Selective Catalytic Cross-Coupling Reactions Using Carbonyl Compounds and Alcohols: Sustainable Synthesis of β-Branched Unsaturated Ketones and N-Heterocyclic Aromatic Compounds

A dissertation submitted to the

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Doctor of Philosophy

Submitted by

Priyanka Adhikari

Roll no- 186122027

Supervisor: Dr. Animesh Das

Department of Chemistry

Indian Institute of Technology Guwahati

Guwahati, Assam-781039

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Dedicated to

My Parents

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INDIAN INSTITUTE OF TECHNOLOGY GUWAHATI
Department of Chemistry
Guwahati, Assam-781039, INDIA

STATEMENT

I, hereby declared that the work comprised in this thesis entitled "***Selective Catalytic Cross-Coupling Reactions Using Carbonyl Compounds and Alcohols: Sustainable Synthesis of β-Branched Unsaturated Ketones and N-Heterocyclic Aromatic Compounds***" is the outcome of the research work carried out by me under the supervision of **Dr. Animesh Das, Department of Chemistry, Indian Institute of Technology Guwahati, India**, for the award of the degree of Doctor of Philosophy.

In harmony with the general practice of reporting scientific observations, due acknowledgements have been made if the work is established on the findings of other investigators.

Priyanka Adhikari

Guwahati
September, 2024

Priyanka Adhikari
Roll No: 186122027
Department of Chemistry
IIT Guwahati, Assam, India-781039

TH-3606_186122027

INDIAN INSTITUTE OF TECHNOLOGY GUWAHATI
Department of Chemistry
Guwahati, Assam-781039, INDIA

Dr. Animesh Das, E-mail: adas@iitg.ac.in
Associate Professor, Department of Chemistry Phone: +91-361-2583478

CERTIFICATE

This is to certify that the work incorporated in the thesis entitled "***Selective Catalytic Cross-Coupling Reactions Using Carbonyl Compounds and Alcohols: Sustainable Synthesis of β-Branched Unsaturated Ketones and N-Heterocyclic Aromatic Compounds***" which is being submitted to the Indian Institute of Technology Guwahati for the award of Doctor of Philosophy in Chemistry by **Miss. Priyanka Adhikari** (Roll No: 186122027) was carried out by her under my supervision at this institute. The work presented in her thesis is original and that has not been submitted elsewhere for a degree.

Guwahati
September, 2024

Dr. Animesh Das
(Thesis Supervisor)
Associate Professor
Department of Chemistry
IIT Guwahati, Assam, India-781039

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Sincerely,

Priyanka Adhikari

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Abbreviation

Ac	Acetyl
α	Alpha
Å	Angstrom
Ar	Argon
ACN	Acetonitrile
AD	Acceptorless dehydrogenation
ADC	Acceptorless dehydrogenative coupling
br.	Broad
bi pyridine	2,2′-bipyridine
β	Beta
Bn	Benzyl
Bu	Butyl
BH	Borrowing hydrogen
CCDC	Cambridge crystallographic data centre
COD	1,5-Cyclooctadiene
$CDCl_3$	Chloroform-d
Cy	Cyclohexyl
Cat	Catalyst
°C	Degree Celsius
d	Doublet or day
dd	Doublet of doublet
δ	Chemical shift or delta
DA	Donor-acceptor
DCE	Dichloroethane
DCM	Dichloromethane
DFT	Density functional theory
DMSO	Dimethylsulfoxide
DMF	Dimethylformamide
DMA	Dimethylacetamide
dppe	1,2-Bis(diphenylphosphino)ethane

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dppf	1,1′-Bis(diphenylphosphino)ferrocene
dppp	1,3-Bis(diphenylphosphino)propane
EtOAc	Ethyl acetate
equiv.	Equivalent
ESI	Electrospray ionization
Et	Ethyl
EWG	Electron withdrawing group
EDG	Electron donating group
g	Grams
γ	Gamma
HE	Hantzsch ester
HA	Hydrogen-autotransfer
h	Hours
HRMS	High resolution mass spectrometry
Hz	Hertz
MHz	Mega Hertz
i	Iso
FT-IR	Fourier transform infrared spectroscopy
J	Coupling constant
m	Multiplet
m	Meta
Me	Methyl
mg	Milligram
mL	Milliliter
mmol	Millimole
Mp	Melting point
MS	Molecular sieve
MLC	Metal-ligand cooperation
NMR	Nuclear magnetic resonance
Ts	Tosylate
Tol	Tolyl
o	Ortho
ω	Omega
ORTEP	Oak ridge thermal ellipsoid plot program

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p	Para
Ph	Phenyl
Py	Pyridine
Pr	Propyl
PNP	2,6-bis-(di-tert-butylphosphinomethyl)pyridine
ppm	Parts per million
q	Quartet
rt	Room temperature
s	Singlet
TH	Transfer hydrogenation
THF	Tetrahydrofuran
THQ	Tetrahydroquinoline
t	Tert
TMS	Tetramethylsilane
TEMPO	2,2,6,6-Tetramethylpiperidine-1-oxyl
Tp'	Tris(3,5-dimethylpyrazolyl)borate
TS	Transition state
XRD	X-ray diffraction

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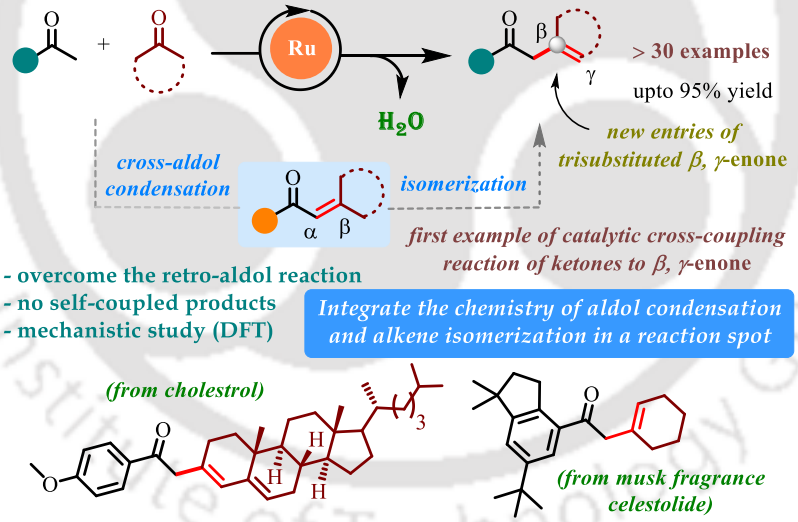
Abstract

The present thesis, entitled "***Selective Catalytic Cross-Coupling Reactions Using Carbonyl Compounds and Alcohols: Sustainable Synthesis of β-Branched Unsaturated Ketones and N-Heterocyclic Aromatic Compounds***" is divided into six chapters based on the results obtained from the experimental works during the course of PhD research period.

Chapter 1 includes a brief introduction about the basic concepts of aldol reaction, alkene isomerization, acceptorless dehydrogenation *via* metal-ligand cooperation, and a general background of transfer hydrogenation reactions.

Each of the following chapters (Chapter 2 to Chapter 6) contains an introduction, previous literature reports, present results and discussion, experimental section and references. The spectral data for selected synthesized molecules are provided in the **Annexure I-V**.

Chapter 2 describe a ruthenium-catalyzed chemoselective and regioselective cross-coupling reaction of ketones for the synthesis of *β*- branched *β*, *γ*-unsaturated ketones. Interestingly, single crossed aldol condensation products are formed even in reactions where a mixture of products is possible. Notably, this transformation is environmentally benign with H_2O as the only by-product. The detailed mechanistic studies reveal the origin of high chemoselectivity and regioselectivity. Method is compatible with a wide variety of sensitive functional group and applicable for even problematic aliphatic ketones as substrates. The process can further be extended to the gram-scale reaction and late-stage functionalization of natural products.



Chapter 3 reports the synthesis and characterization of new bench-stable triazine-based *NNN*-pincer ligands and their corresponding cost-effective chromium complexes. I have explored their utility in the cross-coupling of methyl ketones with cyclic ketones to *β*-branched *β*, *γ*-unsaturated ketones. The reaction is highly chemoselective and regioselective. This catalytic route gives a unique opportunity to integrate the chemistry of the synthetic challenge cross-coupling reaction of ketones and the alkene migration reaction into a single reaction pot.

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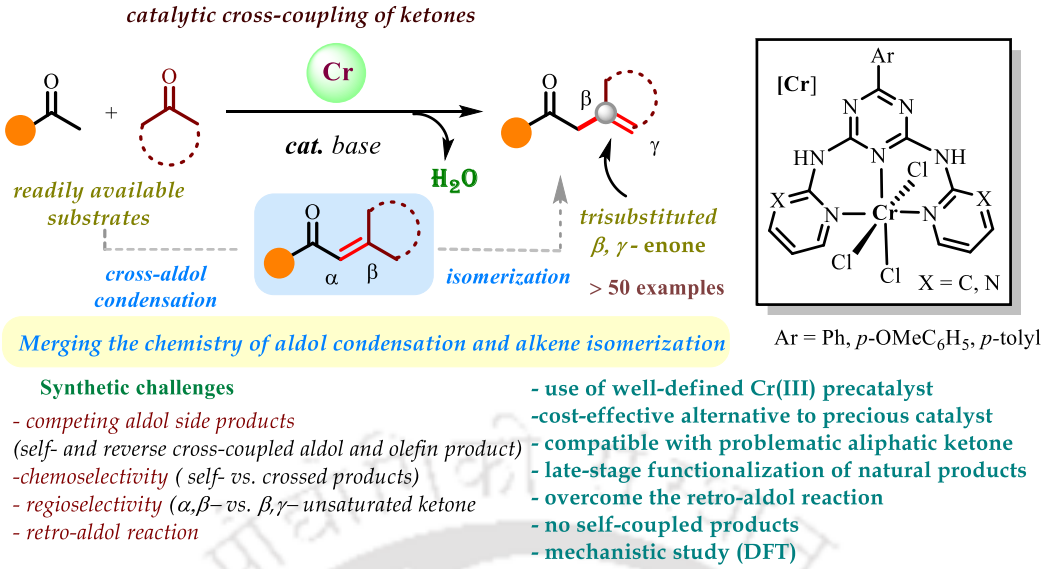
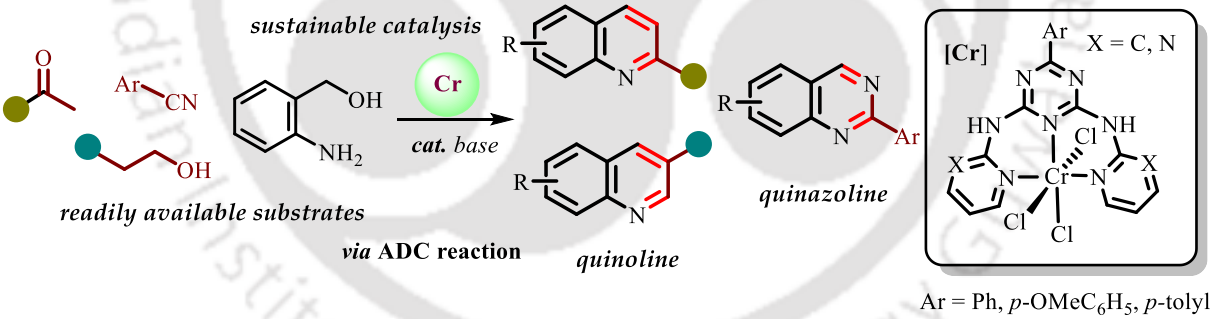


Chapter 4 describe an efficient method for the synthesis of C2 substituted quinoline, C3 substituted quinoline and quinazoline derivatives *via* ADC reaction catalyzed by well defined, bench-stable Cr(III) complex as precatalyst. Reaction is highly chemoselective and produces molecular hydrogen and water as the only byproducts making the protocol green, atom-economical, and environmentally benign. Method is compatible with a wide variety of sensitive functional group and applicable for even problematic aliphatic alcohols as substrates. The process can further be extended to the gram-scale reaction and late-stage functionalization of various natural products. This protocol gives a unique opportunity to dehydrogenative synthesis of *N*-heterocycles by underexplored chromium catalysis.



Chapter 5 illustrates chromium-catalyzed annulation of 2-aminoaryl alcohol with phenoxy acetophenone to 3-oxo-quinoline derivatives is reported. Phenoxy acetophenones are employed as *β*-O-4′ lignin models for this conversion. The efficacy of the process was further extended by producing 3-aminoquinolines using α-amino ketone. Notably, these are hard to prepare using conventional method. The catalyst tolerates numerous functional groups, including hydrogenation sensitive examples and is applicable for even problematic α-hydroxyacetophenone as substrate. The process can further be extended to the gram-scale reaction and late-stage functionalization of natural products. Notably, the use of non-precious catalyst, a catalytic amount of base, aerobic conditions, functional group diversity and late-stage modification of complex molecules are important practical features.

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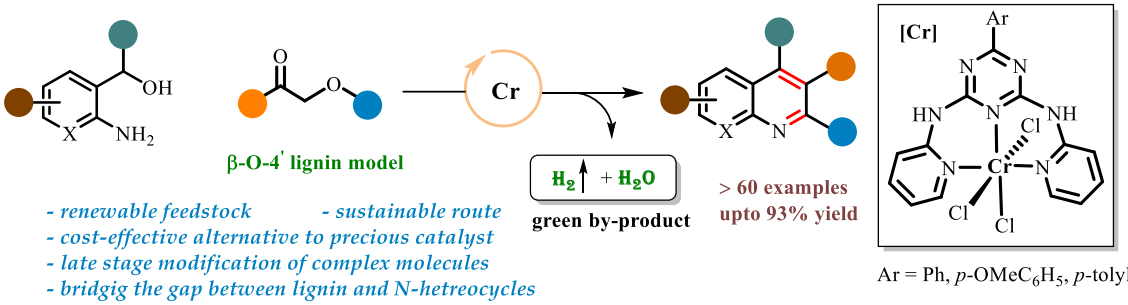
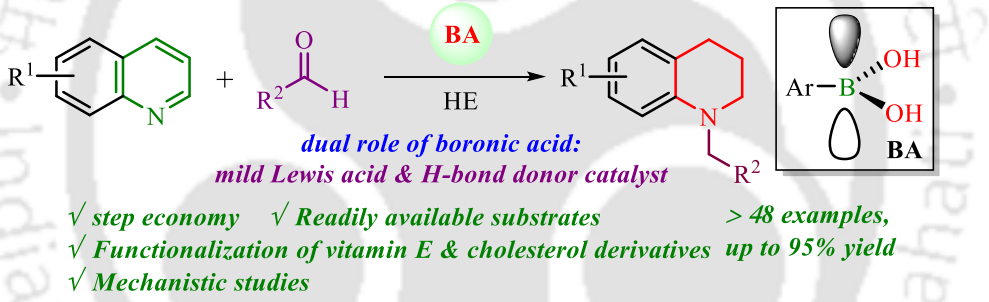


Chapter 6 demonstrates a boronic acid catalyzed one-pot tandem reduction of quinolines to tetrahydroquinolines followed by reductive alkylation by the aldehyde has been demonstrated. This step-economcial synthesis of *N*-alkyl tetrahydroquinolines has been achieved directly from readily available quinolines, aldehydes, and Hantzsch ester under mild reaction conditions. Contrary to the reported procedures, the current protocol employs a commercially available, air- and moisture-tolerant boronic acid that is compatible with a wide variety of substrates and afforded the desired *N*-alkyl tetrahydroquinolines with a very high yield. The mechanistic study demonstrates the unique behavior of organoboron catalysts as both Lewis acids and hydrogen-bond donors. The synthetic utility of the present protocol was explored towards several bioactive molecules such as lipoprotein receptor and antimicrobial active *N*-diarylmethyl THQ efficiently.



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Chapter 1

A brief introduction to aldol condensation, alkene isomerization, acceptorless dehydrogenative coupling and transfer hydrogenation strategies

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1.1. Introduction

In present world, the growing population has increased the consumption of the natural resources drastically. This, also results in the increasing accumulation of industrial waste which is toxic to our environment and its ecosystem. So, currently, it is very desirable to the develop new chemical and synthetic protocols which would lessen the waste generation and utilize renewable feedstock. In this regard, catalytic reactions provide a great precedence in terms of sustainability and energy efficacy. Among such reactions, aldol condensation, alkene isomerization, acceptorless dehydrogenative coupling (ADC) reaction and transfer hydrogenation (TH) reactions represent extremely powerful synthetic strategies to synthesize a diverse range of valuable organic building blocks *via* homogenous catalysis.

Ketones and alcohols are important classes of organic compounds which are cheap, abundant in nature, biorenewable (derived from lignocellulosic biomass) and easy to handle and store. In recent years, the construction of carbon-carbon and carbon-heteroatom bonds by using ketones and alcohols has gained importance in the field of pharmaceutical and agrochemical industries.

This thesis work will discuss the synthesis of *β*-branched *β, γ*-unsaturated ketone *via* base-metal catalyzed cross-coupling reaction ketones, and synthesis of *N*-heteroarenes such as quinoline and quinazolines derivatives *via* transition-metal-catalyzed dehydrogenative coupling of alcohols. Furthermore, the synthesis of *N*-alkyl tetrahydroquinolines directly from quinolines and aldehydes by transition metal-free aryl boronic acid-catalyzed transfer hydrogenation of quinoline with Hantzsch ester will also be described.

1.2. Aldol condensation reaction

Carbon-carbon bond formation reactions constitute the essential core of the organic chemistry.[1] Thus, development of new novel environment friendly methodologies for this well-known transformation is high in demand. Over the past few years, abundant methods have been developed. Among them cross-coupling reactions consist of aldol condensation has gained much of attention. Aldol condensation is one of the important carbon-carbon bond formation reactions which occurs at the carbon center adjacent to a carbonyl group for examples- ketone, aldehyde etc. The aldol condensation reaction was first introduced by *Charles Wurtz* in 1872[2], for the preparation of *β*-hydroxy aldehyde from acetaldehyde. The fundamental step[3] involved in aldol condensation reactions are-

i) Formation of Aldol: Conventionally, two carbonyl compounds i.e., aldehyde and ketone are used for the formation of aldol. A *α*-H containing carbonyl compound in presence of base or acid undergoes deprotonation to form carbonyl enolate (or enol tautomer) then this reacts with another carbonyl molecule to form *β*-hydroxy carbonyl compound known as aldol product.

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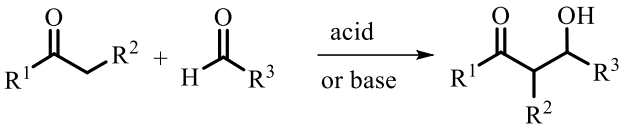
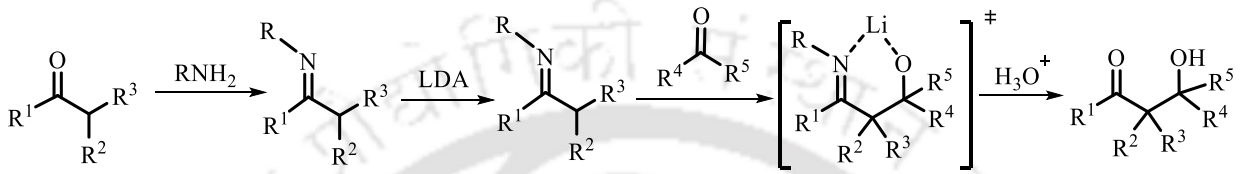


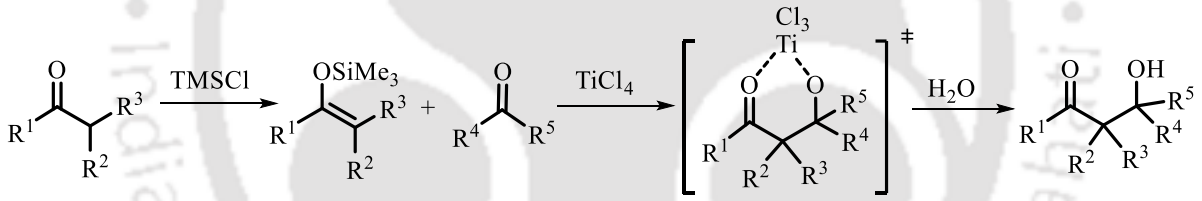
Scheme 1.1. Aldol condensation of ketone with aldehyde

Then several metal enolate mediated aldol reactions have been evolved. In 1963, a lithium enolate-based method for a directed cross-aldol product was reported by *G. Wittig* and co-workers (Scheme 1.2).[4]



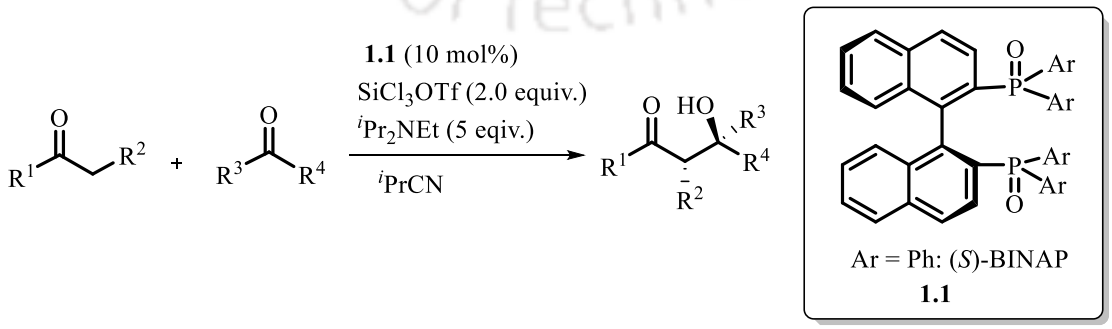
Scheme 1.2. *Wittig*'s method for a directed cross-aldol reaction

Whereas, in similar reactions, Mg, Al or Zn also provides a mild reaction condition for the synthesis of these cross-aldol products. Other Lewis acids such as $TiCl_4$, BF_3, $SnCl_4$, OEt_2, $AlCl_3$, and so on can also promote this kind of reactions. But in terms of yield $TiCl_4$ is considered superior to other Lewis acids.[5]



Scheme 1.3. $TiCl_4$ catalyzed aldol reaction.

Then this strategy has been extended to asymmetric synthesis, pioneering contribution by *Mukaiyama*, *Tanabe* and others. Recent representative example demonstrated trichlorosilyl triflate-promoted directed cross-aldol reaction between ketones in the presence of a chiral phosphine oxide as an organocatalyst. Protocol provided *β*-hydroxy carbonyl compounds bearing a tetra-substituted chiral carbon with good enantioselectivity.[6]



Scheme 1.4. Enantioselective cross-aldol reaction.

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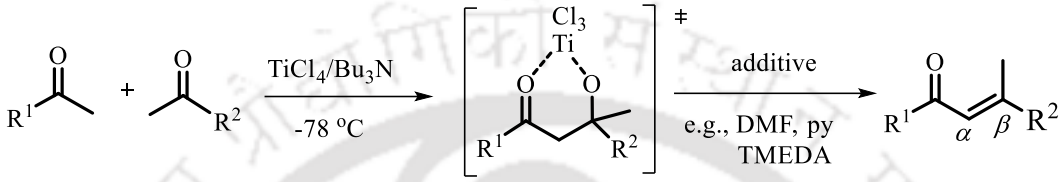
ii) Dehydration/Elimination reaction: The second step is condensation of the aldol product. The process involves the liberation of a water molecule from aldol or *β*-hydroxy ketone to form *α, β*-unsaturated carbonyl compound. Various additives are often required for this, otherwise it can give retro-adol products. For instance, a group of *Sugiura* reported $TiCl_4$-promoted aldol reaction of ketones as aldol acceptors followed by elimination of the titanoxy group from the Ti-aldolates affords *β, β*-disubstituted *α, β*-unsaturated carbonyl compounds in a one-pot procedure. The use of additives, such as DMF, *N*,*N*,*N*′,*N*′-tetramethylethylenediamine, and pyridine, in the elimination step was found to be critical.[7]

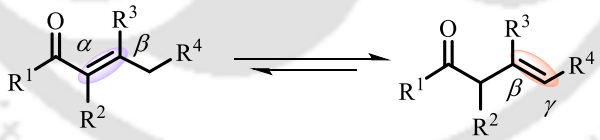


Scheme 1.5. $TiCl_4/Bu_3N$ promoted one-pot synthesis of *β, β*-disubstituted *α, β*-unsaturated carbonyl.

Further, the aldol reaction has wide applicability in pharmaceutical and industrial products synthesis such as enzymatic synthesis of fatty acids, highly concise total synthesis of epothilone B, synthesis of numerous macrolide and ionophore antibiotics (natural products), synthesis of high polymers of poly(glutaraldehyde). This is also useful in the synthesis of macrolide and ionophore antibiotics.

1.3. Isomerization of *α, β*- to *β, γ*-unsaturated carbonyl compounds

It is worth noting that the C=C bond in *α, β*-unsaturated carbonyl compound can be isomerized to form *β, γ*-unsaturated carbonyl compounds where metal catalyst was found to play important role.



Scheme 1.6. General representation for isomerization *α, β* to *β, γ* -unsaturated compounds

Wendlandt and *co-workers* recently disclosed a catalytic system for the isomerization of *α, β*-unsaturated carbonyl compounds catalyzed by decatungstate photocatalyst, cobaltoxime **1.2** and 2,4,6-triisopropylbenzene disulfide $(TripS)_2$ under photochemical irradiation.[8]

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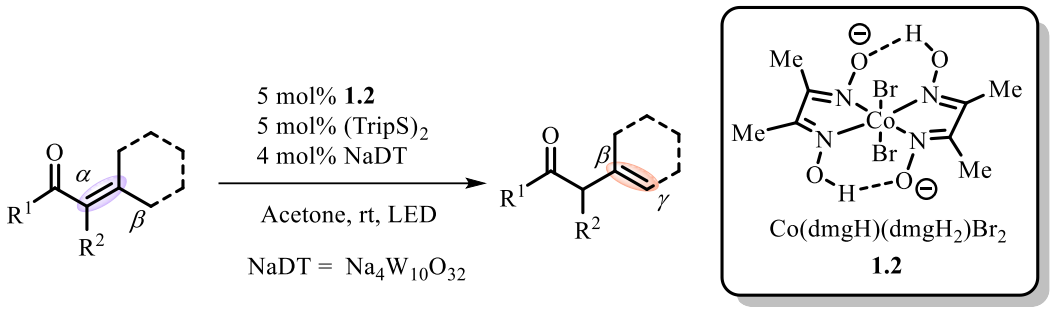
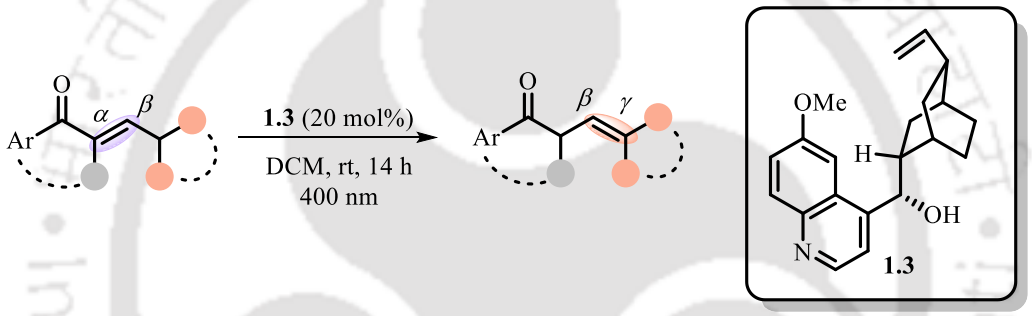


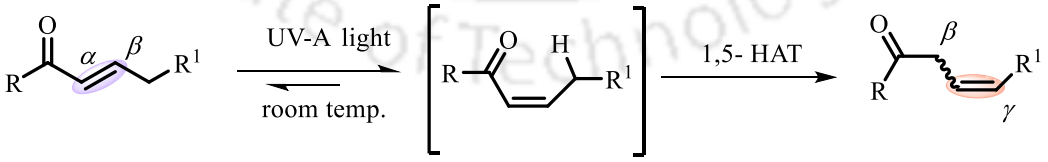
Scheme 1.7. Isomerization *α, β* to *β, γ*-unsaturated compounds

Photoisomerization of *α, β*- to *β, γ*-carbonyl compounds are also an alternative and straightforward approach towards these synthetic intermediates in synthetic chemistry. Recently, *Gilmour*, *Morack*, and *coworkers* executed a light-enabled deconjugative isomerization of *α, β*-unsaturated ketones that include an aryl ketone group. [9]



Scheme 1.8. Photoisomerization of *α, β* to *β, γ*-unsaturated compounds

In 2022, *Lemcoff* and *group* reported photochemical isomerization of *α, β*- to *β, γ*-unsaturated ketones *via* a 1,5-hydrogen atom transfer (HAT) mechanism under mild conditions. The reaction proceeds in absence of any metal catalyst or additives with high efficiency and selectivity. Mechanistic investigations reveal that the *E* to *Z* isomerization is the first step in the reaction, followed by a 1,5-hydride shift and consequent tautomerization to produce the corresponding isomerized products[10]



Scheme 1.9. UV light mediated alkene isomerization

In general, transition metal-catalyzed alkene isomerization occurs in two possible pathways, these are (a) alkene insertion to the metal-hydride, followed by *β*-hydride elimination and (b) *π*-allyl pathway (Scheme 1.10).

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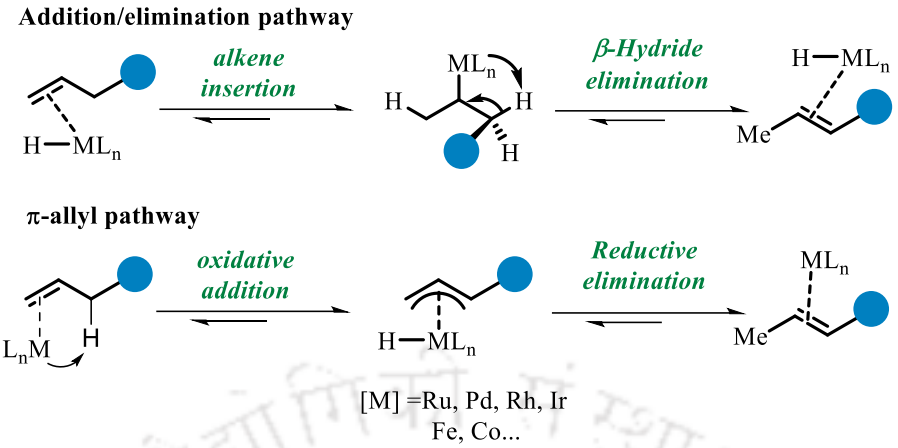
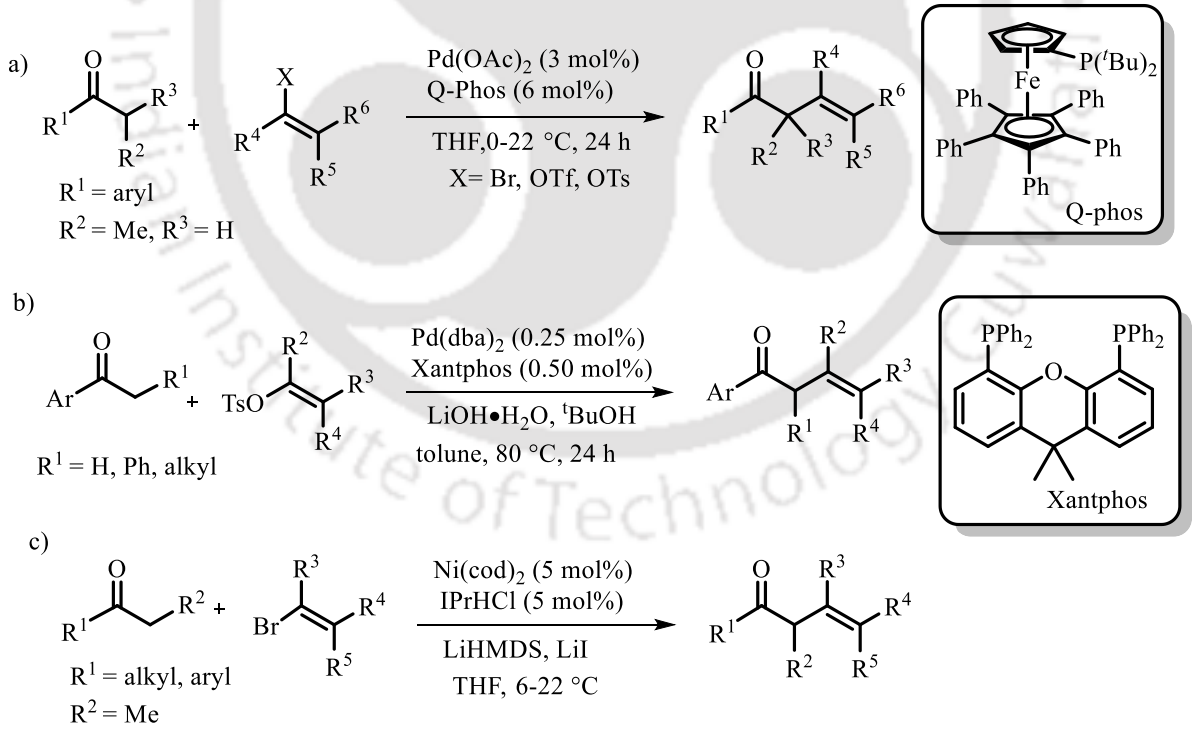


Scheme 1.10. General mechanism for metal-catalyzed alkene isomerization.

1.4. Synthesis of *β, γ*-unsaturated ketones by cross-coupling reaction

Transition-metal-catalyzed cross-coupling reaction of ketones (or enolates) with alkenyl bromides, alkenyltriflates, or alkenyl tosylates can provide a direct route for the synthesis of *β, γ*-unsaturated ketones.[11, 12] However, the process required a pre-functionalized precursor, hence, restricting the applications of these techniques to relatively straightforward and small target molecules. Besides, the *β, γ*-regioselectivity of these protocols is low.[13-17]



Scheme 1.11. (a) Palladium-catalyzed mono-*α*-alkenylation of ketones with alkenyl tosylates (b) palladium-catalyzed *α*-vinylation of carbonyl compounds (c) Ni-catalyzed alkenylation of ketone

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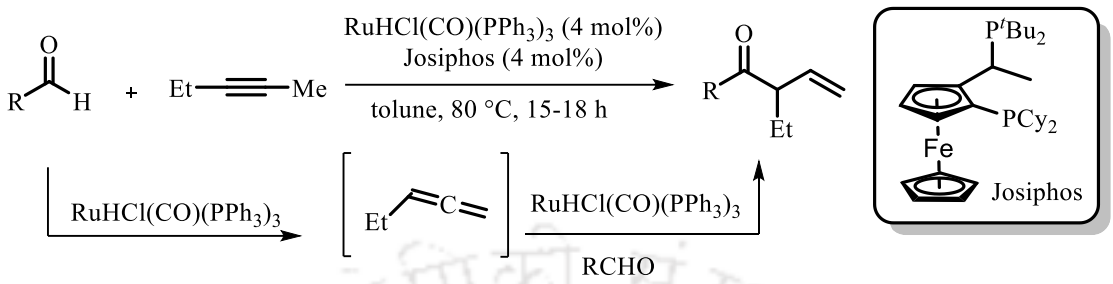
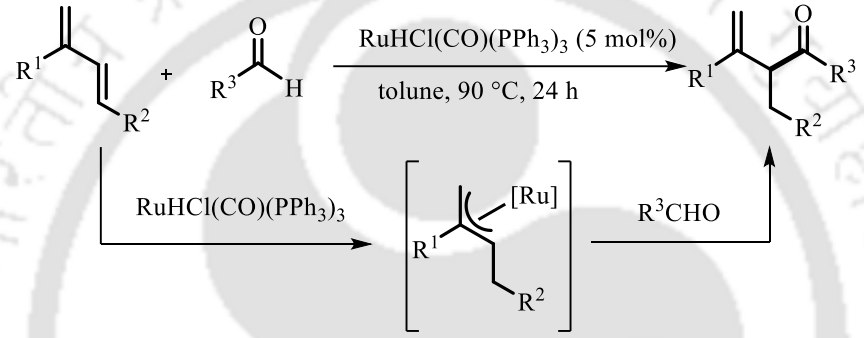
Alternatively, the use of ruthenium catalyst $RuHCl(CO)(PPh_3)_3$ was found to be superior for the synthesis of *β, γ*-unsaturated ketones with aldehyde as a readily available precursors.[18, 19]



Scheme 1.12. Ru−H catalyzed cross-coupling reaction of alkynes with aldehydes



Scheme 1.13. Ru−H catalyzed cross-coupling reaction of dienes with aldehydes.

Despite these developments, none of the known catalytic methods can give *β, γ*-unsaturated ketones directly from readily available ketones *via* one-pot aldol-condensation reaction. Therefore, it is deemed desirable to develop a mild and efficient method for the construction of *β, γ*-unsaturated ketones by tandem process.

1.5. Acceptorless dehydrogenation

The dehydrogenation of unactivated small molecules are an important class of transformation in the organic synthesis, and also widely utilized in both industrial and biological systems. The extrusion of hydrogen from adjacent atoms of an organic molecule is thermodynamically unfavorable process.[20] Conventionally, substrate oxidations occur with the stoichiometric amount of inorganic oxidants such as dichromates,[21] permanganates[22] etc., in the presence of strong mineral acids,[23] silver oxide[24] and lead tetraacetate.[25] Alternatively, catalytic hydrogen transfers reactions using sacrificial organic acceptor (e.g., *tert*-butylethene)[26] has also been mentioned. Both the reactions generate a copious amount of waste, thus causing an adverse effect on the environment (Scheme 1.14). Thus, from an environmental perspective, it is necessary to develop synthetic protocols with high atom economy, inexpensive and safe reagents and no hazardous waste. Towards this goal, acceptorless dehydrogenation provides a new sustainable approach as the process does not require any external oxidant, pre-functionalization of the substrates, or any

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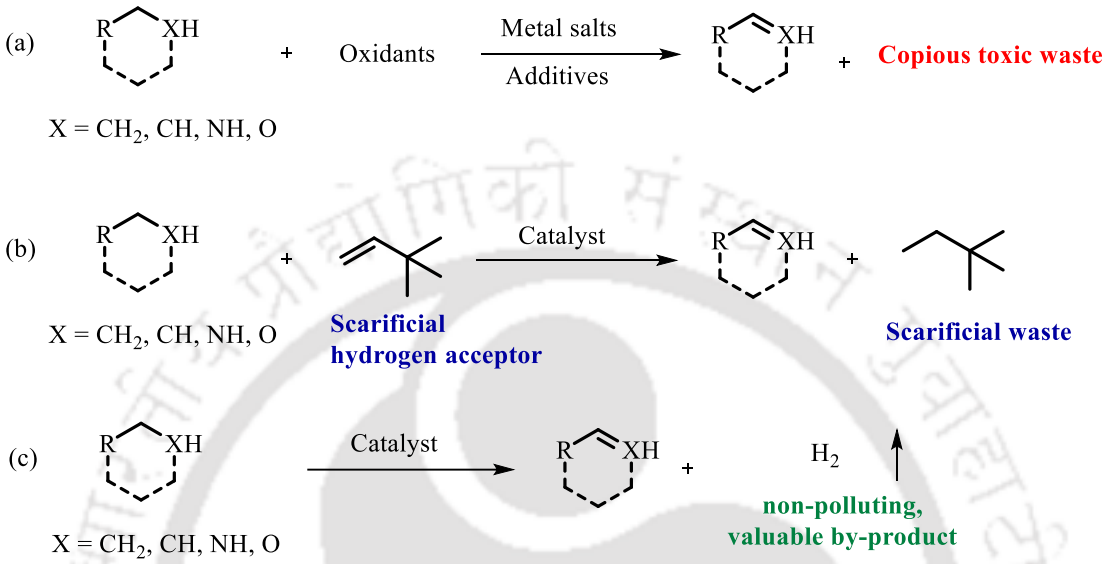
hydrogen scavengers. Liberated molecular hydrogen is the only by-product that makes the process green, atom-economical, and environmentally benign. Therefore, catalytic acceptorless dehydrogenation reaction has become convenient tool for the commodity chemicals. In the majority of cases, the reaction proceeds effectively *via* metal-ligand cooperation effect (MLC).



Scheme 1.14. Conventional routes for dehydrogenation of substrates (a) oxidation reaction (b) hydrogen transfer reaction (c) acceptorless dehydrogenation

1.5.1. Alcohol dehydrogenation

Fossil fuels are currently the primary suppliers for the bulk chemicals and also for the energy required to maintain a quality life. The utilization of this scarce natural feedstock is a major reason for the CO_2 emissions. A potential solution can be achieved to overcome these problems is by considering the use of stable, high-density and renewable hydrogen storage compounds. Due to its high hydrogen content, biowaste derived alcohols are main alternative to fossil fuel-based resources for hydrogen which can easily be derived from lignocellulosic wastes, biomass and sewage sludge etc. The dehydrogenation of an alcohol to a more reactive carbonyl is required for formation of C-C, C-N bond in order to synthesize fine chemicals. Conventionally, alcohols can effectively be oxidized by a variety of strong inorganic oxidants, such as chromium-based,[27] manganese-based,[28] silver based[29] and some well-defined oxidants such as Dess-Martin Periodinane,[30] *o*-iodoxybenzoic acid (IBX),[31] sodium hypochlorite (NaOCl),[32] TEMPO (2,2,6,6-tetramethyl-1-piperidinyloxy)[33] etc. have been known to successfully carry out the oxidation of alcohols. However, these methods often suffer from several disadvantages including the production of significant amounts of by-products or waste materials. Therefore, direct conversion of alcohols into valuable chemicals and H_2, *via* green, sustainable and atom-economic approach is highly demanding.

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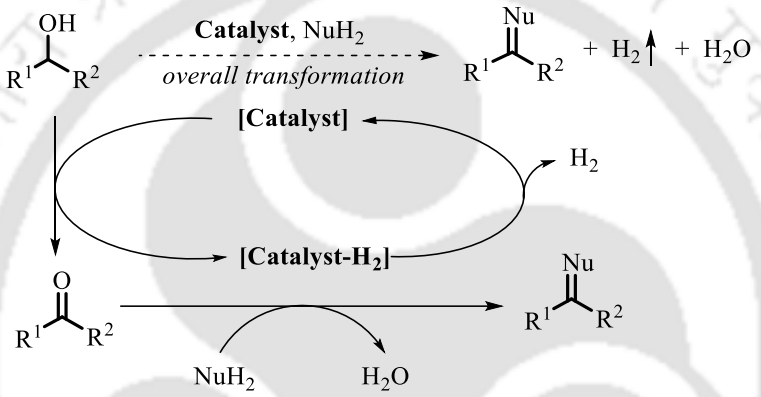
In this context, acceptorless alcohol dehydrogenation has gained remarkable amount of attention. Because i) it procced in absence of any sacrificial oxidant or hydrogen acceptor ii) do not involve in the production of stoichiometric amount of sacrificial waste thus environmentally benign, iii) use of easily accessible low-cost alcohols, iv) formation of useful products. For oxidation of alcohols, transition metal catalyst plays a crucial role in activating the alcohol molecules to form new reactive carbonyl compound (aldehyde, ketone) by abstracting two adjacent hydrogen atoms forming transition metal-H_2 (**catalyst-H_2**) complex. Then the transition metal-H_2 complex releases the hydrogen molecule and regenerates the catalyst in the reaction medium. A brief overview of alcohol dehydrogenation has been shown below where acceptorless dehydration of alcohol forms aldehyde/ketone which undergoes amine/alcohol coupling to form imine or amide and various heterocyclic compounds (Scheme 1.15).



Scheme 1.15. General overview for acceptorless dehydrogenation of alcohols

1.5.2. Dehydrogenation of alcohols to form aldehyde/ketone

Over the past three decades, a significant amount study has been executed for acceptorless dehydrogenation of alcohol to aldehydes/ketones by homogeneous catalysts with the direct evolution of molecular hydrogen.

In one of the earliest findings *Dobson* and *Robinson* demonstrated the application of the complex $[Ru(OCOCF_3)_2(CO)(PPh_3)_2]$ **1.4** in the dehydrogenation of various primary and secondary alcohols.[34] In this protocol an excess amount of a fluorinated carboxylic acid is required which is termed as acid-promoted reaction (Scheme 1.16) *Jung* and *Garrou* reported a series of analogous catalysts based on bidentate diphosphine ligands and demonstrate their mechanistic aspect for the dehydrogenation of primary alcohols.[35] *Hulshof* further investigated this reaction and found that the dehydrogenation of primary alcohols was tangled by decarbonylation (leading to catalyst deactivation) and aldol condensations under the reaction condition.[36]

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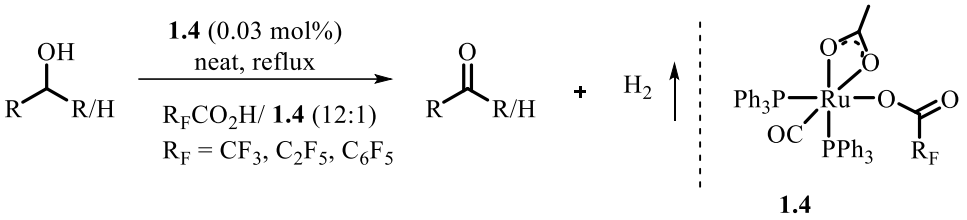
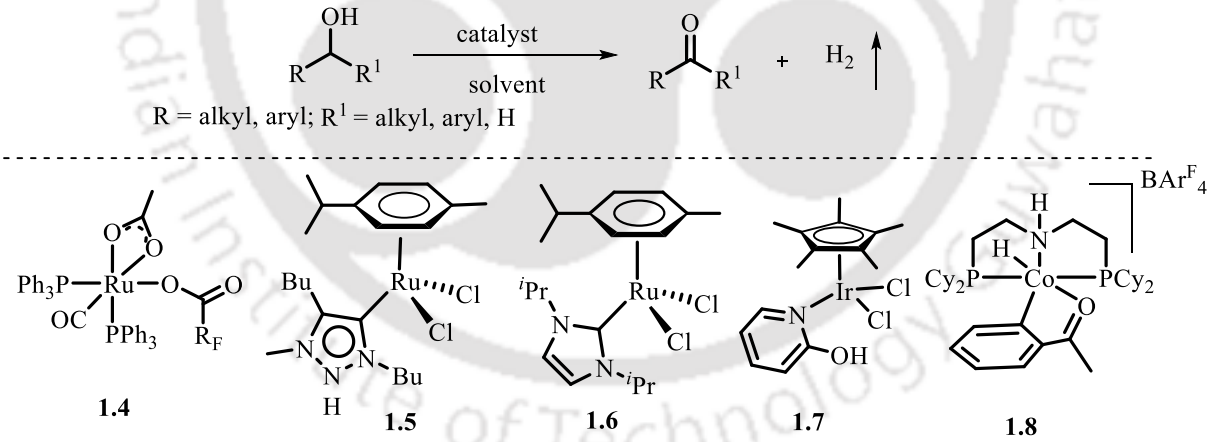


Scheme 1.16. Acid promoted dehydrogenation of alcohol

Morton and Cole-Hamilton independently reported dehydrogenation of alcohol with a series of ruthenium and rhodium catalyst toward the dehydrogenation of low molecular weight containing alcohols such as ethanol, propanol and isopropanol etc.[37] It is found that *Wilkinson*'s catalyst is not active for dehydrogenation of isopropanol but in presence of triethylamine it becomes effective for hydrogen generation from isopropanol.[38, 39] *Beller and coworkers* screened variety of ruthenium catalysts to identify suitable precursors for dehydrogenation of isopropanol and found two precursors, $[RuCl_3 \bullet xH_2O]$ and $[RuCl_2(p\text{-cymene})]_2$, to have higher TOF for the dehydrogenation of isopropanol in the presence of two equivalents of PCy_3 compare to other catalysts that have been tested.[40] *Albrecht,*[41] *Madsen*[42] *groups* independently reported a numbers of catalysts based on various phosphine, mesoionic triazolylidene, *N*-heterocyclic carbene and *N,N,N–b*Mepi (*b*Mepi = 1,3-bis(6-methyl-2-pyridylimino)isoindolate) ligands which could effectively dehydrogenate alcohol.[43] In recent times, dehydrogenation of secondary alcohols to ketones with earth-abundant transition metal complex was reported by various groups.[44]



Scheme 1.17. Selected transition metal complexes for acceptorless dehydrogenation of alcohol

In general, acceptorless alcohol dehydrogenation proceeds through three important steps, namely, (i) oxidative addition of the alcohol to the metal site to form metal-alkoxide species, (ii) next, *β*-hydride elimination of the metal-alkoxide leading to metal-dihydride intermediate and carbonyl product (iii) finally, the metal catalyst is regenerated by liberation of H_2 from metal-dihydride species *via* reductive elimination (Scheme 1.18). However, conventional alcohol dehydrogenations are associated with several limitations.[45]

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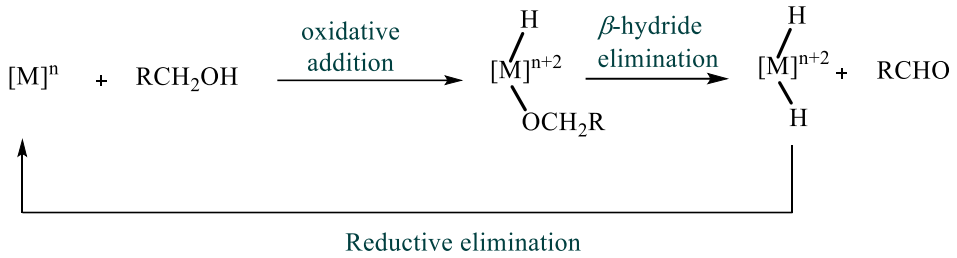
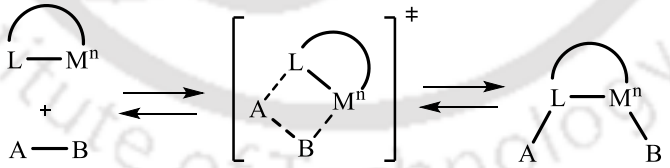


Scheme 1.18. Classical mechanism for alcohol dehydrogenation

Under basic media, product aldehyde undergoes aldol-type rearrangement and making the product separation very difficult thereby, limits the product yield. Furthermore, in case of some metals like ruthenium, the metal alkoxide is so stable which impeded further *β*-hydride elimination.[46] During the catalytic process, the redox adjustment of metal is energetically uphill process thus usually it requires elevated temperature to proceed. Thus, from synthetic prospective, an alternative approach was necessary which could prevent such kind of drawbacks. This has been achieved by introduction of bifunctional catalysts also called metal-ligand cooperative catalyst whose working principle is different from a classical catalyst. In the following sections, I present a brief introduction about the metal-ligand cooperation effect and its mechanistic implications.

1.5.3. Metal-ligand cooperation

In the catalytic cycle, metal centre is often found as an active site, and supported ligands help to modulate the steric and the electronic behaviour of the metal ions. In modern metal-ligand cooperation (MLC) strategy, both the metal and the ligand are actively taking part in the bond activation processes, and their collective interaction facilitates substrate activation and transformation with low energy barriers and avoiding the traditional oxidative addition and/ or reductive elimination steps in the catalytic cycle.



Scheme 1.19. Bond activation *via* metal–ligand cooperation

The MLC catalyst consists of a Lewis acidic site (metal ion), and Lewis basic site (ligand).[47] Both the sites are located in such a way that synergistic manner can activate the small molecules. Proton responsive groups such as -NH and -OH groups are usually used as a Lewis basic site in the cooperating ligand framework because of their easy accessibility, chemical stability and synthetic feasibility. Depending upon the positioning of these groups with respect to the metal, MLC catalyst is classified into three categories. These are *α*-, *β*- and *γ*-protic functionalized MLC. Few *α*-, *β*- and *γ*-protic complexes have been discussed below.[43, 48-54]

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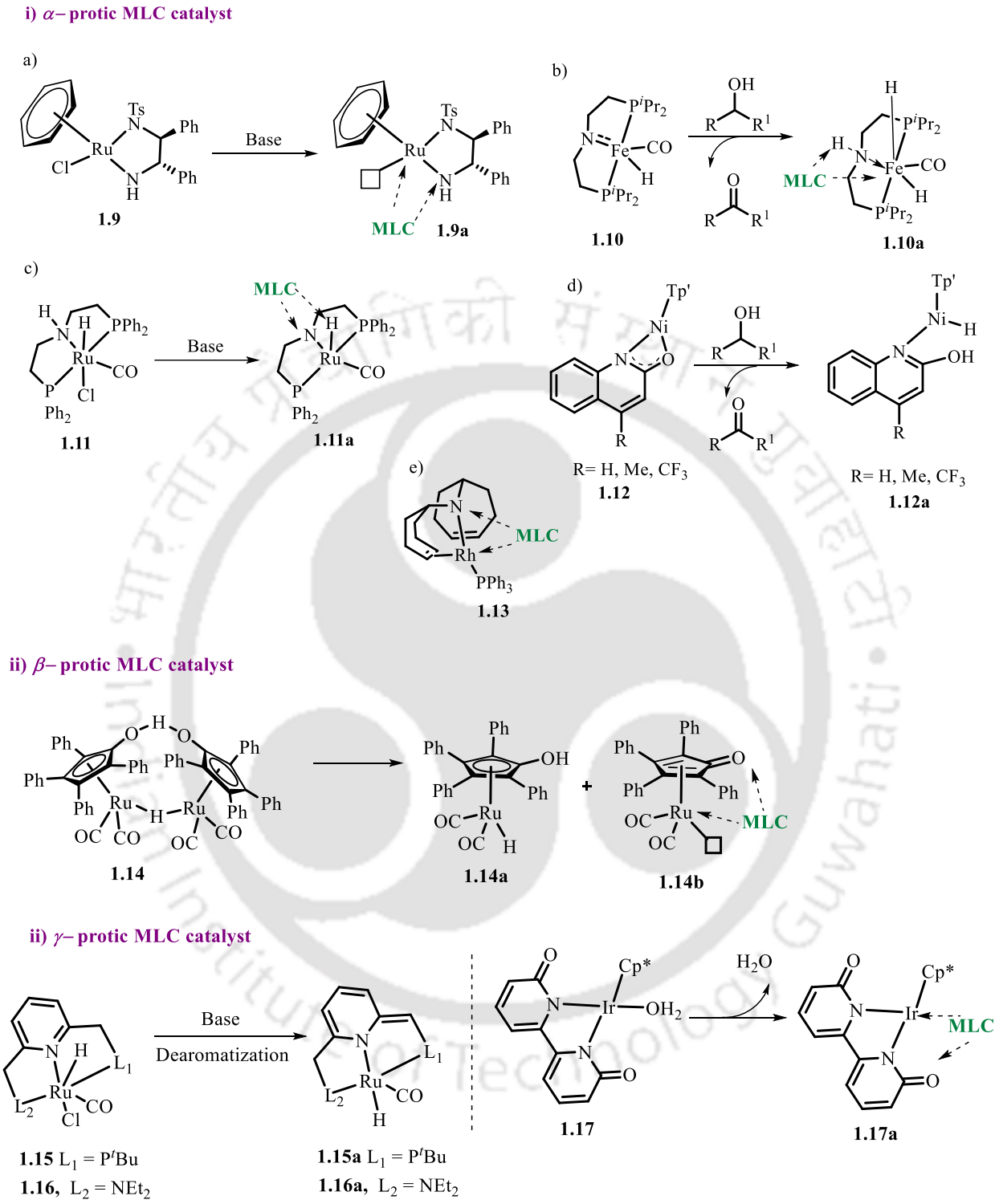

Scheme 1.20. as α-, β- and γ-protic functionalized MLC catalyst

Catalytic reaction proceeds in two different pathways, one is the inner-sphere mechanism, and another is the outer sphere mechanism. In the inner-sphere mechanism, metal-hydride intermediate is formed by stepwise manner. First the oxidative addition takes place at metal center forming

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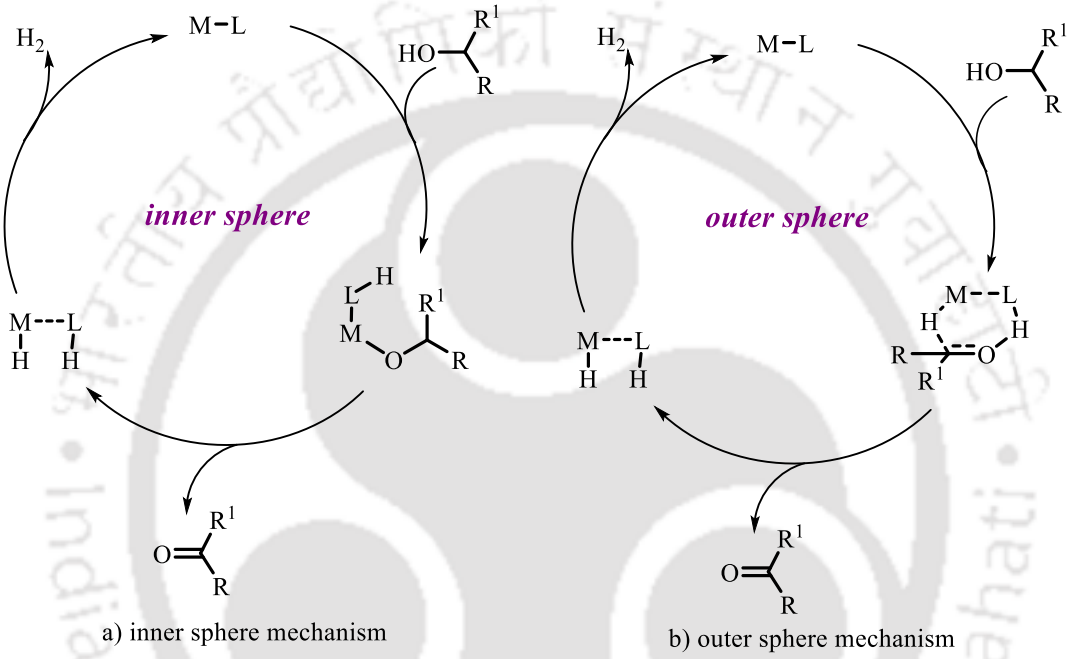
metal-alkoxide species, followed by *β*-H elimination to generate the metal hydride species.[42] In contrast, outer sphere mechanism direct substrate binding is not occur at the metal center, rather the metal-hydride intermediate is generated *via* concerted hydride transfer (form the *α*-C–H of alcohol to the metal center) and proton transfer (from the –OH group to a ligand heteroatom) pathway proceeds through six-membered cyclic transition states.[55] By using MLC strategy, along with O-H bond various other different bonds like N-H, H-H, B-H, and Si-H can also be activated thereby promoting various useful organic transformations.[56]



Scheme 1.21. Mechanistic pathway for a) inner sphere and b) outer sphere mechanism

In 2004, *Milstein* and *coworkers* reported efficient catalytic dehydrogenation of secondary alcohols by ruthenium PNP [2,6-bis-(di-*tert*-butylphosphinomethyl)pyridine] pincer complex **1.18** with low catalyst loading in presence of base.[57] However, this catalytic system failed to give dehydrogenation of primary alcohols to the corresponding aldehydes. Then, the same group developed modified ruthenium (II) hydrido borohydride pincer complex **1.19a-b**[58] where dehydrogenation of secondary alcohols can occur in the absence of base. Interestingly, "hemilabile" amine arm bearing pincer complex **1.19b** shown the higher catalytic efficiency compared to **1.19a,** and the dehydrogenation of 1-phenylethanol to corresponding ketone was achieved with 0.1 mol% catalyst **1.20b**. The iridium complexes **1.7** and **1.20** were also found to be effective for this reaction.[43, 59] The catalytic performance of complex **1.20** is similar to that of ruthenium complex **1.19b**, while complex **1.7** demonstrates greater efficacy.

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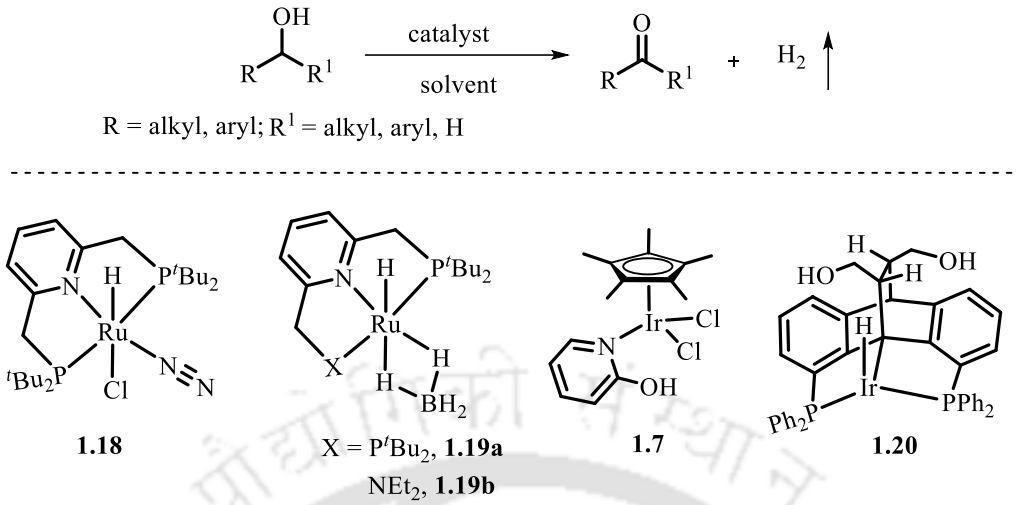
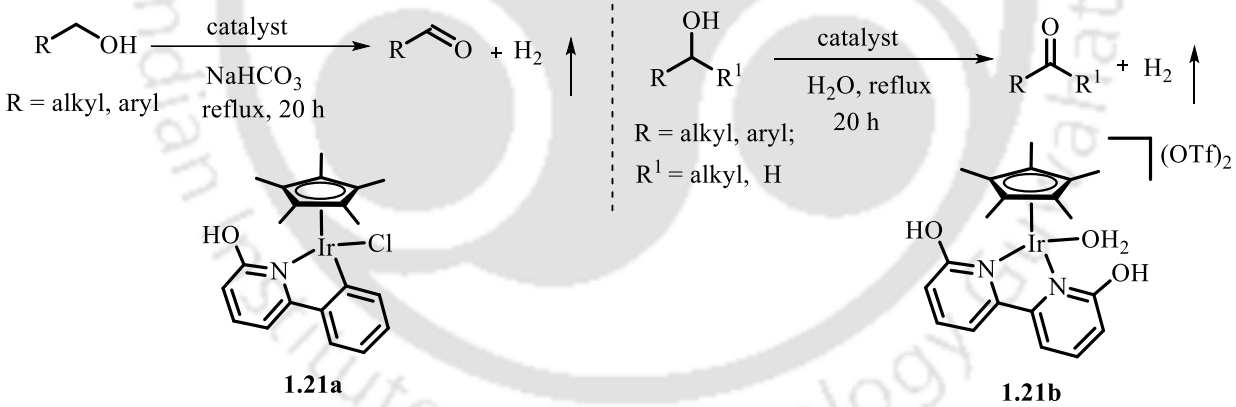


Scheme 1.22. Catalysts used in acceptorless dehydrogenation reaction

It is less common for AD of primary alcohols to produce the respective aldehyde (Scheme 1.23) as decarbonylation of the aldehydes frequently deactivates the ruthenium complexes. *Fujita* and *Yamaguchi* recently reported the synthesis of aldehydes from alcohol by using the iridium catalyst **1.21a-b**.[60] Both secondary and primary alcohols are dehydrogenated by the redesigned water soluble catalyst. Metal-ligand cooperation (MLC) mechanism drives the activity for this series of catalyst.[61, 62]



Scheme 1.23. Catalysts used in acceptorless dehydrogenation of primary and secondary alcohols

1.5.4. Dehydrogenative coupling of alcohols to form esters

Dehydrogenative coupling of alcohols with amines is the most cost-effective technique for the synthesis of imines. *Milstein* first introduced a ruthenium *PNP* pincer complex for the synthesis of imines by dehydrogenative coupling of alcohols and amines *via* de-aromatized Ru-PNP pincer complex with the liberation of H_2.[63] In 2013, *Zhang* and *Hanson* first time introduced Co-pincer complexes for such chemical transformation.[64] Lately, two groups namely *Milstein*[65] and *Kempe*[66]

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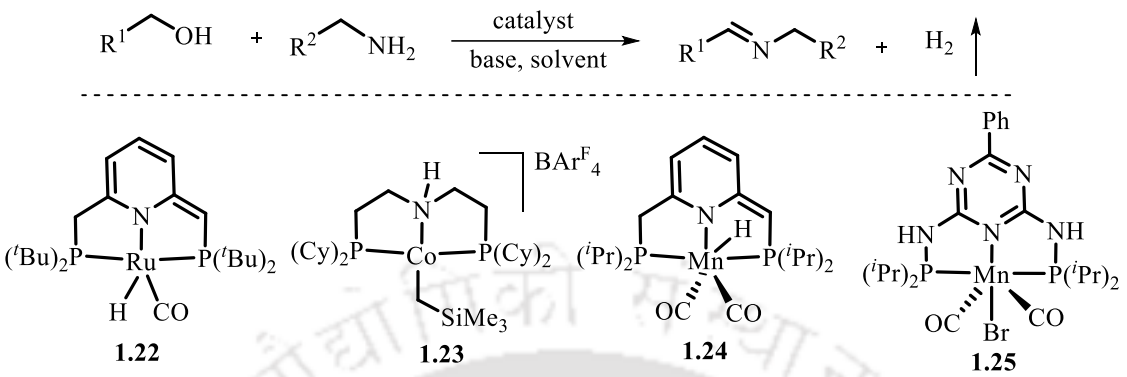
have independently able to synthesize series of earth abundant Mn-pincer complexes for the dehydrogenative coupling of alcohol with amines to form imines.



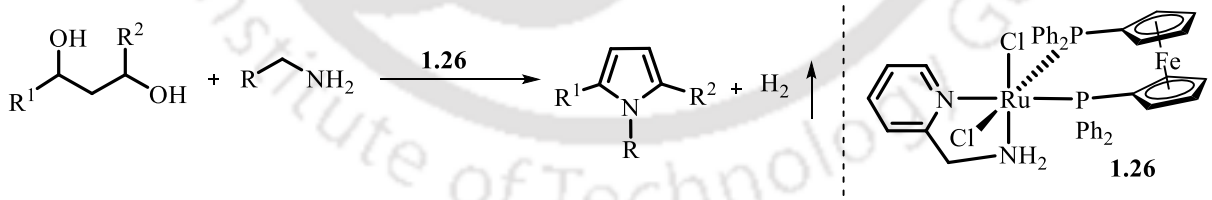
Scheme 1.24. Pincer-metal complex catalyzed dehydrogenative synthesis of imines

1.5.5. Dehydrogenative coupling of alcohols to form *N*-heteroaromatic compounds

N-heteroaromatic compounds are crucial components for both laboratory and industrial processes. They are the core building blocks for many pharmaceuticals, agrochemicals, dyes and other functional materials.[67] Acceptorless dehydrogenative coupling (ADC) is considered to be one of the most environmentally benign strategies for the synthesis of these *N*-heterocyclic compounds where benign alcohols are used coupling partner and water and hydrogen being the only byproducts formed.[68] In the following segment, I present the brief overview for the synthesis of *N*-heteroaromatic compounds catalyzed by selected MLC pincer complexes.

1.5.5.1. Dehydrogenative synthesis of pyrroles and pyridines

In 2011, *Crabtree* and *co-workers* first reported ruthenium catalysed dehydrogenative synthesis of pyrrole from the reaction of 2,5-diol and amines *via* ADC strategy.[69]



Scheme 1.25. Ru catalyzed dehydrogenative synthesis of pyrrole from 2,5-diol

Functionalized pyrroles have also been synthesized by the metal-catalyzed dehydrogenative reaction from secondary alcohols and *β*-amino alcohols. *Kempe*[70] and *Milstein*[71] have independently reported various bifunctional metal catalysts **1.27**, **1.28** respectively, (bearing NH and CH_2 functionality in the pincer system) for the synthesis of pyrroles. Then strategy has been extended to the synthesis of pyridine derivatives by the coupling of *γ*-amino alcohols and secondary alcohols with the catalyst **1.28**. [71]

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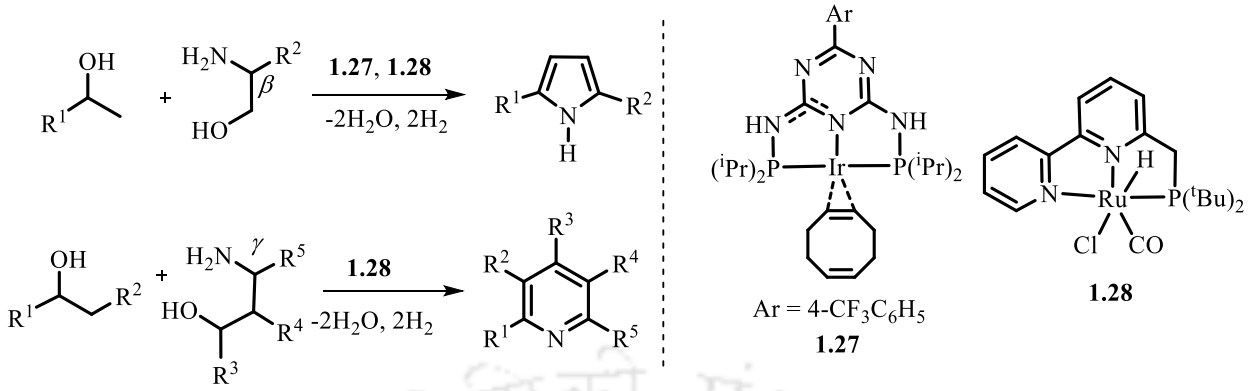
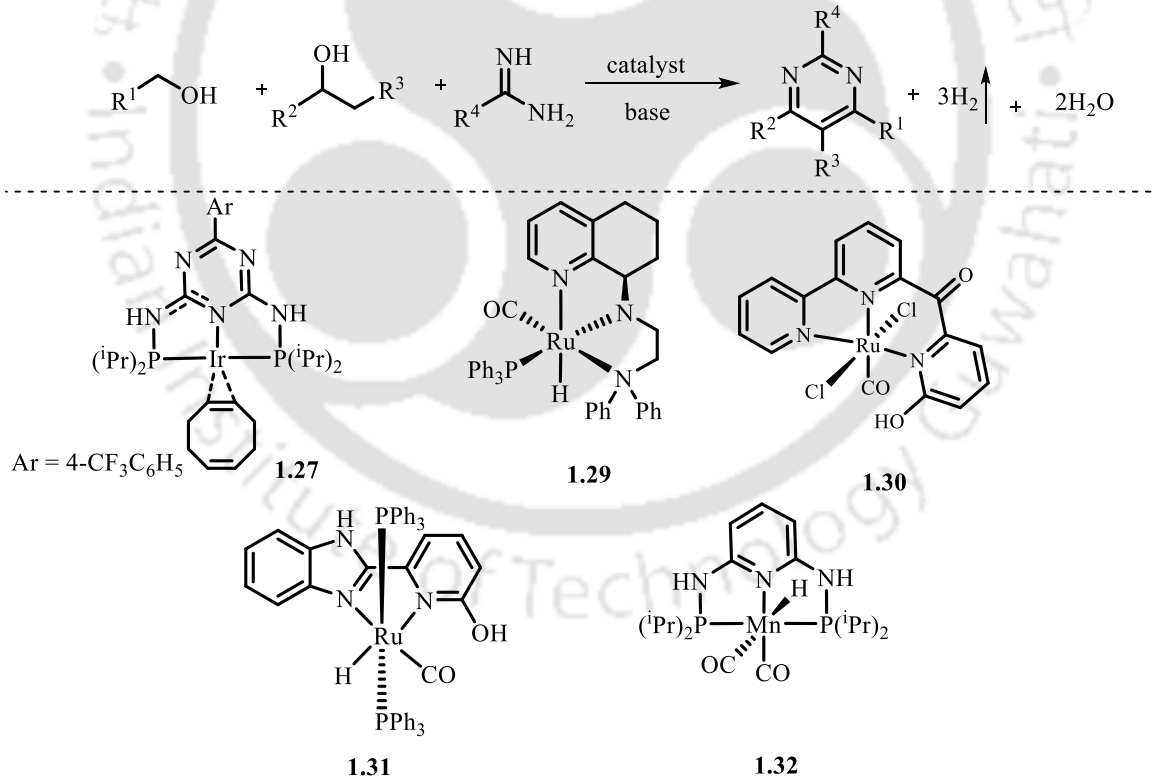


Scheme 1.26. Pyrrole and pyridine synthesis *via* dehydrogenative coupling

1.5.5.2. Dehydrogenative synthesis of pyrimidines

Acceptorless dehydrogenation strategies are also very useful for the synthesis of pyrimidine which proceeds *via* one-pot multicomponent reaction. Various groups namely *Kempe,*[72] *Kirchner,*[73] *Sun,*[74] *Chen,*[75] *Kundu*[76] have reported a series of homogeneous transition metal complexes the synthesis of pyrimidines through ADC condensation in presence of base.



Scheme 1.27. Dehydrogenative synthesis of pyrimidine

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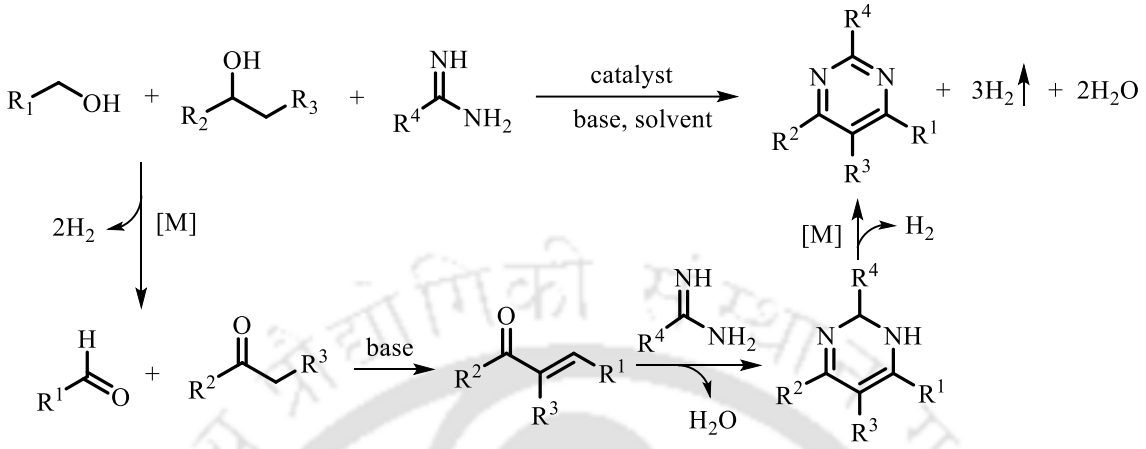
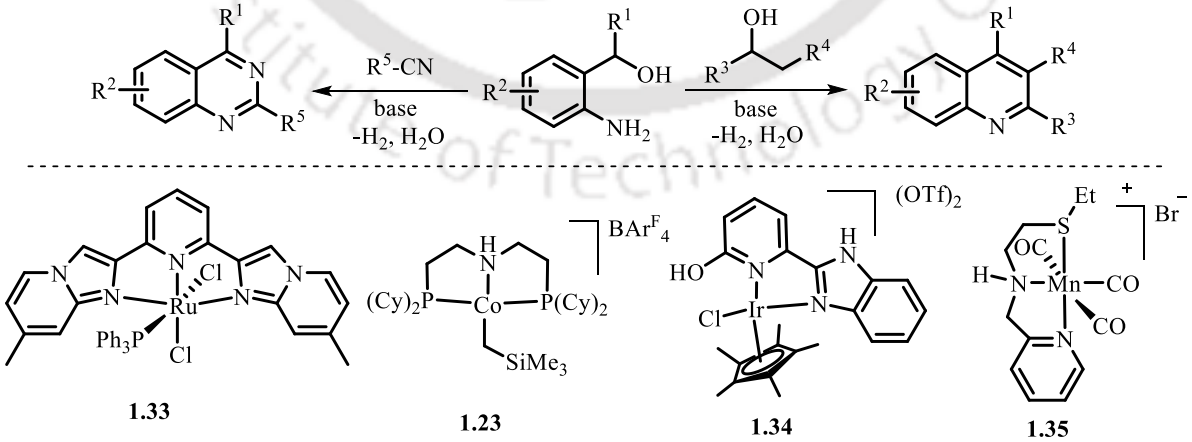
The plausible mechanism for the synthesis of pyrimidine *via* ADC reaction has been demonstrated below in Scheme 1.28.



Scheme 1.28. Plausible mechanism for the synthesis of pyrimidine *via* ADC reaction

1.5.5.3. Dehydrogenative synthesis of quinolines and quinazolines

In recent times, transition-metal-catalyzed dehydrogenative cyclization has been employed for the one-pot synthesis of quinoline and quinazolines. It uses simple and abundant starting materials and releases water and hydrogen as the only by-products thus proving to be a greener approach compared to the traditional protocols. Till now, various groups have developed a wide range of transition metal complexes for the synthesis of quinoline and quinazoline *via* dehydrogenative annulation pathway.[77-81] Most of the methodologies have been developed by using precious metals like Ir, Rh, Ru etc. Lately, earth abundant first row transition metals such Mn, Fe, Co, Ni etc. are gaining popularity as a viable alternative to these precious metals. Numerous research groups are now solely dedicated to develop new earth abundant metal complexes and employing them in the synthesis of different classes of *N*-heteroarene compounds *via* ADC pathway.



Scheme 1.29. Dehydrogenative synthesis of quinoline and quinazoline

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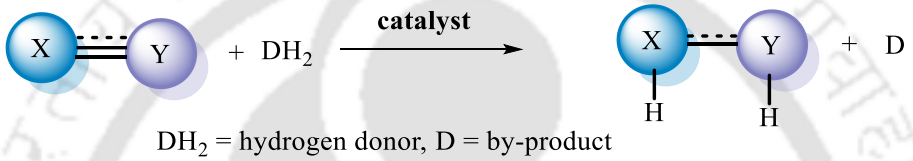
1.6. Transfer hydrogenation reaction

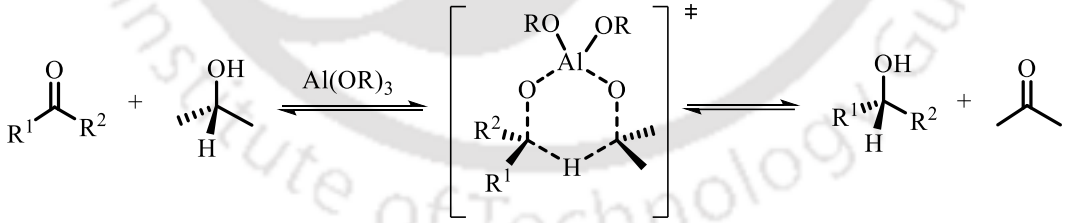
1.6.1. Basic concept of transfer hydrogenation reaction

One of the foremost elemental chemical transformations in organic synthesis is hydrogenation reaction. In general, two methods are used for this, one is direct approach (uses molecular H_2) and the another is transfer hydrogenation (TH, uses hydrogen donor DH_2). Transfer hydrogenation (TH), is an alternative to direct hydrogenation which gained tremendous attention in recent years because it does not require the use of flammable gas nor elaborate sophisticated experimental equipment. In this case hydrogen sources are readily available, inexpensive, and easy to handle reagents such as alcohols (including isopropanol, methanol, ethanol, glycerol), formic acid, Hantzsch esters, hydrazine, benzothiazoles, and dimethylamine-borane.[82] The catalyst is often required for this transformation.



Scheme 1.30. The general transfer hydrogenation reaction

Meerwein–Ponndorf–Verley (MPV) reduction illustrates the reduction of a ketone to its respective alcohol where secondary alcohol act as a hydrogen donor and aluminum alkoxide as a promoter. It was the first example of TH of carbonyl compound. The reduction proceeds *via* a direct hydrogen transfer pathway where a cyclic six membered transition state.[83, 84] However, the main drawback involved with this strategy is the requirement of large amounts of the aluminum reagent, thereby forming undesired side products.



Scheme 1.31. TH in the MPV reduction *via* a cyclic transition state

1.6.2. Transfer hydrogenation with transition metal catalyst

The next milestone was the transition metal catalyse transfer hydrogenation of ketones. In 1986, *Shvo* and *co-workers* in their pioneer work, demonstrated the synthesis of the ruthenium complex **1.14**[85]. which was originally found to be very efficient in direct hydrogenation of ketones, later applied in the transfer hydrogenation reaction. As mentioned in Scheme 1.20-(ii) the dinuclear complex **1.14** dissociates upon heating into the active, reducing form **1.14a** and the coordinatively

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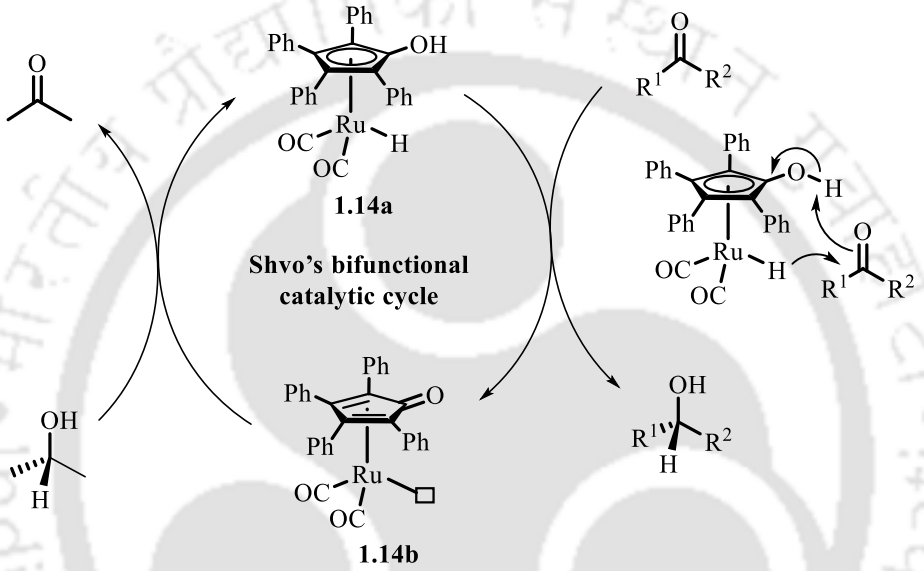
unsaturated and therefore, highly reactive species **1.14b**. The complex **1.14a** operates through an outer-sphere mechanism involving a simultaneous transfer of hydride from the ruthenium centre and proton from the hydroxyl group on cyclopentadienyl ligand the carbonyl group of the ketone substrate. **1.14b** upon dehydrogenation of the hydrogen donor isopropanol, the active transfer hydrogenation catalyst is regenerated. This is the first "metal-ligand bifunctional catalyst" for transfer hydrogenation (Scheme 1.32). Subsequently, many other metal catalysts containing rhodium,[86] iridium,[87] earth-abundant metals[88] are employed to facilitate transfer hydrogenation. Organocatalysts such as chiral secondary amine,[89] phosphoric acid derivative[90] are also found well-suitable for this transformation.



Scheme 1.32. Transfer hydrogenation by Shvo's catalyst

1.6.3. Reduction of *N*-heteroarenes with biomimetic Hantzsch ester as a mild H_2 source

Besides the transfer hydrogenation of multiple bonds such as C=O, C=N, and C=C, reduction of *N*-heteroarenes are also extensively studied using hydrogen transfer reagents such as formates (HCO_2H/NEt_3, HCO_2Na/H_2O), alcohol (isopropanol, ethanol), Hantzsch ester, benzothiazoline etc. Among them, Hantzsch ester is quite promising as it is the synthetic analog of nature's fundamental reduction co-factors such as NADH (nicotinamide adenine dinucleotide hydrogen) or its phosphate, NADPH. Besides, Hantzsch ester can be easily oxidized to Hantzsch pyridine in the presence of the catalytic amount of small organic molecules or metal complexes.[91]. This is primarily driven by aromatization energy. As a hydride is being abstracted in the aromatization process, Hantzsch esters can serve as very mild reducing agents.[92]

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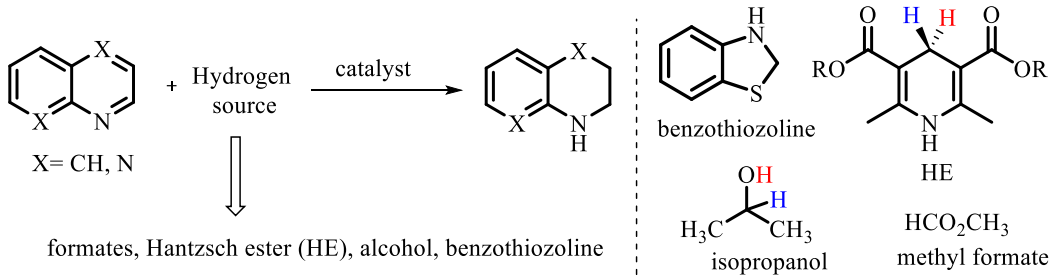
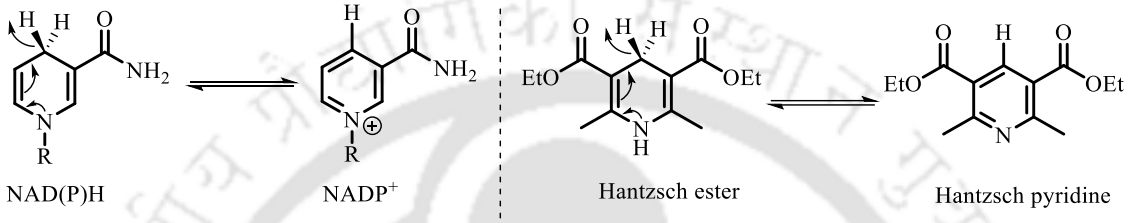


Scheme 1.33. Transfer hydrogenation of quinoline to THQs



Scheme 1.34. The structures of naturally occurring hydride-reduction cofactors and Hantzsch esters

Inspired by this biomimetic reduction approach, in early 2006, *Rueping* and *colleagues* examined the reduction of quinolines by using first highly enantioselective Brønsted acids in presence of Hantzsch ester.[93] The reduced product tetrahydroquinolines are an important class of compounds, ambiguously found in many natural products and used as synthetic intermediates in pharmaceutical, agrochemistry or material science. A highly enantiopure tetrahydroquinoline derivative was obtained in good yield by using 1-2 mol% of phenanthryl-substituted phosphoric acid (Scheme 1.35). It was suggested that the reaction proceeded *via* a cascade hydrogenation that consisted of a 1,4-hydride addition followed by a proton induced enamine-imine isomerization and finally 1,2-hydride addition (Scheme 1.36). The scope of the reaction was further explored to the synthesis of biologically active tetrahydroquinoline alkaloid such as (+)-galipinine, (+)-cuspareine and (±)-angustureine etc.[94] Later on, the same research group have shown their methodology in aqueous medium as well. After the successful enantioselective transfer hydrogenation of quinolines, reduction of other imine containing heterocycles including pyridine, indole, 1,10-phenanthrolines, benzoxazines, benzothiazines, benzoxazinones, quinoxalines, and quinoxalinones accomplished using Hantzsch ester as a mild hydrogen source[95] with Brønsted acids employed as catalysts. [92, 96] Metal-catalyzed transfer hydrogenation of quinoline with Hantzsch esters is also reported with metal triflates such as $Fe(OTf)_2$ and AgOTf.[97, 98] Herein, Lewis acidic metal ions play an important role in the activation of quinoline.

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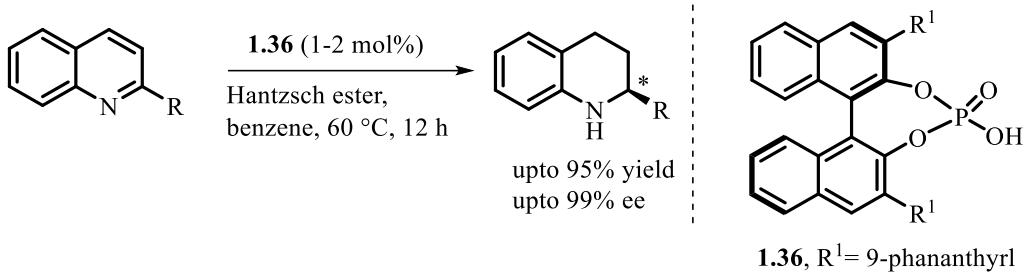
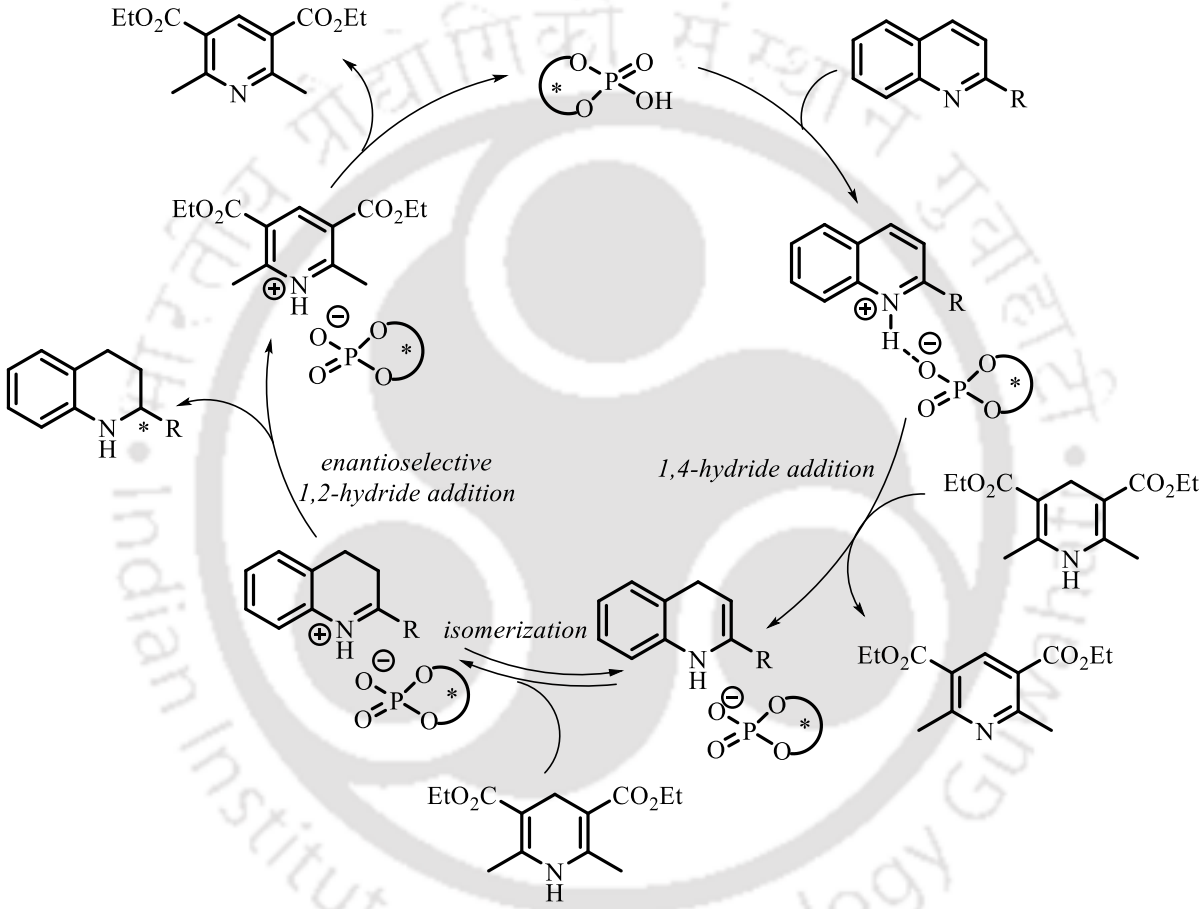


Scheme 1.35. Asymmetric transfer hydrogenation of 2-substituted quinolines



Scheme 1.36. Proposed mechanism for asymmetric reduction of quinoline

Zhang, *Bolm*, *Tan* and *Matile* independently demonstrated the reduction of quinoline with Hantzsch ester by utilizing various non-covalent hydrogen-bond (HB)-donor, halogen-bond (XB)-donor, and chalcogen-bond (ChB)-donor organocatalyst. [99] They found that activation of the quinoline by halogen bonding, or chalcogen bonding was played crucial role for this chemical transformation (Scheme 1.37). Despite various reports on Lewis acidic metals, Brønsted acids, non-covalent bond donor-catalyzed reduction of quinoline to tetrahydroquinoline were reported, there is still potential for development of new earth-abundant catalytic systems to overcome the limitations and functional group tolerance in the transfer hydrogenation reaction.

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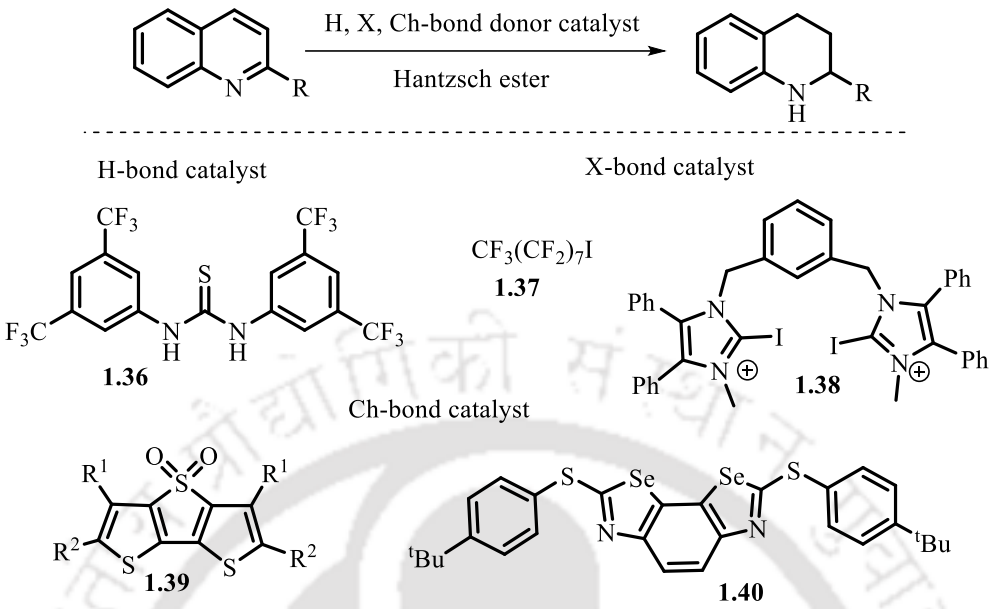

Scheme 1.37. Noncovalent bond donor catalyzed reduction of quinoline with Hantzsch ester

1.7. Summary

The aldol reaction is one of the most useful synthetic tools in forming carbon-carbon bonds especially in attaining *β*-branched carbonyl compounds which act as potential building blocks for the synthesis of fine chemicals such as natural products and bio-active molecules. These *β*-branched carbonyl compounds further can be achieved by transition-metal catalyzed cross-coupling reaction of ketones (or enolates) with prefunctionalized starting precursors. Likewise, the literature studies also showcase that the acceptorless dehydrogenation of alcohol is another important tool to affords aldehyde or carbonyl compounds and produces molecular hydrogen making it atom-economical, environmentally benign sustainable methodology compare to the traditional approaches. This dehydrogenation reaction can be catalyzed by a variety of metal complexes without the use stoichiometric amounts of oxidants or acceptor molecules. The reaction provides a wide range of C-C, C-O, and C-N coupled products such as branched ketones, esters, imines, and *N*-heteroarenes. In the majority of cases, metal–ligand cooperation facilitates substrate activation without changing the redox state of the metals and subsequently proceeds through a low-energy dehydrogenation pathway. Literature suggested that the application of earth-abundant transition metals for acceptorless dehydrogenative reaction is still in the nascent stage. Thus, there is an ample scope to develop new earth-abundant transition metal complexes and to study their scope and limitation in various dehydrogenative transformations. Furthermore, from literature studies, it has been found that transfer hydrogenation is a powerful alternative tool to direct hydrogenation where organic hydrogen sources are used for hydrogenation. In this regard, biomimetic Hantzsch ester as hydrogen source has gained tremendous popularity for the reduction of *N*-heteroarene.

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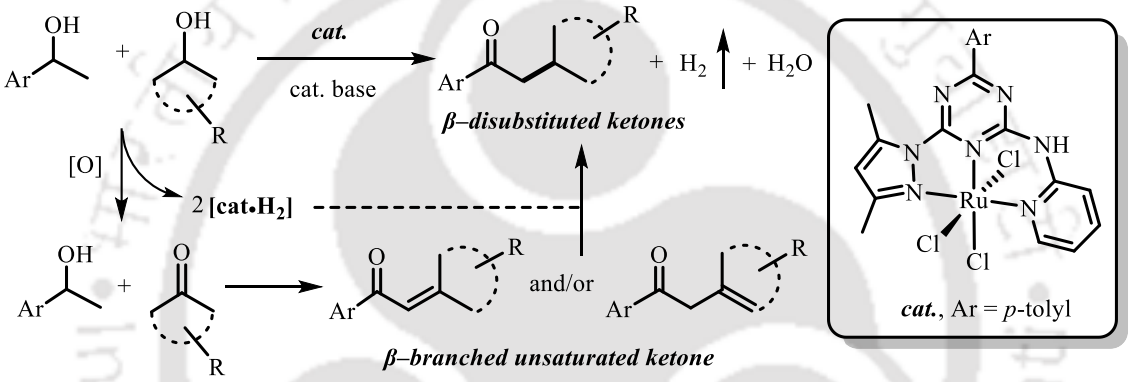
1.8. Scope and objective of the thesis

Based on the literature survey it has been found that aldol condensation, alkene isomerization, acceptorless dehydrogenative coupling, and transfer hydrogenation are the powerful synthetic strategy for the synthesis of diverse range of useful organic building blocks. In contrast to the classical catalyst, MLC-catalyst proved to be efficient in various organic transformations.

Very recently our group reported bifunctional ruthenium(III) complex catalyzed cross-coupling of secondary alcohols to *β*-branched ketone. Study suggests that *β*-branched unsaturated ketone is the key intermediate in the catalytic cycle (Scheme 1.38). Since there is a handful synthetic assay for the *β*-branched unsaturated ketone in particular *β, γ*-unsaturated ketones (see section 1.3, 1.4), herein I am interested to explore this.



Scheme 1.38. Ruthenium-catalyzed cross-coupling of secondary alcohols.

Aldol condensation of two different ketones may offer a straightforward and boosting approach to access this class of *β, γ*-unsaturated ketones. Possibly due to the relatively low reactivity of ketones as electrophiles (aldol acceptors), its propensity for retro-aldol reaction. The reactions often suffer from unsatisfactory chemoselectivity (self- *vs*. crossed aldol, alkene products) and regioselectivity (thermodynamic *vs.* kinetic enolate). Hence, new strategies with high efficiency are highly desired. Present study is focused on the synthetic scope of *β, γ*-unsaturated ketones. Initial attempt was made with air-stable Ru(III)-catalysts, followed by cost-effective chromium(III) catalysts using triazine-based tridentate pincer ligands (Scheme 1.39). Then base-metal chromium(III) catalysed dehydrogenative synthesis of quinoline, and quinazoline derivatives are attempted under sustainable manner (Scheme 1.40).

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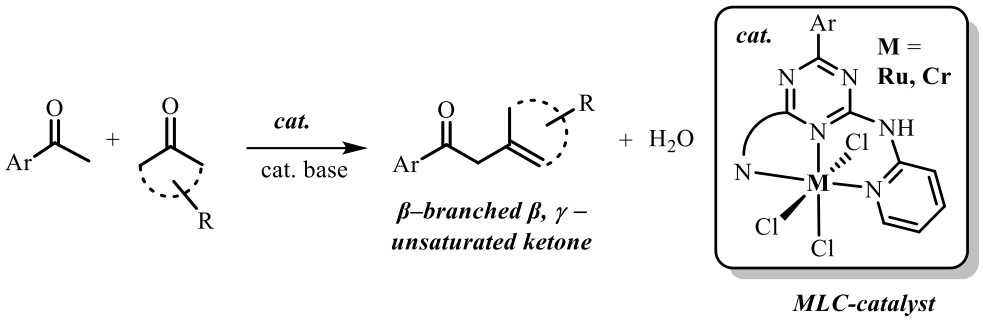
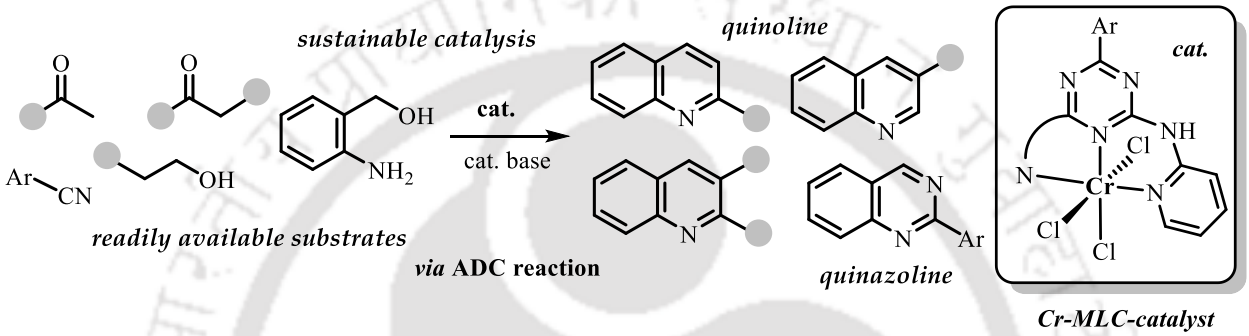
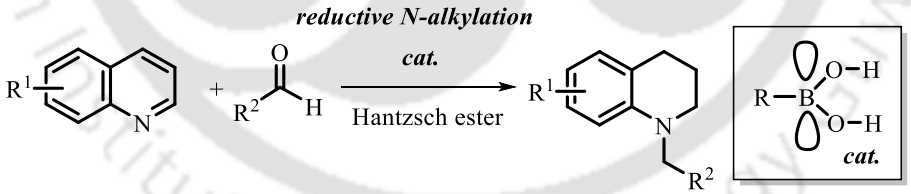


Scheme 1.39. Sustainable synthesis of β-branched β, γ-unsaturated ketones.



Scheme 1.40. Sustainable synthesis of quinoline and quinazoline derivatives.

Another objective of this study was to investigate the boronic acid catalyzed reductive alkylation of quinolines to *N*-alkyl tetrahydroquinolines using Hantzsch ester under mild conditions since tetrahydroquinoline derivatives are an important class of compounds that are widely utilized in pharmaceutical and agrochemical industries (Scheme 1.41).



Scheme 1.41. Boronic acid catalyzed reductive *N*-alkylation of quinolines

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Chapter 2

Chemo- and regioselective catalytic cross-coupling reaction of ketones for the synthesis of β, γ-disubstituted β, γ-unsaturated ketones

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2.1. Introduction

β, γ-unsaturated ketone compounds are ubiquitous in nature. These important molecular scaffolds are found in various natural products and bio-active molecules (as shown in Figure 2.1).[1-5] These high-value synthons are also extensively used as building blocks in a number of total synthesis by manipulating their carbonyl and alkene moieties. In addition, they are found as key intermediates in the synthesis of *β*–branched saturated ketones *via* catalytic cross-coupling reaction of secondary alcohols and the *α*-alkylation of ketones with secondary alcohols (as discussed in chapter 1, section 1.8).[6-9] These unsaturated ketones are also useful in photochemical reactions.[10]

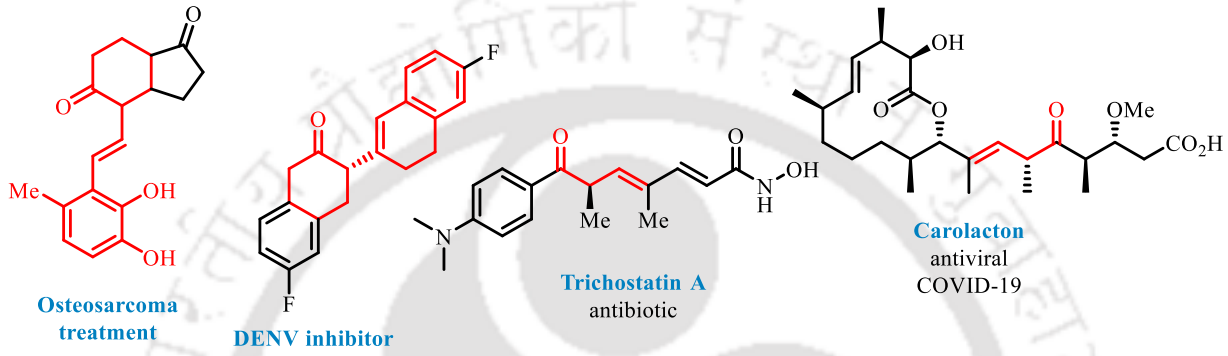

Figure 2.1. Selected *β, γ*-unsaturated carbonyl compounds and their potential medicinal applications.

α, β-unsaturated ketones are common motifs and can be easily synthesized, however methods for the synthesis of *β, γ*-unsaturated ketone remains at an early stage.[11] The conversion of unsaturated esters to corresponding ketones *via Weinreb* amides is encompassed in early studies.[12-14] Though addition of nucleophiles to ester appears to be a simple and straightforward approach for the synthesis of ketone, in reality these reactions typically result in bis-alkylation to form tertiary alcohols, as the initial ketone product is more electrophilic than the starting ester. To offset the inherent reactivity challenges, *Weinreb* amides has been utilized as carboxylate synthons which stabilize and prevent the breakdown of the initial tetrahedral adduct formed upon nucleophilic addition, thereby favouring ketone formation over tertiary alcohol formation. However, the reaction involves three discrete steps: ester hydrolysis, amide bond formation, followed by reaction with nucleophile. Further, the reactivity of the organometallic reagent must be considered during synthetic transformation since these are reactive and incompatible with a number of functional groups. A second strategy to control monoalkylation is the use of transition-metal catalyzed cross-coupling reaction of ketones (or enolates) with alkenylbromides, alkenyltriflates or alkenyl tosylates.[15-18] The use of palladium and nickel is dominated as a choice of catalyst in these reactions. Further, ruthenium hydride-catalyzed[19,20] and photoredox conditions[3] has been employed to enrich this chemistry. In most of the cases, reaction was directed with a pre-functionalized coupling partners which restricts the synthetic efficiency. Further, in some case method suffers low *β, γ*-regioselectivity.[17] Hence, new strategies with high efficiency are highly desired.

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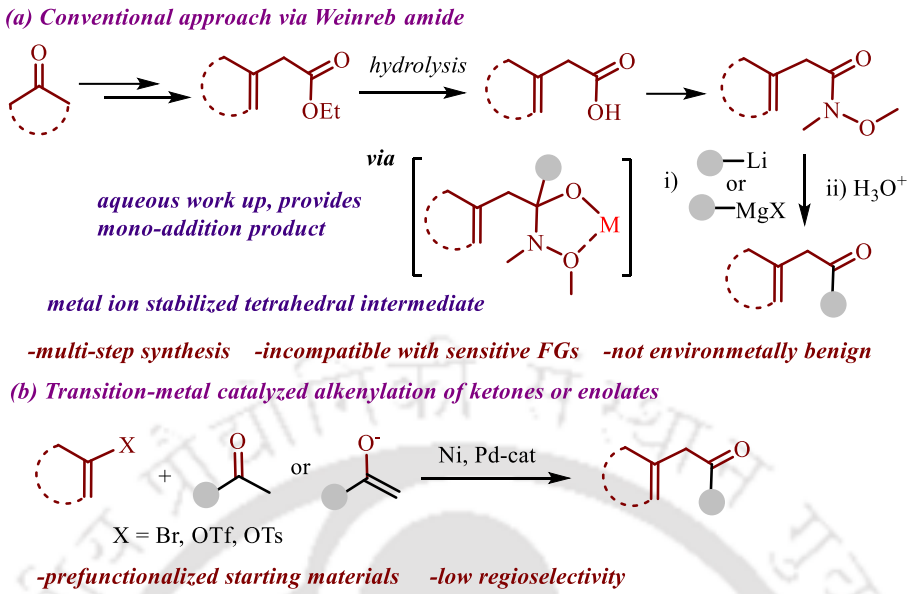

Scheme 2.1. Synthesis of *β*-branched *β, γ*-unsaturated ketones.

2.2. Present work

In this quest, I believe that cross-aldol condensation of ketones may offer a straightforward and boosting approach to access this class of *β*-branched *β, γ*-unsaturated ketones *via* alkene isomerization. Since the starting material ketones are easily available and inexpensive, this may provide access to broad substrate scope. As mentioned in the chapter 1 section 1.2, aldol condensation of ketone with aldehyde is well-explored,[21, 22] however reaction of two different ketones to unsaturated carbonyl compound has not yet been systematically studied.[23] Probably due to the relatively low reactivity of ketones as electrophiles (aldol acceptors), its propensity for retro-aldol reaction. The reactions often suffers from unsatisfactory chemo-selectivity (self- *vs* crossed aldol, alkene products) and regioselectivity (thermodynamic *vs* kinetic enolate).[22] I report here ruthenium- and base- catalyzed aldol-condensation of two different ketones to *β, γ*-disubstituted *β, γ*-unsaturated ketones. Interestingly, single crossed aldol condensation products are formed even in reactions where a mixture of products is possible. The reaction is highly chemoselective, tolerates a wide range of functional groups and exhibits high *β, γ* regioselectivity. Notably, the reaction produces H_2O as the only byproducts making the protocol greener, atom-economical and environmentally benign. To the best of our knowledge, this is a first example of catalytic reaction to integrate the chemistry of synthetic challenge aldol condensation of two different ketones and alkene migration into a reaction pot.

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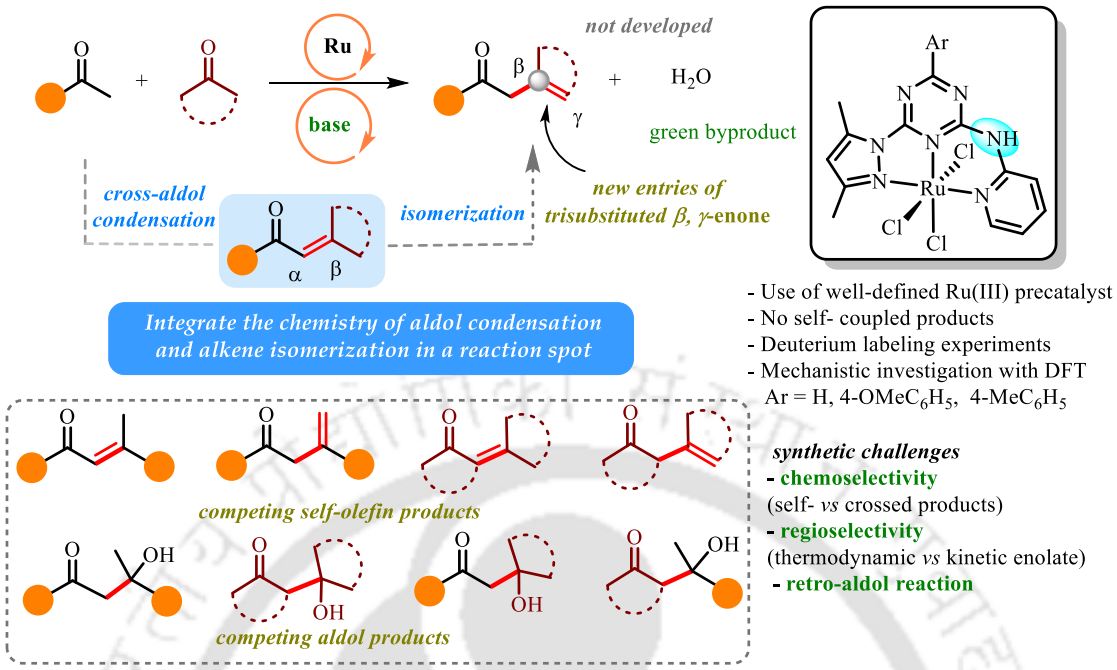

Scheme 2.2. Ruthenium catalyzed cross-coupling of ketones.

2.3. Results and discussion

2.3.1 Synthesis and spectroscopic characterization of ligands and their corresponding ruthenium complexes:

The triazine-based tridentate NNN-pincer ligands **2.5a-c** were synthesized according to the reported procedure.[8] Multistep synthetic process involved as outlined in Scheme 2.3, using cyanuric chloride as starting precursor. A new ligand **2.5b** has been synthesized using the similar procedure.[8] 2,4-dichloro-6-(4-methoxyphenyl)-1,3,5-triazine **2.3b** was initially prepared in 90% yield by reacting cyanuric chloride **2.1** with arylmagnesium bromide at 0 °C in dry THF under argon atmosphere. To the reaction mixture, the deprotonated 3,5 dimethylpyrazole solution in THF was slowly added at low temperature to afford triazine containing 2-chloro disubstituted derivatives **2.4b** as a white solid in good yield. Finally, pincer ligand **2.5b** was readily obtained in 83% yield by reacting **2.4b** with 2-pyridylamine in the presence of NaH. Compound **2.5a-c** was characterized by HRMS, NMR spectroscopy (for details, see experimental section in the section 2.5).

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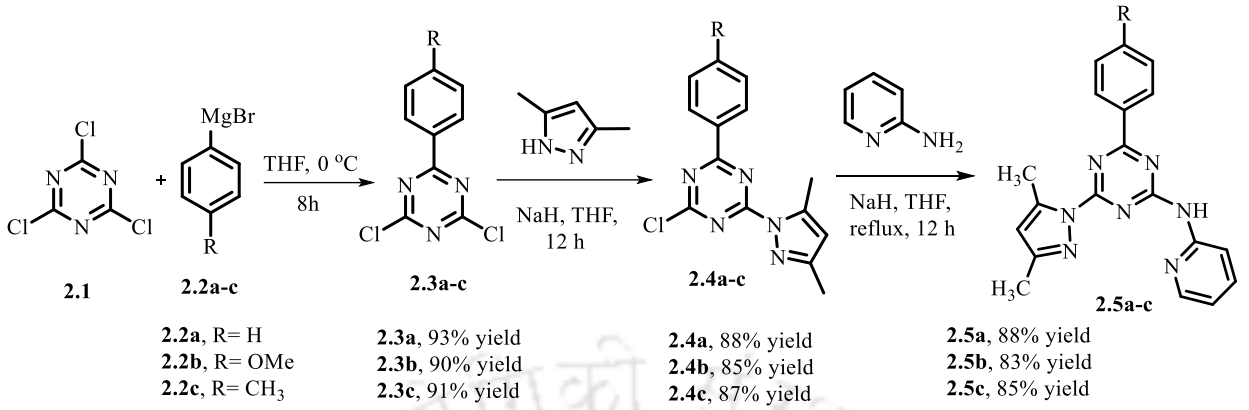
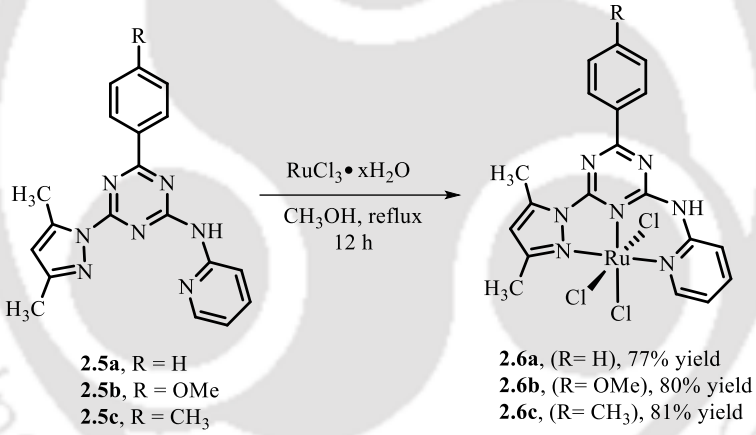


Scheme 2.3. Synthesis of ligands.

The complexes **2.6a-c** were prepared by refluxing $RuCl_3 \bullet xH_2O$ with the corresponding tridentate ligand in methanol for 12 h. The pincer ruthenium (III) complexes were formed as brown solids and are stable in moisture and air. The complex **2.6c^{Me}** was synthesized in 95% yield by treating the complex **2.6c** with KO^{t}Bu, methyl iodide in toluene.[8] The new complex **2.6b** was characterized by HRMS and SC-XRD.



Scheme 2.4. Synthesis of ruthenium complexes.

Among the ruthenium complexes, **2.6b** is the newly synthesized complex and single crystals of complex **2.6b** suitable for X-ray diffraction were obtained by slow evaporation of the saturated solution of the complex in CH_3OH at room temperature. The complex **2.6b** crystallizes in the P-1 space group and consists of one molecule of water in the lattice (Figure 2.2). The water molecule is located in close proximity to the one N−H group of the ligand backbone, indicates a strong hydrogen bonding interaction (N-H•••OH_2 1.972 Å). The molecular structure of complex **2.6b** adopts distorted octahedral geometry with the ruthenium center, which is formed by the three meridional sites with the pyridyl, pyrazolyl and triazine nitrogen atoms of the ligand **2.6b**. The other coordination sites are occupied by three chlorine atoms. Notably, the two chloride ligands are seated in trans position to each other and the other chlorine atom Cl is situated trans to the *s*-

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triazine nitrogen atom of the NNN coordinating units. The Ru-N bond length for the central triazine rings of the complexes is shorter than those for the nitrogen atom of pyrazolyl and pyridyl rings.

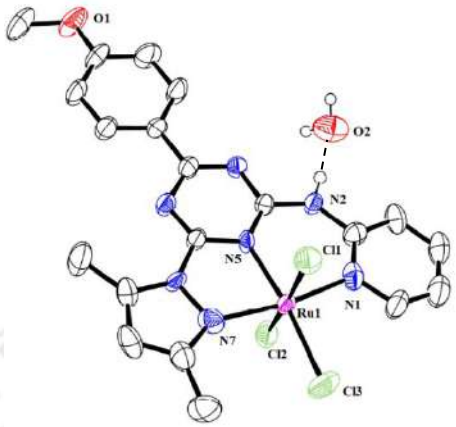

Figure 2.2. ORTEP diagram of ruthenium complex **2.6b**, (CCDC-2361370) (Thermal ellipsoids are drawn with 50% probability level). Selected bond lengths (in Å): Ru1–N5 2.002(4), Ru1–N7 2.056(5), Ru1–N1 2.105(5), Ru1–Cl1 2.3474(17), Ru1–Cl2 2.3545(18), Ru1–Cl3 2.3560(17), NH(22)···O(1) hydrogen bond 1.972. Selected bond angles: N1–Ru1–Cl1 92.60(15), N7–Ru1–N1 170.6(2), N5–Ru1–Cl1 85.57(13), N7–Ru1–Cl2 94.26(16), Cl1–Ru1–Cl2 92.13(7), Cl1–Ru1–Cl3 173.24(6), Cl2–Ru1–Cl3 93.86(7).

2.3.2. Optimization studies of catalytic cross coupling of ketones

To inspect the catalytic applicability of the as-prepared ruthenium complex **2.6a-c**, optimization studies were performed with 4-phenylacetophenone (**2.7c**, 1 mmol) and cyclohexanone (**2.8a**, 1 mmol) as model substrates for the catalytic cross coupling of ketones (Table 2.1). The reaction was initiated with complex **2.6c** (2 mol%), KO^{t}Bu (20 mol%), and 4 Å molecular sieves in dry toluene at 150 °C. After 4 h, the *β, γ*-unsaturated ketone **2.9c** was obtained in 55% yield along with unreacted ketone **2.7c**, 37% (entry 1). Upon further increasing the reaction time to 8 h, the yield of **2.9c** was improved to 82% (entry 3). Under the identical conditions, when the reaction was carried out with complex **2.9a** and **2.9b**, respectively, lower yield of **2.9c** suggested that the complex **2.6c** is more efficient with respect to others (entry 3). Notably, no self-coupled unsaturated ketone and reverse-coupled unsaturated ketone were observed, indicating the reaction is highly chemoselective. The yield of **2.9c** was dramatically decreased in the absence of molecular sieves, indicating the key role of molecular sieves in the current catalytic process (entry 6, Table 2.1). The reaction was also checked with Dean–Stark apparatus (instead of using molecular sieves) *via* azeotropic removal of water, a decrease in the yield has been observed (entry 7). Further, on low catalyst and base loading, resulted in considerably lower yields (entry 8). Use of $RuCl_3 \bullet xH_2O$ as the catalyst provided only 15% yield indicating importance of the ligand backbone in the catalysis (entry 9). The temperature effect on the reaction was also noticeable. When the reaction temperature was decreased to 125 °C, the aldol condensation product formation was gradually decreased suggesting lower temperature (<120 °C) impedes the condensation and propensity of

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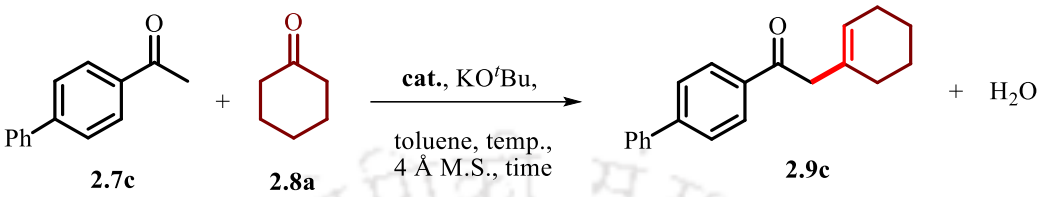
retro-aldol reaction (entries 10–14). Control experiments confirmed that no product was formed in the absence of catalyst and/or base, implying their necessity in the cross-coupling reaction of ketones (entries 15–19).

Table 2.1. Optimization table for catalytic cross coupling of ketones[a], [b]



2.7c **2.8a** **2.9c**

Entry	cat. (mol%)	KO^{t}Bu (mol%)	temp (°C)	time (h)	yield (%)	
					2.9c	**2.7c**
1	**2.6c** (2)	20	150	4	55%	37%
2	**2.6c** (2)	20	150	6	68%	20%
3	**2.6c** (2)	20	150	8	82%	0%
4	**2.6a** (2)	20	150	8	73%	12%
5	**2.6b** (2)	20	150	8	77%	8%
6[c]	**2.6c** (2)	20	150	8	21%	60%
7[d]	**2.6c** (2)	20	150	8	30%	58%
8	**2.6c** (1)	10	150	8	34%	58%
9	**$RuCl_3$•xH_2O** (2)	20	150	8	15%	80%
10	**2.6c** (2)	20	140	8	57%	25%
11	**2.6c** (2)	20	130	8	40%	48%
12	**2.6c** (2)	20	125	8	14%	81%
13	**2.6c** (2)	20	120	8	0%	88%
14	**2.6c** (2)	20	25	8	0%	98%
15	–	20	150	8	0%	98%
16	–	20	25	8	0%	98%
17	–	200	25	8	10%	86%
18	–	200	150	8	14%	51%
19	**2.6c** (2)	–	150	8	0%	97%

Reaction conditions: [a] **2.7c** (1 mmol), cyclohexanone **2.8a** (1 mmol), KO^{t}Bu (x mol%), dry toluene (2 mL) and 4 Å mol sieves were heated in a closed 50 mL reaction tube for given time under argon. [b] Isolated yield. [c] Under air in the absence of 4 Å mol sieves. [d] Using Dean-Stark apparatus.

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When the reaction was performed with 2 equiv. of base at different temperature such as 25 °C and 150 °C, respectively, the desired product **2.9c** was obtained in low yield (at 25 °C, **2.9c**, 10% yield, and at 150 °C, **2.9c**, 14% yield), along with substantial amount of aromatic ketone **2.7c** was recovered (at 25 °C, **2.7c**, 86% yield, and at 150 °C, **2.7c**, 51% yield) (entries 17–18). Notably, in absence of base the reaction did not proceed indicating the necessity of base in the cross-coupling reaction (entry 19). Nevertheless, no self-coupled unsaturated ketone and/ or reverse-coupled unsaturated ketone were observed.

In order to shed some more light on the reaction profile, a model reaction was conducted under the optimized conditions, and the product analysis was performed at different time intervals (Figure 2.3). The initial conversion of the ketones, **2.7c** and **2.8a** was found to be rapid, leading to about 35% conversion in the first hour and then decreases gradually over the period of time.

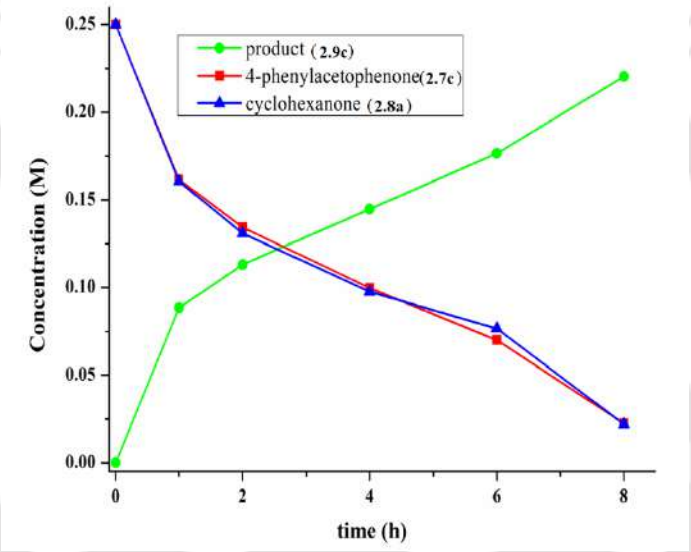

Figure 2.3. Monitoring of the reaction progress by GC.

2.3.3. Substrate scope for catalytic cross coupling of ketones

Further, under the optimized conditions, a wide variety of aromatic ketones **2.7a**–**l** were reacted with cyclohexanone (**2.8a**) to obtain the corresponding *β*-branched-unsaturated carbonyl compounds **2.9a**–**l** (Table 2.2). Different substituted aromatic ketones, such as 4-OCH_2Ph, 4-OMe, 4-Ph, 4-Cl, 4-Br, 4-C≡CPh, 3-Br, and 3-CF_3 acetophenone provided the *β*, *γ*-disubstituted *β*, *γ*-unsaturated ketones **2.9a**–**h** (78–92%). Next, the reactions of *α*- and *β*- naphthyl methyl ketones, 3,4-dimethoxy and 3,4,5- trimethoxy-substituted aromatic ketones were also found to proceed efficiently to obtain the corresponding *β*, *γ*-unsaturated ketones **2.9i**–**l** in moderate to good yields. Furthermore, various 4-substituted cyclohexanones (**2.8b**–**2.8e**) were also well-suited as substrates under the optimized reaction conditions, giving the corresponding *β*, *γ*-unsaturated ketones **2.9m**–**2.9s** in good yields. Interestingly, 4-substituted cyclic ketal bearing cyclohexanone **2.8e** gave a *β*, *γ*-isomer of **2.9q** in 65% yield. Notably, -$OCH_2CH{=}CH_2$ group as a substituent at the para-position

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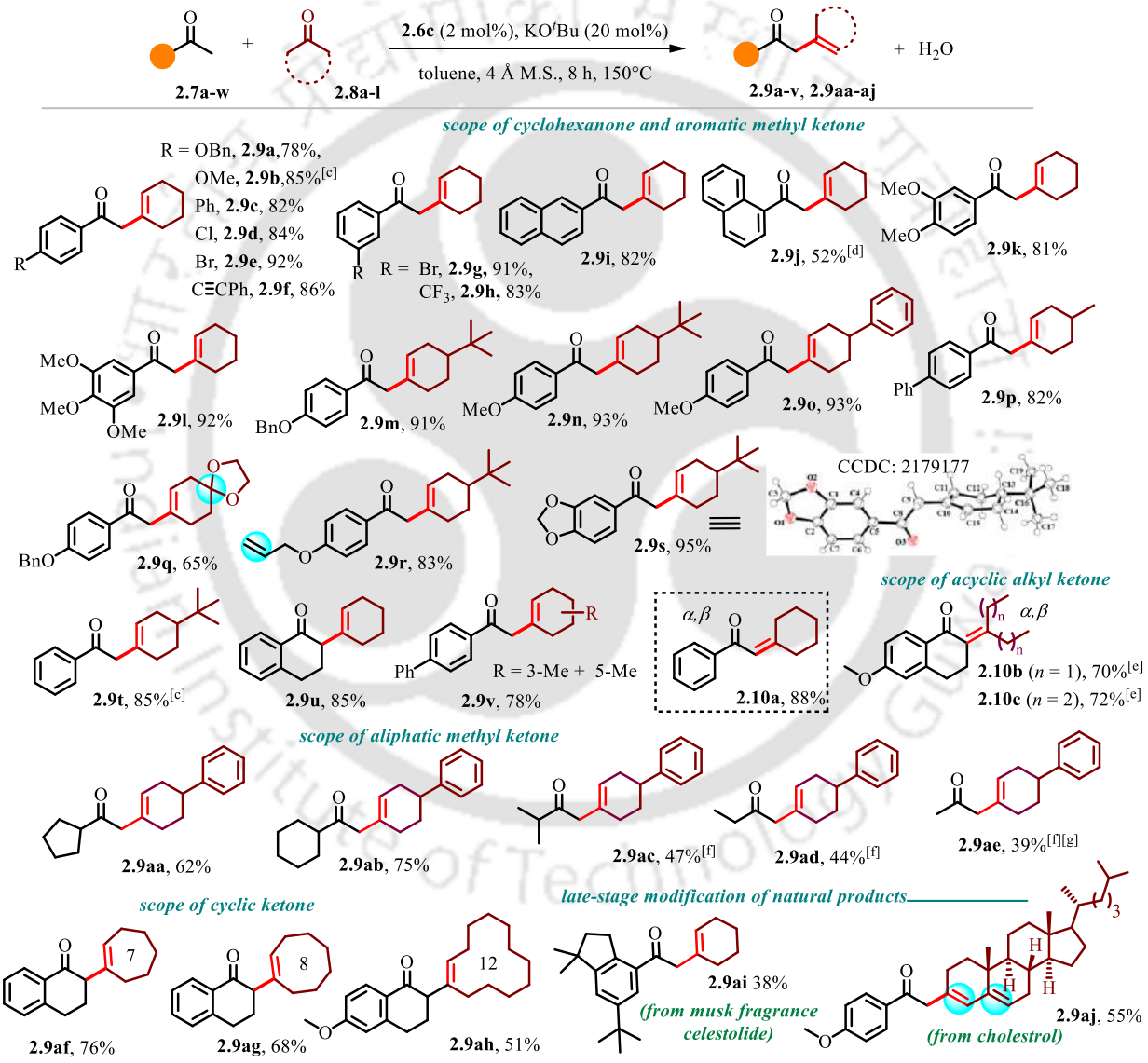
in the aromatic ketone afforded the desired ketone **2.9r** in 83% yield. The entity of the *β*-branched *β*, *γ*-enone was confirmed by X-ray crystallography (**2.9s** in Table 2.2). To my surprise, simple acetophenone was reacted with cyclohexanone yielded the *β*, *β*- disubstituted *α, β*-unsaturated ketone **2.10a** in 88% yield, whereas the reaction with 4-*tert*-butyl cyclohexanone afforded *β*, *γ*-unsaturated ketone **2.9t** in 85% yield (*vide infra in details for the isomerization of olefin*). Hence, switching selectivity was obtained by simply incorporating the substituent in the cyclohexyl ring.

Table 2.2. Substrate scope for catalytic cross coupling of ketones[a], [b]



Reaction conditions: [a] aromatic ketone (1 mmol), cyclohexanone derivative (1 mmol), **2.6c** (2 mol%), KO^{t}Bu (20 mol%), and dry toluene (2 mL) and 4 Å mol sieves were heated at 150 °C in a closed 50 mL reaction tube for 8 h under argon. [b] Isolated yield. [c] with 6 mol% of cat **2.6c** and 40 mol% of base. [d] along with **2.7j** was recovered in 41% yield. [e] with 6 mmol of acyclic alkyl ketone. [f] with 6 mol% of **2.6c** and 60 mol% of base. [g] with 10 equiv. of aliphatic methyl ketone.

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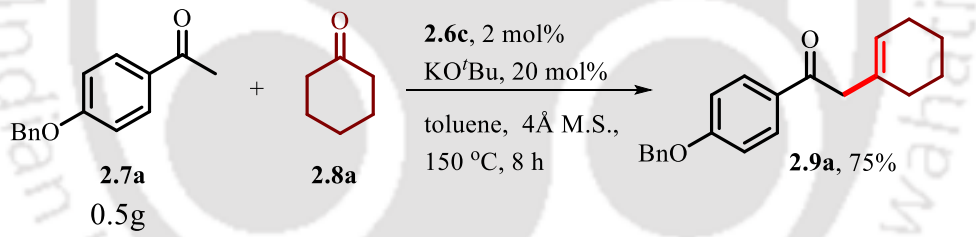
The reaction is also compatible to ketones other than aryl methyl ketones such as benzo-fused cyclohexanone in a good yield (**2.9u**, 85%). Next, 3-substituted cyclohexanone **2.8f** was also successfully employed in the reaction to provide a mixture of *β*, *γ*-unsaturated ketones **2.8v** in 78% yield. Intriguingly, acyclic alkyl ketones for example, diethyl ketone, dipropyl ketone was also amenable to this method. However, it leads to *α*, *β*-enone **2.10b-c**. Finally, synthetically challenging aliphatic methyl ketone was also found to be amenable to this method, giving **2.9aa-ae** in good to moderate yields. To our delight, *β*, *γ*-unsaturated ketone **2.9ae** was successfully prepared using acetone as a simple three carbon feedstock. Further, scope of the reaction was expanded to a variety of other higher analogues of cyclic aliphatic ketones such as, cycloheptanone, cyclooctanone, and cyclododecane (**2.9af-ah**). Synthetic application of the current catalytic protocol was further emphasized by the late-stage functionalization of musk fragrance celestolide, **2.7w** and complex (±) cholesterol, **2.8l** derivatives without affecting the parent moiety (**2.9ai**, 38%, **2.9aj**, 55% respectively).

2.3.4. Gram-scale reactions and synthetic transformation

To demonstrate the practical applicability of this process, gram-scale reaction was performed for the synthesis of **2.9a** as shown in Scheme 2.5. The compound **2.9a** was obtained in 75% yield using 0.5 g of 1-(4-(benzyloxy)phenyl)ethan-1-one (**2.7a**) under standard conditions.



Scheme 2.5. Gram-scale reaction.

2.3.5. Post-synthetic modification

Additionally, synthetic transformation of the *β*, *β*-disubstituted *β*, *γ*-unsaturated ketones **2.9a** have been explored by the reduction of carbonyl group with sodium borohydride to form **2.11** (Scheme 2.6a). A double bond functionality of the **2.9b** could also be easily reduced by the cyclohexanol *via* borrowing hydrogen catalysis to obtain **2.12** in 92% yield (Scheme 2.6b).

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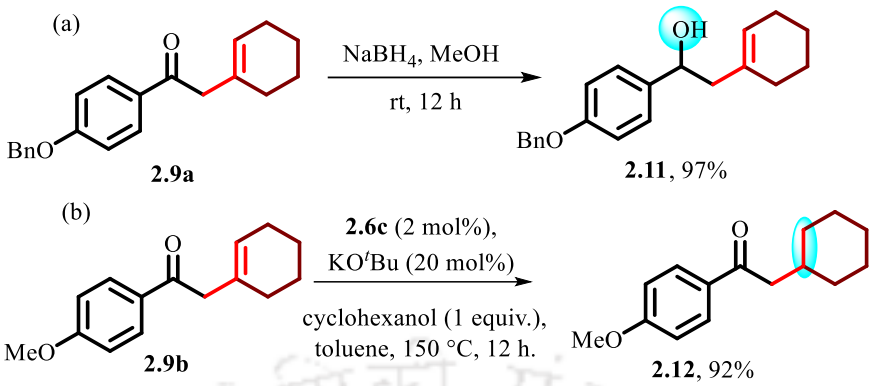
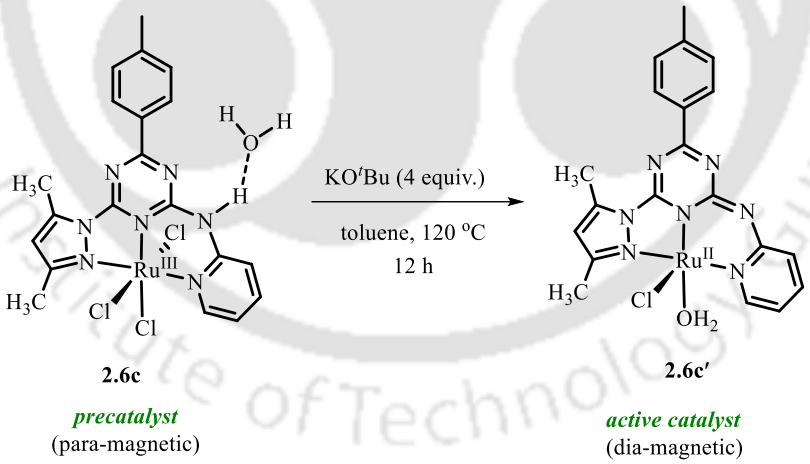


Scheme 2.6. Synthetic transformation.

2.3.6. Spectroscopic characterization for active catalyst 2.6c'

To gain more insights into the active ruthenium species [Ru(III) or Ru(II)] in the catalytic cycle, a titration experiment was performed by adding a base into precatalyst **2.6c** and monitoring the EPR spectra. Upon loading the base, the paramagnetic signal of ruthenium(III) slowly disappeared and formed EPR-silent diamagnetic Ru(II) species by using 4 equiv. of KO^{t}Bu (Scheme 2.7). It infers that 8 mol% of KO^{t}Bu (compared to 2 mol% of **2.6c**) is necessary for activation of precatalyst. Notably, 20 mol% of base was used in the reaction condition which is higher than the needed base loading (8 mol%) for active ruthenium species. Herein, we are presuming that 8 mol% of base is required for the activation of 2 mol% of pre-catalyst and remaining 12 mol% base is required for the cross-coupling reactions.



Scheme 2.7. Active species formation.

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EPR study:

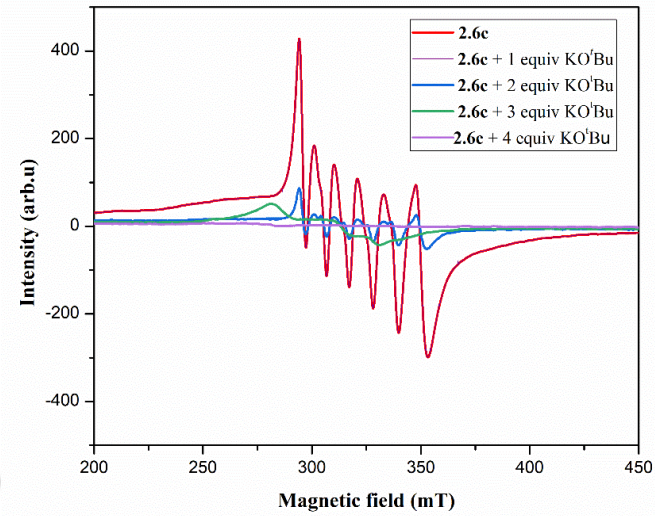


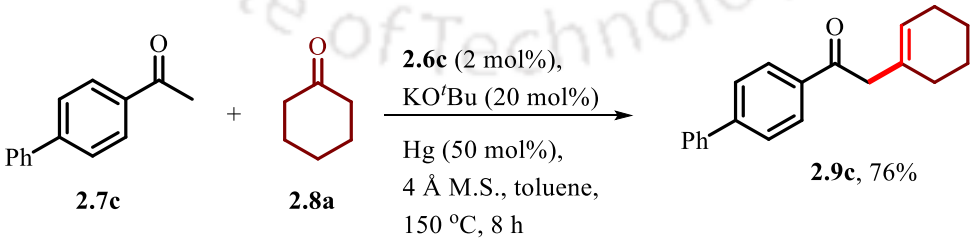
Figure 2.4. EPR spectrum of **2.6c** with varying equivalent of base. X-band microwave frequency(GHz): 9.14, modulation frequency(KHz): 100.

Experimental procedure: The reaction tube was equipped with a stir bar, complex **2.6c** (10 mg, 1 equiv.), varying equivalency of KO^{t}Bu (1-4 equiv.), and toluene (1 mL). The reaction mixture was stirred at 120 °C for 12 h. The resulting solution was cooled to room temperature; all the volatiles were removed under reduced pressure. The obtained residue was then dissolved in CH_3OH (0.5 mL) and subjected for EPR analysis at 77 K. The EPR spectrum was silent by using four equivalents of KO^{t}Bu.

Further active species of ruthenium(II) complex **2.6c'** was confirmed by ^{1}H NMR spectra ESI-HRMS as previously reported by our group.[8, 9]

2.3.7. Mechanistic studies

In order to confirm the homogeneous nature of the ruthenium complex **2.6c** in the catalytic reaction, the mercury drop experiment was conducted. No inhibition of reaction or reduction of product yield of **2.9c** was observed, suggesting the reaction is homogeneous (Scheme 2.8).[24]



Scheme 2.8. Mercury drop experiment

To examine the role of the -NH functionality of the ligand framework on the catalysis, a *N*-methylated complex, **2.6c^{Me}** was employed in the reaction. A lower yield of **2.9c** was observed,

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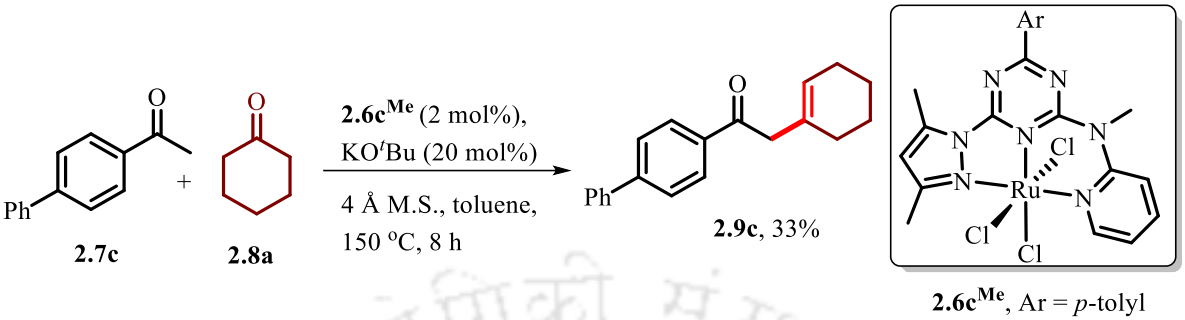
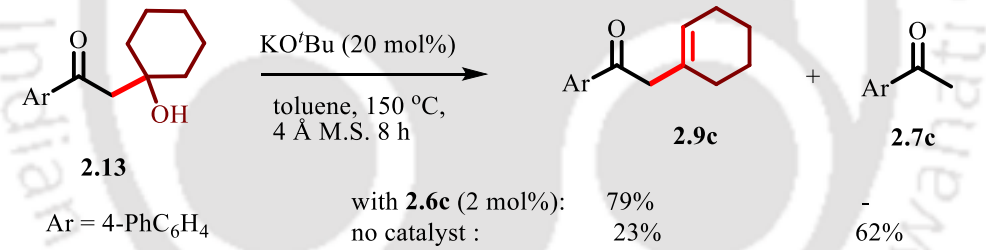
indicating the key role of the -NH functionality and metal-ligand cooperativity (MLC) in the reaction pathway (scheme 2.9).[25]



Scheme 2.9. The impact of the –NH functionality in catalysis.

To probe further the involvement of aldol product in the cross-aldol reaction, the reaction was examined with aldol product **2.13** under the standard conditions (Scheme 2.10). As expected, a dehydration product **2.9c** was obtained with 79% yield in the presence of catalyst, and 23% yield attained in the absence of catalyst (along with 62% of **2.9c** was recovered from the reaction mixture). The result suggests that aldol product **2.13** is the probable reaction intermediate, and a retro-aldol pathway is pronounced in absence of catalyst. Hence, the catalyst was found to play an important role not only in the selective C-C bond formation but also in the condensation step.



Scheme 2.10. Proof for the aldol product as an intermediate in cross-aldol reaction.

To probe the origin of high chemoselectivity, reaction was examined with self-aldol product **2.14** under the standard reaction conditions. A condensation product **2.15** was obtained in 18% yield, along with 74% of **2.9c** which indicates that retro-aldol reaction is evident in this case. Likewise, when the reaction was performed by using reverse cross-aldol product **2.16**, corresponding condensation product **2.17** was obtained in 25% yield along with cross-aldol condensation product **2.9c** in 32%. Compound **2.9c** is possibly formed *via* retroaldol reaction, followed by aldol condensation of in-situ formed ketone and enolates. Both the result suggests that the self- and reverse cross-aldol condensation product is suppressed possibly due to involvement of retro-aldol reaction. Rate of the retro-aldol reaction is possibly much faster than corresponding condensation (since there was no any self- or reverse cross-aldol condensation product **2.15** and **2.17**, respectively, identified from the reaction of **2.7c** and **2.8a**).

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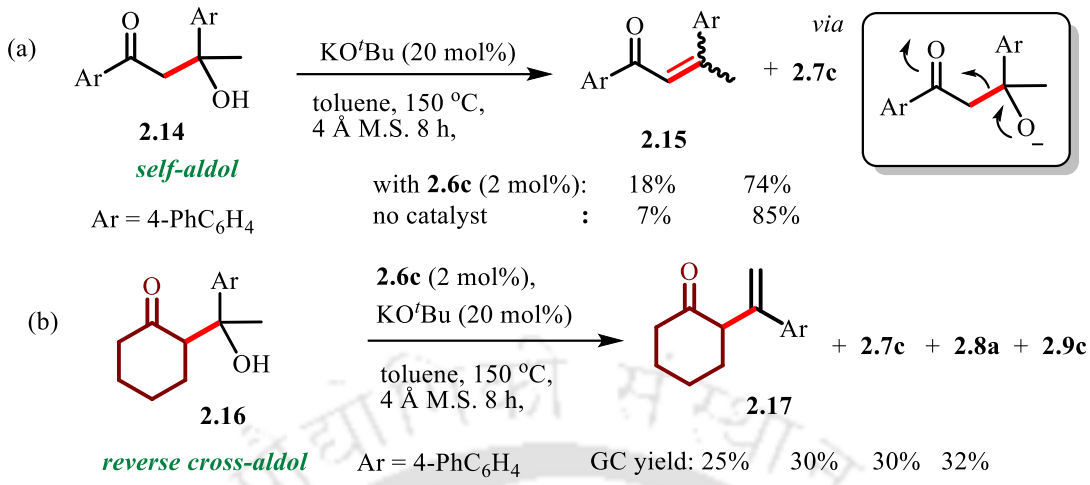
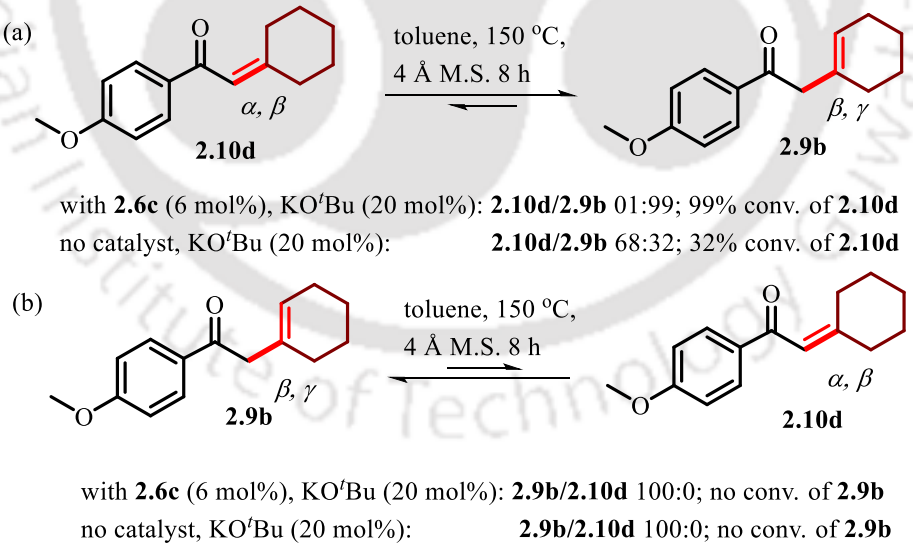


Scheme 2.11. Proof for the origin of high chemoselectivity.

Further, the equilibria between *α*, *β*- and *β*, *γ*- unsaturated ketones were examined by using 4-methoxy substituted enone **2.10d** and **2.9b** (Scheme 2.12a and Scheme 2.12b). It was found that the *α*, *β*-isomer **2.10d** was converted to *β*, *γ*-isomer **2.9b** exclusively under the reaction conditions. On the other hand, no conversion was achieved from **2.9b** to **2.10d**. The result may infer that the *α*, *β*-enone **2.10d** is formed as a kinetic product, which undergoes subsequent isomerization to provide thermodynamically stable *β*, *γ*-isomer **2.9b**.



Scheme 2.12. Equilibria study between *α*, *β*- and *β*, *γ*-unsaturated ketones

Additionally, deuterium-labeling experiments were performed in the cross-coupling reaction to validate the involvement of isomerization. Under the reaction conditions, the reaction of 4-benzyloxyacetophenone **2.7a** with deuterated 4- *tert*-butylcyclohexanone **2.8b**–***d*₄** (Scheme 2.13a)

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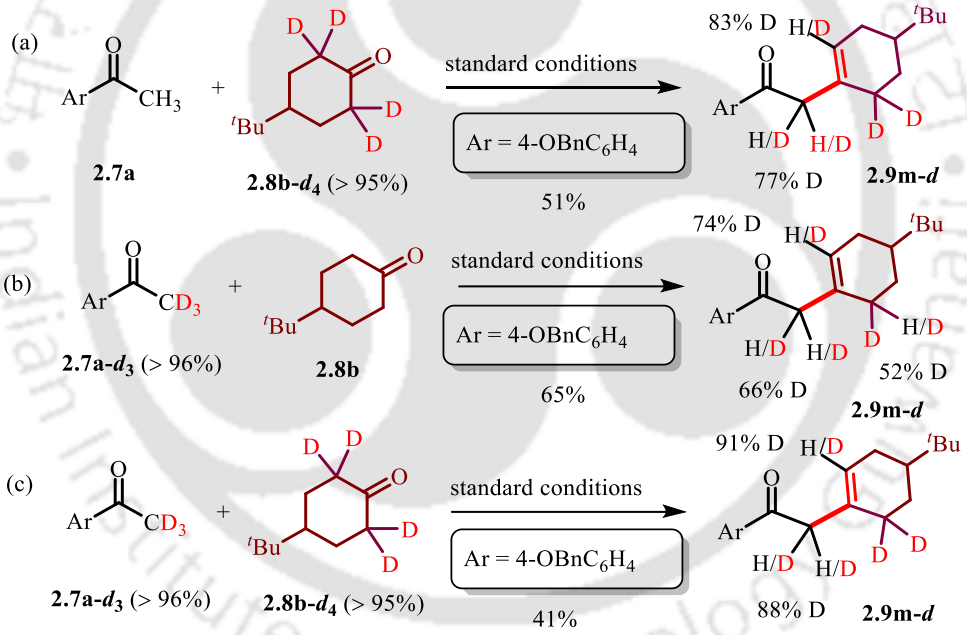
yielded the corresponding deuterated product **2.9m–*d*** in 51% yield and showed 77% D incorporation at the α-position. Likewise, the reaction of deuterated 4-benzyloxy acetophenone **2.7a–*d*$_3$** with 4-*tert*-butylcyclohexanone **2.8b** (Scheme 2.13b) afforded the deuterated product **2.9m–*d*** in 65% yield and exhibited 66% D incorporation at the *α*-position. The higher D incorporation in the first case and the higher H incorporation in the latter case at the *α*-position, suggests that the formation of *β*, *γ*-unsaturated ketone proceeds via the isomerization of the kinetic *α*, *β*- unsaturated ketone product could be the major reaction pathway, presumably with possible involvement of Ru-H/D intermediate in the process. Also, the lack of 100% H/D incorporation reveals that the direct formation of the *β*, *γ*- unsaturated ketone as a minor pathway cannot be ruled out. Further, the reaction of deuterated 4-benzyloxyacetophenone **2.7a–*d*$_3$** and deuterated 4-*tert*-butyl cyclohexanone **2.8b–*d*$_4$** also provided the deuterated product **2.9m–*d*** in 41% yield (Scheme 2.13c). The minor H incorporation at *α*-position and *γ*-position can be attributed to a small amount of base catalysed H/D scrambling of ketones prior to the coupling with the *in-situ* formed H_2O/D_2O.



Scheme 2.13. Deuterium-labeling experiments.

Since the role of both ruthenium catalyst and base are significant in this reaction, experimental support has been given for their importance in catalysis. Study suggests that the reaction proceeds *via* potassium enolate followed by transmetallation. To investigate the mechanistic pathway for the formation of potassium enolate followed by transmetallation, following reaction was designed: a reaction mixture of freshly prepared active Ru(II) species **2.6c'** and aldol acceptor **2.8a** was added to the solution of potassium enolate **2.7c'** (presuming **2.7c'** is formed by the reaction of aldol donor **2.7c** and 1 equiv. of base under the reaction condition) and stirred the reaction mixture for 8 h at

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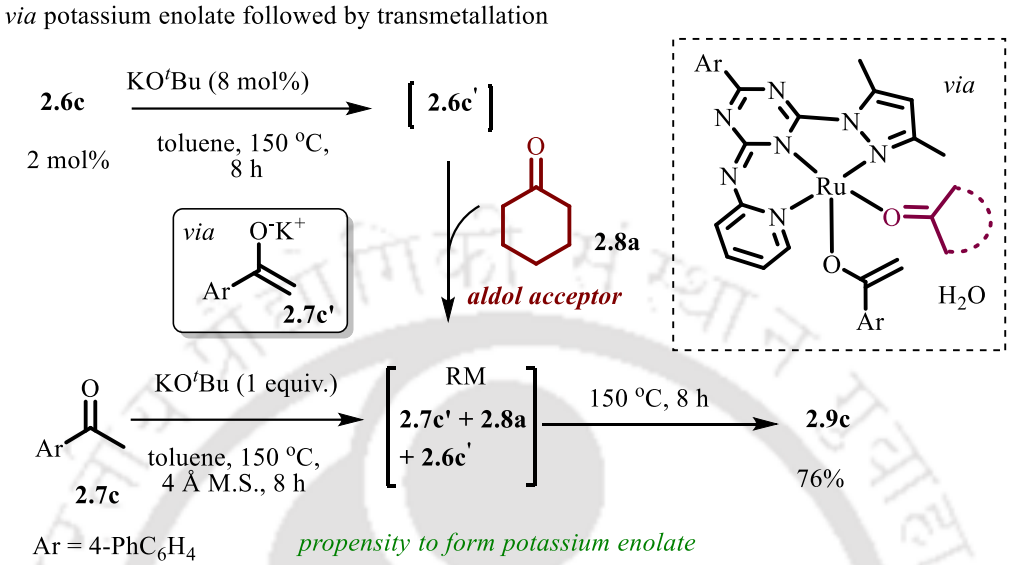
150 °C. A desired condensation product **2.9c** was obtained in 76% yield (Scheme 2.14). The result indicates that there is possible involvement of potassium enolate of aldol donor, followed by transmetallation with Ru-complex.



Scheme 2.14. Mechanistic understanding of Ru-aldol reaction in the presence of base.

The reaction involves three steps (a) aldol product formation (b) dehydration of aldol to unsaturated ketone and then (c) isomerization of *β*-branched unsaturated ketone. To further validate this statement, I have performed theoretical calculations using M06-L level of theory. Acetophenone enol **2.7o'** and cyclohexanone **2.8a** were chosen as the model substrates (Scheme 2.15).

Step I: Cross-coupling reaction of acetophenone **2.7o** and cyclohexanone **2.8a** to provide β-hydroxy ketone **2.18** (Scheme 2.15). The alkenyloxo coordinated ruthenium species **I4** is formed in slightly uphill fashion **(ΔG (I1 → I4)** = -12.8 kcal/mol) *via* an outer sphere MLC pathway of intermediate I3 and proton shuttle type of **TS-1** ($\Delta G^{\ddagger}$ = 14.3 kcal/mol). The complex **I4** then transformed into a ruthenium alkoxo complex **I5** with an energy barrier of 13.2 kcal/mol ($\Delta G^{\ddagger}$ value). Thereafter, the complex **I5** follows at Ru-O bond cleavage and deprotonation of the N-H site in the ligand backbone to generate **I6** in which alkoxide species forms hydrogen bonding with ^{t}BuOH. The process (**I5 → I6**) is thermodynamically downhill with 25.5 kcal/mol. The intermediate **I6** leads to ruthenium *β*-hydroxy ketone-coordinated complex **I8** *via* the intermediate **I7**. Subsequent complex **I8** releases aldol product **18** and *tert*-butoxide in an endothermic fashion with concomitant regeneration of the active catalyst **I1**.

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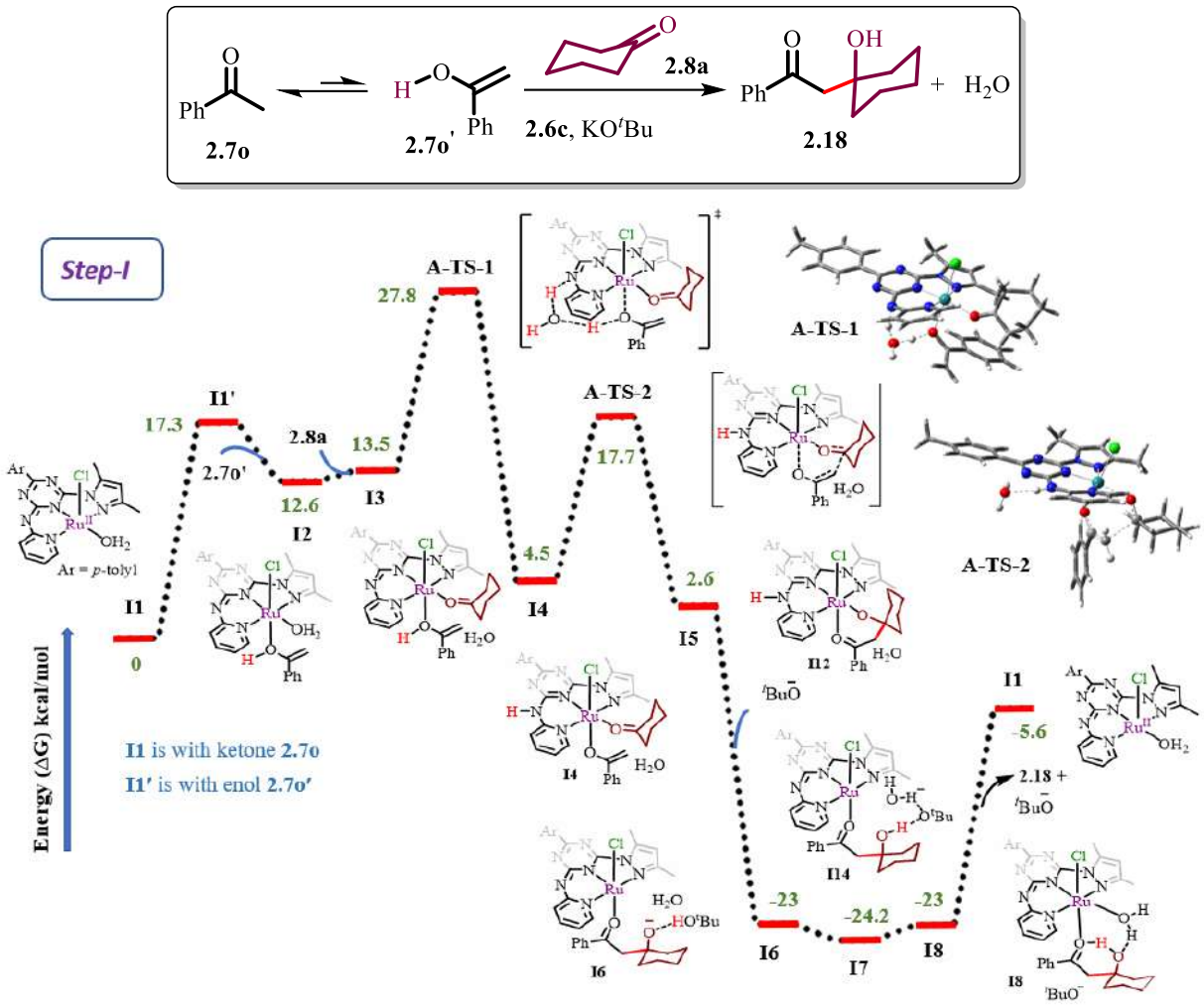

Figure 2.5. Energy profile diagram and proposed reaction pathway for aldol product formation.

Step-II: In general, it is expected that the base catalyzed dehydration of aldol product might give two possible unsaturated ketone such as *α, β*-enone **2.10a** and *β, γ*-enone **2.9w** (Figure 2.6).[9, 26] The *α, β*-enone **2.10a** is formed *via* the E1cb mechanism, which involves the C*α*–H deprotonation of **2.18**, followed by hydroxyl elimination with **D-TS-1** ($\Delta G^{\ddagger}$ = 18.5 kcal/mol). On the other hand, *β, γ*-enone **2.9w** can be formed *via* E2 mechanism, which includes endergonic protonation of **I10** with *t*BuOH to form enolate **I12** (ΔG = 30.9 kcal/mol), followed by hydroxyl elimination *via* **D-TS-2** ($\Delta G^{\ddagger}$ = 18.5 kcal/mol) or otherwise *via* direct **D-TS-3** ($\Delta G^{\ddagger}$ = 37.9 kcal/mol). These results suggested that unsaturated ketone is kinetically favored and *β, γ*-unsaturated ketone is thermodynamically favored.

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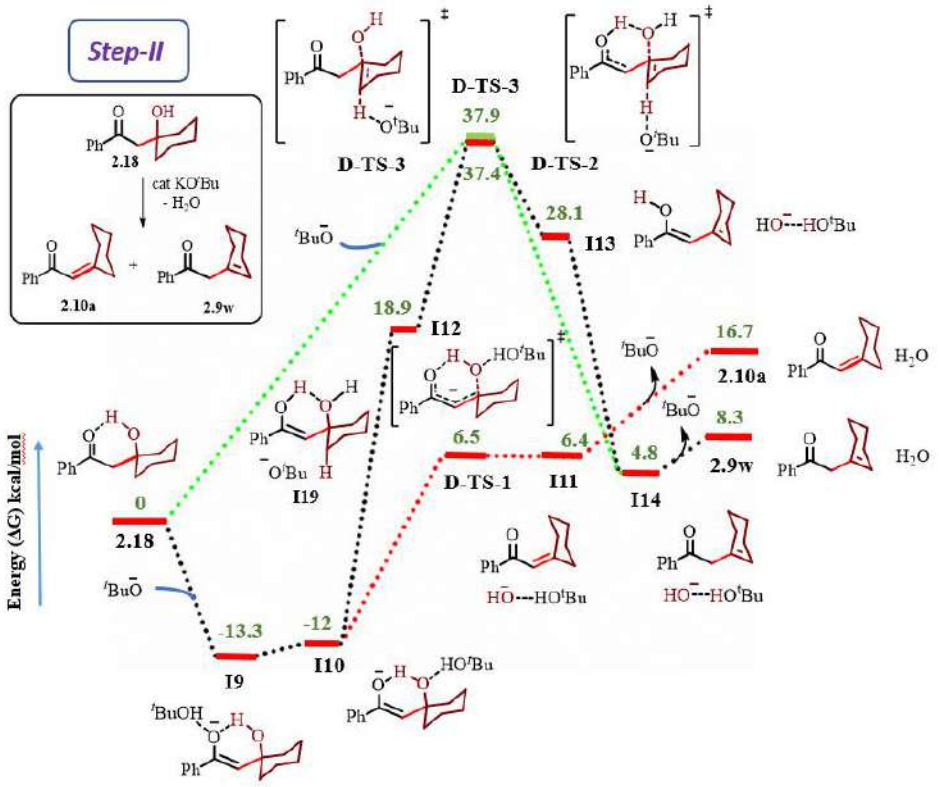
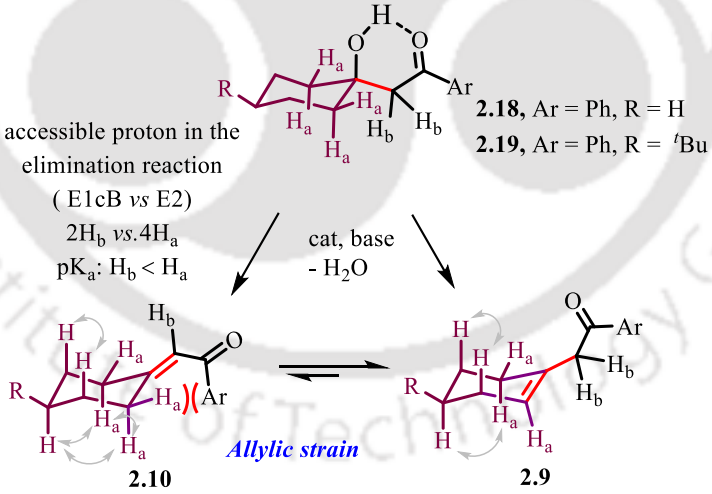


Figure 2.6. Energy profile diagram and proposed pathway for the formation of *β*, *β*-disubstituted *α*, *β*-unsaturated ketone.



Relative energy (150 ^{0}C) of *α*, *β*- and *β*, *γ*-enones isomer (calcd. M06-L)

Ar = Ph, R = H; **2.10a** (**0**) **2.9w** (**-5.4** kcal/mol)

Ar = Ph, R = ^{t}Bu; **2.10d** (**0**) **2.9t** (**-5.2** kcal/mol)

Scheme 2.15. Dehydration of *β*-hydroxy ketone to *α*, *β*- and *β*, *γ*-enones.

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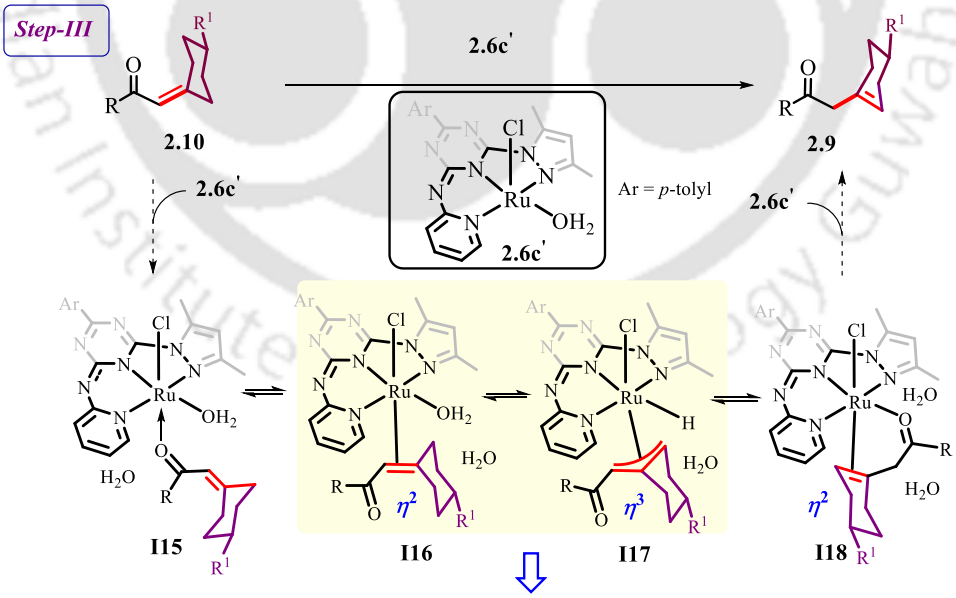
Notably, *α, β*-unsaturated ketone **2.10a** is conjugated one, likely to be less stable with respect to *β, γ*-enone **2.9w**. They might be in equilibrium under the reaction conditions and is predicted in favor of the *β, γ*-isomer because of minimal 1,3-diaxial interactions and relief of ring strain/allylic strain with flattened cyclohexene conformation. The calculated results also in accordance with the *β, γ*-isomer (Scheme 2.15).

Step-III: Since the active catalyst **2.6c'** is able to convert *α, β*-enone **2.10a** to *β, γ*-enone **2.9w** (> 99%) under the reaction condition (in Scheme 2.16), I have examined the pathway for the isomerization of unsaturated ketones with active Ru(II) species **2.6c'** (Scheme 2.16). Calculated data suggests that *α, β*- → *β, γ*- isomerization occurs by the catalyst *via* η^3-allyl ruthenium complex. As expected, the process is thermodynamically favored. [15-18, 27-29] However, the pathway for the η^2-alkene (exo) to η^3-allyl ruthenium complex is kinetically uphill (according to Hammond's postulate). The energy (ΔG) required for **I16-2.10a → I17-2.10a** (27.5 kcal mol^{-1}), **I16-2.10e → I17-2.10e** (23.5 kcal mol^{-1}), **I16-2.10f → I17-2.10f** (23.5 kcal mol^{-1}). The calculated data suggested that electron-withdrawing substituent (e.g., 4-Cl) have favorable impact. The highest ΔG value (27.5 kcal mol^{-1}) was obtained when there is no substituent at the aryl moiety, indicating the process **I16-2.10a** (*α, β*-) → **I17-2.10a** (*β, γ*-) is likely to be energetically unfavorable. On the other hand, 4-*tert*-butyl substituted cyclohexyl ring containing *α, β*-unsaturated ketone **2.10d** proceeds through a relatively lower ΔG value (23.5 kcal mol^{-1}) possibly due to rigid structure of the cyclohexenyl entity. These findings are in line with the experimental results where the substituent-induced switchable olefin isomerization follows by the pincer-ruthenium complex (Scheme 2.16, Figure 2.7).



Relative energy (150 °C) of intermediates in kcal/mol Δ G (**I16→ I17**)

R = Ph, R^1 = H; **I15-2.10a** (0)	**I16-2.10a** (-3.6) 27.5	**I17-2.10a** (23.9)	**I18-2.9w** (-6.9)
R = C_6H_5, R^1 = ^{t}Bu; **I15-2.10e** (0)	**I16-2.10e** (-4.7) 23.5	**I17-2.10e** (18.8)	**I18-2.9t** (-11.3)
R = 4-ClC_6H_4, R^1 = H; **I15-2.10f** (0)	**I16-2.10f** (-4.5) 23.5	**I17-2.10f** (19.0)	**I18-2.9e** (-10.8)

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Scheme 2.16. Isomerization of unsaturated ketones with the catalyst.

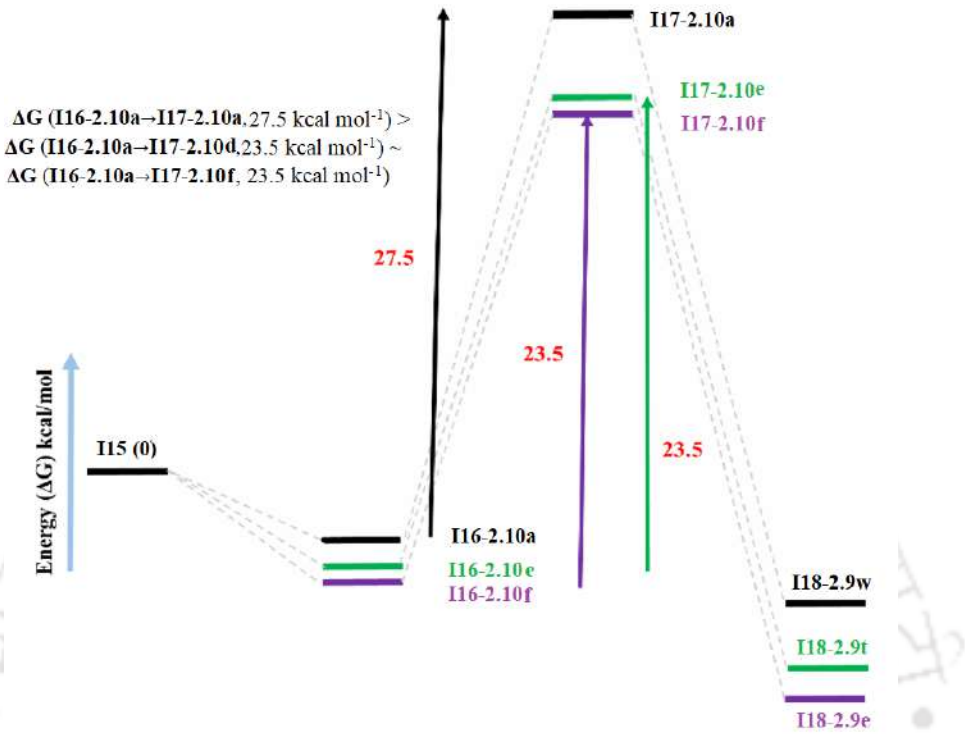

Figure 2.7. Energy profile diagram for the isomerization of *α, β*-unsaturated ketone to *β, γ*-unsaturated ketone with **2.6c'**.

Furthermore, to understand the origin of regioselectivity for the compound **2.9aa-2.9ae** (Scheme 2.17), I have performed theoretical calculations using unsaturated ketone **2.9ae** as a model substrate. Notably, *β*, *γ*-unsaturated ketone **2.9ae** can be further isomerized to give a compound conjugated with a phenyl ring as depicted in Scheme 2.17 (the α, *β*-isomer is denoted as **2.9ae-A**, the *β*, *γ*-isomer is denoted **2.9ae-B**, the *γ*, *δ*-isomer is denoted as **2.9ae-C** and the *δ*, *ω*-isomer is denoted as **2.9ae-D**). The calculated results are in accordance with the stable *δ*, *ω*-isomer **2.9ae-D**. However, when examining the interaction of unsaturated ketone (*β*, *γ*-isomer **2.9ae-B** or *δ*, *ω*-isomer **2.9ae-D**) with catalyst **2.6c'**, a higher adduct stability (~ 11 kcal mol^{-1}) was observed with the *β*, *γ*-isomer **2.9ae-B** compared to *δ*, *ω*-isomer **2.9ae-D**. Hence, a favorable interaction with the bidentate chelating arm of *β*, *γ*-unsaturated ketone may dictate the selectivity.

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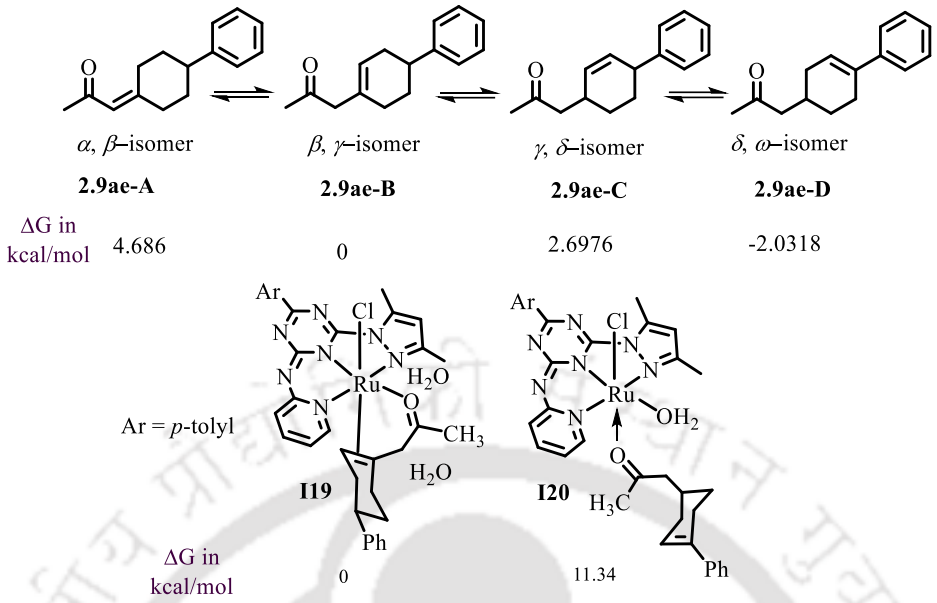

Scheme 2.17. Origin of regioselectivity for *β*, *γ*-unsaturated ketone **2.9ae**.

2.4. Summary

In summary, a ruthenium- and base- catalyzed cross-coupling reaction of ketones to *β*-branched *β*, *γ*-unsaturated ketones were demonstrated. The successful modification of various natural product demonstrates the potential utility of the method. The work has discussed about the origin of regioselectivity between *α*, *β*- and *β*, *γ*-unsaturated ketone by performing various control experiments, deuterium labeling experiments and DFT studies. Also argued about the origin of high chemoselectivity. Further, the reason for the suppression of self- and reverse-cross aldol-condensations is deliberated. This catalytic route gives a unique opportunity to integrate the chemistry of synthetic challenge cross-coupling reaction of ketones and alkene migration reaction into a reaction pot. To the best of our knowledge, this is the first example of catalytic cross-coupling reaction of ketones to *β*- branched *β*, *γ*-enones. The present study provides the precise role of catalyst in the selective C-C bond formation and also in aldol condensation and alkene migration step, otherwise, its propensity of retro-aldol reaction only with base.

2.5. Experimental section

General Information

All the reagents and chemicals were purchased from common commercial suppliers like Sigma Aldrich, Alfa Aesar, Merck, Spectrochem, Avra Synthesis Pvt. Ltd., Finar Chemicals and directly used as received without any further purification unless otherwise mentioned. 4-(phenylethynyl)acetophenone (**2.7f**),[30] 5-cholestenone (**2.7x**), 2-cyclohexylidene-1-(4-methoxyphenyl)ethan-1-one (**2.10d**),[31] 1-([1,1'-biphenyl]-4-yl)-2-(1-hydroxycyclohexyl)ethan-1-one (**2.13**),[32] 3-di([1,1'-biphenyl]-4-yl)-3-hydroxybutan-1-one (**2.14**),[32] 2-(1-([1,1'-biphenyl]-4-

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yl)-1-hydroxyethyl) cyclohexan-1-one (**2.16**),[32] **2.6a**,[8] **2.6c**,[8] **2.6c'**,[8] **2.6c^{Me}** [8] were prepared according to the reported literature. THF and toluene were freshly distilled over sodium–benzophenone before use. ^{1}H, ^{13}C, and ^{19}F NMR spectra of the compounds were measured in $CDCl_3$, DMSO-d_6, CD_3OD as a solvent by using TMS as an internal standard. Chemical shifts, δ (in ppm), are reported relative to TMS δ (^{1}H) 0.0 ppm, δ (^{13}C) 0.0 ppm, which was used as the internal reference. Otherwise, the solvents residual proton resonance and carbon resonance ($CHCl_3$, δ (^{1}H) 7.26 ppm, δ (^{13}C) 77.16 ppm; DMSO-d_6, (^{1}H) 2.50 ppm, δ (^{13}C) 39.52 ppm; CD_3OD, δ (^{1}H) 3.31 ppm, δ (^{13}C) 49 ppm) were also used for calibration. Bruker Avance III 600 and 400 spectrometers were used to record the NMR spectra. Chemical shifts (δ) values were reported in ppm and spin-spin coupling constant (J) were expressed in Hz, and other data were reported as follows: s = singlet, d = doublet, dd = doublet of doublet, dt = doublet of triplet, t = triplet, m = multiplet, q = quartet, sext = sextet, br = broad, and brs = broad singlet. IR spectra were recorded on Perkin Elmer Instrument at normal temperature making KBr pellet grinding the sample with KBr (IR Grade). MS (ESI-HRMS): Mass spectra were recorded on an Agilent Accurate-Mass Q-TOF LC/MS 6520. Merck silica gel 60-120 was used for column chromatography. GC analyses were performed on a Perkinelmer-Clarus 590 GC instrument fitted with Elite-1 column (30 m length, 0.32 mm ID) using the following method: Injection volume: 1 µL, inlet temperature: 280 °C, FID detector temperature: 280 °C, oven temperature: start at 60 °C hold time 1 min, ramp: 12 °C /min, upto 320 °C, Flow rate (carrier): 25 mL/min (N_2). All the catalytic cross coupling of alcohols was carried out under argon atmosphere and in preheated oil baths. Ligand synthesis was performed in oven-dried glassware under argon atmosphere using standard Schlenk techniques. 4 Å M.S. were dried by heating in a furnace oven at 400 ℃ for 6 hours following which it was transferred and stored under argon atmosphere.

A. Synthesis of ligands, and ruthenium complexes

i) Synthesis of ligands (Scheme 2.3)

Synthesis of 2.3b:

Magnesium turnings (1.318 g, 54.22 mmol, 1.5 equiv.) along with catalytic amount of iodine (0.043g, 0.34 mmol, 0.016 equiv.) were taken in two-necked round bottom flask, then 35 mL of dry THF was added and stirred at 60 ℃ for 15 minutes to activate the metal surface. An intense iodine color was observed. This mixture was brought to room temperature and 4-bromo anisole (4.882 g, 23.87 mmol, 1.1 equiv.) was added. Then, heating was applied using a heat gun to initiate the reaction until the iodine color gets disappeared. The solution was refluxed for 2 hours to get the Grignard solution. This solution was then slowly transferred to another two-neck flask containing THF (60 mL) solution of freshly sublimed 2,4,6-trichloro-1,3,5-triazine (4 g, 21.7 mmol, 1 equiv.) at 0 ℃ using cannula technique. The resulting mixture was stirred at 0 ℃ for 8 hours. The reaction was quenched with 2N hydrochloric acid (20 mL) solution followed by dilution

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with water (50 mL). The product was then extracted in ethyl acetate (3×40 mL). The combined organic layer was dried over Na_2SO_4 and solvent was removed under reduced pressure to give yellow solid. It was then washed with cold isopropanol using vacuum filtration technique to discard unreacted cyanuric chloride and obtain light yellow solid. Further purification was done by recrystallization with petroleum ether, and leads to colorless needle shaped crystals of **2.3b** (5.50 g, 90%). This was directly used for subsequent reactions.

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.45 (d, J = 9 Hz, 2H), 6.99 (d, J = 9 Hz, 2H), 3.91 (s, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 174.3, 171.7, 165.3, 132.4, 125.1, 114.6, 55.8. Spectral data is in accordance with the literature.[33]

Synthesis of 2.4b:

Sodium hydride (60% suspension in paraffin oil, 0.315 g, 7.88 mmol, 1.5 equiv.) was taken in a dry two neck flask and washed with dry petroleum ether to remove the paraffin oil. 3,5-dimethylpyrazole (0.505 g, 5.26 mmol, 1 equiv.) was added to the stirring suspension of sodium hydride in dry THF (20 mL) and then refluxed for 2 hours for complete deprotonation. The solution was brought to room temperature and then placed on an ice bath. This solution was added portion-wise to a separate two neck flask containing a solution of **2.3b** (1.34 g, 5.26 mmol, 1 equiv.) in THF (20 mL) at 0 ℃. After complete addition it was left to stir at 0 ℃ for 2 hours followed by room temperature stirring for another 8 hours. Completion of reaction was monitored by TLC with pet-ether and ethyl acetate (v/v = 4:1, R_f = 0.5). The reaction mixture was quenched with water and extracted in ethyl acetate 3 × 20 mL. Solvent was removed under reduced pressure to give white powder of **2.4b** (1.40 g, 85%).

^{1}H NMR (600 MHz, $CDCl_3$): δ 8.49 – 8.47 (m, 2H), 7.02 – 7.01 (m, 2H), 6.13 (s, 1H), 3.91 (s, 3H), 2.82 (s, 3H), 2.37 (s, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 173.7, 172.3, 164.5, 163.4, 154.2, 144.7, 131.8, 114.3, 112.6, 55.6, 16.4, 14.1. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{15}H_{15}ClN_5O$ 316.0960; found: 316.0961.

Synthesis of 2.5b:

Sodium hydride (60% suspension in paraffin oil, 0.256 g, 6.4 mmol, 1.5 equiv.) was taken in a dry two neck flask and washed with dry petroleum ether to remove the paraffin oil. 2-aminopyridine (0.401 g, 4.27 mmol, 1 equiv.) was added to the stirred suspension of sodium hydride in THF (10 mL) and refluxed over night for the complete deprotonation the 2-aminopyridine. Afterwards the reaction mixture was brought to room temperature. A solution of **2.4b** (1.34 g, 4.27 mmol, 1 equiv.) in dry THF (20 mL) was added dropwise to the reaction mixture. The resultant solution was refluxed for 8 hours. The reaction mixture was then quenched with water and extracted three times

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with ethyl acetate (3 × 20 mL). Solvent was removed under reduced pressure to give pale yellow powder of **2.5b** (1.32g, 83%).

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.59 (d, J = 8.0 Hz, 1H), 8.51 (brs, 1H), 8.46 (d, J = 8.5 Hz, 2H), 8.39 (d, J = 4.5 Hz, 1H), 7.81 (t, J = 8.5 Hz, 1H), 7.03 (d, J = 8.5 Hz, 3H), 6.10 (s, 1H), 3.91 (s, 3H), 2.84 (s, 3H), 2.37 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 172.6, 164.8, 163.65, 163.58, 152.8, 151.9, 148.4, 144.3, 138.2, 131.1, 128.3, 119.0, 114.3, 114.1, 111.6, 55.6, 16.5, 14.2. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{20}H_{19}Cl_3N_7O$ 374.1724; found: 374.1737.

ii) Synthesis of ruthenium complexes (Scheme 2.4)

Synthesis of 2.6b:

A mixture of $RuCl_3$•xH_2O (0.184 g, 0.72 mmol, 1 equiv.) and **2.5b** (0.54 g, 0.72 mmol, 1 equiv.) was taken in a round bottom flask equipped with stirring bar. Methanol (5 mL) was added to the mixture and refluxed for 12 hours with continuous stirring. It was then brought to ambient temperature. The resulting mixture was filtered and the filtrate was collected and removed the solvent in vacuum to afford dark brown solid of **2.6b** (0.335 g, 80%). The complex was stable in air and moisture. HRMS (ESI) *m/z*: $[M–Cl]^+$ calculated for $C_{20}H_{19}Cl_2N_7ORu$ 545.0072; found: 545.0087.

B. General procedure for synthesis of *β*-Branched *β, γ*-unsaturated ketones (GP-1)

In a pyrex tube a mixture of ketone (1 mmol, 1 equiv.), cyclohexanone (1 mmol, 1 equiv.), **2.6c** (2 mol%), KO^{t}Bu (20 mol%), 4 Å molecular sieves and dry toluene (2 mL) were taken. The reaction tube was properly closed and placed in a preheated oil bath at 150 ℃ with continuous stirring for 8 h. The resulting mixture was then passed through a bed of celite, the filtrate was collected and concentrated under reduced pressure. The crude reaction mixture was purified by column chromatography over silica gel using petroleum ether or ethyl acetate/ petroleum ether mixture as an eluent.

Gram-scale synthesis of 2.9a (Scheme 2.5): A mixture of **2.7a** (0.5 gm, 2.2 mmol, 1 equiv.), **2.8a** (2.2 mmol, 1equiv.), **2.6c** (2 mol%), KO^{t}Bu (20 mol%), 4 Å molecular sieves and toluene (8 mL) was added into a pyrex tube (100 mL) equipped with stirring bar. The reaction tube was properly closed and placed in a pre-heated oil bath at 150 ℃ with continuous stirring for 8 hours. The resulting mixture was then passed through a bed of celite, the filtrate was collected and concentrated under reduced pressure. The crude reaction mixture was purified by column chromatography over silica gel using petroleum ether or ethyl acetate/ petroleum ether mixture as an eluent to get analytically pure product 0.483 g (75% yield).

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C. General procedure for synthesis of *β*-branched *α*, *β*-unsaturated ketones using acyclic alkyl ketones (GP-2)

In a pyrex tube a mixture of aromatic ketone (1 mmol, 1 equiv.), acyclic alkyl ketone (6 mmol, 6 equiv.), **2.6c** (2 mol%), KO^{t}Bu (20 mol%), 4 Å molecular sieves and dry toluene (2 mL) were taken. The reaction tube was properly closed and placed in a preheated oil bath at 150 °C with continuous stirring for 8 h. The resulting mixture was then passed through a bed of celite, the filtrate was collected and concentrated under reduced pressure. The crude reaction mixture was purified by column chromatography over silica gel using petroleum ether or ethyl acetate/ petroleum ether mixture as an eluent.

D. Mechanistic studies

i) Mercury drop test (Scheme 2.8)

To establish the homogeneity of **2.6c** in cross-aldol reaction of ketones, mercury drop experiment was carried out.

Catalytic cross-aldol reaction of aromatic and aliphatic ketones: In this test, the pyrex tube was charged with 1 mmol of **2.7c** (196 mg), 1 mmol of **2.8a** (98 mg), 0.5 mmol of mercury (100 mg), 20 mol% of KO^{t}Bu (22 mg) and 2 mol% of complex **2.6c** (12 mg). To this reaction mixture, 4 Å molecular sieves and 2 mL of dry toluene was added and heated at 150 ºC for 8 h. The product **2.9c** was obtained in 76% of yield (152 mg), confirmed the homogenous behavior of the catalyst.

ii) The influence of the NH functionality in ruthenium complex (Scheme 2.9)

Experimental procedure: A mixture of **2.7c** (196 mg, 1 mmol, 1 equiv.), **2.8a** (98 mg, 1 mmol, 1 equiv.), **2.6c^{Me}** (2 mol%), KO^{t}Bu (20 mol%), 4 Å molecular sieves and dry toluene (2 mL) was added into a pyrex tube (25 mL) equipped with stirring bar. The reaction tube was properly closed and placed in a preheated oil bath at 150 ºC with continuous stirring for 8 hours. The resulting mixture was then passed through a bed of celite, the filtrate was collected and concentrated under reduced pressure. Analytically pure product (91 mg, 33%) was obtained by column chromatography over silica gel using ethyl acetate / petroleum ether mixture as an eluent.

iii) Proof for the aldol intermediate in cross-aldol reactions of ketones (Scheme 2.10)

a) **Formation of *β, γ*-unsaturated ketone from aldol product in presence of catalyst:** The schlenk tube was loaded with **2.13** (0.5 mmol, 1 equiv.), KO^{t}Bu (11 mg, 0.1 mmol, 0.2 equiv.), **2.6c** (6 mg, 0.01 mmol, 0.02 equiv.), 4 Å molecular sieves and dry toluene (1 mL) and the reaction mixture was heated at 150 °C for 8 h. The product **2.9c** was isolated as white solid (79% yield).

b) **Formation of *α, β*-unsaturated ketone from aldol product in absence of catalyst:** The schlenk tube was loaded with **2.13** (0.5 mmol, 1 equiv.), KO^{t}Bu (11 mg, 0.1 mmol, 0.2 equiv.), 4 Å molecular sieves and dry toluene (1 mL) and the reaction mixture was heated at 150 °C

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for 8 h. The product **2.9c** was isolated as white solid in 23% of yield along with the formation of corresponding ketone **2.7c** with 62% yield.

iv) Proof for the origin of high chemoselectivity (Scheme 2.11)

Using self-aldol 2.14 under the reaction condition: The schlenk tube was loaded with self-aldol product **2.14** (0.5 mmol, 1 equiv.), KO^{t}Bu (11 mg, 0.1 mmol, 0.2 equiv.), **2.6c** (6 mg, 0.01 mmol, 0.02 equiv.), 4 Å molecular sieves and dry toluene (1 mL) and the reaction mixture was heated at 150 °C for 8 h. After the standard aqueous work up, ketone **2.7c** was isolated in 74% of yield along with the formation of self-aldol condensation product **2.15**, 18% yield. In the absence of catalyst, ketone **2.7c** was attained in 85% of yield and product **2.15** was obtained only in 7% yield.

Using reverse cross-aldol product 2.16 under the reaction condition: The schlenk tube was loaded with reverse cross-aldol product **2.16** (120 mg, 0.5 mmol, 1 equiv.), KO^{t}Bu (11 mg, 0.1 mmol, 0.2 equiv.), **2.6c** (6 mg, 0.01 mmol, 0.02 equiv.), 4 Å molecular sieves and dry toluene (1 mL) and the reaction mixture was heated at 150 °C for 8 h. After the standard aqueous work up, condensation product **2.17** (25%), *β, γ*-unsaturated ketone **2.9c** (32%), ketone **2.7c** (30%) and cyclohexanone **2.8a** (30%) was obtained in the GC. Overall conversion of **2.16** was attained in 87%.

v) The equilibria between *β*-branched *α, β*- and *β, γ*- unsaturated ketones (Scheme 2.12)

From pure *α, β*- isomer 2.10d to *β, γ*-isomer 2.9b (Scheme 2.12a):

a) **Treatment of pure *α, β*-isomer 2.10d in the presence of catalyst with base (20 mol%):** A reaction tube (25 mL) was equipped with a stir bar, **2.6c** (0.02 mmol), KO^{t}Bu (0.2 mmol), **2.10d** (1 mmol, 1 equiv.), 4 Å molecular sieves and toluene (1.5 mL). The flask was closed and the solution was stirred at 150 °C (oil bath temperature) for 4 h and 8 h, respectively. The reaction mixture was then monitored using GC analysis. It suggested that the ratio of *α, β*- isomer (**2.10d**): *β, γ*-isomer (**2.9b**) is 01:99 after 8 h. Notably, there was no any other isomers/products.

b) **Treatment of pure *α, β*-isomer 2.10d in the absence of catalyst with base (20 mol%):** A reaction tube (25 mL) was equipped with a stir bar, KO^{t}Bu (0.2 mmol), **2.10d** (1 mmol, 1 equiv.), 4 Å molecular sieves and toluene (1.5 mL). The flask was closed and the solution was stirred at 150 °C (oil bath temperature) for 8 h. The reaction was monitored using GC analysis. It suggested that ratio of *α, β*- isomer (**2.10d**): *β, γ*-isomer (**2.9b**) is 68:32 after 8 h. Notably, there was no any other products. The result suggested that there is ~32% conversion of **2.10d** to **2.9b** in the absence of catalyst.

From pure *β, γ*-isomer 2.9b to *α, β*- isomer 2.10d (Scheme 2.12b)

a) **Treatment of pure *β, γ*-isomer 2.9b in the presence of catalyst:** A reaction tube (25 mL) was equipped with a stir bar, **2.6c** (0.02 mmol), KO^{t}Bu (0.2 mmol), **2.9b** (1 mmol, 1 equiv.), 4 Å molecular sieves and toluene (1.5 mL). The flask was closed and the solution was stirred

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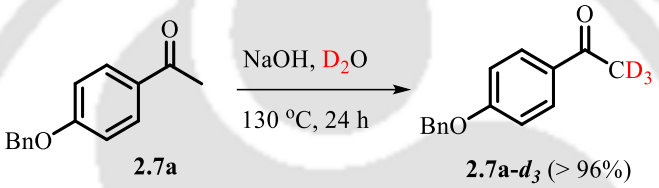
at 150 °C (oil bath temperature) for 8 h. The reaction mixture was then monitored using GC and NMR analysis. It suggested that the ratio of *β, γ*-isomer (**2.9b**) / *α, β*- isomer (**2.10d**) is 100:0 after 8 h; indicating no conversion of **2.9b** to **2.10d**. Notably, there was no any other isomers/products.

b) **Treatment of pure *β, γ*-isomer in the absence of catalyst:** A reaction tube (25 mL) was equipped with a stir bar, KO^{t}Bu (0.2 mmol), **2.9b** (1 mmol, 1equiv.), 4 Å molecular sieves and toluene (1.5 mL). The flask was closed and the solution was stirred at 150 °C (oil bath temperature) for 8 h. The reaction was monitored using GC and NMR analysis. It suggested that there is no formation of *α, β*-isomer **2.10d**.

vi) Deuterium-labeling experiments

Synthesis of deuterated 4-benzyloxyacetophenone 2.7a-*d*$_3$:



2.7a **2.7a-*d*$_3$** (> 96%)

Scheme 2.18. Synthesis of **2.7a-*d*$_3$.**

Procedure: In a pyrex tube degassed D_2O (99.9% D, 3 mL) was taken and to it under nitrogen flow a mixture of 4-benzyloxyacetophenone **2.7a** (452 mg, 2 mmol) and NaOH (40 mg, 1.0 mmol) was added. The reaction tube was properly closed and placed in a preheated oil bath at 130 °C with continuous stirring for 24 hours under nitrogen atmosphere. Upon completion of the reaction, the reaction mixture was extracted with chloroform (5 mL × 3) and dried over Na_2SO_4. The solvent was evaporated under vacuum to afford the desired product **2.7a-*d*$_3$** (95%, 430 mg) with 96% D as a light brown solid.

^{1}H NMR (600 MHz, $CDCl_3$): *δ* 7.93 – 7.91 (m, 2H), 7.43 – 7.39 (m Hz, 4H), 7.35 – 7.32 (m, 2H), 7.00 (d, J = 8.7 Hz, 2H), 5.11 (s, 2H), 2.50 (brs, 0.12 H). ^{13}C{1H} NMR (151 MHz, $CDCl_3$): *δ* 197.1, 162.7, 136.3, 130.7, 130.6, 128.8, 128.6, 128.3, 127.6, 127.0, 114.6, 70.2. 25.8 (sept, JC-D = 19.2 Hz)

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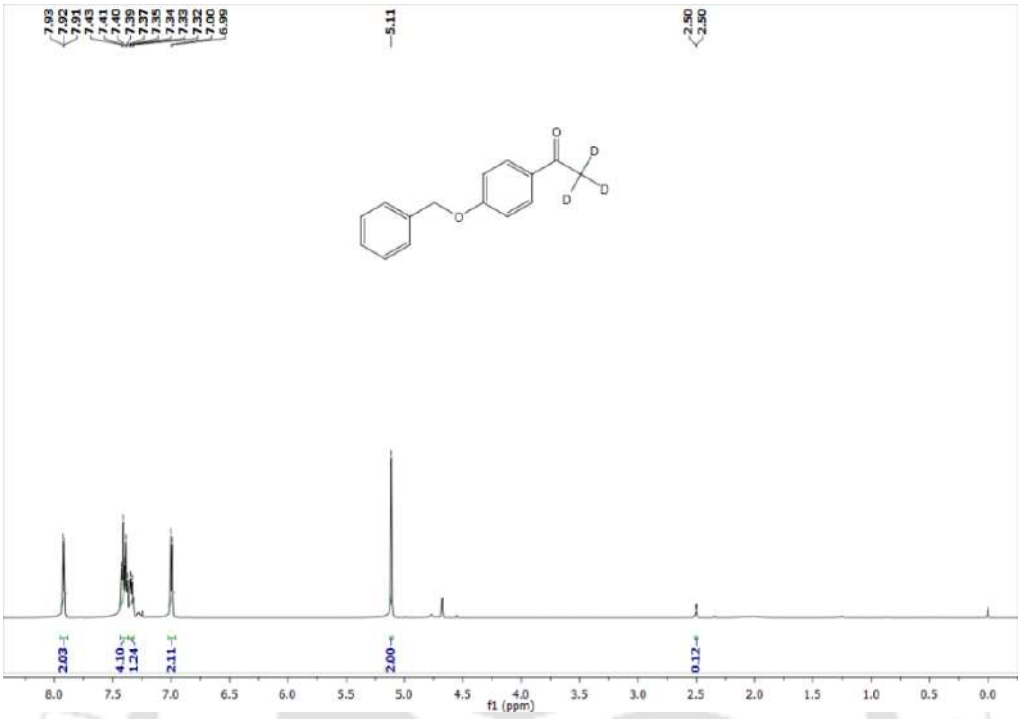

Figure 2.8. ^{1}H NMR spectrum of **2.7a-*d*$_3$** ($CDCl_3$, 600 MHz, 298 K)

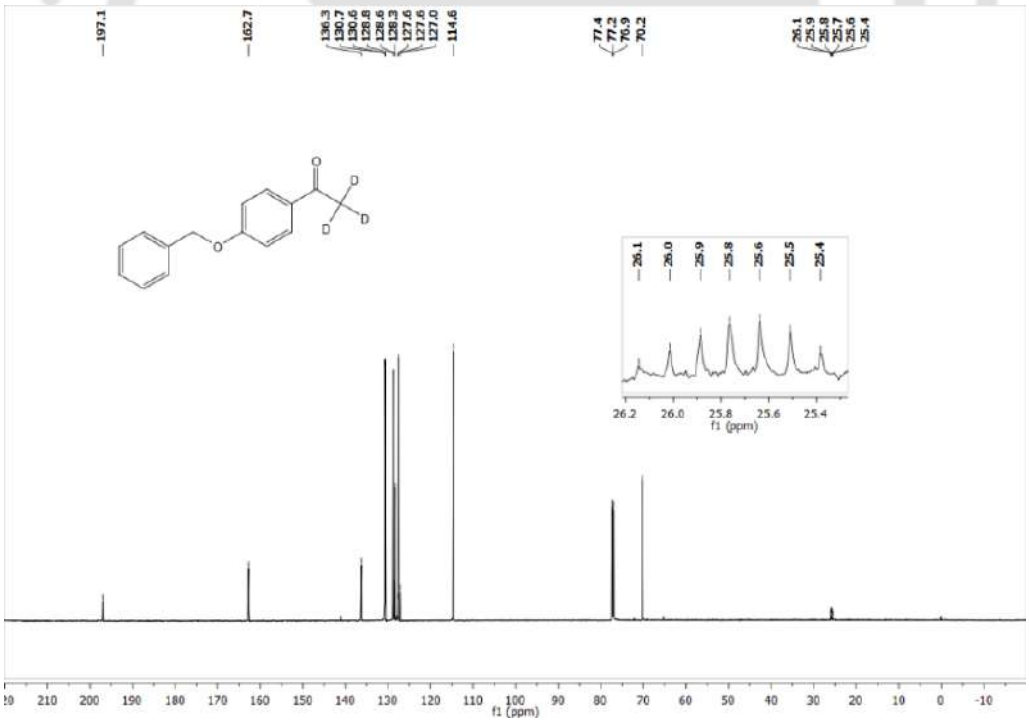

Figure 2.9. $^{13}C\{^{1}H\}$ NMR spectrum of **2.7a-*d*$_3$** ($CDCl_3$, 151 MHz, 298 K)

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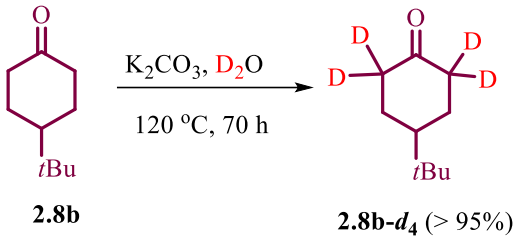
Synthesis of 4-*tert*-butylcyclohexanone 2.8b-d_4



Scheme 2.19. Synthesis of **2.8b-d_4**

Procedure: In a pyrex tube degassed D_2O (99.9% D, 4 mL) was taken and to it under nitrogen flow of 4-*tert*-butylcyclohexanone **2.8b** (386 mg, 2.5 mmol) and K_2CO_3 (24 mg, 0.18 mmol) was added. The reaction tube was properly closed and placed in a preheated oil bath at 120 °C with continuous stirring for 70 hours under nitrogen atmosphere. Upon completion of the reaction, the reaction mixture was extracted with chloroform (5 mL × 3) and dried over Na_2SO_4.The solvent was evaporated under vacuum to afford the desired product **2.8b-d_4** (90%, 321 mg) with 95% D as a light brown solid.

^{1}H NMR (600 MHz, $CDCl_3$): δ 2.32– 2.31 (m, 0.10 H), 2.26 – 2.24 (m, 0.10 H), 2.04 (d, J = 12.4 Hz, 2H), 1.46 – 1.37 (m, 3H), 0.88 (s, 9H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): 213.0, 46.7, 41.2 – 40.5 (m), 32.5, 27. 7, 27.6.

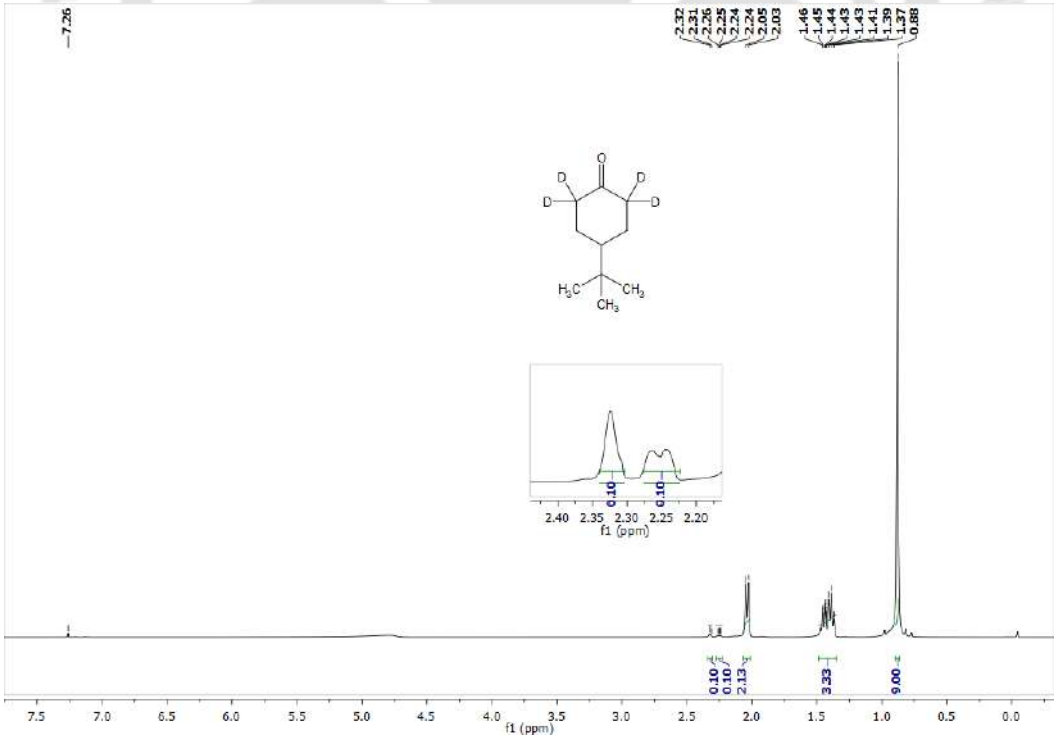


Figure 2.10. ^{1}H NMR spectrum of **2.8b-d_4** ($CDCl_3$, 600 MHz, 298 K)

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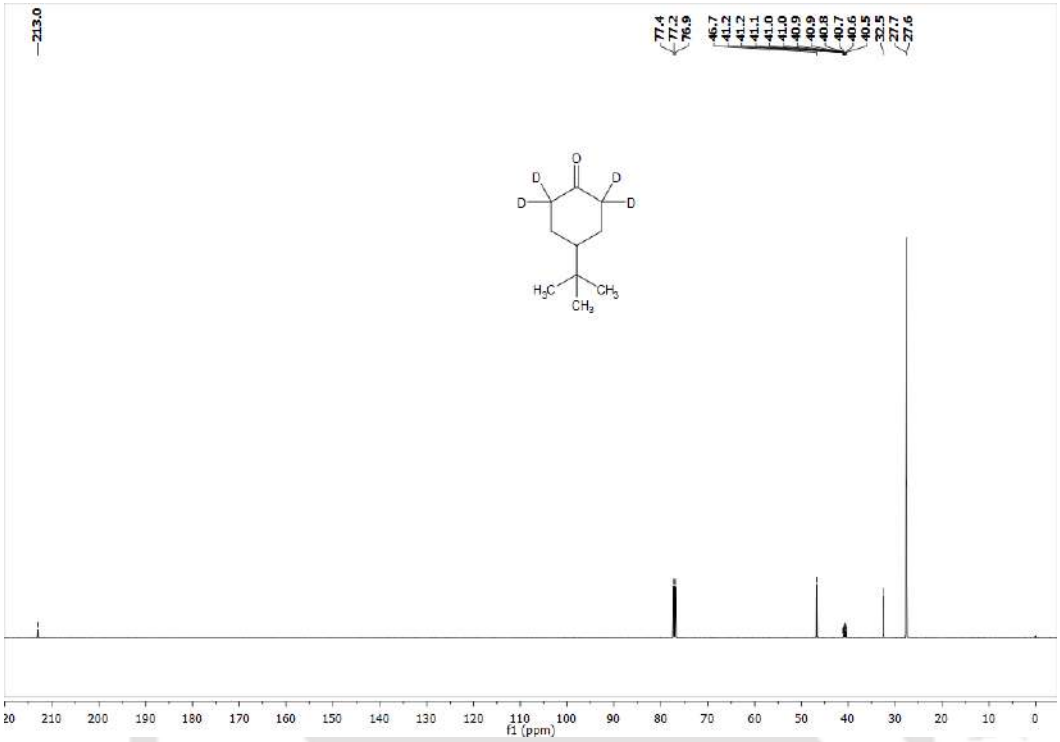

Figure 2.11. $^{13}C\{^{1}H\}$ NMR spectrum of **2.8b-*d*$_4$** ($CDCl_3$, 151 MHz, 298 K)

Synthesis of deuterated 2.9m-*d* using the reaction of 2.7a and 2.8b-*d*$_4$ (Scheme 2.13a)

Procedure: In a pyrex tube a mixture of **2.7a** (115 mg, 0.5 mmol, 1 equiv.), **2.8b-*d*$_4$** (77 mg, 0.5 mmol, 1equiv.), **2.6c** (2 mol%), KO^{t}Bu (20 mol%), 4 Å molecular sieves and dry toluene (2 mL) were taken. The reaction tube was properly closed and placed in a preheated oil bath at 150 °C with continuous stirring for 8 h. The resulting mixture was then passed through a bed of celite, the filtrate was collected and concentrated under reduced pressure. The crude reaction mixture was checked the ^1H NMR and followed by purified by column chromatography over silica gel using petroleum ether or ethyl acetate/ petroleum ether mixture as an eluent to get analytically pure product 92 mg (51% yield).

Based on ^1H-^1H COSY and HSQC NMR, the Ha, H_b, H_c, H_d H_e and H_f are assigned below;

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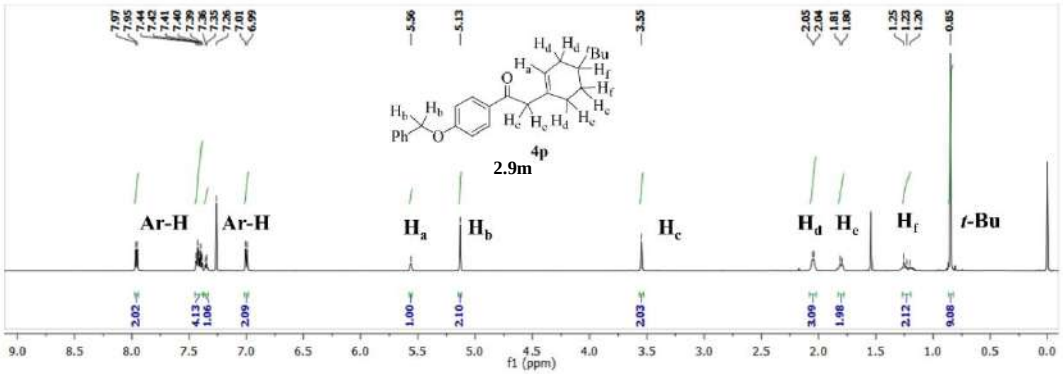

Figure 2.12. ^{1}H NMR spectra of compound **2.9m**

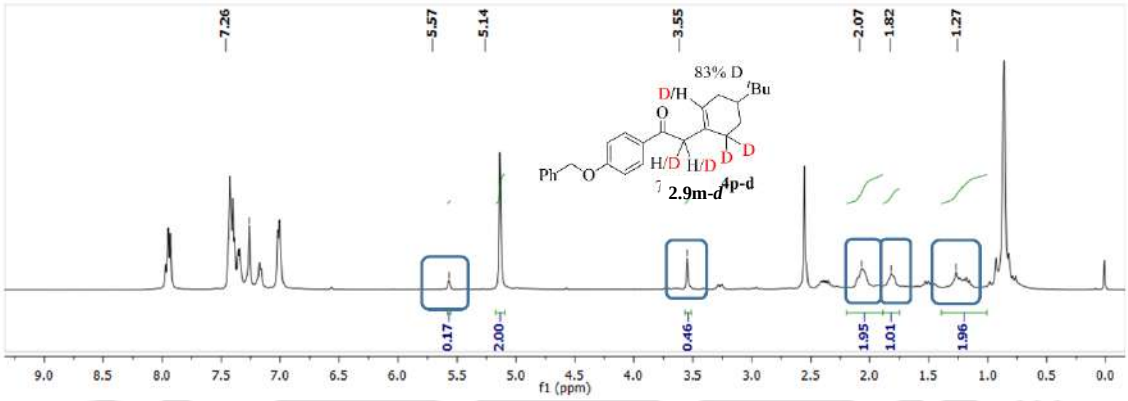

Figure 2.13. Crude ^{1}H NMR spectra of **2.9m-*d*** ($CDCl_3$, 600 MHz, 298 K)

Synthesis of deuterated 2.9m-*d* using the reaction of 2.7a-d_3 and 2.8a (Scheme 2.13b)

Procedure: In a pyrex tube a mixture of **2.7a-d_3** (115 mg, 0.5 mmol, 1 equiv.), **2.8b** (77 mg, 0.5 mmol, 1equiv), **2.6c** (2 mol%), KO^{t}Bu (20 mol%), 4 Å molecular sieves and dry toluene (2 mL) were taken. The reaction tube was properly closed and placed in a preheated oil bath at 150 °C with continuous stirring for 8 h. The resulting mixture was then passed through a bed of celite, the filtrate was collected and concentrated under reduced pressure. The crude reaction mixture was checked the ^{1}H NMR in $CDCl_3$ and followed by purified by column chromatography over silica gel using petroleum ether or ethyl acetate/ petroleum ether mixture as an eluent to get analytically pure product 118 mg (65% yield).

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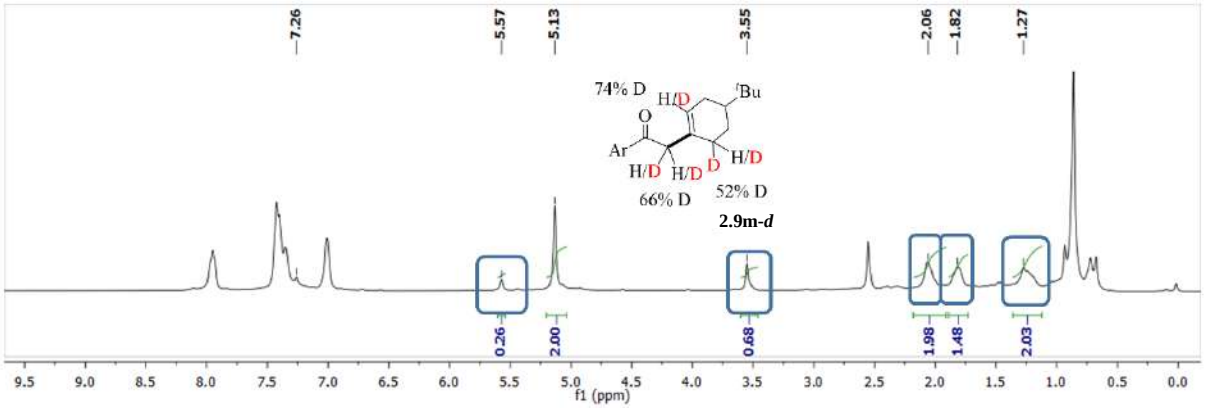

Figure 2.14. Crude ^{1}H NMR spectra of **2.9m-*d*** ($CDCl_3$, 600 MHz, 298 K)

Synthesis of deuterated of 2.9m-*d* using the reaction of 2.7a-d_3 and 2.8b-d_4 (Scheme 2.13c)

Procedure: In a pyrex tube a mixture of **2.7a-d_3** (115 mg, 0.5 mmol, 1 equiv.), **2.8b-d_4** (77 mg, 0.5 mmol, 1equiv), **2.6c** (2 mol%), KO^{t}Bu (20 mol%), 4 Å molecular sieves and dry toluene (2 mL) were taken. The reaction tube was properly closed and placed in a preheated oil bath at 150 °C with continuous stirring for 8 h. The resulting mixture was then passed through a bed of celite, the filtrate was collected and concentrated under reduced pressure. The crude reaction mixture was checked the ^{1}H NMR in $CDCl_3$ and followed by purified by column chromatography over silica gel using petroleum ether or ethyl acetate/ petroleum ether mixture as an eluent to get analytically pure product 74 mg (41% yield).

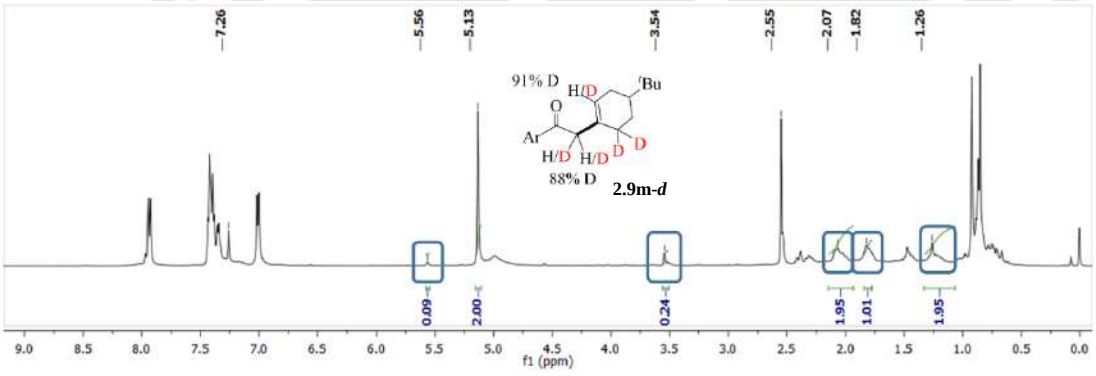

Figure 2.15. Crude ^{1}H NMR spectra of **2.9m-*d*** ($CDCl_3$, 600 MHz, 298 K)

vii) Mechanistic understanding of Ru-aldol reaction in the presence of base (Scheme 2.14)

Since the role of ruthenium catalyst and base is significant in this reaction, experimental support has been given for their importance in catalysis. Study suggests that the reaction proceeds *via*

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potassium enolate followed by transmetallation and alternatively -OH bond addition of enol to the active Ru complex, followed by aromatization/ dearomatization strategy.

For the formation of potassium enolate followed by transmetallation: At first active Ru(II) species **2.6c'** was prepared by using 2 mol% of **2.6c** (11 mg, 0.02 mmol) and 8 mol% of KO^{t}Bu (9 mg, 0.08 mmol) in toluene (2 ml) at 150 ℃ for 8 h. To the reaction mixture aldol acceptor **2.8a** (1 mmol), and 4 Å molecular sieves was added and subsequently added a freshly prepared solution of potassium enolate **2.6c'** [presuming **2.6c'** is formed by the reaction of aldol donor **2.7c** (1 mmol) and base (112 mg, 1 mmol)] under the reaction condition. Then stirred the reaction mixture for 8 h at 150 ℃. A desired cross-coupled condensation product **2.9c** was obtained in 76% yield.

E. Crystallographic data

Crystallographic data of 2.6b:

Single crystals of compound **2.6b** suitable for X-ray diffraction were obtained by slow evaporation of the saturated solution of the complex in CH_3OH at room temperature. X-ray crystallographic data were collected using Bruker D8 QUEST diffractometer. Data refinement and cell reduction were carried out by *APEX4*. Structures were solved by direct methods using Olex2 v1.5 and refined by a full-matrix least-squares method using Olex2 v1.5. All of the non-H atoms were refined anisotropically. The ORTEP diagram was obtained with ORTEP3 software with 50% thermal ellipsoid (Figure 2.2). The crystallographic parameters and refinement data were listed in Table 2.3.

Table 2.3. Crystal data and structure refinement for **2.6b**

Identification code	PA_Ru_NNN
CCDC	2361370
Empirical formula	$C_{40}H_{40}Cl_6N_{14}O_3Ru_2$
Formula weight	1179.70
Temperature/K	298.00
Crystal system	triclinic
Space group	P-1
a/Å	10.8790(12)
b/Å	15.1173(16)
c/Å	15.4491(16)

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α/°	96.955(4)
β/°	105.480(4)
γ/°	108.497(4)
Volume/Å3	2262.5(4)
Z	2
ρcalcg/cm3	1.732
μ/mm-1	1.079
F(000)	1184.0
Crystal size/mm3	0.41 × 0.37 × 0.33
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	2.808 to 50.13
Index ranges	$-12 \leq h \leq 12$, $-17 \leq k \leq 17$, $-18 \leq l \leq 18$
Reflections collected	43815
Independent reflections	7969 [R_{int} = 0.0505, R_{sigma} = 0.0490]
Data/restraints/parameters	7969/0/595
Goodness-of-fit on F2	1.032
Final R indexes [I>=2σ (I)]	R1 = 0.0510, wR2 = 0.1258
Final R indexes [all data]	R1 = 0.0748, wR2 = 0.1341
Largest diff. peak/hole / e Å-3	2.25/-0.67

Crystallographic data of 2.9s

Single crystals of compound **2.9s** suitable for X-ray diffraction were obtained by slow evaporation of the saturated solution of the complex in CH_3CN at room temperature using slow evaporation technique. X-ray crystallographic data were collected using Bruker D8 QUEST diffractometer. Data refinement and cell reduction were carried out by *APEX4*. Structures were solved by direct methods using Olex2 1.5 and refined by a full-matrix least-squares method using Olex2 1.5. All of the non-H atoms were refined anisotropically. The ORTEP diagram was obtained with ORTEP3 software with 50% thermal ellipsoid (see below, Figure 2.16). The crystallographic parameters and refinement data were listed in Table 2.4.

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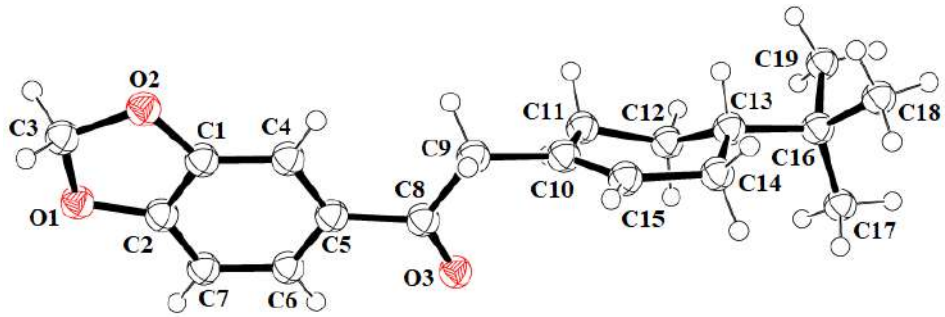

Figure 2.16: Molecular structure of compound **2.9s** (thermal ellipsoid 50% probability level). Selected Bond lengths (in Å): C(10)-C(15) 1.323(2), C(10)-C(11) 1.484, C(11)-C(12) 1.499, C(8)-O(3) 1.214, C(3)-O(2) 1.421, C(3)-O(1) 1.413, C(1)-O(2) 1.367, C(1)-O(1) 1.362, Selected Bond Angles (in °): C(15)-C(10)-C(11) 120.71, C(10)-C(11)-C(12) 124.69, C(11)-C(12)-C(13) 112.77, C(5)-C(8)-C(9) 118.08, C(5)-C(8)-O(3) 120.52, C(9)-C(8)-O(3) 120.80, O(2)-C(3)-O(1) 107.95, C(1)-O(2)-C(3) 106.11, C(2)-O(2)-C(3) 105.90, C(4)-C(1)-O(2) 127.95, C(7)-C(2)-O(1) 128.18.

Table 2.4. Crystal data and structure refinement for **2.9s**

Identification code	PA-543	
CCDC:	2179177	
Empirical formula	$C_{19}H_{24}O_3$	
Formula weight	300.38	
Temperature	296(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	$P2_1/c$	
Unit cell dimensions	a = 9.4165(15) Å	α = 90°.
	b = 25.989(4)Å	β = 96.153(5)°
	c = 6.8202(11) Å	γ = 90°.
Volume	1659.4(5) Å3	
Z	4	
Density (calculated)	1.202 mg/m^3	
Absorption coefficient	0.080 mm^{-1}	
F(000)	648	
Crystal size	0.32 × 0.24 × 0.20 mm^3	
Theta range for data collection	2.175 to 24.247°	

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Index ranges	$-10 \leq h \leq 10, -30 \leq k \leq 30, -7 \leq l \leq 7$
Reflections collected	38235
Independent reflections	2658 [R_{int} = 0.0796, R_{sigma} = 0.054]
Completeness to theta = 24.247°	99%
Refinement method	Full-matrix least-squares on F2
Data / restraints / parameters	2658 / 0 / 202
Goodness-of-fit on F^2	1.080
Final R indices [I>2sigma(I)]	R1 = 0.0964, wR2 = 0.2105
R indices (all data)	R1 = 0.1253, wR2 = 0.2362
Largest diff. peak and hole	0.517 and -0.350 e.$Å^{-3}$

Crystallographic data of 2.13

Single crystals of compound **2.13** suitable for X-ray diffraction were obtained by slow evaporation of the saturated solution of the complex in CH_3CN at room temperature using slow evaporation technique. X-ray crystallographic data were collected using Bruker D8 QUEST diffractometer. Data refinement and cell reduction were carried out by *APEX4*. Structures were solved by direct methods using Olex2 1.5 and refined by a full-matrix least-squares method using Olex2 1.5. All of the non-H atoms were refined anisotropically. The ORTEP diagram was obtained with ORTEP3 software with 50% thermal ellipsoid (see below, Figure 2.17). The crystallographic parameters and refinement data were listed in Table 2.5.

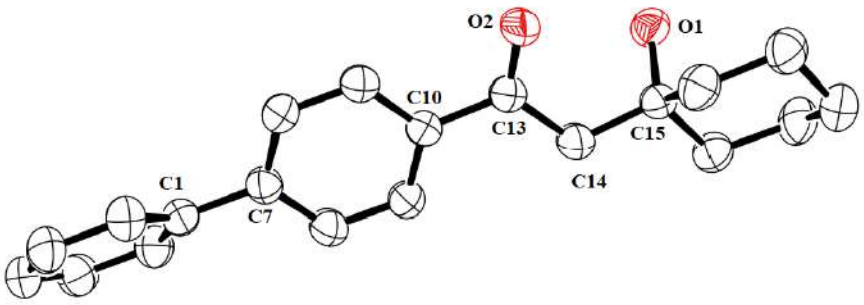

Figure 2.17: Molecular structure of compound **2.13** (thermal ellipsoid 50% probability level). Selected Bond lengths (in Å): O1-C15 1.4359(18), O2-C13 1.2188(18), C1-C7 1.483(2), C10-C13 1.489(2), C13-C14 1.507(2), C14-C15 1.530(2). Selected Bond Angles (in °): O2-C13-C10 119.86(14), C13-C14-C15 117.06(13), O1-C15-C14 108.90(12), C8-C7-C1 120.93(14).

Table 2.5. Crystal data and structure refinement for **2.13**

Identification code	PA_ALDOL_0m_a

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CCDC	2308887
Empirical formula	$C_{20}H_{21}O_2$
Formula weight	293.37
Temperature/K	294.00
Crystal system	triclinic
Space group	P-1
a/Å	7.5846(4)
b/Å	10.2861(5)
c/Å	11.9565(6)
α/°	108.8620(10)
β/°	94.5620(10)
γ/°	110.7890(10)
Volume/Å^3	805.09(7)
Z	2
ρ_{calc}g/cm^3	1.210
μ/mm^{-1}	0.077
F(000)	314.0
Crystal size/mm^3	0.42 × 0.38 × 0.31
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	3.69 to 51.356
Index ranges	$-9 \leq h \leq 9$, $-12 \leq k \leq 12$, $-14 \leq l \leq 14$
Reflections collected	19547
Independent reflections	3032 [R_{int} = 0.0269, R_{sigma} = 0.0191]
Data/restraints/parameters	3032/0/199
Goodness-of-fit on F^2	1.175
Final R indexes [I>=2σ (I)]	R_1 = 0.0453, wR_2 = 0.1048
Final R indexes [all data]	R_1 = 0.0582, wR_2 = 0.1144
Largest diff. peak/hole / e Å^{-3}	0.49/-0.15

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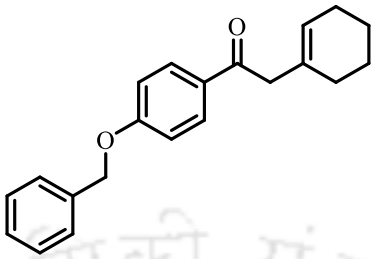
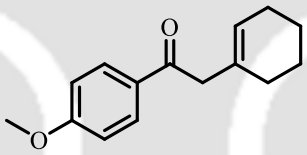
2.6. Analytical data of the products

1-(4-(benzyloxy)phenyl)-2-(cyclohex-1-en-1-yl)ethan-1-one (2.9a):



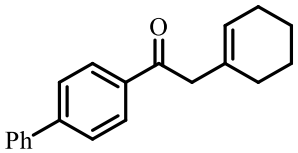
Using **GP-1** with compound **2.7a** (1 mmol, 226 mg) and **2.8a** (1 mmol, 98 mg), the title compound **2.9a** was isolated as white solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.50); 78% yield (239 mg). M.p. 72-74 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.96 (d, J = 8.2 Hz, 2H), 7.42 (t, J = 7.5 Hz, 2H), 7.39 (t, J = 7.5 Hz, 2H), 7.36 – 7.34 (m, 1H), 7.00 (d, J = 8.2 Hz, 2H), 5.56 (brs, 1H), 5.13 (s, 2H), 3.53 (s, 2H), 2.02 – 1.99 (m, 4H), 1.65 – 1.61 (m, 2H), 1.57 –1.54 (m, 2H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 197.5, 162.7, 136.4, 132.7, 130.9, 130.5, 128.8, 128.4, 127.6, 125.8, 114.6, 70.3, 47.8, 28.9, 25.6, 22.9, 22.2. HRMS (ESI) *m/z*: $[M+H]^+$calculated for $C_{21}H_{23}O_2$ 307.1693; found 307.1690.

2-(cyclohex-1-en-1-yl)-1-(4-methoxyphenyl)ethan-1-one (2.9b)[13]



Using **GP-1** with compound **2.7b** (1 mmol, 150 mg) and **2.8a** (1 mmol, 98 mg) and 6 mol% of cat **1** and 40 mol% base, the title compound **2.9b** was isolated as colourless liquid using silica gel column chromatography with petroleum ether and ethyl acetate (v/v = 50:1, R_f = 0.80); 85% yield (195 mg). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.97 – 7.95 (d, J = 8.8 Hz, 2H), 6.93 – 6.91 (d, J = 8.8 Hz, 2H), 5.56 (brs, 1H) 3.87 (s, 3H), 3.53 (s, 2H), 2.03 – 1.99 (m, 4H), 1.64 – 1.61 (m, 2H), 1.57 – 1.54 (m, 2H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 197.6, 163.5, 132.7, 130.9, 130.3, 125.8, 113.8, 55.6, 47.8, 28.9, 25.5, 22.9, 22.2. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{15}H_{19}O_2$ 231.1385; found 231.1392.

1-([1,1'-biphenyl]-4-yl)-2-(cyclohex-1-en-1-yl)ethan-1-one (2.9c)



Using **GP-1** with compound **2.7c** (1 mmol, 196 mg) and **2.8a** (1 mmol, 98 mg), the title compound **2.9c** was isolated as off white solid using silica gel column chromatography with petroleum

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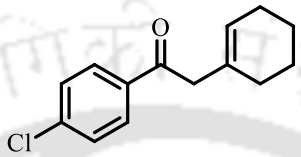
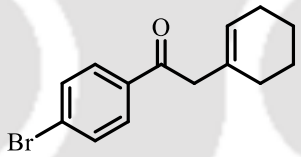
ether/ethyl acetate (v/v = 100:1, R_f = 0.60); 82% yield (226 mg). M.p. 69-71 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.05 (d, J = 8.2 Hz, 2H), 7.68 (d, J = 8.2 Hz, 2H), 7.63 (d, J = 7.4 Hz, 2H), 7.47 (t, J = 7.4 Hz, 2H), 7.40 (t, J = 7.4 Hz, 1H), 5.61 (brs, 1H), 3.62 (s, 2H), 2.04 – 2.03 (m, 4H), 1.66 – 1.64 (m, 2H), 1.58 – 1.55 (m, 2H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 198.5, 145.8, 140.1, 135.9, 132.4, 129.2, 129.1, 128.3, 127.4, 127.3, 126.2, 48.1, 29.0, 25.9, 22.9, 22.2. HRMS (ESI) *m/z*: $[M+H]^+$calculated for $C_{20}H_{21}O$ 277.1587; found 277.1593.

1-(4-chlorophenyl)-2-(cyclohex-1-en-1-yl)ethan-1-one (2.9d)



Using **GP-1** with compound **2.7d** (1 mmol, 154 mg) and **2.8a** (1 mmol, 98 mg), the title compound **2.9d** was isolated as colourless liquid using silica gel column chromatography with petroleum ether and ethyl acetate (v/v = 100:1, R_f = 0.70); 84% yield (197 mg). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.91 (d, J = 8.5 Hz, 2H), 7.42 (d, J = 8.5 Hz, 2H), 5.56 (brs, 1H), 3.55 (s, 2H), 2.03 – 2.02 (m, 2H), 1.99 – 1.97 (m, 2H), 1.65 – 1.61 (m, 2H), 1.56 – 1.54 (m, 2H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 197.7, 139.5, 135.4, 132.1, 130.0, 129.0, 126.4, 48.1, 28.9, 25.5, 22.9, 22.1. HRMS (ESI) *m/z*: $[M+H]^+$calculated for $C_{14}H_{16}ClO$ 235.0885; found 235.0889.

1-(4-bromophenyl)-2-(cyclohex-1-en-1-yl)ethan-1-one (2.9e)



Using **GP-1** with compound **2.7e** (1 mmol, 197 mg) and **2.8a** (1 mmol, 98 mg), the title compound **2.9e** was isolated as yellow liquid using silica gel column chromatography with petroleum ether and ethyl acetate (v/v = 100:1, R_f = 0.80); 92% yield (247 mg). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.83 (d, J = 8.5 Hz, 2H), 7.58 (d, J = 8.5 Hz, 2H), 5.56 (s, 1H), 3.54 (s, 2H), 2.03 – 2.02 (m, 2H), 2.00 – 1.97 (m, 2H), 1.65 – 1.61 (m, 2H), 1.57 – 1.53 (m, 2H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 197.9, 135.8, 132.1, 132.0, 130.1, 128.3, 126.4, 48.0, 38.6, 30.9, 29.8, 28.9, 28.1, 26.4, 25.5, 22.9, 22.1. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{14}H_{16}BrO$ 279.0380; found 279.0375.

2-(cyclohex-1-en-1-yl)-1-(4-(phenylethynyl)phenyl)ethan-1-one (2.9f)

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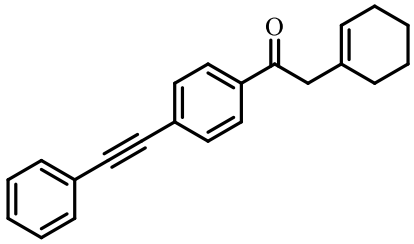
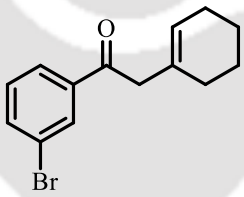


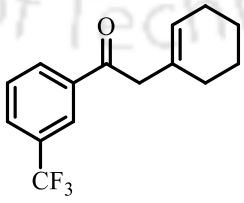
Using **GP-1** with compound **2.7f** (1 mmol, 220 mg) and **2.8a** (1 mmol, 98 mg), the title compound **2.9f** was isolated as off white solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 100:1, R_f = 0.60); 86% yield (258 mg). M.p. 72-74 ℃. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.96 (d, J = 8.2 Hz, 2H), 7.59 (d, J = 8.2 Hz, 2H), 7.56 – 7.55 (m, 2H), 7.37 – 7.36 (m, 3H), 5.58 (brs, 1H), 3.59 (s, 2H), 2.03 – 2.00 (m, 4H), 1.65 – 1.62 (m, 2H), 1.57 – 1.55 (m, 2H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 198.2, 136.2, 132.1, 131.9, 131.8, 128.9, 128.6, 128.5, 128.2, 126.3, 122.8, 92.8, 88.8, 48.1, 28.9, 25.6, 22.9, 22.2. HRMS (ESI) *m/z*: $[M+H]^+$calculated for $C_{22}H_{21}O$ 301.1587; found 301.1571.

1-(3-bromophenyl)-2-(cyclohex-1-en-1-yl)ethan-1-one (2.9g)



Using **GP-1** with compound **2.7g** (1 mmol, 197 mg) and **2.8a** (1 mmol, 98 mg), the title compound **2.9g** was isolated as yellow oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 100:1, R_f = 0.80); 91% yield (253 mg). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.09 (s, 1H), 7.88 (d, J = 7.8 Hz, 1H), 7.67 (d, J = 7.8 Hz, 1H), 7.33 (t, J = 7.8 Hz, 1H), 5.57 (brs, 1H), 3.55 (s, 2H), 2.03 – 1.98 (m, 4H), 1.65 – 1.61 (m, 2H), 1.58 – 1.56 (m, 2H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 197.5, 138.9, 135.9, 131.9, 131.6, 130.27, 127.1, 126.6, 123.0, 48.1, 28.9, 25.6, 22.9, 22.1. HRMS (ESI) *m/z*: $[M+H]^+$calculated for $C_{14}H_{16}BrO$ 279.0380; found 279.0375.

2-(cyclohex-1-en-1-yl)-1-(3-(trifluoromethyl)phenyl)ethan-1-one (2.9h)



Using **GP-1** with compound **2.7h** (1 mmol, 188 mg) and **2.8a** (1 mmol, 98 mg), the title compound **2.9h** was isolated as yellow oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 100:1, R_f = 0.70); 83% yield (222 mg). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.24 (s, 1H), 8.15 (d, J = 7.7 Hz, 1H), 7.81 (d, J = 7.6 Hz, 1H), 7.60 (t, J = 7.6 Hz, 1H), 5.60 (brs, 1H), 3.61 (s,

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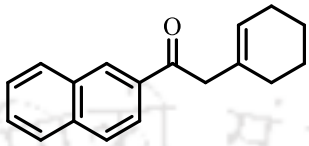
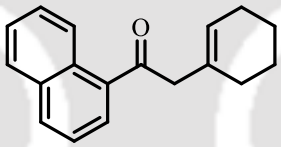
2H), 2.04 (brs, 2H), 1.99 (brs, 2H), 1.66 – 1.62 (m, 2H), 1.58 – 1.54 (m, 2H). $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$): δ 197.5, 137.6, 131.8, 131.7, 129.5 (q, J = 3.6 Hz), 129.4, 126.8, 125.44, 125.42, 48.2, 28.9, 25.6, 22.9, 22.1. $^{19}F\{^{1}H\}$ NMR (377 MHz, $CDCl_3$): δ –62.84. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{15}H_{16}F_3O$ 269.1153; found 269.1158.

2-(cyclohex-1-en-1-yl)-1-(naphthalen-2-yl)ethan-1-one (2.9i)



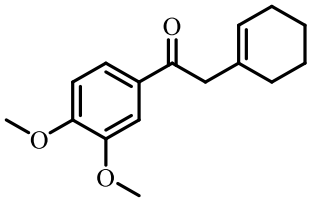
Using **GP-1** with compound **2.9i** (1 mmol, 170 mg) and **2.8a** (1 mmol, 98 mg), the title compound **2.9i** was isolated as yellow oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.70); 82% yield (205 mg). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.51 (s, 1H), 8.04 (d, J = 8.6 Hz, 1H), 7.97 (d, J = 8.0 Hz, 1H), 7.88 (t, J = 8.0 Hz, 2H), 7.60 (t, J = 7.4 Hz, 1H), 7.55 (t, J = 7.4 Hz, 1H), 5.63 (brs, 1H), 3.72 (s, 2H), 2.05 – 2.04 (m, 4H), 1.66 – 1.63 (m, 2H), 1.59 – 1.56 (m, 2H). $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$): δ 198.9, 135.7, 134.5, 132.7, 132.5, 130.3, 129.8, 128.5, 128.5, 127.9, 126.8, 126.2, 124.4, 48.1, 29.0, 25.6, 22.9, 22.2. HRMS (ESI) *m/z*: $[M+H]^+$calculated for $C_{18}H_{19}O$ 251.1430; found 251.1421.

2-(cyclohex-1-en-1-yl)-1-(naphthalen-1-yl)ethan-1-one (2.9j)



Using **GP-1** with compound **2.7j** (1 mmol, 170 mg) and **2.8a** (1 mmol, 98 mg), the title compound **2.9j** was isolated as yellow oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.70); 52% yield (130 mg). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.56 (d, J = 8.5 Hz, 1H), 7.98 (d, J = 8.5 Hz, 1H), 7.88 (dd, J = 12.9, 7.5 Hz, 2H), 7.58 (t, J = 7.5 Hz, 1H), 7.53 (t, J = 7.5 Hz, 1H), 7.49 (t, J = 7.5 Hz, 1H), 5.61 (brs, 1H), 3.68 (s, 2H), 2.03 – 2.02 (m, 4H), 1.63 –1.59 (m, 2H), 1.56 – 1.54 (m, 2H). $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$): δ 203.1, 136.2, 134.0, 132.6, 132.2, 128.5, 128.0, 127.8, 126.5, 126.5, 125.9, 124.4, 51.6, 28.9, 25.5, 22.9, 22.1. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{18}H_{19}O$ 251.1430; found 251.1430.

2-(cyclohex-1-en-1-yl)-1-(3,4-dimethoxyphenyl)ethan-1-one (2.9k)



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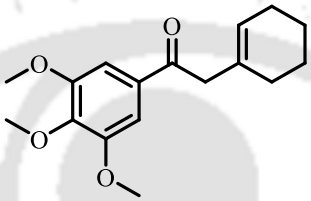
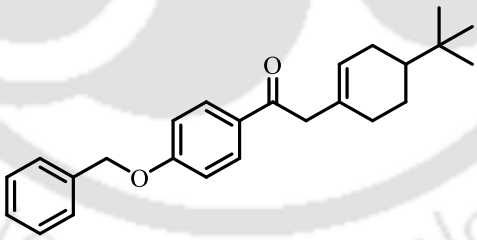
Using **GP-1** with compound **2.7k** (1 mmol, 180 mg) and **2.8a** (1 mmol, 98 mg), the title compound **2.9k** was isolated as yellow oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.50); 81% yield (211 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.62 (dd, J = 8.4, 1.5 Hz, 1H), 7.55 (d, J = 1.5 Hz, 1H), 6.88 (d, J = 8.4 Hz, 1H), 5.57 (brs, 1H), 3.94 (s, 3H), 3.93 (s, 3H), 3.55 (s, 2H), 2.03 – 2.00 (m, 4H), 1.64 – 1.62 (m, 3H), 1.55 – 1.54 (m, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 197.5, 153.4, 149.1, 132.8, 130.5, 125.8, 123.4, 110.7, 110.1, 56.2, 56.1, 47.8, 28.9, 25.6, 23.0, 22.2. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{16}H_{21}O_3$ 261.1485; found 261.1490.

2-(cyclohex-1-en-1-yl)-1-(3,4,5-trimethoxyphenyl)ethan-1-one (2.9l)



Using **GP-1** with compound **2.7l** (1 mmol, 210 mg) and **2.8a** (1 mmol, 98 mg), the title compound **2.9l** was isolated as yellow oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.50); 92% yield (267 mg). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.27 (s, 2H), 5.61 (brs, 1H), 3.92 (s, 3H), 3.91 (s, 6H), 3.56 (s, 2H), 2.04 (brs, 2H), 2.00 (brs, 2H), 1.64 – 1.62 (m, 3H), 1.59 –1.57 (m, 1H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 197.6, 153.1, 142.7, 132.8, 132.4, 126.1, 106.2, 61.1, 56.4, 48.2, 28.9, 25.6, 22.9, 22.2. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{17}H_{23}O_4$ 291.1591; found 291.1591.

1-(4-(benzyloxy)phenyl)-2-(4-(tert-butyl)cyclohex-1-en-1-yl)ethan-1-one (2.9m)



Using **GP-1** with compound **2.9a** (1 mmol, 226 mg) and **2.8b** (1 mmol, 154 mg), the title compound **2.9m** was isolated as white solid (322 mg, 89% yield) using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 20:1, R_f = 0.50), followed by recrystallization from petroleum ether. M.p. 85-87 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.96 (d, J = 8.9 Hz, 2H), 7.44 – 7.39 (m, 4H), 7.36 – 7.33 (m, 1H), 7.00 (d, J = 8.9 Hz, 2H), 5.56 (brs, 1H), 5.13 (s, 2H), 3.55 (s, 2H), 2.05 – 2.04 (m, 3H), 1.81 – 1.79 (m, 2H), 1.25 – 1.20 (m, 2H), 0.85 (s, 9H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 197.5, 162.7, 136.4, 132.4, 130.9, 130.5, 128.9, 128.4, 127.6, 126.1, 114.6, 70.3, 47.3, 43.8, 32.3, 30.4, 27.4, 27.2, 24.3. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{25}H_{31}O_2$ 363.2319; found 363.2321.

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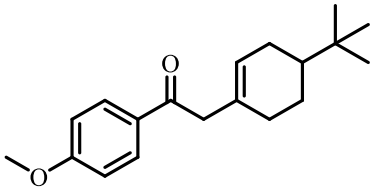
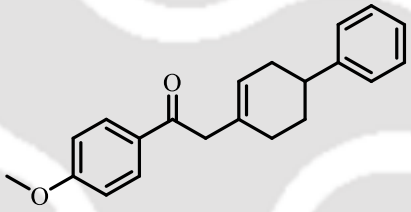
2-(4-(tert-butyl)cyclohex-1-en-1-yl)-1-(4-methoxyphenyl)ethan-1-one (2.9n)



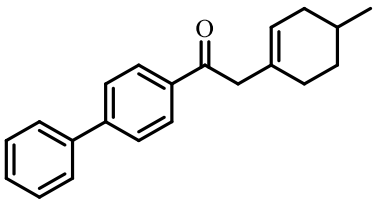
Using **GP-1** with compound **2.7b** (1 mmol, 150 mg) and **2.8b** (1 mmol, 154 mg), the title compound **2.9n** was isolated as white solid (266 mg, 93% yield) using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.50). M.p. 82-84 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.96 (d, J = 8.9 Hz, 2H), 6.92 (d, J = 8.9 Hz, 2H), 5.56 (brs, 1H), 3.86 (s, 3H), 3.54 (s, 2H), 2.05 – 2.04 (m, 3H), 1.81 – 1.78 (m, 2H), 1.27 – 1.22 (m, 1H), 1.20 – 1.15 (m, 1H), 0.84 (s, 9H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 197.5, 163.5, 132.4, 130.9, 130.3, 126.0, 113.8, 55.6, 47.2, 43.8, 32.3, 30.4, 27.3, 27.2, 24.2. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{19}H_{27}O_2$ 287.2010; found 287.2016.

1-(4-methoxyphenyl)-2-(1,2,3,6-tetrahydro-[1,1'-biphenyl]-4-yl)ethan-1-one (2.9o)



Using **GP-1** with compound **2.7b** (1 mmol, 150 mg) and **2.8c** (1 mmol, 174 mg), the title compound **2.9o** was isolated as white solid (285 mg, 93%) using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.60), followed by recrystallization from petroleum ether. M.p. 89-90 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.99 (d, J = 8.9 Hz, 2H), 7.28 (t, J = 7.5 Hz, 2H), 7.21 – 7.17 (m, 3H), 6.94 (d, J = 8.9 Hz, 2H), 5.66 (brs, 1H), 3.88 (s, 3H), 3.61 (s, 2H), 2.81 – 2.76 (m, 1H), 2.34 – 2.31 (m, 1H), 2.24 – 2.19 (m, 2H), 2.13 – 2.10 (m, 1H), 1.96 – 1.94 (m, 1H), 1.84 – 1.77 (m, 1H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 197.3, 163.6, 147.1, 132.6, 130.9, 130.2, 128.5, 127.0, 126.1, 125.5, 113.8, 55.6, 47.3, 39.9, 33.8, 30.0, 29.6. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{21}H_{23}O_2$ 307.1693; found 307.1682.

1-([1,1'-biphenyl]-4-yl)-2-(4-methylcyclohex-1-en-1-yl)ethan-1-one (2.9p)



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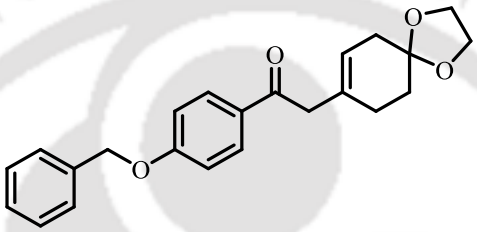
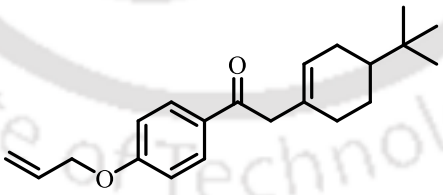
Using **GP-1** with compound **2.7c** (1 mmol, 196 mg) and **2.8d** (1 mmol, 112 mg), the title compound **2.9p** was isolated as white solid (237 mg, 82% yield) using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.60), followed by recrystallization from petroleum ether. M.p. 68-70 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.05 (d, J = 8.0 Hz, 2H), 7.68 (d, J = 8.0 Hz, 2H), 7.63 (d, J = 8.0 Hz, 2H), 7.47 (t, J = 7.4 Hz, 2H), 7.40 (t, J = 7.4 Hz, 1H), 5.57 (brs, 1H), 3.63 (s, 2H), 2.13 – 2.10 (m, 2H), 2.05 – 2.02 (m, 1H), 1.72 – 1.66 (m, 3H), 1.29 – 1.25 (m, 1H), 0.94 (d, J = 5.8 Hz, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 198.5, 145.8, 140.1, 135.9, 132.1, 129.2, 129.1, 128.3, 127.4, 127.3, 125.7, 47.8, 34.1, 31.1, 29.0, 28.2, 21.8. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{21}H_{22}O$ 291.1744; found 291.1739.

1-(4-(benzyloxy)phenyl)-2-(1,4-dioxaspiro[4.5]dec-7-en-8-yl)ethan-1-one (2.9q)



Using **GP-1** with compound **2.7a** (1 mmol, 226 mg) and **2.8e** (1 mmol, 156 mg), the title compound **2.9q** was isolated as colourless solid using silica gel column chromatography with petroleum ether and ethyl acetate (v/v = 20:3, R_f = 0.40); 65% yield (237 mg). M.p. 93-95 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.95 (d, J = 8.8 Hz, 2H), 7.43 – 7.39 (m, 4H), 7.36 – 7.33 (m, 1H), 7.00 (d, J = 8.8 Hz, 2H), 5.48 (brs, 1H), 5.13 (s, 2H), 3.97 (s, 4H), 3.60 (s, 2H), 2.31 (brs, 2H), 2.27 (brs, 2H), 1.79 (t, J = 6.5 Hz, 2H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 197.0, 162.8, 136.3, 132.4, 130.8, 130.4, 128.9, 128.4, 127.6, 123.2, 114.7, 107.9, 70.3, 64.6, 46.5, 36.0, 31.2, 28.1. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{23}H_{25}O_4$ 365.1748 found 365.1749.

1-(4-(allyloxy)phenyl)-2-(4-(tert-butyl)cyclohex-1-en-1-yl)ethan-1-one (2.9r)



Using **GP-1** with compound **2.7m** (1 mmol, 176 mg) and **2.8b** (1 mmol, 154 mg), the title compound **2.9r** was isolated as viscous oil (259 mg, 83% yield) using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.50). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.99 – 7.92 (m, 2H), 6.94 (d, J = 8.9 Hz, 2H), 6.09 – 6.01 (m, 1H), 5.57 – 5.56 (m, 1H), 5.43 (d, J = 17.3, 1.4 Hz, 1H), 5.32 (d, J = 10.5, 1.4 Hz, 1H), 4.61 (dt, J = 5.3, 1.4 Hz, 2H), 3.54 (s, 2H), 2.06 – 2.04 (m, 3H), 1.84 – 1.79 (m, 2H), 1.26 – 1.23 (m, 1H), 1.21 – 1.18 (m, 1H), 0.85 (s, 9H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 197.4, 162.6, 132.7, 132.5, 130.9, 130.5, 126.1,

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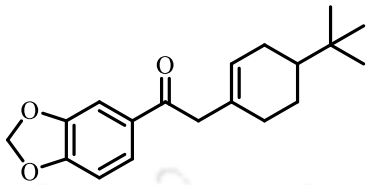
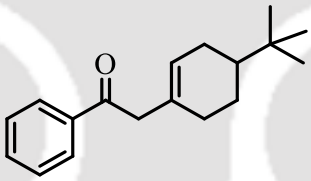
118.3, 114.5, 69.1, 47.3, 43.9, 32.3, 30.4, 27.4, 27.2, 24.3. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{21}H_{29}O_2$ 313.2163; found 313.2165.

1-(benzo[*d*][1,3]dioxol-5-yl)-2-(4-(*tert*-butyl)cyclohex-1-en-1-yl)ethan-1-one (2.9s)



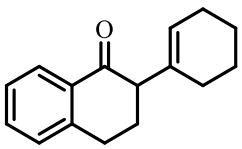
Using **GP-1** with compound **2.7n** (1 mmol, 164 mg) and **2.8b** (1 mmol, 154 mg), the title compound **2.9s** was isolated as white solid (285 mg, 95% yield) using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 20:1, R_f = 0.50), followed by recrystallization from petroleum ether. M.p. 90-92 °C. ^{1}H NMR 1H NMR (500 MHz, $CDCl_3$): δ 7.60 – 7.59 (d, J = 8.2 Hz, 1H), 7.44 (brs, 1H), 6.84 (d, J = 8.2 Hz, 1H), 6.03 (s, 2H), 5.55 (s, 1H), 3.52 (s, 2H), 2.03 – 2.00 (m, 3H), 1.83 – 1.79 (m, 2H), 1.28 – 1.14 (m, 2H), 0.85 (s, 9H). ^{13}C{1H} NMR (126 MHz, $CDCl_3$): δ 196.9, 151.8, 148.2, 132.3, 132.1, 126.2, 124.9, 108.4, 108.0, 101.9, 47.3, 43.9, 32.3, 30.4, 27.3, 27.2, 24.3. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{19}H_{25}O_3$ 301.1799; found. 301.1802.

2-(4-(*tert*-butyl)cyclohex-1-en-1-yl)-1-phenylethan-1-one (2.9t)



Using **GP-1** with compound **2.7o** (1 mmol, 120 mg) and **2.8b** (1 mmol, 154 mg) with 6 mol% of **2.6c** and 40 mol% base, the title compound **2.9t** was isolated as colourless liquid using silica gel column chromatography with petroleum ether and ethyl acetate (v/v = 50:1, R_f = 0.50; 90% yield. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.98 – 7.97 (d, J = 7.4 Hz, 2H), 7.56 – 7.53 (m, 1H), 7.46 – 7.43 (m, 2H), 5.57 (brs, 1H), 3.60 (s, 2H,) 2.06 – 2.03 (m, 3H), 1.82 – 1.79 (m, 2H), 1.29 – 1.18 (m, 2H) 0.85 (s, 9H). ^{13}C{1H} NMR (126 MHz, $CDCl_3$): δ 198.9, 137.1, 133.1, 132.1, 128.6, 128.5, 126.4, 47.4, 43.8, 32.3, 32.4, 30.4, 27.3, 27.1, 24.2. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{18}H_{25}O$: 257.1900; found 257.1988.

2-(cyclohex-1-en-1-yl)-3,4-dihydronaphthalen-1(2H)-one (2.9u)



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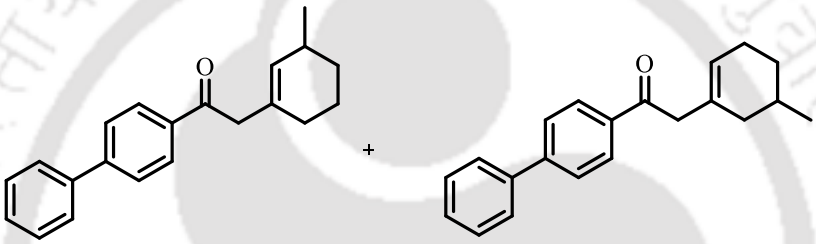
Using **GP-1** with compound **2.7o** (1 mmol, 146 mg) and **2.9a** (1 mmol, 98 mg), the title compound **2.9u** was isolated as yellow oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:2, R_f = 0.50); 85% yield (192 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.04 (d, J = 8.0 Hz, 1H), 7.47 – 7.43 (m, 1H), 7.30 (t, J = 7.6 Hz, 1H), 7.23 (d, J = 7.6 Hz, 1H), 5.45 (s, 1H), 3.11 (dd, J = 10.4, 4.4 Hz, 1H), 3.01 – 2.97 (m, 2H), 2.29 – 2.20 (m, 1H), 2.17 – 2.11 (m, 1H), 2.05 – 2.03 (m, 2H), 2.00 – 1.99 (m, 2H), 1.71 – 1.65 (m, 2H), 1.62 – 1.58 (m, 2H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 199.2, 144.3, 136.1, 133.3, 133.2, 128.8, 127.6, 126.7, 124.9, 56.3, 28.6, 28.5, 26.9, 25.5, 23.0, 22.5. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{15}H_{19}O$ 227.1431; found 227.1446.

1-([1,1'-biphenyl]-4-yl)-2-(3-methylcyclohex-1-en-1-yl)ethan-1-one and 1-([1,1'-biphenyl]-4-yl)-2-(3-methylcyclohex-1-en-1-yl)ethan-1-one (2.9v)



Using **GP-1** with compound **2.7c** (1 mmol, 196 mg) and **2.8f** (1 mmol, 112 mg), the title compound **2.9v-1** + **2.9v-2** was isolated as white solid (229 mg, 85% yield) using silica gel column chromatography with petroleum ether and ethyl acetate (v/v = 50:1, R_f = 0.70), followed by recrystallization from petroleum ether. ^{1}H NMR analysis of the crude reaction mixture showed **2.9v-1**/**2.9v-2** mixture of 71:29, as determined by comparison of the following signals: δ 5.59 (brs, 1H, C*H*, **2.9v-1**)–major, 5.46 (brs, 1H, C*H*, **2.9v-2**)–minor. M.p. 85-88 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.06 – 8.05 (m, 2H, major, 71% + m, 2H, minor, 29%), 7.68 – 7.67 (m, 2H, major, 71% + m, 2H, minor, 29%), 7.64 – 7.62 (m, 2H, major, 71% + m, 2H, minor, 29%), 7.48 – 7.46 (m, 2H, major, 71% + m, 2H, minor, 29%), 7.41 – 7.39 (m, 1H, major, 71% + m, 1H, minor, 29%), 5.59 (brs, 1H, minor, 71%), 5.46 (brs, 1H, major, 29%), 3.62 (s, 2H, major, 71% + s, 2H, minor, 29%), 2.22 (brs, 2H, minor, 29%), 2.09 – 2.05 (m, 3H, major, 71%), 1.99 (brs, 2H, minor, 29%), 1.76 – 1.65 (m, 3H, major, 71% + m, 2H, minor, 29%), 1.20 – 1.12 (m, 1H, major, 71% + m, 1H, minor, 29%), 0.97 – 0.95 (m, 3H, major, 71% + m, 3H, minor, 29%). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 198.5, 145.8, 140.1, 135.9, 132.6, 132.0, 129.2, 129.1, 128.3, 127.4, 127.33, 127.29, 125.8, 48.1, 47.9, 37.5, 31.0, 30.7, 30.4, 28.94, 28.91, 25.7, 21.92, 21.85, 21.84. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{21}H_{22}O$ 291.1744; found 291.1742.

1-cyclopentyl-2-(1,2,3,6-tetrahydro-[1,1'-biphenyl]-4-yl)ethan-1-one (2.9aa)

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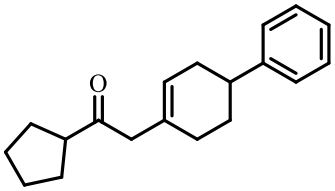
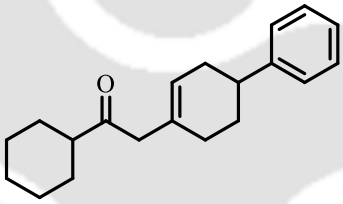


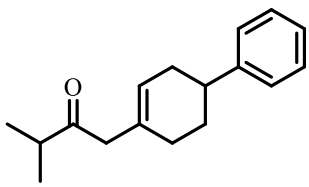
Using **GP-1** with compound **2.7r** (1 mmol) and **2.8c** (1 mmol), the title compound **2.9aa** was isolated as colourless liquid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 100:1, R_f = 0.60); 62% yield. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.31 – 7.29 (m, 2H), 7.23 – 7.19 (m, 3H), 5.62 (s, 1H), 3.14 (s, 2H), 2.98 (p, J = 16.2 Hz, 1H), 2.80 – 2.75 (m, 1H), 2.35 – 2.32 (m, 1H), 2.22 – 2.15 (m, 2H), 2.04 – 2.01 (m, 1H), 1.96 – 1.93 (m, 1H), 1.83 – 1.80 (m 3H), 1.75 – 1.73 (m, 2H), 1.69 – 1.66 (m, 2H), 1.60 – 1.58 (m, 2H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 211.99, 147.0, 132.0, 128.5, 127.0, 126.2, 125.7, 51.2, 50.7, 39.9, 33.8, 30.0, 29.5, 29.3, 29.3, 26.2. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{19}H_{25}O$ 296.1900; found 269.1895.

1-cyclohexyl-2-(1,2,3,6-tetrahydro-[1,1'-biphenyl]-4-yl)ethan-1-one (2.9ab)



Using **GP-1** with compound **2.7s** (1 mmol) and **2.8c** (1 mmol), the title compound **2.9ab** was isolated as colourless liquid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 100:1, R_f = 0.60); 75% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32 – 7.30 (m, 2H), 7.21 – 7.19 (m, 3H), 5.60 (brs, 1H), 3.12 (s, 2H), 2.78 (m, 1H), 2.47 – 2.32 (m, 1H), 2.37 – 2.32 (m, 1H), 2.23 – 2.12 (m, 2H), 2.03 – 1.93 (m, 3H), 1.83 – 1.78 (m, 4H), 1.37 – 1.22 (m, 6H).^{13}C NMR (151 MHz, $CDCl_3$): δ 212.7, 147.0, 132.0, 128.5, 127.0, 126.2, 125.6, 50.3, 49.9, 39.8, 33.7, 30.0, 29.5, 28.75, 28.67, 26.0, 25.84, 25.81. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{20}H_{27}O$ 283.2057; found 283.2056.

3-methyl-1-(1,2,3,6-tetrahydro-[1,1'-biphenyl]-4-yl)butan-2-one (2.9ac)



Using **GP-1** with 6 mol% **2.6c** and 60 mol% base, compound **2.7t** (10 mmol) and **2.8c** (1 mmol), the title compound **2.9ac** was isolated as colourless liquid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 100:2, R_f = 0.60); 39% yield. ^{1}H NMR (400 MHz,

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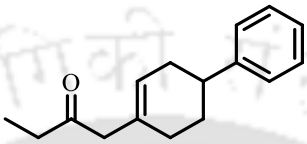
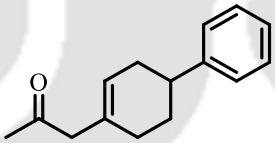
$CDCl_3$): δ 7.33 – 7.29 (m, 2H), 7.24 – 7.18 (m, 3H), 5.62 (brs, 1H), 3.15 (s, 2H), 2.81 – 2.70 (m, 2H), 2.38 – 2.33 (m, 1H), 2.24 – 2.17 (m, 2H), 2.05 – 1.94 (m, 2H), 1.85 – 1.76 (m, 1H), 1.13 – 1.11 (m, 6H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 213.3, 147.0, 131.9, 128.5, 127.0, 126.1, 125.7, 49.7, 40.2, 39.8, 33.7, 30.0, 29.4, 18.5, 18.4. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{17}H_{23}O$ 243.1744; found 243.1746.

1-(1,2,3,6-tetrahydro-[1,1'-biphenyl]-4-yl)butan-2-one (2.9ad)



Using **GP-1** with 6 mol% **2.6c** and 60 mol% base and compound **2.7u** (1 mmol) and **2.8c** (1 mmol), the title compound **2.9ad** was isolated as colourless liquid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v= 100:2, R_f = 0.40); 44% yield. ^1H NMR (400 MHz, $CDCl_3$): δ 7.32 – 7.28 (m, 2H), 7.23 – 7.20 (m, 3H), 5.63 (brs, 1H), 3.08 (s, 2H), 2.80 – 2.74 (m, 1H), 2.52 – 2.46 (m, 2H), 2.36 – 2.32 (m, 1H), 2.23 – 2.17 (m, 2H), 2.05 2.01 (m, 1H), 1.97 – 1.94 (m, 1H), 1.77 (brs, 1H), 1.06 (t, J = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 210.3, 146.9, 132.0, 128.5, 127.0, 126.2, 125.8, 51.7, 39.8, 35.3, 33.7, 30.0, 29.5. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{16}H_{21}O$ 229.1587; found 229.1593.

1-(1,2,3,6-tetrahydro-[1,1'-biphenyl]-4-yl)propan-2-one (2.9ae)



Using **GP-1** with 6 mol% **2.6c** and 60 mol% base and compound **2.7v** (1 mmol) and **2.8c** (1 mmol), the title compound **2.9ae** was isolated as colourless liquid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 100:2, R_f = 0.40); 47% yield. ^1H NMR (400 MHz, $CDCl_3$): δ 7.32 – 7.29 (m, 2H), 7.23 – 7.18 (m, 3H), 5.65 (s, 1H), 3.09 (s, 2H), 2.82 – 2.74 (m, 1H), 2.54 – 2.50 (m, 1H), 2.37 – 2.33 (m, 1H), 2.24 – 2.21 (m, 1H), 2.17 (s, 3H), 2.06 – 1.95 (m, 2H), 1.84 – 1.74 (m, 1H). $^{13}C\{1H\}$ NMR (126 MHz, CDCl3): δ 207.7, 146.9, 131.8, 128.5, 127.0, 126.2, 126.1, 53.0, 39.8, 33.7, 30.0, 29.3. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{15}H_{19}O$ 215.1431; found 215.1429.

2-(cyclohept-1-en-1-yl)-3,4-dihydronaphthalen-1(2*H*)-one (2.9af)

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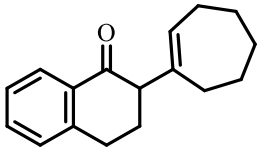
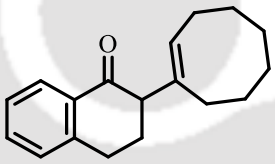


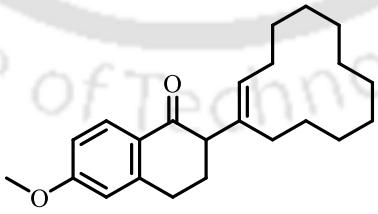
Using **GP-1** with compound **2.7p** (1 mmol) and **2.8i** (1 mmol), the title compound **2.9af** was isolated as yellow oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:2, R_f = 0.50); 76% yield (183 mg).^{1}H NMR (400 MHz, $CDCl_3$): δ 8.04 (d, J = 8.0 Hz, 1H), 7.47 –7.44 (m, 1H), 7.31 (d, J = 7.2 Hz, 1H), 7.23 (d, J = 7.7 Hz, 1H), 5.62 (t, J = 6.4 Hz, 1H), 3.20 – 3.16 (dd, J = 11.2, 4.8 Hz, 1H), 3.06 – 2.96 (m, 2H), 2.36 – 2.30 (m, 1H), 2.28 – 2.25 (m, 1H), 2.23 – 2.12 (m, 5H), 1.52 – 1.42 (m, 7H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 199.4, 144.3, 143.2, 133.3, 133.2, 123.0, 128.8, 127.6, 126.7, 58.6, 32.9, 33.0, 28.9, 28.9, 28.7, 27.2. HRMS (ESI) *m/z*: $[M+Na]^+$ calculated for $C_{17}H_{20}NaO$ 263.1407; found 263.1421.

(*E*)-2-(cyclooct-1-en-1-yl)-3,4-dihydronaphthalen-1(2*H*)-one (2.9ag)



Using **GP-1** with compound **2.7p** (1 mmol, 146 mg) and **2.8j** (1 mmol, 126 mg), the title compound **2.9ag** was isolated as yellow oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:2, R_f = 0.50); 68% yield (173 mg).^{1}H NMR (500 MHz, $CDCl_3$): δ 8.04 (d, J = 7.4 Hz, 1H), 7.45 (t, J = 7.0 Hz, 1H), 7.30 (t, J = 7.5 Hz, 1H), 7.23 (d, J = 7.5 Hz, 1H), 5.37 (t, J = 8.5 Hz, 1H), 3.21 (dd, J = 10.5, 4.5 Hz, 1H), 3.06 – 2.96 (m, 2H), 2.36 – 2.30 (m, 1H), 2.28 – 2.23 (m, 1H), 2.20 – 2.12 (m, 5H), 1.52 – 1.43 (m, 7H).^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 199.5, 144.2, 139.0, 133.28, 133.25, 128.8, 127.9, 127.6, 126.7, 56.7, 29.7, 29.5, 29.0, 28.8, 28.7, 26.47, 26.49, 26.4. HRMS (ESI) m/z: $[M+H]^+$ calculated for $C_{18}H_{23}O$ 255.1744; found 255.1747.

(*Z*)-2-(cyclododec-1-en-1-yl)-6-methoxy-3,4-dihydronaphthalen-1(2*H*)-one (2.9ah)



Using **GP-1** with compound **2.7q** (1 mmol, 176 mg) and **2.8k** (1 mmol, 182 mg), the title compound **2.9ah** was isolated as yellow oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:3, R_f = 0.50); 51% yield (174 mg). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.02 (d, J = 9.0 Hz, 1H), 6.82 (dd, J = 9.0, 3.0 Hz, 1H), 6.68 – 6.67 (m, 1H), 5.06 (t, J = 7.8 Hz, 1H), 3.85 (s, 3H), 3.18 – 3.16 (m, 1H), 2.99 – 2.94 (m, 1H), 2.88 – 2.85 (m, 1H), 2.34 – 2.21 (m, 1H), 2.20 (m, 2H), 2.19 – 2.14 (m, 2H), 2.05 – 2.02 (m, 1H), 1.51 – 1.49 (m, 2H), 1.43 –

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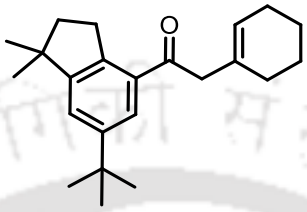
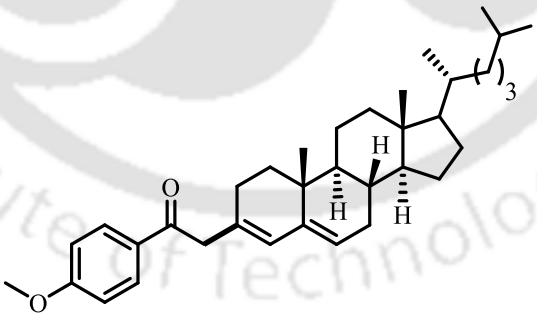
1.41 (m, 3H), 1.40 – 1.39 (m, 3H), 1.33 – 1.28 (m, 8H). $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$): δ 198.6, 163.4, 146.6, 137.7, 130.1, 128.9, 127.1, 113.1, 112.6, 55.5, 53.1, 29.9, 29.1, 28.7, 27.3, 26.6, 25.8, 25.3, 25.2, 24.9, 24.7, 24.6, 22.8. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{23}H_{33}O_2$ 341.2476; found 341.2485.

1-(6-(*tert*-butyl)-1,1-dimethyl-2,3-dihydro-1H-inden-4-yl)-2-(cyclohex-1-en-1-yl)ethan-1-one (2.9ai)



Using **GP-1** with compound **2.7w** (1 mmol) and **2.8a** (1 mmol), the title compound **2.9ai** was isolated as colourless liquid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 100:1, R_f = 0.50); 38% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.79 (brs 1H), 7.32 (brs, 1H), 5.60 (s, 1H), 3.57 (s, 2H), 3.17 (t, *J* = 7.2 Hz, 2H), 2.05 – 2.00(m, 4H), 1.92 (t, *J* = 7.2 Hz, 2H), 1.66 – 1.63 (m, 2H), 1.58 – 1.55 (m, 2H), 1.35 (s, 9H), 1.26 (s, 6H). $^{13}C\{^{1}H\}$ (126 MHz, $CDCl_3$): δ 201.0, 149.8, 141.5, 133.5, 132.9, 125.9, 124.8, 123.2, 50.0, 43.5, 41.6, 34.9, 31.7, 30.9, 28.9, 25.6, 23.0, 22.3. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{23}H_{33}O$ 325.2526; found 325.2529.

2-((8S,9S,10R,13R,14S)-10,13-dimethyl-17-(6-methylheptan-2-yl)-2,7,8,9,10,11,12,13,14,15,16,17-dodecahydro-1H-cyclopenta[*a*]phenanthren-3-yl)-1-(4-methoxyphenyl)ethan-1-one (2.9aj)



The title compound **2.9aj** was isolated as white solid using silica gel column chromatography with petroleum ether and ethyl acetate (v/v = 20:1, R_f = 0.5). The title compound **2.9aj** was 284 mg, 55% yield, starting from **2.7b** (1 mmol, 150 mg) and **2.8l** (1 mmol, 356 mg) using **GP-1** method. M.p. 94-96 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.96 (d, *J* = 8.9 Hz, 2H, ArH), 6.92 (d, *J* = 8.6 Hz, 2H, ArH), 5.84 (s, 1H, C=C*H*), 5.36 (br, 1H, C=C*H*), 3.86 (s, 3H, CH_3), 3.62 (brs, 1H), 3.61 (br, 1H), 2.24 – 2.13 (m, 2H), 2.05 – 2.00 (m, 2H), 1.84 – 1.79 (m, 2H), 1.68 – 1.51 (m, 6H), 1.43 – 1.33 (m, 6H), 1.23 – 1.15 (m, 3H), 1.14 – 1.07 (m, 4H), 1.02 – 0.96 (m, 3H), 0.92 – 0.90 (m, 6H),

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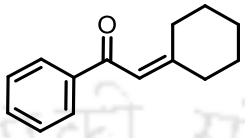
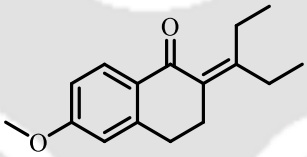
0.87 – 0.85 (m, 7H), 0.69 (brs, 3H). $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$): δ 197.1, 163.5, 141.6, 130.9, 130.8, 130.2, 128.3, 123.2, 113.8, 57.1, 56.3, 55.6, 48.3, 47.4, 42.6, 39.9, 39.7, 36.3, 35.9, 34.9, 34.1, 32, 31.9, 28.4, 28.2, 26.8, 24.3, 24.0, 23.0, 22.7, 21.2, 19.1, 18.8, 12.1. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{36}H_{53}O_2$: 517.4041; found 517.4020.

2-cyclohexylidene-1-phenylethan-1-one (2.10a)[8]



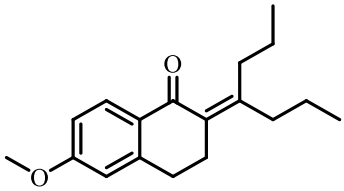
Using **GP-1** with compound **2.7o** (1 mmol, 120 mg) and **2.8a** (1 mmol, 98 mg), the title compound **2.10a** was isolated as colourless oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 100:1, R_f = 0.80); 88% yield (176 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95 – 7.93 (m, 2H), 7.55 – 7.50 (m, 1H), 7.46 – 7.42 (m, 2H), 6.60 (s, 1H), 2.78 – 2.75 (m, 2H), 2.33 – 2.28 (m, 2H), 1.74 – 1.61 (m, 6H). $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$): δ 192.6, 163.0, 139.4, 132.5, 128.5, 128.9, 118.9, 38.6, 30.8, 29.0, 28.1, 26.4.

6-methoxy-2-(pentan-3-ylidene)-3,4-dihydronaphthalen-1(2H)-one (2.10b)



Using **GP-2** with compound **2.7q** (1 mmol, 176 mg) and **2.8g** (6 mmol, 516 mg), the title compound **2.10b** was isolated as colourless liquid using silica gel column chromatography with petroleum ether and ethyl acetate (v/v = 50:2, R_f = 0.50); 70% yield (171 mg). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.07 (d, J = 9.0 Hz, 1H), 6.83 (dd, J = 9.0, 3.0 Hz, 1H), 6.67 (d, J = 2.4 Hz, 1H), 3.85 (s, 3H), 2.93 (t, J = 6.0 Hz, 2H), 2.76 (t, J = 6.6 Hz, 2H), 2.50 (q, J = 7.2 Hz, 2H), 2.24 (q, J = 7.2 Hz, 2H), 1.15 (t, J = 7.8 Hz, 3H), 1.08 (t, J = 7.2 Hz, 3H). $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$): δ 189.1, 163.0, 156.2, 146.0, 130.4, 130.1, 128.7, 113.0, 112.3, 55.5, 31.3, 28.6, 27.6, 27.2, 13.8, 13.5. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{16}H_{21}O_2$ 245.1537; found 245.1540.

2-(heptan-4-ylidene)-6-methoxy-3,4-dihydronaphthalen-1(2H)-one (2.10c)



Using **GP-2** with compound **2.7q** (1 mmol, 176 mg) and **2.8h** (6 mmol, 684 mg), the title compound **2.10c** was isolated as white solid using silica gel column chromatography with

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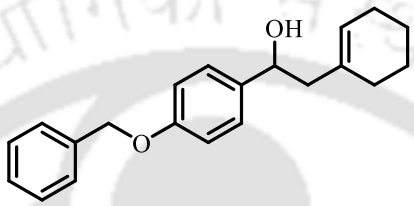
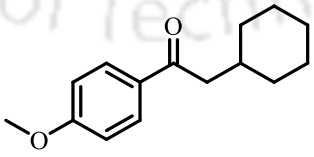
petroleum ether and ethyl acetate (v/v = 50:2, R_f = 0.50); 72% yield (196 mg). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.09 (d, J = 9.0 Hz, 1H), 6.85 (dd, J = 8.4, 2.4 Hz, 1H), 6.69 (d, J = 2.4 Hz, 1H), 3.87 (s, 3H), 2.94 (t, J = 6.0 Hz, 2H), 2.78 (t, J = 6.6 Hz, 2H), 2.50 – 2.48 (m, 2H), 2.23 – 2.20 (m, 2H), 1.60 – 1.55 (m, 2H), 1.53 – 1.49 (m, 2H), 1.01 (q, J = 7.8 Hz, 6H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 189.9, 163.0, 153.4, 146.0, 130.9, 130.4, 128.8, 113.0, 112.3, 36.9, 31.3, 28.9, 22.8, 22.4, 14.69, 14.66. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{18}H_{25}O_2$ 273.1850; found $C_{18}H_{25}O_2$ 273.1853.

1-(4-(benzyloxy)phenyl)-2-(cyclohex-1-en-1-yl)ethan-1-ol (2.11)



Procedure: To a solution of **2.9a** (50 mg, 0.16 mmol, 1 equiv.) in methanol (2 mL), solid $NaBH_4$ (12 mg, 0.16 mmol, 2 equiv.) was added at 0 ℃ portion wise. After the completion of the addition, the reaction mixture was allowed to stirred for 6 h at room temperature. Then water was added to the reaction mixture, and extracted by using dichloromethane (5 mL). Afterwards, in the organic layer Na_2SO_4 was added to remove excess water. Product was obtained as white solid **2.11** (48 mg, 97%) after removable of the dichloromethane solution under reduced pressure. The title compound **2.11** was isolated as white solid using silica gel column chromatography with petroleum ether and ethyl acetate (v/v = 10:1, R_f = 0.5). M.p. 43-45 ℃. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.45 – 7.43 (m, 2H), 7.39 (t, J = 7.5 Hz, 2H), 7.36 – 7.31 (m, 1H), 7.30 (d, J = 8.6 Hz, 2H), 6.96 (d, J = 8.6 Hz, 2H), 5.60 (brs, 1H), 5.06 (s, 2H), 4.72 – 4.70 (m, 1H), 2.31 – 2.29 (m, 1H), 2.16 (br, 1H), 2.04 (brs, 2H), 1.93 –1.90 (m, 1H), 1.65 – 1.64 (m, 2H), 1.59 – 1.58 (m, 2H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 158.2, 137.1, 136.8, 134.6, 128.7, 128.1, 127.6, 127.1, 125.8, 114.7, 70.9, 70.1, 49.0, 28.3, 25.4, 22.9, 22.4. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{21}H_{25}O_2$ 309.1850; found 309.1854.

2-cyclohexyl-1-(4-methoxyphenyl)ethanone (2.12)[8]



Procedure: A freshly synthesized **2.9b** (50 mg, 0.22 mmol, 1 equiv.), cyclohexanol (22 mg, 0.22 mmol, 1 equiv.), **2.6c** (2 mol%), KO^{t}Bu (20 mol%) and toluene (1 mL) were taken into a reaction tube (25 mL) equipped with a stirring bar. Then the reaction tube was properly closed and placed in a preheated oil bath at 150 ℃ with continuous stirring for 12 h. The resulting mixture was then passed through a bed of celite, the filtrate was collected and concentrated under reduced pressure.

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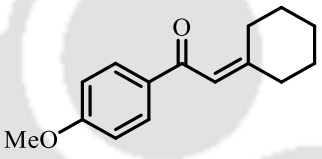
The crude reaction mixture was purified by column chromatography over silica gel using petroleum ether or ethyl acetate/ petroleum ether mixture as an eluent to get analytically pure product **2.12** (47 mg, 92% yield).

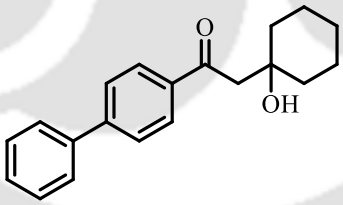
Using above procedure, the title compound **2.12** was isolated as colourless liquid using silica gel column chromatography with petroleum ether and ethyl acetate (v/v = 100:1, R_f = 0.5); 94% yield (0.206 g). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93 (d, J = 8.8 Hz, 2H, ArH), 6.93 (d, J = 8.8 Hz, 2H, ArH), 3.86 (s, 3H, CH_3), 2.76 (d, J = 6.8 Hz, 2H, COCH_2), 1.98 – 1.91 (m, 1H), 1.74 – 1.65 (m, 5H), 1.30 – 1.25 (m, 2H), 1.19 – 1.16 (m, 1H), 1.05 – 0.99 (m, 2H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 199.1 (C=O), 163.4, 130.7, 130.6, 113.8, 55.6 (CH_3), 46.1 (COCH_2), 34.9, 33.6, 26.4, 26.3.

2-cyclohexylidene-1-(4-methoxyphenyl)ethan-1-one (2.10d)



^{1}H NMR (600 MHz, $CDCl_3$): δ 7.95 – 7.93 (m, 2H), 6.93 – 6.92 (m, 2H), 3.87 (s, 3H), 2.73 – 2.72 (m, 2H), 2.31 – 2.28 (m, 2H), 1.74 – 1.70 (m, 2H), 1.64 – 1.61 (m, 4H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 191.1, 163.1, 161.5, 132.2, 130.8, 113.6, 55.6, 38.5, 30.8, 29.0, 28.1, 26.4. The title compound **2.10d** was obtained using reported method.[11]

1-([1,1'-biphenyl]-4-yl)-2-(1-hydroxycyclohexyl)ethan-1-one (2.13)



^{1}H NMR (600 MHz, $CDCl_3$): δ 8.03 (d, J = 8.4 Hz, 2H), 7.70 (d, J = 8.4 Hz, 2H), 7.63(d, J = 7.2 Hz, 2H), 7.48 (t, J = 7.2 Hz, 2H), 7.41 (t, J = 7.2 Hz, 2H), 4.03 (s, 1H), 3.15 (s, 2H), 1.75 (d, J = 21.5 Hz, 4H), 1.60 – 1.56 (m, 1H), 1.48 (s, 4H), 1.27 (s, 1H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 201.7, 146.4, 139.9, 136.3, 129.1, 128.9, 128.5, 127.5, 127.4, 71.2, 38.0, 25.9, 22.1. HRMS (ESI) *m/z*: $[M+Na]^+$ calculated for $C_{20}H_{22}O_2Na$ 317.1517; found 317.1515.

1,3-di([1,1'-biphenyl]-4-yl)-3-hydroxybutan-1-one (2.14)

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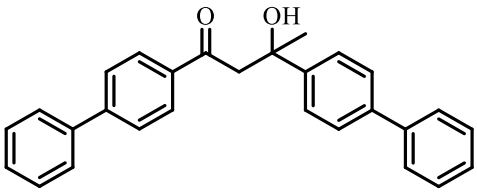
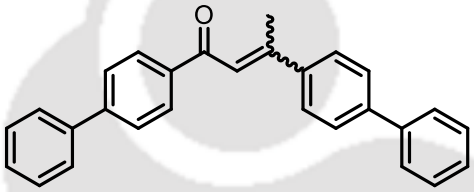


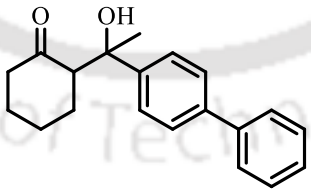
^{1}H NMR (600 MHz, $CDCl_3$): δ 8.01 (d, J = 8.4 Hz, 2H), 7.69 (d, J = 7.8 Hz, 2H), 7.62 (d, J = 7.8 Hz, 2H), 7.58 – 7.55 (m, 6H), 7.48 (t, J = 7.4 Hz, 2H), 2H), 7.43 – 7.40 (m, 3H), 7.33 (t, J = 7.8 Hz, 1H), 4.95 (s, 1H), 3.87 (d, J = 17.3 Hz, 1H), 3.41 (d, J = 17.3 Hz, 1H), 1.68 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 201.1, 146.9, 146.6, 140.9, 139.8, 139.7, 135.7, 129.1, 128.9, 128.8, 128.6, 127.5, 127.4, 127.3, 127.2, 125.0, 73.7, 48.9, 31.7. HRMS (ESI) *m/z*: $[M+Na]^+$ calculated for $C_{28}H_{24}O_2Na$ 415.1674; found 415.1670.

1,3-di([1,1'-biphenyl]-4-yl)but-2-en-1-one (2.15)



^{1}H NMR (400 MHz, $CDCl_3$): δ 8.11 – 8.09 (m, 2H, *E*-isomer + *Z*-isomer), 7.73 – 7.71 (m, 3H, *E*-isomer + *Z*-isomer), 7.68 – 7.67 (m, 3H, *E*-isomer + *Z*-isomer), 7.66 – 7.63 (m, 4H, *E*-isomer + *Z*-isomer) 7.50 – 7.46 (m, 4H, *E*-isomer + *Z*-isomer), 7.42 – 7.39 (m, 2H, *E*-isomer + *Z*-isomer), 7.28 (brs, 1H, *E*-isomer + *Z*-isomer), 2.66 (d, J = 1.2 Hz, 3H, *E*-isomer, 80%), 2.65 (s, 3H, *Z*-isomer, 20%). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 191.5, 154.7, 145.4, 142.2, 141.7, 140.4, 140.2, 138.3, 129.10, 129.05, 128.3, 127.89, 127.86, 127.45, 127.44, 127.39, 127.23, 127.15, 122.1, 18.9. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{28}H_{23}O$ 375.1744 found 375.1745.

2-(1-([1,1'-biphenyl]-4-yl)-1-hydroxyethyl)cyclohexan-1-one (2.16)



^{1}H NMR (600 MHz, $CDCl_3$): δ 7.59 – 7.58 (m, 1H), 7.56 – 7.55 (m, 2H), 7.51 – 7.50 (m, 2H), 7.44 – 7.41 (m, 2H), 7.33 (t, J = 7.4 Hz, 1H), 4.45 (s, 1H), 2.93 (dd, J = 12.6, 5.2 Hz, 1H), 2.36 – 2.34 (m, 2H), 2.17 – 2.10 (m, 2H), 1.95 – 1.93 (m, 1H), 1.74 – 1.64 (m, 1H), 1.53 (s, 2H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 216.0, 147.0, 141.0, 139.6, 128.8, 127.3, 127.2, 126.9, 125.5, 74.9, 59.8, 43.8, 29.9, 28.4, 25.7, 25.6. HRMS (ESI) *m/z*: $[M+Na]^+$ calculated for $C_{20}H_{22}O_2Na$ 317.1512; found 317.1517.

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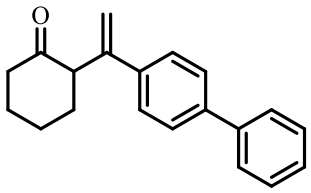
2-(1-([1,1'-biphenyl]-4-yl)vinyl)cyclohexan-1-one (2.17)



^{1}H NMR (600 MHz, $CDCl_3$): δ 7.59 – 7.57 (m, 2H), 7.53 (d, J = 8.4 Hz, 2H), 7.44 – 7.42 (m, 2H), 7.37 (d, J = 8.4 Hz, 2H), 7.33 (t, J = 7.2 Hz, 1H), 5.56 (s, 1H), 5.14 (s, 1H), 3.63 (dd, J = 11.6, 4.8 Hz, 1H), 2.54 – 2.51 (m, 1H), 2.47 – 2.43 (m, 1H), 2.24 – 2.21 (m, 1H), 2.14 – 2.10 (m, 1H), 1.99 – 1.94 (m, 2H), 1.83 – 1.76 (m, 2H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 210.9, 146.3, 140.88, 140.86, 140.3, 128.9, 127.4, 127.15, 127.10, 127.03, 126.95, 125.2, 115.3, 56.6, 42.6, 33.4, 28.1, 25.2. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{20}H_{21}O$ 277.1587; found 277.1598.

2.7. Computational details

All calculations were performed using the Gaussian-16 program package[34] in the gas phase. Full geometry optimizations were carried out using Minnesota 2006 local (M06-L) functional[35] and BS1 basis set. BS1 is defined as an SDD[36] basis set for Ru atom and 6-31G (d, p) for all other atoms. Method and basis set was selected based on a previous report on similar complexes. Frequency calculations at the same method and basis set were performed to make sure that all structures are at minima on the potential energy surface based on the absence of imaginary frequencies. Free energies were calculated by using frequency calculations at 150 °C to match the experimental conditions.

Table 2.5: Free Energies (G) and Total Energies (E) of all the optimized structures given in Hartree along with the number of imaginary frequencies[a]

Species	Free energy (G)	Total energy (E)	# Imaginary Frequency (NImag)
H_2O	-76.416076	-76.4110228	0
acetophenone (**2.7o**)	-384.77127600	-384.858511	0
cyclohexanone (**2a'**)	-309.757132	-309.861046	0
acetophenone enol (**2.7o'**)	-384.743691	-384.831153	0
ter-butoxide anion ($^{-}$**O^{t}Bu**)	-232.942634	-233.017462	0
2-cyclohexylidene-1-phenylethan-1-one (**2.10a**)	-618.078846	-618.279281	0
2-(cyclohex-1-en-1-yl)-1-phenylethan-1-one (**2.9w**)	-618.087507	-618.286856	0
2-(4-(*tert*-butyl)cyclohexylidene)-1-phenylethan-1-one (**2.10e**)	-775.220292	-775.521983	0
2-(4-(tert-butyl)cyclohex-1-en-1-yl)-1-phenylethan-1-one (**2.9t**)	-775.228626	-775.528034	0

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Step I: Pathway for aldol product formation			
I1	-2714.998969	-2715.546358	0
I1′	-2714.971384	-2715.519	0
I2	-2714.978949	-2715.560072	0
I3	-2714.977513	-2715.585023	0
A-TS-1	-2714.954697	-2715.562076	1
I4	-2714.99172	-2715.602426	0
A-TS-2	-2714.970777	-2715.587548	1
I5	-2714.994854	-2715.608892	0
I6	-2715.035492	-2715.674624	0
I7	-2715.0376	-2715.685906	0
I8	-2715.035634	-2715.681026	0
Step II: Pathway for the condensation step (formation of α,β- unsaturated ketone 3a-I1)			
2.18	-927.47995	-927.810721	0
I9	-927.50114	-927.832054	0
I10	-927.499098	-927.828826	0
D-TS-1	-927.469633	-927.799022	1
I11	-927.469754	-927.792828	0
2.10a	-927.453369	-927.776191	0
Step II: Pathway for the condensation step (formation of β,γ- unsaturated ketone 3a-I2)			
2.18	-927.47995	-927.810721	0
I9	-927.50114	-927.832054	0
I10	-927.499098	-927.828826	0
I12	-927.44976	-927.778152	0
D-TS-2	-927.420349	-927.746838	1
I13	-927.435184	-927.753929	0
I24	-927.47229	-927.796765	0
2.9w	-927.466672	-927.787479	0
Step II: Pathway for the condensation step (formation of β, γ-unsaturated ketone (direct route))			
2.18	-927.47995	-927.810721	0
D-TS-3	-927.419625	-927.745482	1
I14	-927.47229	-927.796765	0
2.9w	-927.466672	-927.787479	0
Step III: Isomerisation of β-branched unsaturated ketones with the active catalyst (2.6c)			
I15-2.10a	-2482.043171	-2482.576799	0
I16-2.10a	-2482.048949	-2482.592916	0
I17-2.10a	-2482.005151	2482.541369	0
I18-2.9w	-2482.054181	-2482.593617	0
I15-2.10e	-2639.182990	-2639.820536	0
I16-2.10e	-2639.190481	-2639.834867	0
I17-2.10e	-2639.153074	-2639.786192	0
I18-2.9t	-2639.20097	-2639.839142	0
I15-2.10f	-2941.631267	2942.153721	0
I16-2.10f	-2941.638377	2942.171841	0
I17-2.10f	-2941.600902	2942.120507	0
I18-2.9e	-2941.648507	2942.169684	0
2.9ae-A	-657.365594	-657.5877196	0
2.9ae-B	-657.373063	-657.5935541	0
2.9ae-C	-657.368764	-657.5902701	0
2.9ae-D	-657.376301	-657.5988156	0
I19	-2521.342649	-2521.9052313	0
I20	-2521.324580	-2521.8847025	0

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[a](G) is calculated at 150 °C to meet the experimental conditions. All the figures were generated using (G) values. All the reactants, intermediates and products have zero NImag. All the calculations were performed at M06-L level of DFT.

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Chapter 3

Chromium-catalyzed cross-coupling of methyl ketones with cyclic ketones toward the selective synthesis of β-branched β, γ-unsaturated ketones

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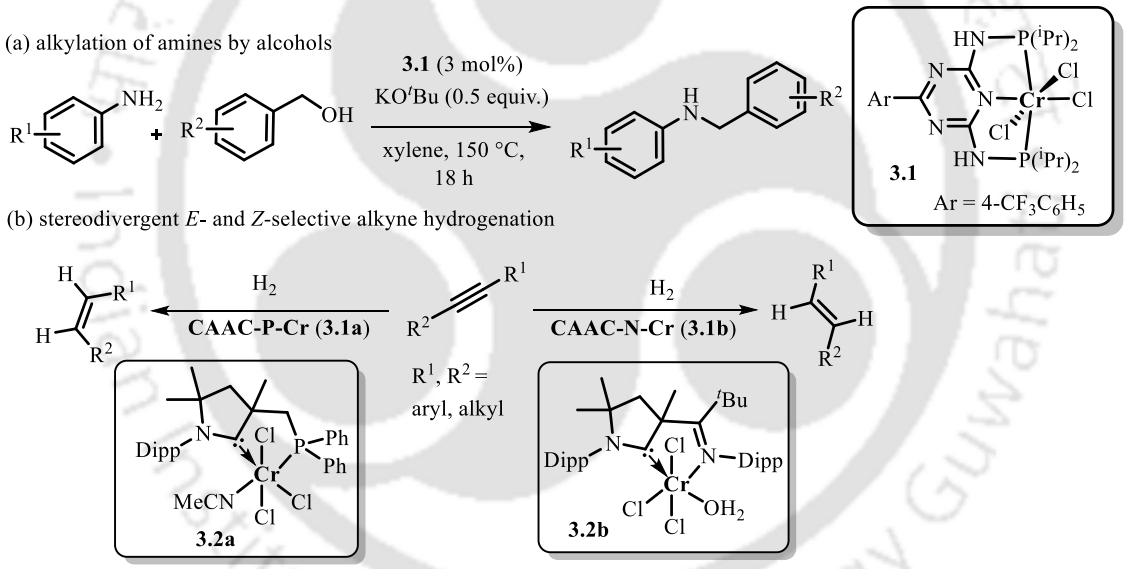
3.1. Introduction

As mentioned in chapter 2, the *β*-branched *β, γ*-unsaturated ketone compounds are an eminent class of structural motif which are often found in various natural products and bioactive molecules.[1-5] They are extensively used as structural building blocks for complex structures by manipulating their carbonyl and alkene moieties.[6, 7] Owing to their great demand, synthesis of these *β, γ*-unsaturated ketones attracts significant attention in chemical research.

Transition-metal catalyzed cross-coupling reaction of ketones (or enolates) with alkenylbromides, alkenyltriflates or alkenyl tosylates has been developed through seminal contributions by *Lei*, *Helquist*, and *Buchwald*.[8-11] The use of palladium and nickel is dominant as the catalyst of choice in these reactions. Further, ruthenium hydride-catalyzed[12, 13] and photoredox[3] conditions were also employed to enrich this chemistry. However, in most of the cases, the reaction was directed with a prefunctionalized coupling partner which restricts the synthetic efficiency. Further, in some cases, the methods suffer from low *β, γ*-regioselectivity.[10] Hence, new strategies with high efficiency are highly desired.



Scheme 3.1. Chromium catalyzed (a) alkylation of amines by alcohols (b) stereodivergent *E* and *Z*- alkyne hydrogenation

Owing to the high price of palladium, ruthenium, and the toxicity associated with nickel, the development of alternative metal catalyst is urgently needed. In this regard, chromium(III/II) catalysis has emerged as an alternative to precious catalysts because of their low cost, acceptably low toxicity, and abundancy in nature.[14] Chromium salts are widely used as catalysts in various cross-coupling reactions, hydrofunctionalization, hydrogenation, and aldol reactions.[15, 16] Further, Cr-pincer complex is employed in the dehydrogenation catalysis for *N*-alkylation of amines by alcohols (Scheme 3.1a).[15a] In contrast to the bond-forming reactions, isomerization of alkene enabled by chromium catalyst has rarely been investigated (Scheme 3.1b).[16] In particular, dual

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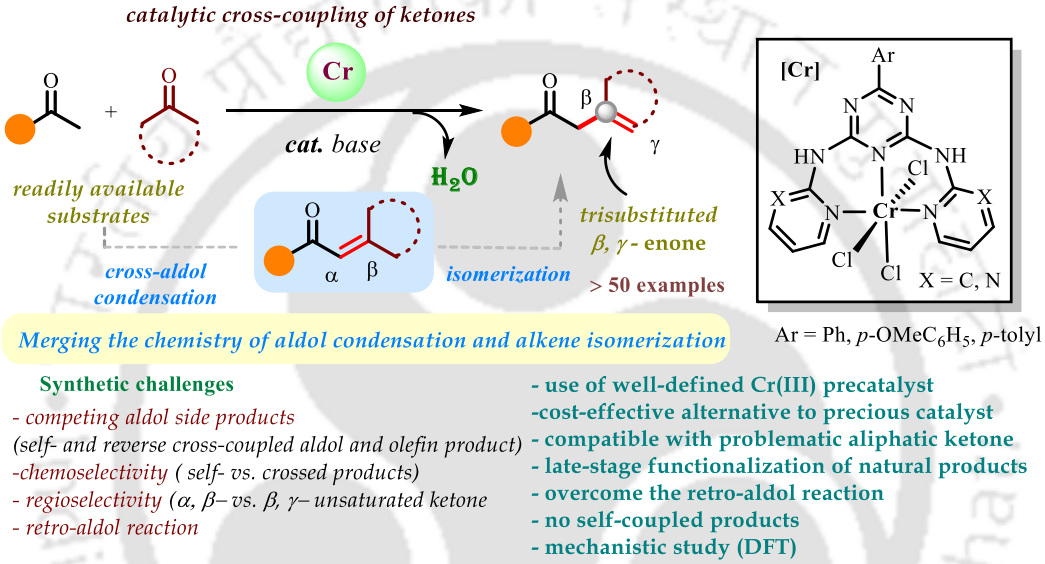
roles of a single catalytic system in both the C-C bond forming reaction and alkene isomerization remain underexplored. Herein, I hypothesize that cost-effective chromium-catalysed aldol condensation of two different ketones and alkene isomerization may offer a straightforward and boosting approach to access *β*, *γ*-unsaturated ketones from readily available ketones.

3.2. Present work

Chromium-catalyzed cross-coupling of methyl ketones with cyclic ketones to *β*-branched *β*, *γ*-unsaturated ketones are reported. A detailed mechanistic study of the catalytic cross-coupling of ketones including spectroscopic characterization of active chromium species has been discussed.



Scheme 3.2. Chromium catalyzed cross-coupling of ketones toward the selective synthesis of *β*-branched *β*, *γ*-unsaturated ketones

3.3. Results and discussion

3.3.1 Synthesis and spectroscopic characterization of ligands and their corresponding chromium complexes

Herein, I have synthesized new bench-stable triazine-based Cr-NNN pincer complexes as outlined in Scheme 3.4. The ligands feature a central triazine ring with potentially tridentate pockets, constituted by pyridyl groups connected by NH functionality on both sides. 2,4-dichloro-6-(4-aryl)-1,3,5-triazine **2.3a-c** was prepared *via* Grignard reaction as mentioned chapter 2, section 2.3.1. To the reaction mixture, the deprotonated 2-picolylamine (or 2-aminopyrimidine) was added to afford pincer ligand **3.3a-d** as a yellow-orange solid in 90%-93% yield. Complexation was performed by refluxing a solution of the NNN ligands **3.3a-d** and $CrCl_3$•3THF in THF afforded the corresponding pincer chromium (III) complexes **3.4a**, **3.4b**, **3.4c** and **3.4d** respectively, in good yields. The complex **3.5** (for $CrCl_2$ complex) was synthesized in 85% yield by treating the ligand **3.3a** with $CrCl_2$ in dry THF. Compound **3.4a-d** were characterized by ESI-MS (for details, see

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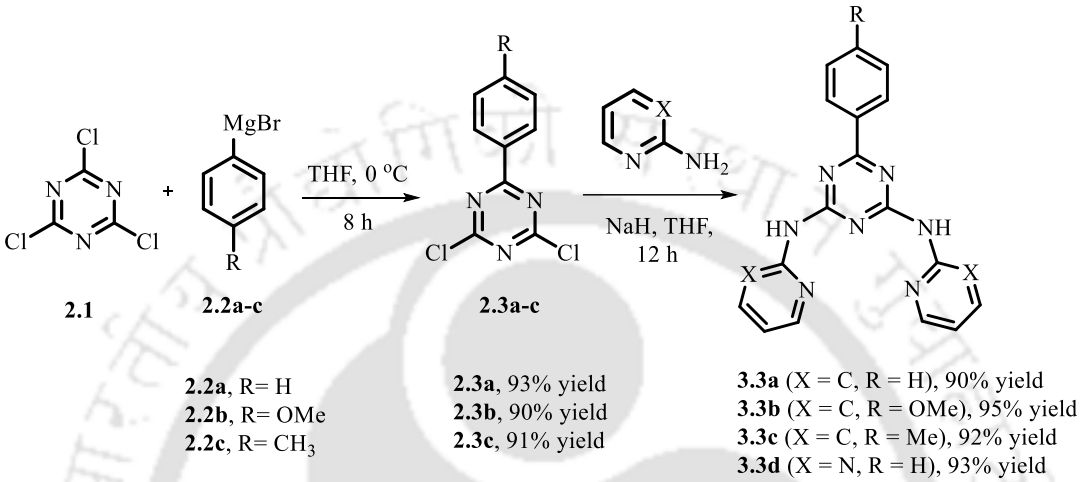
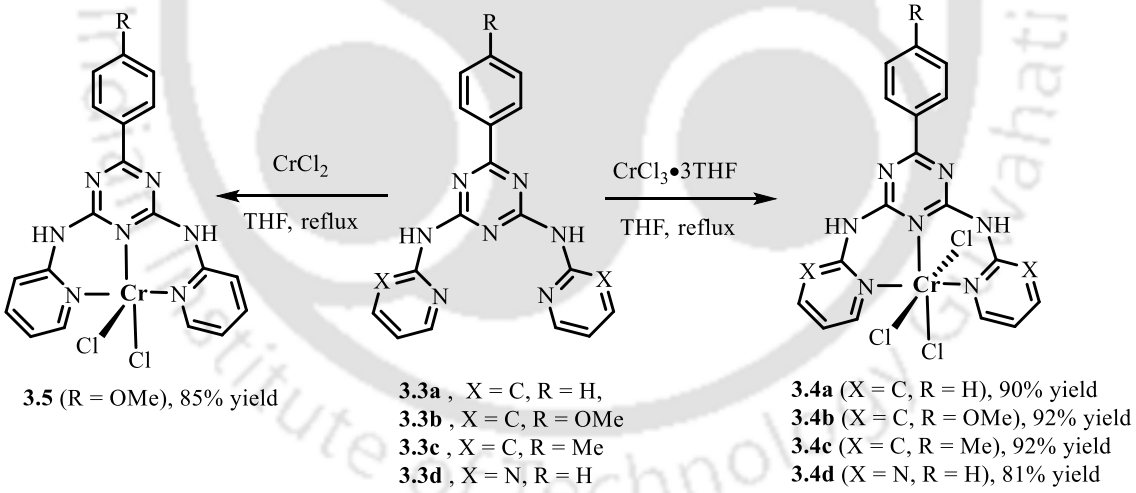
experimental section in the section 3.5). The positive ion ESI-MS analysis revealed molecular ion peak at *m/z* = 463.0170 (for **3.4a**), 493.0274 (for **3.4b**), 477.0320 (for **3.4c**), 465.0060 (for **3.4d**) and 463.0167 (for **3.5**) which are characteristic for corresponding cationic species of $[M\text{-}Cl]^+$ (M = molecular ion). Simulations of the isotopic distribution for all fragments are matched well with their experimental spectra. The chromium (III) complexes **3.4a-d** were paramagnetic and their NMR analysis could not be successfully performed.



Scheme 3.3. Ligand synthesis



Scheme 3.4. Synthesis of chromium complexes

Among the chromium complexes, single crystals of complex **3.4a** and **3.4b** suitable for X-ray diffraction were obtained by slow diffusion of OEt_2 into the saturated solution of the complex in DMF at room temperature. The complexes **3.4a** and **3.4b** crystallizes in the C12/c1 and *P* $2_1/n$ space group respectively. Both the crystals consist of one molecule of DMF in the lattice (Figure-3.1). The DMF molecule is located in close proximity to the one N−H group of the ligand backbone, indicating a strong hydrogen bonding interaction (N-H•••DMF 2.042 Å in **3.4a** and N-H•••DMF 1.952 Å in **3.4b**). The molecular structures of complexes **3.4a** and **3.4b** adopt a distorted

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octahedral geometry with the chromium center, with the three meridional sites occupied with the pyridyl and triazine nitrogen atoms of the ligand **3.4a** and **3.4b**. In both cases two chloride ligands are located in *trans* position with each other and other chlorine atom is situated *trans* to the *s*-triazine nitrogen atom of the NNN coordinating units. The Cr-N bond length for the central triazine rings of the complexes is shorter than those for the nitrogen atom of pyrazolyl and pyridyl rings.

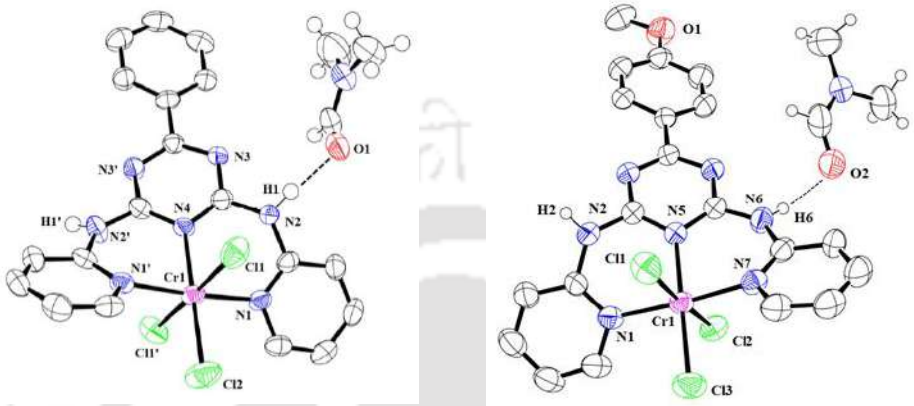

Figure 3.1. ORTEP diagram of chromium complexes **3.4a** (CCDC-2295250), **3.4b** (CCDC-2295248) (Thermal ellipsoids are drawn with 50% probability level). Selected bond lengths (in Å) for **3.4a**: Cr1-Cl1 2.320(10), Cr1-Cl2 2.308(14), Cr1-N4 2.066(3), Cr1-N1 2.078(2), N2-C6 1.358(4), N2-C1 1.387(4), NH(2)···O(1) hydrogen bond 2.042. Selected Bond Angles (in °) for **3.4a**: Cl2-Cr1-Cl1 91.67(3), N4-Cr1-Cl1 88.33(3), N1-Cr1-Cl2 92.62(6). Selected bond angles for **3.4b**: Cr(1)–N(1), 2.084(3), Cr(1)–N(5) 2.069(2), Cr(1)–N(7) 2.089(3), Cr(1)–Cl(1) 2.3050(10), Cr(1)–Cl(2) 2.3205(9), Cr(1)–Cl(3) 2.3400(10), NH(6)···O(2) hydrogen bond 1.952. Selected Bond Angles (in °) for **3.4b**: N(7)–Cr(1)–Cl(2) 91.51(7), N(1)–Cr(1)–N(7) 176.10(10), N(5)–Cr(1)–Cl(1) 88.04(7), N(1)–Cr(1)–Cl(3) 91.78(7), Cl(2)–Cr(1)–Cl(3) 91.81(4), Cl(1)–Cr(1)–Cl(2) 174.89(4).

3.3.2. Optimization studies of catalytic cross coupling of ketones

To inspect the catalytic applicability of the as-prepared chromium complex **3.4a-d**, optimization studies were initiated with 4-methoxyacetophenone (**2.7b**, 1 mmol) and cyclohexanone (**2.8a**, 1 mmol) as model substrates for catalytic cross-coupling of ketones (Table 3.1). When the reaction was carried out with 5 mol% **3.4a** complex, 4 Å molecular sieves, dry toluene (2 mL) for 8 h at 150 °C, *β*-branched *β, γ*-unsaturated ketone **2.9b** was obtained in 72% yield. The yield of **3.4a** was very similar with chromium(II) complex **3.5** (70%, entry 1) and chromium(III) complex **3.4d** (71%, entry 4). Then different substituent bearing chromium(III) complexes **3.4a-d** have been examined, which suggested that –OMe substituent containing chromium(III) complex **3.4b** showed best catalytic activity with 83% yield. Notably, no self-coupled unsaturated ketone or reverse-coupled unsaturated ketone was formed under the reaction conditions, showing excellent chemoselectivity. A decrease in the yield of **2.9b** has been observed when the reaction temperature was decreased to 130 °C (23%, entry 8), and at 120 °C, no conversion was acquired (entry 9), indicating the pronounced temperature effect in the reaction. When catalyst **3.4b** was decreased to

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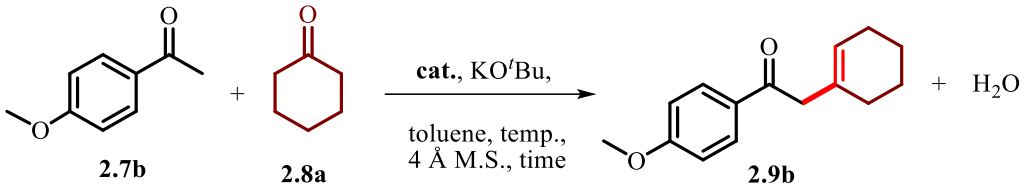
2 mol%, the yield was only 44% (entry 10), while reducing the base to 20 mol% resulted in 64% yield (entry 11).

Table 3.1. Optimization table of catalytic cross coupling of ketones[a]



2.7b + **2.8a** → **2.9b**

Entry	cat. (mol%)	KO^{t}Bu (mol%)	temp (°C)	time (h)	yield (%)	
					2.9b	**2.7b**
1	**3.4a** (5)	30	150	8	72%	8%
2	**3.4b** (5)	30	150	8	83%	0%
3	**3.4c** (5)	30	150	8	78%	5%
4	**3.4d** (5)	30	150	8	71%	6%
5	**3.5** (5)	30	150	8	70%	12%
6	**$CrCl_3$•3THF** (5) + **3.3b** (5)	30	150	8	67%	15%
7	**3.4b** (5)	30	140	8	62%	20%
8	**3.4b** (5)	30	130	8	23%	61%
9	**3.4b** (5)	30	120	8	n.d.	94%
10	**3.4b** (2)	30	150	8	44%	36%
11	**3.4b** (5)	20	150	8	64%	18%
12[b]	**3.4b** (5)	30	150	8	24%	51%
13[c]	**3.4b** (5)	30	150	8	34%	60%
14	**$CrCl_3$•3THF** (5)	30	150	8	12%	85%
15	**$CrCl_3$•6H_2O** (5)	30	150	8	10%	86%
16	**3.4b** (5)	30	150	4	35%	48%
17	–	30	150	8	n.d.	n.d.
18	–	200	150	8	14%	51%
19	**3.4b** (5)	–	150	8	10%	78%

Reaction conditions: [a] **2.7b** (1 mmol), **2.8a** (1 mmol), KO^{t}Bu (x mol%), dry toluene (2 mL) and 4 Å molecular sieves (0.04 g) were heated in a closed 50 mL reaction tube for given time under argon. Isolated yield. [b]Under air in the absence of 4 Å molecular sieves. [c] Using Dean-Stark apparatus.

The yield of **2.9b** was dramatically decreased in the absence of molecular sieves, indicating an important role of molecular sieves in the current process (24%, entry 12). Also, a decrease in the

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yield of **2.9b** was observed when the reaction was performed with Dean–Stark apparatus *via* azeotropic removal of water (entry 13). Control experiments suggest the necessity of catalyst and base in the cross-coupling reaction (entries 14-19).

3.3.3. Substrate scope for catalytic cross coupling of ketones

With the optimized reaction conditions in hand, we probed the scope of various functionalized cyclohexanones employing acetophenone **2.7o**. Various 4- substituted cyclohexanones (**2.8a-d** and **3.7a-d**) were well-suited as substrates under the optimized reaction conditions, leading to the formation of the corresponding *β*, *γ*-unsaturated ketones **2.9w**, **2.9t**, **3.8a-f** in good yields. Likewise, acetophenones bearing either electron-donating or electron-withdrawing groups on the phenyl ring at different positions (*ortho*, *meta*, and *para*) reacted well with cyclohexanone **2.8a**, delivering the corresponding *β*, *γ*-unsaturated ketone **2.9a-l** and **3.8g-j** in 70%−92% yields. Ketones with electron-withdrawing substituents such as 4-Cl, 4-Br gave higher yields for the corresponding products than the ketones containing electron-donating substituents like 4-OMe, 4-NMe_2. Single-crystal XRD analysis of the −NMe_2 derivative **3.8g** unambiguously confirms the structure. Notably, the retention of sensitive functional groups (4-Cl, 4-Br, 4-I, 4- C≡CPh, 3-Br, 3-CF_3, 4-O-allyl, 4-SMe, and −ketal) in the final products showcases the excellent chemoselectivity of the present protocol. Polysubstituted aromatic methyl ketone and fused aromatic methyl ketone also led to the effective formation of the desired product, **2.9i**−**2.9l**. Gratifyingly, a redox-active ferrocenyl moiety was compatible with this method (**3.8j**, 52% yield). I, then examined the hybrid synthesis of a substituted aromatic ketone with substituted cyclohexanone. Fortunately, the desired unsaturated ketones **3.8aa**−**ah**, **2.9p**−**s** were obtained with moderate to good yield. 3-Methyl cyclohexanone **2.8f** was also successfully employed in the reaction to provide *β*, *γ*-unsaturated ketones **2.9v** in 78% yield. Since *β*, γ-unsaturated ketone motifs are present in many natural products and pharmaceutical active intermediates, we performed modification of natural products with various biological activities to access a new pool of functionalized analogues. Naturally occurring musk fragrance celestolide **2.7w**, synthetic fragrance tonalide **3.6g**, and pregnancy hormone progesterone **3.6h** were subjected to the optimized reaction conditions with cyclohexanone to afford the products **2.9ai**, **3.8ai-ak** respectively. In addition, modification of derivatives of cholesterol could be achieved by means of this method, which gave product **2.9aj** in 52% yield.

Furthermore, the scope of the methodology was expanded to a variety of other higher analogues of cyclic aliphatic ketones, such as cycloheptanone, cyclooctanone, cyclododecane, and cyclopentadecanone to obtain **2.9af**−**ah** and **3.11a**. Intriguingly, acyclic alkyl ketones such as acetone, diethyl ketone, and dipropyl ketone were also suitably created with this method; however, it leads to the formation of the *α*, *β*-enones **3.12a**−**c**, **2.9b**−**c**. It is noteworthy that the synthetically challenging aliphatic methyl ketone was also found to be amenable to this method, giving **3.11b**, **2.9aa-ac** and **2.9ae** in moderate to good yields. To our delight, *β*, *γ*-unsaturated ketone **2.9ae** was

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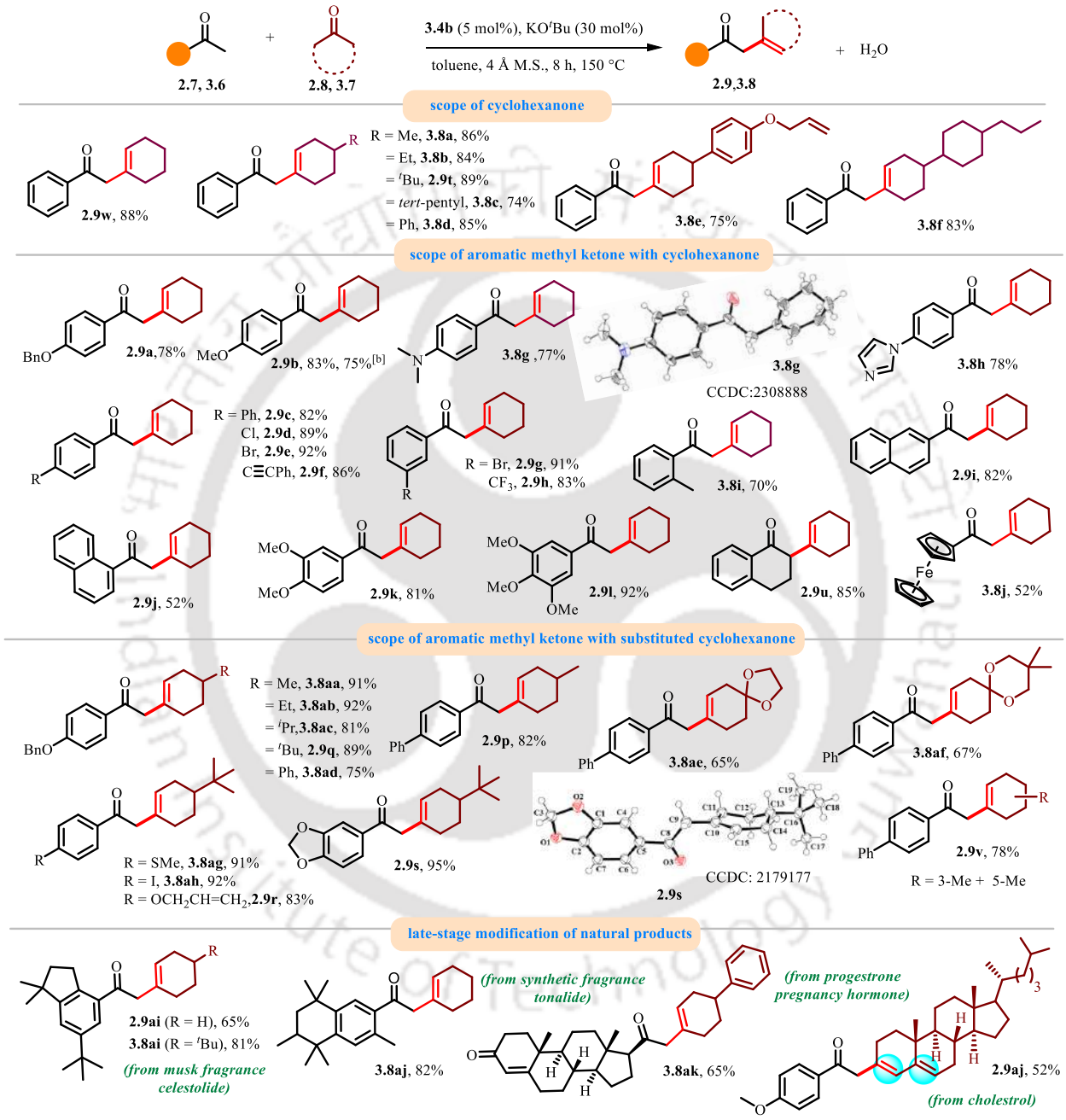
successfully prepared using acetone as a simple three-carbon feedstock. A 5 mmol-scale synthesis of **2.9b** in 75% yield proved the scalability of the present protocol.

Table 3.2. Substrate scope for catalytic cross coupling of ketones[a]



Reaction condition: [a] aromatic ketone (1 mmol), cyclohexanone derivatives (1 mmol), **3.4b** (5 mol%), KO^{t}Bu (30 mol%), dry toluene (2 mL) and 4 Å molecular sieves (0.04 g) were heated at 150 °C in a closed reaction tube for 8 h, isolated yield. [b] 5 mmol scale.

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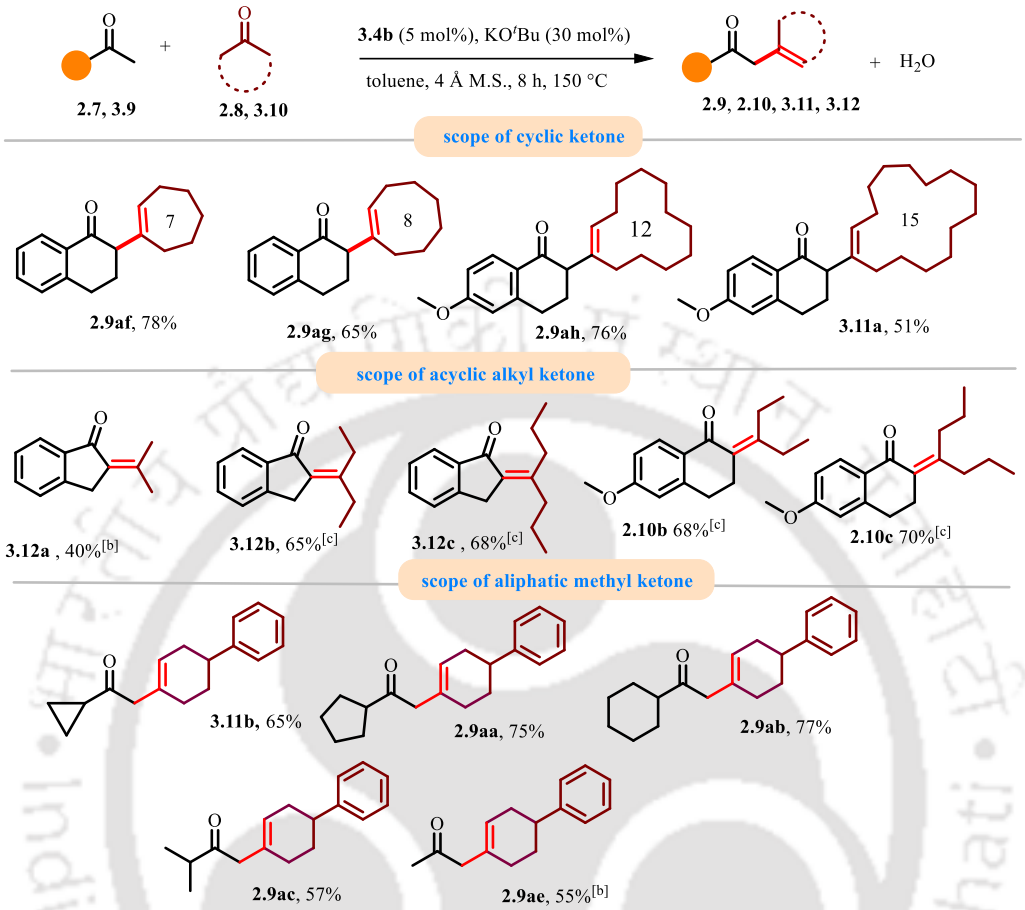
Table 3.3. Substrate scope for catalytic cross coupling of ketones[a]



Reaction condition: [a] **2.7** or **3.9** (1 mmol), **2.8** or **3.10** (1 mmol), **3.4b** (5 mol%), KO^{t}Bu (30 mol%), dry toluene (2 mL) and 4 Å molecular sieves (0.04 g) were heated at 150 °C in a closed reaction tube for 8 h, isolated yield. [b] with 10 equiv. acetone. [c] with 6 equiv. acyclic alkyl ketone.

3.3.4. Post synthetic modification

Next, the *β*, *γ*-unsaturated ketones were easily transformed to other useful molecules. For instance, compound **2.9c** undergo reductive amination to form secondary amine **3.13**. The reaction of **2.9c** with NH_2OH•HCl afforded corresponding ketoxime **3.14**, (details in experimental section 3.4.D, Scheme 3.22) which could then further be transformed into new class of oxa-azaspiro derivative **3.15**. The C=C bond of **2.9c** could be selectively reduced to afford **3.16**. The compound **3.8f** was easily converted into corresponding *β*, *γ*-unsaturated alcohol **3.17** *via* sodium borohydride reduction. Again, treatment of **3.8f** with DDQ delivered selectively an oxidized product **3.18** in 82% yield. Furthermore, *para*-functionalized *β*, *γ*-unsaturated ketone **2.9e** was accomplished by using block buster metal-catalyzed cross-coupling strategy, delivering **3.8h**, and **2.9c**, respectively (Scheme 3.5) (Detailed synthetic procedure is discussed in section 3.5).

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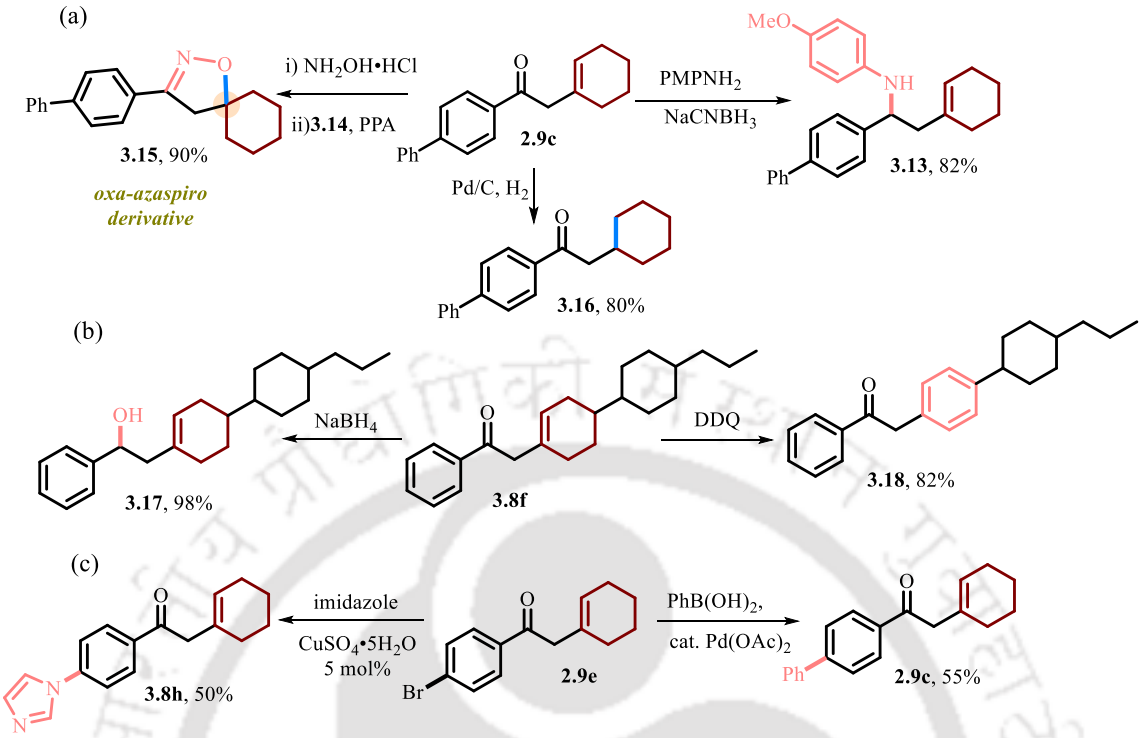
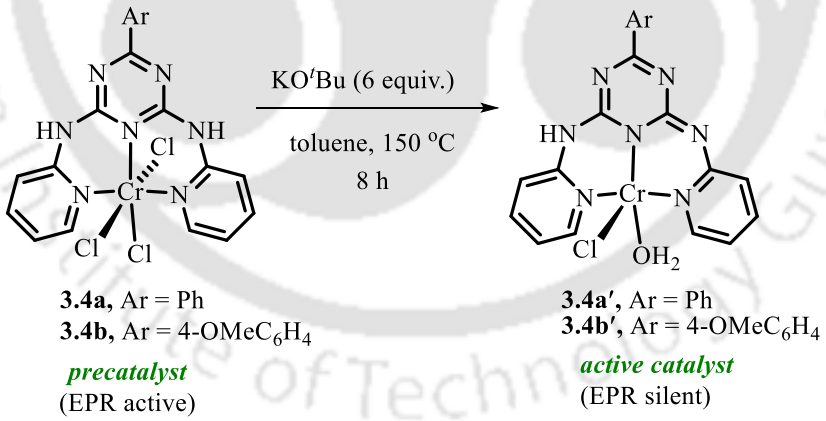


Scheme 3.5. Post synthetic transformation

3.3.5. Spectroscopic characterization of chromium complexes 3.4a and 3.4b and the corresponding active catalyst 3.4a' and 3.4b'



Scheme 3.6. Active chromium species

3.3.5.1. EPR study

To gain more insight into the active chromium species [Cr(III) or Cr(II)] in the catalytic cycle, a titration experiment was performed by adding a base into precatalyst **3.4a** and **3.4b** individually, and monitoring the EPR spectra. Upon loading the base, the paramagnetic signal of chromium (III)

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is disappeared and formed EPR-silent chromium (II) species. Due to non-Kramers $S = 2$ ground states, it is expected not to observe EPR signal.[17]

Experimental procedure: The reaction tube was equipped with a stir bar, complex **3.4a** or **3.4b** (10 mg, 1 equiv.), KO^{t}Bu (6 equiv.), and toluene (0.5 mL). The reaction mixture was stirred at 150 ^{o}C for 8 h in an oil bath. The resulting solution was cooled to room temperature; all the volatile was removed under reduced pressure. The obtained green residue was then dissolved in toluene (0.5 mL) and subjected for EPR analysis at 298 K.

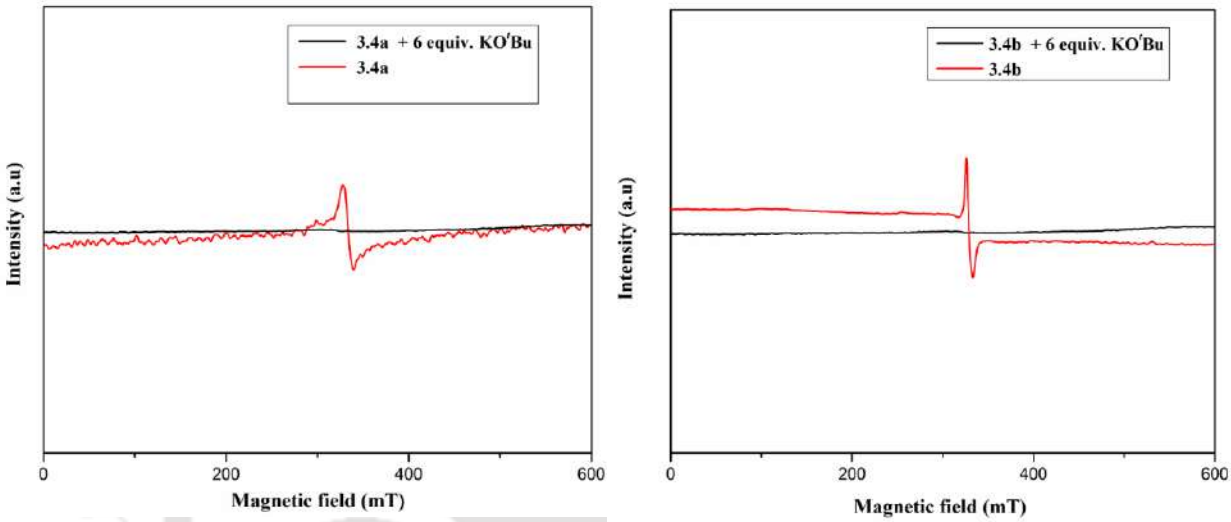

Figure 3.2. EPR spectrum of **3.4a** (left) and **3.4b** (right) w/t base. X-band microwave frequency (GHz): 9.14, modulation frequency (KHz): 100.

3.3.5.2. HRMS study

The complex **3.4a** and **3.4b** were dissolved in methanol and then analyzed the ESI-HRMS. The spectral data for complexes **3.4a** and **3.4b** are given in Figure 3.3 and 3.4.

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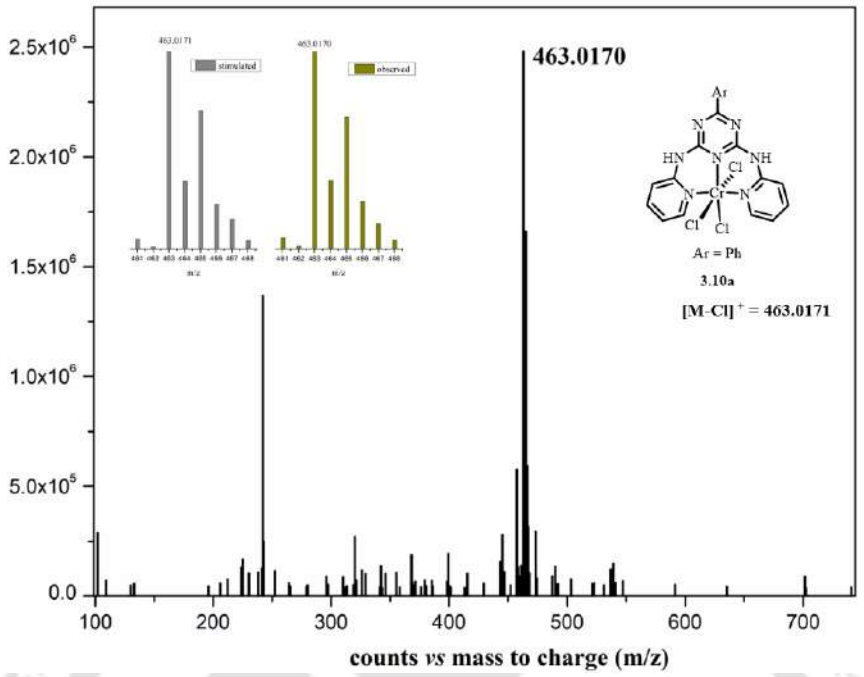

Figure 3.3. HRMS spectra of complex **3.4a**

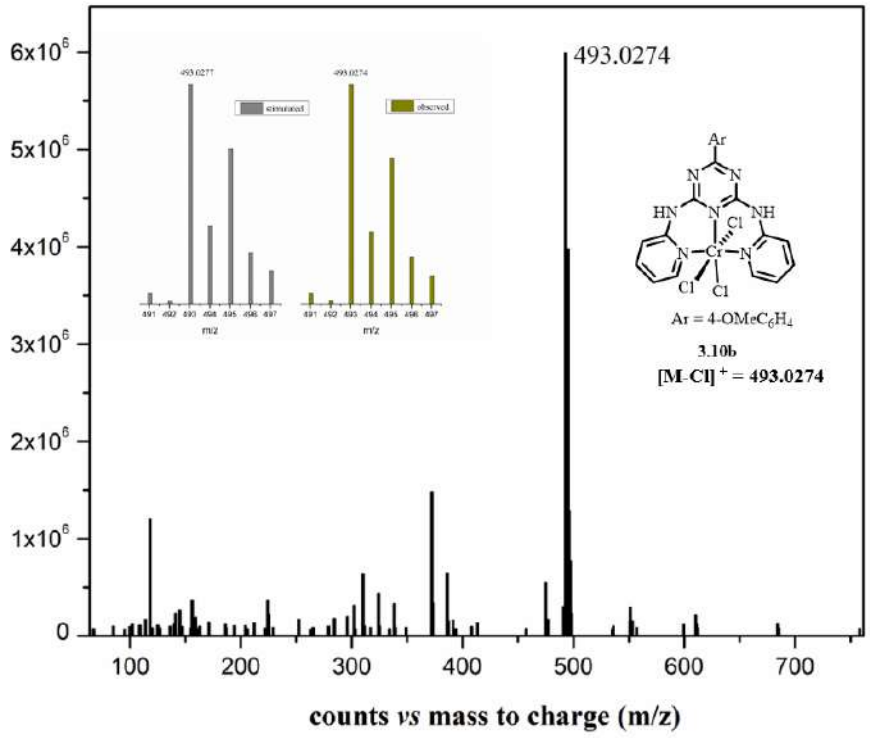

Figure 3.4. HRMS spectra of complex **3.4b**

Procedure: The reaction tube was equipped with a stir bar, complex **3.4a** (10 mg, 1 equiv.), varying equivalent of KO^{t}Bu (6 equiv.), and toluene (0.5 mL). The reaction mixture was stirred at

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150 ºC for 8 h in an oil bath. The resulting solution was cooled to room temperature, all the volatile was removed under reduced pressure. The obtained green residue was then dissolved in methanol, and analyzed the ESI-HRMS (Figure 3.5 and 3.6).

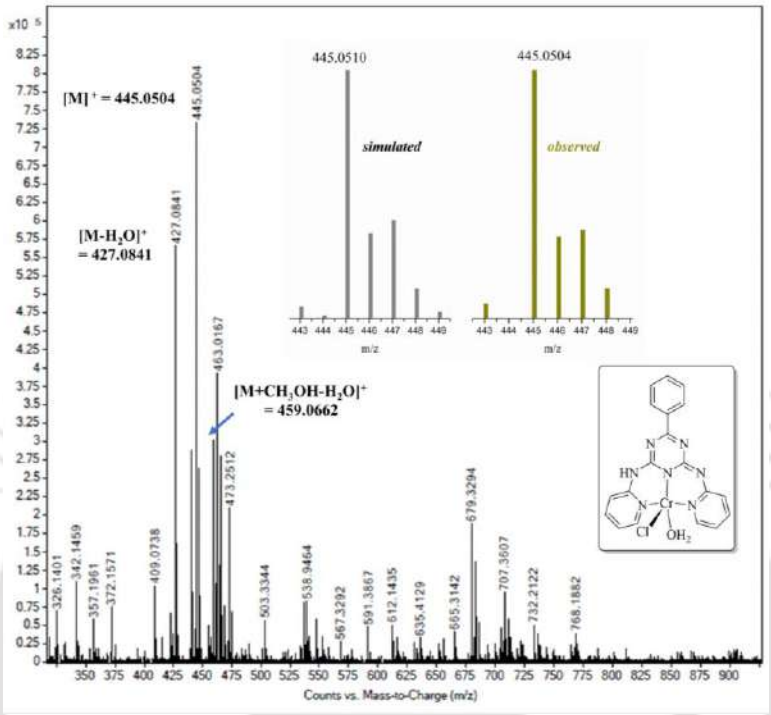

Figure 3.5. HRMS (ESI) spectra of active species **3.4a'**.

Procedure: The reaction tube was equipped with a stir bar, complex **3.4b** (10 mg, 1 equiv.), varying equivalent of KO^{t}Bu (6 equiv.), and toluene (0.5 mL). The reaction mixture was stirred at 150 ºC for 8 h in an oil bath. The resulting solution was cooled to room temperature; all the volatile was removed under reduced pressure. The obtained green residue was then dissolved in methanol, and quickly analyzed the ESI-HRMS.

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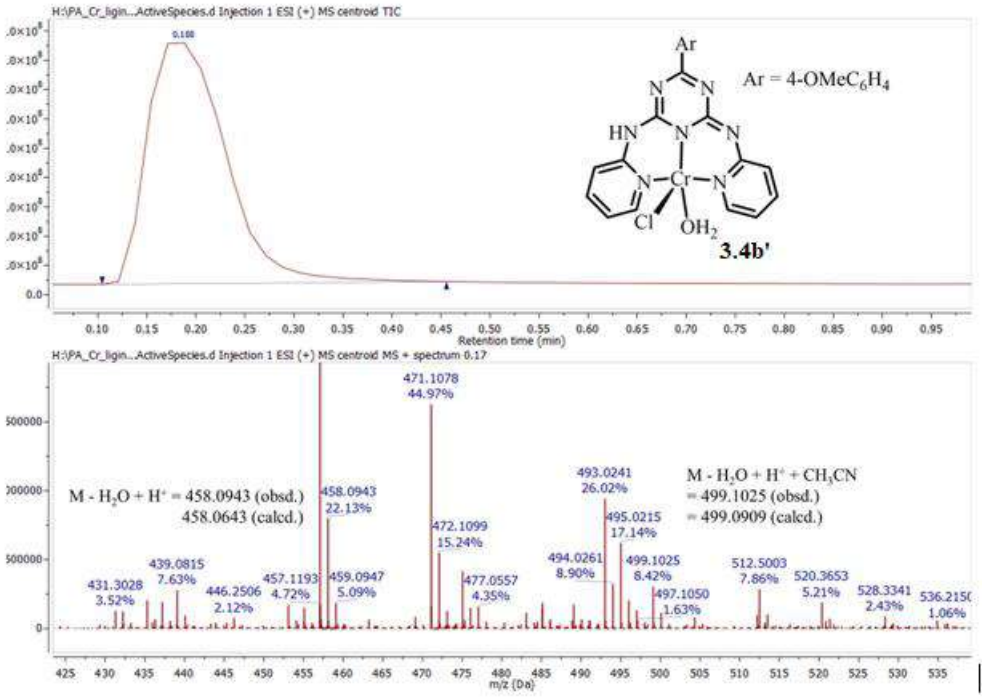

Figure 3.6. HRMS (ESI) spectra of active species **3.4b'**

3.3.5.3. Magnetic moments of 3.4b and 3.4b' in solution (using Evans method)

Magnetic moments of **3.4b** and **3.4b'** in solution were measured according to NMR method described by Evans.[18]

Experimental procedure for 3.4b: A solution of **3.4b** (2.9 mg, 0.0055 mmol) in a 1 mL mixture of DMSO-d_6/^{t}BuOH (98:2) was prepared and loaded in the NMR tube. To the same NMR tube, a capillary containing 2% ^{t}BuOH in DMSO-d_6 solution was put in. Then NMR spectrum was measured at 25 ºC on a Bruker 600 MHz NMR spectrometer. A chemical shift difference of the ^{t}BuOH signal between the inner and outer tubes was observed at 90 Hz. The magnetic moment was calculated using the following equation: $\mu_{eff} = 798(\sqrt{(\chi_M T)}$, $\chi_M = (3\Delta f)/(1000fc)$, T = 298 K, f = frequency of NMR instrument in MHz, Δf = paramagnetic shift of the solvent in Hz, c = molar concentration of the complex. $\mu_{eff} = 798\sqrt{(\chi_M T)} = (4.91 \times 10^{-3} \times 798) = 3.92$ B.M. The magnetic moment for **3.4b** was obtained as 3.92 B.M.

Experimental procedure for 3.4b': The sample for **3.4b'** was obtained by the reaction of complex **3.4b** (4.1 mg, 1 equiv.), KO^{t}Bu (6 equiv.), in dry toluene (0.5 mL) at 150 ºC in an oil bath for 8 h under the nitrogen atmosphere. After removal of the volatiles under reduced pressure, the compound was loaded in 1 mL mixture of DMSO-d_6/^{t}BuOH (98:2) and then the magnetic moment of the **3.4b'** was measured as mentioned above. NMR spectrum was measured at 25 ºC on a Bruker 600 MHz NMR spectrometer. A chemical shift difference of the ^{t}BuOH signal between the inner and outer tubes was observed at 198 Hz. The magnetic moment was calculated for **3.4b'** using

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above equation. $\mu_{eff} = 798\sqrt{(\chi_M T)} = (6.13 \times 10^{-3} \times 798) = 4.9$ B.M. The result is in agreement with the line of HS Cr(II) species.

3.3.5.4. XPS Analysis

XPS studies was performed by using freshly synthesized **3.4b** complex and **3.4b'** species.

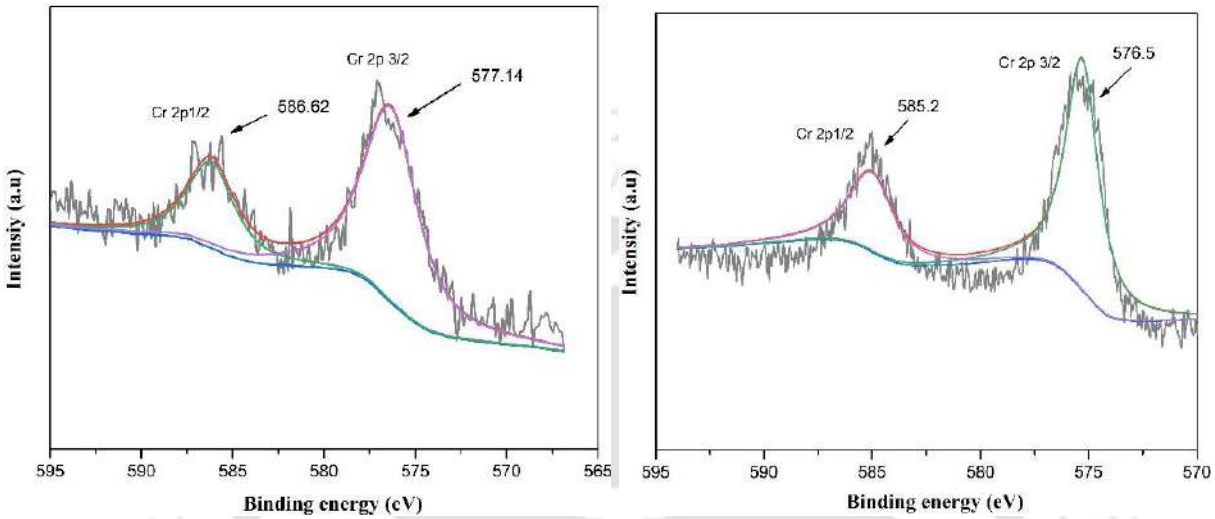

Figure 3.7. Binding energies of XPS spectra for the analysis of Cr(III) (left figure) and Cr(II)-species (right figure).

Sample preparation for **3.4b':** The sample for XPS studies was obtained by reaction of complex **3.4b** (10 mg, 1 equiv.), KO^{t}Bu (6 equiv.), in toluene (0.5 mL) at 150 ºC for 8 h in an oil bath. After removal of the volatiles under reduced pressure, the sample was analyzed by XPS studies without further purification.

I examined the oxidation state of Cr after the reaction of **3.4b** with base by analysis of Cr 2p by core-level X-ray photoelectron spectroscopy (XPS), which was fitted with spin–orbital split $2p_{1/2}$ and $2p_{3/2}$ components (Figure 3.7, right figure). Two sets of XPS peaks appeared at 585.2 and 576.5 eV for the binding energies of the $2p_{1/2}$ and $2p_{3/2}$ components, respectively (Figure 3.7, right figure). In comparison with the related data that were obtained for the **3.4b** mixture (Figure 3.7, right figure), the formation of Cr(II) by a reaction with base can be considered. Observation is in accordance with the literature.[19]

3.3.6. Mechanistic studies

In order to confirm the homogeneous nature of the chromium complex **3.4b** in the catalytic reaction with 0.5 equiv. mercury was carried out, which did not affect the yield of product **2.9c**, hence ruling out the possibilities of heterogeneous pathway (Scheme 3.7).

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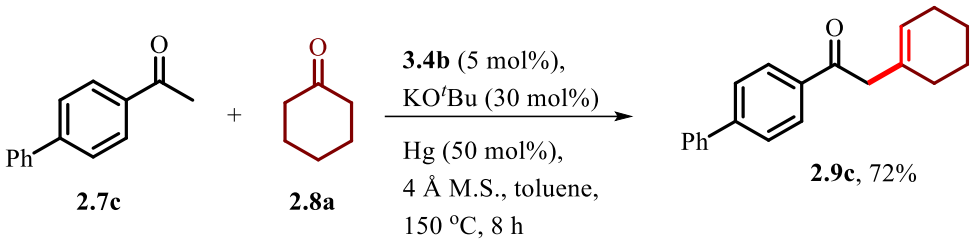
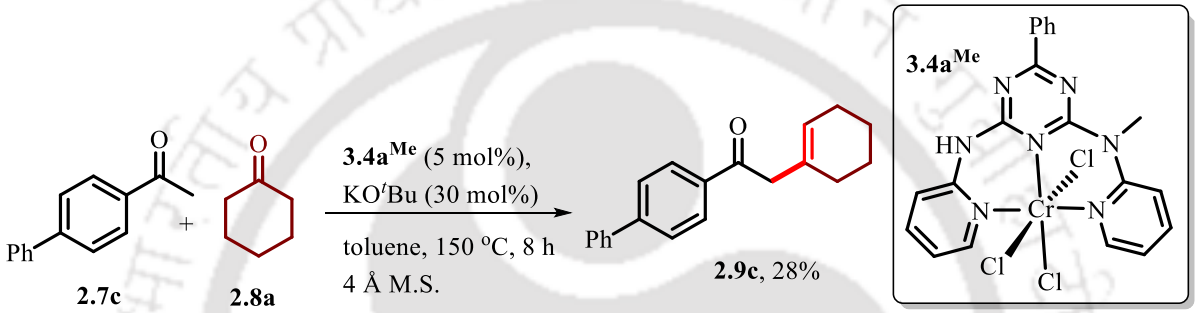


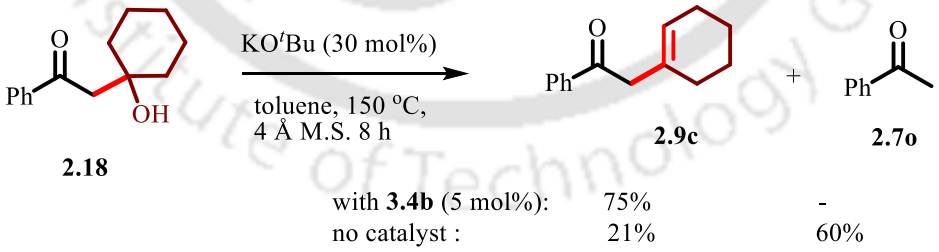
Scheme 3.7. Mercury drop experiment

The impact of the -NH functionality was elucidated by using complex **3.4a^{Me}** as the precatalyst, resulting a lower yield of **2.9c** upto 28% suggesting the importance of the -NH functionality and metal-ligand cooperativity (MLC) in the reaction pathway (Scheme 3.8).



Scheme 3.8. The impact of the –NH functionality in catalysis

To probe further the involvement of aldol product in the cross-coupling reaction, the reaction was examined with aldol product **2.18** under standard conditions, product **2.9c** was obtained with 75% yield in the presence of catalyst, and 21% yield obtained in the absence of catalyst (along with 60% of **2.7o** recovered from the reaction mixture) (Scheme 3.9). The result suggests that aldol product **2.18** is likely to be the reaction intermediate, and a retro-aldol pathway is dominated only with base.



Scheme 3.9. Proof for the aldol product as an intermediate in cross-aldol reaction

In order to probe the origin of high chemoselectivity, the reaction was examined with self-aldol product **2.14** and reverse cross-aldol product **2.16**, independently, under standard reaction conditions (Scheme 3.10). A lower yield of corresponding condensation product **3.15** (20%) and **2.17** (29%), along with recovered ketone **2.7c** suggests the suppression of self- and reverse cross-aldol condensation product, possibly due to involvement of retro-aldol reaction. Rate of the retro-

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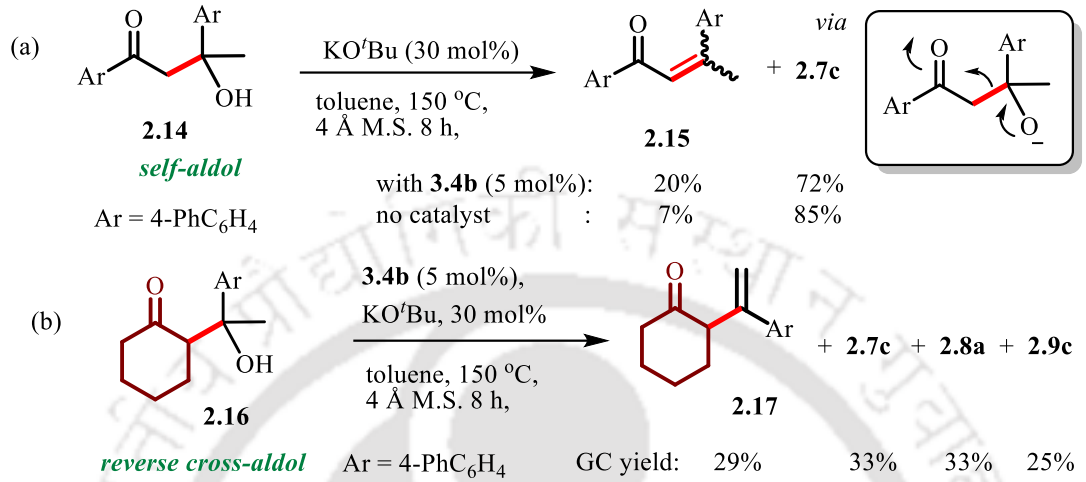
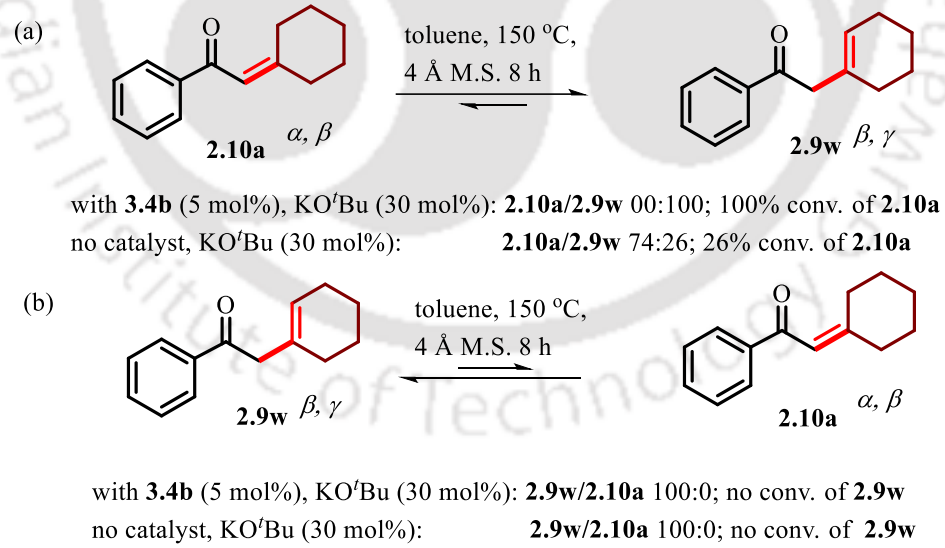
aldol reaction is possibly much faster than corresponding condensation (since there was no any self- or reverse cross-aldol condensation product **2.15** and **2.17**, respectively, identified from the reaction mixture of **2.7c** and **2.8a**).



Scheme 3.10. Proof for the origin of high chemoselectivity

Furthermore, study of the equilibria between *α, β*- and *β, γ*- unsaturated ketones suggests that the *α, β*-isomer **2.10a** is the kinetically controlled product, which undergoes subsequent isomerization to provide thermodynamically stable *β, γ*-isomer of **2.9w** (Scheme 3.11, the reason for the stability of *β, γ*-isomer is already discussed in chapter 2 section Scheme 2.17).



Scheme 3.11. Study the equilibria between *α, β*- and *β, γ*-unsaturated ketones

Also, it is worthy to note that a stoichiometric reaction of Cr(III)-complex **3.4a** showed no conversion from **2.10a** to **2.9w**. On the other hand, Cr(II)-complex **3.5** afforded 62% conversion of **2.10a**, indicating the importance of Cr(II) species in the isomerization (Scheme 3.12).

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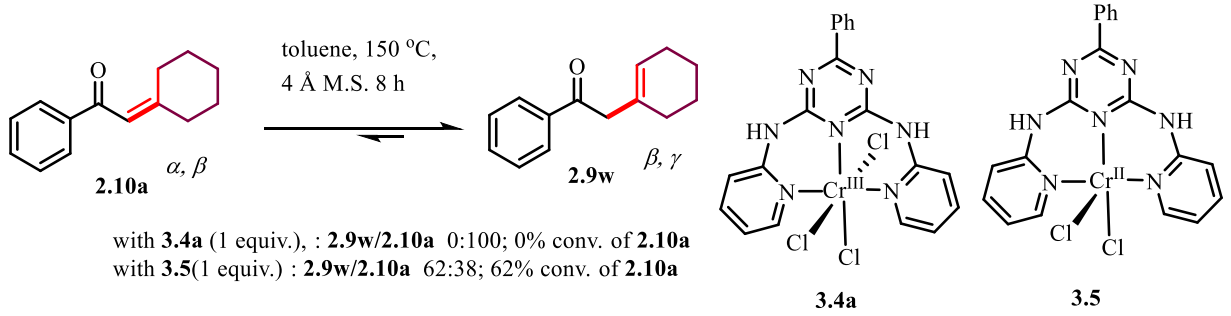
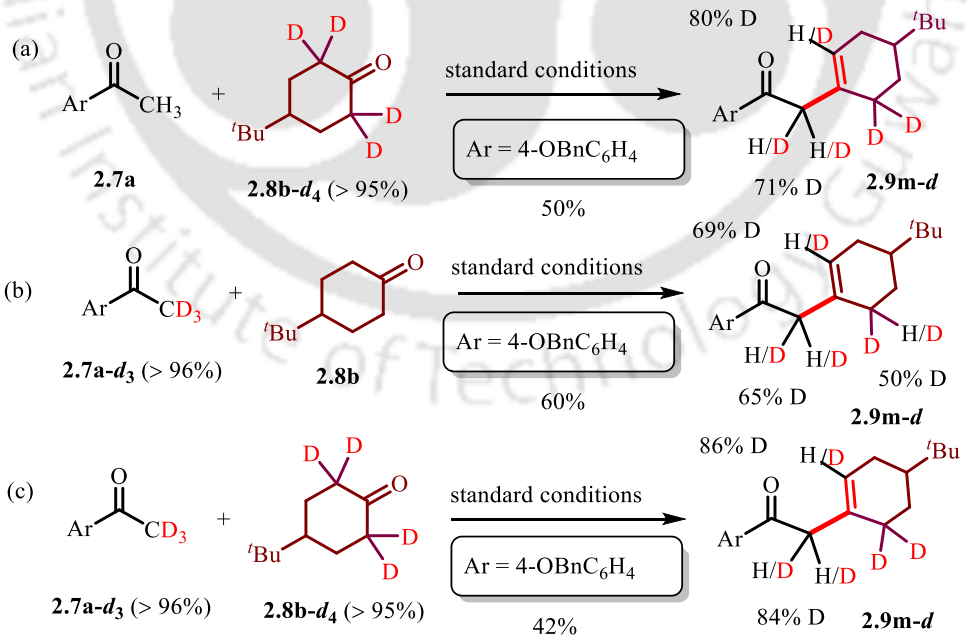


Scheme 3.12. Study the equilibria between *β*-branched *α, β*- and *β, γ*-unsaturated ketones using **3.4a** and **3.5** complexes.

Additionally, a deuterium-labeling experiment was performed in the cross-coupling reaction to validate the involvement of isomerization (Scheme 3.13). The reaction between **2.7a** and **2.8b**–***d*₄** led to the 71% D incorporated product at the *α*-position of **2.9m**–***d***. On the other hand, when the reaction was conducted with **2.8b** and **2.7a**–***d*₃**, 65% D incorporated product at the *α*-position of **2.9m**–***d*** was observed. The higher D incorporation in the first case and the higher H incorporation in the latter case at the *α*-position, suggests that the major reaction pathway for the formation of *β, γ*-unsaturated ketone proceeds *via* the isomerization of *α, β*-unsaturated ketone. Also, the lack of 100% H/D incorporation reveals that the direct formation of the *β, γ*- unsaturated ketone as a minor pathway cannot be ruled out. Further, the reaction between **2.7a**–***d*₃** and **2.8b**–***d*₄** provided minor H incorporated product at the *α*-position and *γ*-position which can be attributed to a small amount of base catalysed H/D scrambling of ketones prior to the coupling with the *in situ* formed H_2O/D_2O.



Scheme 3.13. Deuterium-labelling experiments

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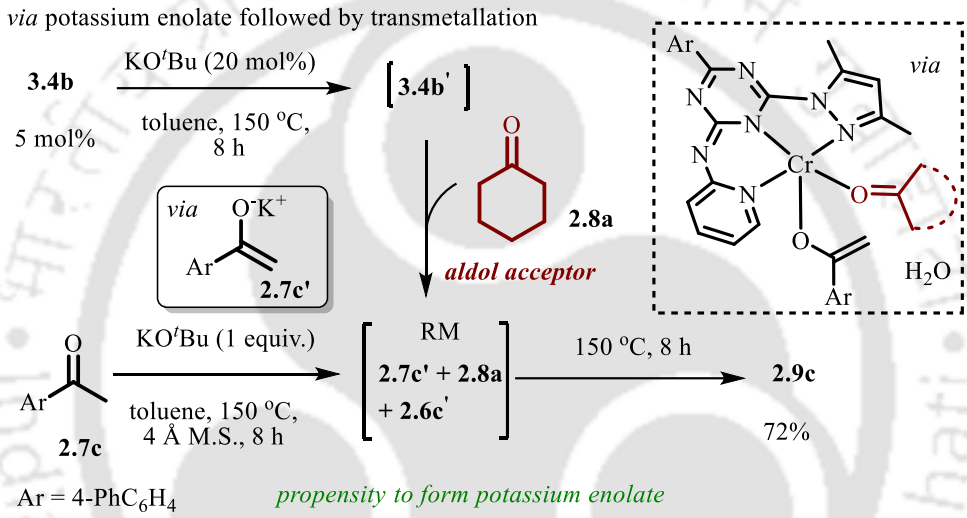
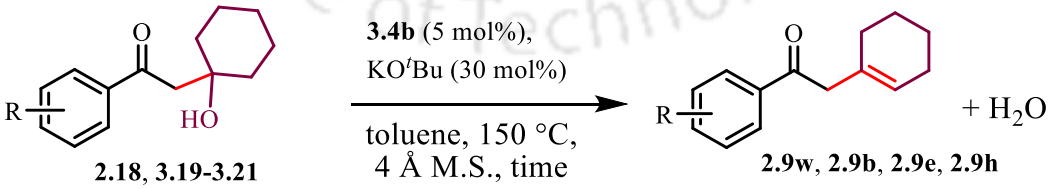
Since the roles of chromium catalyst and base are significant in this reaction, experimental support has been given for their importance in catalysis. Study suggests that the reaction proceeds *via* potassium enolate followed by transmetallation with Cr-complex. To investigate the mechanistic pathway for the formation of potassium enolate followed by transmetallation, following reaction was designed: a reaction mixture of freshly prepared active Cr(II) species **3.4b'** and aldol acceptor **2.8a** was added to the solution of potassium enolate **2.7c'** (presuming **2.7c'** is formed by the reaction of aldol donor **2.7c** and 1 equiv. of base under the reaction condition) and stirred the reaction mixture for 8 h at 150 °C. The desired condensation product **2.9c** was obtained in 72% yield (Scheme 3.14). The result indicates that there is possible involvement of potassium enolate of aldol donor, followed by transmetallation with Cr-complex.



Scheme 3.14. Mechanistic understanding of Cr-aldol reaction in the presence of base.

To study the electronic influence in the reaction, the Hammett correlation study was performed using various aldol substituents under standard reaction conditions (Scheme 3.15). A positive slope of +0.92 suggests little development of negative charge in the transition state which is stabilised by the electron-withdrawing substituents.



2.18, R = H; **3.19**, R = 4-OMe; **3.20**, R = 4-Br; **3.21**, R = 3-CF$_3$

Scheme 3.15. Hammett correlation study

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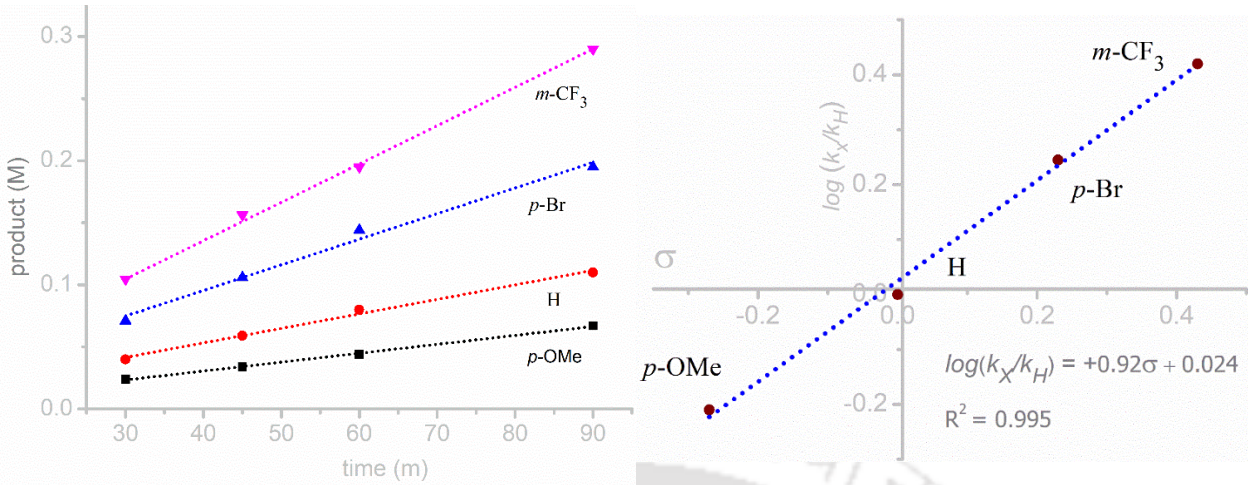
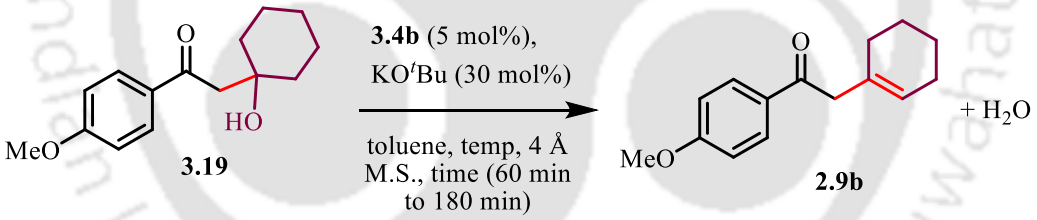


Figure 3.8. Kinetic profile for the initial rates (left figure) and Hammett plot (right figure)

Further, the effect of temperature on the rate of aldol condensation was examined by using Eyring analysis (Scheme 3.16). The activation parameters $\Delta H^{\ddagger}$ = + 26.81 ± .047 kJ mol^{-1} and $\Delta S^{\ddagger}$ = +244.6 ± 5 J mol^{-1} K^{-1} suggested the involvement of dissociative pathway in the turnover-limiting step. Since the process involved aldol-condensation, followed by isomerization leading to desired *β*, *γ*-unsaturated ketone, electronic effect on the isomerization step was also examined using competitive experiments with *α*, *β*-isomer of **2.10a**, and **2.10d** in 1:1 ratio. A comparable yield of **2.9w** (30%) and **2.9b** (28%) ruled out any possible involvement of electronic effect on the isomerization step.



Scheme 3.16. Eyring study

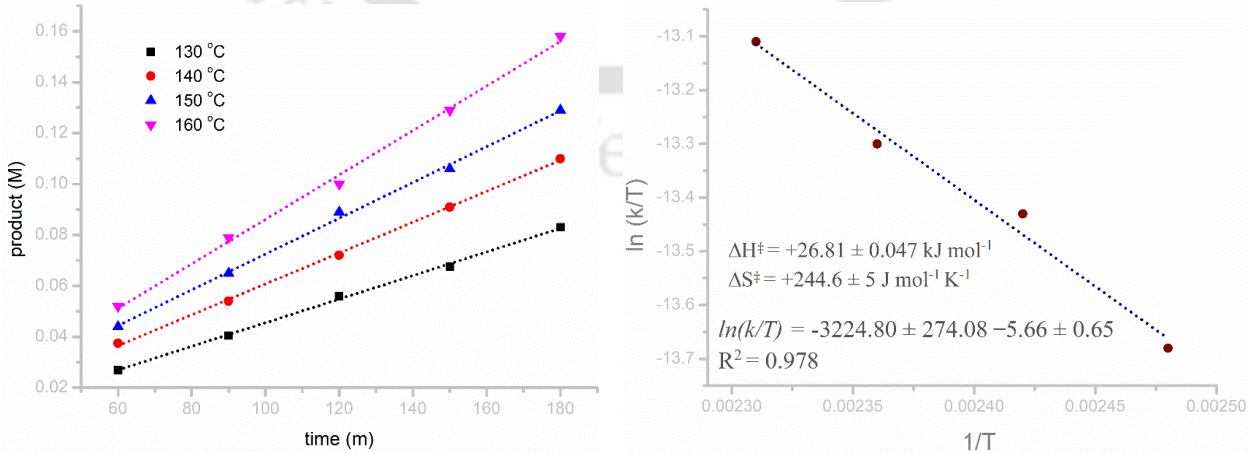


Figure 3.9. Concentration [Product] vs time plot at different temperatures (left) and Eyring plot (right)

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$ln(k/T)$ = -3224.8 ± 274.08 − 5.66 ± 0.65, R^2 = 0.978

$\Delta H^{\ddagger}$ = +26.81 ± 0.047 kJ mol^{-1}

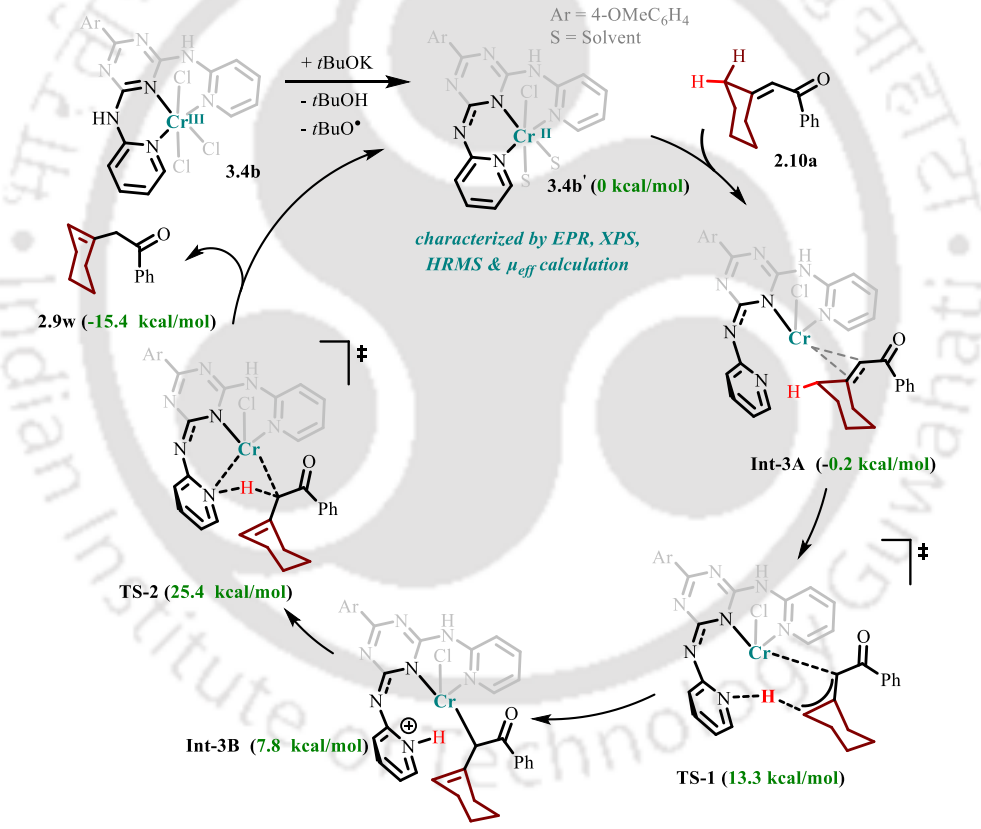
$\Delta S^{\ddagger}$ = +244.6 ± 5 J mol^{-1} K^{-1}

Activation enthalpy ($\Delta H^{\ddagger}$) and activation entropy ($\Delta S^{\ddagger}$) values were obtained from the slope and intercept of plots of ln(k/T) vs 1/T (Figure X.) using the following equation:

$$\ln(k/T) = -\Delta H^{\ddagger}/R(1/T) + \ln(k_B/h) + \Delta S^{\ddagger}/R$$

where k_B (Boltzmann constant) = 1.380649 × 10^{-23} m^2 kg s^{-2} K^{-1}, R (universal gas constant) = 8.3144598 $J{\cdot}mol^{-1}{\cdot}K^{-1}$, and h (Planck's constant) = 6.62607015 × 10^{-34} m^2 kg / s.

To gain insight the pathway for the isomerization of *α, β-* to *β, γ*-unsaturated ketone, I have performed DFT calculations using M06L/6-31G(d) level of theory (Scheme 3.17). The pyridyl-N of the NNN ligand in catalyst **3.4b′** undergoes arm di-coordination, creating an open site for **2.10a** coordination.



Scheme 3.17. Proposed pathway for the isomerization

The resulting coordination of **2.10a** forms the intermediate **Int-3A** (ΔG = -0.2 kcal/mol). Furthermore, this interaction complex demonstrates a preference for an η^2-type interaction between the Cr centre and the exocyclic double bond of the ketone. Following this **Int-3A** undergoes a proton transfer to the pyridinic nitrogen through **TS-1** with a $\Delta G^{\ddagger}$ of 13.3 kcal/mol, leading to the formation of intermediate **Int-3B** (ΔG = 7.8 kcal/mol). Subsequently, a proton transfer to the *α-*

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position of the **2.10a** *via* **TS-2** occurs with a $\Delta G^{\ddagger}$ of 25.4 kcal/mol, completing the cycle (ΔG = -15.4 kcal/mol). The overall reaction profile indicates that **TS-2** represents the energy-demanding step for the proton transfer from the γ- to α-centre, facilitated by a plausible η^2-type interaction originating from the Cr centre of the complex.

3.4. Summary

In summary, chromium-catalyzed cross-coupling of ketones to β-branched β, γ-unsaturated ketones were demonstrated. The work has disclosed about the origin of regioselectivity between α, β- and β, γ-unsaturated ketone by performing various control experiments, deuterium labeling experiments and DFT studies and also argued about the origin of high chemoselectivity. Further, a vast range of sensitive and challenging functional groups were amenable in the current protocol. I hope that this report shades a way towards further development of molecular catalysts using cost-effective chromium catalysts for the synthesis of complex molecular architecture from simple building blocks.

3.5. Experimental section

General Experimental

All the reagents and chemicals were purchased from common commercial suppliers like Sigma-Aldrich, Alfa Aesar, Merck, BLD Pharma, Spectrochem, Avra Synthesis Pvt. Ltd., Finar Chemicals and directly used as received without any further purification unless otherwise mentioned. Compound 2,4-dichloro-6-aryl-1,3,5-triazine (**2.3a-c**),[20] 4-(phenylethynyl)acetophenone (**2.7f**),[21] 1-(4-(1*H*-imidazol-1-yl)phenyl)ethan-1-one (**3.6b**),[22] aldol products, 2-cyclohexylidene-1-(4-methoxyphenyl)ethan-1-one (**2.10d**)[23] 1-([1,1'-biphenyl]-4-yl)-2-(1-hydroxycyclohexyl)ethan-1-one (**2.13**), [23] 1,3-di([1,1'-biphenyl]-4-yl)-3-hydroxybutan-1-one (**2.14**), [23]2-(1-([1,1'-biphenyl]-4-yl)-1-hydroxyethyl) cyclohexan-1-one (**2.16**), 2-(1-hydroxycyclo hexyl)-1-phenylethan-1-one (**2.18**), 2-(1-hydroxy cyclohexyl)-1-(4-methoxyphenyl)ethan-1-one (**2.19**),[23] 1-(4-bromophenyl)-2-(1-hydroxycyclo hexyl) ethan-1-one (**2.20**),[23] 2-(1-hydroxycyclohexyl)-1-(3-(trifluoromethyl)phenyl)ethan-1-one (**2.21**) [23] were prepared according to the reported literature. THF and toluene were freshly distilled over sodium–benzophenone before use. ^{1}H, ^{13}C, and ^{19}F NMR spectra of the compounds were measured in $CDCl_3$, DMSO-d_6, CD_3OD as a solvent by using TMS as an internal standard. Chemical shifts, δ (in ppm), are reported relative to TMS δ (^{1}H) 0.0 ppm, δ (^{13}C) 0.0 ppm, which was used as the internal reference. Otherwise the solvents residual proton resonance and carbon resonance ($CHCl_3$, δ (^{1}H) 7.26 ppm, δ (^{13}C) 77.16 ppm; DMSO-d_6, (^{1}H) 2.50 ppm, δ (^{13}C) 39.52 ppm; CD_3OD, δ (^{1}H) 3.31 ppm, δ (^{13}C) 49 ppm) were also used for calibration. Bruker Avance III 600 and 400 spectrometers were used to record the NMR spectra. Chemical shifts (δ) values were reported in ppm and spin-spin coupling constant (J) were expressed in Hz, and other data were reported as follows: s = singlet, d = doublet, dd = doublet of doublet, dt = doublet of triplet, t = triplet, m = multiplet, q = quartet, sext = sextet, br = broad, and brs = broad singlet. IR spectra were recorded on Perkin Elmer Instrument at normal temperature making KBr pellet grinding the sample with KBr (IR Grade). MS (ESI-HRMS): Mass

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spectra were recorded on an Agilent Accurate-Mass Q-TOF LC/MS 6520. Merck silica gel 60-120 was used for column chromatography. GC analyses were performed on a Perkinelmer-Clarus 590 GC instrument fitted with Elite-1 column (30 m length, 0.32 mm ID) using the following method: Injection volume: 1 µL, inlet temperature: 280 °C, FID detector temperature: 280 °C, oven temperature: start at 60 °C hold time 1 min, ramp: 12 °C /min, upto 320 °C, Flow rate (carrier): 25 mL/min (N_2). All the catalytic cross coupling of alcohols was carried out under argon atmosphere and in preheated oil baths unless mentioned. X-ray photoelectron spectroscopy (XPS) data were collected with a Thermo Fisher ESCALAB Xi+ spectrometer (UK) using monochromatic Al Kα source (284.8 eV). Ligand synthesis was performed in oven-dried glassware under argon atmosphere using standard Schlenk techniques. 4 Å M.S. were dried by heating in a furnace oven at 400 ℃ for 6 hours following which it was transferred and stored under argon atmosphere.

A. Synthesis of ligands, and chromium complexes

i) Synthesis of ligands

Synthesis of 3.3a (Scheme 3.3):

Sodium hydride (60% suspension in paraffin oil, 0.512 g, 12.8 mmol, 3.0 equiv.) was taken in a dry two neck flask and washed with dry petroleum ether to remove the paraffin oil. 2-aminopyridine (0.80 g, 8.54 mmol, 2 equiv.) was added to the stirred suspension of sodium hydride in THF (10 mL) and refluxed over night for the complete deprotonation the 2-aminopyridine. Afterwards the reaction mixture was brought to room temperature. A solution of 2,4-dichloro-6-phenyl-1,3,5-triazine **2.3a** (0.96 g, 4.27 mmol, 1 equiv.) in dry THF (20 mL) was added dropwise to the reaction mixture. The resultant solution was refluxed for 12 hours. The reaction mixture was then quenched with water and extracted three times with ethyl acetate (3 × 20 mL). Solvent was removed under reduced pressure and washed with water to give grey powder of **3.3a** (1.33 g, 92%).

^{1}H NMR (600 MHz, $CDCl_3$): δ 8.53 – 8.48 (m, 6H), 7.82 (t, J = 8.4 Hz, 2H), 7.60 (t, J = 7.2 Hz, 1H), 7.55 (t, J = 7.8 Hz, 2H), 7.08 – 7.06 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 172.9, 164.5, 148.3, 138.0, 132.3, 128.9, 128.7, 118.7. HRMS (ESI) *m/z:* $[M+H]^+$ calculated for $C_{19}H_{16}N_7$: 342.1462; found 342.1459.

Synthesis of 3.3b (Scheme 3.3):

Sodium hydride (60% suspension in paraffin oil, 0.512 g, 12.8 mmol, 3.0 equiv.) was taken in a dry two neck flask and washed with dry petroleum ether to remove the paraffin oil. 2-aminopyridine (0.80 g, 8.54 mmol, 2 equiv.) was added to the stirred suspension of sodium hydride in THF (10 mL) and refluxed over night for the complete deprotonation the 2-aminopyridine. Afterwards the reaction mixture was brought to room temperature. A solution of 2,4-dichloro-6-(4-methoxyphenyl)-1,3,5-triazine **2.3b** (1.09 g, 4.27 mmol, 1 equiv.) in dry THF (20 mL) was added dropwise to the reaction mixture. The resultant solution was refluxed for 12 hours. The reaction mixture was then quenched with water and extracted three times with ethyl acetate (3 ×

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20 mL). Solvent was removed under reduced pressure and washed with water to give light orange powder of **3.3b** (1.50 g, 90%).

^{1}H NMR (600 MHz, $CDCl_3$): δ 8.50 – 8.48 (m Hz, 4H), 8.44 (d, J = 9.0 Hz, 2H), 7.79 – 7.77 (m, 2H), 7.05 – 7.02 (m, 4H), 3.91 (s, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 171.6, 164.3, 163.2, 152.5, 148.3, 138.0, 130.7, 118.6, 114.0, 55.6. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{20}H_{18}N_7O$ 372.1568; found 372.1569.

Synthesis of 3.3c (Scheme 3.3):

Sodium hydride (60% suspension in paraffin oil, 0.512 g, 12.8 mmol, 3.0 equiv.) was taken in a dry two neck flask and washed with dry petroleum ether to remove the paraffin oil. 2-aminopyridine (0.80 g, 8.54 mmol, 2 equiv.) was added to the stirred suspension of sodium hydride in THF (10 mL) and refluxed over night for the complete deprotonation the 2-aminopyridine. Afterwards the reaction mixture was brought to room temperature. A solution of 2,4-dichloro-6-(4-methoxyphenyl)-1,3,5-triazine **2.3c** (1.02 g, 4.27 mmol, 1 equiv.) in dry THF (20 mL) was added dropwise to the reaction mixture. The resultant solution was refluxed for 12 hours. The reaction mixture was then quenched with water and extracted three times with ethyl acetate (3 × 20 mL). Solvent was removed under reduced pressure and washed with water to give light orange powder of **3.3c** (1.51 g, 92%).

^{1}H NMR (600 MHz, $CDCl_3$): δ 8.51 – 8.49 (m, 4H), 8.35 (d, J = 8.4 Hz, 2H), 7.78 (t, J = 7.2 Hz, 2H), 7.34 – 7.32 (m, 2H), 7.05 – 7.03 (m, 2H), 2.46 (s, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 172.0, 164.3, 148.3, 142.9, 138.0, 129.4, 128.9, 118.6, 21.8. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{20}H_{18}N_7$ 356.1619; found 356.1620.

Synthesis of 3.3d (Scheme 3.3):

Sodium hydride (60% suspension in paraffin oil, 0.512 g, 12.8 mmol, 3.0 equiv.) was taken in a dry two neck flask and washed with dry petroleum ether to remove the paraffin oil. 22-aminopyrimidine (0.81 g, 8.54 mmol, 2 equiv.) was added to the stirred suspension of sodium hydride in THF (10 mL) and refluxed over night for the complete deprotonation the 2-aminopyridine. Afterwards the reaction mixture was brought to room temperature. A solution of 2,4-dichloro-6-(4-methoxyphenyl)-1,3,5-triazine **2.3a** (0.96 g, 4.27 mmol, 1 equiv.) in dry THF (20 mL) was added dropwise to the reaction mixture. The resultant solution was refluxed for 12 hours. The reaction mixture was then quenched with water and extracted three times with ethyl acetate (3 × 20 mL). Solvent was removed under reduced pressure and washed with water to give light orange powder of **3.3d** (1.46 g, 93%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 10.86 (s, 2H), 8.82 (d, J = 4.8 Hz, 4H), 8.54 (d, J = 7.2 Hz, 2H), 7.53 – 7.52 (m, 1H), 7.49 – 7.45 (m, 2H), 7.06 (t, J = 4.8 Hz, 2H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 173.3, 165.0, 158.5, 158.5, 136.3, 132.5, 129.3, 128.6, 116.0. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{17}H_{14}N_9$ 344.1367; found 344.1360.

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ii) Synthesis of chromium complexes

Synthesis of 3.4a (Scheme 3.4):

Procedure: A mixture of $CrCl_3$•3THF (0.375 g, 1.0 mmol, 1 equiv.) and **3.3a** (0.341 g, 1.0 mmol, 1 equiv.) was taken in a round bottom flask equipped with stirring bar. and under nitrogen flow dry THF (5mL) was added to the mixture and refluxed for 12 hours with continuous stirring. It was then brought to ambient temperature. The resulting mixture was filtered and the filtrate was collected and removed the solvent in vacuum to afford dark brown solid. Solvent was removed in vacuum to afford dark brown solid. Slow diffusion of diethyl ether in DMF gave **3.4a** as green crystal (0.448 g, 90%). The complex was stable in air and moisture. HRMS (ESI) *m/z*: $[M–Cl]^+$ calculated for $C_{18}H_{14}Cl_2N_7Cr$ 463.0171; found: 463.0170.

Synthesis of 3.4b (Scheme 3.4):

Procedure: A mixture of $CrCl_3$•3THF (0.375 g, 1.0 mmol, 1 equiv.) and **3.3b** (0.371 g, 1.0 mmol, 1 equiv.) was taken in a round bottom flask equipped with stirring bar. and under nitrogen flow dry THF (5mL) was added to the mixture and refluxed for 12 hours with continuous stirring. It was then brought to ambient temperature. The resulting mixture was filtered and the filtrate was collected and removed the solvent in vacuum to afford dark brown solid. Solvent was removed in vacuum to afford dark brown solid. Slow diffusion of diethyl ether in DMF afforded **3.4b** as green crystal (0.484 g, 92%). The complex was stable in air and moisture. HRMS (ESI) *m/z*: $[M–Cl]^+$ calculated for $C_{20}H_{17}Cl_2N_7Cr$ 493.0277; found: 493.0274.

Synthesis of 3.4c (Scheme 3.4):

Procedure: A mixture of $CrCl_3$•3THF (0.375 g, 1.0 mmol, 1 equiv.) and **3.3c** (0.355 g, 1.0 mmol, 1 equiv.) was taken in a round bottom flask equipped with stirring bar. and under nitrogen flow dry THF (5mL) was added to the mixture and refluxed for 12 hours with continuous stirring. It was then brought to ambient temperature. The resulting mixture was filtered and the filtrate was collected and removed the solvent in vacuum to afford dark brown solid. Solvent was removed in vacuum to afford **3.4c** as green solid in 92% yield (0.471 g). The complex was stable in air and moisture. HRMS (ESI) *m/z*: $[M–Cl]^+$ calculated for $C_{20}H_{17}Cl_2N_7Cr$ 477.0328; found 477.0320.

Synthesis of 3.4d (Scheme 3.4):

Procedure: A mixture of $CrCl_3$•3THF (0.375 g, 1.0 mmol, 1 equiv.) and **3.3d** (0.343 g, 1.0 mmol, 1 equiv.) was taken in a round bottom flask equipped with stirring bar. and under nitrogen flow dry THF (5mL) was added to the mixture and refluxed for 12 hours with continuous stirring. It was then brought to ambient temperature. The resulting mixture was filtered and the filtrate was collected and removed the solvent in vacuum to afford dark brown solid. Solvent was removed in vacuum to afford **3.4d** as green solid in 81% yield (0.404 g). The complex was stable in air and moisture. HRMS (ESI) *m/z*: $[M–Cl]^+$ calculated $C_{17}H_{13}Cl_2N_9Cr$ 465.0076; found: 465.0060.

Synthesis of 3.5 (Scheme 3.4):

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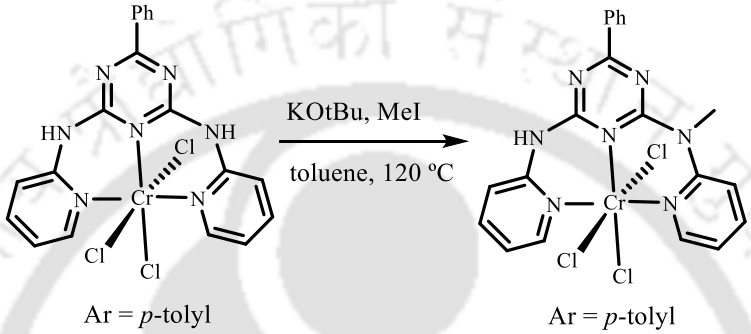
Procedure: A mixture of anhydrous $CrCl_2$ (0.111 g, 1.0 mmol, 1 equiv.) and **3.3a** (0.341 g, 1.0 mmol, 1 equiv.) was taken in a round bottom flask equipped with stirring bar. Under nitrogen atmosphere, dry THF (5 mL) was added to the mixture and refluxed for 12 hours with continuous stirring. It was then brought to ambient temperature. The resulting mixture was filtered and the filtrate was collected and removed the solvent in vacuum to afford green solid. Solvent was removed in vacuum to afford green solid. HRMS (ESI) *m/z*: $[M]^+$ calculated for $C_{31}H_{15}Cl_2N_7Cr$ 463.0171; found: 463.0167.

Synthesis of 3.4a^{Me}:



Scheme 3.18. Synthesis of **3.4a^{Me}**

Procedure: A mixture of **3.4a** (0.050 g, 0.01 mmol, 1 equiv.), KO^{t}Bu (0.020 g, 0.18 mmol, 2 equiv), toluene (1 mL) was taken in a reaction tube equipped with stirring bar, reaction mixture was refluxed for 2 hours with continuous stirring, then methyl iodide (0.051 g, 0.36 mmol, 4 equiv.) was added to the reaction mixture, further stirred for 12 h at 120 ºC in an oil bath. Volatile component was removed in vacuum to provide dark brown solid of **3.4a^{Me}** (0.047 g, 92%). The complex was stable in air and moisture. HRMS (ESI) *m/z*: $[M–Cl]^+$ calculated for $C_{20}H_{17}Cl_2N_7Cr$ 477.0328; found: 477.0318.

B. General procedure

i) General procedure for synthesis of *β*-Branched *β, γ*-unsaturated ketones (GP-1)

In a pyrex tube a mixture of ketone (1 mmol, 1 equiv), cyclic ketone (1 mmol, 1 equiv.), **3.4b** (5 mol%), KO^{t}Bu (30 mol%), 4 Å molecular sieves (0.04 g) and dry toluene (2 mL) were taken. The reaction tube was properly closed and placed in a preheated oil bath at 150 ºC with continuous stirring for 8 h. The resulting mixture was then passed through a bed of celite, the filtrate was collected and concentrated under reduced pressure. The crude reaction mixture was purified by column chromatography over silica gel using petroleum ether or ethyl acetate/ petroleum ether mixture as an eluent.

Gram-scale synthesis of 2.9b: A mixture of **2.7b** (0.75 gm, 5 mmol, 1 equiv.), **2.8a** (5 mmol, 1 equiv.), **3.4b** (5 mol%), KO^{t}Bu (30 mol%), 4 Å molecular sieves (0.15 g) and toluene (8 mL) was added into a pyrex tube (100 mL) equipped with stirring bar. The reaction tube was properly closed and placed in a preheated oil bath at 150 ºC with continuous stirring for 8 hours. The resulting

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mixture was then passed through a bed of celite, the filtrate was collected and concentrated under reduced pressure. The crude reaction mixture was purified by column chromatography over silica gel using petroleum ether or ethyl acetate/ petroleum ether mixture as an eluent to get analytically pure product 0.483 g (75% yield).

C. Mechanistic studies

i) Mercury drop test (Scheme 3.7)

To establish the homogeneity of **3.4b** in cross-aldol reaction of ketones, mercury drop experiment was carried out.

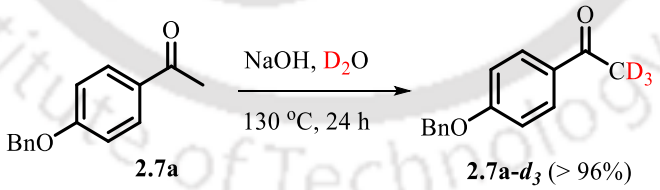
Experimental procedure: In this test, the pyrex tube was charged with 1 mmol of **2.7c** (196 mg), 1 mmol of **2.8a** (98 mg), 0.5 mmol of mercury (100 mg), 30 mol% of KO^{t}Bu (22 mg) and 5 mol% of complex **3.4b** (26 mg). To this reaction mixture, 4 Å molecular sieves (0.04 g) and 2 mL of dry toluene was added and heated at 150 ºC for 8 h in an oil bath. The product **2.9c** was obtained in 72% of yield (198 mg), suggests that homogenous behaviour of the catalyst.

ii) The influence of the NH functionality in chromium complex (Scheme 3.8)

Experimental procedure: A mixture of **2.7c** (196 mg, 1 mmol, 1 equiv.), **2.8a** (98 mg, 1 mmol, 1 equiv.), **3.4a^{Me}** (5 mol%), KO^{t}Bu (30 mol%), 4 Å molecular sieves (0.04 g) and dry toluene (2 mL) was added into a pyrex tube (25 mL) equipped with stirring bar. The reaction tube was properly closed and placed in a preheated oil bath at 150 ºC with continuous stirring for 8 hours. The resulting mixture was then passed through a bed of celite, the filtrate was collected and concentrated under reduced pressure. Analytically pure product (78 mg, 28%) was obtained by column chromatography over silica gel using ethyl acetate / petroleum ether mixture as an eluent.

iii) Deuterium-labeling experiments

Synthesis of deuterated 4-benzyloxyacetophenone 2.7a-*d*$_3$:



Scheme 3.19. Synthesis of **2.7a-*d*$_3$**

Procedure: In a pyrex tube degassed D_2O (99.9% D, 3 mL) was taken and to it under nitrogen flow a mixture of 4-benzyloxyacetophenone **2.7a** (452 mg, 2 mmol) and NaOH (40 mg, 1.0 mmol) was added. The reaction tube was properly closed and placed in a preheated oil bath at 130 ℃ with continuous stirring for 24 hours under nitrogen atmosphere. Upon completion of the reaction, the reaction mixture was extracted with chloroform (5 mL × 3) and dried over Na_2SO_4. The solvent was evaporated under vacuum to afford the desired product **2.7a-*d*$_3$** (95%, 430 mg) with 96% D as a light brown solid.

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^{1}H NMR (600 MHz, $CDCl_3$): δ 7.93 – 7.91 (m, 2H), 7.43 – 7.39 (m Hz, 4H), 7.35 – 7.32 (m, 2H), 7.00 (d, J = 8.7 Hz, 2H), 5.11 (s, 2H), 2.50 (brs, 0.12 H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 197.1, 162.7, 136.3, 130.7, 130.6, 128.8, 128.6, 128.3, 127.6, 127.0, 114.6, 70.2. 25.8 (sept, $J_{C\text{-}D}$ = 19.2 Hz).

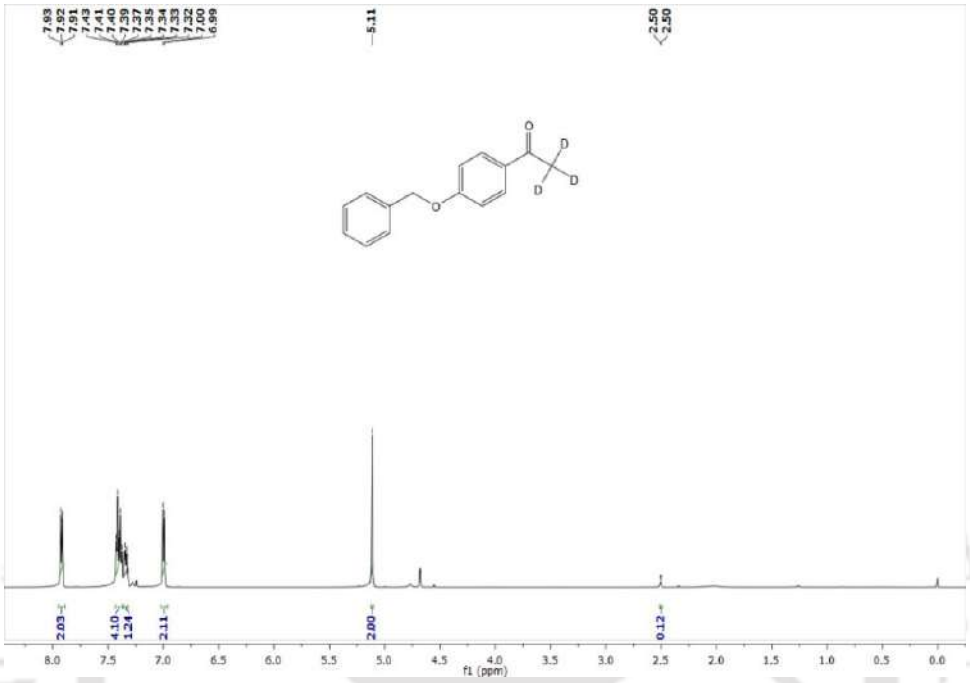

Figure 3.10. ^{1}H NMR spectrum of **2.7a-*d*$_3$** ($CDCl_3$, 600 MHz, 298 K)

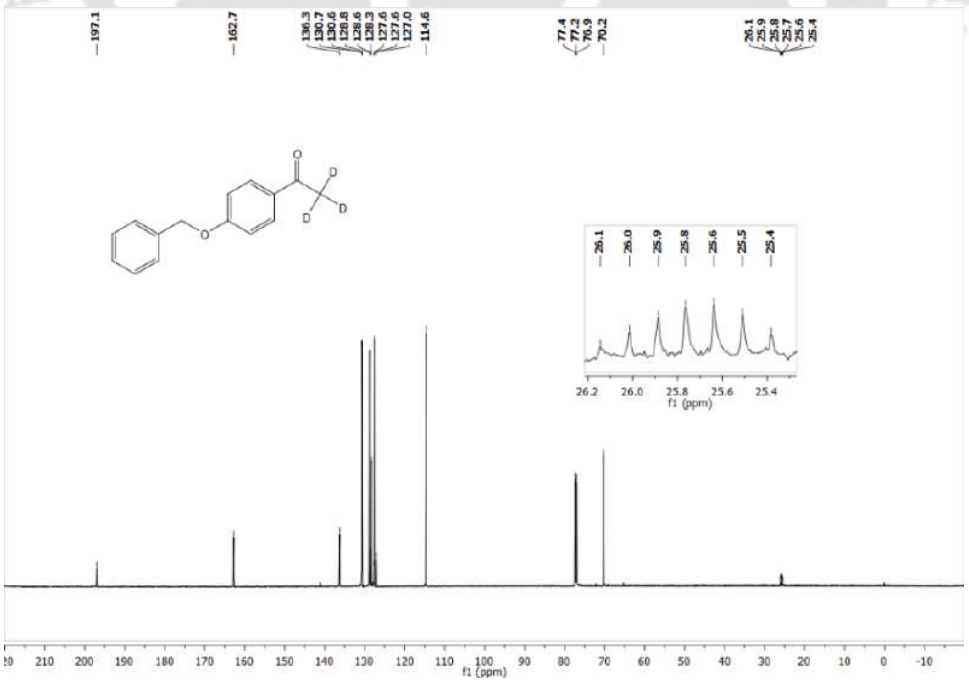

Figure 3.11. ^{13}C{^{1}H} NMR spectrum of **2.7a-*d*$_3$** ($CDCl_3$, 151 MHz, 298 K)

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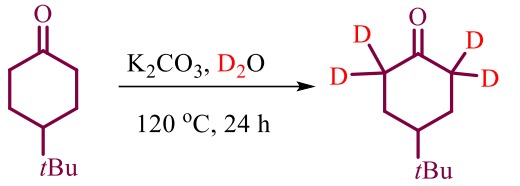
Synthesis of 4-*tert*-butylcyclohexanone 2.8b-d_4:



2.8b **2.8b-d_4** (> 95%)

Scheme 3.20. Synthesis of **2.8b -d_4**

Procedure: In a pyrex tube degassed D_2O (99.9% D, 4 mL) was taken and to it under nitrogen flow of 4-*tert*-butylcyclohexanone **2.8b** (386 mg, 2.5 mmol) and K_2CO_3 (24 mg, 0.18 mmol) was added. The reaction tube was properly closed and placed in a preheated oil bath at 120 ºC with continuous stirring for 70 hours under nitrogen atmosphere. Upon completion of the reaction, the reaction mixture was extracted with chloroform (5 mL × 3) and dried over Na_2SO_4.The solvent was evaporated under vacuum to afford the desired product **2.8b-d_4** (91%, 324 mg) with 95% D as a light brown solid.

^{1}H NMR (600 MHz, $CDCl_3$): δ 2.32– 2.31 (m, 0.10 H), 2.26 – 2.24 (m, 0.10 H), 2.04 (d, J = 12.4 Hz, 2H), 1.46 – 1.37 (m, 3H), 0.88 (s, 9H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 213.0, 46.7, 41.2 – 40.5 (m), 32.5, 27. 7, 27.6.

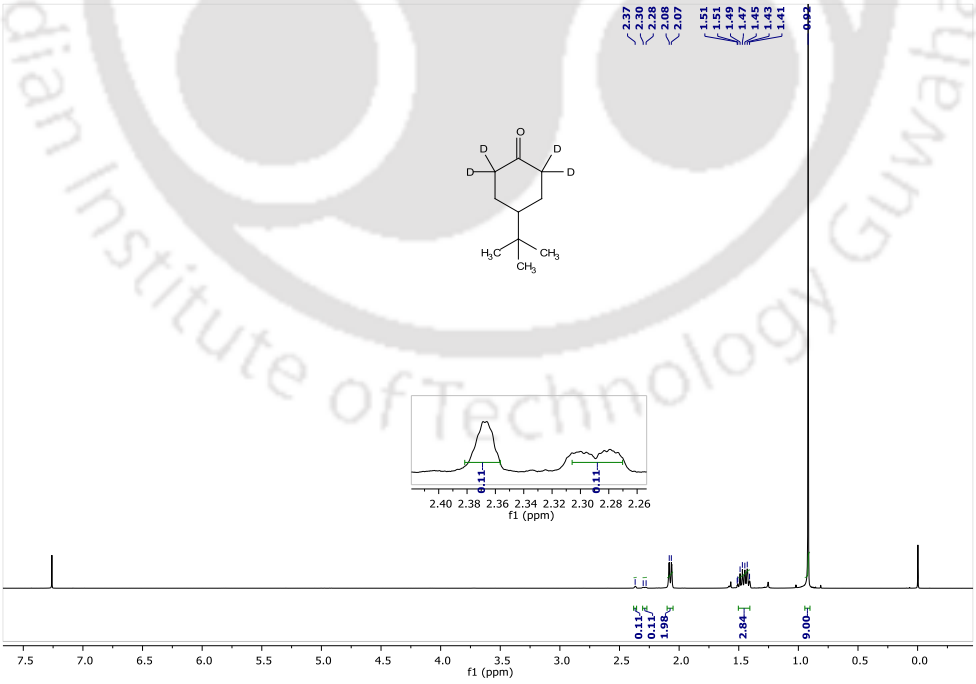


Figure 3.12. ^{1}H NMR spectrum of **2.8b-d_4** ($CDCl_3$, 600 MHz, 298 K)

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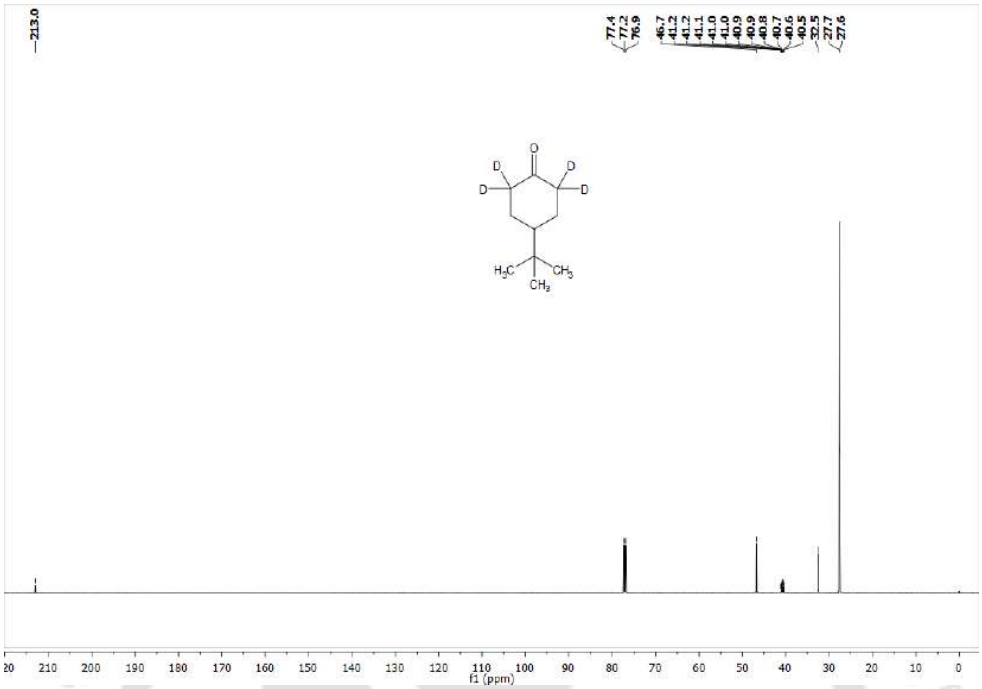

Figure 3.13. $^{13}C\{^{1}H\}$ NMR spectrum of **2.8b-*d*$_4$** ($CDCl_3$, 151 MHz, 298 K)

Synthesis of deuterated 2.9m-*d* using the reaction of 2.7a and 2.8b-*d*$_4$ (Scheme 3.13a):

Procedure: In a pyrex tube a mixture of **2.7a** (115 mg, 0.5 mmol, 1 equiv.), **2.8b-*d*$_4$** (77 mg, 0.5 mmol, 1equiv.), **3.4b** (5 mol%), KO^{t}Bu (30 mol%), 4 Å molecular sieves and dry toluene (2 mL) were taken. The reaction tube was properly closed and placed in a preheated oil bath at 150 ℃ with continuous stirring for 8 h. The resulting mixture was then passed through a bed of celite, the filtrate was collected and concentrated under reduced pressure. The crude reaction mixture was checked the ^{1}H NMR and followed by purified by column chromatography over silica gel using petroleum ether or ethyl acetate/ petroleum ether mixture as an eluent to get analytically pure product 90 mg (50% yield).

Based on ^{1}H-^{1}H COSY and HSQC NMR, the Ha, H_b, H_c, H_d H_e and H_f are assigned below for the compound **2.9m**.

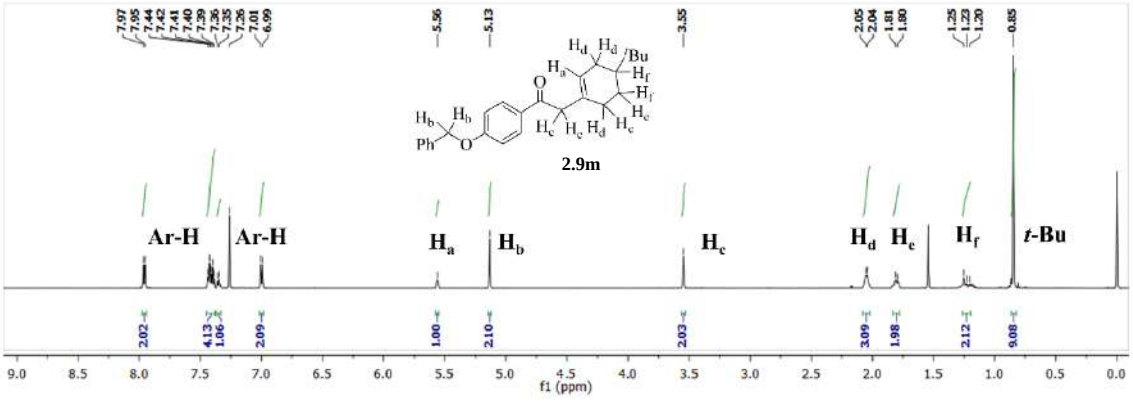

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Figure 3.14. ^{1}H NMR spectra of compound **2.9m** ($CDCl_3$, 600 MHz, 298 K)

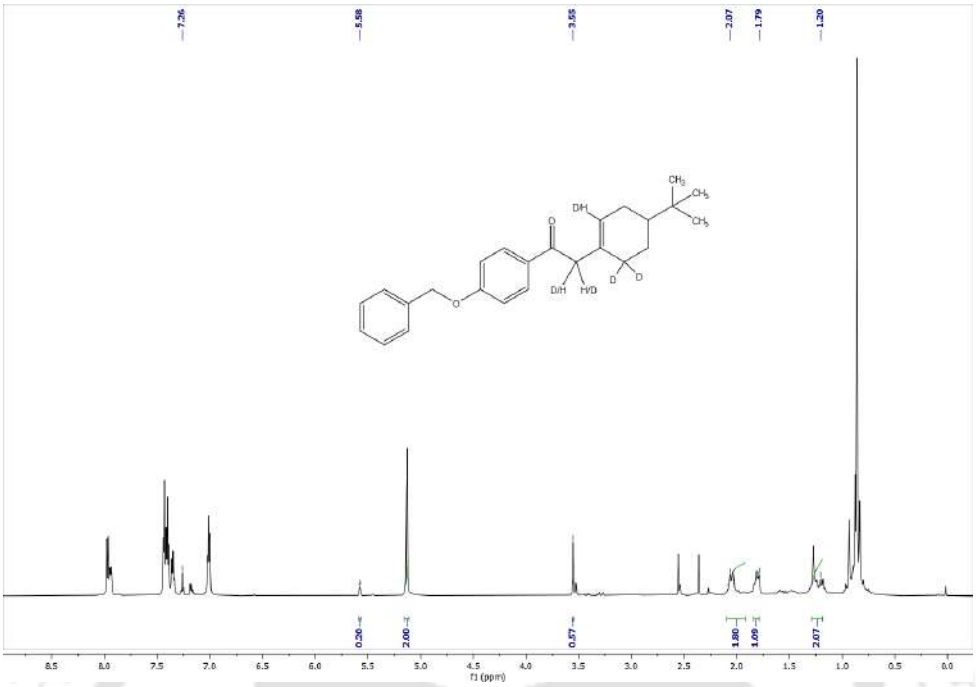

Figure 3.15. Crude ^{1}H NMR spectra of **2.9m-*d*** ($CDCl_3$, 600 MHz, 298 K)

Synthesis of deuterated 2.9m-*d* using the reaction of 2.7a-d_3 and 2.8b (Scheme-3.13b):

Procedure: In a pyrex tube a mixture of **2.7a-d_3** (115 mg, 0.5 mmol, 1 equiv.), **2.8b** (77 mg, 0.5 mmol, 1equiv.), **3.4b** (5 mol%), KO^{t}Bu (30 mol%), 4 Å molecular sieves and dry toluene (2 mL) were taken. The reaction tube was properly closed and placed in a preheated oil bath at 150 °C with continuous stirring for 8 h. The resulting mixture was then passed through a bed of celite, the filtrate was collected and concentrated under reduced pressure. The crude reaction mixture was checked the ^{1}H NMR in $CDCl_3$ and followed by purified by column chromatography over silica gel using petroleum ether or ethyl acetate/ petroleum ether mixture as an eluent to get analytically pure product 110 mg (60% yield).

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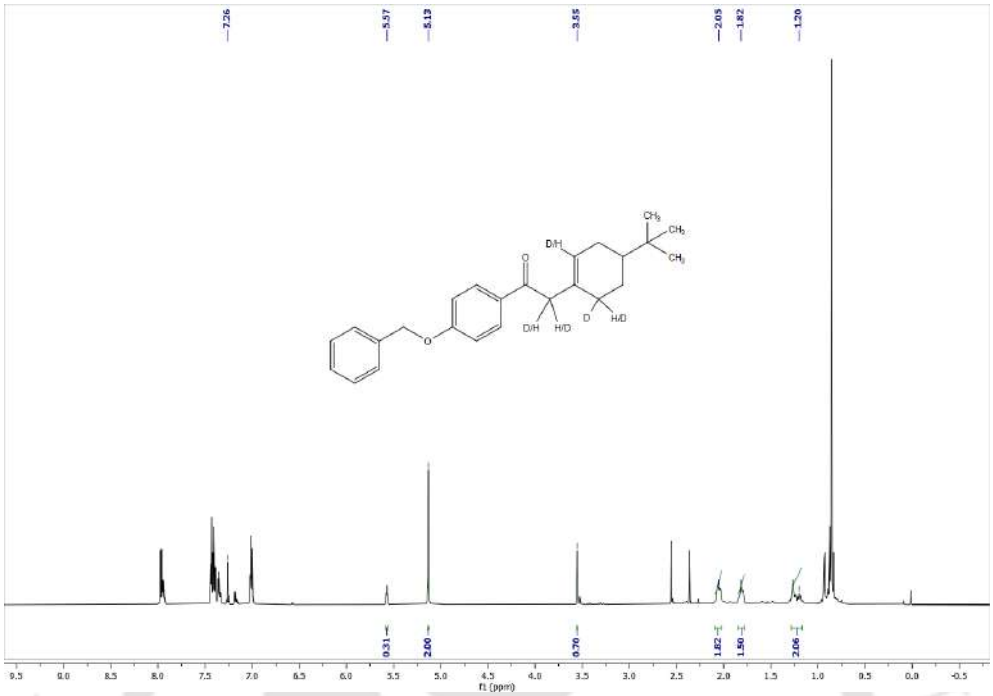

Figure 3.16. Crude ^{1}H NMR spectra of **2.9m-*d*** ($CDCl_3$, 600 MHz, 298 K)

Synthesis of deuterated of 2.9m-*d* using the reaction of 2.7a-d_3 and 2.8b-d_4 (Scheme-3.13c):

Procedure: In a pyrex tube a mixture of **2.7a-d_3** (115 mg, 0.5 mmol, 1 equiv.), **2.8b-d_4** (77 mg, 0.5 mmol, 1equiv), **3.4b** (5 mol%), KO^{t}Bu (30 mol%), 4 Å molecular sieves and dry toluene (2 mL) were taken. The reaction tube was properly closed and placed in a preheated oil bath at 150 °C with continuous stirring for 8 h. The resulting mixture was then passed through a bed of celite, the filtrate was collected and concentrated under reduced pressure. The crude reaction mixture was checked the ^{1}H NMR in $CDCl_3$ and followed by purified by column chromatography over silica gel using petroleum ether or ethyl acetate/ petroleum ether mixture as an eluent to get analytically pure product 76 mg (42% yield).

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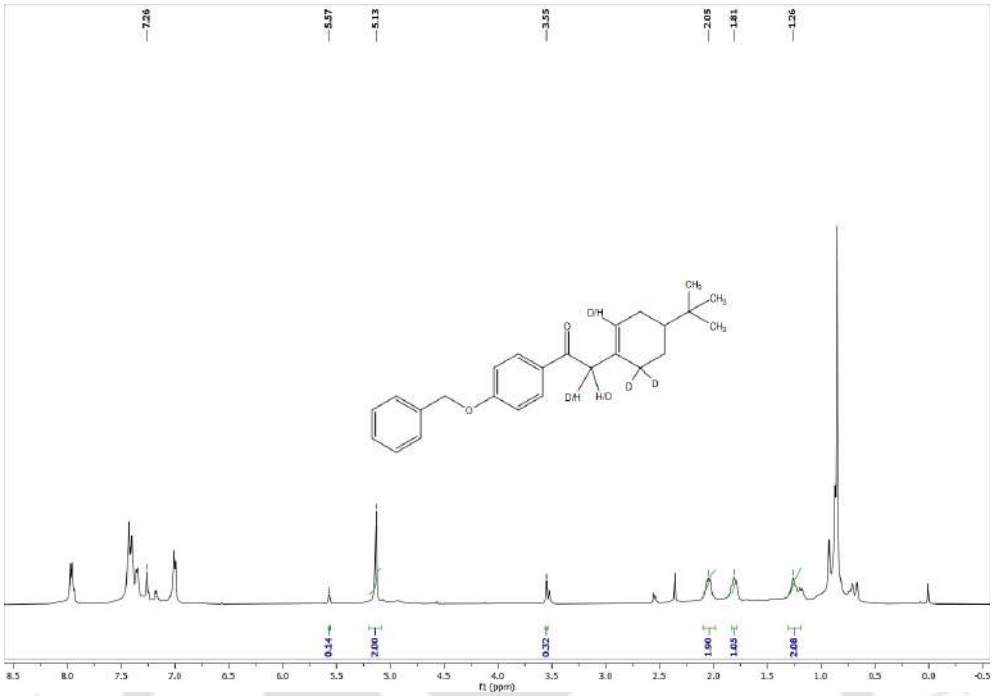

Figure 3.17. Crude ^{1}H NMR spectra of **2.9m-*d*** ($CDCl_3$, 600 MHz, 298 K)

iv) Proof for the aldol intermediate in cross-aldol condensation of ketones (Scheme 3.9):

a) **Formation of *β, γ*-unsaturated ketone from aldol product in presence of catalyst:** The schlenk tube was loaded with **2.14** (0.5 mmol, 1 equiv.), KO^{t}Bu (17 mg, 0.15 mmol, 0.3 equiv.), **3.4b** (6 mg, 0.01 mmol, 0.02 equiv.), 4 Å molecular sieves (20 mg) and dry toluene (1 mL) and the reaction mixture was heated at 150 ºC for 8 h in an oil bath. The product **2.9w** was isolated as white solid (75% yield).

b) **Formation of *α,β*-unsaturated ketone from aldol product in absence of catalyst:** The schlenk tube was loaded with **2.18** (0.5 mmol, 1 equiv.), KO^{t}Bu (17 mg, 0.15 mmol, 0.3 equiv.), 4 Å molecular sieves (20 mg) and dry toluene (1 mL) and the reaction mixture was heated at 150 ℃ for 8 h in an oil bath. The product **2.9w** was isolated as white solid in 21% of yield along with the formation of corresponding ketone **2.7o** with 60% yield.

v) Experimental support for the origin of chemoselectivity (Scheme 3.10):

Using self-aldol 2.14 under the reaction condition: The schlenk tube was loaded with self-aldol product **2.14** (0.5 mmol, 1 equiv.), KO^{t}Bu (16.8 mg, 0.15 mmol, 0.3 equiv.), **3.4b** (14 mg, 0.025 mmol, 0.05 equiv.), 4 Å molecular sieves (20 mg) and dry toluene (1 mL) and the reaction mixture was heated at 150 ℃ for 8 h in an oil bath. After the standard aqueous work up, ketone **2.7c** was isolated in 72% of yield along with the formation of self-aldol condensation product **2.15**, 20% yield. In the absence of catalyst, ketone **2.7c** was attained in 85% of yield and product **2.15** was obtained only in 7% yield.

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Using reverse cross-aldol product 2.16 under the reaction condition: The schlenk tube was loaded with reverse cross-aldol product **2.16** (120 mg, 0.5 mmol, 1 equiv.), KO^{t}Bu (16.8 mg, 0.15 mmol, 0.3 equiv.), **3.4b** (14 mg, 0.025 mmol, 0.05 equiv.), 4 Å molecular sieves (20 mg) and dry toluene (1 mL) and the reaction mixture was heated at 150 ℃ for 8 h in an oil bath. After the standard aqueous work up, condensation product **2.17** (29%), *β, γ*-unsaturated ketone **2.9m** (25%), ketone **2.7c** (33%) and cyclohexanone **2.8a** (33%) was obtained in the GC. Overall conversion of **2.16** was attained in 94%.

vi) The equilibria between *β*-branched *α, β*- and *β, γ*-unsaturated ketones (Scheme 3.11):

From pure *α, β*-isomer 2.10a to *β, γ*-isomer 2.9w (Scheme 3.11a):

a) **Treatment of pure *α, β*-isomer 2.10a in the presence of catalyst with base (30 mol%):** A reaction tube (25 mL) was equipped with a stir bar, **3.4b** (0.05 mmol), KO^{t}Bu (0.3 mmol), **2.10a** (1 mmol, 1 equiv.), 4 Å molecular sieves (0.04 g) and toluene (1.5 mL). The flask was closed and the solution was stirred at 150 °C (oil bath temperature) for 8 h. The reaction mixture was then monitored using GC analysis. It suggested that the ratio of *α, β*-isomer (**2.10a**): *β, γ*-isomer (**2.9w**) is 00:100 after 8 h. Notably, there was no any other isomers/products.

b) **Treatment of pure *α, β*-isomer 2.10a in the absence of catalyst with base (30 mol%):** A reaction tube (25 mL) was equipped with a stir bar, KO^{t}Bu (0.3 mmol), **2.10a** (1 mmol, 1 equiv.), 4 Å molecular sieves (0.04 mg) and toluene (1.5 mL). The flask was closed and the solution was stirred at 150 °C (oil bath temperature) for 8 h. The reaction was monitored using GC analysis. It suggested that ratio of *α, β*-isomer (**2.10a**): *β, γ*-isomer (**2.9w**) is 74:26 after 8 h. Notably, there was no any other products. The result suggested that there is ~26% conversion of **2.10a** to **2.9w** in the absence of catalyst.

From pure *β, γ*-isomer 2.9w to *α, β*- isomer 2.10a (Scheme 3.11b):

a) **Treatment of pure *β, γ*-isomer 2.9w in the presence of catalyst:** A reaction tube (25 mL) was equipped with a stir bar, **3.4b** (0.05 mmol), KO^{t}Bu (0.3 mmol), **2.9w** (1 mmol, 1 equiv.), 4 Å molecular sieves (0.04 g) and toluene (1.5 mL). The flask was closed and the solution was stirred at 150 °C (oil bath temperature) for 8 h. The reaction mixture was then monitored using GC and NMR analysis. It suggested that the ratio of *β, γ* -isomer (**2.9w**) / *α, β*- isomer (**2.10a**) is 100:0 after 8 h; indicating no conversion of **2.9w** to **2.10a**. Notably, there was no any other isomers/products.

b) **Treatment of pure *β, γ*-isomer in the absence of catalyst:** A reaction tube (25 mL) was equipped with a stir bar, KO^{t}Bu (0.2 mmol), **2.9w** (1 mmol, 1equiv), 4 Å molecular sieves (40 mg) and toluene (1.5 mL). The flask was closed and the solution was stirred at 150 °C (oil bath temperature) for 8 h. The reaction was monitored using GC and NMR analysis. It suggested that there is no formation of *α, β*-isomer **2.10a**.

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viii) The equilibria study using a stoichiometric reaction of Cr-complex (Scheme 3.12):

Study the equilibria between *β*-branched *α, β*- and *β, γ*-unsaturated ketones using **3.4a** and **3.5** complexes.

a) **Treatment of pure *α, β*-isomer 2.10a in the presence of chromium(III) complex 3.4a:** A reaction tube (25 mL) was equipped with a stir bar, **2.10a** (1 mmol, 1equiv), **3.4a** (1 mmol, 1 equiv.), 4 Å molecular sieves (40 mg) and toluene (1.5 mL). The flask was closed and the solution was stirred at 150 °C (oil bath temperature) for 8 h. The reaction was monitored using GC, suggested there is no conversion of **2.10a** to **2.9w .**

b) **Treatment of pure *α, β*-isomer 2.10a in the presence of chromium(II) complex 3.5:** A reaction tube (25 mL) was equipped with a stir bar, **2.10a** (1 mmol, 1equiv), **3.5** (1 mmol, 1 equiv.), 4 Å molecular sieves (40 mg) and toluene (1.5 mL). The flask was closed and the solution was stirred at 150 °C (oil bath temperature) for 8 h. The reaction mixture was then monitored using GC analysis. It suggested that the ratio of *β*, *γ*-isomer (**2.9w**):*α*, *β*- isomer (**2.10a**) is 62:38. Notably, there was no any other isomers/products.

viii) Mechanistic understanding of Cr-aldol reaction in the presence of base (Scheme 3.14):

Since the role of ruthenium catalyst and base is significant in this reaction, experimental support has been given for their importance in catalysis. Study suggests that the reaction possibly proceeds *via* potassium enolate followed by transmetallation.

For the formation of potassium enolate followed by transmetallation: At first active Cr(II) species **3.4b'** was prepared by using 5 mol% of **3.4b** (27 mg, 0.05 mmol) and 30 mol% of KO^{t}Bu (33.6 mg, 0.3 mmol) in toluene (2 ml) at 150 ºC for 8 h in an oil bath. To the reaction mixture aldol acceptor **2.8a** (1 mmol), and 4 Å molecular sieves (40 mg) was added and subsequently added a freshly prepared solution of potassium enolate **2.7c'** [presuming **2.7c'** is formed by the reaction of aldol donor **2.7c** (1 mmol) and base (112 mg, 1 mmol)] under the reaction condition. Then stirred the reaction mixture for 8 h at 150 ºC in an oil bath. A desired cross-coupled condensation product **2.9c** was obtained in 72% yield.

ix) Kinetic studies

Hammett Studies (Scheme 3.15):

Reaction conditions: An oven-dried screw cap tube, a mixture of substituted aldol derivative (1 mmol), KO^{t}Bu (30 mol%), **3.4b** (5 mol%), 4 Å molecular sieves and dry toluene (2 mL) were taken. The reaction tube was properly closed and placed in a preheated oil bath at 150 ºC for the specified times. The progress of the reaction was analysed by GC using mesitylene as an internal standard. The measure yield of product was plotted against time to obtain the slope which gave the rate constant for each substrate.

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R	σ	k_X	k_X/k_H	$\log(k_X/k_H)$
m-CF_3	0.43	3.05×10^{-3}	2.61	0.42
p-Br	0.23	2.06×10^{-3}	1.76	0.245
H	0	1.17×10^{-3}	0	0
p-OMe	-0.27	0.72×10^{-3}	0.61	-0.21

The individual rate constants ($\log k_x/k_H$) were then plotted against the substituent constants (σ) and a Hammett correlation with a positive slope was obtained (ρ = +0.92, R^2 = 0.9995) (Figure-3.8).

Reaction conditions: In a reaction tube, a mixture of **2.10d** (0.5 mmol), and **2.10a** (0.5 mmol), KO^{t}Bu (30 mol%), **3.4b** (5 mol%), 4 Å molecular sieves (40 mg) and dry toluene (2 mL) were taken. The reaction tube was properly closed and placed in a preheated oil bath at 150 ºC with continuous stirring for 30 min. The ratio of yields **2.9b**:**2.9w** = 28:30 was estimated using GC analysis with mesitylene as standard.

Eyring Studies (Scheme 3.16):

Reaction conditions: In reaction tube, aldol **3.19** (1 mmol), KO^{t}Bu (30 mol%), **3.4b** (5 mol%), 4 Å molecular sieves (20 mg) and dry toluene (2 mL) were taken. The reaction tube was properly closed and placed in a preheated oil bath at respective temperature (130 ºC, 140 ºC, 150 ºC, 160 ºC). The progress of the reaction was analysed by GC using mesitylene as an internal standard. The measure yield of product **2.9b** was plotted against time to obtain the slope which gave the rate constant (k) for each case. Then activation parameters were determined from the plot of ln(k/T) vs 1/T, which was linear over the temperature range studied (130 ºC, 140 ºC, 150 ºC, 160 ºC).

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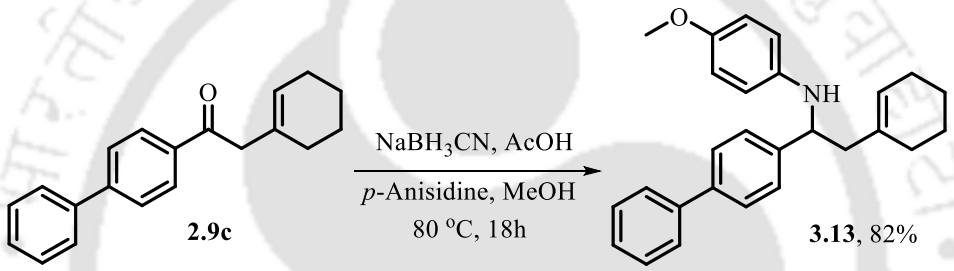
temp	1/T	*k*	*ln(k/T)*
403 K (130 ºC)	0.002481	4.6×10^{-4}	-13.68
413 K (140 ºC)	0.002421	6.06×10^{-4}	-13.43
423 K (150 ºC)	0.002364	7.03×10^{-4}	-13.30
433 K (160 ºC)	0.002309	8.73×10^{-4}	-13.11

D. Post Synthetic Modification:

N-(1-([1,1'-biphenyl]-4-yl)-2-(cyclohex-1-en-1-yl)ethyl)-4-methoxyaniline (3.13):



Scheme 3.21. Synthesis of **3.13**

To a solution of **2.9c** (55.2 mg, 0.2 mmol, 1.0 equiv.) in MeOH (2.0 mL) were added 4-methoxyaniline (70.2 mg, 0.6 mmol, 3.0 equiv.), $NaBH_3CN$ (37.8 mg, 0.6 mmol, 3.0 equiv.), and two drops of AcOH sequentially. The mixture was stirred at 80 ºC for 18 hours in a preheated oil bath and monitored by TLC. After the completion of the reaction, the solvent was removed under reduced pressure. The title compound **3.13** was isolated as light yellow oil using silica gel column chromatography with petroleum ether and ethyl acetate (v/v = 15:1, R_f = 0.50); 82% yield (63 mg).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60 – 7.54 (m, 4H), 7.46 – 7.40 (m, 4H), 7.32 (t, *J* = 7.2 Hz,, 1H), 6.68 (d, *J* = 9.2 Hz, 2H), 6.47 (d, *J* = 8.8 Hz, 2H), 5.61 (s, 1H), 4.30 (dd, *J* = 10.0 Hz, 4.0 Hz, 1H), 3.95 (brs, 1H), 3.69 (s, 3H), 2.48 – 2.44 (m, 1H), 2.33 – 2.26 (m, 1H), 2.06 – 1.93 (m, 4H), 1.63 – 1.59 (m, 4H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 152.1, 144.4, 142.5, 141.2, 139.8, 134.8, 128.8, 127.5, 127.21, 127.16, 126.7, 125.7, 114.8, 56.4, 55.9, 48.8, 27.8, 25.5, 22.9, 22.5. HRMS (ESI) m/z: $[M+H]^+$ calculated for $C_{27}H_{30}NO$ 384.2322; found: 384.2331.

1-([1,1'-biphenyl]-4-yl)-2-(cyclohex-1-en-1-yl)ethan-1-one oxime (3.14):

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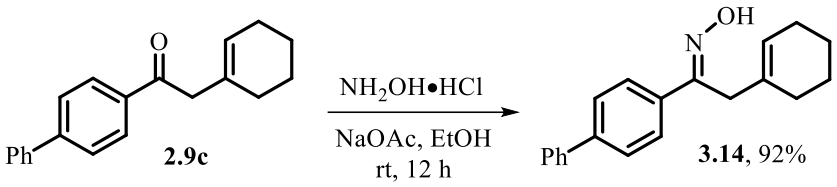
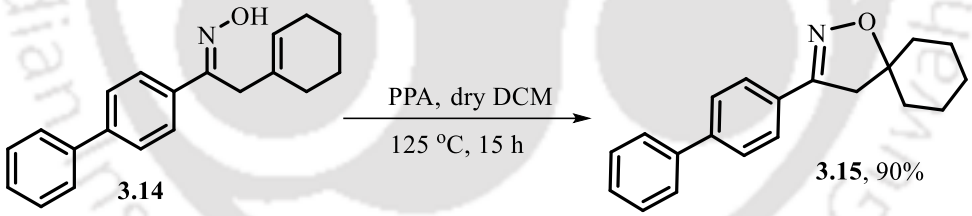


Scheme 3.22. Synthesis of **3.14**

A round-bottom flask a solution of hydroxylamine hydrochloride (69 mg, 1.0 mmol, 5.0 equiv.) in ethanol (1 mL) was taken. To this Sodium acetate (190 mg, 1.4 mmol, 7.0 equiv.) was added followed by the addition of ketone **2.9c** (55.5 mg, 0.2 mmol, 1.0 equiv.) was added to the solution. The resulting suspension was stirred for 12 h at room temperature and monitored by TLC. After completion of the reaction the solution was concentrated in vacuo and extracted with ethyl acetate three times. The organic layers were dried over Na_2SO_4 and removed under vacuum which give the title compound **3.14** white solid with 92% yield (53 mg).

^{1}H NMR (400 MHz, $CDCl_3$: 7.71 (d, J = 8.4 Hz, 2H), 7.62 – 7.58 (m, 4H), 7.45 (t, *J* = 7.2 Hz, 2H), 7.36 (t, *J* = 7.2 Hz, 1H), 5.47 (s, 1H), 3.49 (s, 2H), 2.02 – 1.97 (m, 4H), 1.67 – 1.65 (m, , 2H), 1.57 – 1.53 (m, 2H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) : δ 157.2, 142.0, 140.6, 135.1, 132.6, 129.0, 127.7, 127.2, 127.2, 126.9, 123.20, 29.1, 25.4, 23.0, 22.3. HRMS (ESI) m/z: $[M+H]^+$ calculated for $C_{20}H_{22}NO$ 292.1696; found. 292.1692.

3-([1,1'-biphenyl]-4-yl)-1-oxa-2-azaspiro[4.5]dec-2-ene (3.15):



Scheme 3.23. Synthesis of **3.15**

In an oven dried sealed tube, a solution of oxime **3.14** (58 mg, 2.0 mmol) in dry DCM (2 mL) was taken and to this polyphosphoric acid (10 mmol, 5.0 equiv.) was added. The resulting suspension was stirred for 15 h at 125 ºC in a preheated oil bath and monitored by TLC. After completion of the reaction the solution was concentrated in vacuum and extracted with DCM three times. The organic layers were dried over Na_2SO_4 and removed under vacuum which give the title compound **3.15** white solid with 90% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.73 (d, *J* = 8.4 Hz, 2H), 7.64 – 7.60 (m, 4H), 7.47 – 7.43 (m, 2H), 7.39 – 7.35 (m, 1H), 3.08 (s, 2H), 1.85 – 1.83 (m, 4H), 1.72 – 1.68 (m, 2H), 1.49 (brs, 4H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 155.8, 142.6, 140.4, 129.4, 129.0, 127.9, 127.4, 127.2, 127.0, 87.4,

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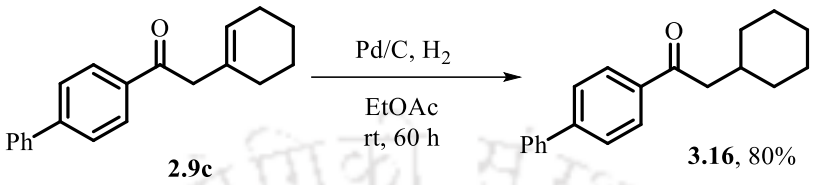
60.6, 45.1, 36.7, 25.2, 23.6. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{20}H_{22}NO$ 292.1696; found: 292.1694.

1-([1,1'-biphenyl]-4-yl)-2-cyclohexylethan-1-one (3.16):



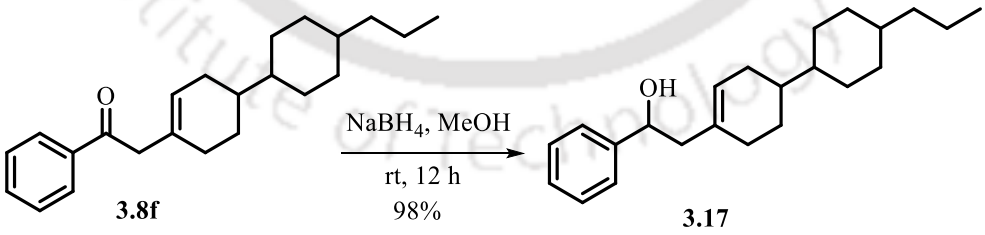
Scheme 3.24. Synthesis of **3.16**

To a Schlenk tube fulfilled with argon were added Pd/C (8.5 mg, 0.004 mmol, 2 mol%) and the ketone **2.9c** (55.3 mg, 0.2 mmol, 1.0 equiv.) sequentially. After addition of these chemicals, the tube was degassed and refilled with H_2 by a balloon of H_2. Then EtOAc (2 mL) was added and the resulting mixture was stirred at room temperature for 60 h. The H_2 balloon was removed and the resulting mixture was filtered through a short column of silica gel, eluted with ethyl acetate. The solvent was removed under vacuum and purified by silica gel chromatography using petroleum ether and ethyl acetate (v/v = 15:1, R_f = 0.50) to afford **3.16** as a colorless oil with 80% yield

.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.03 (d, J = 8.4 Hz, 2H), 7.68 (d, J = 8.4 Hz, 2H), 7.64 – 7.61 (m, 2H), 7.47 (t, J = 7.6 Hz, 2H), 7.40 (t, J = 7.2 Hz, 1H), 2.85 (d, J = 6.8 Hz, 2H, COCH_2), 2.03 – 1.95 (m, 1H), 1.80 – 1.65 (m, 5H), 1.35 – 1.26 (m, 2H), 1.22 – 1.16 (m, 1H), 1.08 – 0.99 (m, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 200.1, 129.1, 128.9, 128.3, 127.4, 127.4, 46.4, 34.9, 33.6, 26.4, 26.3. Spectral data is in accordance with the literature.[17]

1-phenyl-2-(4'-propyl-[1,1'-bi(cyclohexan)]-3-en-4-yl)ethan-1-one (3.17):



Scheme 3.25. Synthesis of **3.17**

To a solution of **3.8f** (48.4 mg, 0.2 mmol, 1 equiv.) in methanol (2 mL), solid $NaBH_4$ (11.3 mg, 0.3 mmol, 1.5 equiv) was added at 0 ºC portion wise. After the completion of the addition, the reaction mixture was allowed to stirred for 6 h at room temperature. Then water was added to the reaction mixture, and extracted by using dichloromethane (5 mL). Afterwards, in the organic layer

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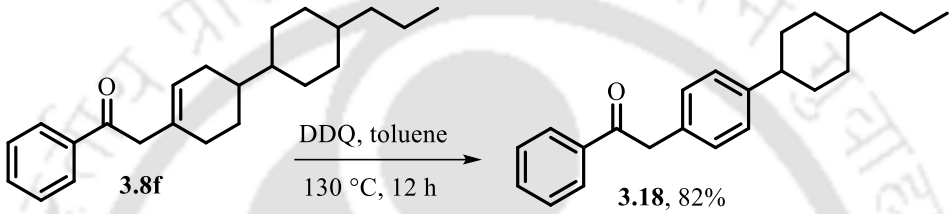
Na_2SO_4 was added to remove excess water. Product was obtained as white solid **3.17** (48 mg, 98%) after removing the solvents under reduced pressure.

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.38 – 7.33 (m, 4H), 7.27 – 7.25 (m, 1H), 5.59 (s, 1H), 4.76 – 4.74 (m, 1H), 2.38 – 2.28 (m, 2H), 2.10 – 2.05 (m, 1H), 1.97 – 1.95 (m, 1H), 1.81 – 1.77 (m, 3H), 1.73 – 1.71 (m, 3H), 1.73 (s, 3H), 1.32 – 1.28 (m, 3H), 1.16 – 1.14 (m, 3H), 1.00 – 0.95 (m, 2H), 0.89 – 0.86 (m, 6H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 128.5, 127.5, 126.0, 125.98, 125.8, 71.5, 71.2, 49.1, 48.2, 42.6, 39.9, 39.2, 39.2, 37.7, 33.6, 30.3, 30.1, 29.5, 29.4, 29.2, 29.1, 26.7, 26.5, 20.2, 14.6. HRMS (ESI) *m/z*: $[M-H]^+$ calculated for $C_{23}H_{33}O$ 325.2536; found: 325.2529.

1-phenyl-2-(4-(4-propylcyclohexyl)phenyl)ethan-1-one (3.18):

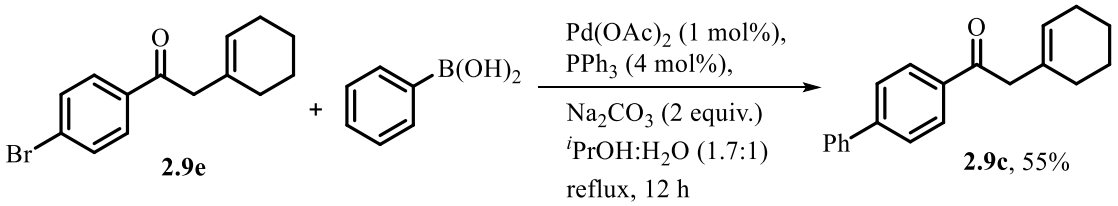


Scheme 3.26. Synthesis of **3.18**

To a solution of **3.8f** (48 mg, 0.2 mmol, 1 equiv.) in toluene (2 mL), DDQ (91 mg, 0.4 mmol, 2 equiv) was added and then the reaction mixture was allowed to stirred for 12 h at 130 ºC in a preheated oil bath. After completion of the reaction solvent was removed under vacuum and purified by silica gel column chromatography with petroleum ether and ethyl acetate (v/v = 20:2, R_f = 0.50); 82% yield (63 mg).

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.05 – 8.01 (m, 2H), 7.57 – 7.53 (m, 1H), 7.46 (t, J = 7.6 Hz, 2H), 7.20 – 7.15 (m, 4H), 4.25 (s, 2H), 2.46 – 2.40 (m, 1H), 1.88 – 1.83 (m, 4H), 1.40 – 1.33 (m, 2H), 1.28 – 1.25 (m, 1H), 1.23 – 1.19 (m, 2H), 1.04 – 1.01 (m, 2H), 0.89 (t, J = 7.2 Hz, 3H), 0.85 – 0.81 (m, 2H).^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 198.0, 146.6, 133.3, 131.9, 129.5, 128.8, 128.8, 127.3, 45.2, 44.4, 39.9, 37.2, 34.4, 33.7, 20.2, 14.6. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{23}H_{29}O$ 321.2213; found 321.2214.

1-([1,1'-biphenyl]-4-yl)-2-(cyclohex-1-en-1-yl)ethan-1-one (2.9c) from 2.9e:



Scheme 3.27. Synthesis of **2.9c**

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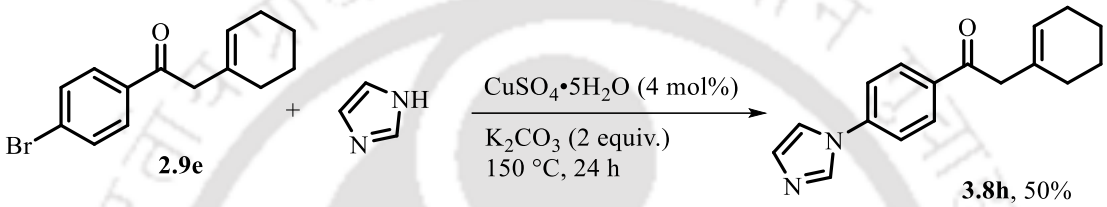
2.9e (56 mg, 0.2 mmol) and phenyl boronic acid (0.3 mmol, 1.5 equiv.) were stirred at room temperature in isopropanol (5 mL) for 15 minutes. To this, $Pd(OAc)_2$ (0.5 mg, 0.002 mmol, 1.0 mol%), PPh_3 (2.1 mg, 0.008 mmol, 4.0 mol%), Na_2CO_3 (42.3 mg, 0.4 mmol, 2.0 equiv.) and water (3ml) were added. Then reaction mixture was reflux for 12 hours. After cooling to room temperature, 5 ml of water was added to the reaction mixture and stirred for 5 minutes. The mixture was extracted using ethyl acetate and solvent was removed under vacuum. The crude compound was purified by column chromatography eluting with pet ether-ethyl acetate mixture to give the pure product **2.9c** as off white solid with 55% yield.

1-(4-(1*H*-imidazol-1-yl)phenyl)-2-(cyclohex-1-en-1-yl)ethan-1-one (3.8h) from 2.9e:



Scheme 3.28. Synthesis of **3.8h**

A pressure tube was charged with **2.9e** (140 mg, 0.5 mmol), imidazole (68 mg, 1.0 mmol, 2 equiv.), K_2CO_3 (138 mg, 1.0 mmol, 2 equiv.), and $CuSO_4 \cdot 5H_2O$ (5 mg, 0.02 mmol, 4 mol%). The solid mixture was then heated to 150 ºC for 24 h in an oil bath. The reaction mixture was then cooled to ambient temperature and distilled water was added to it. The precipitate was filtered and washed three times with distilled water and then with petroleum ether. The remaining solid residue was brought to dryness to give compound **3.8h** as light yellow solid with 50% yield.

E. Crystallographic data

Crystallographic data of 3.4a

Single crystals of compound **3.4a** suitable for X-ray diffraction were obtained by slow evaporation of the diethyl ether in DMF at room temperature. X-ray crystallographic data were collected using Bruker D8 QUEST diffractometer. Data refinement and cell reduction were carried out by APEX4. Structures were solved by direct methods using Olex2 1.5 and refined by a full-matrix least-squares method using Olex2 1.5. All of the non-H atoms were refined anisotropically. The ORTEP diagram was obtained with ORTEP3 software with 50% thermal ellipsoid (see Figure 3.1). The crystallographic parameters and refinement data were listed in Table S2

Table 3.4. Crystal data and structure refinement for **3.4a**

Identification code	PA-3_Cr

TH-3606_186122027

CCDC	2295250
Empirical formula	$C_{21}H_{14}FNO$
Formula weight	107.65
Temperature	131 K
Wavelength	0.71073 Å
Crystal system	monoclinic
Space group	$C_1\ 2/c_1$
Unit cell dimensions	a = 19.977(6) Å α = 90° b = 17.502(5) Å β = 104.986(11)° c = 8.487(2) Å γ = 90°
Volume	2866.6(14) $Å^3$
Z	24
Density (calculated)	1.497 g/cm^3
Absorption coefficient	0.720 mm^{-1}
F(000)	1332.0
Crystal size	0.21 × 0.12 × 0.09 mm^3
2Θ range for data collection	2.33 to 24.60°
Index ranges	$-23 \le h \le 23, -20 \le k \le 20, -10 \le l \le 10$
Reflections collected	28368
Independent reflections	2532 [R_{int} = 0.0692, R_{sigma} = 0.067]
Completeness to theta = 25.094°	99.5%
Data/restraints/parameters	2532/0/186
Goodness-of-fit on F^2	1.096
Final R indexes [I>=2σ (I)]	R_1 = 0.0428, wR_2 = 0.1076
Final R indexes [all data]	R_1 = 0.0648, wR_2 = 0.1127
Largest diff. peak and hole	0.377 and -0.425 e $Å^{-3}$

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Crystallographic data of 3.4b

Single crystals of compound **3.4b** suitable for X-ray diffraction were obtained by slow diffusion of the diethyl ether in DMF at room temperature. X-ray crystallographic data were collected using Bruker D8 QUEST diffractometer. Data refinement and cell reduction were carried out by APEX4. Structures were solved by direct methods using Olex2 v1.5 and refined by a full-matrix least-squares method using Olex2 v1.5. All of the non-H atoms were refined anisotropically. The ORTEP diagram was obtained with ORTEP3 software with 50% thermal ellipsoid (see Figure 3.1). The crystallographic parameters and refinement data were listed in Table 3.5

Table 3.5. Crystal data and structure refinement for **3.4b**

Identification code	PA_Cr_5	
CCDC:	2295248	
Empirical formula	$C_{20}H_{17}Cl_3CrN_7O$	
Formula weight	602.85	
Temperature	297K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	*P 21/n*	
Unit cell dimensions	a = 10.4284(13)Å	α = 90°.
	b = 24.577(3) Å	β = 106.257(3)
	c = 12.9275(16) Å	γ = 90°.
Volume	3180.8(7) $Å^3$	
Z	4	
Density (calculated)	1.259 mg/m^3	
Absorption coefficient	0.643 mm^{-1}	
F(000)	1236.0	
Crystal size	0.46 × 0.36 × 0.30 mm^3	
Theta range for data collection	2.38 to 25.86°	
Index ranges	$-12 \le h \le 12$, $-29 \le k \le 29$, $-15 \le l \le 15$	
Reflections collected	76227	
Independent reflections	5917 [R_{int} = 0.0403, R_{sigma} = 0.065]	

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Completeness to theta = 25.50°	99.7%
Refinement method	Full-matrix least-squares on F2
Data / restraints / parameters	5917 / 0/ 337
Goodness-of-fit on F^2	1.089
Final R indices [I>2sigma(I)]	R1 = 0.0473, wR2 = 0.1448
R indices (all data)	R1 = 0.0599, wR2 = 0.1638
Largest diff. peak and hole	0.413 and -0.314 e.$Å^{-3}$

Crystallographic data of 3.8g

Single crystals of compound **3.8g** suitable for X-ray diffraction were obtained by slow evaporation of the saturated solution of the complex in CH_3CN at room temperature. X-ray crystallographic data were collected using Bruker D8 QUEST diffractometer. Data refinement and cell reduction were carried out by *APEX4*. Structures were solved by direct methods using Olex2 v1.5 and refined by a full-matrix least-squares method using Olex2 v1.5. All of the non-H atoms were refined anisotropically. The ORTEP diagram was obtained with ORTEP3 software with 50% thermal ellipsoid (see below, Figure 3.18). The crystallographic parameters and refinement data were listed in Table 3.6.

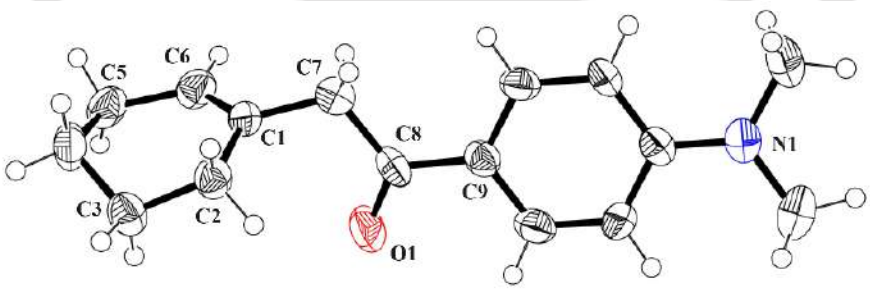

Figure 3.18: Molecular structure of compound **3.8g** (thermal ellipsoid 50% probability level). Selected Bond lengths (in Å): C(1)–C(6) 1.315(7), C(1)–C(2) 1.502(6), C(1)–C(7) 1.500(7), C(7)–C(8) 1.513(8), O(1)–C(8) 1.221(6), C(8)–C(9) 1.473(6). Selected Bond Angles (in °): C(6)–C(1)–C(2) 121.8(4), C(1)–C(2)–C(3) 113.1(4), C(1)–C(7)–C(8) 114.8(4), C(7)–C(1)–C(2) 115.8(4), C(1)–C(6)–C(5) 124.1(5).

Table 3.6. Crystal data and structure refinement for **3.8g**

Identification code	adpa583
CCDC:	2308888
Empirical formula	$C_{16}H_{21}NO$
Formula weight	294.37

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Temperature	297 K	
Wavelength	0.73 Å	
Crystal system	monoclinic	
Space group	P 1 21 1	
Unit cell dimensions	a = 6.2655(8)Å	α = 90
	b = 8.0269(10)Å	β = 92.592(4)
	c = 13.5085(17)Å	γ = 90
Volume	678.68(15) $Å^3$	
Z	2	
Density (calculated)	1.191 mg/m^3	
Absorption coefficient	0.077 mm^{-1}	
F(000)	316	
Crystal size	0.28 × 0.22 × 0.18 mm^3	
Theta range for data collection	2.33 to 25.59°	
Index ranges	$-7 \leq h \leq 7, -9 \leq k \leq 9, -16 \leq l \leq 16$	
Reflections collected	15125	
Independent reflections	2386 [R_{int} = 0.0626, R_{sigma} = 0.048]	
Completeness to theta = 24.999°	99.3%	
Refinement method	Full-matrix least-squares on F2	
Data / restraints / parameters	2386 / 1 / 165	
Goodness-of-fit on F^2	1.178	
Final R indices [I>2sigma(I)]	R1 = 0.0713, wR2 = 0.0713	
R indices (all data)	R1 = 0.0841, wR2 = 0.1745	
Largest diff. peak and hole	0.205 and -0.230e. $Å^{-3}$	

3.6. Analytical data

A. For the precursors

1-(4-(1*H*-imidazol-1-yl)phenyl)ethan-1-one (3.6h)

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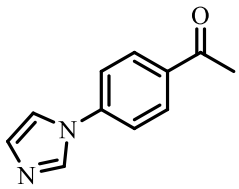
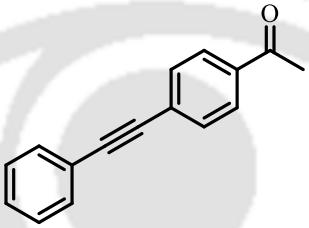


^{1}H NMR (600 MHz, $CDCl_3$): δ 8.09 (d, J = 8.6 Hz, 2H), 7.96 (s, 1H), 7.51 (d, J = 8.7 Hz, 2H), 7.37 (s, 1H), 7.25 (s, 1H), 2.65 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 196.6, 140.8, 135.9, 135.5, 131.3, 130.4, 120.8, 117.8, 26.7. Spectral data is in accordance with the literature.[19]

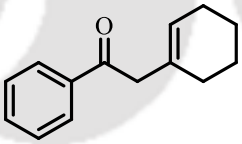
1-(4-(phenylethynyl)phenyl)ethan-1-one (2.7f)



^{1}H NMR (600 MHz, $CDCl_3$): δ 7.95 (d, J = 8.4 Hz, 2H), 7.62 (d, J = 8.4 Hz, 2H), 7.56 – 7.55 (m, 2H), 7.38 – 7.37 (m, 3H), 2.62 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 197.5, 136.3, 131.9, 131.8, 129.0, 128.6, 128.42, 128.35, 122.8, 92.9, 88.7, 26.8. Spectral data is in accordance with the literature.[21]

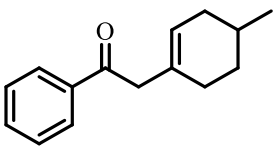
B. For the products

2-(cyclohex-1-en-1-yl)-1-phenylethan-1-one (2.9w)



Using GP-1 with compound **2.7o** (120 mg, 1 mmol) and **2.8a** (98 mg, 1 mmol), the title compound **2.9w** was isolated as colourless liquid using silica gel column chromatography with petroleum ether and ethyl acetate (v/v = 50:1, R_f = 0.70); 88% yield (176 mg). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.97 (d, J = 7.3 Hz, 2H), 7.55 (t, J = 7.3 Hz, 1H), 7.45 (t, J = 7.8 Hz, 2H), 5.57 (s, 1H), 3.59 (s, 2H), 2.03 – 2.00 (m, 4H), 1.66 – 1.64 (m, 1H), 1.63 – 1.62 (m, 1H), 1.57 – 1.54 (m, 2H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 198.9, 137.2, 133.1, 132.3, 128.7, 128.6, 126.2, 48.0, 29.0, 25.6, 22.9, 22.2. Spectral data is in accordance with the literature.[24]

2-(4-methylcyclohex-1-en-1-yl)-1-phenylethan-1-one (3.8a)



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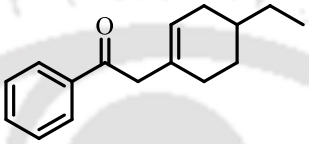
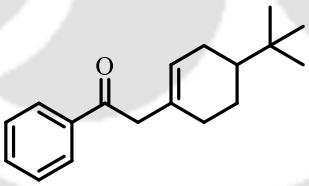
Using GP-1 with compound **2.7o** (120 mg, 1 mmol) and **2.8d** (112 mg, 1 mmol), the title compound **3.8a** was isolated as colourless liquid using silica gel column chromatography with petroleum ether and ethyl acetate (v/v = 50:1, R_f = 0.50); 86% yield (184 mg). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.97 (d, J = 7.4 Hz, 2H), 7.56 – 7.53 (m, 1H), 7.46 – 7.43 (m, 2H), 5.54 (brs, 1H), 3.59 (s, 2H), 2.10 – 2.08 (m, 2H), 2.02 – 1.99 (m, 1H), 1.71 – 1.66 (m, 3H), 1.27 – 1.24 (m, 1H), 0.93 (d, J = 6.2 Hz, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 198.9, 137.1, 133.1, 132.0, 128.6, 128.5, 125.7, 47.7, 34.1, 31.1, 29.0, 28.1, 21.7. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{15}H_{19}O$ 215.1431; found 215.1436.

2-(4-ethylcyclohex-1-en-1-yl)-1-phenylethan-1-one (3.8b)



Using GP-1 with compound **2.7o** (120 mg, 1 mmol) and **3.7a** (126 mg, 1 mmol), the title compound **3.8b** was isolated as colourless liquid using silica gel column chromatography with petroleum ether and ethyl acetate (v/v = 50:1, R_f = 0.50); 84% yield (190 mg). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.98 (d, J = 7.1 Hz, 2H), 7.55 (t, J = 7.3 Hz, 1H), 7.45 (t, J = 7.3 Hz, 2H), 5.55 (s, 1H), 3.60 (s, 2H), 2.15 – 2.12 (m, 1H), 2.04 – 1.99 (m, 2H), 1.77 – 1.75 (m, 1H), 1.69 – 1.65 (m, 2H), 1.28 – 1.26 (m, 3H), 0.89 (t, J = 6.8 Hz, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 199.0, 137.2, 133.1, 132.2, 128.7, 128.6, 125.8, 47.7, 35.0, 32.0, 29.1, 29.0, 28.9, 11.6. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{16}H_{21}O$ 229.1587; found: 229.1592.

2-(4-(*tert*-butyl)cyclohex-1-en-1-yl)-1-phenylethan-1-one (2.9t)



Using GP-1 with compound **2.7o** (120 mg, 1 mmol) and **2.8b** (154 mg, 1 mmol), the title compound **2.9t** was isolated as colourless liquid using silica gel column chromatography with petroleum ether and ethyl acetate (v/v = 50:1, R_f = 0.50); 89% yield (228 mg). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.98 (d, J = 7.4 Hz, 2H), 7.56 – 7.53 (m, 1H), 7.46 – 7.43 (m, 2H), 5.57 (brs, 1H), 3.60 (s, 2H,) 2.06 – 2.03 (m, 3H), 1.82 – 1.79 (m, 2H), 1.28 – 1.19 (m, 2H) 0.85 (s, 9H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 198.9, 137.1, 133.1, 132.1, 128.6, 128.5, 126.4, 47.4, 43.8, 32.3, 30.4, 27.3, 27.1, 24.2. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{18}H_{25}O$: 257.1900; found 257.1906.

2-(4-(tert-pentyl)cyclohex-1-en-1-yl)-1-phenylethan-1-one (3.8c)

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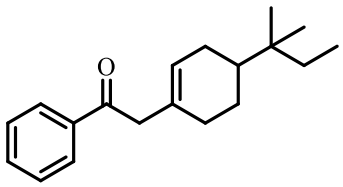
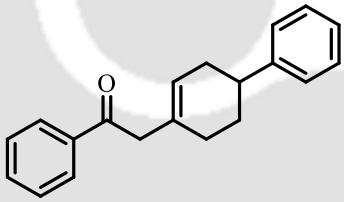


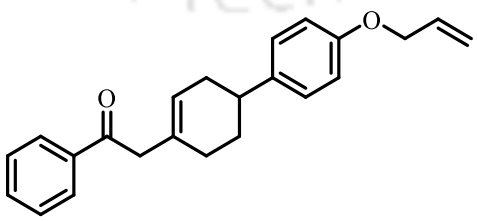
Using GP-1 with compound **2.7o** (120 mg, 1 mmol) and **3.7b** (168 mg, 1 mmol), the title compound **3.8c** was isolated as colourless liquid using silica gel column chromatography with petroleum ether and ethyl acetate (v/v = 50:1, R_f = 0.50); 74% yield (202 mg). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.98 – 7.97 (m, 2H), 7.56 – 7.54 (m, 1H), 7.47 – 7.44 (m, 2H), 5.58 (brs, 1H), 3.60 (s, 2H,) 2.07 – 1.98 (m, 3H), 1.86 – 1.81 (m, 1H), 1.78 – 1.75 (m, 1H), 1.39 – 1.34 (m, 1H), 1.29 – 1.17 (m, 4H), 0.80 – 0.79 (m, 5H), 0.78 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 198.9, 137.2, 133.1, 132.1, 128.7, 128.6, 126.5, 47.4, 41.2, 34.6, 32.6, 30.4, 26.8, 24.0, 23.9, 23.9, 8.3. HRMS (ESI) *m/z:* $[M+H]^+$ calculated for $C_{19}H_{27}O$: 271.2057; found 271.2061.

1-phenyl-2-(1,2,3,6-tetrahydro-[1,1'-biphenyl]-4-yl)ethan-1-one (3.8d)



Using GP-1 with compound **2.7o** (120 mg, 1 mmol) and **2.8c** (174 mg, 1 mmol), the title compound **3.8d** was isolated as white solid using silica gel column chromatography with petroleum ether and ethyl acetate (v/v = 50:1, R_f = 0.50); 85% yield (234 mg); M.p.= 91-92 ºC. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.01 (d, J = 7.9 Hz, 2H), 7.59 – 7.56 (m, 1H), 7.49 – 7.46 (m, 2H), 7.30 – 7.27 (m, 2H), 7.22 – 7.18 (m, 3H), 5.67 (brs, 1H), 3.67 (s, 2H), 2.81 – 2.77 (m, 1H), 2.35 – 2.32 (m, 1H), 2.25 – 2.17 (m, 2H), 2.13 – 2.10 (m, 1H), 1.97 – 1.95 (m, 1H), 1.83 – 1.80 (m, 1H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 198.8, 147.0, 137.1, 133.2, 132.3, 128.7, 128.6, 128.5, 127.0, 126.2, 125.8, 47.5, 39.8, 33.7, 30.0, 29.6. HRMS (ESI) *m/z:* $[M+H]^+$ calculated for $C_{20}H_{21}O$: 277.1587; found 277.1592.

2-(4'-(allyloxy)-1,2,3,6-tetrahydro-[1,1'-biphenyl]-4-yl)-1-phenylethan-1-one (3.8e)



Using GP-1 with compound **2.7o** (120 mg, 1 mmol) and **3.7c** (230 mg, 1 mmol), the title compound **3.8e** was isolated as white solid using silica gel column chromatography with petroleum ether and ethyl acetate (v/v = 50:1, R_f = 0.50); 75% yield (249 mg); M.p.= 94-95 °C. ^{1}H NMR (600 MHz,

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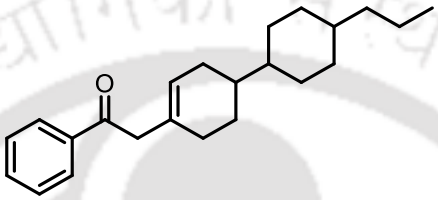
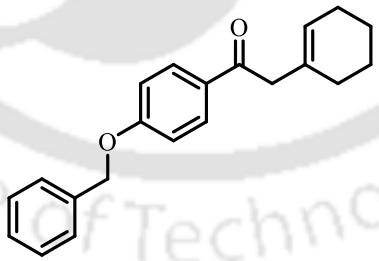
$CDCl_3$): δ 8.00 – 7.99 (m, 2H), 7.58 – 7.56 (m, 1H), 7.49 – 7.46 (m, 2H), 7.11 (d, J = 8.6 Hz, 2H), 6.84 (d, J = 8.6 Hz, 2H), 6.09 – 6.02 (m, 1H), 5.66 (brs, 1H), 5.42 – 5.39 (m, 1H), 5.28 – 5.26 (m, 1H), 4.52 – 4.51 (m, 2H), 3.66 (s, 2H), 2.76 – 2.71 (m, 1H), 2.32 – 2.29 (m, 1H), 2.23 – 2.22 (m, 1H), 2.15 – 2.09 (m, 2H), 1.94 – 1.91 (m, 1H), 1.79 – 1.74 (m, 1H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 198.8, 157.0, 139.4, 137.1, 133.7, 133.2, 132.2, 128.7, 128.6, 127.8, 125.9, 117.7, 114.7, 69.0, 47.5, 38.9, 33.9, 30.3, 29.6. HRMS (ESI) *m/z*: $[M+Na]^+$ calculated for $C_{23}H_{24}O_2Na$ 355.1674; found: 355.1670.

1-phenyl-2-(4'-propyl-[1,1'-bi(cyclohexan)]-3-en-4-yl)ethan-1-one (3.8f)



Using GP-1 with compound **2.7o** (200 mg, 1 mmol) and **3.7d** (222 mg, 1 mmol), the title compound **3.8f** was isolated as light yellow solid using silica gel column chromatography with petroleum ether and ethyl acetate (v/v = 50:1, R_f = 0.50); 83% yield. ^1H NMR (600 MHz, $CDCl_3$): δ 7.97 (d, J = 7.98 Hz, 2H), 7.56 – 7.54 (m, 1H), 7.46 – 7.44 (m, 2H), 5.56 (brs, 1H), 3.59 (s, 2H), 2.07 – 2.03 (m, 2H), 1.78 – 1.74 (m, 5H), 1.70 – 1.68 (m, 1H), 1.31 – 1.25 (m, 5H), 1.14 – 1.12 (m, 3H), 1.06 – 1.04 (m, 1H), 0.99 – 0.92 (m, 2H), 0.88 – 0.85 (m, 5H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 199.0, 137.2, 133.1, 132.2, 128.7, 128.6, 126.2, 47.6, 42.6, 39.9, 38.9, 37.7, 33.6, 30.3, 30.1, 29.7, 29.5, 26.5, 20.2, 14.6. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{23}H_{33}O$: 325.2526; found 325.2530.

1-(4-(benzyloxy)phenyl)-2-(cyclohex-1-en-1-yl)ethan-1-one (2.9a)



Using GP-1 with compound **2.7a** (226 mg, 1 mmol) and **2.8a** (98 mg, 1 mmol), the title compound **2.9a** was isolated as white solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.60); 78% yield (239 mg). M.p. 72-74 °C. ^1H NMR (600 MHz, $CDCl_3$): δ 7.96 (d, J = 8.8 Hz, 2H), 7.44 – 7.39 (m, 4H), 7.36 – 7.34 (m, 1H), 7.00 (d, J = 8.8 Hz, 2H), 5.56 (brs, 1H), 5.13 (s, 2H), 3.54 (s, 2H), 2.03 – 1.99 (m, 4H), 1.65 – 1.61 (m, 2H), 1.57 – 1.54 (m, 2H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 197.5, 162.7, 136.3, 132.6, 130.9, 130.4, 128.8, 128.4, 127.6, 125.8, 114.6, 70.3, 47.8, 28.9, 25.5, 22.9, 22.2. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{21}H_{23}O_2$ 307.1693; found 307.1690.

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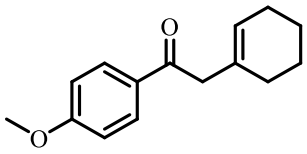
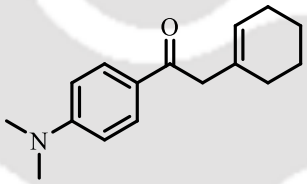
2-(cyclohex-1-en-1-yl)-1-(4-methoxyphenyl)ethan-1-one (2.9b)



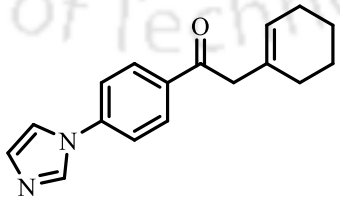
Using GP-1 with compound **2.7b** (150 mg, 1 mmol) and **2.8a** (98 mg, 1 mmol), the title compound **2.9b** was isolated as colourless liquid using silica gel column chromatography with petroleum ether and ethyl acetate (v/v = 50:1, R_f = 0.80); 85% yield (195 mg). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.96 (d, J = 8.8 Hz, 2H), 6.92 (d, J = 8.8 Hz, 2H), 5.56 (brs, 1H) 3.86 (s, 3H), 3.53 (s, 2H), 2.02 – 1.99 (m, 4H), 1.64 – 1.60 (m, 2H), 1.57 – 1.54 (m, 2H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 197.6, 163.5, 132.7, 130.9, 130.3, 125.8, 113.8, 55.6, 47.8, 28.9, 25.5, 22.9, 22.2. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{15}H_{19}O_2$ 231.1385; found 231.1392. Spectral data in accordance with the literature.[25]

2-(cyclohex-1-en-1-yl)-1-(4-(dimethylamino)phenyl)ethan-1-one (3.8g)



Using GP-1 with compound **3.6a** (163 mg, 1 mmol) and **2.8a** (98 mg, 1 mmol), the title compound **3.8g** was isolated as white solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:2, R_f = 0.60); 77% yield (186 mg). M.p. 95-98 °C. ^{1}H NMR (600 MHz, Chloroform-*d*): δ 7.90 (d, J = 7.4 Hz, 2H), 6.65 (d, J = 7.5 Hz, 2H), 5.55 (brs, 1H), 3.49 (s, 2H), 3.05 (s, 6H), 2.01 – 2.00 (m, 4H), 1.63 – 1.61 (m, 2H), 1.55 – 1.54 (m, 2H). ^{13}C NMR (151 MHz, Chloroform-*d*): δ 197.1, 153.5, 133.3, 130.9, 125.3, 125.2, 110.7, 47.5, 40.2, 28.9, 25.6, 23.0, 22.3. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{16}H_{22}NO$ 244.1696; found 244.1695.

1-(4-(1H-imidazol-1-yl)phenyl)-2-(cyclohex-1-en-1-yl)ethan-1-one (3.8h)



Using GP-1 with compound **3.6b** (186 mg, 1 mmol) and **2.8a** (98 mg, 1 mmol), the title compound **3.8h** was isolated as light yellow solid (208 mg, 78% yield) using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 10:100, R_f = 0.50). M.p. 105-109 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.10 (d, J = 8.7 Hz, 2H), 7.94 (brs, 1H), 7.48 (d, J = 8.7 Hz, 2H), 7.35

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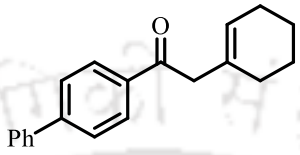
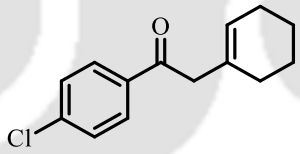
(brs, 1H), 7.24 (brs, 1H), 5.59 (brs, 1H), 3.60 (s, 2H), 2.04 – 2.00 (m, 4H), 1.67 – 1.61 (m, 2H), 1.59 – 1.53 (m, 2H). $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$): δ 197.4, 140.7, 135.8, 135.5, 132.1, 131.3, 130.6, 126.5, 120.8, 117.8, 48.1, 28.9, 25.6, 22.9, 22.1. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{17}H_{19}N_2O$ 267.1492; found 267.1494.

1-([1,1'-biphenyl]-4-yl)-2-(cyclohex-1-en-1-yl)ethan-1-one (2.9c)



Using GP-1 with compound **2.7c** (196 mg, 1 mmol) and **2.8a** (98 mg, 1 mmol), the title compound **2.9c** was isolated as off white solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 100:1, R_f = 0.60); 82% yield (226 mg). M.p. 69-71 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.05 (d, J = 8.3 Hz, 2H), 7.68 (d, J = 8.3 Hz, 2H), 7.63 (d, J = 7.3 Hz, 2H), 7.49 – 7.45 (m, 2H), 7.42 – 7.38 (m, 1H), 5.61 (brs, 1H), 3.62 (s, 2H), 2.04 – 2.03 (m, 4H), 1.67 – 1.64 (m, 2H), 1.60 – 1.57 (m, 2H). $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$): δ 198.5, 145.8, 140.1, 135.8, 132.4, 129.2, 129.1, 128.3, 127.4, 127.3, 126.2, 48.1, 29.0, 25.6, 22.9, 22.2. HRMS (ESI) m/z: [M+H]+calculated for $C_{20}H_{21}O$ 277.1587; found 277.1593. $[M+Na]^+$ calculated for $C_{20}H_{20}NaO$ 299.1407; found 299.1415.

1-(4-chlorophenyl)-2-(cyclohex-1-en-1-yl)ethan-1-one (2.9d)



Using GP-1 with compound **2.7d** (154 mg, 1 mmol) and **2.8a** (98 mg, 1 mmol), the title compound **2.9d** was isolated as colourless liquid using silica gel column chromatography with petroleum ether and ethyl acetate (v/v = 100:1, Rf = 0.70); 89% yield (208 mg). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.91 (d, J = 8.5 Hz, 2H), 7.42 (d, J = 8.5 Hz, 2H), 5.56 (brs, 1H), 3.55 (s, 2H), 2.03 – 1.97 (m, 4H), 1.64 – 1.61 (m, 2H), 1.56 – 1.54 (m, 2H). $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$): δ 197.7, 139.5, 135.4, 132.1, 130.0, 129.0, 126.4, 48.1, 28.9, 25.5, 22.9, 22.1. HRMS (ESI) m/z: $[M+H]^+$calculated for $C_{14}H_{16}ClO$ 235.0885; found 235.0889.

1-(4-bromophenyl)-2-(cyclohex-1-en-1-yl)ethan-1-one (2.9e)

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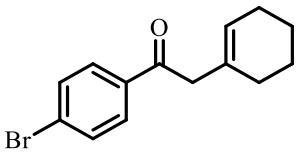
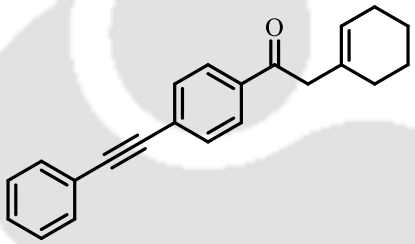


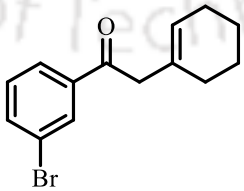
Using GP-1 with compound **2.7e** (199 mg, 1 mmol) and **2.8a** (98 mg, 1 mmol), the title compound **2.9e** was isolated as yellow liquid using silica gel column chromatography with petroleum ether and ethyl acetate (v/v = 100:1, R_f = 0.80); 92% yield (257 mg). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.84 –7.83 (m, 2H), 7.59 – 7.58 (m, 2H), 5.56 (brs, 1H), 3.54 (s, 2H), 2.02 – 1.97 (m, 4H), 1.64 – 1.62 (m, 2H), 1.56 – 1.54 (m, 2H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 197.9, 135.8, 132.1, 132.0, 130.1, 128.3, 126.4, 48.0, 28.9, 28.5, 26.4, 25.5, 22.9, 22.1. HRMS (ESI) m/z: $[M+H]^+$calculated for $C_{14}H_{16}BrO$ 279.0380; found 279.0375.

2-(cyclohex-1-en-1-yl)-1-(4-(phenylethynyl)phenyl)ethan-1-one (2.9f)



Using GP-1 with compound **2.7f** (220 mg, 1 mmol) and **2.8a** (98 mg, 1 mmol), the title compound **2.9f** was isolated as off white solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 100:1, R_f = 0.60); 86% yield (258 mg). M.p. 72-74 ºC. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.96 (d, J = 8.2 Hz, 2H), 7.59 (d, J = 8.2 Hz, 2H), 7.56 – 7.55 (m, 2H), 7.37 – 7.36 (m, 3H), 5.58 (brs, 1H), 3.59 (s, 2H), 2.03 – 2.00 (m, 4H), 1.65 – 1.62 (m, 2H), 1.57 – 1.55 (m, 2H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 198.2, 136.2, 132.2, 131.9, 131.8, 128.9, 128.6, 128.5, 128.2, 126.3, 122.8, 92.8, 88.8, 48.1, 28.9, 25.6, 22.9, 22.2. HRMS (ESI) m/z: $[M+H]^+$calculated for $C_{22}H_{21}O$ 301.1587; found 301.1571.

1-(3-bromophenyl)-2-(cyclohex-1-en-1-yl)ethan-1-one (2.9g)



Using GP-1 with compound **2.7g** (199 mg, 1 mmol) and **2.8a** (98 mg, 1 mmol), the title compound **2.9g** was isolated as yellow oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 100:1, R_f = 0.80); 91% yield (254 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.09 (s, 1H), 7.88 (d, J = 7.7 Hz, 1H), 7.67 (d, J = 7.8 Hz, 1H), 7.33 (t, J = 7.8 Hz, 1H), 5.57 (brs, 1H), 3.55 (s, 2H), 2.03 – 1.98 (m, 4H), 1.65 – 1.61 (m, 2H), 1.57 – 1.54 (m, 2H). ^{13}C{^{1}H} NMR (126 MHz,

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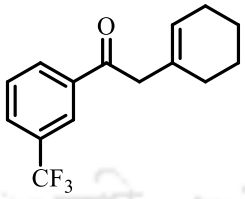
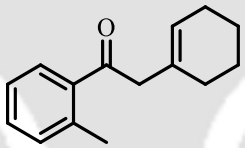
$CDCl_3$): δ 197.5, 138.9, 135.9, 131.9, 131.6, 130.3, 127.1, 126.6, 123.0, 48.0, 28.9, 25.6, 22.9, 22.1. HRMS (ESI) m/z: $[M+H]^+$calculated for $C_{14}H_{16}BrO$ 279.0380; found 279.0378.

2-(cyclohex-1-en-1-yl)-1-(3-(trifluoromethyl)phenyl)ethan-1-one (2.9h)



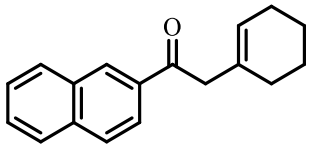
Using GP-1 with compound **2.7h** (188 mg, 1 mmol) and **2.8a** (98 mg, 1 mmol), the title compound **2.9h** was isolated as yellow oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 100:1, R_f = 0.70); 83% yield (222 mg). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.24 (s, 1H), 8.15 (d, J = 7.7 Hz, 1H), 7.81 (d, J = 7.6 Hz, 1H), 7.60 (t, J = 7.6 Hz, 1H), 5.60 (brs, 1H), 3.61 (s, 2H), 2.04 (brs, 2H), 1.99 (brs, 2H), 1.66 – 1.62 (m, 2H), 1.58 – 1.54 (m, 2H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 197.5, 137.6, 131.8, 131.7, 129.5 (q, J = 3.6 Hz), 129.4, 126.8, 125.44, 125.42, 48.2, 28.9, 25.6, 22.9, 22.1. ^{19}F NMR (377 MHz, CDCl3): δ –62.84. HRMS (ESI) m/z: [M+H]+calculated for C15H16F3O 269.1153; found 269.1158.

2-(cyclohex-1-en-1-yl)-1-(o-tolyl)ethan-1-one (3.8i)



Using GP-1 with compound **3.6c** (134 mg, 1 mmol) and **2.8a** (98 mg, 1 mmol), the title compound **3.8i** was isolated as colourless oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 100:1, R_f = 0.70); 70% yield (149 mg) using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 20:1, R_f = 0.60) ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.64 (d, J = 7.2 Hz, 1H), 7.35 (t, J = 7.6 Hz, 1H), 7.26 – 7.22 (m, 2H), 5.55 (brs, 1H), 3.51 (s, 2H), 2.48 (s, 3H), 2.04 – 1.97 (m, 4H), 1.66 – 1.60 (m, 2H), 1.56 – 1.54 (m, 2H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 203.0, 138.4, 138.2, 132.1, 132.0, 131.2, 128.7, 126.4, 125.6, 51.0, 29.0, 25.6, 22.9, 22.2, 21.3. HRMS (ESI) *m/z*: $[M+H]^+$calculated for $C_{15}H_{19}O$ 215.1431; found 215.1431.

2-(cyclohex-1-en-1-yl)-1-(naphthalen-2-yl)ethan-1-one (2.9i)



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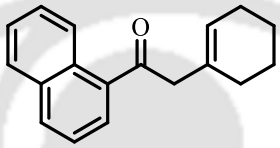
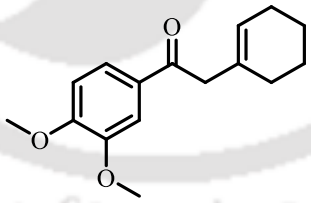
Using GP-1 with compound **2.7i** (170 mg, 1 mmol) and **2.8a** (98 mg, 1 mmol), the title compound **2.8i** was isolated as yellow oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.70); 82% yield (205 mg). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.51 (s, 1H), 8.04 (d, J = 8.6 Hz, 1H), 7.97 (d, J = 8.0 Hz, 1H), 7.88 (t, J = 8.0 Hz, 2H), 7.60 (t, J = 7.4 Hz, 1H), 7.55 (t, J = 7.4 Hz, 1H), 5.63 (brs, 1H), 3.72 (s, 2H), 2.05 – 2.04 (m, 4H), 1.66 – 1.63 (m, 2H), 1.59 – 1.56 (m, 2H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 198.9, 135.7, 134.5, 132.7, 132.5, 130.3, 129.8, 128.5, 128.5, 127.9, 126.8, 126.2, 124.4, 48.1, 29.0, 25.6, 22.9, 22.2. HRMS (ESI) m/z: $[M+H]^+$ calculated for $C_{18}H_{19}O$ 251.1430; found 251.1421.

2-(cyclohex-1-en-1-yl)-1-(naphthalen-1-yl)ethan-1-one (2.9j)



Using GP-1 with compound **2.7j** (170 mg, 1 mmol) and **2.8a** (98 mg, 1 mmol), the title compound **2.9i** was isolated as colourless oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.70); 52% yield (130 mg). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.56 (d, J = 8.4 Hz, 1H), 7.98 (d, J = 8.4 Hz, 1H), 7.89 – 7.86 (m, 2H), 7.58 (t, J = 7.2 Hz, 1H), 7.53 (t, J = 7.2 Hz, 1H), 7.49 (t, J = 7.8 Hz, 1H), 5.61 (brs, 1H), 3.68 (s, 2H), 2.03 – 2.02 (m, 4H), 1.64 –1.60 (m, 2H), 1.56 – 1.53 (m, 2H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 203.0, 136.1, 134.0, 132.4, 132.1, 130.3, 128.4, 127.8, 127.6, 126.42, 126.39, 125.9, 124.3, 51.5, 28.9, 25.4, 22.8, 22.0. HRMS (ESI) *m/z*: $[M+H]^+$calculated for $C_{18}H_{19}O$ 251.1430; found 251.1430.

2-(cyclohex-1-en-1-yl)-1-(3,4-dimethoxyphenyl)ethan-1-one (2.9k)



Using GP-1 with compound **2.7k** (180 mg, 1 mmol) and **2.8a** (98 mg, 1 mmol), the title compound **2.9k** was isolated as yellow oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.50); 81% yield (211 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.62 (dd, J = 8.4, 1.5 Hz, 1H), 7.56 – 7.55 (m, 1H), 6.88 (d, J = 8.4 Hz, 1H), 5.57 (brs, 1H), 3.94 (s, 3H), 3.93 (s, 3H), 3.55 (s, 2H), 2.03 – 2.00 (m, 4H), 1.63 – 1.62 (m, 3H), 1.57 – 1.54 (m, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 197.5, 153.4, 149.1, 132.8, 130.5, 125.8, 123.4, 110.7, 110.1, 56.2, 56.1, 47.8, 28.9, 25.6, 23.0, 22.2. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{16}H_{21}O_3$ 261.1485; found 261.1490.

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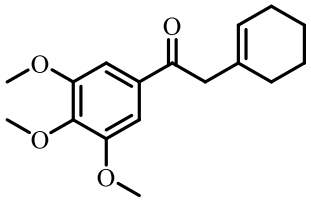
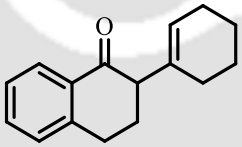
2-(cyclohex-1-en-1-yl)-1-(3,4,5-trimethoxyphenyl)ethan-1-one (2.9l)



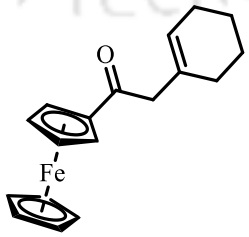
Using GP-1 with compound **2.7l** (210 mg, 1 mmol) and **2.8a** (98 mg, 1 mmol), the title compound **2.9l** was isolated as yellow oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.50); 92% yield (267 mg). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.32 – 7.31 (m, 2H), 5.66 (brs, 1H), 3.97 – 3.96 (m, 9H), 3.61 (s, 2H), 2.10 – 2.04 (m, 4H), 1.71 – 1.69 (m, 2H), 1.63 – 1.61 (m, 2H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 197.6, 153.0, 142.5, 132.6, 132.2, 125.9, 106.0, 61.0, 56.2, 48.1, 28.7, 25.5, 22.8, 22.1. HRMS (ESI) m/z: $[M+H]^+$calculated for $C_{17}H_{23}O_4$ 291.1591; found 291.1591.

2-(cyclohex-1-en-1-yl)-3,4-dihydronaphthalen-1(2H)-one (2.9u)



Using GP-1, with compound **2.7p** (146 mg, 1 mmol) and **2.8a** (98 mg, 1 mmol), the title compound **2.9u** was isolated as colourless liquid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:2, R_f = 0.50); 85% yield (192 mg). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.04 (d, J = 7.9 Hz, 1H), 7.47 – 7.43 (m, 1H), 7.30 (t, J = 7.4 Hz, 1H), 7.23 (d, J = 7.6 Hz, 1H), 5.45 (s, 1H), 3.11 (dd, J = 10.5, 4.5 Hz, 1H), 3.02 – 2.97 (m, 2H), 2.27 – 2.21 (m, 1H), 2.16 – 2.11 (m, 1H), 2.05 – 1.98 (m, 4H), 1.70 – 1.66 (m, 2H), 1.63 – 1.58 (m, 2H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 199.3, 144.3, 136.0, 133.3, 133.1, 128.8, 127.6, 126.7, 124.9, 56.3, 28.6, 28.4, 26.9, 25.5, 23.0, 22.5. HRMS (ESI) m/z: $[M+H]^+$ calculated for $C_{16}H_{19}O$ 227.1431; found 227.1436.

Compound 3.8j



Using GP-1, with compound **3.6d** (228 mg, 1 mmol) and **2.8a** (98 mg, 1 mmol), the title compound **3.8d** was isolated as red solid using silica gel column chromatography with petroleum ether/ethyl

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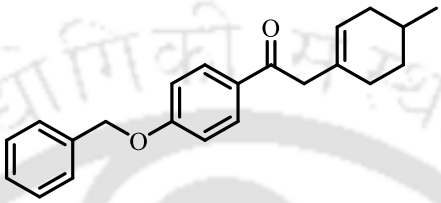
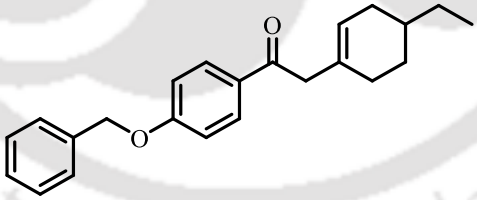
acetate (v/v = 50:2, R_f = 0.50); 52% yield (160 mg). ^{1}H NMR (600 MHz, $CDCl_3$): δ 5.58 (s, 1H), 4.80 (s, 2H), 4.49 (s, 2H), 4.21 – 4.19 (m, 5H), 3.34 (s, 2H), 2.05 – 2.04 (m, 4H), 1.67 – 1.63 (m, 2H), 1.60 – 1.58 (m, 2H).^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 202.8, 132.7, 125.7, 79.3, 72.4, 70.0, 69.8, 49.3, 29.9, 29.0, 25.5, 22.9, 22.2. HRMS (ESI) m/z: $[M+H]^+$ calculated for $C_{18}H_{21}FeO$ 309.0937 ; found 309.0935.

1-(4-(benzyloxy)phenyl)-2-(4-methylcyclohex-1-en-1-yl)ethan-1-one (3.8aa)



Using GP-1, with compound **2.7a** (226 mg, 1 mmol) and **2.8d** (112 mg, 1 mmol), the title compound **3.8aa** was isolated as red solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:2, R_f = 0.50); 91% yield (292 mg). ^{1}H NMR (600 MHz, Chloroform-*d*): δ 7.96 (d, *J* = 8.9 Hz, 2H), 7.44 – 7.35 (m, 4H), 7.36 – 7.35 (m, 1H), 7.00 (d, *J* = 8.9 Hz, 2H), 5.53 (s, 1H), 5.13 (s, 2H), 3.54 (s, 2H), 2.11 – 2.02 (m, 3H), 1.70 – 1.64 (m, 3H), 1.28 – 1.23 (m, 1H), 0.93 (d, *J* = 6.3 Hz, 3H). ^{13}C NMR (151 MHz, Chloroform-*d*): δ 197.5, 162.6, 136.4, 132.3, 130.9, 130.5, 128.8, 128.4, 127.6, 125.4, 114.6, 70.3, 47.5, 34.1, 31.1, 29.0, 28.1, 21.78. HRMS (ESI) m/z: $[M+H]^+$ calculated for $C_{22}H_{25}O_2$ 321.1850; found 321.1854.

1-(4-(benzyloxy)phenyl)-2-(4-ethylcyclohex-1-en-1-yl)ethan-1-one (3.8ab)



Using GP-1, with compound **2.7a** (226 mg, 1 mmol) and **3.7a** (126 mg, 1 mmol), the title compound **3.8ab** was isolated as white solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:2, R_f = 0.50); 92% yield (307 mg). M.p = 93-95 ºC. ^{1}H NMR (600 MHz, Chloroform-*d*): δ 7.96 (d, *J* = 8.8 Hz, 2H), 7.44 – 7.39 (m, 4H), 7.36 – 7.35 (m, 1H), 7.00 (d, *J* = 8.7 Hz, 2H), 5.54 (s, 1H), 5.13 (s, 2H), 3.54 (s, 2H), 2.14 – 2.11 (m, 1H), 2.04 – 1.99 (m, 2H), 1.76 – 1.74 (m, 1H), 1.68 – 1.64 (m, 1H), 1.60 – 1.58 (m, 1H), 1.40 (brs, 1H), 1.29 – 1.26 (m, 1H), 1.24 – 1.21 (m, 1H), 0.89 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (151 MHz, Chloroform-*d*): δ 197.52, 162.66, 136.36, 132.54, 130.88, 130.46, 128.84, 128.38, 127.62, 125.45, 114.63,

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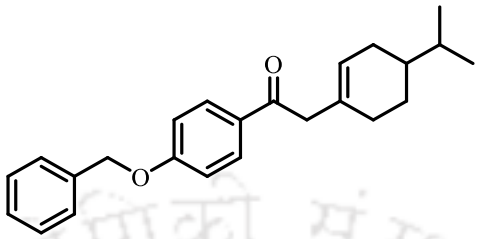
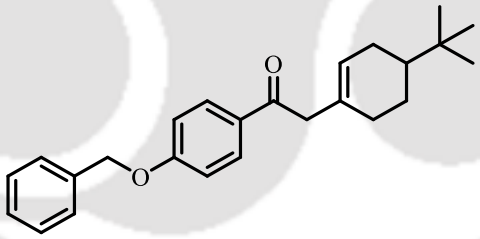
70.27, 47.48, 34.98, 31.98, 29.10, 29.03, 28.88, 11.64. HRMS (ESI) m/z: $[M+H]^+$ calculated for $C_{23}H_{27}O_2$ 335.2006; found 335.2007

1-(4-(benzyloxy)phenyl)-2-(4-isopropylcyclohex-1-en-1-yl)ethan-1-one (3.8ac)



Using GP-1 with compound **2.7a** (1 mmol, 226 mg) and **3.7e** (1 mmol, 140 mg), the title compound **3.8ac** was isolated as light yellow solid (287 mg, 81%) using silica gel column chromatography with petroleum ether and ethyl acetate (v/v = 50:1, R_f = 0.50) followed by recrystallization from petroleum ether. M.p. 91-93 ℃. 1H NMR (600 MHz, $CDCl_3$): δ 7.96 (d, J = 8.8 Hz, 2H), 7.44 – 7.39 (m, 4H), 7.36 – 7.34 (m, 1H), 7.00 (d, J = 8.8 Hz, 2H), 5.56 (brs, 1H), 5.13 (s, 2H), 3.54 (s, 2H), 2.06 – 2.04 (m, 3H), 1.80 – 1.75 (m, 2H), 1.48 – 1.44 (m, 1H), 1.28 – 1.22 (m, 2H), 0.87 (m, 6H). 13C{1H} NMR (151 MHz, $CDCl_3$): δ 197.5, 162.7, 136.4, 132.5, 130.9, 130.5, 128.8, 128.4, 127.6, 125.8, 114.6, 70.3, 47.4, 39.8, 32.3, 29.7, 29.2, 26.4, 20.9, 19.8. HRMS (ESI) m/z: $[M+H]^+$calculated for $C_{24}H_{29}O_2$ 349.2163; found 349.2165

1-(4-(benzyloxy)phenyl)-2-(4-(tert-butyl)cyclohex-1-en-1-yl)ethan-1-one (2.9q)



Using GP-1, with compound **2.7a** (226 mg, 1 mmol) and **2.8b** (154 mg, 1 mmol), the title compound **2.9q** was isolated as white solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 20:1, R_f = 0.50) followed by recrystallization from petroleum ether.; 89% yield (292 mg). M.p. 85-87 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.96 (d, J = 9.0 Hz, 2H), 7.44 – 7.39 (m, 4H), 7.36 – 7.34 (m, 1H), 7.00 (d, J = 8.4 Hz, 2H), 5.56 (brs, 1H), 5.13 (s, 2H), 3.55 (s, 2H), 2.05 – 2.04 (m, 3H), 1.84 – 1.79 (m, 2H), 1.29 – 1.17 (m, 2H), 0.85 (s, 9H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 197.5, 162.7, 136.4, 132.4, 130.9, 130.5, 128.8, 128.4, 127.6, 126.1, 114.6, 70.3, 47.3, 43.8, 32.3, 30.4, 27.3, 27.2, 24.3. HRMS (ESI) m/z: $[M+H]^+$calculated for $C_{25}H_{31}O_2$ 363.2319; found 363.2321.

1-(4-(benzyloxy)phenyl)-2-(1,2,3,6-tetrahydro-[1,1'-biphenyl]-4-yl)ethan-1-one (3.8ad)

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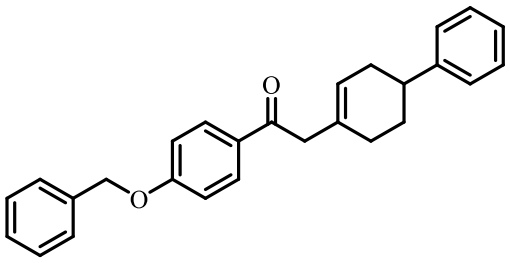
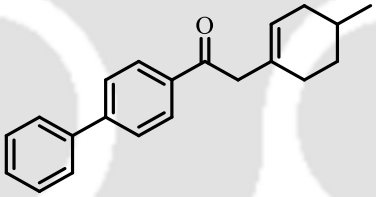


Using GP-1 with compound **2.7a** (1 mmol, 226 mg) and **2.8c** (1 mmol, 174 mg), the title compound **3.8ad** was isolated as light yellow solid (287 mg, 75%) using silica gel column chromatography with petroleum ether and ethyl acetate (v/v = 50:1, R_f = 0.50) followed by recrystallization from petroleum ether. M.p. 105-107 °C ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.01 – 7.99 (m, 2H), 7.46 – 7.40 (m, 4H), 7.37 – 7.35 (m, 1H), 7.30 (t, J = 7.0 Hz, 2H), 7.23 – 7.19 (m, 3H), 7.04 – 7.03 (d, J = 7.7 Hz, 2H), 5.67 (brs, 1H), 5.15 (s, 2H), 3.62 (s, 2H), 2.81 – 2.78 (m, 1H), 2.35 – 2.33 (m, 1H), 2.25 – 2.18 (m, 2H), 2.14 – 2.11 (m, 1H), 1.98 – 1.95 (m, 1H), 1.85 – 1.78 (m, 1H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 197.5, 162.7, 147.0, 136.3, 132.6, 130.9, 130.4, 128.8, 128.5, 128.4, 127.6, 127.0, 126.1, 125.5, 114.7, 70.3, 47.3, 39.8, 33.8, 30.0, 29.6. HRMS (ESI) *m/z*: $[M+H]^+$calculated for $C_{27}H_{27}O_2$ 383.2006; found 383.2011.

1-([1,1'-biphenyl]-4-yl)-2-(4-methylcyclohex-1-en-1-yl)ethan-1-one (2.9p)



Using GP-1 with compound **2.7c** (196 mg, 1 mmol) and **2.8d** (112 mg, 1 mmol), the title compound **2.9p** was isolated as white solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.60), followed by recrystallization from petroleum ether; 82% yield (237 mg). M.p. 68-70 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.05 (d, J = 8.4 Hz, 2H), 7.68 (d, J = 8.4 Hz, 2H), 7.63 – 7.62 (m, 2H), 7.47 (t, J = 7.8 Hz, 2H), 7.40 (t, J = 7.4 Hz, 1H), 5.57 (brs, 1H), 3.63 (s, 2H), 2.13 – 2.05 (m, 3H), 1.73 – 1.63 (m, 3H), 1.30 – 1.23 (m, 1H), 0.94 (d, J = 6.3 Hz, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 198.6, 145.8, 140.1, 135.8, 132.1, 129.2, 129.1, 128.3, 127.4, 127.3, 125.8, 47.8, 34.1, 31.1, 29.0, 28.2, 21.8. HRMS (ESI) *m/z*: $[M+H]^+$calculated for $C_{21}H_{22}O$ 291.1744; found 291.1739.

1-([1,1'-biphenyl]-4-yl)-2-(1,4-dioxaspiro[4.5]dec-7-en-8-yl)ethan-1-one (3.8ae)

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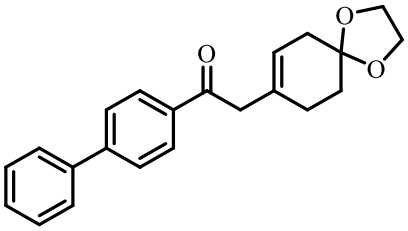
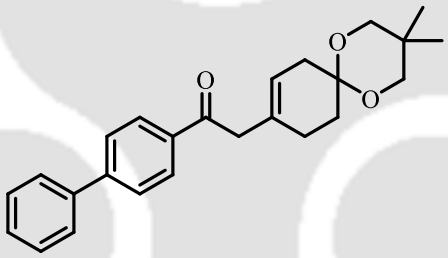


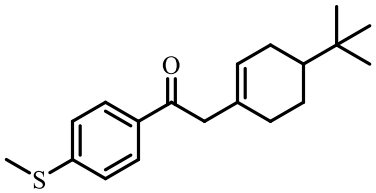
Using GP-1 with compound **2.7c** (196 mg, 1 mmol) and **2.8e** (156 mg, 1 mmol), the title compound **3.8ae** was isolated as white solid using silica gel column chromatography with petroleum ether and ethyl acetate (v/v = 20:3, R_f = 0.40); 65% yield (217 mg). M.p. 89-92 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.05 (d, J = 7.7 Hz, 2H), 7.68 (d, J = 7.7 Hz, 2H), 7.63 (d, J = 7.6 Hz, 2H), 7.47 (t, J = 7.2 Hz, 2H), 7.41 – 7.39 (m, 1H), 5.52 (s, 1H), 3.99 (s, 4H), 3.69 (s, 2H), 2.33 – 2.30 (m, 4H), 1.83 – 1.81 (m, 2H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 198.0, 145.9, 140.0, 135.7, 132.1, 129.12, 129.10, 128.4, 127.41, 127.39, 123.4, 107.9, 64.6, 46.8, 36.0, 31.2, 28.1. HRMS (ESI) *m/z:* $[M+H]^+$ calculated for $C_{22}H_{23}O_3$ 335.1642. found 335.1654.

1-([1,1'-biphenyl]-4-yl)-2-(3,3-dimethyl-1,5-dioxaspiro[5.5]undec-8-en-9-yl)ethan-1-one (3.8af)



Using GP-1 with compound **2.7c** (196 mg, 1 mmol) and **3.7f** (1 mmol, 198.3 mg), the title compound **3.8af** was isolated as white solid using silica gel column chromatography with petroleum ether and ethyl acetate (v/v = 20:3, R_f = 0.50); 67% yield (247 mg). M.p. 92-94 ^{o}C.^{1}H NMR (600 MHz, $CDCl_3$): δ 8.04 (d, J = 8.3 Hz, 2H), 7.68 (d, J = 8.3 Hz, 2H), 7.63 (d, J = 7.3 Hz, 2H), 7.47 (t, J = 7.4 Hz, 2H), 7.40 (t, J = 7.4 Hz, 1H), 5.47 (s, 1H), 3.67 (s, 2H), 3.59 (d, J = 11.4 Hz, 2H), 3.48 (d, J = 11.4 Hz, 2H), 2.42 (s, 2H), 2.18 (brs, 2H), 2.02 (t, J = 6.4 Hz, 2H), 1.04 (s, 3H), 0.91 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 198.1, 145.9, 140.0, 135.7, 132.0, 129.14, 129.10, 128.4, 127.41, 127.37, 122.5, 97.0, 70.4, 46.9, 35.3, 30.4, 27.4, 27.1, 22.9, 22.6. HRMS (ESI) *m/z:* $[M+H]^+$ calculated for $C_{25}H_{29}O_3$ 377.2112. found 377.2114.

2-(4-(tert-butyl)cyclohex-1-en-1-yl)-1-(4-(methylthio)phenyl)ethan-1-one (3.8ag)



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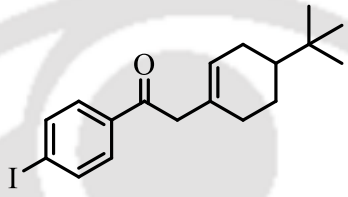
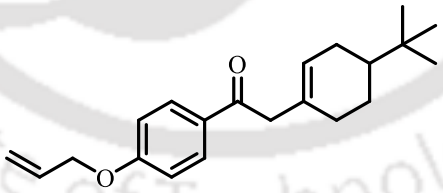
Using GP-1 with compound **3.6e** (166 mg, 1 mmol) and **2.8b** (154 mg, 1 mmol), the title compound **3.8ag** was isolated as white solid using silica gel column chromatography with petroleum ether and ethyl acetate (v/v = 50:3, R_f = 0.50); 91% yield (275 mg). M.p. 92-95 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.89 (d, J = 8.1 Hz, 2H), 7.25 (d, J = 8.4 Hz, 2H), 5.56 (s, 1H), 3.55 (s, 2H), 2.52 (s, 3H), 2.05 – 2.04 (m, 3H), 1.82 (brs, 2H), 1.25 – 1.19 (m, 2H), 0.85 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 197.9, 145.8, 133.5, 132.2, 129.0, 126.3, 125.1, 47.4, 43.8, 32.3, 30.4, 27.3, 27.2, 24.3, 14.9. HRMS (ESI) m/z: $[M+H]^+$ calculated for $C_{19}H_{27}OS$ 303.1778. found 303.1769.

2-(4-(tert-butyl)cyclohex-1-en-1-yl)-1-(4-iodophenyl)ethan-1-one (3.8ah)



Using GP-1 with compound **3.6f** (1 mmol, 226 mg) and **2.8b** (154 mg, 1 mmol), the title compound **3.8ah** was isolated as light yellow liquid using silica gel column chromatography with petroleum ether and ethyl acetate (v/v = 20:1, R_f = 0.50); 92% yield (352 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82 (d, J = 8.4 Hz, 2H), 7.68 (d, J = 8.4 Hz, 2H), 5.56 (brs, 1H), 3.55 (s, 2H), 2.06 – 2.00 (m, 3H), 1.82 – 1.79 (m, 2H), 1.26 – 1.20 (m, 2H), 0.85 (s, 9H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 198.2, 138.0, 136.4, 131.8, 130.0, 126.7, 101.0, 47.5, 43.8, 32.3, 30.4, 27.3, 27.2, 24.3. HRMS (ESI) m/z: $[M+H]^+$ calculated for $C_{18}H_{24}IO$ 383.0867; found. 383.0866.

1-(4-(allyloxy)phenyl)-2-(4-(tert-butyl)cyclohex-1-en-1-yl)ethan-1-one (2.9r)



Using GP-1 with compound **2.7m** (176 mg, 1 mmol) and **2.8b** (154 mg, 1 mmol), the title compound **2.9r** was isolated as viscous oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.50); 83% yield (259 mg). ^{1}H NMR (600 MHz, $CDCl_3$): 7.95 (d, J = 9.0 Hz, 2H), 6.93 (d, J = 9.0 Hz, 2H), 6.08 – 6.02 (m, 1H), 5.55 (brs, 1H), 5.42 (d, J = 17.4 Hz, 1H), 5.32 (d, J = 10.8 Hz, 1H), 4.60 (d, J = 4.8 Hz, 2H), 3.55 (s, 2H), 2.05 – 2.04 (m, 3H), 1.83 – 1.78 (m, 2H), 1.27 – 1.17 (m, 2H), 0.84 (s, 9H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 197.5, 162.5, 132.6, 132.4, 130.8, 130.3, 126.1, 118.3, 114.5, 69.0, 47.2, 43.8, 32.3, 30.4, 27.3, 24.3. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{21}H_{29}O_2$ 313.2163; found 313.2165.

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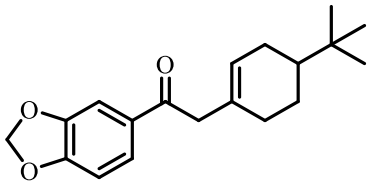
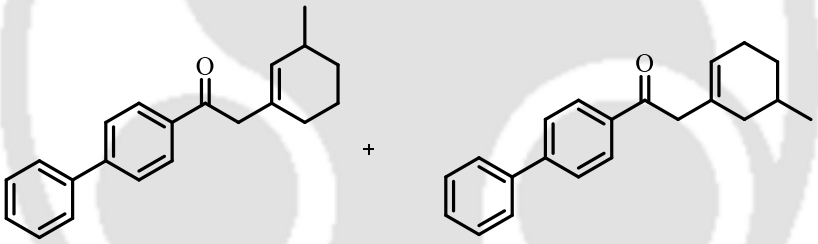
1-(benzo[d][1,3]dioxol-5-yl)-2-(4-(tert-butyl)cyclohex-1-en-1-yl)ethan-1-one (2.9s)



Using GP-1 with compound **2.7n** (164 mg, 1 mmol) and **2.8b** (154 mg, 1 mmol), the title compound **2.9s** was isolated as white solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 20:1, R_f = 0.50), followed by recrystallization from petroleum ether; 95% yield (285 mg). M.p. 90-92 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.59 (d, J = 10.2 Hz, 1H), 7.45 (s, 1H), 6.84 (d, J = 8.4 Hz, 1H), 6.04 (s, 2H), 5.56 (s, 1H), 3.52 (s, 2H), 2.06 – 2.03 (m, 3H), 1.83 – 1.79 (m, 2H), 1.27 – 1.15 (m, 3H), 0.85 (s, 9H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 197.0, 151.8, 148.2, 132.33, 132.0, 126.2, 124.9, 108.4, 108.0, 101.9, 47.4, 43.8, 32.3, 30.4, 27.3, 27.2, 24.3. HRMS (ESI) m/z: $[M+H]^+$ calculated for $C_{19}H_{25}O_3$ 301.1799; found. 301.1802.

1-([1,1'-biphenyl]-4-yl)-2-(3-methylcyclohex-1-en-1-yl)ethan-1-one + 1-([1,1'-biphenyl]-4-yl)-2-(5-methylcyclohex-1-en-1-yl)ethan-1-one (2.9v)



Using GP-1 with compound **2.7c** (196 mg, 1 mmol) and **2.8f** (112 mg, 1 mmol), the title compound **2.9v** was isolated as white solid using silica gel column chromatography with petroleum ether and ethyl acetate (v/v = 50:1, R_f = 0.70), followed by recrystallization from petroleum ether; 78% yield (227 mg). ^{1}H NMR analysis of the crude reaction mixture showed an **2.9v-1**/**2.9v-2** mixture of 71:29, as determined by comparison of the following signals: δ 5.58 (brs, 1H, C*H*, **2.9v-1**)–major, 5.45 (brs, 1H, C*H*, **2.9v-2**)–minor. M.p. 85-88 ºC. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.06 – 8.05 (m, 2H, major, 71% + m, 2H, minor, 29%), 7.68 – 7.67 (m, 2H, major, 71% + m, 2H, minor, 29%), 7.64 – 7.62 (m, 2H, major, 71% + m, 2H, minor, 29%), 7.48 – 7.46 (m, 2H, major, 71% + m, 2H, minor, 29%), 7.41 – 7.39 (m, 1H, major, 71% + m, 1H, minor, 29%), 5.59 (brs, 1H, major, 71%), 5.46 (brs, 1H, minor, 29%), 3.62 (s, 2H, major, 71% + s, 2H, minor, 29%), 2.22 (brs, 1H, minor, 29%), 2.09 – 2.04 (m, 3H, major, 71%), 1.98 (brs, 2H, minor, 29%), 1.73 – 1.64 (m, 3H, major, 71% + m, 2H, minor, 29%), 1.18 – 1.13 (m, 1H, major, 71% + m, 1H, minor, 29%), 0.97 – 0.94 (m, 3H, major, 71% + m, 3H, minor, 29%). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 198.5, 145.8, 140.1, 135.9, 132.6, 132.0, 129.2, 129.1, 128.3, 127.4, 127.33, 127.29, 125.8, 48.1, 47.9, 37.5, 31.0, 30.7, 30.4, 28.94, 28.91, 25.7, 21.92, 21.85, 21.84. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{21}H_{22}O$ 291.1744; found 291.1742.

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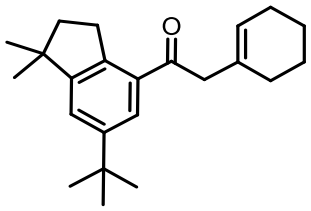
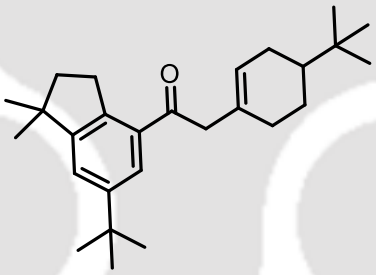
1-(6-(*tert*-butyl)-1,1-dimethyl-2,3-dihydro-1*H*-inden-4-yl)-2-(cyclohex-1-en-1-yl)ethan-1-one (2.9ai)



Using GP-1 with compound **2.7w** (1 mmol, 244 mg) and **2.8a** (1 mmol, 98 mg), the title compound **2.9ai** was isolated as light yellow solid (210 mg, 65% yield) using silica gel column chromatography with petroleum ether and ethyl acetate (v/v = 20:3, R_f = 0.50). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.79 (brs 1H), 7.32 (brs, 1H), 5.60 (s, 1H), 3.57 (s, 2H), 3.17 (t, J = 7.2 Hz, 2H), 2.05 – 2.00(m, 4H), 1.92 (t, J = 7.2 Hz, 2H), 1.66 – 1.63 (m, 2H), 1.58 – 1.55 (m, 2H), 1.35 (s, 9H), 1.26 (s, 6H). ^{13}C{^{1}H} (126 MHz, $CDCl_3$): δ 201.0, 149.8, 141.5, 133.5, 132.9, 125.9, 124.8, 123.2, 50.0, 43.5, 41.6, 34.9, 31.7, 30.9, 28.9, 25.6, 23.0, 22.3. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{23}H_{33}O$ 325.2526; found 325.2529.

1-(6-(*tert*-butyl)-1,1-dimethyl-2,3-dihydro-1H-inden-4-yl)-2-(4-(*tert*-butyl)cyclohex-1-en-1-yl)ethan-1-one (3.8ai)



Using GP-1 with compound **2.7w** (1 mmol, 244 mg) and **2.8b** (1 mmol, 154 mg), the title compound **3.8ai** was isolated as light yellow solid (262 mg, 81% yield) using silica gel column chromatography with petroleum ether and ethyl acetate (v/v = 20:3, R_f = 0.50). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80 (brs, 1H), 7.33 – 7.32 (m, 1H), 5.61 (s, 1H), 3.59 (s, 2H), 3.17 (t, J = 7.2 Hz, 2H), 2.09 – 2.05 (m, 3H), 1.92 (t, J = 7.2 Hz, 3H), 1.36 (s, 9H), 1.26 (s, 6H), 1.13 – 1.12 (m, 1H), 1.09 – 1.08 (m, 2H), 0.86 (s, 9H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 149.8, 133.5, 132.7, 126.2, 124.7, 123.2, 49.4, 43.9, 43.5, 41.6, 34.9, 32.3, 31.7, 31.7, 30.9, 30.4, 28.9, 27.4, 27.4, 27.2, 24.3. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{27}H_{41}O$ 381.3152 ; found 381.3160.

2-(cyclohex-1-en-1-yl)-1-(3,5,5,6,8,8-hexamethyl-5,6,7,8-tetrahydronaphthalen-2-yl)ethan-1-one (3.8aj)

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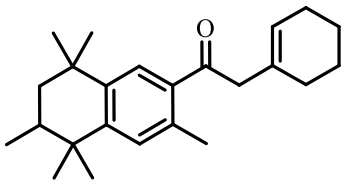
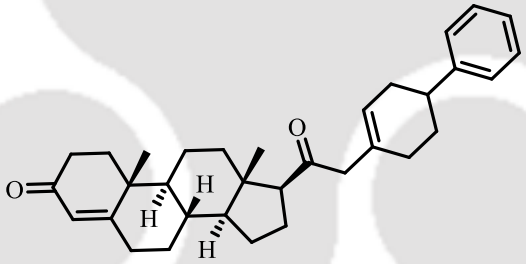


Using GP-1 with compound **3.6g** (1 mmol, 258 mg) and **2.8a** (1 mmol, 98mg), the title compound **3.8aj** was isolated as light yellow solid (277 mg, 82% yield) using silica gel column chromatography with petroleum ether and ethyl acetate (v/v = 20:3, R_f = 0.50). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.73 (s, 1H), 7.18 (s, 1H), 5.59 (s, 1H), 3.52 (s, 2H), 2.47 (s, 3H), 2.04 (brs, 2H), 1.98 (brs, 2H), 1.88 –1.85 (m, 1H), 1.65 – 1.63 (m, 2H), 1.62 – 1.61 (m, 1H) 1.56 – 1.54 (m, 2H), 1.41–1.38 (m,1H), 1.32 (s, 3H), 1.30 (s, 3H), 1.25 (s, 3H), 1.06 (s, 3H), 0.99 (d, J = 6.6 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 202.2, 150.0, 142.1, 135.6, 135.0, 132.9, 130.6, 128.2, 126.0, 51.1, 43.5, 38.0, 34.6, 34.2, 32.6, 32.1, 28.8, 28.4, 25.6, 24.8, 23.0, 22.2, 21.6, 16.9. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{24}H_{35}O$ 339.2683 ; found 339.2684.

(8S,9S,10R,13S,14S,17S)-10,13-dimethyl-17-(2-(1,2,3,6-tetrahydro-[1,1'-biphenyl]-4 yl)acetyl)-1,2,6,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-3H-cyclopenta[a]phenanthren-3-one (3.8ak)



Using GP-1 with compound **3.6h** (1 mmol, 314 mg) and **2f** (1 mmol, 174 mg), the title compound **3.8ak** was isolated as light yellow solid (305 mg, 65% yield) using silica gel column chromatography with petroleum ether and ethyl acetate (v/v = 20:3, R_f = 0.50); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31 – 7.28 (m, 2H), 7.23 – 7.19 (m, 3H), 5.74 (s, 1H), 5.58 (s, 1H), 3.011 – 3.07 (m, 2H), 2.81 – 2.75 (m, 1H), 2.67 – 2.62 (m, 1H), 2.40 – 2.37 (m, 4H), 2.33 – 2.28 (m, 2H), 2.22 – 2.13 (m, 5H), 2.08 – 2.02 (m, 4H), 1.97 – 1.93 (m, 2H), 1.88 – 1.85 (m, 2H), 1.78 – 1.71 (m, 5H), 1.67 – 1.63 (m, 4H), 1.19 – 1.18 (m, 3H), 0.70 – 0.67 (m, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 199.5, 171.0, 128.4, 126.9, 126.1, 125.5, 123.9, 61.6, 56.1, 53.7, 53.1, 44.3, 39.7, 38.8, 38.6, 35.6, 34.0, 33.6, 32.8, 31.9, 29.9, 29.6, 29.4, 24.5, 23.4, 21.1, 17.4, 13.7. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{33}H_{43}O_2$ 471.3258 ; found 471.3255.

2-((8S,9S,10R,13R,14S)-10,13-dimethyl-17-(6-methylheptan-2-yl)-2,7,8,9,10,11,12,13,14, 15,16,17-dodecahydro-1H-cyclopenta[*a*]phenanthren-3-yl)-1-(4-methoxyphenyl)ethan-1-one (2.9aj)

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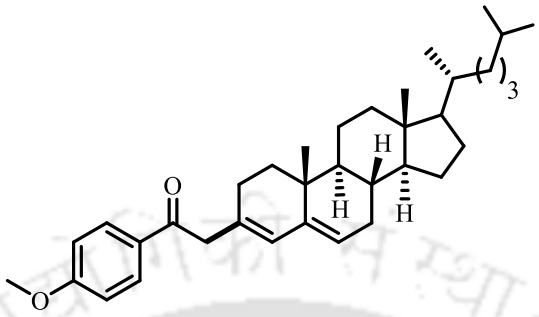
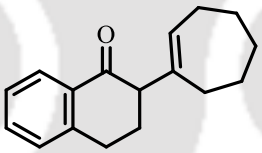
The title compound **2.9aj** was isolated as white solid using silica gel column chromatography with petroleum ether and ethyl acetate (v/v = 20:1, R_f = 0.5). The title compound **5e** was 276 mg, 52% yield, starting from **2.7b** (1 mmol) and **2.8x** (1 mmol, 356 mg) using GP-1 method.



M.p. 94-96 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.96 (d, J = 8.9 Hz, 2H, ArH), 6.92 (d, J = 8.6 Hz, 2H, ArH), 5.84 (s, 1H, C=C*H*), 5.36 (br, 1H, C=C*H*), 3.86 (s, 3H, CH_3), 3.62 (brs, 1H), 3.61 (brs, 1H), 2.24 – 2.13 (m, 2H), 2.05 – 2.00 (m, 2H), 1.84 – 1.79 (m, 2H), 1.68 – 1.51 (m, 6H), 1.43 – 1.33 (m, 6H), 1.23 – 1.15 (m, 3H), 1.14 – 1.07 (m, 4H), 1.02 – 0.96 (m, 3H), 0.92 – 0.90 (m, 6H), 0.87 – 0.85 (m, 7H), 0.69 (brs, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 197.1, 163.5, 141.6, 130.9, 130.8, 130.2, 128.3, 123.2, 113.8, 57.1, 56.3, 55.6, 48.3, 47.4, 42.6, 39.9, 39.7, 36.3, 35.9, 34.9, 34.1, 32, 31.9, 28.4, 28.2, 26.8, 24.3, 24.0, 23.0, 22.7, 21.2, 19.1, 18.8, 12.1. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{36}H_{53}O_2$: 517.4041; found 517.4020.

2-(cyclohept-1-en-1-yl)-3,4-dihydronaphthalen-1(2H)-one (2.9af)



Using GP-1 with compound **2.7p** (146 mg, 1 mmol) and **2.8i** (112 mg 1 mmol), the title compound **2.9af** was isolated as light yellow liquid (186 mg, 78% yield) using neutralized silica column chromatography with petroleum ether/ethyl acetate (v/v = 50:2, R_f = 0.50).^{1}H NMR (600 MHz, $CDCl_3$): δ 8.04 (d, J = 7.8 Hz, 1H), 7.46 (t, J = 7.2, 1H), 7.30 (t, J = 7.8 Hz, 1H), 7.23 (d, J = 7.8 Hz, 1H), 5.62 (t, J = 6.6 Hz, 1H), 3.18 (dd, J = 11.4, 4.8 Hz, 1H), 3.02 – 3.00 (m, 2H), 2.23 – 2.07 (m, 6H), 1.78 – 1.75 (m, 2H), 1.64 – 1.61(m, 1H), 1.52 – 1.43 (m, 3H).^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 199.4, 144.3, 143.2, 133.3, 133.2, 123.0, 128.8, 127.6, 126.7, 58.6, 32.9, 33.0, 28.9, 28.9, 28.7, 27.2. HRMS (ESI) *m/z*: $[M+Na]^+$ calculated for $C_{17}H_{20}NaO$ 263.1407; found 263.1421.

(*E*)-2-(cyclooct-1-en-1-yl)-3,4-dihydronaphthalen-1(2H)-one (2.9ag)

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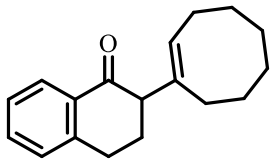
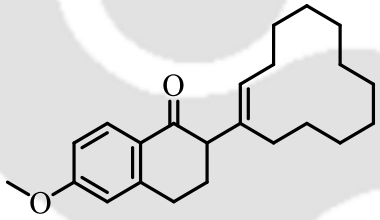


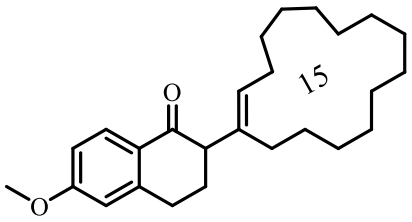
Using GP-1 with compound **2.7p** (146 mg, 1 mmol) and **2.8j** (112 mg 1 mmol), the title compound **2.9ag** was isolated as light yellow liquid (165 mg, 65% yield) using silica column chromatography with petroleum ether/ethyl acetate (v/v = 50:2, R_f = 0.50). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.04 (d, J = 7.8 Hz, 1H), 7.46 – 7.44 (m, 1H), 7.30 (t, J = 7.8 Hz, 1H), 7.23 (d, J = 7.8 Hz, 1H), 5.37 (t, J = 8.4 Hz, 1H), 3.20 (dd, J = 10.8, 4.8 Hz, 1H), 3.05 – 2.95 (m, 2H), 2.28 – 2.24 (m, 1H), 2.20 – 2.12 (m, 5H), 1.56 – 1.48 (m, 7H).^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): 199.5, 144.2, 138.9, 133.3, 133.2, 128.8, 127.9, 127.6, 126.7, 56.7, 29.7, 29.4, 29.0, 28.8, 28.7, 26.5, 26.45, 26.40. HRMS (ESI) m/z: $[M+H]^+$ calculated for $C_{18}H_{23}O$ 255.1744; found 255.1747.

(Z)-2-(cyclododec-1-en-1-yl)-6-methoxy-3,4-dihydronaphthalen-1(2H)-one (2.9ah)



Using GP-1 with compound **2.7q** (1 mmol, 176 mg) and **2.8k** (1 mmol, 154 mg), the title compound **2.9ah** was isolated as light yellow liquid (76% yield) using silica gel column chromatography with petroleum ether/ethyl acetate/ (v/v = 50:3, R_f = 0.50). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.02 (d, J = 9.0 Hz, 1H), 6.82 (dd, J = 9.0, 3.0 Hz, 1H), 6.68 – 6.67 (m, 1H), 5.06 (t, J = 7.8 Hz, 1H), 3.85 (s, 3H), 3.18 – 3.16 (m, 1H), 2.96 – 2.94 (m, 1H), 2.89 – 2.88 (m, 1H), 2.47 – 2.45 (m, 1H), 2.33 – 2.30 (m, 1H), 2.23 – 2.20 (m, 2H), 2.16 – 2.12 (m, 2H), 1.52 – 1.48 (m, 2H), 1.43 – 1.40 (m, 3H), 1.40 – 1.37 (m, 3H), 1.33 – 1.25 (m, 8H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 198.6, 146.6, 137.7, 130.1, 128.9, 127.1, 113.1, 112.6, 55.5, 53.1, 29.8, 29.1, 28.7, 27.3, 26.6, 25.9, 25.3, 25.2, 24.9, 24.6, 24.6, 22.8, 22.7, 14.3. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{23}H_{33}O_2$ 341.2476; found 341.2485.

(*E*)-2-(cyclopentadec-1-en-1-yl)-6-methoxy-3,4-dihydronaphthalen-1(2H)-one (3.11a)



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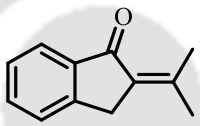
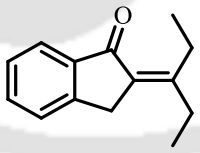
Using GP-1 with compound **2.7q** (1 mmol, 176 mg) and **3.7g** (1 mmol, 154 mg), the title compound **3.11b** was isolated as lightyellow liquid (195 mg, 51% yield) using silica gel column chromatography with petroleum ether/ethyl acetate/ (v/v = 20:2, R_f = 0.50). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.02 (d, J = 8.4 Hz, 1H), 6.82 (d, J = 10.4 Hz, 1H), 6.68 (s, 1H), 5.13 (t, J = 7.6 Hz, 1H), 3.85 (s, 3H), 3.13 (dd, J = 9.6, 4.8 Hz, 1H), 2.95 –2.91 (m, 2H), 2.21 – 2.14 (m, 3H), 2.05 – 1.97 (m, 3H), 1.39 – 1.29 (m, 22H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 198.5, 146.6, 138.0, 130.1, 128.9, 113.1, 112.5, 55.7, 55.5, 30.3, 29.2, 29.0, 28.3, 28.00, 27.96, 27.88, 27.5, 27.2, 27.10, 27.06, 26.99, 26.96, 26.9, 26.8, 26.8, 26.5, 26.1, 26.1, 25.8, 23.3. HRMS (ESI) m/z: $[M+H]^+$ calculated for $C_{26}H_{39}O_2$ 383.2945; found. 383.2938.

2-(propan-2-ylidene)-2,3-dihydro-1H-inden-1-one (3.12a)



Using GP-2 with compound **3.6i** (1 mmol, 132 mg) and **2.7v** (10 mmol, 580 mg), the title compound **3.12a** was isolated as colourless liquid (68.8 mg, 40% yield) using silica gel column chromatography with petroleum ether/ethyl acetate/ (v/v = 50:2, R_f = 0.40). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.80 (d, J = 7.8 Hz, 1H), 7.55 (t, J = 7.8 Hz, 1H), 7.46 (d, J = 7.8 Hz, 1H), 7.37 (d, J = 7.2 Hz, 1H), 3.65 (s, 2H), 2.44 (s, 3H), 2.01 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 194.2, 148.0, 140.5, 133.8, 130.6, 127.3, 126.1, 124.0, 32.4, 24.7, 20.6. Spectral data in accordance with the literature.[26]

2-(pentan-3-ylidene)-2,3-dihydro-1H-inden-1-one (3.12b)



Using GP-2 with compound **3.6i** (1 mmol, 132 mg) and **2.8g** (6 mmol, 516 mg), the title compound **3.12b** was isolated as colourless liquid (130 mg, 65% yield) using silica gel column chromatography with petroleum ether/ethyl acetate/ (v/v = 50:1, R_f = 0.50). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80 (d, J = 7.6 Hz, 1H), 7.56 – 7.52 (m, 1H), 7.45 (d, J = 7.6 Hz, 1H), 7.36 (J = 7.2 Hz, 1H), 3.66 (s, 2H), 2.93 (q, J = 7.2 Hz, 2H), 2.31 (q, J = 7.6 Hz, 2H), 1.16 – 1.11 (m, 6H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 194.0, 161.1, 148.2, 140.6, 133.8, 129.4, 127.3, 126.1, 124.0, 31.7, 28.9, 24.2, 13.8, 12.0. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{14}H_{17}O$ 201.1274; found 201.1277.

2-(heptan-4-ylidene)-2,3-dihydro-1H-inden-1-one (3.12c)

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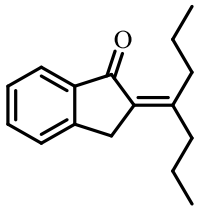
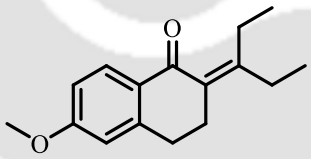


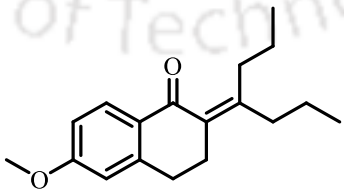
Using GP-2 with compound **3.6i** (1 mmol, 132 mg) and **2.8h** (6 mmol, 684 mg), the title compound **3.12c** was isolated as yellow oil (155 mg, 68% yield) using silica gel column chromatography with petroleum ether/ethyl acetate/ (v/v = 50:2, R_f = 0.40).^{1}H NMR (400 MHz, $CDCl_3$): δ 7.72 (d, J = 7.6 Hz, 1H), 7.49 – 7.46 (m, 1H), 7.38 (d, J = 7.6 Hz, 1H), 7.32 – 7.30 (t, J = 8.0 Hz 1H), 3.61 (s, 2H), 2.82 – 2.78 (m, 2H), 2.21 – 2.18 (m, 2H), 1.55 – 1.51 (m, 2H), 1.49 – 1.44 (m, 2H), 0.96 – 0.91 (m, 6H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 194.0, 158.7, 148.2, 140.7, 133.8, 130.6, 127.3, 126.0, 124.0, 38.4, 33.5, 32.1, 22.4, 21.1, 14.65, 14.61. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{16}H_{21}O$ 229.1587; found 229.1600.

6-methoxy-2-(pentan-3-ylidene)-3,4-dihydronaphthalen-1(2*H*)-one (2.10b)



Using GP-2 with compound **2.7q** (1 mmol, 176 mg) and **2.8g** (6 mmol, 516 mg), the title compound **2.10b** was isolated as colourless oil (166 mg, 68% yield) using silica gel column chromatography with petroleum ether/ethyl acetate/ (v/v = 50:2, R_f = 0.50).^{1}H NMR (600 MHz, $CDCl_3$): δ 8.07 (d, J = 9.0 Hz, 1H), 6.83 (dd, J = 9.0, 3.0 Hz, 1H), 6.67 (brs, 1H), 3.85 (s, 3H), 2.93 (t, J = 6.0 Hz, 2H), 2.76 (t, J = 6.0 Hz, 2H), 2.50 (q, J = 7.2 Hz, 2H), 2.24 (q, J = 7.2 Hz, 2H), 1.15 (t, J = 7.8 Hz, 3H), 1.08 (t, J = 7.8 Hz, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 189.1, 163.0, 156.2, 146.0, 130.4, 130.1, 128.7, 113.0, 112.3, 55.5, 31.3, 28.6, 27.6, 27.2, 13.8, 13.5. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{16}H_{21}O_2$ 245.1537; found 245.1540.

2-(heptan-4-ylidene)-6-methoxy-3,4-dihydronaphthalen-1(2H)-one (2.10c)



Using GP-2 with compound **2.7q** (1 mmol, 176 mg) and **2.8h** (6 mmol, 684 mg), the title compound **2.10c** was isolated as white solid (190 mg, 70% yield) using silica gel column chromatography with petroleum ether/ethyl acetate/ (v/v = 50:2, R_f = 0.50). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.09 (d, J = 9.0 Hz, 1H), 6.85 (dd, J = 8.4, 2.4 Hz, 1H), 6.69 (brs, 1H), 3.87 (s, 3H),

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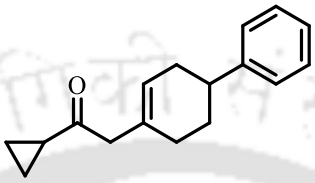
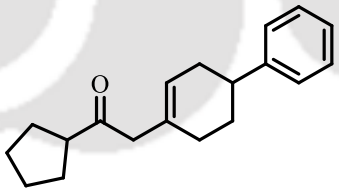
2.94 (t, *J* = 6.0 Hz, 2H), 2.78 (t, *J* = 6.0 Hz, 2H), 2.50 – 2.48 (m, 2H), 2.23 – 2.20 (m, 2H), 1.60 – 1.55 (m, 2H), 1.53 – 1.49 (m, 2H), 1.01 (q, *J* = 7.8 Hz, 6H). $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$): *δ* 189.1, 163.0, 153.4, 146.0, 130.9, 130.4, 128.8, 113.0, 112.3, 36.9, 31.3, 28.9, 22.8, 22.4, 14.7. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{18}H_{25}O_2$ 273.1850; found $C_{18}H_{25}O_2$ 273.1853.

1-cyclopropyl-2-(1,2,3,6-tetrahydro-[1,1'-biphenyl]-4-yl)ethan-1-one (3.11b)



Using GP-1 with compound **3.6j** (1 mmol, 84 mg) and **2.8c** (1 mmol, 174 mg), the title compound **3.11b** was isolated as colourless liquid (165 mg, 65% yield) using silica gel column chromatography with petroleum ether/ethyl acetate/ (v/v = 50:2, R_f = 0.50). ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 7.32 – 7.28 (m, 2H), 7.24 – 7.18 (m, 3H), 5.68 (brs, 1H), 3.21 (s, 2H), 2.82 – 2.76 (m, 1H), 2.38 – 2.34 (m, 1H), 2.24 – 2.18 (m, 2H), 2.07 – 2.02 (m, 2H), 1.98 – 1.94 (m, 1H), 1.85 – 1.78 (m, 1H), 1.04 – 1.02 (m, 2H), 0.89 – 0.85 (m, 2H). $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$): *δ* 209.7, 147.0, 132.0, 128.5, 127.0, 126.2, 125.9, 52.9, 39.8, 33.7, 30.0, 29.4, 19.9, 11.2. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{17}H_{21}O$ 241.1587; found 241.1585

1-cyclopentyl-2-(1,2,3,6-tetrahydro-[1,1'-biphenyl]-4-yl)ethan-1-one (2.9aa)



Using GP-1 with compound **2.7r** (1 mmol, 112 mg) and **2.8c** (1 mmol, 174 mg), the title compound **2.9aa** was isolated as colourless liquid (201 mg, 75% yield) using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:2, R_f = 0.50)^{1}H NMR (600 MHz, $CDCl_3$): *δ* 7.31 – 7.29 (m, 2H), 7.22 – 7.19 (m, 3H), 5.62 (brs, 1H), 3.14 (s, 2H), 2.98 (p, *J* = 8.4 Hz, 1H), 2.80 – 2.75 (m, 1H), 2.35 – 2.32 (m, 1H), 2.20 – 2.15 (m, 2H), 2.04 – 2.01 (m, 1H), 1.96 – 1.93 (m, 1H), 1.83 – 1.78 (m, 3H), 1.76 – 1.73 (m, 2H), 1.69 – 1.66 (m, 2H), 1.60 – 1.58 (m, 2H). $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$): *δ* 211.99, 147.0, 132.0, 128.5, 127.0, 126.2, 125.7, 51.2, 50.7, 39.9, 33.8, 30.0, 29.5, 29.3, 29.3, 26.2. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{19}H_{25}O$ 269.1900; found 269.1895

1-cyclohexyl-2-(1,2,3,6-tetrahydro-[1,1'-biphenyl]-4-yl)ethan-1-one (2.9ab)

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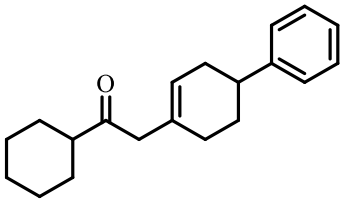
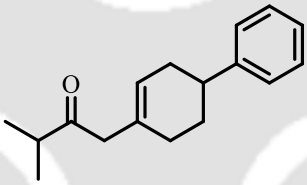


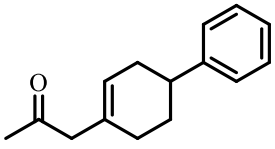
Using GP-1 with compound **2.7s** (1 mmol, 126 mg) and **2.8c** (1 mmol, 174 mg), the title compound **2.9ab** was isolated as colourless liquid (217 mg, 77% yield) using silica gel column chromatography with petroleum ether/ethyl acetate/ (v/v = 100:1, R_f = 0.60). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.31 – 7.28 (m, 2H), 7.23 – 7.19 (m, 3H), 5.60 (brs, 1H), 3.12 (s, 2H), 2.80 – 2.75 (m, 1H), 2.47 – 2.42 (m, 1H), 2.36 – 2.32 (m, 1H), 2.21 – 2.14 (m, 2H), 2.02 – 1.9 (m, 3H), 1.83 – 1.79 (m, 4H), 1.34 – 1.26 (m, 6H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 212.6, 147.0, 132.0, 128.5, 127.0, 126.2, 125.6, 50.3, 49.9, 39.8, 33.7, 30.0, 29.5, 28.8, 28.7, 26.0, 25.8, 25.8. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{20}H_{27}O$ 283.2057; found 283.2056.

3-methyl-1-(1,2,3,6-tetrahydro-[1,1'-biphenyl]-4-yl)butan-2-one (2.9ac)



Using GP-1 with compound **2.7t** (1 mmol, 86 mg) and **2.8c** (1 mmol, 174 mg), the title compound **2.9ac** was isolated as colourless liquid (135 mg, 57% yield) using silica gel column chromatography with petroleum ether/ethyl acetate/ (v/v = 50:1, R_f = 0.60). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.32 – 7.29 (m 2H), 7.24 – 7.19 (m, 3H), 5.62 (brs, 1H), 3.15 (s, 2H), 2.80 – 2.72 (m, 2H), 2.37 – 2.33 (m, 1H), 2.23 – 2.16 (m, 2H), 2.04 – 2.02 (m 1H), 1.97 – 1.94 (m, 1H), 1.83 – 1.77 (m, 1H), 1.12 – 1.11 (m, 6H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 213.3, 131.9, 128.5, 127.0, 126.1, 125.7, 49.7, 40.1, 39.8, 33.7, 30.0, 29.4, 18.5, 18.4. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{17}H_{23}O$ 243.1744; found 243.1746.

1-(1,2,3,6-tetrahydro-[1,1'-biphenyl]-4-yl)propan-2-one (2.9ae)



Using GP-1 with compound **2.7v** (10 mmol, 580 mg) and **2.8c** (1 mmol, 174 mg), the title compound **2.9ae** was isolated as colourless liquid (165 mg, 55% yield) using silica gel column

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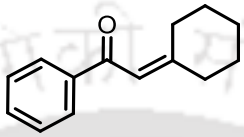
chromatography with petroleum ether/ethyl acetate/ (v/v = 100:2, R_f = 0.60). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.32 – 7.29 (m, 2H), 7.23 – 7.20 (m, 3H), 5.66 (brs, 1H), 3.09 (m, 2H), 2.80 – 2.75 (m, 1H), 2.38 – 2.33 (m, 1H), 2.22 – 2.21 (m, 1H), 2.17 (s, 3H), 2.05 – 1.94 (m, 3H), 1.83 – 1.78 (m, 1H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 207.7, 146.9, 131.8, 128.5, 127.0, 126.2, 126.05, 53.01, 39.81, 33.71, 30.02, 29.3. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{15}H_{19}O$ 215.1431 found 215.1430.

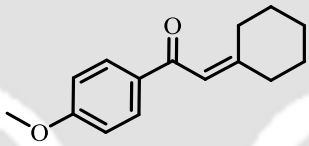
2-cyclohexylidene-1-phenylethan-1-one (2.10a)



The title compound **2.10a** was obtained using reported method.[26]

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95 – 7.93 (m, 2H), 7.55 – 7.50 (m, 1H), 7.46 – 7.42 (m, 2H), 6.60 (s, 1H), 2.78 – 2.75 (m, 2H), 2.33 – 2.28 (m, 2H), 1.74 – 1.61 (m, 6H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 192.6, 163.0, 139.4, 132.5, 128.5, 128.9, 118.9, 38.6, 30.8, 29.0, 28.1, 26.4.

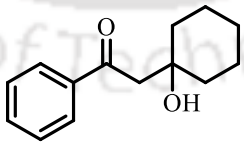
2-cyclohexylidene-1-(4-methoxyphenyl)ethan-1-one (2.10d)



The title compound **2.10d** was obtained using reported method.[26]

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.95 – 7.93 (m, 2H), 6.93 – 6.92 (m, 2H), 3.87 (s, 3H), 2.73 – 2.72 (m, 2H), 2.31 – 2.28 (m, 2H), 1.74 – 1.70 (m, 2H), 1.64 – 1.61 (m, 4H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 191.1, 163.1, 161.5, 132.2, 130.8, 113.6, 55.6, 38.5, 30.8, 29.0, 28.1, 26.4.

2-(1-hydroxycyclohexyl)-1-phenylethan-1-one (2.18)



^{1}H NMR (600 MHz, $CDCl_3$): δ 7.96 – 7.95 (m, 2H), 7.59 (t, J = 7.4 Hz, 1H), 7.48 (t, J = 7.8 Hz, 2H), 3.99 (s, 1H), 3.12 (s, 2H), 1.77 – 1.69 (m, 4H), 1.58 – 1.56 (s, 1H), 1.48 – 1.44 (m, 4H), 1.31 – 1.25 (m, 1H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 202.1, 137.6, 133.7, 128.8, 128.2, 124.5, 71.1, 47.8, 37.9, 25.9, 22.1. The spectral data is in accordance with the literature.[27]

1,3-di([1,1'-biphenyl]-4-yl)-3-hydroxybutan-1-one (2.14)

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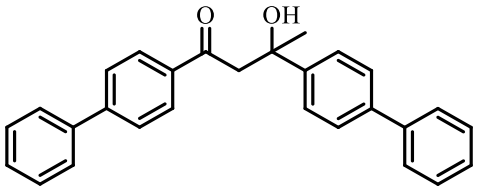
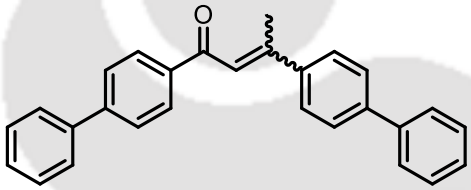


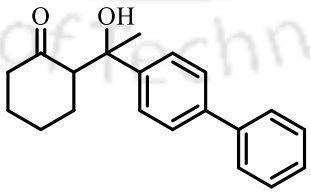
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.01 (d, J = 8.3 Hz, 2H), 7.68 (d, J = 8.4 Hz, 2H), 7.62 (d, J = 8.4 Hz, 2H), 7.58 – 7.56 (m, 6H), 7.49 – 7.46 (m, 2H), 7.43 – 7.40 (m, 3H), 7.34 – 7.31 (m, 1H), 4.94 (s, 1H), 3.86 (d, J = 17.3 Hz, 1H), 3.41 (d, J = 17.3 Hz, 1H), 1.68 (s, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 201.1, 146.9, 146.6, 140.9, 139.8, 139.7, 135.8, 129.1, 128.9, 128.8, 128.6, 127.5, 127.4, 127.3, 127.2, 125.0, 73.7, 49.0, 31.1. HRMS (ESI) *m/z*: $[M+Na]^+$ calculated for $C_{28}H_{24}O_2Na$ 415.1674; found 415.1670.

1,3-di([1,1'-biphenyl]-4-yl)but-2-en-1-one (2.15)



^{1}H NMR (400 MHz, $CDCl_3$): δ 8.11 – 8.09 (m, 2H, *E*-isomer + *Z*-isomer), 7.73 – 7.71 (m, 3H, *E*-isomer + *Z*-isomer), 7.68 – 7.67 (m, 3H, *E*-isomer + *Z*-isomer), 7.66 – 7.63 (m, 4H, *E*-isomer + *Z*-isomer) 7.50 – 7.46 (m, 4H, *E*-isomer + *Z*-isomer), 7.42 – 7.39 (m, 2H, *E*-isomer + *Z*-isomer), 7.28 (brs, 1H, *E*-isomer + *Z*-isomer), 2.66 (d, J = 1.2 Hz, 3H, *E*-isomer, 80%), 2.65 (s, 3H, *Z*-isomer, 20%). ^{13}C NMR (151 MHz, $CDCl_3$): δ 191.5, 154.7, 145.4, 142.2, 141.7, 140.4, 140.2, 138.3, 129.10, 129.05, 128.3, 127.89, 127.86, 127.45, 127.44, 127.39, 127.23, 127.15, 122.1, 18.9. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{28}H_{23}O$ 375.1744 found 375.1745.

2-(1-([1,1'-biphenyl]-4-yl)-1-hydroxyethyl)cyclohexan-1-one (2.16)



^{1}H NMR (600 MHz, $CDCl_3$): δ 7.58 (d, J = 7.4 Hz, 2H), 7.56 – 7.55 (m, 2H), 7.51 – 7.50 (m, 2H), 7.44 – 7.41 (m, 2H), 7.33 (t, J = 7.4 Hz, 1H), 4.45 (s, 1H), 2.93 (dd, J = 12.6, 5.2 Hz, 1H), 2.36 – 2.34 (m, 2H), 2.17 – 2.10 (m, 2H), 1.95 – 1.93 (m, 1H), 1.73 – 1.66 (m, 3H), 1.53 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 216.0, 147.0, 141.0, 139.6, 128.8, 127.3, 127.2, 126.9, 125.5, 74.9,

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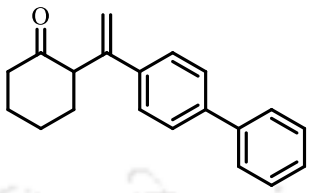
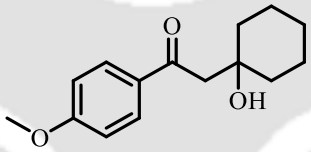
59.8, 43.8, 29.9, 28.4, 25.7, 25.6. HRMS (ESI) m/z: $[M+Na]^+$ calculated for $C_{20}H_{22}O_2Na$ 317.1512; found 317.1517.

2-(1-([1,1'-biphenyl]-4-yl)vinyl)cyclohexan-1-one (2.17)



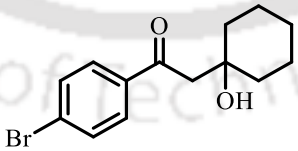
^1H NMR (600 MHz, $CDCl_3$): δ 7.59 – 7.57 (m, 2H), 7.53 (d, J = 8.4 Hz, 2H), 7.44 – 7.42 (m, 2H), 7.37 (d, J = 8.4 Hz, 2H), 7.33 (t, J = 7.2 Hz, 1H), 5.56 (s, 1H), 5.14 (s, 1H), 3.63 (dd, J = 11.6, 4.8 Hz, 1H), 2.54 – 2.51 (m, 1H), 2.47 – 2.43 (m, 1H), 2.24 – 2.21 (m, 1H), 2.13 – 2.10 (m, 1H), 1.99 – 1.92 (m, 2H), 1.82 – 1.76 (m, 2H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 210.9, 146.3, 140.88, 140.86, 140.3, 128.9, 127.4, 127.15, 127.10, 127.03, 126.95, 125.2, 115.3, 56.6, 42.6, 33.4, 28.1, 25.2. HRMS (ESI) *m/z*: $[M+H]^+$calculated for $C_{20}H_{21}O$ 277.1587; found 277.1598.

2-(1-hydroxycyclohexyl)-1-(4-methoxyphenyl)ethan-1-one (3.19)



^1H NMR (600 MHz, $CDCl_3$): δ 7.92 (d, J = 8.9 Hz, 2H), 6.92 (d, J = 8.9 Hz, 2H), 4.19 (s, 1H), 3.85 (s, 3H), 3.03 (s, 2H), 1.73 – 1.69 (m, 4H), 1.55 – 1.53 (m, 1H), 1.44 – 1.40 (m, 4H), 1.29 – 1.24 (m, 1H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 200.5, 163.9, 130.6, 113.9, 71.1, 55.6, 47.1, 37.9, 25.8, 22.0. HRMS (ESI) *m/z*: $[M+Na]^+$ calculated for $C_{15}H_{20}O_3Na$ 271.1305; found 271.1304.

1-(4-bromophenyl)-2-(1-hydroxycyclohexyl)ethan-1-one (3.20)



^1H NMR (400 MHz, $CDCl_3$): δ 7.81 (d, J = 8.5 Hz, 2H), 7.61 (d, J = 8.5 Hz, 2H), 3.75 (s, 1H), 3.07 (s, 2H), 1.76 – 1.67 (m, 4H), 1.58 – 1.56 (m, 1H), 1.47 – 1.42 (m, 4H), 1.32 – 1.26 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 200.8, 136.4, 132.1, 129.8, 128.9, 71.1, 48.0, 37.9, 25.9, 22.1. HRMS (ESI) *m/z:* $[M-H_2O+H^+]$ calculated for $C_{14}H_{17}BrO_2$ 279.0380; found 279.0377. During the measurement dehydration occurs.

2-(1-hydroxycyclohexyl)-1-(3-(trifluoromethyl)phenyl)ethan-1-one (3.21)

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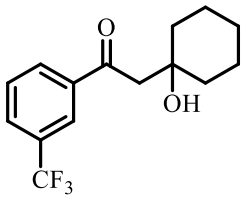

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.19 (s, 1H), 8.13 (d, J = 7.9 Hz, 1H), 7.82 (d, J = 7.8 Hz, 1H), 7.61 (t, J = 7.8 Hz, 1H), 3.63 (s, 1H), 3.12 (s, 2H), 1.77 – 1.73 (m, 2H), 1.69 – 1.65 (m, 2H), 1.58 – 1.56 (m, 1H), 1.49 – 1.44 (m, 4H), 1.29 – 1.26 (m, 1H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 200.2, 138.0, 131.3, 129.9 (q, J = 3.6 Hz), 129.4, 125.0, 124.9, 71.0, 48.2, 37.7, 25.7, 21.9. ^{19}F NMR (565 MHz, $CDCl_3$): δ -62.80. HRMS (ESI) *m/z:* $[M+Na]^+$ calculated for $C_{15}H_{17}F_3O_2Na$ 309.1073; found 309.1073.

3.7. Computational details:

All density functional theory computations, including geometry optimization, single-point calculations, vibrational frequency, and reaction free energies, were performed using the Gaussian16 suite of programs.[28] For 3d elements, M06L is highly recommended for thermochemical calculations. Consequently, the M06L functional was employed consistently throughout the computations, utilizing a 6-31G(d) basis set for C, H, N, and an SDD pseudopotential basis set for Cr. Harmonic vibrational frequencies were determined at the same theoretical level to ensure the absence of saddle points in intermediate geometries and the presence of only one imaginary frequency in transition state structures. Furthermore, an IRC calculation was conducted to verify the connectivity of the transition state structure with reactants and products. Coordinates for all the optimized structures is given in Annexure VII.

Table 3.7: Free Energies (G) and Total Energies (E) of all the optimized structures given in Hartree along with the number of imaginary frequencies

Species	Free energy (G)	Total energy (E)	# Imaginary Frequency (NImag)
3.4b' + 2.10a	-2395.132622	-2395.814347	0
Int-3A	-2395.132876	-2395.742928	0
TS-1	-2395.111296	-2395.716772	-1037.65 cm^{-1}
Int-3B	-2395.120122	-2395.730376	0
TS-2	-2395.092083	-2395.697457	-1268.57 cm^{-1}
3.4b'+2.9w	-2395.157203	-2395.767804	0

3.8. References

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Chapter 4

Chromium complex catalyzed an efficient and sustainable synthesis of N-heteroaromatic compounds via acceptorless dehydrogenative coupling reactions

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4.1. Introduction

Aromatic *N*-heterocyclic compounds are important class of compounds due to their versatile pharmaceutical and biological activities. Among them quinolines and quinazoline have gained remarkable attention over the past decades owing to their versatile role in pharmaceutical and agrochemical industries.[1, 2] Quinoline derivatives play an important role in drug development as they have been widely used as antimicrobial, antimalarial, anti-inflammatory, anti-Alzheimer and anticancer agents.[3] Chloroquine, a 4-aminoquinoline derivative, has been shown to be an effective drug for treatment of malaria.[4] Furthermore, a dimethoxy derivatives of 3-aryl quinolines inhibit platelet derived growth factor receptor tyrosine kinase (PDGF-RTK).[5] Quinoline derivatives also have promising applications as sensors, agrochemicals, luminescent material and anti-foaming agents in refineries. In addition, quinoline derivatives are important components of various natural products with hereditary therapeutic properties. Quinazolines derivatives also exhibit diverse pharmaceutical properties such as antibacterial, antiviral, anti-inflammatory, anticancer, anticoccidial, antileishmanial, antioxidant, anti-obesity, anti-tubercular, neuroprotective and hypertensive activities.[6, 7] Some quinazoline-based compounds are used as drugs e.g., prazosin is used for the treatment of high blood pressure, anxiety, and panic disorder.[8] Lapatinib demonstrated promising clinical activity as epidermal growth factor inhibitor and is used in combination therapy for breast cancer.[9] In fact, Vandetanib is the first FDA-approved drug for the treatment of medullar thyroid cancer.[10] There are several antitumor drugs such as erlotinib and gefitinib are presently used in the market place. Recently, 2-arylquinazolines have been discovered as novel inhibitors of HIV-1 capsid assembly.[11]

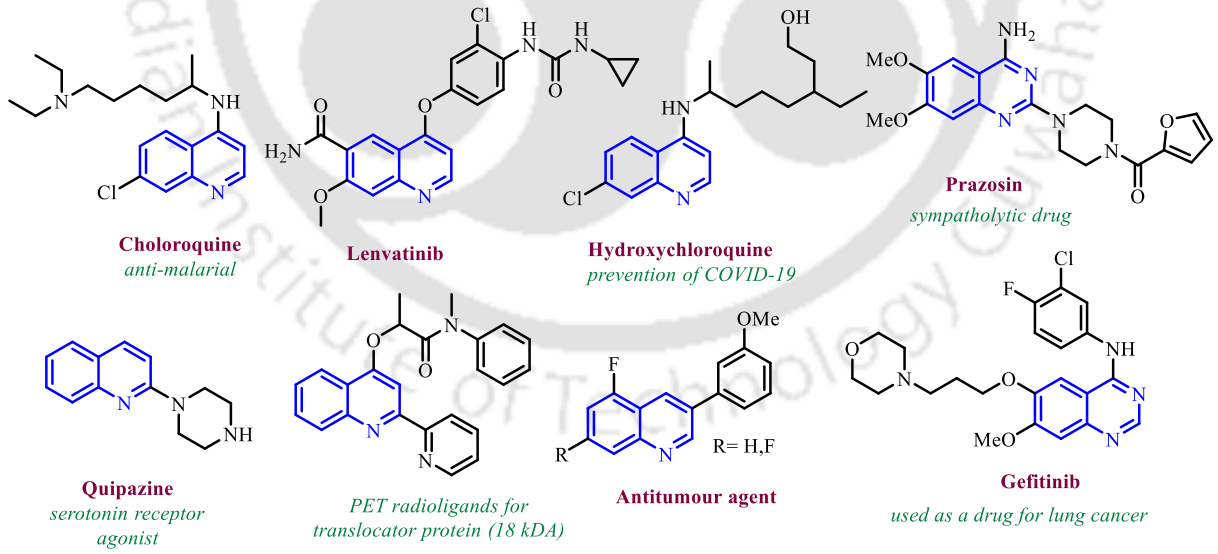

Figure 4.1. Selected bio-active compounds with quinoline and quinazoline motif

Owing to their immense ubiquity in medicinal chemistry and synthetic chemistry, the development of new synthetic approach for the synthesis of quinoline and quinazoline derivatives has gained enormous popularity among the researchers.

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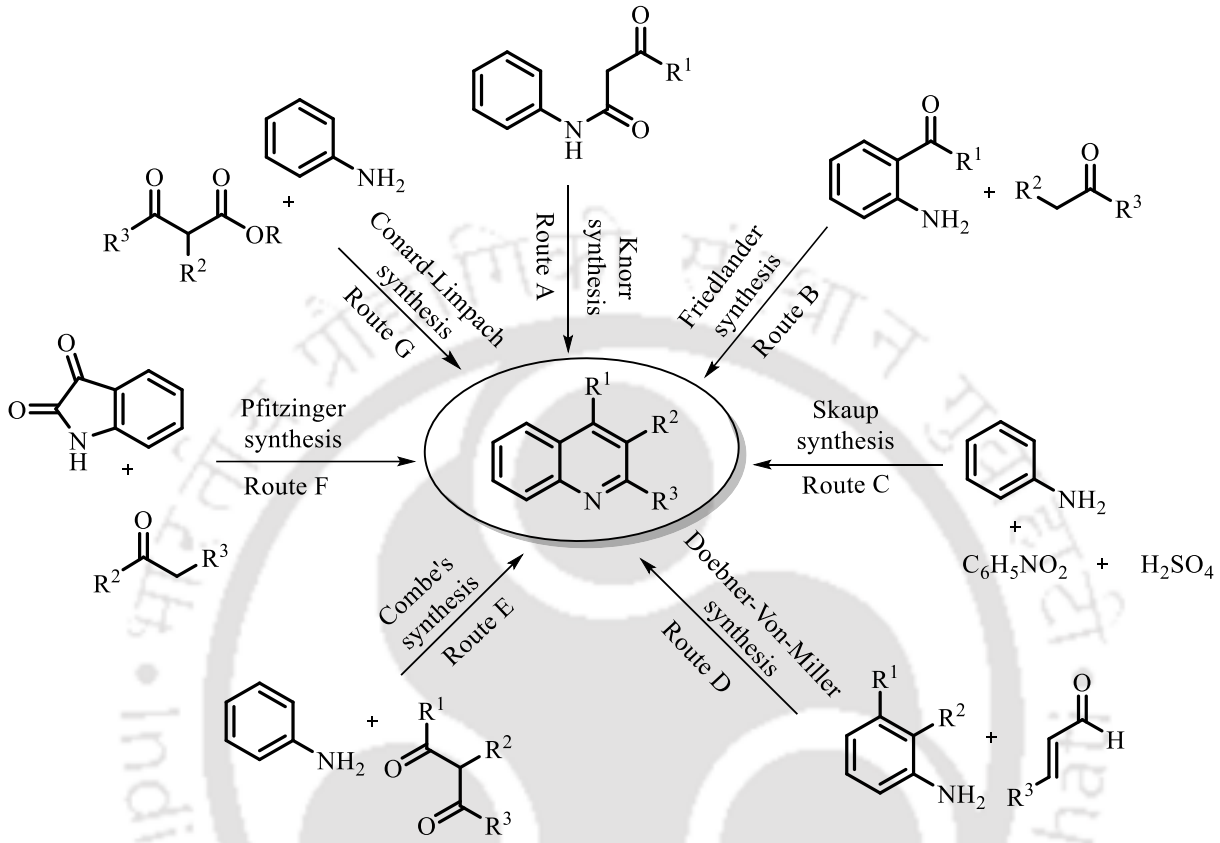
Variety of synthetic strategies for the synthesis of quinolines have been documented in literature. Among them the most important approaches are (A) Knorr[12] (B) Friedlander[13] (C) Skraup[14] (D) Doebner-von-Miller[15] (E) Combes[16] (F) Pfitzinger[17] and (G) Conrad-Limpach synthesis.[18]



Scheme 4.1. Various conventional synthetic strategies for the construction of quinoline derivatives

Among them, the simplest and straightforward synthetic approach for the construction of quinoline scaffolds is Friedländer annulation, involving the condensation of *o*-aminobenzaldehydes or *o*-aminoketones with active *α*-methylene containing carbonyl compounds to give *o*-amino chalcone intermediate followed by intramolecular cyclization and dehydration. However, this synthetic methodology has few disadvantages such as (a) harsh reaction conditions and (b) limited accessibility of the functionalize *o*-aminobenzaldehydes substrates.

In recent times, transition-metal-catalyzed acceptorless dehydrogenative annulation 2-aminobenzyl alcohols with active methylene bearing ketones has been employed as atom economical, and environmentally benign approach for synthesis of the *N*-heteroaromatic compounds. The success of this approach relies on gradual dehydrogenation-driven in situ generation of 2-aminobenzaldehydes, which then rapidly undergo condensation with different coupling partners to yield a wide range of *N*-heterocycles. This method proceeds in absence of any external hydrogen acceptor or oxidant and releases water and hydrogen as the only by-products.

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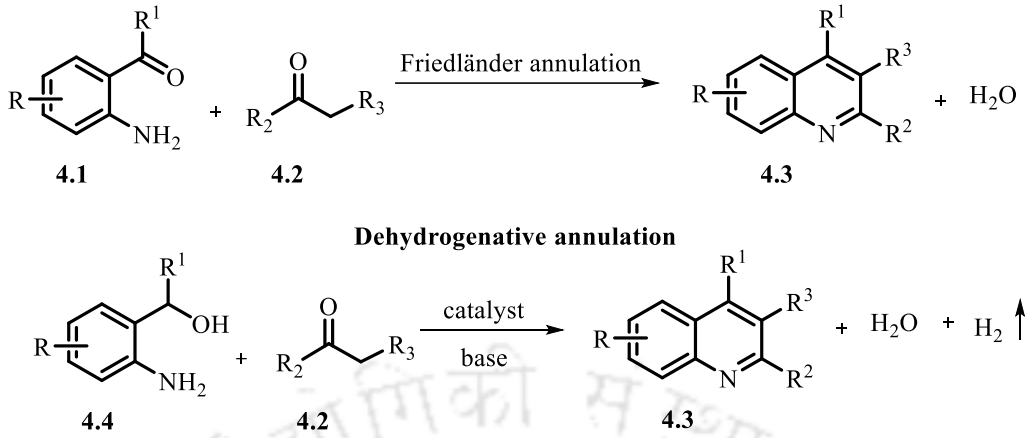
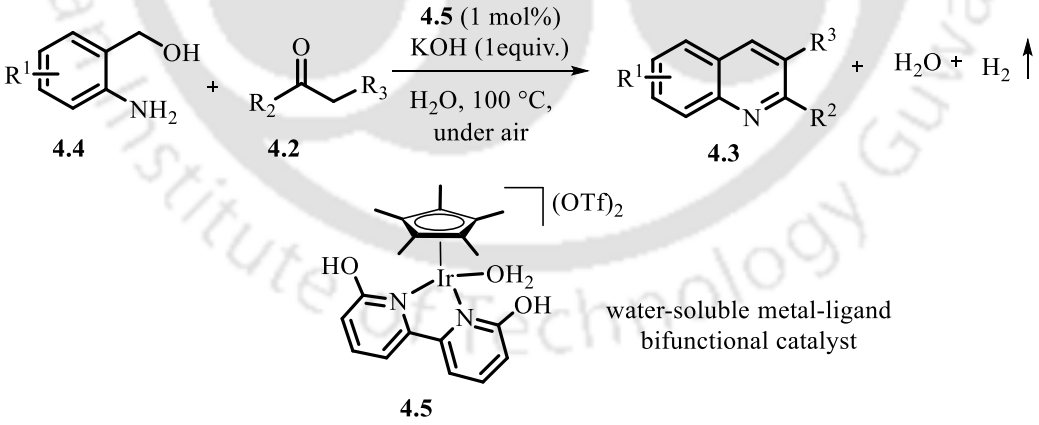


Scheme 4.2. The synthesis of quinoline derivatives *via* dehydrogenative annulations

Presently, the significant progress has been made in dehydrogenative synthesis of quinolines by acceptorless dehydrogenative coupling strategies. However, precious metals such as Ru, Rh, and Ir are predominantly used as the catalysts for this purpose. Hence, with regard to sustainability, it is necessary to substitute these expensive noble metals with affordable and environmentally benign earth-abundant first-row base metals like Mn, Fe, Co, and Ni.[19] Some of the reported efficient earth-abundant metal-based catalytic approaches are discussed below.

In the year 2016, *Li* and *co-workers* reported a novel approach for the synthesis of substituted *via* acceptorless dehydrogenative cyclization of 2-aminobenzyl alcohols with ketones. The cyclization reaction was catalyzed by a water-soluble bifunctional iridium complex **4.5** as a catalyst in presence of KOH as base.[20]



Scheme 4.3. Dehydrogenative quinoline synthesis by iridium complex

In 2021, *Yang* and *Li* were successfully synthesized a diverse range of quinolines by using bifunctional catalyst **4.6**. The presence of accessible -NH units in the ligand backbone, aids to interact with the substrates *via* hydrogen-bonding interaction.[21]

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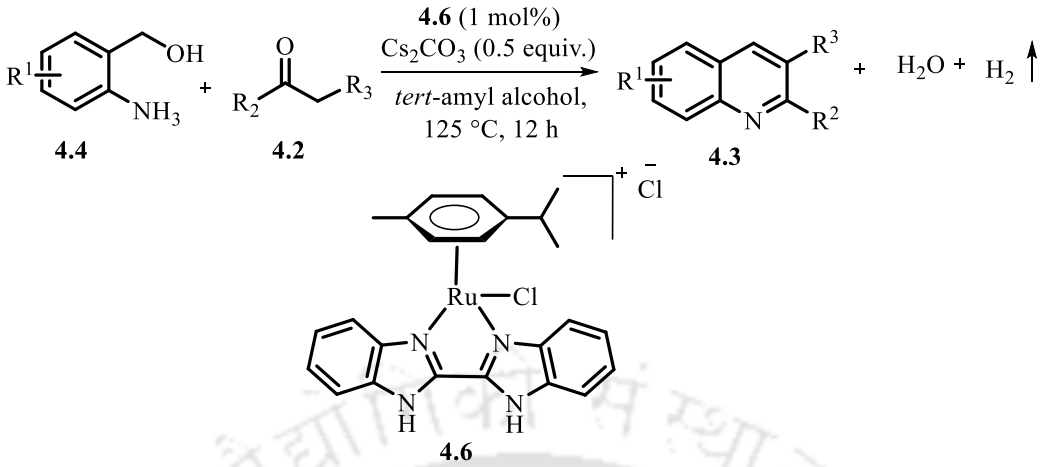
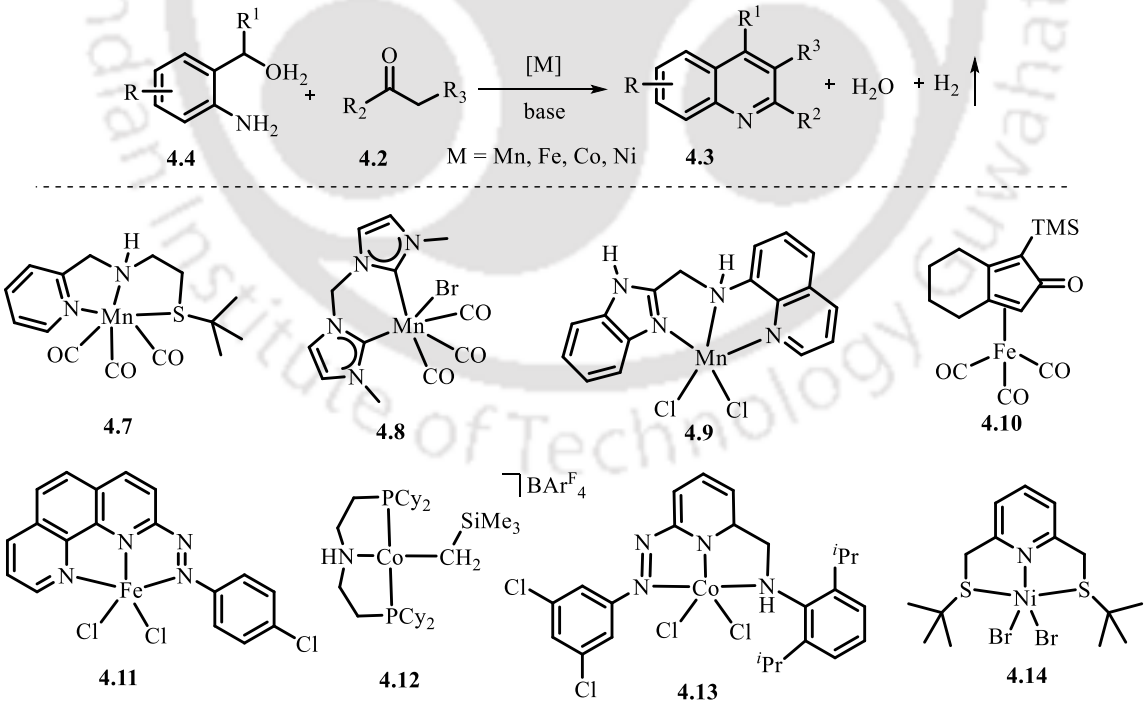


Scheme 4.4. Ru-catalyzed reaction of 2-aminobenzyl alcohols with ketones.

In recent times, tremendous efforts have been made by scientists all over the world for the replacement of these cost effective noble-metal catalysts with earth-abundant metal catalyst. In this quest different groups have reported various 3d-metal based homogenous metal complexes effective for these types of chemical transformation such as acceptorless dehydrogenative coupling for the synthesis of *N*-heteroaromatic compounds. In 2019 *Srimani* and *group* investigated the applicability of NNS-Mn pincer complexes towards the synthesis of 2-phenylquinoline derivatives.[22a]



Scheme 4.5. The synthesis of quinoline derivatives by earth-abundant metal

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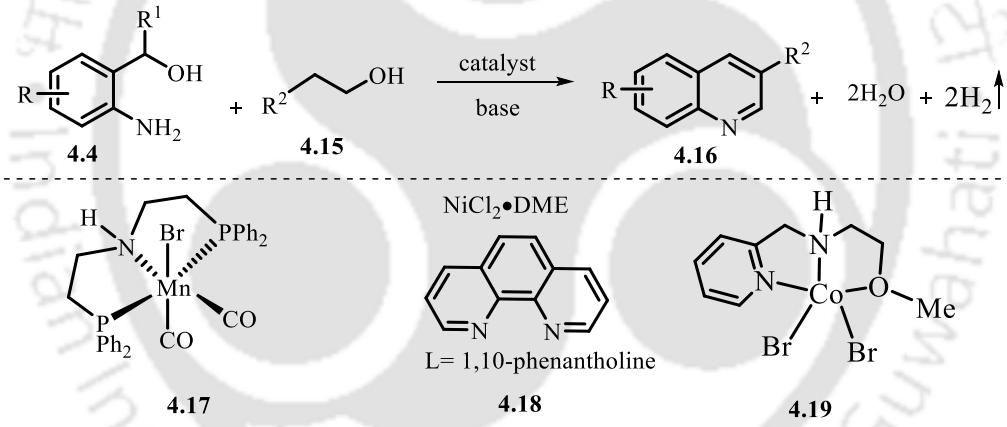
Likewise, *Ke*[23] and *Kundu*[24] groups individually have explored the synthetic scope of quinoline derivatives by variation of ligand supports with manganese metal. Other earth-abundant metal catalysts such as Fe, Co, Ni were also well tested for this purpose.[19] In 2015, *Sortais* and *Darcel* successfully produced quinolines by utilizing 2 mol% of an iron complex **4.10** in *Friedländer* annulation between 2-amino benzyl alcohol and ketones in the presence of PPh_3 and Cs_2CO_3.[25] *Samanta* and *co-workers* developed synthesis of quinoline catalyzed by cobalt(II) complex where they have shown how Co(II) complex **4.13** containing non-innocent azo-aromatic system with amine functionalized ligand was the well suited for dehydrogenative coupling of 2-aminobenzyl alcohols with ketones.[26] Furthermore, *Srimani* and *group* showed that the SNS-Ni complex were also found to be well suited for the dehydrogenative quinoline synthesis.[22b]

Unlike 2-substituted quinolines, C3-substituted quinolines directly from *o*-aminobenzyl alcohol and aliphatic primary alcohols, such as, 2-phenylethanol less studied. The selective synthesis of C3-substituted quinolines is relatively challenging due to deoxygenative self-coupling of 2-aryl ethanol and the Guerbet type reaction of aliphatic alcohols. In 2022, *Balaraman* and *co-workers* were successfully overcome this issue by employing Mn(I)-MACHO **4.17** to generate C3-substituted quinolines with high efficacy.[27]



Scheme 4.6. The synthesis of C-3-substituted quinolines *via* ADC

Later the same transformation was achieved by nickel catalysis with relatively high catalyst loading (5 mol %)[28] and air-stable pincer NNO-cobalt complex **4.19**[29]. Also, it was found that base loading (> 50 mol%) is required to synthesize these heterocycles. Thus, the study of a new and efficient catalytic system with cost-effective metals and catalytic amount of base is highly desired in this regard.

Consequently, various synthetic approaches have been formulated to create wide range of quinazoline scaffolds. These approaches are included as (A) condensation of 2-aminobenzylamines with aldehydes followed by oxidation with oxidants such as MnO_2, DDQ, and sodium hypochlorite;[30-32] a reaction between 2-aminobenzylamines with imines using $K_2S_2O_8$ as oxidant,[33] (B) microwave promoted synthesis of quinazolines from *N*-arylamidines and aldehydes.[34] (C) oxidative cyclization between 2-aminobenzophenones and benzylamines[33] (D)

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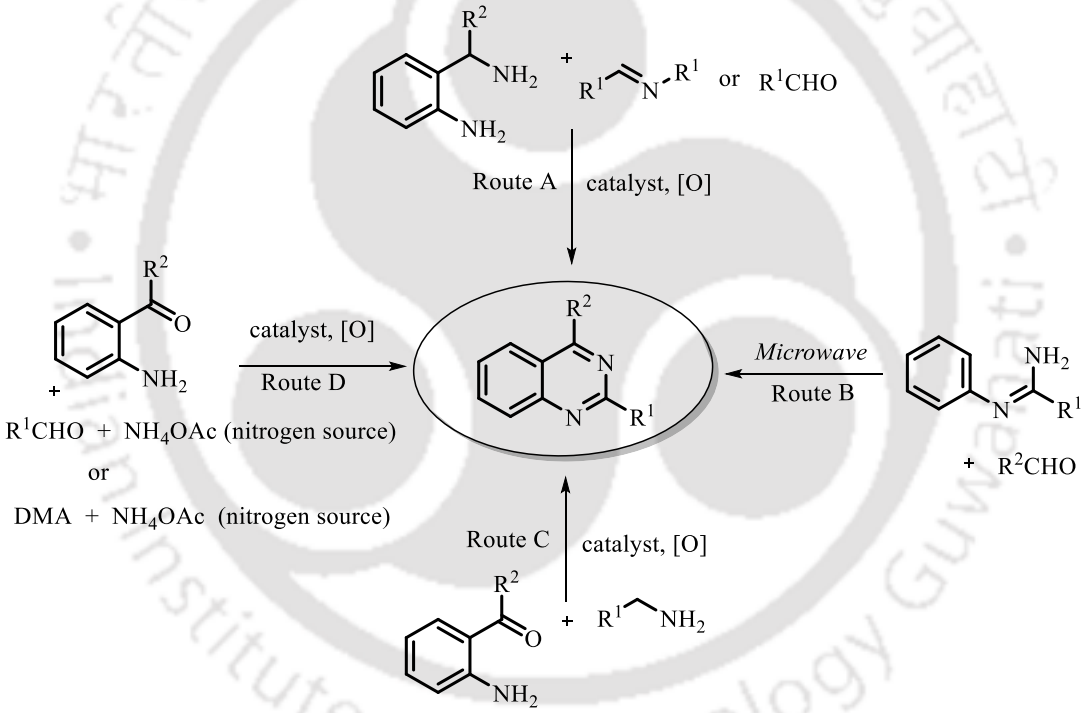
one-pot three-component reaction of 2-aminobenzophenones, aldehyde, and NH_4OAc in mixtures of maltose-dimethylurea (DMU)-NH_4Cl;[35] NS/TBHP-system-catalyzed reaction with NH_4OAc as a nitrogen source and dimethylacetamide (DMA) as a one carbon synthon.[36] Regardless the effectiveness of these methods, they are associated with drawbacks such as the use of stoichiometric amount of dangerous peroxide reagents, toxic solvents, toxic oxidants such as NaOCl, longer reaction times, elevated temperatures, and the need for strong and hazardous oxidizing agents.

However, most of the reactions have their own limitations such as involvement of less environmentally benign halogenated reagents, the use of stoichiometric or excess amounts of strong oxidants /base, incompatibility with pre-functionalized starting precursors, which result not only in the preparation difficulties but also create an adverse effect on the environment. Therefore, development of new, efficient and environmentally benign alternatives for accessing quinazolines from readily available substrates are still a major challenge in the catalysis research.



Scheme 4.7. Classical strategies for the synthesis of quinazolines

In 2018, *Paul* and *group* explored earth-abundant Ni-complexes **4.23** for the synthesis of quinazoline derivatives through the dehydrogenative coupling of 2-aminobenzylalcohol with benzonitrile and 2-aminobenzylamine with benzyl alcohol (Scheme 4.8).[37]

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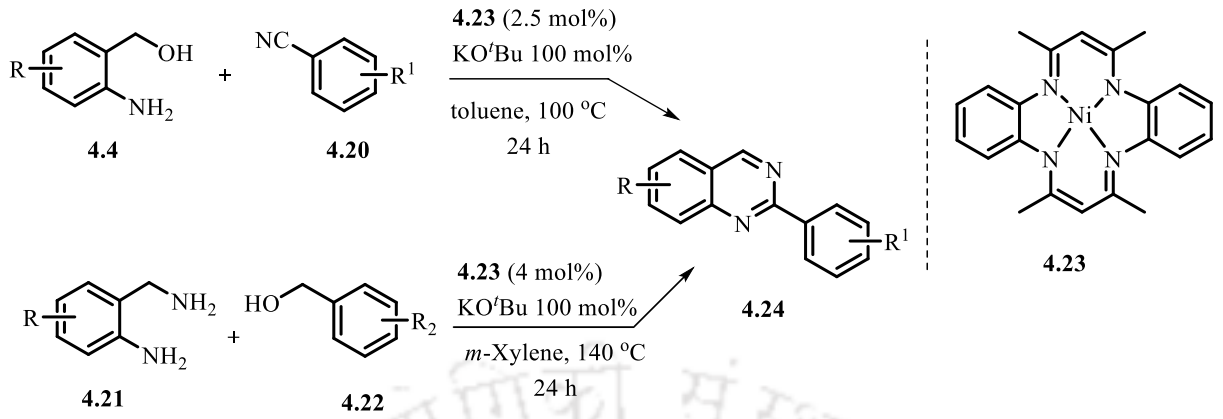
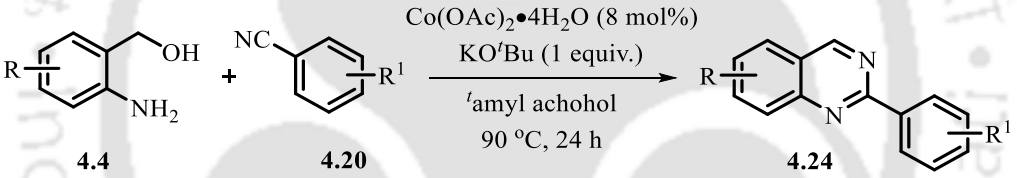


Scheme 4.8. Quinazoline synthesis by nickel (II) complex from 2-aminobenzyl alcohol and benzonitrile (top) and benzyl amine and benzonitrile (bottom) derivatives

Meanwhile, the *Zhang* and *Lin* research group outline the acceptorless dehydrogenative synthesis of quinazolines from 2-aminobenzyl alcohols and ketones where the reaction conducted by cobalt catalysis with good efficiency in the absence of any external ligand. However, relatively high catalyst loading is required.[38]

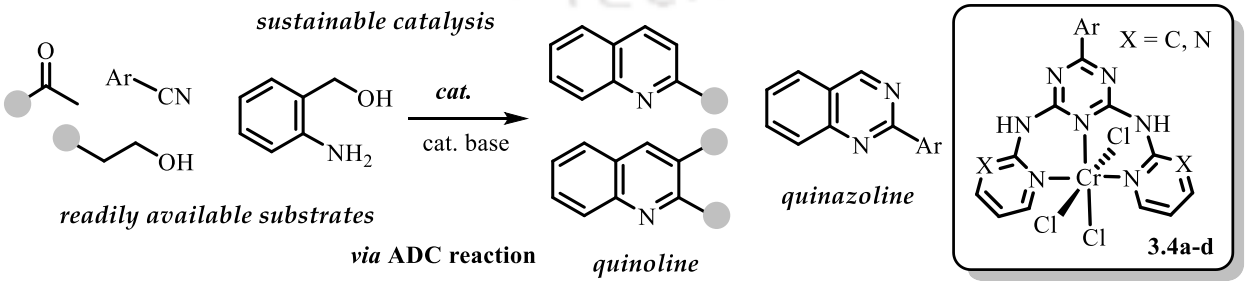


Scheme 4.9. Quinazoline synthesis by cobalt salt from 2-aminobenzyl alcohol and benzonitrile

With this brief introduction, my interest is to develop a new method for the synthesis of N-heteroaromatic compounds by earth abundant and cost-effective metal complexes.

4.2. Present work

Herein chromium (III)-catalyzed dehydrogenative synthesis of quinoline, and quinazoline derivatives is described using 2-aminobenzyl alcohols, methyl ketone, aliphatic primary alcohol and aromatic nitrile as readily available coupling partner.



Scheme 4.10. Chromium catalyzed sustainable synthesis of *N*-heteroaromatic compounds

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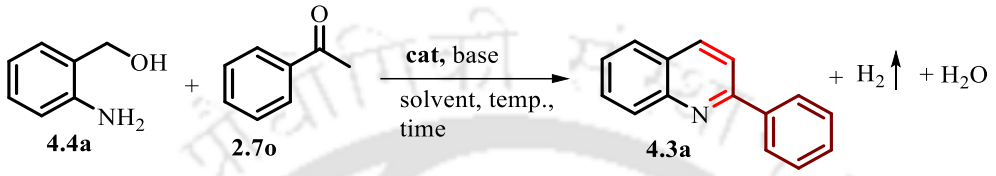
4.3. Results and discussion

4.3.1 Optimization of reaction condition for 2-substituted quinoline

The synthesized chromium complexes **3.4a-d** and **3.5** were used to explore the scope of synthesis of 2-substituted quinoline *via* simultaneous C-C and C-N bond formation through dehydrogenation and condensation reaction between 2-aminobenzylalcohol (**4.4a**) and ketones (**2.7o**).

Table 4.1. Optimization of reaction condition for 2-substituted quinoline[a]



Entry	**cat.** (mol%)	KO^{t}Bu (mol%)	temp (°C)	time (h)	yield (%)
1	**3.4a** (5)	40	120	12	76%
2	**3.4b (5)**	40	120	12	91%
3	**3.4c** (5)	40	120	12	82%
4	**3.4d** (5)	40	120	12	73%
5	**3.5** (5)	40	120	12	74%
6	**$CrCl_3$•3THF** (5) + **3.3b** (5)	40	120	12	73%
7	**3.4b** (5)	40	110	12	65%
8	**3.4b** (5)	40	100	12	38%
9	**3.4b** (5)	40	90	12	14%
10	**3.4b** (5)	30	120	12	68%
11	**3.4b** (2)	40	120	12	46%
12	**$CrCl_3$•3THF** (5)	40	120	12	22%
13	**$CrCl_3$•6H_2O** (5)	40	120	12	12%
14	**3.4b** (5)	40	120	6	46%
15	–	40	120	12	15%
16	**3.4b** (5)	–	120	12	n.d.

Reaction conditions: [a] **4.4a** (1 mmol), **2.7o** (1 mmol), KO^{t}Bu (x mol%), toluene (2 mL) were heated in a closed 50 mL reaction tube for given time. Isolated yield. **3.3b** is [6-(4-methoxyphenyl)-N^2, N^4-di(pyridin-2-yl)-1,3,5-triazine-2,4-diamine].

The initial experiment was performed by stirring a mixture of 2-aminobenzyl alcohol **4.4a** (1 mmol), acetophenone **2.7o** (1 mmol), **3.4b** (5 mol%) and KO^{t}Bu (40 mol%) in toluene at 120 °C

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for 12 h under air. Gratifyingly, both the starting material was completely consumed and the desired 2-phenylquinoline **4.3a** was isolated in 91% yield. Under the identical conditions, other Cr(III) complexes **3.4a**, **3.4c-d** showed less efficient (entries 1, 3-4). Further the mixture of **$CrCl_3$•3THF** and **3.3b** is also effective for this transformation, suggesting in-situ generated corresponding chromium(III) complex is also equally efficient (entry 6). When the reaction temperature was decreased from 120 °C → 110 °C→ 100 °C → 90 °C, the yield of the desired product **4.3a** gradually decreases 91% → 65% → 38% → 14%, indicating the temperature effect on the reaction. With 2 mol% complex **3.4b**, only 46% yield of **4.3a** was obtained (entry 11). The reaction has not proceeded in the absence of base. Only with base there was 17% yield of **4.3a** possibly due to the base mediated partial dehydrogenation of 2-aminobenzylalcohol to 2-aminobenzaldehyde under air, followed by annulation. Based on the above results, the best optimized condition was therefore considered to be fixed to be **3.4b** (5 mol%), KO^{t}Bu (40 mol%), 120°C, 12 h in toluene.

4.3.2. Substrates scope for synthesis of 2-substituted quinoline

In order to investigate the scope of reaction, a variety of ketones and 2-aminobenzylalcohol **4.4a** were employed. In each instance, excellent to moderate yields were obtained with a wide range of ketones tolerating various functional groups. Acetophenones bearing electron donating group (e.g., –OCH_3, –OCH_2Ph) reacted well with **4.4a** to form the desired products **4.3b**, and **4.3d** in excellent yields (92% and 88% respectively). Acetophenone with electron-withdrawing group (e.g., –Cl) was also efficiently reacted to obtain the desired product **4.3c** in 82% yield. The reducible functional groups such as, –$OCH_2CH{=}CH_2$, –C≡C–Ph, –CN intact in the current protocol to give the product **4.3f, 4.3h**, and **4.3i** selectively. Arylmethyl ketones with 1,3-dioxolone substituent leading the product **4.3j** in 85 % yield. Likewise, *meta*-and *ortho*-substituted acetophenone also gave the corresponding product **4.3k-4.3m** in 91-73% yield. Gratifyingly, a redox-active ferrocenyl moiety was compatible with this protocol (**4.3n**, 75%). Heteroatom bearing aromatic methyl ketone is also amenable for this reaction, affording the product **4.3o** and **4.3p** in 82%, and 78% yield respectively. Gratifyingly, 2,3-disubstituted quinoline **4.3q** was synthesized in 83% yield by the reaction between propiophenone and 2-aminobenzylalcohol under the standard reaction conditions. Further, challenging acyclic aliphatic ketones were found to be amenable to this method, giving **4.3r-4.3w** in moderate to good yields. It is worth mentioning that compound **4.3u** was found as an important building block of angustureine, a natural alkaloid. When acetophenone and acetone was reacted individually with (2-aminopyridin-3-yl)methanol **4.4b** under the optimized conditions, 1,8-naphthyridine derivatives **4.3w−4.3x** were obtained in 43%, and 58% yield respectively. Interestingly, 2-methylquinoline **4.3v** and 2-methyl-1,8-naphthyridine **4.3w** were successfully synthesized from simple three carbon feedstock acetone. The reaction of 1,3-indandione with **4.4a**, yielded product **4.3aa** in 70% yield. Polysubstituted aromatic methyl ketones such as 3',4'-dimethoxyacetophenone and 3',4', 5'-trimethoxyacetophenone were also reacted smoothly with substituted 2-aminobenzyl alcohol leading to the product **4.3ab**, **4.34ac** with 79-93% yield. Additionally, product **4.3ac** was confirmed by the single-crystal XRD analysis.

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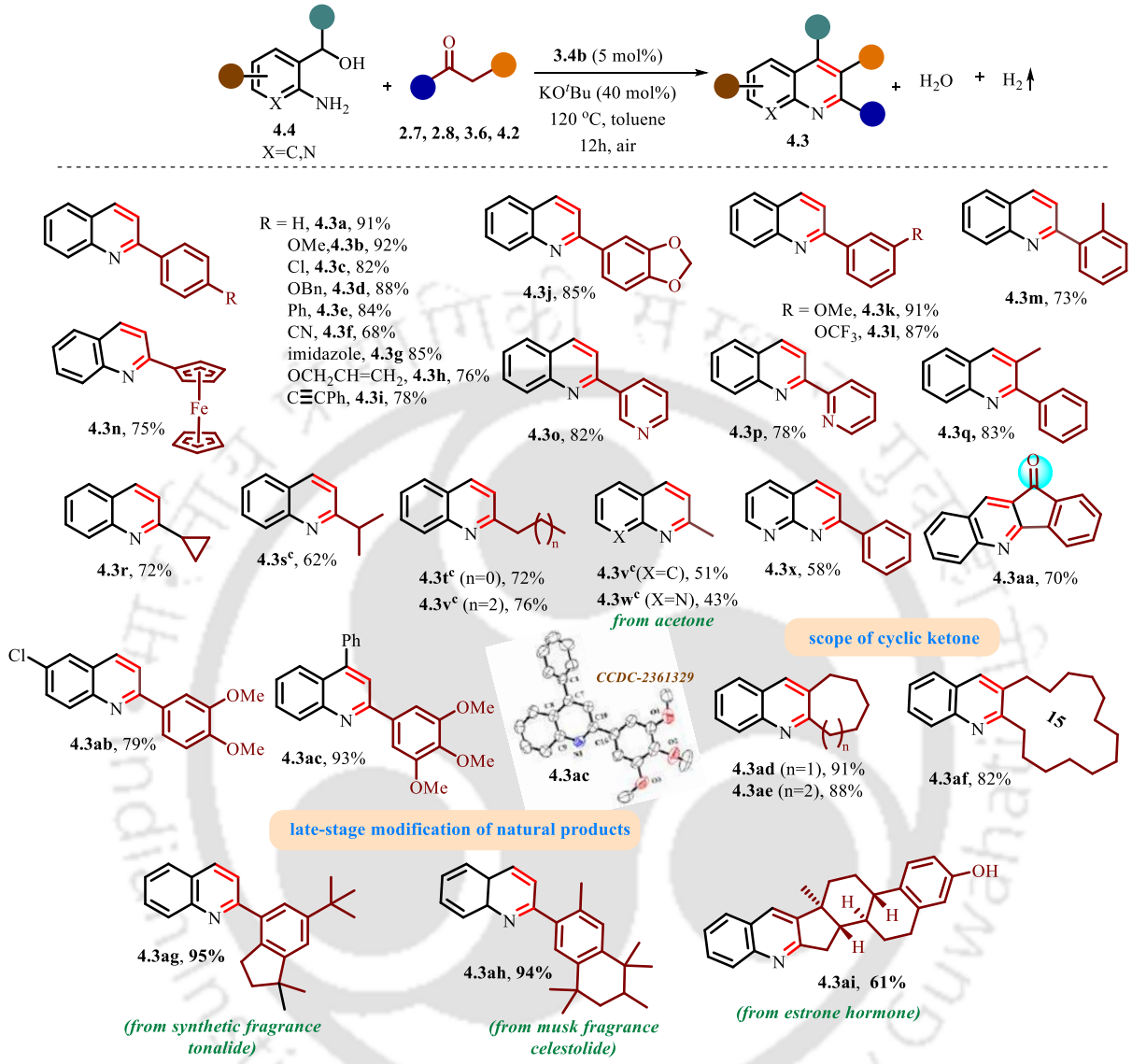
Table 4.2. Synthesis of 2-substituted quinolines[a],[b]



Reaction conditions: [a] 2-aminoaryl alcohol (1 mmol), ketone (1 mmol), catalyst, **3.4b** (5 mol%), KO^{t}Bu (40 mol%), and toluene (2 mL) were heated at 120 °C under air for 12 h. [b] Isolated yield. [c] Aliphatic ketones alcohol (6mmol) was used.

Furthermore, the scope of the methodology was expanded to a variety of other higher analogues of cyclic aliphatic ketones, such as cycloheptanone, cyclooctanone, and cyclopentadecanone to obtain **4.4d−4.4f**. Naturally occurring musk fragrance celestolide **2.7w**, synthetic fragrance tonalide **3.6g**, estrone hormone progesterone **4.2h** were reacted well with **4.4a** under identical reaction conditions, resulting the formation of the products **4.3ag-ai** respectively.

4.3.3. Optimization of reaction condition for 3-substituted quinoline

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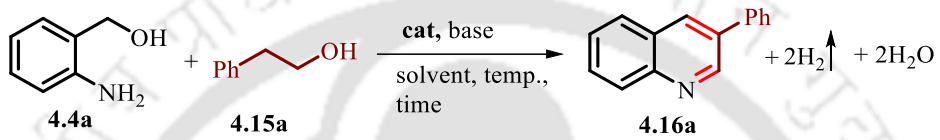
The reaction with 2-aminobenzyl alcohol (**4.4a**), 2-phenylethanol (**4.15a**), **3.4b** (5 mol %), and KO^{t}Bu (50 mol %) at 120 °C for 18 h in toluene was found to be optimal for the synthesis of 3-phenylquinoline **4.16a** in 87% yield. Complex **3.4b** showed higher activity than complex **3.4a** and **3.4c**, **3.4d**. The yield of **4.16a** was dramatically decreased to 38% when the reaction temperature was decreased from 120 °C to 100 °C implying the role of temperature in the catalytic system. Further, a lower catalyst loading and base loading also affected the product yield (entries 9,11). When the reaction was run for shorter time, at 10 h resulted in 56% yield. No product was found in absence of base and a trace amount of product was detected only with base. Control experiments indicate the essential role of both catalyst and base in the ADC reaction (entries 12-16).

Table 4.3. Optimization of reaction condition for 3-substituted quinazoline[a]



Entry	**cat.** (mol%)	KO^{t}Bu (mol%)	temp (°C)	time (h)	yield (%)
1	**3.4a** (5)	50	120	18	73%
2	**3.4b** (5)	50	120	18	87%
3	**3.4c** (5)	50	120	18	79%
4	**3.4d** (5)	50	120	18	70%
5	**3.5** (5)	50	120	18	68%
6	**CrCl$_3$•3THF** (5) + **3.3b** (5)	50	120	18	62%
7	**3.4b** (5)	50	110	18	65%
8	**3.4b** (5)	50	100	18	38%
9	**3.4b** (5)	30	120	18	35%
10	**3.4b** (5)	40	120	18	61%
11	**3.4b** (2)	50	120	18	43%
12	**CrCl$_3$•3THF** (5)	50	120	18	15%
13	**CrCl$_3$•6H$_2$O** (5)	50	120	18	8%
14	**3.4b** (5)	50	120	10	56%
15	–	50	120	18	12%
16	**3.4b** (5)	–	120	18	n.d.

Reaction conditions: [a] **4.4a** (1 mmol), **4.15a** (1 mmol), KO^{t}Bu (x mol%), toluene (2 mL) were heated in a closed 50 mL reaction tube for given time. Isolated yield. **3.3b** is [6-(4-methoxyphenyl)-N^2, N^4-di(pyridin-2-yl)-1,3,5-triazine-2,4-diamine].

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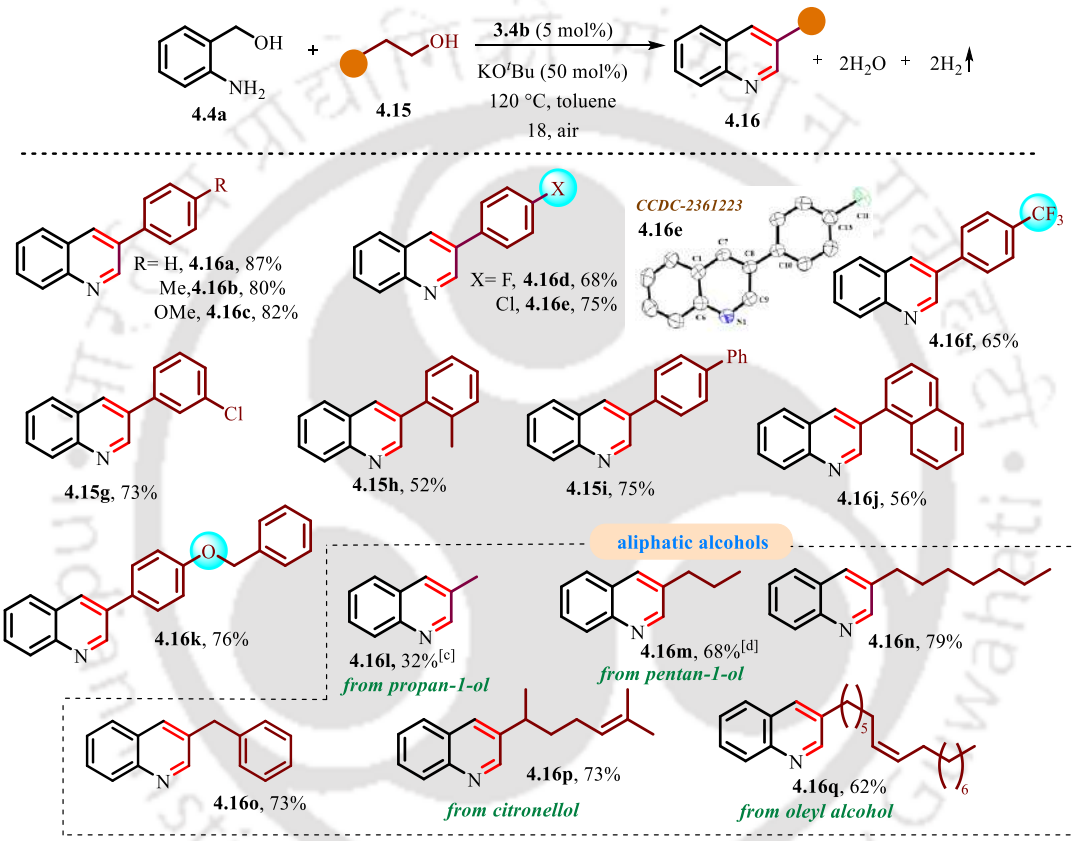
4.3.4. Substrates scope for synthesis of 3-substituted quinoline

Under the optimum reaction condition the substrate scope of the reaction was screened by utilizing various phenyl ethyl alcohols **4.15a-k**, the corresponding 3-substituted quinolines **4.16a-k** were obtained in moderate to good yield (table 4.4). The presence of electron donating substituents (−CH_3, −OMe) and electron withdrawing substituents (−Cl, −F, −CF_3) at different positions (*ortho*, *meta, para*) resulted in the formation of desired products (**4.16a- 4.16h**).

Table 4.4. Synthesis of 3-substituted quinolines[a],[b]



Reaction conditions: [a] **4.4a** (1 mmol), primary alcohol **4.15** (1 mmol), **3.4b** (5 mol%) KO^{t}Bu (40 mol%), toluene (2 mL) were heated in a closed 50 mL reaction tube at 120 °C under air for 12 h. Isolated yield. [b] Isolated yield. [c] with 6 mmol of alcohol was used. [d] with 3 mmol of alcohol was used.

Additionally, product **4.16e** was confirmed by the single-crystal XRD analysis. Furthermore, the product **4.16i** and **4.16j** were obtained in 75% and 56% yield, respectively, by reacting 2-aminobenzyl alcohol **4.1a** with 2-([1,1'-biphenyl]-4-yl)ethan-1-ol (**4.15i**), and 2-(naphthalen-1-yl)ethan-1-ol (**4.15j**), respectively. Interestingly, −OBn containing phenyl ethyl alcohol was also well suited in this reaction giving the expected product **4.16k**. Next, the scope of the reaction was expanded to more challenging long branching aliphatic primary alcohols. The dehydrogenative coupling reaction of 1-propanol (**4.15l**), 1-pentanol (**4.15m**), 1-nonanol (**4.15n**), 3-phenylpropan-1-ol (**4.15o**) with **4.4a**, yielded 3-alkyl quinoline **4.16l** −**4.16o** in 32-73% yield. Remarkably, mono-terpenoid alcohol citronellol and naturally occurring unsaturated oleyl alcohol were also

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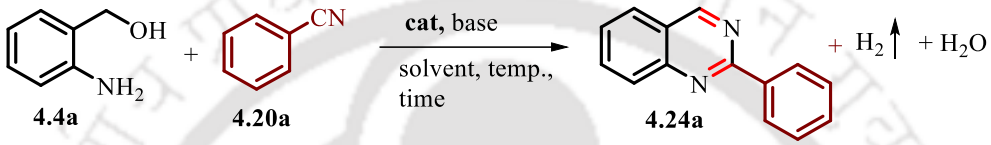
reacted selectively *via* double dehydrogenative coupling reaction to provide the 3-substituted quinolines **4.16p** and **4.16q**, respectively.

4.3.5. Optimization of reaction condition for quinazoline

Next, the synthesis of quinazoline derivatives *via* dehydrogenative annulation reaction of 2-aminobenzylalcohol and aryl nitrile was attempted. The reaction was initiated with 2-aminobenzylalcohol **4.4a** (1 mmol), benzonitrile **4.20a** (1 mmol), **3.4b** (5 mol%) and KO^{t}Bu **(**40 mol%) in toluene at 120 °C under air for 12 h, afforded 2-phenylquinazoline **4.24a** in 88% yield (entry 2).

Table 4.5. Optimization of reaction condition for quinazoline[a]



Entry	**cat.** (mol%)	KO^{t}Bu (mol%)	temp (°C)	time (h)	yield (%)
1	**3.4a** (5)	40	120	12	74%
2	**3.4b** (5)	40	120	12	88%
3	**3.4c** (5)	40	120	12	77%
4	**3.4d** (5)	40	120	12	69%
5	**3.5** (5)	40	120	12	65%
6	**$CrCl_3$•3THF** (5) + **3.3b** (5)	40	120	12	68%
7	**3.4b** (5)	40	110	12	63%
8	**3.4b** (5)	40	100	12	34%
9	**3.4b** (5)	30	120	12	62%
10	**3.4b** (2)	40	120	12	44%
11	**$CrCl_3$•3THF** (5)	40	120	12	18%
12	**$CrCl_3$•6H_2O** (5)	40	120	12	10%
13	**3.4b** (5)	40	120	8	56%
14	–	40	120	12	18%
15	**3.4b** (5)	–	120	12	n.d.

Reaction conditions: [a] **4.4a** (1 mmol), **4.20a** (1 mmol), KO^{t}Bu (x mol%), toluene (2 mL) were heated in a closed 50 mL reaction tube for given time. Isolated yield. **3.3b** is [6-(4-methoxyphenyl)-N^2, N^4-di(pyridin-2-yl)-1,3,5-triazine-2,4-diamine].

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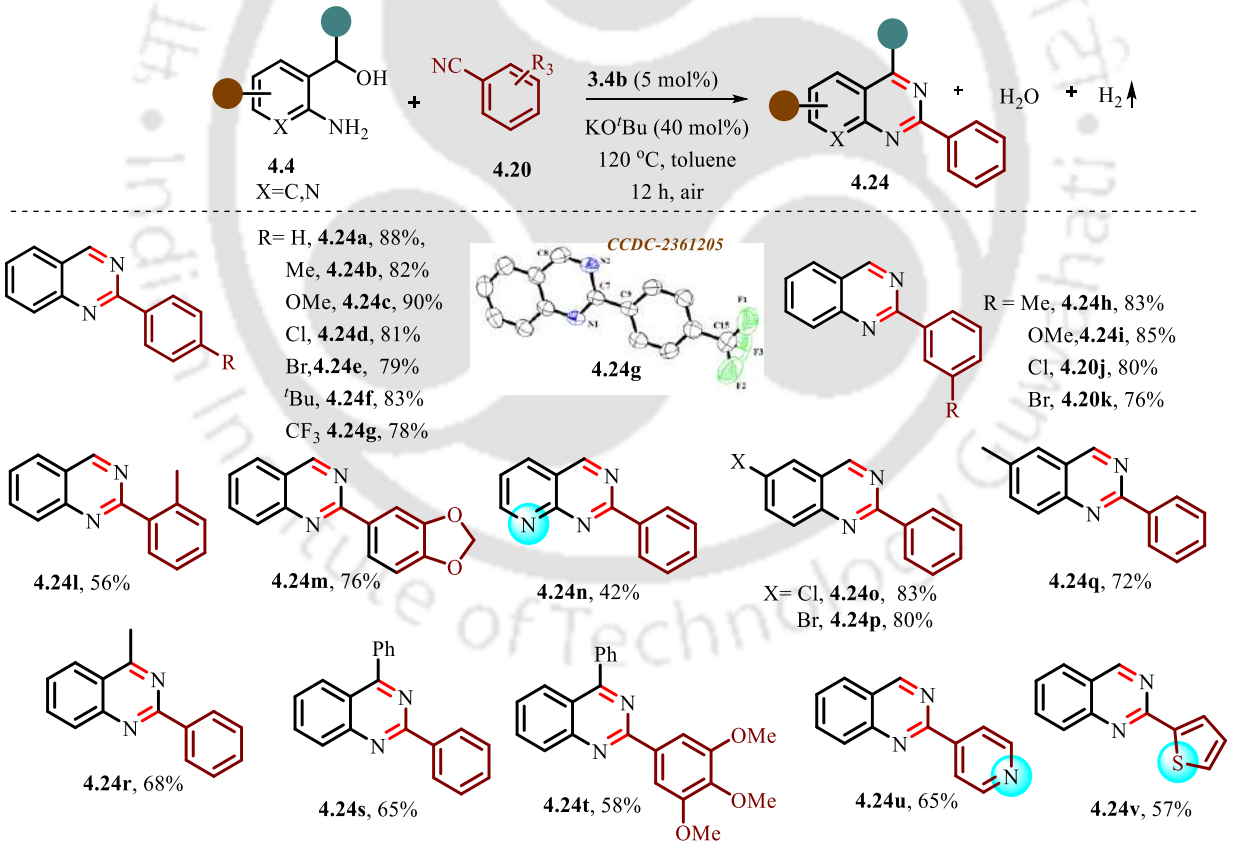
Complex **3.4b** showed the superior activity with respect to other chromium(III) pincer complexes. With decrease in reaction temperature or shortening the reaction time, yield of the desired product is decreased (entries 7−8, entry 13). Likewise, a lowering the base loading (30 mol%), product **4.24a** was obtained in 62% yield (entry 9). When the catalyst loading was reduced to 2 mol%, the yield of product dropped to 44 mol% (entry 10). In absence of base the reaction failed to achieve the desired product (entry 15). Further study suggests that the necessity of catalyst and base in this transformation.

4.3.6. Substrates scope for synthesis of quinazoline

The reaction involving benzonitrile bearing either electron-donating or electron-withdrawing groups on the phenyl ring at different positions (*meta*, and *para*) reacted well with 2-aminobenzylalcohol **4.4a**, resulting the corresponding quinazolines **4.24a**−**4.24k** in excellent yields (table 4.6). It was observed that benzonitrile featuring an electron donating groups (-CH_3, -OCH_3, -^{t}Bu) gave slightly superior results compared to those with electron withdrawing substituent (-Cl, -Br, -CF_3).

Table. 4.6 Synthesis of quinazolines[a],[b]



Reaction conditions: [a] 2-aminoaryl alcohol (1 mmol), nitriles (1 mmol), catalyst **3.4b** (5 mol%), KO^{t}Bu (40 mol%), and toluene (2 mL) were heated at 120 °C under air for 12 h. [b] isolated yield.

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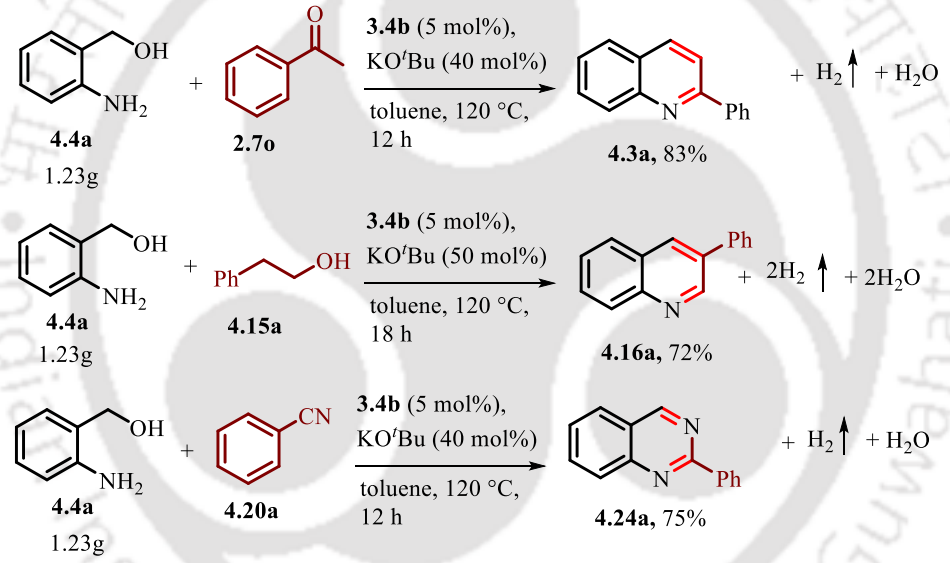
Additionally, product **4.24g** was confirmed by the single-crystal XRD analysis. Sterically hindered *ortho*-methylbenzonitrile underwent dehydrogenative coupling reaction efficiently, resulting the target quinazoline **4.24l** in 56% yield. The piperonylonitrile was also well-suited as it ended with corresponding quinazolines **4.24m** in 76% yield. It is worth mentioning that 2-amino-3-hydroxymethyl pyridine **4.4b** successfully participated in the reaction to provide the *N*-rich quinazoline **4.24n** in 42% yield. The scope of the reaction was then extended to a series of substituted 2-aminoaryl alcohol with both electron donating and withdrawing group, afforded quinazolines **4.24o -4.24t** in 83-58% yield. Polysubstituted aromatic nitrile such as 3,4,5-trimethoxybenzonitrilewere also reacted smoothly with (2-aminophenyl)(phenyl)methanol leading to the product **4.24t** in 58% yield. Nitriles containing heteroaromatic moieties also reacted effectively, resulting the desired quinazoline derivative **4.24u** and **4.24v** in 65% and 57% yield respectively.

4.3.7. Gram Scale synthesis



Scheme 4.11. Gram-scale synthesis of quinoline and quinazoline derivatives

In order to highlight the practical utility of this ADC reactions, gram scale reactions were performed for all the three cases, where it worked effectively (Scheme 4.11).

4.3.8. Post synthetic transformation

The synthetic utility of this catalytic protocol was further explored by converting C2-substituted quinolines **4.3v** and **4.3w** to other valuable molecules such as natural alkaloids (±) angustureine **4.26**, (±)-*α*-tocopherol derived quinoline **4.30** (Scheme 4.12). C3-substituted quinolines **4.16k** and **4.16l** could also be easily functionalized into **4.32**, **4.34** *via* C-H activation (Scheme 4.13).

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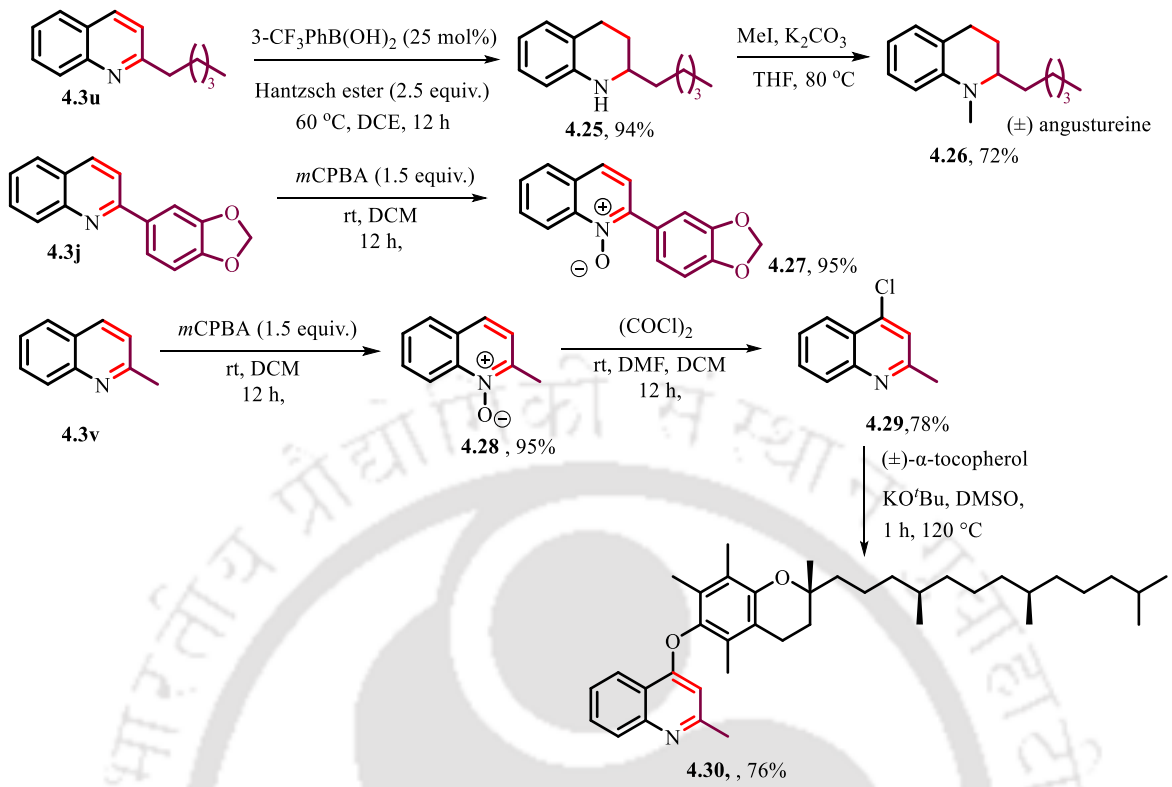
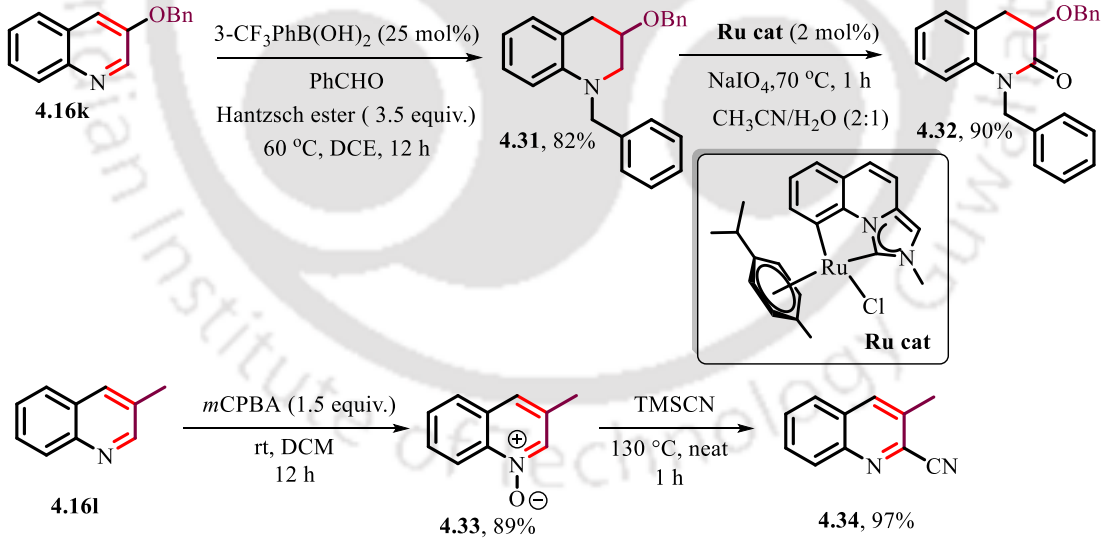


Scheme 4.12. Useful post-synthetic transformations of C2-substituted quinolines



Scheme 4.13. Useful post-synthetic transformations of C3-substituted quinolines

4.3.9. Photophysical properties

It is noteworthy to showcase that some selected 2-substituted quinoline and quinazoline compound for examples **4.3ab**, **4.24v** shows photophysical properties. The absorption spectrum of **4.3ab** and **4.24v** shows an intense peak centered at 270 nm. In the emission spectrum, the emission maxima

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of **4.3ab** was red-shifted to about 457 nm. respectively. The emission maxima of **4.24v** was red-shifted with dual emission at 408 nm and 428 nm. The Stoke's shift in the case of **4.3ab** is 186 nm, and for **4.24v**, it is 138 nm and 160 nm.

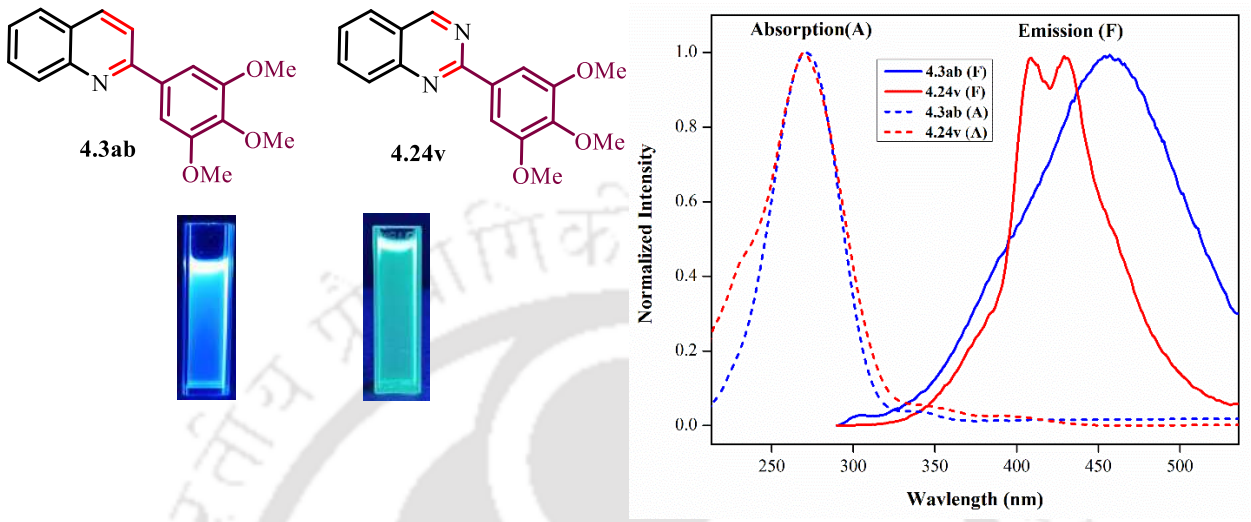
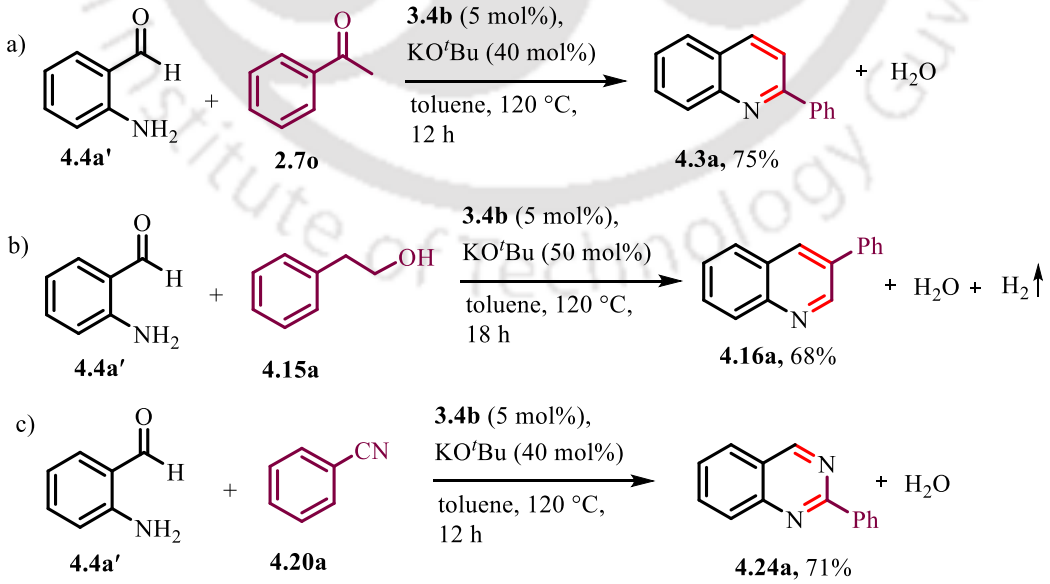


Figure 4.2. Normalized emission and absorbance spectra of some selected molecules. Concentration: 10 μM in Methanol. Excitation wavelength: 270 nm

4.3.10. Mechanistic Studies

In order to gain more mechanistic insights into the synthesis of these heterocycles, few control experiments were carried out. When the reaction between 2-aminobenzylaldehyde and acetophenone was executed under optimized condition, the desired 2-phenylquinoline,**4.3a** was obtained in 75% yield.



Scheme 4.14. Evidence for 2-aminobenzaldehyde intermediate in ADC reactions

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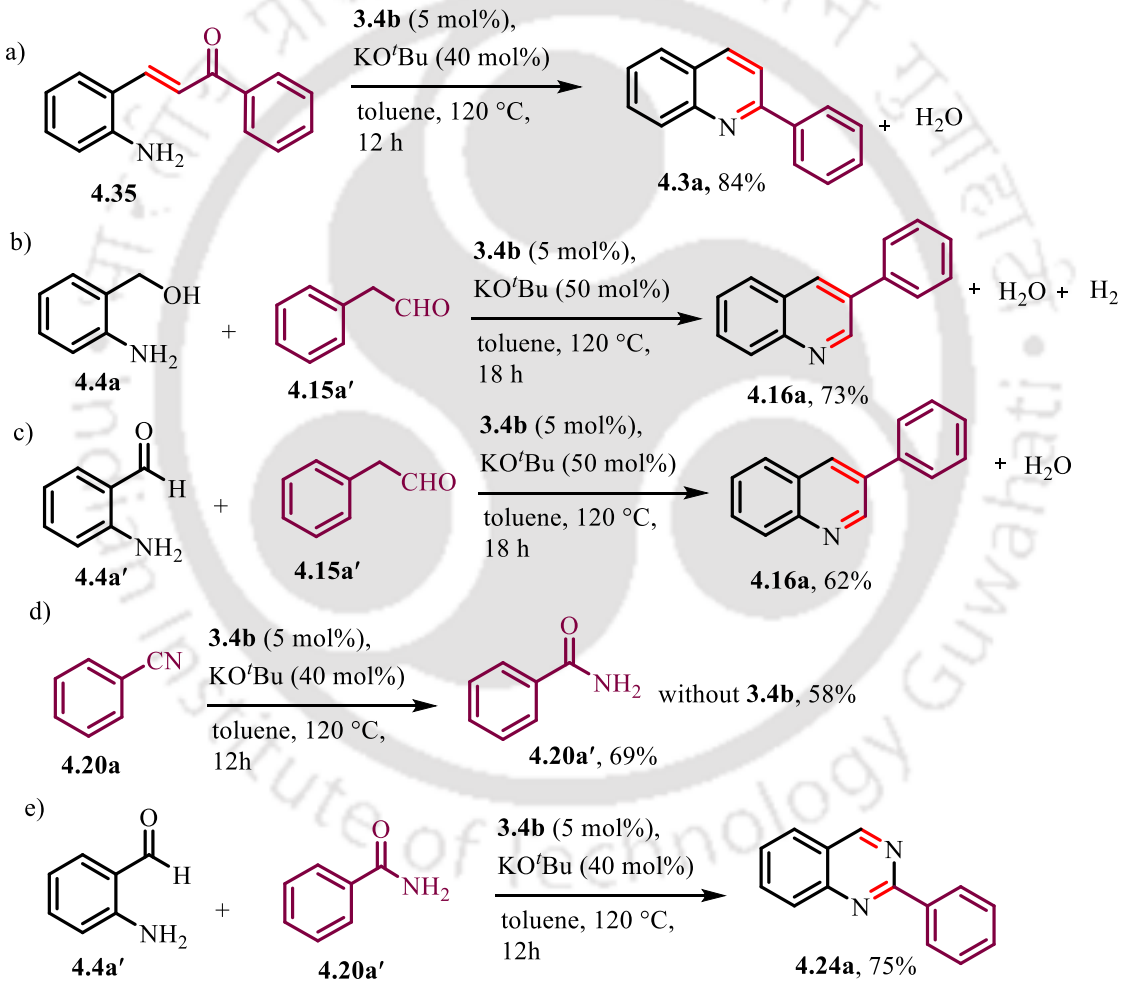
Likewise, the reaction of 2-aminobenzylaldehyde with 2-phenylethanol yielded 3-phenylquinoline **4.16a** in 68% yield. The reaction of 2-aminobenzylaldehyde with benzonitrile delivers quinazoline **4.24a** in 71% yield. These experimental observations suggest that reaction is likely proceeds *via* 2-aminobenzylaldehyde intermediate (Scheme 4.14).

To probe 2-aminochalcone **4.35** as an intermediate, I have independently synthesized **4.35**, and performed the reaction under standard conditions afforded corresponding quinoline **4.3a** in 84% yield (Scheme 4.15a). Study suggests that 2-aminochalcone could be a possible intermediate in the process. For 3-phenylquinoline the involvement of phenylacetaldehyde (**4.15a'**) was confirmed by performing the reaction between **4.4a** and **4.15a'** and **4.4a'** with **4.15a'**, providing the desired 3-phenylquinoline in 73% and 62% yield (Scheme 4.15b-c).



Scheme 4.15. Control experiments for synthesis of quinoline and quinazoline

To understand the possible involvement of benzamide *via* base mediated conversion of nitriles in the quinazoline synthesis, I have performed the reaction with benzonitrile alone. Almost comparable yield of benzamide **4.20a'** (Scheme 4.15d) was obtained while performing the reaction with only base and the base and catalyst together. Further, the reaction of benzamide with 2-

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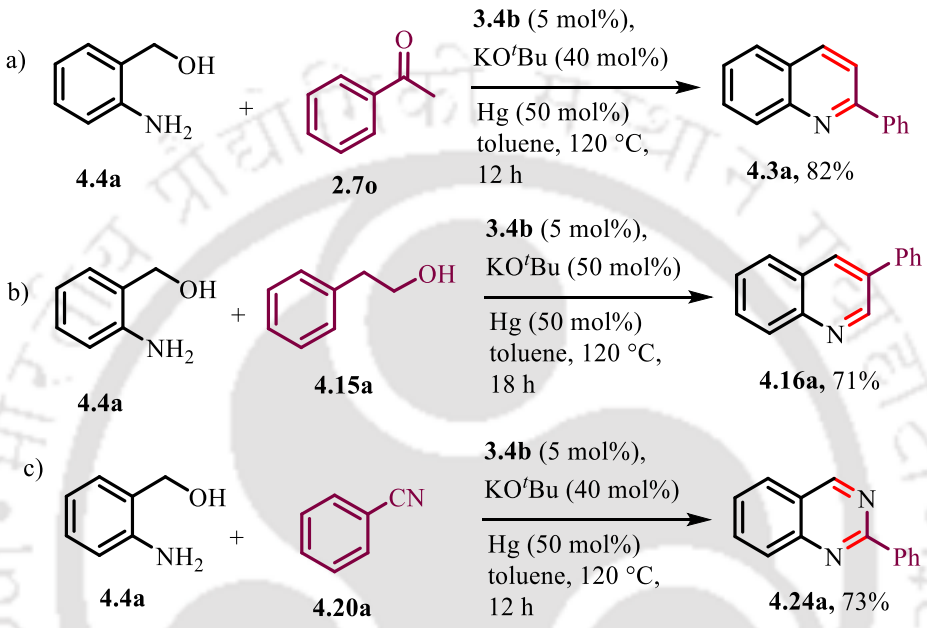
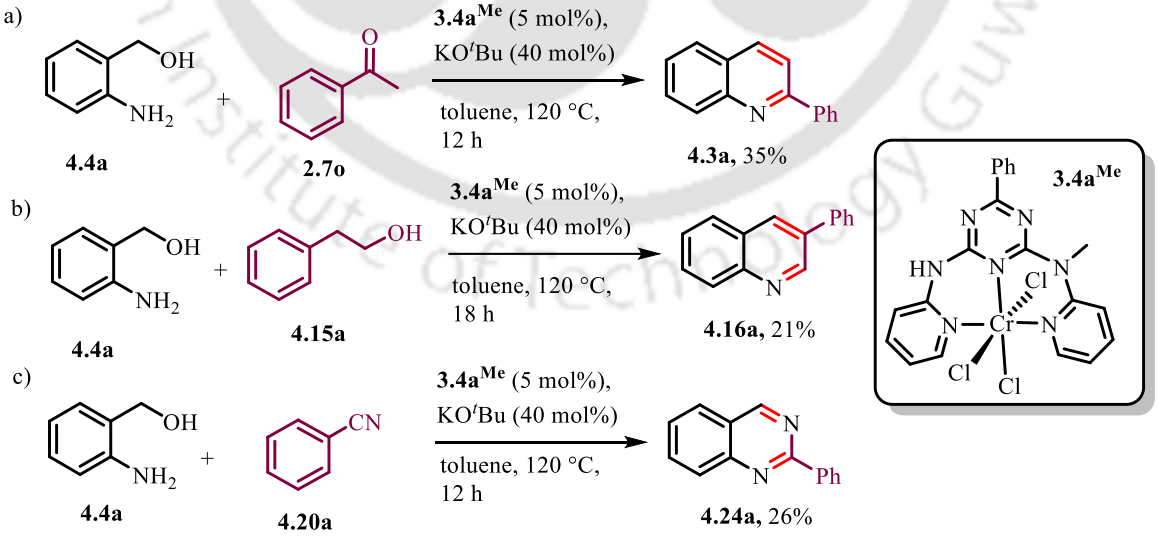
aminobenzaldehyde under the standard reaction conditions afforded the desired quinazoline in 75% yield (Scheme 4.15e). This hinted that the reaction may proceeded through both pathways directly *via* nitrile or benzamide (which is *in- situ* formed in the reaction medium).

To validate the homogeneity of the chromium complex in these catalytic reactions, mercury drop experiment was performed. The consistent yield of the desired products confirms the homogeneity nature of the complex which is not affected by the presence of mercury (Scheme 4.16).[39]



Scheme 4.16. Mercury drop test



Scheme 4.17. The effect of −NH functionality in chromium complex

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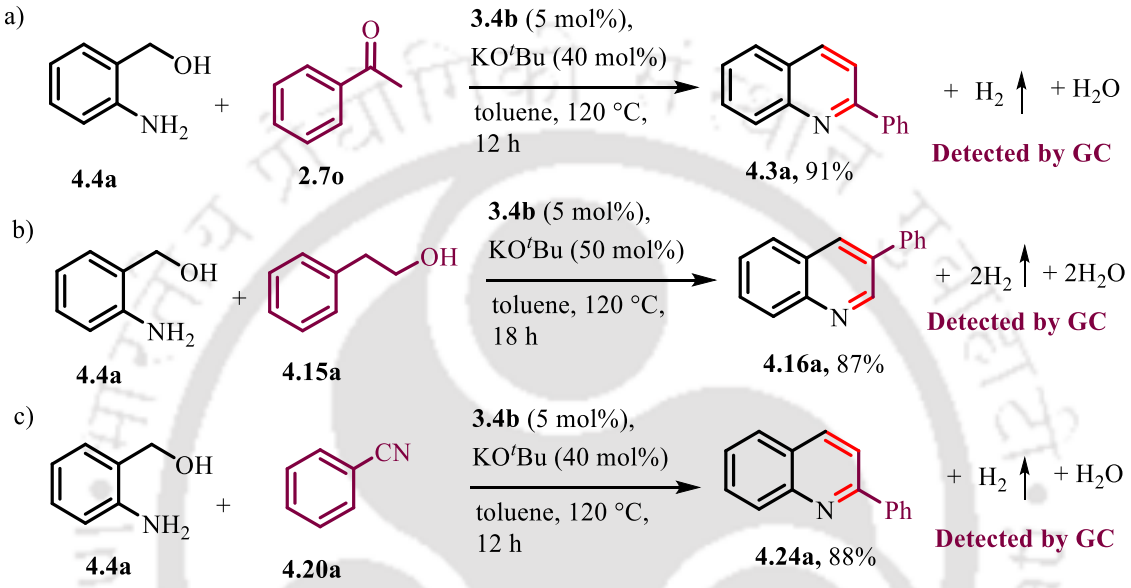
The role of the −NH functionality was examined by employing the ADC reaction by using complex **3.4a^{Me}** as the pre-catalyst, leading to lower yields of **4.3a, 4.16a** and **4.24a**, indicating the importance of the −NH functionality through metal-ligand cooperativity (MLC) in the reaction pathway (Scheme 4.17).[40]

Finally, the dehydrogenative pathway for the synthesis of these heterocycles was further confirmed by detecting the evolved H_2 gas (detection of H_2 gas by GC) under the reaction conditions.



Scheme 4.18. Detection of evolved gas by GC

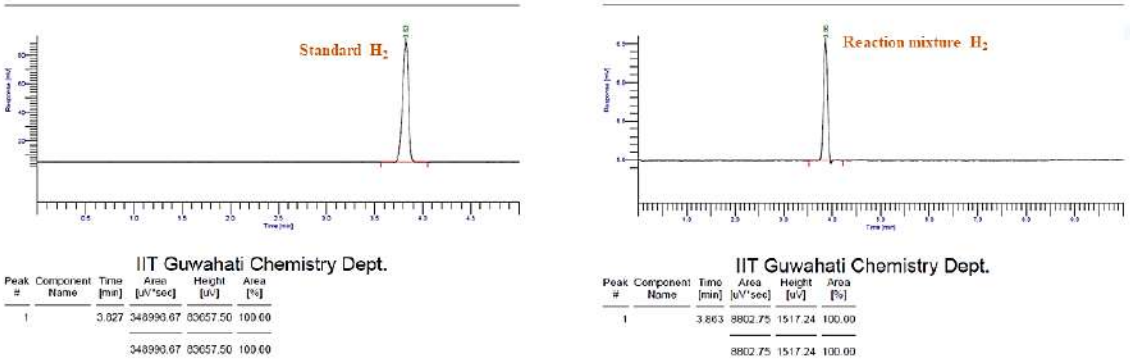


Figure 4.3. GC-TCD analysis of the standard H_2 gas and H_2 gas evolved from the reaction mixture (representative GC spectra for Scheme 4.18b).

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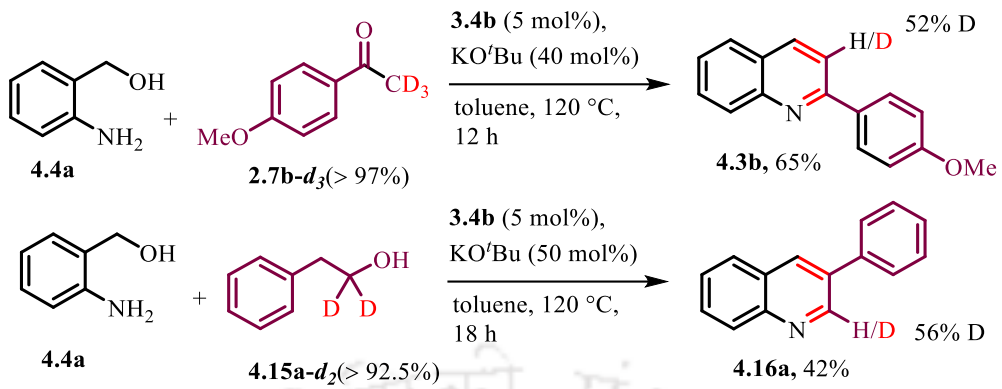
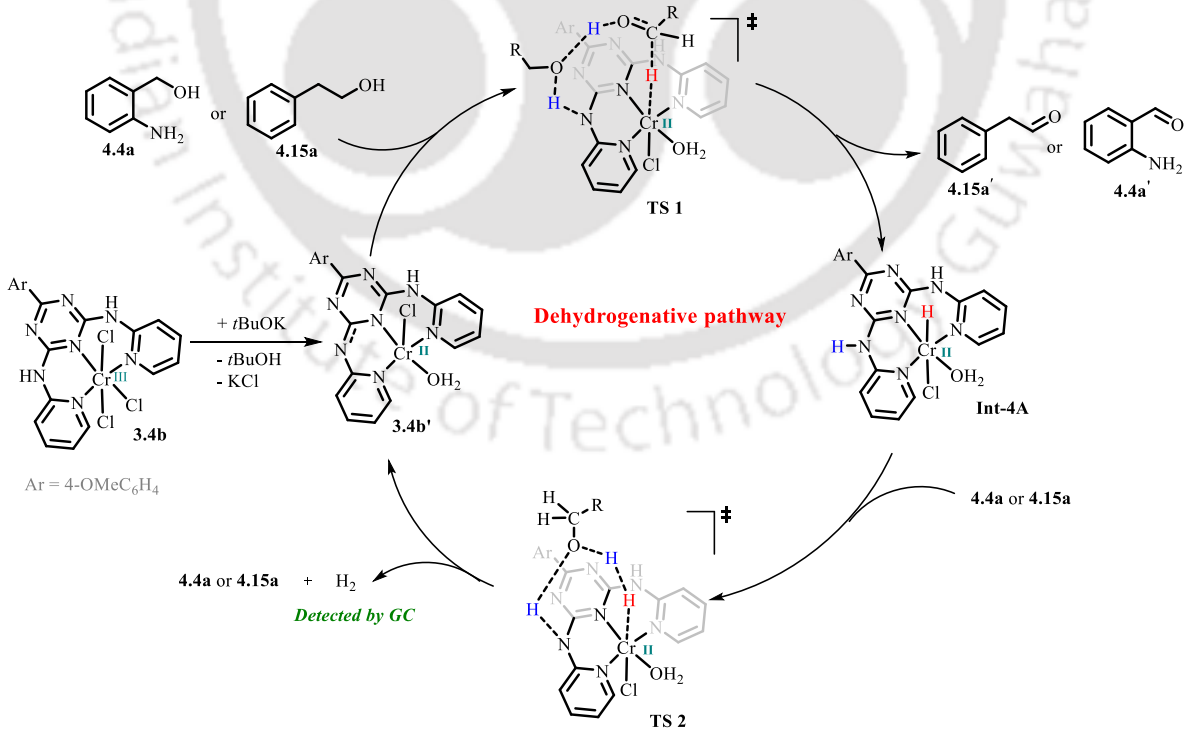


Scheme 4.19. Deuterium-labelled experiment

Furthermore, deuterium labelling experiments suggests that there is no H/D scrambling between two coupling partners (Scheme 4.19).

On the basis of the above experimental observation and related literature, a plausible mechanism is depicted in Schemes 4.20 and 4.21. The precatalyst **3.4b** is initially reduced by base to form the Cr (II) species **3.4b'** which was believed to be considered as active species in the catalytic cycle. The active species **3.4b'** was characterized by ESI-MS, EPR, XPS and magnetic moment (μ_{eff}) calculation as mentioned in chapter 3 section 3.3.5. The resultant active Cr (II) species **3.4b'** then reacted with alcohol **4.4a** or **4.15a** to form aldehyde **4.4a'** or **4.15a'** and chromium hydride complex (**Int-4A**) *via* outer sphere MLC pathway.



Scheme 4.20. Chromium catalyzed acceptorless dehydrogenation of alcohols

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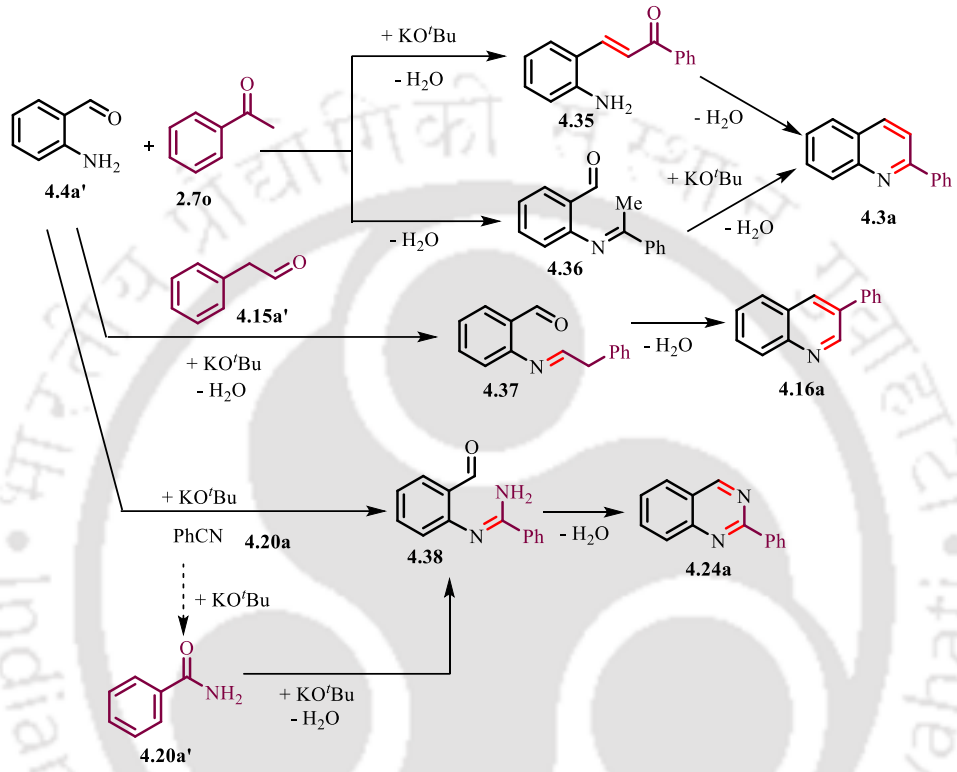
Next the **Int-4A** reacts with another molecule of alcohol **4.4a** or **4.15a** to regenerate the active species **3.4b'** with the liberation of H_2 molecule. Released aldehydes **4.4a'** and **4.15a'** undergo aldol condensation and subsequent intermolecular cyclization to form 3-phenyl quinoline **4.16a**. Likewise, released 2-aminobenzaldehyde **4.4a'** can readily reacts with methyl ketone or benzonitrile (or benzamide, generated *in-situ* from benzonitrile) to form C2-substituted quinoline **4.3a** and quinazoline **4.24a**.



Scheme 4.21. Plausible mechanism of quinoline and quinazoline synthesis

4.4. Summary

In summary, synthesis of C2 substituted quinoline, C3 substituted quinoline and quinazoline derivatives *via* ADC reaction catalyzed by well defined, bench-stable Cr(III) complex as precatalyst is reported. Reaction is highly chemoselective and produces molecular hydrogen and water as the only byproducts making the protocol green, atom-economical, and environmentally benign. Method is compatible with a wide variety of sensitive functional group and applicable for even problematic aliphatic alcohols as substrates. The process can further be extended to the gram-scale reaction and late-stage functionalization of various natural products. This protocol gives a unique opportunity to dehydrogenative synthesis of *N*-heterocycles by underexplored chromium catalysis.

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4.5. Experimental Section

General Information

All the reagents and chemicals were purchased from common commercial suppliers like Sigma-Aldrich, Alfa Aesar, Merck, BLD Pharma, Spectrochem, Avra Synthesis Pvt. Ltd., Finar Chemicals and directly used as received without any further purification unless otherwise mentioned. Compound 4-(phenylethynyl)acetophenone (**2.7f**),[41] 1-(4-(1*H*-imidazol-1-yl)phenyl)ethan-1-one (**3.6b**),[42] and **3.3a-d**, **3.4a-d**, **3.5** **3.4a^{Me}** was prepared according to the reported literature.[43] THF and toluene were freshly distilled over sodium–benzophenone before use. ^{1}H, ^{13}C, and ^{19}F NMR spectra of the compounds were measured in $CDCl_3$, DMSO-d_6, CD_3OD as a solvent by using TMS as an internal standard. Chemical shifts, δ (in ppm), are reported relative to TMS δ (^{1}H) 0.0 ppm, δ (^{13}C) 0.0 ppm, which was used as the internal reference. Otherwise the solvents residual proton resonance and carbon resonance ($CHCl_3$, δ (^{1}H) 7.26 ppm, δ (^{13}C) 77.16 ppm; DMSO-d_6, (^{1}H) 2.50 ppm, δ (^{13}C) 39.52 ppm; CD_3OD, δ (^{1}H) 3.31 ppm, δ (^{13}C) 49 ppm) were also used for calibration. Bruker Avance III 600 and 400 spectrometers were used to record the NMR spectra. Chemical shifts (δ) values were reported in ppm and spin-spin coupling constant (J) were expressed in Hz, and other data were reported as follows: s = singlet, d = doublet, dd = doublet of doublet, dt = doublet of triplet, t = triplet, m = multiplet, q = quartet, sext = sextet, br = broad, and brs = broad singlet. IR spectra were recorded on Perkin Elmer Instrument at normal temperature making KBr pellet grinding the sample with KBr (IR Grade). MS (ESI-HRMS): Mass spectra were recorded on an Agilent Accurate-Mass Q-TOF LC/MS 6520. Merck silica gel 60-120 was used for column chromatography. GC instrument fitted with Elite-1 column (30 m length, 0.32 mm ID) using the following method: Injection volume: 1 µL, inlet temperature: 280 °C, FID detector temperature: 280 °C, oven temperature: start at 60 °C hold time 1 min, ramp: 12 °C /min, upto 320 °C, Flow rate (carrier): 25 mL/min (N2). UV experiments were performed in 1mL quartz cuvettes of path length 1cm at 25°C in UV/V spectrometer in HPLC grade solvent. All the annulation reaction was performed under air in the closed reaction tube.

A. Synthesis of *N*-heterocycles:

i) General procedure for synthesis of C2-substituted quinolines (GP-I)

In a reaction tube a mixture of substituted 2-aminoaryl alcohol, (0.5 mmol, 1 equiv.), ketone (0.5 mmol, 1 equiv.), **3.4b** (5 mol%), KO^{t}Bu (40 mol%), toluene (2 mL) were taken. The reaction tube was properly closed under air and placed in a preheated oil bath at 120 ºC with continuous stirring for 12 h. The resulting mixture was then passed through a bed of celite, the filtrate was collected and concentrated under reduced pressure. The crude reaction mixture was purified by column chromatography over silica gel using petroleum ether or ethyl acetate/ petroleum ether mixture as an eluent.

ii) General procedure for synthesis of C3-substituted quinolines (GP-II)

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In a reaction tube a mixture of substituted 2-aminobenzylalcohol, (0.5 mmol, 1 equiv.), alcohol (0.5 mmol, 1 equiv.), **3.4b** (5 mol%), KO^{t}Bu (50 mol%), toluene (2 mL) were taken. The reaction tube was properly closed under air and placed in a preheated oil bath at 120 ºC with continuous stirring for 18 h. The resulting mixture was then passed through a bed of celite, the filtrate was collected and concentrated under reduced pressure. The crude reaction mixture was purified by column chromatography over silica gel using petroleum ether or ethyl acetate/ petroleum ether mixture as an eluent.

iii) General procedure for synthesis of C2-substituted quinolines (GP-III)

In a reaction tube a mixture of substituted 2-aminoaryl alcohol, (0.5 mmol, 1 equiv.), nitrile (0.5 mmol, 1 equiv.), **3.4b** (5 mol%), KO^{t}Bu (40 mol%), toluene (2 mL) were taken. The reaction tube was properly closed under air and placed in a preheated oil bath at 120 ºC with continuous stirring for 12 h. The resulting mixture was then passed through a bed of celite, the filtrate was collected and concentrated under reduced pressure. The crude reaction mixture was purified by column chromatography over silica gel using petroleum ether or ethyl acetate/ petroleum ether mixture as an eluent.

iv) Experimental procedure for gram-scale cross-coupling reactions (Scheme 4.11)

For 4.3a: In a reaction tube a mixture of substituted 2-aminobenzylalcohol **4.4a**, (1.23g, 10.0, 1 equiv.), ketone **2.7o** (1.20g, 10.0 mmol, 1 equiv.), **3.4b** (5 mol%), KO^{t}Bu (40 mol%), toluene (2 mL) were taken. The reaction tube was properly closed under air and placed in a preheated oil bath at 120 ºC with continuous stirring for 12 h. The resulting mixture was then passed through a bed of celite, the filtrate was collected and concentrated under reduced pressure. The crude reaction mixture was purified by column chromatography over silica gel using petroleum ether or ethyl acetate/ petroleum ether mixture as an eluent to get the analytically pure product **4.3a** in 83% yield (1.7g).

For 4.16a: In a reaction tube a mixture of substituted 2-aminobenzylalcohol **4.4a**, (1.23g, 10.0 mmol, 1 equiv.), alcohol **4.15a** (1.22g, 10.0 mmol, 1 equiv.), **3.4b** (5 mol%), KO^{t}Bu (50 mol%), toluene (2 mL) were taken. The reaction tube was properly closed under air and placed in a preheated oil bath at 120 ºC with continuous stirring for 18 h. The resulting mixture was then passed through a bed of celite, the filtrate was collected and concentrated under reduced pressure. The crude reaction mixture was purified by column chromatography over silica gel using petroleum ether or ethyl acetate/ petroleum ether mixture as an eluent to get the analytically pure product **4.16a** in 72% yield (1.47g).

For 4.24a: In a reaction tube a mixture of substituted 2-aminobenzylalcohol **4.4a**, (1.23g, 10.0 equiv.), ketone **4.20a** (1.03g, 10.0 mmol, 1 equiv.), **3.4b** (5 mol%), KO^{t}Bu (40 mol%), toluene (2 mL) were taken. The reaction tube was properly closed under air and placed in a preheated oil bath at 120 ºC with continuous stirring for 12 h. The resulting mixture was then passed through a bed of celite, the filtrate was collected and concentrated under reduced pressure. The crude reaction mixture was purified by column chromatography over silica gel using petroleum ether or ethyl

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acetate/ petroleum ether mixture as an eluent to get the analytically pure product **4.24a** in 75% yield (1.54g).

B. Mechanistic studies

i) Mercury drop test (Scheme 4.16)

To establish the homogeneity of **3.4b** in ADC reaction mercury drop experiment was carried out.

Experimental procedure for 4.3a: In this test, the reaction tube was charged with 0.4 mmol of **4.4a** (50 mg), 0.4 mmol of **2.7o** (48 mg), 0.2 mmol of mercury (50 mg), 40 mol% of KO^{t}Bu (18 mg) and 5 mol% of complex **3.4b** (11 mg) along with 2 mL of toluene. The whole reaction mixture was then allowed to heated at 120 ºC for 12 h in an oil bath. The product **4.3a** was obtained in 82% of yield (67.3 mg), suggests that homogenous behavior of the catalyst.

Experimental procedure for 4.16a: In this test, the reaction tube was charged with 0.4 mmol of **4.4a** (50 mg), 0.4 mmol of **4.15a** (49 mg), 0.2 mmol of mercury (50 mg), 50 mol% of KO^{t}Bu (18 mg) and 5 mol% of complex **3.4b** (11 mg) along with 2 mL of toluene. The whole reaction mixture was then allowed to heated at 120 ºC for 18 h in an oil bath. The product **4.16a** was obtained in 71% of yield (58 mg), suggests that homogenous behavior of the catalyst.

Experimental procedure for 4.24a: In this test, the reaction tube was charged with 0.4 mmol of **4.4a** (50 mg), 0.4 mmol of **4.20a** (41 mg), 0.2 mmol of mercury (50 mg), 40 mol% of KO^{t}Bu (18 mg) and 5 mol% of complex **3.4b** (11 mg) along with 2 mL of toluene. The whole reaction mixture was then allowed to heated at 120 ºC for 12 h in an oil bath. The product **4.24a** was obtained in 73% of yield (60 mg), suggesting that homogenous behavior of the catalyst.

ii) The influence of the –NH functionality in chromium complex (Scheme 4.17)

Experimental procedure for 4.3a: A mixture of **4.4a** (0.5 mmol, 1 equiv.), **2.7o** (0.5 mmol, 1 equiv.), **3.4a^{Me}** (5 mol%), KO^{t}Bu (40 mol%) and toluene (2 mL) was added into a reaction tube equipped with stirring bar. The reaction tube was properly closed and placed in a preheated oil bath at 120 ºC with continuous stirring for 12 hours. The resulting mixture was then passed through a bed of celite, the filtrate was collected and concentrated under reduced pressure. Analytically pure product (36 mg, 35%) was obtained by column chromatography over silica gel using ethyl acetate / petroleum ether mixture as an eluent.

Experimental procedure for 4.16a: A mixture of **4.4a** (0.5 mmol, 1 equiv.), **4.15a** (0.5 mmol, 1 equiv.), **3.4a^{Me}** (5 mol%), KO^{t}Bu (50 mol%) and toluene (2 mL) was added into a reaction tube equipped with stirring bar. The reaction tube was properly closed and placed in a preheated oil bath at 120 ºC with continuous stirring for 18 hours. The resulting mixture was then passed through a bed of celite, the filtrate was collected and concentrated under reduced pressure. Analytically pure product (22 mg, 21%) was obtained by column chromatography over silica gel using ethyl acetate / petroleum ether mixture as an eluent.

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Experimental procedure for 4.24a: A mixture of **4.4a** (0.5 mmol, 1 equiv.), **4.20a** (0.5 mmol, 1 equiv.), **3.4a^{Me}** (5 mol%), KO^{t}Bu (40 mol%) and toluene (2 mL) was added into a reaction tube equipped with stirring bar. The reaction tube was properly closed and placed in a preheated oil bath at 120 ºC with continuous stirring for 12 hours. The resulting mixture was then passed through a bed of celite, the filtrate was collected and concentrated under reduced pressure. Analytically pure product (27 mg, 26%) was obtained by column chromatography over silica gel using ethyl acetate / petroleum ether mixture as an eluent.

iii) Detection of evolved gas by GC-Thermal Detector (GC-TCD) (Scheme 4.18):

For 4.3a: A mixture of 2-aminobenzyl alcohol, **4.4a** (246 mg, 2.0 mmol, 1.0 equiv.), acetophenone **2.7o** (241 mg, 2.0 mmol, 1 equiv.), **3.4b** (5 mol %), KO^{t}Bu (40 mol%) was added into a pressure tube (50 mL) equipped with stirring bar. The reaction tube was then properly closed without exclusion of air and kept it in a preheated oil bath at 120 ℃ with continuous stirring for 12 hours. After completion of the reaction, the pressure tube was cooled at 0 °C, the evolved gas was syringe out and detected from PerkinElmer clarus-590 GC instrument using Elite Plot-Q column (30 m length x 530 μm x 20 μm ID) employing the following method:

TCD starting temperature: 40 °C

Oven temperature: 60 °C

Time at starting temperature: 0 min

Hold time: 5 min

Ramp: 28 °C/ min up to 200 °C

Flow rate: 5 ml/ min (N2)

Split ration: 20

Inlet temperature: 40 °C

Detector temperature TCD: 200 °C

For 4.16a: A mixture of 2-aminobenzyl alcohol, **4.4a** (246 mg, 2.0 mmol, 1.0 equiv.), acetophenone **4.15a** (244 mg, 2.0 mmol, 1 equiv.), **3.4b** (5 mol %), KO^{t}Bu (50 mol%) was added into a pressure tube (50 mL) equipped with stirring bar. The reaction tube was then properly closed without exclusion of air and kept it in a preheated oil bath at 120 ℃ with continuous stirring for 18 hours. After completion of the reaction, the pressure tube was cooled at 0 °C, the evolved gas was syringe out and detected from PerkinElmer clarus-590 GC instrument similarly as in above mentioned experiment.

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For 4.24a: A mixture of 2-aminobenzyl alcohol, **4.4a** (246 mg, 2.0 mmol, 1.0 equiv.), acetophenone **4.20a** (206 mg, 2.0 mmol, 1 equiv.), **3.4b** (5 mol %), KO^{t}Bu (40 mol%) was added into a pressure tube (50 mL) equipped with stirring bar. The reaction tube was then properly closed without exclusion of air and kept it in a preheated oil bath at 120 ℃ with continuous stirring for 12 hours. After completion of the reaction, the pressure tube was cooled at 0 °C, the evolved gas was syringe out and detected from PerkinElmer clarus-590 GC instrument similarly as in above mentioned experiment.

iv) Proof for the formation of intermediate 2-aminobenzaldehyde (Scheme 4.14)

Experimental procedure for 4.3a: A mixture of **4.4a'** (0.5 mmol, 1 equiv.), **2.7o** (0.5 mmol, 1 equiv.), **3.4b** (5 mol%), KO^{t}Bu (40 mol%) and toluene (2 mL) was loaded into the reaction tube and heated at 120 ℃ for 12 h. The product **4.3a** was isolated in 75% of yield.

Experimental procedure for 4.16a: A mixture of **4.4a'** (0.5 mmol, 1 equiv.), **4.15a** (0.5 mmol, 1 equiv.), **3.4b** (5 mol%), KO^{t}Bu (50 mol%) and toluene (2 mL) was loaded into the reaction tube and heated at 120 ℃ for 18 h. The product **4.16a** was isolated in 68% of yield.

Experimental procedure for 4.24a: A mixture of **4.4a'** (0.5 mmol, 1 equiv.), **4.20a** (0.5 mmol, 1 equiv.), **3.4b** (5 mol%), KO^{t}Bu (40 mol%) and toluene (2 mL) was loaded into the reaction tube and heated at 120 ℃ for 12 h. The product **4.24a** was isolated in 71% of yield.

v) Proof for the formation of 2-aminochalcone in C3-substituted quinoline synthesis (Scheme 4.15a)

Experimental procedure: A mixture of **4.35** (0.5 mmol, 1 equiv.), **3.4b** (5 mol%), KO^{t}Bu (40 mol%) and toluene (2 mL) was loaded into the reaction tube and heated at 120 ℃ for 12 h. The product **4.3a** was isolated in 84% of yield.

vi) Proof for the formation of intermediate phenylacetaldehyde in C3-substituted quinoline synthesis

Scheme 4.16b: A mixture of **4.4a** (0.5 mmol, 1 equiv.), **4.15a'** (0.5 mmol, 1 equiv.), **3.4b** (5 mol%), KO^{t}Bu (50 mol%) and toluene (2 mL) was loaded into the reaction tube and heated at 120 ℃ for 18 h. The product **4.16a** was isolated in 73% of yield.

Scheme 4.16c: A mixture of **4.4a'** (0.5 mmol, 1 equiv.), **4.15a'** (0.5 mmol, 1 equiv.), **3.4b** (5 mol%), KO^{t}Bu (50 mol%) and toluene (2 mL) was loaded into the reaction tube and heated at 120 ℃ for 18 h. The product **4.16a** was isolated in 62% of yield.

vii) Proof for the formation of intermediate benzamide intermediate in quinazoline synthesis:

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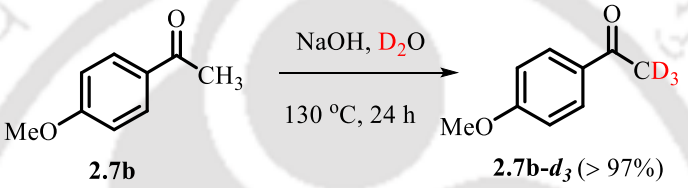
Scheme 4.16d: A mixture of **4.20a** (0.5 mmol, 1 equiv.), **3.4b** (5 mol%), KO^{t}Bu (40 mol%) and toluene (2 mL) was loaded into the reaction tube and heated at 120 °C for 12 h. The product **4.20a'** was isolated in 69% of yield. In absence of **3.4b**, 58% conversion also took place.

Scheme 4.16e: A mixture of **4.4a** (0.5 mmol, 1 equiv.), **4.20a'** (0.5 mmol, 1 equiv.), **3.4b** (5 mol%), KO^{t}Bu (40 mol%) and toluene (2 mL) was loaded into the reaction tube and heated at 120 °C for 12 h. The product **4.24a** was isolated in 75% of yield.

viii) Deuterium-labeling experiments:

Synthesis of deuterated 4′-methoxyacetophenone 2.7b-*d*$_3$:



2.7b **2.7b-*d*$_3$** (> 97%)

Scheme 4.22. Synthesis of **2.7b-*d*$_3$**

Procedure: In a pyrex tube degassed D_2O (99.9% D, 3 mL) was taken and to it under nitrogen flow a mixture of 4′-methoxyacetophone **2.7b** (300 mg, 3 mmol) and NaOH (40 mg, 1.0 mmol) was added. The reaction tube was properly closed and placed in a preheated oil bath at 130 °C with continuous stirring for 24 hours under nitrogen atmosphere. Upon completion of the reaction, the reaction mixture was extracted with chloroform (5 mL × 3) and dried over Na_2SO_4. The solvent was evaporated under vacuum to afford the desired product **2.7b-*d*$_3$** (94%, 282 mg) with 97% D as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.92 (d, J = 6.8 Hz, 2H), 6.91 (d, J = 10.0 Hz, 2H), 3.85 (s, 3H), 2.52 – 2.50 (m, 0.09 H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 197.0, 163.6, 130.7, 130.4, 113.8, 55.5, 25.8 (sept, $J_{C\text{-}D}$ =19.3 Hz).

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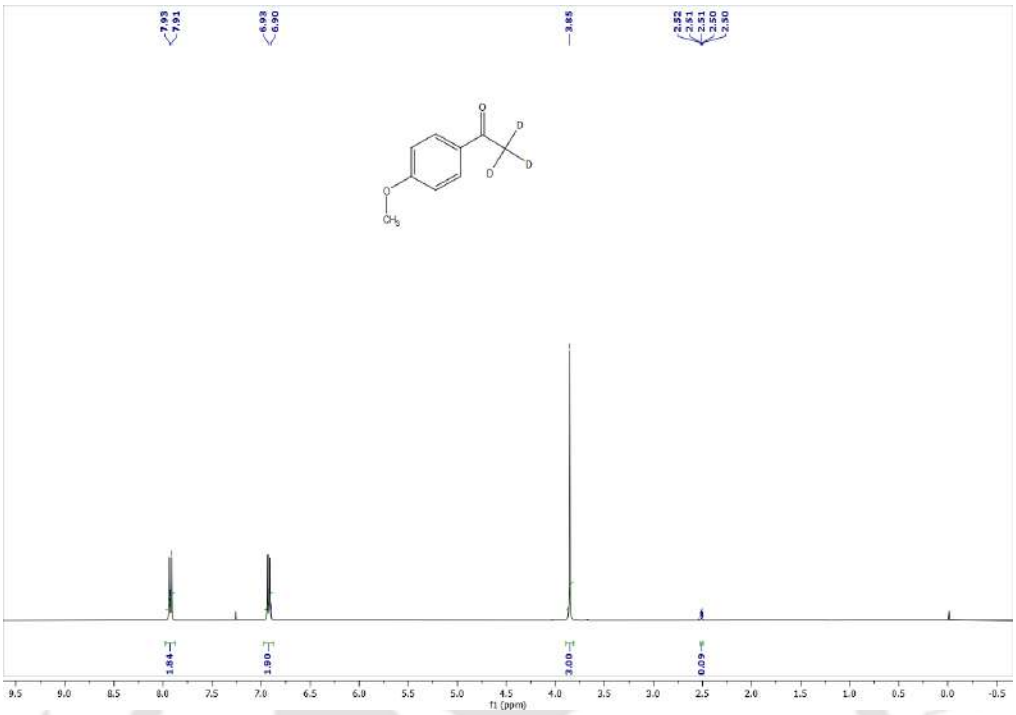

Figure **4.4.** ^{1}H NMR spectrum of **2.7b-*d*$_3$** ($CDCl_3$, 400 MHz, 298 K)

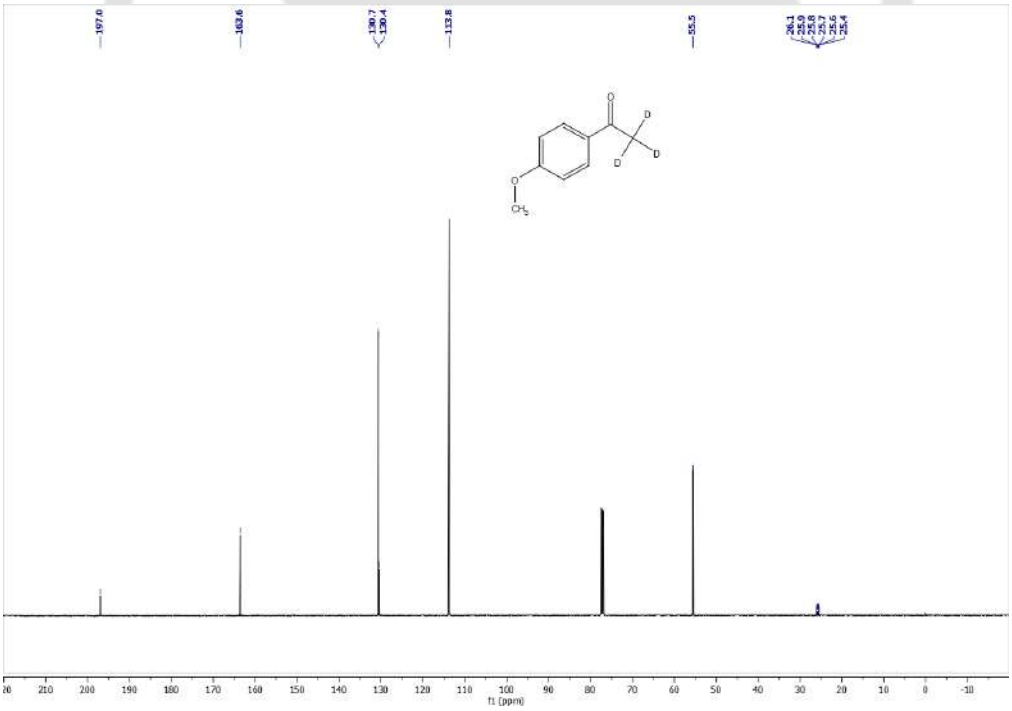

Figure 4.5. $^{13}C\{^{1}H\}$ NMR spectrum of **2.7b-*d*$_3$** ($CDCl_3$, 151 MHz, 298 K)

Synthesis of deuterated 2-(4-methoxyphenyl)quinoline 4.3b-*d* using the reaction of 4.4a and 2.7b-*d*$_3$ (Scheme 4.19a)

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In a reaction tube a mixture of substituted 2-aminobenzylalcohol **4.4a** (0.5 mmol, 1 equiv.), ketone **2.7b-*d*$_3$** (0.5 mmol, 1 equiv.), **3.4b** (5 mol%), KO^{t}Bu (40 mol%), toluene (2 mL) were taken. The reaction tube was properly closed under air and placed in a preheated oil bath at 120 ºC with continuous stirring for 12 h. The resulting mixture was then passed through a bed of celite, the filtrate was collected and concentrated under reduced pressure. The crude reaction mixture was purified by column chromatography over silica gel using petroleum ether or ethyl acetate/ petroleum ether mixture as an eluent to get the desired product **4.3b-*d*** in 65% yield.

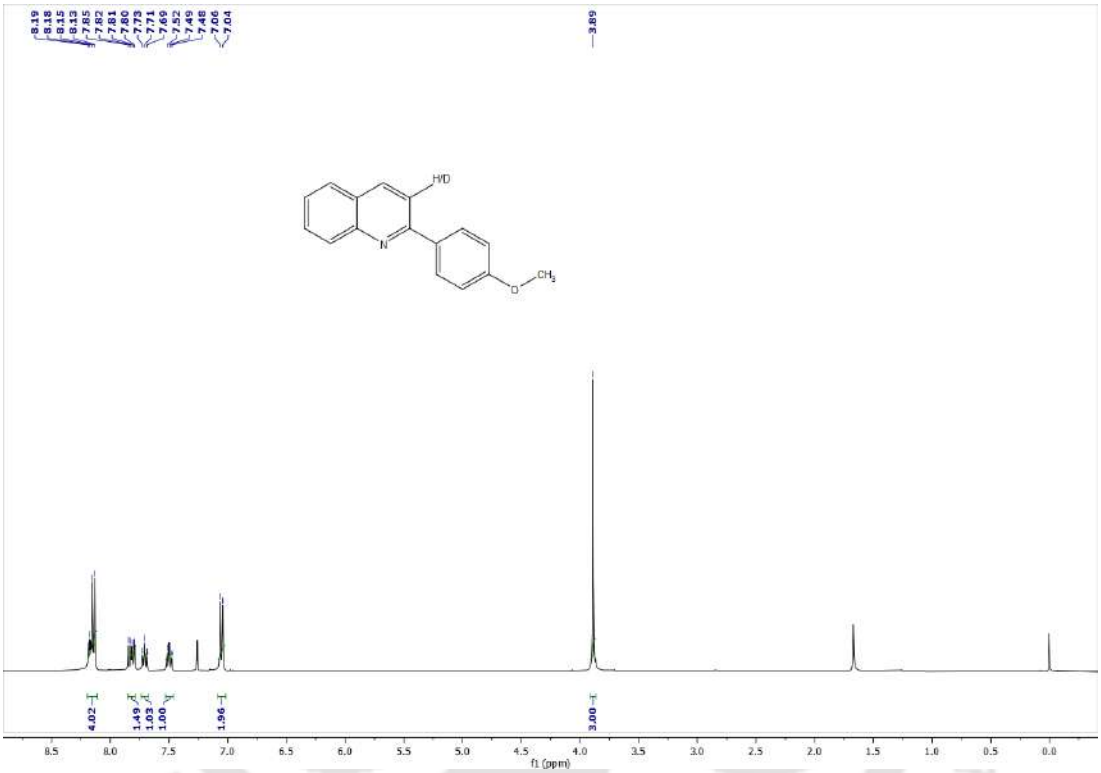
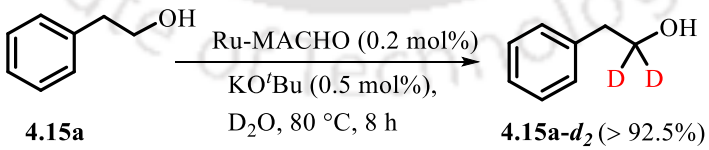


Figure 4.6. ^{1}H NMR spectra of **4.3b-*d*** ($CDCl_3$, 400 MHz, 298 K)

Synthesis of deuterated 2-phenyl ethanol 4.15-*d*$_2$:



4.15a **4.15a-*d*$_2$** (> 92.5%)

Scheme 4.23. Synthesis of **4.15-*d*$_2$**

Procedure: In a pyrex tube degassed D_2O (99.9% D, 3 mL) was taken and to it under nitrogen flow a mixture of 2-phenyl ethanol **4.15a** (3 mmol, 1 equiv.), Ru-MACHO (0.06 mmol, 0.2 mol%) and KO^{t}Bu (0.15 mmol, 0.5 mol%) was added. The pyrex tube was properly closed and the whole reaction mixture was degassed three times and then placed in a preheated oil bath at 80 ºC with continuous stirring for 8 hours under nitrogen atmosphere. Upon completion of the reaction, the

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reaction mixture was extracted with chloroform (5 mL × 3) and dried over Na_2SO_4. The solvent was evaporated under vacuum to afford the desired product **4.15-*d*$_2$** in 96% yield with 92.5% D as a light yellow oil.[44] The ^{1}H-NMR data reveals that 70% deuterium incorporation also occur in *β*-position of 2-phenylethanol **4.15a**.

^{1}H NMR (500 MHz, $CDCl_3$): *δ* 7.30 – 7.25 (m, 2H), 7.22 – 7.17 (m, 3H), 3.74 (brs, 0.15H), 2.78 (brs, 0.61H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): *δ* 138.6, 129.0, 128.6, 126.4, 63.1–62.7 (m), 39.0 – 38.1 (m).

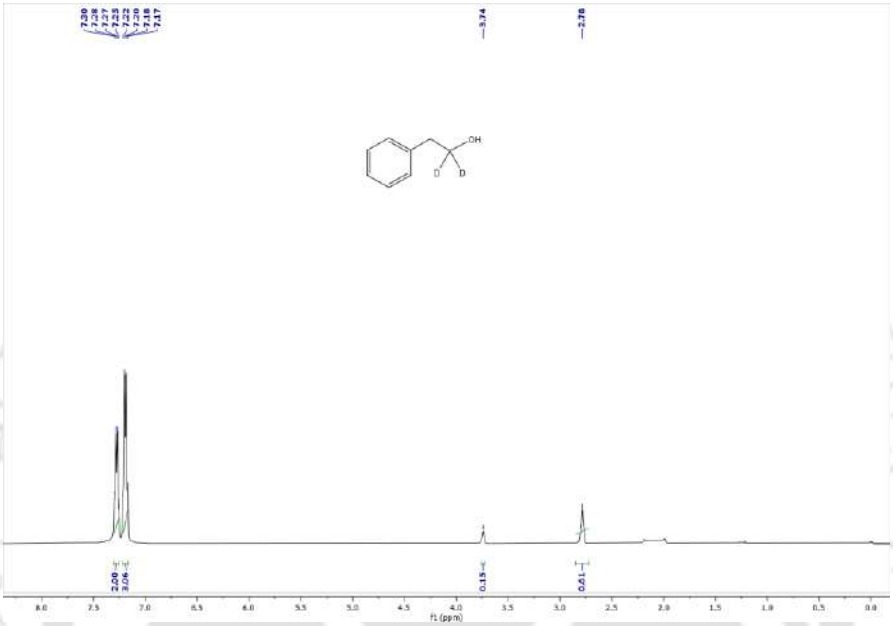

Figure 4.7. ^{1}H NMR spectrum of **4.15a-*d*$_2$** ($CDCl_3$, 500 MHz, 298 K)

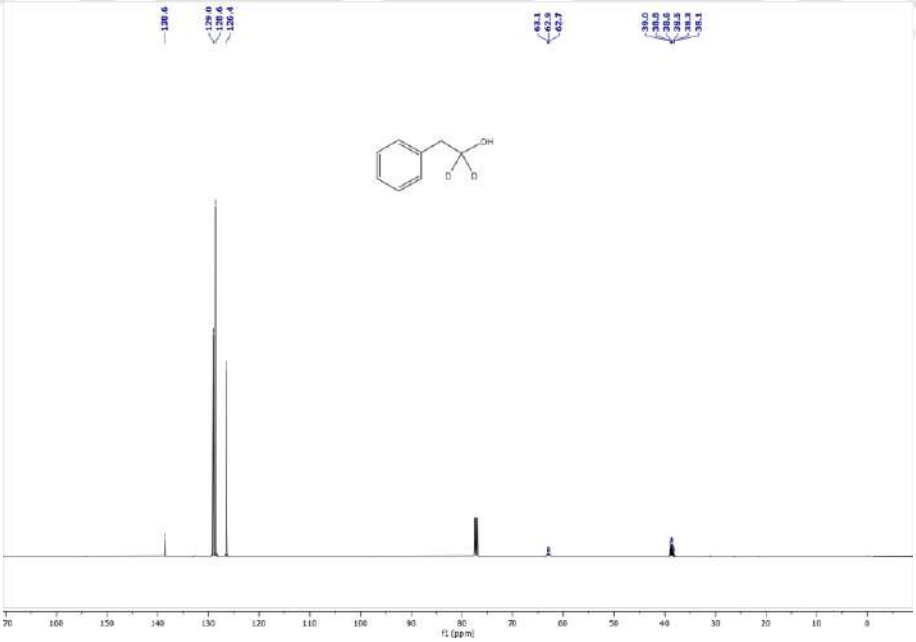

Figure 4.8. ^{13}C{^{1}H} NMR spectrum of **4.15a-*d*$_2$** ($CDCl_3$, 126 MHz, 298 K)

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Synthesis of deuterated 3-phenylquinoline 4.16a-*d* using the reaction of 4.1a and 4.15a-d_2 (Scheme 4.19b):

In a reaction tube a mixture of substituted 2-aminobenzylalcohol **4.4a** (0.5 mmol, 1 equiv.), ketone **4.15a-d_2** (0.5 mmol, 1 equiv.), **3.4b** (5 mol%), KOtBu (50 mol%), toluene (2 mL) were taken. The reaction tube was properly closed under air and placed in a preheated oil bath at 120 ºC with continuous stirring for 18 h. The resulting mixture was then passed through a bed of celite, the filtrate was collected and concentrated under reduced pressure. The crude reaction mixture was purified by column chromatography over silica gel using petroleum ether or ethyl acetate/ petroleum ether mixture as an eluent to get the desired product **4.16a-*d*** in 42% yield.

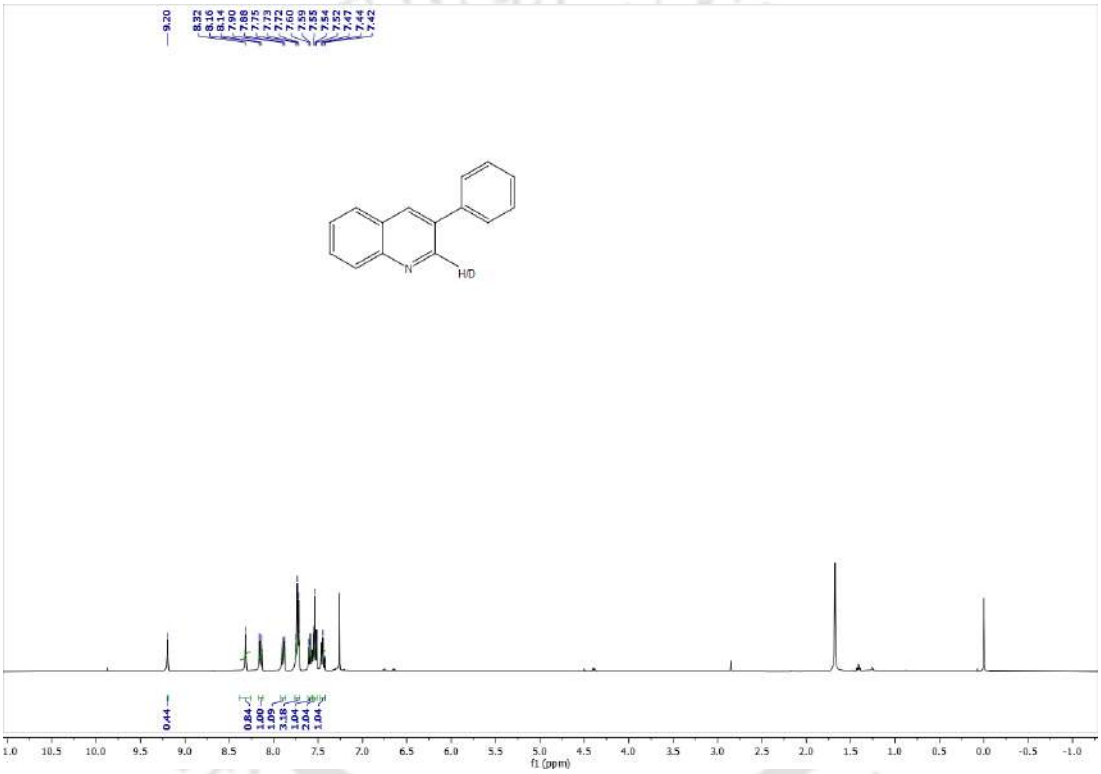

Figure 4.9. ^{1}H NMR spectrum of **4.16a-*d*** ($CDCl_3$, 400 MHz, 298 K)

ix) Synthesis and spectroscopic characterization for active chromium species:

The synthetic procedure and characteristic data for active chromium species **3.4a'** and **3.4b'** already have been discussed in chapter 3 section 3.3.5.

C. Post-synthetic Modification:

Synthesis of 2-pentyl-1,2,3,4-tetrahydroquinoline (4.25) from 4.3v:

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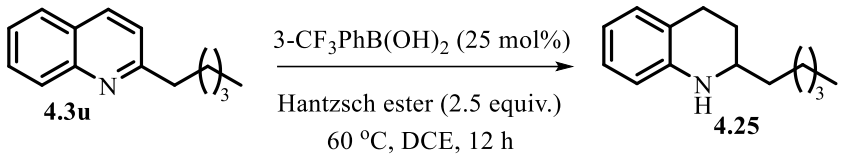
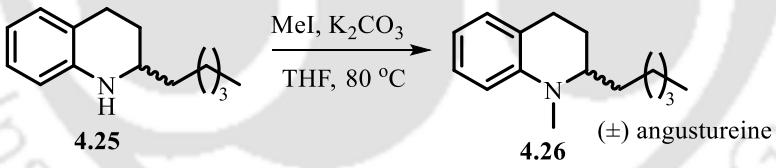


Scheme 4.24. Synthesis of **4.25**

In a reaction tube (25 mL), **4.3u** (199 mg, 1.0 mmol), Hantzsch ester (2.5 equiv.), 3-trifluoromethylphenylboronic acid (25 mol%), and DCE (5 mL) were taken. Then the tube was properly closed and placed on a preheated oil bath at 60 ℃ with continuous stirring. After 12 h, volatile solvent was removed and the resulting crude compound was purified by silica gel column chromatography using petroleum ether/ ethyl acetate mixture as eluent (v/v = 50:1, R_f = 0.50) to get the title compound **4.25** as light yellow oil with 94% yield (191 mg). The spectral data is in accordance to literature. [45]

1H NMR (600 MHz, $CDCl_3$): (*cis : trans* = 6.4:3.6) δ 6.98 – 6.96 (m, 2H, major + minor), 6.62 – 6.60 (m, 1H, major + minor), 6.49 (d, *J* = 7.2 Hz, 1H, major + minor), 3.78 (s, 1H), 3.26 – 3.22 (m, 1H, major + minor), 2.85 – 2.81 (m, 1H, major + minor), 2.75 (t, *J* = 4.8 Hz, 1H, major, 64%), 2.72 (t, *J* = 4.8 Hz, 1H, minor, 36%), 1.99 – 1.95 (m, 1H, major + minor), 1.64 – 1.57 (m, 1H, major + minor), 1.52 – 1.48 (m, 2H, major + minor), 1.43 – 1.39 (m, 2H, major + minor), 1.36 – 1.32 (m, 4H, major + minor), 0.92 (t, *J* = 6.6 Hz, 3H, major + minor). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 144.9, 129.4, 126.8, 121.5, 117.0, 114.1, 51.7, 36.8, 32.1, 28.24, 26.6, 25.5, 22.8, 14.2.

Synthesis of 1-methyl-2-pentyl-1,2,3,4-tetrahydroquinoline, (±) angustureine 4.26 from 4.25:



Scheme 4.25. Synthesis of **4.26**

In a schlenk flask, **4.25** (0.5 mmol, 1 equiv.) was taken in dry THF (1.0 mL). To this solution, methyl iodide (3.0 mmol, 6 equiv.) and potassium carbonate (1.5 mmol, 3 equiv.) was added was under nitrogen flow. The reaction mixture was then stirred for 12h at 80 ℃. After completion of the reaction, the solution was concentrated in vacuo and extracted with ethyl acetate three times. The organic layers were dried over Na_2SO_4 and removed under vacuum. The resulting crude compound was then purified by using silica gel column chromatography using petroleum ether/ ethyl acetate mixture as eluent (v/v = 2:50, R_f = 0.50) to get the title compound **4.26** as yellow oil with 72% yield (78 mg). The spectral data is in accordance to literature. [45, 46]

1H NMR (600 MHz, $CDCl_3$): (*cis : trans* = 6:4) δ 7.13 (t, *J* = 6.0 Hz, 1H, major + minor), 7.02 (d, J = 6.0 Hz, 1H, major + minor), 6.63 (t, *J* = 7.2 Hz, 1H, major + minor), 6.57 (d, *J* = 8.4 Hz, 1H,

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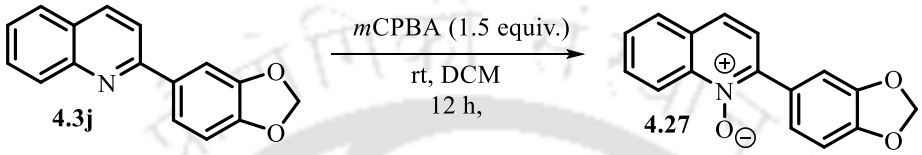
major + minor), 3.29 – 3.26 (m, 1H, major + minor), 2.97 (s, 3H, major + minor), 2.88 – 2.82 (m, 1H, major + minor), 2.71 (t, *J* = 4.2 Hz, 1H, major, 60%), 2.68 (t, *J* = 4.2 Hz, 1H minor, 40%), 1.95 – 1.91 (m, 2H, major + minor), 1.67 – 1.61 (m, 1H, major + minor), 1.46 – 1.40 (m, 2H, major + minor), 1.38 – 1.31 (s, 5H, major + minor), 0.95 (t, *J* = 7.2 Hz, 3H, major + minor). $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$): *δ* 145.5, 128.7, 127.1, 121.9, 115.3, 110.5, 59.0, 38.1, 32.1, 31.2, 25.9, 24.5, 23.6, 22.8, 14.2. The spectral data is in accordance to literature.

Synthesis of 2-(benzo[*d*][1,3]dioxol-5-yl)quinoline 1-oxide (4.27) from 4.3j:

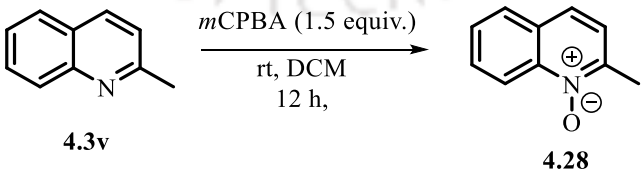


Scheme 4.26. Synthesis of **4.27**

In a round-bottom flask, **4.3j** (0.5 mmol, 1 equiv.) was dissolved in dichloromethane (2 mL). Then, to this solution *m*-chloroperbenzoic acid (*m*-CPBA) (1 mmol, 2 equiv.) in dichloromethane (2 mL) was added portion wise at 0 °C. After completion of the addition, the reaction mixture was allowed to cool down to room temperature and stirred for 12 hours. The mixture was diluted with dichloromethane (5 mL) after completion and combined organic part was washed with 6 N aqueous KOH solution followed by brine solution. The organic part was dried over Na_2SO_4 and solvent was removed under reduced pressure. The resulting crude compound was purified by silica gel column chromatography using petroleum ether/ ethyl acetate mixture as eluent (v/v = 50:25, R_f = 0.40) to get the title compound **4.27** as light brown solid with 95% yield (123 mg). The spectral data is in accordance to literature.[47]

^{1}H NMR (600 MHz, $CDCl_3$): *δ* 8.84 (d, *J* = 9.0 Hz, 1H), 7.85 (d, *J* = 7.8 Hz, 1H), 7.80 – 7.75 (m, 2H), 7.65 – 7.62 (m, 2H), 7.49 (d, *J* = 9.0 Hz, 1H), 7.40 – 7.39 (m, 1H), 6.95 (d, *J* = 8.4 Hz, 1H), 6.04 (s, 2H). $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$): *δ* 148.9, 147.6, 145.1, 142.3, 130.9, 129.5, 128.5, 128.1, 127.2, 126.0, 124.4, 123.4, 120.4, 110.2, 108.4, 101.6.

Synthesis of 2-methylquinoline 1-oxide (4.28) from 4.3w:



Scheme 4.27. Synthesis of **4.28**

In a round-bottom flask, **4.3v** (2 mmol, 1 equiv.) was dissolved in dichloromethane (2 mL). Then, to this solution *m*-chloroperbenzoic acid (*m*-CPBA) (4 mmol, 2 equiv.) in dichloromethane (2 mL) was added portion wise at 0 °C. After completion of the addition, the reaction mixture was allowed

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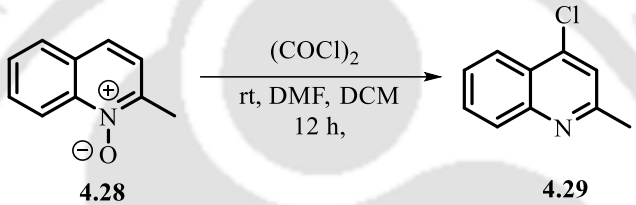
to cool down to room temperature and stirred for 12 hours. The mixture was diluted with dichloromethane (5 mL) after completion and combined organic part was washed with 6 N aqueous KOH solution followed by brine solution. The organic part was dried over Na_2SO_4 and solvent was removed under reduced pressure. The resulting crude compound was purified by silica gel column chromatography using petroleum ether/ ethyl acetate mixture as eluent (v/v = 50:25, R_f = 0.40) to get the title compound **4.28** as brown oil with 95% yield (304 mg).

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.03 (t, J = 8.0 Hz, 2H), 7.76 (d, J = 8.0 Hz, 1H), 7.70 – 7.65 (m, 1H), 7.49–7.46 (m, 1H), 7.29–7.27 (d, J = 8.5 Hz, 1H), 2.75 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 159.1, 148.0, 136.3, 129.6, 128.7, 127.6, 126.6, 125.8, 122.1, 25.5.The spectral data is in accordance to literature.[48]

Synthesis of 4-chloro-2-methylquinoline (4.29) from 4.28:



4.28 **4.29**

Scheme 4.28. Synthesis of **4.29**

In a schlenk flask, 2-methylquinoline 1-oxide (**4.28**) (2 mmol, 1 equiv.) was dissolved in DCM (1.0 mL). To this solution, dry DMF (2.0 mL) was added under nitrogen flow at 0 ºC followed by the addition of $(COCl)_2$ (4.0 mmol). The reaction mixture was stirred for 12 h. The resulting mixture was evaporated under reduced pressure. The resulting crude compound was purified by using silica gel column chromatography using petroleum ether/ ethyl acetate mixture as eluent (v/v = 50:10, R_f = 0.50) to get the tittle compound **4.29** as yellow solid with 78% yield (276 mg).

^{1}H NMR (600 MHz, $CDCl_3$): δ 8.18 – 8.16 (m, 1H), 8.02 (d, J = 8.4 Hz, 1H), 7.74 – 7.72 (m, 1H), 7.58 – 7.56 (m, 1H), 7.39 – 7.38 (m, 1H), 2.72 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 159.0, 148.8, 142.7, 130.5, 129.1, 129.1, 126.8, 124.9, 124.1, 122.1, 25.3. The spectral data is in accordance to literature.[49]

Synthesis of 2-methyl-4-((2,5,7,8-tetramethyl-2-(4,8,12-trimethyltridecyl)chroman-6-yl)oxy)quinoline (4.30) from 4.29:

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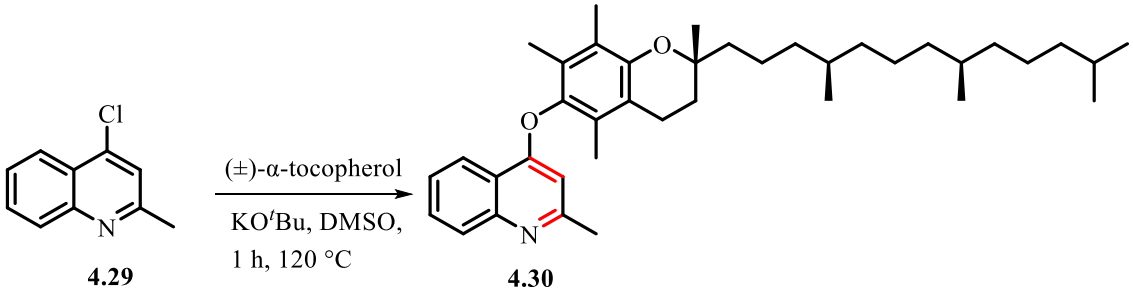
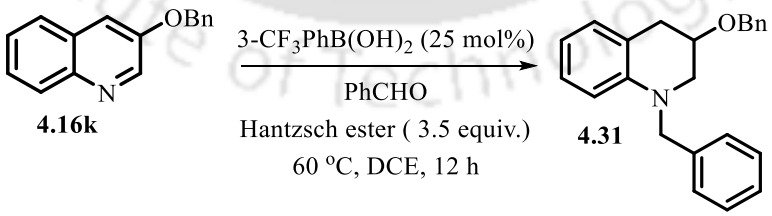


Scheme 4.29. Synthesis of **4.30**

In an oven-dried Schlenk tube, potassium *tert*-butoxide (236 mg, 2.1 mmol, 1.5 equiv.) was taken and dried under vacuum. Then, (±) *α*-tocopherol (724 mg, 1.6 mmol, 1.2 equiv.) in dry DMF (3 mL) was added and stirred at 120 °C for 2 hours. Then 4-chloro-2-methylquinoline (248 mg, 1.4 mmol, 1 equiv.) was added to the mixture and stirred at 120 °C for overnight. After completion of the reaction as confirmed by TLC, the reaction mixture was quenched with water and extracted with dicholromethane (3 × 15 mL). The reaction mixture was evaporated in a vacuum, and purified by using silica gel column chromatography with petroleum ether/ ethyl acetate (v/v = 10/1, R_f = 0.7) as the eluent to afford the desired product **4.30** as a brown viscous liquid in 76% yield (570 mg).

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.42 (d, J = 8.0, 1H), 8.03 (d, J = 8.5 Hz, 1H), 7.71 – 7.68 (m, 1H), 7.51 – 7.48 (m, 1H), 6.16 (d, J = 2.2 Hz, 1H), 2.67 – 2.63 (m, 2H), 2.56 (s, 3H), 2.18 (s, 3H), 2.02 (s, 3H), 1.97 (s, 3H), 1.92 – 1.79 (m, 2H), 1.75 – 1.60 (m, 2H), 1.57 – 1.50 (m, 2H), 1.46 – 1.40 (m, 2H), 1.35 – 1.25 (m, 12H), 1.18 – 1.09 (m, 6H), 0.91– 0.86 (m, 12H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 161.5, 160.3, 149.4, 142.8, 129.9, 128.3, 127.6, 125.8, 125.0, 123.8, 123.7, 121.7, 119.5, 118.2, 102.9, 75.3, 39.5, 37.5, 37.4, 34.7, 32.9, 32.7, 31.6, 31.4, 31.2, 28.0, 25.8, 25.3, 24.9, 24.5, 22.8, 22.7, 20.7, 19.82, 19.76, 14.2, 12.8, 11.94, 11.89. The spectral data is in accordance to literature.[50]

Synthesis of 1-benzyl-3-(benzyloxy)-1,2,3,4-tetrahydroquinoline (4.31) from 4.16k:



Scheme 4.30. Synthesis of **4.31**

In a reaction tube (25 mL) **4.16k** (1.0 mmol, 1 equiv.), benzaldehyde (1 equiv.), Hantzsch ester (2.5 equiv.), 3-trifluoromethylphenylboronic acid (25 mol%), and DCE (5 mL) were taken. Then the tube was properly closed and placed on a preheated oil bath at 60 °C with continuous stirring. After 12 h, volatile solvent was removed and the resulting crude compound was purified by silica

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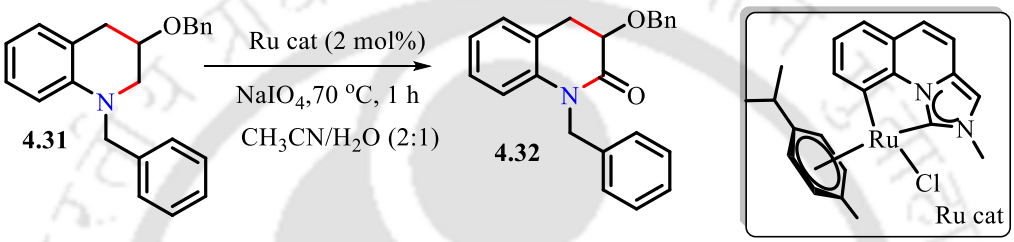
gel column chromatography using petroleum ether/ ethyl acetate mixture as eluent (v/v = 50:1, R_f = 0.60) to get the title compound **4.31** as orange solid with 82% yield (134 mg)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47 – 7.20 (m, 10H), 7.14 (d, J = 8.6 Hz, 2H), 7.02 (t, J = 7.6 Hz, 2H), 6.93 (d, J = 8.6 Hz, 2H), 6.63 – 6.57 (m, 2H), 5.04 (s, 2H), 4.50 (s, 2H), 3.41 (d, J = 7.9 Hz, 2H), 3.23 – 3.16 (m, 1H), 3.04 – 2.95 (m, 2H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 157.7, 145.1, 138.9, 137.2, 136.0, 129.3, 128.73, 128.72, 128.3, 128.1, 127.6, 127.5, 127.0, 126.8, 122.3, 116.2, 115.1, 111.2, 70.2, 56.6, 55.4, 38.0, 35.9. The spectral data is in accordance to literature.[51]

Synthesis of 1-benzyl-3-(benzyloxy)-3,4-dihydroquinolin-2(1*H*)-one (4.28) from 4.27:



Scheme 4.31. Synthesis of **4.32**

$NaIO_4$ (1.5 mmol, 3 equiv.) was taken in a screw-capped reaction tube and dissolved it in water (1 mL). **4.31** (0.5 mmol, 1 equiv.), Ru-cat (2 mol%), and acetonitrile (2 mL) were added to the reaction tube and stirred the reaction mixture in a preheated oil bath at 70 ºC for 1 hour. After the completion of the reaction as confirmed by TLC, the reaction mixture was worked up with CH2Cl2 and water. The organic layer was separated and the aqueous layer was again extracted with CH2Cl2 (two times, 5 mL). The combined organic layer was washed with brine solution (8 mL). The organic layer was separated and dried over anhydrous Na_2SO_4 and the solvent was evaporated under a vacuumThe resulting crude compound was purified by silica gel column chromatography using petroleum ether/ ethyl acetate mixture as eluent (v/v = 10:1, R_f = 0.40) to get the title compound **4.32** as white solid 90% yield (155 mg).

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.41 – 7.40 (m, 2H), 7.37 (t, J = 7.3 Hz, 2H), 7.33 – 7.30 (m, 1H), 7.17 – 7.14 (m, 3H), 7.13 – 7.10 (m, 1H), 6.97 (t, J = 7.8 Hz, 1H), 6.92 – 6.90 (m, 3H), 5.12 (s, 2H), 5.02 (s, 2H), 2.98 – 2.95 (m, 2H), 2.79 – 2.76 (m, 2H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 170.7, 158.0, 140.0, 137.1, 129.5, 128.7, 128.1, 127.94, 127.86, 127.6, 127.5, 126.5, 123.0, 115.8, 115.2, 70.2, 45.7, 32.1, 25.7. The spectral data is in accordance to literature.[51]

Synthesis of 2-methylquinoline 1-oxide (4.33) from 4.16l:

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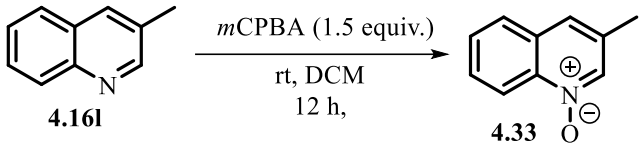
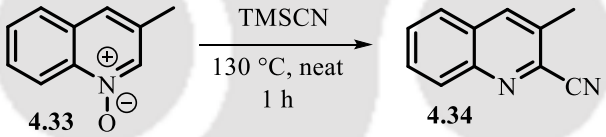


Scheme 4.32. Synthesis of **4.33**

In a round-bottom flask, **4.16l** (0.5 mmol, 1 equiv.) was dissolved in dichloromethane (2 mL). Then, to this solution *m*-chloroperbenzoic acid (*m*-CPBA) (1 mmol, 2 equiv.) in dichloromethane (2 mL) was added portion wise at 0 ℃. After completion of the addition, the reaction mixture was allowed to cool down to room temperature and stirred for 12 hours. The mixture was diluted with dichloromethane (5 mL) after completion and combined organic part was washed with 6 N aqueous KOH solution followed by brine solution. The organic part was dried over Na_2SO_4 and solvent was removed under reduced pressure. The resulting crude compound was purified by silica gel column chromatography using petroleum ether/ ethyl acetate mixture as eluent (v/v = 50:25, R_f = 0.40) to get the title compound **4.33** as yellow liquid with 89% yield (71 mg).

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.66 (d, J = 8.5 Hz, 1H), 8.42 (s, 1H), 7.76 (d, J = 8.0 Hz, 1H), 7.67 (t, J = 8.5 Hz, 1H), 7.58 (t, J = 7.0 Hz, 1H), 7.52 (s, 1H), 2.43 (s, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 139.8, 137.3, 131.3, 130.4, 129.6, 128.9, 127.6, 126.0, 119.7, 18.9. The spectral data is in accordance to literature.[48]

Synthesis of 3-methylquinoline-2-carbonitrile (4.34) from 4.33:



Scheme 4.33. Synthesis of **4.34**

In a schlenk flask, quinoline *N*-oxide, **4.33** (0.5 mmol, 1 equiv.) was taken and to this TMSCN (0.4 mmol, 1 equiv.) was added and stirred the reaction mixture at 130 ºC for 12h. The resulting mixture was collected by using DCM and then evaporated under reduced pressure. The resulting crude compound was purified by using silica gel column chromatography using petroleum ether/ ethyl acetate mixture as eluent (v/v = 10:2, R_f = 0.40) to get the title compound **4.34** as white solid with 897% (73 mg).

1H NMR (600 MHz, $CDCl_3$): δ 8.13 – 8.11 (m, 2H), 7.81 (d, J = 8.2 Hz, 1H), 7.76 (t, J = 7.7 Hz, 1H), 7.66 (t, J = 7.5 Hz, 1H), 2.72 (s, 3H). 13C NMR (151 MHz, $CDCl_3$): δ 146.83, 136.86, 135.26, 132.74, 130.36, 129.82, 129.57, 129.03, 127.21, 116.69, 18.94. HRMS FT-IR (KBr, selected band): 2232 cm^{-1} (CN).The spectral data is in accordance to literature.[52]

D. Crystallographic data

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Crystallographic data of 4.3ac:

Single crystals of compound **4.3ac** suitable for X-ray diffraction were obtained by slow evaporation of the saturated solution of the compound in $CHCl_3$ at room temperature. X-ray crystallographic data were collected using Bruker D8 QUEST diffractometer. Data refinement and cell reduction were carried out by *APEX4*. Structures were solved by direct methods using Olex2 v1.5 and refined by a full-matrix least-squares method using Olex2 v1.5. All of the non-H atoms were refined anisotropically. The ORTEP diagram was obtained with ORTEP3 software with 50% thermal ellipsoid (see below, Figure 4.10). The crystallographic parameters and refinement data were listed in Table 4.7.

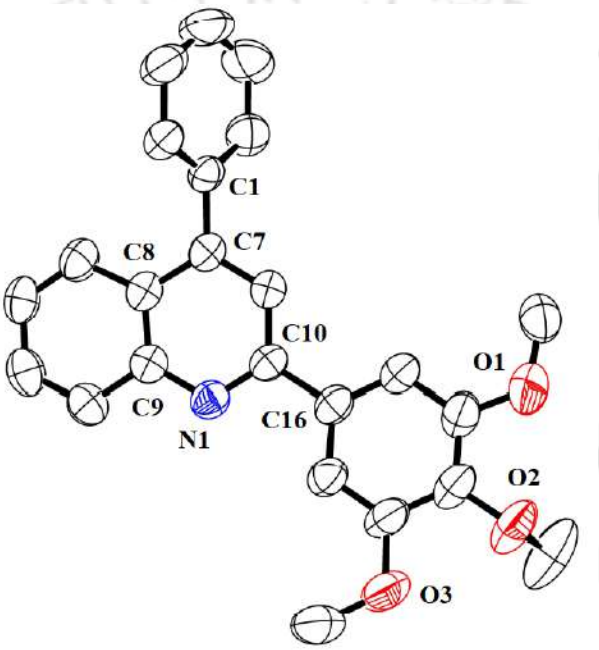

Figure 4.10: Molecular structure of compound **4.3ac** (thermal ellipsoid 50% probability level). Selected Bond lengths (in Å): N1-C9 1.360(2), N1-C10 1.324(2), C1-C7 1.487(3), C10-C16 1.487(3), O2-C20 1.368(3), O3-C19 1.376(2), O4-C18 1.362(2). Selected Bond Angles (in °): C10-N1-C9 118.62(16), N1-C10-C16 116.11(16), C11-C10-C16 122.17(17), C6-C1-C7 120.37(18)

Table 4.7. Crystal data and structure refinement for **4.3ac**

Identification code	3OMe_645_0m_a
CCDC	2361329
Empirical formula	$C_{24}H_{21}NO_3$
Formula weight	371.42
Temperature/K	297.00

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Crystal system	triclinic
Space group	P-1
a/Å	7.8455(6)
b/Å	9.7839(7)
c/Å	14.6769(11)
α/°	96.043(2)
β/°	105.226(2)
γ/°	112.871(2)
Volume/Å3	973.96(13)
Z	2
ρcalcg/cm3	1.266
μ/mm-1	0.083
F(000)	392.0
Crystal size/mm3	0.37 × 0.21 × 0.15
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	4.646 to 50.616
Index ranges	$-9 \leq h \leq 9$, $-11 \leq k \leq 11$, $-17 \leq l \leq 17$
Reflections collected	23912
Independent reflections	3525 [R_{int} = 0.0391, R_{sigma} = 0.0290]
Data/restraints/parameters	3525/0/256
Goodness-of-fit on F2	1.113
Final R indexes [I>=2σ (I)]	R1 = 0.0568, wR2 = 0.1111
Final R indexes [all data]	R1 = 0.0788, wR2 = 0.1230
Largest diff. peak/hole / e Å-3	0.15/-0.14

Crystallographic data of 4.4e:

Single crystals of compound **4.16e** suitable for X-ray diffraction were obtained by slow evaporation of the saturated solution of the compound in $CHCl_3$ at room temperature. X-ray crystallographic data were collected using Bruker D8 QUEST diffractometer. Data refinement and cell reduction were carried out by *APEX4*. Structures were solved by direct methods using Olex2

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v1.5 and refined by a full-matrix least-squares method using Olex2 v1.5. All of the non-H atoms were refined anisotropically. The ORTEP diagram was obtained with ORTEP3 software with 50% thermal ellipsoid (see below, Figure 4.11). The crystallographic parameters and refinement data were listed in Table 4.8.

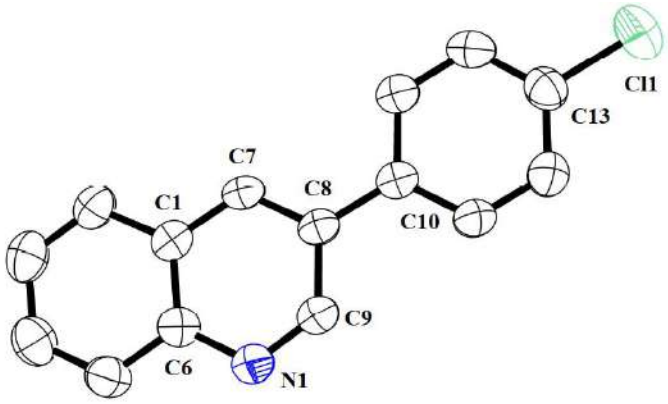

Figure 4.11: Molecular structure of compound **4.16e** (thermal ellipsoid 50% probability level). Selected Bond lengths (in Å): Cl1-C13 1.732(3), N1-C6 1.365(4), N1-C9 1.311(4), C8-C10 1.479(4), C7-C8 1.371(4), C8-C9 1.418(5). Selected Bond Angles (in °): C9-N1-C6 117.6(3), C9-C8-C10 120.7(3) , C7-C8-C10 124.0(3).

Table 4.8. Crystal data and structure refinement for **4.16e**

Identification code	PA_702_0m_a
CCDC	2361223
Empirical formula	$C_{15}H_{10}ClN$
Formula weight	239.69
Temperature/K	298.00
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	13.8866(17)
b/Å	5.9015(7)
c/Å	14.7636(19)
α/°	90
β/°	109.473(4)
γ/°	90
Volume/Å^3	1140.7(2)

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Z	4
ρ_{calc}g/cm^3	1.396
μ/mm^{-1}	0.307
F(000)	496.0
Crystal size/mm^3	0.31 × 0.25 × 0.15
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	5.64 to 50
Index ranges	$-16 \leq h \leq 16$, $-7 \leq k \leq 7$, $-17 \leq l \leq 17$
Reflections collected	21549
Independent reflections	1999 [R_{int} = 0.0816, R_{sigma} = 0.0375]
Data/restraints/parameters	1999/0/154
Goodness-of-fit on F^2	1.134
Final R indexes [I>=2σ (I)]	R_1 = 0.0638, wR_2 = 0.1349
Final R indexes [all data]	R_1 = 0.1006, wR_2 = 0.1678
Largest diff. peak/hole / e Å^{-3}	0.28/-0.25

Crystallographic data of 4.24g:

Single crystals of compound **4.24g** suitable for X-ray diffraction were obtained by slow evaporation of the saturated solution of the compound in $CHCl_3$ at room temperature. X-ray crystallographic data were collected using Bruker D8 QUEST diffractometer. Data refinement and cell reduction were carried out by *APEX4*. Structures were solved by direct methods using Olex2 v1.5 and refined by a full-matrix least-squares method using Olex2 v1.5. All of the non-H atoms were refined anisotropically. The ORTEP diagram was obtained with ORTEP3 software with 50% thermal ellipsoid (see below, Figure 4.12). The crystallographic parameters and refinement data were listed in Table 4.9.

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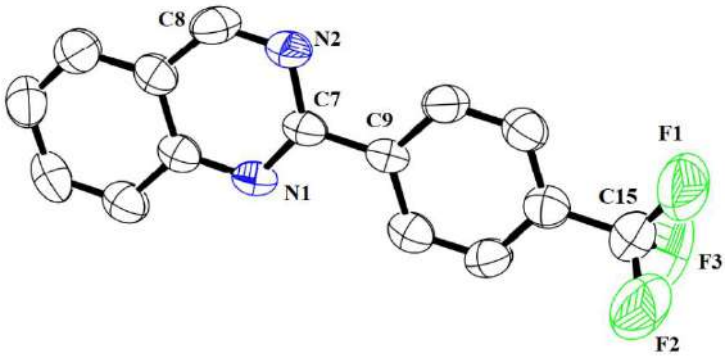

Figure 4.12: Molecular structure of compound **4.24g** (thermal ellipsoid 50% probability level). Selected Bond lengths (in Å): F1-C15 1.282(9), C7-C9 1.478(8), N2-C7 1.371(7), N2-C8 1.309(8), N1-C7 1.305(7) Selected Bond Angles (in °): F1-C15-C12 114.7(7), N1-C7-C9 118.4(5), N2-C7 -C9 115.5(5), C8-N2-C7 116.1(5), N1-C7-N2 126.1(6)

Table 4.9. Crystal data and structure refinement for **4.24g**

Identification code	PA_613_0m_a
CCDC	2361205
Empirical formula	$C_{15}H_9F_3N_2$
Formula weight	274.24
Temperature/K	298.00
Crystal system	orthorhombic
Space group	Pbca
a/Å	14.8264(11)
b/Å	6.1317(5)
c/Å	27.253(2)
α/°	90
β/°	90
γ/°	90
Volume/Å^3	2477.6(3)
Z	8
ρ_{calc}g/cm^3	1.470
μ/mm^{-1}	0.120

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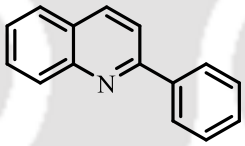
F(000)	1120.0
Crystal size/mm^3	0.38 × 0.32 × 0.31
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	2.988 to 49.99
Index ranges	-17 ≤ h ≤ 17, -7 ≤ k ≤ 7, -32 ≤ l ≤ 32
Reflections collected	48302
Independent reflections	2177 [R_{int} = 0.0524, R_{sigma} = 0.0237]
Data/restraints/parameters	2177/0/181
Goodness-of-fit on F^2	1.301
Final R indexes [I>=2σ (I)]	R_1 = 0.1279, wR_2 = 0.2108
Final R indexes [all data]	R_1 = 0.1639, wR_2 = 0.2346
Largest diff. peak/hole / e Å^{-3}	0.47/-0.36

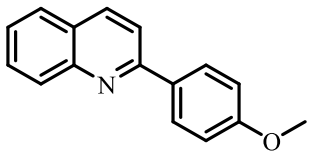
4.6. Analytical data of the products

2-phenylquinoline (4.3a)[53]



Using **GP-I** the title compound **4.3a** was isolated as white solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.50); (93 mg, 91%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.23 – 8.17 (m, 4H), 7.88 (d, J = 8.4 Hz, 1H), 7.83 (d, J = 7.8 Hz, 1H), 7.75 – 7.73 (m, 1H), 7.55 – 7.52 (m, 3H), 7.49 – 7.46 (t, J = 7.3 Hz, 1H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 157.5, 148.4, 139.8 136.9, 129.9, 129.8, 129.4, 129.0, 127.7, 127.6, 127.3, 126.4, 119.1.

2-(4-methoxyphenyl)quinoline (4.3b)[53]



Using **GP-I** the title compound **4.3b** was isolated as light yellow solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.40); (108 mg, 92%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.20 – 8.16 (m, 4H), 7.86 (d, J = 9.0 Hz, 1H), 7.83 (d, J = 7.8 Hz, 1H), 7.75 – 7.72 (t, J = 8.4 Hz, 1H), 7.52 (t, J = 7.2 Hz, 1H), 7.08 – 7.07 (m, 2H). ^{13}C{^{1}H} NMR (151

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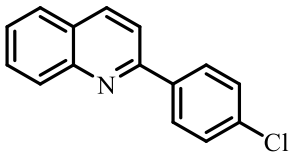
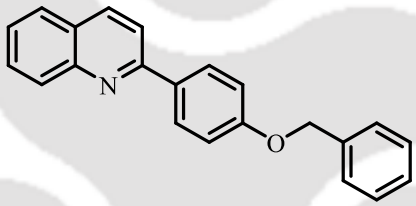
MHz, $CDCl_3$) δ 160.9, 157.0, 148.4, 136.8, 132.4, 129.7, 129.7, 129.0, 127.6, 127.0, 126.0, 118.7, 114.4, 55.5.

2-(4-chlorophenyl)quinoline (4.3c)[53]



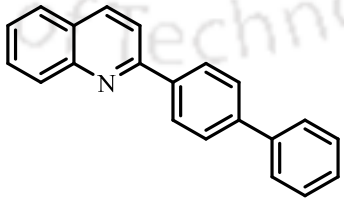
Using **GP-I** the title compound **4.3c** was isolated as white solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.50); (98 mg, 82%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.19 (d, J = 9.0 Hz, 1H), 8.16 (d, J = 9.0 Hz, 1H), 8.11 (d, J = 9.0 Hz, 2H), 7.82 – 7.80 (m, 2H), 7.75 – 7.73 (m, 1H), 7.55 – 7.52 (m, 1H), 7.49 (d, J = 8.4 Hz, 2H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 156.2, 148.3, 138.1, 137.1, 135.6, 129.9, 129.8, 129.1, 128.9, 127.6, 127.3, 126.6, 118.6.

2-(4-(benzyloxy)phenyl)quinoline (4.3d)[53]



Using **GP-I** the title compound **4.3d** was isolated as white solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v= 20/1, R_f = 0.5) (137 mg, 88%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.18 (d, J = 8.6 Hz, 1H), 8.15 – 8.13 (m, 3H), 7.83 (d, J = 6.0 Hz, 1H), 7.81 (d, J = 6.0 Hz, 1H), 7.72 – 7.70 (m, 1H), 7.51 – 7.47 (m, 3H), 7.41 (t, J = 6.0 Hz, 2H), 7.36 – 7.33 (m, 1H), 7.14 – 7.12 (m, 2H), 5.16 (s, 2H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 160.1, 157.0, 148.4, 136.9, 136.8, 132.6, 129.72, 129.7, 129.0, 128.8, 128.2, 127.6, 127.6, 127.1, 126.1, 118.7, 115.3, 70.2.

2-([1,1'-biphenyl]-4-yl)quinoline (4.3e)[53]



Using **GP-I** the title compound **4.3e** was isolated as white solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50/1, R_f = 0.5) (118 mg, 84%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.28 (d, J = 8.2 Hz, 2H), 8.22 (d, J = 8.4 Hz, 2H), 7.92 (d, J = 8.4 Hz, 1H), 7.84 (d, J = 8.4 Hz, 1H), 7.79 – 7.74 (m, 3H), 7.70 (d, J = 7.8 Hz, 2H), 7.57 – 7.53 (m, 1H), 7.49

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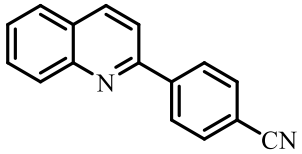
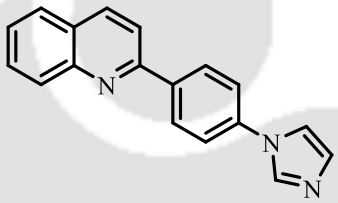
(t, J = 7.8 Hz, 2H), 7.42 – 7.39 (m, 1H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 157.0, 148.5, 142.2, 140.7, 138.6, 136.9, 129.9, 129.8, 129.0, 128.1, 127.7, 127.7, 127.6, 127.3, 127.3, 126.4, 119.0.

4-(quinolin-2-yl)benzonitrile(4.3f)[53]



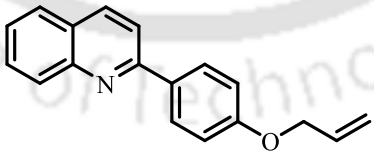
Using **GP-I** the title compound **4.3f** was isolated as off-white solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.40); (78 mg, 68%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.30 – 8.28 (m, 3H), 8.18 (d, J = 8.5 Hz, 1H), 7.90 – 7.86 (m, 2H), 7.81 (d, J = 8.0 Hz, 2H), 7.79 – 7.76 (t, J = 7.4 Hz, 1H), 7.59 (t, J = 7.5 Hz, 1H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 155.1, 148.4, 143.9, 137.4, 132.7, 130.3, 130.0, 128.2, 127.7, 127.7, 127.3, 119.0, 118.7, 112.9.

2-(4-(1H-imidazol-1-yl)phenyl)quinoline (4.3g)



Using **GP-I** the title compound **4.3g** was isolated as off-white solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.40); (115 mg, 85%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.29 (d, J = 8.4 Hz, 2H), 8.25 (d, J = 8.4 Hz, 1H), 8.17 (d, J = 9.0 Hz, 1H), 7.95 (s, 1H), 7.88 (d, J = 8.4 Hz, 1H), 7.84 (d, J = 8.4 Hz, 1H), 7.75 (t, J = 7.8 Hz, 1H), 7.56 – 7.53 (m, 3H), 7.36 (s, 1H), 7.25 (s, 1H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 155.8, 148.4, 138.9, 138.1, 137.2, 135.6, 130.8, 130.1, 129.8, 129.2, 127.6, 127.4, 126.7, 121.6, 118.7, 118.2. HRMS (ESI) m/z: $[M+H]^+$ calculated for $C_{18}H_{14}N_3$ 272.1183; found 272.1181.

2-(4-(allyloxy)phenyl)quinoline (4.3h)[53]



Using **GP-I** the title compound **4.3h** was isolated as colorless oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.40); (102 mg, 76%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.19 (d, J = 8.5 Hz, 1H), 8.13 (d, J = 8.5 Hz, 3H), 7.84 – 7.80 (m, 2H), 7.71 (t, J = 7.0 Hz, 1H), 7.50 (t, J = 7.5 Hz, 1H), 7.07 (d, J = 9.0 Hz, 2H), 6.14 – 6.06 (m, 1H), 5.46 (d, J = 17.0 Hz, 1H), 5.33 (d, J = 10.5, 1H), 4.63 (d, J = 5.0 Hz, 2H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 160.0, 157.1, 148.5, 136.8, 133.2, 132.6, 129.7, 129.7, 129.0, 127.6, 127.1, 126.1, 118.7, 118.0, 115.2, 69.0.

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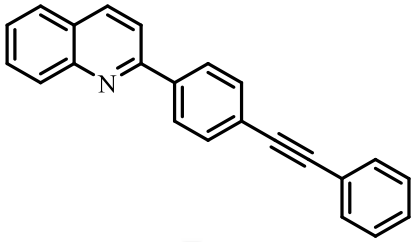
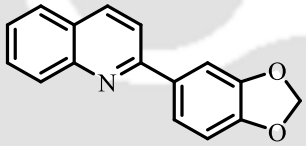
2-(4-(phenylethynyl)phenyl)quinoline (4i)[53]



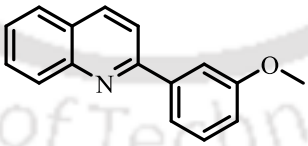
Using **GP-I** the title compound **4.3i** was isolated as colorless oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v= 20/1, R_f = 0.5) (118 mg, 78%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.24 (d, J = 8.4 Hz, 1H), 8.20 – 8.17 (m, 3H), 7.91 (d, J = 8.5 Hz, 1H), 7.84 (d, J = 8.0 Hz, 1H), 7.75 (t, J = 7.5 Hz, 1H), 7.70 (d, J = 8.1 Hz, 2H), 7.58 – 7.55 (m, 3H), 7.38 – 7.36 (m, 3H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 156.5, 148.4, 139.4, 137.0, 132.2, 131.8, 130.0, 129.9, 128.5, 127.6, 127.6, 127.4, 126.6, 124.4, 123.3, 118.9, 91.0, 89.5.

2-(benzo[*d*][1,3]dioxol-5-yl)quinoline (4.3j)[47]



Using **GP-I** the title compound **4.3j** was isolated as yellow solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:3, R_f = 0.50); (106 mg, 85%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.17 (d, J = 9.0 Hz, 1H), 8.13 (d, J = 8.5 Hz, 1H), 7.81 – 7.78 (m, 2H), 7.75 (brs, 1H), 7.71 (t, J = 7.0 Hz, 1H), 7.67 – 7.65 (m, 1H), 7.50 (t, J = 8.0 Hz, 1H), 6.95 (d, J = 8.0 Hz, 1H), 6.04 (s, 2H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 156.81, 148.97, 148.5, 148.3, 136.8, 134.3, 129.8, 129.7, 127.5, 127.1, 126.2, 121.9, 118.7, 108.6, 108.1, 101.5.

2-(3-methoxyphenyl)quinoline (4.3k)[53]



Using **GP-I** the title compound **4.3k** was isolated as light yellow solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.40); (107 mg, 91%).^{1}H NMR (600 MHz, $CDCl_3$): δ 8.22 (d, J = 8.4 Hz, 2H), 7.88 (d, J = 8.4 Hz, 1H), 7.84 (d, J = 8.4 Hz, 1H), 7.82 (s, 1H), 7.77 – 7.74 (m, 2H), 7.55 (t, J = 7.8 Hz, 1H), 7.47 (t, J = 7.8 Hz, 1H), 7.06 – 7.05(m, 1H), 3.96 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 160.2, 148.3, 141.3, 136.8, 129.9, 129.84, 129.75, 127.6, 127.4, 126.4, 120.1, 119.2, 115.5, 112.8, 55.5.

2-(3-(trifluoromethoxy)phenyl)quinoline (4.3l)

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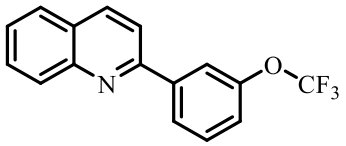
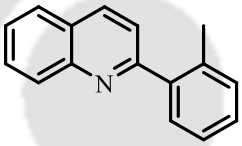


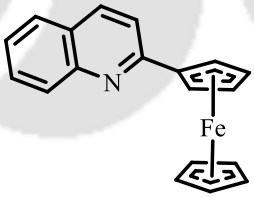
Using **GP-I** the title compound **4.3l** was isolated as white solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:2, R_f = 0.40); (125 mg, 87%).^{1}H NMR (500 MHz, $CDCl_3$): δ 8.25 (d, J = 8.4 Hz, 1H), 8.18 (d, J = 8.5 Hz, 1H), 8.12 – 8.07 (m, 2H), 7.87 – 7.83 (m, 2H), 7.76 (t, J = 7.6 Hz, 1H), 7.58 – 7.53 (m, 2H), 7.32 (d, J = 8.1 Hz, 1H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 155.7, 150.0, 148.4, 141.9, 137.2, 130.3, 130.1, 130.0, 127.6, 127.5, 126.8, 125.9. ^{19}F NMR (471 MHz, $CDCl_3$): δ -57.59. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{16}H_{11}F_3NO$ 290.0788; found 290.0786.

2-(o-tolyl)quinoline (4.3m)[54]



Using **GP-I** the title compound **4.3m** was isolated as white solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:2, R_f = 0.40); (80 mg, 73%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.22 (d, J = 8.5 Hz, 1H), 8.16 (d, J = 8.5 Hz, 1H), 7.87 (d, J = 8.0 Hz, 1H), 7.74 (t, J = 7.5 Hz, 1H), 7.58 – 7.54 (m, 2H), 7.51 – 7.49 (m, 1H), 7.35 – 7.32 (m, 3H), 2.42 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 160.5, 140.9, 136.2, 136.1, 131.0, 129.8, 129.7, 129.7, 128.6, 127.6, 126.9, 126.5, 126.2, 122.5, 20.5.

2-(ferrocenyl)quinoline (4.3n)[54]



Using **GP-I** the title compound **4.3n** was isolated as reddish solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:4, R_f = 0.50); (117 mg, 75%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.04 (d, J = 8.4 Hz, 2H), 7.75 (d, J = 8.0 Hz, 1H), 7.68 – 7.64 (m, 1H), 7.58 (d, J = 8.4 Hz, 1H), 7.49 – 7.45 (m, 1H), 5.08 – 5.07 (m, 2H), 4.48 – 4.47 (m, 2H), 4.06 (s, 4H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 159.7, 148.5, 135.6, 129.5, 129.2, 127.6, 126.9, 125.5, 119.7, 84.1, 70.6, 69.8, 68.1.

2-(pyridin-3-yl)quinoline (4.3o)[53]

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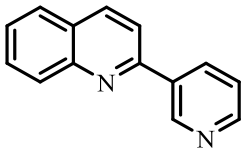
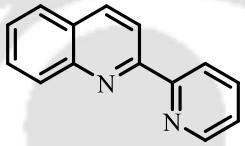


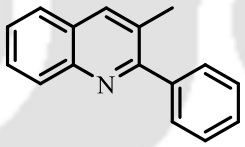
Using **GP-I** the title compound **4.3o** was isolated as reddish solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v= 20/1, R_f = 0.5); (84 mg, 82%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 9.35 (d, J = 1.8 Hz, 1H), 8.70 (dd, J = 1.6, 4.8 Hz, 1H), 8.52 (dt, J = 2, 8 Hz, 1H), 8.29 (d, J = 8.0 Hz, 1H), 8.18 (d, 8.4 Hz, 1H), 7.90 (d, J = 8.4 Hz, 1H), 7.87 (d, J = 8.0 Hz, 1H), 7.78 – 7.75 (m, 1H), 7.59 – 7.56 (m, 1H), 7.48 – 7.46 (m, 1H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 154.8, 150.4, 149.0, 148.5, 137.4, 135.3, 135.1, 130.2, 129.9, 127.7, 127.5, 127.0, 123.9, 118.7.

2-(pyridin-2-yl)quinoline (4.3p)[53]



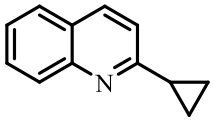
Using **GP-I** the title compound **4.3p** was isolated as reddish solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 20/1, R_f = 0.5); (80 mg, 78%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.74 – 8.73 (m, 1H), 8.65 (d, J = 7.9 Hz, 1H), 8.56 (d, J = 8.6 Hz, 1H), 8.28 (d, J = 8.6 Hz, 1H), 8.18 (d, J = 8.6 Hz, 1H), 7.88 – 7.84 (m, 2H), 7.75 – 7.72 (m, 1H), 7.56 – 7.53 (m, 1H), 7.36 – 7.34 (m, 1H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 156.4, 156.3, 149.3, 148.0, 137.1, 136.9, 129.9, 129.7, 128.3, 127.7, 126.9, 124.1, 121.9, 119.1.

3-methyl-2-phenylquinoline (4.3q)[53]



Using **GP-I** the title compound **4.3q** was isolated as yellow oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:3, R_f = 0.50); (91 mg, 83%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.15 (d, J = 8.5 Hz, 1H), 8.00 (s, 1H), 7.77 (d, J = 8.0 Hz, 1H), 7.68 – 7.65 (m, 1H), 7.61 – 7.59 (m, 2H), 7.53 – 7.48 (m, 3H), 7.45 – 7.43 (m, 1H), 2.46 (s, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 160.6, 146.7, 141.0, 136.8, 129.4, 129.3, 128.9, 128.8, 128.4, 128.3, 127.7, 126.8, 126.5, 20.7.

2-cyclopropylquinoline (4.3r)[55]



Using **GP-1** the title compound **4.3r** was isolated as yellow solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:3, R_f = 0.50); (61 mg, 72%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.99 (d, J = 7.8 Hz, 1H), 7.95 (d, J = 8.4 Hz, 1H), 7.71 (d, J = 9.6 Hz, 1H),

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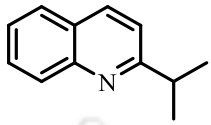
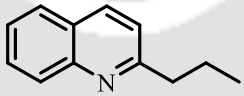
7.65 – 7.62 (m, 1H), 7.43 – 7.41 (m, 1H), 7.13 (d, J = 8.4 Hz, 1H), 2.26 – 2.21 (m, 1H), 1.18 – 1.16 (m, 2H), 1.11 – 1.08 (m, 2H). $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$): δ 163.4, 148.0, 135.8, 129.3, 128.7, 127.5, 126.8, 125.2, 119.4, 18.1, 10.4.

2-isopropylquinoline (4.3s) [53]



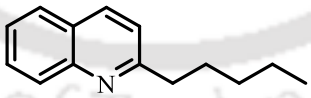
Using **GP-1** the title compound **4.3s** was isolated as yellow solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 100/1, R_f = 0.5) (53 mg, 62%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.07 (d, J = 8.4 Hz, 1H), 8.04 (d, J = 8.6 Hz, 1H), 7.73 (d, J = 8.1 Hz, 1H), 7.67–7.64 (m, 1H), 7.45 (t, J = 7.0 Hz, 1H), 7.30 (d, J = 8.6 Hz, 1H), 3.27 (hept, J = 7.0 Hz, 1H), 1.40 (d, J = 7.0 Hz, 6H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 167.7, 147.8, 136.4, 129.3, 129.0, 127.5, 127.0, 125.7, 119.2, 37.3, 22.6.

2-propylquinoline (4.3t)[56]



Using **GP-I** the title compound **4.3t** was isolated as yellow oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:3, R_f = 0.50); (62 mg, 72%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.06 – 8.04 (m, 2H), 7.77 (d=, J = 8.4, 1H), 7.67 (t, J = 7.2 Hz, 1H), 7.47 (d, J = 8.4 Hz, 1H), 7.29 (d, J = 8.4 Hz, 1H), 2.96 – 2.94 (m, 2H), 1.88 – 1.82 (m, 2H), 1.02 (t, J = 7.2 Hz, 3H). $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$): δ 163.0, 148.0, 136.3, 129.4, 129.0, 127.6, 126.9, 125.8, 121.5, 41.4, 23.4, 14.1.

2-pentylquinoline (4.3u)[53]



Using **GP-I** the title compound **4.3u** was isolated as yellow oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:3, R_f = 0.50); (77 mg, 76%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.05 (d, J = 8.4 Hz, 2H), 7.76 (d, J = 8.4 Hz, 1H), 7.67 (t, J = 7.8 Hz, 1H), 7.47 (t, J = 7.2 Hz, 1H), 7.29 (d, J = 8.4 Hz, 1H), 2.98 – 2.95 (m, 2H), 1.82 (p, J = 7.8 Hz, 2H), 1.41 – 1.37 (m, 4H), 0.91 – 0.89 (m, 3H). $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$): δ 163.2, 148.0, 136.3, 129.4, 128.9, 127.6, 126.8, 125.7, 121.5, 39.5, 31.9, 29.9, 22.7, 14.1.

2-methylquinoline (4.3v)[53]

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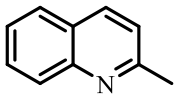
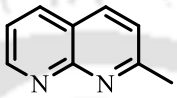


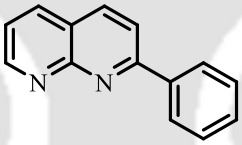
Following the general procedure **GP-I** the title compound **4.3v** was isolated as light yellow oil using silica gel column chromatography with pet-ether/ ethyl acetate (v/v= 95/5, R_f = 0.5) (36 mg, 51%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.99 (d, J = 8.2 Hz, 1H), 7.92 (d, J = 8.4 Hz, 1H), 7.67 (d, J = 8.0 Hz, 1H), 7.61 (t, J = 8.4 Hz, 1H), 7.43 – 7.37 (m, 1H), 7.16 (d, J = 8.4 Hz, 1H), 2.67 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 158.9, 158.9, 147.8, 136.1, 129.3, 128.5, 127.4, 126.4, 125.6, 121.9, 25.3.

2-methyl-1,8-naphthyridine (4.3w)[57]



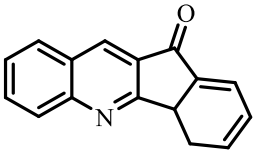
Using **GP-I** the title compound **4.3w** was isolated as brown solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:3, R_f = 0.50); (31 mg, 43%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.08 – 9.07 (m, 1H), 8.15 – 8.13 (m, 1H), 8.07 (d, J = 8.5 Hz, 1H), 7.44 – 7.42 (m 1H), 7.38 (d, J = 8.5 Hz, 1H), 2.82 (s, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 163.2, 156.1, 153.4, 137.0, 136.8, 123.1, 121.5, 120.9, 25.8.

2-phenyl-1,8-naphthyridine (4.3x)[57]



Using **GP-I** the title compound **4.3x** was isolated as yellow solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:4, R_f = 0.50); (60 mg, 58%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 9.14 – 9.12 (m, 1H), 8.33 – 8.31 (m, 2H), 8.25 – 8.23 (m, 1H), 8.20 – 8.17 (m, 1H), 8.02 – 8.00 (m, 1H), 7.54 – 7.51 (m, 2H), 7.50 – 7.44 (m, 2H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 160.4, 156.3, 154.0, 138.6, 137.9, 136.8, 130.2, 128.9, 128.1, 121.9, 121.8, 119.8.

11H-indeno[1,2-b]quinolin-11-one (4.3aa)[58]



Using **GP-I** the title compound **4.3aa** was isolated as reddish solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:3, R_f = 0.50); (82 mg, 70%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.39 (s, 1H), 8.14 – 8.11 (m, 2H), 7.89 (d, J = 7.8 Hz, 1H), 7.84 (d, J = 7.8 Hz, 1H), 7.79 – 7.77 (m, 1H), 7.71 – 7.69 (m, 1H), 7.56 –7.52 (m, 2H). ^{13}C{^{1}H} NMR (151 MHz,

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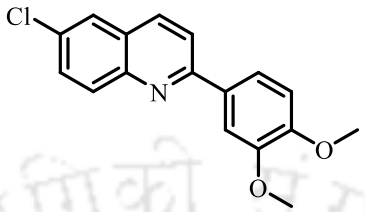
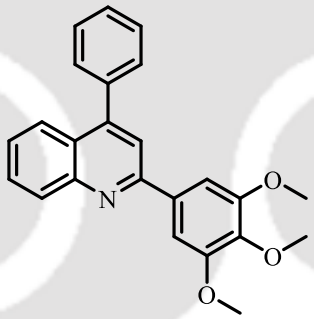
$CDCl_3$): δ 191.1, 162.3, 150.9, 144.1, 137.7, 135.8, 132.7, 132.3, 131.8, 130.7, 130.0, 127.9, 127.4, 127.3, 124.4, 122.0.

6-chloro-2-(3,4-dimethoxyphenyl)quinoline (4.3ab)[59]



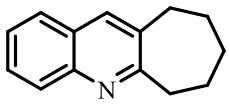
Using **GP-I** the title compound **4.3ab** was isolated as white solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:2, R_f = 0.40); (118 mg, 79%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.10 – 8.07 (m, 2H), 7.88 – 7.86 (m, 2H), 7.79 (brs, 1H), 7.67 – 7.63 (m, 2H), 7.00 (d, J = 8.5 Hz, 1H), 4.05 (s, 3H), 3.97 (s, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 157.2, 150.8, 149.6, 135.8, 132.2, 131.7, 131.2, 130.6, 127.7, 126.3, 120.4, 119.6, 111.2, 110.5, 56.2, 56.2.

4-phenyl-2-(3,4,5-trimethoxyphenyl)quinoline (4.3ac)[60]



Using **GP-I** the title compound **4.3ac** was isolated as white solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:3, R_f = 0.40); (172 mg, 93%).^{1}H NMR (600 MHz, $CDCl_3$): δ 8.24 (d, J = 8.4 Hz, 1H), 7.89 (d, J = 8.4 Hz, 1H), 7.76 – 7.73 (m, 2H), 7.58 – 7.57 (m, 4H), 7.55 – 7.53 (m, 1H), 7.49 – 7.47 (m, 1H), 7.43 (s, 2H), 4.00 (s, 6H), 3.93 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 156.7, 153.7, 149.3, 148.8, 139.6, 138.6, 135.4, 130.2, 129.75, 129.71, 128. 8, 128.6, 126.5, 125.9, 125.8, 119.3, 105.0, 61.1, 56.5.

7,8,9,10-tetrahydro-6*H*-cyclohepta[*b*]quinoline (4.3ad)[61]



Using **GP-I** the title compound **4.3ad** was isolated as white solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:3, R_f = 0.50); (90 mg, 91%). ^{1}H NMR

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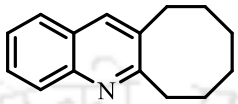
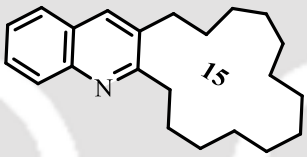
(600 MHz, $CDCl_3$): δ 7.99 (d, J = 8.4 Hz, 1H), 7.79 –7.77 (m, 1H), 7.71 – 7.68 (m, 1H), 7.61 – 7.59 (m, 1H), 7.46 – 7.42 (m, 1H), 3.21 – 3.19 (m, 2H), 2.94 – 2.90 (m, 2H), 1.89 – 1.86 (m, 2H), 1.80 – 1.78 (m, 2H), 1.74 – 1.74 (m, 2H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 164.7, 146.3, 136.59, 136.57, 134.7, 134.6, 128.5, 127.4, 126.9, 125.8, 40.1, 35.5, 32.3, 28.9, 27.1.

6,7,8,9,10,11-hexahydrocycloocta[*b*]quinoline (4.3ae)[61]



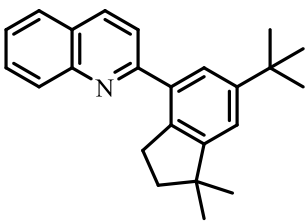
Using **GP-I** the title compound **4.3ae** was isolated as white solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:3, R_f = 0.50); (93 mg, 88%).^{1}H NMR (600 MHz, $CDCl_3$): δ 8.03 (d, J = 8.4 Hz, 1H), 7.83 (s, 1H), 7.72 (d, J = 7.8 Hz, 1H), 7.62 (t, J = 7.8 Hz, 1H), 7.45 (t, J = 7.2 Hz, 1H), 3.18 – 3.16 (m, 2H), 2.97 – 2.94 (m, 2H), 1.90 – 1.89 (m, 2H), 1.81 – 1.78 (m, 2H), 1.42 – 1.40 (m, 4H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 163.4, 147.1, 135.3, 135.2, 128.6, 128.5, 127.8, 127.0, 125.7, 35.4, 32.9, 32.2, 31.1, 26.2, 26.1.

7,8,9,10,11,12,13,14,15,16,17,18-dodecahydro-6*H*-cyclopentadeca[*b*]quinoline (4.3af)[61]



Using **GP-I** the title compound **4.3af** was isolated as white solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:3, R_f = 0.50); (127 mg, 82%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.01 (d, J = 8.4 Hz, 1H), 7.85 (s, 1H), 7.70 (d, J = 8.4 Hz, 1H), 7.60 (t, J = 7.2 Hz, 1H), 7.43 (t, J = 7.8 Hz, 1H), 2.98 – 2.96 (m, 2H), 2.79 – 2.76 (m, 2H), 1.84 – 1.79 (m, 2H), 1.75 – 1.70 (m, 2H), 1.61 – 1.58 (m, 2H), 1.56 – 1.53 (m, 2H), 1.46 – 1.43 (m, 4H), 1.39 – 1.32 (m, 10H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 162.5, 146.6, 135.4, 134.5, 128.5, 127.4, 126.9, 125.7, 36.1, 32.5, 29.4, 28.4, 27.6, 27.5, 27.0, 26.9, 26.7, 26.1, 26.0, 25.7, 25.6. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{22}H_{32}N$ 310.2530; found 310.2539.

2-(6-(tert-butyl)-1,1-dimethyl-2,3-dihydro-1*H*-inden-4-yl)quinoline (4.3ag)



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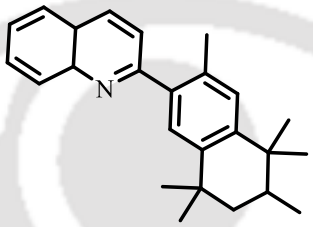
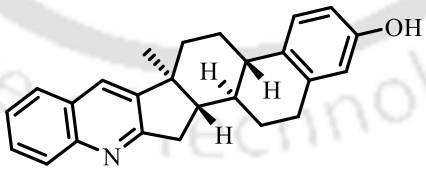
Using **GP-I** the title compound **4.3ag** was isolated as yellow solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:4, R_f = 0.50); (156 mg, 95%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.21 (d, J = 8.4 Hz, 1H), 8.17 (d, J = 8.4 Hz, 1H), 7.85 (d, J = 8.4), 7.77 – 7.70 (m, 2H), 7.63 (brs, 1H), 7.56 – 7.53 (m, 1H), 7.29 (s, 1H), 3.15 (t, J = 7.2 Hz, 2H), 1.97 (t, J = 6.0, 2H), 1.42 (s, 9H), 1.35 (s, 6H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 160.0, 153.7, 150.3, 148.2, 139.0, 136.5, 136.1, 129.9, 129.5, 127.6, 126.8, 126.3, 124.3, 121.7, 119.7, 44.0, 41.9, 35.0, 31.8, 29.8, 28.90. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{24}H_{28}N$ 330.2217; found 330.2226.

2-(3,5,5,6,8,8-hexamethyl-5,6,7,8-tetrahydronaphthalen-2-yl)-4a,8a-dihydroquinoline (4.3ah)



Using **GP-I** the title compound **4.3ah** was isolated as light yellow solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:4, R_f = 0.50); (162 mg, 94%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.20 (d, J = 8.4 Hz, 1H), 8.15 (d, J = 8.4 Hz, 1H), 7.86 (d, J = 6.6 Hz, 1H), 7.74 – 7.72 (m, 1H), 7.56 – 7.54 (m, 2H), 7.41 (s, 1H), 7.30 (s, 1H), 2.39 (s, 3H), 1.94 – 1.90 (m, 1H), 1.70 – 1.68 (m, 2H), 1.38 (s, 3H), 1.33 (s, 3H), 1.29 (s, 3H), 1.11 (s, 3H), 1.01 (d, J = 6.6 Hz, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 160.8, 148.0, 146.6, 142.5, 138.2, 136.1, 133.1, 129.8, 129.6, 128.0, 127.6, 126.8, 126.3, 122.5, 43.9, 37.7, 34.7, 34.3, 32.6, 32.2, 28.7, 25.1, 20.3, 17.0. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{25}H_{32}N$ 346.2530; found 346.2512.

(6bS,8aS,15aS,15bS)-8a-methyl-2,6b,7,8,8a,15,15a,15b-octahydro-1H naphtho[2',1':4,5]indeno[2,1-b]quinolin-4-ol (4.3ai)



Using **GP-I** the title compound **4.3ai** was isolated as white solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:20, R_f = 0.50); (108 mg, 61%). ^{1}H NMR (600 MHz, DMSO): δ 9.08 (s, 1H), 8.10 (s, 1H), 7.95 (d, J = 8.4 Hz, 1H), 7.86 (d, J = 9.6 Hz, 1H), 7.65 – 7.62 (m, 1H), 7.51 – 7.48 (m, 1H), 7.11 (d, J = 8.4 Hz, 1H), 6.55 – 6.53 (m, 1H), 6.48 (brs, 1H), 2.98 (dd, J = 15.6, 6.10 Hz, 1H), 2.86 – 2.69 (m, 3H), 2.46 – 2.44 (m, 1H), 2.38 – 2.28 (m, 2H), 2.00 – 1.97 (m, 1H), 1.85 – 1.78 (m, 1H), 1.77 – 1.67 (m, 2H), 1.63 – 1.56 (m, 1H), 1.48 – 1.42 (m, 1H), 1.00 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, DMSO): δ 174.2, 155.1, 146.7, 137.2, 135.0, 131.1, 130.4, 128.4, 127.9, 127.4, 126.0, 125.6, 115.1, 112.9, 54.2, 45.8, 43.9, 37.7, 33.7,

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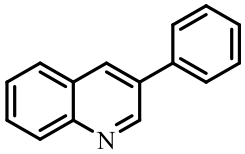
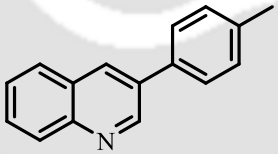
29.5, 29.1, 27.2, 26.1, 17.8. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{25}H_{26}NO$ 356.2006; found 356.1972.

3-phenylquinoline (4.16a) [27]



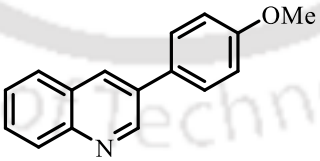
Using **GP-II** the title compound **4.16a** was isolated as light yellow solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:3, R_f = 0.50); (89 mg, 87%).^{1}H NMR (600 MHz, $CDCl_3$): δ 9.19 (s, 1H), 8.32 (s, 1H), 8.15 (d, J = 8.4 Hz, 1H), 7.89 (d, J = 7.8 Hz, 1H), 7.74 – 7.72 (m, 3H), 7.59 (t, J = 7.2 Hz, 1H), 7.54 (t, J = 7.2 Hz, 2H), 7.45 (t, J = 7.2 Hz, 1H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 150.1, 147.5, 138.1, 134.0, 133.4, 129.6, 129.4, 129.3, 128.3, 128.2, 128.2, 127.6, 127.2.

3-(*p*-tolyl)quinoline (4.16b)[27]



Using **GP-II** the title compound **4.16b** was isolated as white solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:3, R_f = 0.50); (88 mg, 80%).^{1}H NMR (600 MHz, $CDCl_3$): δ 9.18 (d, J = 2.4 Hz, 1H), 8.28 (d, J = 2.4 Hz, 1H), 8.14 (d, J = 9.0 Hz, 1H), 7.87 (d, J = 7.8 Hz, 1H), 7.73 – 7.70 (m, 1H), 7.62 (d, J = 8.4 Hz, 2H), 7.57 (t, J = 7.2 Hz, 1H), 7.34 (d, J = 7.8 Hz, 2H), 2.44 (s, 3H).^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 150.1, 147.3, 138. 2, 135. 1, 133.9, 133.0, 130.0, 129.4, 129.3, 128.2, 128.1, 127.4, 127.1, 21.3.

3-(4-methoxyphenyl)quinoline (4.16c)[27]



Using **GP-II** the title compound **4.16bc** was isolated as white solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:3, R_f = 0.50); (96 mg, 82%).^{1}H NMR (600 MHz, $CDCl_3$): δ 9.16 (d, J = 2.4 Hz, 1H), 8.25 – 8.24 (m, 1H), 8.13 (d, J = 9.6 Hz, 1H), 7.86 (d, J = 7.8 Hz, 1H), 7.71 – 7.69 (m, 1H), 7.67 – 7.65 (m, 2H), 7.58 – 7.55 (m, 1H), 7.07 – 7.05 (m, 2H), 3.88 (s, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 159.9, 150.0, 147.2, 133.6, 132.5, 129.4, 129.2, 128.6, 128.0, 127.1, 114.8, 55.5.

3-(4-fluorophenyl)quinoline (4.16d)[27]

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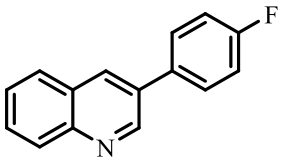
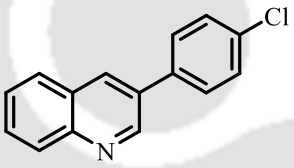


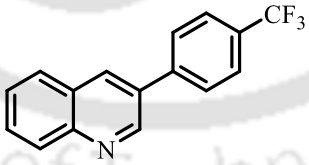
Using **GP-II** the title compound **4.16d** was isolated as light white solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:3, R_f = 0.50); (76 mg, 68%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 9.14 (s, 1H), 8.26 (s, 1H), 8.14 (d, J = 8.4 Hz, 1H), 7.88 (d, J = 7.8 Hz, 1H), 7.73 (t, J = 7.2 Hz, 1H), 7.69 – 7.67 (m, 2H), 7.59 (t, J = 7.5 Hz, 1H), 7.22 (t, J = 8.4 Hz, 2H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 163.9, 162.3, 149.9, 147.5, 134.2, 134.2, 133.2, 133.1, 129.6, 129.4, 129.3, 129.2, 128.10, 127.3, 116.4, 116.3. ^{19}F{^{1}H} NMR (565 MHz, $CDCl_3$): δ -114.10.

3-(4-chlorophenyl)quinoline (4.16e)[27]



Using **GP-II** the title compound **4.16e** was isolated as light white solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:3, R_f = 0.50); (89 mg, 78%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 9.14 (d, J = 2.4 Hz, 1H), 8.28 (d, J = 1.8 Hz, 1H), 8.15 (d, J = 8.0 Hz, 1H), 7.88 (d, J = 7.8 Hz, 1H), 7.75 – 7.72 (m, 1H), 7.64 (d, J = 8.4 Hz, 2H), 7.60 (d, J = 7.8 Hz, 1H), 7.49 (d, J = 8.4 Hz, 2H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 149.5, 147.4, 136.4, 134.6, 133.5, 132.8, 129.9, 129.6, 129.5, 129.2, 128.8, 128.15, 128.07, 127.4.

3-(4-(trifluoromethyl)phenyl)quinoline (4.16f)[62]



Using **GP-II** the title compound **4.16f** was isolated as light white solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:3, R_f = 0.50); (89 mg, 65%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.19 (d, J = 2.0 Hz, 1H), 8.33 (s, 1H), 8.19 (d, J = 8.5 Hz, 1H), 7.90 (d, J = 8.5 Hz, 1H), 7.82 – 7.74 (m, 5H), 7.62 – 7.59 (m, 1H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 149.4, 147.6, 141.4, 134.0, 132.4, 130.1, 129.3, 128.2, 127.8, 127.4, 126.2 (q, J = 3.8 Hz). ^{19}F{^{1}H} NMR (471 MHz, $CDCl_3$): δ -62.52.

3-(3-chlorophenyl)quinoline (4.16g) [27]

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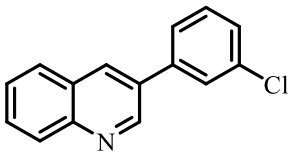
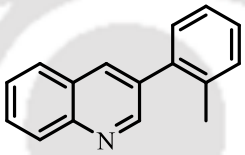


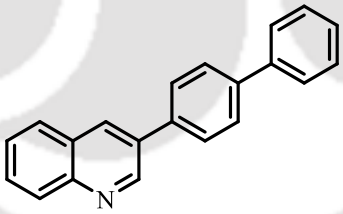
Using **GP-II** the title compound **4.16g** was isolated as white solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:3, R_f = 0.40); (88 mg, 73%).^{1}H NMR (600 MHz, $CDCl_3$): δ 9.14 (brs, 1H), 8.30 (s, 1H), 8.16 (d, J = 8.4 Hz, 1H), 7.89 (d, J = 7.8 Hz, 1H), 7.75 (t, J = 7.8 Hz, 1H), 7.70 – 7.69 (m, 1H), 7.62 – 7.58 (m, 2H), 7.46 (t, J = 7.8 Hz, 1H), 7.42 – 7.40 (m, 1H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 149.5, 147.5, 139.8, 135.29, 133.8, 132.7, 130.6, 130.0, 129.2, 129.2, 128.3, 128.2, 128.0, 127.7, 127.4, 125.7.

3-(*o*-tolyl)quinoline (4.16h) [27]



Using **GP-II** the title compound **4.16h** was isolated as white solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:3, R_f = 0.40); (57 mg, 52%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.93 (d, J = 2.4 Hz, 1H), 8.17 (d, J = 8.4 Hz, 1H), 8.08 (brs, 1H), 7.83 (d, J = 8.0 Hz, 1H), 7.74 – 7.70 (m, 1H), 7.58 – 7.55 (m, 1H), 7.33 – 7.30 (m, 4H), 2.32 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 151.5, 147.0, 138.1, 135.9, 135.4, 134.9, 130.7, 130.2, 129.5, 129.3, 128.3, 127.9, 127.8, 127.0, 126.3, 20.5.

3-([1,1'-biphenyl]-4-yl)quinoline (4.16i) [27]



Using **GP-II** the title compound **4.16i** was isolated as white solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:3, R_f = 0.40); (105 mg, 75%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 9.25 (d, J = 2.4 Hz, 1H), 8.37 (brs, 1H), 8.17 (d, J = 8.4 Hz, 1H), 7.91 (d, J = 7.8 Hz, 1H), 7.82 – 7.81(m, 2H), 7.78 – 7.73 (m, 2H), 7.74 – 7.33 (m, 1H), 7.68 (d, J = 7.2 Hz, 2H), 7.60 (t, J = 7.8 Hz, 1H), 7.51 – 7.48 (m, 2H), 7.41 – 7.39 (m, 1H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 149.9, 147.4, 141.16, 140.49, 136.81, 133.30, 129.63, 129.30, 129.05, 128.2, 128.1, 127.9, 127.8, 127.2.

3-(naphthalen-1-yl)quinoline (4.16j[27]

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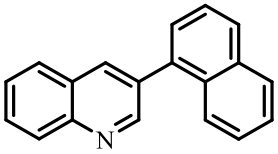
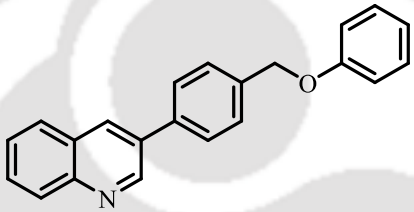


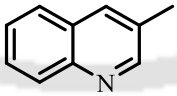
Using **GP-II** the title compound **4.16j** was isolated as white solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:3, R_f = 0.40); (71 mg, 56%).^{1}H NMR (600 MHz, $CDCl_3$): δ 9.08 (d, J = 2.4 Hz, 1H), 8.24 (d, J = 8.4 Hz, 1H), 8.21 (brs, 1H), 7.89 (t, J = 7.2 Hz, 2H), 7.82 (t, J = 7.8 Hz, 2H), 7.73 (t, J = 7.2 Hz, 1H), 7.57 – 7.52 (m, 2H), 7.49 – 7.46 (m, 2H), 7.42 – 7.40 (t, J = 7.5 Hz, 1H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 151.9, 147.2, 136.6, 136.3, 133.9, 133.9, 131.7, 129.8, 129.2, 128.7, 128.6, 128.1, 128.0, 127.9, 127.2, 126.8, 126.3, 126.2, 125.5, 125.4.

3-(4-(phenoxymethyl)phenyl)quinoline (4.16k)



Using **GP-II** the title compound **4.16k** was isolated as light white solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:4, R_f = 0.40); (118 mg, 78%).^{1}H NMR (500 MHz, $CDCl_3$): δ 9.16 (s, 1H), 8.25 (s, 1H), 8.12 (d, J = 8.0 Hz, 1H), 7.86 (d, J = 8.0 Hz, 1H), 7.70 (t, J = 7.5 Hz, 1H), 7.66 (d, J = 8.5 Hz, 2H), 7.57 (t, J = 8.0 Hz, 1H), 7.48 – 7.47 (m, 2H), 7.41 (t, J = 7.5 Hz, 2H), 7.36 – 7.34 (m, 1H), 7.13 (d, J = 8.5 Hz, 2H), 5.15 (s, 2H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 159.2, 150.0, 147.2, 136.9, 133.6, 132.6, 130. 129.4, 129.2, 128.8, 128.7, 128.3, 128.2, 128.0, 127.6, 127.1, 115.8, 70.3. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{22}H_{18}NO$ 312.1383; found 313.1386.

3-methylquinoline (4.16l)[63]



Using **GP-II** the title compound **4.16l** was isolated as light yellow oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:3, R_f = 0.40); (23 mg, 32%).^{1}H NMR (500 MHz, $CDCl_3$): δ 8.78 (brs, 1H), 8.07 (d, J = 8.5 Hz, 1H), 7.92 (s, 1H), 7.74 (d, J = 8.0 Hz, 1H), 7.66 – 7.63 (m, 1H), 7.51 (t, J = 8.0 Hz, 1H), 2.52 (s, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 152.6, 146.7, 134.8, 130.6, 129.3, 128.6, 128.3, 127.3, 126.70, 18.90.

3-propylquinoline (4.16m)[28]

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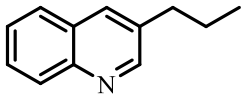
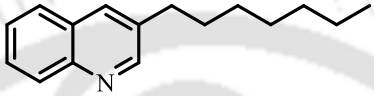


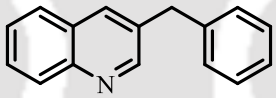
Using **GP-II** the title compound **4.16m** was isolated as light yellow oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:3, R_f = 0.40); (58 mg, 68%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.78 (d, J = 2.0 Hz, 1H), 8.07 (d, J = 8.4 Hz, 1H), 7.91 (s, 1H), 7.76 (d, J = 9.2 Hz, 1H), 7.67 – 7.63 (t, J = 8.4 Hz, 1H), 7.53 – 7.50 (m, 1H), 2.78 (t, J = 7.2 Hz, 2H), 1.78 – 1.73 (m, 2H), 1.00 (t, J = 7.6 Hz, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 152.3, 146.9, 135.3, 134.4, 129.2, 128.6, 128.3, 127.4, 126.6, 35.4, 24.4, 13.8.

3-heptylquinoline (4.16n)[29]



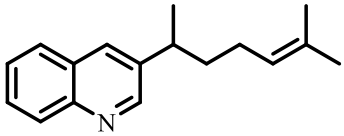
Using **GP-II** the title compound **4.16n** was isolated as light yellow oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:3, R_f = 0.40); (90 mg, 79%).^{1}H NMR (400 MHz, $CDCl_3$): δ 8.77 (d, J = 2.4 Hz, 1H), 8.08 (d, J = 8.8 Hz, 1H), 7.90 (s, 1H), 7.76 (d, J = 8.0 Hz, 1H), 7.66 – 7.62 (m, 1H), 7.53 – 7.51 (m, 1H), 2.78 (t, J = 7.6 Hz, 2H), 1.75 – 1.68 (m, 2H), 1.36 – 1.35 (m, 4H), 1.30 – 1.27 (m, 4H), 0.90 – 0.86 (m, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 152.2, 146.8, 135.5, 134.3, 129.2, 128.6, 128.3, 127.4, 126.6, 33.3, 31.9, 31.3, 29.3, 29.2, 22.8, 14.2.

3-benzylquinoline (4.16o)[27]



Using **GP-II** the title compound **4.16o** was isolated as light yellow oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:3, R_f = 0.40); (78.8 mg, 72%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.82 (d, J = 2.5 Hz, 1H), 8.09 (d, J = 8.5 Hz, 1H), 7.88 (s, 1H), 7.74 (d, J = 9.5 Hz, 1H), 7.66 (t, J = 7.7 Hz, 1H), 7.51 (t, J = 7.5 Hz, 1H), 7.33 – 7.31 (m, 2H), 7.26 – 7.22 (m, 3H), 4.17 (s, 2H).^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 152.2, 147.0, 139.8, 135.0, 133.9, 129.3, 129.2, 129.1, 129.0, 128.9, 128.2, 127.6, 126.8, 126.7, 39.3.

3-(6-methylhept-5-en-2-yl)quinoline (4.16p)[28]



Using **GP-II** the title compound **4.16p** was isolated as light yellow oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:3, R_f = 0.40); (87 mg, 73%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.79 (d, J = 2.4 Hz, 1H), 8.08 (d, J = 8.4 Hz, 1H), 7.90 (brs, 1H), 7.77 (d, J = 9.2 Hz, 1H), 7.67 – 7.63 (m, 1H), 7.59 – 7.54 (m, 1H), 5.11 – 5.07 (m, 1H), 2.96 – 2.91 (m, 1H),

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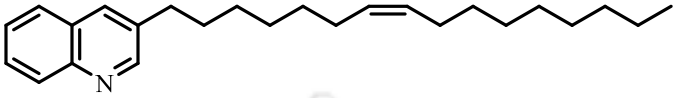
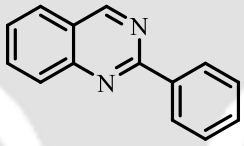
1.95 – 1.92 (m, 2H), 1.76 – 1.67 (m, 2H), 1.67 (s, 3H), 1.50 (s, 3H), 1.36 (d, J = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 151.5, 147.2, 140.2, 132.9, 132.1, 129.3, 128.7, 128.4, 127.6, 126.6, 124.1, 38.2, 37.2, 26.2, 25.8, 22.2, 17.8.

(*Z*)-3-(hexadec-7-en-1-yl)quinoline (4.16q)[29]



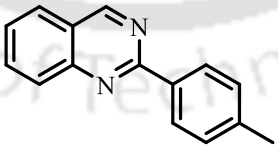
Using **GP-II** the title compound **4.16q** was isolated as light yellow oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:3, R_f = 0.40); (109 mg, 62%).^{1}H NMR (600 MHz, $CDCl_3$): δ 8.77 (s, 1H), 8.07 (d, J = 8.4 Hz, 1H), 7.91 (s, 1H), 7.76 (d, J = 7.8 Hz, 1H), 7.65 (t, J = 7.2 Hz, 1H), 7.51 (t, J = 7.2 Hz, 1H), 5.38 – 5.32 (m, 2H), 2.79 (t, J = 7.8 Hz, 2H), 2.04 – 1.98 (m, 4H), 1.74 – 1.69 (m, 2H), 1.36 – 1.25 (m, 18H), 0.88 – 0.86 (m, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 152.26, 146.89, 135.48, 134.22, 130.24, 129.77, 129.27, 128.62, 128.33, 127.42, 126.64, 33.33, 32.04, 31.24, 29.89, 29.77, 29.66, 29.46, 29.23, 29.20, 27.36, 27.28, 22.82, 14.25.

2-phenylquinazoline (4.24a)[53]



Using **GP-III** the title compound **4.24a** was isolated as solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:3, R_f = 0.40); (85 mg, 82%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 9.48 (s, 1H), 8.62 – 8.61 (m, 2H), 8.10 (d, J = 8.2 Hz, 1H), 7.94 – 7.90 (m, 2H), 7.64 – 7.61 (m, 1H), 7.56 – 7.51 (m, 3H).^{13}C NMR (151 MHz, $CDCl_3$): δ 161.2, 160.7, 150.9, 138.2, 134.3, 130.8, 128.8, 128.7, 127.4, 127.3, 123.8.

2-(4-methylphenyl)quinazoline (4.24b) [53]



Using **GP-III** the title compound **4.24b** was isolated as solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:3, R_f = 0.40); (90 mg, 82%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.44 (s, 1H), 8.52 (d, J = 9.6 Hz, 2H), 8.07 (d, J = 9.6 Hz, 1H), 7.90 – 7.87 (m, 2H), 7.58 (t, J = 8.8 Hz, 1H), 7.35 (d, J = 9.6 Hz, 2H), 2.45 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 161.3, 160.6, 150.9, 141.0, 135.4, 134.2, 129.6, 128.7, 128.6, 127.3, 127.2, 123.6, 21.7.

2-(4-methoxyphenyl)quinazoline (4.24c) [53]

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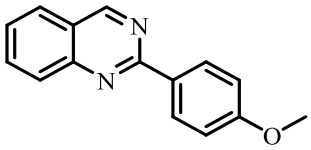
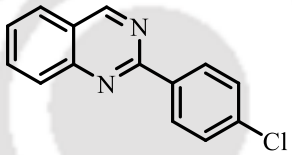


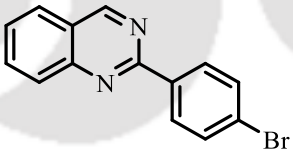
Using **GP-III** the title compound **4.24c** was isolated as solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:3, R_f = 0.40); (108mg, 90%). yield (0.68 g). ^{1}H NMR (600 MHz, $CDCl_3$): δ 9.42 (s, 1H), 8.58 (d, J = 8.8 Hz, 2H), 8.04 (d, J = 7.8 Hz, 1H), 7.90 – 7.87 (m, 2H), 7.57 (t, J = 7.2 Hz, 1H), 7.05 (d, J = 8.8 Hz, 2H), 3.90 (s, 3H).^{13}C NMR (151 MHz, $CDCl_3$): δ 162.0, 161.0, 160.5, 151.0, 134.2, 130.9, 130.3, 128.6, 127.3, 126.9, 123.5, 114.1, 55.5.

2-(4-chlorophenyl)quinazoline (4.24d) [53]



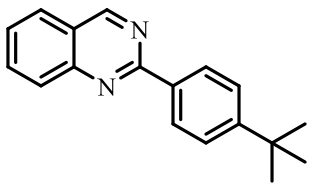
Using **GP-III** the title compound **4.24d** was isolated as yellow solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:3, R_f = 0.40); (109 mg, 62%).^{1}H NMR (500 MHz, $CDCl_3$): δ 9.46 (s, 1H), 8.58 (d, J = 8.5 Hz, 2H), 8.08 (d, J = 8.5 Hz, 1H), 7.95 – 7.91 (m, 2H), 7.64 (t, J = 7.5 Hz, 1H), 7.51 (d, J = 8.5 Hz, 2H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 160.7, 160.2, 150.9, 137.0, 136.7, 134.4, 130.1, 129.0, 128.8, 127.6, 127.3, 123.8.

2-(4-bromophenyl)quinazoline (4.24e)[53]



Using **GP-III** the title compound **4.24e** was isolated as yellow solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:3, R_f = 0.40); (109 mg, 62%).^{1}H NMR (500 MHz, $CDCl_3$): δ 9.45 (s, 1H), 8.50 (d, J = 8.5 Hz, 2H), 8.08 (d, J = 8.5 Hz, 1H), 7.94 – 7.90 (m, 2H), 7.67 – 7.62 (m, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 160.7, 160.3, 150.9, 137.1, 134.4, 132.0, 130.3, 128.8, 127.7, 127.3, 125.6, 123.8.

2-(4-(tert-butyl)phenyl)quinazoline (4.24f)[64]



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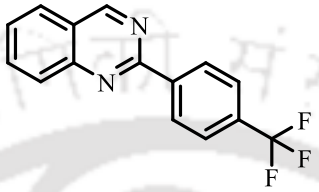
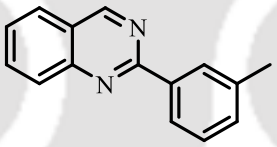
Using **GP-III** the title compound **4.24f** was isolated as white solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:3, R_f = 0.40); (109 mg, 83%).^{1}H NMR (500 MHz, $CDCl_3$): δ 9.45 (s, 1H), 8.54 (d, J = 8.0 Hz, 2H), 8.08 (d, J = 8.5 Hz, 1H), 7.92 – 7.89 (m, 2H), 7.61 – 7.55 (m, 3H), 1.39 (s, 9H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 161.4, 160.6, 154.1, 151.0, 135.5, 134.1, 128.8, 128.5, 127.3, 127.2, 125.8, 123.7, 35.0, 31.4.

2-(4-(trifluoromethyl)phenyl)quinazoline (4.24g)[62]



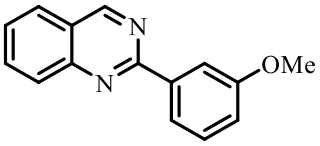
Using **GP-III** the title compound **4.24g** was isolated as white solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:3, R_f = 0.40); (107 mg, 78%).^{1}H NMR (600 MHz, $CDCl_3$): δ 9.50 (s, 1H), 8.75 (d, J = 8.4 Hz, 2H), 8.12 (d, J = 8.4 Hz, 1H), 7.98 – 7.94 (m, 2H), 7.79 (d, J = 8.4 Hz, 2H), 7.67 (t, J = 7.4 Hz, 1H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 160.81, 159.81, 150.84, 141.47, 134.56, 132.40, 132.19, 128.99, 128.94, 128.04, 127.34, 125.68 (q, J = 3.7 Hz), 124.01. ^{19}F NMR (377 MHz, $CDCl_3$): δ -62.68.

2-(m-tolyl)quinazoline (4.24h)[53]



Using **GP-III** the title compound **4.24h** was isolated as white solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:4, R_f = 0.50); (92 mg, 83%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.45 (s, 1H), 8.43 – 8.41 (m, 2H), 8.10 – 8.07 (m, 1H), 7.91 – 7.86 (m, 2H), 7.60 – 7.56 (m, 1H), 7.44 (t, J = 8.0 Hz, 1H), 7.33 (d, J = 8.0 Hz, 1H), 2.49 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 161.3, 160.5, 150.8, 138.4, 138.1, 134.2, 131.5, 129.2, 128.7, 127.3, 127.2, 125.9, 123.7, 21.6.

2-(3-methoxyphenyl)quinazoline (4.24i)[37]



Using **GP-III** the title compound **4.24i** was isolated as light yellow solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:4, R_f = 0.40); (100 mg, 85%).^{1}H

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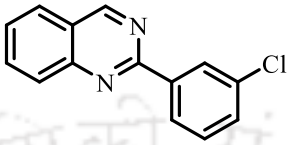
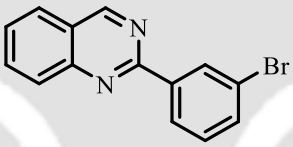
NMR (600 MHz, $CDCl_3$): δ 9.46 (s, 1H), 8.23 (d, J = 7.2 Hz, 1H), 8.19 (s, 1H), 8.09 (d, J = 8.4 Hz, 1H), 7.93 – 7.89 (m, 2H), 7.61 (t, J = 7.8 Hz, 1H), 7.45 (t, J = 7.8 Hz, 1H), 7.08 – 7.06 (m, 1H), 3.95 (s, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 161.0, 160.6, 160.2, 150.9, 139.6, 134.2, 129.8, 128.8, 127.4, 127.2, 123.8, 121.3, 117.4, 113.2, 55.6.

3-(3-chlorophenyl)isoquinoline (4.24j)[37]



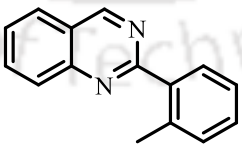
Using **GP-III** the title compound **4.24j** was isolated as white solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:4, R_f = 0.50); (962 mg, 80%). ^1H NMR (500 MHz, $CDCl_3$): δ 9.47 (s, 1H), 8.64 (s, 1H), 8.52 – 8.51 (m, 1H), 8.10 (d, J = 8.5 Hz, 1H), 7.96 – 7.95 (m, 2H), 7.65 (t, J = 7.0 Hz, 1H), 7.48 – 7.46 (m, 2H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 160.7, 159.9, 150.8, 140.0, 134.9, 134.5, 133.4, 132.1, 130.7, 130.6, 130.4, 130.0, 128.8, 128.8, 127.8, 127.3, 126.8, 123.9.

2-(3-bromophenyl)quinazoline (4.24k)[53]



Using **GP-III** the title compound **4.24k** was isolated as yellow solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:4, R_f = 0.50); (107 mg, 76%). ^1H NMR (600 MHz, $CDCl_3$): δ 9.46 (s, 1H), 8.79 (t, J = 1.8 Hz, 1H), 8.56 (dt, J = 1.2, 7.8 Hz, 1H), 8.09 (d, J = 6.0 Hz, 1H), 7.94 – 7.91 (m, 2H), 7.65 – 7.62 (m, 2H), 7.40 (t, J = 7.8 Hz, 1H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 160.7, 159.7, 150.8, 140.2, 134.5, 133.6, 131.7, 130.3, 128.8, 127.8, 127.3, 127.2, 123.9, 123.1.

2-(o-tolyl)quinazoline (4.24l)[53]



Using **GP-III** the title compound **4.24l** was isolated as white solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:4, R_f = 0.40); (62 mg, 56%).^1H NMR (600 MHz, $CDCl_3$): δ 9.45 (s, 1H), 8.44 – 8.40 (m, 2H), 8.09 (d, J = 8.5 Hz, 1H), 7.89 (t, J = 9.2 Hz, 2H), 7.59 (t, J = 7.5 Hz, 1H), 7.44 (s, 1H), 7.33 (d, J = 7.4 Hz, 1H), 2.49 (s, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 161.3, 160.6, 150.4, 138.4, 138.1, 134.2, 131.5, 129.2, 128.7, 128.7, 127.3, 127.2, 125.9, 123.7, 21.7.

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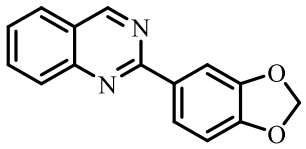
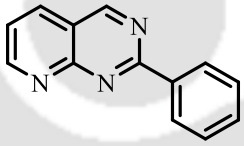
2-(benzo[*d*][1,3]dioxol-5-yl)quinazoline (4.24m)[29]



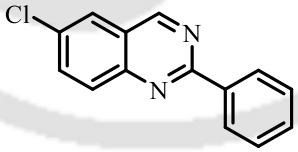
Using **GP-III** the title compound **4.24m** was isolated as white solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:5, R_f = 0.40); (95 mg, 76%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.40 (s, 1H), 8.23 (dd, J = 8.4, 1.8 Hz, 1H), 8.12 (d, J = 1.8 Hz, 1H), 8.03 (d, J = 8.4 Hz, 1H), 7.90 – 7.87 (m, 2H), 7.59 – 7.57 (m, 1H), 6.96 (d, J = 8.4 Hz, 1H), 6.05 (s, 2H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 160.7, 160.5, 150.9, 150.1, 148.4, 134.2, 132.7, 128.6, 127.3, 127.1, 123.7, 123.6, 108.9, 108.5, 101.6.

2-phenylpyrido[2,3-d]pyrimidine (4.24n)[65]



Using **GP-III** the title compound **4.24n** was isolated as white solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:10, R_f = 0.40); (44 mg, 42%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 9.54 (s, 1H), 9.29 – 9.28 (m, 1H), 8.76 – 8.74 (m, 2H), 8.33 – 8.31 (m, 1H), 7.59 – 7.57 (m, 1H), 7.56 – 7.55 (d, J = 6.7 Hz, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 164.7, 162.0, 159.0, 158.4, 137.3, 136.5, 131.6, 129.4, 128.8, 123.0, 118.4.

6-chloro-2-phenylquinazoline (4.24o) [53]



Using **GP-III** the title compound **4.24o** was isolated as white solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:4, R_f = 0.40); (100 mg, 83%).^{1}H NMR (600 MHz, $CDCl_3$): δ 9.41 (s, 1H), 8.61– 8.59 (m, 2H), 8.04 (d, J = 12.0 Hz, 1H), 7.92 (d, J = 1.8 Hz, 1H), 7.85– 7.83 (m, 1H), 7.56 – 7.51 (m, 3H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 161.45, 159.68, 149.40, 137.73, 135.27, 132.95, 131.03, 130.54, 128.85, 128.72, 125.98, 124.13.

6-bromo-2-phenylquinazoline (4.24p) [66]

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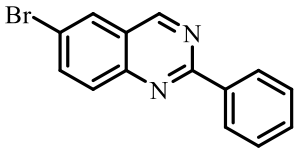
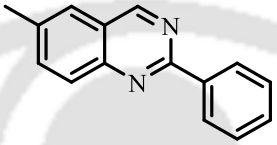


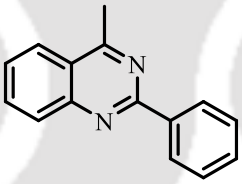
Using **GP-III** the title compound **4.24p** was isolated as white solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:4, R_f = 0.40); (114 mg, 85%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.40 (s, 1H), 8.62 – 8.59 (m, 2H), 8.10 – 8.09 (m, 1H), 7.97 (d, J = 2.0 Hz, 2H), 7.55 – 7.53 (m, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 161.5, 159.6, 149.6, 137.8, 137.8, 131.1, 130.6, 129.4, 128.9, 128.8, 124.7, 120.9.

6-methyl-2-phenylquinazoline (4.24q) [37]



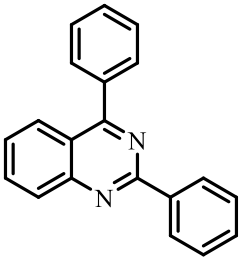
Using **GP-III** the title compound (**4.24q)** was isolated as white solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:4, R_f = 0.40); (80 mg, 72%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.38 (s, 1H), 8.60 (d, J = 7.8 Hz, 2H), 7.99 (d, J = 8.4 Hz, 1H), 7.73 (d, J = 8.4 Hz, 1H), 7.68 (s, 1H), 7.55 – 7.48 (m, 3H), 2.57 (s, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 160.6, 159.9, 149.5, 138.3, 137.6, 136.5, 130.5, 128.7, 128.6, 128.4, 125.9, 123.7, 21.8.

4-methyl-2-phenylquinazoline 4.24r [29]



Using **GP-III** the title compound **4.24r** was isolated as white solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:4, R_f = 0.40); (75 mg, 68%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.62 (d, J = 7.0 Hz, 2H), 8.11 – 8.07 (m, 2H), 7.87 (t, J = 8.5 Hz, 1H), 7.59 (t, J = 8.0 Hz, 1H), 7.54 – 7.48 (m, 3H), 3.03 (s, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 168.4, 160.4, 150.6, 138.5 133.7, 130.5, 129.4, 128.7, 127.0, 125.1, 123.2, 22.2.

2,4-diphenylquinazoline (4.24s) [67]



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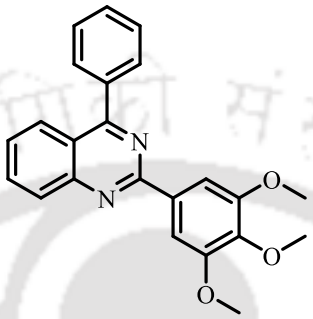
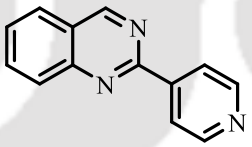
Using **GP-III** the title compound **4.24s** was isolated as white solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:4, R_f = 0.40); (92 mg, 65%).^{1}H NMR (600 MHz, $CDCl_3$): δ 8.70 (d, J = 7.2 Hz, 2H), 8.17 – 8.13 (m, 2H), 7.90 – 7.88 (m, 3H), 7.61 – 7.60 (m, 3H), 7.57 – 7.50 (m, 4H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 168.5, 160.4, 152.2, 138.4, 137.8, 133.7, 130.6, 130.3, 130.1, 129.3, 128.8, 128.7, 127.2, 127.1, 121.85.9

4-phenyl-2-(3,4,5-trimethoxyphenyl)quinazoline (4.24s)[67]



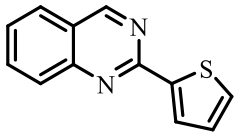
Using **GP-III** the title compound **4.24t** was isolated as light yellow solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:4, R_f = 0.40); (108 mg, 65%).^{1}H NMR (500 MHz, $CDCl_3$): δ 8.15 (d, J = 9.0 Hz, 1H), 8.11 (d, J = 8.2 Hz, 1H), 8.00 (s, 2H), 7.91 – 7.87 (m, 3H), 7.62 – 7.60 (m, 3H), 7.56 – 7.53 (m, 1H), 4.03 (s, 6H), 3.94 (s, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 168.39, 159.9, 153.5, 152.1, 140.6, 137.8, 133.9, 133.7, 130.33, 130.0, 129.2, 128.7, 127.2, 127.1, 121.7, 106.0, 61.1, 56.5.

2-(pyridin-4-yl)quinazoline (4.24u)[53]



Using **GP-III** the title compound **4.24u** was isolated as off white solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:5, R_f = 0.40); (62 mg, 65%). $^{13}C\{^1H\}$NMR (600 MHz, $CDCl_3$): δ 9.52 (s, 1H), 8.82 – 8.81 (m, 2H), 8.47– 8.46 (m, 2H), 8.14 (d, J = 8.4 Hz, 1H), 8.00 – 7.96 (m, 2H), 7.72– 7.69 (m, 1H).^{13}C NMR (151 MHz, $CDCl_3$): δ 160.9, 159.1, 150.7, 150.7, 145.4, 134.7, 129.0, 128.5, 127.4, 124.3, 122.5.

2-(thiophen-2-yl)quinazoline (4.24v)[37]



Using **GP-III** the title compound **4.24v** was isolated as light yellow solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:5, R_f = 0.40); (60 mg, 57%).^{1}H NMR (500 MHz, $CDCl_3$): δ 9.36 (s, 1H), 8.15 (d, J = 3.0 Hz, 1H), 8.02 (d, J = 9.0 Hz, 1H), 7.90 – 7.88

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(m, 2H), 7.58 (t, *J* = 7.5 Hz, 1H), 7.52 (d, *J* = 5.0 Hz, 1H), 7.20 (d, *J* = 4.0 Hz, 1H). $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$): *δ* 160.7, 158.0, 150.8, 144.0, 134.5, 130.1, 129.4, 128.5, 128.4, 127.4, 127.2, 123.6.

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Chapter 5

Chromium-catalysed selective synthesis of 3-oxo and 3-amino quinolines using β-O-4' lignin models or α-amino ketones

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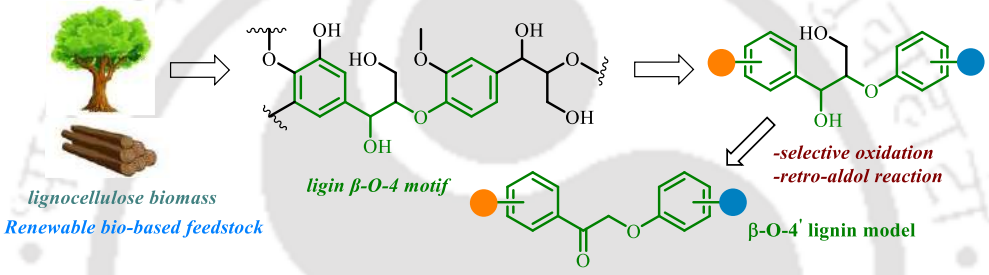
5.1. Introduction

Lignin is a major component of lignocellulosic biomass (approx. 30%), serving as a renewable resource, provided by nature, for the manufacturing of aromatic compounds.[1, 2] Thus, nowadays lignin molecules are considered as an alternative feedstock for the synthesis of valuable compounds. Structurally, lignin is comprised of *p*-hydroxyphenyl, guaiacyl, and syringyl units joined through a variety of different ether and C-C linkage. The *β*-O-4′ linkage is the most frequent unit among all. In this context, phenoxy acetophenone derivatives are extensively utilized lignin model molecules. Considerable efforts have been made for the degradation of the lignin model such as phenoxy acetophenone derivatives to afford various valuable aromatics.[3, 4] Direct production of heterocyclic aromatic compounds from lignin *β*-O-4′ models remains a great challenge due to the incompatible catalysis for aryl ether bond cleavage and heterocyclic ring formation.



Scheme 5.1. *β*-O-4′ lignin model

Recently, *Zhang* and *co-workers* developed oxidative annulation between 2-amino-azaarenes with lignin model 2-phenoxyacetophenones to afford valuable 3-phenoxy imidazo heterocycles.[3, 4] Very recently, the same group has reported an iridium-catalyzed annulation reaction between 2-aminobenzylalcohol and phenoxy acetophenone to afford 3-oxo quinolines. The benzoquinone was used as a sacrificial hydrogen acceptor and reaction was performed under inert reaction conditions.[5] Owing to the high price of iridium, the development of alternative cost-effective metal catalyst with less waste and environmentally benign condition is highly desired. Notably, 3-position oxygen atom containing quinoline have a potential application value in the field of medicine and materials (Figure 5.1).[6-8]

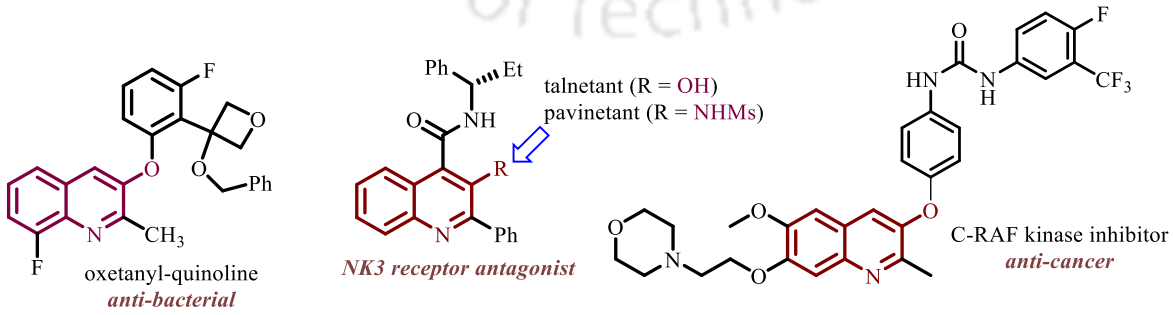


Figure 5.1. Selected bioactive 3-oxouinoline derivatives

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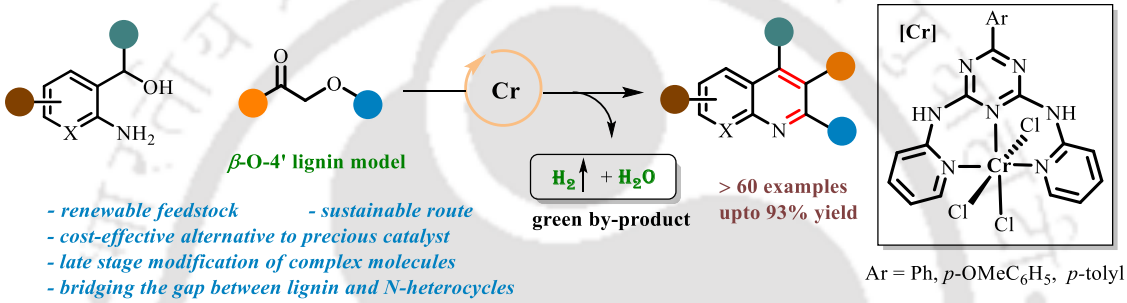
5.2. Present work

Herein, the scope of the synthesized chromium complexes **3.4a-b** and **3.5** has been explored towards the synthesis of 3-oxoquinoline derivatives *via* dehydrogenative coupling of 2-aminobenzyal alcohol and phenoxyacetophenone as *β*-O-4′ lignin model. The reaction provides an efficient route for the construction of 3-oxo substituted quinolines *via* acceptorless dehydrogenative coupling (ADC) reaction without the need of any external chemical oxidant or additives. Interestingly, this catalytic route gives a unique opportunity to provide hydroxyl motif at the C3-position of the heteroaromatic moiety which otherwise can be achieved by hydroxyl group incorporated at the C3 position *via N*-oxide using aryldiazonium salt.[9] Notably, the synthetic applicability of the present protocol is further extended toward the synthesis of 3-aminoquinoline derivatives.



Scheme 5.2. Chromium catalyzed synthesis of 3-oxo quinoline derivatives

5.3. Results and discussion

5.3.1. Optimization of reaction condition for 3-oxo quinoline

The above hypothesis was initially executed by the reaction of 2-aminobenzyl alcohol (**4.4a**, 1 equiv.) and 2-phenoxyacetophenone (**5.1a**, 1 equiv.) in the presence of **3.4a** (5 mol %) in toluene at 120 °C for 14 h (Table 1). Gratifyingly, the desired 3-phenoxy-2-phenylquinoline **5.2a** was obtained in 79% yield (entry 1). Furthermore, the yield of **5.2a** was enhanced up to 86% when **3.4b** complex was used, suggesting **3.4b** showed better activity compared to **3.4a** (entry 2). The yield of **5.2a** was very similar to chromium(III) complex **3.4a** (entry 1) and chromium(II) complex **3.5** (entry 3). The reaction is also effective with a mixture of **3.3a** (5 mol%) or **3.3b** (5 mol%) with **$CrCl_3$•3THF** (5 mol%) (**5.2a**, 68% and 71% respectively, entry 4 and 5). When the reaction temperature was decreased to 100 °C a decrease in the yield of **5.2a** to 35% has been observed (entry 7), and further decreases drastically to 11% at 90 °C (entry 8), highlighting the influence of the temperature on the reaction. When catalyst loading was decreased to 2 mol %, the yield of **5.2a** was only 43% (entry 10), and base was reduced to 30 mol%, the yield of **5.2a** was 64% (entry 9). Control experiments indicate that both catalyst and base are essential for the cyclization reaction (entries 9-10). In absence of **3.4b**, 13% of product **5.2a** was obtained, which may be due to the possible base-mediated partial dehydrogenation of 2-aminobenzyl alcohol to corresponding 2-aminobenzyl aldehyde under air, followed by aldol condensation with **5.1a** and annulation.

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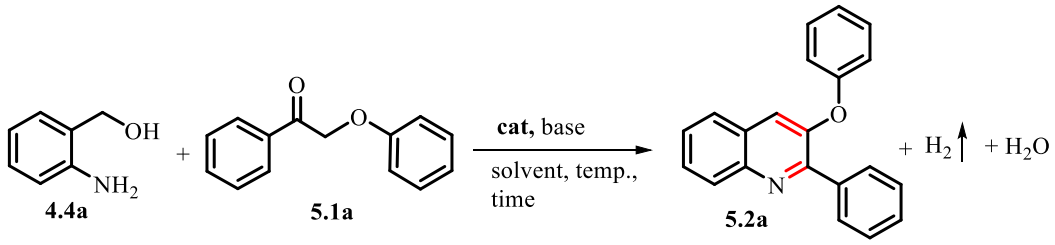
Table 5.1. Optimization studies[a]



Entry	**cat.** (mol%)	KO^{t}Bu (mol%)	temp (°C)	time (h)	yield (%)
1	**3.4a** (5)	40	120	14	79%
2	**3.4b** (5)	40	120	14	86%
3	**3.5** (5)	40	120	14	75%
4	**CrCl$_3$•3THF** (5) + **3.3a** (5)	40	120	14	68%
5	**CrCl$_3$•3THF** (5) + **3.3b** (5)	40	120	14	71%
6	**3.4b** (5)	40	110	14	60%
7	**3.4b** (5)	40	100	14	35%
8	**3.4b** (5)	40	90	14	11%
9	**3.4b** (5)	30	120	14	64%
10	**3.4b** (2)	40	120	14	43%
11	**CrCl$_3$•3THF** (5)	40	120	14	20%
12	**CrCl$_3$•6H$_2$O** (5)	40	120	14	15%
13	**3.4b** (5)	40	120	8	53%
14	–	40	120	14	13%, 0%[b]
15	**3.4b** (5)	–	120	14	n.d.
16	**3.4b** (5)	40	120	14	46%[c]

Reaction conditions: [a] **4.4a** (1 mmol), **5.1a** (1 mmol), KO^{t}Bu (x mol%), toluene (2 mL) were heated in a closed 50 mL reaction tube for given time. Isolated yield. **3.4b** is [6-(4-methoxyphenyl)-N^2, N^4-di(pyridin-2-yl)-1,3,5-triazine-2,4-diamine]. [b] Under air-free conditions. [c] In xylene at 150 °C.

In order to comprehend the role of air on the dehydrogenation of 2-aminobenzyl alcohol, I have performed the same reaction in the absence of air and subsequently compared the outcome with aerobic conditions as outlined in entry 14. The above findings suggest that the synergistic effect of air and base is responsible for this conversion (entries 9-10, entries 14-15).[10]

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5.3.2. Substrates scope for synthesis of 3-oxo quinoline

With the optimized reaction conditions in hand, next I investigated the substrate scope of this reaction by employing varieties of phenoxyacetophenone derivative **5.1a**-**5.1x** with 2-aminobenzyl alcohol **4.4a** as the standard substrate (Table 5.2). The phenoxy acetophenones, containing both electron-donating (e.g., −Et, −OMe) and electron-withdrawing (e.g., −F, −Br, −I, and −CN) groups as substituents on the *O*-terminal benzene ring were reacted well with **4.4a** under the standard reaction condition, result the desired 2-phenyl-3-aryloxy quinoline derivatives **5.2a**-**5.2i** in 62−86% yield. The phenoxy acetophenone with electron-donating substituents such as 4-Et (**5.1b**), 4-OMe (**5.1c**) gave higher yields for the corresponding products compared to the electron-withdrawing substituent containing phenoxyacetophenone like 4-F (**5.1f**), 4-CN (**5.1i**). The structures of **5.2a**, **5.2f** and **5.2h** were unambiguously confirmed by the SC-XRD. It is noteworthy that sulfur containing functionality such as thioether remain compatible under the reductive conditions (**5.2e**, 82%). The imidazole bearing phenoxy acetophenone **5.1j** also well suited in the reaction condition giving the desired product **5.2j** efficiently in 81% yield. Additionally, *meta*- and *ortho*- substituted substrate with functional group such as $–CF_3$, −OMe also showed good reactivity. The reaction involving poly-substituted phenoxy acetophenone also reacted efficiently leading to the formation of the desired product **5.2o**-**5.2p** effectively with excellent yield (92% and 95% respectively). Interestingly, pyrene moiety bearing substrate **5.1q** successfully participated in the reaction to provide the corresponding product **5.2q** in 85% yield. Surprisingly, when naturally occurring phenol derivatives like sesamol, thymol-derived phenoxyacetophenone were tested under the standard reaction conditions with **4.4a**, also lead to the formation of expected products **5.2r**, **5.2s** respectively.

Later, I have explored the reaction with a series of phenoxy acetophenones bearing functionalities different positions (*ortho*, *meta*, and *para*) such as *p*-OMe (**5.1aa**), *p*-Br (**5.1ab**), *p*-Ph (**5.1ac**), *m*-OMe (**5.1ad**), *m*-Cl (**5.1ae**), and *p*,*m*- 2OMe (**5.1af**) on the *C*-terminal benzene ring; all of them afforded the corresponding 3-oxo quinolines **5.2aa**-**5.2af** in good to excellent yields (73−83%). The reaction was further screened with phenoxy acetophenones derivatives having substituents on both *O*- and *C*- terminal benzene rings, they were reacted well with **4.4a** to give the 3-oxo quinolines **5.2ag**-**5.2aj** in 82-87% yields. In addition to the phenoxyacetophenone derivatives, the reaction was compatible with alkoxyacetophenone **5.1u** and aliphatic ketone **5.1ak** resulting the formation of **5.2t** and **5.2ak**-**5.2al**, respectively. Given the significance of the 3-oxoquinoline motif in various biologically and pharmaceutically relevant complex molecular settings,[6-8] substrates containing naturally occurring synthetic fragrance tonalide **5.1am**, musk fragrance celestolide **5.1an**, and nonsteroidal anti-inflammatory drug naproxen **5.1u** and ibuprofen **5.1v** were efficiently transformed into functionalized quinolines **5.2am**, **5.2an**, **5.2u**, **5.2v** respectively.

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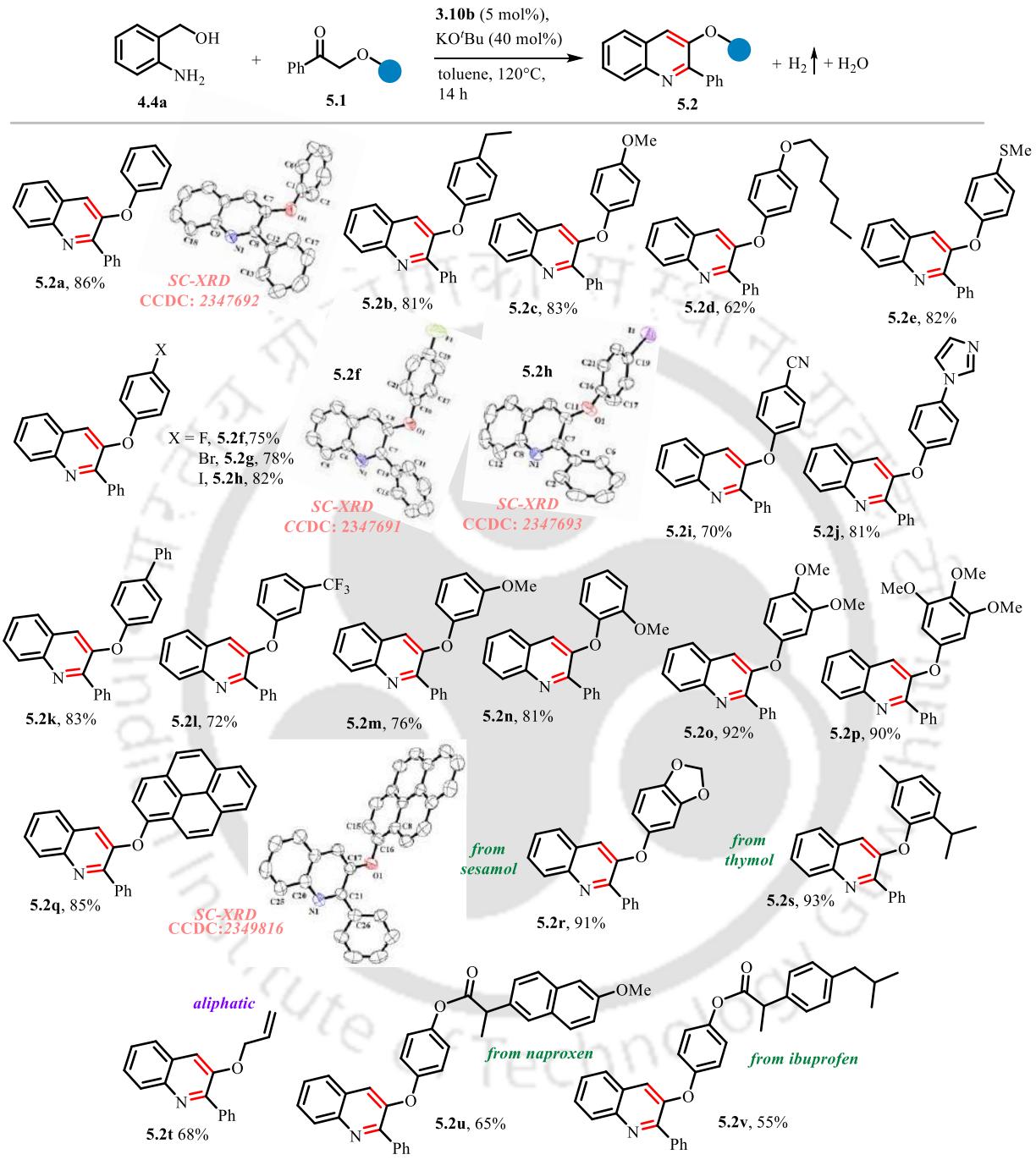
Table 5.2. Substrate scope of *α*-oxy ketones[a]



Reaction condition: [a] **4.4a** (1 mmol), **5.1** (1 mmol), **3.4b** (5 mol%), KO^{t}Bu (40 mol%) and toluene (2 mL) were heated at 120 °C in a closed reaction tube for 14 h, isolated yield.

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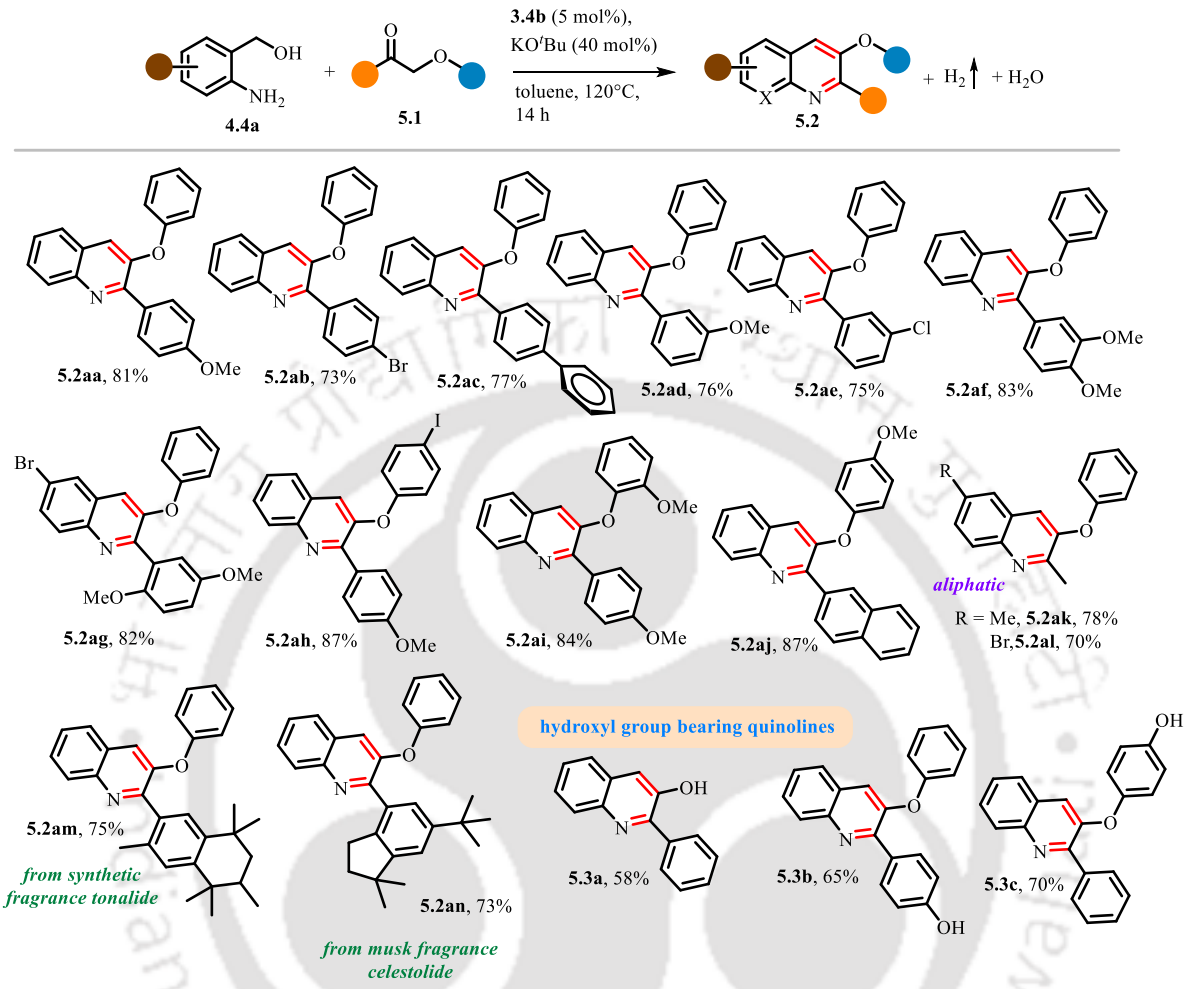
Table 5.3. Substrate scope of α-oxy ketone and of 2-aminoaryl alcohol[a]



Reaction condition: [a] **4.4a** (1 mmol), **5.1** (1 mmol), **3.4b** (5 mol%), KO^{t}Bu (40 mol%) and toluene (2 mL) were heated at 120 °C in a closed reaction tube for 14 h, isolated yield.

Notably, the protocol is applicable for even challenging *α*-hydroxyacetophenone **5.1w** as substrate, provided **5.3a** with excellent selectivity. Furthermore, hydroxyl group bearing phenoxyacetophenone are also amenable to give **5.3b** and **5.3c**, clearly showcasing the effectiveness of the chromium catalyst. The scope of the reaction was further expanded to a series of 2-aminoaryl alcohol **4.4b-4.4g** and **5.4a-5.4e** while maintaining 2-phenoxy acetophenone **5.1a** as the standard substrate (Table 5.4). Interestingly, substrates having substituents near the cyclization site of 2-aminobenzyl alcohol such as C3 substituted 2-aminobenzyl alcohol **4.4g** and a C6 substituted 2-aminobenzyl alcohol **5.4b** reacted efficiently with **5.1a** resulting in the formation of the desired 3-oxo quinoline **5.5e** and **5.5f** respectively. Notably, polysubstituted quinoline **5.5g-5.5j** was gladly obtained by varying the substituent at the benzyl position in the 2-aminobenzyl alcohol moiety. Interestingly, aminopyridine-3-methanol **4.4b** was efficiently involved in the reaction to provide the desired product **5.5k** in 92% yield. Additionally, structures of **5.5e** and **5.5k** were confirmed by SC-XRD.

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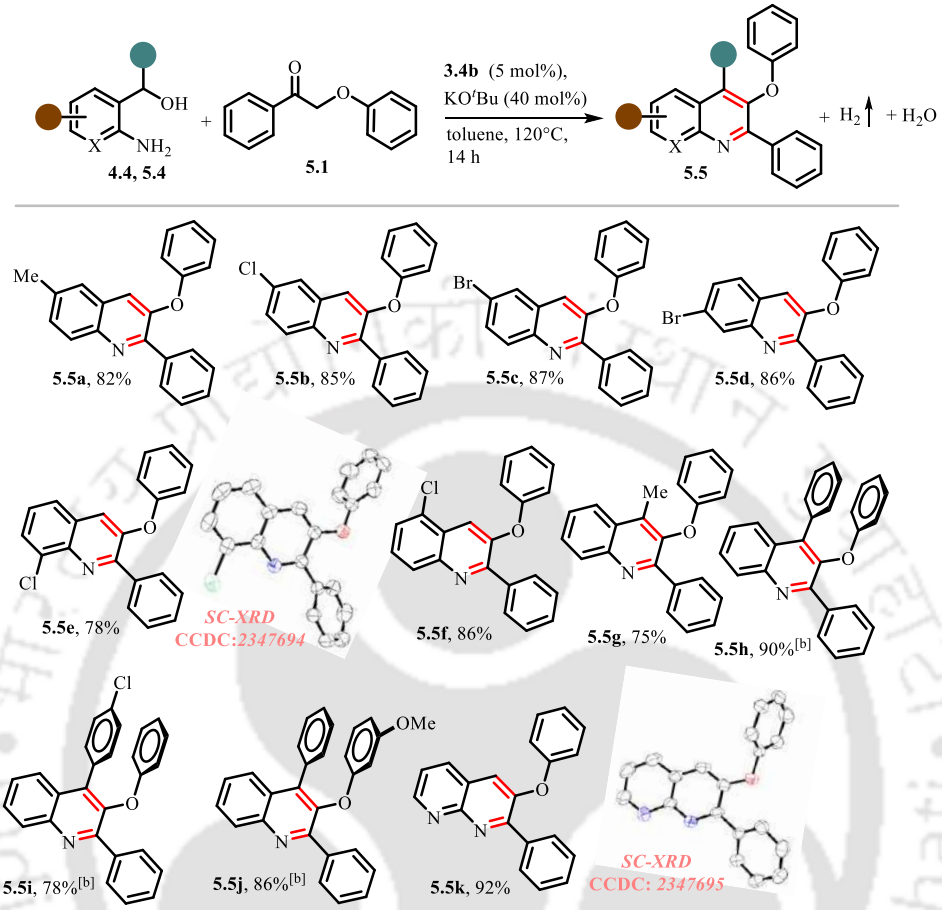
Table 5.4. Substrate Scope of 2-aminoaryl alcohols[a]



Reaction condition: [a] 2-aminoaryl alcohol (1 mmol), **5.1** (1 mmol), **3.4b** (5 mol%), KO^{t}Bu (40 mol%) and toluene (2 mL) were heated at 120 °C in a closed reaction tube for 14 h, isolated yield. [b] with reaction time 24 h.

5.3.3. Substrates scope for synthesis of 3-amino quinoline

Fortunately, the current protocol was not limited to *α*-oxy ketones. When I tested the reaction with α-amino ketones in place of *α*-oxy ketones under the standard reaction condition, desired 3-amino quinolines were formed effectively in excellent yield (**5.7a-5.7e)** including functional groups such as morpholine **5.7a**, pyrazole **5.7d**, imidazole **5.7f**. It is noteworthy to mention that product **5.7e** showed good inhibitory activity against citrus green mold, wheat blight, wheat fusarium, and wheat stand blight and is used as a fungicide.[11] Thus, this straightforward cost-effective method offers a new approach for the screening of potent bioactive molecules from a wealth of raw materials.

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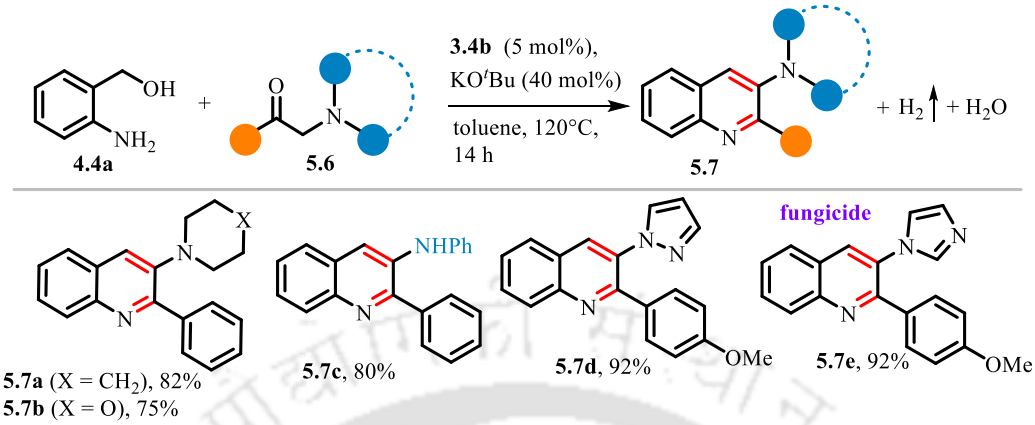
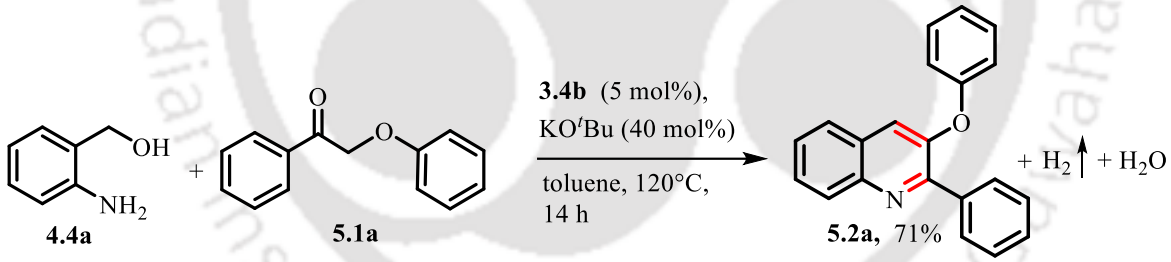
Table 5.5. Substrate Scope of α-aminoketone[a]



Reaction condition: [a] **4.4a** (1 mmol), **5.6** (1 mmol), **3.4b** (5 mol%), KO^{t}Bu (40 mol%) and toluene (2 mL) were heated at 120 °C in a closed reaction tube for 14 h, isolated yield.

5.3.4. Gram Scale synthesis

In order to highlight the practical utility of the present protocol, gram scale reactions were performed for the synthesis of 3-phenoxy-2-phenylquinoline **5.2a**, as shown in Scheme 5.3. The compound **5.2a** was isolated in 71% yield using 1.23 g of 2-aminobenzylacohol (**4.4a**) under the standard condition.



Scheme 5.3. Gram-scale reaction

5.3.5. Post synthetic modification

The usefulness of the 3-oxo quinolines was further explored by using them in various post synthetic transformations (Scheme 5.4). The pyrene moiety could be incorporated in the backbone by using palladium-catalysis, affording **5.8** in 55% yield. The α-alkylation of 2-methyl-3-oxo quinoline **5.2ak** was successfully achieved by using biorenewable alcohol *via* ruthenium-catalyzed borrowing hydrogen catalysis.[12] In addition, selective C-H chlorination[13] of **5.2a** and cyanation[14] of **5.2a** was executed *via* *N*-oxide **5.10** under transition metal-free conditions. Next, the selective reduction of **5.2a** was attained by performing the reaction with the use of arylbornic acid catalyst and Hantzsch ester as hydrogen source,[15] followed by *N*-alkylation using MeI leading to the formation of **5.14** in 68% yield. The demethylation of methyl ether in **5.2c** was effectively

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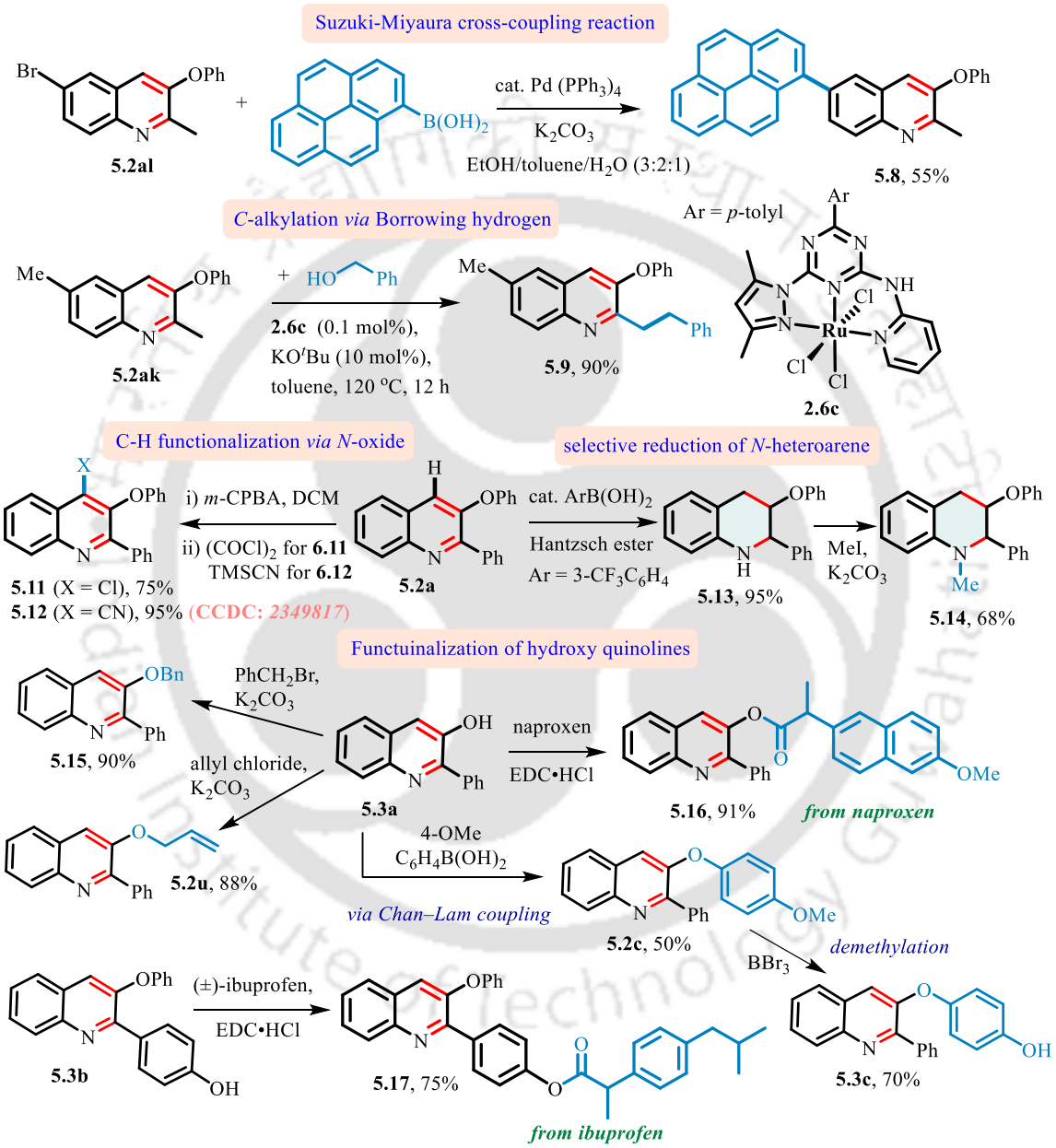
achieved by treating with BBr_3, provided **5.3c** in 70% yield. Given that the current reaction conditions are compatible with the hydroxyl functional group, further functionalization was accomplished at the C3-position of **5.3a**, delivering **5.15** and **5.2u** *via* nucleophilic reaction and affording **5.2c** and **5.16** *via* Chan-lam-coupling reaction and esterification, respectively. A coupled product **5.17** was readily obtained by treating **5.3b** with anti-inflammatory drug ibuprofen.



Scheme 5.4. Post synthetic modification

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5.3.6. Photophysical properties

It is noteworthy to showcase that some selected 3-oxo substituted quinoline for examples **5.2a**, **5.3a** with 260 nm photoexcitation display a fluorescence emission band at 377-405 nm.

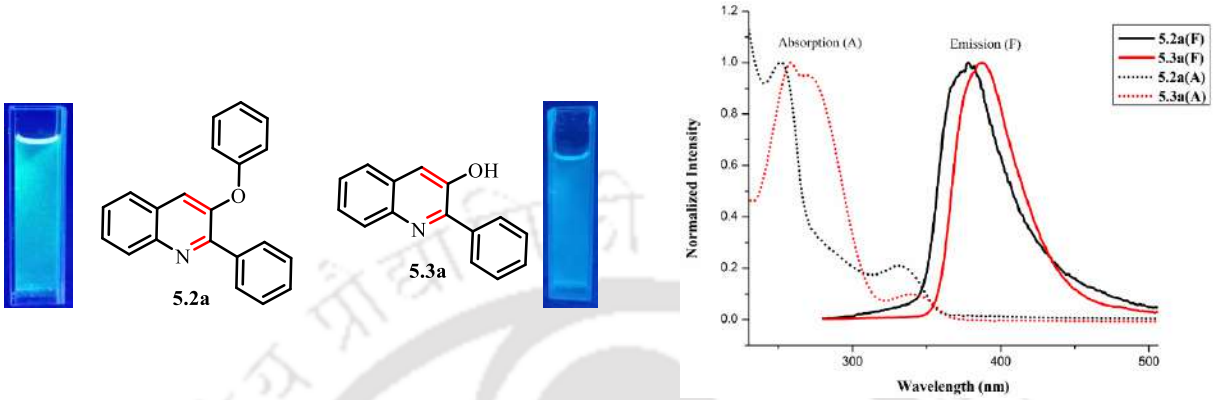
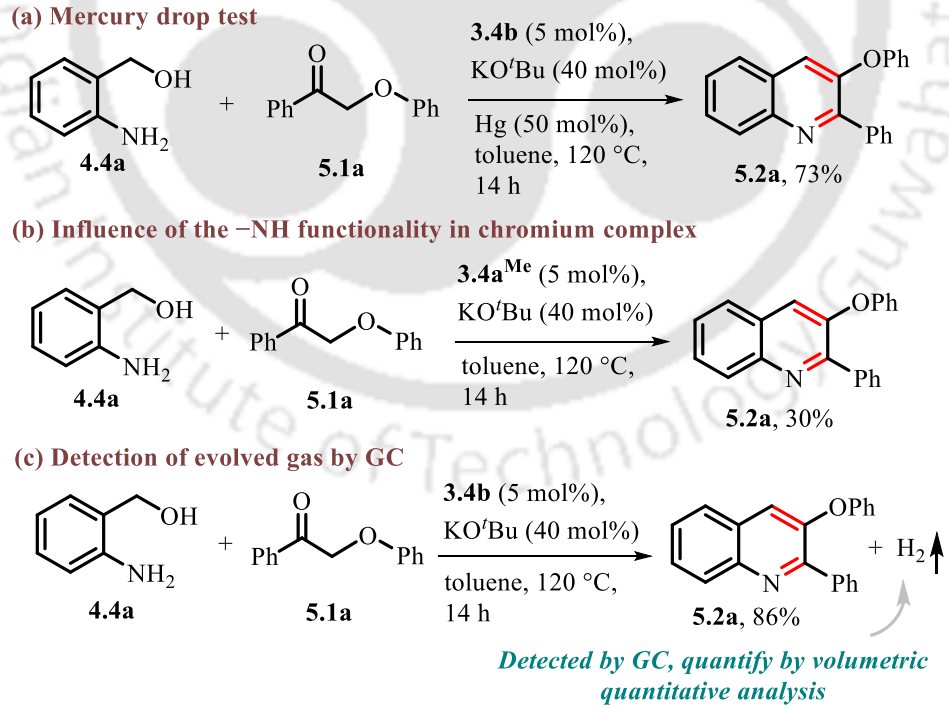


Figure 5.2: Normalized emission and absorbance spectra of some selected molecules. Concentration: 10 μM in Methanol. Excitation wavelength: 260 nm.

5.3.7. Mechanistic studies

In order to gain mechanistic insight into the synthesis of C3-subsituted quinolines various control experiments were performed.



Scheme 5.5. Control experiments

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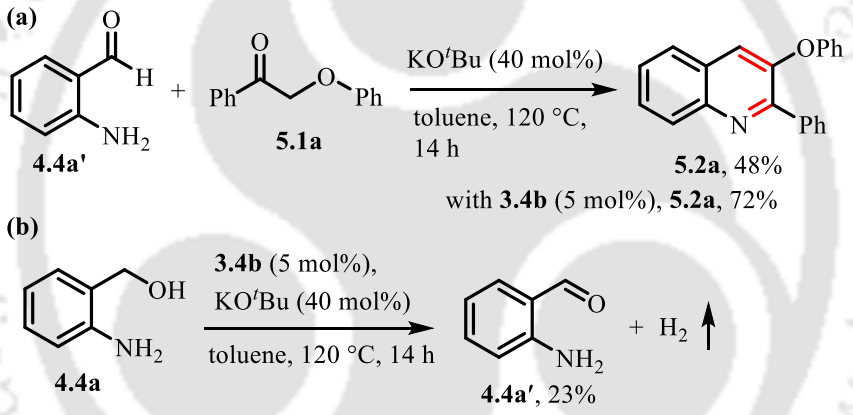
To establish the homogeneity of **3.4b** in ADC reaction of 2-aminobenzylalcohol and *α*-aryloxy ketone mercury drop experiment was carried out and there was no inhibition of the reaction or effect on the product yield confirming the homogeneity nature of the chromium complex (Scheme 5.5a).[16] The significance of the −NH functionality was elucidated by using complex **3.4a^{Me}** as the precatalyst, a lower yield of **5.2a** indicating the impact of the −NH functionality and metal−ligand cooperativity (MLC) in the reaction pathway (Scheme 5.5b).[17] The dehydrogenative pathway was confirmed by the detection of evolved H_2 gas (90%) under the reaction conditions using gas chromatography (GC), further the amount of H_2 gas has been quantified by volumetric quantitative analysis (Scheme 5.5c).[18, 19]

The reaction of 2-aminobenzylaldehyde **4.4a'** and **5.1a** under standard catalytic conditions gave the desired 3-oxo quinoline **5.2a** in a 72% yield, suggesting that 2-aminobenzylaldehyde act as a reaction intermediate in the process (Scheme 5.6). It has been further supported by conducting the reaction with **4.4a** in the absence of coupling partner **5.1a** under the reaction conditions which result in the formation of **4.4a'** in 23% of yield.



Scheme 5.6. Proof for the formation of intermediate 2-aminobenzaldehyde

The reaction of *β*-O-4′ lignin model **5.18** with **4.4a** was also investigated to afford **5.2a** in 21% yield (Scheme 5.7). Under the reaction conditions, compound **5.18** possibly undergoes retro-aldol reaction leading to the generation of 2-phenoxy-1-phenylethan-1-one **5.1a**. This conclusion is further supported by the control experiment using **5.18** in the absence of coupling partner **5.1a** giving the 2-phenoxy-1-phenylethan-1-one **5.1a** in 25% yield (Scheme 5.7b).

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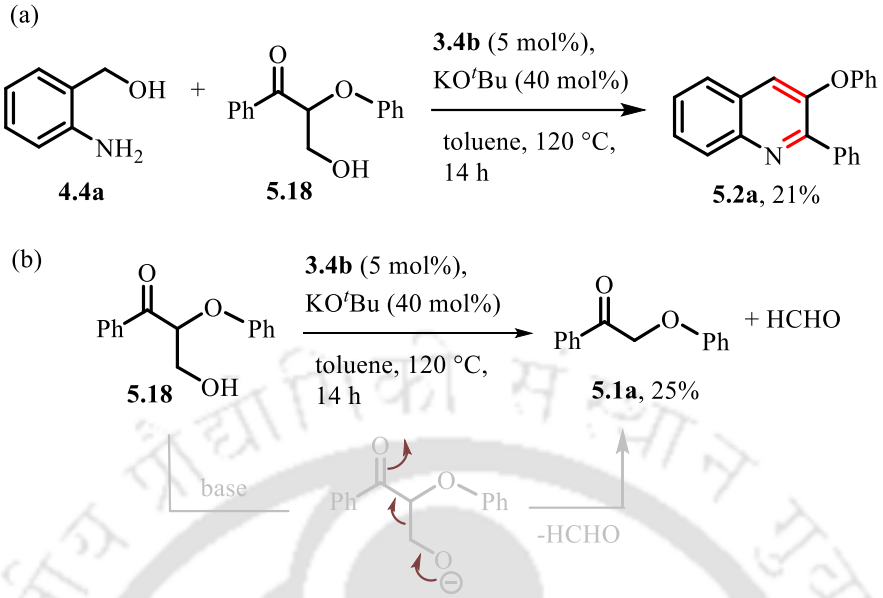
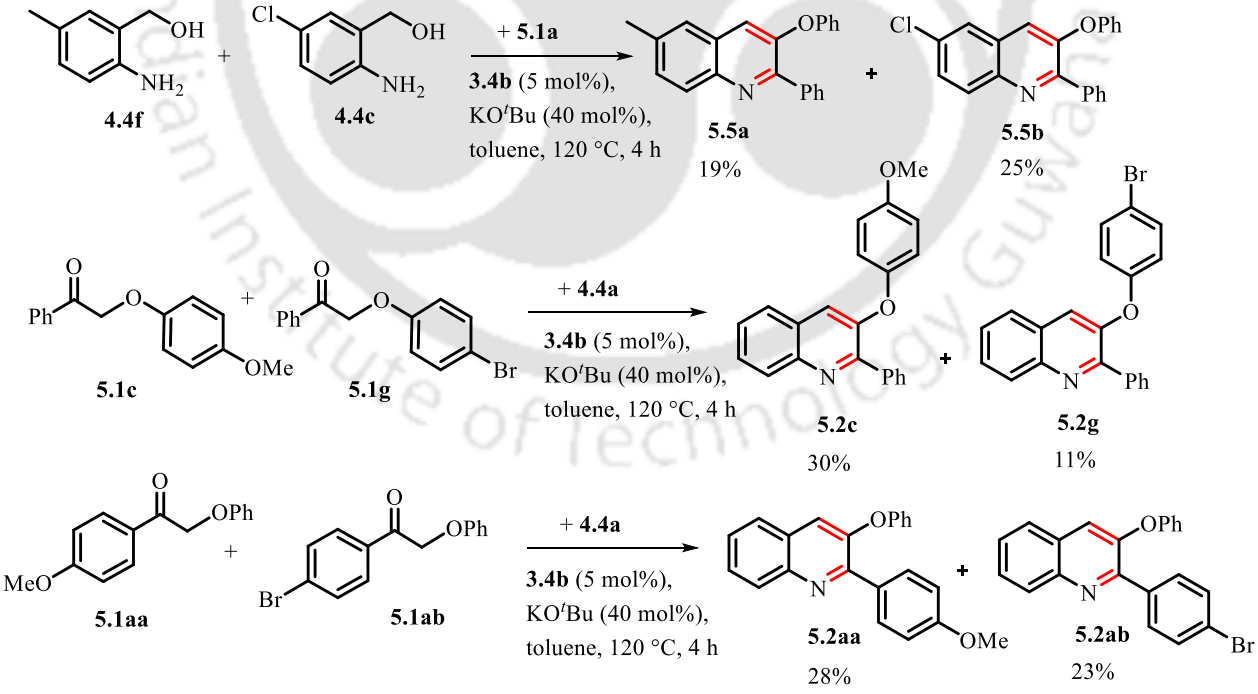


Scheme 5.7. Reaction with *β*-O-4′ lignin model

To understand the electronic effect on the rate of the reaction few competitive reactions were performed by taking various electron ring and electron deficient substrates. For that electronic effect of the 2-aminobenzyl alcohol 5-Me (**4.4f**), 5-Cl (**4.4c**) and phenoxy acetophenone **5.1c**, **5.1g** and **5.1aa**, **5.1ab** substrates on the rate of the reaction was examined (Scheme 5.8).



Scheme 5.8. Competitive cyclization reaction with electronically different substrates

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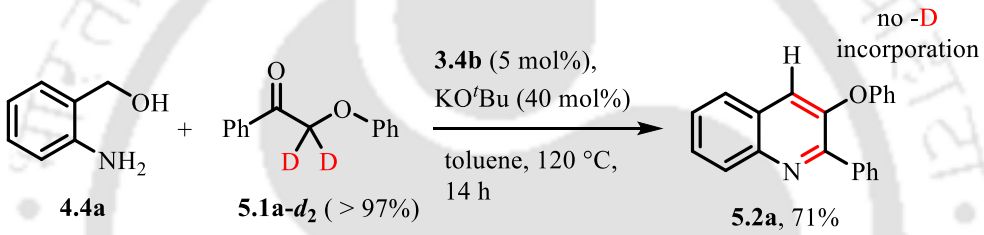
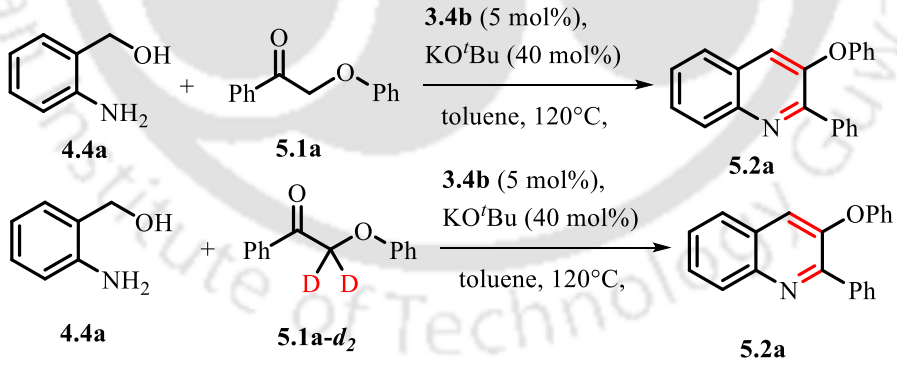
A competitive annulation reaction suggested that the electron-withdrawing group (−Cl) on the aminobenzyl alcohol afforded higher yield with respect to an electron-donating group (−Me) attributed to more favourable dehydrogenation (Scheme 5.8a). Competitive reaction between **5.1c** containing the electron donating group (−OMe) and **5.1g** containing an electron-withdrawing substituent (−Br) on the *C*-terminal of benzene ring highlighted that electron rich substrate enhanced the rate of the reaction more efficiently compare to electron deficient substrate (Scheme 5.8b). Furthermore, when the competitive experiments were performed using phenoxyacetophenone **5.1aa**, **5.1ab** bearing −OMe and −Br group on the *O*-terminal of the benzene ring, revealed that electron rich substituent exhibited better reactivity (Scheme 5.8c).

Additionally, a deuterium-labelling experiment was conducted in the cyclization reaction between **4.4a** and **5.1a-*d*$_2$** under standard conditions (Scheme 5.9). Lack of D incorporation in the product **5.2a** indicating that there is no H/D scrambling between the compound **5.1a-*d*$_2$** and the *in-situ* generated aldehyde **4.4a'**.



Scheme 5.9. Deuterium labeling experiment

Furthermore, the initial kinetics was performed in two parallel experiments with the reaction of **4.4a** and **5.1a** and **4.4a** with **5.1a-*d*$_2$** under the standard conditions (Scheme 5.10 and Figure 5.3).



Scheme 5.10. Deuterium kinetic isotope effect (DKIE) experiment

The DKIE value was found to be 2.62, indicating the α-C−H bond cleavage of **5.1a** as the turnover-limiting step in the aldol condensation segment which is distinctly different from most other conventional dehydrogenative annulation process.

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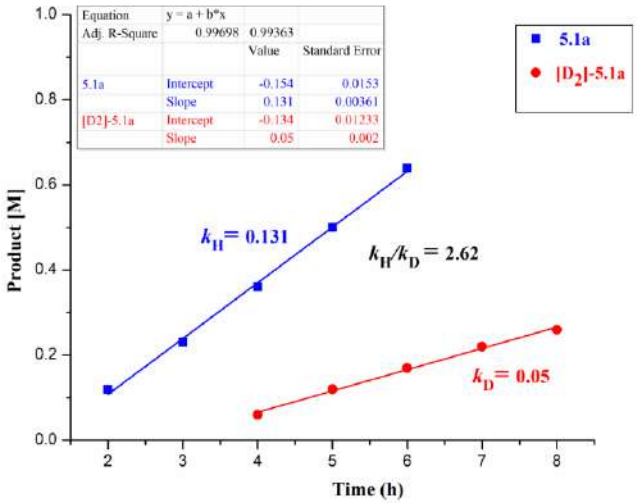
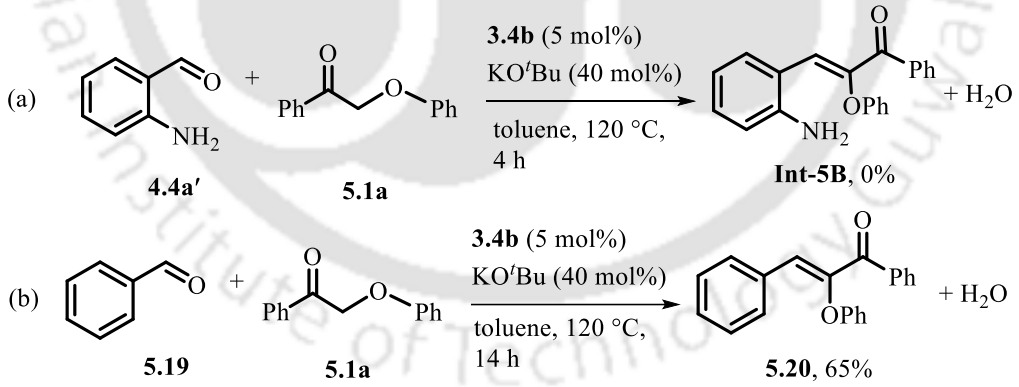


Figure 5.3. Concentration [Product] *vs* time plot of ADC reactions of **5.1a** and **5.1a-*d*$_2$**

In order to investigate the mode of cyclization during the initial condensation, the reaction was performed with **4.4a'** and **5.1a**, I failed to obtain the anticipated unsaturated ketone 3-(2-aminophenyl)-2-phenoxy-1-phenylprop-2-en-1-one **Int-5D** (Scheme 5.11). On the otherhand, in the absence of -NH_2 group in **4.4a'**, i.e., compound **5.19** can readily reacted with **5.1a** under the standard conditions, leading to formation of the desired *α*-substituted chalcone derivative **5.20** in 65% yield *via* intermolecular nucleophilic condensation. The result indirectly suggests that the presence of –NH_2 group at the *ortho*-position is crucial to obtain the desired product **5.1a**.



Scheme 5.11. Proof for the formation of unsaturated ketone

On the basis of the above mechanistic investigation and existing literature, a plausible mechanism for the dehydrogenative synthesis of 3-oxo quinolines has been proposed and is shown in Scheme 5.12.

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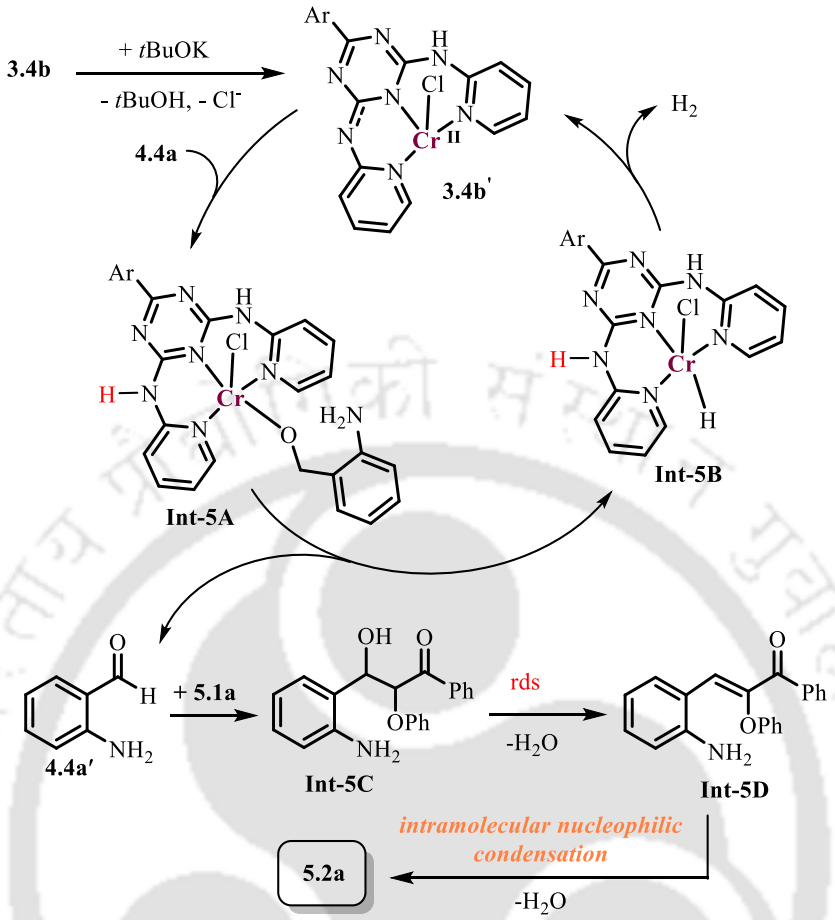

Scheme 5.12. Plausible mechanism

Catalytic cycle inititated with the *in-situ* of the active **3.4b'**[17] from precatalyst **3.4b** in presence of KO^{t}Bu which dehydrogenate 2-aminobenzyl alcohol to 2-aminobenzaldehyde *via* the outer sphere and/or inner sphere MLC pathway.[12] Following this, the 2-aminobenzaldehyde reacts with phenoxy acetophenone to give *β*-hydroxy ketone **Int-5C**. Subsequently **Int-5C** undergoes condensation to form intermediate **Int-5D**, and then an intramolecular nucleophilic condensation occurred to produce the desired product **5.2a**. Finally the release of H_2 gas through MLC, facillitates the regenaration of active **3.4b'** catalyst from **Int-5B**.

5.4. Summary

In summary, I have established an efficient and sustainable strategy for the synthesis of 3-oxo quinolines *via* ADC reaction of 2-aminoaryl alcohols with *β*-O-4′ lignin model. The effectiveness of the process was further enhanced by successfully producing 3-aminoquinolines using *α*-amino ketone. The catalytic system is compatible with various challenging functional groups such as iodide, bromide, CN, CF_3, and other hydrogenation-sensitive groups like benzyl ether, thioether, O-allyl, alkene, and alkyne groups, and unprotected hydroxyl are efficiently converted. The findings from the kinetic study and control experiments suggested that the aldol condensation segment is probably the rate-determining step. The strategy outlines the use of renewable

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substrates, cost-effective chromium catalysis, aerobic reaction conditions, functional group diversity, late stage diversification of complex molecular settings, and hydride scavenger free reagents, thus make it an appealing alternative for the construction of biologically significant *N*-heterocyclic compounds.

5.5. Experimental Section

General Information

All the reagents and chemicals were purchased from common commercial suppliers like Sigma-Aldrich, Alfa Aesar, Merck, BLD Pharma, Spectrochem, Avra Synthesis Pvt. Ltd., Finar Chemicals and directly used as received without any further purification unless otherwise mentioned. Compound 2-(allyloxy)-1-phenylethan-1-one (**5.1t**),[20] and **3.3a**, **3.3b**, **3.4a**, **3.4a^{Me}**, **3.3b**, **3.5** was prepared according to the reported literature.[17] THF and toluene were freshly distilled over sodium–benzophenone before use. ^{1}H, ^{13}C, and ^{19}F NMR spectra of the compounds were measured in $CDCl_3$, DMSO-d_6, CD_3OD as a solvent by using TMS as an internal standard. Chemical shifts, δ (in ppm), are reported relative to TMS δ (^{1}H) 0.0 ppm, δ (^{13}C) 0.0 ppm, which was used as the internal reference. Otherwise the solvents residual proton resonance and carbon resonance ($CHCl_3$, δ (^{1}H) 7.26 ppm, δ (^{13}C) 77.16 ppm; DMSO-d_6, (^{1}H) 2.50 ppm, δ (^{13}C) 39.52 ppm; CD_3OD, δ (^{1}H) 3.31 ppm, δ (^{13}C) 49 ppm) were also used for calibration. Bruker Avance III 600 and 400 spectrometers were used to record the NMR spectra. Chemical shifts (δ) values were reported in ppm and spin-spin coupling constant (J) were expressed in Hz, and other data were reported as follows: s = singlet, d = doublet, dd = doublet of doublet, dt = doublet of triplet, t = triplet, m = multiplet, q = quartet, sext = sextet, br = broad, and brs = broad singlet. IR spectra were recorded on Perkin Elmer Instrument at normal temperature making KBr pellet grinding the sample with KBr (IR Grade). MS (ESI-HRMS): Mass spectra were recorded on an Agilent Accurate-Mass Q-TOF LC/MS 6520. Merck silica gel 60-120 was used for column chromatography. GC instrument fitted with Elite-1 column (30 m length, 0.32 mm ID) using the following method: Injection volume: 1 μL, inlet temperature: 280 °C, FID detector temperature: 280 °C, oven temperature: start at 60 °C hold time 1 min, ramp: 12 °C /min, upto 320 °C, Flow rate (carrier): 25 mL/min (N2). UV experiments were performed in 1mL quartz cuvettes of path length 1cm at 25°C in UV/V spectrometer in HPLC grade solvent. All the annulation reaction was performed under air in the closed reaction tube.

A. Starting material employed in the reaction

2-aminobenzyl alcohol employed in the reaction:

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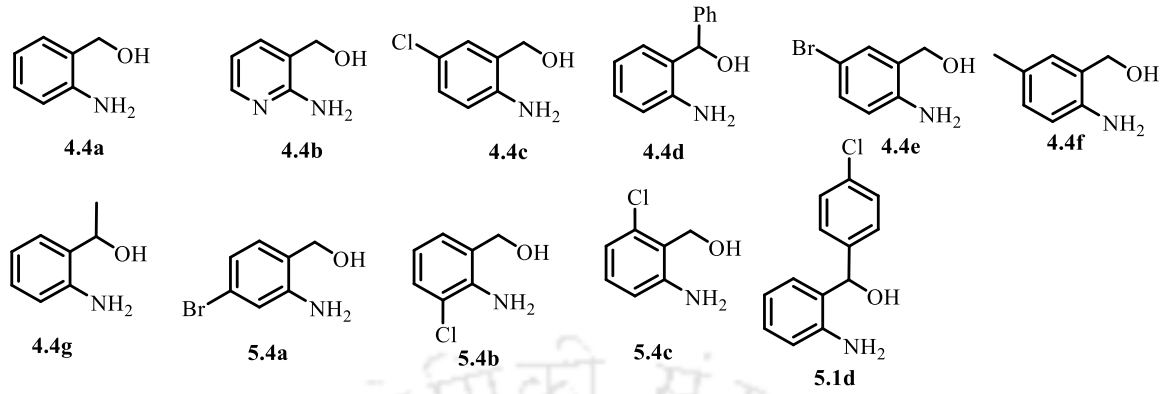
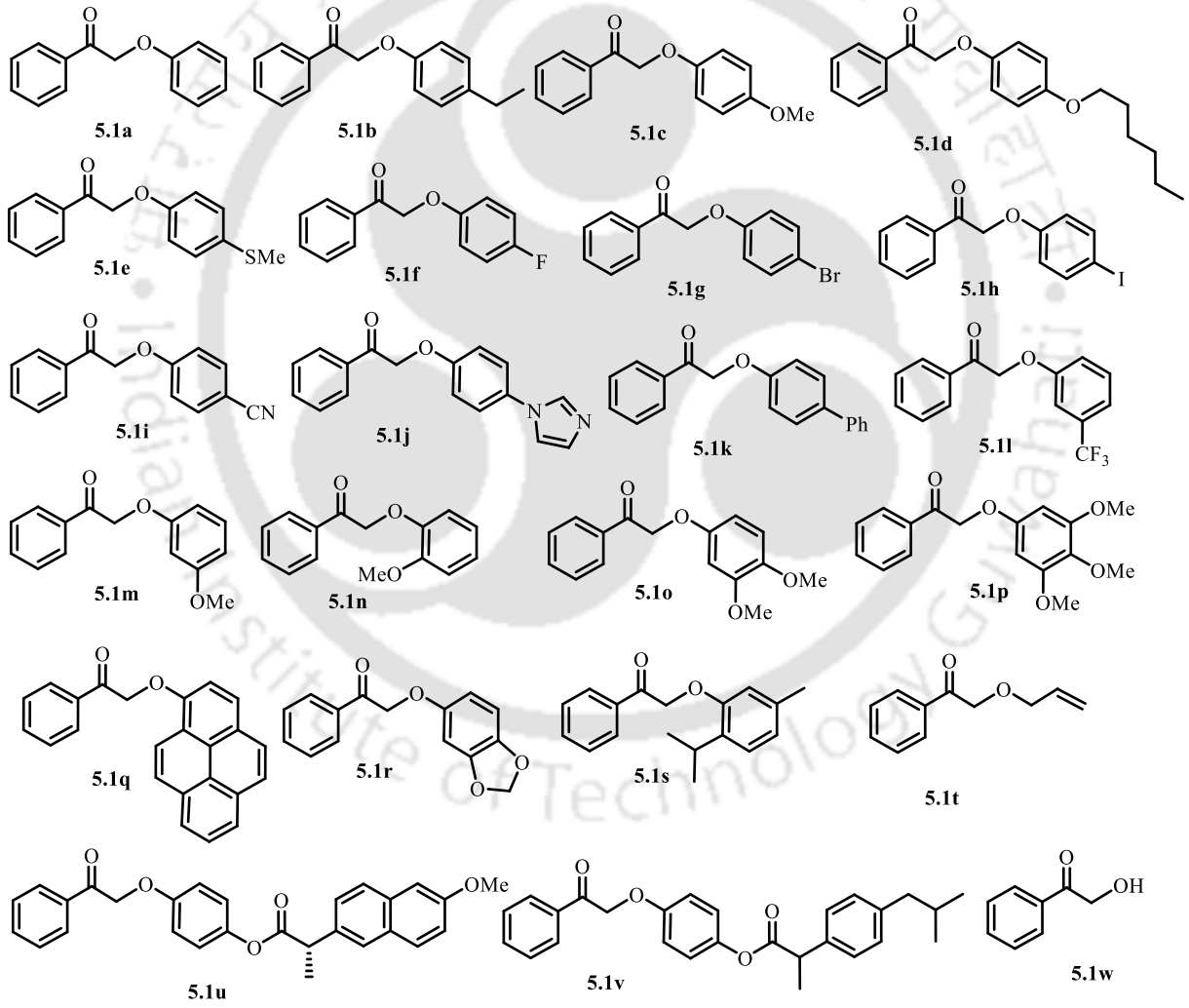


α-aryloxy, α-alkoxy, or α-hydoxy ketones substrates employed in the reaction:



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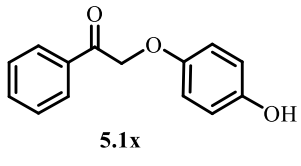

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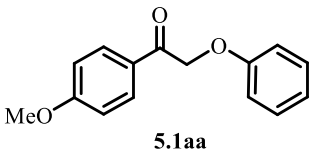

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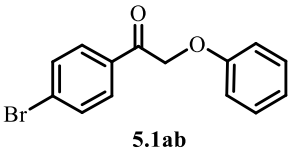

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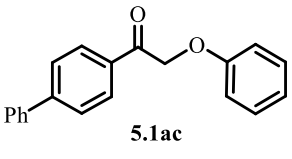

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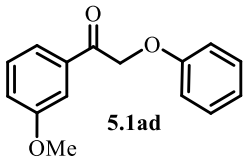

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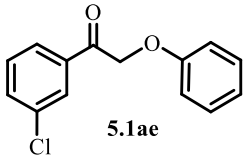

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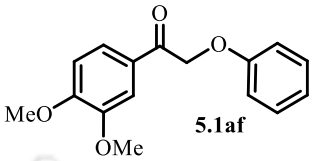

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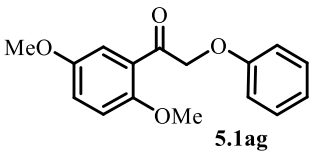

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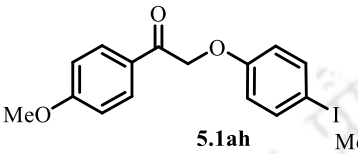

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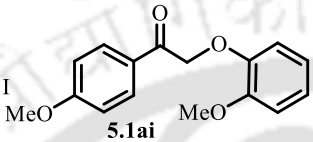

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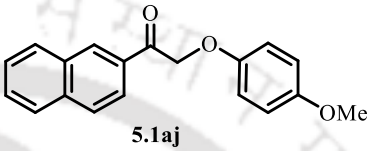

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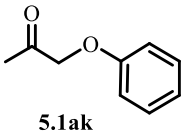

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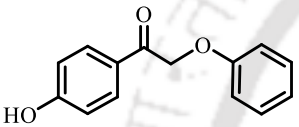

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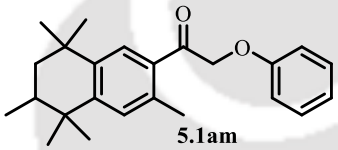

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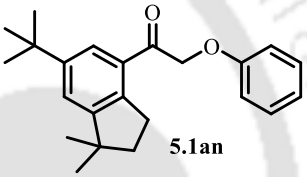

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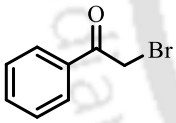
α-bromoacetophenone substrates employed in the reaction:



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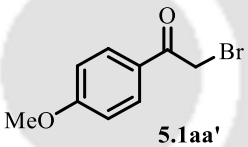

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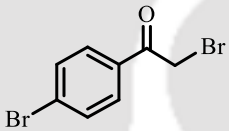

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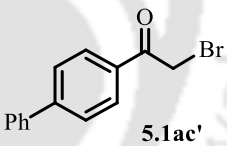

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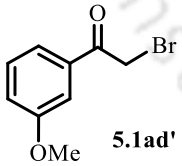

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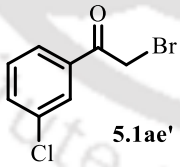

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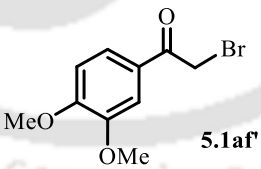

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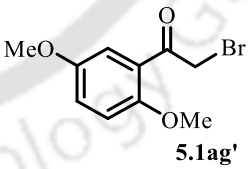

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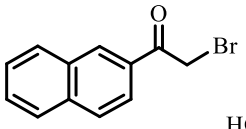

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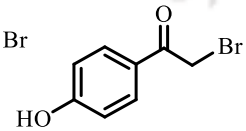

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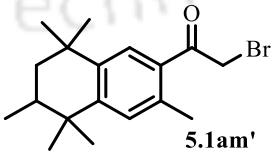

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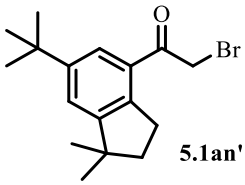

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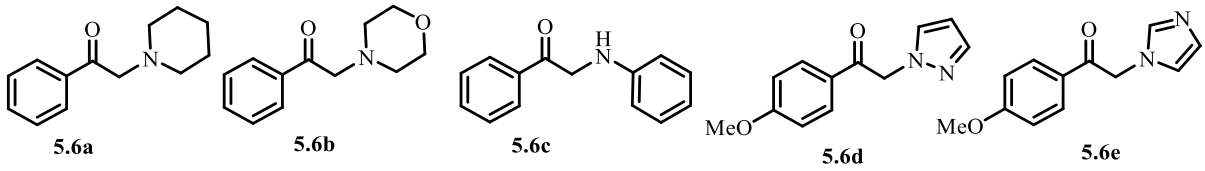
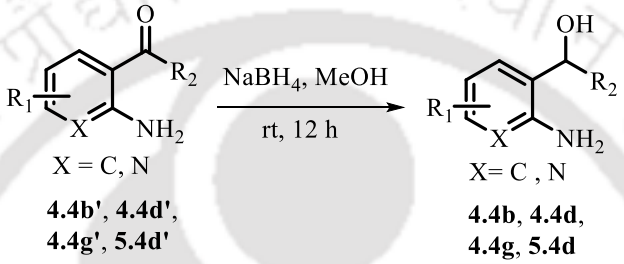
α-Amino ketones substrates employed in the reaction:



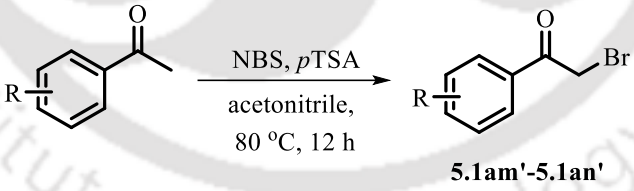
B. Experimental procedure for the synthesis of starting material and products:

i) General Procedure I (GP-I)



To a solution of substituted 2-aminoaryl ketone (1 equiv.) in methanol (2 mL), solid $NaBH_4$ (1.5 equiv.) was added at 0 ºC portion wise. After the completion of the addition, the reaction mixture was allowed to stirred for 12 h at room temperature. Then water was added to the reaction mixture, and extracted by using dichloromethane (5 mL). Afterwards, in the organic layer Na_2SO_4 was added to remove excess water. The corresponding product was obtained after removing the solvents under reduced pressure. Compound **4.4b**, **4.4d**, **4.4g** and **5.4d** were prepared by the above method.[21]

ii) General Procedure II (GP-II)



A mixture of acetophenone (2.0 mmol), *N*-bromosuccinimide (4.0 mmol), *p*-toluenesulfonic acid (1.0 mmol, 50 mol%), and acetonitrile (5 mL) was loaded in an oven-dried Schleck tube equipped with stirring bar. The reaction mixture was allowed to stirred at 90 ℃ for 12hrs. After completion of the reaction, all the volatiles were removed under reduced pressure and the compound was extracted from ethyl acetate and the crude reaction mixture was purified by column chromatography using ethyl acetate and petroleum ether as eluents to get the tittle compounds.

2-bromo-1-(3,5,5,6,8,8-hexamethyl-5,6,7,8-tetrahydronaphthalen-2-yl)ethan-1-one (5.1am'):

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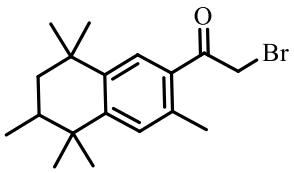
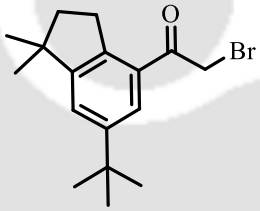


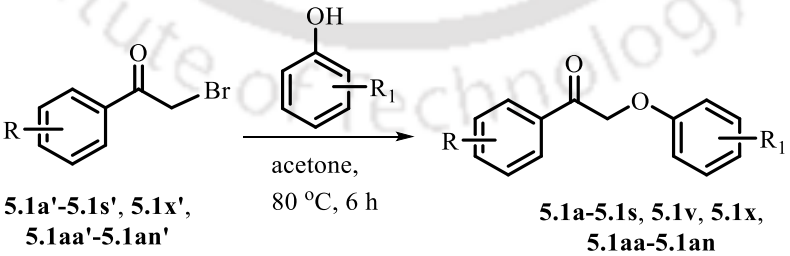
Using **GP-II** the title compound **5.1am'** was isolated as colourless liquid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.40); (225 mg, 60%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67 (s, 1H), 7.24 (s, 1H), 4.43 (s, 2H), 2.50 (s, 3H), 1.91 – 1.85(s, 1H), 1.67 – 1.64 (m, 1H), 1.61 – 1.59 (m, 1H), 1.33 (s, 6H), 1.27 (s, 3H), 1.08 (s, 3H), 1.00 (d, *J* = 6.8 Hz, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 193.7, 151.5, 142.6, 136.8, 131.6, 131.1, 128.5, 43.4, 38.2, 34.5, 34.2, 33.8, 32.5, 32.1, 28.4, 24.89, 21.69, 16.9. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{17}H_{24}BrO$ 336.1162; found 337.1168.

2-bromo-1-(6-(tert-butyl)-1,1-dimethyl-2,3-dihydro-1H-inden-4-yl)ethan-1-one (5.1an'):



Using **GP-II** the title compound **5.1an'** was isolated as colourless liquid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.50); (257 mg, 80%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.71 (brs, 1H), 7.39 (s, 1H), 4.48 (s, 2H), 3.18 (t, *J* = 7.2 Hz, 2H), 1.95 (t, *J* = 7.2 Hz, 2H), 1.36 (s, 9H), 1.27 (s, 6H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 192.9, 155.1, 150.2, 142.5, 130.4, 124.9, 124.4, 43.6, 41.4, 34.9, 33.2, 31.6, 30.9, 30.2, 28.9. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{17}H_{24}BrO$ 323.1006; found 323.1004.

iii) General Procedure III (GP-III)



5.1a'-5.1s', **5.1x'**, **5.1aa'-5.1an'**

5.1a-5.1s, **5.1v**, **5.1x**, **5.1aa-5.1an**

A mixture of substituted phenacyl bromide (1.0 mmol, 1 equiv.), substituted phenol (1.5 mmol, 1 equiv.), K_2CO_3 (2.0 mmol, 1 equiv.) and acetone (5 mL) was taken in an oven-dried Schleck tube equipped with stirring bar. The reaction mixture was allowed to stirred at 80 °C for 6 h. After completion of the reaction, all the volatiles were removed under reduced pressure and the compound was extracted from ethyl acetate. Afterwards the organic layers were dried over Na_2SO_4

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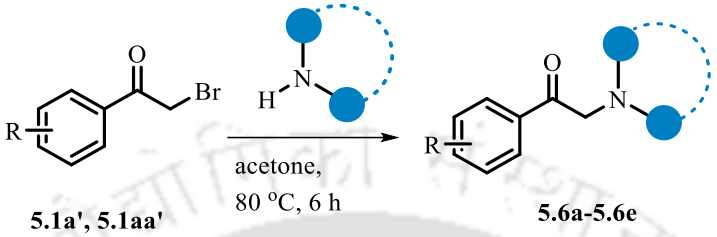
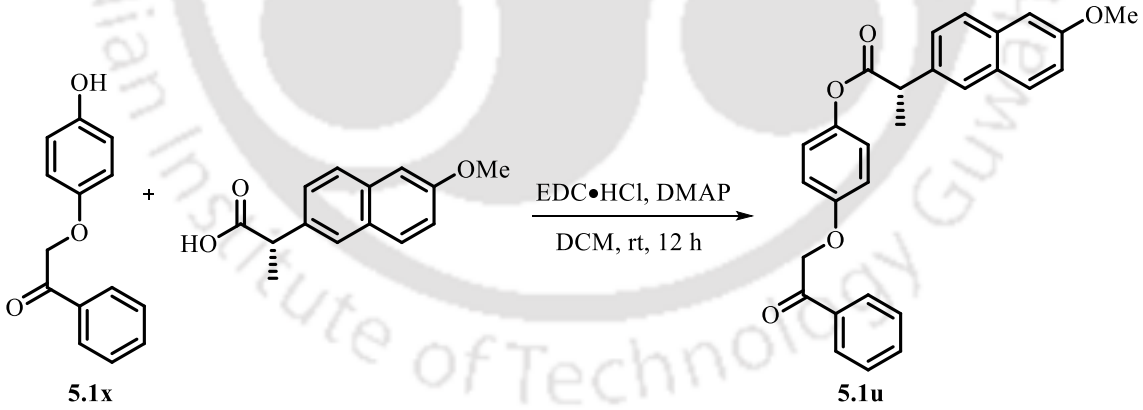
and removed under vacuum which give the corresponding compound. **5.1a-5.1s**, **5.1v**, **5.1x**, **5.1aa-5.1an** were prepared by following this method.[22] All compounds spectral data were in accordance with the literature.[5, 22]

iv) General Procedure IV (GP-IV)



A mixture of substituted phenacyl bromide (1.0 mmol, 1 equiv.), α-amino ketones (1.5 mmol, 1 equiv.), K_2CO_3 (2.0 mmol, 1 equiv.) and acetone (5 mL) was taken in an oven-dried Schleck tube equipped with stirring bar. The reaction mixture was allowed to stirred at 80 °C for 6 hrs. After completion of the reaction, all the volatiles were removed under reduced pressure and the compound was extracted from ethyl acetate. Afterwards the organic layers were dried over Na_2SO_4 and removed under vacuum which give the corresponding compound. **5.6a-5.6e** were prepared by following the above method.[22] All compounds spectral data were in accordance with the literature.[23-27]

v) Synthesis of 4-(2-oxo-2-phenylethoxy)phenyl (*S*)-2-(6-methoxynaphthalen-2-yl)propanoate (5.1u):



Scheme 5.13. Synthesis of **5.1u**

In a pressure tube 2-(4-hydroxyphenoxy)-1-phenylethan-1-one, **5.1x** (0.5 mmol, 1 equiv.) was taken in DCM (4.0 mL). To this (*S*)-2-(6-Methoxynaphthalen-2-yl)propanoic acid (1.0 mmol, 2 equiv.), EDC•HCl (1.5 mmol, 3 equiv.) and DMAP (0.13 mmol, 0.25 equiv.) was added. The reaction mixture was then stirred for 12 h at room temperature. After completion of the reaction the solution was concentrated in vacuo. The resulting crude compound was then purified by using

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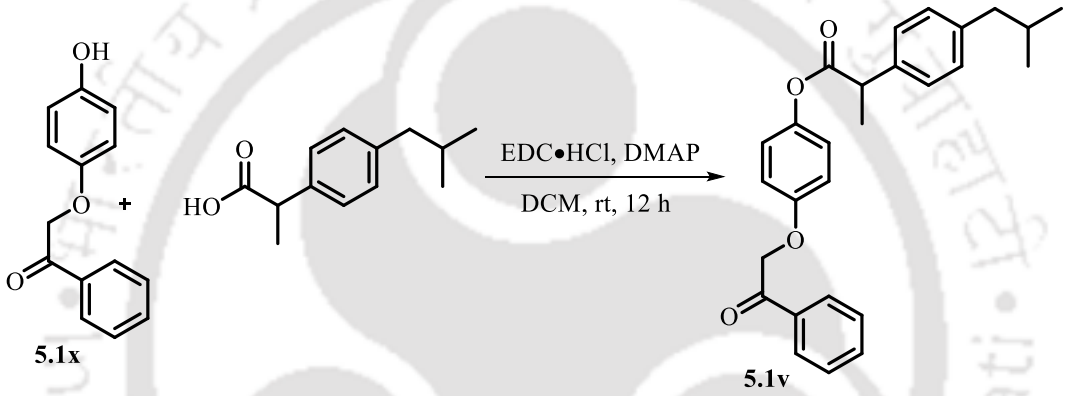
silica gel column chromatography using petroleum ether/ ethyl acetate mixture as eluent (v/v = 1:10, R_f = 0.40) to get the tittle compound **5.1u** as colourless liquid with 95% yield (209 mg).

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.00 – 7.98 (m, 2H), 7.76 – 7.72 (m, 2H), 7.63 – 7.59 (m, 1H), 7.51 – 7.49 (m, 3H), 7.15 – 7.14 (m, 1H), 6.83 – 6.79 (m, 3H), 6.74 – 6.71 (m, 3H), 5.22 (s, 2H), 4.10 – 4.08 (m, 1H), 3.92 (s, 2H), 1.68 (d, J = 7.2 Hz, 3H).^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 195.4, 174.2, 157.8, 153.6, 152.1, 150.8, 134.6, 134.1, 133.9, 129.5, 129.0, 128.2, 127.5, 126.3, 126.2, 122.3, 119.2, 116.3, 116.2, 116.0, 105.7, 71.8, 55.5, 45.6, 18.6. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{28}H_{25}NO_5$ 441.1697; found 441.1706.

vi) Synthesis of 4-(2-oxo-2-phenylethoxy)phenyl 2-(4-isobutylphenyl)propanoate (5.1v):



Scheme 5.14. Synthesis of **5.1v**

In a pressure tube 2-(4-hydroxyphenoxy)-1-phenylethan-1-one (0.5 mmol, 1 equiv.) was taken in DCM (4.0 mL). To this 2-(4-isobutylphenyl)propanoic acid (1.0 mmol, 2 equiv.), EDC•HCl (1.5 mmol, 3 equiv.) and DMAP (0.13 mmol, 0.25 equiv.) was added. The reaction mixture was then stirred for 12 h at room temperature. After completion of the reaction the solution was concentrated in vacuo. The resulting crude compound was then purified by using silica gel column chromatography using petroleum ether/ ethyl acetate mixture as eluent (v/v = 1:10, R_f = 0.40) to get the tittle compound **5.1v** as colourless oil with 92% yield (191 mg).

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.99 – 7.97 (m, 2H), 7.61 (t, J = 7.2 Hz, 1H), 7.49 (t, J = 7.8 Hz, 2H), 7.28 (d, J = 8.4 Hz, 2H), 7.13 (d, J = 7.8 Hz, 2H), 6.92 – 6.89 (m, 4H), 5.23 (s, 2H), 3.91 (q, J = 7.2 Hz, 1H), 2.46 (d, J = 7.2 Hz, 2H), 1.88 – 1.85 (m, 1H), 1.59 (d, J = 7.2 Hz, 3H), 0.91 (d, J = 6.6 Hz, 6H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 194.5, 173.6, 155.7, 145.3, 140.9, 137.4, 134.1, 129.6, 129.0, 128.3, 127.3, 122.5, 115.6, 71.4, 45.3, 45.2, 30.3, 22.5, 18.7. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{27}H_{29}NO_3$ 417.2061; found 417.2065.

vi) General procedure for synthesis of 3-oxo quinolines (GP-V)

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In a reaction tube a mixture of substituted 2-aminoaryl alcohol (0.4 mmol, 1 equiv.), α-substituted ketone (0.4 mmol, 1 equiv.), **3.4b** (5 mol%), KO^{t}Bu (40 mol%), toluene (2 mL) were taken. The reaction tube was properly closed under air and placed in a preheated oil bath at 120 ºC with continuous stirring for 14 h. The resulting mixture was then passed through a bed of celite, the filtrate was collected and concentrated under reduced pressure. The crude reaction mixture was purified by column chromatography over silica gel using petroleum ether or ethyl acetate/ petroleum ether mixture as an eluent.

vii) General procedure for synthesis of 3-amino quinolines (GP-VI)

In a reaction tube a mixture of substituted 2-aminobenzylalcohol **4.4a** (0.4 mmol, 1 equiv.), substituted *α*-amino ketone **5.6** (0.4 mmol, 1 equiv.), **3.4b** (5 mol%), KO^{t}Bu (40 mol%), toluene (2 mL) were taken. The reaction tube was properly closed under air and placed in a preheated oil bath at 120 ºC with continuous stirring for 14 h. The resulting mixture was then passed through a bed of celite, the filtrate was collected and concentrated under reduced pressure. The crude reaction mixture was purified by column chromatography over silica gel using petroleum ether or ethyl acetate/ petroleum ether mixture as an eluent.

D. Mechanistic studies

i) Mercury drop test (Scheme 5.5a)

To establish the homogeneity of **3.4b** in ADC reaction of 2-aminobenzylalcohol and *α*-aryloxy ketone mercury drop experiment was carried out.

Experimental procedure: In this test, the reaction tube was charged with 0.4 mmol of **4.4a** (50 mg), 0.4 mmol of **5.1a** (85 mg), 0.2 mmol of mercury (50 mg), 40 mol% of KO^{t}Bu (18 mg) and 5 mol% of complex **3.4b** (11 mg) along with 2 mL of toluene. The whole reaction mixture was then allowed to heated at 120 ºC for 14 h in an oil bath. The product **5.2a** was obtained in 73% of yield (86 mg), suggests that homogenous behavior of the catalyst.

ii) The influence of the −NH functionality in chromium complex (Scheme 5.5b)

Experimental procedure: A mixture of **4.4a** (0.4 mmol, 1 equiv.), **5.1a** (0.4 mmol, 1 equiv.), **3.4a^{Me}** (5 mol%), KO^{t}Bu (40 mol%) and toluene (2 mL) was added into a reaction tube equipped with stirring bar. The reaction tube was properly closed and placed in a preheated oil bath at 120 ºC with continuous stirring for 14 hours. The resulting mixture was then passed through a bed of celite, the filtrate was collected and concentrated under reduced pressure. Analytically pure product (32 mg, 30%) was obtained by column chromatography over silica gel using ethyl acetate /petroleum ether mixture as an eluent.

iii) Detection of evolved gas (Scheme 5.5c):

a) Detection of evolved gas by GC-Thermal Detector (GC-TCD)

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A mixture of 2-aminobenzyl alcohol, **4.4a** (246 mg, 2.0 mmol, 1.0 equiv.), 2-phenoxy-1-phenylethan-1-one, **5.1a** (424 mg, 2.0 mmol, 1 equiv.), **3.4b** (5 mol %), KO^{t}Bu (40 mol%) was added into a pressure tube (50 mL) equipped with stirring bar. The reaction tube was then properly closed without exclusion of air and kept it in a preheated oil bath at 120 ℃ with continuous stirring for 14 h. After completion of the reaction, the pressure tube was cooled at 0 °C, the evolved gas was syringe out and detected from PerkinElmer clarus-590 GC instrument using Elite Plot-Q column (30 m length x 530 µm x 20 µm ID) employing the following method:

TCD starting temperature: 40 °C

Oven temperature: 60 °C

Time at starting temperature: 0 min

Hold time: 5 min

Ramp: 28 °C/ min up to 200 °C

Flow rate: 5 ml/ min (N_2)

Split ration: 20

Inlet temperature: 40 °C

Detector temperature TCD: 200 °C

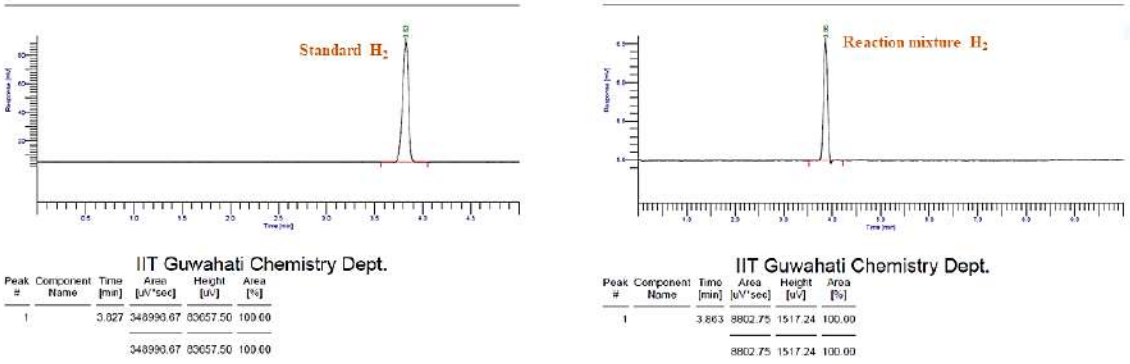

Figure 5.4. GC-TCD analysis of the standard H_2 gas and H_2 gas evolved from the reaction mixture.

b) Hydrogen gas quantification- A volumetric quantitative analysis:

The volumetric quantification of hydrogen gas was accomplished according to the previously reported literature methods.[18, 19] A mixture of 2-aminobenzylalcohol **4.4a** (1 mmol, 1equiv.), 2-phenoxy-1-phenylethan-1-one, **5.1a** (1.0 mmol, 1 equiv.), **3.4b** (5 mol%) KO^{t}Bu (40 mol%) was added into schenck flask (10 mL) equipped with stirring bar after that 2 mL of toluene was added to the reaction mixture and joined with a one neck adapter condenser set up. The adapter was

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connected to the gas collection apparatus (standard water displacement apparatus, using a graduated cylinder to determine the volume) and the entire system was flushed with argon for 5 minutes and allowed to equilibrate for 5 minutes. The reaction vessel was placed in a preheated oil-bath to the appropriate temperature (120 °C). The reaction was stirred vigorously at a constant temperature until gas evolution ceased. The volume of collected gas was noted. After 14 h, the reaction mixture was removed from preheated oil-bath, subjected to cool at room temperature. The desired compound **5.2a** was purified by using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:2) with 86% of yield. The collected volume of gas in that experiment was 23 mL. The experiment was repeated twice to obtain consistent readings and the number of moles of hydrogen was evolved was calculated considering the vapor pressure of water at 298 K = 23.7695 Torr. Volume of water displaced = 23 mL. Atmospheric Pressure = 758.3124 Torr, R = 62.3635 L Torr K^{-1} mol^{-1}

$nH_2 = [(P_{atm} – P_{water}) \times V] / RT$ = 0.00090 moles = 0.90 mmoles. The yield of molecular hydrogen 90%.

iv) Proof for the formation of intermediate 2-amino benzaldehyde (Scheme 5.6):

Experimental procedure for 5.2a: A mixture of **4.4a'** (0.4 mmol, 1 equiv.), **5.1a** (0.4 mmol, 1 equiv.), **3.4b** (5 mol%), KO^{t}Bu (40 mol%) and toluene (2 mL) was loaded into the reaction tube and heated at 120 °C for 14 h. The product **5.2a** was isolated in 72% of yield. In the absence of **3.4b**, product **5.2a** was isolated in 48% yield.

Experimental procedure for 4.4a': A mixture of **4.4a** (0.4 mmol, 1 equiv.), **3.4b** (5 mol%), KO^{t}Bu (40 mol%) and toluene (2 mL) was loaded into the reaction tube and heated at 120 °C for 14 h. The product **4.4a'** was isolated in 23% yield.

v) Reaction with *β*-O-4' lignin model (5.18) (Scheme 5.7):

Experimental procedure (Scheme 5.7a): A mixture of **4.4a** (0.4 mmol, 1 equiv.), **5.18** (0.4 mmol, 1 equiv.), **3.4b** (5 mol%), KO^{t}Bu (40 mol%) and toluene (2 mL) was loaded into the reaction tube and heated at 120 °C for 14 h. The product **5.2a** was isolated in 21% of yield.

Experimental procedure (Scheme 5.7b): A mixture of **5.18** (0.4 mmol, 1 equiv.), **3.4b** (5 mol%), KO^{t}Bu (40 mol%) and toluene (2 mL) was loaded into the reaction tube and heated at 120 °C for 14 h. The product **5.1a** was isolated in 25% of yield.

vi) Competitive cyclization reaction with electronically different substrates (Scheme 5.8)

Reaction conditions: In an oven-dried reaction tube, a mixture of substituted 2-aminobenzyl alcohol (1 mmol, 1 equiv.), substituted *α*-aryloxy (1 mmol, 1 equiv.), KO^{t}Bu (40 mol%), **3.4b** (5 mol%), and toluene (2 mL) were taken. The reaction tube was properly closed and placed in a

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preheated oil bath at 120 °C for 4 h. The compound **5.5a, 5.5b**, **5.2c, 5.2g, 5.2aa, 5.2ab** were isolated in each case after specified time.

It has been observed that the electron-withdrawing group (-Cl) on the aminobenzyl alcohol afforded higher yield with respect to an electron-donating group (-Me) and the electron donating group (-OMe) on the *C*-terminal and *O*-terminal benzene ring bearing phenoxy acetophenone enhanced the reaction rate with respect to an electron-withdrawing substituent (-Br).

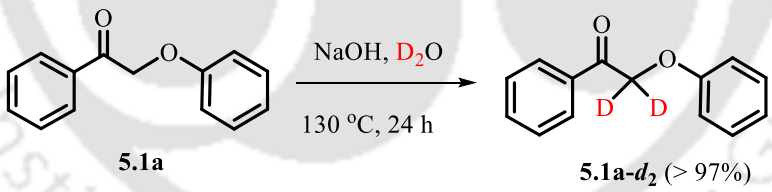
vii) Proof for the formation of intermediate unsaturated ketone (Scheme 5.11)

Reaction conditions for (a): In an oven-dried reaction tube, a mixture of 2-aminobenzaldehyde **4.4a'** (1 mmol, 1 equiv.), 2-phenoxyacetophenone **5.1a** (1 mmol, 1 equiv.), KO^{t}Bu (40 mol%), **3.4b** (5 mol%), and toluene (2 mL) were taken. The reaction tube was properly closed and placed in a preheated oil bath at 120 °C for 4 h. The unsaturated ketone **Int-5D** was not isolated.

Reaction conditions for (b): In an oven-dried reaction tube, a mixture of benzaldehyde **5.19** (1 mmol, 1 equiv.), 2-phenoxyacetophenone **5.1a** (1 mmol, 1 equiv.), KO^{t}Bu (40 mol%), **3.4b** (5 mol%), and toluene (2 mL) were taken. The reaction tube was properly closed and placed in a preheated oil bath at 120 °C for 14 h. The unsaturated ketone **5.20** was isolated in 65% yield.

viii) Deuterium-labeling experiments

a) Synthesis of deuterated 2-phenoxy-1-phenylethan-1-one 5.1a-*d*$_2$:



5.1a **5.1a-*d*$_2$** (> 97%)

Scheme 5.15. Synthesis of **5.1a-*d*$_2$**

Procedure: In a pyrex tube degassed D_2O (99.9% D, 3 mL) was taken and to it under nitrogen flow a mixture of 2-phenoxy-1-phenylethan-1-one **5.1a** (424 mg, 2 mmol) and NaOH (40 mg, 1.0 mmol) was added. The reaction tube was properly closed and placed in a preheated oil bath at 130 °C with continuous stirring for 24 hours under nitrogen atmosphere. Upon completion of the reaction, the reaction mixture was extracted with chloroform (5 mL × 3) and dried over Na_2SO_4. The solvent was evaporated under vacuum to afford the desired product **5.1a-*d*$_2$** (93%, 390mg) with 97% D as a light brown solid.

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^{1}H NMR (600 MHz, $CDCl_3$): δ 8.01 (d, J = 7.2 Hz, 2H), 7.62 (t, J = 7.2 Hz, 1H), 7.51 (t, J = 7.8 Hz, 2H), 7.29 (t, J = 8.4 Hz, 2H), 6.99 (t, J = 7.2 Hz, 1H), 6.95 (d, J = 8.4 Hz, 2H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 194.8, 158.1, 129.7, 129.0, 128.3, 121.8, 115.0, 70.6 – 70.0 (m).

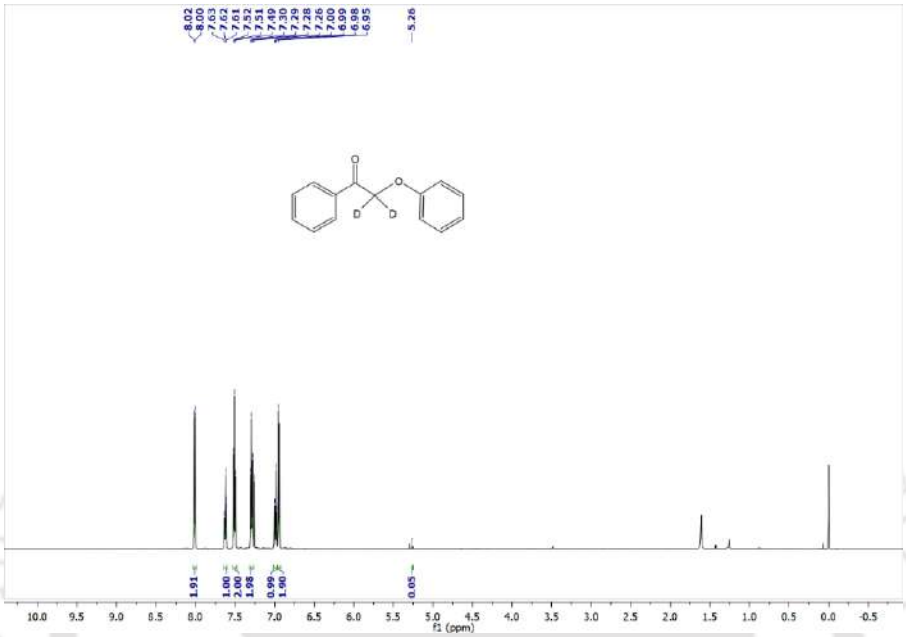

Figure 5.5. ^{1}H NMR spectrum of **5.1a-*d*$_2$** ($CDCl_3$, 600 MHz, 298 K)

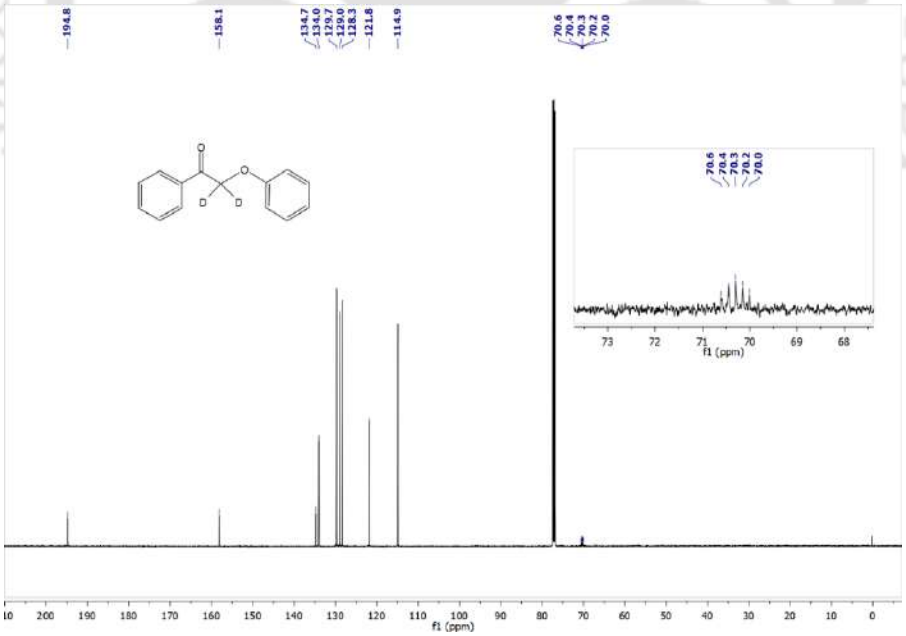

Figure 5.6. ^{13}C{^{1}H} NMR spectrum of **5.1a-*d*$_2$** ($CDCl_3$, 151 MHz, 298 K)

b) Deuterium kinetic isotope effect (DKIE) experiment (Scheme 5.10):

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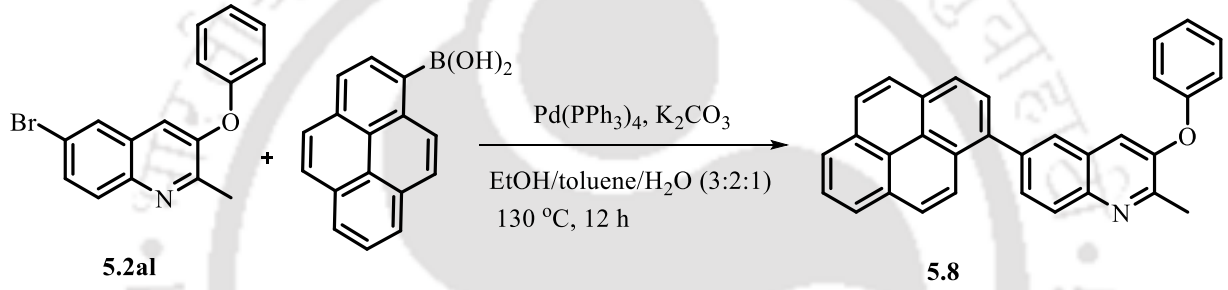
By following the standard catalytic procedure, two parallel reactions were performed by using **5.1a** (1 mmol) and **5.1a-*d*$_2$** (1.0 mmol) as substrates. Then the compound **5.2a** was isolated at different time intervals. Then the initial rates of product formation were obtained from the plot of the concentration of product *vs* time (Figure 5.3). The $k_H/k_D = 2.62 \pm 0.26$ was obtained by comparing the initial rates of these two reactions.

ix) Synthesis and spectroscopic characterization for active chromium species:

Synthesis and spectroscopic characterization for active chromium species have been discussed in chapter 3, section 3.3.5.

E. Post Synthetic Modification

2-methyl-3-phenoxy-6-(pyren-1-yl)quinoline (5.8):



5.2al **5.8**

Scheme 5.16. Synthesis of **5.8**

5.2al (63 mg, 0.2 mmol) and pyrene boronic acid (0.3 mmol, 1.5 equiv.) were stirred at room temperature in mixture of solvents EtOH/toluene/H_2O (3:2:1) (4 mL) for 15 minutes. To this, $Pd(PPh_3)_4$ (11.56 mg, 0. 01 mmol, 5.0 mol%), K_2CO_3 (110 mg, 0.8 mmol, 4.0 equiv.) were added. Then reaction mixture was reflux for 12 hours with continuous stirring on a preheated oil bath at 130 °C. After completion of the reaction the solvent was removed under vacuum pressure. The mixture was extracted using ethyl acetate and solvent was removed under vacuum. The crude compound was purified by column chromatography eluting with pet ether-ethyl acetate mixture (v/v = 2:50, R_f = 0.50) to give the pure product **5.8** as off-white solid with 55% yield (48 mg).

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.25 – 8.20 (m, 3H), 8.20 – 8.15 (m, 3H), 8.11 (s, 1H), 8.04 – 8.02 (m, 3H), 7.90 – 7.85 (m, 2H), 7.49 (s, 1H), 7.44 – 7.40 (m, 2H), 7.21 – 7.18 (m, 1H), 7.12 – 7.10 (m, 2H), 2.82 (s, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 156.4, 154.3, 150.8, 139.4, 137.0, 131.6, 131.1, 131.0, 130.4, 128.7, 128.4, 128.2, 127.9, 127.8, 127.6, 126.2, 125.4, 125.2, 125.1, 124.8, 124.3, 120.2, 119.3, 20.8. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{32}H_{22}NO$ 436.1696; found 436.1692.

6-methyl-2-phenethyl-3-phenoxyquinoline (5.9):

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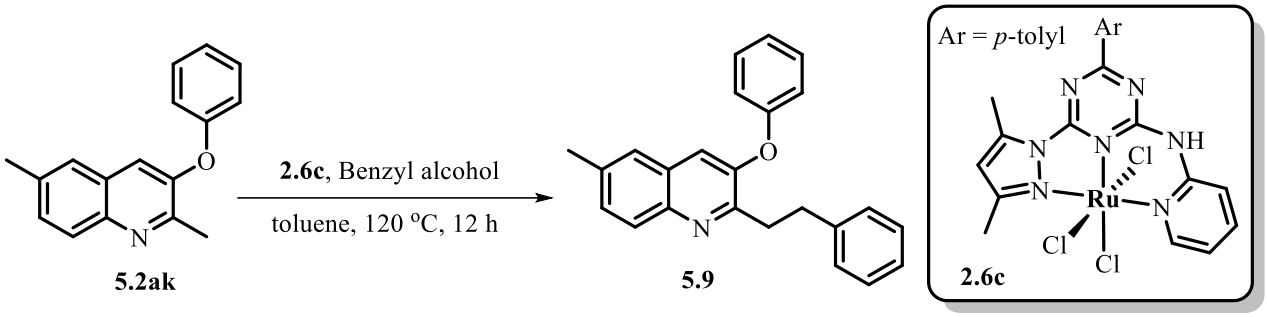
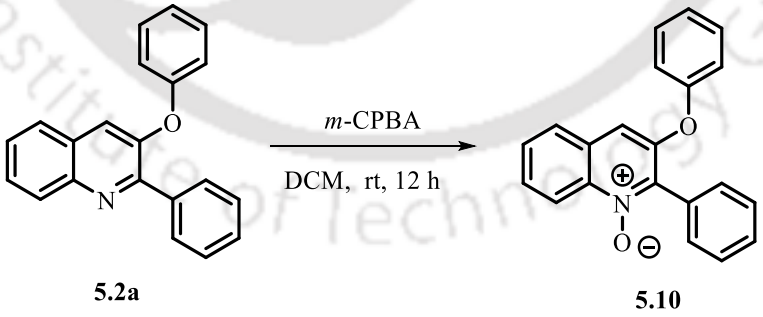


Scheme 5.17. Synthesis of **5.9**

A mixture of 2,6-dimethyl-3-phenoxyquinoline (0.2 mmol, 1 equiv.), benzyl alcohol (0.24 mmol, 1.2 equiv.), **2.6c** (0.1 mol%),[12] KO^{t}Bu (10 mol%) and toluene (1 mL) was added into a reaction tube (25 mL) equipped with stirring bar. The reaction tube was then properly closed without exclusion of air and kept it on a preheated oil bath at 120 °C with continuous stirring for 12 hours. After completion of the reaction, the resulting mixture was passed through a bed of celite, the filtrate was collected and concentrated under reduced pressure. The resulting crude compound was purified by silica gel column chromatography using petroleum ether/ ethyl acetate mixture as eluent (v/v = 1:50, R_f = 0.50) to get the tittle compound **5.9** as light yellow oil with 90% yield (61 mg).

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.96 (d, J = 9.0 Hz, 1H), 7.44 (d, J = 8.4 Hz, 1H), 7.40 – 7.38 (m, 3H), 7.32 (s, 1H), 7.26 – 7.25 (d, J = 4.8 Hz, 4H), 7.19 – 7.17 (m, 2H), 7.00 (d, J = 7.8 Hz, 2H), 3.37 – 3.34 (m, 2H), 3.18 – 3.15 (m, 2H), 2.49 (s, 3H).^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 156.6, 155.4, 150.1, 142.1, 136.3, 130.2, 130.2, 128.7, 128.5, 126.0, 125.8, 124.1, 112.0, 119.2, 35.7, 34.9, 21.7. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{24}H_{22}NO$ 340.1696; found 340.1688.

3-phenoxy-2-phenylquinoline 1-oxide (5.10):



Scheme 5.18. Synthesis of **5.10**

In a round-bottom flask, **5.2a** (0.5 mmol, 1 equiv.) was dissolved in dichloromethane (2 mL). Then, to this solution *m*-chloroperbenzoic acid (*m*-CPBA) (1 mmol, 2 equiv.) in dichloromethane (2 mL) was added portion wise at 0 °C. After completion of the addition, the reaction mixture was allowed to cool down to room temperature and stirred for 12 hours. The mixture was diluted with dichloromethane (5 mL) after completion and combined organic part was washed with 6 N

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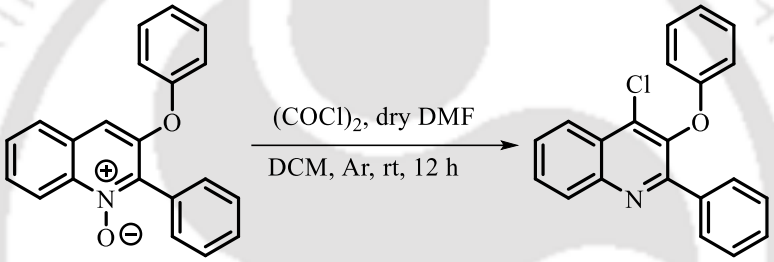
aqueous KOH solution followed by brine solution. The organic part was dried over Na_2SO_4 and solvent was removed under reduced pressure. The resulting crude compound was purified by silica gel column chromatography using petroleum ether/ ethyl acetate mixture as eluent (v/v = 50:25, R_f = 0.40) to get the title compound **5.10** as light brown solid with 95% yield (147 mg).

^{1}H NMR (600 MHz, $CDCl_3$): δ 8.74 (d, J = 8.4 Hz, 1H), 7.68 – 7.65 (m, 4H), 7.60 (t, J = 7.8 Hz, 1H), 7.49 (t, J = 7.8 Hz, 2H), 7.45 – 7.42 (m, 1H), 7.36 (t, J = 7.8 Hz, 2H), 7.19 – 7.16 (m, 2H), 7.01 (d, J = 7.8 Hz, 2H).^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ ^{13}C NMR (151 MHz, $CDCl_3$): δ 155.9, 150.8, 141.8, 139.4, 130.3, 130.2, 129.5, 129.4, 129.2, 129.0, 128.6, 128.3, 127.4, 124.7, 120.4, 119.6, 111.8. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{21}H_{16}NO_2$ 314.1176; found 314.1169.

4-chloro-3-phenoxy-2-phenylquinoline (5.11) from 5.10:



Scheme 5.19. Synthesis of **5.11**

In a schlenk flask, quinoline *N*-oxide (0.5 mmol, 1 equiv.) was dissolved in DCM (1.0 mL). To this solution, dry DMF (1.0 mL) was added under nitrogen flow at 0 ºC followed by the addition of $(COCl)_2$ (1.0 mmol). The reaction mixture was stirred for 12 h. The resulting mixture was evaporated under reduced pressure. The resulting crude compound was purified by using silica gel column chromatography using petroleum ether/ ethyl acetate mixture as eluent (v/v = 50:15, R_f = 0.50) to get the tittle compound **5.11** as light brown oil with 75% yield (124 mg).

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.25 – 8.22 (m, 2H), 7.94 – 7.92 (m, 2H), 7.80 – 7.77 (m, 1H), 7.69 – 7.65 (m, 1H), 7.41 – 7.36 (m, 3H), 7.21 – 7.17 (m, 2H), 6.98 – 6.93 (m, 1H), 6.75 – 6.77 (m, 2H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 157.1, 155.4, 146.1, 143.0, 137.0, 135.2, 130.1, 129.9, 129.7, 129.4, 129.4, 128.4, 127.9, 126.7, 124.0, 122.5, 115.4. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{21}H_{15}ClNO$ 332.0837; found 332.0842.

3-phenoxy-2-phenylquinoline-4-carbonitrile (5.12) from 5.10:

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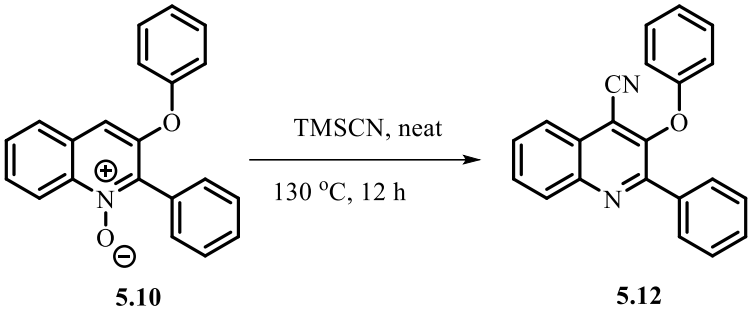
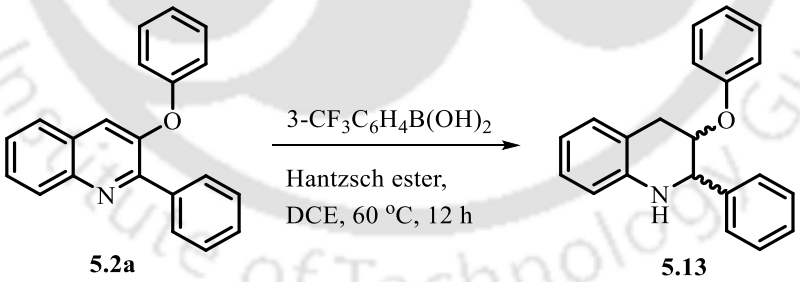


Scheme 5.20. Synthesis of **5.12**

In a schlenk flask, quinoline *N*-oxide (0.2 mmol, 1 equiv.) was taken and to this TMSCN (0.4 mmol, 1 equiv.) was added and stirred the reaction mixture at 130 °C for 12h. The resulting mixture was collected by using DCM and then evaporated under reduced pressure. The resulting crude compound was purified by using silica gel column chromatography using petroleum ether/ ethyl acetate mixture as eluent (v/v = 50:20, R_f = 0.40) to get the title compound **5.12** as white solid with 95% yield (61 mg).

^{1}H NMR (600 MHz, $CDCl_3$): δ 8.27 (d, J = 8.4 Hz, 1H), 8.14 (d, J = 8.3 Hz, 1H), 7.93 (d, J = 5.5 Hz, 2H), 7.84 (t, J = 7.4 Hz, 1H), 7.76 (t, J = 7.5 Hz, 1H), 7.40 (d, J = 6.6 Hz, 3H), 7.22 (t, J = 7.9 Hz, 2H), 7.01 (t, J = 7.4 Hz, 1H), 6.81 (d, J = 8.1 Hz, 2H).^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 157.4, 154.9, 149.9, 145.3, 136.0, 130.5, 130.4, 129.9, 129.5, 129.4, 128.6, 126.4, 124.5, 123.6, 116.5, 112.9, 112.0. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{22}H_{15}N_2O$ 323.1179; found 323.1181. FT-IR (KBr, selected band): 2232 cm^{-1} (CN).

3-phenoxy-2-phenyl-1,2,3,4-tetrahydroquinoline (5.13):



Scheme 5.21. Synthesis of **5.13**

In a reaction tube (25 mL), **5.2a** (149 mg, 0.5 mmol), Hantzsch ester (2.5 equiv.), 3-trifluoromethylphenylboronic acid (25 mol%), and DCE (5 ml) were taken. Then the tube was properly closed and placed on a preheated oil bath at 60 °C with continuous stirring. After 12 h, volatile solvent was removed and the resulting crude compound was purified by silica gel column chromatography using petroleum ether/ ethyl acetate mixture as eluent (v/v = 50:1, R_f = 0.50) to get the title compound **5.13** as colourless oil with 95% yield (143 mg).

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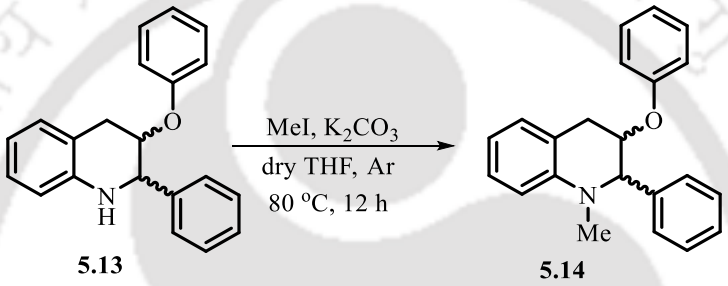
^{1}H NMR (500 MHz, $CDCl_3$): (*cis : trans* = 6:4) δ 7.40 (d, *J* = 7.0 Hz, 2H, major + minor), 7.31 – 7.27 (m, 3H, major + minor), 7.24 – 7.21 (m, 2H, major + minor), 7.07 (t, *J* = 7.5 Hz, 1H, major + minor), 6.98 (d, *J* = 7.5 Hz, 1H, major + minor), 6.92 (t, *J* = 7.5 Hz, 1H, major + minor), 6.84 (d, *J* = 8.0 Hz, 2H, major + minor), 6.69 (t, *J* = 7.5 Hz, 1H, major + minor), 6.64 (d, *J* = 8.0 Hz, 1H, major + minor), 4.87 – 4.84 (m, 1H), 4.75 (brs, 1H), 4.23 (s, 1H), 3.13 (d, *J* = 4.0 Hz, 1H, minor, 40%), 3.10 (d, *J* = 4.0 Hz, 1H, major, 60%), 2.99 (d, *J* = 6.5 Hz, 1H, major, 60%), 2.96 (d, *J* = 6.5 Hz, 1H, minor, 40%). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 157.8, 143.9, 140.9, 130.1, 129.6, 128.3, 128.1, 127.9, 127.5, 121.3, 117.9, 116.4, 113.9, 73.1, 58.1, 30.8. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{21}H_{20}NO$ 304.1540; found 302.1547.

1-methyl-3-phenoxy-2-phenyl-1,2,3,4-tetrahydroquinoline (5.14) from 5.13:



Scheme 5.22. Synthesis of **5.14**

In a schlenk flask, **5.13** (0.5 mmol, 1 equiv.) was taken in dry THF (1.0 mL). To this solution, methyl iodide (3.0 mmol, 6 equiv.) and potassium carbonate (1.5 mmol, 3 equiv.) was added was under nitrogen flow. The reaction mixture was then stirred for 12h at 80 °C. After completion of the reaction, the solution was concentrated in vacuo and extracted with ethyl acetate three times. The organic layers were dried over Na_2SO_4 and removed under vacuum. The resulting crude compound was then purified by using silica gel column chromatography using petroleum ether/ ethyl acetate mixture as eluent (v/v = 2:50, R_f = 0.50) to get the title compound **5.14** as light brown oil with 68% yield (107 mg).

^{1}H NMR (600 MHz, $CDCl_3$):): (*cis : trans* = 6:4) δ 7.31 (t, *J* = 7.2 Hz, 2H, major + minor), 7.26 – 7.25 (m, 3H, major + minor), 7.20 (t, *J* = 7.8 Hz, 1H, major + minor), 7.09 – 7.08 (m, 2H, major + minor), 7.02 (d, *J* = 7.2 Hz, 1H, major + minor), 6.99 – 6.96 (m, 3H, major + minor), 6.71 – 6.67 (m, , 2H, major + minor), 5.05 – 5.03 (m, 1H, major + minor), 4.79 (brs, 1H), 3.00 (d, *J* = 4.8 Hz, minor, 40%), 2.97 (d, *J* = 4.2 Hz, 1H, major, 60%), 2.93 (s, 3H, major + minor), 2.89 – 2.86 (m, 1H, minor, 40%), 2.84 – 2.82 (m, 1H, major, 60%). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 157.5, 145.5, 138.5, 129.8, 129.7, 128.3, 128.2, 128.1, 127.6, 121.3, 119.0, 116.5, 115.9, 109.8, 71.9, 65.0, 38.2, 30.1. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{22}H_{22}NO$ 316.1696; found 316.1705.

3-(benzyloxy)-2-phenylquinoline (5.15) from 5.3a:

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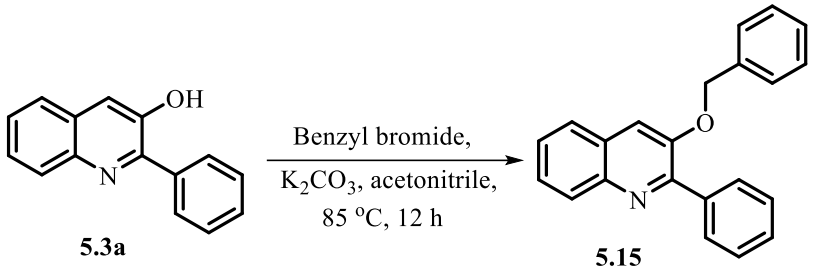
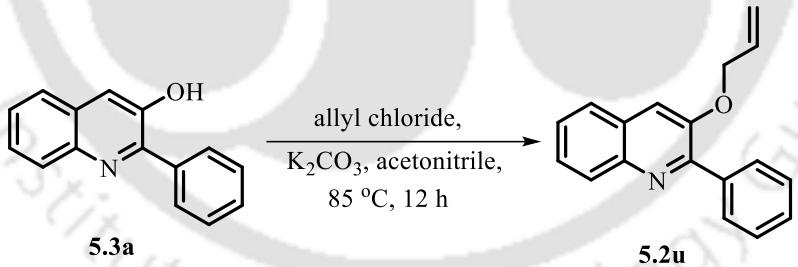


Scheme 5.23. Synthesis of **5.15**

In a pressure tube, **5.3a** (0.2 mmol, 1 equiv.) was taken in acetonitrile (1.0 mL). To this solution benzyl bromide (0.6 mmol, 3 equiv.) and potassium carbonate (0.6 mmol, 3 equiv.). The reaction mixture was then stirred for 12 h at 85 °C. After completion of the reaction the solution was concentrated in vacuo and extracted with ethyl acetate three times. The organic layers were dried over Na_2SO_4 and removed under vacuum. The resulting crude compound was then purified by using silica gel column chromatography using petroleum ether/ ethyl acetate mixture as eluent (v/v = 1:10, R_f = 0.40) to get the title compound **5.15** as white solid with 90% yield (56 mg).

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.11 (d, J = 8.4 Hz, 1H), 8.04 – 8.01 (m, 2H), 7.72 (d, J = 8.8 Hz, 1H), 7.59 – 7.56 (m, 1H), 7.56 (s, 1H), 7.51 – 7.46 (m, 4H), 7.43 – 7.34 (m, 5H), 5.26 (s, 2H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 152.4, 150.8, 143.4, 138.0, 136.4, 130.0, 129.5, 128.9, 128.8, 128.7, 128.1, 127.2, 127.1, 126.9, 126.4, 114.8, 70.6. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{22}H_{18}NO$ 312.1383; found 312.1375.

3-(allyloxy)-2-phenylquinoline (5.2u) from 5.3a:



Scheme 5.24. Synthesis of **5.2u**

In a pressure tube **5.3a** (0.2 mmol, 1 equiv.) was taken in acetonitrile (1.0 mL). To this solution allyl chloride (0.6 mmol, 3 equiv.) and potassium carbonate (0.6 mmol, 3 equiv.). The reaction mixture was then stirred for 12 h at 85 °C. After completion of the reaction the solution was concentrated in vacuo and extracted with ethyl acetate three times. The organic layers were dried over Na_2SO_4 and removed under vacuum. The resulting crude compound was then purified by using silica gel column chromatography using petroleum ether/ ethyl acetate mixture as eluent (v/v = 1:10, R_f = 0.50) to get the title compound **5.2u** as colourless oil with 88% yield (46 mg).

3-(4-methoxyphenoxy)-2-phenylquinoline(5.2c) from 5.3a:

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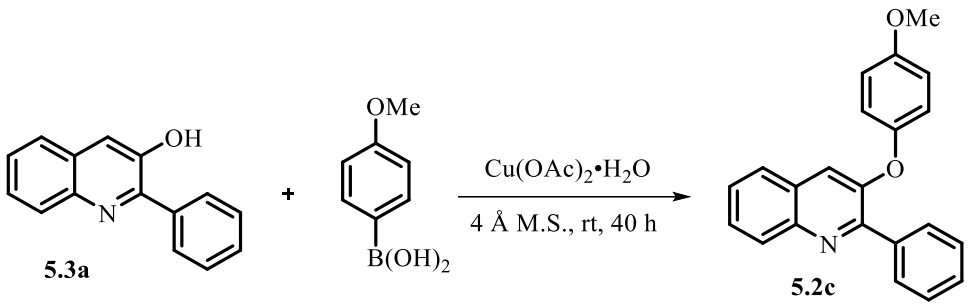
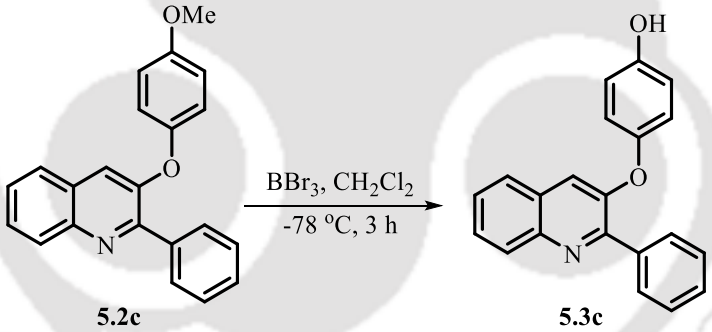


Scheme 5.25. Synthesis of **5.2c**

In a reaction tube **5.3a** (0.2 mmol, 1 equiv.), 4-Methoxyphenylboronic acid (0.2 mmol, 1.0 equiv.), $Cu(OAc)_2•H_2O$ (0.16 mmol, 0.7 equiv.), 4 Å M.S. and DCE (1 mL) was taken. The reaction mixture was allowed to stirred on a preheated oil bath at 60 °C with continuous stirring for 40 h at room temperature. After completion of the reaction, the reaction mixture was then passed through a bed of celite, the filtrate was collected and concentrated under reduced pressure. The crude reaction mixture was purified by petroleum ether/ ethyl acetate mixture as eluent (v/v = 50:3, R_f = 0.40) to get the tittle compound **5.2c** as white with 50% yield (33 mg).

4-((2-phenylquinolin-3-yl)oxy)phenol (5.3c) from 5.2c:



Scheme 5.26. Synthesis of **5.3c**

In a schlenk flask, **5.2c** (0.2 mmol, 1 equiv.) was taken in dry DCM and cooled the solution to -20 °C. To this solution, BBr_3 (0.6 mmol, 3 equiv.) was added dropwise over the time period of 30 minutes under an inert atmosphere. The reaction was allowed to stirrer for about 3h at -78 °C until all the substrate was consumed which is monitored by TLC. After completion of the reaction the solution was allowed to warm to room temperature. The reaction mixture was quenched with saturated NaCl solution and then extracted three times with ethyl acetate. The solution was then dried over anhydrous Na_2SO_4, and the solvent was removed in vacuum. The crude compound was purified by column chromatography using petroleum ether/ ethyl acetate mixture as eluent (v/v = 1:10, R_f = 0.50) to get the title compound **5.3c** as yellow solid with 70% yield (44 mg).

2-phenylquinolin-3-yl (S)-2-(6-methoxynaphthalen-2-yl)propanoate (5.16) from 5.3a:

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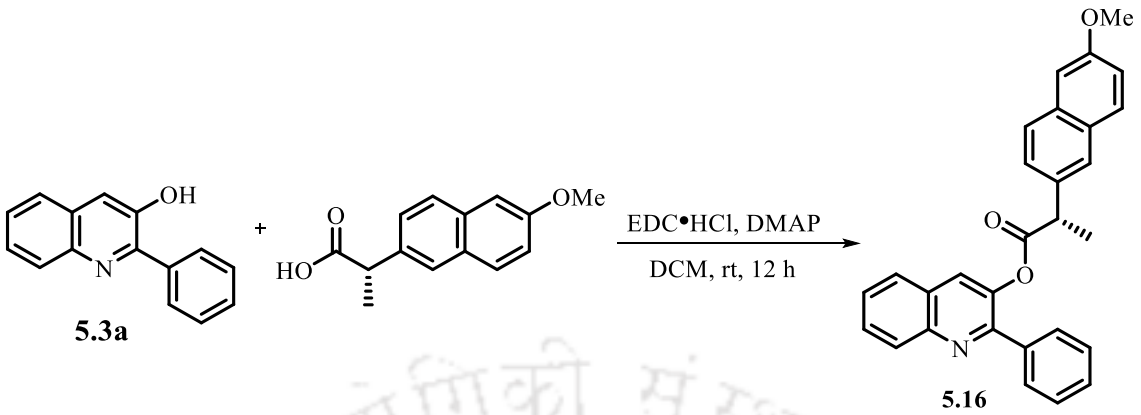
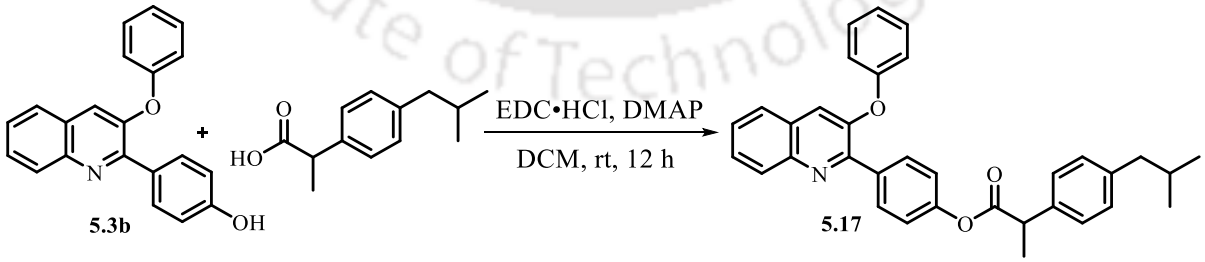


Scheme 5.27. Synthesis of **5.16**

In a pressure tube, 2-phenylquinolin-3-ol (0.2 mmol, 1 equiv.) was taken in DCM (2.0 mL). To this (*S*)-2-(6-Methoxynaphthalen-2-yl)propanoic acid (0.4 mmol, 2 equiv.), EDC•HCl (0.6 mmol, 3 equiv.) and DMAP (0.05 mmol, 0.25 equiv.) was added. The reaction mixture was then stirred for 12 h at room temperature. After completion of the reaction the solution was concentrated in vacuum. The resulting crude compound was then purified by using silica gel column chromatography using petroleum ether/ ethyl acetate mixture as eluent (v/v = 1:10, R_f = 0.40) to get the title compound **5.16** as white solid with 91% yield (78 mg).

^{1}H NMR (600 MHz, $CDCl_3$): δ 8.14 (d, J = 8.4 Hz, 1H), 7.88 (s, 1H), 7.77 (d, J = 7.8 Hz, 1H), 7.71 – 7.68 (m, 3H), 7.62 – 7.59 (m, 3H), 7.53 (t, J = 7.2 Hz, 1H), 7.34 (d, J = 9.6 Hz, 1H), 7.24 – 7.22 (m, 1H), 7.19 – 7.15 (m, 4H), 4.00 (q, J = 7.2 Hz, 1H), 3.95 (s, 3H), 1.61 (s, 3H), 1.55 (d, J = 7.2 Hz, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 172.9, 158.0, 154.0, 146.3, 134.4, 134.1, 129.6, 129.5, 129.5, 129.1, 129.1, 128.8, 128.2, 128.0, 127.5, 127.3, 127.2, 126.5, 126.2, 119.2, 105.7, 55.5, 45.7, 18.5. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{29}H_{24}NO_3$ 434.1751; found 434.1755.

4-(3-phenoxyquinolin-2-yl)phenyl 2-(4-isobutylphenyl)propanoate (5.17) from 5.3b:



Scheme 5.28. Synthesis of **5.17**

In a pressure tube, **5.3b** (0.2 mmol, 1 equiv.) was taken in DCM (2.0 mL). To this 2-(4-Isobutylphenyl)propanoic acid (0.4 mmol, 2 equiv.), EDC•HCl (0.6 mmol, 3 equiv.) and DMAP (0.05 mmol, 0.25 equiv.) was added. The reaction mixture was then stirred for 12 h at room

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temperature. After completion of the reaction, the solution was concentrated in vacuum. The resulting crude compound was then purified by using silica gel column chromatography using petroleum ether/ ethyl acetate mixture as eluent (v/v = 1:10, R_f = 0.40) to get the tittle compound **5.17** as colourless oil with 75% yield (75 mg).

^{1}H NMR (600 MHz, $CDCl_3$): δ 8.13 (d, J = 8.4 Hz, 1H), 8.07 – 8.06 (d, J = 8.4 Hz, 2H), 7.64 – 7.62 (m, 2H), 7.55 (s, 1H), 7.50 – 7.47 (m,1H), 7.37 (t, J = 7.8 Hz, 2H), 7.30 (d, J = 7.8 Hz, 2H), 7.18 – 7.14 (m, 3H), 7.11 (d, J = 8.4 Hz, 2H), 7.05 (d, J = 7.8 Hz, 2H), 3.95 (q, J = 7.2 Hz, 1H), 2.47 (d, J = 7.2 Hz, 2H), 1.89 – 1.83 (m, 1H), 1.62 (s, 3H), 0.91 (d, J = 6.6 Hz, 6H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 173.2, 156.4, 151.9, 149. 9, 141.0, 137.4, 135.0, 130.9, 130.2, 129.7, 129.5, 128.4, 128.3, 127.4, 127.17, 126.7, 124.3, 122.0, 121.3, 119.5, 45.5, 45.2, 30.3, 22.5, 18.7. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{34}H_{31}NO_3$ 502.2377; found 502.2382.

F. Crystallographic data

Crystallographic data of 5.2a:

Single crystals of compound **5.2a** suitable for X-ray diffraction were obtained by slow evaporation of the saturated solution of the compound in $CHCl_3$ at room temperature. X-ray crystallographic data were collected using Bruker D8 QUEST diffractometer. Data refinement and cell reduction were carried out by *APEX4*. Structures were solved by direct methods using Olex2 v1.5 and refined by a full-matrix least-squares method using Olex2 v1.5. All of the non-H atoms were refined anisotropically. The ORTEP diagram was obtained with ORTEP3 software with 50% thermal ellipsoid (see below, Figure 5.7). The crystallographic parameters and refinement data were listed in Table 5.6.

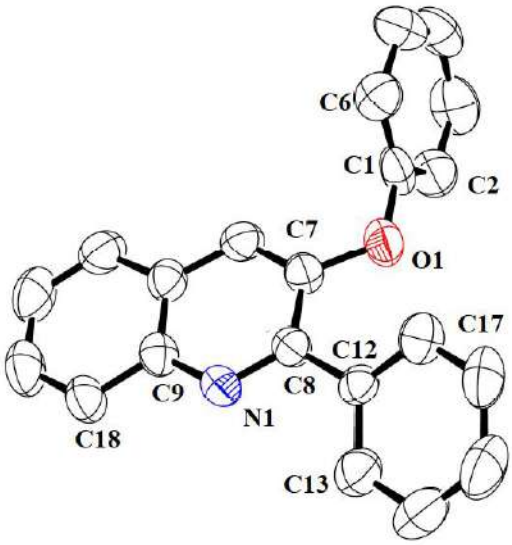

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Figure 5.7. Molecular structure of compound **5.2a** (thermal ellipsoid 50% probability level). Selected Bond lengths (in Å): O1-C1 1.394(5), O1-C7 1.386(5), N1-C8 1.318(5), N1-C9 1.376(5), C7-C8 1.428(6). Selected Bond Angles (in °): C7-O1-C1 119.4(3), C8-N1-C9 119.8(4), O1-C7-C8 115.8(4), C11-C7-O1 123.5(4).

Table 5.6. Crystal data and structure refinement for **5.2a**

Identification code	PA_LIGN_Q	
CCDC	2347692	
Empirical formula	$C_{42}H_{30}N_2O_2$	
Formula weight	594.68	
Temperature	297 K	
Wavelength	0.71073 Å	
Crystal system	triclinic	
Space group	P-1	
Unit cell dimensions	a = 10.9446(12) Å	α = 98.612(3)°
	b = 11.0130(11) Å	β = 100.767(3)°
	c = 15.4815(16) Å	γ = 116.484(3)°
Volume	1582.1(3) $Å^3$	
Z	2	
Density (calculated)	1.248 g/cm^3	
Absorption coefficient	0.077 mm^{-1}	
F(000)	624.0	
Crystal size	0.24 × 0.22 × 0.20 mm^3	
2Θ range for data collection	2.778 to 48.994°	
Index ranges	$-12 \leq h \leq 12$, $-12 \leq k \leq 12$, $-18 \leq l \leq 18$	
Reflections collected	30619	
Independent reflections	5104 [R_{int} = 0.0575, R_{sigma} = 0.0451]	
Completeness to theta = 24.497°	97.0%	
Data/restraints/parameters	5104/0/415	
Goodness-of-fit on F^2	1.122	

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Final R indexes [I>=2σ (I)]	R_1 = 0.0986, wR_2 = 0.2212
Final R indexes [all data]	R_1 = 0.1354, wR_2 = 0.2497
Largest diff. peak and hole	0.34 and -0.23 e $Å^{-3}$

Crystallographic data of 5.2f:

Single crystals of compound **5.2f** suitable for X-ray diffraction were obtained by slow evaporation of the saturated solution of the compound in $CHCl_3$ at room temperature. X-ray crystallographic data were collected using Bruker D8 QUEST diffractometer. Data refinement and cell reduction were carried out by *APEX4*. Structures were solved by direct methods using Olex2 v1.5 and refined by a full-matrix least-squares method using Olex2 v1.5. All of the non-H atoms were refined anisotropically. The ORTEP diagram was obtained with ORTEP3 software with 50% thermal ellipsoid (see below, Figure 5.8). The crystallographic parameters and refinement data were listed in Table 5.7.

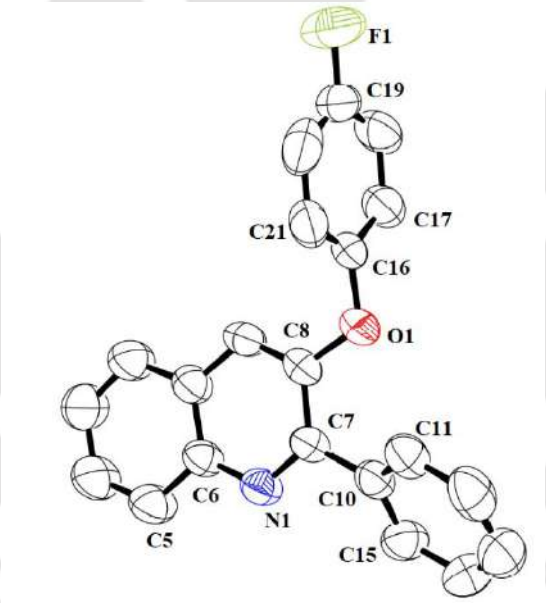

Figure 5.8. Molecular structure of compound **5.2f** (thermal ellipsoid 50% probability level). Selected Bond lengths (in Å): F1-C19 1.357(3), O1-C8 1.380(3), O1-C16 1.397(3), O1-C22 1.279(5), N1-C6 1.367(3), N1-C7 1.316(3), C7-C8 1.424(3). Selected Bond Angles (in °): C8-O1-C16 118.20(18), C7-N1-C6 119.65(19), N1-C6-C5 118.6(2), O1-C8-C7 115.3(2), F1-C19-C18 118.7(3).

Table 5.7. Crystal data and structure refinement for **5.2f**

Identification code	AH_PA_40
CCDC	2347691

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Empirical formula	$C_{21}H_{14}FNO$	
Formula weight	315.33	
Temperature	295 K	
Wavelength	0.71073 Å	
Crystal system	monoclinic	
Space group	$P2_1/n$	
Unit cell dimensions	a = 9.8424(7) Å	α = 90°
	b = 10.3061(7) Å	β = 93.515(2)°
	c = 16.0655(11) Å	γ = 90°
Volume	1626.57(19) $Å^3$	
Z	4	
Density (calculated)	1.288 g/cm^3	
Absorption coefficient	0.087 mm^{-1}	
F(000)	656.0	
Crystal size	0.39 × 0.35 × 0.30 mm^3	
2Θ range for data collection	4.698 to 52.914°	
Index ranges	$-12 \leq h \leq 12, -12 \leq k \leq 12, -20 \leq l \leq 20$	
Reflections collected	40066	
Independent reflections	3330 [R_{int} = 0.0544, R_{sigma} = 0.0306]	
Completeness to theta = 26.457°	99.3%	
Data/restraints/parameters	3330/0/217	
Goodness-of-fit on F^2	1.154	
Final R indexes [I>=2σ (I)]	R_1 = 0.0642, wR_2 = 0.1241	
Final R indexes [all data]	R_1 = 0.1152, wR_2 = 0.1516	
Largest diff. peak and hole	0.18 and -0.18 e $Å^{-3}$	

Crystallographic data of 5.2h:

Single crystals of compound **5.2h** suitable for X-ray diffraction were obtained by slow evaporation

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of the saturated solution of the compound in CH_3CN at room temperature. X-ray crystallographic data were collected using Bruker D8 QUEST diffractometer. Data refinement and cell reduction were carried out by *APEX4*. Structures were solved by direct methods using Olex2 v1.5 and refined by a full-matrix least-squares method using Olex2 v1.5. All of the non-H atoms were refined anisotropically. The ORTEP diagram was obtained with ORTEP3 software with 50% thermal ellipsoid (see below, Figure 5.9). The crystallographic parameters and refinement data were listed in Table 5.8.

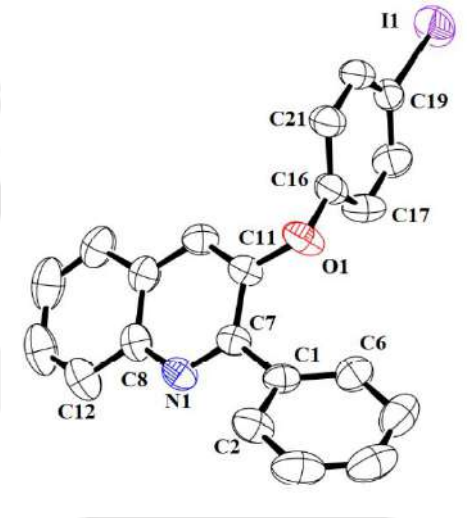

Figure 5.9. Molecular structure of compound **5.2h** (thermal ellipsoid 50% probability level). Selected Bond lengths (in Å): I1-C1 92.097(2), O1-C11 1.380(3), O1-C16 1.392(3), N1-C7 1.320(3), N1-C8 1.369(3), C7-C11 1.423(3). Selected Bond Angles (in °): C16-O1-C11 116.42(17), C8-N1-C7 118.98(19), C7-C11-O1 116.97(19), C18-C19-I1 120.04(17).

Table 5.8. Crystal data and structure refinement for **5.2h**

Identification code	PA_I_N	
CCDC	2347693	
Empirical formula	$C_{21}H_{14}INO$	
Formula weight	423.256	
Temperature	297 K	
Wavelength	0.71073 Å	
Crystal system	triclinic	
Space group	P-1	
Unit cell dimensions	a = 9.7474(5) Å	α = 88.270(1)°

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	b = 9.9183(5) Å	β = 73.649(1)°
	c = 10.3831(5) Å	γ = 64.637(1)°
Volume	865.63(8) $Å^3$	
Z	2	
Density (calculated)	1.624 g/cm^3	
Absorption coefficient	1.856 mm^{-1}	
F(000)	415.4	
Crystal size	0.36 × 0.30 × 0.21 mm^3	
2Θ range for data collection	4.12 to 50.06°	
Index ranges	$-11 \leq h \leq 11$, $-11 \leq k \leq 11$, $-12 \leq l \leq 12$	
Reflections collected	18709	
Independent reflections	2977 [R_{int} = 0.0290, R_{sigma} = 0.0178]	
Completeness to theta = 25.030°	97.0%	
Data/restraints/parameters	2977/0/217	
Goodness-of-fit on F^2	1.079	
Final R indexes [I>=2σ (I)]	R_1 = 0.0262, wR_2 = 0.0608	
Final R indexes [all data]	R_1 = 0.0608, wR_2 = 0.0630	
Largest diff. peak and hole	0.61 and -0.60 e $Å^{-3}$	

Crystallographic data of 5.2q:

Single crystals of compound **5.2q** suitable for X-ray diffraction were obtained by slow evaporation of the saturated solution of the compound in CH_3CN at room temperature. X-ray crystallographic data were collected using Bruker D8 QUEST diffractometer. Data refinement and cell reduction were carried out by *APEX4*. Structures were solved by direct methods using Olex2 v1.5 and refined by a full-matrix least-squares method using Olex2 v1.5. All of the non-H atoms were refined anisotropically. The ORTEP diagram was obtained with ORTEP3 software with 50% thermal ellipsoid (see below, Figure 5.10). The crystallographic parameters and refinement data were listed in Table 5.9.

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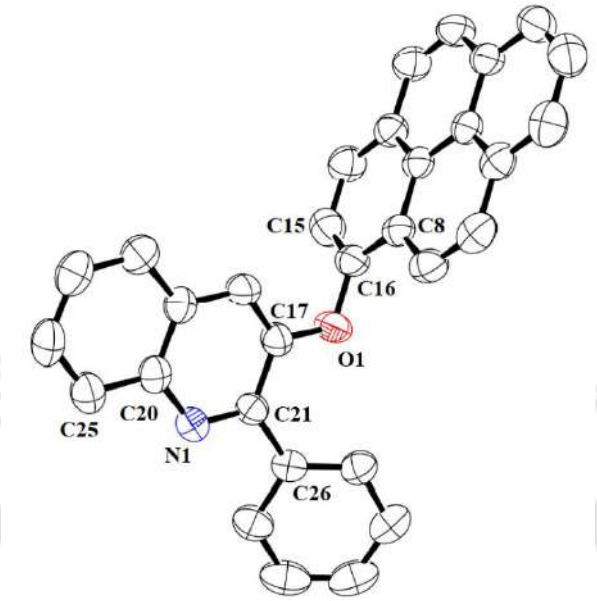

Figure 5.10. Molecular structure of compound **5.2q** (thermal ellipsoid 50% probability level). Selected Bond lengths (in Å): O1-C16 1.406(3), O1-C17 1.380(3), N1-C20 1.366(3), N1-C21 1.321(3), C17-C21 1.429(3). Selected Bond Angles (in °): C17-O1-C16 117.16(19), C21-N1-C20 119.8(2), N1-C21-C26 115.6(2), C8-C16-O1 118.7(2), N1-C20-C19 122.2(2), N1-C20-C25 118.8(2).

Table 5.9. Crystal data and structure refinement for **5.2q**

Identification code	PA_1115	
CCDC	2349816	
Empirical formula	$C_{31}H_{19}NO$	
Formula weight	421.47	
Temperature	300.00 K	
Wavelength	0.71073 Å	
Crystal system	triclinic	
Space group	P-1	
Unit cell dimensions	a = 9.7290(9) Å	α = 82.158(2) °
	b = 10.2569(9) Å	β = 81.034(3) °
	c = 10.7927(10)Å	γ = 84.630(3) °

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Volume	1051.01(17) $Å^3$
Z	2
Density (calculated)	1.332 g/cm^3
Absorption coefficient	0.080 mm^{-1}
F(000)	440.0
Crystal size	0.25 × 0.21 × 0.17 mm^3
2Θ range for data collection	3.85 to 50.874°
Index ranges	$-11 \leq h \leq 11$, $-12 \leq k \leq 12$, $-13 \leq l \leq 12$
Reflections collected	23376
Independent reflections	3835 [R_{int} = 0.0435, R_{sigma} = 0.0351]
Completeness to theta = 25.437°	98.7%
Data/restraints/parameters	3835/0/298
Goodness-of-fit on F^2	1.147
Final R indexes [I>=2σ (I)]	R_1 = 0.0649, wR_2 = 0.1203
Final R indexes [all data]	R_1 = 0.1009, wR_2 = 0.1381
Largest diff. peak and hole	0.18 and -0.21 e $Å^{-3}$

Crystallographic data of 5.5e:

Single crystals of compound **5.5e** suitable for X-ray diffraction were obtained by slow evaporation of the saturated solution of the compound in $CHCl_3$ at room temperature. X-ray crystallographic data were collected using Bruker D8 QUEST diffractometer. Data refinement and cell reduction were carried out by *APEX4*. Structures were solved by direct methods using Olex2 v1.5 and refined by a full-matrix least-squares method using Olex2 v1.5. All of the non-H atoms were refined anisotropically. The ORTEP diagram was obtained with ORTEP3 software with 50% thermal ellipsoid (see below, Figure 5.11). The crystallographic parameters and refinement data were listed in Table 5.10.

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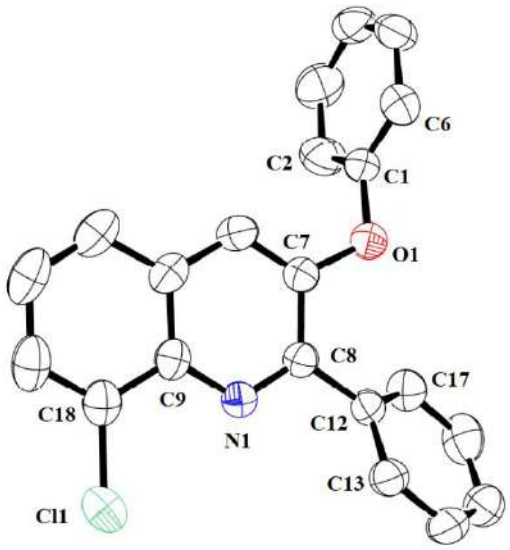

Figure 5.11. Molecular structure of compound **5.5e** (thermal ellipsoid 50% probability level). Selected Bond lengths (in Å): Cl1-C18 1.732(2), O1-C1 1.398(2), O1-C7 1.376(2), N1-C8 1.319(2), N1-C9 1.362(2), N1-C9 1.362(2). Selected Bond Angles (in °): C7-O1-C1 117.51(13), C9-N1-C8 119.47(14), C8-C7-O1 116.64(15), C9-C18-Cl1 119.14(14).

Table 5.10. Crystal data and structure refinement for **5.5e**

Identification code	AH_PA_1061	
CCDC	2347694	
Empirical formula	$C_{21}H_{14}ClNO$	
Formula weight	331.804	
Temperature	297 K	
Wavelength	0.71073 Å	
Crystal system	triclinic	
Space group	P-1	
Unit cell dimensions	a = 9.6282(4) Å	α = 78.651(1)°
	b = 10.0026(4) Å	β = 63.960(1)°
	c = 10.3941(4) Å	γ = 66.233(1) °
Volume	822.89(6)Å^3	
Z	2	
Density (calculated)	1.339 g/cm^3	

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Absorption coefficient	0.238 mm^{-1}
F(000)	344.5
Crystal size	0.32 × 0.27 × 0.21 mm^3
2Θ range for data collection	4.46 to 52.7°
Index ranges	$-12 \leq h \leq 12$, $-12 \leq k \leq 12$, $-12 \leq l \leq 12$
Reflections collected	14000
Independent reflections	3326 [R_{int} = 0.0495, R_{sigma} = 0.0381]
Completeness to theta = 26.350°	99.0%
Data/restraints/parameters	3326/0/217
Goodness-of-fit on F^2	1.112
Final R indexes [I>=2σ (I)]	R_1 = 0.0475, wR_2 = 0.1043
Final R indexes [all data]	R_1 = 0.0607, wR_2 = 0.1159
Largest diff. peak and hole	0.19 and -0.27 e $Å^{-3}$

Crystallographic data of 5.5k:

Single crystals of compound **5.5k** suitable for X-ray diffraction were obtained by slow evaporation of the saturated solution of the compound in CH_3CN at room temperature. X-ray crystallographic data were collected using Bruker D8 QUEST diffractometer. Data refinement and cell reduction were carried out by *APEX4*. Structures were solved by direct methods using Olex2 v1.5 and refined by a full-matrix least-squares method using Olex2 v1.5. All of the non-H atoms were refined anisotropically. The ORTEP diagram was obtained with ORTEP3 software with 50% thermal ellipsoid (see below, Figure 5.12). The crystallographic parameters and refinement data were listed in Table 5.11.

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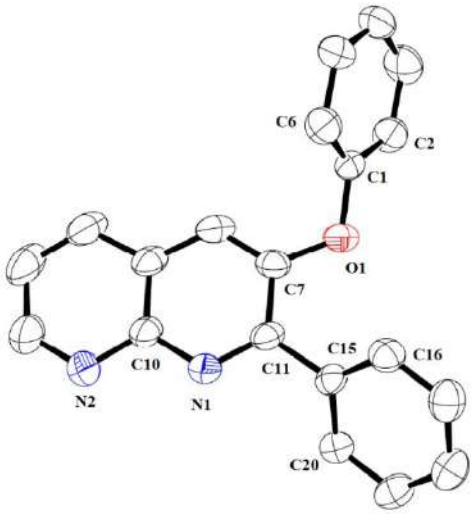

Figure 5.12. Molecular structure of compound **5.5k** (thermal ellipsoid 50% probability level). Selected Bond lengths (in Å): O1-C1 1.388(5), O1-C7 1.386(5), N1-C10 1.370(5), N1-C11 1.320(5), N2-C10 1.360(6), N2-C14 1.312(6), C7-C11 1.421(6). Selected Bond Angles (in °): C7-O1-C1 117.9(3), C11-N1-C10 118.7(4), C14-N2-C10 115.8(5), C6-C1-O1 117.4(4), N2-C10-N1 114.6(4), C9-C10-N1 121.9(4), C9-C10-N2 123.5(4), C7-C11-N1 121.9(4), C15-C11-N1 115.8(4)

Table 5.11. Crystal data and structure refinement for **5.5k**

Identification code	PA_917	
CCDC	2347695	
Empirical formula	$C_{20}H_{14}N_2O$	
Formula weight	298.347	
Temperature	296 K	
Wavelength	0.71073 Å	
Crystal system	monoclinic	
Space group	$P2_1/n$	
Unit cell dimensions	a = 13.6973(12) Å	α = 90°
	b = 9.7865(9) Å	β = 102.578(3)°
	c = 11.7031(10)Å	γ = 90(1) °
Volume	1531.1(2)$Å^3$	
Z	4	
Density (calculated)	1.294 g/cm^3	

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Absorption coefficient	0.081 mm^{-1}
F(000)	624.4
Crystal size	0.37 × 0.24 × 0.21 mm^3
2Θ range for data collection	5.16 to 50°
Index ranges	$-16 \leq h \leq 16$, $-11 \leq k \leq 11$, $-14 \leq l \leq 14$
Reflections collected	33515
Independent reflections	2694 [R_{int} = 0.0892, R_{sigma} = 0.0599]
Completeness to theta = 25.0°	100%
Data/restraints/parameters	2694/0/208
Goodness-of-fit on F^2	1.156
Final R indexes [I>=2σ (I)]	R_1 = 0.0999, wR_2 = 0.1443
Final R indexes [all data]	R_1 = 0.1459, wR_2 = 0.1640
Largest diff. peak and hole	0.52 and -0.49 e $Å^{-3}$

Crystallographic data of 5.12:

Single crystals of compound **5.12** suitable for X-ray diffraction were obtained by slow evaporation of the saturated solution of the compound in CH_3CN at room temperature. X-ray crystallographic data were collected using Bruker D8 QUEST diffractometer. Data refinement and cell reduction were carried out by *APEX4*. Structures were solved by direct methods using Olex2 v1.5 and refined by a full-matrix least-squares method using Olex2 v1.5. All of the non-H atoms were refined anisotropically. The ORTEP diagram was obtained with ORTEP3 software with 50% thermal ellipsoid (see below, Figure 5.13). The crystallographic parameters and refinement data were listed in Table 5.12.

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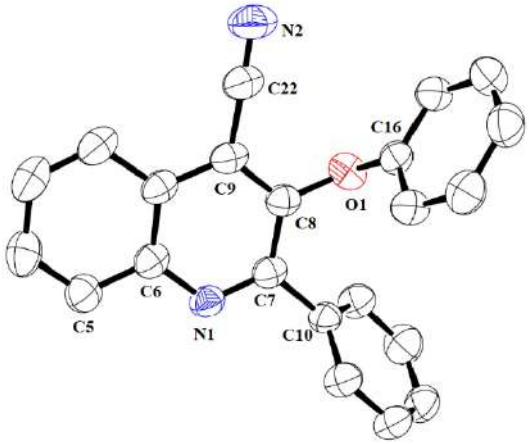

Figure 5.13. Molecular structure of compound **5.12** (thermal ellipsoid 50% probability level). Selected Bond lengths (in Å): O1-C8 1.3755(16), O1-C16 1.3997(16), N1-C6 1.3686(17), N1-C7 1.3208(17), N2-C22 1.1395(19), C9-C22 1.4410(19). Selected Bond Angles (in °): C8-O1-C16 117.41(10), C7-N1-C6 119.64(11), N1-C6-C1 122.43(13), N1-C6-C5 118.37(12), N1-C7-C8 121.51(12), N2-C22-C9 178.26(18).

Table 5.12. Crystal data and structure refinement for **5.12**

Identification code	PA_1116	
CCDC	2349817	
Empirical formula	$C_{22}H_{14}N_2O$	
Formula weight	322.35	
Temperature	299.00 K	
Wavelength	0.71073 Å	
Crystal system	monoclinic	
Space group	$P2_1/c$	
Unit cell dimensions	a = 12.8115(9) Å	α = 90 °
	b = 5.8300(4) Å	β = 103.523(2) °
	c = 22.4700(16) Å	γ = 90 °
Volume	1631.8(2) $Å^3$	
Z	4	
Density (calculated)	1.312 g/cm^3	
Absorption coefficient	0.082 mm^{-1}	

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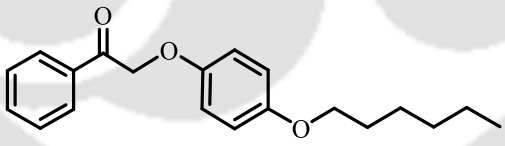
F(000)	672.0
Crystal size	0.28 × 0.23 × 0.12 mm^3
2Θ range for data collection	3.728 to 51.388°
Index ranges	$-15 \leq h \leq 15$, $-7 \leq k \leq 7$, $-27 \leq l \leq 27$
Reflections collected	36842
Independent reflections	3074 [R_{int} = 0.0476, R_{sigma} = 0.0200]
Completeness to theta = 25.694°	99.2%
Data/restraints/parameters	3074/0/226
Goodness-of-fit on F^2	1.102
Final R indexes [I>=2σ (I)]	R_1 = 0.0378, wR_2 = 0.0863
Final R indexes [all data]	R_1 = 0.0485, wR_2 = 0.0967
Largest diff. peak and hole	0.15 and -0.13 e $Å^{-3}$

5.6. Analytical data

A. For the starting materials

2-(4-(hexyloxy)phenoxy)-1-phenylethan-1-one (5.1d):



^{1}H NMR (400 MHz, $CDCl_3$): δ 8.01 – 7.99 (m, 2H), 7.61 (t, *J* = 7.6 Hz, 1H), 7.49 (t, *J* = 7.6 Hz, 2H), 6.90 – 6.87 (m, 2H), 6.83 – 6.80 (m, 2H), 5.22 (s, 2H), 3.89 (t, *J* = 6.4 Hz, 2H), 1.78 – 1.71 (m, 2H), 1.47 – 1.42 (m, 2H), 1.34 – 1.34 (m, 4H), 0.90 (t, *J* = 6.8 Hz, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 195.1, 154.2, 152.2, 134.8, 133.9, 128.9, 128.3, 116.1, 116.1, 115.7, 115.6, 72.0, 68.7, 31.7, 29.4, 25.9, 22.7, 14.2. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{20}H_{25}NO_3$ 313.1799; found 313.1804.

2-(4-(1H-imidazol-1-yl)phenoxy)-1-phenylethan-1-one (5.1j):

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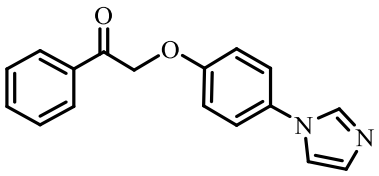
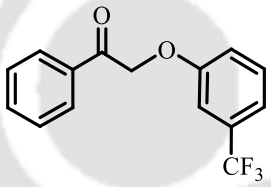


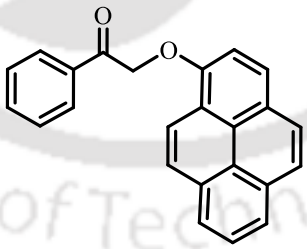
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.02 – 8.00 (m, 2H), 7.79 (brs, 1H), 7.67 – 7.63 (m, 1H), 7.55 – 7.53 (m 2H), 7.30 (d, *J* = 8.8 Hz, 2H), 7.20 – 7.19 (m, 2H), 7.03 (d, *J* = 8.8 Hz, 2H), 5.35 (s, 2H).^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 194.0, 157.5, 134.4, 134.3, 129.1, 128.2, 123.4, 116.8, 116.0, 70.9. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{17}H_{15}N_2O_2$ 279.1129; found 279.1139.

1-phenyl-2-(3-(trifluoromethyl)phenoxy)ethan-1-one (5.1l):



^{1}H NMR (600 MHz, $CDCl_3$): δ 8.00 (d, *J* = 7.8 Hz, 2H), 7.65 (t, *J* = 7.8 Hz, 1H), 7.54 – 7.50 (t, *J* = 7.8 Hz, 2H), 7.40 (t, *J* = 7.8 Hz, 1H), 7.26 – 7.25 (m, 1H), 7.19 (s, 1H), 7.12 – 7.10 (m, 1H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 193.7, 158.3, 134.4, 134.3, 130.3, 129.1, 128.2, 118.51 (q, *J* = 3.7 Hz), 118.2 112.0, 112.0, 70.8. ^{19}F{^{1}H} NMR (565 MHz, $CDCl_3$): δ -62.69. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{15}H_{12}NF_3O_2$ 281.0784; found 281.0788.

1-phenyl-2-(pyren-1-yloxy)ethan-1-one (5.1q):



^{1}H NMR (400 MHz, $CDCl_3$): δ 8.55 (d, *J* = 9.2 Hz, 1H), 8.14 – 8.07 (m, 5H), 8.00 – 7.90 (m, 3H), 7.65 – 7.62 (m, 1H), 7.53 – 7.48 (m, 3H), 5.62 (s, 2H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 194.8, 152.1, 134.8, 134.1, 131.8, 131.8, 129.0, 128.4, 127.3, 127.0, 126.4, 126.2, 126.1, 125.7, 125.4, 124.9, 124.7, 124.6, 121.4, 120.9, 109.7, 72.2. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{24}H_{17}NO_2$ 337.1224; found 337.1232.

2-(4-iodophenoxy)-1-(4-methoxyphenyl)ethan-1-one (5.1ah):

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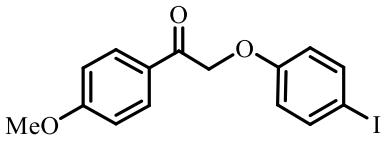
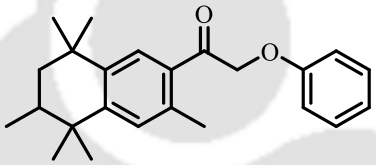


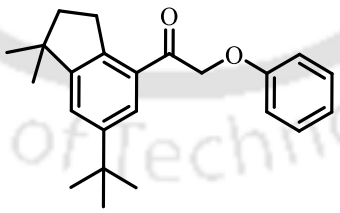
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.98 (d, J = 8.8 Hz, 2H), 7.55 (d, J = 9.2 Hz, 2H), 6.97 (d, J = 8.8 Hz, 2H), 6.71 (d, J = 9.2 Hz, 2H), 5.19 (s, 2H), 3.89 (s, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 192.7, 164.3, 158.2, 138.5, 130.6, 127.6, 117.3, 114.2, 83.9, 70.7, 55. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{15}H_{14}IO_3$ 368.9983; found 368.9988.

1-(3,5,5,6,8,8-hexamethyl-5,6,7,8-tetrahydronaphthalen-2-yl)-2-phenoxyethan-1-one (5.1am):



^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66 (s, 1H), 7.29 – 7.23 (m, 4H), 6.99 – 6.95 (m, 1H), 6.93 – 6.90 (m, 2H), 5.14 (s, 2H), 2.49 (s, 3H), 1.90 – 1.85 (m 1H), 1.67 – 1.60 (m, 1H), 1.42 – 1.38 (m, 1H), 1.32 (d, J = 6.0 Hz, 6H), 1.26 (s, 3H), 1.07 (s, 3H), 1.00 (d, J = 6.8 Hz, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 197.8, 158.2, 151. 1, 142.4, 136.2, 132.2, 131.0, 129.7, 127.6, 121.6, 114.8, 71.8, 43.5, 38.1, 34.5, 34.2, 32.6, 32.1, 28.4, 24.8, 21.3, 16.9. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{24}H_{31}O_2$ 351.2319; found 351.2320.

1-(6-(tert-butyl)-1,1-dimethyl-2,3-dihydro-1H-inden-4-yl)-2-phenoxyethan-1-one (5.1an):



^{1}H NMR (600 MHz, $CDCl_3$): δ 7.72 (brs, 1H), 7.39 (brs, 1H), 7.30 – 7.27 (m, 2H), 6.99 – 6.95 (m, 1H), 6.94 (d, J = 7.8 Hz, 2H), 5.24 (s, 2H), 3.18 (t, J = 7.2 Hz, 2H), 1.95 (t, J = 7.2 Hz, 2H), 1.36 (s, 9H), 1.27 (s, 6H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 196.3, 158.2, 154.9, 150.2, 141.9, 129.7, 124.2, 123.6, 121.6, 114.9, 71.7, 43.6, 41.5, 34.9, 31.6, 30.7, 30.2, 28.9. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{23}H_{29}O_2$ 337.2163; found 337.2169.

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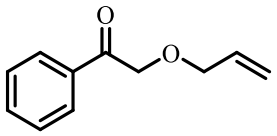
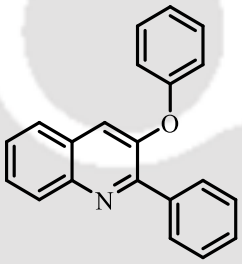
2-(allyloxy)-1-phenylethan-1-one (5.1t):



^{1}H NMR (600 MHz, $CDCl_3$): δ 7.93 (d, J = 7.2 Hz, 2H), 7.58 (t, J = 7.2 Hz, 1H), 7.47 (t, J = 7.2 Hz, 2H), 5.99 – 5.93 (m, 1H), 5.33 (d, J = 17.4 Hz, 1H), 5.25 (d, J = 10.2 Hz, 1H), 4.76 (s, 2H), 4.16 (d, J = 5.4 Hz, 2H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 196.4, 135.1, 134.1, 133.7, 128.8, 128.0, 118.4, 72.7, 72.6. The spectral data is in accordance with the literature.[28]

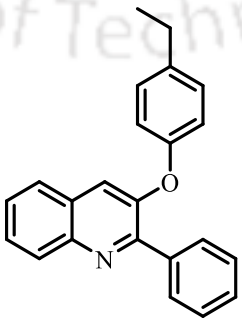
Analytical data for the products

3-phenoxy-2-phenylquinoline (5.2a):



Using **GP-V** the title compound **5.2a** was isolated as light yellow solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:2, R_f = 0.50); (102 mg, 86%). M.p. 129-131 ºC. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.17 (d, J = 8.4 Hz, 1H), 8.06 – 8.05 (m, 2H), 7.67 – 7.63 (m, 2H), 7.58 (s, 1H), 7.51 – 7.46 (m, 3H), 7.46 – 7.42 (m, 1H), 7.39 – 7.36 (m, 2H), 7.17 – 7.15 (m, 1H), 7.09 – 7.06 (m, 2H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 156.6, 153.1, 149.9, 144.9, 137.6, 130.2, 129.8, 129.6, 129.1, 128.5, 128.3, 128.3, 127.0, 126.7, 124.2, 122.0, 119.5. The spectral data is in accordance with the literature.[5]

3-(4-ethylphenoxy)-2-phenylquinoline (5.2b):



Using **GP-V** the title compound **5.2b** was isolated as yellow oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:2, R_f = 0.40); (106 mg, 81%).^{1}H

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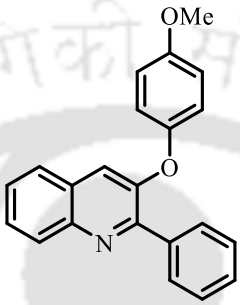
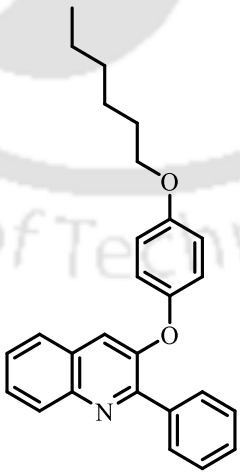
NMR (600 MHz, $CDCl_3$): δ 8.15 (d, J = 8.4 Hz, 1H), 8.07 (d, J = 7.8 Hz, 2H), 7.65 – 7.61 (m, 2H), 7.52 (s, 1H), 7.48 (t, J = 7.8 Hz, 3H), 7.43 (t, t, J = 7.8 Hz, 1H), 7.22 (d, J = 8.4 Hz, 2H), 7.02 (d, J = 8.4 Hz, 2H), 2.67 (q, J = 7.2 Hz, 2H), 1.26 (t, J = 7.2 Hz, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 154.1, 152.8, 144.6, 140.4, 137.6, 129.8, 129.5, 129.1, 128.5, 128.3, 128.1, 127.0, 126.6, 121.0, 119.7, 28.3, 15.8. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{23}H_{20}NO$ 326.1540; found 326.1544.

3-(4-methoxyphenoxy)-2-phenylquinoline (5.2c):



Using **GP-V** the title compound **5.2c** was isolated as white solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:3, R_f = 0.40); (109 mg, 83%). ^1H NMR (600 MHz, $CDCl_3$): δ 8.15 (d, J = 8.4 Hz, 1H), 8.10 – 8.07 (d, J = 7.2 Hz, 2H), 7.62 – 7.60 (m, 2H), 7.51 – 7.45 (m, 4H), 7.43 (s, 1H), 7.06 (d, J = 9.0 Hz, 2H), 6.95 (d, J = 9.0 Hz, 2H), 3.83 (s, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 156.6, 152.5, 151.2, 149.3, 144.4, 137.6, 129.8, 129.5, 129.1, 128.5, 128.3, 128.0, 127.0, 126.6, 121.4, 119.8, 115.3, 55.8. The spectral data is in accordance with the literature.[5]

3-(4-(hexyloxy)phenoxy)-2-phenylquinoline (5.2d):



Using **GP-V** the title compound **5.2d** was isolated as colourless oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:2, R_f = 0.50); (98 mg, 62%). ^1H NMR

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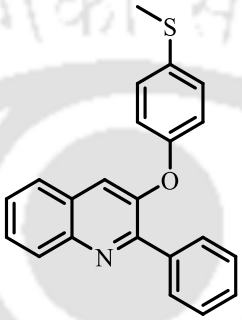
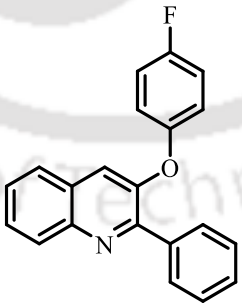
(600 MHz, $CDCl_3$): δ 8.17 – 8.13 (m, 1H), 8.08 (d, J = 7.8 Hz, 2H), 7.62 – 7.59 (m, 2H), 7.55 – 7.52 (m, 1H), 7.49 – 7.45 (m, 3H), 7.42 (s, 1H), 7.04 (d, J = 9.0 Hz, 2H), 6.93 (d, J = 9.0 Hz, 2H), 3.96 (t, J = 6.6 Hz, 2H), 1.81 – 1.78 (m, 2H), 1.36 – 1.35 (m, 3H), 0.93 – 0.91 (m, 3H), 0.89 – 0.88 (m, 3H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 156.2, 152.5, 149.2, 129.8, 129.5, 129.1, 129.0, 128.3, 127.9, 127.0, 126.6, 121.3, 119.8, 115.9, 68.7, 31.8, 29.9, 29.4, 25.9, 22.8, 14.2. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{27}H_{27}NO_2$ 398.2115; found 398.2122.

3-(4-(methylthio)phenoxy)-2-phenylquinoline (5.2e):



Using **GP-V** the title compound **5.2e** was isolated as yellow oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:3, R_f = 0.40); (112 mg, 82%). ^1H NMR (400 MHz, $CDCl_3$): δ 8.16 (d, J = 8.4 Hz, 1H), 8.04 – 8.02 (m, 2H), 7.66 – 7.63 (m, 2H), 7.56 (s, 1H), 7.56 – 7.44 (m, 4H), 7.30 – 7.28 (m, 2H), 7.02 – 7.00 (m, 2H), 2.49 (s, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 154.4, 152.9, 149.9, 144.8, 137.4, 133.6, 129.7, 129.6, 129.2 129.2, 128.4, 128.4, 128.3, 127. 1, 126.7, 121.8, 120.1, 17.0. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{28}H_{18}NOS$ 344.1104; found 344.1109.

3-(4-fluorophenoxy)-2-phenylquinoline (5.2f):



Using **GP-V** the title compound **5.2f** was as light yellow solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:3, R_f = 0.50); (95 mg, 75%). M.p. 131-133 ºC. ^1H NMR (400 MHz, $CDCl_3$): δ 8.17 (d, J = 9.2 Hz, 1H), 8.05 – 8.03 (m, 2H), 7.67 – 7.62 (m, 2H), 7.51 – 7.44 (m, 6H), 7.09 – 7.04 (m, 4H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 160.1, 158.5, 152.8 152.1, 150.2, 144.8, 137.4, 129.7, 129.6, 129.2, 128.4, 128.35, 128.33, 127.1, 126.6,

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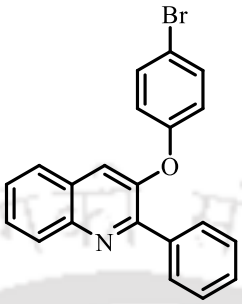
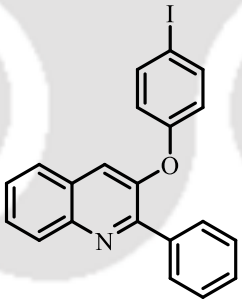
121.3, 121.1, 121.0, 116.9, 116.7. ^{19}F NMR (565 MHz, $CDCl_3$): δ -121.88. HRMS (ESI) *m/z:* $[M+H]^+$ calculated for $C_{21}H_{15}FNO$ 316.1133; found 316.1141.

3-(4-bromophenoxy)-2-phenylquinoline (5.2g):



Using **GP-V** the title compound **5.2g** was isolated as yellow oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.50); (117 mg, 78%). M.p. 140-142 ºC. ºC. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.17 (d, J = 8.4 Hz, 1H), 8.00 – (m, 2H), 7.70 – 7.65 (m, 2H), 7.61 (s, 1H), 7.54 – 7.50 (m, 1H), 7.48 – 7.44 (m, 5H), 6.92 (d, J = 8.8 Hz, 2H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 155.9, 149.1, 145.1, 137.3, 133.1, 129.6, 129.3, 128.7, 128.4, 128.3, 127.2, 126.8, 122.8, 120.8, 116.6. HRMS (ESI) *m/z:* $[M+H]^+$ calculated for $C_{21}H_{15}BrNO$ 376.0332; found 376.0336.

3-(4-iodophenoxy)-2-phenylquinoline (5.2h):



Using **GP-V** the title compound **5.2h** was isolated was isolated as white solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.50); (138 mg, 82%). M.p. 142-144 ºC. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.17 (d, J = 8.5 Hz, 1H), 7.99 (d, J = 7.0 Hz, 2H), 7.70 – 7.67 (m, 2H), 7.64 – 7.63 (m, 3H), 7.52 (t, J = 7.5 Hz, 1H), 7.47 – 7.42 (m, 3H), 6.80 (d, J = 8.5 Hz, 2H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 156.81, 153.14, 148.98, 145.19, 139.09, 137.25, 129.63, 129.6, 129.3, 128.7, 128.4, 128.3, 127.2, 126.8, 123.0, 121.1. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{21}H_{15}INO$ 424.0193; found 424.0194.

4-((2-phenylquinolin-3-yl)oxy)benzonitrile (5.2i):

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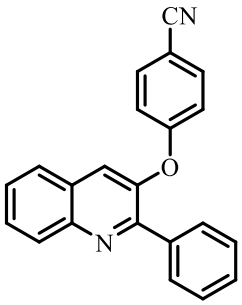
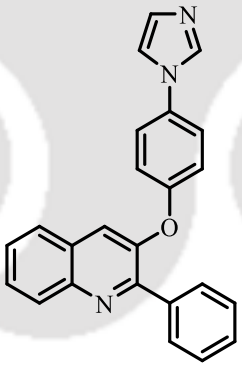


Using **GP-V** the title compound **5.2i** was isolated as white solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:3, R_f = 0.50); (90 mg, 70%). M.p. 145-147 ºC. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.21 (d, J = 8.4 Hz, 1H), 7.91 (d, J = 7.2 Hz, 2H), 7.83 (s, 1H), 7.78 (d, J = 8.4 Hz, 1H), 7.74 (t, J = 7.8 Hz, 1H), 7.58 (d, J = 7.8 Hz, 1H), 7.55 (d, J = 8.4 Hz, 1H), 7.43 – 7.39 (m, 3H), 6.98 (d, J = 8.4 Hz, 2H).^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 161.0, 153.6, 146.9, 146.0, 136.8, 134.4, 129.8, 129.5, 129.4, 129.4, 128.5, 128.2, 127.5, 127.0, 126.0, 118.7, 118.0, 106.6. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{22}H_{15}N_2O$ 323.1179; found 323.1181. FT-IR (KBr, selected band): 2234 cm^{-1} (CN).

3-(4-(1H-imidazol-1-yl)phenoxy)-2-phenylquinoline (5.2j):



Using **GP-V** the title compound **5.2j** was isolated as dark brown solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 2:10, R_f = 0.50); (117 mg, 81%). M.p. 140-142 ºC. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.19 (d, J = 9.0 Hz, 1H), 8.02 – 8.01 (m, 2H), 7.81 (s, 1H), 7.72 – 7.68 (m, 3H), 7.54 (t, J = 7.2 Hz, 1H), 7.48 – 7.43 (m, 3H), 7.35 – 7.34 (m, 2H), 7.23 (s, 1H), 7.20 (s, 1H), 7.13 – 7.12 (m, 2H) .^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 156.2, 153.2, 148.0, 145.3, 137.2, 135.8, 133.2, 130.3, 129.3, 128.8, 128.4, 128.3, 127.3, 126.8, 123.5, 123.4, 120.0, 118, 116.7, 116.0. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{24}H_{18}N_3O$ 364.1445; found 364.1450.

3-([1,1'-biphenyl]-4-yloxy)-2-phenylquinoline (5.2k):

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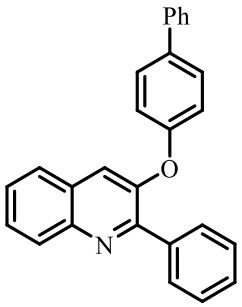
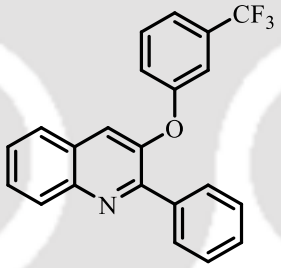


Using **GP-V** the title compound **5.2k** was isolated as white solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:2, R_f = 0.50); (124 mg, 83%). M.p. 99 -100 ºC. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.18 (d, J = 8.4 Hz, 1H), 8.08 – 8.07 (m, 2H), 7.69 (d, J = 7.8 Hz, 1H), 7.66 – 7.65 (m, 2H), 7.59 (t, J = 8.4 Hz, 4H), 7.51 – 7.44 (m, 6H), 7.35 (t, J = 7.8 Hz, 1H), 7.14 (d, J = 8.4 Hz, 2H).^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 156.1, 149.8, 145.0, 140.4, 137.5, 137.2, 129.8, 129.6, 129.2, 129.0, 128.9, 128.45, 128.38, 128.37, 127.38, 127.1, 127.1, 126.7, 122.3, 119.6. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{27}H_{20}NO$ 374.1540; found 374.1547.

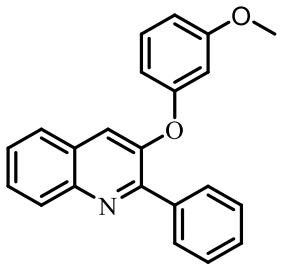
2-phenyl-3-(3-(trifluoromethyl)phenoxy)quinoline (5.2l):



Using **GP-V** the title compound **5.2l** as yellow oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.50); (105 mg, 72%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.22 (d, J = 8.4 Hz, 1H), 7.99 (d, J = 7.2 Hz, 2H), 7.73 – 7.69 (m, 2H), 7.68 (s, 1H), 7.55 (t, J = 7.2 Hz, 1H), 7.47 – 7.42 (m, 4H), 7.38 – 7.37 (m, 1H), 7.28 (s, 1H), 7.17 – 7.16 (m, 1H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 157.1, 153.2, 148.6, 145.2, 137.0, 132.6 (q, J = 33.0 Hz), 130.7, 129.6, 129.5, 129.4, 129.0, 128. 4, 128.3, 127.4, 126.9, 123.7, 121.9, 120.5, 115.8. ^{19}F NMR (565 MHz, $CDCl_3$): δ -62.70. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{22}H_{15}F_3NO$ 366.1101; found 366.1107.

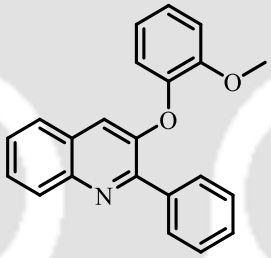
3-(3-methoxyphenoxy)-2-phenylquinoline (5.2m):

TH-3606_186122027



Using **GP-V** the title compound **5.2m** was isolated as yellow oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:2, R_f = 0.50); (99 mg, 76%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.17 (d, J = 8.4 Hz, 1H), 8.04 (d, J = 7.2 Hz, 2H), 7.68 – 7.64 (m, 2H), 7.62 (s, 1H), 7.52 – 7.46 (m, 3H), 7.44 – 7.42 (m, 1H), 7.28 – 7.25 (m, 1H) 6.72 – 6.70 (m, 1H), 6.65 – 6.64 (m, 1H), 6.63 – 6.62 (m, 1H), 3.78 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 161.3, 157.7, 153.0, 149.6, 144.9, 137.5, 130.6, 129.7, 129.6, 129.1, 128.4, 128.4, 128.3, 127.0, 126.7, 122.4, 111.4, 109.8, 105.4, 55.6. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{22}H_{18}NO_2$ 328.1333; found 328.1335.

3-(2-methoxyphenoxy)-2-phenylquinoline (5.2n):



Using **GP-V** the title compound **5.2n** was isolated as colourless oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:2, R_f = 0.50); (106 mg, 81%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.17 – 8.14 (m, 3H), 7.60 – 7.58 (m, 2H), 7.51 – 7.48 (m, 2H), 7.47 – 7.43 (m, 2H), 7.28 (s, 1H), 7.25 – 7.22 (m, 1H), 7.10 (d, J = 7.8 Hz, 1H), 7.05 (d, J = 8.2 Hz, 1H), 6.99 (t, J = 7.8 Hz, 1H), 3.79 (s, 3H). ^{13}C {^{1}H} NMR (151 MHz, $CDCl_3$): δ 152.1, 151.7, 150.9, 143.8, 137.8, 129.9, 129.5, 129.0, 128.5, 128.2, 127.6, 126.8, 126.5, 126.1, 122.5, 121.4, 118.2, 113.2, 56.0. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{22}H_{18}NO_2$ 328.1333; found 328.1342.

3-(3,4-dimethoxyphenoxy)-2-phenylquinoline (5.2o):

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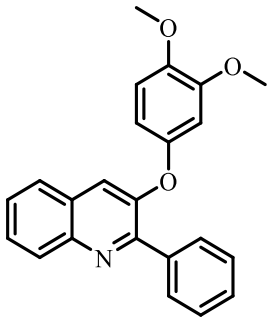
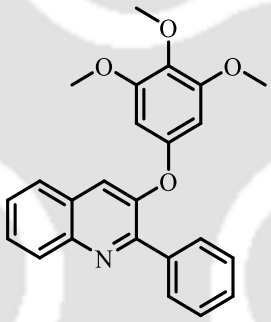


Using **GP-V** the title compound **5.2o** was isolated as yellow oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:2, R_f = 0.40); (131 mg, 92%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.15 (d, J = 8.4 Hz, 1H), 8.09 – 8.07 (m, 2H), 7.65 – 7.60 (m, 2H), 7.51 – 7.44 (m, 4H), 6.88 – 6.85 (m, 2H), 6.69 – 6.68 (m, 1H), 6.66 – 6.63 (m, 1H), 3.90 (s, 3H), 3.84 (s, 3H). ^{13}C {^{1}H} NMR (151 MHz, $CDCl_3$): δ 151.0, 150.3, 149.6, 146.1, 144. 4, 137.6, 129.8, 129.5, 129.2, 128.4, 128.0, 127.0, 126.6, 120.1, 111.9, 111.4, 104.8, 56.4, 56.2. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{23}H_{19}NO_3$ 358.1438; found 358.1435.

2-phenyl-3-(3,4,5-trimethoxyphenoxy)quinoline (5.2p):



Using **GP-V** the title compound **5.2p** was isolated as white solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:3, R_f = 0.30); (139 mg, 90%). M.p. 160-162 ºC. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.16 (d, J = 8.4 Hz, 1H), 8.07 – 8.05 (m, 2H), 7.69 – 7.62 (m, 2H), 7.56 (s, 1H), 7.52 – 7.44 (m, 4H), 6.33 (s, 2H), 3.85 (s, 3H), 3.79 (s, 6H). ^{13}C {^{1}H} NMR (151 MHz, $CDCl_3$): δ 154.3, 152.5, 152.3, 150.4, 144.7, 137.5, 134.8, 129.8, 129.6, 129.2, 128.4, 128.4, 128.2, 127.1, 126.7, 120.9, 97.5, 61.2, 56.3. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{24}H_{22}NO_4$ 388.1548; found 388.1544.

2-phenyl-3-(pyren-1-yloxy)quinoline (5.2q):

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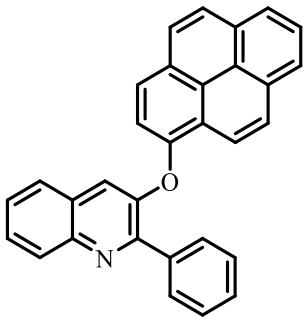
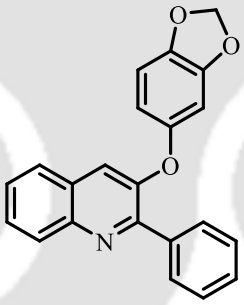


Using **GP-V** the title compound **5.2q** was isolated as yellow solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:2, R_f = 0.50); (143 mg, 85%). M.p. 151-152 ºC. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.29 – 8.27 (m, 3H), 8.22 – 8.16 (m, 4H), 8.08 – 8.03 (m, 4H), 7.69 (d, J = 8.4 Hz, 1H), 7.63 – 7.61 (m, 1H), 7.53 – 7.50 (m, 2H), 7.48 – 7.42 (m, 3H), 7.35 (s, 1H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 152.4, 151.4, 149.4, 144.7, 137.6, 131.45, 131.43, 129.9, 129.6, 129.3, 128.50, 128.45, 128.2, 128.1, 127.2, 127.1, 127.0, 126.6, 126.3, 125.9, 125.5, 125.3, 123.2, 121.0, 120.6, 117.6. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{31}H_{20}NO$ 422.1540; found 422.1536.

3-(benzo[d][1,3]dioxol-5-yloxy)-2-phenylquinoline (5.2r):



Using **GP-V** the title compound **5.2r** was isolated as yellow liquid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:2, R_f = 0.50); (124 mg, 91%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.15 (d, J = 8.4 Hz, 1H), 8.05 (d, J = 7.2 Hz, 2H), 7.66 – 7.62 (m, 2H), 7.50 – 7.43 (m, 4H), 7.46 – 7.43 (m, 1H), 6.80 (d, J = 8.4 Hz, 1H), 6.64 (s, 1H), 6.55 (d, J = 8.4 Hz, 1H), 6.00 (s, 2H). ^{13}C {^{1}H} NMR (151 MHz, $CDCl_3$): δ 152.5, 150.8, 150.6, 148.8, 144.55, 144.49, 137.5, 129.8, 129.5, 129.1, 128.4, 128.3, 128.1, 127.0, 126.6, 120.5, 112.4, 108.7, 102.5, 101.8. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{22}H_{16}NO_3$ 342.1125; found 342.1132.

3-(2-isopropyl-5-methylphenoxy)-2-phenylquinoline (5.2s):

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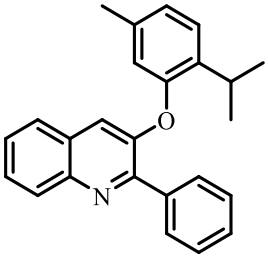
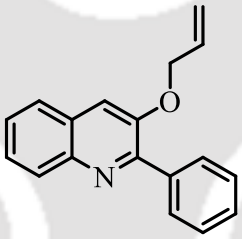


Using **GP-V** the title compound **5.2s** was isolated as white solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:2, R_f = 0.50); (131 mg, 93%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.17 (d, J = 8.5 Hz, 1H), 8.10 (d, J = 7.5 Hz, 2H), 7.64 – 7.60 (m, 2H), 7.51 – 7.44 (m, 4H), 7.37 (s, 1H), 7.29 (d, J = 7.5 Hz, 1H), 7.02 (d, J = 7.5 Hz, 1H), 6.79 (s, 1H), 3.23 – 3.17 (m, 1H), 2.29 (s, 3H), 1.19 (d, J = 7.0 Hz, 6H). ^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$): δ 152.7, 152.5, 150.9, 144.3, 137.7, 137.4, 137.4, 129.8, 129.5, 129.1, 128.56, 128.25, 127.8, 127.2, 127.0, 126.6, 125.9, 120.7, 119.4, 27.1, 23.3, 21.1. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{25}H_{24}NO$ 354.1853; found 354.1857.

3-(allyloxy)-2-phenylquinoline (5.2t):



Using **GP-V** the title compound **5.2t** was isolated as colourless oil using silica gel column chromatography using petroleum ether/ ethyl acetate mixture as eluent (v/v = 1:10, R_f = 0.50) ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.11 (d, J = 8.4 Hz, 1H), 8.02 – 8.00(m, 2H), 7.74 (d, J = 9.2 Hz, 1H), 7.59 – 7.55 (m, 1H), 7.52 – 7.44 (m, 5H), 6.12 – 6.06 (m, 1H), 5.46 – 5.41 (m, 1H), 5.32 – 5.29 (m, 1H), 4.71 – 4.70 (m, 2H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 152.3, 150.6, 143.3, 137.9, 132.5, 130.0, 129.5, 128.9, 128.7, 128.1, 127.1, 126.9, 126.3, 117.8, 114.4, 69.2. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{18}H_{16}NO$ 262.1227; found 262.1224.

4-((2-phenylquinolin-3-yl)oxy)phenyl (S)-2-(6-methoxynaphthalen-2-yl)propanoate (3u):

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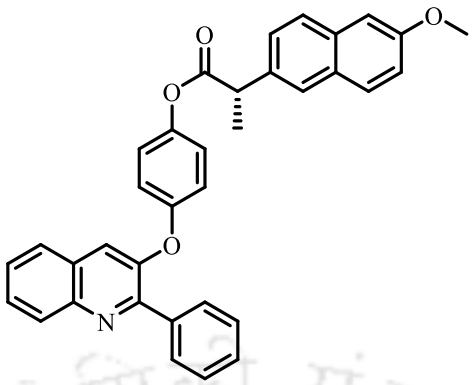
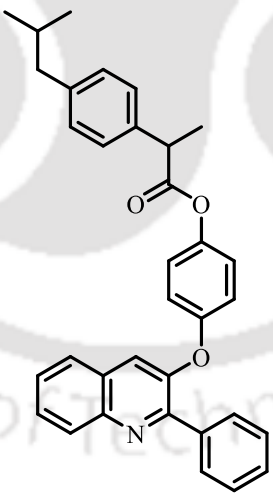


Using **GP-V** the title compound **5.2u** was isolated as colourless oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:2, R_f = 0.50); (136 mg, 65%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.16 (d, J = 8.0 Hz, 1H), 8.03 – 8.01(m, 2H), 7.75 – 7.73 (m, 3H), 7.66 – 7.62 (m, 2H), 7.55 (s, 1H), 7.49 – 7.43 (m, 5H), 7.18 – 7.15 (m, 2H), 7.03 – 6.98 (m, 4H), 4.12 – 4.08 (m, 1H), 3.92 (s, 3H), 1.70 (d, J = 7.2 Hz, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 173.5, 157.9, 153.8, 152.8, 149.9, 147.0, 144.8, 137.4, 135.1, 134.0, 129.7, 129.5, 129.4, 129.2, 128.4, 127.6, 127.1, 126.7, 126.3, 126.2, 123.1, 121.8, 120.2, 119.3, 105.7, 55.5, 45.7, 18.6. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{35}H_{28}NO_4$ 526.2013; found 526.2015.

4-((2-phenylquinolin-3-yl)oxy)phenyl 2-(4-isobutylphenyl)propanoate (5.2v):



Using **GP-V** the title compound **5.2v** was isolated as colourless oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:2, R_f = 0.50); (110 mg, 55%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.15 (d, J = 8.0 Hz, 1H), 8.02 (d, J = 7.5 Hz, 2H), 7.66 – 7.62 (m, 2H), 7.56 (s, 1H), 7.51 – 7.42 (m, 4H), 7.30 (d, J = 8.0 Hz, 2H), 7.15 (d, J = 8.0 Hz, 2H), 7.05 – 6.99 (m, 4H), 3.94 (q, J = 7.0 Hz, 1H), 2.47 (d, J = 7.0 Hz, 2H), 1.89 – 1.84 (m, 1H), 1.61 (d, J = 7.0 Hz, 3H), 0.91 (d, J = 6.5 Hz, 6H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 173.5, 153.9, 149.9, 147.1,

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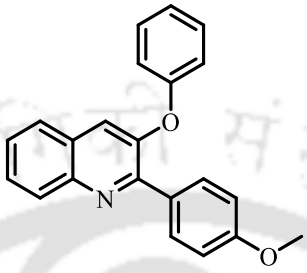
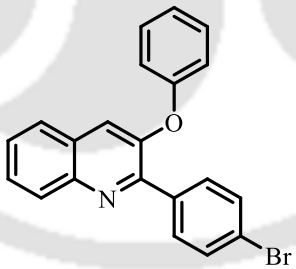
144.9, 141.1, 137.3, 129.7, 129.6, 129.2, 128.4, 128.4, 127.3, 127.1, 126.7, 123.1, 121.8, 120.2, 45.4, 45.2, 30.3, 22.5, 18.6. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{34}H_{32}NO_4$ 502.2377; found 502.2371.

2-(4-methoxyphenyl)-3-phenoxyquinoline (5.2aa):



Using **GP-V** the title compound **5.2aa** was isolated as colourless liquid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:2, R_f = 0.50); (106 mg, 81%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.16 (d, J = 8.4 Hz, 1H), 8.09 (d, J = 7.8 Hz, 2H), 7.64 – 7.63 (m, 2H), 7.55 (s, 1H), 7.47 (t, J = 7.2 Hz, 1H), 7.38 (t, J = 7.5 Hz, 2H), 7.17 (t, J = 7.2 Hz, 1H), 7.08 (d, J = 7.2 Hz, 2H), 7.01 (d, J = 8.4 Hz, 2H), 3.86 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 160.5, 156.6, 152.5, 149.8, 144.9, 131.2, 130.2, 130.0, 129.4, 128.2, 128.2, 126.7, 126.61, 124.1, 122.1, 119.4, 113.8, 55.4. The spectral data is in accordance with the literature.[5]

2-(4-bromophenyl)-3-phenoxyquinoline (5.2ab):



Using **GP-V** the title compound **5.2ab** was isolated as yellow solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:2, R_f = 0.50); (109 mg, 73%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.14 (d, J = 8.8 Hz, 1H), 7.97 (d, J = 8.4 Hz, 2H), 7.67 – 7.65 (m, 2H), 7.61 (s, 1H), 7.58 – 7.57 (m, 2H), 7.52 – 7.48 (m, 1H), 7.40 – 7.36 (m, 2H), 7.18 (t, J = 7.2 Hz, 1H), 7.05 (d, J = 8.0 Hz, 2H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 156.3, 151.6, 149.8, 144.8, 136.4, 131.5, 131.4, 130.3, 129.5, 128.5, 128.5, 127.3, 126.7, 124.4, 123.7, 122.2, 119.4. The spectral data is in accordance with the literature.[5]

2-([1,1'-biphenyl]-4-yl)-3-phenoxyquinoline (5.2ac):

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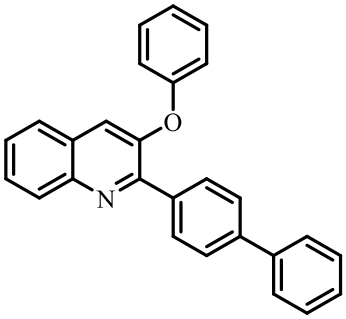
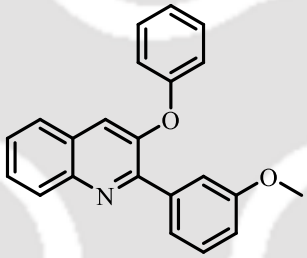


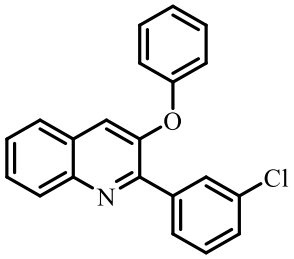
Using **GP-V** the title compound **5.2ac** was isolated as light red solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:2, R_f = 0.50); (114 mg, 77%). M.p. 101-103 ºC. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.19 – 8.17 (m, 3H), 7.72 – 7.70 (m, 2H), 7.67 – 7.63 (m, 4H), 7.58 (s, 1H), 7.52 – 7.44 (m, 3H), 7.42 – 7.34 (m, 3H), 7.20 – 7.17 (m, 1H), 7.13 – 7.10 (m, 2H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 156.5, 152.5, 150.1, 144.9, 141.9, 136.5, 130.3, 130.2, 129.6, 128.9, 128.4, 128.3, 127.6, 127.3, 127.1, 127.1, 126.7, 124.3, 121.9, 119.6. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{27}H_{20}NO$ 374.1540; found 374.1551.

2-(3-methoxyphenyl)-3-phenoxyquinoline (5.2ad):



Using **GP-V** the title compound **5.2ad** was isolated as yellow oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:2, R_f = 0.50); (99 mg, 76%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.20 (d, J = 8.4 Hz, 1H), 7.69 – 7.68 (m, 3H), 7.63 (s, 1H), 7.61 (s, 1H), 7.53 (t, J = 7.2 Hz, 1H), 7.40 (t, J = 7.8 Hz, 3H), 7.19 (t, J = 7.2 Hz, 1H), 7.10 (d, J = 7.8 Hz, 2H), 7.01 (d, J = 7.2 Hz, 1H), 3.87 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 159.5, 156.9, 149.8, 144.8, 138.7, 130.2, 129.7, 129.5, 129.3, 128.5, 128.3, 127.1, 126.7, 124.1, 122.3, 119.3, 115.3, 114.9, 55.4. The spectral data is in accordance with the literature.[5]

2-(3-chlorophenyl)-3-phenoxyquinoline (5.2ae):



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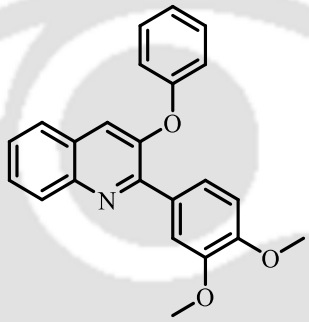
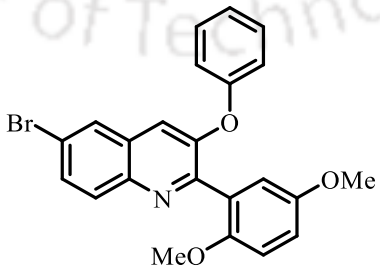
Using **GP-V** the title compound **5.2ae** was isolated as yellow liquid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:2, R_f = 0.60); (99 mg, 75%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.15 (d, J = 8.5 Hz, 1H), 8.09 (s, 1H), 7.97 – 7.96 (m, 1H), 7.67 – 7.64 (m, 2H), 7.58 (s, 1H), 7.53 – 7.50 (m, 1H), 7.40 – 7.37 (m, 3H), 7.19 – 7.16 (m, 1H), 7.06 (d, J = 8.0 Hz, 2H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 156.3, 151.3, 149.8, 144.8, 139.2, 134.3, 130.3, 129.9, 129.6, 129.5, 129.2, 128.6, 128.5, 128.0, 127.4, 126.7, 124.4, 122.1, 119.5. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{21}H_{15}NClO$ 332.0837; found 332.0847.

2-(3,4-dimethoxyphenyl)-3-phenoxyquinoline (5.2af):



Using **GP-V** the title compound **5.2af** was isolated as yellow liquid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:2, R_f = 0.50); (118 mg, 83%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.15 (d, J = 8.4 Hz, 1H), 7.73 – 7.72 (m, 1H), 7.69 (brs, 1H), 7.66 – 7.63 (m, 2H), 7.59 (s, 1H), 7.48 (t, J = 7.8 Hz, 1H), 7.37 (t, J = 7.8 Hz, 2H), 7.15 (t, J = 7.2 Hz, 1H), 7.06 (d, J = 8.4 Hz, 2H), 6.95 (d, J = 8.4 Hz, 1H), 3.93 (s, 3H), 3.92 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 156.8, 150.1, 149.5, 148.8, 145.0, 130.2, 130.2, 129.4, 128.4, 128.2, 126.8, 126.7, 124.0, 122.9, 122.8, 119.0, 112.9, 110.9, 56.1, 56.0. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{23}H_{20}NO_3$ 358.1438; found 358.1436.

6-bromo-2-(2,5-dimethoxyphenyl)-3-phenoxyquinoline (5.2ag):



Using **GP-V** the title compound **5.2ag** was isolated as yellow oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:2, R_f = 0.40); (142 mg, 82%). ^{1}H

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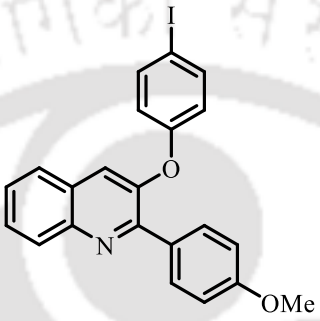
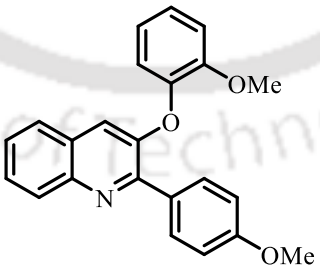
NMR (600 MHz, $CDCl_3$): δ 8.00 (d, J = 9.0 Hz, 1H), 7.81 (d, J = 2.1 Hz, 1H), 7.66 (dd, J = 9.0, 2.4 Hz, 1H), 7.38 – 7.36 (m, 3H), 7.17 (t, J = 7.2 Hz, 1H), 7.08 – 7.07 (m, 3H), 6.96 – 6.94 (m, 1H), 6.89 (d, J = 9.0 Hz, 1H), 3.81 (s, 3H), 3.66 (s, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 156.3, 153.8, 153.1, 151.9, 151.7, 142.9, 131.2, 131.1, 130.1, 129.9, 128.7, 127.6, 124.4, 121.0, 119.9, 118.6, 116.1, 115.8, 112.2, 56.2, 56.0. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{23}H_{18}BrNO_3$ 436.0543; found 436.0440.

3-(4-iodophenoxy)-2-(4-methoxyphenyl)quinoline (5.2ah):



Using **GP-V** the title compound **5.2ah** was isolated as yellow liquid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:2, R_f = 0.50); (122 mg, 87%). ^1H NMR (500 MHz, $CDCl_3$): δ 8.14 (d, J = 8.5 Hz, 1H), 8.01 (d, J = 8.5 Hz, 2H), 7.67 – 7.62 (m, 4H), 7.60 (s, 1H), 7.51 – 7.48 (m, 1H), 6.98 (d, J = 9.0 Hz, 2H), 6.79 (d, J = 8.5 Hz, 2H), 3.85 (s, 3H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 160.6, 156.9, 152.6, 148.9, 145.3, 139.1, 131.1, 129.8, 129.5, 128.6, 128.1, 126.9, 126.7, 123.2, 121.0, 113.9, 55.5. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{23}H_{17}NIO_2$ 354.0299; found 354.0300.

3-(2-methoxyphenoxy)-2-(4-methoxyphenyl)quinoline (5.2ai):



Using **GP-V** the title compound **3ai** was isolated as yellow liquid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:2, R_f = 0.50); (119 mg, 84%). ^1H NMR (600 MHz, $CDCl_3$): δ 8.17 (d, J = 9.0 Hz, 2H), 8.11 (d, J = 9.0 Hz, 1H), 7.59 – 7.56 (m, 2H), 7.43 (t, J = 7.8 Hz, 1H), 7.25 (s, 1H), 7.24 – 7.21 (m, 1H), 7.09 – 7.03 (m, 2H), 7.02 (d, J = 9.0 Hz, 2H), 7.00 – 6.98 (m, 1H), 3.87 (s, 3H), 3.79 (s, 3H).$^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 160.4,

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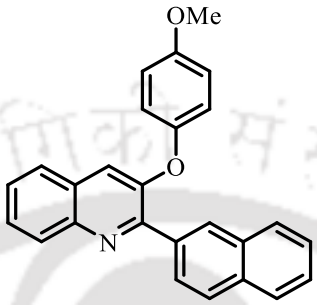
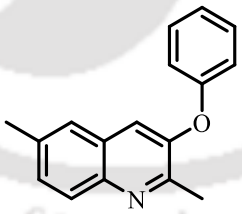
151.7, 151.6, 150.8, 144.3, 131.4, 130.4, 129.3, 128.3, 127.6, 126.5, 126.5, 126.0, 122.4, 121.4, 118.2, 113.7, 113.2, 56.0, 55.5. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{23}H_{20}NO_3$ 358.1438; found 358.1440.

3-(4-methoxyphenoxy)-2-(naphthalen-2-yl)quinoline (5.2aj):



Using **GP-V** the title compound **5.2aj** was isolated as yellow liquid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:2, R_f = 0.50); (131 mg, 87%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.61 (s, 1H), 8.23 (d, J = 8.5 Hz, 1H), 8.19 (d, J = 8.5 Hz, 1H), 7.96 – 7.94 (m, 2H), 7.89 – 7.87 (m, 1H), 7.65 – 7.62 (m, 2H), 7.51 – 7.48 (m, 4H), 7.08 (d, J = 9.0 Hz, 2H), 6.94 (d, J = 9.0 Hz, 2H), 3.83 (s, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 156.6, 151.4, 149.4, 144.5, 135.1, 133.7, 133.4, 129.7, 129.5, 129.0, 128.5, 128.0, 127.7, 127.3, 127.0, 126.7, 126.6, 126.1, 121.3, 120.1, 115.3, 55.8. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{26}H_{20}NO_2$ 378.1489; found 378.1492.

2,6-dimethyl-3-phenoxyquinoline (5.2ak):



Using **GP-V** the title compound **5.2ak** was isolated as yellow liquid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:2, R_f = 0.50); (68 mg, 78%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.91 (d, J = 8.5 Hz, 1H), 7.44 – 7.37 (m, 4H), 7.34 (s, 1H), 7.17 (t, J = 7.4 Hz, 1H), 7.03 (d, J = 8.0 Hz, 2H), 2.70 (s, 3H), 2.48 (s, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 156.7, 153.0, 150.2, 143.1, 136.2, 130.3, 130.2, 128.2, 125.8, 124.0, 120.1, 118.9, 21.6, 20.7. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{17}H_{16}NO$ 250.1227; found 250.1223.

6-bromo-2-methyl-3-phenoxyquinoline (3al):

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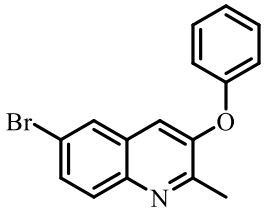
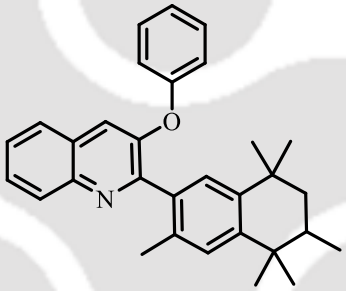


Using **GP-V** the title compound **5.2al** was isolated as yellow liquid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:10, R_f = 0.50); (87 mg, 70%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87 (d, J = 8.8 Hz, 1H), 7.75 – 7.74(m, 1H), 7.65 – 7.62 (m, 1H), 7.44 – 7.40 (m, 2H), 7.24 – 7.20 (m, 2H), 7.07 – 7.05 (m, 2H), 2.73 (s, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 155.9, 154.5, 151.3, 142.8, 131.2, 130.4, 130.2, 129.4, 128.8, 124.7, 120.2, 119.6, 118.0, 20.8. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{17}H_{16}NO$ 314.0176; found 314.0183.

2-(3,5,5,6,8,8-hexamethyl-5,6,7,8-tetrahydronaphthalen-2-yl)-3-phenoxyquinoline (5.2am):



Using **GP-V** the title compound **5.2am** was isolated as colourless oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:2, R_f = 0.50); (130 mg, 75%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.14 (d, J = 8.4 Hz, 1H), 7.69 (d, J = 8.4 Hz, 1H), 7.63 (t, J = 7.2 Hz, 1H), 7.59 (s, 1H), 7.51 (t, J = 7.2 Hz, 1H), 7.32 – 7.29 (s, 3H), 7.20 (s, 1H), 7.10 (t, J = 7.2 Hz, 1H), 6.97 (d, J = 7.8 Hz, 2H), 2.28 (s, 3H), 1.87 – 1.83 (m, 1H), 1.62 – 1.61 (m, 2H), 1.32 (s, 3H), 1.19 (s, 3H), 1.17 (s, 3H), 1.05 (s, 3H), 0.97 (d, J = 6.6 Hz, 3H).^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 156.7, 146.3, 144.5, 141.7, 133.3, 129.9, 129.5, 128.9, 128.4, 128.1, 127.9, 126.9, 126.7, 123.9, 121.5, 119.3, 43.9, 37.7, 34.7, 34.1, 32.6, 32.1, 28.7, 25.0, 19.8, 17.0. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{31}H_{34}NO$ 434.2635; found 436.2641.

2-(6-(tert-butyl)-1,1-dimethyl-2,3-dihydro-1H-inden-4-yl)-3-phenoxyquinoline (5.2an):

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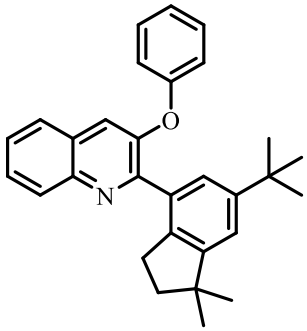
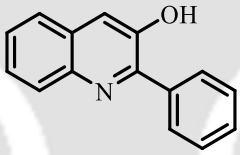


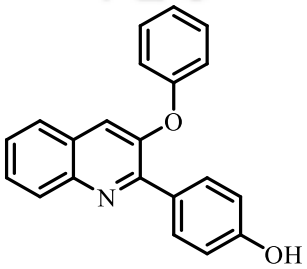
Using **GP-V** the title compound **5.2an** was isolated as colourless oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:2, R_f = 0.50); (122 mg, 73%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.13 (d, J = 8.5 Hz, 1H), 7.69 (d, J = 8.0 Hz, 1H), 7.63 (t, J = 7.5 Hz, 1H), 7.59 (s, 1H), 7.50 (t, J = 7.5 Hz, 1H), 7.40 (s, 1H), 7.31 – 7.28 (m, 2H), 7.16 (s, 1H), 7.11 – 7.08 (m, 1H), 6.96 (d, J = 7.5 Hz, 2H), 2.93 (t, J = 7.1 Hz, 2H), 1.89 (t, J = 7.1 Hz, 2H), 1.29 (d, J = 1.7 Hz, 9H), 1.27 (s, 6H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 156.7, 152.8, 149.9, 144.6, 139.4, 129.9, 129.5, 128.4, 128.1, 126.9, 126.7, 124.8, 123.9, 121.6, 119.5, 119.3, 44.1, 41.8, 34.8, 31.7, 29.9, 29.0, 28.9. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{30}H_{32}NO$ 422.2479; found 422.2489.

2-phenylquinolin-3-ol (5.3a):



Using **GP-V** the title compound **5.3a** was isolated as light yellow solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:10, R_f = 0.50); (51 mg, 58%). M.p. 210-212 ºC. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.10 (d, J = 8.4 Hz, 1H), 7.86 – 7.84 (m, 2H), 7.71 (d, J = 8.0 Hz, 1H), 7.58 – 7.54 (m, 4H), 7.52 – 7.48 (m, 2H), 5.77 (s, 1H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 150.7, 147.5, 143.8, 136.7, 129.6, 129.4, 129.4, 129.1, 127.3, 127.1, 126.3, 118.2. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{15}H_{12}NO$ 222.0914; found 222.0922.

4-(3-phenoxyquinolin-2-yl)phenol (5.3b):



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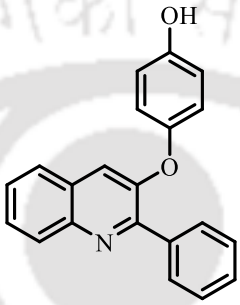
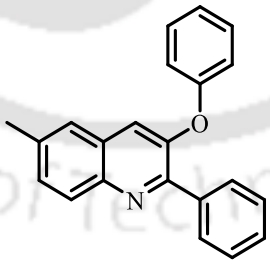
Using **GP-V** the title compound **5.3b** was isolated as light yellow solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:10, R_f = 0.50); (81 mg, 65%). M.p. 201-203 ºC. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.18 (d, J = 8.4 Hz, 1H), 7.90 (d, J = 8.8 Hz, 2H), 7.62 – 7.60 (m, 2H), 7.56 (s, 1H), 7.47 (t, J = 7.6 Hz, 1H), 7.37 (t, J = 7.6 Hz, 2H), 7.16 (t, J = 7.2 Hz, 1H), 7.06 (d, J = 7.6 Hz, 2H), 6.81 (d, J = 8.8 Hz, 2H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 157.5, 156.4, 153.0, 149.9, 144.5, 131.4, 130.2, 128.7, 128.5, 128.2, 126.9, 126.7, 124.2, 122.2, 119.5, 115.6. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{21}H_{16}NO_2$ 314.1176; found 314.1180.

4-((2-phenylquinolin-3-yl)oxy)phenol (5.3c):



Using **GP-V** the title compound **5.3c** was isolated as light yellow solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 10:1, R_f = 0.50); (87 mg, 70%).^{1}H NMR (600 MHz, $CDCl_3$): δ 8.15 (d, J = 8.4 Hz, 1H), 8.05 (d, J = 7.8 Hz, 2H), 7.63 – 7.60 (m, 2H), 7.49 – 7.47 (m, 3H), 7.45 – 7.43 (m, 2H), 6.97 (d, J = 8.4 Hz, 2H), 6.83 (d, J = 7.8 Hz, 2H), 5.45 (brs, 1H).^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 152.6, 152.6, 151.2, 149.3, 144.3, 137.5, 129.8, 129.4, 129.2, 128.5, 128.3, 128.0, 127.1, 126.6, 121.5, 119.9, 116.8. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{21}H_{16}NO_2$ 314.1176; found 314.1179.

6-methyl-3-phenoxy-2-phenylquinoline (5.5a):



Using **GP-V** the title compound **5.5a** was isolated as yellow oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.50); (102 mg, 82%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.06 – 8.02 (m, 3H), 7.50 (s, 1H), 7.48 – 7.44 (m, 3H), 7.42 – 7.40 (m, 2H), 7.36 (t, J = 8.4 Hz, 2H), 7.15 (t, J = 7.2 Hz, 1H), 7.05 (d, J = 8.4 Hz, 2H), 2.51 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 156.7, 152.1, 149.9, 143.5, 137.0, 130.6, 130.1, 129.7, 129.2,

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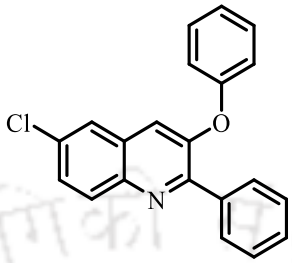
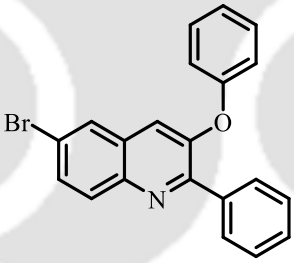
129.0, 128.5, 128.3, 125.6, 124.0, 121.7, 119.3, 21.8. The spectral data is in accordance with the literature.[5]

6-chloro-3-phenoxy-2-phenylquinoline (5.5b):



Using **GP-V** the title compound **5.5b** was isolated as colourless oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:2, R_f = 0.50); (112 mg, 85%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.09 – 8.05 (m 3H), 7.62 (d, J = 1.8 Hz, 1H), 7.55 (dd, J = 9.0, 2.4 Hz, 1H), 7.49 – 7.44 (m, 3H), 7.42 – 7.39 (m, 3H), 7.20 (t, J = 7.2 Hz, 1H), 7.08 (d, J = 7.8 Hz, 2H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 155.9, 153.0, 151.0, 143.0, 137.2, 132.8, 131.1, 130.3, 129.7, 129.4, 129.1, 129.1, 128.4, 125.3, 124.7, 120.2, 119.9. The spectral data is in accordance with the literature.[5]

6-bromo-3-phenoxy-2-phenylquinoline (5.5c):



Using **GP-V** the title compound **5.5c** was isolated as colourless oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:2, R_f = 0.50); (130 mg, 87%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.06 (d, J = 7.2 Hz, 2H), 8.01 (d, J = 9.0 Hz, 1H), 7.80 (brs, 1H), 7.69 – 7.67 (m, 1H), 7.49 – 7.44 (m, 3H), 7.42 – 7.39 (m, 3H), 7.20 (d, J = 7.2 Hz, 1H), 7.09 (d, J = 8.4 Hz, 2H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 155.9, 153.1, 150.9, 143.2, 137.1, 131.6, 131.2, 130.3, 129.7, 129.4, 128.6, 128.4, 124.7, 121.0, 120.0, 119.9. The spectral data is in accordance with the literature.[5]

7-bromo-3-phenoxy-2-phenylquinoline (5.5d):

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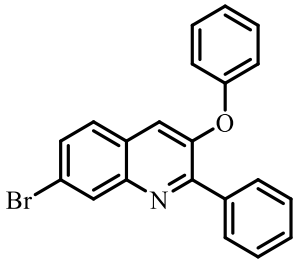
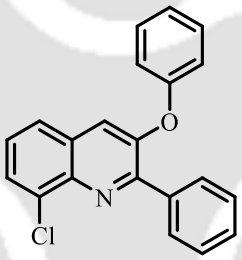


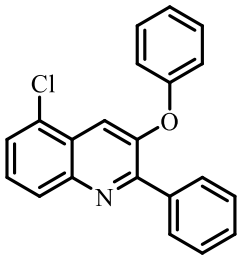
Using **GP-V** the title compound **5.5d** was isolated as colourless oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:2, R_f = 0.40); (129 mg, 86%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.35 (s, 1H), 8.06 (d, J = 7.8 Hz, 2H), 7.57 – 7.56 (m, 1H), 7.52 – 7.44 (m, 5H), 7.40 (t, J = 7.8 Hz, 2H), 7.19 (t, J = 7.8 Hz, 1H), 7.08 (d, J = 8.4 Hz, 2H).^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 156.1, 153.7, 150.4, 137.1, 131.8, 130.5, 130.3, 129. 8, 129.5, 128.4, 127.9, 127.0, 124.6, 121.9, 121.3, 119.7. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{21}H_{15}NBrO$ 376.0332; found 376.0335.

8-chloro-3-phenoxy-2-phenylquinoline (5.5e):



Using **GP-V** the title compound **5.5e** was isolated as yellow solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:3, R_f = 0.40); (103 mg, 78%). M.p 133-135 ºC ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.24 – 8.22 (m, 2H), 7.74 (d, J = 7.2 Hz, 1H), 7.56 – 7.53 (m, 2H), 7.50 – 7.45 (m, 3H), 7.42 – 7.38 (m, 3H), 7.20 (t, J = 7.2 Hz, 1H), 7.09 (d, J = 8.0 Hz, 2H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 156.1, 152.7, 151.0, 140.7, 137.2, 133.9, 130.3, 130.2, 129.8, 129.6, 128.4, 128.3, 127.0, 125.7, 124.6, 121.7, 119.8. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{21}H_{15}NClO$ 332.0837; found 332.0839.

5-chloro-3-phenoxy-2-phenylquinoline (5.5f):



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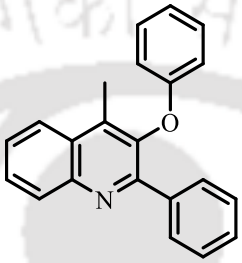
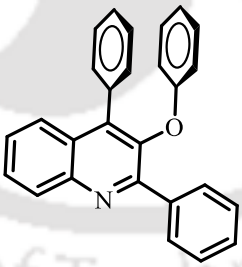
Using **GP-V** the title compound **5.5f** was isolated as yellow solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:3, R_f = 0.40); (113 mg, 86%).^{1}H NMR (400 MHz, $CDCl_3$): δ 8.10 – 8.06 (m, 3H), 7.96 (s, 1H), 7.56 – 7.54 (m, 2H), 7.48 – 7.46 (m, 3H), 7.42 – 7.38 (m, 2H), 7.20 – 7.17 (m, 1H), 7.10 – 7.08 (m, 2H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 156.1, 153.7, 150.8, 145.2, 136.9, 130.3, 130.2, 130.0, 129.9, 129.7, 129.5, 128.7, 128.4, 128.3, 127.8, 126.9, 126.8, 124.5, 119.5, 119.4, 118.9. The spectral data is in accordance with the literature.[5]

4-methyl-3-phenoxy-2-phenylquinoline (5.5g):



Using **GP-V** the title compound **5.5g** was isolated as colourless oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:2, R_f = 0.50); (93 mg, 75%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.20 (d, J = 8.4 Hz, 1H), 8.00 (d, J = 8.0 Hz, 1H), 7.87 – 7.85 (m, 2H), 7.74 – 7.70 (m, 1H), 7.62 – 7.58 (m, 1H), 7.36 – 7.30 (m, 3H), 7.14 (t, J = 8.0 Hz, 2H), 6.89 (t, J = 7.6 Hz, 1H), 6.67 (d, J = 8.0 Hz, 2H), 2.56 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 157.9, 155.0, 145.7, 144.3, 137.9, 136.6, 130.4, 129.7, 129.4, 128.9, 128.8, 128.6, 128.2, 126.8, 124.0, 121.9, 115.2, 12.0. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{22}H_{18}NO$ 312.1383; found 312.1381.

3-phenoxy-2,4-diphenylquinoline (5.5h):



Using **GP-V** the title compound **5.5h** was isolated as yellow solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:3, R_f = 0.50); (134 mg, 90%). M.p. 129-131 ºC. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.26 (d, J = 8.4 Hz, 1H), 7.95 – 9.93 (m, 2H), 7.74 – 7.72 (m, 1H), 7.62 – 7.60 (m, 1H), 7.49 – 7.47 (m, 1H), 7.37 – 7.31 (m, 8H), 6.98 – 6.94 (m, 2H), 6.76 – 6.73 (m, 1H), 6.50 – 6.48 (m, 2H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 158.1, 155.3, 146.2, 143.8, 140.8, 137.8, 133.3, 130.1, 129.9, 129.5, 129.1, 129.0, 128.9, 128.28, 128.25, 128.22, 128.18, 126.9, 125.9, 121.6, 116.0. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{27}H_{20}NO$ 374.1540; found 374.1546.

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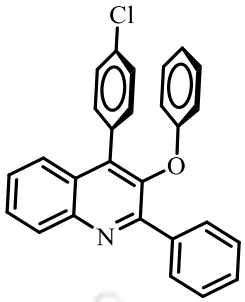
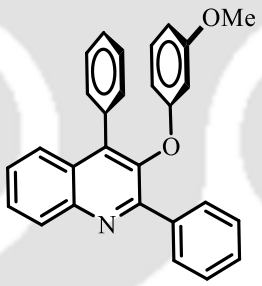
4-(4-chlorophenyl)-3-phenoxy-2-phenylquinoline (5.5i):



Using **GP-V** the title compound **5.5i** was isolated as yellow solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:3, R_f = 0.60); (126 mg, 78%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.25 (d, J = 8.0 Hz, 1H), 7.93 – 7.91 (m, 2H), 7.74 – 7.70 (m, 1H), 7.58 – 7.55 (m, 1H), 7.50 – 7.46 (m, 1H), 7.36 – 7.31 (m, 5H), 7.27 (s, 1H), 7.26 – 7.25 (m, 1H), 7.00 – 6.95 (m, 2H), 6.77 (t, J = 7.2 Hz, 1H), 6.48 (d, J = 7.8 Hz, 2H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 158.0, 146.2, 143.8, 139.5, 137.6, 134.4, 131.8, 131.5, 130.0, 129.5, 129.2, 129.1, 129.1, 128.6, 128.3, 127.9, 127.2, 125.5, 121.987, 115.9. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{27}H_{19}ClNO$ 408.1150; found 408.1152.

3-(3-methoxyphenoxy)-2,4-diphenylquinoline (5.5j):



Using **GP-V** the title compound **5.5j** was isolated as yellow solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:3, R_f = 0.40); (138 mg, 86%).^{1}H NMR (600 MHz, $CDCl_3$): δ 8.25 (d, J = 8.4 Hz, 1H), 7.94 – 7.93 (m, 2H), 7.72 (t, J = 7.8 Hz, 1H), 7.61 (d, J = 8.4 Hz, 1H), 7.48 (t, J = 7.8 Hz, 1H), 7.37 – 7.32 (m, 8H), 6.86 (t, J = 7.8 Hz, 1H), 6.31 (d, J = 7.2 Hz, 1H), 6.08 (d, J = 11.9 Hz, 2H), 3.59 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 160.4, 159.3, 143.7, 140.8, 137.8, 133.3, 130.1, 129.9, 129.5, 129.5, 129.0, 128.9, 128.30, 128.3, 128.2, 128.1, 126.9, 125.9, 108.5, 107.4, 102.5, 55.3. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{28}H_{22}NO_2$ 404.1646; found 406.1651.

3-phenoxy-2-phenyl-1,8-naphthyridine (5.5k):

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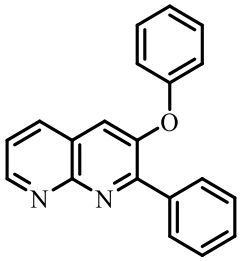
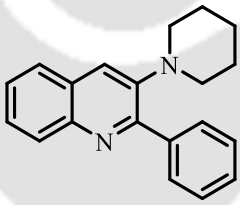


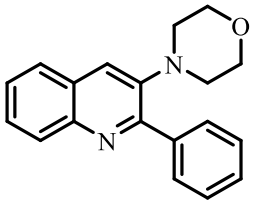
Using **GP-V** the title compound **5.5k** was isolated as white solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:50, R_f = 0.60); (84 mg, 92%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 9.06 – 9.05 (m, 1H), 8.26 – 8.24 (m, 2H), 8.02 – 8.00 (m, 1H), 7.51 (s, 1H), 7.48 – 7.45 (m, 3H), 7.43 – 7.40 (m, 3H), 7.23 – 7.21 (m, 1H), 7.12 – 7.10 (m, 2H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 155.8, 155.4, 152.4, 152.2, 151.0, 136.7, 135.9, 130.4, 130.2, 129.8, 128.2, 124.8, 122.8, 122.3, 121.6, 119.9. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{20}H_{15}N_2O$ 299.1179; found 229.1175.

2-phenyl-3-(piperidin-1-yl)quinoline (5.7a):



Using **GP-VI** the title compound **5.7a** was isolated as yellow liquid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:4, R_f = 0.40); (94 mg, 82%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.05 (d, J = 7.6 Hz, 3H), 7.71 (d, J = 8.4 Hz, 1H), 7.58 (s, 1H), 7.54 (t, J = 7.2 Hz, 1H), 7.47 – 7.43 (m, 3H), 7.41 – 7.39 (m, 1H), 2.86 (s, 4H), 1.55 – 1.54 (m, 4H), 1.51 – 1.50 (m, 2H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 155.9, 146.5, 144.1, 140.7, 129.329, 128.9, 128.3, 128.3, 127.2, 126.6, 126.5, 121.9, 52.8, 25.9, 24.1. HRMS (ESI) *m/z*: $[M+H]^{]+}$ calculated for $C_{20}H_{21}N_2O$ 289.1700; found 289.1694.

4-(2-phenylquinolin-3-yl)morpholine (5.7b):



Using **GP-VI** the title compound **5.7b** was isolated as yellow liquid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:4, R_f = 0.40); (87 mg, 75%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.06 – 8.02 (m, 3H), 7.74 (d, J = 6.8 Hz, 1H), 7.60 (s, 1H), 7.57 – 7.56 (m,

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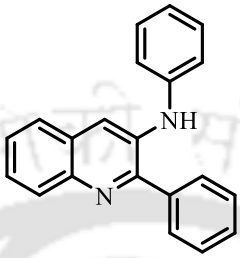
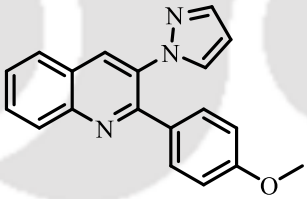
1H), 7.51 – 7.46 (m, 3H), 7.43 – 7.41 (m, 1H), 3.70 – 3.68 (m, 4H), 2.94 – 2.91 (m, 4H). $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$): δ 155.5, 144.9, 144.4, 140.3, 129.4, 128.9, 128.8, 128.5, 128.3, 127.7, 126.9, 126.6, 122.0, 66.9, 51.7. HRMS (ESI) *m/z*: $[M+H]^{]+}$ calculated for $C_{19}H_{19}N_2O$ 291.1492; found 291.1493.

N,2-diphenylquinolin-3-amine (5.7c):



Using **GP-VI** the title compound **5.7c** was isolated as yellow liquid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:4, R_f = 0.40); (94 mg, 80%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.05 (d, J = 8.4 Hz, 1H), 7.92 (s, 1H), 7.78 – 7.76 (m, 2H), 7.65 – 7.62 (m, 1H), 7.56 – 7.45 (m, 5H), 7.37 – 7.33 (m, 2H), 7.19 – 7.17 (m, 2H), 7.07 – 7.04 (m, 1H), 5.82 (brs, 1H). $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$): δ 152.6, 143.4, 141.9, 138.1, 135.7, 129.8, 129.35, 129.28, 129.26, 129.2, 128.7, 127.0, 126.7, 126.2, 122.8, 119.8, 117.1. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{21}H_{17}N_2$ 297.1387; found 297.1396.

2-(4-methoxyphenyl)-3-(1H-pyrazol-1-yl)quinoline (5.7d):



Using **GP-VI** the title compound **5.7d** as yellow solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:20, R_f = 0.40); (108 mg, 90%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.36 (s, 1H), 8.20 (d, J = 8.5 Hz, 1H), 7.87 (d, J = 8.0 Hz, 1H), 7.78 – 7.75 (m, 2H), 7.60 – 7.56 (m, 1H), 7.36 – 7.56 (d, J = 8.8 Hz, 2H), 7.27 – 7.26 (m, 1H), 6.89 – 6.86 (m, 2H), 6.33 – 6.32 (m, 1H), 3.82 (s, 3H). $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$): δ 160.5, 154.3, 147.5, 141.2, 133.6, 133.2, 131.8, 130.50, 130.45, 130.3, 129.6, 127.8, 127.3, 127.1, 114.1, 107.4, 55.4. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{19}H_{16}N_3O$ 302.1288; found 302.1297.

3-(1H-imidazol-1-yl)-2-(4-methoxyphenyl)quinoline (5.7e):

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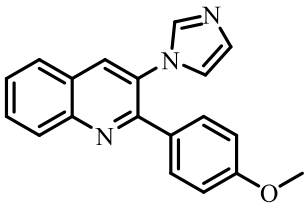
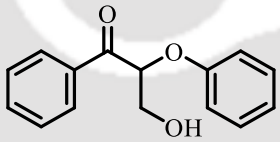


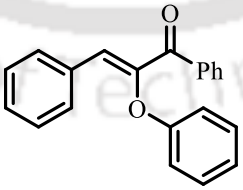
Using **GP-VI** the title compound **5.7e** was isolated as yellow oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:20, R_f = 0.40); (111 mg, 92%).^{1}H NMR (600 MHz, $CDCl_3$): δ 8.21 (d, J = 8.4 Hz, 1H), 8.14 (s, 1H), 7.88 (d, J = 7.8 Hz, 1H), 7.80 (t, J = 8.4 Hz, 1H), 7.63 – 7.61 (m, 2H), 7.33 (d, J = 9.0 Hz, 2H), 7.18 (s, 1H), 6.97 (s, 1H), 6.87 (d, J = 8.4 Hz, 2H), 3.81 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 160.7, 154.6, 147.8, 133.4, 130.9, 130.0 129.7, 129.7, 127.7, 127.5, 126.8, 121.0, 114.3, 55.4. Spectral data is in accordance with the literature.[11]

3-hydroxy-2-phenoxy-1-phenylpropan-1-one (5.18):



^{1}H NMR (600 MHz, $CDCl_3$): δ 8.05 (d, J = 7.8 Hz, 2H), 7.60 (t, J = 7.2 Hz, 1H), 7.47 (t, J = 7.8 Hz, 2H), 7.23 (t, J = 7.8 Hz, 2H), 6.96 (t, J = 7.2 Hz, 1H), 6.89 (d, J = 8.4 Hz, 2H), 5.60 – 5.58 (m, 1H), 4.18 – 4.09 (m, 2H), 2.87 (s, 1H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 196.9, 157.3, 134.1, 129.7, 129.0, 128.8, 122.0, 115.3, 81.2, 63.3. Spectral data is in accordance with the literature.[29]

(Z)-2-phenoxy-1,3-diphenylprop-2-en-1-one (5.20):



The title compound 20 was isolated as yellow oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:10, R_f = 0.40); (111 mg, 65%).^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88 – 7.86 (m, 2H), 7.76 – 7.74 (m, 2H), 7.51 – 7.49 (m, 1H), 7.42 – 7.38 (m, 3H), 7.35 – 7.33 (m, 2H), 7.22 – 7.18 (m, 2H), 7.01 – 6.93 (m 4H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 192.20,

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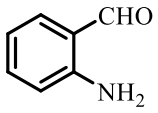
156.18, 148.19, 137.11, 132.96, 132.71, 130.58, 129.83, 129.76, 129.44, 128.87, 128.42, 128.21, 122.95, 116.22. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{21}H_{17}O_2$ 301.1224; found 301.1216.

2-aminobenzaldehyde (4.4a'):



^{1}H NMR (500 MHz, $CDCl_3$): δ 9.87 (s, 1H), 7.48 (d, J = 8.0 Hz, 1H), 7.31 (t, J = 7.0 Hz, 1H), 6.75 (t, J = 7.5 Hz, 1H), 6.65 (d, J = 8.0 Hz, 1H), 6.11 (brs, 2H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 194.1, 149.9, 135.7, 135.2, 118.9, 116.4, 116.0. Spectral data is in accordance with the literature.[30]

5.7. References

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Chapter 6

Reductive alkylation of quinolines to N-alkyl tetrahydroquinolines catalyzed by arylboronic acid

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6.1. Introduction

1,2,3,4-Tetrahydroquinoline (THQ) derivatives are an important class of compounds and are widely utilized in pharmaceutical and agrochemical industries, and for the total synthesis of natural products.[1-3] In addition, THQ core was found to be the key structural unit of many natural products, including cuspareine, galipinine, and angustrureine. [4-6] Among these, the *N*-benzyltetrahydroquinolines (BTHQs) are of paramount interest in medicinal chemistry due to their excellent therapeutic potential.[4-8] They are useful as β_3-adrenergic receptor agonists,[4] HDAC6 inhibitor,[5] UCM1014 melatonin receptor agonists,[6a] antihyperlipidemic,[6b] antitumor and anti-HIV agents.[7] Few selected examples are listed in Figure 6.1.

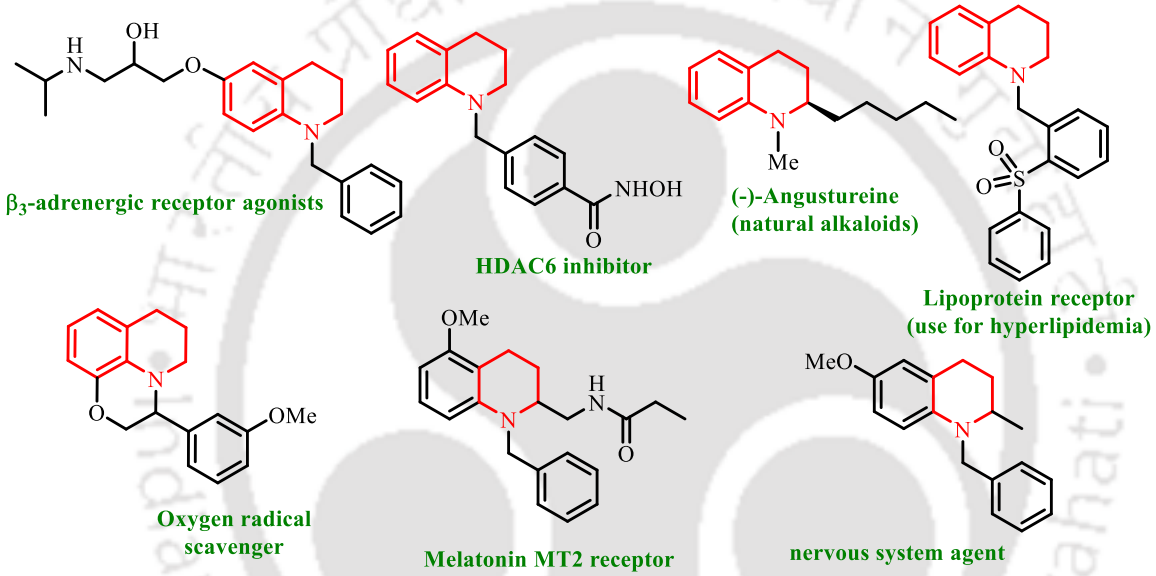

Figure 6.1. Representative bioactive compounds containing *N*-benzyltetrahydroquinolines (BTHQs) framework

Owing to their significance and utility, a considerable amount of research efforts has been dedicated for the development of synthetic methods that facilitate access to the BTHQ skeleton. Conventionally, these BTHQs are synthesized in two step sequence reaction i) the reduction of quinolines to THQs[1-3] ii) subsequent *N*-benzylation of THQs using a range of different alkylating agents[9-20] such as $PhCH_2X$ (X = OH, Cl, Br),[9-18] $PhCO_2H$,[19] PhCN,[20] and others[21] (Scheme 6.1). However, these methods suffer from various drawbacks such as limited substrate scope and low yields. On the other hand, the reduction of quinolines for synthesizing THQs represents the most common and well-known approach.[1-3] Thus, direct *N*-benzylation of readily available quinolines can offer a straightforward and boosting approach to access BTHQs in terms of easiness and step efficiency.

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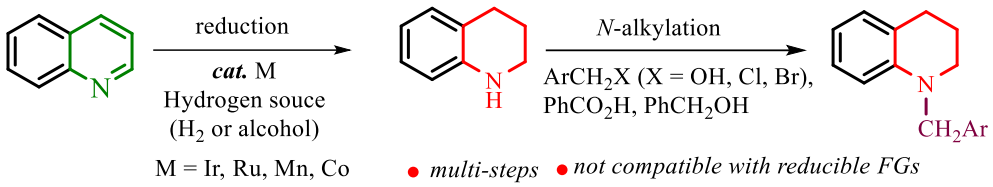
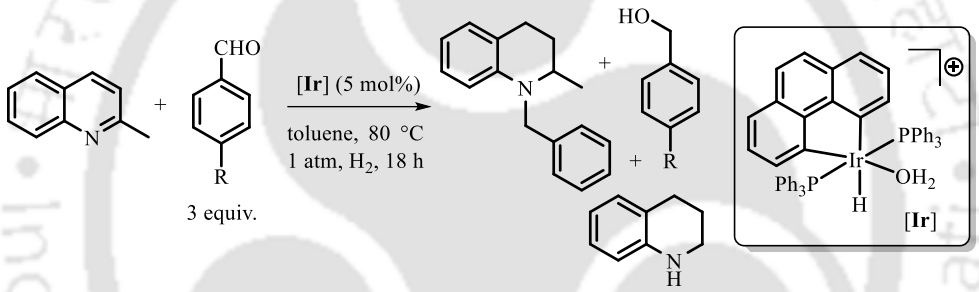


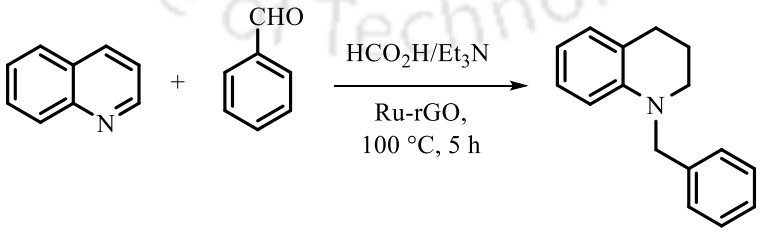
Scheme 6.1. Synthesis of BTHQs

To this date, there has been limited synthetic protocol available in literature for the direct *N*-benzylation of quinolines. In 2013, *Crabtree* and *group* introduced the *N*-benzylation of 2-methyl quinoline for the first time, employing an iridium-benzoquinoline catalyst under mild reaction condition (Scheme 6.2).[22] However, the process afforded the *N*-benzylation product along with the undesired hydrogenated product 2-methyl-THQs and benzyl alcohol. The reductive alkylation process was found to compete with the hydrogenation of aldehydes hampering the selectivity. Unfortunately, an excess amount of aldehyde (3 equiv.) has to be used to get a good yield, and the reaction does not proceed with either strongly EDG or EWG bearing aromatic aldehydes.



Scheme 6.2. Iridium catalyzed reductive *N*-alkylation of quinaldine

Later, the *Lee* and *group* developed another method for the direct reductive *N*-benzylation by using bifunctional Ru-rGO NSs catalyst (Scheme 6.3).[23] Despite these developments, none of the known catalytic methods can directly give BTHQs in the presence of other reducible functional groups such as ester, nitro, alkyne, nitrile groups. The methods require the use of precious metals. Therefore, it is deemed desirable to develop a mild and efficient method for the construction of BTHQ derivatives under metal-free conditions.



Scheme 6.3. Bifunctional Ru-rGO NSs catalyzed reductive benzylation of quinoline

Boronic acid catalysis (BAC) can emerge as an alternative to metal catalysis due to their readily availability, tractability and low toxicity.[24] In spite of their large popularity as

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reagent in Suzuki–Miyaura cross-coupling reaction, boronic acids also served as a catalyst in various C–C, C–O bond forming reaction, hydrosilylation, glycosylation, and amidation in peptide synthesis. In contrast to the mild Lewis acid properties of boronic acids, limited attention to the hydrogen-bonding interactions in solution has appeared in the literature. Specifically, the dual roles of both hydrogen bonding and Lewis acid properties in a single organoboronic system remain underdeveloped (Figure 6.2).[24, 25]

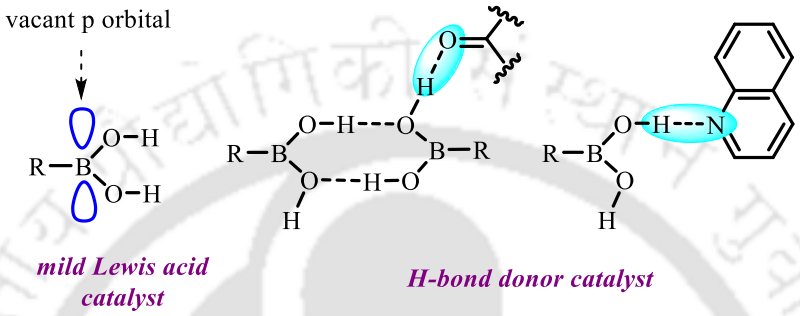
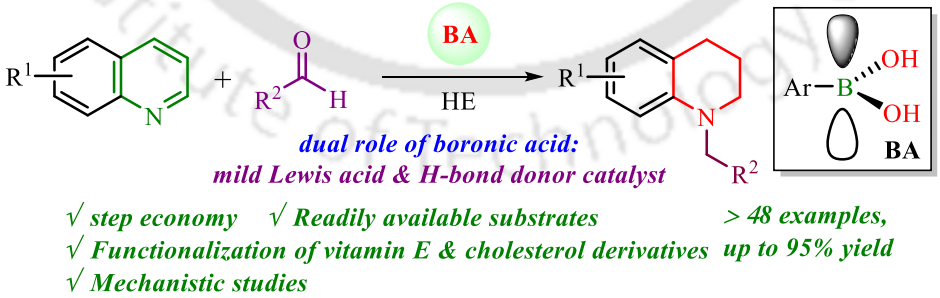


Figure 6.2. Role of boronic acid in organocatalysis

6.2. Present work

Recently our group reported boronic acid catalyzed chemoselective reduction of quinolines using Hantzsch ester (close analogue of biological NAD(P)H) organic hydride source under mild reaction conditions.[26] Inspired by this, a one-pot tandem procedure involving quinoline reduction to tetrahydroquinoline and sequential reductively alkylated by the aldehyde under boronic acid catalysis (**BA**) has been demonstrated. This step-economical synthesis of *N*-alkyl tetrahydroquinolines has been achieved directly from readily available quinolines, aldehydes, and Hantzsch ester under mild reaction conditions (Scheme 6.4). The mechanistic study demonstrates a unique behaviour of both Lewis acid and hydrogen-bonding properties in organoboronic catalysts.



Scheme 6.4. Synthetic approach towards BTHQs

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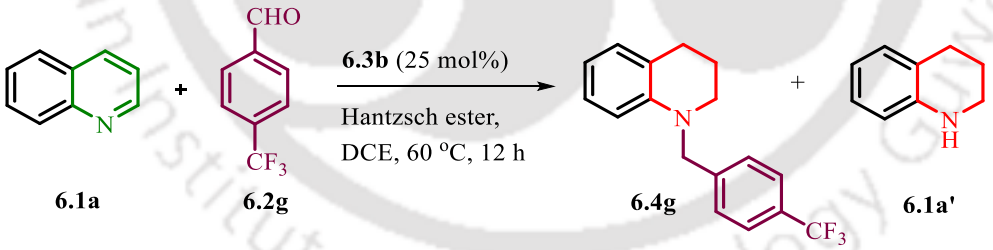
6.3. Results and discussion

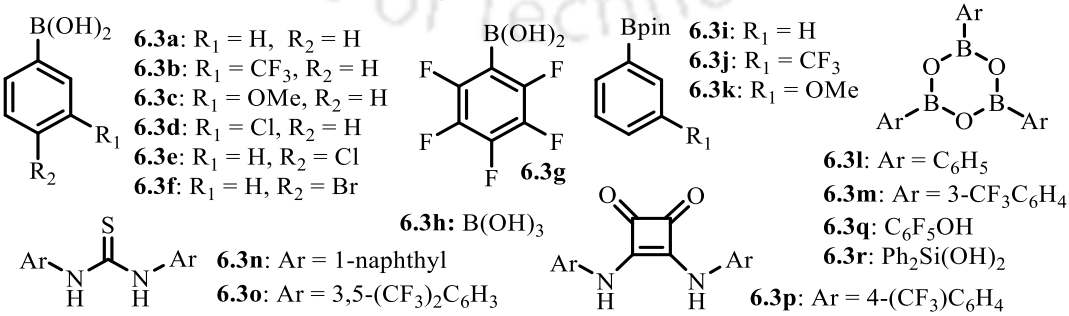
6.3.1. Optimization of reaction condition

The above hypothesis was initially executed with quinoline (**6.1a**), 4-trifluoromethyl benzaldehyde (**6.2g**), Hantzsch ester (**HE**) (3.5 equiv.), and 25 mol % of $PhB(OH)_2$ (**6.3a**) in DCE at 60 °C. Gratifyingly, after 12 h, the targeted *N*-alkylated product **6.4g** was obtained in 72% yield, along with 27% intermediate hydrogenated product THQ (**6.1a′**, Table 6.1, entry 7) was achieved. In order to enhance the yield of the desired product **6.4g**, various arylboronic acids with different substituents (**6.3c-g**) were examined (entries 8−12). Boronic acids **6.3b** and **6.3g** with electron-withdrawing $-CF_3$ and −F respectively have been demonstrated as the superior catalytic activity for current transformation by improving the desired product **6.4g** yield upto 93% in both cases (Table 6.1, entries 1 and 12). The yield of **6.4g** remained consistent in the presence of molecular sieves (entry 6), whereas a decrease in the yield has been observed in the presence of water (Table 6.1, entry 2). When the reaction was performed with arylboronic acid containing electron -donating group −OMe, the yield of **6.4g** dropped upto 80% (entry 8). Subsequently, this reaction was evaluated with different hydrogen-bond donors and Brønsted acids (Table 6.1, entries 16−21). When $-CF_3$ functionalized thiourea (**6.3o**) and squaramide (**6.3p**) were utilized as the H-bond donor catalysts, product **6.4g** was achieved in 81% and 74% yields respectively (Table 6.1, entries 17 and 18). Silanol **6.3r** was unsuccessful to catalyze the transformation (Table 6.1, entry 20). Additionally, Pentafluorobenzoic acid and oxalic acid resulted in moderate to low yields of **6.4g**. (N.B- All the boronic acids used in this study were recrystallized from water prior to use). Thus **6.3b** has been selected as the best catalyst for the synthesis of this *N*-benzylated molecules.

Table 6.1. Optimization of reaction conditions[a]



catalyts



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Entry	Deviation from above	Yield (%)
1	none	93%
2	with H_2O	[23%, (20% of **6.1a'**)] [b]
3	at 45 °C	10%
4	at 80 °C	60%
5	no catalyst	2%
6	4Å M.S.	93%
7	**6.3a**	[72%, (27% of **6.1a'**)]
8	**6.3c**	80%
9	**6.3d**	85%
10	**6.3e**	85%
11	**6.3f**	80%
12	**6.3g**	93%
13	**6.3h**	[12%, (80% of **6.1a'**)]
14	**6.3j**	72%
15	**6.3k**	61%, 63%[b], 58%[c]
16	**6.3n**	7%
17	**6.3o**	81%
18	**6.3p**	74%
19	**6.3q**	51%
20	**6.3r**	0%
21	Brønsted acid	28%[d], 10%[e], 31%[f], 64%[g], 57%[h]

Reaction conditions: [a] **6.1a** (0.5 mmol), **6.2g** (0.5 mmol), catalyst (25 mol%), HE (1.75 mmol) in DCE (2 mL) at 60 °C for 12 h under air, isolated yields. [b] 5 equiv. H_2O. [c] with 4Å M.S. [d] with *p*-TsOH. [e] with $PhCO_2H$. [f] with TfOH. [g] with $C_6F_5CO_2H$. [h] with oxalic acid.

Additionally, in order to shed some more light on the reaction profile, a model reaction was conducted under the optimized conditions, and the desired *N*-benzylTHQ formation was analysed at different time intervals. As shown in the Figure 6.2, the initial consumption of the aldehyde **6.2g** is rapid (~70% conversion in the first 2 h) after which it requires reaction for another 10 h for the complete conversion of **6.2g**.

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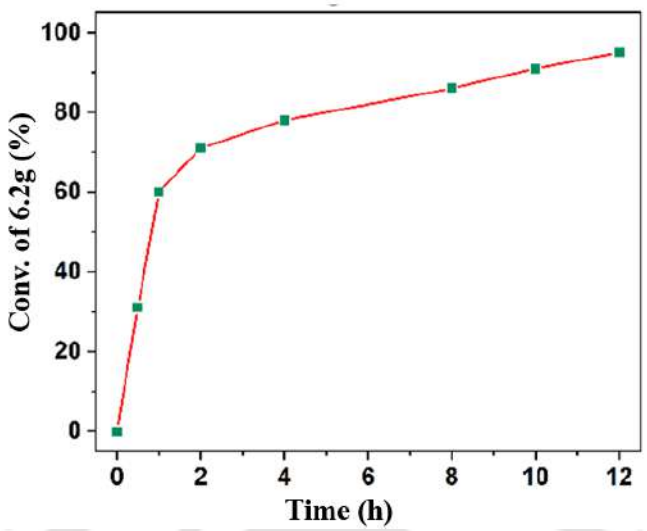

Figure 6.3. Reaction kinetic profile for the conversion of **6.2g**. The conversion of **6.2g** was determined by ^{19}F NMR using fluorobenzene as an internal standard.

6.3.2. Substrate scope of the synthesis of *N*-alkyl tetrahydroquinolines

With the optimized condition in hand, the scope of the reaction was screened with a variety of aldehydes **6.2a−6.2z**, **6.2aa−6.2ac** and different quinolines **6.1a−6.1m** (Table 6.2). The quinoline **6.1a** reacted with benzaldehyde **6.2a−6.2q** containing both electron-donating and electron-withdrawing groups at different positions, resulting the desired *N*-benzylated THQs (**6.4a−6.4q**) in 85−88% yields and 82−96% yields, respectively. Notably, the retention of reducible functional groups (4-Cl, 4-CN, 4-CF_3, 4- CO_2Me, 4-C≡CPh, 4-O-allyl, 4-OBn, 4-SMe, 3-Br, 2-NO_2, 3-Br) in the final products showcases the excellent chemoselectivity of the present reductive protocol. With heteroaromatic aldehydes **6.2r** and **6.2s**, the desired products **6.4r** and **6.4s** were formed in excellent yields (86% and 85% respectively). Fused aromatic aldehyde such as 1- napthaldehyde and 1-pyrene aldehyde also reacted well leading to the formation of the desired products **6.4t** and **6.4u** efficiently (Table 6.2). It is important to highlight that the reaction of aliphatic aldehydes proceeded smoothly to provide desired products **6.4aa−6.4ad**, including biologically relevant *N*-methyltetrahydroquinoline motif. In addition to aldehydes, aliphatic cyclic ketone **6.2ad** was also amenable to this method to give the desired product **6.4ae** in 83% yield. Unfortunately, aromatic ketones were not suitable for this process. Intriguingly, when 1,4-benzenedialdehyde was used as an alkylating agent the bistetrahydroquinoline **6.4af** was obtained in notable selectivity. Since the *N*-alkylated THQ motif is found in various biologically and pharmaceutically relevant compounds,[1-3] we attempted to explore the present approach in complex molecular settings. A substrate comprising seven contiguous stereocenters, derived from cholestan-3-ol of the steroid cholesterol family, was successfully converted into *N*-alkylated THQ **6.4ah** in 91% yield. Synthetic application of the catalytic protocol was further corroborated by treating vitamin *E*, (±)-

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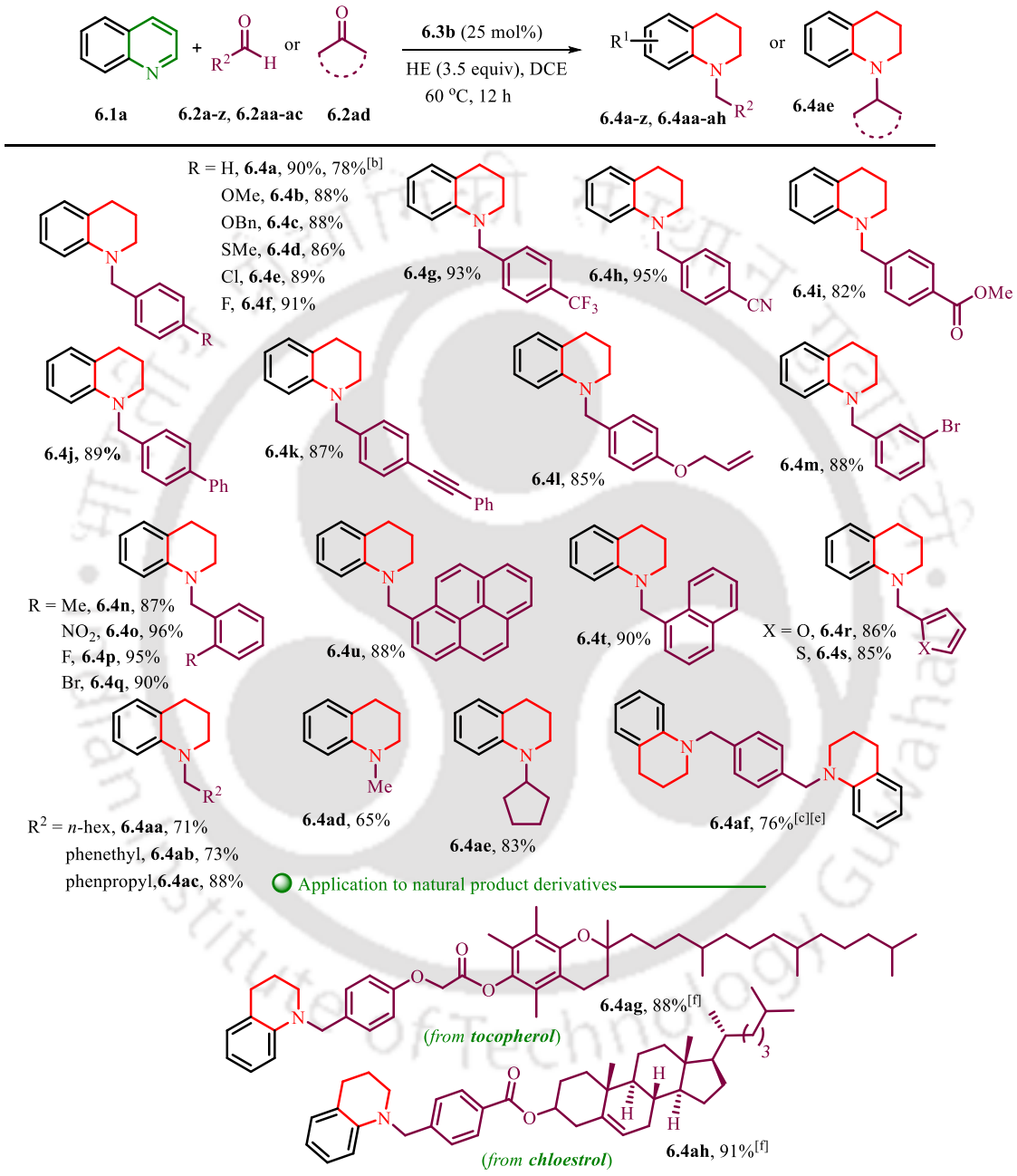
α-tocopherol derived aldehyde **6.2ab** with quinoline to provide **6.4ag** in 88% yield without affecting the parent tocopherol moiety.

Table 6.2. Substrate Scope of the aldehydes[a]



Reaction conditions: [a] Substituted quinoline (0.5 mmol), aldehyde or ketone (0.5 mmol), **6.3b** (0.125 mmol), HE (1.75 mmol), in DCE (2mL), at 60 °C for 12 h under air, isolated yields. [b] 8 mmol scale, 24 h. [c] With 4 mmol of HE. [d] With 1 mmol of PhCHO. [e] With 0.5 equiv. of aldehyde. [f] With 0.25 mmol scale

Diversely substituted quinolines (**6.1b−6.1m**) and *N*-heteroarene are also best-suited as substrates under the reaction conditions, giving the desired products **6.5a−6.5n** efficiently (Table 6.3). The

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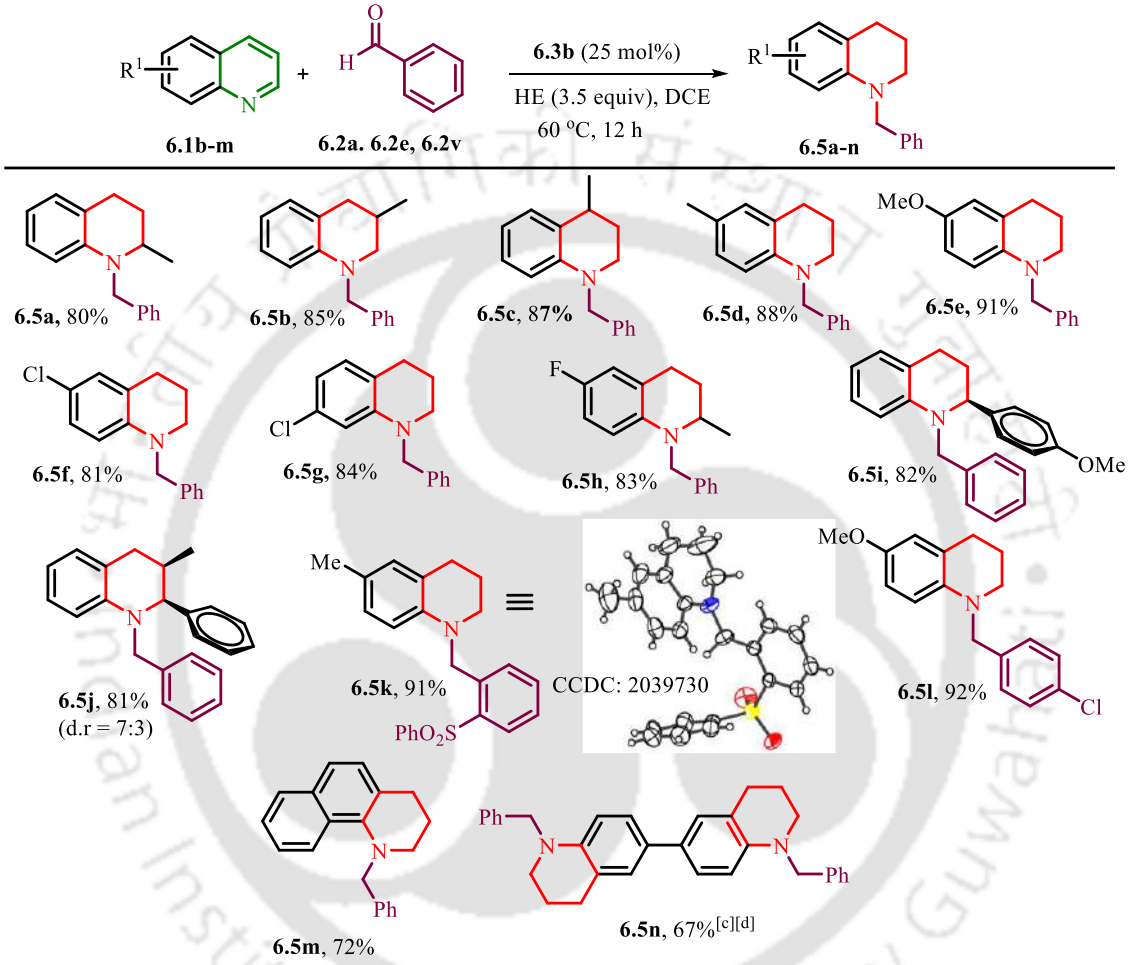
present reductive *N*-alkylation protocol was also effectively employed to synthesize a lipoprotein receptor[6b] **6.5k** (Table 6.3). Interestingly, poly-*N*-alkylated THQ was also successfully synthesized under the current reaction conditions resulting **6.5n** in 67% yield.

Table 6.3. Substrate Scope of quinolines[a]



Reaction conditions: [a] Substituted quinoline (0.5 mmol), aldehyde (0.5 mmol), **6.3b** (0.125 mmol), HE (1.75 mmol), in DCE (2mL), at 60 °C for 12 h under air, isolated yields. [b] 8 mmol scale, 24 h. [c] With 4 mmol of HE. [d] With 1 mmol of PhCHO.

Furthermore, the protocol was extended to include a multicomponent Petasis-borono Mannich (PBM) reaction, facilitating the synthesis the antimicrobial active *N*-diarylmethyl THQ[27] skeleton **6.6a**, **6.6b** in one pot using readily accessible starting materials such as boronic acid, quinoline, and salicylaldehyde (Table 6.4). Herein, boronic acid function not only as a catalyst for the reduction of quinoline to THQ but also act as a coupling partner in the PBM reaction, thus reducing the number of steps and making the process more step-economical.

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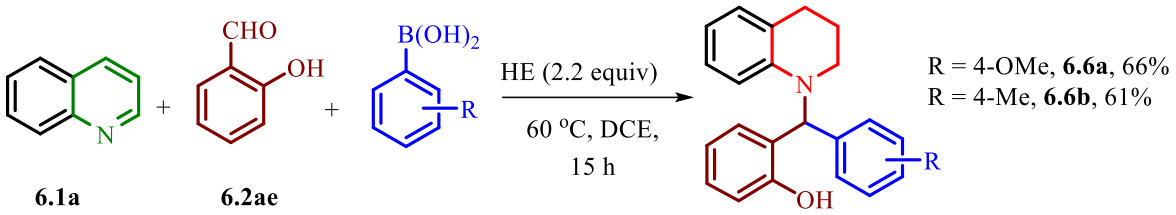
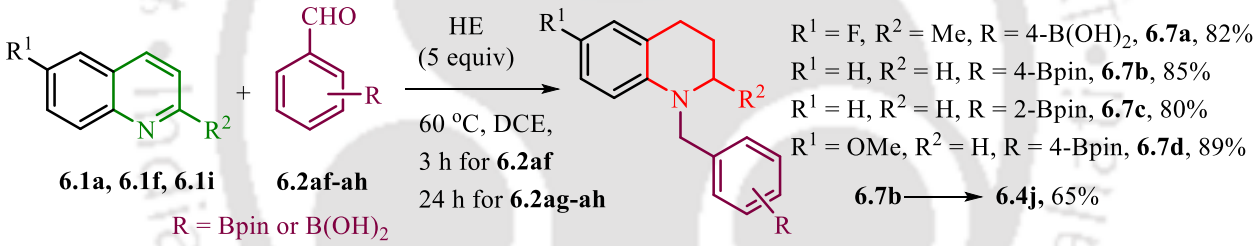
Table 6.4. Multicomponent PBM reaction: preparation of alkylaminophenols[a]



Reaction conditions: [a] **6.1a** (0.5 mmol), arylboronic acid (0.5 mmol), HE (1.1 mmol) in DCE (2 mL), at 60 °C for 3 h under air, then salicylaldehyde (0.34 mmol) at 90 °C for 12 h. Isolated yields.

Afterwards, I have tested the present *N*-alkylation reaction using aldehyde containing boronic acid or boronic acid pinacol ester under the standard reaction conditions. The reaction was sluggish for boronic ester; however, it furnishes the desired product with boronic acid in good yield without the hampering of the boron moiety (Table 6.5). The synthetic utility of the −Bpin group in **6.7b** has been further demonstrated by subjecting it to the Pd-catalyzed Suzuki−Miyaura coupling with bromobenzene to produce **6.4j** in good yield (Table 6.5).[28]

Table 6.5. *N*-alkylation with boronic acid or boronic ester bearing aromatic aldehydes[a]



Reaction conditions: [a] Substituted quinoline (0.5 mmol), **6.2af-ah** (0.5 mmol), HE (2.5 mmol) in DCE (2 mL) at 60 °C, 3 h for **6.2af** and 24 h for 2ag-ah. Isolated yields are reported.

Given that the final product **6.7a** and the substrate 4-boronobenzaldehyde **6.2af** both possess a boronic acid moiety, which allows possibility for the reaction to be a product induced or substrate promoted transformation. To elucidate this, an experiment was carried out by adding the corresponding product **6.7a** as a 25 mol% catalyst in the reaction mixture. This resulted in a notably higher percentage of conversion of **6.1i** compared to adding the same mole% of boronic acid bearing aldehyde **6.2af** (>99% vs 64%). This indicates the process is likely to be a product prompted transformation (Scheme 6.5).

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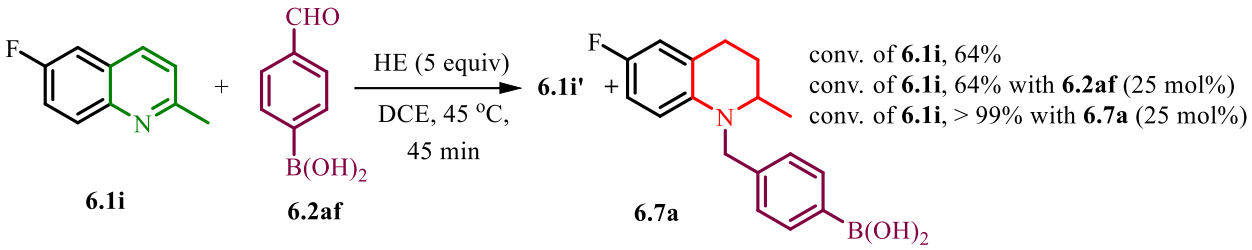
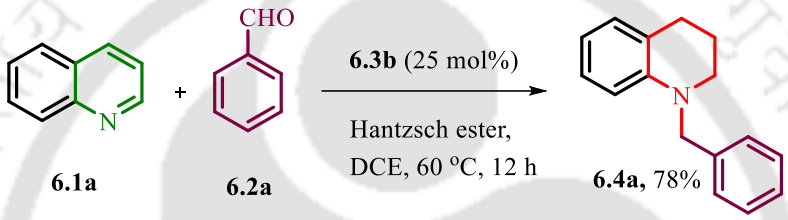


Scheme 6.5. Conversion of substituted quinoline with boronic acid-containing aldehyde

6.3.3. Gram scale synthesis

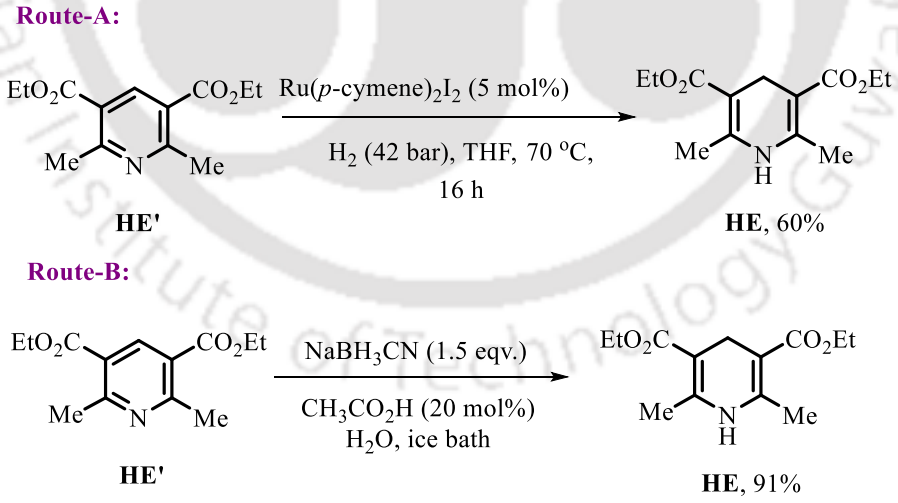
To understand the efficiency of this process, gram-scale reaction was performed for bulk utilization. The desired product **6.4a** was achieved with 78% yield using 1 gram of quinoline (Scheme 6.6).



Scheme 6.6. Gram-scale reduction-reductive *N*-alkylation

6.3.4. Regeneration of Hantzsch ester (HE)

Moreover, regeneration of Hantzsch ester can be achieved by rereducing the Hantzsch pyridine by using the synthetic protocols given in Scheme 6.7.



Scheme 6.7. Reduction of Hantzsch pyridine (**HE'**) to Hantzsch-1,4-dihydropyridine (**HE**)

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6.3.5. Mechanistic investigation

The mechanism of the reaction was studied, noting both hydrogen bonding and Lewis acid [24] properties of boronic acid. The mild Lewis acidic behavior of boronic acid in transfer hydrogenation of quinoline to THQs by HE was recently reported.[26] Close inspection of the nature of binding in solution reveals weak hydrogen bond interaction between B-OH of **6.3b** and N-atom of quinoline moiety, which was confirmed by ^{1}H NMR *via* a downfield shift of the signal of B-OH protons in **6.3b** from δ = 4.92 ppm to 5.85 ppm. In ^{11}B NMR, approximately 7 ppm upfield shift was observed, which suggests complexation may take place between boronic acid and quinoline. The above upfield shift in ^{11}B NMR for boronic acid likely to be attributed as hydrogen bonding interaction rather than complexation with quinoline in solution. Notably, the signals corresponding to aromatic protons H2, H4, and H8 in quinoline **6.1a** shifted downfield, and along with aromatic proton of boronic acid was shifted to upfield in **6.3b** (Figure 6.4).

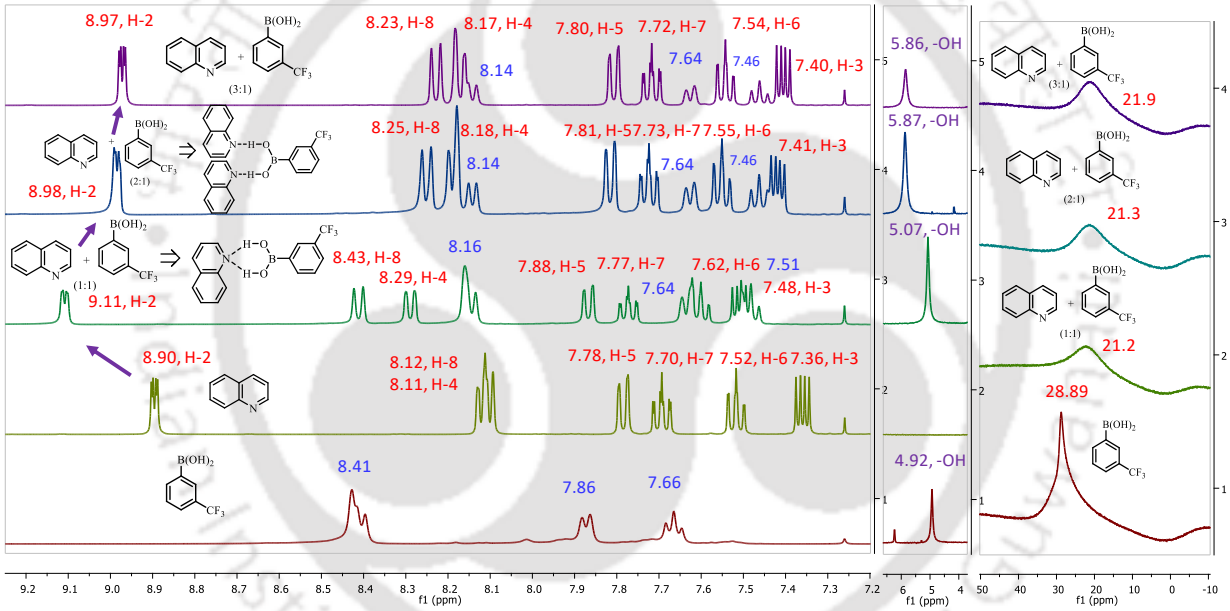

Figure 6.4. ^{1}H, and ^{11}B spectra of quinoline (10 mg, 0.077 mmol), 3-trifluoromethylphenyl boronic acid (15 mg, 0.077 mmol), and a combination of quinoline and 3-trifluoromethylphenylboronic acid (molar ratio 1:1, 2:1, and 3:1) in $CDCl_3$ at 298 K.

Furthermore, the interaction of boronic acid with the aldehyde (or keto group in **HE**) was also established with the help of ^{1}H, ^{13}C, ^{11}B NMR, and IR spectroscopic experiments by using acid, and 4-trifluoromethylbenzaldehyde. While one equivalent of 3-trifluoromethylphenylboronic acid was added to 4-trifluoromethyl benzaldehyde in $CDCl_3$, a downfield shift of approximately 0.22 ppm for hydroxyl peak of boronic acid in ^{1}H NMR and 0.16 ppm for carbonyl signal of aldehyde in ^{13}C NMR were observed (Figure 6.5, 6.6), and for 4-fluoro benzaldehyde, the downfield shift of approximately 0.4 ppm in ^{1}H NMR for –OH group of boronic acid and 0.13 ppm in ^{13}C NMR for keto group of aldehyde was found (Figure 6.7, 6.8). On the other hand, no shift was observed in ^{11}B NMR, which rules out the possibility of adduct formation with boron (Figure 6.9).

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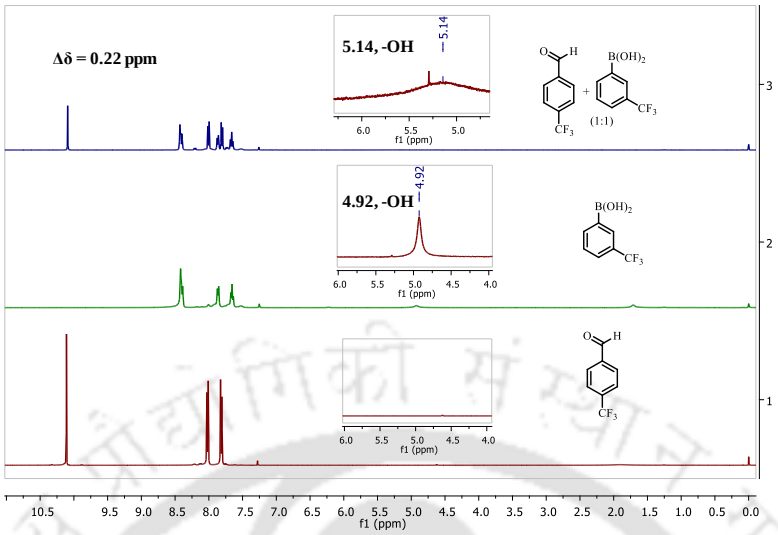

Figure 6.5. ^{1}H spectra of 4-trifluoromethylbenzaldehyde (14 mg, 0.079 mmol), 3-trifluoromethylphenylboronic acid (16 mg, 0.079 mmol), and mixture of 4-trifluoromethylbenzaldehyde and 3-trifluoromethylphenylboronic acid (molar ratio 1:1) in $CDCl_3$ at 298 K.

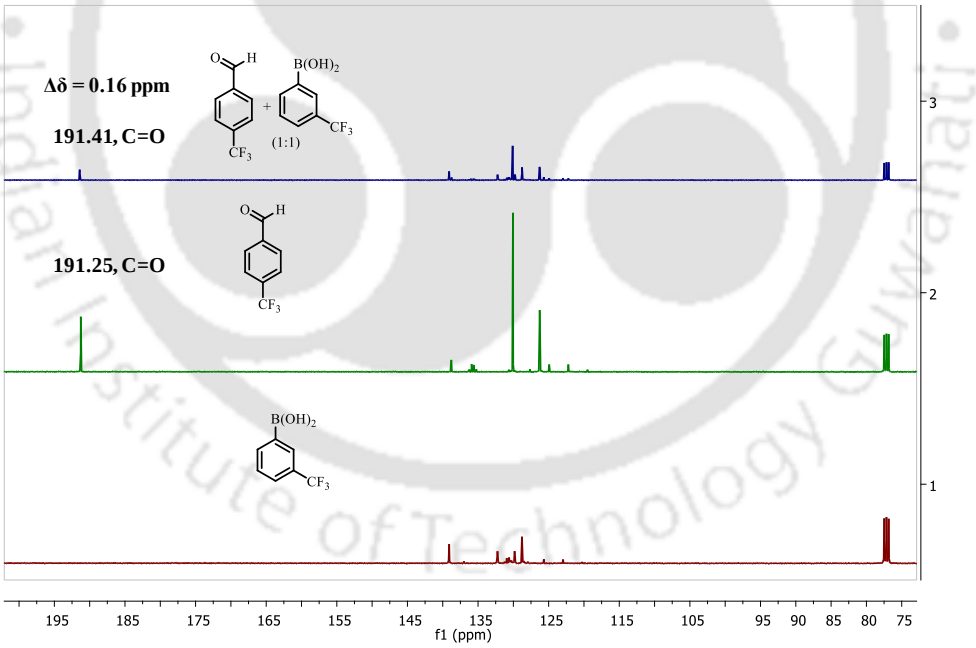

Figure 6.6. ^{13}C NMR spectra of 4-trifluoromethylbenzaldehyde (14 mg, 0.079 mmol), 3-trifluoromethylphenylboronic acid (16 mg, 0.079 mmol), and mixture of 4-trifluoromethylbenzaldehyde and 3-trifluoromethylphenylboronic acid (molar ratio 1:1) in $CDCl_3$ at 298 K.

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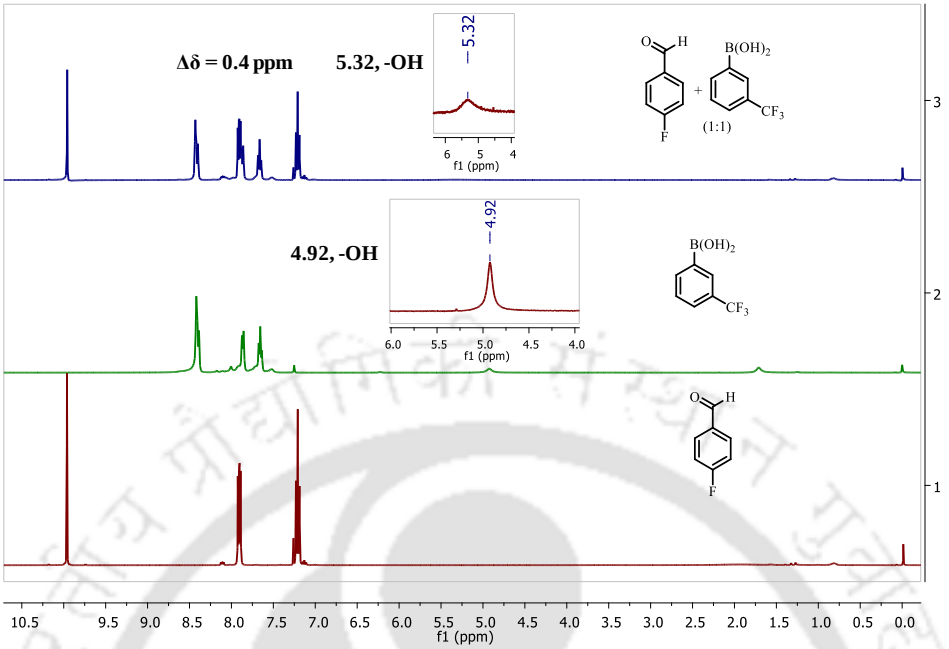

Figure 6.7. ^{1}H NMR spectra of 4-fluorobenzaldehyde (10 mg, 0.079 mmol), 3-trifluoromethylphenylboronic acid (15 mg, 0.079 mmol), and the mixture of 4-fluorobenzaldehyde and 3-trifluoromethylphenylboronic acid (molar ratio 1:1) in $CDCl_3$ at 298 K.

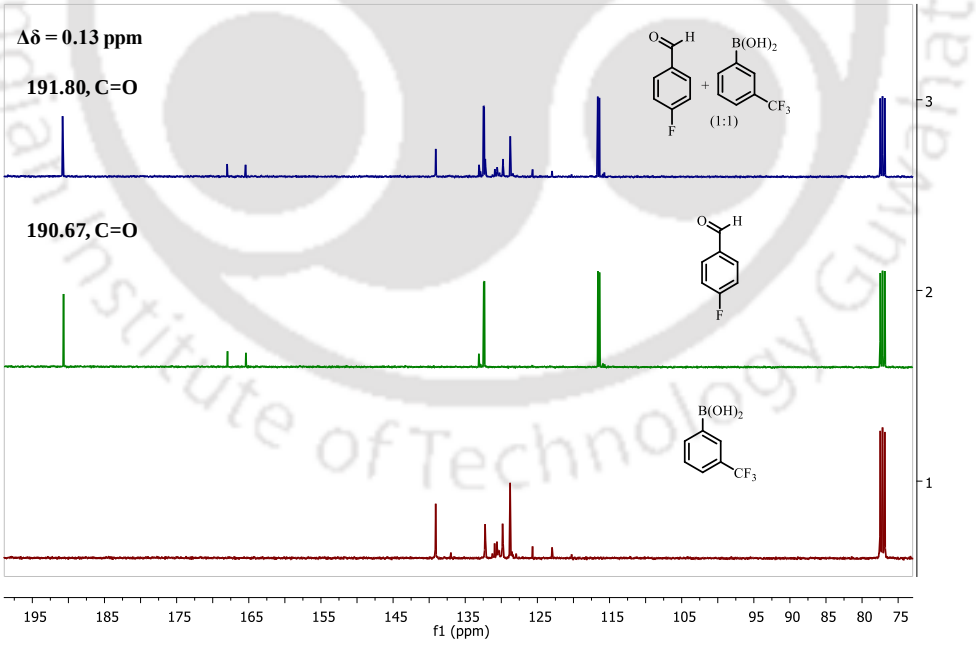

Figure 6.8. ^{13}C NMR spectra of 4-fluorobenzaldehyde (10 mg, 0.079 mmol), 3-trifluoromethylphenylboronic acid (15 mg, 0.079 mmol), and the mixture of 4-fluorobenzaldehyde and 3-trifluoromethylphenylboronic acid (molar ratio 1:1) in $CDCl_3$ at 298 K.

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For comparison, one equivalent of TBAF was added to the same reaction mixture, about 25 ppm upfield shift was observed, which indicates the same boron acts as a Lewis acid and take part in complexation with TBAF within. In IR, the carbonyl value shifted to a lower wave number from 1712.4 cm^{-1} to 1701.3 cm^{-1} after mixing with 3-trifluoromethylphenylboronic acid at room temperature (Figure 6.10). Approximately 10 cm^{-1} lower wave number has been observed for the carbonyl group in a mixture compared to free aldehyde, which supports hydrogen bonding interaction between aldehyde and boronic acid. A downfield shift for hydroxyl peak of boronic acid in ^{1}H NMR and ensuing downfield shift for carbonyl in aldehyde in ^{13}C NMR supports hydrogen bonding interaction with aldehyde and boronic acid rather than complexation with boron. It has been further reinforced by using IR spectroscopic experiments in the solid-state. Likewise, weak hydrogen bonding interaction was also observed while mixing **6.3b** or **6.3a** with Hantzsch ester (Figure 6.16-6.18)

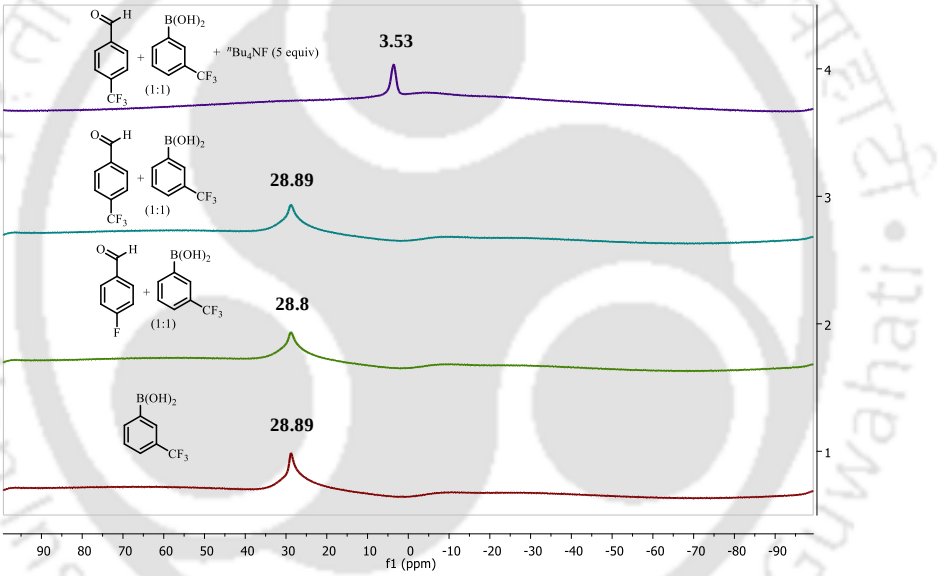

Figure 6.9. ^{11}B NMR spectra of 3-trifluoromethylphenylboronic acid (15 mg, 0.079 mmol), mixture of 4-fluorobenzaldehyde and 3-trifluoromethylphenylboronic acid (molar ratio 1:1), 4-trifluoromethylbenzaldehyde and 3-trifluoromethylphenylboronic acid (molar ratio 1:1) and with TBAF (0.534 mmol) in $CDCl_3$ at 298 K.

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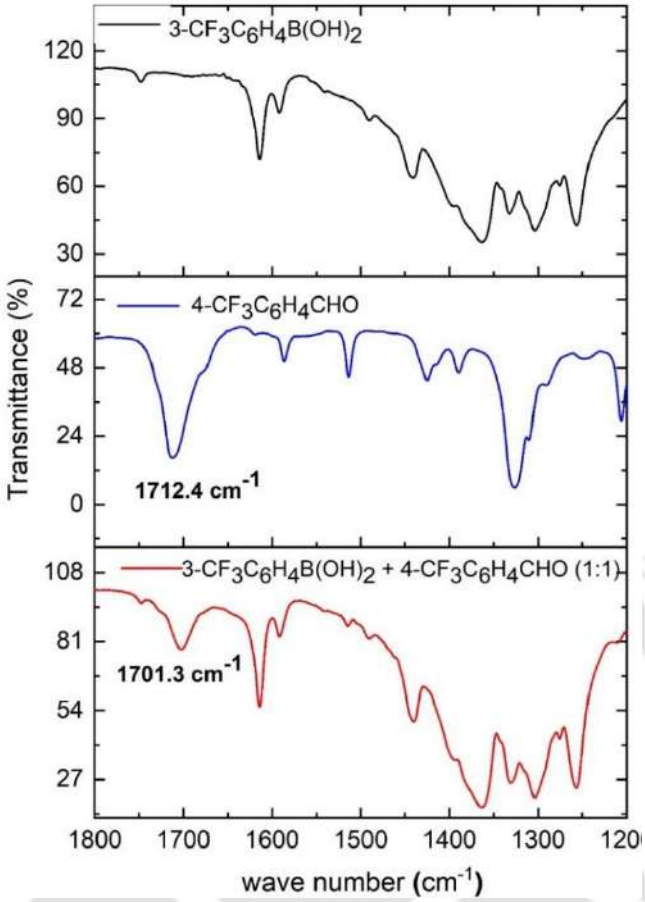

Figure 6.10. IR spectroscopy experiment to support the interaction of 4-trifluoromethyl benzaldehyde and 3-trifluoromethylphenylboronic acid.

To further probe the Lewis acidic nature of boron and hydrogen bonding activation mode of boronic acids, I have examined the conversion of **6.1a** to **6.1a'** (for reduction step) and **6.1a'** to **6.4f** (for reductive *N*-alkylation step) with different electronic substituents of boronic acids **6.3a**, **6.3b**, **6.3c** boronic esters **6.3i**, **6.3j**, **6.3k** under the reaction condition mentioned in Scheme 6.8. The boronic esters with increased Lewis acidic character did not show any considerable effect (e.g., **6.3b**; **6.1a′**, 78%, **6.4f**, 75% *vs* **6.3j**; **6.1a′**, 16%, **6.4f**, 35%, **6.3a**; **6.1a′,** 11%, **6.4af**, 45% vs **6.3i**; **6.1a′**, 9%, **6.4af**, 18% and **6.3c**, **6.1a'**, 32%, **6.4f**, 67% *vs* **6.3k**, **6.1a'**, 14%, **6.4f**, 30%). It suggests that the activation of quinoline or aldehyde by boronic acid is superior to boronic ester, probably due to hydrogen bonding interaction rather than Lewis acid activation. The catalytic activity is further enhanced while increasing the Lewis acidic behavior of boron either in boronic acid or in boronic ester. These results demonstrate that both the Lewis acidic behavior of boron and the importance of the hydroxyl group present in the catalytic system. Following this, the role of boronic acid in condensation reaction was also probed by performing the reaction with THQ, aldehyde **6.2g**, and Hantzsch ester under optimized conditions, giving the anticipated product **6.4g** in 96% (with **6.3b**), and 36% (without **6.3b**) respectively, indicating boron-assisted condensation is beneficial (Scheme 6.9).

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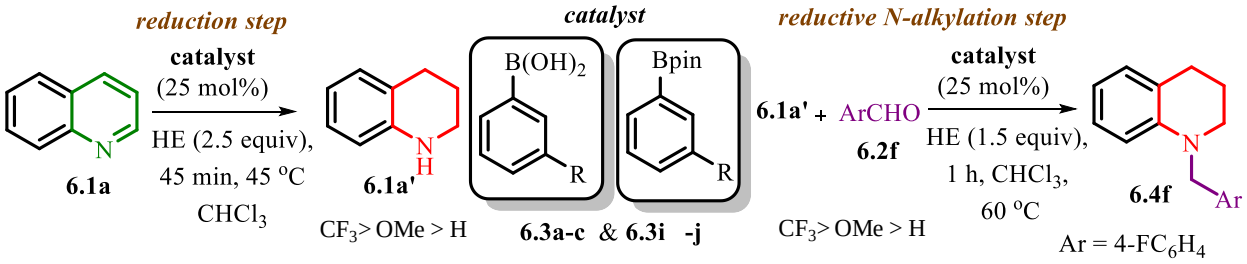
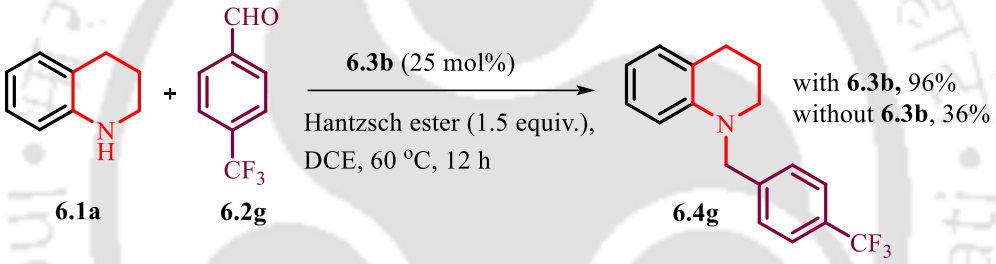


catalyst	6.3b (R= CF_3)	6.3c (R= OMe)	6.3a (R= H)	6.3j (R= CF_3)	6.3k (R= OMe)	6.3i (R= H)	none
yield (%), **6.1a'**	78%	32%	11%	16%	14%	9%	7%
yield (%), **6.4f**	75%	67%	45%	35%	30%	18%	3%

Scheme 6.8. Effect of hydrogen bonding ability and Lewis acidic properties of boronic acid and ester in catalysis



Scheme 6.9. Synthesis of *N*-alkyl THQs from THQs

In order to investigate the mechanistic pathway of the condensation reaction, the reaction was performed with and without 3-trifluormethylphenylboronic acid in the equal molar ratio 1,2,3,4-THQ, and 4-trifluoromethylbenzaldehyde at 45 ℃ in $CDCl_3$ and the reaction was monitored by ^1H and ^{11}B NMR spectroscopy at different time intervals. (Scheme 6.10). Over the time of 7 h, the signal of –CHO proton in aldehyde slowly disappeared, and a new peak was raised at 5.25 ppm in ^1H NMR (Figure 6.11), and a new signal appeared at 55.4 ppm in ^{13}C NMR (assignment based on 2D HSQC correlation spectra). These are likely to be attributed to hemiaminal formation (Figure 6.12).[29, 30] Due to the presence of vacant *p*-orbital of boron in boronic acid, the iminium species can transiently be stabilized by the borate anion (the ion pair that may form after the capture of the hydroxyl group of hemiaminal) that may shift the equilibrium toward the Schiff base formation. (In ^{11}B NMR, a new signal originated at 1.69 ppm, which may correspond to borate anion (Figure 6.13). During the reaction of 2-formylboronic acid with THQ, benzoxaborole derivative **6.9** was isolated in 66% yield (Scheme 6.10) that could have formed after the elimination of water molecule from the zwitter ionic species. Notably, no conversation of aldehyde was observed without boronic acid under the same condition after 24 h.

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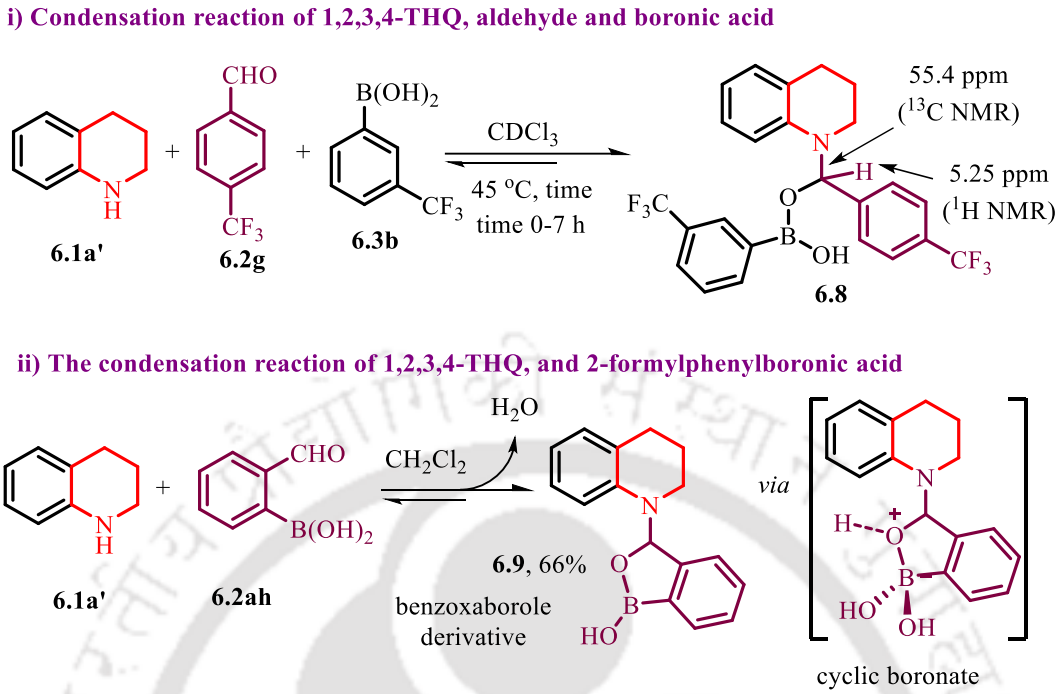

Scheme 6.10. Role of boronic acid in condensation reaction.

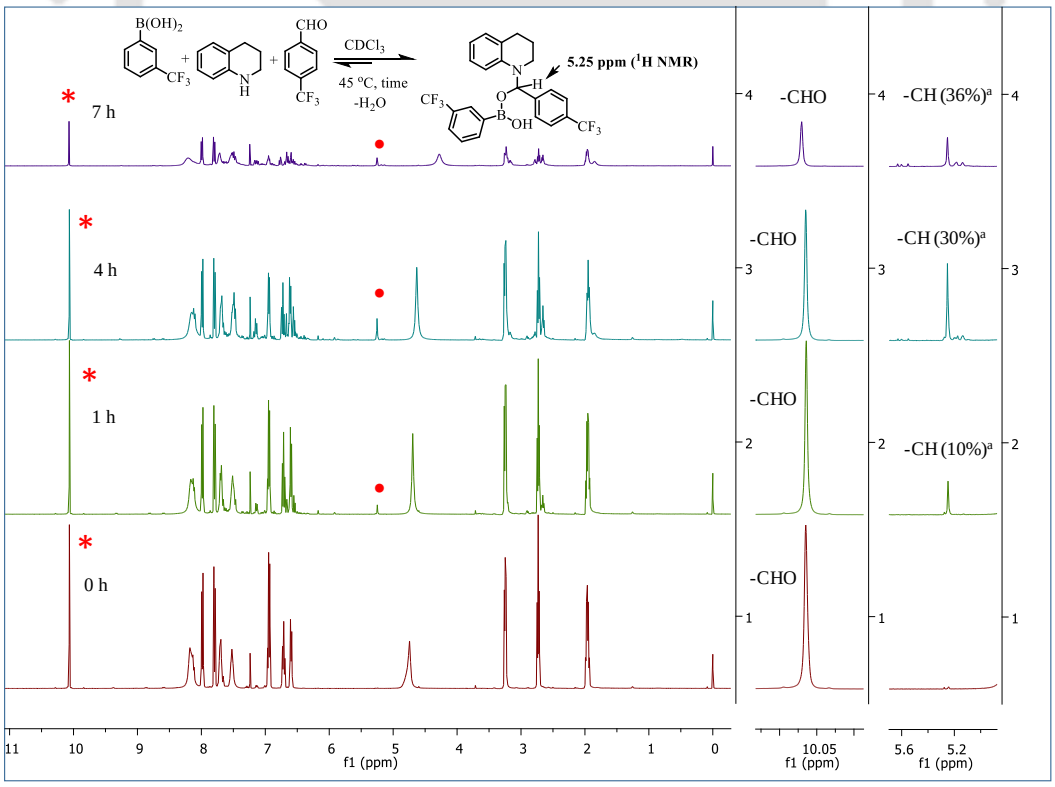

Figure 6.11. ^{1}H spectra of the combination of tetrahydroquinoline (11 mg, 0.079 mmol), 3-trifluoromethyl phenylboronic acid (15 mg, 0.079 mmol), and 4-trifluoromethylbenzaldehyde (14

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mg, 0.079 mmol) (molar ratio 1:1:1) in $CDCl_3$ at 298 K at different time interval. [a]conversion with respect to 4-trifluoromethylbenzaldehyde.

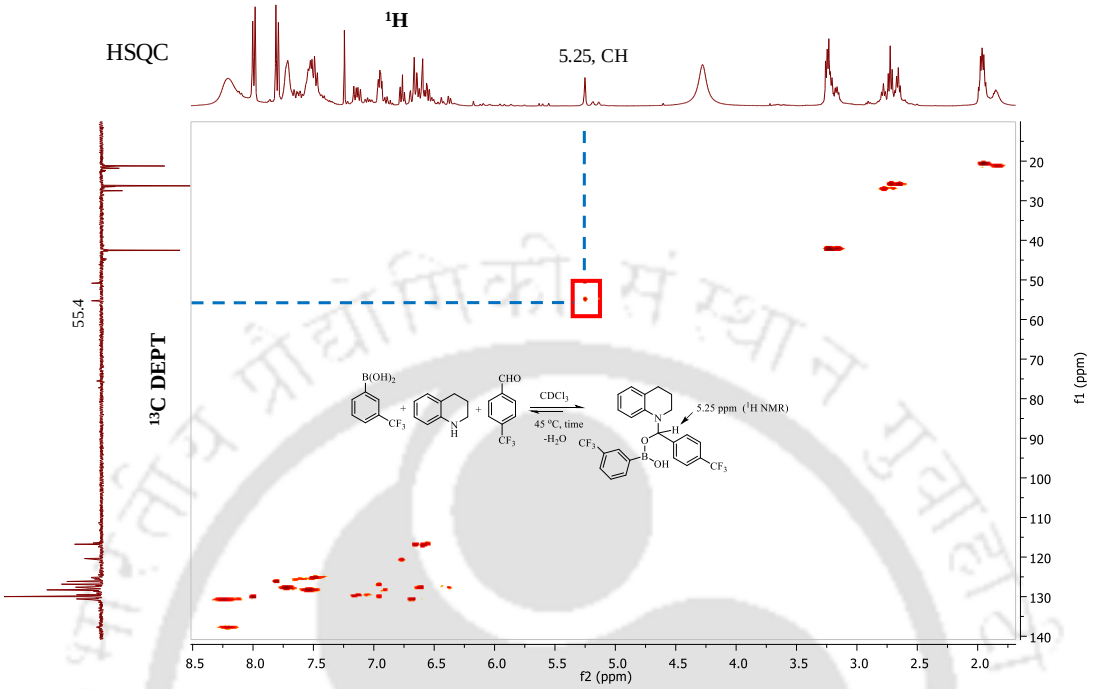

Figure 6.12. HSQC correlation spectra after 7 h for the mixture of tetrahydroquinoline (11 mg, 0.079 mmol), 3-trifluoromethyl phenylboronic acid (15 mg, 0.079 mmol), and 4-trifluoromethylbenzaldehyde (14 mg, 0.079 mmol) (molar ratio 1:1:1) in $CDCl_3$ at 298 K.

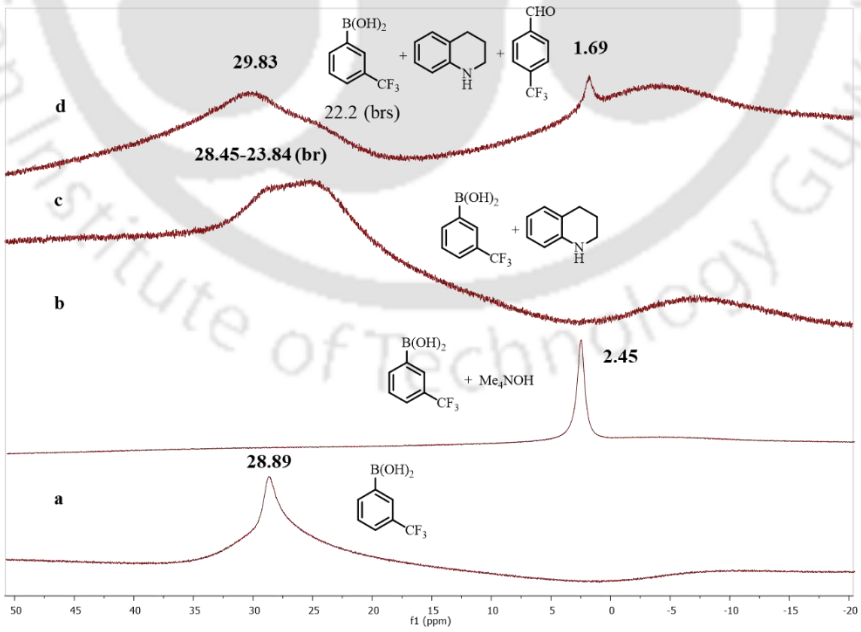

Figure 6.13. ^{11}B spectra of (a) 3-trifluoromethylphenylboronic acid (15 mg, 0.079 mmol), in $CDCl_3$ at 298 K, (b) a combination of 3-trifluoromethylphenylboronic acid (15 mg, 0.079 mmol),

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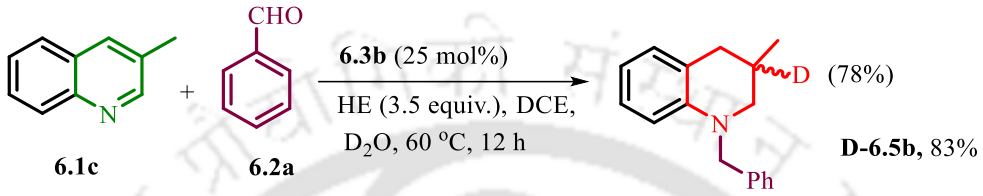
and Me_4NOH (molar ratio 1:5) in D_2O at 298 K (c) a combination of 3-trifluoromethylphenylboronic acid, 1,2,3,4-THQ, 4-trifluoromethylbenzaldehyde (molar ratio 1:1:1) in $CDCl_3$ at 298 K under the reaction condition.

In order to locate the hydridic proton and acidic proton in the *N*-alkyl-THQ product, we have performed the catalytic experiment with 3-methyl quinoline **6.1c** in the presence of D_2O. The outcome demonstrated that the deuterium atom was incorporated at the C-3 position of *N*-alkyl-THQ derivative **D-6.5b** (Scheme 6.11).



Scheme 6.11. Deuterium-labeled experiment with 3-methyl quinoline.

Role of water in reductive amination of quinoline

As the reaction produces H_2O as one of the by-products, the the effect of water in this transformation was also studied. Initially, when the reaction was carried out with 5 equiv. water under the optimized conditions, the yield of *N*-alkylated product **6.4g** is dropped to 23% within 12 h along with, 20% of the intermediate hydrogenated product 1,2,3,4-THQ (**6.1a'**) was also observed.

To further understand the effect of water in this tandem process, we have examined the conversion of quinoline (**6.1a**) to 1,2,3,4-THQ (**6.1a'**) (for reduction step) and 1,2,3,4-THQ (**6.1a'**) to *N*-alkylated product **6.4f** (for reductive *N*-alkylation step) by adding different equivalents of water in the reaction mixture. It was found that the yield of **6.1a'** is decreased from 96% to 72% to 45% with 0, 1 and 4 equiv. of H_2O respectively, (Scheme 6.12b). Likewise, the yield of **6.4f** also decreases from 94% to 48% to 21% with 0, 1 and 4 equiv. of H_2O respectively, (Scheme 6.12c). It suggests that both the reaction steps are suppressed in the presence of water.

To inspect the nature of binding interaction with boronic acid and quinoline in presence of water, the combination of quinoline, 3-trifluoromethylphenylboronic acid (molar ratio 3:1), and water (3 equiv.) in $CDCl_3$ at rt was examined. The result was compared to the absence of water. The chemical shift for H2 in quinoline is shifted to upfield from δ = 8.97 ppm to 8.90 ppm (H2 chemical shift in free quinoline), indicating the disruption of the H-bonding interaction. In addition, a downfield shift was observed from δ = 21.9 ppm to 27.8 ppm in ^{11}B NMR that also suggests the same. These results clearly indicate not-only the significance of the H-bonding interaction between the boronic acid and quinoline in the current protocol, but also explains the decrease in yields of the products in the presence of excess amounts of water.

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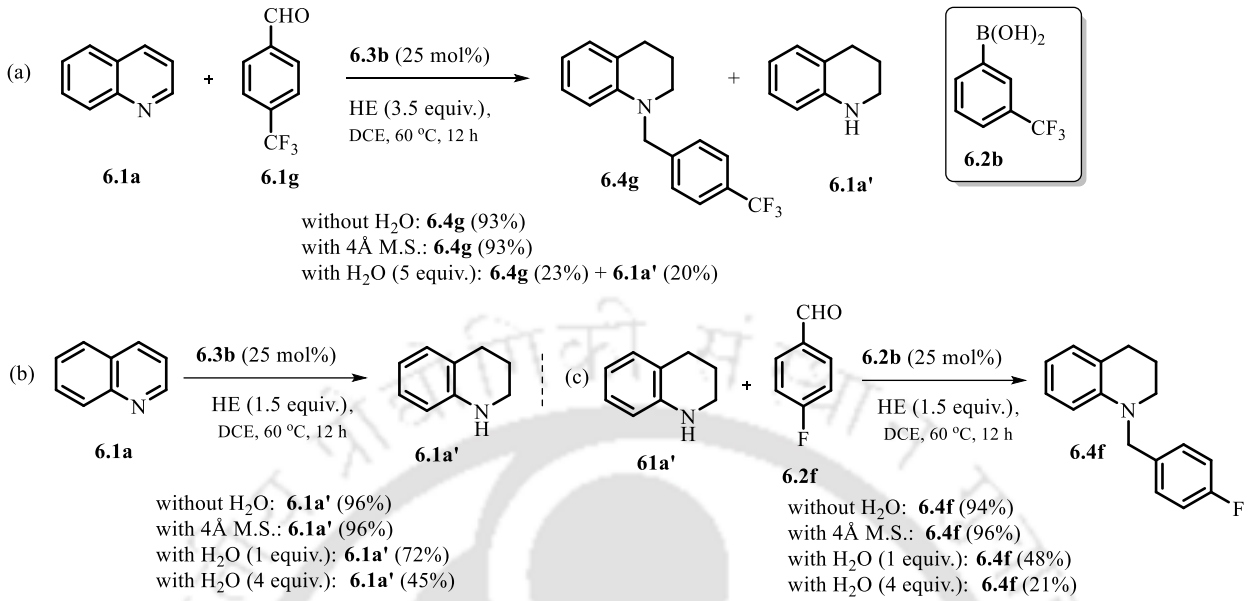
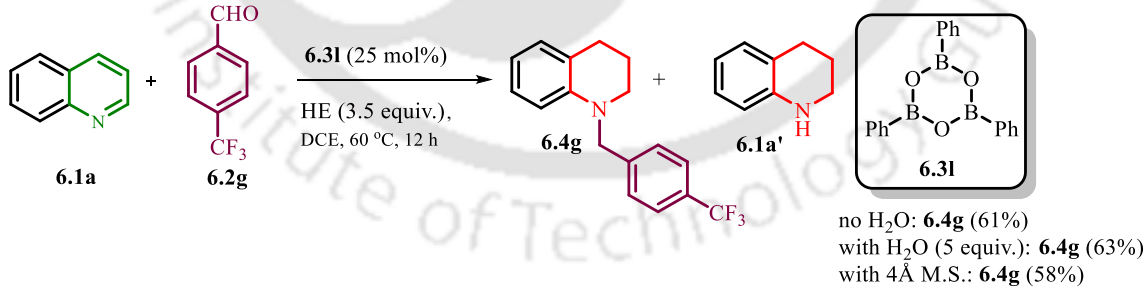


Scheme 6.12. Effect of water with **6.3b** in reduction-reductive *N*-alkylation reaction

In order to understand the effect of the water on the Lewis acidic property of boron derivatives in the current protocol, we have performed the following reaction with triphenylboroxine (**6.3l**) as the catalyst under i) 4 Å molecular sieves, ii) no water, and iii) in the presence of water where the *N*-alkylated product **6.4g** was obtained in 58%, 61%, and 63% yield respectively, (Scheme 6.14). These experiments suggest that the reaction can be facilitates by Lewis acidic boroxine to certain extent. Also, the similar yields obtained in the presence and absence of water under boroxine catalysis suggest that the boroxine under the reaction conditions does not hydrolyze to give free boronic acid.



Scheme 6.13. Effect of water with triphenylboroxine

To understand the possible involvement of boronic anhydride in boronic acid catalysis, we have examined the dehydration of phenyl boronic acid (**6.3a**), and 3-triflouromethylphenyl boronic acid (**6.3b**), independently in DCE at 60 °C for 12 h under our reaction conditions. Interestingly, complete conversion of phenylboronic acid (**6.3a**) to triphenyl boroxine (**6.3l**) was observed by using (**6.3b**), and no conversion was observed from **6.3b** to tris(3-triflouromethylphenyl)boroxine (**6.3m**) (Scheme 6.14).

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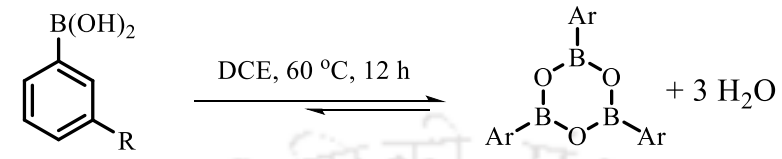
These observations suggest that the reaction possibly occur *via* the combined effect of boronic anhydride and residual boronic acid in the case of phenylboronic acid (**6.3a**). But, for boronic acid with electron-withdrawing $–CF_3$ substituent **6.3b** the reaction is most likely to proceed through boronic acid and not by the catalysis of boronic anhydride as there is no formation of corresponding boroxine under the reaction conditions.



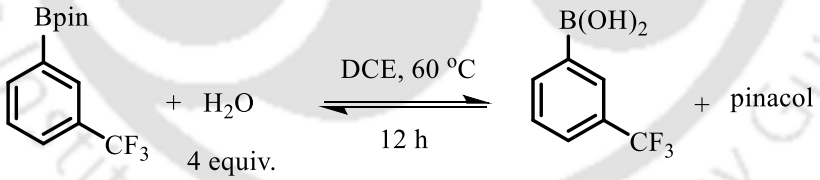
6.3a (R = H)
6.3b (R = CF_3)

6.3l (Ar = Ph), > 99%
6.3m (Ar = 3-$CF_3C_6H_3$), 0%
6.3m (Ar = 3-$CF_3C_6H_3$) (with 4 Å M.S.,), 0%

Scheme 6.14. Dehydration of arylboronic acid

Based on all of the above observations, we would like to postulate that, under the current reaction conditions, the involvement of boronic anhydride arising from **6.3b** is unlikely and the reaction is more likely to be catalysed by only 3-triflouromethylphenyl boronic acid (**6.3b**).

To understand the partial hydrolysis of arylboronic acid pinacol ester in presence of water, we have also performed the NMR experiment with 3-trifluoromethylphenylboronic acid pinacol ester (**6.3j**) and H_2O (4 equiv.) in DCE at 60 °C for 12 h. We have not observed any partial hydrolysis product (such as aryl boronic acid **6.3b** and free pinacol) under our reaction conditions (Scheme 6.15). This control experiment suggests that the possibility of partial hydrolysis for arylboronic acid pinacol ester is unlikely under the reaction conditions.



6.3j **6.3b**

Scheme 6.15. Hydrolysis study of **6.3j**

On the basis of all of the above experimental findings, a weak Lewis acid and hydrogen-bond interaction promoted catalytic cycle of boronic acid is proposed for tandem-reduction and reductive *N*-alkylation of quinoline (Scheme 6.16). First, the 1,4 position of the quinoline ring is activated by the hydroxyl group of boronic acid *via* hydrogen bonding interaction and forms the specie **6.1A** (Scheme 6.16, Cycle 1), Following this, a Hantzsch ester hydride atom attacks the C-4 position of the quinoline moiety and generates 1,4-dihydroquinoline species **6.1B**. This intermediate can easily undergo isomerization to give 3,4-dihydroquinoline **6.1C**, after which 1,2-hydride transfer takes place, resulting the 1,2,3,4-THQ **6.1a'**. Then the in situ generated THQ can participate in boron assisted condensation reaction with the aldehyde to form iminium intermediate

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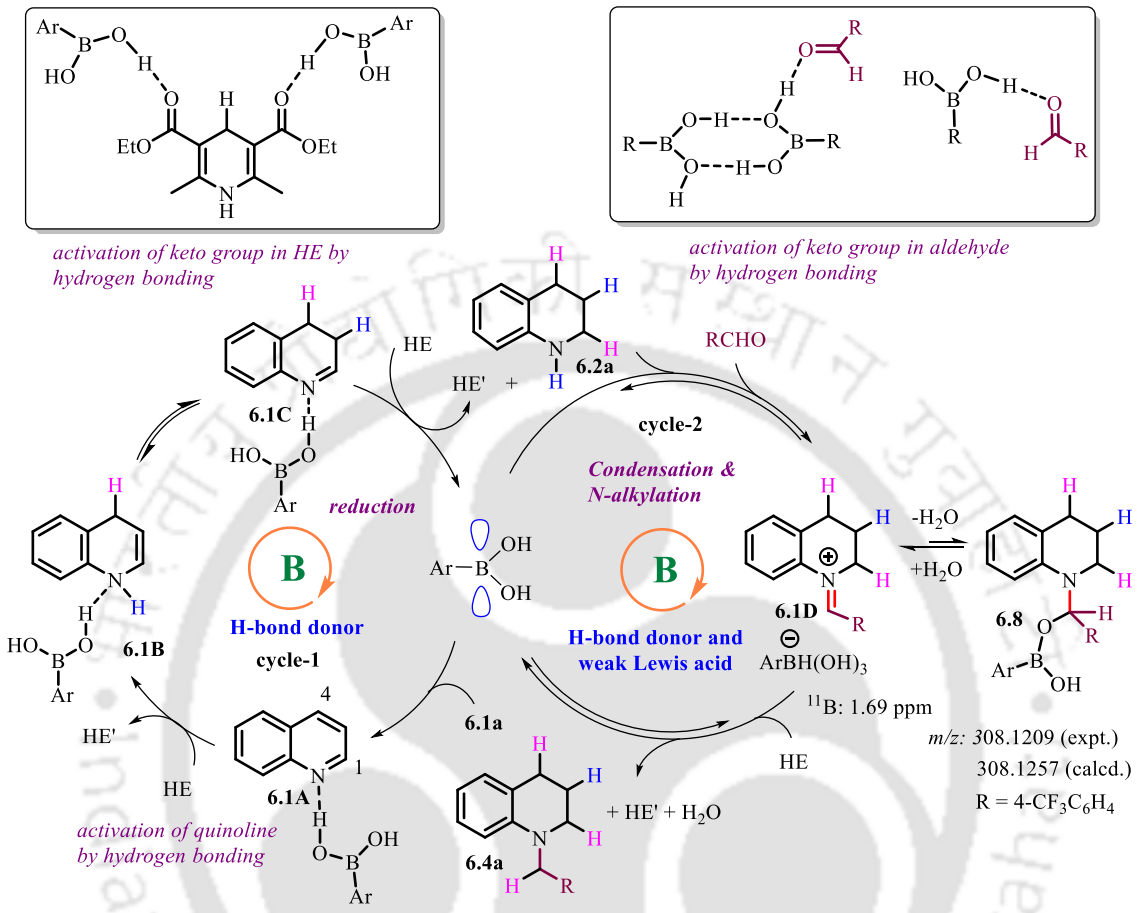
6.1D. Intermediate **6.1D** reduced by HE to provide the desired *N*-alkylated THQ and simultaneously regenerates the catalyst (Cycle 2).



Scheme 6.16. Probable mechanistic pathway

6.4. Summary

In summary, I have developed a one-pot tandem reduction of quinoline with subsequent reductive alkylation using aldehydes to form *N*-alkylated tetrahydroquinolines without the aid of any transition metal. Contrary to the reported procedures, the current protocol employs a commercially available, air- and moisture-tolerant boronic acid that is compatible with a wide variety of substrates. This convenient method tolerates diverse reducible groups such as ester, halo, nitro, nitrile, alkyne, allyl, benzyl etc. The protocol is further extended to the functionalization of complex Vitamin-*E* and (±) cholesterol derivative efficiently. Method enables facile access to the antimicrobial active *N*-diarylmehyl THQ motif *via* a multicomponent Petasis borono-Mannich (PBM) reaction. The detailed mechanistic finding demonstrates the dual role of boronic acid as a mild-Lewis acid and H-bond donor catalyst, in which H-bond donor property was found to be superior in boronic acid catalysis. The role of boronic acid as a hydrogen bond donor has been discussed in the reductive chemistry for the first time herein. Furthermore, the effect of boronic acid in the condensation pathway was also disclosed.

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6.5. Experimental section

A. General information

All the reagents and chemicals were purchased from common commercial suppliers like Sigma-Aldrich, Alfa Aesar, Merck, Spectrochem, Avra Synthesis Pvt. Ltd. and directly used as received without any further purification unless otherwise mentioned. 3-methyl-2-phenylquinoline,[31] 6-fluoro-2-methylquinoline,[32] [1,1'-biphenyl]-4-carbaldehyde,[33] 4-(phenylethynyl)benzaldehyde,[34] 4-(allyloxy)benzaldehyde,[35] 4-(benzyloxy)benzaldehyde,[36] 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborola-2-yl)benzaldehyde,[37]2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzaldehyde,[37] 2-(phenyl sulfonyl)benzaldehyde,[38] cholester-3-yl-4-formylbenzoate,[39] 3,4-bis[[4-(trifluoromethyl)phenyl] amino]-3-cyclobutene-1,2-dione[40] were prepared according to the reported literature. All boronic acids are recrystallized from water, prior to use. Boronic acid pinacol esters are synthesized by overnight reflux in toluene with boronic acid, and pinacol. Hantzsch ester was synthesized according to the reported literature.[41] All the reductive N-alkylation reactions were performed in a pyrex tube. All synthesized compounds were characterized by spectroscopic methods and compared to reported literature wherever applicable, otherwise stated. ^{1}H, ^{13}C, ^{19}F, and ^{11}B NMR spectra of all the compounds were measured in $CDCl_3$ or DMSO-d_6 as a solvent by using TMS as an internal standard. Chemical shifts, δ (in ppm), are reported relative to TMS δ (^{1}H) 0.0 ppm, δ (^{13}C) 0.0 ppm, which was used as the inner reference. Otherwise the solvents residual proton resonance and carbon resonance ($CHCl_3$, δ (^{1}H) 7.26 ppm, δ (^{13}C) 77.16 ppm; DMSO-d_6, (^{1}H) 2.50 ppm, δ (^{13}C) 39.52 ppm) were also used for calibration. Bruker Avance III 600 and 400 spectrometers were used to record the NMR spectra. Chemical shifts (δ) values were reported in ppm and spin-spin coupling constant (J) were expressed in Hz, and other data were reported as follows: s = singlet, d = doublet, dd = doublet of doublet, dt = doublet of triplet, t = triplet, m = multiplet, q = quartet, sext = sextet, br = broad, and brs = broad singlet. IR spectra were recorded on Perkin Elmer Instrument at normal temperature making KBr pellet grinding the sample with KBr (IR Grade). MS (ESI-HRMS): Mass spectra were recorded on an Agilent Accurate-Mass Q-TOF LC/MS 6520. Merck silica gel 60-120 was used for column chromatography. GC analyses were performed on a Perkinelmer-Clarus 590 GC instrument fitted with Elite-1 column (30 m length, 0.32 mm ID) using the following method: Injection volume: 1 µL, inlet temperature: 280 °C, FID detector temperature: 280 °C, oven temperature: start at 60 °C hold time 1 min, ramp: 12 °C /min, upto 320 °C, Flow rate (carrier): 25 mL/min (N2).

B. General procedure for preparation of starting materials

Preparation of 2,5,7,8-tetramethyl-2-(4,8,12-trimethyltridecyl)chroman-6-yl 2-(4-formyl phenoxy)acetate (6.2ab):

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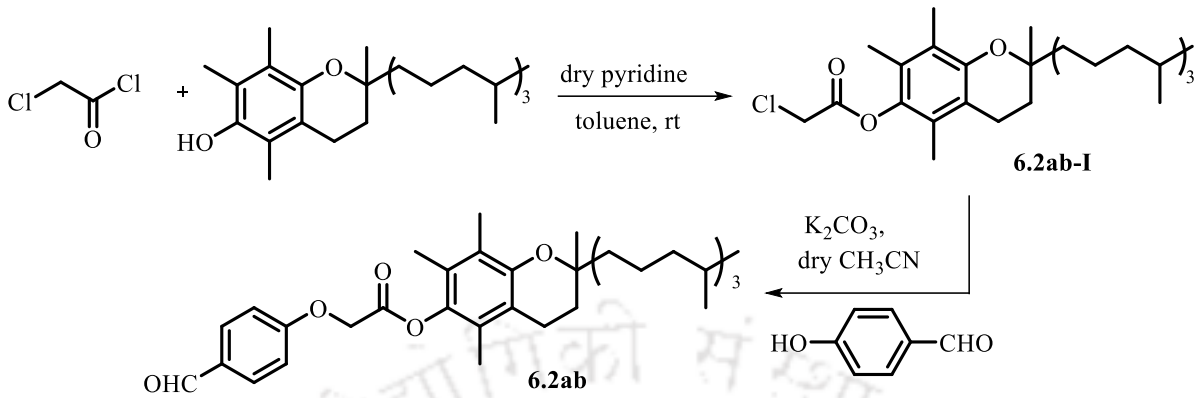

Scheme 6.17. Synthesis of 2,5,7,8-tetramethyl-2-(4,8,12-trimethyltridecyl)chroman-6-yl-2-(4-formylphenoxy)acetate

Step-1: To a stirred solution of (±)-α-tocopherol (250 mg, 0.6 mmol) and pyridine (0.1 mL) in toluene (2.0 mL), a solution of 2-chloroacetyl chloride (0.1 mL) in toluene (2 mL) was added dropwise over 15 min under nitrogen atmosphere and allowed to stir for 8 h. The reaction mixture was then filtered, and filtrate was washed with brine solution. The resulting organic layer was dried with sodium sulfate and solvent was evaporated under reduced pressure in rotary evaporator to afford the compound **6.2ab-I**.[42]

Step-2: A mixture of 4-hydroxybenzaldehyde (61 mg, 0.5 mmol) and K_2CO_3 (166 mg, 1.2 mmol) was refluxed in dry CH_3CN for 2 h and then, to the reaction mixture compound **6.2ab-I** (304 mg, 0.6 mmol) was added and refluxed for 5 h. After completion of the reaction, the required product was extracted in DCM dried over sodium sulfate and dried under reduced pressure. Evaporation of the solvent gave the crude product, which was purified by column chromatography eluted by pet ether–ethyl acetate mixture (9:1 v/v) to obtain the desired product in 75% yield.

Light yellow liquid (267 mg, 75%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.92 (s, 1H), 7.89 – 7.87 (m, 2H), 7.12 (d, J = 8.8 Hz, 2H), 5.02 (s, 2H), 2.58 (t, J = 6.8 Hz, 2H), 2.08 (s, 3H), 2.01 (s, 3H), 1.96 (s, 3H), 1.83-1.73 (m, 2H), 1.57 – 1.58 (m, 3H), 1.55 – 1.48 (m, 2H), 1.43 – 1.34 (m, 3H), 1.27 – 1.20 (m, 10H), 1.15 – 1.04 (m, 6H), 0.87 – 0.83 (m, 12H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 190.8, 166.9, 162.7, 150.0, 140.0, 132.1, 131.1, 126.5, 124.9, 123.5, 117.8, 115.2, 75.4, 65.2, 39.5, 37.6, 37.5, 37.4, 32.9, 32.8, 28.1, 25.0, 24.6, 22.9, 22.8, 21.2, 20.7, 19.9, 19.8, 13.2, 12.3, 12.0. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{38}H_{57}O_5$ 593.4201; found 593.4241.

C. Synthetic scope of *N*-alkyl tetrahydroquinolines

i) General procedure

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General procedure for synthesis of *N*-alkyl tetrahydroquinolines (GP-1)

In a reaction tube (15 mL), substituted quinoline (0.5 mmol), substituted aldehyde (0.5 mmol) or cyclic ketone (0.5 mmol), Hantzsch ester (1.75 mmol), **6.3b** (25 mol%) and DCE (2 mL) were taken. Then the reaction tube was properly closed and placed in a preheated oil bath at 60 ℃ for 12 h with continuous stirring. The reaction was monitored by thin layered chromatography (TLC) in petroleum ether and ethyl acetate solvent system. After completion of the reaction, the reaction tube was brought to room temperature and the crude compound was purified through silica gel column chromatography.

General procedure for the synthesis of *N*-diarylmethyl THQs (GP-2)

In a reaction tube (15 mL), quinoline (0.5 mmol), arylboronic acid (0.5 mmol), Hantzsch ester (1.1 mmol), and DCE (2 mL) were taken. The reaction tube was properly closed and placed in a preheated oil bath at 60 ℃ for 3 h with continuous stirring. To the reaction mixture, then salicylaldehyde (0.34 mmol) was added and heated at 90 ℃ for 12 h. After completing the reaction, the reaction tube was brought to room temperature, and the crude compound was purified through silica gel column chromatography.

General procedure for synthesis of 6.7a-6.7d (GP-3)

In a reaction tube (15 mL), quinoline (0.5 mmol) or substituted quinoline (0.5 mmol), formylphenylboronic acid (0.5 mmol) or formylphenylboronic acid pinacol ester (0.5 mmol), Hantzsch ester (2.5 mmol), and DCE (2 mL) were taken. The reaction tube was properly closed and placed in a preheated oil bath at 60 ℃ with continuous stirring. All the starting material was completely consumed after 3 h for formylphenylboronic acid and 24 h for formylphenylboronic acid pinacol ester. The crude compound was then purified through silica gel column chromatography.

ii) Gram scale-reaction (Scheme 6.6)

Experimental procedure: In a reaction tube (100 mL), quinoline (1.0 g, 8 mmol), benzaldehyde (8 mmol), Hantzsch ester (3.5 equiv.), 3-trifluoromethylphenylboronic acid (25 mol%), and DCE (15 ml) were taken. Then the tube was properly closed and placed in a preheated oil bath at 60 ℃ with continuous stirring. After 24 h, volatile solvent was removed and the resulting crude compound was purified by silica gel column chromatography using petroleum ether/ ethyl acetate mixture as eluent (v/v = 50:1, R_f = 0.80) to obtain **6.4a** in 78% yield (1.4 g, 6.24 mmol).

iii) Recovery of Hantzsch-1,4-dihydropyridine (HE) (Scheme 6.7)

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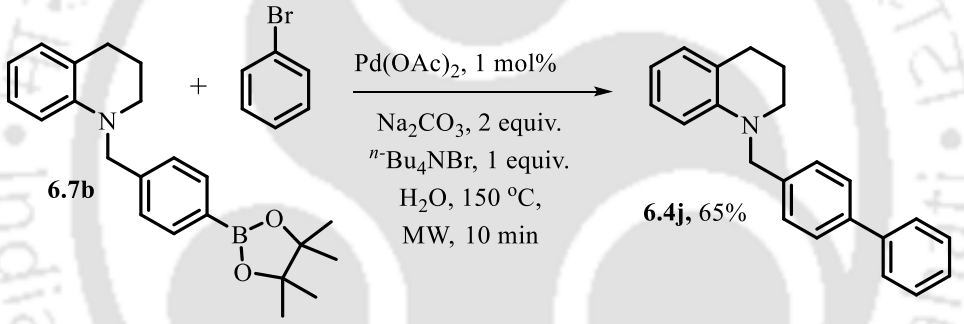
Experimental procedure for route A: A mixture of [Ru(*p*-cymene)I_2]$_2$ (10 mg, 0.01 mmol) and Hantzsch pyridine (50.0 mg, 0.2 mmol) in THF (10 mL) was stirred at room temperature for 10 min in glove box, then the mixture was loaded to an autoclave. The hydrogenation was performed at 70 ^oC under H_2 (42 bar) for 16 h. After carefully release of the hydrogen, the autoclave was opened. Isolated yield (yellow solid, 30 mg, 60%).

Experimental procedure for route B: In a 50 mL round bottom flask, Hantzsch pyridine (1 gm, 3.9 mmol), water (10 mL) and acetic acid (45 µmL, 20 mol%) were charged and placed in an ice bath. In the reaction mixture $NaBH_3CN$ (294 mg, 1.2 equiv.) was slowly added and stirred for overnight. The reaction was monitored by thin layered chromatography (TLC) in hexane and ethyl acetate solvent system. After completion of the reaction, solid precipitate was filtered. Then it was washed thoroughly by water and ice cold acetone and dried on vacuum desiccator. Isolated yield (yellow solid, 0.9 g, 91%).

iv) Pd-catalyzed Suzuki-Miyaura coupling reaction of 6.7b



Scheme 6.18. Functionalization of **6.7b**

1-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzyl)-1,2,3,4-tetrahydroquinoline (0.2 mmol, 70 mg), bromobenzene (0.2 mmol, 31 mg), palladium(II) acetate (0.002 mmol, 0.5 mg), sodium carbonate (0.4 mmol, 42 mg), tetrabutylammonium bromide (0.2 mmol, 65 mg), and water (1 mL) were mixed in a microwave vial. The mixture was stirred under microwave irradiation at 150 °C for 15 min. The mixture was cooled and diluted with EtOAc and water, then washed with a saturated sodium chloride solution, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure to give coupling product **6.4j** in 65% yield (yellow liquid, 39 mg).

D. Mechanistic studies

i) Interaction of boronic ester and triphenyl boroxine with quinoline

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To clarity the Lewis acidic behavior of boron, the interaction of boronic ester with quinoline was investigated; no reasonable shift was observed in ^{1}H and ^{11}B NMR while mixing with quinoline and 3-trifluoromethylphenylboronic acid pinacol ester (**6.3j**) (molar ratio 3:1), which indicates no noticeable Lewis acid-base adduct formation in boronic ester in the NMR time frame (Figure 6.14). To check the interaction of boronic anhydride and quinoline in the reaction, we have examined the ^{1}H and ^{11}B NMR in $CDCl_3$ for the mixture of quinoline and triphenyl boroxine (molar ratio 3:1). The chemical shift for H2, H4, and H8 in quinoline is shifted to downfield along with aromatic proton of boronic acid was shifted to upfield (Figure 6.15). In addition, at 22.6 ppm a upfield shift was observed in ^{11}B NMR, which suggests the possibility of Lewis acid-base adduct formation.

Likewise, we attempted to study the interaction with electron-withdrawing $–CF_3$ substituent boronic anhydride. Despite several attempts, unlike simple phenyl boronic acid, we failed to obtain the desired tris(3-triflouromethylphenyl)boroxine (**6.3l**) from 3-triflouromethylphenyl boronic acid (**6.3b**) in good yield by heating at 140 ℃ in toluene with 4 Å M.S for 24 h. Only 7% conversion was achieved by heating **6.3b** at 120 ℃ under vacuum for 12 h using a Kugelrohr apparatus. It is likely that the dehydration of boronic acid is an unfavorable process with an electron withdrawing $–CF_3$ substituent.

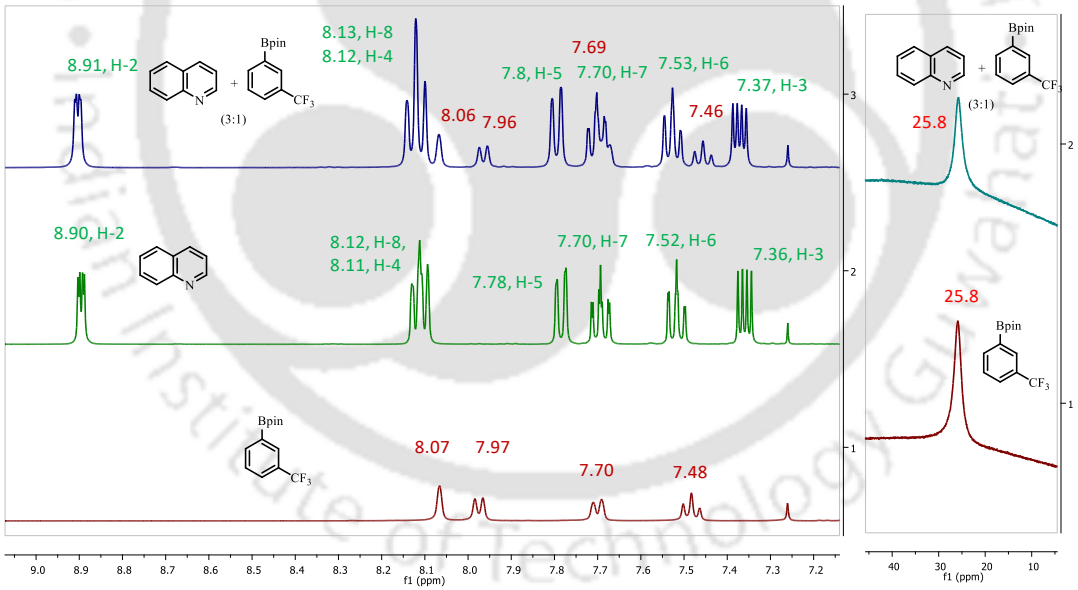

Figure 6.14. ^{1}H, and ^{11}B spectra of quinoline (10 mg, 0.077 mmol), 3-trifluoromethylphenylboronic acid pinacol ester (21 mg, 0.077 mmol), and a combination of quinoline and 3-trifluoromethylphenylboronic acid pinacol ester (molar ratio 3:1) in $CDCl_3$ at 298 K.

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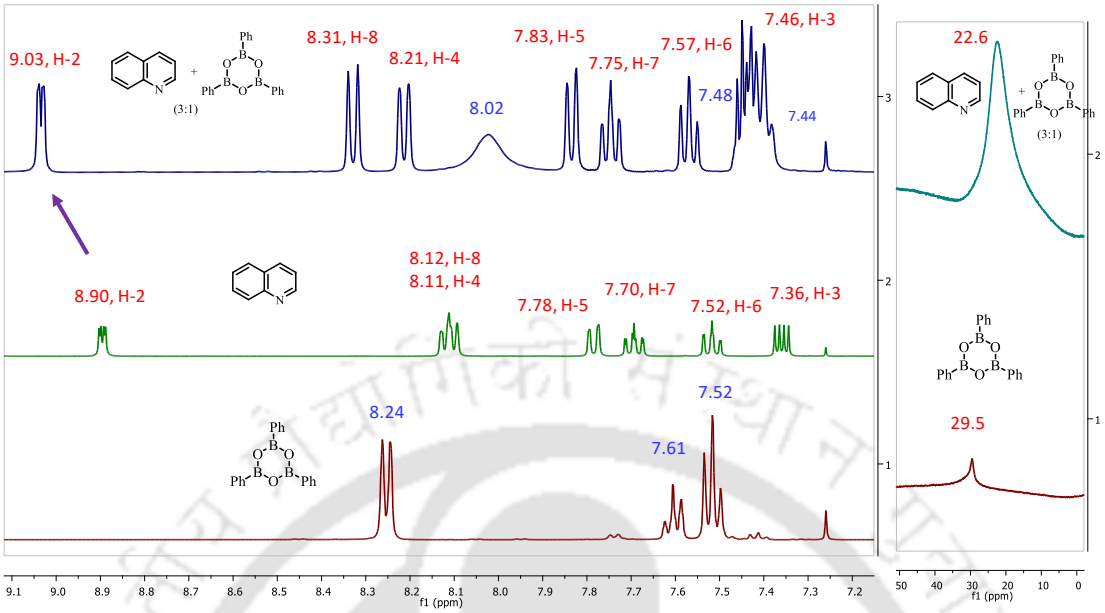

Figure 6.15. ^{1}H, and ^{11}B spectra of quinoline (10 mg, 0.077 mmol), triphenyl boroxine (24 mg, 0.077 mmol), a combination of quinoline and triphenyl boroxine (molar ratio 3:1) in $CDCl_3$ at 298 K.

ii) Interaction of boronic acid with Hantzsch ester

To examine the interaction of boronic acid and Hantzsch ester, we have checked the ^{1}H NMR with the combination of (a) Hantzsch ester and phenylboronic acid (molar ratio 1:1) (b) Hantzsch ester and 3-trifluoromethyl boronic acid (molar ratio 1:2) in $CDCl_3$ at rt. In the case of phenylboronic acid approximately 0.41 ppm downfield was shifted for the hydroxyl peak (Figure 6.16), whereas no characteristic –OH proton signal was observed while mixing with 3-trifluoromethylphenylboronic acid (Figure 6.17). However, in ^{13}C NMR, the carbonyl value in Hantzsch ester was shifted downfield from 168.22 to 168.43 ppm ($\Delta\delta$ = 0.18 ppm). Using ^{11}B NMR spectroscopy, no noticeable shift was observed in boronic acid, which implies exclude Lewis acid-base adduct, and hydrogen bonding interaction may exist between Hantzsch ester and –OH of boronic acid (Figure 6.18)

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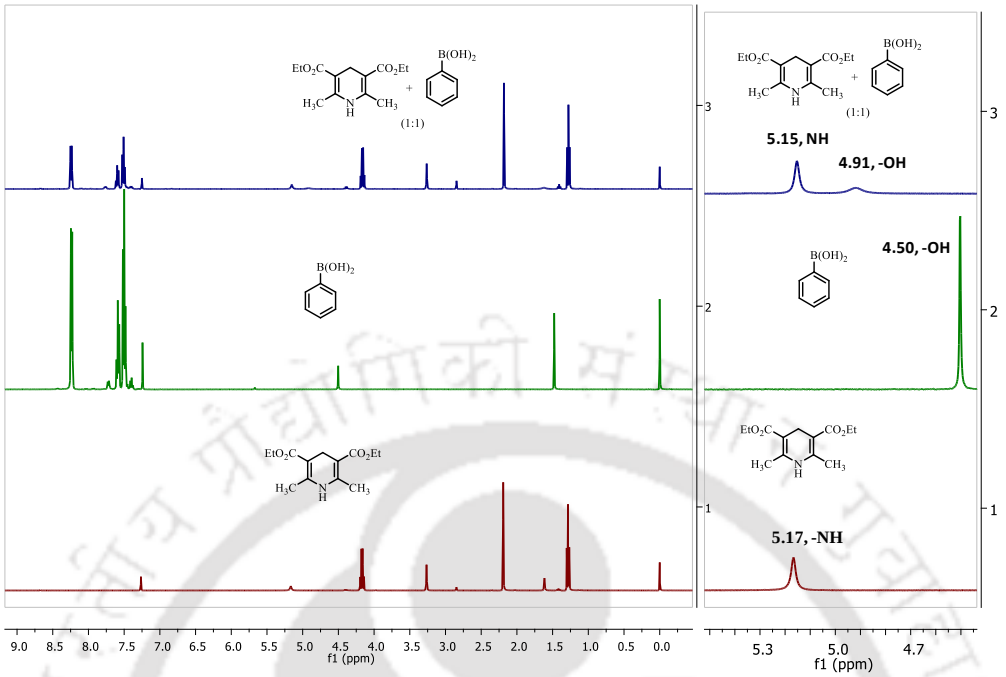

Figure 6.16. ^{1}H NMR spectra of phenylboronic acid (10 mg, 0.079 mmol), Hantzsch ester (10 mg, 0.079 mmol), and combination of phenylboronic acid, Hantzsch ester (molar ratio 1:1).

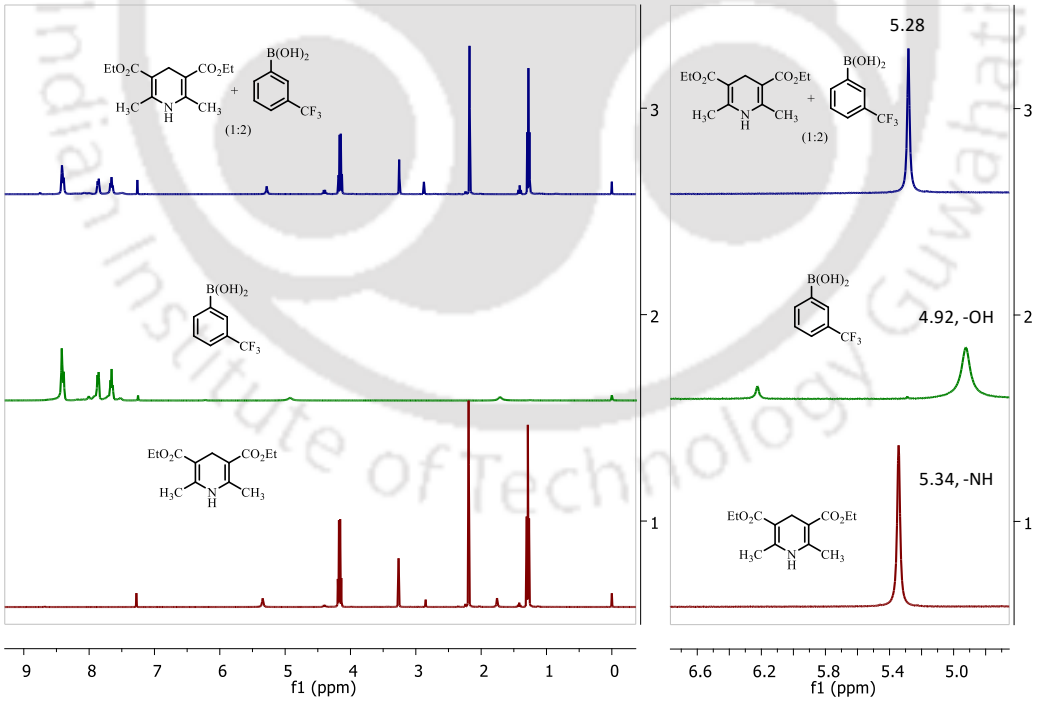

Figure 6.17. ^{1}H NMR spectra of 3-trifluoromethylphenylboronic acid (15 mg, 0.079 mmol), Hantzsch ester (5 mg, 0.0.039 mmol), and combination of 3-trifluoromethylphenylboronic acid and Hantzsch ester (molar ratio 2:1) in $CDCl_3$ at 298 K.

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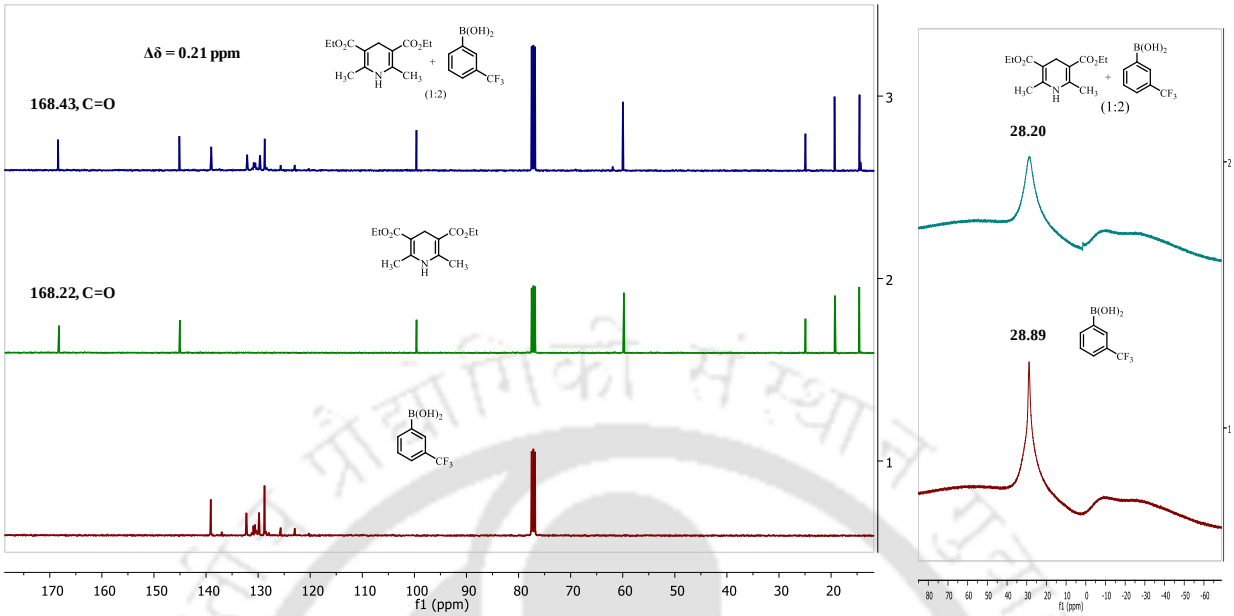

Figure 6.18. ^{13}C, and ^{11}B NMR spectra of 3-trifluoromethylphenylboronic acid (15 mg, 0.079 mmol), Hantzsch ester (5 mg, 0.0.039 mmol), and combination of 3-trifluoromethylphenylboronic acid and Hantzsch ester (molar ratio 2:1) (left, right) in $CDCl_3$ at 298 K.

iii) Interaction of boronic acid with 1,2,3,4 THQ

To probe the interaction of boronic acid and 1,2,3,4 THQ, we have analyzed the ^{1}H NMR and ^{11}B NMR of the mixture of 1,2,3,4-THQ and 3-trifluoromethylphenylboronic acid (molar ratio 1:1) in $CDCl_3$ at rt and compare with individuals (Figure 6.19). In ^{1}H NMR, the chemical shift of aromatic proton of 1,2,3,4-THQ is shifted to the downfield, and aromatic proton of boronic acid moved to upfield. In ^{11}B NMR, a broad upfield signal was observed (28.45-23.84 ppm). As distinct shift was not found in vide infra, these observations likely to be weak hydrogen bonding interaction with -NH of THQ moiety and boronic acid; however, the possibility of weak complexation with THQ in solution cannot be excluded.

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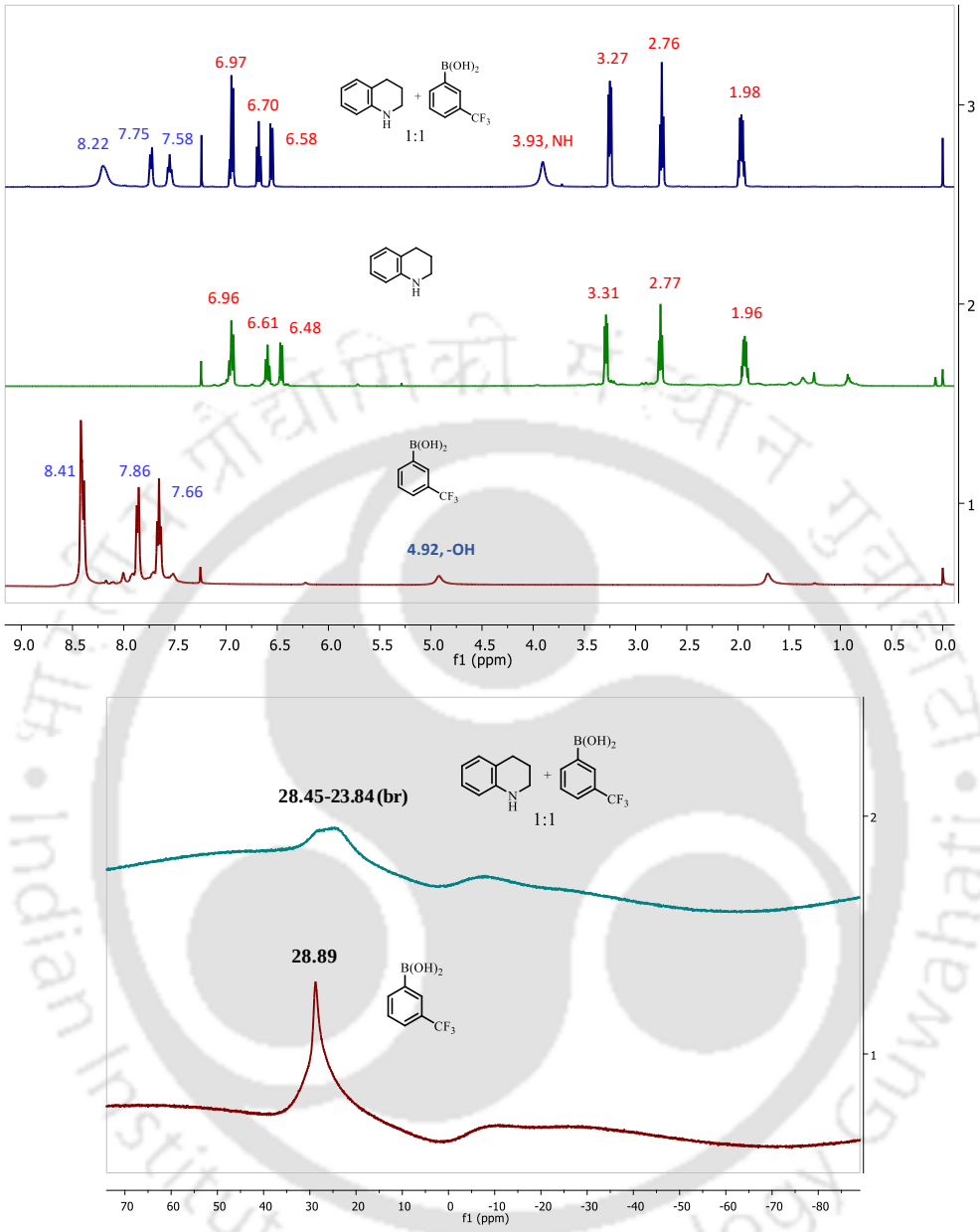

Figure 6.19. ^{1}H, and ^{11}B NMR spectra of 3-trifluoromethylpheylboronic acid (15 mg, 0.079 mmol), 1,2,3,4-THQ (11 mg, 0.079 mmol), and combination of 3-trifluoromethylphenylboronic acid and 1,2,3,4-THQ (molar ratio 1:1) in $CDCl_3$ at 298 K.

iv) Proposed pathway for condensation reaction:

Based on the above experimental finding with different time interval ^{1}H NMR, ^{11}B NMR, 2-D HSQC correlation spectra (Figure 6.11-6.12), and mass spectrometry studies (Figure 6.20), the following condensation pathway is proposed in Scheme 6.19.

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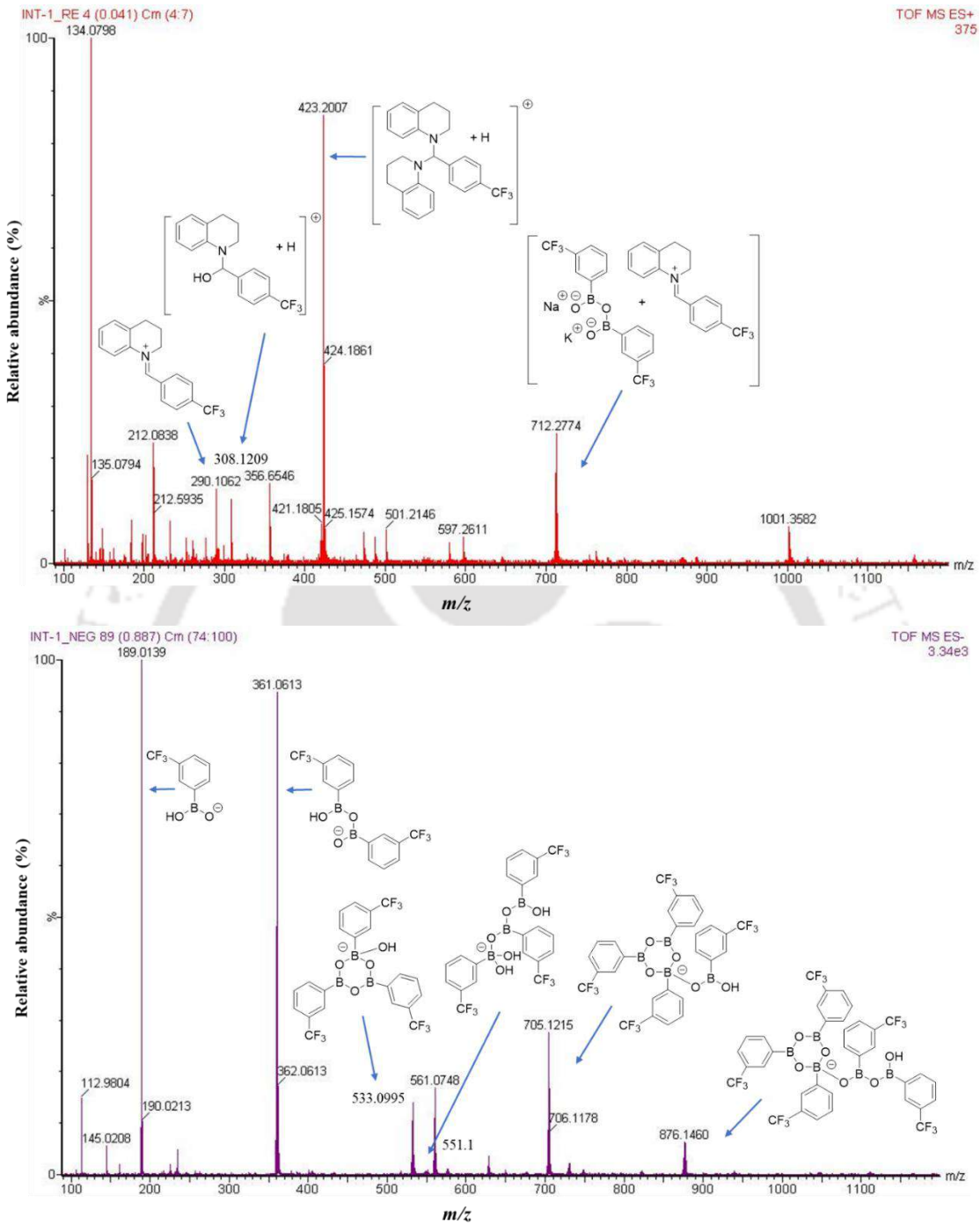

Figure 6.20. MS(ESI) spectra of the reaction mixture obtained from 3-trifluoromethylphenyl boronic acid, 1,2,3,4-THQ, 4-trifluoromethyl benzaldehyde (molar ratio 1:1:1) under the above reaction condition.

First, condensation occurs between 4-trifluoromethyl benzaldehyde and 1,2,3,4-THQ to form hemiaminal intermediate **I-1**, which reacts 3-trifluoromethylphenyl boronic acid (**6.3b**) to produce iminium and borate ion pair **I-2**. The resulted intermediate **I-2** can form the hemiaminal species

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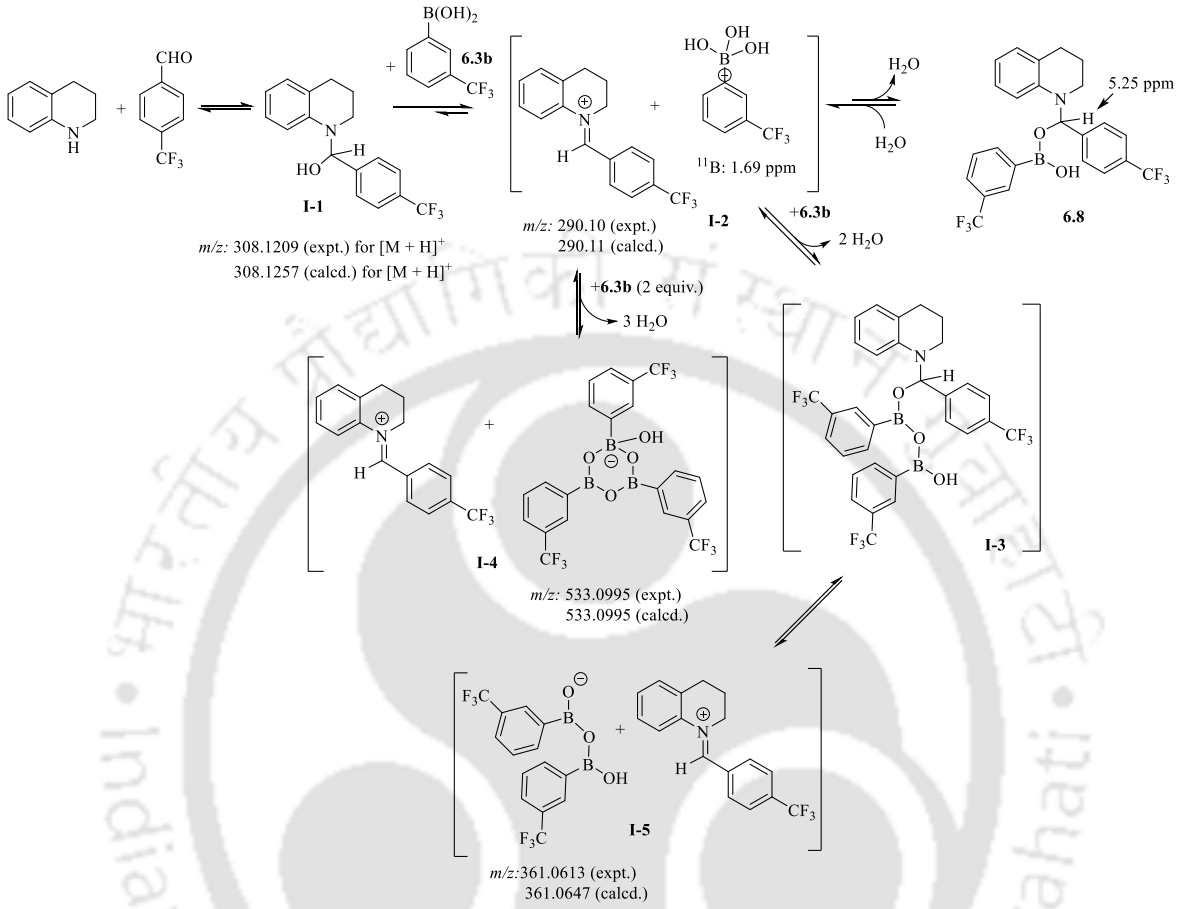
6.8 by releasing one water molecule. The imino intermediate **I-2** can further react with 3-trifluoromethylphenylboronic acid to afford **I-3**, **I-4**, and **I-5** subsequently.



Scheme 6.19. Plausible mechanistic pathway for the condensation reaction

v) Condensation reaction of 1,2,3,4-THQ, and 2-formylphenylboronic acid (Scheme 6.10b)

To probe the formation of hemiaminal or imino intermediate in condensation reaction, the reaction has been examined with 1,2,3,4-THQ, and 2-formylphenylboronic acid in dry CH_2Cl_2 at rt (Scheme 6.10b). After 12 h, benzoxaborole derivative **6.9** was obtained with 66% yield. It likely to be formed *via* cyclic boronate intermediate[17] subsequently releases one molecule of water.

Reaction condition: In a round bottom flask (25 mL), 1,2,3,4-THQ (1 mmol), 2-formylphenylboronic acid (1 mmol), dry CH_2Cl_2 (5 mL), and $MgSO_4$ (0.6 g) were taken. Then the flask was closed with a glass stopper and stirred at rt for 12 h. The reaction mixture was then filtered, and the volatile solvent was evaporated under reduced pressure in a rotary evaporator. Pure compound (66%) was obtained by using silica column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.80).

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vi) Impact of hydrogen bonding ability of boronic acid in catalysis (Scheme 6.9)

Reaction conditions for 6.1a' and 6.4f:

For 6.1a': In a reaction tube (15 mL), quinoline (0.062 mmol), catalyst (0.0155 mmol), Hantzsch ester (2.5 equiv.), catalyst (25 mol%), and $CHCl_3$ (0.6 ml) were taken. The tube was then properly closed and placed in a preheated oil bath at 45 ℃ with continuous stirring. After 45 minutes, the yield of each case was determined by GC with internal standard benzene.

For 6.4f: In a reaction tube (15 mL), 1,2,3,4-THQs (0.060 mmol), 4-fluorobenzaldehyde (0.06 mmol), Hantzsch ester (3.5 equiv.), catalyst (25 mol%), and $CHCl_3$ (0.6 ml) were taken. The tube was then properly closed and placed in a preheated oil bath at 60 ℃ with continuous stirring. After 1 h, the volatile solvent was removed and dissolved in $CDCl_3$, the yield of each case was determined by ^{19}F NMR with internal standard fluorobenzene (δ = –115.3 ppm).

vii) Preparation of *N*-alkyl THQs from 1,2,3,4-THQ (Scheme 6.9)

When performing the reaction with 1,2,3,4-THQ **6.1g'**, 4-trifluoromethylbenzaldehyde **6.2g** and HE under optimized reaction condition, we have observed the desired product **6.4g** in 96% yield with **6.3b** and 36% yield without catalyst.

Reaction condition: In a reaction tube (15 mL), 1,2,3,4-THQ (0.5 mmol), 4-trifluoromethylbenzaldehyde (0.5 mmol), 3-trifluoromethylphenyl boronic acid (**cat.2**) (0.125 mmol), Hantzsch ester (3.5 equiv.) and DCE (2 ml) were taken. The tube was properly closed and placed in a preheated oil bath at 60 ℃ with continuous stirring for 12 h, the volatile solvent was then removed, and crude compound was purified by using silica column chromatography.

viii) Effect of *N*-alkylation with boronic acid bearing aromatic aldehydes (Scheme 6.5)

As shown in scheme 6.6, boronic acid or boronic ester bearing aromatic aldehyde takes part in *N*-alkylation reaction and leads to the desired product without disruption of boron moiety under the reaction condition, whether the reaction is product induced or substrate promoted transformation, the conversion of **6.1g** was monitored by adding the corresponding product **6.7a** as 25 mol% or aldehyde **6.2af** as 25 mol% in the reaction mixture. The conversion of **6.1g** has been enhanced while adding 25 mol% of **6.7a** in the reaction mixture compared to same mole% of **6.2af** (> 99% *vs* 64%), which suggests the process likely to be product prompted transformation. However, more detailed mechanistic investigations for the autocatalyzed reaction are ongoing in our laboratory and will be reported in due course.

Reaction conditions: In a reaction tube (15 mL), 6-fluoro-2-methylquinoline **6.1i** (0.03 mmol), 4-formylphenylboronic acid **6.2af** (0.03 mmol), Hantzsch ester (5 equiv.) and $CHCl_3$ (0.6 ml) were taken. The tube was then properly closed and placed in a preheated oil bath at 45 ℃ with

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continuous stirring. After 45 min, the volatile solvent was removed and dissolved in $CDCl_3$ (0.5 mL), the conversion of **6.1g** was determined by ^{19}F NMR with internal standard fluorobenzene (δ = –115.3 ppm). Similarly, by adding 25% of **6.2af** or 25 mol% of **6.7a** in the reaction mixture, the conversion of **6.1i** was analyzed.

ix) Deuterium-labeling experiment (Scheme 6.11)

In order to locate the hydridic proton and acidic proton in the *N*-alkyl-THQ product, we have performed the catalytic experiment with 3-methyl quinoline **6.1c** in the presence of D_2O. The outcome demonstrated that the deuterium atom was incorporated at the C3 position of *N*-alkyl-THQ derivative **6.5b.**

Reaction conditions: In a pyrex tube (15 mL), 3-methyl quinoline (0.5 mmol), Hantzsch ester (3.5 equiv.), 3-trifluoromethylphenyl boronic acid (**6.3b**) (25 mol%), dichloroethane (2 mL) and D_2O (0.30 mmol) were charged. The reaction tube was properly closed and placed in a preheated oil bath (60 °C) with continuous stirring. The reaction was monitored by thin layered chromatography (TLC) in *n*-hexane and ethyl acetate solvent system. After 12 h, the reaction tube was brought to room temperature and purified by silica column chromatography using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.80) (99 mg, 83%).

^{1}H NMR spectrum of deuterated 1-benzyl-3-methyl-1,2,3,4-tetrahydroquinoline (6.5b + D-6.5b):

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.33-7.30 (m, 4H, **6.5b + D-6.5b**), 7.27-7.24 (m, 6H, **6.5b + D-6.5b**), 6.98-6.96 (m, 4H, **6.5b + D-6.5b**), 6.57 (t, *J* = 7.2 Hz, 2H, **6.5b + D-6.5b**), 6.50 (d, *J* = 8.4 Hz, 2H, **6.5b + D-6.5b**), 4.48 (s, 4H, **6.5b + D-6.5b**), 3.29-3.27 (m, 2H, **6.5b + D-6.5b**), 3.04–3.02 (m, 2H, **6.5b + D-6.5b**), 2.82–2.80 (m, 2H, **6.5b + D-6.5b**), 2.51–2.49 (m, 2H, **6.5b + D-6.5b**), 2.20–2.14 (m, 1H, **6.5b**) 1.04 (s, 6H, **6.5b + D-6.5b**).

E. Crystallographic data

The crystal was obtained by the crystallization of compound **6.5k** in the presence of a pet-ether as solvent at room temperature using a slow evaporation technique. X-ray crystallographic data were collected using Supernova, a single source at offset, Eos diffractometer. Data refinement and cell reduction were carried out by *CrysAlisPro*. Structures were solved by direct methods using SHELXL-2014/7 and WinGX and refined by a full-matrix least-squares method using SHELXL-2014/7. All of the non-H atoms were refined anisotropically. The ORTEP diagram was obtained with ORTEP software with 40% thermal ellipsoid (see below, Figure 6.20). The crystallographic parameters and refinement data were listed in Table 6.6.

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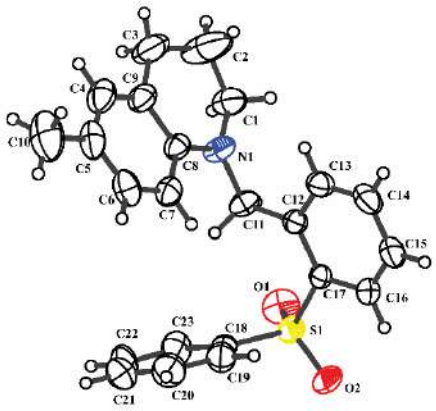

Figure 6.21. Molecular structure of compound **6.5k** (thermal ellipsoid 40% probability level). Selected Bond lengths (in Å): S(1)-O(1) 1.439(2), S(1)-O(2) 1.431(2), N(1)-C(1) 1.443(4), N(1)-C(8) 1.389(4), N(1)-C(11) 1.446(3), C(1)-C(2) 1.441(5), C(4)-C(5) 1.373(5), C(12)-C(13) 1.406(3), C(18)-C(19) 1.374(4). Selected Bond Angles (in °) O(1)-S(1)-C(17) 107.58(13), O(1)-S(1)-C(18) 107.81(14), O(1)-S(1)-O(2) 118.39(14), N(1)-C(11)-C(12) 114.4(2), N(1)-C(1)-C(2) 114.5(3), C(6)-C7(1)-C(8) 120.9(3)

Table 6.6. Crystal data and structure refinement for **6.5k**

Identification code	PA-281	
CCDC:	2039730	
Empirical formula	$C_{23}H_{23}NO_2S$	
Formula weight	377.48	
Temperature	293(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	$P2_1/n$	
Unit cell dimensions	a = 10.9095(17) Å	α = 90°.
	b = 8.5692(14) Å	β = 98.982(5)°
	c = 21.390(3) Å	γ = 90°.
Volume	1975.1(5) $Å^3$	
Z	4	
Density (calculated)	1.269 mg/m^3	
Absorption coefficient	0.181 mm^{-1}	
F(000)	800.0	
Crystal size	0.35 × 0.32 × 0.30 mm^3	
Theta range for data collection	3.856 to 49.994°.	
Index ranges	$-12 \le h \le 12$, $-10 \le k \le 10$, $-25 \le l \le 25$	

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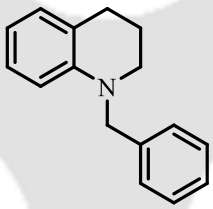
Reflections collected	78209
Independent reflections	3481 [R_{int} = 0.0811, R_{sigma} = 0.0227]
Completeness to theta = 25.242°	98%
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3481/0/245
Goodness-of-fit on F^2	1.102
Final R indices [I>2sigma(I)]	R_1 = 0.0602, wR_2 = 0.1423
R indices (all data)	R_1 = 0.0787, wR_2 = 0.1631
Extinction coefficient	n/a
Largest diff. peak and hole	0.47 and -0.51 e.$Å^{-3}$

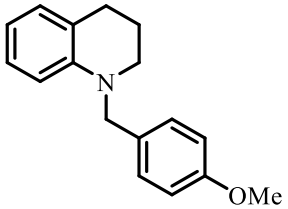
6.6. Analytical data

1-benzyl-1,2,3,4-tetrahydroquinoline (6.4a)[23]



Using **GP-1**, the title compound **6.4a** was isolated as light yellow oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.80); (100 mg, 90%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32 – 7.18 (m, 5H), 6.97– 6.94 (m, 2H), 6.56 (td, J = 0.8, 7.2 Hz, 1H), 6.49 (d, J = 8.4 Hz, 1H), 4.46 (s, 2H), 3.34 (t, J = 5.6 Hz, 2H), 2.80 (t, J = 6.3 Hz, 2H), 2.03-1.97 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 145.7, 139.1, 129.1, 128.7, 127.3, 126.9, 126.7, 122.4, 116.0, 111.1, 55.3, 50.0, 28.4, 22.5.

1-(4-methoxybenzyl)-1,2,3,4-tetrahydroquinoline (6.4b)[23]



Using **GP-1**, the title compound **6.4b** was isolated as colorless oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.80); (111 mg, 88%). ^{1}H

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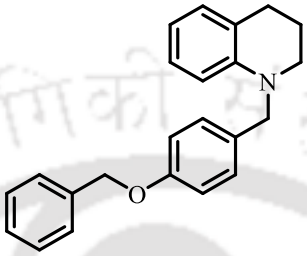
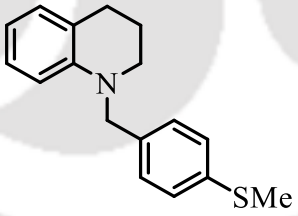
NMR (400 MHz, $CDCl_3$): δ 7.22 (d, J = 8.4 Hz, 2H), 7.01 – 6.99 (m, 2H), 6.90 – 6.88 (m, 2H), 6.63 – 6.56 (m, 2H), 4.45 (s, 2H), 3.82 (s, 3H), 3.38 – 3.35 (m, 2H), 2.85 – 2.82 (m, 2H), 2.04 – 2.00 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 158.7, 145.8, 131.0, 129.1, 127.9, 127.3, 122.4, 115.9, 114.1, 111.1, 55.4, 54.7, 49.8, 28.4, 22.5.

1-(4-(benzyloxy)benzyl)-1,2,3,4-tetrahydroquinoline (6.4c)



Using **GP-1**, the title compound **6.4c** was isolated as yellow oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.80); (145 mg, 88%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45 – 7.33 (m, 5H), 7.20 (d, J = 8.4 Hz, 2H), 7.01 – 6.93 (m, 4H), 6.59 – 6.54 (m, 2H), 5.06 (s, 2H), 4.43 (s, 2H), 3.36 – 3.34 (m, 2H), 2.82 (t, J = 6.2 Hz, 2H), 2.04 – 1.98 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 157.9, 145.8, 137.2, 131.2, 129.1, 128.7,128.1, 127.9, 127.6, 127.3, 122.4, 115.9, 115.1, 111.1, 70.2, 54.7, 49.8, 28.4, 22.5. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{23}H_{24}NO$: 330.1853; found 330.1852.

1-(4-(methylthio)benzyl)-1,2,3,4-tetrahydroquinoline (6.4d)



Using **GP-1**, the title compound **6.4d** was isolated as yellow oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.80); (116 mg, 86%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.24 – 7.19 (m, 4H), 7.00 – 6.96 (m, 2H), 6.61 – 6.57 (m, 1H), 6.49 (d, J = 8.4 Hz, 1H), 4.44 (s, 2H), 3.37 – 3.34 (m, 2H), 2.82 (t, J = 6.4 Hz, 2H), 2.48 (s, 3H), 2.05 – 1.99 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 145.6, 136.6, 136.1, 129.1, 127.3, 127.3, 127.2, 122.4, 116.0, 111.1, 54.9, 50.0, 28.3, 22.5, 16.3. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{17}H_{20}NS$ 270.1311; found 270.1317.

1-(4-chlorobenzyl)-1,2,3,4-tetrahydroquinoline (6.4e)[23]

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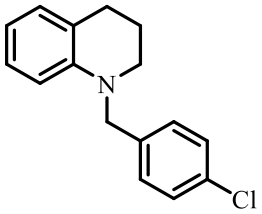
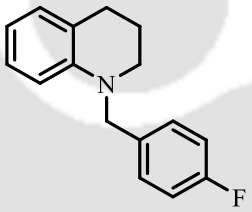


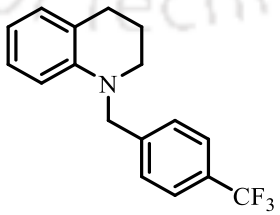
Using **GP-1**, the title compound **6.4e** was isolated as colorless oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.80); (114 mg, 89%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26 – 7.24 (m, 2H), 7.18– 7.15 (m 2H), 6.97 – 6.93 (m, 2H), 6.57 (t, J = 7.2 Hz, 1H), 6.43 (d, J = 8.2 Hz, 1H), 4.39 (s, 2H), 3.31 (t, J = 5.6 Hz, 2H), 2.79 (t, J = 6.0 Hz, 2H), 2.01 – 1.95 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 145.5, 137.6, 132.5, 129.2, 128.8, 128.1, 127.3, 122.5, 116.3, 111.1, 54.8, 50.0, 28.3, 22.5.

1-(4-fluorobenzyl)-1,2,3,4-tetrahydroquinoline (6.4f)



Using **GP-1**, the title compound **6.4f** was isolated as colorless oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.80); (110 mg, 91%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.23 – 7.20 (m, 2H), 7.01– 6.95 (m 4H), 6.58 (td, J = 0.8, 7.2 Hz, 1H), 6.47 (d, J = 8.8 Hz, 1H), 4.43 (s, 2H), 3.35-3.32 (m, 2H), 2.81 (t, J = 6.4 Hz, 2H), 2.03 – 1.97 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 163.2–162.7 (C-F, $^1J_{C\text{-}F}$ = 245.4 Hz), 145.6, 134.6 (C-F, $^4J_{C\text{-}F}$ = 3 Hz), 129.2, 128.2 (C-F, $^3J_{C\text{-}F}$ = 8 Hz), 127.3, 122.5, 116.2, 115.6–115.4 (C-F, $^2J_{C\text{-}F}$ = 21 Hz), 111.1, 54.7, 50.0, 28.3, 22.5. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{16}H_{17}FN$ 242.1340; found 242.1341. ^{19}F NMR (377 MHz, $CDCl_3$): -118.7.

1-(4-(trifluoromethyl)benzyl)-1,2,3,4-tetrahydroquinoline (6.4g)



Using **GP-1**, the title compound **6.4g** was isolated as colorless oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.80); (135 mg, 93%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.60 (d, J = 8.4 Hz, 2H), 7.42 (d, J = 7.8 Hz, 2H), 7.04 – 7.00 (m, 2H),

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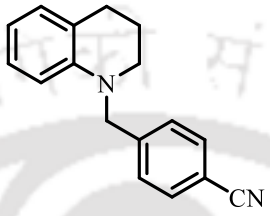
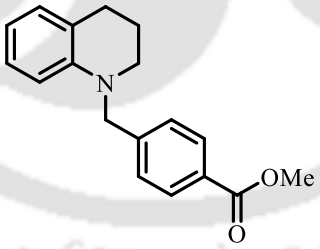
6.65 (t, *J* = 7.2 Hz, 1H), 6.45 (d, *J* = 8.4 Hz, 1H), 4.55 (s, 1H), 3.42-3.40 (m, 2H), 2.88 (t, *J* = 6.2 Hz, 2H), 2.10-2.06 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): 145.4, 143.5, 130.1, 129.3, 127.3, 127.0, 125.6 (q, C-F, $^1J_{C-F}$ = 3.8 Hz), 122.6, 116.5, 111.0, 55.2, 50.3, 28.2, 22.5. ^{19}F NMR (377 MHz, $CDCl_3$): -64.4. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{17}H_{17}F_3N$ 292.1308; found 292.1315.

4-((3,4-dihydroquinolin-1(2H)-yl)methyl)benzonitrile (6.4h)



Using **GP-1**, the title compound **6.4h** was isolated as white solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.80); (117 mg, 95%). m.p. 62-64 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.61 (d, *J* = 8.4 Hz, 2H), 7.39 – 7.36 (d, *J* = 8.4 Hz, 2H), 7.01 – 6.94 (m, 2H), 6.61 (td, *J* = 0.8, 7.4 Hz, 1H), 6.35 (d, *J* = 8.0 Hz, 1H), 4.51 (s, 2H), 3.37 (t, *J* = 5.6 Hz, 2H), 2.84 (t, *J* = 6.2 Hz, 2H), 2.07– 2.01 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 145.2, 145.1, 132.6, 129.4, 127.4, 127.4, 122.6, 119.1, 116.7, 111.0, 110.8, 55.4, 50.4, 28.2, 22.5. IR (KBr, selected band): 2227.78 cm^{-1}. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{17}H_{17}N_2$ 249.1386; found 249.1386.

Methyl 4-((3,4-dihydroquinolin-1(2H)-yl)methyl)benzoate (6.4i)[5]



Using **GP-1**, the title compound **6.4i** was isolated as colorless oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.80); (115 mg, 82%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.98 (d, *J* = 8.4 Hz, 2H), 7.34 (d, *J* = 7.8 Hz, 2H), 6.98 (d, *J* = 7.2 Hz, 1H), 6.96 (t, *J* = 7.2 Hz, 1H), 6.59 (t, *J* = 7.2 Hz, 1H), 6.41 (d, *J* = 7.8 Hz, 1H), 4.51 (s, 2H), 3.90 (s, 3H), 3.38-3.36 (m, 2H), 2.85-2.82 (m, 2H), 2.05–2.01 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 167.2, 145.5, 144.8, 130.1, 129.3, 129.0, 127.3, 126.6, 123.5, 116.3, 111.1, 55.4, 52.2, 50.3, 28.3, 22.5. IR (KBr, selected band): 1722.6 cm^{-1}.

1-([1,1'-biphenyl]-4-ylmethyl)-1,2,3,4-tetrahydroquinoline (6.4j)

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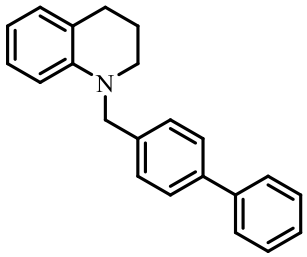
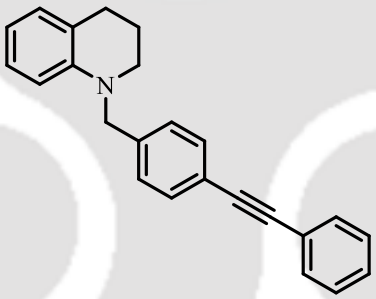


Using **GP-1**, the title compound **6.4j** was isolated as yellow oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.80); (133 mg, 89%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59 – 7.53 (m, 5H), 7.43 (t, J = 7.6 Hz, 2H), 7.34 (d, J = 7.6 Hz, 2H), 7.00-6.97 (m, 2H), 6.60 – 6.53 (m, 2H), 4.52 (s, 2H), 3.41 – 3.39 (m, 2H), 2.84 (t, J = 6.0 Hz, 2H), 2.07 – 2.01 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 145.7, 141.1, 139.9, 138.2, 129.2, 128.9, 127.5, 127.3, 127.3, 127.2, 127.1, 122.4, 116.0, 111.1, 55.1, 50.1, 28.4, 22.5. HRMS (ESI) *m/z*: $[M+H]^+$calculated for $C_{22}H_{22}N$ 300.1747; found 300.1753.

1-(4-(phenylethynyl)benzyl)-1,2,3,4-tetrahydroquinoline (6.4k)



Using **GP-1**, the title compound **6.4k** was isolated as yellow oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.80); (140 mg, 87%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54 – 7.47 (m, 4H), 7.37 – 7.32 (m, 3H), 7.26 – 7.24 (m, 2H), 6.99-6.96 (m, 2H), 6.59 (td, J = 0.8, 7.2 Hz, 1H), 6.46 (d, J = 8.0 Hz, 1H), 4.48 (s, 2H), 3.38-3.35 (m, 2H), 2.83 (t, J = 6 Hz, 2H), 2.06 – 2.00 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 145.6, 139.6, 132.0, 131.7, 129.2, 128.5, 128.3, 127.3, 126.7, 123.5, 122.5, 121.8, 116.2, 111.1, 89.5, 89.2, 55.3, 50.1, 28.3, 22.5. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{24}H_{22}N$ 324.1747; found 324.1751. IR (KBr, selected band): 2217.5 cm^{-1}.

1-(4-(allyloxy)benzyl)-1,2,3,4-tetrahydroquinoline (6.4l)

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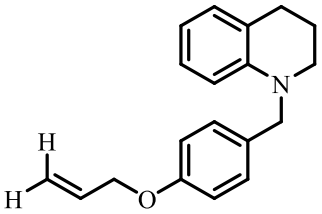
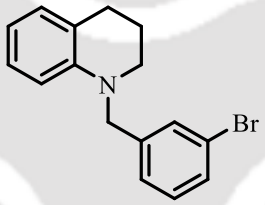


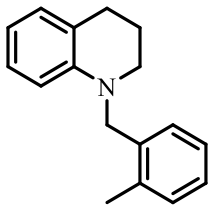
Using **GP-1**, the title compound **6.4l** was isolated as colorless oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.80); (118 mg, 85%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.20 (d, J = 8.0 Hz, 2H), 7.02-6.98 (m, 2H), 6.89 (d, J = 8.4 Hz, 2H), 6.61-6.54 (m, 2H), 6.12-6.02 (m, 1H), 5.43 (d, J = 17.2 Hz, 1H), 5.30 (d, J = 10.4 Hz, 1H), 4.53 (d, J = 5.2 Hz, 2H), 4.43 (s, 2H), 3.35 (t, J = 5.6 Hz, 2H), 2.83 (t, J = 6.4 Hz, 2H), 2.05 – 1.99 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 157.7, 145.8, 133.5, 131.2, 129.1, 127.9, 127.3, 122.4, 117.7, 115.9, 115.0, 111.1, 69.0, 54.7, 49.8, 28.4, 22.5. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{19}H_{22}NO$ 280.1696; found: 280.1698.

1-(2-bromobenzyl)-1,2,3,4-tetrahydroquinoline (6.4m)



Using **GP-1**, the title compound **6.4m** was isolated as yellow oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.80); (133 mg, 88%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40 (brs, 1H), 7.34 (d, J = 7.2 Hz, 1H), 7.18 – 7.12 (m, 2H), 6.98-6.94 (m, 2H), 6.58 (t, J = 7.6 Hz, 1H), 6.43 (d, J = 8.4 Hz, 1H), 4.40 (s, 2H), 3.32 (t, J = 5.6 Hz, 2H), 2.80 (t, J = 6.4 Hz, 2H), 2.03-1.97 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 145.4, 141.8, 130.3, 130.0, 129.6, 129.2, 127.3, 125.2, 122.9, 122.5, 116.3, 111.1, 55.1, 50.2, 28.2, 22.5. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{16}H_{17}BrN$ 302.0539; found 302.0529.

1-(2-methylbenzyl)-1,2,3,4-tetrahydroquinoline (6.4n)[23]



Using **GP-1**, the title compound **6.4n** was isolated as light yellow oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.80); (103 mg, 87%). ^{1}H

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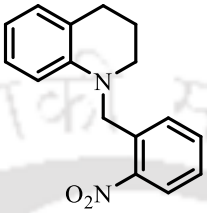
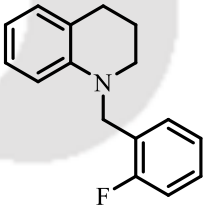
NMR (400 MHz, $CDCl_3$): δ 7.22 – 7.14 (m, 4H), 7.01 – 6.96 (m, 2H), 6.59 (td, J = 0.8, 7.2 Hz, 1H), 6.39 (d, J = 8.4 Hz, 1H), 4.41 (s, 2H), 3.36 (t, J = 5.6 Hz, 2H), 2.86 (t, J = 6.3 Hz, 2H), 2.34 (s, 3H), 2.08-2.04 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 145.8, 136.1, 135.7, 130.4, 129.0, 127.3, 126.8, 126.2, 126.2, 122.4, 115.9, 111.0, 53.6, 49.9, 28.4, 22.6, 19.1.

1-(2-nitrobenzyl)-1,2,3,4-tetrahydroquinoline (6.4o)



Using **GP-1**, the title compound **6.4o** was isolated as red solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.76); (128 mg, 96%). m.p. 120-122 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.16 (dd, J = 8.0, 1.2 Hz, 1H), 7.59 – 7.50 (m, 2H), 7.43 (td, J = 1.6, 7.6 Hz, 1H), 7.02 (d, J = 7.3 Hz, 1H), 6.96 (td, J = 1.6, 7.2 Hz, 1H), 6.62 (td, J = 1.6, 7.2 Hz, 1H), 6.27 (d, J = 8.1 Hz, 1H), 4.85 (s, 2H), 3.41 (t, J = 5.6 Hz, 2H), 2.87 (t, J = 6.4 Hz, 2H), 2.11-2.05 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 148.3, 145.1, 135.3, 134.1, 129.2, 128.6, 127.9, 127.4, 125.6, 122.5, 116.6, 110.8, 54.0, 50.4, 28.2, 22.5. HRMS (ESI) *m/z*: $[M+H]^+$calculated for $C_{16}H_{17}N_2O_2$: 269.1285; found: 269.1287.

1-(2-fluorobenzyl)-1,2,3,4-tetrahydroquinoline (6.4p)



Using **GP-1**, the title compound **6.4p** was isolated as white solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.80); (114 mg, 95%). m.p. 61-63 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.25-7.19 (m, 7.3 Hz, 2H), 7.08 – 7.03 (m, 2H), 6.99-6.96 (m, 2H), 6.59 (t, J = 7.3 Hz, 1H), 6.46 (d, J = 8.4 Hz, 1H), 4.52 (s, 2H), 3.39 (t, J = 6.2 Hz, 2H), 2.83 (t, J = 6.2 Hz, 2H), 2.06 – 2.00 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 162.3–159.8 (C-F, $^1J_{C\text{-}F}$ = 245.8 Hz), 145.5, 129.2, 128.4 (C-F, $^3J_{C\text{-}F}$ = 3.6 Hz), 128.4, 127.4, 125.8–125.6 (C-F, $^2J_{C\text{-}F}$ = 14.5 Hz), 124.3–124.2 (C-F, $^3J_{C\text{-}F}$ = 3.4 Hz), 122.4, 116.1, 115.5–115.3 (C-F, $^2J_{C\text{-}F}$ = 21.1 Hz), 110.9, 50.1, 49.3 (C-F, $^3J_{C\text{-}F}$ = 4.5 Hz), 28.3, 22.5. ^{19}F NMR (377 MHz, $CDCl_3$): -118.62. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{16}H_{17}FN$ 242.1340; found: 242.1339.

1-(2-bromobenzyl)-1,2,3,4-tetrahydroquinoline (6.4q)[43]

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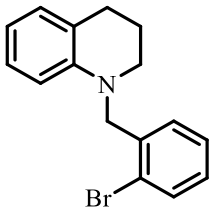
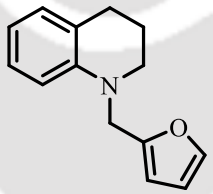


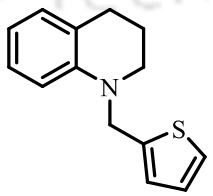
Using **GP-1**, the title compound **6.4q** was isolated as yellow oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.80); (136 mg, 90%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.62 (d, J = 7.7 Hz, 1H), 7.27 – 7.26 (m, 2H), 7.17 – 7.15 (m, 1H), 7.04 (d, J = 7.3 Hz, 1H), 7.0 (t, J = 7.7 Hz, 1H), 6.64 (t, J = 7.3 Hz, 1H), 6.34 (d, J = 8.2 Hz, 1H), 4.51 (s, 2H), 3.45 (t, J = 5.4 Hz, 2H), 2.90 (t, J = 6.0 Hz, 2H), 2.12 – 2.08 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 145.2, 137.1, 132.9, 129.1, 128.4, 127.8, 127.6, 127.4, 123.0, 122.2, 116.2, 110.9, 56.3, 50.3, 28.3, 22.6.

1-(furan-2-ylmethyl)-1,2,3,4-tetrahydroquinoline (6.4r)[23]



Using **GP-1**, the title compound **6.4r** was isolated as light yellow oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.80); (92 mg, 86%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35 (d, J = 1.2 Hz, 1H), 7.04 (t, J = 1.6, 8 Hz, 1H), 6.96 (d, J = 7.2 Hz, 1H), 6.72 (d, J = 8.4 Hz, 1H), 6.60 (t, J = 0.8, 7.6 Hz, 1H), 6.30 – 6.29 (m, 1H), 6.16 (d, J = 7.2 Hz, 1H), 4.42 (s, 2H), 3.38 – 3.35 (m, 2H), 2.77 (t, J = 6.4 Hz, 2H), 2.01 – 1.95 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 152.5, 145.1, 141.9, 129.2, 127.1, 122.9, 116.4, 111.4, 110.3, 107.2, 49.7, 48.5, 28.2, 22.4. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{14}H_{16}NO$ 214.1227; found 214.1226.

1-(thiophen-2-ylmethyl)-1,2,3,4-tetrahydroquinoline (6.4s)[23]



Using **GP-1**, the title compound **6.4s** was isolated as light yellow oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.80); (97 mg, 85%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.19 – 7.17 (m, 1H), 7.07 – 7.03 (m, 1H), 6.98 – 6.95 (m, 3H), 6.72 (d, J =

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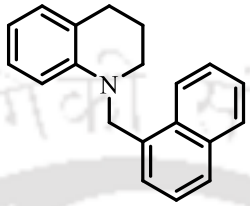
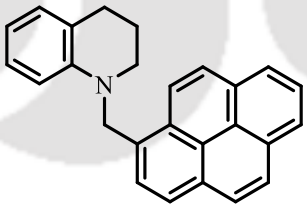
8.2 Hz, 1H), 6.63 (t, *J* = 7.2 Hz, 1H), 4.64 (s, 2H), 3.39 – 3.36 (m, 2H), 2.80 (t, *J* = 6.4 Hz, 2H), 2.04 – 1.98 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 145.1, 142.6, 129.3, 127.2, 126.9, 124.8, 124.3, 123.0, 116.6, 111.6, 50.7, 49.6, 28.2, 22.4. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{14}H_{16}NS$ 230.0998; found 230.0996.

1-(naphthalen-1-ylmethyl)-1,2,3,4-tetrahydroquinoline (6.4t) [23]



Using **GP-1**, the title compound **6.4t** was isolated as off white solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.80); (122 mg, 90%). m.p. 100-102 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.01 (d, *J* = 7.8 Hz, 1H), 7.93 – 7.91 (m, 1H), 7.79 – 7.77 (m, 1H), 7.58 – 7.53 (m, 2H), 7.41-7.40 (m, 2H), 7.04 (d, *J* = 7.2 Hz, 1H), 6.96 (t, *J* = 7.8 Hz, 1H), 6.61 (t, *J* = 7.2 Hz, 1H), 6.46 (d, *J* = 8.2 Hz, 1H), 4.93 (s, 2H), 3.43 – 3.40 (m, 2H), 2.89 (t, *J* = 6.0 Hz, 2H), 2.10 – 2.04 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 145.8, 134.0, 132.9, 131.3, 129.1, 129.0, 127.5, 127.4, 126.1, 125.8, 125.8, 123.7, 122.8, 122.5, 116.0, 111.1, 53.4, 49.8, 28.4, 22.6.

1-(pyren-1-ylmethyl)-1,2,3,4-tetrahydroquinoline (6.4u)



Using **GP-1**, the title compound **6.4u** was isolated as light green solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.80); (152 mg, 88%). m.p. 175-177 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.28 – 8.26 (m, 1H), 8.22 – 8.19 (m, 2H), 8.16 – 8.11 (m, 2H), 8.05 – 8.00 (m, 3H), 7.96 (d, *J* = 8 Hz, 1H), 7.06 (d, *J* = 7.2 Hz, 1H), 6.97 (td, *J* = 1.6, 7.6 Hz, 1H), 6.63 (td, *J* = 0.8, 7.2 Hz, 1H), 6.55 (d, *J* = 8 Hz, 1H), 5.20 (s, 2H), 3.46 – 3.43 (m, 2H), 2.91 (t, *J* = 6.2 Hz, 2H), 2.12 – 2.06 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 145.9, 131.6, 131.5, 130.9, 130.6, 129.2, 128.5, 127.7, 127.7, 127.4, 127.0, 126.1, 125.3, 125.3, 125.1, 125.0, 124.7, 122.8, 122.4, 116.2, 111.2, 53.7, 49.8, 28.4, 22.7. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{26}H_{22}N$ 348.1747; found 348.1754.

1-heptyl-1,2,3,4-tetrahydroquinoline (6.4aa)

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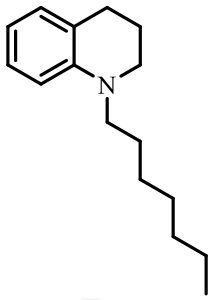
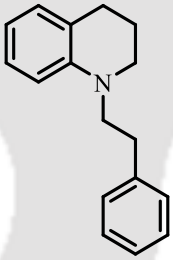


Using **GP-1**, the title compound **6.4aa** was isolated as light green oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.80); (82 mg, 71%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.04 (t, J = 7.2 Hz, 1H), 6.93 (d, J = 7.2 Hz, 1H), 6.57 – 6.52 (m, 2H), 3.29 – 3.26 (m, 2H), 3.24 – 3.21 (m, 2H), 2.75 (t, J = 6.2 Hz, 2H), 1.98 – 1.92 (m, 2H), 1.32 – 1.30 (m, 10H), 0.90 (t, J = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 145.5, 129.2, 127.2, 122.3, 115.3, 110.6, 51.7, 49.6, 32.0, 29.4, 28.4, 27.4, 26.3, 22.8, 22.4, 14.2. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{16}H_{26}N$ 232.2060; found: 232.2045.

1-phenethyl-1,2,3,4-tetrahydroquinoline (6.4ab)



Using **GP-1**, the title compound **6.4ab** was isolated as colorless oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.81); (87 mg, 73%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.32 – 7.30 (m, 2H), 7.24 – 7.21 (m, 3H), 7.08 (td, J = 1.2, 7.8 Hz, 1H), 6.96 (d, J = 7.2 Hz, 1H), 6.66 (d, J = 7.8 Hz, 1H), 6.58 (t, J = 7.2 Hz, 1H), 3.50 – 3.47 (m, 2H), 3.21 (t, J = 6 Hz, 2H), 2.88 – 2.86 (m, 2H), 2.74 (t, J = 6.3 Hz, 2H), 1.92 – 1.88 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 144.9, 140.1, 129.4, 129.0, 128.6, 127.3, 126.3, 122.5, 115.6, 110.5, 53.5, 49.7, 32.5, 28.3, 22.3. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{17}H_{20}N$ 238.1590; found 238.1596.

1-(3-phenylpropyl)-1,2,3,4-tetrahydroquinoline (6.4ac)

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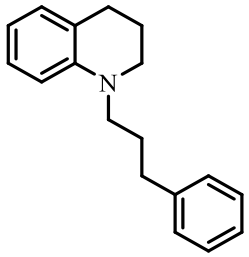
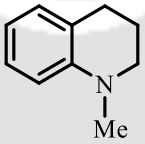


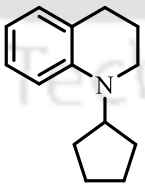
Using **GP-1**, the title compound **6.4ac** was isolated as colorless oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.82); (110 mg, 88%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.31 – 7.28 (m, 2H), 7.21 (d, J = 7.8 Hz, 3H), 7.02 (t, J = 7.8 Hz, 1H), 6.93 (d, J = 7.2 Hz, 1H), 6.54 (t, J = 7.2 Hz, 1H), 6.49 (d, J = 7.8 Hz, 1H), 3.29 – 3.25 (m, 4H), 2.75 (t, J = 6.6 Hz, 2H), 2.67 (t, J = 7.8 Hz, 2H), 1.96 – 1.91 (m, 4H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 145.4, 142.0, 129.3, 128.5, 128.5, 127.2, 126.0, 122.4, 115.5, 110.6, 51.1, 49.6, 33.6, 28.3, 27.8, 22.4. HRMS (ESI) *m/z*: [M+H$^+$] calculated for $C_{18}H_{22}N$ 252.1747; found 252.1737.

1-methyl-1,2,3,4-tetrahydroquinoline (6.4ad)[44]



Using **GP-1**, the title compound **6.4ad** was isolated as colorless oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.84); (47 mg, 65%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.11 (t, J = 7.8 Hz, 1H), 6.99 (d, J = 7.2 Hz, 1H), 6.66-6.63 (m, 2H), 3.27-3.24 (m, 2H), 2.92 (s, 3H), 2.81 (t, J = 6.4 Hz, 2H), 2.05–1.99 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 146.9, 128.9, 127.2, 123.0, 116.3, 111.1, 51.4, 39.2, 27.9, 22.6.

1-cyclopentyl-1,2,3,4-tetrahydroquinoline (6.4ae)



Using **GP-1**, the title compound **6.4ae** was isolated as light yellow oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.80); (83 mg, 83%). ^{1}H NMR (400 MHz, $CDCl_3$): 7.06 (td, J = 1.6, 7.8 Hz, 1H), 6.95 (d, J = 7.2 Hz, 1H), 6.74 (d, J = 8.0 Hz, 1H), 6.56 (t, J = 7.2 Hz, 1H), 4.20 (p, J = 7.6 Hz, 1H), 3.21 – 3.18 (m, 2H), 2.75 (t, J = 6.2 Hz, 2H), 1.95 – 1.89 (m, 4H), 1.73 – 1.61 (m, 6H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 146.4, 129.1, 127.1,

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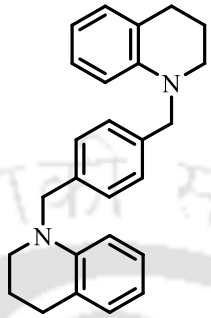
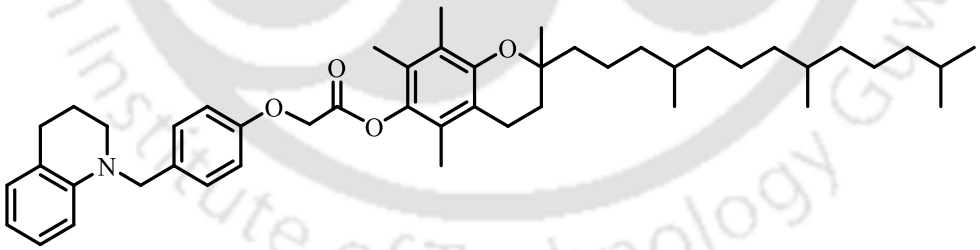
123.5, 115.4, 111.2, 58.7, 42.1, 28.6, 28.1, 24.3, 22.8. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{14}H_{20}N$ 202.1590; found: 202.1584.

1,4-bis((3,4-dihydroquinolin-1(2H)-yl)methyl)benzene (6.4f)



Using **GP-1**, the title compound **6.4f** was isolated as white solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.79); (139 mg, 76%). m.p. 139-141 °C. Using 1 equiv. of 1,4-benzenedialdehyde, 2 equiv. of quinoline, and 8 equiv. of Hantzsch ester. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.22 (s, 4H), 6.99 – 6.96 (m, 4H), 6.58 (t, J = 7.2 Hz, 2H), 6.51 (d, J = 8.4 Hz, 2H), 4.46 (s, 4H), 3.38– 3.35 (m, 4H), 2.82 (t, J = 6.2 Hz, 4H), 2.04 – 1.98 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 145.7, 137.6, 129.1, 127.3, 127.0, 122.4, 116.0, 111.1, 55.1, 50.0, 28.3, 22.5. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{26}H_{29}N_2$ 369.2623; found: 369.2627.

2,5,7,8-tetramethyl-2-(4,8,12-trimethyltridecyl)chroman-6-yl 2-(4-((3,4-dihydroquinolin-1(2H)-yl)methyl)phenoxy)acetate (6.4g)



Using **GP-1**, the title compound **6.4g** was isolated as colorless oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.77); (156 mg, 88%). Using 0.25 mmol of quinoline, 0.25 mmol of **6.2ab** and 1 mmol of Hantzsch ester. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.21 (d, J = 8.4 Hz, 2H), 7.00 – 7.95 (m, 4H), 6.58 (t, J = 7.2 Hz, 1H), 6.51 (d, J = 8.8 Hz, 1H), 4.91 (s, 2H), 4.43 (s, 2H), 3.35 – 3.33 (m, 2H), 2.81 (t, J = 6.2 Hz, 2H), 2.58 (t, J = 6.6 Hz, 1H), 2.08 (s, 3H), 2.05 – 2.00 (m, 2H), 1.99 (s, 3H), 1.95 (s, 3H), 1.85 – 1.73 (m, 2H), 1.58 – 1.57 (m, 3H), 1.56 – 1.52 (m, 2H), 1.42 – 1.34 (m, 3H), 1.30 – 1.23 (m, 12H), 1.16 – 1.05 (m, 6H), 0.90 – 0.83 (m, 12H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 167.9, 156.9, 149.8, 145.7, 140.0, 132.4, 129.2, 128.0, 127.3, 126.7, 125.0, 123.4, 122.4, 117.7, 116.0, 115.1, 111.1, 75.3, 65.5, 54.7, 49.9,

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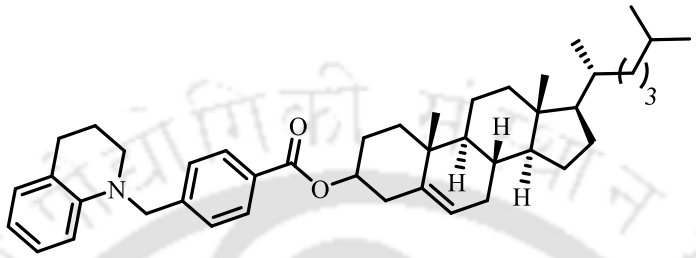
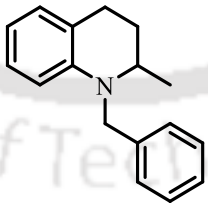
39.5, 37.6, 37.5, 37.4, 32.9, 32.8, 28.3, 28.1, 25.0, 24.6, 22.9, 22.8, 22.5, 21.2, 20.7, 19.9, 19.8, 13.1, 12.3, 12.0. HRMS (ESI) *m/z*: [M+H$^+$] calculated for $C_{47}H_{68}NO_4$ 710.5143; found: 710.5143.

(8S,9S,10R,13R,14S,17R)-10,13-dimethyl-17-((R)-6-methylheptan-2-yl)-2,3,4,7,8,9,10,11, 12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl-4-((3,4-dihydro quinolin-1(2H)-yl)methyl)benzoate (6.4h)



Using **GP-1**, the title compound **6.4h** was isolated as white solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.78); (138 mg, 91%). m.p. 158-160 °C. Using 0.25 mmol of quinoline, 0.25 mmol of **6.2aa** and 1 mmol of Hantzsch ester. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.99 (d, J = 8.0 Hz, 2H), 7.33 (d, J = 8.0 Hz, 2H), 6.98 (d, J = 7.6 Hz, 1H), 6.94 (d, J = 7.2 Hz, 1H), 6.59 (t, J = 7.0 Hz, 1H), 6.41 (d, J = 8.0 Hz, 1H), 5.41 (d, J = 4 Hz, 1H), 4.89 – 4.81 (m, 1H), 4.51 (s, 2H), 3.39 – 3.36 (m, 2H), 2.83 (t, J = 6.4 Hz, 2H), 2.45 (d, J = 8 Hz, 2H), 2.05 – 1.00 (m, 31H), 0.92 (d, J = 6.4 Hz, 3H), 0.87 (dd, J = 6.4, 2 Hz, 6H), 0.69 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 166.0, 145.5, 144.6, 139.8, 130.1, 129.7, 129.2, 127.3, 126.6, 122.9, 122.5, 116.3, 111.1, 74.6, 56.8, 56.3, 55.4, 50.2, 50.2, 42.5, 39.9, 39.7, 38.4, 37.2, 36.8, 36.3, 35.9, 32.1, 32.0, 28.4, 28.3, 28.2, 28.0, 24.4, 24.0, 23.0, 22.7, 22.5, 21.2, 19.5, 18.9, 12.0. HRMS (ESI) *m/z*: [M+H$^+$] calculated for $C_{44}H_{62}NO_2$ 636.4775; found 636.4741.

1-benzyl-2-methyl-1,2,3,4-tetrahydroquinoline (6.5a)[45]



Using **GP-1**, the title compound **6.5a** was isolated as colourless oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.80); (95 mg, 80%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32 – 7.20 (m, 5H), 7.01 (d, J = 7.3 Hz, 1H), 6.94 (t, J = 7.8 Hz, 1H), 6.57 (td, J = 7.3, 0.8 Hz, 1H), 6.40 (d, J = 8.2 Hz, 1H), 4.51 (m, 2H), 3.62 – 3.55 (m, 1H), 2.97 – 2.88 (m, 1H), 2.79 – 2.72 (m, 1H), 2.09 – 2.00 (m, 1H), 1.87 – 1.81 (m, 1H), 1.18 (d, J = 6.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): 144.9, 139.6, 128.9, 128.7, 127.2, 126.7, 126.4, 121.9, 115.6, 111.5, 53.5, 53.1, 28.3, 24.2, 19.1.

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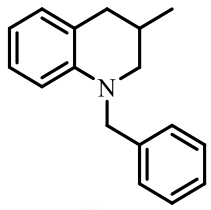
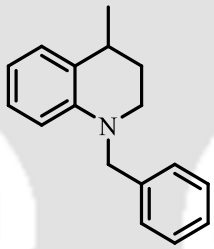
1-benzyl-3-methyl-1,2,3,4-tetrahydroquinoline (6.5b) [45]



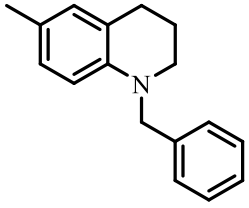
Using **GP-1**, the title compound **6.5b** was isolated as yellow oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v= 50:1, R_f = 0.80); (100 mg, 85%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34 – 7.22 (m, 5H), 6.99-6.96 (m, 2H), 6.58 (t, J = 7.4 Hz, 1H), 6.51 (d, J = 8.4 Hz, 1H), 4.48 (s, 2H), 3.31-3.27 (m, 1H), 3.07 – 3.01 (m, 1H), 2.85 – 2.80 (m, 1H), 2.54 – 2.48 (m, 1H), 2.22 – 2.13 (m, 1H), 1.06 (d, J = 6.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 145.3, 139.1, 129.2, 128.7, 127.3, 126.9, 126.7, 122.0, 116.0, 110.8, 57.0, 55.3, 36.6, 27.4, 19.2.

1-benzyl-4-methyl-1,2,3,4-tetrahydroquinoline (6.5c)[45]



Using **GP-1**, the title compound **6.5c** was isolated as yellow oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 98:2, R_f = 0.83); (103 mg, 87%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33 – 7.22 (m, 5H), 7.07 (d, J = 7.2 Hz, 1H), 6.97 (t, J = 7.2 Hz, 1H), 6.60 (t, J = 7.2 Hz, 1H), 6.50 (d, J = 8.4 Hz, 1H), 4.49 (s, 2H), 3.45 – 3.39 (m, 1H), 3.34 – 3.29 (m, 1H), 2.96 – 2.89 (m, 1H), 2.09 – 2.03 (m, 1H), 1.77– 1.72 (m, 1H), 1.33 – 1.31 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 145.0, 139.0, 128.7, 128.0, 127.4, 127.2, 126.9, 126.7, 115.9, 111.1, 55.3, 46.7, 31.2, 29.8, 22.4.

1-benzyl-6-methyl-1,2,3,4-tetrahydroquinoline (6.5d)[45]



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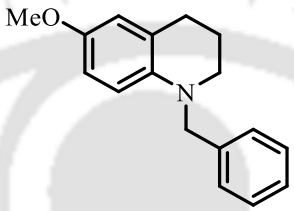
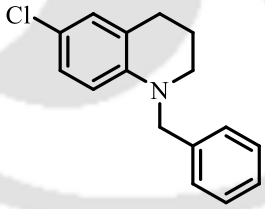
Using **GP-1**, the title compound **6.5d** was isolated as colorless oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.80); (104 mg, 88%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.32 – 7.21 (m, 5H), 6.81 (brs, 1H), 6.78 (d, J = 7.8 Hz, 1H), 6.42 (d, J = 8.2 Hz, 1H), 4.44 (s, 2H), 3.33 – 3.32 (m, 2H), 2.79 (t, J = 6.6 Hz, 2H), 2.19 (s, 3H), 2.02 – 1.98 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 143.6, 139.3, 129.9, 128.7, 127.7, 126.8, 126.8, 125.1, 122.4, 111.3, 55.5, 50.0, 28.3, 22.7, 20.3.

1-benzyl-6-methoxy-1,2,3,4-tetrahydroquinoline (6.5e)[23]



Using **GP-1**, the title compound **6.5e** was isolated as light yellow oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.80); (115 mg, 91%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33 – 7.23 (m, 5H), 6.61 – 6.56 (m, 2H), 6.46 – 6.44 (m, 1H), 4.41 (s, 2H), 3.71 (s, 3H), 3.30 – 3.27 (m, 2H), 2.80 (t, J = 6.4 Hz, 2H), 2.03 – 1.97 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 151.0, 140.5, 139.5, 128.7, 126.9, 126.8, 123.9, 115.4, 112.5, 112.4, 56.1, 55.9, 50.1, 28.5, 22.7.

1-benzyl-6-chloro-1,2,3,4-tetrahydroquinoline (6.5f)



Using **GP-1**, the title compound **6.5f** was isolated as colorless oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.80); (104 mg, 81%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33 – 7.30 (m, 2H), 7.25 – 7.21 (m, 3H), 6.93 (d, J = 2.4 Hz, 1H), 6.88 (dd, J = 2.4, 8.8 Hz, 1H), 6.37 (d, J = 8.4 Hz, 1H), 4.45 (s, 2H), 3.37 – 3.34 (m, 2H), 2.78 (t, J = 6.2 Hz, 2H), 2.02 – 1.96 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 144.2, 138.5, 128.8, 128.7, 127.0, 126.9, 126.6, 123.9, 120.4, 112.1, 55.3, 50.0, 28.2, 22.3. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{16}H_{17}ClN$ 258.1044; found: 258.1065

1-benzyl-7-chloro-1,2,3,4-tetrahydroquinoline (6.5g)

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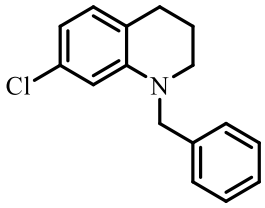
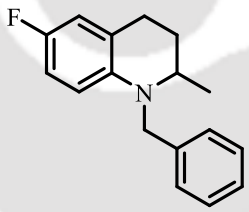


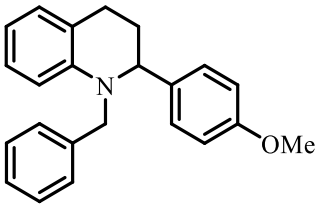
Using **GP-1**, the title compound **6.5g** was isolated as colorless oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.80); (108 mg, 84%). Using 4,7 dichloro quinoline and 4.5 equiv. of Hantzsch ester. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34-7.30 (m, 2H), 7.24-7.22 (m, 3H), 6.85 (d, J = 8 Hz, 1H), 6.51 (dd, J = 2, 4.0 Hz, 1H), 6.46 (d, J = 1.6 Hz, 1H), 4.44 (s, 2H), 3.34 – 3.32 (m, 2H), 2.75 (t, J = 6.0 Hz, 2H), 2.00-1.94 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 146.6, 138.1, 132.7, 129.9, 128.8, 127.1, 126.6, 120.7, 115.6, 110.6, 55.0, 49.6, 27.8, 22.2. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{16}H_{17}ClN$ 258.1044; found: 258.1045.

1-benzyl-6-fluoro-2-methyl-1,2,3,4-tetrahydroquinoline (6.5h)



Using **GP-1**, the title compound **6.5h** was isolated as yellow oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.80); (106 mg, 83%). ^{1}H NMR (400 MHz, $CDCl_3$): 7.33 – 7.22 (m, 5H), 6.74 (dd, J = 2.8, 9.2 Hz, 1H), 6.63 (td, J = 3.2, 8.8 Hz, 1H), 6.26 (dd, J = 4.8, 9.2 Hz, 1H), 4.51 – 4.40 (m, 2H), 3.59 – 3.52 (m, 1H), 2.93 – 2.85 (m, 1H), 2.76 – 2.70 (m, 1H), 2.08 – 1.99 (m, 1H), 1.86 – 1.79 (m, 1H), 1.16 (d, J = 6.8 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$): 155.4–154.9 (C-F, $^1J_{C\text{-}F}$ = 234 Hz), 141.3, 139.5, 128.7, 126.8, 126.4, 123.3 (C-F, $^3J_{C\text{-}F}$ = 6.5 Hz), 115.4–115.2 (C-F, $^2J_{C\text{-}F}$ = 21.7 Hz), 113.3–113.1 (C-F, $^2J_{C\text{-}F}$ = 21.6 Hz), 112.2 (C-F, $^3J_{C\text{-}F}$ = 7.2 Hz), 54.1, 53.2, 28.3, 24.4, 18.9. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{17}H_{19}FN$ 256.1496; found: 256.1502.

1-benzyl-2-(4-methoxyphenyl)-1,2,3,4-tetrahydroquinoline (6.5i)



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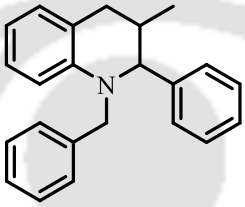
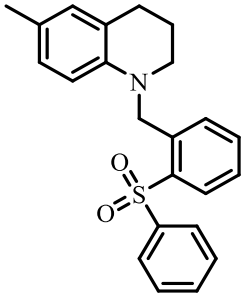
Using **GP-1**, the title compound **6.5i** was isolated as yellow oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.80); (135 mg, 82%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32-7.28 (m, 2H), 7.24 – 7.20 (m, 3H), 7.10 (d, J = 8.8 Hz, 2H), 7.01 (d, J = 7.2 Hz, 2H), 6.84 (d, J = 8.4 Hz, 2H), 6.61 (t, J = 7.0 Hz, 1H), 6.54 (d, J = 8.4 Hz, 1H), 4.71-4.64 (m, 2H), 4.24 (d, J = 17.6 Hz, 1H), 3.79 (s, 3H), 2.66 – 2.63 (m, 2H), 2.31-2.23 (m, 1H), 2.08 – 2.02 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 158.7, 145.3, 138.8, 136.2, 128.9, 128.7, 127.9, 127.5, 126.8, 126.4, 122.2, 115.7, 113.9, 110.5, 60.8, 55.4, 52.8, 29.7, 23.7. HRMS (ESI) *m/z*: $[M+H]^+$calculated for $C_{23}H_{24}NO$ 330.1852; found 330.1853.

1-benzyl-3-methyl-2-phenyl-1,2,3,4-tetrahydroquinoline (6.5j)



Using **GP-1**, the title compound **6.5j** was isolated as colorless oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.80); (126 mg, 81%). *cis : trans* = 7:3. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.32 – 7.20 (m, 10H, major + minor), 7.13 – 7.11 (m, 1H, major, 68%), 7.03 – 6.98 (m, 3H, major + minor), 6.65 (t, J = 7.2 Hz, 1H, major, 68%), 6.61 (t, J = 7.2 Hz, 1H, minor, 32%), 6.54 (d, J = 7.8 Hz, 1H, major, 68%), 6.48 (d, J = 8.4 Hz, 1H, minor, 32%), 4.53 (d, J = 17.4 Hz, 1H, minor, 32%), 4.49 (d, J = 3.6 Hz, 1H, major, 68%), 4.42 (d, J = 4.2 Hz, 1H, minor, 32%), 4.19 (d, J = 11.4 Hz, 1H, minor, 32%), 4.11 (s, 1H, major, 68%), 2.96 (dd, J = 4.8, 16.2 Hz, 1H, major, 68%), 2.58 – 2.47 (m, 3H, major + minor), 2.31 – 2.27 (m, 3H, major, 68%), 0.88 (d, 3H, J = 6 Hz, minor, 32%), 0.81 (d, 3H, J = 6.6 Hz, major, 68%). ^{13}C NMR (151 MHz, $CDCl_3$): δ 145.2, 144.3, 143.0, 140.6, 138.9, 129.8, 128.9, 128.8, 128.6, 128.2, 128.0, 127.6, 127.4, 127.3, 127.2, 127.0, 126.9, 126.3, 121.6, 120.1, 117.2, 115.6, 113.8, 110.1, 67.1, 59.5, 53.2, 33.5, 32.0, 31.6, 31.6, 18.6, 15.3. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{23}H_{24}N$ 314.1904; found: 314.1904. The relative *cis*-configuration was tentatively assigned by comparison with previous observation.[14, 21]

6-methyl-1-(2-(phenylsulfonyl)benzyl)-1,2,3,4-tetrahydroquinoline (6.5k)



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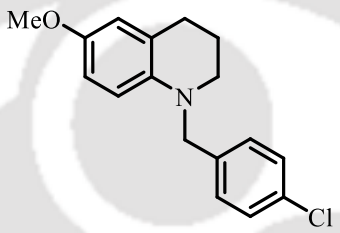
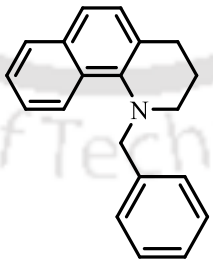
Using GP-1, the title compound **6.5k** was isolated as white solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.80); (171 mg, 91%). m.p. 175-177 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.28 (dd, J = 7.6, 1.6 Hz, 1H), 7.91-7.89 (m, 2H), 7.62 (tt, J = 1.2, 7.6 Hz, 1H), 7.55-7.40 (m, 5H), 6.77 (s, 1H), 6.46 (dd, J = 8.4, 1.6 Hz, 1H), 5.44 (d, J = 8.4 Hz, 1H), 4.57 (s, 2H), 3.26 (t, J = 5.6 Hz, 2H), 2.76 (t, J = 6.4 Hz, 2H), 2.13 (s, 3H), 2.13 – 1.96 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 142.6, 141.2, 139.0, 137.8, 134.3, 133.4, 130.0, 129.9, 129.4, 128.0, 127.8, 127.5, 127.4, 125.3, 122.2, 110.5, 53.2, 50.5, 28.1, 22.6, 20.2. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{23}H_{24}NO_2S$ 378.1523; found 378.1520.

1-(4-chlorobenzyl)-6-methoxy-1,2,3,4-tetrahydroquinoline (6.5l)



Using **GP-1**, the title compound **6.5l** was isolated as yellow oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.80); (132 mg, 92%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28 – 7.25 (m, 2H), 7.22 – 7.20 (m, 2H), 6.62 – 6.53 (m, 2H), 6.39 (d, J = 8.0 Hz, 1H), 4.36 (s, 2H), 3.71 (s, 3H), 3.28 – 3.25 (m, 2H), 2.80 (t, J = 6.4 Hz, 2H), 2.03 – 1.96 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): 151.19, 140.15, 138.02, 132.49, 128.80, 128.26, 124.11, 115.41, 112.50, 112.41, 55.90, 55.67, 50.15, 28.44, 22.67. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{17}H_{19}ClNO$ 288.1150; found 288.1151.

1-benzyl-1,2,3,4-tetrahydrobenzo[*h*]quinoline (6.5m)[45]



Using **GP-1**, the title compound **6.5m** was isolated as colorless oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.80); (98 mg, 72%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.15 – 8.13 (m, 1H), 7.78 – 7.76 (m, 1H), 7.64 (d, J = 7.2 Hz, 2H), 7.47 – 7.40 (m, 3H), 7.39 – 7.30 (m, 3H), 7.18 (d, J = 9.2 Hz, 1H), 4.35 (s, 2H), 3.18 – 3.15 (m, 2H), 2.95 (t, J = 6.6 Hz, 2H), 1.93 – 1.87 (m, 2H).). ^{13}C NMR (101 MHz, $CDCl_3$): δ 144.3, 139.9, 133.6,

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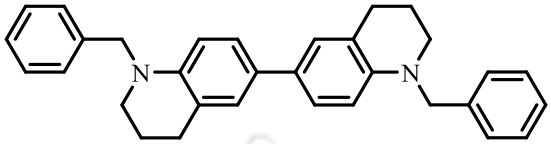
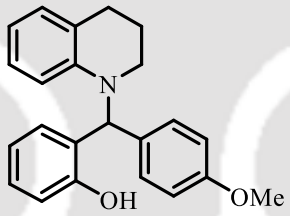
129.0, 128.9, 128.8, 128.5, 128.3, 127.5, 127.1, 127.0, 125.4, 125.4, 125.1, 123.0, 122.2, 59.2, 47.0, 28.1, 16.6.

1,1'-dibenzyl-1,1',2,2',3,3',4,4'-octahydro-6,6'-biquinoline (6.5n)[18]



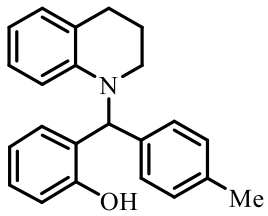
Using **GP-1**, the title compound **6.5n** was isolated as light brown solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.80); (148 mg, 67%). m.p. 168-170 °C. Using 6,6'-diquinoline, 2 equiv of benzaldehyde, and 8 equiv of Hantzsch ester. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34-7.28 (m, 8H), 7.24-7.22 (m, 2H), 7.14-7.12 (m, 4H), 6.52 (d, J = 8 Hz, 2H), 4.49 (s, 4H), 3.38-3.35 (m, 4H), 2.85 (t, J = 6.4 Hz, 4H), 2.06-2.0 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 144.3, 139.2, 129.5, 128.7, 127.1, 126.9, 126.8, 125.1, 122.5, 111.4, 55.5, 50.1, 28.5, 22.7.

2-((3,4-dihydroquinolin-1(2H)-yl)(4-methoxyphenyl)methyl)phenol (6.6a)[27]



Using **GP-2**, the title compound **6.6a** was isolated as yellow oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 10:1, R_f = 0.5); (113 mg, 66%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.16-7.11 (m, 1H), 7.09-7.07 (m, 2H), 6.86-6.79 (m, 6H), 6.76-6.73 (m, 2H), 6.42 (d, J = 8 Hz, 1H), 5.47 (s, 1H), 3.81 (s, 3H), 3.28-3.25 (m, 2H), 2.71-2.68 (m, 2H), 1.98 (s, 1H), 1.93-1.89 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 158.2, 153.8, 143.6, 135.2, 131.3, 130.6, 130.4, 130.3, 127.8, 127.6, 121.9, 120.6, 116.3, 114.6, 114.0, 55.3, 49.9, 42.1, 27.1, 22.2.

2-((3,4-dihydroquinolin-1(2H)-yl)(*p*-tolyl)methyl)phenol (6.6b)[27]



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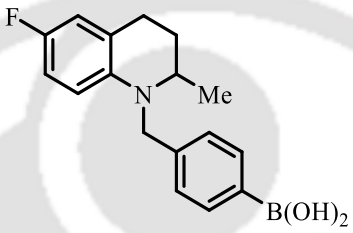
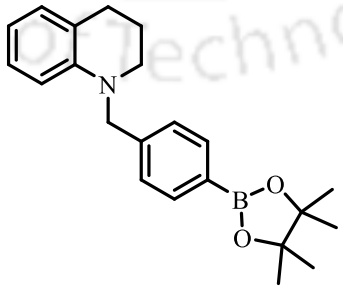
Using **GP-2**, the title compound **6.6b** was isolated as light yellow oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 10:1, R_f = 0.5); (100 mg, 61%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.16-7.11 (m, 3H), 7.05-7.03 (m, 2H), 6.86-6.84 (m, 1H), 6.84-6.82 (m, 2H), 6.82-6.81 (m, 1H), 6.74 (br, 1H), 6.71 (d, J = 8.4 Hz, 1H), 6.41 (d, J = 7.8 Hz, 1H), 5.46 (s, 1H), 3.29-3.27 (m, 2H), 2.69-2.67 (m, 2H), 2.33 (s, 3H), 2.01 (s, 1H), 1.93-1.89 (m, 2H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 153.9, 143.6, 140.0, 136.2, 131.1, 130.4, 130.4, 130.2, 129.3, 129.3, 127.8, 127.7, 122.0, 120.7, 116.4, 114.7, 50.5, 42.1, 27.1, 22.2, 21.2.

6-fluoro-2-methyl-1-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzyl)-1,2,3,4-tetrahydroquinoline (6.7a)



Using **GP-3**, the title compound **6.7a** was isolated as white solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 20:1, R_f = 0.8); (61 mg, 82%). using 0.25 mmol scale. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.15 (d, J = 7.8 Hz, 2H), 7.39 (d, J = 7.7 Hz, 2H), 6.76 (dd, J = 9.0, 2.8 Hz, 1H), 6.64 (td, J = 8.6, 3.0 Hz, 1H), 6.26 (dd, J = 9.0, 4.6 Hz, 1H), 4.58 – 4.49 (m, 2H), 3.64 – 3.59 (m, 1H), 2.91–2.88 (m, 1H), 2.78–2.74 (m, 1H), 2.10 – 2.07 (m, 1H), 1.91 – 1.86 (m, 1H), 1.19 (d, J = 6.0 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 144.8–143.2 (C-F, $^1J_{C\text{-}F}$ = 240.1 Hz), 141.2, 136.1, 134.0, 127.8, 126.2–126.1 ($^3J_{C\text{-}F}$ = 10.6 Hz), 123.5, 115.5–115.4 (C-F, $^2J_{C\text{-}F}$ = 16.6 Hz), 113.3–113.2 (C-F, $^2J_{C\text{-}F}$ = 21.1 Hz), 112.2, 54.5, 53.4, 28.4, 24.4, 19. ^{19}F NMR (565 MHz, $CDCl_3$): -132.72. ^{11}B (193 MHz, $CDCl_3$): 29.37. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{17}H_{20}BFNO_2$ 300.1566; found: 300.1566.

1-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzyl)-1,2,3,4-tetrahydroquinoline (6.7b)



Using **GP-3**, the title compound **6.7b** was isolated as off white solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.80); (148 mg, 85%). m.p.

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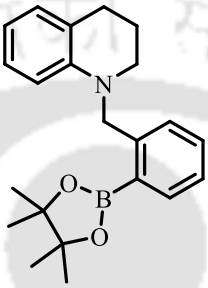
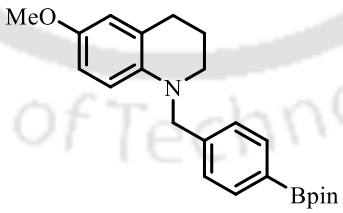
118-120 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.79 (d, J = 8 Hz, 2H), 7.30 (d, J = 8 Hz, 2H), 7.00 – 6.96 (m, 2H), 6.59 (t, J = 7.2 Hz, 1H), 6.49 (d, J = 8.0 Hz, 1H), 4.50 (s, 2H), 3.38 – 3.35 (m, 2H), 2.84 (t, J = 6.2 Hz, 2H), 2.06 – 2.00 (m, 2H), 1.36 (s, 12H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 145.7, 142.6, 135.2, 129.1, 127.3, 126.1, 122.4, 116.0, 111.1, 83.8, 55.5, 50.0, 28.3, 25.0, 22.5. ^{11}B (128.4 Hz, $CDCl_3$): 31.27. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{22}H_{29}BNO_2$ 350.2286; found 350.2284.

1-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzyl)-1,2,3,4-tetrahydroquinoline (6.7c)



Using **GP-3**, the title compound **6.7c** was isolated as colorless oil using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.80); (140 mg, 80%). m.p. 120-122 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84 (dd, J = 1.2, 7.2 Hz, 1H), 7.34 (td, J = 1.2, 7.4 Hz 1H), 7.28 – 7.21 (m, 2H), 6.98 – 6.93 (m, 2H), 6.55 (t, J = 7.2 Hz, 1H), 6.43 (d, J = 8.4 Hz, 1H), 4.73 (s, 2H), 3.36 (t, J = 5.6 Hz, 2H), 2.83 (t, J = 6.2 Hz, 2H), 2.05 – 1.99 (m, 2H), 1.33 (s, 12H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 145.9, 145.5, 136.5, 131.3, 128.9, 127.3, 126.0, 125.7, 122.2, 115.6, 111.2, 83.8, 55.4, 49.9, 28.3, 25.1, 22.5. ^{11}B (128.4 Hz, $CDCl_3$): 31.55. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{22}H_{29}BNO_2$ 350.2286; found 350.2267.

6-methoxy-1-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzyl)-1,2,3,4-tetrahydroquinoline (6.7d)



Using **GP-3**, the title compound **6.7d** was isolated as off white solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.80); (168 mg, 89%). m.p. 91-94 °C. ^{1}H NMR (400 MHz, $CDCl_3$): 7.76 (d, J = 8 Hz, 2H), 7.29 (d, J = 8 Hz, 2H), 6.61 (d, J = 2.8 Hz, 1H), 6.55 (dd, J = 2.8, 5.8 Hz, 1H), 6.42 (d, J = 8.8 Hz, 1H), 4.41 (s, 2H), 3.71 (s, 3H), 3.29 – 3.26 (m, 2H), 2.80 (t, J = 6.4 Hz, 2H), 2.01 – 1.98 (m, 2H), 1.33 (s, 12H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 151.0, 143.0, 140.5, 135.2, 126.3, 123.9, 115.4, 112.5, 112.4, 83.8, 56.4, 55.9,

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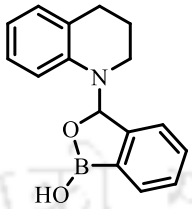
50.1, 28.5, 25.0, 22.7. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{23}H_{31}BNO_3$ 380.2392; found: 380.2391.

3-(3,4-dihydroquinolin-1(2H)-yl)benzo[c][1,2]oxaborol-1(3H)-ol (6.9)



Using the reaction condition given in Scheme 6.11 the title compound **6.9** was isolated as off white solid using silica gel column chromatography with petroleum ether/ethyl acetate (v/v = 50:1, R_f = 0.50); (87 mg, 66%). m.p. 108-110 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.79 (d, J = 7.2 Hz, 1H), 7.54 (t, J = 7.2 Hz 1H), 7.44 (t, J = 7.2 Hz 1H), 7.39 (d, J = 7.2 Hz 1H), 7.26 (s, 1H), 6.96 (d, J = 7.2 Hz, 1H), 6.66 (d, J = 7.8 Hz, 1H), 6.50 (t, J = 7.4 Hz, 1H), 6.25 (s, 1H), 3.43 – 3.41 (m, 2H), 2.85 – 2.79 (m, 2H), 1.99 – 1.95 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 154.6, 144.4, 130.0, 130.7, 130.2, 127.7, 125.4, 123.8, 123.1, 122.5, 116.2, 80.7, 42.4, 27.6, 21.9. ^{11}B (128.4 Hz, $CDCl_3$): 32.5. HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{16}H_{17}BNO_2$ 266.1347; found: 266.1347.

Triphenyl boroxine (6.3l):[46]

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.25 (d, J = 7.2 Hz, 6H), 7.61 (t, J = 7.2 Hz, 3H), 7.52 (t, J = 7.6 Hz, 6H); ^{11}B NMR (128.4 MHz, $CDCl_3$): δ 29.5 (brs).

6.7. References

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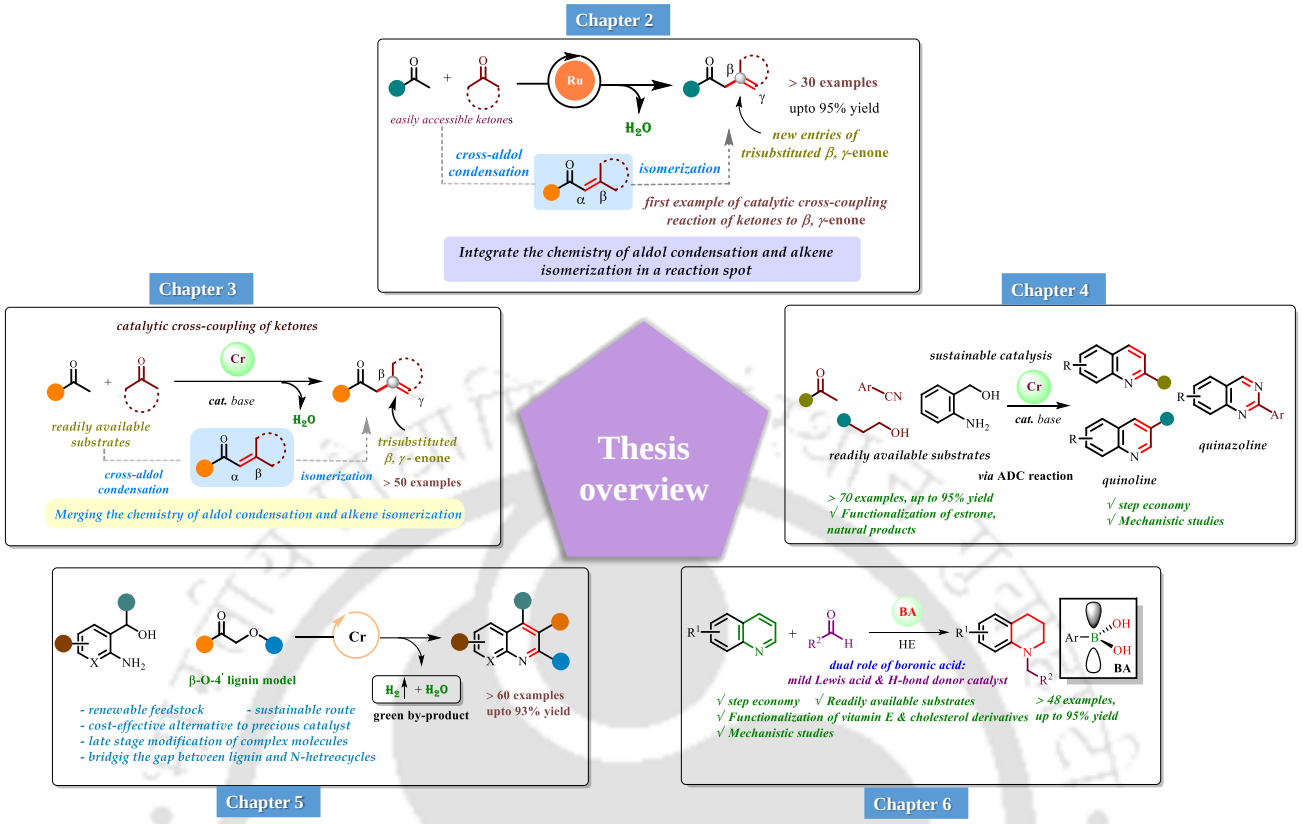

Chapter 1 outlines includes a brief introduction about the basic concepts of aldol reaction, alkene isomerization, acceptorless dehydrogenation *via* metal-ligand cooperation, and a general background of transfer hydrogenation reactions.

Chapter 2 deals with the ruthenium-catalyzed chemoselective and regioselective cross-coupling reaction of ketones for the synthesis of *β*- branched *β*, *γ*-unsaturated ketones with water as only by product, making this process environmentally benign. The detailed mechanistic studies were done in order to disclose the origin of high chemoselectivity and regioselectivity between *α*, *β*- and *β*, *γ*-unsaturated ketone. Thus, with the help of DFT calculations, several control experiments, and deuterium-labeling experiments, the mechanistic finding illustrate that the initial aldol condensation of ketones to a *β*, *β*-disubstituted *α*, *β*-unsaturated ketone, which further isomerizes to a *β*, *γ*- unsaturated ketone *via* η^3-allyl ruthenium complex. This protocol is compatible with wide range of sensitive and reduceable functional group and even suitable for challenging aliphatic ketones. Further the practical applicability of this process was further extended to the gram-scale reaction and late-stage functionalization of natural products.

Chapter 3 deals with the synthesis and characterization of new bench-stable triazine-based NNN-pincer ligands and their corresponding cost-effective chromium complexes. I have explored their utility in the cross-coupling of methyl ketones with cyclic ketones to *β*-branched *β*, *γ*- unsaturated ketones. The reaction is highly chemoselective and regioselective. This catalytic route gives a

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unique opportunity to integrate the chemistry of the synthetic challenge cross-coupling reaction of ketones and the alkene migration reaction into a single reaction pot.

Chapter 4 describe an efficient method for the synthesis of C2 substituted quinoline, C3 substituted quinoline and quinazoline derivatives *via* ADC reaction catalyzed by well defined, bench-stable Cr(III) complex as precatalyst. Reaction is highly chemoselective and produces molecular hydrogen and water as the only byproducts making the protocol green, atomeconomical, and environmentally benign. Method is compatible with a wide variety of sensitive functional group and applicable for even problematic aliphatic alcohols as substrates. The process can further be extended to the gram-scale reaction and late-stage functionalization of various natural products. This protocol gives a unique opportunity to dehydrogenative synthesis of N-heterocycles by underexplored chromium catalysis.

Chapter 5 illustrates chromium-catalyzed annulation of 2-aminoaryl alcohol with phenoxy acetophenone to 3-oxo-quinoline derivatives is reported. Phenoxy acetophenones are employed as β-O-4′ lignin models for this conversion. The efficacy of the process was further extended by producing 3-aminoquinolines using α-amino ketone. Notably, these are hard to prepare using conventional method. The catalyst tolerates numerous functional groups, including hydrogenation sensitive examples and is applicable for even problematic α-hydroxyacetophenone as substrate. The process can further be extended to the gram-scale reaction and late-stage functionalization of natural products. Notably, the use of non-precious catalyst, a catalytic amount of base, aerobic conditions, functional group diversity and late-stage modification of complex molecules are important practical features

Chapter 6 demonstrates a boronic acid catalyzed one-pot tandem reduction of quinolines to tetrahydroquinolines followed by reductive alkylation by the aldehyde has been demonstrated. This step-economcial synthesis of N-alkyl tetrahydroquinolines has been achieved directly from readily available quinolines, aldehydes, and Hantzsch ester under mild reaction conditions. Contrary to the reported procedures, the current protocol employs a commercially available, air- and moisture-tolerant boronic acid that is compatible with a wide variety of substrates and afforded the desired *N*-alkyl tetrahydroquinolines with a very high yield. The mechanistic study demonstrates the unique behavior of organoboron catalysts as both Lewis acids and hydrogen-bond donors. The synthetic utility of the present protocol was explored towards several bioactive molecules such as lipoprotein receptor and antimicrobial active *N*-diarylmethyl THQ efficiently.

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Annexure I

^{1}H, ^{13}C, ^{19}F, 2D and nOe NMR spectra of representative compounds (*Chapter 2*)

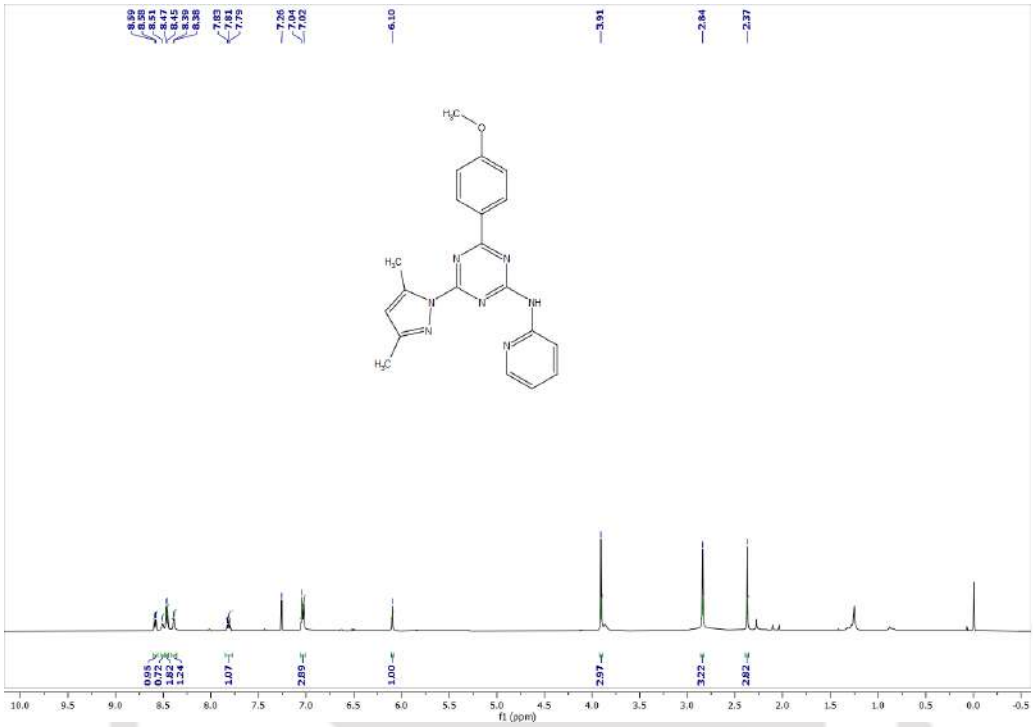

Figure S1: ^{1}H NMR Spectrum of **2.5b** ($CDCl_3$, 500 MHz, 298 K)

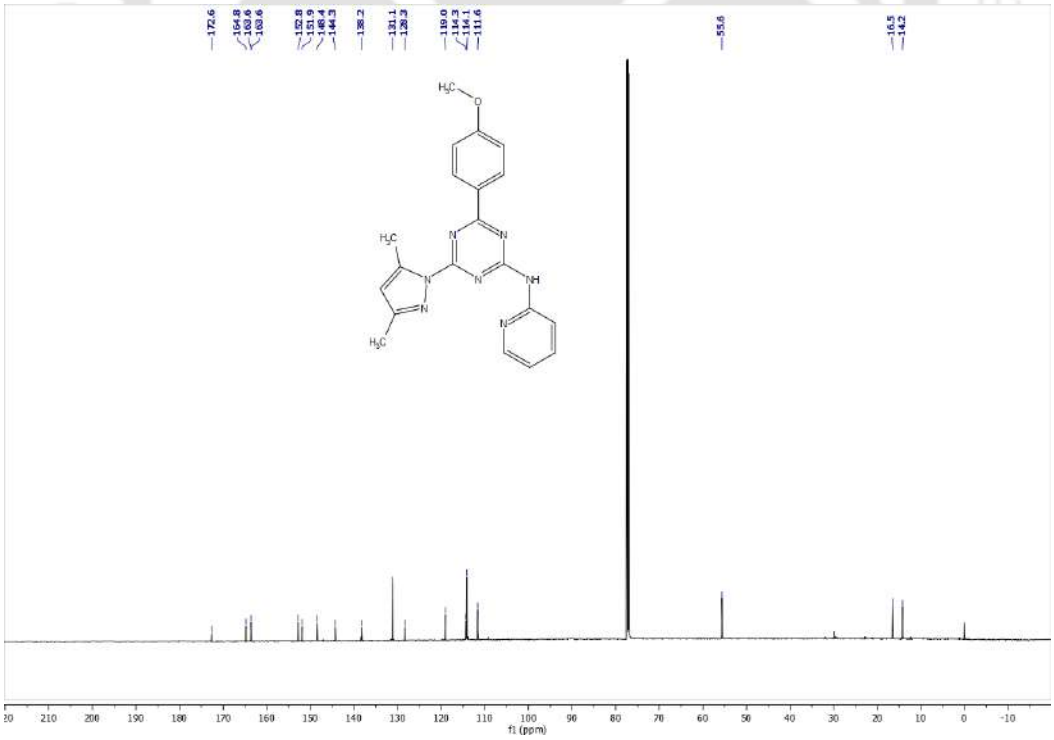

Figure S2: $^{13}C\{^{1}H\}$ NMR Spectrum of **2.5b** ($CDCl_3$, 101 MHz, 298 K)

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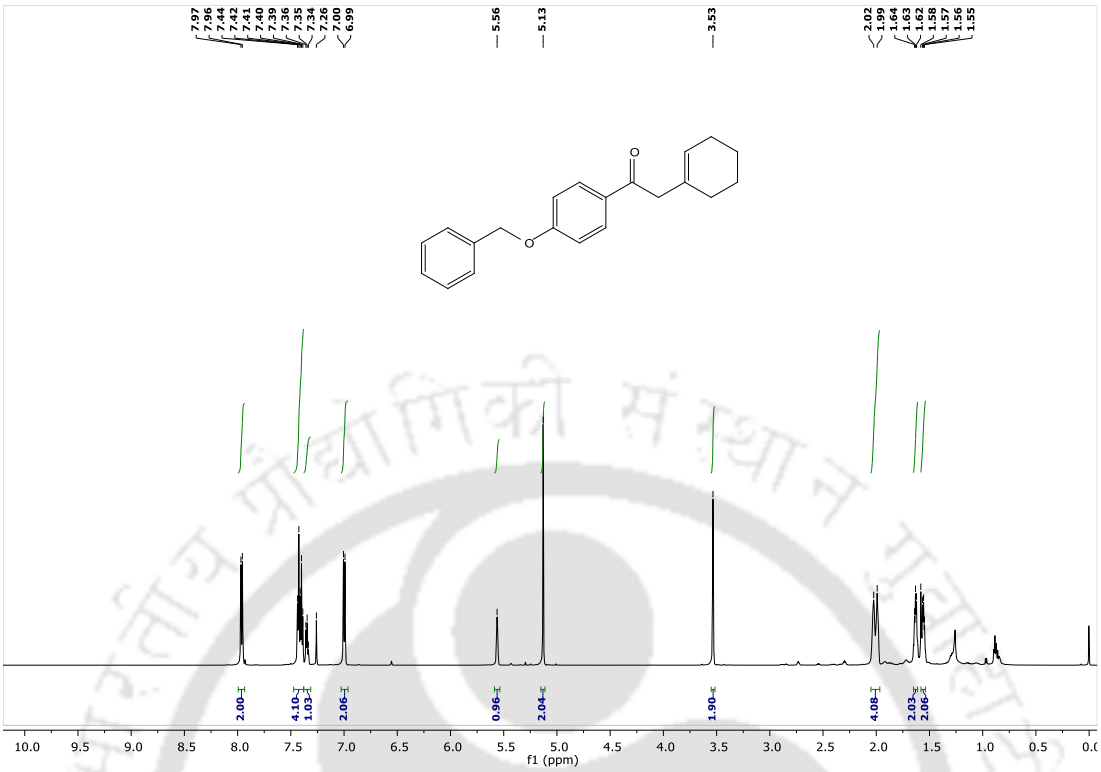

Figure S3: ^{1}H NMR Spectrum of **2.9a** ($CDCl_3$, 600 MHz, 298 K)

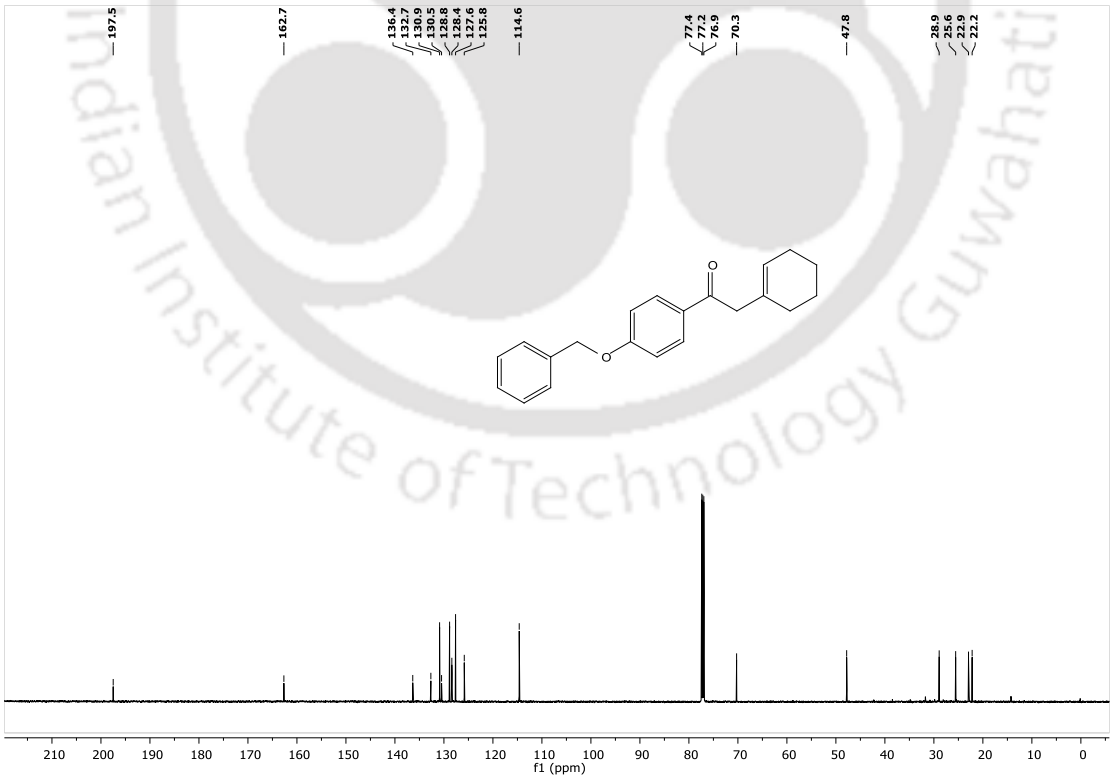

Figure S4: $^{13}C\{^{1}H\}$ NMR Spectrum of **2.9a** ($CDCl_3$, 151 MHz, 298 K)

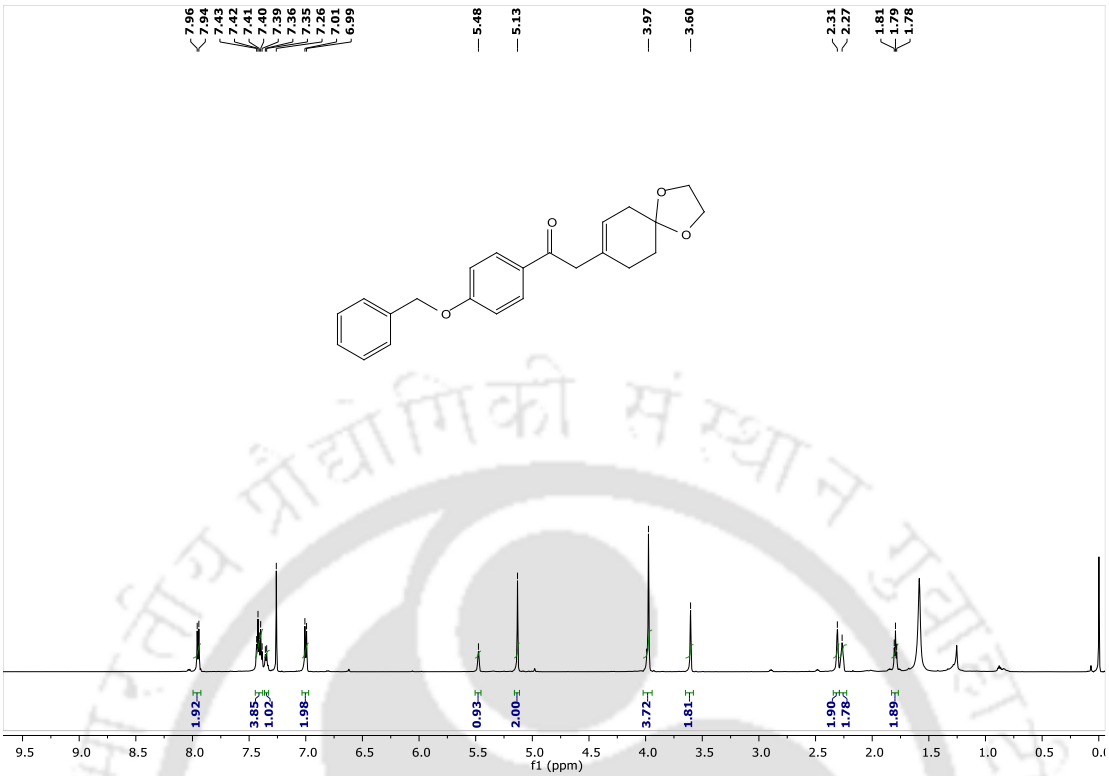

Figure S5: ^{1}H NMR Spectrum of **2.9q** ($CDCl_3$, 600 MHz, 298 K)

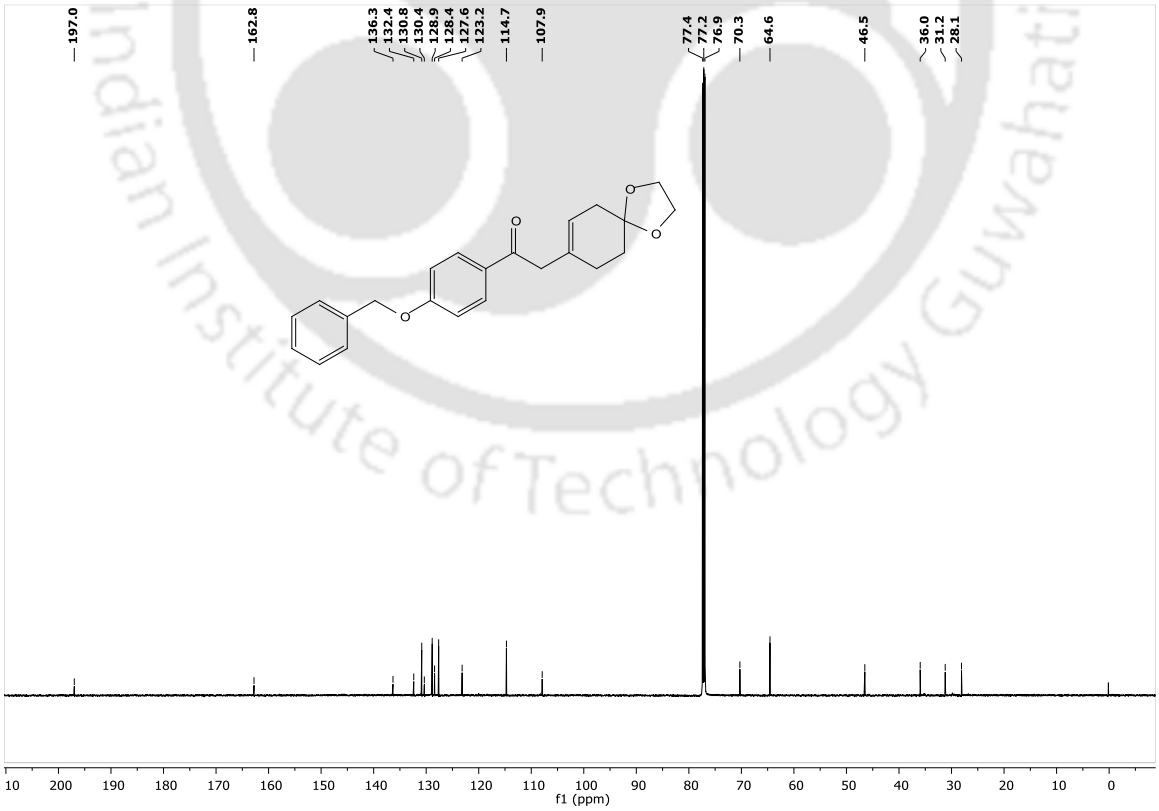

Figure S6: $^{13}C\{^{1}H\}$ NMR Spectrum of **2.9q** ($CDCl_3$, 151 MHz, 298 K)

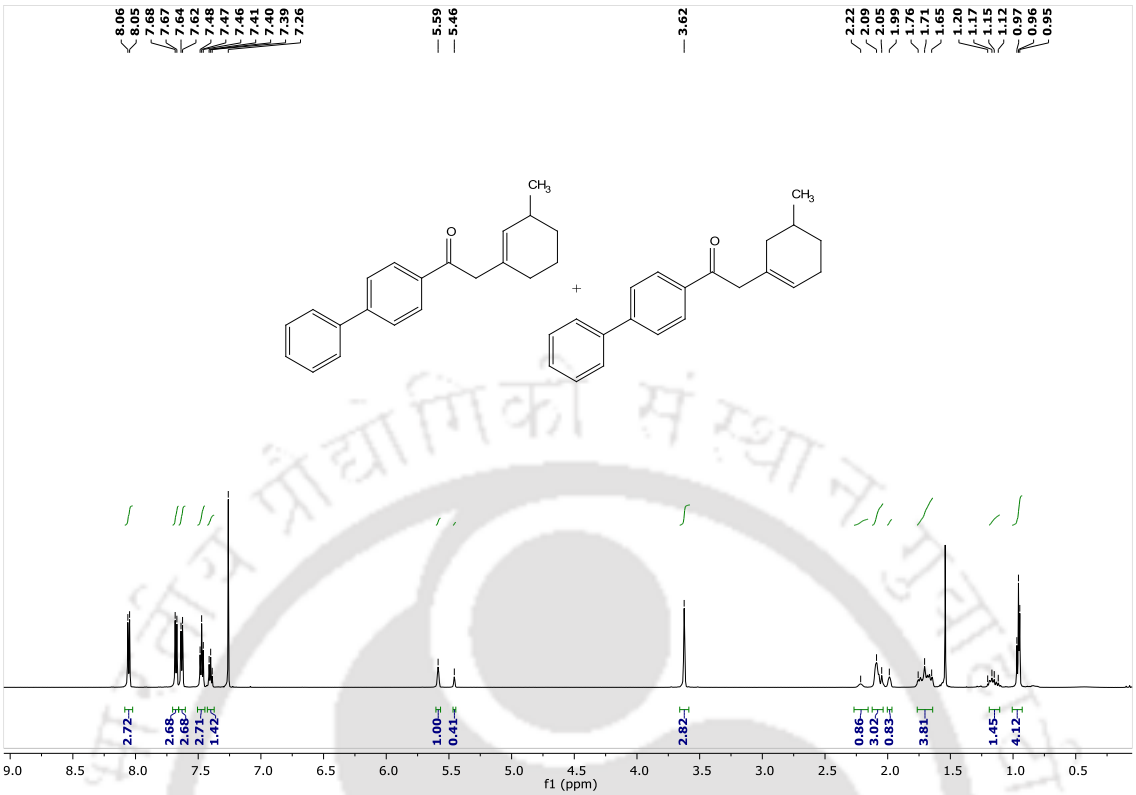

Figure S7: ^{1}H NMR Spectrum of **2.9v** ($CDCl_3$, 600 MHz, 298 K)

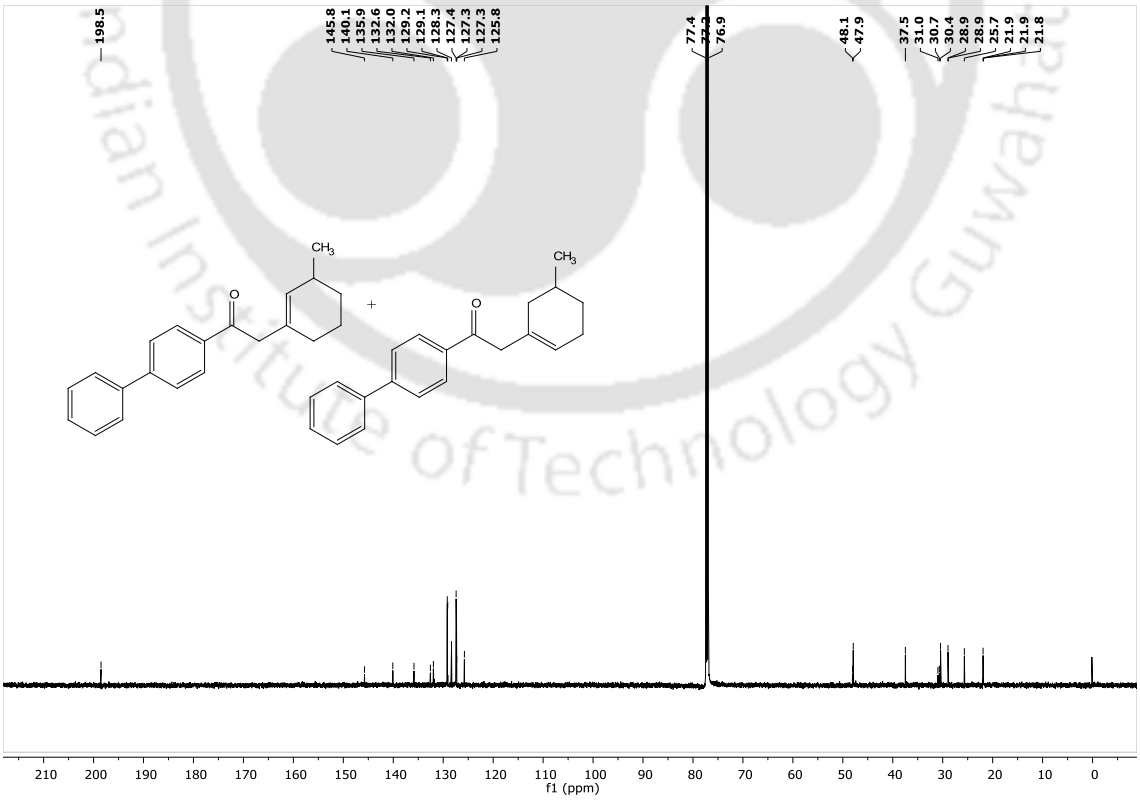

Figure S8: $^{13}C\{^{1}H\}$ NMR Spectrum of **2.9v** ($CDCl_3$, 151 MHz, 298 K)

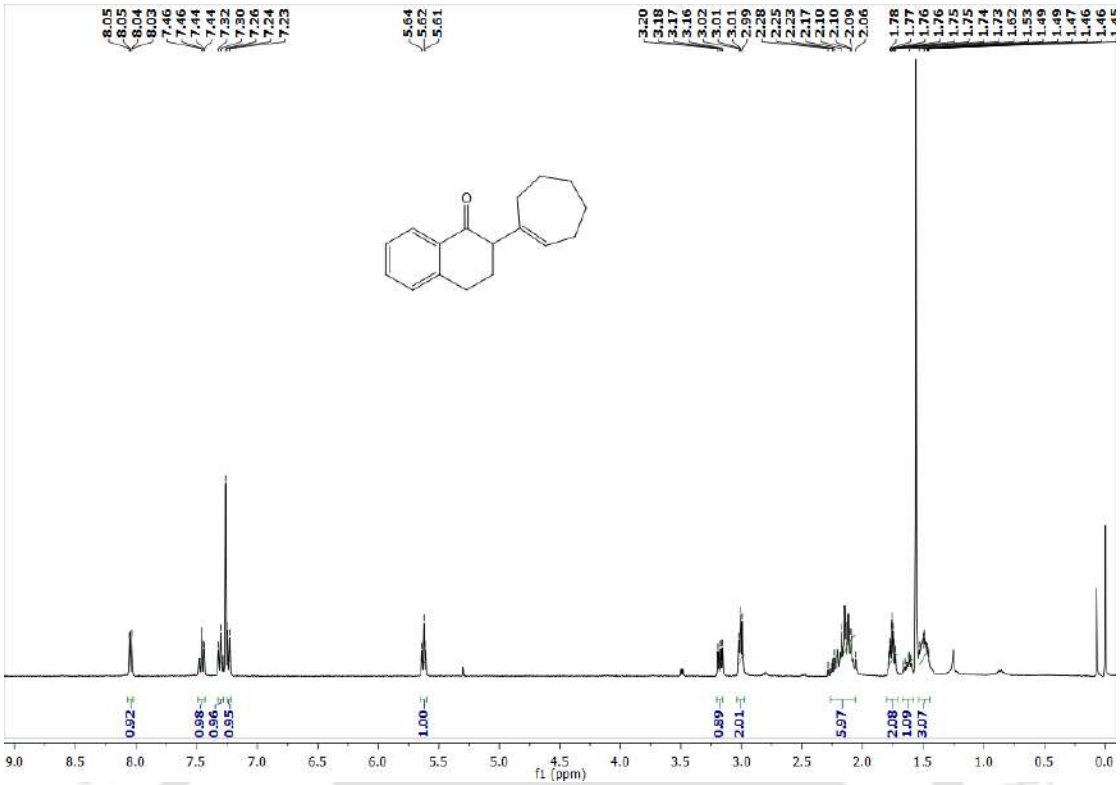

Figure S9: ^{1}H NMR Spectrum of **2.9af** ($CDCl_3$, 400 MHz, 298 K)

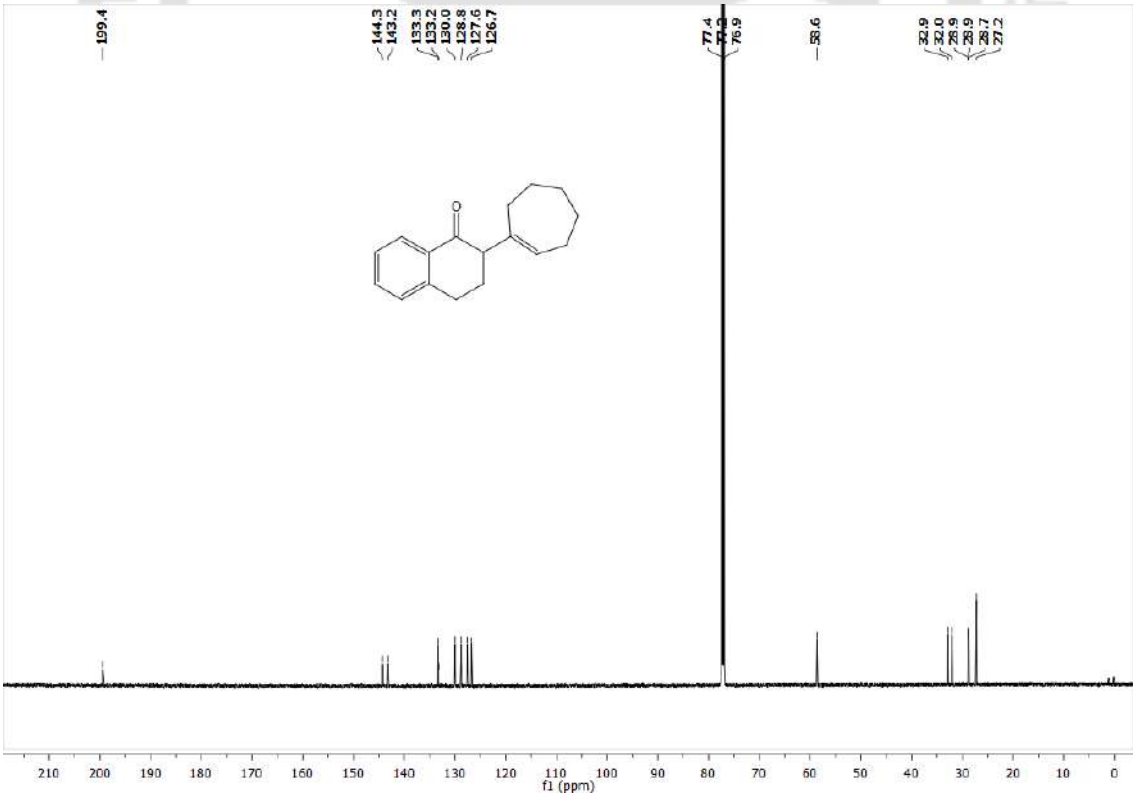

Figure S10: $^{13}C\{^{1}H\}$ NMR Spectrum of **2.9af** ($CDCl_3$, 151 MHz, 298 K)

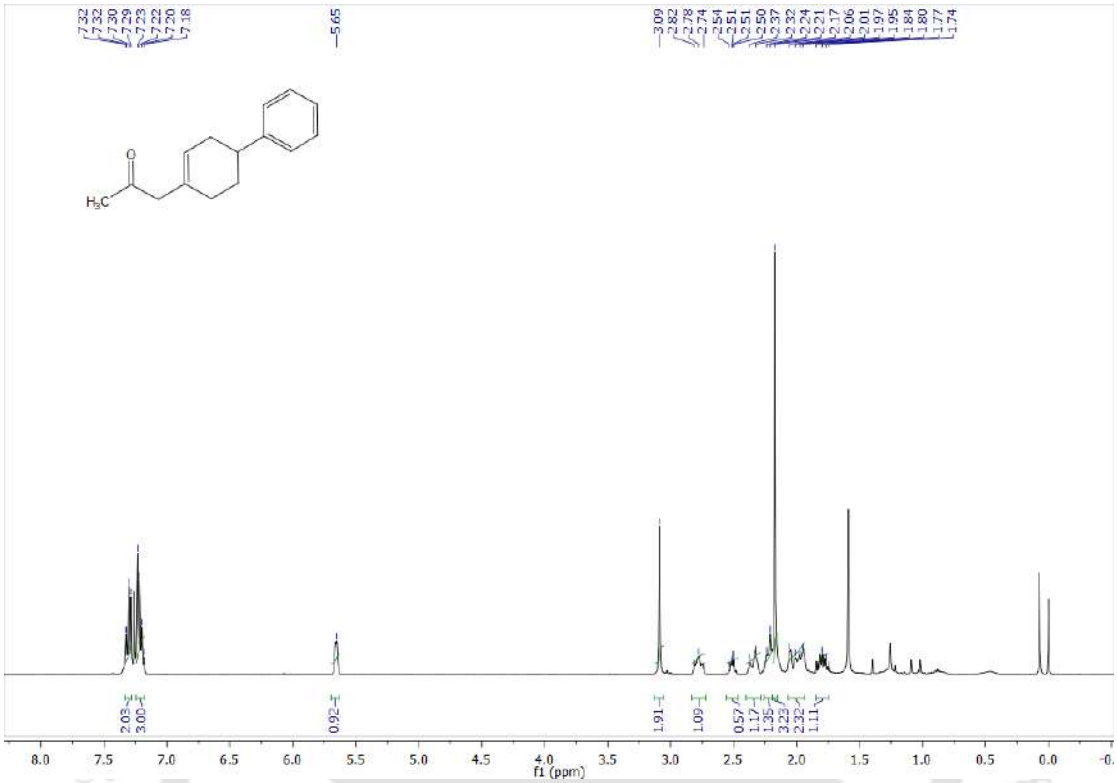

Figure S11: ^{1}H NMR Spectrum of **2.9ae** ($CDCl_3$, 400 MHz, 298 K)

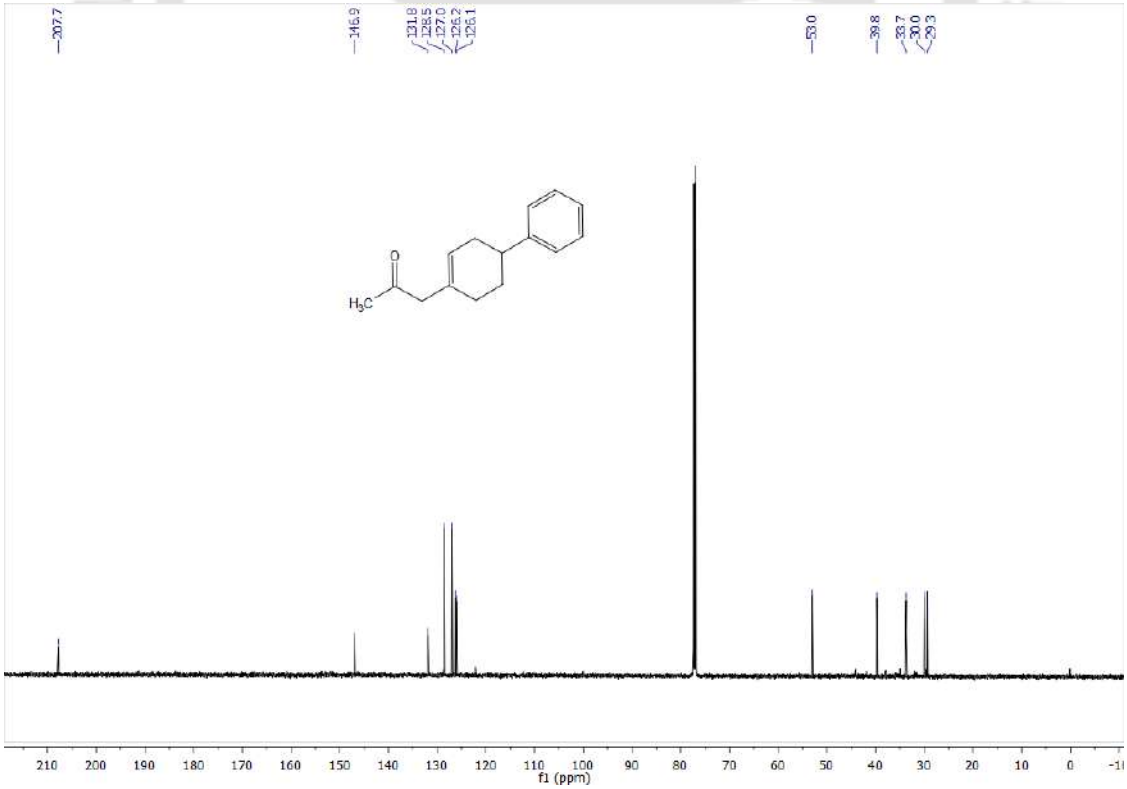

Figure S12: $^{13}C\{^{1}H\}$ NMR Spectrum of **2.9ae** ($CDCl_3$, 126 MHz, 298 K).

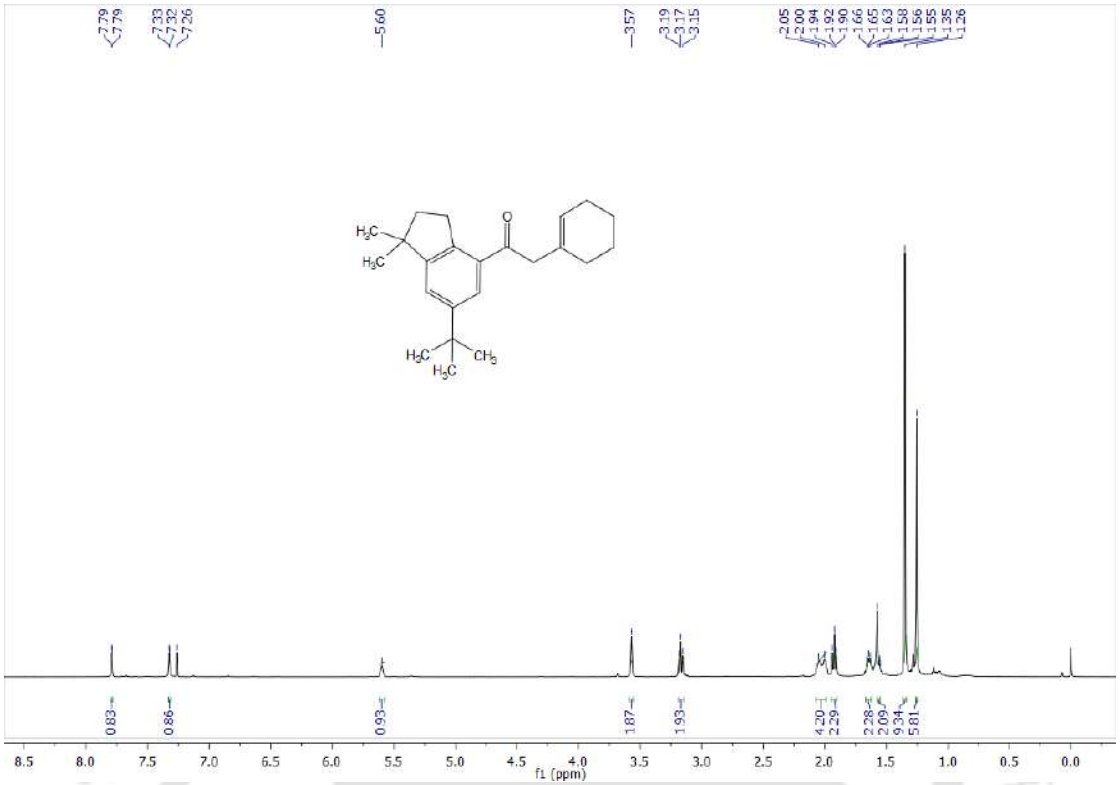

Figure S13: ^{1}H NMR Spectrum of **2.9ai** ($CDCl_3$, 400 MHz, 298 K).

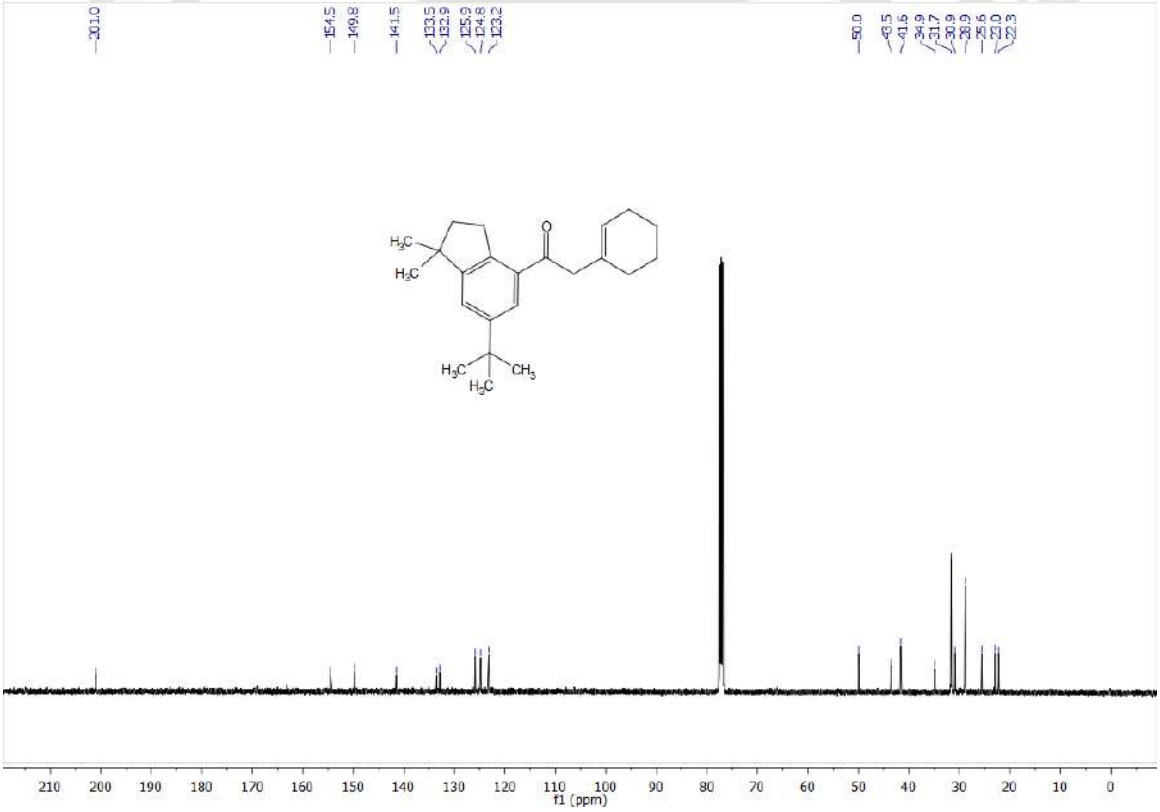

Figure S14: $^{13}C\{^{1}H\}$ NMR Spectrum of **2.9ai** ($CDCl_3$, 126 MHz, 298 K).

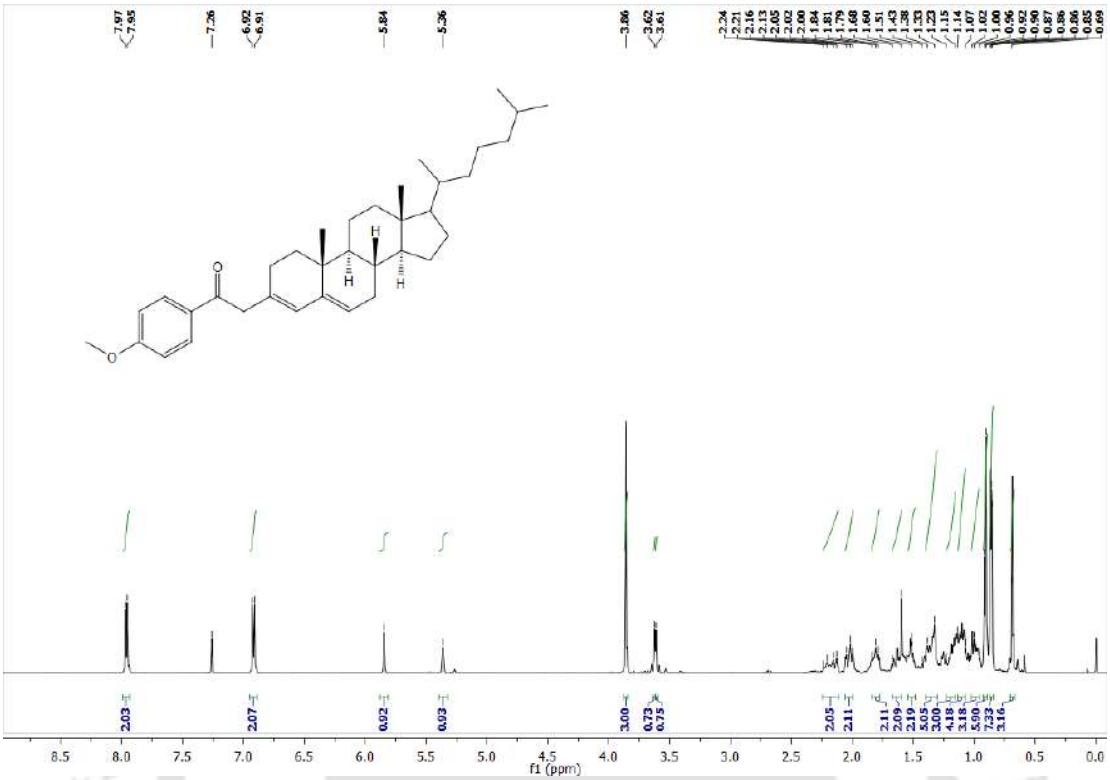

Figure S15: ^{1}H NMR Spectrum of **2.9aj** ($CDCl_3$, 600 MHz, 298 K)

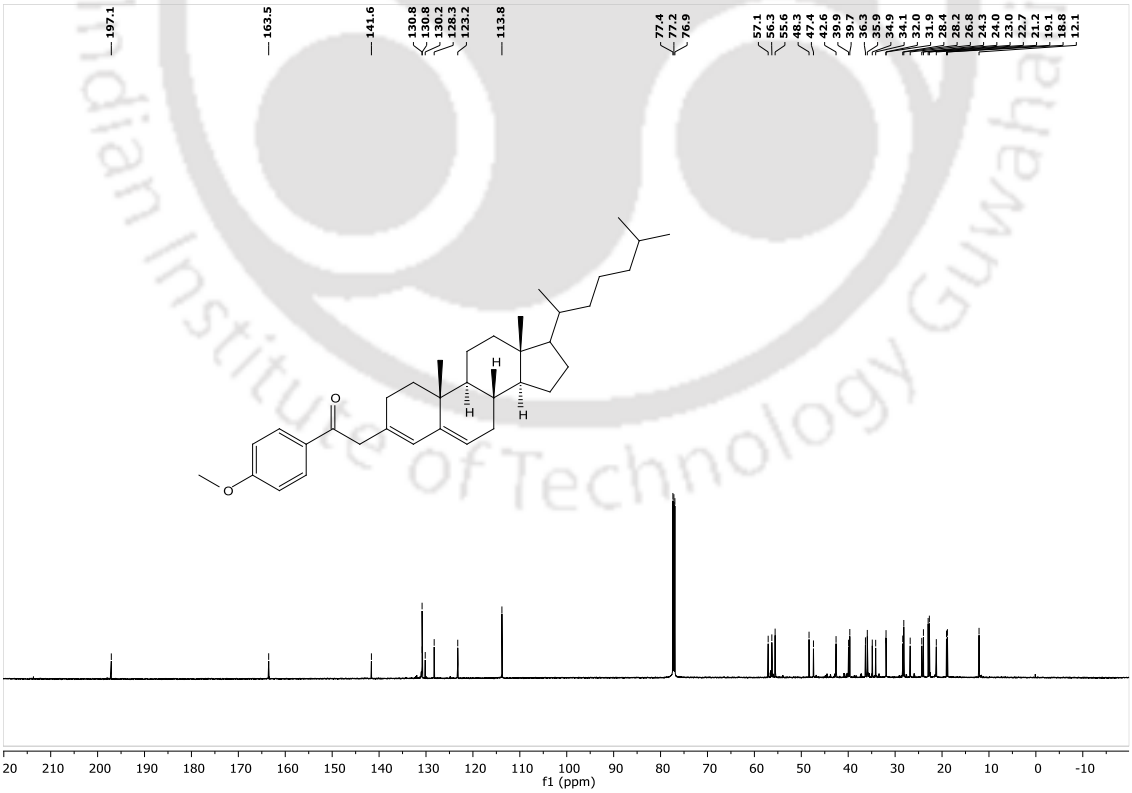

Figure S16: $^{13}C\{^{1}H\}$ NMR Spectrum of **2.9aj** ($CDCl_3$, 151 MHz, 298 K)

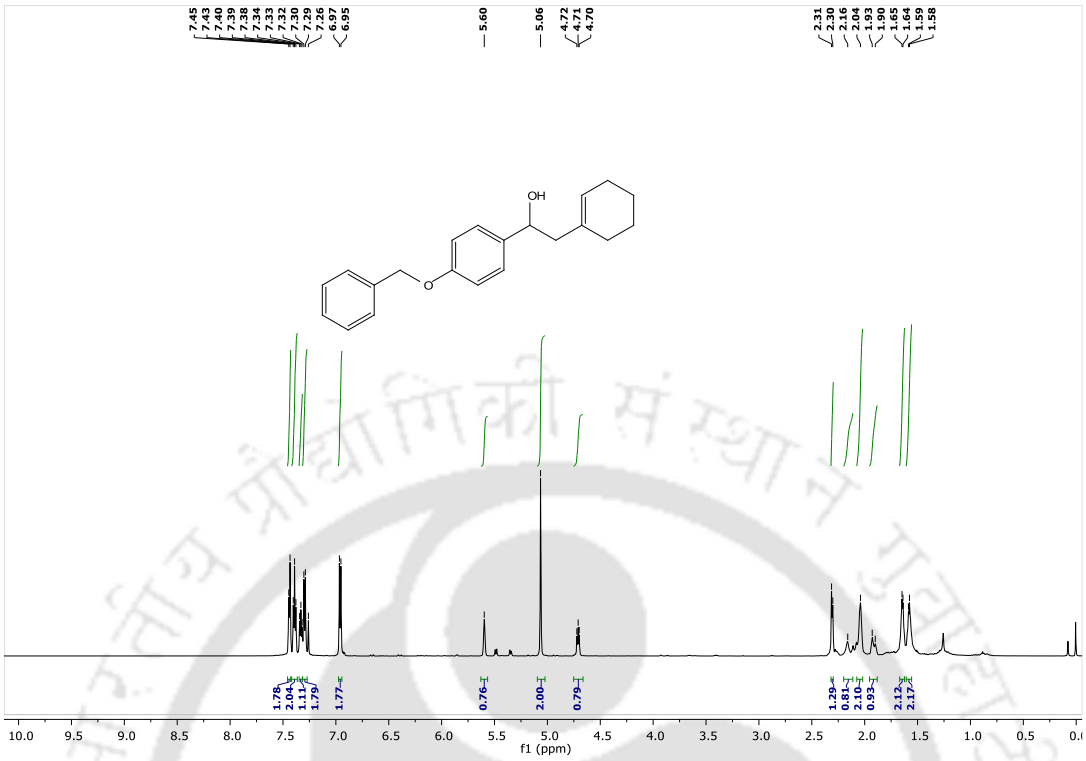

Figure S17: ^{1}H NMR Spectrum of **2.11** ($CDCl_3$, 600 MHz, 298 K)

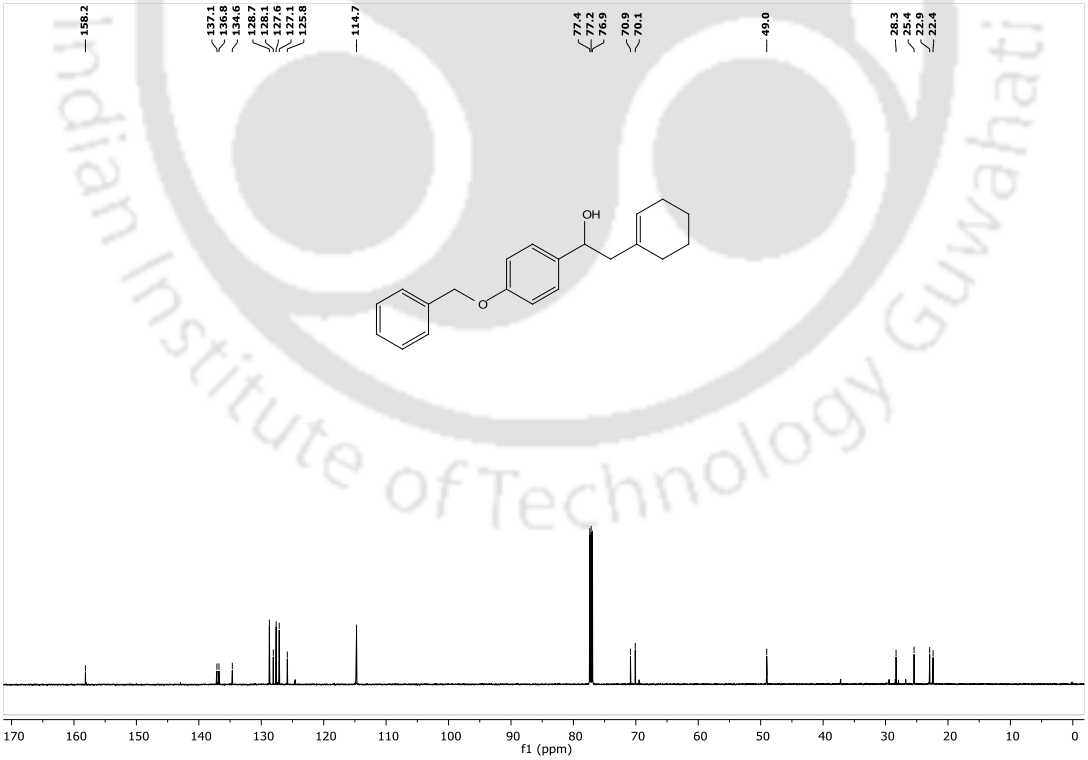

Figure S18: $^{13}C\{^{1}H\}$ NMR Spectrum of **2.11** ($CDCl_3$, 151 MHz, 298 K)

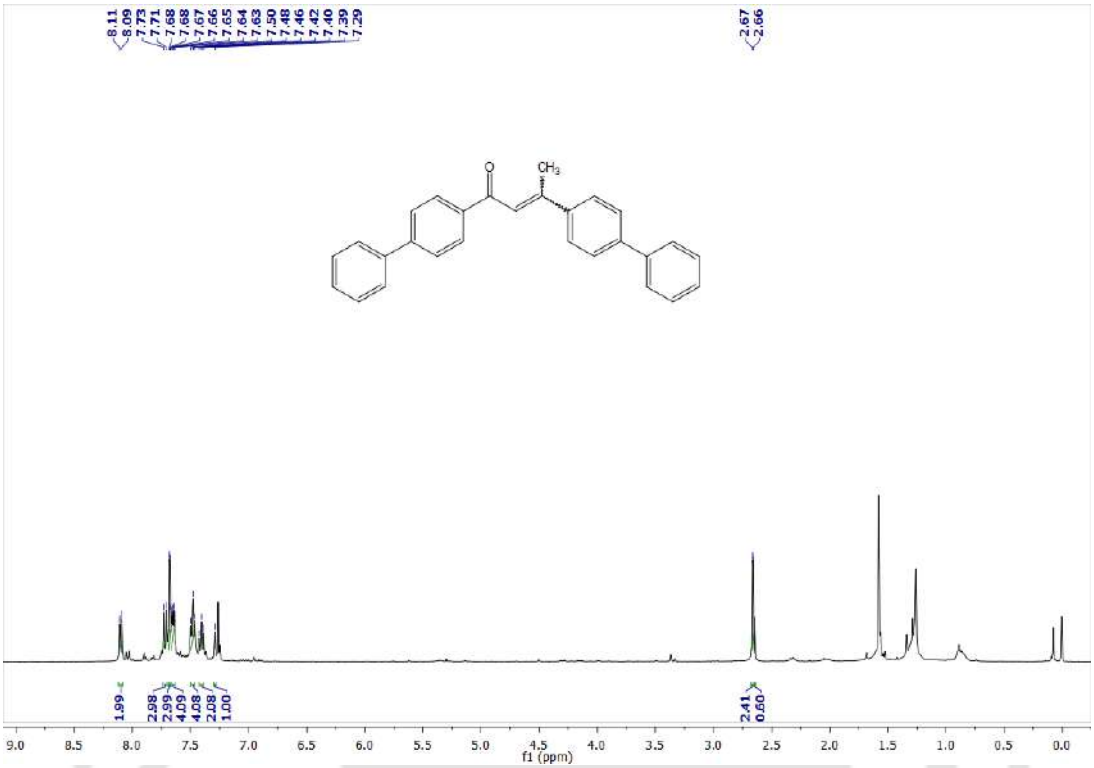

Figure S19: ^{1}H NMR Spectrum of **2.15** ($CDCl_3$, 400 MHz, 298 K)

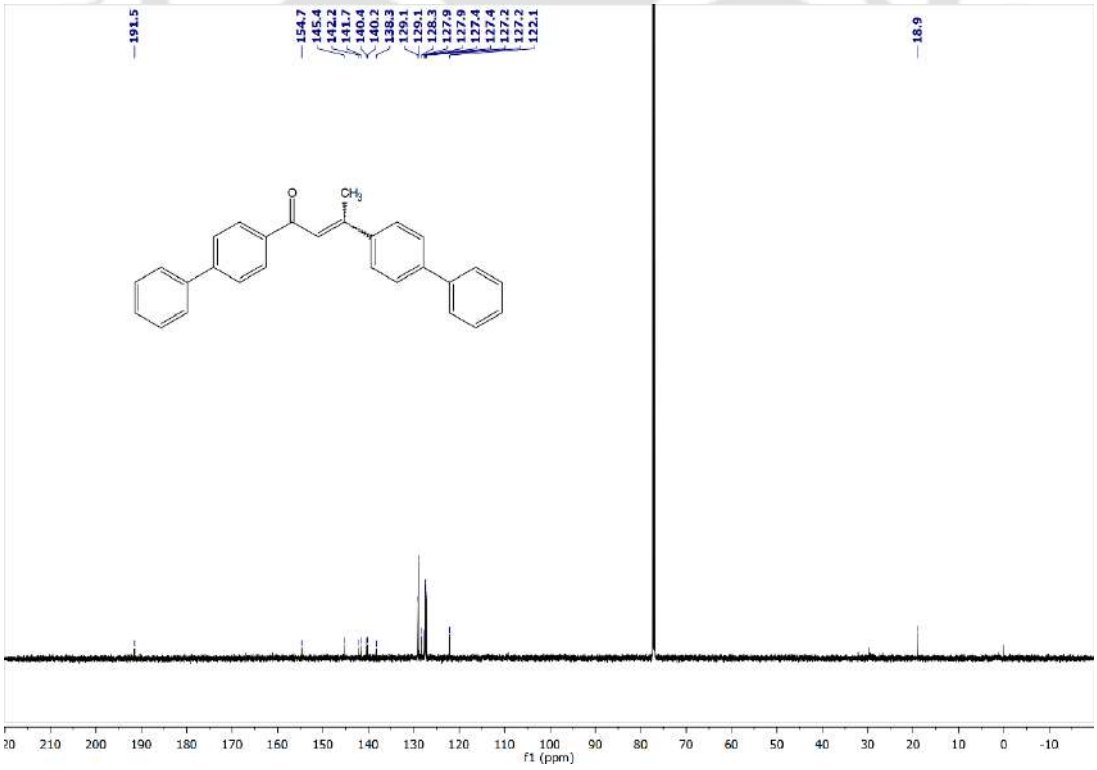

Figure S20: $^{13}C\{^{1}H\}$ NMR Spectrum of **2.15** ($CDCl_3$, 151 MHz, 298 K)

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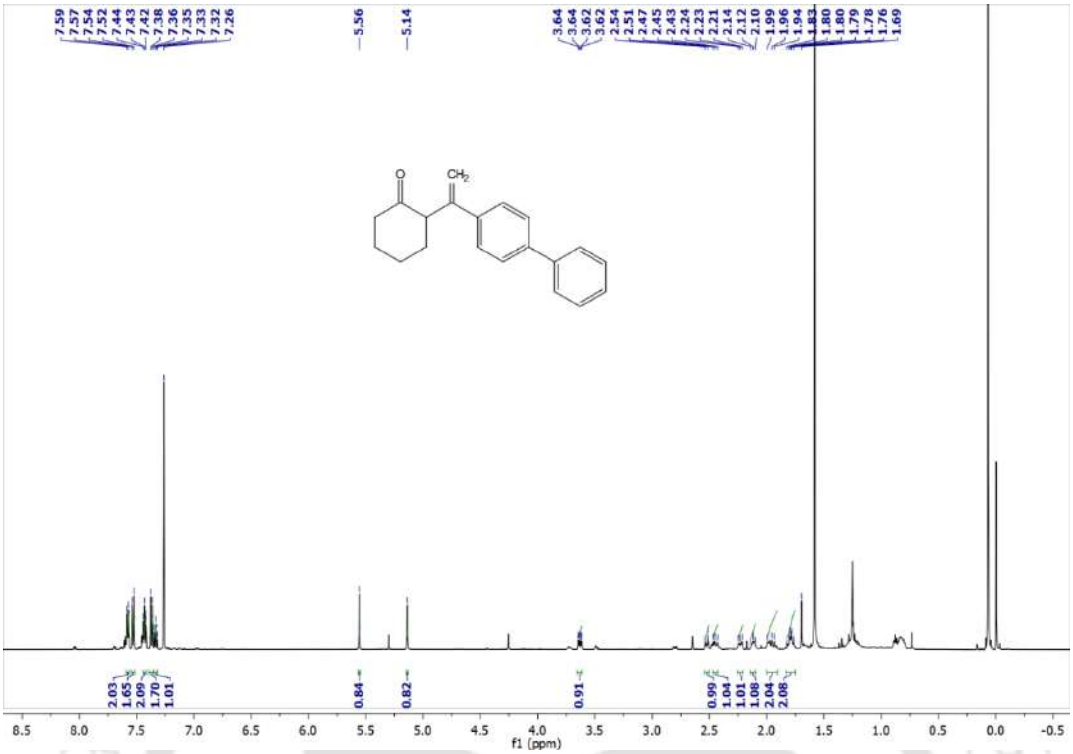

Figure S21: ^{1}H NMR Spectrum of **2.17** ($CDCl_3$, 600 MHz, 298 K)

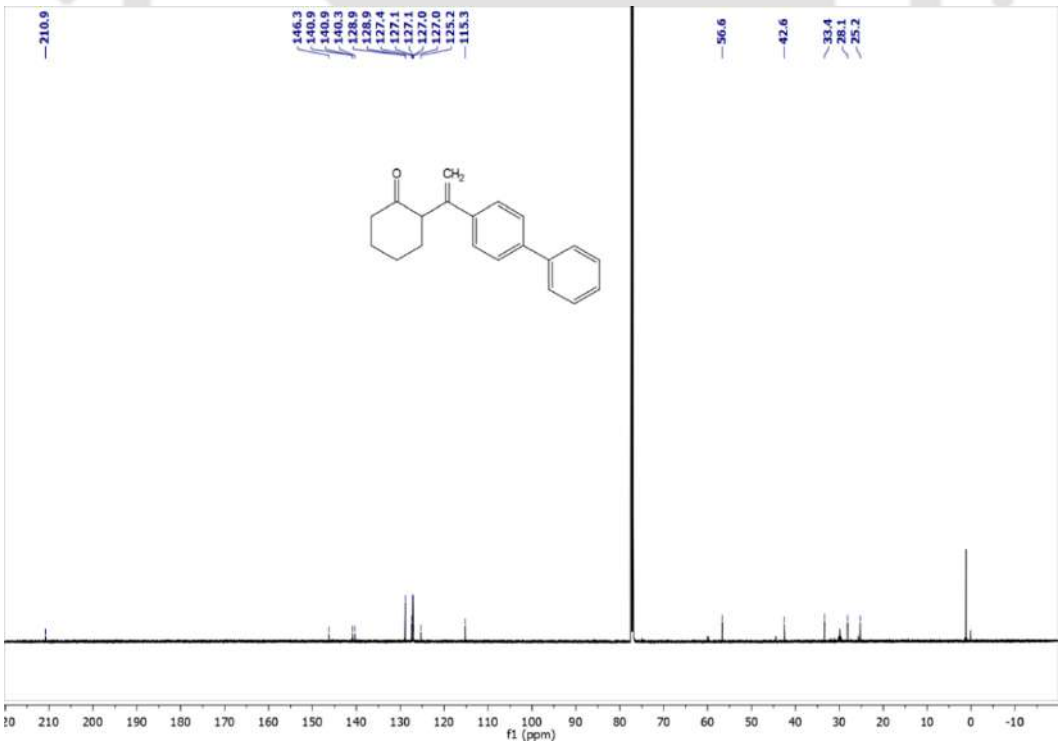

Figure S22: $^{13}C\{^{1}H\}$ NMR Spectrum of **2.17** ($CDCl_3$, 151 MHz, 298 K)

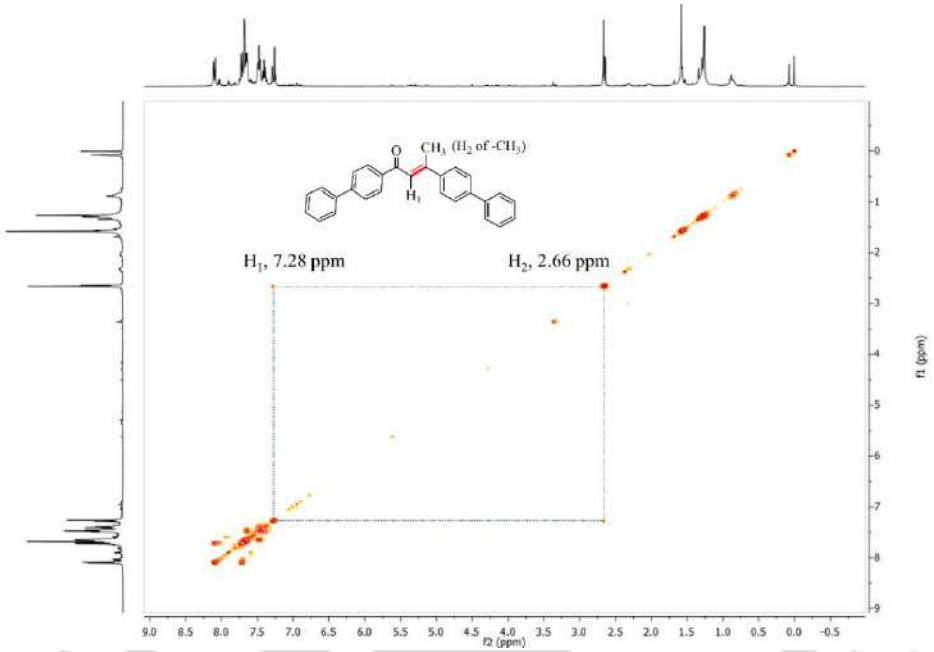

Figure S23: COSY NMR Spectrum of **2.15**

nOe Experiment of compound 2.15.

Irradiation of H_1: Upon irradiation of olefinic proton **H_1** (at 7.28 ppm), the enhancement on aromatic proton **H_3** is found in 2% and **H_4** is found in 1%. There was no effect on methyl H_2 proton.

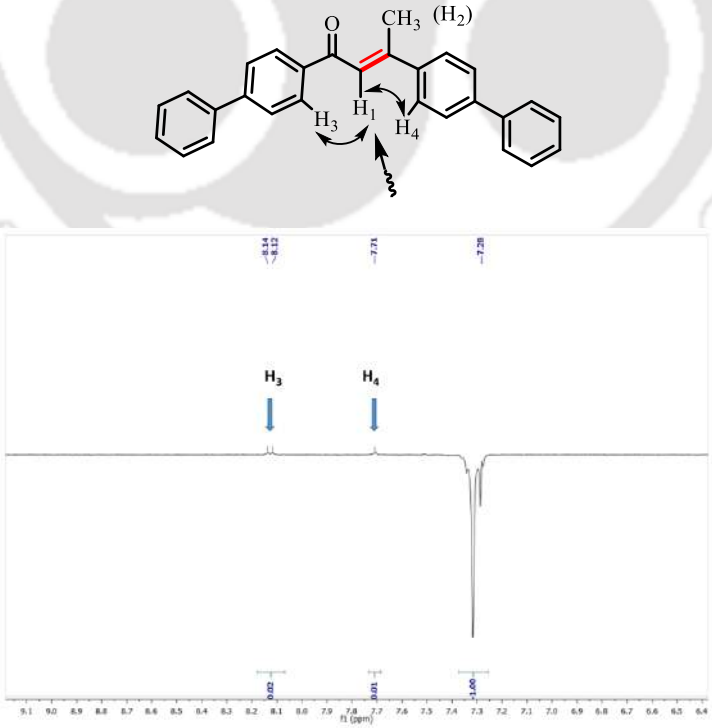

Figure S24: nOe Experiment of **2.15** by irradiating H_1

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Irradiation of H_2: Upon irradiation of olefinic proton **H_2** (at 2.66 ppm), the enhancement on aromatic proton **H_5** is found in 1%.

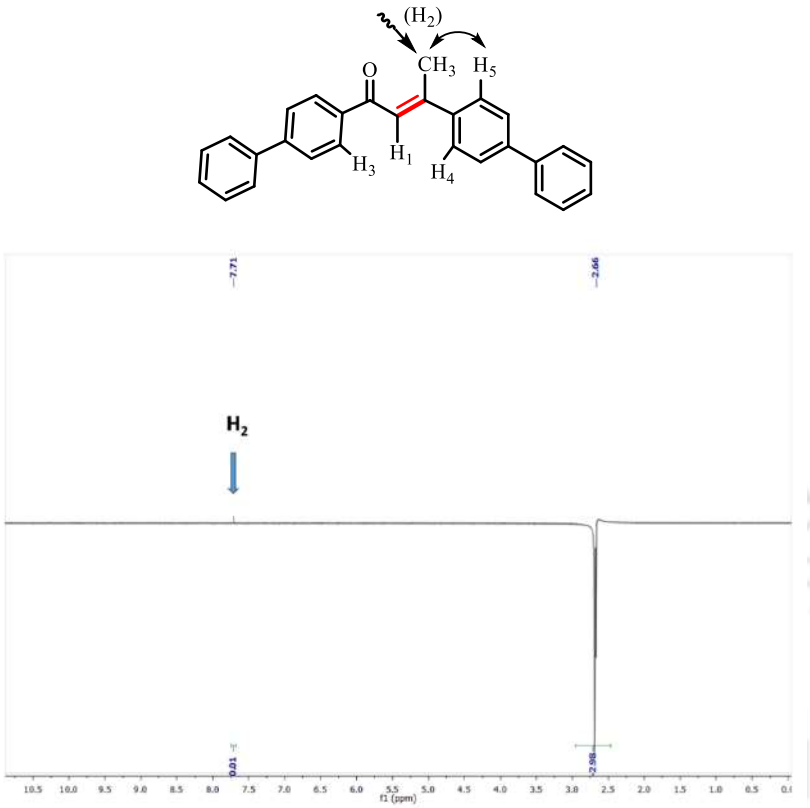

Figure S25: nOe Experiment of **2.15** by irradiating H_2

From the above observation it can be concluded that the major compound is *E*-isomer.

The supporting information and all other product spectra for chapter 2 is available at https://doi.org/10.1002/chem.202303206

Annexure II

^{1}H, ^{13}C, and ^{19}F NMR spectra of representative compounds (*Chapter 3*)

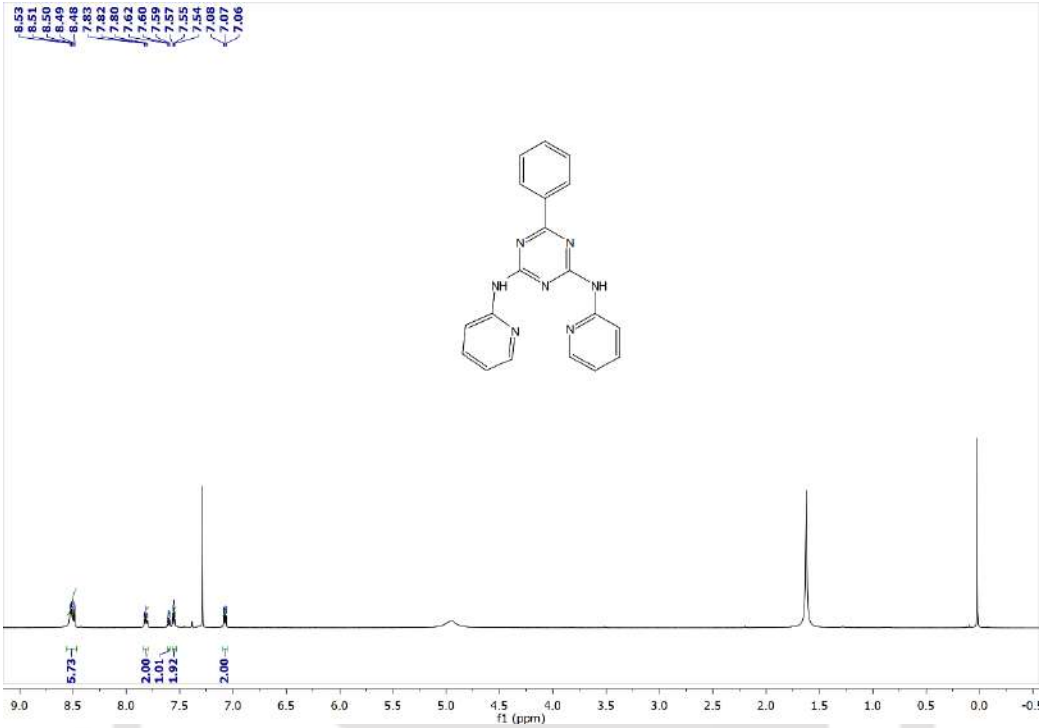

Figure S26: ^{1}H NMR Spectrum of **3.3a** ($CDCl_3$, 600 MHz, 298 K)

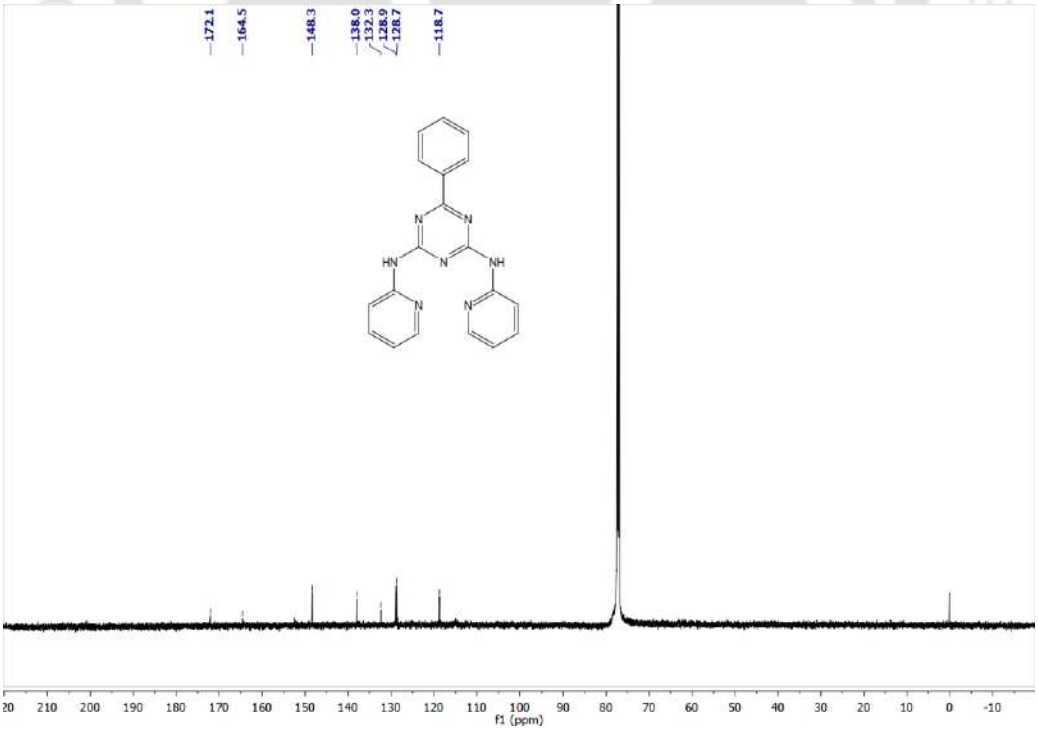

Figure S27: $^{13}C\{^{1}H\}$ NMR Spectrum of **3.3a** ($CDCl_3$, 151 MHz, 298 K)

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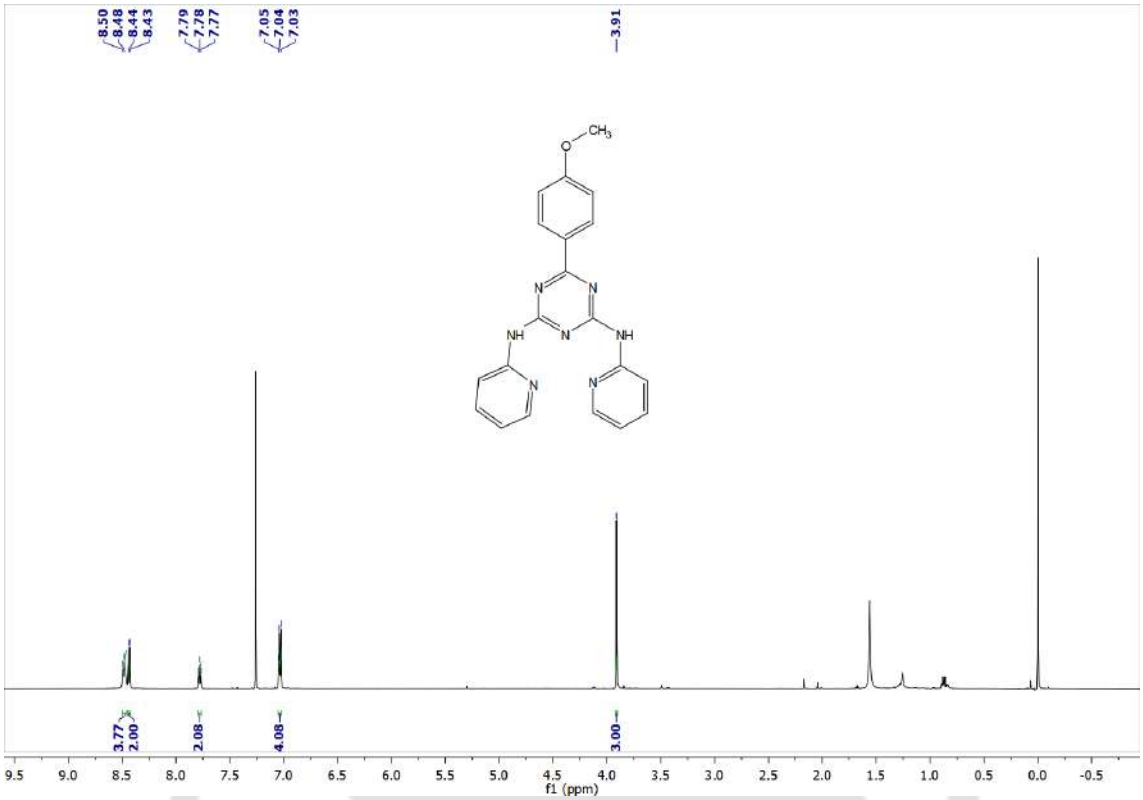

Figure S28: ^{1}H NMR Spectrum of **3.3b** ($CDCl_3$, 600 MHz, 298 K)

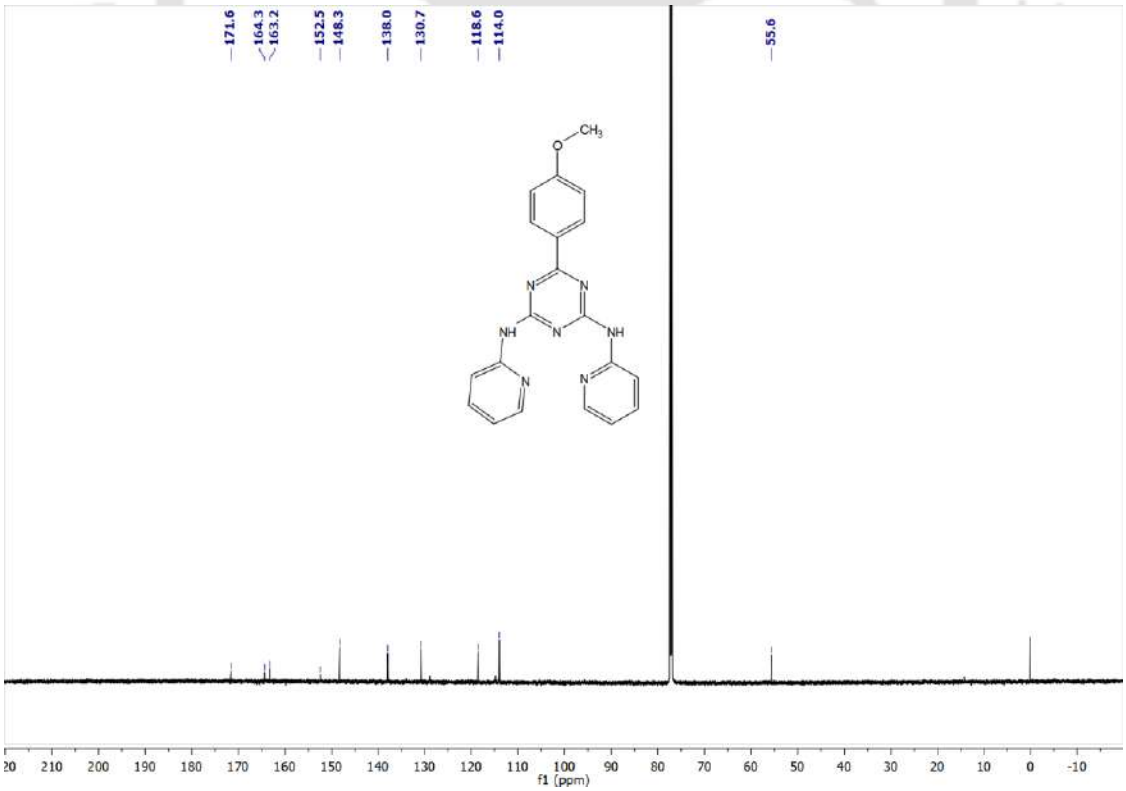

Figure S29: $^{13}C\{^{1}H\}$ NMR Spectrum of **3.3b** ($CDCl_3$, 151 MHz, 298 K)

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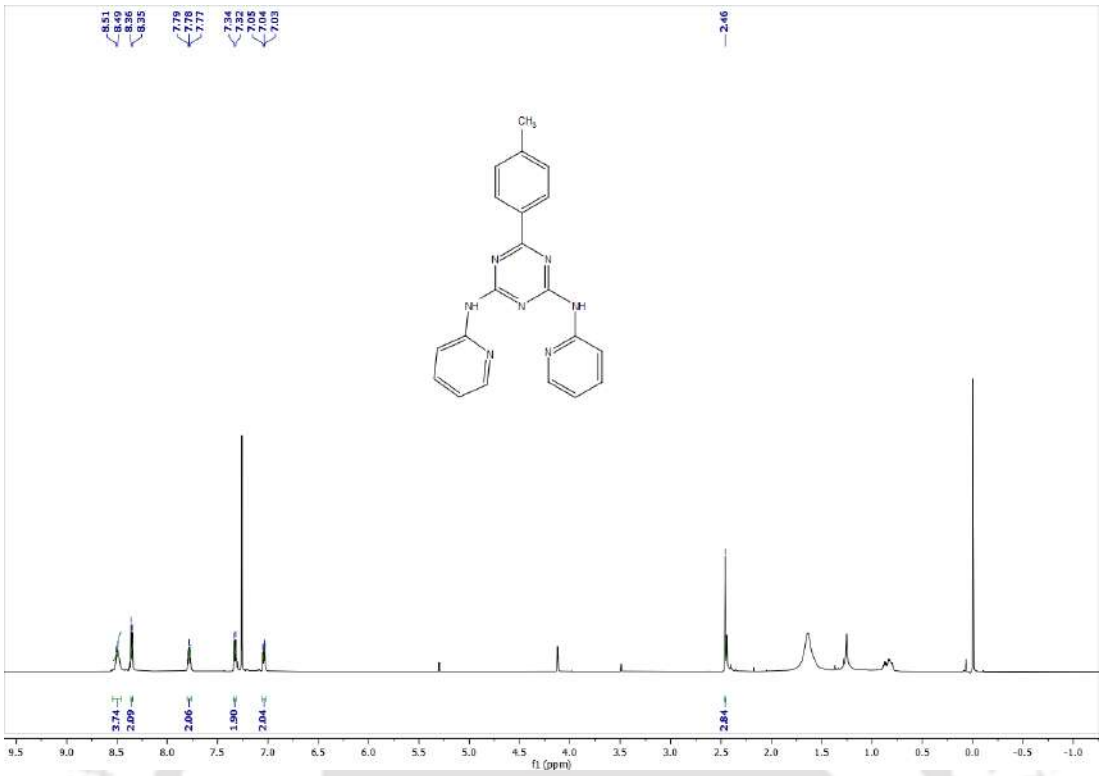

Figure S30: ^{1}H NMR Spectrum of **3.3c** ($CDCl_3$, 600 MHz, 298 K)

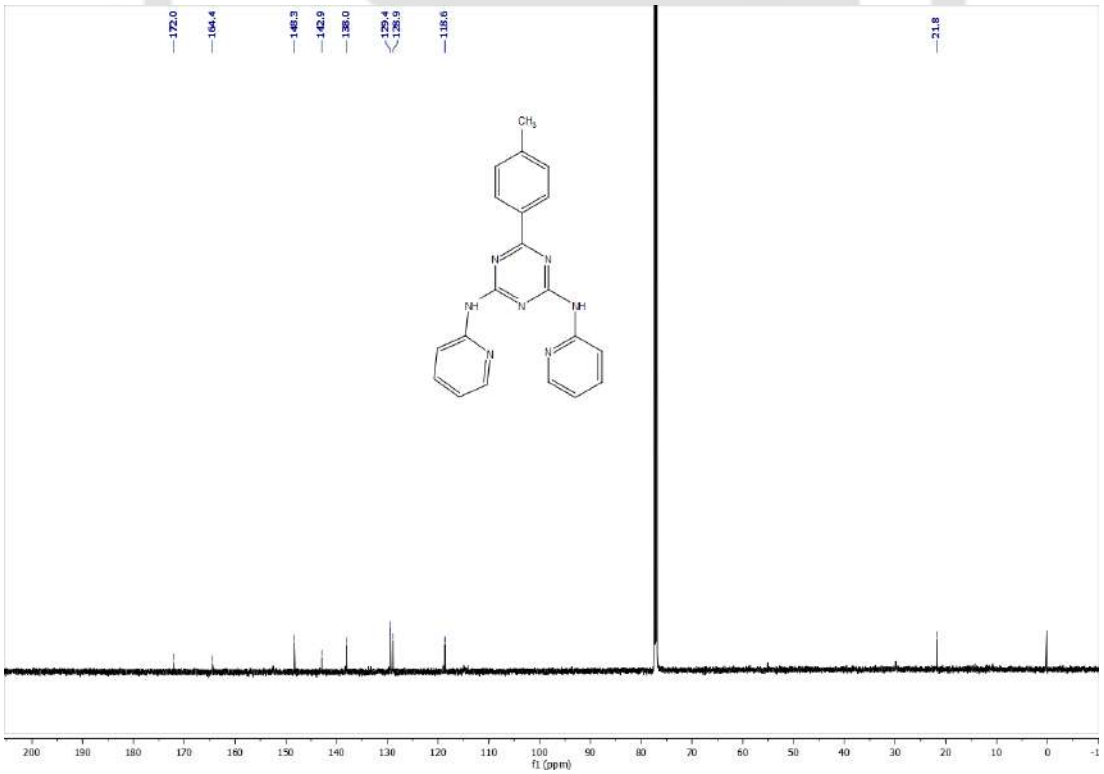

Figure S31: $^{13}C\{^{1}H\}$ NMR Spectrum of **3.3c** ($CDCl_3$, 151 MHz, 298 K)

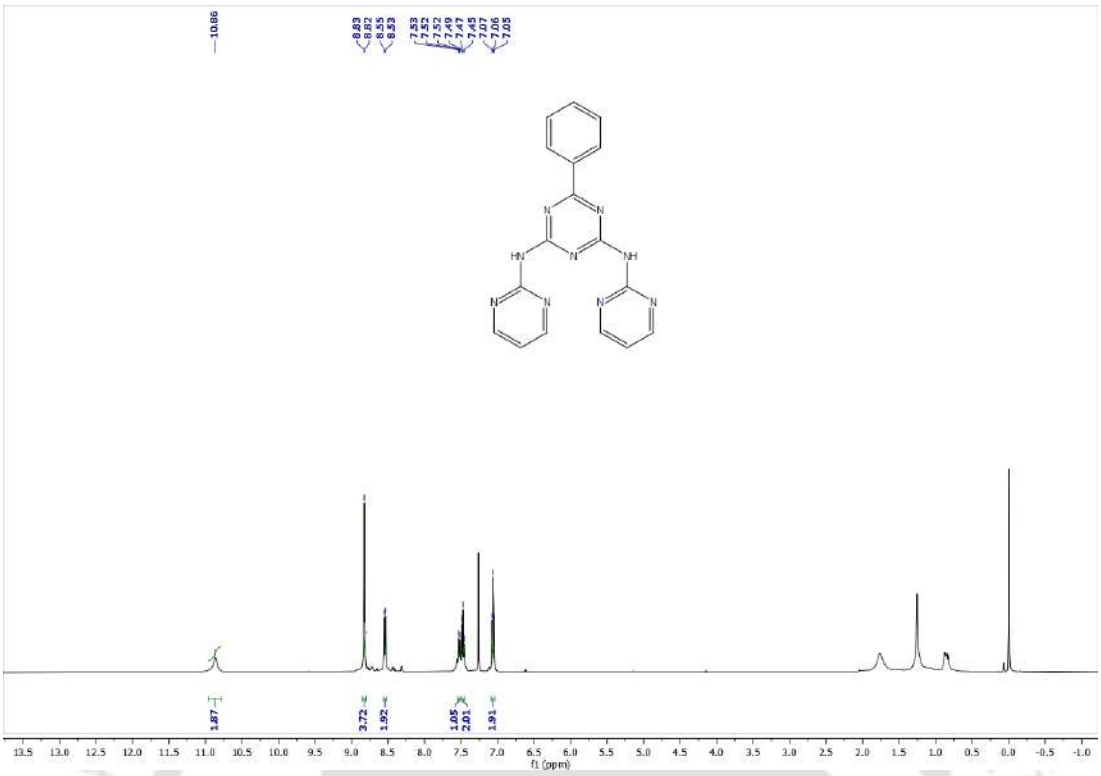

Figure S32: ^{1}H NMR Spectrum of **3.3d** ($CDCl_3$, 400 MHz, 298 K)

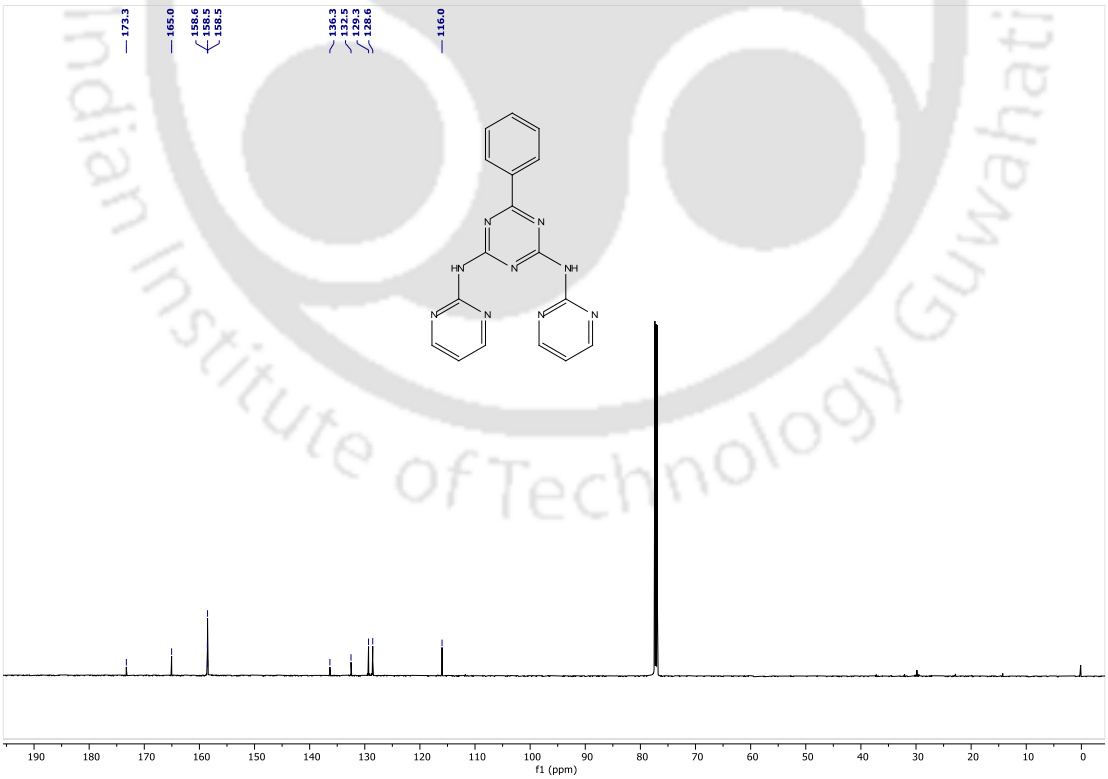

Figure S33: $^{13}C\{^{1}H\}$ NMR Spectrum of **3.3d** ($CDCl_3$, 151 MHz, 298 K)

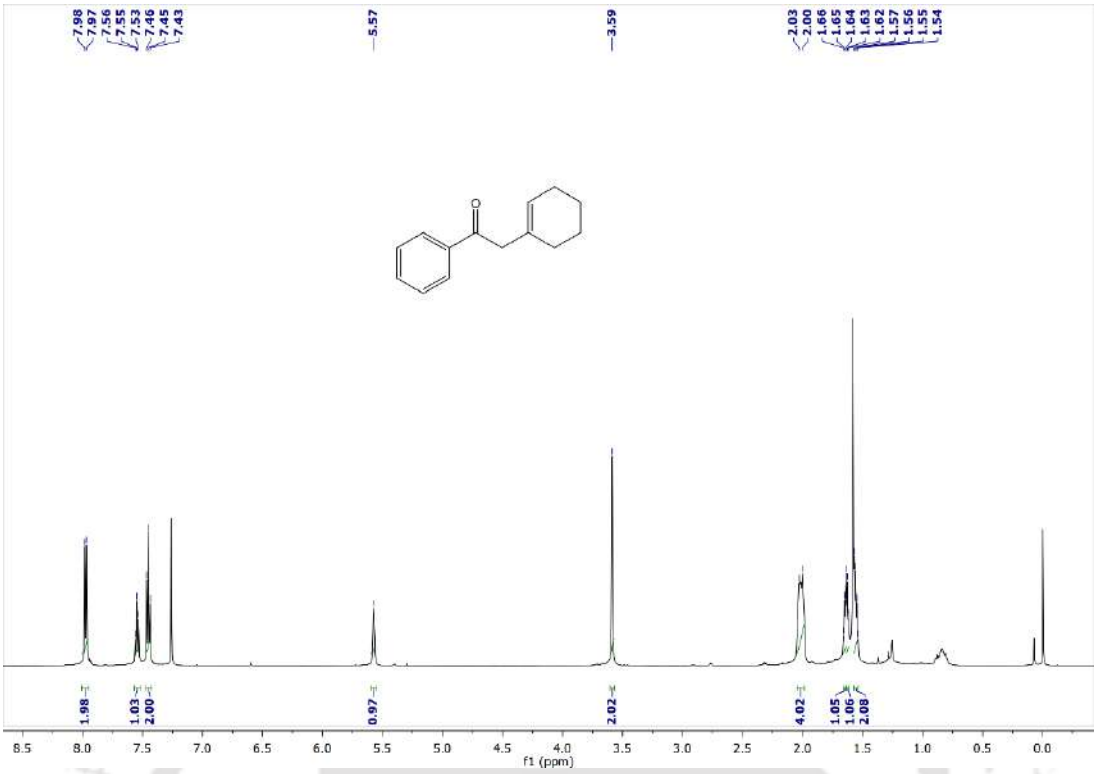

Figure S34: ^{1}H NMR Spectrum of **2.9w** ($CDCl_3$, 500 MHz, 298 K)

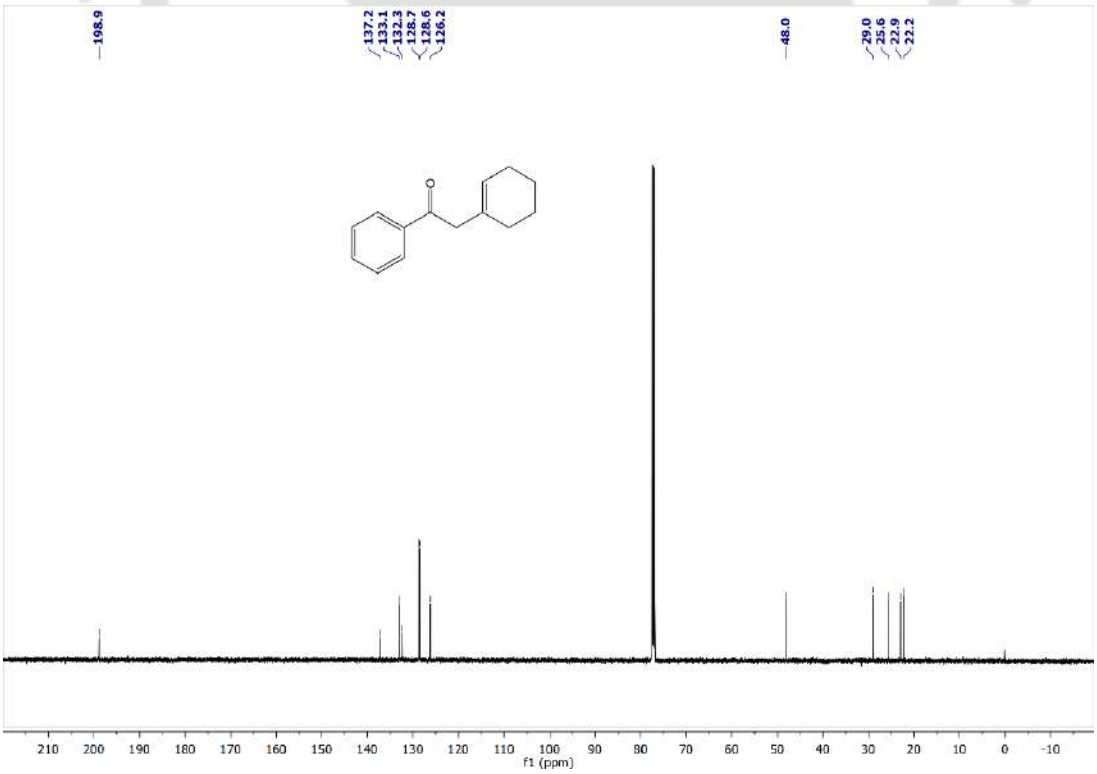

Figure S35: $^{13}C\{^{1}H\}$ NMR Spectrum of **2.9w** ($CDCl_3$, 126 MHz, 298 K)

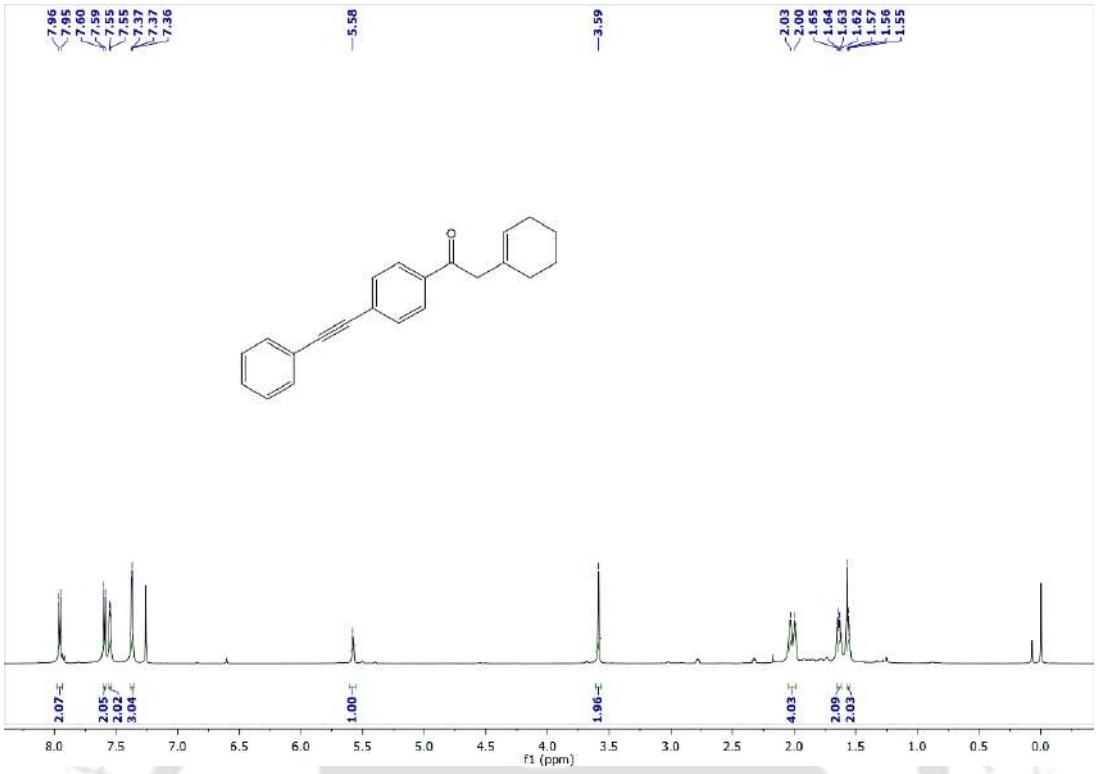

Figure S36: ^{1}H NMR Spectrum of **2.9f** ($CDCl_3$, 600 MHz, 298 K)

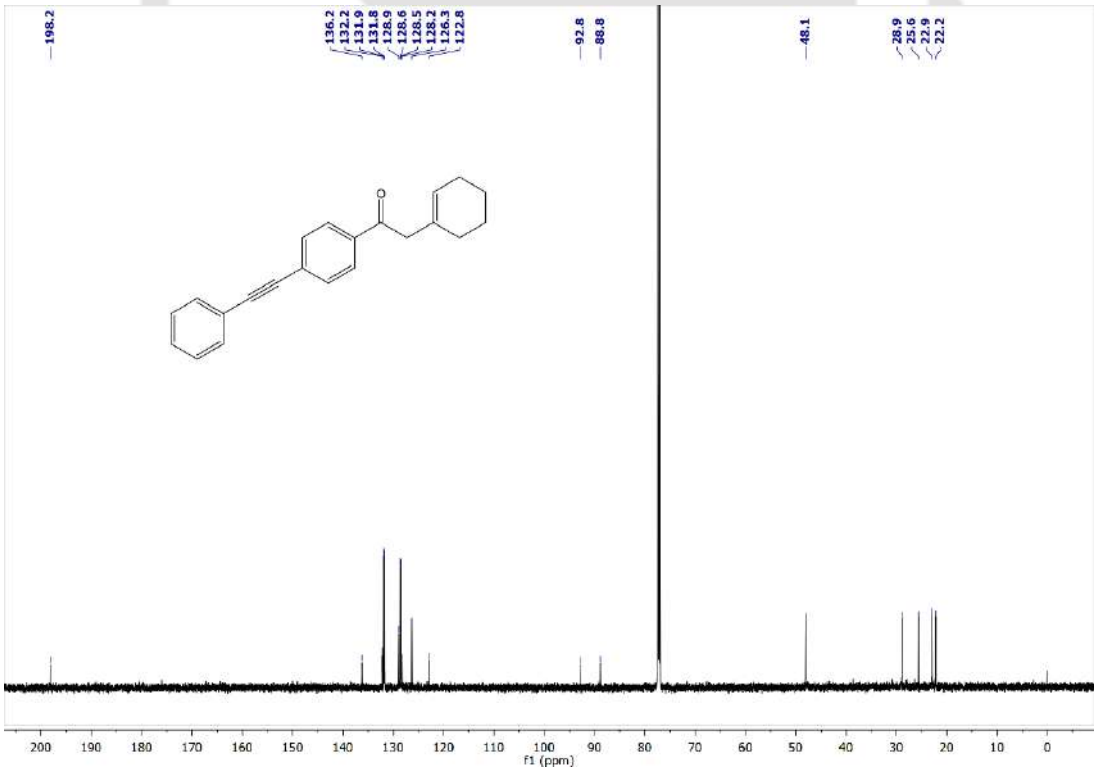

Figure S37: $^{13}C\{^{1}H\}$ NMR Spectrum of **2.9f** ($CDCl_3$, 151 MHz, 298 K)

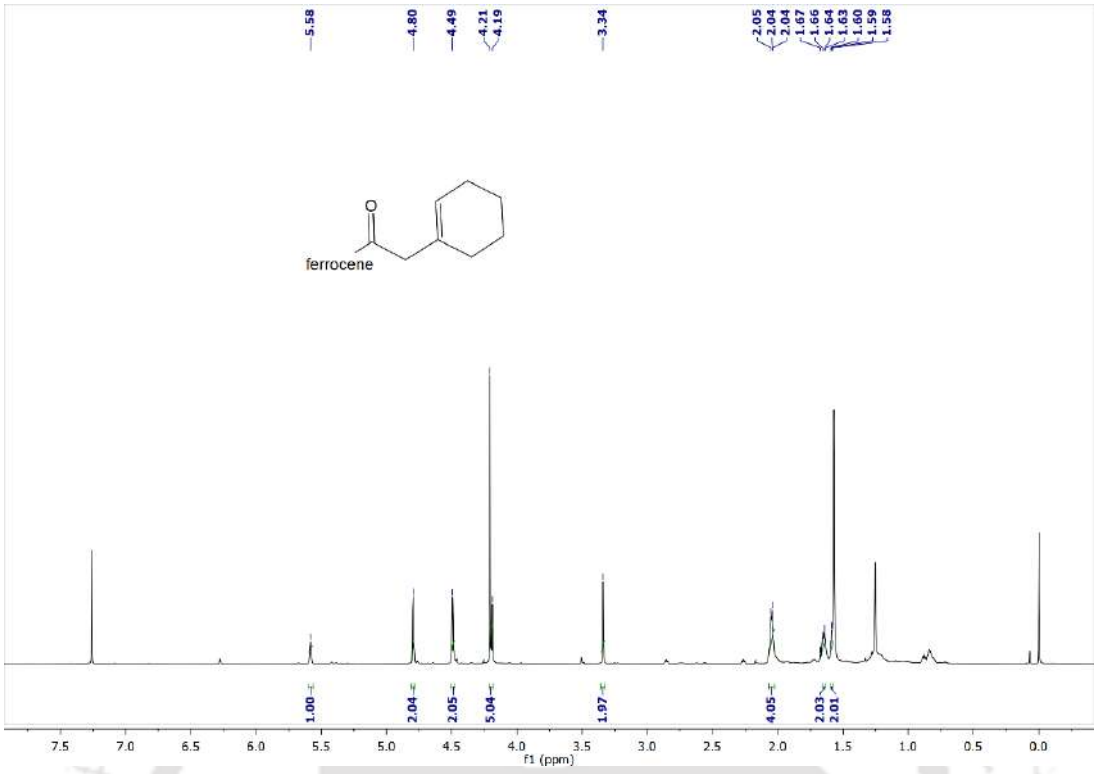

Figure S38: ^{1}H NMR Spectrum of **3.8j** ($CDCl_3$, 600 MHz, 298 K)

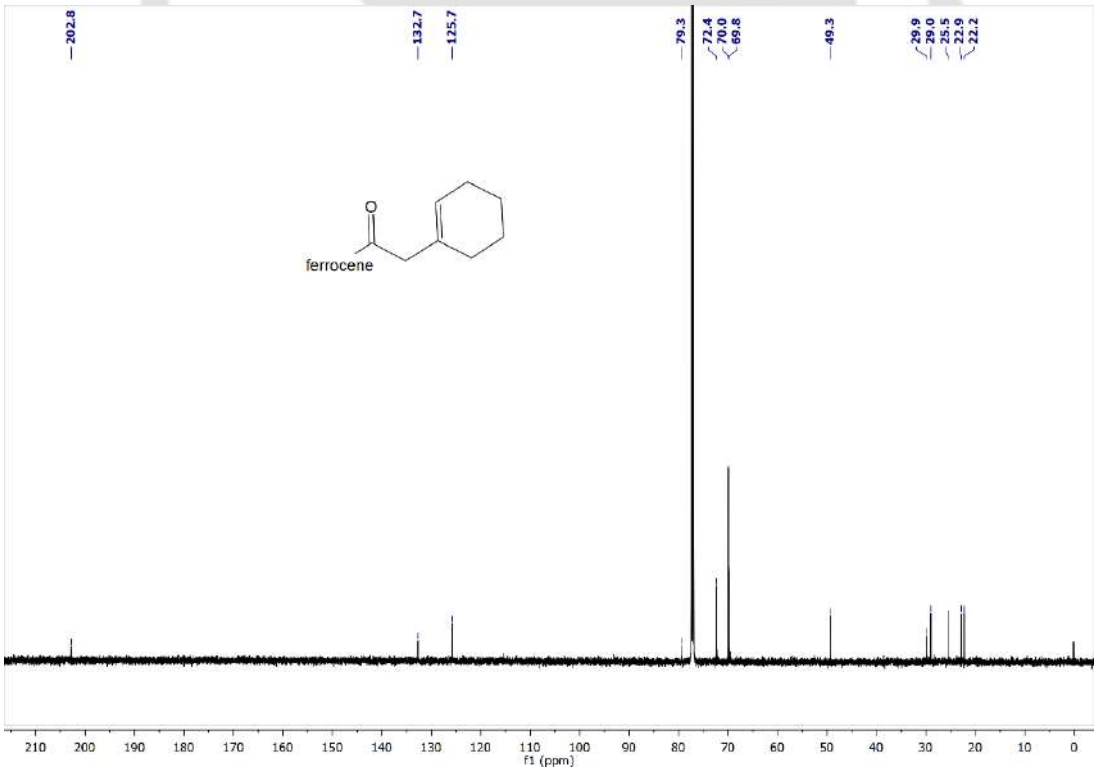

Figure S39: $^{13}C\{^{1}H\}$ NMR Spectrum of **3.8j** ($CDCl_3$, 151 MHz, 298 K)

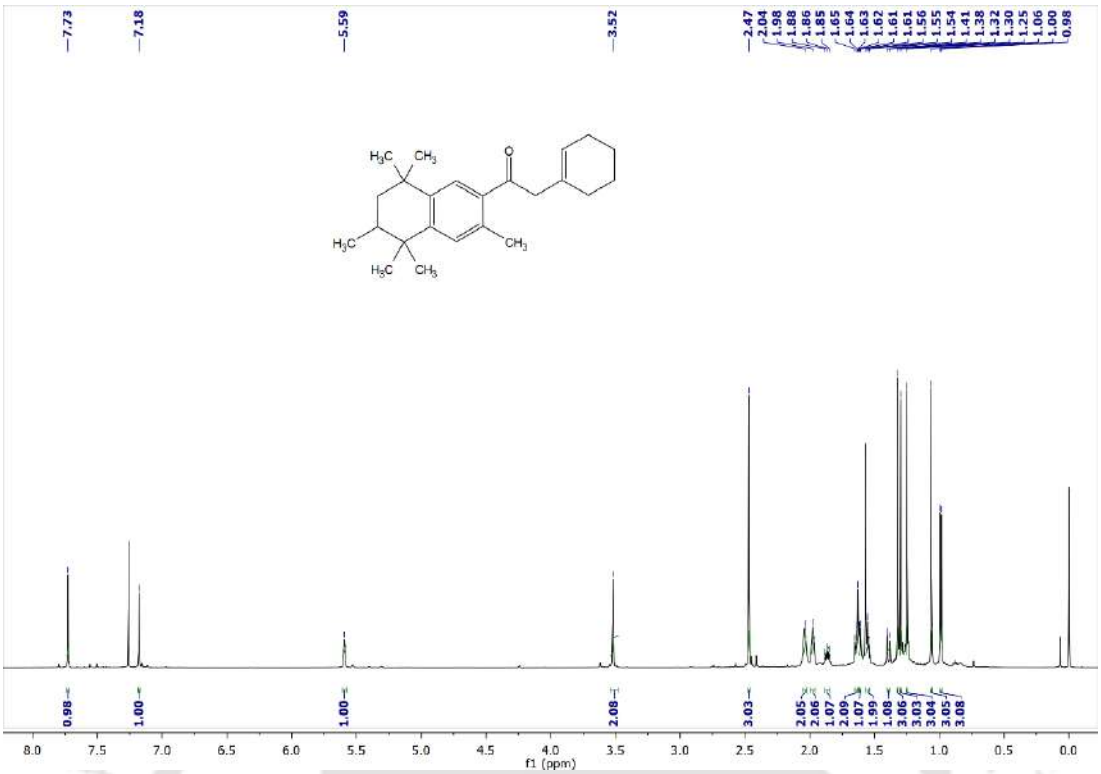

Figure S40: ^{1}H NMR Spectrum of **3.8aj** ($CDCl_3$, 600 MHz, 298 K)

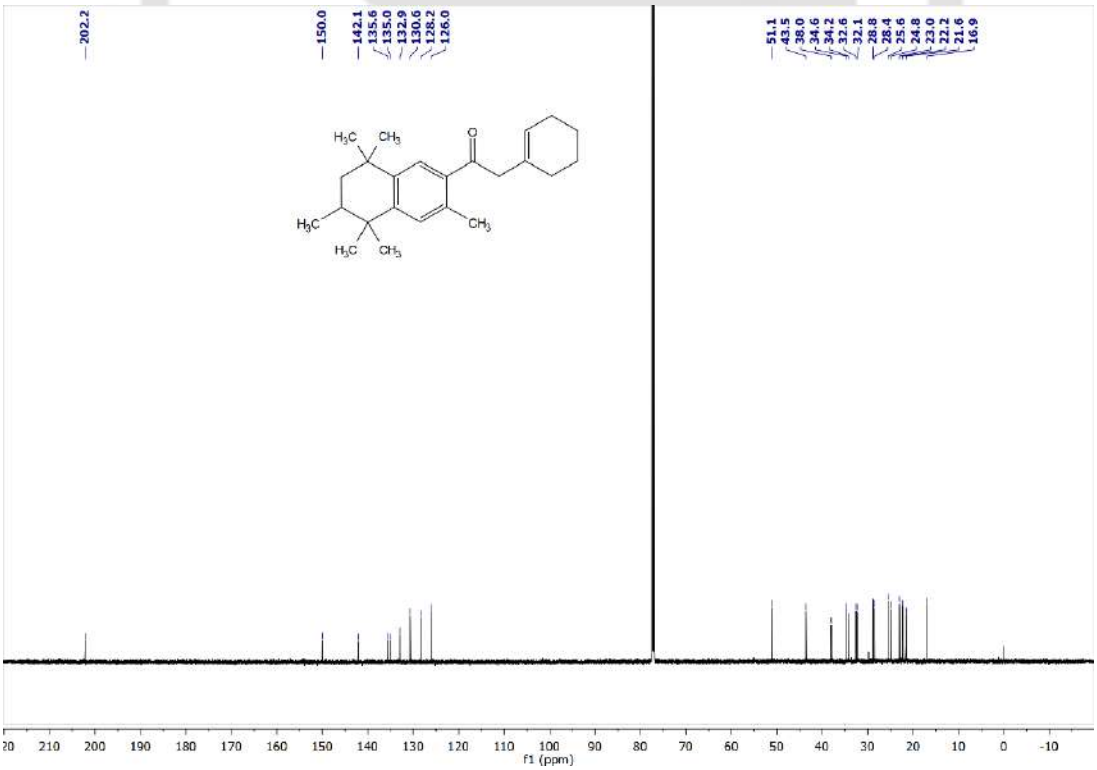

Figure S41: $^{13}C\{^{1}H\}$ NMR Spectrum of **3.8aj** ($CDCl_3$, 151 MHz, 298 K)

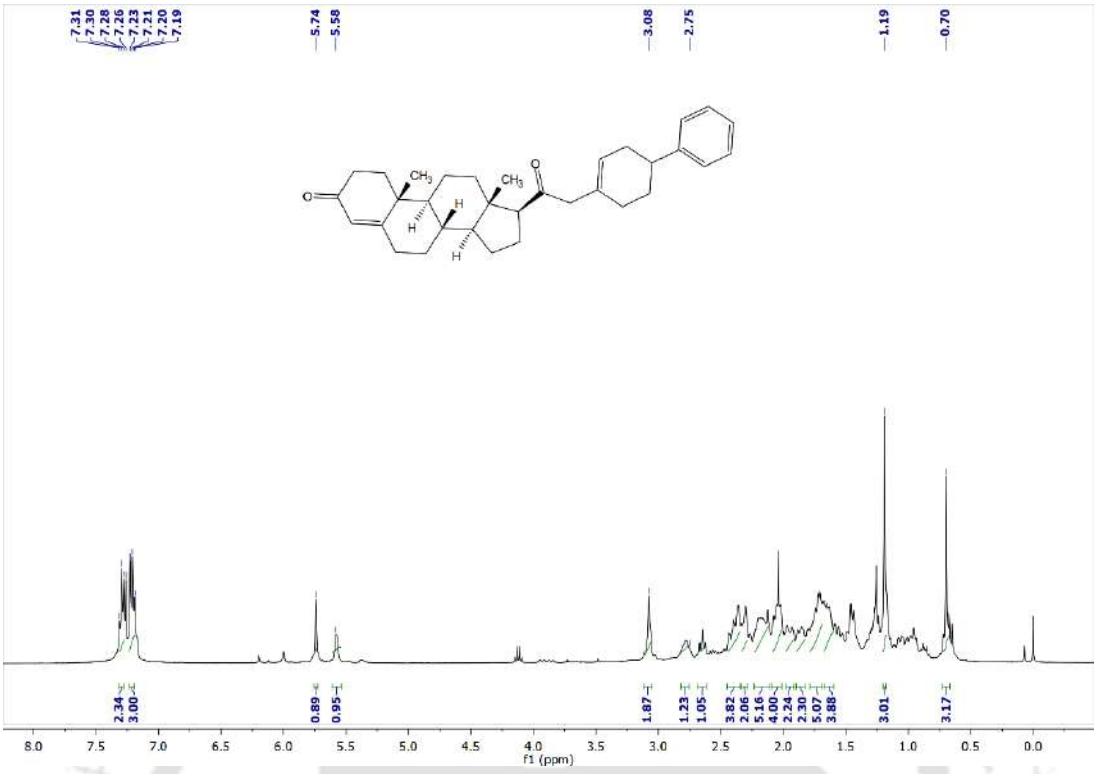

Figure S42: ^{1}H NMR Spectrum of **3.8ak** ($CDCl_3$, 400 MHz, 298 K)

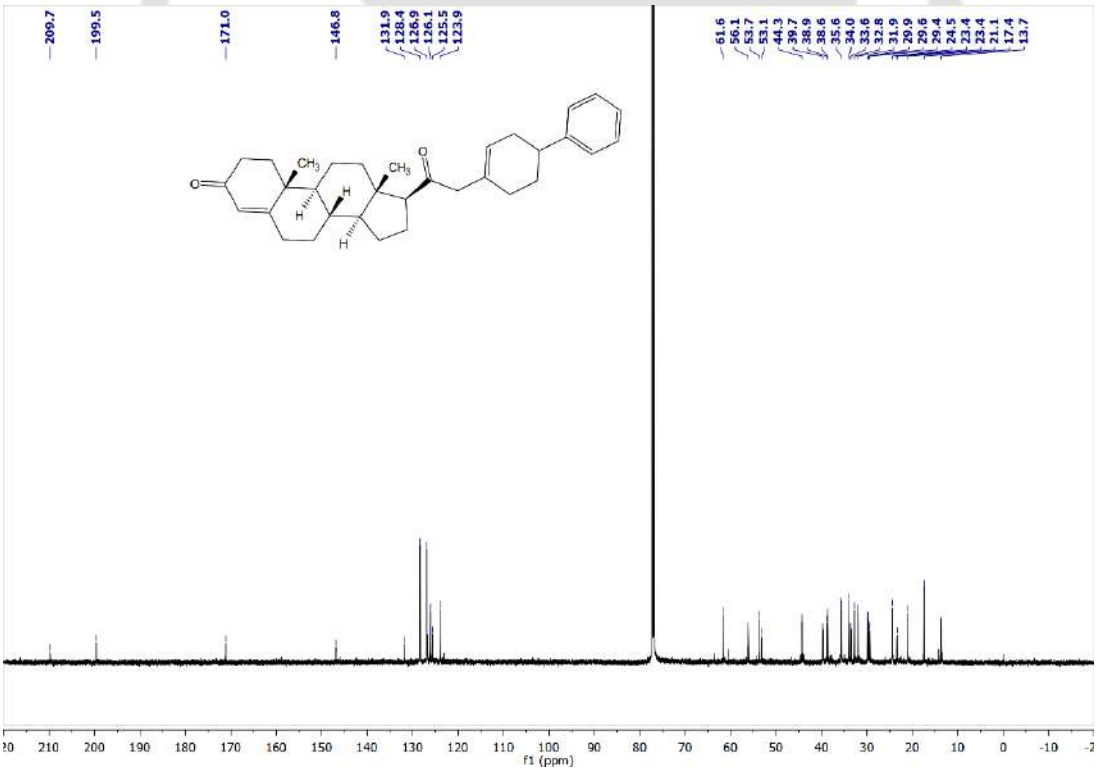

Figure S43: $^{13}C\{^{1}H\}$ NMR Spectrum of **3.8ak** ($CDCl_3$, 151 MHz, 298 K)

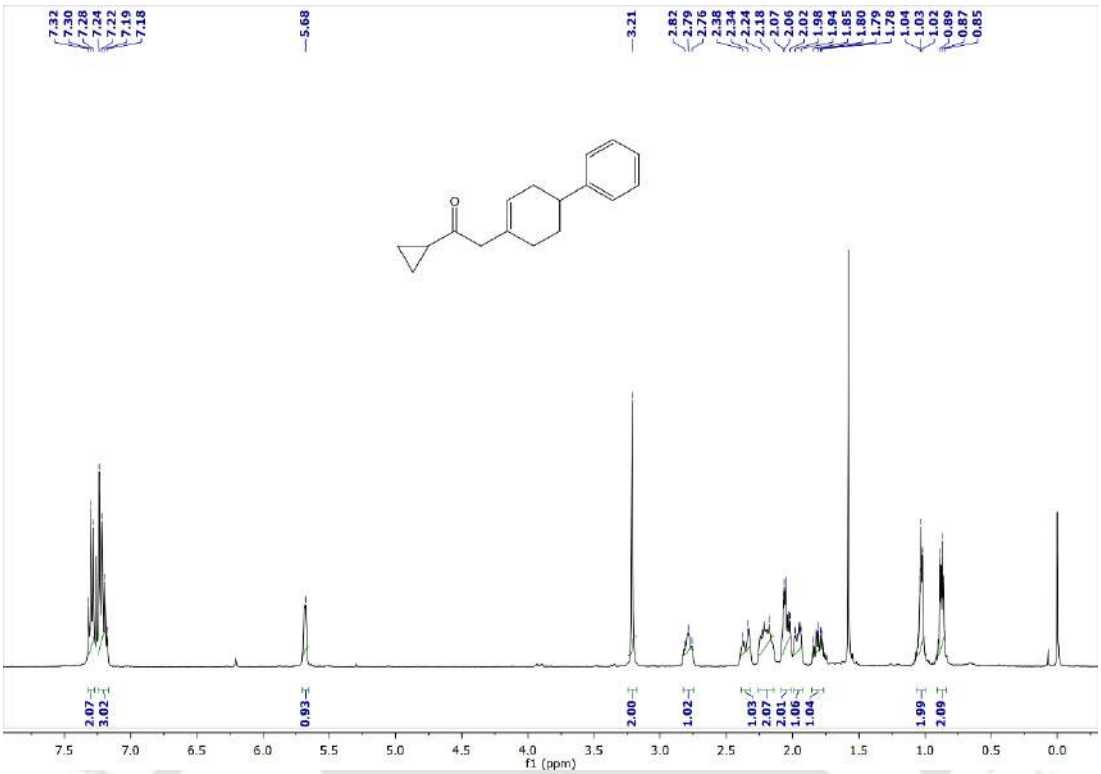

Figure S44: ^{1}H NMR Spectrum of **3.11b** ($CDCl_3$, 400 MHz, 298 K)

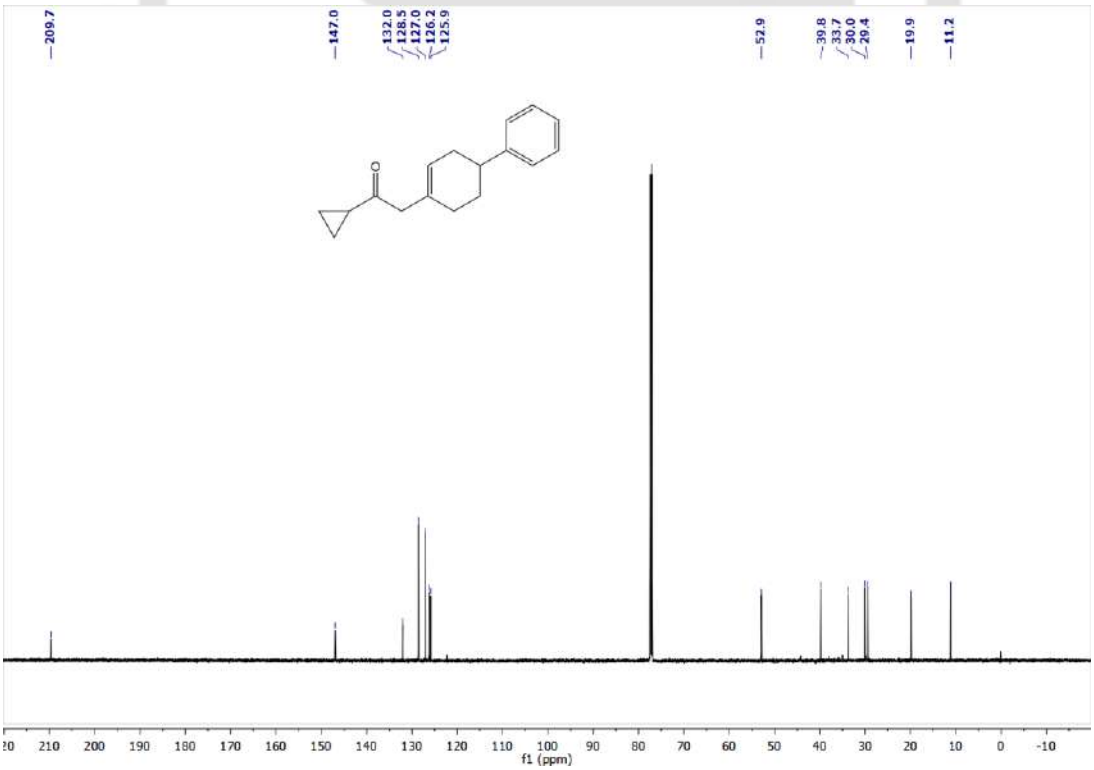

Figure S45: $^{13}C\{^{1}H\}$ NMR Spectrum of **3.11b** ($CDCl_3$, 151 MHz, 298 K)

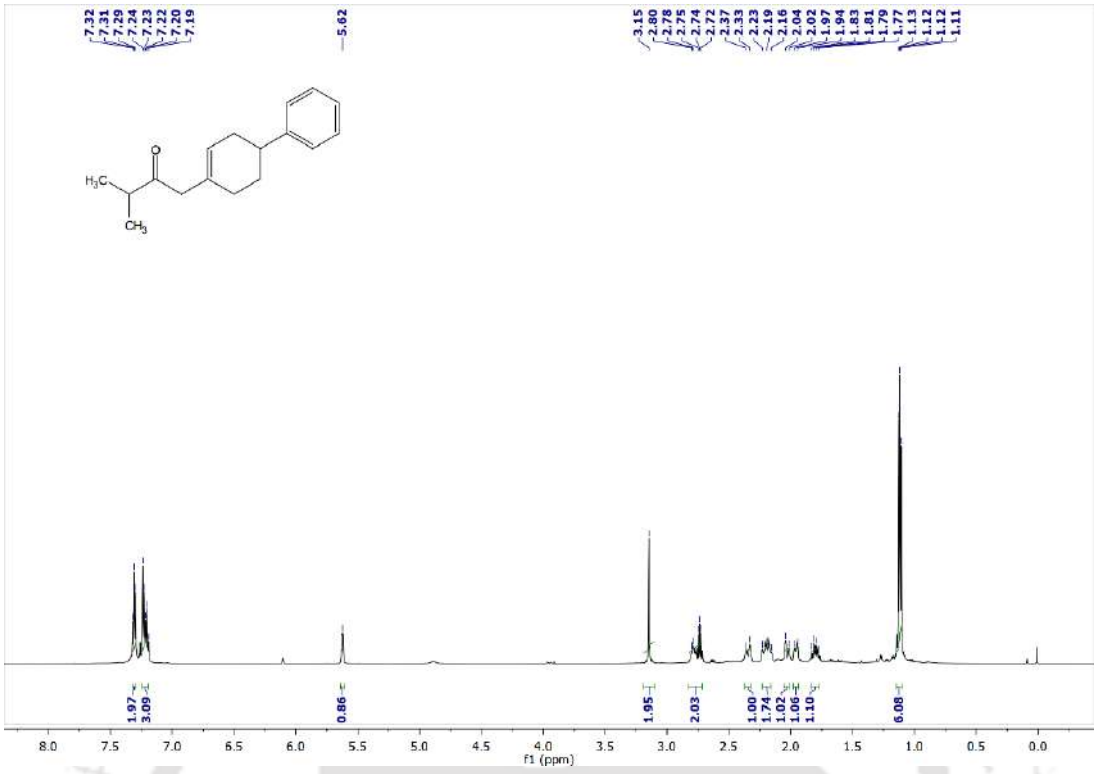

Figure S46: ^{1}H NMR Spectrum of **2.9ac** ($CDCl_3$, 600 MHz, 298 K)

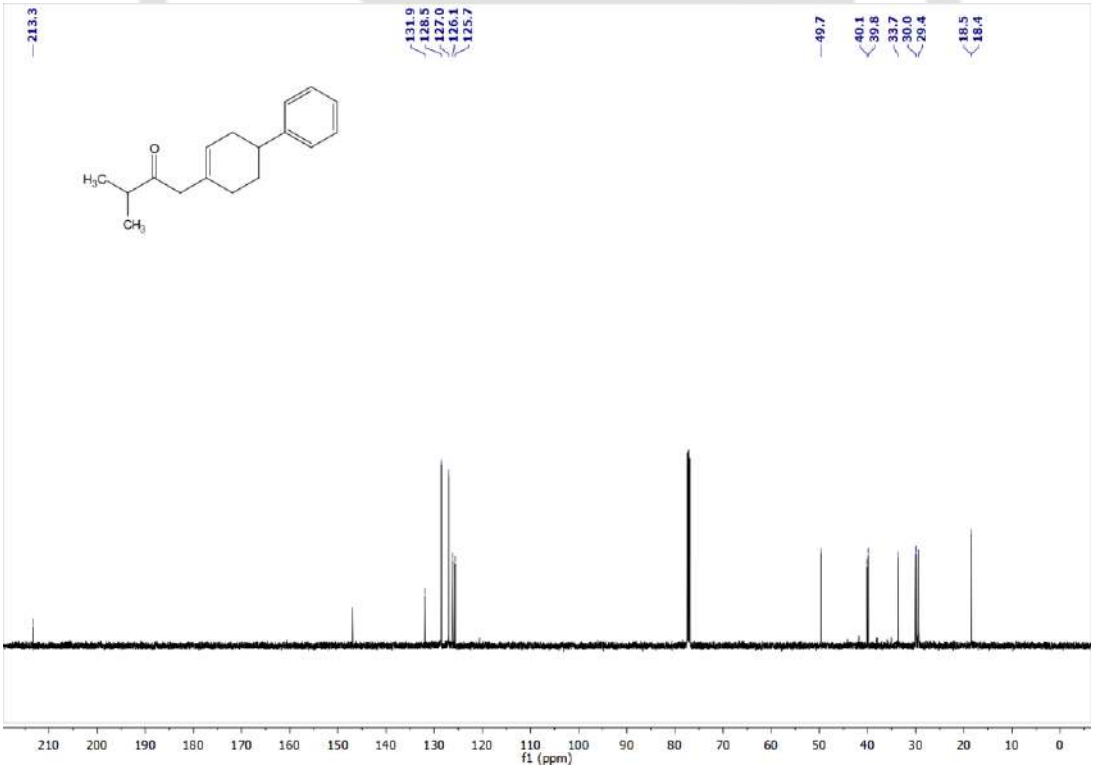

Figure S47: $^{13}C\{^{1}H\}$ NMR Spectrum of **2.9ac** ($CDCl_3$, 151 MHz, 298 K)

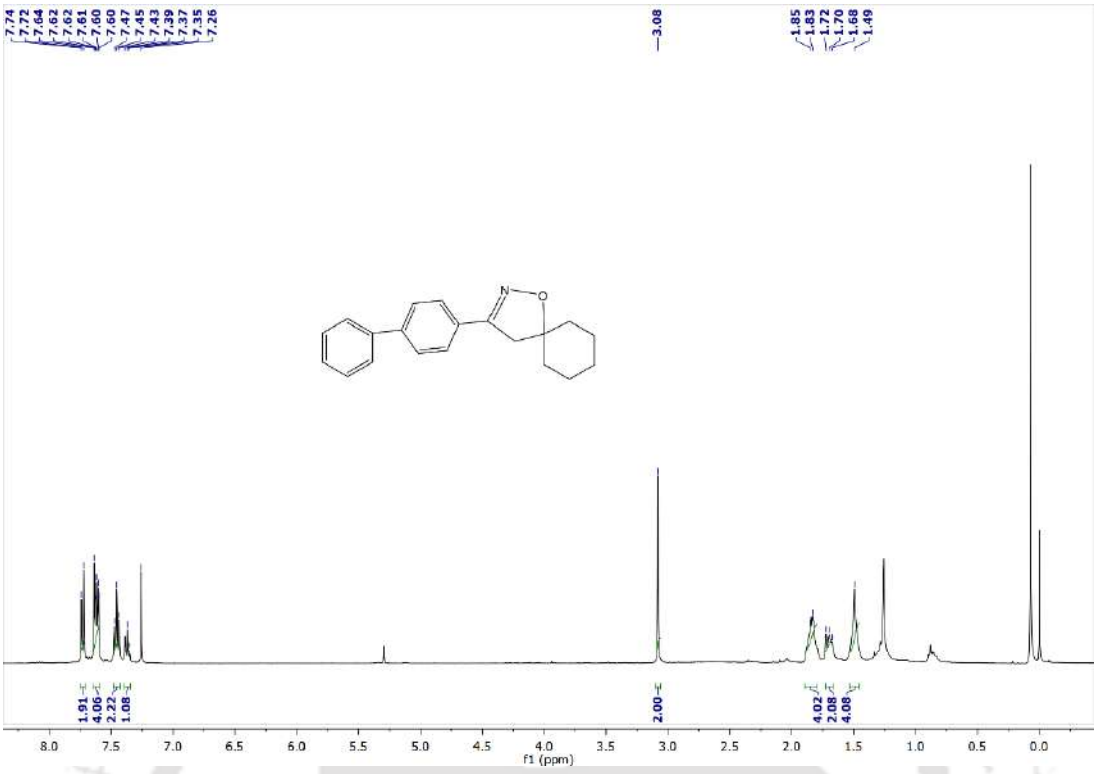

Figure S48: ^{1}H NMR Spectrum of **3.15** ($CDCl_3$, 400 MHz, 298 K)

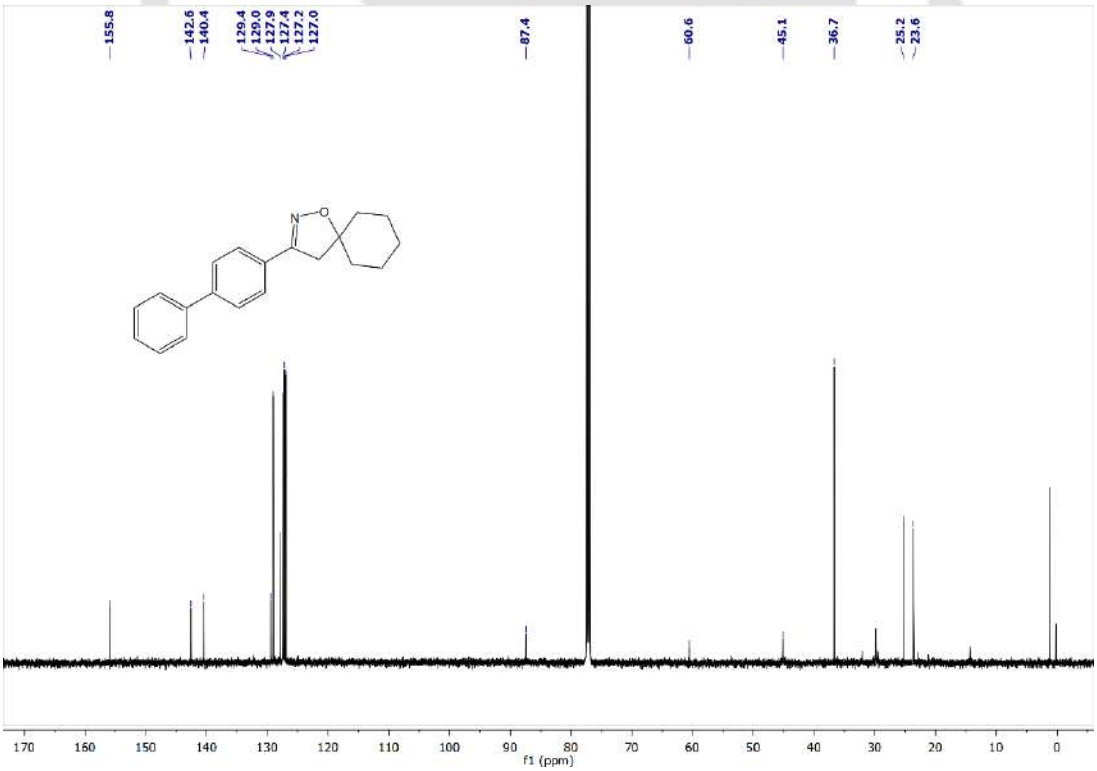

Figure S49: $^{13}C\{^{1}H\}$ NMR Spectrum of **3.15** ($CDCl_3$, 151 MHz, 298 K)

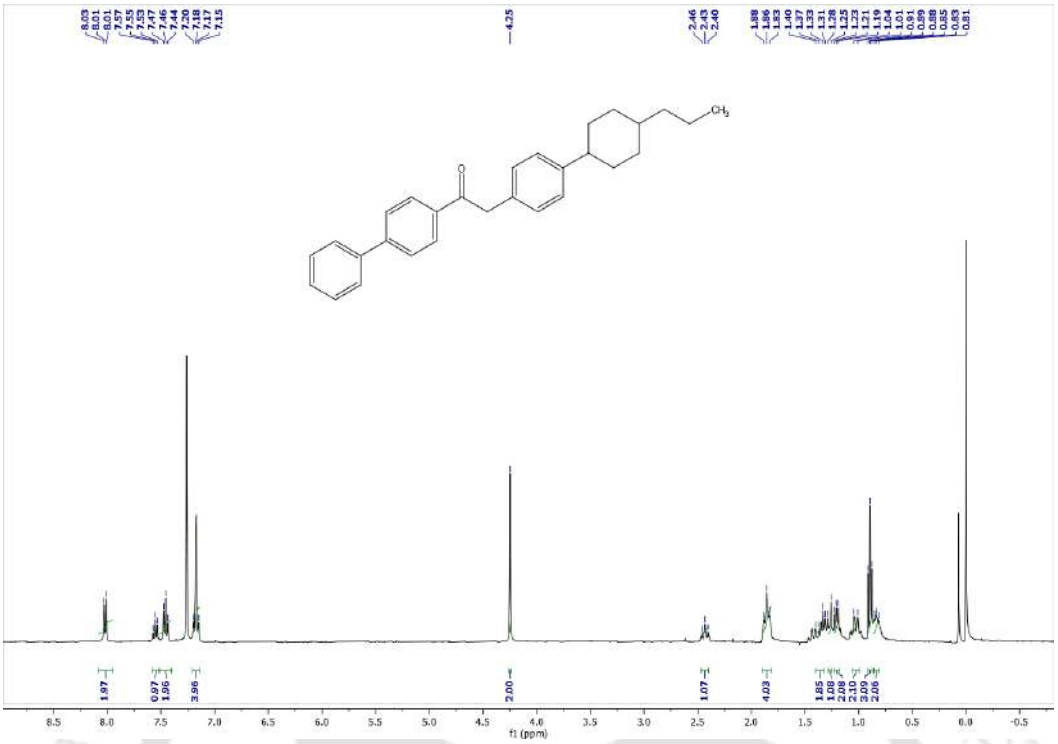

Figure S50: ^{1}H NMR Spectrum of **3.18** ($CDCl_3$, 400 MHz, 298 K)

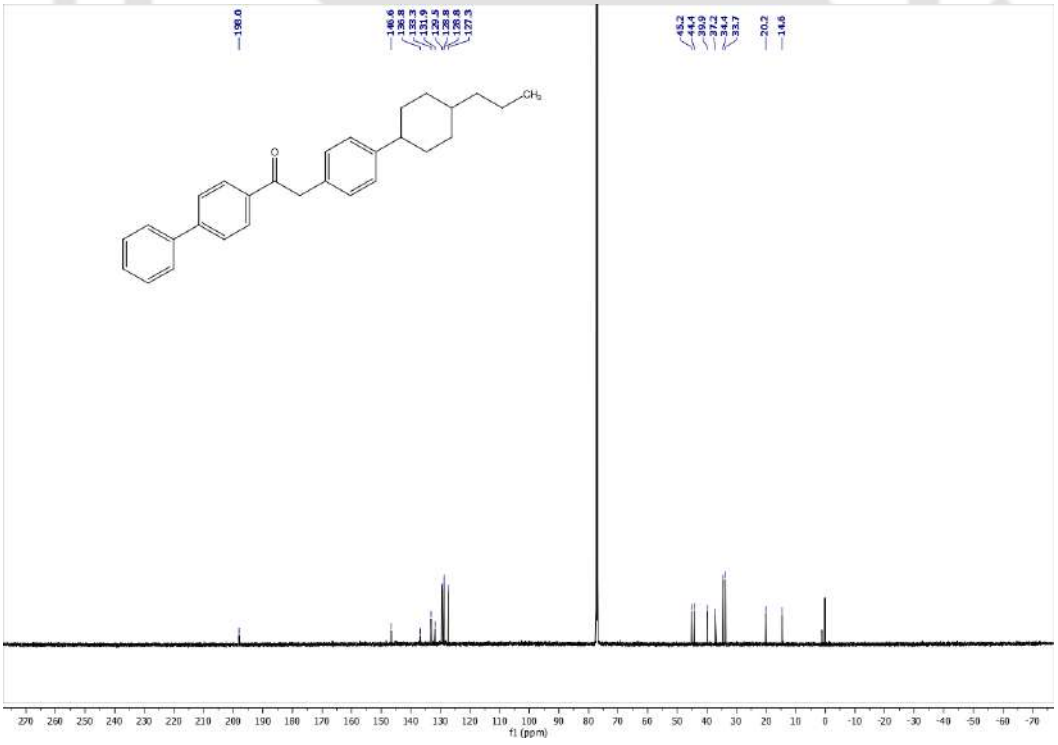

Figure S51: $^{13}C\{^{1}H\}$ NMR Spectrum of **3.18** ($CDCl_3$, 151 MHz, 298 K)

The supporting information and all other product spectra for chapter 3 is available at https://doi.org/10.1021/acs.orglett.3c03960

Annexure III

^{1}H, ^{13}C, and ^{19}F NMR spectra of representative compounds (*Chapter 4*)

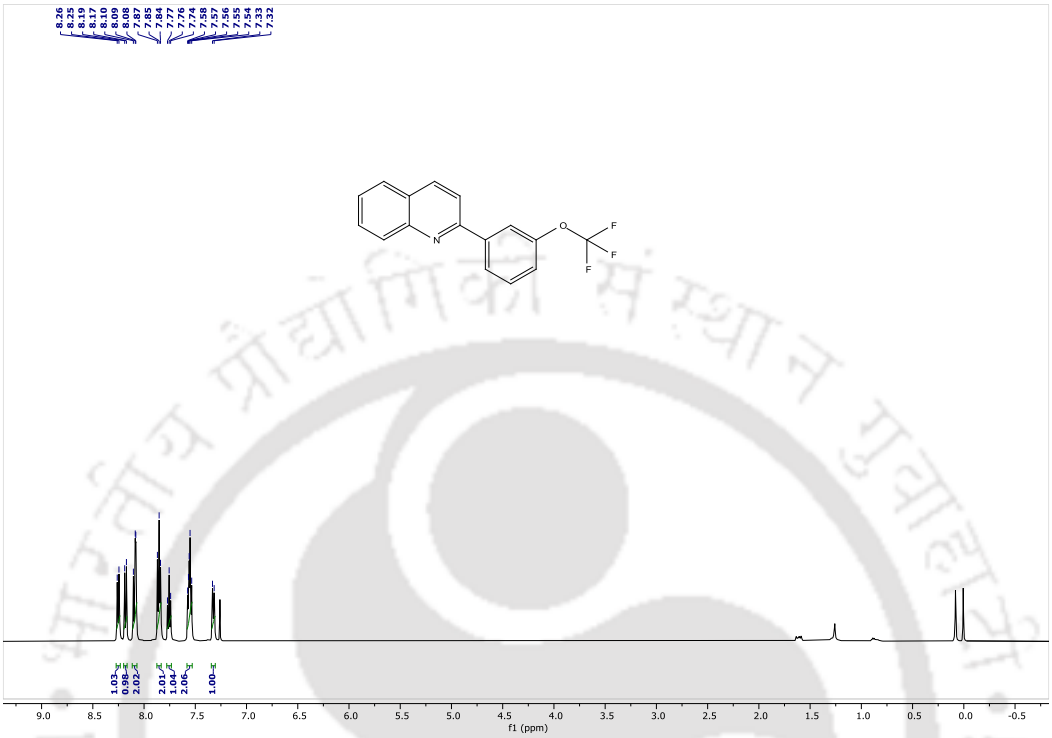

Figure S52: ^{1}H NMR Spectrum of **4.3k** ($CDCl_3$, 500 MHz, 298 K)

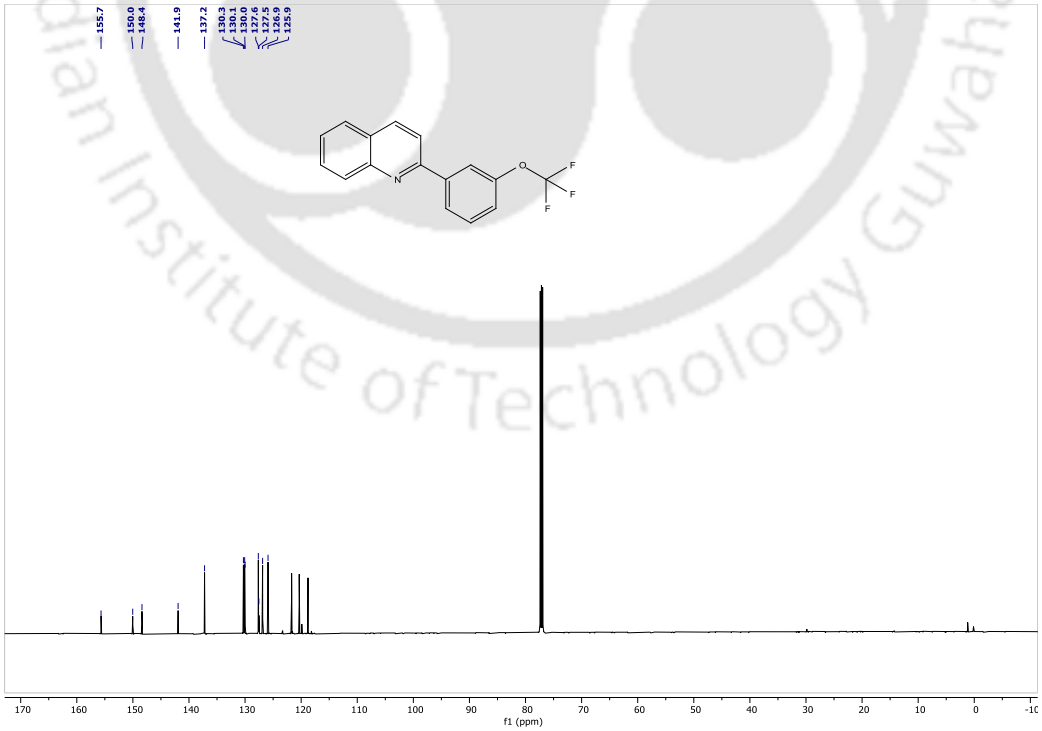

Figure S53: $^{13}C\{^{1}H\}$ NMR Spectrum of **4.3k** ($CDCl_3$, 151 MHz, 298 K)

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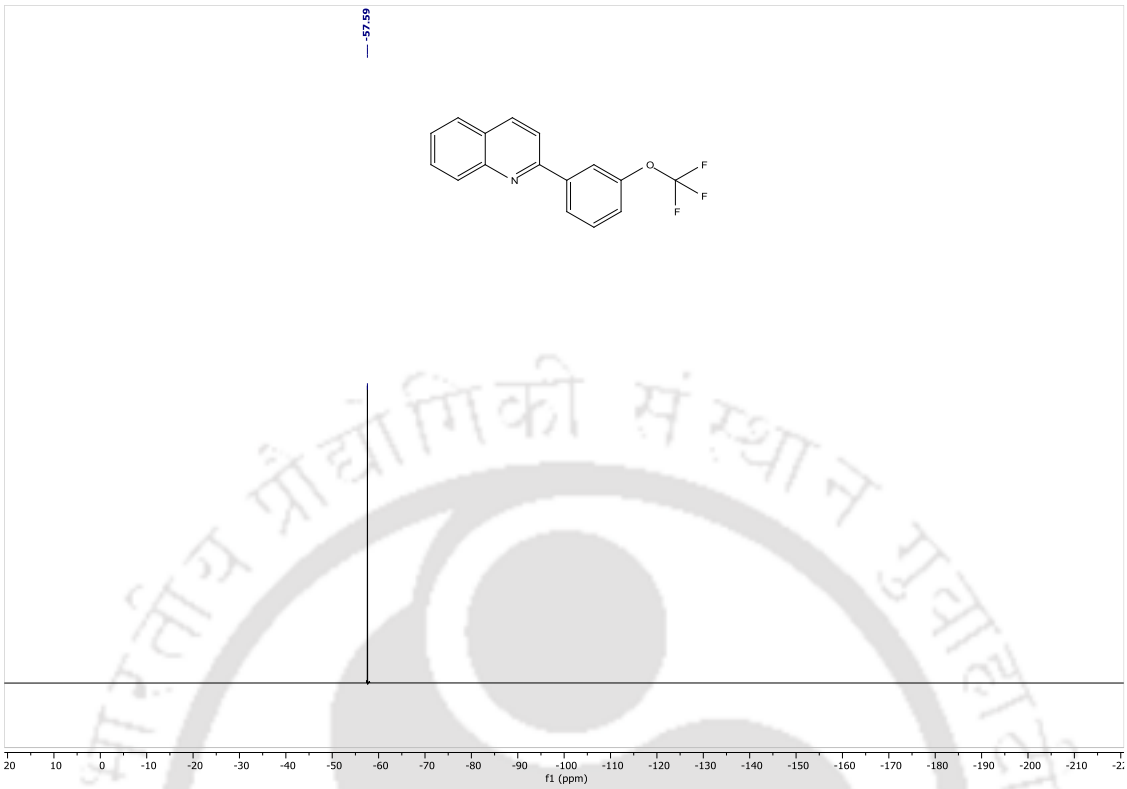

Figure S54: $^{19}F\{^{1}H\}$ NMR Spectrum of **4.3k** ($CDCl_3$, 471 MHz, 298 K)

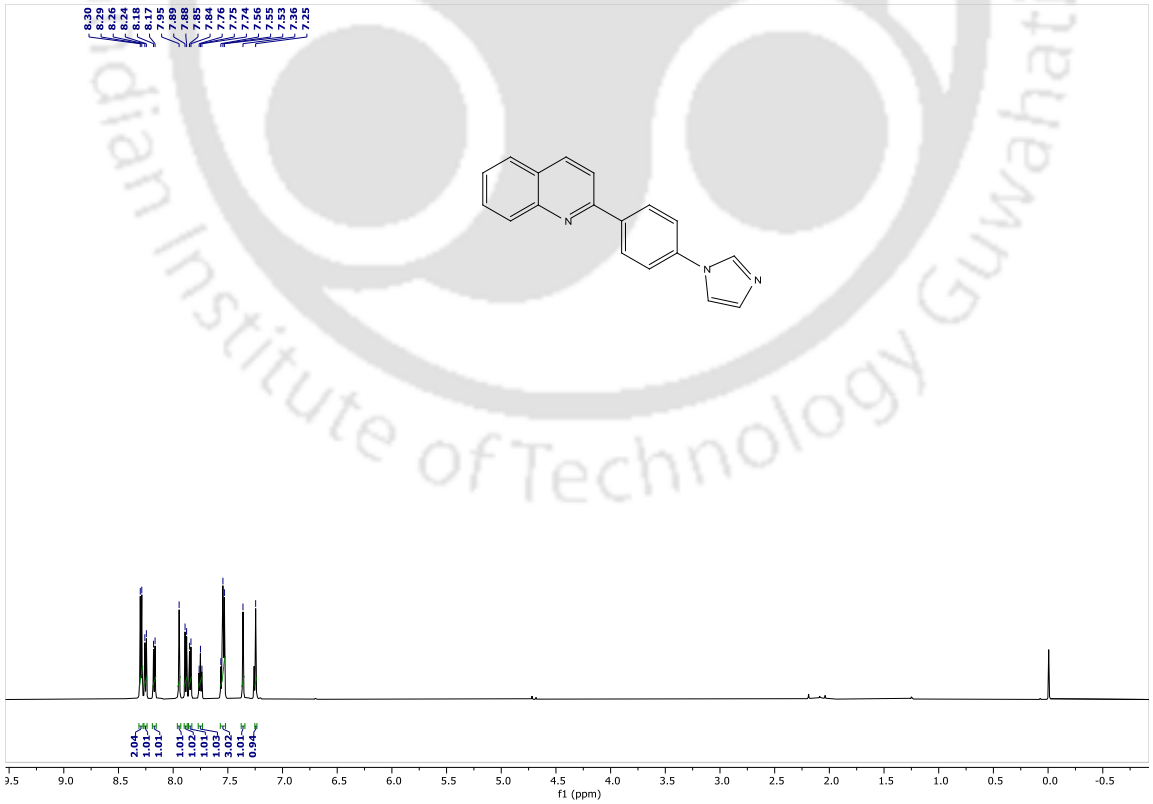

Figure S55: ^{1}H NMR Spectrum of **4.3g** ($CDCl_3$, 600 MHz, 298 K)

TH-3606_186122027

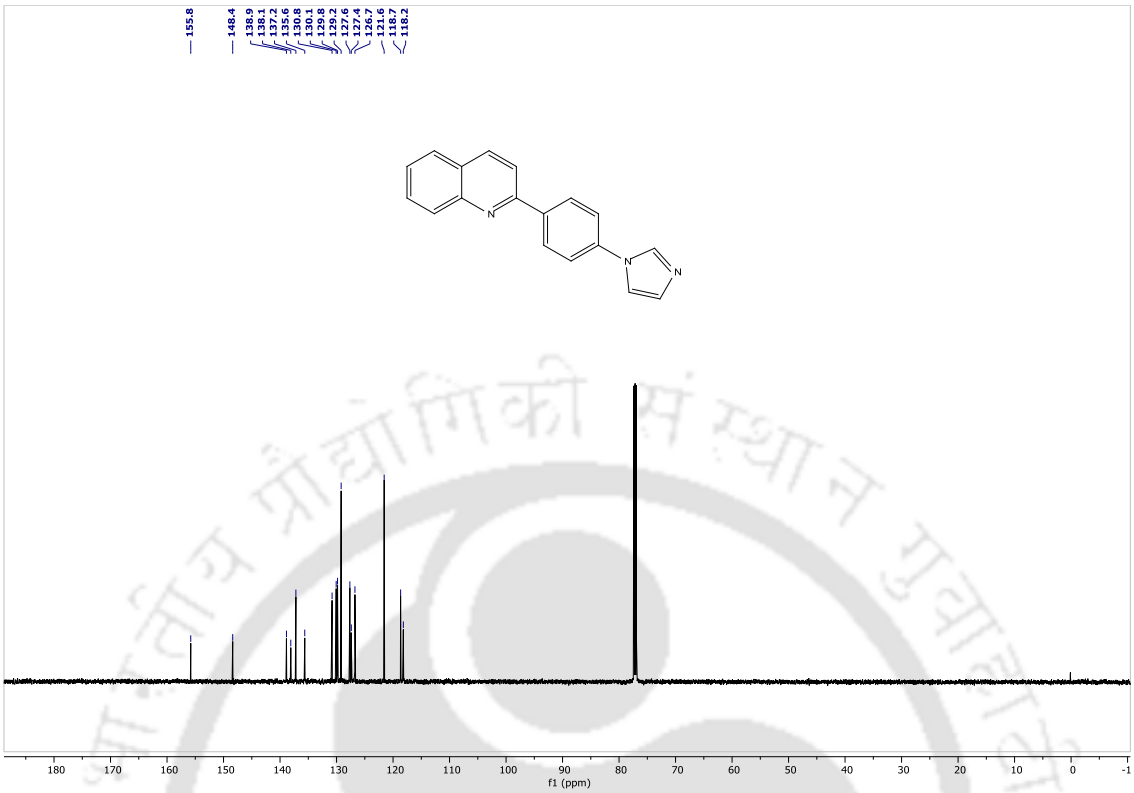

Figure S56: $^{13}C\{^{1}H\}$ NMR Spectrum of **4.3g** ($CDCl_3$, 151 MHz, 298 K)

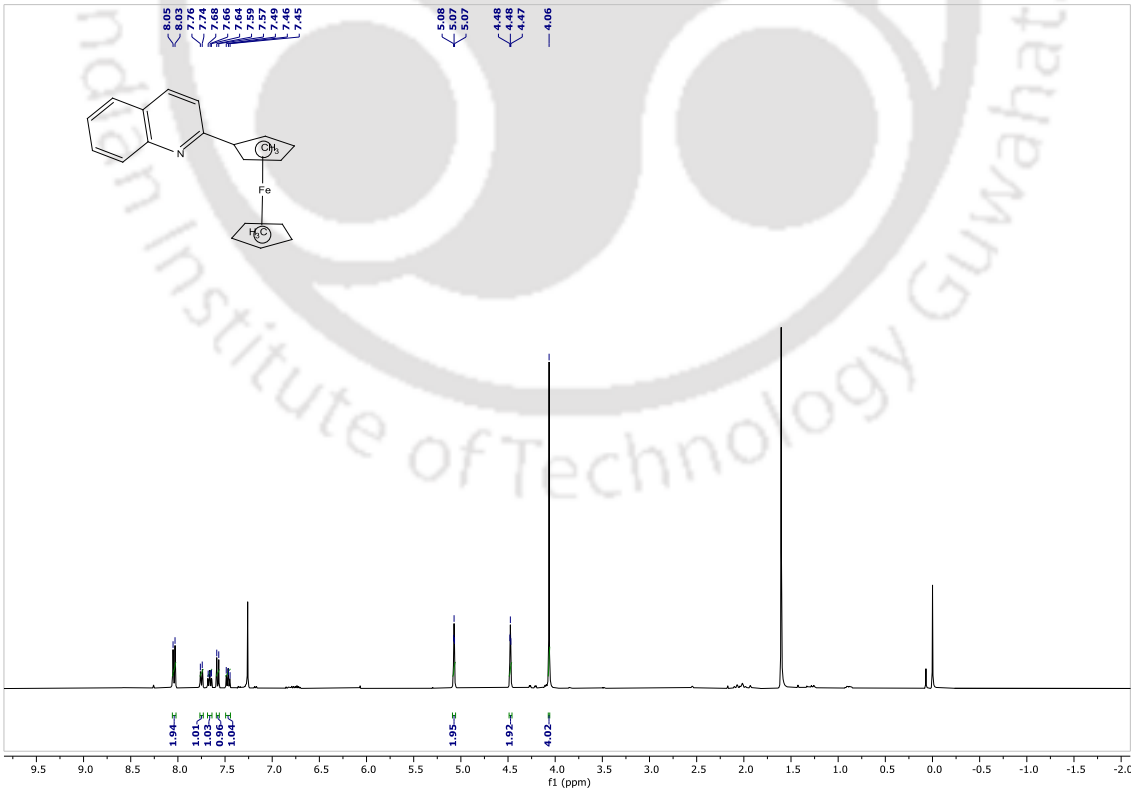

Figure S57: ^{1}H NMR Spectrum of **4.3n** ($CDCl_3$, 400 MHz, 298 K)

TH-3606_186122027

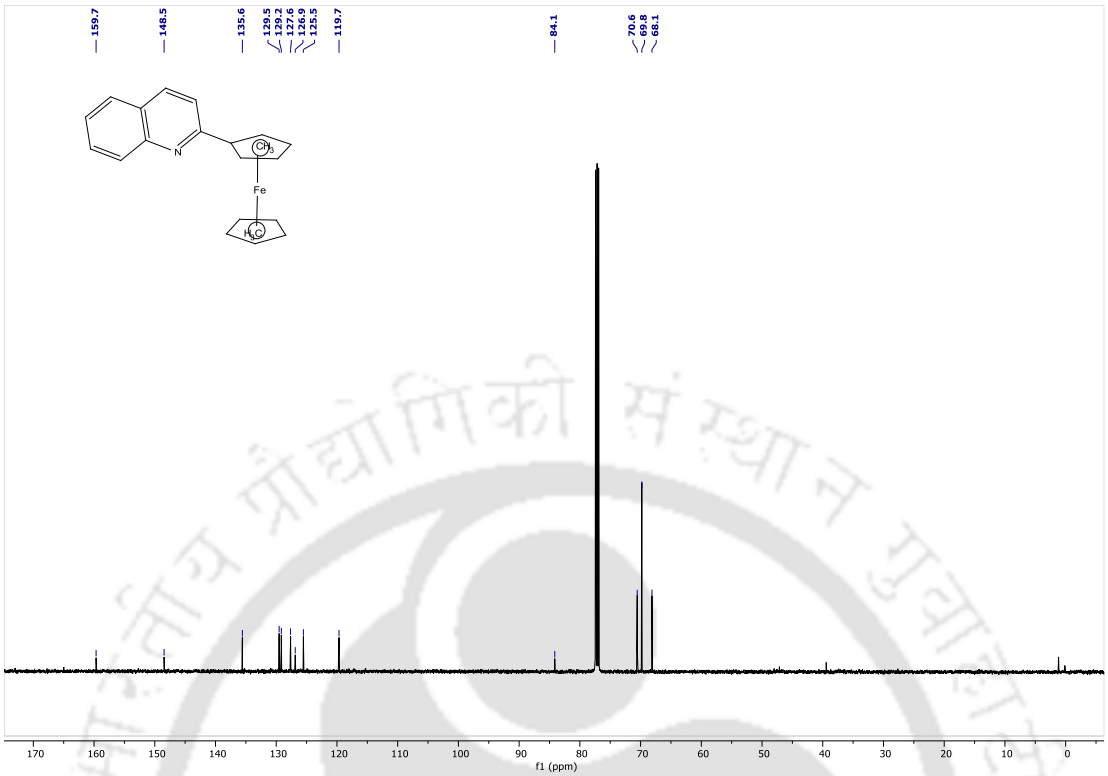

Figure S58: $^{13}C\{^{1}H\}$ NMR Spectrum of **4.3n** ($CDCl_3$, 126 MHz, 298 K)

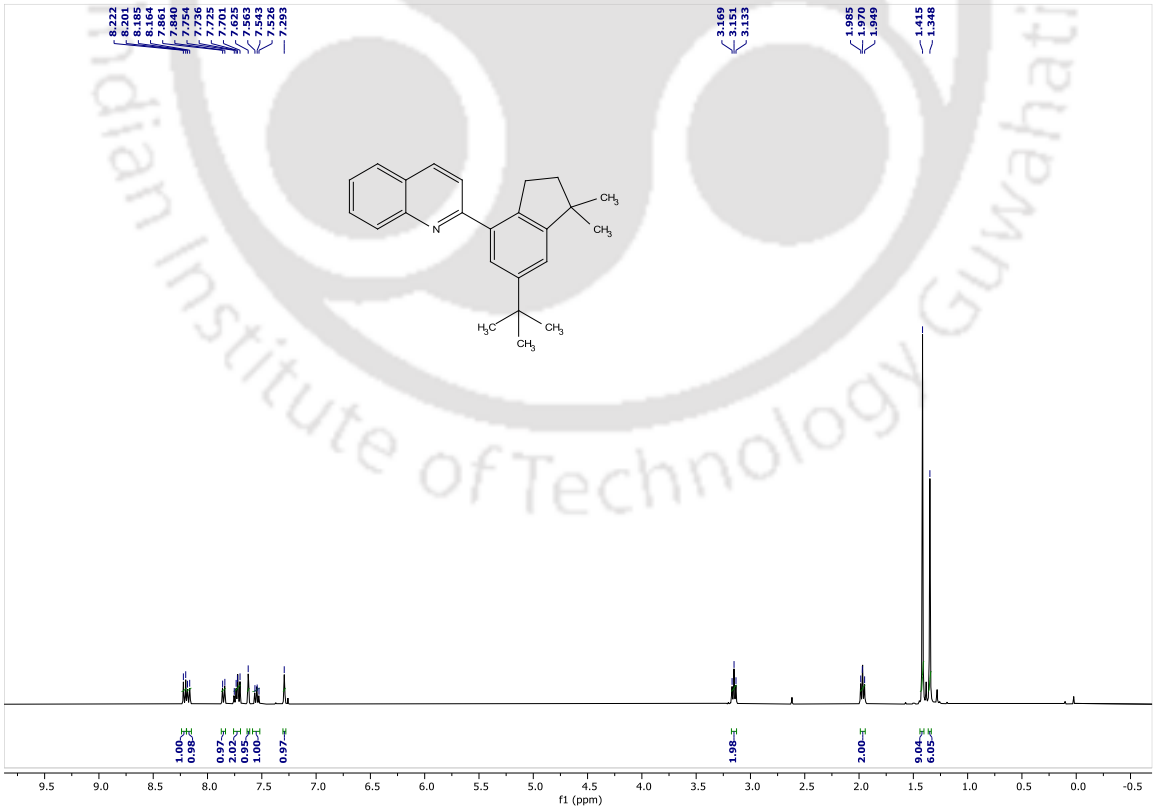

Figure S59: ^{1}H NMR Spectrum of **4.3ag** ($CDCl_3$, 400 MHz, 298 K)

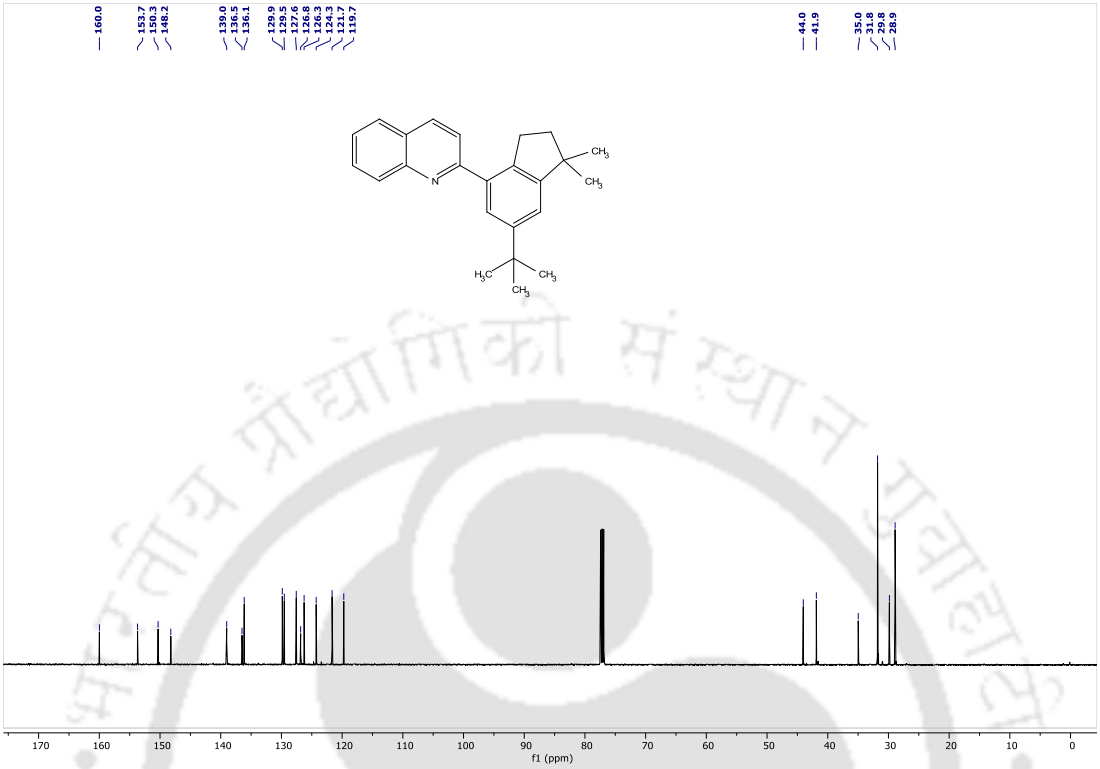

Figure S60: $^{13}C\{^{1}H\}$ NMR Spectrum of **4.3ag** ($CDCl_3$, 126 MHz, 298 K)

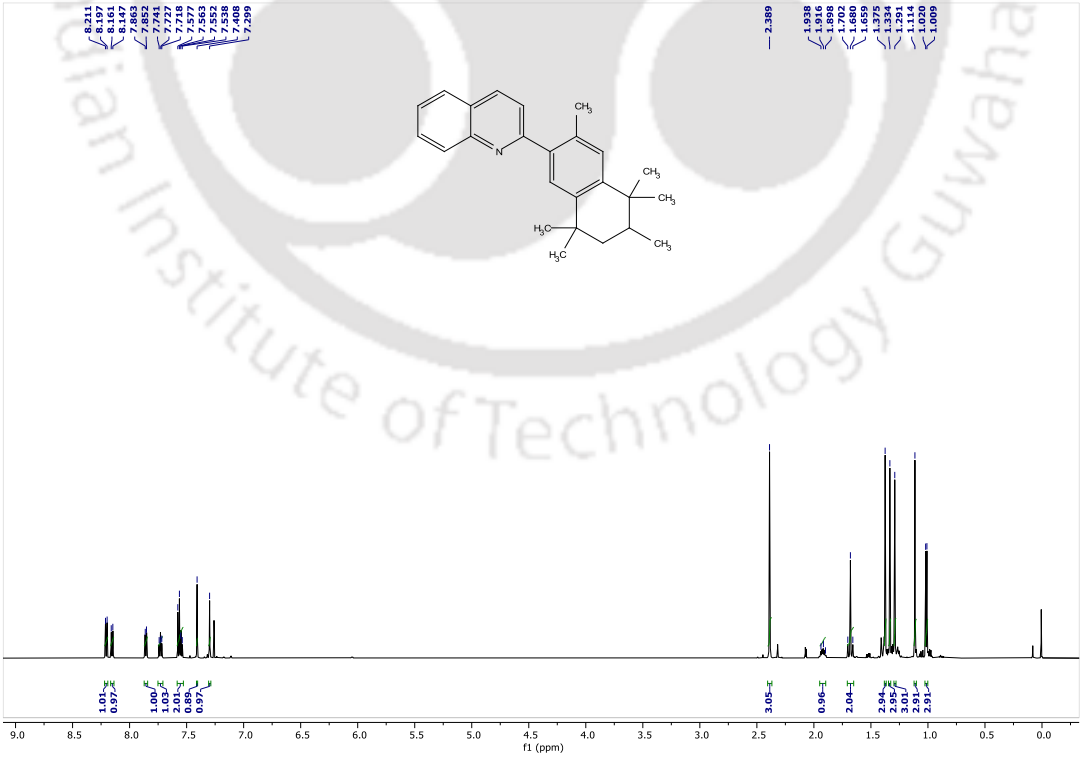

Figure S61: ^{1}H NMR Spectrum of **4.3ah** ($CDCl_3$, 600 MHz, 298 K)

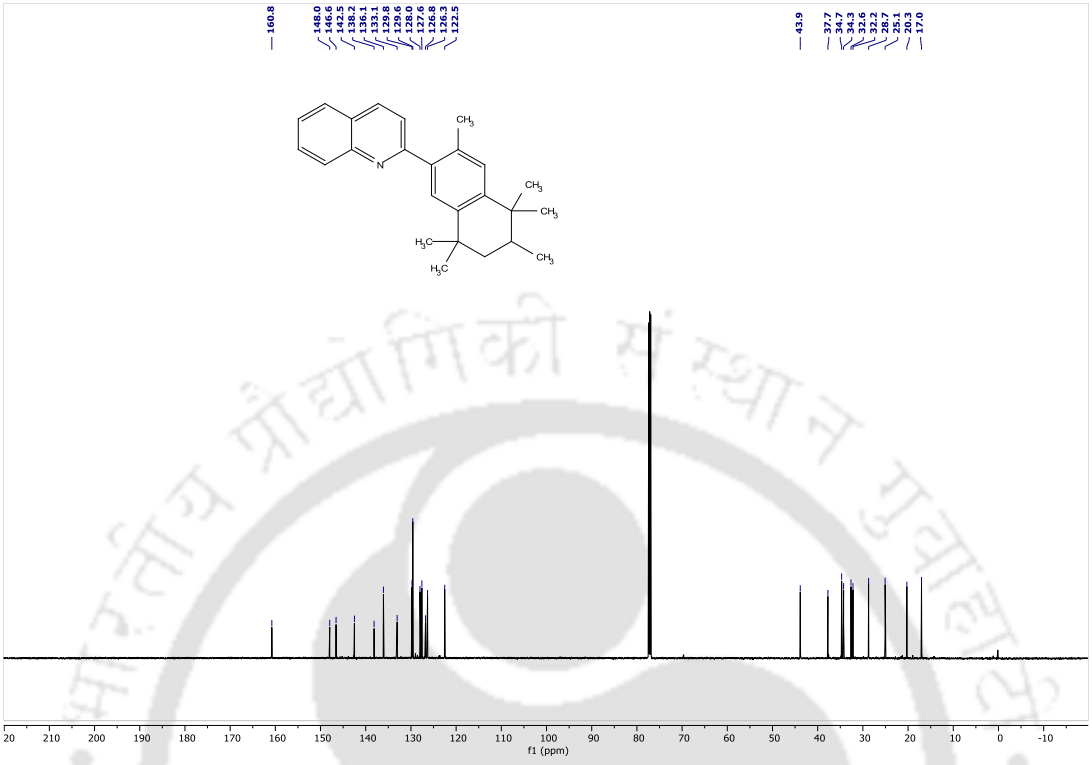

Figure S62: $^{13}C\{^{1}H\}$ NMR Spectrum of **4.3ah** ($CDCl_3$, 151 MHz, 298 K)

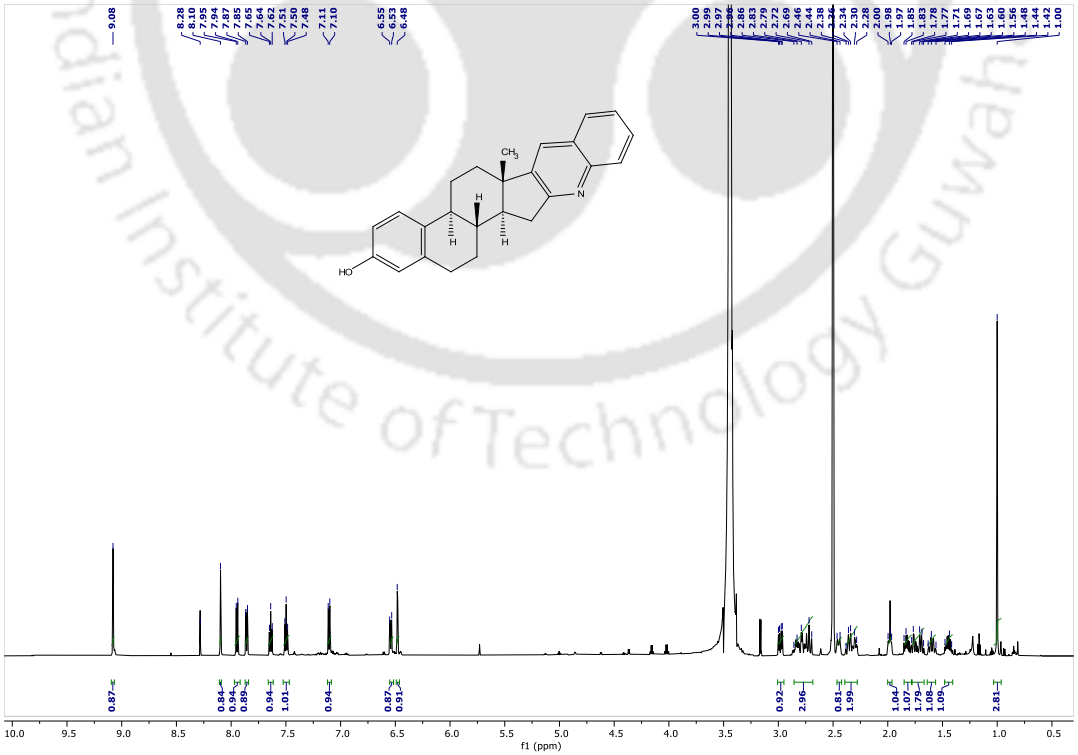

Figure S63: ^{1}H NMR Spectrum of **4.3ai** (DMSO, 600 MHz, 298 K)

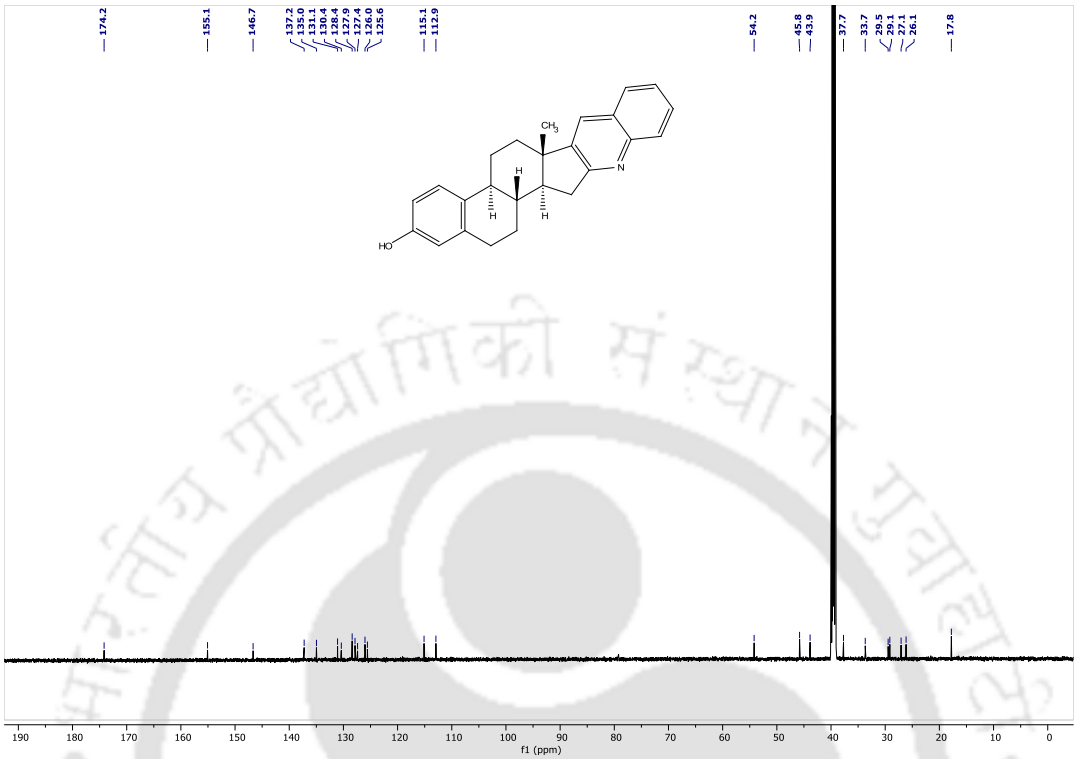

Figure S64: $^{13}C\{^{1}H\}$ NMR Spectrum of **4.3ai** (DMSO, 151 MHz, 298 K)

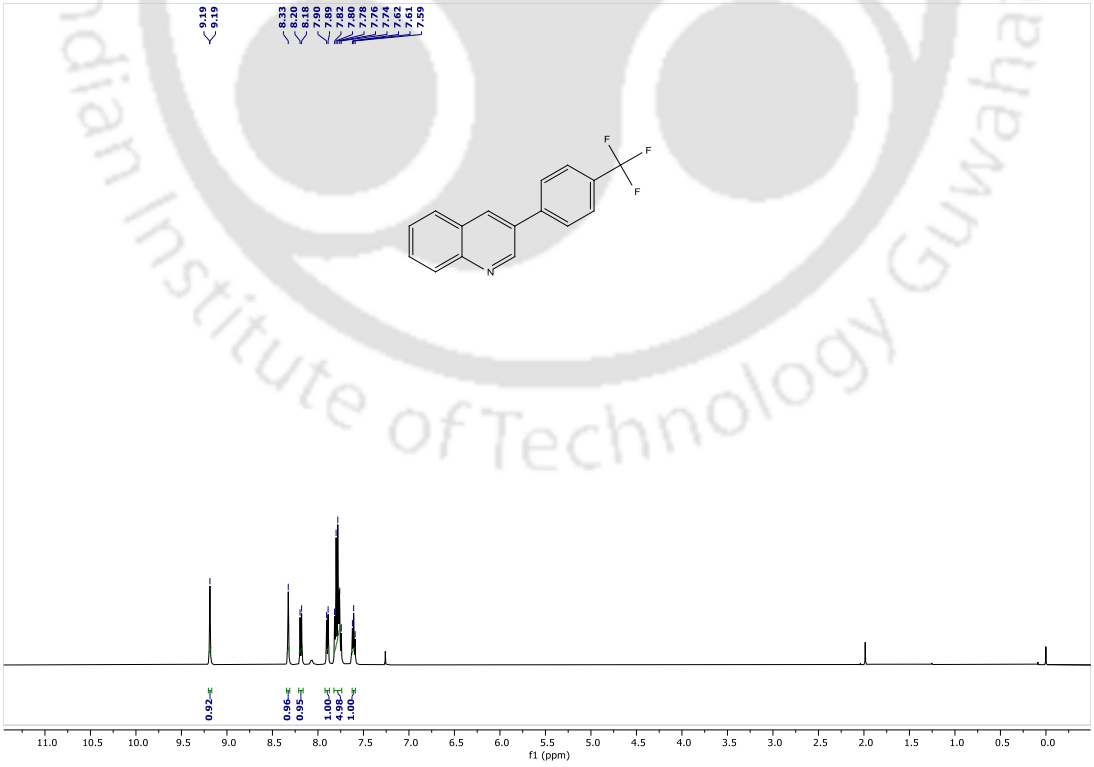

Figure S65: ^{1}HNMR Spectrum of **4.16af** ($CDCl_3$, 500 MHz, 298 K)

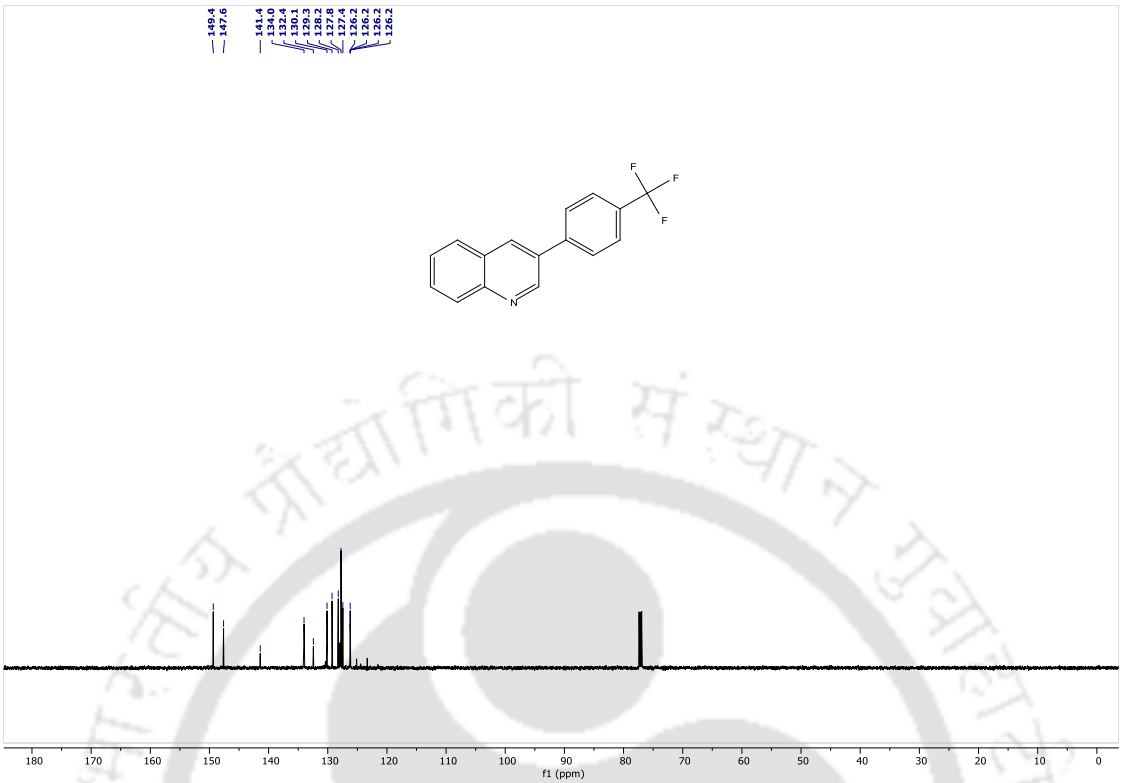

Figure S66: $^{13}C\{^{1}H\}$ NMR Spectrum of **4.16af** ($CDCl_3$, 121 MHz, 298 K)

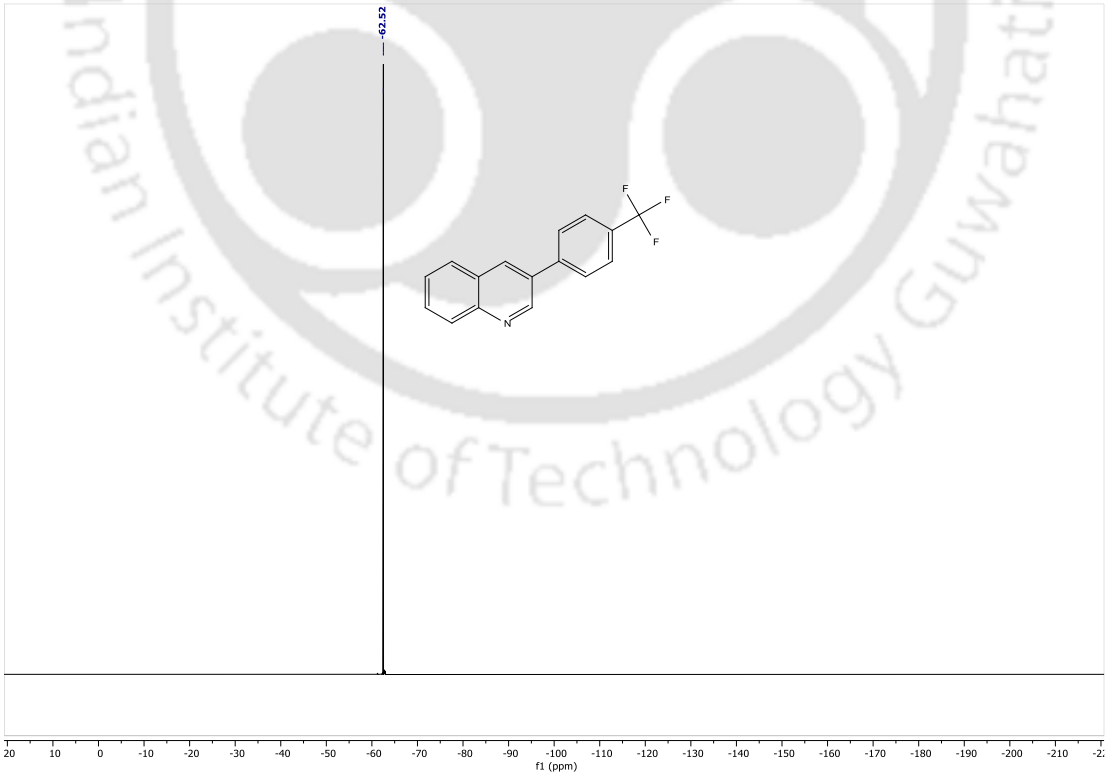

Figure S67: $^{19}F\{^{1}H\}$ NMR Spectrum of **4.16af** ($CDCl_3$, 471 MHz, 298 K)

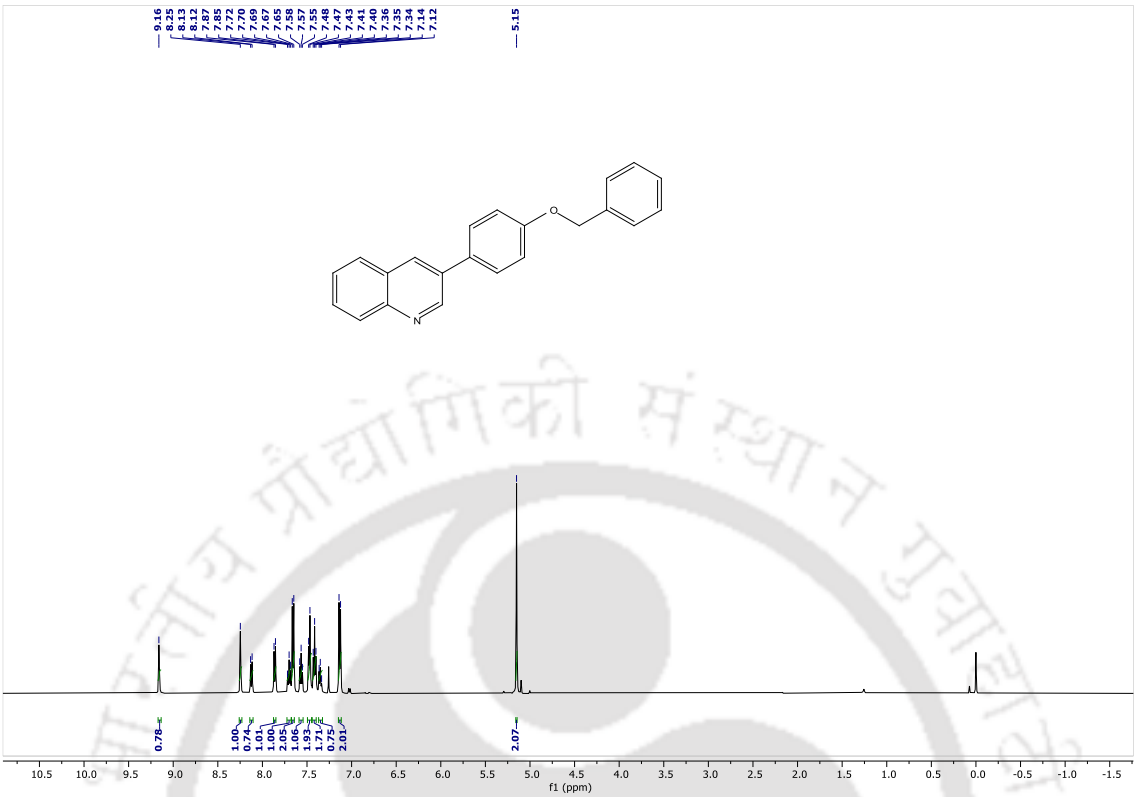

Figure S68: ^{1}HNMR Spectrum of **4.16ak** ($CDCl_3$, 500 MHz, 298 K)

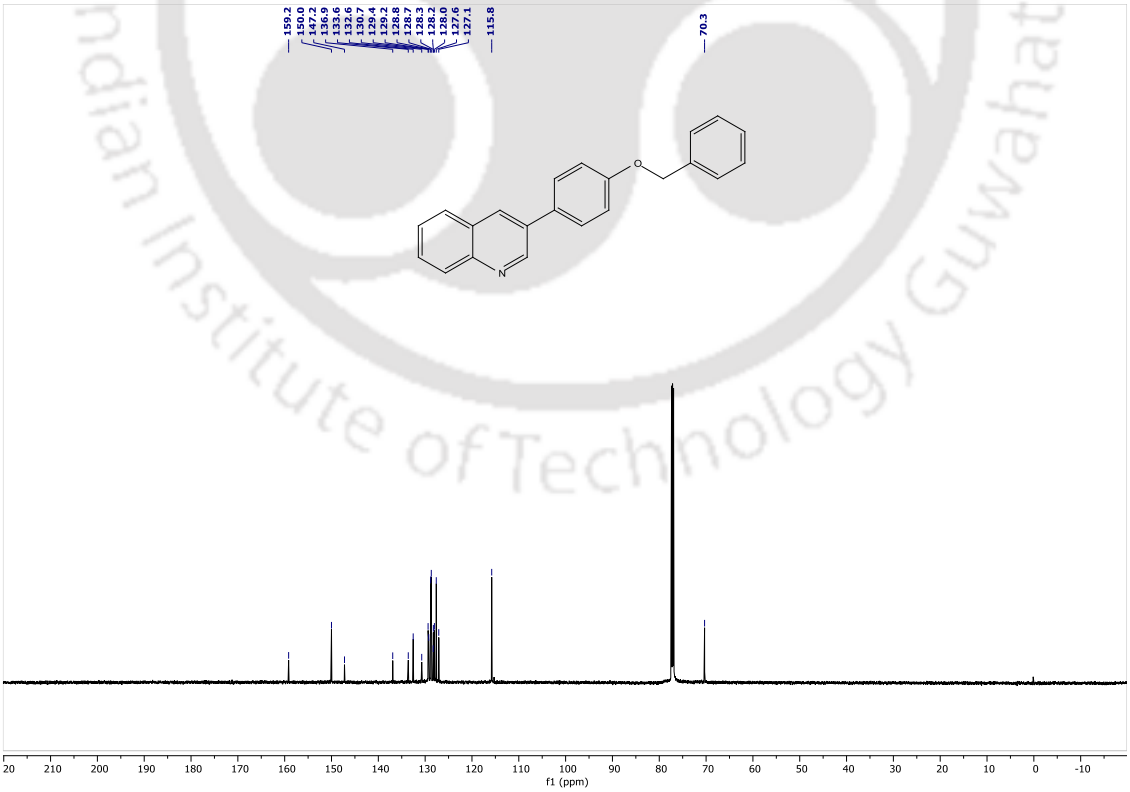

Figure S69: $^{13}C\{^{1}H\}$ NMR Spectrum of **4.16ak** ($CDCl_3$, 151 MHz, 298 K)

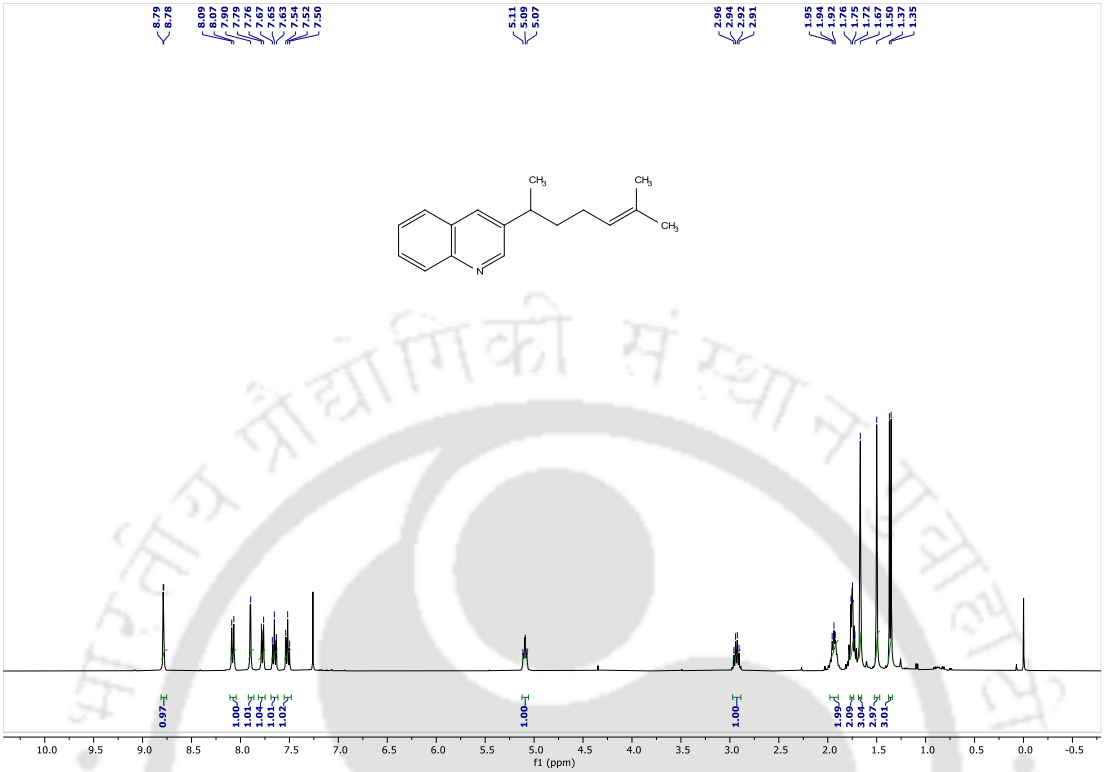

Figure S70: ^{1}HNMR Spectrum of **4.16p** ($CDCl_3$, 400 MHz, 298 K)

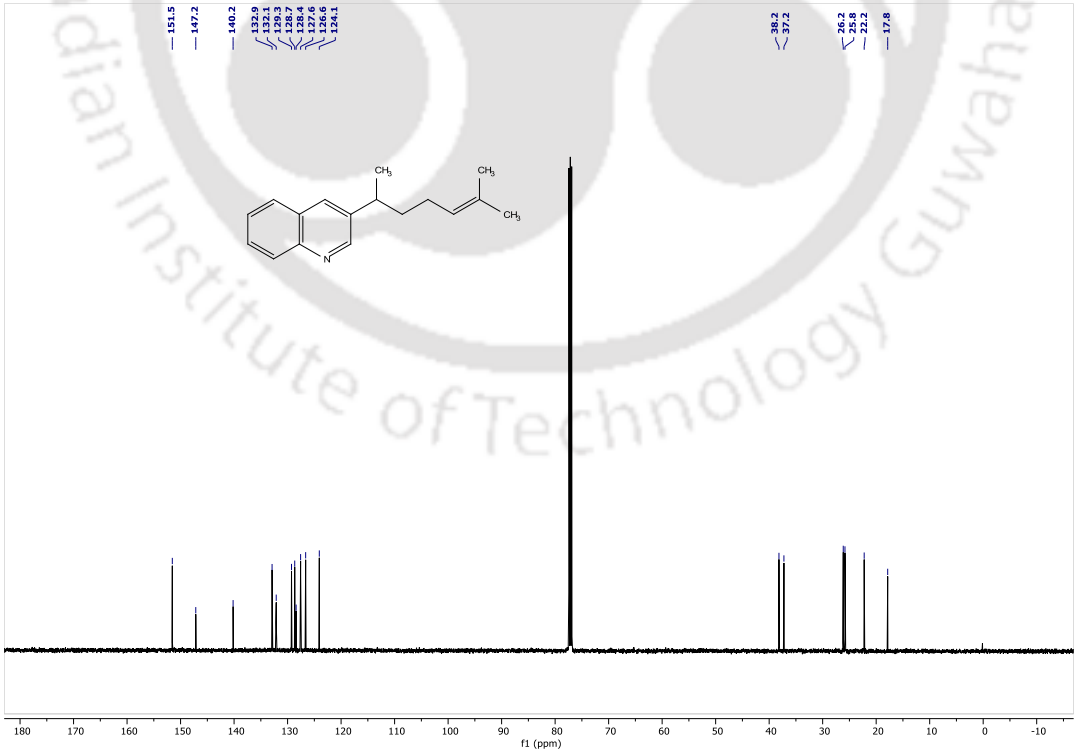

Figure S71: $^{13}C\{^{1}H\}$ NMR Spectrum of **4.16p** ($CDCl_3$, 126 MHz, 298 K)

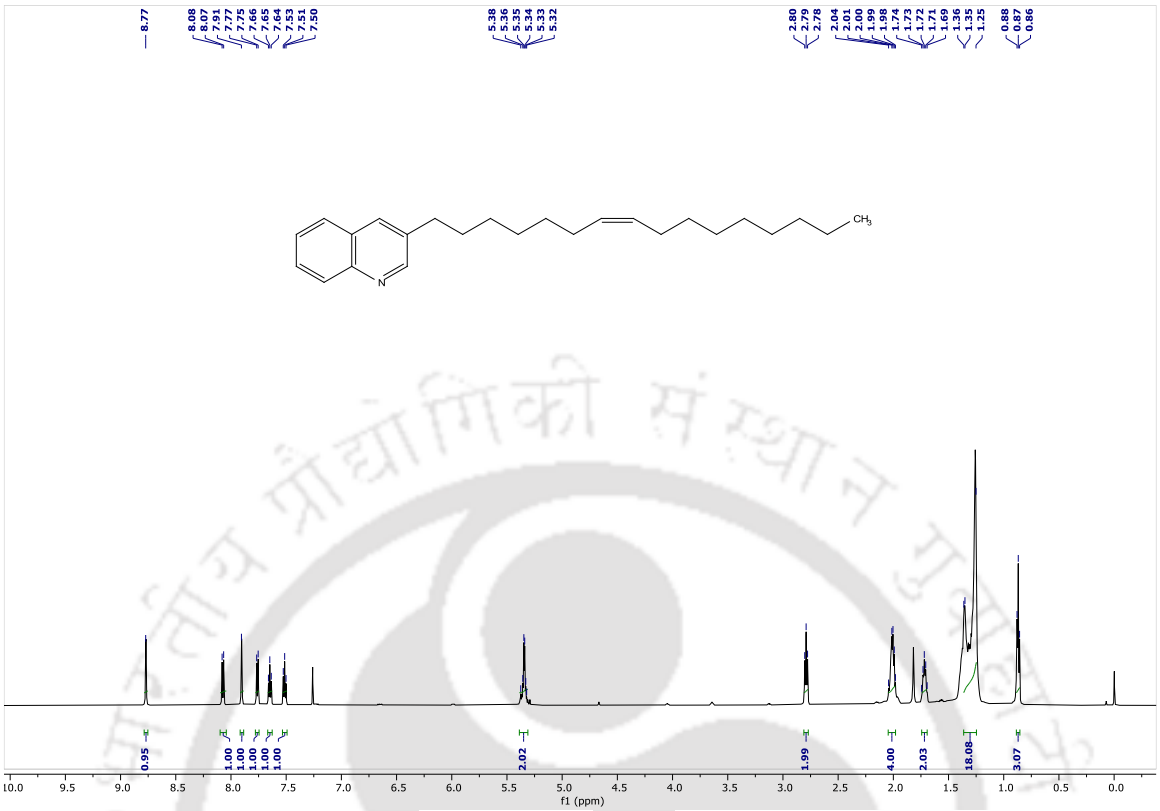

Figure S72: ^{1}HNMR Spectrum of **4.16q** ($CDCl_3$, 600 MHz, 298 K)

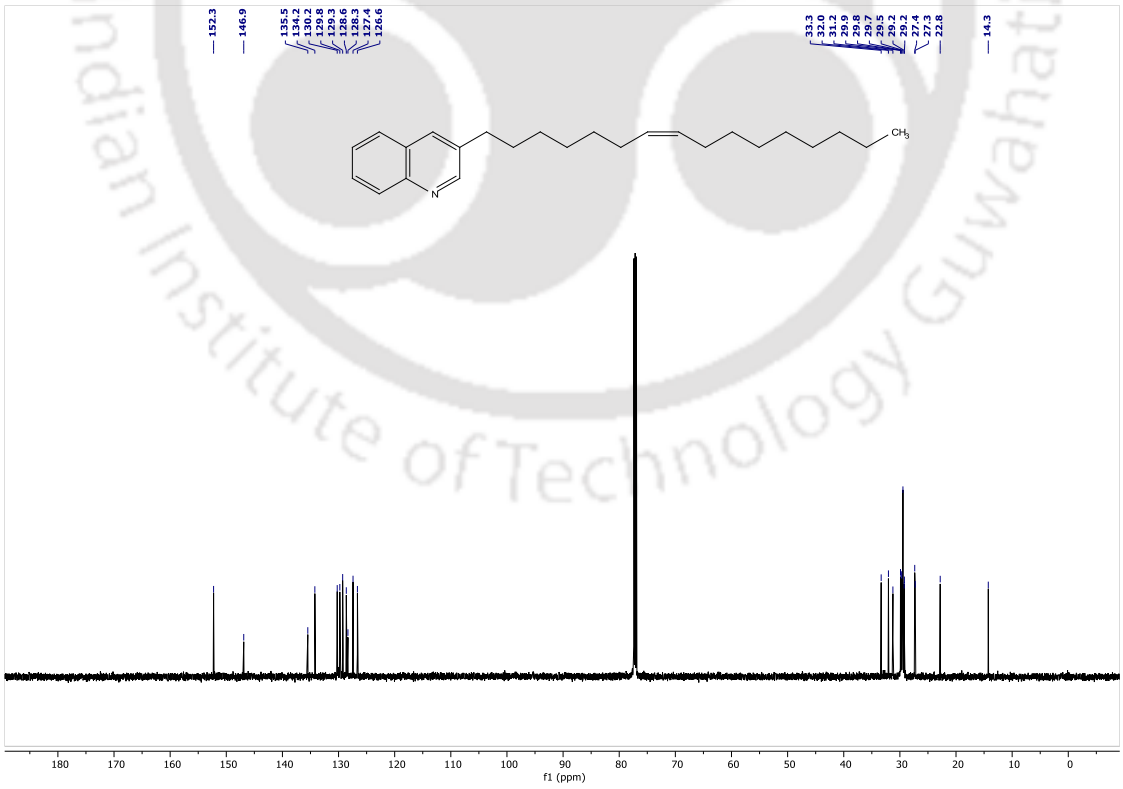

Figure S73: $^{13}C\{^{1}H\}$ NMR Spectrum of **4.16q** ($CDCl_3$, 151 MHz, 298 K)

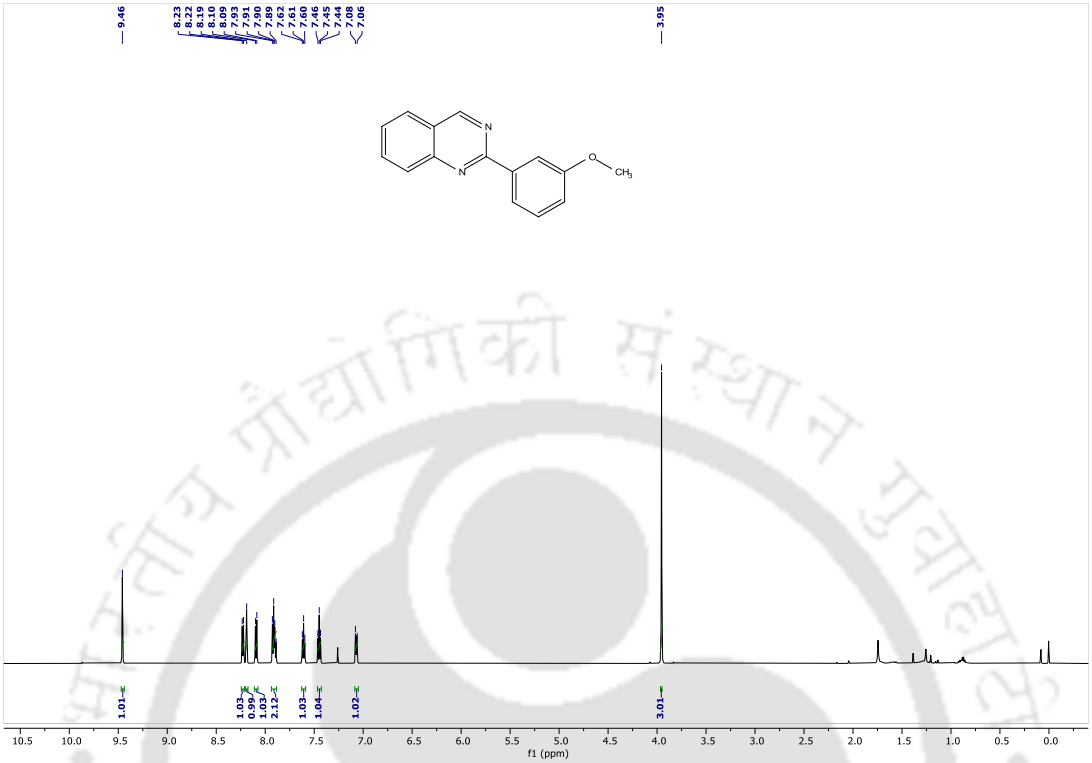

Figure S74: ^{1}HNMR Spectrum of **4.24i** ($CDCl_3$, 600 MHz, 298 K)

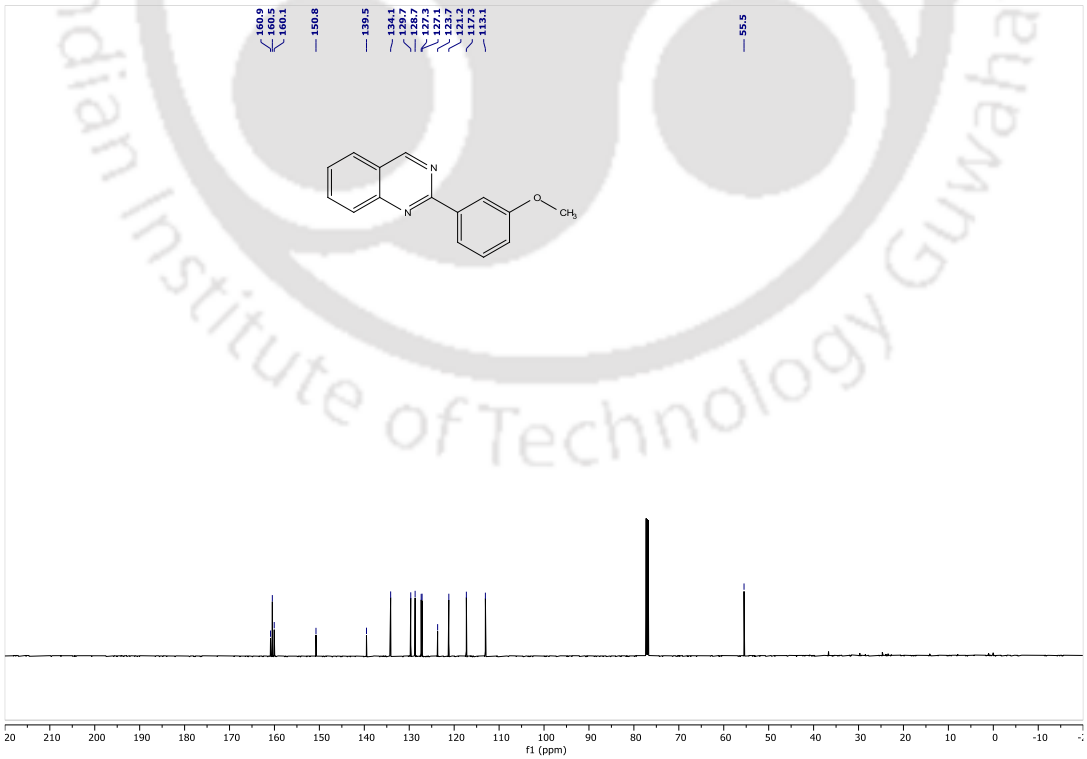

Figure S75: $^{13}C\{^{1}H\}$ NMR Spectrum of **4.24i** ($CDCl_3$, 151 MHz, 298 K)

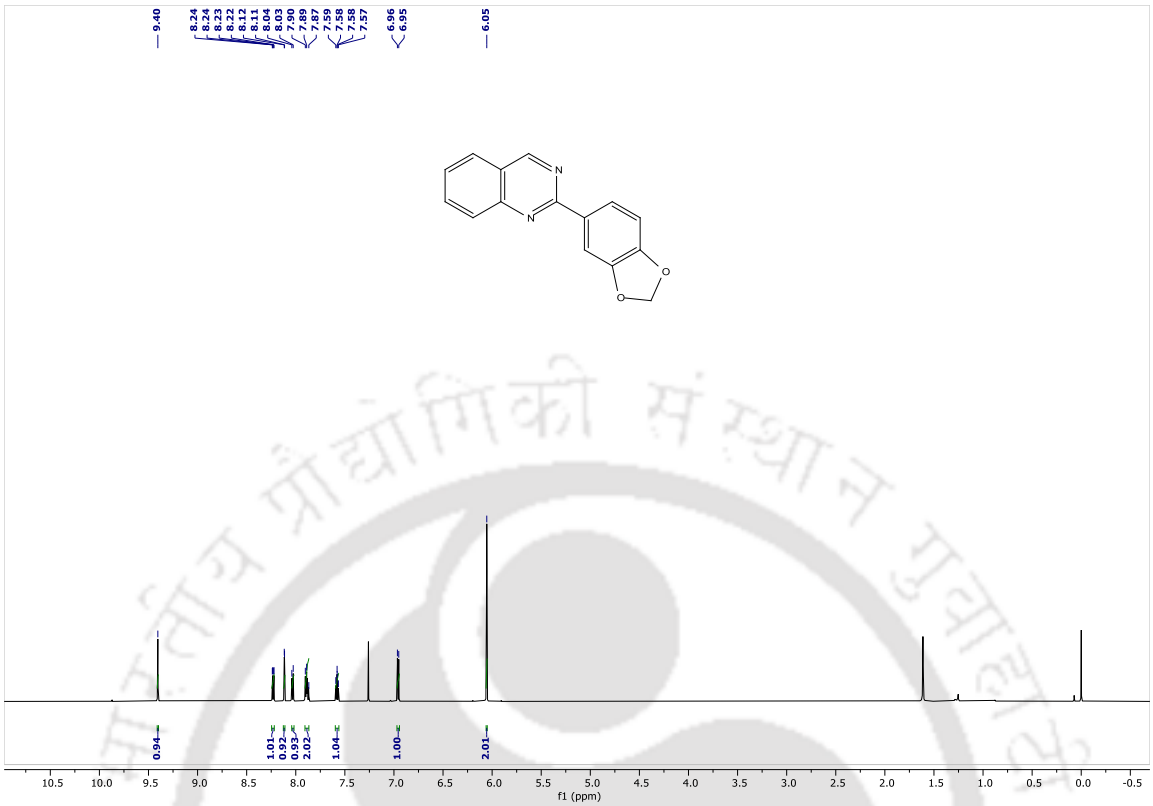

Figure S76: ^{1}HNMR Spectrum of **4.24m** ($CDCl_3$, 400 MHz, 298 K)

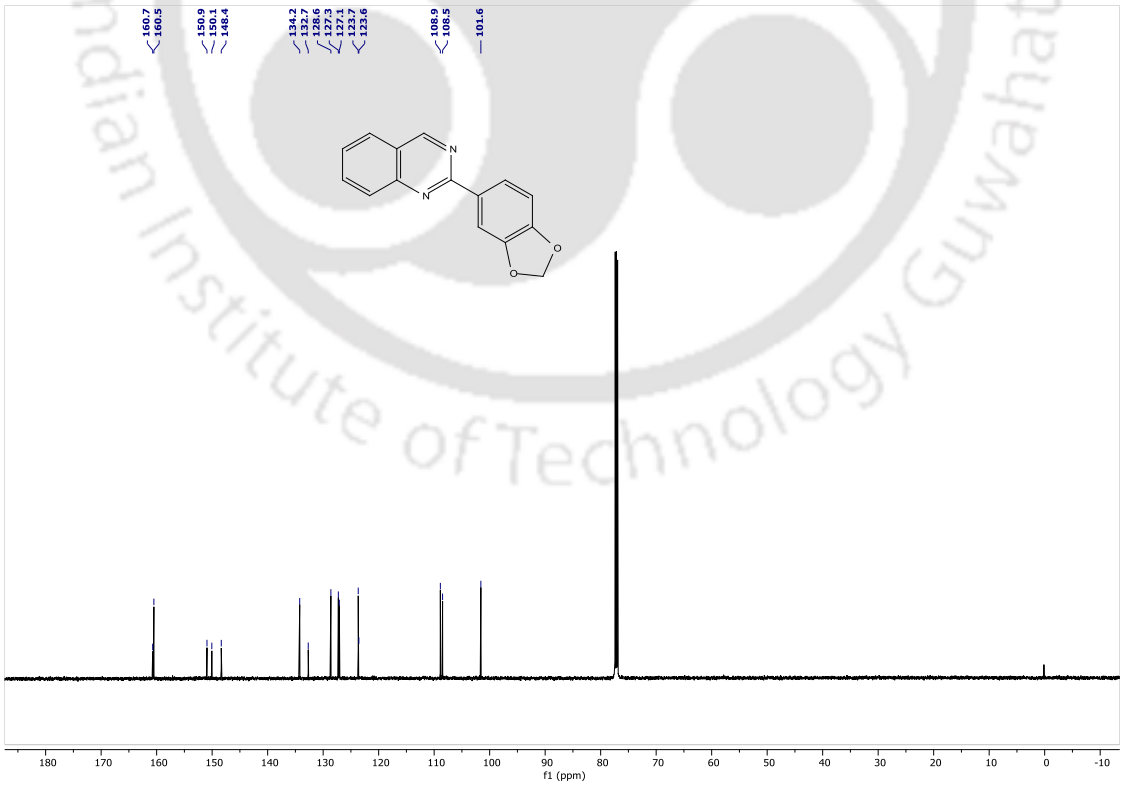

Figure S77: $^{13}C\{^{1}H\}$ NMR Spectrum of **4.24m** ($CDCl_3$, 151 MHz, 298 K)

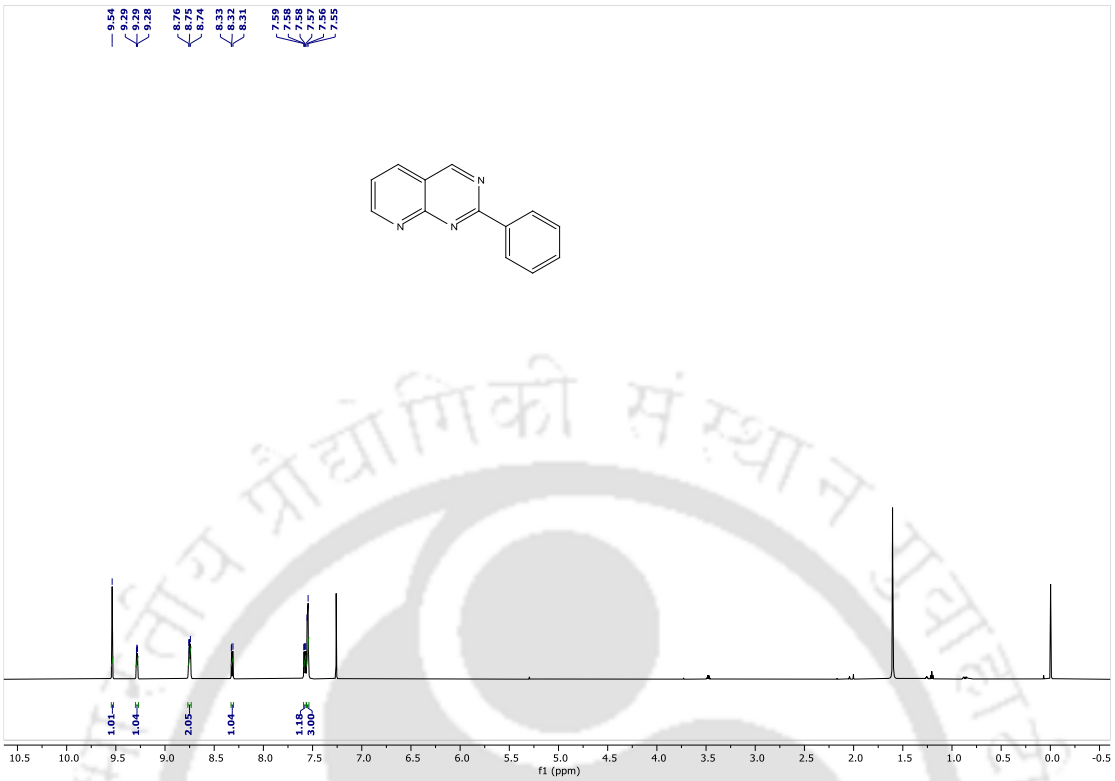

Figure S78: ^{1}HNMR Spectrum of **4.24n** ($CDCl_3$, 600 MHz, 298 K)

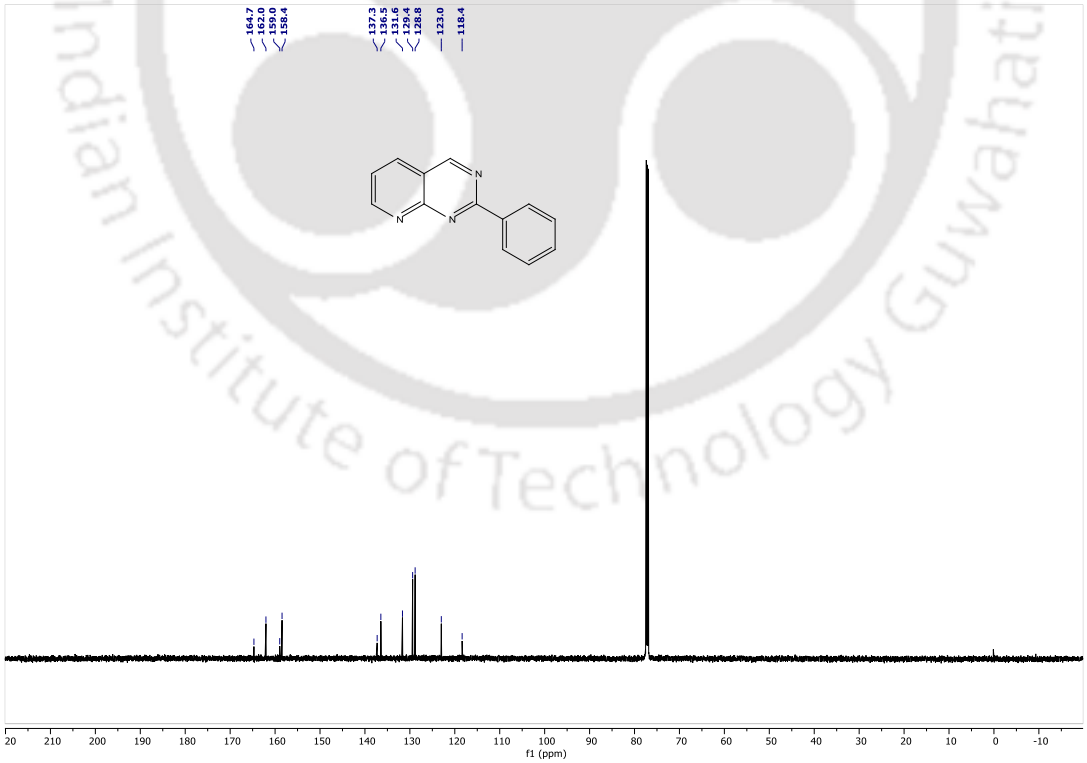

Figure S79: $^{13}C\{^{1}H\}$ NMR Spectrum of **4.24n** ($CDCl_3$, 151 MHz, 298 K)

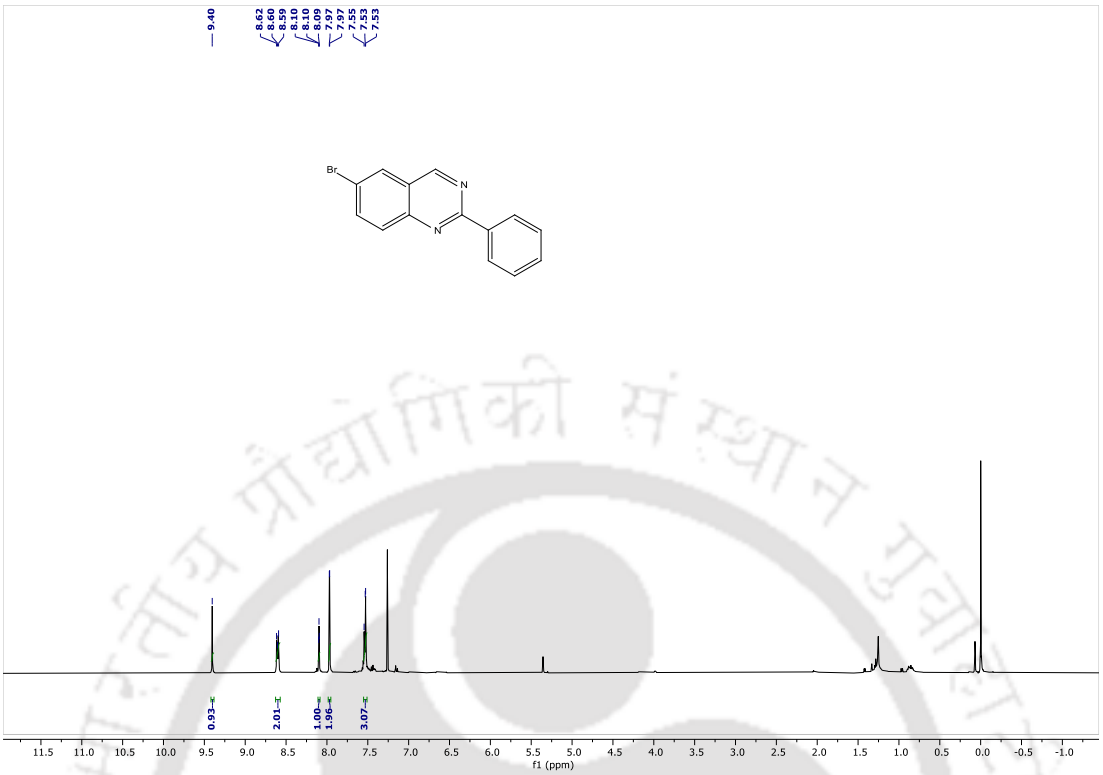

Figure S80: ^{1}HNMR Spectrum of **4.24p** ($CDCl_3$, 400 MHz, 298 K)

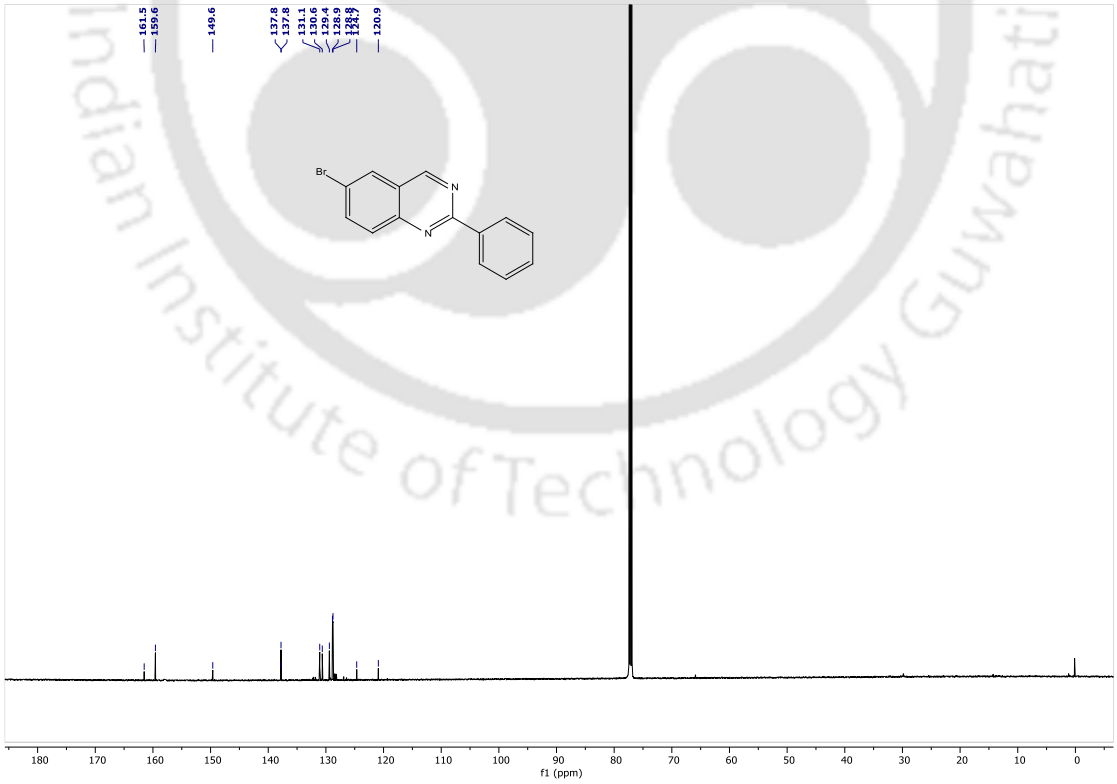

Figure S81: $^{13}C\{^{1}H\}$ NMR Spectrum of **4.24p** ($CDCl_3$, 151 MHz, 298 K)

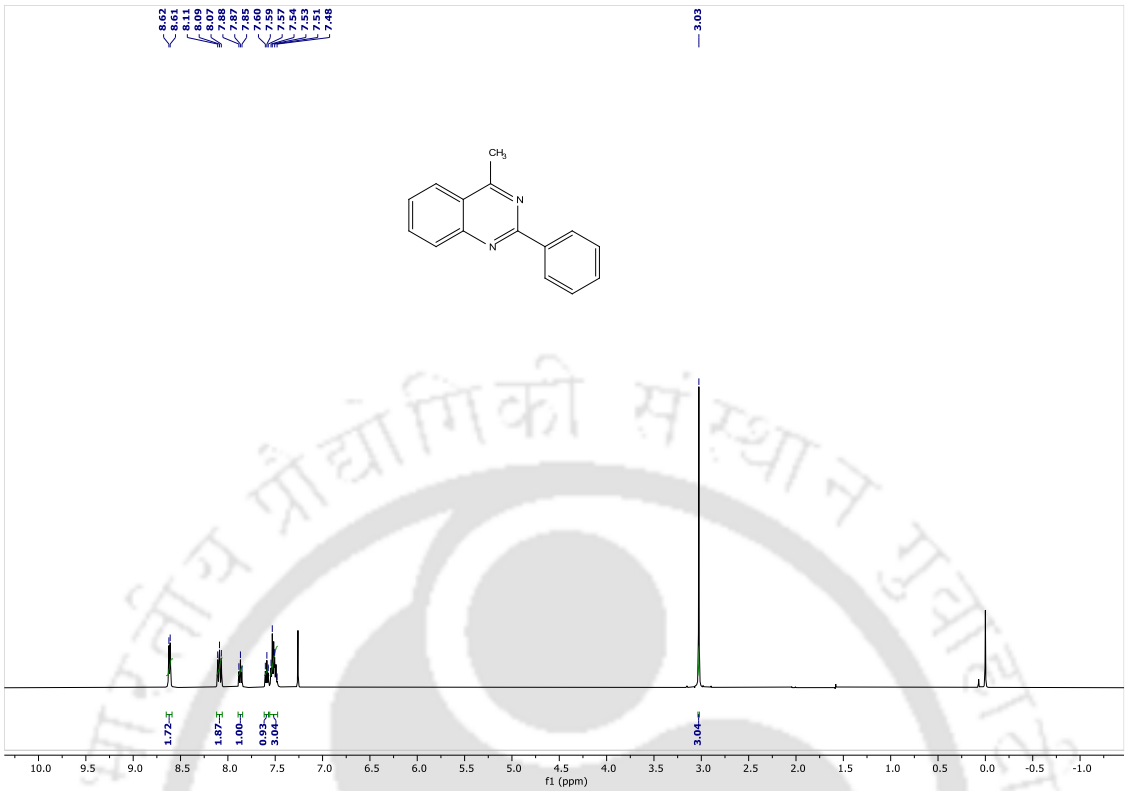

Figure S82: ^{1}HNMR Spectrum of **4.24r** ($CDCl_3$, 500 MHz, 298 K)

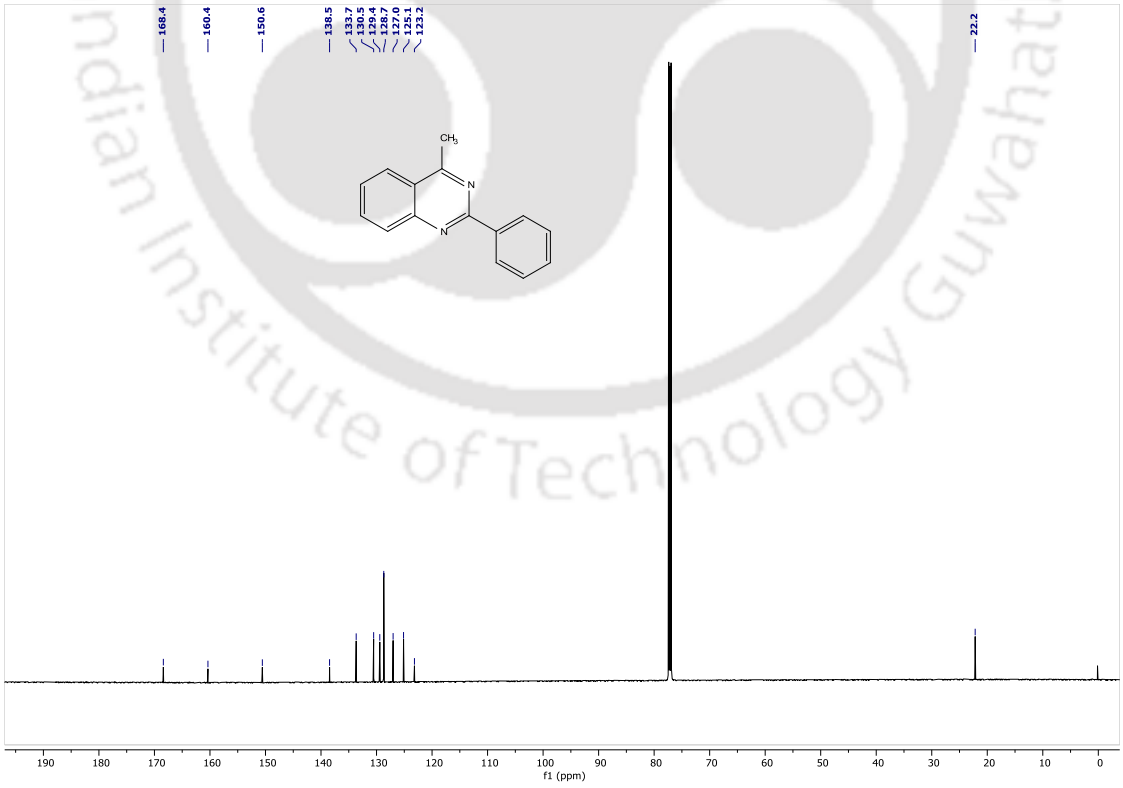

Figure S83: $^{13}C\{^{1}H\}$ NMR Spectrum of **4.24r** ($CDCl_3$, 151 MHz, 298 K)

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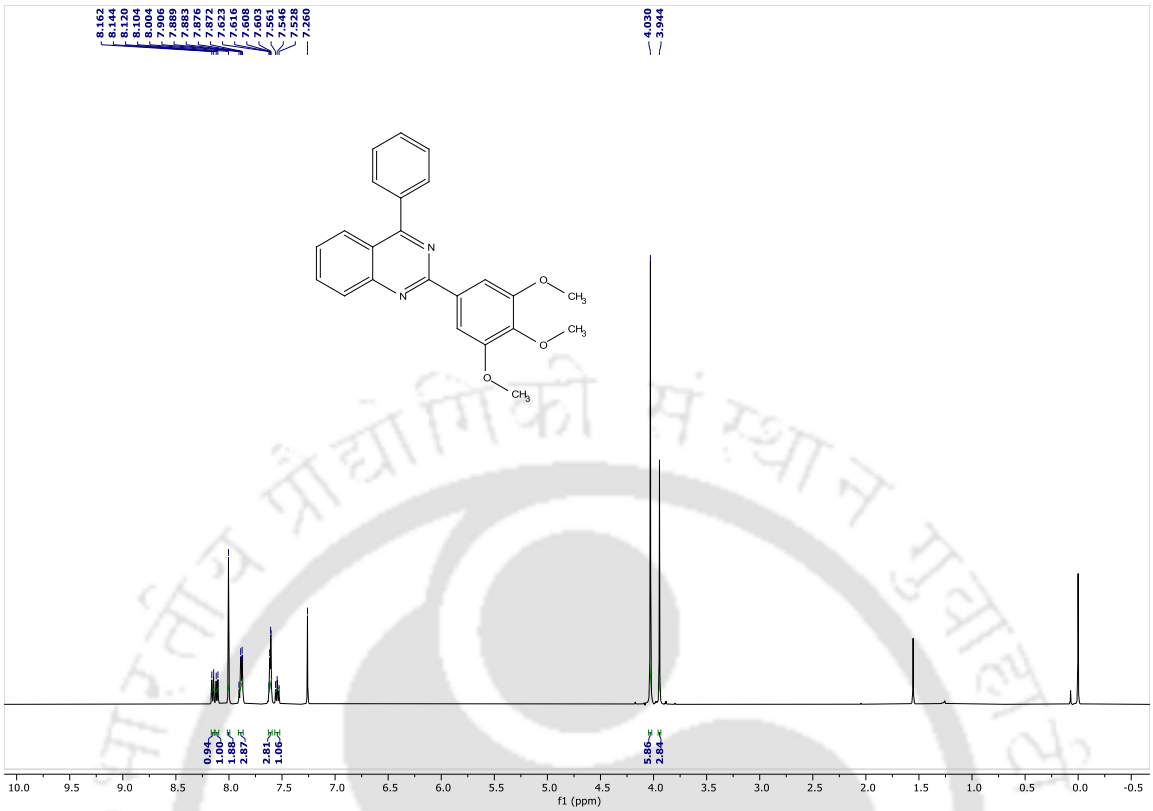

Figure S84: ^{1}HNMR Spectrum of **4.24t** ($CDCl_3$, 500 MHz, 298 K)

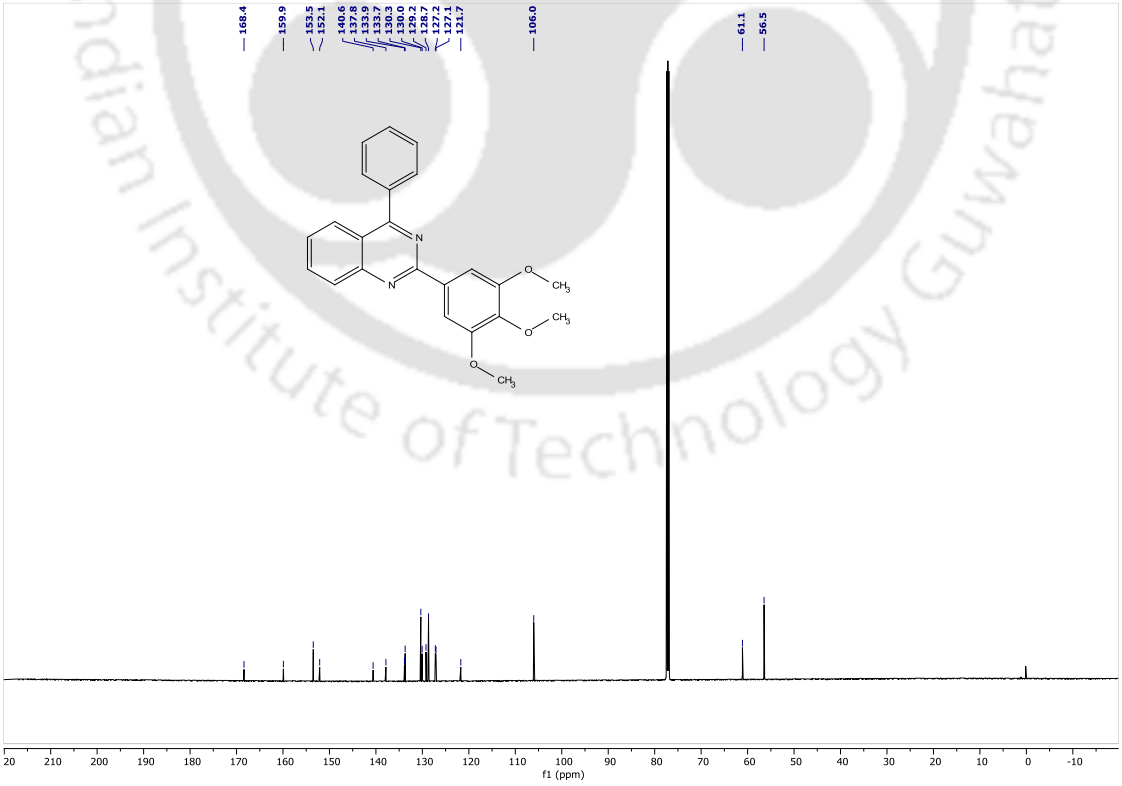

Figure S85: $^{13}C\{^{1}H\}$ NMR Spectrum of **4.24t** ($CDCl_3$, 151 MHz, 298 K)

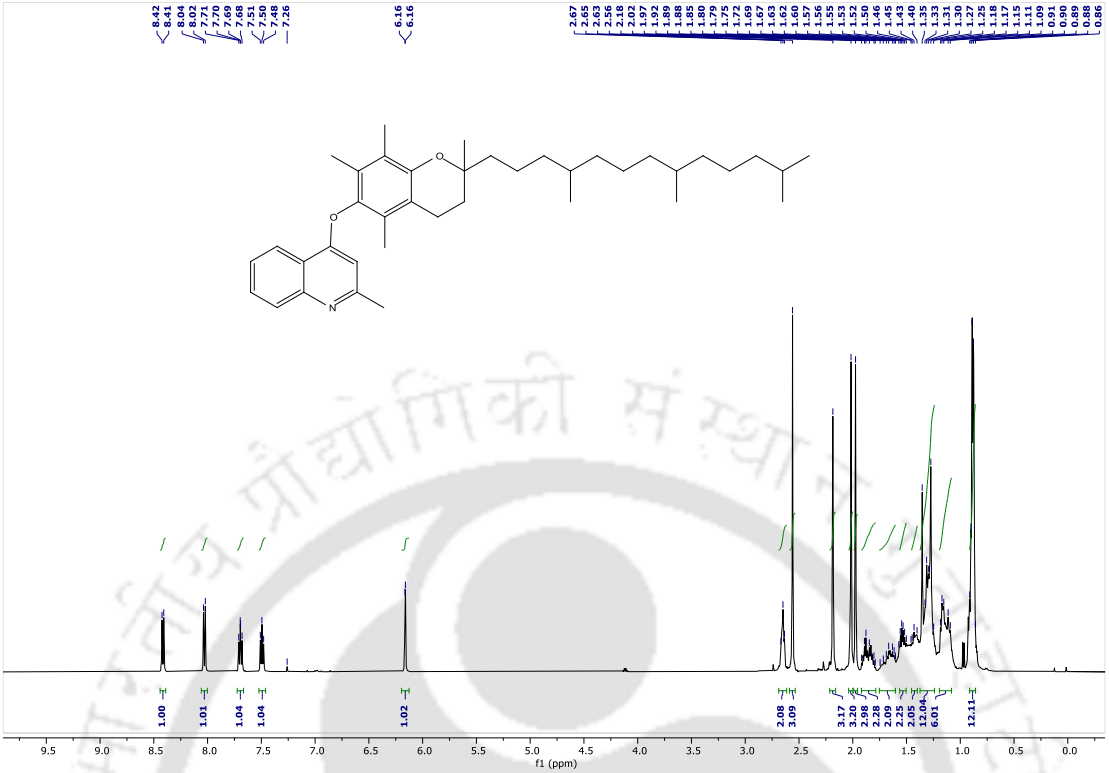

Figure S86: ^{1}HNMR Spectrum of **4.30** ($CDCl_3$, 500 MHz, 298 K)

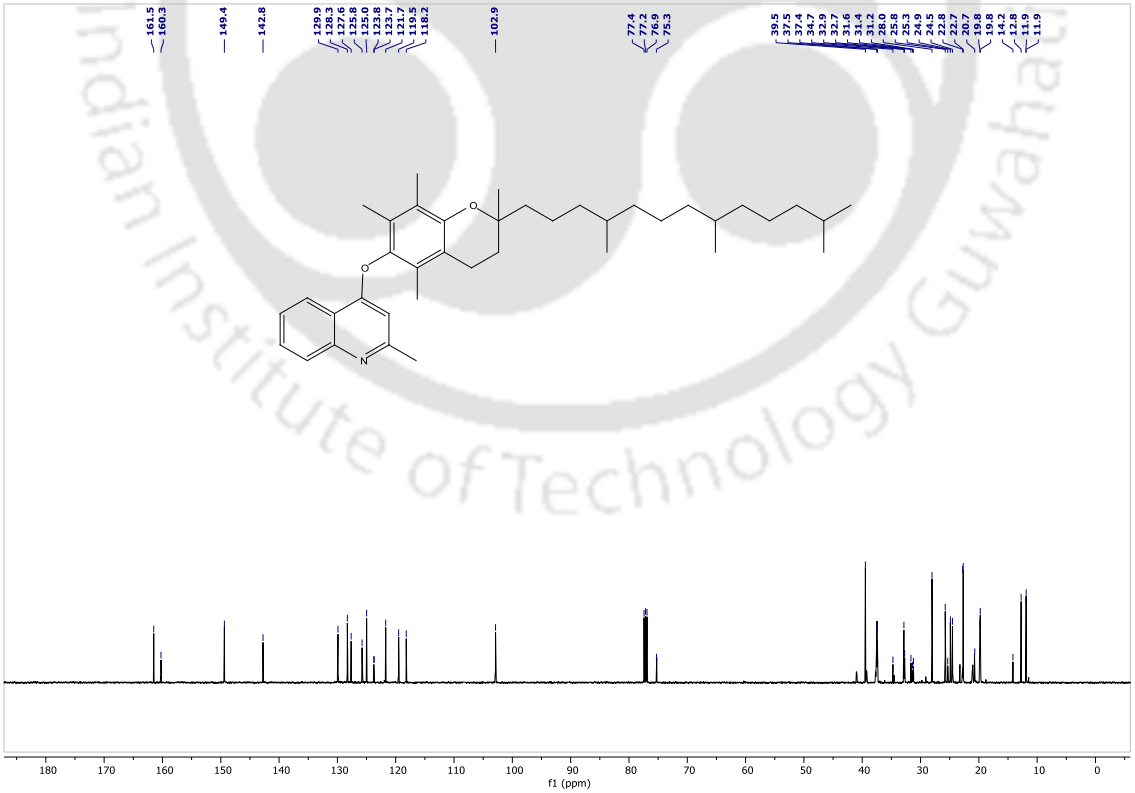

Figure S87: $^{13}C\{^{1}H\}$ NMR Spectrum of **4.30** ($CDCl_3$, 126 MHz, 298 K)

Annexure IV

^{1}H, ^{13}C, and ^{19}F NMR spectra representative compounds (*Chapter 5*)

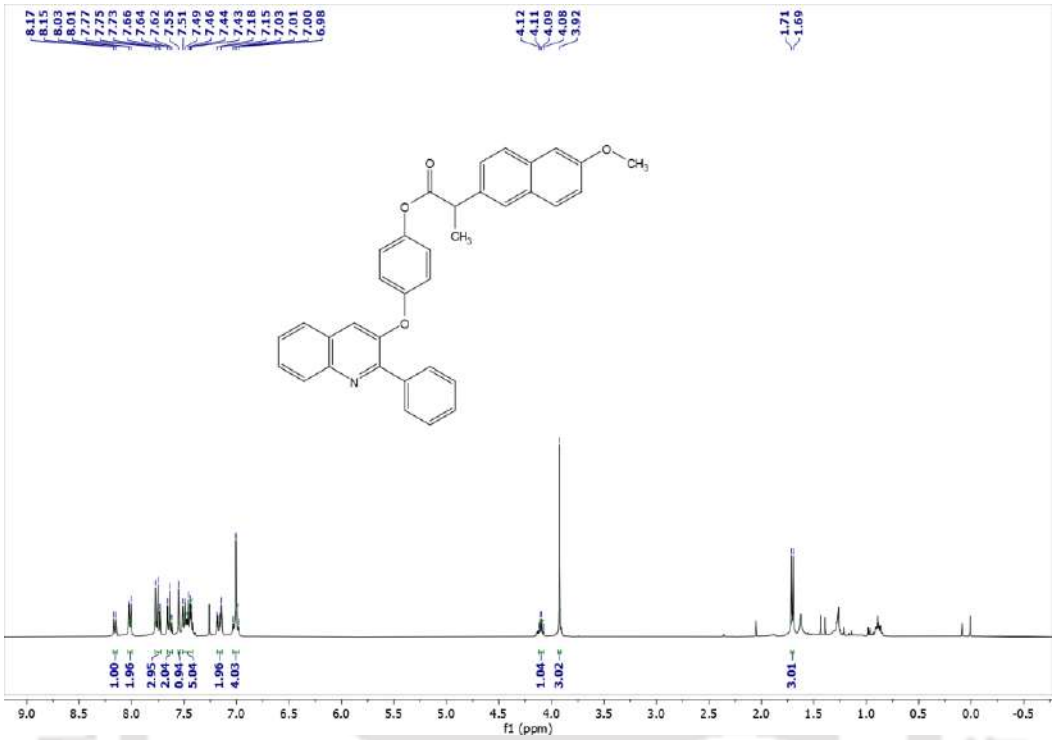

Figure S88: ^{1}H NMR Spectrum of **5.2u** ($CDCl_3$, 400 MHz, 298 K)

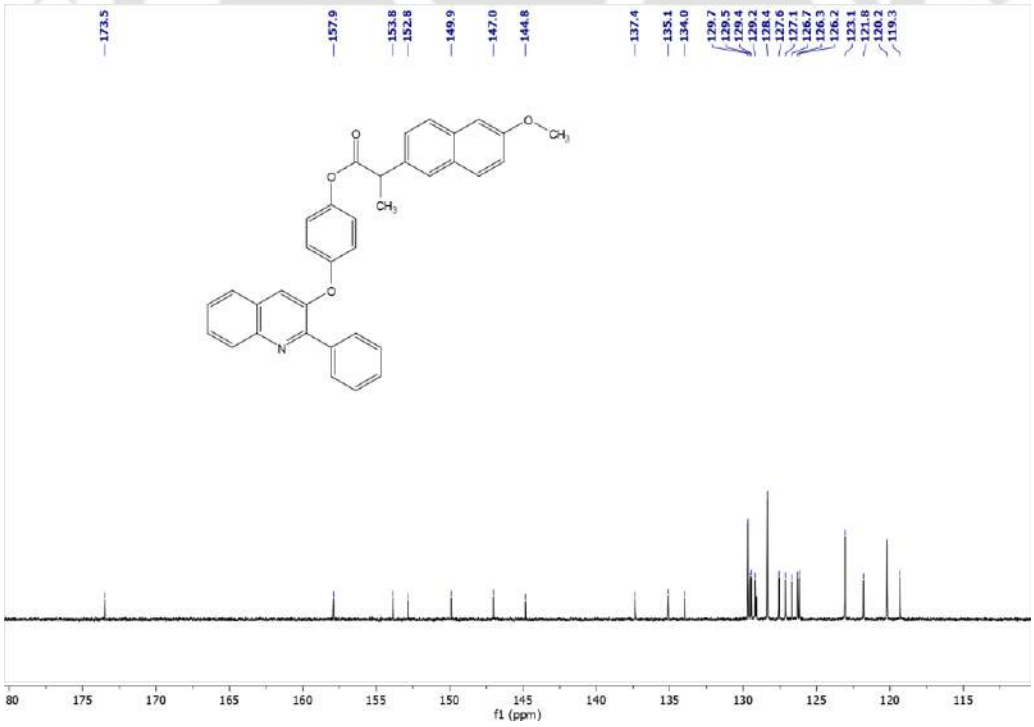

Figure S89: $^{13}C\{^{1}H\}$ NMR Spectrum of **5.2u** ($CDCl_3$, 151 MHz, 298 K)

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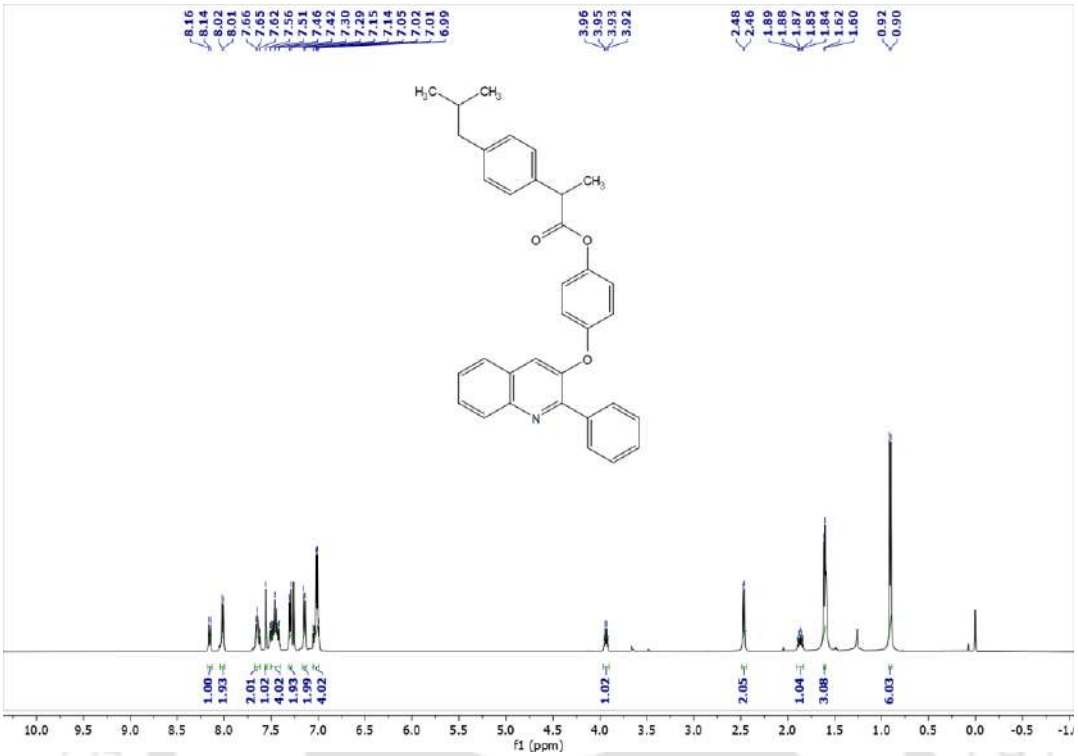

Figure S90: ^{1}H NMR Spectrum of **5.2v** ($CDCl_3$, 500 MHz, 298 K)

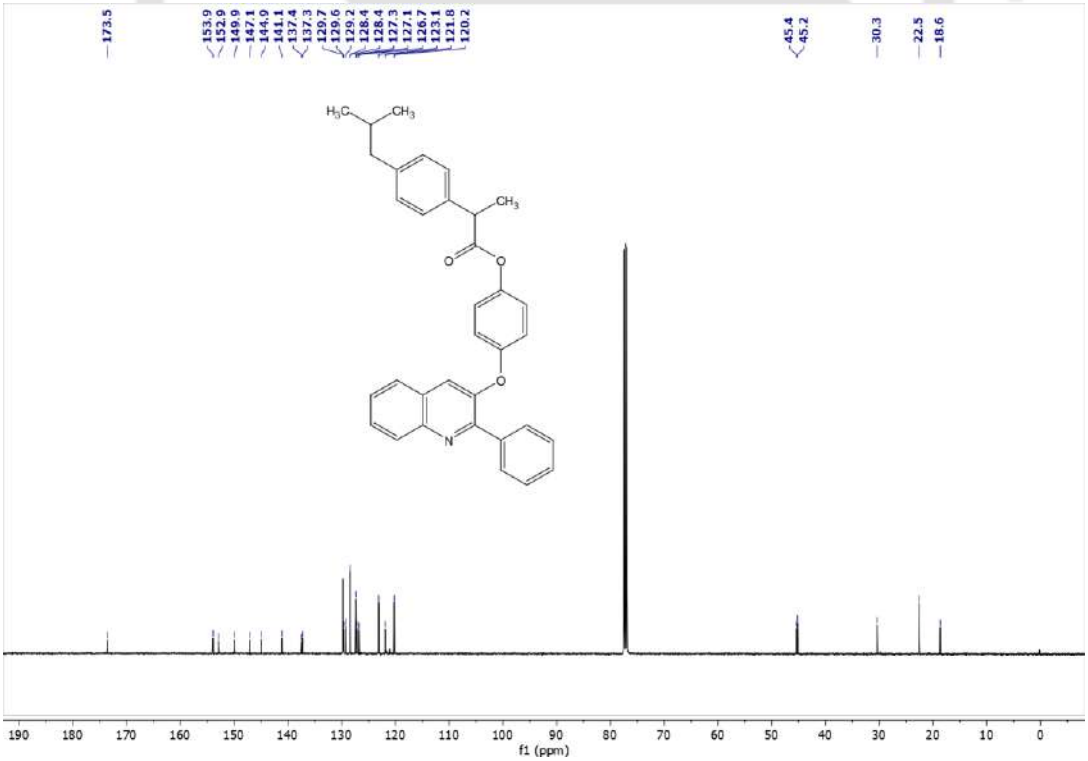

Figure S91: $^{13}C\{^{1}H\}$ NMR Spectrum of **5.2v** ($CDCl_3$, 126 MHz, 298 K)

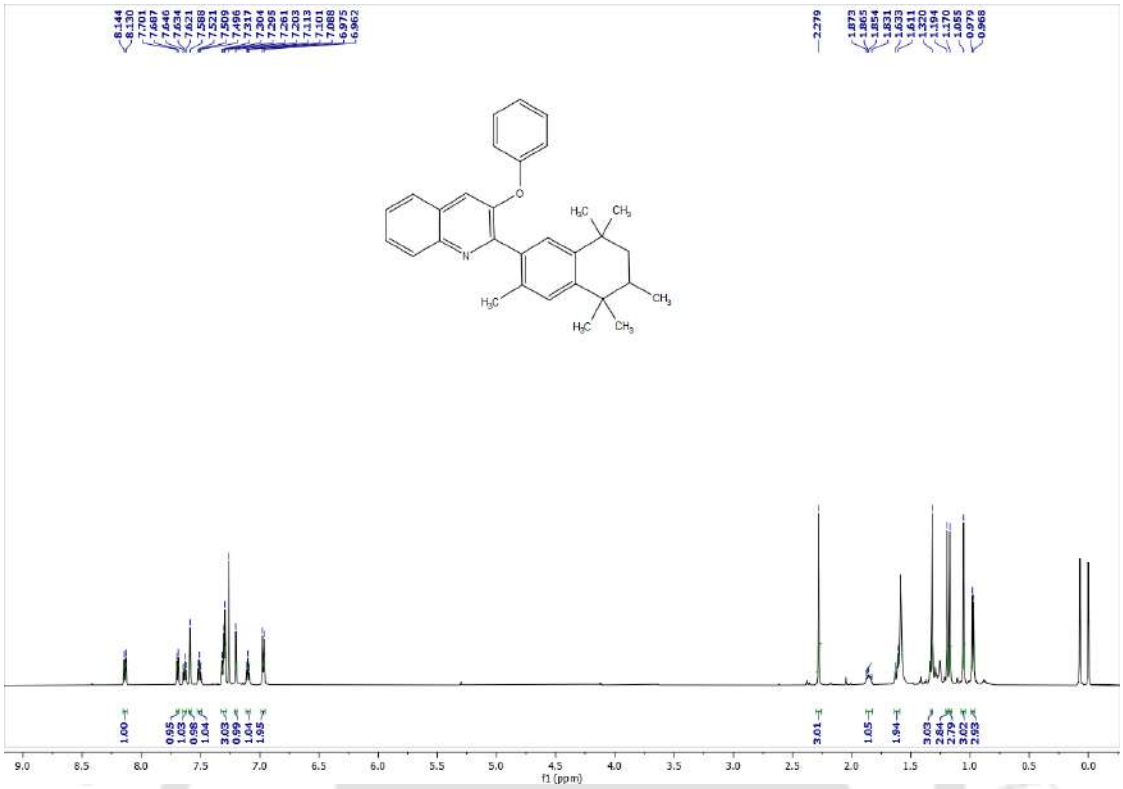

Figure S92: ^{1}H NMR Spectrum of **5.2am** ($CDCl_3$, 600 MHz, 298 K)

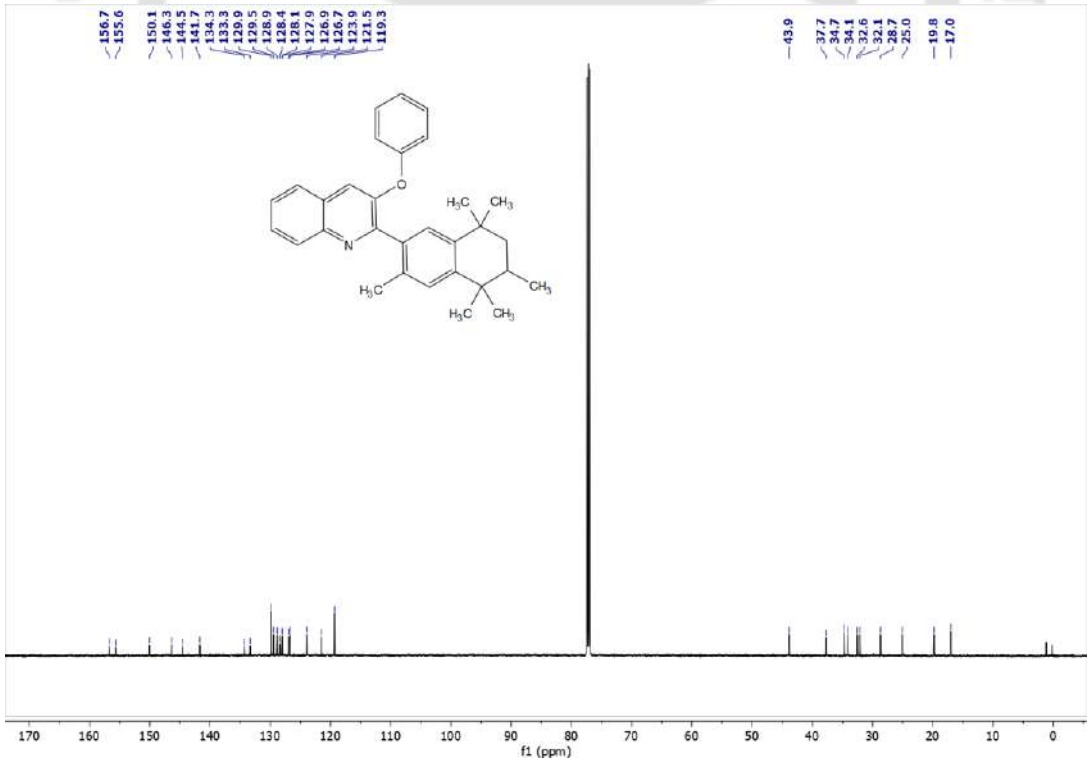

Figure S93: $^{13}C\{^{1}H\}$ NMR Spectrum of **5.2am** ($CDCl_3$, 151 MHz, 298 K)

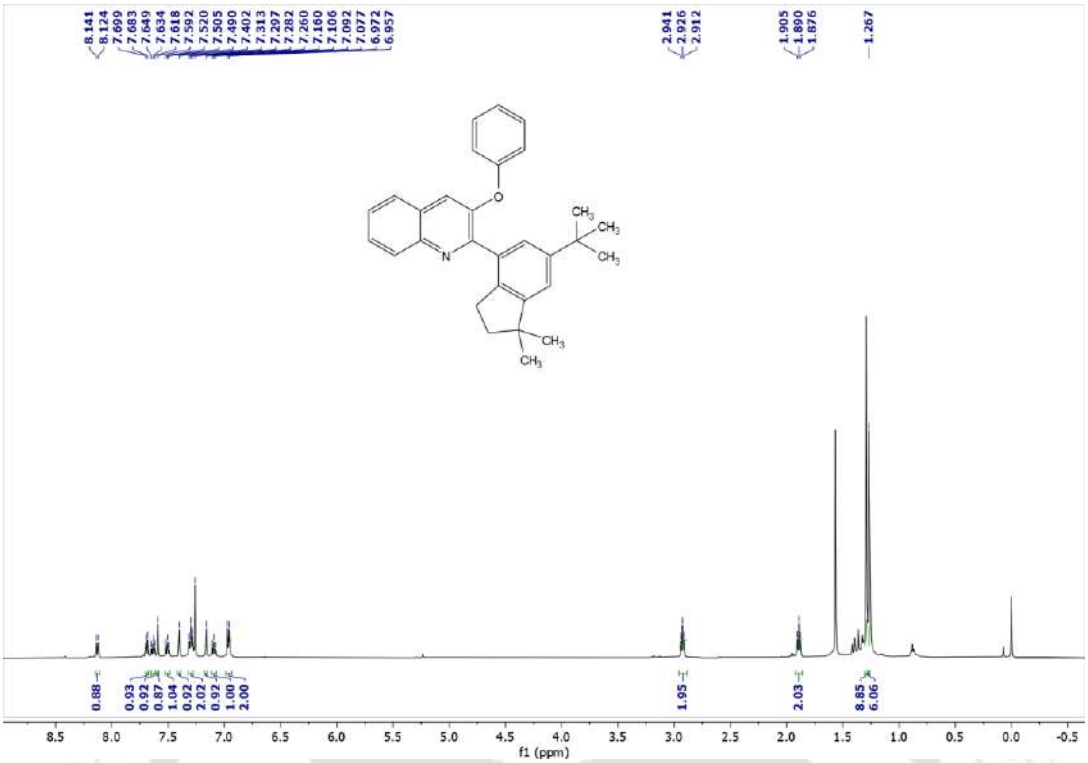

Figure S94: ^{1}H NMR Spectrum of **5.2an** ($CDCl_3$, 500 MHz, 298 K)

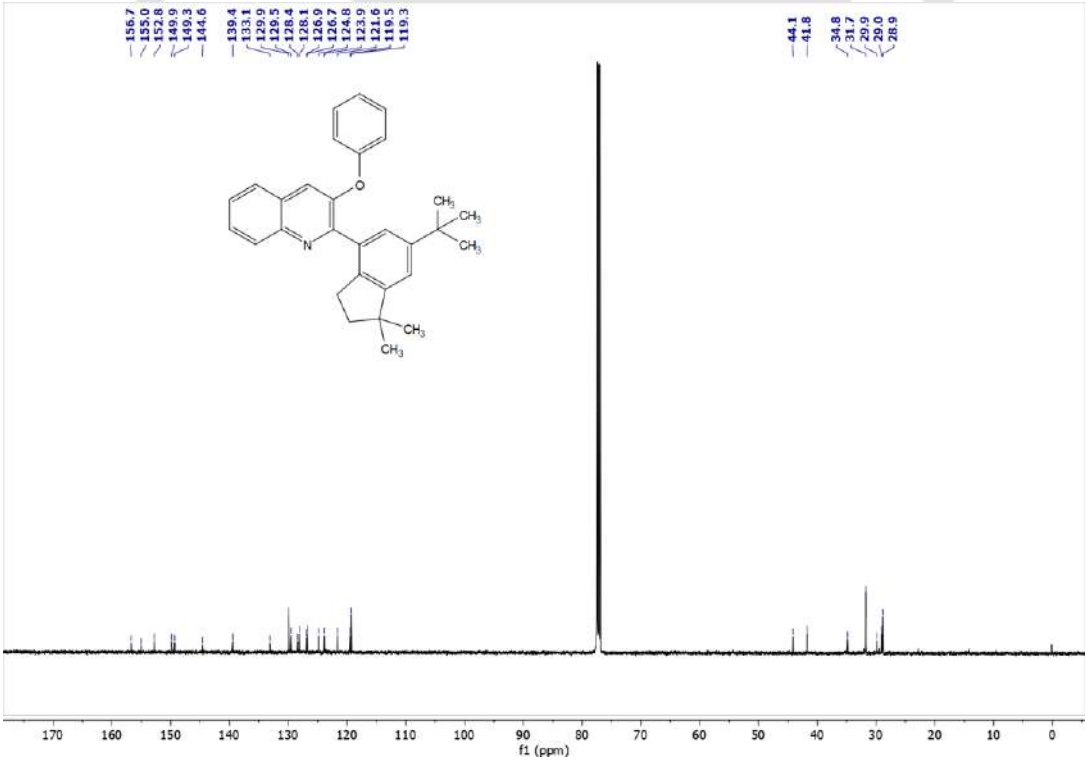

Figure S95: $^{13}C\{^{1}H\}$ NMR Spectrum of **5.2an** ($CDCl_3$, 126 MHz, 298 K)

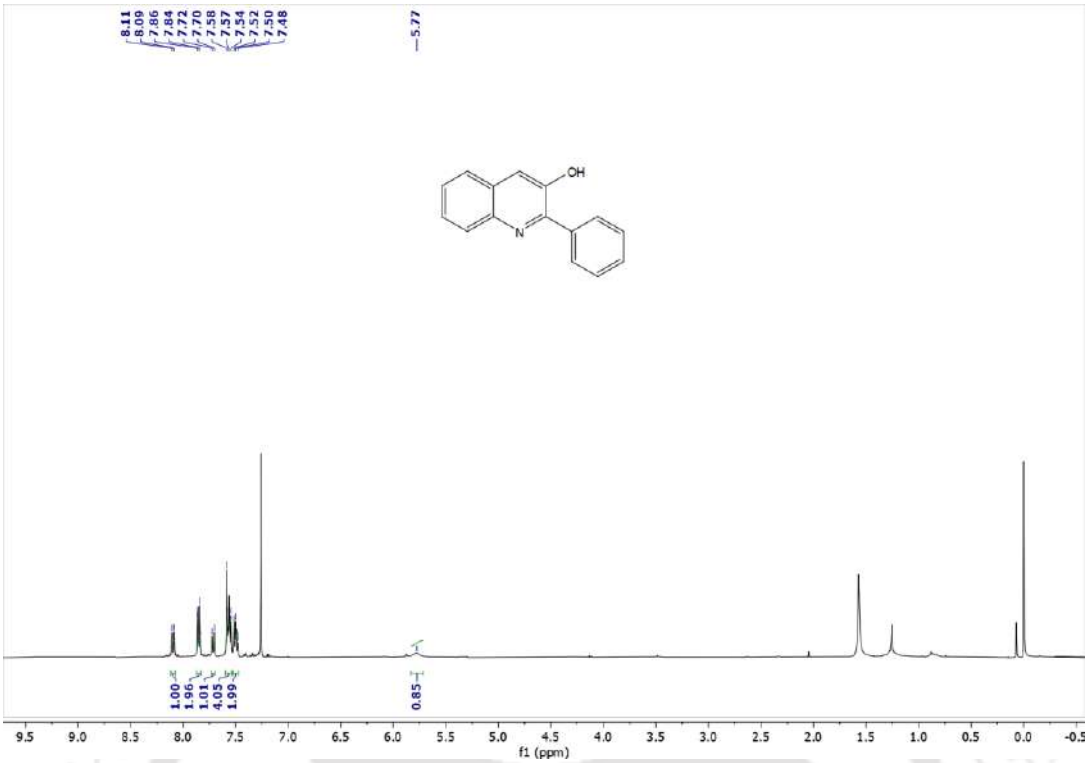

Figure S96: ^{1}H NMR Spectrum of **5.3a** ($CDCl_3$, 400 MHz, 298 K)

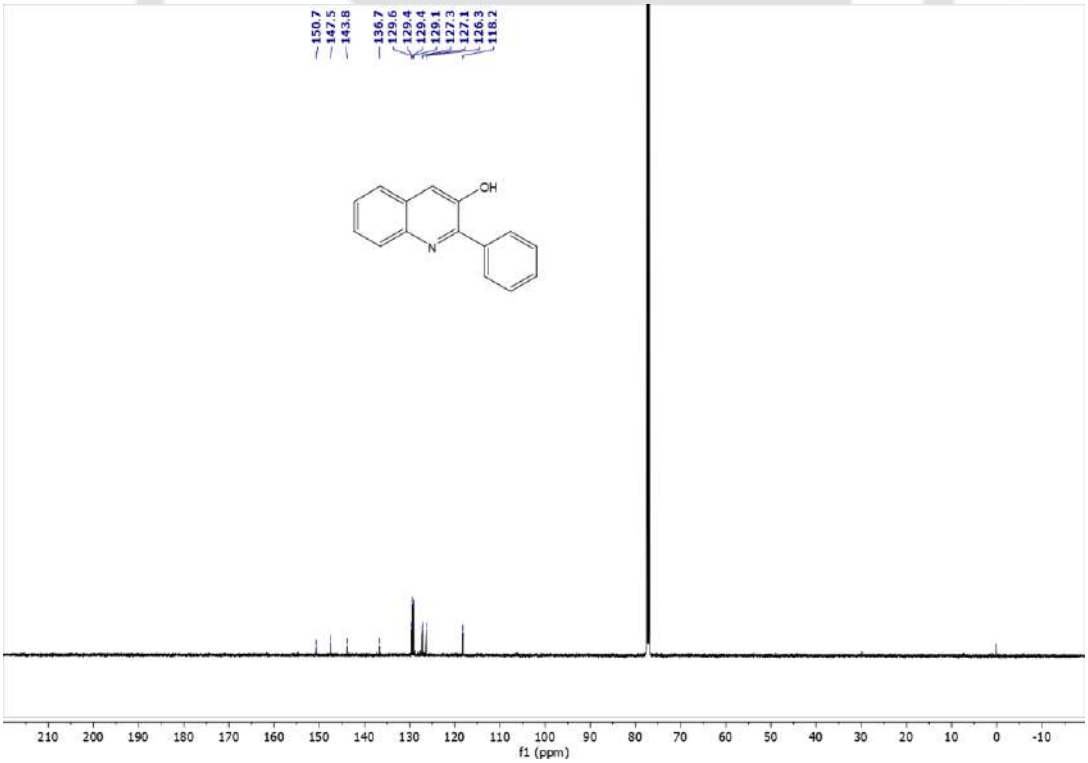

Figure S97: $^{13}C\{^{1}H\}$ NMR Spectrum of **5.3a** ($CDCl_3$, 126 MHz, 298 K)

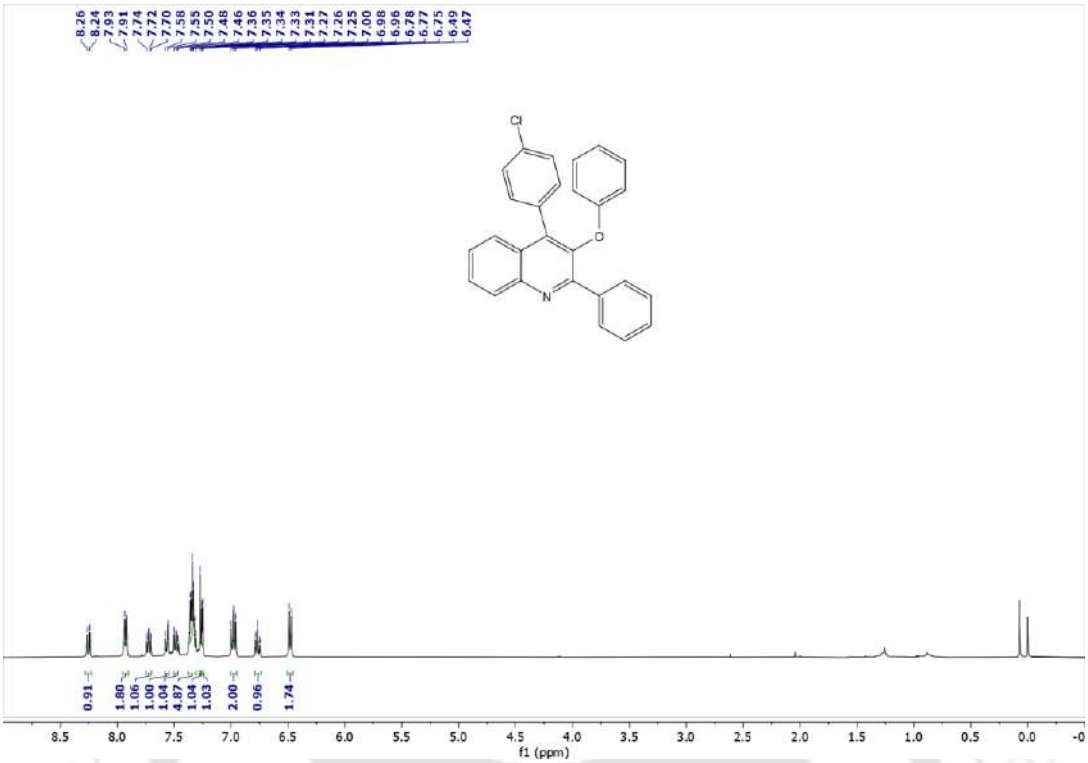

Figure S98: ^{1}H NMR Spectrum of **5.5i** ($CDCl_3$, 400 MHz, 298 K)

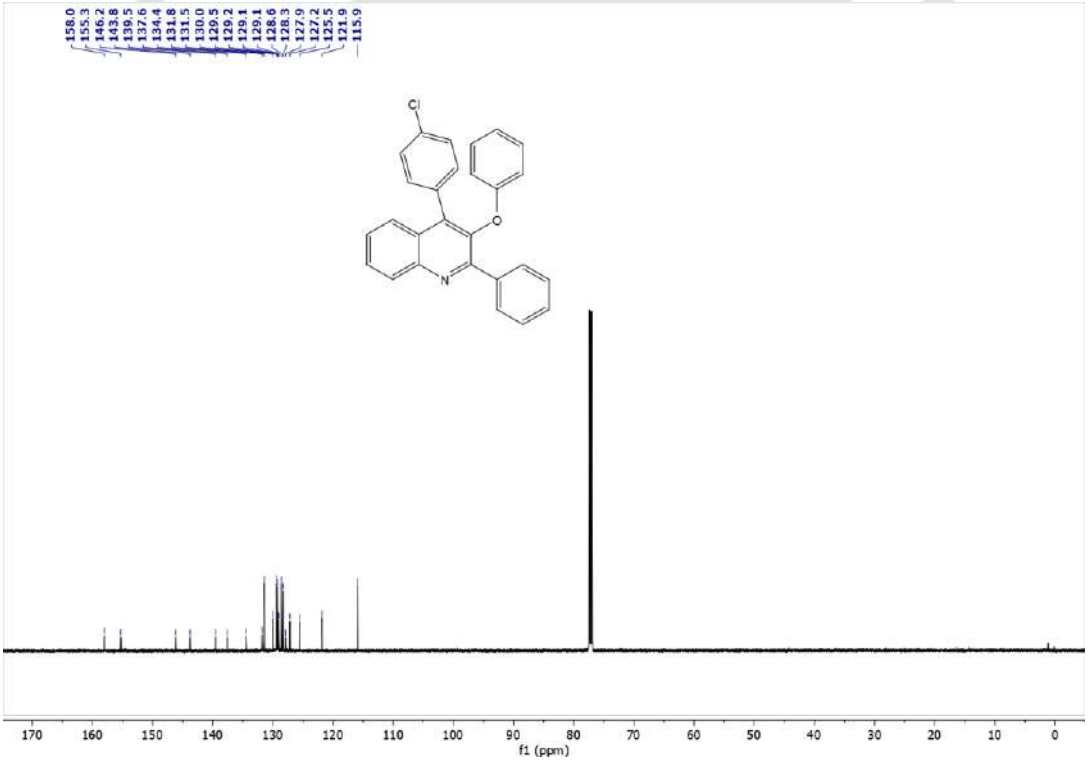

Figure S99: $^{13}C\{^{1}H\}$ NMR Spectrum of **5.5i** ($CDCl_3$, 151 MHz, 298 K)

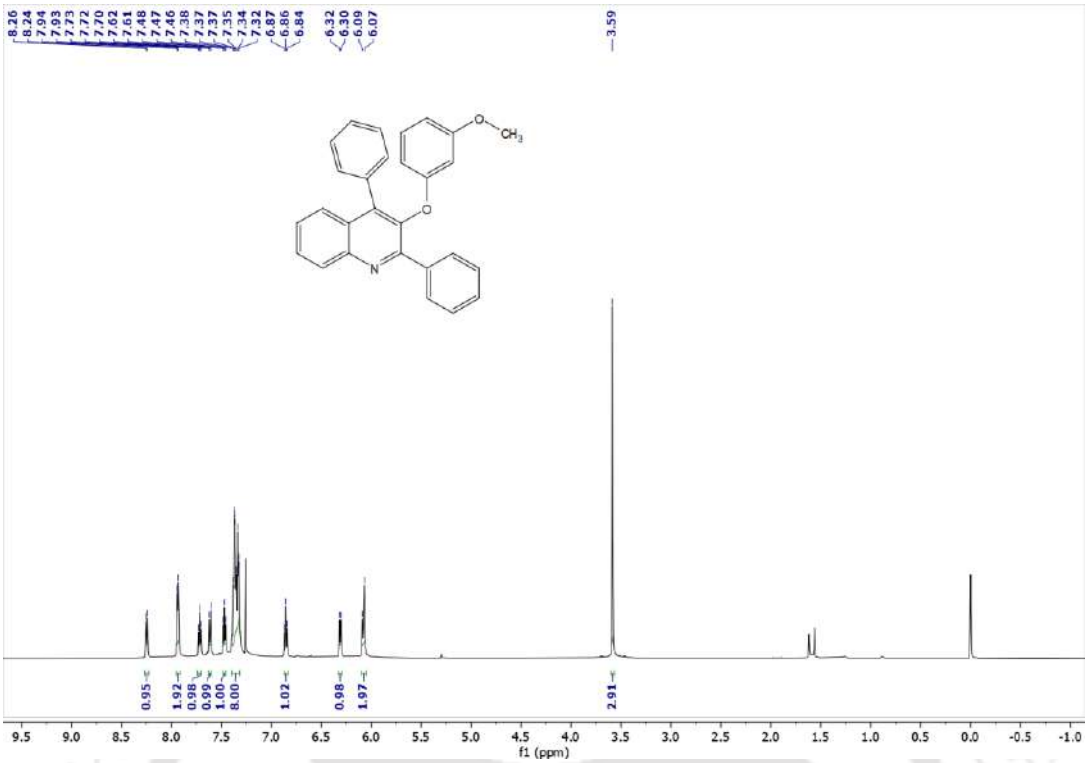

Figure S100: ^{1}H NMR Spectrum of **5.5j** ($CDCl_3$, 600 MHz, 298 K)

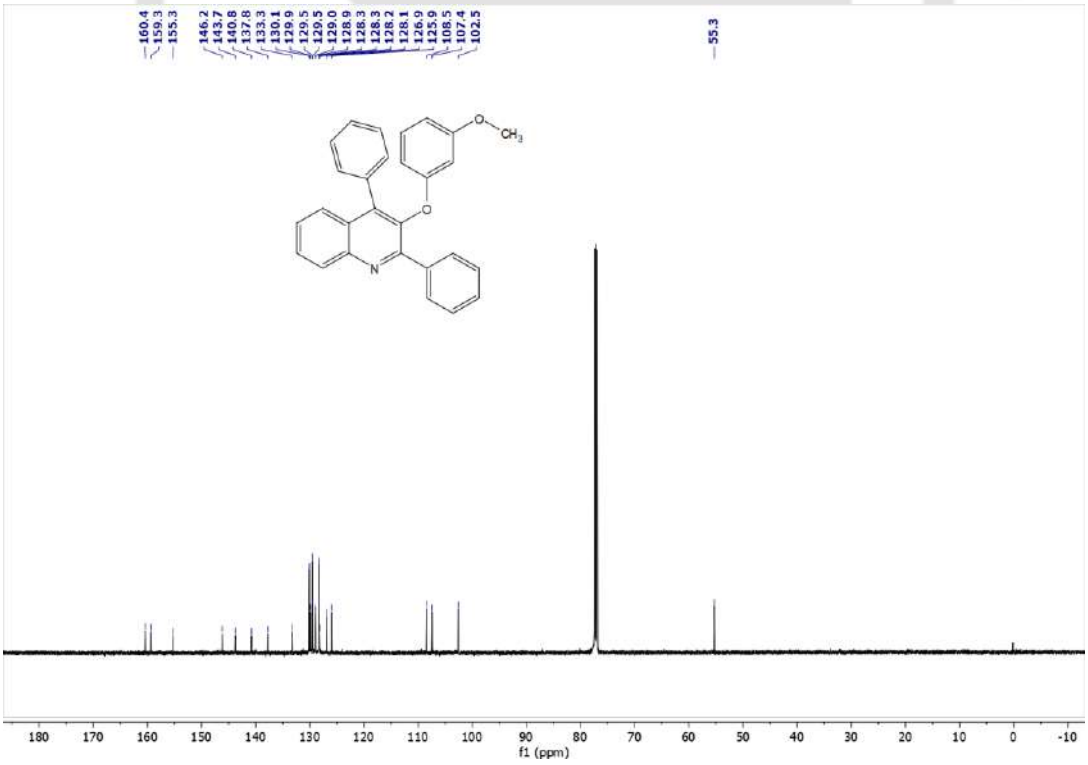

Figure S101: $^{13}C\{^{1}H\}$ NMR Spectrum of **5.5j** ($CDCl_3$, 151 MHz, 298 K)

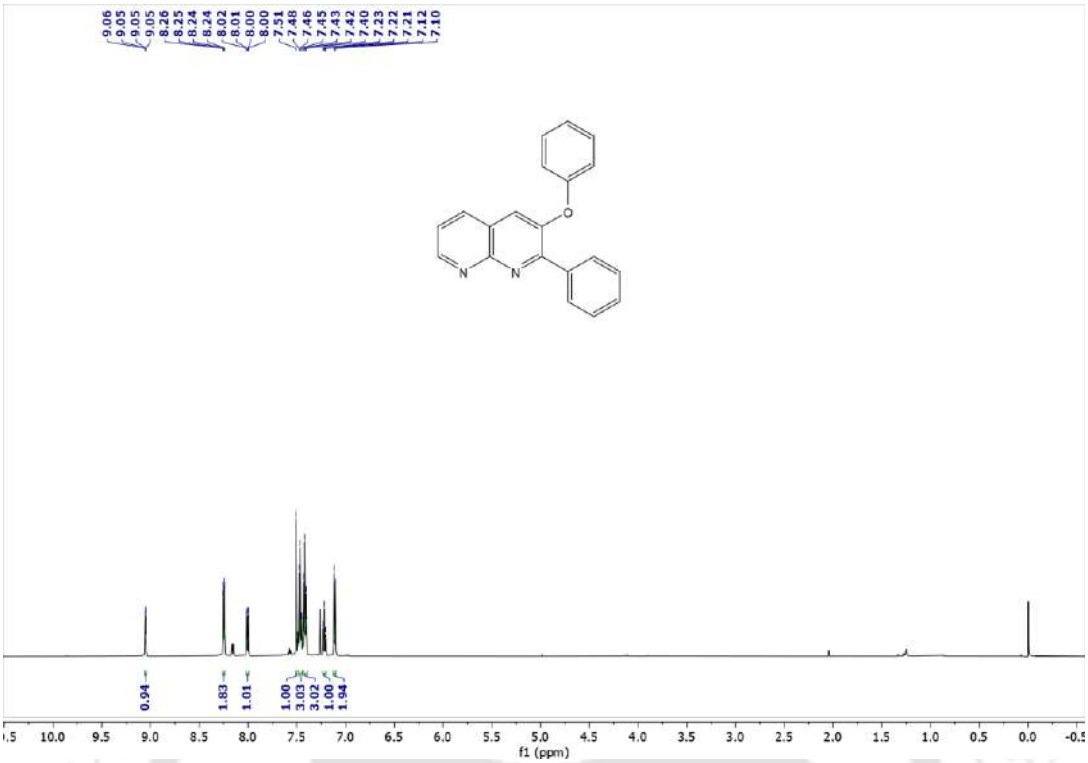

Figure S102: ^{1}H NMR Spectrum of **5.5k** ($CDCl_3$, 600 MHz, 298 K)

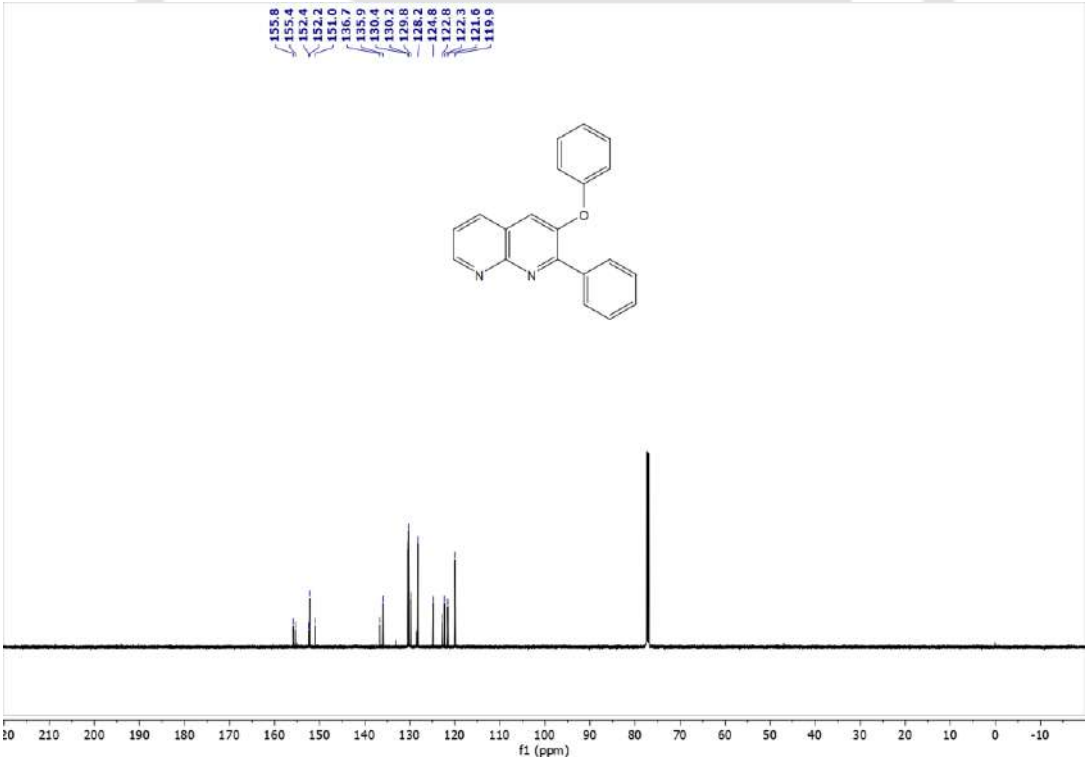

Figure S103: $^{13}C\{^{1}H\}$ NMR Spectrum of **5.5k** ($CDCl_3$, 151 MHz, 298 K)

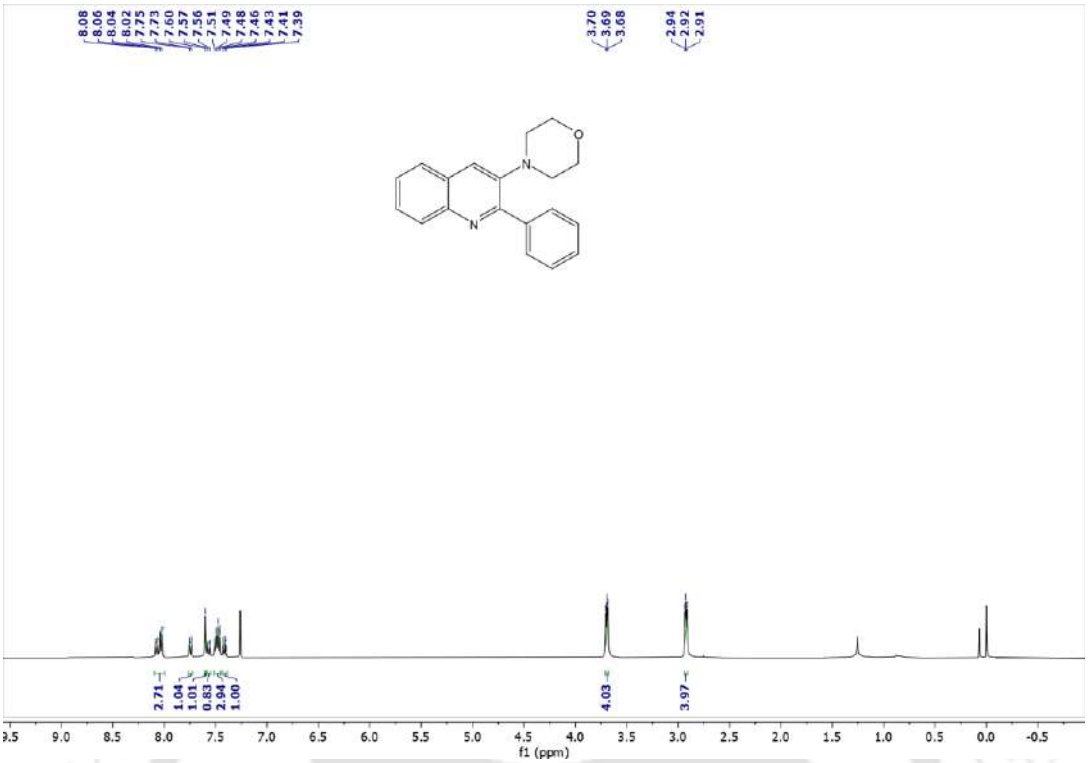

Figure S104: ^{1}H NMR Spectrum of **5.7b** ($CDCl_3$, 400 MHz, 298 K)

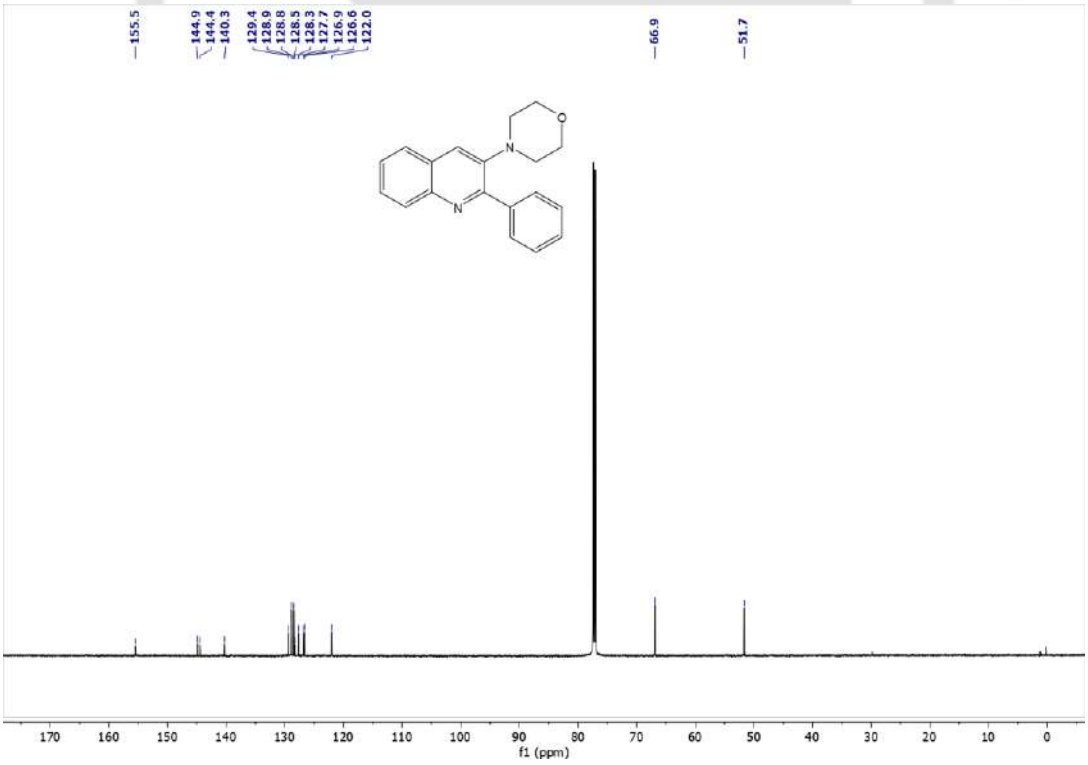

Figure S105: $^{13}C\{^{1}H\}$ NMR Spectrum of **5.7b** ($CDCl_3$, 151 MHz, 298 K)

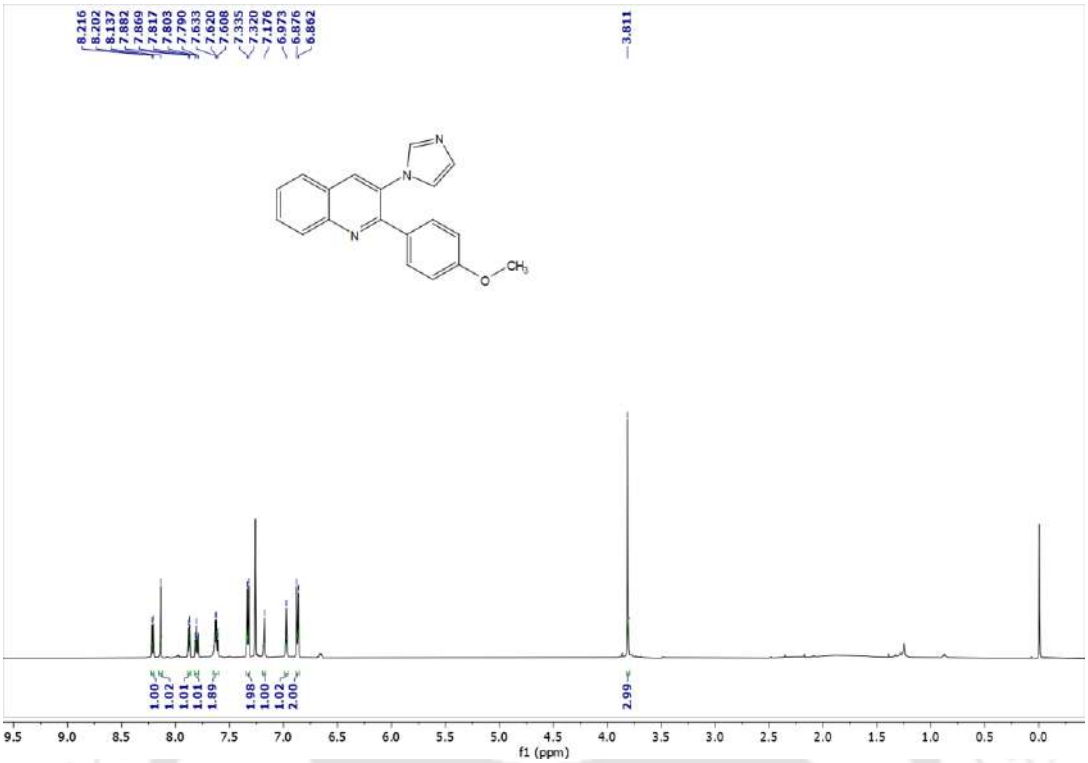

Figure S106: ^{1}H NMR Spectrum of **5.7e** ($CDCl_3$, 600 MHz, 298 K)

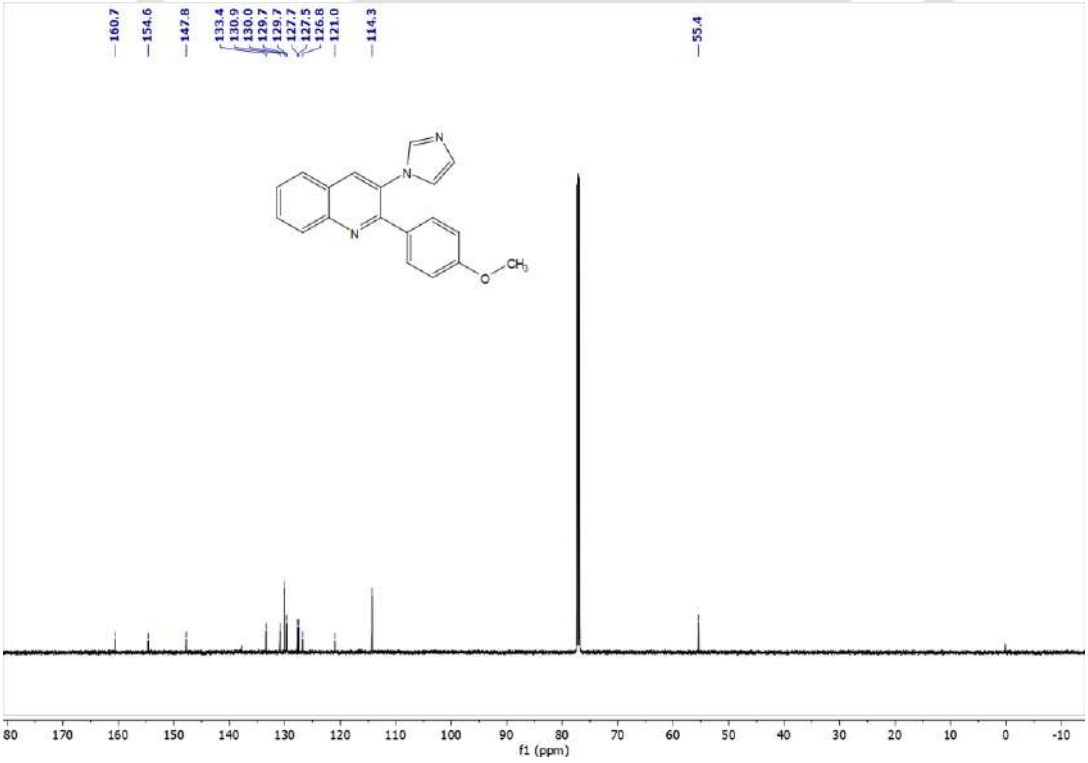

Figure S107: $^{13}C\{^{1}H\}$ NMR Spectrum of **5.7e** ($CDCl_3$, 151 MHz, 298 K)

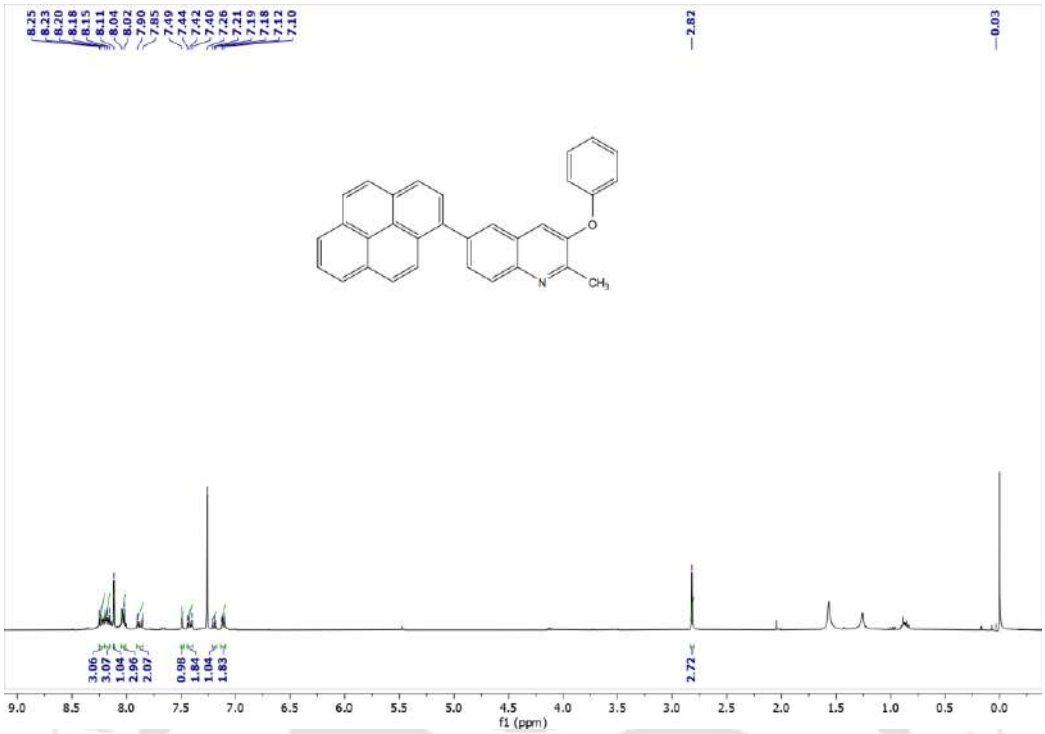

Figure S108: ^{1}H NMR Spectrum of **5.8** ($CDCl_3$, 400 MHz, 298 K)

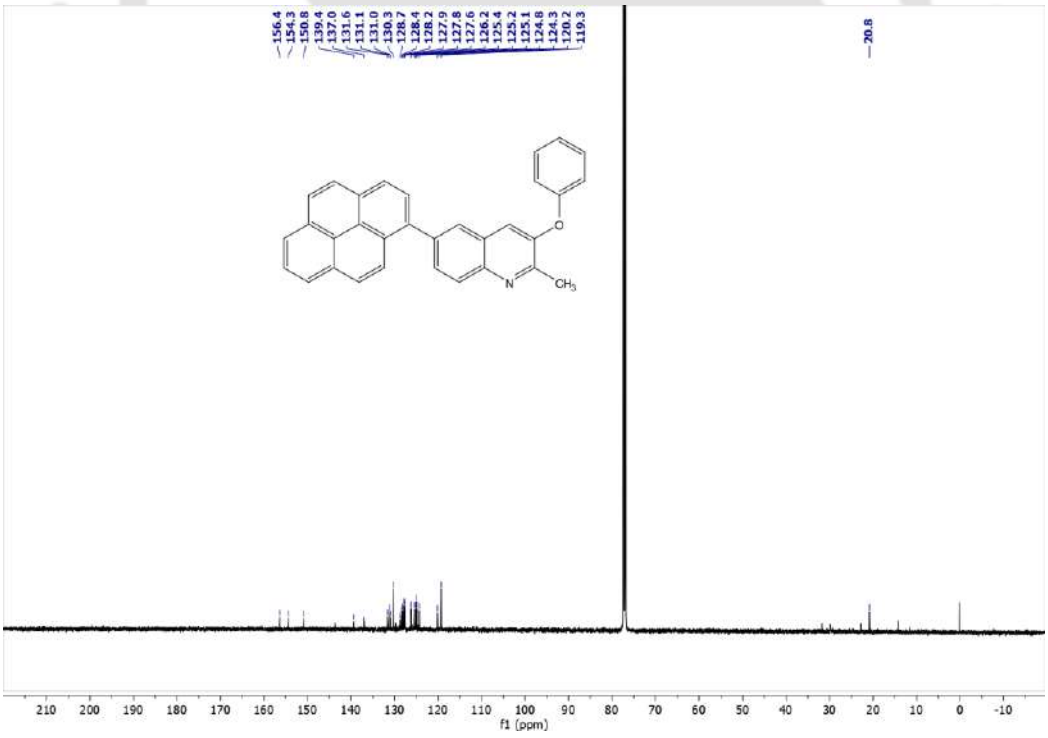

Figure S109: $^{13}C\{^{1}H\}$ NMR Spectrum of **5.8** ($CDCl_3$, 126 MHz, 298 K)

The supporting information and all other product spectra for chapter 5 is available at https://doi.org/10.1039/D4QO01089B

Annexure V

^{1}H, ^{13}C, and ^{19}F NMR spectra representative compounds (*Chapter 6*)

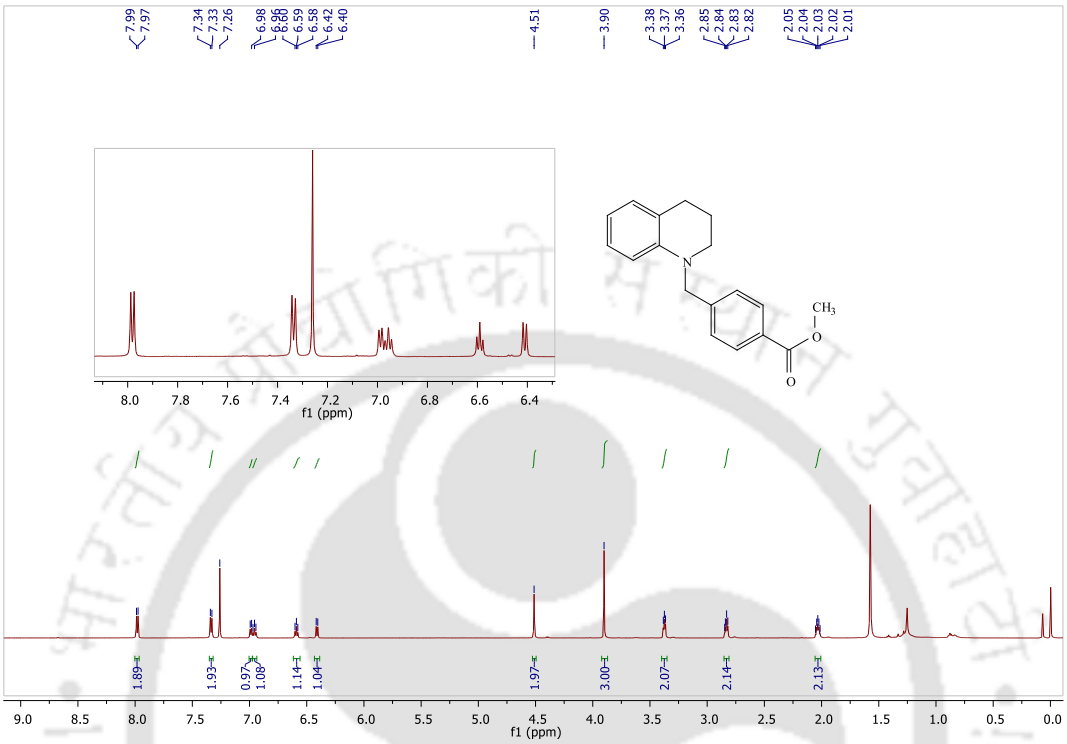

Figure S110: ^{1}H NMR Spectrum of **6.4i** ($CDCl_3$, 400 MHz, 298 K)

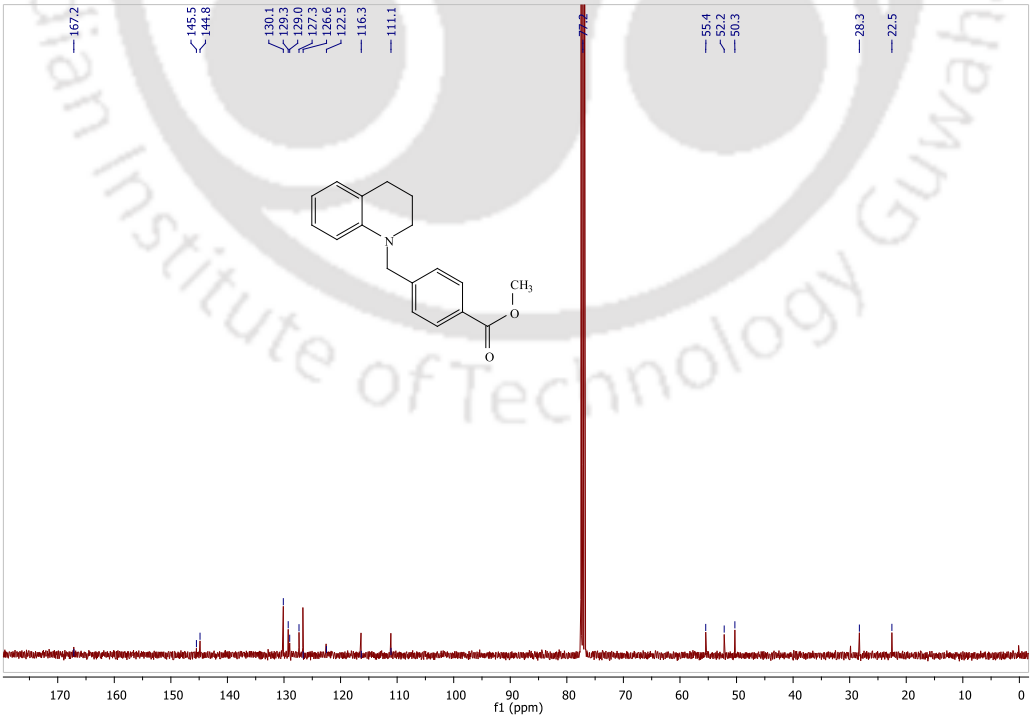

Figure S111: $^{13}C\{^{1}H\}$ NMR Spectrum of **6.4i** ($CDCl_3$, 151 MHz, 298 K)

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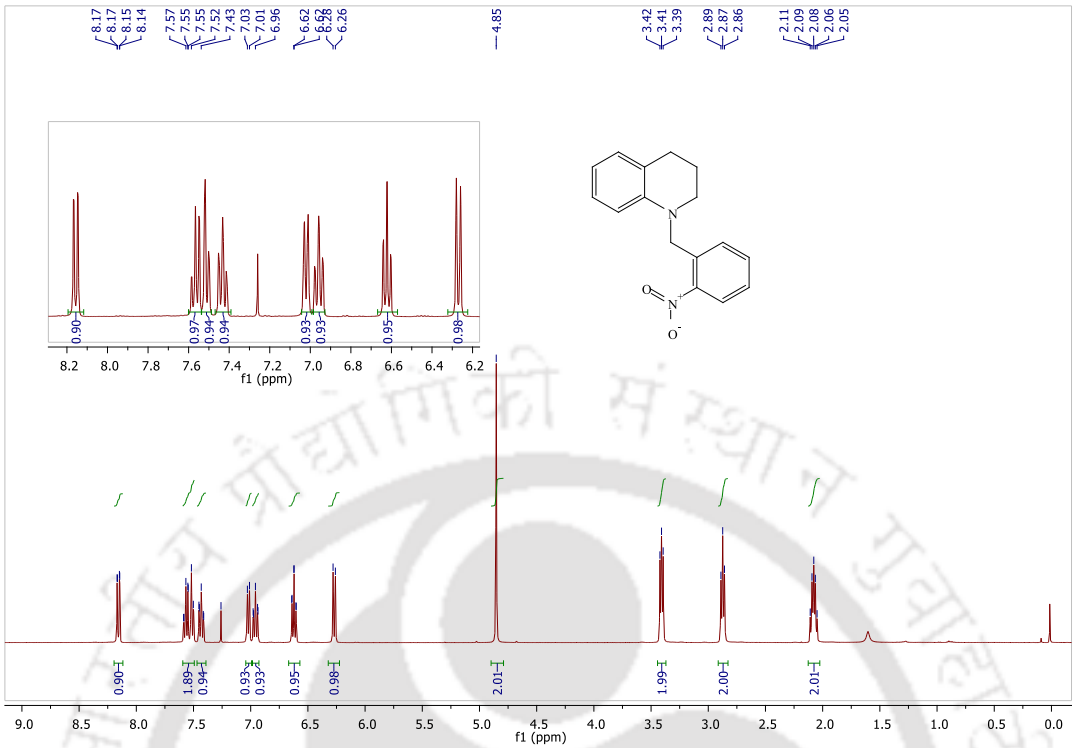

Figure S112: ^{1}H NMR Spectrum of **6.4o** ($CDCl_3$, 400 MHz, 298 K)

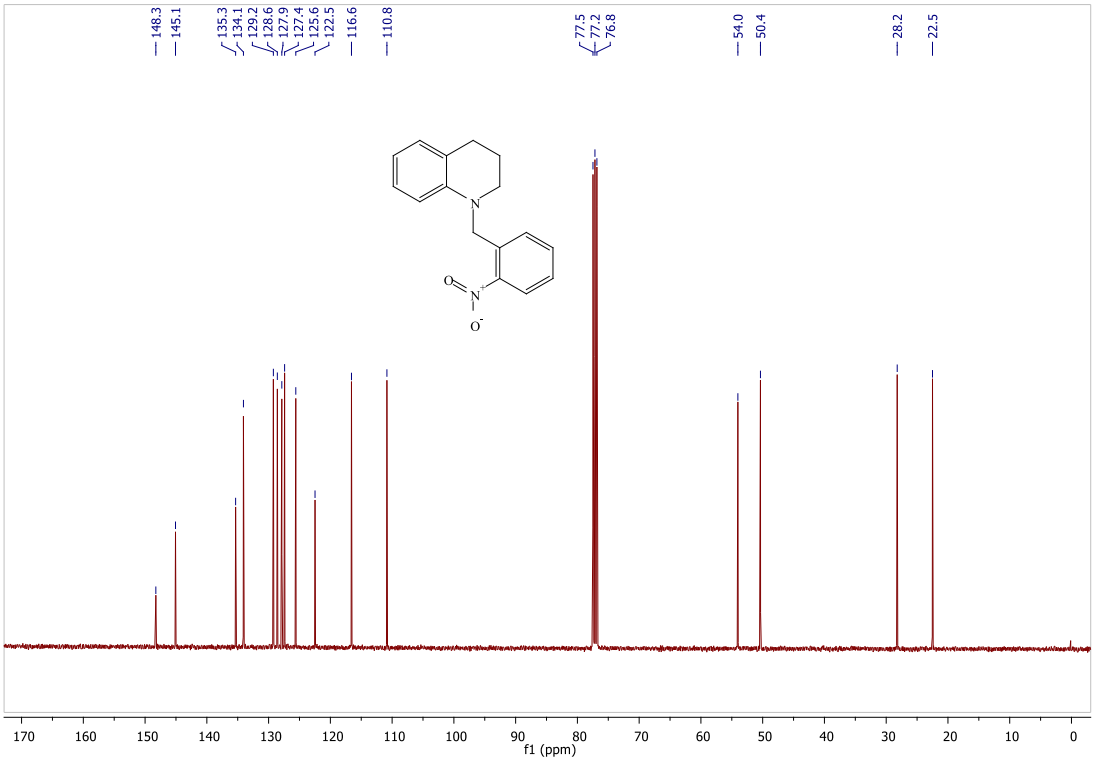

Figure S113: $^{13}C\{^{1}H\}$ NMR Spectrum of **6.4o** ($CDCl_3$, 101 MHz, 298 K)

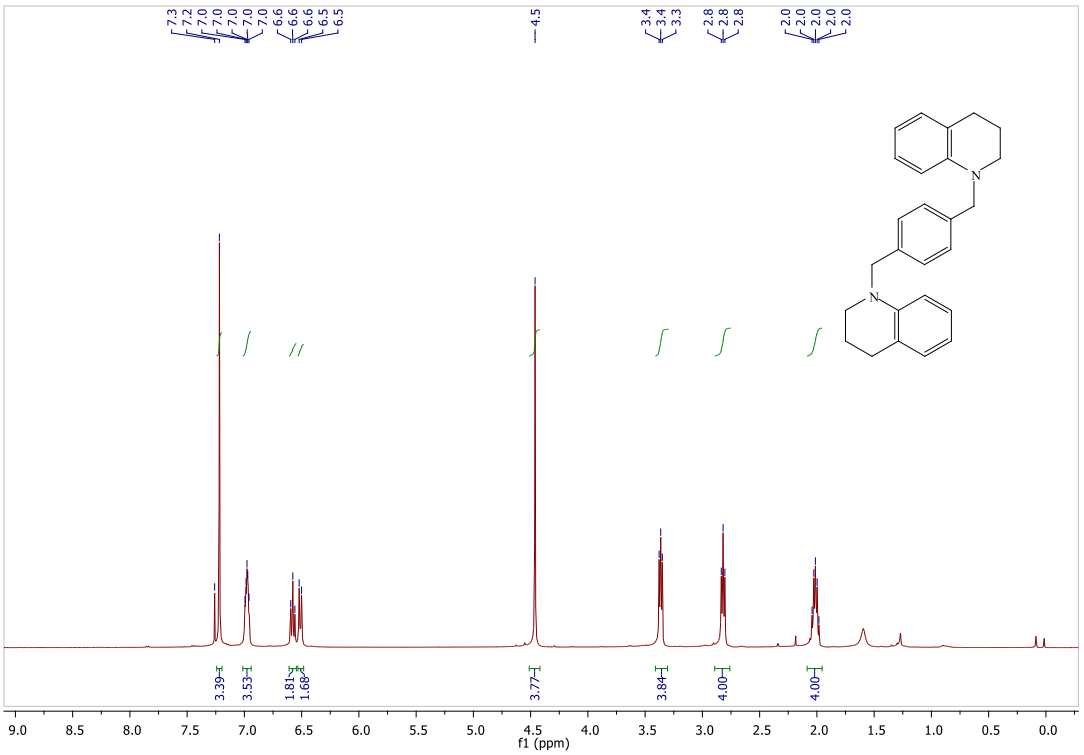

Figure S114: ^{1}H NMR Spectrum of **6.4af** ($CDCl_3$, 400 MHz, 298 K)

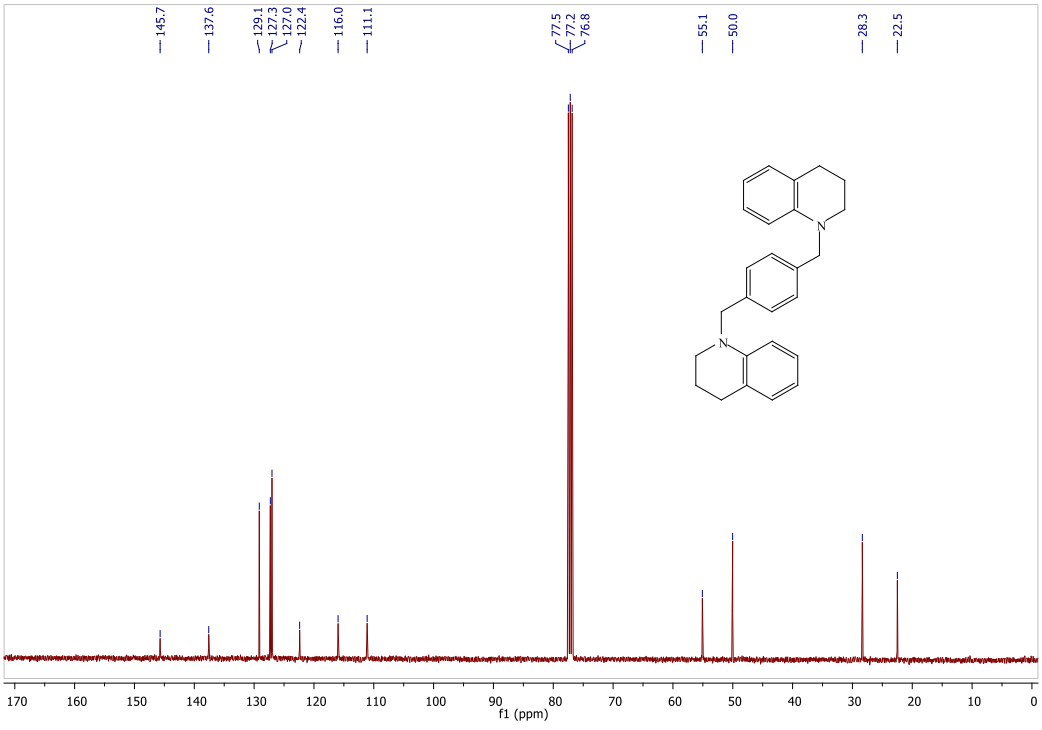

Figure S115: $^{13}C\{^{1}H\}$ NMR Spectrum of **6.4af** ($CDCl_3$, 101 MHz, 298 K)

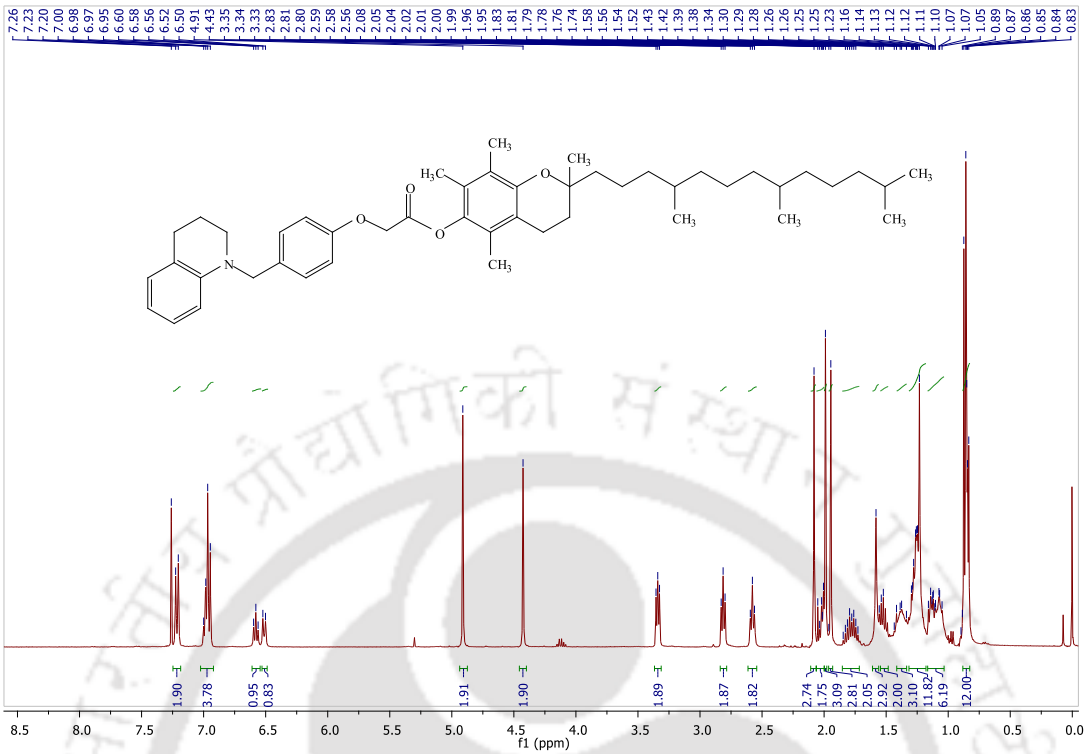

Figure S116: ^{1}H NMR Spectrum of **6.4ag** ($CDCl_3$, 400 MHz, 298 K)

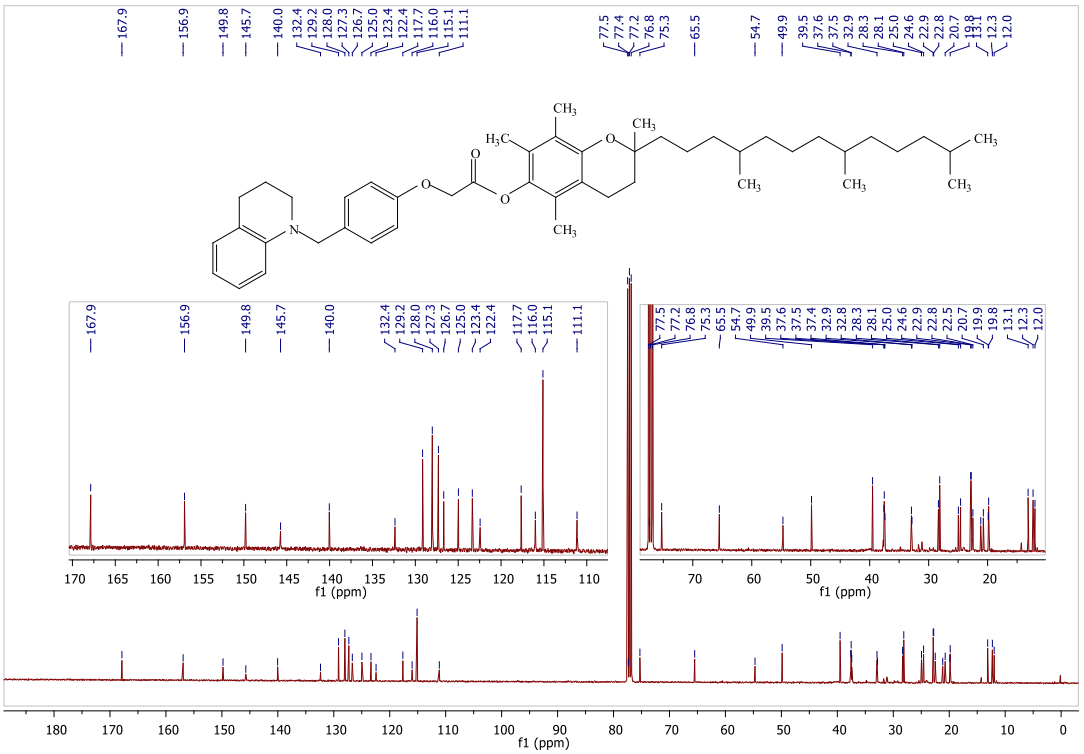

Figure S117: $^{13}C\{^{1}H\}$ NMR Spectrum of **6.4ag** ($CDCl_3$, 101 MHz, 298 K)

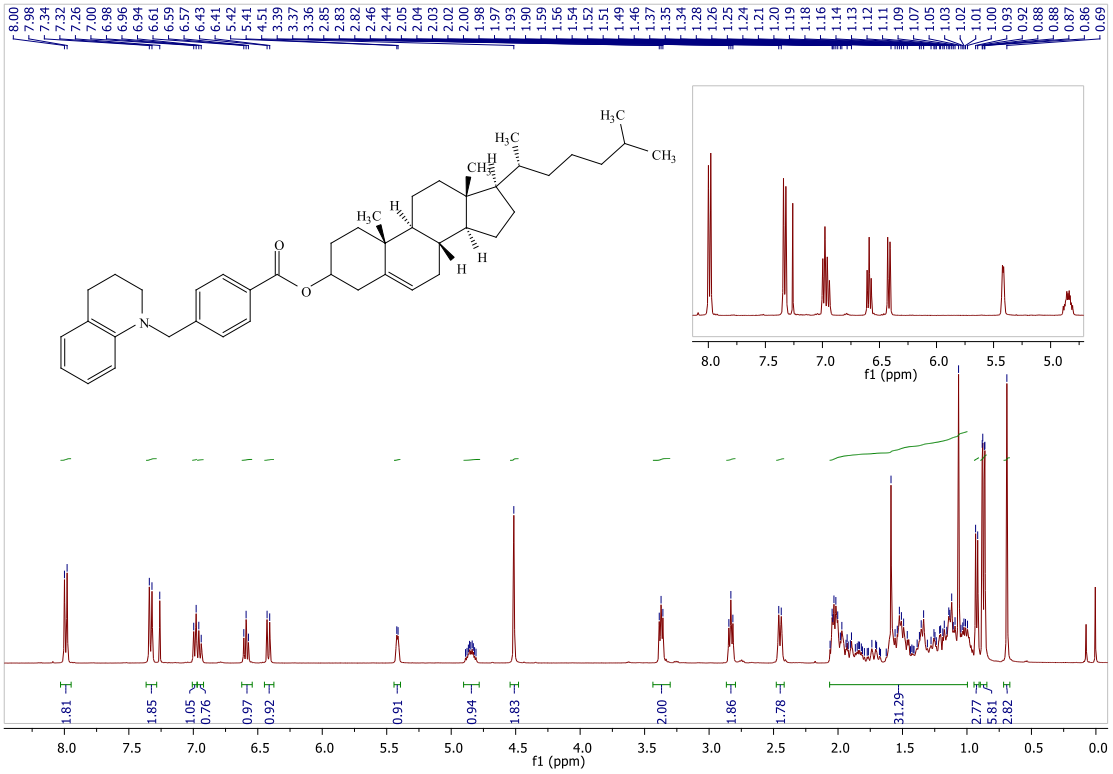

Figure S118: ^{1}H NMR Spectrum of **6.4ah** ($CDCl_3$, 400 MHz, 298 K)

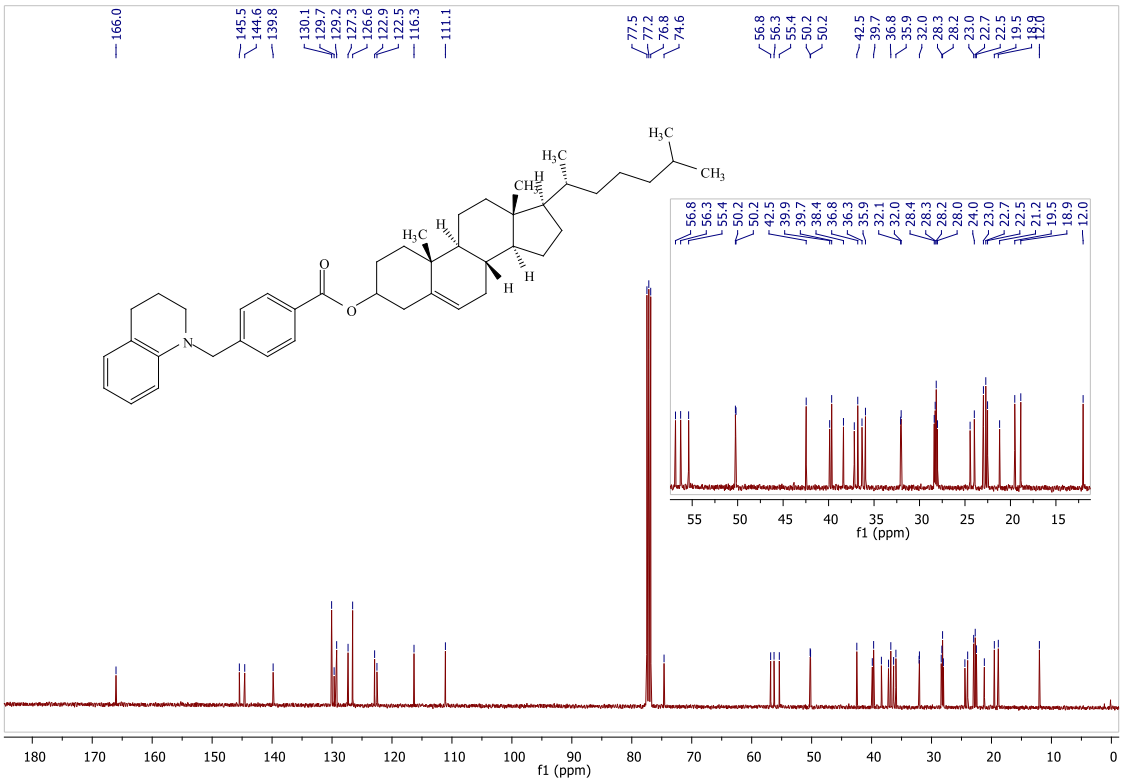

Figure S119: $^{13}C\{^{1}H\}$ NMR Spectrum of **6.4ah** ($CDCl_3$, 101 MHz, 298 K)

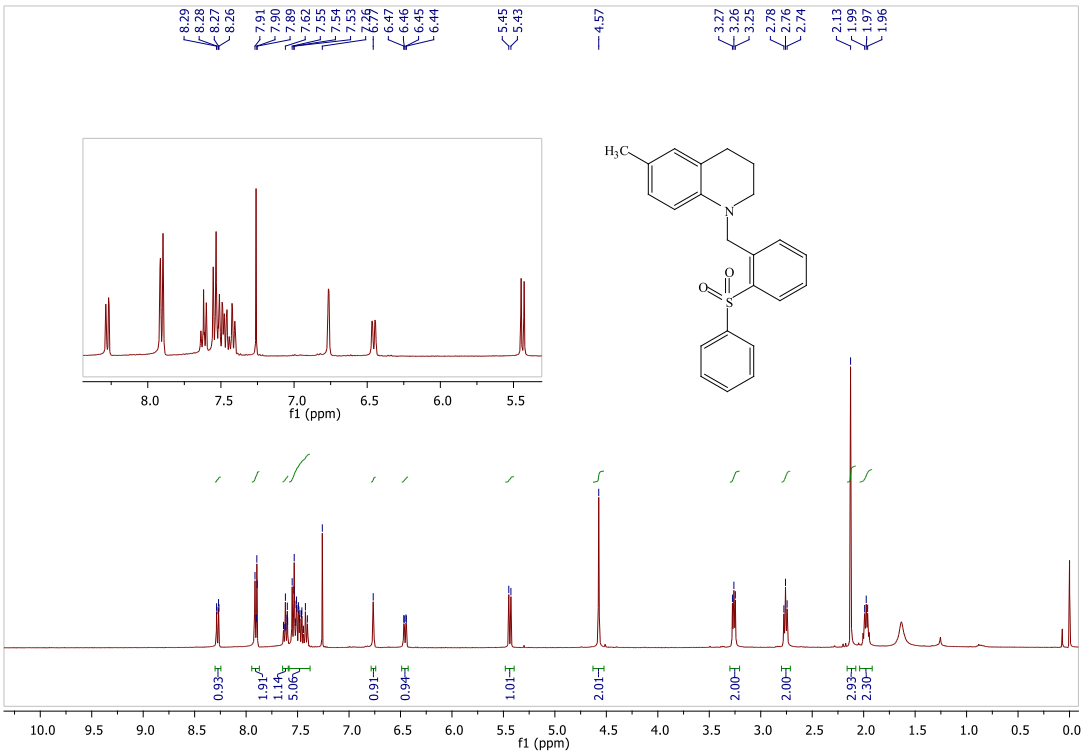

Figure S120: ^{1}H NMR Spectrum of **6.5k** ($CDCl_3$, 400 MHz, 298 K)

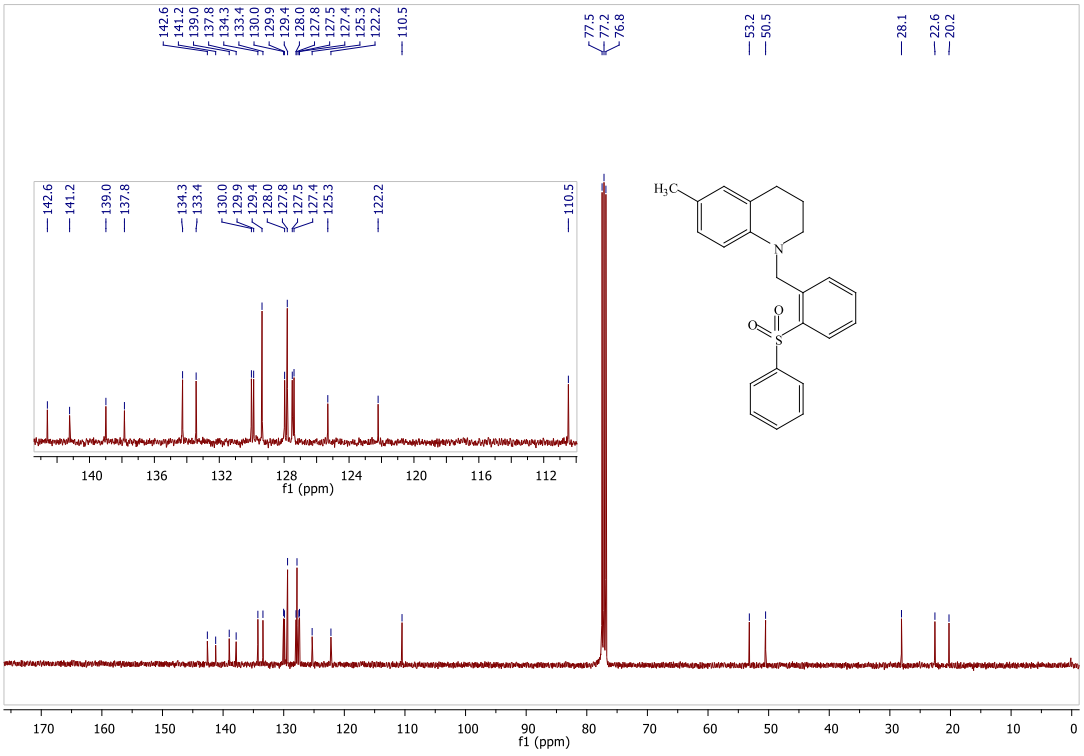

Figure S121: $^{13}C\{^{1}H\}$ NMR Spectrum of **6.5k** ($CDCl_3$, 101 MHz, 298 K)

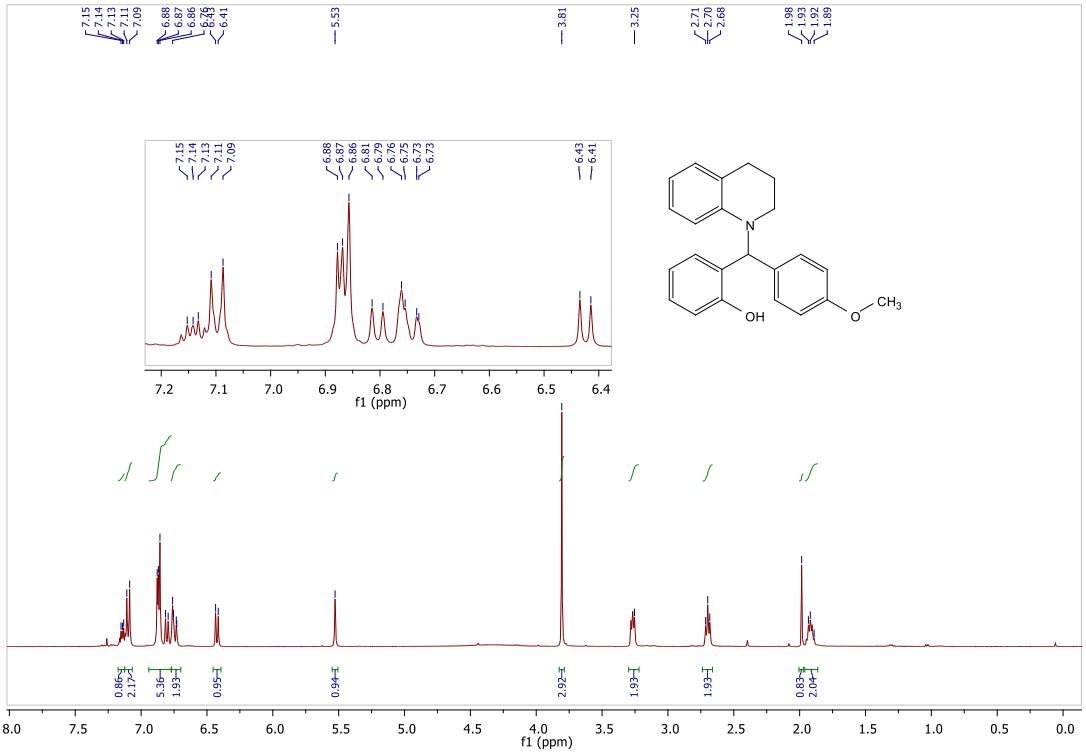

Figure S122: ^{1}H NMR Spectrum of **6.6a** ($CDCl_3$, 400 MHz, 298 K)

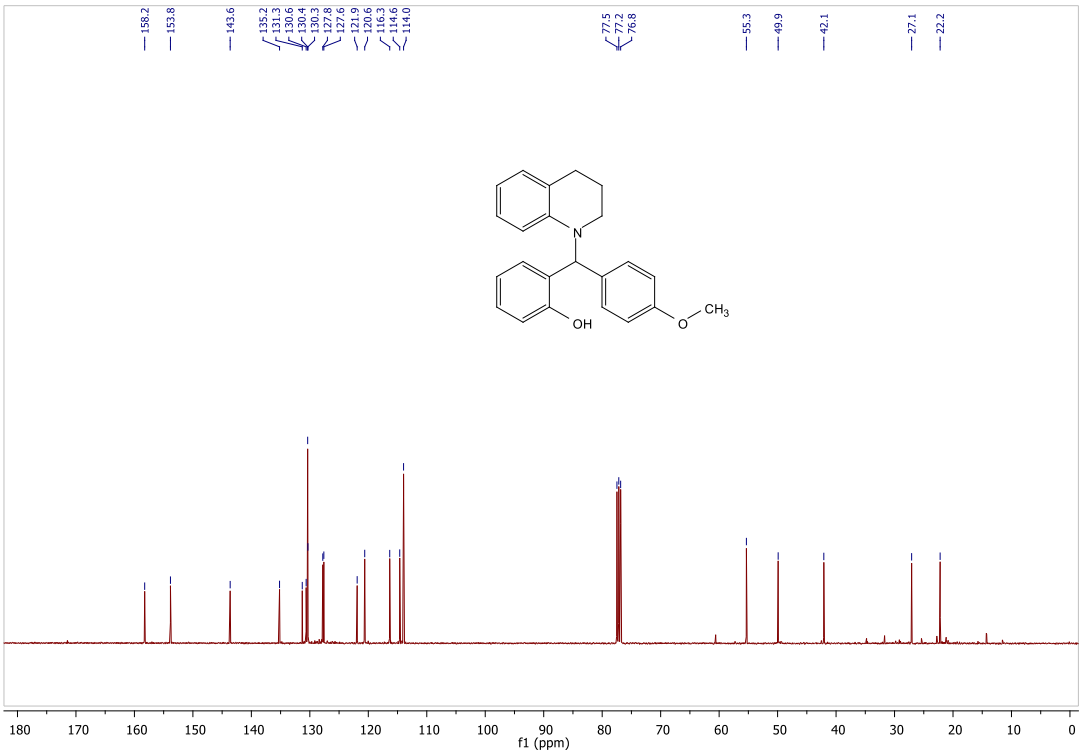

Figure S123: $^{13}C\{^{1}H\}$ NMR Spectrum of **6.6a** ($CDCl_3$, 101 MHz, 298 K)

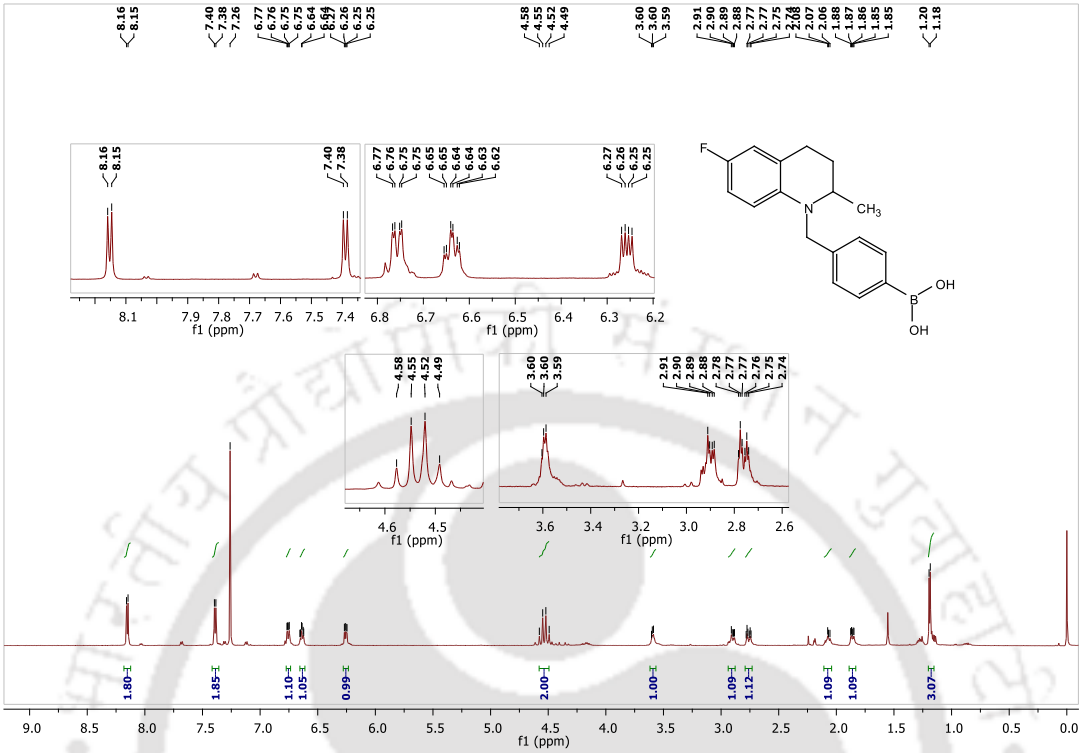

Figure S124: ^{1}H NMR Spectrum of **6.7a** ($CDCl_3$, 600 MHz, 298 K)

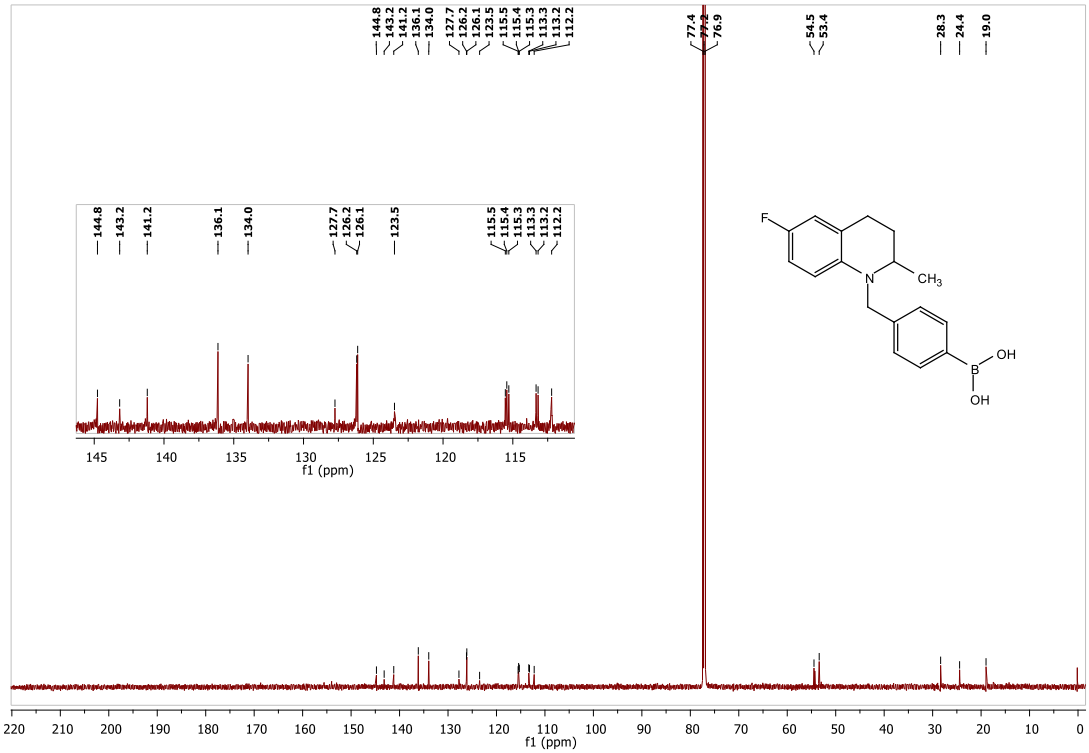

Figure S125: $^{13}C\{^{1}H\}$ NMR Spectrum of **6.7a** ($CDCl_3$, 151 MHz, 298 K)

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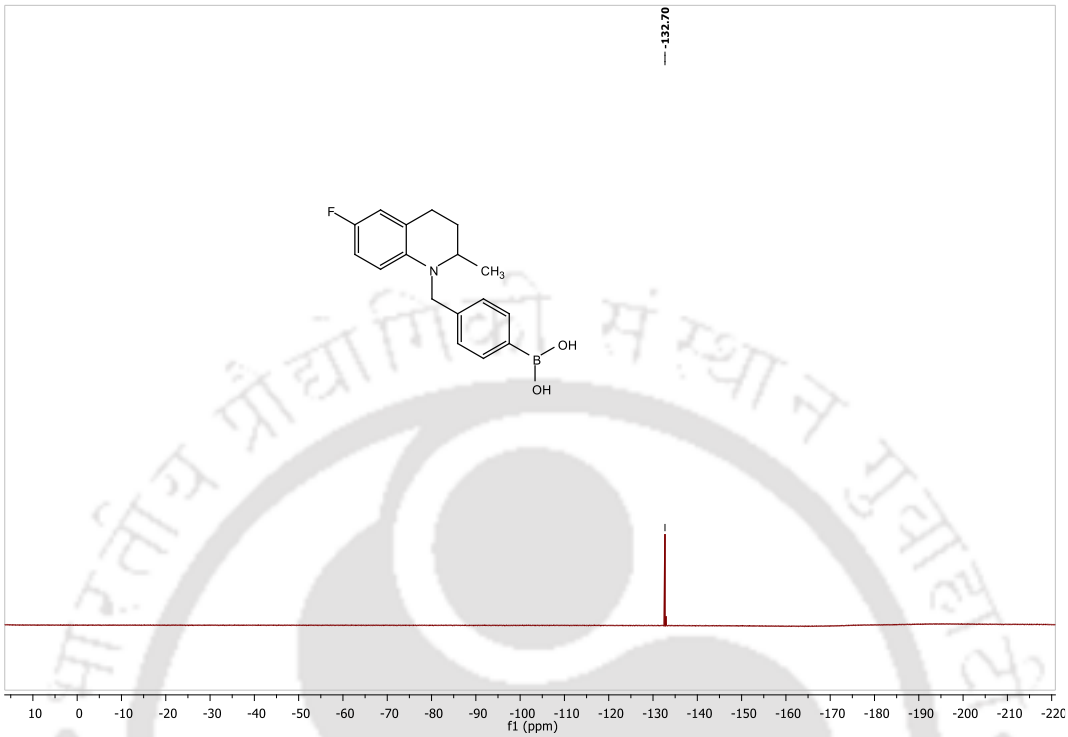

Figure S126: $^{19}F\{^{1}H\}$ NMR Spectrum of **6.7a** ($CDCl_3$, 565 MHz, 298 K)

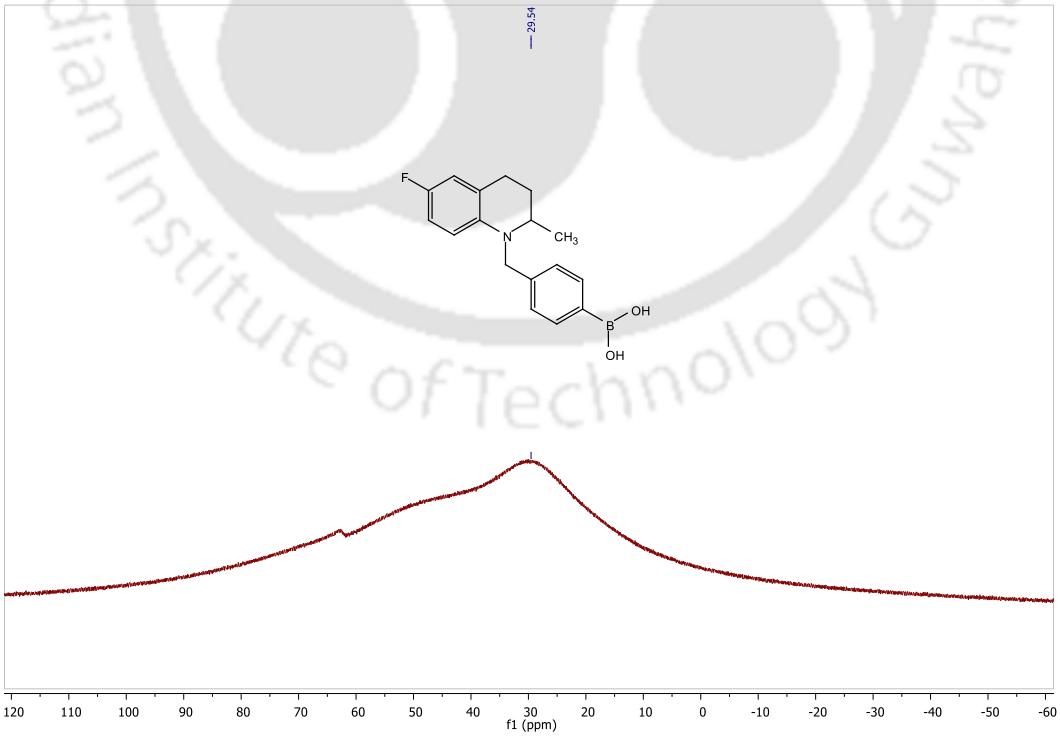

Figure S127: $^{11}B\{^{1}H\}$ NMR Spectrum of **6.7a** ($CDCl_3$, 193 MHz, 298 K)

TH-3606_186122027

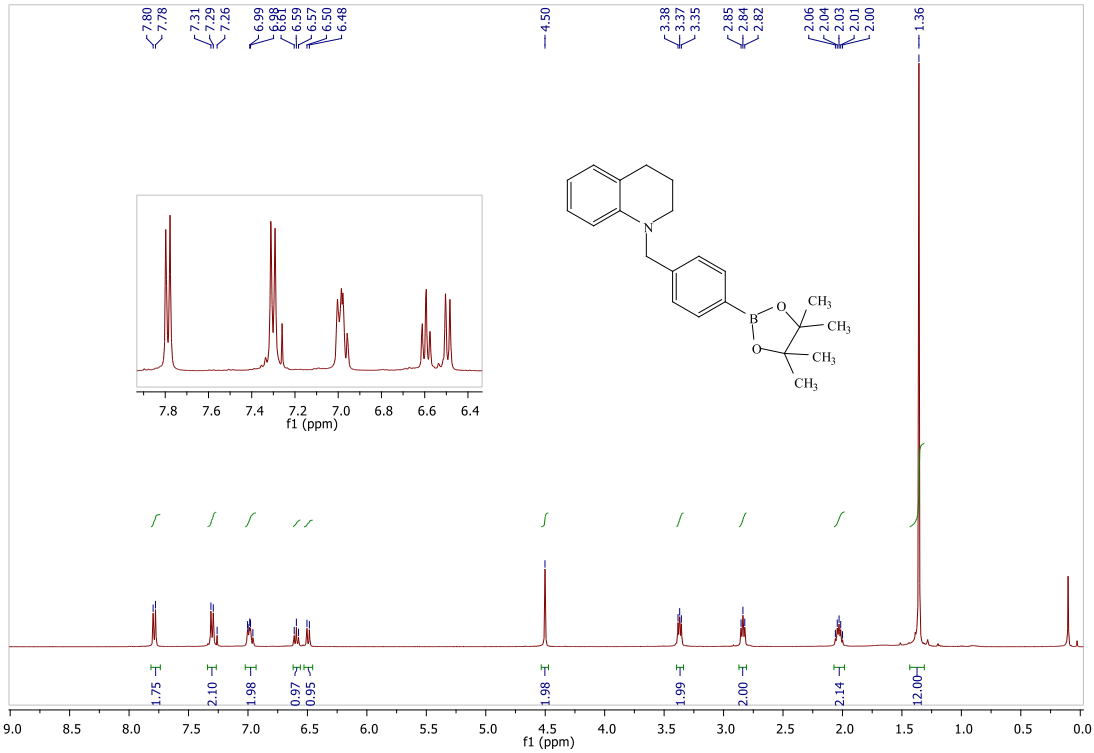

Figure S128: ^{1}H NMR Spectrum of **6.7b** ($CDCl_3$, 400 MHz, 298 K)

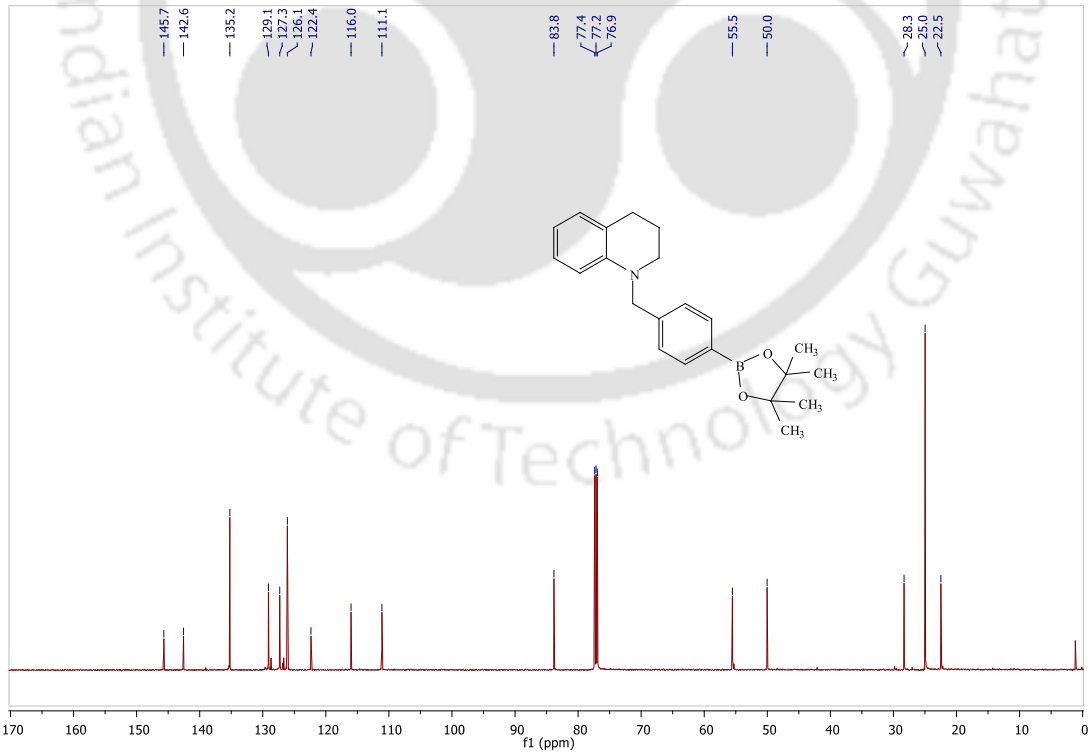

Figure S129: $^{13}C\{^{1}H\}$ NMR Spectrum of **6.7b** ($CDCl_3$, 151 MHz, 298 K)

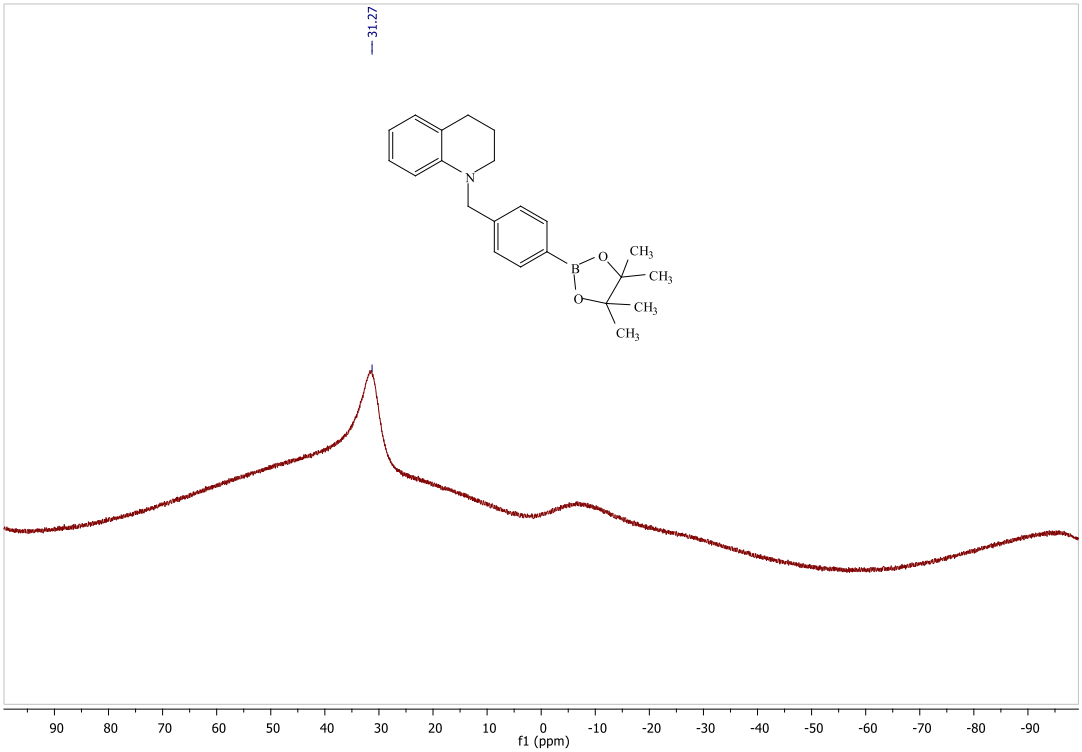

Figure S130: $^{11}B\{^{1}H\}$ NMR Spectrum of **6.7b** ($CDCl_3$, 128.4 MHz, 298 K)

The supporting information and all other product spectra for chapter 6 is available at https://doi.org/10.1021/acs.orglett.1c00302

Annexure VI

The Cartesian coordinates (xyz) for all optimized structures *(Chapter 2)*

Step I: Pathway for aldol product formation

Cyclohexanone (**2.8a**)

C	1.51157	-0.09578	0.10137
C	3.03971	-0.12188	0.19701
C	3.61936	1.28648	0.21043
C	3.04124	2.10053	1.36054
C	1.51312	2.1659	1.28547
C	0.88477	0.79292	1.15674
H	4.7117	1.24758	0.2833
H	3.33398	-0.64208	1.11873
H	3.45414	-0.70857	-0.62988
H	1.22838	0.31641	-0.87895
H	1.07011	-1.09278	0.17404
H	3.33555	1.63911	2.31303
H	3.45676	3.11391	1.37134
H	1.0727	2.67468	2.14649
H	1.23004	2.73703	0.38836
H	3.39058	1.78564	-0.7427
O	-0.0569	0.43658	1.8386

Acetophenone (**2.7o**)

C	-3.75677	-1.32833	0.02999
C	-2.36887	-1.34505	0.17022
C	-1.64165	-0.16277	0.05624
C	-2.29965	1.03558	-0.19761
C	-3.69207	1.06257	-0.33991
C	-4.41255	-0.13266	-0.2232
H	-4.32266	-2.25126	0.11915
H	-1.85394	-2.28107	0.36861
H	-0.56081	-0.1759	0.16551
H	-1.72469	1.95382	-0.28513
H	-5.49172	-0.08454	-0.33771
C	-4.44753	2.31799	-0.6123
C	-3.67109	3.6056	-0.73789
H	-4.36202	4.42404	-0.93488
H	-3.10958	3.8197	0.17728
H	-2.93875	3.54826	-1.5497
O	-5.6637	2.30306	-0.7305

2.7o'

C	2.58837	-0.01595	0.01493
C	1.86483	-1.20049	0.11295
C	0.47432	-1.17768	0.10102
C	-0.21821	0.03577	-0.00492
C	0.52144	1.2214	-0.11617
C	1.90903	1.19593	-0.10188
H	3.67446	-0.0351	0.02187
H	2.38503	-2.15045	0.19953
H	-0.09005	-2.10041	0.17889
H	0.00348	2.16878	-0.23612
H	2.46431	2.12521	-0.19298
C	-1.68963	0.05111	0.00077
C	-2.45334	1.13567	0.21307
H	-2.01436	2.09898	0.43162
H	-3.53689	1.07982	0.19374
O	-2.2121	-1.19158	-0.22113
H	-3.17	-1.12877	-0.14599

(**$^{-}$O^{t}Bu**)

C	-0.00006	-0.00001	-0.1654
C	0.79079	-1.21488	0.43592
H	1.82306	-1.18257	0.06118
H	0.82736	-1.26942	1.54016
H	0.34179	-2.14548	0.06268

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C	-1.4476	-0.07736	0.43604	H	-2.88202	-2.32963	-0.06706
H	-1.51305	-0.081	1.54028	H	-2.83896	-0.01704	1.92051
H	-2.0294	0.77631	0.06218	H	-4.19399	-1.11874	1.7641
H	-1.93542	-0.98789	0.06191	H	-4.13927	1.18739	0.38732
C	0.65685	1.2921	0.43614	H	-4.8366	-0.24884	-0.33965
H	1.68697	1.36925	0.0621	**2.9w**			
H	0.11208	2.16982	0.06225	C	-4.30628	0.97619	-0.35122
H	0.68667	1.35049	1.54037	C	-2.93069	1.14286	-0.42304
O	0.00001	0.00017	-1.48117	C	-2.06748	0.10133	-0.05979
2.10a				C	-2.61223	-1.11286	0.37662
O	0.84632	2.68241	0.44336	C	-3.99108	-1.28016	0.44885
C	0.61946	1.58247	-0.0551	C	-4.83907	-0.23665	0.08549
C	1.67941	0.53319	-0.05356	H	-4.96795	1.7897	-0.63492
C	2.68796	0.60571	0.91436	H	-2.48633	2.075	-0.75917
C	1.74279	-0.46292	-1.03419	H	-1.96007	-1.93382	0.66192
C	3.7199	-0.32278	0.92421	H	-4.40507	-2.22514	0.7885
H	2.63621	1.40585	1.64716	C	-0.59807	0.34155	-0.15962
C	2.78909	-1.37929	-1.03869	O	-0.16792	1.418	-0.54549
H	0.97544	-0.49753	-1.80432	C	0.33722	-0.79613	0.22766
C	3.77238	-1.31646	-0.05354	H	0.08795	-1.09454	1.25881
H	4.49102	-0.27151	1.68773	H	0.08631	-1.6683	-0.39126
H	2.84071	-2.14096	-1.81167	C	1.79082	-0.45939	0.10848
H	4.5847	-2.03811	-0.05178	C	2.33871	0.53125	1.09884
C	-0.69724	1.33313	-0.67809	C	2.55913	-1.01721	-0.83593
C	-1.47745	0.23691	-0.58753	C	3.68669	1.09419	0.66852
H	-1.13158	2.2284	-1.12218	H	2.42798	0.04189	2.08284
C	-2.88182	0.25547	-1.11382	H	1.61424	1.34206	1.23602
H	-3.01698	-0.62052	-1.76471	C	4.02056	-0.74096	-1.00386
H	-3.06092	1.13829	-1.73413	C	4.61259	-0.02128	0.20341
C	-1.13589	-1.04609	0.13255	H	4.13995	1.66568	1.48569
H	-0.62607	-1.73559	-0.55433	H	3.5272	1.80053	-0.15727
H	-0.41504	-0.85001	0.93355	H	4.55875	-1.67891	-1.19317
C	-3.90095	0.17634	0.04112	H	4.17417	-0.13807	-1.91249
C	-2.39197	-1.72013	0.70425	H	5.60885	0.36679	-0.03477
C	-3.36752	-0.66492	1.20841	H	4.74702	-0.74016	1.0236
H	-2.1063	-2.41448	1.50032	H	2.1015	-1.71444	-1.53902

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H	-5.916	-0.36869	0.14227	H	-6.38169 -2.88936 0.14323
I1				C	1.71203 3.42185 -0.27514
Ru	2.13377	0.19302	-0.25699	C	-6.14616 0.4874 0.01491
Cl	2.5148	0.47675	2.04209	H	-6.77094 1.37827 0.00201
N	-0.025	2.14029	-0.22214	C	-1.96172 3.75849 -0.0462
N	0.17773	-0.15802	-0.20344	H	-2.06772 4.84395 0.00329
N	2.58147	-1.82305	-0.24424	H	-2.42109 3.31302 0.83999
N	-1.76833	-1.51168	-0.0466	H	-2.52737 3.38184 -0.90234
N	0.25558	-2.55051	-0.07631	C	-6.75428 -0.76931 0.07773
N	1.34723	2.13962	-0.31055	C	3.14366 3.81076 -0.31462
N	-1.97351	0.86625	-0.1293	H	3.63164 3.45623 -1.23063
C	-0.6649	0.89358	-0.17929	H	3.68117 3.40901 0.55202
C	1.58541	-2.77249	-0.13582	H	3.25231 4.89611 -0.29256
C	-0.40938	-1.42123	-0.10461	O	4.36376 0.71008 -0.23675
C	-4.76366	0.61523	-0.03098	H	4.49538 1.61331 -0.54405
H	-4.30182	1.59658	-0.07982	H	4.3815 0.77102 0.74025
C	-2.48016	-0.40265	-0.06666	**I2**	
C	-3.94501	-0.51954	-0.01531	Ru	-1.31653 0.49235 0.62035
C	-0.52511	3.41852	-0.14547	Cl	-1.37339 0.67624 3.00325
C	1.95455	-4.14273	-0.09259	N	0.46425 -1.79942 0.72503
H	1.13924	-4.85124	-0.00441	N	0.65455 0.46145 0.33253
C	0.57475	4.24649	-0.18103	N	-1.42449 2.54228 0.31893
H	0.55699	5.32576	-0.13801	N	2.75172 1.38791 -0.27475
C	4.26167	-3.55976	-0.26261	N	0.92807 2.75458 -0.30961
H	5.31498	-3.81087	-0.31646	N	-0.87618 -1.5336 0.87831
C	-4.54863	-1.78393	0.04847	N	2.57315 -0.94482 0.20673
H	-3.90769	-2.65973	0.06143	C	1.29548 -0.71737 0.40705
C	3.87302	-2.23996	-0.29833	C	-0.31855 3.24289 -0.11745
H	4.60696	-1.44732	-0.38577	C	1.41524 1.55473 -0.07418
C	3.26765	-4.54049	-0.15353	C	5.33373 -1.22515 -0.15866
H	3.52604	-5.59497	-0.11609	H	4.72186 -2.08358 0.10111
C	-8.24414	-0.90976	0.1271	C	3.26977 0.1833 -0.11371
H	-8.7436	0.06189	0.10106	C	4.71919 0.02333 -0.30723
H	-8.56866	-1.4261	1.03693	C	0.74893 -3.11734 0.99653
H	-8.61996	-1.49988	-0.71565	C	-0.46767 4.62279 -0.41751
C	-5.92786	-1.90145	0.0939	H	0.42062 5.13233 -0.77292

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C	-0.45649	-3.69168	1.33407	C	-4.61915	-1.22163	-1.74058
H	-0.60931	-4.72338	1.61648	C	-2.90606	-3.41134	-1.87976
C	-2.75981	4.5527	0.2489	H	-1.31956	-1.96767	-2.07138
H	-3.72439	5.01584	0.42362	C	-5.13146	-2.51181	-1.65736
C	5.51412	1.12815	-0.64442	H	-5.28226	-0.36311	-1.66333
H	5.03102	2.09334	-0.75917	C	-4.27735	-3.61159	-1.73198
C	-2.58819	3.21068	0.5106	H	-2.23166	-4.26208	-1.92343
H	-3.41022	2.60408	0.87238	H	-6.19974	-2.65876	-1.52689
C	-1.6653	5.27517	-0.24153	H	-4.67854	-4.61865	-1.66464
H	-1.7526	6.33403	-0.46887	C	-3.36028	1.41991	-2.51851
C	8.98176	-0.40908	-0.85722	H	-2.89674	2.40093	-2.54932
H	9.28927	-1.45785	-0.86379	H	-4.37615	1.33156	-2.87999
H	9.533	0.08898	-0.05154	**I3**			
H	9.32006	0.04655	-1.79338	Ru	0.75462	0.50174	-0.34538
C	6.87991	0.98105	-0.82511	Cl	0.86826	1.01001	-2.68024
H	7.48376	1.84764	-1.08757	N	-1.0048	-1.7141	-0.99218
C	-1.43484	-2.6796	1.26265	N	-1.24069	0.49403	-0.38986
C	6.70357	-1.36303	-0.34181	N	0.81688	2.5435	0.05185
H	7.16798	-2.34015	-0.22386	N	-3.3887	1.36074	0.1121
C	2.10055	-3.71697	0.93088	N	-1.603	2.7626	0.29314
H	2.03549	-4.77259	1.20213	N	0.34419	-1.47815	-0.86818
H	2.7958	-3.21654	1.61017	N	-3.16242	-0.89131	-0.64775
H	2.53754	-3.62969	-0.06729	C	-1.86816	-0.65911	-0.67784
C	7.5023	-0.26568	-0.67601	C	-0.34071	3.26467	0.20515
C	-2.88399	-2.74954	1.56981	C	-2.04894	1.55433	-0.01095
H	-3.48861	-2.45044	0.70405	C	-5.93537	-1.23358	-0.44737
H	-3.12901	-2.09974	2.41784	H	-5.30162	-2.05456	-0.76851
H	-3.17935	-3.76769	1.82965	C	-3.88628	0.18081	-0.22725
O	-3.56134	0.42433	1.03653	C	-5.3423	-0.00543	-0.13202
H	-3.9005	-0.44983	0.80585	C	-1.25188	-3.00001	-1.41366
H	-3.4051	0.40674	2.00448	C	-0.25754	4.67068	0.35855
O	-1.37607	0.41907	-1.65755	H	-1.1972	5.19762	0.47902
H	-1.0132	1.27695	-1.92646	C	-0.01289	-3.58105	-1.56316
C	-2.70895	0.34799	-2.05435	H	0.17669	-4.5938	-1.88902
C	-3.24148	-1.01101	-1.90892	C	2.11796	4.57544	0.17014
C	-2.38877	-2.12359	-1.96366	H	3.10027	5.03361	0.14293

C	-6.1663 1.05117 0.28113	H	0.83554 -4.66226 1.57165
H	-5.70227 2.00282 0.52031	H	4.83187 -3.57035 2.71611
C	1.99415 3.2104 0.02725	H	3.19824 -5.30435 2.00693
H	2.87022 2.58731 -0.11274	H	1.77342 1.67449 3.57207
C	0.9511 5.32734 0.3395	H	2.9605 0.36612 4.15243
H	0.99298 6.40723 0.44961	O	2.84832 0.29331 0.01917
C	-9.62312 -0.52002 0.14716	C	3.93869 0.22427 -0.56588
H	-10.02698 -0.09723 1.07235	C	4.1179 0.41347 -2.03806
H	-9.91313 -1.57293 0.10284	C	5.18761 -0.03545 0.22897
H	-10.1311 -0.00773 -0.6781	C	5.39663 -0.2593 -2.525
C	-7.53776 0.87703 0.37684	C	6.36924 0.71727 -0.37998
H	-8.16379 1.70668 0.69991	C	6.65115 0.28047 -1.8257
C	0.95068 -2.60902 -1.22243	H	5.48498 -0.1554 -3.60989
C	-7.3107 -1.39859 -0.34935	H	5.3085 -1.33835 -2.33824
H	-7.75717 -2.36002 -0.59576	H	6.13582 1.78961 -0.35399
C	-2.60067 -3.5642 -1.64515	H	7.2581 0.59348 0.24543
H	-2.50018 -4.5811 -2.02997	H	7.43179 -0.48789 -1.84229
H	-3.17188 -2.96682 -2.3605	H	7.05631 1.13054 -2.38508
H	-3.1943 -3.5875 -0.72721	H	5.00193 0.23505 1.27262
C	-8.13787 -0.34937 0.06249	H	5.38055 -1.12082 0.21791
C	2.42958 -2.71872 -1.2139	H	4.14884 1.49907 -2.22616
H	2.73952 -3.7612 -1.31162	H	3.21159 0.09005 -2.56167
H	2.84174 -2.32483 -0.27888	O	-1.01088 1.99785 2.9775
H	2.8672 -2.15384 -2.04495	H	-1.73754 1.59042 3.45699
C	1.61444 -0.22065 2.64257	H	-1.43833 2.46774 2.23391
C	2.15491 0.66273 3.49232	**A-TS-1**	
O	0.51301 0.09452 1.87389	Ru	-0.73111 -0.44943 -0.42646
H	0.0126 0.85348 2.28441	Cl	-0.85773 -0.60303 -2.8298
C	2.05906 -1.60717 2.44922	N	1.01214 1.83026 -0.8622
C	1.14906 -2.59199 2.04198	N	1.25001 -0.41081 -0.41728
C	3.38912 -1.98094 2.68866	N	-0.75609 -2.50505 -0.31274
C	1.55615 -3.91354 1.89018	N	3.3661 -1.26521 0.19681
H	0.12029 -2.30693 1.84281	N	1.52616 -2.58822 0.52504
C	3.79539 -3.30024 2.53197	N	-0.33497 1.59763 -0.67538
H	4.10803 -1.22102 2.98474	N	3.17319 0.98317 -0.56977
C	2.87939 -4.27332 2.1323	C	1.87819 0.76438 -0.6343

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C	0.32211	-3.17549	0.17368	H	-2.88554	2.78659	-1.74117
C	2.0441	-1.42135	0.057	O	1.11689	-1.95435	2.84653
C	5.96582	1.25523	-0.49273	H	1.49709	-2.44834	1.79679
H	5.34699	2.07925	-0.83453	C	-1.64466	-0.3217	2.51298
C	3.89101	-0.09176	-0.16794	C	-2.22736	-1.3495	3.16525
C	5.34786	0.05754	-0.1091	O	-0.51928	-0.47649	1.78975
C	1.25755	3.1529	-1.15874	H	0.32259	-1.28031	2.39984
C	0.23387	-4.5579	0.41821	C	-2.15294	1.06586	2.58256
H	1.11199	-5.04891	0.82392	C	-1.26695	2.1378	2.40996
C	0.025	3.76036	-1.16646	C	-3.50423	1.35096	2.82218
H	-0.165	4.80418	-1.37099	C	-1.71418	3.4523	2.49398
C	-1.9736	-4.57288	-0.49445	H	-0.22297	1.91544	2.20689
H	-2.88179	-5.07811	-0.80337	C	-3.95406	2.66463	2.89784
C	6.15232	-1.00254	0.3331	H	-4.20554	0.52724	2.93498
H	5.67059	-1.928	0.63159	C	-3.05929	3.72236	2.7371
C	-1.84609	-3.212	-0.68603	H	-1.00952	4.26975	2.35917
H	-2.63539	-2.62433	-1.14234	H	-5.00711	2.86535	3.07983
C	-0.91297	-5.25956	0.09866	H	-3.4106	4.74912	2.79639
H	-0.97039	-6.32921	0.27736	H	-1.85902	-2.36456	3.04335
C	9.64536	0.46289	0.03638	H	-3.06588	-1.19682	3.83434
H	10.08021	-0.0674	0.88845	H	0.6731	-2.60723	3.39639
H	9.95884	1.50871	0.09117	O	-2.84256	-0.42509	-0.11584
H	10.10149	0.03781	-0.86549	C	-3.91732	-0.1999	-0.68601
C	7.52999	-0.86207	0.38869	C	-4.05274	0.13543	-2.13795
H	8.14112	-1.69188	0.73798	C	-5.19436	-0.25404	0.10493
C	-0.93571	2.76911	-0.8674	C	-5.31199	0.96046	-2.3856
C	7.34577	1.38496	-0.43536	C	-6.35349	-0.71829	-0.7731
H	7.81165	2.32169	-0.73463	C	-6.59029	0.22343	-1.96374
C	2.60195	3.71757	-1.41303	H	-5.3658	1.25519	-3.43742
H	2.49839	4.76142	-1.71554	H	-5.22538	1.89771	-1.81915
H	3.12827	3.17107	-2.20016	H	-6.12019	-1.72693	-1.1379
H	3.23932	3.66626	-0.526	H	-7.26257	-0.82422	-0.17411
C	8.15454	0.33078	0.00345	H	-7.36402	0.95806	-1.71542
C	-2.40769	2.90699	-0.76209	H	-6.98574	-0.35447	-2.80601
H	-2.67729	3.89414	-0.37911	H	-5.03683	-0.88664	0.98365
H	-2.81493	2.15715	-0.0777	H	-5.38682	0.76146	0.48896

H	-4.09424 -0.81404 -2.6946	H	-7.40277 1.16219 -1.26558
H	-3.1285 0.60339 -2.49109	C	1.48132 -3.27944 1.24047
I4		C	-6.61686 -2.07605 -0.66125
Ru	1.41357 -0.23164 0.15758	H	-7.08402 -3.04921 -0.52495
Cl	1.73636 -1.03869 -2.15242	C	-2.04831 -4.35236 0.89869
N	-0.4017 -2.46277 0.55891	H	-1.9997 -5.37199 1.28539
N	-0.51868 -0.3016 -0.20491	H	-2.42965 -4.38172 -0.12599
N	1.55123 1.76074 -0.38283	H	-2.77906 -3.78561 1.48228
N	-2.57056 0.53763 -1.05054	C	-7.42395 -0.96133 -0.92021
N	0.93557 -2.18114 0.7303	C	2.92952 -3.33872 1.54836
N	-2.48458 -1.65166 -0.1329	H	3.23994 -2.45202 2.10663
C	-1.19666 -1.45305 0.04134	H	3.51898 -3.36067 0.62508
C	0.5411 2.41033 -1.00314	H	3.16478 -4.23376 2.12704
C	-1.26079 0.64947 -0.82066	N	-0.68339 1.80859 -1.23932
C	-5.23861 -1.96142 -0.5751	O	1.35223 0.24738 2.1926
H	-4.62335 -2.83247 -0.37249	C	-0.3351 1.95343 2.287
C	-3.15756 -0.60234 -0.64773	C	-1.40209 1.0483 2.38982
C	-4.61078 -0.71896 -0.75446	C	-0.62199 3.27653 1.92865
C	-0.69931 -3.7475 0.96279	C	-2.71165 1.45123 2.15402
C	0.65436 3.74954 -1.40714	H	-1.17254 0.01977 2.6612
H	-0.18759 4.21395 -1.91218	C	-1.9312 3.68304 1.67932
C	0.49166 -4.27618 1.39831	H	0.20145 3.98075 1.82349
H	0.63586 -5.27293 1.78929	C	-2.98284 2.7718 1.79081
C	2.82652 3.81184 -0.41758	H	-3.52631 0.73599 2.24601
H	3.7374 4.32537 -0.13221	H	-2.13145 4.71625 1.40085
C	-5.41659 0.40205 -1.00258	H	-4.0084 3.08884 1.61082
H	-4.95661 1.37995 -1.11097	O	3.53817 -0.47779 0.51843
C	2.64779 2.49039 -0.06186	O	-3.07181 3.32377 -1.64431
H	3.39099 1.95127 0.51438	H	-3.06395 3.47178 -0.68916
C	1.80929 4.45341 -1.12614	H	-3.29175 2.3777 -1.69851
H	1.90591 5.49006 -1.43257	H	-1.38566 2.45826 -1.60596
C	-8.90945 -1.09698 -1.04168	C	1.05694 1.4879 2.55156
H	-9.30272 -1.86546 -0.3703	H	1.63017 3.26858 3.57387
H	-9.199 -1.38701 -2.05858	H	2.94384 1.96034 3.39247
H	-9.4219 -0.15724 -0.81997	C	1.93546 2.30328 3.18452
C	-6.79572 0.27861 -1.0809	C	4.56282 -0.36495 -0.16657

C	4.64708 0.3561 -1.47702	C	-2.27309 -4.58875 0.65451
H	5.30275 1.22785 -1.31774	H	-3.19397 -5.14723 0.53057
H	3.65864 0.70529 -1.77998	C	5.87025 -0.72175 0.72557
C	5.83756 -1.00584 0.30474	H	5.45892 -1.65309 1.10271
H	6.56395 -0.20811 0.51878	C	-2.16033 -3.33234 0.09231
H	5.65163 -1.54466 1.23729	H	-2.96372 -2.86629 -0.46661
C	5.26821 -0.54067 -2.5564	C	-1.18901 -5.11132 1.35869
H	5.40012 0.04298 -3.47274	H	-1.23631 -6.09387 1.81737
H	4.54234 -1.32896 -2.79106	C	9.25896 0.99288 0.55377
C	6.4155 -1.91128 -0.79206	H	9.68007 0.46477 1.41319
H	7.36514 -2.33621 -0.45064	H	9.46311 2.06015 0.67684
H	5.73429 -2.75815 -0.95198	H	9.81863 0.66361 -0.32966
C	6.58727 -1.14851 -2.0991	C	7.22111 -0.45491 0.89023
H	7.33509 -0.35378 -1.95872	H	7.84947 -1.1761 1.40837
H	6.98634 -1.81282 -2.87297	C	-1.02241 1.71468 -2.86939
A-TS-2		C	6.96106 1.62899 -0.26757
Ru	-0.96016 -0.73215 -0.77419	H	7.38378 2.55423 -0.65368
Cl	-1.12307 -1.96847 -2.82736	C	2.49302 2.88548 -2.89579
N	0.83669 1.28776 -1.84518	H	2.45889 3.65055 -3.67358
N	1.01183 -0.64122 -0.60625	H	3.2356 2.13179 -3.17247
N	-1.0514 -2.55953 0.21003	H	2.84938 3.34098 -1.96761
N	3.06104 -1.13071 0.49236	C	7.79515 0.72278 0.39883
N	-0.49696 0.94655 -1.92225	C	-2.43586 1.54355 -3.26765
N	2.91412 0.77791 -0.90734	H	-2.87335 0.71107 -2.71024
C	1.65139 0.45868 -1.09029	H	-2.50426 1.30798 -4.3336
C	0.01698 -3.09831 0.83243	H	-3.02123 2.45201 -3.09067
C	1.77011 -1.37484 0.24476	N	1.2288 -2.42269 0.92331
C	5.61103 1.37009 -0.44067	O	-0.86824 0.54894 0.91742
H	4.97424 2.08194 -0.95623	C	-1.74391 0.64178 1.85779
C	3.61166 -0.07188 -0.12835	C	-1.72586 1.93715 2.58982
C	5.03765 0.18932 0.0577	C	-1.10846 3.04775 1.99698
C	1.14431 2.29772 -2.73657	C	-2.30903 2.0908 3.85427
C	-0.02936 -4.36242 1.43528	C	-1.08715 4.27719 2.64355
H	0.8601 -4.73884 1.93186	H	-0.65688 2.91959 1.01644
C	-0.03106 2.5835 -3.38523	C	-2.28504 3.32066 4.50264
H	-0.16156 3.32857 -4.15656	H	-2.76356 1.233 4.34266

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C	-1.67672	4.41887	3.89866	N	-2.98536	-0.63349	-1.02061
H	-0.61145	5.13076	2.16767	C	-1.70632	-0.36061	-1.16546
H	-2.73623	3.42121	5.48613	C	0.0983	2.8804	1.1262
H	-1.65869	5.37972	4.40588	C	-1.7338	1.29353	0.39206
C	-2.74477	-0.29705	2.09425	C	-5.71053	-1.12703	-0.64571
H	-2.58828	-1.32394	1.78834	H	-5.11108	-1.78048	-1.27152
C	-3.85201	-0.02	0.17059	C	-3.63916	0.14563	-0.13475
C	-5.16597	-0.62257	0.62802	C	-5.07633	-0.06652	0.02292
C	-3.89903	1.48722	0.03564	C	-1.26804	-1.99764	-3.03341
C	-6.2663	-0.24825	-0.37102	C	0.19263	4.09783	1.81441
H	-5.43474	-0.22168	1.61238	H	-0.67705	4.46929	2.34837
H	-5.05546	-1.70723	0.72219	C	-0.09176	-2.29532	-3.67536
C	-5.02796	1.8571	-0.93901	H	0.0138	-2.95269	-4.52618
H	-4.1032	1.95065	1.00896	C	2.43308	4.31621	1.00568
H	-2.92668	1.85605	-0.31392	H	3.36442	4.86131	0.90063
C	-6.36411	1.26711	-0.50351	C	-5.86217	0.77099	0.82903
H	-7.22219	-0.67775	-0.05084	H	-5.40553	1.6111	1.34308
H	-6.03193	-0.69085	-1.34854	C	2.27619	3.10456	0.36103
H	-5.08963	2.94799	-1.02933	H	3.04305	2.63747	-0.25224
H	-4.78832	1.47343	-1.93799	C	1.37462	4.81497	1.76515
H	-7.1497	1.54168	-1.21633	H	1.45675	5.76365	2.28651
H	-6.65936	1.69737	0.46503	C	-9.3336	-0.72853	0.4259
H	-3.43175	-0.14109	2.91991	H	-9.57818	-1.79173	0.50767
O	-3.14533	-0.71531	-0.62877	H	-9.86806	-0.35039	-0.45337
O	3.54201	-3.1486	2.44276	H	-9.74742	-0.21751	1.29879
H	3.51316	-2.78701	3.33283	C	-7.22516	0.55001	0.96159
H	3.70818	-2.37285	1.87292	H	-7.81589	1.21397	1.58896
H	1.92066	-2.88298	1.52357	C	0.94058	-1.57361	-3.02837
I5				C	-7.07145	-1.34115	-0.50403
Ru	0.98655	0.64103	-0.6914	H	-7.54052	-2.1727	-1.02605
Cl	1.08579	2.08447	-2.59245	C	-2.64931	-2.45578	-3.30301
N	-0.92563	-1.12408	-2.01998	H	-2.6441	-3.10947	-4.17706
N	-1.00928	0.61997	-0.53182	H	-3.32672	-1.61821	-3.49209
N	1.14729	2.36067	0.45796	H	-3.06855	-3.00445	-2.45486
N	-3.03629	1.09225	0.61196	C	-7.85876	-0.50755	0.3007
N	0.43363	-0.88038	-2.0165	C	2.38228	-1.47138	-3.33737

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H	2.89896	-2.42451	-3.17978
H	2.83259	-0.70872	-2.69395
H	2.52965	-1.18548	-4.38275
N	-1.13211	2.22883	1.18526
O	0.936	-0.77134	0.84638
C	1.86787	-1.02385	1.65392
C	1.73204	-2.22118	2.49105
C	0.54677	-2.97619	2.41394
C	2.74757	-2.65554	3.35948
C	0.38206	-4.11651	3.18315
H	-0.23253	-2.64314	1.73566
C	2.58077	-3.80355	4.1243
H	3.67868	-2.10229	3.43176
C	1.399	-4.53582	4.04261
H	-0.54017	-4.6865	3.11399
H	3.37802	-4.12833	4.7865
H	1.27059	-5.43143	4.64385
C	3.04765	-0.128	1.68566
H	2.68575	0.8908	1.87024
C	3.82506	-0.08533	0.32361
C	5.09468	0.7565	0.59152
C	4.26056	-1.52161	-0.04723
C	6.02508	0.76452	-0.60958
H	5.63185	0.34133	1.45963
H	4.7866	1.77353	0.86758
C	5.24679	-1.53615	-1.20984
H	4.72075	-2.00994	0.82855
H	3.36234	-2.10473	-0.29934
C	6.46192	-0.65784	-0.93887
H	6.89434	1.40464	-0.41756
H	5.48821	1.19394	-1.46532
H	5.55049	-2.56592	-1.43554
H	4.74304	-1.15238	-2.10338
H	7.13864	-0.66858	-1.80128
H	7.03389	-1.06639	-0.09089
H	3.73553	-0.38476	2.49457
O	3.09971	0.49756	-0.69759
O	-3.43826	2.96379	2.72007
H	-3.47284	2.50437	3.56352
H	-3.63412	2.26962	2.06075
H	-1.80187	2.66702	1.82536
I6			
Ru	-0.40502	-1.65444	1.62216
Cl	-1.74834	-2.36922	3.46981
N	-0.75188	1.15531	2.23646
N	-1.80175	-0.45805	0.97659
N	-1.04355	-3.2255	0.48727
N	-3.74147	0.0772	-0.26765
N	0.10864	0.13842	2.56803
N	-2.66301	1.76596	1.02844
C	-1.81124	0.82601	1.38821
C	-2.16749	-3.13732	-0.29149
C	-2.8336	-0.85195	0.12959
C	-4.63987	3.60021	0.18142
H	-4.01444	3.84647	1.03461
C	-3.60601	1.32294	0.15927
C	-4.54177	2.32218	-0.37837
C	-0.3278	2.35542	2.75911
C	-2.52324	-4.24139	-1.10231
H	-3.40709	-4.12406	-1.72162
C	0.83028	2.06891	3.4465
H	1.44574	2.78362	3.97391
C	-0.6242	-5.46144	-0.30648
H	0.00798	-6.34177	-0.27425
C	-5.33633	2.01022	-1.49198
H	-5.22596	1.02781	-1.94569
C	-0.31591	-4.36233	0.46915
H	0.5586	-4.35832	1.11851
C	-1.76247	-5.3901	-1.11729
H	-2.04398	-6.22493	-1.75346
C	-7.28488	5.23169	-2.01261
H	-7.15949	6.21442	-1.54983

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H	-8.3263 4.92653 -1.85654	H	2.49607 1.04507 -2.73822
H	-7.155 5.35248 -3.09341	C	3.96746 2.21105 0.73444
C	-6.20892 2.95193 -2.01457	H	2.6118 0.54967 0.97511
H	-6.8104 2.70067 -2.88664	H	4.32292 0.08863 1.03348
C	1.07127 0.68508 3.30331	C	2.99998 3.12786 -0.00858
C	-5.52393 4.53375 -0.34521	H	2.23391 3.43407 -2.01628
H	-5.59505 5.52315 0.10362	H	3.92709 2.94286 -1.94656
C	-1.02088 3.64726 2.55542	H	3.98187 2.45824 1.80589
H	-0.46255 4.43484 3.06608	H	4.98355 2.37891 0.35192
H	-2.04348 3.62583 2.94212	H	3.28344 4.17923 0.13
H	-1.10122 3.89931 1.49419	H	1.99064 3.01681 0.42474
C	-6.32571 4.22831 -1.44845	O	4.7846 0.44117 -1.54364
C	2.17721 -0.1536 3.82596	H	3.31889 -1.4837 -2.13251
H	2.45277 -0.91536 3.09093	H	5.92387 1.70274 -1.49658
H	1.88464 -0.66698 4.74839	O	6.70967 2.29898 -1.3963
H	3.06199 0.45172 4.03518	C	7.78835 1.44206 -1.06181
N	-2.9776 -2.056 -0.38353	C	7.48641 0.70283 0.24232
O	1.27682 -1.34891 0.40843	H	7.32326 1.41873 1.05609
C	1.66231 -1.38524 -0.80528	H	6.56966 0.11878 0.10712
C	0.66084 -1.45688 -1.89695	H	8.30439 0.0305 0.53153
C	-0.47985 -0.6465 -1.89246	C	8.00441 0.42893 -2.18649
C	0.81357 -2.40164 -2.92003	H	8.20788 0.94917 -3.12848
C	-1.46737 -0.80068 -2.85815	H	8.84432 -0.24532 -1.97524
H	-0.57649 0.11616 -1.1246	H	7.09602 -0.16806 -2.31292
C	-0.18396 -2.57176 -3.87486	C	9.00527 2.34199 -0.90399
H	1.70201 -3.02923 -2.93324	H	9.20215 2.88208 -1.83582
C	-1.33152 -1.78151 -3.83839	H	8.82887 3.08245 -0.11711
H	-2.36956 -0.19426 -2.8227	H	9.89843 1.76335 -0.64228
H	-0.07023 -3.33309 -4.64257	H	3.7217 -1.71214 -0.38461
H	-2.12861 -1.92887 -4.56198	H	-4.07014 -1.75591 -1.98919
C	3.06037 -1.23054 -1.10512	O	-4.71755 -1.5922 -2.70347
C	3.60693 0.42101 -0.9816	H	-5.45278 -1.24642 -2.19044
C	2.55646 1.31358 -1.67606	**I7**	
C	3.59824 0.74402 0.53071	Ru	-0.04354 -1.53343 1.48467
C	2.94081 2.77731 -1.49284	Cl	-0.92465 -2.05699 3.61418
H	1.55782 1.15273 -1.23594	N	-0.5544 1.30701 1.66144

N	-1.65296	-0.57249	0.9025	H	-1.84616	3.8673	1.99422
N	-0.72846	-3.33519	0.80002	H	-1.24734	3.74373	0.35233
N	-3.88121	-0.41865	0.12063	C	-7.23338	3.26634	-0.66666
N	0.4412	0.42862	2.02511	C	2.77645	0.53426	2.73001
N	-2.73393	1.54679	0.85335	H	2.63133	-0.5302	2.93873
C	-1.71154	0.75891	1.1206	H	3.21316	1.004	3.61684
C	-2.01117	-3.47626	0.3262	H	3.50541	0.64516	1.90534
C	-2.79996	-1.19556	0.41129	N	-2.91674	-2.48425	0.16737
C	-4.96276	3.09274	0.17529	O	1.25845	-1.08749	-0.1486
H	-4.06601	3.55919	0.57169	C	1.68305	-1.15986	-1.32432
C	-3.79981	0.88311	0.33718	C	0.89004	-1.8093	-2.3866
C	-4.976	1.70499	-0.00285	C	-0.47277	-2.05079	-2.16733
C	-0.1177	2.61385	1.77467	C	1.4505	-2.18893	-3.61703
C	-2.43535	-4.7655	-0.08084	C	-1.25614	-2.66565	-3.13302
H	-3.45197	-4.8422	-0.45085	H	-0.90584	-1.73544	-1.22613
C	1.17324	2.54073	2.23365	C	0.66897	-2.81257	-4.58195
H	1.87977	3.35232	2.35299	H	2.50157	-2.00212	-3.81586
C	-0.29544	-5.68362	0.47082	C	-0.6835	-3.05426	-4.34342
H	0.40721	-6.50565	0.54876	H	-2.31051	-2.83721	-2.93247
C	-6.13323	1.10657	-0.52	H	1.11644	-3.11045	-5.52648
H	-6.13365	0.02983	-0.65797	H	-1.29023	-3.54107	-5.10278
C	0.07804	-4.41525	0.86619	C	2.97404	-0.48699	-1.61612
H	1.07436	-4.22094	1.26232	C	2.85426	1.02915	-2.03203
C	-1.59601	-5.85599	-0.01647	C	2.20431	1.20623	-3.4044
H	-1.94219	-6.83438	-0.33937	C	2.0491	1.80739	-0.98089
C	-8.44017	4.08813	-1.00364	C	2.12729	2.684	-3.77652
H	-8.21462	5.15809	-0.99687	H	1.19387	0.77097	-3.39151
H	-9.25345	3.92227	-0.287	H	2.78392	0.64927	-4.1535
H	-8.83957	3.836	-1.99169	C	2.00179	3.28633	-1.33601
C	-7.23905	1.87689	-0.84463	H	1.0228	1.40815	-0.91902
H	-8.12988	1.39677	-1.24689	H	2.51435	1.65898	-0.00219
C	1.48984	1.16621	2.36884	C	1.38234	3.48898	-2.71461
C	-6.07553	3.8571	-0.15363	H	1.65019	2.80442	-4.75761
H	-6.04904	4.93635	-0.01244	H	3.15138	3.06589	-3.86504
C	-0.93126	3.79247	1.3998	H	1.44774	3.84097	-0.56846
H	-0.33247	4.6942	1.54482	H	3.02707	3.67655	-1.3271

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H	1.36701	4.55265	-2.98482	H	4.85804 -2.48971 1.945
H	0.32953	3.16294	-2.68641	C	4.04772 -0.58414 0.20858
O	4.15797	1.52236	-2.12271	C	5.27136 -1.40416 0.14316
H	3.54129	-0.98128	-2.41097	C	1.25672 -0.92799 3.4461
H	4.51258	1.50577	-1.16438	C	1.69188 3.55301 -3.11702
O	4.84041	1.28763	0.36027	H	2.61915 3.4121 -3.66136
C	6.19336	1.03871	0.53332	C	0.14756 -0.54387 4.16815
C	6.62108	-0.15253	-0.33772	H	-0.16029 -0.95038 5.12113
H	6.06631	-1.05024	-0.03828	C	-0.46055 4.52873 -2.79705
H	6.37956	0.05149	-1.387	H	-1.27213 5.18801 -3.08601
H	7.69505	-0.37351	-0.2639	C	6.17911 -1.23884 -0.91257
C	7.00887	2.27976	0.13363	H	5.95087 -0.49361 -1.66829
H	6.66839	3.13924	0.722	C	-0.57068 3.77235 -1.64676
H	8.09021	2.15345	0.28535	H	-1.45057 3.83372 -1.01635
H	6.83699	2.5135	-0.92342	C	0.71125 4.41634 -3.5502
C	6.48465	0.70716	2.00485	H	0.84846 4.99261 -4.46201
H	6.19439	1.55088	2.64348	C	8.86256 -3.80246 -0.08928
H	5.89841	-0.16525	2.31676	H	9.0194 -4.3894 0.82014
H	7.54581	0.49406	2.19316	H	9.75589 -3.18884 -0.24891
H	3.58132	-0.4641	-0.70287	H	8.81525 -4.50708 -0.92816
H	4.39941	2.67319	1.21861	C	7.33138 -2.00661 -0.97854
O	4.17813	3.42816	1.83966	H	8.0262 -1.86372 -1.80498
H	4.48387	3.0864	2.68323	C	-0.49641 0.46955 3.42992
I8				C	6.71515 -3.12495 1.05079
Ru	0.12114	1.88097	0.57211	H	6.92371 -3.86379 1.82323
Cl	1.22872	3.64661	1.77318	C	2.28196 -1.94976 3.75846
N	1.24455	-0.15299	2.31236	H	2.02015 -2.43975 4.69942
N	1.80148	0.85026	0.31548	H	3.27857 -1.50894 3.84919
N	0.38018	2.91873	-1.20639	H	2.35612 -2.70452 2.97098
N	3.84696	0.29483	-0.75789	C	7.62238 -2.96595 0.
N	0.16546	0.69522	2.29734	C	-1.7024 1.26403 3.76766
N	3.23278	-0.8029	1.27318	H	-2.41148 1.27225 2.93263
C	2.15455	-0.0445	1.25035	H	-1.42951 2.30119 3.99815
C	1.53745	2.77862	-1.93992	H	-2.21057 0.8482 4.64063
C	2.71517	1.0553	-0.7203	N	2.5614 1.92799 -1.69008
C	5.55761	-2.35948	1.12476	O	-1.40111 0.51913 -0.13109

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C	-2.08308	0.04167	-1.07467
C	-1.48642	-0.32087	-2.37337
C	-0.15288	0.01612	-2.63997
C	-2.21245	-1.057	-3.32982
C	0.44117	-0.31954	-3.84764
H	0.40913	0.53733	-1.87555
C	-1.607	-1.39929	-4.53459
H	-3.21075	-1.43402	-3.09522
C	-0.29211	-1.02096	-4.80489
H	1.47453	-0.03519	-4.03087
H	-2.16554	-1.98108	-5.26431
H	0.1671	-1.28916	-5.75385
C	-3.51148	-0.24048	-0.88594
C	-4.14945	-0.05402	0.47387
C	-5.64707	-0.34406	0.32008
C	-3.54422	-1.01499	1.50232
C	-6.40252	-0.37414	1.6431
H	-5.71639	-1.31942	-0.18818
H	-6.07771	0.40202	-0.36008
C	-4.30192	-1.02286	2.82449
H	-3.5937	-2.01803	1.05434
H	-2.48579	-0.7727	1.64582
C	-5.77172	-1.36444	2.61478
H	-7.45647	-0.61643	1.46415
H	-6.4155	0.6266	2.11359
H	-3.82654	-1.72063	3.52503
H	-4.23469	-0.03119	3.30146
H	-6.31302	-1.37462	3.56921
H	-5.85141	-2.37622	2.19238
O	-3.97755	1.33048	0.93277
O	-1.77686	3.00899	0.9606
H	-2.5053	2.34781	1.01778
H	-1.64232	3.40203	1.82983
H	-4.63729	1.47698	1.62082
H	-3.75299	-1.34213	-1.16574
C	-4.08409	-3.8975	-1.42701
C	-2.56859	-3.90575	-1.14101
H	-2.02218	-3.47561	-1.98824
H	-2.34304	-3.29225	-0.25851
H	-2.17246	-4.91431	-0.95572
C	-4.80283	-4.55704	-0.23122
H	-4.58786	-3.9946	0.68743
H	-5.88671	-4.52173	-0.39225
H	-4.50966	-5.60363	-0.06075
C	-4.33653	-4.75425	-2.68378
H	-5.4079	-4.76245	-2.91362
H	-3.81813	-4.30499	-3.53943
H	-3.99481	-5.79481	-2.58159
O	-4.56532	-2.63289	-1.63572
H	-4.08485	0.28044	-1.66584

Step II: Pathway for the condensation step (formation of α,β- unsaturated ketone 2.10a)

2.18

O	-0.85777	-2.79323	-0.37862
C	-1.02692	-1.63554	0.03468
C	-2.3973	-1.04449	-0.0014
C	-3.50195	-1.90525	0.02791
C	-2.59477	0.34165	-0.09425
C	-4.79325	-1.39485	0.007
H	-3.31528	-2.97567	0.07011
C	-3.89476	0.84161	-0.13592
H	-1.7281	1.01253	-0.21239
C	-4.99147	-0.01536	-0.07081
H	-5.64784	-2.0672	0.04767
H	-4.05003	1.91488	-0.22624
H	-6.00248	0.38739	-0.09089
C	0.06242	-0.79077	0.59039
C	1.48157	-1.29648	0.35611
C	1.82592	-1.13714	-1.13551
C	2.44993	-0.44953	1.1776
C	3.27547	-1.50278	-1.42191
H	1.61894	-0.08908	-1.40405

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H	1.14478	-1.76357	-1.72499	H	2.75419	-1.18251	-0.24045
C	3.90687	-0.79368	0.89915	C	4.41218	2.25631	0.34883
H	2.24833	0.60002	0.91844	H	2.43976	3.06385	0.09941
H	2.21452	-0.57609	2.24292	C	5.20742	1.10946	0.3657
C	4.22619	-0.65321	-0.58565	H	5.21761	-1.03465	0.16427
H	3.49694	-1.38852	-2.49105	H	4.86673	3.23466	0.49722
H	3.43046	-2.56279	-1.17451	H	6.27982	1.18555	0.53358
H	4.56997	-0.1551	1.49788	C	0.07938	1.75284	-0.03792
H	4.09317	-1.82976	1.21346	C	-1.39978	1.5359	-0.20298
H	5.27214	-0.92538	-0.78366	C	-1.97095	0.74625	0.99741
H	4.11505	0.40205	-0.87861	C	-2.15556	2.86118	-0.32893
O	1.66057	-2.65573	0.78028	C	-3.47091	0.51898	0.8616
H	0.92867	-3.12182	0.34417	H	-1.75912	1.307	1.92158
H	0.01936	0.25956	0.17044	H	-1.4271	-0.20363	1.07244
O	0.13831	1.77954	-0.69323	C	-3.65841	2.64779	-0.46196
C	0.39632	2.9525	-0.05939	H	-1.94075	3.47098	0.56285
C	1.86798	3.37968	-0.26933	H	-1.75934	3.4066	-1.19442
H	2.11856	4.3578	0.17128	C	-4.21108	1.84466	0.71201
H	2.53888	2.62942	0.16895	H	-3.86069	-0.04779	1.71821
H	2.08084	3.41846	-1.34415	H	-3.64552	-0.0928	-0.03341
C	0.13644	2.86249	1.46346	H	-4.1803	3.61087	-0.54955
H	-0.90433	2.56225	1.64419	H	-3.84457	2.0975	-1.39306
H	0.78119	2.09396	1.90892	H	-5.29087	1.67985	0.59159
H	0.31563	3.80718	2.00015	H	-4.09059	2.43182	1.63748
C	-0.50855	4.07374	-0.62478	O	-1.68681	0.80508	-1.40585
H	-0.32976	5.06404	-0.17633	H	-0.94097	0.16217	-1.43618
H	-0.3553	4.15112	-1.70736	O	0.16817	-2.49857	0.92042
H	-1.56143	3.81031	-0.46114	C	-0.53667	-3.34938	0.03434
H	-0.14268	-0.65631	1.6652	C	0.28577	-3.57574	-1.23575
I9				H	-0.22717	-4.24247	-1.94098
O	0.58577	-0.42962	-0.76131	H	0.47856	-2.6175	-1.72692
C	0.96001	0.73895	-0.30751	H	1.25214	-4.02435	-0.979
C	2.42418	0.91638	-0.07352	C	-1.89349	-2.73605	-0.31647
C	3.23988	-0.22524	-0.06792	H	-2.48758	-2.5954	0.59374
C	3.04279	2.15938	0.13158	H	-1.76033	-1.7519	-0.77841
C	4.6093	-0.13155	0.1557	H	-2.46497	-3.37112	-1.00606

C	-0.72989	-4.66186	0.78299	H	3.64524	3.41402	0.97369
H	-1.28122	-5.39066	0.17748	O	1.54933	0.24743	-0.86524
H	0.24079	-5.09338	1.04866	H	0.70647	0.11604	-1.40241
H	-1.28655	-4.48934	1.7099	O	2.2057	-2.07148	0.49638
H	0.41268	2.6998	0.37983	C	1.24832	-3.06045	0.14972
H	0.36333	-1.67795	0.40082	C	-0.17157	-2.53803	0.35736
I10				H	-0.91383	-3.33285	0.20913
O	-0.89132	0.19351	-1.67242	H	-0.28686	-2.14233	1.37167
C	-1.2017	0.70766	-0.52165	H	-0.39891	-1.73141	-0.34754
C	-2.64609	0.62702	-0.13406	C	1.53183	-4.24003	1.07028
C	-3.47878	-0.22976	-0.86831	H	2.56479	-4.58177	0.94416
C	-3.22943	1.37045	0.90273	H	1.40098	-3.94206	2.1153
C	-4.82958	-0.35966	-0.56425	H	0.85922	-5.07956	0.86171
H	-3.01371	-0.77778	-1.68347	C	1.43968	-3.4702	-1.31242
C	-4.58044	1.2467	1.20709	H	0.7459	-4.26758	-1.60736
H	-2.61438	2.07029	1.46388	H	1.26114	-2.61243	-1.96938
C	-5.39179	0.37654	0.47731	H	2.46375	-3.82179	-1.4782
H	-5.45289	-1.03847	-1.14497	H	-0.60082	1.59377	1.34515
H	-5.00867	1.83971	2.01391	H	1.97116	-1.25541	-0.00301
H	-6.44996	0.2824	0.71332	**D-TS-1**			
C	-0.29253	1.23383	0.36712	O	1.10512	2.83291	0.72408
C	1.17093	1.30961	0.03758	C	1.15024	1.79482	0.02826
C	1.52649	2.64319	-0.65623	C	2.48895	1.1064	-0.10382
C	2.03727	1.15077	1.29168	C	3.6484	1.85581	0.12419
C	3.01306	2.74793	-0.97468	C	2.61365	-0.26682	-0.35953
H	1.22199	3.47223	0.0019	C	4.90524	1.2659	0.0618
H	0.91741	2.72036	-1.56468	H	3.52091	2.90908	0.36262
C	3.52631	1.26234	0.98638	C	3.873	-0.86099	-0.40298
H	1.74329	1.93167	2.01057	H	1.71775	-0.87672	-0.48433
H	1.80742	0.18229	1.75149	C	5.02264	-0.09871	-0.20397
C	3.85413	2.57771	0.28606	H	5.79881	1.86548	0.22773
H	3.24339	3.7032	-1.46656	H	3.95457	-1.93134	-0.58532
H	3.26682	1.95072	-1.68513	H	6.00467	-0.5663	-0.24363
H	4.11498	1.15887	1.90761	C	0.0636	1.17991	-0.66378
H	3.8138	0.42407	0.33845	C	-1.29012	1.35512	-0.42502
H	4.92588	2.63446	0.0507	C	-1.82083	2.49121	0.40412

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C	-2.25595	0.74431	-1.40925	C	-4.45387	-0.72485	-0.17144
C	-3.25473	2.29555	0.88267	C	-4.83432	-2.06041	-0.1493
H	-1.76371	3.39514	-0.22821	C	-3.87414	-3.04859	0.0784
H	-1.13548	2.69406	1.23011	H	-1.78742	-3.46513	0.41692
C	-3.68181	0.59053	-0.89773	H	-1.07768	-1.0857	0.34804
H	-2.26703	1.40909	-2.29247	H	-5.17176	0.06753	-0.37183
H	-1.85591	-0.21827	-1.74686	H	-5.87338	-2.33731	-0.31615
C	-4.17869	1.87921	-0.25434	H	-4.16824	-4.09676	0.08824
H	-3.61665	3.21885	1.35613	C	-2.73748	1.07639	0.02174
H	-3.24478	1.49949	1.63511	O	-3.37002	1.86558	-0.68499
H	-4.34187	0.29245	-1.72435	C	-1.61084	1.46537	0.88105
H	-3.69568	-0.21061	-0.15196	H	0.41801	-1.15016	-1.18375
H	-5.20822	1.75684	0.10936	H	-1.50707	0.89562	1.8053
H	-4.21431	2.67949	-1.01344	H	2.18304	-0.53827	-0.66936
O	-1.71977	-0.21635	1.06817	C	3.74313	-1.54037	-0.07065
H	-0.98202	0.11912	1.5919	C	3.37831	-1.40154	1.41188
O	-0.45161	-1.88351	-0.49471	H	2.28626	-1.37964	1.49519
C	-0.6481	-3.11213	0.16911	H	3.77097	-2.22915	2.01948
C	-0.03317	-3.04378	1.56971	H	3.77625	-0.46079	1.81026
H	-0.15779	-3.98241	2.12605	C	3.16104	-2.85616	-0.6013
H	1.03759	-2.81975	1.50219	H	2.07046	-2.79219	-0.50731
H	-0.51956	-2.23483	2.12494	H	3.41533	-2.98019	-1.66054
C	0.04593	-4.17745	-0.66863	H	3.5289	-3.73334	-0.05079
H	-0.37825	-4.20176	-1.67784	C	5.25622	-1.50805	-0.25272
H	1.11367	-3.94726	-0.75947	H	5.51033	-1.59435	-1.31495
H	-0.05717	-5.17451	-0.22338	H	5.65909	-0.55618	0.11086
C	-2.14858	-3.39335	0.28333	H	5.75079	-2.32406	0.28996
H	-2.35647	-4.35205	0.77752	O	3.21603	-0.46278	-0.80039
H	-2.613	-2.58476	0.85744	C	1.80939	2.0268	0.90769
H	-2.60385	-3.41015	-0.71341	H	1.71761	0.93999	0.8104
H	0.31458	0.35976	-1.33181	H	2.65695	2.23874	1.57259
H	-0.91875	-1.18586	0.09009	C	0.5124	2.56979	1.51934
I11				H	0.31407	2.10291	2.49156
C	-2.54181	-2.69345	0.27685	H	0.61799	3.65479	1.69223
C	-2.15159	-1.35434	0.28935	C	2.05031	2.59872	-0.48343
C	-3.12277	-0.36666	0.0697	H	2.931	2.10847	-0.91205

H	2.2625	3.68059	-0.41922
C	0.83746	2.35882	-1.37474
H	0.69147	1.26917	-1.44453
H	0.99863	2.76521	-2.3816
C	-0.63416	2.34287	0.58142
C	-0.43744	2.9672	-0.76473
H	-0.30463	4.05574	-0.65002
H	-1.3085	2.80953	-1.40336
O	0.72149	-0.77459	-0.34967

2.10a

O	-0.56646	0.93217	2.63569
C	-0.94941	1.22855	1.49898
C	-0.04177	1.82225	0.49924
C	1.33966	1.64017	0.64969
C	-0.52394	2.55216	-0.60525
C	2.22277	2.13695	-0.30574
H	1.72454	1.0564	1.47793
C	0.35935	3.08307	-1.53045
H	-1.59696	2.69809	-0.71663
C	1.73715	2.86888	-1.3846
H	3.26935	1.86582	-0.21093
H	-0.01725	3.65725	-2.37473
C	-2.36899	0.94006	1.16698
C	-2.85213	0.30715	0.08004
H	-3.04453	1.07864	2.01263
C	-4.27108	-0.18073	0.03841
H	-4.73052	0.14685	-0.90664
H	-4.86698	0.25581	0.84674
C	-2.04756	-0.12846	-1.11944
H	-2.05887	0.65893	-1.88696
H	-0.99593	-0.24916	-0.84489
C	-4.30821	-1.72229	0.09865
C	-2.58397	-1.44141	-1.70825
C	-3.08208	-2.34287	-0.58633
H	-1.79322	-1.92872	-2.28759
H	-3.40763	-1.24613	-2.4111
H	-2.26868	-2.45989	0.14196
H	-3.31524	-3.34935	-0.95079
H	-4.35291	-2.04533	1.14472
H	-5.23173	-2.07888	-0.37602
H	2.42502	3.26009	-2.13163
H	1.22799	-0.56405	2.70999
O	2.05929	-1.04042	2.80255
H	2.55102	-0.82918	1.95694
O	3.2809	-0.46665	0.45614
C	2.92873	-1.46384	-0.39867
C	1.39973	-1.47601	-0.64641
H	1.05104	-2.31809	-1.26677
H	0.88726	-1.5221	0.32473
H	1.10766	-0.54003	-1.14068
C	3.32522	-2.84144	0.18092
H	3.07514	-3.6862	-0.48042
H	4.40546	-2.85797	0.36825
H	2.81818	-2.98263	1.14181
C	3.63166	-1.27889	-1.76097
H	3.39006	-2.06212	-2.49694
H	3.34915	-0.30809	-2.18761
H	4.71799	-1.2706	-1.61129

Step II: Pathway for the condensation step (formation of β,γ-unsaturated ketone 2.9w)

2.18

O	-0.85777	-2.79323	-0.37862
C	-1.02692	-1.63554	0.03468
C	-2.3973	-1.04449	-0.0014
C	-3.50195	-1.90525	0.02791
C	-2.59477	0.34165	-0.09425
C	-4.79325	-1.39485	0.007
H	-3.31528	-2.97567	0.07011
C	-3.89476	0.84161	-0.13592
H	-1.7281	1.01253	-0.21239
C	-4.99147	-0.01536	-0.07081
H	-5.64784	-2.0672	0.04767

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H	-4.05003	1.91488	-0.22624	H	-0.14268	-0.65631	1.6652
H	-6.00248	0.38739	-0.09089	**I9**			
C	0.06242	-0.79077	0.59039	O	0.58577	-0.42962	-0.76131
C	1.48157	-1.29648	0.35611	C	0.96001	0.73895	-0.30751
C	1.82592	-1.13714	-1.13551	C	2.42418	0.91638	-0.07352
C	2.44993	-0.44953	1.1776	C	3.23988	-0.22524	-0.06792
C	3.27547	-1.50278	-1.42191	C	3.04279	2.15938	0.13158
H	1.61894	-0.08908	-1.40405	C	4.6093	-0.13155	0.1557
H	1.14478	-1.76357	-1.72499	H	2.75419	-1.18251	-0.24045
C	3.90687	-0.79368	0.89915	C	4.41218	2.25631	0.34883
H	2.24833	0.60002	0.91844	H	2.43976	3.06385	0.09941
H	2.21452	-0.57609	2.24292	C	5.20742	1.10946	0.3657
C	4.22619	-0.65321	-0.58565	H	5.21761	-1.03465	0.16427
H	3.49694	-1.38852	-2.49105	H	4.86673	3.23466	0.49722
H	3.43046	-2.56279	-1.17451	H	6.27982	1.18555	0.53358
H	4.56997	-0.1551	1.49788	C	0.07938	1.75284	-0.03792
H	4.09317	-1.82976	1.21346	C	-1.39978	1.5359	-0.20298
H	5.27214	-0.92538	-0.78366	C	-1.97095	0.74625	0.99741
H	4.11505	0.40205	-0.87861	C	-2.15556	2.86118	-0.32893
O	1.66057	-2.65573	0.78028	C	-3.47091	0.51898	0.8616
H	0.92867	-3.12182	0.34417	H	-1.75912	1.307	1.92158
H	0.01936	0.25956	0.17044	H	-1.4271	-0.20363	1.07244
O	0.13831	1.77954	-0.69323	C	-3.65841	2.64779	-0.46196
C	0.39632	2.9525	-0.05939	H	-1.94075	3.47098	0.56285
C	1.86798	3.37968	-0.26933	H	-1.75934	3.4066	-1.19442
H	2.11856	4.3578	0.17128	C	-4.21108	1.84466	0.71201
H	2.53888	2.62942	0.16895	H	-3.86069	-0.04779	1.71821
H	2.08084	3.41846	-1.34415	H	-3.64552	-0.0928	-0.03341
C	0.13644	2.86249	1.46346	H	-4.1803	3.61087	-0.54955
H	-0.90433	2.56225	1.64419	H	-3.84457	2.0975	-1.39306
H	0.78119	2.09396	1.90892	H	-5.29087	1.67985	0.59159
H	0.31563	3.80718	2.00015	H	-4.09059	2.43182	1.63748
C	-0.50855	4.07374	-0.62478	O	-1.68681	0.80508	-1.40585
H	-0.32976	5.06404	-0.17633	H	-0.94097	0.16217	-1.43618
H	-0.3553	4.15112	-1.70736	O	0.16817	-2.49857	0.92042
H	-1.56143	3.81031	-0.46114	C	-0.53667	-3.34938	0.03434

C	0.28577	-3.57574	-1.23575	H	1.74329	1.93167	2.01057
H	-0.22717	-4.24247	-1.94098	H	1.80742	0.18229	1.75149
H	0.47856	-2.6175	-1.72692	C	3.85413	2.57771	0.28606
H	1.25214	-4.02435	-0.979	H	3.24339	3.7032	-1.46656
C	-1.89349	-2.73605	-0.31647	H	3.26682	1.95072	-1.68513
H	-2.48758	-2.5954	0.59374	H	4.11498	1.15887	1.90761
H	-1.76033	-1.7519	-0.77841	H	3.8138	0.42407	0.33845
H	-2.46497	-3.37112	-1.00606	H	4.92588	2.63446	0.0507
C	-0.72989	-4.66186	0.78299	H	3.64524	3.41402	0.97369
H	-1.28122	-5.39066	0.17748	O	1.54933	0.24743	-0.86524
H	0.24079	-5.09338	1.04866	H	0.70647	0.11604	-1.40241
H	-1.28655	-4.48934	1.7099	O	2.2057	-2.07148	0.49638
H	0.41268	2.6998	0.37983	C	1.24832	-3.06045	0.14972
H	0.36333	-1.67795	0.40082	C	-0.17157	-2.53803	0.35736
I10				H	-0.91383	-3.33285	0.20913
O	-0.89132	0.19351	-1.67242	H	-0.28686	-2.14233	1.37167
C	-1.2017	0.70766	-0.52165	H	-0.39891	-1.73141	-0.34754
C	-2.64609	0.62702	-0.13406	C	1.53183	-4.24003	1.07028
C	-3.47878	-0.22976	-0.86831	H	2.56479	-4.58177	0.94416
C	-3.22943	1.37045	0.90273	H	1.40098	-3.94206	2.1153
C	-4.82958	-0.35966	-0.56425	H	0.85922	-5.07956	0.86171
H	-3.01371	-0.77778	-1.68347	C	1.43968	-3.4702	-1.31242
C	-4.58044	1.2467	1.20709	H	0.7459	-4.26758	-1.60736
H	-2.61438	2.07029	1.46388	H	1.26114	-2.61243	-1.96938
C	-5.39179	0.37654	0.47731	H	2.46375	-3.82179	-1.4782
H	-5.45289	-1.03847	-1.14497	H	-0.60082	1.59377	1.34515
H	-5.00867	1.83971	2.01391	H	1.97116	-1.25541	-0.00301
H	-6.44996	0.2824	0.71332	**I12**			
C	-0.29253	1.23383	0.36712	O	-1.56264	-2.90051	0.11714
C	1.17093	1.30961	0.03758	C	-1.37186	-1.55179	-0.06177
C	1.52649	2.64319	-0.65623	C	-2.61478	-0.76847	-0.01212
C	2.03727	1.15077	1.29168	C	-3.86256	-1.39778	-0.11993
C	3.01306	2.74793	-0.97468	C	-2.57383	0.62758	0.17015
H	1.22199	3.47223	0.0019	C	-5.04007	-0.65582	-0.07686
H	0.91741	2.72036	-1.56468	H	-3.89162	-2.47663	-0.24119
C	3.52631	1.26234	0.98638	C	-3.75348	1.35827	0.205

H	-1.60948	1.12905	0.30473	H	5.12316 -1.25464 0.40811
C	-4.99319	0.72663	0.07933	H	4.02128 0.12754 0.38729
H	-5.99987	-1.1617	-0.16722	O	1.11098 -3.00705 -0.32675
H	-3.70316	2.43655	0.34509	H	1.84742 -3.37482 0.17338
H	-5.91289	1.30722	0.11295	H	-0.67301 -3.28625 0.01509
C	-0.18257	-0.96343	-0.27304	H	-0.12536 0.12439 -0.37473
C	1.1807	-1.55158	-0.1648	C	1.06261 2.93333 -0.01144
C	2.08715	-0.95194	-1.24559	C	0.48082 3.30014 -1.3987
C	1.74685	-1.19092	1.21907	H	-0.60803 3.16162 -1.38218
C	3.54431	-1.36092	-1.08543	H	0.69119 4.33284 -1.72272
H	1.97694	0.13896	-1.13406	H	0.88507 2.61357 -2.15357
H	1.69924	-1.23731	-2.23055	C	2.59546 3.15405 -0.06555
C	3.21071	-1.58708	1.38563	H	2.90149 4.18536 -0.30694
H	1.63158	-0.09662	1.30217	H	3.03137 2.88475 0.90512
H	1.1153	-1.65625	1.98726	H	3.03247 2.48432 -0.81897
C	4.06996	-0.96621	0.29051	C	0.4767 3.92565 1.02432
H	4.15588	-0.90762	-1.8756	H	-0.61353 3.80352 1.06314
H	3.64097	-2.4525	-1.2135	H	0.86757 3.6818 2.01954
H	3.5679	-1.28977	2.37948	H	0.697 4.98543 0.81527
H	3.33267	-2.68718	1.3549	O	0.

76927 1.65831 0.32146

D-TS-2

O	-1.84679	-2.33248	0.42986
C	-1.65546	-1.0565	-0.01371
C	-2.8802	-0.24778	-0.0121
C	-4.13037	-0.86745	0.1463
C	-2.85259	1.15177	-0.14576
C	-5.30462	-0.12266	0.1487
H	-4.15547	-1.94583	0.26331
C	-4.02699	1.89119	-0.15063
H	-1.89614	1.66257	-0.23044
C	-5.26388	1.26097	-0.00414
H	-6.26092	-0.62787	0.27002
H	-3.97684	2.97263	-0.2559
H	-6.18155	1.84441	-0.00004

C	-0.45053	-0.61463	-0.44091
C	0.82492	-1.39405	-0.35245
C	1.9187	-0.787	-1.1389
C	1.26233	-1.60466	1.11209
C	3.20314	-1.5944	-1.07621
H	2.43085	0.57771	-0.48097
H	1.59306	-0.6165	-2.17636
C	2.5625	-2.396	1.21332
H	1.42201	-0.61104	1.55123
H	0.45845	-2.08933	1.68195
C	3.66304	-1.75711	0.37302
H	3.99273	-1.08783	-1.6494
H	3.13171	-2.61419	-1.52688
H	2.86831	-2.48719	2.26499
H	2.39474	-3.43275	0.87047

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H	4.58547 -2.35346 0.43917	H	1.68682 2.82341 0.15468
H	3.88218 -0.7597 0.77643	H	-3.69005 -0.84679 -0.50331
O	0.37745 -2.81334 -0.8383	C	-5.41549 -0.03511 -0.05292
H	1.15959 -3.36549 -0.72981	C	-4.91086 1.38363 -0.34722
H	-1.05881 -2.82675 0.08902	H	-4.16035 1.32115 -1.1427
H	-0.37999 0.37713 -0.87269	H	-5.71829 2.06041 -0.6623
C	2.15584 2.53405 0.11005	H	-4.43566 1.8059 0.54618
C	1.4525 2.84818 -1.21969	C	-6.0733 -0.59482 -1.32179
H	0.85058 1.99046 -1.5386	H	-5.29724 -0.64638 -2.0944
H	0.79726 3.72817 -1.15201	H	-6.44933 -1.60778 -1.13435
H	2.19846 3.02897 -2.00143	H	-6.90796 0.02508 -1.67916
C	3.03703 3.72043 0.50509	C	-6.41031 -0.01484 1.1032
H	2.45795 4.64519 0.63655	H	-6.76023 -1.03107 1.31713
H	3.55712 3.50123 1.44391	H	-5.92394 0.36739 2.00784
H	3.79769 3.89268 -0.26399	H	-7.28355 0.61455 0.88554
C	1.09881 2.30894 1.20346	O	-4.35033 -0.8584 0.32851
H	0.46837 1.4479 0.95322	C	-1.47547 0.42751 1.14773
H	1.59474 2.0893 2.15582	H	-2.04568 0.70659 0.25341
H	0.44435 3.18099 1.34818	H	-2.13277 0.61431 2.00508
O	2.98674 1.42565 -0.01794	C	-0.20248 1.25939 1.25184
I13		H	-0.42232 2.32914 1.1045
C	4.47007 -1.9059 0.81764	H	0.21116 1.19911 2.27362
C	3.67839 -0.7725 0.7196	C	-1.14387 -1.05218 1.0175
C	4.06429 0.30872 -0.09298	H	-2.07255 -1.63016 1.01567
C	5.28615 0.21187 -0.77984	H	-0.53826 -1.38035 1.87988
C	6.0744 -0.93079 -0.6831	C	-0.39037 -1.26093 -0.28947
C	5.67206 -1.99895 0.11174	H	-1.16681 -1.0954 -1.09438
H	4.14899 -2.72588 1.45523	H	-0.02887 -2.29382 -0.40073
H	2.74384 -0.71353 1.26848	C	0.86328 0.83807 0.26617
H	5.60759 1.04809 -1.39159	C	0.73162 -0.30994 -0.44102
H	7.0109 -0.98355 -1.23408	O	-2.88886 -0.70478 -1.72721
H	6.28577 -2.89318 0.18605	H	1.49121 -0.5305 -1.19382
C	3.28633 1.55006 -0.16282	H	3.52109 3.37136 -0.64544
O	4.10365 2.61945 -0.49551	**I14**	
C	1.96918 1.76372 0.08972	C	-3.00889 -2.19612 -0.96323
H	-3.03087 -1.56039 -2.14718	C	-2.27932 -1.34498 -0.1324

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C	-2.91956	-0.22687	0.42335
C	-4.27247	0.01411	0.14215
C	-4.98324	-0.83458	-0.69333
C	-4.34791	-1.94684	-1.25017
H	-2.51568	-3.06561	-1.39353
H	-1.21587	-1.57397	0.09188
H	-4.73621	0.88357	0.60127
H	-6.03016	-0.63632	-0.91416
H	-4.90137	-2.61609	-1.90685
C	-2.22277	0.72515	1.34231
O	-2.87359	1.56603	1.95725
C	-0.7184	0.64447	1.49969
H	0.48251	-2.90509	0.68417
H	-0.35215	-0.40207	1.46537
H	1.76498	-1.68811	-0.33726
C	3.60918	-1.26476	0.13379
C	3.21451	-0.1394	1.0952
H	2.24852	-0.39036	1.54623
H	3.95933	0.00779	1.89003
H	3.09976	0.80597	0.55194
C	3.76249	-2.56543	0.93131
H	2.79012	-2.7915	1.38291
H	4.03875	-3.38893	0.2623
H	4.52175	-2.48952	1.7219
C	4.90786	-0.91947	-0.58589
H	5.17647	-1.71784	-1.28663
H	4.78388	0.00407	-1.16277
H	5.73914	-0.779	0.11686
O	2.62616	-1.43283	-0.85659
C	1.40168	3.39577	-0.26448
H	2.48288	3.28976	-0.07009
H	1.19004	4.46538	-0.11768
C	0.62913	2.57743	0.7254
C	1.10295	2.98742	-1.70303
H	1.82195	3.45356	-2.3895
H	0.11018	3.36926	-1.98494
C	1.11278	1.47153	-1.83674
H	2.09119	1.06555	-1.5456
H	0.96159	1.16968	-2.88024
C	0.01106	1.42336	0.43036
C	0.05391	0.82965	-0.95038
H	-0.94295	0.91783	-1.41424
H	0.24759	-0.24661	-0.85279
O	0.59246	-1.95229	0.60549
H	-0.49472	1.09045	2.4744
H	0.60036	2.9382	1.75448

2.9w

O	-0.12543	-1.84524	0.87414
C	-0.42029	-1.11401	-0.08661
C	-1.85293	-0.90332	-0.45905
C	-2.80167	-1.88382	-0.13879
C	-2.26819	0.28152	-1.08978
C	-4.13927	-1.70357	-0.47139
H	-2.47731	-2.77609	0.39187
C	-3.6148	0.46086	-1.39732
H	-1.54494	1.08935	-1.25807
C	-4.5495	-0.53056	-1.10552
H	-4.8665	-2.4764	-0.23088
H	-3.93601	1.39122	-1.8614
C	0.57094	-0.35347	-0.86919
H	0.32955	-0.45921	-1.93921
C	2.02046	-0.61086	-0.5922
C	2.53611	-2.02375	-0.66994
C	2.83214	0.42643	-0.33319
C	3.93639	-2.17121	-0.0862
H	2.53313	-2.34893	-1.72485
H	1.83441	-2.6869	-0.15289
C	4.30949	0.30303	-0.11703
H	2.37691	1.41933	-0.30727
C	4.84747	-1.05085	-0.56956
H	4.35672	-3.15466	-0.33332
H	3.87125	-2.1284	1.01024

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H	4.83461	1.11483	-0.64004
H	4.54708	0.45705	0.94891
H	5.87744	-1.19761	-0.21867
H	4.88672	-1.07429	-1.66856
H	0.36198	0.77871	-0.70737
H	-5.59803	-0.3861	-1.35893
O	-1.82429	-3.21155	2.68672
H	-2.45497	-2.49558	2.79605
H	-1.15916	-2.7925	2.10752
C	-0.13755	2.95162	0.49399
C	0.98557	3.93738	0.8849
H	1.93448	3.39537	0.98253
H	1.11049	4.67987	0.08815
H	0.79828	4.46977	1.83055
C	-1.46782	3.73484	0.43838
H	-1.41385	4.48891	-0.35563
H	-2.28873	3.05026	0.19046
H	-1.72148	4.2425	1.38197
C	-0.25315	1.89393	1.61326
H	-1.08564	1.20899	1.40622
H	0.66362	1.29226	1.66341
H	-0.42664	2.33718	2.60472
O	0.13174	2.39377	-0.72511

Step II: Pathway for the condensation step (formation of β,γ-unsaturated ketone (direct route))

2.18

O	-0.85777	-2.79323	-0.37862
C	-1.02692	-1.63554	0.03468
C	-2.3973	-1.04449	-0.0014
C	-3.50195	-1.90525	0.02791
C	-2.59477	0.34165	-0.09425
C	-4.79325	-1.39485	0.007
H	-3.31528	-2.97567	0.07011
C	-3.89476	0.84161	-0.13592
H	-1.7281	1.01253	-0.21239
C	-4.99147	-0.01536	-0.07081
H	-5.64784	-2.0672	0.04767
H	-4.05003	1.91488	-0.22624
H	-6.00248	0.38739	-0.09089
C	0.06242	-0.79077	0.59039
C	1.48157	-1.29648	0.35611
C	1.82592	-1.13714	-1.13551
C	2.44993	-0.44953	1.1776
C	3.27547	-1.50278	-1.42191
H	1.61894	-0.08908	-1.40405
H	1.14478	-1.76357	-1.72499
C	3.90687	-0.79368	0.89915
H	2.24833	0.60002	0.91844
H	2.21452	-0.57609	2.24292
C	4.22619	-0.65321	-0.58565
H	3.49694	-1.38852	-2.49105
H	3.43046	-2.56279	-1.17451
H	4.56997	-0.1551	1.49788
H	4.09317	-1.82976	1.21346
H	5.27214	-0.92538	-0.78366
H	4.11505	0.40205	-0.87861
O	1.66057	-2.65573	0.78028
H	0.92867	-3.12182	0.34417
H	0.01936	0.25956	0.17044
O	0.13831	1.77954	-0.69323
C	0.39632	2.9525	-0.05939
C	1.86798	3.37968	-0.26933
H	2.11856	4.3578	0.17128
H	2.53888	2.62942	0.16895
H	2.08084	3.41846	-1.34415
C	0.13644	2.86249	1.46346
H	-0.90433	2.56225	1.64419
H	0.78119	2.09396	1.90892
H	0.31563	3.80718	2.00015
C	-0.50855	4.07374	-0.62478
H	-0.32976	5.06404	-0.17633
H	-0.3553	4.15112	-1.70736

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H	-1.56143	3.81031	-0.46114
H	-0.14268	-0.65631	1.6652

D-TS-3

O	1.01854	1.52665	1.18264
C	1.40245	0.81885	0.25792
C	2.88414	0.66033	0.03374
C	3.74338	1.36676	0.88241
C	3.45129	-0.09591	-0.99985
C	5.12225	1.31548	0.71409
H	3.28537	1.95007	1.67613
C	4.82948	-0.14518	-1.17598
H	2.80775	-0.66442	-1.66656
C	5.67342	0.56078	-0.31904
H	5.77234	1.86869	1.38901
H	5.24935	-0.74167	-1.98303
H	6.75166	0.52063	-0.4567
C	0.41505	0.23117	-0.72496
C	-0.25419	-0.99419	-0.12279
C	-1.26158	-0.76855	0.833
C	-0.51425	-2.10985	-1.11686
C	-1.91087	-1.97251	1.46904
H	-2.45512	0.00921	-0.38732
H	-1.05077	0.05639	1.5194
C	-1.0381	-3.35751	-0.42283
H	-1.25142	-1.75212	-1.85564
H	0.40315	-2.33369	-1.68317
C	-2.26305	-3.02579	0.42239
H	-2.82683	-1.68095	2.00851
H	-1.26004	-2.45203	2.22832
H	-1.26097	-4.14649	-1.15547
H	-0.23847	-3.7289	0.23291
H	-2.6614	-3.93724	0.89224
H	-3.05581	-2.62885	-0.23141
O	1.28924	-1.62838	0.67858
H	1.83431	-1.97509	-0.04221
H	-0.33676	0.99449	-0.96645
O	-3.09488	0.47977	-1.02174
C	-3.6385	1.56307	-0.29999
C	-4.70626	2.17838	-1.1969
H	-5.1797	3.04744	-0.72362
H	-4.26188	2.49921	-2.14484
H	-5.48231	1.43973	-1.42341
C	-2.55171	2.5967	0.01094
H	-1.7495	2.14613	0.60641
H	-2.10873	2.96443	-0.92158
H	-2.94951	3.45863	0.56351
C	-4.26886	1.06452	1.00357
H	-4.77146	1.87119	1.55365
H	-5.00247	0.28008	0.78642
H	-3.49689	0.63244	1.64795
H	0.90832	-0.04102	-1.66622

I14

C	-3.00889	-2.19612	-0.96323
C	-2.27932	-1.34498	-0.1324
C	-2.91956	-0.22687	0.42335
C	-4.27247	0.01411	0.14215
C	-4.98324	-0.83458	-0.69333
C	-4.34791	-1.94684	-1.25017
H	-2.51568	-3.06561	-1.39353
H	-1.21587	-1.57397	0.09188
H	-4.73621	0.88357	0.60127
H	-6.03016	-0.63632	-0.91416
H	-4.90137	-2.61609	-1.90685
C	-2.22277	0.72515	1.34231
O	-2.87359	1.56603	1.95725
C	-0.7184	0.64447	1.49969
H	0.48251	-2.90509	0.68417
H	-0.35215	-0.40207	1.46537
H	1.76498	-1.68811	-0.33726
C	3.60918	-1.26476	0.13379
C	3.21451	-0.1394	1.0952
H	2.24852	-0.39036	1.54623

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H	3.95933	0.00779	1.89003	C	-3.6148	0.46086	-1.39732
H	3.09976	0.80597	0.55194	H	-1.54494	1.08935	-1.25807
C	3.76249	-2.56543	0.93131	C	-4.5495	-0.53056	-1.10552
H	2.79012	-2.7915	1.38291	H	-4.8665	-2.4764	-0.23088
H	4.03875	-3.38893	0.2623	H	-3.93601	1.39122	-1.8614
H	4.52175	-2.48952	1.7219	C	0.57094	-0.35347	-0.86919
C	4.90786	-0.91947	-0.58589	H	0.32955	-0.45921	-1.93921
H	5.17647	-1.71784	-1.28663	C	2.02046	-0.61086	-0.5922
H	4.78388	0.00407	-1.16277	C	2.53611	-2.02375	-0.66994
H	5.73914	-0.779	0.11686	C	2.83214	0.42643	-0.33319
O	2.62616	-1.43283	-0.85659	C	3.93639	-2.17121	-0.0862
C	1.40168	3.39577	-0.26448	H	2.53313	-2.34893	-1.72485
H	2.48288	3.28976	-0.07009	H	1.83441	-2.6869	-0.15289
H	1.19004	4.46538	-0.11768	C	4.30949	0.30303	-0.11703
C	0.62913	2.57743	0.7254	H	2.37691	1.41933	-0.30727
C	1.10295	2.98742	-1.70303	C	4.84747	-1.05085	-0.56956
H	1.82195	3.45356	-2.3895	H	4.35672	-3.15466	-0.33332
H	0.11018	3.36926	-1.98494	H	3.87125	-2.1284	1.01024
C	1.11278	1.47153	-1.83674	H	4.83461	1.11483	-0.64004
H	2.09119	1.06555	-1.5456	H	4.54708	0.45705	0.94891
H	0.96159	1.16968	-2.88024	H	5.87744	-1.19761	-0.21867
C	0.01106	1.42336	0.43036	H	4.88672	-1.07429	-1.66856
C	0.05391	0.82965	-0.95038	H	0.36198	0.77871	-0.70737
H	-0.94295	0.91783	-1.41424	H	-5.59803	-0.3861	-1.35893
H	0.24759	-0.24661	-0.85279	O	-1.82429	-3.21155	2.68672
O	0.59246	-1.95229	0.60549	H	-2.45497	-2.49558	2.79605
H	-0.49472	1.09045	2.4744	H	-1.15916	-2.7925	2.10752
H	0.60036	2.9382	1.75448	C	-0.13755	2.95162	0.49399
2.9w				C	0.98557	3.93738	0.8849
O	-0.12543	-1.84524	0.87414	H	1.93448	3.39537	0.98253
C	-0.42029	-1.11401	-0.08661	H	1.11049	4.67987	0.08815
C	-1.85293	-0.90332	-0.45905	H	0.79828	4.46977	1.83055
C	-2.80167	-1.88382	-0.13879	C	-1.46782	3.73484	0.43838
C	-2.26819	0.28152	-1.08978	H	-1.41385	4.48891	-0.35563
C	-4.13927	-1.70357	-0.47139	H	-2.28873	3.05026	0.19046
H	-2.47731	-2.77609	0.39187	H	-1.72148	4.2425	1.38197

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C	-0.25315	1.89393	1.61326	H	-0.42664	2.33718	2.60472
H	-1.08564	1.20899	1.40622	O	0.13174	2.39377	-0.72511
H	0.66362	1.29226	1.66341				

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Step III: Pathway for alkene isomerization

2.10e

O	2.34449	2.17796	1.61361
C	2.08742	1.4967	0.62406
C	2.95173	0.33224	0.27594
C	3.70728	-0.2683	1.28987
C	3.09305	-0.11918	-1.04094
C	4.5593	-1.32487	0.99827
H	3.6061	0.11825	2.29996
C	3.96355	-1.16255	-1.33718
H	2.52908	0.37047	-1.83161
C	4.68921	-1.77306	-0.31648
H	5.13116	-1.79754	1.79187
H	4.07967	-1.49852	-2.36379
C	0.93815	1.86793	-0.2284
C	0.0064	1.06235	-0.7766
H	0.76279	2.94284	-0.26189
C	-1.2094	1.63671	-1.43933
H	-1.30219	1.18595	-2.43807
H	-1.10649	2.71507	-1.59092
C	-0.03414	-0.44456	-0.69531
H	0.52906	-0.88062	-1.53177
H	0.4764	-0.79017	0.21028
C	-2.47943	1.31548	-0.62835
C	-1.47718	-0.96409	-0.71984
C	-2.38674	-0.04182	0.09385
H	-1.49859	-1.99235	-0.34466
H	-1.84464	-1.01379	-1.75433
H	-1.87468	0.13732	1.05523
H	-2.65275	2.11077	0.10438
H	-3.3441	1.32797	-1.30474
H	5.36272	-2.59416	-0.54626
C	-3.7672	-0.6488	0.451
C	-3.57876	-1.80812	1.43253
H	-4.54734	-2.22591	1.72751
H	-2.99234	-2.62627	1.00237
H	-3.0701	-1.47556	2.34434
C	-4.63324	0.41361	1.1326
H	-4.88633	1.23518	0.45507
H	-5.5747	-0.023	1.4827
H	-4.12323	0.84291	2.00293
C	-4.48974	-1.16619	-0.79438
H	-3.94597	-1.99229	-1.26477
H	-5.48578	-1.53827	-0.53191
H	-4.62509	-0.38285	-1.54861

2.9t

O	2.93578	-2.2538	-1.11595
C	2.48611	-1.53527	-0.23523
C	3.03692	-0.16717	-0.01046
C	4.13392	0.23614	-0.78152
C	2.50594	0.71937	0.93503
C	4.6936	1.49427	-0.60794
H	4.52607	-0.46706	-1.51046
C	3.06402	1.98104	1.10666
H	1.64254	0.42961	1.52866
C	4.15908	2.36917	0.33744
H	5.54689	1.79753	-1.208
H	2.64448	2.66425	1.83953
H	4.59549	3.35483	0.47405
C	1.34967	-2.0088	0.64806
H	1.2783	-3.09701	0.53594
C	0.02102	-1.36252	0.34535
C	-1.00238	-1.43604	1.44213
C	-0.25201	-0.77347	-0.8263

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C	-2.40294	-1.1003	0.95189
H	-0.70937	-0.75672	2.26035
H	-0.98287	-2.43936	1.89068
C	-1.53963	-0.07771	-1.13825
C	-2.3992	0.17221	0.10416
H	-3.08702	-1.01276	1.80334
H	-2.77378	-1.93464	0.34039
H	-1.88648	0.95494	0.69132
H	1.60035	-1.82263	1.70292
H	0.50575	-0.7722	-1.61009
H	-2.10758	-0.66148	-1.88182
H	-1.31385	0.87177	-1.63967
C	-3.81547	0.72241	-0.21203
C	-3.71559	1.88528	-1.20271
H	-3.38839	1.55584	-2.19369
H	-4.69081	2.36833	-1.3264
H	-3.01019	2.64845	-0.85294
C	-4.45452	1.253	1.07402
H	-5.4472	1.66831	0.86925
H	-4.58172	0.47096	1.82917
H	-3.84729	2.05045	1.51738
C	-4.72013	-0.36009	-0.80506
H	-4.91739	-1.16385	-0.08838
H	-5.68756	0.06586	-1.09198
H	-4.28496	-0.81212	-1.70338

2.6c′

Ru	2.13377	0.19302	-0.25699
Cl	2.5148	0.47675	2.04209
N	-0.025	2.14029	-0.22214
N	0.17773	-0.15802	-0.20344
N	2.58147	-1.82305	-0.24424
N	-1.76833	-1.51168	-0.0466
N	0.25558	-2.55051	-0.07631
N	1.34723	2.13962	-0.31055
N	-1.97351	0.86625	-0.1293
C	-0.6649	0.89358	-0.17929
C	1.58541	-2.77249	-0.13582
C	-0.40938	-1.42123	-0.10461
C	-4.76366	0.61523	-0.03098
H	-4.30182	1.59658	-0.07982
C	-2.48016	-0.40265	-0.06666
C	-3.94501	-0.51954	-0.01531
C	-0.52511	3.41852	-0.14547
C	1.95455	-4.14273	-0.09259
H	1.13924	-4.85124	-0.00441
C	0.57475	4.24649	-0.18103
H	0.55699	5.32576	-0.13801
C	4.26167	-3.55976	-0.26261
H	5.31498	-3.81087	-0.31646
C	-4.54863	-1.78393	0.04847
H	-3.90769	-2.65973	0.06143
C	3.87302	-2.23996	-0.29833
H	4.60696	-1.44732	-0.38577
C	3.26765	-4.54049	-0.15353
H	3.52604	-5.59497	-0.11609
C	-8.24414	-0.90976	0.1271
H	-8.7436	0.06189	0.10106
H	-8.56866	-1.4261	1.03693
H	-8.61996	-1.49988	-0.71565
C	-5.92786	-1.90145	0.0939
H	-6.38169	-2.88936	0.14323
C	1.71203	3.42185	-0.27514
C	-6.14616	0.4874	0.01491
H	-6.77094	1.37827	0.00201

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C	-1.96172	3.75849	-0.0462
H	-2.06772	4.84395	0.00329
H	-2.42109	3.31302	0.83999
H	-2.52737	3.38184	-0.90234
C	-6.75428	-0.76931	0.07773
C	3.14366	3.81076	-0.31462
H	3.63164	3.45623	-1.23063
H	3.68117	3.40901	0.55202
H	3.25231	4.89611	-0.29256
O	4.36376	0.71008	-0.23675
H	4.49538	1.61331	-0.54405
H	4.3815	0.77102	0.74025

I15-2.10a

Ru	0.54333	-0.59119	0.90891
Cl	0.05531	-2.13712	2.71565
N	-1.64419	1.08425	1.84016
N	-1.35538	-0.60404	0.29894
N	1.02262	-2.21997	-0.2764
N	-3.15456	-1.25696	-1.09811
N	-0.30324	0.93316	2.08452
N	-3.47749	0.44414	0.54766
C	-2.21147	0.26916	0.84853
C	0.11679	-2.71826	-1.18581
C	-1.85007	-1.40118	-0.72978
C	-6.16339	0.65891	-0.21802
H	-5.76718	1.27864	0.58055
C	-3.90007	-0.37711	-0.4571
C	-5.31185	-0.25116	-0.85366
C	-2.20295	2.0241	2.67166
C	0.52195	-3.79691	-2.01646
H	-0.20626	-4.13799	-2.74321
C	-1.16941	2.47722	3.46266
H	-1.24735	3.22405	4.23955
C	2.62397	-3.91539	-0.89045
H	3.59576	-4.364	-0.71254
C	-5.82974	-1.05102	-1.8823
H	-5.16381	-1.75655	-2.36897
C	2.21368	-2.84451	-0.12527
H	2.86091	-2.42062	0.63573
C	1.75418	-4.39067	-1.88045
H	2.03682	-5.22399	-2.51785
C	-9.45057	0.0869	-2.04377
H	-9.9927	0.81308	-1.43285
H	-9.97148	-0.87298	-1.96114
H	-9.54101	0.40026	-3.08964
C	-7.15815	-0.93759	-2.25864
H	-7.5458	-1.56607	-3.05822
C	-0.01186	1.77515	3.07288
C	-7.4944	0.7653	-0.60164
H	-8.14602	1.47645	-0.09758
C	-3.63162	2.41125	2.66828
H	-3.79944	3.16028	3.44488
H	-4.28242	1.55271	2.85286
H	-3.93791	2.82115	1.70244
C	-8.01685	-0.02783	-1.62684
C	1.37122	1.86795	3.60295
H	2.03998	2.38081	2.89976
H	1.78045	0.86941	3.78873
H	1.39353	2.43031	4.53812
O	2.70846	-0.39621	1.54434
H	2.93904	0.53798	1.53819
H	2.84211	-0.71101	2.47709
N	-1.14769	-2.2925	-1.39105
O	0.98688	0.94618	-0.40588

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C	1.94211	1.18614	-1.20396
C	2.11301	2.58132	-1.62336
C	1.53617	3.61151	-0.85936
C	2.8018	2.91566	-2.80068
C	1.66873	4.93546	-1.25066
H	0.98375	3.3445	0.03805
C	2.92462	4.2421	-3.19273
H	3.21497	2.11924	-3.41413
C	2.36564	5.25635	-2.41655
H	1.2258	5.72413	-0.6489
H	3.44956	4.48701	-4.11167
H	2.46548	6.2937	-2.72297
C	2.78754	0.10387	-1.69166
C	4.13584	0.08135	-1.77759
H	2.25075	-0.81901	-1.90026
C	4.85447	-1.16885	-2.18177
H	5.53525	-0.92297	-3.01001
H	4.15333	-1.92038	-2.55816
C	5.05617	1.20146	-1.36089
H	5.23205	1.88042	-2.20687
H	4.56882	1.8203	-0.59622
C	5.68163	-1.73512	-1.00821
C	6.39567	0.66463	-0.8379
C	6.17232	-0.62948	-0.06738
H	6.88168	1.42534	-0.219
H	7.07987	0.47504	-1.67596
H	5.41506	-0.45056	0.70823
H	7.08037	-0.94518	0.45552
H	5.0696	-2.45138	-0.45053
H	6.53115	-2.29803	-1.4114
O	2.81799	-1.55728	3.93544
H	2.6856	-1.13209	4.78655
H	1.94539	-1.96097	3.72805

I15-2.10e

Ru	-0.03929	-0.96862	-0.34713
Cl	0.42776	-2.61874	-2.05605
N	1.63552	0.88906	-1.81992
N	1.91383	-0.6543	-0.12776
N	-0.0459	-2.48307	1.07182
N	4.05486	-1.00636	0.82088
N	0.30096	0.59187	-1.70803
N	3.78917	0.52713	-0.99231
C	2.51386	0.21845	-0.94833
C	1.08089	-2.74185	1.8187
C	2.72418	-1.30096	0.79945
C	6.54144	1.04364	-0.94409
H	5.90373	1.52471	-1.67944
C	4.52536	-0.13977	-0.0562
C	5.96835	0.14981	-0.03304
C	1.83932	1.96431	-2.65041
C	0.99406	-3.7217	2.84501
H	1.89255	-3.87836	3.4307
C	0.58367	2.35451	-3.06549
H	0.36489	3.17151	-3.73799
C	-1.26004	-4.21578	2.2289
H	-2.18087	-4.78051	2.32571
C	6.79826	-0.47248	0.91043
H	6.34736	-1.16663	1.61252
C	-1.15183	-3.24176	1.2609
H	-1.97582	-3.01664	0.59095
C	-0.15282	-4.44748	3.05645
H	-0.19055	-5.19919	3.84018
C	10.20845	0.97159	0.06343
H	10.50073	1.699	-0.69811

H	10.79478 0.06165 -0.10459	C	-2.46569 0.03515 1.89263
H	10.51914 1.36583 1.03702	C	-3.79208 0.28793 1.80794
C	8.15686 -0.20274 0.93672	H	-2.15469 -1.00649 1.97679
H	8.78794 -0.69382 1.67513	C	-4.77984 -0.83848 1.82229
C	-0.34371 1.48879 -2.45247	H	-5.58247 -0.59697 2.53306
C	7.90512 1.30702 -0.91116	H	-4.31684 -1.76764 2.16846
H	8.33759 2.00322 -1.62724	C	-4.42501 1.62051 1.50262
C	3.16505 2.52834 -2.9904	H	-4.6864 2.13735 2.43665
H	3.03355 3.34159 -3.70717	H	-3.70489 2.27723 1.00018
H	3.82506 1.7727 -3.42364	C	-5.38561 -1.02087 0.41354
H	3.68212 2.90907 -2.10569	C	-5.67707 1.44133 0.63154
C	8.73779 0.69138 0.02718	C	-5.45225 0.30465 -0.3672
C	-1.82876 1.51674 -2.5013	H	-5.91295 2.38694 0.13341
H	-2.24972 1.73814 -1.51093	H	-6.54787 1.20268 1.25715
H	-2.2482 0.55792 -2.82234	H	-4.45332 0.48158 -0.81412
H	-2.18103 2.28983 -3.1867	H	-4.78833 -1.75103 -0.14215
O	-2.23631 -1.29584 -0.75883	H	-6.39136 -1.44909 0.50743
H	-2.76056 -0.52777 -0.50018	O	-2.25612 -1.91071 -3.3839
H	-2.36029 -1.41943 -1.73332	H	-2.01223 -1.28947 -4.07564
N	2.29894 -2.17802 1.68036	H	-1.40249 -2.34467 -3.15922
O	-0.37112 0.59109 0.9815	H	-1.12323 5.89955 3.72117
C	-1.35609 0.95884 1.68458	C	-6.42716 0.27429 -1.56912
C	-1.31662 2.31108 2.24477	C	-6.18723 1.5022 -2.45099
C	-0.46882 3.27402 1.66978	H	-6.84137 1.48031 -3.32879
C	-2.08178 2.66187 3.36899	H	-6.3855 2.44094 -1.92389
C	-0.40738 4.55593 2.19518	H	-5.15236 1.53274 -2.8126
H	0.12787 2.9902 0.80638	C	-6.15583 -0.97578 -2.40937
C	-2.00861 3.94395 3.89707	H	-6.4098 -1.89579 -1.87431
H	-2.71367 1.9097 3.8348	H	-6.75004 -0.9591 -3.32887
C	-1.17682 4.89592 3.30915	H	-5.09962 -1.04296 -2.69979
H	0.24332 5.29649 1.73892	C	-7.88384 0.27487 -1.10316
H	-2.59458 4.2012 4.77478	H	-8.13481 1.19219 -0.55982

H	-8.55955	0.20797	-1.96207	H	-8.87565 -1.06382 0.23593
H	-8.10828	-0.57428	-0.44859	H	-9.01444 0.08226 -1.09432
I16-2.10a				H	-8.83296 0.6783 0.54772
Ru	1.90649	-0.23184	-0.74265	C	-6.30424 1.08964 -0.40617
Cl	1.96091	-0.70621	-3.16645	H	-6.84053 2.03348 -0.3296
N	-0.06702	-2.38804	-0.63154	C	1.77613 -3.50343 -0.5492
N	-0.10507	-0.09741	-0.85474	C	-6.30659 -1.31153 -0.39871
N	2.13986	1.79627	-1.17458	H	-6.8439 -2.2545 -0.32112
N	-2.15986	1.068	-0.9183	C	-1.85621 -4.17649 -0.62955
N	1.29994	-2.26011	-0.56245	H	-1.86445 -5.26783 -0.60426
N	-2.13552	-1.31534	-0.74816	H	-2.38923 -3.8347 -1.52023
C	-0.82698	-1.22339	-0.7574	H	-2.41514 -3.79385 0.22895
C	1.06001	2.64114	-1.14766	C	-7.0196 -0.11177 -0.31149
C	-0.79872	1.09223	-0.94342	C	3.23202 -3.78983 -0.58886
C	-4.92942	-1.3164	-0.57683	H	3.77851 -3.24035 0.18398
H	-4.38212	-2.25248	-0.63174	H	3.64897 -3.5358 -1.57064
C	-2.7591	-0.10186	-0.80177	H	3.41925 -4.85205 -0.4237
C	-4.2232	-0.11272	-0.67505	O	4.10116 -0.62934 -1.2094
C	-0.45347	-3.70628	-0.61089	H	4.36323 -1.46722 -0.80818
C	1.27182	4.03449	-1.29445	H	3.88217 -0.83865 -2.14624
H	0.39666	4.66885	-1.18612	N	-0.24097 2.28167 -1.00167
C	0.7146	-4.42923	-0.56273	O	0.39803 -1.56208 2.18821
H	0.79507	-5.50617	-0.5433	C	0.31752 -0.3572 1.93488
C	3.5908	3.64326	-1.71321	C	-0.9695 0.3593 2.18892
H	4.591	3.97633	-1.96579	C	-2.08684 -0.43368 2.50099
C	-4.93063	1.09424	-0.58728	C	-1.14227 1.74705 2.0778
H	-4.3719	2.02444	-0.63719	C	-3.33736 0.13858 2.67372
C	3.35083	2.30281	-1.50042	H	-1.9408 -1.50797 2.57302
H	4.15389	1.57664	-1.55964	C	-2.39846 2.32297 2.24627
C	2.52274	4.53569	-1.57186	H	-0.31065 2.39802 1.82476
H	2.66977	5.6049	-1.69441	C	-3.49503 1.51923 2.54158
C	-8.50693	-0.10651	-0.14118	H	-4.19973 -0.48953 2.88286

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H	-2.51348 3.39031 2.08546	C	0.71261 1.15736 -0.85646
C	1.43861 0.39841 1.32447	C	-0.95171 -2.79651 -0.39771
C	2.78851 -0.03836 1.27701	C	0.81853 -1.14227 -0.59153
H	1.29741 1.47719 1.27148	C	4.81189 1.50081 -0.78278
C	3.2522 -1.31902 1.93072	H	4.21628 2.38205 -1.0005
H	4.25281 -1.55801 1.53441	C	2.70657 0.1583 -0.72948
H	2.58569 -2.15486 1.72523	C	4.16883 0.26671 -0.6408
C	3.87041 1.02907 1.36293	C	0.17856 3.58934 -1.22301
H	4.57672 0.94451 0.52968	C	-1.07762 -4.20204 -0.26648
H	3.40944 2.02032 1.27946	H	-0.16084 -4.74868 -0.06255
C	3.36232 -1.0992 3.45437	C	-1.0307 4.23626 -1.30039
C	4.64706 0.91152 2.69192	H	-1.17667 5.28303 -1.52271
C	3.76076 0.3425 3.79063	C	-3.41021 -4.04101 -0.75043
H	5.05117 1.89122 2.96616	H	-4.38013 -4.47861 -0.95641
H	5.51671 0.25319 2.5602	C	4.93782 -0.86796 -0.34291
H	2.86181 0.96775 3.88077	H	4.42684 -1.8168 -0.20351
H	4.25914 0.3872 4.76432	C	-3.25927 -2.67293 -0.77685
H	2.40321 -1.35106 3.91676	H	-4.09559 -2.01321 -0.98745
H	4.10154 -1.8009 3.859	C	-2.29123 -4.82212 -0.43922
O	-1.84621 4.48902 -0.09754	H	-2.37047 -5.90258 -0.36357
H	-2.55397 4.60774 -0.73489	C	8.45139 0.56864 -0.20238
H	-1.41924 3.66204 -0.40019	H	8.77797 1.60168 -0.05901
H	-4.48126 1.96387 2.64881	H	8.95864 0.18914 -1.09685
I17-2.10a		H	8.81942 -0.02402 0.64043
Ru	-2.02465 0.07018 -0.48634	C	6.31093 -0.76188 -0.19435
Cl	-1.99648 -0.06826 -2.94689	H	6.89618 -1.64714 0.04662
N	-0.11936 2.27738 -0.94361	C	-2.0354 3.27614 -1.05831
N	0.06096 -0.00466 -0.73798	C	6.18955 1.5962 -0.63564
N	-2.08387 -2.04022 -0.54148	H	6.6786 2.5617 -0.74706
N	2.17711 -1.04539 -0.61503	C	1.5477 4.12448 -1.39023
N	-1.47649 2.09557 -0.80672	H	1.48657 5.19095 -1.61476
N	2.0143 1.32819 -0.87685	H	2.08802 3.61937 -2.19453

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H	2.14114	3.98201	-0.48298
C	6.96418	0.46984	-0.3412
C	-3.50489	3.45187	-1.13806
H	-3.86784	4.19718	-0.42362
H	-4.0171	2.50353	-0.95901
H	-3.78609	3.79475	-2.13826
N	0.33169	-2.34868	-0.38591
O	-0.21298	1.99295	1.95981
C	-0.21511	0.76084	2.02218
C	1.03328	0.03317	2.37804
C	2.20867	0.7967	2.47878
C	1.11503	-1.3573	2.54581
C	3.42972	0.18633	2.71778
H	2.13138	1.87045	2.33352
C	2.34177	-1.9714	2.77766
H	0.23088	-1.98291	2.46535
C	3.49766	-1.20036	2.85955
H	4.33736	0.7833	2.76202
H	2.39754	-3.05275	2.83999
C	-1.42676	-0.01627	1.65602
C	-2.72039	0.57761	1.58509
H	-1.39808	-1.09232	1.82227
C	-3.7407	-0.2556	1.07579
C	-3.15024	1.94135	2.04616
C	-5.12371	0.33063	1.05684
H	-5.86647	-0.39892	0.72191
O	2.19773	-4.31488	0.62587
H	2.72855	-4.56911	-0.13224
H	1.687	-3.5526	0.28871
H	-3.64935	-1.33238	1.20068
H	-2.32561	2.48166	2.50794
O	-0.84136	-3.13428	-3.37318
H	-1.2827	-2.27299	-3.39886
H	0.01716	-2.92082	-2.99773
H	-3.4008	0.46491	-1.17085
H	4.45939	-1.68242	3.01531
C	-5.44858	0.84859	2.46687
H	-6.41593	1.36103	2.44952
H	-5.57606	-0.01067	3.13488
C	-4.34074	1.77771	3.0088
H	-4.74289	2.77154	3.22863
H	-3.96572	1.39174	3.96271
H	-5.17251	1.16886	0.35164
H	-3.46525	2.53978	1.1866

I18-2.9w

Ru	1.10033	0.26767	-0.23803
Cl	1.12522	0.3485	-2.7115
N	-0.60007	-2.10648	-0.46932
N	-0.91351	0.16094	-0.20566
N	1.03726	2.36625	-0.43863
N	-3.10472	1.03982	-0.04596
N	0.73263	-1.78484	-0.58131
N	-2.77031	-1.32165	-0.10188
C	-1.49488	-1.04936	-0.25096
C	-0.15641	3.03439	-0.48637
C	-1.76927	1.24548	-0.19558
C	-5.5247	-1.69681	0.31358
H	-4.8576	-2.55161	0.25715
C	-3.54286	-0.20654	0.01656
C	-4.98605	-0.41026	0.20412
C	-0.84119	-3.37069	-0.95062
C	-0.14464	4.43663	-0.70301
H	-1.11511	4.92679	-0.71486
C	0.38481	-3.86156	-1.33908

H	0.56826	-4.83301	-1.77422
C	2.24275	4.40529	-0.852
H	3.20101	4.88858	-1.00431
C	-5.84959	0.69397	0.26882
H	-5.42767	1.69028	0.1699
C	2.18794	3.04646	-0.62897
H	3.08795	2.4392	-0.6099
C	1.03668	5.11565	-0.88477
H	1.02901	6.1886	-1.05518
C	-9.2325	-0.96844	0.73877
H	-9.49409	-2.02221	0.86282
H	-9.79305	-0.58691	-0.12162
H	-9.60266	-0.42647	1.61544
C	-7.21094	0.50553	0.44253
H	-7.87092	1.36957	0.48726
C	1.33407	-2.84429	-1.11907
C	-6.89083	-1.87404	0.49045
H	-7.29827	-2.87942	0.57584
C	-2.18352	-3.97642	-1.07155
H	-2.08429	-4.98487	-1.47766
H	-2.80171	-3.37486	-1.74389
H	-2.70557	-4.02275	-0.1134
C	-7.7582	-0.77995	0.55779
C	2.77618	-2.81797	-1.47009
H	3.04691	-1.83034	-1.85583
H	2.98597	-3.55859	-2.24386
H	3.42691	-3.05072	-0.61855
N	-1.3915	2.502	-0.31804
O	3.21732	0.20501	-0.26636
C	3.7802	-0.44635	0.64455
C	5.23126	-0.61865	0.608
C	5.95523	-0.06977	-0.4656
C	5.91762	-1.34534	1.59441
C	7.32878	-0.23625	-0.54057
H	5.41251	0.47512	-1.23208
C	7.29421	-1.51073	1.51271
H	5.37496	-1.78414	2.42673
C	8.00191	-0.9552	0.44871
H	7.88039	0.1901	-1.373
H	7.81705	-2.07328	2.28017
C	2.91073	-1.09729	1.67441
H	2.80894	-2.15718	1.3857
C	1.53259	-0.4697	1.77669
C	0.55053	-1.33854	2.53245
C	1.41463	0.93877	1.81373
C	-0.67627	-0.60423	3.06529
H	1.10265	-1.74719	3.3959
H	0.26761	-2.21767	1.93867
C	0.31893	1.63911	2.59001
C	-0.27979	0.73667	3.6636
H	-1.17715	-1.23374	3.80841
H	-1.40984	-0.43567	2.26823
H	-1.14259	1.22467	4.12862
H	0.45676	0.57304	4.46399
H	3.40101	-1.11547	2.65833
H	2.33893	1.51356	1.71026
H	-0.48054	1.98596	1.92555
H	0.73327	2.54925	3.03844
O	-3.52012	4.50022	-0.35871
H	-3.58614	4.5825	0.59522
H	-2.95959	3.70831	-0.45608
O	-1.65332	-1.23098	-3.10582
H	-0.76126	-0.84255	-3.13759
H	-2.21777	-0.47801	-3.3005

H	9.07861	-1.0849	0.38777
I16-2.10e			
Ru	1.17093	1.47673	0.57161
Cl	0.57625	3.70733	1.45311
N	-0.77152	2.08779	-1.52769
N	-0.7944	1.01734	0.51015
N	1.345	0.78695	2.53344
N	-2.75443	-0.05352	1.28159
N	0.57083	2.28023	-1.30127
N	-2.76353	1.11028	-0.80571
C	-1.50079	1.37796	-0.57133
C	0.33924	0.04796	3.1019
C	-1.44816	0.27772	1.47482
C	-5.41387	0.30888	-1.22181
H	-4.93108	0.99095	-1.91496
C	-3.33968	0.34663	0.16866
C	-4.71916	-0.0964	-0.07723
C	-1.18061	2.69688	-2.68942
C	0.54989	-0.5378	4.37494
H	-0.24406	-1.17888	4.74752
C	-0.06246	3.32101	-3.18882
H	-0.01354	3.90847	-4.09389
C	2.65957	0.57013	4.54134
H	3.56658	0.83441	5.07294
C	-5.33847	-0.9898	0.80781
H	-4.78158	-1.32042	1.67991
C	2.44113	1.06713	3.27448
H	3.17501	1.70249	2.79132
C	1.69775	-0.28477	5.09006
H	1.84188	-0.73011	6.07024
C	-8.70796	-1.553	-0.85309
H	-9.00103	-1.41247	-1.8966
H	-9.44088	-1.01972	-0.23659
H	-8.81013	-2.61517	-0.61171
C	-6.61504	-1.46126	0.54823
H	-7.08068	-2.16267	1.23781
C	0.9954	3.05403	-2.29792
C	-6.69474	-0.16587	-1.4721
H	-7.22355	0.15474	-2.36736
C	-2.55541	2.64396	-3.23372
H	-2.59081	3.21671	-4.1624
H	-3.28766	3.05266	-2.53301
H	-2.86415	1.6146	-3.43574
C	-7.31942	-1.057	-0.59404
C	2.3821	3.58059	-2.35071
H	3.12607	2.78725	-2.22883
H	2.5369	4.33833	-1.57343
H	2.575	4.05997	-3.31177
O	3.15325	2.58642	0.73737
H	3.48912	2.77163	-0.1484
H	2.69126	3.40675	1.02561
N	-0.88747	-0.18685	2.56992
O	0.4381	-0.53695	-2.26326
C	0.3353	-0.9994	-1.12405
C	-0.81385	-1.89857	-0.8001
C	-1.84497	-1.98056	-1.75109
C	-0.95162	-2.60928	0.40147
C	-2.98371	-2.73006	-1.50007
H	-1.73009	-1.41646	-2.67259
C	-2.09632	-3.35908	0.65686
H	-0.18555	-2.56677	1.17006
C	-3.1121	-3.41752	-0.29206
H	-3.78873	-2.75904	-2.23026
H	-2.20468	-3.8426	1.62249

C	1.28063	-0.64401	-0.0376	H	6.02381	-5.02205	-0.9862
C	2.5559	-0.04948	-0.22443	H	5.84479	-3.83529	0.3041
H	1.16532	-1.21447	0.88299	**I17-2.10e**			
C	3.1371	0.21712	-1.59257	Ru	-1.40703	0.1319	-0.57775
H	3.98603	0.90993	-1.47212	Cl	-1.8866	-0.36556	-2.94269
H	2.41318	0.66645	-2.27029	N	0.77025	1.71841	-1.73113
C	3.6578	-0.43548	0.75216	N	0.54106	-0.46228	-1.01967
H	4.10319	0.45059	1.2178	N	-1.92235	-1.86145	-0.1513
H	3.22941	-1.03195	1.56671	N	2.45742	-1.72017	-0.42441
C	3.65609	-1.10704	-2.18731	N	-0.56457	1.86564	-1.43851
C	4.76538	-1.22924	0.03282	N	2.69712	0.43922	-1.43364
C	4.19039	-2.06707	-1.10909	C	1.38412	0.49611	-1.40698
H	5.29999	-1.84384	0.76491	C	-0.94788	-2.79822	0.07417
H	5.51266	-0.53601	-0.37845	C	1.09201	-1.61282	-0.48067
H	3.32392	-2.61669	-0.70132	C	5.45858	0.28986	-1.03385
H	2.84319	-1.58023	-2.74666	H	4.99746	1.21273	-1.37239
H	4.44566	-0.87944	-2.91609	C	3.18209	-0.72336	-0.89777
O	-2.1348	-2.48363	3.77142	C	4.64353	-0.81623	-0.7674
H	-2.97696	-2.19297	4.12849	C	1.26569	2.84086	-2.3532
H	-1.82513	-1.69599	3.28015	C	-1.33375	-4.11806	0.39441
H	-4.01758	-3.98224	-0.08463	H	-0.53491	-4.82041	0.60212
C	5.15459	-3.1473	-1.66154	C	0.19946	3.7039	-2.4635
C	4.53113	-3.80854	-2.89314	H	0.2226	4.68343	-2.91816
H	4.43484	-3.11076	-3.7308	C	-3.62548	-3.55132	0.05794
H	5.14816	-4.64685	-3.23422	H	-4.681	-3.79356	0.00879
H	3.53219	-4.20102	-2.66993	C	5.24285	-2.00345	-0.32059
C	6.50989	-2.54862	-2.04275	H	4.61104	-2.86373	-0.12006
H	7.03673	-2.14829	-1.17004	C	-3.21195	-2.26264	-0.20031
H	7.1535	-3.31363	-2.49011	H	-3.92736	-1.48884	-0.45966
H	6.41202	-1.73905	-2.77477	C	-2.65581	-4.49925	0.38901
C	5.37272	-4.22958	-0.60151	H	-2.93228	-5.52368	0.61976
H	4.42402	-4.69346	-0.30907	C	8.91866	-1.05876	-0.21525

H	9.41341	-0.10803	-0.4274	H	-3.02313	2.13359	0.57915
H	9.36168	-1.81747	-0.86919	C	-0.58926	0.01602	1.61936
H	9.17206	-1.34654	0.81039	C	-0.47232	2.48104	1.53955
C	6.61504	-2.07469	-0.14784	C	0.86732	0.12773	1.95333
H	7.06548	-3.00316	0.19645	C	0.20316	2.39868	2.91401
C	-0.91993	3.06155	-1.89365	C	1.18375	1.20962	3.01532
C	6.83324	0.21013	-0.85357	H	-0.57781	2.30393	3.67708
H	7.45502	1.0791	-1.05807	H	0.71382	3.34464	3.12462
C	2.67054	3.00935	-2.78741	H	1.05089	0.74642	4.00275
H	2.76174	3.94373	-3.344	H	1.27437	-0.84449	2.24922
H	3.00673	2.18229	-3.41674	H	1.42063	0.42257	1.05349
H	3.35029	3.0392	-1.93085	O	2.28678	-2.95301	2.30547
C	7.43714	-0.96941	-0.40842	H	2.98371	-2.59746	1.74403
C	-2.32073	3.53272	-1.77485	H	1.60272	-3.13045	1.63853
H	-2.49404	4.06555	-0.83263	H	-1.14152	-0.86057	1.93746
H	-3.00339	2.67908	-1.82159	H	-1.12147	3.36043	1.45914
H	-2.56794	4.21836	-2.58749	H	0.30278	2.59144	0.77129
N	0.40327	-2.59632	0.04533	O	-1.08222	-3.52503	-2.83191
O	-3.38284	-0.49416	2.44352	H	-1.43914	-2.63672	-2.98304
C	-3.66293	0.28697	1.54227	H	-0.13481	-3.3725	-2.79724
C	-5.06488	0.36873	1.03102	H	-2.95227	0.42774	-0.85845
C	-6.01522	-0.47297	1.62478	H	-8.74913	0.36996	-0.20123
C	-5.46464	1.20895	-0.01699	C	2.68275	1.63038	2.94031
C	-7.3321	-0.47147	1.18758	C	3.0403	2.42783	4.19632
H	-5.683	-1.12443	2.42784	H	4.09538	2.72187	4.1811
C	-6.78408	1.20887	-0.45638	H	2.44953	3.34536	4.29042
H	-4.7445	1.8579	-0.50839	H	2.87495	1.83175	5.10052
C	-7.71945	0.37043	0.14528	C	3.57231	0.38394	2.89496
H	-8.06018	-1.12801	1.65533	H	3.35525	-0.29759	3.7249
H	-7.08103	1.85919	-1.2738	H	3.43927	-0.18333	1.96771
C	-2.63086	1.16984	0.90817	H	4.62962	0.66612	2.95253
C	-1.26465	1.2136	1.35111	C	2.98068	2.48888	1.70559

H	2.41023 3.42544 1.70341	C	-8.95998 -1.29158 0.68781
H	4.0432 2.75696 1.68415	H	-9.18694 -2.20735 1.23941
H	2.77397 1.95958 0.76681	H	-9.53523 -1.31895 -0.24453
I18-2.9t		H	-9.34494 -0.44542 1.26579
Ru	1.3058 -0.09755 -0.5791	C	-6.97066 0.03797 -0.10113
Cl	1.63361 -1.15517 -2.79195	H	-7.64156 0.8726 -0.29412
N	-0.26243 -2.46555 0.13535	C	1.76151 -3.24205 0.08509
N	-0.6881 -0.35387 -0.68	C	-6.61077 -2.21005 0.66509
N	1.18478 1.66141 -1.72939	H	-6.99918 -3.1425 1.06975
N	-2.91529 0.36694 -1.00236	C	-1.69714 -4.53318 0.27317
N	1.0614 -2.10984 0.03095	H	-1.51797 -5.60696 0.35354
N	-2.48554 -1.75585 -0.00242	H	-2.24858 -4.32783 -0.64876
C	-1.21492 -1.49552 -0.20575	H	-2.32787 -4.20894 1.10372
C	-0.02484 2.1676 -2.12246	C	-7.49353 -1.15424 0.4186
C	-1.58422 0.56907 -1.17799	C	3.23563 -3.24838 -0.08954
C	-5.25307 -2.08569 0.40163	H	3.52226 -2.52694 -0.86105
H	-4.57258 -2.90959 0.59459	H	3.57071 -4.23863 -0.40298
C	-3.3056 -0.74248 -0.39697	H	3.7754 -3.00413 0.83336
C	-4.74046 -0.89413 -0.12285	N	-1.24937 1.67873 -1.80902
C	-0.39935 -3.82706 0.24666	O	3.41343 0.01259 -0.35553
C	-0.04286 3.35155 -2.90411	C	3.86249 -0.11676 0.80754
H	-1.02338 3.7485 -3.15113	C	5.30858 -0.17986 1.01362
C	0.88221 -4.33096 0.24335	C	6.16056 -0.11322 -0.10327
H	1.15213 -5.37489 0.30726	C	5.86871 -0.34244 2.29116
C	2.34903 3.38835 -2.92972	C	7.53425 -0.19599 0.05895
H	3.29873 3.81188 -3.23558	H	5.71667 -0.0048 -1.0882
C	-5.61862 0.1722 -0.37206	C	7.24612 -0.42736 2.44739
H	-5.21495 1.09781 -0.77465	H	5.227 -0.40538 3.16518
C	2.32336 2.25477 -2.14588	C	8.08056 -0.35158 1.33411
H	3.23782 1.7652 -1.82404	H	8.18523 -0.14389 -0.80852
C	1.12539 3.95543 -3.30555	H	7.6706 -0.55241 3.43886
H	1.09414 4.85832 -3.90892	C	2.87795 -0.29773 1.92202

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H	2.82516	-1.37917	2.13329
C	1.49273	0.2173	1.58122
C	0.42338	-0.25218	2.53986
C	1.35776	1.47188	0.94913
C	-0.86939	0.55493	2.49467
H	0.85031	-0.16381	3.55342
H	0.22525	-1.32491	2.41009
C	0.18919	2.3986	1.19982
C	-0.60098	2.05826	2.46815
H	-1.48529	0.2803	3.35805
H	-1.4593	0.2879	1.61151
H	0.04718	2.29432	3.33197
H	3.24193	0.15884	2.85359
H	2.28191	1.98602	0.67267
H	-0.49655	2.41802	0.345
H	0.58658	3.41743	1.26816
O	-3.3436	3.69753	-1.90316
H	-2.88648	4.1637	-1.19873
H	-2.83686	2.86719	-1.96366
O	-1.07388	-2.9072	-2.68689
H	-0.18985	-2.51683	-2.80529
H	-1.62465	-2.35599	-3.24913
C	-1.88448	2.91945	2.63396
C	-1.55149	4.39848	2.41843
H	-2.41302	5.0249	2.67272
H	-0.712	4.71851	3.0478
H	-1.28989	4.61403	1.37705
C	-2.97875	2.51106	1.64404
H	-2.65224	2.55759	0.59867
H	-3.34214	1.49393	1.82596
H	-3.84192	3.17987	1.73562
C	-2.41929	2.76091	4.05975
H	-1.6718	3.06646	4.80136
H	-3.30757	3.38396	4.20899
H	-2.71009	1.72938	4.28194
H	9.15757	-0.41691	1.45889

I14-2.10f

Ru	0.32026	-1.17357	0.73543
Cl	-0.37027	-3.11223	2.01757
N	-1.72817	0.38224	2.09392
N	-1.54929	-0.82005	0.13661
N	0.68508	-2.43474	-0.86653
N	-3.35265	-0.86302	-1.3997
N	-0.41798	0.02972	2.29356
N	-3.56741	0.32751	0.66015
C	-2.33627	-0.05518	0.90709
C	-0.23078	-2.55387	-1.88804
C	-2.08093	-1.23559	-1.08102
C	-6.18778	1.03428	-0.03609
H	-5.75879	1.36816	0.90376
C	-4.03231	-0.12904	-0.53942
C	-5.41031	0.24742	-0.89275
C	-2.22131	1.10191	3.15499
C	0.10085	-3.37864	-2.99582
H	-0.62977	-3.41844	-3.79543
C	-1.17713	1.20303	4.04868
H	-1.20922	1.70376	5.00554
C	2.14013	-4.03075	-1.93925
H	3.05786	-4.60778	-1.89388
C	-5.96988	-0.18194	-2.10472
H	-5.36128	-0.79288	-2.76379
C	1.80564	-3.19325	-0.89648
H	2.46266	-3.07679	-0.04055
C	1.26594	-4.10677	-3.03143

H	1.49196	-4.74234	-3.88316
C	-9.45276	1.32785	-1.9648
H	-9.92048	1.96201	-1.20751
H	-10.08281	0.44043	-2.0895
H	-9.4846	1.86763	-2.91732
C	-7.26667	0.1691	-2.4424
H	-7.68737	-0.17209	-3.38641
C	-0.08079	0.52314	3.4826
C	-7.48732	1.3817	-0.38326
H	-8.08081	1.99452	0.29245
C	-3.60391	1.62131	3.25278
H	-3.72666	2.12879	4.21174
H	-4.34244	0.81938	3.17511
H	-3.83127	2.32195	2.44526
C	-8.05127	0.95734	-1.58946
C	1.28502	0.31848	4.02602
H	2.02617	0.9327	3.49842
H	1.58623	-0.72982	3.92846
H	1.33032	0.59427	5.08103
O	2.46911	-1.38647	1.41364
H	2.78638	-0.51995	1.68631
H	2.54128	-1.97247	2.21309
N	-1.44219	-1.96398	-1.96779
O	0.95054	0.6206	-0.08063
C	1.95299	0.98085	-0.76932
C	2.26408	2.41221	-0.77023
C	1.74132	3.23827	0.24117
C	3.03384	3.00108	-1.78678
C	2.00000	4.59884	0.2555
H	1.12475	2.78749	1.01448
C	3.29344	4.36343	-1.78848
H	3.40711	2.37969	-2.59625
C	2.78022	5.1525	-0.76039
H	1.60475	5.23541	1.03985
H	3.87769	4.81974	-2.58021
C	2.71324	0.00504	-1.53941
C	4.05616	-0.12772	-1.611
H	2.1023	-0.7603	-2.01305
C	4.6718	-1.27534	-2.35053
H	5.40536	-0.87232	-3.06417
H	3.91981	-1.8131	-2.93645
C	5.05771	0.72713	-0.87525
H	5.33337	1.59833	-1.48592
H	4.59745	1.14645	0.02904
C	5.39502	-2.23421	-1.38094
C	6.31809	-0.06938	-0.51029
C	5.94263	-1.50076	-0.1521
H	6.84411	0.4285	0.31021
H	7.01818	-0.07761	-1.35649
H	5.17072	-1.47647	0.62935
H	4.69899	-3.01797	-1.0648
H	6.20712	-2.73674	-1.91852
O	2.39413	-3.19364	3.36387
H	2.28054	-3.02071	4.30193
H	1.49354	-3.43272	3.04996
H	6.79349	-2.04309	0.27148
Cl	3.11075	6.85983	-0.74786

I16-2.10f

Ru	-2.19476	0.27979	-0.65424
Cl	-2.49016	1.1279	-2.95486
N	-0.40049	2.56708	-0.33648
N	-0.19584	0.35197	-0.92867
N	-2.30219	-1.66503	-1.40112
N	1.93623	-0.59915	-1.29882

N	-1.74073	2.30195	-0.1862	H	1.14804	5.57079	-0.01147
N	1.7325	1.71719	-0.74589	H	1.70935	4.33471	-1.16237
C	0.43854	1.50995	-0.69348	H	1.8898	4.0549	0.55541
C	-1.16	-2.39719	-1.60111	C	6.71306	0.91887	-0.7617
C	0.58276	-0.74111	-1.25284	C	-3.78645	3.62876	0.17106
C	4.51713	1.95222	-0.74093	H	-4.21539	2.91338	0.87961
H	3.89139	2.83267	-0.632	H	-4.26609	3.49644	-0.80608
C	2.44688	0.58842	-1.03	H	-4.04476	4.62822	0.52458
C	3.90942	0.71464	-0.98025	O	-4.44545	0.54431	-0.89539
C	-0.12325	3.89856	-0.14161	H	-4.73933	1.28191	-0.34653
C	-1.27243	-3.75757	-1.98138	H	-4.32263	0.91643	-1.79875
H	-0.34442	-4.31717	-2.05369	N	0.11671	-1.95025	-1.4776
C	-1.33791	4.49283	0.10525	O	-0.49681	1.23078	2.31022
H	-1.50448	5.5428	0.29619	C	-0.381	0.08472	1.86803
C	-3.64396	-3.52229	-2.14673	C	0.95594	-0.58143	1.9151
H	-4.6332	-3.901	-2.3771	C	2.05392	0.21815	2.27316
C	4.72024	-0.42171	-1.11104	C	1.19129	-1.92183	1.57593
H	4.24226	-1.38421	-1.27062	C	3.34168	-0.2912	2.28595
C	-3.49378	-2.22151	-1.71712	H	1.86594	1.25986	2.51738
H	-4.35447	-1.57535	-1.58496	C	2.47632	-2.45181	1.58201
C	-2.49915	-4.31944	-2.25072	H	0.38232	-2.57765	1.26916
H	-2.5702	-5.36031	-2.55284	C	3.53739	-1.62954	1.94294
C	8.20137	1.01594	-0.63448	C	-1.50693	-0.63968	1.23295
H	8.52615	2.04168	-0.44383	C	-2.87935	-0.29867	1.36574
H	8.70506	0.67017	-1.54342	H	-1.31035	-1.68318	0.99058
H	8.57306	0.39033	0.18407	C	-3.35548	0.81837	2.26446
C	6.0966	-0.31642	-1.00244	H	-4.40131	1.04297	1.99836
H	6.71115	-1.21025	-1.08757	H	-2.76412	1.72531	2.14928
C	-2.3144	3.47897	0.05528	C	-3.88247	-1.44414	1.35602
C	5.89854	2.0484	-0.6364	H	-4.66752	-1.27658	0.61047
H	6.35956	3.01606	-0.44944	H	-3.37222	-2.37012	1.06591
C	1.22857	4.49765	-0.19462	C	-3.30918	0.3423	3.73186

C	-4.53628 -1.60657 2.74506	H	0.10182 4.61795 -0.82811
C	-3.58684 -1.16109 3.84813	C	1.61488 -4.36975 -0.75569
H	-4.85255 -2.64575 2.88032	H	1.84319 -5.42296 -0.82698
H	-5.4528 -1.0033 2.79993	C	3.43056 4.04823 -1.17275
H	-2.64733 -1.72336 3.75614	H	4.38615 4.52003 -1.37006
H	-3.98815 -1.40311 4.83743	C	-4.72524 0.3489 -0.86724
H	-2.32842 0.58553 4.1516	H	-4.2982 1.34578 -0.80129
H	-4.04817 0.90997 4.30983	C	3.36379 2.68269 -1.01195
O	1.9096 -4.14361 -1.01861	H	4.25162 2.05982 -1.06486
H	2.65592 -4.08791 -1.61963	C	2.24569 4.78391 -1.05924
H	1.42381 -3.3112 -1.19033	H	2.25358 5.86702 -1.13715
H	2.6433 -3.47063 1.2511	C	-8.12687 -1.33512 -0.77498
Cl	5.15312 -2.28024 1.95234	H	-8.38944 -2.38786 -0.6452
H	4.19338 0.33461 2.53375	H	-8.61771 -0.985 -1.68998
I17-2.10f		H	-8.57036 -0.77127 0.05153
Ru	2.27571 -0.07296 -0.43132	C	-6.09391 0.1519 -0.79337
Cl	2.43882 -0.2692 -2.88168	H	-6.75355 1.00953 -0.67924
N	0.5586 -2.4519 -0.7317	C	2.53451 -3.31747 -0.56335
N	0.2196 -0.18035 -0.84388	C	-5.77287 -2.22222 -0.96673
N	2.21257 2.00852 -0.77204	H	-6.18273 -3.22939 -1.00325
N	-1.96307 0.7111 -0.99397	C	-0.94725 -4.45516 -1.0659
N	1.88507 -2.15767 -0.51391	H	-0.8013 -5.53386 -1.14673
N	-1.62738 -1.65883 -0.94547	H	-1.4436 -4.09226 -1.96921
C	-0.34496 -1.39261 -0.8549	H	-1.62699 -4.24603 -0.23546
C	1.02942 2.69565 -0.81646	C	-6.64501 -1.13595 -0.8439
C	-0.61794 0.90918 -0.89802	C	4.01322 -3.3961 -0.50254
C	-4.39862 -2.03501 -1.03633	H	4.35659 -4.01694 0.3307
H	-3.72806 -2.88472 -1.12023	H	4.44871 -2.3983 -0.41053
C	-2.4035 -0.53429 -0.99471	H	4.40155 -3.84174 -1.42318
C	-3.85689 -0.74554 -0.98989	N	-0.22274 2.16344 -0.8222
C	0.3664 -3.80658 -0.85953	O	0.36602 -1.76774 2.10732
C	1.06089 4.11067 -0.88388	C	0.30227 -0.53996 2.00519

C	-1.0055 0.149 2.17223	H	5.40205 -0.83396 0.79283
C	-2.14633 -0.66407 2.27832	H	3.7067 -2.1946 1.66847
C	-1.17423 1.5413 2.15528	Cl	-5.13681 1.9794 2.35529
C	-3.41527 -0.1141 2.34405	**I18-2.9e**	
H	-2.00761 -1.74137 2.27413	Ru	0.69006 0.3336 -0.25795
C	-2.43924 2.11163 2.21924	Cl	0.69036 0.42646 -2.72986
H	-0.32382 2.20963 2.05944	N	-0.9363 -2.09285 -0.48195
C	-3.54651 1.27473 2.30921	N	-1.31904 0.1626 -0.20745
H	-4.29961 -0.74216 2.39115	N	0.55787 2.43026 -0.44808
H	-2.56535 3.18395 2.13122	N	-3.53542 0.97078 -0.0253
C	1.49485 0.25844 1.62623	N	0.38398 -1.72802 -0.60691
C	2.82093 -0.25281 1.73591	N	-3.12699 -1.37856 -0.09297
H	1.39374 1.34283 1.64159	C	-1.86238 -1.06551 -0.252
C	3.83211 0.5725 1.19663	C	-0.65674 3.06042 -0.4816
C	3.28552 -1.51146 2.41154	C	-2.20876 1.21959 -0.18523
C	5.2428 0.08548 1.36847	C	-5.86776 -1.84038 0.33929
H	5.96874 0.81355 0.99568	H	-5.17664 -2.67508 0.27211
O	-2.19742 4.13418 -0.09734	C	-3.93363 -0.28886 0.03598
H	-2.87052 4.18034 -0.77987	C	-5.36816 -0.53776 0.23388
H	-1.65098 3.36995 -0.37004	C	-1.1414 -3.36317 -0.96393
H	3.66904 1.64765 1.16299	C	-0.69122 4.4635 -0.69087
H	2.45611 -2.04122 2.877	H	-1.6768 4.92265 -0.69151
O	1.14693 2.62822 -3.80609	C	0.0958 -3.81326 -1.36625
H	1.62635 1.79601 -3.68449	H	0.30614 -4.77733 -1.8056
H	0.26447 2.41396 -3.49173	C	1.69447 4.50849 -0.86152
H	3.74787 -0.44472 -0.95749	H	2.63548 5.02268 -1.02007
C	5.47023 -0.21502 2.85833	C	-6.26343 0.54007 0.3128
H	6.46517 -0.65201 2.99121	H	-5.87198 1.54901 0.21712
H	5.48273 0.73263 3.40845	C	1.68455 3.14768 -0.64517
C	4.37793 -1.14329 3.43231	H	2.60352 2.56931 -0.63753
H	4.81876 -2.07057 3.81121	C	0.46625 5.18054 -0.8796
H	3.90142 -0.66679 4.29567	H	0.42314 6.25353 -1.04418

C	-9.59195	-1.22447	0.79753
H	-9.81936	-2.28467	0.93344
H	-10.16791	-0.87035	-0.06447
H	-9.97548	-0.68506	1.6699
C	-7.61704	0.31062	0.49644
H	-8.30165	1.15457	0.55243
C	1.01374	-2.76626	-1.15355
C	-7.22659	-2.05876	0.526
H	-7.6035	-3.07622	0.60814
C	-2.46452	-4.01205	-1.07161
H	-2.33695	-5.01635	-1.47999
H	-3.10926	-3.43033	-1.73641
H	-2.97451	-4.07608	-0.10799
C	-8.12526	-0.99115	0.6075
C	2.45065	-2.69255	-1.51896
H	2.68581	-1.69516	-1.90301
H	2.67611	-3.42277	-2.29815
H	3.11676	-2.90863	-0.67491
N	-1.87247	2.48811	-0.30487
O	2.80557	0.33936	-0.30712
C	3.39832	-0.29362	0.59858
C	4.85229	-0.41214	0.54883
C	5.54702	0.15836	-0.53323
C	5.57904	-1.10624	1.52962
C	6.92292	0.05043	-0.62925
H	4.98006	0.67899	-1.29897
C	6.95838	-1.22204	1.4433
H	5.06699	-1.56337	2.37112
C	7.62102	-0.63928	0.36425
H	7.52225	-1.75564	2.20017
C	2.56223	-0.97771	1.63413
H	2.49396	-2.03994	1.34372
C	1.16439	-0.39744	1.75045
C	0.21926	-1.30175	2.51154
C	1.00041	1.00609	1.79441
C	-1.02603	-0.61074	3.05932
H	0.79305	-1.69513	3.36791
H	-0.03985	-2.18751	1.91678
C	-0.1108	1.66666	2.58325
H	-1.49783	-1.25921	3.8051
H	-1.77298	-0.46461	2.27036
H	3.06125	-0.98121	2.614
H	1.90435	1.61151	1.68496
H	-0.92748	1.98888	1.92747
H	0.27703	2.58852	3.03134
O	-4.06346	4.41958	-0.31704
H	-4.12282	4.49728	0.63771
H	-3.47971	3.64585	-0.42255
O	-2.03895	-1.24272	-3.10332
H	-1.16236	-0.8216	-3.14454
H	-2.63295	-0.51379	-3.30135
C	-0.66889	0.74066	3.65877
H	-1.54309	1.19786	4.13358
H	0.08009	0.5991	4.45178
Cl	9.34609	-0.77763	0.25156
H	7.46103	0.48802	-1.46285

2.9ae-A

O	-4.69613	-1.94317	-0.15046
C	-4.04497	-0.90439	-0.1377
C	-2.58321	-0.9798	-0.29379
C	-1.63486	-0.01747	-0.29671
H	-2.25194	-2.00773	-0.43688
C	-0.19835	-0.39676	-0.49537

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H	0.17234	0.07851	-1.41667
H	-0.0907	-1.47557	-0.64223
C	-1.84544	1.46598	-0.09868
H	-2.43363	1.88019	-0.92802
H	-2.45258	1.63842	0.79883
C	0.70473	0.0712	0.67065
C	-0.5273	2.22282	0.04658
C	0.37196	1.5336	1.06516
H	-0.72667	3.25603	0.34787
H	-0.0192	2.28603	-0.92504
H	-0.14069	1.53886	2.03517
H	1.2962	2.10237	1.21021
H	0.47829	-0.57941	1.52498
C	2.15294	-0.1485	0.30538
C	2.84553	-1.26552	0.77707
C	2.82009	0.73274	-0.55274
C	4.16924	-1.49566	0.41093
H	2.33738	-1.95981	1.4442
C	4.14198	0.50772	-0.92215
H	2.29655	1.60935	-0.93283
C	4.82196	-0.60876	-0.44013
H	4.69179	-2.36777	0.79431
H	4.64368	1.2056	-1.58698
H	5.85512	-0.78449	-0.72563
C	-4.74604	0.42311	0.02957
H	-4.46001	0.9064	0.96979
H	-4.49371	1.12383	-0.77223
H	-5.82264	0.25266	0.03654

2.9ae-B

C	4.2352	0.43786	-0.0088
O	3.74058	1.54071	-0.13588
C	3.40293	-0.83702	0.03958
H	3.70904	-1.44288	-0.82951
H	3.72765	-1.41946	0.91274
C	1.92188	-0.6241	0.04957
C	1.30314	-0.10699	-1.21874
C	1.1881	-0.88149	1.13977
C	-0.11367	0.40776	-1.01162
H	1.30912	-0.91062	-1.97348
H	1.93682	0.68838	-1.62724
C	-0.29555	-0.71128	1.21312
C	-0.94092	-0.56957	-0.17099
H	-0.60382	0.59052	-1.9742
H	-0.07224	1.37655	-0.495
H	-0.75015	-1.55468	1.74957
H	-0.54189	0.17391	1.82138
H	-0.88665	-1.55374	-0.66211
H	1.69032	-1.24085	2.03887
C	-2.39386	-0.17944	-0.07804
C	-3.40044	-1.04946	-0.50282
C	-2.77081	1.06496	0.44063
C	-4.74387	-0.69292	-0.41522
H	-3.12173	-2.02076	-0.90814
C	-4.11065	1.42719	0.5293
H	-2.00258	1.75913	0.77775
C	-5.10351	0.54821	0.10134
H	-5.51012	-1.38622	-0.7518
H	-4.38168	2.39898	0.93336
H	-6.15034	0.83024	0.17049
C	5.72531	0.24059	0.12438
H	5.9665	-0.09193	1.13992
H	6.0864	-0.54236	-0.55002
H	6.25096	1.17437	-0.07445

2.9ae-C

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C	4.31925	-0.11502	-0.3616
O	4.09408	-0.53637	-1.48092
C	3.25746	0.58259	0.4635
H	3.30317	0.21841	1.50062
H	3.55682	1.64021	0.53168
C	1.846	0.45971	-0.09985
C	1.32122	-0.97363	-0.00788
C	-0.16854	-1.03357	-0.3049
H	1.50284	-1.35287	1.00985
H	1.88416	-1.61553	-0.69202
C	-0.97921	-0.23226	0.72422
H	-0.52802	-2.06841	-0.33407
H	-0.3607	-0.61297	-1.30201
H	-0.96923	-0.79453	1.67359
H	1.29143	2.41594	0.78402
C	-2.42419	-0.11018	0.29697
C	-3.38155	-1.02049	0.75065
C	-2.82287	0.88326	-0.60275
C	-4.70331	-0.94227	0.3211
H	-3.08214	-1.79828	1.4517
C	-4.14306	0.96652	-1.034
H	-2.08294	1.59694	-0.9617
C	-5.08851	0.05337	-0.57282
H	-5.43451	-1.65749	0.68831
H	-4.4356	1.74724	-1.73114
H	-6.12026	0.119	-0.90657
C	5.67552	-0.24704	0.28348
H	5.99097	0.69133	0.75038
H	5.62725	-0.98995	1.08733
H	6.41707	-0.56917	-0.4474
C	0.90925	1.41404	0.583
H	1.91598	0.72714	-1.16689
C	-0.33244	1.10494	0.96704
H	-0.93902	1.85423	1.47463

2.9ae-D

C	4.29633	-0.29355	-0.38299
O	3.91591	-1.05151	-1.256
C	3.35707	0.67197	0.30983
H	3.52976	0.6203	1.39634
H	3.68162	1.68746	0.03286
C	1.88757	0.47005	-0.01784
C	1.33003	-0.81225	0.59064
C	-0.10009	-1.06447	0.13481
H	1.35494	-0.71788	1.68718
H	1.96275	-1.66549	0.32736
H	-0.53766	-1.86589	0.7415
H	-0.10551	-1.45608	-0.89334
C	-2.43065	0.00148	0.03937
C	-3.09269	-1.1693	0.43991
C	-3.21031	1.02059	-0.53374
C	-4.47018	-1.30431	0.30017
H	-2.52895	-1.98317	0.88687
C	-4.58553	0.88888	-0.67247
H	-2.71725	1.91735	-0.89998
C	-5.22588	-0.27575	-0.25375
H	-4.95453	-2.22008	0.62839
H	-5.15911	1.69308	-1.12561
H	-6.3006	-0.38377	-0.36869
C	5.73438	-0.25715	0.07022
H	6.10823	0.76944	0.13716
H	5.81288	-0.67968	1.07808
H	6.36209	-0.83961	-0.60407
H	1.79749	0.38516	-1.11025
C	1.04411	1.65055	0.45354

H	1.28751	2.54813	-0.13314
H	1.32168	1.91223	1.48946
C	-0.42361	1.38257	0.37622
H	-1.08253	2.24383	0.47786
C	-0.97057	0.16512	0.19607

I6

Ru	-2.13352	-0.0265	0.16001
Cl	-2.99133	-1.32212	2.08503
N	-0.73007	-2.47701	-0.6056
N	-0.2352	-0.54852	0.55368
N	-2.04682	1.51476	1.58552
N	1.9667	-0.1622	1.31458
N	-2.00149	-1.96271	-0.69464
N	1.49739	-2.06634	-0.03575
C	0.24349	-1.6796	0.01076
C	-0.89961	1.76007	2.29374
C	0.64644	0.17677	1.33093
C	4.22906	-2.71906	-0.02165
H	3.49695	-3.46602	-0.31316
C	2.34369	-1.21578	0.6037
C	3.78004	-1.49397	0.48573
C	-0.72194	-3.8251	-0.86358
C	-0.94884	2.72373	3.33313
H	-0.02425	2.89739	3.87274
C	-2.02759	-4.15491	-1.15295
H	-2.39224	-5.14202	-1.39654
C	-3.27035	3.10604	2.90926
H	-4.21747	3.58967	3.11803
C	4.72597	-0.52621	0.85729
H	4.38899	0.4366	1.23197
C	-3.18463	2.16656	1.90439
H	-4.05408	1.88316	1.31877
C	-2.11214	3.38847	3.642
H	-2.12811	4.11781	4.4469
C	8.0043	-2.29632	0.11397
H	8.19996	-3.21401	-0.44636
H	8.46706	-2.40955	1.10087
H	8.53156	-1.47705	-0.38479
C	6.07993	-0.78984	0.72481
H	6.80228	-0.02704	1.00756
C	-2.79587	-2.98289	-1.01757
C	5.58808	-2.97492	-0.14095
H	5.92471	-3.93383	-0.5297
C	0.47346	-4.68568	-0.7458
H	0.19733	-5.71539	-0.97994
H	0.86023	-4.6396	0.2764
H	1.27932	-4.36712	-1.41054
C	6.53786	-2.01802	0.22999
C	-4.26736	-2.81381	-1.11288
H	-4.61768	-2.14827	-0.31806
H	-4.76411	-3.77853	-0.99651
H	-4.5842	-2.40581	-2.0806
N	0.32027	1.2043	2.08857
O	-4.16742	0.41486	-0.44133
C	-4.33475	0.50023	-1.66895
C	-3.16826	0.29096	-2.58002
H	-3.20094	-0.76919	-2.88528
C	-1.83678	0.58643	-1.91674
C	-0.64128	0.1088	-2.71021
C	-1.72492	1.72682	-1.08965
C	0.68548	0.75885	-2.32854
H	-0.84866	0.35312	-3.76574
H	-0.56698	-0.98691	-2.68624
C	-0.4475	2.52448	-0.9681

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H	1.42473	0.5623	-3.11275
H	1.10176	0.32207	-1.41318
H	-3.30229	0.85924	-3.51391
H	-2.63432	2.31129	-0.92554
H	0.05834	2.32308	-0.0191
H	-0.69866	3.59125	-0.93188
O	3.28467	2.19979	2.51416
H	2.54067	2.78618	2.3479
H	2.866	1.33288	2.3799
O	-0.44954	-3.31414	2.23887
H	-1.30808	-2.85525	2.2487
H	0.02213	-2.89588	2.96403
C	0.53433	2.26702	-2.11759
H	0.09745	2.68541	-3.03944
C	1.86779	2.93648	-1.88976
C	2.42719	3.75711	-2.87225
C	2.58886	2.73208	-0.70697
C	3.66877	4.35916	-2.68282
H	1.87736	3.9261	-3.7973
C	3.82758	3.33448	-0.5097
H	2.19123	2.10152	0.08761
C	4.37211	4.14997	-1.49961
H	4.08396	4.99591	-3.45997
H	4.34315	3.15928	0.43131
H	5.33852	4.62347	-1.3483
C	-5.68878	0.75648	-2.23064
H	-5.71256	1.73841	-2.71604
H	-5.92329	0.02596	-3.01248
H	-6.44841	0.72219	-1.45024

I7

Ru	-1.47537	-0.95971	-0.97922
Cl	-1.57721	-2.17551	-3.06421
N	0.51765	0.82212	-2.14474
N	0.49624	-0.97424	-0.71176
N	-1.7403	-2.69066	0.14532
N	2.46586	-1.58346	0.44694
N	-0.85141	0.69426	-2.1295
N	2.52845	0.19853	-1.13483
C	1.24251	-0.0243	-1.29555
C	-0.69774	-3.20151	0.88239
C	1.14159	-1.77781	0.21331
C	5.26545	0.55795	-0.56131
H	4.75022	1.25339	-1.21791
C	3.10209	-0.64517	-0.22979
C	4.53919	-0.48369	0.02587
C	0.92404	1.79446	-3.02618
C	-0.93635	-4.32067	1.72093
H	-0.09163	-4.67313	2.30361
C	-0.23267	2.28684	-3.58907
H	-0.29203	3.06228	-4.33879
C	-3.20586	-4.4155	0.98371
H	-4.19503	-4.85903	0.97227
C	5.20537	-1.38431	0.87265
H	4.64049	-2.19895	1.32211
C	-2.94055	-3.31403	0.19838
H	-3.71656	-2.87558	-0.41963
C	-2.17032	-4.92479	1.77638
H	-2.3314	-5.78606	2.41854
C	8.76033	-0.04464	0.80994
H	9.17852	0.83672	0.3173
H	9.32153	-0.91786	0.45993
H	8.96261	0.04445	1.88258
C	6.56043	-1.23338	1.11835
H	7.06744	-1.93958	1.77284

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C	-1.30668	1.57797	-3.01784
C	6.62312	0.7001	-0.30483
H	7.17757	1.51578	-0.76473
C	2.33387	2.16913	-3.27691
H	2.37054	2.88445	-4.1007
H	2.94654	1.29996	-3.52764
H	2.79611	2.62384	-2.39599
C	7.29528	-0.19057	0.53711
C	-2.75635	1.67974	-3.31717
H	-3.34477	1.84286	-2.40523
H	-3.11258	0.76715	-3.80994
H	-2.9601	2.51735	-3.98614
O	-3.73064	-0.93746	-1.5053
H	-3.94332	-0.06773	-1.86325
H	-3.51046	-1.47771	-2.29968
N	0.57285	-2.73787	0.91183
O	-1.33942	-0.07065	0.96715
C	-2.1186	0.02506	1.92993
C	-4.43497	1.22945	1.76819
C	-4.1157	2.17353	2.92824
H	-4.09672	1.62628	3.88054
H	-4.93801	2.89656	3.03609
C	-4.29155	2.0213	0.46909
H	-4.6096	1.40767	-0.384
H	-4.99463	2.86302	0.5142
C	-2.87456	2.54256	0.25207
H	-2.87725	3.37039	-0.4711
H	-2.25898	1.7638	-0.21924
H	2.23353	-3.52331	1.94939
O	2.86728	-3.6637	2.6724
H	3.02747	-2.75534	2.94034
C	-1.50841	0.11434	3.29279
H	-2.18422	0.53698	4.03835
H	-1.25843	-0.90675	3.61051
H	-0.57621	0.68105	3.25846
C	-3.61178	-0.08714	1.78221
H	-3.97559	-0.69847	2.61865
H	-3.81652	-0.6363	0.85659
C	-0.83473	3.53524	1.41888
C	-0.39126	4.5925	2.22557
C	0.08668	2.93374	0.54773
C	0.92919	5.02445	2.17181
H	-1.09972	5.08597	2.88728
C	1.41309	3.35132	0.50974
H	-0.23352	2.099	-0.06871
C	1.83889	4.40171	1.31914
H	1.25022	5.85229	2.79829
H	2.11852	2.83469	-0.13905
H	2.87291	4.73284	1.28729
C	-2.80973	2.87529	2.71899
H	-2.2734	3.21056	3.60611
C	-2.20945	3.00742	1.51951
H	-5.48108	0.91148	1.85511

Annexure VII

The Cartesian coordinates (xyz) for all optimized structures (*Chapter 3*)

Coordinate file:

3.4b'

Cr	-2.351820000000	0.073787000000	0.544331000000
Cl	-3.399601000000	0.017543000000	2.515603000000
O	7.765031000000	-0.459452000000	0.069014000000
N	-0.498893000000	0.026051000000	0.161403000000
N	1.602286000000	1.131146000000	-0.083564000000
N	-0.527286000000	-2.308120000000	-0.226358000000
H	0.109265000000	-3.079243000000	-0.372243000000
N	-2.816829000000	-1.644723000000	-0.263198000000
N	-2.658766000000	1.780381000000	-0.316850000000
N	-0.297824000000	2.387807000000	-0.211462000000
N	1.479853000000	-1.246150000000	-0.229190000000
C	4.392532000000	1.012044000000	0.008751000000
H	3.878867000000	1.968018000000	0.031457000000
C	5.778006000000	0.954848000000	0.060243000000
H	6.349941000000	1.873921000000	0.125469000000
C	6.419472000000	-0.288899000000	0.025392000000
C	5.660219000000	-1.463591000000	-0.061334000000
H	6.181873000000	-2.415024000000	-0.086893000000
C	4.281545000000	-1.392895000000	-0.110890000000
H	3.688242000000	-2.299038000000	-0.177506000000
C	2.160608000000	-0.070689000000	-0.113569000000
C	0.174932000000	-1.125185000000	-0.091752000000
C	0.254902000000	1.202555000000	-0.042833000000
C	8.561124000000	0.705036000000	0.160216000000
H	9.595814000000	0.364075000000	0.185452000000
H	8.344238000000	1.272924000000	1.073796000000
H	8.417327000000	1.362573000000	-0.706513000000
C	-1.865153000000	-2.608522000000	-0.398417000000

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C	-4.116198000000	-2.015470000000	-0.456488000000
H	-4.837833000000	-1.214201000000	-0.324724000000
C	-4.507797000000	-3.291543000000	-0.774818000000
H	-5.559114000000	-3.514419000000	-0.912843000000
C	-3.522311000000	-4.281397000000	-0.905262000000
H	-3.787334000000	-5.302279000000	-1.158600000000
C	-2.201699000000	-3.935167000000	-0.710666000000
H	-1.409110000000	-4.671375000000	-0.804810000000
C	-3.921121000000	2.216517000000	-0.585512000000
H	-4.693621000000	1.452163000000	-0.523958000000
C	-4.229042000000	3.515977000000	-0.893069000000
H	-5.256114000000	3.797757000000	-1.094069000000
C	-3.180704000000	4.454702000000	-0.924884000000
H	-3.381760000000	5.496409000000	-1.157005000000
C	-1.899395000000	4.038079000000	-0.666933000000
H	-1.055594000000	4.718022000000	-0.689053000000
C	-1.602444000000	2.678800000000	-0.376727000000
C	3.621487000000	-0.153291000000	-0.075569000000

2.10a'

C	1.548800000000	0.834936000000	0.128014000000
C	1.301098000000	-0.256847000000	1.131103000000
C	1.890272000000	-1.594694000000	0.672395000000
C	3.361087000000	-1.455852000000	0.298765000000
C	3.565544000000	-0.356831000000	-0.736903000000
C	2.997786000000	0.978108000000	-0.243183000000
H	1.757488000000	-2.345820000000	1.458503000000
H	0.241954000000	-0.358451000000	1.377632000000
H	3.941360000000	-1.212002000000	1.200858000000
H	3.753853000000	-2.409599000000	-0.070556000000
H	4.627363000000	-0.244061000000	-0.981365000000
H	3.058369000000	-0.636531000000	-1.671264000000
H	3.568877000000	1.288118000000	0.646004000000
H	3.128291000000	1.764496000000	-0.993676000000

H	1.323966000000	-1.957765000000	-0.197124000000
C	0.620427000000	1.658822000000	-0.394824000000
C	-0.831434000000	1.722721000000	-0.107628000000
O	-1.356794000000	2.814248000000	0.093557000000
C	-1.664471000000	0.484739000000	-0.128386000000
C	-2.922425000000	0.517060000000	0.484724000000
C	-1.260141000000	-0.676941000000	-0.796738000000
C	-3.744844000000	-0.601134000000	0.459260000000
H	-3.227117000000	1.436935000000	0.975388000000
C	-2.089407000000	-1.792561000000	-0.834749000000
H	-0.294896000000	-0.690831000000	-1.297907000000
C	-3.329237000000	-1.758324000000	-0.200061000000
H	-4.714098000000	-0.574309000000	0.949194000000
H	-1.770880000000	-2.687548000000	-1.362119000000
H	-3.975376000000	-2.631543000000	-0.224168000000
H	0.966887000000	2.488378000000	-1.011265000000
H	1.809982000000	0.037337000000	2.062670000000

Int-3A

Cr	1.789863000000	0.605290000000	-0.481300000000
Cl	3.975029000000	1.293070000000	-0.110068000000
O	-8.275435000000	-1.287428000000	-0.135061000000
N	-0.143748000000	0.133527000000	-0.862551000000
N	-2.381853000000	0.977704000000	-0.903552000000
N	0.144549000000	-2.198576000000	-0.830290000000
H	-0.395013000000	-3.049986000000	-0.732170000000
N	2.265320000000	-1.289664000000	-1.362255000000
N	1.256688000000	3.796356000000	-1.015048000000
N	-0.609588000000	2.426888000000	-1.159177000000
N	-1.974334000000	-1.377757000000	-0.798764000000
C	-5.119066000000	0.544989000000	-0.607666000000
H	-4.726532000000	1.551546000000	-0.731020000000
C	-6.481805000000	0.335026000000	-0.450008000000
H	-7.158917000000	1.184796000000	-0.449855000000

C	-6.966015000000	-0.969318000000	-0.294997000000
C	-6.073518000000	-2.049772000000	-0.300125000000
H	-6.474494000000	-3.053105000000	-0.176783000000
C	-4.719080000000	-1.826912000000	-0.457404000000
H	-4.021359000000	-2.660312000000	-0.460087000000
C	-2.780012000000	-0.279652000000	-0.773150000000
C	-0.685198000000	-1.085697000000	-0.833547000000
C	-1.049476000000	1.203227000000	-1.013188000000
C	-9.202673000000	-0.221887000000	-0.121238000000
H	-10.183712000000	-0.679533000000	0.018175000000
H	-9.190823000000	0.335286000000	-1.068551000000
H	-9.003712000000	0.474945000000	0.705045000000
C	1.448425000000	-2.357457000000	-1.244370000000
C	3.517330000000	-1.494150000000	-1.833151000000
H	4.126608000000	-0.595130000000	-1.901884000000
C	4.014976000000	-2.739774000000	-2.156519000000
H	5.032011000000	-2.839928000000	-2.523051000000
C	3.186131000000	-3.849399000000	-1.971862000000
H	3.543567000000	-4.854443000000	-2.186691000000
C	1.897021000000	-3.660688000000	-1.520126000000
H	1.219992000000	-4.499758000000	-1.376186000000
C	2.421664000000	4.201206000000	-1.512915000000
H	2.847993000000	5.085371000000	-1.033969000000
C	3.099603000000	3.590828000000	-2.569477000000
H	4.042002000000	3.992545000000	-2.930926000000
C	2.536159000000	2.445875000000	-3.111658000000
H	3.018823000000	1.918753000000	-3.934546000000
C	1.335687000000	1.962270000000	-2.591076000000
H	0.826466000000	1.122633000000	-3.062736000000
C	0.672522000000	2.694256000000	-1.558809000000
C	-4.216678000000	-0.524757000000	-0.613459000000
C	0.834184000000	1.609272000000	2.044654000000
C	1.571980000000	2.903798000000	2.169587000000

C	1.006064000000	3.698537000000	3.353622000000
C	-0.475606000000	4.057540000000	3.142979000000
C	-1.135357000000	3.162169000000	2.090728000000
C	-0.653461000000	1.722216000000	2.186152000000
H	1.128518000000	3.098260000000	4.266911000000
H	2.651250000000	2.732342000000	2.258915000000
H	-1.010182000000	3.975134000000	4.099328000000
H	-0.571694000000	5.105435000000	2.831869000000
H	-2.227229000000	3.191854000000	2.186297000000
H	-0.912008000000	3.533432000000	1.080955000000
H	-0.909371000000	1.277853000000	3.164579000000
H	-1.171582000000	1.063706000000	1.481897000000
H	1.612489000000	4.599625000000	3.502509000000
C	1.525753000000	0.420098000000	1.949511000000
H	2.608946000000	0.492454000000	2.039566000000
C	0.927903000000	-0.921569000000	2.050657000000
O	-0.285316000000	-1.099915000000	2.184051000000
C	1.846186000000	-2.106042000000	1.992821000000
C	1.288018000000	-3.364075000000	2.259523000000
C	3.203442000000	-2.027456000000	1.648064000000
C	2.062915000000	-4.513702000000	2.193398000000
H	0.231159000000	-3.403481000000	2.517111000000
C	3.977417000000	-3.182686000000	1.573529000000
H	3.664474000000	-1.070749000000	1.399397000000
C	3.412700000000	-4.425404000000	1.849068000000
H	1.618663000000	-5.483358000000	2.413396000000
H	5.026911000000	-3.107213000000	1.293668000000
H	4.022993000000	-5.325909000000	1.795875000000
H	1.419519000000	3.491704000000	1.247563000000

HF energy = -2395.74292834 a.u.

Int-3B

Cr	1.934776000000	0.049252000000	-0.179118000000

Cl	4.149155000000	0.775194000000	-0.055544000000
O	-8.229310000000	-0.883127000000	-0.189139000000
N	0.002278000000	-0.249531000000	-0.863359000000
N	-2.142712000000	0.782240000000	-0.997752000000
N	0.081699000000	-2.587669000000	-0.717643000000
H	-0.520617000000	-3.388998000000	-0.577607000000
N	2.313097000000	-1.876774000000	-1.109392000000
N	1.742362000000	3.219825000000	-1.322661000000
N	-0.230357000000	2.049488000000	-1.233924000000
N	-1.959117000000	-1.585339000000	-0.740351000000
C	-4.909967000000	0.621348000000	-0.691414000000
H	-4.423043000000	1.580664000000	-0.848193000000
C	-6.287806000000	0.548018000000	-0.544841000000
H	-6.880956000000	1.457251000000	-0.587416000000
C	-6.895183000000	-0.696945000000	-0.342342000000
C	-6.109356000000	-1.857032000000	-0.288723000000
H	-6.605485000000	-2.811309000000	-0.128641000000
C	-4.739329000000	-1.770243000000	-0.434914000000
H	-4.123520000000	-2.664822000000	-0.391199000000
C	-2.662167000000	-0.431200000000	-0.788672000000
C	-0.644121000000	-1.415954000000	-0.776166000000
C	-0.807377000000	0.856383000000	-1.064004000000
C	-9.052822000000	0.264491000000	-0.230452000000
H	-10.073546000000	-0.093806000000	-0.086055000000
H	-8.979380000000	0.778066000000	-1.199285000000
H	-8.796972000000	0.972399000000	0.570077000000
C	1.407500000000	-2.869608000000	-0.988741000000
C	3.583790000000	-2.218628000000	-1.422101000000
H	4.270122000000	-1.376467000000	-1.492525000000
C	4.005522000000	-3.522640000000	-1.593414000000
H	5.043548000000	-3.730275000000	-1.835388000000
C	3.071478000000	-4.546903000000	-1.425754000000
H	3.360595000000	-5.590331000000	-1.532442000000

C	1.764037000000	-4.220741000000	-1.126575000000
H	1.005680000000	-4.990114000000	-0.997236000000
C	2.944192000000	3.569404000000	-1.833914000000
H	3.447411000000	4.386579000000	-1.326167000000
C	3.461881000000	2.902570000000	-2.911122000000
H	4.421737000000	3.193529000000	-3.322296000000
C	2.737387000000	1.807082000000	-3.420013000000
H	3.134956000000	1.242097000000	-4.261262000000
C	1.540051000000	1.427558000000	-2.858073000000
H	0.971611000000	0.588244000000	-3.248720000000
C	0.977624000000	2.167579000000	-1.775847000000
C	-4.113800000000	-0.528751000000	-0.639197000000
C	0.860110000000	2.368016000000	1.788625000000
C	1.771835000000	3.377331000000	1.754025000000
C	1.455289000000	4.838603000000	1.890147000000
C	0.018717000000	5.076620000000	2.338661000000
C	-0.919268000000	4.145743000000	1.586455000000
C	-0.611466000000	2.687710000000	1.894612000000
H	2.162298000000	5.306729000000	2.592154000000
H	2.829044000000	3.105843000000	1.667760000000
H	-0.061124000000	4.870375000000	3.416928000000
H	-0.259250000000	6.129992000000	2.199338000000
H	-1.968131000000	4.364746000000	1.825475000000
H	-0.812320000000	4.310542000000	0.500382000000
H	-0.947991000000	2.428979000000	2.911150000000
H	-1.196427000000	2.030897000000	1.245893000000
H	1.630179000000	5.377579000000	0.935192000000
C	1.335669000000	0.974871000000	1.764632000000
H	2.366507000000	0.902866000000	2.121840000000
C	0.507152000000	-0.163274000000	2.114477000000
O	-0.735513000000	-0.171665000000	2.129436000000
C	1.210686000000	-1.494494000000	2.325338000000
C	0.393896000000	-2.615663000000	2.529869000000

C	2.601354000000	-1.687674000000	2.276297000000
C	0.938001000000	-3.887820000000	2.655320000000
H	-0.681004000000	-2.445403000000	2.567692000000
C	3.147341000000	-2.964843000000	2.389641000000
H	3.279427000000	-0.846637000000	2.133129000000
C	2.319287000000	-4.069195000000	2.575778000000
H	0.284790000000	-4.745254000000	2.817332000000
H	4.227583000000	-3.091885000000	2.332131000000
H	2.748695000000	-5.066410000000	2.665711000000
H	1.442350000000	3.596340000000	-0.417049000000

HF energy = -2395.73037618 a.u.

TS-1

Cr	1.943782000000	0.123736000000	-0.246813000000
Cl	4.139679000000	0.832240000000	0.063254000000
O	-8.184191000000	-1.012150000000	-0.217836000000
N	0.032654000000	-0.203378000000	-0.895281000000
N	-2.132926000000	0.795943000000	-0.993956000000
N	0.153070000000	-2.541775000000	-0.769817000000
H	-0.440905000000	-3.354802000000	-0.664850000000
N	2.378809000000	-1.789265000000	-1.107484000000
N	1.737077000000	3.273959000000	-1.123228000000
N	-0.251902000000	2.105300000000	-1.230464000000
N	-1.904122000000	-1.576595000000	-0.809266000000
C	-4.898909000000	0.573253000000	-0.701622000000
H	-4.432936000000	1.545803000000	-0.840536000000
C	-6.274402000000	0.467181000000	-0.551261000000
H	-6.886964000000	1.364264000000	-0.572768000000
C	-6.854350000000	-0.794470000000	-0.373511000000
C	-6.043806000000	-1.937860000000	-0.349454000000
H	-6.518437000000	-2.906090000000	-0.208753000000
C	-4.676123000000	-1.818233000000	-0.499361000000
H	-4.041265000000	-2.700201000000	-0.478227000000
C	-2.627075000000	-0.427604000000	-0.827104000000

C	-0.595165000000	-1.379339000000	-0.829461000000
C	-0.791636000000	0.909013000000	-1.077170000000
C	-9.030857000000	0.118729000000	-0.229188000000
H	-10.043361000000	-0.263199000000	-0.087020000000
H	-8.973972000000	0.655284000000	-1.186683000000
H	-8.784811000000	0.814324000000	0.585261000000
C	1.482780000000	-2.796494000000	-1.031831000000
C	3.658192000000	-2.102124000000	-1.418226000000
H	4.333068000000	-1.249443000000	-1.456621000000
C	4.099455000000	-3.393447000000	-1.626375000000
H	5.142347000000	-3.578294000000	-1.865138000000
C	3.178080000000	-4.435432000000	-1.499674000000
H	3.483252000000	-5.470805000000	-1.636150000000
C	1.863503000000	-4.137800000000	-1.206301000000
H	1.114593000000	-4.921186000000	-1.111904000000
C	2.941941000000	3.618049000000	-1.604083000000
H	3.457519000000	4.397866000000	-1.044045000000
C	3.500227000000	3.025920000000	-2.717409000000
H	4.466723000000	3.351045000000	-3.089061000000
C	2.799445000000	1.968206000000	-3.309452000000
H	3.214978000000	1.450211000000	-4.172622000000
C	1.580686000000	1.569016000000	-2.794257000000
H	1.010426000000	0.763201000000	-3.251093000000
C	1.009310000000	2.266974000000	-1.693308000000
C	-4.077884000000	-0.559920000000	-0.677647000000
C	0.698812000000	2.268138000000	1.762360000000
C	1.558012000000	3.364183000000	1.542937000000
C	1.167342000000	4.797409000000	1.868229000000
C	-0.268246000000	4.918444000000	2.364922000000
C	-1.165072000000	3.965343000000	1.591103000000
C	-0.776050000000	2.523003000000	1.871459000000
H	1.866786000000	5.206563000000	2.610870000000
H	2.625629000000	3.134067000000	1.650615000000

H	-0.312314000000	4.659129000000	3.434476000000
H	-0.614284000000	5.956741000000	2.281676000000
H	-2.221153000000	4.114709000000	1.848449000000
H	-1.074768000000	4.155582000000	0.510254000000
H	-1.070584000000	2.228846000000	2.892760000000
H	-1.337899000000	1.830904000000	1.238553000000
H	1.292552000000	5.429035000000	0.971267000000
C	1.245148000000	0.945203000000	1.810105000000
H	2.299692000000	0.924168000000	2.092392000000
C	0.471186000000	-0.248739000000	2.125931000000
O	-0.766347000000	-0.291696000000	2.158041000000
C	1.225243000000	-1.547736000000	2.317492000000
C	0.453265000000	-2.705539000000	2.488483000000
C	2.622310000000	-1.677212000000	2.276725000000
C	1.050446000000	-3.955167000000	2.590218000000
H	-0.628292000000	-2.583664000000	2.517588000000
C	3.221502000000	-2.931656000000	2.369558000000
H	3.263962000000	-0.805972000000	2.150957000000
C	2.439373000000	-4.073649000000	2.522438000000
H	0.433747000000	-4.843604000000	2.723688000000
H	4.306458000000	-3.011233000000	2.319304000000
H	2.910274000000	-5.053364000000	2.593758000000
H	1.530199000000	3.369956000000	0.165047000000

HF energy = -2395.71677237

TS-2

Cr	-2.002919000000	0.683602000000	-0.171306000000
Cl	-4.157844000000	0.750320000000	0.711034000000
O	7.994649000000	-0.433344000000	0.010698000000
N	-0.142200000000	0.562935000000	-1.075771000000
N	1.816364000000	-0.746173000000	-1.494538000000
N	0.217887000000	2.851648000000	-0.597378000000
H	0.978586000000	3.495693000000	-0.418144000000
N	-2.113341000000	2.646739000000	-0.882615000000

N	-2.289232000000	-1.597501000000	-1.051658000000
N	-0.188657000000	-1.555969000000	-2.179752000000
N	2.028802000000	1.522276000000	-0.823134000000
C	4.540709000000	-1.169845000000	-1.020826000000
H	3.914949000000	-1.974650000000	-1.398655000000
C	5.887613000000	-1.383589000000	-0.765881000000
H	6.319120000000	-2.363799000000	-0.948535000000
C	6.672168000000	-0.334308000000	-0.272230000000
C	6.093507000000	0.921212000000	-0.038940000000
H	6.724309000000	1.717994000000	0.347977000000
C	4.751726000000	1.121315000000	-0.297684000000
H	4.294569000000	2.091286000000	-0.114810000000
C	2.525154000000	0.278727000000	-1.046057000000
C	0.709360000000	1.579587000000	-0.851642000000
C	0.478951000000	-0.595890000000	-1.562053000000
C	8.610623000000	-1.687340000000	-0.201577000000
H	9.655900000000	-1.560049000000	0.085356000000
H	8.555540000000	-1.989683000000	-1.256721000000
H	8.153698000000	-2.470441000000	0.419239000000
C	-1.009604000000	3.421057000000	-0.848977000000
C	-3.298045000000	3.236149000000	-1.166423000000
H	-4.151142000000	2.563352000000	-1.170033000000
C	-3.436304000000	4.592466000000	-1.380694000000
H	-4.415665000000	5.008867000000	-1.594567000000
C	-2.299515000000	5.398527000000	-1.286957000000
H	-2.366102000000	6.474972000000	-1.429666000000
C	-1.077736000000	4.811931000000	-1.024363000000
H	-0.166130000000	5.402222000000	-0.966534000000
C	-3.558636000000	-2.084195000000	-0.976705000000
H	-4.074421000000	-1.861859000000	-0.046039000000
C	-4.133229000000	-2.774861000000	-2.010805000000
H	-5.150268000000	-3.143244000000	-1.922030000000
C	-3.363016000000	-2.991350000000	-3.171376000000

H	-3.789574000000	-3.531556000000	-4.014972000000
C	-2.068637000000	-2.540988000000	-3.236084000000
H	-1.436969000000	-2.717304000000	-4.101699000000
C	-1.483841000000	-1.843367000000	-2.143091000000
C	3.951418000000	0.079199000000	-0.794875000000
C	-1.505895000000	-2.558032000000	1.637584000000
C	-2.622144000000	-3.077083000000	2.186392000000
C	-2.937684000000	-4.538016000000	2.256251000000
C	-1.741587000000	-5.409656000000	1.891440000000
C	-1.015664000000	-4.834078000000	0.684283000000
C	-0.468802000000	-3.447181000000	0.996471000000
H	-3.313129000000	-4.798714000000	3.257412000000
H	-3.371793000000	-2.390370000000	2.590188000000
H	-1.043827000000	-5.444855000000	2.742039000000
H	-2.063168000000	-6.443594000000	1.708422000000
H	-0.201757000000	-5.496421000000	0.361733000000
H	-1.718530000000	-4.769686000000	-0.163944000000
H	0.407938000000	-3.516982000000	1.655985000000
H	-0.073922000000	-2.971933000000	0.087429000000
H	-3.779388000000	-4.758857000000	1.573482000000
C	-1.363547000000	-1.074488000000	1.524397000000
H	-2.169339000000	-0.586338000000	2.082133000000
C	-0.046277000000	-0.463826000000	1.762612000000
O	1.024377000000	-1.038714000000	1.547476000000
C	0.009656000000	0.981931000000	2.212200000000
C	1.279883000000	1.564332000000	2.318075000000
C	-1.114293000000	1.776581000000	2.491006000000
C	1.426632000000	2.904349000000	2.655080000000
H	2.141529000000	0.933551000000	2.108476000000
C	-0.968690000000	3.123912000000	2.818085000000
H	-2.120292000000	1.357590000000	2.466363000000
C	0.300776000000	3.693556000000	2.893554000000
H	2.423999000000	3.336972000000	2.730189000000

H	-1.854750000000	3.723926000000	3.020910000000
H	0.413053000000	4.745058000000	3.155634000000
H	-1.779362000000	-1.294661000000	0.064560000000

HF energy = -2395.69745716 a.u.

3.4b'+2.9w

Cr	1.222013000000	-0.041471000000	-1.615134000000
Cl	2.823458000000	-0.272019000000	-3.263441000000
O	-8.912486000000	-0.849550000000	-0.196533000000
N	-0.648704000000	-0.120840000000	-0.776048000000
N	-2.806035000000	0.914919000000	-0.539238000000
N	-0.622758000000	-2.483990000000	-0.463248000000
H	-1.272253000000	-3.221094000000	-0.217147000000
N	1.639796000000	-1.960847000000	-0.857457000000
N	1.197672000000	2.023856000000	-1.580292000000
N	-0.994163000000	2.254803000000	-0.607734000000
N	-2.605368000000	-1.446886000000	-0.390904000000
C	-5.591562000000	0.719336000000	-0.420539000000
H	-5.109250000000	1.690726000000	-0.499891000000
C	-6.974571000000	0.621353000000	-0.363048000000
H	-7.578069000000	1.524116000000	-0.398449000000
C	-7.574113000000	-0.639715000000	-0.259880000000
C	-6.774976000000	-1.790504000000	-0.215127000000
H	-7.264659000000	-2.758108000000	-0.134803000000
C	-5.399328000000	-1.679022000000	-0.273703000000
H	-4.774401000000	-2.567888000000	-0.240196000000
C	-3.324264000000	-0.296958000000	-0.448866000000
C	-1.302587000000	-1.279192000000	-0.555383000000
C	-1.457306000000	1.027407000000	-0.657136000000
C	-9.749460000000	0.287953000000	-0.243066000000
H	-10.771738000000	-0.089450000000	-0.182869000000
H	-9.620094000000	0.845044000000	-1.181462000000
H	-9.558899000000	0.963258000000	0.602754000000
C	0.710612000000	-2.808529000000	-0.377494000000

TH-3606_186122027

C	2.940999000000	-2.328737000000	-0.761227000000
H	3.649428000000	-1.620303000000	-1.182754000000
C	3.354764000000	-3.520829000000	-0.202707000000
H	4.414441000000	-3.750942000000	-0.153468000000
C	2.383863000000	-4.402143000000	0.276171000000
H	2.664252000000	-5.354215000000	0.721545000000
C	1.053211000000	-4.047687000000	0.187117000000
H	0.267326000000	-4.699710000000	0.561087000000
C	2.340681000000	2.675419000000	-1.925725000000
H	3.026457000000	2.095055000000	-2.539839000000
C	2.637625000000	3.962245000000	-1.536988000000
H	3.572324000000	4.418782000000	-1.849417000000
C	1.703365000000	4.648616000000	-0.745714000000
H	1.902821000000	5.663116000000	-0.404292000000
C	0.519304000000	4.030010000000	-0.429371000000
H	-0.259319000000	4.522859000000	0.146576000000
C	0.240936000000	2.707029000000	-0.868066000000
C	-4.782271000000	-0.421763000000	-0.378422000000
C	0.909360000000	1.019073000000	2.324818000000
C	0.265709000000	2.155308000000	2.626449000000
C	-1.088579000000	2.215170000000	3.256676000000
C	-1.522199000000	0.866304000000	3.820875000000
C	-1.199846000000	-0.248716000000	2.835225000000
C	0.302628000000	-0.331388000000	2.597440000000
H	-1.108241000000	2.985318000000	4.041759000000
H	0.734081000000	3.107438000000	2.363973000000
H	-0.990234000000	0.676733000000	4.765704000000
H	-2.593144000000	0.879464000000	4.059709000000
H	-1.586533000000	-1.214327000000	3.188172000000
H	-1.714163000000	-0.034344000000	1.885612000000
H	0.807836000000	-0.787210000000	3.462095000000
H	0.526648000000	-1.003869000000	1.750686000000
H	-1.811626000000	2.555845000000	2.494745000000

C	2.207329000000	1.042319000000	1.585416000000
H	2.561719000000	2.074720000000	1.430058000000
C	3.338076000000	0.207448000000	2.155035000000
O	3.278617000000	-0.299410000000	3.265878000000
C	4.522132000000	-0.017647000000	1.273235000000
C	5.500269000000	-0.926423000000	1.697586000000
C	4.666959000000	0.602045000000	0.024287000000
C	6.585876000000	-1.224063000000	0.884958000000
H	5.370686000000	-1.394722000000	2.671519000000
C	5.753519000000	0.303243000000	-0.792127000000
H	3.927397000000	1.321666000000	-0.326529000000
C	6.710674000000	-0.614781000000	-0.365232000000
H	7.338470000000	-1.935782000000	1.220758000000
H	5.838421000000	0.774277000000	-1.769540000000
H	7.556396000000	-0.855809000000	-1.006968000000
H	2.033714000000	0.660486000000	0.559439000000

List of Publications

1. Chemo- and Regioselective Catalytic Cross-Coupling Reaction of Ketones for the Synthesis of *β*, *γ*-Disubstituted *β*, *γ*-Unsaturated Ketones.

Adhikari, P.; Bhattacharyya, D.; Deori, K.; Sarmah, B. K.; Das A. *Chem. Eur. J.* **2024***, 30,* e202303206.

2. Chromium-Catalyzed Cross-Coupling of Methyl Ketones with Cyclic Ketones toward the Selective Synthesis of *β*-Branched *β*, *γ*-Unsaturated Ketones.

Adhikari, P.; Hazarika, N.; Bhattacharyya, K.; Das A. *Org. Lett.* **2024***, 26,* 286−291.

3. Chromium-catalysed selective synthesis of 3-oxo and 3-amino quinolines using β-O-4′ lignin models or α-amino ketones.

Adhikari, P.; Borah, A.; Das A. *Org. Chem. Front.* **2024**, *11*, 5454-5461.

4. Reductive Alkylation of Quinolines to *N*-Alkyl Tetrahydroquinolines Catalyzed by Arylboronic Acid.

Adhikari, P.; Bhattacharyya, D.; Nandi, S.; Kancharla, P. K; Das, A. *Org. Lett.* **2021***, 23,* 2437-2442.

5. Chromium catalyzed efficient and sustainable synthesis of *N*-heteroaromatic compounds *via* acceptorless dehydrogenative coupling reactions.

Adhikari, P.; Das A. (Manuscript under preparation).

6. Phosphine-Free Pincer Ruthenium-Catalyzed *α*-Alkylation of Ketones with Secondary Alcohols to form *β*-Branched Ketones.

Bhattacharyya, D.; **Adhikari, P.;** Hazarika, N.; Sarmah, B. K.; Das, A. *ChemCatChem* **2023**, *15*, e202300542.

7. Ruthenium pincer complex catalyzed efficient synthesis of quinoline, 2-styrylquinoline and quinazoline derivatives via acceptorless dehydrogenative coupling reactions.

Bhattacharyya, D.; **Adhikari, P.**; Deori, K.; Das, A. *Catal. Sci. Technol*. **2022**,*12*, 5695-5702.

8. Boric acid catalyzed chemoselective reduction of quinolines.

Bhattacharyya, D.; Nandi, S.; **Adhikari, P**.; Sarmah, B. K.; Konwar, M.; Das, A. *Org. Biomol. Chem.* **2020**, *18*, 1214-1220.

9. Regioselective Cyanation of Six-Membered *N*-Heteroaromatic Compounds Under Metal-, Activator-, Base- and Solvent-Free Conditions.

Sarmah, B. K.; Konwar, M.; Bhattacharyya, D.; **Adhikari, P.**; Das, A. *Adv. Syn. Cat.* **2019**, *361*, 5616-5625.

TH-3606_186122027

List of Conferences

1. **30th International Conference on Organometallic Chemistry (ICOMC 2024)** from 14th-18th July 2024, Agra. Poster presentation with entitled "Chromium-catalyzed selective synthesis of *β*-branched *β*, *γ*-unsaturated ketones *via* cross-aldol-condensation of ketones."
2. **Junior National Organic Symposium Trust (JNOST-XIX)** from 10th-12th October 2023, IISER Pune, Pune. Oral presentation with entitled "Reductive *N*-alkylation and N-arylation of Quinolines catalysed by Aryl boronic acid."
3. **Research and Industrial Conclave (RIC-2023)** from 14th-16th August 2023, IIT Guwahati, Guwahati. Oral presentation with entitled "Reductive Alkylation of Quinolines to *N*-Alkyl Tetrahydroquinolines Catalysed by Arylboronic acid"
4. **International Conference on Modern Trends in Inorganic Chemistry (MTIC-XIX)** from 15th-17th December 2022, BHU, Varanasi. Poster presentation with entitled "Selective Catalytic Synthesis of *β*-branched Unsaturated Ketones via Cross-Aldol Condensation of Ketones."
5. **Frontiers in Chemical Sciences - 2022 (FICS-2022)** from 2nd-4th December 2022, IIT Guwahati. Poster presentation with entitled "Ruthenium pincer complex catalyzed efficient synthesis of quinoline, 2-styrylquinoline and quinazoline derivatives via acceptorless dehydrogenative coupling (ADC) reactions."
6. **North-East Research Conclave (NERC)** from 20th-22nd May 2022, IIT Guwahati. Poster presentation with entitled "Reductive Alkylation of Quinolines to *N*-Alkyl Tetrahydroquinolines Catalyzed by Arylboronic Acid."
7. **Chemical Research Society of India 28th National Symposium in Chemistry (CRSI NSC-28)** from 4th-6th February 2022, IIT Guwahati. Poster presentation with entitled "Reductive Alkylation of Quinolines to N-Alkyl Tetrahydroquinolines Catalyzed by Arylboronic Acid." (**Best Poster Award**)
8. **International Conference on Progress and Challenges in Modern Day Science (PCMDS-2021)** from 17h-18th June 2021, B. Borooah College, Assam. Poster presentation with entitled "Reductive Alkylation of Quinolines to *N*-Alkyl Tetrahydroquinolines Catalyzed by Arylboronic Acid." (**Best Poster Award**)
9. **The Present and Future of Excellence in Organic Synthesis (PFEOS-2021)** from 7th-8th January 2021, Tezpur University, Assam. Poster presentation with entitled "Boric acid catalysed chemoselective reduction of quinolines."

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