

Catalytic Synthesis of Branched Ketones, and N-Heteroaromatic Compounds Using Acceptorless Dehydrogenative Coupling and Hydrogen Transfer Strategies

A Dissertation

Submitted in partial fulfilment of the

Requirements for the Degree of

Doctor of Philosophy

by

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INDIA, April, 2021



***Dedicated
To
My Parents, Family
And
All My Teachers***





INDIAN INSTITUTE OF TECHNOLOGY GUWAHATI

Department of Chemistry

Guwahati, Assam-781039, INDIA

STATEMENT

I, hereby declared that the work comprised in this thesis entitled “*Catalytic Synthesis of Branched Ketones, and N-Heteroaromatic Compounds Using Acceptorless Dehydrogenative Coupling and Hydrogen Transfer Strategies*” 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.

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CERTIFICATE

This is to certify that the work incorporated in the thesis entitled “*Catalytic Synthesis of Branched Ketones, and N-Heteroaromatic Compounds Using Acceptorless Dehydrogenative Coupling and Hydrogen Transfer Strategies*” which is being submitted to the Indian Institute of Technology Guwahati for the award of Doctor of Philosophy in Chemistry by **Mr. Dipanjan Bhattacharyya** (Roll No: 166122033) was carried out by him under my supervision at this institute. The work presented in his thesis is original and that has not been submitted elsewhere for a degree.

Guwahati
April, 2021


Dr. Animesh Das



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Sincerely,
Dipanjan Bhattacharyya



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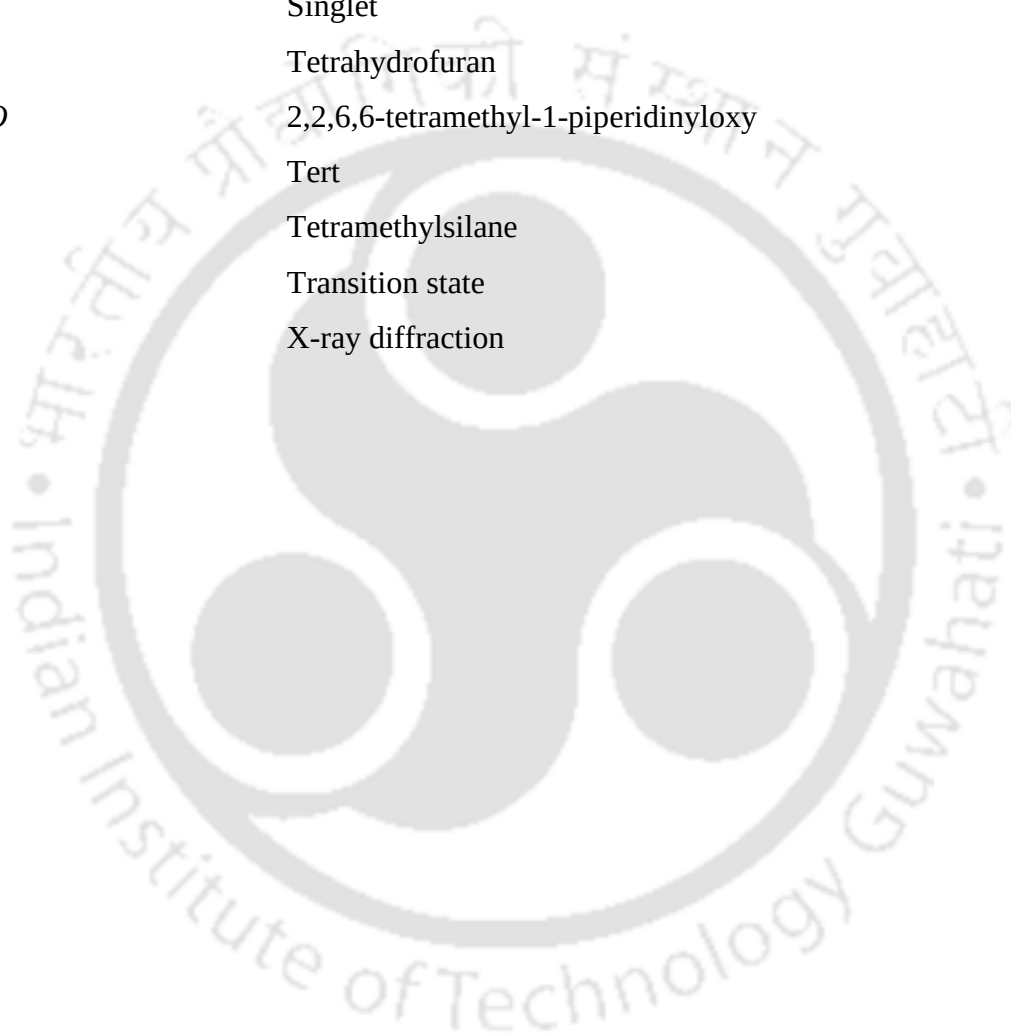
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Abbreviation

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
oC	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
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
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	Millilitre
mmol	Millimole
Mp	Melting point
MS	Molecular seive
MLC	Metal-ligand cooperation
NMR	Nuclear magnetic resonance
Ts	Tosylate
o	Ortho
ω	Omega
ORTEP	Oak ridge thermal ellipsoid plot program
p	Para
Ph	Phenyl

<i>Py</i>	Pyridine
<i>Pr</i>	propyl
<i>PNP</i>	2,6-bis-(di-tert-butylphosphinomethyl)pyridine
<i>ppm</i>	Parts per million
<i>q</i>	Quartet
<i>rt</i>	Room temperature
<i>s</i>	Singlet
<i>THF</i>	Tetrahydrofuran
<i>TEMPO</i>	2,2,6,6-tetramethyl-1-piperidinyloxy
<i>t</i>	Tert
<i>TMS</i>	Tetramethylsilane
<i>TS</i>	Transition state
<i>XRD</i>	X-ray diffraction



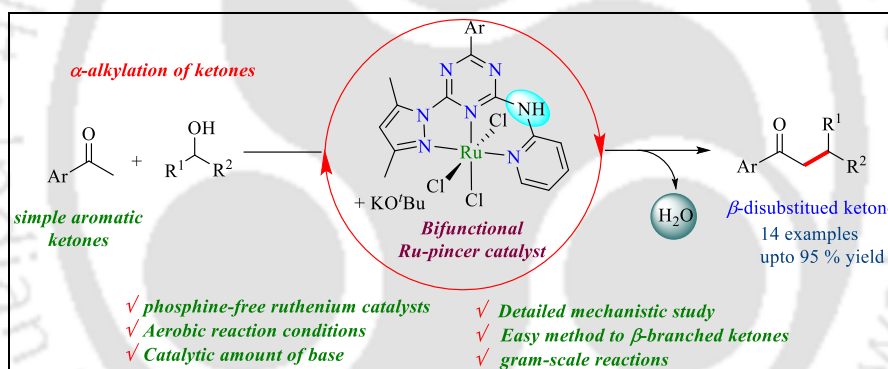
Abstract

The present thesis, entitled as “**Catalytic Synthesis of Branched Ketones, and N-Heteroaromatic Compounds Using Acceptorless Dehydrogenative Coupling and Hydrogen Transfer Strategies**” is divided into six chapter based on the obtained results of experimental works performed during the complete course of the PhD research period.

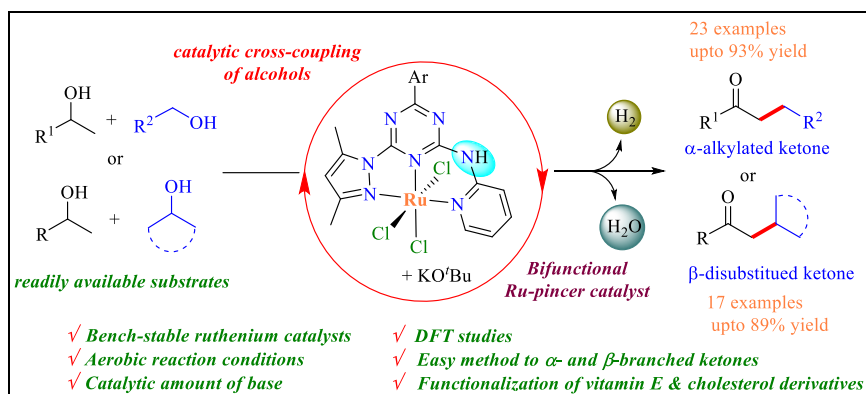
Chapter-1 includes a brief introduction about the basic concepts of acceptorless dehydrogenation, borrowing hydrogen catalysis *via* metal-ligand cooperation, and a general background of transfer hydrogenation reactions.

Each of the following chapters (chapter-2 to chapter-5) contains an introduction, previous studies, present results and discussion, experimental section, and references. All the spectral data for newly synthesized compounds are given in annexure I – V.

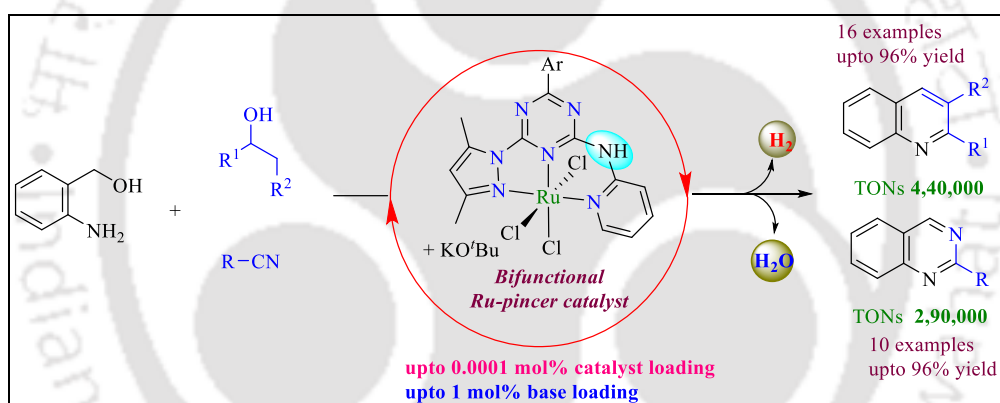
Chapter-2 reports the synthesis and characterization of new phosphine-free triazine-based NNN-pincer ligands and their ruthenium (III) complexes. I have explored their utility in the catalytic synthesis of β -branched ketones *via* α -alkylation of ketones using secondary alcohols. Remarkably, challenging substrates such as simple acetophenone derivatives are effectively alkylated under the reaction conditions. The detailed mechanistic studies indicated the involvement of “borrowing hydrogen” catalysis and the role of the metal-ligand cooperation for the success of such catalysis.



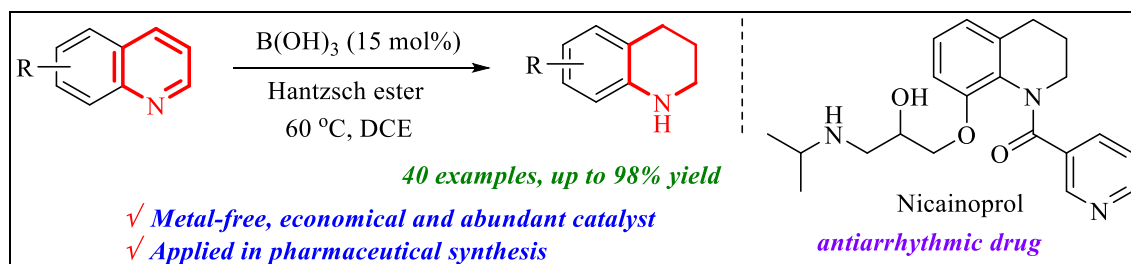
Chapter-3 demonstrates catalytic cross-coupling of primary and secondary alcohols to α -substituted ketones and two different secondary alcohols to β -disubstituted ketones with good to excellent yield. Notably, this transformation is environmentally benign and atom efficient with H₂O and H₂ gas as the only by-products. The protocol is extended to gram-scale reaction and for functionalization of complex Vitamin-E and cholesterol derivatives. The preliminary mechanistic studies indicated that the dehydrogenation of alcohol follows the proton-shuttle type of TS and the involvement of “borrowing hydrogen” catalysis. The use of air-stable catalyst, a catalytic amount of base, aerobic reaction condition, and high selectivity in the C-C bond formation are the important practical features.



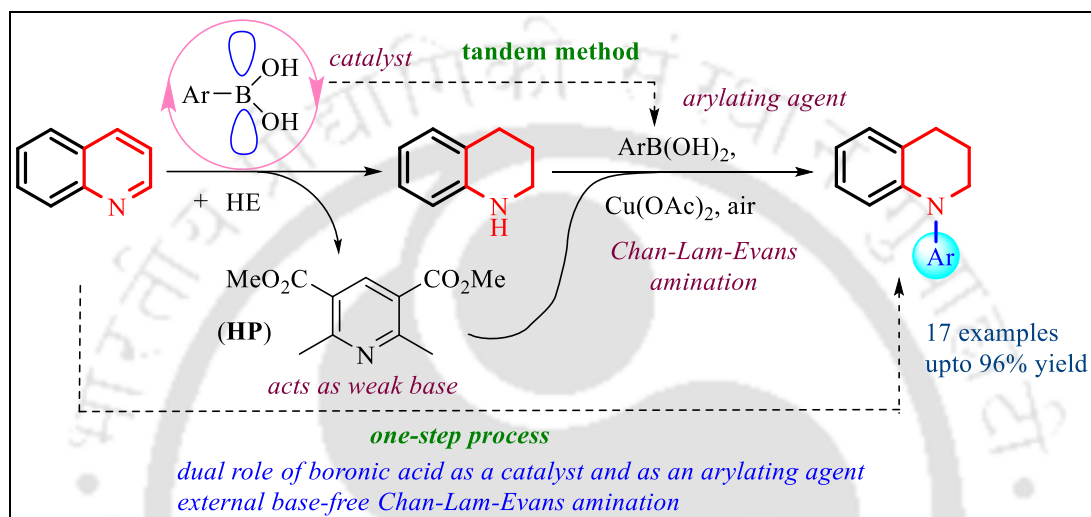
Chapter-4 describes an efficient and atom-economic method for the facile synthesis of quinolines, and quinazolines *via* acceptorless dehydrogenative coupling of alcohols using a simple phosphine-free Ru(III) complex. The reaction enables low catalyst loading (0.1 mol%) and base loading (1 mol%) under the aerial condition with a wide variety of substituted quinolines and quinazolines in moderate to good yield. Notably, the catalytic system has shown remarkably high TONs of **4,40,000** (for 2-phenylquinoline) and TONs of **2,90,000** (for 2-phenylquinazoline), which are the highest among all the reported transition metal complexes in the homogeneous catalysis.



Chapter-5 reports boric acid-catalyzed reduction of quinolines to synthetically versatile 1,2,3,4-tetrahydroquinolines (1,2,3,4-THQs) under mild reaction conditions using Hantzsch ester as an organic hydrogen source. This methodology has high functional group tolerance and afforded the desired THQ derivatives with a very high yield. The process can also be scaled up to obtain gram-quantities. Based on various control experiments and NMR studies, a plausible mechanism is proposed, highlighting the Lewis acidic behavior of boron in the boric acid/boronic acid in catalysis. The synthetic utility of the present protocol was explored towards several bioactive molecules such as antiarrhythmic drug nicainoprol, antitrypanosomal active compound, natural alkaloid ($\pm$) cuspareine, and TB inhibitor efficiently.



Chapter-6 illustrates arylboronic acid-catalyzed one-pot reduction of quinoline to tetrahydroquinoline followed by *N*-arylation by external base-free Chan-Lam-Evans amination under air. This step-economical synthesis of *N*-aryl tetrahydroquinoline has been achieved directly from quinoline, Hantzsch ester, and arylboronic acid under an external base-free *N*-arylation process. The process proved to be versatile and compatible with various reducible functional groups at quinoline and boronic acid moiety. The use of arylboronic acid as a catalyst and as an arylating agent and bypassing isolation of THQs as the intermediate in the C-N bond-forming step is the important practical feature. Because of the ready accessibility of starting materials and the low cost of the amination protocol, the methodology proved to be useful alternative for the construction of bio-relevant *N*-heterocycles.



The basic concepts of acceptorless dehydrogenative coupling, borrowing hydrogen and hydrogen transfer strategies

1.1. Introduction

Population growth increases the demand for standard requirements in daily life. Hence, industrial development is necessary to fulfil the requirements. However, such development additionally causes environmental damage by the release of hazardous chemical waste. So, the development of new chemical processes by minimizing waste generation and the use of renewable feedstock is an important task in chemical research. In this perspective, acceptorless dehydrogenative coupling (ADC) reaction, borrowing hydrogen (BH) catalysis, transfer hydrogenation (TH) reactions are found to be powerful synthetic strategies to synthesize a diverse range of value-added chemical products.

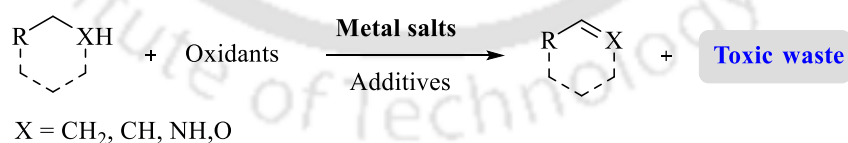
Alcohol is considered a valuable industrial feedstock as they are cheap, abundant in nature, bio-renewable (derived from lignocellulosic biomass), easy to handle and store. The construction of carbon-carbon and carbon-heteroatom bonds by using alcohols has gained importance in recent years.

This thesis will discuss the synthesis of α -alkylated ketones, β -branched ketones, and *N*-heteroarenes such as quinolines and quinazolines *via* transition-metal-catalyzed dehydrogenative coupling of alcohols. Furthermore, transition metal-free boric acid and aryl boronic acid-catalyzed transfer hydrogenation of quinoline with Hantzsch ester will be described. The synthesis of biologically relevant *N*-aryl tetrahydroquinolines directly from quinoline, Hantzsch ester, and arylboronic acid under external base-free Chan-Lam-Evans *N*-arylation will also be presented.

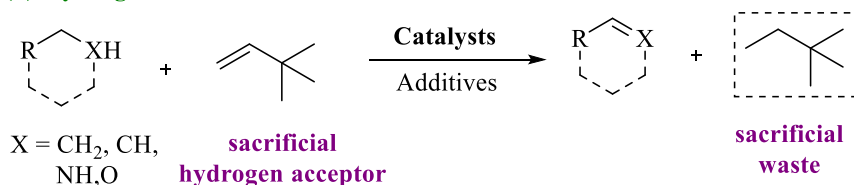
1.2. Acceptorless dehydrogenation

The dehydrogenation of organic molecules seems like a thermodynamically uphill process as the process requires high energy to abstract the hydrogen atoms from neighboring atoms of an organic molecule.¹ Conventionally, substrate oxidations rely on the use of the stoichiometric amount of inorganic oxidants such as dichromates,² permanganates³ etc., in the presence of strong mineral acids,⁴ silver oxide⁵ and lead tetraacetate.⁶ Alternatively, catalytic hydrogen transfers reactions using sacrificial organic acceptor (e.g. *tert*-butylethene)⁷ has also been mentioned. Both the reactions generate a copious amount of waste, thus causing an adverse effect on the environment (Scheme 1.1).

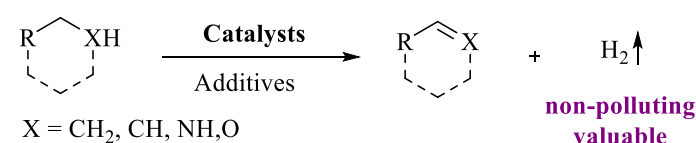
(a) Conventional oxidation



(b) Hydrogen transfer reaction



(c) Acceptorless dehydrogenation



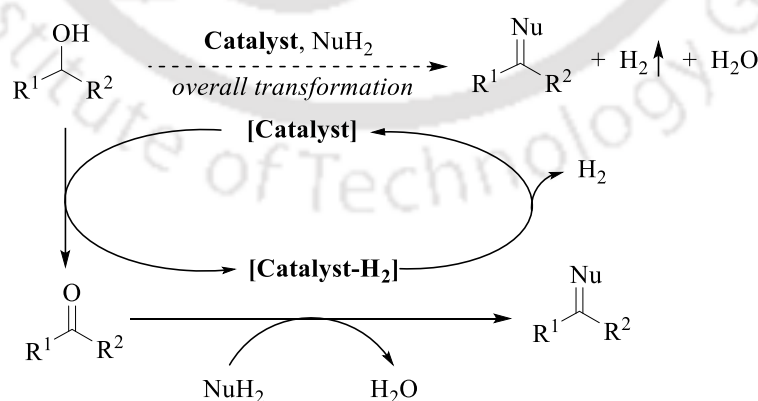
Scheme 1.1. Conventional routes for dehydrogenation of substrates

Contrary to traditional approach,²⁻⁷ acceptorless dehydrogenation reactions are well-recognized sustainable processes as the process does not require any external oxidant, pre-functionalization of the substrates, or any hydrogen scavengers.⁸ Liberated molecular hydrogen in the process is the only by-product that makes the process green, atom-economical, and environmentally benign. Therefore, catalytic acceptorless dehydrogenation reaction has become convenient approach for the commodity chemicals. In current study, this reaction has shown a significant impact on organic synthesis. In the majority of cases, the reaction proceeds effectively *via* metal-ligand cooperation effect (MLC).⁹

1.2.1. Alcohol dehydrogenation

A number of strong inorganic oxidants, such as chromium-based,¹⁰ manganese-based,¹¹ silver based⁵ and some well-defined oxidants such as Dess-Martin Periodinane,¹² *o*-iodoxybenzoic acid (IBX),¹³ sodium hypochlorite (NaOCl),¹⁴ TEMPO (2,2,6,6-tetramethyl-1-piperidinyloxy)¹⁵ etc. have been known to successfully carry out the oxidation of alcohols. These processes have broad applicability and high efficiency in various organic syntheses. However, they often suffer from multiple drawbacks, including the generation of considerable amounts of by-products or wastes.¹⁶ Hence, greener alternatives for the oxidation reaction of alcohol have been explored in recent years.

In this regard, acceptorless dehydrogenation of alcohol strategy has attracted considerable attention as the reactions do not require the use of conventional oxidants or sacrificial acceptors; thereby process does not produce stoichiometric amounts of sacrificial waste. Recent trends in the area of homogeneous catalysis have enabled ADC reactions to be applied for the synthesis of various organic substrates.¹⁷⁻¹⁹ Among them, the use of alcohols has a particular interest. This is primarily due to (i) the ready accessibility and usually low cost of alcohols,²⁰ and (ii) the environmentally benign and atom economical nature of these processes. In this strategy, alcohol is oxidized to form aldehyde or ketone. Then in-situ formed carbonyl compound reacted with different nucleophiles ensued in the construction of new carbon-carbon or carbon-heteroatom bonds. For the oxidation of alcohols, transition metal catalyst plays an important role where two hydrogen atom is transferred to the catalyst and form as **Catalyst-H₂** (by transferring one hydrogen atom from a C-H bond adjacent to the hydroxyl group and another hydrogen atom from the alcoholic hydroxyl group). Then **Catalyst-H₂** releases hydrogen molecule and regenerate the active catalyst. A brief overview of alcohol dehydrogenation is given in Scheme 1.2.

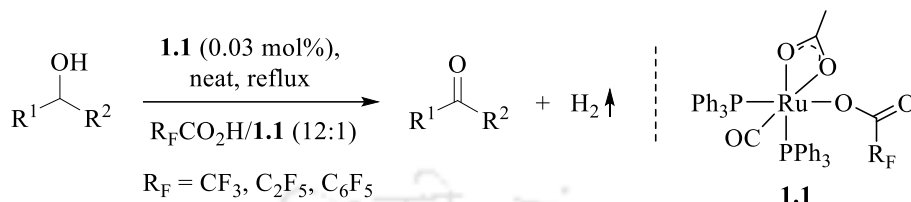


Scheme 1.2. General overview of acceptorless dehydrogenation of alcohols

1.2.2. Dehydrogenation of alcohols to form aldehyde/ketone

During the last three decades, catalytic dehydrogenation of alcohols into aldehydes and ketones in the absence of hydrogen-acceptors was studied with several transition metal catalysts to develop a large-scale procedure. Initially, Dobson and Robinson group reported a series of examples for dehydrogenation of primary and secondary alcohols catalysed by $[\text{Ru}(\text{OCOCF}_3)_2(\text{CO})(\text{PPh}_3)_2]$ (1.1).²¹ With excess alcohol (RCH_2OH), first the alkoxide complex

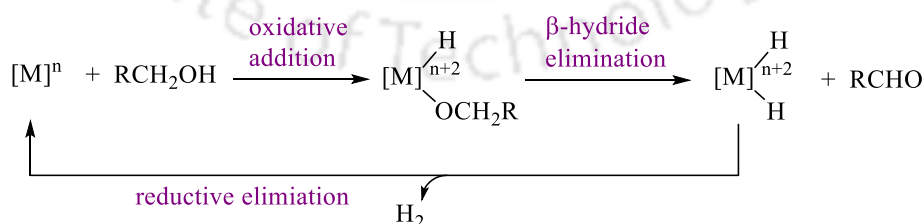
$[\text{Ru}(\text{OCH}_2\text{R})(\text{OCOCF}_3)(\text{CO})(\text{PPh}_3)_2]$ is formed and consequently releases $\text{CF}_3\text{CO}_2\text{H}$. Then, metal hydride complex $[\text{RuH}(\text{OCOCF}_3)(\text{CO})(\text{PPh}_3)_2]$ is generated as a reactive intermediate *via* β -hydride elimination and released corresponding aldehyde or ketone. The final step in the catalytic cycle, excess fluorinated carboxylic acid helps to regenerate the active catalytic species with the liberation of the hydrogen molecule. As this reaction required excess of carboxylic acid, therefore process is named as “acid-promoted” strategy (Scheme 1.3). Later *Jung and Garrou* reported a class of parallel catalysts based on bidentate diphosphine ligands and reported their mechanistic aspects for dehydrogenation of primary alcohols.²²



Scheme 1.3. Acid promoted dehydrogenation of alcohol

The catalytic dehydrogenation of alcohols was also illustrated by *Hulshof* and co-workers.²³ They have demonstrated dehydrogenation of several secondary alcohols with high selectivity in short reaction times. However, the dehydrogenation of primary alcohols is problematic due to decarbonylation (reason of catalyst poisoning) and aldol condensations under the reaction conditions. *Morton and Cole-Hamilton* carried out their studies with various ruthenium and rhodium complexes toward the dehydrogenation of low molecular weight alcohols such as ethanol, propanol and isopropanol etc.²⁴ *Wilkinson's* catalyst in the presence of triethylamine is also effective for the dehydrogenation of isopropanol.²⁵ *Beller and co-workers* examined simple and commercially available ruthenium precursor for dehydrogenation of isopropanol and found $[\text{RuCl}_3 \cdot x\text{H}_2\text{O}]$ and $[\text{RuCl}_2(p\text{-cymene})]_2$ gave best TOF when the reaction was performed in the presence of two equivalents of PCy_3 .²⁶ Subsequently, different ligand derived metal Ru, and Ir metal complexes were also found to be active for this process.²⁷

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 1.4). However, conventional alcohol dehydrogenations are associated with several shortcomings.¹



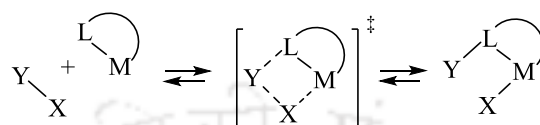
Scheme 1.4. Classical mechanism of alcohol dehydrogenation

Under basic media, product aldehyde undergoes aldol-type rearrangement rendering the product separation very difficult.²⁸ Moreover, for certain metals like ruthenium, the metal alkoxide is so stable that further β -hydride elimination is hindered.²⁹ Also, redox adjustment of metal during the catalytic cycle makes this an energetically unfavorable process and usually requires the elevated temperature to occur. Hence, from synthetic and selectivity viewpoints, an alternative approach was necessary, which is devoid of such limitation. This has been achieved by the introduction of metal-ligand

cooperative catalysts whose working principle is different from a classical catalyst.³⁰ In the following sections, I present a brief introduction about the metal-ligand cooperation effect.

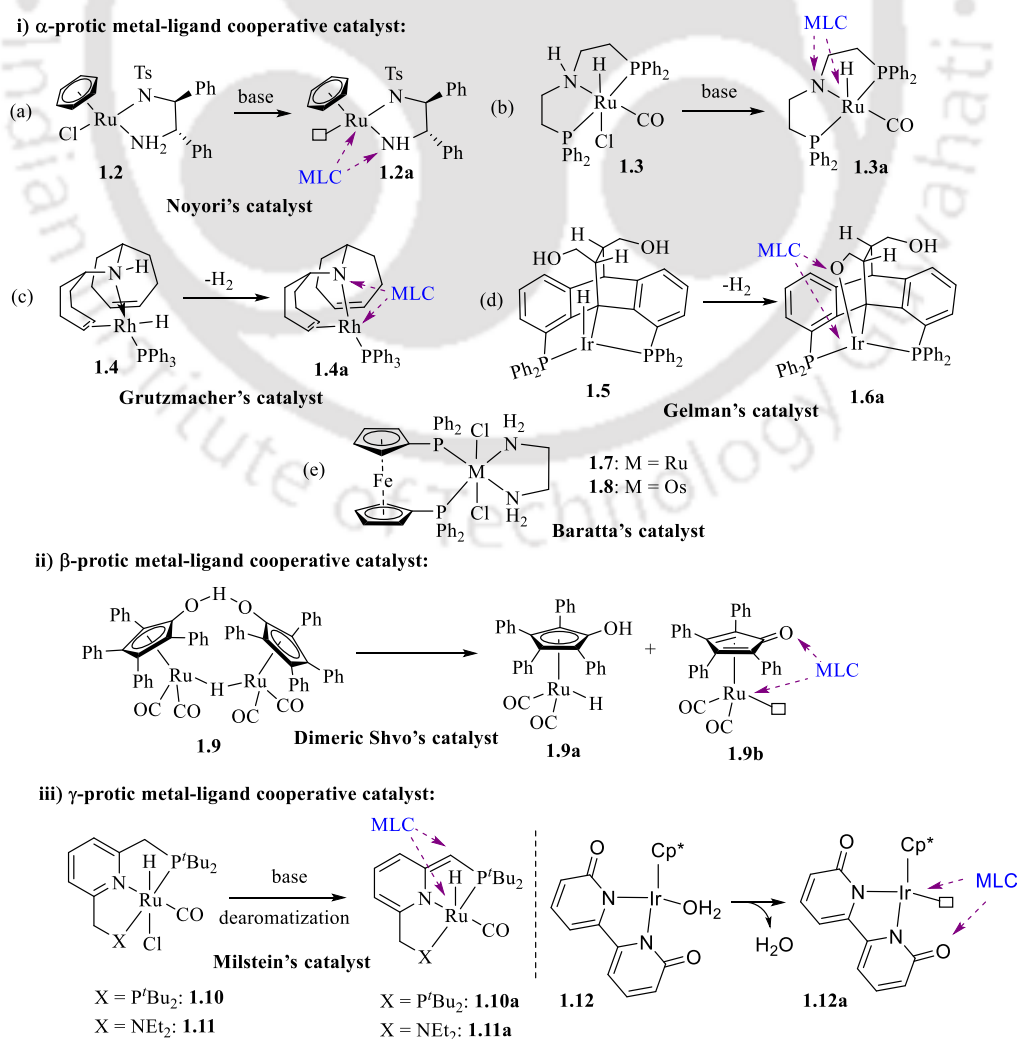
1.2.3. Metal-ligand cooperation

During catalytic process, it was found that the metal center is the active site, and supported ligands help to modulate the steric and the electronic behavior of the metal ions.³¹ In modern metal-ligand cooperation (MLC) strategy, both the metal and the ligand are actively take part in the bond activation processes, and their synergistic interplay facilitates chemical transformation with low energy barriers and bypassing the traditional oxidative addition and/ or reductive elimination steps in the catalytic cycle (Scheme 1.5).



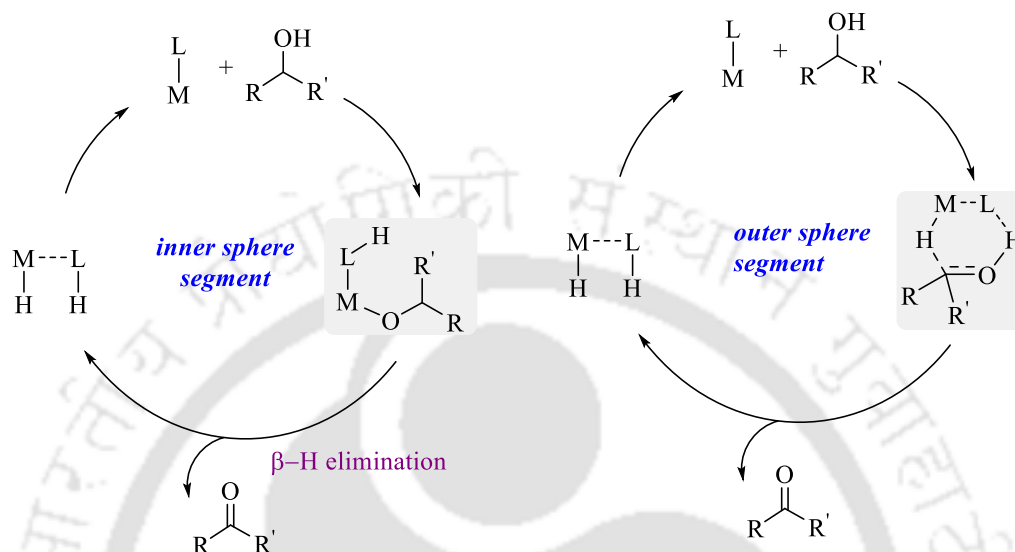
Scheme 1.5. Bond activation via metal–ligand cooperation

The MLC catalyst consists of a Lewis acidic site (metal ion), and Lewis basic site (ligand).³⁰ 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 functional units are normally 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 (α -, β -, and γ -protic). Some representative MLC catalysts are shown below (Scheme 1.6).^{32–39}



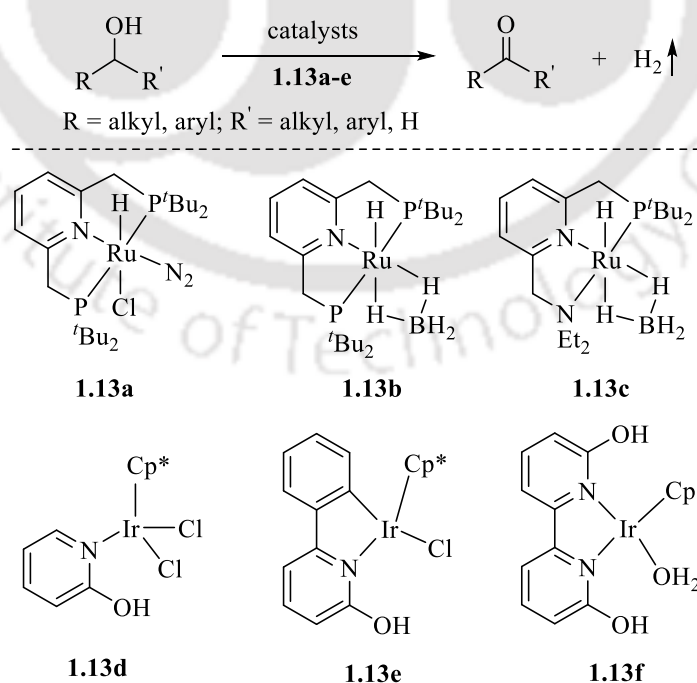
Scheme 1.6. Different types of protic functionalized MLC catalyst

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 *via* oxidative addition of alcohol, followed by β -H elimination.⁴⁰ Whereas, in the outer sphere mechanism, metal-hydride intermediate is generated *via* concerted hydride transfer (from 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.⁴¹ Using this MLC strategy, not only O-H bond is activated, but also different other bonds like N-H, H-H, B-H, and Si-H can also be activated which will lead to various useful organic transformations.³⁸



Scheme 1.7. Generalized mechanistic pathway for inner sphere (left) and outer sphere (right) mechanism

In 2004, the *Milstein* and co-workers demonstrated efficient catalytic dehydrogenation of secondary alcohols by ruthenium PNP [2,6-bis-(di-*tert*-butylphosphinomethyl)pyridine] pincer complex **1.13a** with low catalyst loading (0.4 mol%) in the presence of base (Scheme 1.8).



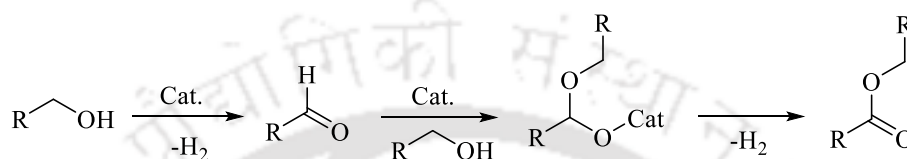
Scheme 1.8. Catalysts used in acceptorless dehydrogenation reaction

However, their catalytic system failed to give dehydrogenation of primary alcohols to the corresponding aldehydes. Then, same group has developed modified ruthenium (II) hydrido pincer complex **1.13b-c**⁴² where dehydrogenation of secondary alcohols can occur in the absence of base. Interestingly, “hemilabile” amine arm bearing pincer complex **1.13c** shown the

higher catalytic efficiency compared to **1.13b**, and the dehydrogenation of 1-phenylethanol to corresponding ketone was achieved with 0.1 mol% catalyst **1.13c**. Iridium-based complex **1.13d** was also showed efficient conversion for the dehydrogenation of secondary alcohols to corresponding ketones. But, benzyl alcohol gave only 24% benzaldehyde even with 1 mol% catalyst loading. Recently, *Fujita and Yamaguchi* reported the iridium catalyst **1.13e** for catalytic dehydrogenation of both primary and secondary alcohols to obtain the corresponding aldehydes or ketones in good yield. Similar type of dehydrogenation in the water medium also proceeded with the water-soluble catalyst **1.13f**.³⁹

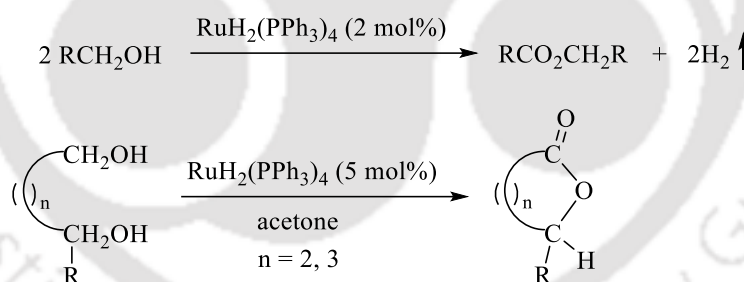
1.2.4. Dehydrogenative coupling of alcohols to form esters

In recent years, the synthesis of esters *via* the dehydrogenative coupling of alcohols was found to be the green approach. The proposed mechanistic pathway is depicted in Scheme 1.9.



Scheme 1.9. A plausible mechanism for dehydrogenative ester formation reaction

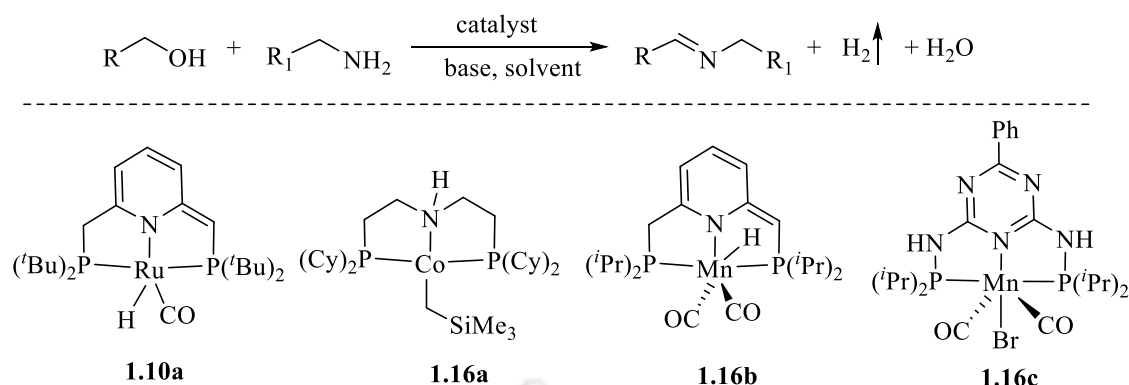
In 1985, Shvo's and co-workers reported catalytic dehydrogenation of primary alcohols to an ester using $(\eta^4\text{-tetracyclone})(\text{CO})_3\text{Ru}$ and $[(\eta^4\text{-tetracyclone})(\text{CO})_2\text{Ru}]_2$ complexes.³⁷ Later, Murahashi and co-workers reported conversion of alcohols to esters by 2 mol% of $\text{RuH}_2(\text{PPh}_3)_4$ at very high temperature 180 °C in the absence of hydrogen acceptor.⁴³ Their catalytic protocol is also effective for the synthesis of γ - and δ -lactones from 1,4- and 1,5-diol, respectively (Scheme 1.10). They also stated that the presence of hydrogen acceptor (such as acetone) lactonization process is greatly improved.



Scheme 1.10. Ruthenium catalysed oxidative transformation of alcohols to esters and ketones

In 2005, Milstein group demonstrated efficient conversion of alcohol to the corresponding ester under mild and neutral conditions catalyzed by ruthenium PNP and PNN-type pincer complexes.⁴⁴ The reaction proceeds through the aromatization/dearomatization strategy, and “hemilabile” amine “arm” in the ligand backbone plays an important role in the efficacy of this transformation. The same research group also reported cross dehydrogenative coupling of primary and secondary alcohols to form mix-ester (Scheme 1.11). The catalytic cycle for the formation of the ester by Ru-PNP catalyst **1.10a** is depicted in Scheme 1.12.⁴⁵

Pullarkat,⁴⁸ and Ozawa⁴⁹ have developed other catalytic systems with noble metals for this transformation (Scheme 1.13). Earth-abundant Mn and Co-complexes **1.16a-c** were also utilized for dehydrogenative synthesis of imine.^{50, 51}



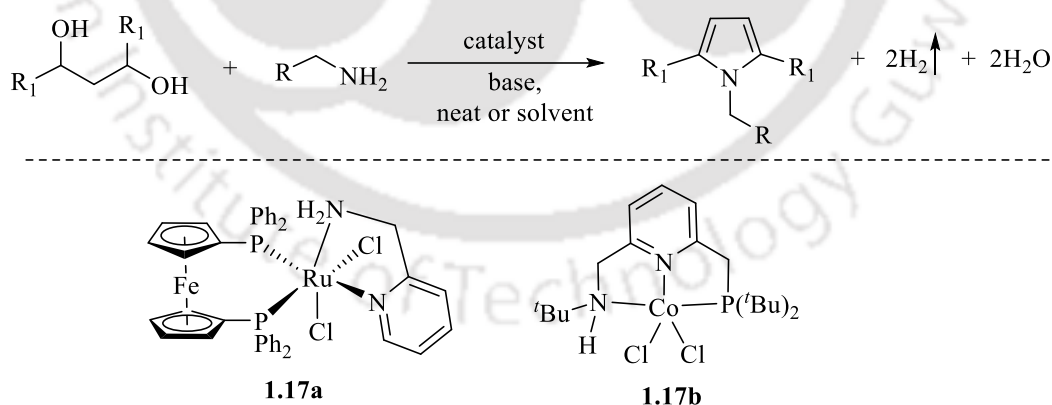
Scheme 1.13. Metal-catalyzed dehydrogenative synthesis of imines

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

Transition metal-catalyzed sustainable synthesis of *N*-heteroaromatics from readily available alcohols found to be an emerging area of chemical research considering their high importance in pharmaceuticals, material chemistry, and natural product synthesis. Among them, metal-ligand cooperative catalysts having NH, OH, or CH₂ functionality in the ligand backbone display pronounced efficacy for such transformations. In the following section, I present the brief synthesis of *N*-heteroaromatic compounds using selected MLC catalysts.

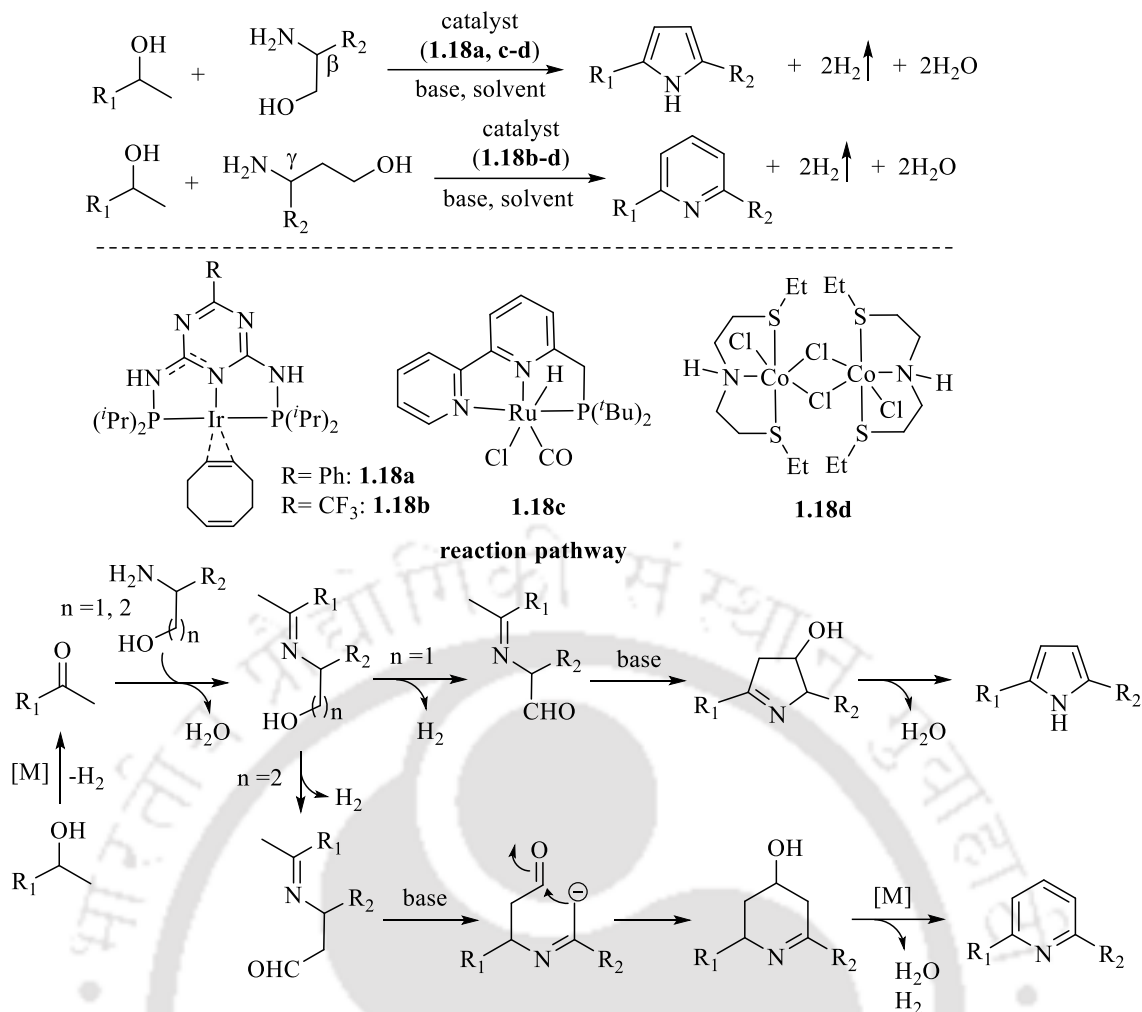
1.2.6.1. Dehydrogenative synthesis of pyrroles

2011, Crabtree group first reported a Ru-catalysed **1.17a** synthesis of pyrrole in moderate yield from the reaction of 2,5-diol and amines via ADC strategy.⁵² Later on, in 2016, Milstein and co-workers developed a methodology for a similar reaction with Co-PNN pincer complexes **1.17b** extended the strategy with broader substrate scopes (Scheme 1.14).⁵³



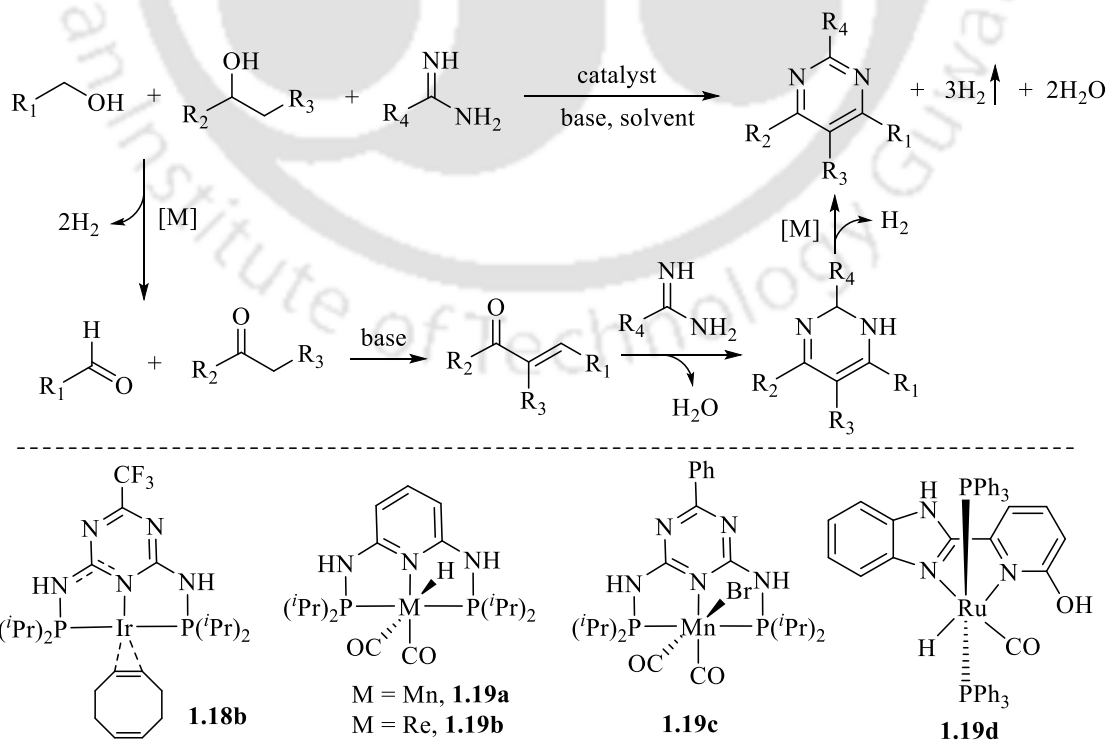
Scheme 1.14. Metal catalyzed dehydrogenative synthesis of pyrrole from 2,5-diol

Functionalized pyrroles have also been synthesized by the metal-catalyzed dehydrogenative reaction from secondary alcohols and β-amino alcohols. Kempe,⁵⁴ Milstein,⁵⁵ and Balaraman⁵⁶ have independently developed various bifunctional metal catalysts **1.18a**, **1.8c**, **1.18d** respectively, (bearing NH and CH₂ 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 **1.18b-d**. A plausible mechanistic pathway for the synthesis of these *N*-heterocycles is depicted in Scheme 1.15.⁵⁷



Scheme 1.15. Metal catalysed synthesis of pyrrole and pyridine with plausible mechanism

1.2.6.2. Dehydrogenative synthesis of pyrimidines

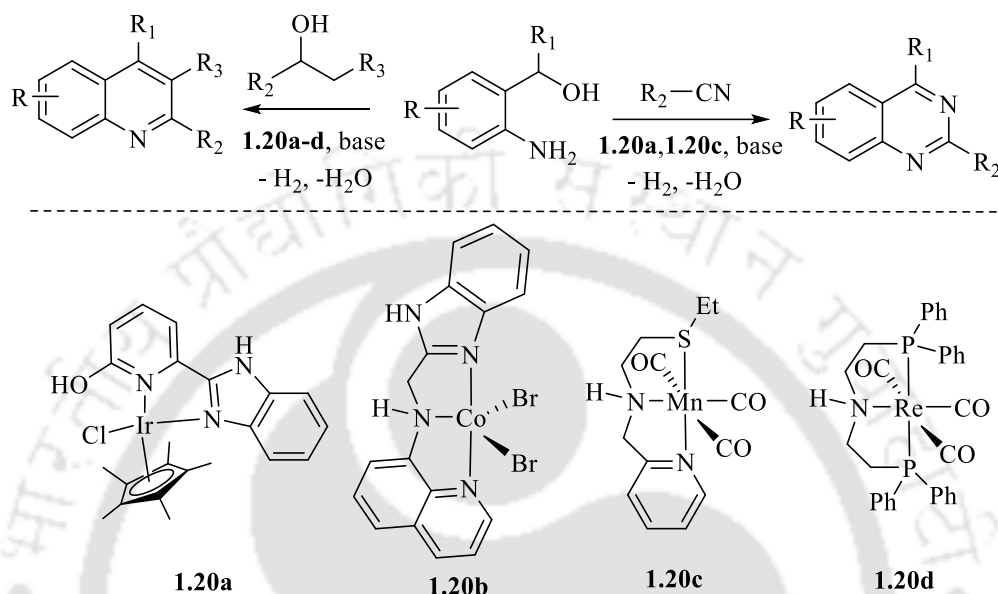


Scheme 1.16. Dehydrogenative synthesis of pyrimidine by the coupling of alcohol amidine with mechanism

Transition metal catalyzed multi-component synthesis of other heterocycles like pyrimidine has also been achieved by the reaction of alcohols and amidines following the acceptorless dehydrogenative coupling strategy. A general reaction pathway is shown in Scheme 1.16.⁵⁸⁻⁶⁰

1.2.6.3. Dehydrogenative synthesis of quinolines and quinazolines

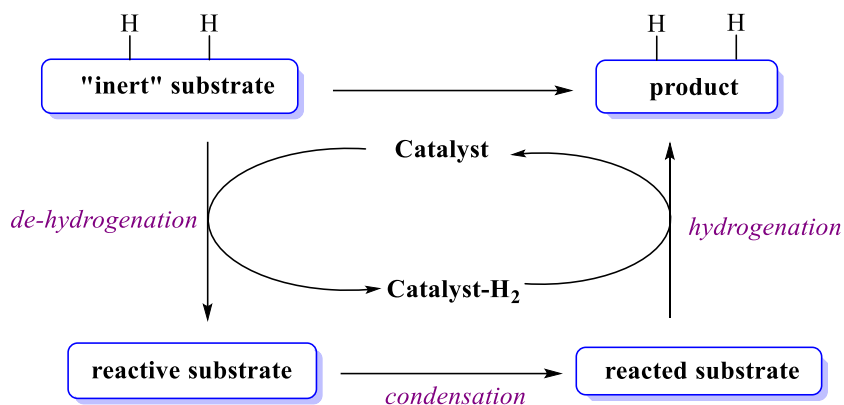
Moreover, metal-catalyzed dehydrogenative synthesis of quinoline was accomplished by the reaction of 2-aminoaryl alcohol and secondary alcohol, and quinazoline was achieved from 2-aminoaryl alcohol and aryl nitrile or 2-aminobenzylamine with primary alcohols. Some selected metal catalyst is given in Scheme 1.17.^{57, 61-64}



Scheme 1.17. Dehydrogenative synthesis of quinoline and quinazoline from the 2-aminoaryl alcohol

1.3. Hydrogen Autotransfer (HA) or Borrowing Hydrogen (BH) Strategy

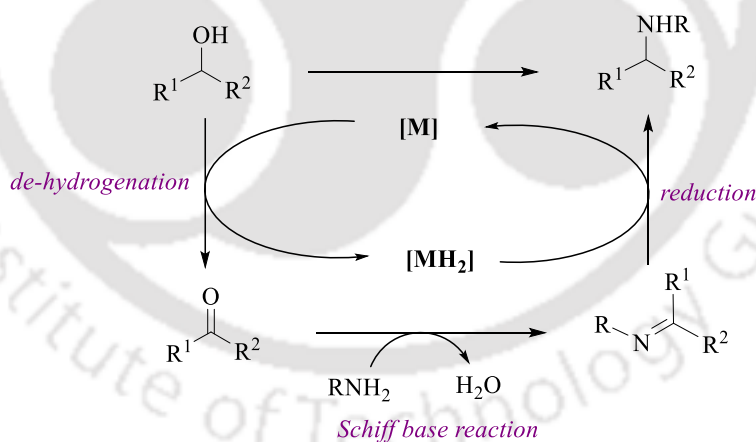
The ‘hydrogen atom-transfer’ methodology called ‘borrowing hydrogen’ (BH) is a synthetic approach that associates acceptorless dehydrogenation with a transfer hydrogenation process concurrent to the *in-situ* generations of the reaction intermediate.⁶⁵⁻⁶⁷ This one-pot oxidation–condensation–reduction sequence has received much attention due to its intrinsic high atom economy and permitting alcohols or amines to be employed as alkylating agents, generating water or ammonia as the only by-products, respectively. This strategy has become a topic of great interest due to its widespread application for various transformations of cheap and harmless starting materials, most commonly alcohols. In general, this reaction sequence leads to new carbon-carbon or carbon-nitrogen bonds, and the strategy consists of three distinct steps (Scheme 1.18). In the first step, the substrate gets activated by catalyst through dehydrogenation (oxidation), and then condensation reaction (e.g., Schiff base formation, aldol condensation, Michael additions etc.) occurs. Finally, to complete this cascade reaction, the formed condensation product got hydrogenated (or reduced) and regenerated the catalyst. The overall process is redox neutral, and after the completion of the reaction sequence, there is no gain or loss of hydrogen. The process is evading the application of further reducing agents or external hydrogen.



Scheme 1.18. The general schematic diagram for borrowing hydrogen strategy

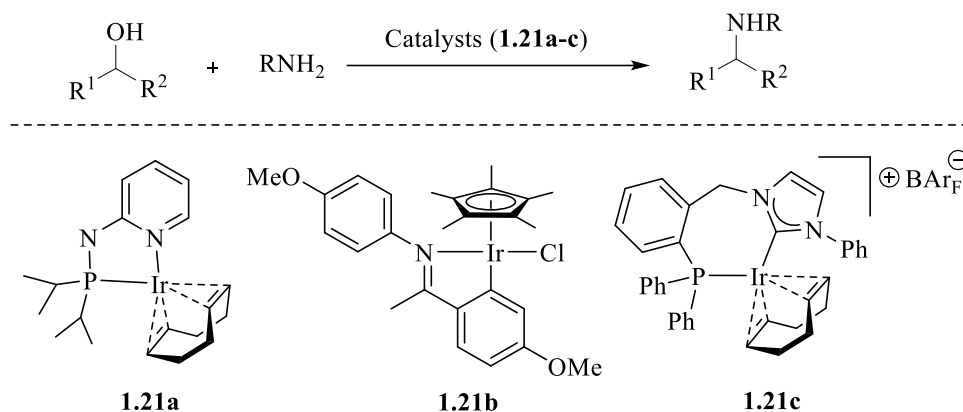
1.3.1. Borrowing Hydrogen Strategy in *N*-alkylation reaction

Catalytic *N*-alkylation of amines by alcohol using the BH approach is a promising atom-economical and environmentally benign process for the selective synthesis of various amine derivatives with water the only by-product. Conventionally, an *N*-alkylation reaction has been carried out using the reaction of amines with mutagenic alkyl halides.⁶⁸ However, over alkylation often occurs after the first alkylation under the reaction conditions. Therefore, selective synthesis of *N*-alkylated amines is challenging using this route. Amine derivatives can also be synthesized by the reduction of the amide by generating stoichiometric copious waste. Alternatively, the alkylation of amines using alcohol is a precious approach in the current study. The catalyst first oxidizes the substrate alcohol *via* acceptorless dehydrogenation to form aldehyde or ketone and subsequently generate **Catalyst-H₂**. Corresponding carbonyl compound (aldehyde or ketone) eventually undergoes a condensation reaction with amines to form an imine intermediate. Finally, the imine is reduced with the hydrogen atom equivalents gained in the oxidation/dehydrogenation step (Scheme 1.19).



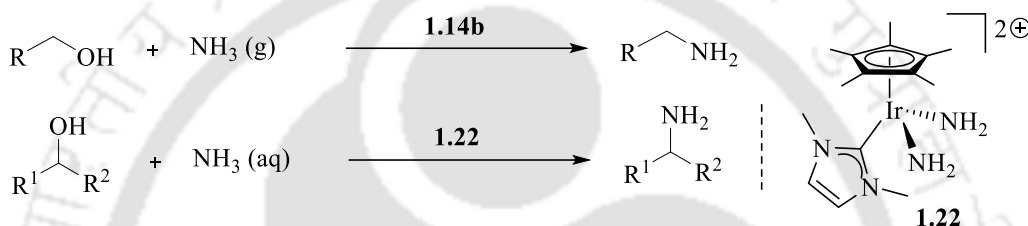
Scheme 1.19. General schematic diagram for *N*-alkylation of amines with alcohols.

N-alkylation of amine with alcohols was first discovered by Grigg,⁶⁹ and Watanabe⁷⁰ at the beginning of 1980s using RuH(PPh₃)₄ and Ru(PPh₃)₂Cl₂, respectively. Inspired by their pioneering work, in 2003 Yamaguchi and co-workers introduced the activity of [Cp*IrCl₂]₂ for the *N*-alkylation of alcohols.⁷¹ Later on, Kempe,⁷² Xiao,⁷³ and Anderson⁷⁴ have independently reported other Iridium-based complexes **1.21a**, **1.21b**, **1.21c**, respectively, for this transformation with good substrate scope. Very recently, earth-abundant metal complexes such as Fe, Co, and Mn have also been shown to catalyze such transformation.^{51, 75, 76}



Scheme 1.20. *N*-Alkylation of the aliphatic and/or aromatic amine with primary alcohol catalyzed by Ir-complex.

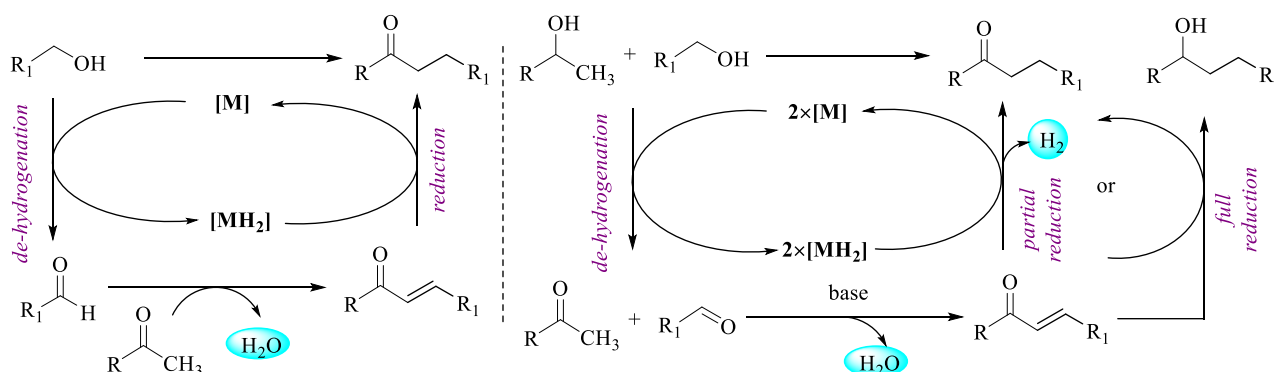
The strategy is further extended to achieve the synthesis of primary amine directly from the reaction of primary alcohol and ammonia gas using acridine-based ruthenium-complex **1.14** (Scheme 1.21). Recently, Yamaguchi and co-workers reported an elegant way to synthesize primary amines using aqueous ammonia by water-soluble iridium *N*-heterocyclic carbene Ir-catalyst **1.22**.⁷⁷



Scheme 1.21. Catalytic synthesis of primary amines by *N*-alkylation of ammonia with alcohol

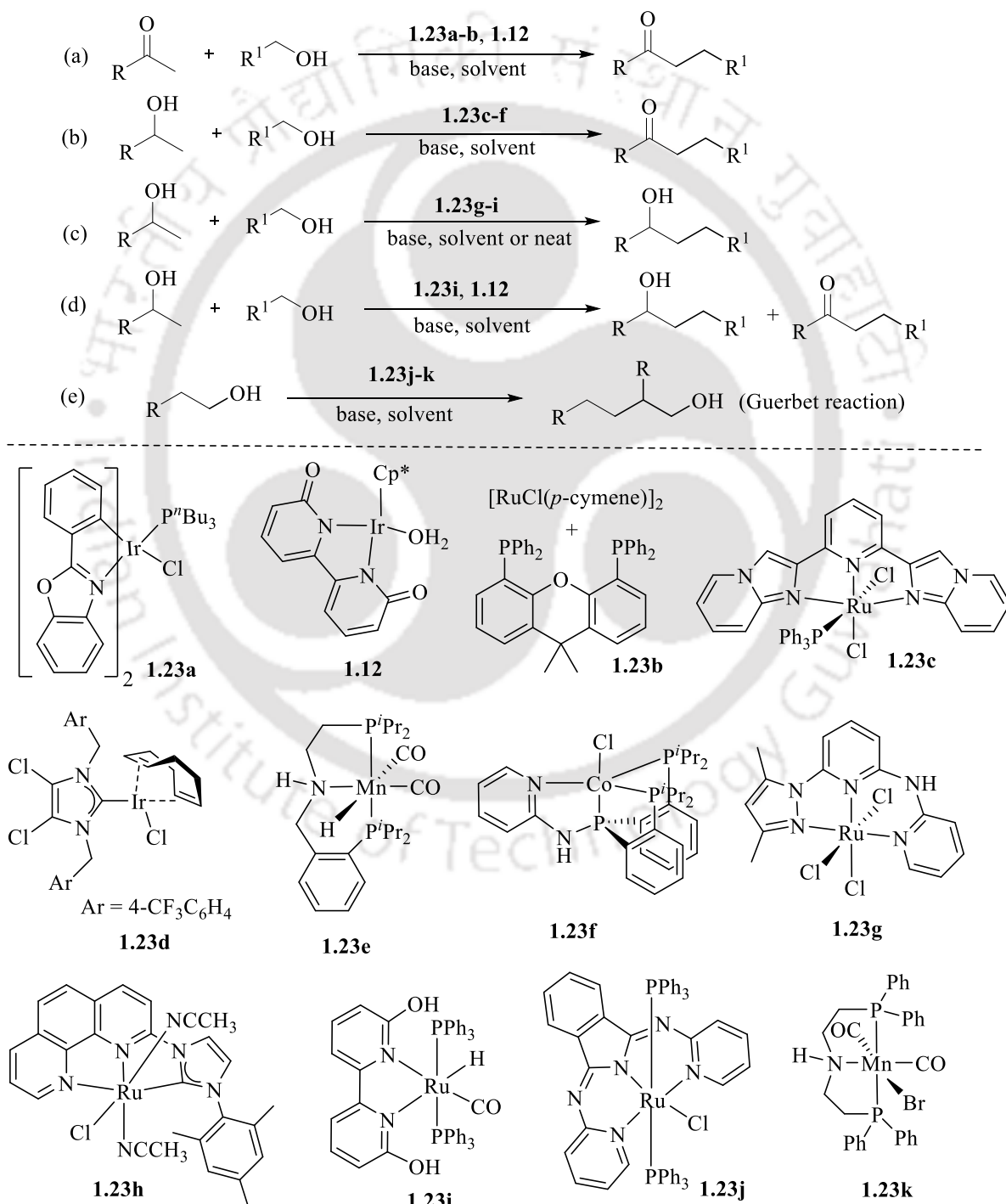
1.3.2. Borrowing Hydrogen Strategy in C-alkylation reaction

Transition metal-catalysed C-alkylation using alcohol as an alkylating agent represents the highly atom efficient and environmentally benign synthetic approach. The water is generated as the only major by-product in the overall process. A variety of alkylated ketone or branched alcohol could be obtained from readily available alcohol using the concept of BH principle and aldol condensation. The reaction primarily involved three steps; these are i) oxidation of the alcohol substrate through a hydrogen transfer process to give the corresponding aldehyde or ketone and metal-hydride intermediate ii) aldol condensation of the enol to form corresponding α , β -unsaturated ketone iii) reduction of unsaturated ketone with metal hydride to give α -alkylated ketone or branched alcohol (Scheme 1.22). Depending on the coupling partners, the reaction can be categorized as follows: 1) the α -alkylation of ketones and carbonyl compounds; (2) alcohol-alcohol coupling reactions to afford α -branched ketone or β -alkylated secondary alcohol. The product distribution depends on the selectivity of the reduction step in the catalytic cycle. Full reduction leads to β -alkylated secondary alcohol, and partial reduction gives to α -branched ketone; and (3) β -alkylation by alcohol dimerization, which is denoted as a Guerbet reaction.⁷⁸



Scheme 1.22. General schematic diagram for C-alkylation reactions using BH strategy.

To date, several research groups have reported the development of effective C-alkylation catalysts by the ligand modification of the transition-metal complex. One of the interesting examples reported by Ding and co-workers using benzoxazolyl ligand supported iridium complex **1.23a**,⁷⁹ which exhibited high catalytic activity towards the C-alkylation of numerous ketones and primary alcohols (Scheme 1.22a). Later on, Li and co-workers modified the ligand backbone by bipyridonate iridium Cp* complex **1.12**⁸⁰ for the similar type of reaction. They proposed that carbonyl group of the bipyridonate ligand facilitates activating the alcohol substrate by accepting a proton from the species, which would serve as an important step in the transfer hydrogenation reaction. It is worthy to note that the corresponding complex showed high catalytic activity towards α -alkylation of ketone with methanol as well. Several ruthenium-based catalysts have also been developed as effective C-alkylation catalysts. Zhang and co-workers reported the use of Ru-catalyzed (**1.23b**) α -alkylation methodology to synthesize a series of α -pyridyl methylated ketones using pyridyl methanol derivatives in good yield. In 2018, Song et. al. reported NNN pincer Ru(II)-complex **1.23c**⁸¹, which showed high catalytic



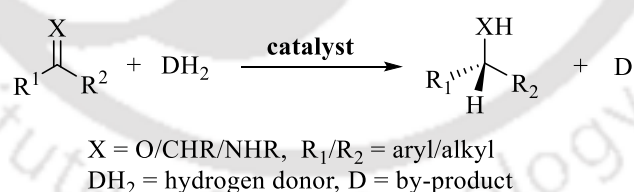
Scheme 1.22. Metal-catalyzed (a) α -alkylation of ketone with alcohol (b-d) Cross-coupling reaction of primary and secondary alcohol to ketone or branched alcohol (e) β -alkylation by alcohol dimerization (Guerbet reaction).

activity in the coupling of secondary and primary alcohols to afford the linear or branched ketones. They have shown that the protocol could also be utilized for the synthesis of biologically active drug donepezil directly from readily available alcohols. Metal-catalyzed cross-coupling of secondary alcohol with primary alcohol can provide the α -alkylated ketone selectively reported by Guelcema (using Ir-based complex **1.23d**),⁸² Milstein (by Mn-based complex **1.23e**),⁸³ Ding (by a PNP-co catalyst **1.23e**),⁸⁴ and others,⁸⁵ independently, (Scheme 1.22b). In 2016, Yu and co-workers⁸⁶ synthesized a ruthenium(III)-NNN pincer complex **1.23g**, which catalyzes β -alkylation of secondary alcohols with primary alcohols to afford β -branched secondary alcohol (Scheme 1.22c). Subsequently, Kundu and co-workers⁸⁷ reported efficient catalytic protocol for the synthesis of β -substituted secondary alcohol using 1,10-phenanthroline-based-NNC-Ru(II) complex **1.23h** with high TONs. Very recently Kumar et. al.⁸⁸ found even high TONs for the same transformation by phosphine-free NNN-pincer Ru(II) complex. In this reaction, corresponding β -substituted secondary alcohol can further dehydrogenate under the catalytic condition to form α -branched ketone, leading to challenges in the selectivity (Scheme 1.22d). Considerable research interest has also recently been directed towards using ethanol as a bioresource substrate to provide access to *n*-butanol and higher alcohols using the Guerbet process. Upgrading ethanol to butanol (>50% conversion) was achieved using air-stable ruthenium complex **1.23j** reported by Szymczak and co-workers in the year 2016 (Scheme 1.22e).⁸⁹ Recently, Jones group reported the same transformation with manganese complex **1.23k** as a catalyst; about 34% yield of *n*-butanol was obtained with high selectivity.⁹⁰ The limited attention has been made for catalytic cross-coupling of two secondary alcohols⁹¹ and C-alkylation of secondary alcohol with ketones.⁹²

1.4. Transfer hydrogenation reaction

1.4.1. General background of transfer hydrogenation reaction

Transfer hydrogenation or hydrogen transfer (H-transfer) is defined as “the reduction of multiple bonds with the aid of a hydrogen donor (DH₂) in the presence of a catalyst”, as depicted in Scheme 1.23.⁹³ The hydrogen donor (DH₂) is characterized by the presence of hydrogen that, under the influence of a suitable promoter, can be mobilized in such a way as to add to an unsaturated functional group in the substrate. At the same time, the hydrogen donor is converted to its dehydrogenated counterpart D. In the large majority of cases, the two hydrogens of the donor are non-equivalent and they are transferred sequentially, one as a formal hydride and the other as a formal proton.



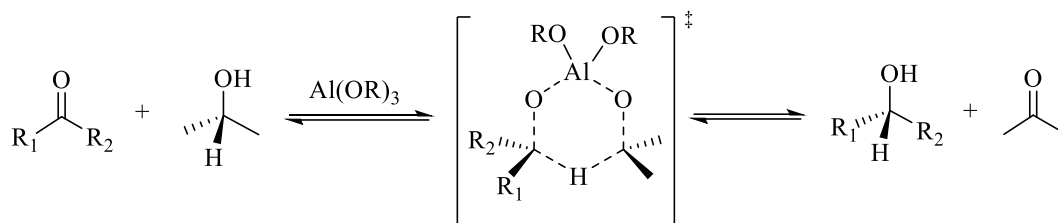
Scheme 1.23. The general transfer hydrogenation reaction

In contrast to the hydrogenation process, formation of a co-product D is the main drawback in the hydrogen transfer processes. Furthermore, upon losing two hydrogen atoms, the hydrogen donor (DH₂) itself becomes a hydrogen acceptor that may be in competition with the substrate until equilibrium is reached. An example is where isopropyl alcohol is used as the hydrogen source in the transfer hydrogenation of ketones. There is an added advantage when the products of the decomposing donor have large negative enthalpies of formation. Thus, CO₂ from formic acid and N₂, from hydrazine provides added driving force to the reactivity of these substances as hydrogen donors.⁹⁴

1.4.2. Transfer hydrogenation reaction in polar multiple bonds

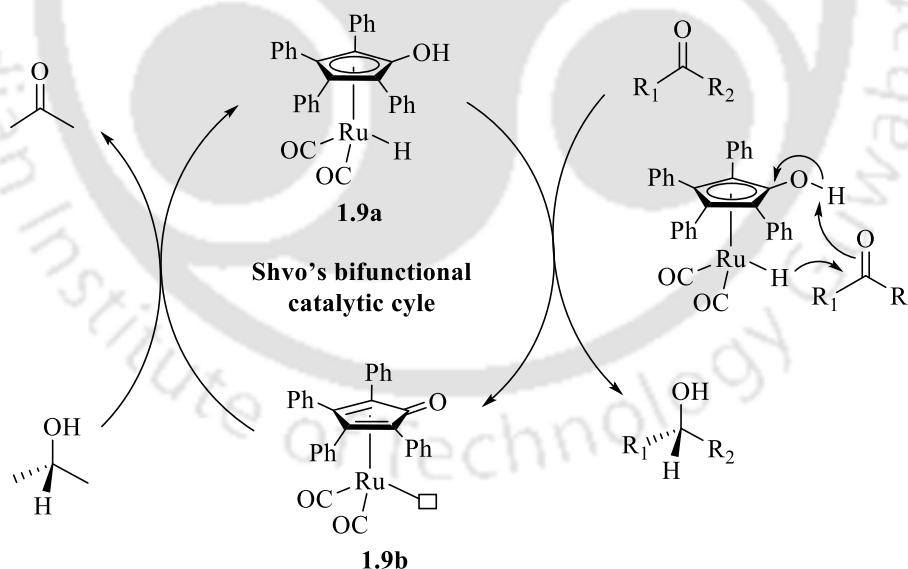
In the 1920s, Meerwein, Ponndorf, and Verley⁹⁵ reported that aluminium alkoxides were able to reduce ketones to the corresponding alcohols with isopropanol. The reduction occurs *via* a direct hydrogen transfer route, which proceeds through the formation of a cyclic six-membered transition

state whereby the ketone and isopropanol are simultaneously coordinated to the metal center (Scheme 1.24). It is known as the Meerwein-Ponndorf-Verley (MPV) reduction. However, the drawbacks of the MPV reduction are the large amounts of the aluminum reagent required and undesired side products.



Scheme 1.24. Hydrogen transfer in Meerwein-Ponndorf-Verley reduction

The next milestone was the discovery that transition metal complexes could catalyze the transfer hydrogenation of ketones. In 1986, Shvo's and co-workers⁹⁶, in their pioneer work, demonstrated the synthesis of the ruthenium complex **1.9**, which was originally found to be very efficient in direct hydrogenation of ketones, was later applied in the transfer hydrogenation reaction. As mentioned in Scheme 1.6-(ii) the dinuclear complex **1.9** dissociates upon heating into the active, reducing form **1.9a** and the coordinatively unsaturated and therefore, highly reactive species **1.9b**.⁹⁶ The complex **1.9a** operates through an outer-sphere mechanism involving a simultaneous transfer of hydride from the ruthenium center and proton from the hydroxyl group on cyclopentadienyl ligand the carbonyl group of the ketone substrate. **1.9b** 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 1.25). Subsequently, many other metal catalysts containing rhodium,⁹⁷ iridium,⁹⁸ earth-abundant metals⁹⁹ are employed to facilitate transfer hydrogenation. Organocatalysts such as chiral secondary amine,¹⁰⁰ phosphoric acid derivative¹⁰¹ are also found well-suitable for this transformation.

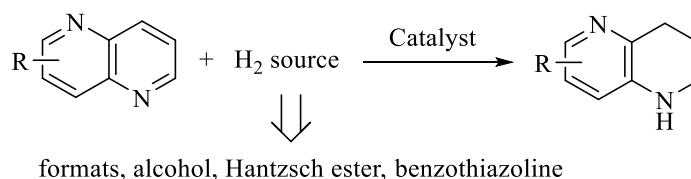


Scheme 1.25. Transfer hydrogenation by Shvo's catalyst

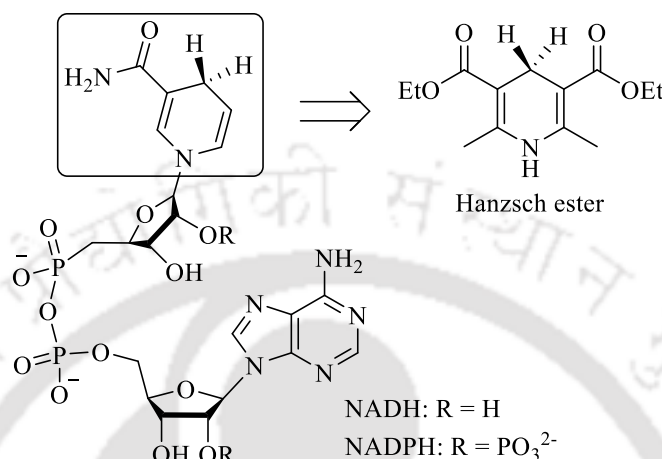
1.4.3. Reduction of *N*-heteroarenes with biomimetic Hantzsch ester as a mild H₂ source

Besides the transfer hydrogenation of multiple bonds such as C=C, C=N, and C=O, reduction of *N*-heteroarenes are also extensively studied using hydrogen transfer reagent, for instance, formates (HCO₂H/NEt₃, HCO₂Na/H₂O), alcohol (isopropanol, ethanol), Hantzsch ester, benzothiazoline etc.⁹³ Among them, Hantzsch ester is quite promising as it is synthetic analogs of nature's fundamental reduction co-factors such as NADH (nicotinamide adenine dinucleotide) 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. 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.¹⁰²

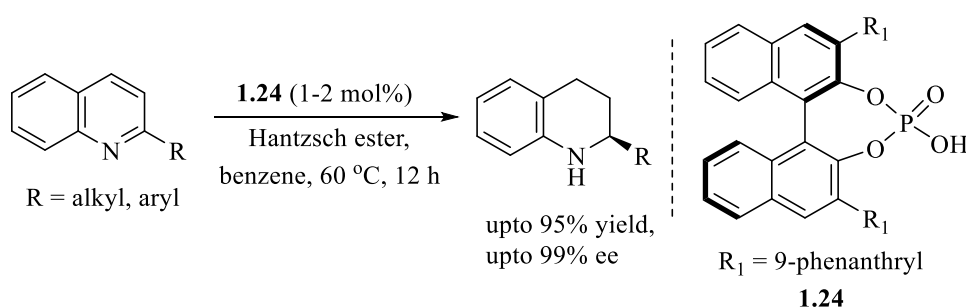


Scheme 1.25. Transfer hydrogenation of quinoline to THQs

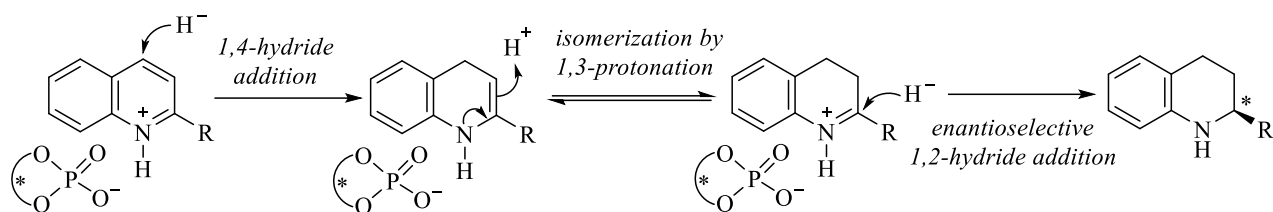


Scheme 1.26. The structures of naturally occurring hydride-reduction cofactors and Hantzsch esters.

Inspired by this biomimetic reduction process, in early 2006, Rueping and co-workers reported a highly enantioselective Brønsted acid catalyzed transfer hydrogenation of quinoline.¹⁰³ The resulting products tetrahydroquinolines are an important class of compounds found in many natural and medicinal products and used as synthetic intermediates in pharmacy, agrochemistry or material science. They found that the use of Hantzsch ester as a reducing agent and 1-2 mol% of phenanthryl-substituted phosphoric acid afforded highly enantiopure tetrahydroquinoline derivatives in good yield (Scheme 1.26). It was also proposed that the reaction involves cascade hydrogenation consisting of a 1,4-hydride addition, an enamine-imine isomerization by protonation, and a final 1,2-hydride addition (Scheme 1.27). The scope of the reaction was further explored to the synthesis of biologically active tetrahydroquinoline alkaloid such as (+)-galipinine, (+)-cuspareine and (–)-angustureine etc.¹⁴⁶ Later on, the same research group have shown their methodology in aqueous medium as well. After the successful enantioselective transfer hydrogenation of quinolines, imine containing other heterocycles including pyridine, indole, 1,10-phenanthrolines, benzoxazines, benzothiazines, benzoxazinones, quinoxalines, and quinoxalinones accomplished using Hantzsch ester as a mild hydrogen source¹⁰² In general, the Brønsted acids were employed as catalysts for these transformations.¹⁰⁴ Metal-catalyzed transfer hydrogenation of quinoline with Hantzsch esters is also reported by metal triflate such as Fe(OTf)₂ and AgOTf.^{105, 106} Herein, Lewis acidic metal ions play an important role for the activation of quinoline.

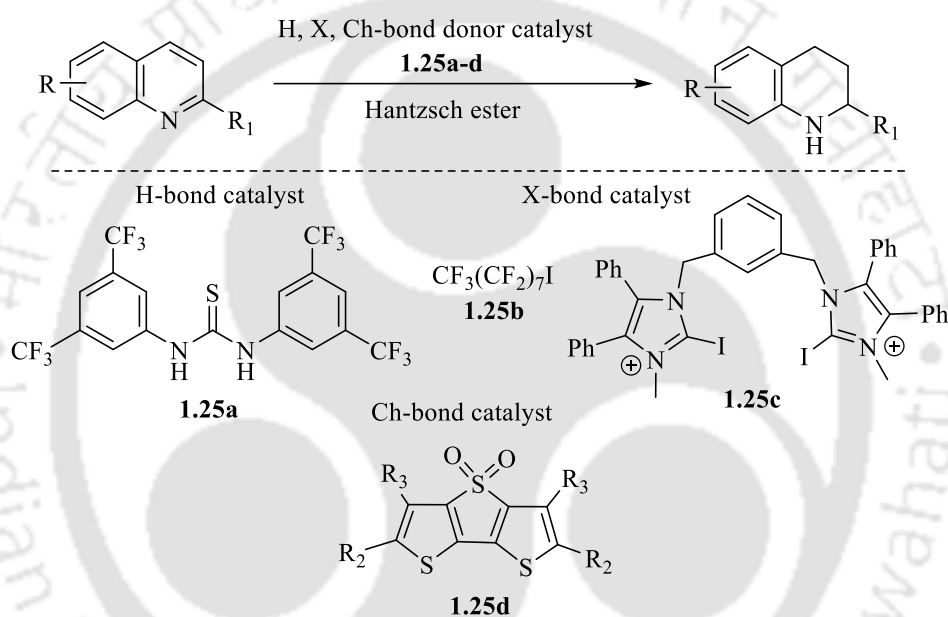


Scheme 1.26. Asymmetric transfer hydrogenation of 2-substituted quinolines



Scheme 1.27. Proposed mechanism for asymmetric reduction of quinoline

Subsequently, non-covalent hydrogen-bond (HB)-donor, halogen-bond (XB)-donor, and chalcogen-bond (ChB)-donor catalyzed reduction of quinoline with Hantzsch ester were described independently by Zhang,¹⁰⁷ Bolm,¹⁰⁸ Tan,¹⁰⁹ and Matile.¹¹⁰ They have demonstrated that activation of the quinoline by halogen bonding, halogen bonding, or chalcogen bonding was crucial for this transformation (Scheme 1.28). Though various Lewis acidic metals, Brønsted acids, non-covalent bond donor-catalyzed reduction of quinoline to tetrahydroquinoline were reported, there is still ample scope to develop a new earth-abundant catalytic system to study their scope and limitation in the transfer hydrogenation reaction.



Scheme 1.28. noncovalent bond donor catalysed reduction of quinoline with Hantzsch ester

1.5. Summary

Acceptorless dehydrogenation of alcohol is an important reaction that affords aldehyde or carbonyl compounds and produces molecular hydrogen. The liberated hydrogen can be used as a potential energy source in the energy sector. This raises the prospect of using the catalysts for reversible dehydrogenation of organic liquid fuel for energy storage and generation. This dehydrogenation reaction can be catalyzed by a variety of metal complexes without the use stoichiometric amount 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 proceeded through a low-energy dehydrogenation pathway. Likewise, the borrowing hydrogen principle is shown to be effective for *N*-alkylation and *C*-alkylation reaction. Furthermore, it has been found that transfer hydrogenation is another powerful tool for the reduction of *N*-heteroarene with biomimetic Hantzsch ester as the hydrogen source.

1.6. Scope and objective of the thesis

As discussed above, acceptorless dehydrogenative coupling reaction, borrowing hydrogen catalysis, and transfer hydrogenation is the powerful synthetic approach to synthesize the diverse range of useful organic building blocks in the sustainable manner. In contrast to the classical catalyst, MLC-

catalyst has shown efficacy in various organic transformations. Considering the literature facts, the present study was focused on the synthesis of new tridentate ligand supported ruthenium (III) complexes as a metal-ligand cooperative catalyst, study their applicability and shortcoming towards

- ❖ α -alkylation of simple aromatic ketone with secondary alcohol to form β -disubstituted ketone
- ❖ Selective catalytic cross-coupling of secondary alcohol and primary alcohol to form α -alkylated ketone, and two different secondary alcohols to form β -disubstituted ketones.
- ❖ Practical dehydrogenative synthesis of quinolines and quinazoline derivatives.

Another objective of this study was to investigate

- ❖ transition-metal-free chemoselective reduction of quinolines with Hantzsch ester under mild conditions
- ❖ synthesis of biologically relevant *N*-aryl tetrahydroquinolines directly from readily available quinolines

1.7. References

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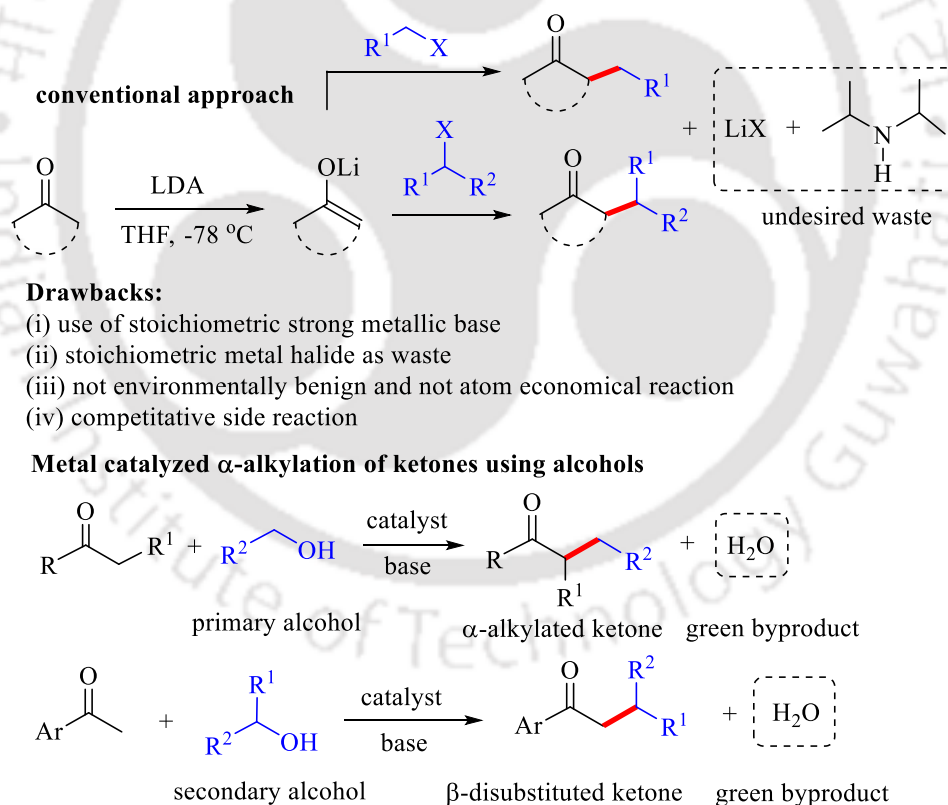
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Synthesis of triazine-based NNN-pincer ruthenium (III) complexes and their catalytic application for sustainable synthesis of β -disubstituted ketones via α -alkylation of ketones using secondary alcohols

2.1. Introduction

In this chapter, I have mainly discussed the synthesis of new nitrogen rich triazine-based pincer ligands and their ruthenium (III) complexes, and explored their utility in borrowing–hydrogen catalysis. The sustainable synthesis of β -disubstituted ketones was achieved by using these well-defined ruthenium complexes efficiently.

Ketones are of great importance in organic synthesis and widely applied in material, biological, pharmaceutical and agrochemical industries.¹ They are produced on a large scale as solvents in manufacturing industry. Traditionally, α -alkylated ketones and β -disubstituted ketones are synthesized by the reaction of an alkyl halide with a ketone in the presence of a strong base such as n BuLi or LDA (Scheme 2.1).^{2,3} Such alkylation methods have several disadvantages, such as the use of toxic alkyl halides, the requirement for cryogenic conditions, and the elimination can occur as a competitive side reaction with secondary alkyl halides. The formation of stoichiometric amounts of metal salts as chemical waste is another concern,^{4,5} thereby the overall process is not environmentally benign and less atom economical. It is desirable to develop an alternative approach where these hazardous and toxic reagents can be replaced by cheap, readily available, and bio-renewable alcohols^{6,7} and the process become more atom economical, practical, and environmentally friendly.

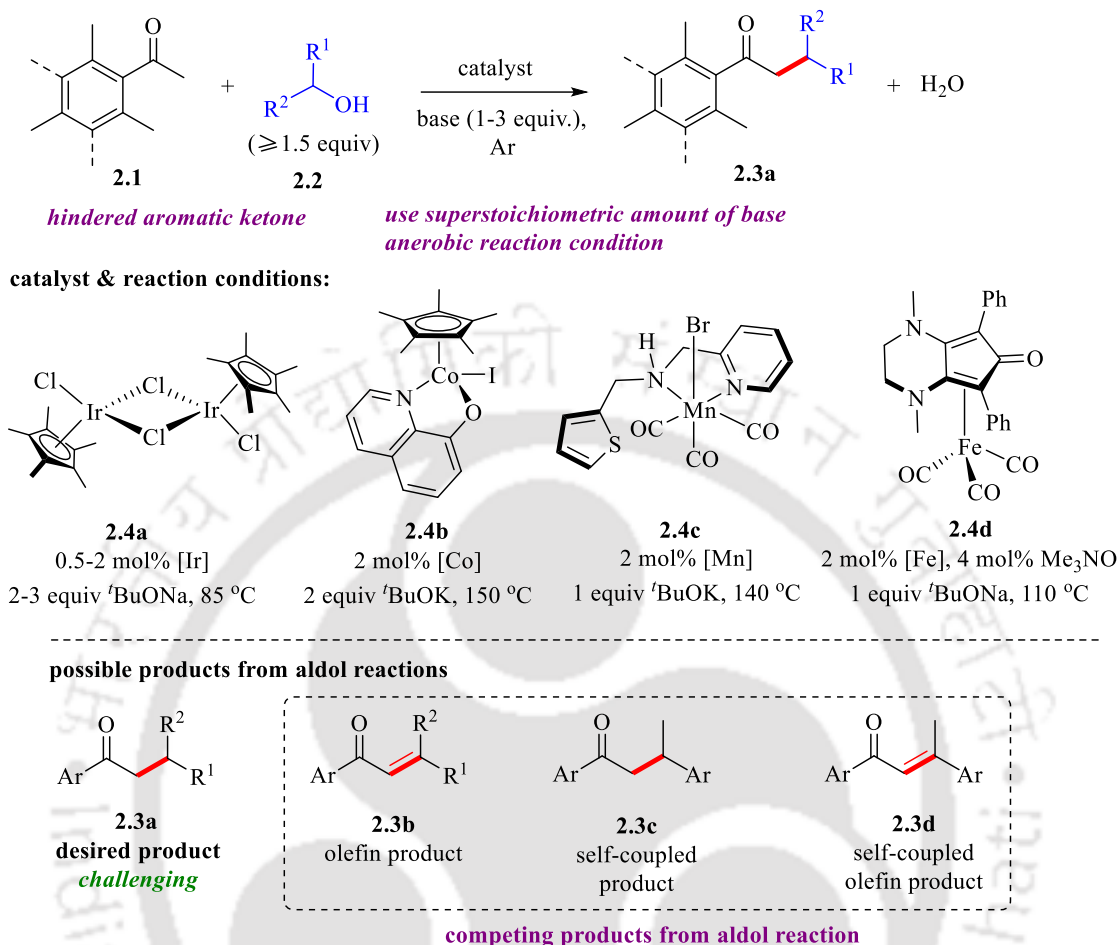


Scheme 2.1. Traditional and selective catalytic α -alkylation of ketones using primary and secondary alcohols

In this context, transition-metal-catalysed α -alkylation of ketone using alcohol as alkylating agent is a promising approach.⁸⁻³⁸ The process yields only water as the side product, which makes the process green, atom economical, and environmentally benign. The use of primary alcohol for α -alkylation of ketone to generate linear α -alkylated ketones has been well documented in the literature by using borrowing hydrogen catalysis.³⁹⁻⁴⁷ On the other hand, the use of secondary alcohols for alkylation reactions is very limited.⁴⁸⁻⁵¹ In contrast to α -alkylated ketones, formation of β -branched products is more challenging and relatively underdeveloped. The self-coupling of secondary alcohols is one of the common undesired side products which reduce the atom economy in an overall process.

Moreover, selectivity is another major concern in this transformation.^{52, 53} Initially, the pioneering work on the C-alkylation of ketones using secondary alcohol to form β -disubstituted ketones reported by Donohoe and co-workers⁴⁸ in 2017. Soon after, Co,⁴⁹ Mn,⁵⁰ and Fe-catalyzed⁵¹ α -alkylation of ketones with secondary alcohols was described with earth-abundant metals (Scheme 2.2).

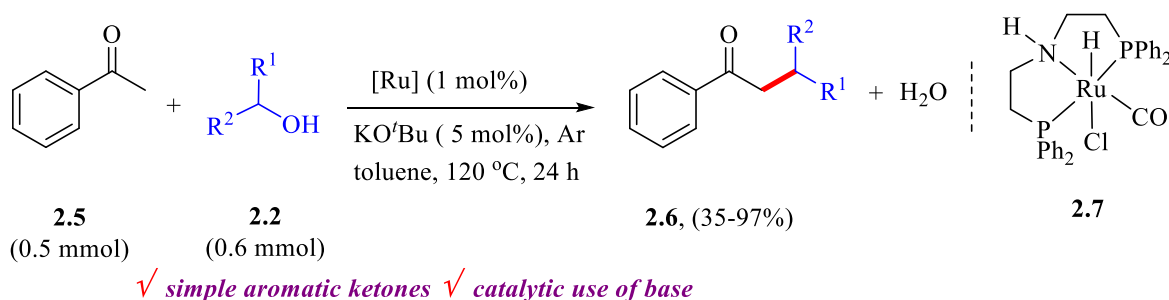
Transition metal-catalyzed α -alkylation of ketones with secondary alcohols



Scheme 2.2. Selective catalytic α -alkylation of ketones using secondary alcohols

All the encouraging developments is summarized as follows: (i) The reactions require equivalent or excess amount of base (2 equiv), which can give to aldol side reactions (ii) To avoid base-promoted self-condensation of the starting ketones, highly hindered aryl ketones are used. In general, these methods work only for pentamethylphenyl (Ph*) ketone or trisubstituted aryl ketones (iii) Unsubstituted or other aryl ketones are less successful and thus, suffer from a limited substrate scope (iv) air-sensitive catalyst and anaerobic reaction condition is used to achieve the outcome. To overcome these shortcomings, Gunanathan group⁵⁴ very recently demonstrated efficient protocol with Ru-MACHO catalyst, which can tolerate simple aromatic ketone substrate with good selectivity (Scheme 2.3). They have used phosphine-based ruthenium(II) complex **2.7** as the pre-catalyst.

Ruthenium catalyzed α -alkylation of ketones with secondary alcohols

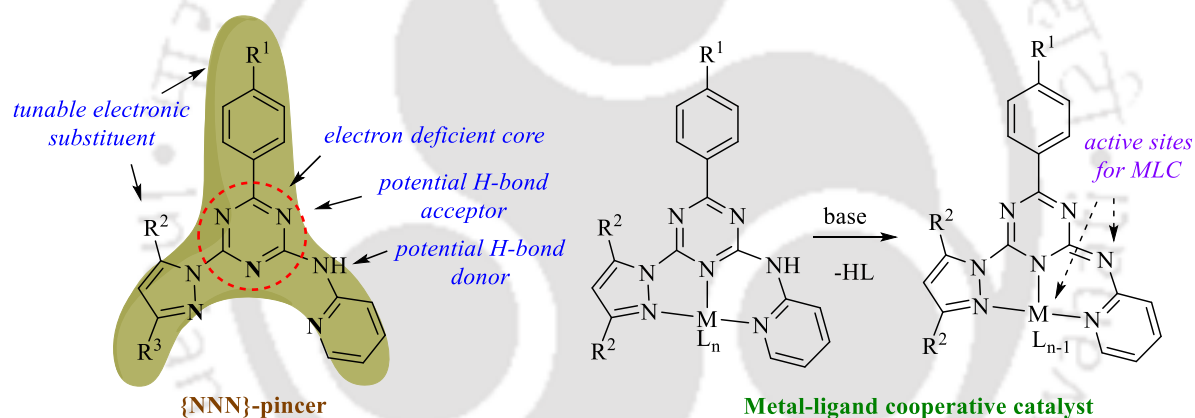


Scheme 2.3. Ruthenium-catalysed α -alkylation of simple aromatic ketones using secondary alcohols

The above reports suggest that the synthesis of β -branched ketones *via* BH catalysis is inevitably significant. The development of a new selective, environmentally benign, sustainable method is highly desired. The reported catalyst **2.7** containing MACHO ligand, which is $\text{HN}(\text{CH}_2\text{CH}_2\text{PPh}_2)_2$. In general, the phosphine-bearing pincer ligands are a milestone in homogeneous catalysis. However, in practical aspects, they are associated with some limitations such as these are often air and moisture sensitive, involved in complex synthetic procedures, and high cost. Therefore, I am interested in developing suitable alternative nitrogen-based ligands at their place. These will be employed to synthesize ruthenium complexes and investigate their applicability in ADC and BH catalysis.

2.2. Present work

Herein I have endeavored to design nitrogen rich new triazine-based tridentate NNN-pincer ligand system. The triazine moiety is remarkable primarily because of its unique electron-deficient nature.⁵⁵ s-triazine has shown the ability to exhibit unusual anion- π contacts and intricate H-bonding networks in the supramolecular chemistry.⁵⁶ Its electronic behavior can also be modulated by varying substituent in the backbone which may show prospective aspect in homogeneous metal catalysis. The designed ligands feature a central triazine ring with potentially tridentate pockets, in where pyrazolyl group is located at one side and -NH functionality containing pyridyl group is situated on the other side (Scheme 2.4). Notably, the Lewis basic site of deprotonated -NH moiety in the ligand framework can activate the alcohol substrate in synergetic manner with Lewis acidic metal site *via* metal ligand cooperation, thereby the catalytic activity of the dehydrogenation of alcohols or coupling of alcohols can be enhanced.

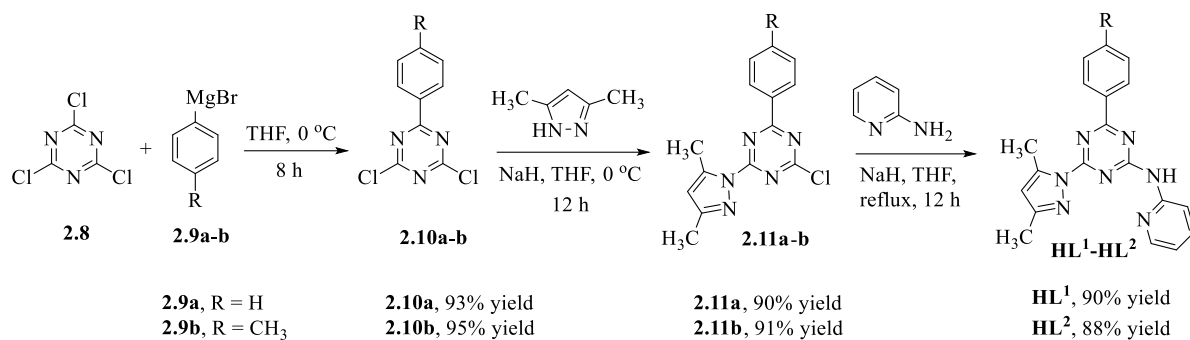


Scheme 2.4. Design of new triazine-based phosphine-free pincer ligand and their metal complexes in MLC

Chapter-2 discusses the synthesis and spectroscopic characterization of triazine-based NNN pincer ligands and their ruthenium complexes. The newly synthesized ruthenium complexes efficiency was examined in α -alkylation of simple aromatic ketones with secondary alcohols and their reaction pathway is also studied in detail.

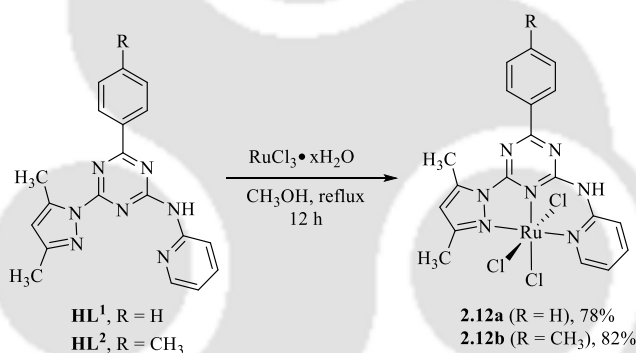
2.2.1. Synthesis and spectroscopic characterization of ligands and their corresponding Ru(III) complexes

The new triazine-based tridentate NNN-pincer ligands were synthesized in a multistep process as outlined in Scheme 2.5, using cyanuric chloride as a starting precursor. Cyanuric chloride **2.8** was transformed into the corresponding monoaryl dichloro s-triazine derivatives of **2.10a** and **2.10b** using the Grignard reaction by treating with arylmagnesium bromide at 0 °C in dry THF under argon atmosphere. To this, the deprotonated 3,5-dimethylpyrazole solution in THF was slowly added at low temperature to afford triazine containing 2-chloro disubstituted derivatives **2.11a** and **2.11b** as a white solid in good yield. Finally, the desired pincer ligands **HL**¹ and **HL**² were readily obtained in 88-90% yields by reacting **2.11a** and **2.11b** with 2-pyridylamine in the presence of NaH. These were characterized by HRMS, NMR, and IR spectroscopy (for details, see experimental section).



Scheme 2.5. Ligand synthesis

Complexation was performed by refluxing a solution of the NNN ligands **HL¹-HL²** and RuCl₃·xH₂O in methanol for 12 h afforded the corresponding pincer ruthenium (III) complexes as brown solids **2.12a** and **2.12b** respectively, in good yields. The complex **2.12b^{Me}** was synthesized in 95% yield by treating the complex **2.12b**, KO^tBu, methyl iodide, and toluene. Complexes **2.12a** and **2.12b** were characterized by HRMS, and IR spectroscopy. The positive ion HRMS analysis revealed molecular ion peak at $m/z = 514.9987$ (for **2.12a**), and 529.0157 (for **2.12b**) which are characteristic for corresponding cationic species of [M-Cl]⁺ (M = molecular ion). Simulations of the isotopic distribution for both fragments are included in Figure 2.1 and are matched well with their experimental spectrum. Infrared spectroscopy of the complexes showed broad absorption bands at 3408.00 (for **2.12a**) and 3475.40 cm⁻¹ (for **2.12b**), which can be assigned to the N-H stretch of the aminopyridyl moiety. The ruthenium (III) complexes **2.12a** and **2.12b** were paramagnetic, and their NMR analysis could not be successfully performed.



Scheme 2.6. Synthesis of ruthenium (III) complexes

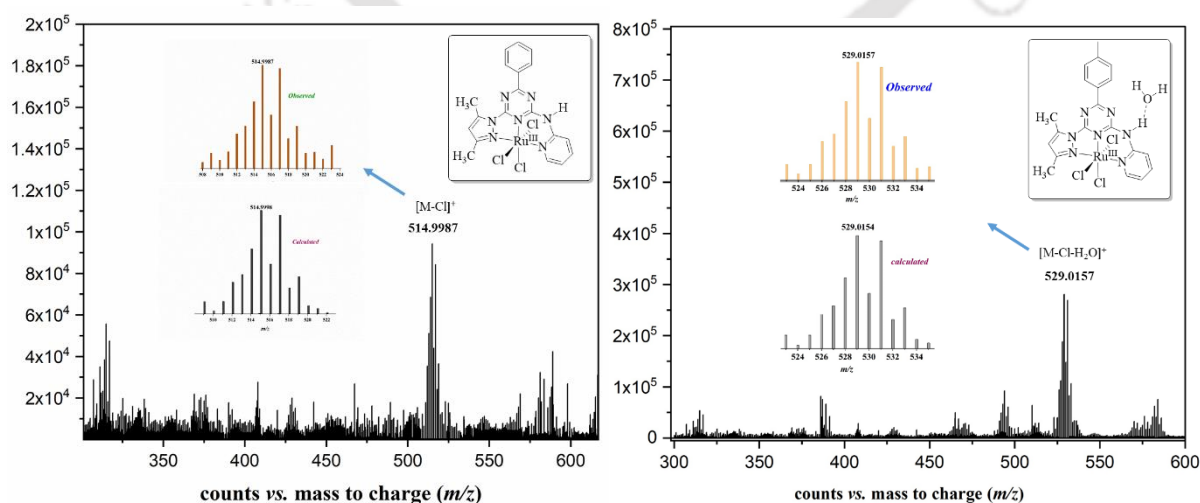


Figure 2.1. HRMS spectra of ruthenium (III) complexes

Among the ruthenium complexes, single crystals of complex **2.12b** suitable for X-ray diffraction was obtained by slow evaporation of the saturated solution of the complex in CH₃CN/CH₃OH (v/v 9/1) at room temperature. It crystallizes in the *P*2₁/*c* space group, and consists of one molecule of water and one acetonitrile molecule in the lattice (Figure 2.2). The water molecule is located in close

proximity to the N–H group of the ligand backbone, indicates a strong hydrogen bonding interaction (N–H...OH₂ 1.926 Å). The molecular structure of complex **2.12b** adopts an 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 **HL**² and other coordination sites are occupied by three chlorine atoms. The Ru–N bond length for the central triazine rings (N5) of the complex **2.12b** is shorter than those for the nitrogen atom of pyrazolyl and pyridyl rings (N1 and N3). The Cl(1)–Ru(1)–Cl(2), and N(5)–Ru(1)–Cl(3) in the ruthenium complex are 175.91(11)° and 173.81(8)° respectively, which indicates that chlorido ligands Cl(1) and Cl(2) are in *trans* position, and other chlorine atom Cl(3) is situated *trans* to the s-triazine nitrogen atom of the NNN coordinating units. The aryl and pincer-type NNN coordinating moiety is nearly coplanar, as shown by the respective torsional angles.

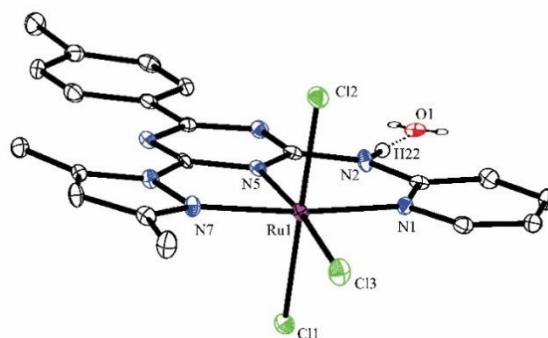


Figure 2.2. Molecular structure of **2.12b** (Thermal ellipsoids are drawn with 50% probability level). Selected bond lengths (in Å): Ru(1)–N(5) 2.015(3), Ru(1)–N(7) 2.071(3), Ru(1)–N(1) 2.091(3), Ru(1)–Cl(2) 2.3448(9), Ru(1)–Cl(1) 2.3603(9), Ru(1)–Cl(3) 2.3624(9) NH(22)...O(1) hydrogen bond 1.926. Selected bond angles: N(1)–Ru(1)–Cl(1) 89.66(7), N(1)–Ru(1)–N(7) 170.28(10), N(5)–Ru(1)–Cl(2) 90.88(8), N(7)–Ru(1)–Cl(3) 96.73(8), Cl(1)–Ru(1)–Cl(3) 90.31(3), Cl(1)–Ru(1)–Cl(2) 175.91(3).

2.2.2. Optimization studies

To inspect the catalytic applicability of the as-prepared ruthenium complex **2.12a** and **2.12b**, optimization studies was performed with 1-(4-methoxyphenyl)ethan-1-one **2.5c** (1 equiv.) and cyclohexanol **2.2a** (1.5 equiv.) as model substrates for the α -alkylation of ketone with secondary alcohol (Table 2.1).

Table 2.1. Optimization for α -alkylation of ketone using secondary alcohols^{a,b}

entry	catalyst	cat. (mol%)	base (mol%)	temp (°C)	yield (%)
1	2.12a	1	10	120	0
2	2.12b	1	10	120	0
3	2.12a	1	10	150	36
4	2.12b	1	10	150	50
5	2.12b	2	20	150	94
6 ^c	2.12b	2	20	150	85
7 ^d	2.12b	2	20	150	92
8 ^e	2.12b	2	30	150	n.d.
9	2.12b	2	–	150	n.d.
10	RuCl₃	2	20	150	n.d.
11	–	–	20	150	n.d.

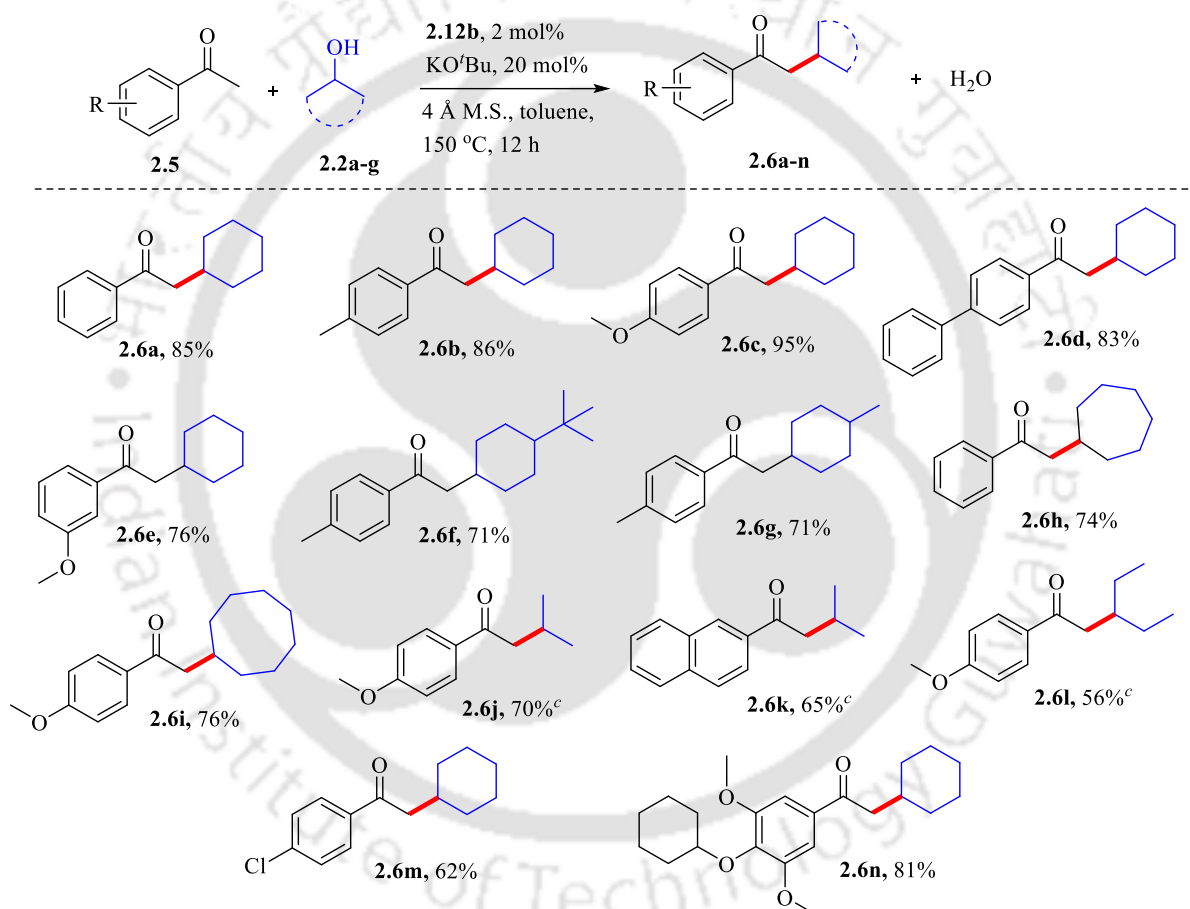
^aReaction conditions: 4-methoxyacetophenone (1 mmol), cyclohexanol (1.5 mmol), **Cat.** (x mol%), KO^tBu (x mol%), and dry toluene (2 mL) were heated under argon for 12 h in the presence of 4 Å M.S. ^bIsolated yields. ^c1 equiv. cyclohexanol was used. ^dwithout 4 Å M.S. ^eSelf-coupling product 1,3-bis(4-methoxyphenyl)butan-1-one was obtained in 40% yield.

The initial experiment was carried out with complex **2.12a** (1 mol%) or **2.12b** (1 mol%), KO^tBu (10 mol%), and 4 Å molecular sieves in toluene at 120 °C for 12 h. However, no desired product was

obtained (Table 2.1). Interestingly, when the temperature was increased from 120 °C to 150 °C, product **2.6c** was observed in 36% yield by **2.12a** and 50% yield by **2.12b**. Obtaining the higher yield for **2.12b** compared to **2.12a**, suggests that **2.12b** showed better activity compared to **2.12a**. The yield has been further improved upto 94% by increasing the catalyst loading from 1 mol% to 2 mol% and base loading from 10 mol% to 20 mol%. It was found that base loading was very crucial for outcome of the reaction. For instance, when the reaction was carried out with 30 mol% of base, only self-coupling product 1,3-bis(4-methoxyphenyl)butan-1-one was obtained in 40% yield. The reaction did not occur in the absence of base and catalyst. Based on the above observations, the optimized condition was therefore fixed to be **2.12b** (2 mol%), KO^tBu (20 mol%), 150°C, 12 h in toluene with 4 Å molecular sieves.

Encouraged by these results, at first, I focused on exploring the catalytic reaction of various aromatic ketones. As displayed in Table 2.2, a wide variety of aromatic ketones was used for the synthesis of β -disubstituted ketones.

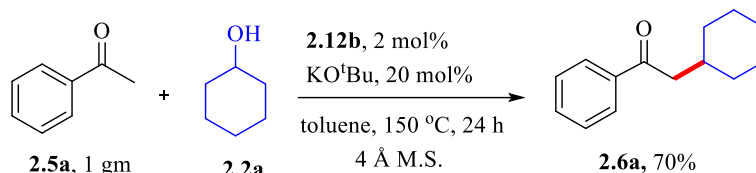
Table 2.2. Substrate scopes for the synthesis of β -disubstituted ketones^{a,b}



^aReaction conditions: Aromatic ketones (1 mmol), aliphatic secondary alcohols (1.5 mmol), **2.12b** (2 mol%), KO^tBu (20 mol%), and dry toluene (2 mL) were heated under argon for 12 h in the presence of 4 Å M.S. ^bIsolated yields. ^c8 equiv. aliphatic secondary alcohol was used.

An array of diverse functionalities such as 4-methyl, 4-methoxy, 4-phenyl on the acetophenone (**2.5a-d**) reacted effectively with cyclohexanol and were successfully transformed to desired β -disubstituted ketones **2.6a-d** in good to excellent yields (56-95%). Similarly, *meta*-substituted 3-methoxyacetophenone also provided to the corresponding β -branched ketone in high yield. Notably, the -Cl group on the benzene ring is compatible with the reaction conditions, giving the desired product **2.6m** efficiently. Polysubstituent aromatic ketone **2.5n** can also proceed to afford the desired compound **2.6n** in good yield. Notably, the substitution on cyclohexyl ring such as 4-*tert*-butyl cyclohexanol **2.5f** (or 4-methyl-butylcyclohexanol **2.5g**) gave a mixture of diastereomers with the diastereomeric ratio of 81:19 (or 70:30) as determined from ¹H NMR of the reaction mixture. The major isomer is 1,4-*cis* confirmation of cyclohexyl ring, which was consistent with reported literature. The result suggested that C-alkylation occurred in selective manner with substituted cyclohexanol.

Gratifyingly, the scope of the reaction methodology was expanded to a variety of other higher analog cyclic alcohols, for instance, cycloheptanol and cyclooctanol. Finally, the highly challenging unactivated acyclic aliphatic secondary alcohol was also amenable to this method to provide **2.6j-l**. To demonstrate the practical applicability of this process, gram-scale reaction was performed for the synthesis of **2.6a** as shown in Scheme 2.7. The compound **2.6a** was obtained in 70% yield using 1 g of acetophenone (**2.5a**) under the standard condition.



Scheme 2.7. Gram-scale reaction

2.2.3. Spectroscopic characterization for active catalyst I

To gain more insight 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 **2.12b**, and monitoring the EPR spectra. Upon loading the base, the paramagnetic signal of ruthenium(III) was slowly disappeared and formed EPR-silent diamagnetic Ru(II) species by using four equivalent of KO^tBu (Figure 2.3).

2.2.3.1. EPR study

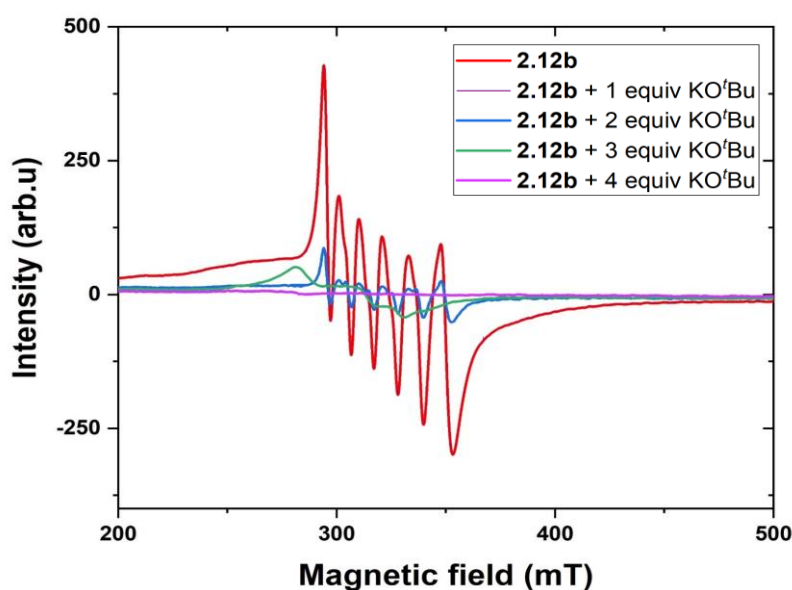


Figure 2.3. EPR spectrum of **2.12b** with varying equivalent of base. X-band microwave frequency(GHz): 9.14, modulation frequency(KHz): 100.

Experimental procedure: The reaction tube was equipped with a stir bar, complex **2.12b** (10 mg, 1 equiv), varying equivalent of KO^tBu (1 to 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 volatile was removed under reduced pressure. The obtained residue was then dissolved in CH₃OH (0.5 mL) and subjected for EPR analysis at 77 K. The EPR spectrum was silent by using four equivalent of KO^tBu.

It infers that 4 mol% of KO^tBu (compared to **2.12b**) is necessary for the activation of pre-catalyst. As the resulting active species (**I**) is diamagnetic, the NMR analysis was executed in CD₃OD (see Figure 2.4). For further clarity, the experiment has been performed in the presence of PPh₃. A singlet at 28.5 ppm was observed in ³¹P {¹H} NMR, indicating the phosphine ligand is coordinated to the ruthenium (II) center (see Figure 2.5). Besides, species **I** was also confirmed by the mass spectrometry analysis (see Figure 2.6). Based on these experimental evidence, it can reasonably conclude that an *in-situ* generated ruthenium (II) species is the active species in this catalytic cycle. The resulting complex **I** can react with cyclohexanol to provide reactive ruthenium hydride species **II**. Despite several attempts, it failed to isolate ruthenium hydride species under the reaction conditions.

2.2.3.2. ^1H NMR spectrum

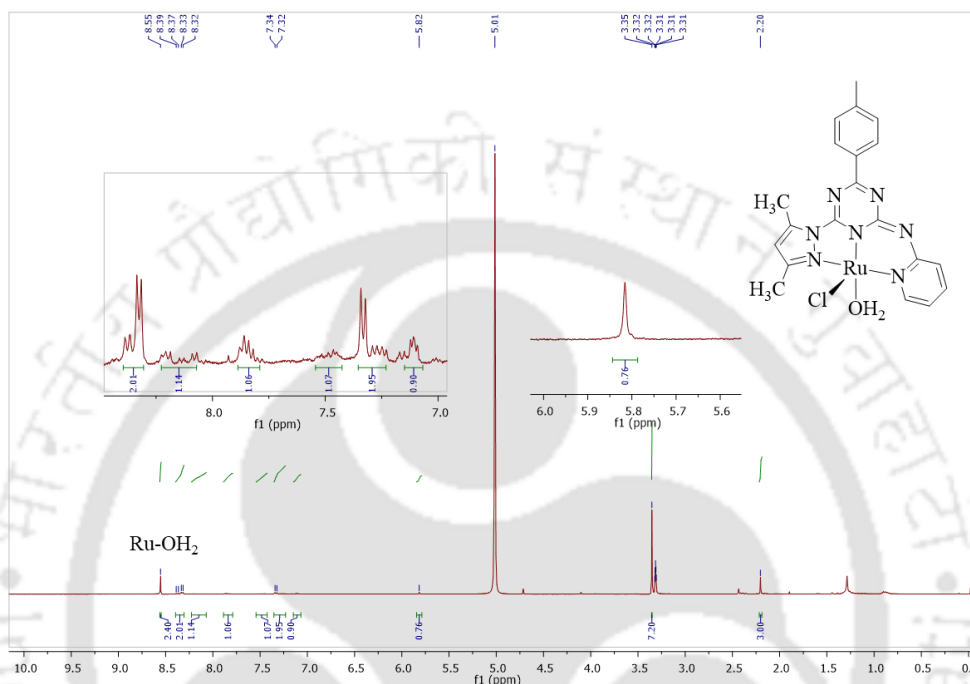
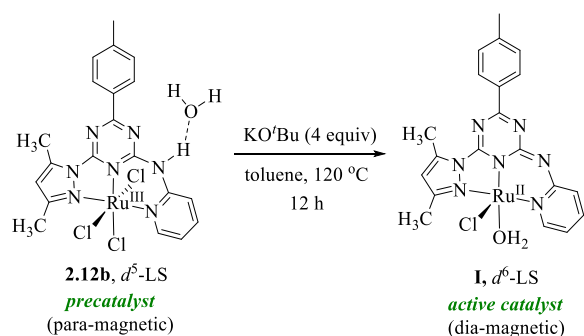


Figure 2.4. ^1H NMR spectrum of active species **I** (CD_3OD , 400 MHz, 298 K)

Experimental procedure: The reaction tube was equipped with a stir bar, complex **2.12b** (30 mg, 0.05 mmol, 1 equiv.) KOtBu (4 equiv.), and toluene (1.5 mL). The reaction mixture was stirred at 120 °C for 12 h. The resulting solution was then cooled to room temperature; all the volatile was removed under reduced pressure. The obtained residue was dissolved in methanol- d_4 and subjected for NMR analysis at room temperature.

2.2.3.3. In-situ reduction of the **2.12b** in the presence of PPh_3

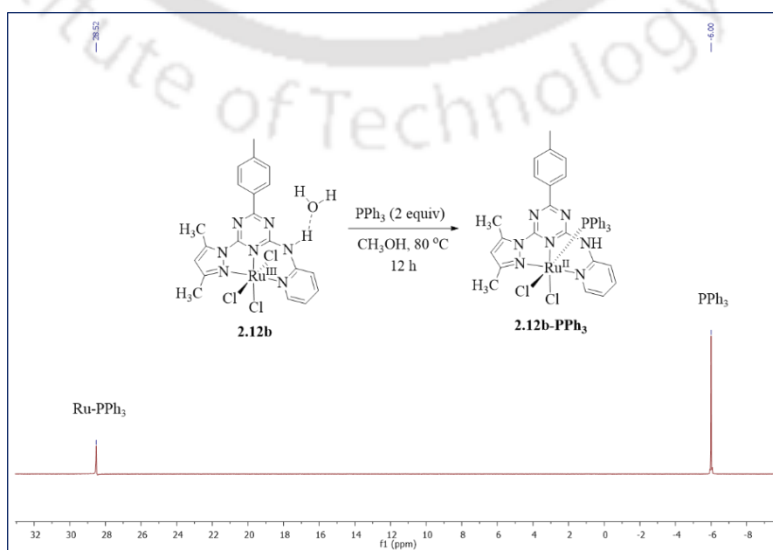


Figure 2.5. $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum of **2.12b-PPh₃** (CDCl_3 , 400 MHz, 298 K)

Experimental procedure: The round bottom flask was equipped with a stir bar, complex **2.12b** (30 mg, 0.05 mmol, 1 equiv.), PPh_3 (2 equiv.), and methanol (2 mL). The reaction mixture was then heated at 80 °C for 12 h with continuous

stirring. All the volatile was removed under reduced pressure and the resulting brown solid was dissolved in chloroform-*d* and subjected for $^{31}\text{P}\{^1\text{H}\}$ NMR at room temperature.

2.2.3.4. HRMS spectrum for complex I

The above brown residue was dissolved in equimolar ratio of acetonitrile and water, and then analyze the ESI-HRMS. The spectral data for compound **I** is given in Figure 2.6.

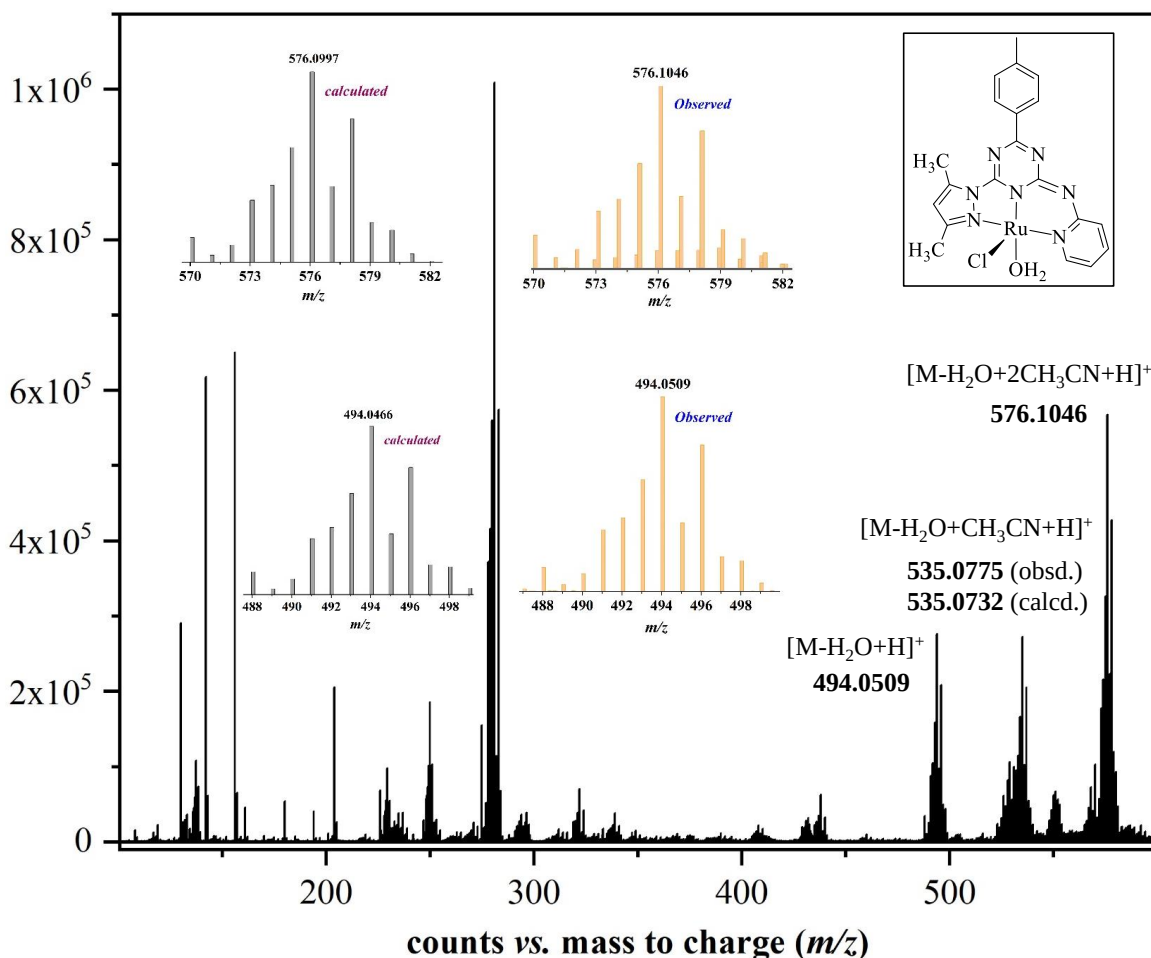
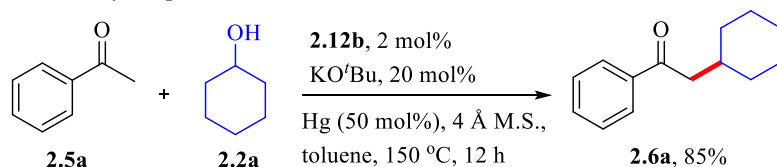


Figure 2.6. HRMS (ESI) spectra of complex **I**

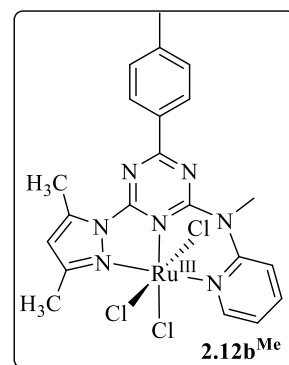
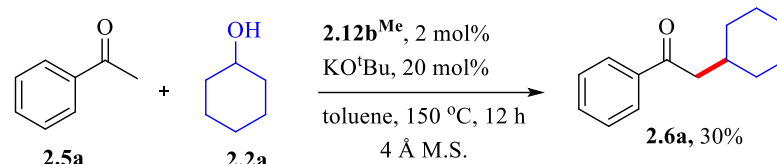
2.2.4. Mechanistic studies

To validate the homogenous catalytic system for this *C*-alkylation, the mercury drop test was conducted, showing no inhibition of the reaction or reduction of the product yield (Scheme 2.8a). The effect of the NH functionality was examined by using complex **2.12b^{Me}** as the pre-catalyst, leading to lower yields of **2.6a**, indicating the importance of the NH functionality through metal-ligand cooperative (MLC) pathway (Scheme 2.8b). Next, in the presence of KO^tBu , the base mediated cross-aldol condensation of acetophenone with cyclohexanone afforded α,β -unsaturated enone **2.6a-I**, suggesting the *in-situ* form cyclohexanone as the intermediates. The reaction of **2.6a-I** with cyclohexanol under optimized condition afforded desired ketone **2.6a** in good yield. Similar results were also observed with molecular H_2 in its place of alcohol (Scheme 2.8c). These data suggest that α,β -unsaturated ketone **2.6a-I** is the reaction intermediate and the reaction is likely proceeded *via* ruthenium hydride species, either derived from dehydrogenation of alcohol or from produced molecular H_2 . Furthermore, deuterium-labelling experiment was performed in *C*-alkylation reactions to validate the involvement of hydrogen-borrowing methodology. Under the standard condition, the reaction of **2.5c** with **2.2a-D** yielded expected H/D scrambled product **2.6c-D** in 73% yields (Scheme 2.8d). The above results demonstrated the reaction proceeded *via* hydrogen-borrowing pathway.

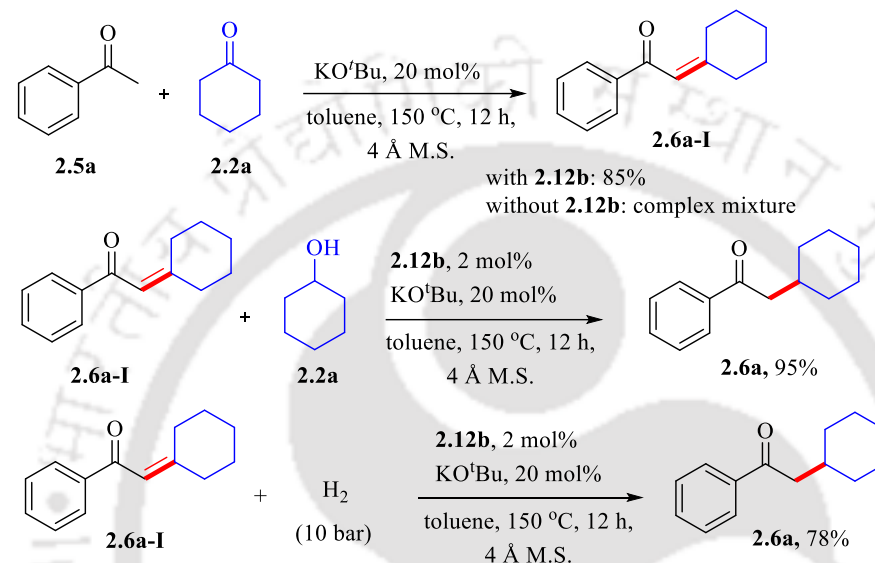
(a) Mercury drop test



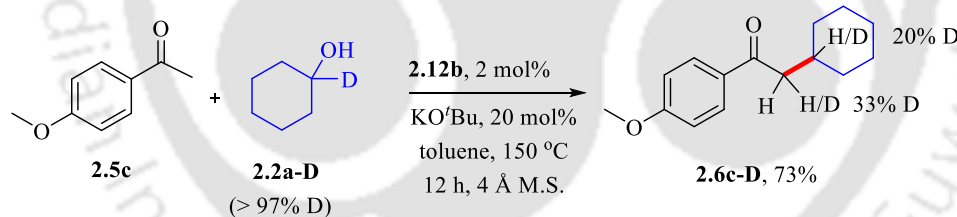
(b) The effect of the NH functionality in ruthenium complex



(c) Proof for the formation of intermediates cyclohexanone or α,β -unsaturated ketone

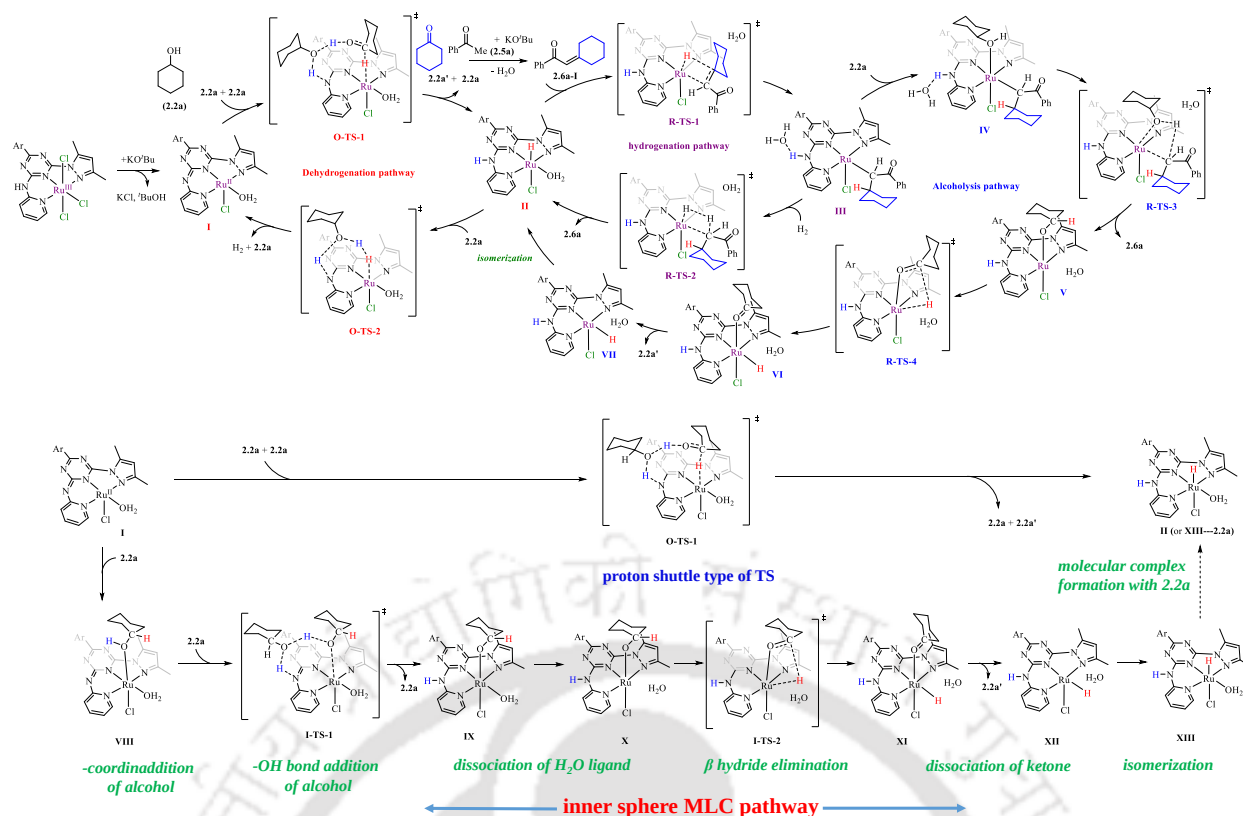


(d) Deuterium labelling experiment



Scheme 2.8. Mechanistic studies

On the basis of previous reports,^{45, 57-62} our observations, and DFT calculations, a plausible mechanistic pathway has been proposed and is presented in Scheme 2.9. Acetophenone **2.5a** and cyclohexanol **2.2a** were used as the model substrates for this transformation. All calculations were performed using the Gaussian-09 program package in the gas phase. All calculations were performed at M06-L level of theory (please see the experimental section for details). The calculated free energy result and some important optimized structures are shown in Table 2.4. The precatalyst **2.12b** is initially reduced *in situ* to form the Ru(II) species under the reaction conditions. The resultant active species **I** is then reacted with alcohol **2.2a** converted into ruthenium-hydride intermediate **II** in a downhill process ($\Delta G = -22.7$ kcal/mol) *via* outer sphere MLC pathway and proton shuttle type of TS (**O-TS-1**) with a low energy barrier $\Delta G^\ddagger = 9.7$ kcal/mol (Figure 2.8).



Scheme 2.9. Proposed mechanism

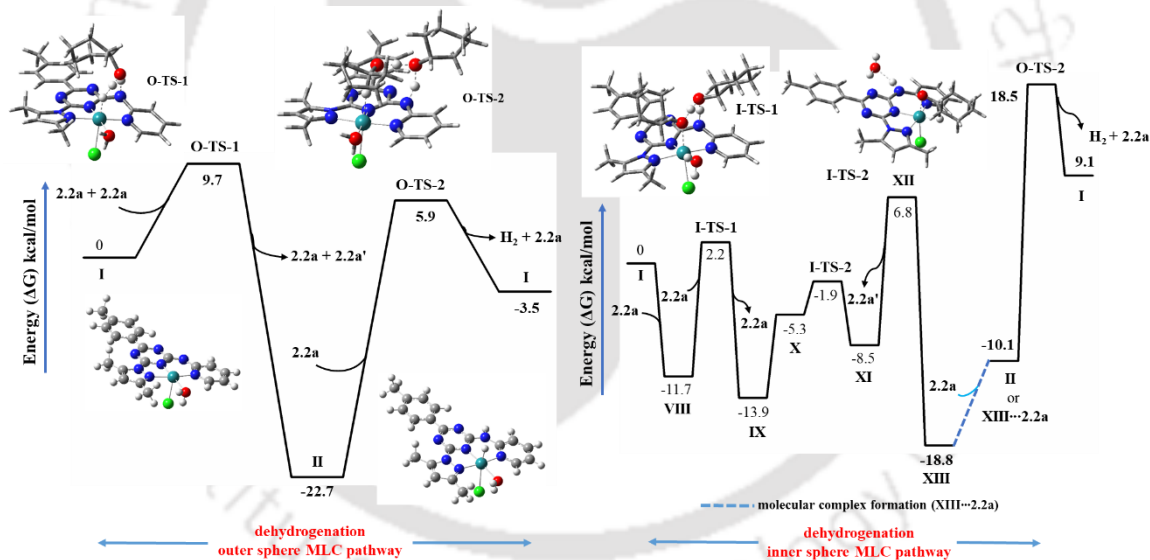


Figure 2.8. Dehydrogenation of alcohol via outer sphere and inner sphere MLC pathway

Complex **II** can also form via multiple-step involving inner sphere MLC pathway. In the first step, the complex **I** converted into aromatized intermediate **IX** by the $-\text{OH}$ bond addition of alcohol in a downhill process (**I-TS-1** $\rightarrow$ **IX**, $\Delta G = -16.1$ kcal/mol) through the proton shuttle type of mechanism. Then β -hydride elimination takes place and gives ketone coordinated intermediate **XI** in uphill way (**IX** $\rightarrow$ **XI**, $\Delta G = 5.4$ kcal/mol). The energy barrier acquired for this step is $\Delta G^\ddagger = 15.8$ kcal/mol which is comparable (**XI** $\rightarrow$ **XII**; $\Delta G = 15.3$ kcal/mol) to release corresponding ketone **2.2a'** from **XI**. Subsequent isomerization can give to the complex **II** in a downhill process of 25.6 kcal/mol (**XII** $\rightarrow$ **XIII**).

Additionally, nucleus independent chemical shift index (NICS) calculation was performed to evaluate the change in the aromaticity during **I** $\rightarrow$ **II** or vice versa (Scheme 2.10). The higher positive NICS(0) value for triazine ring in **I** compared to **II** suggests that complex **I** is anti-aromatized species and complex **II** is aromatized species.

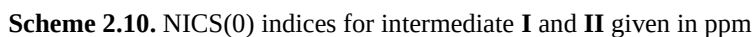


Figure 1 displays the energy profiles for the hydrogenation and alcoholysis pathways. The y-axis represents Energy (ΔG) in kcal/mol.

Hydrogenation Pathway (Left):

- Reaction: $\text{III} \rightarrow \text{II}$
- Transition States: R-TS-1, R-TS-2
- Intermediates: II, III
- Energy values (kcal/mol): II (0), 2.6a-I (2.6), R-TS-1 (3.3), III (2.4), R-TS-2 (12.7), R-TS-3 (18.2), II (-14.5)
- Molecular complex formation (III...H₂) is indicated by a dashed blue line.

Alcoholysis Pathway (Right):

- Reaction: $\text{II} \rightarrow \text{VII}$
- Transition States: R-TS-1, R-TS-3, R-TS-4, R-TS-5
- Intermediates: II, III, IV, V, VI, VII
- Energy values (kcal/mol): II (0), 2.6a-I (2.6), R-TS-1 (3.3), III (2.4), R-TS-2 (12.7), R-TS-3 (23.8), IV (32.5), R-TS-4 (-11.6), V (-8.2), VI (-14.8), VII (0.5), R-TS-5 (-28.4)
- Molecular complex formation (III...2.2a) is indicated by a dashed blue line.

Figure 2.9. Energy profile for hydrogenation pathway (left) and alcoholysis pathway (right)

The alternative alcoholysis of **III** involves co-ordination of **2.2a** to the ruthenium center to give **IV** via molecular complex (**III**...**2.2a**) (Figure 2.9, right). This process is an endothermic (**III**...**2.2a** $\rightarrow$ **IV**, $\Delta G = 11.1$ kcal/mol), followed by σ -bond metathesis of Ru-C with the O-H of **2.2a** in **IV**, giving product **2.6a** and intermediate **V**. It affords an energy barrier **R-TS-3**, $\Delta G^\ddagger = 8.7$ kcal/mol. Complex **V** undergoes β -hydride elimination, the liberation of ketone, and isomerization to regenerate intermediate **II**. The process (**V** $\rightarrow$ **II**) is thermodynamically downhill ($\Delta G = -16.8$ kcal/mol). These observations open up the possibility of both the alcoholysis and hydrogenation pathways giving rise to the formation product **2.6a**.

Lastly, the Ru-H and N-H cooperation involving the metal hydride intermediate **II** and the –OH group of the alcohol to yield H₂ regenerates active catalyst **I** *via* the transition state **O-TS-2** with energy barrier $\Delta G^\ddagger = 28.6$ kcal/mol (Figure 2.8).

2.2.5. Summary

In summary, I have demonstrated the use of a phosphine-free, bench-stable, and well-defined ruthenium(III) pincer catalyst for the α -alkylation of ketones with secondary alcohols to form β -branched ketones. Contrary to previously reported procedures, this method explored the utility of unhindered acetophenone compounds with a variety of secondary alcohols, which are used as alkylating agents. The preliminary mechanistic studies indicated the involvement of “borrowing

hydrogen'' catalysis and the role of the metal-ligand cooperation was found to be important for the success of such catalytic reaction. This convenient method produces only water as the only byproduct, making it highly atom-economical and environmentally benign.

2.3. 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. 1-([1,1'-biphenyl]-4-yl)ethan-1-one was prepared according to the reported literature.⁶³ THF and toluene were freshly distilled over sodium–benzophenone before use. ¹H, ¹³C, and ¹⁹F NMR spectra of the compounds were measured in CDCl₃, DMSO-*d*₆, CD₃OD as a solvent by using TMS as an internal standard. Chemical shifts, δ (in ppm), are reported relative to TMS δ (¹H) 0.0 ppm, δ (¹³C) 0.0 ppm, which was used as the internal reference. Otherwise the solvents residual proton resonance and carbon resonance (CHCl₃, δ (¹H) 7.26 ppm, δ (¹³C) 77.16 ppm; DMSO-*d*₆, (¹H) 2.50 ppm, δ (¹³C) 39.52 ppm; CD₃OD, δ (¹H) 3.31 ppm, δ (¹³C) 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 μ L, 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). 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 °C for 6 hours following which it was transferred and stored in a schlenk flask inside a dessicator.

A. Synthesis of ligands, and ruthenium complexes

i) Synthesis of HL¹ and HL²

Synthesis of 2.10a:⁶⁴⁻⁶⁶

Magnesium turnings (1.318 g, 54.22 mmol, 1.5 equiv.) along with catalytic amount of iodine (0.043 g, 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 °C for 15 minutes to activate the metal surface. An intense iodine color was observed. This mixture was brought to room temperature and 4-bromo benzene (3.747 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 °C using cannula technique. The resulting mixture was stirred at 0 °C for 8 hours. The reaction was quenched with 2N hydrochloric acid (20 mL) solution followed by dilution with water (50 mL). The product was then extracted in ethyl acetate (3×40 mL). The combined organic layer was dried over Na₂SO₄ and solvent was removed under reduced pressure to give light brown 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 **2.10a** (4.6 g, 93%). This was directly used for subsequent

reactions. ^1H NMR (600 MHz, CDCl_3): δ 8.52–8.51 (m, 2H), 7.66 (t, J = 7.4 Hz, 1H), 7.54 (t, J = 7.8 Hz, 2H). ^{13}C NMR (101 MHz, CDCl_3): δ 175.0, 172.2, 134.8, 132.8, 130.0, 129.2. HRMS (ESI) m/z : $[\text{M}+\text{H}]^+$ calculated for $\text{C}_9\text{H}_6\text{Cl}_2\text{N}_3$ 225.9933; observed: 225.9976.

Synthesis of **2.10b**:⁶⁴⁻⁶⁶

Compound **2.10b** (4.95 g, 95%) was obtained in a similar method described above for **2.10a**, using 4-bromotoluene instead of 4-bromobenzene. This was directly used for next reactions. ^1H NMR (400 MHz, CDCl_3): δ 8.39 (d, J = 8.3 Hz, 2H), 7.33 (d, J = 8.1 Hz, 2H), 2.46 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3): δ 174.9, 172.0, 146.2, 130.1, 130.1, 130.0, 22.0. HRMS (ESI) m/z : $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{10}\text{H}_8\text{Cl}_2\text{N}_3$ 240.0089; observed: 240.0087.

Synthesis of **2.11a**:

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 **2.10a** (1.19 g, 5.26 mmol, 1 equiv) in THF (20 mL) at 0 °C. After complete addition it was left to stir at 0 °C 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 $\times$ 20 mL. Solvent was removed under reduced pressure to give white powder of **2.11a** (1.36 g, 90%). It was used for next step without further purification. ^1H NMR (400 MHz, CDCl_3): δ 8.52 (d, J = 7.2 Hz, 2H, ArH), 7.64 (t, J = 7.4 Hz, 1H, ArH), 7.54 (t, J = 7.6 Hz, 2H, ArH), 6.15 (s, 1H, 4- H_{pz}), 2.84 (s, 3H, CH_3), 2.37 (s, 3H, CH_3). ^{13}C NMR (101 MHz, CDCl_3): δ 174.4, 172.8, 163.7, 154.6, 144.9, 134.1, 134.1, 129.7, 129.0, 112.9, 16.5 (CH_3), 14.2 (CH_3). HRMS (ESI) m/z : $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{14}\text{H}_{13}\text{ClN}_5$ 286.0854; found: 286.0856. IR (KBr pellet) cm^{-1} : 1585.82 (m), 1544.12 (s), 1512.70 (s), 1453.01 (s), 1378.92 (s), 1250.49 (s).

Synthesis of **2.11b**:

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 **2.10b** (1.26 g, 5.26 mmol, 1 equiv) in THF (20 mL) at 0 °C. After complete addition it was left to stir at 0 °C 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 $\times$ 20 mL. Solvent was removed under reduced pressure to give white powder of **2.11b** (1.43 g, 91%). It was used for next step without further purification. ^1H NMR (400 MHz, CDCl_3): δ 8.40 (d, J = 8.2 Hz, 2H, ArH), 7.33 (d, J = 8.0 Hz, 2H, ArH), 6.14 (s, 1H, 4- H_{pz}), 2.83 (s, 3H, CH_3), 2.46 (s, 3H, Ar CH_3), 2.37 (s, 3H, CH_3). ^{13}C NMR (101 MHz, CDCl_3): δ 174.4, 172.6, 163.6, 154.4, 145.2, 144.9, 131.4, 129.8, 129.7, 112.9, 21.9 (Ar CH_3), 16.5 (CH_3), 14.2 (CH_3). HRMS (ESI) m/z : $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{15}\text{H}_{15}\text{ClN}_5$ 300.1010; found: 300.1015. IR (KBr pellet, selected bands) cm^{-1} : 2925.42 (w), 1610.66 (m), 1590.54 (s), 1548.56 (s), 1515.51 (s), 1504 (s), 1455.22 (s), 1431.13 (s), 1391.19 (s), 1379.14 (s), 1366.05 (s), 1327.94 (s), 1249.90 (s), 1180.73 (s), 1089.87 (s).

Synthesis of **HL**¹:

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 **2.11a** (1.22 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 with ethyl acetate (3 × 20 mL). Solvent was removed under reduced pressure to give pale yellow powder of **HL**¹ (1.20 g, 90%). ¹H NMR (400 MHz, CDCl₃): δ 8.61 (d, *J* = 8.4 Hz, 1H, ArH), 8.54 (brs, 1H, NH), 8.51 – 8.49 (m, 2H, ArH), 8.42 (d, *J* = 4.0 Hz, 1H, ArH), 7.85 – 7.81 (m, 1H, ArH), 7.62-7.53 (m, 4H), 7.06 (dd, *J* = 6.8, 5.1 Hz, 1H, ArH), 6.11 (s, 1H, 4-H_{pz}), 2.86 (s, 3H, CH₃), 2.38 (s, 3H, CH₃). ¹³C NMR (101 MHz, CDCl₃): δ 173.1, 164.9, 163.73, 152.9, 151.8, 148.5, 144.4, 138.2, 135.9, 132.9, 129.1, 128.8, 119.2, 114.4, 111.8, 16.5 (CH₃), 14.2 (CH₃). HRMS (ESI) *m/z*: [M+H]⁺ calculated for C₁₉H₁₈N₇ 344.1618; found: 344.1612.

Synthesis of **HL**²:

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 **2.11b** (1.279 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 with ethyl acetate (3 × 20 mL). Solvent was removed under reduced pressure to give pale yellow powder of **HL**² (1.34 g, 88%). ¹H NMR (400 MHz, CDCl₃) δ 8.60 (d, *J* = 8.4 Hz, 1H, ArH), 8.40-8.38 (m, 4H, ArH), 7.86 – 7.78 (m, 1H, ArH), 7.34 (d, *J* = 8.0 Hz, 2H, ArH), 7.05 (dd, *J* = 6.6, 5.0 Hz, 1H, ArH), 6.11 (s, 1H, 4-H_{pz}), 2.85 (s, 3H, CH₃), 2.47 (s, 3H, ArCH₃), 2.38 (s, 3H, CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 173.1, 164.9, 163.7, 152.9, 151.8, 148.5, 144.4, 143.6, 138.2, 133.2, 129.6, 129.2, 119.1, 114.3, 111.7, 21.9 (ArCH₃), 16.5 (CH₃), 14.2 (CH₃). HRMS (ESI) *m/z*: [M+H]⁺ calculated for C₂₀H₂₀N₇ 358.1774; found: 358.1773.

ii) Synthesis of ruthenium complexes

Synthesis of **2.12a**:

A mixture of RuCl₃•xH₂O (0.368 g, 1.45 mmol, 1 equiv) and **HL**¹ (0.50 g, 1.45 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 (0.429 g, 78%). The complex was stable in air and moisture. HRMS (ESI) *m/z*: [M–Cl]⁺ calculated for C₁₉H₁₇Cl₂N₇Ru 514.9998; found: 514.9987.

Synthesis of **2.12b**:

A mixture of RuCl₃•xH₂O (0.366 g, 1.4 mmol, 1 equiv) and **HL**² (0.50 g, 1.4 mmol, 1 equiv) was taken in a round bottom flask equipped with stirring bar. Methanol (5mL) was added to the mixture and refluxed for 12 hours with continuous stirring. It was then cooled to ambient temperature and the resulting mixture was filtered to afford a brown solution. Solvent was removed in vacuum to afford dark brown solid. Recrystallization in acetonitrile/methanol (v/v = 5:1) gave **2.12b** as dark red crystals (0.644 g, 82%). The complex was stable in air and moisture. HRMS (ESI) *m/z*: [M–Cl]⁺ calculated for C₂₀H₁₉Cl₂N₇Ru 529.0154; found: 529.0157.

Synthesis of **2.12b**^{Me}:

A mixture of **2.12b** (0.050 g, 0.089 mmol, 1 equiv), KO^tBu (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 °C. Volatile component was removed in vacuum to provide

dark brown solid of **2.12b^{Me}** (0.048 g, 95%). The complex was stable in air and moisture. HRMS (ESI) m/z : $[M-Cl+H_2O]^+$ calculated for $C_{21}H_{23}Cl_2N_7ORu$ 561.0385; found: 561.0398.

B. General procedure for synthesis of β -disubstituted ketones:

A mixture of aromatic ketone (1 mmol, 1 equiv.), aliphatic secondary alcohol (1.5 mmol, 1.5 equiv.), **2.12b** (2 mol%), KO^tBu (20 mol%), 4 Å M.S., and 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 °C 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. The crude reaction mixture was purified by column chromatography over silica gel using petroleum ether or ethyl acetate/ petroleum ether mixture as an eluent.

C. Experimental procedure for gram-scale reactions of **2.6a**:

A mixture of **2.5a** (1 gm, 6.6 mmol, 1 equiv), **2.2a** (9.9 mmol, 1.5 equiv), **2.12b** (2 mol%), KO^tBu (20 mol%), 4 Å M.S., and toluene (16 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 °C with continuous stirring for 24 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 1.17 g (70% yield).

D. Mechanistic studies

i) Mercury drop test

In this test, the reaction tube was charged with 1 mmol (120 mg) of **2.5a**, 1.5 mmol (150 mg) of **2.2a**, 0.5 mmol (100 mg) of mercury, 20 mol% of KO^tBu (22 mg), 4 Å M.S., and 2 mol% of complex **2.12b** (12 mg). To this reaction mixture, 2 mL of toluene was added and heated at 150 °C for 12 h. The product **2.6a** was obtained in 85% of yield, demonstrated the homogenous behavior of the catalytic process.

ii) The influence of the NH functionality in catalysis

A mixture of **2.5a** (1 mmol, 1 equiv), **2.2a** (1 mmol, 1 equiv), **2.12b^{Me}** (2 mol%), KO^tBu (20 mol%), 4 Å M.S., and 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 °C 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. The crude reaction mixture was purified by column chromatography over silica gel using petroleum ether or ethyl acetate / petroleum ether mixture as an eluent (30% yield).

iii) Cross-coupling reactions of two ketones

A mixture of **2.5a** (120 mg, 1 mmol, 1 equiv.), **2.2a** (98 mg, 1 mmol, 1 equiv.), KO^tBu (22 mg, 0.2 mmol, 0.2 equiv.), complex **2.12b** (12 mg, 0.02 mmol, 0.02 equiv.), 4 Å M.S., and toluene (1.5 mL) was loaded into the reaction tube and heated at 150 °C for 12 h. The product **2.6a-I** was isolated as colorless liquid in 85% yield. In absence of **2.12b**, complex mixture was observed.

iv) Reaction of α , β -unsaturated ketone with cyclohexanol in the presence of catalyst

A mixture of **2.6a-I** (100 mg, 0.5 mmol, 1 equiv.), **2.2a** (49 mg, 0.5 mmol, 1 equiv.), KO^tBu (11 mg, 0.1 mmol, 0.2 equiv), complex **2.12b** (6 mg, 0.01 mmol, 0.02 equiv.), 4 Å M.S., and toluene (1 mL) was loaded into the reaction tube and heated at 150 °C for 12 h. The product **2.6a** was isolated as colourless liquid in 95% yield.

v) Reaction of α , β -unsaturated ketone with hydrogen in presence of catalyst

A mixture of **2.6a-I** (1 mmol), catalyst **2.12b** (2 mol%), KO^tBu (20 mol%), molecular hydrogen (10 bar), 4 Å M.S., and toluene (1 mL) was loaded in autoclave and heated at 150 °C for 12 h with stirring. Then, autoclave was brought at room temperature. The remaining gas was carefully released and benzene was used as an internal standard and the reaction mixture was analyzed by gas chromatography to get the desired product **2.6a** (78%).

vi) Deuterium labelling experiment

A reaction tube (25 mL) was equipped with a stir bar, catalyst **2.12b** (0.02 mmol), KO^tBu (0.2 mmol), acetophenone **2.5a** (1 mmol, 1equiv.), deuterated cyclohexanol **2.2a-D** (1.5 mmol, 1.5 equiv.), 4 Å M.S., and toluene (1.5 mL). The flask was closed and the solution was stirred at 150 °C (oil bath temperature) for 12 h. The completion of the reaction was monitored using TLC analysis. After cooling to room temperature, solution was filtered and the solvent was evaporated and crude reaction mixture was purified by column chromatography over silica-gel (60-120 mesh) using ethyl acetate / petroleum ether (v/v = 1: 50, R_f = 0.5) mixture as an eluent. Pure product was isolated as colorless oil in 73% (169 mg) of yield (Figure 2.10).

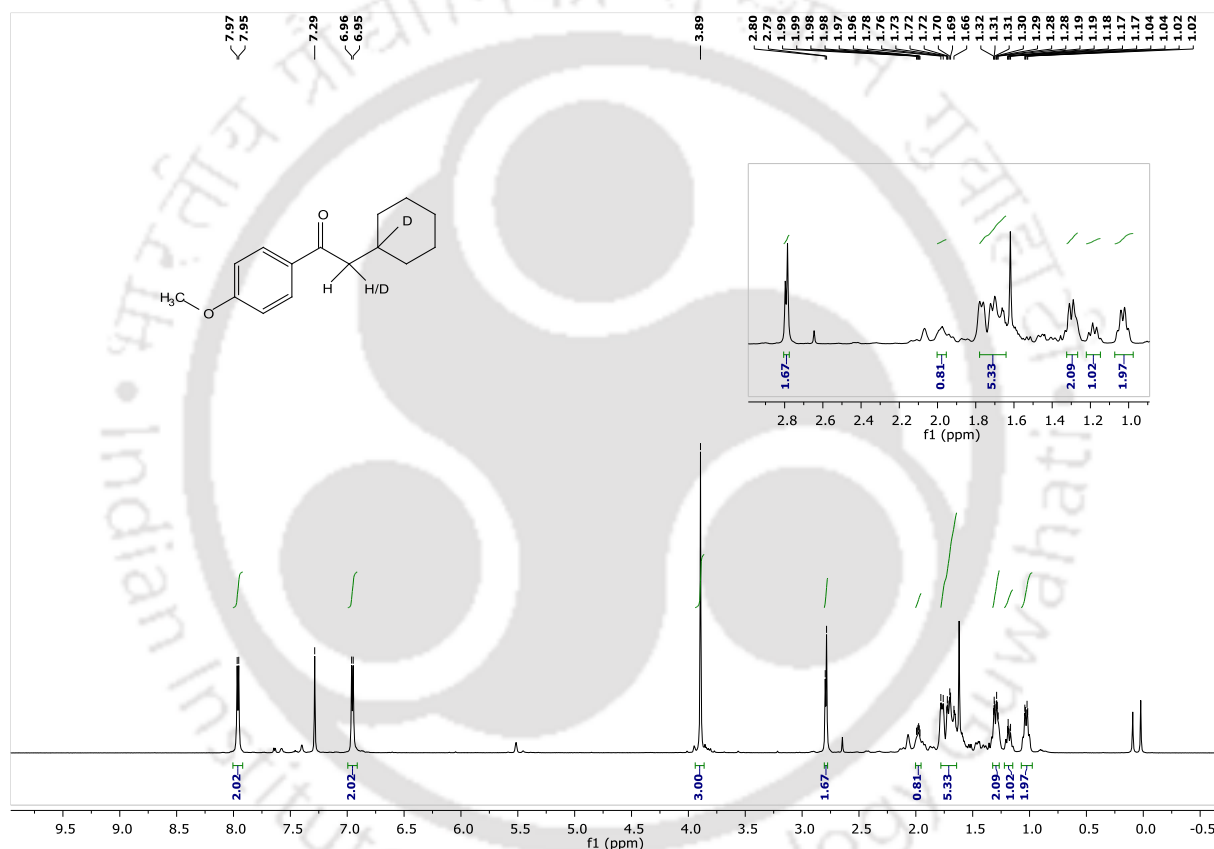


Figure 2.10. Deuterium-labelling experiment for α -alkylation of ketones using secondary alcohol

E. Crystallographic data

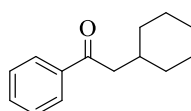
Single crystals of complex **2.12b** suitable for X-ray diffraction were obtained by slow evaporation of the saturated solution of the complex in CH₃CN/CH₃OH (v/v 9/1) at room temperature using slow evaporation technique. X-ray crystallographic data were collected using Supernova, single source at offset, 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 crystallographic parameters and refinement data were listed in Table 2.3.

Table 2.3. Crystal data and structure refinement for **2.12b**

Identification code	DB-366
CCDC:	2047904
Empirical formula	C ₂₂ H ₂₄ C ₁₃ N ₈ ORu
Formula weight	623.91
Temperature	77 K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	<i>P</i> 2 ₁ / <i>c</i>
Unit cell dimensions	<i>a</i> = 13.7170(5) Å α = 90° <i>b</i> = 11.7346(3) Å β = 102.131(3)° <i>c</i> = 15.8302(4) Å γ = 90°
Volume	2491.18(13) Å ³
Z	4
Density (calculated)	1.664 mg/m ³
Absorption coefficient	0.984 mm ⁻¹
F(000)	1260
Crystal size	0.34 x 0.31 x 0.27 mm ³
Theta range for data collection	2.31 to 25.00°
Index ranges	-16 ≤ <i>h</i> ≤ 8, -13 ≤ <i>k</i> ≤ 13, -18 ≤ <i>l</i> ≤ 18
Reflections collected	9313
Independent reflections	4383 [R(int) = 0.0354]
Completeness to theta = 25.00°	100.0 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.767 and 0.723
Refinement method	Full-matrix least-squares on F ²
Data / restraints / parameters	4383 / 0 / 332
Goodness-of-fit on F ²	1.038
Final R indices [I > 2σ(I)]	R ₁ = 0.0343, wR ₂ = 0.0762
R indices (all data)	R ₁ = 0.0474, wR ₂ = 0.0813
Largest diff. peak and hole	0.554 and -0.385 e.Å ⁻³

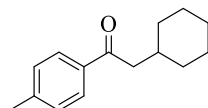
2.4. Analytical data of the products

2-cyclohexyl-1-phenylethanone (2.6a)⁶¹



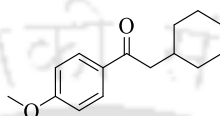
Following the general procedure, the title compound **2.6a** was isolated as colourless oil using silica gel column chromatography with pet-ether (*R_f* = 0.5); 81% yield (0.163 g). ¹H NMR (400 MHz, CDCl₃): δ 7.95 (d, *J* = 7.2 Hz, 2H, ArH), 7.55 (t, *J* = 7.4 Hz, 1H, ArH), 7.46 (t, *J* = 7.6 Hz, 2H, ArH), 2.82 (d, *J* = 6.8 Hz, 2H, COCH₂), 2.02-1.96 (m, 1H), 1.77 – 1.64 (m, 5H), 1.34-1.24 (m, 2H), 1.18-1.14 (m, 1H), 1.06 – 0.97 (m, 2H). ¹³C NMR (101 MHz, CDCl₃): δ 200.5 (C=O), 137.7, 132.98, 128.7, 128.3, 46.4 (COCH₂), 34.7, 33.6, 26.4, 26.3.

2-cyclohexyl-1-(*p*-tolyl)ethanone (2.6b)⁶¹



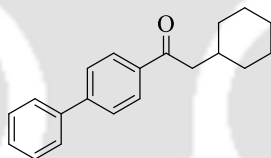
Following the general procedure, the title compound **2.6b** was isolated as colourless liquid using silica gel column chromatography with petroleum ether and ethyl acetate (v/v = 90:1, R_f = 0.5); 85% yield (0.183 g). ^1H NMR (400 MHz, CDCl_3): δ 7.78 (d, J = 8.0 Hz, 2H, ArH), 7.18 (d, J = 8.8 Hz, 2H, ArH), 2.72 (d, J = 6.8 Hz, 2H, COCH_2), 2.33 (s, 3H, CH_3), 1.93 – 1.84 (m, 1H), 1.69 – 1.60 (m, 5H), 1.24 – 1.16 (m, 2H), 1.13-1.07 (m, 1H), 0.98-0.89 (m, 2H). ^{13}C NMR (101 MHz, CDCl_3): δ 200.2 (C=O), 143.7, 135.2, 129.3, 128.4, 46.3 (COCH_2), 34.8, 33.6, 26.4, 26.3, 21.7.

2-cyclohexyl-1-(4-methoxyphenyl)ethanone (2.6c)⁶¹



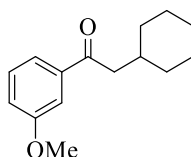
Following the general procedure, the title compound **2.6c** was isolated as colourless liquid using silica gel column chromatography with petroleum ether and ethyl acetate (v/v = 100:1, R_f = 0.5); 89% yield (0.206 g). ^1H NMR (400 MHz, CDCl_3): δ 7.93 (d, J = 8.8 Hz, 2H, ArH), 6.93 (d, J = 8.8 Hz, 2H, ArH), 3.87 (s, 3H, CH_3), 2.76 (d, J = 6.8 Hz, 2H, COCH_2), 2.00 – 1.91 (m, 1H), 1.76-1.61 (m, 5H), 1.29-1.23 (m, 2H), 1.19-1.13 (m, 1H), 1.05-0.96 (m, 2H). ^{13}C 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. HRMS (ESI) m/z : $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{15}\text{H}_{21}\text{O}_2$ 233.1536; found: 233.1531.

1-([1,1'-biphenyl]-4-yl)-2-cyclohexylethanone (2.6d)



Following the general procedure, the title compound **2.6d** was isolated as white solid using silica gel column chromatography with petroleum ether and ethyl acetate (v/v = 100:1, R_f = 0.5); 83% yield (0.226 g) M.p. = 151 – 153 °C. ^1H NMR (400 MHz, CDCl_3): δ 8.02 (d, J = 8.4 Hz, 2H, ArH), 7.68 (d, J = 8.4 Hz, 2H, ArH), 7.64-7.61 (m, 2H, ArH), 7.47 (t, J = 7.6 Hz, 2H, ArH), 7.40 (t, J = 7.2 Hz, 1H, ArH), 2.85 (d, J = 6.8 Hz, 2H, COCH_2), 2.03-1.95 (m, 1H), 1.80 – 1.65 (m, 5H), 1.35 – 1.25 (m, 2H), 1.22 – 1.12 (m, 1H), 1.08 – 0.99 (m, 2H). ^{13}C NMR (101 MHz, CDCl_3): δ 200.1 (C=O), 145.7, 140.1, 136.4, 129.1, 128.9, 128.3, 127.4, 127.4, 46.4 (COCH_2), 34.8, 33.6, 26.4, 26.3. HRMS (ESI) m/z : $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{20}\text{H}_{23}\text{O}$ 279.1743; found: 279.1732.

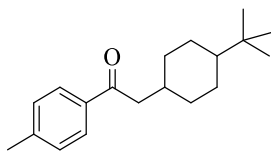
2-cyclohexyl-1-(3-methoxyphenyl)ethanone (2.6e)



Following the general procedure, the title compound **2.6e** was isolated as colourless oil using silica gel column chromatography with petroleum ether and ethyl acetate (v/v = 20:1, R_f = 0.5); 76% yield (0.176 g). ^1H NMR (400 MHz, CDCl_3): δ 7.52 (d, J = 7.6 Hz, 1H, ArH), 7.48 – 7.46 (m, 1H, ArH), 7.36 (t, J = 8 Hz, 1H, ArH), 7.10 (dd, J = 8, 2.0 Hz, 1H, ArH), 3.86 (s, 3H, CH_3), 2.80 (d, J = 6.8 Hz, 2H, COCH_2), 1.98-1.94 (m, 1H), 1.77 – 1.64 (m, 5H), 1.31 – 1.24 (m, 2H), 1.17 – 1.14 (m, 1H), 1.03 – 0.99 (m, 2H). ^{13}C NMR (101 MHz, CDCl_3): δ 200.3 (C=O), 159.9, 139.1, 129.6, 120.9, 119.4,

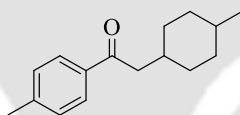
112.6, 55.6 (CH₃), 46.5 (COCH₂), 34.8, 33.6, 26.4, 26.3. HRMS (ESI) *m/z*: [M+H]⁺ calculated for C₁₅H₂₁O₂ 233.1536; found: 233.1526.

2-(4-(*tert*-butyl)cyclohexyl)-1-(*p*-tolyl)ethenone (2.6f)



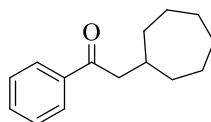
Following the general procedure, the title compound **2.6f** was isolated as colourless liquid using silica gel column chromatography with petroleum ether and ethyl acetate (v/v = 20:1, *R_f* = 0.5); 71% yield (0.193 g). ¹H NMR analysis of the crude reaction mixture showed d.r. of 81:19, as determined by comparison of the following signals: δ 2.97 (d, *J* = 7.2 Hz, 3H, COCH₂)-major, 2.79 (d, *J* = 7.2 Hz, 2H, COCH₂)-minor. ¹H NMR (600 MHz, CDCl₃): δ 7.88-7.85 (m, 2H, ArH, major, 81% + m, 2H, ArH, minor, 19%, minor), 7.27 – 7.26 (m, 2H, ArH, major, 81% + m, 2H, ArH, minor, 19%), 2.97 (d, *J* = 7.2 Hz, 2H, COCH₂, major, 81%), 2.79 (d, *J* = 6.6 Hz, 2H, COCH₂, minor, 19%), 2.42 (s, 3H, major, 81%), 2.42-2.40 (br, 3H, major, 19%), 1.84 – 1.75 (m, 1H, major, 81% + m, 1H, minor, 19%), 1.68 – 1.51 (m, 4H, major, 81% + m, 4H, minor, 19%), 1.26-1.15 (m, 3H, major, 81% + m, 3H, minor, 19%), 1.01-0.93 (m, 2H, major, 81% + m, 2H, minor, 19%), 0.86 (s, 9H, (CH₃)₃, major, 81%), 0.83 (s, 9H, (CH₃)₃, minor, 19%). ¹³C NMR (101 MHz, CDCl₃): δ 200.5 (C=O), 200.2 (C=O), 143.7, 135.2, 135.1, 129.4, 129.3, 128.4, 128.4, 48.5 (COCH₂)-major, 48.0 (COCH₂)-minor, 46.2, 40.4, 35.0, 34.0, 32.7, 32.5, 30.9, 29.4, 27.7, 27.6, 27.3, 22.1, 21.7. HRMS (ESI) *m/z*: [M+H]⁺ calculated for C₁₉H₂₉O 273.2213; found: 273.2221.

2-(4-methylcyclohexyl)-1-(*p*-tolyl)ethan-1-one (2.6g)⁶¹



Following the general procedure, the title compound **2.6g** was isolated as colourless liquid using silica gel column chromatography with petroleum ether and ethyl acetate (v/v = 100:1, *R_f* = 0.5); 71% yield (0.116 g). ¹H NMR analysis of the crude reaction mixture showed a d.r. of 70:30, as determined by comparison of the following signals: δ 2.89 (d, *J* = 6.8 Hz, 2H, COCH₂)-major, 2.79 (d, *J* = 6.8 Hz, 2H, COCH₂)-minor. ¹H NMR (400 MHz, CDCl₃): δ 7.87-7.78 (m, 2H, ArH, major, 70% + m, 2H, ArH, major, 30%), 7.26-7.24 (m, 2H, ArH, major, 70%), 7.11-7.07 (m, 2H, ArH, major, 30%), 2.89 (d, *J* = 7.0 Hz, 2H, COCH₂, major, 70%), 2.79 (d, *J* = 6.8 Hz, 2H, COCH₂, minor, 30%), 2.41 (s, 3H, major, 70%), 2.39 (s, 3H, minor, 30%), 2.20-2.17 (m, 1H, major, 70%), 1.91-1.84 (m, 1H, minor, 30%), 1.77-1.74 (m, 1H), 1.68 – 1.62 (m, 2H), 1.57-1.48 (m, 5H), 1.45-1.37 (m, 2H), 1.32-1.24 (m, 2H), 1.05-0.96 (m, 1H), 0.91 (d, *J* = 6.8 Hz, 3H, CH₃, major, 70%), 0.91 (d, *J* = 6.4 Hz, 3H, CH₃, minor, 30%). ¹³C NMR (101 MHz, CDCl₃): δ 200.4 (C=O), 143.7, 135.1, 129.4, 128.4, 46.2 (COCH₂)-major, 43.3 (COCH₂)-minor, 35.1, 34.6, 33.5, 32.6, 30.9, 29.0, 22.8, 21.8, 20.4.

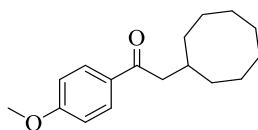
2-cycloheptyl-1-phenylethanone (2.6h)



Following the general procedure, the title compound **2.6h** was isolated as colourless liquid using silica gel column chromatography with petroleum ether and ethyl acetate (v/v = 100:1, *R_f* = 0.5); 74% yield (0.160 g). ¹H NMR (400 MHz, CDCl₃): δ 7.98 – 7.92 (m, 2H, ArH), 7.55 (tt, *J* = 7.2, 2 Hz, 1H, ArH), 7.47 – 7.44 (m, *J* = 2H, ArH), 2.87 (d, *J* = 6.9 Hz, 2H, COCH₂), 2.24 – 2.19 (m, 1H), 1.80 – 1.71 (m, 2H), 1.67 – 1.59 (m, 4H), 1.54 – 1.45 (m, 4H), 1.33 – 1.23 (m, 2H). ¹³C NMR (101 MHz, TH-2648_10612033

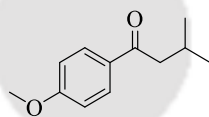
CDCl₃): δ 200.6 (C=O), 137.6, 132.9, 128.7, 128.3, 46.9 (COCH₂), 36.1, 35.0, 28.5, 26.4. HRMS (ESI) m/z : [M+H]⁺ calculated for C₁₅H₂₁O 217.1587; found: 217.1596.

2-cyclooctyl-1-(4-methoxyphenyl)ethanone (2.6i)⁶⁷



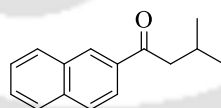
Following the general procedure, the title compound **2.6i** was isolated as white solid using silica gel column chromatography with petroleum ether and ethyl acetate (v/v = 80:1, R_f = 0.5); 76% yield (0.197 g) M.p. = 64 – 66 °C. ¹H NMR (400 MHz, CDCl₃): δ 7.93 (d, J = 8.8 Hz, 2H, ArH), 6.93 (d, J = 9.2 Hz, 2H, ArH), 3.86 (s, 3H, CH₃), 2.80 (d, J = 6.9 Hz, 2H, COCH₂), 2.28 – 2.24 (m, 1H), 1.66 – 1.63 (m, 4H), 1.60 – 1.58 (m, 4H), 1.51 – 1.49 (m, 4H), 1.41 – 1.32 (m, 2H). ¹³C NMR (101 MHz, CDCl₃): δ 199.3 (C=O), 163.4, 130.8, 130.5, 113.8, 55.6 (CH₃), 46.7 (COCH₂), 34.5, 32.7, 27.3, 26.3, 25.5. HRMS (ESI) m/z : [M+H]⁺ calculated for C₁₇H₂₅O₂ 261.1849; found: 261.1850. IR (KBr pellet, selected bands) cm⁻¹: 2924.17 (s), 2853.32 (m), 1676.07 (s), 1600.13 (s), 1511.24 (s), 1256.69 (s), 1170.66 (s).

1-(4-methoxyphenyl)-3-methylbutan-1-one (2.6j)⁶⁸



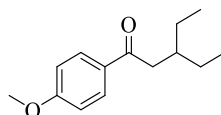
Following the general procedure and 6 equiv. of isopropanol, the title compound **2.6j** was isolated as colourless liquid using silica gel column chromatography with petroleum ether and ethyl acetate (v/v = 100:1, R_f = 0.5); 71% yield. ¹H NMR (600 MHz, CDCl₃): δ 7.94 (d, J = 9 Hz, 2H, ArH), 6.93 (d, J = 9 Hz, 2H, ArH), 3.87 (s, 3H, OCH₃), 2.78 (d, J = 6.9 Hz, 2H, COCH₂), 2.31-2.24 (m, 1H), 0.99 (d, J = 6.6 Hz, 6H, ⁱPr-CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 199.1 (C=O), 163.5, 130.7, 130.5, 113.8, 55.6 (CH₃), 47.4 (COCH₂), 25.6, 22.9 (ⁱPr-CH₃). HRMS (ESI) m/z : [M+H]⁺ calculated for C₁₂H₁₇O₂ 193.1223; found: 193.1226. IR (KBr pellet, selected bands) cm⁻¹: 2958.23 (s), 2933.28 (s), 2870.81 (s), 1601.70 (m), 1514.24 (s), 1249.41 (s).

3-methyl-1-(naphthalen-2-yl)butan-1-one (2.6k)



Following the general procedure and 6 equiv. of isopropanol, the title compound **2.6k** was isolated as colourless liquid using silica gel column chromatography with petroleum ether and ethyl acetate (v/v = 100:1, R_f = 0.5); 67% yield. ¹H NMR (400 MHz, CDCl₃): δ 8.46 (brs, 1H, ArH), 8.03 (dd, J = 8.8, 1.6 Hz, 1H, ArH), 7.97 (d, J = 8 Hz, 1H, ArH), 7.90-7.87 (m, 2H, ArH), 7.62 – 7.53 (m, 2H, ArH), 2.97 (d, J = 6.8 Hz, 2H, COCH₂), 2.40-2.34 (m, 1H), 1.04 (d, J = 6.8 Hz, 6H, CH₃). ¹³C NMR (101 MHz, CDCl₃): δ 200.4 (C=O), 135.7, 134.9, 132.7, 129.8, 129.7, 128.5, 128.5, 127.9, 126.8, 124.2, 47.7 (COCH₂), 25.5, 22.9. HRMS (ESI) m/z : [M+H]⁺ calculated for C₁₅H₁₇O 213.1274; found: 213.1266.

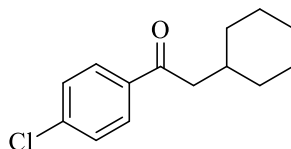
3-ethyl-1-(4-methoxyphenyl)pentan-1-one (2.6l)



Following the general procedure and 6 equiv. of 3-pentanol, the title compound **2.6l** was isolated as colourless liquid using silica gel column chromatography with petroleum ether and ethyl acetate (v/v

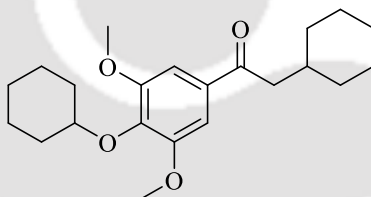
= 50:1, R_f = 0.5); 78% yield (0.171 g). ^1H NMR (600 MHz, CDCl_3): δ 7.94 (d, J = 8.9 Hz, 2H, ArH), 6.93 (d, J = 8.9 Hz, 2H, ArH), 3.87 (s, 3H, OCH_3), 2.81 (d, J = 7.2 Hz, 2H, COCH_2), 2.00–1.93 (m, 1H), 1.39–1.33 (m, 4H), 0.88 (t, J = 7.2 Hz, 6H, CH_3). ^{13}C NMR (101 MHz, CDCl_3): δ 199.6 ($\text{C}=\text{O}$), 163.4, 130.8, 130.5, 113.8, 55.6 (OCH_3), 42.5 (COCH_2), 37.6, 26.2, 11.1. HRMS (ESI) m/z : $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{14}\text{H}_{21}\text{O}_2$ 221.1536; found: 221.1552. IR (KBr pellet, selected bands) cm^{-1} : 2955.70 (s), 2935.78 (m), 1399.39 (m), 1094.52 (s), 1013.26 (s).

1-(4-chlorophenyl)-2-cyclohexylethan-1-one (2.6m)⁶¹



Following the general procedure, the title compound **2.6m** was isolated as colourless liquid using silica gel column chromatography with petroleum ether and ethyl acetate (v/v = 50:1, R_f = 0.5); 62% yield (0.146 g). ^1H NMR (600 MHz, CDCl_3): δ 7.91 (d, J = 8.6 Hz, 2H), 7.45 (d, J = 8.6 Hz, 2H), 2.81 (d, J = 6.8 Hz, 2H), 1.99 – 1.96 (m, 1H), 1.78 – 1.66 (m, 5H), 1.32 – 1.28 (m, 2H), 1.22 – 1.15 (m, 1H), 1.06 – 1.00 (m, 2H). ^{13}C NMR (151 MHz, CDCl_3) δ 199.23, 139.43, 135.87, 129.72, 128.99, 46.34, 34.69, 33.55, 26.35, 26.27.

2-cyclohexyl-1-(4-(cyclohexyloxy)-3,5-dimethoxyphenyl)ethan-1-one (2.6n)



Following the general procedure, the title compound **2.6n** was isolated as colourless liquid using silica gel column chromatography with petroleum ether and ethyl acetate (v/v = 100:1, R_f = 0.5); 81% yield (0.146 g). ^1H NMR (600 MHz, Chloroform- d) δ 7.20 (s, 2H), 4.15 – 4.12 (m, 1H), 3.89 (s, 6H), 2.78 (d, J = 6.7 Hz, 2H), 2.00 – 1.91 (m, 3H), 1.80 – 1.76 (m, 4H), 1.72 – 1.65 (m, 3H), 1.56 (m, 4H), 1.30 – 1.24 (m, 4H), 1.20 – 1.15 (m, 1H), 1.06 – 0.96 (m, 2H). ^{13}C NMR (151 MHz, CDCl_3) δ 199.19, 153.88, 141.13, 132.70, 106.07, 81.37, 56.52, 46.02, 34.89, 33.70, 32.73, 26.45, 26.35, 25.77, 24.32. HRMS (ESI) m/z : $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{16}\text{H}_{23}\text{O}_4$ 361.2374; found: 361.2384.

2.5. Computational studies

All calculations were performed using the Gaussian-09 program package in the gas phase.⁶⁹ Full geometry optimizations were carried out using Minnesota 2006 local (M06-L)⁷⁰ functional and BS1 basis set. BS1 is defined as an SDD⁷¹ basis set for Ru atom and 6-31G(d,p) for all other atoms. Method and basis set was selected based on a previous report⁷² on similar complexes. Frequency calculations at the same method and basis set were performed to distinguish transition state structures and minima structures on the potential energy surface based on the availability of imaginary frequencies. The transition states were verified by the intrinsic reaction coordinate (IRC) calculations, wherever necessary.⁷³ Free energies were calculated by using frequency calculations at 150 °C to match the experimental conditions. The nuclear independent chemical shift (NICS(0)iso) calculations were calculated at the same level of theory using the gauge invariant atomic orbital (GIAO)⁷⁴⁻⁷⁶ method at the geometrical centre of the ring. Negative isotropic values determine the aromaticity of the ring whereas non-aromatic rings show positive isotropic NICS values. Co-ordinates for all the optimized structures is listed in Annexure VII (page 294).

Table 2.4. Free Energies (G) and Total Energies (E) given in Hartree along with the number of imaginary frequencies

Species	Free energy (G)	Total energy (E)	# Imaginary Frequency (NImag)
H ₂	-1.17803400	-1.1700775	0
H ₂ O	-76.416076	-76.4110228	0
cyclohexanol (2.2a)	-310.93162500	-311.0597947	0
cyclohexanone (2.2a')	-309.756482	-309.8609199	0
acetophenone (2.5a)	-384.77127600	-384.858511	0
2.6a	-619.290486	-619.5160333	0
<i>Dehydrogenation outer sphere MLC pathway for 2.6a</i>			
I	-2409.36238800	-2409.9644913	0
O-TS-1	-2409.34690000	-2409.9424804	1
II	-2409.39853700	-2409.96550870	0
O-TS-2	-2409.35294200	-2409.91588560	1
I + H₂	-2409.36797400	-2409.93854400	0
<i>Hydrogenation segment</i>			
II	-2407.97763800	-2408.51309160	0
R-TS-1	-2407.97237500	-2408.50375430	1
III	-2407.97376200	-2408.50980450	0
IV	-2407.957408	-2408.5132625	0
R-TS-2	-2407.94857200	-2408.5040619	1
II	-2408.00075800	-2408.56600960	0
<i>Alcoholysis segment</i>			
II	-2717.73122900	-2718.402809	0
R-TS-1	-2717.72596600	-2718.393472	1
III	-2717.72735300	-2718.399522	0
(III...2.2a)	-2717.710931	-2718.359621	0
IV	-2717.693295	-2718.755802	0
R-TS-3	-2717.679434	-2718.779210	1
V	-2717.74975500	-2718.416445	0
R-TS-4	-2717.74429700	-2718.408192	1
VI	-2717.75477700	-2718.420596	0
VII	-2717.73041200	-2718.363755	0
II	-2717.77129300	-2718.40689	0
<i>Dehydrogenation inner sphere MLC pathway for 2.2a</i>			
I	-2409.38244500	-2409.964341	0
VIII	-2409.40109700	-2409.984620	0
I-TS-1	-2409.37896000	-2409.941273	1
IX	-2409.40462000	-2409.976271	0
X	-2409.39089400	-2409.960207	0
I-TS-2	-2409.38543600	-2409.951953	1
XI	-2409.395916	-2409.964357	0
XII	-2409.371551	-2409.907516	0
XIII	-2409.412432	-2409.950652	0
II or XIII...2.2a	-2409.39853700	-2409.965509	0
O-TS-2	-2409.35294200	-2409.915886	1
I+H₂	-2409.36797400	-2409.938544	0

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

2.6. References

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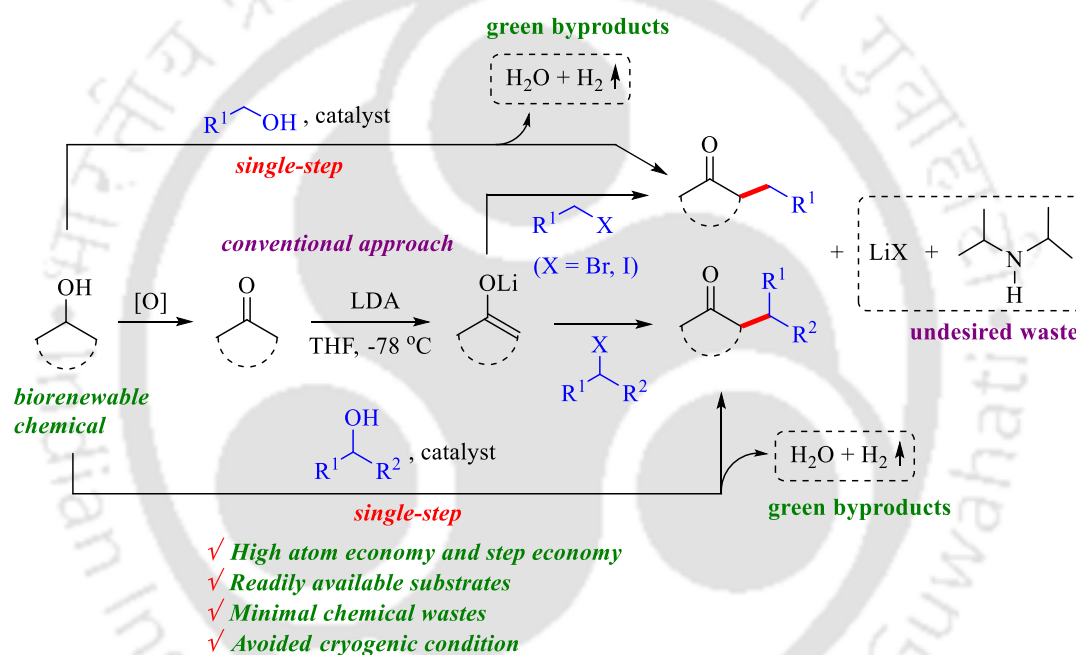
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Catalytic cross-coupling of primary alcohols and secondary alcohols to form α -alkylated ketones and two different secondary alcohols to form β -disubstituted ketones

3.1. Introduction

Transition-metal-catalysed carbon–carbon bond formations have proved to be a powerful tool for the synthesis of a wide range of important organic molecules.¹ Among various methods, β -alkylation of the secondary alcohols for synthesizing α -branched²⁻¹⁸ or β -branched ketones¹⁹⁻²⁵ represents the most efficient synthetic approach. As mentioned in chapter 1, these have been synthesized in a multi-step process, such as stoichiometric oxidation of alcohol, followed by the formation of lithium enolate species by using a strong base under cryogenic condition, and then alkylation with mutagenic alkyl halides,^{26, 27} as a result copious amount of waste has been generated during the reaction.^{28, 29} On the other hand, metal-catalyzed direct cross-coupling of alcohols *via* ADC is a prominent synthetic strategy as the process does not require any external hydrogen acceptor or oxidant source, H_2 and H_2O are the only byproducts, which makes the process green, atom economical, and environmentally benign.

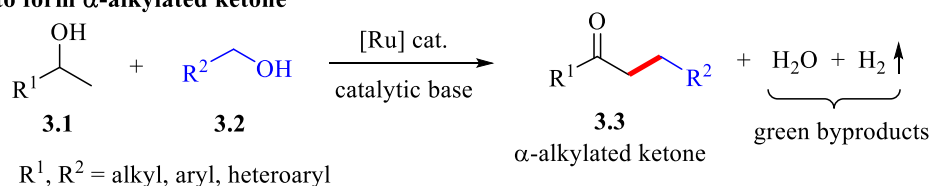


Scheme 3.1. Traditional and selective catalytic synthesis of α -alkylated ketones and β -disubstituted ketones using alcohols

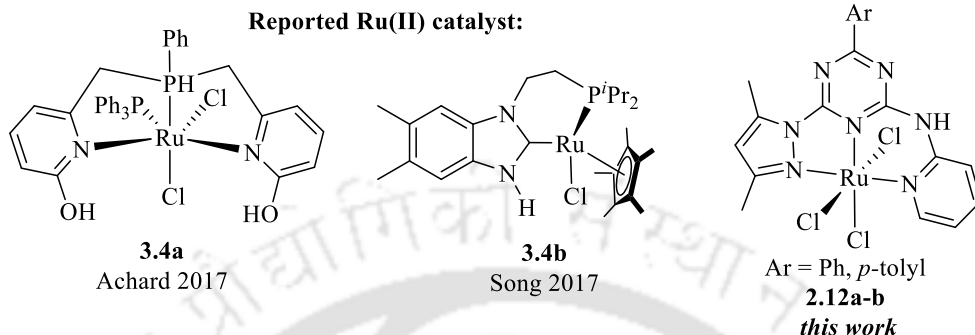
Using this strategy, selective α -substituted ketone formation is described *via* metal-catalyzed cross-coupling of primary and secondary alcohols.²⁻¹⁵ Among various homogenous transition metal catalysts, ruthenium (II) complexes⁶⁻⁹ have shown very well in this transformation, described one each by the group of Archard,⁷ Song⁸ and others^{10, 11} (Scheme 3.2a). As the reaction produces H_2 as one of the by-products, the formed ketones could further be hydrogenated to alcohols,³⁰⁻³⁶ leading to a challenge in the selectivity.³⁷ In contrast, the reports on α -alkylation of ketones, using cross-coupling of secondary alcohols to generate β -branched ketones are very scarce, as self-coupling^{17, 38} of secondary alcohols is one of the common undesired side products which reduce the atom economy in an overall process. Very recently, Gunanathan and co-workers reported catalytic cross-coupling of two different secondary alcohols by well-defined phosphine based Ru–MACHO system, leading to β -branched aromatic ketones in moderate to excellent yield (30-90%).^{23, 24} The protocol was not limited to the use of bulky substituted benzylic alcohol and does not require the excess amount of base and alcohol substrate (Scheme 3.2b). Despite this pioneering work, some limitations are still present from the sustainable and practical perspective. The reaction requires anaerobic reaction conditions, the phosphine-supported ligand, and ruthenium(II) is used as the pre-catalyst for ADC of

alcohol. In this context, synthesis of branched ketones catalyzed by non-phosphine ruthenium complexes is highly desired.

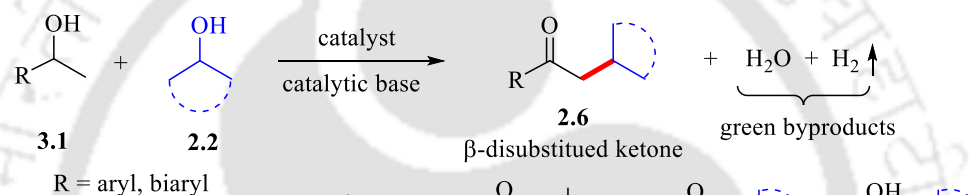
(a) Ruthenium-catalyzed cross-coupling of secondary alcohols with primary alcohols to form α -alkylated ketone



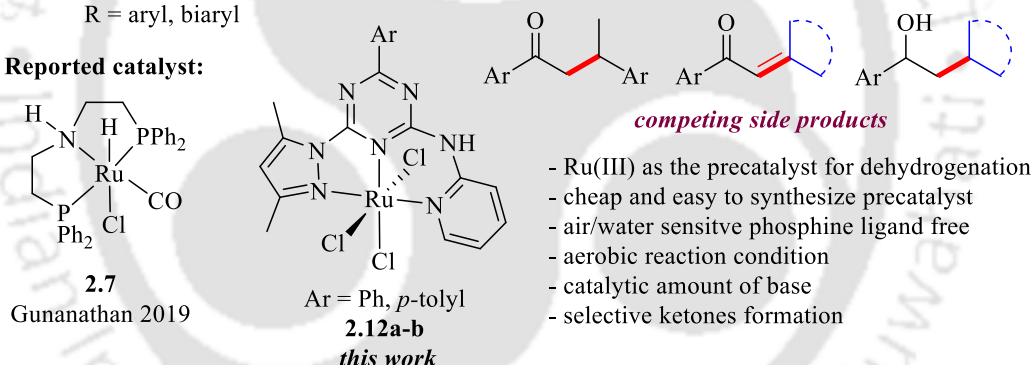
Reported Ru(II) catalyst:



(b) Direct cross-coupling of secondary alcohols: Synthesis of β -disubstituted ketone



Reported catalyst:



Scheme 3.2. Catalytic dehydrogenative cross-coupling of alcohols

3.2. Present work

Herein, the scope of the newly synthesized phosphine-free ruthenium complexes **2.12a-b** is explored towards catalytic cross-coupling of primary and secondary alcohols to α -substituted ketones and two different secondary alcohols to β -disubstituted ketones. Contrary to reported method,²³ a single catalyst can oxidize both alcohols to provide selectively branched ketones under air. A detailed mechanistic study of the catalytic cross-coupling of alcohols has also been discussed.

3.2.1. Optimization studies for cross-coupling of primary and secondary alcohols

Optimization study was initiated with 1-(4-methoxyphenyl)ethanol (**3.1c**) and benzyl alcohol (**3.2a**) as model substrates for the cross-coupling of secondary and primary alcohols. The initial experiment was carried out with **3.1c** (1 mmol) and **3.2a** (1 mmol) in the presence of **2.12a** (2 mol%) and KO^tBu (20 mol%) in toluene at 120 °C for 12 h. Both the alcohols were completely consumed and the ketone **3.3c** was obtained as the only C–C cross-couple product in 78% yield (Table 3.1, entry 1). Notably, I have not observed any fully reduced alcohol, 1-(4-methoxyphenyl)-3-phenyl-1-propanol **3.3c'**, reflecting excellent product selectivity. Interestingly, complex **2.12b** showed better activity compared to **2.12a**. Under the same reaction conditions ketone **3.3c** was obtained in 92% yield using complex

2.12b (entry 2). Encouraged by this result, I further studied the effect of other reaction parameters such as loading catalyst, base, time and temperature etc.

Table 3.1. Screening of reaction conditions for catalytic cross coupling of primary and secondary alcohols^{a,b}

COc1ccc(cc1)C(O)C (3.1c) + c1ccccc1CO (3.2a) $\xrightarrow[\text{toluene, temp.}]{\text{catalyst, base}}$ COc1ccc(cc1)C(=O)Cc2ccccc2 (3.3c) + H₂O + H₂↑

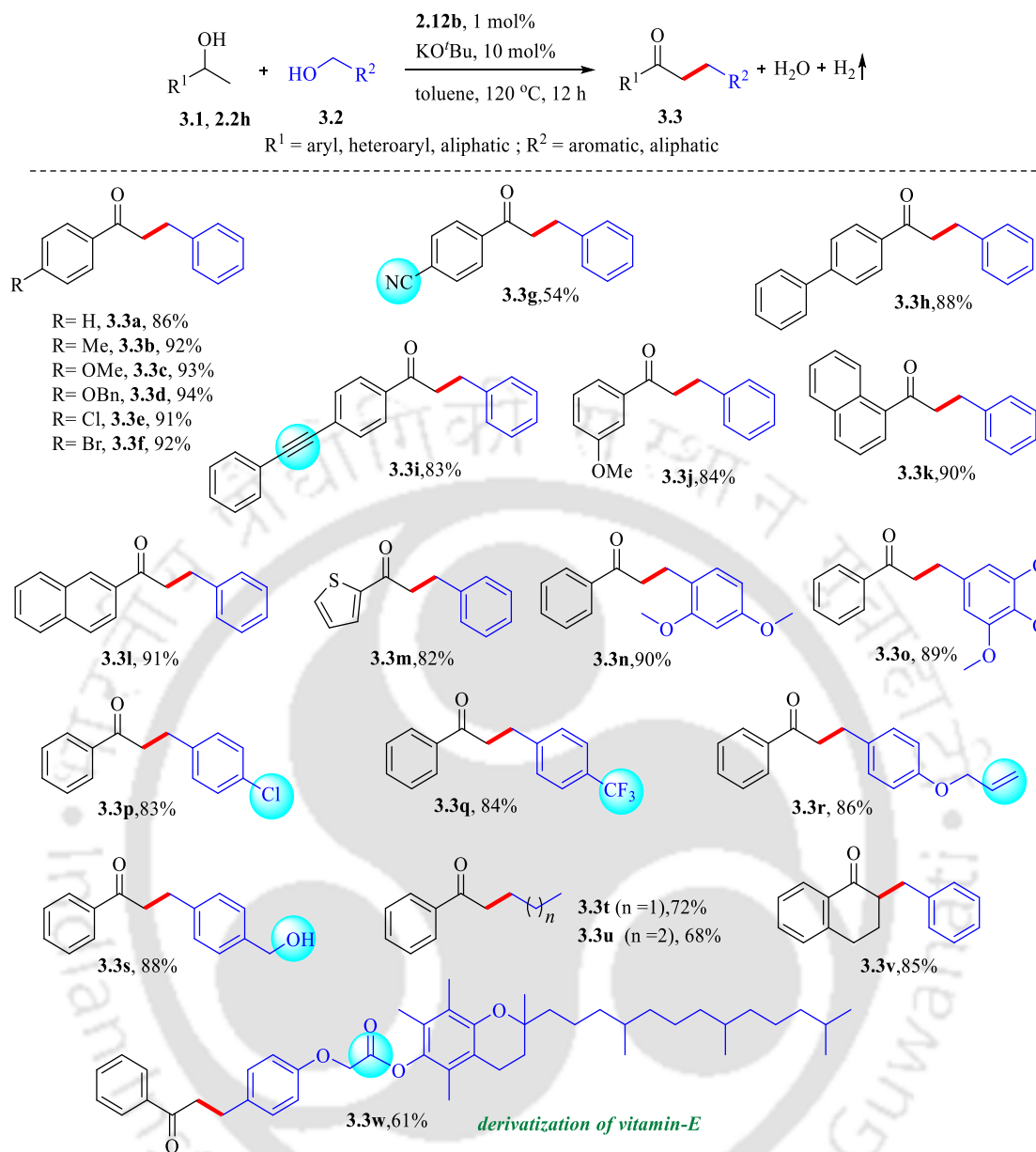
entry	catalyst	mol% cat.	base (mol%)	time (h)	temp (°C)	yield (%)
1	2.12a	2	KO ^t Bu (20)	12	120	78
2	2.12b	2	KO ^t Bu (20)	12	120	92
3	2.12b	2	KO ^t Bu (20)	12	130	89
4	2.12b	2	KO ^t Bu (20)	12	140	85
5	2.12b	2	KO ^t Bu (20)	12	100	78
6	2.12b	1	KO ^t Bu (10)	12	120	93
7	2.12b	0.5	KO ^t Bu (10)	12	120	72
8	2.12b	0.5	KO ^t Bu (5)	12	120	56
9	2.12b	1	NaO ^t Bu (10)	12	120	65
10 ^c	2.12b	1	KOH (10)	12	120	12
11	2.12b	1	KO ^t Bu (10)	6	120	75
12	2.12b	1	KO ^t Bu (10)	10	120	87
13	RuCl₃	1	KO ^t Bu (10)	12	120	44
14 ^d	—	—	KO ^t Bu (10)	12	120	n.d.
15 ^c	HL² + RuCl₃	1	KO ^t Bu (10)	12	120	71
16	2.12b	1	—	12	120	n.d.
17	2.12b + PPh₃	1	KO ^t Bu (10)	12	120	46

^aReaction conditions: 1-(4-methoxyphenyl)ethanol (1 mmol), benzyl alcohol (1 mmol), catalyst (x mol%), base (x mol%), and toluene (2 mL) were heated under air. ^bIsolated yields; ^cConversion of 1-(4-methoxy phenyl)ethanol was determined by ¹H NMR; > 99%. ^dHL² (1 mol%) was used.

The yield of the **3.3c** got notably decreased in both cases either by lowering the reaction temperature from 120 °C to 100 °C or by increasing the reaction temperature from 120 °C to 140 °C, indicating the temperature plays a significant role to the reaction outcome. Gratifyingly, a lower catalyst loading (**2.12b**, 1 mol%) and base loading (KO^tBu, 10 mol%) also showed high yields of **3.3c** with 93% (entry 6). However, decreasing the catalyst loading from 1 mol% to 0.5 mol%, led to lower yields of the desired product (entry 7). It was also found that KO^tBu was the appropriate base for this reaction. Further optimization study was examined with varying reaction time. Low yielded cross-coupled product was observed below 12 hours (entry 11 and 12). Finally, control experiments showed that both the catalyst and the base were indispensable for this particular transformation. The optimized reaction conditions were therefore fixed to be **2.12b** (1 mol%), KO^tBu (10 mol%), 120°C for 12 h in toluene.

3.2.2. Substrate scope for cross-coupling of primary and secondary alcohols:

With the optimized conditions in hand, I next explored the substrate scope of secondary and primary alcohols (Table 3.2). Substrates having both electron-donating (*e.g.* Me, OMe, OCH₂Ph) and electron-withdrawing (*e.g.* Cl, Br) groups at the *para* position of the secondary alcohols were reacted with **3.2a** to obtain the desired ketones, **3.3a-f**, **3.3h** in excellent yields (86-94%). The reducible functional groups such as –CN, –C≡C–Ph can survive the current reaction to give the desired products **3.3g**, **3.3i** selectively. *Meta*-substituted substrate **3.3j** also showed good activity. Furthermore, α- and β-naphthylethanol was reacted with **3.2a** to obtain the corresponding ketones in excellent 90-91% yields. Gratifyingly, the heterocyclic moiety is also well-tolerated. Next, we have investigated the scope of primary alcohols. The electron-donating methoxy group substituted at the different positions of the primary aromatic alcohol furnished the corresponding ketones in good yields.

Table 3.2. β -alkylation of secondary alcohols with primary alcohols to α -alkylated ketones^a

^aReaction conditions: 1-arylethanol (1 mmol), primary alcohol (1 mmol), catalyst **2.12b** (1 mol%), KOtBu (10 mol%), and toluene (2 mL) were heated at 120 °C under air for 12 h. Isolated yield. **2.2h**: 1-tetralol

Notably, the electron-withdrawing groups such as $-\text{Cl}$, $-\text{CF}_3$, and reducible $-\text{OCH}_2\text{CH}=\text{CH}_2$ groups present at the *para* position in the benzyl alcohol afforded the desired ketones **3.3p-r** in 83–86% yields. Intriguingly, when 1,4-phenylenedimethanol was used as an alkylating agent the single α -alkylated ketone **3.3s** was obtained with excellent selectivity. Aliphatic primary alcohols were also well amenable to this method and provided **3.3t-u** in 68–72% yield. Synthetic utility of this reaction was explored using vitamin E, ($\pm$) tocopherol functionalized aromatic primary alcohol (**3.2w**) with 1-phenylethanol **3.1a**. Gratifyingly, 61% yield of cross couple product **3.3w** was obtained without affecting the parent tocopherol moiety.

3.2.3. Optimization studies for cross-coupling of two different secondary alcohols:

I next explored the catalytic cross-coupling of two different secondary alcohols to synthesize β -disubstituted ketones. The major challenge is to overcome the unwanted self-coupled aldol product, while selectivity is also another issue as discussed in above.^{17, 38} Investigation started with the reaction of **3.1c** and cyclohexanol **2.2a** in the presence of **2.12a** (2 mol%) and KOtBu (20 mol%) in toluene at 120 °C for 12 h (Table 3.3). To my delight, I have observed the desired product **2.6c** in 83% yield after 12

hours (Table 3.3, entry 1). Notably, no self-coupled product or fully hydrogenated product 2-cyclohexyl-1-(4-methoxyphenyl)ethan-1-ol **2.6c'** was detected.

Table 3.3. Optimization reaction condition for cross-coupling of secondary alcohols^{a,b}

COc1ccc(cc1)C(O)C (3.1c) + C1CCCCC1O (2.2a) $\xrightarrow[\text{toluene, temp., 12 h}]{\text{catalyst, base}}$ COc1ccc(cc1)C(=O)C2CCCCC2 (2.6c) + H₂O + H₂↑

entry	catalyst	mol% cat.	base (mol%)	temp (°C)	yield (%)
1	2.12a	2	20	150	83
2	2.12b	2	20	150	89
3	2.12b	2	20	140	63
4	2.12b	2	20	120	12
5	2.12b	2	10	150	20
6 ^c	2.12b	2	30	150	10
7 ^d	2.12b	1	20	150	n.d.
8	2.12b	1	10	150	15
9	2.12b	2	—	150	n.d.
10	RuCl₃	2	20	150	n.d.
11	—	—	20	150	n.d.

^aReaction conditions: 1-(4-methoxyphenyl)ethanol (1 mmol), cyclohexanol (1 mmol), catalyst (x mol%), base (x mol%), and toluene (2 mL) were heated under air for 12 h. ^bIsolated yields. ^cSelf-coupling product 1,3-bis(4-methoxyphenyl)butan-1-one was obtained in 44% yield. ^dConversion of 1-(4-methoxyphenyl)ethanol was determined by ¹H NMR; > 72%.

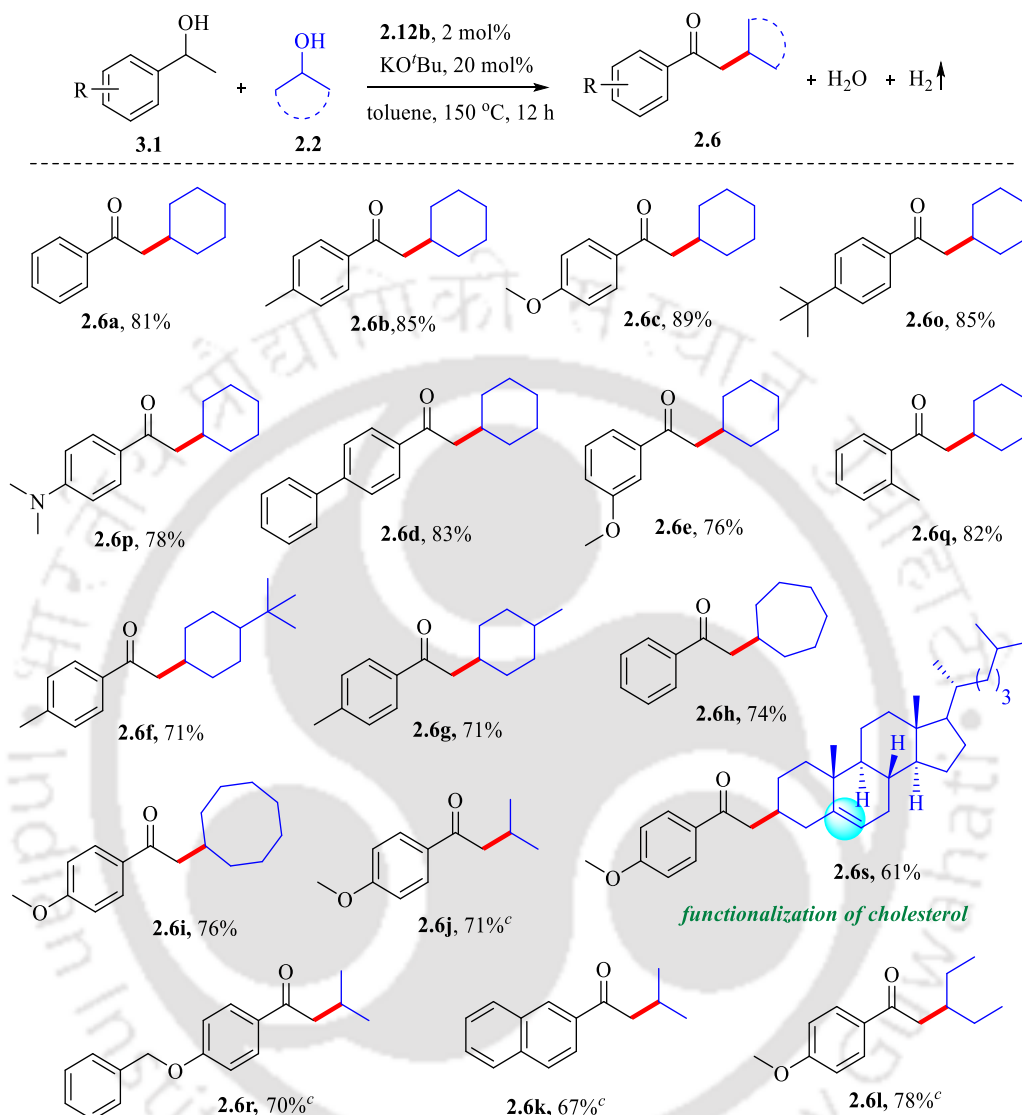
Employing **2.12b** under similar conditions led to better yield of **2.6c**, 90% (entry 2). While inspecting the catalytic protocol with decreasing the catalyst loading from 2 mol% to 1 mol% and/or base loading from 20 mol% to 10 mol%, the yield of desired product **2.6c** was dramatically decreased (entry 7 and 8). In contrast, when the reaction was performed with higher base loading from 20 mol% to 30 mol% and keeping the catalyst loading of 2 mol%, exclusively self-couple product was obtained along with some unreacted ketones (entry 6). These control experiments suggested that optimal base loading and catalyst loading were important for efficiency of the reaction. Furthermore, a temperature of 150 °C was also proved to be crucial for this transformation, as lowering the reaction temperatures gave considerably poor results (entry 3 and 4). To gain more insight about the catalytic system, blank experiments were performed and it indicated that both the catalyst and the base were indispensable for this transformation. Thus, the optimized reaction conditions were catalyst **2.12b** (2 mol%), KO^tBu (20 mol%), 150 °C for 12 hours in toluene.

3.2.4. Substrate scope for cross-coupling of secondary alcohols

Next, above optimized conditions were pursued for the scope of the reaction. As displayed in Table 3.4, a wide variety of secondary alcohol was examined to synthesize β-disubstituted ketones. An array of diverse functionalities such as 4-methyl, 4-methoxy, 4-*ter*-butyl, 4-dimethylamine, and 4-phenyl on the 1-phenylethanol were efficiently reacted with **2.2a** to obtain β-disubstituted ketones **2.6b-c**, **2.6o-p** and **2.6d** in good to excellent yields (78-90%). Likewise, *meta*-substituted aromatic secondary alcohol also resulted to the corresponding ketone **2.6e** in high yield. Remarkably, sterically hindered *ortho*-substituted substrate was well tolerated as witnessed from the 82% yield of 2-cyclohexyl-1-(*o*-tolyl)ethanone (**2.6q**). However, chloro substituted aromatic secondary alcohol showed diminished activity. It was interesting to note that substitution on cyclohexyl ring such as 4-*tert*-butyl cyclohexanol (or 4-methyl-butylcyclohexanol) gave a mixture of diastereomers with the diastereomeric ratio of 81:19 as determined from the ¹H NMR of the reaction mixture. The major isomer is 1,4-*cis* conformation of cyclohexyl ring, which was consistent with reported literature.²³ The result suggests cross-coupling reaction occurred in selective manner with substituted cyclohexanol. Gratifyingly, the scope of the methodology was expanded to a variety of other higher

analog of cyclic alcohols such as cycloheptanol and cyclooctanol. Finally, the highly challenging acyclic aliphatic secondary alcohol was found to be amenable to this method, giving **2.6j-l**, **2.6r** in good yields. Synthetic application of the catalytic protocol was further demonstrated by reacting cholesterol with **3.1c**. Delightfully, cholesterol functionalized β -disubstituted ketone **2.6s** was obtained in 61% yield.

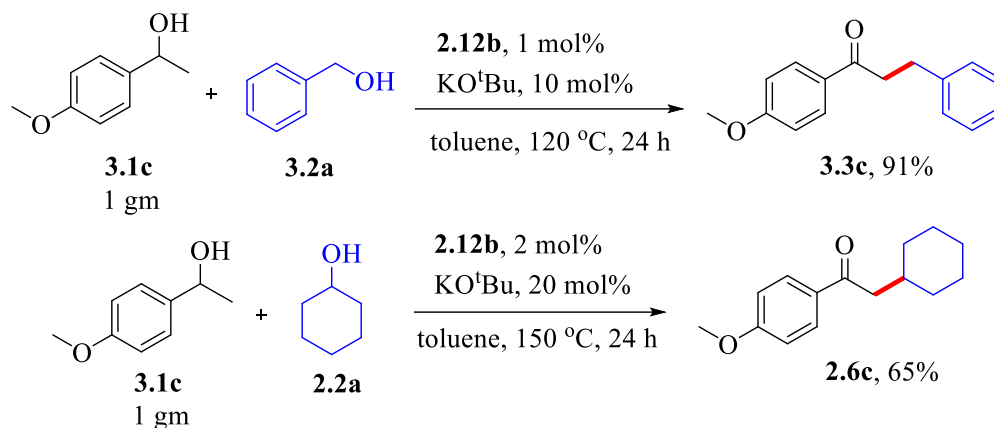
Table 3.4. Ruthenium catalyzed selective cross-coupling of secondary alcohols^a



^aGeneral conditions: 1-arylethanol (1 mmol), secondary alcohol (1 mmol), catalyst **2.12b** (2 mol%), KOtBu (20 mol%), and toluene (2 mL) were heated at 150 °C under air for 12 h. ^bIsolated yield. ^cAliphatic secondary alcohol (6 mmol) was used.

3.2.5. Gram-scale reactions

Both the cross-coupling reactions have been shown to work effectively on a gram-scale, highlighting the practical utility of the present protocol (Scheme 3.3).



Scheme 3.3. Gram-scale cross-coupling reactions of alcohols

3.2.6. Kinetic studies

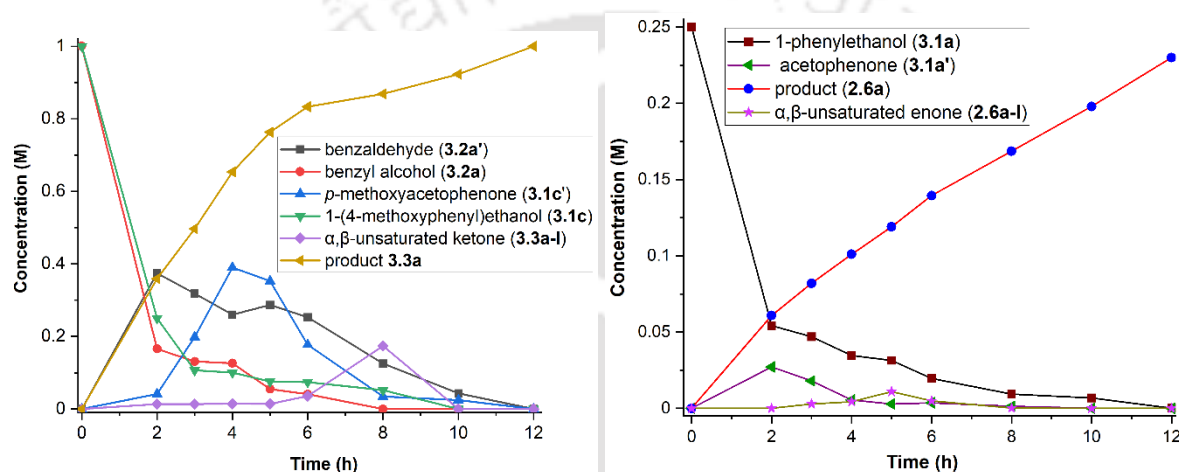
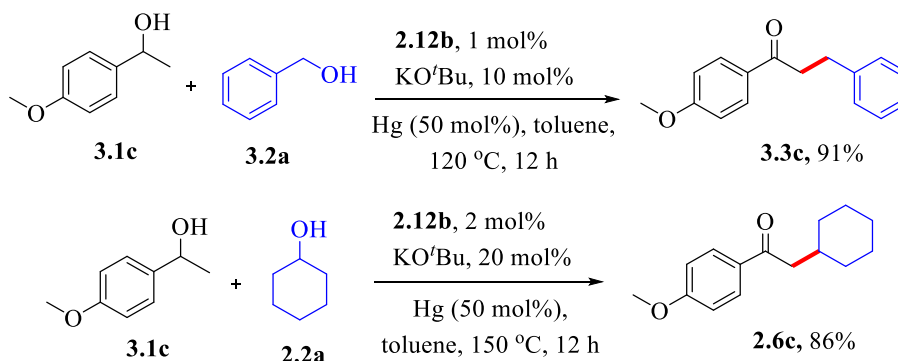


Figure 3.1. Kinetic profile diagram for catalytic cross-coupling of primary and secondary alcohols (left) and for different secondary alcohols (right).

The kinetics analysis for the catalytic cross-coupling of alcohols was carried out under optimized conditions in different time intervals. As shown in the kinetic profile in Figure 3.1, the consumption of alcohol **3.1a** or **3.1c** declines rapidly in the first 2 h, and then gradually decreases over the remaining time. Interestingly, the corresponding aldehyde **3.2a'**, ketone (**2.5a** or **2.5c**), and α,β -unsaturated ketone (**3.3c-I** or **2.6c-I**) were found as intermediates.

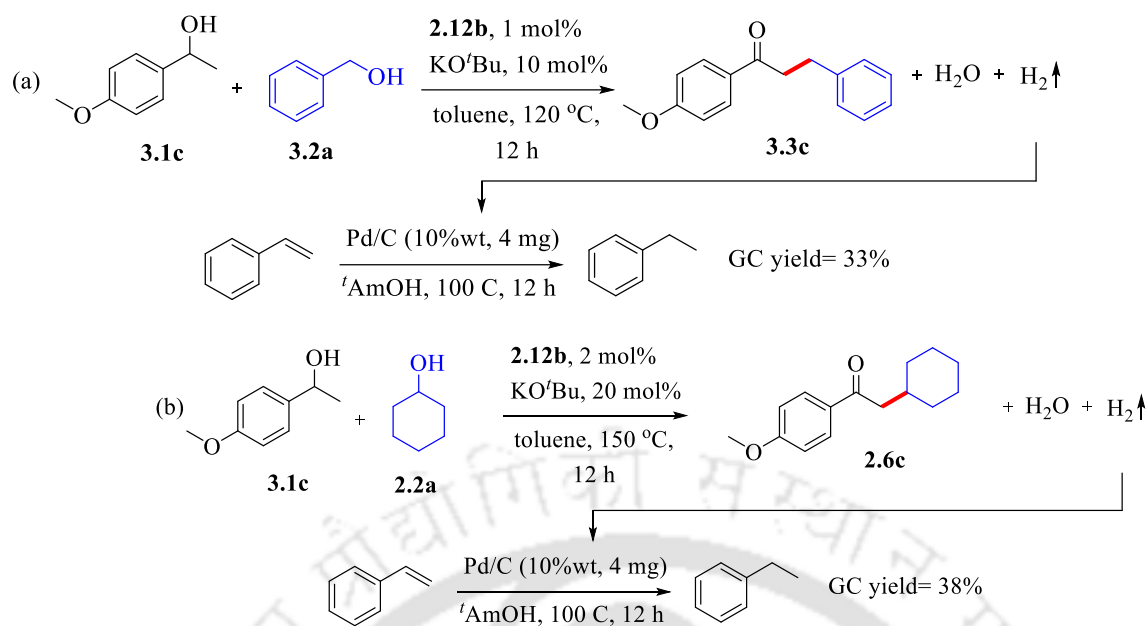
3.2.7. Mechanistic studies:

At first mercury drop experiment was carried out to understand the homogeneity of ruthenium complex in this catalytic reaction. The similar yield was observed in the presence of mercury, suggests the reaction is homogeneous and is not inhibited using mercury (Scheme 3.4).



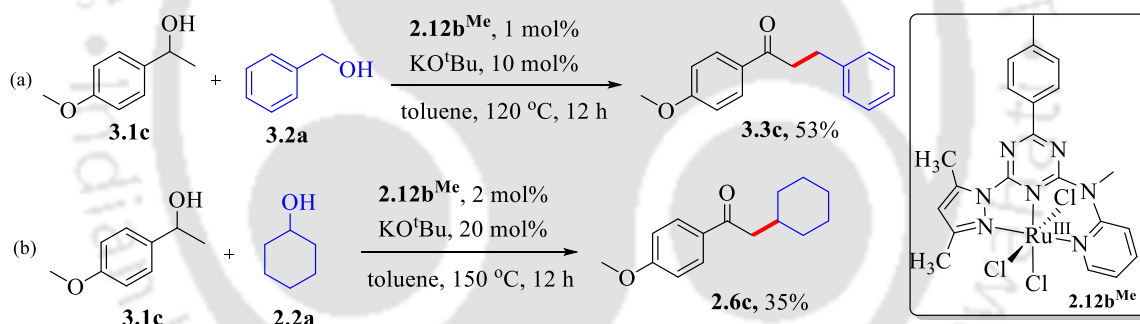
Scheme 3.4. Mercury drop experiment

The liberation of H₂ in ADC reaction was probed by the Pd/C catalyzed hydrogenation of styrene (Scheme 3.5).



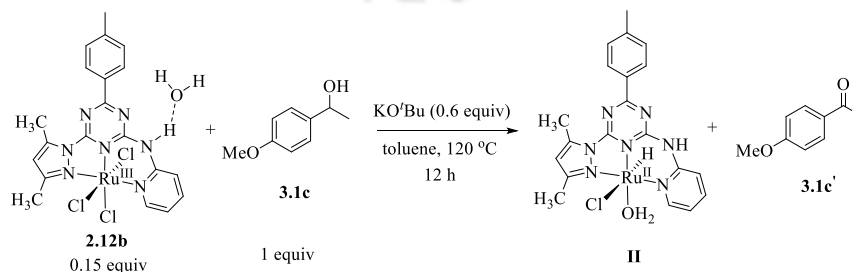
Scheme 3.5. Evidence for evolved hydrogen in cross-coupling reaction

The role of the NH functionality was examined by using complex **2.12b^{Me}** as the precatalyst, leading to lower yields of **3.3c** and **2.6c** and thereby indicating the importance of the NH functionality through metal-ligand cooperative (MLC) pathway (Scheme 3.6).



Scheme 3.6. The influence of the –NH functionality in catalysis

In subsection 2.2.4, it has been shown that ruthenium (III) complex **2.12b** is reduced to ruthenium (II) in the presence of base under the reaction conditions and *in-situ* formed complex **I** was found as an active species in the catalytic process. Complex **I** can react with alcohol **3.1c** to give reactive ruthenium hydride species **II**, which was supported by mass spectrometry analysis (Figure 3.2).



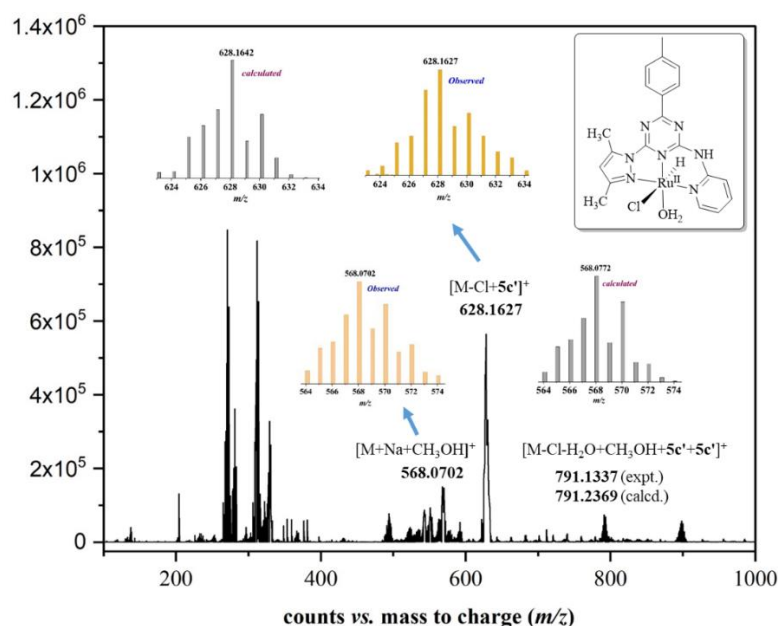
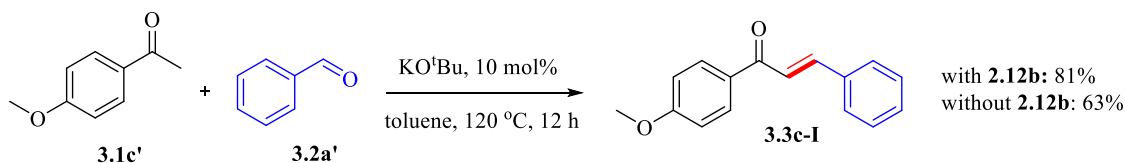


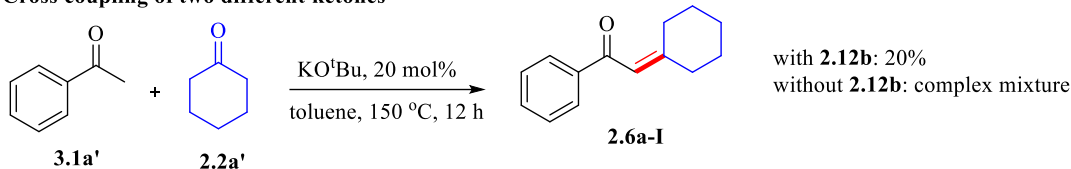
Figure 3.2. HRMS (ESI) spectra for ruthenium hydride **II**

Next, in the presence of KO^tBu, the base mediated cross-aldol condensation of **2.5c** with **3.2a'** (or with **2.5a** and **2.2a'**) afforded α,β -unsaturated ketone **3.3c-I** (or **2.6a-I**), suggesting the formation of a ketone or aldehyde *in-situ* as the intermediates (Scheme 3.7a and Scheme 3.7b). The reaction of **3.3c-I** with **3.2a** under optimized condition afforded desired ketone **3.3c** in good yield (Scheme 3.7c). Likewise, β -branched ketone **2.6a** was obtained by using intermediate **2.6a-I** and cyclohexanol (Scheme 3.7d). Similar results were observed with molecular H₂ in its place of alcohol (Scheme 3.7e). These data suggest that in both cases, α,β -unsaturated ketone (**3.3c-I** or **2.6a-I**) is the reaction intermediate and the reaction is likely proceeded *via* ruthenium hydride species, either derived from dehydrogenation of alcohol or molecular H₂.

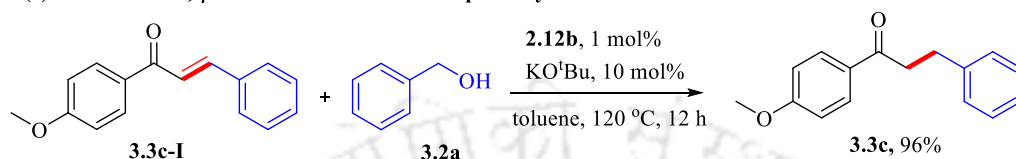
(a) Base catalyzed aldol condensation with aldehyde and ketone



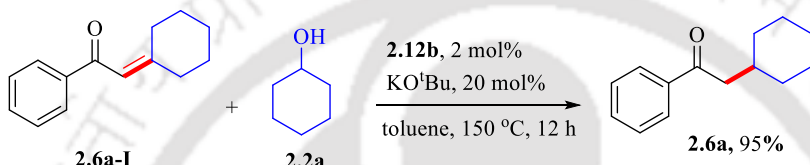
(b) Cross coupling of two different ketones



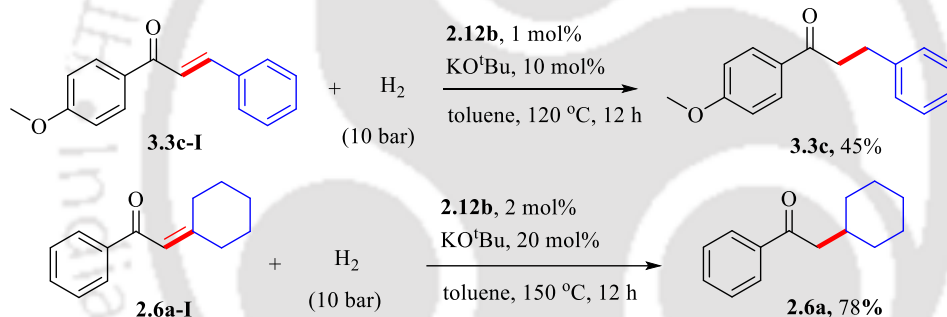
(c) Reaction of α , β -unsaturated ketone with primary alcohol



(d) Reaction of α , β -unsaturated ketone with secondary alcohol

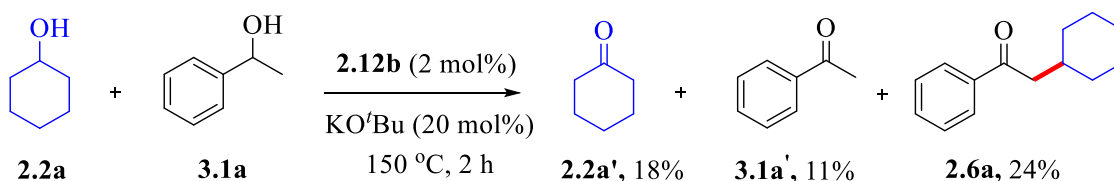


(e) Reaction of α , β -unsaturated ketones with molecular hydrogen



Scheme 3.7. Proof for the formation of intermediate aldehyde, ketone or α,β -unsaturated ketone

In order to understand the rate of dehydrogenation of aliphatic secondary alcohol vs. aromatic secondary alcohol by catalyst **2.12b**, the investigation has been illustrated with **2.2a** and **3.1c** under the standard condition for 2 h. Higher yield of **2.2a'** (18%) was obtained with respect to **2.5c** (11%) by GC analysis, which revealed that dehydrogenation of the aliphatic secondary alcohol was faster than the benzylic ones under the reaction conditions (Scheme 3.8). Furthermore, deuterium-labelling experiment was performed in both cross-coupling reactions to validate the involvement of hydrogen-borrowing methodology. Under the standard condition, the reaction of **5c-D** with **6a** or with **8a** yielded expected H/D scrambled product **7ca-D** or **9ca-D** in 85% and 78% yields, respectively (Scheme 3.9). The above results demonstrated that the dehydrogenative step takes place in the ADC reaction sequence and the involvement of the cooperative bifunctional mechanism.



Scheme 3.8. Comparative study for dehydrogenation of aliphatic secondary vs. aromatic secondary alcohol

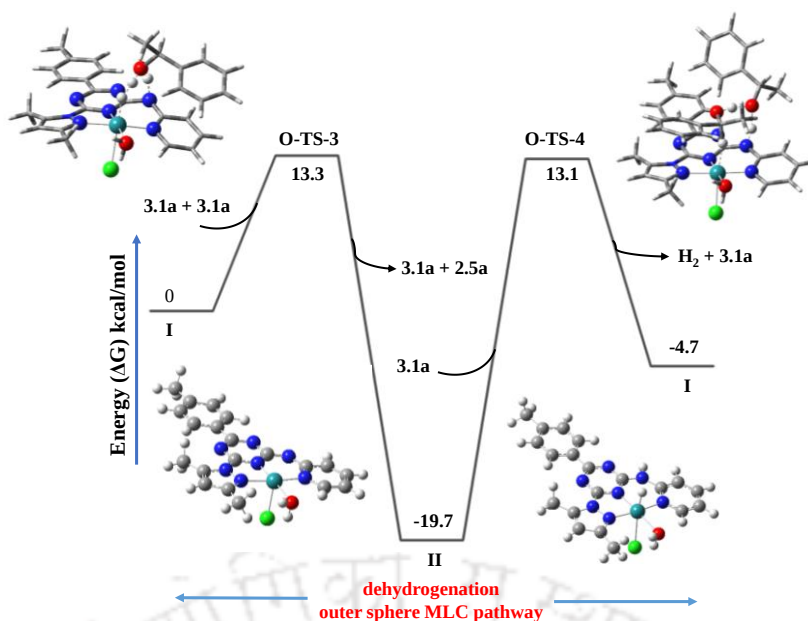


Figure 3.3. Dehydrogenation of alcohol via outer sphere MLC pathway

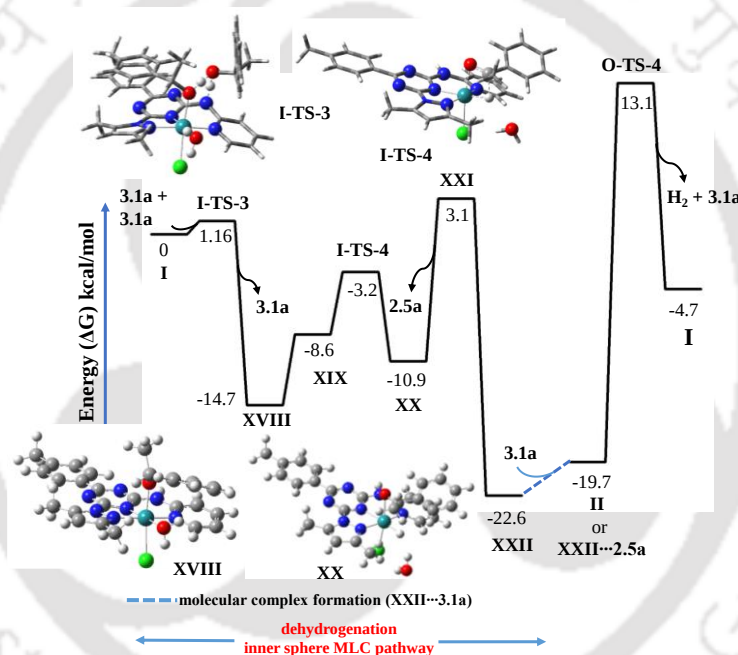


Figure 3.4. Dehydrogenation of alcohol via inner sphere MLC pathway

could be easily formed by the addition of -OH bond of alcohol with the proton shuttle type of mechanism via inner sphere MLC pathway (Figure 3.4). Subsequently, β -hydride elimination reaction takes place and yielded the ketone coordinated intermediate **XX** in uphill way (**XVIII** $\rightarrow$ **XX**, $\Delta G = 3.8$ kcal/mol). To release corresponding ketone **2.5a** from **XX** requires higher energy ($\Delta G = 14.6$ kcal/mol) compared to the energy barrier for β -hydride elimination step ($\Delta G^\ddagger = 11.5$ kcal/mol) (**XVIII** $\rightarrow$ **I-TS4**). Then after isomerization can lead to ruthenium-hydride intermediate **II** in a downhill process of 25.7 kcal/mol (**XXI** $\rightarrow$ **XXII**).

A base mediated cross-aldol reaction between *in-situ* generated ketones **2.5a** and **2.2a'** gives α,β -unsaturated ketone compound **2.6a-I**, which inserts into the Ru-H bond of **II** in an uphill process ($\Delta G = 2.4$ kcal/mol) while crossing a barrier (**R-TS-1**) of only 3.3 kcal/mol (Figure 3.5). The subsequent undergoes σ -bond metathesis with molecular H_2 with slightly higher energy barrier (**R-TS-2**, $\Delta G^\ddagger = 5.5$ kcal/mol), leading to the desired product **2.6a** in exothermic way ($\Delta G = -27.2$ kcal/mol) and regeneration of the active metal hydride intermediate **II**.

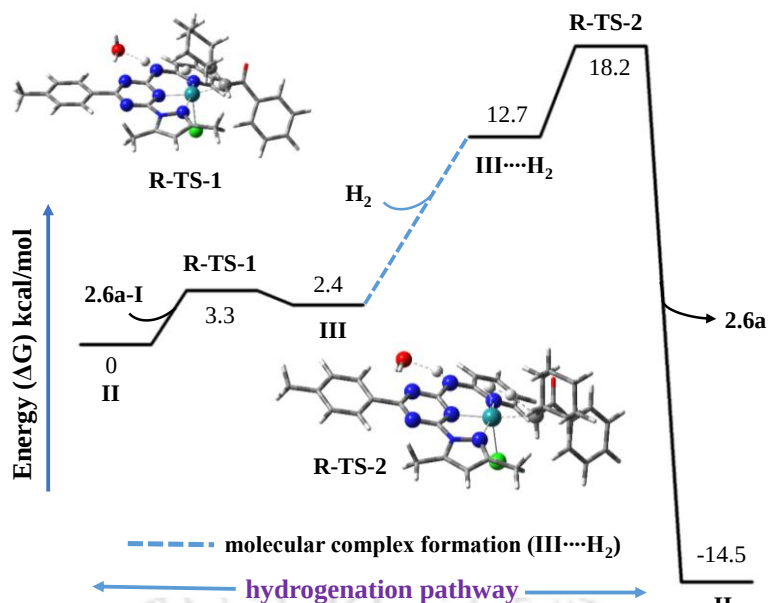


Figure 3.5. Energy profile for hydrogenation pathway

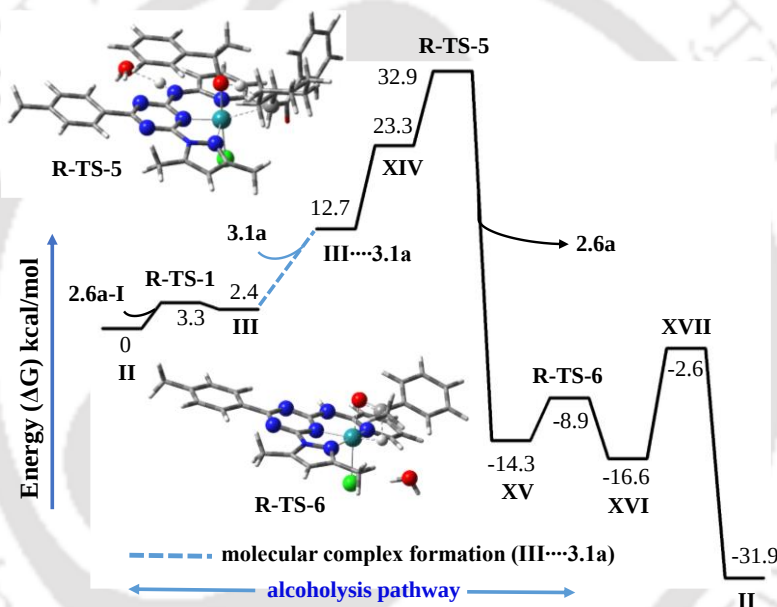


Figure 3.6. Energy profile for alcoholysis pathway

The alternative alcoholysis of **III** comprises coordination of **3.1a** to ruthenium center to give **XIV** via molecular complex **III...3.1a** (Figure 3.6). This process is an endothermic (**III...3.1a** → **XIV**, $\Delta G = 10.6$ kcal/mol), followed by the σ -bond metathesis of Ru-C with O-H of **3.1a**, giving the product **2.6a** and complex **XV**. Then, it undergoes β -hydride elimination and isomerization to re-establish the complex **II**. The process (**XV** → **II**) is thermodynamically downhill ($\Delta G = -17.6$ kcal/mol).

These observations open up the possibility of both the alcoholysis and hydrogenation pathway giving to the formation product **2.6a**. Lastly, the Ru-H and N-H cooperation involved in the metal hydride intermediate **II** by -OH group of the alcohol **3.1a** to yield H_2 and regenerates the active catalyst **I** via the transition state **O-TS-4** with energy barrier $\Delta G^\ddagger = 32.8$ kcal/mol (Figure 3.3).

3.2.8. Summary

In summary, a phosphine-free pincer ruthenium-catalyzed cross-coupling of primary and secondary alcohols to α -substituted ketones and two different secondary alcohols to β -disubstituted ketones were demonstrated. The preliminary mechanistic studies indicated that the dehydrogenation of alcohol follows proton shuttle type of TS and the involvement of “borrowing hydrogen” catalysis.

The use of air-stable catalyst, a catalytic amount of base, aerobic reaction condition, and high selectivity in the C-C bond formation are the important practical features.

3.3. 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. 1-([1,1'-biphenyl]-4-yl)ethan-1-ol,^{42, 43} 1-(4-(phenylethynyl)phenyl)ethan-1-ol,^{44, 45} 4-(allyloxy)-benzyl alcohol⁴⁶ were prepared according to the reported literature. ¹H, ¹³C, and ¹⁹F NMR spectra of the compounds were measured in CDCl₃, DMSO-*d*₆, CD₃OD as a solvent by using TMS as an internal standard. Chemical shifts, δ (in ppm), are reported relative to TMS δ (¹H) 0.0 ppm, δ (¹³C) 0.0 ppm, which was used as the internal reference. Otherwise the solvents residual proton resonance and carbon resonance (CHCl₃, δ (¹H) 7.26 ppm, δ (¹³C) 77.16 ppm; DMSO-*d*₆, (¹H) 2.50 ppm, δ (¹³C) 39.52 ppm; CD₃OD, δ (¹H) 3.31 ppm, δ (¹³C) 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 μ L, 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). All the catalytic cross coupling of alcohols was carried out under air and in preheated oil baths.

A. General procedure for the synthesis of α -alkylated ketones (GP-1):

A mixture of primary alcohol (1 mmol, 1 equiv), secondary alcohol (1 mmol, 1 equiv), **2.12b** (1 mol%), KO^tBu (10 mol%) and 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 120 °C 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 was obtained by column chromatography over silica gel using ethyl acetate / petroleum ether mixture as an eluent.

B. General procedure for synthesis of β -disubstituted ketones (GP-2):

A mixture of aromatic secondary alcohol (1 mmol, 1 equiv), aliphatic secondary alcohol (1 mmol, 1 equiv), **2.12b** (2 mol%), KO^tBu (20 mol%) and 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 °C 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. The crude reaction mixture was purified by column chromatography over silica gel using petroleum ether or ethyl acetate/ petroleum ether mixture as an eluent.

C. Experimental procedure for gram-scale cross-coupling reactions

For 3.3c: A mixture of **3.1c** (6.6 mmol, 1 equiv.), **3.2a** (1 gm, 6.6 mmol, 1 equiv.), **2.12b** (1 mol%), KO^tBu (10 mol%) and toluene (16 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 120 °C with continuous stirring for 24 hours. The resulting mixture was then passed through a bed of celite, the filtrate was collected and concentrated under reduced pressure. Analytically pure product 1.436 g

(91%) was obtained by column chromatography over silica gel using ethyl acetate / petroleum ether mixture as an eluent.

For 2.6c: A mixture of **3.1c** (1 gm, 6.6 mmol, 1 equiv), **2.2a** (6.6 mmol, 1 equiv), **2.12b** (2 mol%), KO^tBu (20 mol%) and toluene (16 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 °C with continuous stirring for 24 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 0.992 g (65% yield).

D. Mechanistic studies

i) Mercury drop test

To establish the homogeneity of **2.12b** in cross-coupling reaction, mercury drop experiment was carried out (Scheme 3.4).

Catalytic cross coupling of primary and secondary alcohols

In this test, the reaction tube was charged with 1 mmol of **3.2a** (108 mg), 1 mmol of **3.1c** (152 mg), 0.5 mmol of mercury (100 mg), 10 mol% of KO^tBu (11 mg) and 1 mol% of complex **2.12b** (6 mg). To this reaction mixture, 2 mL of toluene was added and heated at 120 °C for 12 h. The product **3.3c** was obtained in 91% of yield, confirmed the homogenous behavior of the catalyst.

Catalytic cross coupling of secondary alcohols

In this test, the reaction tube was charged with 1 mmol (152 mg) of **3.1c**, 1 mmol (100 mg) of **2.2a**, 0.5 mmol (100 mg) of mercury, 20 mol% of KO^tBu (22 mg) and 2 mol% of complex **2.12b** (12 mg). To this reaction mixture, 2 mL of toluene was added and heated at 150 °C for 12 h. The product **2.6c** was obtained in 86% of yield, demonstrated the homogenous behavior of the catalytic process.

ii) Hydrogenation of styrene by evolved hydrogen during cross-coupling of alcohols

Experimental procedure

An oven dried H-shaped bridged tube was equipped with a magnetic stir bar. Under Ar atmosphere, chamber one charged with catalyst **2.12b** (1 mol%), 1 mmol of **3.1c**, 1 mmol of **3.2a**, KO^tBu (10 mol%), and toluene (1 mL) and chamber two in which styrene (1 mmol), Pd/C (4 mg) were placed in ^tAmOH (1.5 mL). Both chambers were closed with cap. The sealed bridged tube was placed in preheated oil bath at 120 °C for 12 h. After completion of the reaction, small portion of aliquot taken from chamber two for GC analysis, revealed conversion of styrene to ethyl benzene (33%) (Scheme 3.5a).

Similarly, the following experiment was performed for cross-coupling of two different secondary alcohols with catalyst **2.12b** (2 mol%), KO^tBu (20 mol%), 1 mmol of **3.1c**, and 1 mmol of **2.2a**, in toluene (1 mL). the conversion of styrene to ethyl benzene was observed in 38% (Scheme 3.5b).

iii) The impact of the NH functionality in ruthenium complex

Experimental procedure for 3.3c (Scheme 3.6a): A mixture of **3.1c** (1 mmol, 1 equiv), **3.2a** (1 mmol, 1 equiv), **2.12b**^{Me} (1 mol%), KO^tBu (10 mol%) and 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 120 °C 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 (53%) was obtained by column chromatography over silica gel using ethyl acetate / petroleum ether mixture as an eluent.

Experimental procedure for 2.6c (Scheme 3.6b): A mixture of **3.1c** (1 mmol, 1 equiv), **2.2a** (1 mmol, 1 equiv), **2.12b**^{Me} (2 mol%), KO^tBu (20 mol%) and 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 °C 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. The crude reaction mixture was purified by column chromatography over silica gel using petroleum ether or ethyl acetate / petroleum ether mixture as an eluent (35% yield).

iv) Proof for the formation of intermediate aldehyde, ketone or α,β -unsaturated ketone

Cross coupling of ketone and aldehyde in the absence of catalyst (Scheme 3.7a)

Procedure: A mixture of **3.2a'** (106 mg, 1 mmol, 1 equiv), **2.5c** (150 mg, 1 mmol, 1 equiv), KO^tBu (11 mg, 0.1 mmol, 0.1 equiv) and toluene (1.5 mL) was loaded into the reaction tube and heated at 120 °C for 12 h. The product **3.3c-I** was isolated as white solid in 63% of yield.

Cross coupling of ketone and aldehyde in the presence of catalyst (Scheme 3.7a)

Procedure: A mixture of **2.2a'** (106 mg, 1 mmol, 1 equiv), **2.5a** (150 mg, 1 mmol, 1 equiv.), KO^tBu (11 mg, 0.1 mmol, 0.1 equiv.), complex **2.12b** (6 mg, 0.01 mmol, 0.01 equiv.) and toluene (1.5 mL) was loaded into the reaction tube and heated at 120 °C for 12 h. The product **2.6a-I** was isolated as white solid in 81% (192 mg) of yield.

Cross coupling of two different ketones (Scheme 3.7b)

Procedure: A mixture of **2.5a** (120 mg, 1 mmol, 1 equiv), **2.2a'** (98 mg, 1 mmol, 1 equiv), KO^tBu (22 mg, 0.2 mmol, 0.2 equiv), complex **2.12b** (12 mg, 0.02 mmol, 0.02 equiv) and toluene (1.5 mL) was loaded into the reaction tube and heated at 150 °C for 12 h. The product **2.6a-I** was isolated as colorless liquid in 20% yield. In absence of **2.12b**, complex mixture was observed.

Reaction of α,β -unsaturated ketone (**3.3c-I**) with primary alcohol in the presence of catalyst (Scheme 3.7c)

Procedure: A mixture of **3.3c-I** (50 mg, 0.21 mmol, 1 equiv), **3.2a** (45 mg, 0.42 mmol, 2 equiv.), KO^tBu (3 mg, 0.021 mmol, 0.1 equiv.), complex **2.12b** (2 mg, 0.0021 mmol, 0.01 equiv.) and toluene (1.5 mL) was loaded into the reaction tube and heated at 120 °C for 12 h. The product **3.3c-I** was isolated as white solid in 96% (230 mg) of yield.

Reaction of α,β -unsaturated ketone (**2.6a-I**) with secondary alcohol in presence of catalyst (Scheme 3.7d)

Procedure: A mixture of **2.6a-I** (100 mg, 0.5 mmol, 1 equiv), **2.2a** (49 mg, 0.5 mmol, 1 equiv), KO^tBu (11 mg, 0.1 mmol, 0.2 equiv), complex **2.12b** (6 mg, 0.01 mmol, 0.02 equiv) and toluene (1 mL) was loaded into the reaction tube and heated at 150 °C for 12 h. The product **2.6a** was isolated as colorless liquid in 95% yield.

Reaction of α,β -unsaturated ketone with hydrogen in presence of catalyst (Scheme 3.7e)

For 3.3c: 1 mmol of **3.3c-I**, catalyst **2.12b** (1 mol%), KO^tBu (10 mol%), molecular hydrogen (10 bar) and toluene (1 mL) was loaded in autoclave and heated at 120 °C for 12 h with stirring. Then, autoclave was brought at room temperature. The remaining gas was carefully released and benzene was used as an internal standard and the reaction mixture was analyzed by gas chromatography to get the desired product **3.3c** (45%).

For 3.6a: 1 mmol of **2.6a-I**, catalyst **2.12b** (2 mol%), KO^tBu (20 mol%), molecular hydrogen (10 bar) and toluene (1 mL) was loaded in autoclave and heated at 150 °C for 12 h with stirring. Then, autoclave was brought at room temperature. The remaining gas was carefully released and benzene was used as an internal standard and the reaction mixture was analyzed by gas chromatography to get the desired product **2.6a** (78%).

Procedure: In this test, the reaction tube was charged with **3.1c** (34 mg, 0.22 mmol, 1 equiv), **2.2a** (22 mg, 0.22 mmol, 1 equiv), KO^tBu (5 mg, 0.044 mmol, 0.2 equiv) and complex **2.12b** (3 mg, 0.0044 mmol, 0.02 equiv), heated at 150 °C for 2 h with continuous stirring, then benzene was used as an internal standard and the reaction mixture was analysed by gas chromatography to get the desired product **2.5c** (11%) and **2.2a'** (18%), respectively.

vi) Deuterium labelling experiment

For 3.3c-D:

A reaction tube (25 mL) was equipped with a stir bar, catalyst **2.12b** (6 mg, 0.01 mmol), KO^tBu (0.1 mmol), benzyl alcohol **3.2a** (108 mg, 1 mmol, 1 equiv), deuterated secondary alcohol **3.1c-D** (153 mg, 1 mmol, 1 equiv) and toluene (1.5 mL). The flask was closed and the solution was stirred at 120 °C (oil bath temperature) for 12 h. The completion of the reaction was monitored using TLC analysis. After cooling to room temperature, solution was filtered and the solvent was evaporated and crude reaction mixture was purified by column chromatography over silica-gel (60-120 mesh) using ethyl acetate / petroleum ether (v/v = 1:100, R_f = 0.5) mixture as an eluent. Pure white solid product was isolated in 85% (204 mg) of yield (Figure 3.4).

For 2.6c-D:

A reaction tube (25 mL) was equipped with a stir bar, catalyst **2.12b** (0.02 mmol), KO^tBu (0.2 mmol), cyclohexanol **2.2a** (100 mg, 1 mmol, 1equiv.), deuterated secondary alcohol **3.1c-D** (153 mg, 1 mmol, 1 equiv.) and toluene (1.5 mL). The flask was closed and the solution was stirred at 150 °C (oil bath temperature) for 12 h. The completion of the reaction was monitored using TLC analysis. After cooling to room temperature, solution was filtered and the solvent was evaporated and crude reaction mixture was purified by column chromatography over silica-gel (60-120 mesh) using ethyl acetate / petroleum ether (v/v = 1: 50, R_f = 0.5) mixture as an eluent. Pure product was isolated as colorless oil in 78% (187 mg) of yield (Figure 3.5).

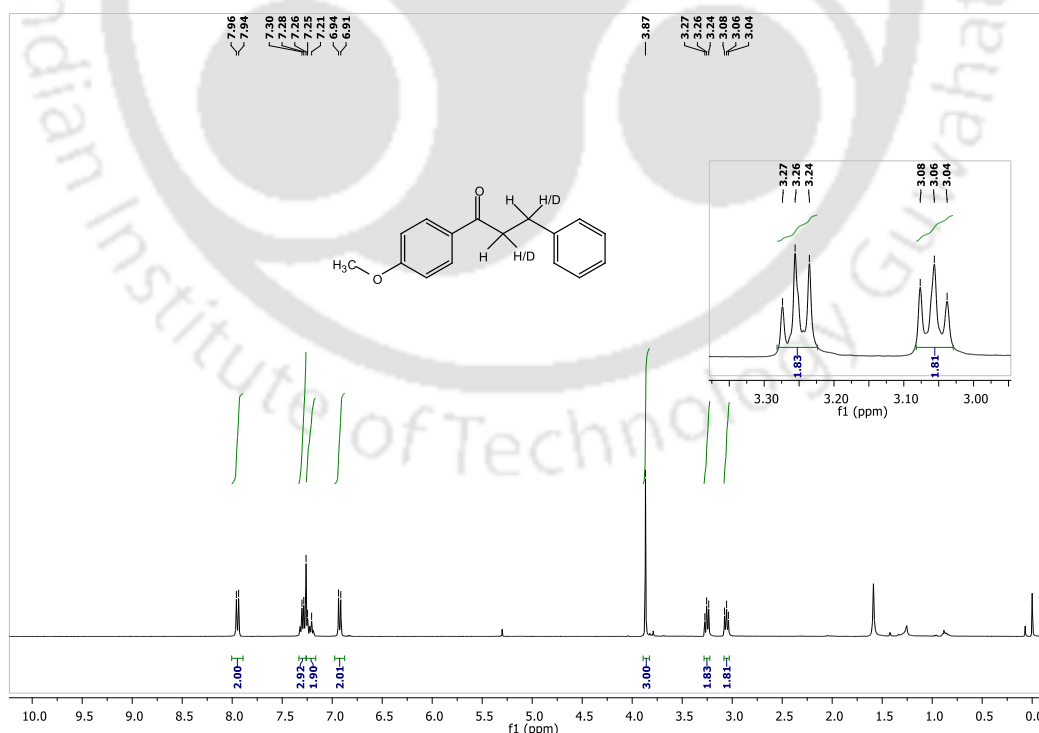


Figure 3.7. Deuterium labelling experiment for cross-coupling of primary and secondary alcohols

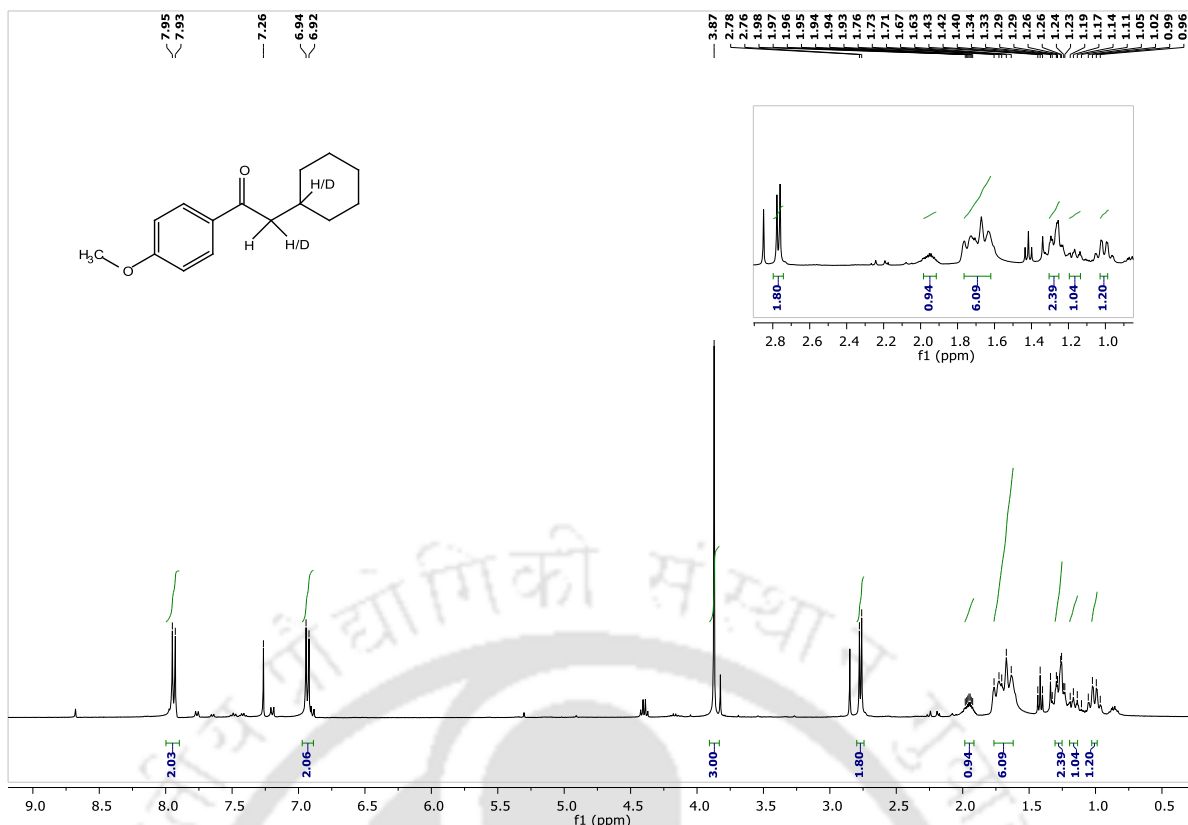
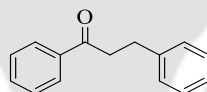


Figure 3.8. Deuterium-labelling experiment for cross-coupling of secondary alcohols

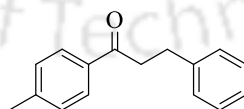
3.4. Analytical data of the products:

1,3-diphenylpropan-1-one (3.3a)⁴⁷



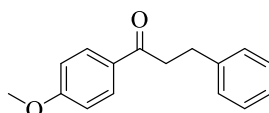
Using GP-1, the title compound **3.3a** was obtained as colourless oil using silica-gel column chromatography with petroleum ether and ethyl acetate (v/v = 50:1, R_f = 0.5); 86% yield (0.181 g). ^1H NMR (400 MHz, CDCl_3): δ 7.96 (d, J = 7.1 Hz, 2H, ArH), 7.56 (t, J = 7.4 Hz, 1H, ArH), 7.46 (t, J = 7.6 Hz, 2H, ArH), 7.33 – 7.27 (m, 3H, ArH), 7.25 – 7.17 (m, 2H, ArH), 3.31 (t, J = 7.2 Hz, 2H, COCH_2), 3.07 (t, J = 7.4 Hz, 2H, CH_2). ^{13}C NMR (101 MHz, CDCl_3): δ 199.4 (CO), 141.4, 137.0, 133.2, 128.7, 128.7, 128.6, 128.2, 126.3, 40.6 (COCH_2), 30.3 (CH_2).

3-phenyl-1-(p-tolyl)propan-1-one (3.3b)⁴⁸



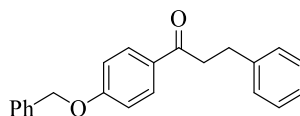
Using GP-1, the title compound **3.3b** was isolated as white solid using silica gel column chromatography with petroleum ether and ethyl acetate (v/v = 20:1, R_f = 0.5); 92% yield (0.206 g) M.p. = 68 – 70 °C. ^1H NMR (400 MHz, CDCl_3): δ 7.86 (d, J = 8.2 Hz, 2H, ArH), 7.32 – 7.28 (m, 2H, ArH), 7.27 – 7.22 (m, 4H, ArH), 3.27 (t, J = 8.2 Hz, 2H, COCH_2), 3.06 (t, J = 7.4 Hz, 2H, CH_2), 2.40 (s, 3H, CH_3). ^{13}C NMR (101 MHz, CDCl_3): δ 199.0 (C=O), 143.9, 141.5, 134.6, 129.4, 128.6, 128.6, 128.3, 126.2, 40.5 (COCH_2), 30.4 (CH_2), 21.8 (CH_3).

1-(4-methoxyphenyl)-3-phenylpropan-1-one (3.3c)⁴⁷



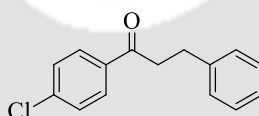
Using GP-1, the title compound **3.3c** was isolated as white solid using silica gel column chromatography with petroleum ether and ethyl acetate (v/v = 20:1, R_f = 0.5); 93% yield (0.223 g) M.p. = 95 – 97 °C. ^1H NMR (400 MHz, CDCl_3): δ 7.95 (d, J = 8.8 Hz, 2H, ArH), 7.32-7.27 (m, 3H, ArH), 7.25-7.19 (m, 2H, ArH), 6.94-6.91 (m, 2H, ArH), 3.87 (s, 3H, CH_3), 3.26 (t, J = 7.2 Hz, 2H, COCH_2), 3.06 (t, J = 8.0 Hz, 2H, CH_2). ^{13}C NMR (151 MHz, CDCl_3): δ 197.9 (C=O), 163.6, 141.6, 130.4, 130.1, 128.6, 128.6, 126.2, 113.8, 55.6 (CH_3), 40.3 (COCH_2), 30.4 (CH_2). HRMS (ESI) m/z : $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{16}\text{H}_{17}\text{O}_2$ 241.1223; found: 241.1237.

1-(4-(benzyloxy)phenyl)-3-phenylpropan-1-one (3.3d)⁴⁹



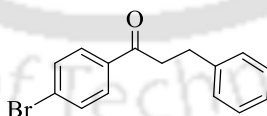
Using GP-1, the title compound **3.3d** was isolated as white solid using silica gel column chromatography with petroleum ether and ethyl acetate (v/v = 20:1, R_f = 0.5); 94% yield (0.297 g) M.p. = 128 – 130 °C. ^1H NMR (400 MHz, CDCl_3): δ 7.93 (d, J = 8.0 Hz, 2H, ArH), 7.46-7.26 (m, 7H, ArH), 7.22-7.18 (m, 3H, ArH), 7.00 (d, J = 8.9 Hz, 2H, ArH), 5.12 (s, 2H, OCH_2), 3.26-3.23 (t, J = 7.1 Hz, 2H, COCH_2), 3.03-3.07 (t, J = 8.1 Hz, 2H, CH_2). ^{13}C NMR (101 MHz, CDCl_3) δ 197.9 (C=O), 162.7, 141.6, 136.3, 130.5, 130.3, 128.8, 128.7, 128.6, 128.4, 127.6, 126.2, 114.7, 70.3 (OCH_2), 40.3 (COCH_2), 30.5 (CH_2). HRMS (ESI) m/z : $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{22}\text{H}_{21}\text{O}_2$ 317.1536; found: 317.1528.

1-(4-chlorophenyl)-3-phenylpropan-1-one (3.3e)⁵⁰



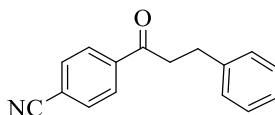
Using GP-1, the title compound **3.3e** was isolated as white solid using silica gel column chromatography with petroleum ether and ethyl acetate (v/v = 20:1, R_f = 0.5); 91% yield (0.221 g) M.p. = 77 – 79 °C. ^1H NMR (600 MHz, CDCl_3): δ 7.88 (d, J = 8.6 Hz, 2H, ArH), 7.41 (d, J = 8.6 Hz, 2H, ArH), 7.29 (t, J = 7.5 Hz, 2H, ArH), 7.24 – 7.19 (m, 3H, ArH), 3.25 (t, J = 7.4 Hz, 2H, COCH_2), 3.05 (t, J = 7.7 Hz, 2H, CH_2). ^{13}C NMR (101 MHz, CDCl_3): δ 198.1 (C=O), 141.2, 139.6, 135.3, 129.6, 129.0, 128.7, 128.5, 126.3, 40.5 (COCH_2), 30.2 (CH_2). HRMS (ESI) m/z : $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{15}\text{H}_{14}\text{ClO}$ 245.0727; found: 245.0728.

1-(4-bromophenyl)-3-phenylpropan-1-one (3.3f)⁵⁰



Using GP-1, the title compound **3.3f** was isolated as white solid using silica gel column chromatography with petroleum ether and ethyl acetate (v/v = 20:1, R_f = 0.5); 92% yield (0.265 g) M.p. = 99 – 101 °C. ^1H NMR (400 MHz, CDCl_3): δ 7.83–7.80 (m, 2H, ArH), 7.62–7.58 (m, 2H, ArH), 7.38–7.14 (m, 5H, ArH), 3.27 (t, J = 7.6 Hz, 2H, COCH_2), 3.06 (t, J = 7.6 Hz, 2H, CH_2). ^{13}C NMR (101 MHz, CDCl_3): δ 198.35 (C=O), 141.2, 135.7, 132.1, 129.7, 128.7, 128.5, 128.4, 126.4, 40.6 (COCH_2), 30.1 (CH_2).

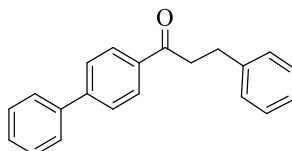
4-(3-phenylpropanoyl)benzonitrile (3.3g)⁵⁰



Using GP-1, the title compound **3.3g** was isolated as white solid using silica gel column chromatography with petroleum ether and ethyl acetate (v/v = 10:1, R_f = 0.5); 54% yield (0.127 g)

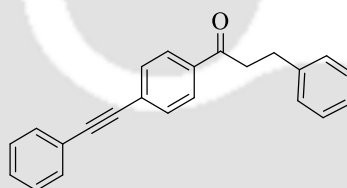
M.p. = 93 – 95 °C. ^1H NMR (400 MHz, CDCl_3): δ 8.03 (d, J = 8.4 Hz, 2H, ArH), 7.76 (d, J = 8.5 Hz, 2H, ArH), 7.32-7.29 (m, 2H, ArH), 7.25-7.20 (m, 3H, ArH), 3.31 (t, J = 7.6 Hz, 2H, COCH_2), 3.08 (t, J = 7.5 Hz, 2H, CH_2). ^{13}C NMR (101 MHz, CDCl_3): δ 197.9 (C=O), 140.8, 139.9, 132.7, 128.8, 128.6, 128.5, 126.5, 118.1, 116.5, 40.9 (COCH_2), 30.0 (CH_2). Additionally, the compound 4-(1-hydroxyethyl)benzonitrile (**5g**, 30%) was recovered after column chromatography.

1-([1,1'-biphenyl]-4-yl)-3-phenylpropan-1-one (**3.3h**)⁶



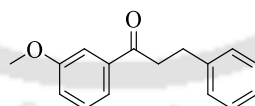
Using GP-1, the title compound **3.3h** was isolated as white solid using silica gel column chromatography with petroleum ether and ethyl acetate (v/v = 10:1, R_f = 0.5); 88% yield (0.251 g) M.p. = 88 – 90 °C. ^1H NMR (400 MHz, CDCl_3): δ 8.04 (d, J = 8.4 Hz, 2H, ArH), 7.68 (d, J = 8.4 Hz, 2H, ArH), 7.64-7.62 (m, 2H, ArH), 7.47 (t, J = 7.5 Hz, 2H, ArH), 7.42-7.38 (m, 1H, ArH), 7.33-7.13 (m, 5H, ArH), 3.36-3.32 (m, 2H, COCH_2), 3.12 – 3.08 (m, 2H, CH_2). ^{13}C NMR (101 MHz, CDCl_3): δ 198.9 (C=O), 145.8, 141.3, 139.9, 135.6, 128.9, 128.7, 128.6, 128.4, 128.2, 127.3, 126.2, 40.5 (COCH_2), 30.2 (CH_2).

3-phenyl-1-(4-(phenylethynyl)phenyl)propan-1-one (**3.3i**)⁵¹



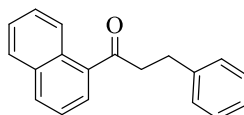
Using GP-1, the title compound **3.3i** was isolated as white solid using silica gel column chromatography with petroleum ether and ethyl acetate (v/v = 50:1, R_f = 0.5); 83% yield (0.257 g) M.p. = 75 – 77 °C. ^1H NMR (400 MHz, CDCl_3): δ 7.94 (d, J = 8.4 Hz, 2H, ArH), 7.70 – 7.54 (m, 4H, ArH), 7.38 – 7.34 (m, 3H, ArH), 7.33 – 7.22 (m, 5H, ArH), 3.33 – 3.29 (m, 2H, COCH_2), 3.10 – 3.06 (m, 2H, CH_2). ^{13}C NMR (101 MHz, CDCl_3): δ 198.6 (C=O), 141.3, 136.1, 131.9, 131.9, 129.1, 128.9, 128.7, 128.6, 128.6, 128.1, 126.3, 122.8, 92.9 ($\text{C}\equiv\text{C}$), 88.7 ($\text{C}\equiv\text{C}$), 40.6 (COCH_2), 30.3 (CH_2).

1-(3-methoxyphenyl)-3-phenylpropan-1-one (**3.3j**)⁵⁰



Using GP-1, the title compound **3.3j** was isolated as colourless liquid using silica gel column chromatography with petroleum ether and ethyl acetate (v/v = 50:1, R_f = 0.5); 84% yield (0.204 g). ^1H NMR (400 MHz, CDCl_3) δ 7.52 (d, J = 7.7 Hz, 1H, ArH), 7.49 – 7.47 (m, 1H, ArH), 7.36 – 7.18 (m, 6H, ArH), 7.09 (dd, J = 2.8, 8 Hz, 1H, ArH), 3.83 (s, 3H, CH_3), 3.28 (t, J = 7.7 Hz, 2H, COCH_2), 3.05 (t, J = 7.7 Hz, 2H, CH_2). ^{13}C NMR (101 MHz, CDCl_3) δ 199.1 (C=O), 159.9, 141.4, 138.3, 129.7, 128.6, 128.5, 126.2, 120.8, 119.6, 112.4, 55.5 (CH_3), 40.6 (COCH_2), 30.3 (CH_2). HRMS (ESI) m/z : $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{16}\text{H}_{17}\text{O}_2$ 241.1223; found: 241.1234.

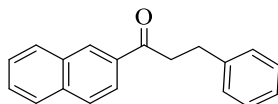
1-(naphthalen-1-yl)-3-phenylpropan-1-one (**3.3k**)⁵²



Using GP-1, the title compound **3.3k** was isolated as colourless oil using silica gel column chromatography with petroleum ether and ethyl acetate (v/v = 20:1, R_f = 0.5); 90% yield (0.234 g).

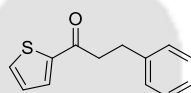
^1H NMR (400 MHz, CDCl_3): δ 8.54 (d, $J = 8.4$ Hz, 1H, ArH), 7.96 (d, $J = 8.0$ Hz, 1H, ArH), 7.86 (d, $J = 8.0$ Hz, 1H, ArH), 7.81 (d, $J = 8.0$ Hz, 1H, ArH), 7.59-7.44 (m, 3H, ArH), 7.31-7.24 (m, 3H, ArH), 7.22-7.12 (m, 2H, ArH), 3.38 (t, $J = 7.2$ Hz, 2H, COCH_2), 3.13 (t, $J = 8$ Hz, 2H, CH_2). ^{13}C NMR (101 MHz, CDCl_3): δ 203.7 (C=O), 136.1, 134.1, 132.7, 130.3, 129.2, 128.7, 128.6, 128.5, 128.0, 127.5, 126.6, 126.3, 125.9, 124.5, 43.9 (COCH_2), 30.7 (CH_2).

1-(naphthalen-2-yl)-3-phenylpropan-1-one (3.3l)⁵³



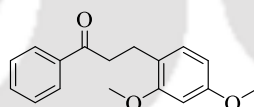
Using GP-1, the title compound **3.3l** was isolated as colourless oil using silica gel column chromatography with petroleum ether and ethyl acetate (v/v = 20:1, $R_f = 0.5$); 91% yield (0.237 g). ^1H NMR (400 MHz, CDCl_3): δ 8.39 (s, 1H, ArH), 7.97 (dd, $J = 8.6, 1.6$ Hz, 1H, ArH), 7.88 – 7.69 (m, 3H, ArH), 7.56 – 7.42 (m, 2H, ArH), 7.27 – 7.04 (m, 5H, ArH), 3.38 ($J = 7.2$ Hz, 2H, COCH_2), 3.06 ($J = 8$ Hz, 2H, CH_2). ^{13}C NMR (101 MHz, CDCl_3): δ 199.3 (C=O), 141.5, 135.7, 134.3, 132.7, 129.8, 129.7, 129.2, 128.7, 128.6, 128.6, 127.9, 126.9, 126.3, 124.0, 40.7 (COCH_2), 30.4 (CH_2).

3-phenyl-1-(thiophen-2-yl)propan-1-one (3.3m)⁴⁷



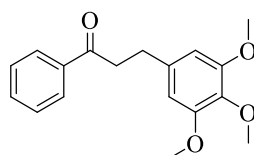
Using GP-1, the title compound **3.3m** was isolated as colourless liquid using silica gel column chromatography with petroleum ether and ethyl acetate (v/v = 50:1, $R_f = 0.5$); 82% yield (0.177 g). ^1H NMR (400 MHz, CDCl_3): δ 7.69 (dd, $J = 3.8, 1.0$ Hz, 1H, ArH), 7.62 (dd, $J = 4.9, 1.0$ Hz, 1H, ArH), 7.32 – 7.19 (m, 5H, ArH), 7.11 (dd, $J = 4.9, 3.8$ Hz, 1H, ArH), 3.25-3.22 (m, 2H, COCH_2), 3.07 (t, $J = 7.7$ Hz, 2H, CH_2). ^{13}C NMR (101 MHz, CDCl_3): δ 192.3 (C=O), 144.3, 141.1, 133.7, 131.9, 128.7, 128.5, 128.2, 126.3, 41.3 (COCH_2), 30.5 (CH_2).

3-(2,4-dimethoxyphenyl)-1-phenylpropan-1-one (3.3n)⁴⁷



Using GP-1, the title compound **3.3n** was isolated as colourless liquid using silica gel column chromatography with petroleum ether and ethyl acetate (v/v = 50:1, $R_f = 0.5$); 90% yield (0.243 g). ^1H NMR (400 MHz, CDCl_3) δ 7.98 (d, $J = 7.2$ Hz, 2H, ArH), 7.54 (t, $J = 7.4$ Hz, 1H, ArH), 7.45 (t, $J = 7.6$ Hz, 2H, ArH), 7.10 (d, $J = 8.2$ Hz, 1H, ArH), 6.46-6.41 (m, 2H, ArH), 3.81 (s, 3H, CH_3), 3.80 (s, 3H, CH_3), 3.23 (t, $J = 7.2$ Hz, 2H, COCH_2), 2.98 (t, $J = 7.3$ Hz, 2H, CH_2). ^{13}C NMR (101 MHz, CDCl_3) δ 200.3 (C=O), 159.6, 158.5, 137.1, 132.9, 130.4, 128.6, 128.2, 122.0, 104.0, 98.7, 55.5 (CH_3), 55.3 (CH_3), 39.3 (COCH_2), 25.3 (CH_2). HRMS (ESI) m/z : $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{17}\text{H}_{19}\text{O}_3$ 271.1328; found: 271.1331.

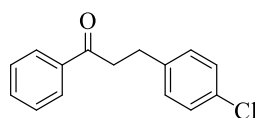
1-phenyl-3-(3,4,5-trimethoxyphenyl)propan-1-one (3.3o)⁵⁰



Using GP-1, the title compound **3.3o** was isolated as colourless liquid using silica gel column chromatography with petroleum ether and ethyl acetate (v/v = 20:1, $R_f = 0.5$); 89% yield (0.267 g). ^1H NMR (400 MHz, CDCl_3): δ 7.96 (d, $J = 7.1$ Hz, 2H, ArH), 7.57 (t, $J = 7.4$ Hz, 1H, ArH), 7.46 (t, $J = 7.6$ Hz, 2H, ArH), 6.46 (s, 2H, ArH), 3.85 (s, 6H, CH_3), 3.82 (s, 3H, CH_3), 3.30 (t, $J = 7.6$ Hz, 2H, COCH_2), 3.02 (t, $J = 7.6$ Hz, 2H, CH_2). ^{13}C NMR (101 MHz, CDCl_3): δ 199.4 (C=O), 153.4,

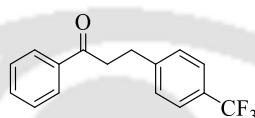
137.2, 137.0, 133.3, 128.8, 128.2, 105.5, 61.0 (CH₃), 56.2 (CH₃), 40.7 (COCH₂), 30.8 (CH₂). HRMS (ESI) *m/z*: [M+H]⁺ calculated for C₁₈H₂₁O₄ 301.1434; found: 301.1435.

3-(4-chlorophenyl)-1-phenylpropan-1-one (3.3p)⁵⁴



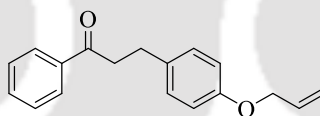
Using GP-1, the title compound **3.3p** was isolated as white solid using silica gel column chromatography with petroleum ether and ethyl acetate (v/v = 10:1, *R_f* = 0.6); 83% yield (0.202 g) M.p. = 57 – 59 °C. ¹H NMR (400 MHz, CDCl₃): δ 7.95 (d, *J* = 8.4 Hz, 2H, ArH), 7.59-7.54 (m, 1H, ArH), 7.48-7.44 (m, 2H, ArH), 7.27-7.25 (m, 2H, ArH), 7.20-7.18 (m, 2H, ArH), 3.29 (t, *J* = 7.2 Hz, 2H, COCH₂), 3.05 (t, *J* = 7.5 Hz, 2H, CH₂). ¹³C NMR (101 MHz, CDCl₃): δ 199.0 (C=O), 139.9, 136.9, 133.3, 132.0, 129.9, 128.8, 128.7, 128.2, 40.3 (COCH₂), 29.5 (CH₂).

1-phenyl-3-(4-(trifluoromethyl)phenyl)propan-1-one (3.3q)^{2, 52}



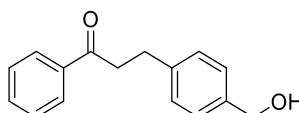
Using GP-1, the title compound **3.3q** was isolated as colourless liquid using silica gel column chromatography with petroleum ether and ethyl acetate (v/v = 10:1, *R_f* = 0.5); 84% yield (0.233 g). ¹H NMR (400 MHz, CDCl₃): δ 7.95 (d, *J* = 7.2 Hz, 2H, ArH), 7.59 – 7.54 (m, 3H, ArH), 7.46 (t, *J* = 7.6 Hz, 2H, ArH), 7.37 (d, *J* = 8.0 Hz, 2H, ArH), 3.33 (t, *J* = 7.4 Hz, 2H, COCH₂), 3.14 (t, *J* = 7.5 Hz, 2H, CH₂). ¹³C NMR (101 MHz, CDCl₃): δ 198.7 (C=O), 145.6, 136.8, 133.4, 128.9, 128.8, 128.1, 125.6 (q, C-F, ¹*J*_{C-F} = 3.8 Hz), 39.9 (COCH₂), 29.9 (CH₂). ¹⁹F NMR (377 MHz, CDCl₃): δ -62.4. HRMS (ESI) *m/z*: [M+H]⁺ calculated for C₁₆H₁₄F₃O 279.0991; found: 279.0990.

3-(4-(allyloxy)phenyl)-1-phenylpropan-1-one (3.3r)⁵⁵



Using GP-1, the title compound **3.3r** was isolated as colourless liquid using silica gel column chromatography with petroleum ether and ethyl acetate (v/v = 100:1, *R_f* = 0.5); 86% yield (0.229 g). ¹H NMR (400 MHz, CDCl₃): δ 7.96 – 7.94 (m, 2H, ArH), 7.55 (dd, *J* = 10.5, 4.2 Hz, 1H, ArH), 7.45 (t, *J* = 7.6 Hz, 2H, ArH), 7.16 (d, *J* = 8.5 Hz, 2H, ArH), 6.88 – 6.82 (m, 2H), 6.10-6.00 (m, 1H), 5.52 – 5.38 (m, 1H), 5.29 – 5.26 (m, 1H), 4.52 (dt, *J* = 5.2, 1.4 Hz, 2H), 3.29-3.25 (m, 2H, COCH₂), 3.01 (t, *J* = 7.6 Hz, 2H, CH₂). ¹³C NMR (101 MHz, CDCl₃): δ 199.6 (C=O), 157.1, 137.0, 133.6, 133.6, 133.2, 129.5, 128.7, 128.2, 117.7, 114.9, 69.0, 40.8 (COCH₂), 29.4 (CH₂).

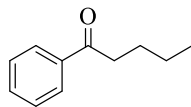
3-(4-(hydroxymethyl)phenyl)-1-phenylpropan-1-one (3.3s)



Using GP-1, the title compound **3.3s** was isolated as colourless liquid using silica gel column chromatography with petroleum ether and ethyl acetate (v/v = 5:1, *R_f* = 0.6); 88% yield (0.211 g). ¹H NMR (400 MHz, CDCl₃): δ 7.96 (d, *J* = 7.2 Hz, 2H, ArH), 7.56 (t, *J* = 7.4 Hz, 1H, ArH), 7.45 (t, *J* = 7.6 Hz, 2H, ArH), 7.33 – 7.30 (m, 2H, ArH), 7.27 – 7.24 (m, 2H, ArH), 4.66 (s, 2H, OCH₂), 3.30 (t, *J* = 7.6 Hz, 2H, COCH₂), 3.07 (t, *J* = 7.6 Hz, 2H, CH₂). ¹³C NMR (101 MHz, CDCl₃): δ 199.3 (C=O), 140.9, 138.9, 136.9, 133.2, 128.8, 128.8, 128.2, 127.5, 65.3 (OCH₂), 40.5 (COCH₂), 29.9 (CH₂). HRMS (ESI) *m/z*: [M+H]⁺ calculated for C₁₆H₁₇O₂ 241.1223; found: 241.1246. IR (KBr pellet,

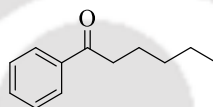
selected bands) cm^{-1} : 3383.99 (br), 3057.00 (w), 2927.97 (w), 1681.97 (s), 1597.13 (m), 1448.57 (s), 1204.16 (s).

1-phenylpentan-1-one (3.3t)⁵⁶



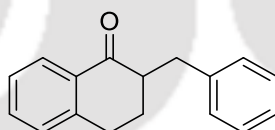
Using GP-1, the title compound **3.3t** was isolated as colourless liquid using silica gel column chromatography with petroleum ether and ethyl acetate (v/v = 100:1, R_f = 0.5); 72% yield. ^1H NMR (600 MHz, CDCl_3): δ 7.96 (d, J = 7.2 Hz, 2H, ArH), 7.55 (t, J = 7.8 Hz, 1H, ArH), 7.47–7.44 (m, 2H, ArH), 2.97 (t, J = 7.8 Hz, 2H, COCH_2), 1.73–1.71 (m, 2H), 1.44–1.38 (m, 2H), 0.96–0.94 (m, 3H, CH_3). ^{13}C NMR (101 MHz, CDCl_3): δ 200.7, 137.2, 132.9, 128.6, 128.2, 38.4, 26.6, 22.6, 14.1. Additionally, the compound acetophenone (**5a'**, 18%) was recovered after column chromatography.

1-phenylhexan-1-one (3.3u)⁵⁷



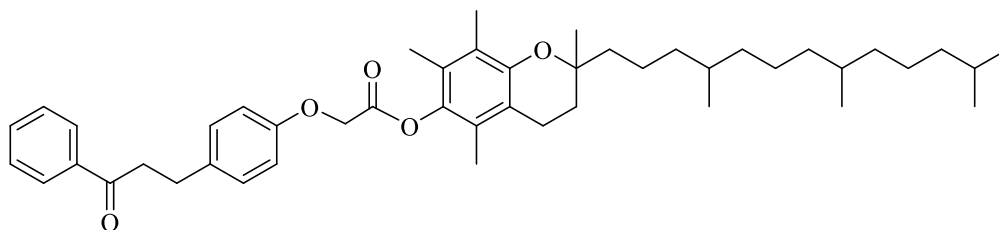
Using GP-1, the title compound **3.3u** was isolated as colourless liquid using silica gel column chromatography with petroleum ether and ethyl acetate (v/v = 100:1, R_f = 0.5); 68% yield (0.120 g). ^1H NMR (400 MHz, CDCl_3): δ 7.97–7.95 (m, 2H, ArH), 7.55 (t, J = 7.2 Hz, 1H, ArH), 7.48–7.44 (m, 2H, ArH), 2.96 (t, J = 7.6 Hz, 2H, COCH_2), 1.78–1.71 (m, 2H), 1.38–1.35 (m, 3H), 1.28–1.25 (m, 1H), 0.93–0.83 (m, 3H, CH_3). ^{13}C NMR (151 MHz, CDCl_3): δ 200.8, 137.2, 133.0, 128.7, 128.2, 38.7, 31.7, 24.2, 22.7, 14.1. Additionally, the compound acetophenone (**5a'**, 21%) was recovered after column chromatography.

2-benzyl-3,4-dihydronaphthalen-1(2H)-one (3.3v)¹⁶



Using GP-1, the title compound **3.3v** was isolated as colourless liquid using silica gel column chromatography with petroleum ether and ethyl acetate (v/v = 100:1, R_f = 0.5); 85% yield (0.20 g). ^1H NMR (600 MHz, CDCl_3): δ 8.10 (d, J = 7.8 Hz, 1H), 7.48 (td, J = 7.8, 1.2 Hz, 1H), 7.35–7.30 (m, 3H), 7.27–7.23 (m, 4H), 3.52 (dd, J = 13.8, 4.2 Hz, 1H), 3.00–2.89 (m, 2H), 2.79–2.75 (m, 1H), 2.69–2.65 (m, 1H), 2.15–2.11 (m, 1H), 1.84–1.77 (m, 1H). ^{13}C NMR (151 MHz, CDCl_3): δ 199.5, 144.1, 140.1, 133.4, 132.6, 129.4, 128.8, 128.5, 127.6, 126.7, 126.2, 49.6, 35.8, 28.7, 27.8.

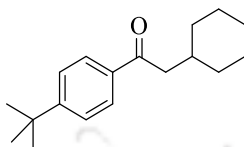
2,5,7,8-tetramethyl-2-(4,8,12-trimethyltridecyl)chroman-6-yl-2-(4-(3-oxo-3-phenylpropyl)phenoxy)acetate (3.3w)



Using GP-1, the title compound **3.3w** was isolated as colourless solid using silica gel column chromatography with pet-ether (v/v = 20:1, R_f = 0.5); 61% yield (0.424 g) M.p. = decomposed above 100 °C. ^1H NMR (600 MHz, CDCl_3): δ 7.98 (d, J = 9.0 Hz, 2H), 7.31–7.29 (m, 2H), 7.26–7.24 (m,

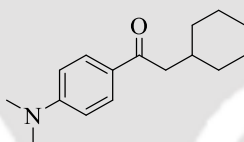
3H), 7.21 (t, $J = 7.2$ Hz, 1H), 7.03 (d, $J = 9.0$ Hz, 2H), 4.99 (s, 2H), 3.26 (t, $J = 7.8$ Hz, 2H), 3.06 (t, $J = 7.8$ Hz, 2H), 2.58 (t, $J = 7.2$ Hz, 2H), 2.08 (s, 3H), 2.01 (s, 3H), 1.96 (s, 3H), 1.82 – 1.80 (m, 1H), 1.77 – 1.73 (m, 1H), 1.66 (br, 1H), 1.58 – 1.49 (m, 3H), 1.39 – 1.34 (m, 4H), 1.32 – 1.20 (m, 10H), 1.15 – 1.12 (m, 2H), 1.11 – 1.05 (m, 4H), 0.89 – 0.84 (m, 12H). ^{13}C NMR (151 MHz, CDCl_3): δ 197.9, 167.1, 161.5, 149.9, 141.5, 139.9, 131.1, 130.5, 128.6, 128.5, 126.5, 126.2, 124.9, 123.4, 117.7, 114.6, 75.3, 65.1, 40.3, 39.5, 37.6, 37.5, 37.4, 32.9, 32.8, 31.7, 30.4, 28.1, 24.9, 24.6, 22.9, 22.8, 21.1, 20.7, 19.9, 19.8, 19.8, 19.7, 14.3, 13.2, 12.3, 11.9. HRMS (ESI) m/z : $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{46}\text{H}_{65}\text{O}_5$ 697.4827; found: 697.4834; $[\text{M}+\text{K}]^+$ calculated for $\text{C}_{46}\text{H}_{64}\text{O}_5\text{K}$ 735.4385; found: 735.4405.

1-(4-(tert-butyl)phenyl)-2-cyclohexylethan-1-one (2.6o)⁵⁸



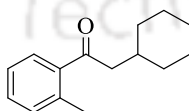
Using GP-2, the title compound **9da** was isolated as colourless liquid using silica gel column chromatography with petroleum ether and ethyl acetate (v/v = 100:1, $R_f = 0.5$); 86% yield (0.222 g). ^1H NMR (600 MHz, CDCl_3): δ 7.89 (d, $J = 8.5$ Hz, 2H), 7.47 (d, $J = 8.5$ Hz, 2H), 2.80 (d, $J = 6.8$ Hz, 2H), 2.01 – 1.95 (m, 1H), 1.76 – 1.74 (m, 2H), 1.70 – 1.64 (m, 2H), 1.34 (s, 9H), 1.30 – 1.29 (m, 2H), 1.28 – 1.25 (m, 2H), 1.02 – 1.01 (m, 2H). ^{13}C NMR (151 MHz, CDCl_3): δ 200.2, 156.7, 135.0, 128.3, 125.6, 77.4, 77.2, 76.9, 46.3, 35.2, 34.8, 33.6, 31.2, 26.4, 26.3. HRMS (ESI) m/z : $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{18}\text{H}_{26}\text{O}$ 259.2056; found: 259.2046.

2-cyclohexyl-1-(4-(dimethylamino)phenyl)ethenone (2.6p)



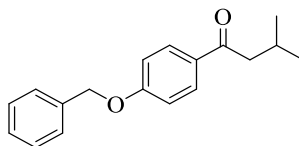
Using GP-2, the title compound **9ea** was isolated as colourless liquid using silica gel column chromatography with petroleum ether and ethyl acetate (v/v = 50:1, $R_f = 0.5$); 78% yield (0.191 g). ^1H NMR (400 MHz, CDCl_3): δ 7.87 (d, $J = 8.8$ Hz, 2H, ArH), 6.65 (d, $J = 9.2$ Hz, 2H, ArH), 3.05 (s, 6H, $\text{N}(\text{CH}_3)_2$), 2.72 (d, $J = 6.9$ Hz, 2H, COCH_2), 2.00 – 1.90 (m, 1H), 1.77 – 1.61 (m, 5H), 1.32 – 1.22 (m, 2H), 1.19 – 1.13 (m, 1H), 1.05 – 0.96 (m, 1H). ^{13}C NMR (101 MHz, CDCl_3): δ 198.8 (C=O), 153.4, 130.6, 125.9, 110.8, 45.7, 40.2, 35.4, 33.7, 26.5, 26.4. HRMS (ESI) m/z : $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{16}\text{H}_{24}\text{NO}$ 246.1853; found: 246.1873.

2-cyclohexyl-1-(o-tolyl)ethanone (2.6q)²³



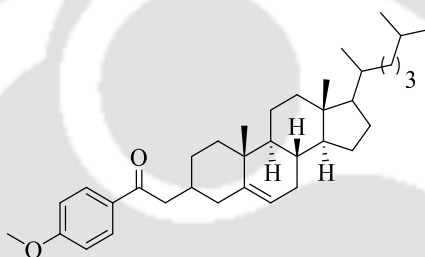
Using GP-2, the title compound **9ha** was isolated as colourless liquid using silica gel column chromatography with petroleum ether and ethyl acetate (v/v = 20:1, $R_f = 0.5$); 82% yield (0.177 g). ^1H NMR (400 MHz, CDCl_3): δ 7.58 (d, $J = 7.6$ Hz, 1H, ArH), 7.35 (td, $J = 1.2, 7.6$ Hz, 1H, ArH), 7.24 (m, 2H, ArH), 2.75 (d, $J = 6.8$ Hz, 2H, COCH_2), 2.48 (s, 3H, CH_3), 1.96 – 1.92 (m, 1H), 1.75 – 1.67 (m, 5H), 1.32 – 1.24 (m, 2H), 1.19 – 1.13 (m, 1H), 1.04 – 0.95 (m, 2H). ^{13}C NMR (101 MHz, CDCl_3): δ 204.9 (C=O), 138.9, 137.8, 132.0, 131.1, 128.4, 125.7, 49.6 (COCH_2), 34.6, 33.5, 26.4, 26.3, 21.2. HRMS (ESI) m/z : $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{14}\text{H}_{21}\text{O}_2$ 217.1586; found: 217.1586.

1-(4-(benzyloxy)phenyl)-3-methylbutan-1-one (2.6r)



Using GP-2 and 6 equiv. of isopropanol, the title compound **9df** was isolated as white solid using silica gel column chromatography with petroleum ether and ethyl acetate (v/v = 20:1, R_f = 0.5); 70% yield. ^1H NMR (400 MHz, CDCl_3): δ 7.93 (d, J = 9.2 Hz, 2H, ArH), 7.44 – 7.34 (m, 5H, ArH), 7.00 (d, J = 8.8 Hz, 2H, ArH), 5.13 (s, 2H, OCH_2), 2.77 (d, J = 6.8 Hz, 2H, COCH_2), 2.31 – 2.24 (m, 1H), 0.99 (d, J = 6.8 Hz, 6H, CH_3). ^{13}C NMR (101 MHz, CDCl_3): δ 199.0 ($\text{C}=\text{O}$), 162.6, 136.4, 130.9, 130.5, 128.8, 128.4, 127.6, 114.7, 70.3 (OCH_2), 47.4 (COCH_2), 25.5, 22.9. HRMS (ESI) m/z : $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{18}\text{H}_{21}\text{O}_2$ 269.1536; found: 269.1554. Additionally, the compound 1-(4-(benzyloxy)phenyl)ethan-1-one (**5d'**, 13%), and 1-(4-(benzyloxy)phenyl)ethan-1-ol (**5d**, 9%) were recovered after column chromatography.

2-((8S,9S,10R,13R,14S)-10,13-dimethyl-17-(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)-1-(4-methoxyphenyl)ethanone (2.6s)



Using GP-2, the title compound **9ch** was isolated as white solid using silica gel column chromatography with petroleum ether and ethyl acetate (v/v = 20:1, R_f = 0.5); 61% yield (0.316 g) M.p. = 129 – 131 °C. ^1H NMR (400 MHz, CDCl_3): δ 7.96 (d, J = 9.2 Hz, 2H, ArH), 6.92 (d, J = 8.8 Hz, 2H, ArH), 5.47 (d, J = 4.8 Hz, 1H, $\text{C}=\text{CH}$), 3.87 (s, 3H, CH_3), 3.54 (br, 1H), 1.98-1.95 (m, 2H), 1.83-1.75 (m, 3H), 1.59-1.49 (br, 5H), 1.51-1.49 (m, 3H), 1.37-1.32 (m, 5H), 1.25 (brs, 2H), 1.14-1.12 (m, 6H), 1.02-0.99 (m, 2H), 0.92-0.89 (m, 4H), 0.87-0.85 (m, 8H), 0.71 (brs, 2H), 0.65 (brs, 2H). ^{13}C NMR (101 MHz, CDCl_3): δ 197.6, 163.5, 131.3, 130.8, 130.2, 124.8, 113.8, 56.6, 56.4, 55.6, 54.0, 47.4, 42.6, 41.8, 40.3, 40.2, 39.7, 36.3, 35.9, 35.7, 34.4, 33.9, 31.9, 28.7, 28.4, 28.1, 24.3, 23.9, 22.9, 22.7, 21.2, 18.8, 12.1, 11.9. HRMS (ESI) m/z : $(\text{M}+\text{H})^+$ calculated for $\text{C}_{36}\text{H}_{55}\text{O}_2$ 519.4197; found: 519.4177.

3.5. Computational studies

All calculations were performed using the Gaussian-09 program package in the gas phase.⁵⁹ Full geometry optimizations were carried out using Minnesota 2006 local (M06-L)⁶⁰ functional and BS1 basis set. BS1 is defined as an SDD⁶¹ basis set for Ru atom and 6-31G(d,p) for all other atoms. Method and basis set was selected based on a previous report⁶² on similar complexes. Frequency calculations at the same method and basis set were performed to distinguish transition state structures and minima structures on the potential energy surface based on the availability of imaginary frequencies. The transition states were verified by the intrinsic reaction coordinate (IRC) calculations, wherever necessary.⁶³ Free energies were calculated by using frequency calculations at 150 °C to match the experimental conditions. The nuclear independent chemical shift (NICS(0)iso) calculations were calculated at the same level of theory using the gauge invariant atomic orbital (GIAO)⁶⁴⁻⁶⁶ method at the geometrical centre of the ring. Negative isotropic values determine the aromaticity of the ring whereas non-aromatic rings show positive isotropic NICS values. Co-ordinates for all the optimized structures is given in Annexure VIII (page 319).

Table 3.5. Free Energies (G) and Total Energies (E) given in Hartree along with the number of imaginary frequencies

Species	Free energy (G)	Total energy (E)	# Imaginary Frequency (NImag)
H ₂	-1.17803400	-1.1700775	0
H ₂ O	-76.416076	-76.4110228	0
cyclohexanol (2.2a)	-310.93162500	-311.0597947	0
cyclohexanone (2.2a')	-309.756482	-309.8609199	0
1-phenylethanol (3.1a)	-385.94151900	-386.0501096	0
acetophenone (2.5a)	-384.77127600	-384.858511	0
2.2a	-619.290486	-619.5160333	0
<i>Dehydrogenation outer sphere MLC pathway for 3.1a</i>			
I	-2559.40115100	-2559.9760588	0
O-TS-3	-2559.37986900	-2559.9478003	1
II	-2559.43249200	-2559.96507290	0
O-TS-4	-2559.38029900	-2559.90886140	1
I + H₂	-2559.40867100	-2559.94970420	0
<i>Hydrogenation segment</i>			
II	-2407.97763800	-2408.51309160	0
R-TS-1	-2407.97237500	-2408.50375430	1
III	-2407.97376200	-2408.50980450	0
IV (III...H₂)	-2407.957408	-2408.5132625	0
R-TS-2	-2407.94857200	-2408.5040619	1
II	-2408.00075800	-2408.56600960	0
<i>Alcoholysis segment</i>			
II	-2792.74112300	-2793.39312370	0
R-TS-1	-2792.73586000	-2793.38378640	1
III	-2792.73724700	-2793.38983660	0
III...3.1a	-2792.720846	-2793.4083892	0
XIV	-2792.703905	-2793.3965573	0
R-TS-5	-2792.688726	-2793.3789152	1
XV	-2792.76391500	-2793.41148760	0
R-TS-6	-2792.75529500	-2793.40302270	1
XVI	-2792.76759100	-2793.41612350	0
XVII	-2792.74520600	-2793.36134570	0
II	-2792.78608700	-2793.40448150	0
<i>Dehydrogenation inner sphere MLC pathway for 3.1a</i>			
I	-2559.40115100	-2559.9760588	0
I-TS-3	-2559.39929500	-2559.9689118	1
XVIII	-2559.42468700	-2559.96304640	0
XIX	-2559.41494800	-2559.94556390	0
I-TS-4	-2559.40632800	-2559.93709900	1
XX	-2559.41862400	-2559.95019980	0
XXI	-2559.396239	-2559.89542200	0
XXII	-2559.437120	-2559.93855780	0
II (XXII...3.1a)	-2559.432492	-2559.96507290	0
O-TS-4	-2559.38029900	-2559.90886140	1
I + H₂	-2559.40867100	-2559.94970420	0

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

3.6. References

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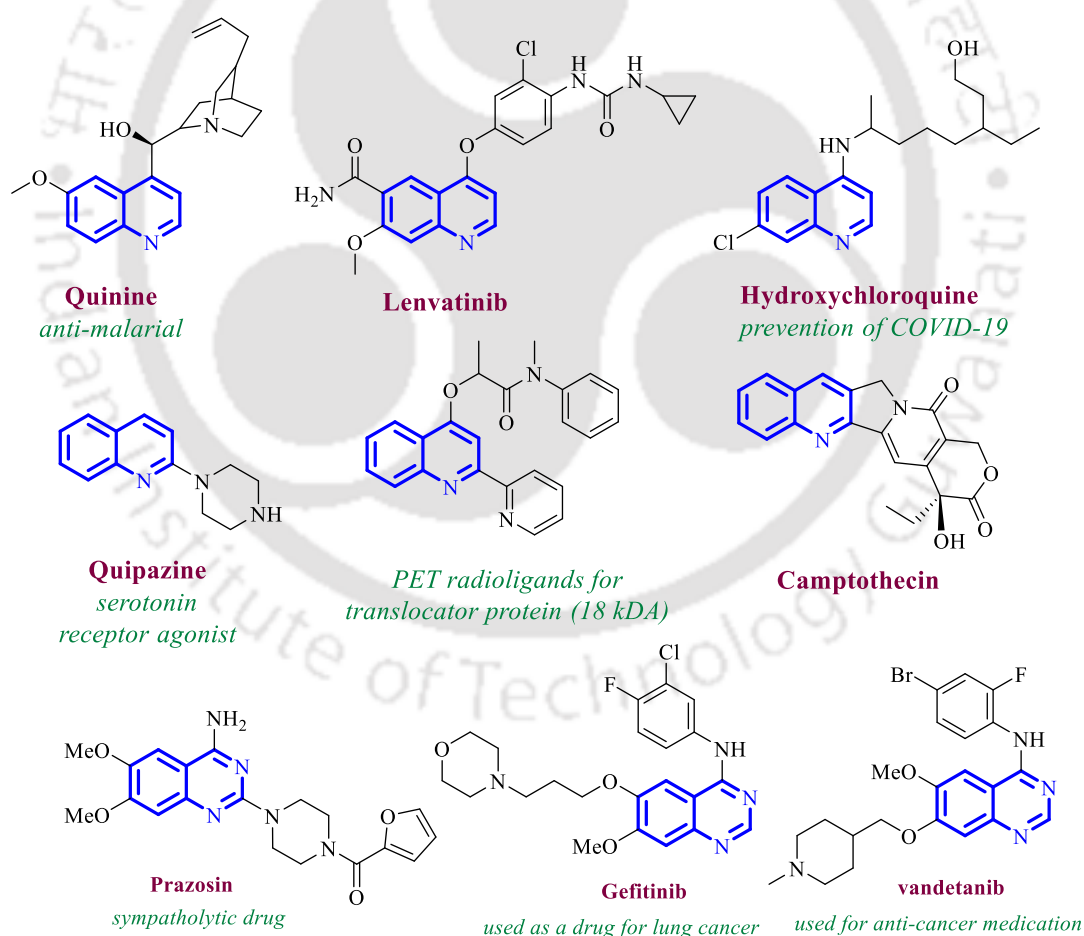
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An efficient ruthenium(III) catalyzed sustainable synthesis of quinolines, and quinazolines via acceptorless dehydrogenative coupling of alcohols

4.1. Introduction

Quinoline, and quinazoline derivatives are important class of nitrogen-containing six-membered aromatic compounds found in many natural products,^{1, 2} and large number of biologically active molecules. Quinoline derivative have shown a wide spectrum of biological and pharmaceutical activities³ such as antimalarial,^{4, 5} antibacterial,⁶ anti-inflammatory,⁷ antiasthmatic,⁸ antihypertensive,⁹ anti-Alzheimer,¹⁰ and anticancer activities.¹¹⁻¹³ Besides, they are widely used as efficient organocatalysts in contemporary organic chemistry for enantioselective synthesis of chiral molecules and also served as potential ligands for the synthesis of phosphorescent complexes. Quinazolines derivatives also exhibit diverse pharmaceutical properties, including antibacterial,¹⁴⁻¹⁶ anticancer,¹⁷⁻²⁰ anticonvulsant,¹⁷ anti-inflammatory,²¹ antiplasmodial,²² antitumor,²³ antimicrobial,²⁴ antioxidant,²⁵ anti-HIV,²⁶ and antitubercular activities²⁷ and as an α -adrenergic blocker.²⁸ Furthermore, its derivatives have been applied as photochemotherapeutic agents,²⁹ DNA-gyrase,³⁰ JAK2, PDE5 and EGFR (epidermal growth factor receptor) tyrosine kinase inhibitors and CB2 receptor agonists.³¹⁻³³ Some quinazoline-based compounds are used as drugs e.g., prazosin, an orally available sympatholytic drug, is used for the treatment of hypertension, anxiety and post-traumatic stress disorder.³⁴

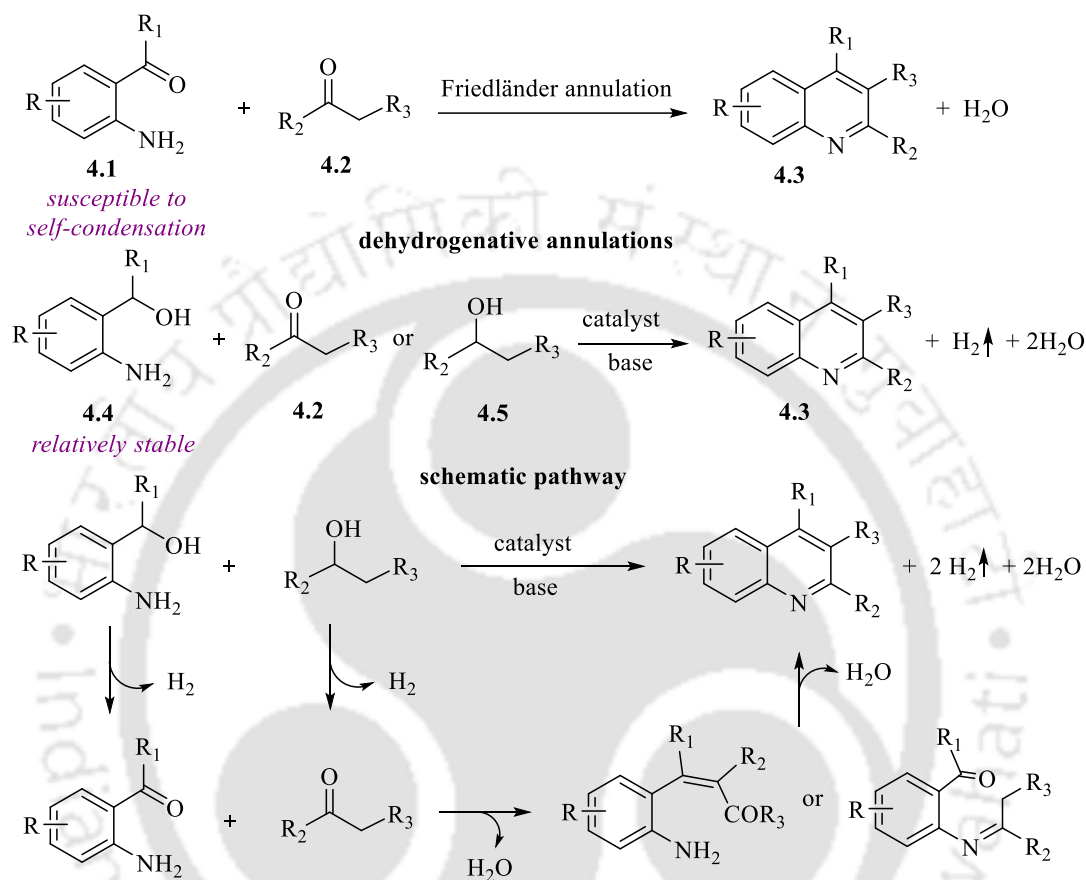


Scheme 4.1. Selected bio-active compounds with quinoline and quinazoline motif

Vandetanib is the first FDA-approved drug applied for the treatment of late-stage medullary thyroid cancer. Gefitinib demonstrated promising clinical activity as EGFR tyrosine kinase inhibitors, and is used for treating lung and pancreatic cancers.³⁵

Due to their huge prevalence in medicinal chemistry as well as in synthetic chemistry, the development of a new synthetic approach for the synthesis of quinoline and quinazoline derivatives has become an active area of research.

Various synthetic approaches have been developed over the past few decades for the synthesis of quinoline derivatives, for instance the Friedländer synthesis,³⁶⁻³⁹ Doebner–von Miller synthesis,⁴⁰ Skraup synthesis,⁴¹ and Gould–Jacobs synthesis.⁴² In addition, various other strategies are also discussed.^{43, 44} 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.

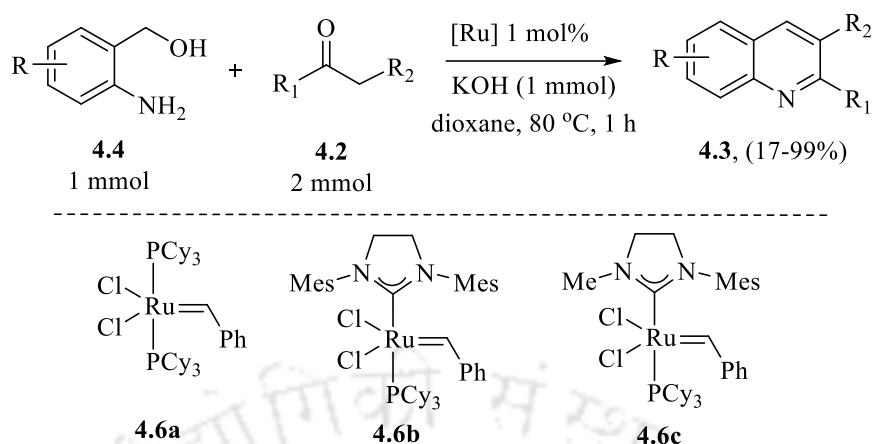


Scheme 4.2. The synthesis of quinoline derivatives via dehydrogenative annulations

Besides, *o*-aminobenzaldehydes are not stable under the reaction condition, and susceptible to self-condensation.⁴⁵ To overcome this issue, comparatively stable *o*-aminobenzyl alcohol is used as a suitable alternative precursor for the synthesis of quinoline moiety. In this context, recent study demonstrated that the atom economical, and environmentally benign approach is *via* transition metal catalyzed acceptorless dehydrogenative reaction of *o*-aminobenzyl alcohols with active methylene bearing ketones or corresponding secondary alcohols. As the process does not require any external hydrogen acceptor or oxidant source, and hydrogen is the only side product, thereby the overall process becomes green and sustainable. The catalytic cycle involves dehydrogenation of alcohols, followed by base promoted cross-aldol condensation with release of water molecule to afford *o*-amino chalcone intermediate which might undergo intramolecular cyclization and dehydration led to the desired product (Scheme 4.2).⁴⁶⁻⁵⁶

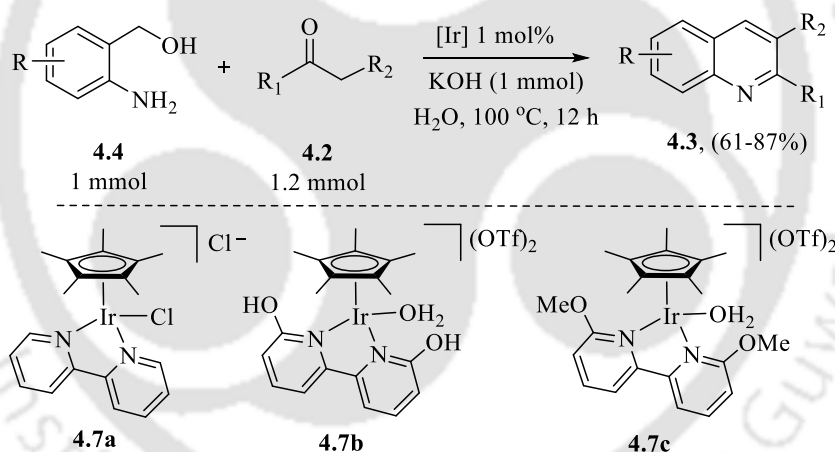
Herein, slowly generating unstable *o*-aminobenzaldehydes not only minimizes the self-condensation, but also process can avoid strong and toxic oxidant. Notably, these were major drawbacks of previous Friedländer annulation. Based on this ADC concept several transition metal catalysed oxidative annulation reaction of *o*-aminobenzyl alcohol derivative have been reported for synthesis of quinoline skeleton. In the context of catalytic efficiency, ruthenium and iridium-based metal complexes have been found the most proficient to date by getting maximum yields at lowest catalyst loading. Recently earth-abundant metal complexes (Ni, Co, Mn)⁵⁷⁻⁶² are also utilized for similar kind of reaction. Some of the reported efficient catalytic approach are discussed below.

In 2007, Verpoort and co-workers⁵⁰ reported ruthenium-catalyzed direct synthesis of quinoline from 2-aminobenzyl alcohol and ketone in the presence of KOH and dioxane solvent (Scheme 4.3). In this method, several ruthenium-based catalyst were screened by varying the ligand backbone. They have used 2 equivalent of ketone with respect to 2-aminobenzyl alcohol.



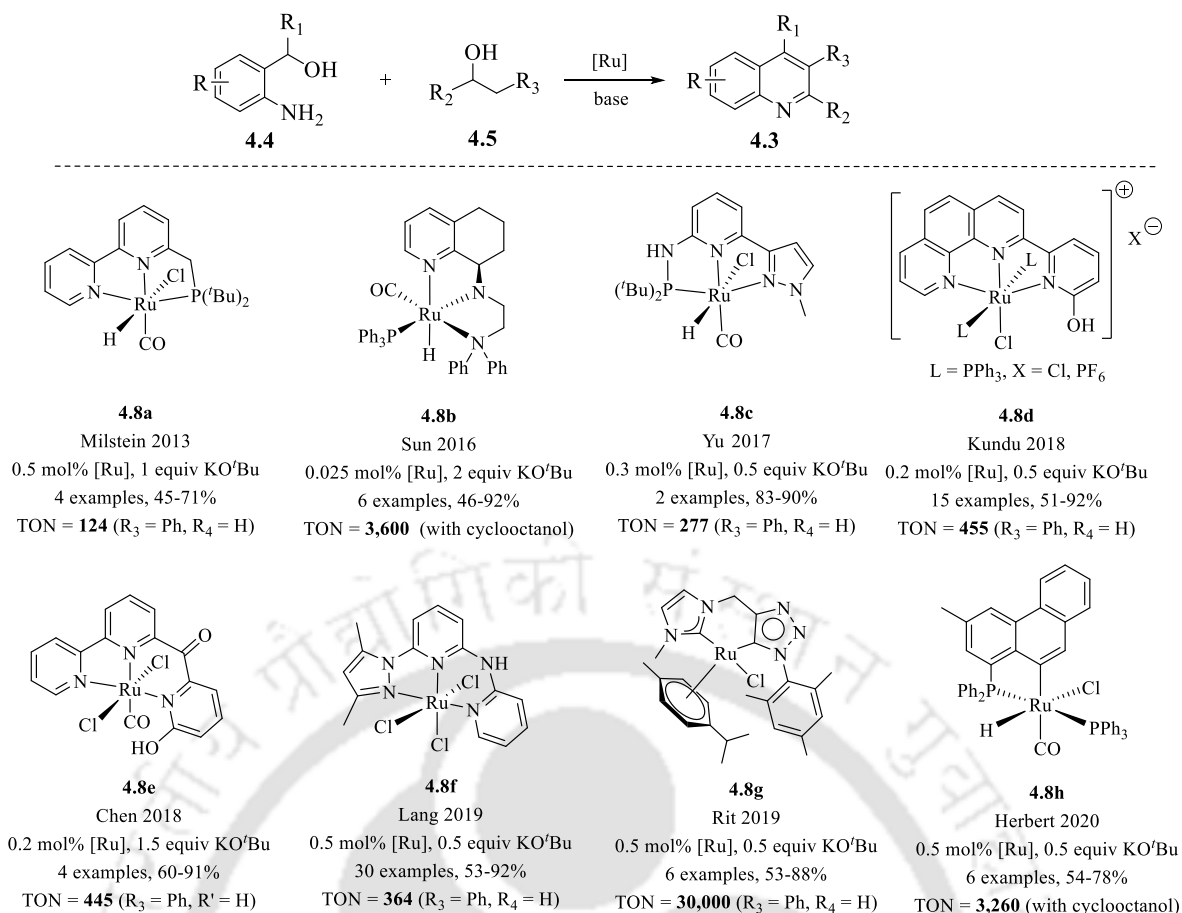
Scheme 4.3. Dehydrogenative quinoline synthesis by ruthenium complexes from 2-aminobenzyl alcohol and ketone derivatives

In 2016, Li and co-workers⁵⁶ demonstrated similar transformation with bifunctional iridium complexes in water with moderate to good yield, using the almost equimolar amount of 2-aminobenzyl alcohol and ketone (Scheme 4.4).



Scheme 4.4. Dehydrogenative quinoline synthesis by iridium complexes from 2-aminobenzyl alcohol and ketone derivatives

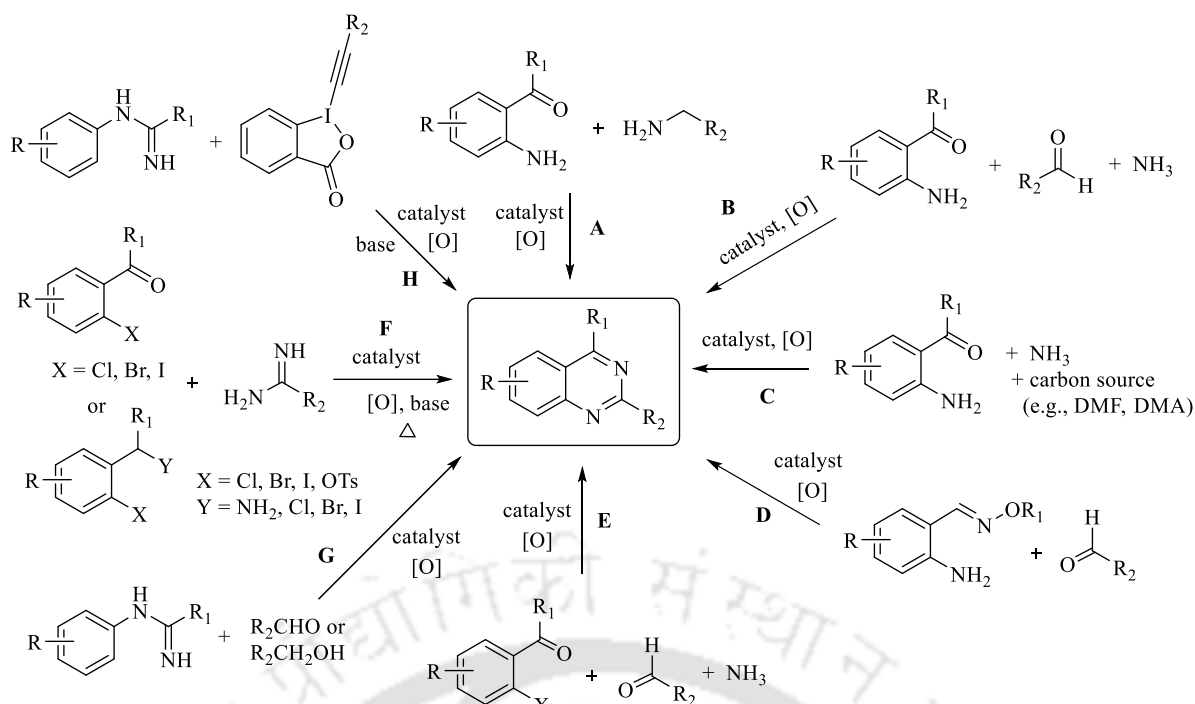
Very recently, efficient Friedländer annulation reaction has been reported for synthesis of quinolines from 2-aminobenzyl alcohol and secondary alcohol. Milstein,⁵³ Sun,⁶³ Yu,⁵⁴ Kundu,⁵⁵ Chen,⁶⁴ Lang,⁶⁵ Rit⁶⁶ and Herbert⁶⁷ independently have shown the synthetic scope of quinoline derivatives by variation of ligand supports with ruthenium metal (Scheme 4.5). The report suggests that catalyst loading (up to 0.2 mol% [Ru]) and base loading (at least 50 mol% KO^tBu) require to achieve the quantitative yield with decent substrate scope.⁵⁵ Furthermore, it was found that maximum TONs of 30,000 is stated so far for the synthesis of dehydronetiave annulation of quinoline.⁷⁴



Scheme 4.5. Dehydrogenative quinoline synthesis by ruthenium complexes from 2-aminobenzyl alcohol and secondary alcohol derivatives

In contrast to ruthenium (II), molecularly defined ruthenium (III) complexes as a pre-catalyst have been less explored in modified Friedländer ADC reactions. Because of air- and moisture-sensitive nature of phosphine and carbene-based ruthenium (II) complexes, the reaction often performed under schlenk techniques. As the reaction produces H₂ as one of the by-products, the formed quinolines could further be hydrogenated to 1,2,3,4-tetrahydroquinoline, leading to a challenge in the selectivity.⁶⁸ Therefore, continuous flow of argon or nitrogen gas was used to prevent hydrogenation of quinoline; the process is not economical. Thereby it is desired more economical and sustainable alternative where the method can proceed in low catalyst loading with catalytic amount of base, under the air atmosphere and open reaction system.

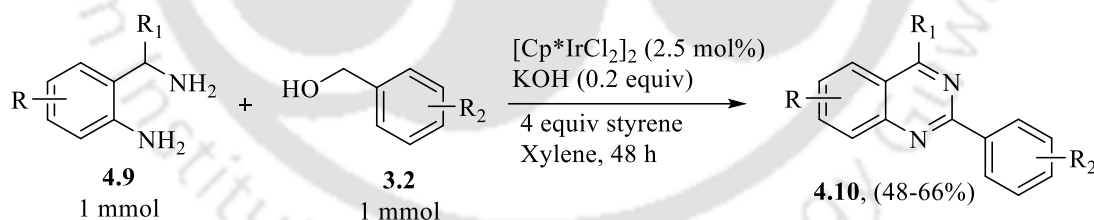
Consequently, many synthetic strategies have been developed for the construction of substituted quinazoline scaffolds. These strategies are included (i) the oxidative condensation of *ortho*-carbonyl functionalized anilines with benzyl amines (Scheme 4.6, **A**)⁶⁹ or ammonia and with various carbon sources such as aldehyde, DMF, DMA etc. (Scheme 4.6, **B**, **C**)⁷⁰ (ii) reaction between oxime derivatives and aldehydes (Scheme 4.6, **D**)⁷¹ (iii) oxidative coupling of *ortho*-carbonyl haloaromatic compounds with ammonia and aldehydes (Scheme 4.6, **E**)⁷² (iv) reaction of amidines with *ortho*-carbonyl haloarenes, *ortho*-halobenzyl halides, or *ortho*-halobenzyl tosylates, and *ortho*-halobenzyl amines (Scheme 4.6, **F**);^{73, 74} (v) oxidative coupling of amidines with benzyl alcohols or arylaldehyde (Scheme 4.6, **G**)⁷⁵ and hypervalent iodine-substituted alkynes (Scheme 4.6, **H**)⁷⁶ and (vi) intramolecular oxidative annulation of *N*-alkylated arylamidines.⁷⁷



Scheme 4.6. Various conventional synthetic strategies for the construction of quinazoline derivatives

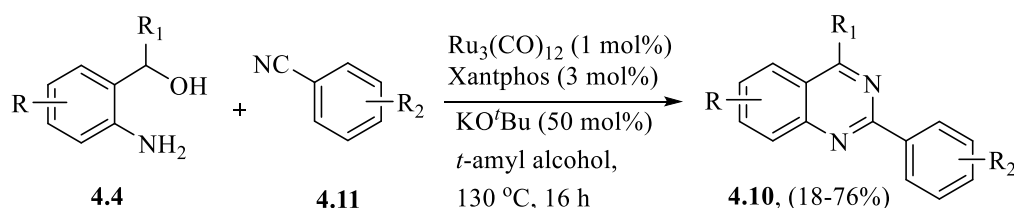
However, most of the reactions have their own limitations such as involvement of less environmentally benign halogenated reagents, the use of stoichiometric or excess amounts of strong oxidants /base, incompatibility with pre-functionalized starting precursors, which result not only in the preparation 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.

In 2013, *Fang and coworkers* reported Ir-catalysed quinazoline synthesis using 2-aminobenzylamine and benzyl alcohol. They have used excess amount of styrene as hydrogen acceptor to promote the reaction (Scheme 4.7).^{78, 79}

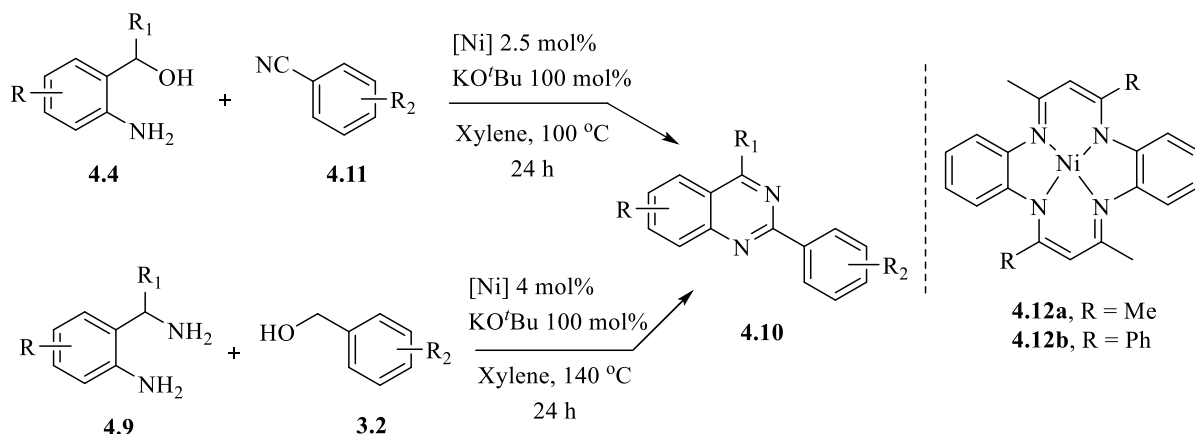


Scheme 4.7. Quinazoline synthesis by iridium complexes from 2-aminobenzyl amine and primary alcohol

In 2014, *Jiang and co-workers* have developed the synthesis of 2-arylquinazoline derivatives via acceptorless dehydrogenative coupling 2-aminobenzylalcohol and benzonitrile (Scheme 4.8). The reaction is catalyzed by 1 mol% $\text{Ru}_3(\text{CO})_{12}$ in presence of 3 mol% Xantphos ligand.⁸⁰

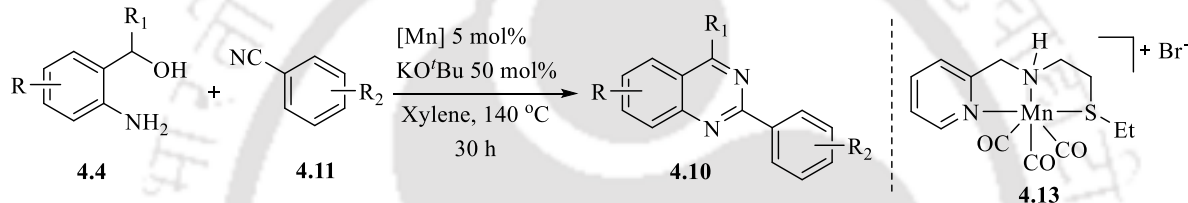


Scheme 4.8. Quinazoline synthesis by ruthenium carbonyl from 2-aminobenzyl alcohol and benzonitrile derivatives



Scheme 4.9. Quinazoline synthesis by nickel (II) complex from 2-aminobenzyl alcohol and benzonitrile (top) and 2-aminobenzyl amine and benzyl alcohol (bottom) derivatives

Very recently, earth-abundant Ni-complexes **4.12a-b** (Scheme 4.9)⁸¹ and Mn complexes **4.13** (Scheme 4.10)⁸² have been applied for the synthesis of quinazoline derivatives through the dehydrogenative coupling of 2-aminobenzylalcohol with benzonitrile or 2-aminobenzylamine with benzyl alcohol.



Scheme 4.10. Quinazoline synthesis by manganese (I) complex from 2-aminobenzyl alcohol and benzonitrile

A number of transition metal-catalyzed dehydrogenative synthesis of quinazoline have been demonstrated; however, it was found that catalyst loading (up to 1 mol%) and base loading (≥ 50 mol% of KOtBu) require to synthesize such heterocycle *via* dehydrogenative coupling of 2-aminobenzyl alcohol and nitrile. Thus the study of a new and efficient catalytic system with low catalyst loading and catalytic amount of base is highly desired for such type of transformation.

4.2. Present work

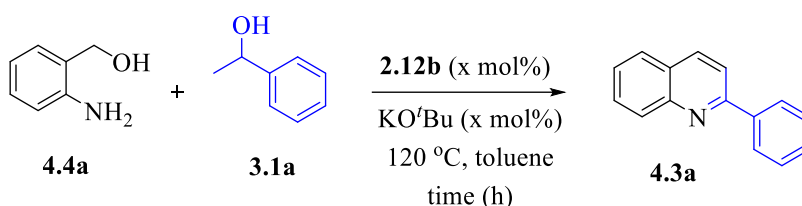
Herein ruthenium (III)-catalyzed dehydrogenative synthesis of quinoline *via* acceptorless dehydrogenative coupling of 2-aminobenzyl alcohols and secondary alcohols and synthesis of quinazoline derivatives from 2-aminobenzyl alcohols and nitriles will be described with low catalyst loading (upto 0.0001 mol%) and base loading (up to 1 mol%). The reaction can proceed under air.

4.2.1. Optimization of reaction condition for quinoline

The synthesized ruthenium complex **2.12b** was used to explore the scope of synthesis of quinoline *via* simultaneous C-C and C-N bond formation through dehydrogenation and condensation reaction between 2-aminobenzylalcohol (**4.4a**) and secondary alcohols (**3.1**). The initial experiment was performed by stirring a mixture of **4.4a** (1 mmol), 1-phenylethanol **3.1a** (1 mmol), **2.12b** (1 mol%) and KOtBu (10 mol%) in toluene at 120 °C for 12 h under air. Gratifyingly, both the starting material was completely consumed and the desired 2-phenylquinoline (**4.3a**) was isolated in 98% yield. With this encouraging result, I then investigated the reaction by gradually decreasing the catalyst loading from 1 mol% $\rightarrow$ 0.5 mol% $\rightarrow$ 0.2 mol% $\rightarrow$ 0.1 mol% and base loading from 10 mol% to 1 mol%, a similar yield of **4.3a** in 96% was obtained (entry 6). However, the yield of **4.3a** got decreased from 96% to 77% when further decrease the catalyst loading from 0.1 mol% to 0.05 mol% with KOtBu (1 mol%) (entry 10). On the other hand, decreasing the reaction time from 12 h to 6 h, the yield of **4.3a** was 166% (entry 14). The optimization condition is therefore fixed to be **2.12b** (0.1 mol%), KOtBu (1 mol%), 120 °C for 6 h under air in toluene. To the best of my knowledge, this is the lowest

base loading hitherto and relatively low catalyst loading for the synthesis of quinolines catalysed by ruthenium metals *via* dehydrogenative annulation of alcohols.

Table 4.1. Optimisation of reaction condition for quinoline synthesis^a



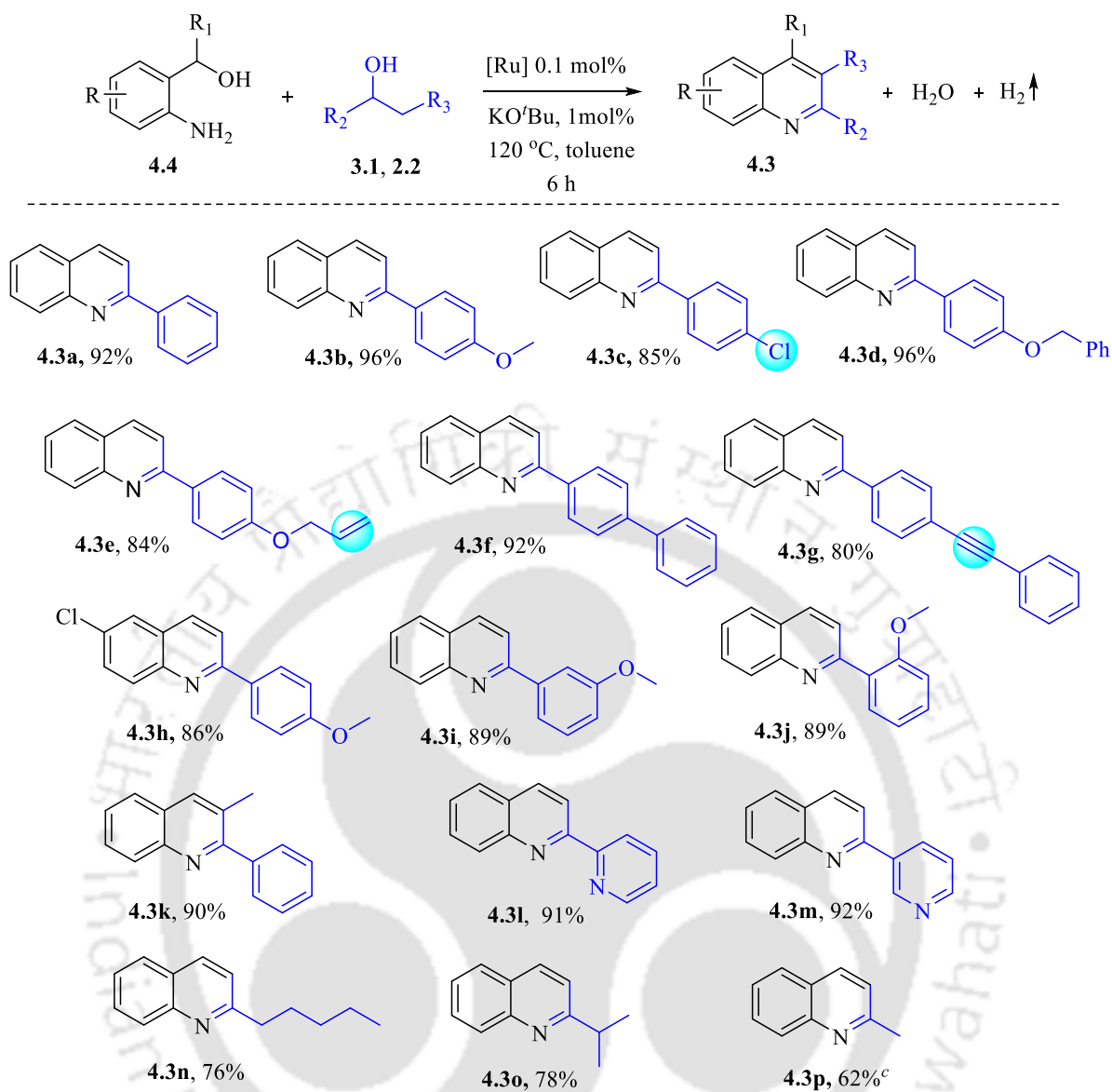
Entry	Catalyst	mol% cat.	base (mol%)	time (h)	Conv. (%) ^b	Yield (%) ^c	TONs
1	2.12b	2	KO ^t Bu (20)	12	>99	98 (96)	49
2	2.12b	1	KO ^t Bu (10)	12	>99	98	98
3	2.12b	0.5	KO ^t Bu (10)	12	>99	98	196
4	2.12b	0.2	KO ^t Bu (10)	12	>99	98	490
5	2.12b	0.1	KO ^t Bu (10)	12	>99	98	980
6	2.12b	0.1 (1000 ppm)	KO ^t Bu (1)	12	>99	96 (92)	960
7	2.12b	0.05 (500 ppm)	KO ^t Bu (1)	12	95	77	1,540
8	2.12b	0.01 (100 ppm)	KO ^t Bu (1)	12	92	68	6,800
9	2.12b	0.001 (10 ppm)	KO ^t Bu (1)	12	88	56	56,000
10 ^d	2.12b	0.0001 (1 ppm)	KO ^t Bu (1)	12	72	44	4,40,000
11	2.12b	0.0001 (1 ppm)	KO ^t Bu (0.1)	12	75	36	3,60,000
12	2.12b	0.00005 (0.5 ppm)	KO ^t Bu (1)	12	53	9	1,80,000
13	2.12b	0.0001 (1 ppm)	KO ^t Bu (1)	6	30	8	80,000
14	2.12b	0.1	KO ^t Bu (1)	6	>99	96 (92)	960
15	2.12b	0.05	KO ^t Bu (1)	6	89	86	1,720
16	2.12b	0.1	KOH (1)	6	85	81	810
17	RuCl₃	0.1	KO ^t Bu (1)	6	76	47	–
18	–	–	KO ^t Bu (1)	6	17	n.d.	–
19	2.12b	0.1	–	6	12	n.d.	–

^aReaction conditions: 2-aminobenzylalcohol (1 mmol), 1-phenylethanol (1 mmol), **2.12b** (x mol%), and toluene (2 mL) were heated under air for 12 h at 120 °C. ^bConversion of 2-aminobenzylalcohol was determined by GC analysis using benzene as internal standard. ^cYields were calculated from GC analysis of the reaction mixture using benzene as an internal standard; isolated yields are given within parentheses. ^dThe same has been repeated three times.

4.2.2. Substrates scope for synthesis of quinoline

To study the scope of reaction, a variety of secondary alcohols and 2-aminobenzylalcohol were employed. In all the cases, excellent to moderate yields were obtained with a series of secondary alcohols tolerating various functional groups. 1-arylethanol having electron donating group (e.g., OCH₃, OCH₂Ph) reacted with **4.4a** to form the desired products **4.3b**, and **4.3d** in 96% yield. 1-arylethanol with electron-withdrawing group (e.g., Cl) was also efficiently reacted to obtain the desired product **4.3c** in 85% yield. The reducible functional groups such as, –OCH₂CH=CH₂, –C≡C–Ph can survive the current reaction to give the product **4.3e**, and **4.3g** selectively. *Meta*- and *ortho*-substituted aromatic secondary alcohol also gave the corresponding product **4.3i** and **4.3j** in high yield. The substrate containing aromatic heterocycles such as pyridine is suitable substrate for this reaction, affording the pyridylquinoline product **4.3l**, **4.3m** in good yields. Gratifyingly, 2,3-disubstituted quinoline **4.3k** was synthesized in 90% yield by employing 1-phenylpropanol and 2-aminobenzylalcohol under the reaction conditions. Notably, challenging acyclic aliphatic secondary alcohol was found to be amenable to this method, giving **4.3n–p** in moderate to good yields.

Table 4.2. Synthesis of quinolines^{a,b}



^aReaction conditions: 2-aminobenzyl alcohol (1 mmol), secondary alcohol (1 mmol), catalyst **2.12b** (0.1 mol%), KOtBu (1 mol%), and toluene (2 mL) were heated at 120 °C under air for 6 h. ^bIsolated yield. ^cAliphatic secondary alcohol (6 mmol) was used.

4.2.3. Optimisation of reaction condition for quinazoline

Next, the synthesis of quinazoline derivatives *via* dehydrogenative annulation reaction of 2-aminobenzylalcohol and aryl nitrile was attempted. When 2-aminobenzyl alcohol (**4.4a**, 1 mmol) and benzonitrile (**4.11a**, 1 mmol) were heated at 120 °C in the presence of **2.12b** (2 mol%) and KOtBu (20 mol%) in toluene for 12 h under air, 95% of the yield of desired quinazoline **4.10a** was isolated (Table 4.2, entry 1). Decreasing the catalyst loading from 2 mol% → 1 mol% → 0.5 mol% → 0.2 mol% → 0.1 mol% and the base loading from 20 mol% to 10 mol% to 1 mol% led to similar yield of **4.10a** in 92% (entry 6). Whereas the yield was dropped to 78% when the reaction was performed using further lower amount of **2.12b** (0.05 mol%). Reducing the reaction time from 12 h to 6 h had almost same outcome (entry 7). Control experiments in the absence of catalyst and only with base showed trace amount of product. The optimized reaction conditions were therefore fixed to be **2.12b** (0.1 mol%), KOtBu (1 mol%), 120°C for 6 h in toluene under air. My knowledge this is the lowest catalyst loading and base loading so far to synthesizing quinazoline catalysed by transition metals *via* dehydrogenative annulation of alcohols.

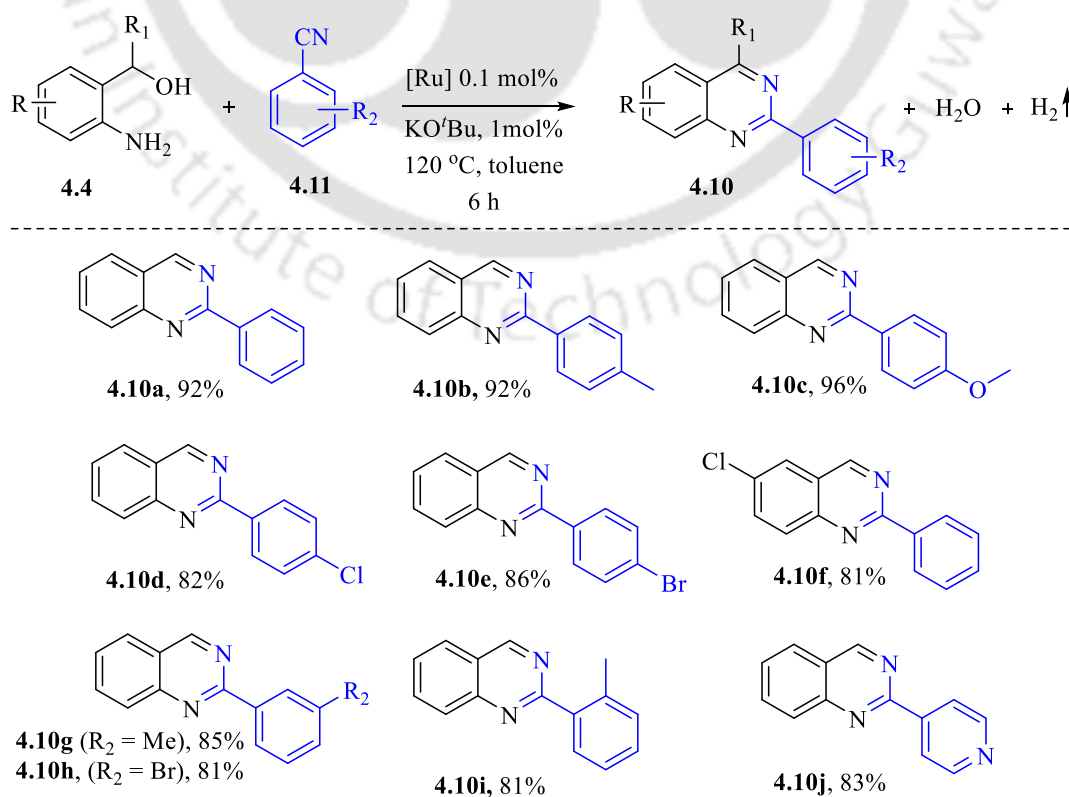
Table 4.2. Optimisation of reaction condition for quinazoline synthesis^a

Entry	Catalyst	mol% cat.	base (mol%)	time (h)	Conv. (%) ^b	Yield ^c	TON
1	2.12b	2	KO ^t Bu (20)	12	> 99	98 (95)	49
2	2.12b	1	KO ^t Bu (10)	12	> 99	97	97
3	2.12b	0.5	KO ^t Bu (10)	12	> 99	97	194
4	2.12b	0.2	KO ^t Bu (10)	12	> 99	97	485
5	2.12b	0.1	KO ^t Bu (10)	12	> 99	96	960
6	2.12b	0.1 (1000 ppm)	KO ^t Bu (1)	12	> 99	95 (92)	950
7	2.12b	0.1 (1000 ppm)	KO ^t Bu (1)	6	> 99	94 (92)	940
8	2.12b	0.05	KO ^t Bu (1)	6	85	80 (78)	1600
9	RuCl₃	0.1	KO ^t Bu (1)	6	70	43 (41)	430
10	–	–	KO ^t Bu (1)	6	18	n.d.	–
11	2.12b	0.1	–	6	12	n.d.	–
12	2.12b	0.01 (100 ppm)	KO ^t Bu (1)	12	84	65	6,500
13	2.12b	0.0001 (1 ppm)	KO ^t Bu (1)	10	61	25	2,50,000
14 ^d	2.12b	0.0001 (1 ppm)	KO ^t Bu (1)	12	67	29	2,90,000

^aReaction conditions: 2-aminobenzylalcohol (1 mmol), benzonitrile (1.2 mmol), **2.12b** (x mol%) and toluene (2 mL) were heated under air for 12 h at 120 °C. ^bConversion of 2-aminobenzylalcohol was determined by GC analysis using benzene as internal standard. ^cYields were calculated from GC analysis of the reaction mixture using benzene as an internal standard; isolated yields are given within parentheses. ^dThe same has been repeated three times.

4.2.4. Substrates scope for synthesis of quinazoline:

After attaining the optimized condition, the current protocol has been applied to synthesize a diverse range of quinazoline using 2-aminobenzylalcohol and aromatic nitriles (Table 4.3).

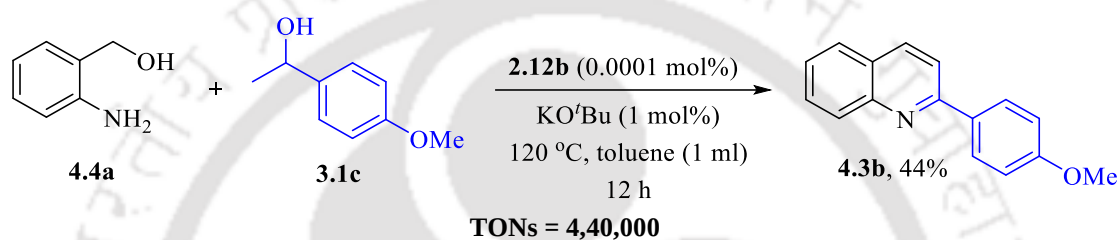
Table 4.3. Substrates scope for quinazoline derivatives^{a,b}

TH-2648-166132033 Reaction conditions: 2-aminobenzyl alcohol (1 mmol), secondary alcohol (1 mmol), catalyst **2.12b** (0.1 mol%), KO^tBu (1 mol%), and toluene (2 mL) were heated at 120 °C under air for 6 h. ^bIsolated yield.

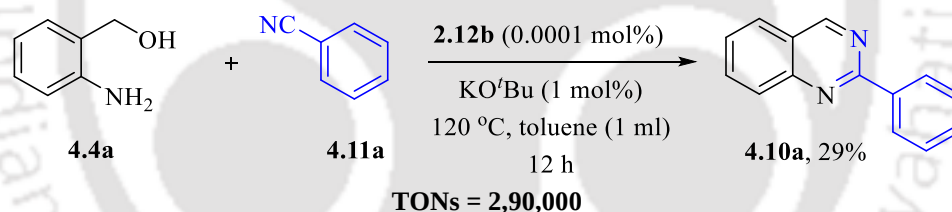
Initially, 2-aminobenzylalcohol was reacted with different electron donating and electron withdrawing group containing benzonitrile efficiently led to the desired product **4.10a-e** in 86-96% yield. It was found that benzonitrile having an electron donating -CH₃, or -OCH₃ substituent gave slightly better yield compared to an electron withdrawing -Cl, or -Br substituent. Meta-substituent benzonitrile also efficiently reacted to obtain the desired product **4.10g-h** in good yield. Sterically hindered nitrile such as *o*-methylbenzonitrile underwent dehydrogenative coupling reaction smoothly, affording the desired quinazoline **4.10i** in 81% yield. Nitriles possessing heteroaromatic moieties such as pyridine also proceeded well. Furthermore, 2-amino-5-chlorobenzyl alcohol was reacted well under the optimized condition to afford desired quinazoline **4.10f** in 81% yield.

4.2.5. Efficiency of the catalytic reaction for the synthesis of quinoline and quinazoline:

I have attempted to examine the efficiency of the ruthenium catalyst for the synthesis of *N*-heterocycles by calculating the turn over number (TON) (Scheme 4.11). Gratifyingly, catalyst **2.12b** showed remarkably high TONs of **4,40,000** for the synthesis of quinoline **4.3b** and TONs of **2,90,000** for the synthesis of quinazoline **4.10a** respectively, using 0.0001 mol% of catalyst, and 1 mol% of KO^tBu in toluene at 120 °C for 12 h under air.



Molecular weight of product **4.3b** = 235.3; Catalyst loading = 1.6×10^{-7} mmol; Yield = 0.0704 mmol. TON = mmol of product/ mmol of catalyst = $0.0704 / (1.6 \times 10^{-7}) = 4,40,000$ (same was repeated for three times).



Molecular weight of product **4.10a** = 206.3; Catalyst loading = 1.6×10^{-7} mmol; Yield = 0.0464 mmol. TON = mmol of product/ mmol of catalyst = $0.0464 / (1.6 \times 10^{-7}) = 2,90,000$ (same was repeated for three times).

Scheme 4.11. Calculation of TONs

4.2.6. Kinetic studies

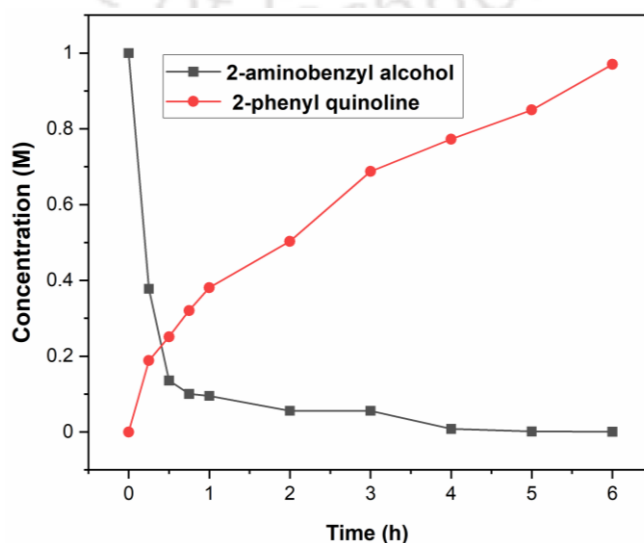
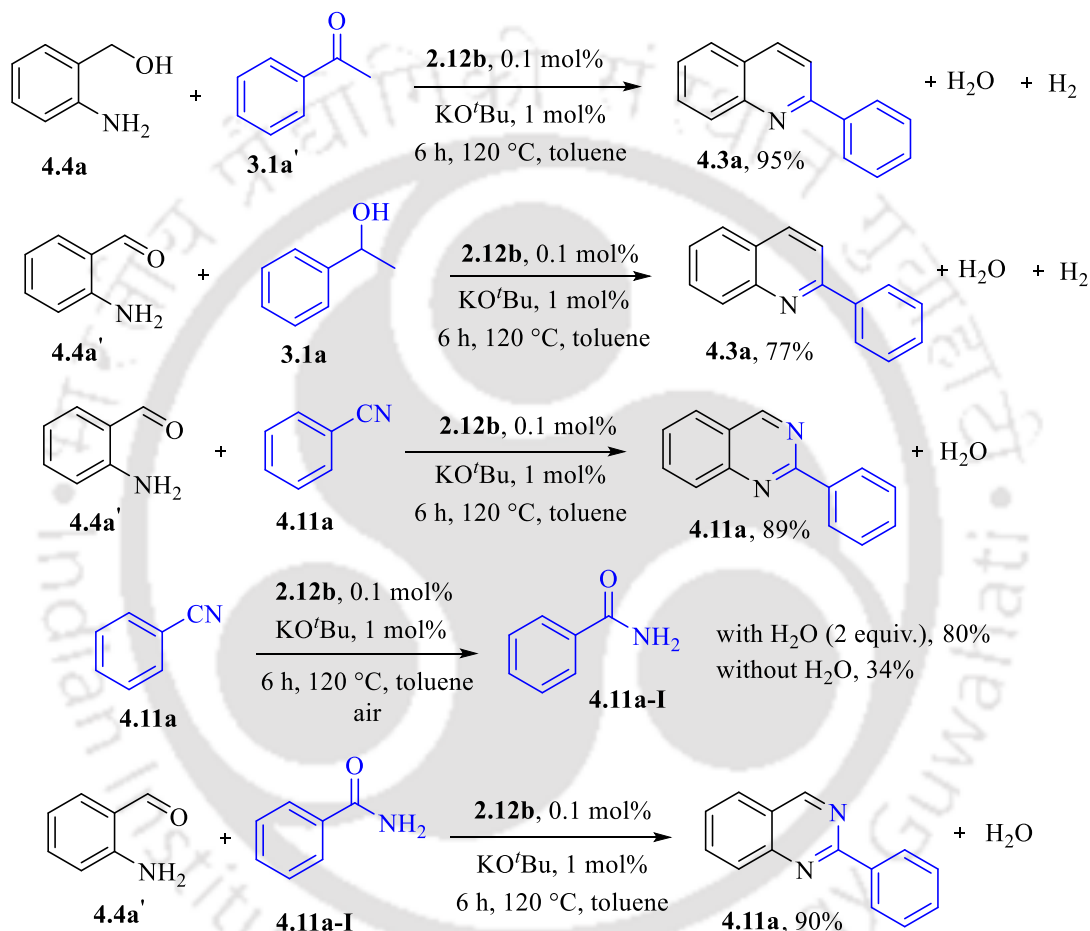


Figure 4.1. Kinetic profile diagram for synthesis of quinoline

The kinetics analysis for the synthesis of 2-phenylquinoline was performed under optimized conditions in different time intervals. As shown in the kinetic profile in Figure 4.1, the consumption of 2-aminobenzyl alcohol sharp decline in first 1 h, and then gradually decreases over the remaining time.

4.2.7. Mechanistic studies

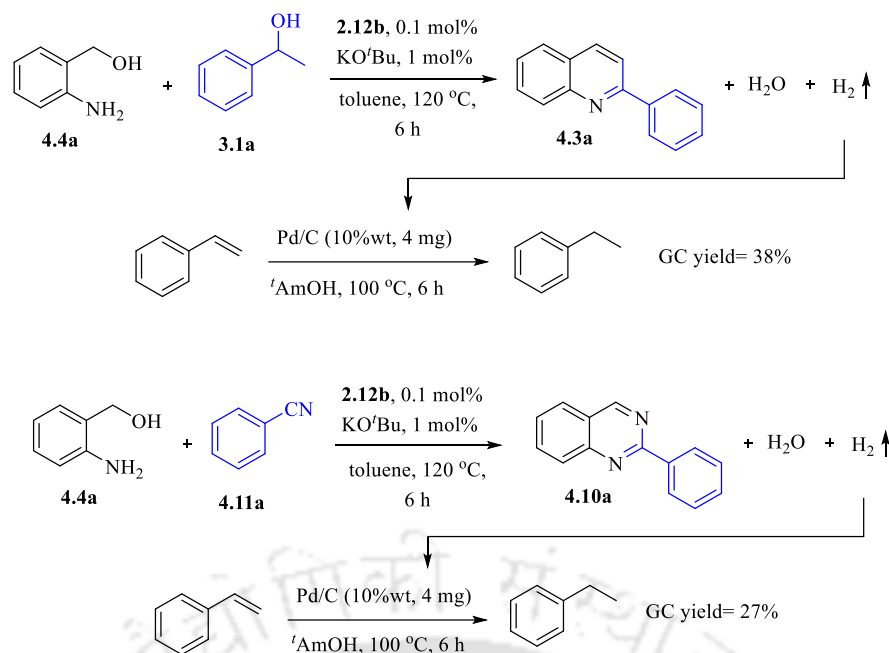
To gain mechanistic insights into the synthesis of quinoline and quinazoline derivatives, a few control experiments were carried out (Scheme 4.11). When the reaction was performed between 2-aminobenzylaldehyde and 1-phenylethanol under optimized condition, desired quinoline was isolated in 77% yield. Likewise, the reaction of 2-aminobenzylaldehyde and benzonitrile **4.11a** afforded 89% yield of the desired quinazoline. These experimental observations suggest that the reaction likely proceeds *via* 2-aminobenzylaldehyde.



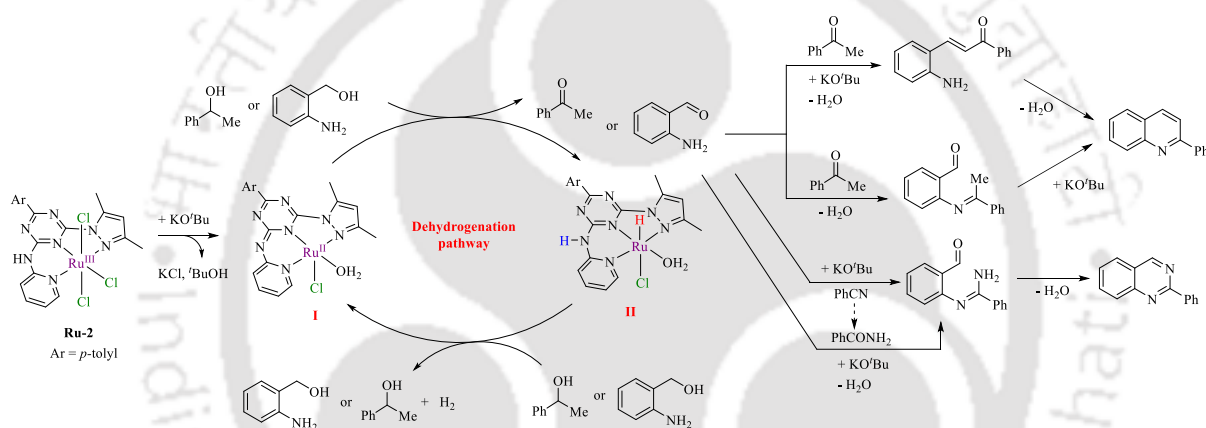
Scheme 4.11. Control experiments for synthesis of quinoline and quinazoline

Further the reaction of 2-aminobenzylalcohol and acetophenone under standard catalytic condition gave the desired quinoline in 95% yield. To check the possibility of KO^tBu mediated conversions of nitriles to amide formation and to subsequent possibility of quinazoline *via* condensation with 2-aminobenzylaldehyde, when the reaction was performed with benzonitrile alone, 80% of benzamide (with 2 equiv. of H₂O) and 34% of benzamide (in the absence of H₂O) were isolated from the reaction medium. Further, reaction of benzamide with 2-aminobenzylaldehyde under the optimized catalytic conditions to provide the desired quinazoline in 90% yield. These observations suggest that the reaction possibly occurs in both pathways either *via* directly nitrile or by the benzamide (which is formed in the reaction medium *in-situ*).

Finally, the liberation of H₂ during the dehydrogenative synthesis of quinoline and quinazolines was confirmed by the Pd/C catalyzed hydrogenation of styrene using H-shaped tube, which clearly shows the formation of ethylbenzene (Scheme 4.12).



Scheme 4.12. Evidence for evolved hydrogen in ADC annulation reaction



Scheme 4.13. Plausible mechanism of quinoline and quinazoline synthesis

On the basis of the above experimental results and available literature, a plausible mechanism for the dehydrogenative synthesis of quinoline and quinazoline is shown in Scheme 4.13. The first step in the catalytic cycle is the dehydrogenation of the 2-aminobenzylalcohol to 2-aminobenzaldehyde or secondary alcohols to the corresponding ketones *via* outer sphere and/or inner sphere MLC pathway as discussed in chapter 2.2.4 and 3.2.7 section for dehydrogenation of alcohol. Then 2-aminobenzaldehyde undergoes cyclocondensation with acetophenone to form the quinoline. Likewise, a base promoted cyclocondensation of 2-aminobenzaldehyde with benzonitrile or benzamide (formed in-situ from benzonitrile) to produce desired quinazoline.

4.2.8. Summary

In summary, I have developed efficient method for synthesis of quinolines, and quinazolines *via* acceptorless dehydrogenative coupling of alcohols catalysed by simple phosphine-free Ru(III) precatalyst. The catalytic process enables by low catalyst loading (0.1 mol%) and base loading (1 mol%) under aerial condition with a wide variety of substituted quinolines and quinoxalines in moderate to good yield. Notably, this catalytic system shown remarkably high TONs of **4,40,000** for 2-phenylquinoline and TONs of **2,90,000** for 2-phenylquinazoline, which are the highest among all the reported transition metal complexes in synthesis of quinolines, and quinazolines. Cheap and readily available alcohols as starting precursors, low catalyst loading and base loading, one-step, atom economical, environmentally benign ADC reaction proved to be valuable alternative for the construction of quinoline, and quinazoline heterocycles.

4.3. 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. **1**-([1,1'-biphenyl]-4-yl)ethan-1-ol,^{83, 84} **1**-(4-(phenylethynyl)phenyl)ethan-1-ol,^{85, 86} 4-(allyloxy) benzyl alcohol⁸⁷ were prepared according to the reported literature. ¹H, ¹³C, and ¹⁹F NMR spectra of the compounds were measured in CDCl₃, DMSO-*d*₆, CD₃OD as a solvent by using TMS as an internal standard. Chemical shifts, δ (in ppm), are reported relative to TMS δ (¹H) 0.0 ppm, δ (¹³C) 0.0 ppm, which was used as the internal reference. Otherwise the solvents residual proton resonance and carbon resonance (CHCl₃, δ (¹H) 7.26 ppm, δ (¹³C) 77.16 ppm; DMSO-*d*₆, (¹H) 2.50 ppm, δ (¹³C) 39.52 ppm; CD₃OD, δ (¹H) 3.31 ppm, δ (¹³C) 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 μ L, 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). All the catalytic cross coupling of alcohols was carried out under air and in preheated oil baths.

A. General procedure for the synthesis of quinolines (GP-1):

In a sealed tube containing a magnetic stir bar, **2.12b** (0.001 mmol) was taken. To it secondary alcohol **3.1** (1 mmol), 2-aminobenzyl alcohol **4.4** (1 mmol) and base KO^tBu (0.01 mmol) were added sequentially. Toluene (2 mL) was added to the mixture and the tube was closed without exclusion of air. It was then stirred at 120 °C for 6 h. Upon completion, the crude mixture was filtered through celite followed by evaporation of the solvent. The residue was purified by column chromatography over silica gel (60-120 mesh) with pet-ether/ethyl acetate mixture as eluent.

B. General procedure for synthesis of quinazolines (GP-2):

In a sealed tube containing a magnetic stir bar, **2.12b** (0.001 mmol) was taken. To it 2-aminobenzyl alcohol **4.4** (1 mmol), aryl nitrile **4.11** (1.2 mmol) and base KO^tBu (0.01 mmol) were added sequentially. Toluene (2 mL) was added to the mixture and the tube was closed without exclusion of air. It was then stirred at 120 °C for 6 h. Upon completion, the crude mixture was filtered through celite followed by evaporation of the solvent. The residue was purified by column chromatography over silica gel (60-120 mesh) with pet-ether/ethyl acetate mixture as eluent.

C. Mechanistic studies

i) Proof for the formation of intermediate 2-amino benzaldehyde, ketone in quinoline synthesis (Scheme 4.11):

Reaction of 2-aminobenzyl alcohol and acetophenone

A mixture of **4.4a** (1 mmol, 1 equiv.), **3.1a'** (1 mmol, 1 equiv.), **2.12b** (0.1 mol%), KO^tBu (1 mol%) and toluene (1.5 mL) was loaded into the reaction tube and heated at 120 °C for 6 h. The product **4.3a** was isolated in 95% of yield.

A mixture of **4.4a'** (1 mmol, 1 equiv.), **3.1a** (1 mmol, 1 equiv.), **2.12b** (0.1 mol%), KO^tBu (1 mol%) and toluene (1.5 mL) was loaded into the reaction tube and heated at 120 °C for 6 h. The product **4.3a** was isolated in 77% of yield.

ii) Proof for the formation of intermediate 2-aminobenzaldehyde, and benzamide in quinazoline synthesis (Scheme 4.11):

Reaction of 2-aminobenzaldehyde and benzonitrile

A mixture of **4.4a'** (1 mmol, 1 equiv.), **4.11a** (1 mmol, 1 equiv.), **2.12b** (0.1 mol%), KO^tBu (1 mol%) and toluene (1.5 mL) was loaded into the reaction tube and heated at 120 °C for 6 h. The product **4.11a** was isolated in 89% of yield.

Formation of benzamide under the reaction conditions

A mixture of **4.11a** (1 mmol, 1 equiv.), **2.12b** (0.1 mol%), KO^tBu (1 mol%) and toluene (1.5 mL) was loaded into the reaction tube under air and heated at 120 °C for 6 h. The product **4.11a-I** was isolated in 34% of yield. In the presence of H₂O (2 equiv.), the yield of **4.11a-I** was obtained in 80% yield.

Reaction of 2-aminobenzaldehyde and benzamide

A mixture of **4.4a'** (1 mmol, 1 equiv.), **4.11a-I** (1 mmol, 1 equiv.), **2.12b** (0.1 mol%), KO^tBu (1 mol%) and toluene (1.5 mL) was loaded into the reaction tube and heated at 120 °C for 6 h. The product **4.11a** was isolated in 90% of yield.

iii) Hydrogenation of styrene by evolved hydrogen during synthesis of quinoline and quinazoline

For 4.3a:

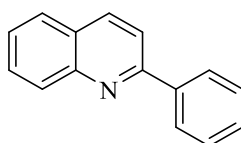
An oven dried H-shaped bridged tube was equipped with a magnetic stir bar. Under Ar atmosphere, chamber one charged with catalyst **2.12b** (0.1 mol%), 1 mmol of **4.4a**, 1 mmol of **3.1a**, KO^tBu (1 mol%), and toluene (2 mL) and chamber two in which styrene (1 mmol), Pd/C (4 mg) were placed in ^tAmOH (1.5 mL). Both chambers were closed with cap. The sealed bridged tube was placed in preheated oil bath at 120 °C for 6 h. After completion of the reaction, small portion of aliquot taken from chamber two for GC analysis, revealed conversion of styrene to ethyl benzene (38%) (Scheme 4.12).

For 4.10a:

Similarly, the following experiment was performed for **4.10a** using catalyst **2.12b** (0.1 mol%), KO^tBu (1 mol%), 1 mmol of **4.4a**, and 1 mmol of **4.11a**, in toluene (2 mL). the conversion of styrene to ethyl benzene was observed in 27% (Scheme 4.12).

4.4. Analytical data of the products:

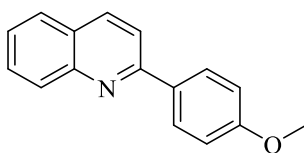
2-phenylquinoline (**4.3a**)⁸⁸



Following the general procedure **GP1** the title compound **3a** was isolated as off white solid using silica gel column chromatography with pet-ether/ ethylacetate (v/v= 50/1, *R_f* = 0.5) in 92% yield (0.189 g). ¹H NMR (400 MHz, CDCl₃): δ ¹H NMR (600 MHz, Chloroform-*d*) δ 8.23 – 8.17 (m, 4H), 7.88 (d, *J* = 8.5 Hz, 1H), 7.83 (d, *J* = 8.0 Hz, 1H), 7.74 (ddd, *J* = 8.3, 6.9, 1.3 Hz, 1H), 7.56 – 7.52 (m, 3H), 7.48 (t, *J* = 7.3 Hz, 1H). ¹³C NMR (151 MHz, CDCl₃): δ 157.47, 148.38, 139.79, 136.89,

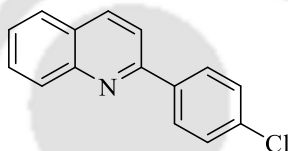
129.84, 129.77, 129.43, 128.96, 127.68, 127.58, 127.28, 126.39, 119.13. Spectral data is in accordance to the reported literature.

2-(4-methoxyphenyl)quinoline (4.3b)⁸⁸



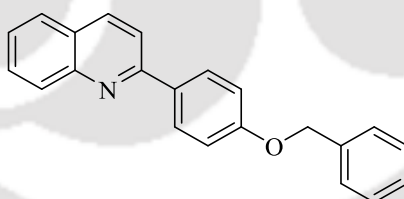
Following the general procedure **GP1** the title compound **3b** was isolated as light yellow solid using silica gel column chromatography with pet-ether/ ethylacetate (v/v= 50/1, R_f = 0.5) in 96% yield (0.225 g). ^1H NMR (600 MHz, CDCl_3): δ 8.19 (d, J = 8.6 Hz, 1H), 8.16 – 8.12 (m, 3H), 7.84 (d, J = 8.6 Hz, 1H), 7.81 (d, J = 8.0 Hz, 1H), 7.71 (s, 1H), 7.51 (d, J = 7.9 Hz, 1H), 7.05 (d, J = 8.8 Hz, 2H), 3.89 (s, 3H). ^{13}C NMR (151 MHz, CDCl_3) δ 160.93, 157.07, 136.80, 129.73, 129.64, 129.03, 127.58, 126.07, 118.73, 114.36, 55.56. Spectral data is in accordance to the reported literature.

2-(4-chlorophenyl)quinoline (4.3c)⁸⁸



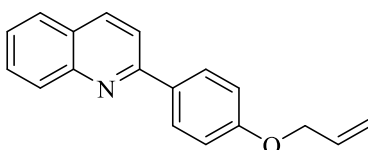
Following the general procedure **GP1** the title compound **3c** was isolated as yellow solid using silica gel column chromatography with pet-ether/ ethylacetate (v/v= 50/1, R_f = 0.5) in 85% yield (0.203 g). ^1H NMR (600 MHz, CDCl_3): δ 8.19 (d, J = 6.0 Hz, 1H), 8.16 (d, J = 6.0 Hz, 1H), 8.11 (d, J = 6.0 Hz, 2H), 7.82 – 7.80 (m, 2H), 7.75 – 7.72 (m, 1H), 7.53 (t, J = 6.0 Hz, 1H), 7.50 – 7.48 (m, 2H). ^{13}C NMR (151 MHz, CDCl_3): δ 156.06, 148.30, 138.11, 137.05, 135.62, 129.94, 129.77, 129.10, 128.90, 127.59, 127.30, 126.59, 118.64.

2-(4-(benzyloxy)phenyl)quinoline (4.3d)



Following the general procedure **GP1** the title compound **3d** was isolated as off white solid using silica gel column chromatography with pet-ether/ ethylacetate (v/v= 20/1, R_f = 0.5) in 96% yield (0.298 g). ^1H NMR (600 MHz, CDCl_3): δ 8.18 (d, J = 12.0 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 160.11, 157.03, 148.43, 136.93, 136.78, 132.65, 129.72, 129.67, 129.05, 128.77, 128.18, 127.64, 127.57, 127.06, 126.07, 118.71, 115.32, 70.21.

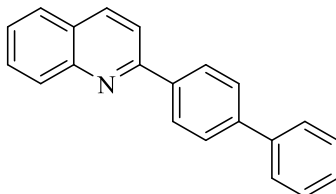
2-(4-(allyloxy)phenyl)quinoline (4.3e)



Following the general procedure **GP1** the title compound **3l** was isolated as colourless oil using silica gel column chromatography with pet-ether/ ethylacetate (v/v= 50/1, R_f = 0.5) in 84% yield (0.219 g). ^1H NMR (600 MHz, CDCl_3): δ 8.20 – 8.11 (m, 4H), 7.82 (dd, J = 17.1, 8.2 Hz, 2H), 7.71 (t, J = 7.4

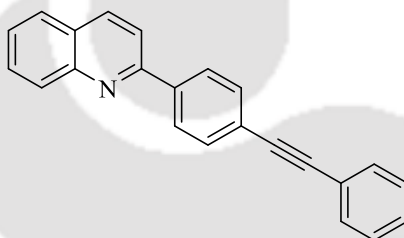
Hz, 1H), 7.50 (t, $J = 7.4$ Hz, 1H), 7.06 (d, $J = 8.6$ Hz, 2H), 6.09 (dq, $J = 15.9, 5.2$ Hz, 1H), 5.46 (d, $J = 17.2$ Hz, 1H), 5.33 (d, $J = 10.4$ Hz, 1H), 4.62 (d, $J = 5.0$ Hz, 2H). ^{13}C NMR (151 MHz, CDCl_3): δ 159.91 (s), 157.03 (s), 148.40 (s), 136.78 (s), 133.17 (s), 132.52 (s), 129.68 (d, $J = 10.9$ Hz), 129.00, 127.57, 127.03, 126.06, 118.71, 118.03, 115.13, 68.98.

2-([1,1'-biphenyl]-4-yl)quinoline (4.3f)⁶⁵



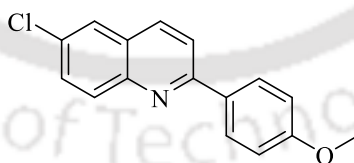
Following the general procedure **GP1** the title compound **3f** was isolated as off white solid using silica gel column chromatography with pet-ether/ ethylacetate (v/v= 50/1, $R_f = 0.5$) in 92% yield (0.258 g). ^1H NMR (600 MHz, CDCl_3): δ 8.31 – 8.25 (m, 2H), 8.22 (d, $J = 8.4$ Hz, 2H), 7.92 (d, $J = 8.4$ Hz, 1H), 7.81 – 7.74 (m, 3H), 7.73 – 7.68 (m, 2H), 7.57 – 7.53 (m, 1H), 7.49 (t, $J = 7.8$ Hz, 2H). ^{13}C NMR (151 MHz, CDCl_3) δ 156.99, 148.47, 142.18, 140.70, 138.65, 136.90, 129.87, 129.82, 128.98, 128.09, 127.71, 127.67, 127.60, 127.34, 127.26, 126.41, 118.99, 77.37, 77.16, 76.95.

2-(4-(phenylethynyl)phenyl)quinoline (4.3g)⁸⁹



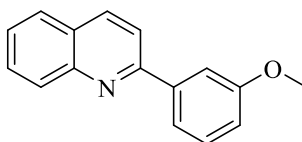
Following the general procedure **GP1** the title compound **3m** was isolated as off white solid using silica gel column chromatography with pet-ether/ ethylacetate (v/v= 20/1, $R_f = 0.5$) in 80% yield (0.244 g). ^1H NMR (600 MHz, CDCl_3): δ 8.27 – 8.15 (m, 4H), 7.91 (d, $J = 8.4$ Hz, 1H), 7.84 (d, $J = 8.0$ Hz, 1H), 7.77 – 7.68 (m, 3H), 7.58 – 7.55 (dd, $J = 14.1, 6.9$ Hz, 3H), 7.37 (d, $J = 6.8$ Hz, 3H). ^{13}C NMR (151 MHz, CDCl_3): δ 156.52, 148.44, 139.37, 137.04, 132.23, 131.82, 129.96, 129.90, 128.56, 128.54, 127.63, 127.58, 127.40, 126.64, 124.39, 123.30, 118.95, 91.04, 89.48.

6-chloro-2-(4-methoxyphenyl)quinoline (4.3h)



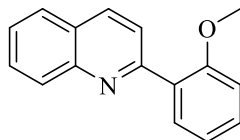
Following the general procedure **GP1** the title compound **3k** was isolated as off white solid using silica gel column chromatography with pet-ether/ ethylacetate (v/v= 20/1, $R_f = 0.5$) in 86% yield (0.220 g). ^1H NMR (400 MHz, CDCl_3): δ 8.14 – 8.05 (m, 4H), 7.86 (d, $J = 8.0$ Hz, 1H), 7.78 (d, $J = 2.0$ Hz, 1H), 7.64 (dd, $J = 8.0, 2.0$ Hz, 1H), 7.08 – 7.02 (m, 2H), 3.89 (s, 3H). ^{13}C NMR (151 MHz, CDCl_3): δ 161.15, 157.27, 146.82, 135.84, 131.92, 131.61, 131.25, 130.60, 129.01, 127.59, 126.26, 119.50, 114.44, 55.57.

2-(3-methoxyphenyl)quinoline (4.3i)



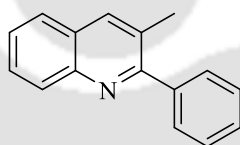
Following the general procedure **GP1** the title compound **3n** was isolated as yellow solid using silica gel column chromatography with pet-ether/ ethylacetate (v/v= 100/1, R_f = 0.5) in 89% yield (0.209 g). ^1H NMR (600 MHz, CDCl_3): δ 8.23 – 8.20 (m, 2H), 7.89 – 7.82 (m, 3H), 7.77 – 7.74 (m, 2H), 7.55 (t, J = 6.0 Hz, 1H), 7.47 (t, J = 6.0 Hz, 1H), 7.06 (m, 1H), 3.96 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3): δ 160.21, 157.21, 148.28, 141.23, 136.86, 129.90, 129.80, 129.76, 127.55, 127.35, 126.42, 120.11, 119.20, 115.46, 112.79, 55.50.

2-(2-methoxyphenyl)quinoline (4.3j)⁸⁸



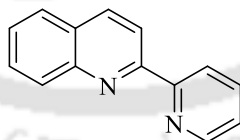
Following the general procedure **GP1** the title compound **3o** was isolated as light yellow liquid using silica gel column chromatography with pet-ether/ ethylacetate (v/v= 100/1, R_f = 0.5) in 84% yield (0.197 g). ^1H NMR (600 MHz, CDCl_3): δ 8.16 (dd, J = 17.0, 8.4 Hz, 2H), 7.89 (d, J = 8.4 Hz, 1H), 7.84 (t, J = 8.6 Hz, 2H), 7.71 (t, J = 7.4 Hz, 1H), 7.53 (t, J = 7.4 Hz, 1H), 7.43 (t, J = 7.4 Hz, 1H), 7.14 (t, J = 7.4 Hz, 1H), 7.04 (d, J = 8.2 Hz, 1H), 3.87 (s, 3H). ^{13}C NMR (151 MHz, CDCl_3) δ 157.30, 157.26, 148.45, 135.20, 131.61, 130.44, 129.77, 129.33, 127.52, 126.30, 123.58, 121.41, 111.53, 55.78.

3-methyl-2-phenylquinoline (4.3k)⁸⁸



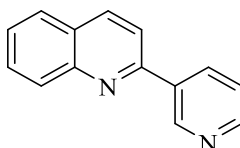
Following the general procedure **GP1** the title compound **3e** was isolated as light yellow liquid using pet-ether/ ethyl acetate (v/v= 50/1, R_f = 0.5) in 90% yield (0.201 g). ^1H NMR (400 MHz, CDCl_3): δ 8.14 (d, J = 8.5 Hz, 1H), 8.02 (s, 1H), 7.78 (d, J = 8.1 Hz, 1H), 7.70 – 7.64 (m, 1H), 7.60 (dd, J = 8.1, 1.3 Hz, 2H), 7.55 – 7.42 (m, 4H), 2.47 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3): δ (ppm) = 160.5, 146.6, 140.9, 136.8, 129.3, 129.2, 128.9, 128.8, 128.3, 128.2, 127.6, 126.7, 126.4, 20.6. Spectral data is in accordance to the reported literature.

2-(pyridin-2-yl)quinoline (4.3l)⁹⁰



Following the general procedure **GP1** the title compound **3g** was isolated as yellow solid using silica gel column chromatography with pet-ether/ ethylacetate (v/v= 20/1, R_f = 0.5) in 91% yield (0.187 g). ^1H NMR (600 MHz, CDCl_3): δ 8.74 – 8.73 (m, 1H), 8.65 (d, J = 12.0 Hz, 1H), 8.56 (d, J = 6.0 Hz, 1H), 8.28 (d, J = 12 Hz, 1H), 8.18 (d, J = 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 156.43, 156.26, 149.27, 148.01, 137.07, 136.93, 129.91, 129.68, 128.35, 127.73, 126.87, 124.15, 121.95, 119.06.

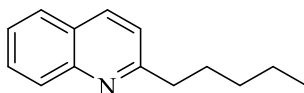
2-(pyridin-3-yl)quinoline (4.3m)⁸⁸



Following the general procedure **GP1** the title compound **3h** was isolated as off yellow solid using silica gel column chromatography with pet-ether/ ethylacetate (v/v= 20/1, R_f = 0.5) in 92% yield

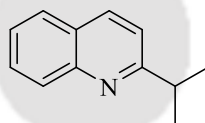
(0.189 g). ^1H NMR (600 MHz, CDCl_3): δ 9.35 (d, $J = 6.0$ Hz, 1H), 8.71 – 8.70 (m, 1H), 8.53 – 8.51 (m, 1H), 8.29 (d, $J = 6.0$ Hz, 1H), 8.18 (d, 12.0 Hz, 1H), 7.90 (d, $J = 6.0$ Hz, 1H), 7.87 (d, $J = 6.0$ Hz, 1H), 7.78 – 7.75 (m, 1H), 7.59 – 7.56 (m, 1H), 7.48 – 7.46 (m, 1H). ^{13}C NMR (151 MHz, CDCl_3): δ 154.80, 150.37, 148.97, 148.50, 137.35, 135.28, 135.12, 130.17, 129.88, 127.71, 127.50, 126.95, 123.85, 118.71.

2-pentylquinoline (4.3n)⁵⁵



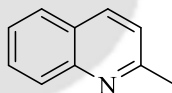
Following the general procedure **GP1** the title compound **3i** was isolated as oily colourless liquid using silica gel column chromatography with pet-ether/ ethylacetate (v/v= 100/1, $R_f = 0.5$) in 76% yield (0.151 g). ^1H NMR (600 MHz, CDCl_3): δ 8.05 (t, $J = 8.5$ Hz, 2H), 7.77 (d, $J = 8.1$ Hz, 1H), 7.71 – 7.66 (m, 1H), 7.48 (t, $J = 7.4$ Hz, 1H), 7.30 (d, $J = 8.3$ Hz, 1H), 2.99 – 2.93 (m, 2H), 1.81 (dt, $J = 15.6, 7.7$ Hz, 2H), 1.42 – 1.33 (m, 4H), 0.90 (t, $J = 7.0$ Hz, 3H). ^{13}C NMR (151 MHz, CDCl_3) δ ^{13}C NMR (151 MHz, CDCl_3) δ 163.28, 147.99, 136.34, 129.46, 128.90, 127.61, 126.83, 125.76, 121.51, 39.47, 31.89, 29.93, 22.71, 14.16.

2-isopropylquinoline (4.3o)⁹¹



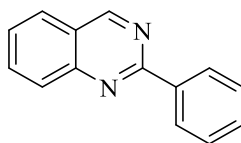
Following the general procedure **GP1** the title compound **3p** was isolated as light yellow liquid using silica gel column chromatography with pet-ether/ ethylacetate (v/v= 100/1, $R_f = 0.5$) in 78% yield (0.133 g). ^1H NMR (600 MHz, CDCl_3): δ 8.07 (d, $J = 12.0$ Hz, 1H), 8.04 (d, $J = 12.0$ Hz, 1H), 7.73 (d, $J = 6.0$ Hz, 1H), 7.68 – 7.67–7.64 (m, 1H), 7.45 (t, $J = 6.0$ Hz, 1H), 7.30 (d, $J = 6.0$ Hz, 1H), 3.27 (hept, $J = 6.0$ Hz, 1H), 1.40 (d, $J = 7.0$ Hz, 6H). ^{13}C NMR (151 MHz, CDCl_3): δ 167.66, 147.79, 136.40, 129.26, 129.04, 127.47, 126.96, 125.66, 119.19, 37.35, 22.58.

2-methylquinoline (4.3p)⁹¹



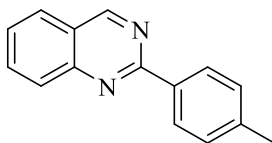
Following the general procedure **GP1** the title compound **3j** was isolated as light yellow oil using silica gel column chromatography with pet-ether/ ethylacetate (v/v= 95/5, $R_f = 0.5$) in 62% yield (0.189 g).

2-phenylquinazoline (4.10a)⁸²



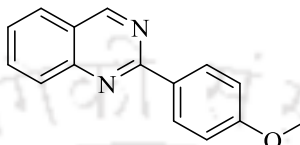
Following the general procedure **GP2** the title compound **5a** was isolated as off white solid using silica gel column chromatography with pet-ether/ ethylacetate (v/v= 100/1, $R_f = 0.5$) in 92% yield (0.189 g). ^1H NMR (600 MHz, CDCl_3): δ 9.48 (s, 1H), 8.62 – 8.61 (m, 2H), 8.10 (d, $J = 6.0$ Hz, 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 161.23, 160.66, 150.93, 138.18, 134.28, 130.76, 128.79, 128.71, 127.43, 127.28, 123.76.

2-(4-methylphenyl)quinazoline (4.10b)⁸⁸



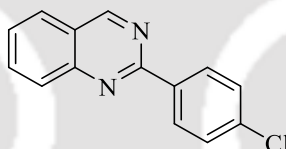
Following the general procedure **GP2** the title compound **5b** was isolated as off white solid using silica gel column chromatography with pet-ether/ ethylacetate (v/v= 100/1, R_f = 0.5) in 92% yield (0.202 g). ^1H NMR (500 MHz, CDCl_3): δ 9.44 (s, 1H), 8.52 (d, J = 8.0 Hz, 2H), 8.07 (d, J = 8.4 Hz, 1H), 7.93 – 7.86 (m, 2H), 7.58 (t, J = 7.5 Hz, 1H), 7.35 (d, J = 7.9 Hz, 2H), 2.45 (s, 3H). ^{13}C NMR (151 MHz, CDCl_3) δ 161.27, 160.57, 150.92, 141.00, 135.44, 134.18, 129.55, 128.67, 128.64, 127.25, 127.17, 123.64, 21.66.

2-(4-methoxyphenyl)quinazoline (4.10c)⁸²



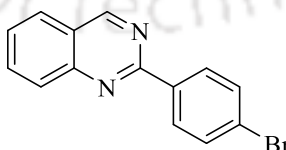
Following the general procedure **GP2** the title compound **5b** was isolated as off white solid using silica gel column chromatography with pet-ether/ ethylacetate (v/v= 100/1, R_f = 0.5) in 96% yield (0.226 g). ^1H NMR (600 MHz, CDCl_3): δ 9.42 (s, 1H), 8.58 (d, J = 8.8 Hz, 2H), 8.04 (d, J = 8.4 Hz, 1H), 7.90 – 7.87 (m, 2H), 7.57 (t, J = 7.4 Hz, 1H), 7.05 (d, J = 8.8 Hz, 2H), 3.90 (s, 3H). ^{13}C NMR (151 MHz, CDCl_3) δ 161.97, 161.01, 160.54, 150.98, 134.16, 130.87, 130.34, 128.55, 127.27, 126.93, 123.46, 114.12, 77.37, 77.16, 76.95, 55.53.

2-(4-chlorophenyl)quinazoline (4.10d)⁸²



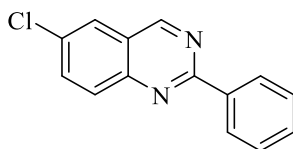
Following the general procedure **GP2** the title compound **5d** was isolated as off white solid using silica gel column chromatography with pet-ether/ ethylacetate (v/v= 50/1, R_f = 0.5) in 82% yield (0.197 g). ^1H NMR (400 MHz, CDCl_3): δ 9.44 (s, 1H), 8.58 – 8.55 (m, 2H), 8.08 – 8.06 (m, 1H), 7.93– 7.89 (m, 2H), 7.64– 7.60 (m, 1H), 7.51 – 7.48 (m, 2H). ^{13}C NMR (151 MHz, CDCl_3): δ 160.68, 160.19, 150.84, 136.98, 136.66, 134.41, 130.04, 128.97, 128.74, 127.61, 127.30, 123.77.

2-(4-bromophenyl)quinazoline (4.10e)⁸²



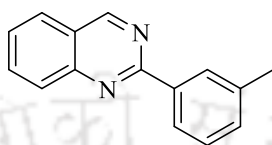
Following the general procedure **GP2** the title compound **5c** was isolated as off white solid using silica gel column chromatography with pet-ether/ ethylacetate (v/v= 50/1, R_f = 0.5) in 86% yield (0.245 g). ^1H NMR (400 MHz, CDCl_3): δ 9.45 (s, 1H), 8.51 – 8.49 (m, 2H), 8.07 (d, J = 8.0 Hz, 1H), 7.94 – 7.92 (m, 2H), 7.67– 7.63 (m, 3H). ^{13}C NMR (101 MHz, CDCl_3): δ 160.70, 160.27, 150.83, 137.11, 134.44, 131.94, 130.29, 128.75, 127.65, 127.31, 125.56, 123.80.

6-chloro-2-phenylquinazoline (4.10f)⁸²



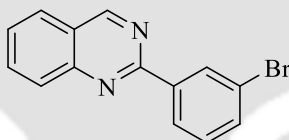
Following the general procedure **GP2** the title compound **3a** was isolated as off white solid using silica gel column chromatography with pet-ether/ ethylacetate (v/v= 95/5, R_f = 0.5) in 81% yield (0.189 g). ^1H NMR (600 MHz, CDCl_3): δ 9.41 (s, 1H), 8.61– 8.59 (m, 2H), 8.04 (d, J = 12.0 Hz, 1H), 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.

2-(*m*-tolyl)quinazoline (**4.10g**)⁸²



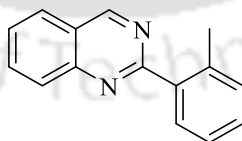
Following the general procedure **GP2** the title compound **5e** was isolated as off white solid using silica gel column chromatography with pet-ether/ ethylacetate (v/v= 100/1, R_f = 0.5) in 85% yield (0.187 g). ^1H NMR (400 MHz, CDCl_3): δ 9.45 (s, 1H), 8.43 – 8.41 (m, 2H), 8.10 – 8.07 (m, 1H), 7.91 – 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 NMR (101 MHz, CDCl_3): δ 161.29, 160.54, 150.85, 138.37, 138.05, 134.18, 131.53, 129.21, 128.68, 127.29, 127.21, 125.89, 123.65, 21.65.

2-(3-bromophenyl)quinazoline (**4.10h**)⁸²



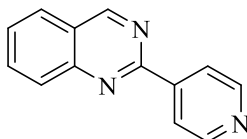
Following the general procedure **GP2** the title compound **3a** was isolated as off white solid using silica gel column chromatography with pet-ether/ ethylacetate (v/v= 95/5, R_f = 0.5) in 92% yield (0.189 g). ^1H NMR (600 MHz, CDCl_3): δ 9.46 (s, 1H), 8.79 (t, J = 6.0 Hz, 1H), 8.56 (d, J = 6.0 Hz, 1H), 8.09 (dd, J = 8.4, 0.5 Hz, 1H), 7.94 – 7.91 (m, 2H), 7.70 – 7.54 (m, 2H), 7.40 (t, J = 6.0 Hz, 1H). ^{13}C NMR (151 MHz, CDCl_3): δ 160.70, 159.72, 150.79, 140.22, 134.46, 133.60, 131.72, 130.27, 128.82, 127.80, 127.29, 127.23, 123.90, 123.07.

2-(*o*-tolyl)quinazoline (**4.10i**)⁹²



Following the general procedure **GP2** the title compound **3a** was isolated as off white solid using silica gel column chromatography with pet-ether/ ethylacetate (v/v= 100/1, R_f = 0.5) in 92% yield (0.178 g). ^1H NMR (600 MHz, CDCl_3): δ 9.51 (s, 1H), 8.10 (d, J = 12.0 Hz, 1H), 7.98 – 7.89 (m, 3H), 7.66 (t, J = 6.0 Hz, 1H), 7.39 – 7.33 (m, 3H), 2.61 (s, 3H). ^{13}C NMR (151 MHz, CDCl_3) δ 164.19, 160.23, 150.53, 138.72, 137.49, 134.27, 131.42, 130.76, 129.44, 128.72, 127.68, 127.21, 126.11, 123.05, 21.15.

2-(pyridin-4-yl)quinazoline (**4.10j**)⁹²



Following the general procedure **GP2** the title compound **3a** was isolated as off white solid using silica gel column chromatography with pet-ether/ ethylacetate (v/v= 95/5, R_f = 0.5) in 92% yield (0.189 g). ^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 = 12.0 Hz, 1H), 8.00 – 7.96 (m, 2H), 7.72– 7.69 (m, 1H). ^{13}C NMR (151 MHz, CDCl_3): δ 160.93, 159.11, 150.73, 150.65, 145.44, 134.70, 129.03, 128.47, 127.36, 124.32, 122.48.

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Boric acid catalyzed chemoselective reduction of quinolines under mild reaction conditions: mechanistic studies and application in the synthesis of antiarrhythmic drug nicainoprol

5.1. Introduction

Nature is the oldest laboratory, producing a wide series of molecules, that has utmost diversity and utility, precisely in the identification of various medicines including antibacterial, antitumor, antifungal compounds.¹ These biologically active molecules are mostly cyclic molecules containing nitrogen atom in their active site.²⁻⁶ In this context, saturated quinolines such as 1,2,3,4-tetrahydroquinolines (1,2,3,4-THQs) core are prevalent in nature and found in the numerous bioactive molecules.⁷⁻¹⁰ Few selected examples¹¹⁻¹⁷ are listed in Figure 5.1.

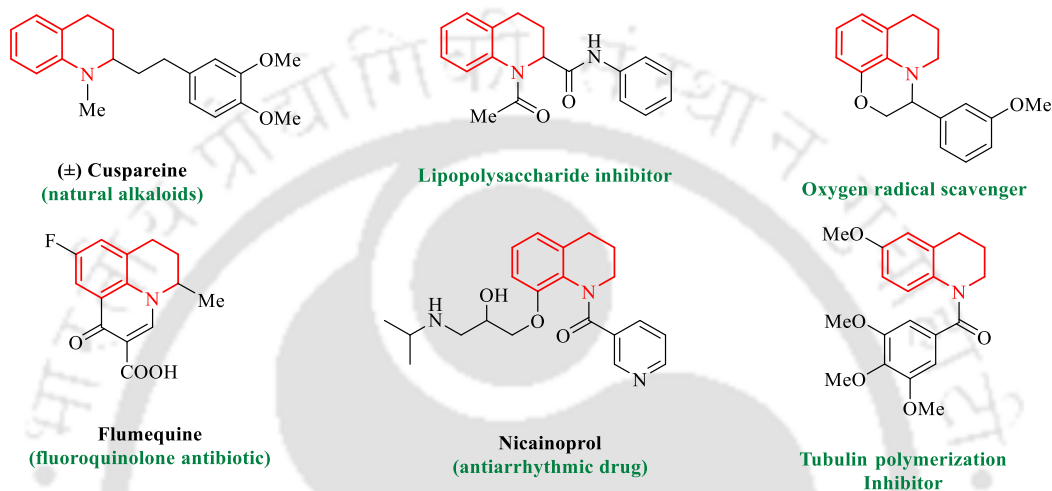


Figure 5.1. Representative bioactive compounds containing 1,2,3,4-THQs framework

Since these molecules have wider applications in the pharmaceuticals, agrochemicals industries and total synthesis of natural products, the scientific community is more inclined towards the development of new and efficient synthetic methodologies for the synthesis of these compounds.⁷⁻¹⁷ Nonetheless there are several synthetic approach known in the literature to construct the 1,2,3,4-THQ derivatives,⁷⁻¹⁰ yet partial hydrogenation of *N*-heteroaromatics is a straightforward and practical method to produce these saturated nitrogen-containing heterocycles (Figure 5.2).^{9, 10} Further, the hydrogenation of quinolines is well explored with the precious as well as non-precious metal catalysts in the presence of suitable hydrogen source.¹⁸⁻²⁴ Despite considerable progress still these protocols possess several disadvantages such as (a) metal contamination; (b) harsh conditions; (c) low substrate scope; (d) functional group intolerance; (e) expensive reagents etc.^{18-20, 25, 26} Occasionally, this reaction is also reported *via* transition-metal-free Lewis acid-catalyzed pathway²⁷⁻³⁵ through hydrogenation,²⁹⁻³¹ hydroborylation,^{27, 28} and hydrosilylation³²⁻³⁴ and very recently iodine catalyzed route¹⁰ (Scheme 5.1). Despite their excellent work where the above-said issues were somehow resolved, yet possess shortcomings like (a) additional step requires in hydroboration and hydrosilylation pathway (for reduction); (b) barely compatible with sensitive reducible functional groups; (c) loss in atom-economy (generates the stoichiometric amount of boron-or silicon-containing by-product); (d) practical methodology that requires less sophisticated techniques; (e) economic reagents etc. (Scheme 5.2), thus improved methodology is highly desired.

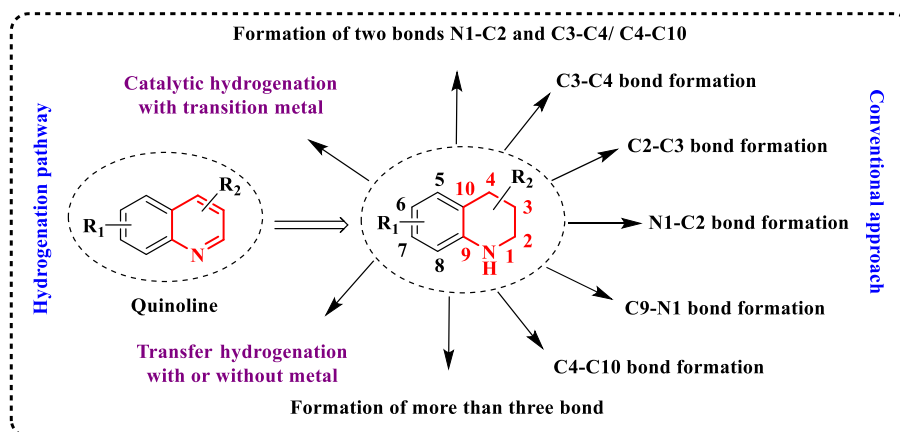
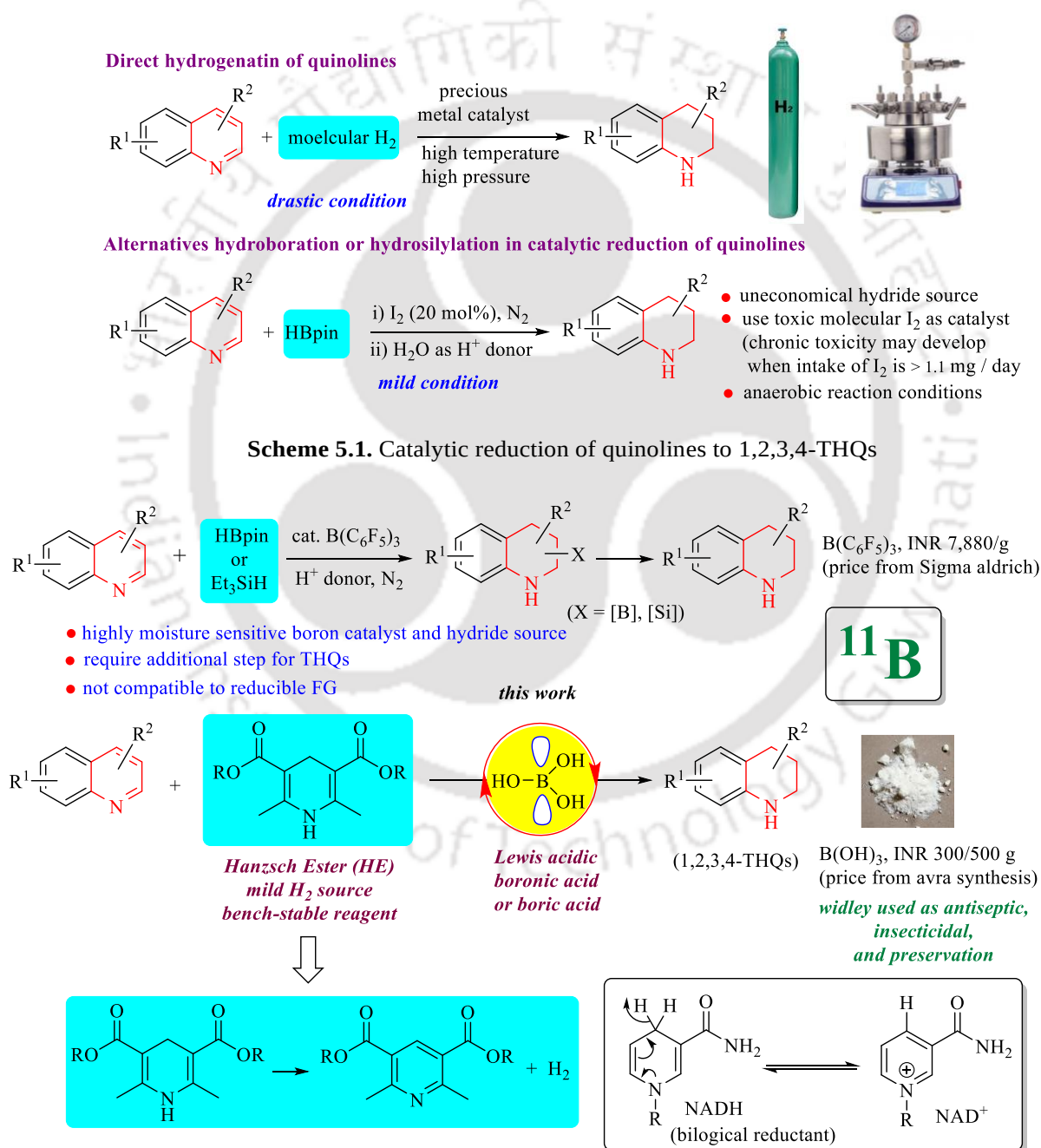


Figure 5.2. Synthetic pathway for the construction of 1,2,3,4-THQs framework



Scheme 5.2. Boron based Lewis acid induced catalytic reduction of quinolines to 1,2,3,4-THQs

As discussed in chapter-1 (section 1.4.2), Hantzsch ester (1,4-dihydropyridines) is widely used as a mild reducing agent for the reduction of quinoline to 1,2,3,4-THQ derivatives.³⁶⁻³⁹ Rueping and co-workers, in their pioneering work, reported biomimetic transfer hydrogenation of quinolines using

chiral phosphoric acid as the catalyst and Hantzsch ester as the hydrogen source.^{40, 41} After that, various research groups independently demonstrated the racemic as well as asymmetric catalytic system for this particular transformation by using different Brønsted acid⁴²⁻⁴⁴, Lewis acidic metals,^{36, 37} and non-covalent bond donors⁴⁵ as the catalyst. Nevertheless, despite the progress made, none of the known catalytic transfer hydrogenation methods can directly reduce *N*-containing fused ring in the presence of other functional groups such as ester, halide, alkyne, amide, nitro, and nitrile groups. The invention of new types of catalysts might be the key to solving this problem.

5.2. Present work

Herein I have demonstrated boric acid (B(OH)₃) catalyzed chemoselective reduction of quinolines with Hantzsch ester under mild conditions. Detailed mechanistic pathways have also been discussed by various control experiments and NMR studies. Finally, the formed tetrahydroquinoline derivatives have been applied into several bioactive molecules including antiarrhythmic drug nicainoprol, antitrypanosomal active compound, natural alkaloid (±) cuspareine, and TB inhibitor.

5.2.1. Results and Discussion

Quinoline ring consists of two fragments (a) nitrogen atom containing the activated ring and (b) an un-activated fused benzene ring. *N*-containing ring can further be activated or polarised by Brønsted acid, Lewis acid etc. Herein I am interested in using of readily available boric acid as the catalyst for the reduction of quinolines to 1,2,3,4-THQs. Owing to weak-Lewis acidic behavior of boric acid, it can selectively reduce *N*-containing fused ring in the presence of other functional groups under mild reaction conditions.

I initiated the reaction with 6-methoxyquinoline **5.1k** as the model substrate, 15 mol% of boric acid as the catalyst, 2.5 equiv. of Hantzsch ester as the hydrogen source at 60 °C in 2 mL of DCE. After 3 h, crude compound was analyzed and obtained the desired product **5.2k** in 70% yield. Interestingly, the yield of **5.2k** has been further improved upto 90% by using phenylboronic acid as the catalyst. However, the yield was dropped to 75% with 4-methoxyphenylboronic acid. This could be due to boron's weaker Lewis acidic behavior of 4-methoxyphenylboronic acid (Table 5.1, entries 1-3).

Table 5.1. Optimization studies for the transfer hydrogenation of 6-methoxyquinoline.^{a,b}

Reaction scheme: 6-methoxyquinoline (**5.1k**) reacts with Hantzsch ester (2.5 equiv) in the presence of a catalyst and solvent at a specific temperature to yield 6-methoxy-1,2,3,4-tetrahydroquinoline (**5.2k**).

entry	catalyst	cat. (mol%)	temp.(°C)	time (h)	solvent	yield (%)
1	B(OH) ₃	15	60	3	DCE	70
2	PhB(OH) ₂	15	60	3	DCE	90
3	4-OMePhB(OH) ₂	15	60	3	DCE	75
4	B(OH) ₃	5	60	7	DCE	16
5	B(OH) ₃	10	60	7	DCE	58
6	B(OH) ₃	15	60	7	DCE	95
7	B(OH) ₃	15	27	7	DCE	nd
8	B(OH) ₃	15	45	7	DCE	63
9	B(OH) ₃	25	60	6	DCE	94
10	B(OH) ₃	15	75	7	DCE	88
11	-	-	60	7	DCE	nd
12	B(OH) ₃	15	60	7	DMC	10
13	B(OH) ₃	15	60	7	toluene	37
14	B(OH) ₃	15	60	7	THF	10
15	B(OH) ₃	15	60	7	CH ₃ CN	46
16	B(OH) ₃	15	60	7	CH ₃ OH	7

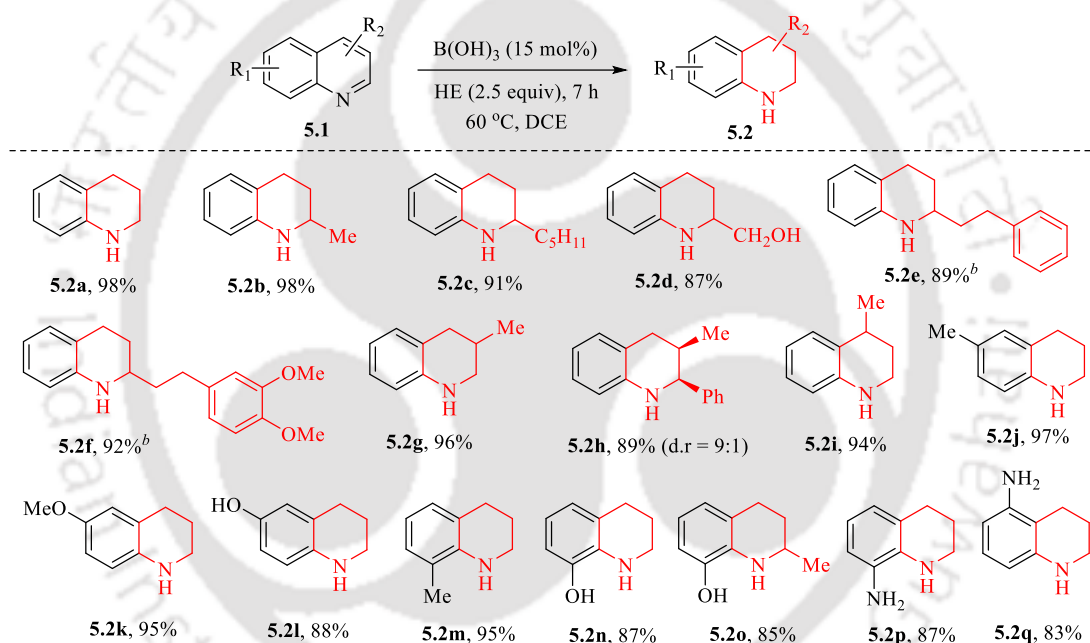
^a Reaction conditions: 6-methoxyquinoline (0.5 mmol), catalyst (mol%), Hantzsch ester (2.5 equiv.) in solvent (2 mL). nd = not detected. DMC = dimethyl carbonate. ^b Isolated yield.

To my delight, the yield of **5.2k** has been increased from 70% to 95% by simply increasing the reaction time from 3 h to 6 h with 15 mol% of boric acid (entry 6). Nevertheless, the yield of desired product is decreased by decreasing the catalyst loading from 15 to 5 mol% (entries 4-9). Notably, the

reaction was failed in the absence of catalyst as well as at room temperature, suggesting both factors were very crucial to achieve the desired product (entries 7, 11). Furthermore, a variety of solvents were investigated. It was found that halogenated solvent (DCE) is the appropriate solvent for the present protocol (entries 6 and 12-16). Based on these observations, the optimized condition is decided that 15 mol% of B(OH)₃, DCE (2 mL), 7 h at 60 °C.

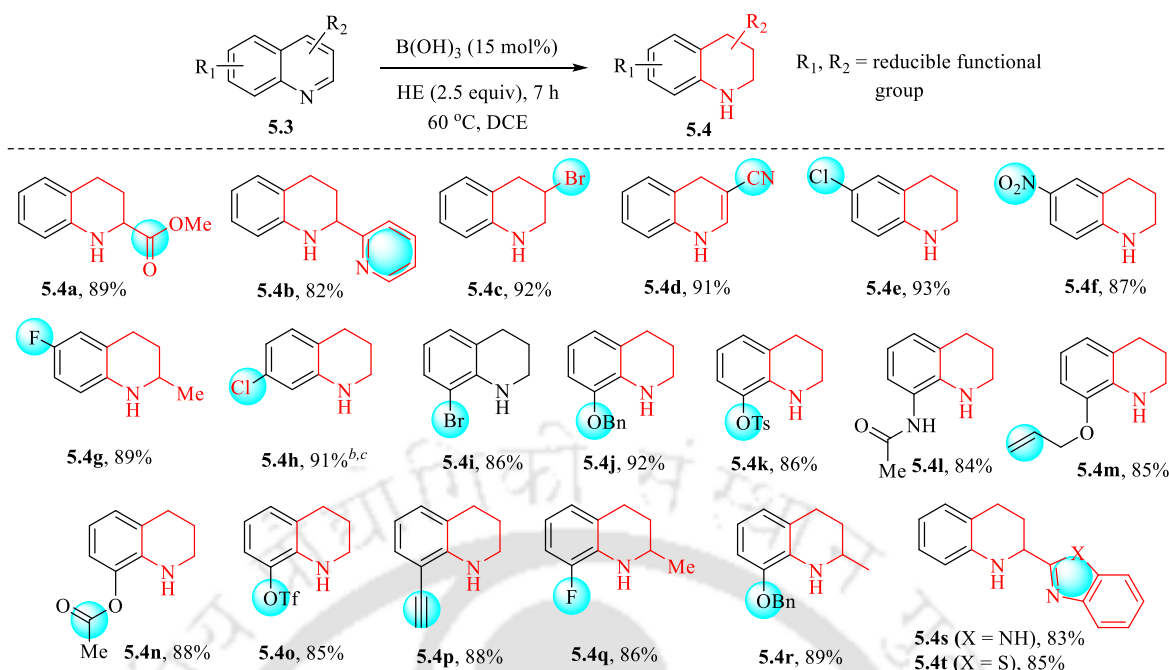
With the optimized conditions in hand, I explored the transfer hydrogenation of various substituted quinolines. For that, I have chosen substitution on both sides, nitrogen-containing ring as well as fused benzene ring, and the results were displayed in the Table 5.2-5.3. The quinolines bearing alkyl, aryl, styryl, methoxy, amine, and hydroxy groups at the different positions were reduced to give the corresponding THQ derivatives **5.2a-q** efficiently in good yield (Table 5.2). In the styryl substrate case, both the quinoline and the conjugated double bond are reduced and lead to the product **5.2f**. For the 2-phenyl-3-methylquinoline, desired product **5.2h** has shown excellent *cis*-selectivity (diastereomeric ratio = 9:1). It is worthy to note that compounds “**5.2a-c**, **5.2f**, **5.2i**, **5.2k-l**” are the useful building blocks for various bioactive compounds (see Experimental section, Table 5.5).^{3b,4} Likewise, tetrahydroquinolin-8-ols (**5.2n** and **5.2o**) can show unique activity e.g., chelation with metal ions, and medicinal activity.^{3b}

Table 5.2. Catalytic transfer hydrogenation of basic quinolines.^a

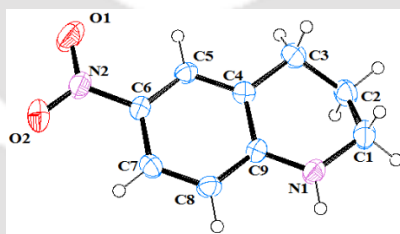


^a Reaction conditions: Substituted quinoline (0.5 mmol), B(OH)₃ (15 mol%), Hantzsch ester (2.5 equiv.) in DCE (2 mL) at 60 °C for 7 h, stirring speed: 400 rpm; isolated yields are reported. ^b 3.5 equiv. HE was used.

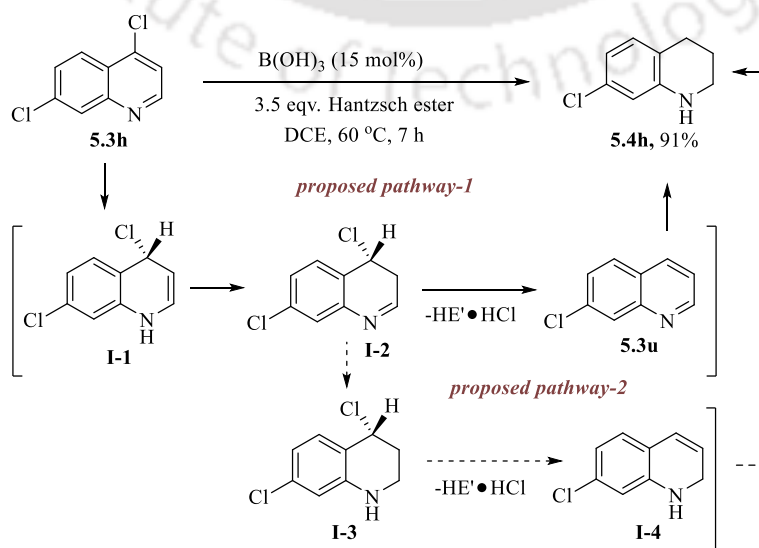
Next, I attempted to explore chemoselective transfer hydrogenation of substituted quinolines with Hantzsch ester (Table 5.3). Quinolines containing various functional groups such as ester, fluoro, chloro, bromo, nitro, nitrile, alkyne, amide, *O*-protected benzyl, tosyl, triflate, and allyl were examined under the reaction conditions. Gratifyingly, all the substituted quinolines were effectively reduced to form corresponding THQs with retaining the functional group (**5.4a**, and **5.4c-r**). The molecular structure of **5.4f** provides evidence for the formation of THQ core and intact the nitro unit. The X-ray crystal structure of compound **5.4f** is depicted in Figure 5.3.

Table 5.3. Chemoselective transfer hydrogenation of substituted quinolines^a

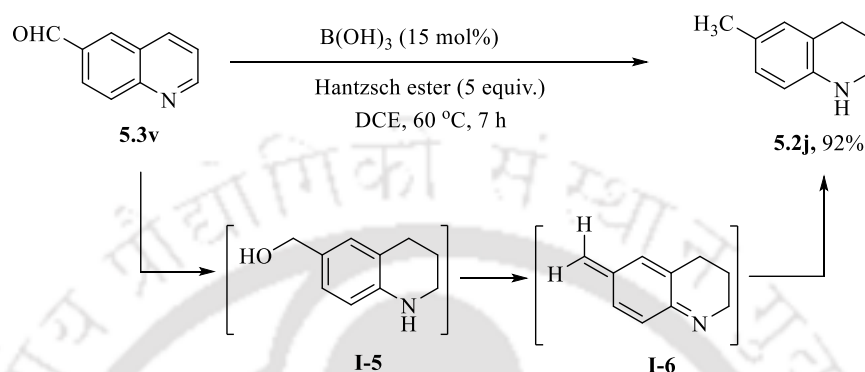
^a Reaction conditions: Substituted quinoline (0.5 mmol), B(OH)₃ (15 mol%), Hantzsch ester (2.5 equiv.) in DCE (2 mL) at 60 °C for 7 h, stirring speed: 400 rpm; isolated yields are reported. ^b 4,7-dichloroquinoline was used as the substrate ^c 3.5 equiv. HE was used.

**Figure 5.3.** Molecular structure of compound **5.4f** (thermal ellipsoid 40% probability level)

In contrast to 3-position substituted bromoquinoline, 3-cyanoquinoline provide 1,4-dihydroquinoline derivative **5.4d** with intact of cyano group, possibly it gains inherent stability by π -electron delocalization. While I subjected to 4,7-dichloroquinoline, interestingly, dehalogenated THQ product **5.4h** was obtained in good yield (proposed reaction pathway is given in Scheme 5.3).

**Scheme 5.3.** Proposed pathway for the reduction of 4,7-dichloroquinoline

In the case of quinoline-6-carbaldehyde, both quinoline ring and carbaldehyde unit were reduced yielded 6-methyl-1,2,3,4-tetrahydroquinoline **5.2j** in 92% yield by using 5 equiv. of Hantzsch ester under the standard conditions. To understand the reaction pathway, the same reaction was conducted with 3.7 equiv. of Hantzsch ester. I have successfully isolated intermediate 6-methylene-2,3,4,6-tetrahydroquinoline (**I-6**) and 6-methyl-1,2,3,4-tetrahydroquinoline (**5.2j**) in 1:3 ratio. The reaction possibly occurs in stepwise manner, first, both the quinoline ring and carbaldehyde unit were reduced to give intermediate **I-5**, then converted to 6-methylene-2,3,4,6-tetrahydroquinoline (**I-6**) via the elimination of hydroxo-group; subsequently further reduction leads to 6-methyl-1,2,3,4-tetrahydroquinoline **5.2j**. The proposed reaction pathway is shown in Scheme 5.4.

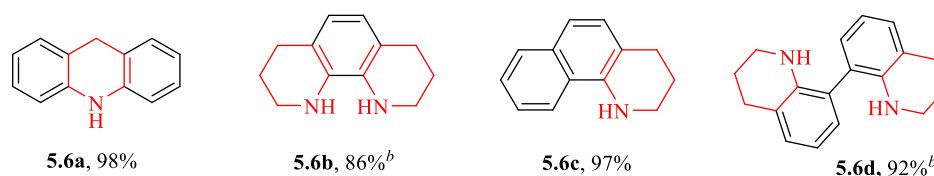


Scheme 5.4. Catalytic reduction of quinoline-6-carbaldehyde

I have also examined C8-substituted *O*- and *N*-atom functionalized quinolines **5.4j-o**, and **5.4r** to know the effect of steric hindrance near the active site. Remarkably, these were also hydrogenated quantitatively and suggested that the catalytic protocol was not only chemoselective but also pleasantly tolerate the functional groups near to the active site. It is worthy of mentioning that the present reduction condition is well tolerated the alkyne functional group into the quinoline moiety (product **5.4p**). Further, I have examined 2,8-disubstituted quinolines to know the effect of steric hindrance near the active site. To my delight, these were also well compatible and provided the desired products (**5.4q** and **5.4r**) in good yields.

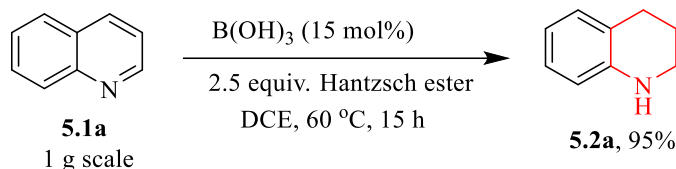
To probe the selective reduction of *N*-heteroaromatic compounds, I have examined the substrate with C-2 substituted pyridyl moiety (**5.3b**), benzimidazole, and benzthiazole moiety (**5.3s-t**). Though these substrates have more than one reaction center, interestingly, *N*-containing fused ring is reduced selectively with good yield (**5.4b**, **5.4s-t**). Besides substituted quinolines, other *N*-heteroarenes **5.5a-d** like acridine, 1,10-phenanthroline, 7,8-benzoquinoline, and 8,8'-biquinoline were also reduced efficiently under the standard conditions (Table 5.4). Overall, this mild catalytic protocol is excellent to showcase the variety of substrates with very good chemoselectivity.

Table 5.4. Selective transfer hydrogenation of substituted quinolines and other *N*-heteroarenes^a



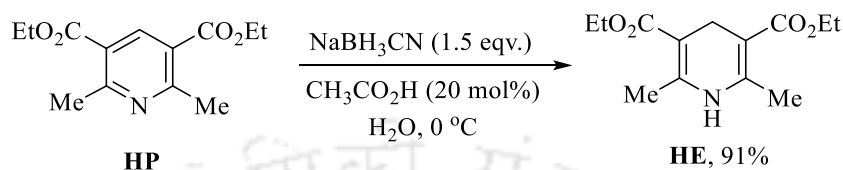
^a Reaction conditions: Substituted quinoline (0.5 mmol), B(OH)₃ (15 mol%), Hantzsch ester (2.5 equiv.) in DCE (2 mL) at 60 °C for 7 h, stirring speed: 400 rpm; isolated yields are reported. ^b 5 equiv. HE was used.

To understand the efficiency of this process, gram-scale reaction was performed for bulk utilization. The reaction takes somewhat longer time (15 h) however, complete conversion was achieved with 95% yield using 1 gram of quinoline (Scheme 5.5).



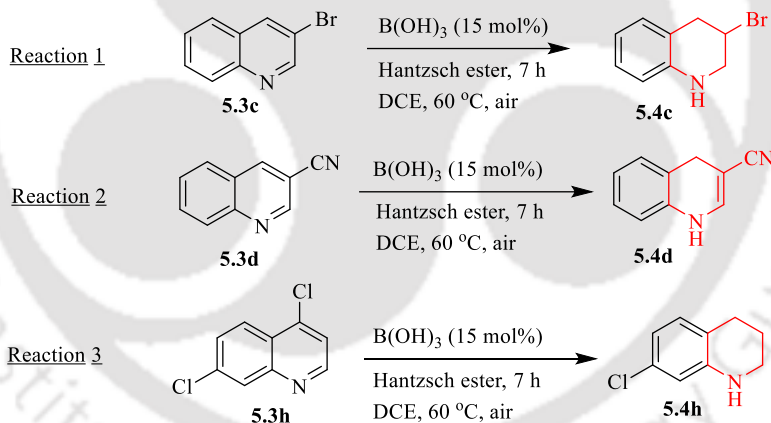
Scheme 5.5. Gram scale transfer hydrogenation of quinoline

Moreover, regeneration of the Hantzsch ester was accomplished by rereducing the aromatized Hantzsch pyridine with sodium cyano borohydride (Scheme 5.6).



Scheme 5.6. Regenerated the by-product of the Hantzsch ester

To gain more clarity about the reaction pathway, I relook the substrate scope studies, particularly for product **5.4c**, **5.4d** and **5.4h** (Scheme 5.7). As shown in Table 5.3, 4,7-dichloroquinoline gives 7-chloro-1,2,3,4-tetrahydroquinoline **5.4h**, and 3-bromoquinoline provides 3-bromo-1,2,3,4-tetrahydroquinoline **5.4c** and no dehalogenated product. On the other hand, the reaction of 3-cyanoquinoline to obtain only 3-cyano-1,4-dihydroquinoline **5.4d** (which might be due to stabilization of conjugation of π electrons). These results suggest that the reaction possibly proceeded via 1,4 addition of hydride into the quinoline moiety.



Scheme 5.7. Transfer hydrogenation of 3-bromo, 3-cyano and 4,7-dichloroquinoline with Hantzsch ester.

To ensure the above results and gain further insight into the reaction pathway I have performed the series of NMR studies as shown in Figure 5.3. [N.B- NMR experiments were performed with quinoline as a substrate and phenylboronic acid as the catalyst (instead of boric acid) since it has very good solubility in CDCl_3]. The bare quinoline in CDCl_3 , ^1H chemical shift for H2 and H4 is δ 8.92–8.93 ppm and δ 8.11–8.13 ppm respectively, which shifted to downfield while interacting with PhB(OH)_2 due to coordinate bond of nitrogen to boron results decreasing of electron density over the nitrogen atom (Figure 5.3).

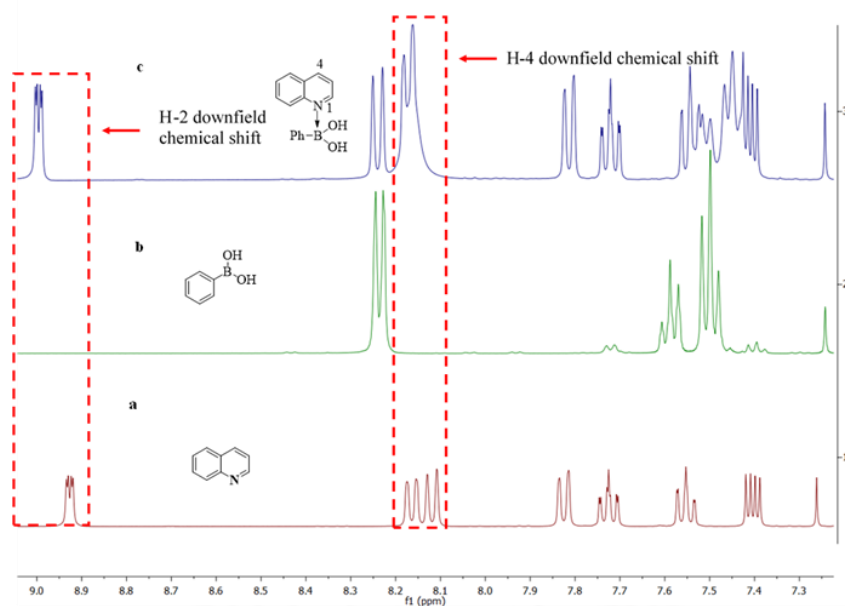


Figure 5.3. Comparative ^1H NMR spectra of (a) quinoline (b) phenylboronic acid and (c) combination of both (NMR experiment and reaction conditions: In a quartz NMR tube, quinoline (26 mg, 0.2 mmol), $\text{PhB}(\text{OH})_2$ (24 mg, 0.2 mmol), CDCl_3 (600 μL) were charged. The NMR tube was properly closed and placed in a preheated oil bath (50 $^\circ\text{C}$) for 1 h. Then, the reaction crude was analysed by ^1H NMR at 50 $^\circ\text{C}$ in 400 MHz Bruker NMR instrument).

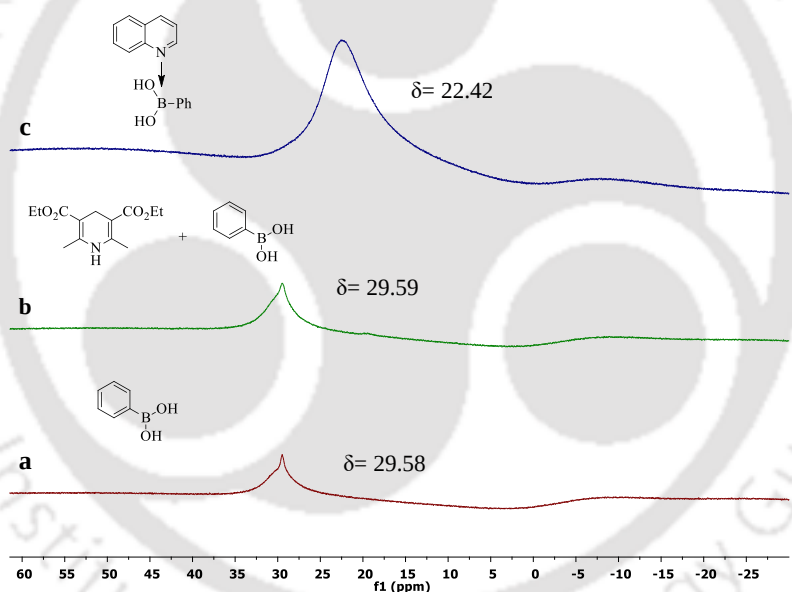


Figure 5.4. Comparative ^{11}B NMR spectra of (a) phenylboronic acid; (b) combination of phenylboronic acid with Hantzsch ester [NMR experiment and reaction conditions: In a quartz NMR tube, Hantzsch ester (86 mg, 0.34 mmol), $\text{PhB}(\text{OH})_2$ (12 mg, 0.1 mmol), CDCl_3 (600 μL) were charged. The NMR tube was properly closed and placed in a preheated oil bath (50 $^\circ\text{C}$) for 1 h. Then, the reaction crude was analysed by ^1H NMR at 50 $^\circ\text{C}$ in 400 MHz Bruker NMR instrument]; and (c) combination of phenylboronic acid with quinoline [NMR experiment and reaction conditions: In a quartz NMR tube, quinoline (44 mg, 0.34 mmol), $\text{PhB}(\text{OH})_2$ (12 mg, 0.1 mmol), CDCl_3 (600 μL) were charged. The NMR tube was properly closed and placed in a preheated oil bath (50 $^\circ\text{C}$) for 1 h. Then, the reaction crude was analysed by ^1H NMR at 50 $^\circ\text{C}$ in 400 MHz Bruker NMR instrument].

A similar effect also observed in the ^{11}B NMR for phenylboronic acid and a combination of phenylboronic acid and quinoline. Where due to the coordinate bonding electron density on boron increases and it shifted to upfield (Figure 5.4). Hence, NMR study demonstrated that a weak adduct was formed with quinoline and phenylboronic acid,^{46, 47} however, there was no interaction with Hantzsch ester and phenylboronic acid (Figure 5.5).

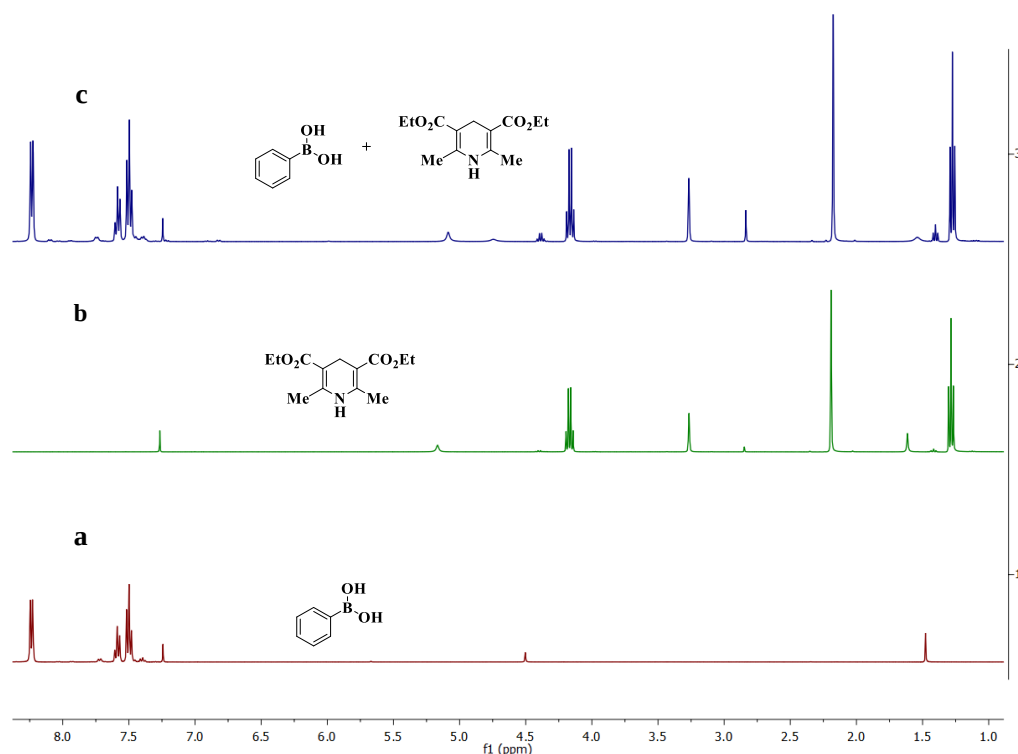
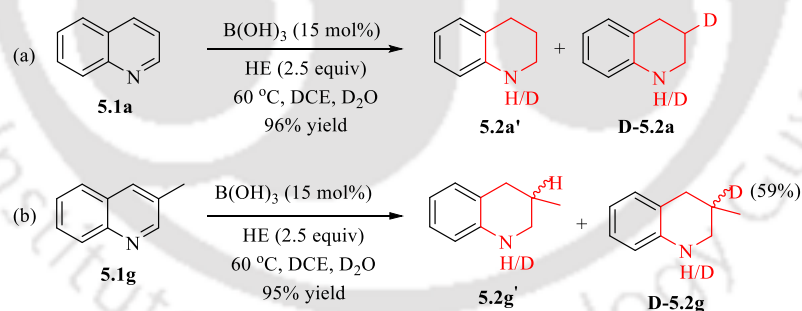


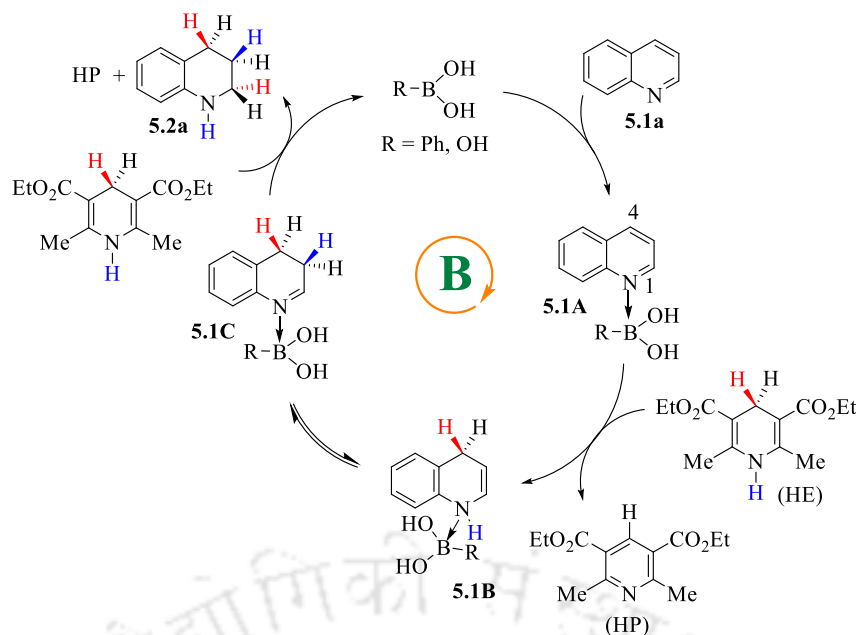
Figure 5.5. Comparative ^1H NMR spectra of (a) phenylboronic acid; (b) Hantzsch ester; and (c) combination of phenylboronic acid with Hantzsch ester (NMR experiment and reaction conditions: In a quartz NMR tube, Hantzsch ester (50 mg, 0.2 mmol), PhB(OH)_2 (24 mg, 0.2 mmol), CDCl_3 (600 μL) were charged. The NMR tube was properly closed and placed in a preheated oil bath (50 $^\circ\text{C}$) for 1 h. Then, the reaction crude was analysed by ^1H NMR at 50 $^\circ\text{C}$ in 400 MHz Bruker NMR instrument).

To locate the hydridic proton and acidic proton in the product, the deuterium-labelled experiments were performed with **5.1a** and **5.1g** independently in presence of D_2O . 59% of deuterium atom was incorporated in both cases at the C3 position of the THQ moiety *via* exchangeable proton of Hantzsch ester and D_2O (Scheme 5.8).

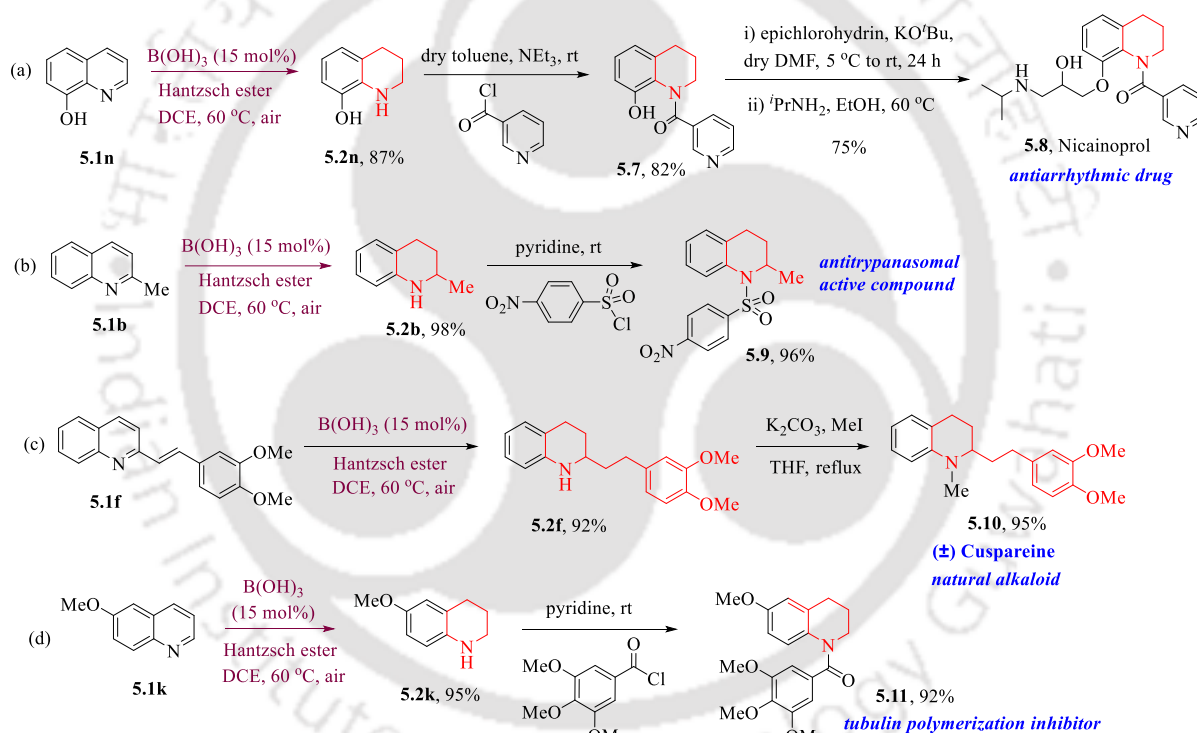


Scheme 5.8. Deuterium-labelled experiment for quinoline and 3-methyl quinoline

On the basis of these experimental findings, a plausible catalytic cycle has been proposed in Scheme 5.9. Atfirst, 1,4-position of quinoline ring is activated by the interaction with boron,^{46,47} and formed the species **5.1A**. Then, hydride atom attacks at the C4 position of the quinoline moiety and generate 1,4-dihydroquinoline⁴⁸ (**5.1B**) intermediate. The resulting species **5.1B** isomerizes to 3,4-dihydroquinoline (**5.1C**), and subsequent 1,2-hydride transfer occurs.^{22, 38-40}



Scheme 5.9. Probable mechanistic pathway



Scheme 5.10. Application in the synthesis of the nicainoprol and other bioactive compounds

As 1,2,3,4-THQs are the important core for various biologically active molecules, the synthetic protocol was utilized towards few bioactive molecules such as antiarrhythmic drug nicainoprol (**5.8**), antitrypanosomal active compound (**5.9**), natural alkaloid ($\pm$) cuspareine (**5.10**), and TB inhibitor (**5.11**) in good yield (Scheme 5.10). The desired molecules can be easily prepared in multi-steps from the readily available starting precursor. For example, an antiarrhythmic drug nicainoprol¹² can be synthesized in multi-steps starting from readily available 8-hydroxyquinoline (**5.1n**). Using the present reaction condition, compound **5.1n** can be easily converted to **5.2n** in good yield, subsequently transformed to *N*-amidation derivative **5.7** with 82% yield. Then it reacted with epichlorohydrin, followed by overnight reflux with isopropyl amine yielded desired product **5.8** with 75% yield. Furthermore, I have utilized building block **5.2b** for the synthesis of other distinct biological active compound *i.e.* antitrypanosomal active compound **5.9**.^{19, 49} Besides, natural alkaloid ($\pm$) cuspareine **5.10**^{16, 17} has also been synthesized in 95% yield from the reaction of **5.2f** and methyl iodide. Tubulin polymerization inhibitor **5.11** has been synthesized from 6-methoxyquinoline in just

two step.^{14, 19, 38, 39} First step is boric acid catalyzed reduction of quinoline with Hantzsch ester and then coupling of formed 6-methoxytetrahydroquinoline with 3,4,5-trimethoxy benzoyl chloride in the presence of pyridine afforded desired product with 92% yield. Additionally, in Table 5.5, I have presented few other bio-active molecules which can be synthesized in multiple steps from the obtained THQs.

5.2.2. Summary

In summary, I have demonstrated boric acid catalyzed transfer hydrogenation of quinolines with Hantzsch ester under mild conditions. The protocol functions under mild catalytic conditions with excellent yield and good chemoselectivity. The mechanistic studies demonstrate that the reaction proceeds via a stepwise 1,4/1,2-hydride addition to the quinoline moiety. The synthetic utility of the tetrahydroquinoline derivatives is exemplified by synthesizing several bio-active molecules including antiarrhythmic drug nicainoprol. Overall, this method for transfer hydrogenation is promising, especially from industrial perspective, as it's an operationally simple, efficient, environment-friendly, scalable, economical, and abundant boric acid used as the catalyst.

5.3. 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. and directly used as received without any further purification unless otherwise mentioned. 2-pentylquinoline,⁵⁰ quinolin-2-ylmethanol,⁵¹ 2-styrylquinoline,⁵² (E)-2-(3,4-dimethoxystyryl)quinoline,⁵² 3-methyl-2-phenylquinoline,⁵⁰ methyl quinoline-2-carboxylate,⁵³ 3-cyanoquinoline,⁵⁴ 8-(benzyloxy)quinoline,⁵⁵ quinolin-8-yl-4-methylbenzenesulfonate,⁵⁶ N-(quinolin-8-yl)acetamide,⁵⁷ quinolin-8-ylacetate,⁵⁸ 2-(2-benzimidazolyl)quinolone⁵⁹ and 2-(quinolin-2-yl)benzo[d]thiazole⁵⁹ were prepared according to the reported literature. Boric acid, phenyl boronic acid, and 4-methoxy phenyl boronic acid were purchased from Avra Synthesis Private Ltd and used without further purification. Hantzsch ester was prepared according to the reported literature.⁶⁰ All the transfer hydrogenation reactions were performed in a pyrex tube. ¹H, ¹³C, ¹⁹F, and ¹¹B NMR spectra of the compounds were measured in CDCl₃ and DMSO-*d*₆ as a solvent by using TMS as an internal standard. Chemical shifts, δ (in ppm), are reported relative to TMS δ (¹H) 0.0 ppm, δ (¹³C) 0.0 ppm) which was used as the inner reference. Otherwise the solvents residual proton resonance and carbon resonance (CHCl₃, δ (¹H) 7.26 ppm, δ (¹³C) 77.16 ppm; DMSO-*d*₆, (¹H) 2.50 ppm, δ (¹³C) 39.52 ppm) were used for calibration. Bruker Avance III 600 and 400 spectrometers were used to record the NMR spectra. Chemical shifts (δ) are reported in ppm and spin-spin coupling constant (*J*) are expressed in Hz, and other data are 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 or Spectrochem silica gel 60-120 was used for column chromatography. All the transfer hydrogenation reactions were carried out under air.

A. General procedure for transfer hydrogenation reaction:

In a pyrex tube (15 mL), substituted quinoline (0.5 mmol), Hantzsch ester (2.5 equiv.), B(OH)₃ (15 mol%) and solvent (2 mL) 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 completing the reaction, the crude compound was purified by column chromatography on silica gel for pure compound.

Note: 1,2,3,4-THQ's are highly iodine active and easily identified in a reaction mixture.

B. Procedure for gram scale transfer hydrogenation reaction (Scheme 5.5):

In a pyrex tube (100 mL), quinoline (1.09 gm, 8.46 mmol), Hantzsch ester (5.35 gm, 2.5 eqv.), B(OH)₃ (79 mg, 15 mol%) and DCE (15 mL) 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 hexane and ethyl acetate solvent system. Once the reaction was completed, reaction tube was brought to room temperature and purified by column chromatography for pure product. The final product was then analysed by ¹H and ¹³C NMR. Isolated yield: 1.07 gm, 95%.

C. Procedure for Hantzsch pyridine (HP) to Hantzsch-1,4-dihydropyridine (HE) recovery (Scheme 5.6):

In a 50 mL round bottom flask, Hantzsch pyridine (1 gm, 3.9 mmol), water (10 mL) and acetic acid (45 µL, 20 mol%) were charged and placed in an ice bath. In the reaction mixture NaBH₃CN (294 mg, 1.2 eqv.) was slowly added and stirred for overnight. The reaction was monitored by thin layered chromatography (TLC) in hexane and ethyl acetate solvent system. Once the reaction was completed, solid precipitate was filtered, washed thoroughly with water and ice cold acetone and dried on vacuum desiccator. Isolated yield: 0.9 g, 91%.

D. Applications of synthesized 1,2,3,4-tetrahydroquinoline derivatives:

i) Synthesis of nicainoprol (5.8):

Transfer hydrogenation of 8-hydroxyquinoline to 8-hydroxy-1,2,3,4-tetrahydroquinoline

In a pyrex tube (100 mL), 8-hydroxyquinoline (1 g, 6.8 mmol, 1 eqv.), Hantzsch ester (4.3 g, 17 mmol, 2.5 eqv.), B(OH)₃ (15 mol%) and DCE (15 mL) 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. Once the reaction was completed, reaction tube was brought to room temperature and purified by silica column chromatography using CH₂Cl₂/ MeOH mixture to get the pure 8-hydroxy-1,2,3,4-tetrahydroquinoline (5.2n). Isolated yield: 0.882 g, 87%, colourless oil.

Synthesis of compound 5.7

In a 50 mL schlenk flask, 8-hydroxy-1,2,3,4-tetrahydroquinoline (0.6 g, 4.02 mmol, 1 eqv.), nicotinoyl chloride (0.681 g, 4.83 mmol, 1.2 eqv.), triethyl amine (0.611 g, 6.04 mmol, 1.5 eqv.) and dry toluene (20 mL) were charged and stirred overnight in argon atmosphere at room temperature. Once the reaction was complete, toluene was evaporated by using rotary evaporator. The solid reaction crude was purified by liquid-liquid separation method (water/ ethyl acetate), the organic layer was added with Na₂SO₄ to remove the excess water and concentrated in a rotary evaporator. Afterwards, the solid crude was purified by silica column chromatography using CH₂Cl₂ : MeOH (5-10% MeOH mixture) solvent system to obtain pure product as white solid (838 mg, 82%); m.p: 121~122 °C.

Synthesis of compound 5.8

In a 50 mL schlenk flask, compound 5 (0.125 g, 0.49 mmol, 1 eqv.) was dissolved in dry DMF (0.5 mL) and potassium *tert*-butoxide (0.066 g, 0.59 mmol, 1.2 eqv.) was charged onto it. The entire solution was stirred in ice cold bath (~0-5 °C) for 30 min followed by the dropwise addition of epichlorohydrin (0.068 g, 0.735 mmol, 1.5 eqv.). After complete addition the reaction mixture was continue to stir at ice cold bath for next 30 minutes and then allowed warm to room temperature and stirred for another 24 h. The reaction was monitored by thin layered chromatography (TLC) in CH₂Cl₂ and methanol solvent system. After completion of the reaction, crude reaction was concentrated in rotary evaporator and purified by using liquid-liquid separation method (water/ ethyl acetate). The organic layer (ethyl acetate fraction) was added with Na₂SO₄ to remove the excess water and concentrated in a rotary evaporator. Afterwards, the solid crude (0.118 g, 78%) was directly

proceeded for the next step without any further purification. The compound was sensitive towards air and moisture, recommendable to store under argon at -20 °C.

In a 50 mL pyrex tube, above crude compound (0.118 g, 0.38 mmol, 1 eqv.) was dissolved in dry ethanol (2 mL) and isopropylamine (0.045 g, 0.76 mmol, 2 eqv.) was charged onto it. The tube was closed under argon flow and the entire solution was stirred at 60 °C for 12 hours. The reaction was monitored using thin layered chromatography (TLC). Upon complete consumption of the starting material, the reaction mixture is concentrated in rotary evaporator to remove ethanol and unreacted isopropylamine. Analytically pure compound **5.8** was obtained by neutral alumina column chromatography using CH₂Cl₂:CH₃OH (4% CH₃OH mixture) solvent system to obtain pure product as white solid (130 mg, 93%); m.p: 120~122 °C. Overall yield in the last step: 75%.

ii) Synthesis of antitrypanosomal active compound (5.9):

Step 1: Transfer hydrogenation of 2-methylquinoline to 2-methyl-1,2,3,4-tetrahydroquinoline (5.2b)

In a pyrex tube (15 mL), 6-methoxyquinoline (159 mg, 1 mmol), Hantzsch ester (633 mg, 2.5 eqv.), B(OH)₃ (10 mg, 15 mol%) and dichloroethane (5 mL) 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 hexane and ethyl acetate solvent system. Once the reaction was completed, reaction tube was brought to room temperature and purified by column chromatography for pure product. Isolated yield-144 mg, 98%, colourless oil.

Step 2: Synthesis of 2-methyl-1-((4-nitrophenyl)sulfonyl)-1,2,3,4-tetrahydroquinoline (5.9)⁴⁹

In a 25 mL round bottom flask, 2-methyl-1,2,3,4-tetrahydroquinoline (100 mg, 0.68 mmol), 4-nitrobenzenesulfonyl chloride (150 mg, 1 eqv.) and pyridine (3 mL) were charged and allowed to stir at room temperature for 20 h. After consuming the substrates, water was added to the reaction mixture and extracted by using ethyl acetate. The organic layer was further washed with diluted HCl solution to remove the pyridine in traces. Afterwards, in the organic layer Na₂SO₄ was added to remove excess water and finally organic solvent was evaporated by using rotary evaporator. The product was further purified by column chromatography using hexane and ethyl acetate solvent system to obtain the pure product as pale yellow solid (217 mg, 96%); m.p: 160~162 °C.

iii) Synthesis of cuspareine (5.10):

Step 1: Transfer hydrogenation of (E)-2-(3,4-dimethoxystyryl)quinolone (5.1f) to 2-(3,4-dimethoxyphenethyl)-1,2,3,4-tetrahydroquinoline (5.2f)

In a pyrex tube (15 mL), (E)-2-(3,4-dimethoxystyryl)quinoline (100 mg, 0.34 mmol), Hantzsch ester (217 mg, 2.5 eqv.), B(OH)₃ (4 mg, 15 mol%) and dichloroethane (3 mL) 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 hexane and ethyl acetate solvent system. Once the reaction was complete, reaction tube was brought to room temperature (30 °C) and purified by column chromatography for pure product. Isolated yield: 93 mg, 92%.

Step 2: Synthesis of 2-(3,4-dimethoxyphenethyl)-1-methyl-1,2,3,4-tetrahydroquinoline (5.10)¹⁷

In a pyrex tube (15 mL), 2-(3,4-dimethoxyphenethyl)-1,2,3,4-tetrahydroquinoline (50 mg, .17 mmol), methyl iodide (32 µL, 3 eqv.), potassium carbonate (1 eqv.) and dry THF (3 mL) were charged. The reaction mixture was allowed to reflux in a pre-heated oil bath for 20 h. Once the substrates were consumed, THF was evaporated using rotary evaporator and directly purified by column chromatography (*n*-hexane/ ethyl acetate) to afford the pure product as yellow oil (50 mg, 95%).

iv) Synthesis of tubulin polymerization inhibitor (5.11):

Step 1: Transfer hydrogenation of 6-methoxyquinoline to 6-methoxy-1,2,3,4-tetrahydroquinoline (5.2k)

In a pyrex tube (15 mL), 6-methoxyquinoline (159 mg, 1 mmol), Hantzsch ester (633 mg, 2.5 eqv.), B(OH)₃ (10 mg, 15 mol%) and dichloroethane (5 mL) 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 hexane and ethyl acetate solvent system. Once the reaction was complete, reaction tube was brought to room temperature and purified by column chromatography for pure product **5.2k**. Isolated yield: 155 mg, 95%.

Step 2: Synthesis of compound **5.11**³⁵

In a 50 mL schlenk flask, 6-methoxy-1,2,3,4-tetrahydroquinoline (100 mg, 0.61 mmol), was dissolved in pyridine (2 mL). Next, 3,4,5-trimethoxybenzoyl chloride (0.92 mmol, 1.5 eqv.) was added to the above solution and resulting mixture was allowed to stir at room temperature for overnight. Once the reaction was completed, water was added to the reaction mixture and extracted by using ethyl acetate. The organic layer was further washed with diluted HCl solution to remove the pyridine in traces. Afterwards, in the organic layer Na₂SO₄ was added to remove excess water and finally organic solvent was evaporated by using rotary evaporator. The product was further purified by column chromatography using hexane and ethyl acetate solvent system to obtain the pure product as light yellow viscous liquid (200 mg, 92%).

E. Reaction mechanism studies:

i) ¹H NMR spectrum of crude reaction mixture:

Further, with close inspection of ¹H NMR spectrum of reaction mixture, I found two of the interesting peaks at $\delta = 4.65$ and 3.43 ppm (H3 and H4 respectively). The chemical shifts are well matched with the previous report⁴⁸ and probably due to the presence of 1,4-dihydroquinoline as an intermediate on the crude reaction.

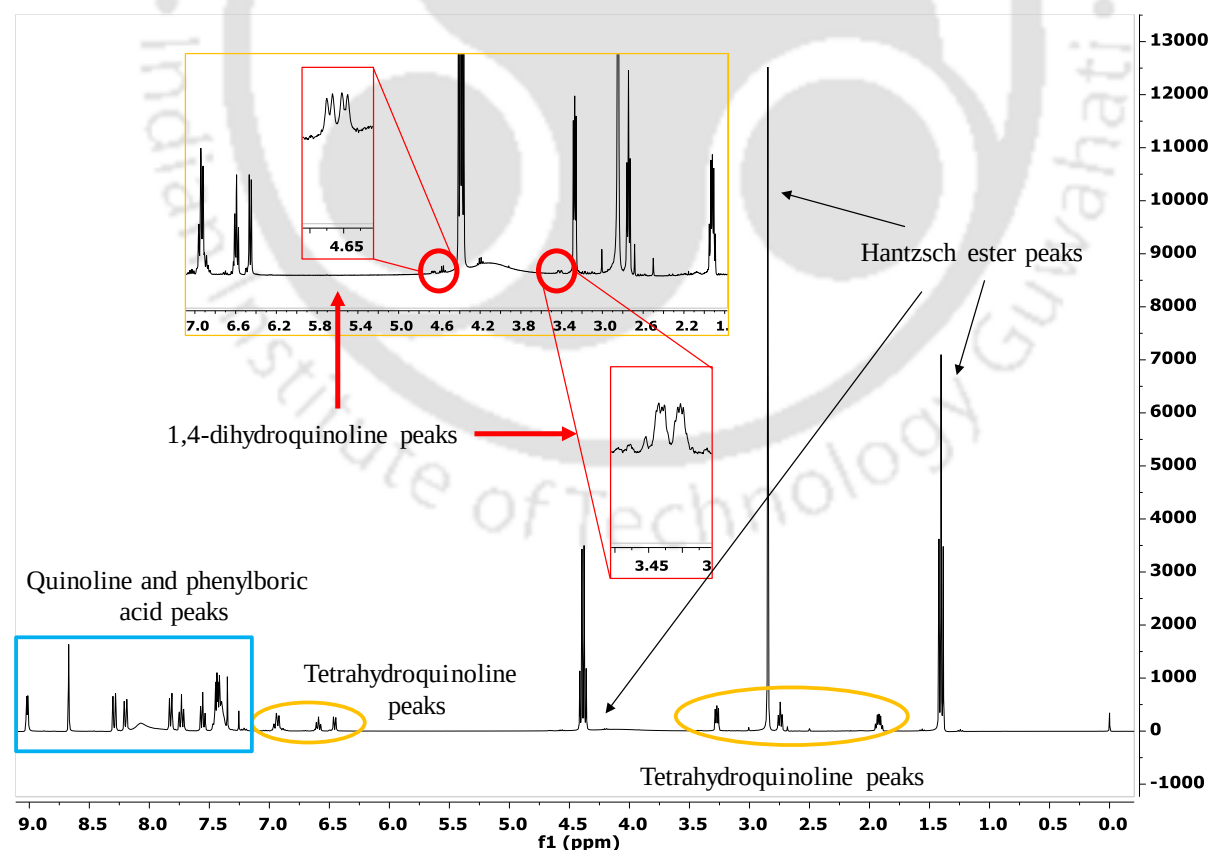


Figure 5.3: ¹H NMR spectra of quinoline reduction crude. NMR experiment and reaction conditions: In a quartz NMR tube, quinoline (54 mg, 0.42 mmol), Hantzsch ester (2.5 eqv.), B(OH)₃ (15 mol%), CDCl₃ (600 μ L) were charged. The NMR tube was properly closed and placed in a preheated oil bath (50 °C) for 1 h. Then, the reaction crude was analysed by ¹H NMR at 50 °C in 400 MHz Bruker NMR instrument.

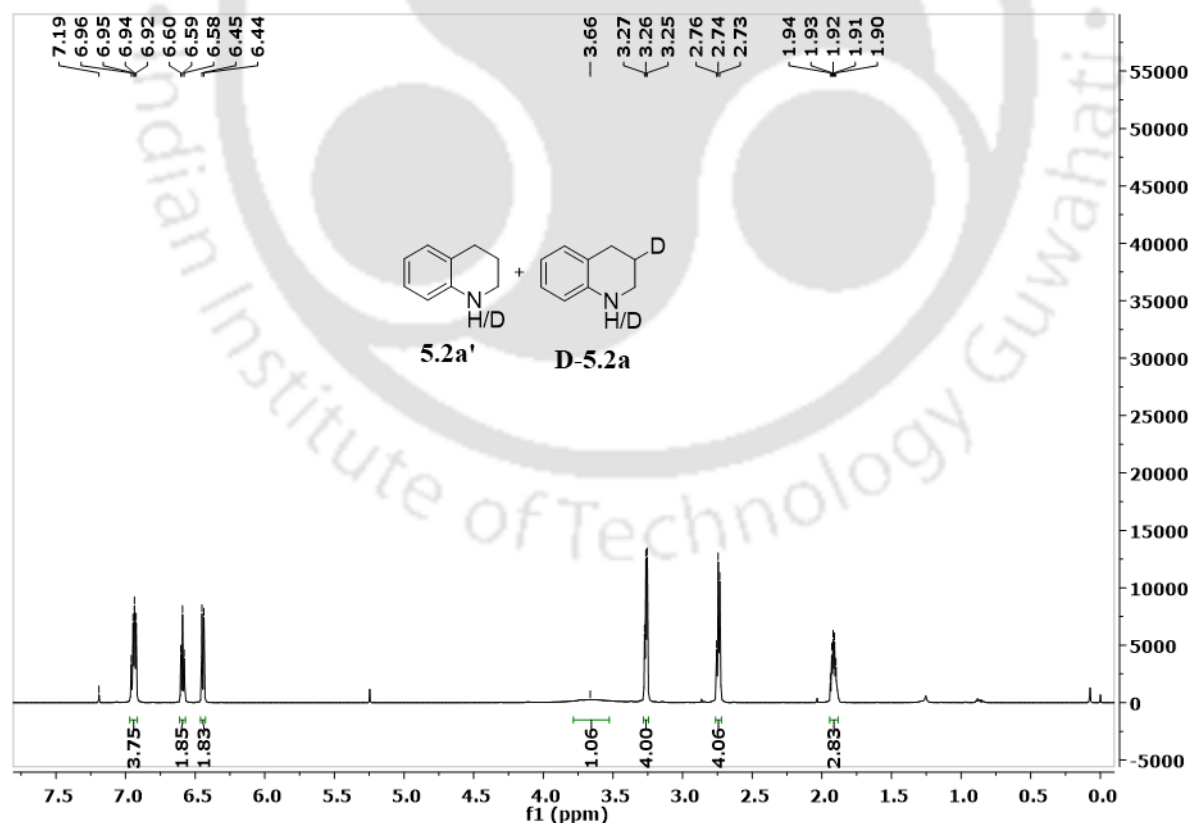
ii) Deuterium-labelling experiment:

To reconfirm the results and more specifically to locate the hydridic proton and acidic proton in the 1,2,3,4-THQ product I have conducted the catalytic experiment in presence of D₂O. To simplify the D₂O experiment results, we have taken two different substrates *i.e.* quinoline and 3-methyl quinoline. The result demonstrated that deuterium atom was incorporated at C3 position of THQ moiety. Thus, from all the results obtained from catalytic reactions and NMR experiments, here we concluded that in catalytic reaction, 1,4-position of quinoline ring gets activated (by decreasing electron density) due to interaction with catalyst where hydride atom attacks and form 1,4-dihydroquinoline. This 1,4-dihydroquinoline gets isomerized to 3,4-dihydroquinoline which again it interacts with the catalyst and another Hantzsch ester, subsequently 1,2-hydride shift occurs and leads to desired product.

Reaction conditions: In a pyrex tube (15 mL), substituted quinoline (1 mmol), Hantzsch ester (2.5 eqv.), B(OH)₃ (15 mol%), dichloroethane (3 mL) and D₂O (0.60 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. Once the reaction complete, reaction tube was brought to room temperature and purified by column chromatography for pure compound. The final product was then analysed by ¹H and ¹³C NMR.

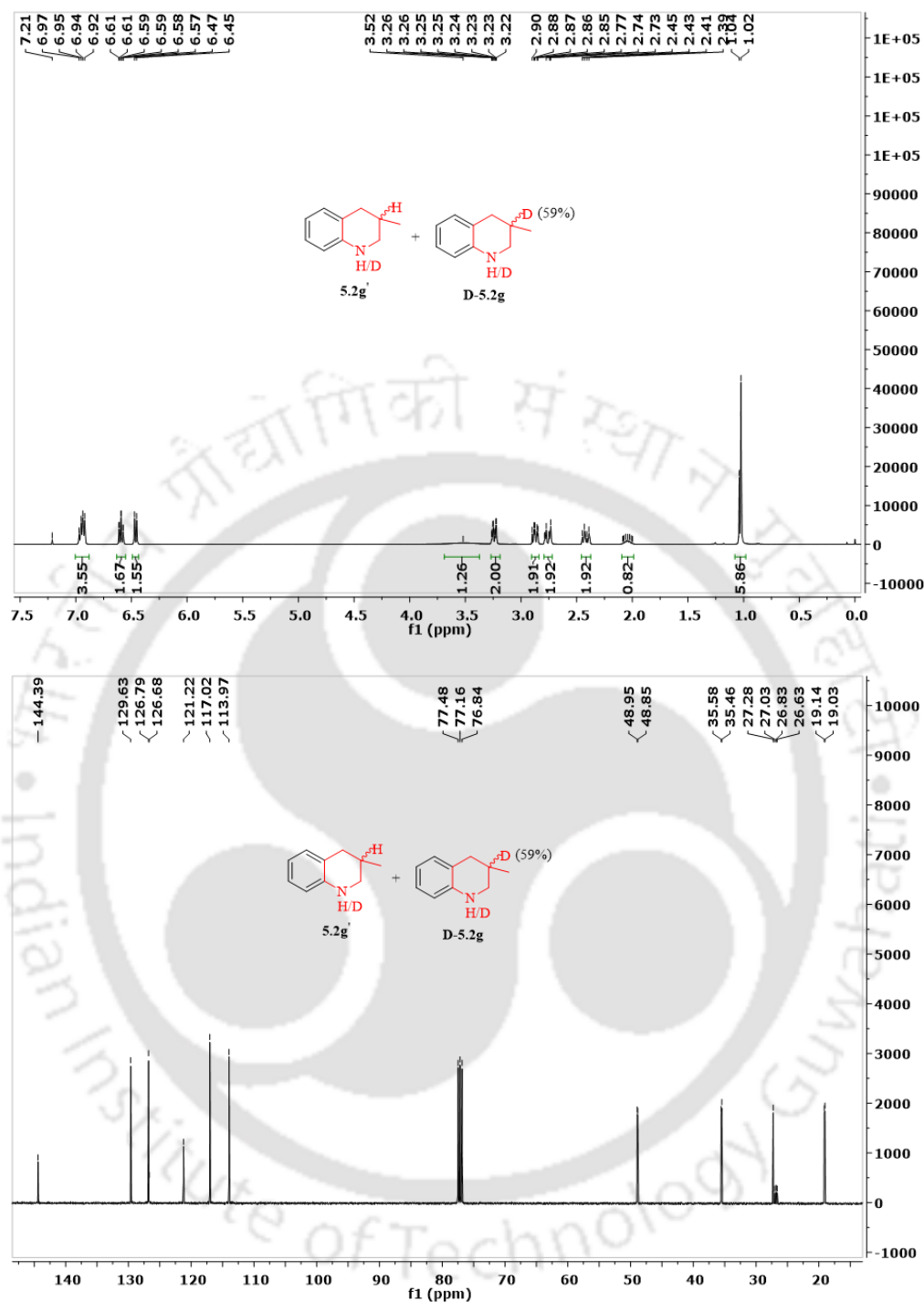
¹H NMR spectrum of deuterated 1,2,3,4-tetrahydroquinoline (5.2a' + D-5.2a):

¹H NMR (600 MHz, CDCl₃): δ 6.96–6.92 (m, 4H, 5.2a' + D-5.2a), 6.60–6.58 (t, *J* = 7.3 Hz, 2H, 5.2a' + D-5.2a), 6.45–6.44 (d, *J* = 7.9 Hz, 2H, 5.2a' + D-5.2a), 3.66 (br, 2H, 5.2a' + D-5.2a), 3.27–3.25 (m, 4H, 5.2a' + D-5.2a), 2.76–2.73 (t, *J* = 6.8 Hz, 2H, 5.2a' + D-5.2a), 1.94–1.90 (m, 3H, 5.2a' + D-5.2a).



¹H NMR spectrum of deuterated 3-methyl-1,2,3,4-tetrahydroquinoline (5.2g' + D-5.2g): ¹H NMR (400 MHz, CDCl₃): δ 6.97–6.92 (dd, *J* = 12.6, 7.1 Hz, 4H, 5.2g' + D-5.2g), 6.61–6.57 (m, 2H, 5.2g' + D-5.2g), 6.47–6.45 (d, *J* = 7.9 Hz, 2H, 5.2g' + D-5.2g), 3.52 (br, 2H, 5.2g' + D-5.2g), 3.26–3.22 (m, 2H, 5.2g' + D-5.2g), 2.90–2.85 (m, 2H, 5.2g' + D-5.2g), 2.79–2.73 (m, 2H, 5.2g' + D-5.2g), 2.45–2.39 (m, 2H, 5.2g' + D-5.2g), 2.07–2.02 (m, 1H, 5.2g') 1.04 (s, 6H, 5.2g' + D-5.2g).

^{13}C NMR spectrum of deuterated 3-methyl-1,2,3,4-tetrahydroquinoline (**5.2g'** + **D-5.2g**): ^{13}C NMR (101 MHz, CDCl_3): δ 144.39, 129.63, 126.79, 126.68, 121.22, 117.02, 113.97, 48.95, 48.85, 35.58, 35.46, 27.28, 27.03, 26.83, 26.63, 19.14, 19.03.



F. Crystallographic study of compound **5.4f**

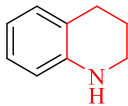
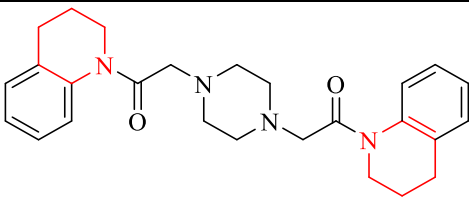
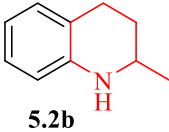
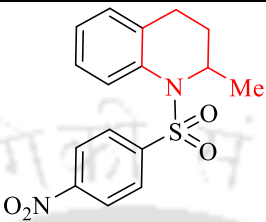
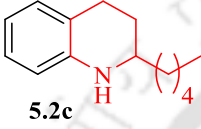
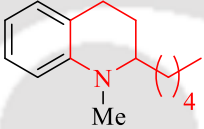
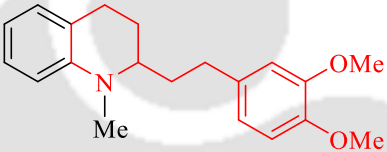
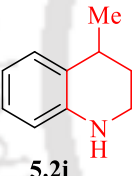
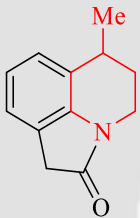
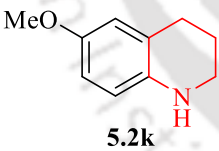
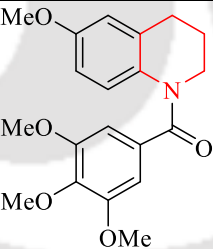
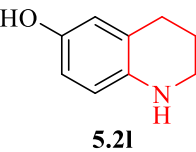
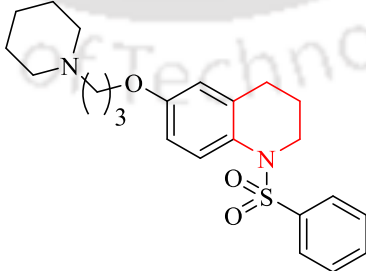
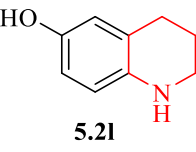
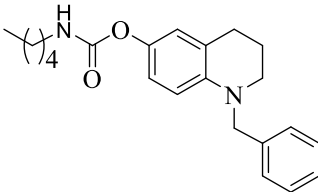
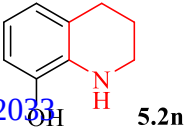
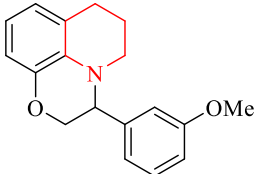
The crystal was obtained by crystallisation of compound **5.4f** in the presence of chloroform as solvent at room temperature using slow evaporation technique. X-ray crystallographic data were collected using Supernova, single source at offset, Eos diffractometer. Data refinement and cell reduction were 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 crystallographic parameters and refinement data were listed in Table 5.4.

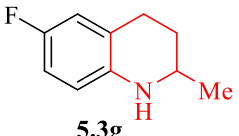
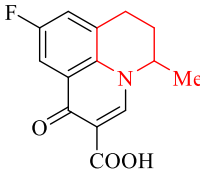
Table 5.4. Crystal data and structure refinement for **5.4f**

Identification code	shelx	
CCDC:	1946184	
Empirical formula	C ₉ H ₁₀ N ₂ O ₂	
Formula weight	178.19	
Temperature	293(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	<i>P</i> 2 ₁ / <i>n</i>	
Unit cell dimensions	<i>a</i> = 7.5569(7) Å	$\alpha = 90^\circ$.
	<i>b</i> = 7.5729(6) Å	$\beta = 101.729(9)^\circ$.
	<i>c</i> = 15.4076(14) Å	$\gamma = 90^\circ$.
Volume	863.33(13) Å ³	
Z		
Density (calculated)	1.371 Mg/m ³	
Absorption coefficient	0.099 mm ⁻¹	
F(000)	376	
Crystal size	0.35 × 0.32 × 0.30 mm ³	
Theta range for data collection	2.700 to 24.982°.	
Index ranges	-8 ≤ <i>h</i> ≤ 5, -5 ≤ <i>k</i> ≤ 9, -12 ≤ <i>l</i> ≤ 18	
Reflections collected	2994	
Independent reflections	1513 [R(int) = 0.0277]	
Completeness to theta = 25.242°	97.7 %	
Refinement method	Full-matrix least-squares on F ²	
Data / restraints / parameters	1513 / 0 / 120	
Goodness-of-fit on F ²	1.139	
Final R indices [I > 2σ(I)]	R1 = 0.0528, wR2 = 0.1192	
R indices (all data)	R1 = 0.0690, wR2 = 0.1387	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.185 and -0.244 e.Å ⁻³	

G. Synthesized precursors for bioactive molecules:

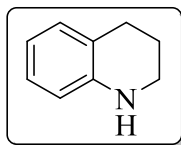
Table 5.5. Some reduced quinoline compound as an active intermediate for the synthesis of biological active molecules

Entry	1,2,3,4-THQ derivative	Bioactive compound	Application	Ref.
1	 5.2a		Aspernigerin, Natural alkaloid	61
2	 5.2b		Anti trypanosomal activity	62
3	 5.2c		(±)Angustureine Natural alkaloid	63
4	5.2f		Cuspareine (natural alkaloids)	17
5	 5.2i		CNS depressant agent	63
6	 5.2k		Tubulin polymerization Inhibitor	35
7	 5.2l		Histamine H3- Receptor antagonist	64
8	 5.2m		AChE inhibitor	65
9	 5.2n		Oxygen radical scavenger	15

10	 5.3g		Flumequine antibiotic	11
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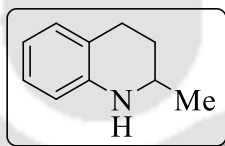
5.4. Analytical data of the products:

1,2,3,4-tetrahydroquinoline (5.2a)



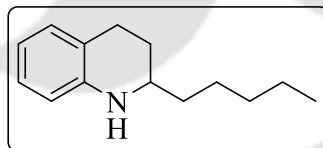
Colourless oil (65 mg, 98%). ^1H NMR (400 MHz, CDCl_3): δ 6.97 – 6.93 (m, 2H), 6.59 (t, $J = 7.4$ Hz, 1H), 6.46 (d, $J = 7.9$ Hz, 1H), 3.30 – 3.28 (m, 2H), 2.76 (t, $J = 6.4$ Hz, 2H), 1.96 – 1.90 (m, 2H). ^{13}C NMR (101 MHz, CDCl_3): δ 144.89, 129.64, 126.84, 121.59, 117.08, 114.32, 42.12, 27.09, 22.31. Spectral data is in accordance with the literature.³⁵

2-methyl-1,2,3,4-tetrahydroquinoline (5.2b)



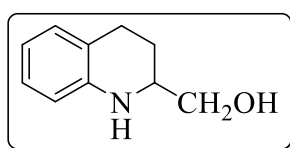
Colourless oil (72 mg, 98%). ^1H NMR (400 MHz, CDCl_3): δ 6.97 – 6.93 (m, 2H), 6.61 – 6.57 (m, 1H), 6.46 – 6.44 (m, 1H), 3.64 (brs, 1H), 3.42 – 3.34 (m, 1H), 2.87–2.79 (m, 1H), 2.74 – 2.68 (m, 1H), 1.94 – 1.88 (m, 1H), 1.62 – 1.53 (m, 1H), 1.20 (d, $J = 6.3$ Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3): δ 144.79, 129.26, 126.68, 121.05, 116.95, 114.02, 47.14, 30.14, 26.61, 22.60. Spectral data is in accordance with the literature.³⁵

2-pentyl-1,2,3,4-tetrahydroquinoline (5.2c)



Colourless oil (92 mg, 91%). Isolated yield: 91%. ^1H NMR (400 MHz, CDCl_3): δ 6.97 – 6.93 (m, 2H), 6.59 (td, $J = 7.4, 1.2$ Hz, 1H), 6.47 (dd, $J = 8.4, 1.3$ Hz, 1H), 3.76 (brs, 1H), 3.23 (dtd, $J = 9.5, 6.3, 2.9$ Hz, 1H), 2.87 – 2.66 (m, 2H), 1.99 – 1.93 (m, 1H), 1.49–1.26 (m, 8H), 1.59 – 1.49 (m, 1H), 0.91 (t, $J = 6.8$ Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3): δ 144.77, 129.39, 126.84, 121.63, 117.12, 114.25, 51.78, 36.79, 32.10, 28.25, 26.57, 25.55, 22.79, 14.19. Spectral data is in accordance to the reported literature.⁶⁶

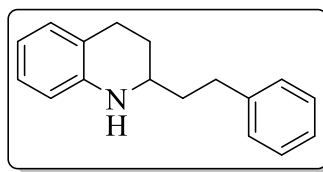
(1,2,3,4-tetrahydroquinolin-2-yl) methanol (5.2d)



Pale yellow oil (70 mg, 87%). ^1H NMR (400 MHz, CDCl_3): δ 7.00 – 6.95 (m, 2H), 6.63 (td, $J = 7.4, 1.2$ Hz, 1H), 6.54 (dd, $J = 7.9, 1.2$ Hz, 1H), 3.75 (dd, $J = 10.4, 3.8$ Hz, 1H), 3.56 (dd, $J = 10.4, 7.7$ Hz, 1H), 3.47 – 3.44 (m, 1H), 2.84 (ddd, $J = 16.4, 10.8, 5.6$ Hz, 1H), 2.74 (dt, $J = 16.3, 4.9$ Hz, 1H), 1.90 (dddd, $J = 13.1, 5.6, 4.3, 3.2$ Hz, 1H), 1.71 (dddd, $J = 12.9, 10.8, 9.4, 5.4$ Hz, 1H). ^{13}C NMR

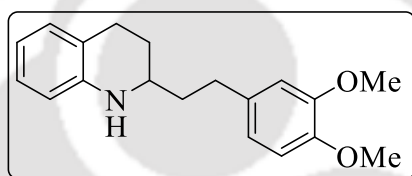
(101 MHz, CDCl₃): δ 144.27, 129.37, 127.02, 121.58, 117.61, 114.68, 66.90, 52.90, 26.03, 24.46. Spectral data is in accordance to the reported literature.⁶⁷

2-phenethyl-1,2,3,4-tetrahydroquinoline (5.2e)



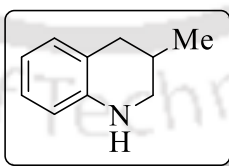
Started with a conjugated double bond containing substrate 2-styrylquinoline. For this, 3.5 equiv. of Hantzsch ester was used. White sticky liquid (105 mg, 89%). ¹H NMR (400 MHz, CDCl₃): δ 7.31 – 7.27 (m, 2H), 7.24 – 7.18 (m, 3H), 6.97-6.93 (m, 2H), 6.60 (t, J = 7.3 Hz, 1H), 6.44 (d, J = 7.8 Hz, 1H), 3.74 (brs, 1H), 3.31-3.28 (m, 1H), 2.79 – 2.72 (m, 4H), 1.99 (ddd, J = 16.0, 8.3, 4.6 Hz, 1H), 1.86 – 1.80 (m, 2H), 1.69 – 1.65 (m, 1H). ¹³C NMR (101 MHz, CDCl₃): δ 144.65, 141.98, 129.38, 128.62, 128.49, 126.87, 126.10, 121.42, 117.16, 114.27, 51.25, 38.39, 32.31, 28.12, 26.35. Spectral data is in accordance with the literature.⁶⁸

2-(3,4-dimethoxyphenethyl)-1,2,3,4-tetrahydroquinoline (5.2f)



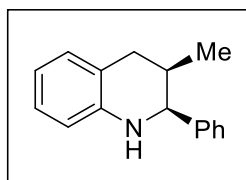
Started with a conjugated double bond containing substrate (*E*)-2-(3,4-dimethoxy styryl)quinoline. For this, 3.5 equiv. of Hantzsch ester was used. Yellow sticky solid (136 mg, 92%); m.p: 52~54 °C. ¹H NMR (600 MHz, CDCl₃): δ 6.96 – 6.94 (m, 2H), 6.79 (d, J = 8.1 Hz, 1H), 6.74 (d, J = 8.1 Hz, 1H), 6.73 (d, J = 1.6 Hz, 1H), 6.60 (t, J = 7.3 Hz, 1H), 6.44 (d, J = 7.7 Hz, 1H), 3.87 (s, 3H), 3.85 (s, 3H), 3.29 (td, J = 9.2, 6.4 Hz, 1H), 2.79 (dd, J = 10.6, 5.5 Hz, 1H), 2.76 – 2.72 (m, 1H), 2.68 (t, J = 8.0 Hz, 2H), 1.99 (dd, J = 8.7, 3.4 Hz, 1H), 1.80 (td, J = 8.9, 7.4, 3.4 Hz, 2H), 1.69 (dd, J = 10.5, 5.3 Hz, 1H). ¹³C NMR (151 MHz, CDCl₃) δ 148.94, 147.30, 144.57, 134.51, 129.32, 126.80, 121.34, 120.16, 117.08, 114.20, 111.62, 111.30, 55.99, 55.89, 51.25, 38.49, 31.88, 28.06, 26.26. Spectral data is in accordance with the literature.¹⁷

3-methyl-1,2,3,4-tetrahydroquinoline (5.2g)



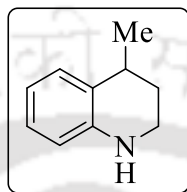
Colourless oil (71 mg, 96%). ¹H NMR (400 MHz, CDCl₃): δ 6.96-6.93 (m, 2H), 6.60 (t, J = 6.9 Hz, 1H), 6.48 (d, J = 7.9 Hz, 1H), 3.84 (brs, 1H), 3.26 (ddd, J = 11.0, 3.6, 2.0 Hz, 1H), 2.91 – 2.86 (m, 1H), 2.77 (ddd, J = 16.0, 4.8, 1.6 Hz, 1H), 2.43 (dd, J = 16.0, 10.3 Hz, 1H), 2.07 – 1.98 (m, 1H), 1.04 (d, J = 6.6 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃): δ 144.39, 129.62, 126.78, 121.19, 117.00, 113.96, 48.94, 35.57, 27.28, 19.14. Spectral data is in accordance with the literature.³⁵

3-methyl-2-phenyl-1,2,3,4-tetrahydroquinoline (5.2h)



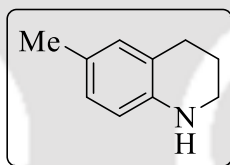
White solid (99 mg, 89%); m.p: 84~86 °C. *cis* : *trans* = 10:1. ^1H NMR (400 MHz, CDCl_3): δ 7.32 – 7.22 (m, 5H, major + minor), 7.04 – 6.98 (m, 2H, major + minor), 6.65 (td, J = 7.4, 1.2 Hz, 1H, major + minor), 6.54 (dd, J = 8.0, 1.2 Hz, 1H, minor major + minor), 4.50 (d, J = 3.6 Hz, 1H, major, 90%), 4.39 (d, J = 3.6 Hz, 1H, minor, 10%), 4.11 (brs, 1H, major, 90%), 3.94 (d, J = 12.4 Hz, 1H, minor, 10%), 3.38 (d, J = 12.4 Hz, 1H, minor, 10%), 2.96 (dd, J = 16.1, 5.0 Hz, 1H, major, 90%), 2.49 (dd, J = 16.1, 6.8 Hz, 2H, major 90% + minor 10%), 2.44-2.39 (m, 1H, minor, 10%), 2.31-2.28 (m, 1H, major, 90%), 0.88 (d, J = 6.4 Hz, 3H, minor, 10%), 0.81 (d, J = 6.9 Hz, 3H, major, 90%). ^{13}C NMR (101 MHz, CDCl_3): δ 144.28, 143.05, 129.83, 128.24, 127.29, 127.23, 127.00, 120.14, 117.19, 113.79, 59.48, 33.50, 32.01, 15.27 (for major 90%). HRMS (ESI) m/z : calculated for $\text{C}_{16}\text{H}_{18}\text{N}$ ($\text{M}+\text{H}^+$): 224.1434; found: 224.1446. Spectral data is in accordance to the literature.⁶⁹⁻⁷¹ The relative *cis*- configuration was tentatively assigned by comparison with literature data.⁶⁹⁻⁷¹

4-methyl-1,2,3,4-tetrahydroquinoline (5.2i)



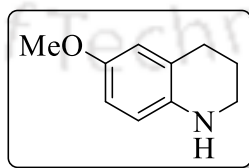
Colourless oil (69 mg, 94%). ^1H NMR (400 MHz, CDCl_3): δ 7.05 (d, J = 7.5 Hz, 1H), 6.96 (t, J = 7.3 Hz, 1H), 6.63 (t, J = 7.4 Hz, 1H), 6.47 (d, J = 7.9 Hz, 1H), 3.36-3.27 (m, 2H), 2.94 – 2.89 (m, 1H), 2.02 – 1.95 (m, 1H), 1.71 – 1.65 (m, 1H), 1.29 (d, J = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3): δ 144.39, 128.58, 126.87, 126.78, 117.11, 114.31, 39.17, 30.38, 30.04, 22.76. Spectral data is in accordance to the reported literature.³⁵

6-methyl-1,2,3,4-tetrahydroquinoline (5.2j)



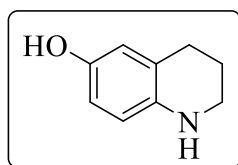
Colourless oil (71 mg, 97%). ^1H NMR (400 MHz, CDCl_3): δ 6.78 – 6.76 (m, 2H), 6.39 (d, J = 8.6 Hz, 1H), 3.43 (brs, 1H), 3.31 – 3.20 (m, 2H), 2.72 (t, J = 6.5 Hz, 2H), 2.19 (s, 3H), 1.94 – 1.88 (m, 2H). ^{13}C NMR (101 MHz, CDCl_3): δ 142.52, 130.16, 127.34, 126.33, 121.69, 114.56, 42.29, 27.02, 22.55, 20.50. Spectral data is in accordance to the reported literature.¹⁸

6-methoxy-1,2,3,4-tetrahydroquinoline (5.2k)



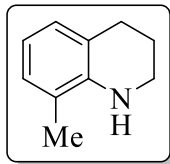
Colourless oil (77 mg, 95%). ^1H NMR (400 MHz, CDCl_3): δ 6.60 – 6.55 (m, 2H), 6.45 – 6.43 (d, J = 8.5 Hz, 1H), 3.72 (s, 3H), 3.26 – 3.23 (m, 2H), 3.14 (brs, 1H), 2.75 (t, J = 6.5 Hz, 2H), 1.95-1.89 (m, 2H). ^{13}C NMR (101 MHz, CDCl_3): δ 151.97, 138.97, 123.03, 115.71, 115.02, 113.03, 55.94, 42.46, 27.28, 22.56. Spectral data is in accordance to the reported literature.¹⁸

6-hydroxy-1,2,3,4-tetrahydroquinoline (5.2l)



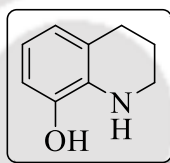
White solid (65 mg, 88%); m.p: 160~162 °C. ^1H NMR (400 MHz, $\text{DMSO}-d_6$): δ 8.47 (s, 1H), 6.47 – 6.34 (m, 3H), 3.10 – 3.07 (m, 2H), 2.58 (t, J = 6.4 Hz, 2H), 1.79 – 1.73 (m, 2H). ^{13}C NMR (101 MHz, $\text{DMSO}-d_6$): δ 149.30, 135.57, 123.05, 116.33, 115.66, 113.69, 41.43, 26.43, 21.64. Spectral data is in accordance to the reported literature.¹⁰

8-methyl-1,2,3,4-tetrahydroquinoline (5.2m)



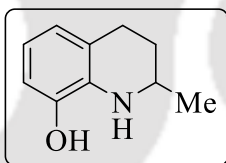
Colourless oil (70 mg, 95%). ^1H NMR (400 MHz, CDCl_3): δ 6.88 – 6.84 (m, 2H), 6.55 (t, J = 7.4 Hz, 1H), 3.65 (brs, 1H), 3.38 – 3.36 (m, 2H), 2.79 (t, J = 6.4 Hz, 2H), 2.07 (s, 3H), 1.97-1.91 (m, 2H). ^{13}C NMR (101 MHz, CDCl_3): δ 142.81, 127.95, 127.49, 121.29, 120.98, 116.50, 42.46, 27.40, 22.27, 17.27. Spectral data is in accordance to the reported literature.³⁵

8-hydroxy-1,2,3,4-tetrahydroquinoline (5.2n)



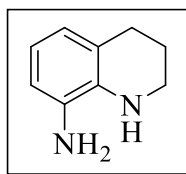
White solid (65 mg, 87%); m.p: 120~122 °C. ^1H NMR (400 MHz, $\text{DMSO}-d_6$): δ 8.94 (s, 1H), 6.45 – 6.26 (m, 3H), 4.60 (s, 1H), 3.20 (brs, 2H), 2.63 (brs, 2H), 1.78 (brs, 2H). ^{13}C NMR (101 MHz, $\text{DMSO}-d_6$): δ 143.18, 133.73, 120.37, 119.86, 114.71, 111.39, 40.80, 26.43, 21.79. Spectral data is in accordance to the reported literature.¹⁰

2-methyl-1,2,3,4-tetrahydroquinolin-8-ol (5.2o)



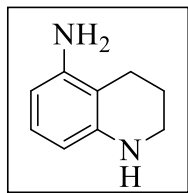
White solid (69 mg, 85%); m.p: 75~77 °C. ^1H NMR (400 MHz, CDCl_3): δ 6.60 – 6.46 (m, 3H), 4.61 (s, 1H), 3.33 (s, 1H), 2.86 – 2.71 (m, 2H), 1.94 – 1.90 (m, 1H), 1.62 – 1.57 (m, 1H), 1.23 – 1.22 (d, J = 6.3 Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3): δ 142.96, 133.69, 123.28, 121.72, 117.29, 112.75, 47.27, 30.19, 26.44, 22.41. Spectral data is in accordance to the reported literature.⁷²

8-amino-1,2,3,4-tetrahydroquinoline (5.2p)



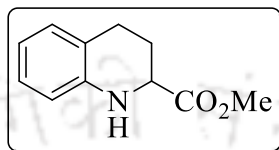
Brown oil (65 mg, 87%). ^1H NMR (400 MHz, CDCl_3): δ 6.59 – 6.51 (m, 3H), 3.32 – 3.29 (m, 2H), 2.76 (t, J = 6.4 Hz, 2H), 1.93 – 1.87 (m, 2H). ^{13}C NMR (101 MHz, CDCl_3): δ 133.99, 133.93, 123.31, 121.19, 118.09, 114.15, 42.65, 27.11, 22.48. HRMS (ESI) m/z : calculated for $\text{C}_9\text{H}_{13}\text{N}_2$ ($\text{M}+\text{H}^+$): 149.1073; found: 149.1086. Spectral data is in accordance to the reported literature.⁷³

1,2,3,4-tetrahydroquinolin-5-amine (5.2q)



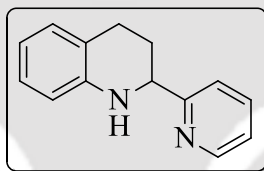
Yellow solid (62 mg, 83%); m.p: 96~98 °C. ^1H NMR (400 MHz, CDCl_3): δ 6.81 (t, J = 8.0 Hz, 1H), 6.09 (d, J = 7.9 Hz, 1H), 6.01 (d, J = 8.0 Hz, 1H), 3.26 – 3.23 (m, 2H), 2.85 (s, 1H), 2.48 (t, J = 6.7 Hz, 2H), 2.06 – 1.95 (m, 2H). ^{13}C NMR (101 MHz, CDCl_3): δ 145.89, 145.05, 127.15, 106.95, 105.71, 104.82, 41.52, 22.48, 21.66. Spectral data is in accordance with literature.⁷²

Methyl 1,2,3,4-tetrahydroquinoline-2-carboxylate (5.4a)



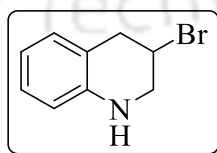
Pale yellow oil (85 mg, 89%). ^1H NMR (400 MHz, CDCl_3): δ 7.02 – 6.94 (m, 2H), 6.65 (td, J = 7.4, 1.2 Hz, 1H), 6.59 (dd, J = 8.0, 1.2 Hz, 1H), 4.05 (dd, J = 8.8, 3.8 Hz, 1H), 3.78 (s, 3H), 2.83 – 2.73 (m, 2H), 2.28 (dtd, J = 13.0, 5.6, 3.8 Hz, 1H), 2.01 (dtd, J = 12.9, 9.0, 5.2 Hz, 1H). ^{13}C NMR (101 MHz, CDCl_3): δ 173.86, 143.08, 129.27, 127.20, 120.69, 117.83, 114.73, 54.06, 52.50, 25.95, 24.85. Spectral data is in accordance to the reported literature.²⁰

2-(pyridin-2-yl)-1,2,3,4-tetrahydroquinoline (5.4b)



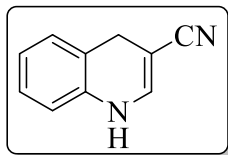
Brown oil (86 mg, 82%). ^1H NMR (400 MHz, CDCl_3): δ 8.58 (d, J = 4.9 Hz, 1H), 7.70 – 7.66 (td, J = 7.7, 1.8 Hz, 1H), 7.43 (d, J = 7.9 Hz, 1H), 7.21 – 7.18 (m, 1H), 7.05 – 6.99 (m, 2H), 6.68 – 6.62 (m, 2H), 4.59 (dd, J = 8.8, 3.5 Hz, 1H), 2.92–2.89 (m, 1H), 2.70 (dt, J = 16.3, 5.2 Hz, 1H), 2.29 – 2.24 (m, 1H), 2.06 – 2.02 (m, 1H). ^{13}C NMR (101 MHz, CDCl_3): δ 163.22, 149.25, 144.28, 136.91, 129.38, 127.10, 122.32, 121.24, 120.74, 117.43, 114.60, 57.00, 28.90, 26.12. HRMS (ESI) m/z : calculated for $\text{C}_{14}\text{H}_{15}\text{N}_2$ ($\text{M}+\text{H}^+$): 211.1235; found: 211.1244. Spectral data is in accordance to the reported literature.⁶⁸

3-bromo-1,2,3,4-tetrahydroquinoline (5.4c)



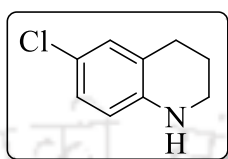
Brown oil (97 mg, 92%). ^1H NMR (400 MHz, CDCl_3): δ 7.05 – 7.00 (m, 1H), 6.93 (d, J = 7.4 Hz, 1H), 6.67 (td, J = 7.5, 0.9 Hz, 1H), 6.53 (d, J = 7.9 Hz, 1H), 4.52 – 4.46 (m, 1H), 3.65 (ddd, J = 12.1, 3.2, 1.8 Hz, 1H), 3.48 (ddd, J = 12.1, 7.6, 0.9 Hz, 1H), 3.39 (dd, J = 16.5, 4.7 Hz, 1H), 3.19 (dd, J = 16.4, 7.6 Hz, 1H). ^{13}C NMR (101 MHz, CDCl_3): δ 142.73, 129.58, 127.68, 118.71, 118.20, 114.66, 49.52, 44.32, 37.96. HRMS (ESI) m/z : calculated for $\text{C}_9\text{H}_{11}\text{BrN}$ ($\text{M}+\text{H}^+$): 212.0069; found: 212.0081.

1,4-dihydroquinoline-3-carbonitrile (5.4d)



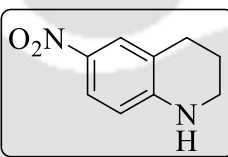
White solid (71 mg, 91%); m.p: 106~107 °C. ^1H NMR (400 MHz, CDCl_3): δ 7.10 – 7.06 (m, 1H), 6.98 – 6.92 (m, 2H), 6.82 (d, J = 5.9 Hz, 1H), 6.58 (d, J = 8.0 Hz, 1H), 6.14 (brs, 1H), 3.72 (s, 2H). ^{13}C NMR (101 MHz, CDCl_3): δ 139.43, 135.82, 129.48, 127.81, 123.93, 121.24, 118.59, 115.30, 78.06, 27.03. HRMS (ESI) m/z : calculated for $\text{C}_{10}\text{H}_9\text{N}_2$ ($\text{M}+\text{H}^+$): 157.0765; found: 157.0778.

6-chloro-1,2,3,4-tetrahydroquinoline (5.4e)



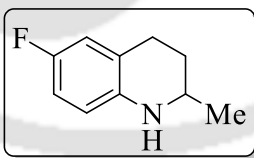
Pale yellow sticky liquid (77 mg, 93%). ^1H NMR (400 MHz, CDCl_3): δ 6.89 (s, 1H), 6.87 (d, J = 2.4 Hz, 1H), 6.35 (d, J = 8.0 Hz, 1H), 3.76 (brs, 1H), 3.27 – 3.24 (m, 2H), 2.70 (t, J = 6.4 Hz, 2H), 1.92 – 1.86 (m, 2H). ^{13}C NMR (101 MHz, CDCl_3): δ 143.40, 129.10, 126.58, 122.95, 121.20, 115.17, 41.94, 26.96, 21.83. Spectral data is in accordance to the reported literature.¹⁸

6-nitro-1,2,3,4-tetrahydroquinoline (5.4f)



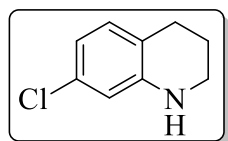
White solid (77 mg, 87%); m.p: 160~162 °C. ^1H NMR (400 MHz, CDCl_3): δ 7.90 – 7.87 (m, 2H), 6.36 (m, J = 9.6 Hz, 1H), 4.75 (brs, 1H), 3.42 (td, J = 6.0, 2.0 Hz, 2H), 2.79 (t, J = 6.3 Hz, 2H), 1.95 (dt, J = 12.4, 6.1 Hz, 2H). ^{13}C NMR (101 MHz, CDCl_3): δ 150.52, 137.32, 126.04, 124.41, 119.95, 112.27, 41.85, 27.00, 20.92. Spectral data is in accordance to the reported literature.⁷⁴

6-fluoro-2-methyl-1,2,3,4-tetrahydroquinoline (5.4g)



Colourless sticky liquid (73 mg, 89%). ^1H NMR (400 MHz, CDCl_3): δ 6.70-6.65 (m, 2H), 6.41 – 6.38 (m, 1H), 3.72 (brs, 1H), 3.36 – 3.32 (m, 1H), 2.85 – 2.81 (m, 1H), 2.79-2.71 (m, 1H), 1.94 – 1.89 (m, 1H), 1.58 – 1.56 (m, 1H), 1.20 (d, J = 6.3 Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3): δ 155.63 (d, J = 235.3 Hz), 141.1 (d, J = 1.8 Hz), 122.61 (d, J = 6.6 Hz), 115.51 (d, J = 21.6 Hz), 114.84 (d, J = 7.7 Hz), 113.28 (d, J = 22.5 Hz), 47.44, 30.02, 26.84, 22.63. Spectral data is in accordance to the reported literature.¹⁸

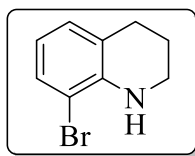
7-chloro-1,2,3,4-tetrahydroquinoline (5.4h)



4,7-dichloroquinoline was used as the substrate. Colourless oil (76 mg, 91%). For this, 3.5 equiv. of 4,7-dichloroquinoline was used. ^1H NMR (400 MHz, CDCl_3): δ 6.83 (d, J = 8 Hz, 1H), 6.53 (dd, J = 8.0, 2.1 Hz, 1H), 6.42 (d, J = 2.1 Hz, 1H), 3.84 (brs, 1H), 3.29 – 3.26 (m, 2H), 2.70 (t, J = 6.4 Hz, 2H), 1.93

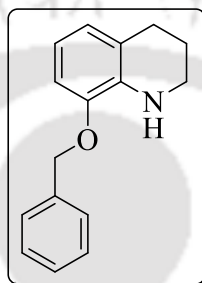
– 1.87 (m, 2H). ^{13}C NMR (101 MHz, CDCl_3): δ 145.80, 132.03, 130.51, 119.72, 116.63, 113.49, 41.79, 26.66, 21.92. Spectral data is in accordance to the reported literature.³⁶

8-bromo-1,2,3,4-tetrahydroquinoline (5.4i)



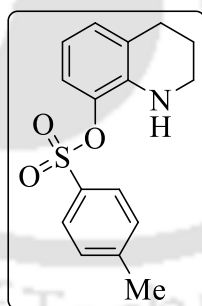
Colourless oil (90 mg, 86%). ^1H NMR (400 MHz, CDCl_3): δ 7.22 (d, J = 8.0 Hz, 1H), 6.88 (dd, J = 7.4, 0.7 Hz, 1H), 6.44 (t, J = 7.7 Hz, 1H), 4.42 (brs, 1H), 3.39 – 3.37 (m, 2H), 2.77 (t, J = 6.3 Hz, 2H), 1.95 – 1.89 (m, 2H). ^{13}C NMR (101 MHz, CDCl_3): δ 141.85, 130.15, 128.52, 122.97, 117.03, 108.84, 42.18, 27.57, 21.83. Spectral data is in accordance to the reported literature.³⁵

8-(benzyloxy)-1,2,3,4-tetrahydroquinoline (5.4j)



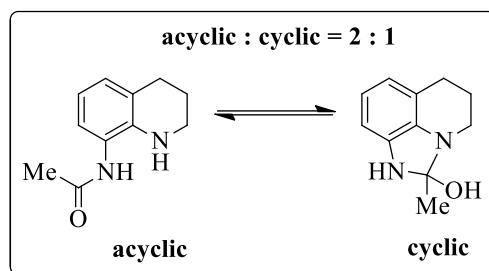
Colourless oil (110 mg, 92%). ^1H NMR (400 MHz, CDCl_3): δ 7.43 – 7.22 (m, 5H), 6.65 (dd, J = 16.2, 7.7 Hz, 2H), 6.54 (t, J = 7.7 Hz, 1H), 5.03 (s, 2H), 4.29 (brs, 1H), 3.32 – 3.29 (m, 2H), 2.78 (t, J = 6.4 Hz, 2H), 1.98 – 1.92 (m, 2H). ^{13}C NMR (101 MHz, CDCl_3): δ 145.53, 137.42, 134.89, 128.64, 128.05, 127.77, 122.12, 121.62, 115.66, 108.88, 70.36, 41.56, 26.82, 22.17. Spectral data is in accordance to the reported literature.³⁵

1,2,3,4-tetrahydroquinolin-8-yl-4'-methylbenzenesulfonate (5.4k)



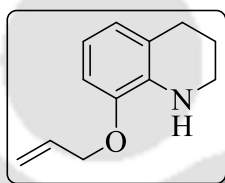
White solid (130 mg, 86%); m.p: 62~64 °C. ^1H NMR (400 MHz, CDCl_3): δ 7.77 (d, J = 8.4 Hz, 2H), 7.32 (d, J = 8.0 Hz, 2H), 6.80 (d, J = 7.2 Hz, 2H), 6.59 (dd, J = 8.2, 1.4 Hz, 1H), 6.39 (t, J = 7.8 Hz, 1H), 4.18 (brs, 1H), 3.20-3.16 (m, 2H), 2.72 – 2.68 (t, J = 6.4 Hz, 2H), 2.45 (s, 3H), 1.85 – 1.79 (m, 2H). ^{13}C NMR (101 MHz, CDCl_3): δ 145.45, 137.95, 136.07, 133.04, 129.79, 128.66, 127.87, 123.65, 120.16, 115.22, 41.36, 27.01, 21.85, 21.50. HRMS (ESI) m/z : calculated for $\text{C}_{16}\text{H}_{18}\text{NO}_3\text{S}$ ($\text{M}+\text{H}^+$): 304.1007; found: 304.1037.

N-(1,2,3,4-tetrahydroquinolin-8-yl)acetamide (5.4l)



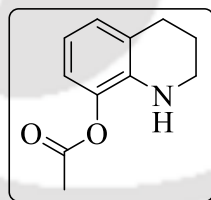
White solid (80 mg, 84%); m.p: 113~115 °C. ^1H NMR (400 MHz, CDCl_3): δ 7.11 (brs, 1H, acyclic, 67%), 7.01 (d, $J = 7.8$ Hz, 1H, acyclic, 67%), 6.93 (d, $J = 7.2$ Hz, 1H, cyclic, 33%), 6.87 (d, $J = 7.2$ Hz, 1H, acyclic, 67%), 6.83 (d, $J = 7.2$ Hz, 1H, cyclic, 33%), 6.68 (brs, 1H, cyclic, 33%), 6.63 (t, $J = 7.6$ Hz, 1H, acyclic, 67%), 6.55 (t, $J = 7.2$ Hz, 1H, cyclic, 33%), 4.14 (brs, 1H, acyclic, 67%), 3.32-3.29 [(m, 2H, acyclic, 67%) + (m, 2H, cyclic, 33%)], 2.78 [(t, 2H, acyclic, 67%) + (t, 2H, cyclic, 33%)], 2.17 (s, 3H, acyclic 67%), 1.91-1.87 [(m, 2H, acyclic, 67%) + (m, 2H, cyclic, 33%) + (s, 3H, cyclic, 33%)]. ^{13}C NMR (101 MHz, CDCl_3): δ 169.25, 139.36, 129.29, 127.87, 126.61, 124.34, 123.42, 123.33, 117.41, 115.95, 42.30, 41.76, 27.45, 27.15, 23.88, 22.00, 21.76, 20.51. HRMS (ESI) m/z : calculated for $\text{C}_{11}\text{H}_{14}\text{N}_2\text{O}$ (M^+): 190.1106; found: 190.1185.

8-(allyloxy)-1,2,3,4-tetrahydroquinoline (5.4m)



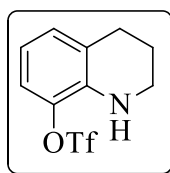
Colourless oil (80 mg, 85%). ^1H NMR (400 MHz, CDCl_3): δ 6.66-6.62 (m, 2H), 6.58 – 6.54 (m, 1H), 6.10-6.05 (m, 1H), 5.42 (dd, $J = 17.3, 1.6$ Hz, 1H), 5.30 (dd, $J = 10.5, 1.5$ Hz, 1H), 4.55 (dt, $J = 5.4, 1.6$ Hz, 2H), 3.37–3.35 (m, 2H), 2.80 (t, $J = 6.4$ Hz, 2H), 1.97 – 1.91 (m, 2H). ^{13}C NMR (101 MHz, CDCl_3): δ 145.29, 134.88, 133.82, 122.03, 121.64, 117.45, 115.68, 108.94, 69.21, 41.59, 26.82, 22.19. Spectral data is in accordance to the reported literature.³⁵

1,2,3,4-tetrahydroquinolin-8-yl acetate (5.4n)



Yellow oil (84 mg, 88%). ^1H NMR (400 MHz, CDCl_3): δ 7.80 (s, 1H), 7.11 (t, $J = 7.8$ Hz, 1H), 6.92 (d, $J = 8.0$ Hz, 1H), 6.74 (d, $J = 7.4$ Hz, 1H), 3.72 – 3.69 (m, 2H), 2.85 (t, $J = 7.0$ Hz, 2H), 2.38 (s, 3H), 2.10 – 2.04 (p, $J = 6.9$ Hz, 2H). ^{13}C NMR (101 MHz, CDCl_3): δ 171.66, 150.52, 133.24, 128.94, 127.43, 121.04, 118.38, 47.87, 26.52, 24.24, 23.36. HRMS (ESI) m/z : calculated for $\text{C}_{11}\text{H}_{14}\text{NO}_2$ ($\text{M}+\text{H}^+$): 192.1024; found: 192.1016.

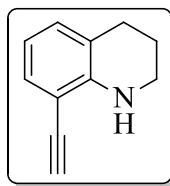
1,2,3,4-tetrahydroquinolin-8-yl trifluoromethanesulfonate (5.4o)



Yellow oil (151 mg, 85%). ^1H NMR (600 MHz, CDCl_3): δ 6.95 (dd, $J = 19.0, 7.9$ Hz, 2H), 6.55 (t, $J = 7.8$ Hz, 1H), 4.17 (brs, 1H), 3.38-3.36 (m, 2H), 2.79 (t, $J = 6.3$ Hz, 2H), 1.96-1.92 (m, 2H). ^{13}C NMR (101 MHz, CDCl_3): δ 137.25, 136.39, 128.99, 124.58, 120.31, 119.22, 115.73, 41.56, 27.01,

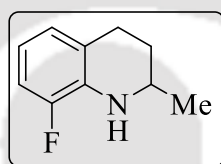
21.35. ^{19}F NMR (377 MHz, CDCl_3): δ -73.98. HRMS (ESI) m/z : calculated for $\text{C}_{10}\text{H}_{11}\text{F}_3\text{NO}_3\text{S}$ ($\text{M}+\text{H}^+$): 282.0406; found: 282.0425.

8-ethynyl-1,2,3,4-tetrahydroquinoline (5.4p)



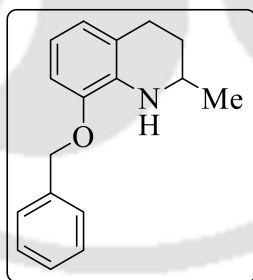
Colourless oil (69 mg, 88%). ^1H NMR (400 MHz, CDCl_3): δ 7.15 (d, J = 7.6 Hz, 1H), 6.92 (d, J = 7.3 Hz, 1H), 6.49 (t, J = 7.5 Hz, 1H), 4.74 (brs, 1H), 3.41-3.38 (m, 2H), 3.37 (s, 1H), 2.76-2.75 (t, J = 6.4 Hz, 2H), 1.96 – 1.90 (m, 2H). ^{13}C NMR (101 MHz, CDCl_3): δ 146.56, 130.48, 130.22, 120.84, 115.61, 104.80, 82.42, 81.20, 41.89, 27.26, 21.74. HRMS (ESI) m/z : calculated for $\text{C}_{11}\text{H}_{12}\text{N}$ ($\text{M}+\text{H}^+$): 158.0969; found: 158.0975.

8-fluoro-2-methyl-1,2,3,4-tetrahydroquinoline (5.4q)



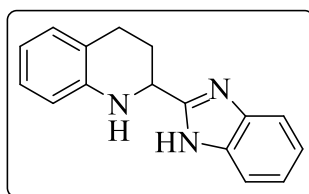
Colourless sticky liquid (71 mg, 86%). ^1H NMR (400 MHz, CDCl_3): δ 6.81 – 6.73 (m, 2H), 6.52 – 6.47 (m, 1H), 3.88 (brs, 1H), 3.45-3.37 (m, 1H), 2.88 – 2.72 (m, 2H), 1.95 – 1.92 (m, 1H), 1.64 – 1.61 (m, 1H), 1.25 (d, J = 6.2 Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3): δ 150.83 (d, J = 238.3 Hz), 133.35 (d, J = 12.2 Hz), 124.4 (d, J = 2.8 Hz), 123.5 (d, J = 3.8 Hz), 115.74 (d, J = 7.5 Hz), 112.25 (d, J = 18.4 Hz), 46.8, 29.86, 26.35 (d, J = 3 Hz), 22.64. HRMS (ESI) m/z : calculated for $\text{C}_{10}\text{H}_{13}\text{FN}$ ($\text{M}+\text{H}^+$): 166.1027; found: 166.1037.

8-(benzyloxy)-2-methyl-1,2,3,4-tetrahydroquinoline (5.4r)



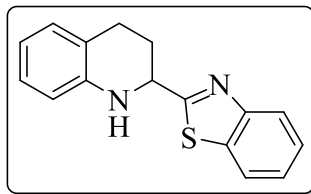
Colourless oil (112 mg, 89%). ^1H NMR (400 MHz, CDCl_3): δ 7.43-7.30 (m, 5H), 6.65 (t, J = 8.6 Hz, 2H), 6.53 (t, J = 7.8 Hz, 1H), 5.07 – 5.01 (m, 2H), 4.18 (brs, 1H), 3.40 – 3.35 (m, 1H), 2.85 (ddd, J = 16.8, 11.2, 5.7 Hz, 1H), 2.77 – 2.71 (m, 1H), 1.94 – 1.90 (m, 1H), 1.63 – 1.56 (m, 1H), 1.22 – 1.21 (d, J = 6.3 Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3): δ 145.33, 137.52, 134.93, 128.64, 128.01, 127.73, 121.95, 121.40, 115.76, 109.11, 70.50, 46.79, 30.15, 26.48, 22.69. HRMS (ESI) m/z : calculated for $\text{C}_{17}\text{H}_{20}\text{NO}$ ($\text{M}+\text{H}^+$): 254.1544; found: 254.1538.

2-(1H-benzo[d]imidazol-2-yl)-1,2,3,4-tetrahydroquinoline (5.4s)



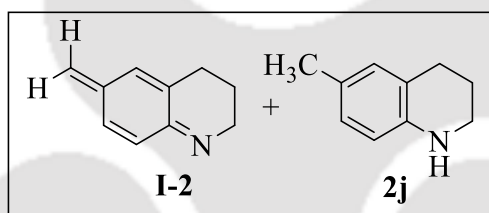
Pale yellow solid (103 mg, 83%); m.p: 156~157 °C. ^1H NMR (400 MHz, CDCl_3): δ 7.56 (brs, 2H), 7.25-7.23 (m, 2H), 7.05 (t, J = 7.5 Hz, 1H), 6.99 (d, J = 7.4 Hz, 1H), 6.72 (t, J = 7.3 Hz, 1H), 6.60 (d, J = 7.9 Hz, 1H), 4.88 (t, J = 4 Hz, 1H), 2.86 – 2.79 (m, 1H), 2.63-2.56 (m, 1H), 2.36 (dd, J = 13.0, 6.6 Hz, 1H), 2.22 (d, J = 4.6 Hz, 1H). ^{13}C NMR (101 MHz, CDCl_3): δ 157.18, 142.79, 129.63, 127.32, 122.68, 121.67, 118.59, 114.98, 50.93, 27.80, 25.07. HRMS (ESI) m/z : calculated for $\text{C}_{16}\text{H}_{16}\text{N}_3$ ($\text{M}+\text{H}^+$): 250.1344; found: 250.1338.

2-(1,2,3,4-tetrahydroquinolin-2-yl)benzo[d]thiazole (5.4t)



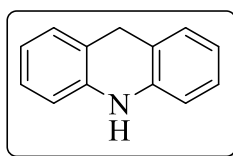
Yellow oil (113 mg, 85%). ^1H NMR (400 MHz, CDCl_3): δ 7.99 (dd, J = 8.2, 1.1 Hz, 1H), 7.86 (dt, J = 8.0, 0.9 Hz, 1H), 7.48 (ddd, J = 8.3, 7.2, 1.3 Hz, 1H), 7.37 (ddd, J = 8.3, 7.2, 1.2 Hz, 1H), 7.07 (td, J = 7.7, 1.6 Hz, 1H), 7.00 (d, J = 7.5 Hz, 1H), 6.74 – 6.67 (m, 2H), 4.97 (ddd, J = 6.2, 4.9, 3.1 Hz, 1H), 4.61 (brs, 1H), 2.95 – 2.82 (m, 1H), 2.78-2.71 (m, 1H), 2.38-2.33 (m, 2H). ^{13}C NMR (101 MHz, CDCl_3): δ 177.39, 153.78, 142.86, 135.08, 129.43, 127.30, 126.19, 125.01, 122.99, 121.97, 121.34, 118.45, 114.85, 54.60, 29.09, 25.22. HRMS (ESI) m/z : calculated for $\text{C}_{16}\text{H}_{15}\text{N}_2\text{S}$ ($\text{M}+\text{H}^+$): 267.0955; found: 267.0981.

6-methylene-2,3,4,6-tetrahydroquinoline (I-2) + 6-methyl-1,2,3,4-tetrahydroquinoline (2j)



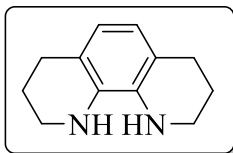
Yellow oil (**I-2** + **2j**): (53 mg, 73%), **I-2:2j** = 1:3 ratio; ^1H NMR (400 MHz, CDCl_3): δ 7.18-7.21 (m, 2H, minor, 25%), 6.77-6.79 [(m, 2H, major, 75%) + (m, 1H, minor, 25%)], 6.40-6.42 (m, 1H, major, 75%), 6.37-6.39 (m, 2H, minor, 25%), 4.28-4.42 (m, 1H, major, 75%), 3.35-3.37 (m, 2H, minor, 25%), 3.25-3.28 (m, 2H, major, 75%), 2.71-2.75 [(m, 2H, major, 75%) + (m, 2H, minor, 25%)], 2.2 (s, 3H, major, 75%), 1.90-1.96 [(m, 2H, major, 75%) + (m, 2H, minor, 25%)]. ^{13}C NMR (101 MHz, CDCl_3): δ 163.01, 142.53, 133.39, 131.43, 130.22, 127.39, 126.45, 121.78, 114.63, 113.39, 42.34, 41.74, 27.05, 26.87, 22.59, 21.13, 20.54. HRMS (ESI) m/z : calculated for $\text{C}_{10}\text{H}_{12}\text{N}$ ($\text{M}+\text{H}^+$) for **I-2**: 146.0970; found: 146.0963. calculated for $\text{C}_{10}\text{H}_{14}\text{N}$ ($\text{M}+\text{H}^+$) for **2j**: 148.1126; found: 148.1127.

9,10-dihydroacridine (5.6a)



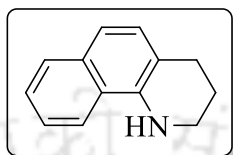
White solid (89 mg, 98%); m.p: 171~173 °C. ^1H NMR (400 MHz, CDCl_3): δ 7.10 – 7.05 (m, 4H), 6.84 (td, J = 7.4, 1.2 Hz, 2H), 6.65 (dd, J = 7.8, 1.2 Hz, 2H), 5.93 (brs, 1H), 4.04 (s, 2H). ^{13}C NMR (101 MHz, CDCl_3) δ 140.25, 128.73, 127.12, 120.76, 120.16, 113.57, 31.51. Spectral data is in accordance to the reported literature.³⁵

1,2,3,4,7,8,9,10-octahydro-1,10-phenanthroline (5.6b)



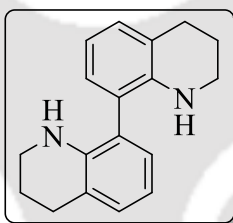
For this, 5 eqv. of Hantzsch ester was used. Yellow solid (81 mg, 86%); m.p: 69~71 °C. ^1H NMR (400 MHz, CDCl_3): δ 6.45 (s, 2H), 3.31 – 3.28 (m, 4H), 2.73 (t, J = 6.3 Hz, 4H), 1.89 – 1.87 (m, 4H). ^{13}C NMR (101 MHz, CDCl_3): δ 132.88, 120.51, 119.20, 42.69, 26.99, 22.59. spectral data is matched with the literature.⁷³

1,2,3,4-tetrahydrobenzo[h]quinoline (5.6c)



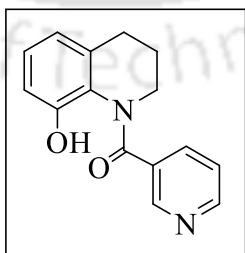
Light brown oil (89 mg, 97%). ^1H NMR (400 MHz, CDCl_3): δ 7.73 – 7.71 (m, 1H), 7.67 – 7.65 (m, 1H), 7.40 – 7.34 (m, 2H), 7.16 (d, J = 8.3 Hz, 1H), 7.10 (d, J = 8.3 Hz, 1H), 4.23 (brs, 1H), 3.46 – 3.44 (m, 2H), 2.89 (t, J = 6.4 Hz, 2H), 2.04 – 1.98 (m, 2H). ^{13}C NMR (101 MHz, CDCl_3): δ 139.03, 133.13, 128.68, 128.62, 125.02, 124.83, 123.37, 119.54, 117.08, 115.96, 42.52, 27.55, 22.22. Spectral data is in accordance to the reported literature.¹⁸

1,1',2,2',3,3',4,4'-octahydro-8,8'-biquinoline (5.6d)



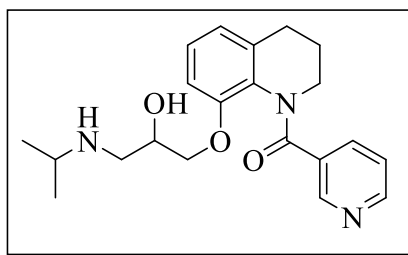
For this, 5 eqv. of Hantzsch ester was used. Isolated yield: 92%. Yellow oil (121 mg, 92%). ^1H NMR (400 MHz, CDCl_3): δ 6.97 (d, J = 7.3 Hz, 2H), 6.91 (d, J = 7.3 Hz, 2H), 6.66 (t, J = 7.4 Hz, 2H), 3.29 – 3.22 (m, 4H), 2.83 (t, J = 6.4 Hz, 4H), 1.98 – 1.89 (m, 4H). ^{13}C NMR (101 MHz, CDCl_3): δ 142.49, 128.98, 128.83, 123.4, 121.59, 116.63, 42.10, 27.58, 22.07. HRMS (ESI) m/z : calculated for $\text{C}_{18}\text{H}_{21}\text{N}_2$ ($\text{M}+\text{H}^+$): 265.1704; found: 265.1709.

(8-hydroxy-3,4-dihydroquinolin-1(2H)-yl)(pyridin-3-yl)methanone (5)



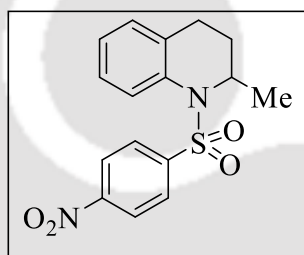
Isolated yield: 82%. ^1H NMR (400 MHz, $\text{DMSO}-d_6$): δ 9.43 (s, 1H), 8.46 (dd, J = 4.8, 1.7 Hz, 1H), 8.38 (d, J = 2.2 Hz, 1H), 7.58 (dt, J = 7.9, 2.0 Hz, 1H), 7.23 (dd, J = 7.9, 4.8 Hz, 1H), 6.89 (t, J = 7.8 Hz, 1H), 6.72 (dd, J = 7.5, 1.3 Hz, 1H), 6.42 (dd, J = 8.1, 1.3 Hz, 1H), 3.4 (brs, 2H), 2.73 (t, J = 6.4 Hz, 2H), 1.91 (brs, 2H). ^1H NMR (400 MHz, CD_3CN): δ 8.48 (br, 2H), 7.68 – 7.66 (m, 1H), 7.23 – 7.21 (m, 1H), 6.98 (t, J = 7.5 Hz, 1H), 6.78 (d, J = 7.4 Hz, 1H), 6.53 – 6.51 (m, 1H), 3.64 (brs, 2H), 2.78 (t, J = 6.6 Hz, 2H), 1.91 (m, 2H). ^{13}C NMR (101 MHz, $\text{DMSO}-d_6$): δ 167.62, 150.20, 149.24, 148.17, 136.31, 134.96, 133.27, 127.11, 126.56, 122.63, 118.22, 114.24, 42.86, 26.28, 24.47. HRMS (ESI) m/z : calculated for $\text{C}_{15}\text{H}_{15}\text{N}_2\text{O}_2$ ($\text{M}+\text{H}^+$): 255.1133; found: 255.1132.

(8-(2-hydroxy-3-(isopropylamino)propoxy)-3,4-dihydroquinolin-1(2H)-yl)(pyridin-3-yl)methanone (6)



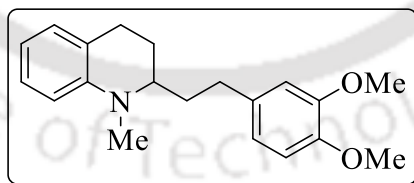
Isolated yield: 75%. ^1H NMR (400 MHz, CDCl_3): δ 8.62 – 8.55 (m, 2H), 7.73 (br, 1H), 7.20 – 7.17 (m, 1H), 7.08 (t, J = 7.9 Hz, 1H), 6.85 (d, J = 7.5 Hz, 1H), 6.64 – 6.61 (m, 1H), 4.22 (br, 1H), 3.80 – 3.76 (m, 2H), 3.58 – 3.48 (m, 2H), 2.86 – 2.66 (m, 4H), 2.56 – 2.51 (m, 1H), 2.22 (br, 2H), 1.89 – 1.80 (m, 2H), 1.05 (d, 6H). ^{13}C NMR (101 MHz, CDCl_3): δ 168.57, 151.13, 151.07, 149.09, 135.67, 132.44, 128.64, 127.04, 122.87, 122.79, 120.79, 111.32, 71.92, 70.98, 68.68, 68.06, 49.10, 26.75, 24.82, 23.07, 22.98. HRMS (ESI) m/z : calculated for $\text{C}_{21}\text{H}_{28}\text{N}_3\text{O}_3$ ($\text{M}+\text{H}^+$): 370.2125; found: 370.2141.

2-methyl-1-((4-nitrophenyl)sulfonyl)-1,2,3,4-tetrahydroquinoline (7)



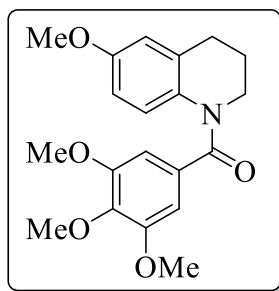
Isolated yield: 96%. ^1H NMR (400 MHz, CDCl_3): δ 8.21 (d, J = 8.9 Hz, 2H), 7.75 (d, J = 8.0 Hz, 1H), 7.64 (d, J = 8.9 Hz, 2H), 7.29 (d, J = 7.4 Hz, 1H), 7.16 (t, J = 7.9 Hz, 1H), 7.00 (d, J = 7.4 Hz, 1H), 4.43 – 4.35 (hext, J = 6.4 Hz, 1H), 2.44 – 2.37 (m, 1H), 1.89 – 1.81 (m, 1H), 1.71 – 1.64 (m, 1H), 1.41 – 1.36 (m, 1H), 1.34 – 1.32 (d, J = 6.5 Hz, 3H). ^{13}C NMR (151 MHz, CDCl_3): δ 144.85, 134.40, 133.80, 128.36, 128.28, 127.62, 127.28, 126.55, 124.17, 53.43, 30.61, 25.02, 22.03. Spectral data is in accordance to the reported literature.⁴⁹

2-(3,4-dimethoxyphenethyl)-1-methyl-1,2,3,4-tetrahydroquinoline (8)



Isolated yield: 95%. ^1H NMR (400 MHz, CDCl_3): δ 7.10–7.06 (m, 1H), 6.98 (d, J = 7.4 Hz, 1H), 6.80 – 6.78 (m, 1H), 6.74 – 6.70 (m, 2H), 6.58 (t, J = 7.3, 1.1 Hz, 1H), 6.52 (d, J = 8.2 Hz, 1H), 3.87 (s, 3H), 3.85 (s, 3H), 3.30 – 3.27 (dq, J = 8.6, 4.3 Hz, 1H), 2.91 (s, 3H), 2.82 – 2.87 (m, 1H), 2.72–2.66 (m, 2H), 2.55 – 2.53 (m, 1H), 1.96 – 1.92 (m, 3H), 1.74 – 1.73 (m, 1H). ^{13}C NMR (101 MHz, CDCl_3): δ 149.08, 147.40, 145.47, 134.82, 128.83, 127.27, 121.90, 120.22, 115.55, 111.79, 111.49, 110.78, 58.58, 56.11, 56.04, 38.24, 33.25, 32.08, 24.58, 23.74. The obtained spectroscopic data were in agreement with the reported data for this compound.⁶²

(6-methoxy-3,4-dihydroquinolin-1(2H)-yl)(3,4,5-trimethoxyphenyl)methanone (9)



Isolated yield: 92%. ^1H NMR (400 MHz, CDCl_3): δ 6.66 (d, J = 2.4 Hz, 1H), 6.55 (d, J = 1.7 Hz, 2H), 6.45 (dd, J = 7.0, 4.3 Hz, 1H), 3.83 (td, J = 6.5, 2.1 Hz, 2H), 3.79 (s, J = 2.1 Hz, 3H), 3.70 (d, J = 2.3 Hz, 3H), 3.65 (d, J = 2.1 Hz, 6H), 2.76 (td, J = 6.7, 2.1 Hz, 2H), 2.02 –1.97 (m, 2H). ^{13}C NMR (101 MHz, CDCl_3): δ 169.37, 156.60, 152.71, 139.56, 132.99, 132.57, 131.24, 126.27, 113.12, 111.44, 106.25, 60.86, 56.04, 55.40, 44.58, 27.18, 24.15. Spectra data is in accordance to the reported literature.³⁵

5.5. References

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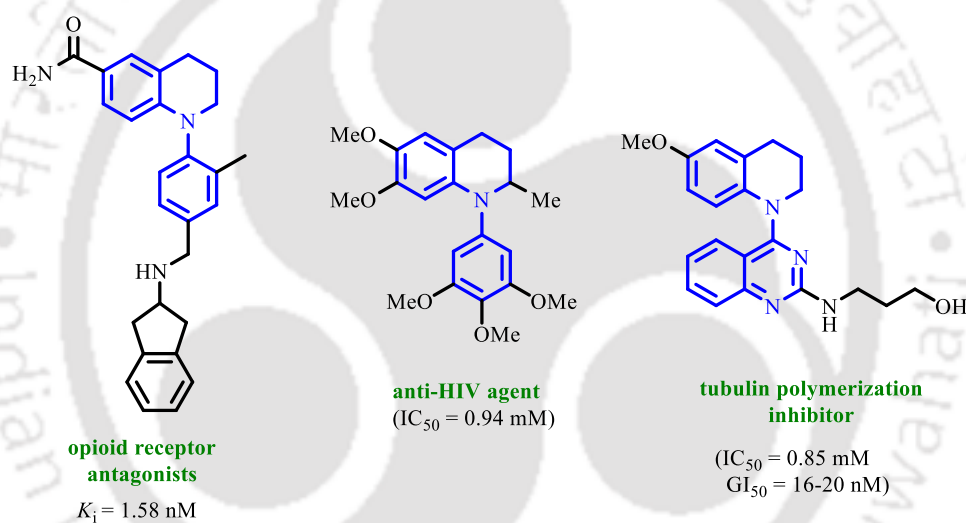
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Synthesis of biologically relevant *N*-aryl tetrahydroquinolines directly from quinoline, Hantzsch ester, and arylboronic acid under external base-free Chan-Lam-Evans *N*-arylation

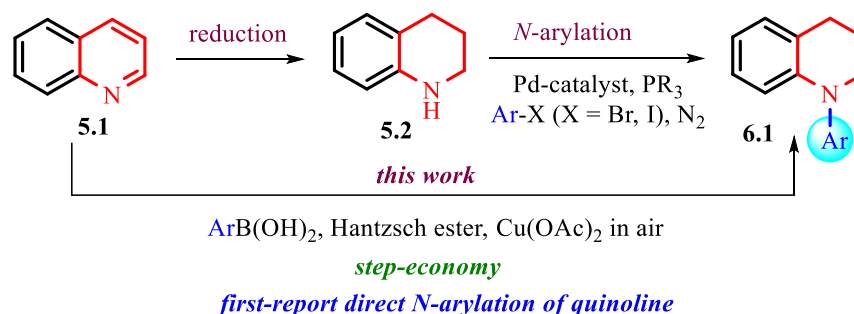
6.1. Introduction

As shown in the previous chapter (chapter-5) 1,2,3,4-tetrahydroquinoline (THQ) derivatives are an important class of bioactive compounds that are widely used as potential drugs against many diseases such as anti-bacterial, anti-cancer, anti-viral, anti-fungal, anti-hypertensive, antiparasitic, oxytocin antagonist, vasopressin antagonist, and calcium antagonist activity etc.¹⁻⁴. Among the various tetrahydroquinoline derivatives, the *N*-aryl tetrahydroquinolines (ATHQs) are found for their application in pharmaceutical chemistry due to their excellent therapeutic potential. These compounds are utilized as opioid receptor agonists,⁵ tubulin polymerization inhibitor,⁶ anti-cancer,⁷ and anti-HIV agents.⁸ Some of the selected bio-active ATHQs are listed in Scheme 6.1. The antioxidant and antimicrobial activities of ATHQs derivatives are also well studied.⁹ Besides their bioactivities, they are widely applied as organic electronic device materials and hole-transporting materials for electrophotography in material science.¹⁰ Thus, given their importance and usefulness, considerable research efforts have been directed towards the development of effective synthetic methodologies for constructing *N*-aryl substituted ATHQs.



Scheme 6.1. Selected bioactive compounds containing the ATHQs motif

To date, very few synthetic protocols have been demonstrated to access the *N*-aryl THQs.¹¹ These are synthesized in a two-step sequence: (1) the reduction of quinolines to THQs^{12, 13} and (2) subsequent Pd-catalyzed *N*-arylation by using aryl halide (Scheme 6.2).¹⁴ For the C-N bond-forming step, precious metals, phosphine-based ligands, air- and moisture-free conditions, and dry solvents are used.¹⁵ Surprisingly, there is no report for the synthesis of *N*-arylated tetrahydroquinolines starting from readily available quinoline in one-step, easy and straightforward manner.



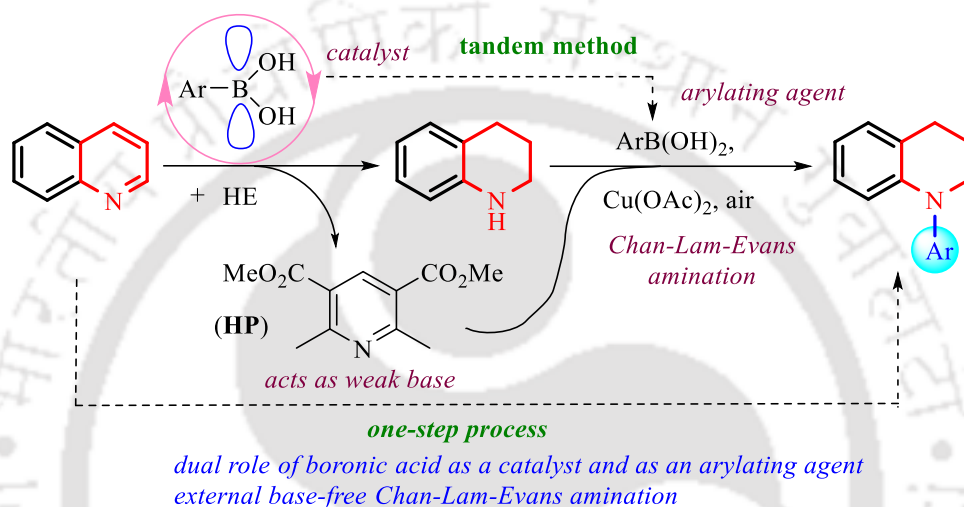
Scheme 6.2. Synthetic approach towards *N*-aryl THQs

6.2. This work

6.2.1. Hypothesis

In chapter-5, I have demonstrated that aryl boronic acid, a weak Lewis acid catalyzed reduction of quinoline with Hantzsch ester to provide reduced heterocycle 1,2,3,4-THQs and concomitant releases of Hantzsch pyridine (**HP**).

Herein I envisaged that *in-situ* formed THQs could take part in C-N bond formation reaction with arylboronic acid *via* Chan-Lam-Evans amination reaction¹⁶ in one-pot. Moreover, from the 1st step generated Hantzsch pyridine can also serve as a weak Lewis base (pK_a 2.81) in the subsequent *N*-arylation reaction (Scheme 6.3). Therefore, bypassing (a) the use of an external base in amination reaction and (b) isolation of THQs as the intermediate for subsequent *N*-arylation, may increase the product scopes and reduces the number of steps to make the process more step-economical and economically beneficial. Besides, aryl boronic acid can show the dual role as a catalyst (for reduction of quinoline to 1,2,3,4-THQs) and as a reagent (in Chan-Lam-Evans amination).



Scheme 6.3. Hypothesis for the one-step synthesis of *N*-aryl substituted THQs. HE = Hantzsch ester, HP = Hantzsch pyridine

6.2.2. Optimization studies

Hence, the study started with a reaction of quinoline (**5.1a**, 1 mmol), Hantzsch ester (2.2 mmol), and 30 mol% of PhB(OH)₂ (**6.2a**) in dichloroethane (DCE) at a 60 °C for 8 h in air. Then, to the reaction mixture phenylboronic acid (**6.2a**, 0.7 mmol), copper(II) acetate (0.2 mmol), and 4 Å molecular sieves were added and stirred at room temperature for 40 hours. Gratifyingly, the desired *N*-phenyl tetrahydroquinolines **6.1a** was obtained in 25% yield (Table 6.1, entry 1).

Table 6.1. Optimization studies for the reductive *N*-alkylation of quinoline^{a,b}

Entry	Cu(OAc) ₂ (equiv.)	Yield (%)
1	0.2	25%
2	0.6	76%
3	0.8	94%
4 ^c	0.8	62%
5 ^d	0.8	60%
6 ^e	0.8	37%

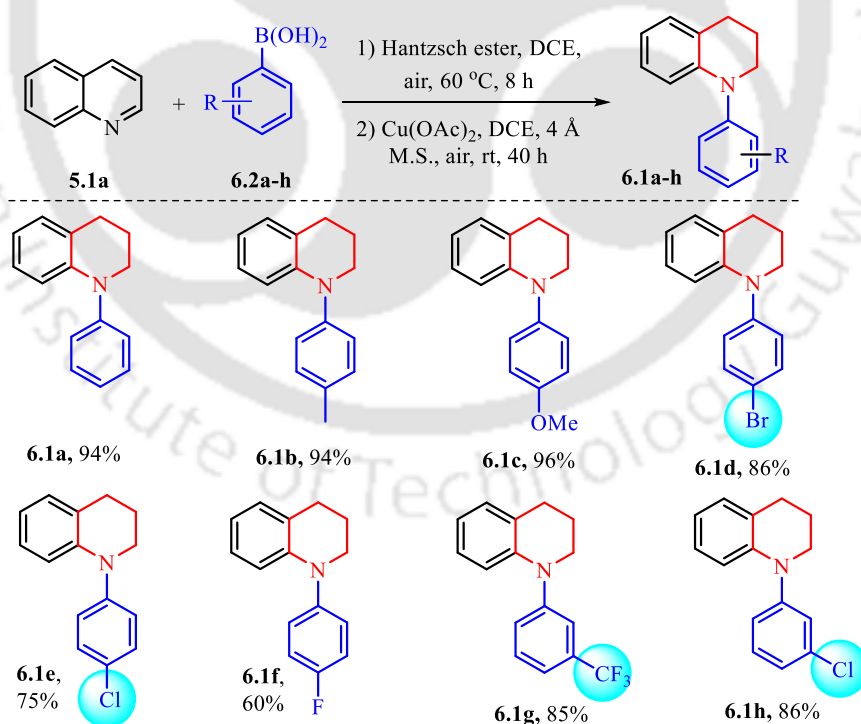
^aReaction conditions: quinoline (1 mmol), phenyl boronic acid (30 mol%), HE (2.2 mmol), DCE (2 mL), 60 °C for 7 h under air; then phenyl boronic acid (0.7 mmol), copper(II)acetate (0.8 equiv.), 4 Å M.S., 40 h, air, rt. ^bYields are those of isolated products. ^cFor 2nd step, 24 h. ^dFor 2nd step, 70 °C, 24 h. ^equinoline (1 mmol), phenyl boronic acid (1 mmol), HE (2.2 mmol), copper(II)acetate (equiv.), 4 Å M.S., DCE (2 mL), 60 °C, 48 h, air.

For further improving the yield of desired product **6.1a**, different reaction condition such as temperature, copper(II) acetate loading has been examined. The best yield of **6.1a** (94%, Table 6.1, entry 3) was obtained by using copper(II) acetate (0.8 mmol), Hantzsch ester (2.2 mmol), phenyl boronic acid (1 mmol) in DCE (2 mL) under air.

6.2.3. Substrate scope

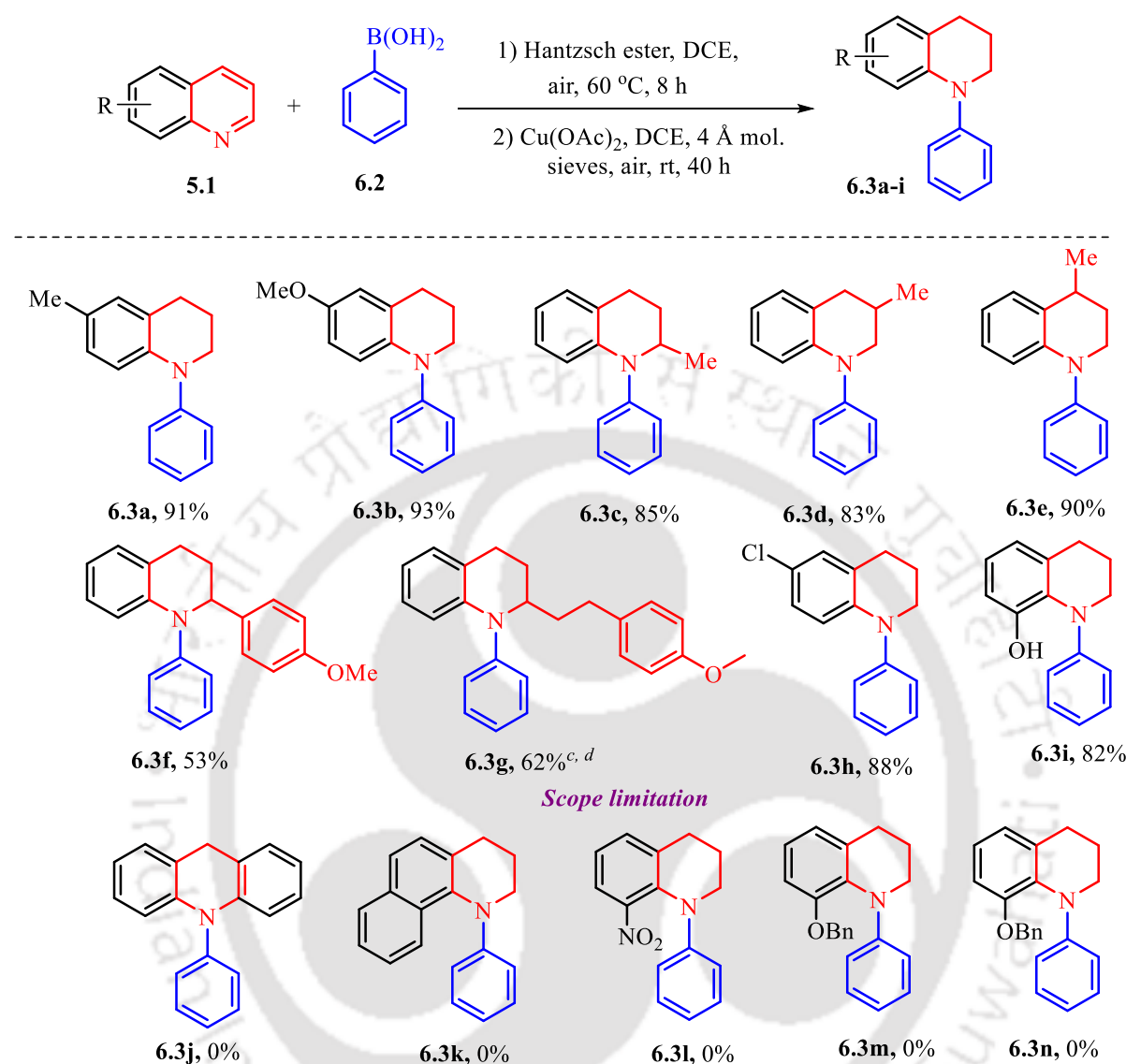
Next, the optimized condition was used to explore the substrate scope of this *N*-arylation reaction employing various boronic acid **6.2a-h**, and quinoline (Table 6.2). The reaction of quinoline **5.1a** with 4-Me (**6.2b**), and 4-OMe (**6.2c**) bearing arylboronic acid underwent the product **6.1b**, and **6.1c** in 94 and 96% yields, respectively, while the substrates with 4-Br (**6.2d**), 4-Cl (**6.2e**), and 4-F (**6.2f**) substituent afforded **6.1d-f** in 60-86% yields. Likewise, the substrates having 3-CF₃, and 3-Cl groups in the aromatic ring were also reacted efficiently to give the desired *N*-aryl substituted THQs **6.1g**, **6.1h** in good yields. Notably, retaining the halogen functional group (4-Br, 4-Cl, 3-Cl) in the final product can offer further functionalization through cross-coupling way. The scope of the above protocol was further extended to synthesize *N*-phenyl tetrahydroquinoline derivatives **6.3a-i** using phenyl boronic acid as the model substrate and varieties of substituents at different positions of the quinoline moiety (Table 6.3). The quinoline bearing 2-Me, 3-Me, 4-Me, 6-Me, 6-OMe, 6-Cl, 8-OH groups afforded the desired products **6.3a-i** in 82-93% yield. In the case of (*E*)-2-(4-methoxystyryl)quinoline substrate, both the conjugated double bond and quinoline ring effectively reduced to obtain **6.3g** in 62% yield. Gratifyingly, 2-(4-methoxyphenyl)quinoline gave the desired product **6.3f** in 53% yield, indicating that bulky aromatic functionality at the C2 position of the quinoline moiety is tolerated in our reaction condition, which is superior to the known Chan-Lam-Evans amination method.¹⁶

Table 6.2. Substrate scope for *N*-aryl tetrahydroquinolines^{a,b}



^aReaction conditions: quinoline (1 mmol), aryl boronic acid (30 mol%), HE (2.2 mmol), DCE (2 mL), 60 °C for 7 h under air; then aryl boronic acid (0.7 mmol), copper(II)acetate (0.8 equiv.), 4 Å M.S., 40 h, air, rt. ^bIsolated yield.

It was found that the desired aminated products **6.3j-n** were not detected when the acridine, benzo[*h*]quinoline, 8-nitroquinoline, 8-benzyloxyquinolines, 8-tosyloxyquinolines were used as substrates, probably because of their steric and electronic effect.

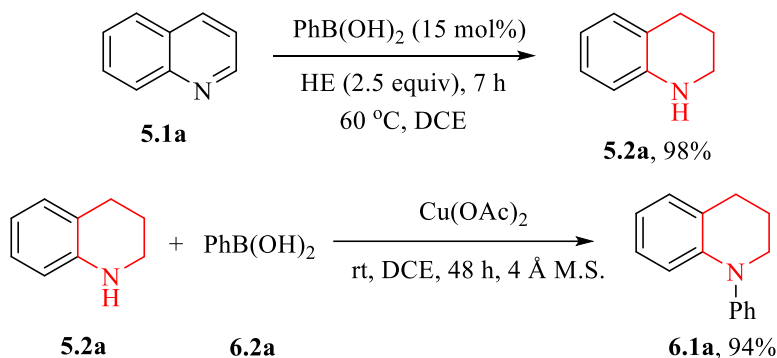
Table 6.3. Substrate scope for *N*-phenyl tetrahydroquinoline derivatives^{a,b}

^aReaction conditions: substituted quinoline (1 mmol), phenyl boronic acid (30 mol%), HE (2.2 mmol), DCE (2 mL), 60 °C for 7 h under air; then phenyl boronic acid (0.7 mmol), copper(II)acetate (0.8 equiv.), 4 Å M.S., 40 h, air, rt. ^bIsolated yield. ^cStarted from 2-(4-methoxystyryl)quinoline. ^d3.5 equivalent HE was used.

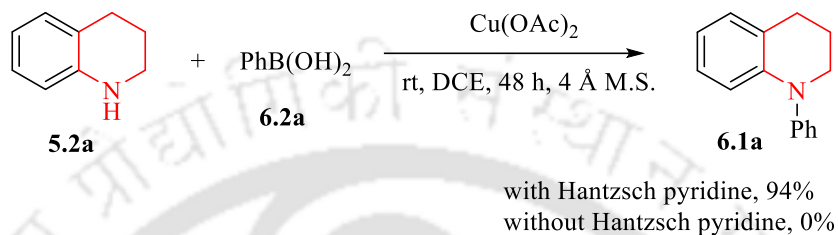
6.2.4. Mechanistic studies

To gain more insight into the reaction pathway, at first I have performed the experiment with quinoline, hantzsch ester and phenylboronic acid (15 mol%) under the following reaction condition as discussed in the section 5.2.1. As expected, 1,2,3,4-tetrahydroquinoline was obtained in 98% yield. For the subsequent step, the reaction was conducted with formed 1,2,3,4-tetrahydroquinoline, phenylboronic acid, and copper(II)acetate in the presence of Hantzsch pyridine, the desired product **6.1a** was obtained in 94% yield. In contrast, there is no formation of **6.1a** in the absence of Hantzsch pyridine. It suggests the role of Hantzsch pyridine is crucial for this transformation. Then I attempted to synthesize the adduct of copper(II)acetate and 1,2,3,4-tetrahydroquinoline in toluene at 60 °C for 12 h, complex **6.4** was obtained in 23% of yield. The structure of compound **6.4** has been proposed based on earlier report¹⁷ and mass-spectrometry analysis. Treating complex **6.4** with phenylboronic acid and Hantzsch pyridine in DCE at rt for 48 h, desired *N*-arylated product **6.1a** was achieved in 87% yield. This observation suggests that amine ligated Cu(II) complex **6.4** is the possible reaction intermediate in the C-N bond formation step.

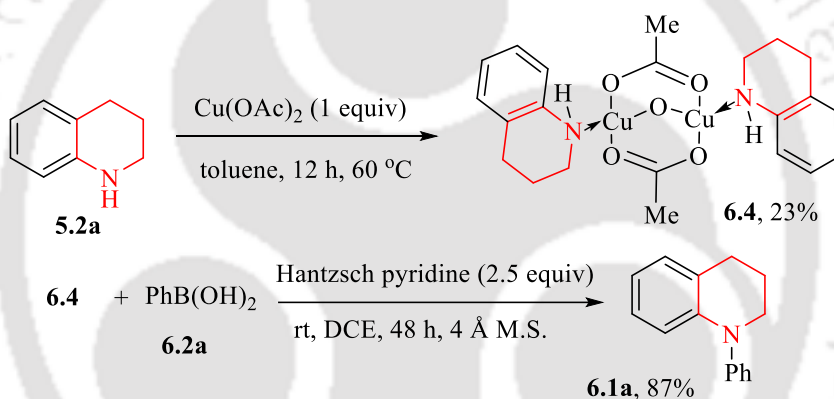
Proof of 1,2,3,4 THQ as the reaction intermediate



Role of Hantzsch pyridine in the *N*-arylation reaction



Scheme 6.4. Control experiments for mechanistic studies



Scheme 6.5. A possible reaction intermediate in the C-N bond formation step

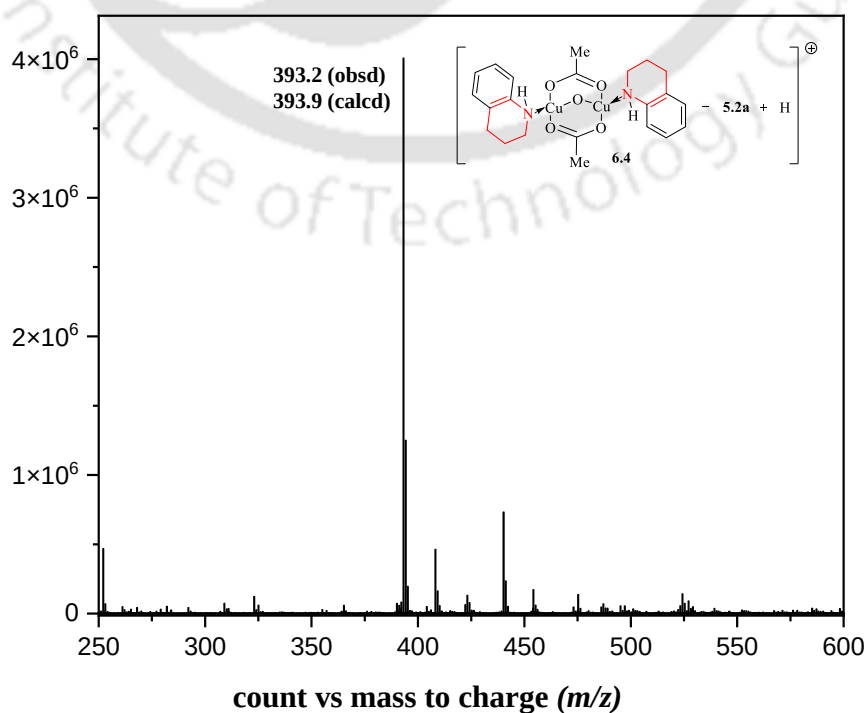


Figure 6.1. ESI spectra of complex 6.4

6.3. Summary

In summary, one-pot tandem method involving quinoline reduction to tetrahydroquinoline and sequential external base-free Chan-Lam-Evans amination has been demonstrated for the step-economical synthesis of *N*-aryl tetrahydroquinoline derivatives. These have been achieved directly from readily available quinolines, aryl boronic acid, and Hantzsch ester under air. The process proved to be versatile and compatible with various functional groups at both quinoline and boronic acid moiety. Because of the ready accessibility of starting materials and the low cost of the amination protocol, the methodology proved to be useful alternative for the construction of bio-relevant *N*-heterocycles.

6.4. 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., Finar Chemicals and directly used as received without any further purification unless otherwise mentioned. ^1H , ^{13}C , and ^{19}F NMR spectra of the compounds were measured in CDCl_3 , $\text{DMSO}-d_6$, CD_3OD as a solvent by using TMS as an internal standard. Chemical shifts, δ (in ppm), are reported relative to TMS δ (^1H) 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 (^1H) 7.26 ppm, δ (^{13}C) 77.16 ppm; $\text{DMSO}-d_6$, (^1H) 2.50 ppm, δ (^{13}C) 39.52 ppm; CD_3OD , δ (^1H) 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.

B. General procedure for synthesis of *N*-aryl tetrahydroquinolines:

A mixture of substituted quinoline (1 mmol, 1 equiv.), Hantzsch ester (2.5 mmol, 2.5 equiv.), aryl-boronic acid (0.3 mmol, 0.3 equiv) and DCE (2 mL) was added into a reaction tube (25 mL) equipped with stirring bar. The reaction tube was properly closed and placed in a preheated oil bath at 60 °C with continuous stirring for 8 hours. To the resulting mixture, aryl-boronic acid (0.7 mmol, 0.7 equiv), copper(II)acetate (0.8 mmol, 0.8 equiv) and 4 Å M.S. was added and stirred at room temperature for 40 hours. 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 column chromatography over silica gel using petroleum ether or ethyl acetate/ petroleum ether mixture as eluent.

C. Reaction mechanism studies:

i. Synthesis of 5.2a

In a pyrex tube (15 mL), quinoline (0.129 g, 1 mmol, 1 equiv), Hantzsch ester (0.632 g, 2.5 mmol 2.5 equiv.), benzenboronic acid (0.19 g, 0.15 mmol, 0.15 equiv) and solvent (2 mL) 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 pet-ether and ethyl acetate solvent system. After completion of the reaction, the crude compound was purified by column chromatography on silica gel for pure compound.

ii. Synthesis of 6.4

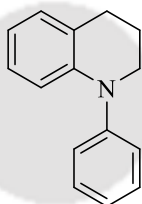
In a pyrex tube (15 mL), **5.1a** (0.133 g, 1 mmol, 1 equiv), copper(II)acetate (0.300 g, 1.5 mmol, 1.5 equiv) and toluene (3 mL) were charged. The reaction tube was properly closed and kept at room temperature with continuous stirring for 12 hours. After 12 hours the reaction mixture is filtered to get rid of excess Cu(OAc)₂. The filtrate was then evaporated under reduced pressure. The residue was washed with cold DCE to get a green solid of **6.4** (0.090 g, 23%) HRMS (ESI) *m/z*: [M+H]⁺ calculated for C₁₃H₁₇Cu₂NO₅ 393.9772; found: 393.2200. It was directly used for the next reaction.

iii. Synthesis of 1-phenyl-1,2,3,4-tetrahydroquinoline (**6.1a**) from **6.4**

In a pyrex tube (15 mL), **6.4** (0.025 g, 0.06 mmol, 1 equiv.), **HP** (0.038 g, 0.15 mmol, 2.5 equiv), benzeneboronic acid (0.008 g, 0.06 mmol, 1 equiv.) and DCE (2 mL) were charged. The reaction tube was properly closed and kept at room temperature with continuous stirring. The reaction was monitored by thin layered chromatography (TLC) in pet-ether and ethyl acetate solvent system. After completion of the reaction, the crude compound was purified by column chromatography on silica gel for pure compound to get pure compound as colourless oil of **6.1a** (0.011 g, 87%).

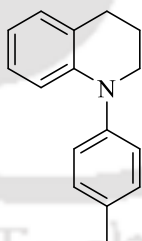
6.5. Analytical data of the products:

1-phenyl-1,2,3,4-tetrahydroquinoline (**6.1a**)¹⁵



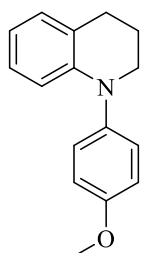
Following the general procedure the title compound **6.1a** was isolated as colourless liquid using silica gel column chromatography with pet-ether/ ethylacetate (v/v= 100/1, *R_f* = 0.5) in 94% yield (0.196 g). ¹H NMR (600 MHz, CDCl₃): δ 7.34 (t, *J* = 8.0 Hz, 2H), 7.24 (d, *J* = 7.4 Hz, 2H), 7.09 (t, *J* = 7.2 Hz, 1H), 7.05 (d, *J* = 7.2 Hz, 1H), 6.93 (t, *J* = 7.4 Hz, 1H), 6.75 (d, *J* = 8.2 Hz, 1H), 6.70 (t, *J* = 7.2 Hz, 1H), 3.64 – 3.62 (m, 2H), 2.85 (t, *J* = 6.4 Hz, 2H), 2.07 – 2.03 (m, 2H). ¹³C NMR (151 MHz, CDCl₃): δ 148.51, 144.54, 129.50, 126.48, 124.77, 123.70, 118.42, 115.89, 50.96, 27.90, 22.87.

1-(p-tolyl)-1,2,3,4-tetrahydroquinoline (**6.1b**)¹⁸



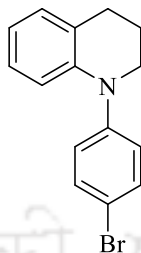
Following the general procedure the title compound **6.1b** was isolated as colourless liquid using silica gel column chromatography with pet-ether/ ethylacetate (v/v= 100/1, *R_f* = 0.5) in 94% yield (0.209 g). ¹H NMR (400 MHz, CDCl₃): δ 7.20 – 7.11 (m, 4H), 7.03 (d, *J* = 7.4 Hz, 1H), 6.91 (dd, *J* = 11.4, 4.2 Hz, 1H), 6.69 – 6.63 (m, 2H), 3.63 – 3.60 (m, 2H), 2.88 (t, *J* = 6.4 Hz, 2H), 2.37 (s, 3H), 2.10 – 2.05 (m, 2H). ¹³C NMR (101 MHz, CDCl₃): δ 145.98, 145.04, 133.78, 130.20, 129.45, 126.50, 125.44, 123.96, 117.85, 115.30, 51.31, 27.96, 22.74, 21.03.

1-(4-methoxyphenyl)-1,2,3,4-tetrahydroquinoline (**6.1c**)¹¹



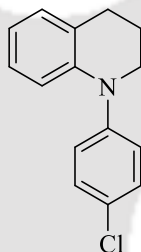
Following the general procedure the title compound **6.1c** was isolated as colourless liquid using silica gel column chromatography with pet-ether/ ethylacetate (v/v= 100/1, R_f = 0.5) in 96% yield (0.229 g). ^1H NMR (600 MHz, CDCl_3) δ 7.18 – 7.16 (m, 2H), 7.02 (d, J = 7.2 Hz, 1H), 7.01 – 6.87 (m, 3H), 6.64 – 6.49 (m, 1H), 6.47 (d, J = 8.2 Hz, 1H), 3.83 (s, 3H), 3.57 – 3.55 (m, 2H), 2.87 (t, J = 6.4 Hz, 2H), 2.08 – 2.05 (m, 2H). ^{13}C NMR (151 MHz, CDCl_3) δ 156.90, 145.68, 141.51, 129.43, 127.80, 126.60, 123.09, 117.30, 114.97, 114.44, 55.62, 51.79, 28.00, 22.64.

1-(4-bromophenyl)-1,2,3,4-tetrahydroquinoline (**6.1d**)¹⁹



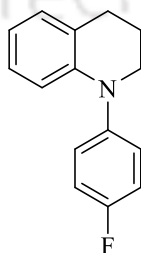
Following the general procedure the title compound **6.1d** was isolated as colourless liquid using silica gel column chromatography with pet-ether/ ethylacetate (v/v= 50/1, R_f = 0.5) in 86% yield (0.247 g). ^1H NMR (400 MHz, CDCl_3) δ 7.45 – 7.38 (m, 2H), 7.13 – 7.07 (m, 2H), 7.05 (d, J = 7.4 Hz, 1H), 6.94 (t, J = 7.8 Hz, 1H), 6.80 – 6.71 (m, 2H), 3.61 – 3.58 (m, 2H), 2.84 (t, J = 6.4 Hz, 2H), 2.03 (dd, J = 12.0, 6.0 Hz, 2H). ^{13}C NMR (101 MHz, CDCl_3) δ 147.63, 143.85, 132.45, 129.58, 126.55, 125.76, 125.56, 119.23, 116.43, 115.82, 50.75, 27.75, 22.89.

1-(4-chlorophenyl)-1,2,3,4-tetrahydroquinoline (**6.1e**)



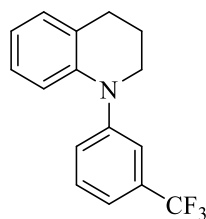
Following the general procedure the title compound **6.1e** was isolated as colourless liquid using silica gel column chromatography with pet-ether/ ethylacetate (v/v= 50/1, R_f = 0.5) in 75% yield (0.182 g). ^1H NMR (400 MHz, CDCl_3): δ 7.36 – 7.26 (m, 2H), 7.18 – 7.13 (m, 2H), 7.05 (d, J = 8.0 Hz, 1H), 6.94 (t, J = 7.6 Hz, 1H), 6.73 (dd, J = 11.8, 4.6 Hz, 2H), 3.61 – 3.60 (m, 2H), 2.82 (t, J = 6.4 Hz, 2H), 2.05 – 2.01 (m, 2H). ^{13}C NMR (151 MHz, CDCl_3): δ 148.18, 143.23, 129.66, 128.98, 126.34, 126.17, 124.87, 124.14, 122.78, 116.97, 50.95, 27.80, 22.54.

1-(4-fluorophenyl)-1,2,3,4-tetrahydroquinoline (**6.1f**)¹¹



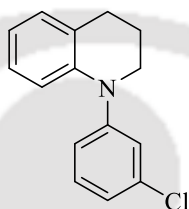
Following the general procedure the title compound **6.1f** was isolated as colourless liquid using silica gel column chromatography with pet-ether/ ethylacetate (v/v= 50/1, R_f = 0.5) in 60% yield (0.136 g). ^1H NMR (600 MHz, CDCl_3): δ 7.22 – 7.19 (m, 2H), 7.09 – 7.03 (m, 3H), 6.93 (t, J = 7.6 Hz, 1H), 6.69 (t, J = 7.2 Hz, 1H), 6.56 (d, J = 8.2 Hz, 1H), 3.59 – 3.57 (m, 2H), 2.88 (t, J = 6.4 Hz, 2H), 2.09 – 2.04 (m, 2H). ^{13}C NMR (126 MHz, CDCl_3): δ 160.68, 158.75, 145.01, 144.61, 144.59, 129.56, 127.44, 127.37, 126.62, 123.94, 118.15, 116.45, 116.27, 115.06, 51.57, 27.89, 22.69. ^{19}F NMR (377 MHz, CDCl_3) δ -118.31.

1-(3-(trifluoromethyl)phenyl)-1,2,3,4-tetrahydroquinoline (6.1g)²⁰



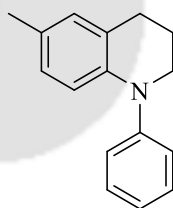
Following the general procedure the title compound **6.1g** was isolated as colourless liquid using silica gel column chromatography with pet-ether/ ethylacetate (v/v= 50/1, R_f = 0.5) in 85% yield (0.235 g). ^1H NMR (400 MHz, CDCl_3): δ 7.45 – 7.39 (m, 3H), 7.26 – 7.25 (m, 1H), 7.08 (d, J = 7.4 Hz, 1H), 7.00 – 6.84 (m, 1H), 6.80 (d, J = 8.0 Hz, 1H), 6.77 (t, J = 7.2 Hz, 1H), 3.66 – 3.63 (m, 2H), 2.83 (t, J = 6.4 Hz, 2H), 2.07 – 2.01 (m, 2H). ^{13}C NMR (101 MHz, CDCl_3): δ 148.96, 143.32, 129.83, 129.64, 126.63, 126.42, 119.92, 119.28, 116.86, 50.48, 27.68, 23.09. ^{19}F NMR (377 MHz, CDCl_3) δ -62.71.

1-(3-chlorophenyl)-1,2,3,4-tetrahydroquinoline (6.1h)



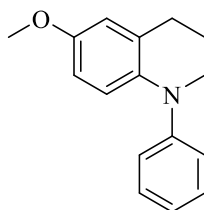
Following the general procedure the title compound **6.1h** was isolated as colourless liquid using silica gel column chromatography with pet-ether/ ethylacetate (v/v= 50/1, R_f = 0.5) in 86% yield (0.209 g). ^1H NMR (400 MHz, CDCl_3): δ 7.25 – 7.18 (m, 2H), 7.12 – 7.04 (m, 2H), 7.02 – 6.94 (m, 2H), 6.86 (d, J = 8.2 Hz, 1H), 6.76 (td, J = 7.4, 1.0 Hz, 1H), 3.62 – 3.59 (m, 2H), 2.81 (t, J = 6.4 Hz, 2H), 2.07 – 1.98 (m, 2H). ^{13}C NMR (101 MHz, CDCl_3): δ 149.77, 143.46, 134.86, 130.27, 129.54, 126.55, 126.16, 123.45, 122.89, 121.55, 119.64, 117.03, 50.52, 27.69, 23.02.

6-methyl-1-phenyl-1,2,3,4-tetrahydroquinoline (6.3a)



Following the general procedure the title compound **6.3a** was isolated as colourless liquid using silica gel column chromatography with pet-ether/ ethylacetate (v/v= 100/1, R_f = 0.5) in 91% yield (0.203 g). ^1H NMR (400 MHz, CDCl_3): δ 7.32 (t, J = 7.8 Hz, 2H), 7.28 (d, J = 7.4 Hz, 2H), 7.19 (t, J = 7.2 Hz, 1H), 7.01 (s, 1H), 6.88 – 6.71 (m, 2H), 3.61 – 3.58 (m, 2H), 2.79 (t, J = 6.4 Hz, 2H), 2.23 (s, 3H), 2.03 – 1.97 (m, 2H). ^{13}C NMR (101 MHz, CDCl_3): δ 148.87, 141.92, 130.01, 129.35, 128.03, 127.02, 125.31, 123.93, 122.98, 116.62, 50.80, 27.78, 22.98, 20.55.

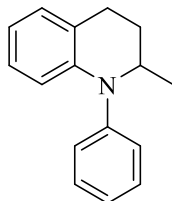
6-methoxy-1-phenyl-1,2,3,4-tetrahydroquinoline (6.3b)



Following the general procedure the title compound **6.3b** was isolated as colourless liquid using silica gel column chromatography with pet-ether/ ethylacetate (v/v= 100/1, R_f = 0.5) in 93% yield (0.222 g). ^1H NMR (400 MHz, CDCl_3): δ 7.31 – 7.25 (m, 2H), 7.16 (dd, J = 8.6, 1.0 Hz, 2H), 7.01 – 6.95

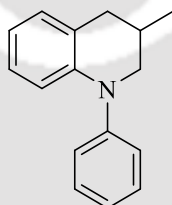
(m, 1H), 6.83 (d, $J = 8.8$ Hz, 1H), 6.65 (d, $J = 3.0$ Hz, 1H), 6.57 (dd, $J = 9.0, 3.0$ Hz, 1H), 3.75 (s, 3H), 3.62 – 3.57 (m, 2H), 2.80 (t, $J = 6.4$ Hz, 2H), 1.98 (dt, $J = 12.0, 6.4$ Hz, 2H). ^{13}C NMR (101 MHz, CDCl_3): δ 153.12, 149.42, 137.94, 129.29, 127.70, 122.78, 122.20, 118.97, 114.41, 112.42, 55.76, 50.64, 28.02, 22.89.

2-methyl-1-phenyl-1,2,3,4-tetrahydroquinoline (6.3c)



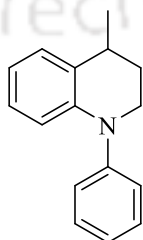
Following the general procedure the title compound **6.3c** was isolated as colourless liquid using silica gel column chromatography with pet-ether/ ethylacetate (v/v= 100/1, $R_f = 0.5$) in 85% yield (0.189 g). ^1H NMR (400 MHz, CDCl_3): δ 7.40 – 7.31 (m, 2H), 7.26 – 7.18 (m, 2H), 7.15 (td, $J = 7.2, 1.2$ Hz, 1H), 7.04 (dd, $J = 7.4, 1.4$ Hz, 1H), 6.89 (ddd, $J = 8.6, 7.2, 1.6$ Hz, 1H), 6.65 (td, $J = 7.2, 1.2$ Hz, 1H), 6.51 (dd, $J = 8.2, 1.2$ Hz, 1H), 3.90 (dt, $J = 6.6, 4.4$ Hz, 1H), 2.89 (dd, $J = 10.6, 5.4$ Hz, 1H), 2.87 – 2.77 (m, 1H), 2.12 – 2.02 (m, 1H), 1.90 – 1.80 (m, 1H), 1.15 (d, $J = 6.4$ Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3): δ 147.53, 144.34, 129.63, 129.31, 127.12, 126.53, 124.67, 123.20, 117.52, 115.93, 54.33, 28.50, 24.37, 19.85.

3-methyl-1-phenyl-1,2,3,4-tetrahydroquinoline (6.3d)



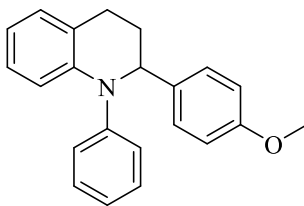
Following the general procedure the title compound **6.3d** was isolated as colourless liquid using silica gel column chromatography with pet-ether/ ethylacetate (v/v= 100/1, $R_f = 0.5$) in 83% yield (0.184 g). ^1H NMR (600 MHz, CDCl_3): δ 7.35 – 7.32 (m, 2H), 7.25 – 7.23 (m, 1H), 7.12 – 7.08 (m, 1H), 7.06 – 6.99 (m, 2H), 6.94 – 6.91 (m, 1H), 6.74 (dd, $J = 8.2, 1.2$ Hz, 1H), 6.69 (td, $J = 7.3, 1.3$ Hz, 1H), 3.63 (ddd, $J = 11.4, 3.9, 1.9$ Hz, 1H), 3.22 (dd, $J = 11.4, 9.6$ Hz, 1H), 2.88 (ddd, $J = 16.0, 5.0, 1.8$ Hz, 1H), 2.52 (dd, $J = 16.0, 10.3$ Hz, 1H), 2.25 – 2.16 (m, 1H), 1.06 (d, $J = 6.6$ Hz, 3H). ^{13}C NMR (151 MHz, CDCl_3): δ 148.40, 143.98, 129.87, 129.66, 129.52, 126.45, 124.96, 124.08, 123.85, 123.35, 119.03, 118.39, 115.40, 57.82, 36.24, 27.80, 19.08.

4-methyl-1-phenyl-1,2,3,4-tetrahydroquinoline (6.3e)



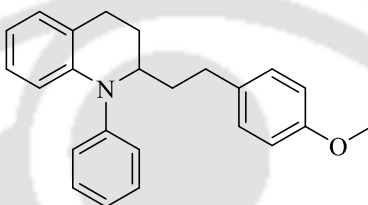
Following the general procedure the title compound **6.3e** was isolated as colourless liquid using silica gel column chromatography with pet-ether/ ethylacetate (v/v= 100/1, $R_f = 0.5$) in 90% yield (0.201 g). ^1H NMR (600 MHz, CDCl_3): δ 7.35 – 7.32 (m, 2H), 7.25 – 7.22 (m, 2H), 7.16 – 7.13 (m, 1H), 7.10 – 7.07 (m, 1H), 6.93 (tdd, $J = 7.1, 1.7, 0.8$ Hz, 1H), 6.79 – 6.71 (m, 2H), 3.66 (ddd, $J = 11.6, 8.3, 4.0$ Hz, 1H), 3.60 (ddd, $J = 11.4, 6.8, 4.4$ Hz, 1H), 2.98 (q, $J = 6.4$ Hz, 1H), 2.16 – 2.09 (m, 1H), 1.80 – 1.74 (m, 1H), 1.36 (d, $J = 6.9$ Hz, 3H). ^{13}C NMR (151 MHz, CDCl_3): δ 148.52, 143.89, 130.05, 129.50, 128.25, 126.45, 124.54, 123.60, 118.49, 116.09, 47.94, 31.01, 30.57, 22.32.

2-(4-methoxyphenyl)-1-phenyl-1,2,3,4-tetrahydroquinoline (6.3f)



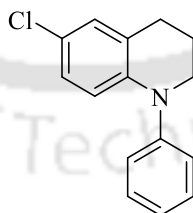
Following the general procedure the title compound **6.3f** was isolated as colourless liquid using silica gel column chromatography with pet-ether/ ethylacetate (v/v= 50/1, R_f = 0.5) in 53% yield (0.167 g). ^1H NMR (400 MHz, CDCl_3): δ 7.27 – 7.22 (m, 3H), 7.21 – 7.16 (m, 4H), 7.06 – 6.95 (m, 3H), 6.86 (d, J = 8.0 Hz, 1H), 6.81 (d, J = 8.7 Hz, 2H), 6.71 (d, J = 6.6 Hz, 1H), 4.89 (t, J = 4.2 Hz, 1H), 3.77 (s, 3H), 2.72 – 2.59 (m, 2H), 2.34 – 2.28 (m, 1H), 2.14 – 2.05 (m, 1H). ^{13}C NMR (101 MHz, CDCl_3): δ 158.46, 148.09, 143.99, 136.04, 129.42, 127.72, 126.68, 125.15, 124.13, 123.93, 118.11, 115.85, 113.87, 62.74, 55.35, 29.18, 23.87.

2-(4-methoxyphenethyl)-1-phenyl-1,2,3,4-tetrahydroquinoline (6.3g)



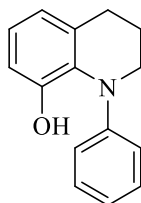
Following the general procedure the title compound **6.3g** was isolated as colourless liquid using silica gel column chromatography with pet-ether/ ethylacetate (v/v= 50/1, R_f = 0.5) in 62% yield (0.213 g). ^1H NMR (600 MHz, CDCl_3): δ 7.39 – 7.36 (m, 2H), 7.33 (t, J = 7.9 Hz, 2H), 7.19 (d, J = 7.5 Hz, 1H), 7.15 – 7.12 (m, 1H), 7.10 (d, J = 6.4 Hz, 1H), 7.07 – 7.04 (m, 3H), 6.96 (t, J = 7.2 Hz, 1H), 6.82 (d, J = 8.6 Hz, 1H), 6.76 (t, J = 8.3 Hz, 1H), 3.80 (s, 3H), 2.92 (ddd, J = 17.2, 11.9, 6.0 Hz, 1H), 2.83 (dt, J = 16.5, 4.7 Hz, 1H), 2.73 (ddd, J = 15.8, 10.5, 5.5 Hz, 1H), 2.67 – 2.60 (m, 1H), 2.06 (ddd, J = 17.4, 8.8, 4.9 Hz, 1H), 2.00 – 1.94 (m, 1H), 1.86 – 1.79 (m, 1H), 1.59 (s, 1H), 1.39 – 1.27 (m, 1H). ^{13}C NMR (126 MHz, CDCl_3): δ 157.91, 157.40, 148.85, 143.51, 134.11, 129.87, 129.50, 129.48, 129.46, 129.29, 126.45, 125.31, 124.68, 123.52, 123.35, 119.03, 118.74, 118.42, 113.93, 58.79, 55.41, 34.17, 31.67, 24.61, 23.76.

6-Chloro-1-phenyl-1,2,3,4-tetrahydroquinoline (6.3h)



Following the general procedure the title compound **6.3h** was isolated as colourless liquid using silica gel column chromatography with pet-ether/ ethylacetate (v/v= 100/1, R_f = 0.5) in 88% yield (0.214 g). ^1H NMR (400 MHz, CDCl_3): δ 7.35 (t, J = 7.9 Hz, 2H), 7.20 (d, J = 7.8 Hz, 2H), 7.11 (t, J = 7.3 Hz, 1H), 7.01 (d, J = 2.2 Hz, 1H), 6.86 (dd, J = 8.8, 2.5 Hz, 1H), 6.64 (d, J = 8.8 Hz, 1H), 3.62 – 3.59 (m, 2H), 2.82 (t, J = 6.5 Hz, 2H), 2.06 – 2.00 (m, 2H). ^{13}C NMR (101 MHz, CDCl_3): δ 149.77, 143.46, 134.86, 130.27, 129.54, 126.55, 126.16, 123.45, 122.89, 121.55, 119.64, 117.03, 50.52, 27.69, 23.02.

1-phenyl-1,2,3,4-tetrahydroquinolin-8-ol (6.3i)



Following the general procedure the title compound **6.3i** was isolated as colourless liquid using silica gel column chromatography with pet-ether/ ethylacetate (v/v= 25/1, R_f = 0.5) in 82% yield (0.184 g). ^1H NMR (400 MHz, CDCl_3): δ 7.28 – 7.22 (m, 2H), 6.98 (dt, J = 14.7, 7.6 Hz, 2H), 6.92 – 6.86 (m, 2H), 6.76 (d, J = 8.2 Hz, 2H), 5.03 (s, 1H), 3.70 – 3.68 (m, 2H), 2.82 (dd, J = 13.2, 6.4 Hz, 2H), 1.85 – 1.81 (m, 2H). ^{13}C NMR (151 MHz, CDCl_3): δ 149.62, 148.35, 132.71, 130.85, 129.51, 124.69, 122.02, 121.25, 120.05, 112.90, 51.83, 26.64, 20.67.

6.6. References

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Annexure I

^1H , ^{13}C , and ^{19}F NMR spectra of the products (*Chapter 2*)

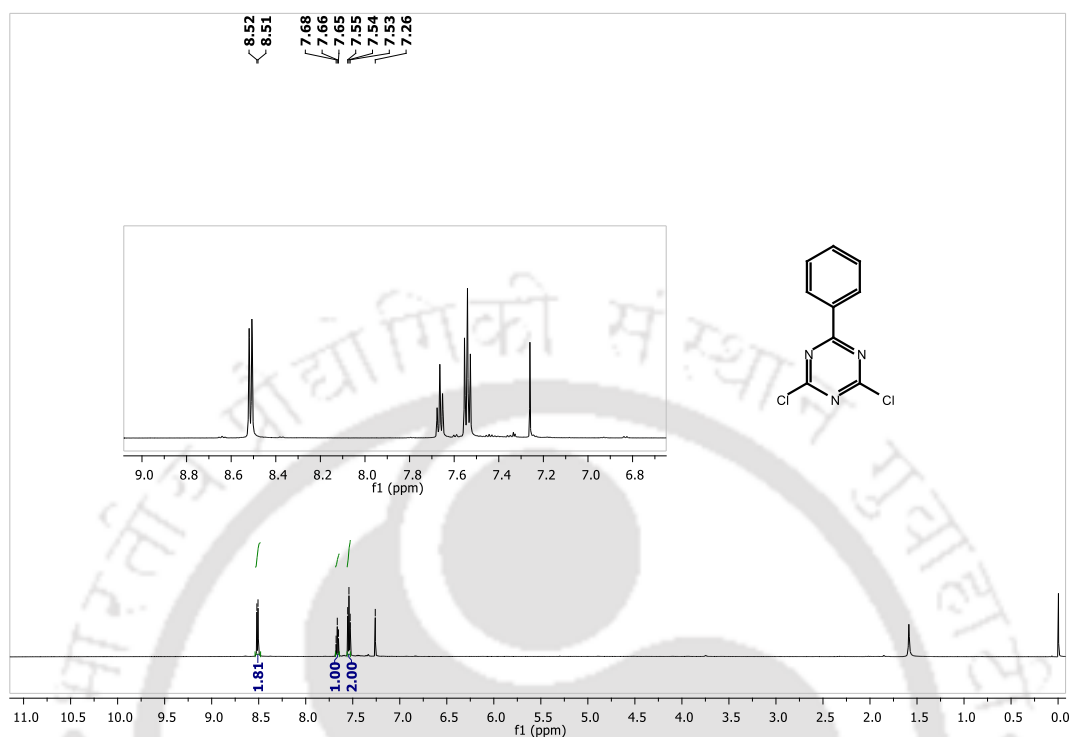


Figure S1: ^1H NMR Spectrum of **2.10a** (CDCl_3 , 600 MHz, 298 K)

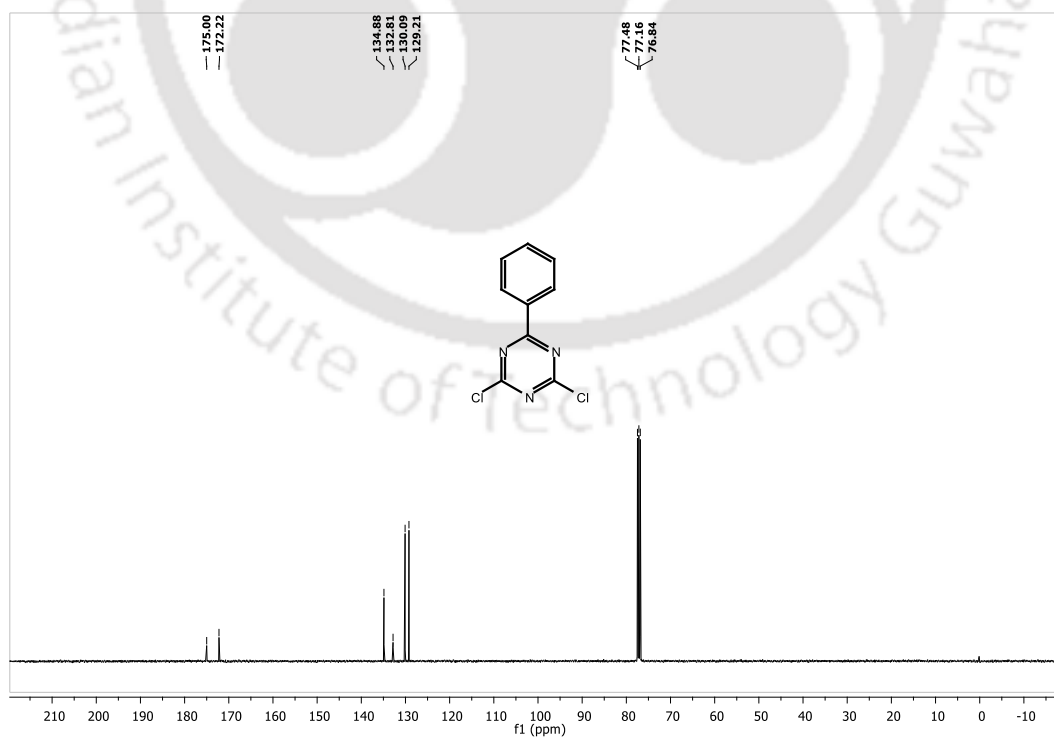


Figure S2: ^{13}C NMR Spectrum of **2.10a** (CDCl_3 , 101 MHz, 298 K)

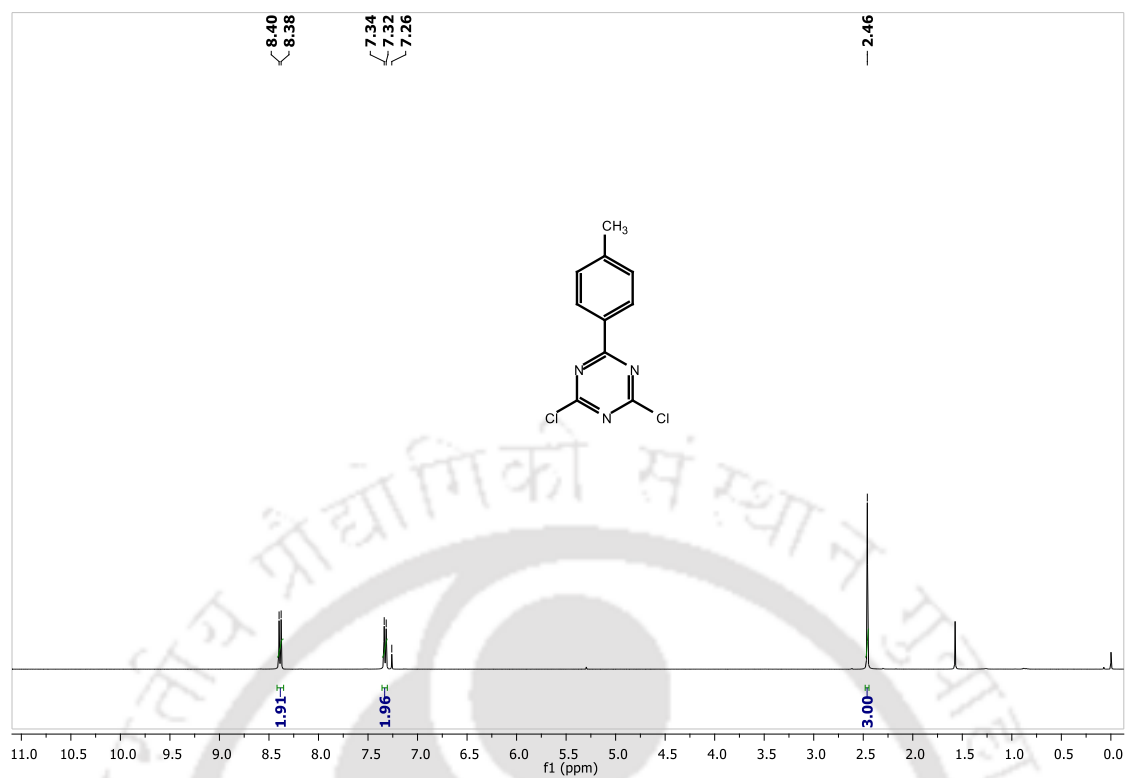


Figure S3: ¹H NMR Spectrum of **2.10b** (CDCl₃, 400 MHz, 298 K)

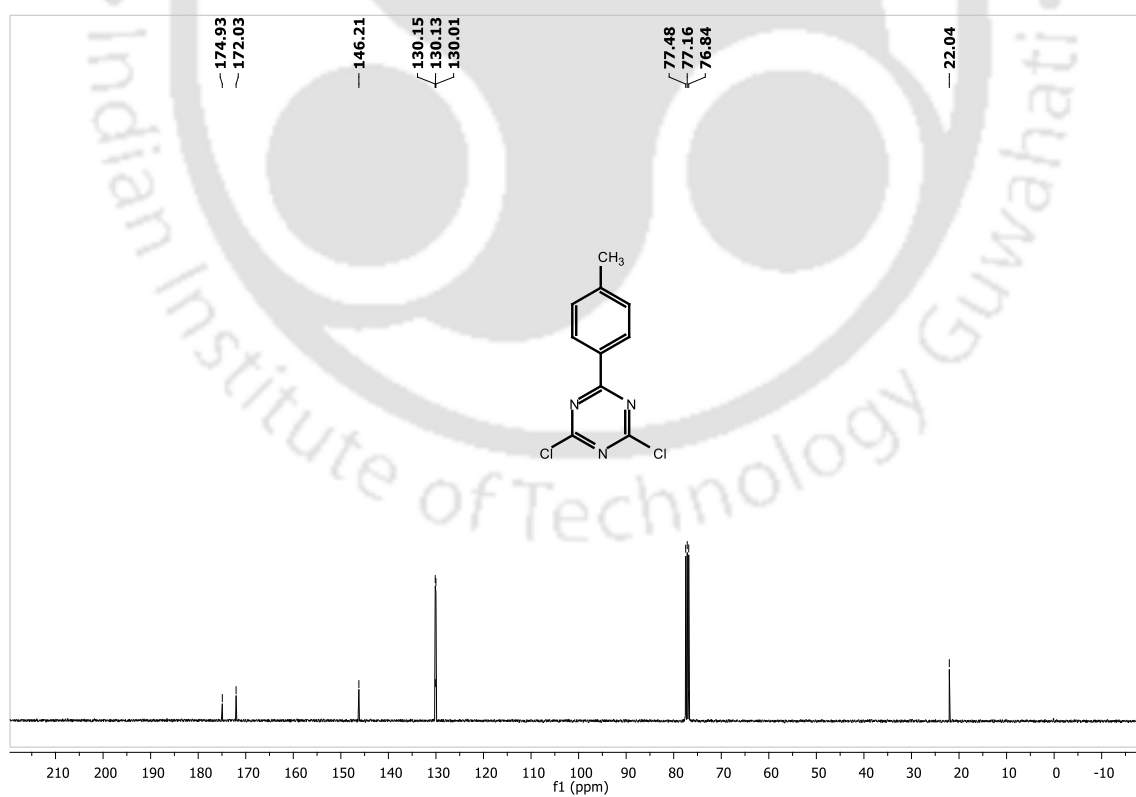


Figure S4: ¹³C NMR Spectrum of **2.10b** (CDCl₃, 101 MHz, 298 K)

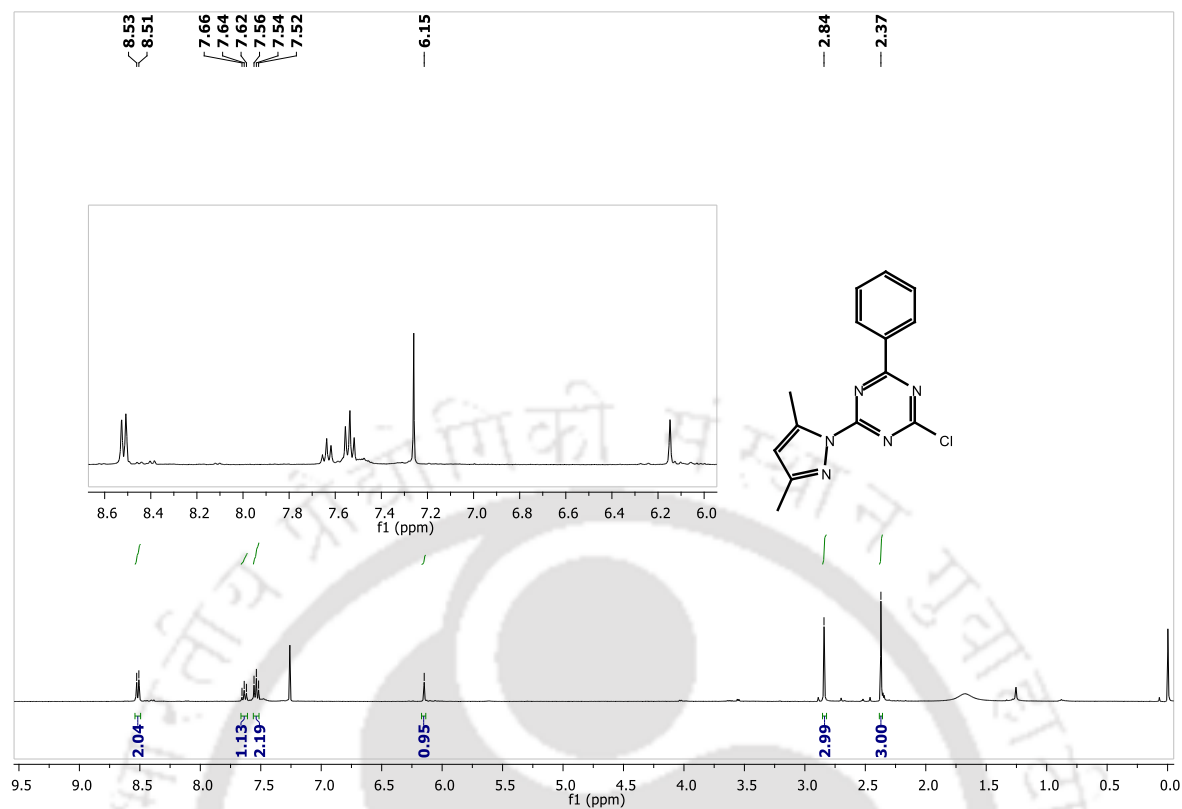


Figure S5: ¹H NMR Spectrum of **2.11a** (CDCl₃, 400 MHz, 298 K)

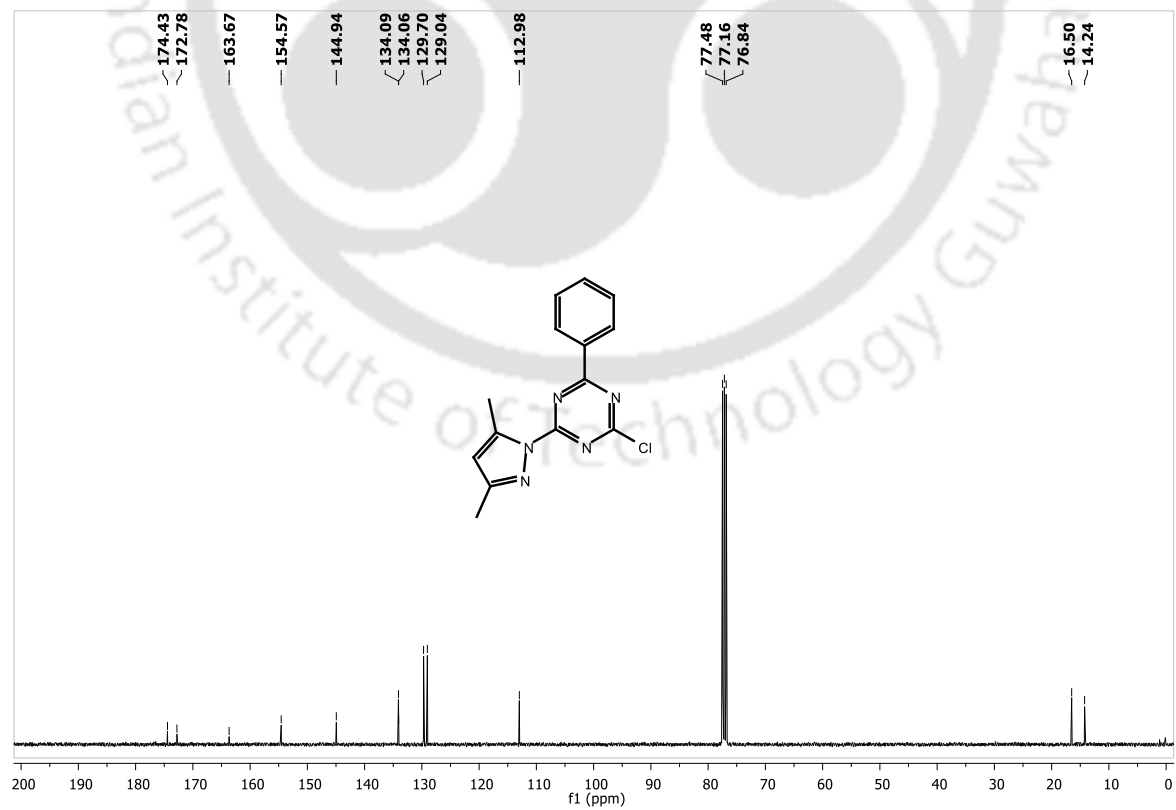
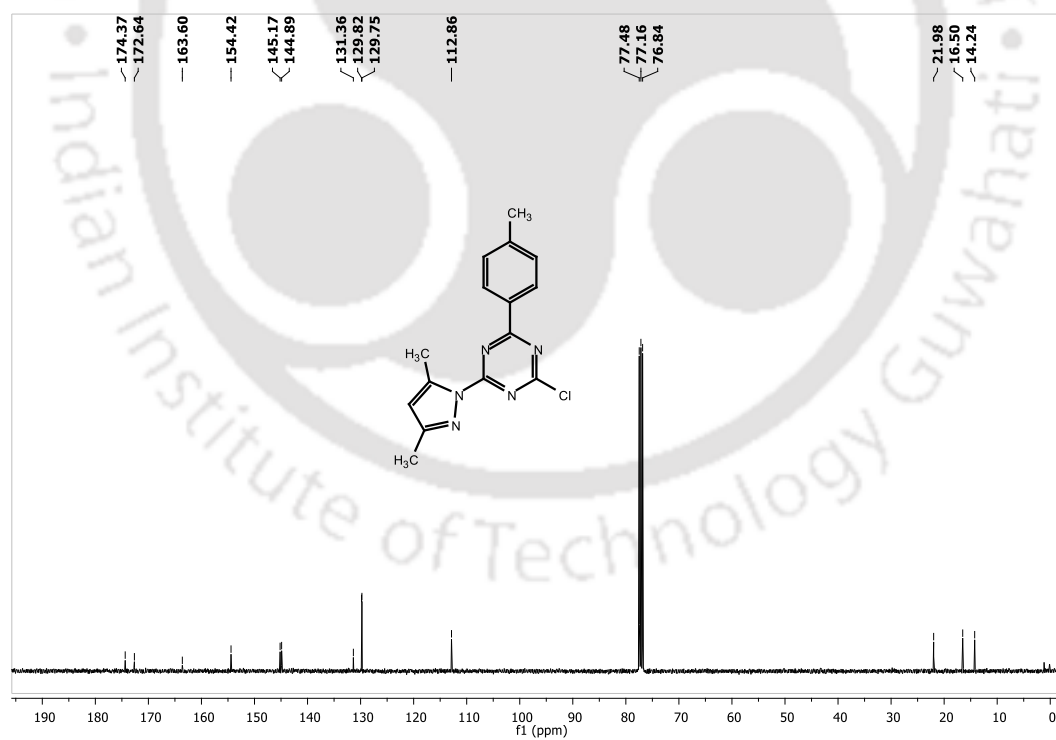
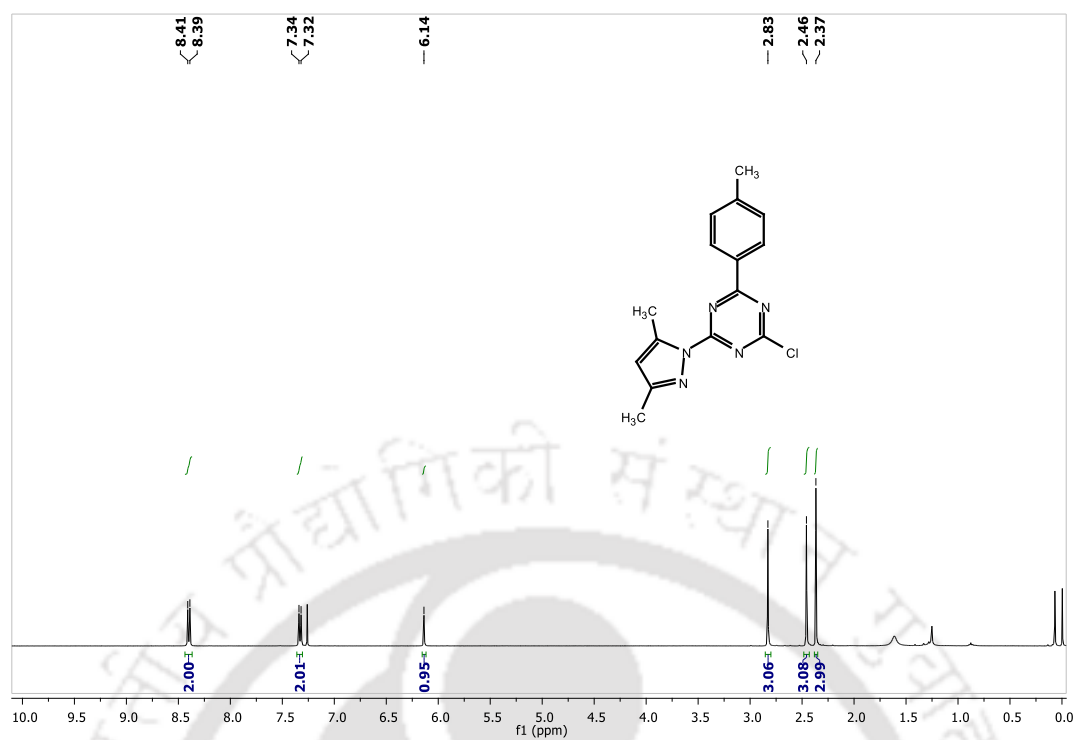


Figure S6: ¹³C NMR Spectrum of **2.11a** (CDCl₃, 101 MHz, 298 K)



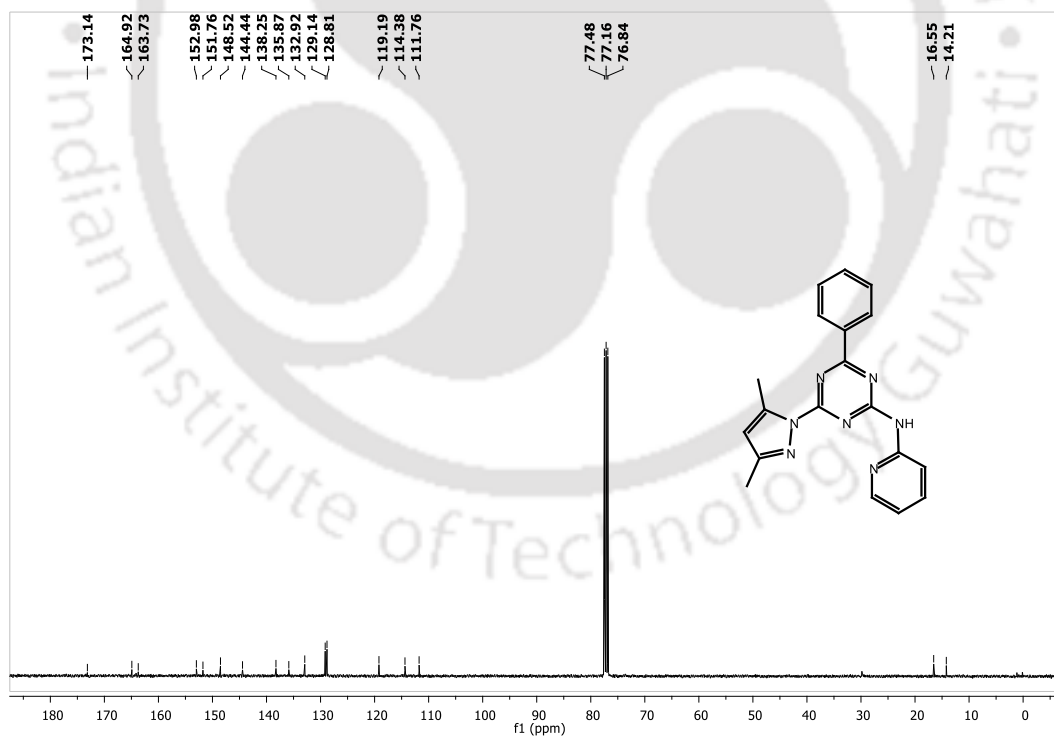
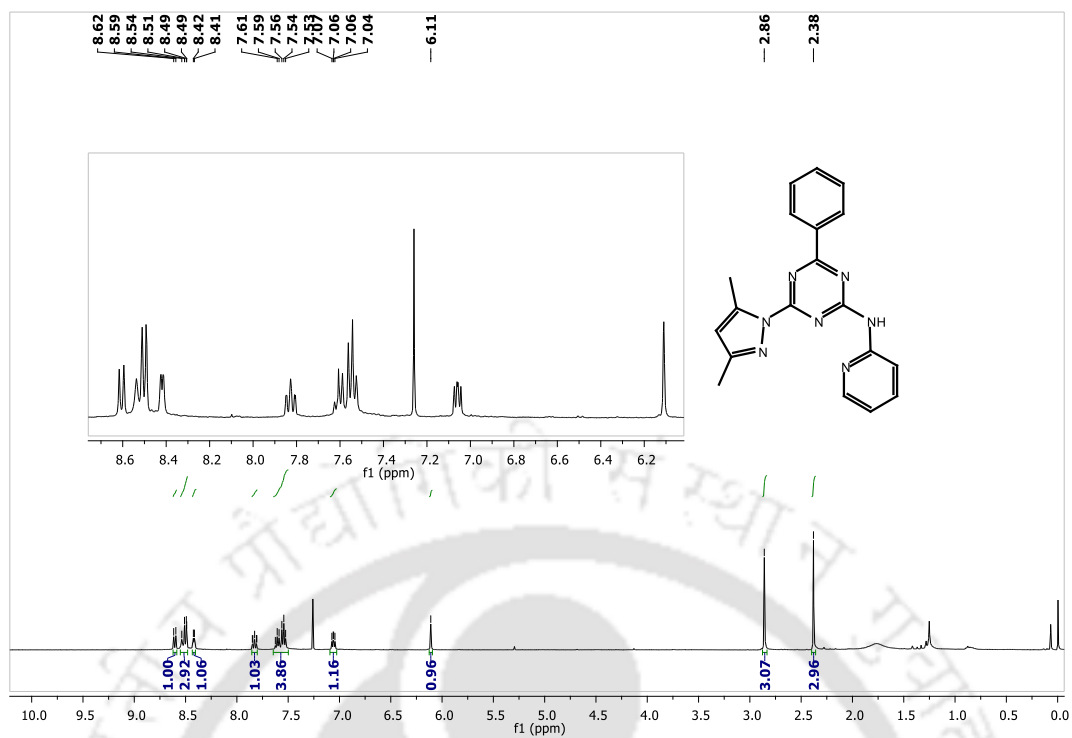


Figure S10: ^{13}C NMR Spectrum of HL^1 (CDCl_3 , 101 MHz, 298 K)

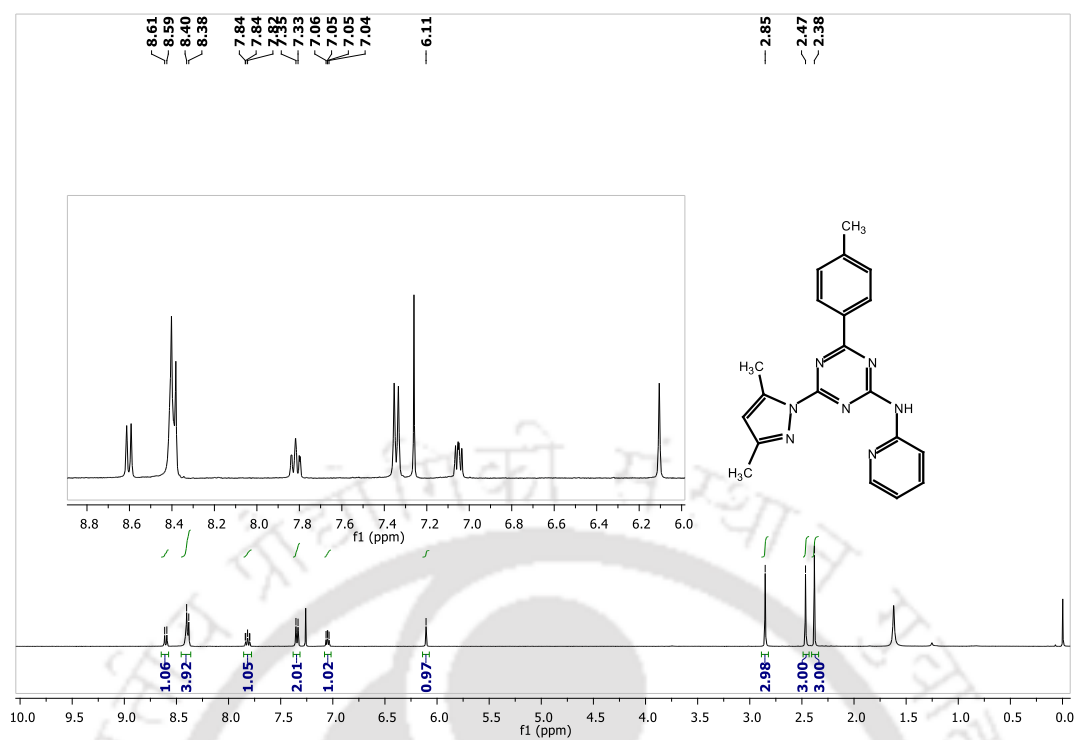


Figure S11: ^1H NMR Spectrum of HL^2 (CDCl_3 , 400 MHz, 298 K)

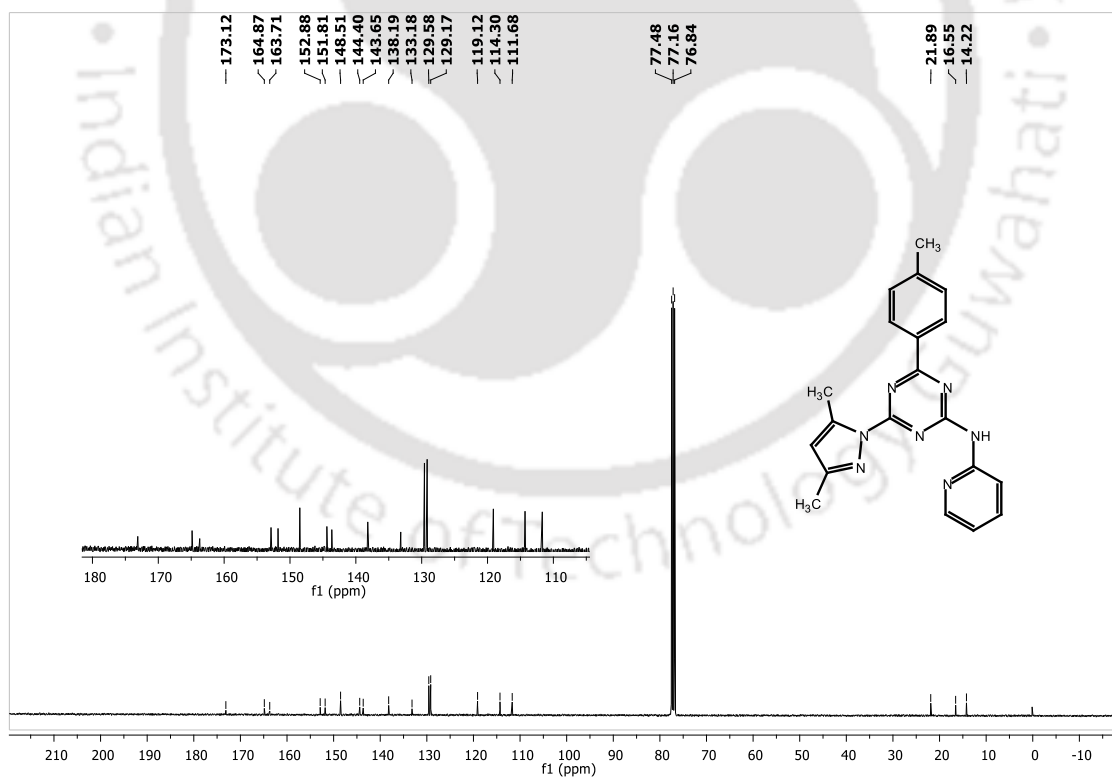


Figure S12: ^{13}C NMR Spectrum of HL^2 (CDCl_3 , 101 MHz, 298 K)

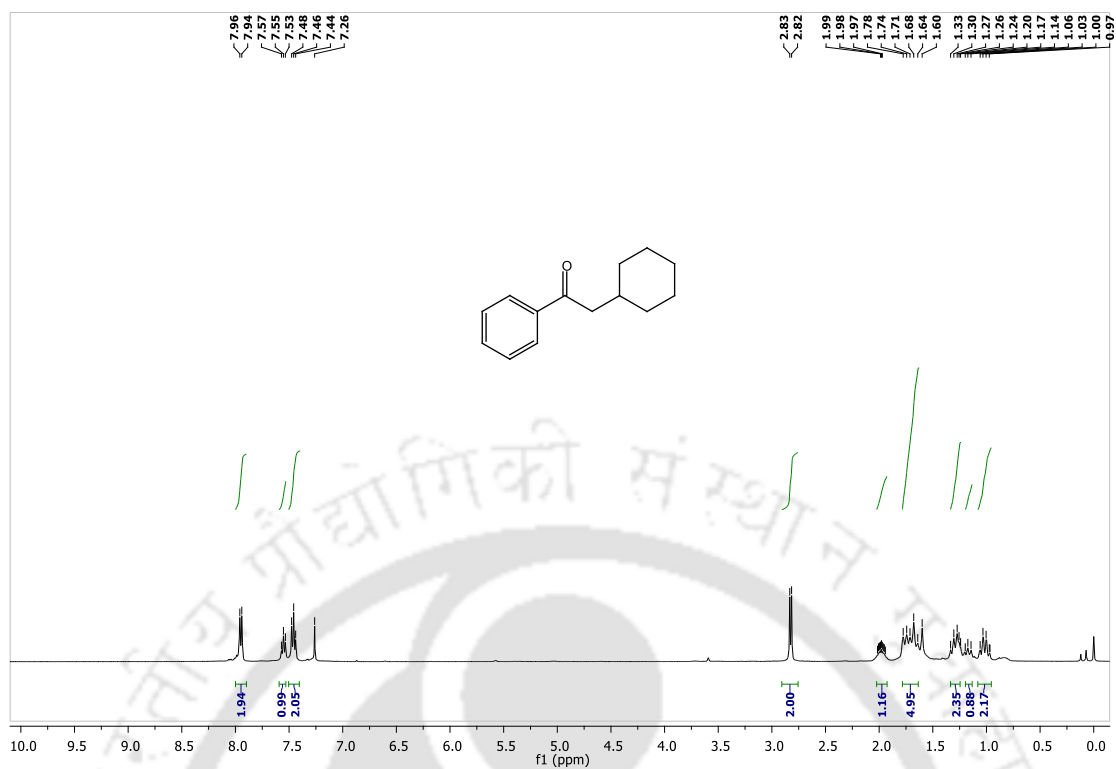


Figure S13: ¹H NMR Spectrum of **2.6a** (CDCl₃, 400 MHz, 298 K)

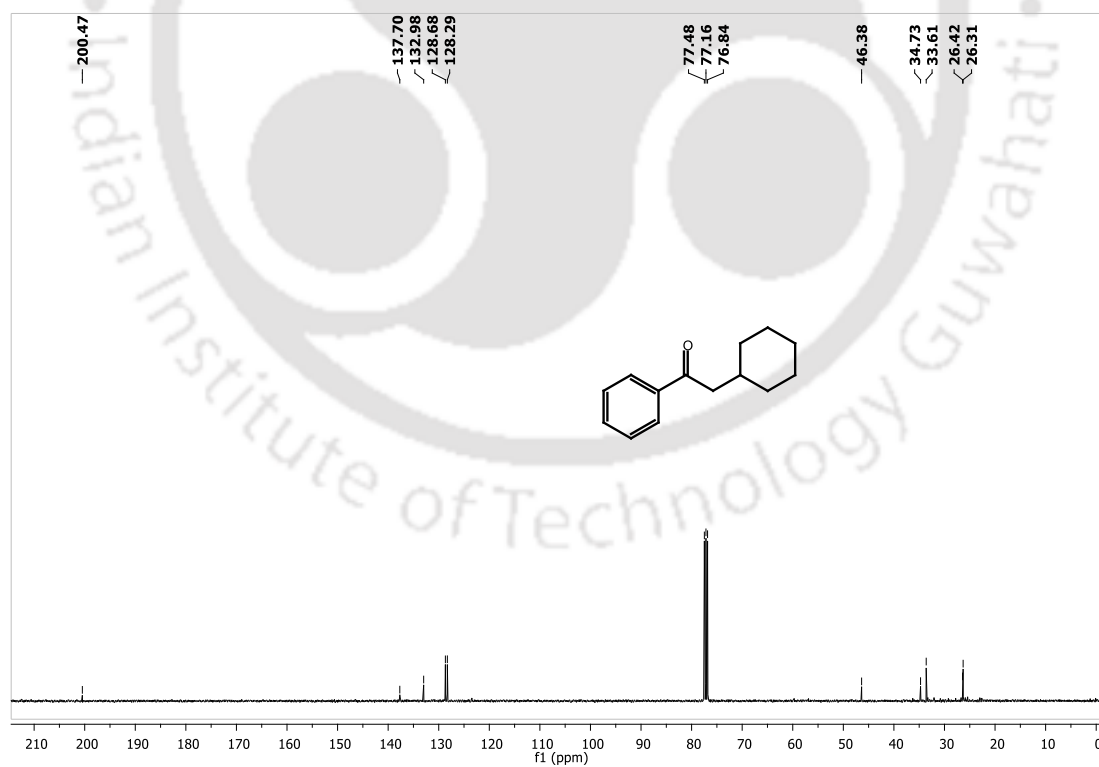


Figure S14: ¹³C NMR Spectrum of **2.6a** (CDCl₃, 101 MHz, 298 K)

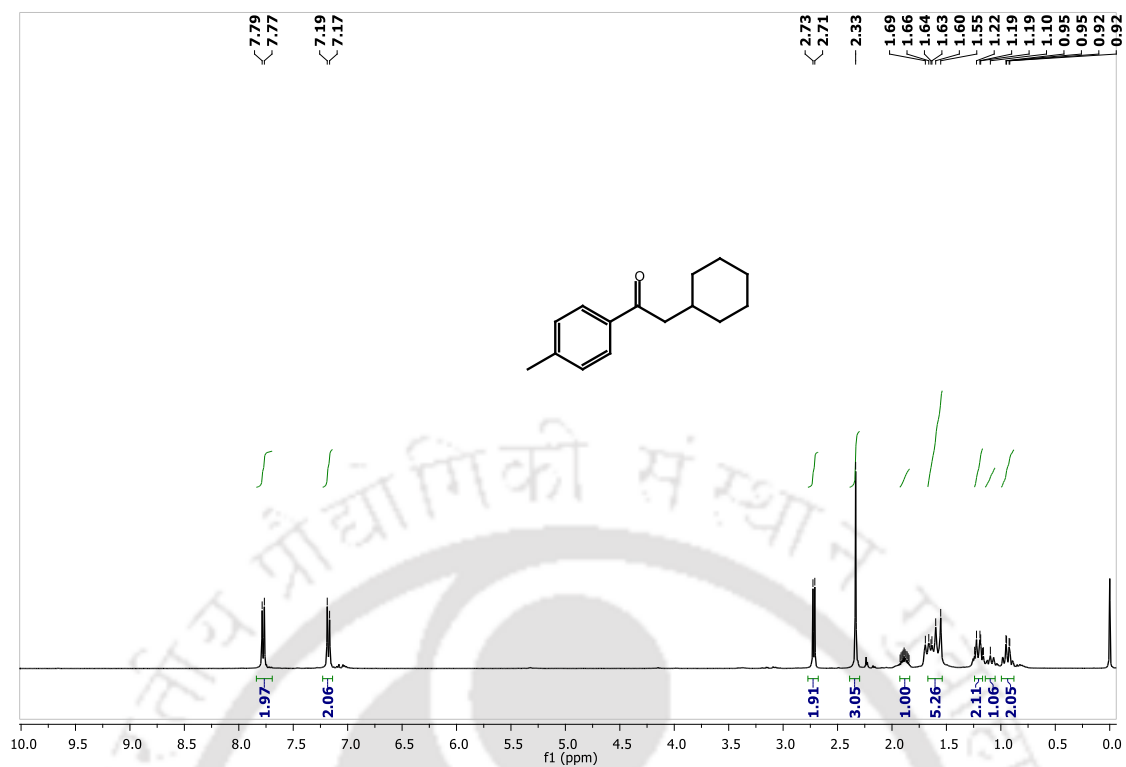


Figure S15: ¹H NMR Spectrum of **2.6b** (CDCl₃, 400 MHz, 298 K)

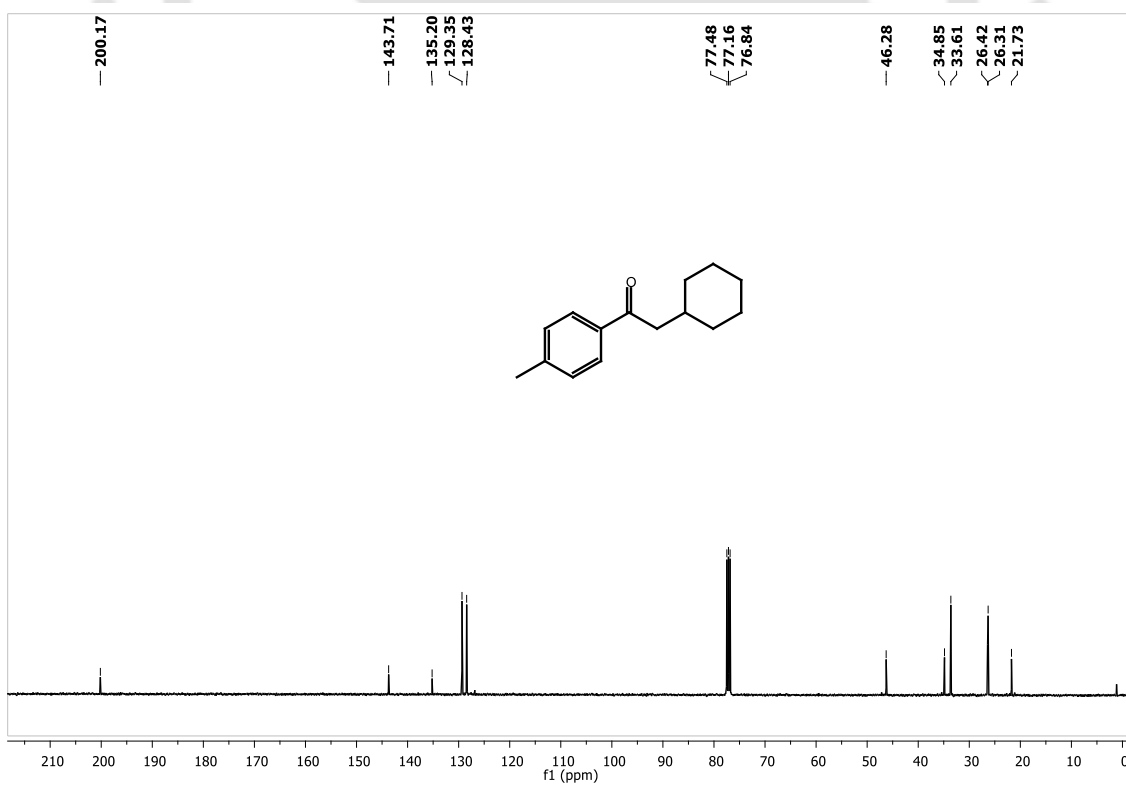


Figure S16: ¹³C NMR Spectrum of **2.6b** (CDCl₃, 101 MHz, 298 K)

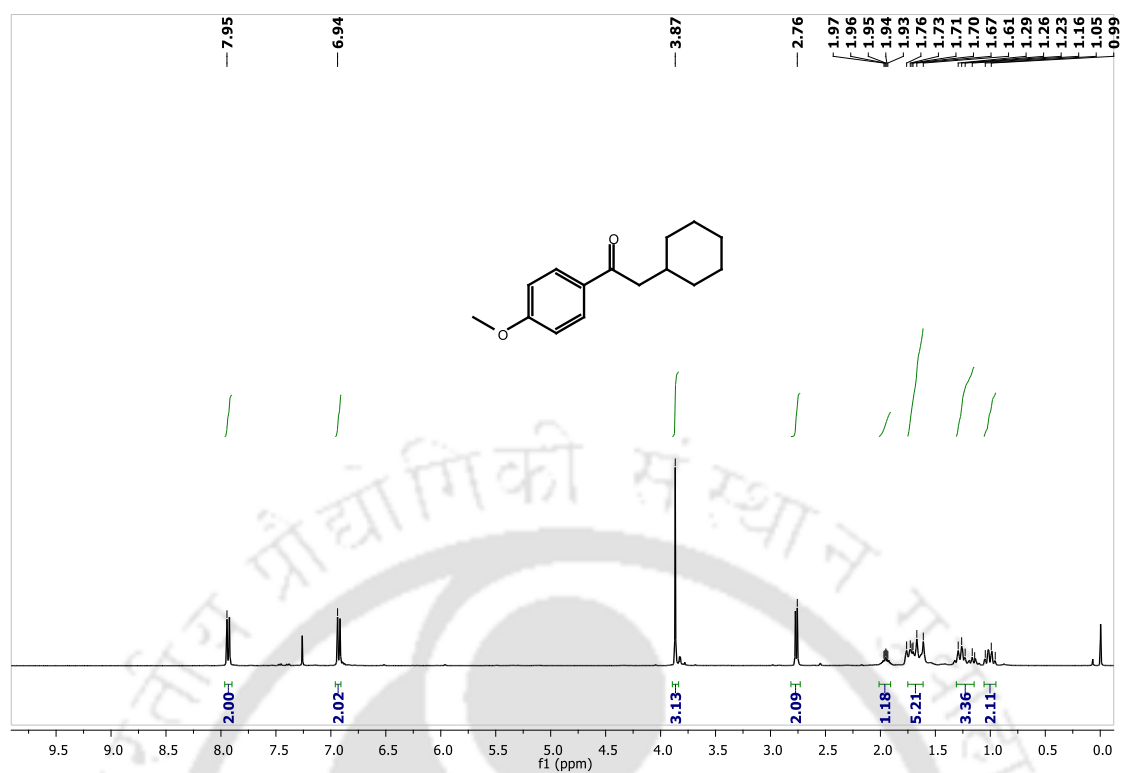


Figure S17: ¹H NMR Spectrum of 2.6c (CDCl₃, 400 MHz, 298 K)

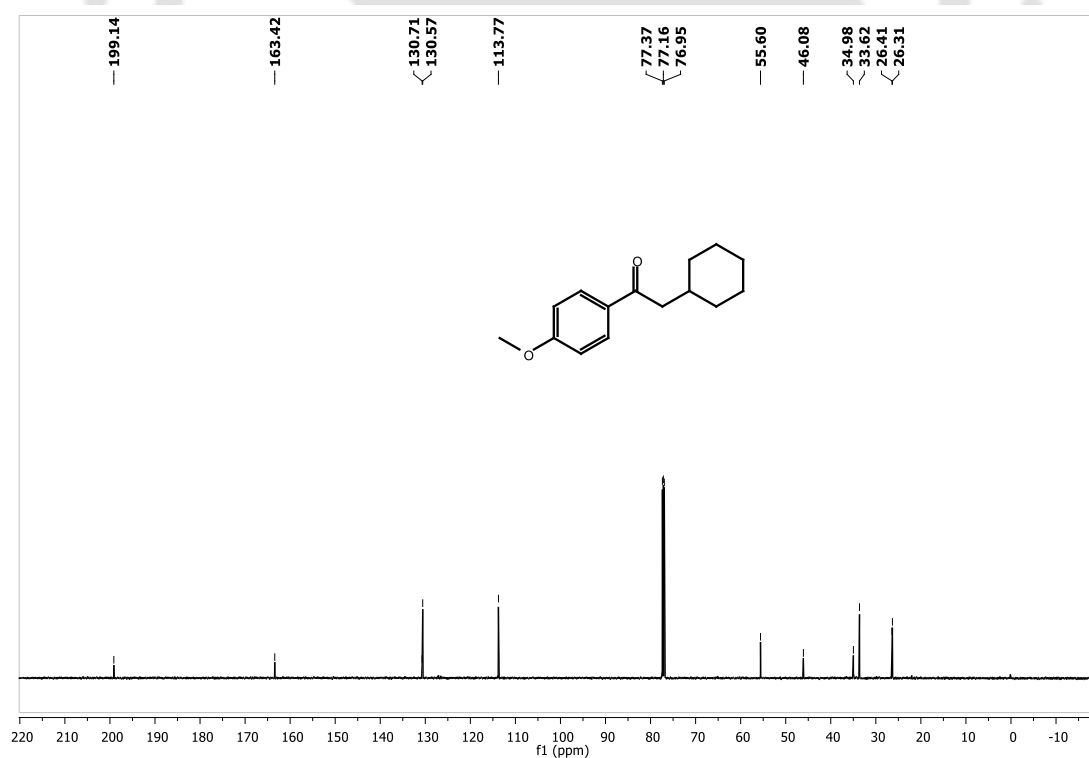


Figure S18: ¹³C NMR Spectrum of 2.6c (CDCl₃, 101 MHz, 298 K)

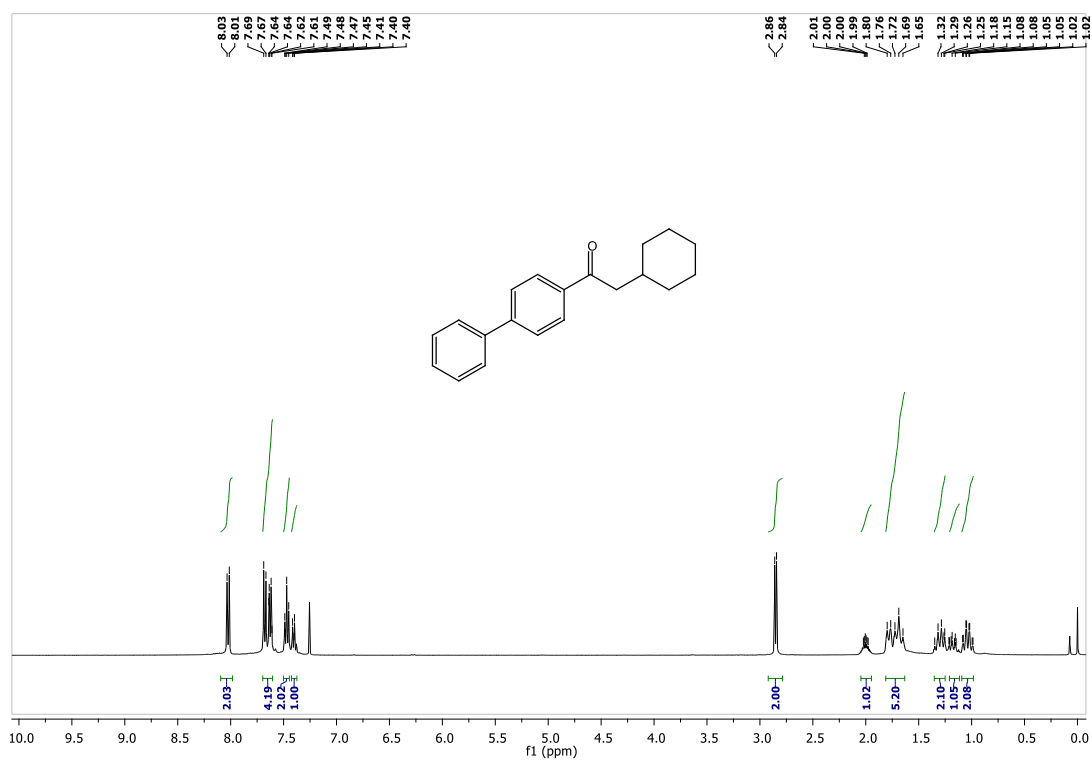


Figure S19: ^1H NMR Spectrum of **2.6d** (CDCl_3 , 400 MHz, 298 K)

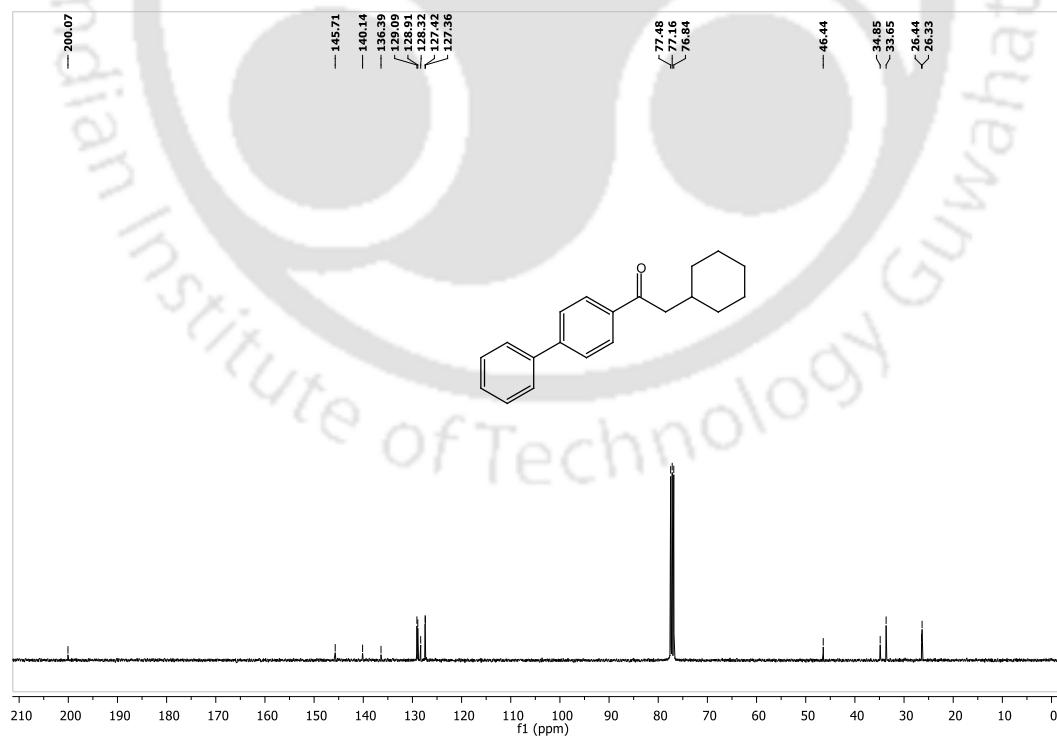


Figure S20: ^{13}C NMR Spectrum of **2.6d** (CDCl_3 , 101 MHz, 298 K)

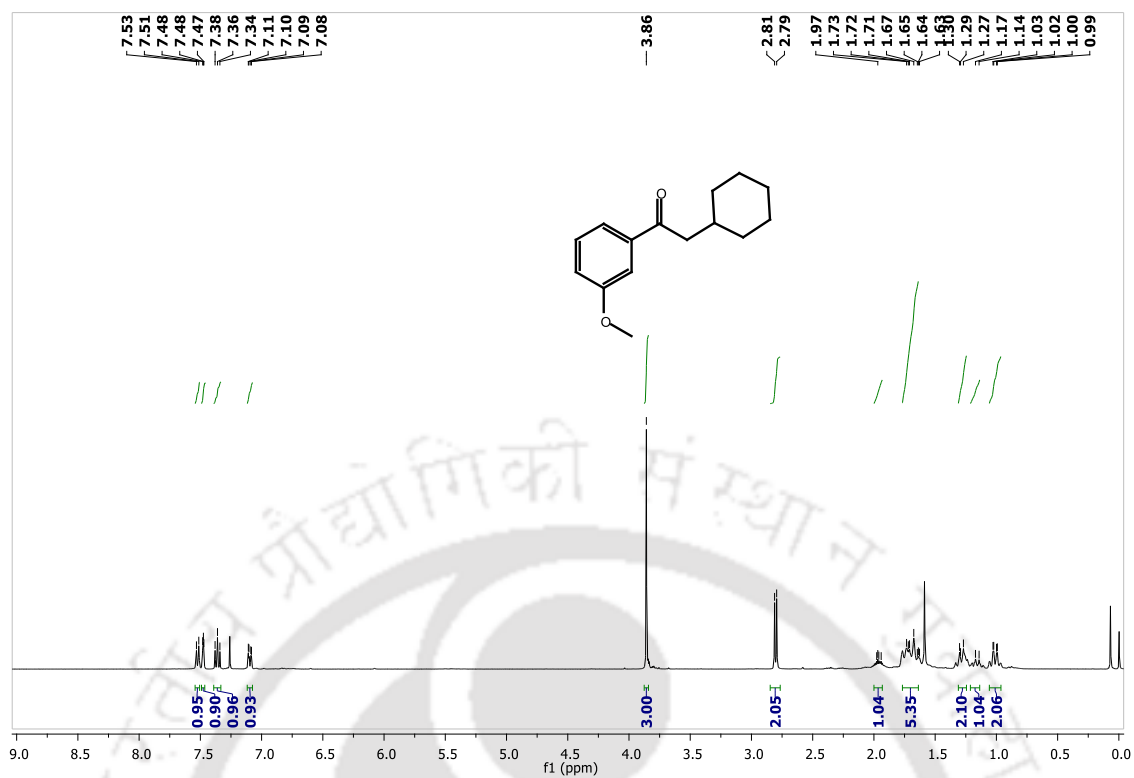


Figure S21: ^1H NMR Spectrum of 2.6e (CDCl₃, 400 MHz, 298 K)

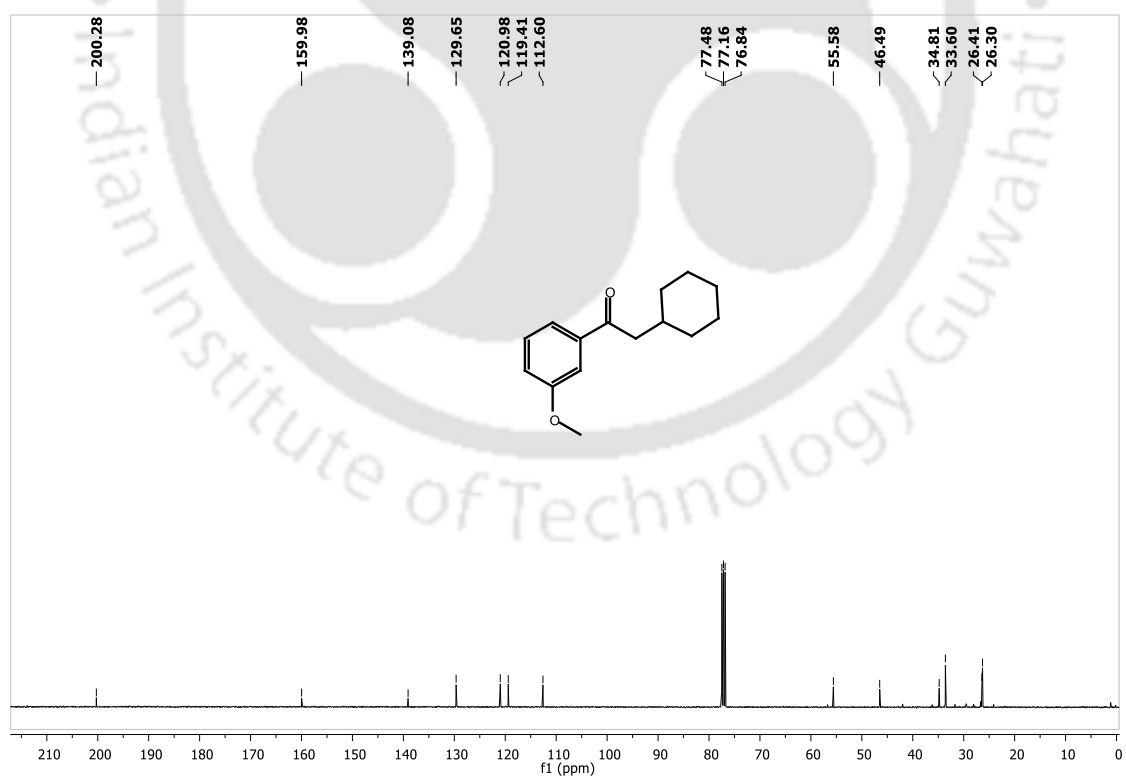


Figure S22: ^{13}C NMR Spectrum of 2.6e (CDCl₃, 101 MHz, 298 K)

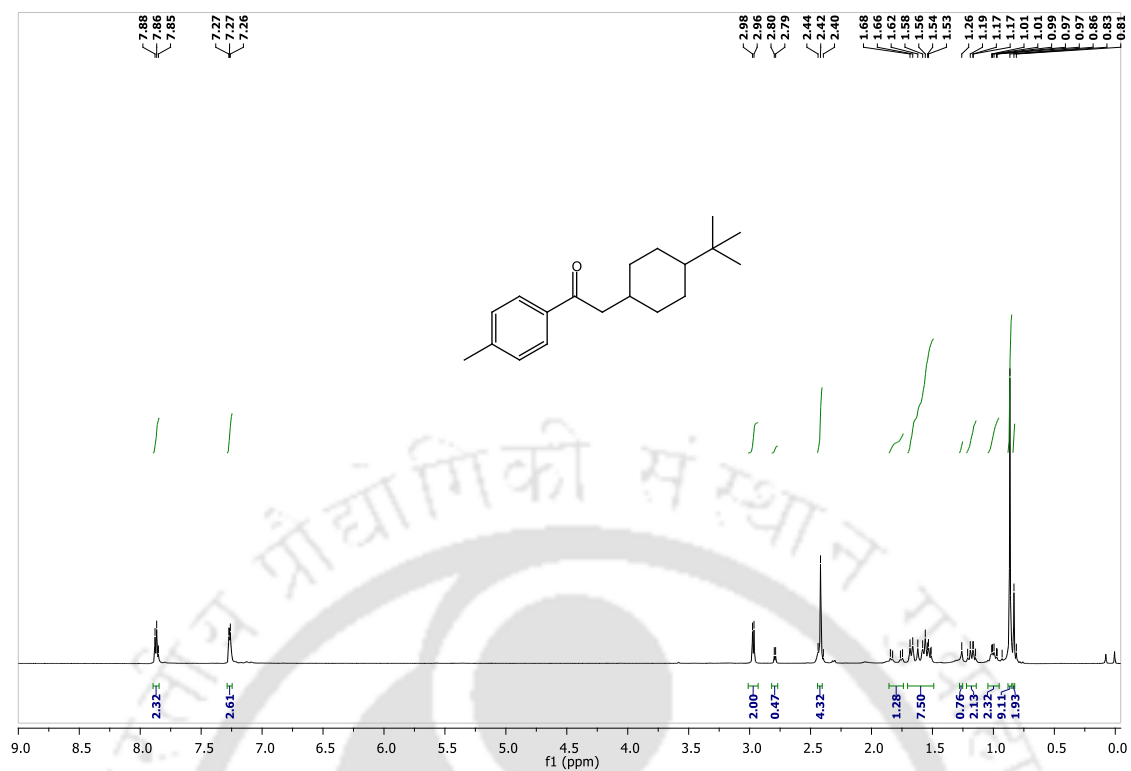


Figure S23: ¹H NMR Spectrum of **2.6f** (CDCl₃, 600 MHz, 298 K)

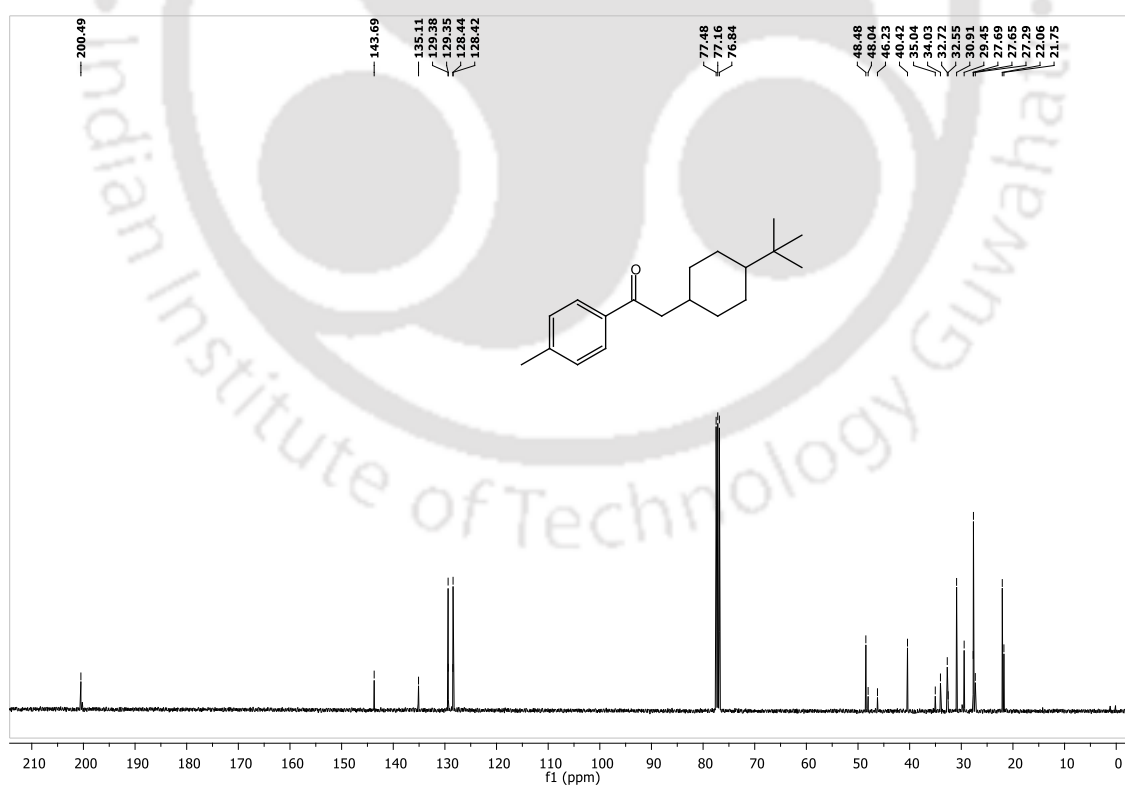


Figure S24: ¹³C NMR Spectrum of **2.6f** (CDCl₃, 101 MHz, 298 K)

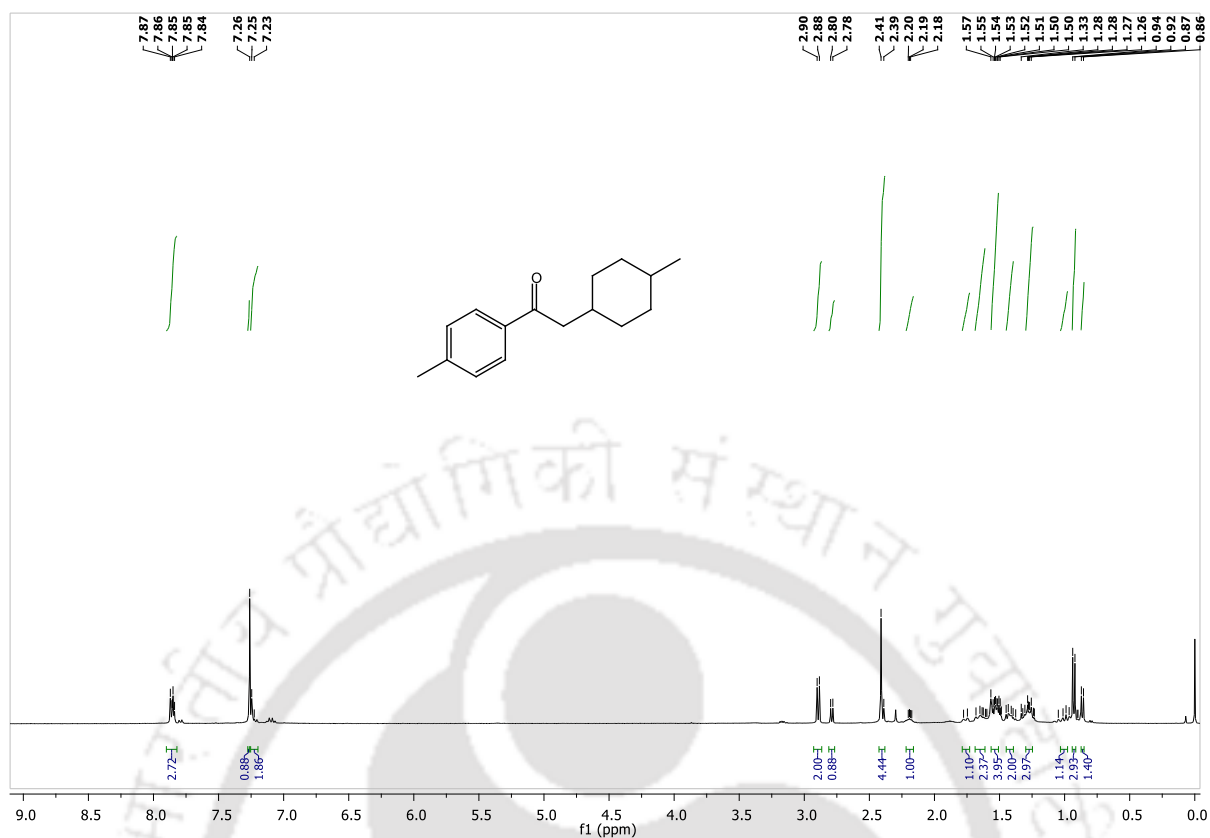


Figure S25: ¹H NMR Spectrum of **2.6g** (CDCl₃, 600 MHz, 298 K)

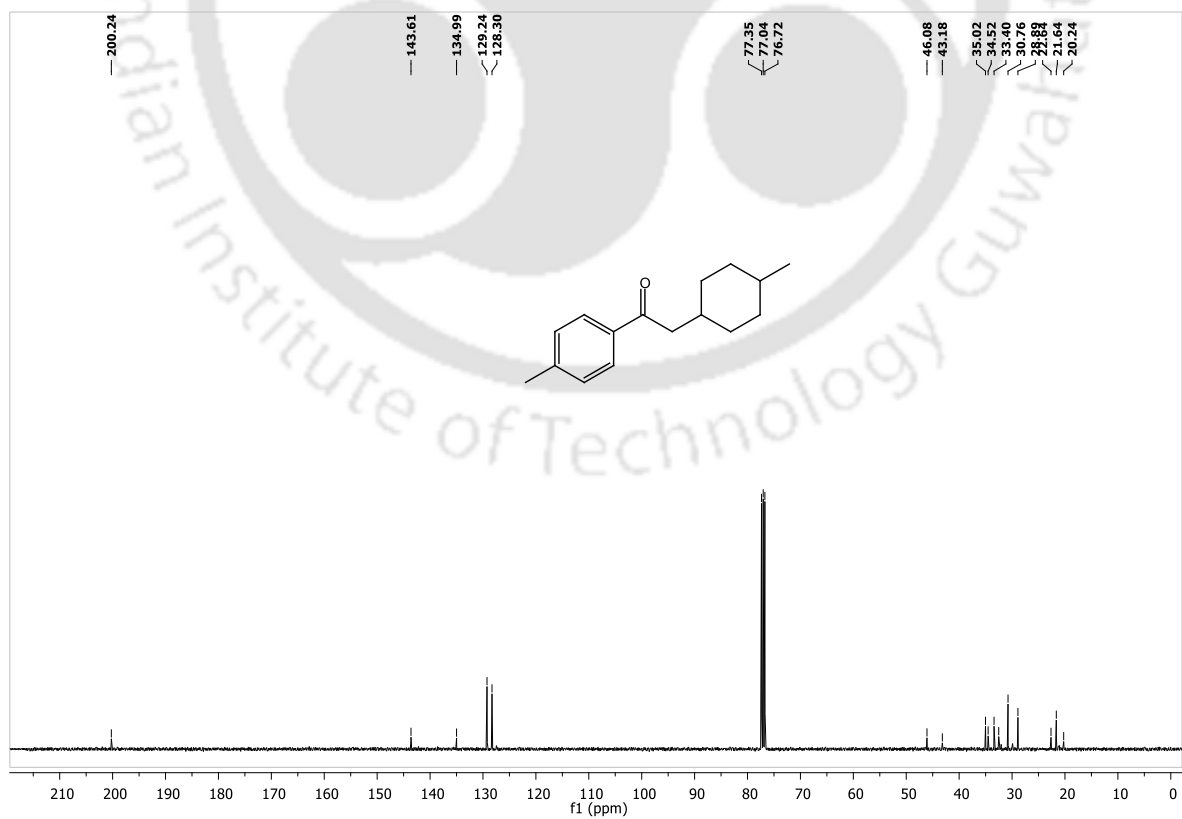


Figure S26: ¹³C NMR Spectrum of **2.6g** (CDCl₃, 101 MHz, 298 K)

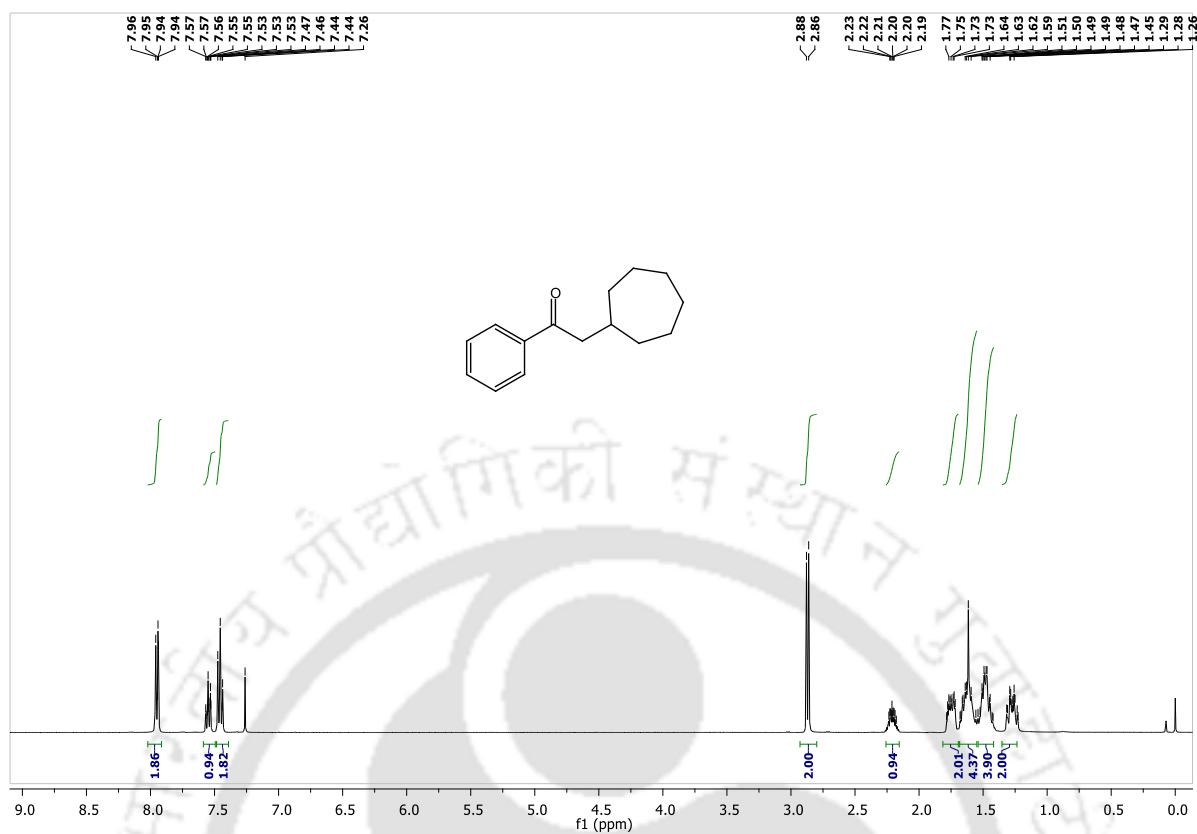


Figure S27: ^1H NMR Spectrum of **2.6h** (CDCl_3 , 600 MHz, 298 K)

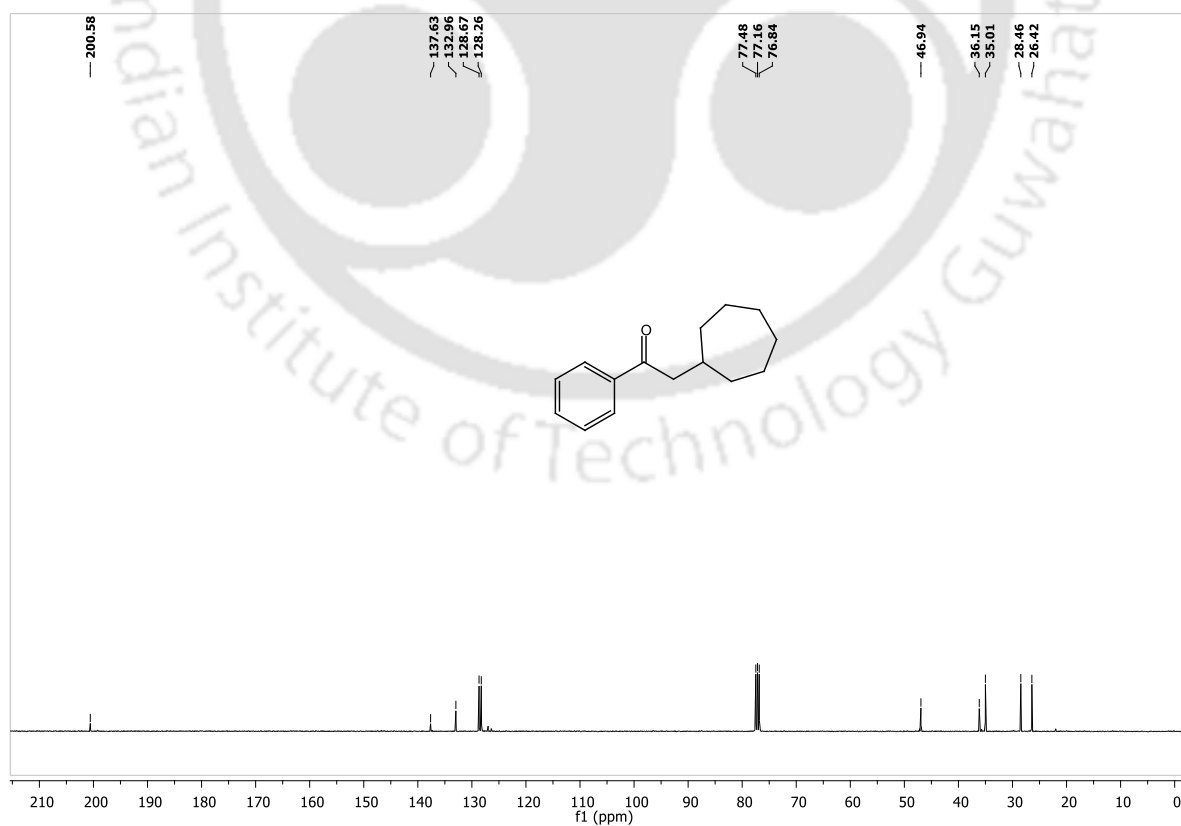


Figure S28: ^{13}C NMR Spectrum of **2.6h** (CDCl_3 , 101 MHz, 298 K)

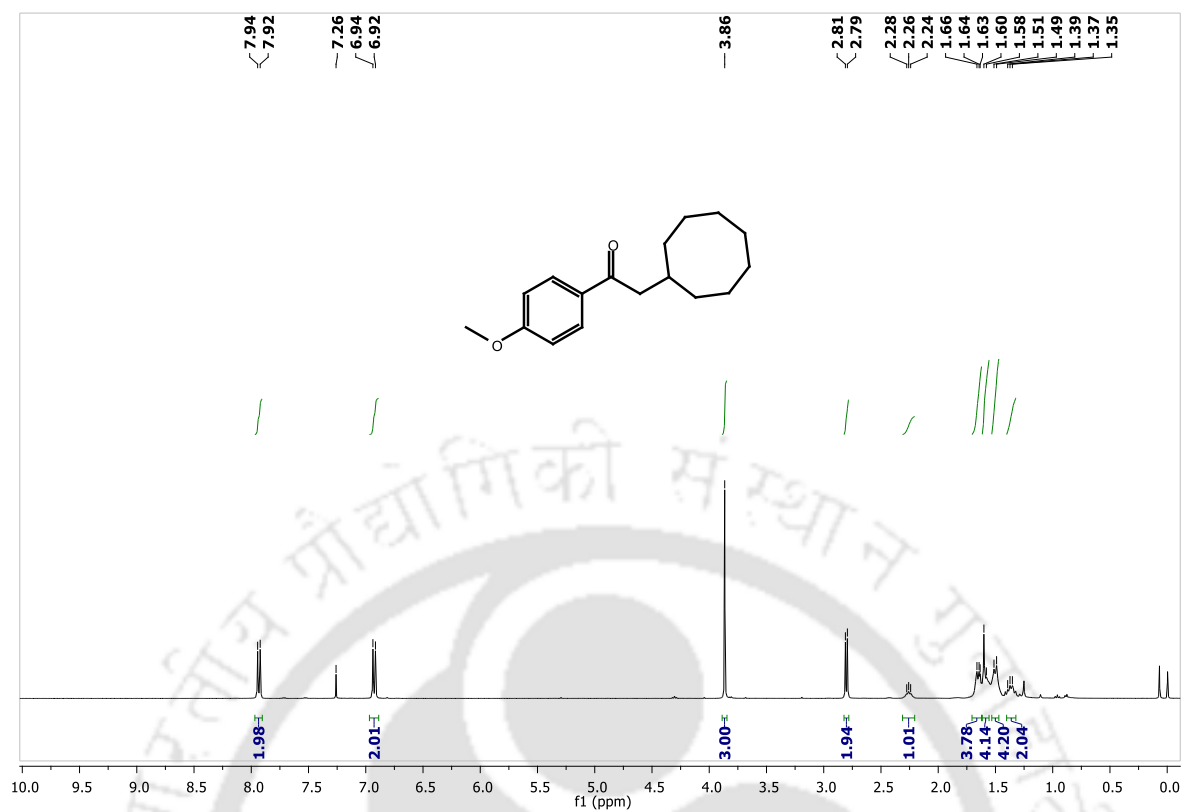


Figure S29: ¹H NMR Spectrum of **2.6i** (CDCl₃, 400 MHz, 298 K)

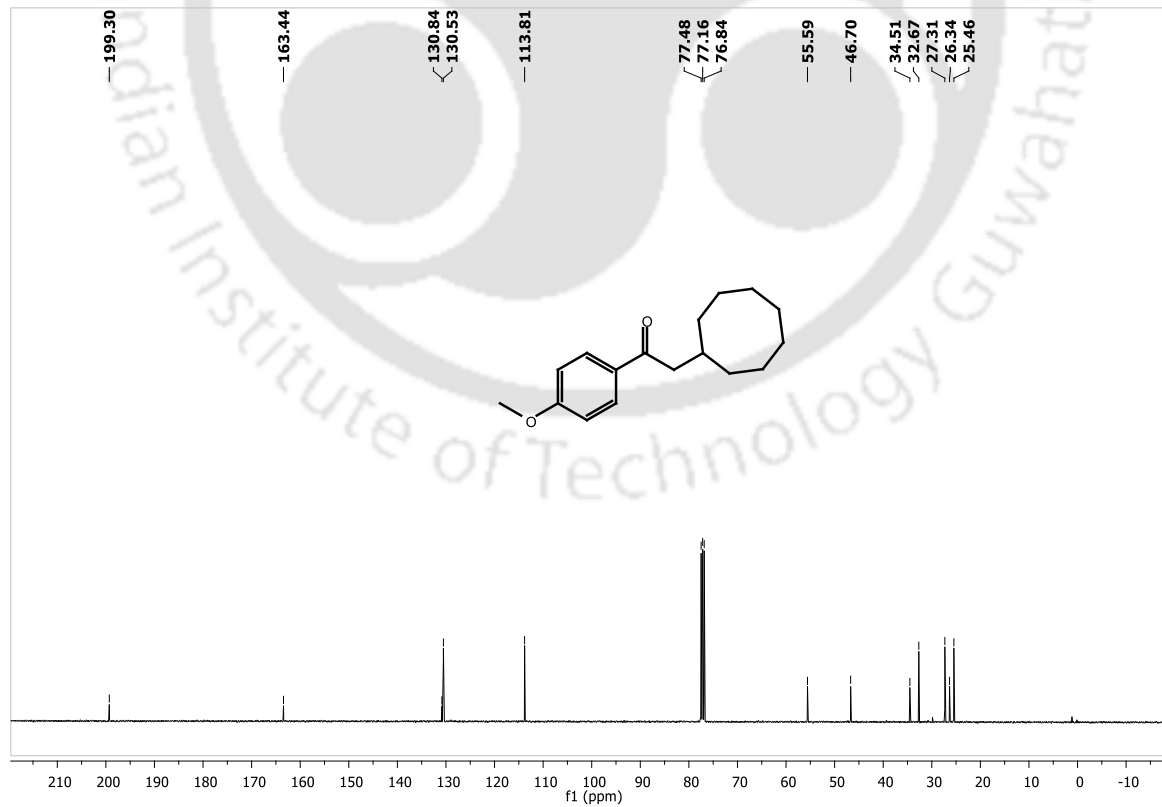


Figure S30: ¹³C NMR Spectrum of **2.6i** (CDCl₃, 101 MHz, 298 K)

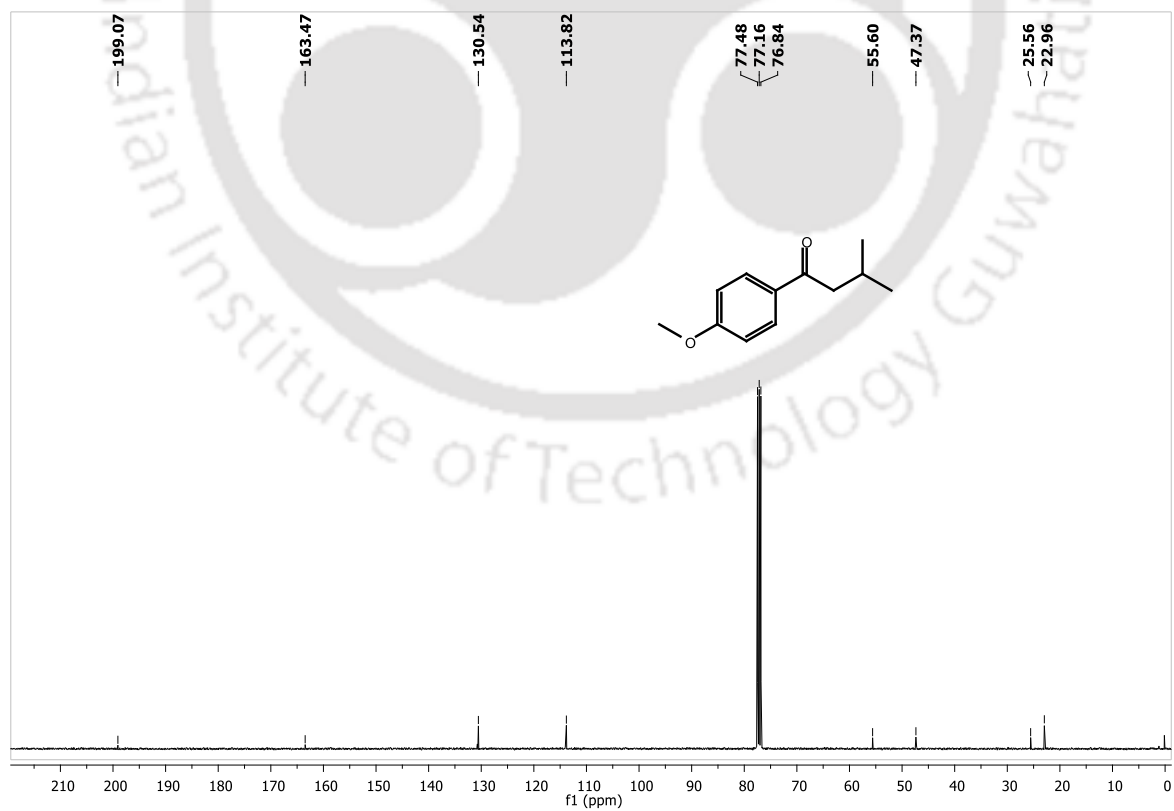
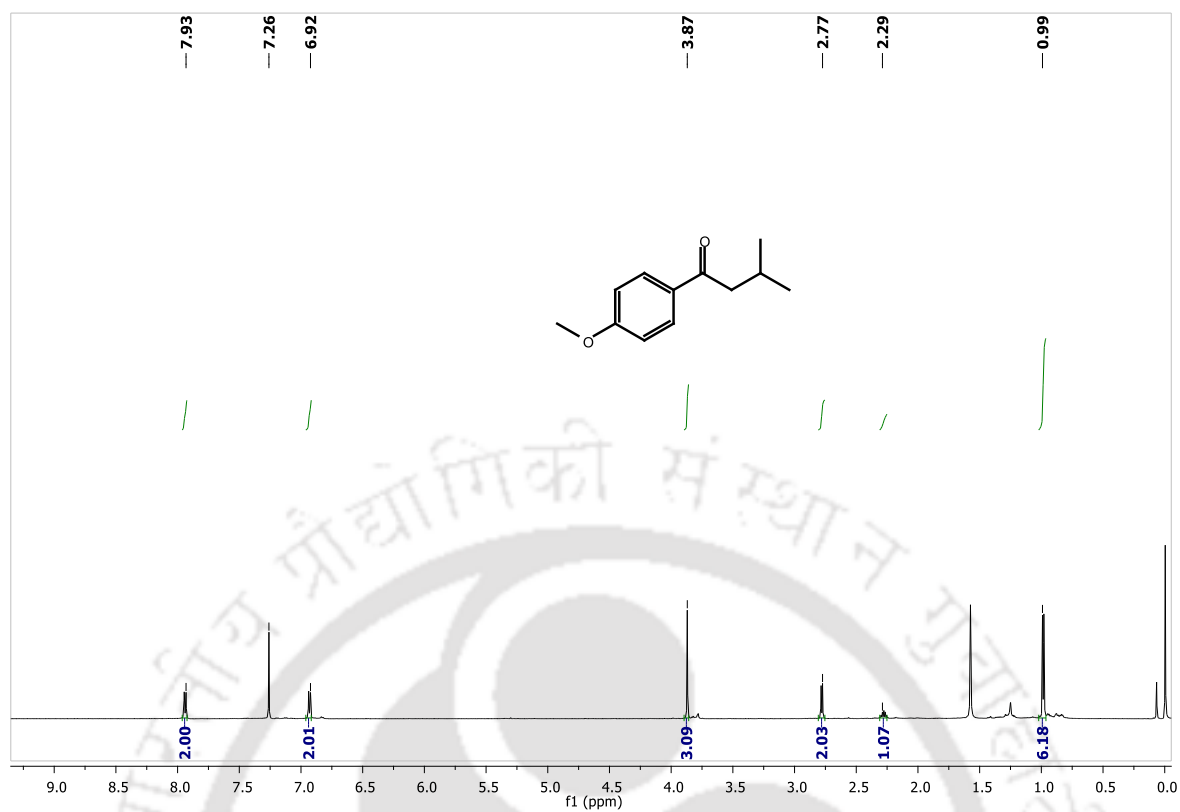


Figure S32: ^{13}C NMR Spectrum of 2.6j (CDCl_3 , 101 MHz, 298 K)

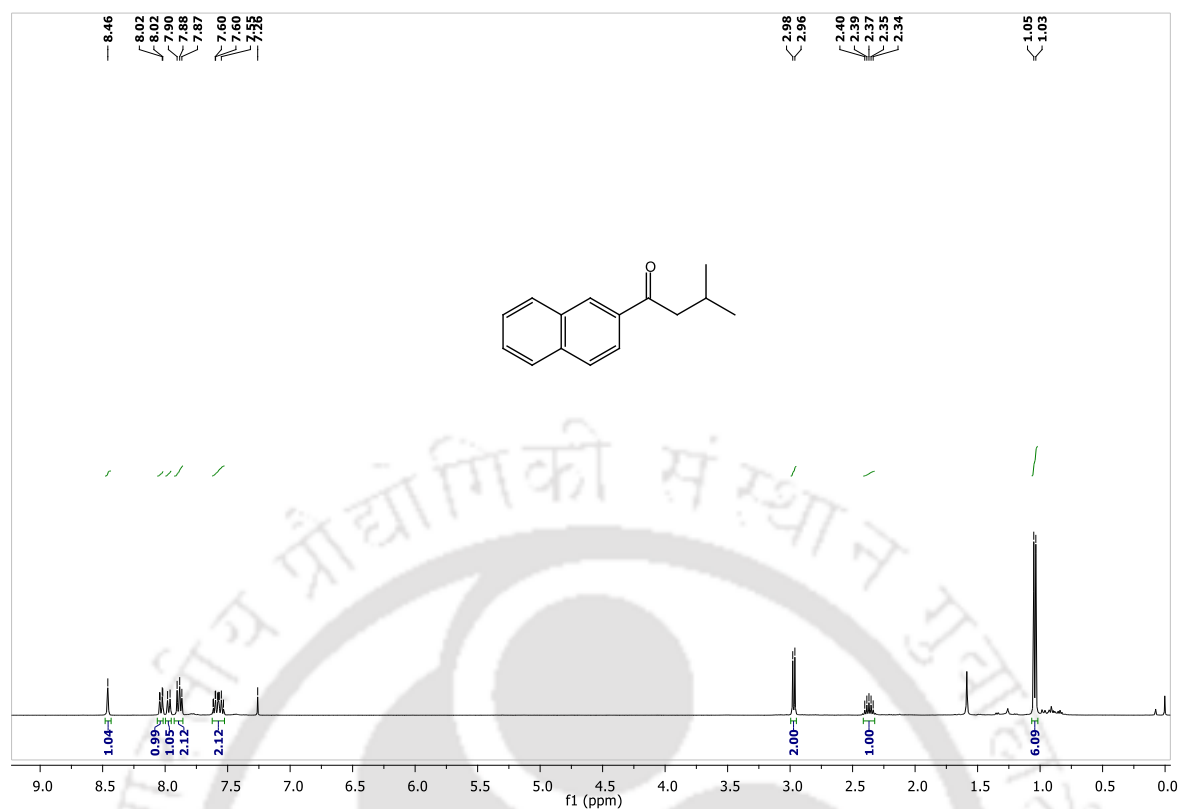


Figure S33: ¹H NMR Spectrum of **2.6k** (CDCl₃, 400 MHz, 298 K)

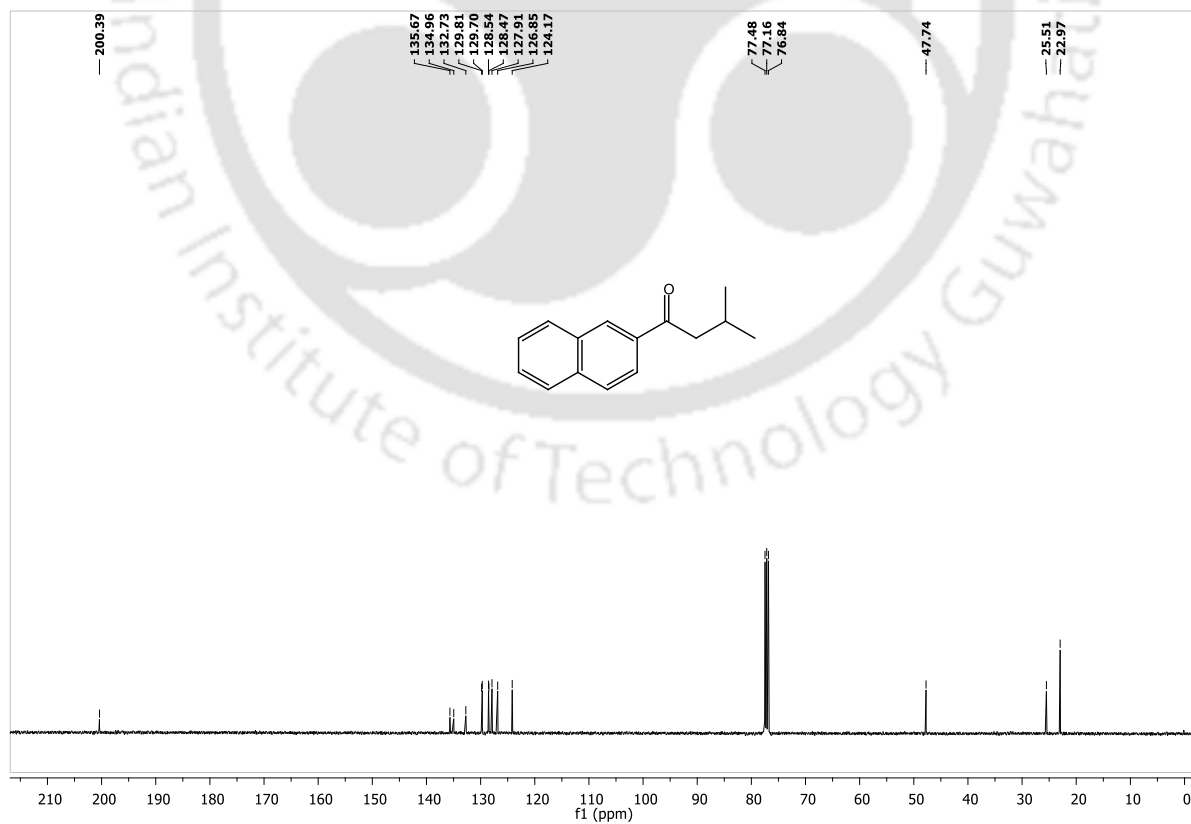


Figure S34: ¹³C NMR Spectrum of **2.6k** (CDCl₃, 101 MHz, 298 K)

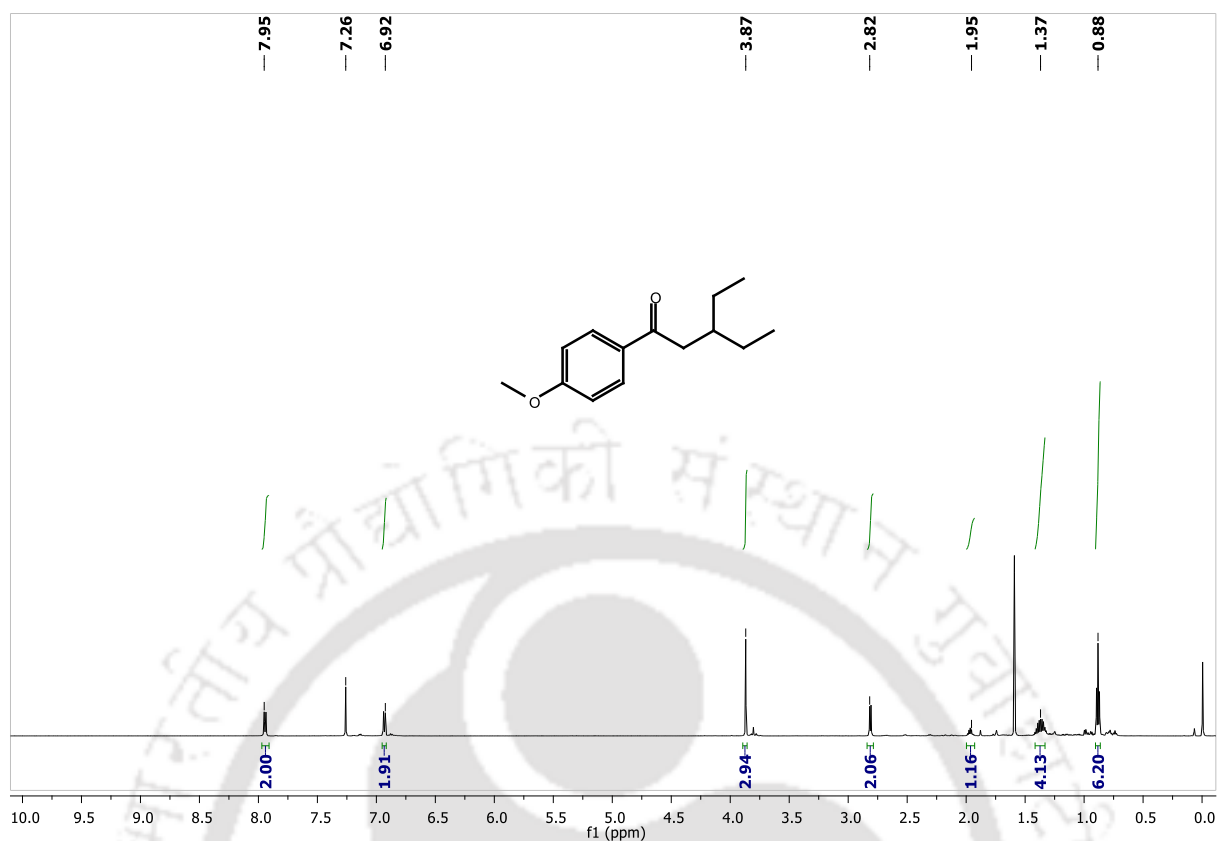


Figure S35: ^1H NMR Spectrum of **2.6l** (CDCl_3 , 400 MHz, 298 K)

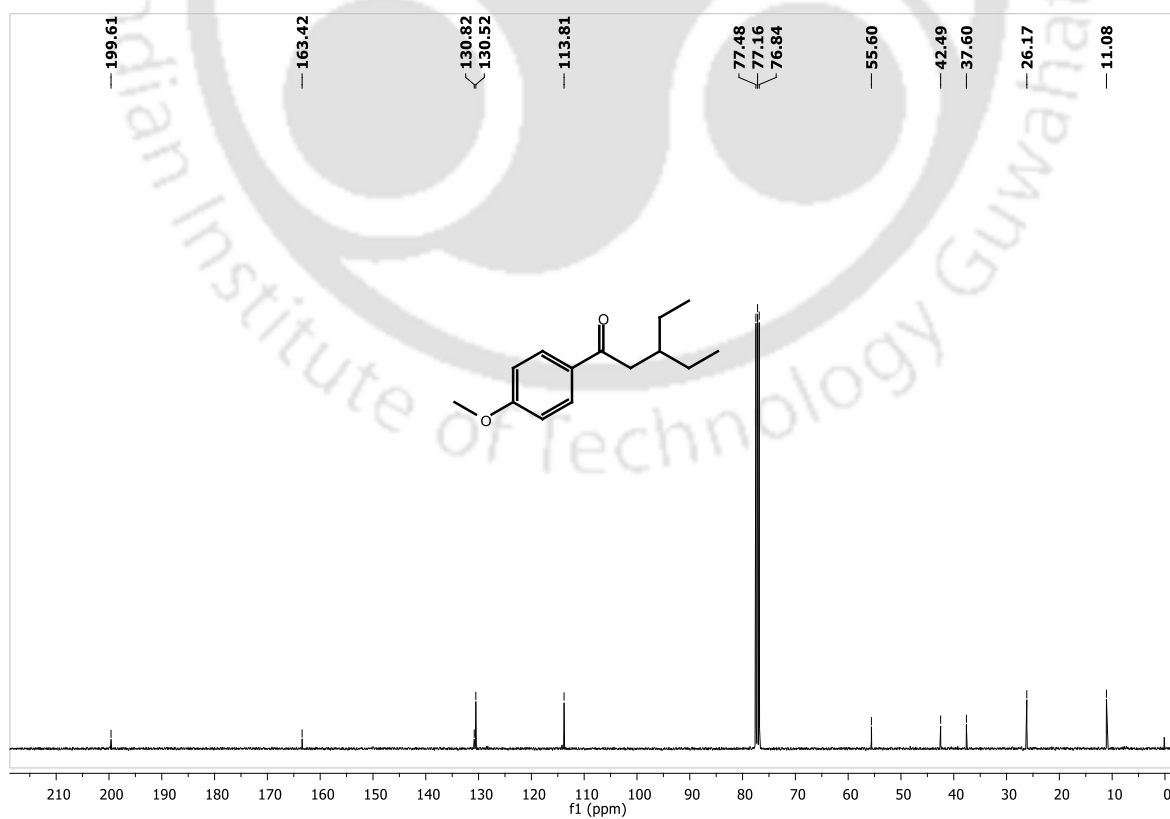


Figure S36: ^{13}C NMR Spectrum of **2.6l** (CDCl_3 , 101 MHz, 298 K)

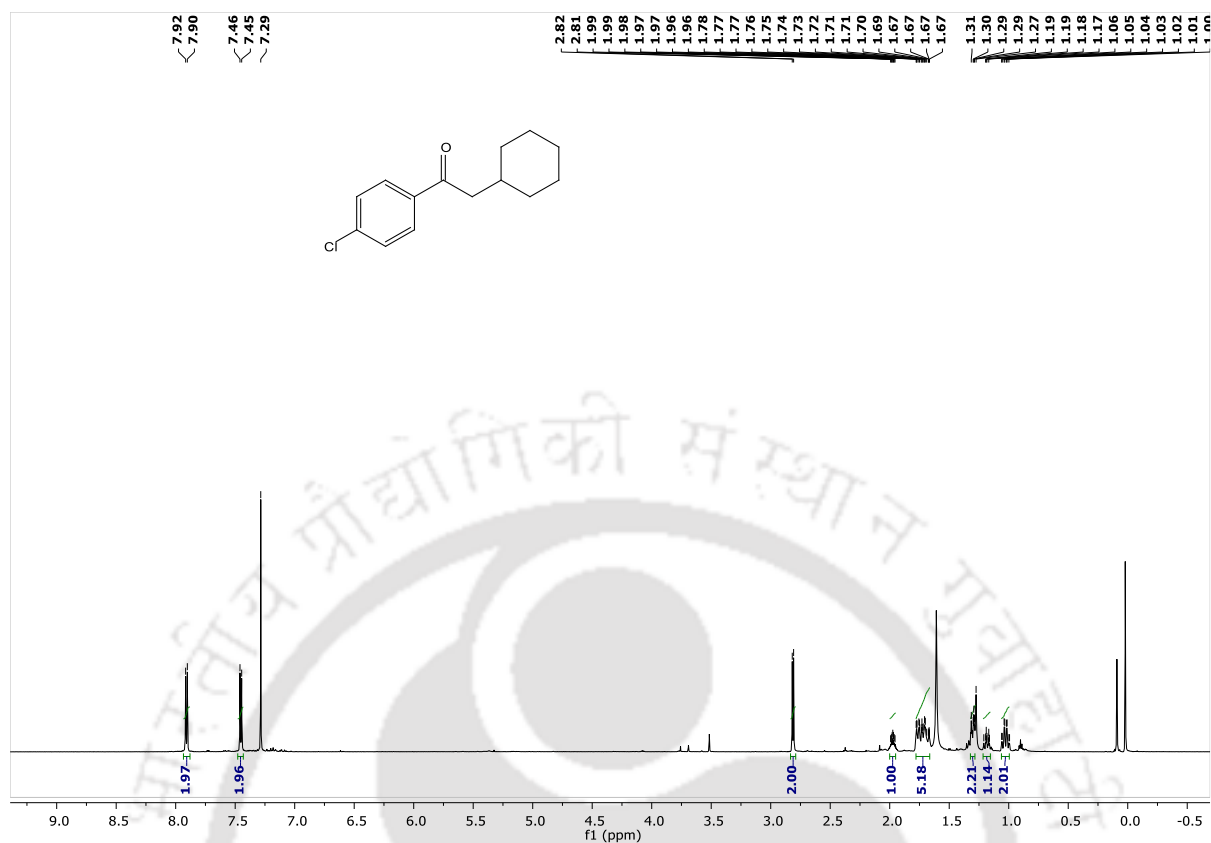


Figure S37: ¹H NMR Spectrum of **2.6m** (CDCl₃, 400 MHz, 298 K)

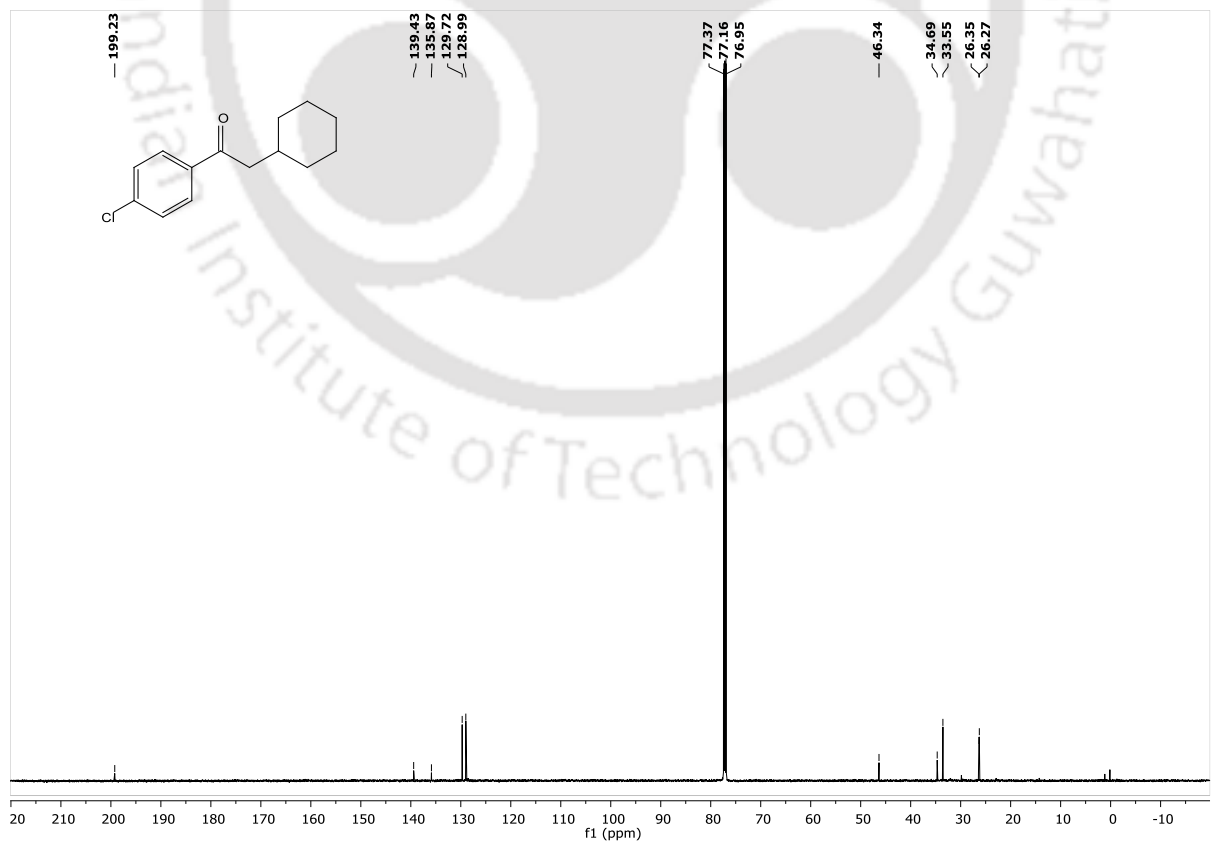


Figure S38: ¹³C NMR Spectrum of **2.6m** (CDCl₃, 101 MHz, 298 K)

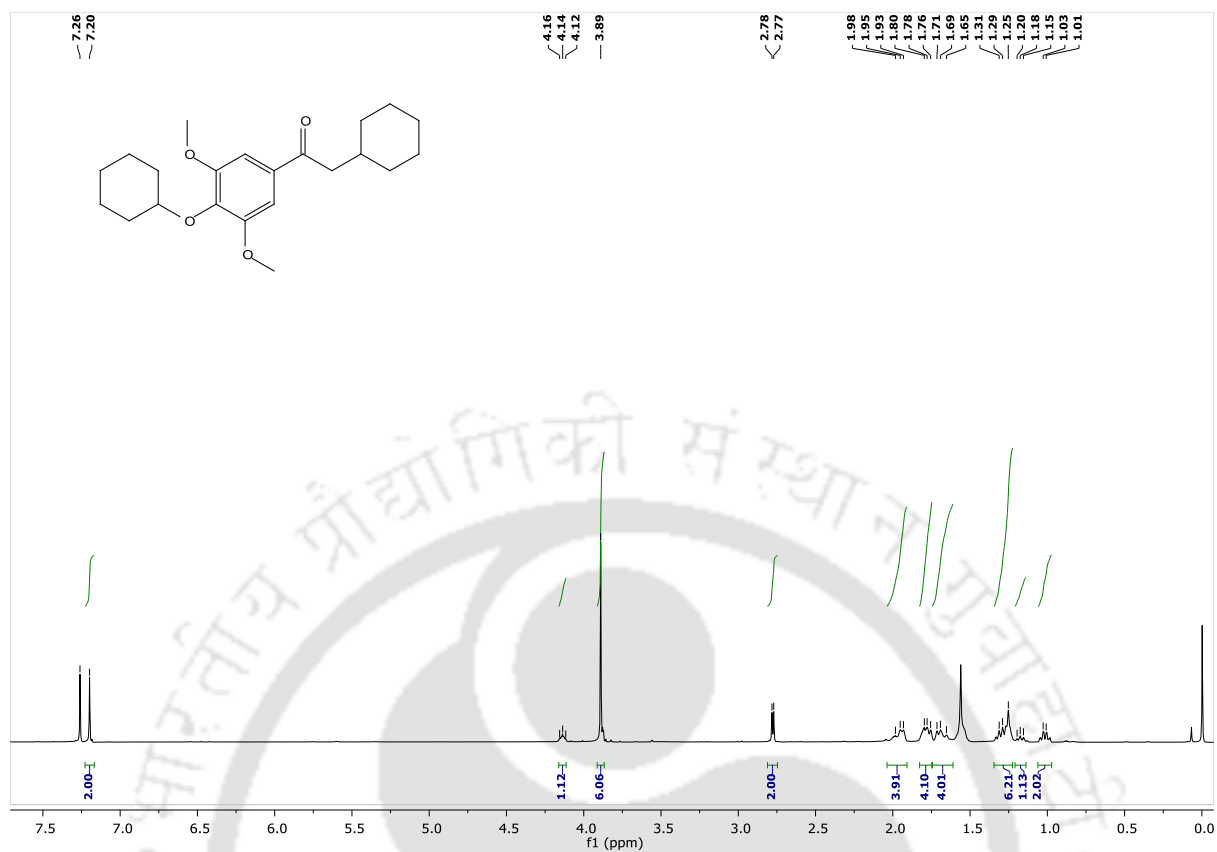


Figure S39: ¹H NMR Spectrum of **2.6n** (CDCl₃, 600 MHz, 298 K)

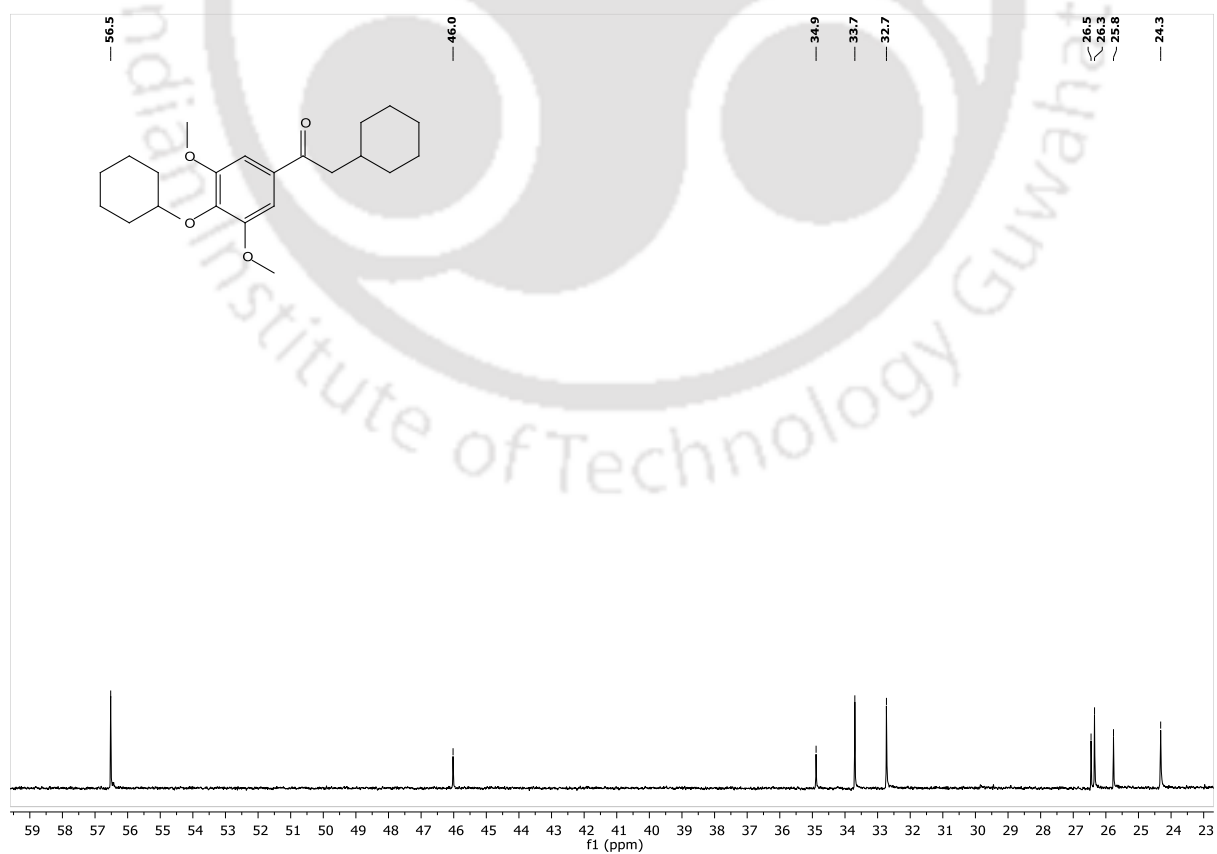


Figure S40: ¹³C NMR Spectrum of **2.6n** (CDCl₃, 151 MHz, 298 K)

Annexure II

^1H , ^{13}C , and ^{19}F NMR spectra of the products (Chapter 3)

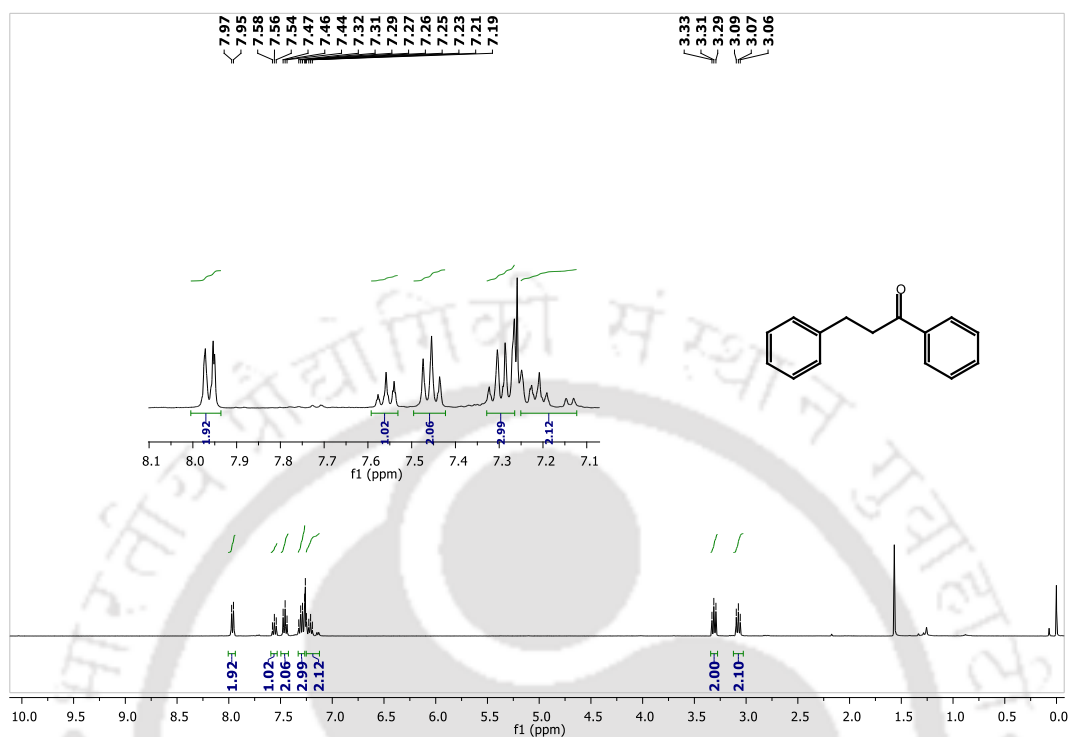


Figure S41: ^1H NMR Spectrum of 3.3a (CDCl₃, 400 MHz, 298 K)

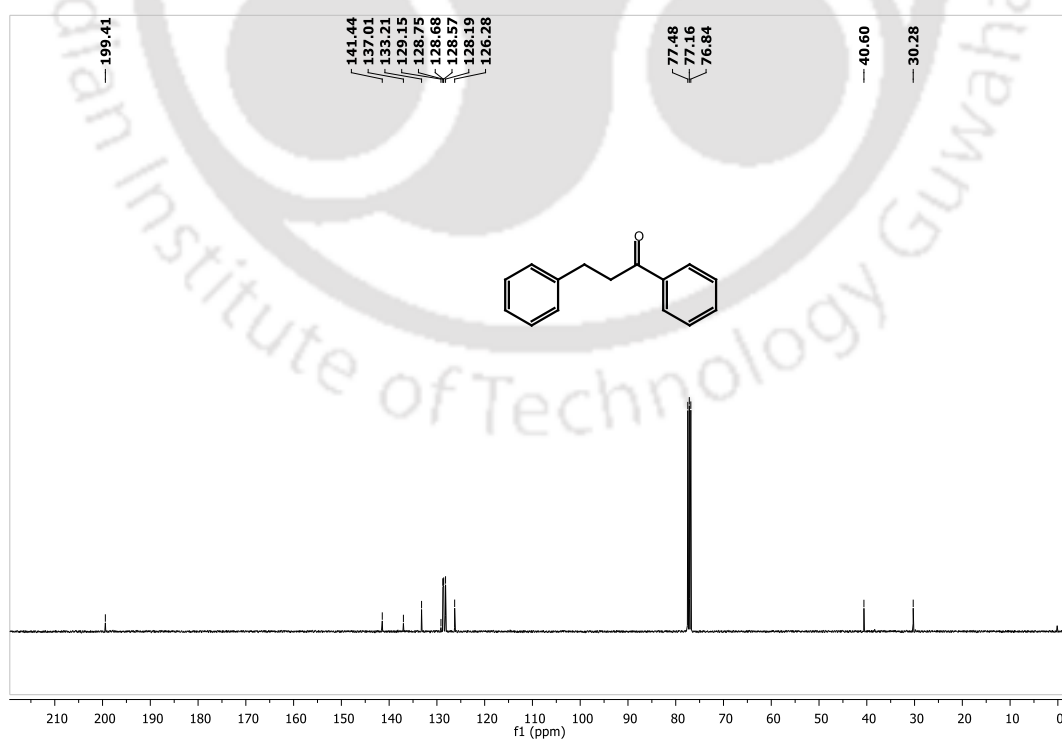


Figure S42: ^{13}C NMR Spectrum of 3.3a (CDCl₃, 101 MHz, 298 K)

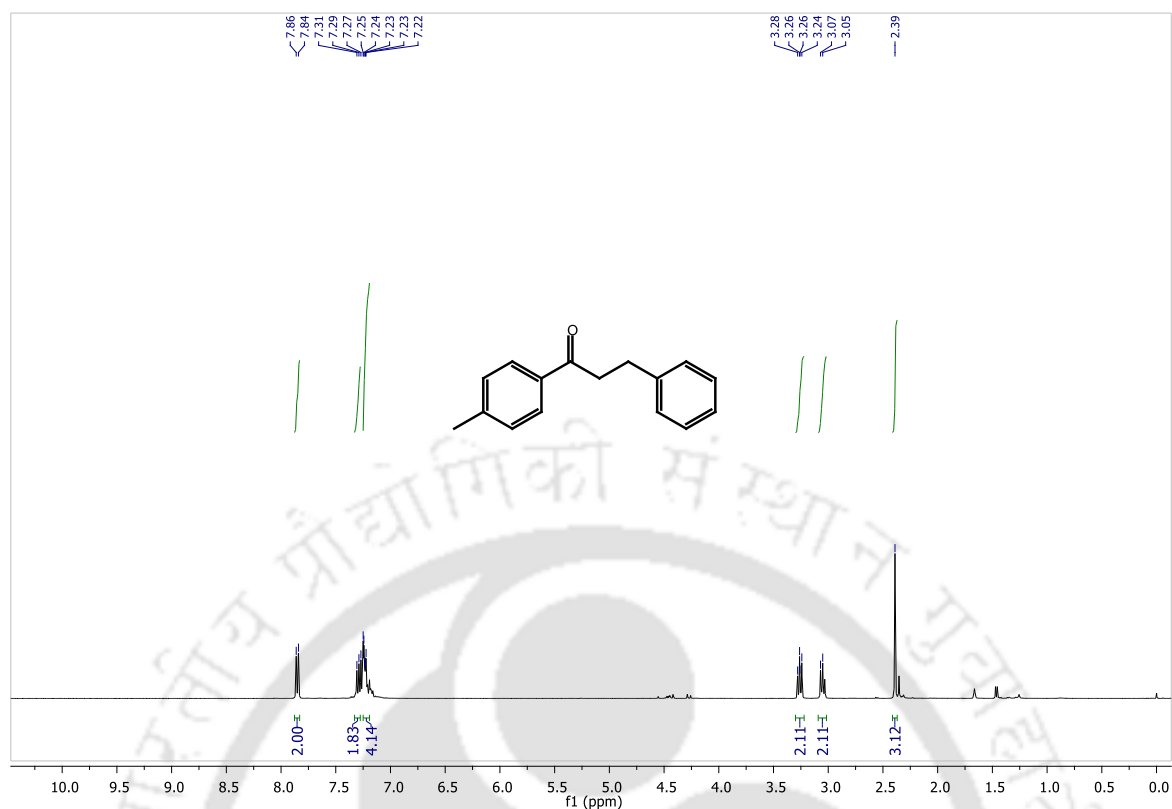


Figure S43: ¹H NMR Spectrum of **3.3b** (CDCl₃, 400 MHz, 298 K)

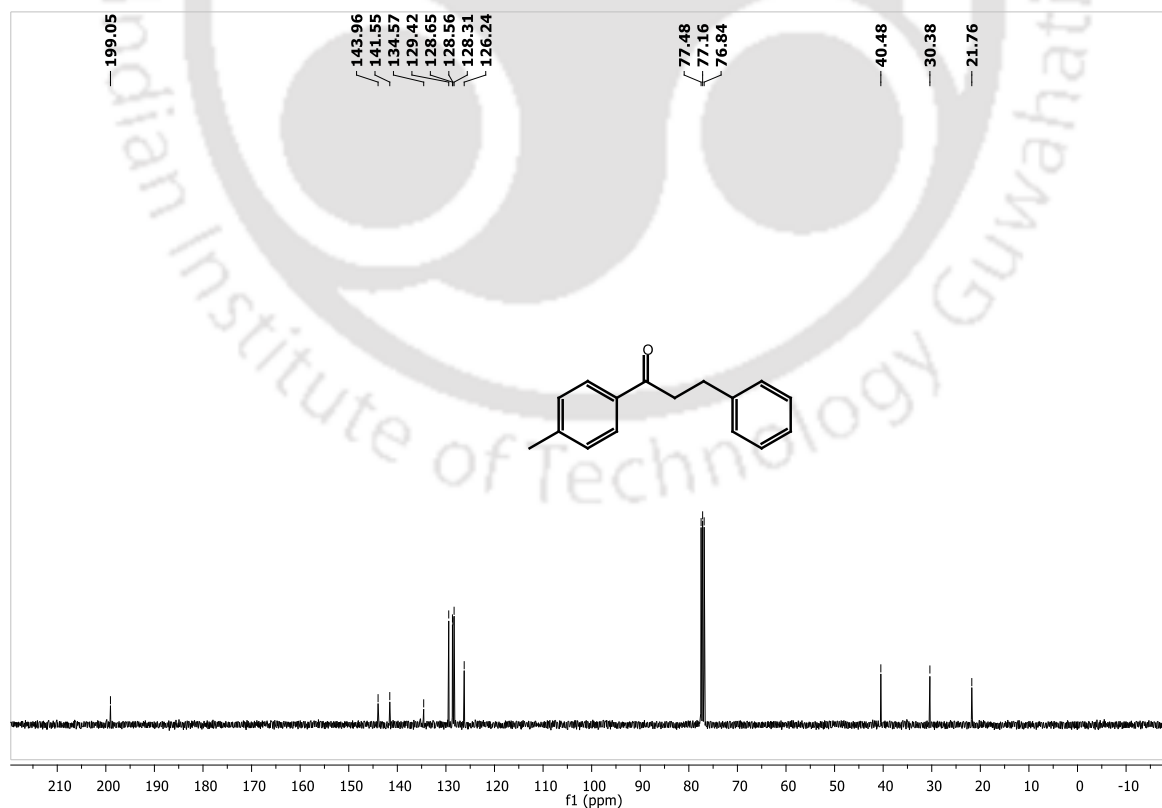
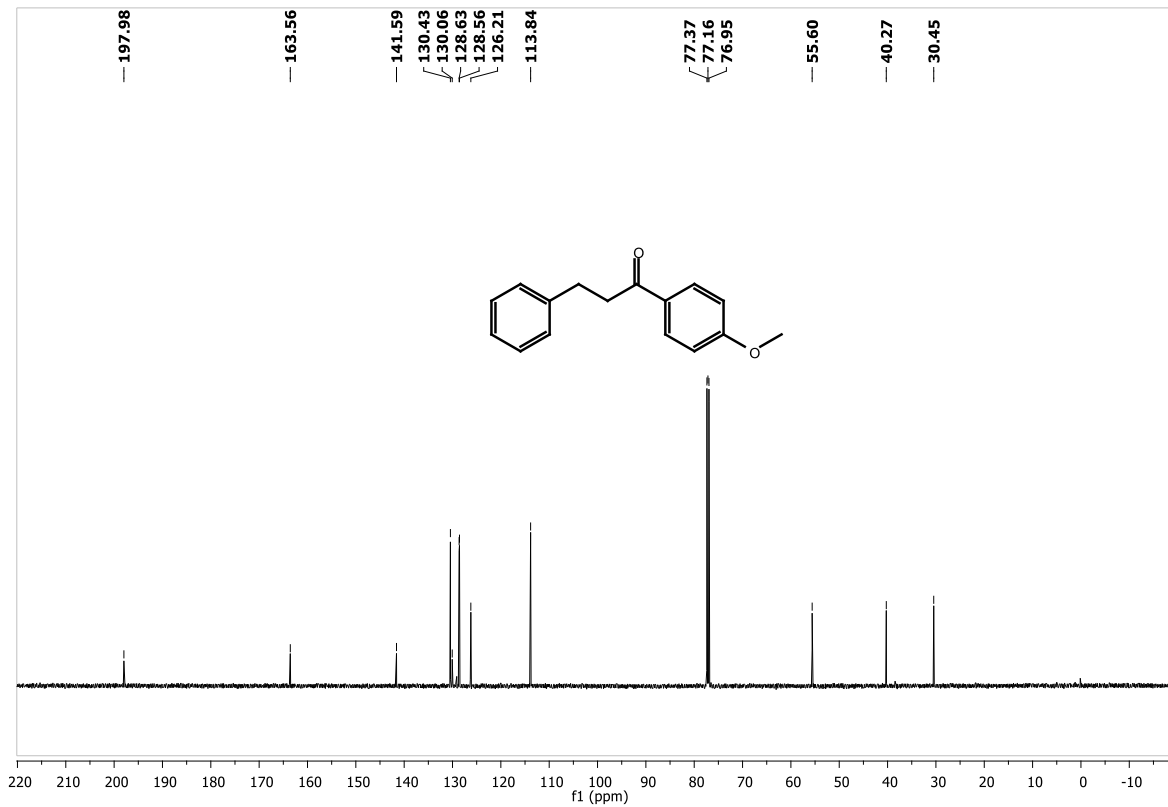
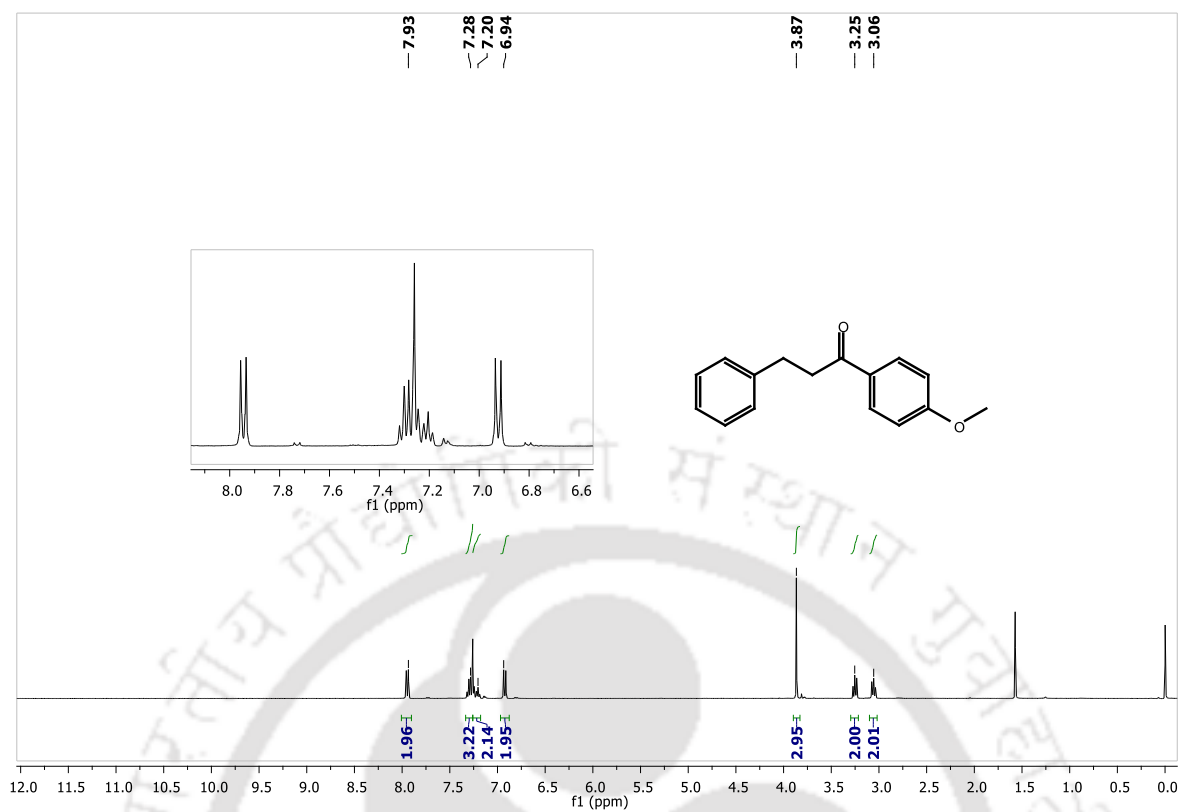
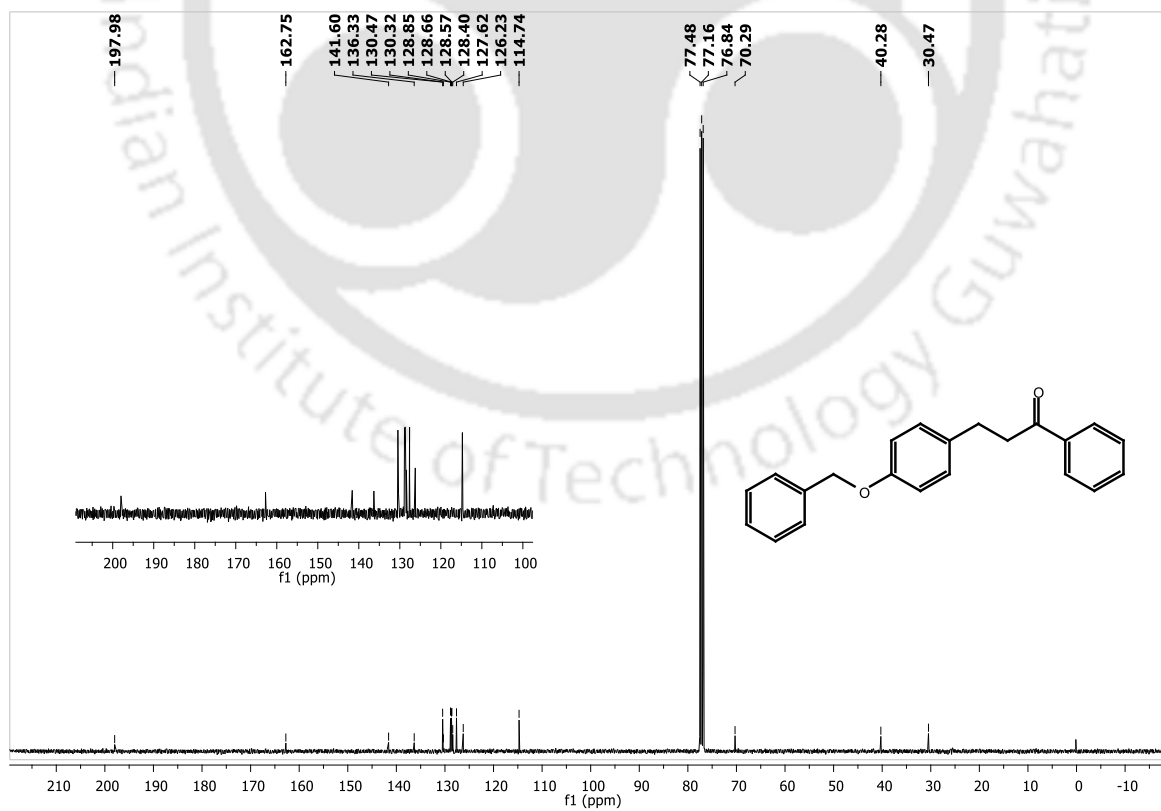
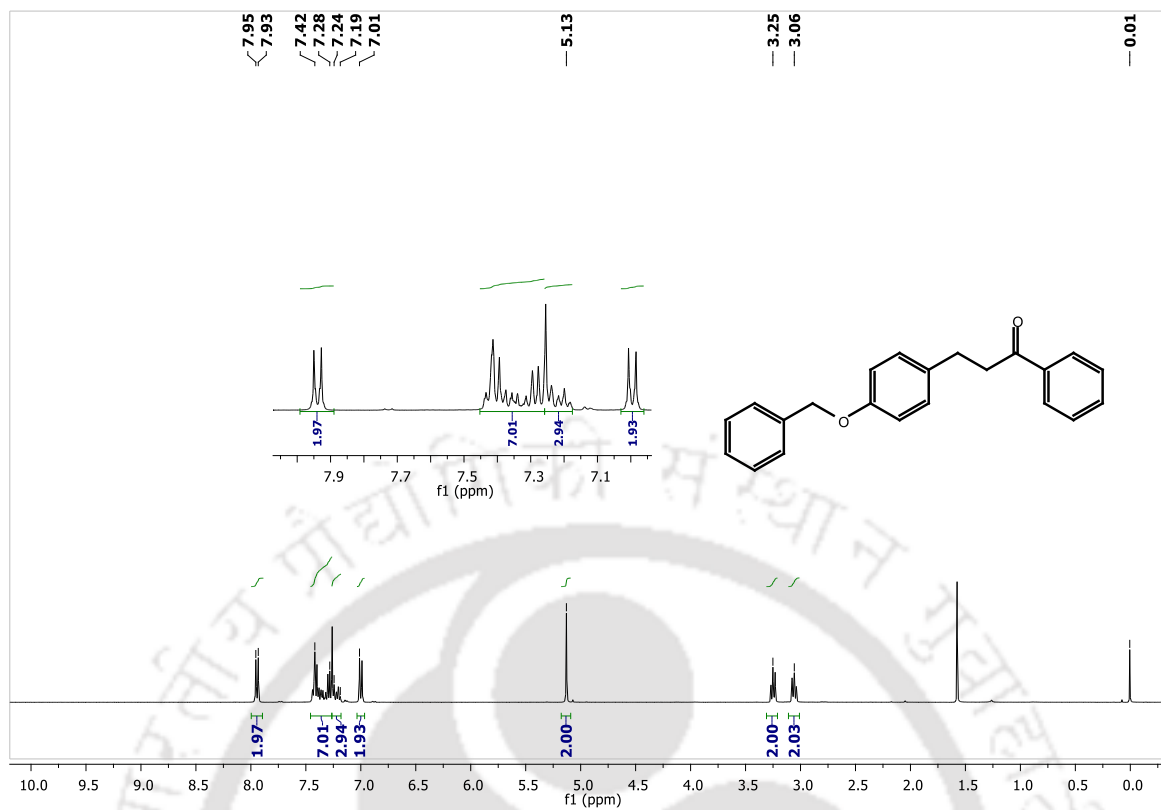


Figure S44: ¹³C NMR Spectrum of **3.3b** (CDCl₃, 101 MHz, 298 K)





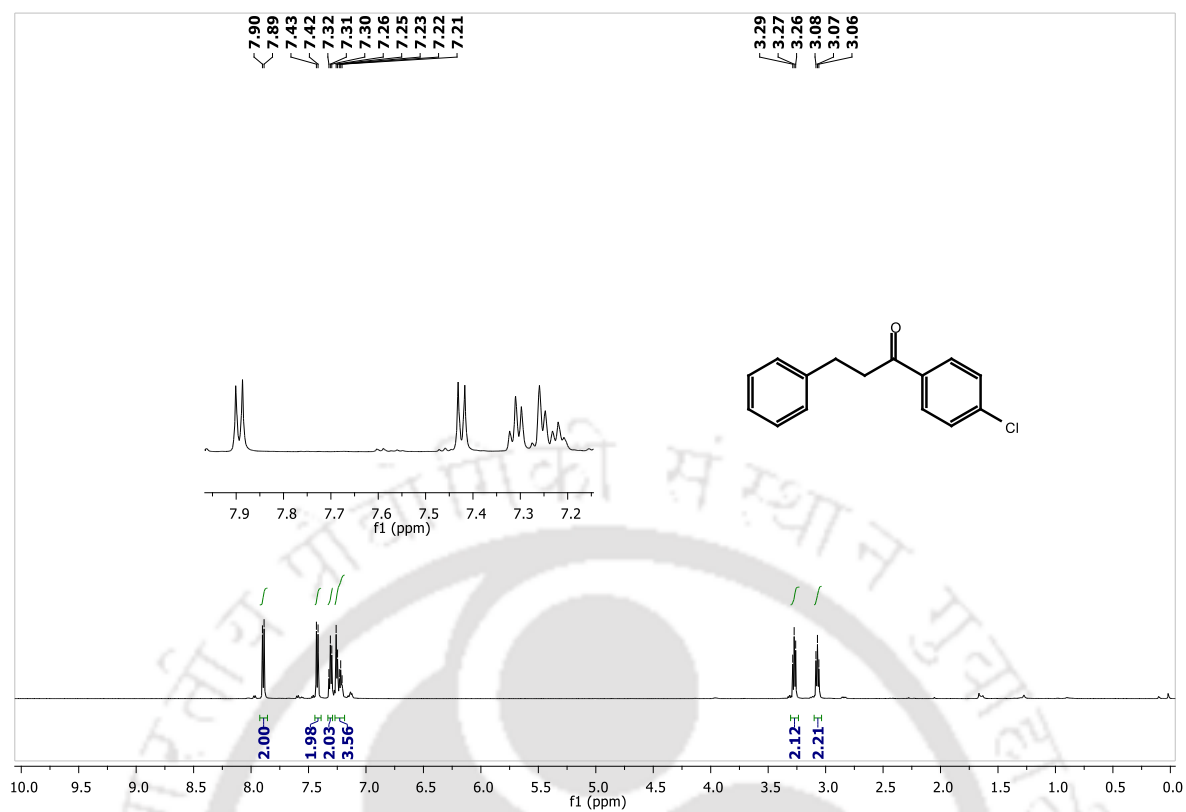


Figure S49: ^1H NMR Spectrum of 3.3e (CDCl_3 , 600 MHz, 298 K)

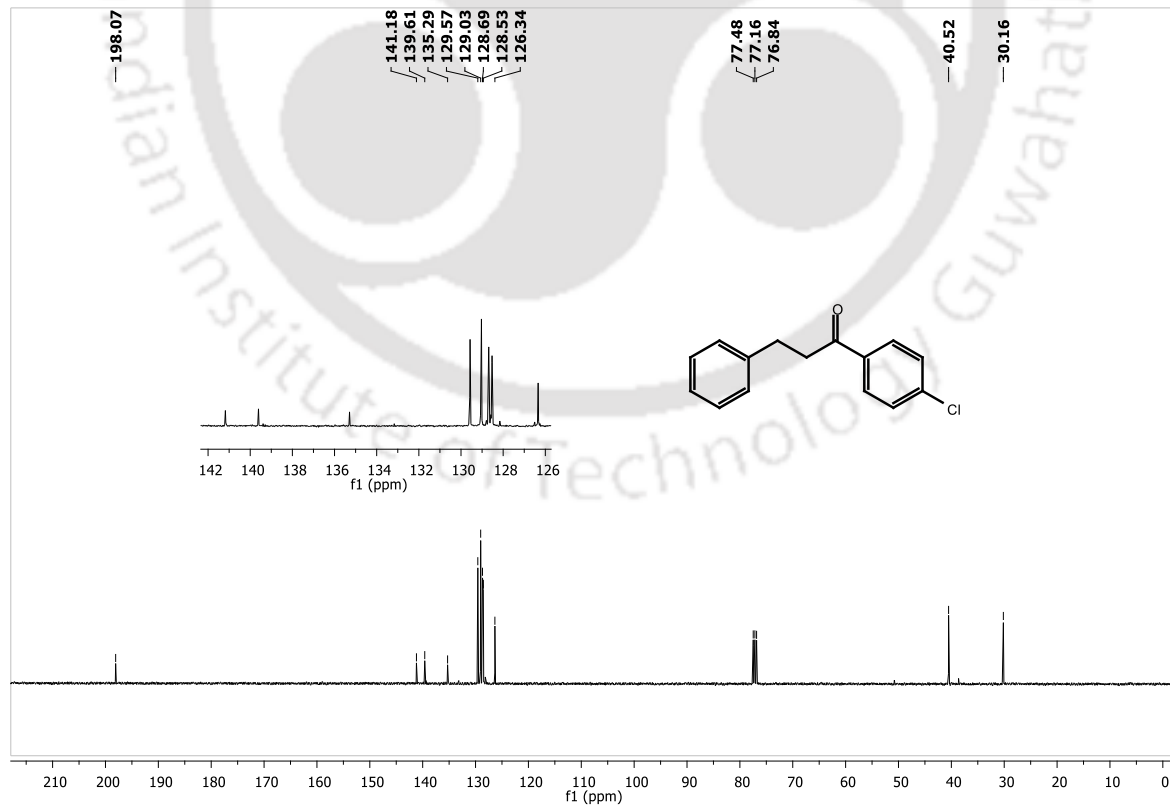


Figure S50: ^{13}C NMR Spectrum of 3.3e (CDCl_3 , 101 MHz, 298 K)

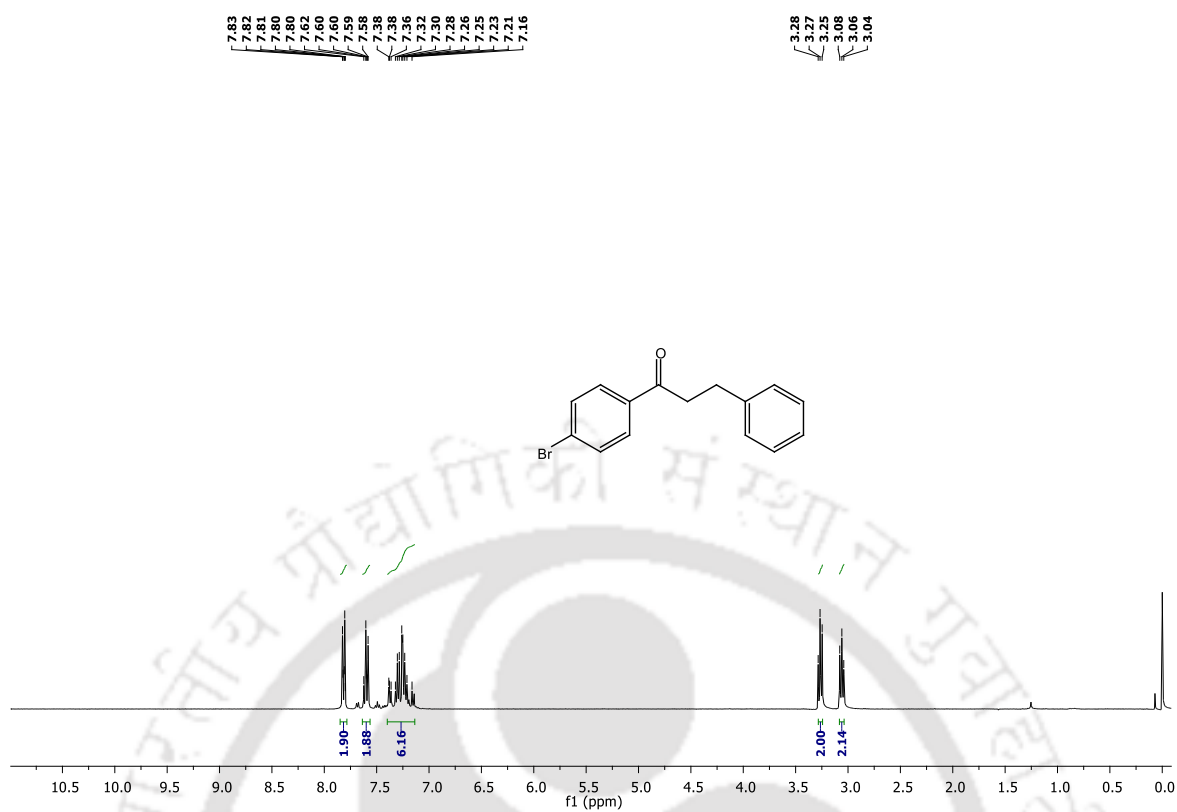


Figure S51: ¹H NMR Spectrum of **3.3f** (CDCl₃, 400 MHz, 298 K)

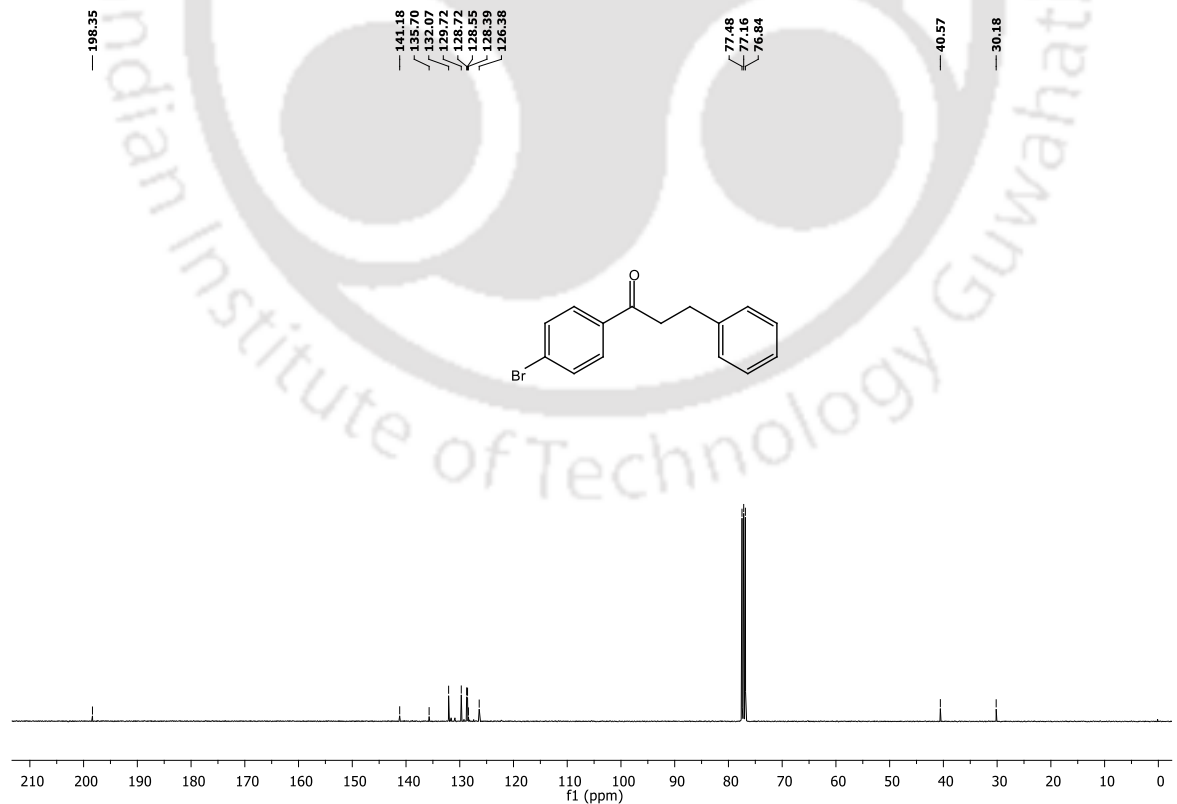


Figure S52: ¹³C NMR Spectrum of **3.3f** (CDCl₃, 101 MHz, 298 K)

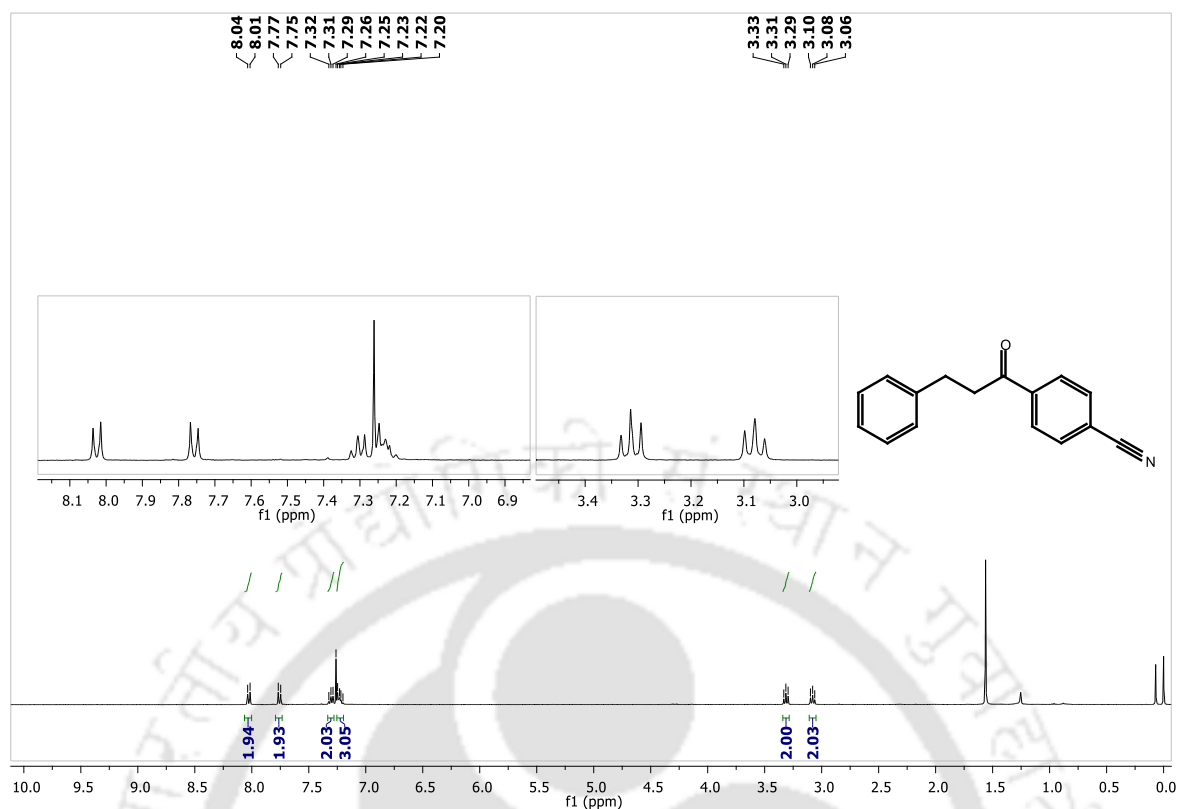


Figure S53: ^1H NMR Spectrum of 3.3g (CDCl_3 , 400 MHz, 298 K)

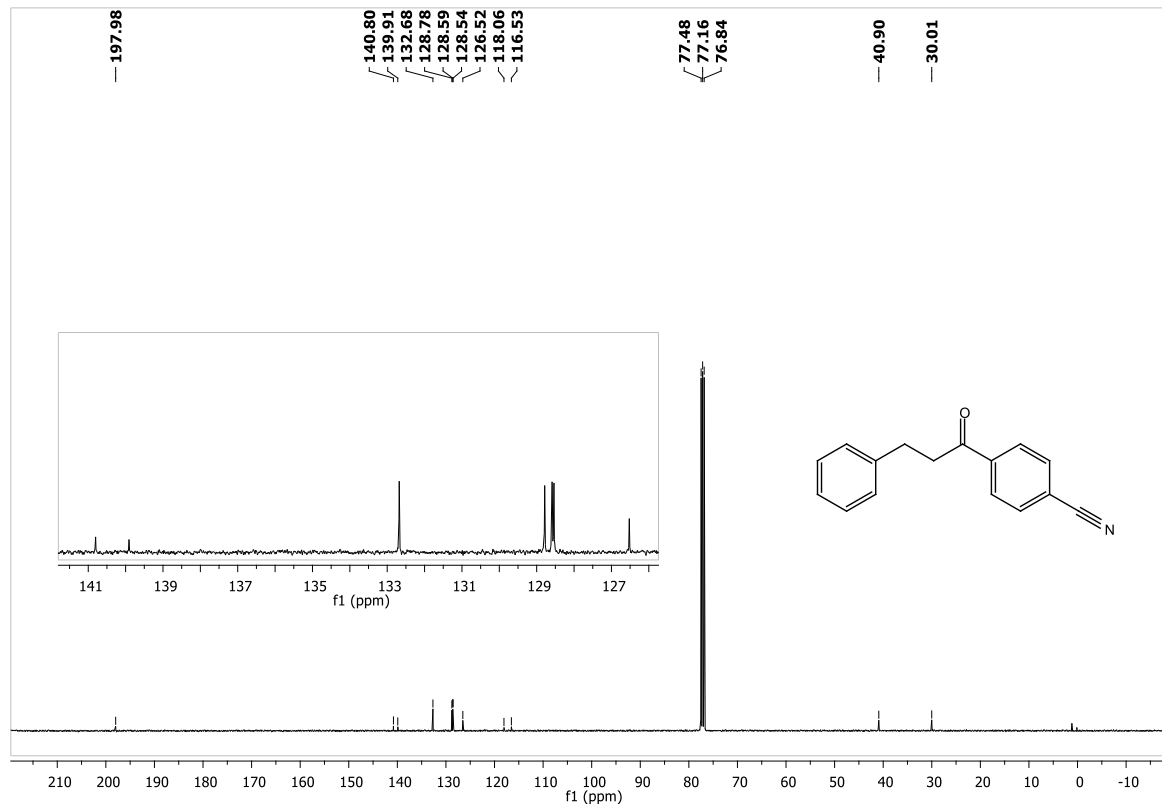


Figure S54: ^{13}C NMR Spectrum of 3.3g (CDCl_3 , 101 MHz, 298 K)

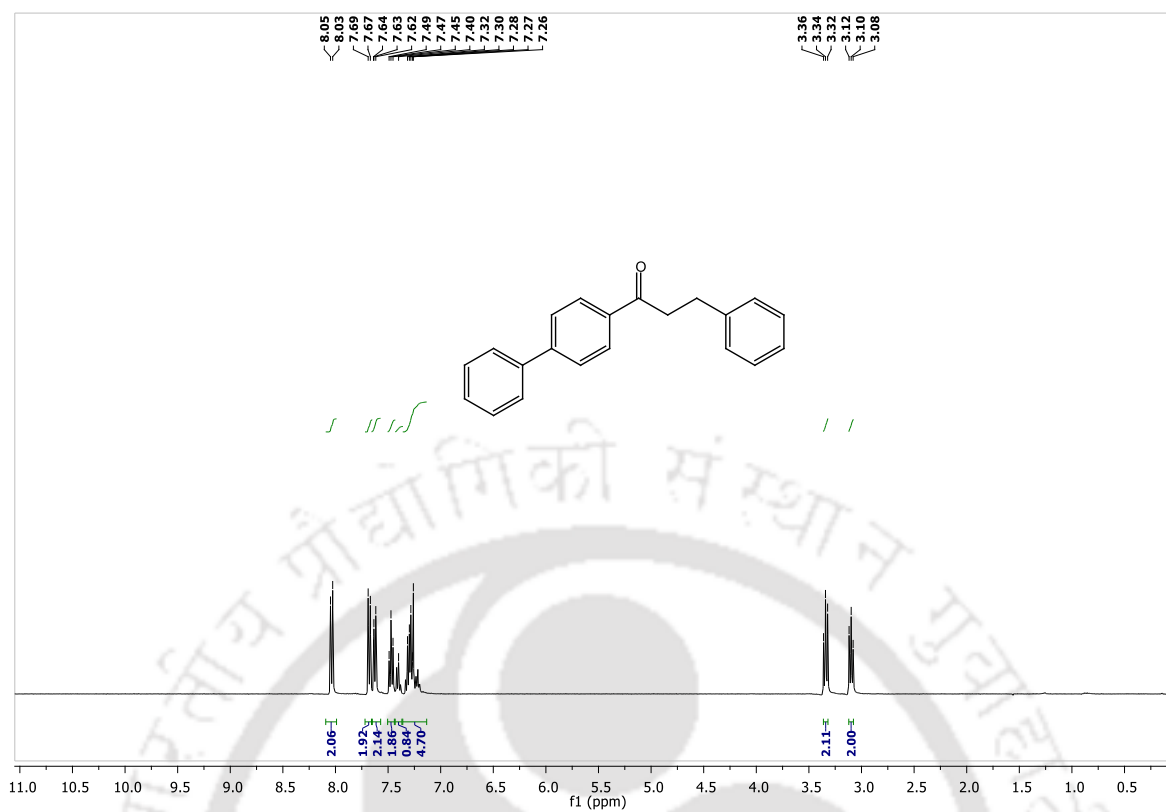


Figure S55: ¹H NMR Spectrum of **3.3h** (CDCl₃, 400 MHz, 298 K)

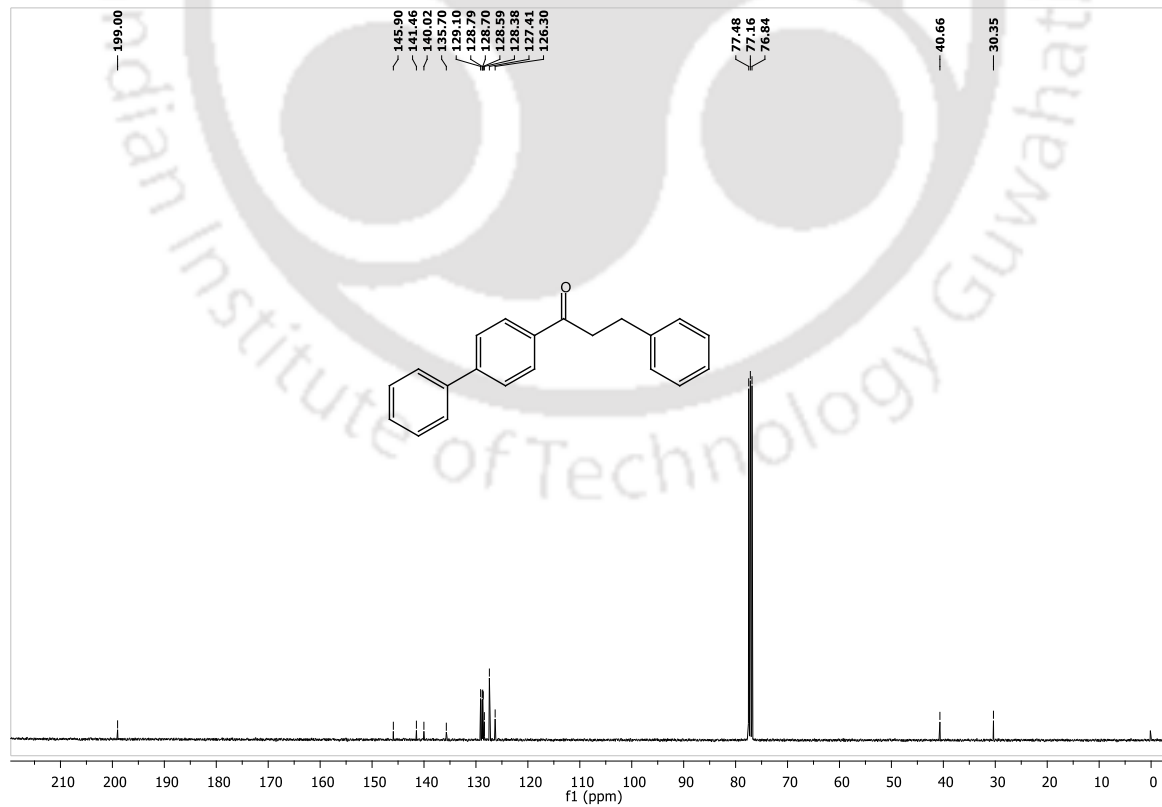


Figure S56: ¹³C NMR Spectrum of **3.3h** (CDCl₃, 101 MHz, 298 K)

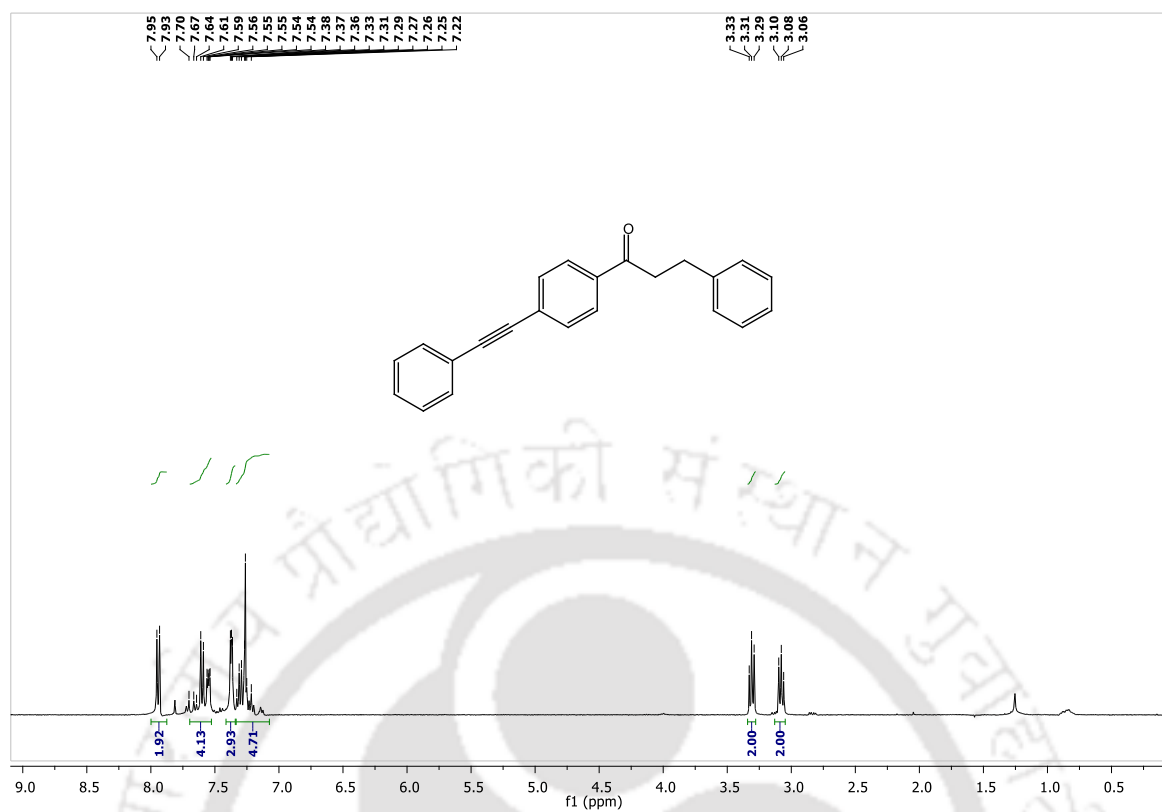


Figure S57: ¹H NMR Spectrum of **3.3i** (CDCl₃, 400 MHz, 298 K)

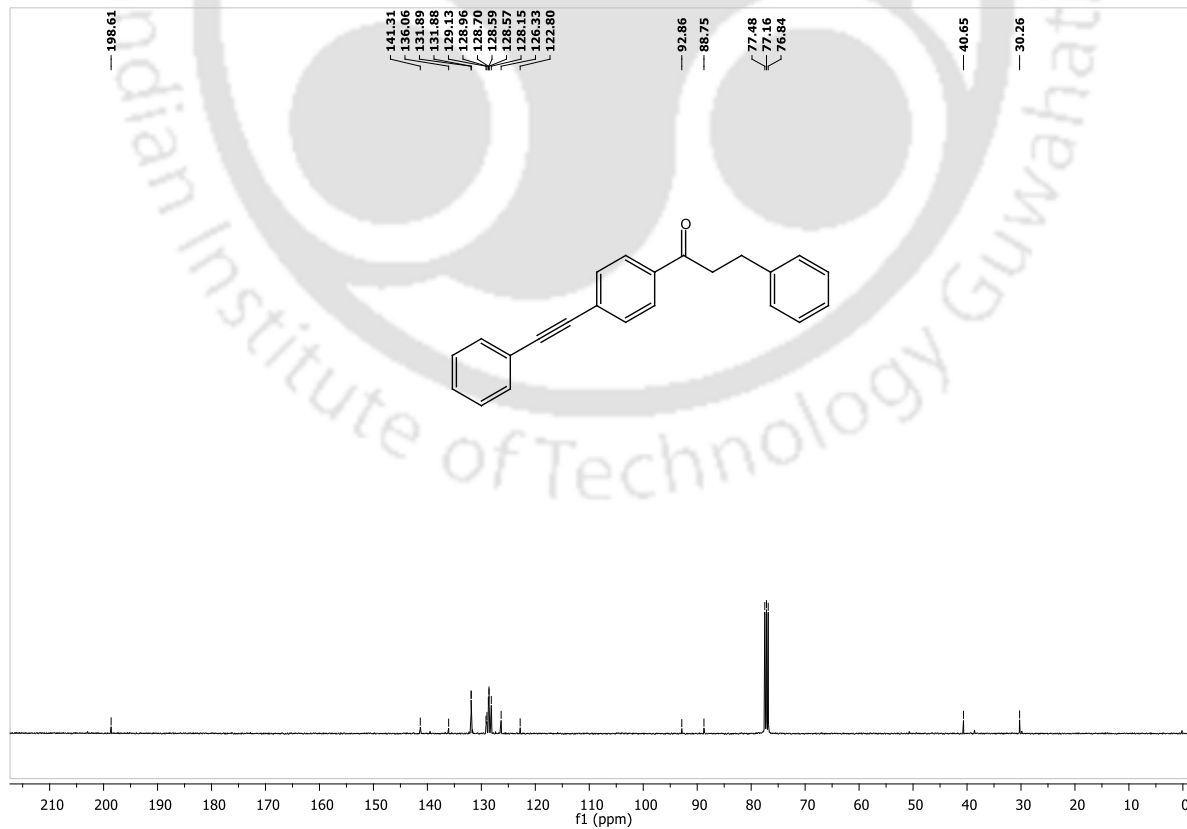


Figure S58: ¹³C NMR Spectrum of **3.3i** (CDCl₃, 101 MHz, 298 K)

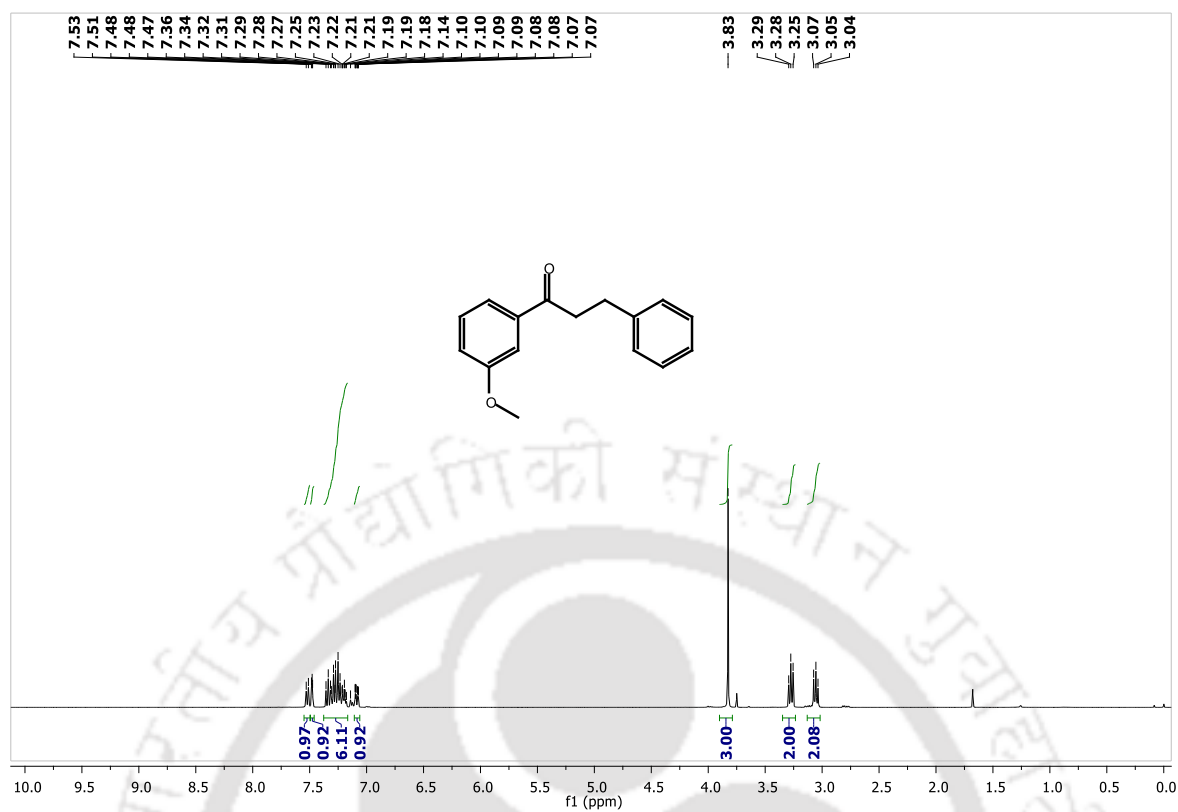


Figure S59: ¹H NMR Spectrum of **3.3j** (CDCl₃, 400 MHz, 298 K)

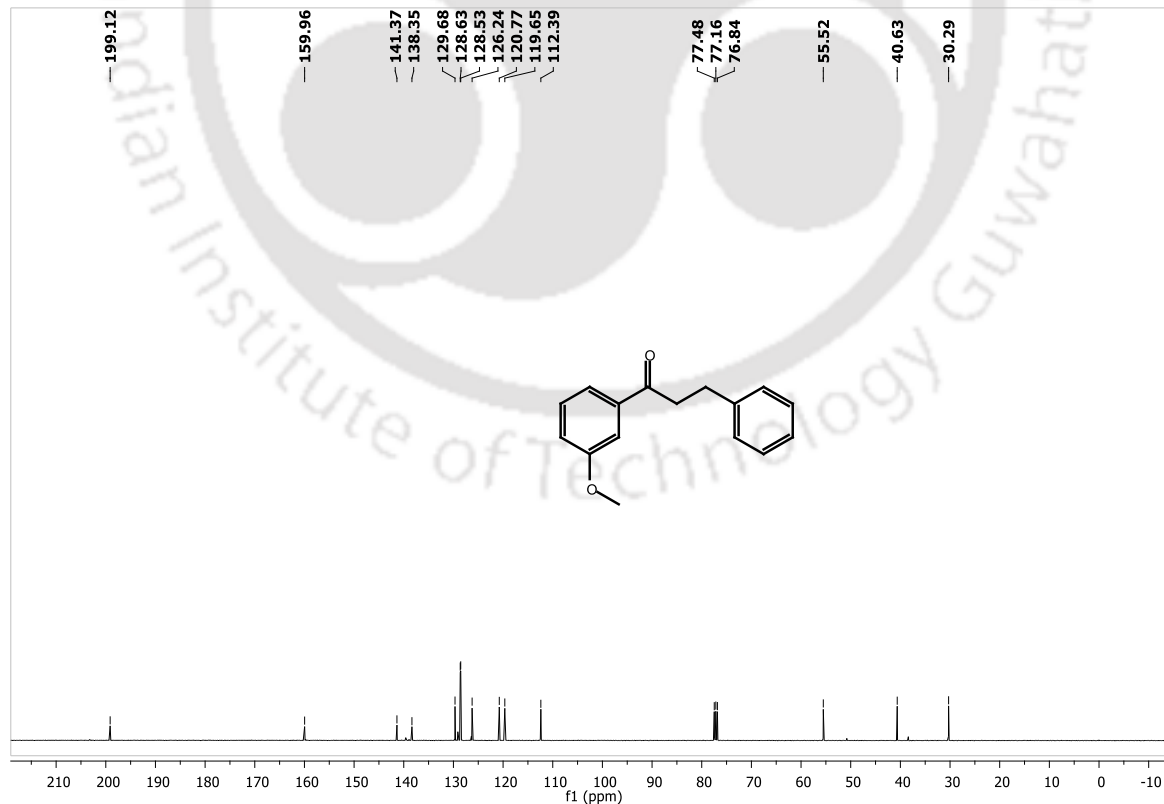


Figure S60: ¹³C NMR Spectrum of **3.3j** (CDCl₃, 101 MHz, 298 K)

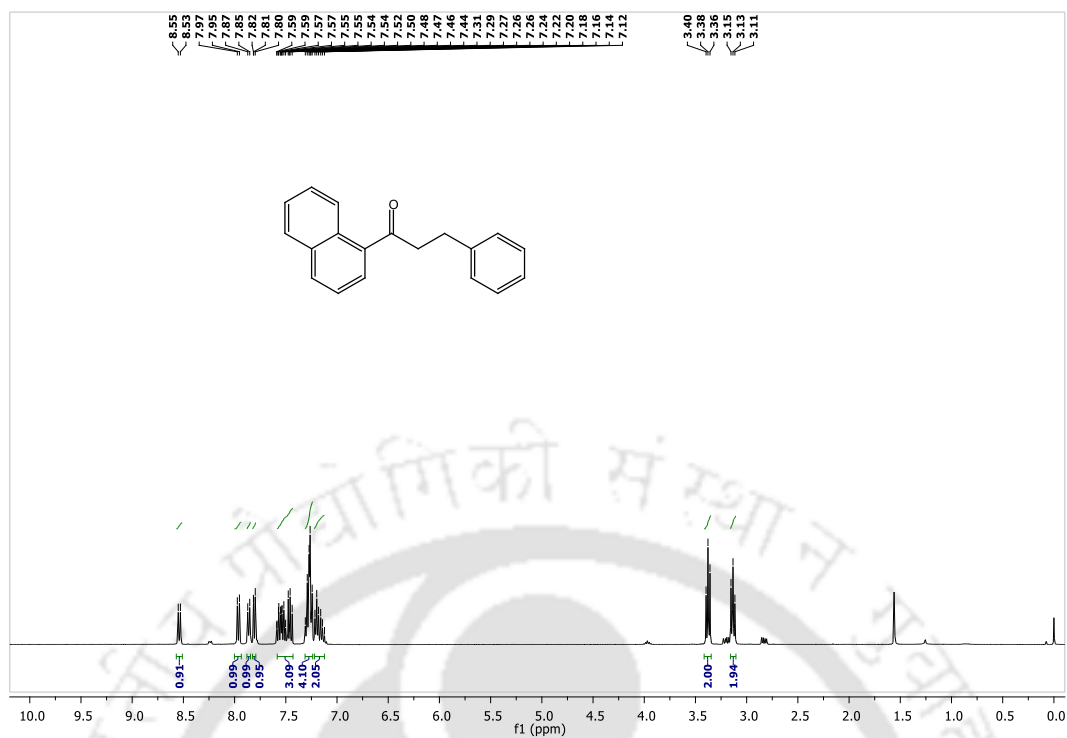


Figure S61: ¹H NMR Spectrum of **3.3k** (CDCl₃, 400 MHz, 298 K)

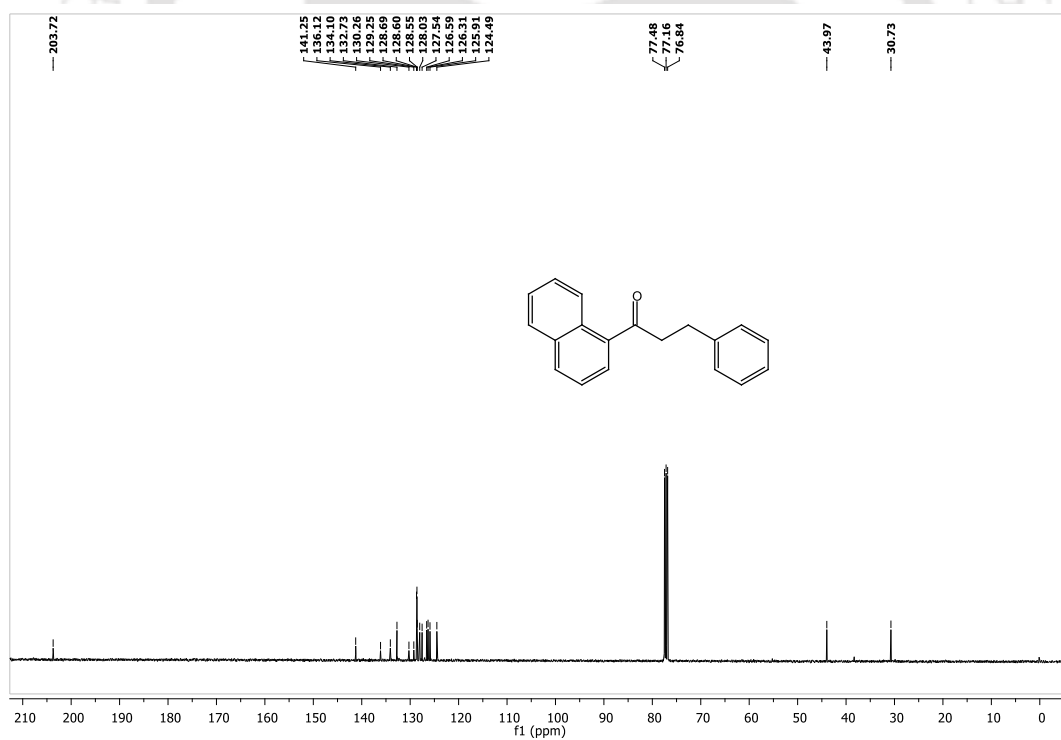


Figure S62: ¹³C NMR Spectrum of **3.3k** (CDCl₃, 101 MHz, 298 K)

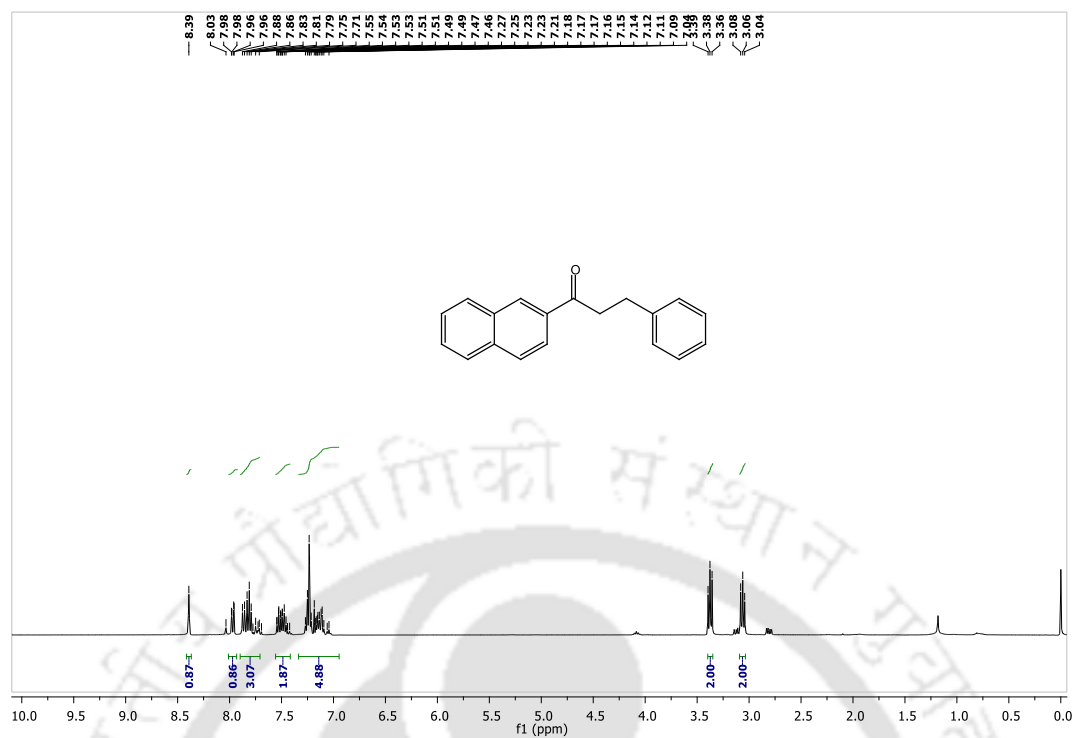


Figure S63: ¹H NMR Spectrum of **3.3I** (CDCl₃, 400 MHz, 298 K)

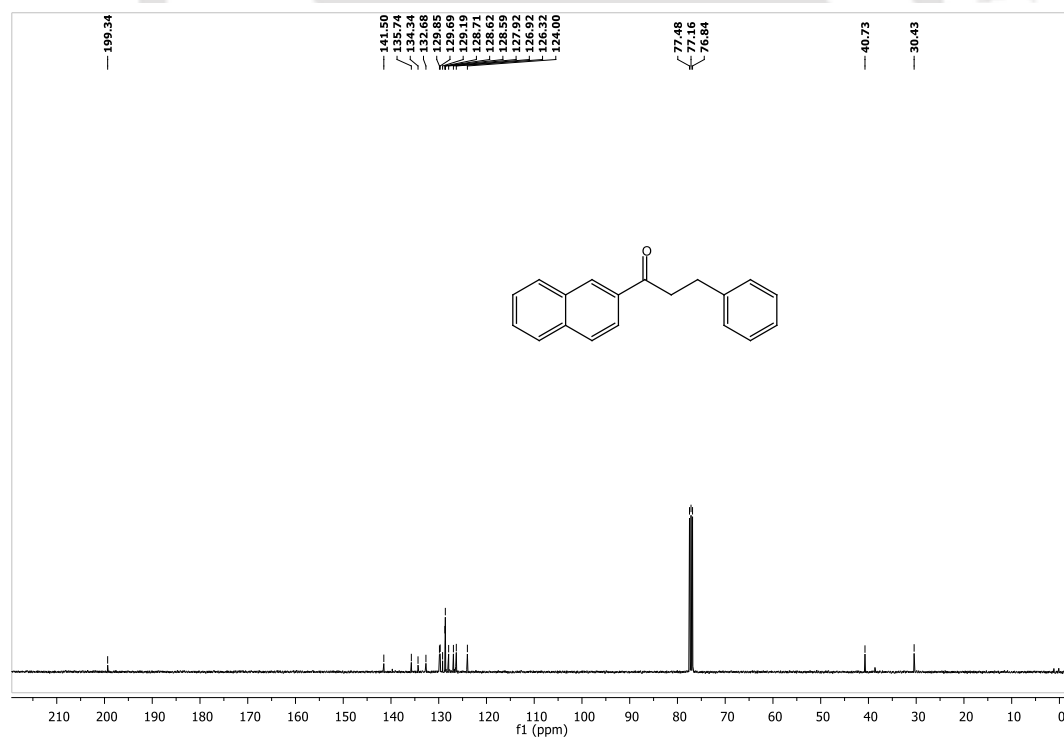


Figure S64: ¹³C NMR Spectrum of **3.3I** (CDCl₃, 101 MHz, 298 K)

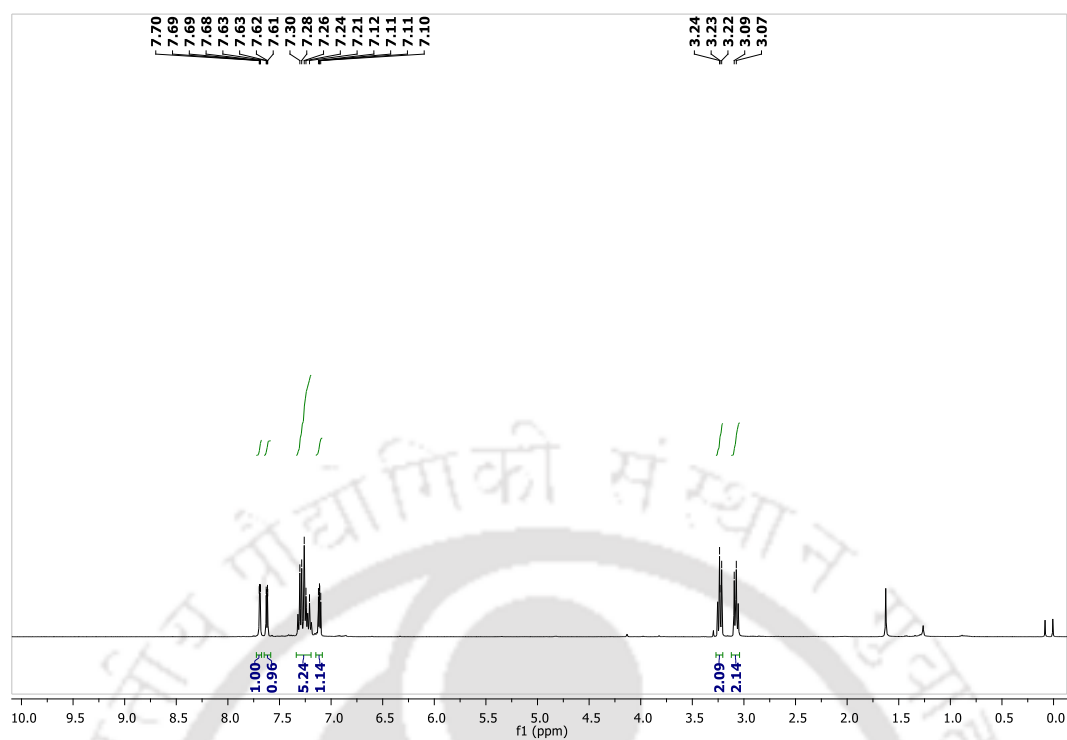


Figure S65: ¹H NMR Spectrum of **3.3m** (CDCl₃, 400 MHz, 298 K)

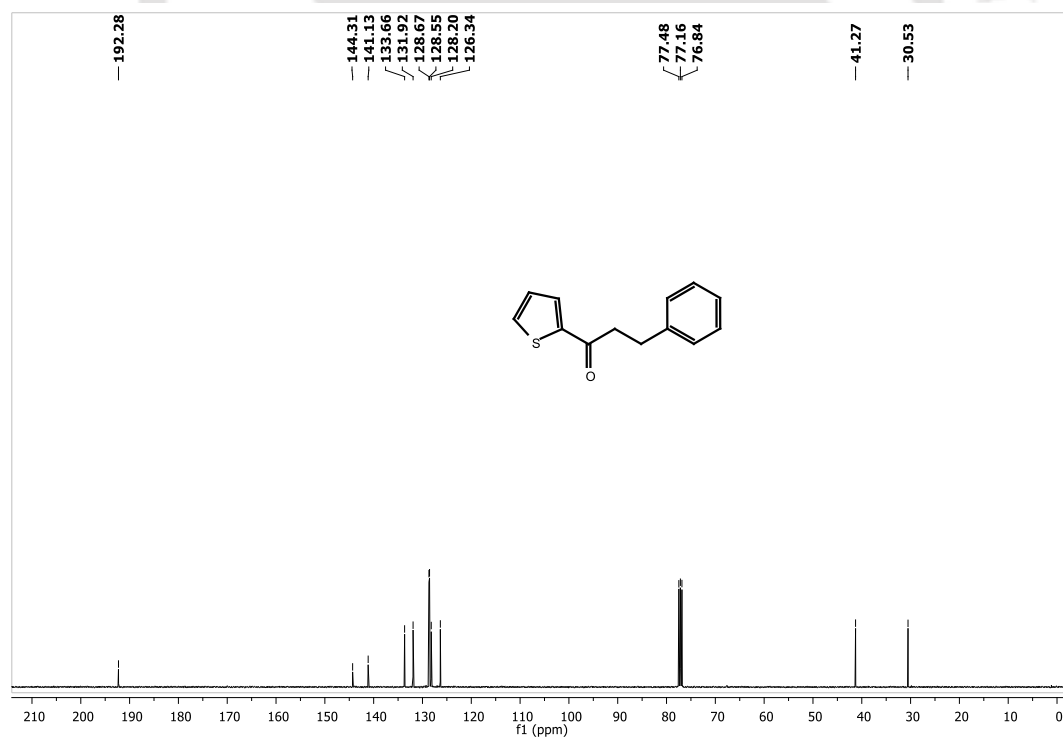


Figure S66: ¹³C NMR Spectrum of **3.3m** (CDCl₃, 101 MHz, 298 K)

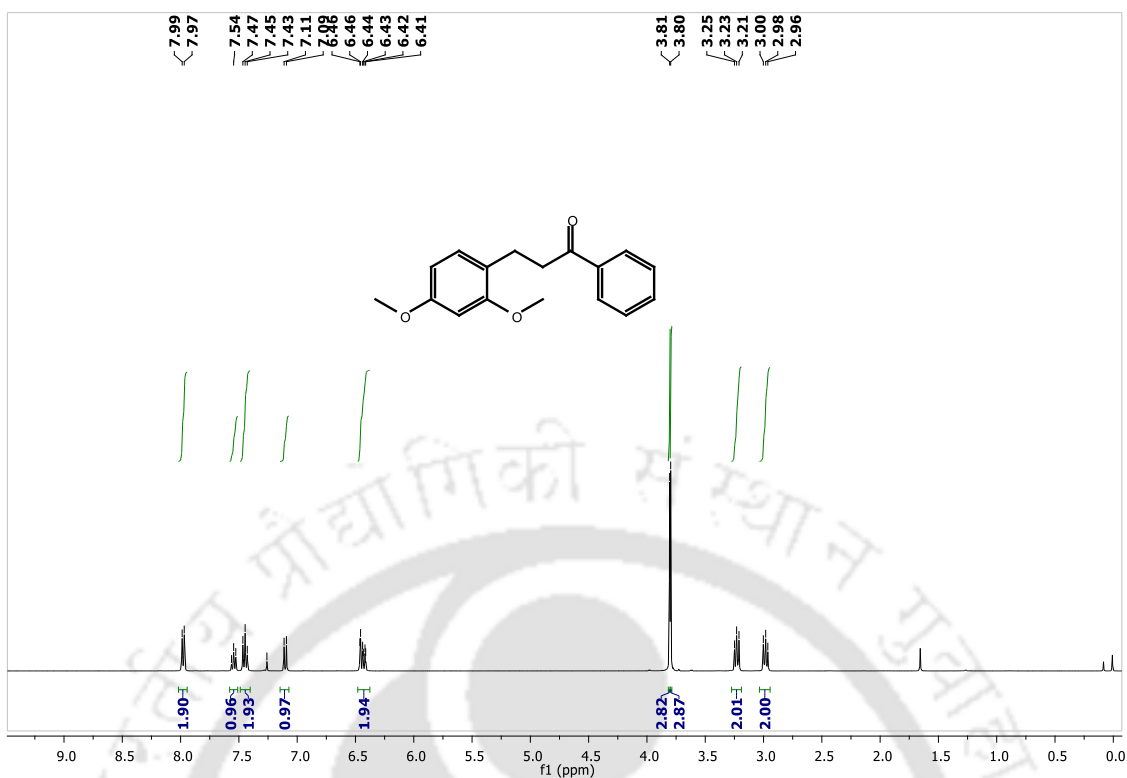


Figure S67: ^1H NMR Spectrum of **3.3n** (CDCl_3 , 400 MHz, 298 K)

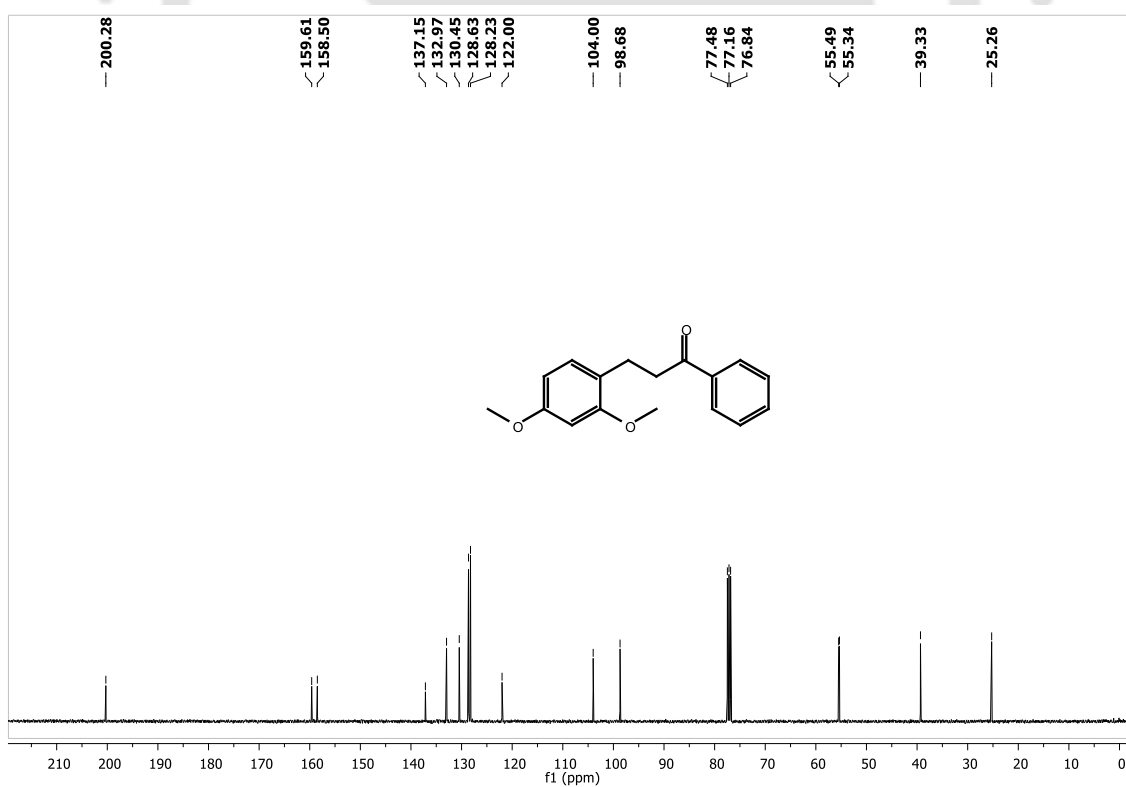


Figure S68: ^{13}C NMR Spectrum of **3.3n** (CDCl_3 , 101 MHz, 298 K)

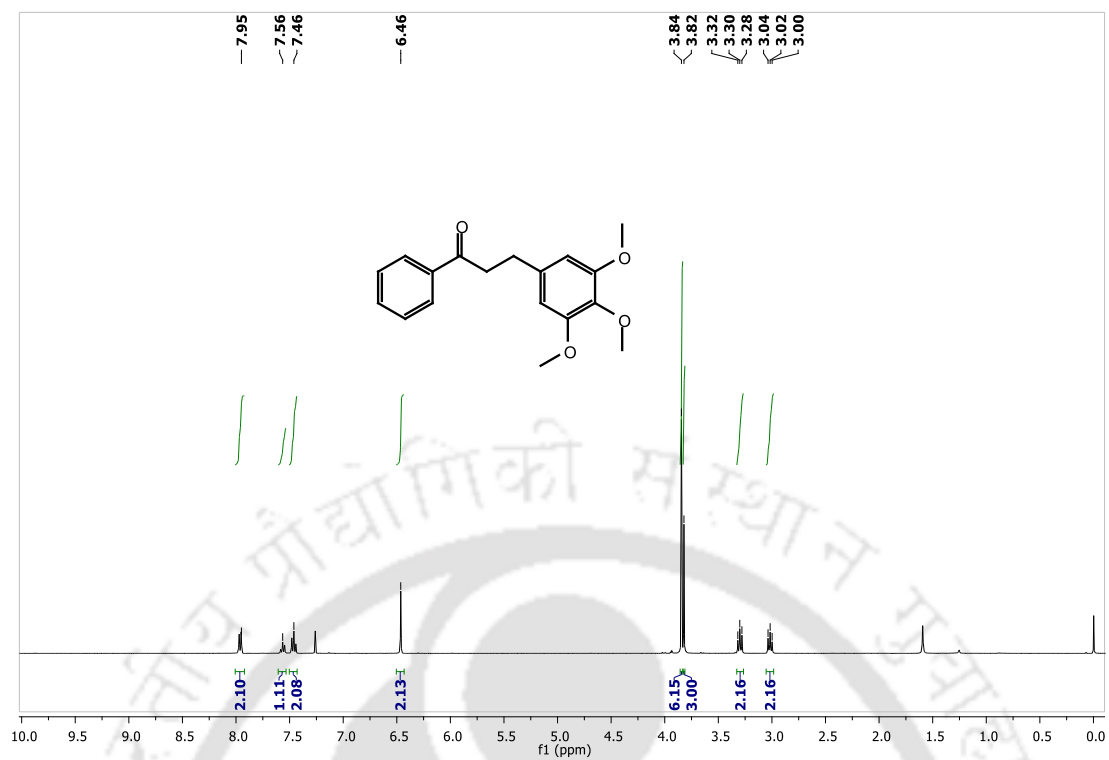


Figure S69: ^1H NMR Spectrum of **3.3o** (CDCl_3 , 400 MHz, 298 K)

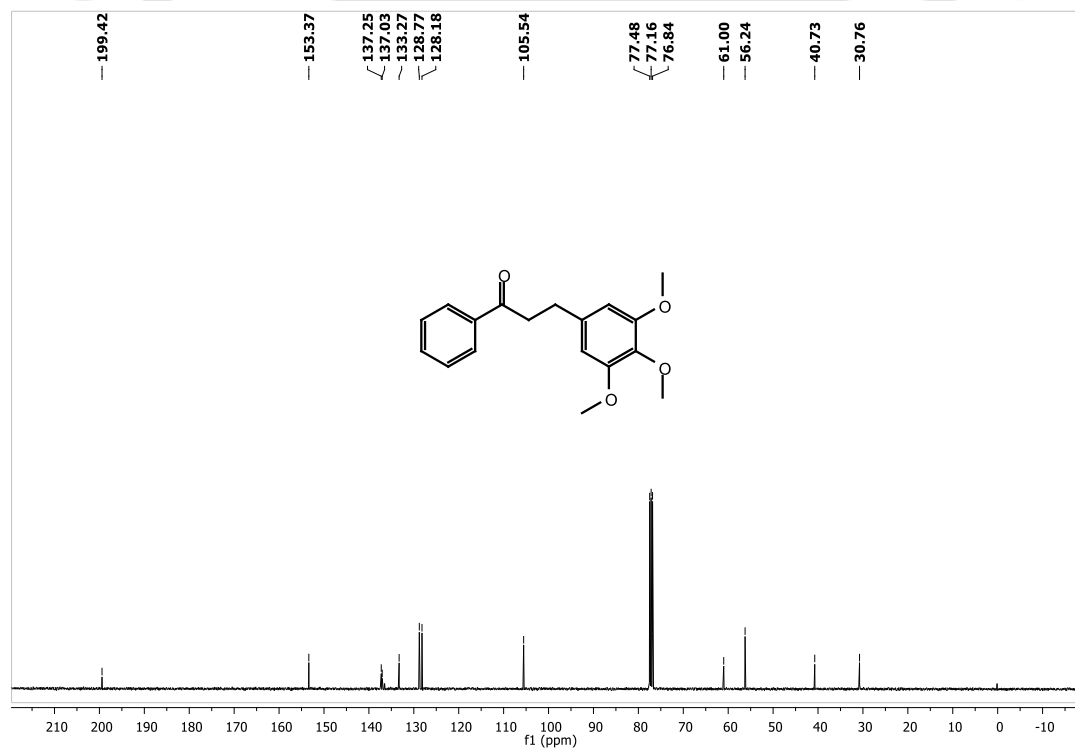


Figure S70: ^{13}C NMR Spectrum of **3.3o** (CDCl_3 , 101 MHz, 298 K)

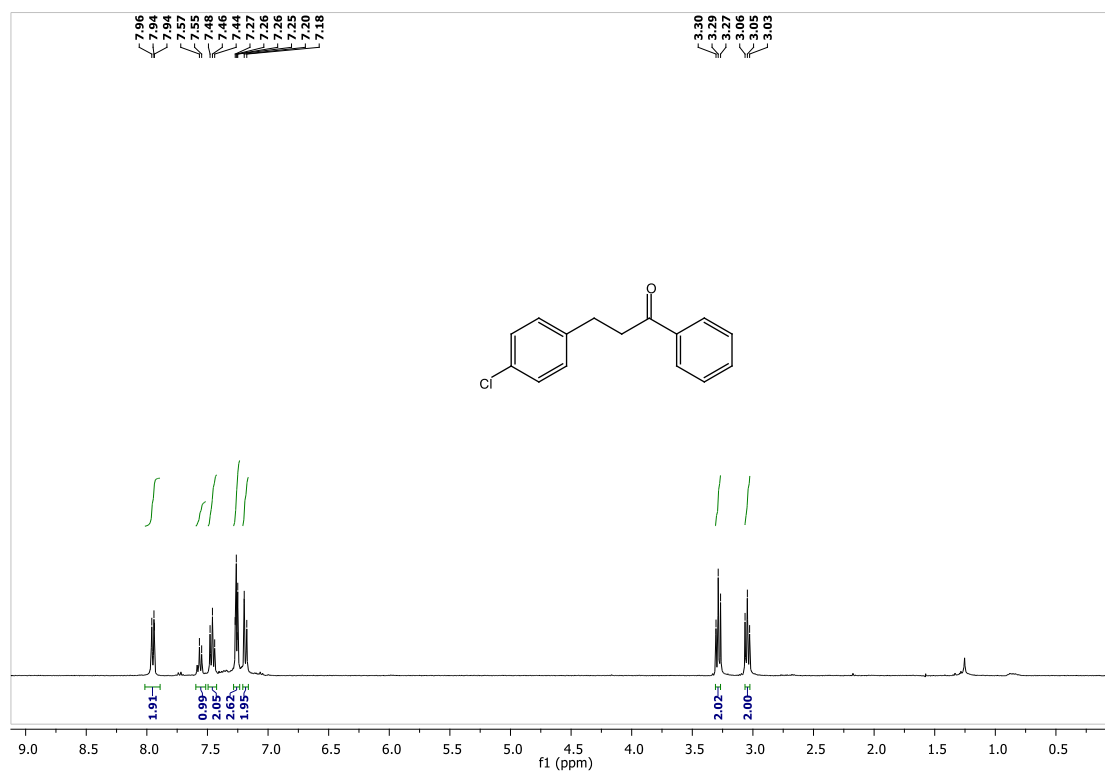


Figure S71: ^1H NMR Spectrum of 3.3p (CDCl_3 , 400 MHz, 298 K)

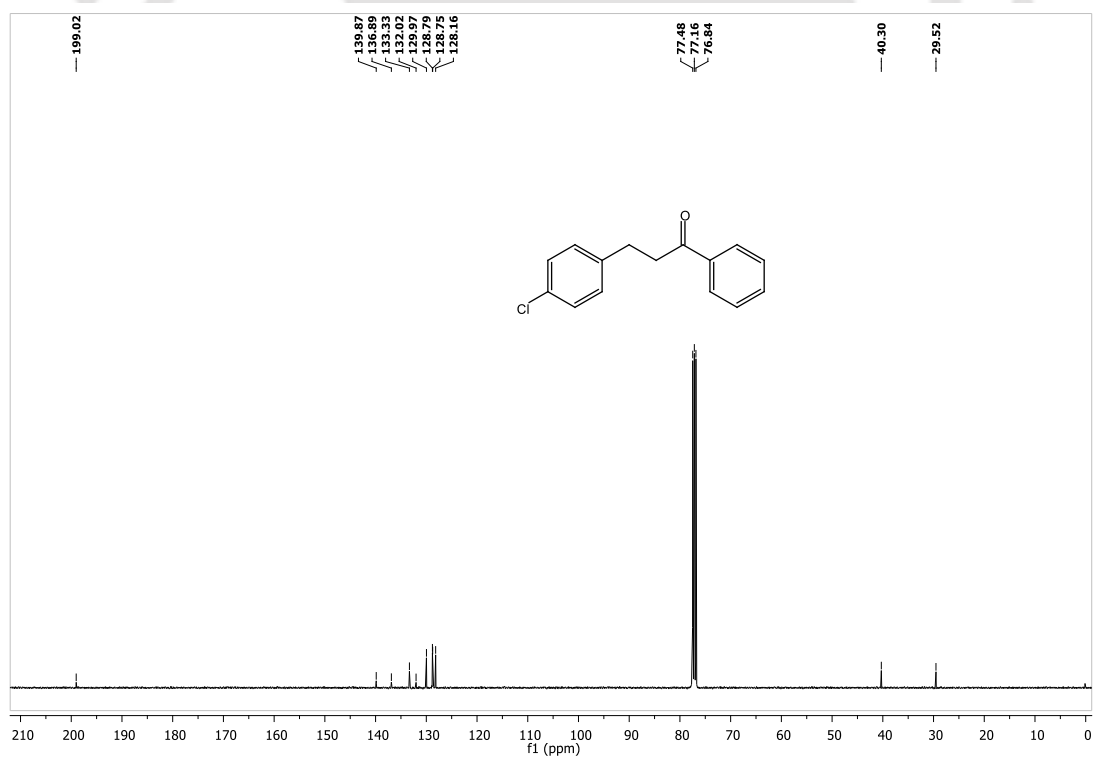


Figure S72: ^{13}C NMR Spectrum of 3.3p (CDCl_3 , 101 MHz, 298 K)

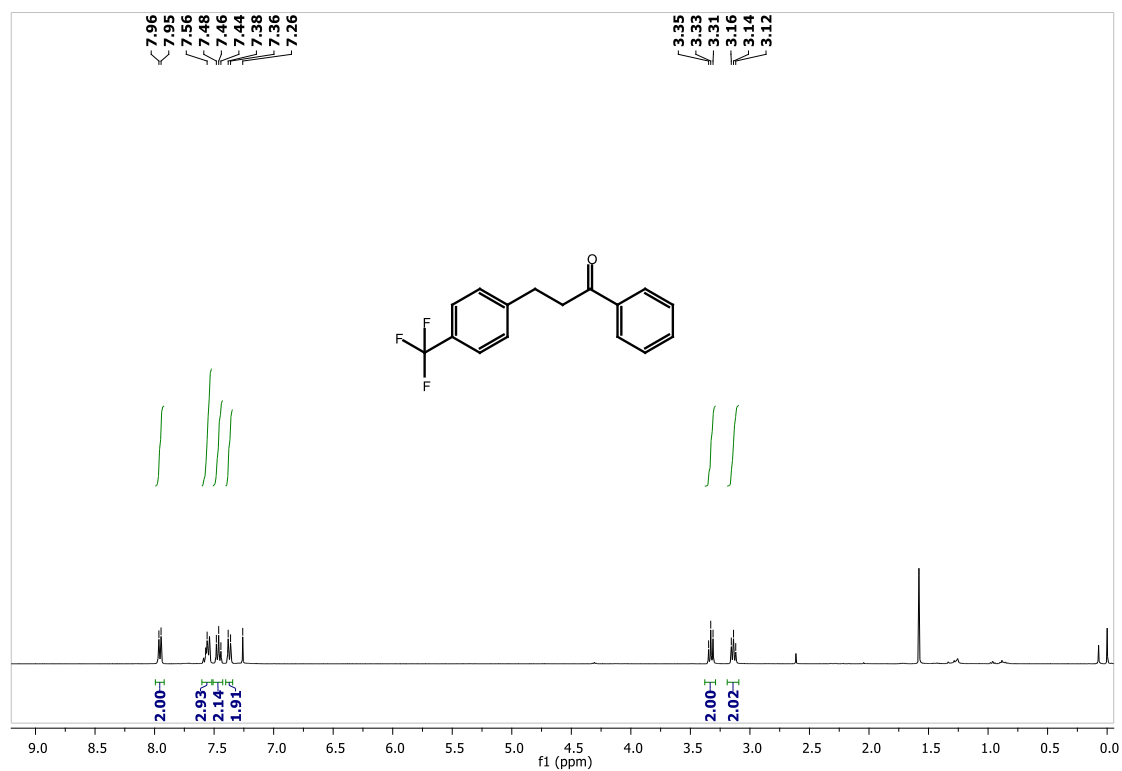


Figure S73: ¹H NMR Spectrum of **3.3q** (CDCl₃, 400 MHz, 298 K)

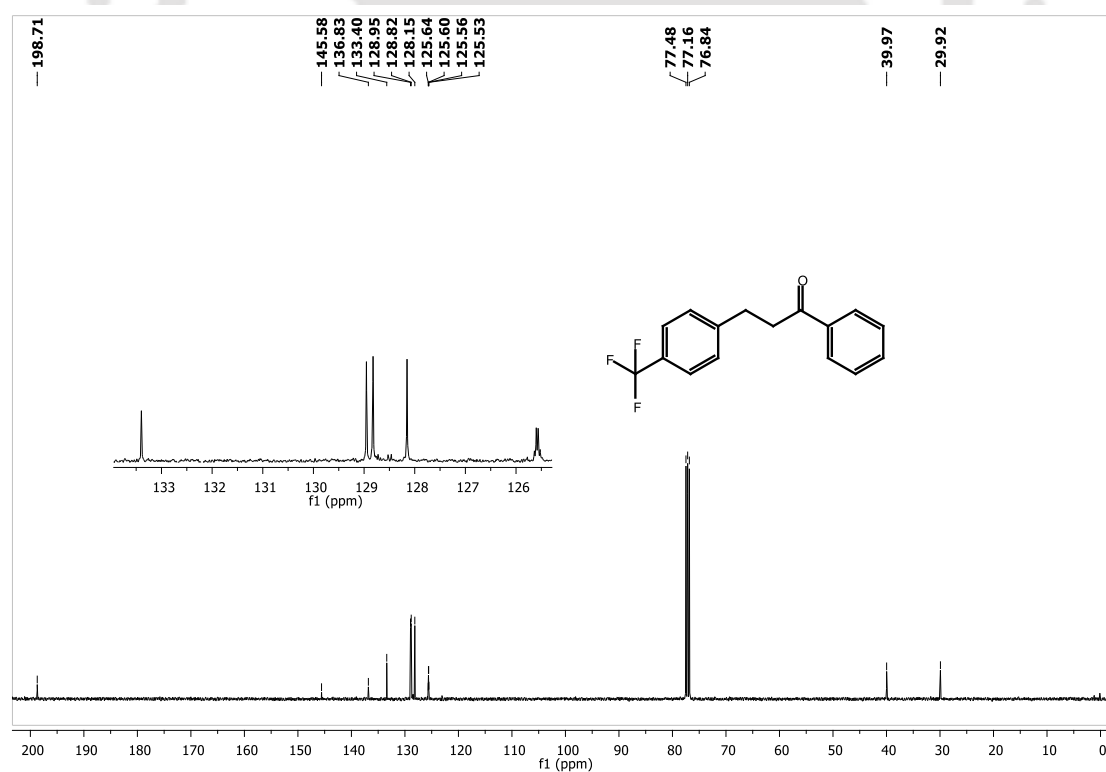


Figure S74: ¹³C NMR Spectrum of **3.3q** (CDCl₃, 101 MHz, 298 K)

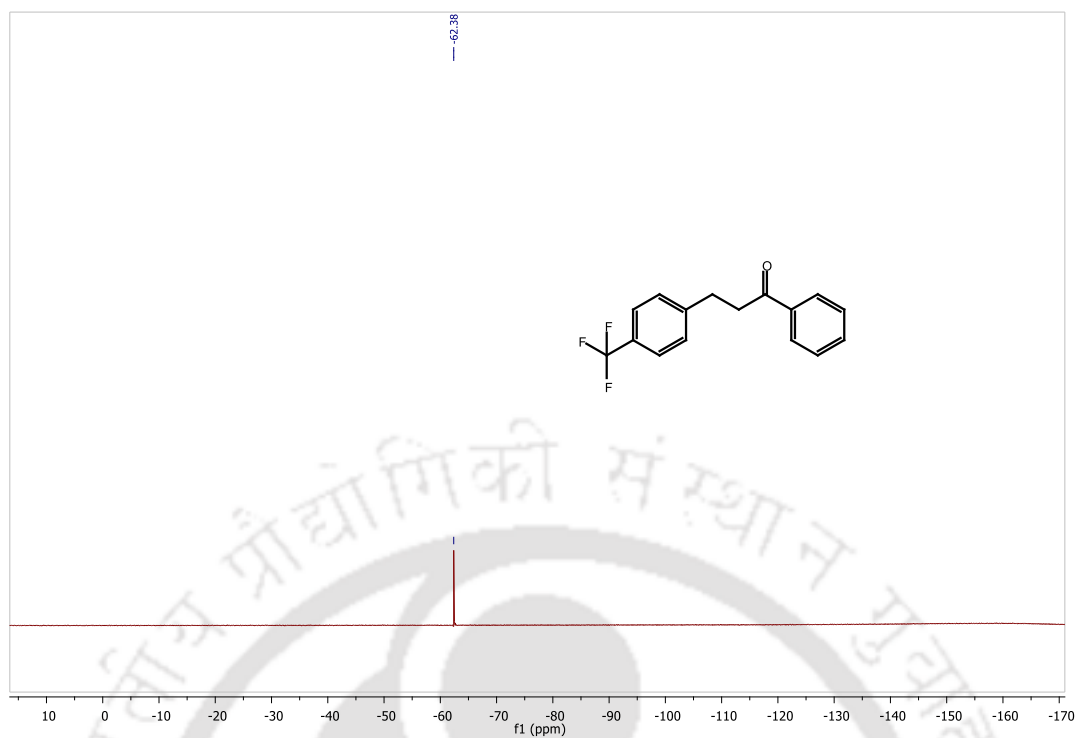


Figure S75: ^{19}F NMR Spectrum of 3.3q (CDCl_3 , 377 MHz, 298 K)

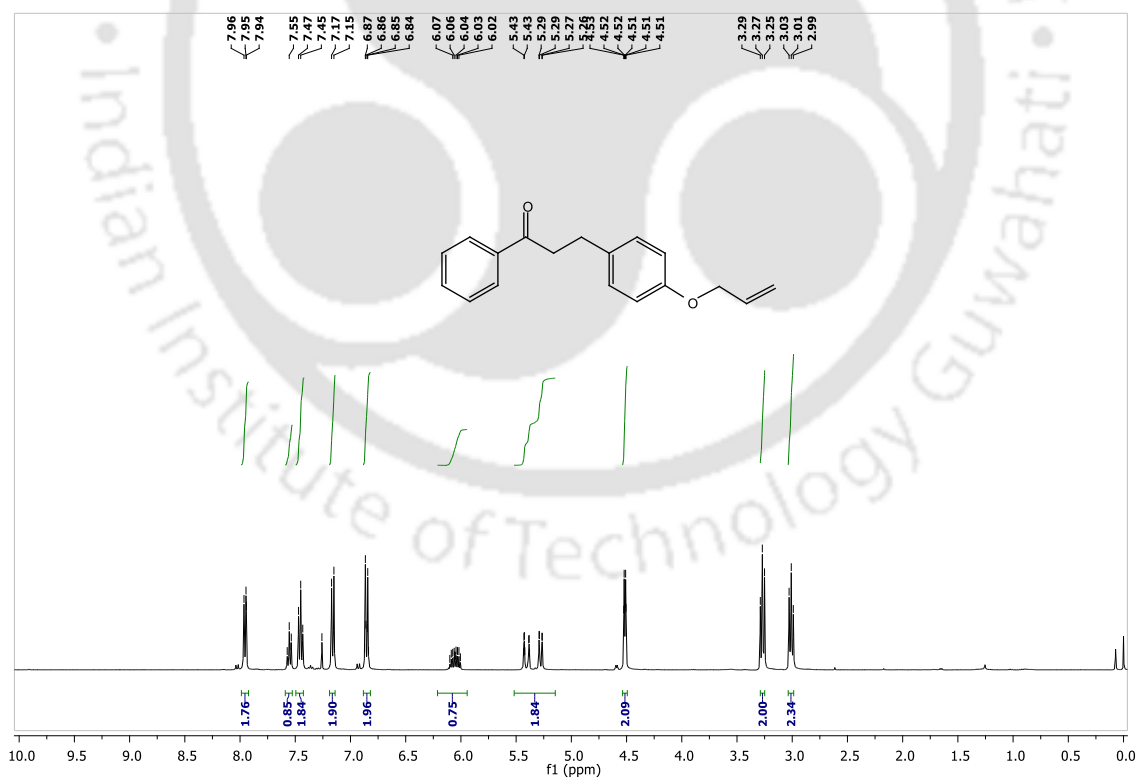


Figure S76: ^1H NMR Spectrum of 3.3r (CDCl_3 , 400 MHz, 298 K)

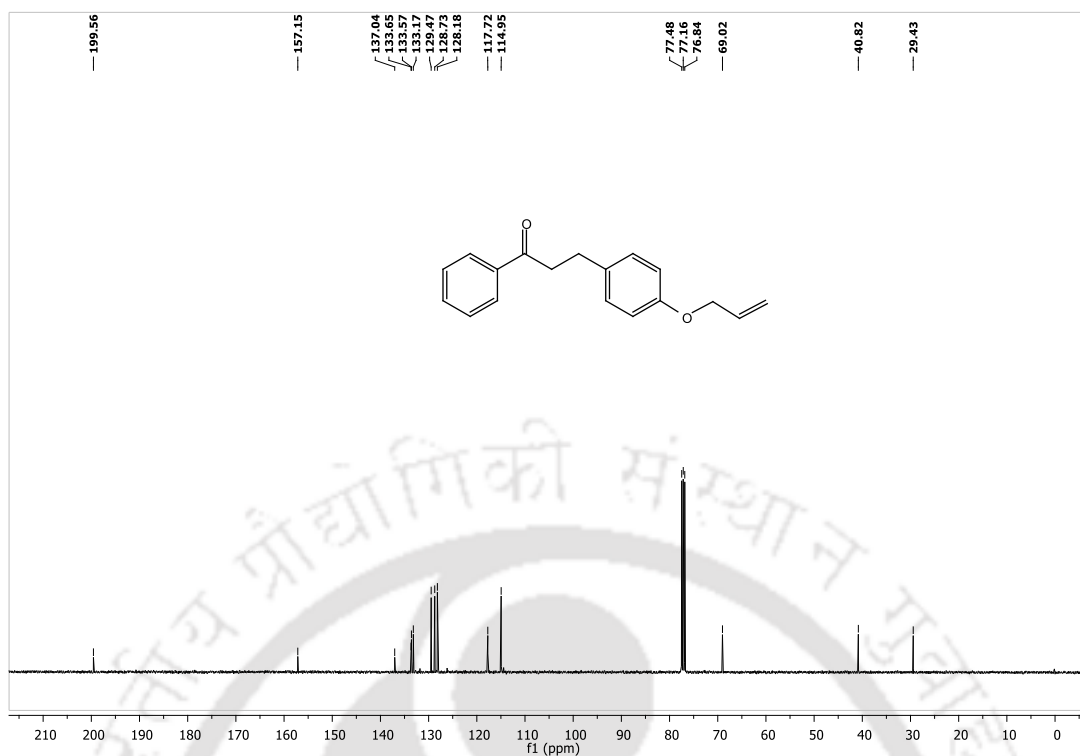


Figure S77: ¹³C NMR Spectrum of 3.3r (CDCl₃, 101 MHz, 298 K)

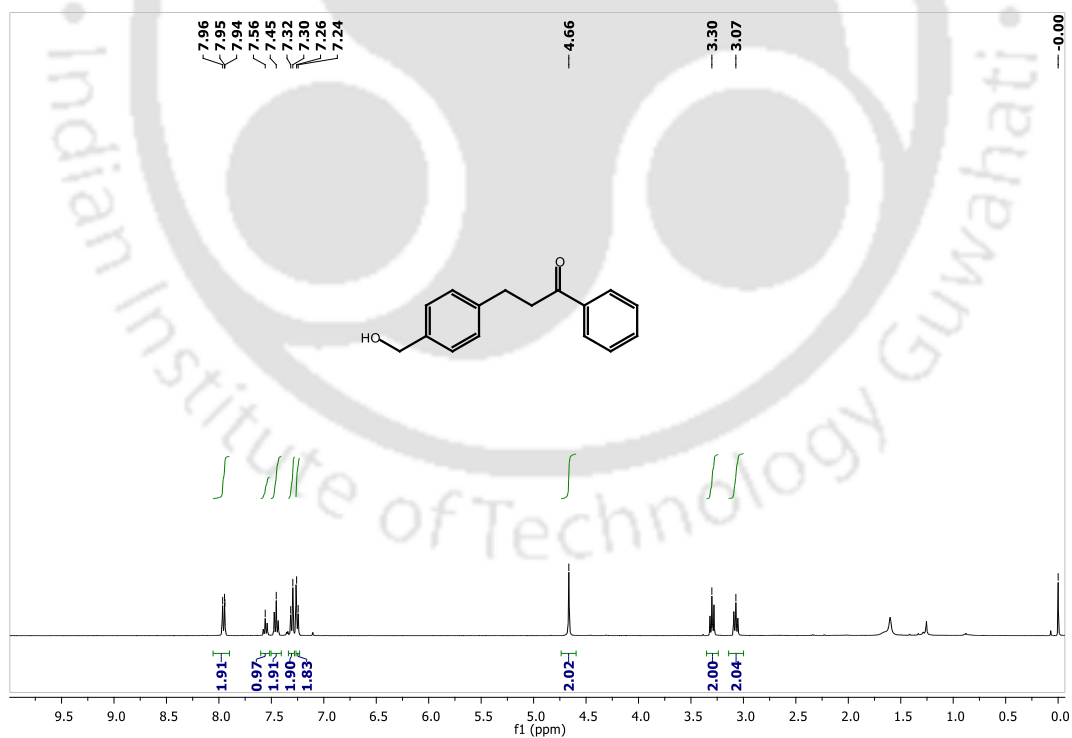


Figure S78: ¹H NMR Spectrum of 3.3s (CDCl₃, 400 MHz, 298 K)

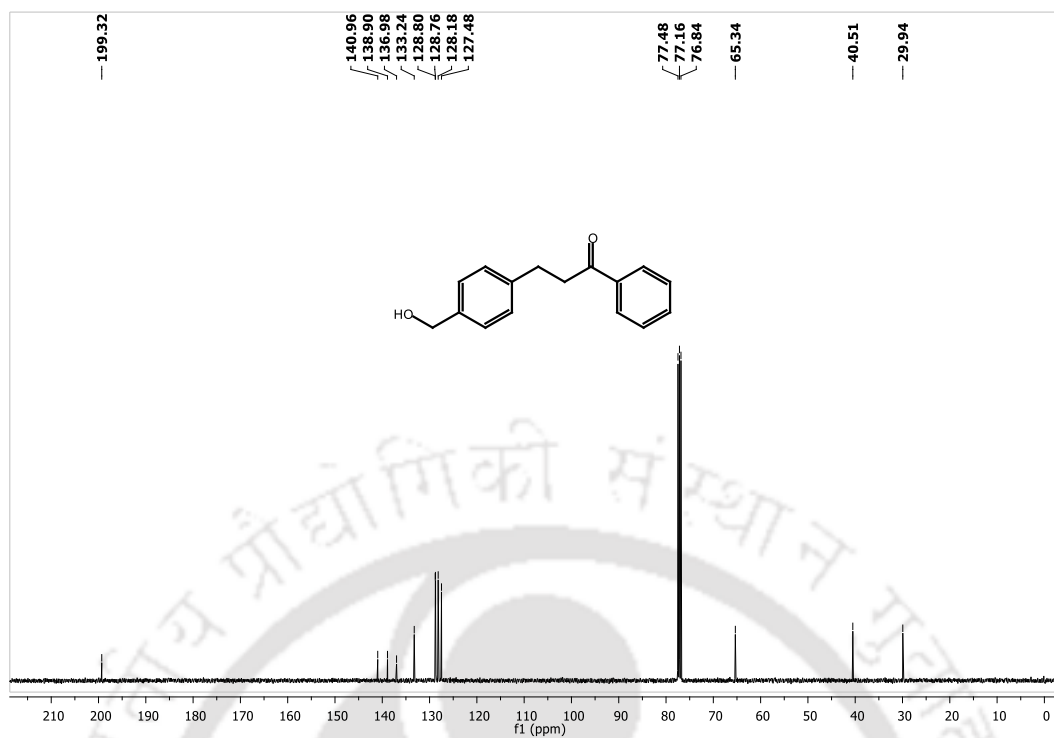


Figure S79: ¹³C NMR Spectrum of 3.3s (CDCl₃, 101 MHz, 298 K)

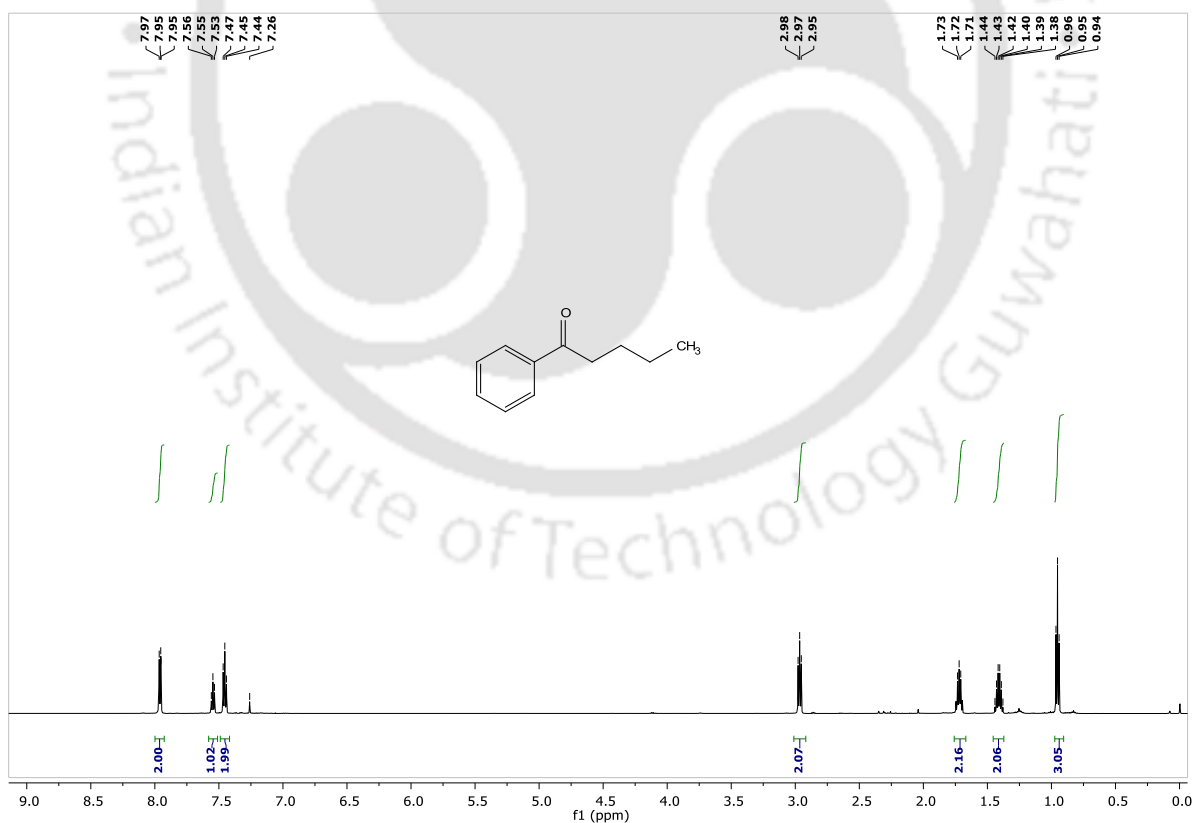
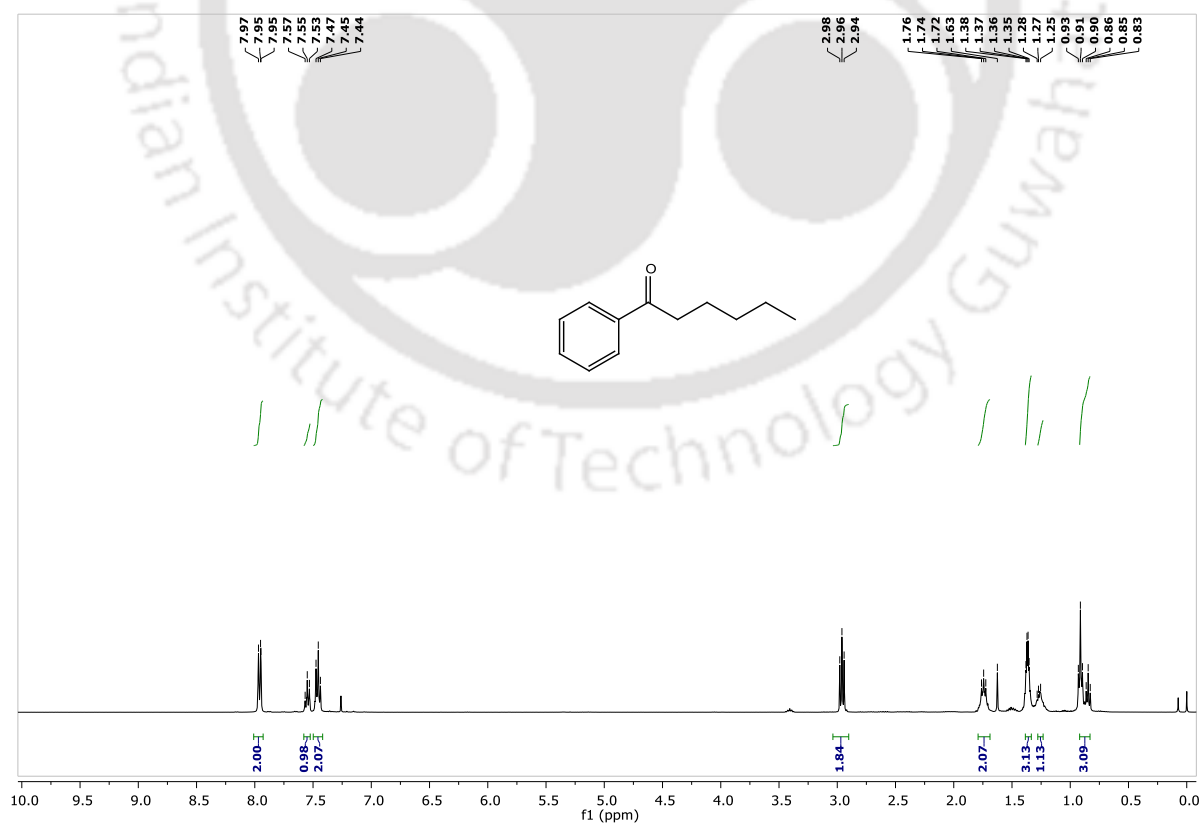
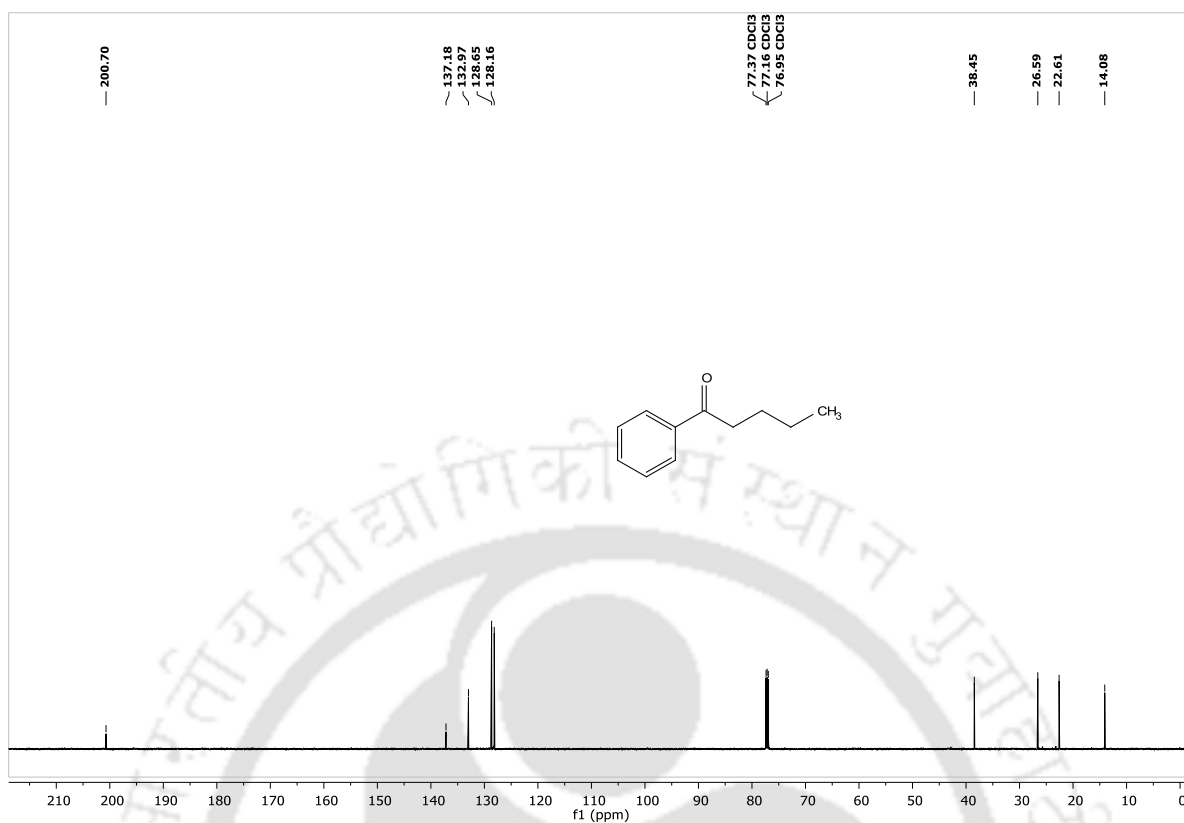


Figure S80: ¹H NMR Spectrum of 3.3t (CDCl₃, 400 MHz, 298 K)



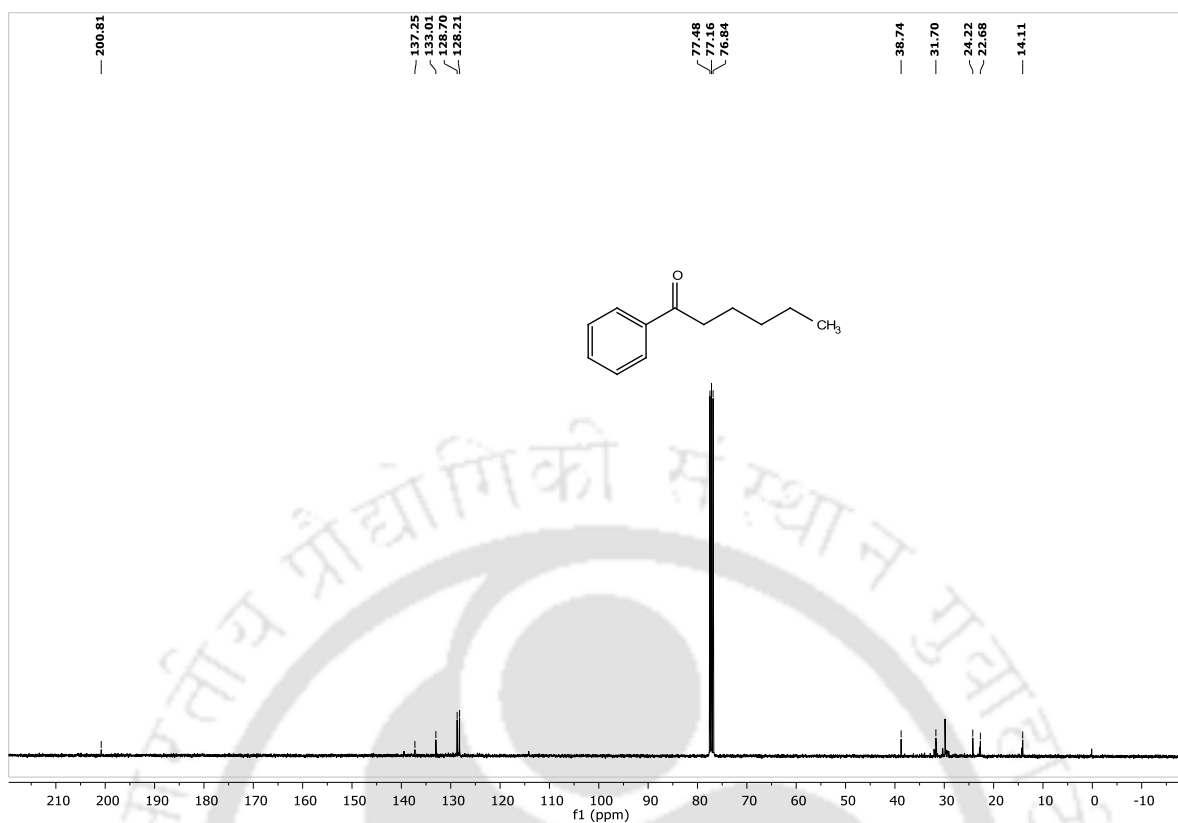


Figure S83: ^{13}C NMR Spectrum of **3.3u** (CDCl_3 , 101 MHz, 298 K)

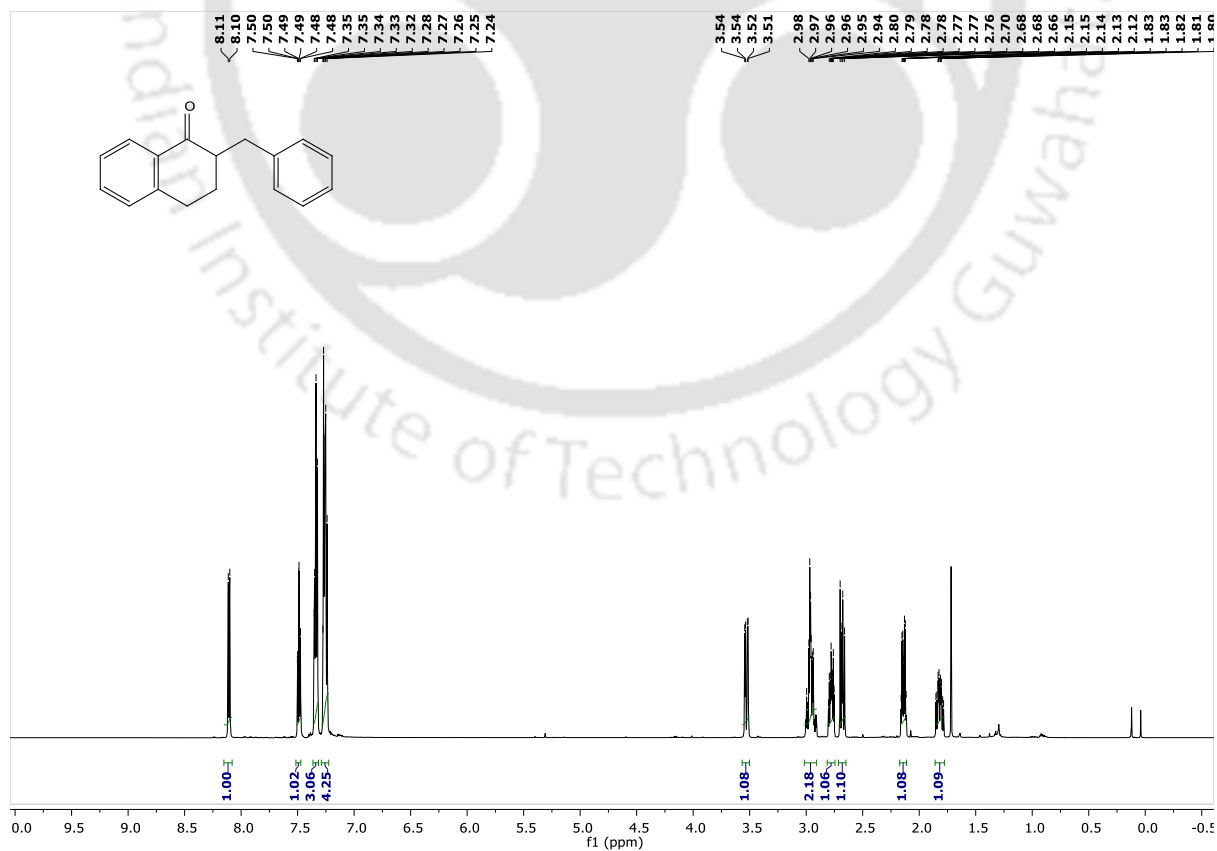


Figure S84: ^1H NMR Spectrum of **3.3v** (CDCl_3 , 400 MHz, 298 K)

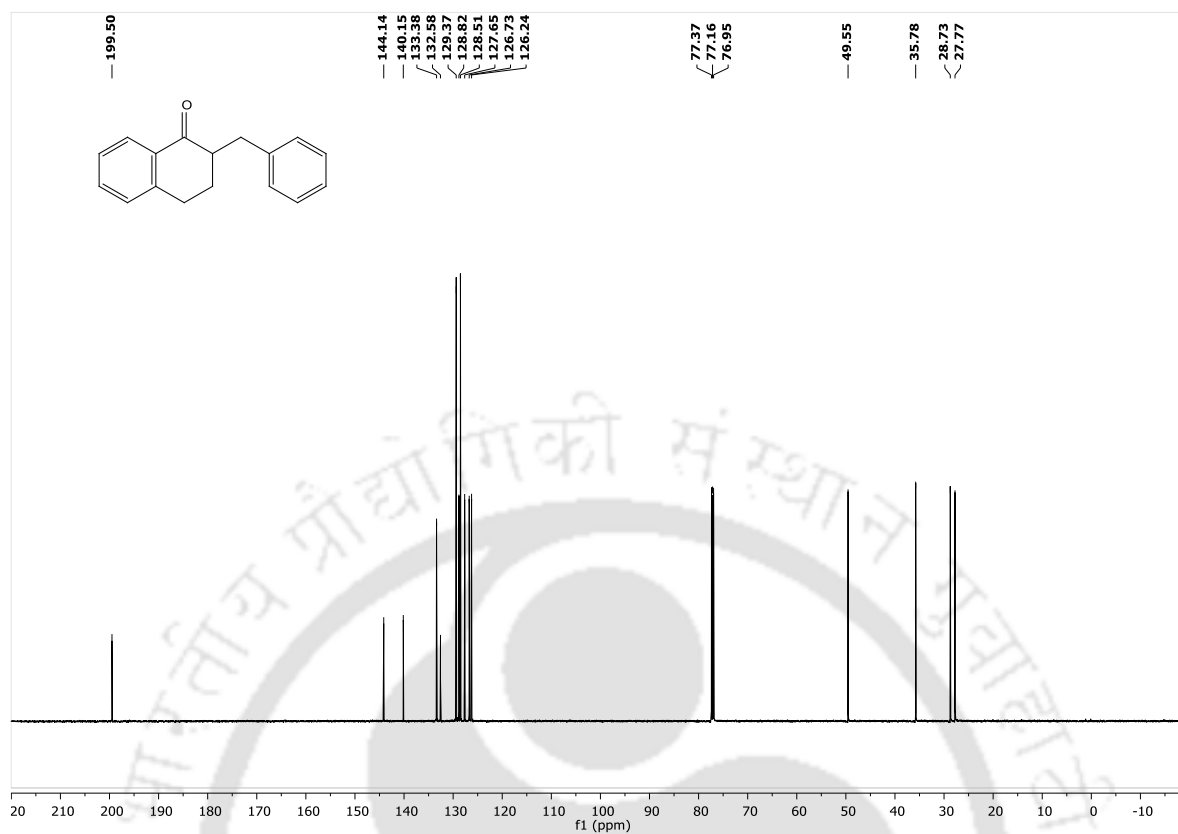


Figure S85: ^{13}C NMR Spectrum of **3.3v** (CDCl_3 , 101 MHz, 298 K)

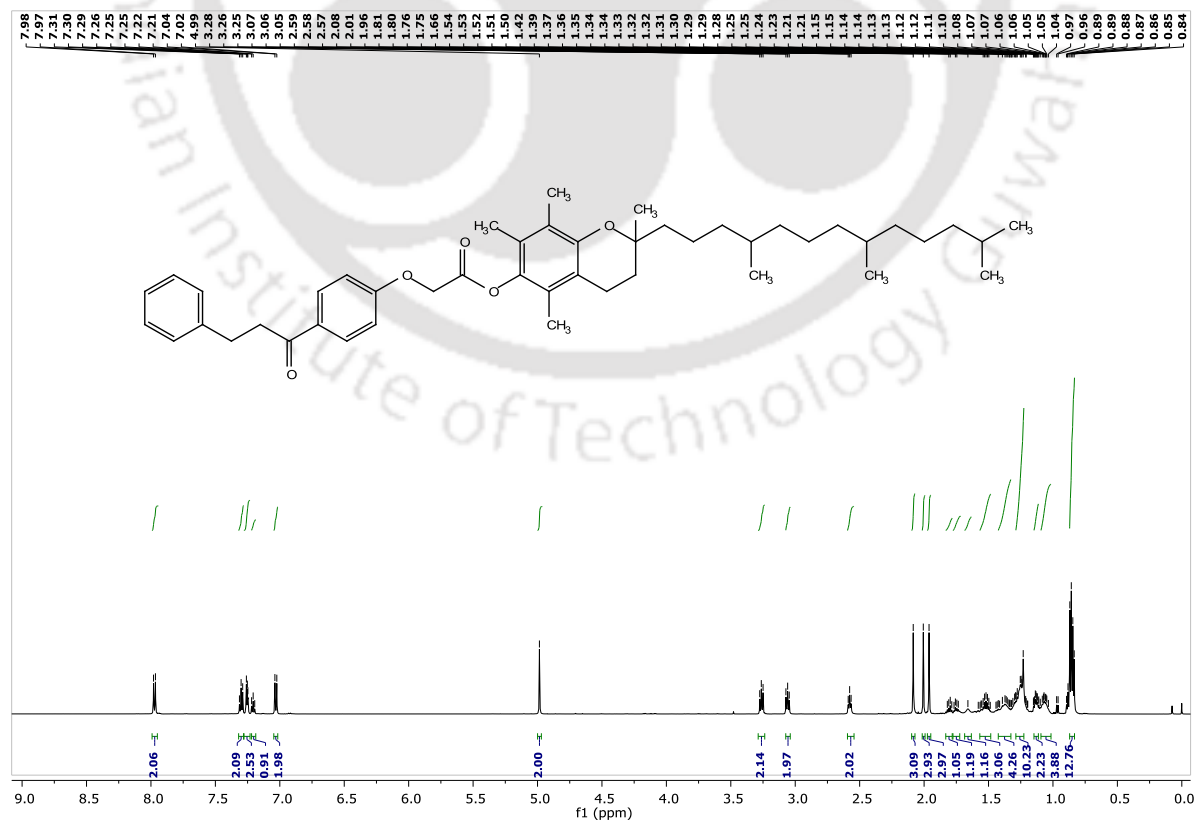


Figure S86: ^1H NMR Spectrum of **3.3w** (CDCl_3 , 400 MHz, 298 K)

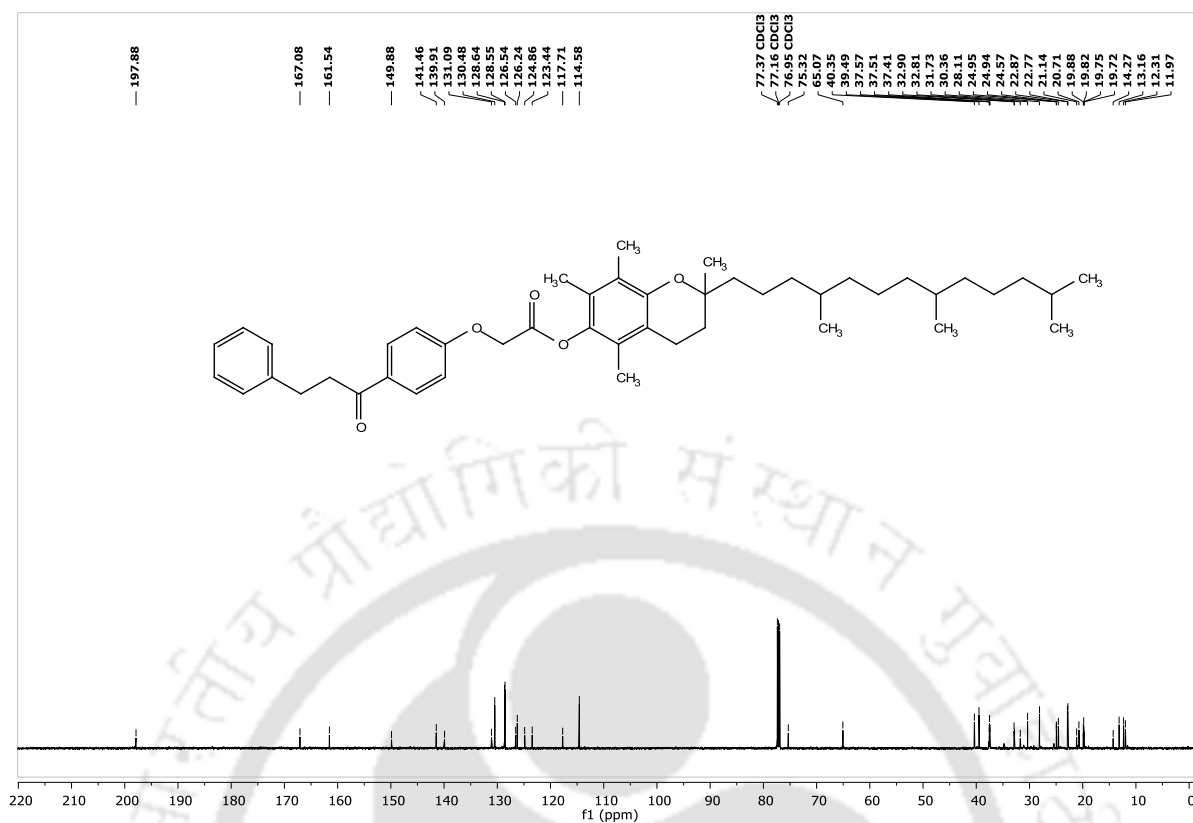


Figure S87: ¹³C NMR Spectrum of **3.3w** (CDCl₃, 101 MHz, 298 K)

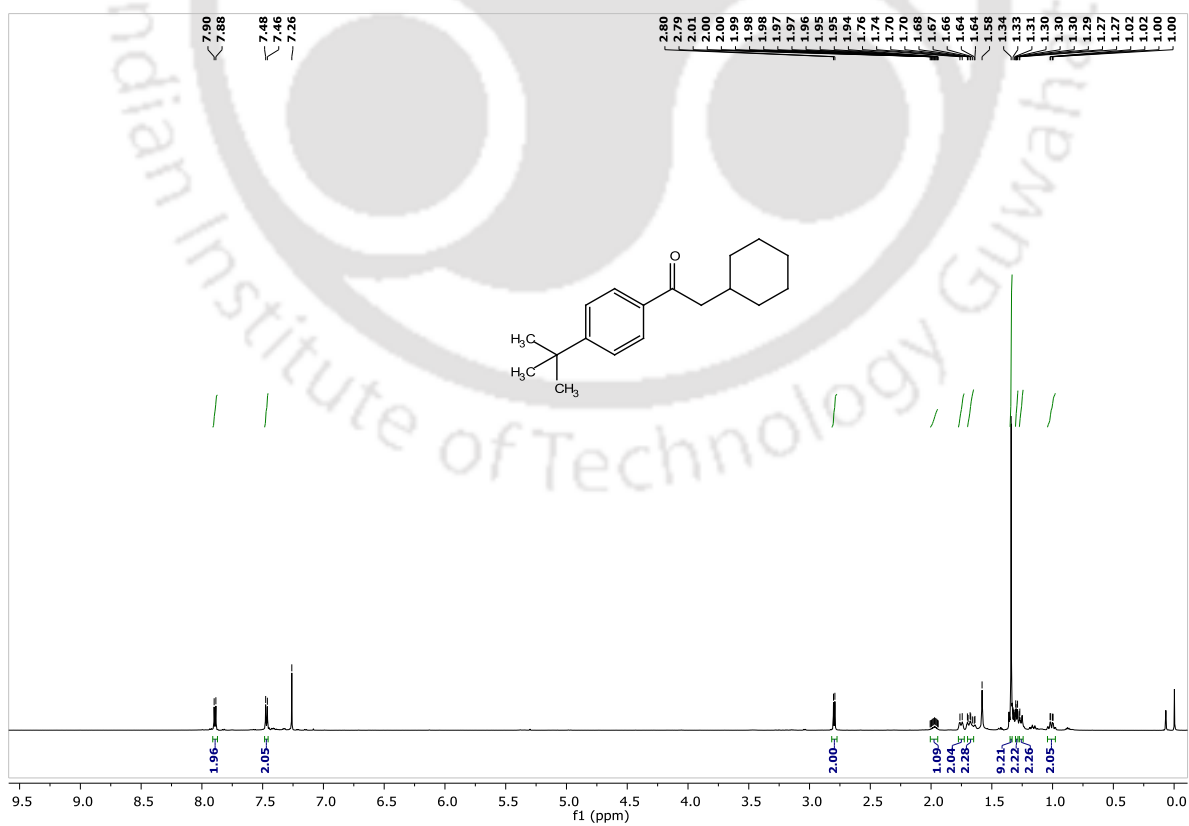


Figure S88: ¹H NMR Spectrum of **3.4a** (CDCl₃, 400 MHz, 298 K)

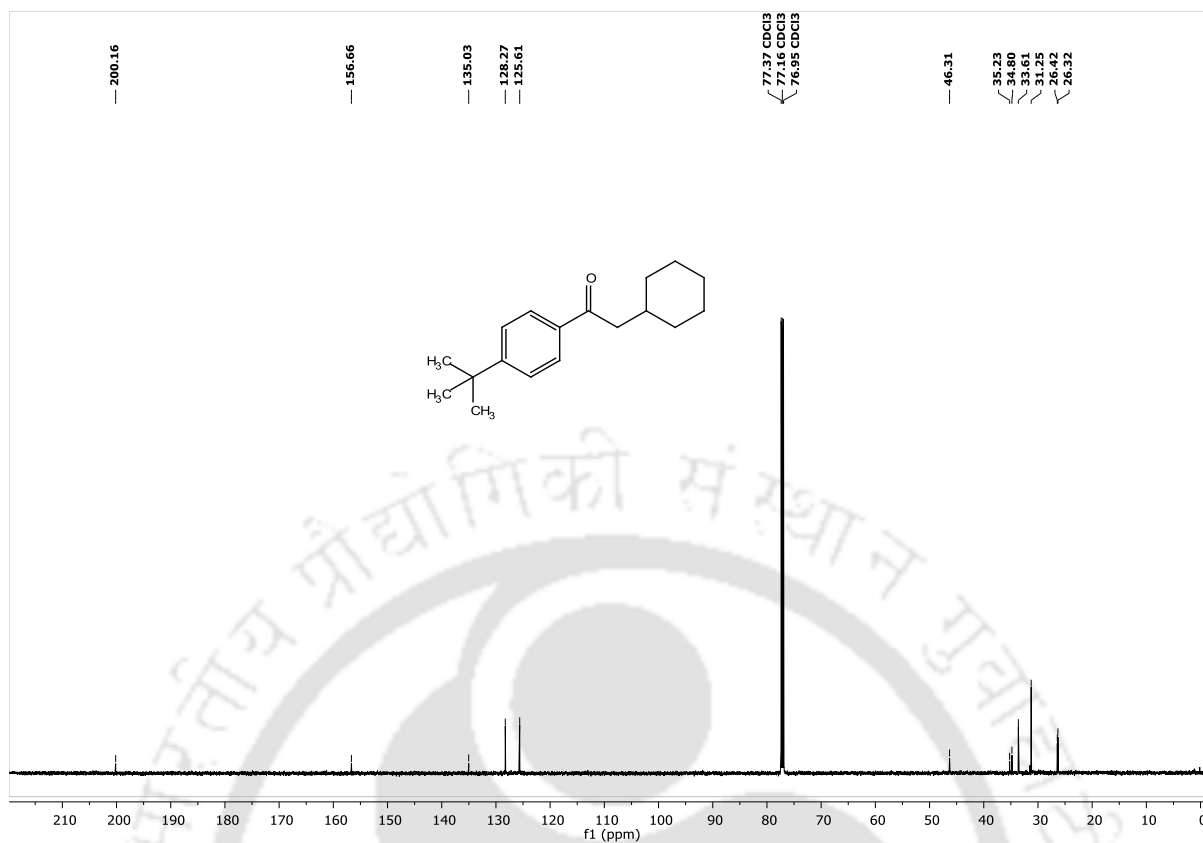


Figure S89: ^{13}C NMR Spectrum of **3.4a** (CDCl_3 , 101 MHz, 298 K)

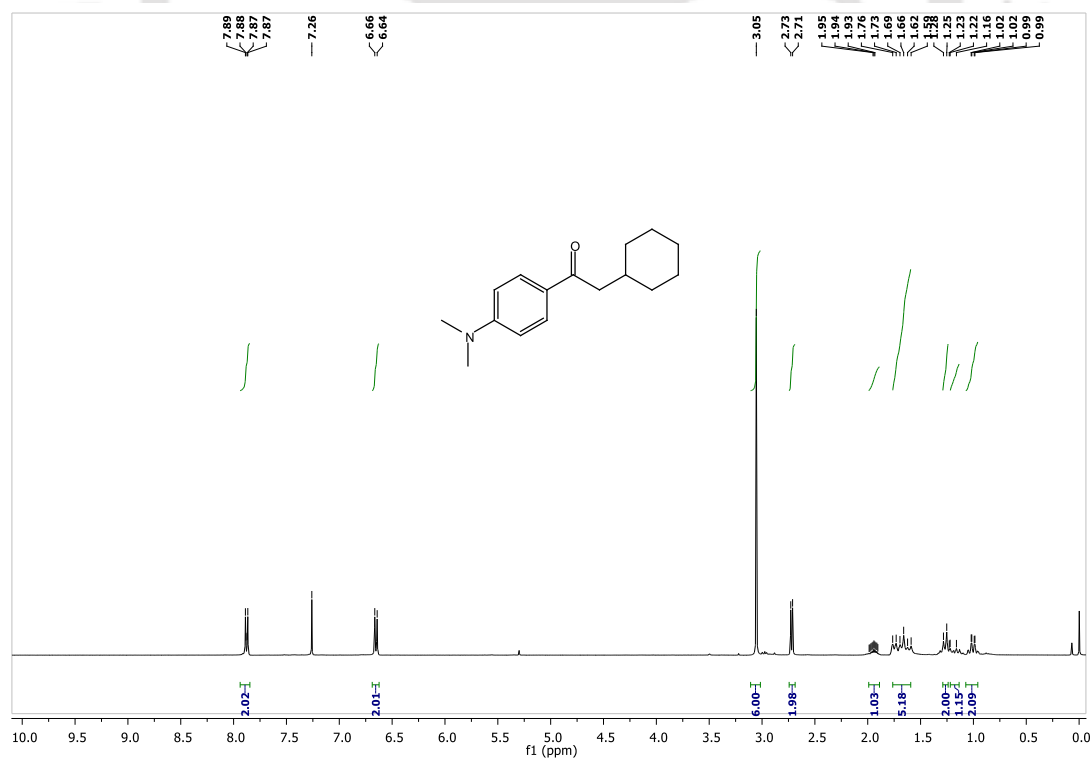


Figure S90: ^1H NMR Spectrum of **3.4b** (CDCl_3 , 400 MHz, 298 K)

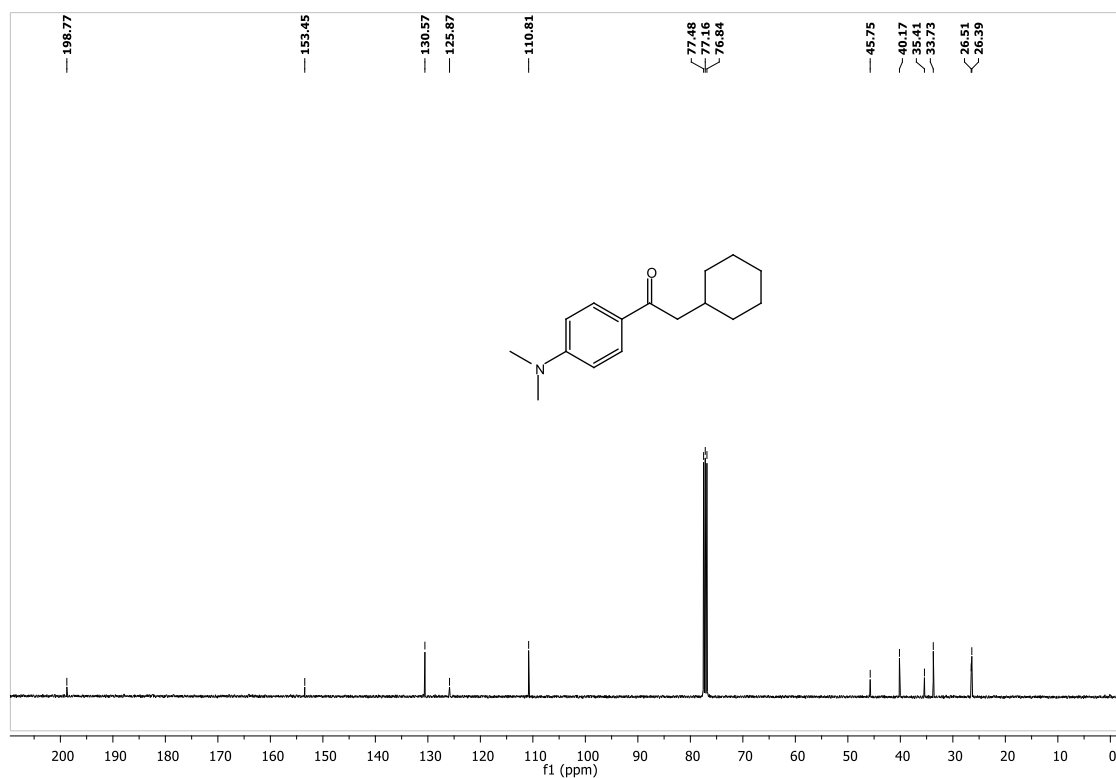


Figure S91: ¹³C NMR Spectrum of **3.4b** (CDCl₃, 101 MHz, 298 K)

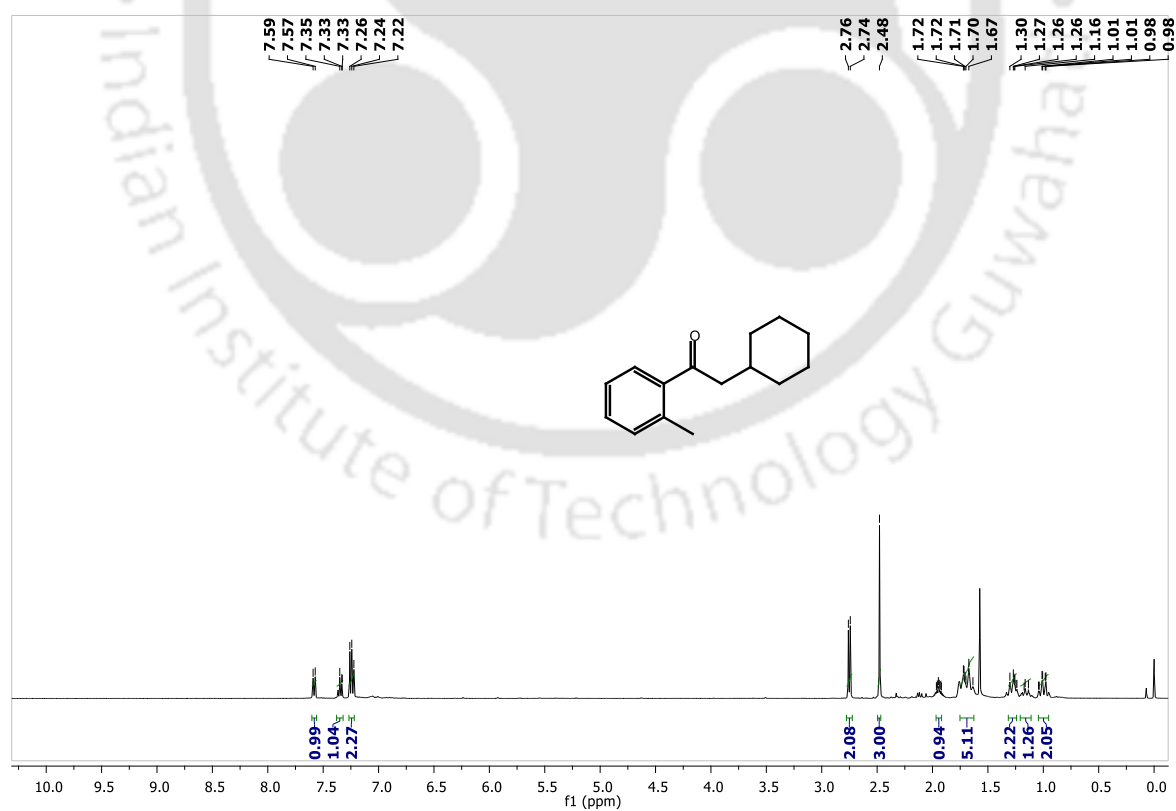


Figure S92: ¹H NMR Spectrum of **3.4c** (CDCl₃, 400 MHz, 298 K)

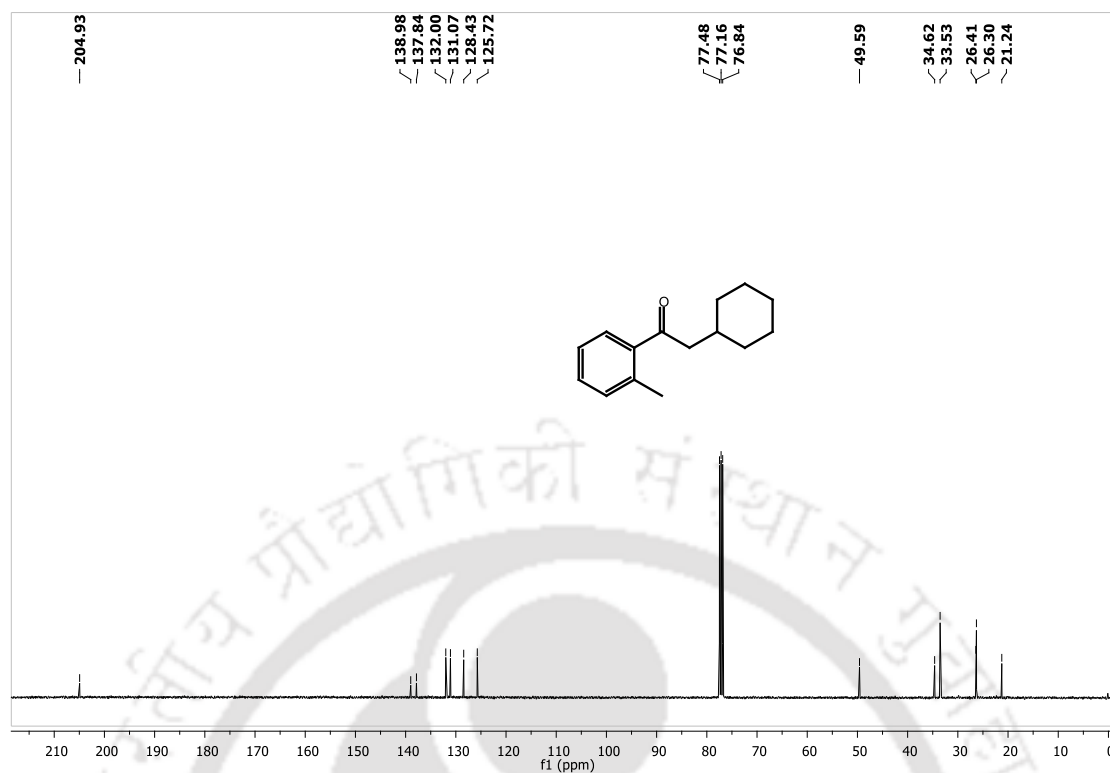


Figure S93: ¹³C NMR Spectrum of 3.4c (CDCl₃, 101 MHz, 298 K)

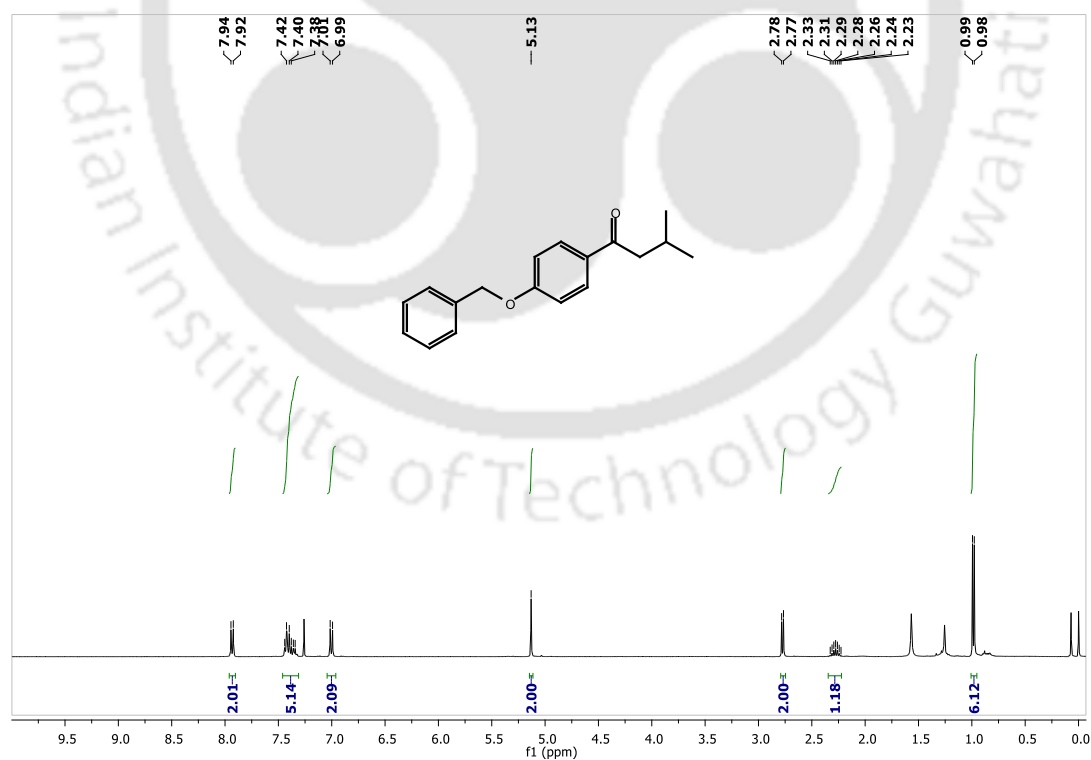


Figure S94: ¹H NMR Spectrum of 3.4d (CDCl₃, 400 MHz, 298 K)

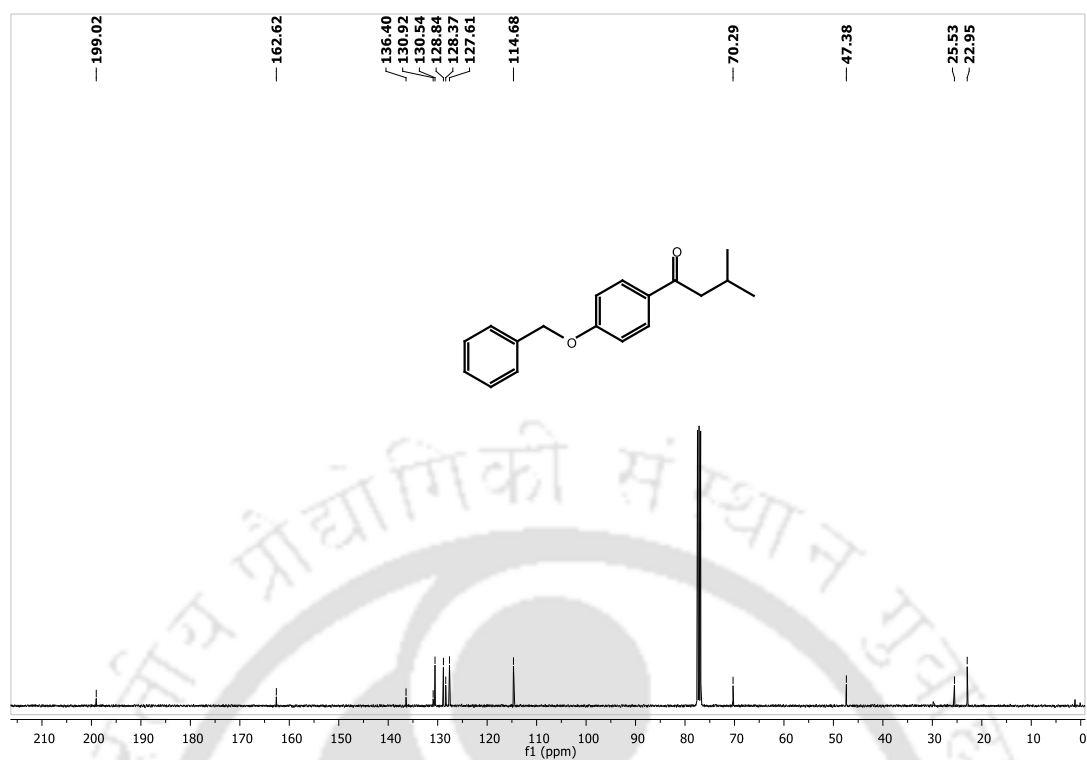


Figure S95: ¹³C NMR Spectrum of 3.4d (CDCl₃, 101 MHz, 298 K)

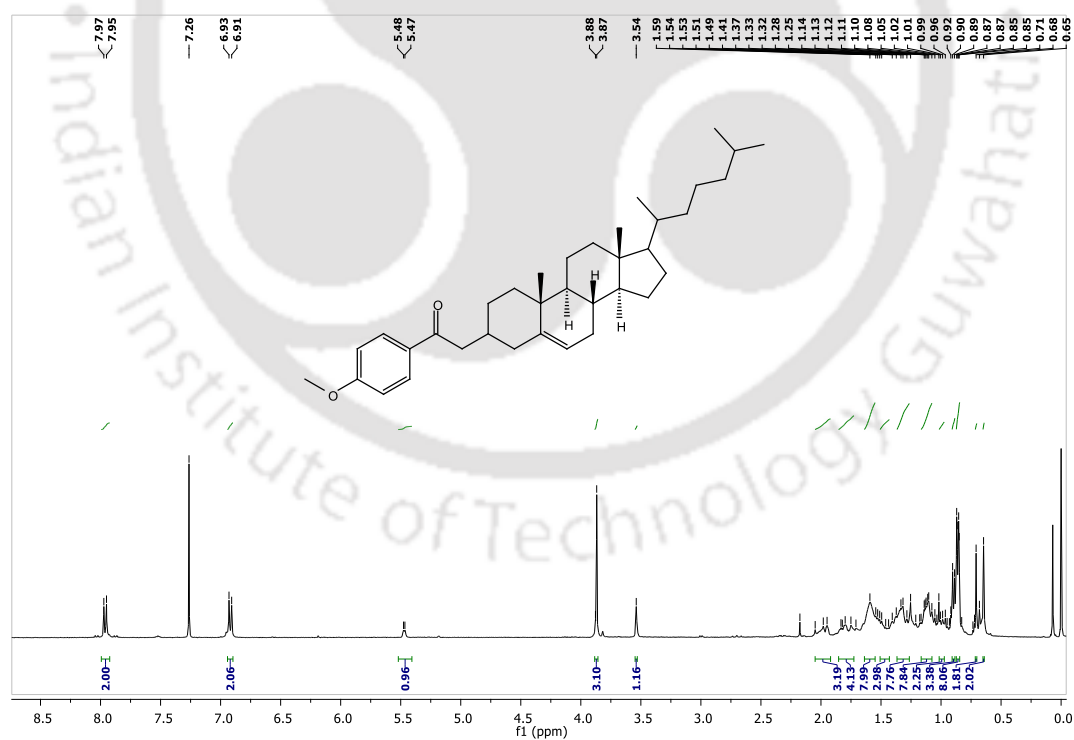


Figure S96: ¹H NMR Spectrum of 3.4e (CDCl₃, 400 MHz, 298 K)

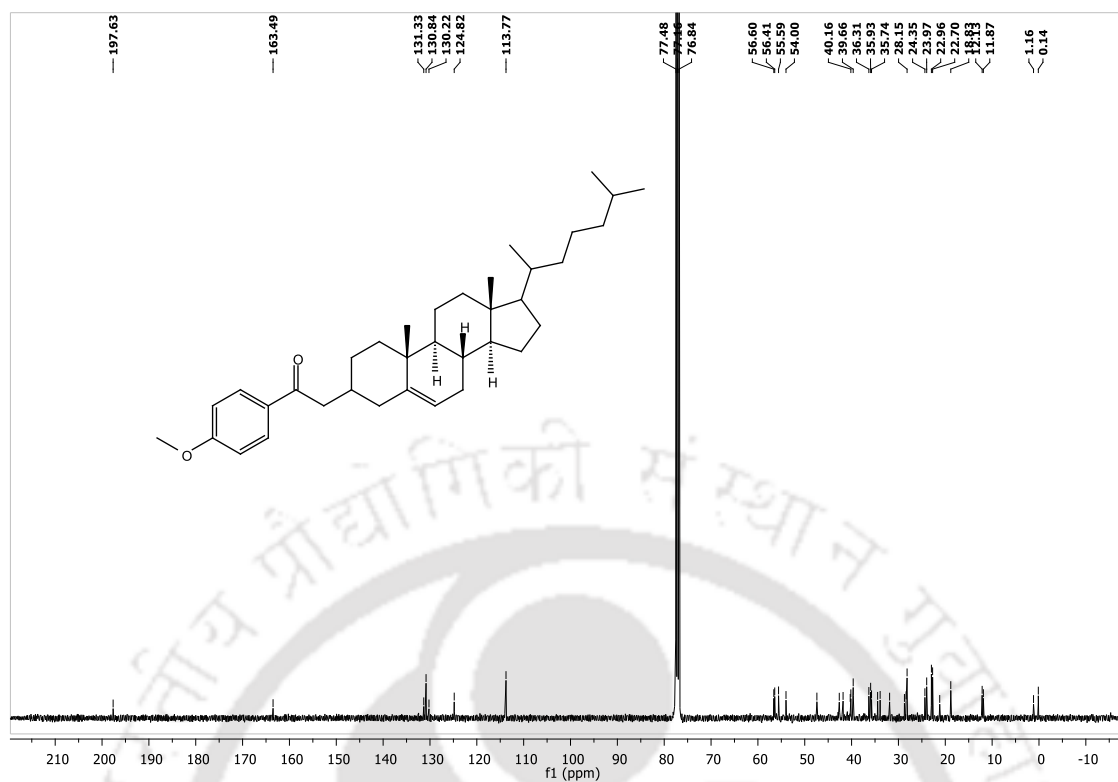


Figure S97: ^{13}C NMR Spectrum of **3.4e** (CDCl_3 , 101 MHz, 298 K)

Annexure III

^1H , ^{13}C , and ^{19}F NMR spectra of the products (*Chapter 4*)

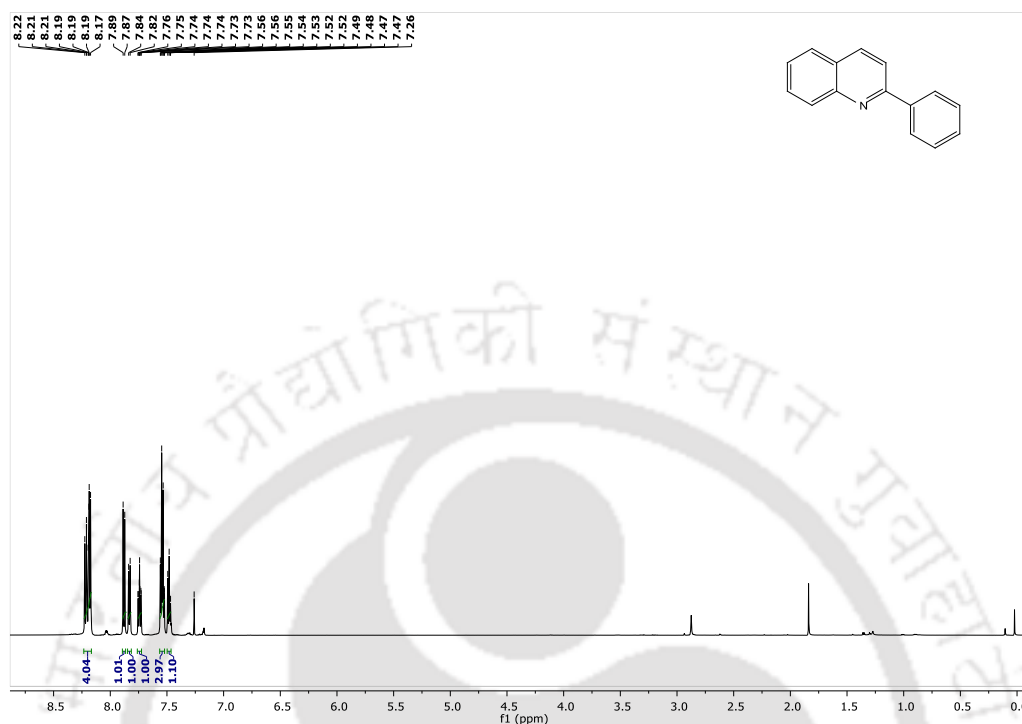


Figure S98: ^1H NMR Spectrum of **4.3a** (CDCl_3 , 400 MHz, 298 K)

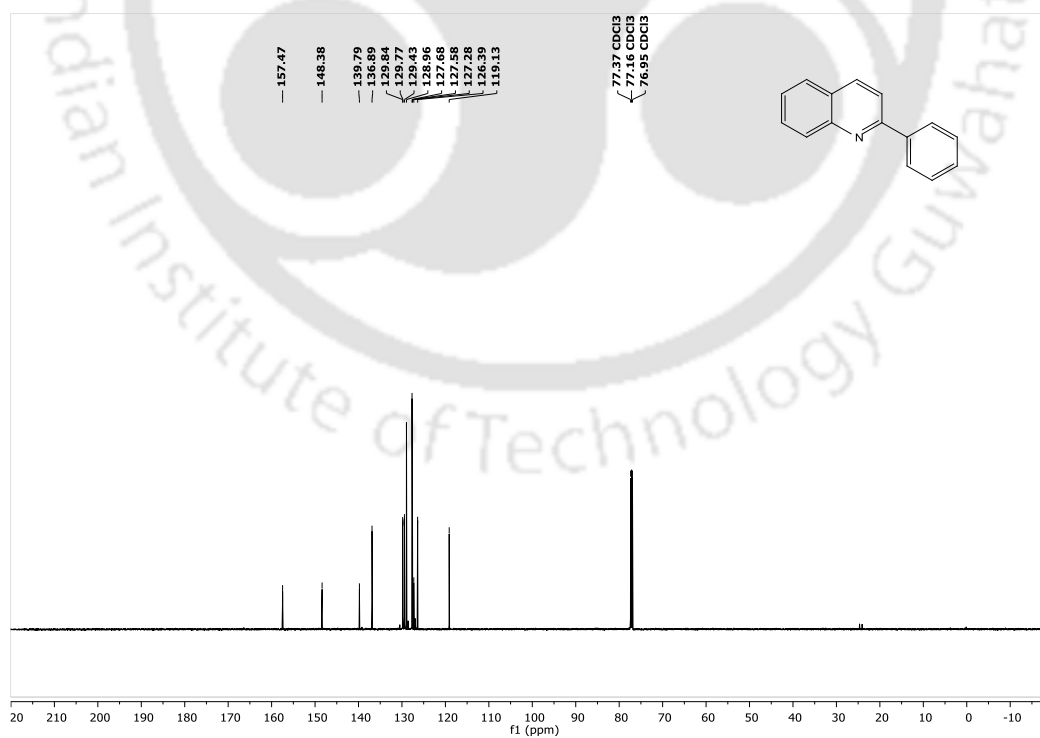


Figure S99: ^{13}C NMR Spectrum of **4.3a** (CDCl_3 , 151 MHz, 298 K)

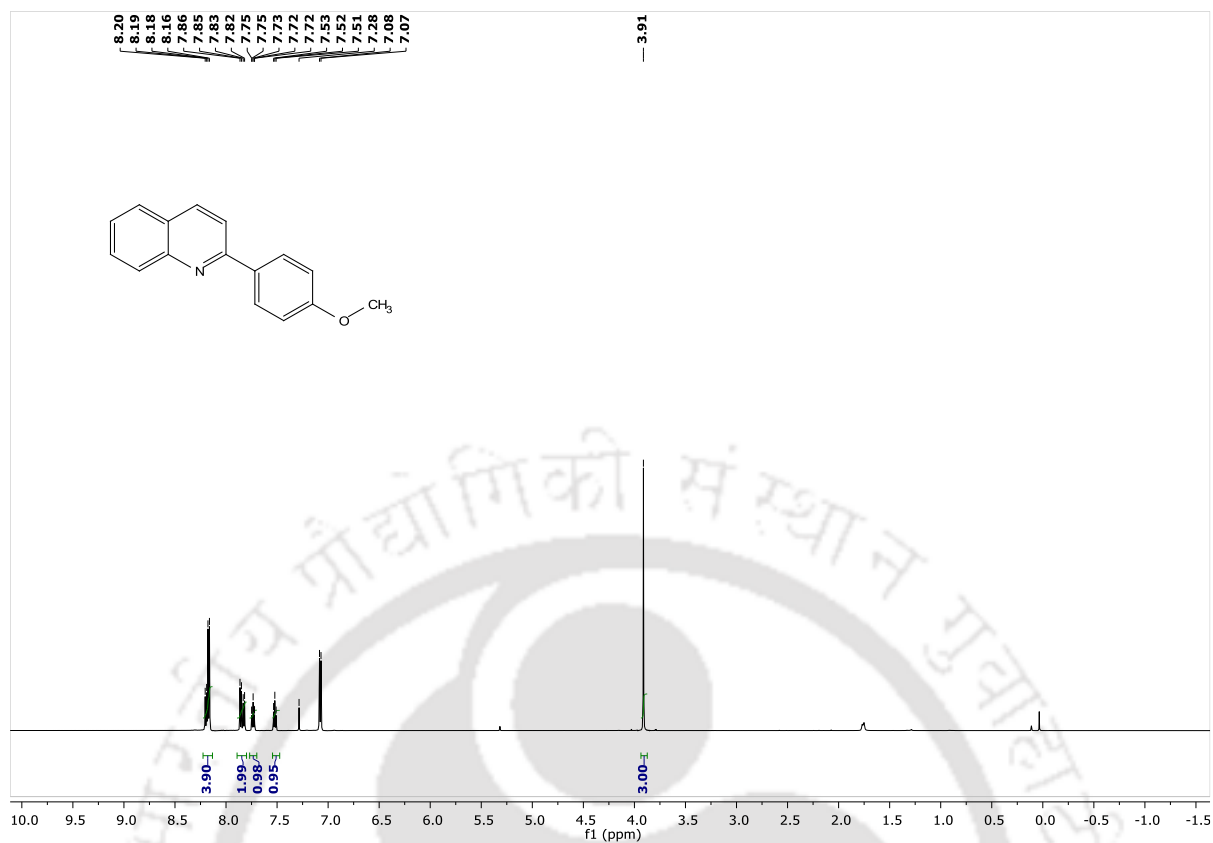


Figure S100: ¹H NMR Spectrum of **4.3b** (CDCl₃, 400 MHz, 298 K)

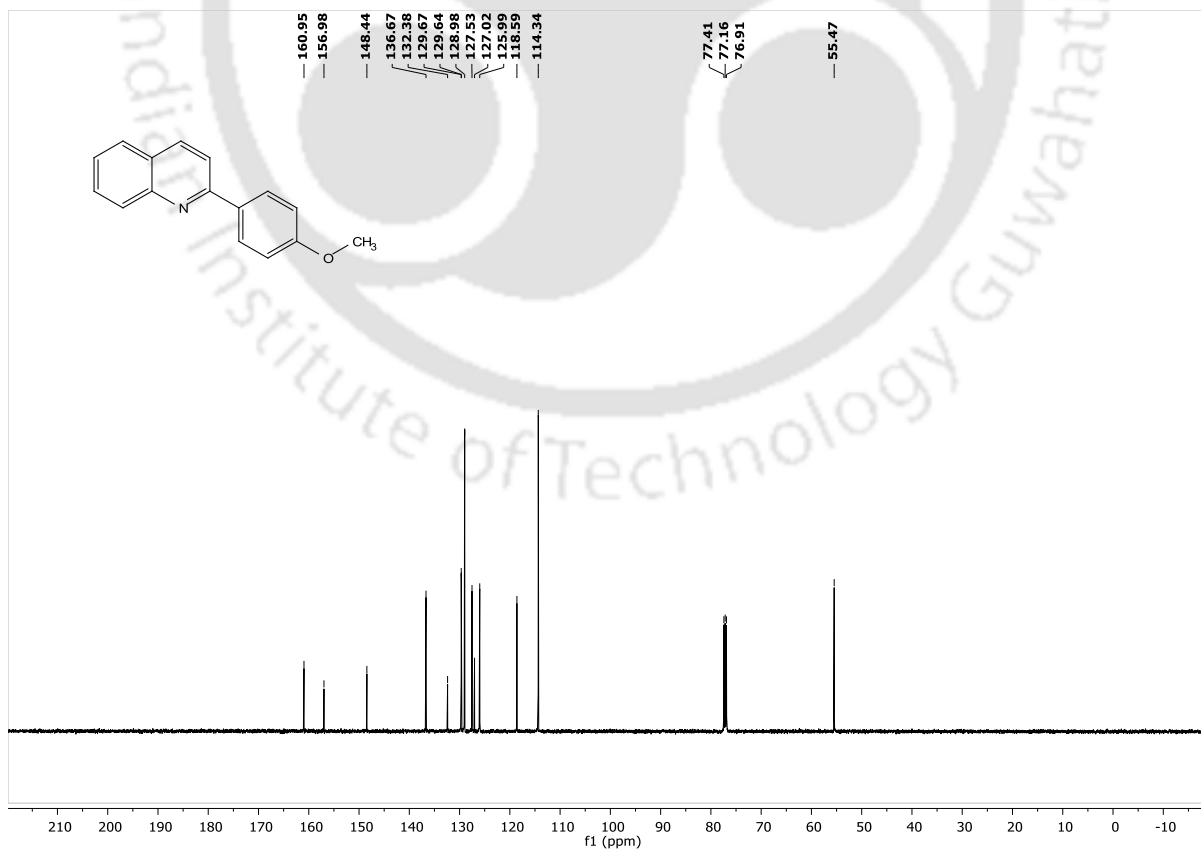
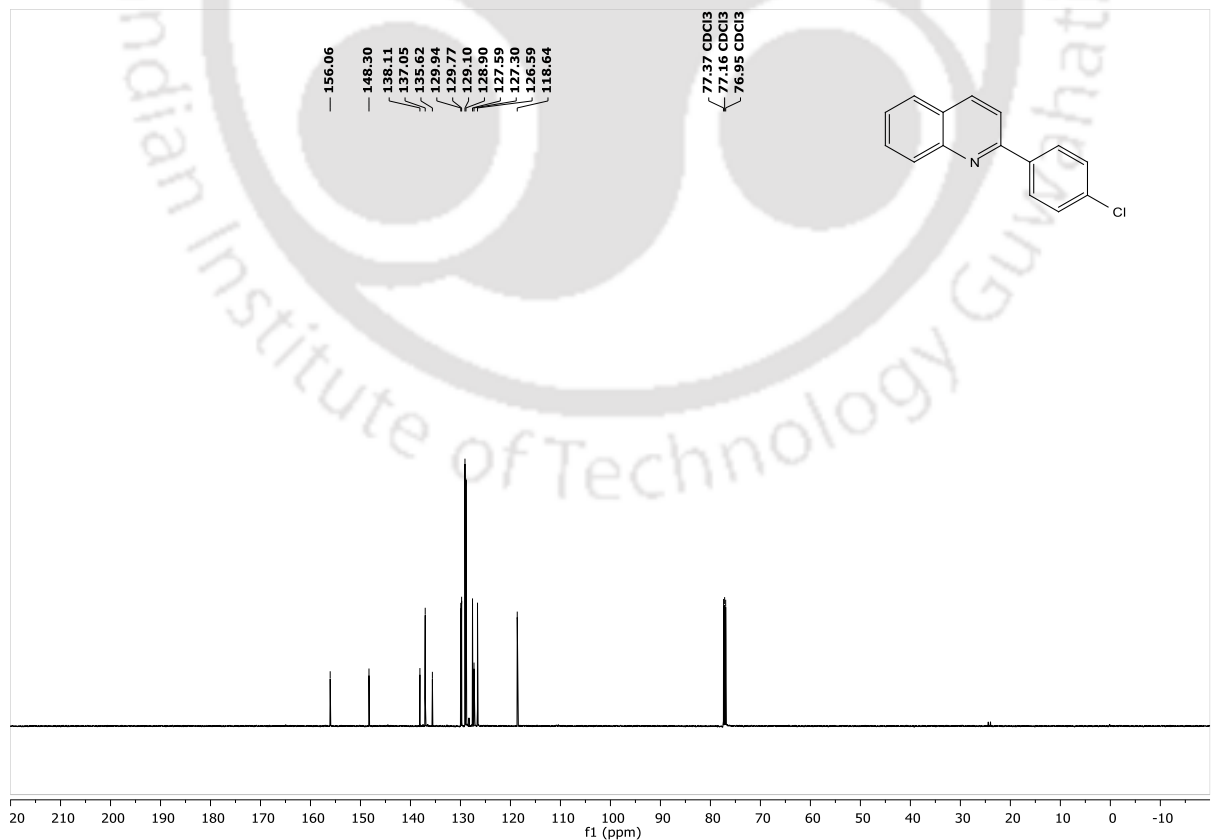
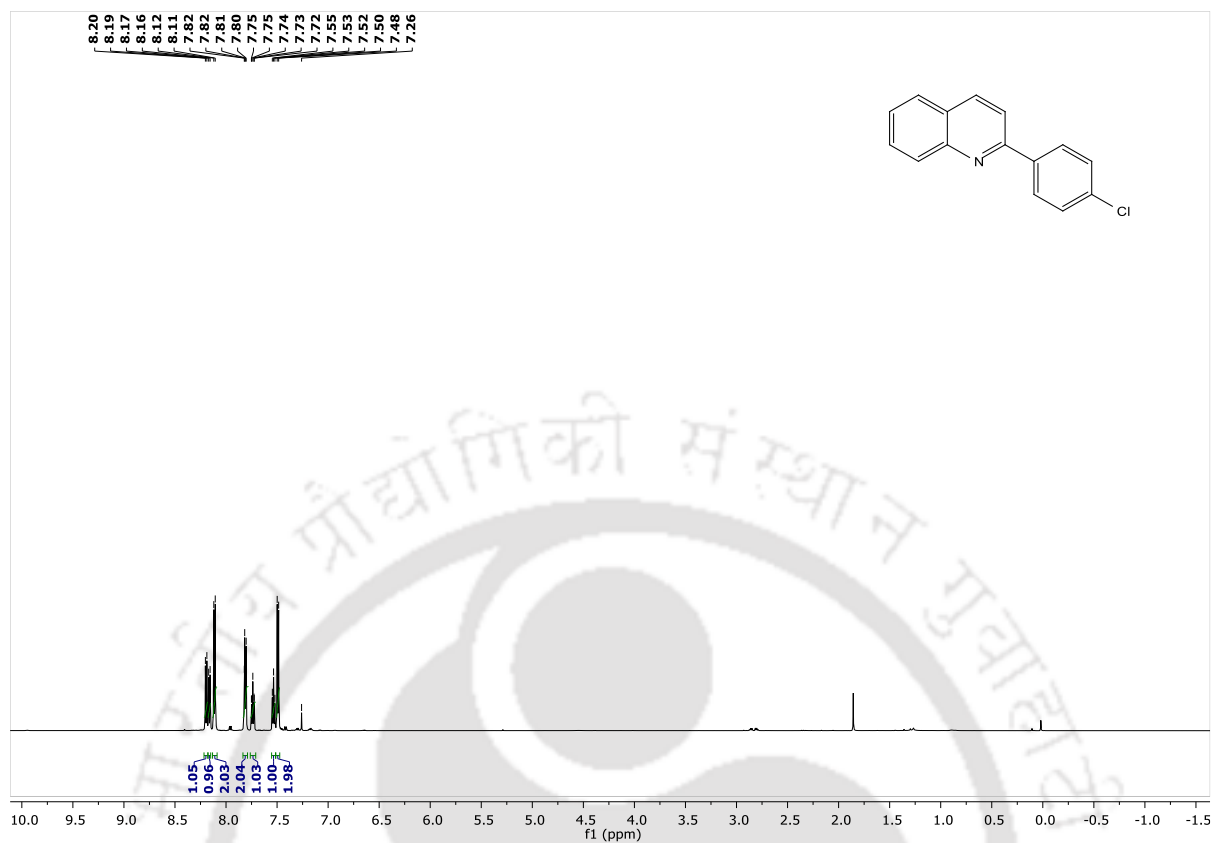


Figure S101: ¹³C NMR Spectrum of **4.3b** (CDCl₃, 101 MHz, 298 K)



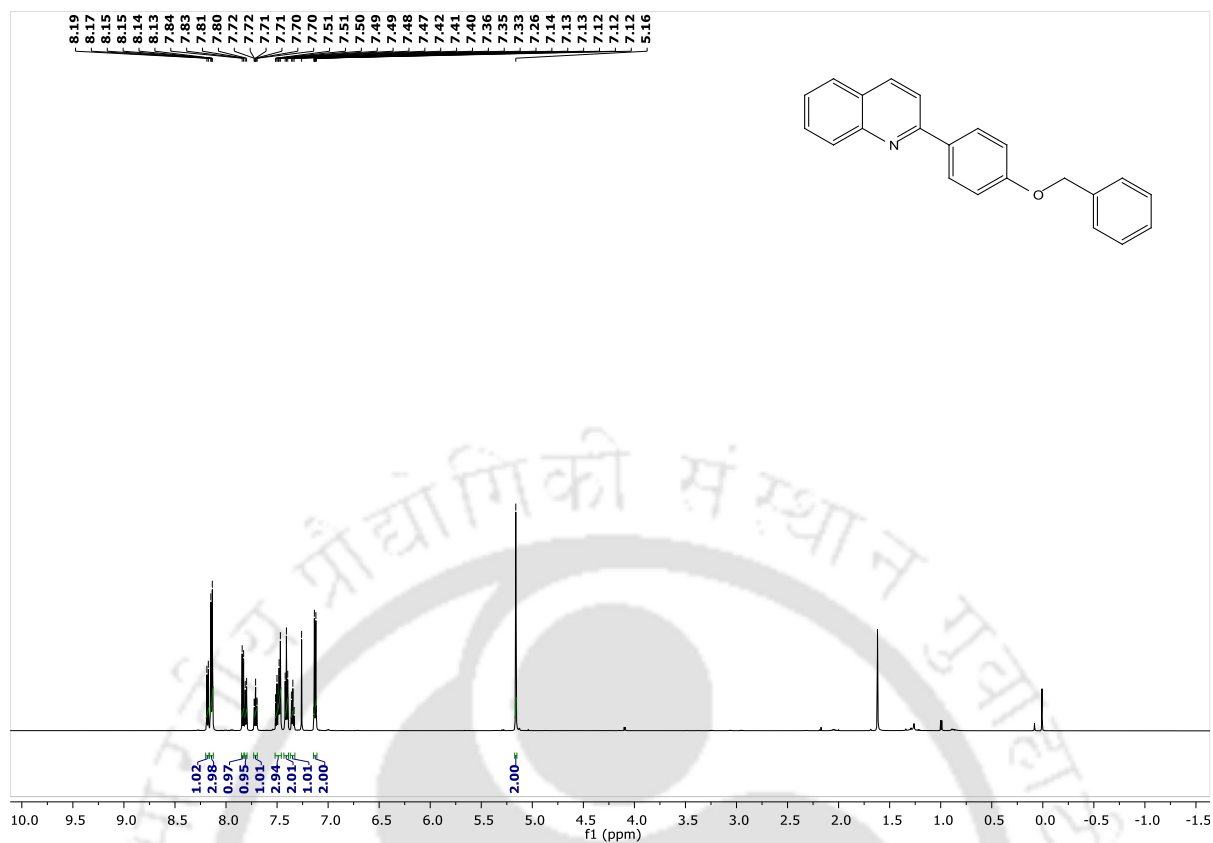


Figure S104: ¹H NMR Spectrum of **4.3d** (CDCl₃, 600 MHz, 298 K)

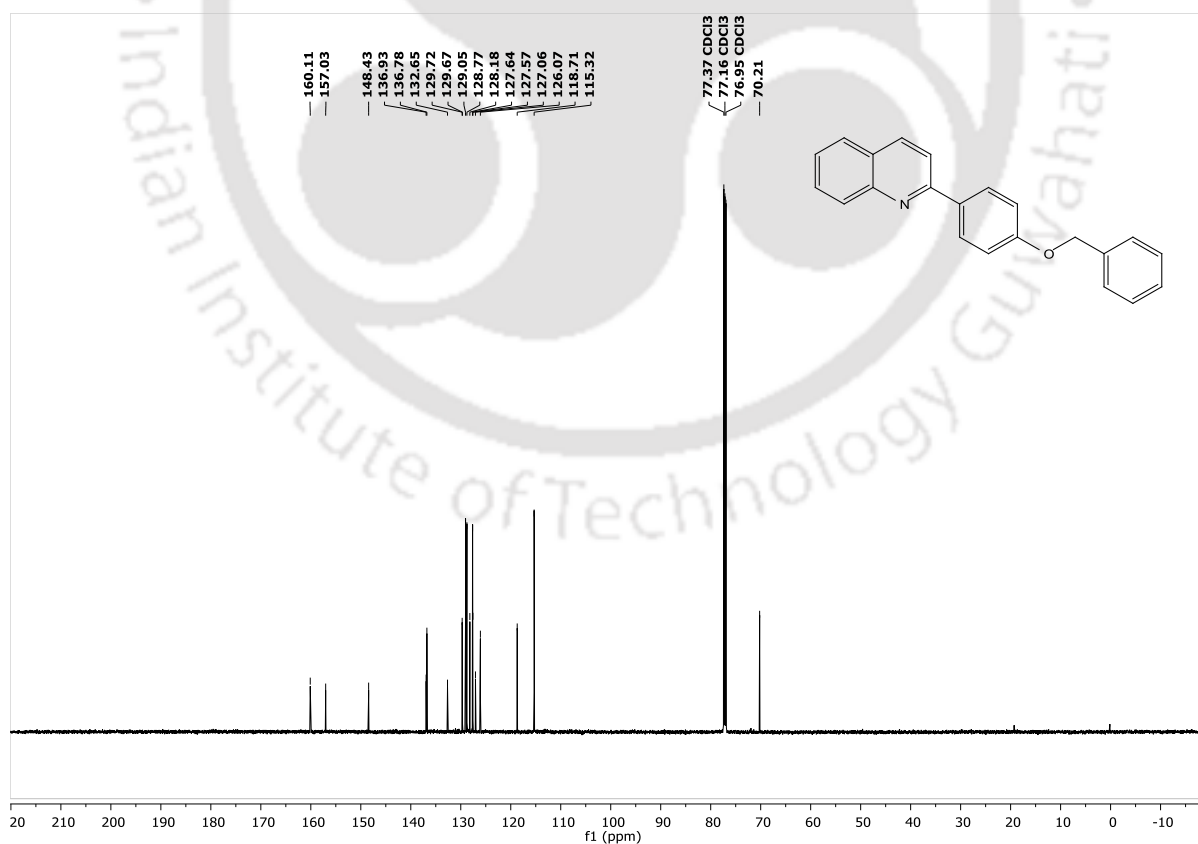


Figure S105: ¹³C NMR Spectrum of **4.3d** (CDCl₃, 151 MHz, 298 K)

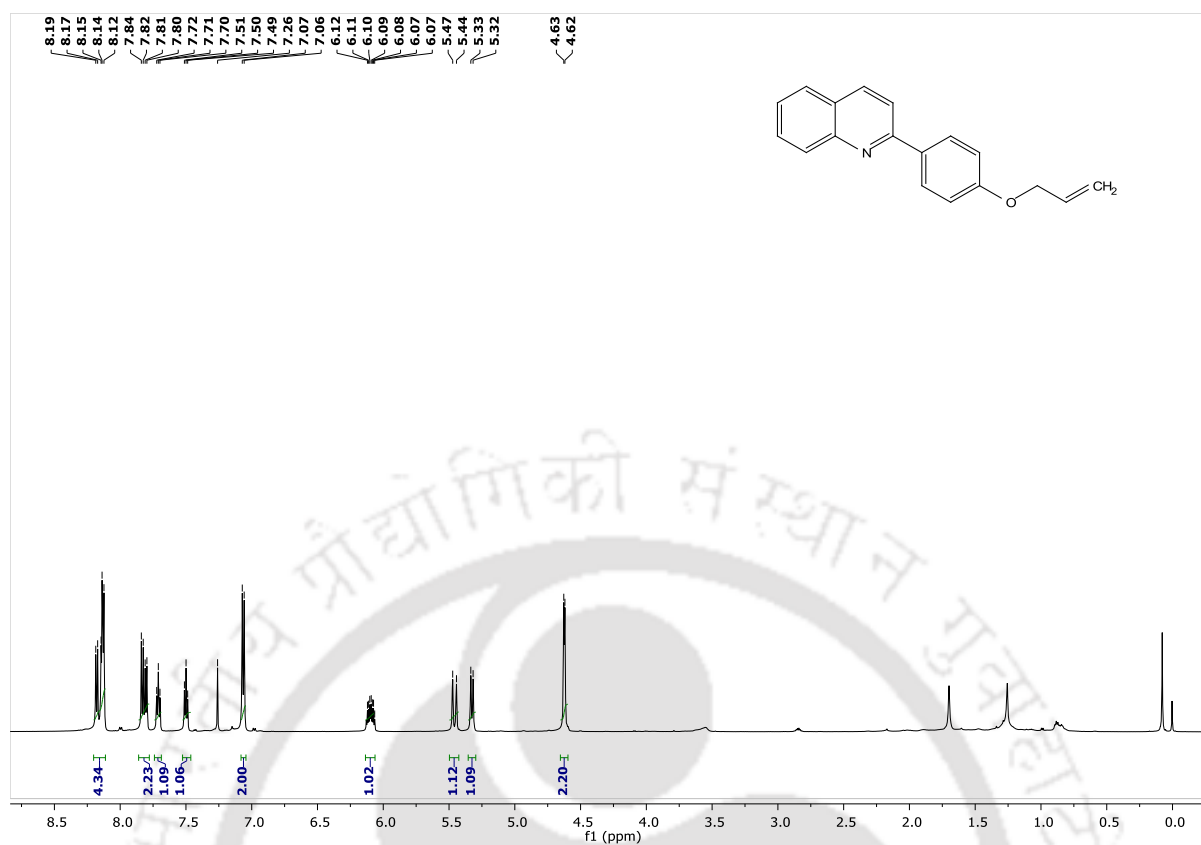


Figure S106: ¹H NMR Spectrum of **4.3e** (CDCl₃, 400 MHz, 298 K)

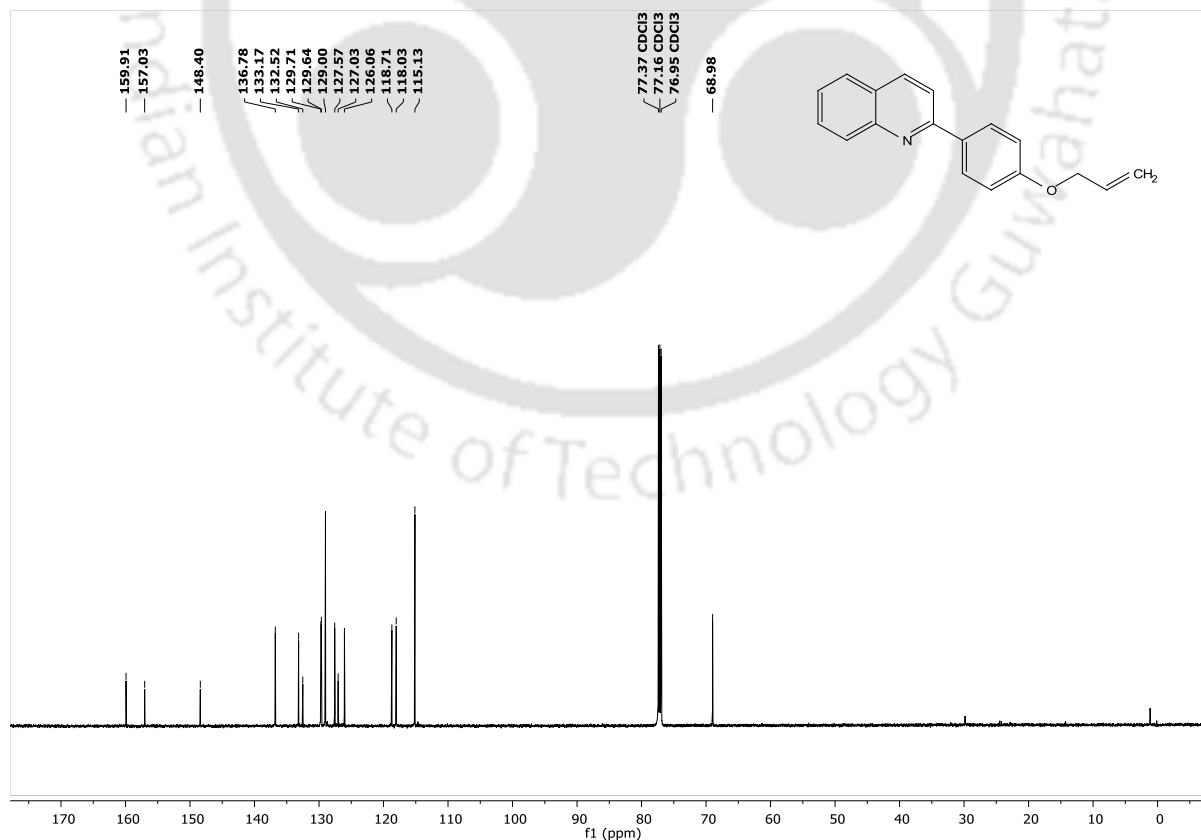


Figure S107: ¹³C NMR Spectrum of **4.3e** (CDCl₃, 101 MHz, 298 K)

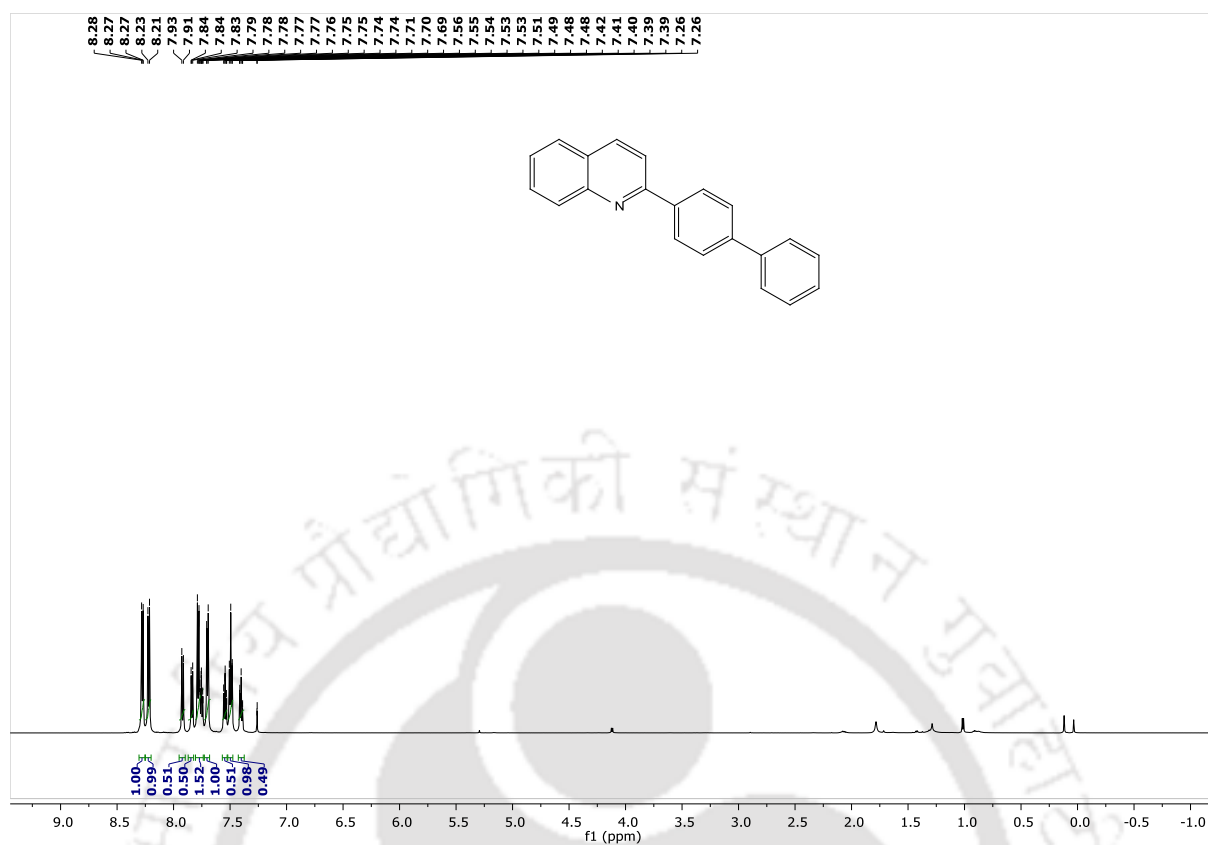


Figure S108: ¹H NMR Spectrum of **4.3f** (CDCl₃, 400 MHz, 298 K)

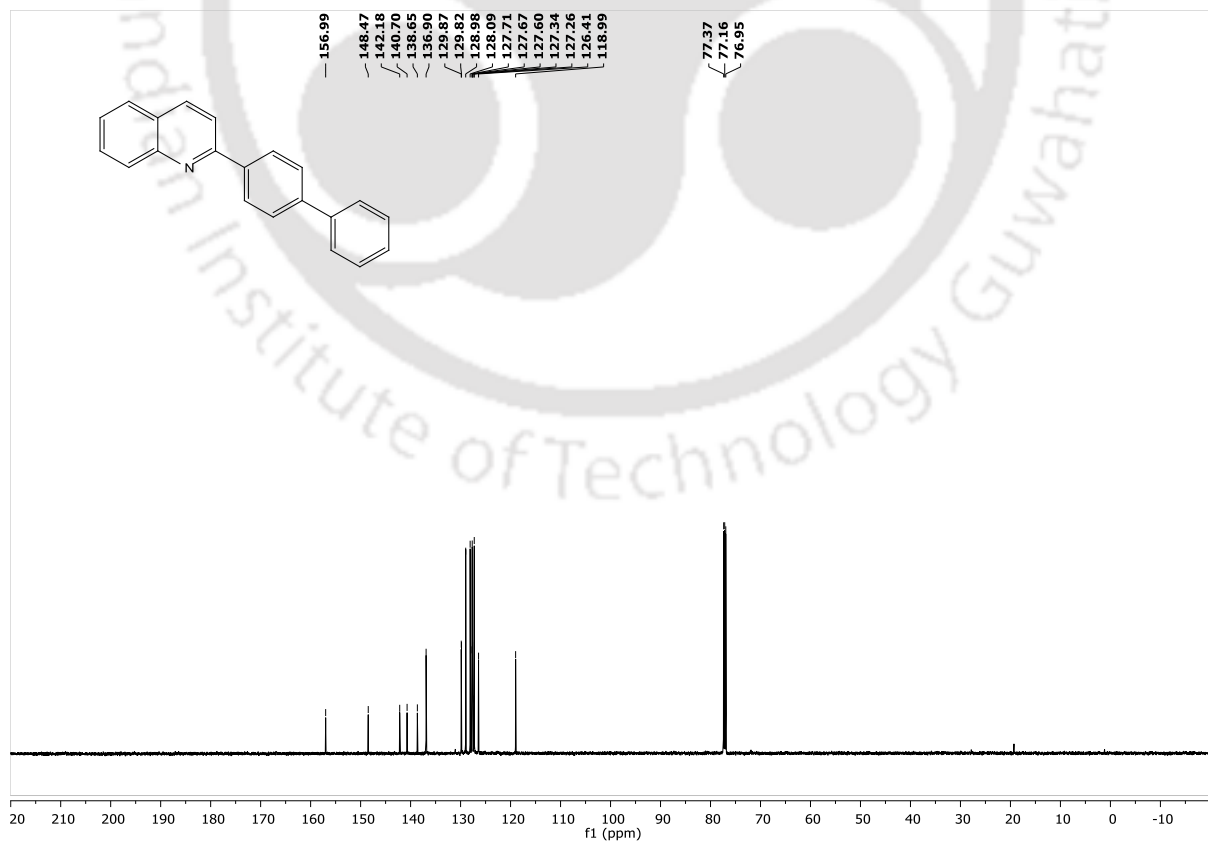


Figure S109: ¹³C NMR Spectrum of **4.3f** (CDCl₃, 101 MHz, 298 K)

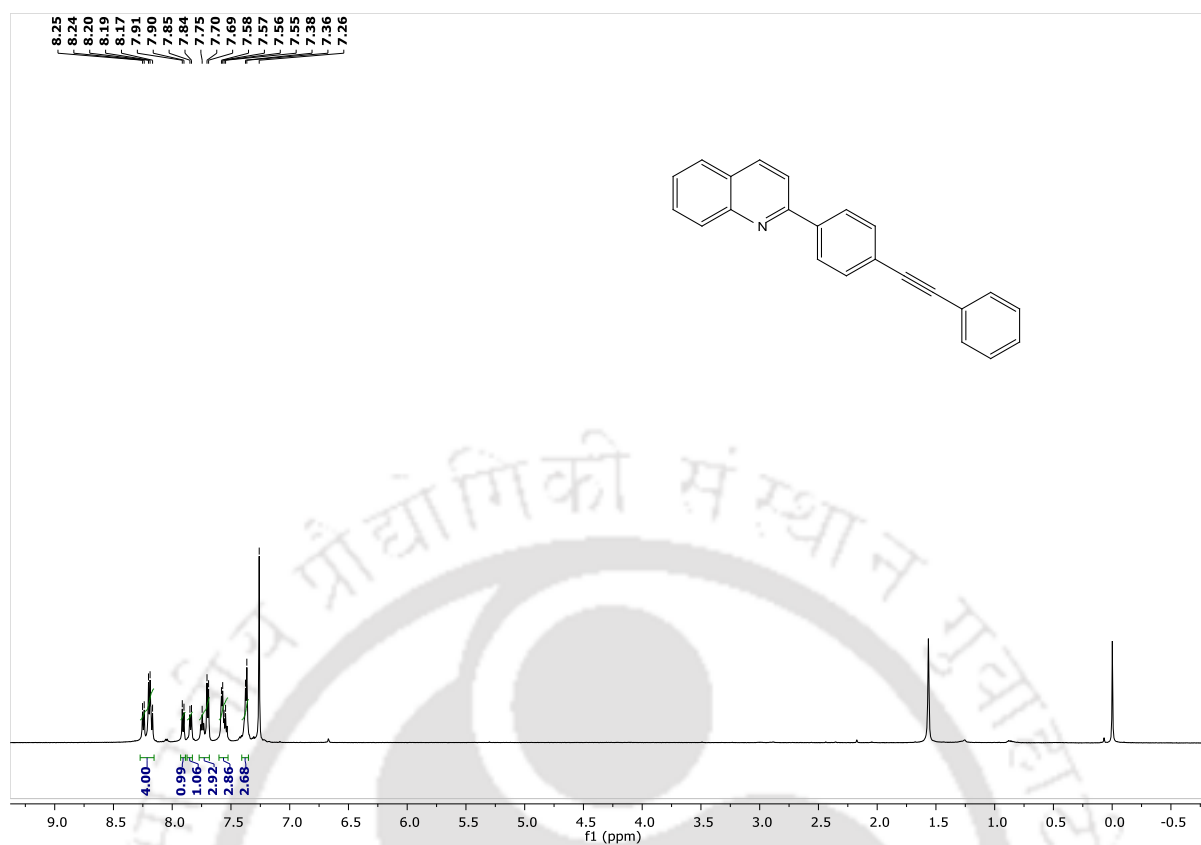


Figure S110: ¹H NMR Spectrum of **4.3g** (CDCl₃, 600 MHz, 298 K)

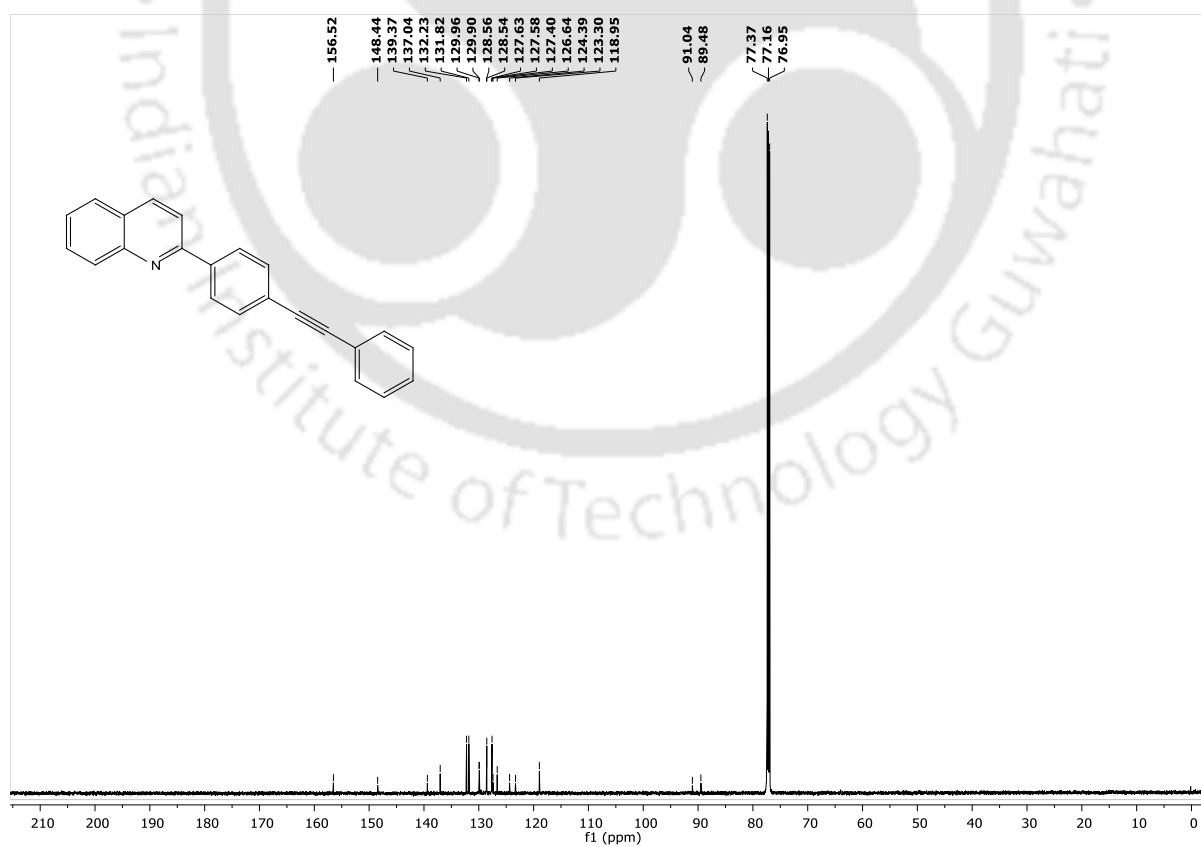


Figure S111: ¹³C NMR Spectrum of **4.3g** (CDCl₃, 151 MHz, 298 K)

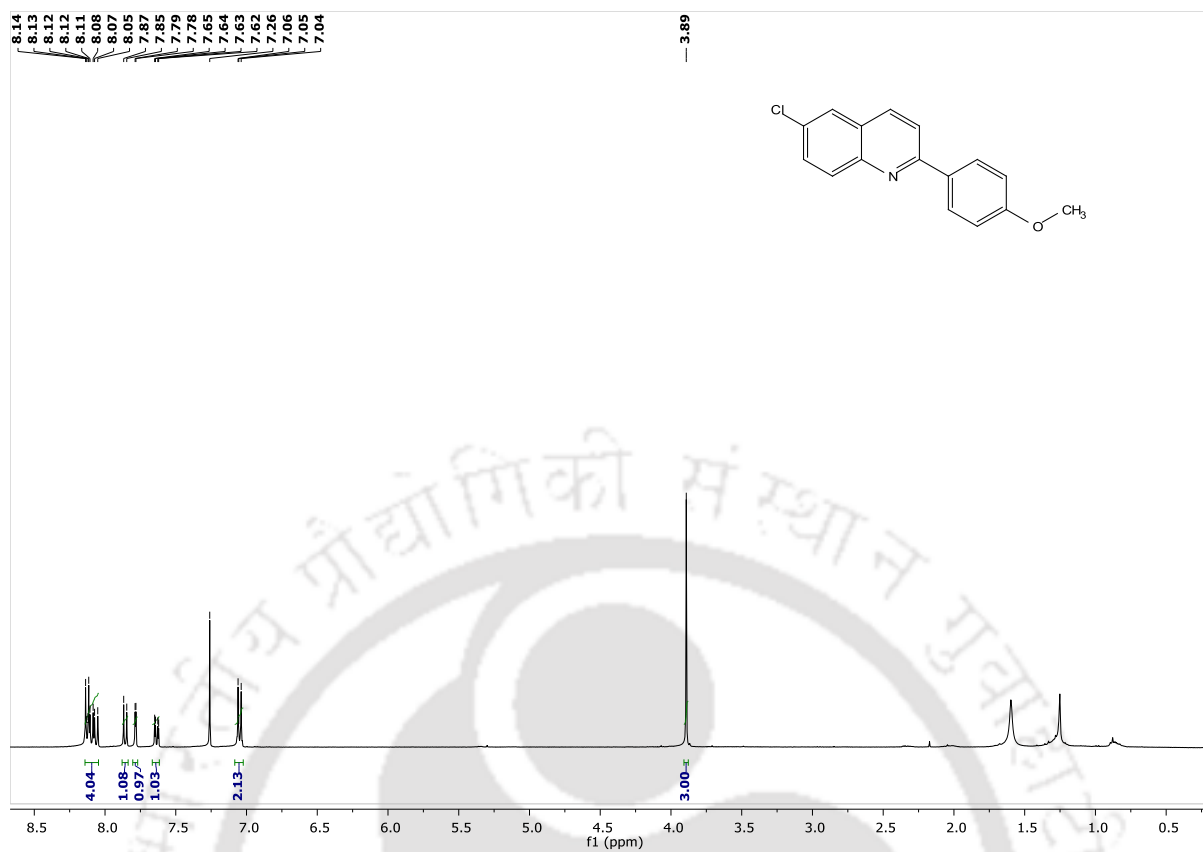


Figure S112: ¹H NMR Spectrum of **4.3h** (CDCl₃, 400 MHz, 298 K)

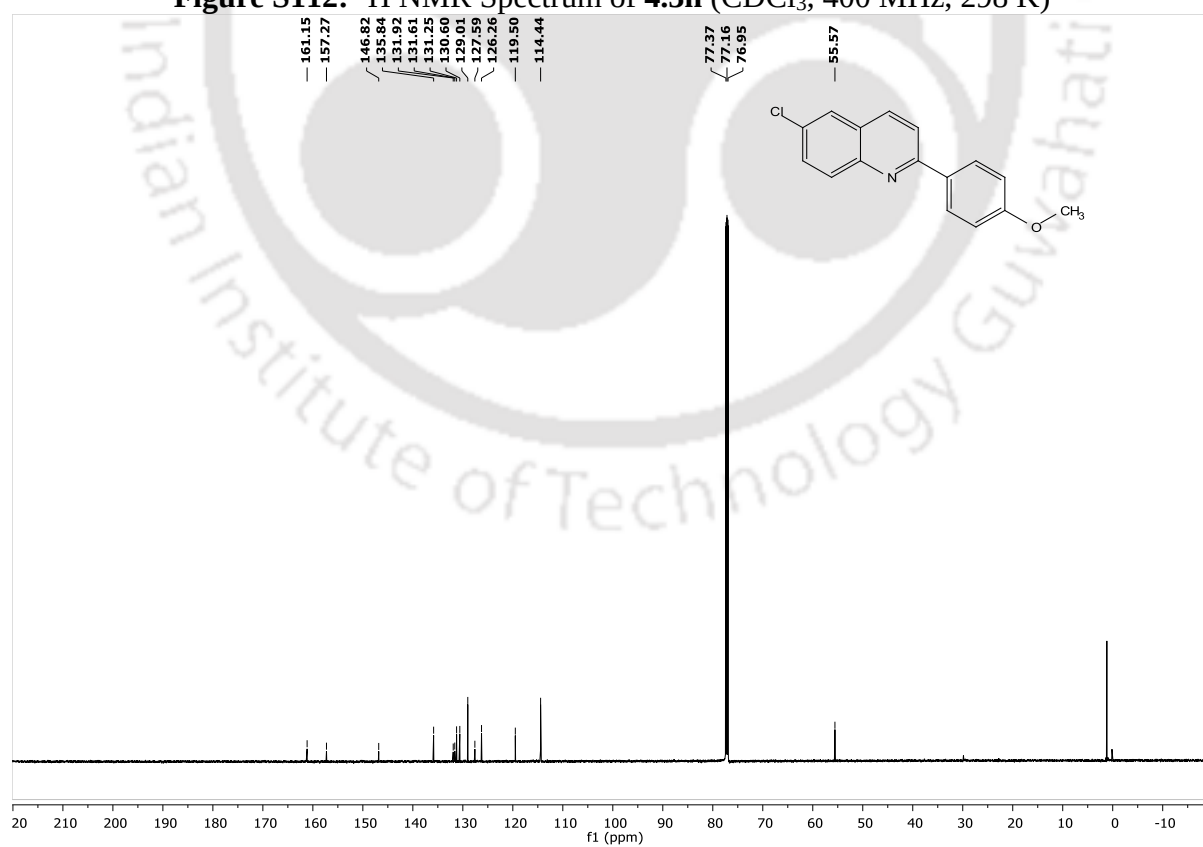


Figure S113: ¹³C NMR Spectrum of **4.3h** (CDCl₃, 151 MHz, 298 K)

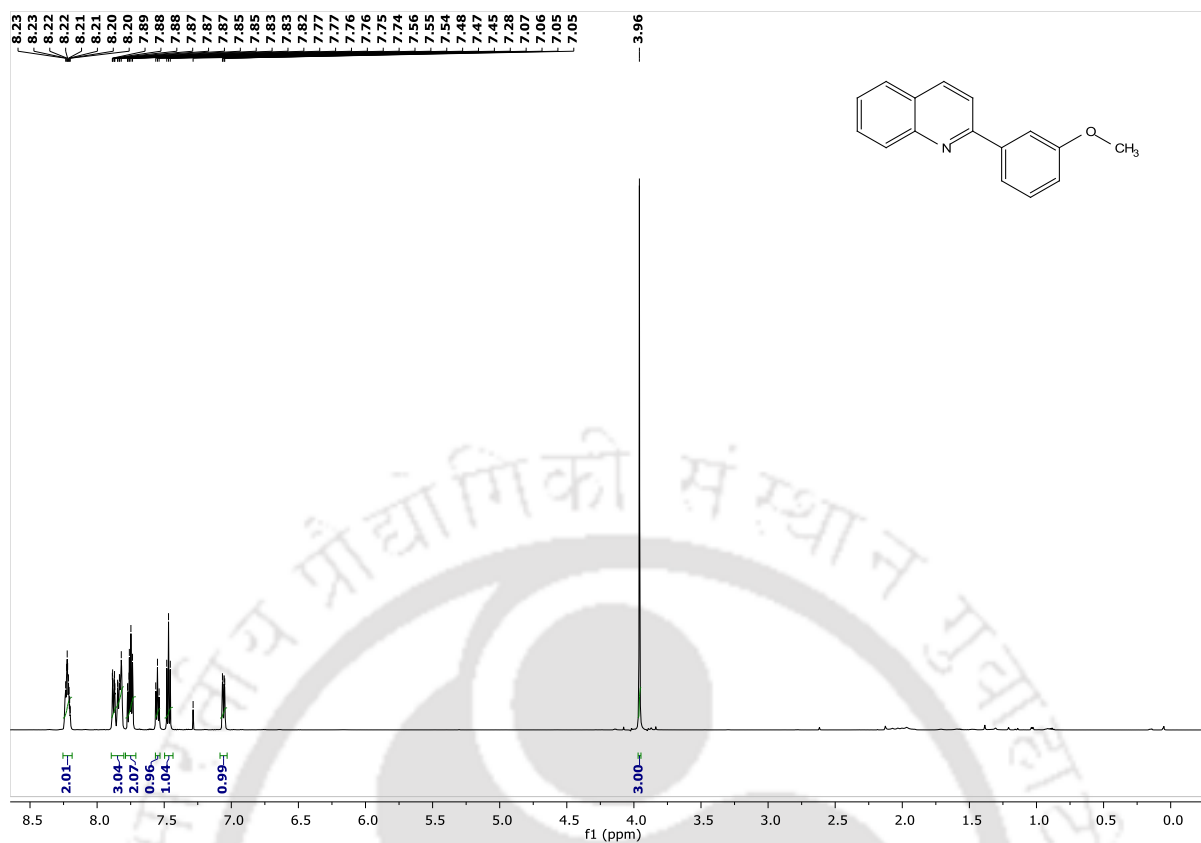


Figure S114: ^1H NMR Spectrum of **4.3i** (CDCl_3 , 600 MHz, 298 K)

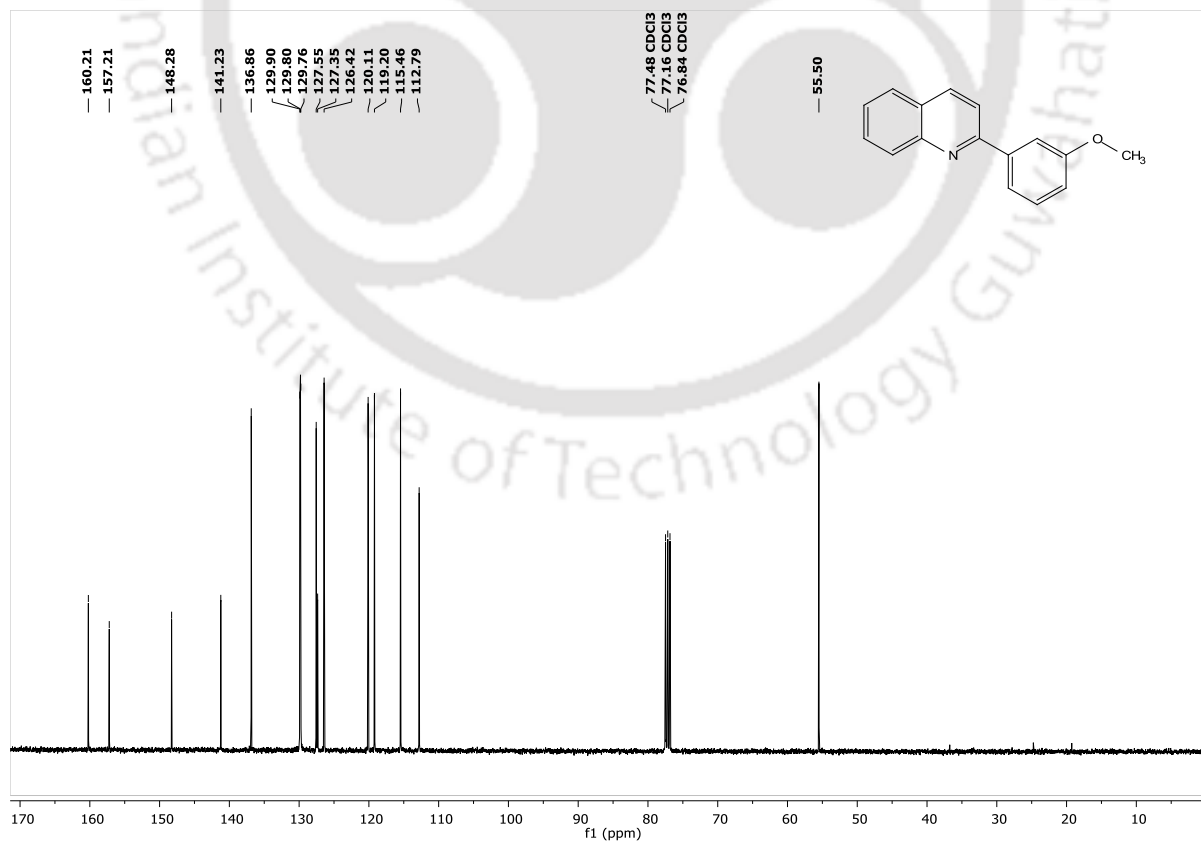


Figure S115: ^{13}C NMR Spectrum of **4.3i** (CDCl_3 , 101 MHz, 298 K)

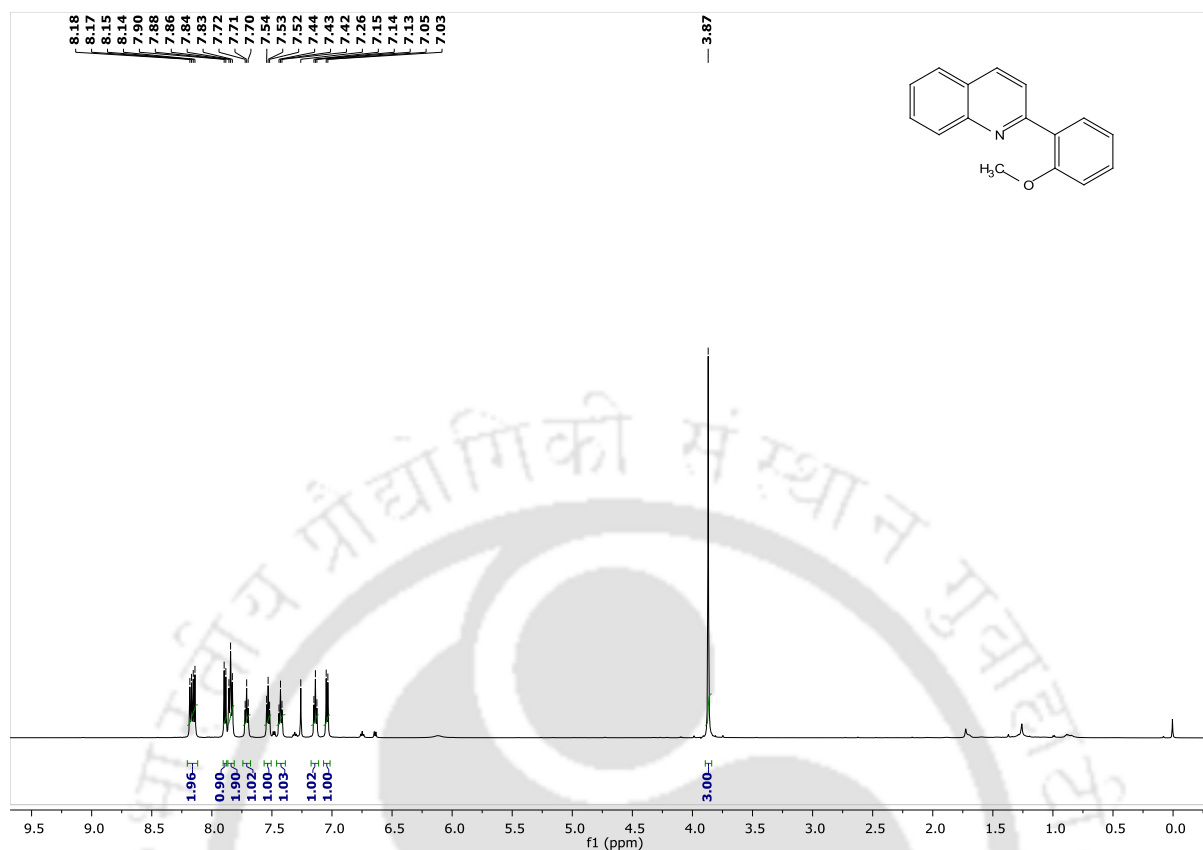


Figure S116: ¹H NMR Spectrum of **4.3j** (CDCl₃, 600 MHz, 298 K)

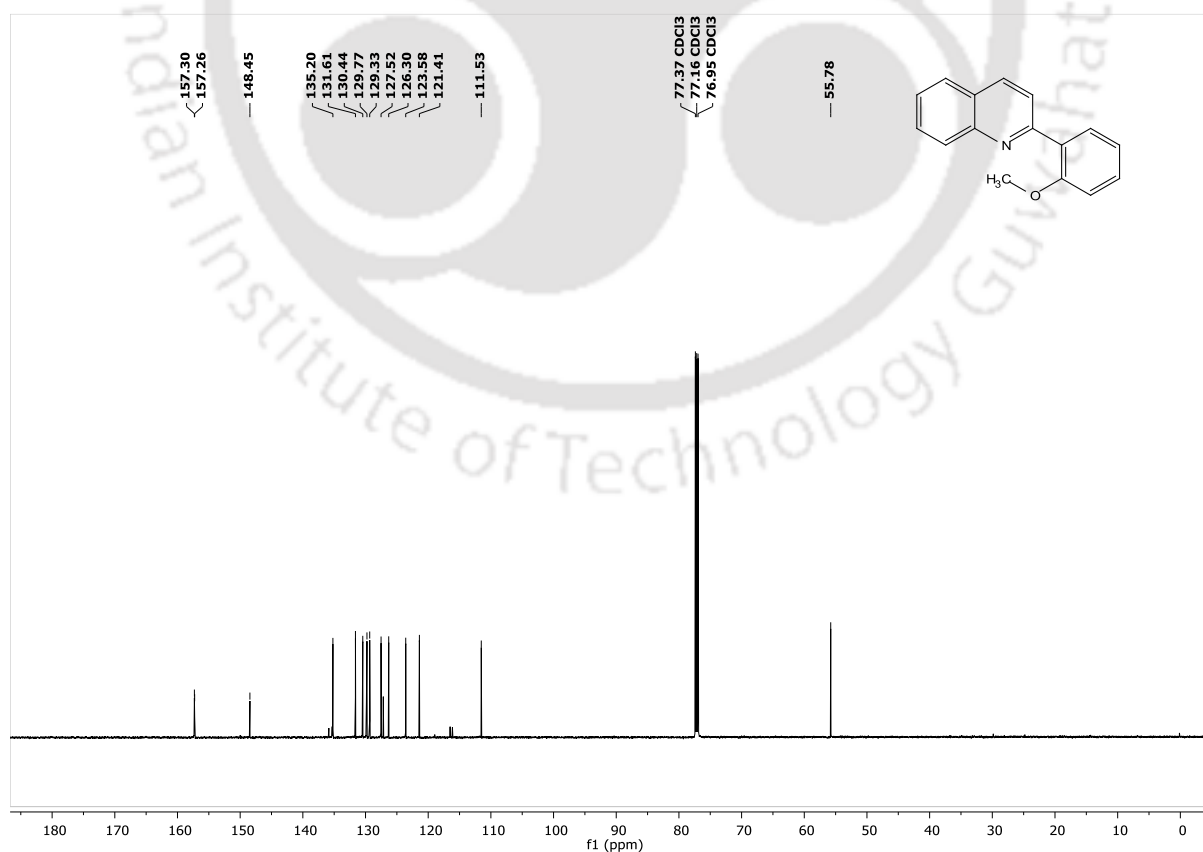


Figure S117: ¹³C NMR Spectrum of **4.3j** (CDCl₃, 151 MHz, 298 K)

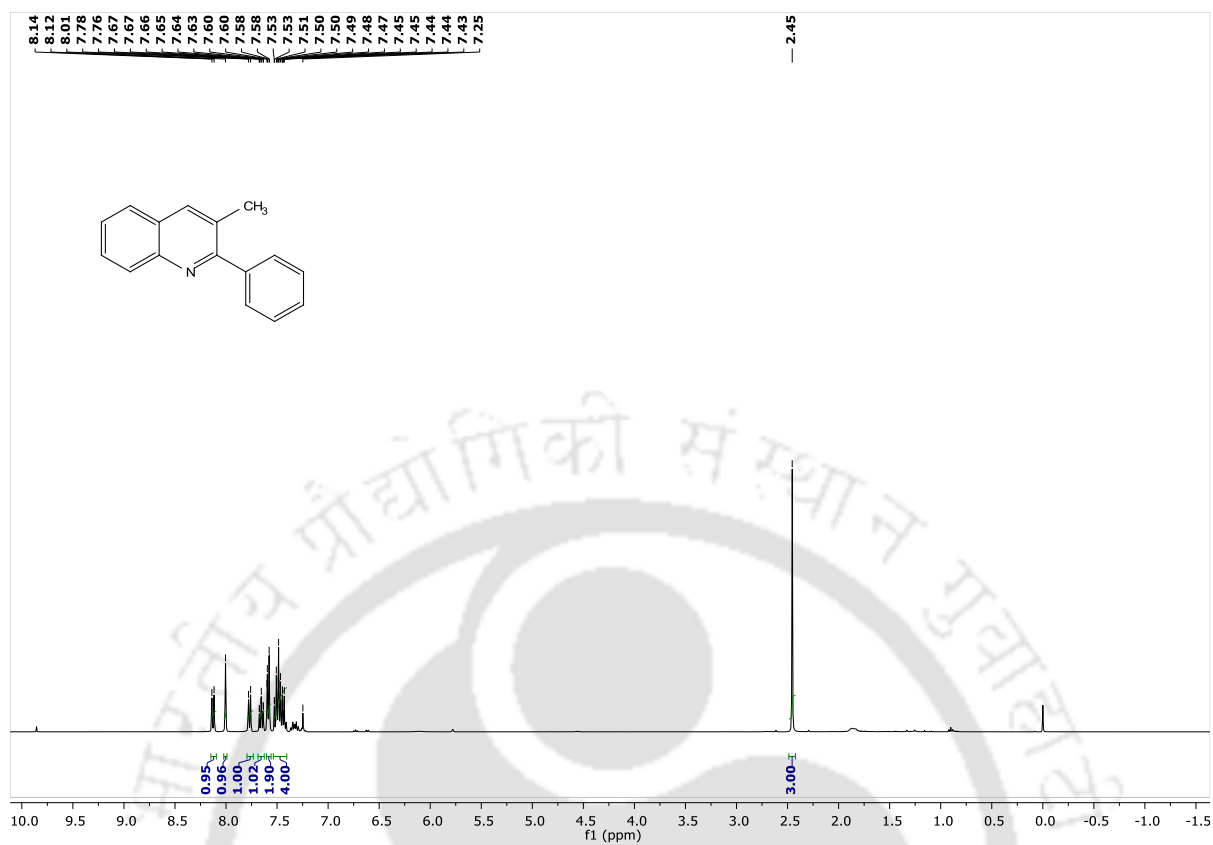


Figure S118: ¹H NMR Spectrum of 4.3k (CDCl₃, 400 MHz, 298 K)

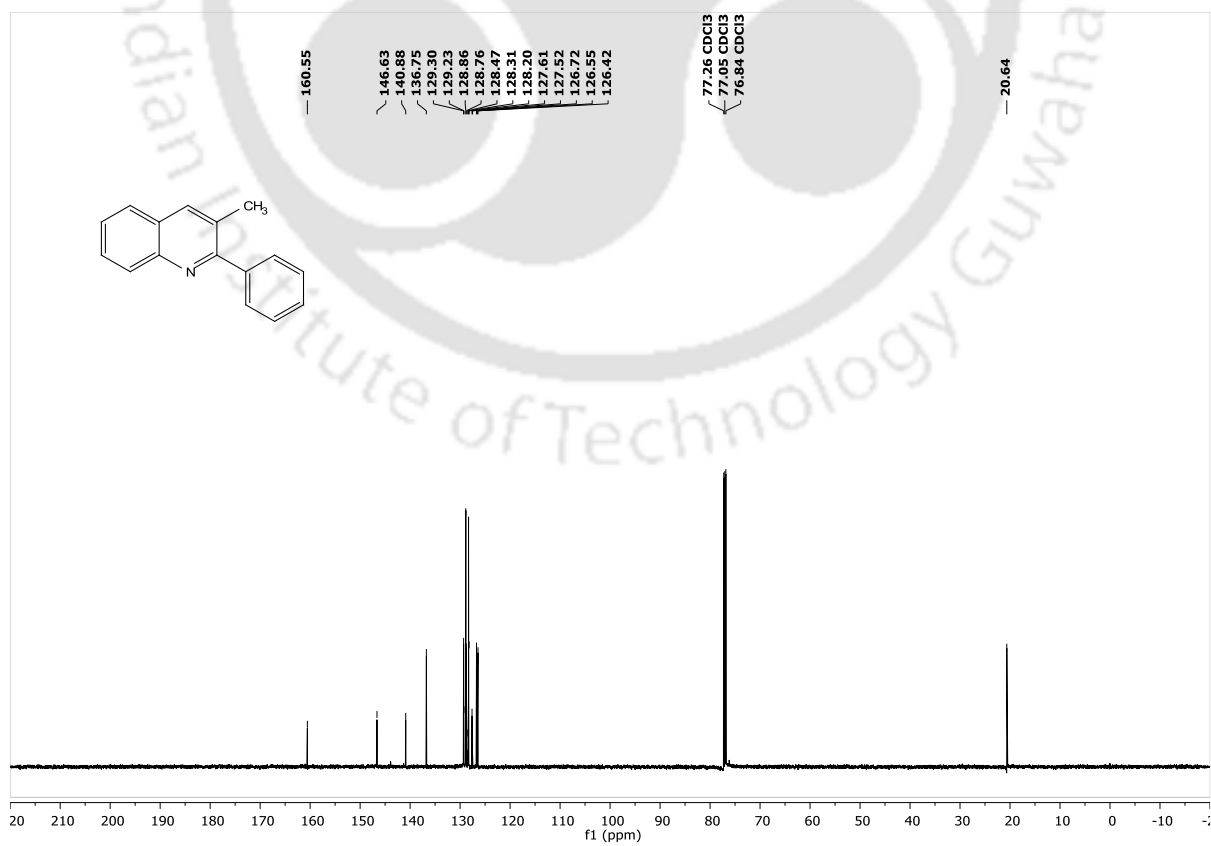


Figure S119: ^{13}C NMR Spectrum of **4.3k** (CDCl_3 , 101 MHz, 298 K)

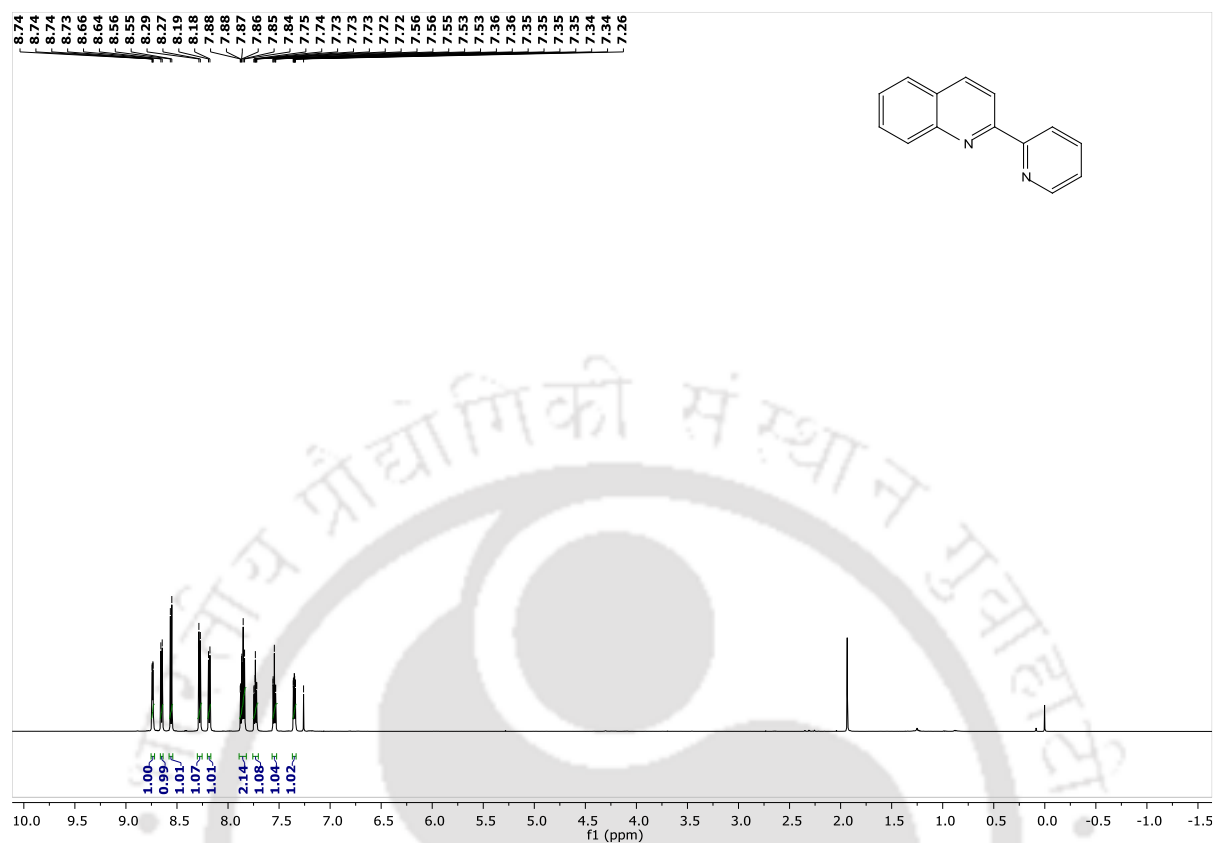


Figure S120: ^1H NMR Spectrum of **4.3l** (CDCl_3 , 600 MHz, 298 K)

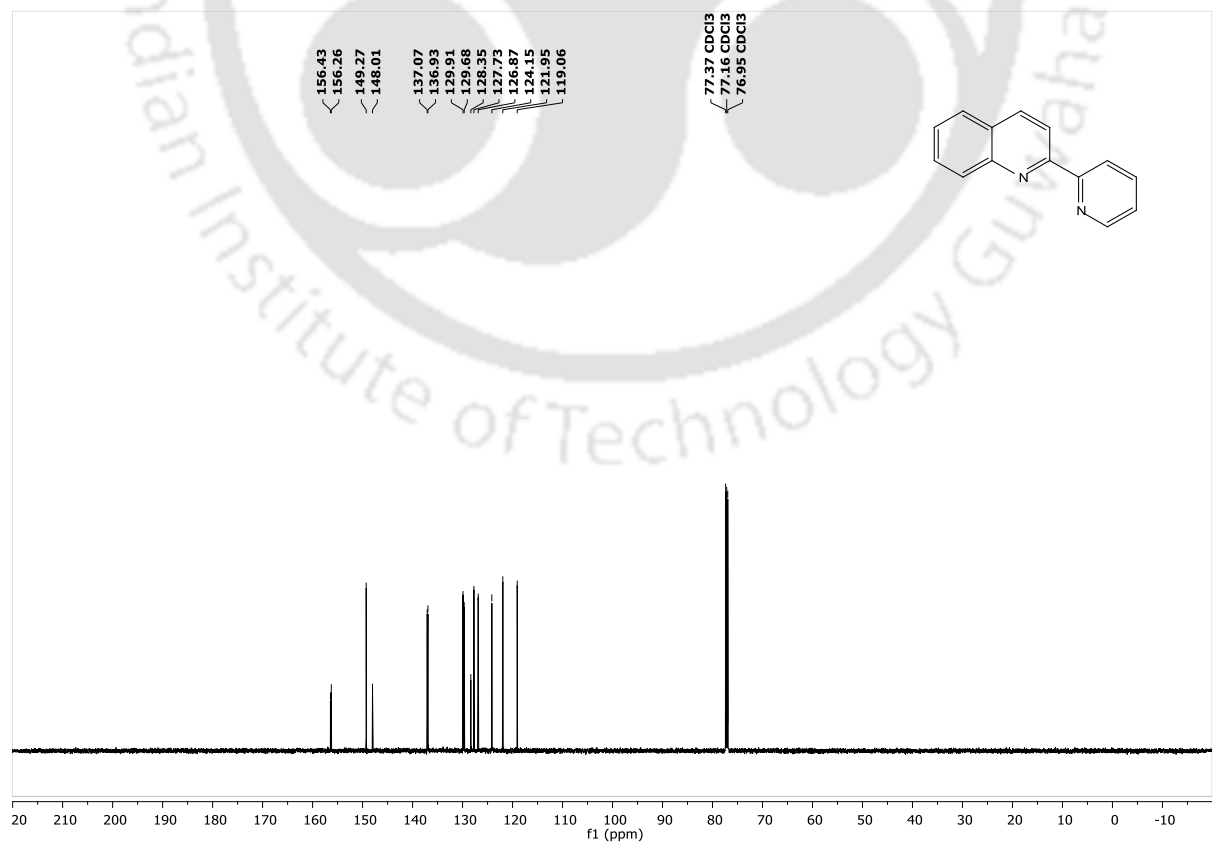


Figure S121: ^{13}C NMR Spectrum of **4.3l** (CDCl_3 , 151 MHz, 298 K)

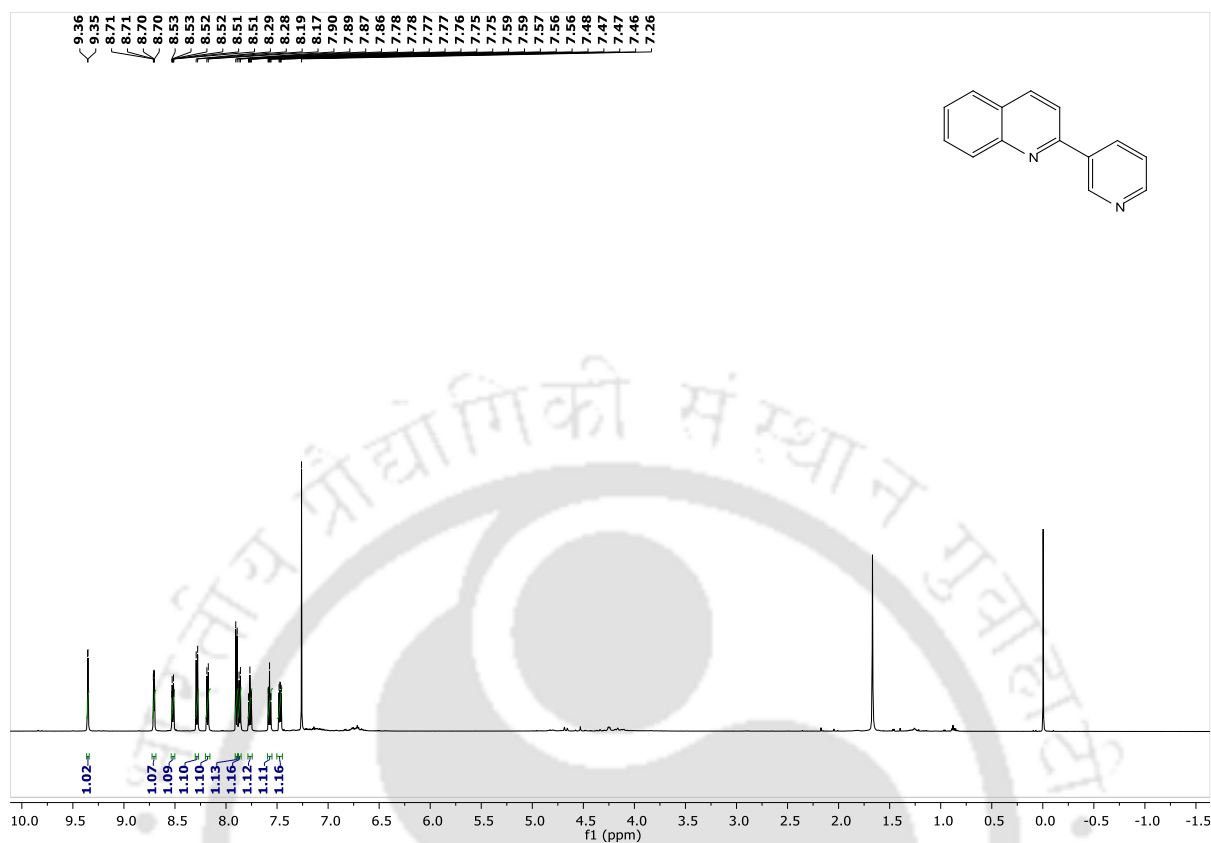


Figure S122: ^1H NMR Spectrum of **4.3m** (CDCl_3 , 600 MHz, 298 K)

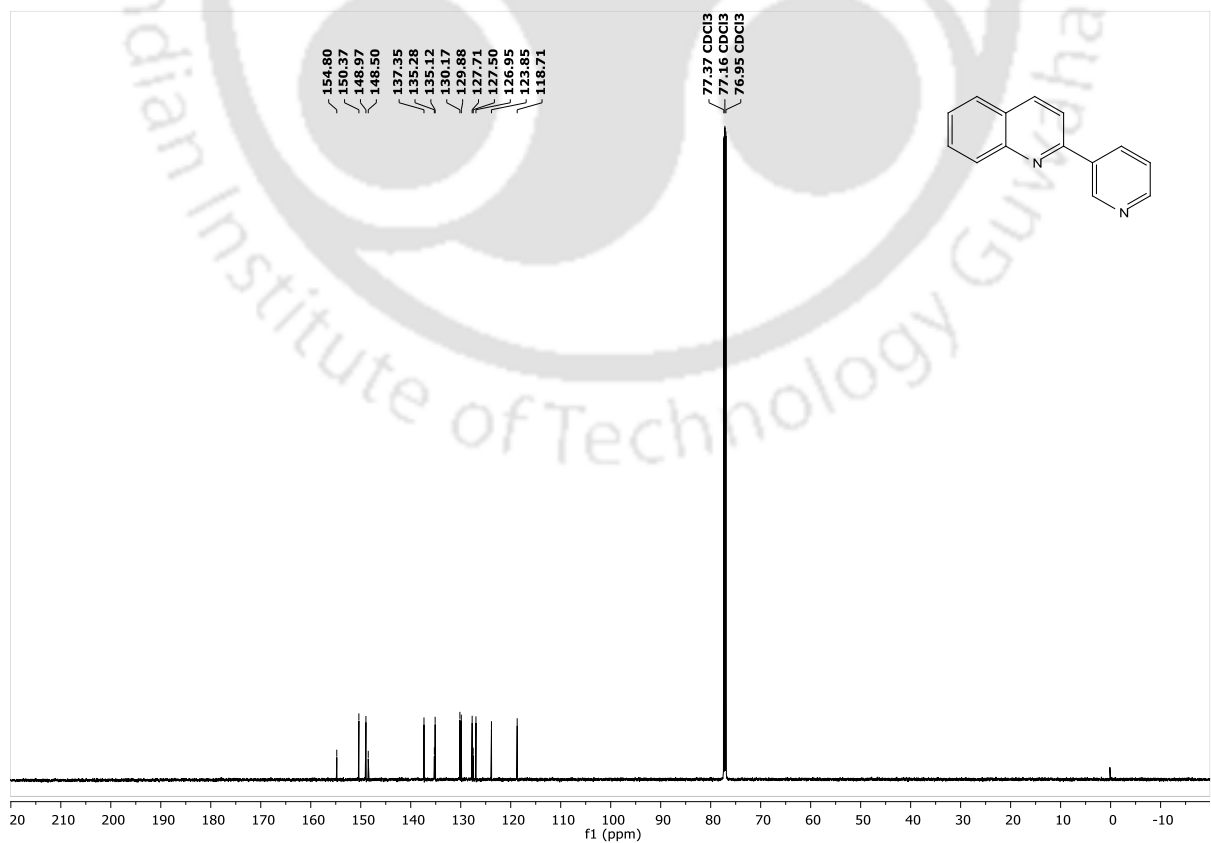


Figure S123: ^{13}C NMR Spectrum of **4.3m** (CDCl_3 , 151 MHz, 298 K)

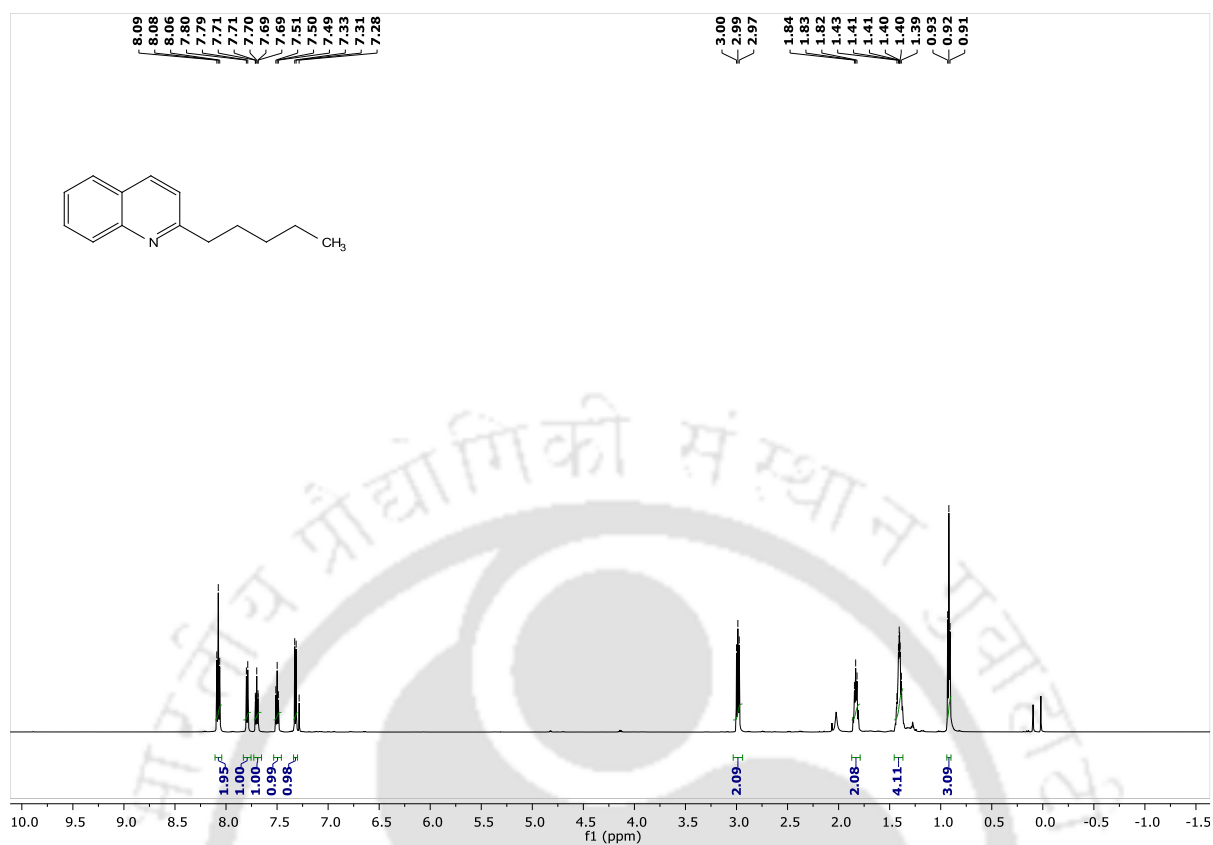


Figure S124: ¹H NMR Spectrum of **4.3n** (CDCl₃, 600 MHz, 298 K)

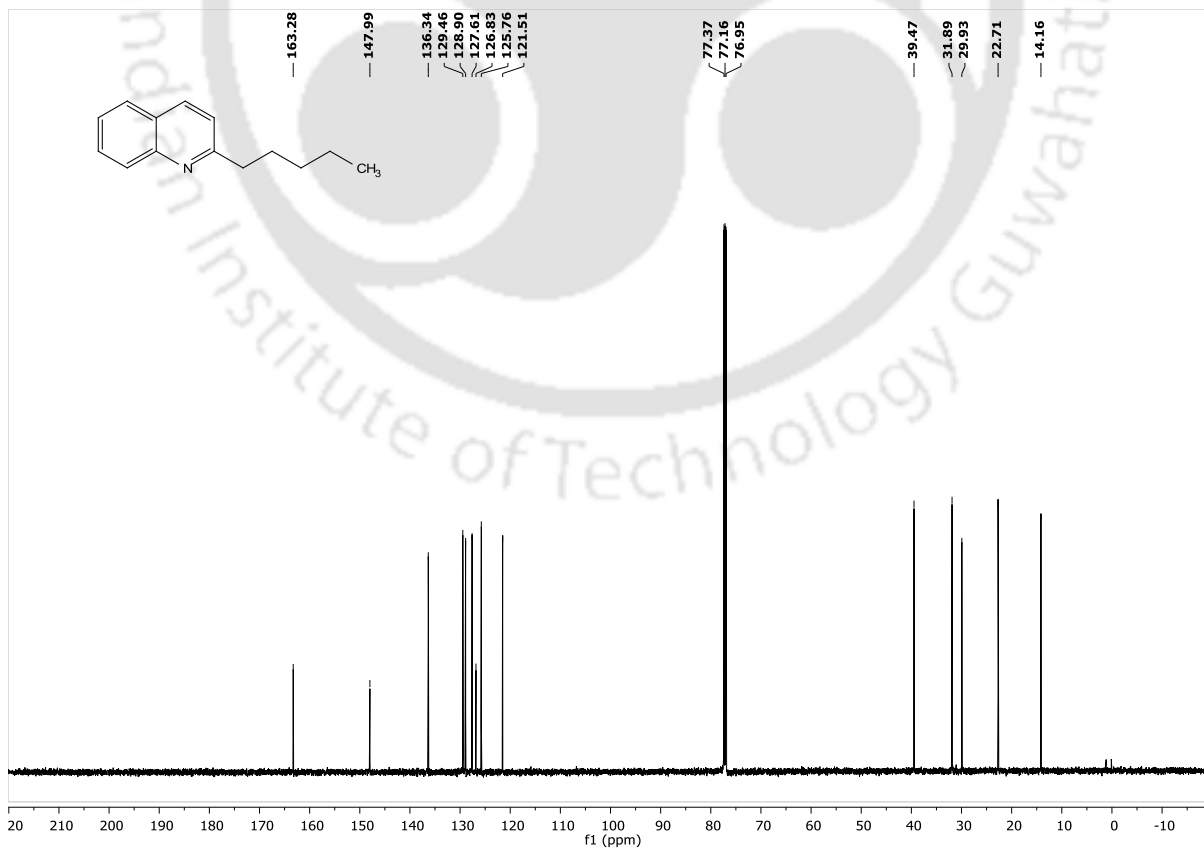


Figure S125: ¹³C NMR Spectrum of **4.3n** (CDCl₃, 151 MHz, 298 K)

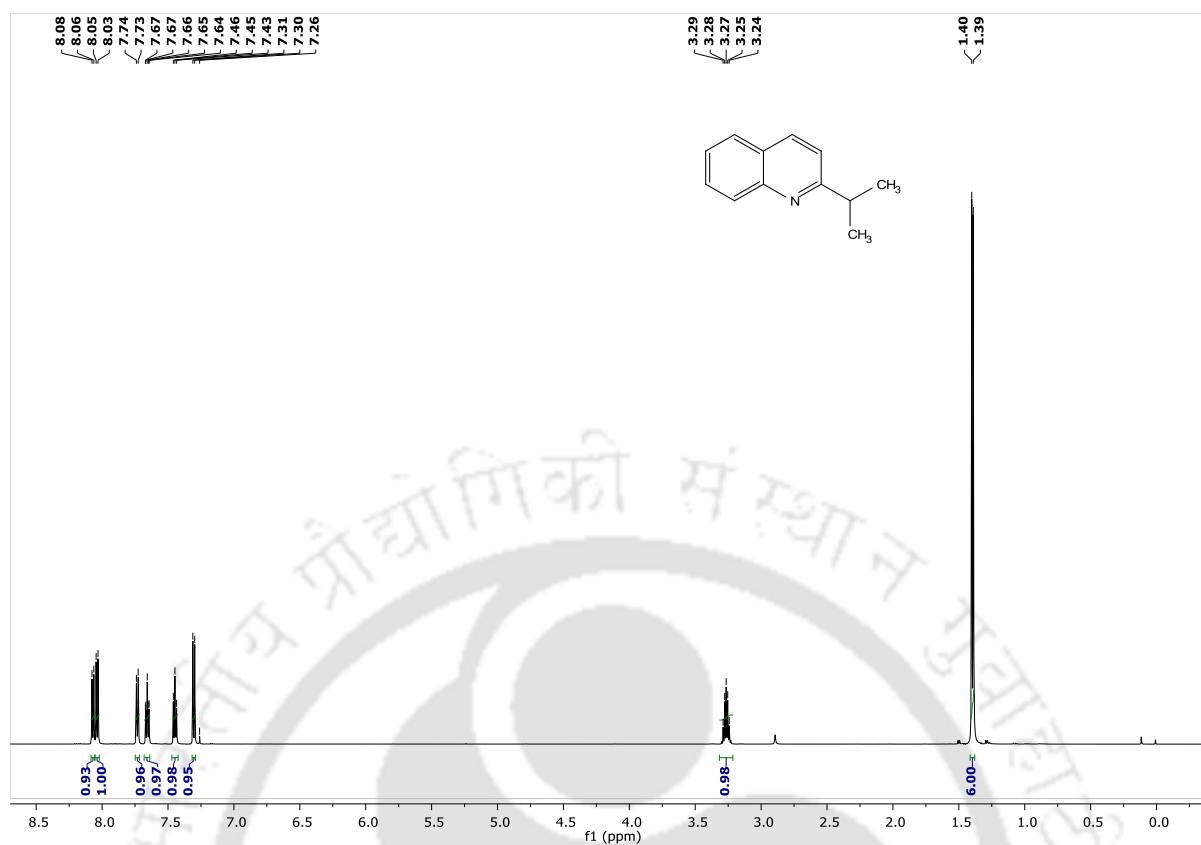


Figure S126: ^1H NMR Spectrum of 4.3o (CDCl_3 , 600 MHz, 298 K)

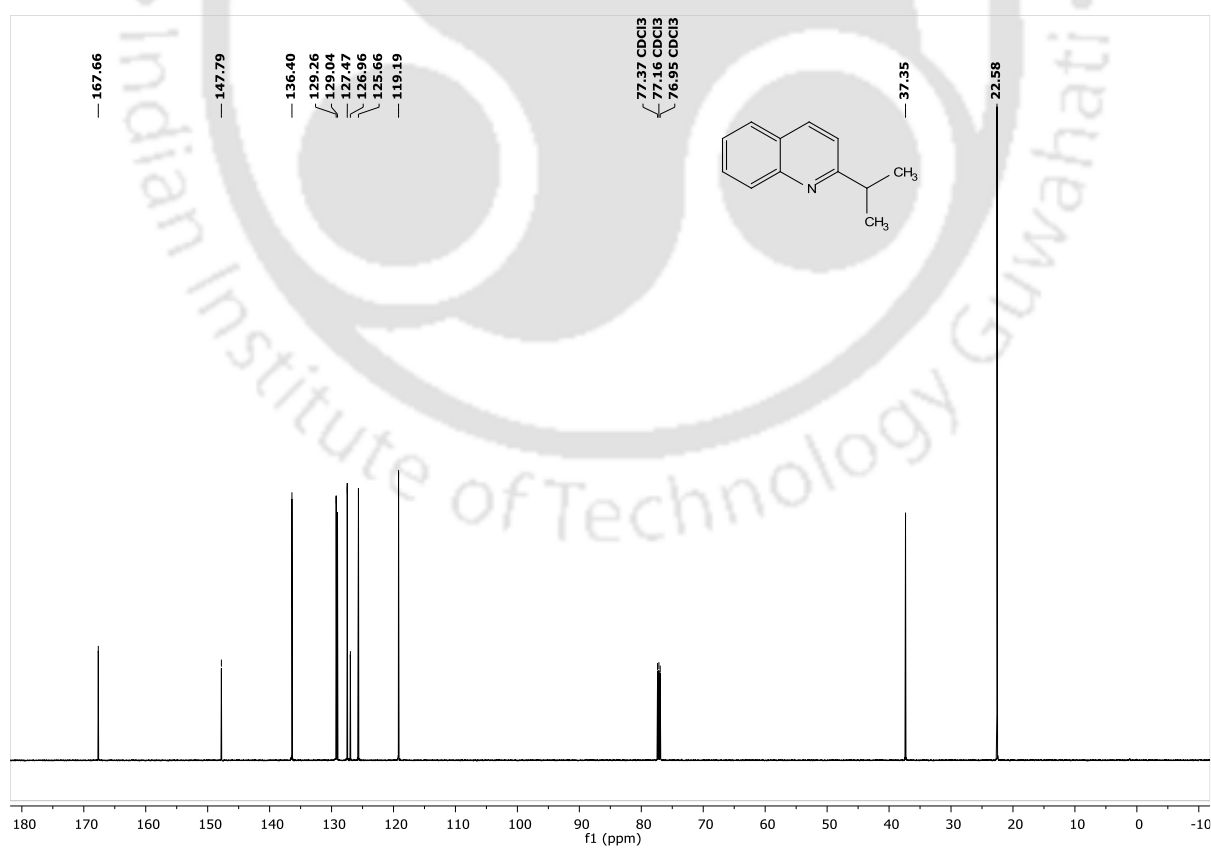


Figure S127: ^{13}C NMR Spectrum of 4.3o (CDCl_3 , 151 MHz, 298 K)

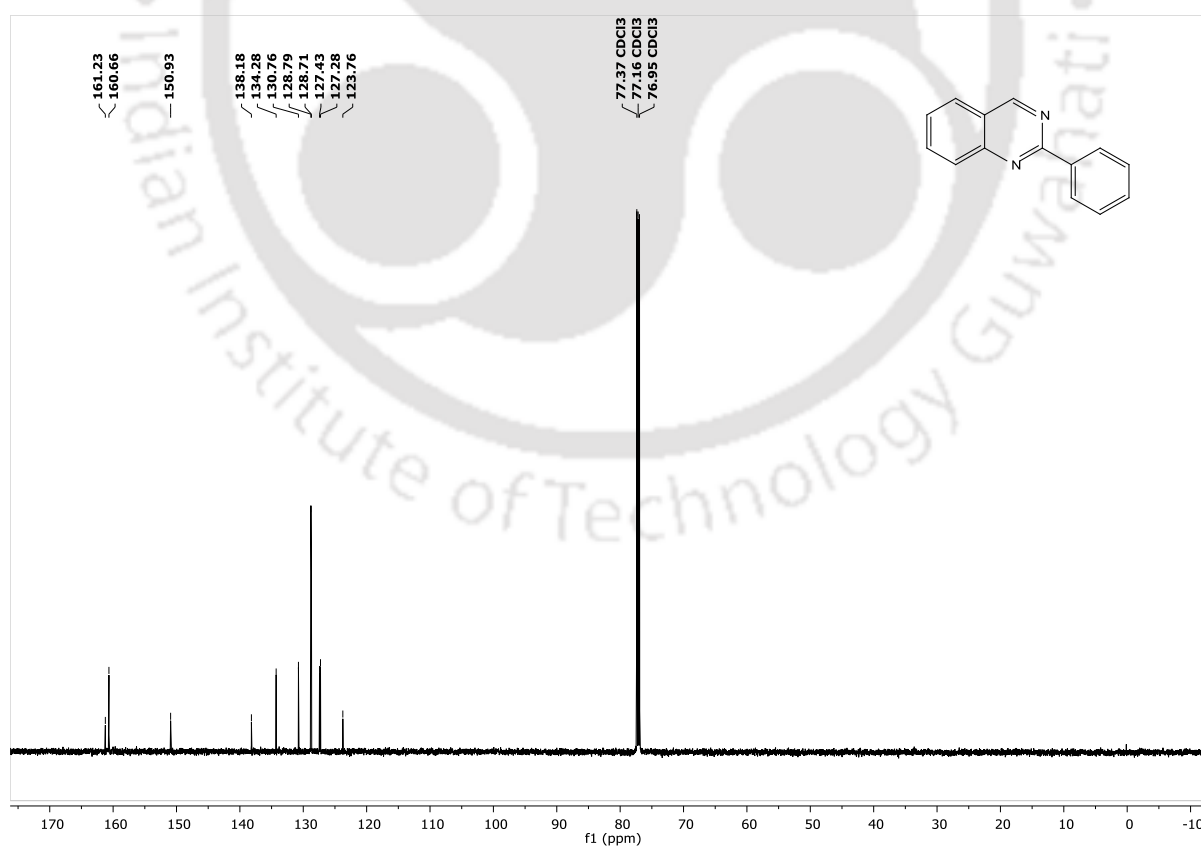
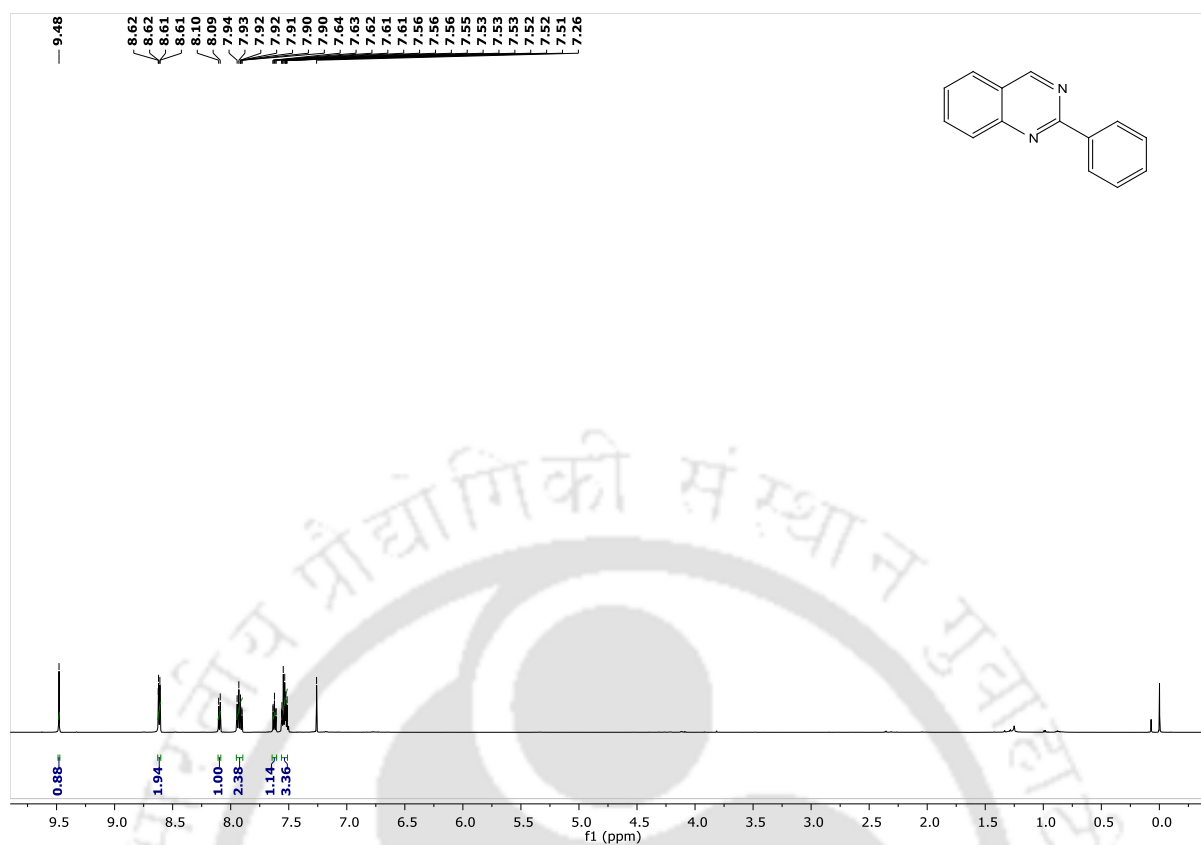
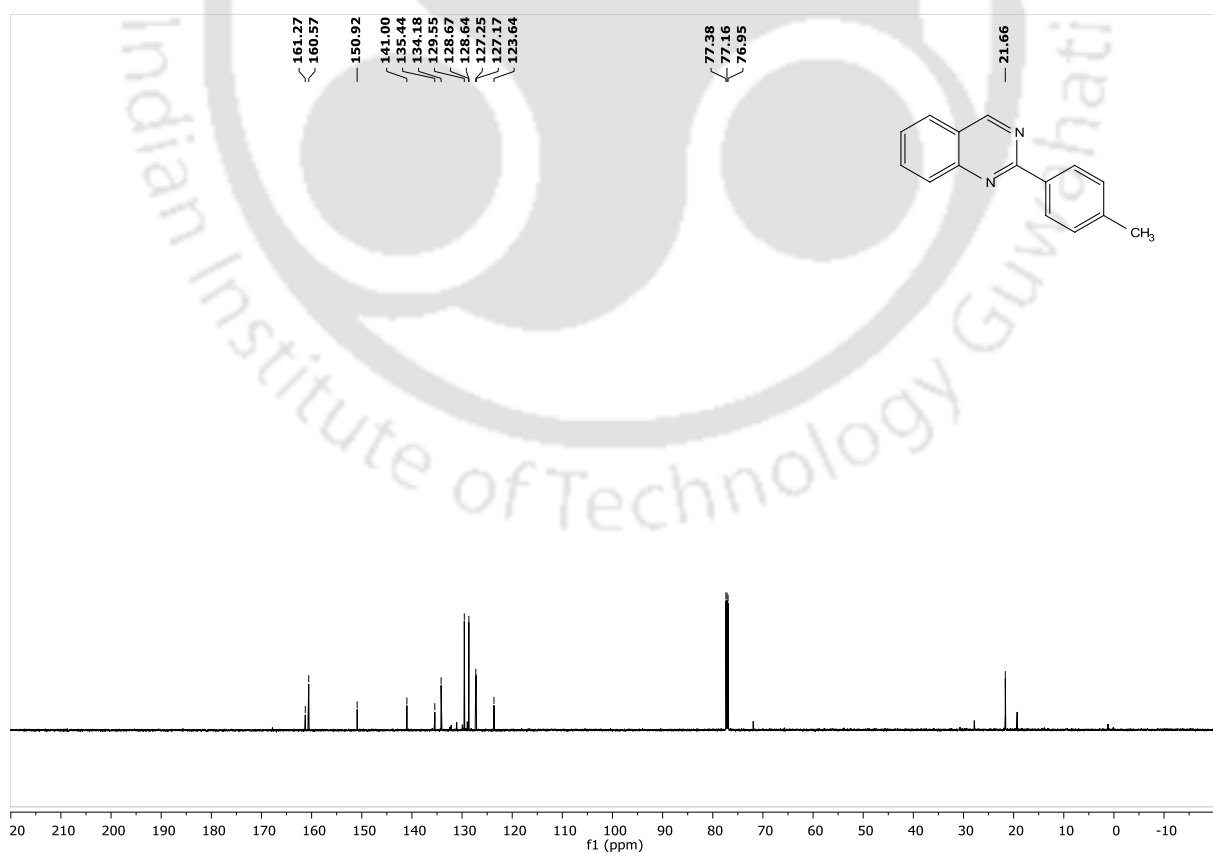
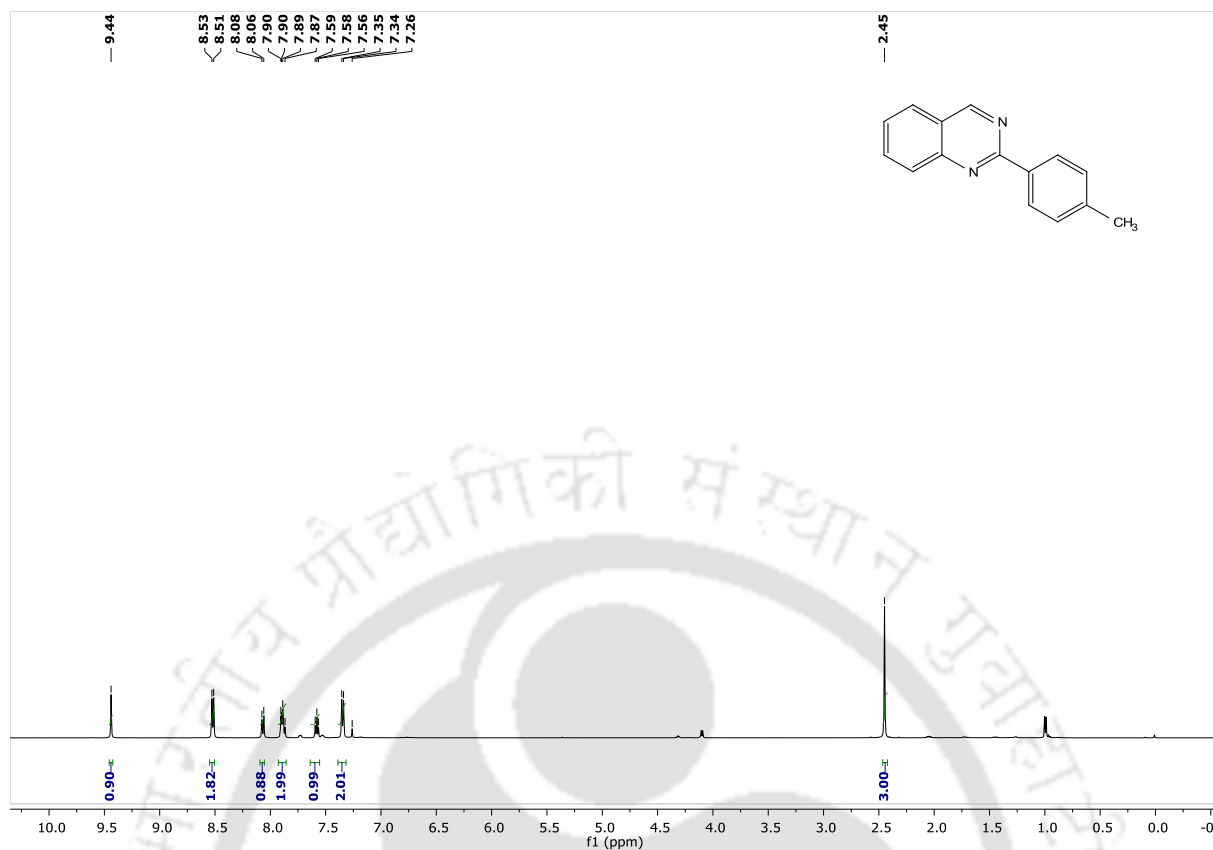
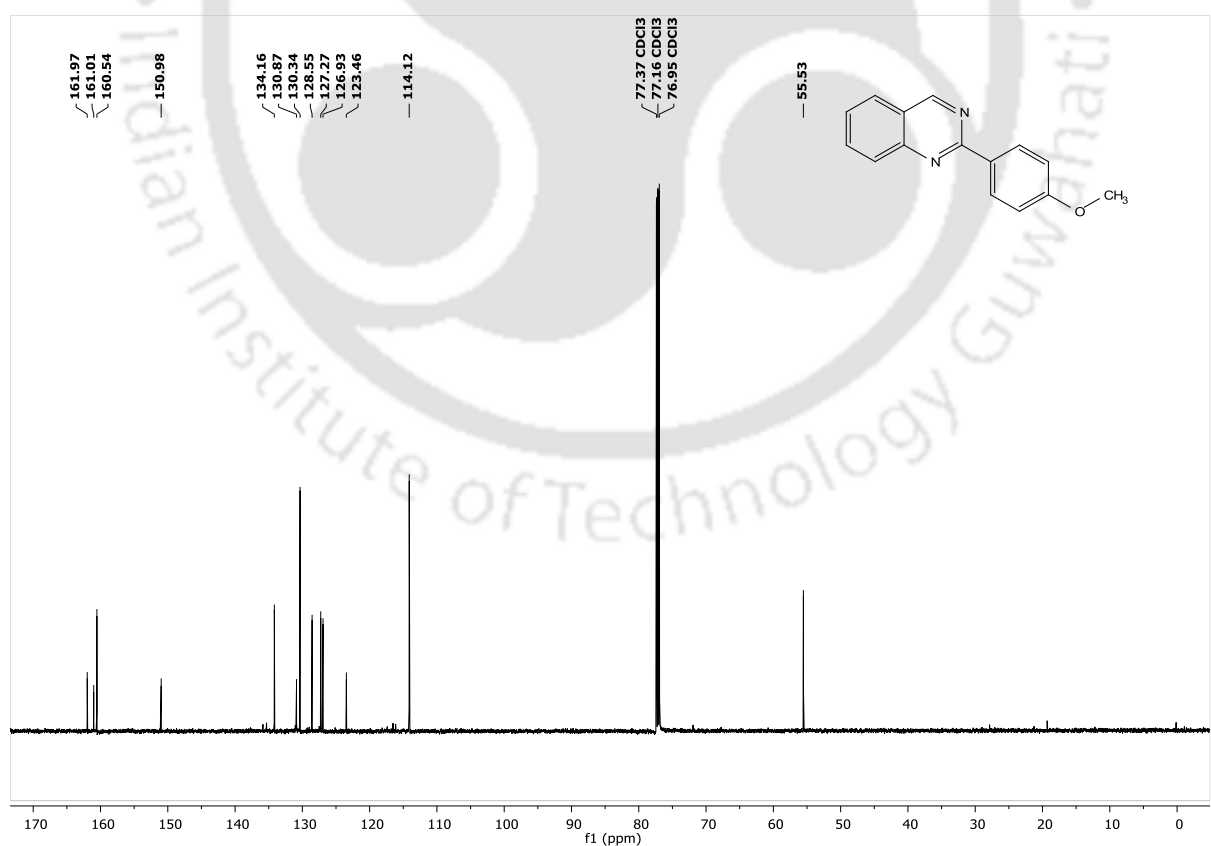
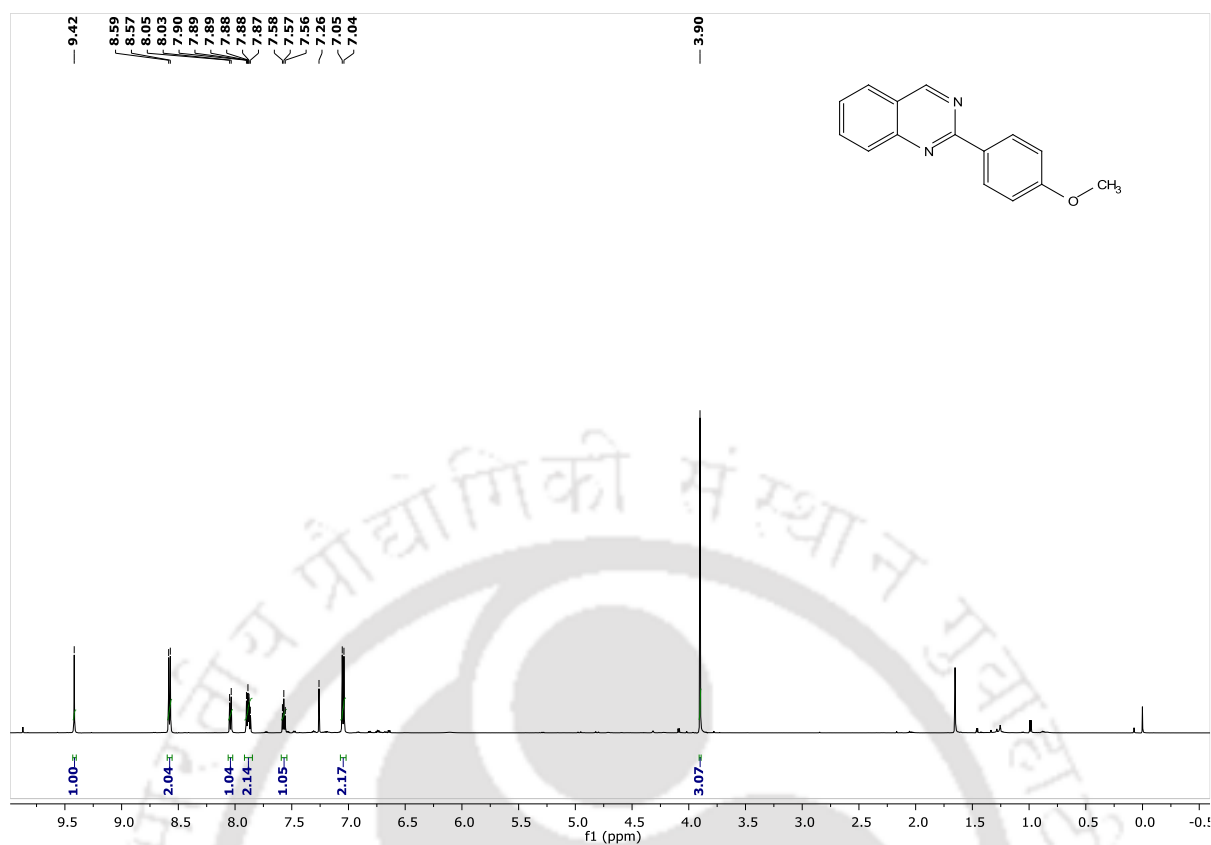


Figure S129: ^{13}C NMR Spectrum of 4.10a (CDCl_3 , 151 MHz, 298 K)





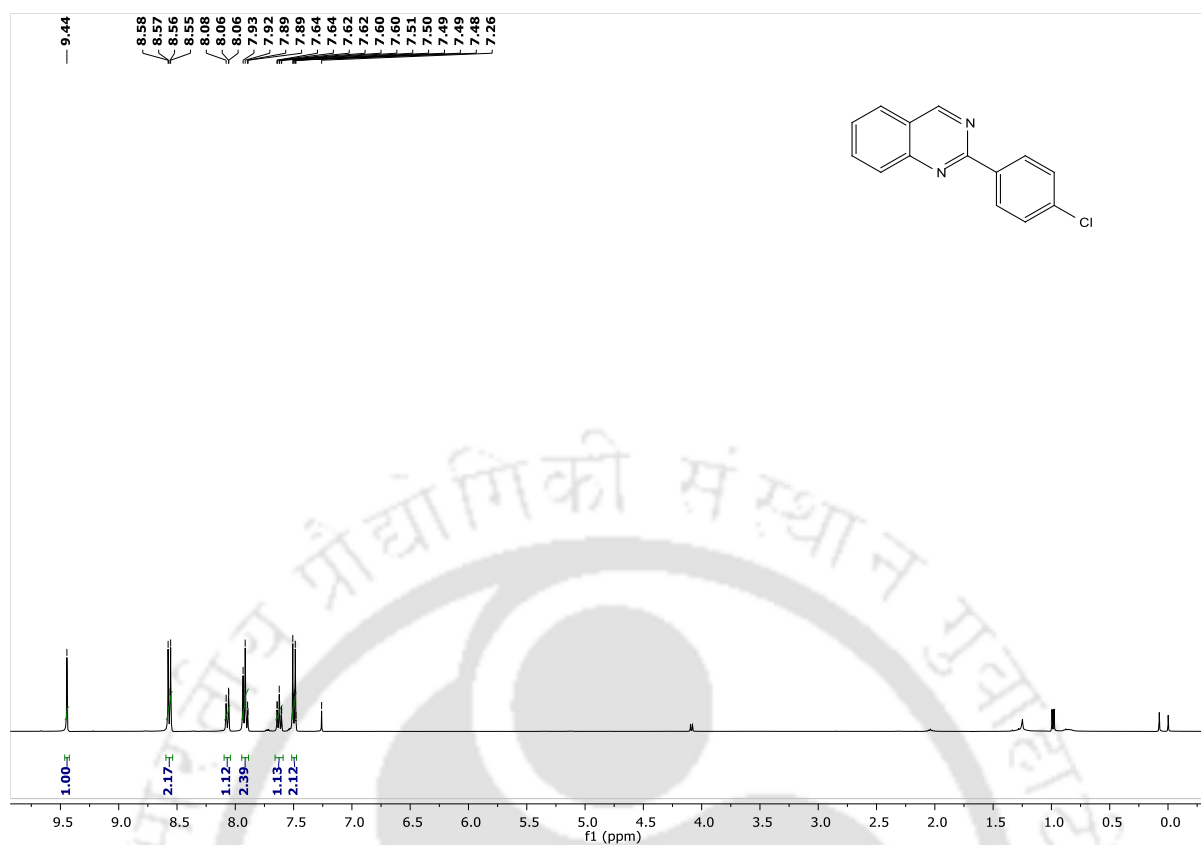


Figure S134: ¹H NMR Spectrum of **4.10d** (CDCl₃, 400 MHz, 298 K)

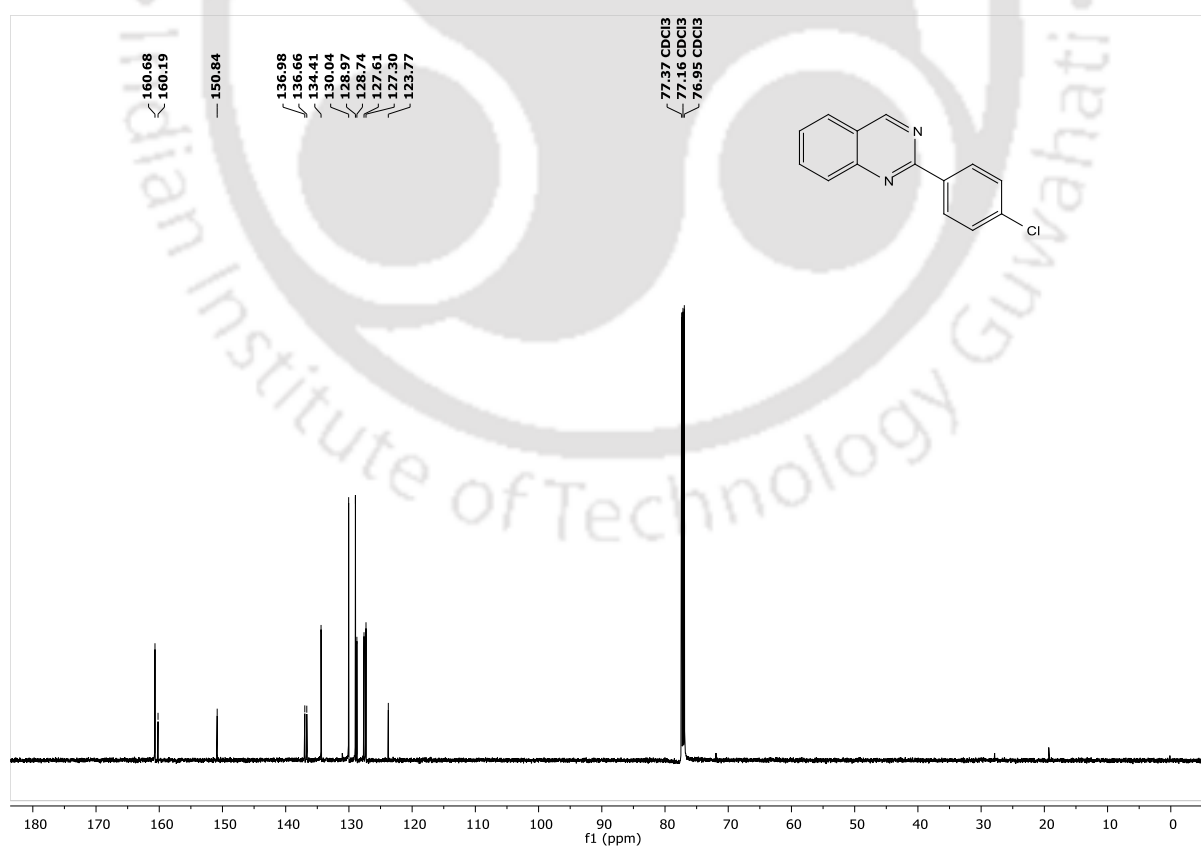
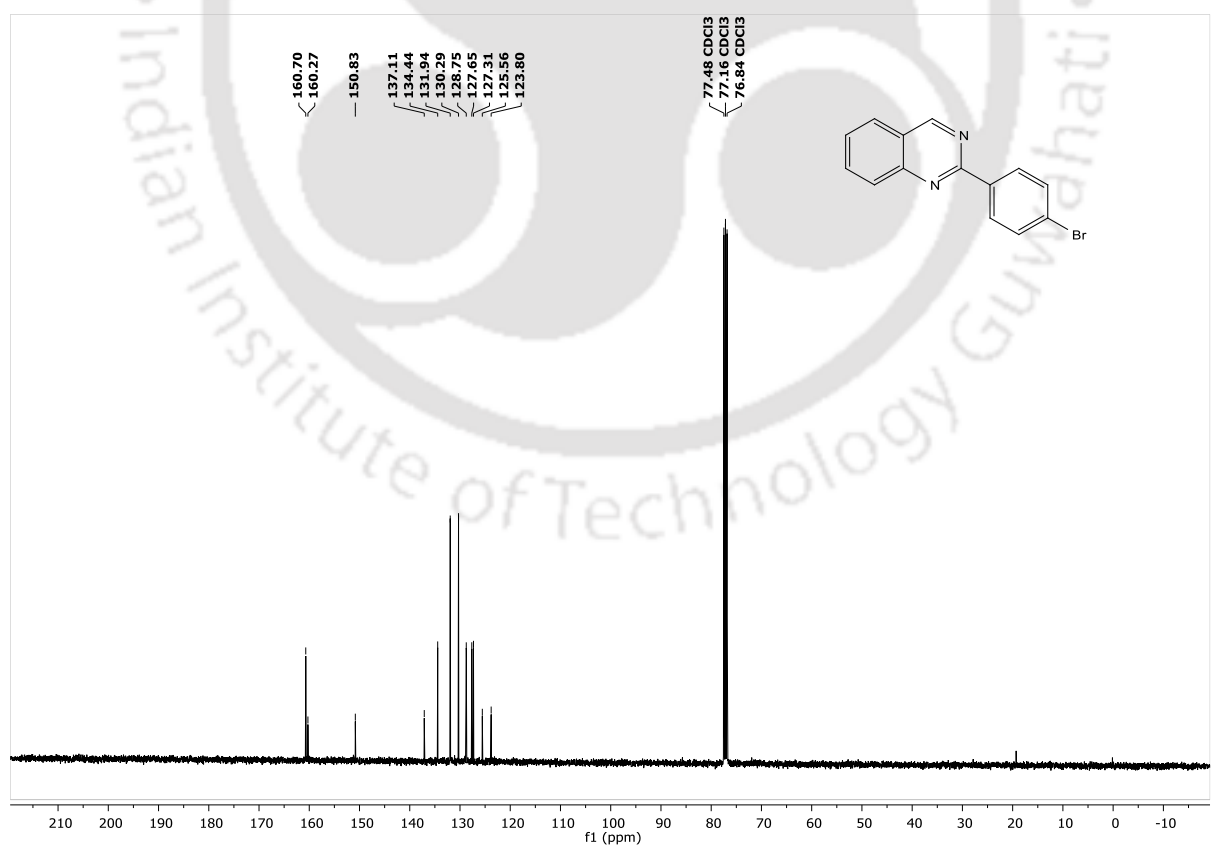
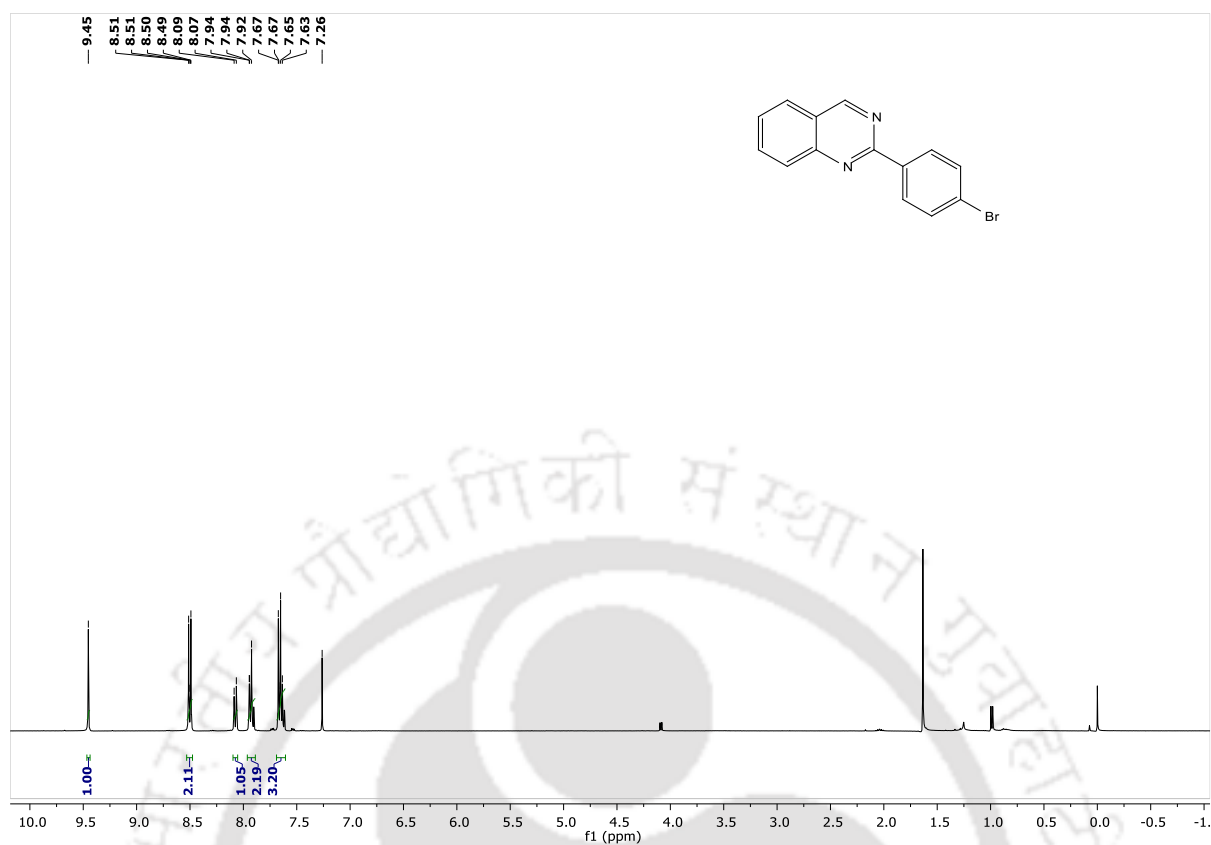
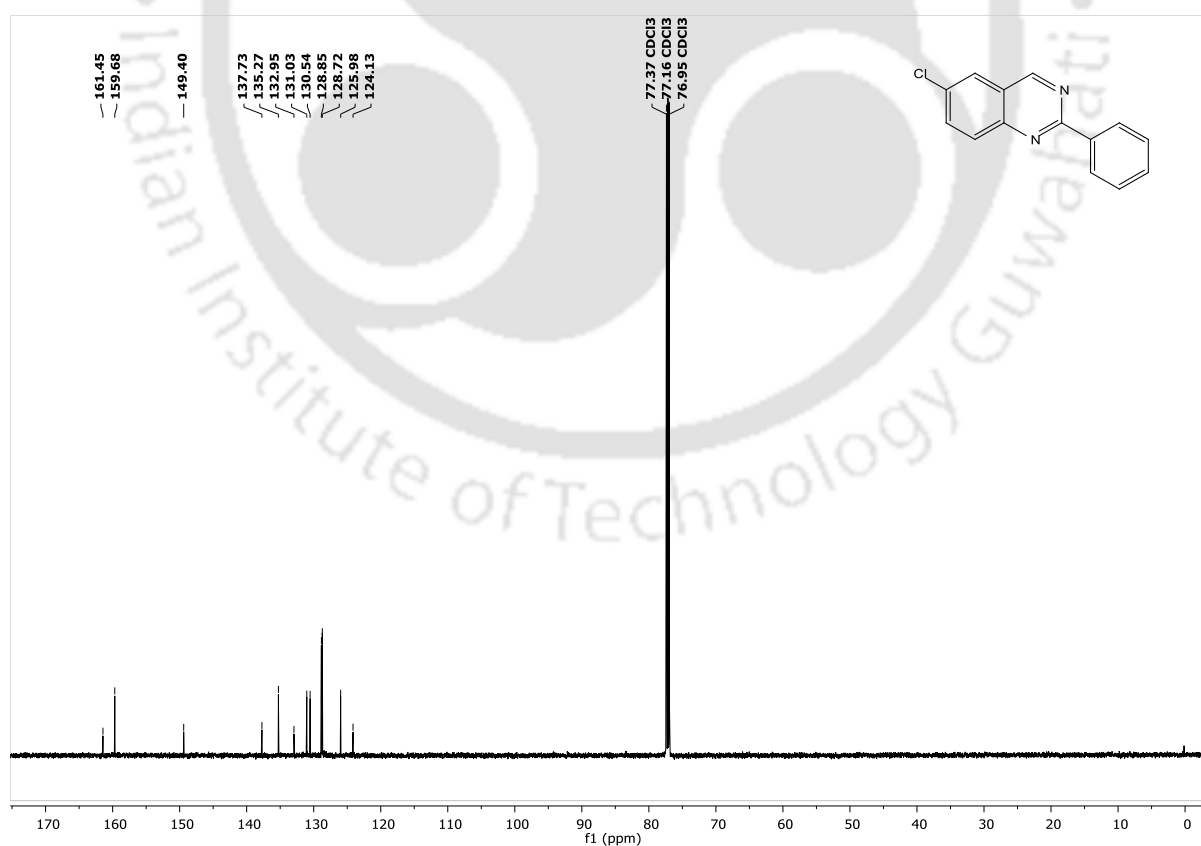
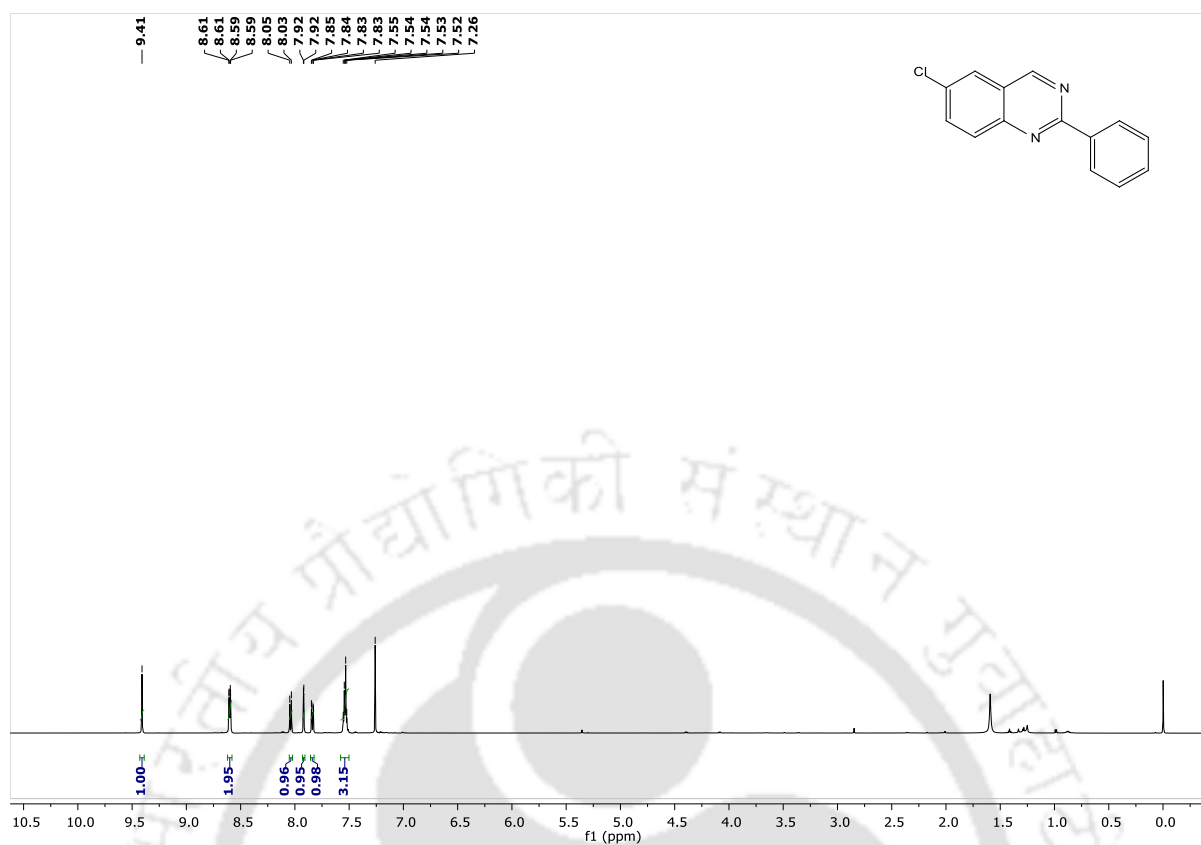
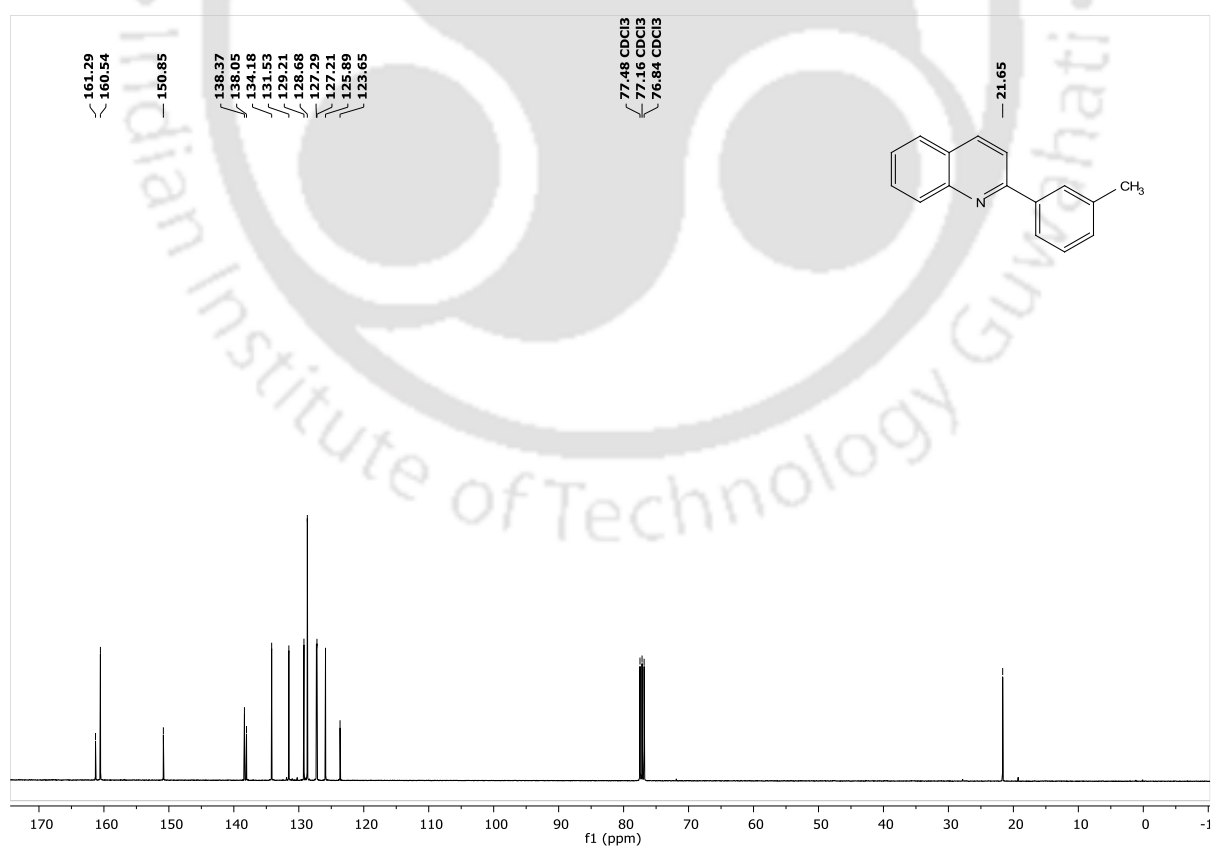
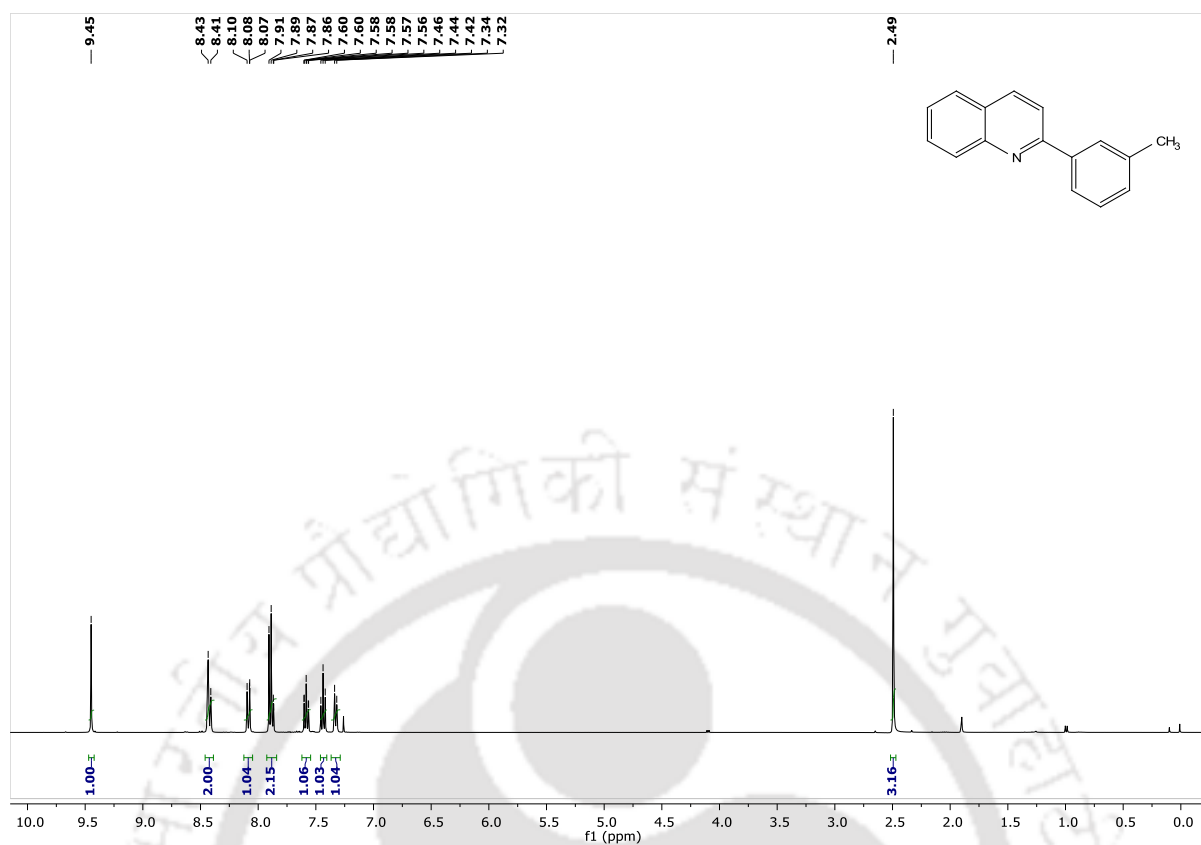
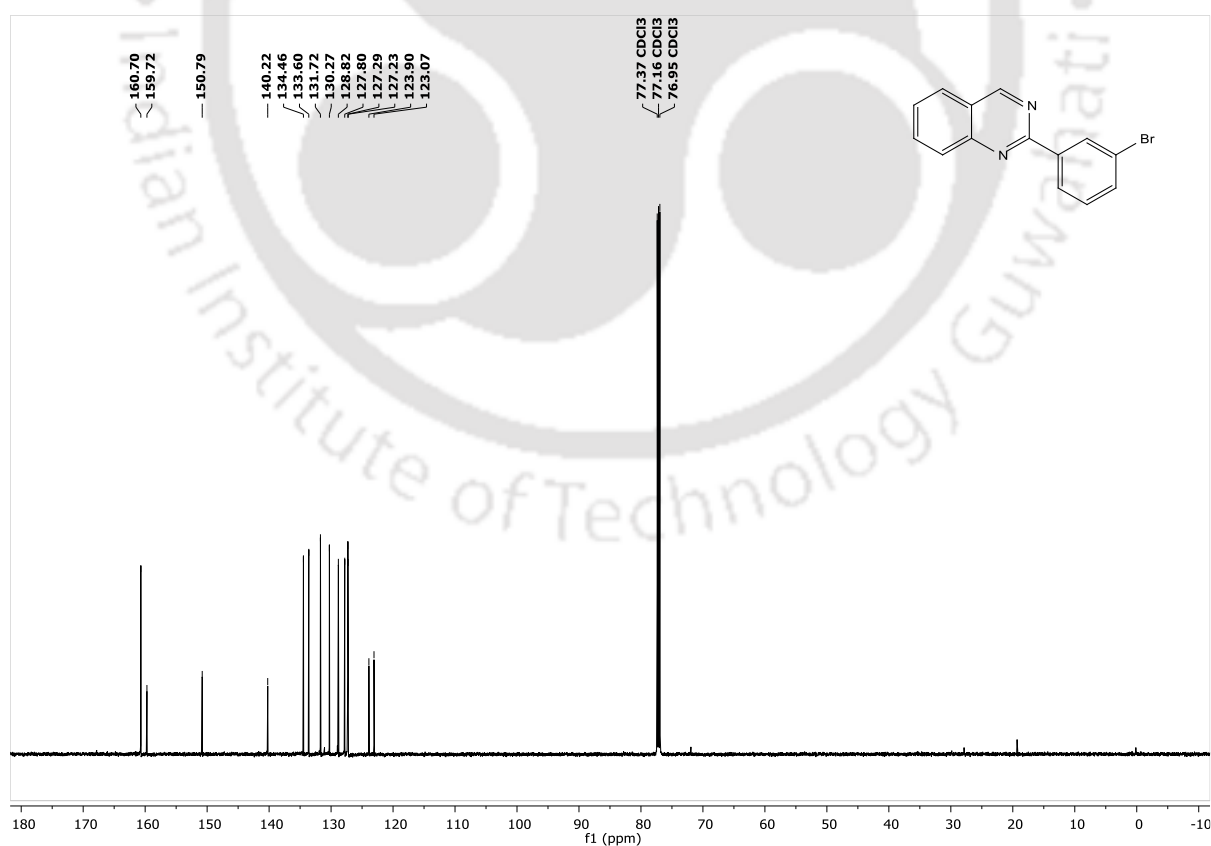
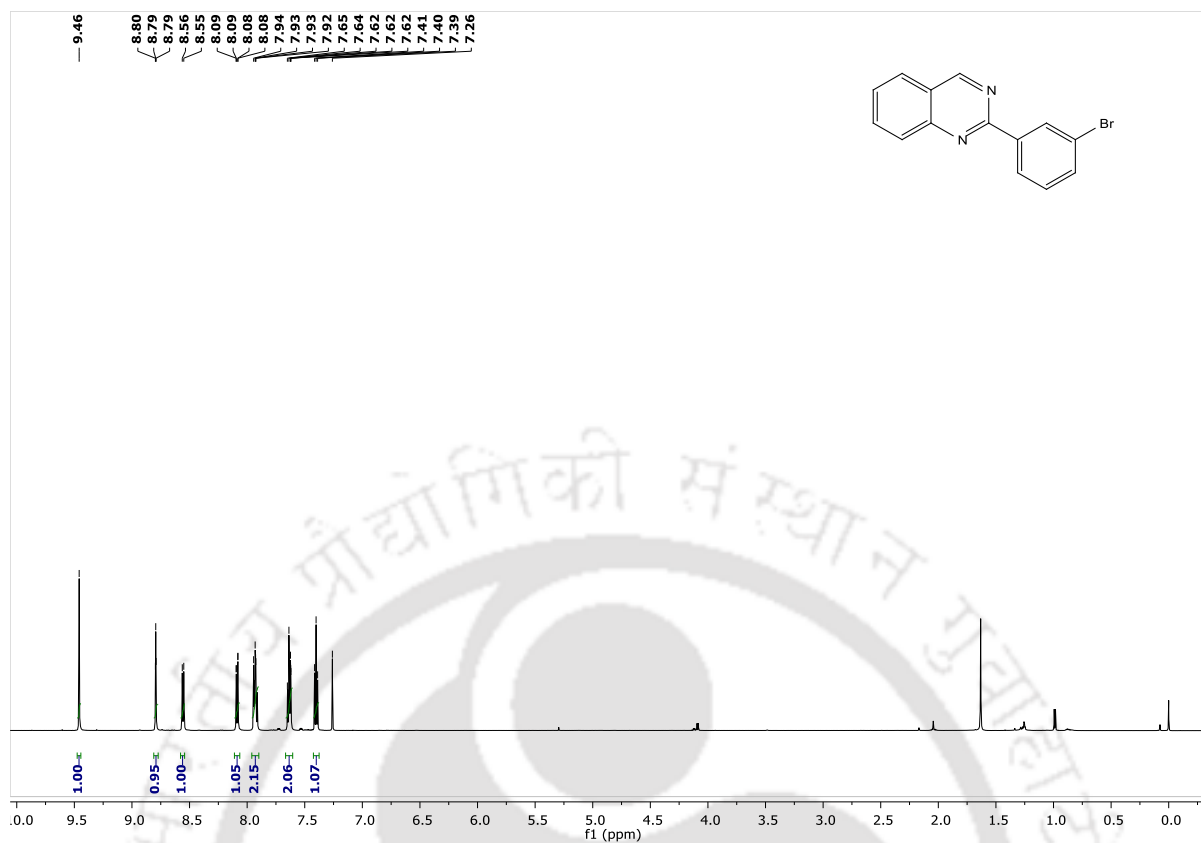


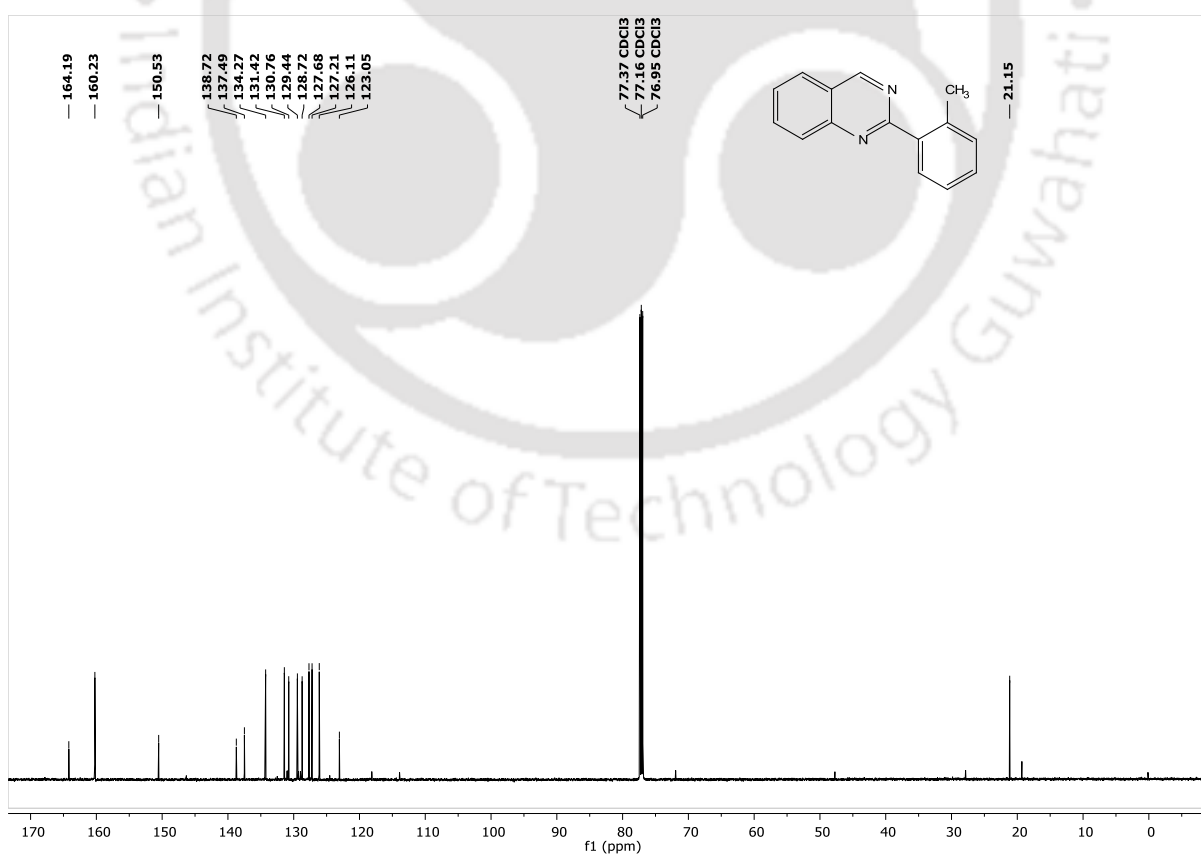
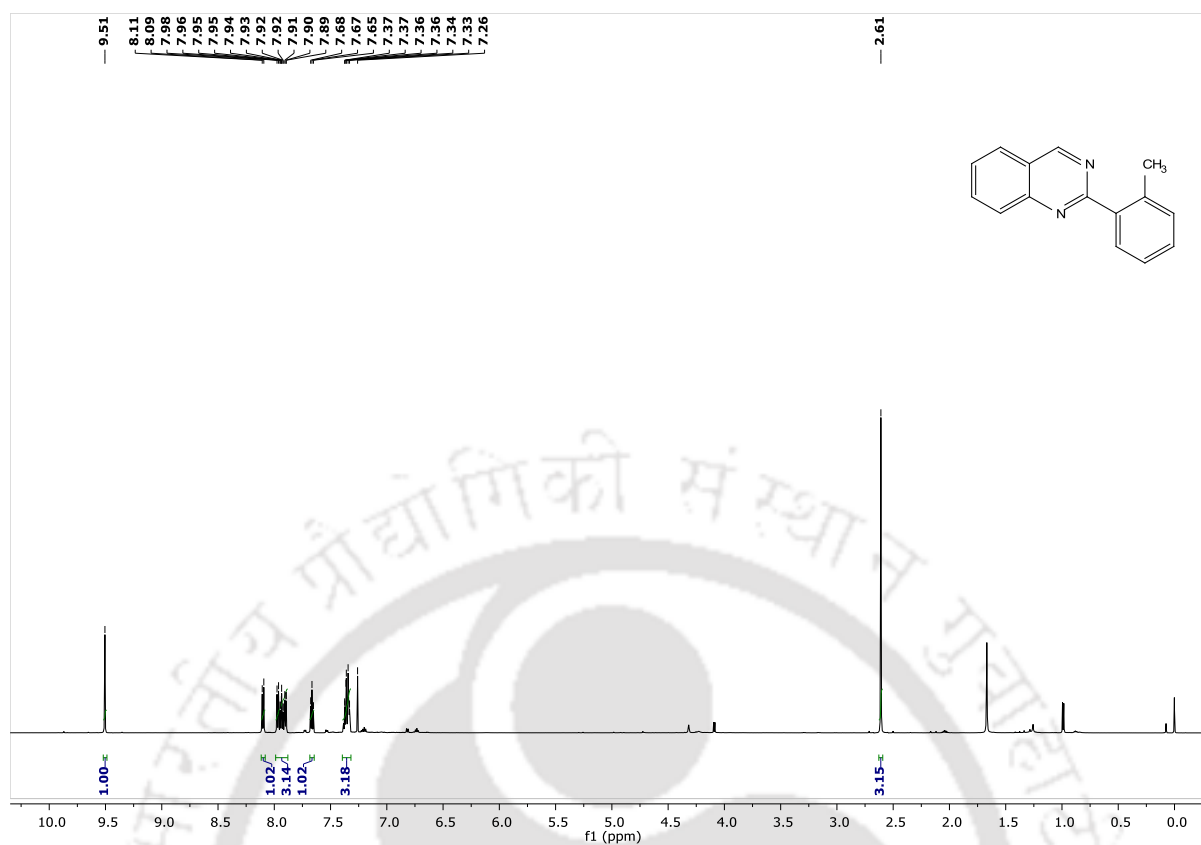
Figure S135: ¹³C NMR Spectrum of **4.10d** (CDCl₃, 151 MHz, 298 K)











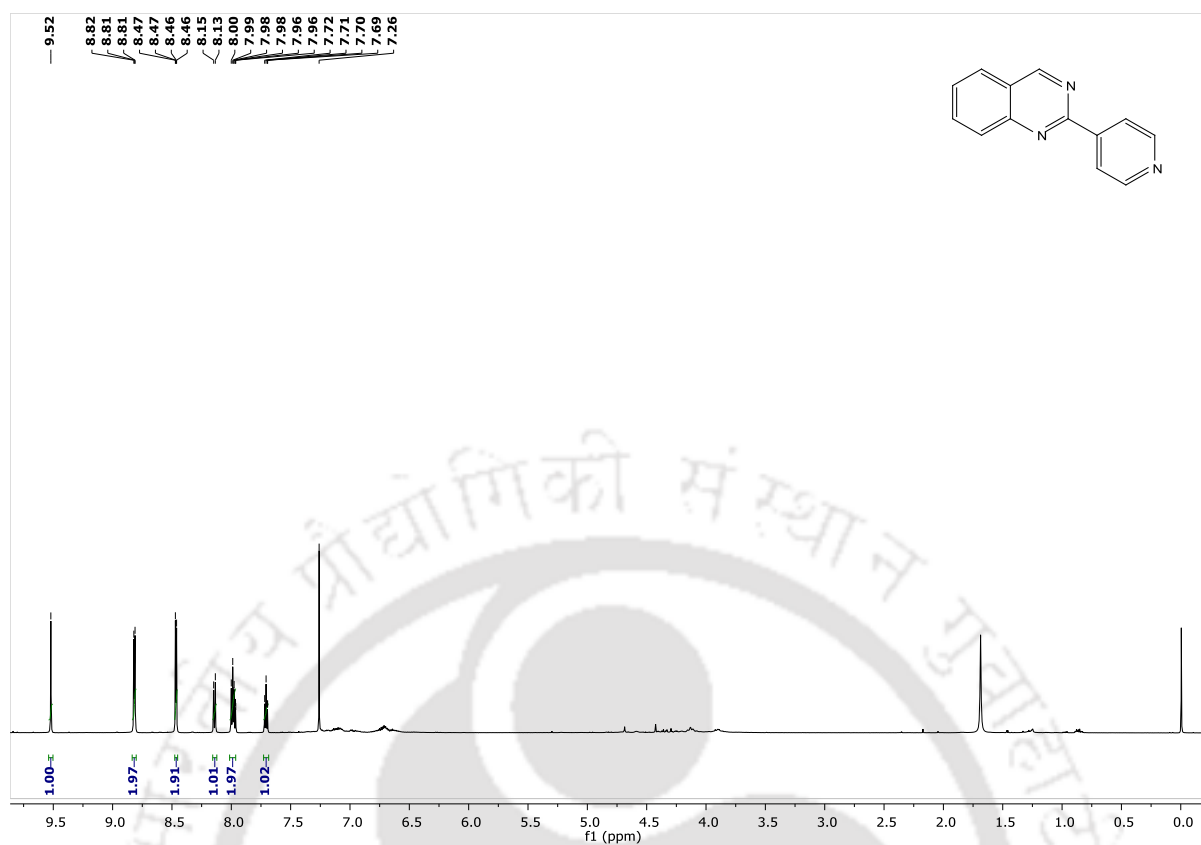


Figure S146: ^1H NMR Spectrum of 4.10j (CDCl_3 , 600 MHz, 298 K)

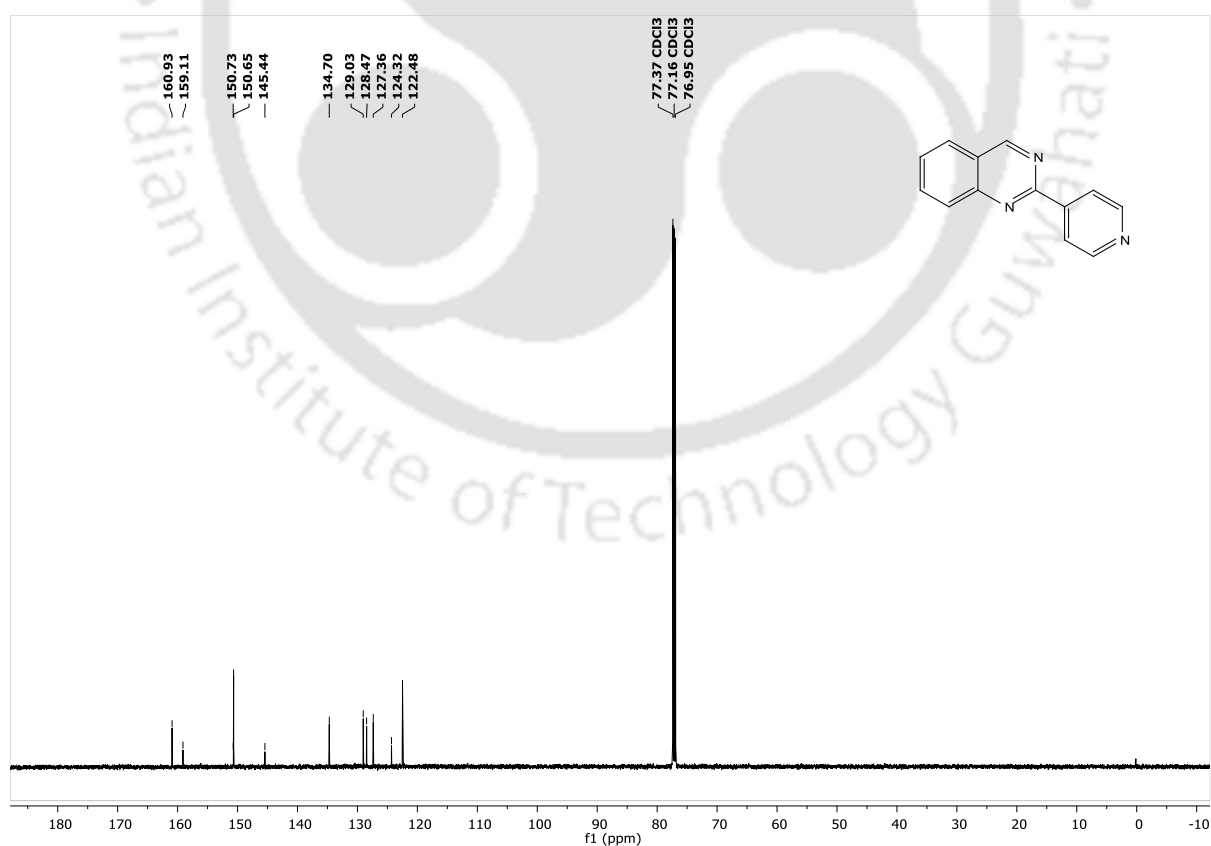


Figure S147: ^{13}C NMR Spectrum of 4.10j (CDCl_3 , 151 MHz, 298 K)

Annexure IV

^1H , ^{13}C , and ^{19}F NMR spectra of the products (Chapter 5)

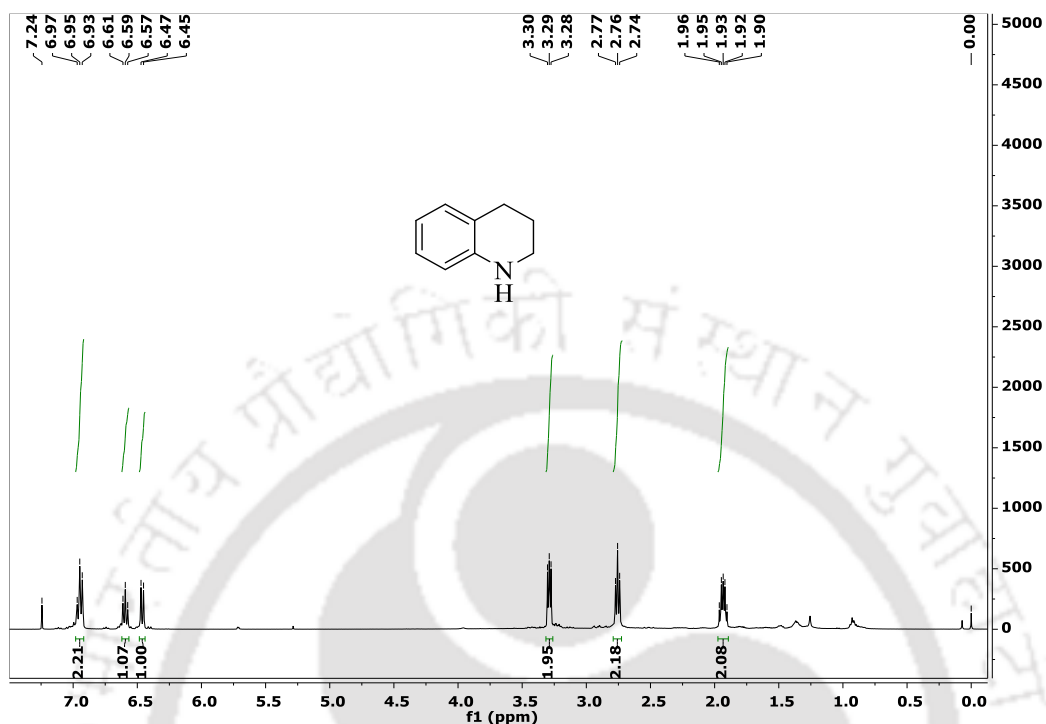


Figure S148: ^1H NMR Spectrum of 5.2a (CDCl₃, 400 MHz, 298 K)

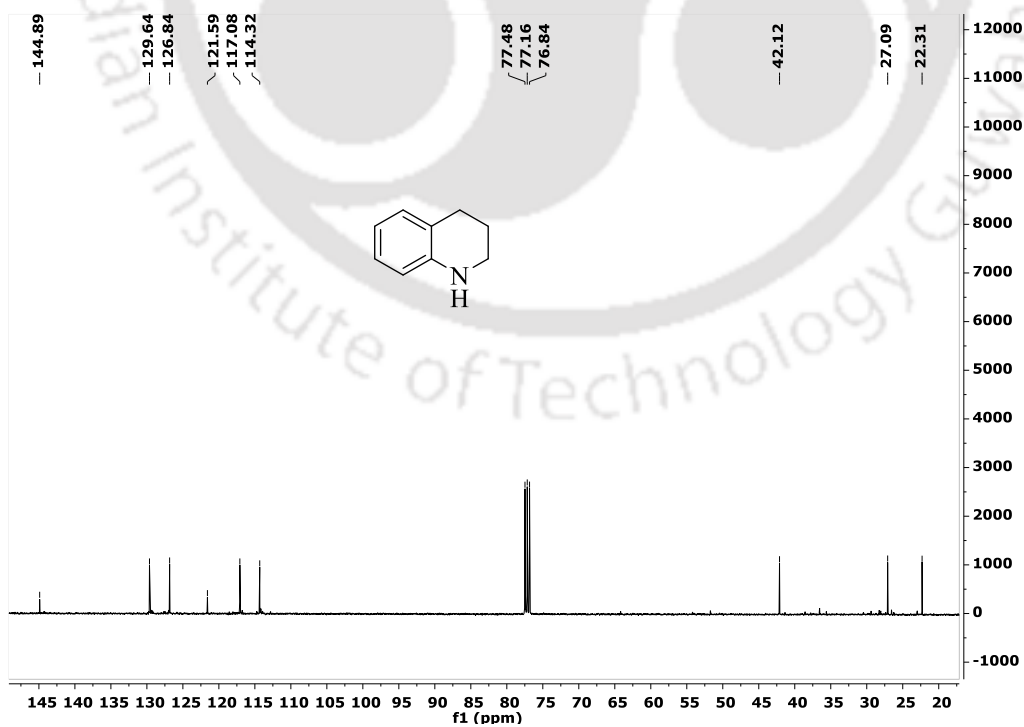


Figure S149: ^{13}C NMR Spectrum of 5.2a (CDCl₃, 101 MHz, 298 K)

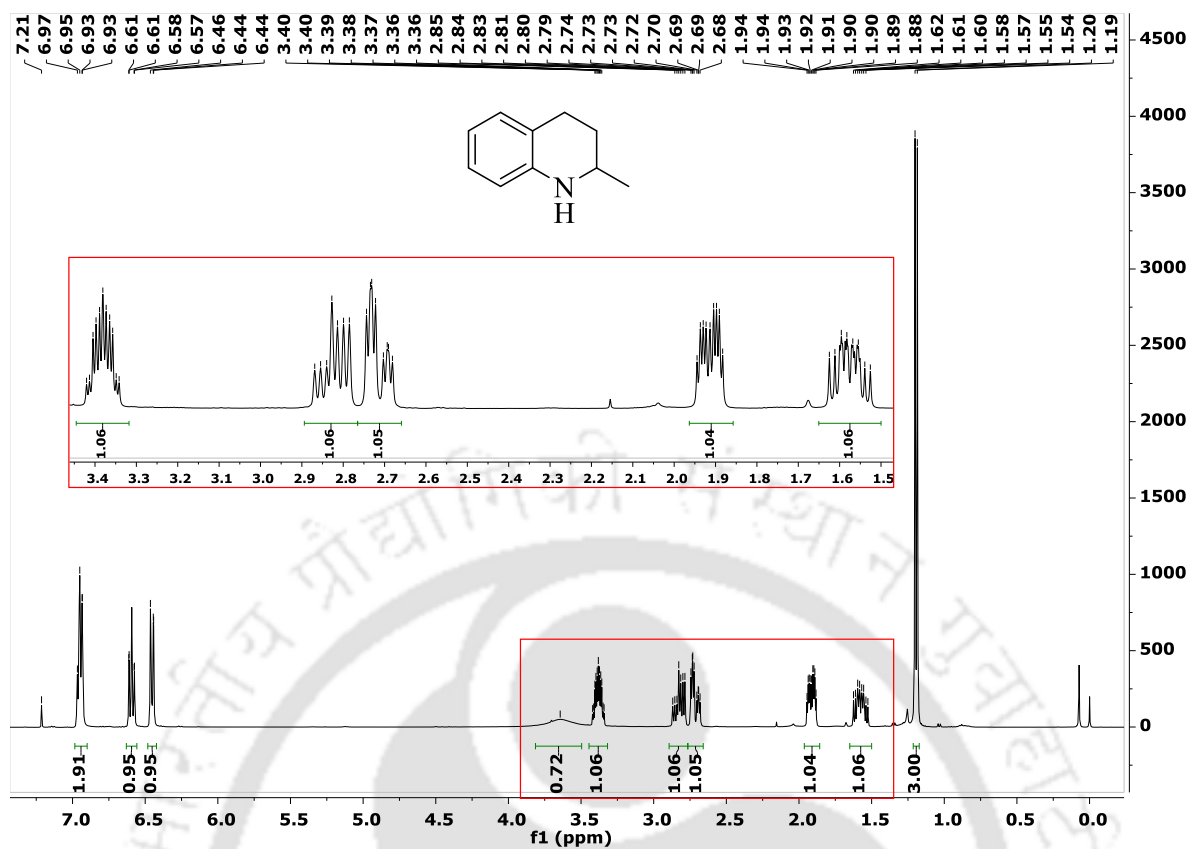


Figure S150: ¹H NMR Spectrum of 5.2b (CDCl₃, 400 MHz, 298 K)

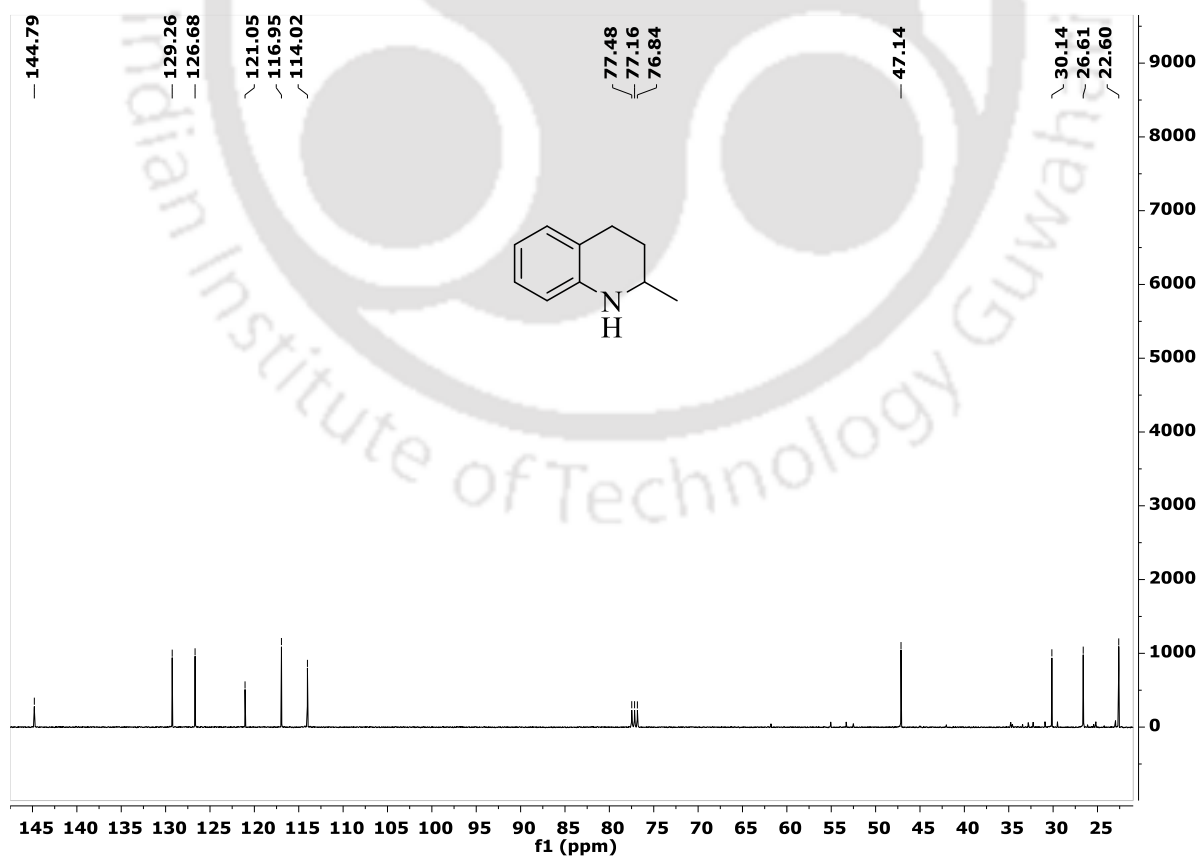


Figure S151: ¹³C NMR Spectrum of 5.2b (CDCl₃, 101 MHz, 298 K)

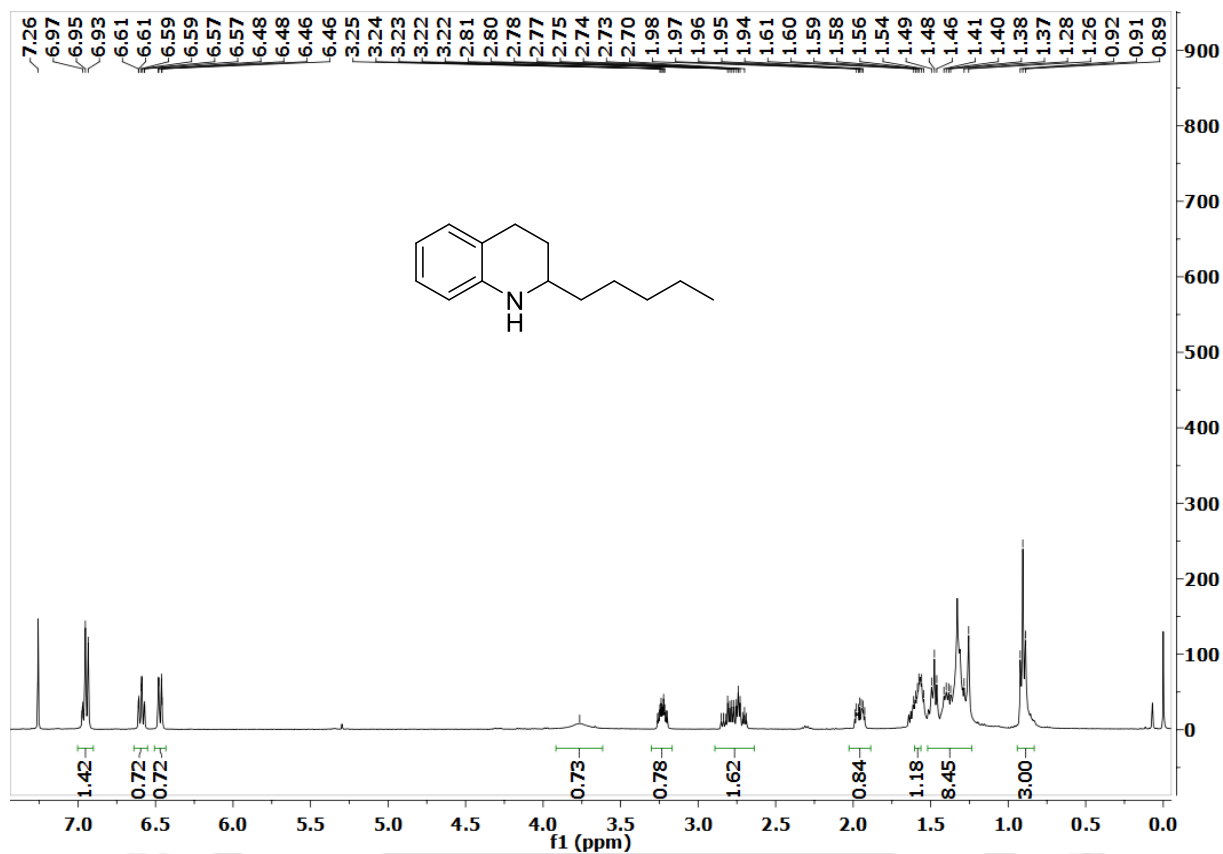


Figure S152: ^1H NMR Spectrum of 5.2c (CDCl_3 , 400 MHz, 298 K)

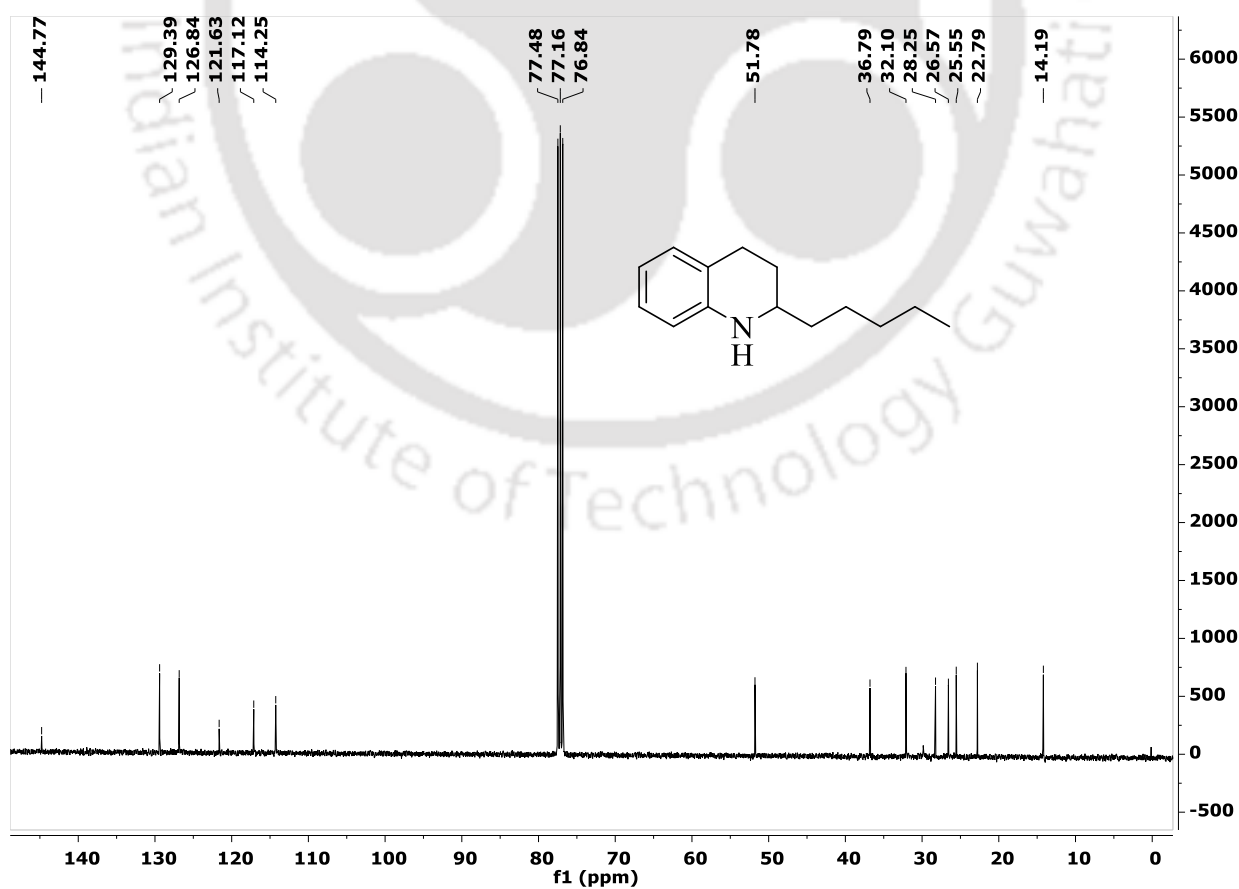


Figure S153: ^{13}C NMR Spectrum of 5.2c (CDCl_3 , 101 MHz, 298 K)

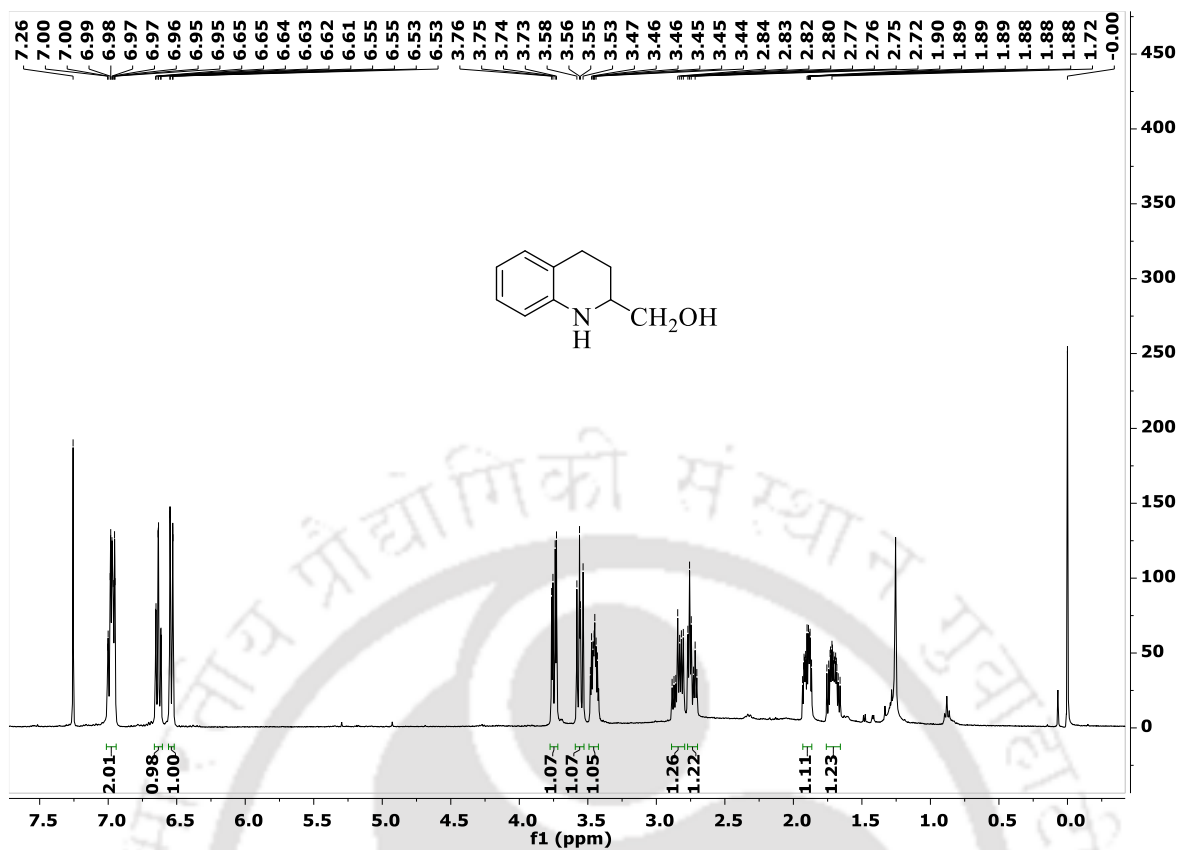


Figure S154: ^1H NMR Spectrum of **5.2d** (CDCl_3 , 400 MHz, 298 K)

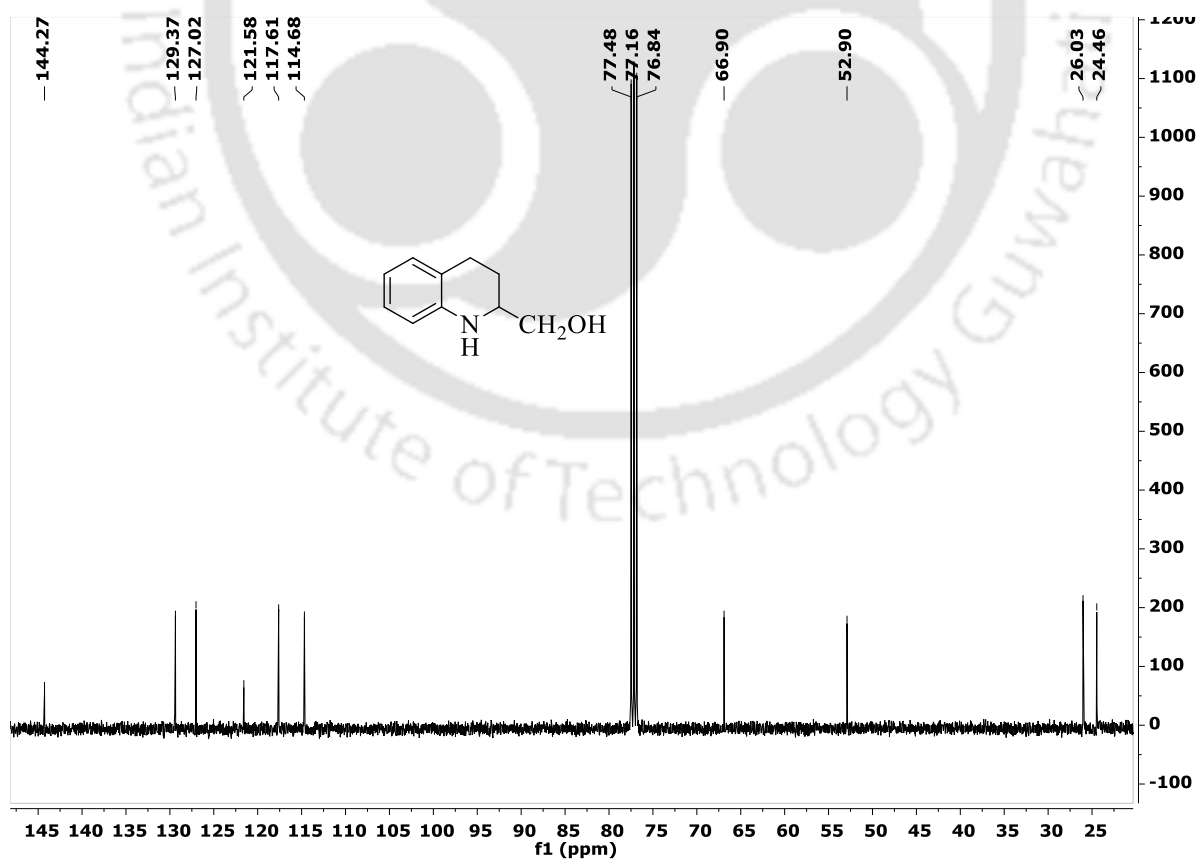


Figure S155: ^{13}C NMR Spectrum of **5.2d** (CDCl_3 , 101 MHz, 298 K)

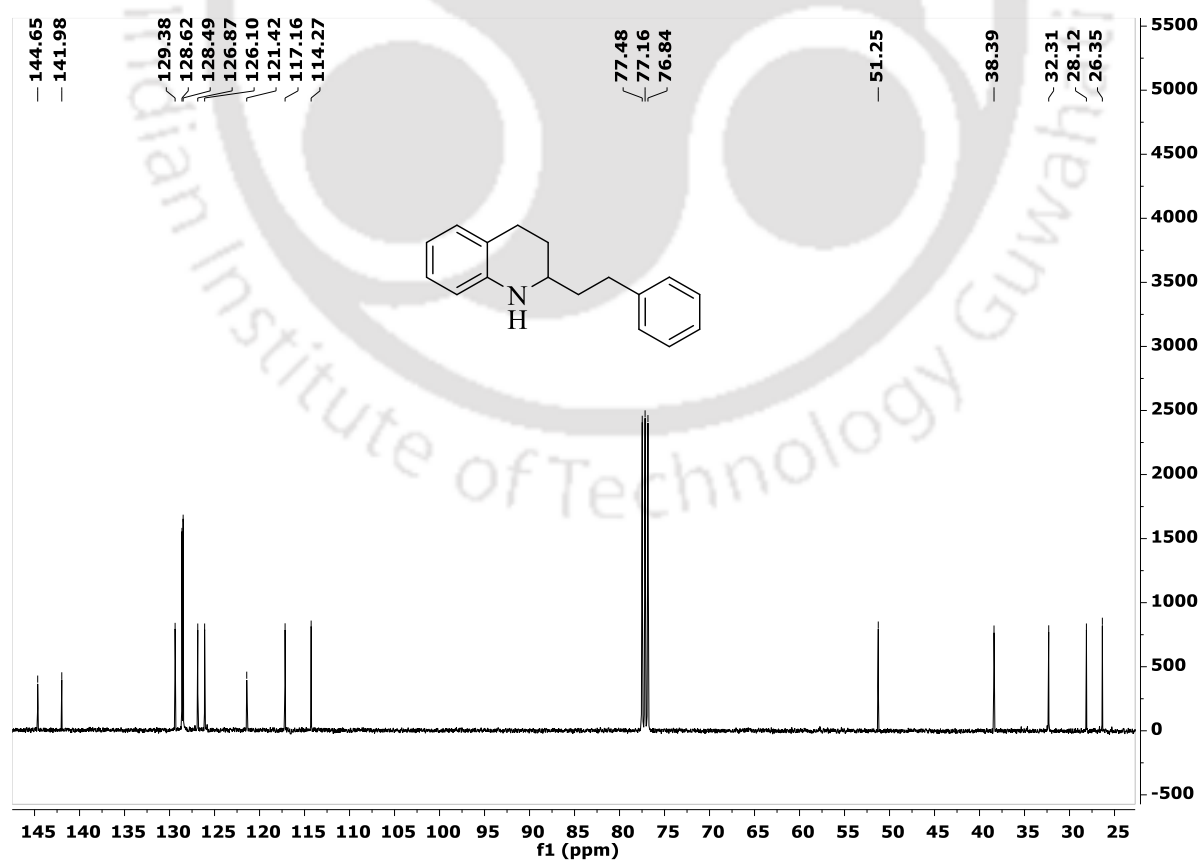
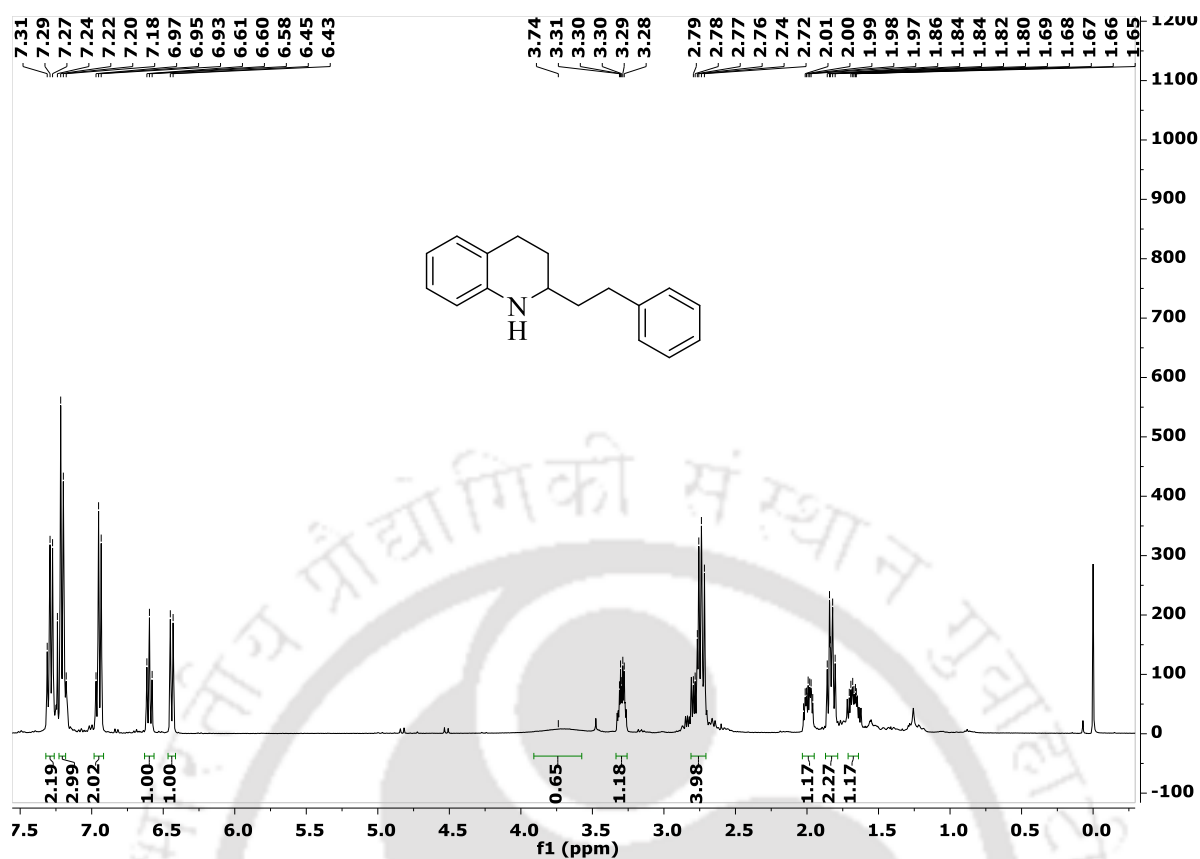
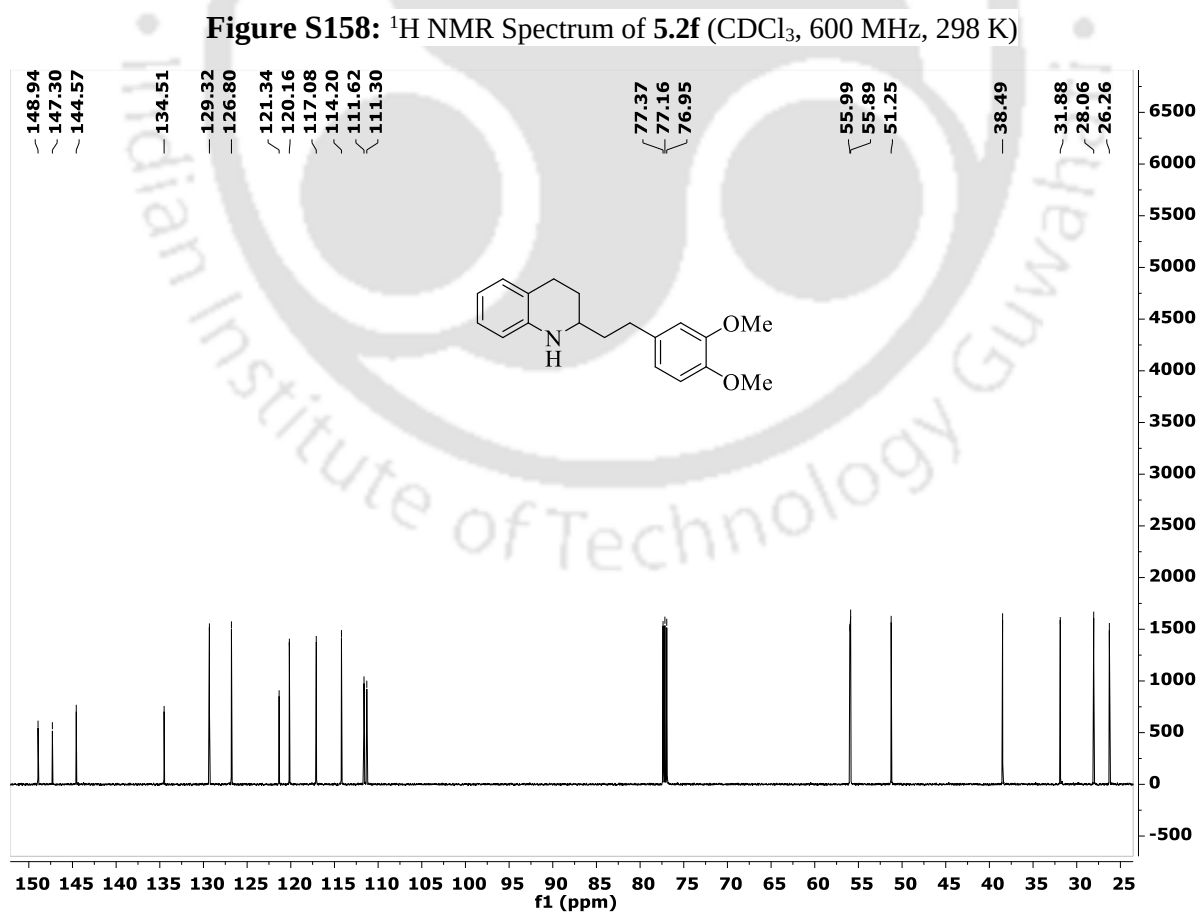
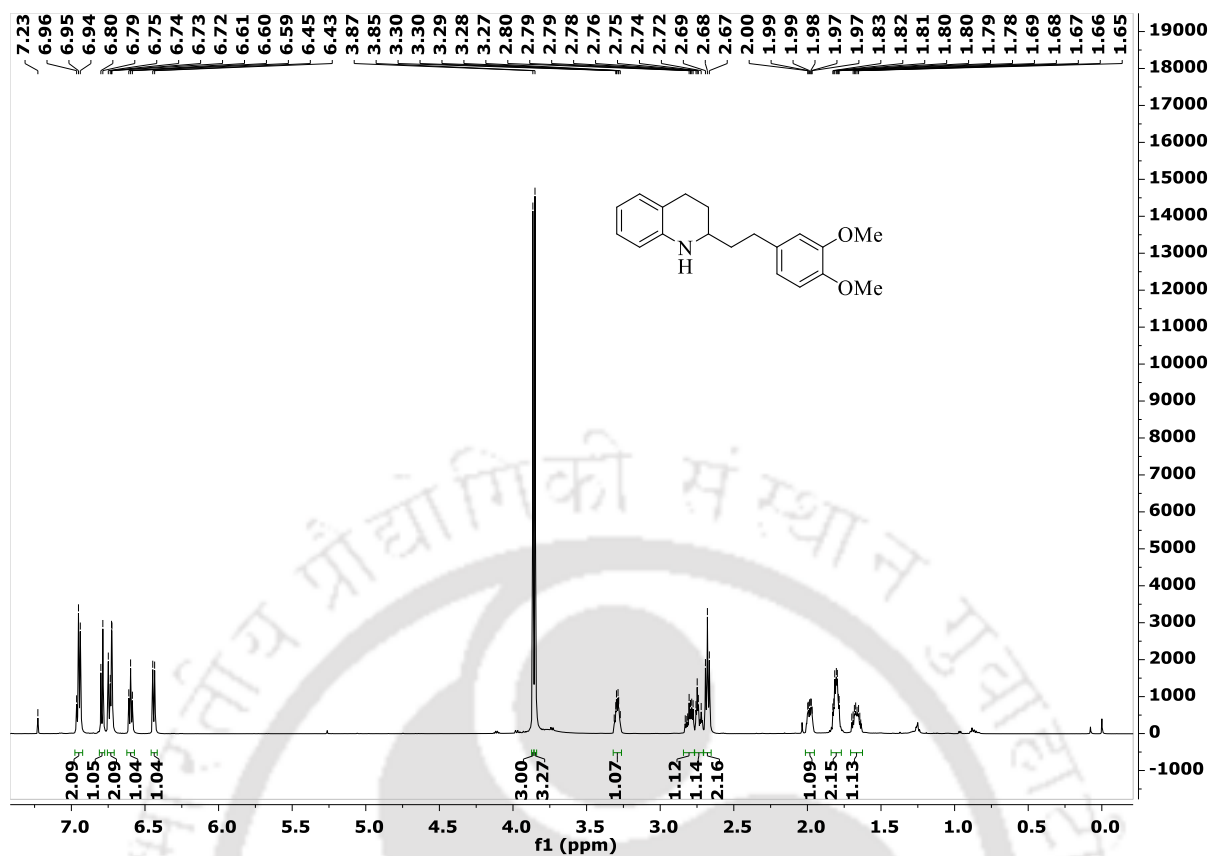


Figure S157: ^{13}C NMR Spectrum of 5.2e (CDCl_3 , 101 MHz, 298 K)



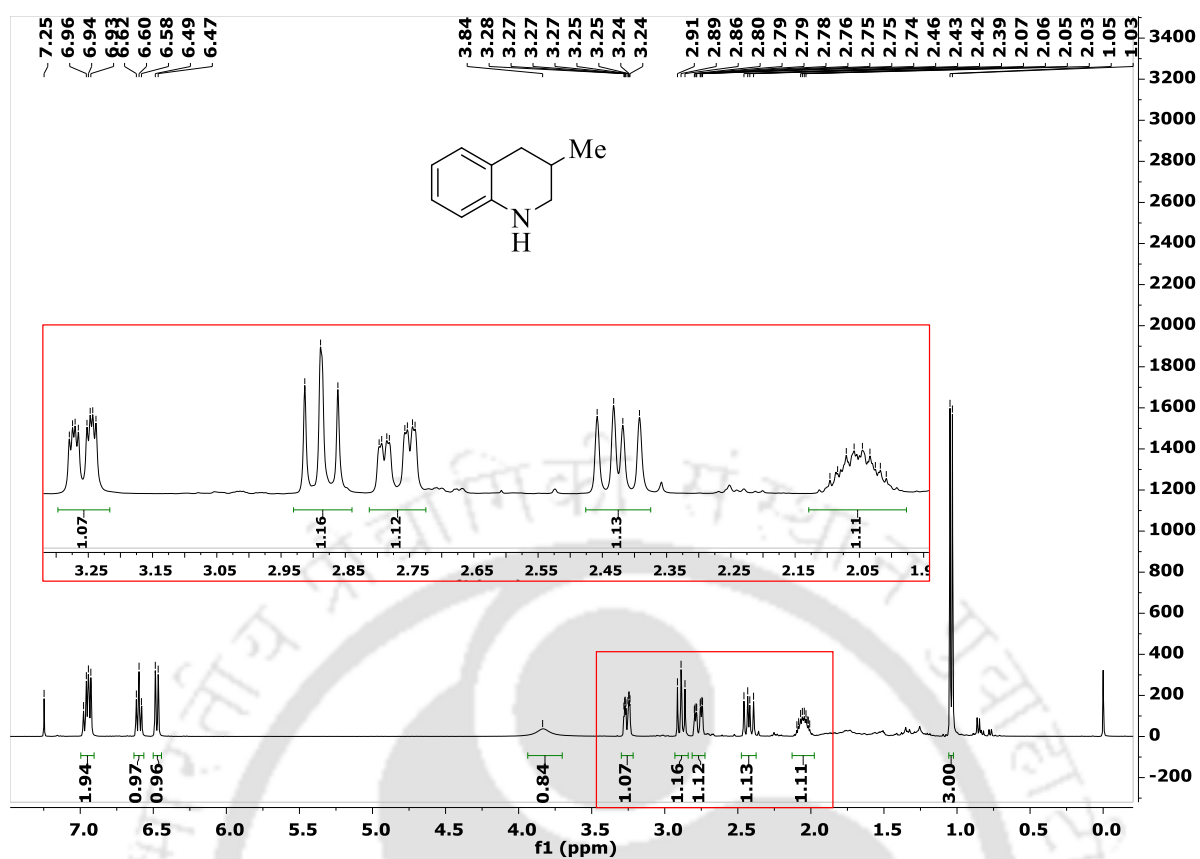


Figure S160: ¹H NMR Spectrum of 5.2g (CDCl₃, 400 MHz, 298 K)

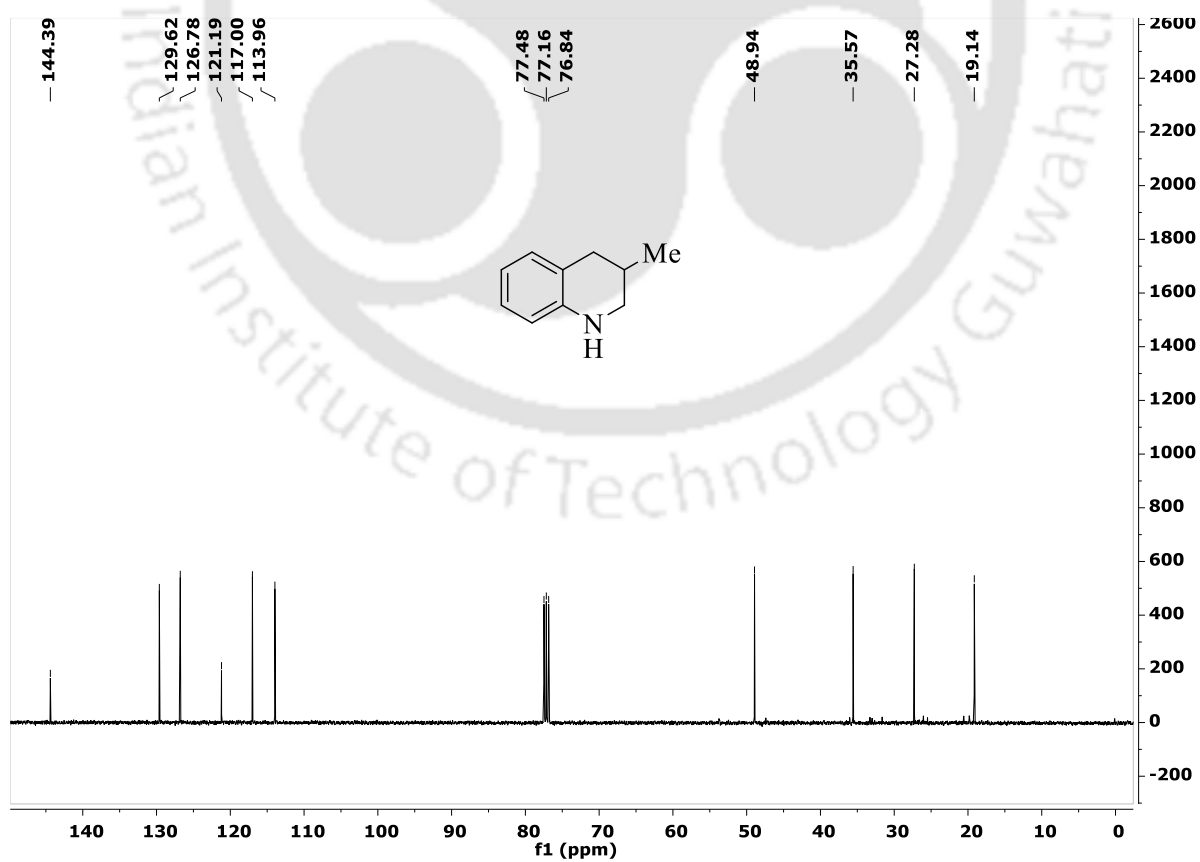


Figure S161: ¹³C NMR Spectrum of 5.2g (CDCl₃, 101 MHz, 298 K)

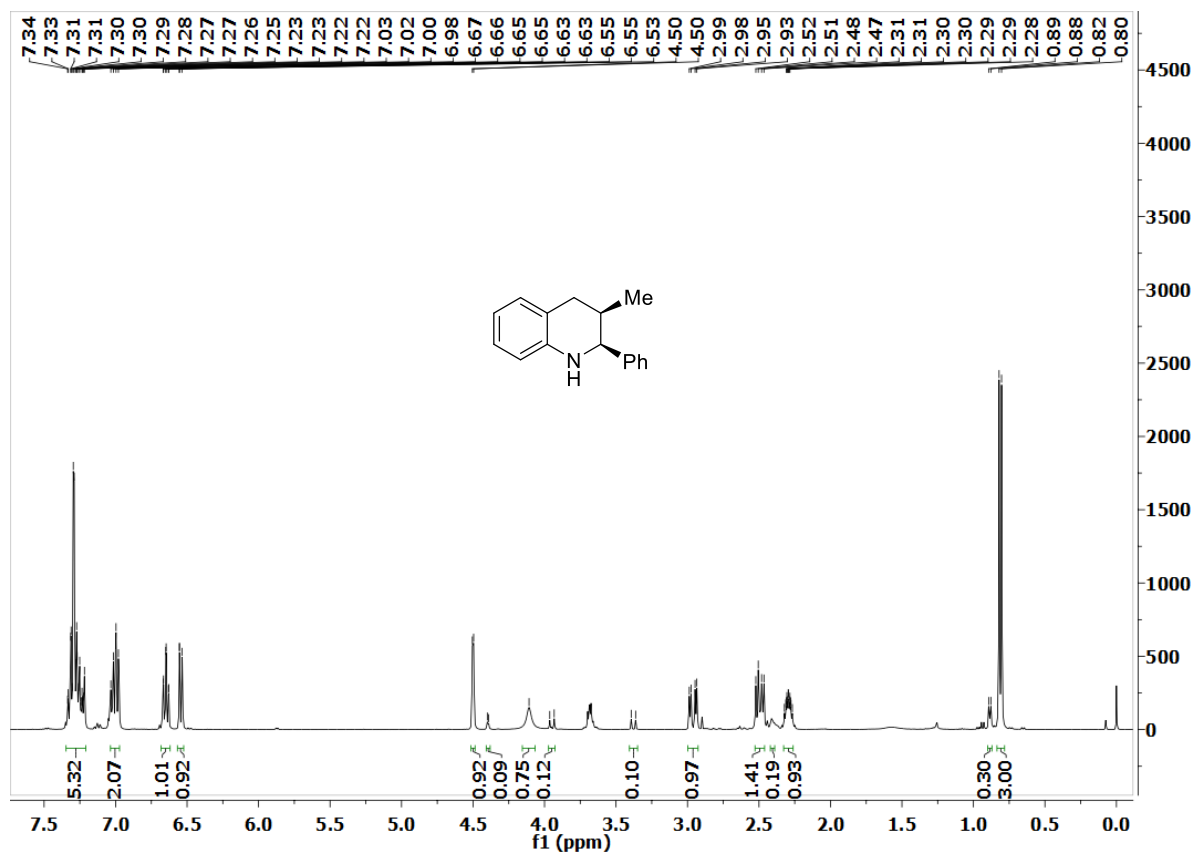


Figure S162: ¹H NMR Spectrum of 5.2h (CDCl₃, 400 MHz, 298 K)

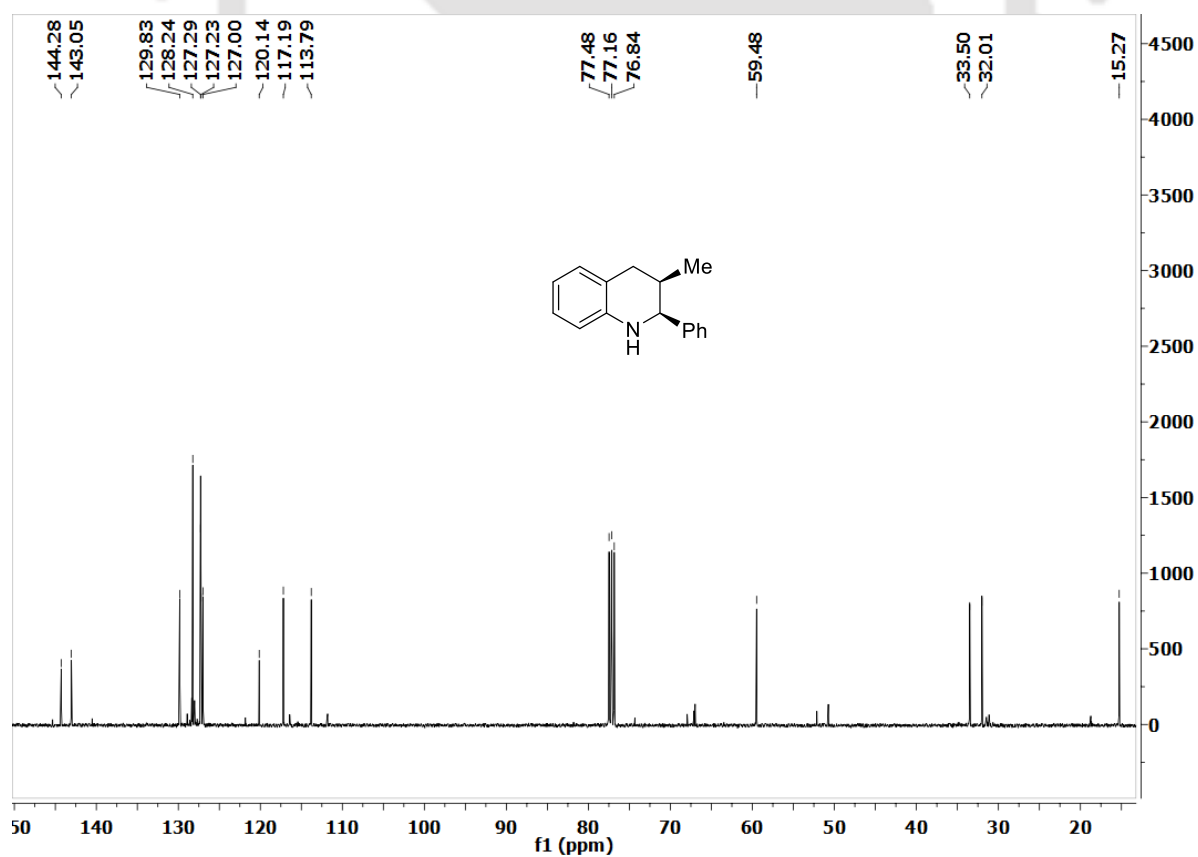


Figure S163: ¹³C NMR Spectrum of 5.2h (CDCl₃, 101 MHz, 298 K)

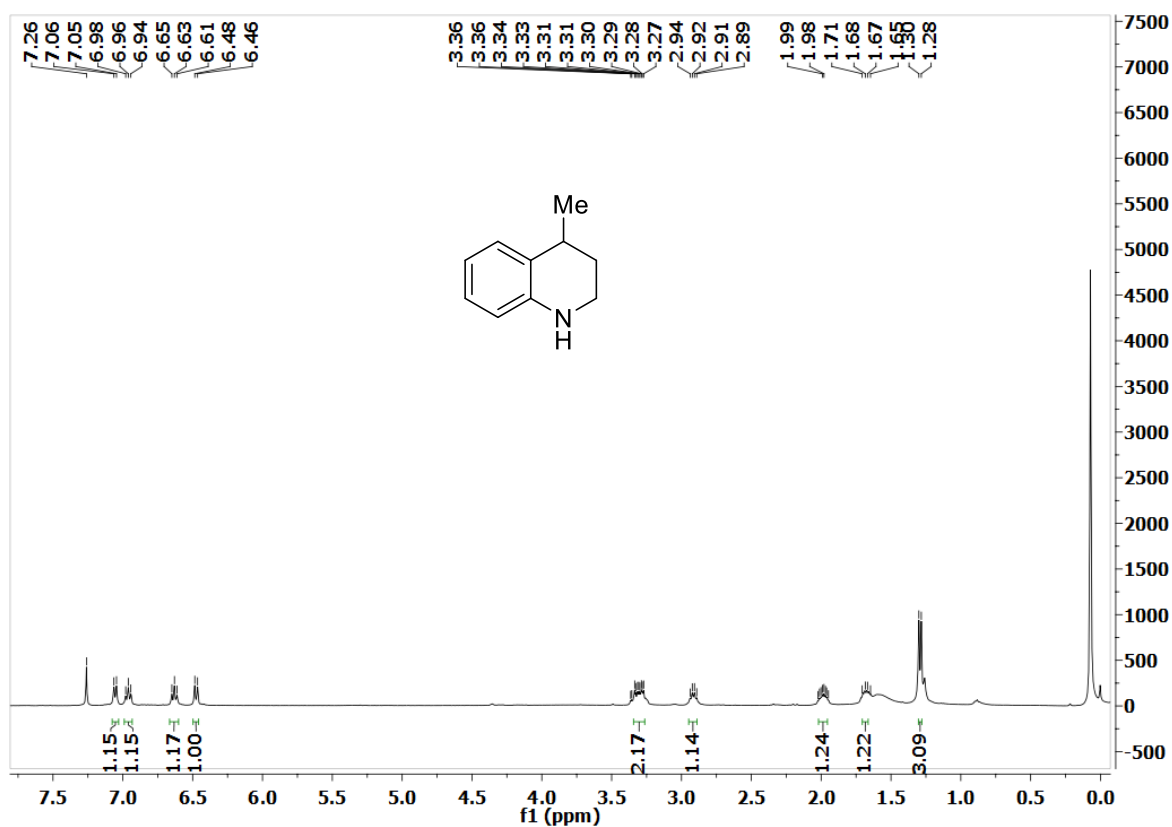


Figure S164: ¹H NMR Spectrum of 5.2i (CDCl₃, 400 MHz, 298 K)

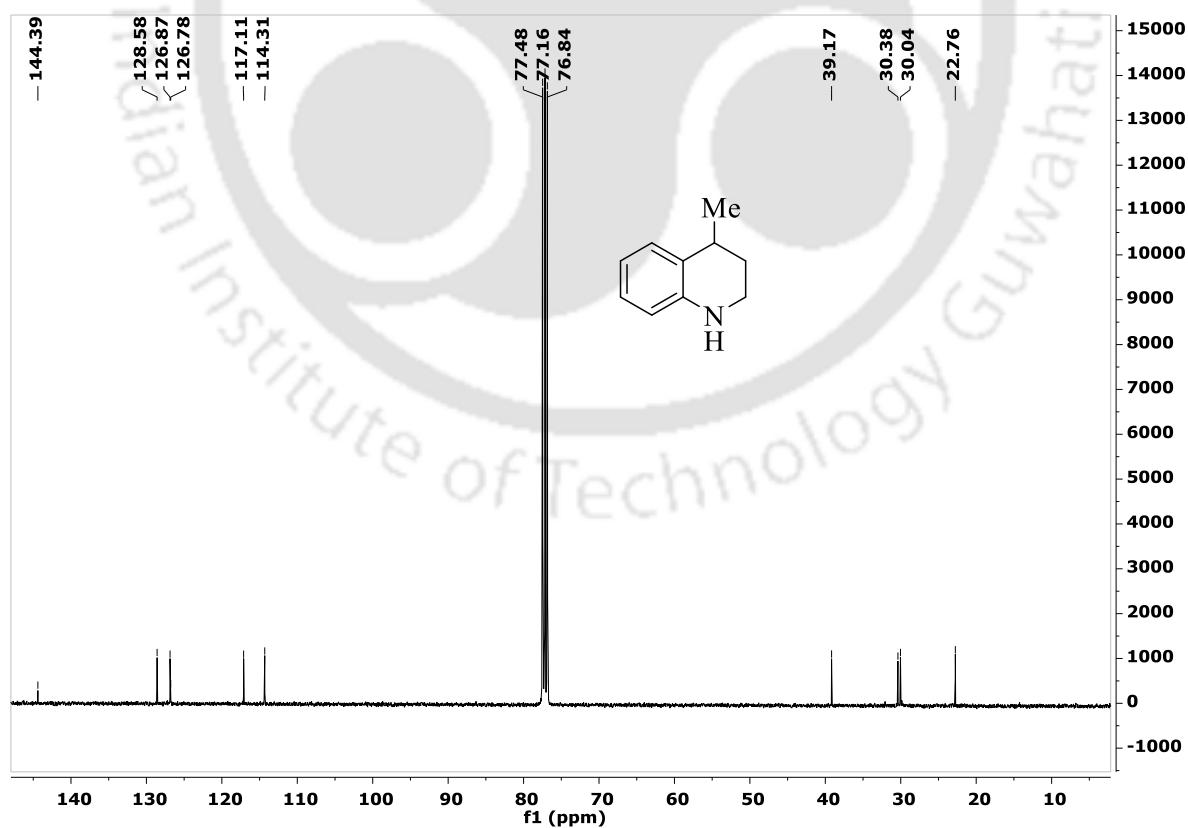


Figure S165: ¹³C NMR Spectrum of 5.2i (CDCl₃, 101 MHz, 298 K)

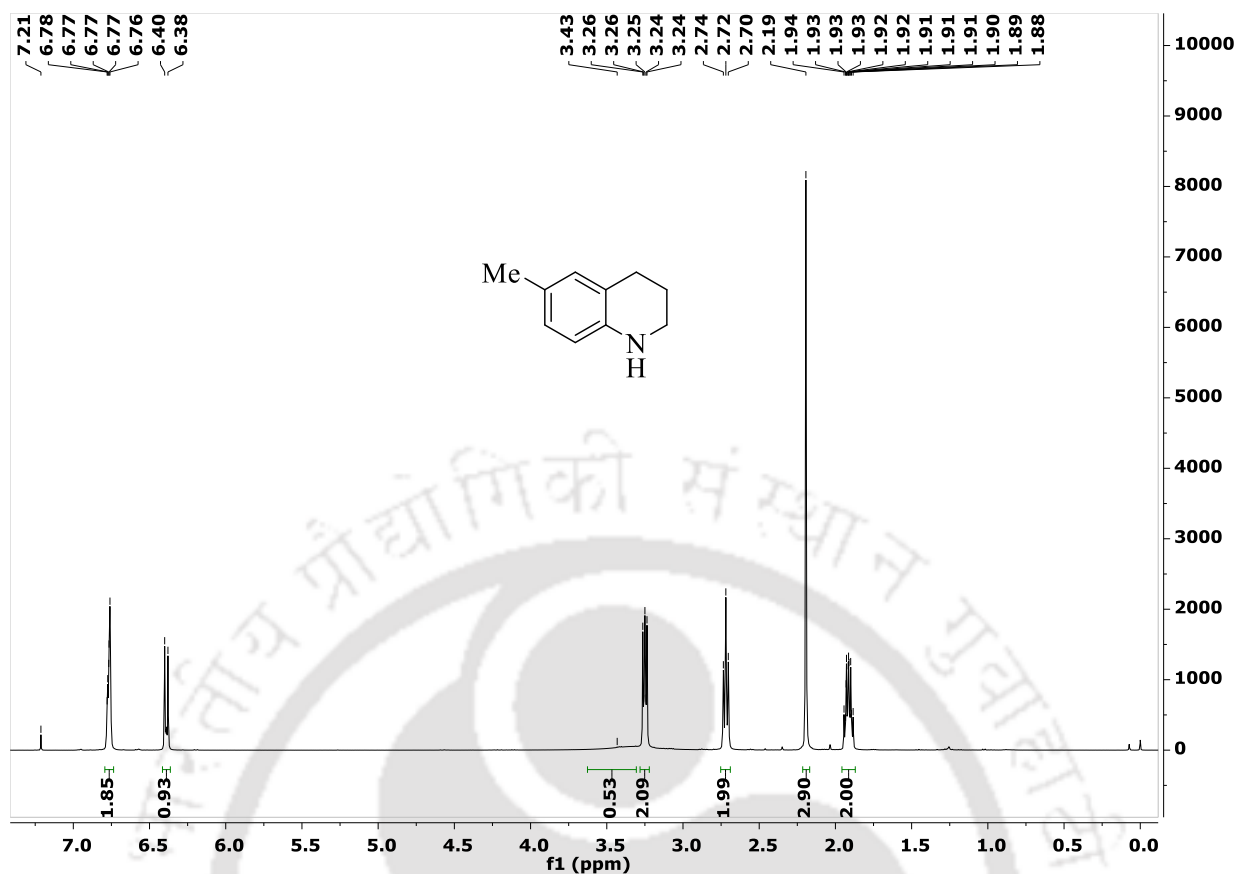


Figure S166: ^1H NMR Spectrum of **5.2j** (CDCl_3 , 400 MHz, 298 K)

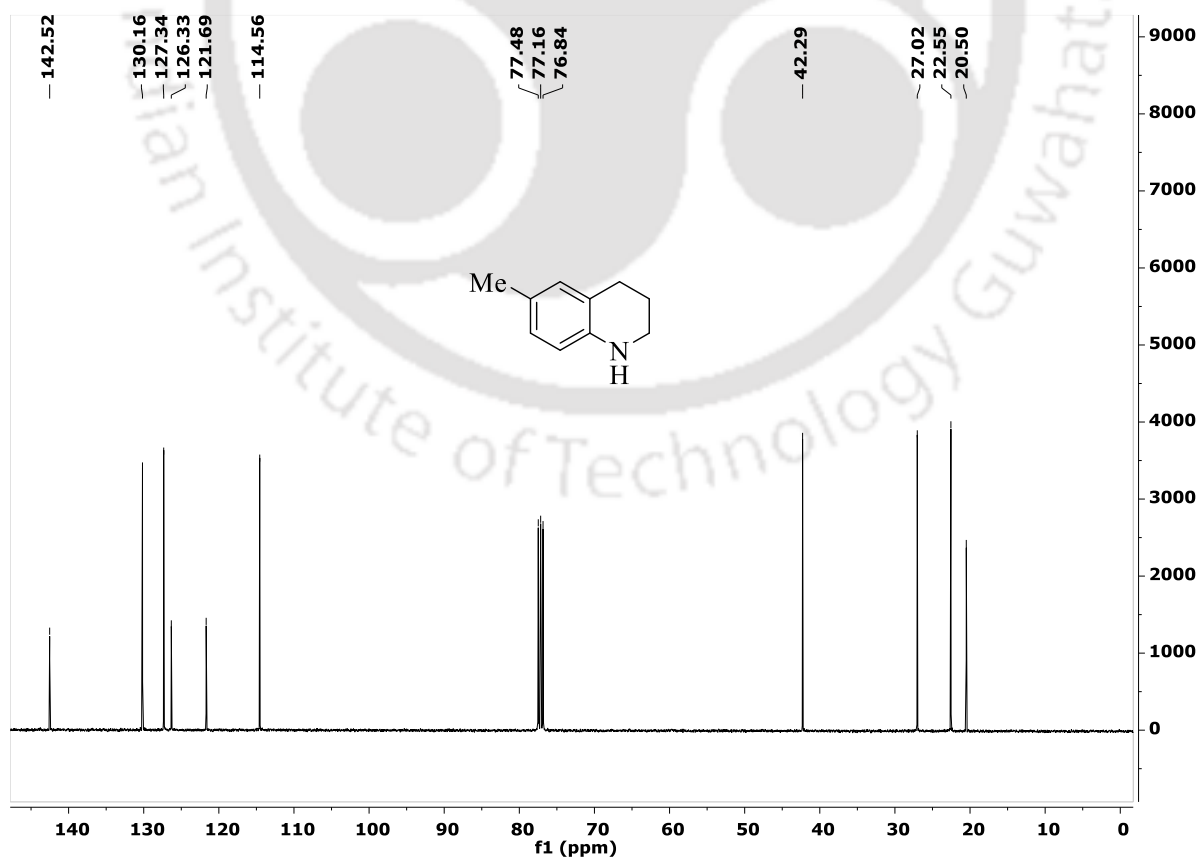


Figure S167: ^{13}C NMR Spectrum of **5.2j** (CDCl_3 , 101 MHz, 298 K)

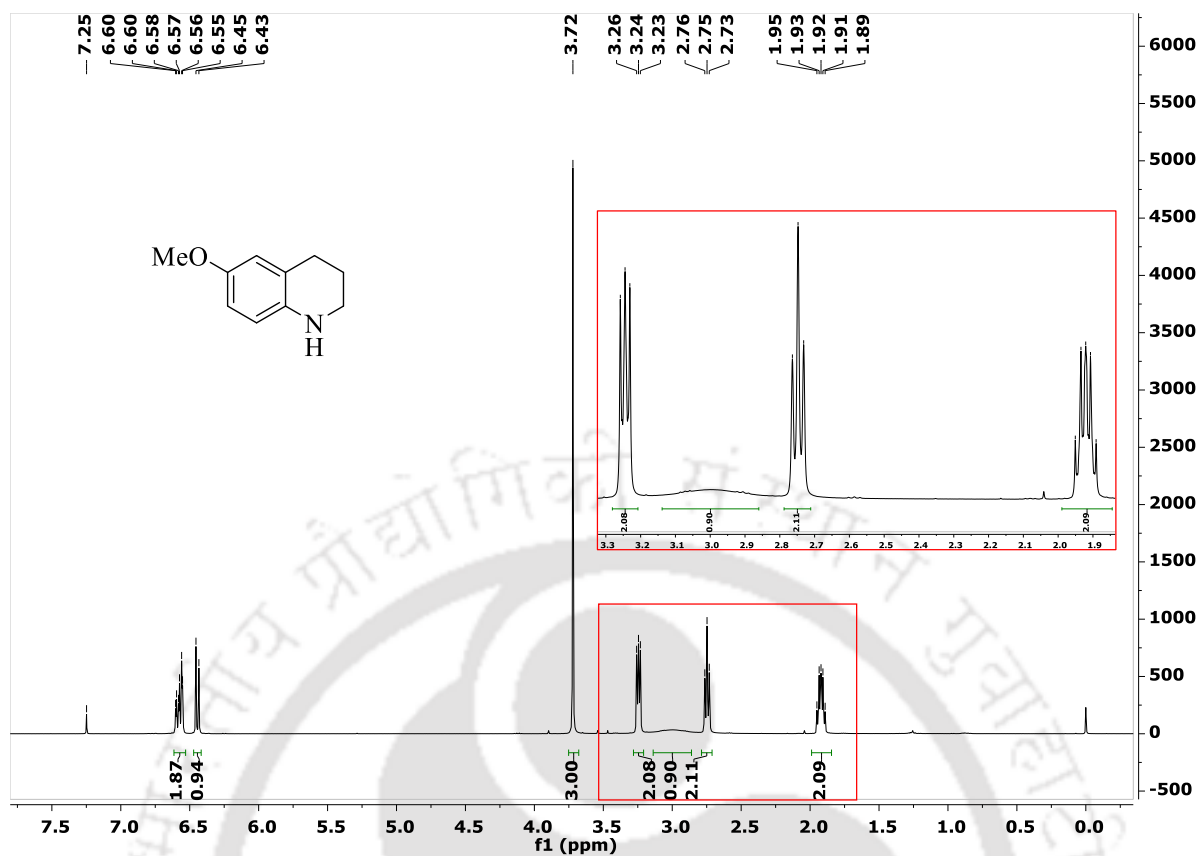


Figure S168: ¹H NMR Spectrum of 5.2k (CDCl₃, 400 MHz, 298 K)

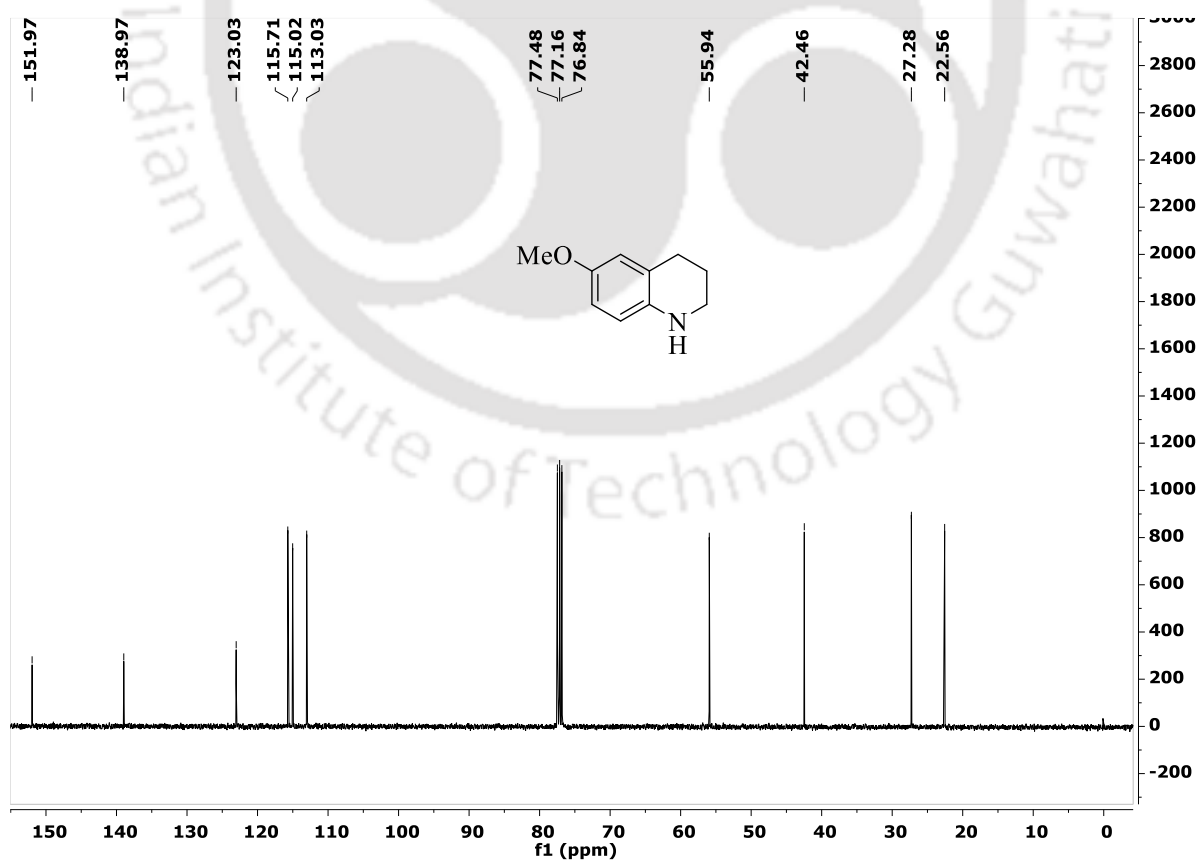
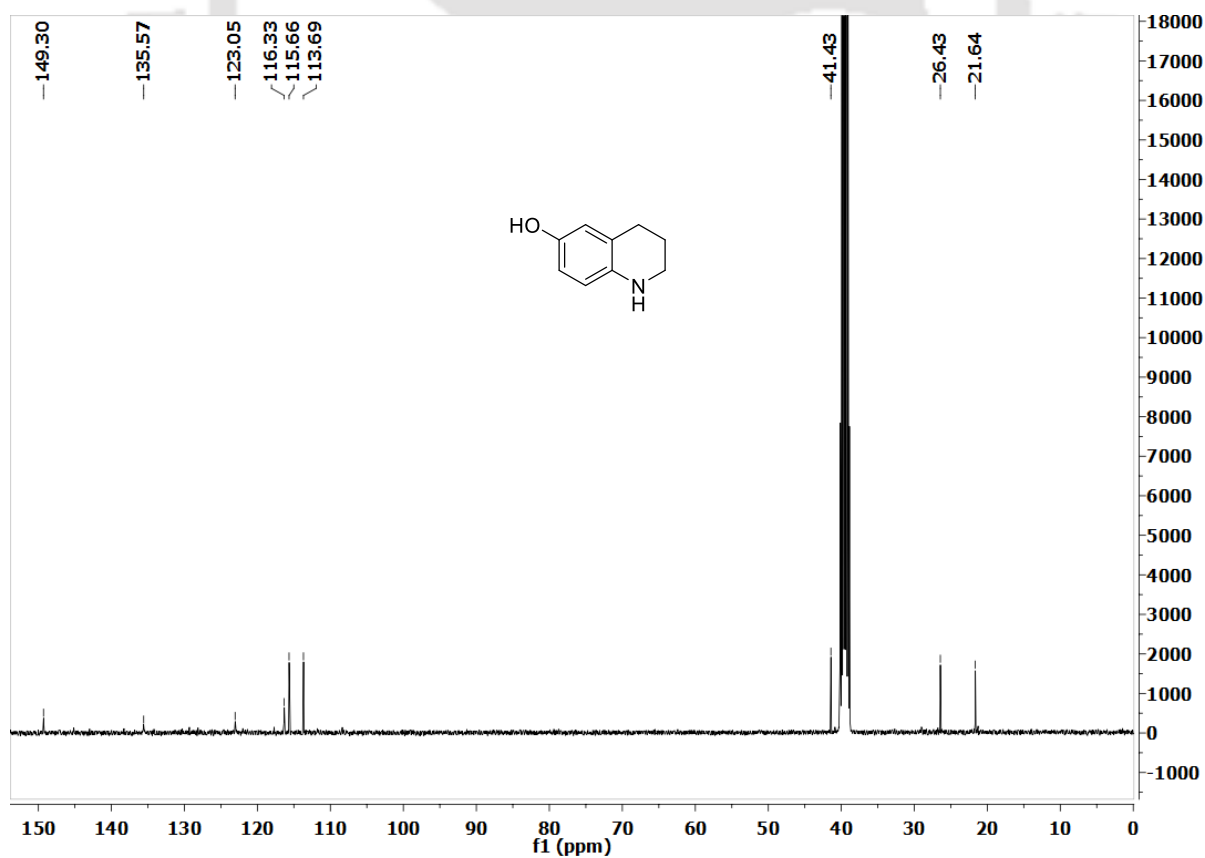
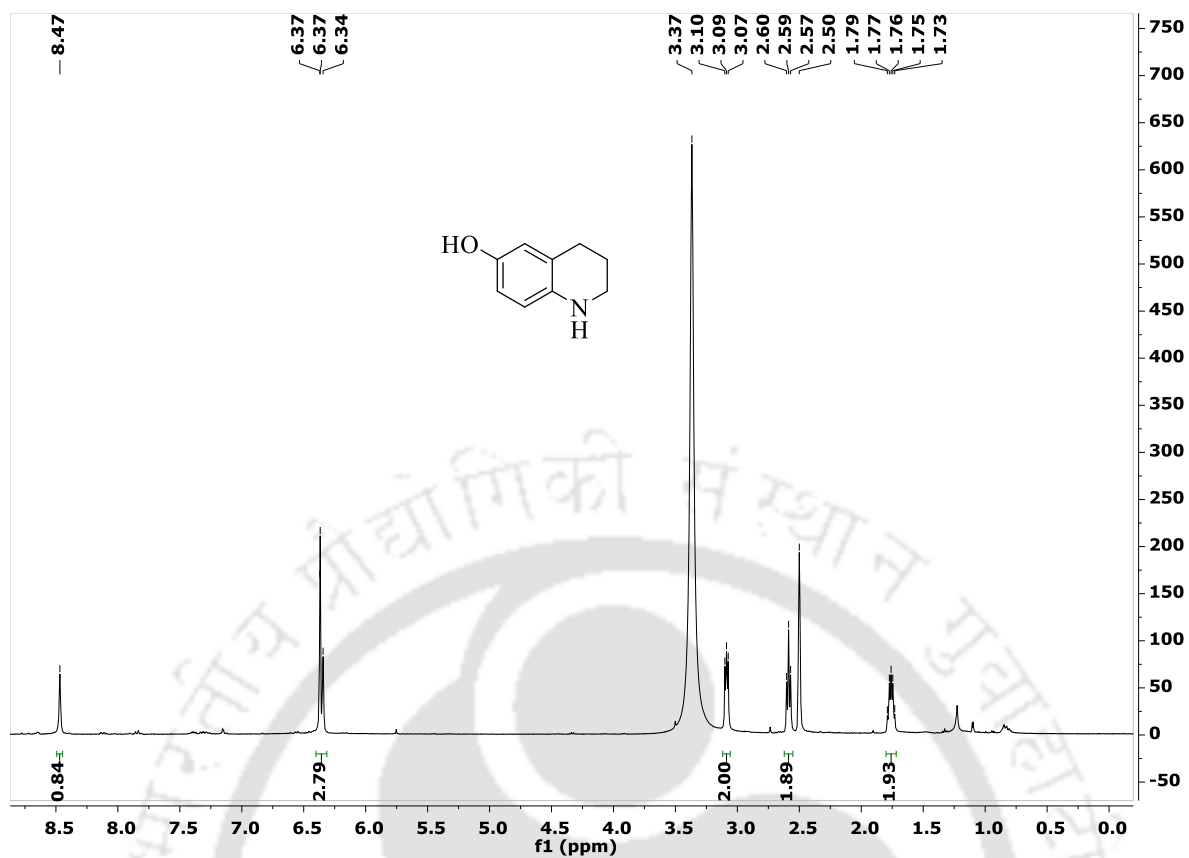


Figure S169: ¹³C NMR Spectrum of 5.2k (CDCl₃, 101 MHz, 298 K)



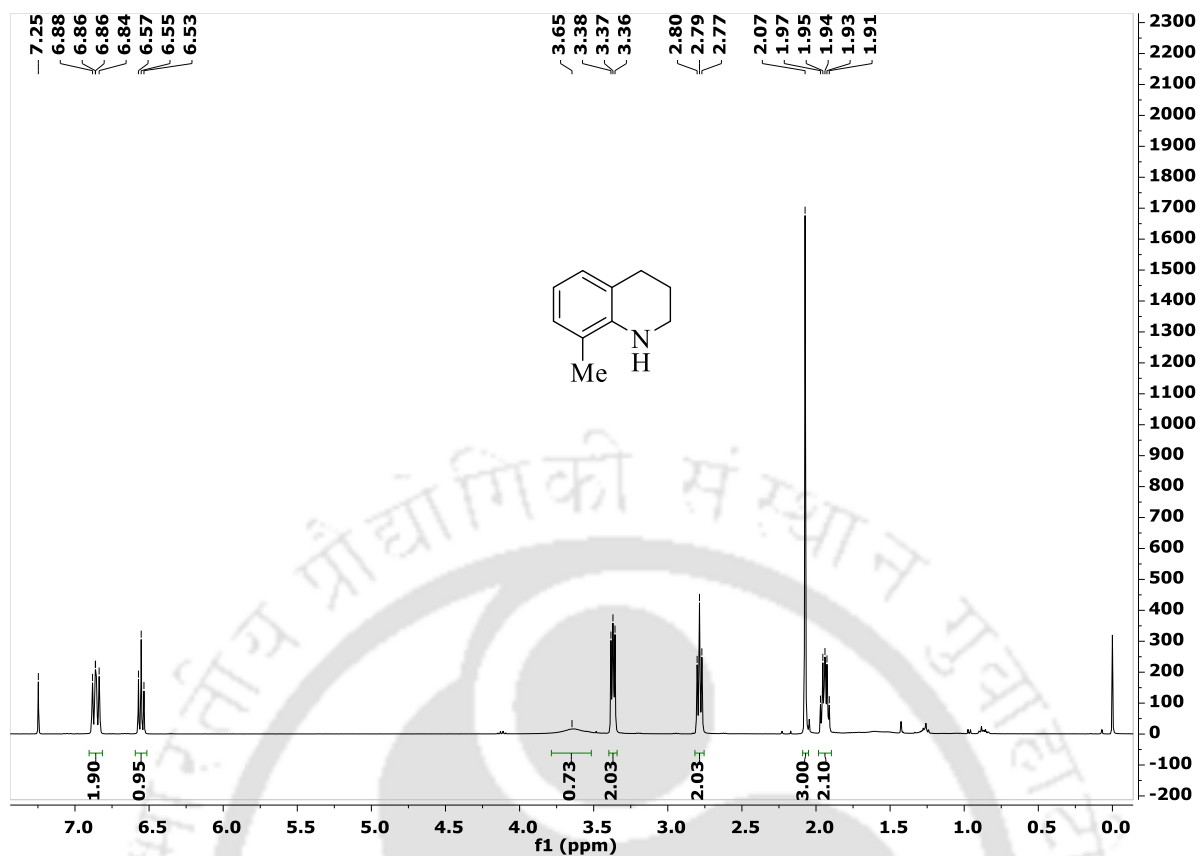


Figure S172: ^1H NMR Spectrum of 5.2m (CDCl_3 , 400 MHz, 298 K)

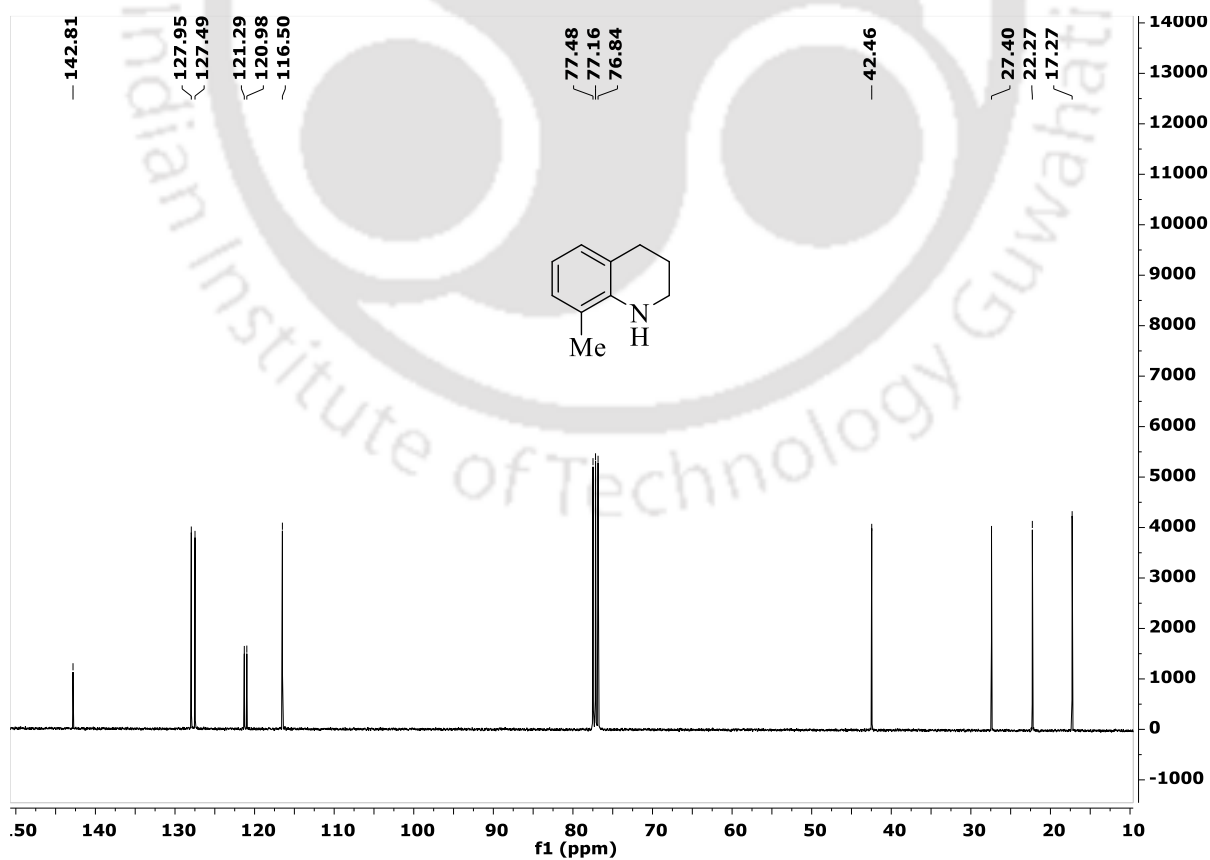


Figure S173: ^{13}C NMR Spectrum of 5.2m (CDCl_3 , 101 MHz, 298 K)

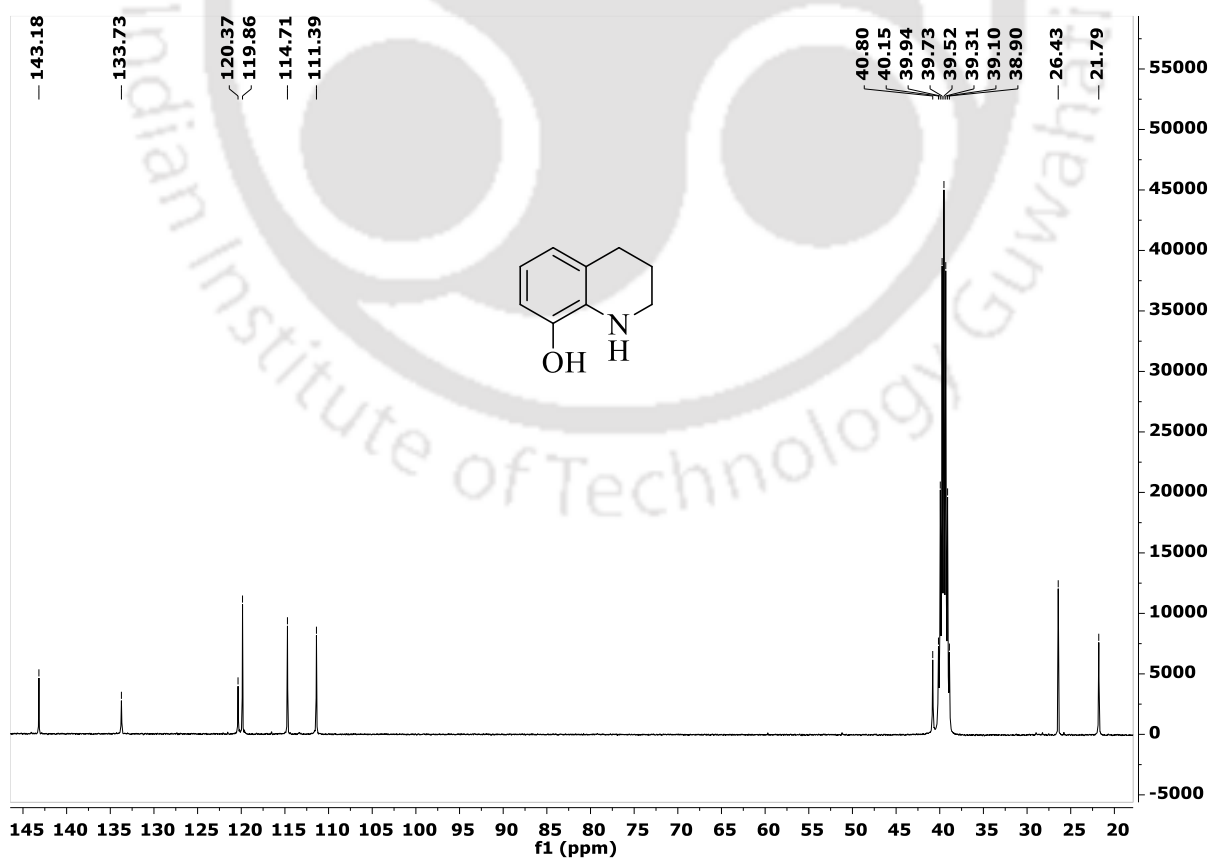
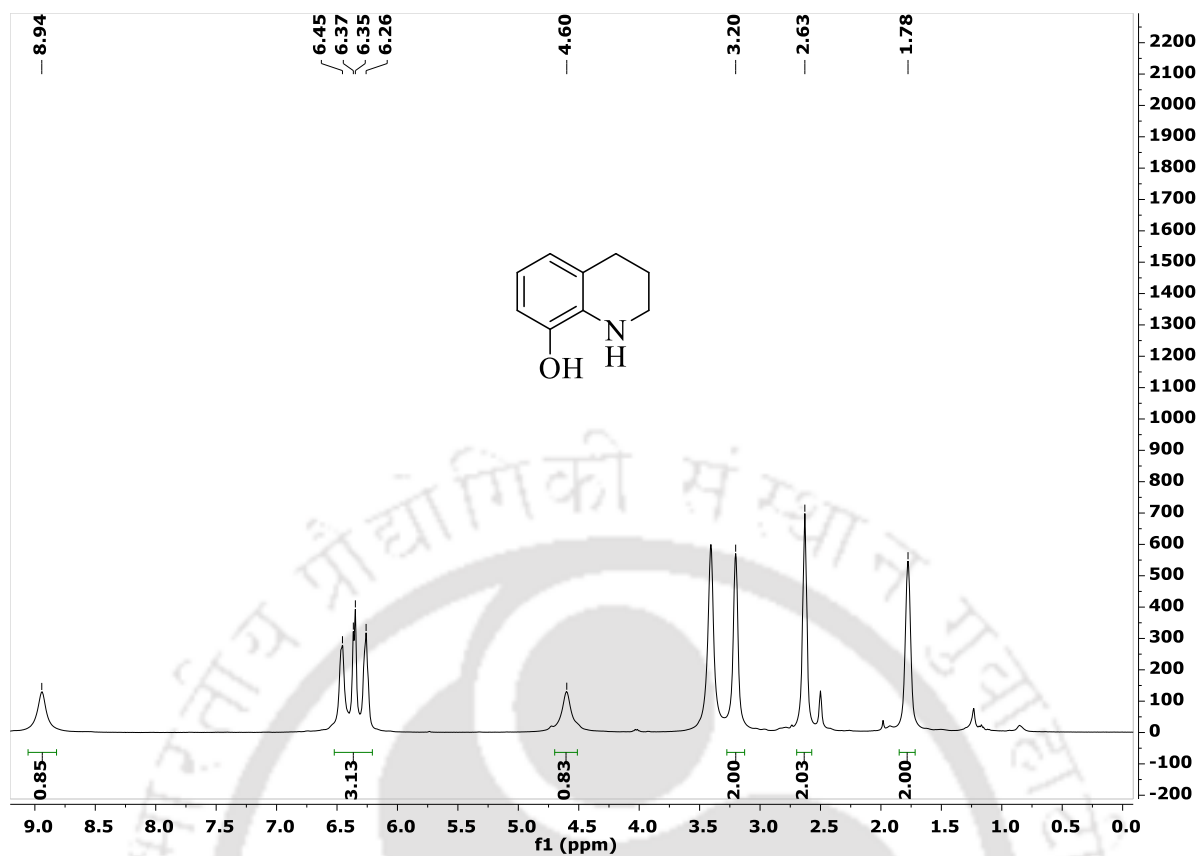


Figure S175: ^{13}C NMR Spectrum of **5.2n** (DMSO- d_6 , 101 MHz, 298 K)

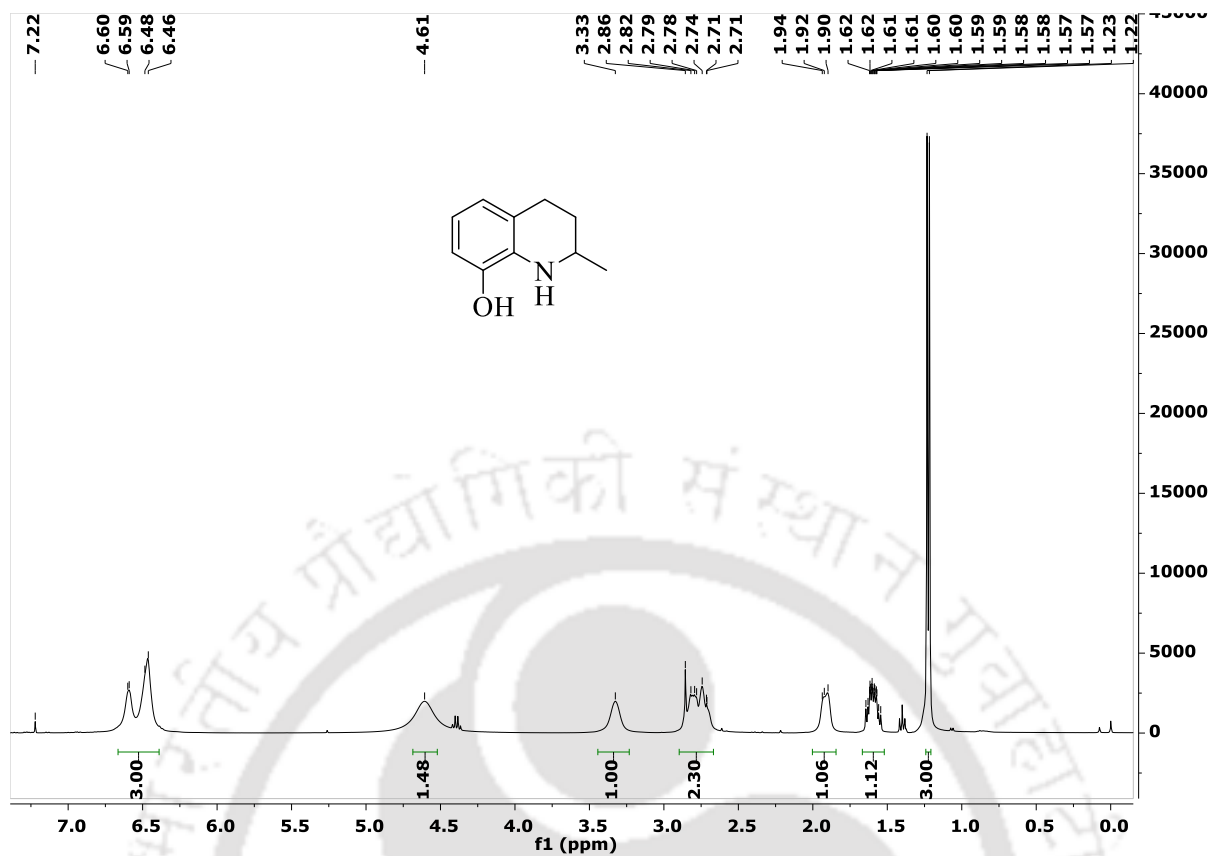


Figure S176: ^1H NMR Spectrum of 5.2o (CDCl_3 , 400 MHz, 298 K)

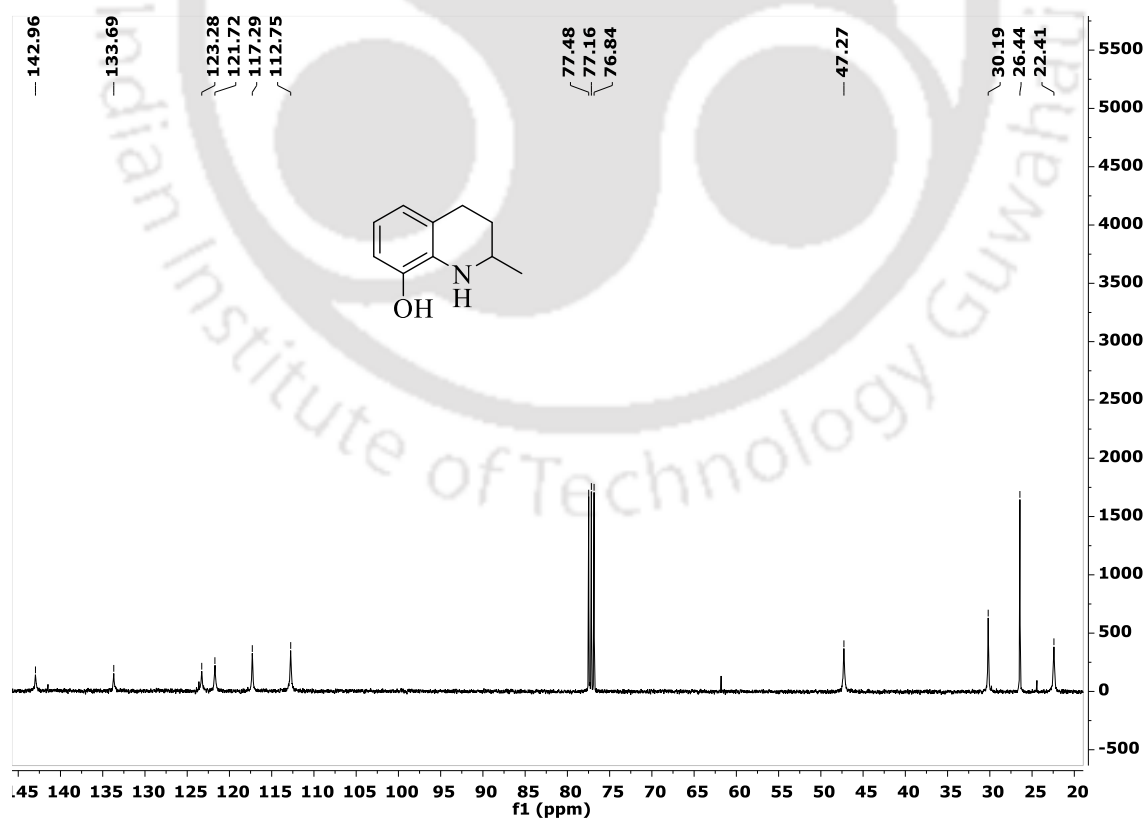
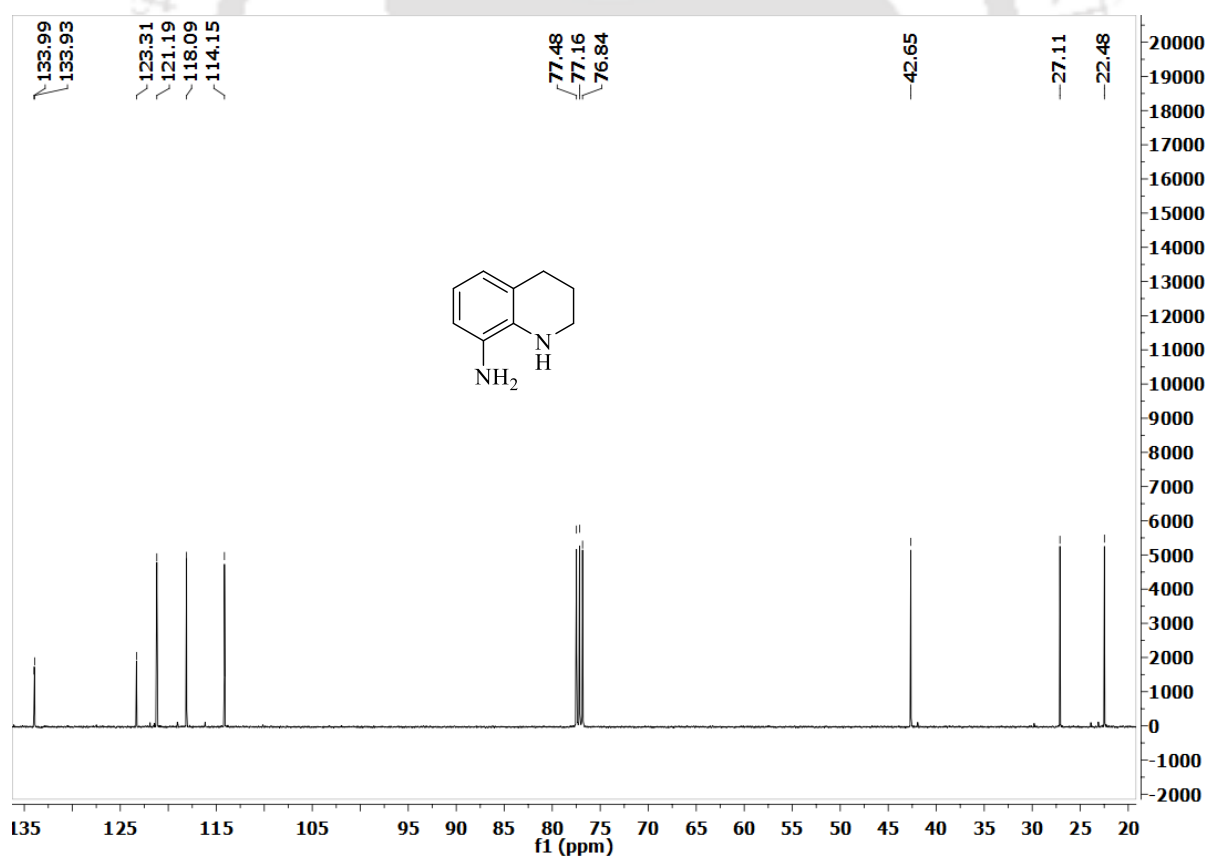
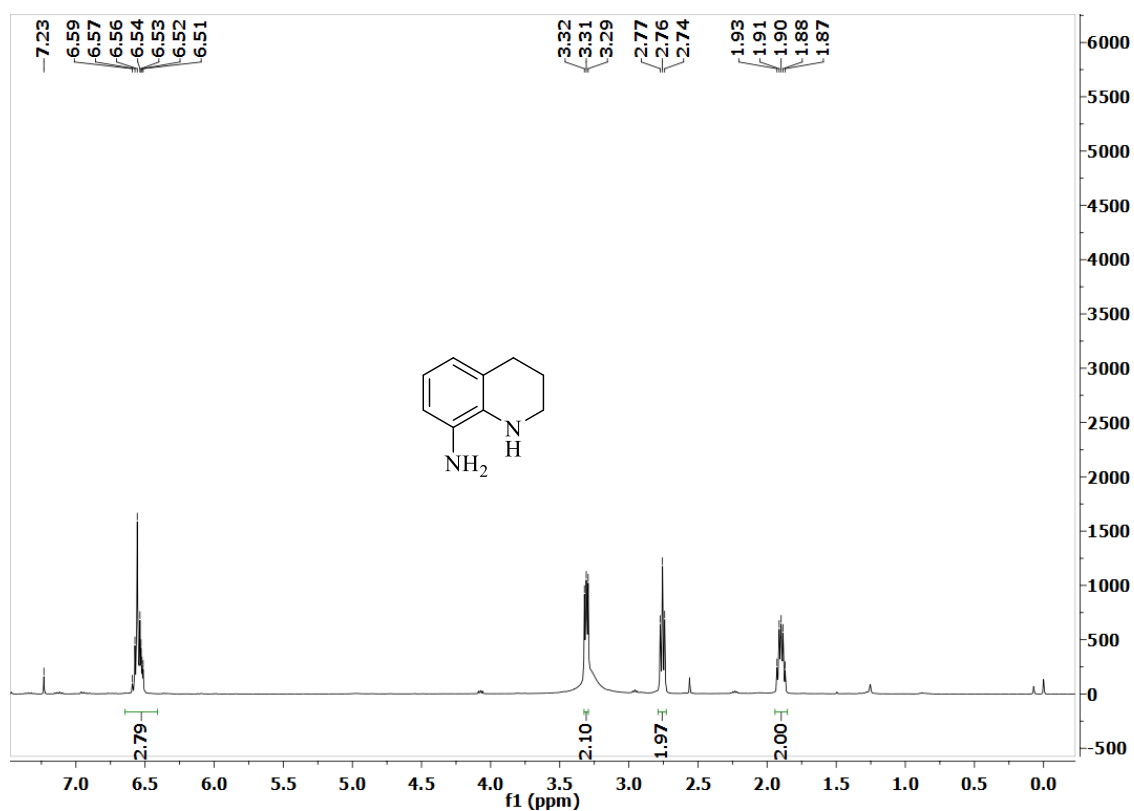


Figure S177: ^{13}C NMR Spectrum of 5.2o (CDCl_3 , 101 MHz, 298 K)



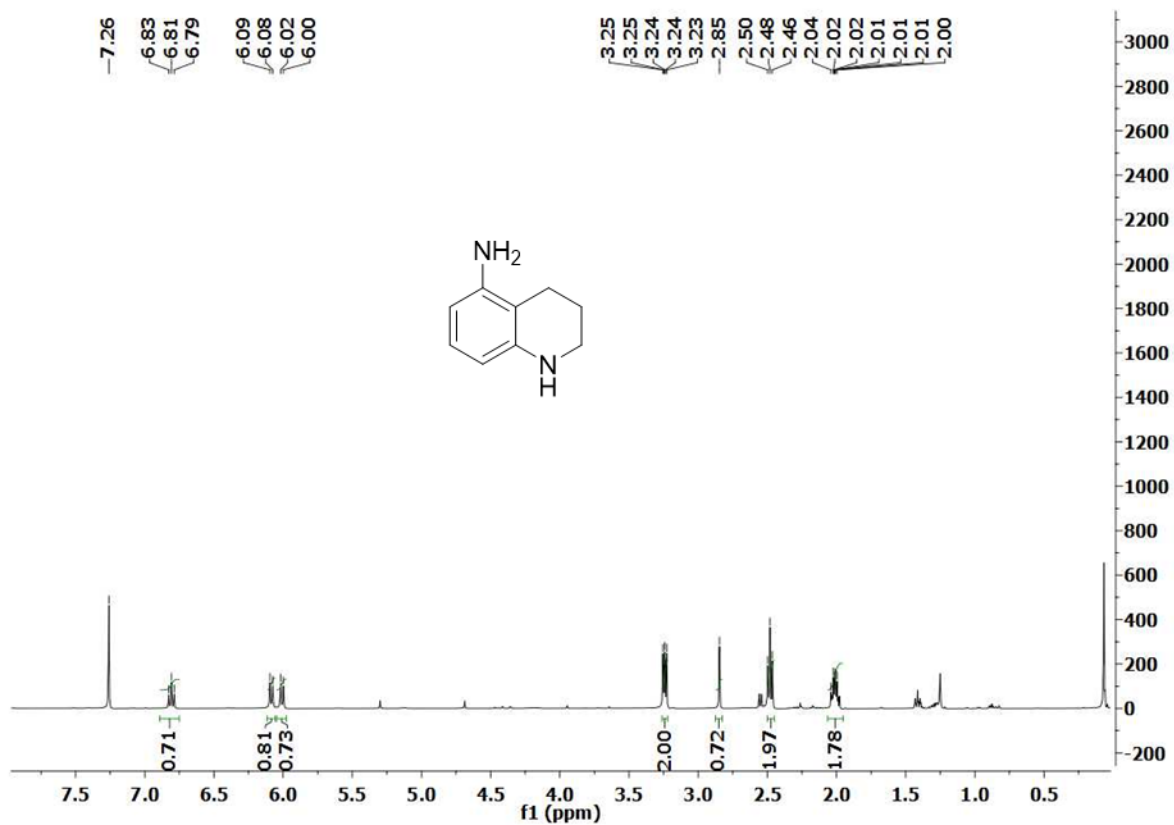


Figure S180: ¹H NMR Spectrum of **5.2q** (CDCl₃, 400 MHz, 298 K)

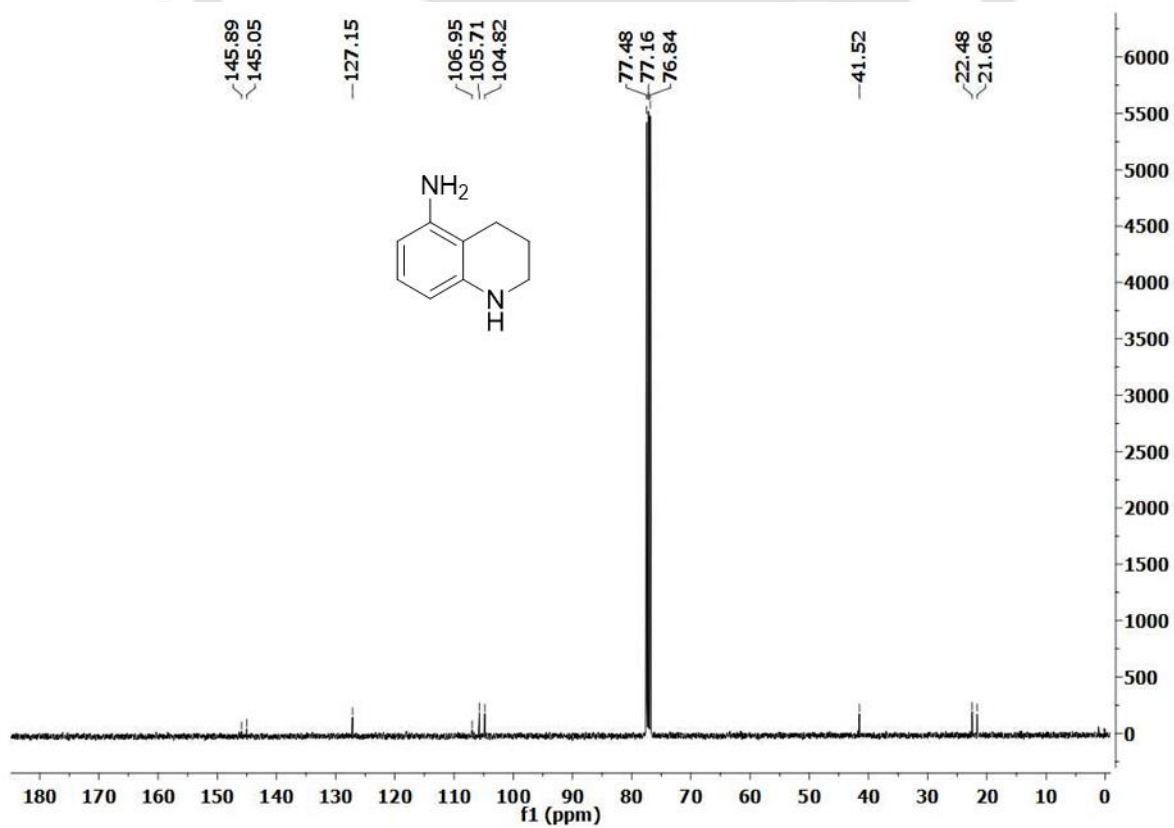


Figure S181: ¹³C NMR Spectrum of **5.2q** (CDCl₃, 101 MHz, 298 K)

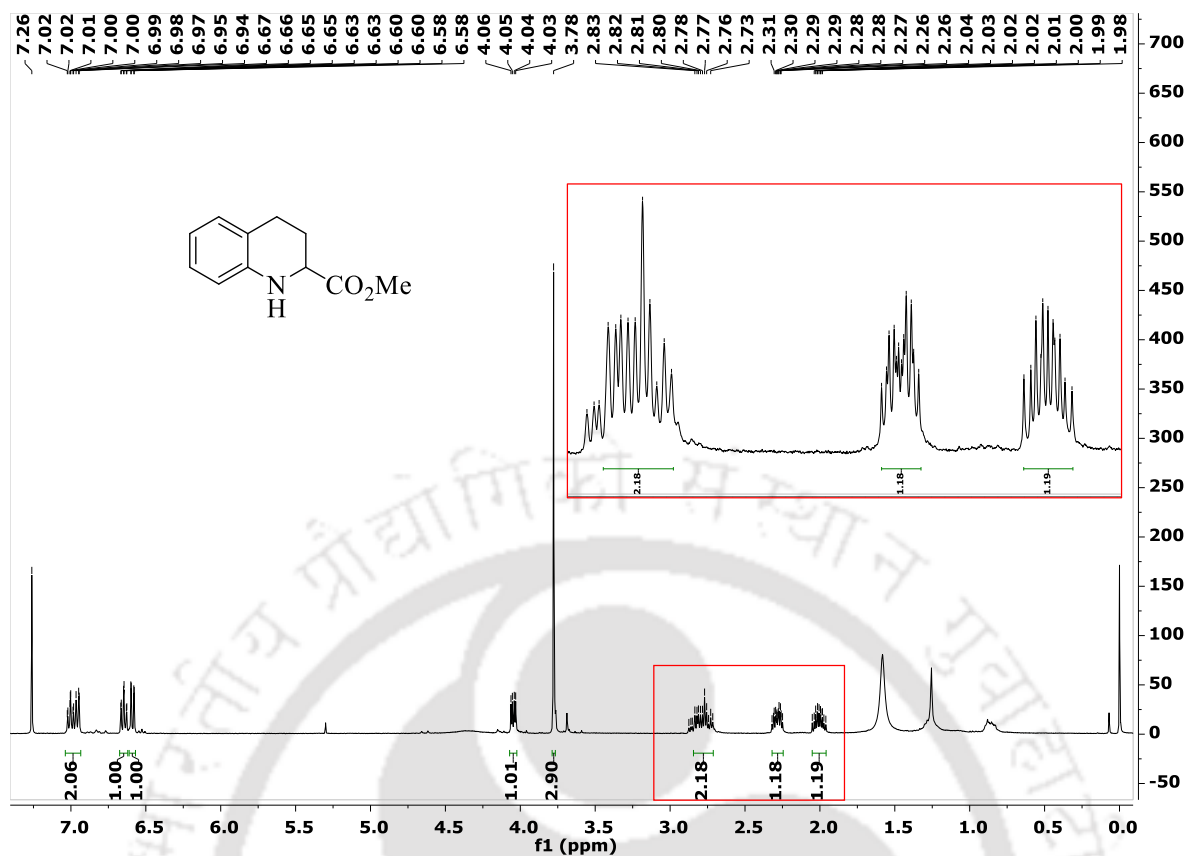


Figure S182: ¹H NMR Spectrum of 5.4a (CDCl₃, 400 MHz, 298 K)

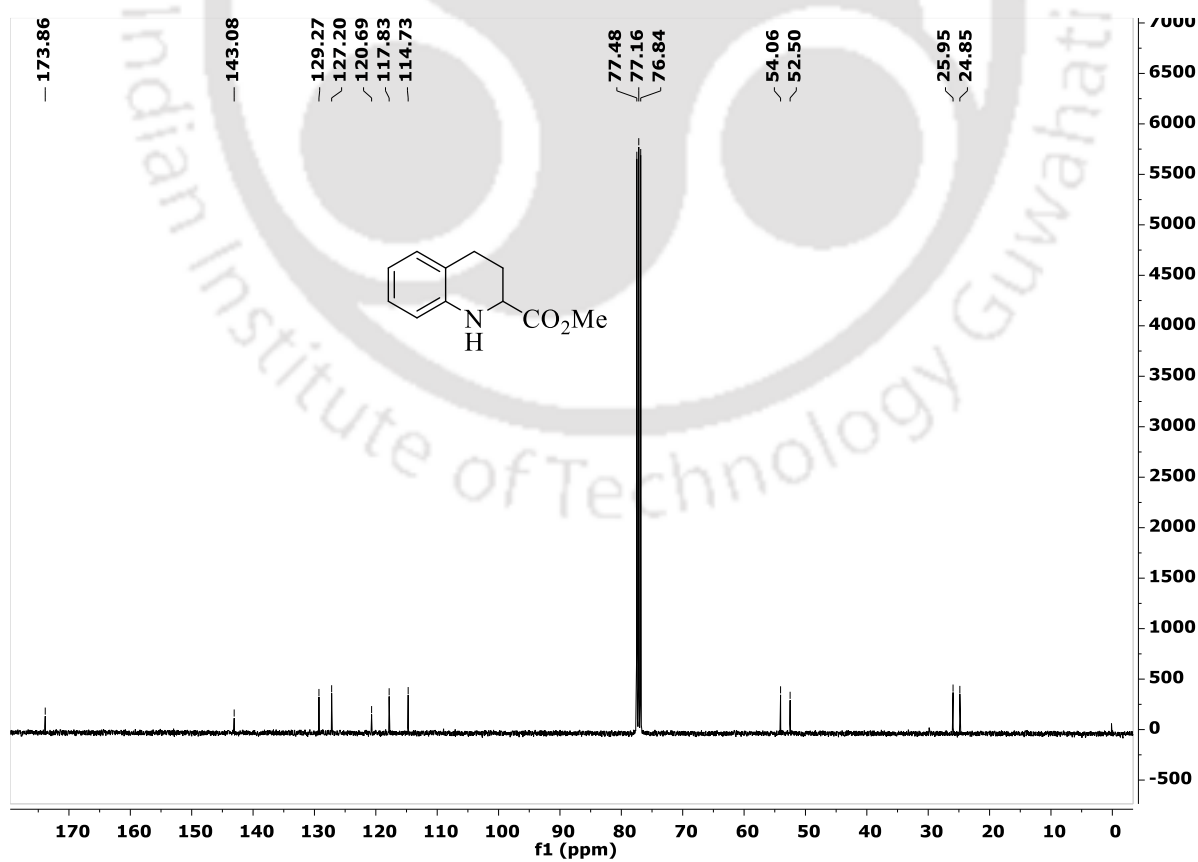


Figure S183: ¹³C NMR Spectrum of 5.4a (CDCl₃, 101 MHz, 298 K)

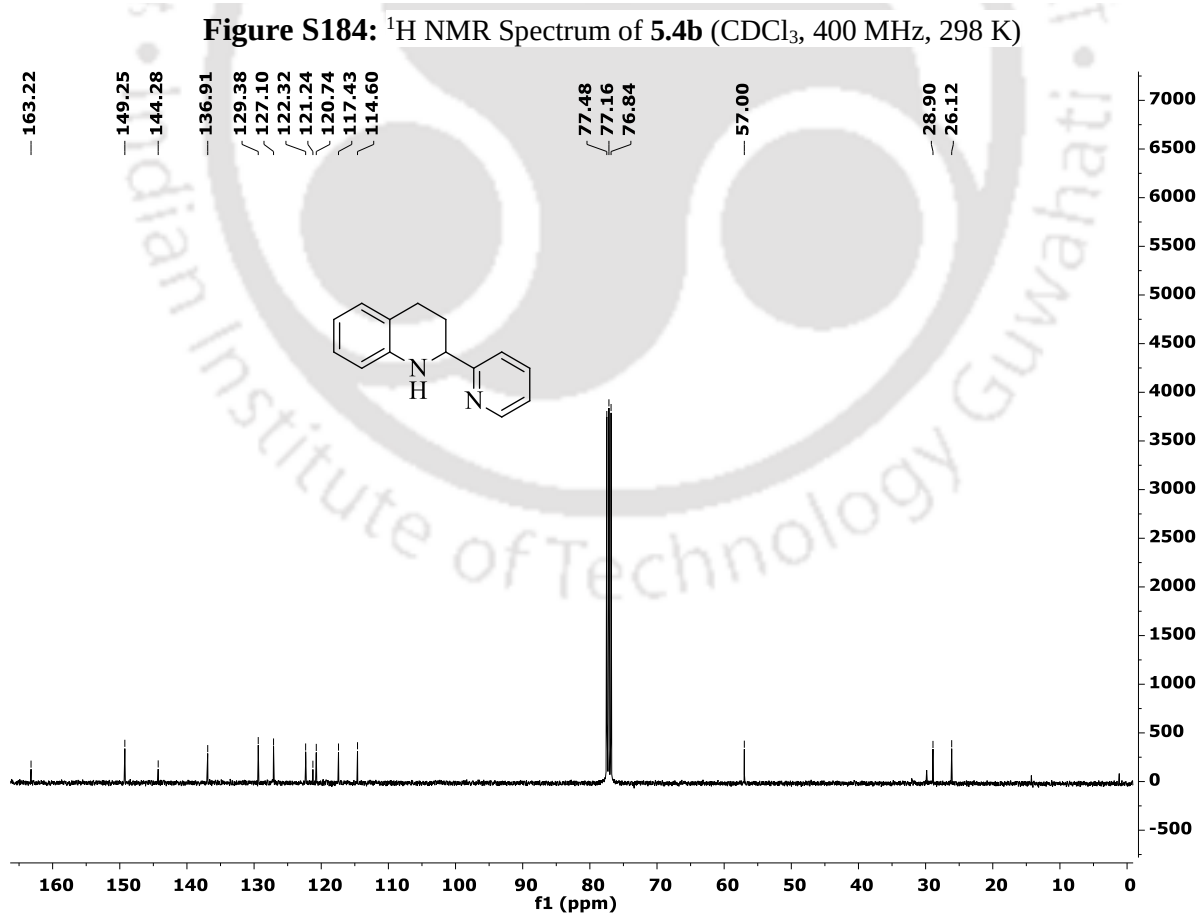
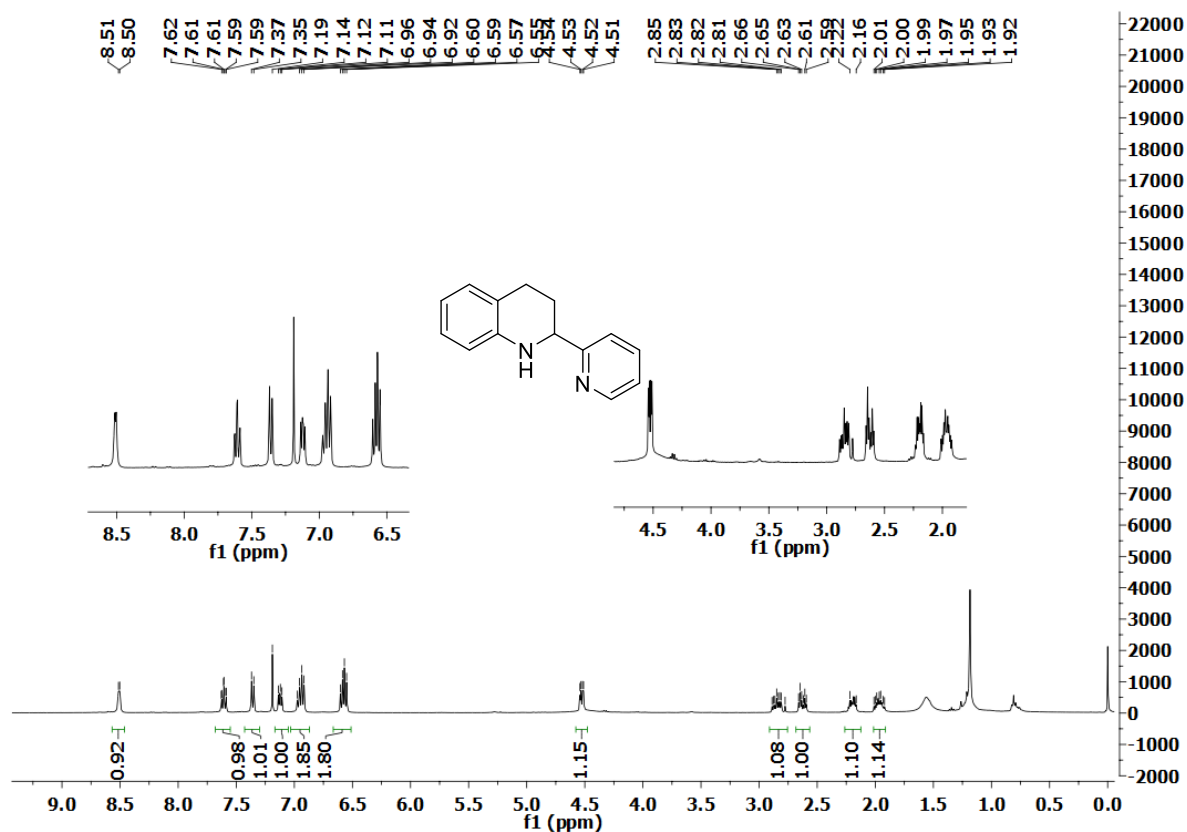


Figure S185: ^{13}C NMR Spectrum of 5.4b (CDCl_3 , 101 MHz, 298 K)

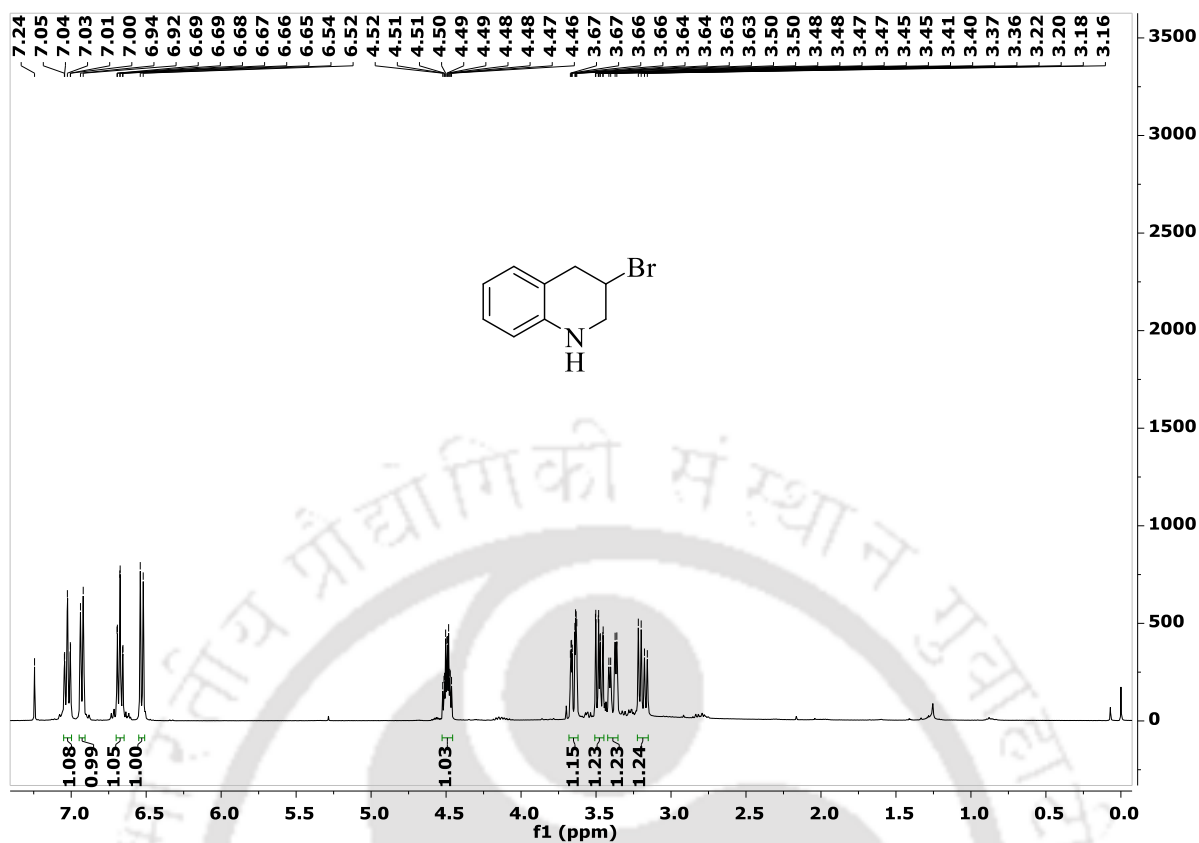


Figure S186: ^1H NMR Spectrum of 5.4c (CDCl_3 , 400 MHz, 298 K)

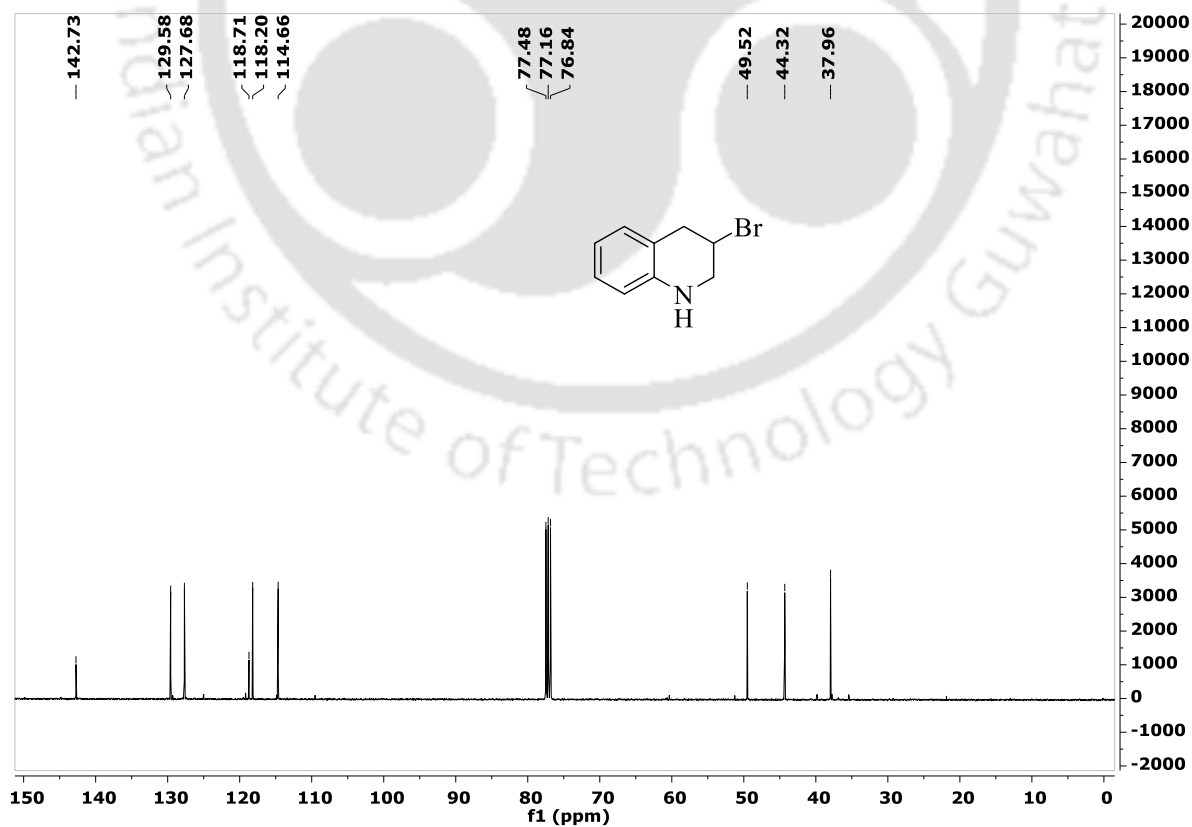


Figure S187: ^{13}C NMR Spectrum of 5.4c (CDCl_3 , 101 MHz, 298 K)

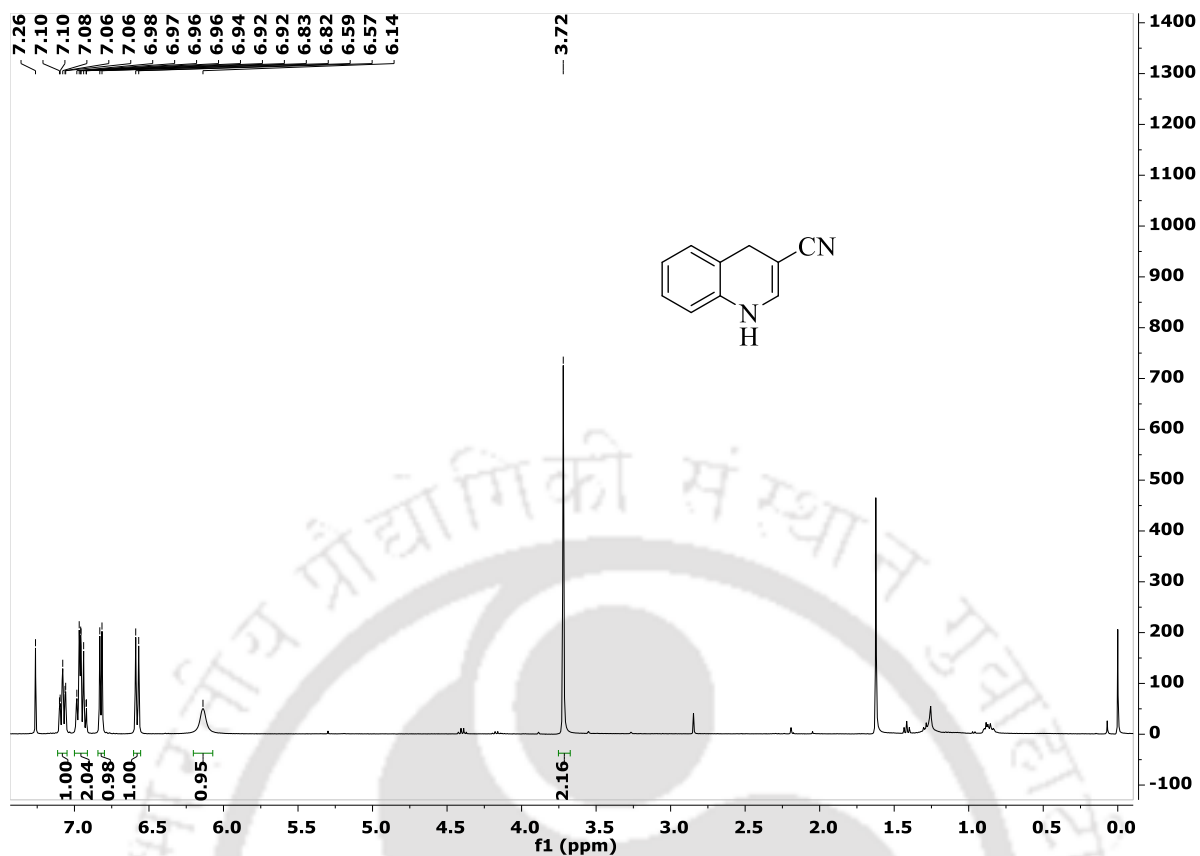


Figure S188: ^1H NMR Spectrum of 5.4d (CDCl_3 , 400 MHz, 298 K)

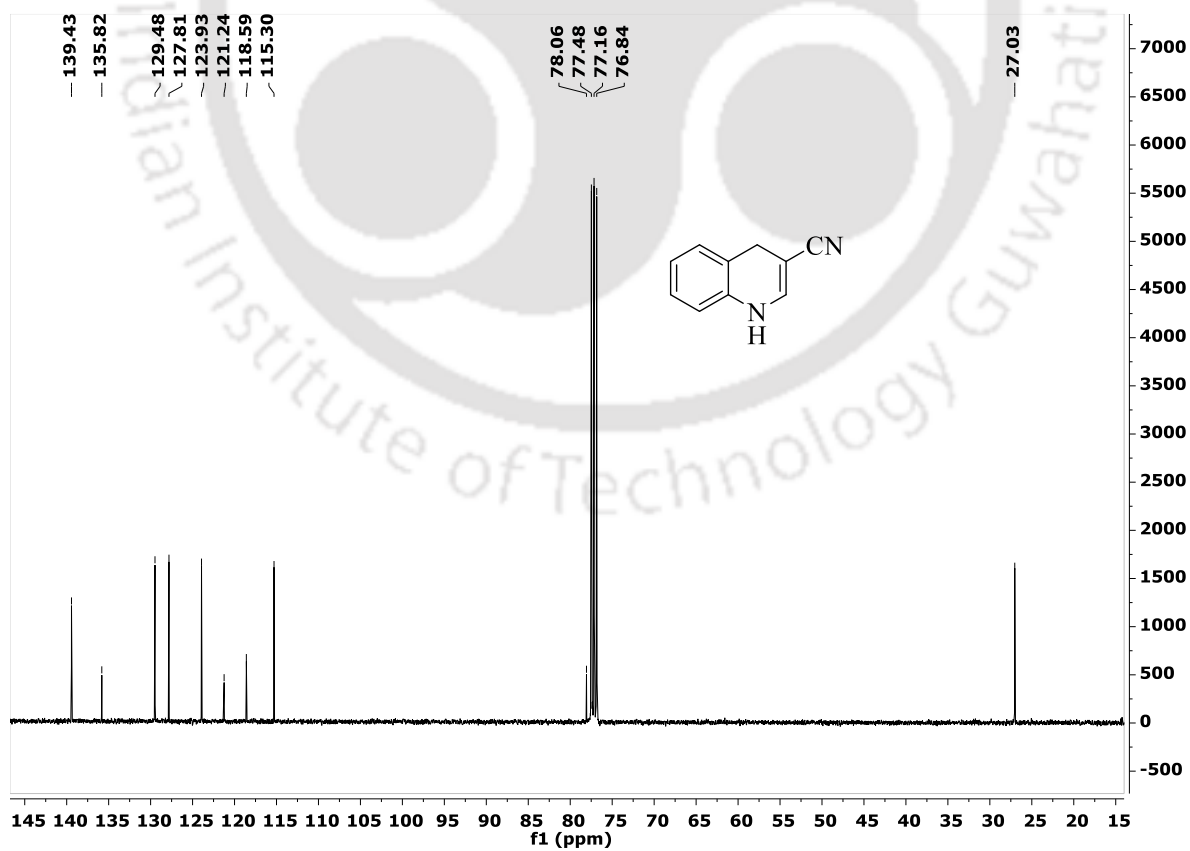


Figure S189: ^{13}C NMR Spectrum of 5.4d (CDCl_3 , 101 MHz, 298 K)

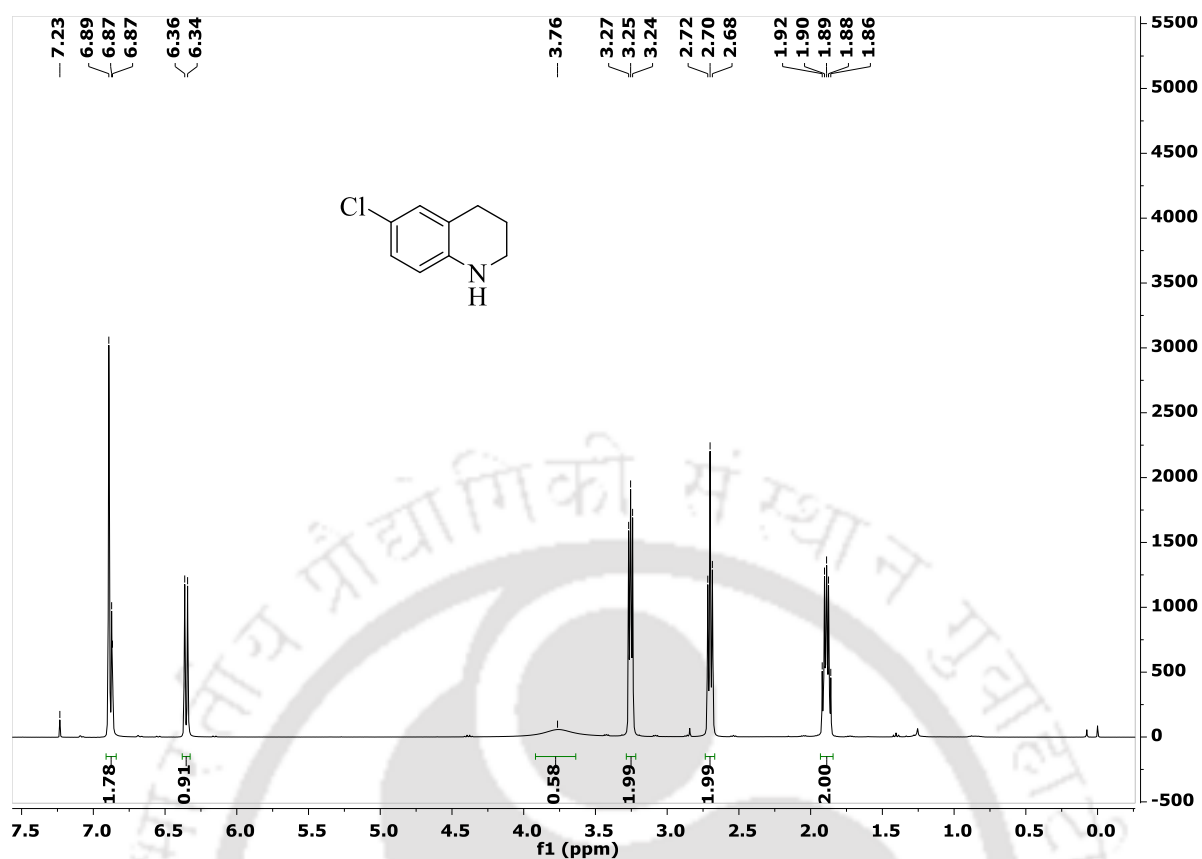


Figure S190: ^1H NMR Spectrum of 5.4e (CDCl_3 , 400 MHz, 298 K)

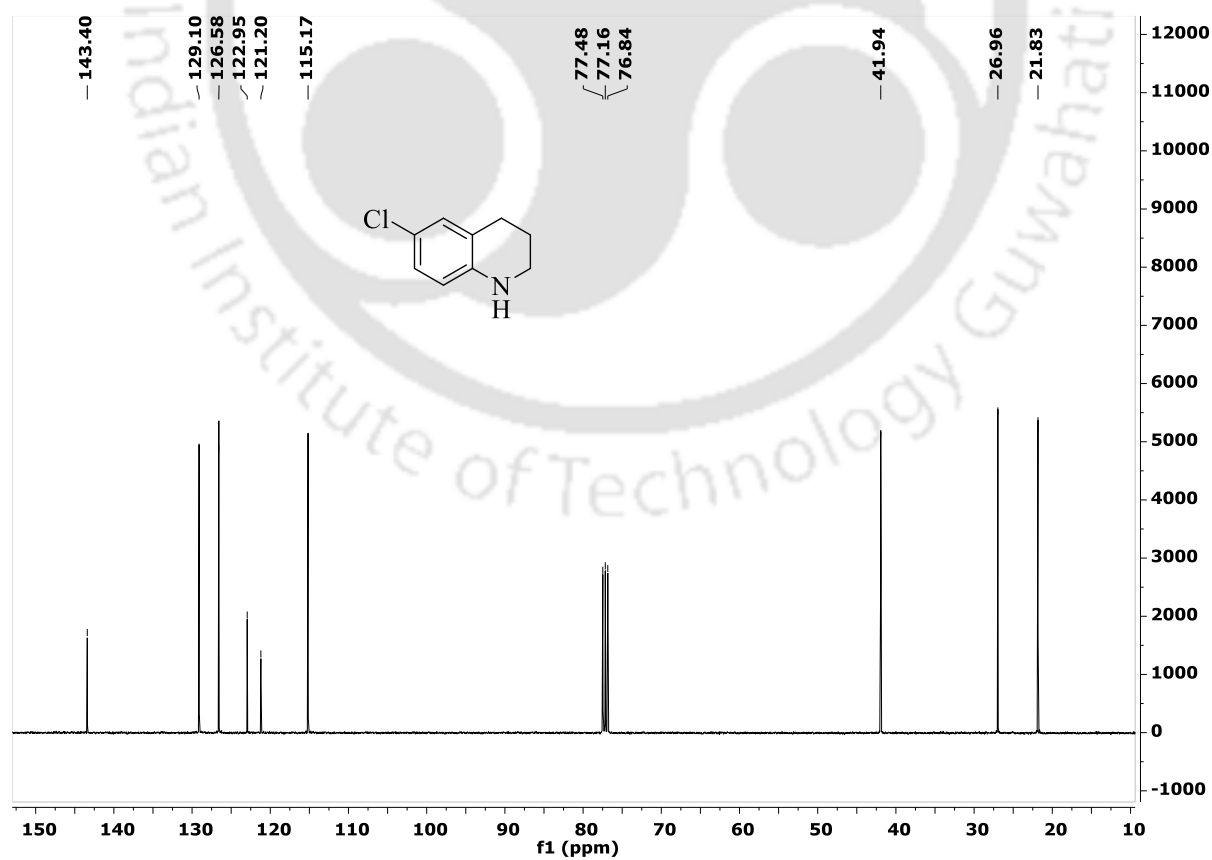


Figure S191: ^{13}C NMR Spectrum of 5.4e (CDCl_3 , 101 MHz, 298 K)

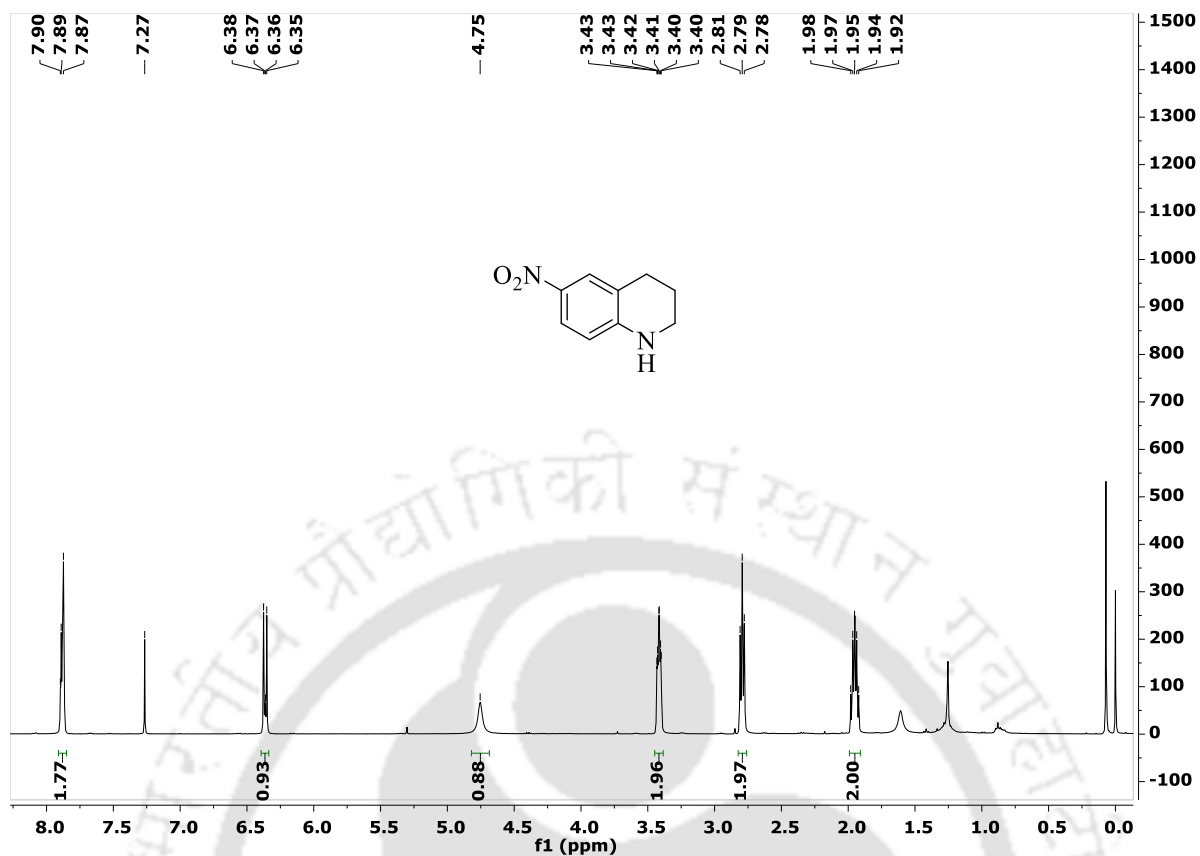


Figure S192: ^1H NMR Spectrum of **5.4f** (CDCl_3 , 400 MHz, 298 K)

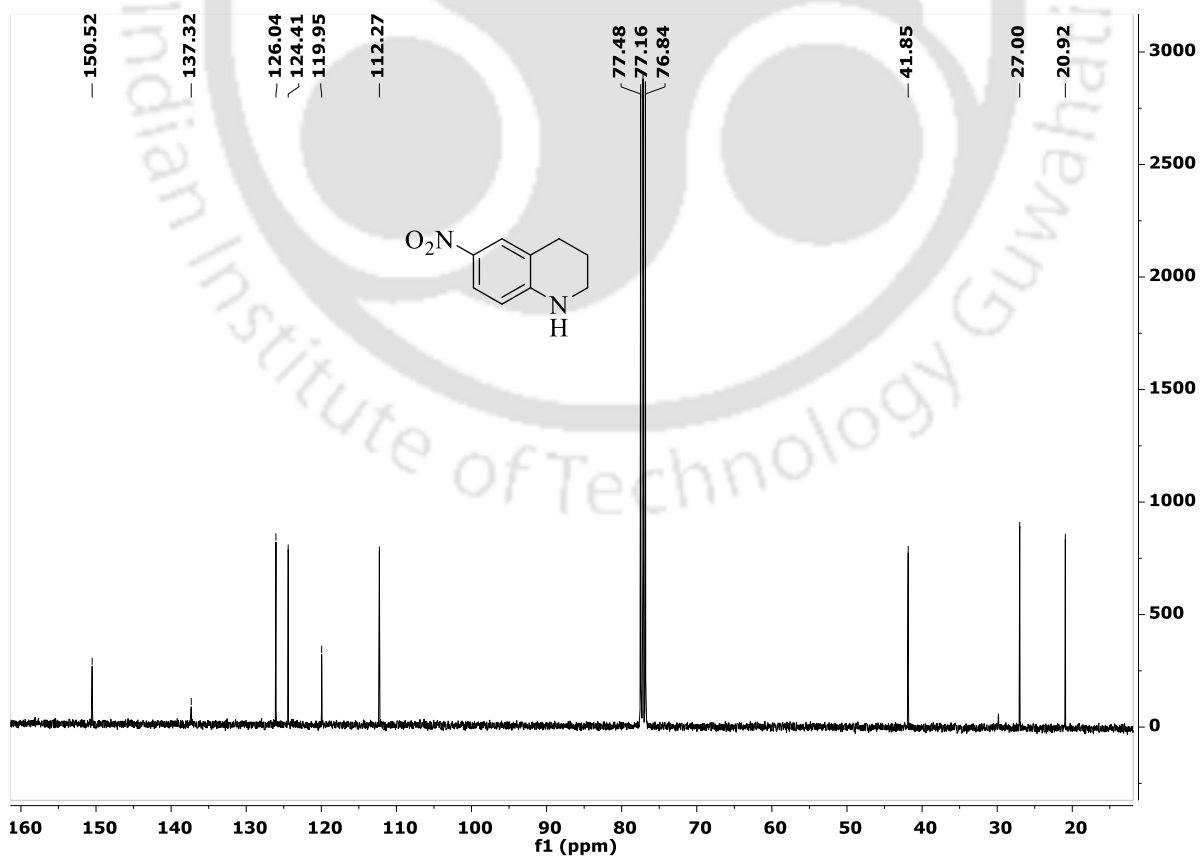
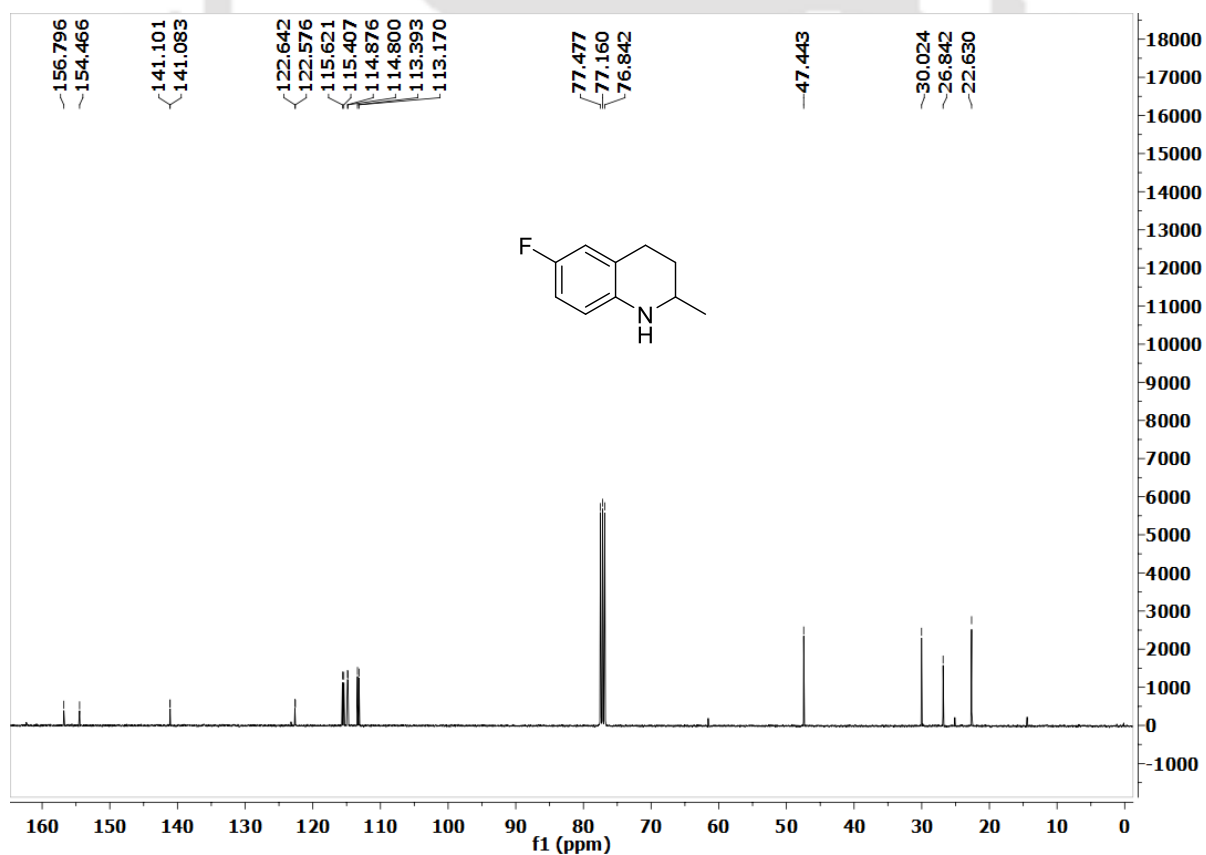
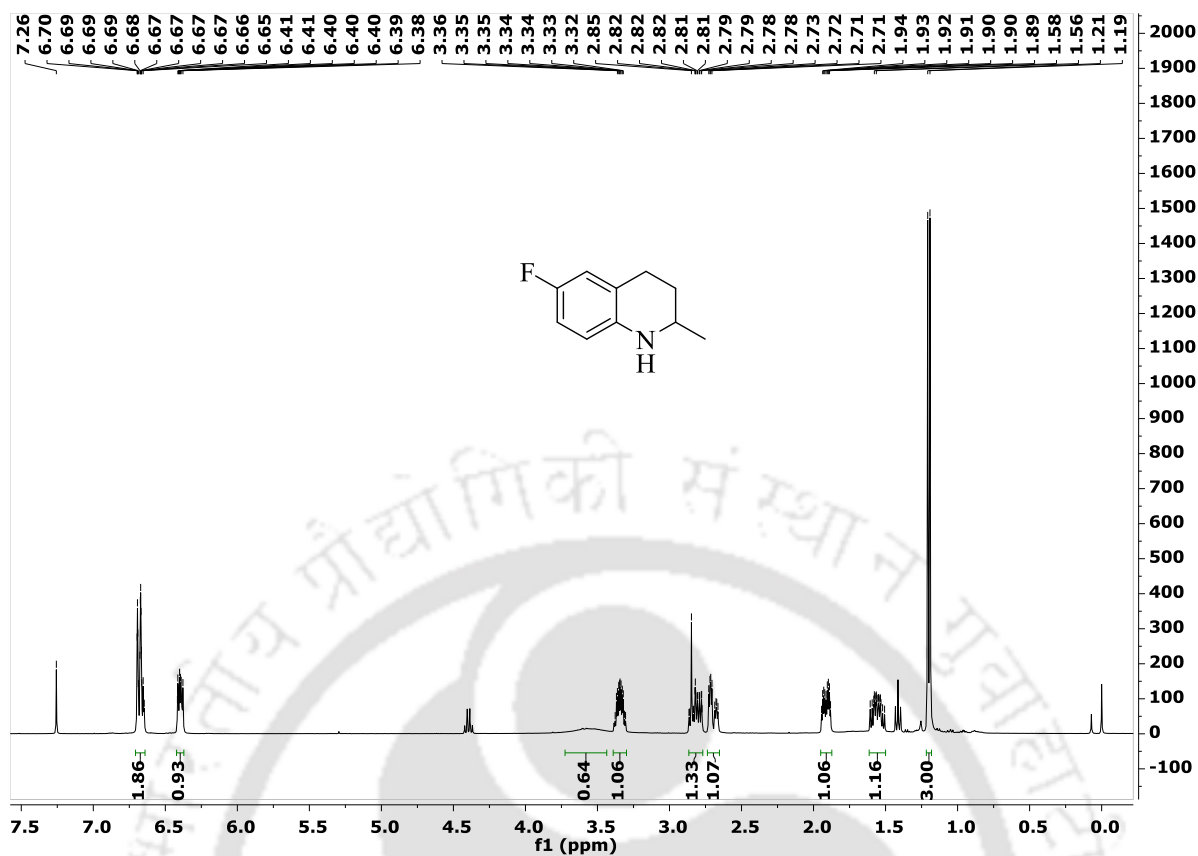


Figure S193: ^{13}C NMR Spectrum of **5.4f** (CDCl_3 , 101 MHz, 298 K)



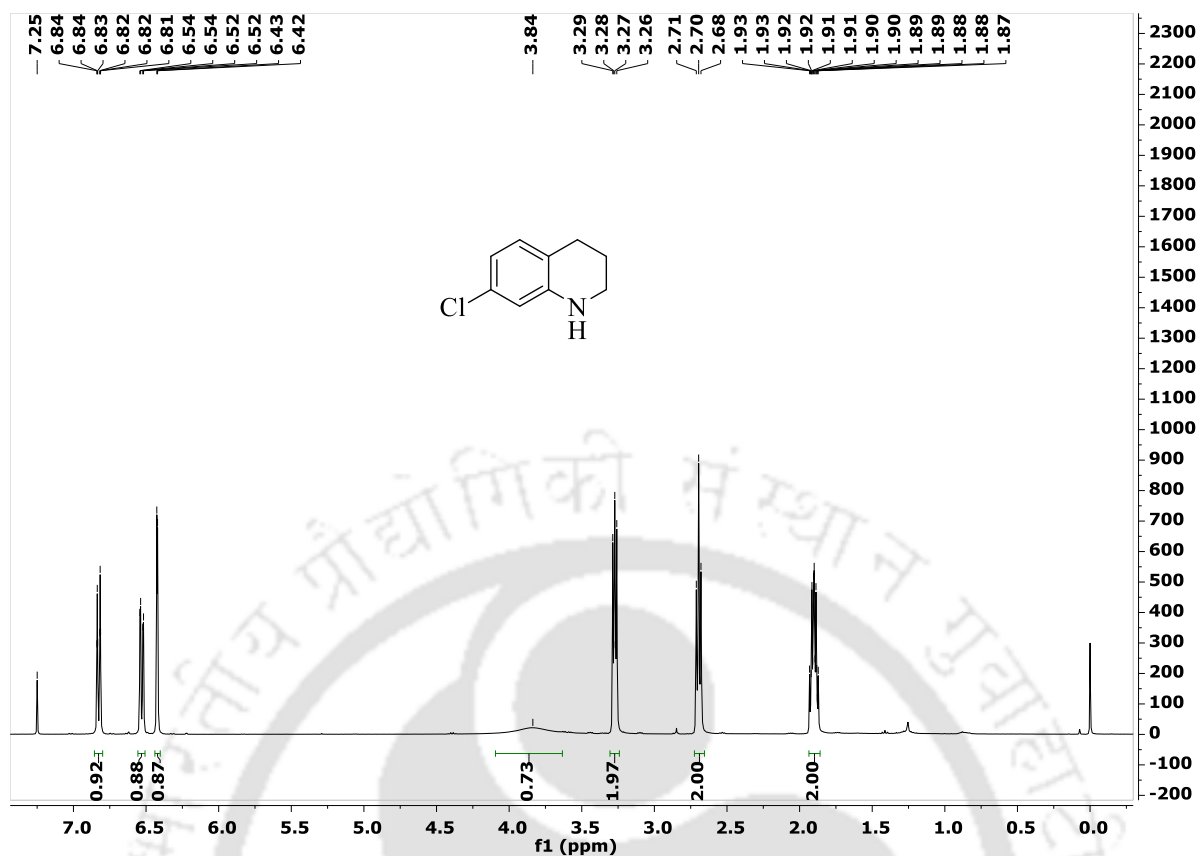


Figure S196: ¹H NMR Spectrum of **5.4h** (CDCl₃, 400 MHz, 298 K)

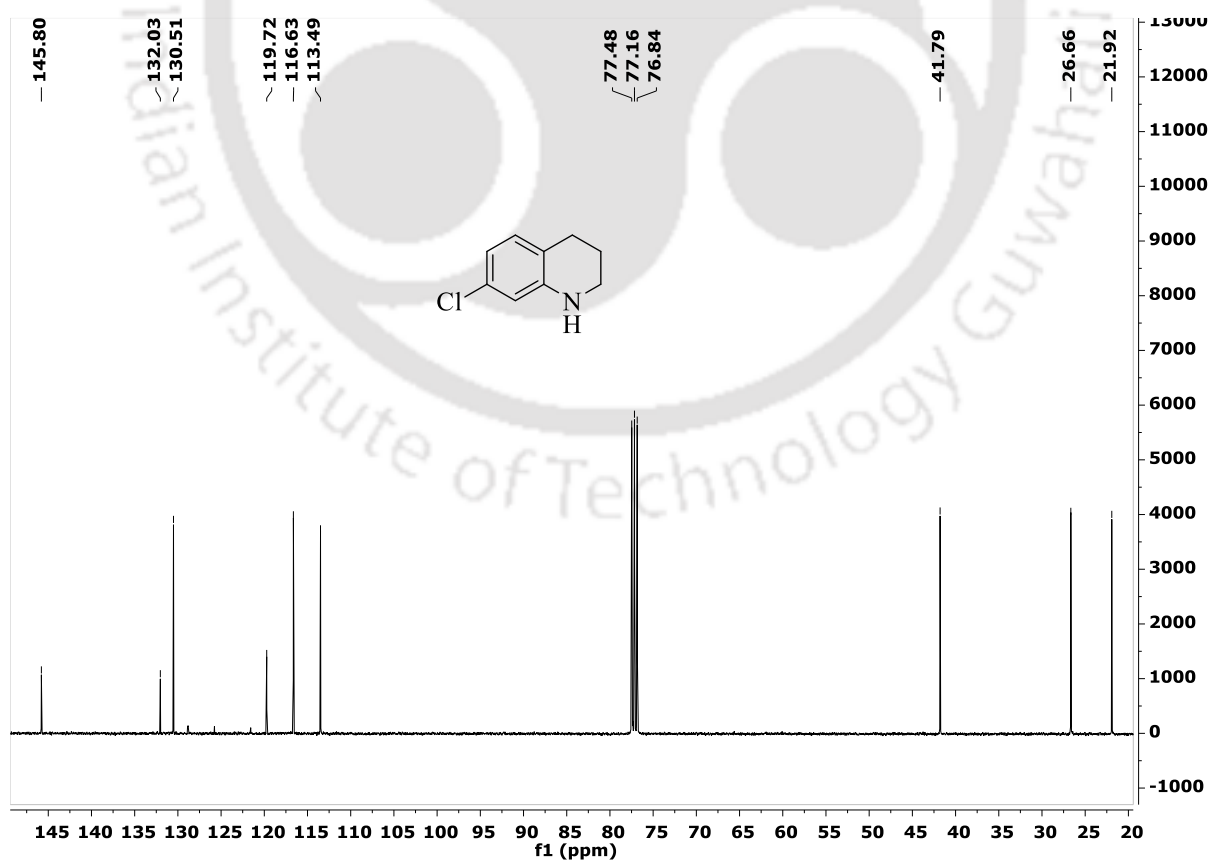


Figure S197: ¹³C NMR Spectrum of **5.4h** (CDCl₃, 101 MHz, 298 K)

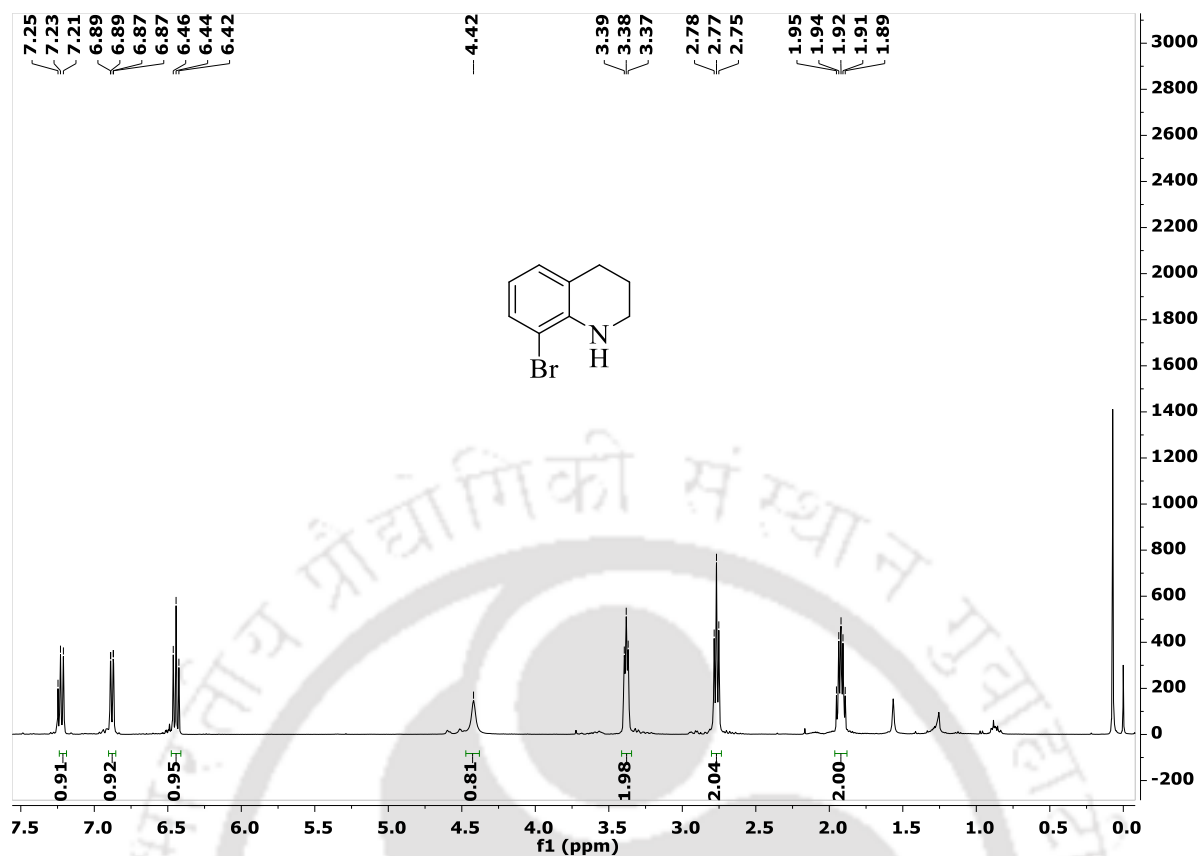


Figure S198: ¹H NMR Spectrum of **5.4i** (CDCl₃, 400 MHz, 298 K)

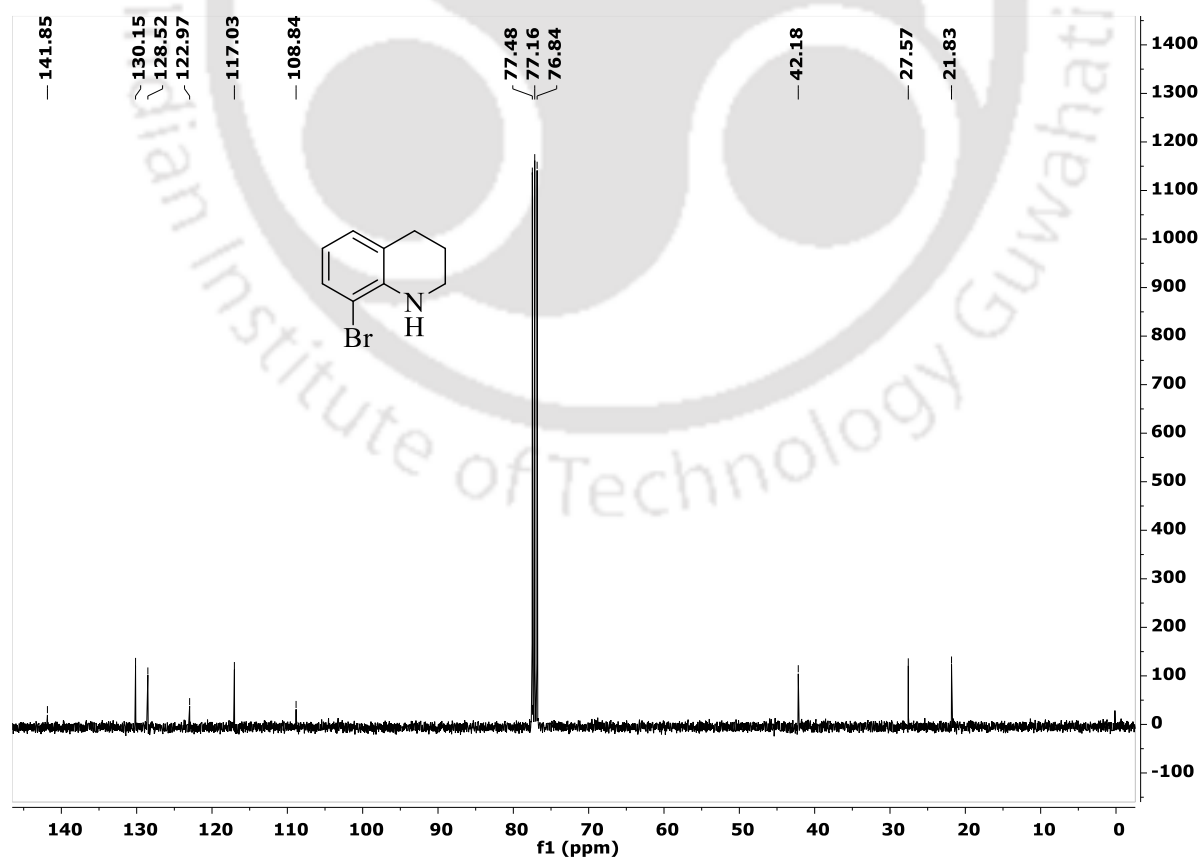


Figure S199: ¹³C NMR Spectrum of **5.4i** (CDCl₃, 101 MHz, 298 K)

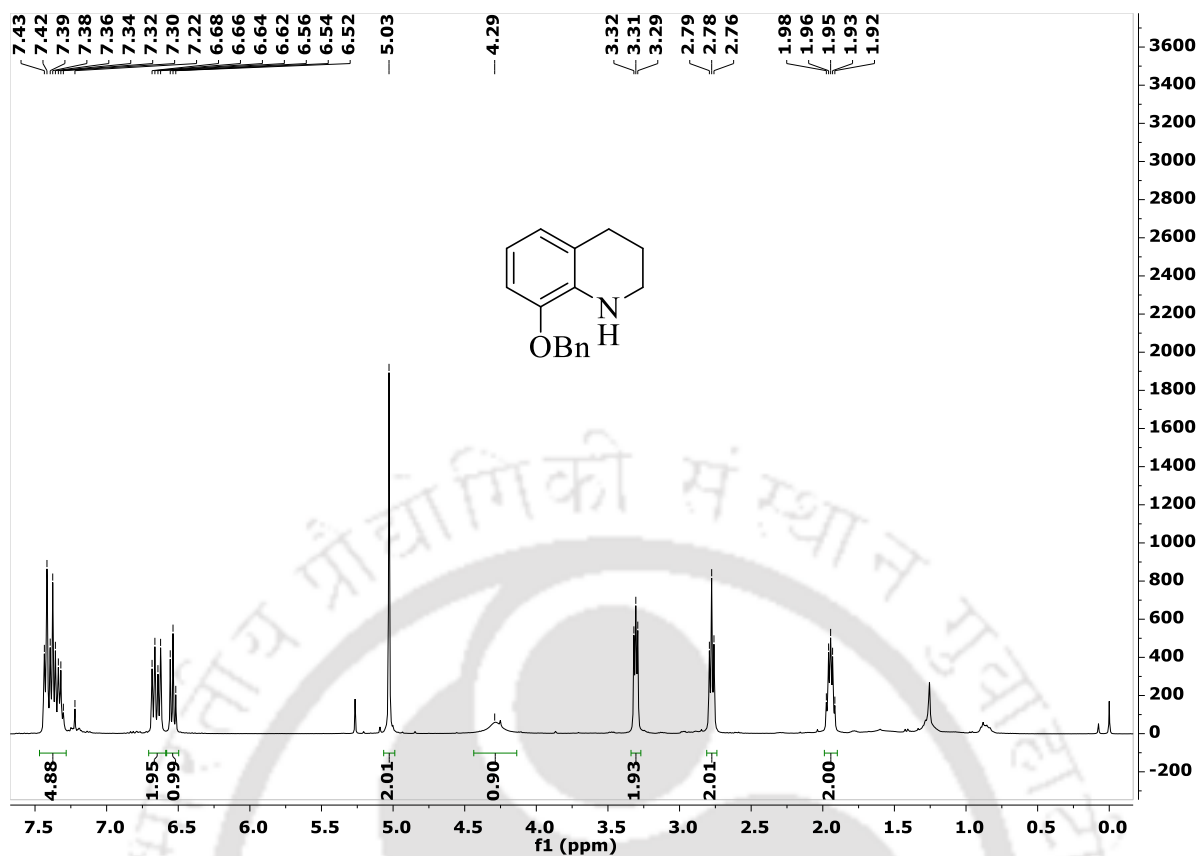


Figure S200: ¹H NMR Spectrum of **5.4j** (CDCl₃, 400 MHz, 298 K)

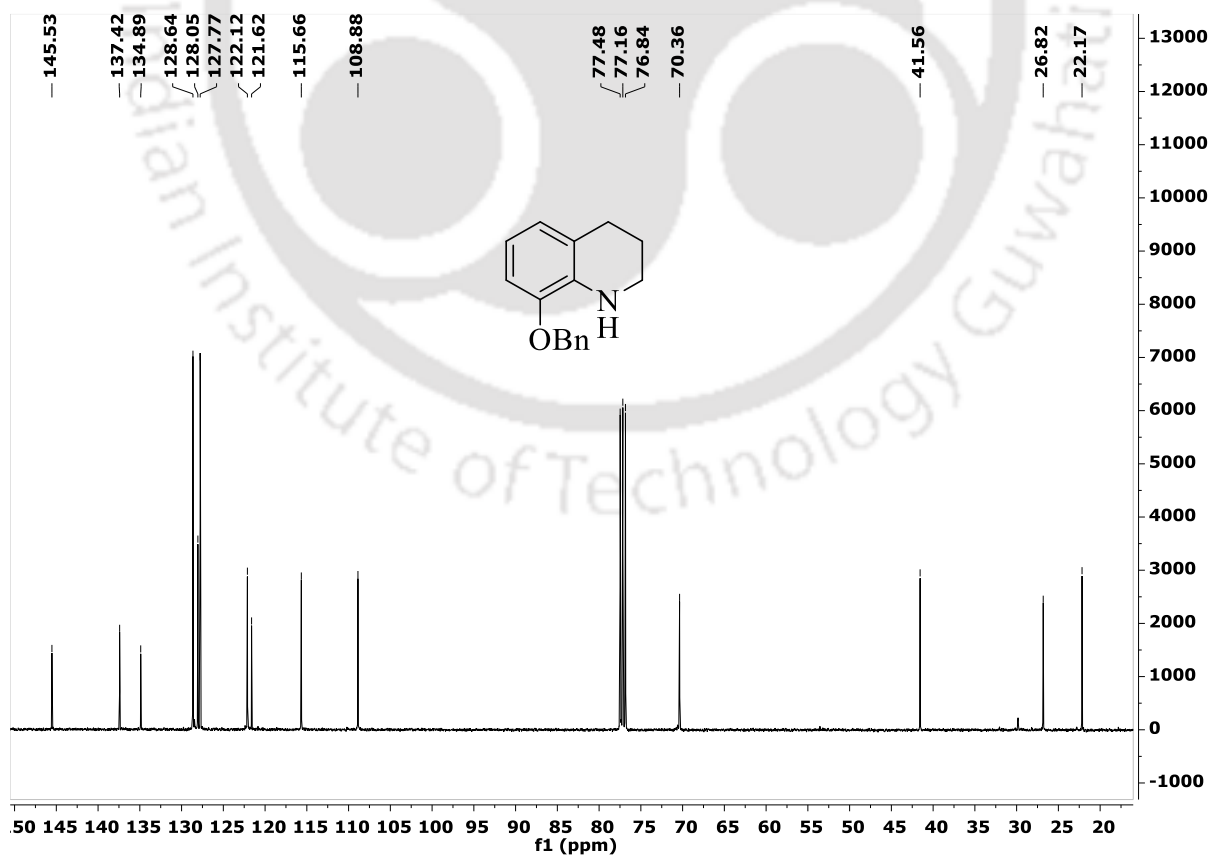


Figure S201: ¹³C NMR Spectrum of **5.4j** (CDCl₃, 101 MHz, 298 K)

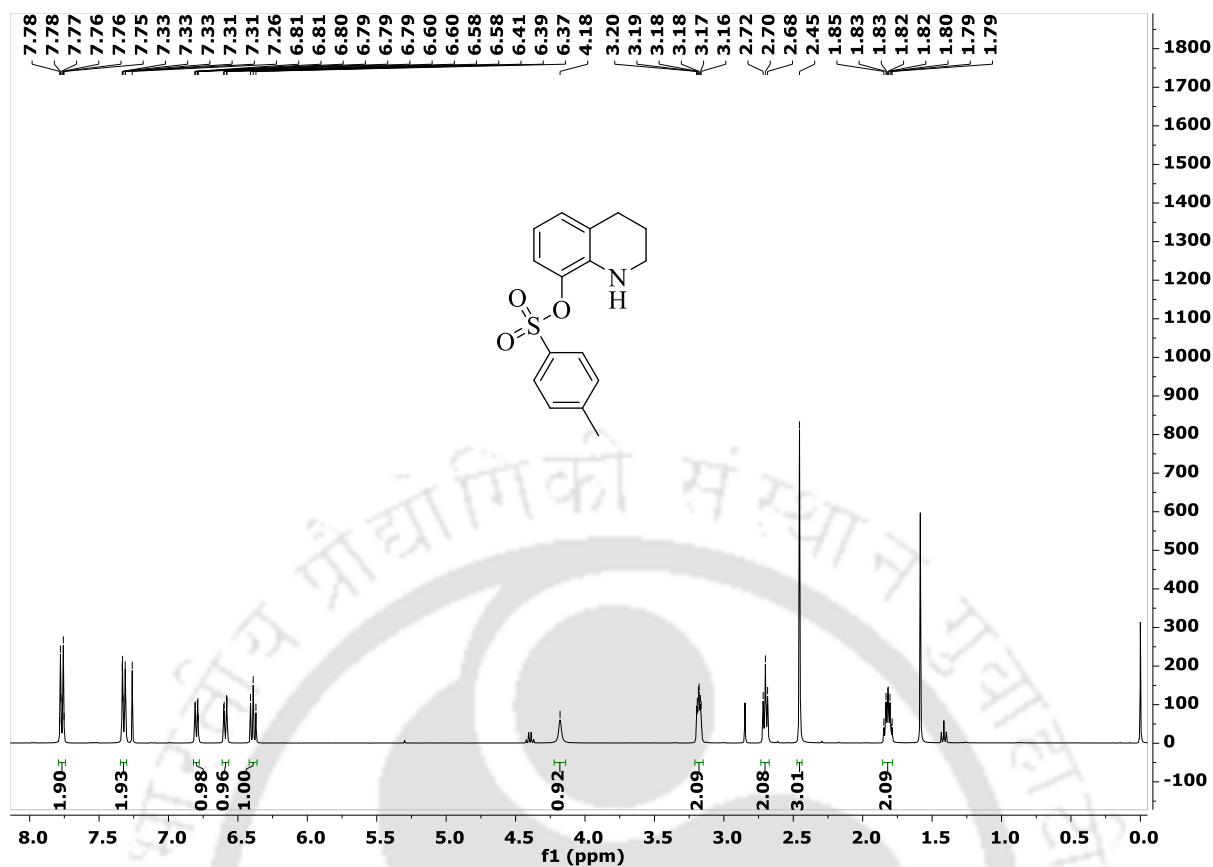


Figure S202: ¹H NMR Spectrum of **5.4k** (CDCl₃, 400 MHz, 298 K)

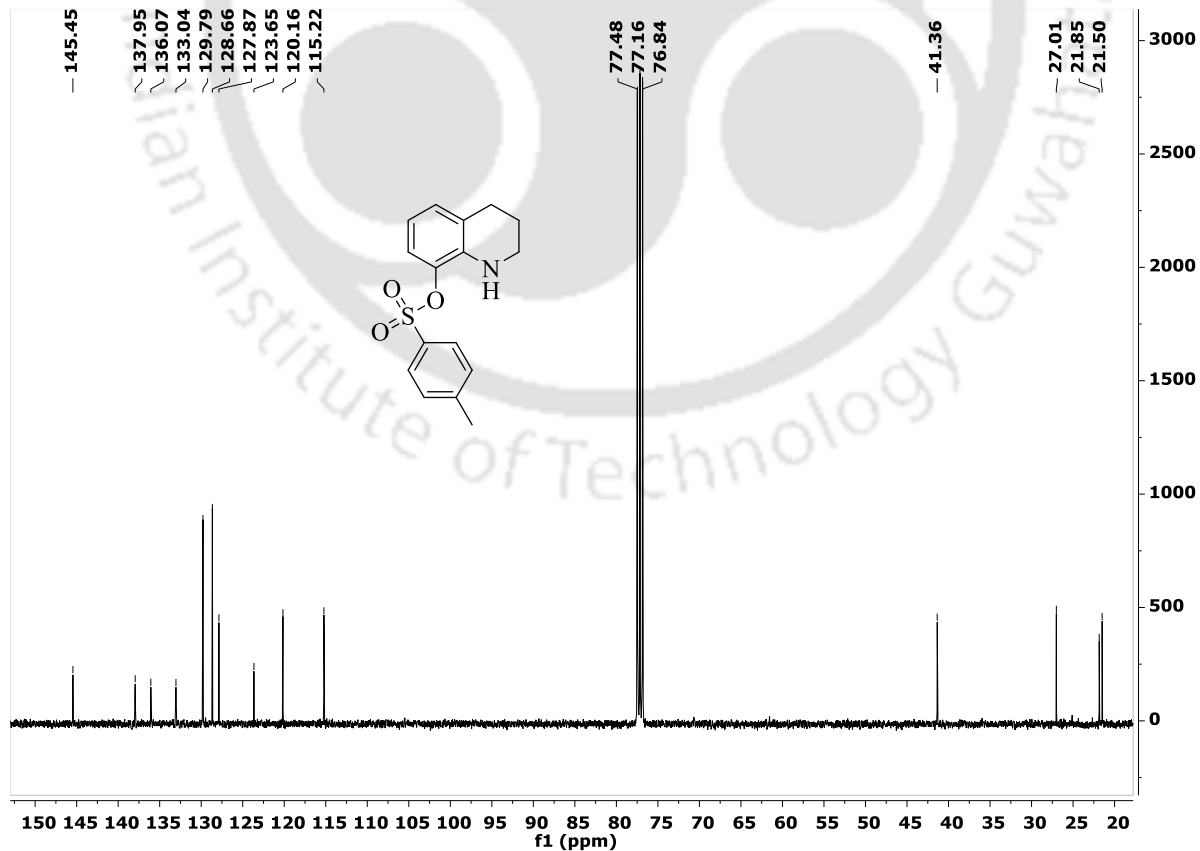


Figure S203: ¹³C NMR Spectrum of **5.4k** (CDCl₃, 101 MHz, 298 K)

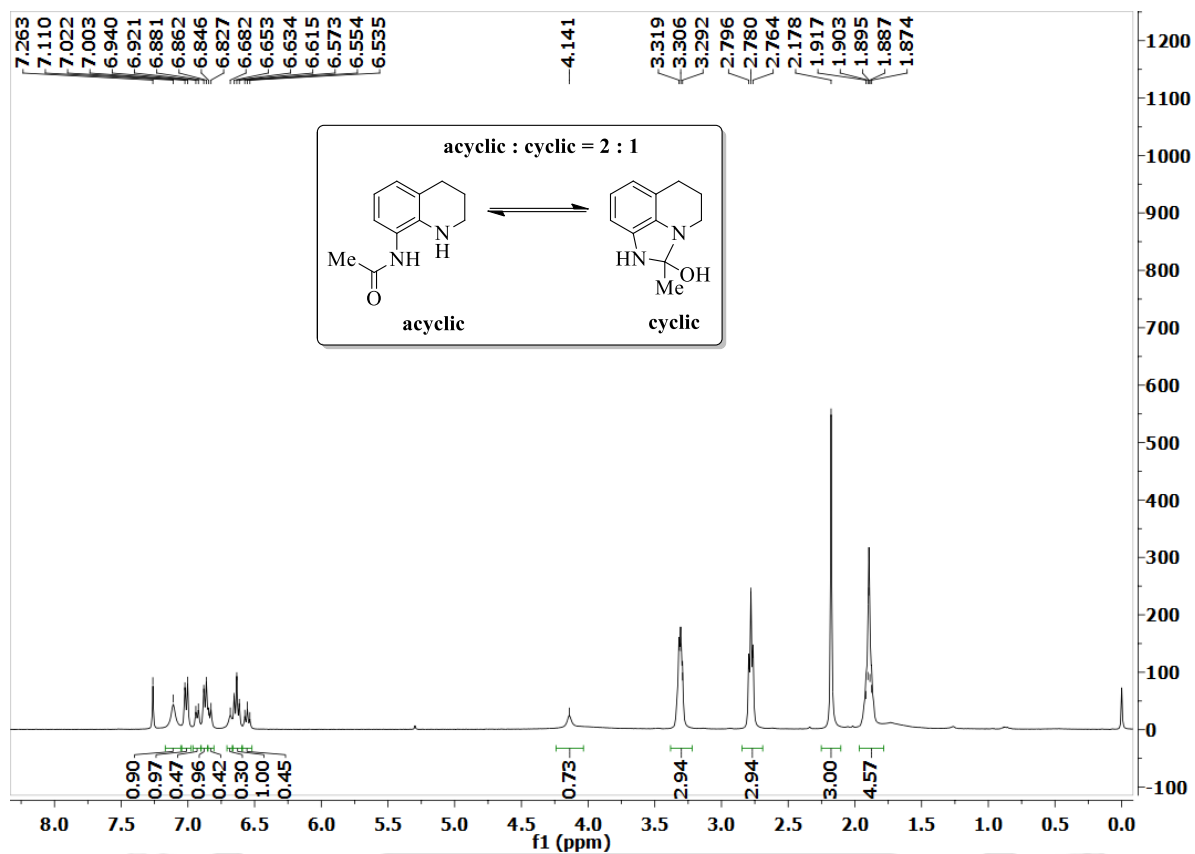


Figure S204: ^1H NMR Spectrum of **5.4I** (CDCl_3 , 400 MHz, 298 K)

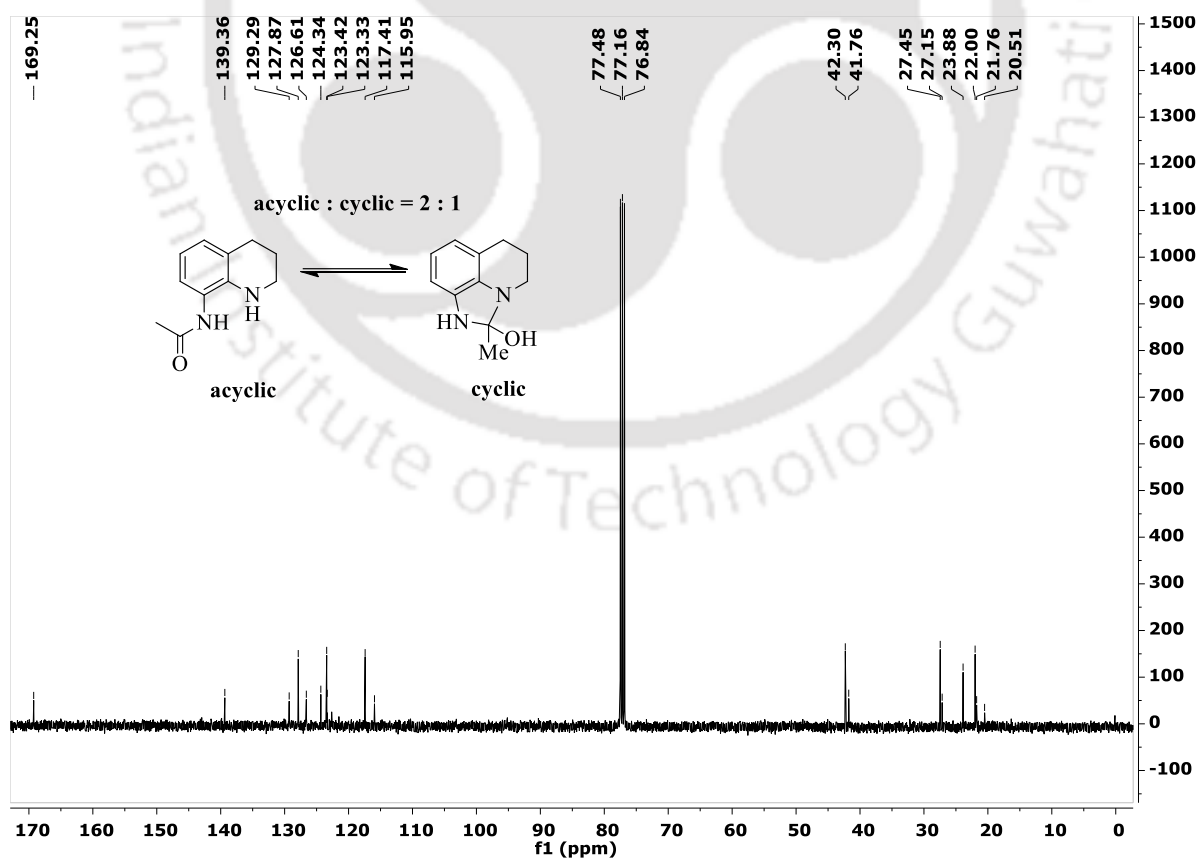


Figure S205: ^{13}C NMR Spectrum of **5.4I** (CDCl_3 , 101 MHz, 298 K)

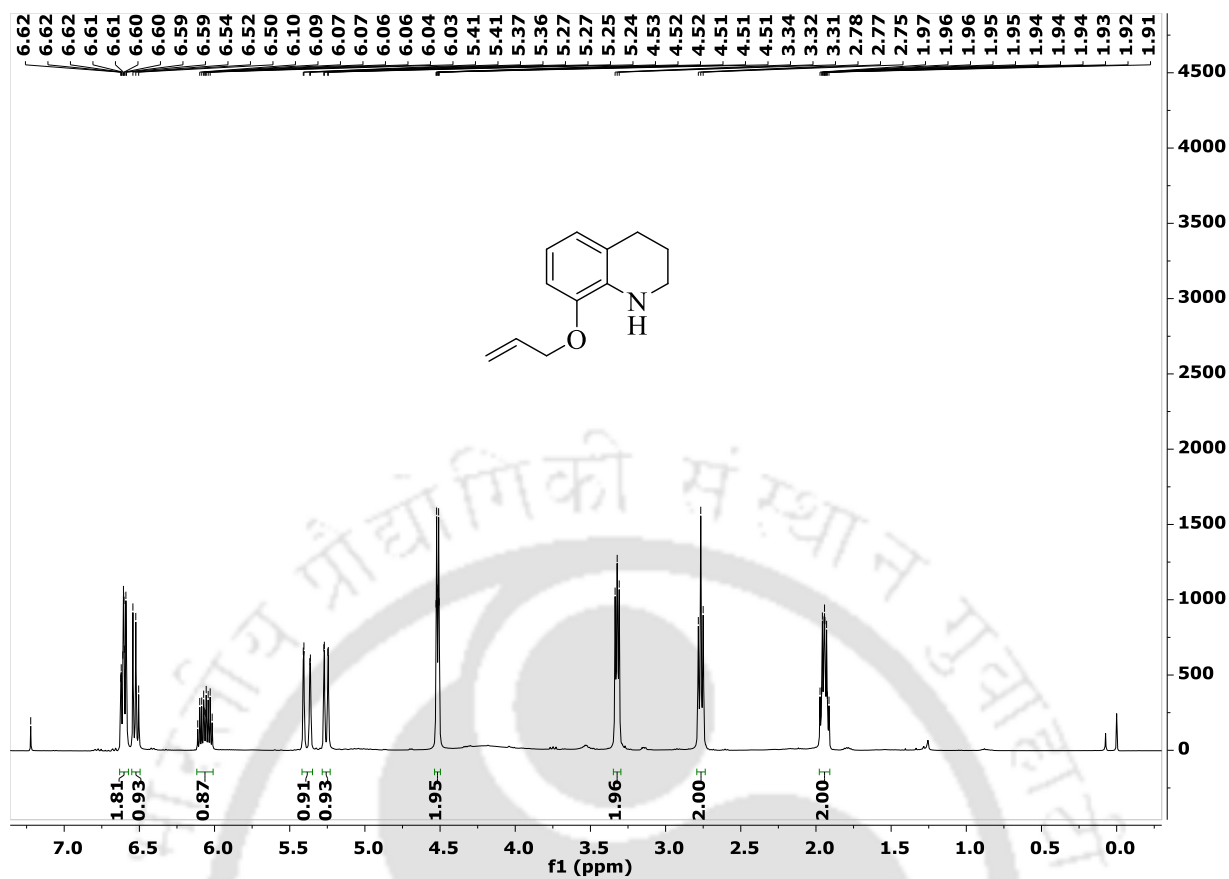


Figure S206: ¹H NMR Spectrum of 5.4m (CDCl₃, 400 MHz, 298 K)

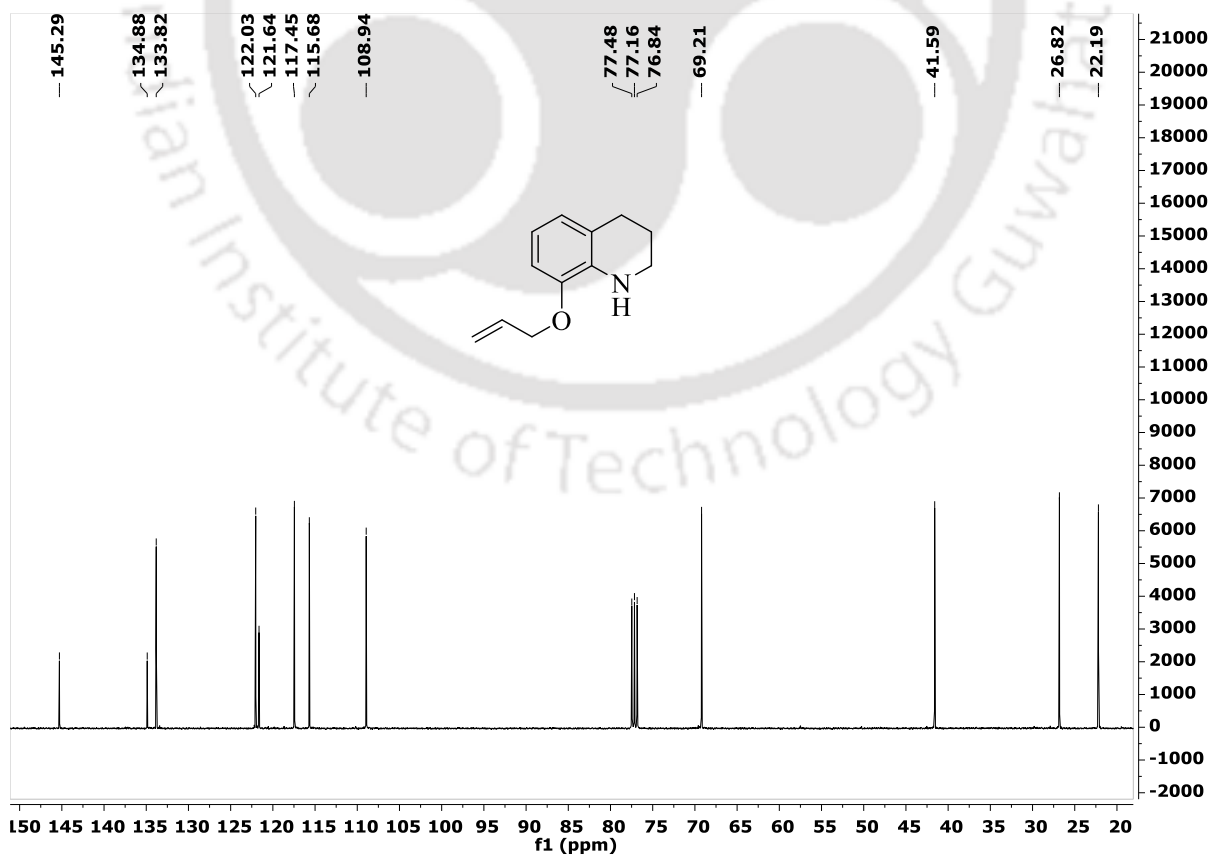


Figure S207: ¹³C NMR Spectrum of 5.4m (CDCl₃, 101 MHz, 298 K)

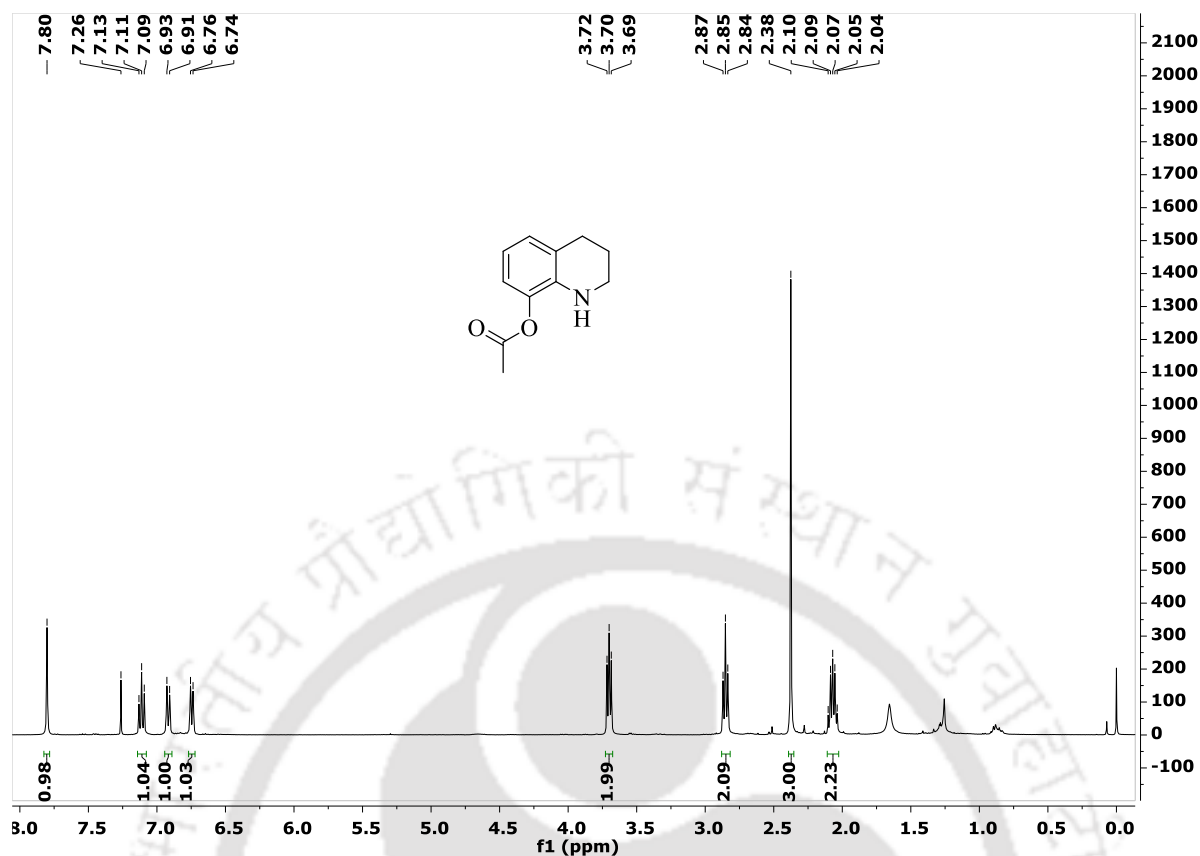


Figure S208: ¹H NMR Spectrum of **5.4n** (CDCl₃, 400 MHz, 298 K)

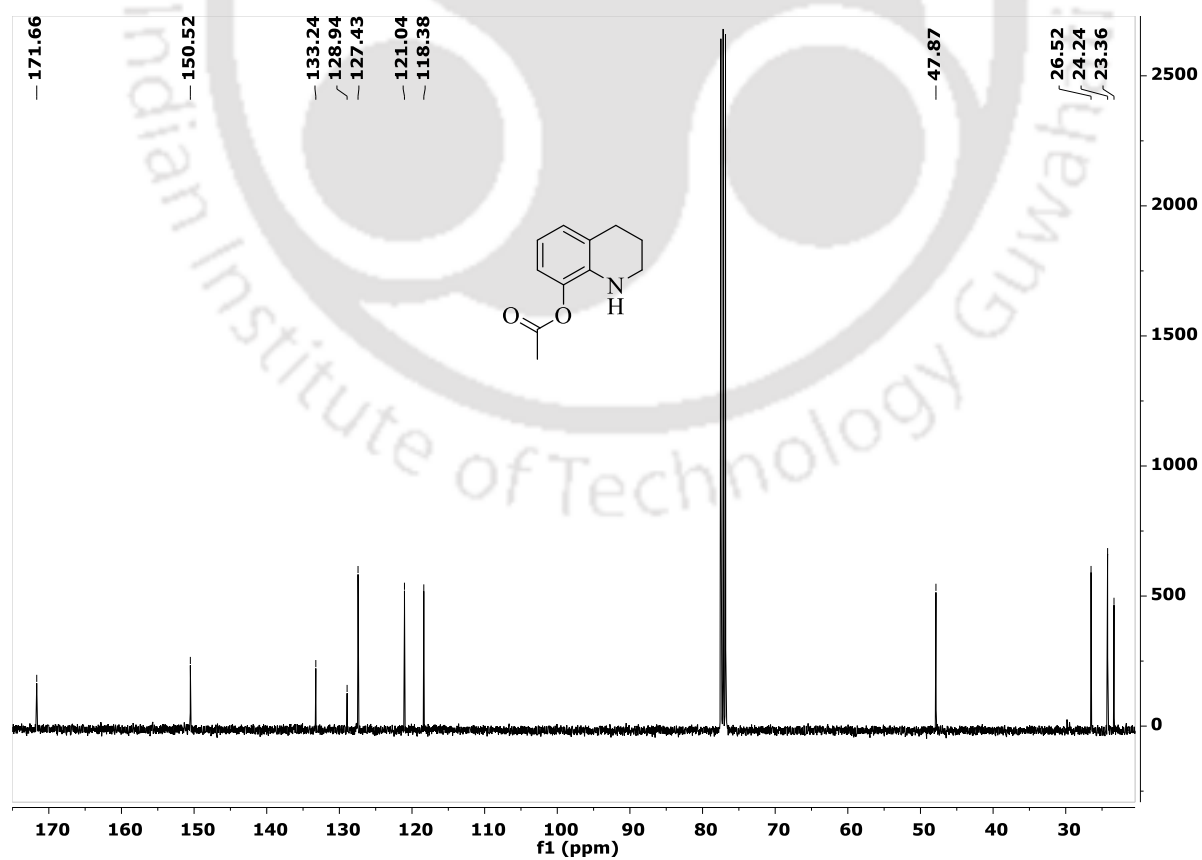


Figure S209: ¹³C NMR Spectrum of **5.4n** (CDCl₃, 101 MHz, 298 K)

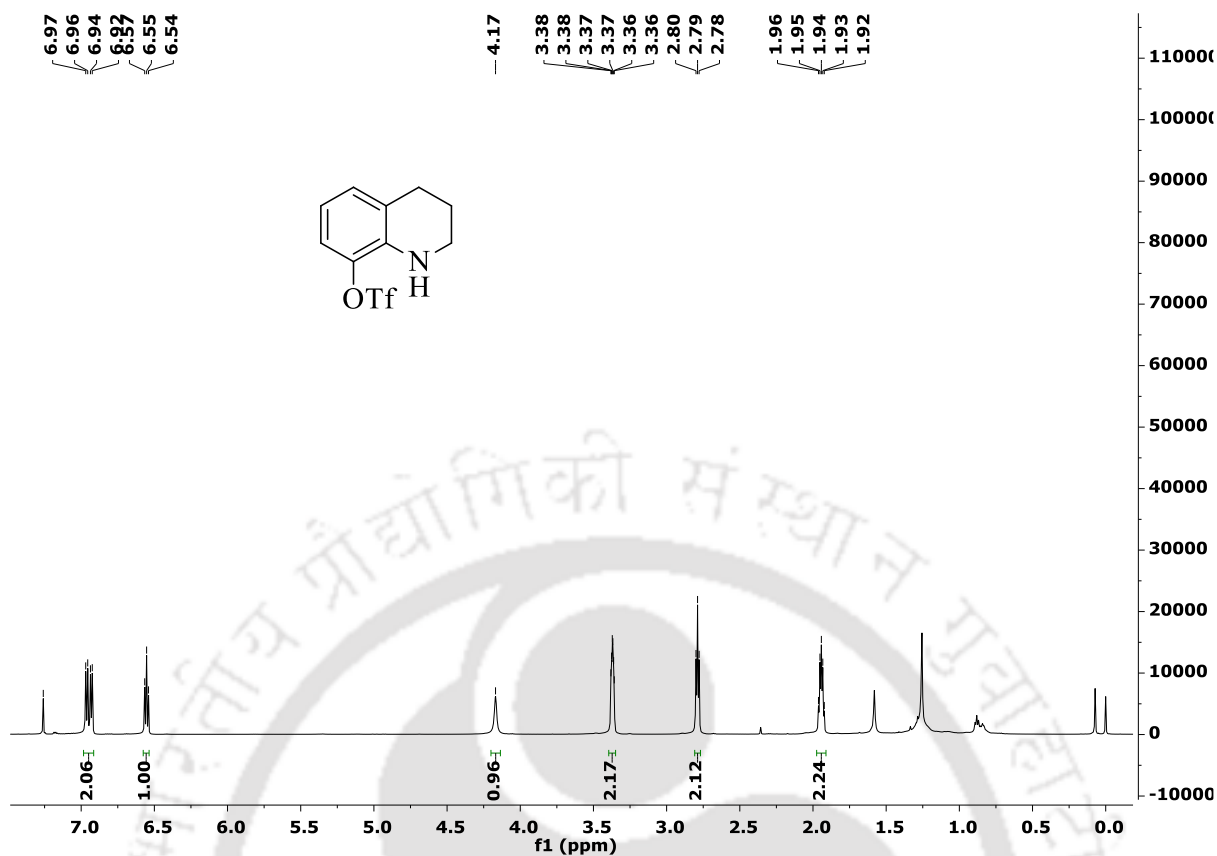


Figure S211: ¹H NMR Spectrum of **5.4o** (CDCl₃, 600 MHz, 298 K)

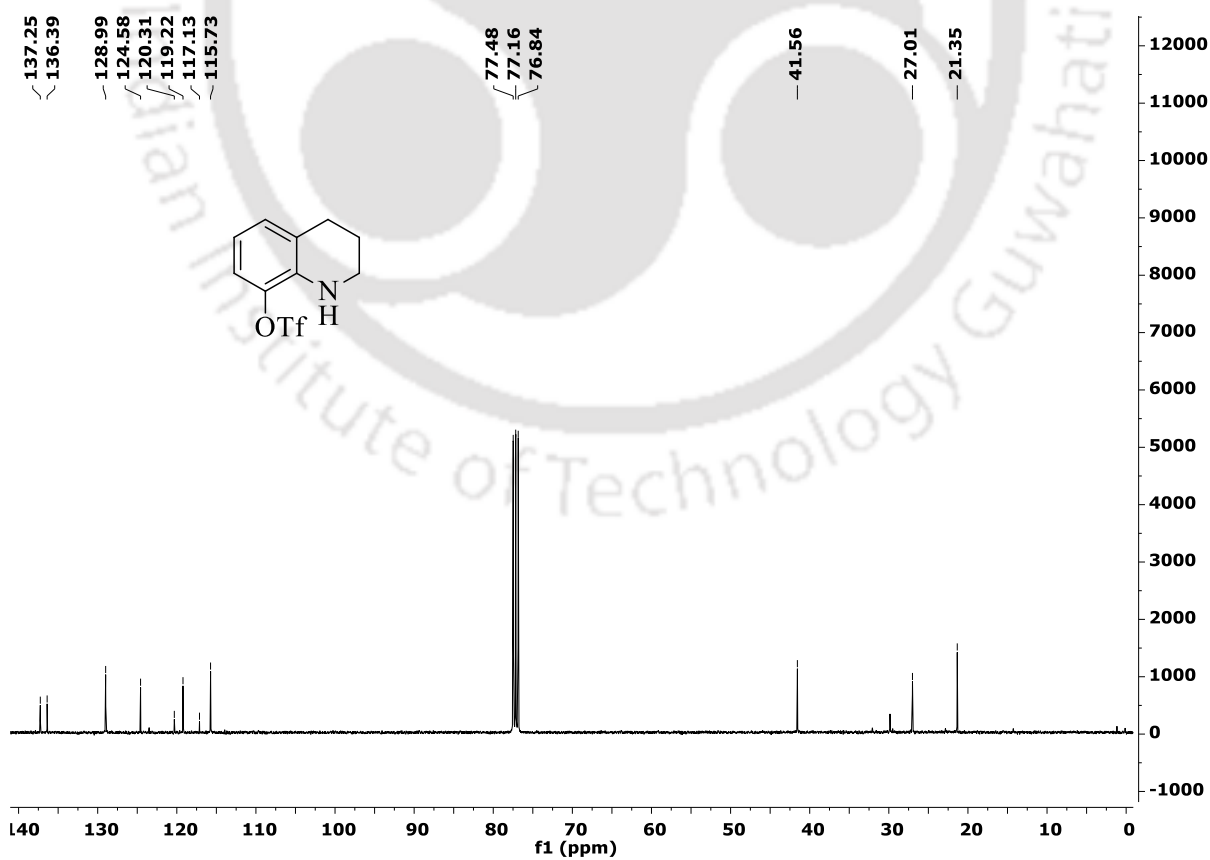


Figure S212: ¹³C NMR Spectrum of **5.4o** (CDCl₃, 101 MHz, 298 K)

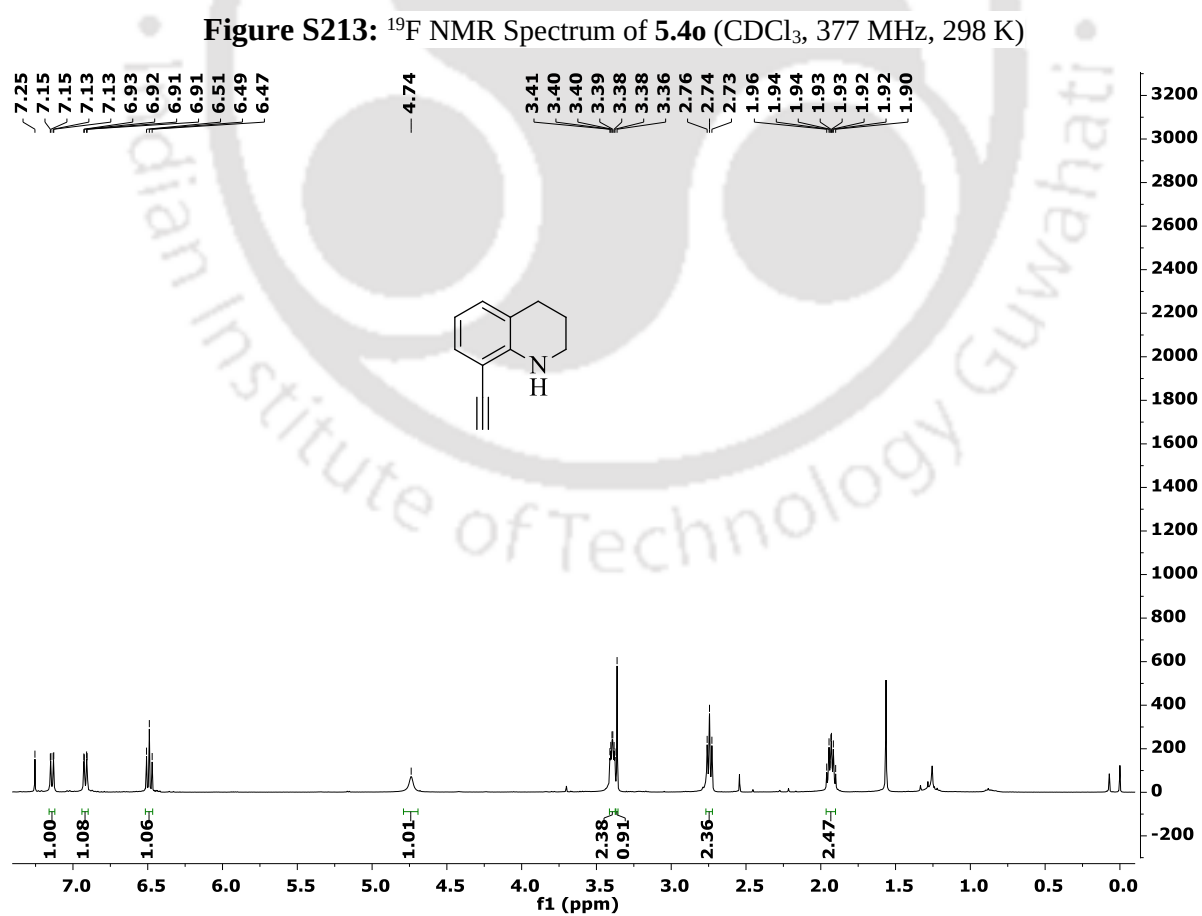
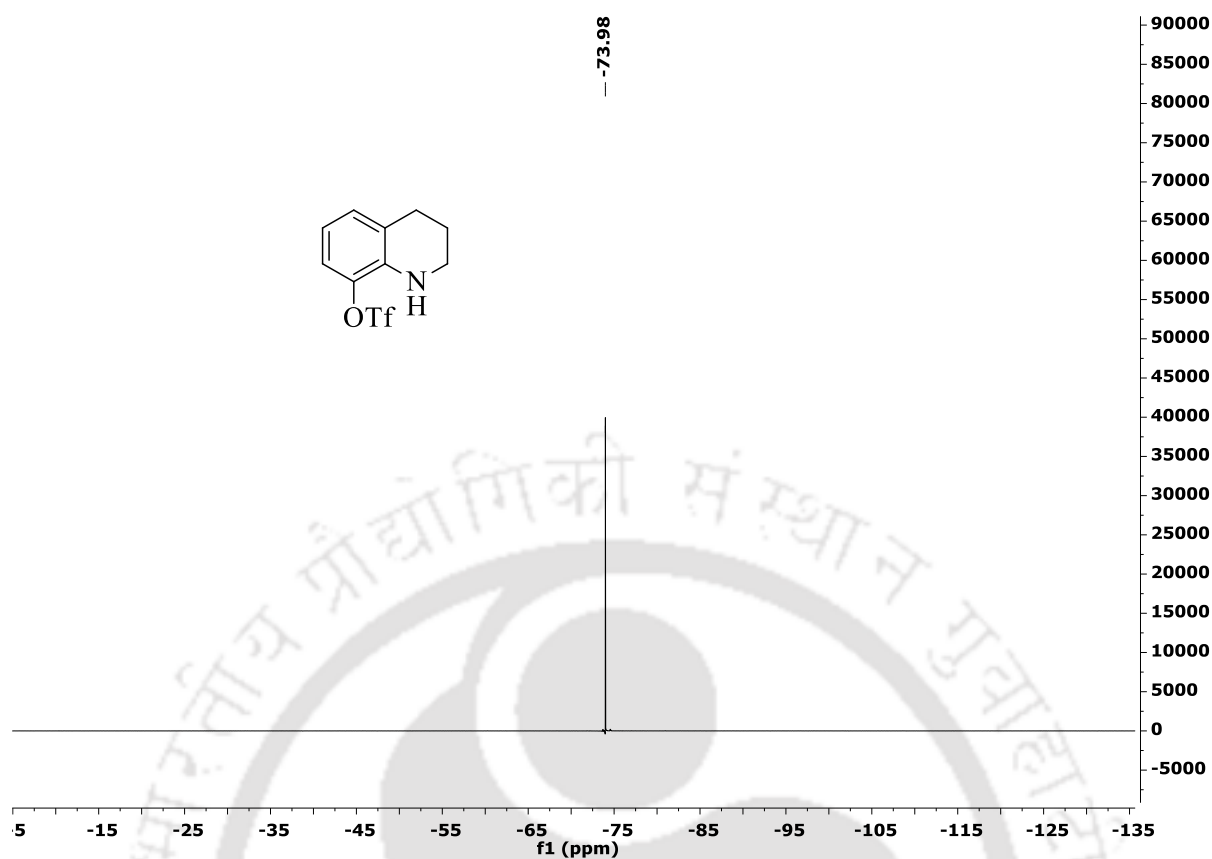


Figure S214: ^1H NMR Spectrum of **5.4p** (CDCl_3 , 400 MHz, 298 K)

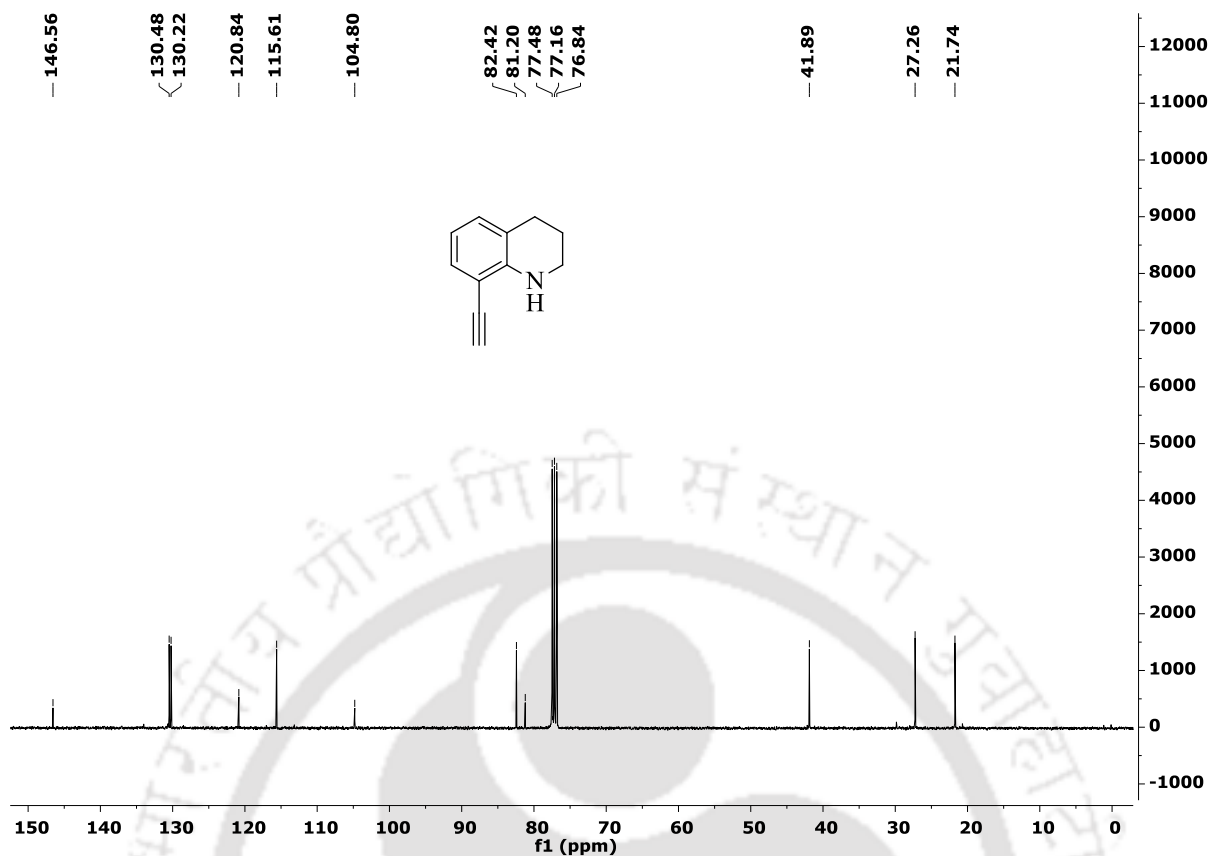


Figure S215: ¹³C NMR Spectrum of 5.4p (CDCl₃, 101 MHz, 298 K)

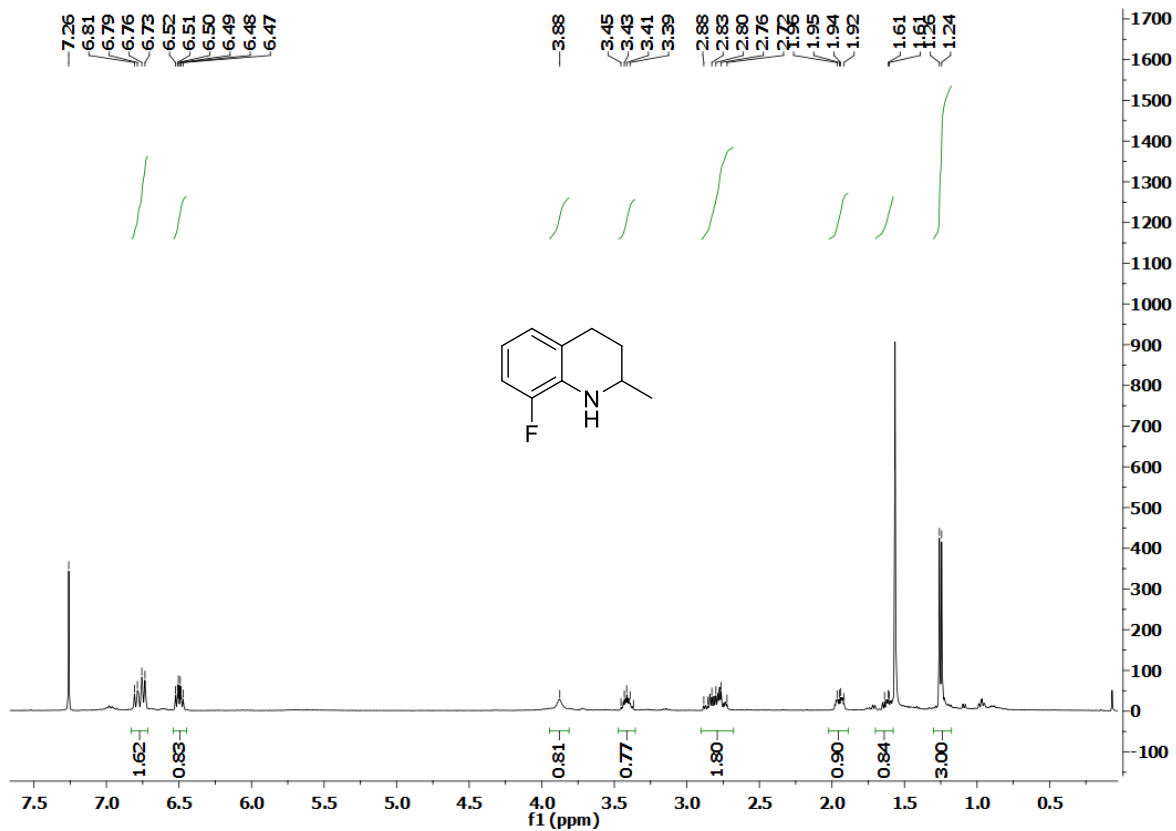
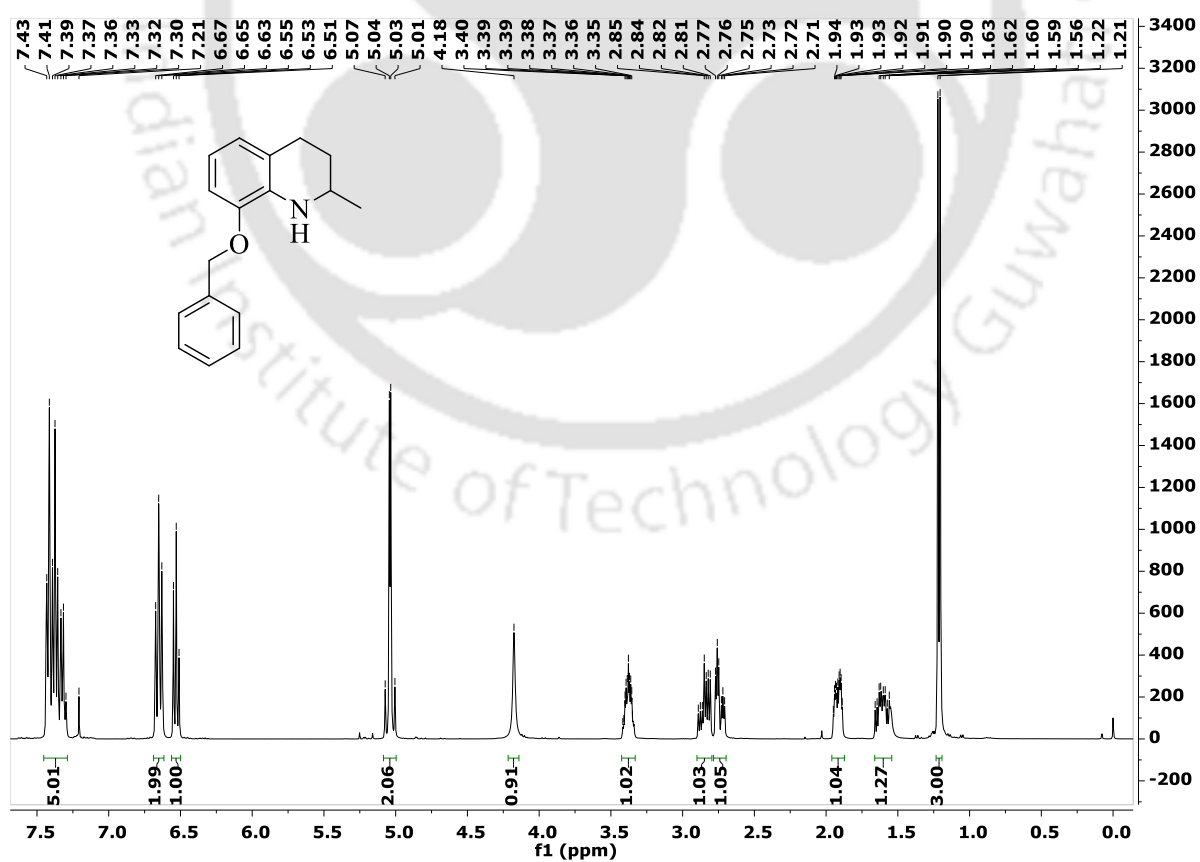
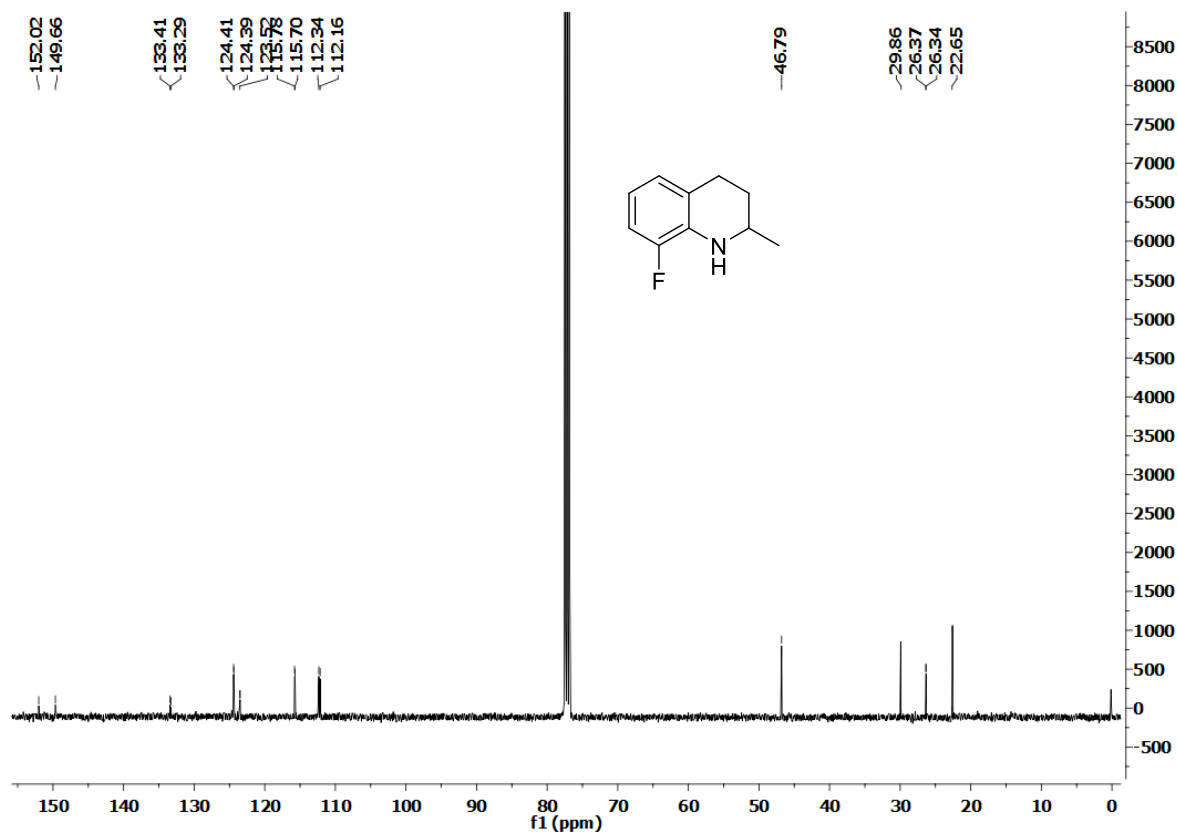


Figure S216: ¹H NMR Spectrum of 5.4q (CDCl₃, 400 MHz, 298 K)



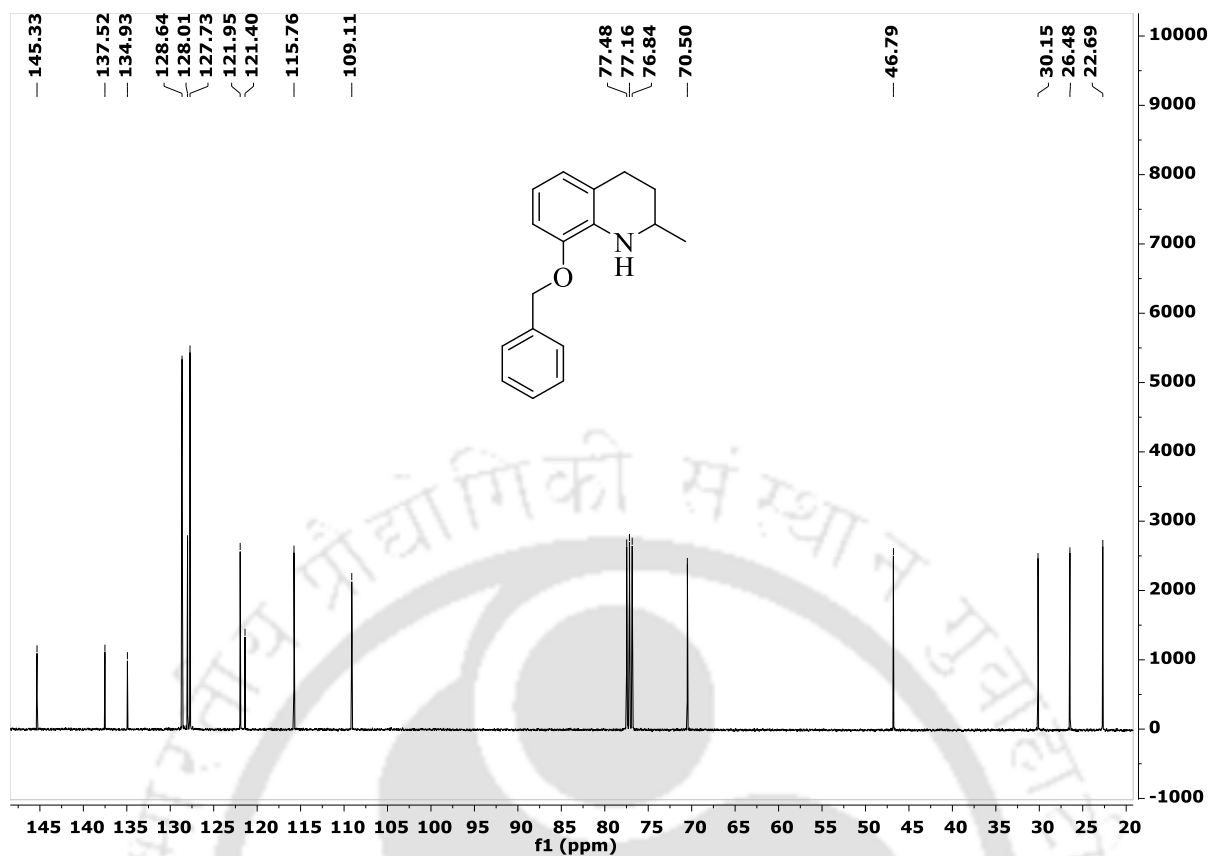


Figure S219: ^{13}C NMR Spectrum of **5.4r** (CDCl_3 , 101 MHz, 298 K)

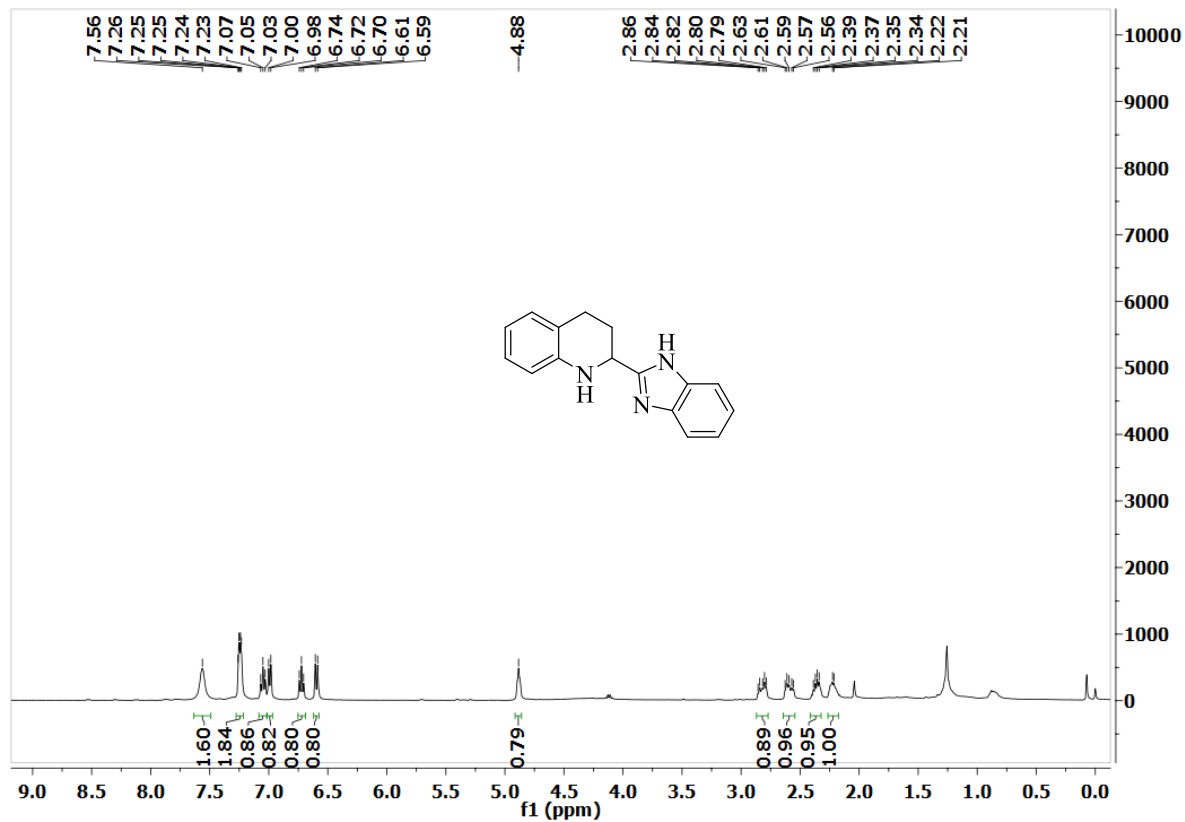
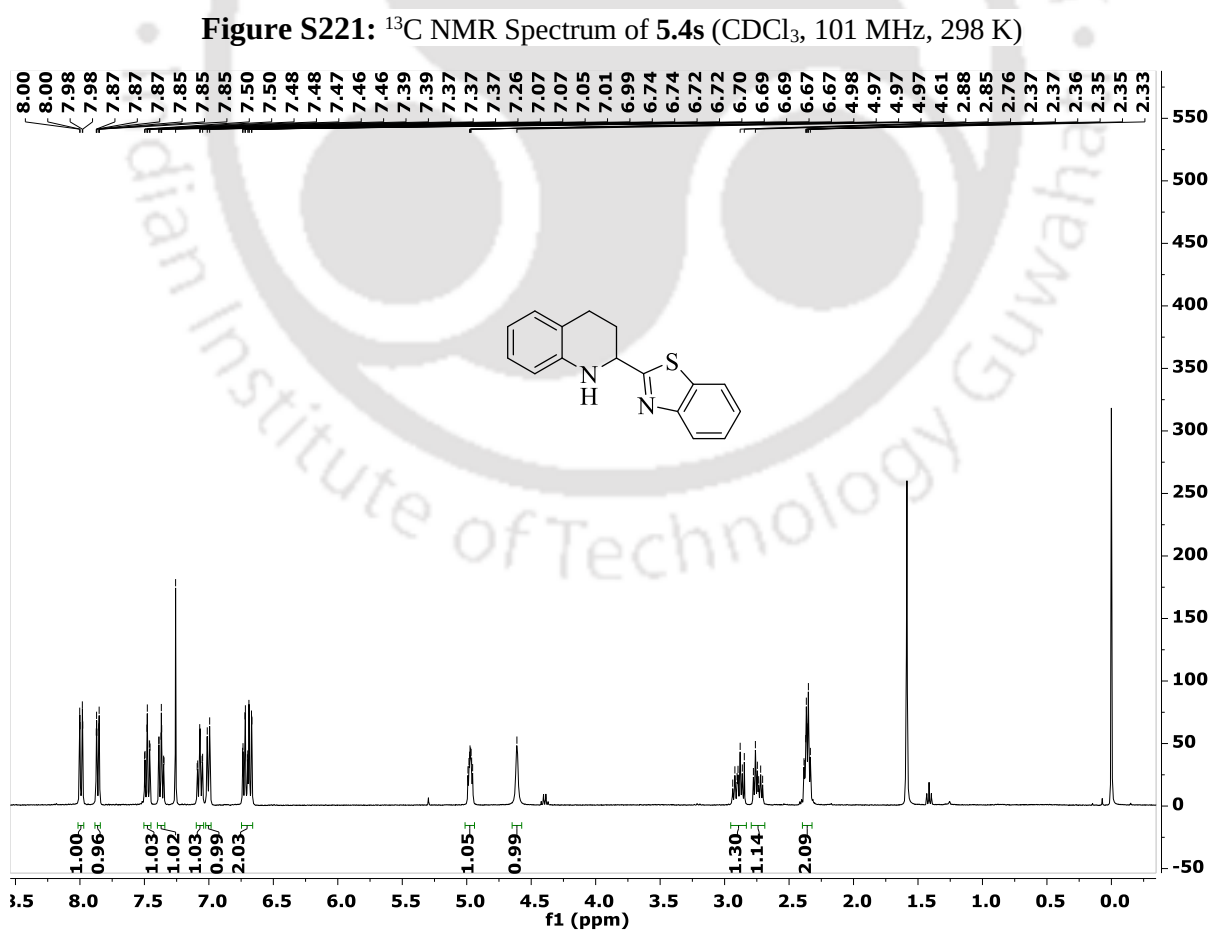
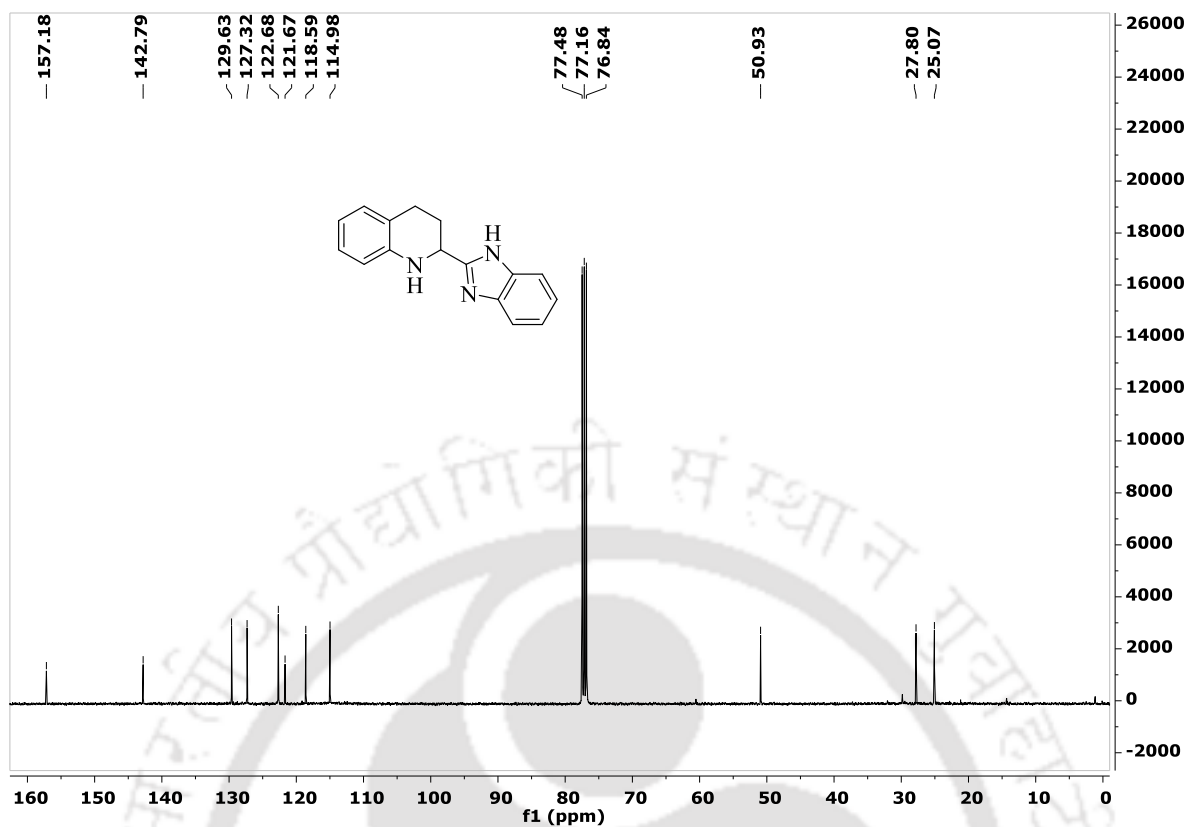
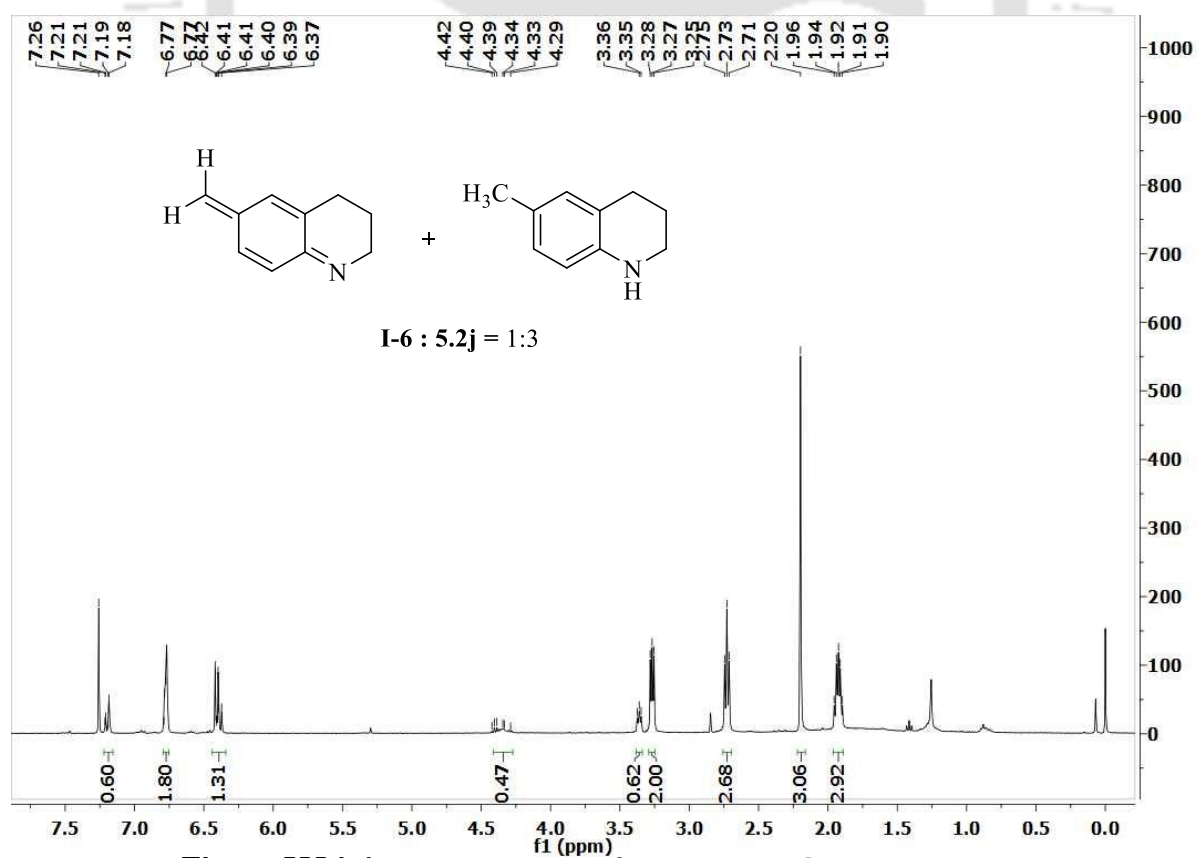
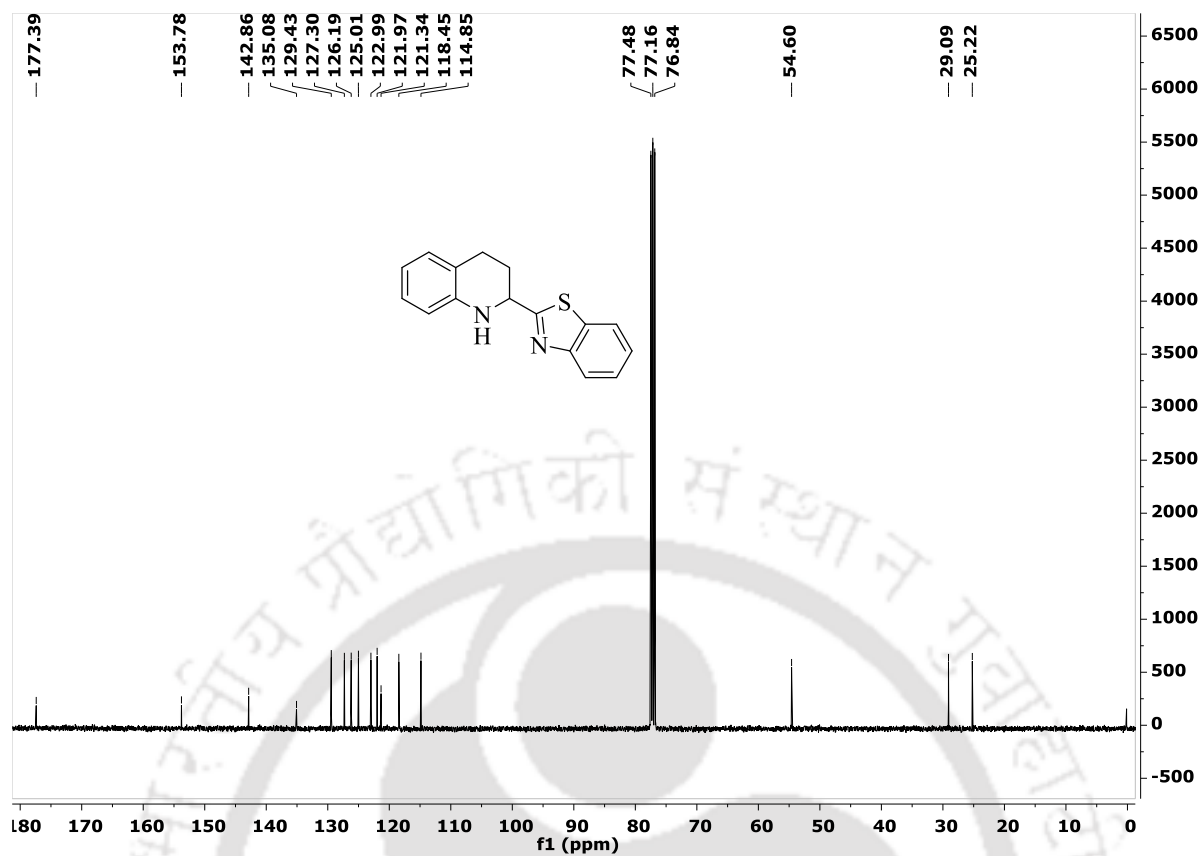


Figure S220: ^1H NMR Spectrum of **5.4s** (CDCl_3 , 400 MHz, 298 K)





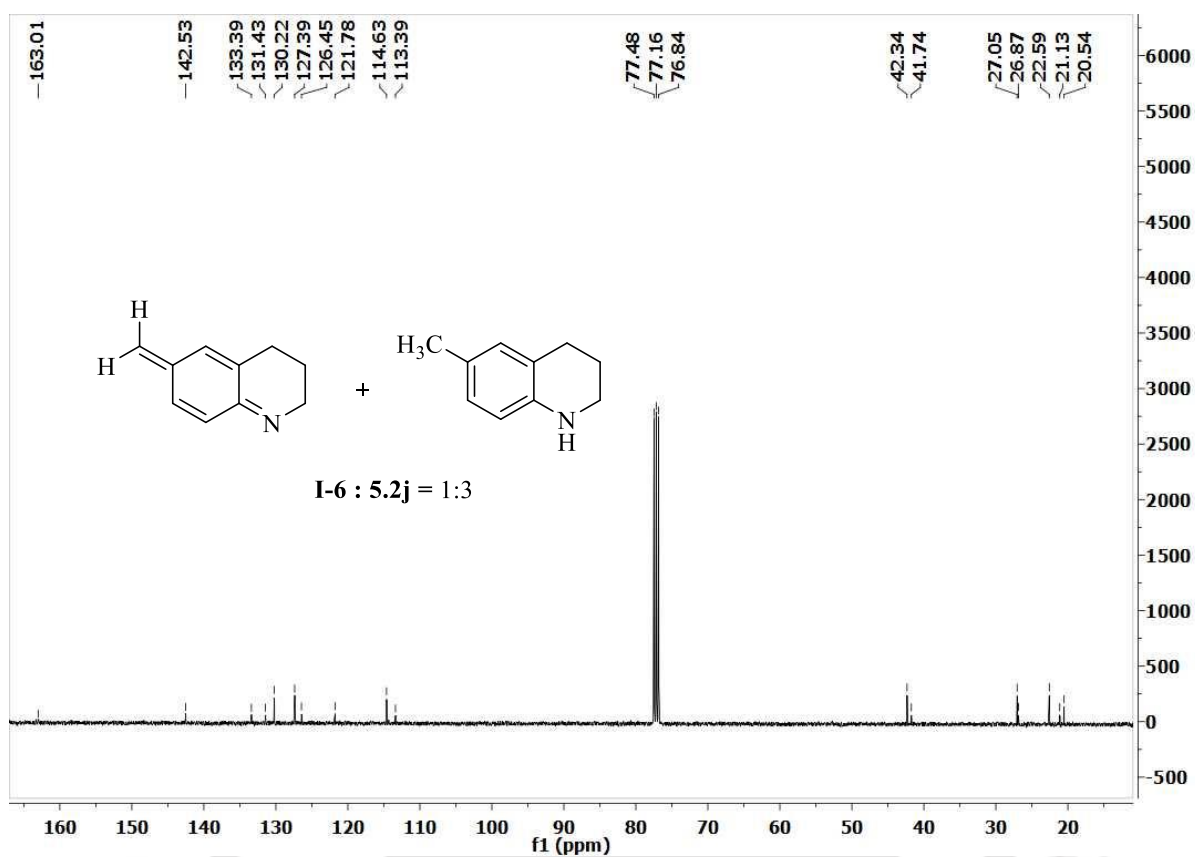


Figure S225: ^1H NMR Spectrum of I-6+5.2j (CDCl_3 , 101 MHz, 298 K)

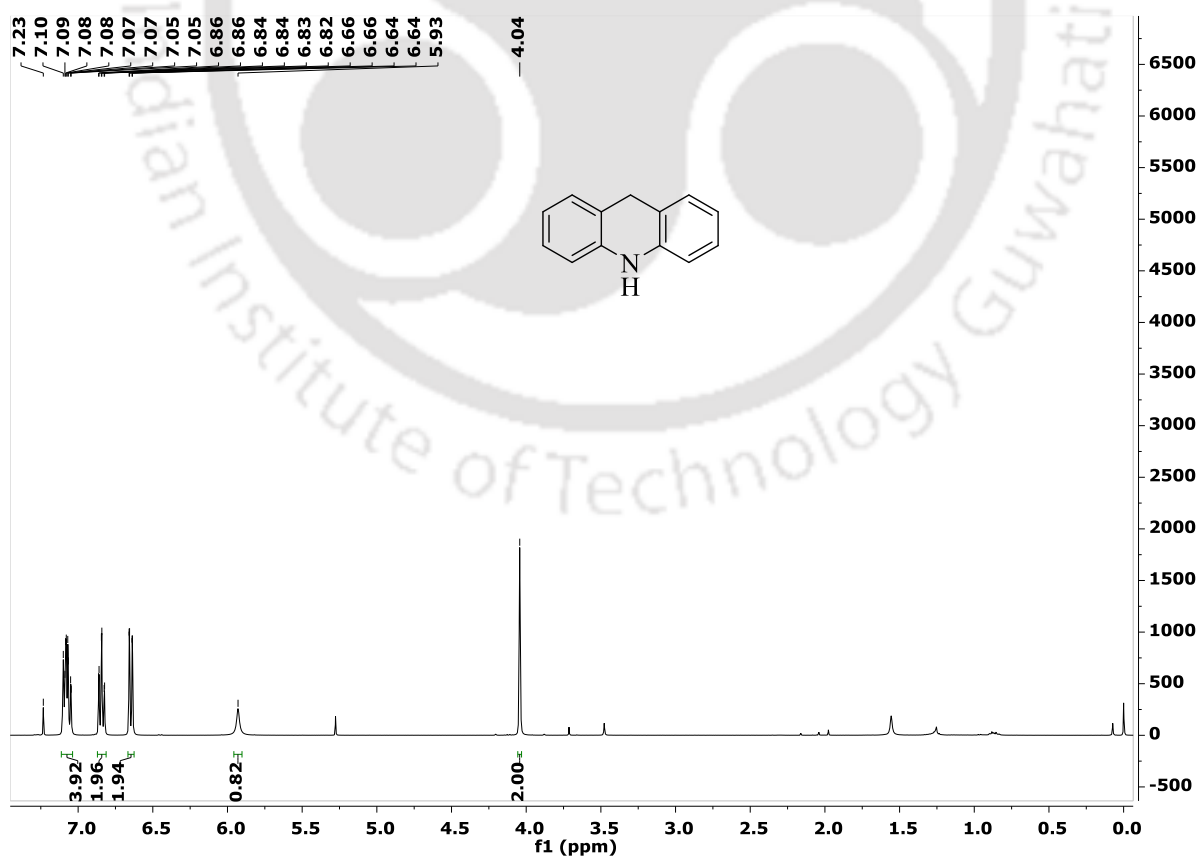


Figure S226: ^1H NMR Spectrum of 5.6a (CDCl_3 , 400 MHz, 298 K)

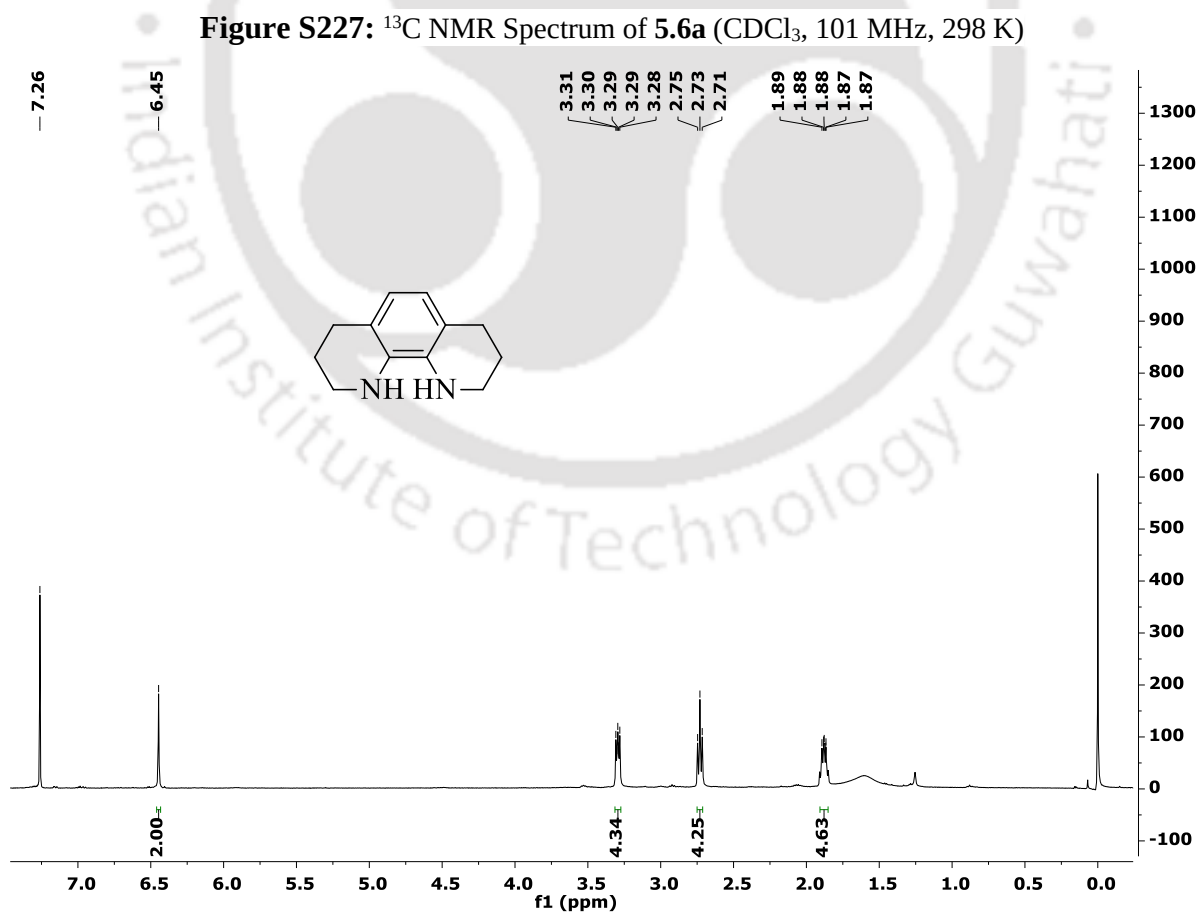
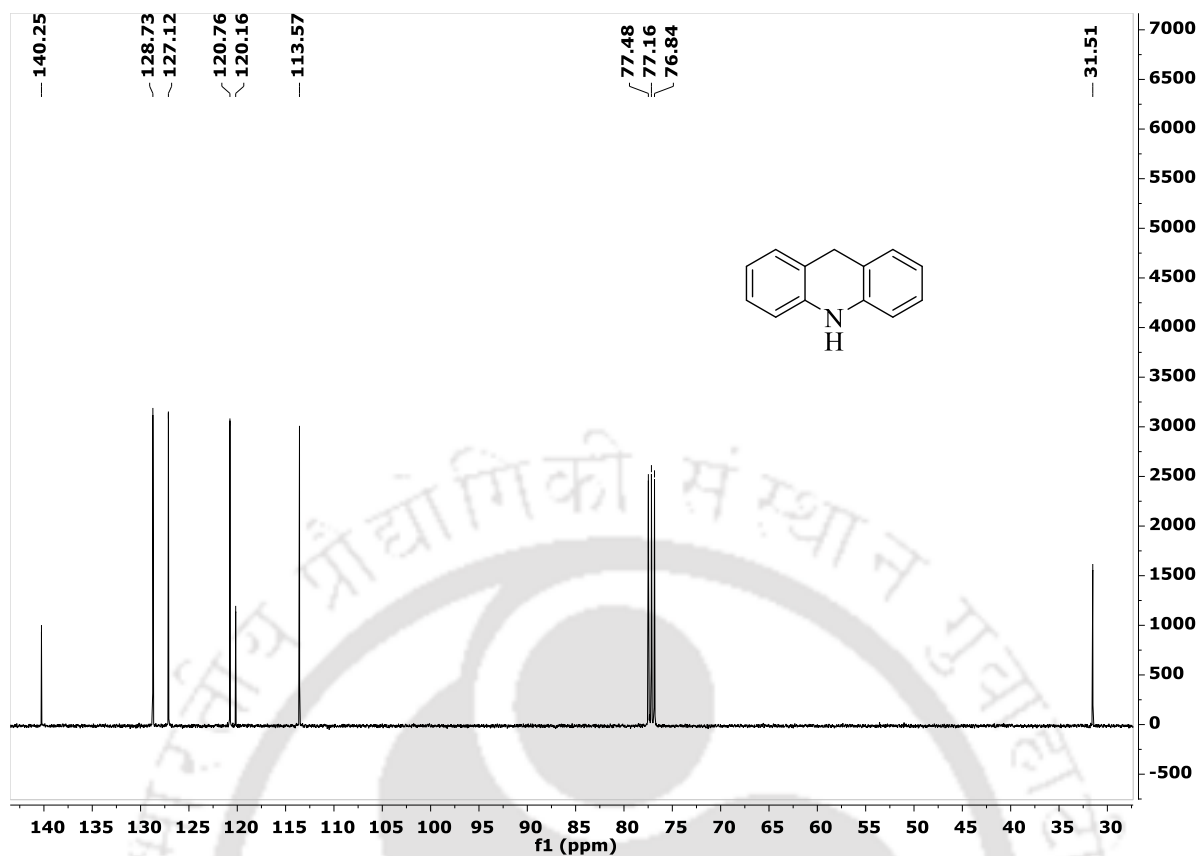
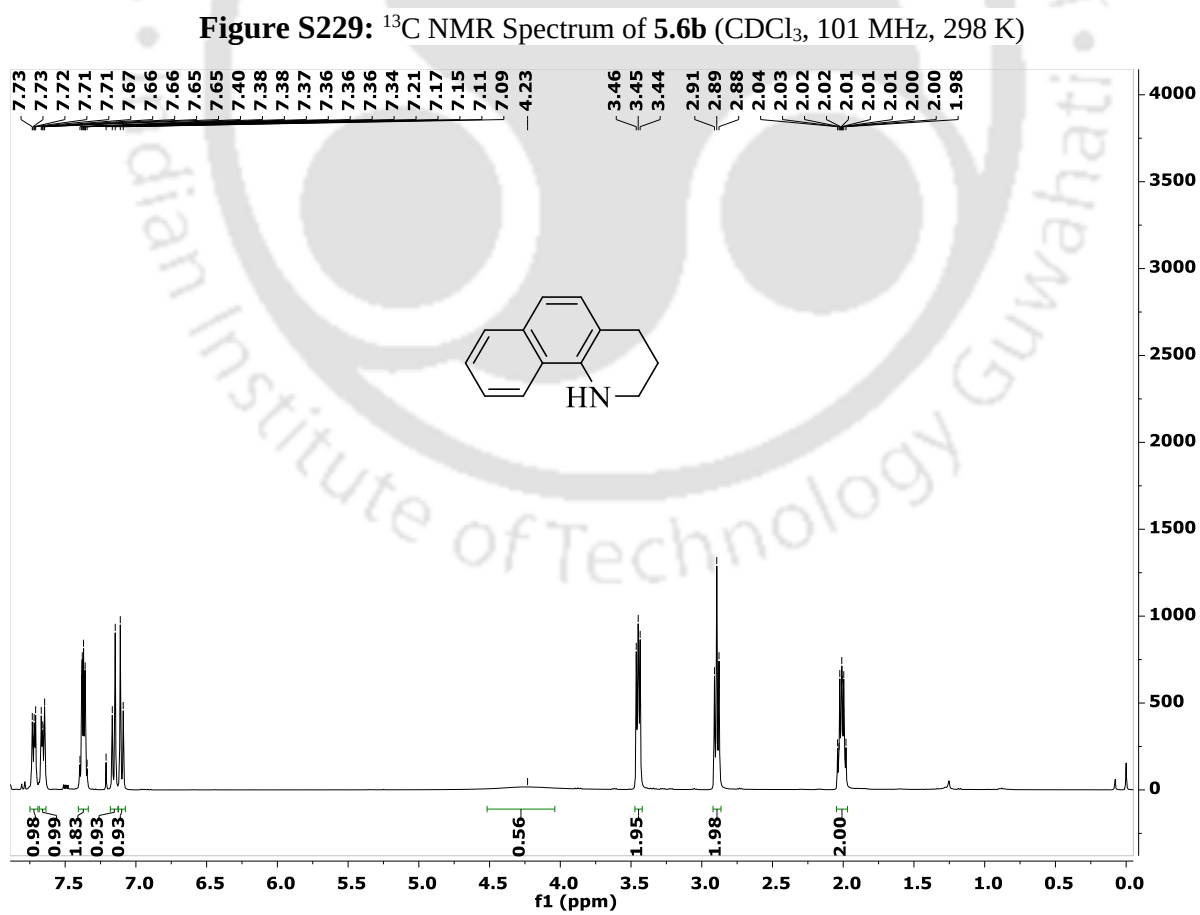
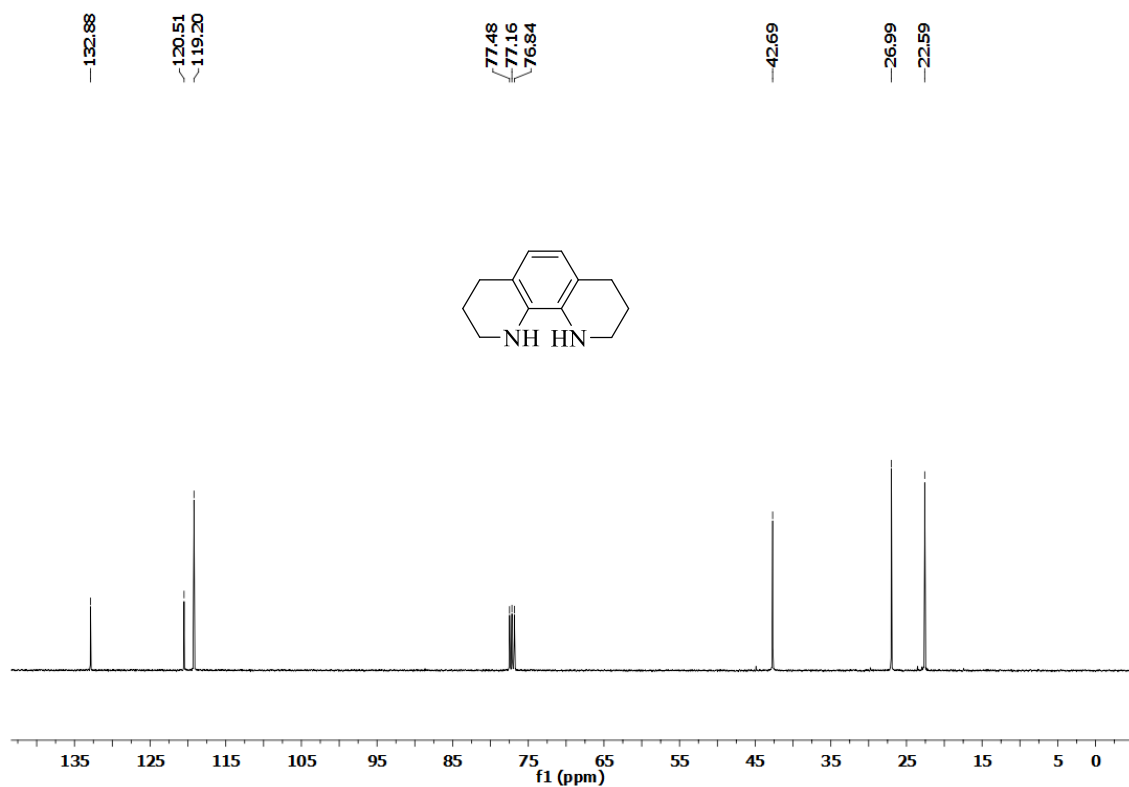


Figure S228: ^1H NMR Spectrum of **5.6b** (CDCl_3 , 400 MHz, 298 K)



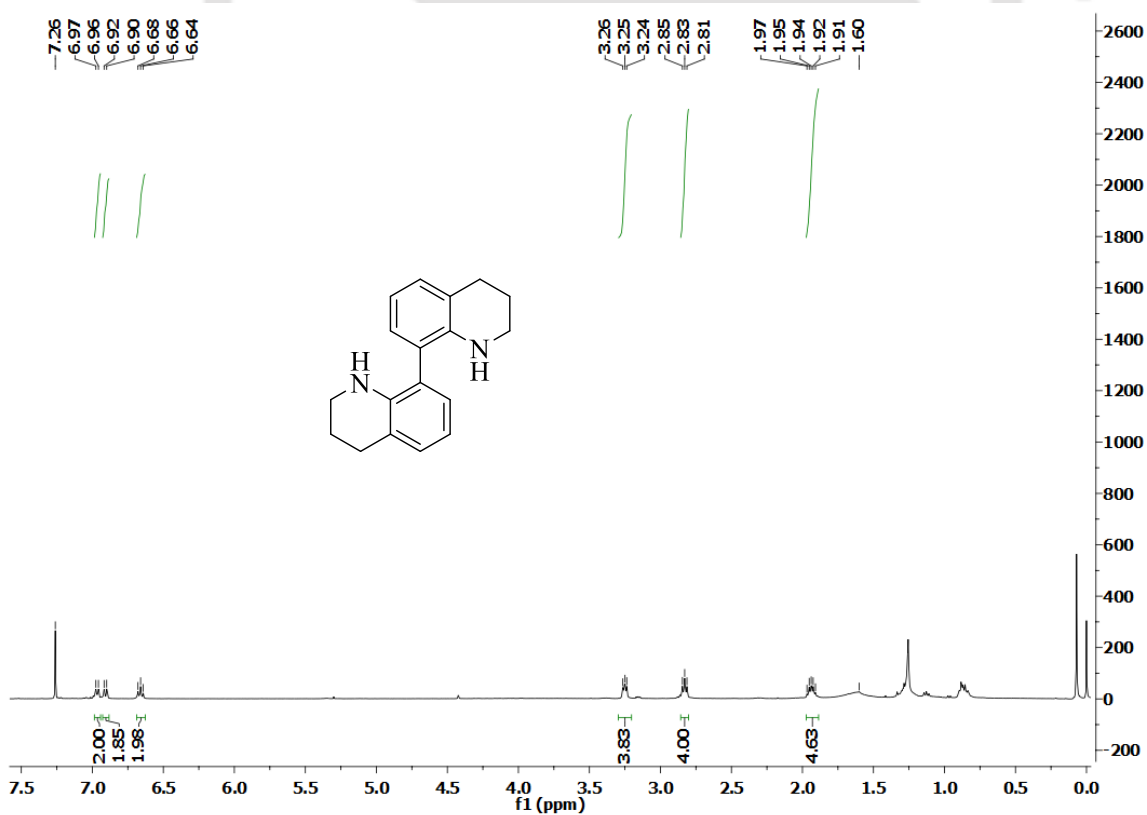
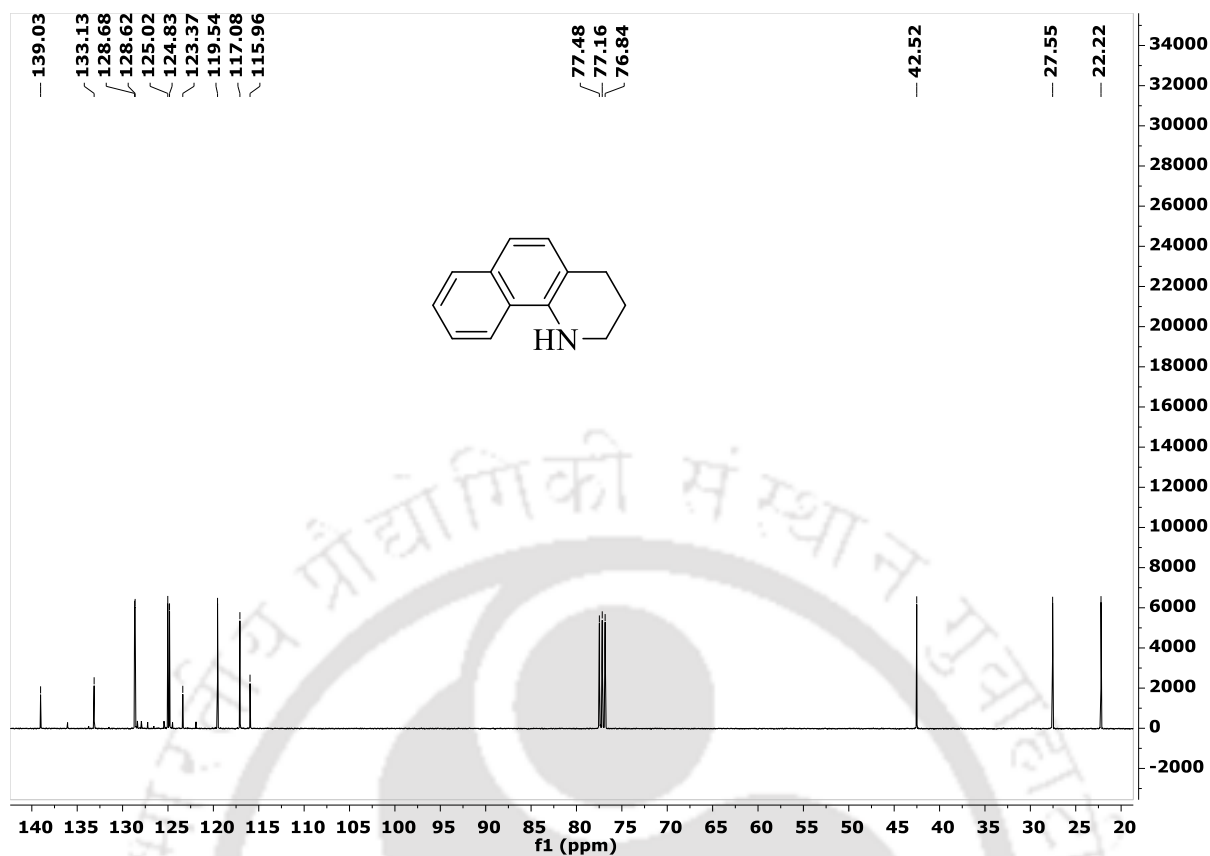


Figure S241: ^1H NMR Spectrum of **5.6d** (CDCl_3 , 400 MHz, 298 K)

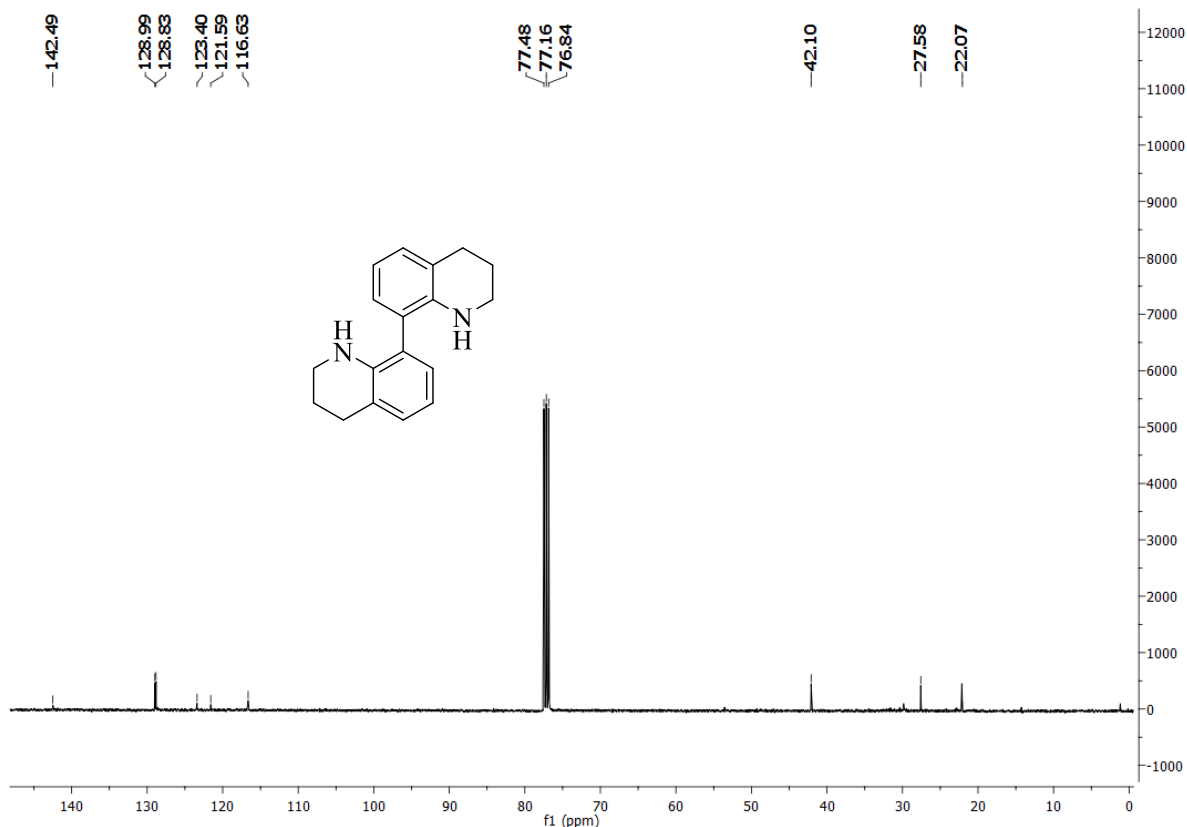


Figure S242: ¹³C NMR Spectrum of 5.6d (CDCl₃, 101 MHz, 298 K)

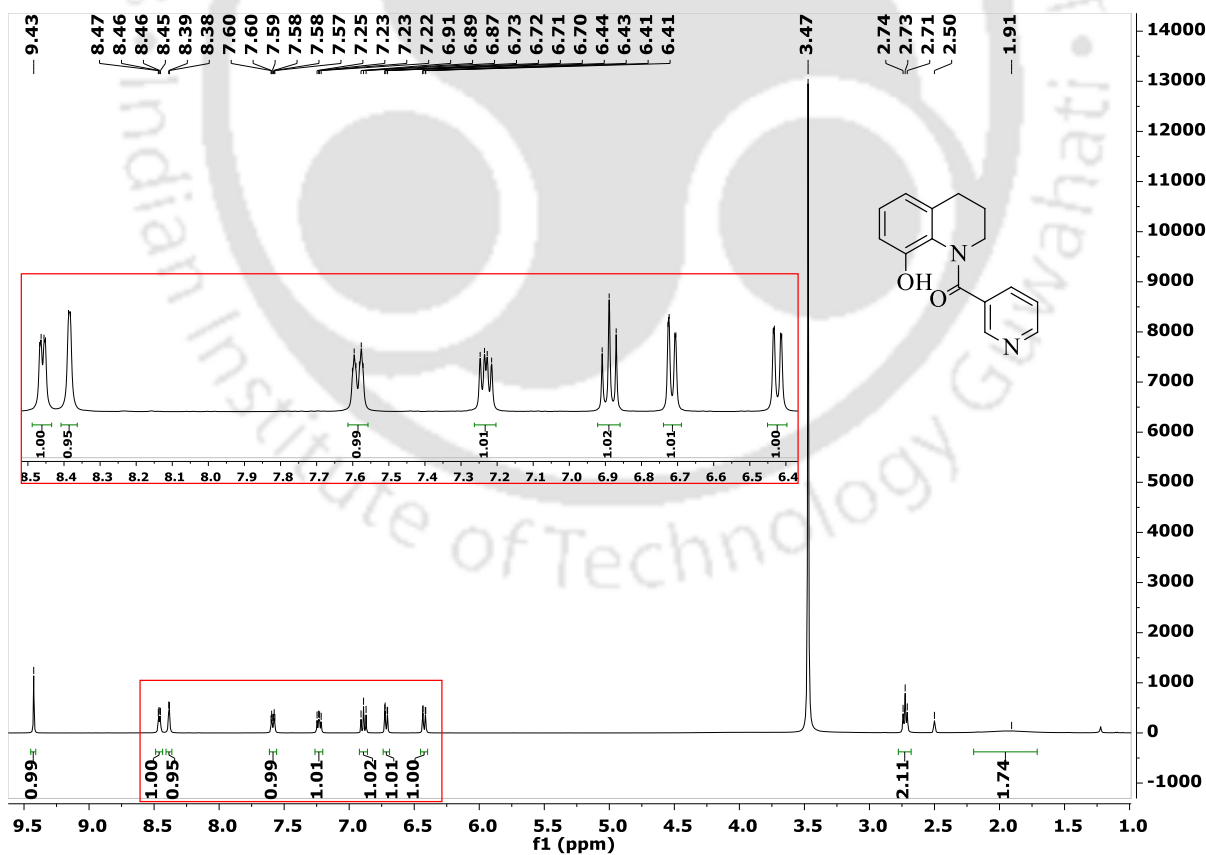


Figure S243: ¹H NMR Spectrum of 5.7 (DMSO-*d*₆, 400 MHz, 298 K)

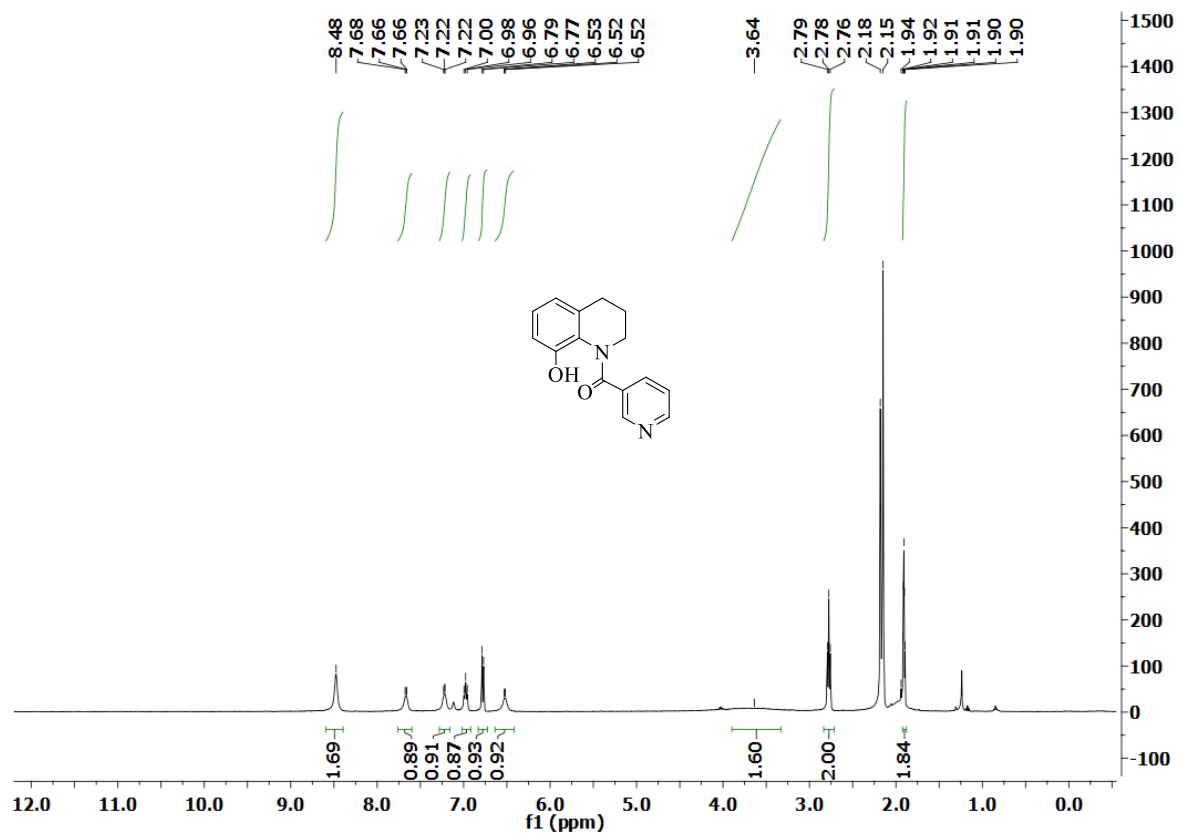


Figure S244: ¹H NMR Spectrum of 5.7 (CD₃CN, 400 MHz, 298 K)

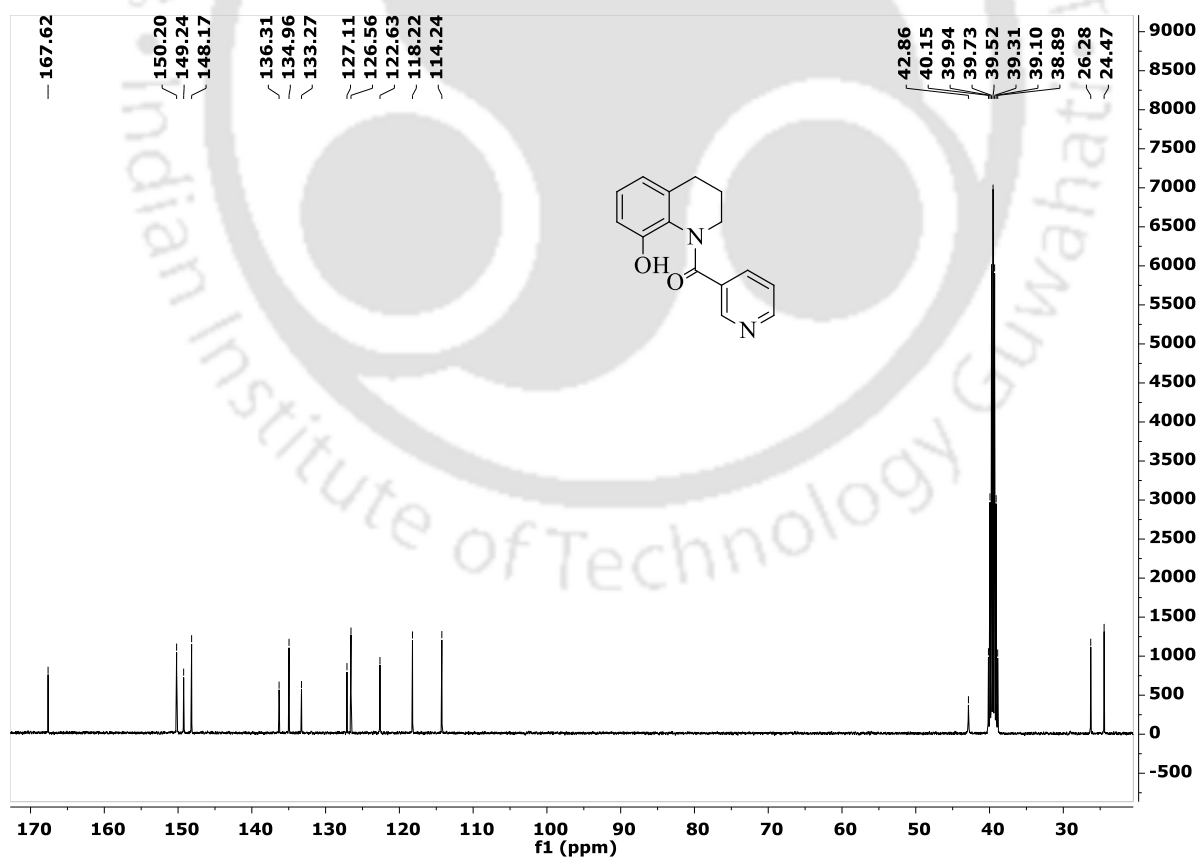


Figure S245: ¹³C NMR Spectrum of 5.7 (DMSO-*d*₆, 101 MHz, 298 K)

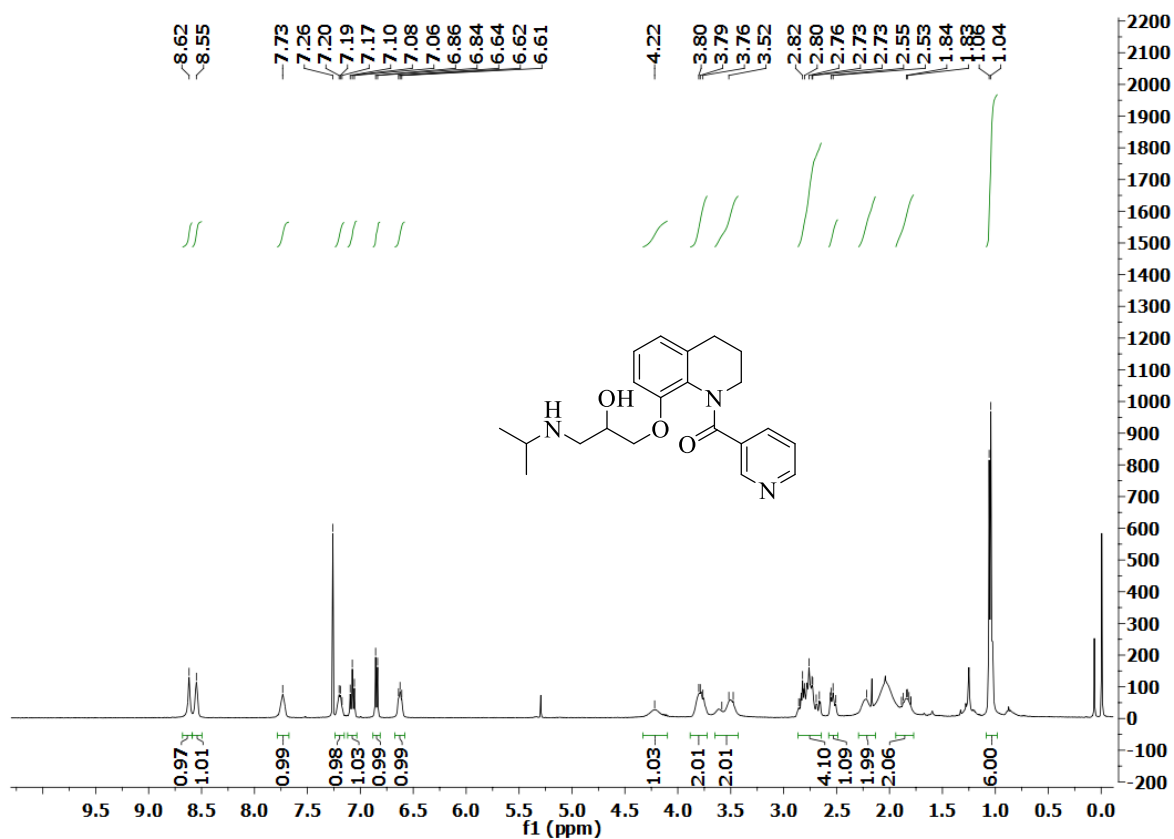


Figure S246: ¹H NMR Spectrum of 5.8 (CDCl₃, 400 MHz, 298 K)

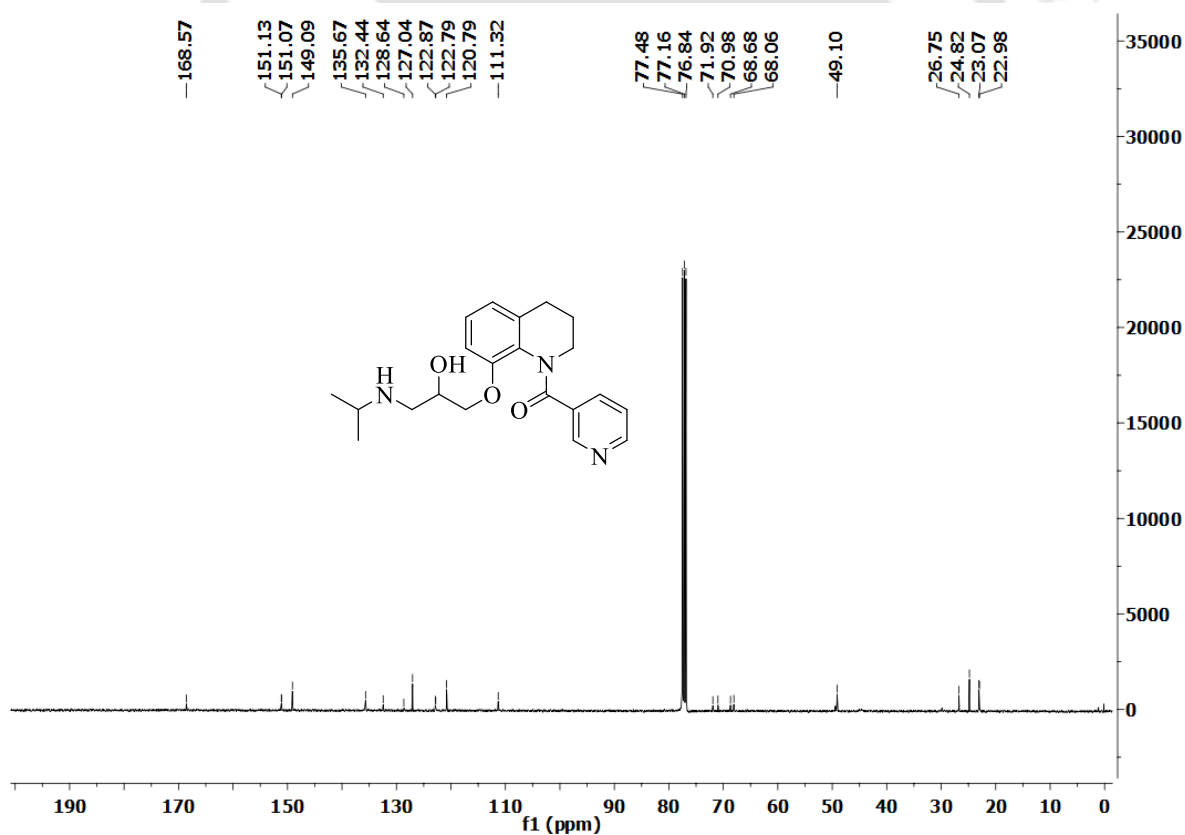


Figure S247: ¹³C NMR Spectrum of 5.8 (CDCl₃, 101 MHz, 298 K)

Sample Name	NCP-2	Position	P1-E1	Instrument Name	Instrument 1
User Name		Inj Vol	20	InjPosition	
Sample Type	Sample	IRM Calibration Status	Success	Data Filename	NCP-2.d
ACQ Method	ESI ALS 100-1000.m	Comment		Acquired Time	09-07-2019 10:31:18 AM (UTC+05:30)

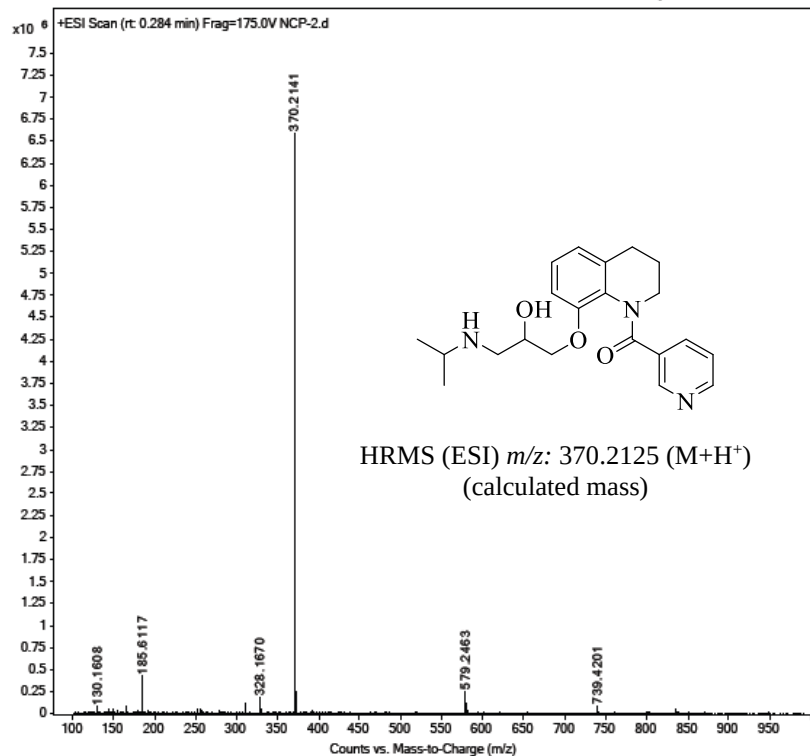


Figure S248: HRMS Spectrum of 5.8

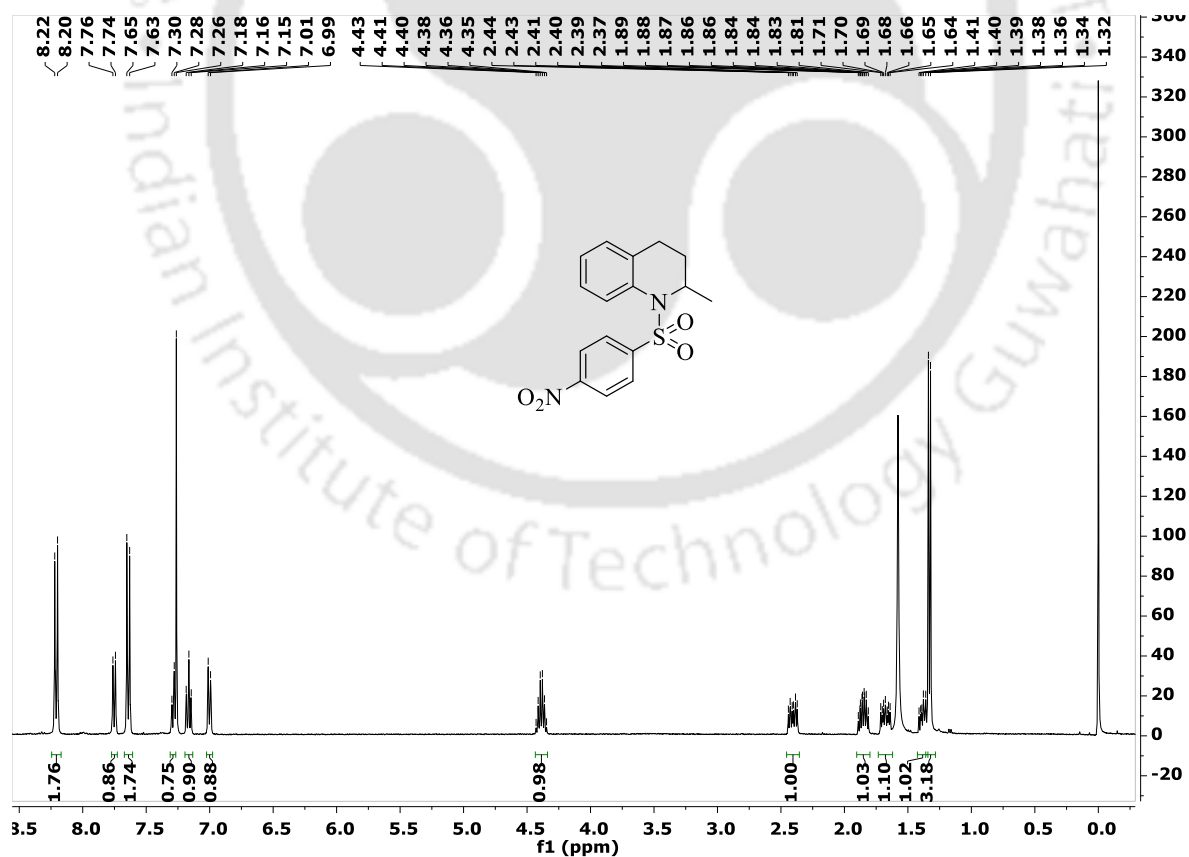


Figure S249: 1H NMR Spectrum of 5.9 ($CDCl_3$, 400 MHz, 298 K)

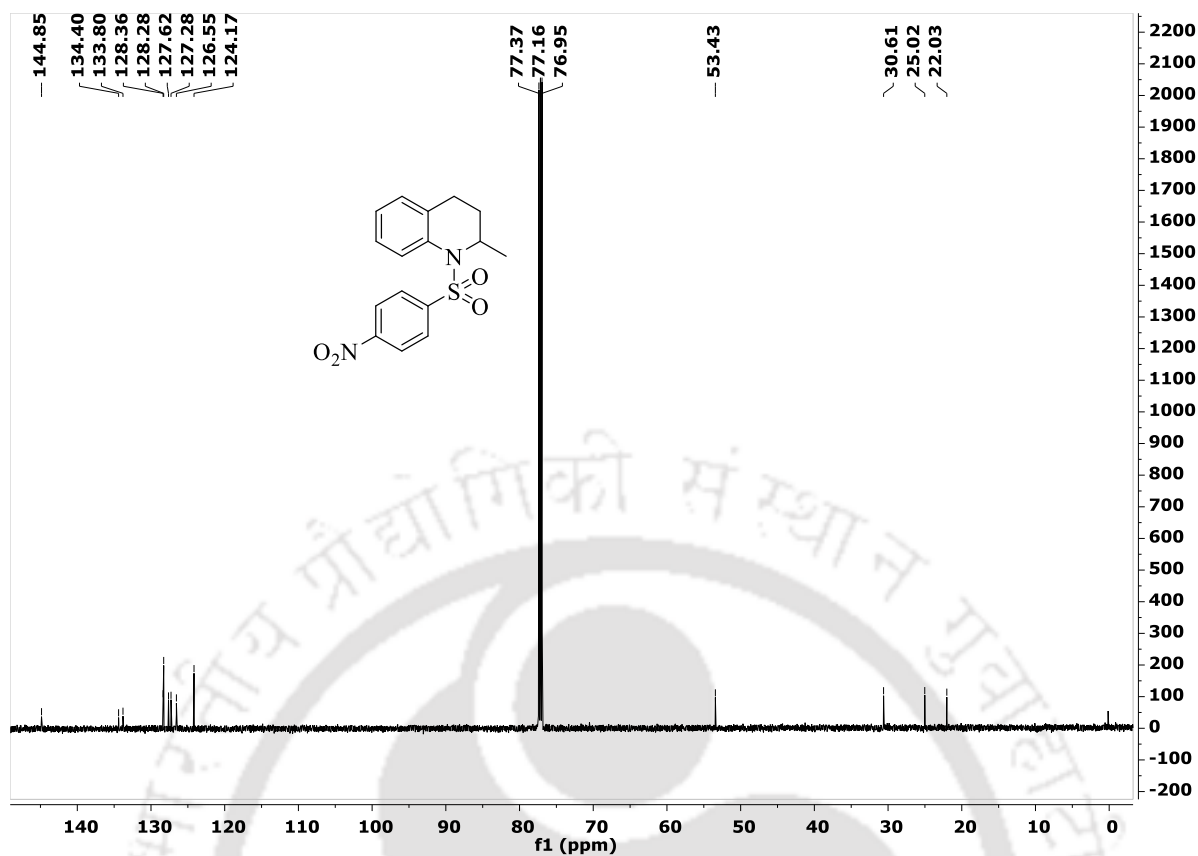


Figure S250: ¹³C NMR Spectrum of 5.9 (CDCl₃, 151 MHz, 298 K)

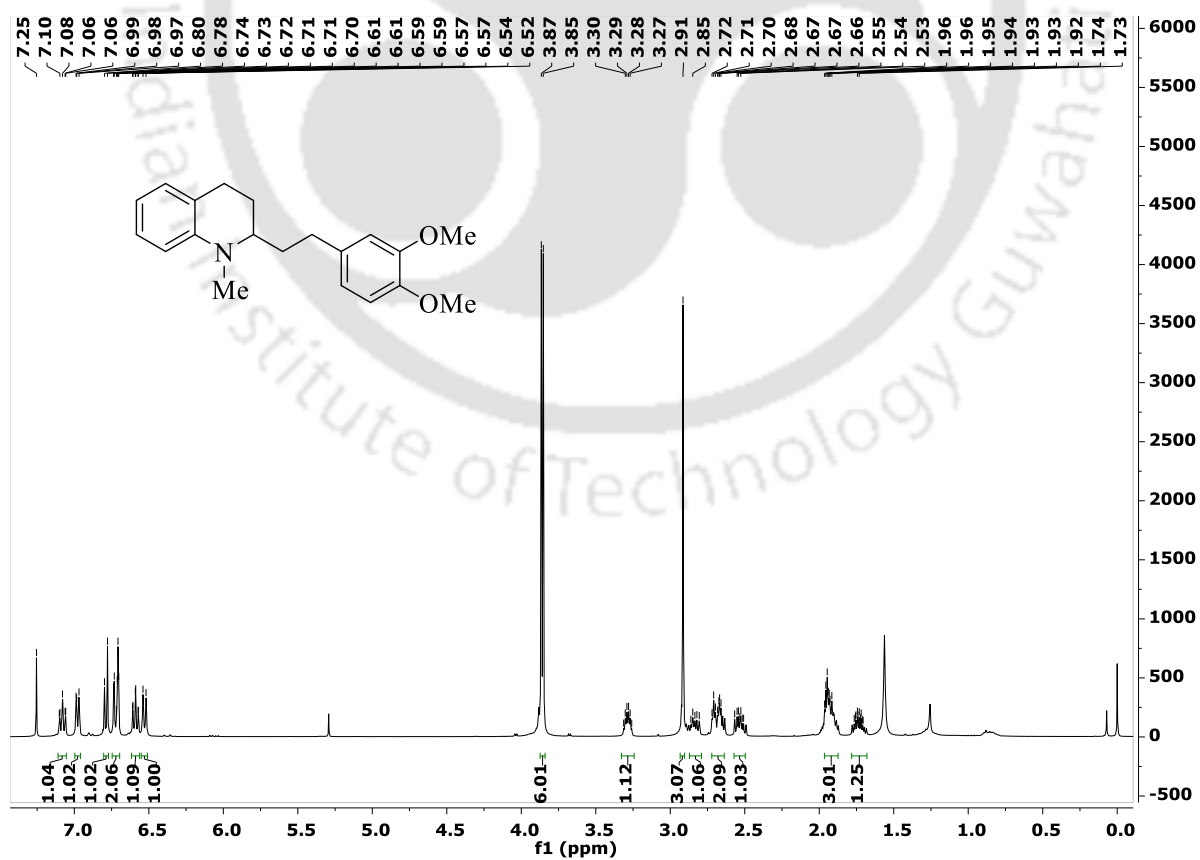


Figure S251: ¹H NMR Spectrum of 5.10 (CDCl₃, 400 MHz, 298 K)

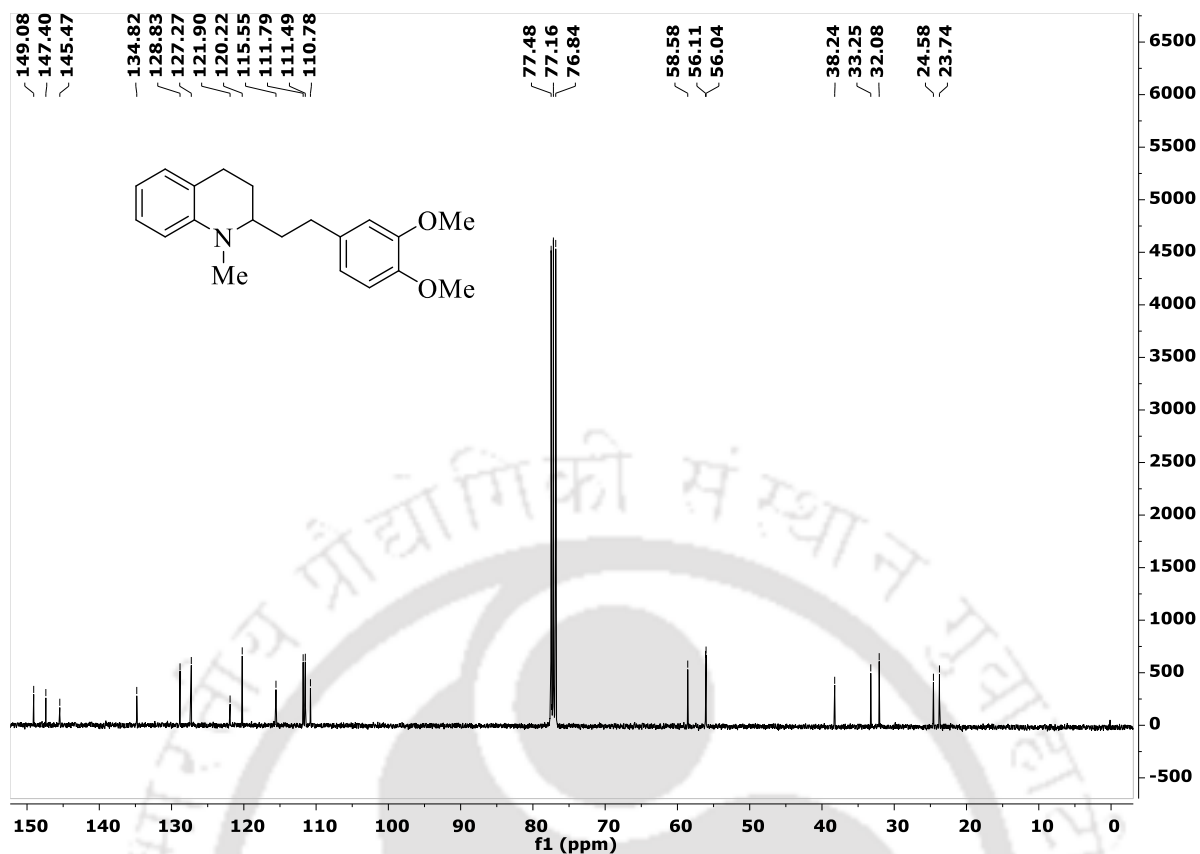


Figure S252: ¹³C NMR Spectrum of 5.10 (CDCl₃, 101 MHz, 298 K)

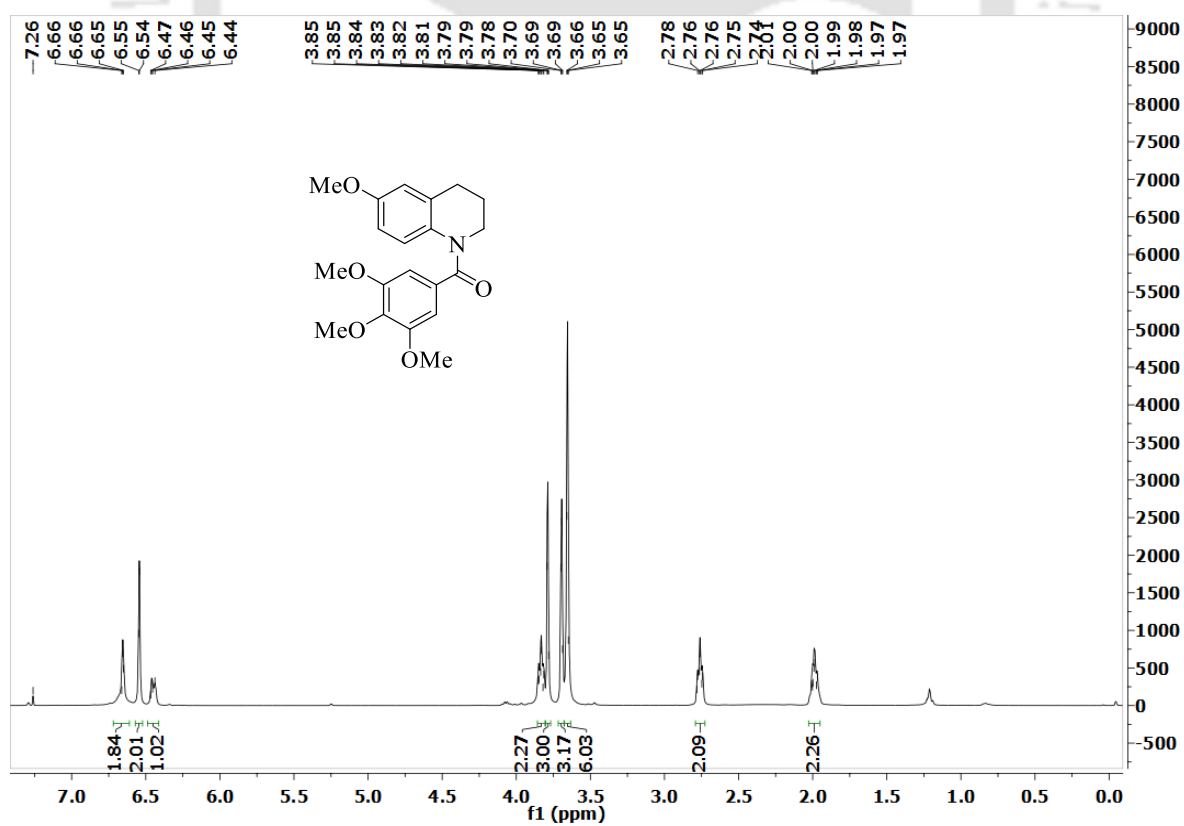


Figure S253: ¹H NMR Spectrum of 5.11 (CDCl₃, 400 MHz, 298 K)

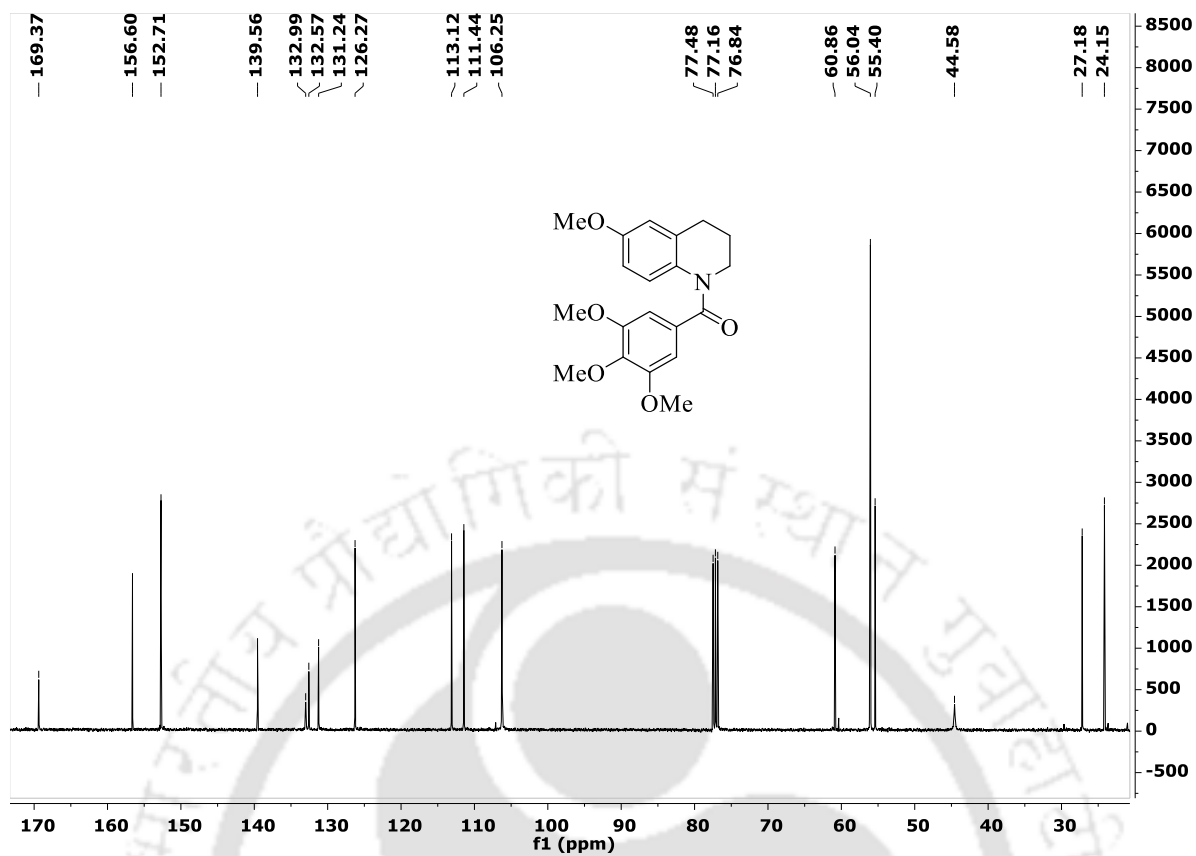


Figure S254: ¹³C NMR Spectrum of 5.11 (CDCl₃, 101 MHz, 298 K)

Annexure V

^1H , ^{13}C , and ^{19}F NMR spectra of the products (*Chapter 6*)

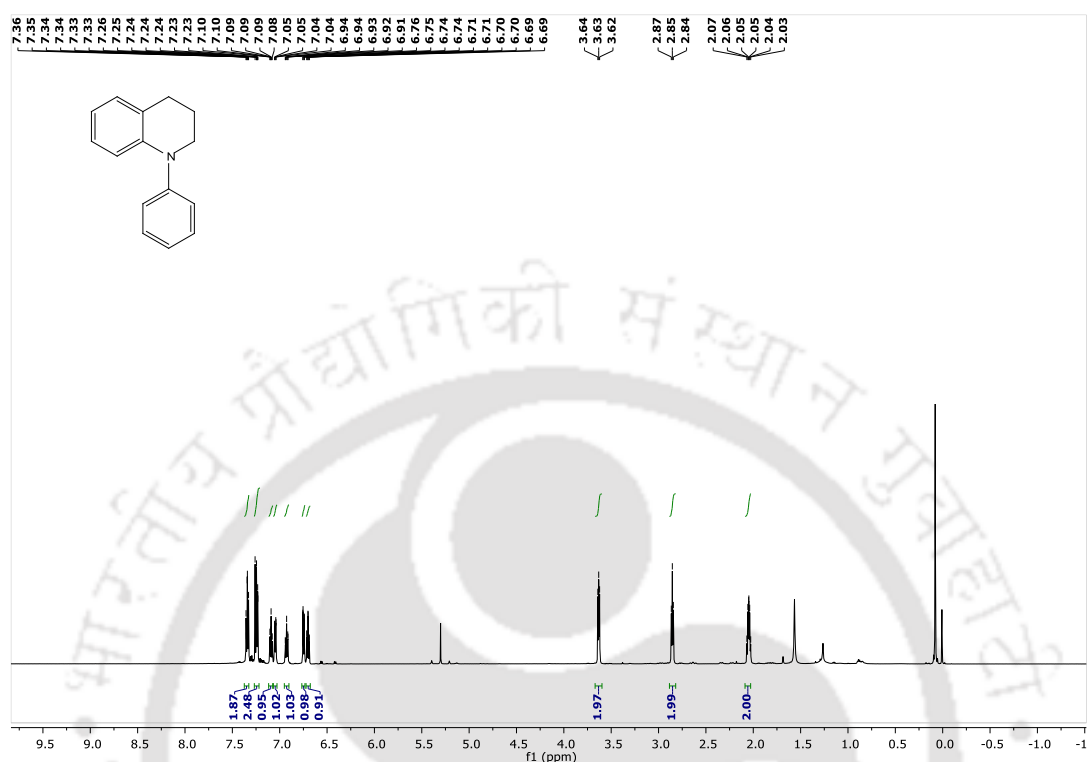


Figure S255: ^1H NMR Spectrum of **6.1a** (CDCl₃, 600 MHz, 298 K)

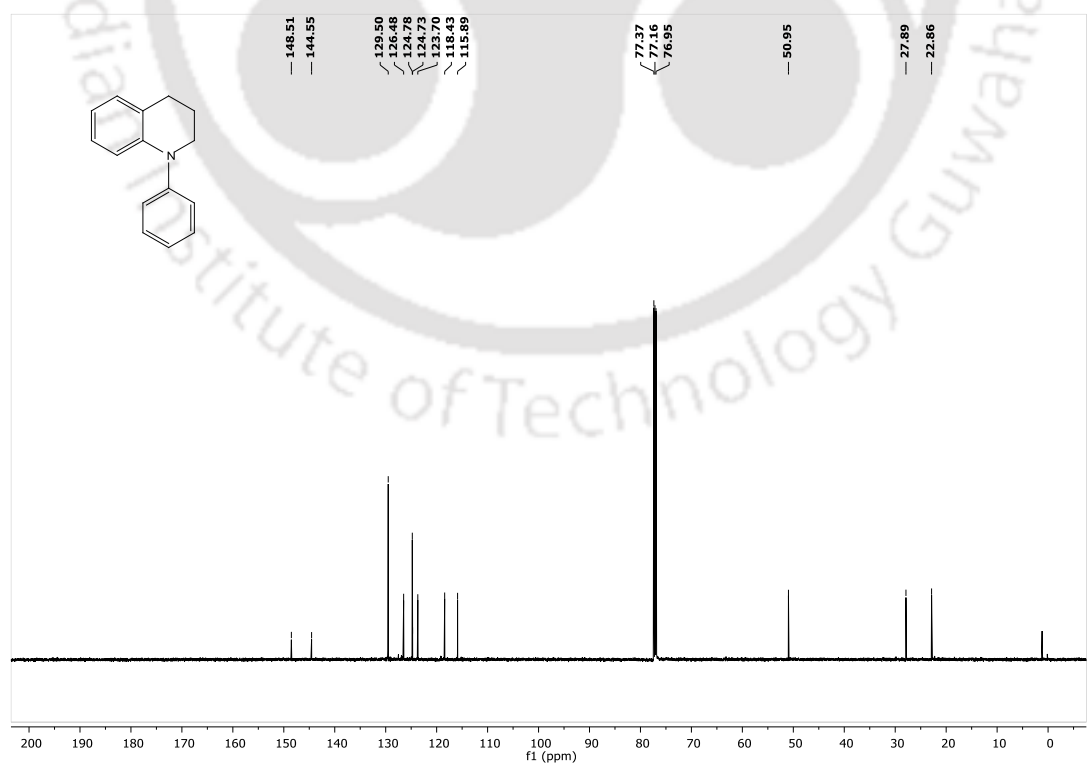


Figure S256: ^{13}C NMR Spectrum of **6.1a** (CDCl₃, 101 MHz, 298 K)

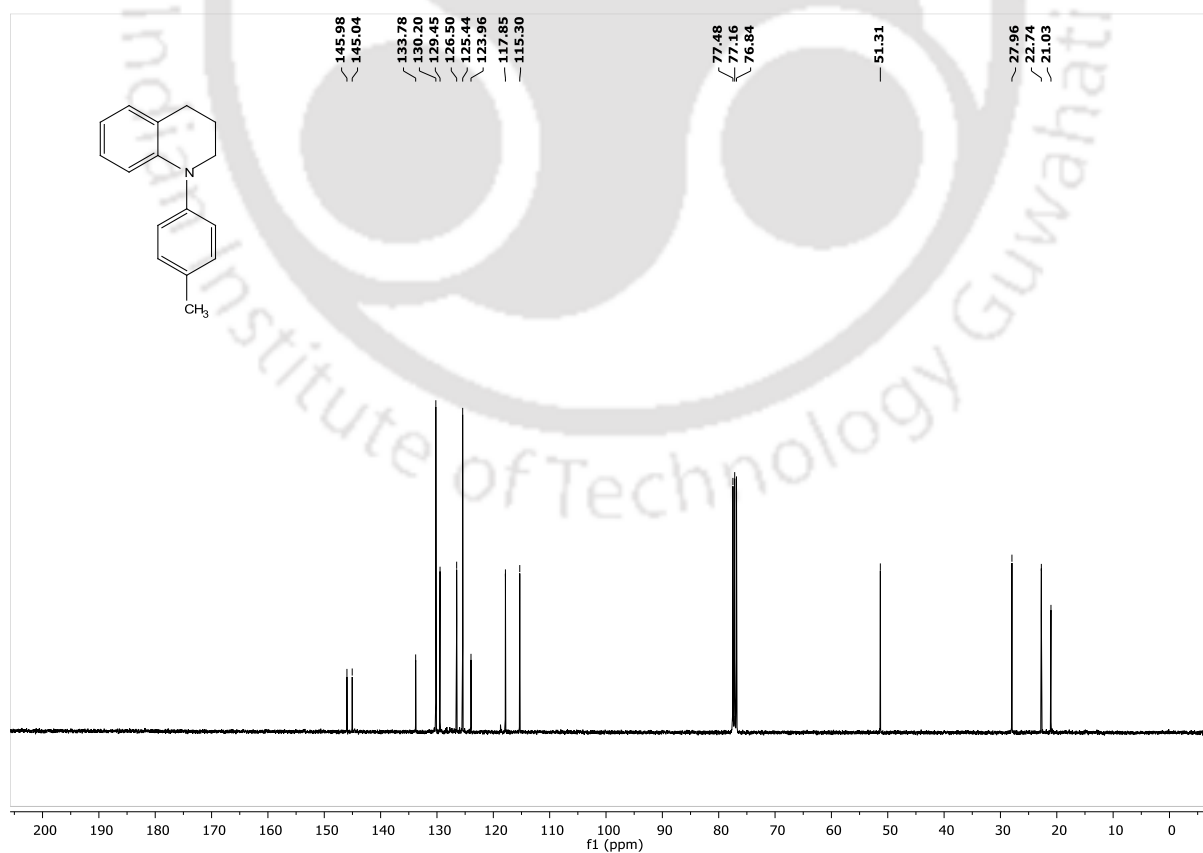
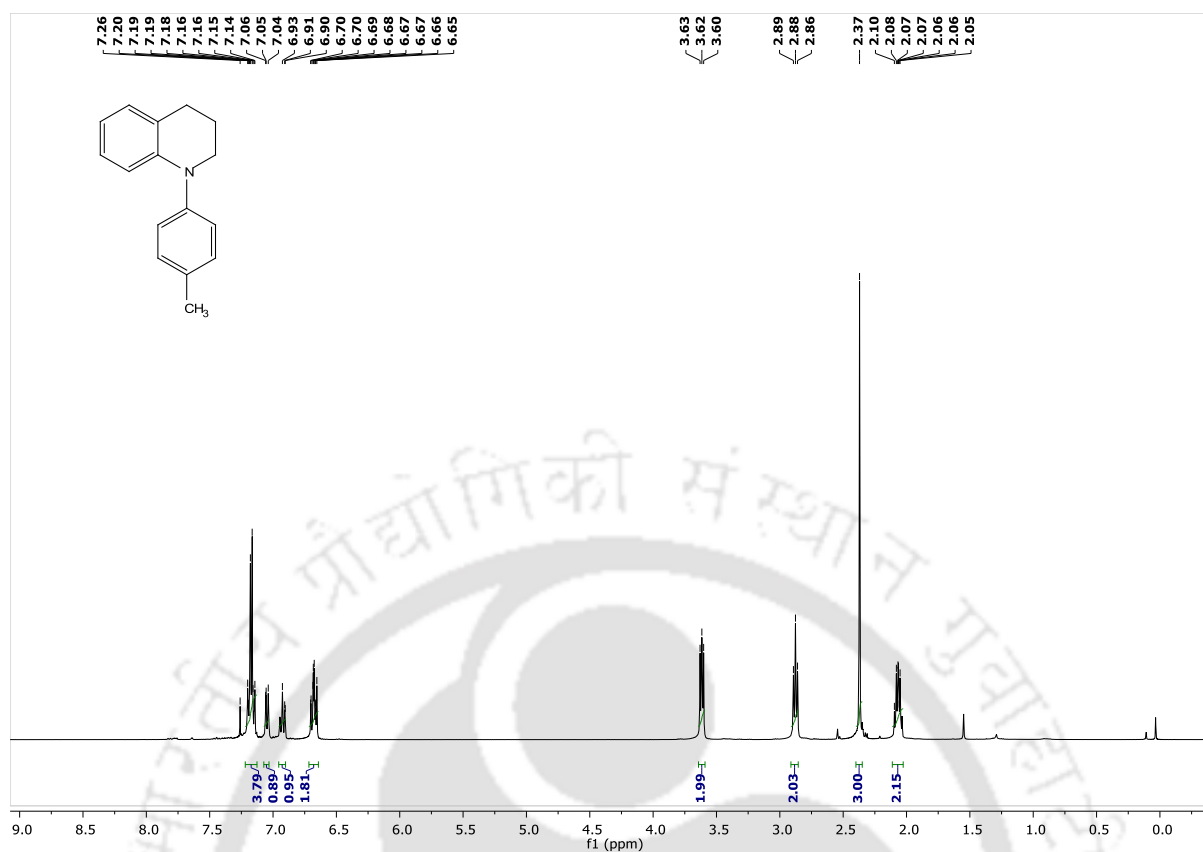
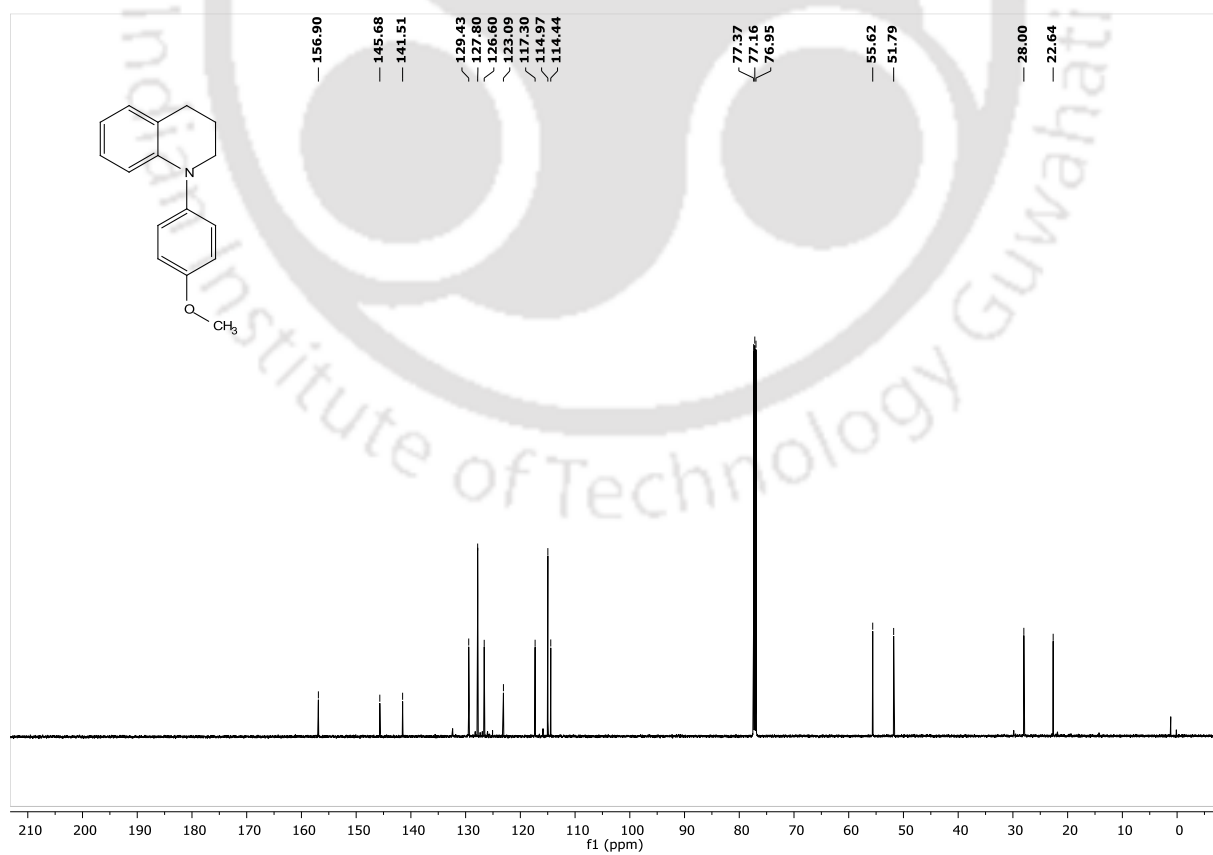
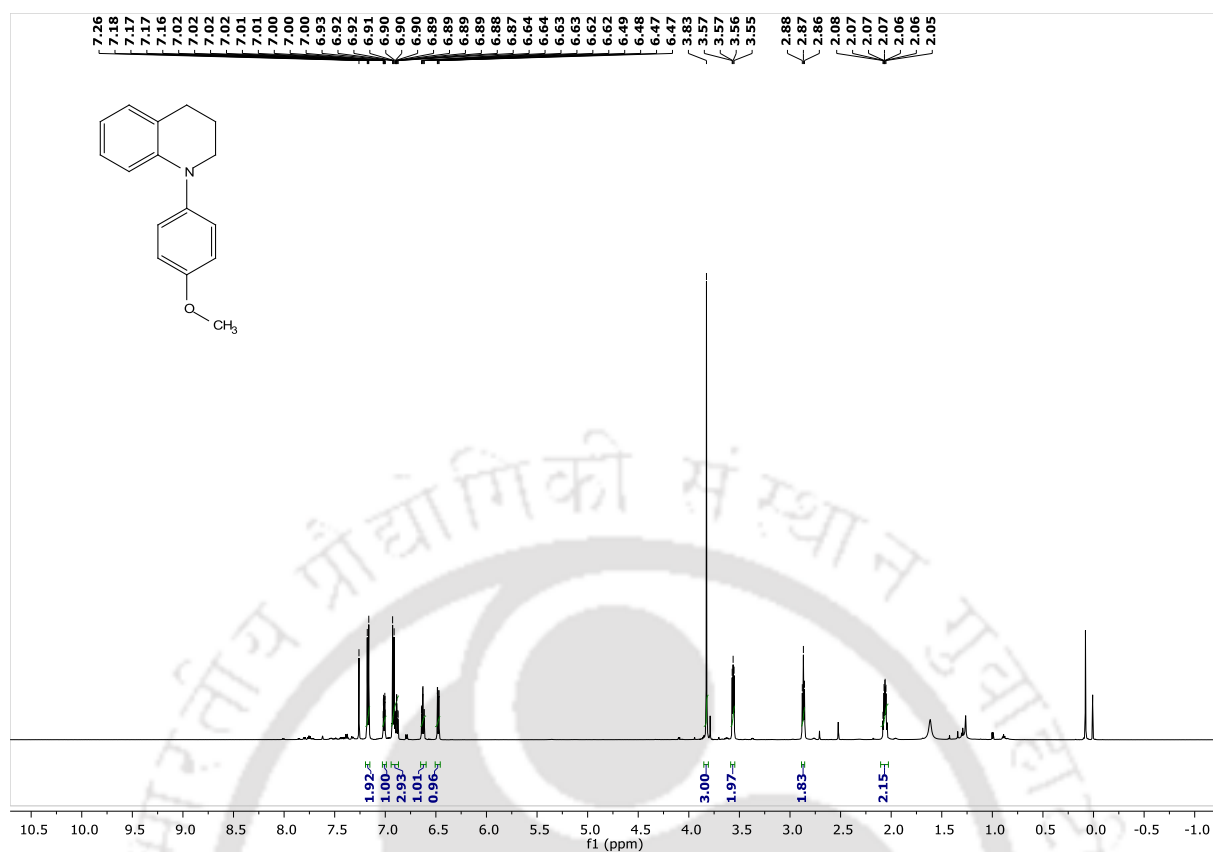


Figure S258: ^{13}C NMR Spectrum of **6.1b (CDCl_3 , 101 MHz, 298 K)**



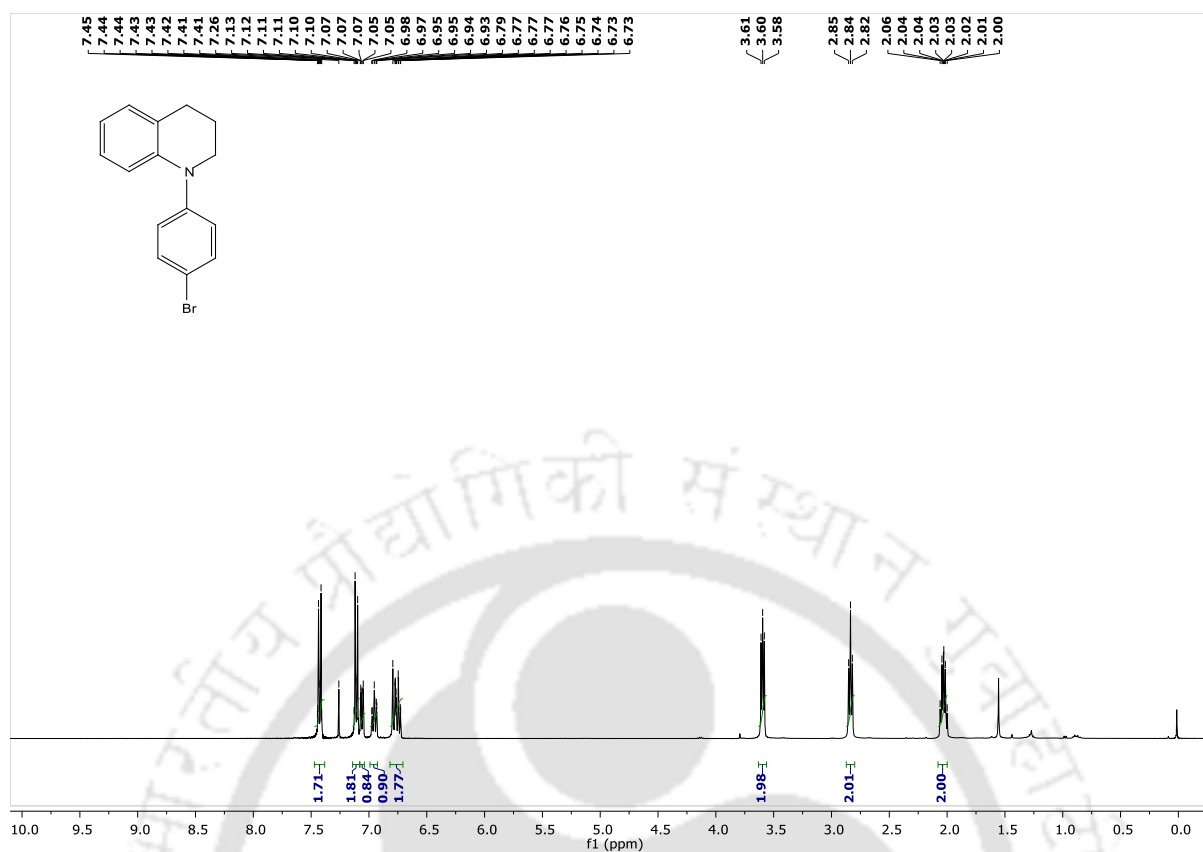


Figure S261: ¹H NMR Spectrum of **6.1d** (CDCl₃, 400 MHz, 298 K)

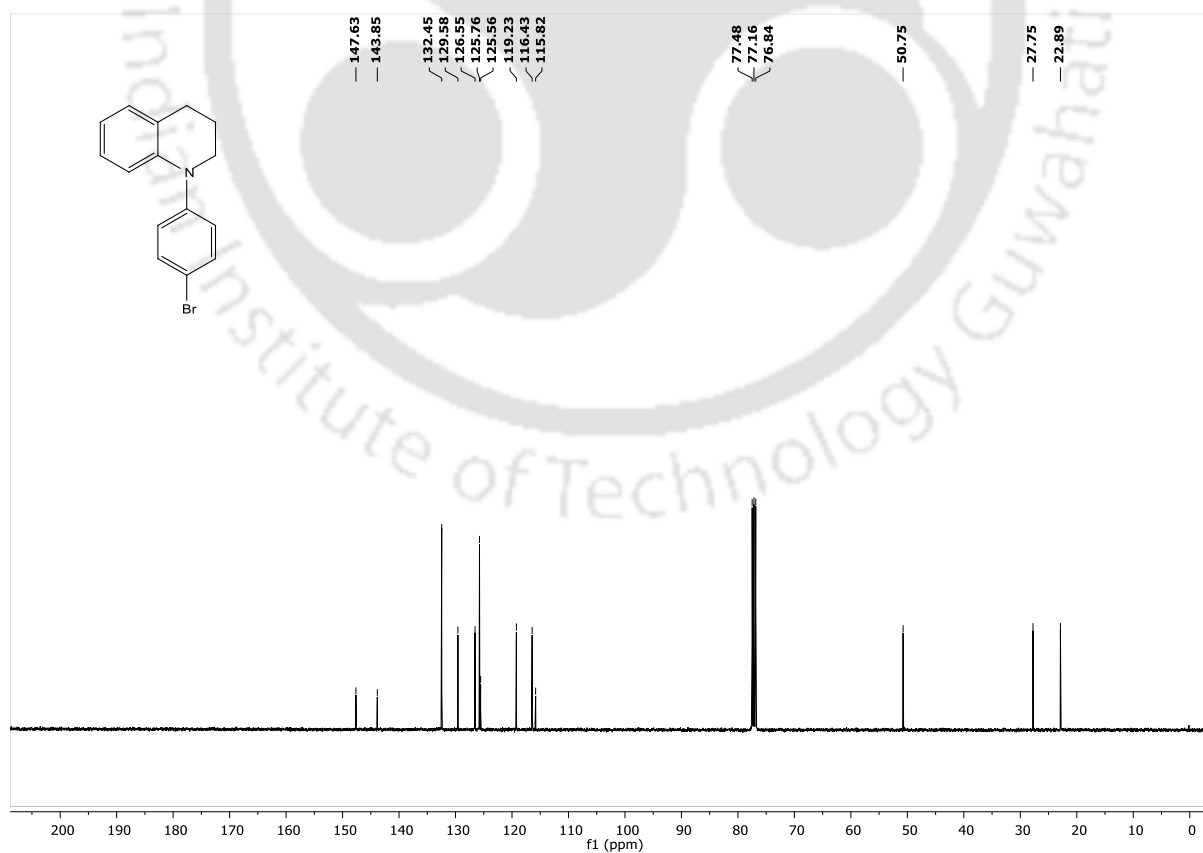


Figure S262: ¹³C NMR Spectrum of **6.1d** (CDCl₃, 101 MHz, 298 K)

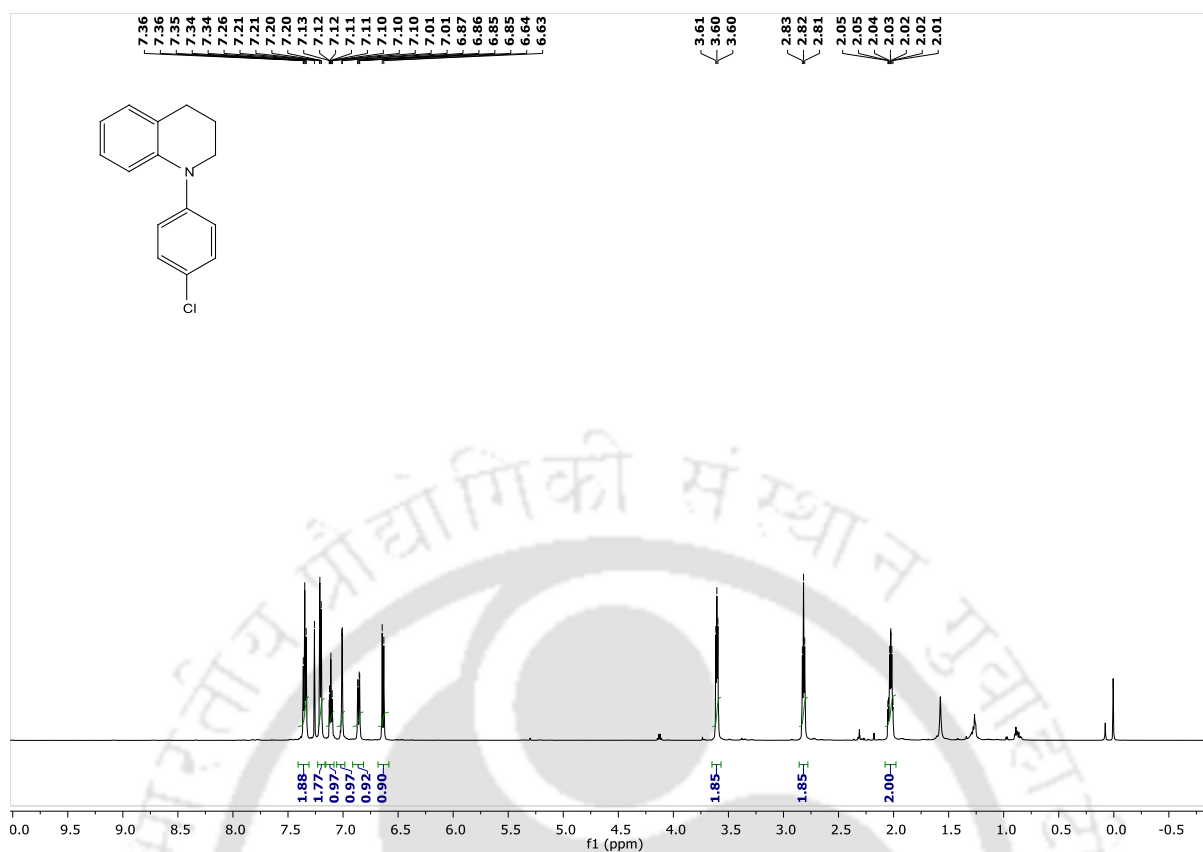


Figure S263: ¹H NMR Spectrum of **6.1e** (CDCl₃, 400 MHz, 298 K)

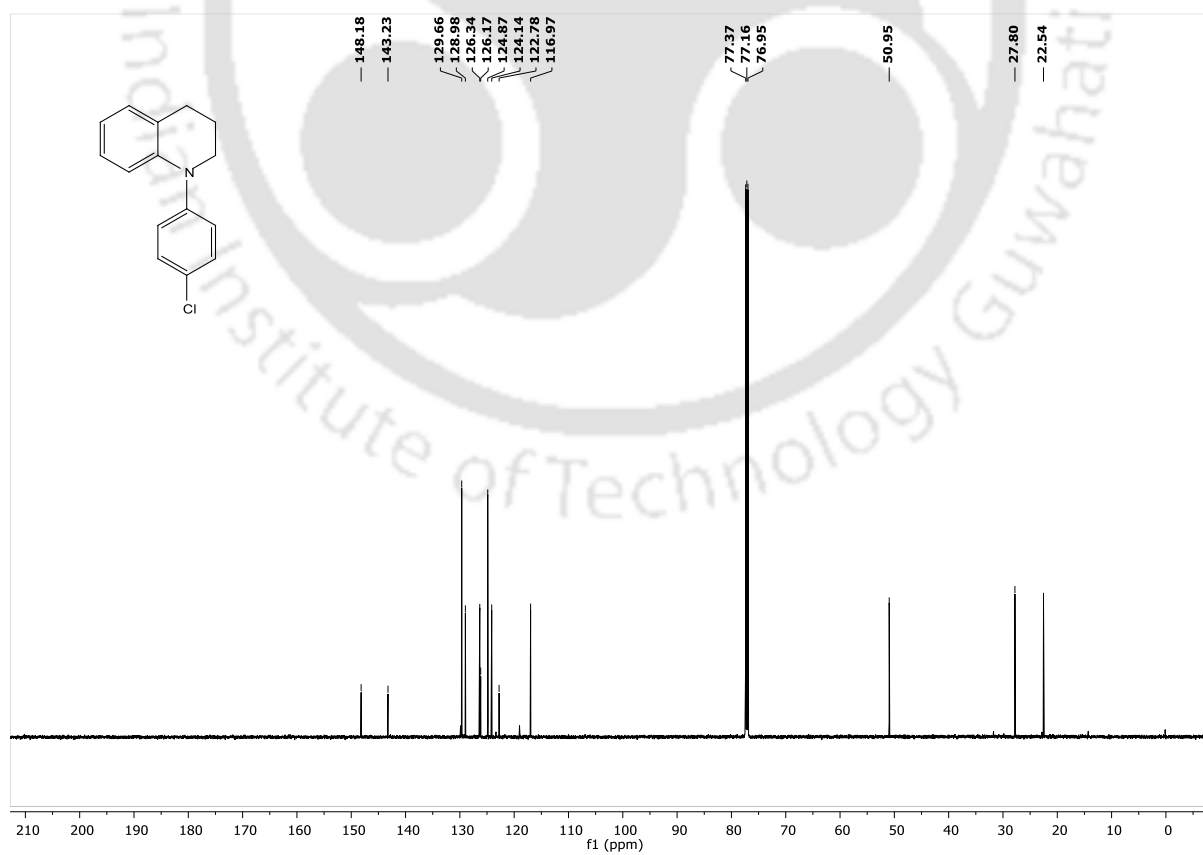


Figure S264: ¹³C NMR Spectrum of **6.1e** (CDCl₃, 101 MHz, 298 K)

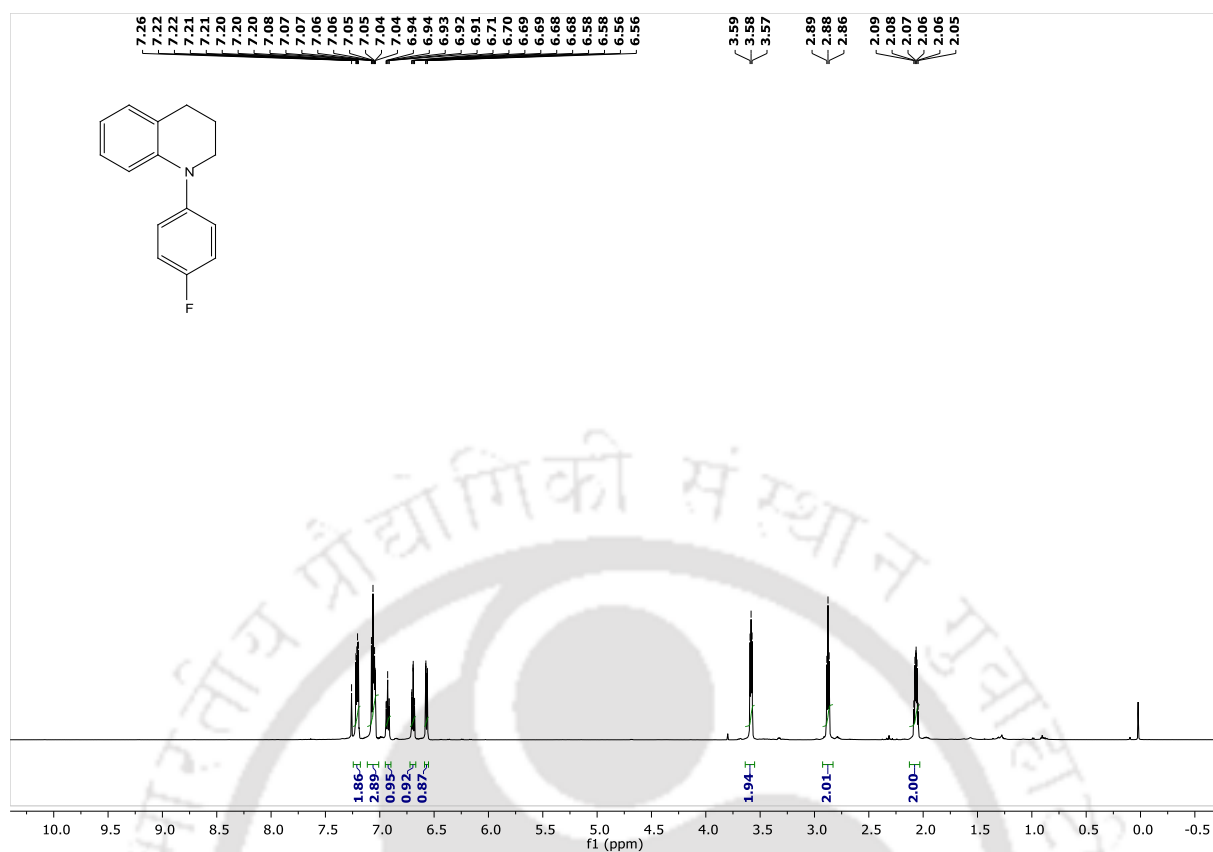


Figure S265: ¹H NMR Spectrum of **6.1f** (CDCl₃, 400 MHz, 298 K)

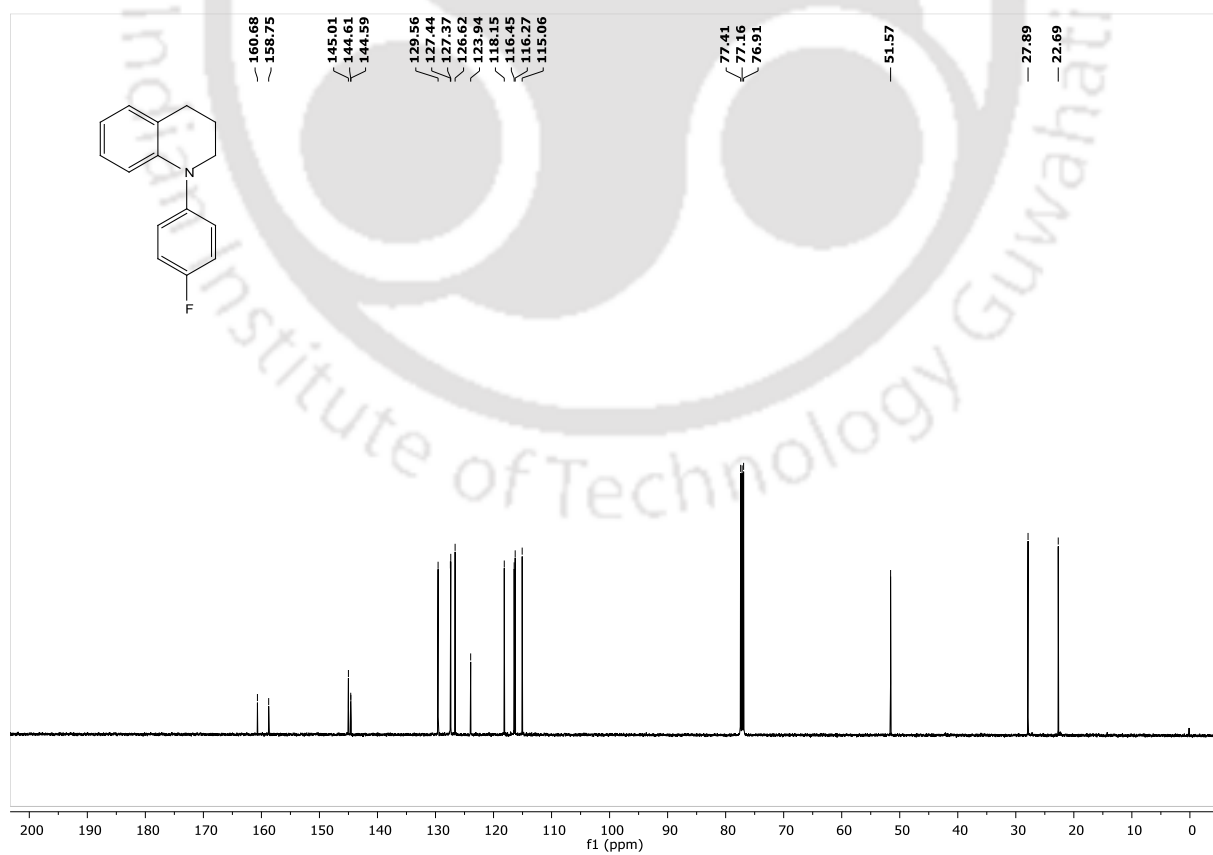


Figure S266: ¹³C NMR Spectrum of **6.1f** (CDCl₃, 101 MHz, 298 K)

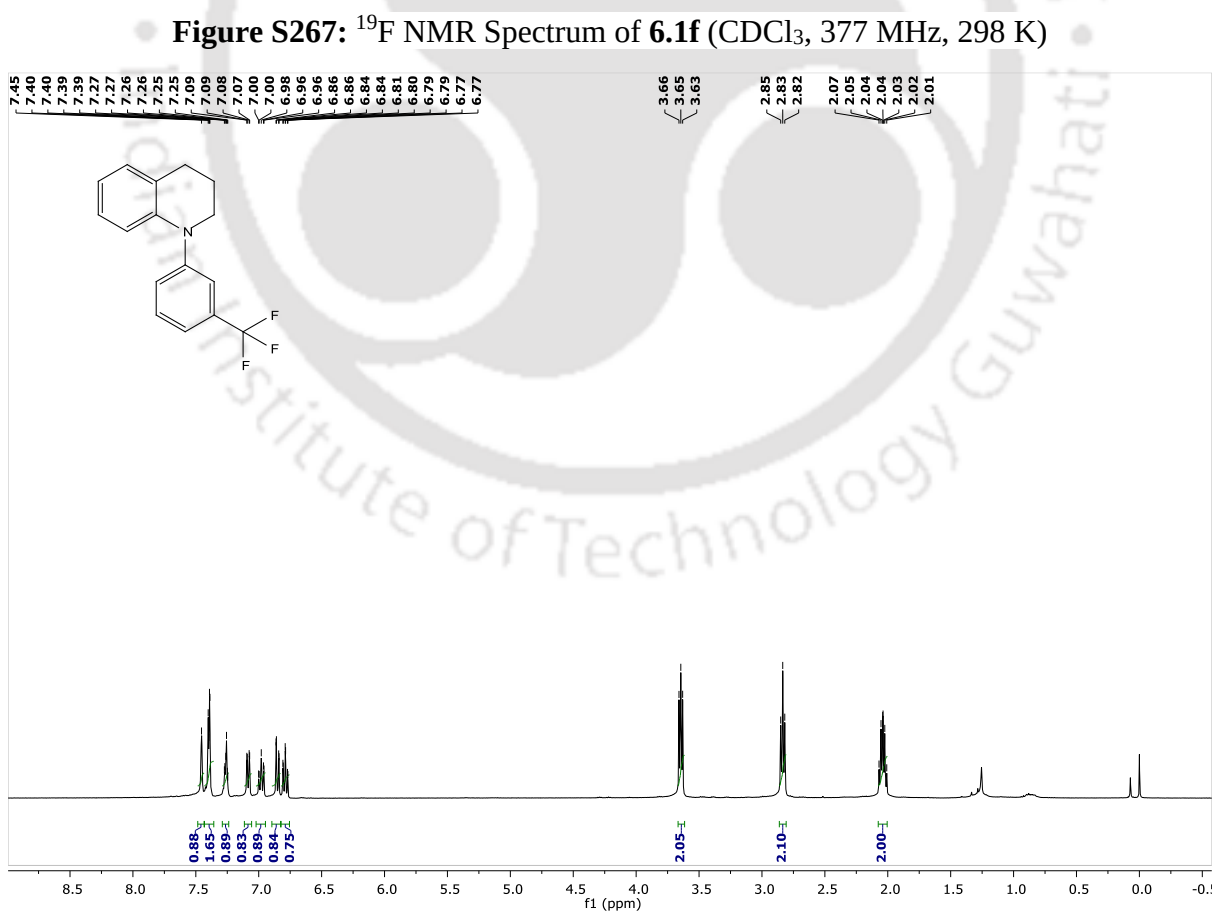
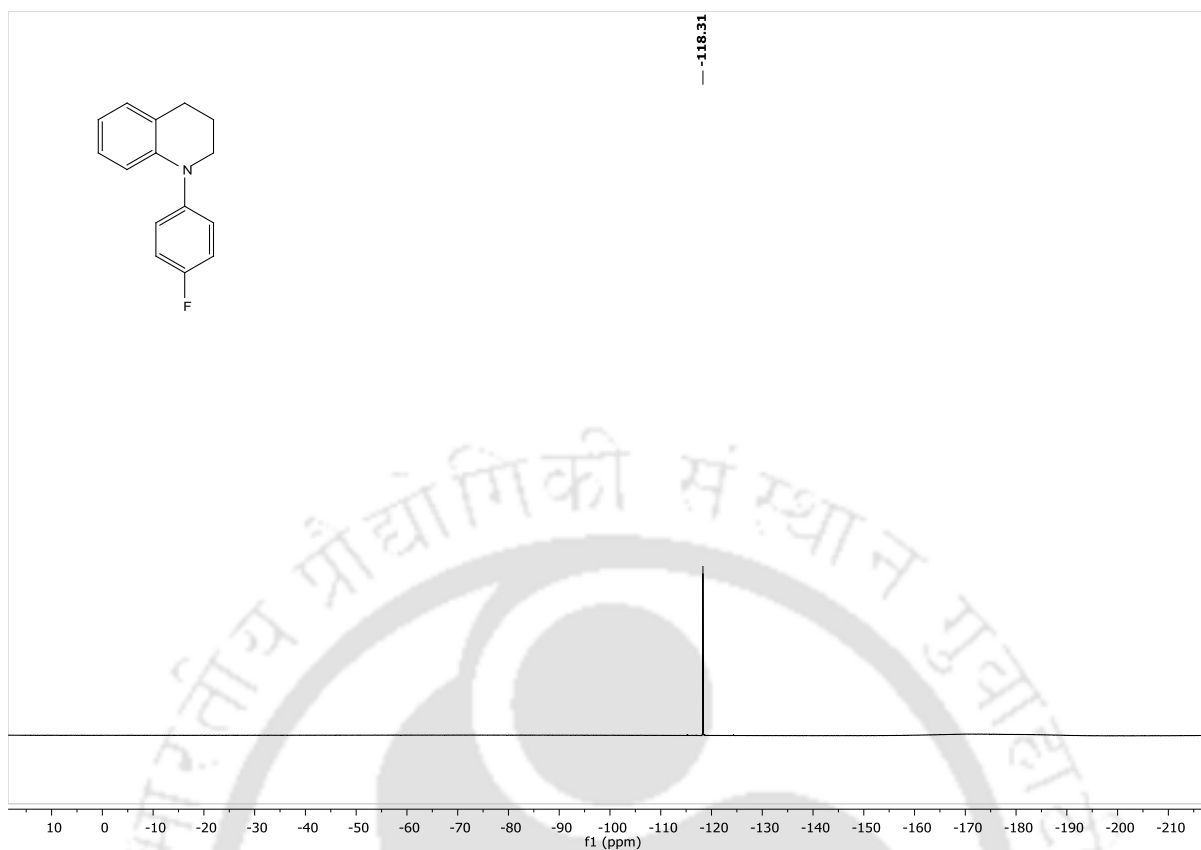


Figure S268: ^1H NMR Spectrum of **6.1g** (CDCl_3 , 400 MHz, 298 K)

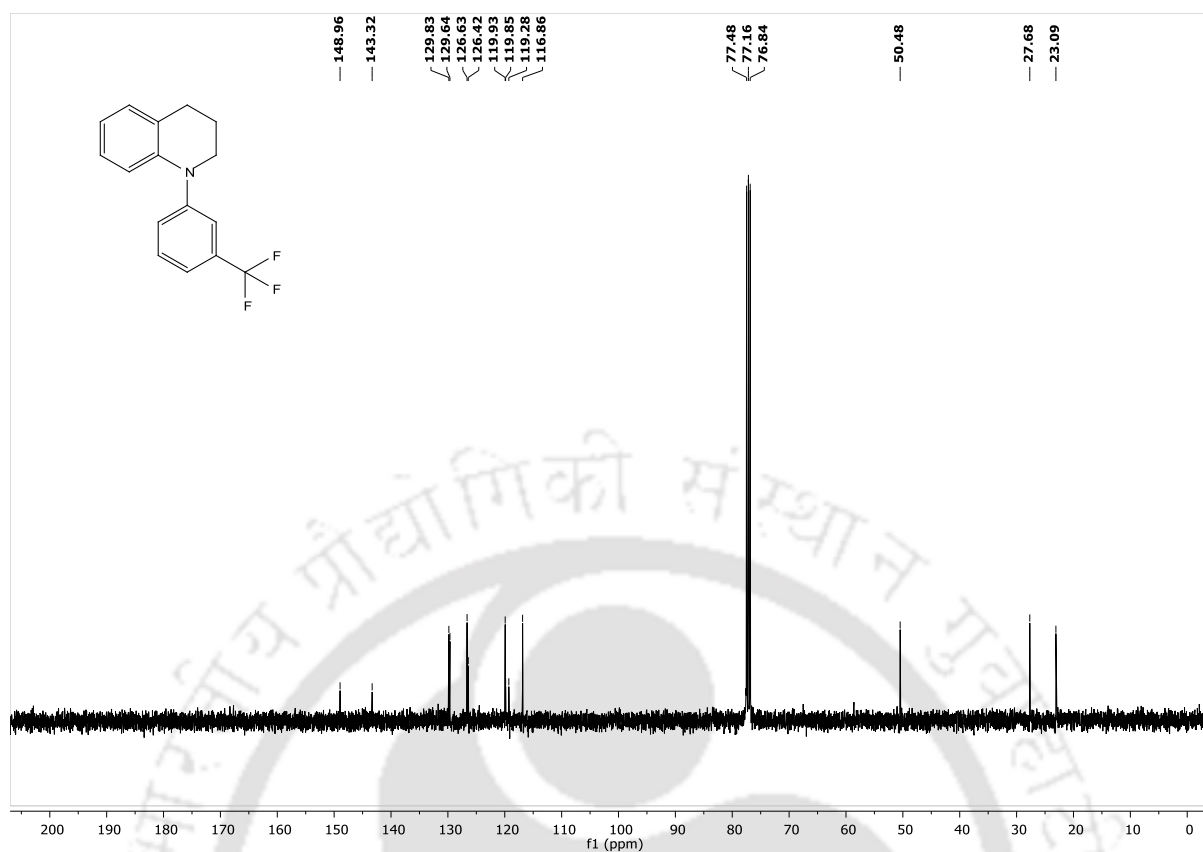


Figure S269: ¹³C NMR Spectrum of **6.1g** (CDCl₃, 101 MHz, 298 K)

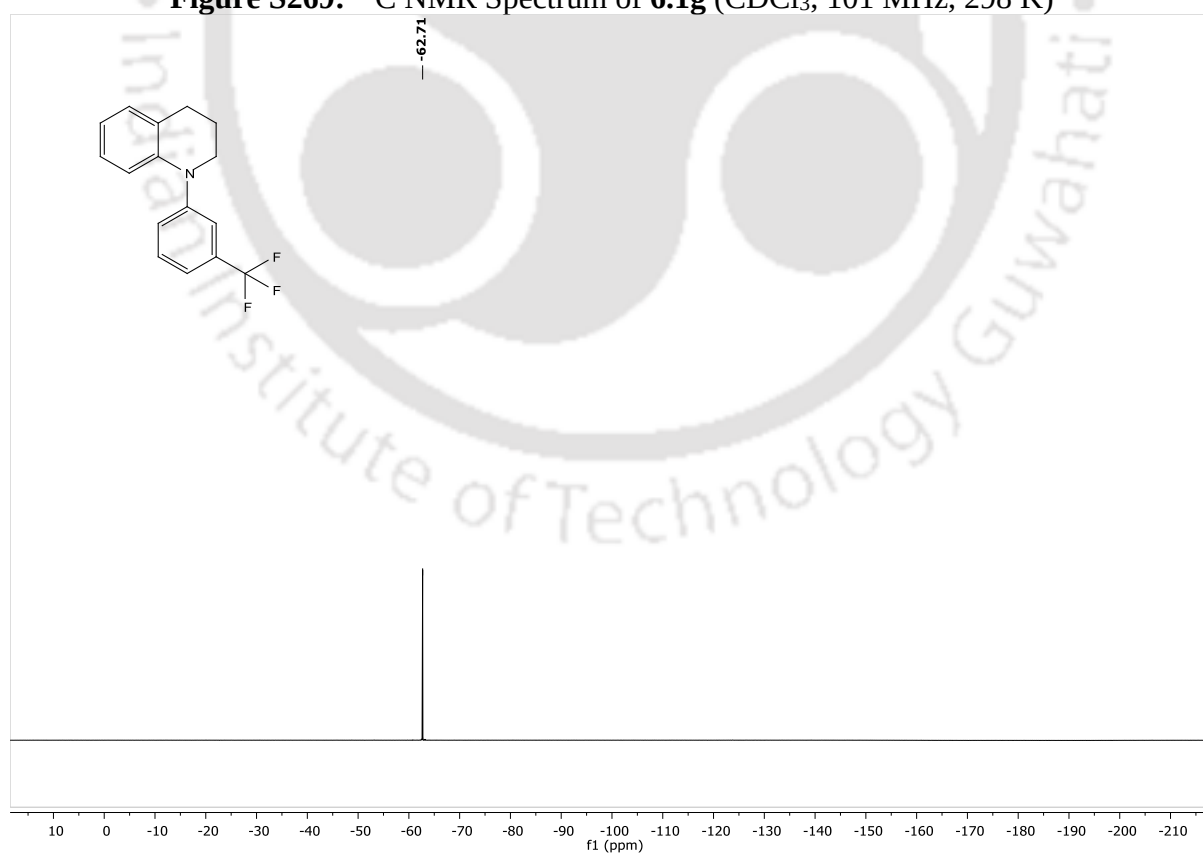


Figure S270: ¹⁹F NMR Spectrum of **6.1g** (CDCl₃, 377 MHz, 298 K)

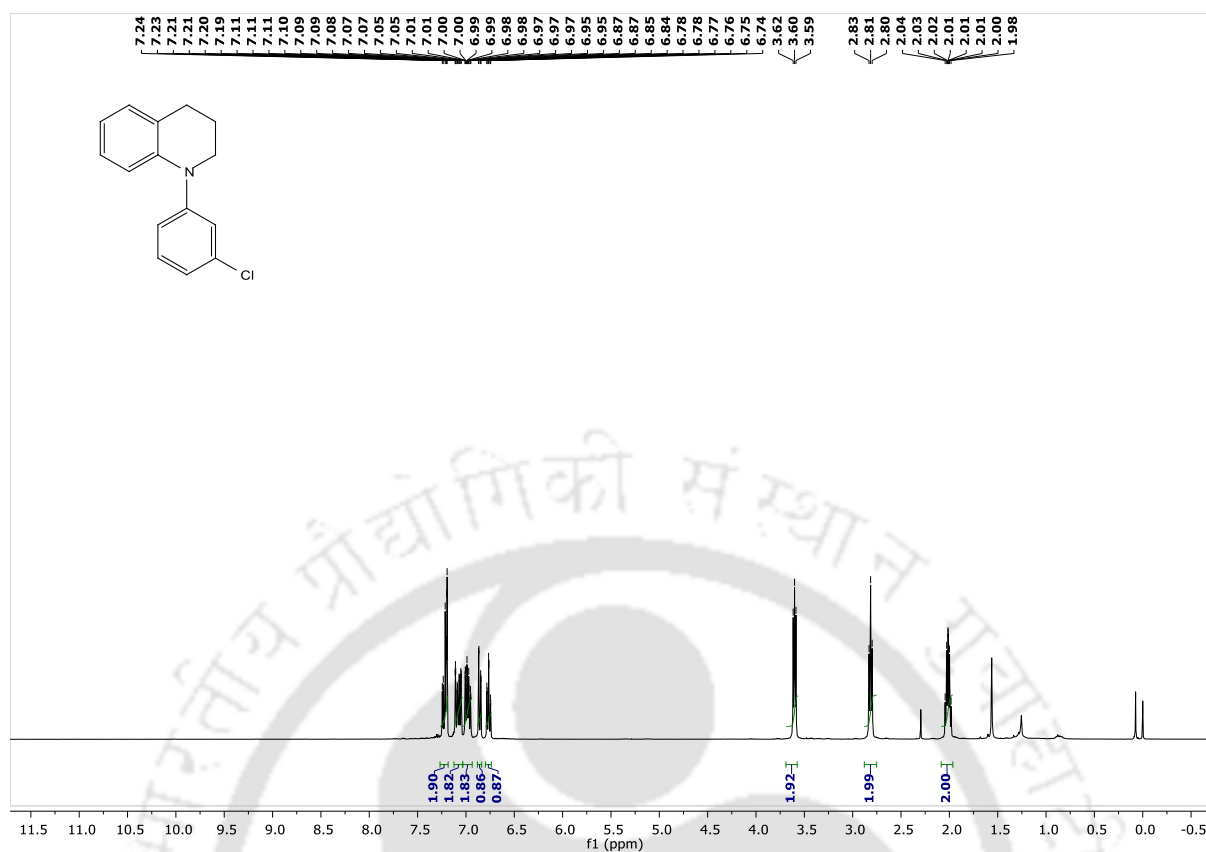


Figure S271: ¹H NMR Spectrum of **6.1h** (CDCl₃, 400 MHz, 298 K)

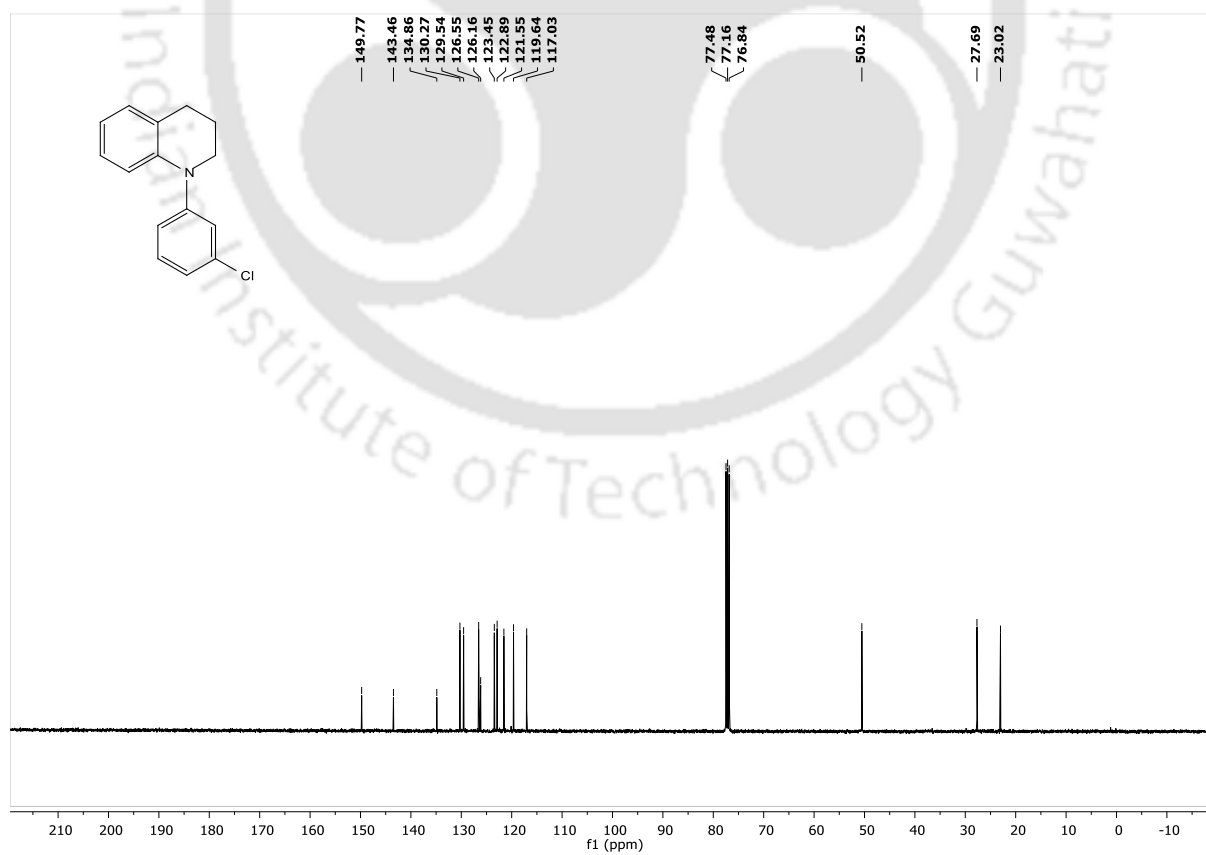


Figure S272: ¹³C NMR Spectrum of **6.1h** (CDCl₃, 101 MHz, 298 K)

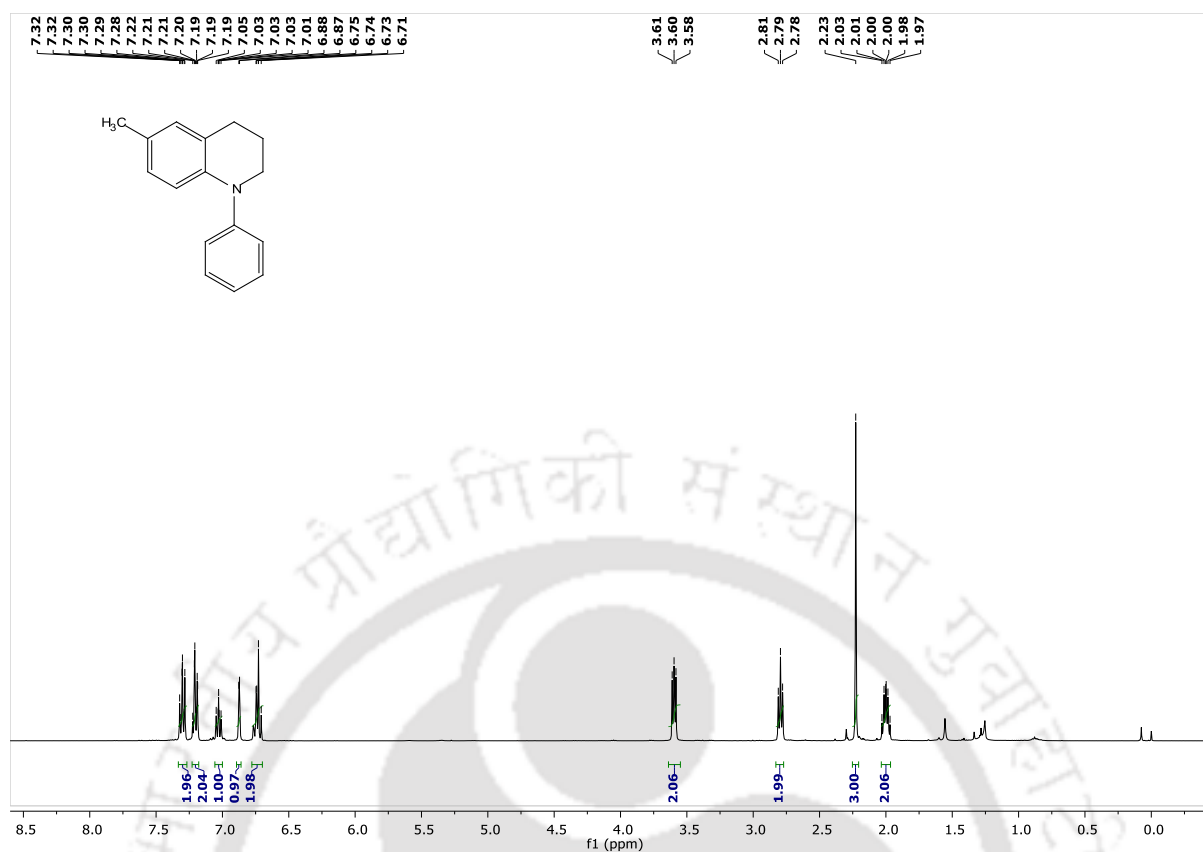


Figure S273: ¹H NMR Spectrum of **6.3a** (CDCl₃, 400 MHz, 298 K)

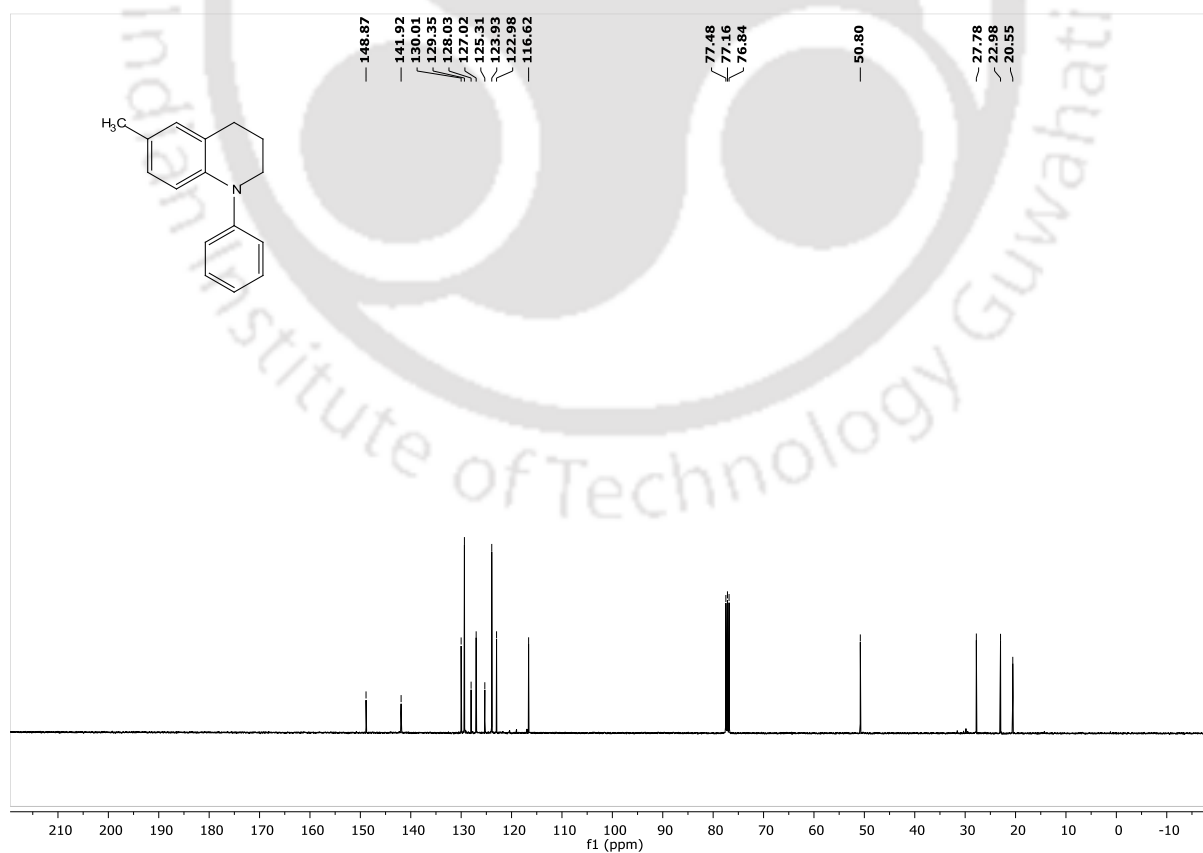
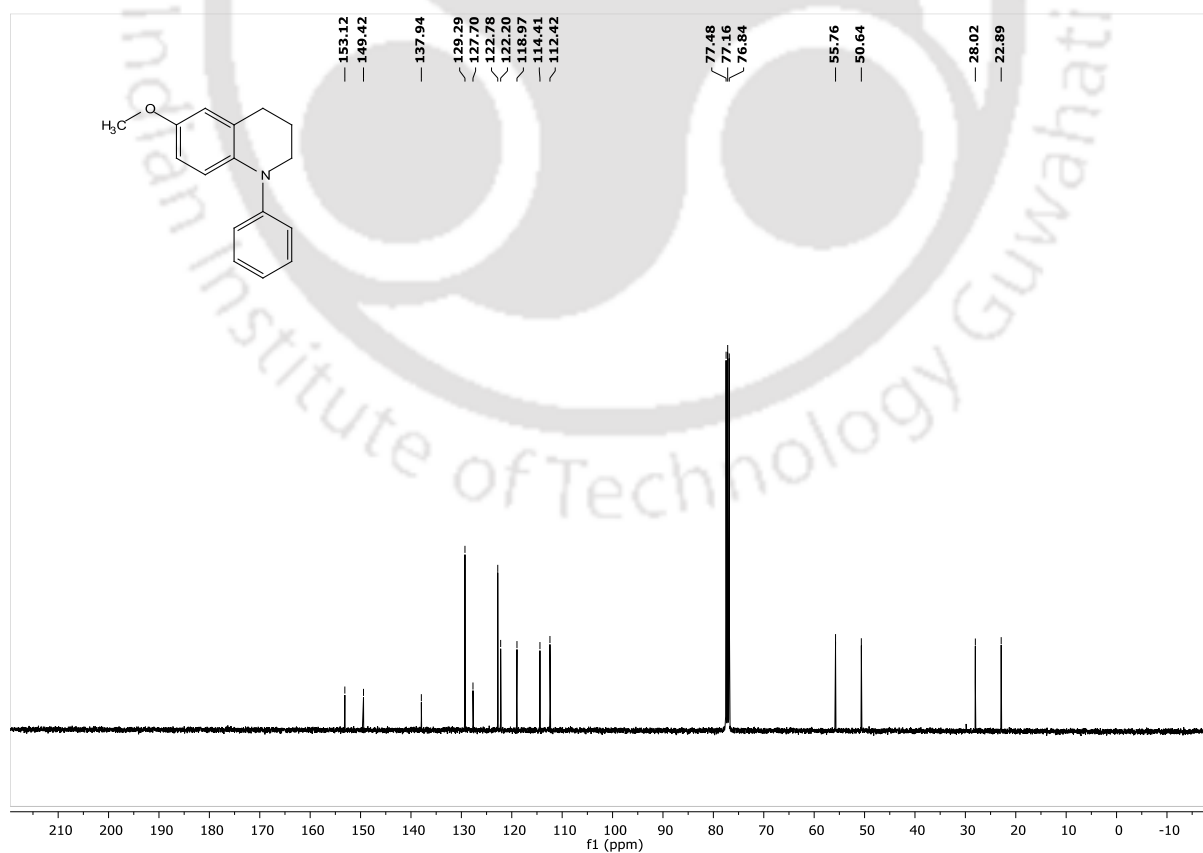
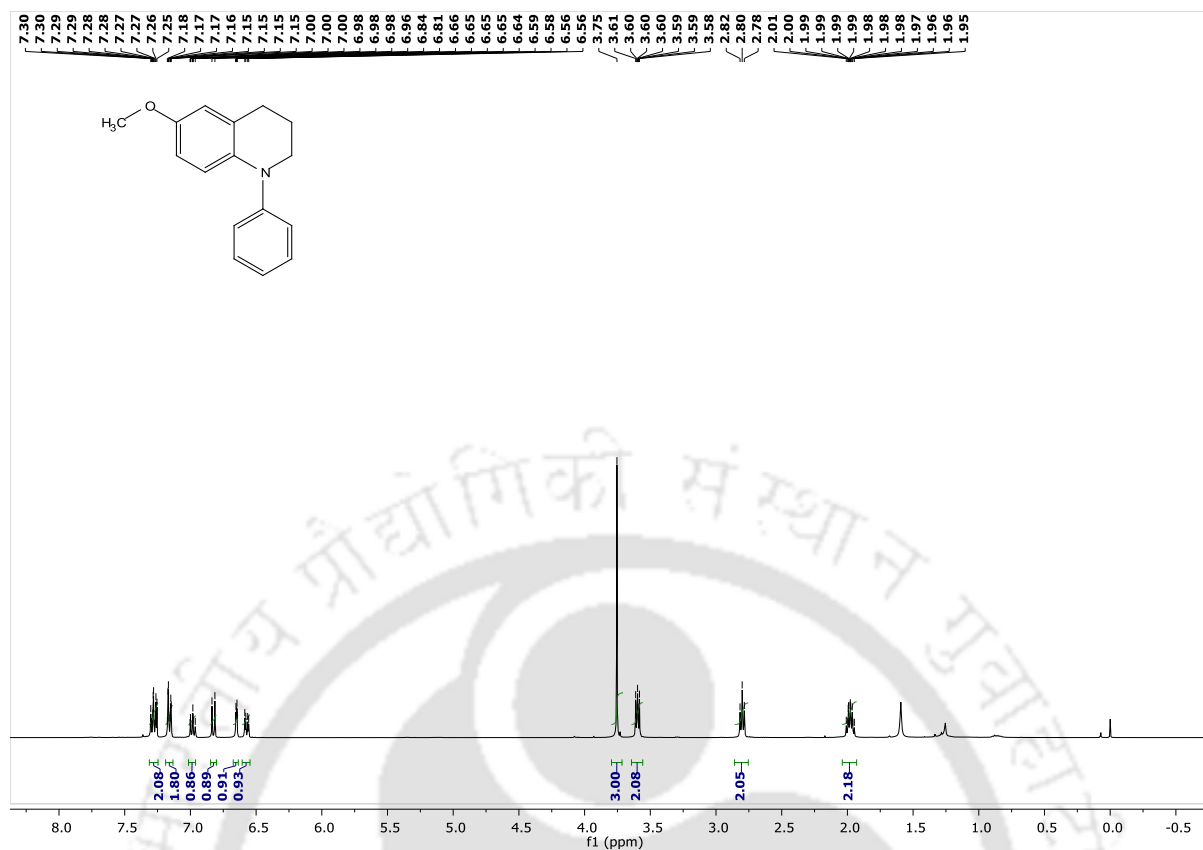
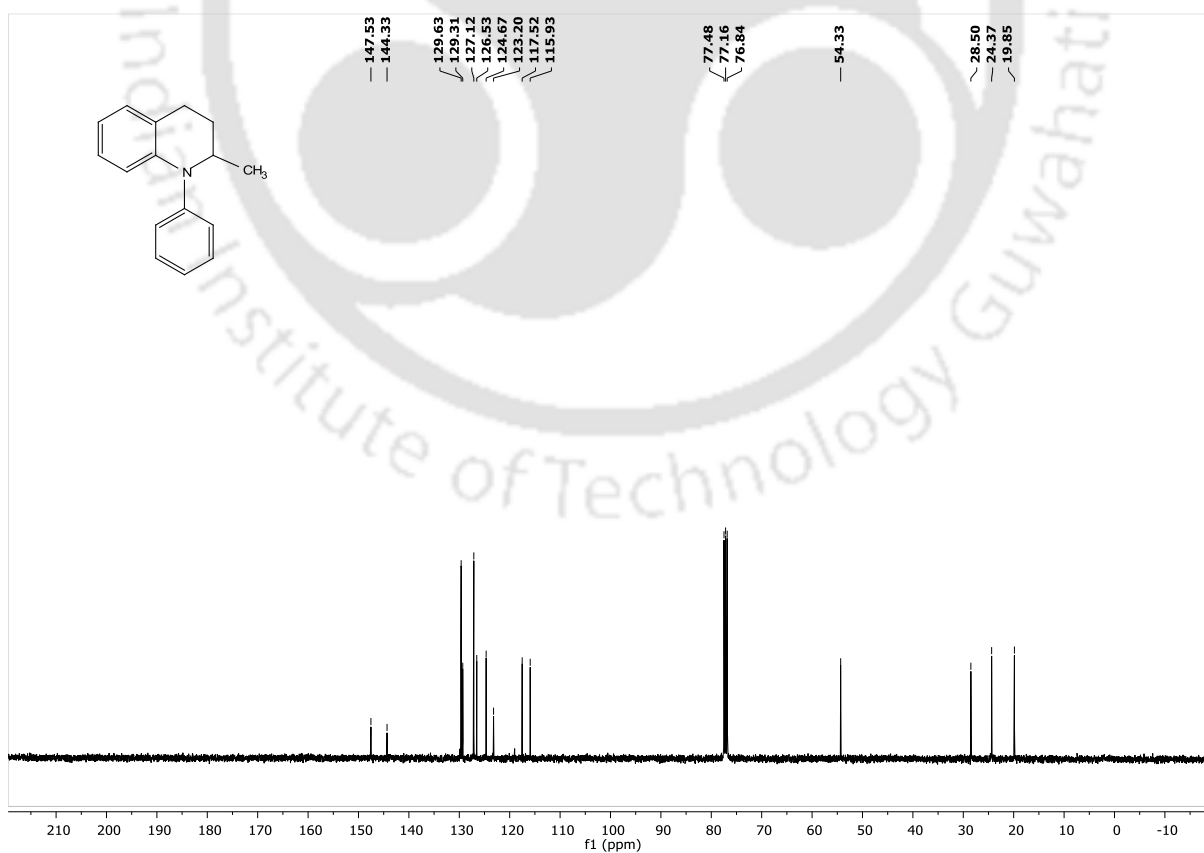
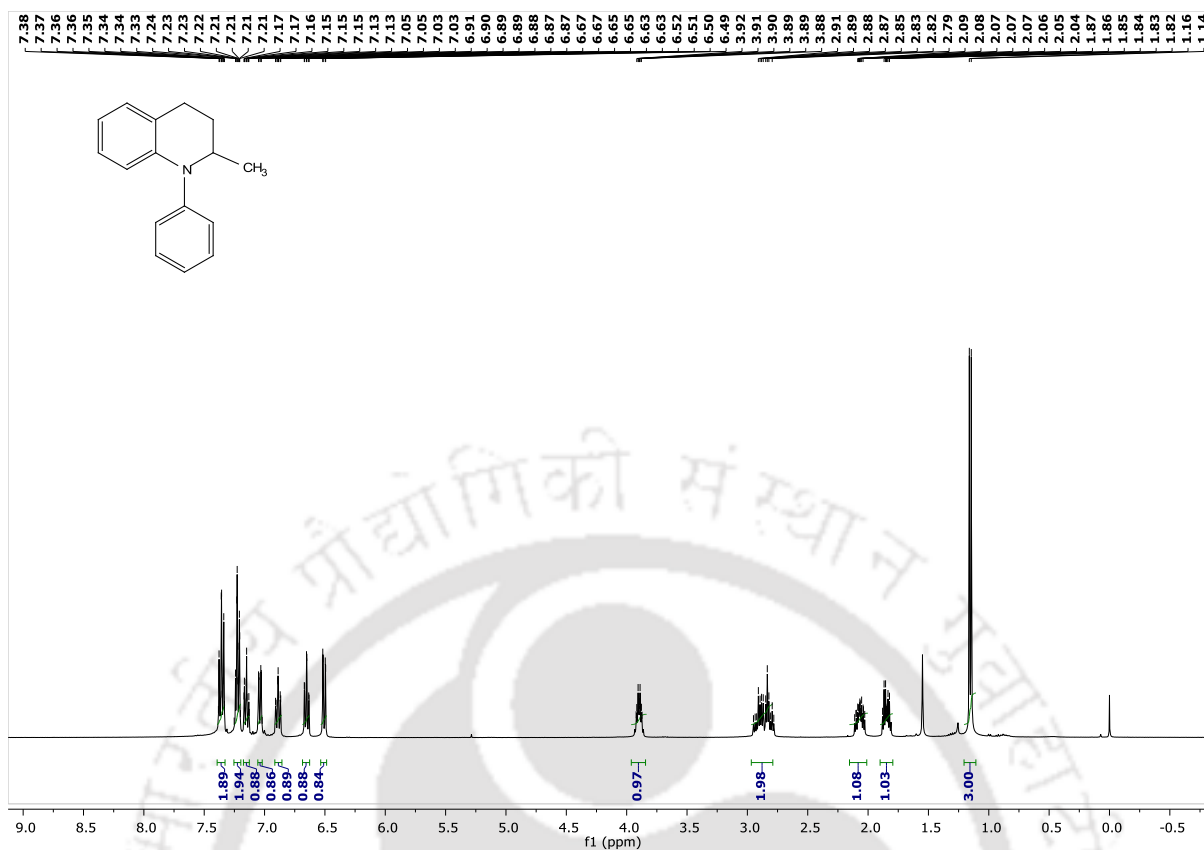


Figure S274: ¹³C NMR Spectrum of **6.3a** (CDCl₃, 101 MHz, 298 K)





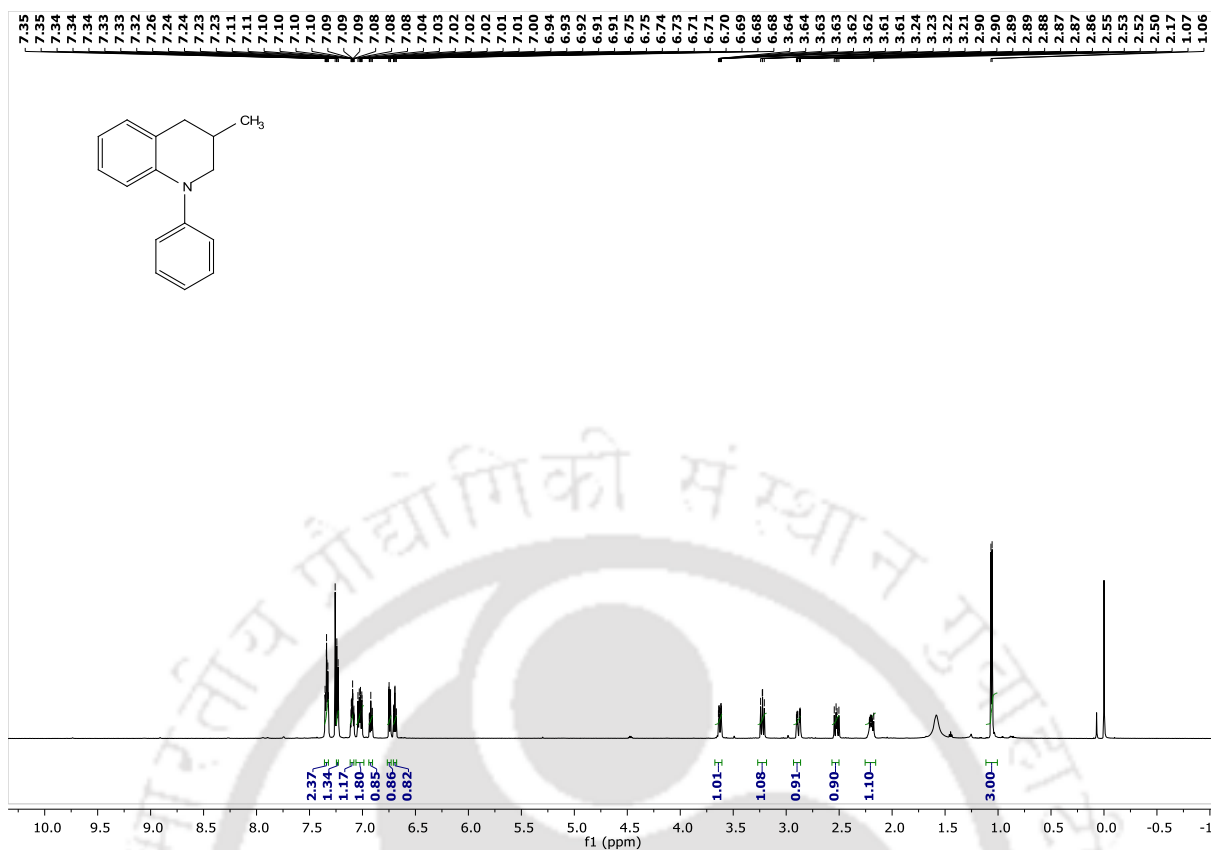


Figure S279: ¹H NMR Spectrum of **6.3d** (CDCl₃, 400 MHz, 298 K)

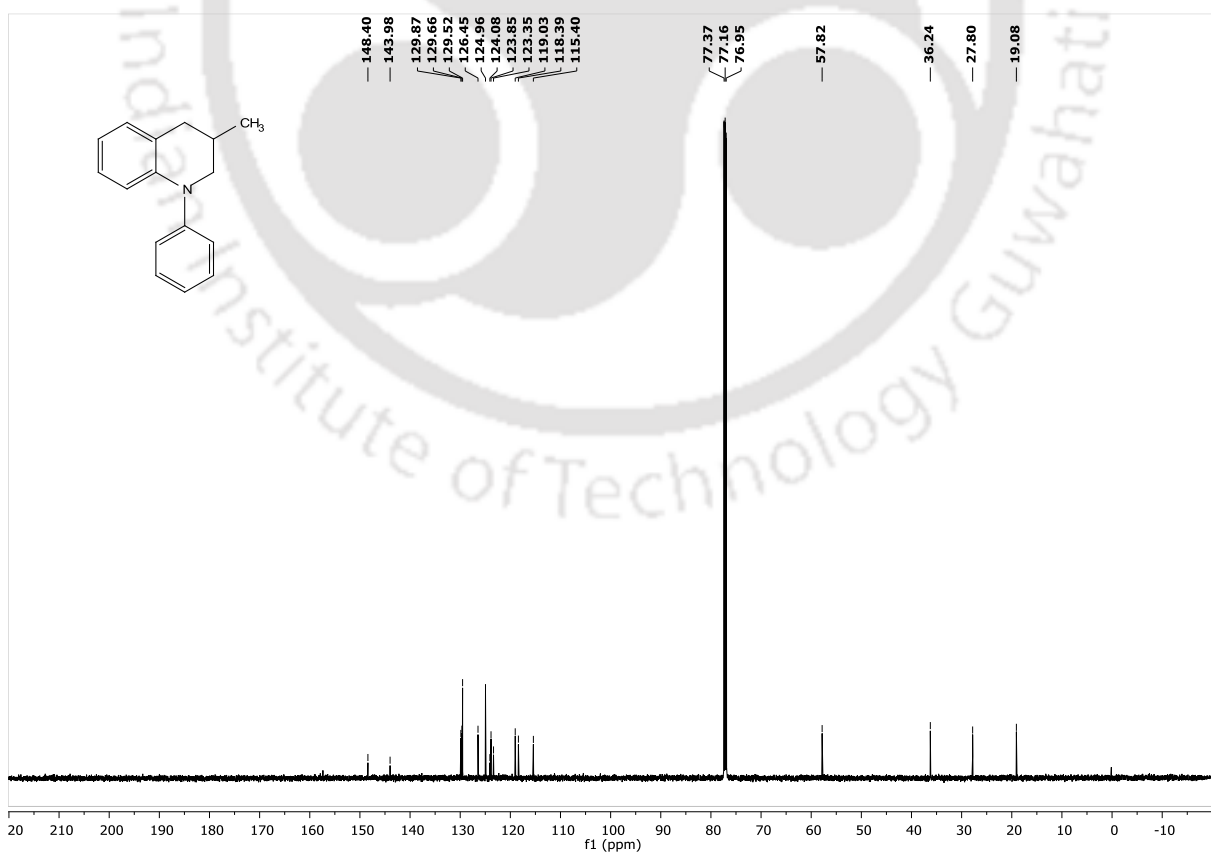


Figure S280: ¹³C NMR Spectrum of **6.3d** (CDCl₃, 101 MHz, 298 K)

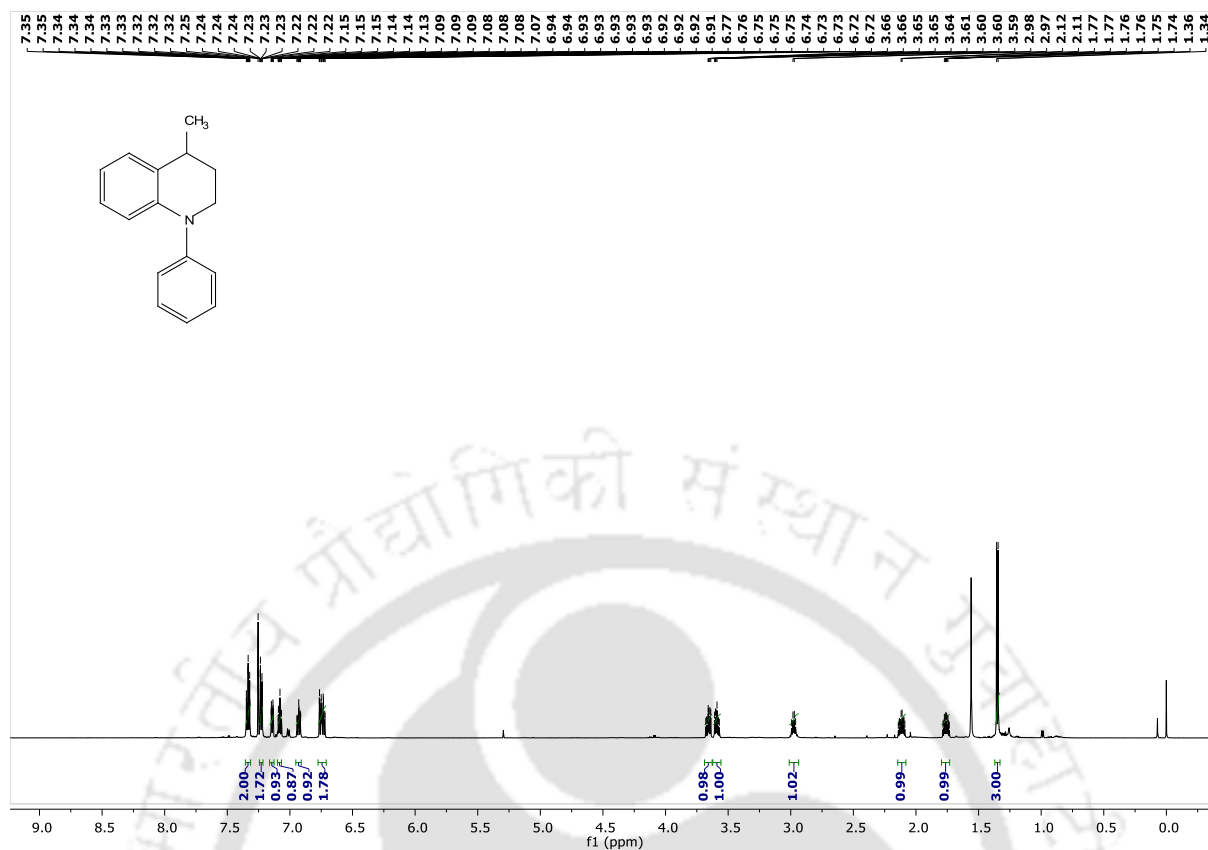


Figure S281: ¹H NMR Spectrum of **6.3e** (CDCl₃, 400 MHz, 298 K)

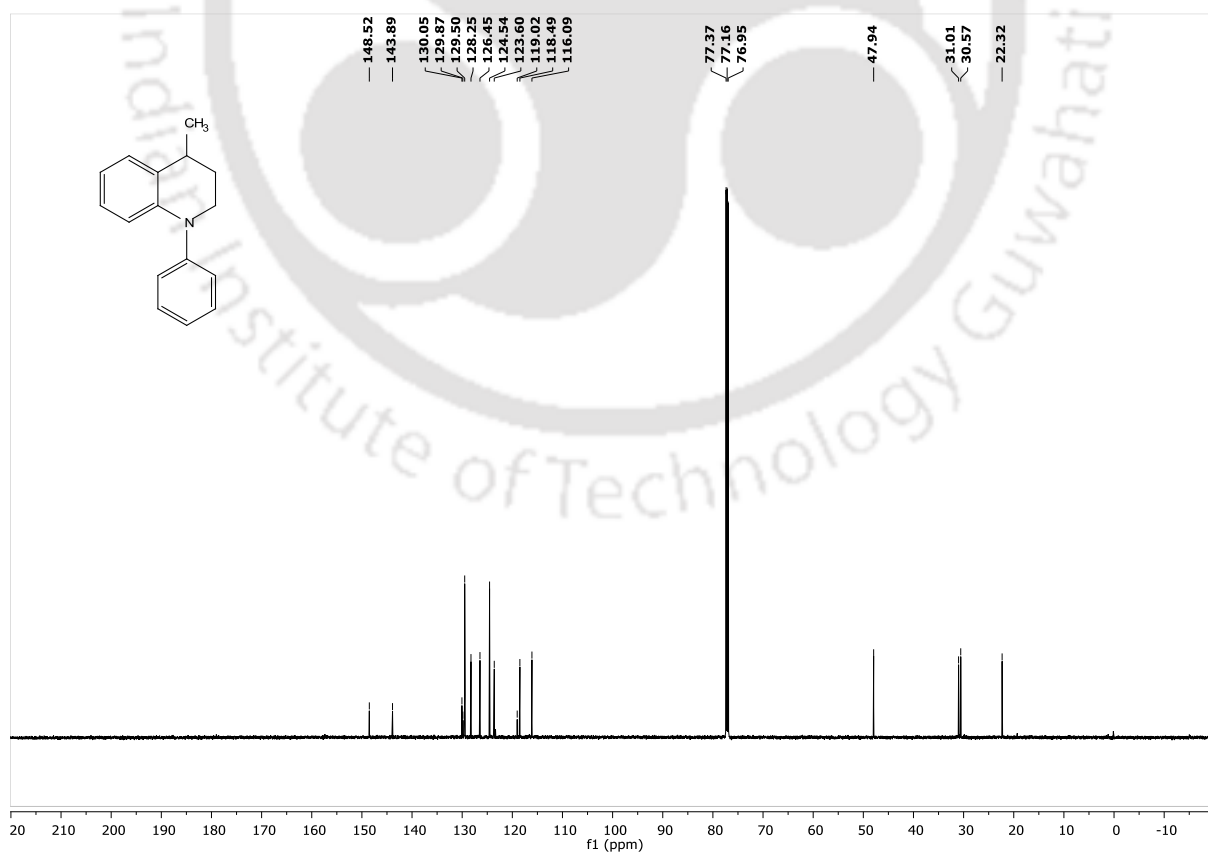


Figure S282: ¹³C NMR Spectrum of **6.3e** (CDCl₃, 101 MHz, 298 K)

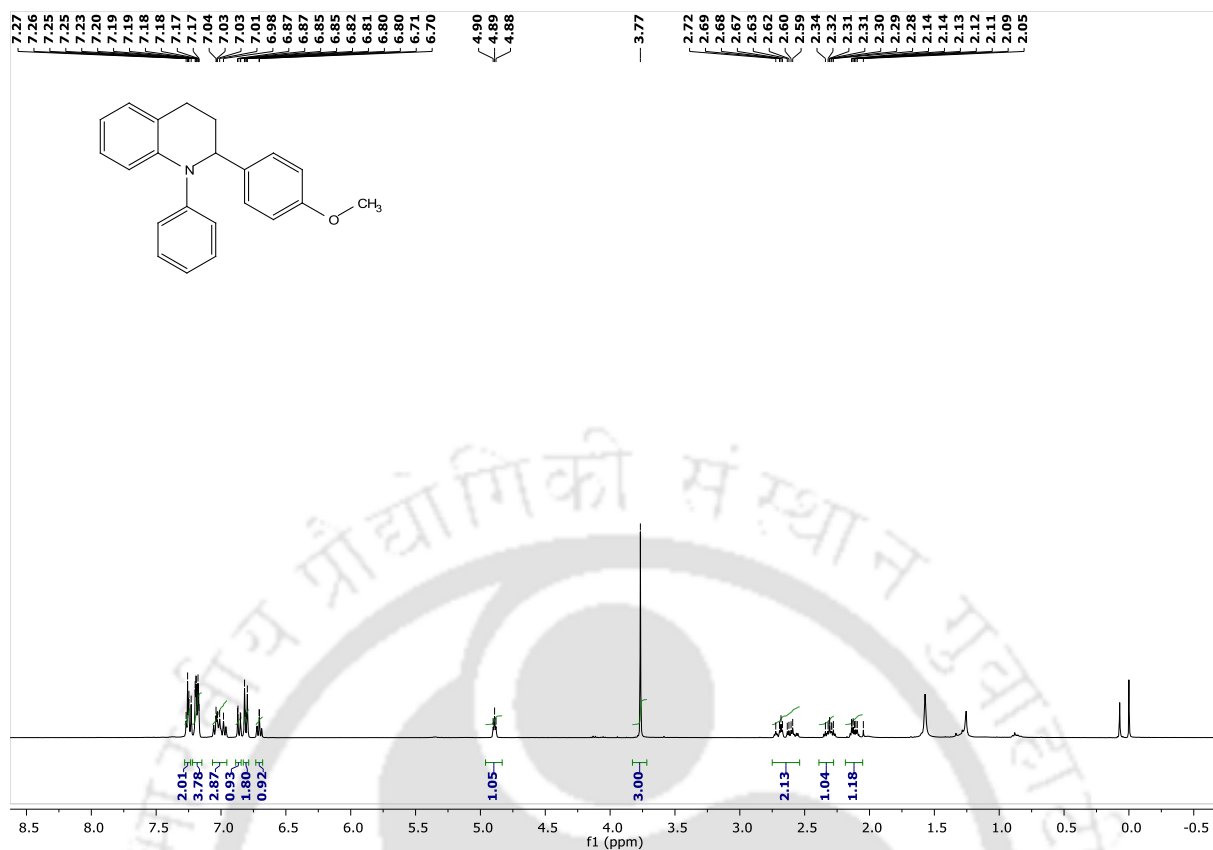


Figure S283: ¹H NMR Spectrum of **6.3f** (CDCl₃, 400 MHz, 298 K)

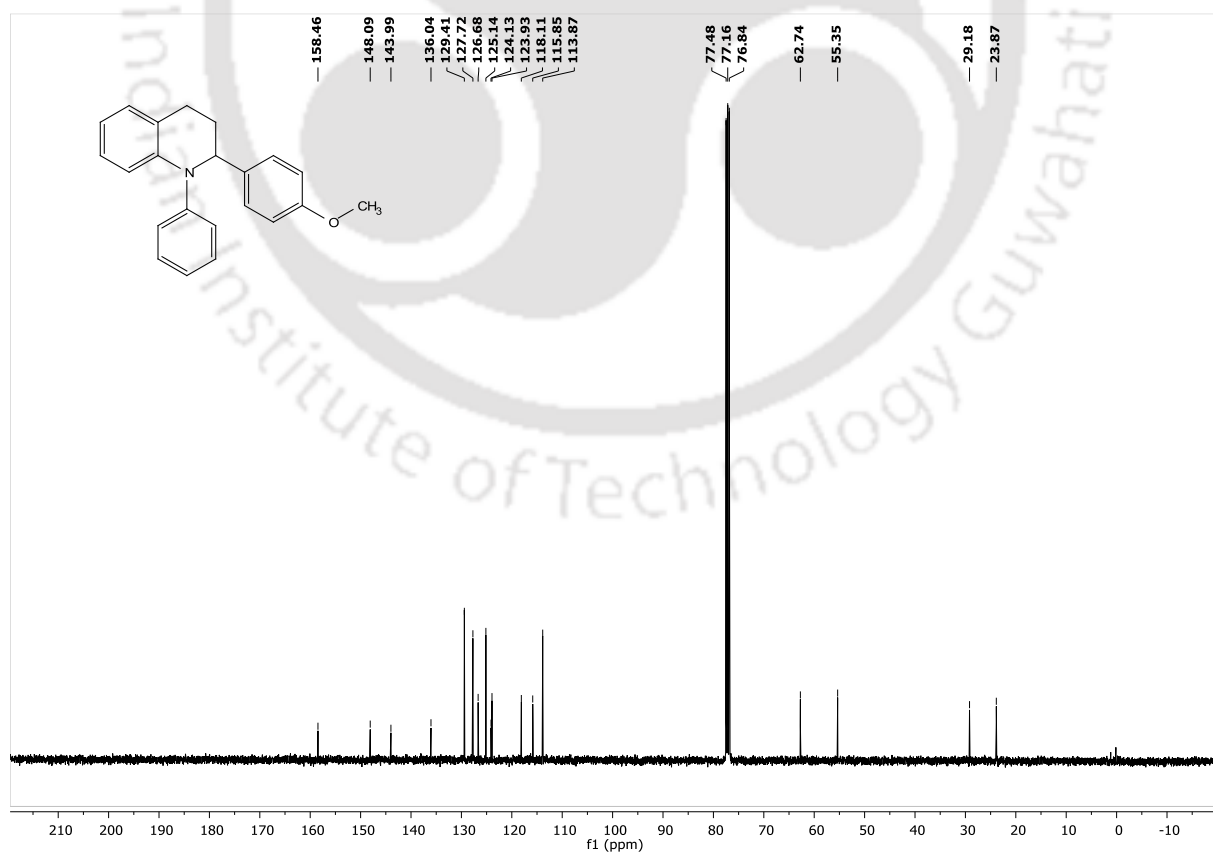


Figure S284: ¹³C NMR Spectrum of **6.3f** (CDCl₃, 101 MHz, 298 K)

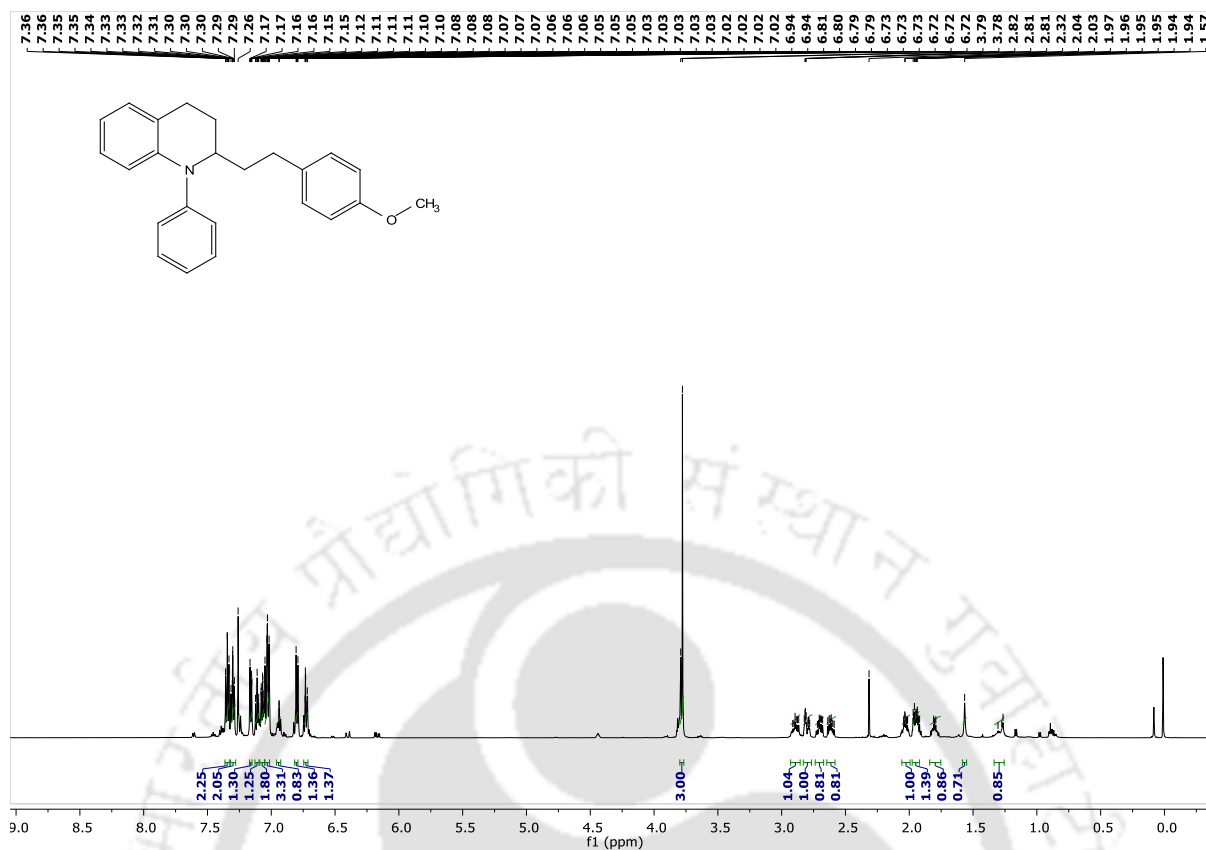


Figure S285: ^1H NMR Spectrum of 6.3g (CDCl_3 , 400 MHz, 298 K)

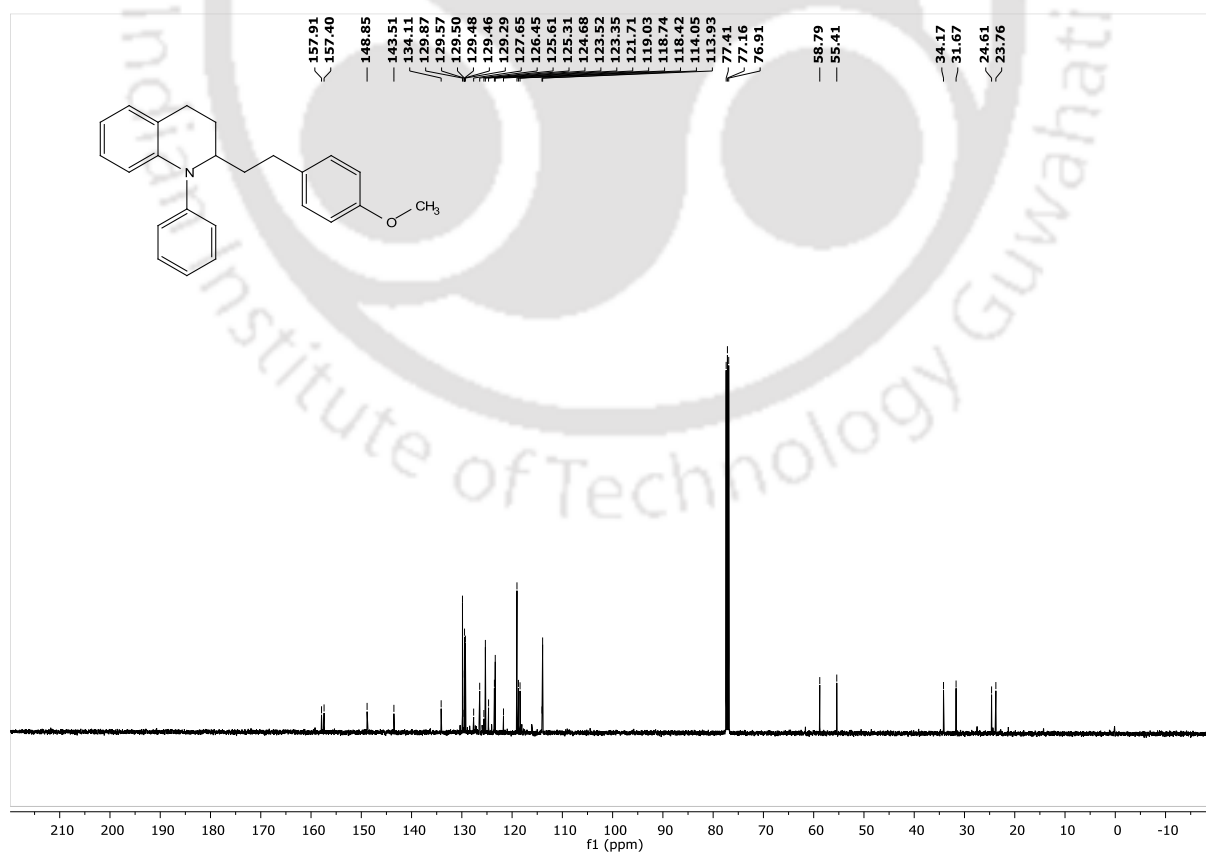


Figure S286: ^{13}C NMR Spectrum of 6.3g (CDCl_3 , 101 MHz, 298 K)

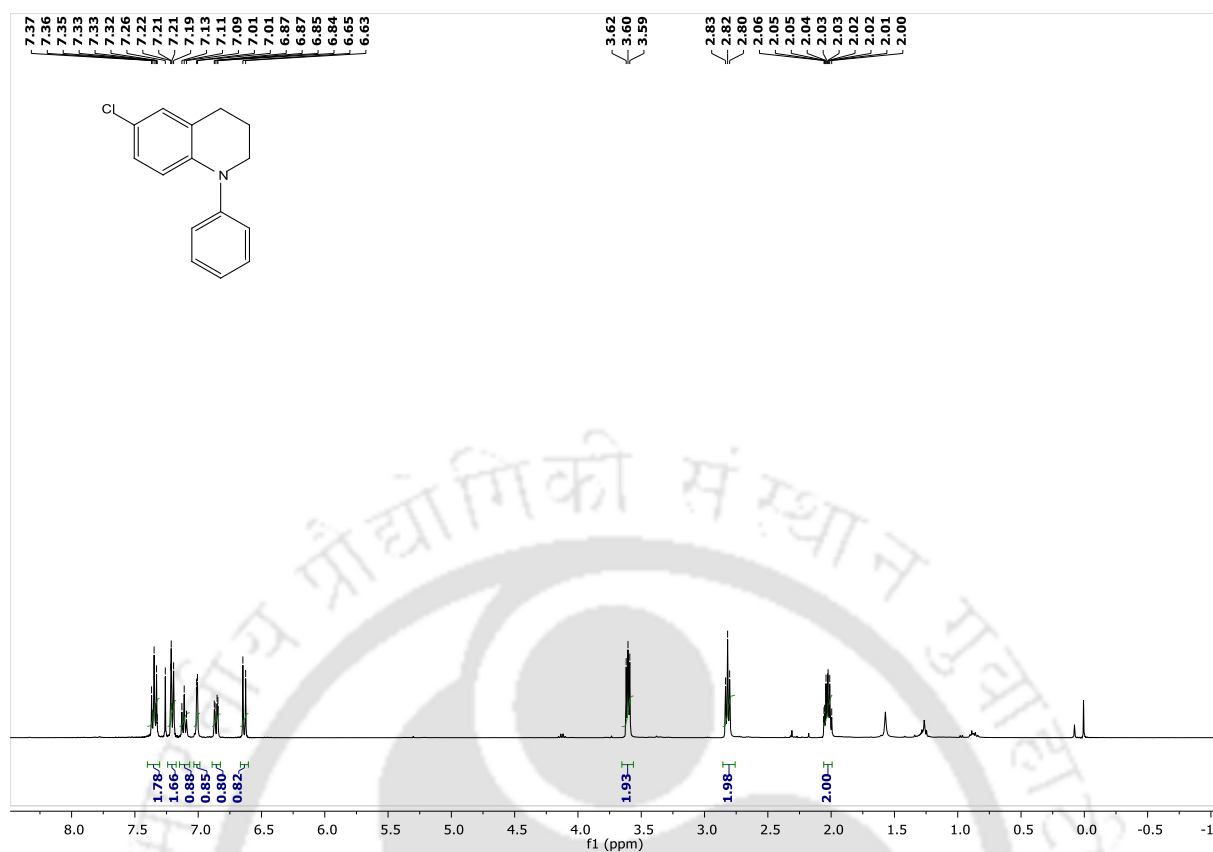


Figure S287: ¹H NMR Spectrum of **6.3h** (CDCl₃, 400 MHz, 298 K)

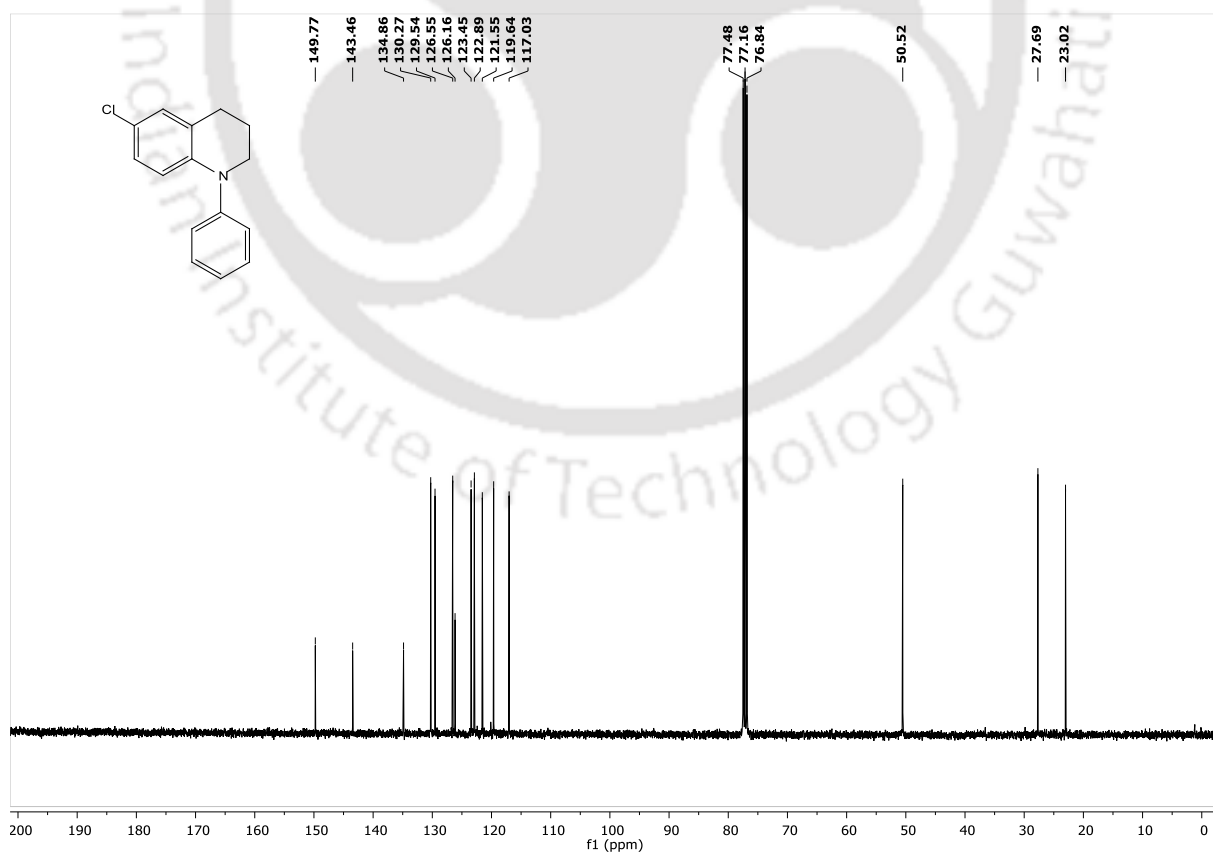


Figure S288: ¹³C NMR Spectrum of **6.3h** (CDCl₃, 101 MHz, 298 K)

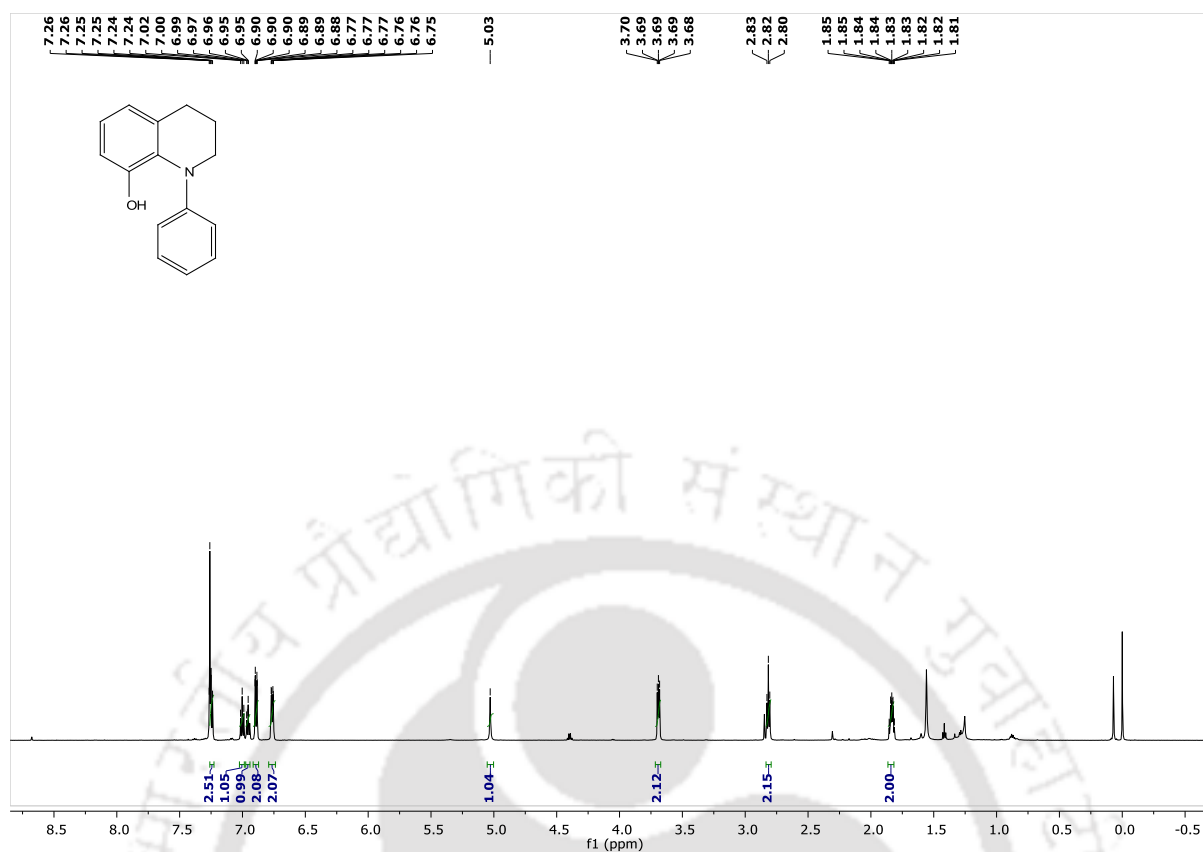


Figure S289: ¹H NMR Spectrum of **6.3i** (CDCl₃, 400 MHz, 298 K)

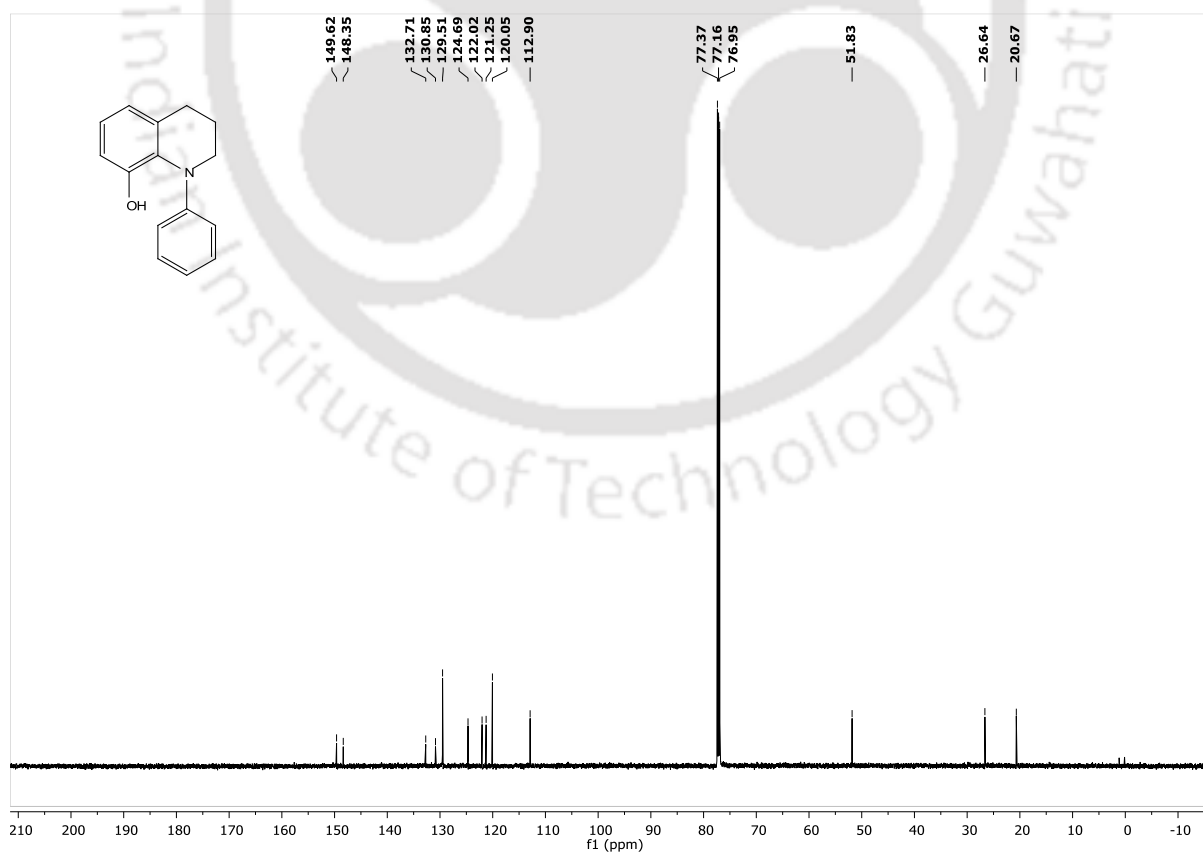
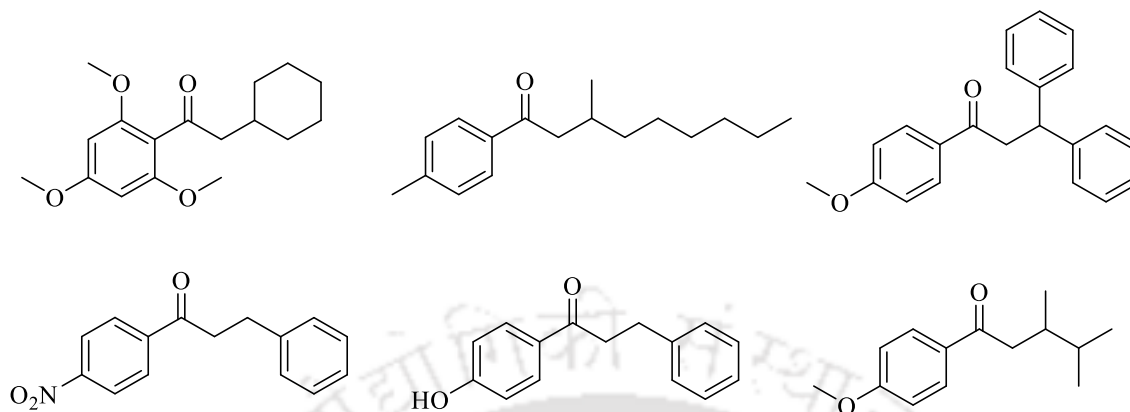


Figure S290: ¹³C NMR Spectrum of **6.3i** (CDCl₃, 101 MHz, 298 K)

Annexure VI

Unsuccessful substrates for cross coupling of secondary alcohols (*Chapter 3*)

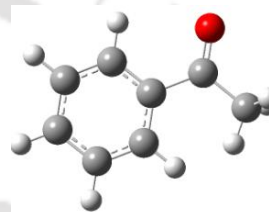
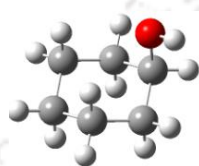


Scheme S1. Unsuccessful substrates for catalytic cross-coupling of secondary alcohols

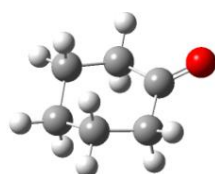
Annexure VII

Table S1. The Cartesian coordinates (xyz) for all optimized structures (*Chapter 2*)

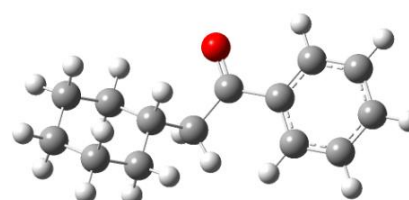
				H	3.33398	-0.64208	1.11873
H ₂				H	3.45414	-0.70857	-0.62988
H	-3.13773	3.75334	3.49986	H	1.22838	0.31641	-0.87895
H	-3.70195	3.82293	3.02075	H	1.07011	-1.09278	0.17404
H ₂ O				H	3.33555	1.63911	2.31303
O	0.82898	-1.24738	-0.07531	H	3.45676	3.11391	1.37134
H	1.78737	-1.19773	-0.07531	H	1.0727	2.67468	2.14649
H	0.55587	-0.32738	-0.07531	H	1.23004	2.73703	0.38836
Cyclohexanol (2.2a)				H	3.39058	1.78564	-0.7427
				O	-0.0569	0.43658	1.8386



C	1.53416	-0.12136	0.20116
C	3.05931	-0.12458	0.19793
C	3.61561	1.29498	0.19421
C	3.06083	2.10126	1.3633
C	1.53568	2.09843	1.36335
C	0.97557	0.68289	1.36679
H	4.71098	1.27924	0.22284
H	3.42277	-0.64922	1.09441
H	3.43764	-0.69234	-0.65955
H	1.15636	0.33311	-0.72559
H	1.13197	-1.14027	0.23233
H	3.42435	1.66298	2.30499
H	3.44029	3.12902	1.34119
H	1.13458	2.65374	2.21871
H	1.15793	2.60158	0.46208
H	1.2802	0.19027	2.30731
H	3.33821	1.7887	-0.74844
O	-0.44794	0.7331	1.27281
H	-0.81231	0.32182	2.05822



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

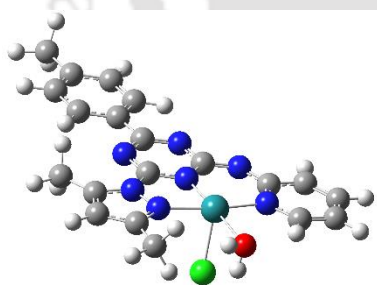


C	1.51157	-0.09578	0.10137
C	3.03971	-0.12188	0.19701
C	3.61936	1.28648	0.21043
C	3.04124	2.10053	1.36054
C	1.51312	2.1659	1.28547
C	0.88477	0.79292	1.15674
H	4.7117	1.24758	0.2833

C	-2.31049	0.12072	-1.26015
C	-3.83313	0.05422	-1.25732
C	-4.35353	-0.63316	0.00042
C	-3.83241	0.05385	1.25804

C	-2.30976	0.12034	1.26014
C	-1.7869	0.8152	-0.00005
H	-5.44952	-0.6551	0.00074
H	-4.24186	1.07533	-1.30319
H	-4.19428	-0.46057	-2.1551
H	-1.89471	-0.89298	-1.30661
H	-1.95147	0.65006	-2.15312
H	-4.24092	1.07505	1.30427
H	-4.19321	-0.461	2.15592
H	-1.95029	0.64935	2.1531
H	-1.89382	-0.89338	1.30598
H	-4.02249	-1.68171	0.00013
C	-0.27256	0.99907	-0.0003
H	0.03079	1.60033	-0.87044
H	0.03097	1.60072	0.86945
C	2.05877	-0.09523	-0.00009
C	2.69001	1.15501	0.00004
C	2.84655	-1.25341	0.00002
C	4.07765	1.24287	0.00021
H	2.09898	2.06667	-0.00002
C	4.2309	-1.1663	0.00018
H	2.33514	-2.21165	0.
C	4.8496	0.08369	0.00026
H	4.55865	2.21701	0.00035
H	4.83284	-2.07056	0.0002
H	5.93388	0.1541	0.00037
C	0.57392	-0.25795	-0.00043
O	0.08166	-1.37857	-0.001
H	-2.21362	1.83342	0.00021

I (Dehydrogenation outer sphere MLC pathway for 2.2a), step-1

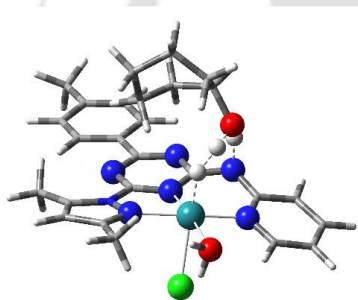


Ru	0.00096	-2.11493	-0.6827
Cl	0.55666	-2.93781	-2.82875
N	-0.13226	0.65018	-1.59567
N	1.37772	-0.67687	-0.46984
N	1.18891	-3.5233	0.26336
N	3.3257	0.28855	0.48336
N	2.94221	-1.92663	0.85044
N	-0.8841	-0.49879	-1.68172
N	1.79523	1.65661	-0.73972
C	1.09024	0.56015	-0.90336
C	2.40124	-3.16744	0.80948
C	2.54288	-0.81122	0.28985
C	3.49595	3.86123	-0.36224

H	2.57999	3.96846	-0.93558
C	2.94523	1.44127	-0.03427
C	3.8183	2.60777	0.17133
C	-0.6622	1.6568	-2.36517
C	3.18803	-4.1747	1.42285
H	4.13161	-3.85204	1.84786
C	-1.77693	1.11143	-2.96925
H	-2.4338	1.61839	-3.66298
C	1.55574	-5.82782	0.87323
H	1.18609	-6.84716	0.8607
C	5.00017	2.47754	0.91328
H	5.24324	1.50359	1.32576
C	0.8107	-4.82307	0.29297
H	-0.14447	-5.03076	-0.17621
C	2.77982	-5.48772	1.4587
H	3.40284	-6.24407	1.92789
C	6.4315	5.99438	0.77209
H	5.90934	6.94599	0.64083
H	7.2558	5.9777	0.04935
H	6.88633	5.99119	1.76704
C	5.8291	3.57014	1.11194
H	6.74165	3.45376	1.69345
C	-1.86794	-0.23131	-2.54186
C	4.33337	4.95032	-0.15909
H	4.06916	5.91944	-0.57807
C	-0.09836	3.0202	-2.47919
H	-0.7196	3.60671	-3.1597
H	0.92772	3.0021	-2.85538
H	-0.05648	3.52488	-1.50978
C	5.51508	4.82636	0.57791
C	-2.83493	-1.27962	-2.95085
H	-3.37593	-1.68728	-2.09144
H	-2.30291	-2.10083	-3.44602
H	-3.57214	-0.87798	-3.64826
O	-1.71572	-3.55807	-0.8163
H	-2.45345	-2.98505	-0.52088
H	-1.78448	-3.66721	-1.77627
C	-4.01822	4.33793	0.42052
C	-4.09861	3.1763	-0.58113
C	-4.35932	1.87454	0.15743
C	-5.75068	1.88453	0.78631
C	-6.16145	3.29336	1.23622
C	-4.93905	4.11372	1.63034
H	-2.98428	4.46366	0.76214
H	-4.90951	3.33276	-1.3051
H	-6.45071	1.49538	0.03867
H	-6.68418	3.80716	0.41865
H	-4.39618	3.57953	2.42276
H	-3.47392	0.83487	-1.23007
H	-3.59364	1.77939	0.95097
H	-3.17225	3.10211	-1.16569
H	-4.28454	5.27128	-0.08715
H	-5.23414	5.07326	2.06605
H	-6.87913	3.23471	2.06002
H	-5.78001	1.18427	1.63009

O	-4.27966	0.73201	-0.70165
C	-2.28727	0.56397	3.45265
C	-3.14676	-0.40263	2.62946
C	-2.4044	-0.82131	1.36983
C	-1.16219	-1.63176	1.7352
C	-0.61548	-1.29469	3.12751
C	-0.79378	0.19271	3.4025
H	-2.42497	1.58846	3.08181
H	-3.39024	-1.3049	3.20517
H	-1.37198	-2.70124	1.64459
H	-1.15229	-1.88097	3.88429
H	-0.28749	0.75548	2.60382
H	-3.83382	-0.95392	0.08147
H	-2.08691	0.09655	0.83878
H	-4.10611	0.05589	2.36397
H	-2.64241	0.56971	4.48874
H	-0.29298	0.48308	4.33058
H	0.43486	-1.59509	3.19466
H	-0.32474	-1.33877	1.05749
O	-3.22232	-1.59433	0.49248

O-TS-1 (Dehydrogenation outer sphere MLC pathway for **2.2a**), step-1

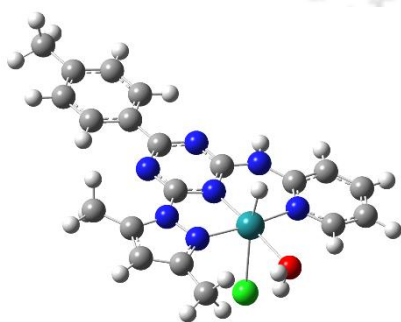


Ru	1.47915	-1.52052	-0.62733
Cl	1.61001	-2.95715	-2.58586
N	-0.8339	-2.96139	0.37105
N	-0.42314	-0.98239	-0.72118
N	2.11273	0.15421	-1.6769
N	-2.16271	0.60378	-0.96538
N	-0.04443	1.24128	-1.48449
N	0.53807	-3.07958	0.39511
N	-2.63829	-1.53601	-0.03879
C	-1.35617	-1.78474	-0.1652
C	1.2826	1.21689	-1.85006
C	-0.87376	0.25787	-1.07272
C	-5.37262	-0.88535	0.04751
H	-5.04519	-1.8898	0.29911
C	-3.00261	-0.30417	-0.47567
C	-4.42017	0.05187	-0.37764
C	-1.4426	-4.02295	1.00111
C	1.76446	2.41841	-2.40573
H	1.06212	3.23895	-2.51399
C	-0.41609	-4.83673	1.42123
H	-0.52558	-5.77428	1.94697
C	3.90683	1.41118	-2.6902

H	4.94048	1.42611	-3.01646
C	-4.84584	1.34614	-0.70199
H	-4.10482	2.07055	-1.02445
C	3.38423	0.26198	-2.13466
H	3.99501	-0.62263	-2.00163
C	3.07671	2.52722	-2.81378
H	3.44428	3.45619	-3.239
C	-8.58961	1.12702	-0.07447
H	-8.97243	0.96903	0.93944
H	-9.2079	0.51408	-0.73927
H	-8.76073	2.17418	-0.33538
C	-6.18614	1.68853	-0.59994
H	-6.50345	2.69868	-0.85028
C	0.79115	-4.22272	1.0283
C	-6.70958	-0.53449	0.14153
H	-7.43826	-1.27272	0.47084
C	-2.90611	-4.18374	1.14704
H	-3.11273	-5.13221	1.64656
H	-3.41216	-4.17764	0.17763
H	-3.34594	-3.36771	1.72631
C	-7.14261	0.75911	-0.17886
C	2.18589	-4.68303	1.23406
H	2.77644	-3.92317	1.76271
H	2.67214	-4.90353	0.27687
H	2.21209	-5.59329	1.83501
O	3.63413	-2.2744	-0.5938
H	3.80484	-2.85744	0.15415
H	3.45161	-2.86446	-1.3583
C	1.66257	5.47508	2.1236
C	0.55246	4.44169	1.90879
C	0.49512	4.0207	0.44621
H	1.53028	3.75048	0.14282
C	0.03863	5.20635	-0.41401
H	0.41074	5.08414	-1.44049
H	-1.0546	5.16262	-0.47395
O	-0.37091	2.92696	0.26948
H	-0.29587	2.21379	-0.87118
C	2.6592	-0.68695	3.585
C	1.24888	-0.5239	3.02041
C	1.19815	0.3687	1.76074
H	1.39652	-0.42577	0.86083
C	2.4459	1.24524	1.63502
H	2.35868	1.88781	0.75029
H	2.45125	1.91966	2.5039
O	0.01596	0.95897	1.62751
H	-0.09553	1.98442	0.98112
C	0.49949	6.55237	0.16179
H	-0.25478	6.93399	0.86291
H	0.57766	7.30469	-0.63025
C	1.82285	6.40079	0.90421
H	2.56796	5.98299	0.21291
H	2.21449	7.37613	1.2123
H	0.69781	3.56087	2.54414
H	-0.42863	4.85275	2.18273
H	1.44542	6.06804	3.01958

H	2.61339	4.96416	2.32241
C	3.73495	0.41965	1.5789
H	3.9398	0.12763	0.54156
H	4.57708	1.04794	1.89091
C	3.66582	-0.84271	2.45409
H	3.33485	-1.69209	1.8378
H	4.65983	-1.10173	2.83541
H	2.70003	-1.54273	4.2684
H	2.92705	0.1917	4.18765
H	0.81112	-1.5028	2.78474
H	0.58328	-0.05508	3.75189

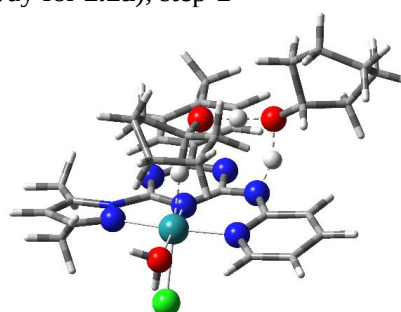
II (Dehydrogenation outer sphere MLC
pathway for **2.2a**), step-2



Ru	-0.07819	-1.52149	-3.6309
Cl	-1.21202	-2.5576	-5.7235
N	-2.22018	-2.261	-1.79292
N	-1.47251	-0.37105	-2.85795
N	0.76239	0.01971	-4.73723
N	-2.5732	1.70521	-2.47299
N	-0.79761	1.63062	-3.89272
N	-1.20899	-2.87538	-2.50708
N	-3.32554	-0.24716	-1.34857
C	-2.37464	-0.89742	-1.98236
C	0.26878	1.27899	-4.71389
C	-1.63891	0.95923	-3.05108
C	-5.33553	1.24056	-0.06685
H	-5.22691	0.18048	0.1398
C	-3.40247	1.07118	-1.6263
C	-4.44987	1.84888	-0.96798
C	-3.03287	-3.18831	-1.1718
C	0.80341	2.30962	-5.49719
H	0.36176	3.30014	-5.43746
C	-2.511	-4.41258	-1.50899
H	-2.89682	-5.37286	-1.19828
C	2.38886	0.7611	-6.36702
H	3.22407	0.49623	-7.00545
C	-4.59289	3.22115	-1.2222
H	-3.90656	3.69689	-1.91561
C	1.81105	-0.20673	-5.56973
H	2.17304	-1.22742	-5.55937
C	1.87434	2.05584	-6.33331
H	2.29254	2.84812	-6.94565
C	-7.57353	4.14096	0.94667

H	-7.9253	3.6688	1.86777
H	-8.4412	4.23615	0.28306
H	-7.25018	5.1577	1.18845
C	-5.58951	3.95313	-0.59682
H	-5.68468	5.01729	-0.80342
C	-1.39649	-4.18404	-2.34642
C	-6.32914	1.98214	0.55382
H	-7.00635	1.49487	1.25254
C	-4.21117	-2.84516	-0.3454
H	-4.6653	-3.76579	0.02631
H	-4.95755	-2.28671	-0.91769
H	-3.94392	-2.21393	0.50695
C	-6.47984	3.34991	0.30017
C	-0.54083	-5.16942	-3.04699
H	0.50541	-5.11319	-2.72905
H	-0.5844	-4.9828	-4.12708
H	-0.8955	-6.18471	-2.85986
O	1.44918	-2.91796	-4.48252
H	1.78085	-3.59152	-3.85339
H	0.81434	-3.33671	-5.09987
H	-1.06233	2.6036	-3.9476
H	0.85958	-1.10426	-2.39087
C	4.47045	-1.58252	-0.99839
C	3.85006	-2.38165	-2.15512
C	3.2783	-3.69234	-1.64011
C	2.08544	-3.4281	-0.73214
C	2.29089	-2.16768	0.12111
C	3.77104	-1.87362	0.33716
H	5.53981	-1.80841	-0.91092
H	3.02807	-1.81776	-2.6187
H	1.20782	-3.28417	-1.37617
H	1.82906	-1.31435	-0.39417
H	4.24235	-2.73754	0.8266
H	3.58883	-4.80043	-3.22628
H	4.06136	-4.23664	-1.08515
H	4.59064	-2.56542	-2.94407
H	4.40364	-0.5135	-1.22838
H	3.90499	-1.03248	1.02517
H	1.7674	-2.26796	1.07723
H	1.89336	-4.31216	-0.11316
O	2.81926	-4.54852	-2.7044

O-TS-2 (Dehydrogenation outer sphere MLC
pathway for **2.2a**), step-2

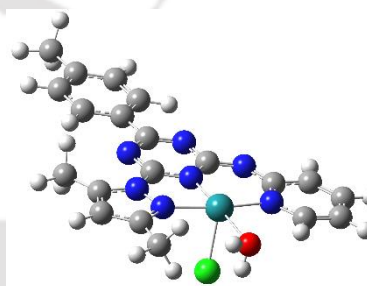


Ru	1.06302	1.37614	0.20413
Cl	1.01421	3.40244	1.71167

N	-1.48043	2.25314	-0.88839
N	-0.74233	0.66667	0.60315
N	1.90302	0.25729	1.74372
N	-2.27632	-0.88916	1.51839
N	-0.03163	-1.22316	1.87846
N	-0.13859	2.47695	-1.11019
N	-3.07223	0.88584	0.14026
C	-1.81123	1.23839	0.0062
C	1.20254	-0.76208	2.32216
C	-1.01622	-0.44745	1.37227
C	-5.71368	0.03705	0.55673
H	-5.51208	0.91675	-0.04688
C	-3.25714	-0.19524	0.93185
C	-4.63699	-0.64825	1.13626
C	-2.26476	3.06333	-1.67835
C	1.76671	-1.48636	3.38627
H	1.17153	-2.29171	3.80162
C	-1.38356	3.82661	-2.40797
H	-1.65015	4.58645	-3.12847
C	3.69764	-0.0875	3.31532
H	4.67147	0.22759	3.67362
C	-4.90465	-1.78308	1.91477
H	-4.06881	-2.31107	2.36283
C	3.1094	0.58444	2.26257
H	3.60897	1.41591	1.78019
C	3.01104	-1.15691	3.8887
H	3.43431	-1.71291	4.7205
C	-8.69655	-1.9854	1.76169
H	-8.755	-3.06623	1.91746
H	-9.3511	-1.72651	0.92475
H	-9.12111	-1.51261	2.65533
C	-6.20878	-2.21536	2.10091
H	-6.40083	-3.0996	2.70545
C	-0.08148	3.44003	-2.02733
C	-7.01461	-0.4021	0.75075
H	-7.83988	0.14025	0.29343
C	-3.74501	3.05827	-1.67815
H	-4.10322	3.83468	-2.35717
H	-4.15145	3.24556	-0.68058
H	-4.14979	2.09321	-1.99712
C	-7.28875	-1.5339	1.52727
C	1.22436	3.96873	-2.49069
H	1.88533	3.15652	-2.81577
H	1.72497	4.53118	-1.69372
H	1.09423	4.64525	-3.33712
O	3.05832	2.40232	-0.15375
H	3.09097	2.74629	-1.05193
H	2.76099	3.15381	0.41135
C	-1.27386	-0.9969	-2.50005
C	-1.2072	-2.20708	-1.57654
C	0.2314	-2.69119	-1.41973
C	1.05519	-2.46458	-2.6863
C	0.16181	-2.54348	-3.91839
C	-0.86163	-1.39726	-3.92522
H	-2.27443	-0.55114	-2.48911

H	-1.65298	-2.02292	-0.59369
H	1.50003	-1.46163	-2.6352
H	0.76875	-2.52509	-4.82827
H	-0.44161	-0.52667	-4.44175
O	0.93447	-2.004	-0.32445
H	0.40987	-1.91809	0.62663
H	1.38293	0.22606	-0.95876
H	1.12795	-0.98743	-0.55511
H	-1.78835	-3.03167	-2.00959
H	-0.59191	-0.22319	-2.1181
H	-1.74251	-1.6985	-4.50358
H	-0.354	-3.51308	-3.92603
H	1.88911	-3.17045	-2.73104
H	0.24866	-3.74268	-1.11585

I (Dehydrogenation outer sphere MLC pathway for **2.2a**), releasing H₂, step-2

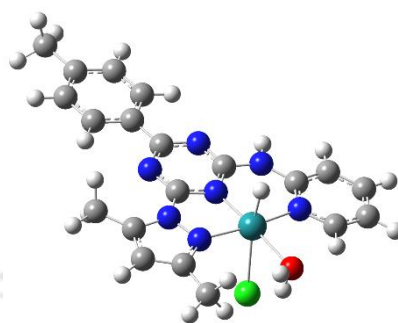


Ru	3.84801	2.59995	1.26026
Cl	4.45401	0.56858	2.28354
N	1.36973	2.43985	2.79586
N	2.04823	1.97334	0.6465
N	4.75198	2.03951	-0.52845
N	0.45997	1.31154	-0.9908
N	2.63443	1.5254	-1.63397
N	2.64897	2.92069	2.97274
N	-0.22229	1.65622	1.27411
C	1.03095	1.98097	1.51736
C	3.98471	1.63791	-1.59721
C	1.75511	1.59993	-0.66645
C	-2.83075	0.92497	0.59194
H	-2.55158	1.0288	1.6378
C	-0.44635	1.3375	-0.03658
C	-1.84316	1.04204	-0.39314
C	0.63128	2.54534	3.95165
C	4.63595	1.29955	-2.80983
H	3.99384	1.00164	-3.63066
C	1.48715	3.07968	4.88691
H	1.24547	3.2887	5.91893
C	6.76555	1.69696	-1.80922
H	7.84924	1.7212	-1.83227
C	-2.21401	0.89601	-1.73719
H	-1.44193	0.98337	-2.49538
C	6.10024	2.0381	-0.65059
H	6.63907	2.33891	0.23999
C	6.00653	1.3254	-2.92305

H	6.48597	1.0523	-3.85906
C	-5.95125	0.26388	-1.47853
H	-6.62216	0.33321	-0.61874
H	-6.06264	-0.74062	-1.90195
H	-6.30759	0.96415	-2.24083
C	-3.53474	0.65439	-2.07803
H	-3.80825	0.5503	-3.12623
C	2.7277	3.2875	4.25163
C	-4.15226	0.67665	0.24069
H	-4.90838	0.58679	1.01874
C	-0.79249	2.16618	4.08834
H	-1.08962	2.27864	5.13274
H	-0.97539	1.1362	3.77359
H	-1.4297	2.80982	3.47211
C	-4.53032	0.53969	-1.09746
C	3.99427	3.79197	4.83687
H	4.40958	4.62156	4.25613
H	4.74039	2.99	4.87832
H	3.83173	4.14077	5.85811
O	5.82381	3.3021	2.01234
H	5.70639	4.24052	2.27642
H	5.96655	2.76834	2.80519
C	-5.26542	4.90725	1.86851
C	-3.99215	4.0836	2.00919
C	-2.98534	4.43715	0.90526
C	-3.09087	5.91683	0.522
C	-3.53634	6.76086	1.7076
C	-4.97003	6.39399	2.11953
H	-5.66448	4.76706	0.8541
H	-3.51752	4.30691	2.97542
H	-2.11901	6.23592	0.13193
H	-2.84541	6.57709	2.54131
H	-5.68891	7.01142	1.56783
H	-1.50295	3.25007	1.39968
H	-3.1971	3.81972	0.01486
H	-4.19979	3.00706	2.00383
H	-6.04688	4.54935	2.54666
H	-5.11959	6.63081	3.1797
H	-3.46235	7.83009	1.48384
H	-3.81138	6.03229	-0.29811
O	-1.64828	4.2066	1.33762
C	1.22298	5.60717	1.32328
C	2.41892	6.17017	2.07602
C	3.73507	5.61272	1.59601
C	3.71981	5.04595	0.19954
C	2.77274	5.86652	-0.68833
C	1.32188	5.79026	-0.19773
H	1.15723	4.53972	1.54557
H	2.4875	7.26181	1.95062
H	4.73528	4.98304	-0.19922
H	3.12822	6.90501	-0.68035
H	0.80485	4.95183	-0.68062
H	2.34554	6.00474	3.15633
H	0.28811	6.02427	1.70516
H	0.79193	6.69485	-0.51477

H	2.85475	5.52402	-1.72412
H	3.25372	4.01933	0.12174
O	4.76792	5.74774	2.25901

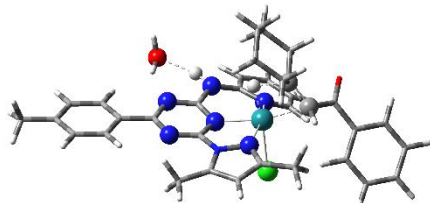
II (Hydrogenation segment), step-1



Ru	-0.60254	1.45585	1.226
Cl	-0.46153	1.98294	3.77048
N	0.49913	-1.23415	1.45585
N	1.14539	0.80106	0.61677
N	-0.17591	3.41526	0.75275
N	3.17888	0.97626	-0.60681
N	1.87145	2.82388	-0.33729
N	-0.66612	-0.56698	1.78519
N	2.54372	-1.1162	0.32397
C	1.46215	-0.51599	0.76908
C	0.95594	3.77514	0.10494
C	2.0695	1.49215	-0.09242
C	4.83853	-2.32035	-0.75155
H	4.12653	-2.91134	-0.18315
C	3.38796	-0.33286	-0.37725
C	4.58837	-0.95269	-0.93398
C	0.52509	-2.50272	1.99686
C	1.26383	5.11161	-0.17458
H	2.1891	5.34248	-0.69469
C	-0.65656	-2.62963	2.6839
H	-0.98345	-3.50217	3.23064
C	-0.75936	5.755	0.90859
H	-1.46956	6.49597	1.25735
C	5.51013	-0.19633	-1.67399
H	5.31787	0.86192	-1.81957
C	-0.99903	4.41749	1.15171
H	-1.88496	4.08768	1.67997
C	0.39999	6.11524	0.22416
H	0.63295	7.15413	0.0145
C	8.13675	-2.7853	-2.58475
H	8.06482	-3.87575	-2.60345
H	9.01733	-2.52917	-1.98405
H	8.34257	-2.44179	-3.60306
C	6.64074	-0.79195	-2.20913
H	7.34396	-0.19113	-2.78248
C	-1.36146	-1.41547	2.5447
C	5.97419	-2.90648	-1.29083
H	6.15351	-3.96921	-1.14133
C	1.64195	-3.45745	1.83001

H	1.41196	-4.37204	2.38016
H	2.58707	-3.04889	2.19911
H	1.79901	-3.70576	0.77598
C	6.89821	-2.15693	-2.02709
C	-2.65315	-1.02568	3.15719
H	-3.43744	-0.8926	2.40195
H	-2.52788	-0.09876	3.72917
H	-2.99946	-1.80486	3.83794
O	-2.70077	2.00722	1.86878
H	-3.22001	1.20134	1.73765
H	-2.4205	2.00937	2.81518
H	-1.0601	1.27226	-0.30053
H	2.65072	3.20469	-0.85423
C	-0.04022	-3.98429	-1.22795
C	0.71003	-3.0676	-1.96543
C	0.23298	-1.77144	-2.1448
C	-0.9801	-1.38676	-1.58304
C	-1.72905	-2.29157	-0.81543
C	-1.24333	-3.59649	-0.6532
H	0.32285	-5.00036	-1.09306
H	1.66564	-3.35973	-2.39444
H	0.81212	-1.0518	-2.71923
H	-1.32564	-0.36947	-1.73171
H	-1.83844	-4.28687	-0.06174
C	-3.01935	-1.94357	-0.14366
O	-3.61834	-2.8057	0.50554
C	-3.508	-0.55852	-0.27069
C	-4.77724	-0.12146	-0.0938
C	-5.97218	-0.97297	0.2159
C	-5.10193	1.33107	-0.30645
C	-7.06421	-0.78399	-0.84532
H	-6.37572	-0.64905	1.18886
H	-5.6899	-2.0196	0.32609
C	-6.17834	1.50248	-1.38222
H	-5.49337	1.74981	0.63491
H	-4.19882	1.89954	-0.55393
C	-7.41775	0.68323	-1.04752
H	-7.9498	-1.36387	-0.56389
H	-6.70818	-1.20619	-1.79506
H	-6.42631	2.56355	-1.49357
H	-5.77098	1.17355	-2.34829
H	-8.17207	0.79028	-1.83512
H	-7.87402	1.07808	-0.12775
H	-2.76668	0.19291	-0.53676

R-TS-1 (Hydrogenation segment), step-1

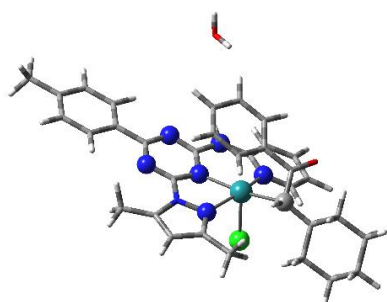


Ru	0.98032	-0.11712	0.00323
Cl	1.40589	-0.7093	-2.37402
N	-1.05049	-2.26733	-0.06757

N	-1.05641	0.00835	-0.32635
N	1.20578	1.86986	-0.58906
N	-3.10767	1.19684	-0.261
N	-1.12111	2.34863	-0.20645
N	0.31377	-2.14165	0.15997
N	-3.11584	-1.18033	-0.22632
C	-1.79719	-1.11112	-0.22939
C	0.16573	2.73225	-0.60413
C	-1.76861	1.15191	-0.28147
C	-5.90417	-1.21482	-0.29454
H	-5.34048	-2.13562	-0.18422
C	-3.74307	0.01095	-0.28361
C	-5.20528	0.00089	-0.35906
C	-1.42108	-3.59013	-0.21231
C	0.30261	4.05994	-1.02229
H	-0.56669	4.71034	-0.99608
C	-0.26206	-4.30815	-0.07951
H	-0.16959	-5.38254	-0.14608
C	2.56774	3.5859	-1.59663
H	3.53257	3.85589	-2.00961
C	-5.94313	1.18348	-0.51246
H	-5.42816	2.13594	-0.59293
C	2.36344	2.29518	-1.14893
H	3.13106	1.53906	-1.24134
C	1.52378	4.50097	-1.50157
H	1.64339	5.52878	-1.82974
C	-9.52203	-0.0962	-0.57982
H	-9.93248	0.82731	-0.99537
H	-9.95591	-0.22322	0.41871
H	-9.88242	-0.932	-1.18652
C	-7.32737	1.14694	-0.59173
H	-7.88062	2.07468	-0.72037
C	0.78713	-3.3868	0.13393
C	-7.28645	-1.24118	-0.37315
H	-7.80875	-2.19432	-0.3225
C	-2.80136	-4.05434	-0.47483
H	-2.78806	-5.13595	-0.62146
H	-3.22887	-3.58258	-1.36387
H	-3.47451	-3.81979	0.35439
C	-8.02777	-0.06169	-0.5192
C	2.23126	-3.69065	0.26878
H	2.59726	-3.53662	1.28943
H	2.82023	-3.05099	-0.39478
H	2.42133	-4.73205	0.00277
H	3.15572	-1.38529	0.96321
H	-1.78287	3.13065	-0.16848
C	2.9316	-0.31941	0.9938
C	1.95342	0.05715	2.00305
C	1.57295	-1.0405	2.98943
C	2.01053	1.41991	2.68781
H	0.50608	0.38411	1.45953
C	0.3018	-0.73806	3.76963
H	2.41373	-1.13462	3.69536
H	1.49387	-2.00111	2.47065
C	0.75544	1.71993	3.50224

H	2.89341	1.41592	3.34243
H	2.19978	2.20774	1.95794
C	0.41127	0.60481	4.48226
H	0.0934	-1.5417	4.48518
H	-0.54877	-0.71683	3.0692
H	0.87877	2.67192	4.03108
H	-0.09063	1.86396	2.81041
H	-0.51601	0.83501	5.02018
H	1.20067	0.53869	5.24552
C	4.10332	0.49352	0.64347
O	4.33073	1.62474	1.08761
C	5.0874	-0.11662	-0.30718
C	4.72476	-1.09589	-1.23918
C	6.40938	0.34435	-0.28121
C	5.67228	-1.61389	-2.11728
H	3.682	-1.39312	-1.32699
C	7.35871	-0.18978	-1.14268
H	6.66416	1.12528	0.43024
C	6.99196	-1.17319	-2.06199
H	5.37246	-2.3536	-2.85512
H	8.38667	0.16195	-1.10468
H	7.73282	-1.58446	-2.74303
O	-3.44125	4.02903	-0.09227
H	-3.66894	4.29097	0.804
H	-3.68334	3.08475	-0.13797

III (Hydrogenation segment), step-2

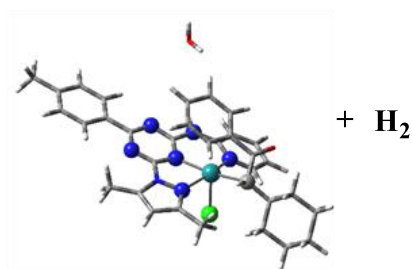


Ru	-1.01468	0.19569	-0.2291
Cl	-1.64347	0.61225	-2.50963
N	1.06096	2.28133	-0.35149
N	1.00114	-0.00622	-0.5266
N	-1.31488	-1.83131	-0.62928
N	3.01663	-1.24666	-0.304
N	1.00365	-2.34298	-0.26273
N	-0.31015	2.18908	-0.18259
N	3.09865	1.12699	-0.35003
C	1.78455	1.09695	-0.43031
C	-0.29657	-2.71872	-0.6106
C	1.68702	-1.1664	-0.38482
C	5.89465	1.0773	-0.29241
H	5.35636	2.01924	-0.25298
C	3.69722	-0.08061	-0.33855
C	5.15705	-0.11748	-0.34079
C	1.46139	3.59379	-0.48969
C	-0.48164	-4.07004	-0.92305
H	0.37153	-4.7404	-0.87719

C	0.30975	4.33843	-0.41546
H	0.24466	5.41388	-0.4957
C	-2.75967	-3.58221	-1.43933
H	-3.74873	-3.86029	-1.78368
C	5.86383	-1.32826	-0.40257
H	5.32289	-2.26734	-0.46878
C	-2.50753	-2.26756	-1.09696
H	-3.2651	-1.50043	-1.20083
C	-1.7308	-4.51147	-1.32352
H	-1.88703	-5.55711	-1.56998
C	9.48327	-0.16851	-0.32119
H	9.88477	-1.10441	-0.71788
H	9.86389	-0.06265	0.70164
H	9.90823	0.65615	-0.90078
C	7.25034	-1.33885	-0.40624
H	7.77776	-2.28871	-0.46336
C	-0.76443	3.44028	-0.23895
C	7.27916	1.0559	-0.29566
H	7.8303	1.99347	-0.25887
C	2.86287	4.02368	-0.69104
H	2.88356	5.10255	-0.85588
H	3.32327	3.52641	-1.54927
H	3.48866	3.78791	0.1741
C	7.98757	-0.15141	-0.34748
C	-2.21314	3.73851	-0.14831
H	-2.56983	3.74074	0.88797
H	-2.78535	2.98681	-0.69868
H	-2.42729	4.72111	-0.57306
H	-3.05405	1.46042	1.03561
H	1.64352	-3.13774	-0.16489
C	-2.76136	0.40865	1.06502
C	-1.65696	0.13618	2.03701
C	-1.29708	1.35597	2.89217
C	-1.65851	-1.14284	2.88619
H	-0.61654	-0.06767	1.47329
C	0.02918	1.18061	3.6176
H	-2.10767	1.49112	3.62282
H	-1.2844	2.25384	2.26432
C	-0.33648	-1.30421	3.63125
H	-2.4978	-1.08487	3.5908
H	-1.86098	-2.01097	2.2583
C	0.01817	-0.08277	4.47046
H	0.2543	2.06262	4.22743
H	0.8355	1.11098	2.86777
H	-0.36716	-2.20521	4.25376
H	0.4661	-1.47341	2.89306
H	0.98475	-0.2223	4.96814
H	-0.72689	0.03438	5.27071
C	-3.91352	-0.48154	0.91589
O	-4.00944	-1.60348	1.42991
C	-5.04162	0.00054	0.05348
C	-4.87094	0.94564	-0.96484
C	-6.30547	-0.57007	0.24753
C	-5.94825	1.32294	-1.76141
H	-3.87496	1.3273	-1.17782

C	-7.38416	-0.17853	-0.53425
H	-6.40869	-1.32544	1.02163
C	-7.20786	0.7716	-1.54062
H	-5.79825	2.03852	-2.5656
H	-8.36464	-0.61739	-0.36765
H	-8.04963	1.07049	-2.16011
O	3.27749	-4.07298	-0.01486
H	3.48827	-4.28779	0.8979
H	3.53505	-3.13536	-0.10712

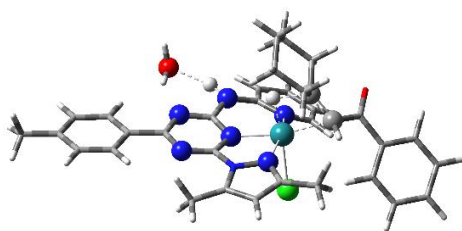
IV (Hydrogenation segment), molecular complex formation, with H₂ step-2



Ru	1.03577	-0.191	-0.23958
Cl	1.67067	-0.74445	-2.49116
N	-1.01234	-2.31056	-0.27287
N	-0.97939	-0.03498	-0.56506
N	1.31464	1.81056	-0.74804
N	-3.01294	1.18811	-0.43962
N	-1.01107	2.30891	-0.40703
N	0.35324	-2.19151	-0.08072
N	-3.06355	-1.1851	-0.34568
C	-1.74947	-1.14216	-0.42213
C	0.28475	2.68491	-0.77383
C	-1.68171	1.12121	-0.49201
C	-5.85755	-1.17582	-0.34986
H	-5.30559	-2.11039	-0.34137
C	-3.67757	0.01312	-0.4017
C	-5.13804	0.03049	-0.38387
C	-1.3947	-3.63287	-0.35133
C	0.45341	4.02127	-1.15165
H	-0.40799	4.68244	-1.13927
C	-0.2366	-4.35797	-0.21419
H	-0.15699	-5.43518	-0.23776
C	2.73996	3.53869	-1.6364
H	3.72661	3.81327	-1.99027
C	-5.86399	1.23151	-0.40265
H	-5.33895	2.18099	-0.4447
C	2.50439	2.2392	-1.23015
H	3.2737	1.47898	-1.29072
C	1.6983	4.45858	-1.57025
H	1.84166	5.49269	-1.86794
C	-9.46442	0.01596	-0.29944
H	-9.88534	0.94697	-0.68756
H	-9.8295	-0.09814	0.72819
H	-9.88455	-0.81326	-0.87586

C	-7.25047	1.22123	-0.38477
H	-7.79269	2.16419	-0.40654
C	0.8228	-3.43816	-0.06171
C	-7.24204	-1.17542	-0.33291
H	-7.7785	-2.12195	-0.31145
C	-2.78654	-4.08919	-0.56139
H	-2.79145	-5.17441	-0.67842
H	-3.23396	-3.63588	-1.45051
H	-3.43291	-3.82242	0.27934
C	-7.96914	0.02167	-0.34621
C	2.27243	-3.71194	0.07424
H	2.60704	-3.65186	1.11603
H	2.84588	-2.98328	-0.50491
H	2.50753	-4.71344	-0.29105
H	3.052	-1.37525	1.13445
H	-1.6591	3.09973	-0.33311
C	2.77145	-0.32082	1.08221
C	1.65995	0.03747	2.01596
C	1.25668	-1.105	2.95443
C	1.67209	1.37555	2.76869
H	0.62885	0.2152	1.42528
C	-0.09046	-0.84939	3.61674
H	2.04	-1.19237	3.72107
H	1.24789	-2.05014	2.39958
C	0.33391	1.6249	3.45758
H	2.48938	1.3452	3.50061
H	1.91823	2.19093	2.08798
C	-0.08503	0.47697	4.36873
H	-0.35432	-1.67579	4.28601
H	-0.87035	-0.82563	2.83611
H	0.37088	2.56692	4.01614
H	-0.43492	1.76495	2.67851
H	-1.06876	0.6739	4.81133
H	0.62225	0.40721	5.20784
C	3.93922	0.53846	0.87998
O	4.0501	1.69626	1.3042
C	5.07289	-0.03411	0.08362
C	4.89167	-1.00997	-0.90316
C	6.35719	0.47579	0.30969
C	5.9783	-1.47635	-1.6378
H	3.88515	-1.3466	-1.14269
C	7.44386	-0.00687	-0.40727
H	6.47229	1.25541	1.05768
C	7.25666	-0.98636	-1.38319
H	5.8217	-2.21469	-2.41981
H	8.43974	0.38424	-0.21434
H	8.10555	-1.35591	-1.95307
O	-3.3008	4.01679	-0.16238
H	-3.48458	4.17324	0.76828
H	-3.54879	3.08209	-0.2978
H	-3.43562	1.48031	2.39574
H	-2.82428	1.76737	2.71491

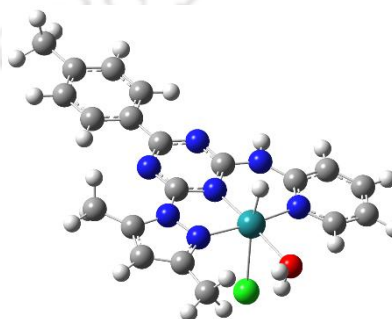
R-TS-2 (Hydrogenation segment), step-2



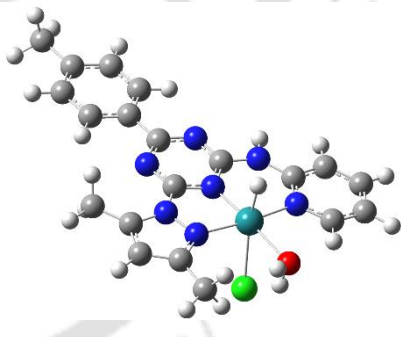
Ru	0.61127	0.04091	-0.14427
Cl	1.19708	0.38251	-2.54462
N	-1.41221	-1.97905	-0.886
N	-1.44095	0.2304	-0.25607
N	0.77597	2.11817	0.09155
N	-3.48458	1.21598	0.44569
N	-1.52344	2.35537	0.74501
N	-0.02912	-1.88466	-0.8071
N	-3.47347	-1.01536	-0.3652
C	-2.1666	-0.88256	-0.50029
C	-0.26035	2.88913	0.48152
C	-2.15571	1.23926	0.28829
C	-6.27191	-1.07898	-0.31134
H	-5.71443	-1.88029	-0.7858
C	-4.11153	0.08201	0.08378
C	-5.56879	0.02206	0.20016
C	-1.80465	-3.12068	-1.55913
C	-0.14072	4.275	0.64202
H	-1.00246	4.83764	0.98917
C	-0.64153	-3.74428	-1.92271
H	-0.56314	-4.66697	-2.47956
C	2.09181	4.12332	-0.17605
H	3.03878	4.55232	-0.48395
C	-6.29797	1.04673	0.82275
H	-5.77704	1.8953	1.25563
C	1.90188	2.76066	-0.29381
H	2.65502	2.124	-0.73574
C	1.05531	4.8986	0.33536
H	1.16178	5.97125	0.46262
C	-9.8776	-0.17966	0.48097
H	-10.25168	0.27749	1.40116
H	-10.24465	-1.20827	0.43798
H	-10.34125	0.36139	-0.35222
C	-7.6784	0.9712	0.91975
H	-8.2241	1.77048	1.41614
C	0.43289	-2.94786	-1.46525
C	-7.65286	-1.1432	-0.21333
H	-8.18067	-2.00455	-0.61728
C	-3.20911	-3.50662	-1.81998
H	-3.2177	-4.42647	-2.40775
H	-3.74789	-2.7324	-2.37346
H	-3.76779	-3.67279	-0.895
C	-8.38502	-0.11998	0.39966
C	1.87309	-3.1621	-1.73767
H	2.43263	-3.48142	-0.8543
H	2.31589	-2.23218	-2.11132
H	1.9917	-3.93298	-2.5015

H	2.94415	-0.94027	-0.64971
H	-2.1939	3.05166	1.08384
C	2.76284	-0.6208	0.37701
C	2.9475	-1.8702	1.26974
C	4.30609	-2.52218	0.97942
C	2.79173	-1.67739	2.7809
H	0.31077	-0.12654	1.47044
C	4.47694	-3.84361	1.71779
H	5.09999	-1.8239	1.28766
H	4.43463	-2.6599	-0.10336
C	2.94042	-3.00551	3.5175
H	3.54556	-0.9664	3.13853
H	1.82074	-1.22294	3.01459
C	4.28235	-3.66225	3.21801
H	5.45928	-4.28028	1.50256
H	3.73152	-4.56247	1.34274
H	2.82019	-2.85459	4.59654
H	2.13134	-3.68619	3.21067
H	4.36851	-4.62388	3.73751
H	5.08892	-3.02518	3.60957
C	3.66163	0.49902	0.76021
O	3.57599	1.04132	1.86574
C	4.71278	0.97695	-0.19961
C	4.74776	0.62932	-1.55784
C	5.69079	1.84874	0.30062
C	5.73896	1.14377	-2.38878
H	3.9713	-0.00058	-1.98558
C	6.69061	2.34287	-0.52484
H	5.63538	2.11917	1.35113
C	6.7163	1.99144	-1.8749
H	5.74297	0.8821	-3.44314
H	7.45017	3.00772	-0.12133
H	7.49444	2.38275	-2.5254
H	1.39574	-0.28234	1.22684
H	2.1597	-2.58239	0.9697
O	-3.88545	3.91497	1.26923
H	-4.10069	3.01258	0.96582
H	-4.12296	4.47816	0.52755

II (Hydrogenation segment, releasing 2.6a)



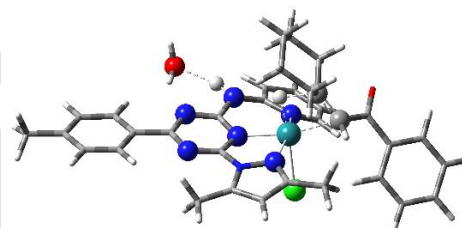
Ru	-0.70377	1.61614	0.43177
Cl	-0.41435	2.89172	2.67997
N	0.57204	-0.73448	1.57322
N	1.12499	0.96896	0.1407

N	-0.39156	3.35701	-0.64833	H	2.63057	-3.54164	-1.27768
N	3.30153	1.0345	-0.81998	H	1.68073	-1.55939	-2.42434
N	1.814	2.69179	-1.3046	H	-0.69537	-0.96579	-2.11628
N	-0.6848	-0.16413	1.53142	H	-1.21499	-4.31416	0.51013
N	2.74207	-0.6991	0.70542	C	-2.55872	-2.31452	-0.56809
C	1.54973	-0.15358	0.78684	O	-3.16959	-2.86687	0.34208
C	0.77017	3.6132	-1.29213	C	-3.2108	-1.31614	-1.49654
C	2.08363	1.53142	-0.6324	C	-4.73633	-1.26319	-1.51299
C	5.25429	-1.87787	0.34378	C	-5.37498	-2.60355	-1.88484
H	4.52057	-2.33506	1.00144	C	-5.35549	-0.72041	-0.22387
C	3.59648	-0.08607	-0.1384	C	-6.8892	-2.4802	-2.00618
C	4.91377	-0.6913	-0.32541	H	-5.12574	-3.34001	-1.11045
C	0.60726	-1.8207	2.42254	H	-4.94277	-2.97475	-2.82353
C	0.98918	4.80466	-1.99541	C	-6.86908	-0.59139	-0.34644
H	1.94361	4.95608	-2.49148	H	-5.10753	-1.40137	0.6
C	-0.66614	-1.93162	2.9239	H	-4.90861	0.25691	0.0137
H	-1.0122	-2.68246	3.61928	C	-7.50236	-1.92576	-0.72494
C	-1.19623	5.51848	-1.37294	H	-7.33366	-3.45019	-2.25712
H	-2.00795	6.2369	-1.36589	H	-7.13164	-1.80511	-2.84089
C	5.8617	-0.10791	-1.17653	H	-7.29877	-0.21186	0.5879
H	5.60205	0.80837	-1.69755	H	-7.10743	0.15349	-1.12051
C	-1.34368	4.32203	-0.7005	H	-8.58791	-1.81901	-0.83193
H	-2.25783	4.07983	-0.17324	H	-7.34006	-2.64435	0.09153
C	0.0007	5.7694	-2.04109	H	-2.78964	-0.32918	-1.23141
H	0.1644	6.6973	-2.57935	H	-2.84054	-1.50376	-2.5134
C	8.80429	-2.49671	-0.85515	H	-5.00213	-0.55036	-2.31207
H	8.72551	-3.50531	-1.27546	II (Alcoholysis segment, step-1)			
H	9.32942	-2.59871	0.1006				
H	9.43946	-1.90887	-1.52205				
C	7.10962	-0.69132	-1.34497	Ru	-0.60254	1.45585	1.226
H	7.83605	-0.22495	-2.00746	Cl	-0.46153	1.98294	3.77048
C	-1.43367	-0.89242	2.35625	N	0.49913	-1.23415	1.45585
C	6.50314	-2.45089	0.16974	N	1.14539	0.80106	0.61677
H	6.75193	-3.36851	0.69957	N	-0.17591	3.41526	0.75275
C	1.81507	-2.63092	2.68855	N	3.17888	0.97626	-0.60681
H	1.56955	-3.40951	3.41371	N	1.87145	2.82388	-0.33729
H	2.63406	-2.02271	3.08353	N	-0.66612	-0.56698	1.78519
H	2.18878	-3.0996	1.77353	N	2.54372	-1.1162	0.32397
C	7.45715	-1.86936	-0.67648	C	1.46215	-0.51599	0.76908
C	-2.85685	-0.55804	2.59048	C	0.95594	3.77514	0.10494
H	-3.37704	-0.3986	1.64038	C	2.0695	1.49215	-0.09242
H	-2.95325	0.34002	3.21246	C	4.83853	-2.32035	-0.75155
H	-3.37085	-1.37834	3.09404	H	4.12653	-2.91134	-0.18315
O	-2.77385	2.3482	1.00692	C	3.38796	-0.33286	-0.37725
H	-3.31951	1.60027	1.27358	C	4.58837	-0.95269	-0.93398
H	-2.39114	2.70683	1.84617				
H	-1.1701	0.91124	-0.93241				
H	2.62551	2.98969	-1.82693				
C	0.76851	-4.07149	-0.32372				
C	1.58018	-3.29088	-1.14701				
C	1.04612	-2.17757	-1.79344				
C	-0.29482	-1.84849	-1.62588				
C	-1.11516	-2.62215	-0.79246				
C	-0.56531	-3.73089	-0.13668				
H	1.18198	-4.94308	0.17808				

C	0.52509	-2.50272	1.99686
C	1.26383	5.11161	-0.17458
H	2.1891	5.34248	-0.69469
C	-0.65656	-2.62963	2.6839
H	-0.98345	-3.50217	3.23064
C	-0.75936	5.755	0.90859
H	-1.46956	6.49597	1.25735
C	5.51013	-0.19633	-1.67399
H	5.31787	0.86192	-1.81957
C	-0.99903	4.41749	1.15171
H	-1.88496	4.08768	1.67997
C	0.39999	6.11524	0.22416
H	0.63295	7.15413	0.0145
C	8.13675	-2.7853	-2.58475
H	8.06482	-3.87575	-2.60345
H	9.01733	-2.52917	-1.98405
H	8.34257	-2.44179	-3.60306
C	6.64074	-0.79195	-2.20913
H	7.34396	-0.19113	-2.78248
C	-1.36146	-1.41547	2.5447
C	5.97419	-2.90648	-1.29083
H	6.15351	-3.96921	-1.14133
C	1.64195	-3.45745	1.83001
H	1.41196	-4.37204	2.38016
H	2.58707	-3.04889	2.19911
H	1.79901	-3.70576	0.77598
C	6.89821	-2.15693	-2.02709
C	-2.65315	-1.02568	3.15719
H	-3.43744	-0.8926	2.40195
H	-2.52788	-0.09876	3.72917
H	-2.99946	-1.80486	3.83794
O	-2.70077	2.00722	1.86878
H	-3.22001	1.20134	1.73765
H	-2.4205	2.00937	2.81518
H	-1.0601	1.27226	-0.30053
H	2.65072	3.20469	-0.85423
C	-0.04022	-3.98429	-1.22795
C	0.71003	-3.0676	-1.96543
C	0.23298	-1.77144	-2.1448
C	-0.9801	-1.38676	-1.58304
C	-1.72905	-2.29157	-0.81543
C	-1.24333	-3.59649	-0.6532
H	0.32285	-5.00036	-1.09306
H	1.66564	-3.35973	-2.39444
H	0.81212	-1.0518	-2.71923
H	-1.32564	-0.36947	-1.73171
H	-1.83844	-4.28687	-0.06174
C	-3.01935	-1.94357	-0.14366
O	-3.61834	-2.8057	0.50554
C	-3.508	-0.55852	-0.27069
C	-4.77724	-0.12146	-0.0938
C	-5.97218	-0.97297	0.2159
C	-5.10193	1.33107	-0.30645
C	-7.06421	-0.78399	-0.84532
H	-6.37572	-0.64905	1.18886

H	-5.6899	-2.0196	0.32609
C	-6.17834	1.50248	-1.38222
H	-5.49337	1.74981	0.63491
H	-4.19882	1.89954	-0.55393
C	-7.41775	0.68323	-1.04752
H	-7.9498	-1.36387	-0.56389
H	-6.70818	-1.20619	-1.79506
H	-6.42631	2.56355	-1.49357
H	-5.77098	1.17355	-2.34829
H	-8.17207	0.79028	-1.83512
H	-7.87402	1.07808	-0.12775
H	-2.76668	0.19291	-0.53676

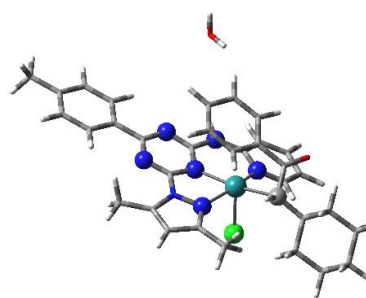
R-TS-1 (Alcoholysis segment, step-1)



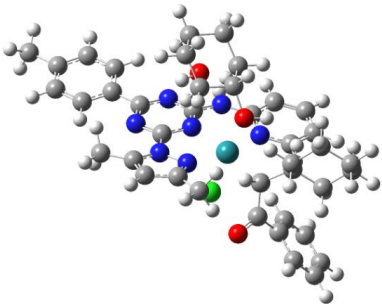
Ru	0.98032	-0.11712	0.00323
Cl	1.40589	-0.7093	-2.37402
N	-1.05049	-2.26733	-0.06757
N	-1.05641	0.00835	-0.32635
N	1.20578	1.86986	-0.58906
N	-3.10767	1.19684	-0.261
N	-1.12111	2.34863	-0.20645
N	0.31377	-2.14165	0.15997
N	-3.11584	-1.18033	-0.22632
C	-1.79719	-1.11112	-0.22939
C	0.16573	2.73225	-0.60413
C	-1.76861	1.15191	-0.28147
C	-5.90417	-1.21482	-0.29454
H	-5.34048	-2.13562	-0.18422
C	-3.74307	0.01095	-0.28361
C	-5.20528	0.00089	-0.35906
C	-1.42108	-3.59013	-0.21231
C	0.30261	4.05994	-1.02229
H	-0.56669	4.71034	-0.99608
C	-0.26206	-4.30815	-0.07951
H	-0.16959	-5.38254	-0.14608
C	2.56774	3.5859	-1.59663
H	3.53257	3.85589	-2.00961
C	-5.94313	1.18348	-0.51246
H	-5.42816	2.13594	-0.59293
C	2.36344	2.29518	-1.14893
H	3.13106	1.53906	-1.24134
C	1.52378	4.50097	-1.50157
H	1.64339	5.52878	-1.82974
C	-9.52203	-0.0962	-0.57982
H	-9.93248	0.82731	-0.99537
H	-9.95591	-0.22322	0.41871
H	-9.88242	-0.932	-1.18652

C	-7.32737	1.14694	-0.59173
H	-7.88062	2.07468	-0.72037
C	0.78713	-3.3868	0.13393
C	-7.28645	-1.24118	-0.37315
H	-7.80875	-2.19432	-0.3225
C	-2.80136	-4.05434	-0.47483
H	-2.78806	-5.13595	-0.62146
H	-3.22887	-3.58258	-1.36387
H	-3.47451	-3.81979	0.35439
C	-8.02777	-0.06169	-0.5192
C	2.23126	-3.69065	0.26878
H	2.59726	-3.53662	1.28943
H	2.82023	-3.05099	-0.39478
H	2.42133	-4.73205	0.00277
H	3.15572	-1.38529	0.96321
H	-1.78287	3.13065	-0.16848
C	2.9316	-0.31941	0.9938
C	1.95342	0.05715	2.00305
C	1.57295	-1.0405	2.98943
C	2.01053	1.41991	2.68781
H	0.50608	0.38411	1.45953
C	0.3018	-0.73806	3.76963
H	2.41373	-1.13462	3.69536
H	1.49387	-2.00111	2.47065
C	0.75544	1.71993	3.50224
H	2.89341	1.41592	3.34243
H	2.19978	2.20774	1.95794
C	0.41127	0.60481	4.48226
H	0.0934	-1.5417	4.48518
H	-0.54877	-0.71683	3.0692
H	0.87877	2.67192	4.03108
H	-0.09063	1.86396	2.81041
H	-0.51601	0.83501	5.02018
H	1.20067	0.53869	5.24552
C	4.10332	0.49352	0.64347
O	4.33073	1.62474	1.08761
C	5.0874	-0.11662	-0.30718
C	4.72476	-1.09589	-1.23918
C	6.40938	0.34435	-0.28121
C	5.67228	-1.61389	-2.11728
H	3.682	-1.39312	-1.32699
C	7.35871	-0.18978	-1.14268
H	6.66416	1.12528	0.43024
C	6.99196	-1.17319	-2.06199
H	5.37246	-2.3536	-2.85512
H	8.38667	0.16195	-1.10468
H	7.73282	-1.58446	-2.74303
O	-3.44125	4.02903	-0.09227
H	-3.66894	4.29097	0.804
H	-3.68334	3.08475	-0.13797

III (Alcoholysis segment, step-2)

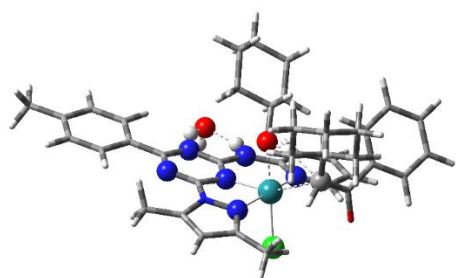


Ru	-1.01468	0.19569	-0.2291
Cl	-1.64347	0.61225	-2.50963
N	1.06096	2.28133	-0.35149
N	1.00114	-0.00622	-0.5266
N	-1.31488	-1.83131	-0.62928
N	3.01663	-1.24666	-0.304
N	1.00365	-2.34298	-0.26273
N	-0.31015	2.18908	-0.18259
N	3.09865	1.12699	-0.35003
C	1.78455	1.09695	-0.43031
C	-0.29657	-2.71872	-0.6106
C	1.68702	-1.1664	-0.38482
C	5.89465	1.0773	-0.29241
H	5.35636	2.01924	-0.25298
C	3.69722	-0.08061	-0.33855
C	5.15705	-0.11748	-0.34079
C	1.46139	3.59379	-0.48969
C	-0.48164	-4.07004	-0.92305
H	0.37153	-4.7404	-0.87719
C	0.30975	4.33843	-0.41546
H	0.24466	5.41388	-0.4957
C	-2.75967	-3.58221	-1.43933
H	-3.74873	-3.86029	-1.78368
C	5.86383	-1.32826	-0.40257
H	5.32289	-2.26734	-0.46878
C	-2.50753	-2.26756	-1.09696
H	-3.2651	-1.50043	-1.20083
C	-1.7308	-4.51147	-1.32352
H	-1.88703	-5.55711	-1.56998
C	9.48327	-0.16851	-0.32119
H	9.88477	-1.10441	-0.71788
H	9.86389	-0.06265	0.70164
H	9.90823	0.65615	-0.90078
C	7.25034	-1.33885	-0.40624
H	7.77776	-2.28871	-0.46336
C	-0.76443	3.44028	-0.23895
C	7.27916	1.0559	-0.29566
H	7.8303	1.99347	-0.25887
C	2.86287	4.02368	-0.69104
H	2.88356	5.10255	-0.85588
H	3.32327	3.52641	-1.54927
H	3.48866	3.78791	0.1741
C	7.98757	-0.15141	-0.34748
C	-2.21314	3.73851	-0.14831
H	-2.56983	3.74074	0.88797

H	-2.78535	2.98681	-0.69868	N	-1.32615	0.08885	-0.0621
H	-2.42729	4.72111	-0.57306	N	1.04098	1.62147	0.88265
H	-3.05405	1.46042	1.03561	N	-3.29993	1.37603	0.26802
H	1.64352	-3.13774	-0.16489	N	-1.31362	2.1261	1.09952
C	-2.76136	0.40865	1.06502	N	-0.04965	-1.90822	-1.17206
C	-1.65696	0.13618	2.03701	N	-3.3911	-0.60026	-1.04122
C	-1.29708	1.35597	2.89217	C	-2.09172	-0.71247	-0.83762
C	-1.65851	-1.14284	2.88619	C	0.02606	2.39762	1.34453
H	-0.61654	-0.06767	1.47329	C	-1.98318	1.16822	0.40325
C	0.02918	1.18061	3.6176	C	-6.13575	-0.2159	-1.46707
H	-2.10767	1.49112	3.62282	H	-5.58848	-0.94158	-2.06095
H	-1.2844	2.25384	2.26432	C	-3.97399	0.45159	-0.43604
C	-0.33648	-1.30421	3.63125	C	-5.42387	0.59604	-0.57063
H	-2.4978	-1.08487	3.5908	C	-1.92394	-2.87371	-2.07736
H	-1.86098	-2.01097	2.2583	C	0.25134	3.5505	2.1146
C	0.01817	-0.08277	4.47046	H	-0.61008	4.11007	2.46801
H	0.2543	2.06262	4.22743	C	-0.86008	-3.71619	-2.25027
H	0.8355	1.11098	2.86777	H	-0.88148	-4.67332	-2.75177
H	-0.36716	-2.20521	4.25376	C	2.59124	3.20255	1.88807
H	0.4661	-1.47341	2.89306	H	3.6306	3.47681	2.03639
H	0.98475	-0.2223	4.96814	C	-6.13932	1.52826	0.19477
H	-0.72689	0.03438	5.27071	H	-5.6162	2.14869	0.91676
C	-3.91352	-0.48154	0.91589	C	2.29443	2.0748	1.15046
O	-4.00944	-1.60348	1.42991	H	3.07841	1.49059	0.70039
C	-5.04162	0.00054	0.05348	C	1.53893	3.95915	2.40033
C	-4.87094	0.94564	-0.96484	H	1.71498	4.8515	2.99252
C	-6.30547	-0.57007	0.24753	C	-9.70786	0.9892	-1.00016
C	-5.94825	1.32294	-1.76141	H	-10.19742	0.02049	-1.136
H	-3.87496	1.3273	-1.17782	H	-9.95269	1.5919	-1.88246
C	-7.38416	-0.17853	-0.53425	H	-10.16362	1.48198	-0.1376
H	-6.40869	-1.32544	1.02163	C	-7.51527	1.64314	0.06184
C	-7.20786	0.7716	-1.54062	H	-8.05379	2.36467	0.67264
H	-5.79825	2.03852	-2.5656	C	0.27748	-3.09943	-1.68255
H	-8.36464	-0.61739	-0.36765	C	-7.50914	-0.08912	-1.59712
H	-8.04963	1.07049	-2.16011	H	-8.04253	-0.72512	-2.3007
O	3.27749	-4.07298	-0.01486	C	-3.33003	-3.03962	-2.5091
H	3.48827	-4.28779	0.8979	H	-3.42018	-3.98578	-3.04686
H	3.53505	-3.13536	-0.10712	H	-3.6475	-2.22698	-3.16789
IV (Alcoholysis segment, step-4) molecular complex formation with 2.2a				H	-4.0263	-3.04212	-1.66591
				C	-8.22755	0.84331	-0.83796
				C	1.63749	-3.68565	-1.64842
				H	1.99932	-3.7921	-0.61975
				H	2.35004	-3.04888	-2.18771
				H	1.61464	-4.67856	-2.10303
				H	-1.94308	2.87489	1.40714
				O	1.1301	-1.43091	1.66418
				H	1.88886	-1.00089	2.08447
				C	2.88352	-0.73817	-0.48819
				H	2.59977	-1.78671	-0.55044
				C	3.87604	-0.68593	0.70775
				C	4.23555	-2.12178	1.13161
				C	5.18275	0.10625	0.55393
Ru	0.71983	-0.15877	-0.17508	H	3.38855	-0.22955	1.5992
Cl	0.42702	1.07075	-2.21391	C	5.06217	-2.16759	2.40948
N	-1.41454	-1.77668	-1.40962	H	4.78984	-2.5939	0.3059

H	3.315	-2.70774	1.24978
C	6.00521	0.08378	1.83772
H	5.76609	-0.33359	-0.26858
H	5.00044	1.14327	0.24873
C	6.33157	-1.33754	2.27763
H	5.30046	-3.20354	2.67803
H	4.45752	-1.76831	3.241
H	6.92389	0.66739	1.70745
H	5.43365	0.58668	2.63483
H	6.89555	-1.33463	3.21785
H	6.98555	-1.80304	1.52606
C	3.35793	-0.42156	-1.85495
O	3.20713	-1.21664	-2.79179
C	4.07491	0.85857	-2.17577
C	3.59968	2.12196	-1.8141
C	5.28011	0.76982	-2.88129
C	4.33591	3.26564	-2.11189
H	2.62075	2.20382	-1.35472
C	6.02614	1.90865	-3.16121
H	5.62596	-0.21269	-3.19381
C	5.55989	3.16228	-2.76808
H	3.94461	4.24283	-1.83692
H	6.97109	1.82097	-3.69188
H	6.13948	4.05466	-2.99057
O	-3.49177	3.93828	1.48754
H	-3.47284	4.65627	0.84866
H	-3.76848	3.15934	0.96752
C	0.18762	-1.82237	2.68646
C	-0.47963	-0.62033	3.33176
C	-0.81407	-2.75521	2.0372
H	0.75646	-2.38095	3.44883
C	-1.57027	-1.04838	4.30865
H	-0.91532	-0.01491	2.52779
H	0.2725	0.01058	3.82485
C	-1.89728	-3.17697	3.02215
H	-1.26864	-2.2222	1.1931
H	-0.28894	-3.61874	1.61429
C	-2.58576	-1.9602	3.62926
H	-2.05888	-0.16513	4.73298
H	-1.11562	-1.58373	5.15513
H	-2.62229	-3.82752	2.52202
H	-1.45054	-3.77846	3.82739
H	-3.35984	-2.26869	4.33994
H	-3.10054	-1.40125	2.83192

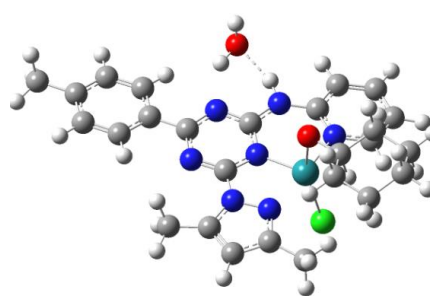
R-TS-3 (Alcoholysis segment, step-5)



Ru	0.53291	-0.12745	-1.24985
Cl	0.51663	0.01407	-3.59978
N	-1.42278	-2.25252	-1.07142
N	-1.39163	0.05124	-0.95406
N	0.8361	1.9298	-1.26734
N	-3.3555	1.2137	-0.29886
N	-1.45887	2.40188	-0.76262
N	-0.10097	-2.10583	-1.44203
N	-3.37864	-1.15856	-0.40793
C	-2.12498	-1.09058	-0.79394
C	-0.16158	2.81247	-1.05702
C	-2.07316	1.19216	-0.6758
C	-6.10261	-1.19491	0.23266
H	-5.60235	-2.10259	-0.08988
C	-3.97799	0.02715	-0.17179
C	-5.3766	0.0079	0.24868
C	-1.87406	-3.53319	-1.33833
C	0.04901	4.19647	-1.0941
H	-0.78502	4.86081	-0.88737
C	-0.80525	-4.18631	-1.89578
H	-0.79658	-5.21398	-2.22912
C	2.3194	3.7748	-1.69923
H	3.31647	4.09449	-1.98079
C	-6.03177	1.17153	0.67872
H	-5.48761	2.10984	0.73125
C	2.03937	2.42209	-1.65144
H	2.77809	1.67771	-1.94811
C	1.30828	4.68322	-1.3938
H	1.48839	5.75366	-1.41295
C	-9.53297	-0.1038	1.44171
H	-10.17894	-0.34273	0.58955
H	-9.86753	0.8528	1.84976
H	-9.71751	-0.87414	2.19735
C	-7.36357	1.13049	1.06571
H	-7.8512	2.04276	1.40266
C	0.27058	-3.26713	-1.97023
C	-7.43219	-1.22417	0.61681
H	-7.97697	-2.16583	0.59212
C	-3.24732	-4.00706	-1.05963
H	-3.32482	-5.05941	-1.33854
H	-3.99306	-3.43641	-1.6211
H	-3.50894	-3.89945	-0.00336
C	-8.0928	-0.06225	1.0385
C	1.6078	-3.45611	-2.57946
H	2.29759	-3.96771	-1.89948
H	2.04649	-2.49412	-2.85987
H	1.51934	-4.07156	-3.47831
H	-2.11355	3.17156	-0.58483
O	0.65304	-0.57977	0.96176
H	1.60926	-0.74127	0.69385
C	3.10082	-1.2212	-0.247
H	2.8571	-1.99768	-0.97222
C	3.49726	-1.84053	1.09459
C	2.67203	-3.1034	1.36874

C	4.99227	-2.18825	1.16874
H	3.30677	-1.15819	1.9439
C	3.03081	-3.74562	2.70258
H	2.8644	-3.8212	0.55453
H	1.59965	-2.87334	1.32609
C	5.36295	-2.82838	2.50179
H	5.225	-2.87746	0.34244
H	5.59007	-1.28591	0.99372
C	4.51907	-4.06646	2.77991
H	2.43181	-4.64912	2.86898
H	2.76754	-3.05037	3.51574
H	6.43052	-3.07688	2.52498
H	5.20224	-2.09484	3.30674
H	4.77224	-4.4973	3.75596
H	4.75627	-4.83713	2.03143
C	3.81584	-0.17041	-0.89802
O	3.86467	-0.0616	-2.14839
C	4.47444	0.93888	-0.11585
C	5.48918	1.66276	-0.75436
C	4.06318	1.35423	1.15588
C	6.08847	2.75228	-0.13418
H	5.77223	1.35085	-1.75605
C	4.63885	2.46457	1.7681
H	3.26032	0.82305	1.66029
C	5.65961	3.16292	1.12765
H	6.88553	3.29316	-0.63855
H	4.28726	2.78665	2.74592
H	6.11625	4.02466	1.60787
C	0.58345	0.15621	2.19493
C	0.53156	1.66152	2.00501
C	-0.62943	-0.33465	2.96698
H	1.49092	-0.09975	2.77225
C	0.45697	2.36581	3.35558
H	-0.37102	1.89972	1.42715
H	1.39042	2.00759	1.41822
C	-0.73975	0.3711	4.31468
H	-1.52785	-0.13214	2.36314
H	-0.56833	-1.42215	3.0867
C	-0.75306	1.88709	4.15081
H	0.42515	3.45137	3.21281
H	1.37566	2.1576	3.92469
H	-1.63316	0.02993	4.84848
H	0.11812	0.08372	4.93997
H	-0.79087	2.37766	5.12969
H	-1.6692	2.18468	3.61937
O	-3.75572	4.03549	-0.30825
H	-3.99067	3.08906	-0.26913
H	-4.15916	4.34951	-1.12225

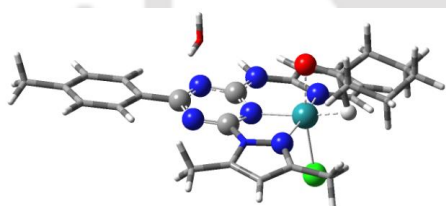
V (Alcohololysis segment, step-6)



Ru	-1.48842	-0.02538	0.41188
N	0.43533	-2.19764	0.36022
N	0.46228	0.10128	0.31254
N	-1.74107	2.01129	0.49316
N	2.50674	1.2354	-0.11037
N	0.57476	2.44575	0.0733
N	-0.9256	-2.02754	0.49904
N	2.49125	-1.13306	0.02768
C	1.1959	-1.04748	0.22361
C	-0.717	2.8781	0.34287
C	1.18877	1.22988	0.09631
C	5.24445	-1.22448	-0.42708
H	4.6568	-2.1365	-0.40938
C	3.13451	0.04283	-0.11424
C	4.58466	0.00635	-0.28769
C	0.79369	-3.51812	0.54686
C	-0.89853	4.26365	0.45186
H	-0.03957	4.91567	0.32244
C	-0.37934	-4.1815	0.80999
H	-0.47451	-5.23933	1.00835
C	-3.20603	3.8753	0.93686
H	-4.2044	4.21367	1.18884
C	5.35951	1.17766	-0.30455
H	4.88273	2.14399	-0.17036
C	-2.95459	2.52422	0.81118
H	-3.72848	1.77888	0.97287
C	-2.15225	4.76887	0.74258
H	-2.3014	5.84001	0.83242
C	8.87775	-0.16982	-0.80076
H	9.15676	0.09323	-1.82783
H	9.27338	-1.16958	-0.60496
H	9.39788	0.53461	-0.14471
C	6.73514	1.11309	-0.46052
H	7.31651	2.03274	-0.46
C	-1.42301	-3.22739	0.787
C	6.62026	-1.27781	-0.58611
H	7.11072	-2.24306	-0.69369
C	2.1823	-4.02135	0.46433
H	2.18625	-5.09378	0.66762
H	2.83999	-3.52259	1.18193
H	2.61808	-3.84832	-0.52388
C	7.39491	-0.11315	-0.60876
C	-2.86739	-3.39941	1.06536
H	-3.35317	-4.04594	0.32645
H	-3.36608	-2.42639	1.07081

H	-3.01696	-3.85041	2.05038
O	-1.76908	-0.01511	-1.64099
Cl	-2.01705	-0.11671	2.77428
H	1.24188	3.20362	-0.10632
C	-3.08784	-0.28323	-1.44339
C	-4.03963	0.78601	-1.98875
C	-3.51288	-1.68073	-1.89992
H	-3.3237	-0.2824	-0.27703
C	-5.49653	0.47781	-1.6623
H	-3.89167	0.81101	-3.07732
H	-3.73502	1.76929	-1.61322
C	-4.97023	-1.98004	-1.57227
H	-3.35487	-1.71568	-2.98684
H	-2.82929	-2.41723	-1.46357
C	-5.89552	-0.91257	-2.14642
H	-6.15527	1.24085	-2.09249
H	-5.6415	0.53072	-0.57156
H	-5.25136	-2.97546	-1.93652
H	-5.09651	-2.00917	-0.47879
H	-6.93782	-1.12521	-1.88331
H	-5.84151	-0.94048	-3.24455
O	2.86272	4.02358	-0.57935
H	3.08983	3.07675	-0.5012
H	2.9112	4.20117	-1.52272

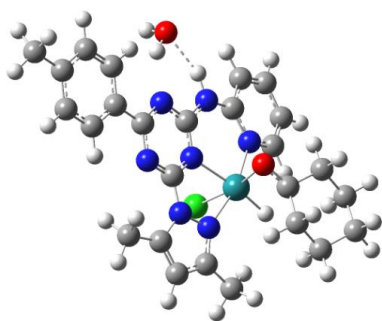
R-TS-4 (Alcoholysis segment, step-7)



Ru	1.58432	-0.07345	-0.27607
N	-0.42643	-2.20838	-0.33311
N	-0.4509	0.08525	-0.33461
N	1.82309	1.96864	-0.43902
N	-2.47135	1.24429	0.11839
N	-0.51303	2.41692	-0.06976
N	0.94802	-2.06851	-0.40621
N	-2.47862	-1.12929	-0.02255
C	-1.17961	-1.04813	-0.22639
C	0.78221	2.82979	-0.37527
C	-1.14942	1.21499	-0.1006
C	-5.23526	-1.18452	0.40332
H	-4.65813	-2.10331	0.39253
C	-3.10521	0.0584	0.11142
C	-4.5598	0.03824	0.27098
C	-0.81093	-3.50926	-0.59923
C	0.94189	4.20449	-0.5995
H	0.07029	4.8488	-0.53022
C	0.3524	-4.19072	-0.84993
H	0.42839	-5.23895	-1.10093
C	3.25243	3.8172	-1.05127

H	4.24456	4.14818	-1.33618
C	-5.31802	1.21923	0.27835
H	-4.82601	2.17855	0.14914
C	3.02545	2.47847	-0.80875
H	3.80988	1.73464	-0.90542
C	2.18544	4.70763	-0.93083
H	2.31562	5.7698	-1.11156
C	-8.85723	-0.08557	0.73977
H	-9.13184	0.01988	1.7961
H	-9.28134	-1.03161	0.39324
H	-9.35304	0.72696	0.2017
C	-6.69647	1.17254	0.41825
H	-7.2668	2.09891	0.40989
C	1.41812	-3.26689	-0.7409
C	-6.61312	-1.22041	0.54657
H	-7.11721	-2.17922	0.6484
C	-2.21413	-3.97832	-0.60041
H	-2.23714	-5.03353	-0.87856
H	-2.8332	-3.412	-1.30201
H	-2.68044	-3.86209	0.38217
C	-7.37249	-0.04502	0.5599
C	2.86358	-3.467	-0.98945
H	3.35294	-4.01478	-0.17608
H	3.34896	-2.49524	-1.11126
H	3.01396	-4.03895	-1.90877
O	1.63154	-0.02733	1.83283
Cl	1.904	-0.16166	-2.68247
H	-1.16682	3.18949	0.09323
C	2.89831	-0.26475	1.57272
C	3.88001	0.83993	1.95455
C	3.42381	-1.65468	1.91642
H	3.23777	-0.30544	0.0474
C	5.30562	0.57554	1.4904
H	3.8526	0.87818	3.05382
H	3.49892	1.80529	1.61017
C	4.85889	-1.8908	1.46307
H	3.36723	-1.72509	3.01317
H	2.7311	-2.40489	1.52378
C	5.7916	-0.79163	1.95675
H	5.97352	1.36929	1.84411
H	5.34112	0.60861	0.39046
H	5.20407	-2.87601	1.79872
H	4.8918	-1.91089	0.36448
H	6.81453	-0.97428	1.60933
H	5.82944	-0.80768	3.05599
O	-2.78487	4.0464	0.53327
H	-3.02148	3.10033	0.48008
H	-2.82855	4.24932	1.47174

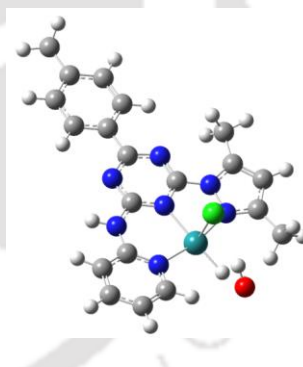
VI (Alcoholysis segment, step-8)



Ru	1.71955	-0.0909	-0.32618
N	-0.36186	-2.19518	-0.40515
N	-0.40141	0.09106	-0.34128
N	1.93827	1.96948	-0.40834
N	-2.41112	1.26224	0.06758
N	-0.43047	2.41262	-0.0969
N	1.01859	-2.07204	-0.49931
N	-2.41876	-1.12119	-0.07139
C	-1.1129	-1.03668	-0.26586
C	0.88802	2.82103	-0.32728
C	-1.07713	1.22011	-0.12386
C	-5.19371	-1.14782	0.15376
H	-4.64925	-2.04975	-0.10601
C	-3.03188	0.07419	0.07757
C	-4.48436	0.05316	0.28504
C	-0.76546	-3.49079	-0.68118
C	1.04839	4.20805	-0.46689
H	0.17376	4.84533	-0.37214
C	0.38398	-4.18238	-0.95699
H	0.44344	-5.22867	-1.22025
C	3.37137	3.8611	-0.87099
H	4.37008	4.21298	-1.10329
C	-5.1945	1.21477	0.62449
H	-4.66387	2.15357	0.75219
C	3.14777	2.51047	-0.70714
H	3.94046	1.77751	-0.80686
C	2.29531	4.73766	-0.73274
H	2.42247	5.80966	-0.84384
C	-8.75596	-0.0682	0.92151
H	-8.99261	0.05474	1.98441
H	-9.19197	-1.01588	0.59691
H	-9.26993	0.73994	0.39227
C	-6.56481	1.16961	0.82217
H	-7.09756	2.07925	1.09074
C	1.46389	-3.273	-0.85054
C	-6.56638	-1.18251	0.34813
H	-7.10167	-2.12285	0.23563
C	-2.17208	-3.9502	-0.67277
H	-2.19932	-5.01119	-0.92799
H	-2.78417	-3.39961	-1.39306
H	-2.64179	-3.80822	0.30436
C	-7.2789	-0.02833	0.68807
C	2.90615	-3.50315	-1.08637
H	3.38562	-3.98096	-0.22418

H	3.40164	-2.54733	-1.27603
H	3.05301	-4.15708	-1.9495
O	1.30876	-0.03479	1.73795
H	3.30256	-0.33693	-0.5153
Cl	1.75388	-0.04484	-2.74718
H	-1.08486	3.19544	-0.00368
C	2.58578	-0.3067	1.66521
C	3.56155	0.7641	2.12796
C	3.04893	-1.70922	2.02174
C	5.01014	0.47654	1.75447
H	3.48051	0.78424	3.2281
H	3.23073	1.74956	1.79004
C	4.50513	-1.97449	1.65432
H	2.9366	-1.80017	3.11567
H	2.37132	-2.44816	1.58479
C	5.43051	-0.90931	2.22824
H	5.66971	1.24706	2.17132
H	5.11752	0.52432	0.66128
H	4.80514	-2.97364	1.99454
H	4.60271	-1.96856	0.56073
H	6.46988	-1.11335	1.94639
H	5.39501	-0.94409	3.32769
O	-2.75757	4.09384	-0.04997
H	-3.00726	4.35555	-0.94054
H	-2.99939	3.14984	-0.00109

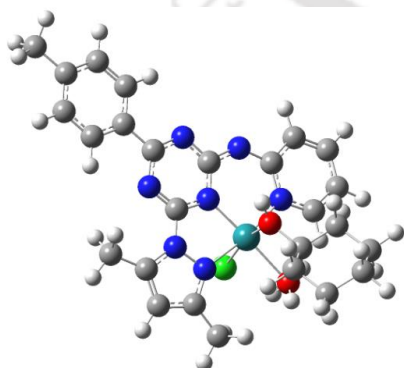
VII (Alcoholysis segment, step-9)



Ru	-2.33957	0.12409	-0.10285
N	-0.11157	2.03672	-0.16341
N	-0.29755	-0.24417	-0.09615
N	-2.77109	-1.90875	-0.1785
N	1.63587	-1.61662	0.00272
N	-0.44675	-2.57177	0.00227
N	-1.50049	2.0302	-0.10394
N	1.85895	0.76139	-0.06837
C	0.54355	0.8121	-0.11326
C	-1.80943	-2.8655	-0.1268
C	0.31674	-1.43622	-0.03885
C	4.64782	0.52067	0.00371
H	4.18097	1.50039	-0.02335
C	2.37269	-0.49126	-0.01961
C	3.82865	-0.61933	0.01096
C	0.37028	3.31891	-0.33622
C	-2.11985	-4.23119	-0.18385

H	-1.3149	-4.95815	-0.12179
C	-0.73824	4.12578	-0.39958
H	-0.73134	5.19768	-0.53483
C	-4.41756	-3.6583	-0.45334
H	-5.4597	-3.91159	-0.61012
C	4.43731	-1.88137	0.04719
H	3.80736	-2.76486	0.05245
C	-4.05027	-2.32976	-0.37963
H	-4.7705	-1.52912	-0.52161
C	-3.43194	-4.63644	-0.33542
H	-3.67553	-5.6932	-0.38033
C	8.13226	-0.98454	0.09201
H	8.45193	-2.02321	0.20458
H	8.56962	-0.40819	0.91375
H	8.57979	-0.59917	-0.83076
C	5.81951	-1.99472	0.07422
H	6.27786	-2.98109	0.10133
C	-1.87657	3.29693	-0.26518
C	6.02652	0.39657	0.0326
H	6.6467	1.2905	0.02894
C	1.80594	3.66542	-0.42746
H	1.90326	4.74129	-0.58365
H	2.29783	3.14228	-1.25255
H	2.35063	3.38853	0.47955
C	6.64108	-0.8627	0.06787
C	-3.31158	3.65295	-0.32741
H	-3.49615	4.64318	0.09555
H	-3.90965	2.90422	0.1965
H	-3.65465	3.66088	-1.36783
H	-3.9154	0.55769	0.01514
Cl	-2.4398	0.22255	-2.45444
H	0.14249	-3.39122	0.04045
O	-5.71772	0.08635	-1.82752
H	-5.19096	0.49341	-1.12128
H	-5.03084	-0.04698	-2.49312

VIII (dehydrogenation inner sphere MLC
pathway for **2.2a**) Step1:

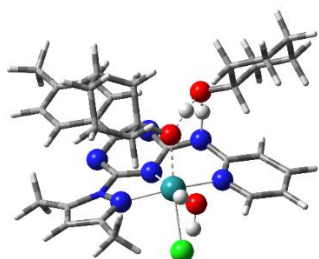


Ru	-0.07819	-1.52149	-3.6309
Cl	-1.21202	-2.5576	-5.7235
N	-2.22018	-2.261	-1.79292
N	-1.47251	-0.37105	-2.85795
N	0.76239	0.01971	-4.73723

N	-2.5732	1.70521	-2.47299
N	-0.79761	1.63062	-3.89272
N	-1.20899	-2.87538	-2.50708
N	-3.32554	-0.24716	-1.34857
C	-2.37464	-0.89742	-1.98236
C	0.26878	1.27899	-4.71389
C	-1.63891	0.95923	-3.05108
C	-5.33553	1.24056	-0.06685
H	-5.22691	0.18048	0.1398
C	-3.40247	1.07118	-1.6263
C	-4.44987	1.84888	-0.96798
C	-3.03287	-3.18831	-1.1718
C	0.80341	2.30962	-5.49719
H	0.36176	3.30014	-5.43746
C	-2.511	-4.41258	-1.50899
H	-2.89682	-5.37286	-1.19828
C	2.38886	0.7611	-6.36702
H	3.22407	0.49623	-7.00545
C	-4.59289	3.22115	-1.2222
H	-3.90656	3.69689	-1.91561
C	1.81105	-0.20673	-5.56973
H	2.17304	-1.22742	-5.55937
C	1.87434	2.05584	-6.33331
H	2.29254	2.84812	-6.94565
C	-7.57353	4.14096	0.94667
H	-7.9253	3.6688	1.86777
H	-8.4412	4.23615	0.28306
H	-7.25018	5.1577	1.18845
C	-5.58951	3.95313	-0.59682
H	-5.68468	5.01729	-0.80342
C	-1.39649	-4.18404	-2.34642
C	-6.32914	1.98214	0.55382
H	-7.00635	1.49487	1.25254
C	-4.21117	-2.84516	-0.3454
H	-4.6653	-3.76579	0.02631
H	-4.95755	-2.28671	-0.91769
H	-3.94392	-2.21393	0.50695
C	-6.47984	3.34991	0.30017
C	-0.54083	-5.16942	-3.04699
H	0.50541	-5.11319	-2.72905
H	-0.5844	-4.9828	-4.12708
H	-0.8955	-6.18471	-2.85986
O	1.44918	-2.91796	-4.48252
H	1.78085	-3.59152	-3.85339
H	0.81434	-3.33671	-5.09987
H	-1.06233	2.6036	-3.9476
H	0.85958	-1.10426	-2.39087
C	4.47045	-1.58252	-0.99839
C	3.85006	-2.38165	-2.15512
C	3.2783	-3.69234	-1.64011
C	2.08544	-3.4281	-0.73214
C	2.29089	-2.16768	0.12111
C	3.77104	-1.87362	0.33716
H	5.53981	-1.80841	-0.91092
H	3.02807	-1.81776	-2.6187

H	1.20782	-3.28417	-1.37617
H	1.82906	-1.31435	-0.39417
H	4.24235	-2.73754	0.8266
H	3.58883	-4.80043	-3.22628
H	4.06136	-4.23664	-1.08515
H	4.59064	-2.56542	-2.94407
H	4.40364	-0.5135	-1.22838
H	3.90499	-1.03248	1.02517
H	1.7674	-2.26796	1.07723
H	1.89336	-4.31216	-0.11316
O	2.81926	-4.54852	-2.7044

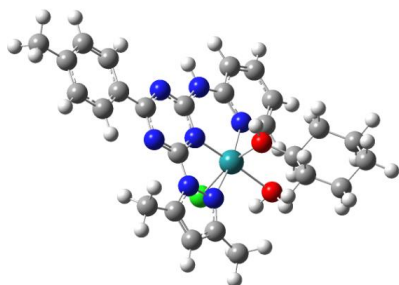
I-TS-1 (dehydrogenation inner sphere MLC pathway for **2.2a**) Step2:



Ru	1.10364	-1.35777	-0.81444
Cl	1.32501	-2.77417	-2.8039
N	-1.58243	-2.36063	-0.27956
N	-0.62386	-0.40707	-1.02342
N	2.14035	0.13262	-1.78055
N	-1.86671	1.60829	-0.89298
N	0.36852	1.74057	-1.3613
N	-0.28435	-2.80737	-0.17225
N	-2.93947	-0.46848	-0.44233
C	-1.75862	-1.0207	-0.6142
C	1.55805	1.34734	-1.9723
C	-0.71778	0.96214	-1.12106
C	-5.39808	0.84968	-0.15611
H	-5.33589	-0.22642	-0.02559
C	-2.94781	0.87349	-0.61392
C	-4.23153	1.5628	-0.46342
C	-2.48742	-3.36943	-0.04128
C	2.21057	2.34214	-2.71373
H	1.69463	3.28754	-2.84161
C	-1.72781	-4.4898	0.20307
H	-2.10774	-5.4788	0.41563
C	4.03601	0.85171	-3.08116
H	5.00359	0.60022	-3.50156
C	-4.3177	2.95276	-0.63002
H	-3.41265	3.50301	-0.86725
C	3.34319	-0.09898	-2.35556
H	3.74475	-1.09314	-2.20318
C	3.45823	2.10622	-3.26487
H	3.9631	2.87816	-3.83797
C	-8.01991	3.59937	-0.07185
H	-8.46752	3.76915	-1.05824
H	-7.91334	4.58161	0.39758

H	-8.74043	3.0202	0.5117
C	-5.53462	3.60141	-0.49215
H	-5.58588	4.68062	-0.62223
C	-0.37328	-4.10864	0.10381
C	-6.61083	1.50842	-0.01985
H	-7.50741	0.94163	0.22302
C	-3.95716	-3.19926	-0.07593
H	-4.43236	-4.17131	0.06876
H	-4.29708	-2.77926	-1.02652
H	-4.3035	-2.51459	0.70305
C	-6.70471	2.89438	-0.18767
C	0.84095	-4.95137	0.21711
H	1.4402	-4.70015	1.10127
H	1.46292	-4.82794	-0.67705
H	0.57171	-6.00589	0.2983
O	3.04858	-2.41727	-0.41292
H	2.99534	-2.88119	0.43076
H	2.92726	-3.08661	-1.11536
O	1.24463	2.20737	0.88363
H	0.71795	2.22281	-0.28293
H	1.24865	1.08725	0.99202
O	1.2626	-0.23904	1.01678
C	0.53641	-0.77425	2.09997
C	1.24716	-1.995	2.67354
C	0.29051	0.25056	3.20453
H	-0.46633	-1.1077	1.75837
C	0.4346	-2.63967	3.78692
H	2.23098	-1.67408	3.04973
H	1.42854	-2.70501	1.85649
C	-0.52024	-0.37395	4.33721
H	1.25914	0.60634	3.58641
H	-0.22245	1.12775	2.79322
C	0.1488	-1.6277	4.89218
H	0.949	-3.52047	4.18981
H	-0.51611	-3.00291	3.36546
H	-0.68449	0.35868	5.13518
H	-1.51797	-0.63898	3.95675
H	-0.47018	-2.07665	5.67736
H	1.0986	-1.34668	5.37061
C	2.60323	2.6561	0.85991
C	2.64936	4.11965	0.45934
C	3.24624	2.42914	2.21858
H	3.1692	2.06899	0.11103
C	4.08445	4.63385	0.4647
H	2.03723	4.69072	1.17143
H	2.18609	4.24788	-0.52698
C	4.67977	2.94874	2.23497
H	2.64292	2.95047	2.97593
H	3.20986	1.36004	2.46097
C	4.74071	4.41583	1.82357
H	4.11072	5.69299	0.18656
H	4.66069	4.09928	-0.30601
H	5.12537	2.80413	3.22521
H	5.28615	2.35401	1.53614
H	5.77844	4.76759	1.80973

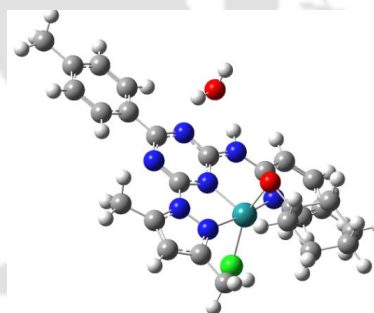
H 4.21762 5.02348 2.57626
IX (dehydrogenation inner sphere MLC
 pathway for **2.2a**) Step 3:



Ru	1.62176	0.47518	-0.59221
N	-0.32559	-1.56998	-1.26207
N	-0.32638	0.56532	-0.41782
N	1.86647	2.44656	0.02537
N	-2.34389	1.47104	0.45815
N	-0.40079	2.61355	0.75078
N	1.04589	-1.40778	-1.26996
N	-2.37241	-0.66616	-0.57923
C	-1.07627	-0.53249	-0.73616
C	0.87635	3.13591	0.6332
C	-1.0379	1.51099	0.24444
C	-5.17049	-0.79465	-0.27252
H	-4.64077	-1.61018	-0.75518
C	-2.99338	0.38106	0.0059
C	-4.44009	0.31541	0.17809
C	-0.6891	-2.79749	-1.77404
C	1.07728	4.42171	1.15436
H	0.25435	4.92191	1.65599
C	0.4907	-3.41018	-2.12123
H	0.58794	-4.3904	-2.56519
C	3.30776	4.367	0.31276
H	4.27743	4.81529	0.13025
C	-5.13605	1.3678	0.79369
H	-4.57509	2.23053	1.13841
C	3.03953	3.09766	-0.15667
H	3.77507	2.55335	-0.73865
C	2.30413	5.04013	1.00875
H	2.46686	6.03516	1.40969
C	-8.72641	0.12914	0.7052
H	-8.97732	-0.19841	1.72119
H	-9.19441	-0.57811	0.01556
H	-9.2008	1.10474	0.56396
C	-6.51082	1.30649	0.95175
H	-7.03404	2.13295	1.42865
C	1.54261	-2.52329	-1.80399
C	-6.54652	-0.84513	-0.10973
H	-7.09878	-1.71151	-0.46842
C	-2.08629	-3.27013	-1.88811
H	-2.09295	-4.25248	-2.36424
H	-2.70044	-2.58537	-2.4799
H	-2.56928	-3.34643	-0.90953

C	-7.24473	0.19947	0.50678
C	2.99856	-2.68975	-2.02455
H	3.22822	-3.71785	-2.31044
H	3.56998	-2.43408	-1.12831
H	3.34289	-2.02476	-2.82439
O	1.79426	-0.00341	1.37451
Cl	2.13537	1.1898	-2.92442
H	-1.06245	3.21551	1.21922
O	3.83326	0.08101	-0.74697
H	3.93814	0.47333	-1.63779
H	4.3339	0.62364	-0.12676
C	2.2075	-1.30435	1.65744
C	3.24146	-1.28221	2.78457
C	1.04501	-2.22597	2.03633
H	2.71331	-1.75991	0.77925
C	3.73278	-2.68408	3.12606
H	2.77985	-0.81533	3.66678
H	4.07505	-0.63133	2.49087
C	1.5299	-3.63327	2.36788
H	0.53222	-1.78748	2.90515
H	0.31161	-2.24675	1.2202
C	2.57213	-3.60658	3.48166
H	4.46357	-2.65154	3.94305
H	4.26445	-3.10027	2.2564
H	0.68927	-4.28264	2.64013
H	1.98046	-4.0786	1.46613
H	2.93582	-4.61878	3.69531
H	2.09823	-3.24667	4.40689

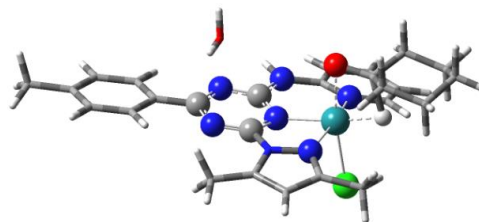
X (dehydrogenation inner sphere MLC
 pathway for **2.2a**) Step 4:



Ru	-1.48842	-0.02538	0.41188
N	0.43533	-2.19764	0.36022
N	0.46228	0.10128	0.31254
N	-1.74107	2.01129	0.49316
N	2.50674	1.2354	-0.11037
N	0.57476	2.44575	0.0733
N	-0.9256	-2.02754	0.49904
N	2.49125	-1.13306	0.02768
C	1.1959	-1.04748	0.22361
C	-0.717	2.8781	0.34287
C	1.18877	1.22988	0.09631
C	5.24445	-1.22448	-0.42708
H	4.6568	-2.1365	-0.40938

C	3.13451	0.04283	-0.11424
C	4.58466	0.00635	-0.28769
C	0.79369	-3.51812	0.54686
C	-0.89853	4.26365	0.45186
H	-0.03957	4.91567	0.32244
C	-0.37934	-4.1815	0.80999
H	-0.47451	-5.23933	1.00835
C	-3.20603	3.8753	0.93686
H	-4.2044	4.21367	1.18884
C	5.35951	1.17766	-0.30455
H	4.88273	2.14399	-0.17036
C	-2.95459	2.52422	0.81118
H	-3.72848	1.77888	0.97287
C	-2.15225	4.76887	0.74258
H	-2.3014	5.84001	0.83242
C	8.87775	-0.16982	-0.80076
H	9.15676	0.09323	-1.82783
H	9.27338	-1.16958	-0.60496
H	9.39788	0.53461	-0.14471
C	6.73514	1.11309	-0.46052
H	7.31651	2.03274	-0.46
C	-1.42301	-3.22739	0.787
C	6.62026	-1.27781	-0.58611
H	7.11072	-2.24306	-0.69369
C	2.1823	-4.02135	0.46433
H	2.18625	-5.09378	0.66762
H	2.83999	-3.52259	1.18193
H	2.61808	-3.84832	-0.52388
C	7.39491	-0.11315	-0.60876
C	-2.86739	-3.39941	1.06536
H	-3.35317	-4.04594	0.32645
H	-3.36608	-2.42639	1.07081
H	-3.01696	-3.85041	2.05038
O	-1.76908	-0.01511	-1.64099
Cl	-2.01705	-0.11671	2.77428
H	1.24188	3.20362	-0.10632
C	-3.08784	-0.28323	-1.44339
C	-4.03963	0.78601	-1.98875
C	-3.51288	-1.68073	-1.89992
H	-3.3237	-0.2824	-0.27703
C	-5.49653	0.47781	-1.6623
H	-3.89167	0.81101	-3.07732
H	-3.73502	1.76929	-1.61322
C	-4.97023	-1.98004	-1.57227
H	-3.35487	-1.71568	-2.98684
H	-2.82929	-2.41723	-1.46357
C	-5.89552	-0.91257	-2.14642
H	-6.15527	1.24085	-2.09249
H	-5.6415	0.53072	-0.57156
H	-5.25136	-2.97546	-1.93652
H	-5.09651	-2.00917	-0.47879
H	-6.93782	-1.12521	-1.88331
H	-5.84151	-0.94048	-3.24455
O	2.86272	4.02358	-0.57935
H	3.08983	3.07675	-0.5012

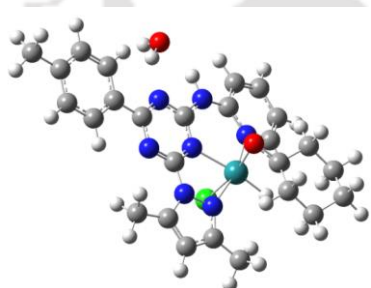
H 2.9112 4.20117 -1.52272
I-TS-2 (dehydrogenation inner sphere MLC
pathway for **2.2a**) Step 5:



Ru	1.58432	-0.07345	-0.27607
N	-0.42643	-2.20838	-0.33311
N	-0.4509	0.08525	-0.33461
N	1.82309	1.96864	-0.43902
N	-2.47135	1.24429	0.11839
N	-0.51303	2.41692	-0.06976
N	0.94802	-2.06851	-0.40621
N	-2.47862	-1.12929	-0.02255
C	-1.17961	-1.04813	-0.22639
C	0.78221	2.82979	-0.37527
C	-1.14942	1.21499	-0.1006
C	-5.23526	-1.18452	0.40332
H	-4.65813	-2.10331	0.39253
C	-3.10521	0.0584	0.11142
C	-4.5598	0.03824	0.27098
C	-0.81093	-3.50926	-0.59923
C	0.94189	4.20449	-0.5995
H	0.07029	4.8488	-0.53022
C	0.3524	-4.19072	-0.84993
H	0.42839	-5.23895	-1.10093
C	3.25243	3.8172	-1.05127
H	4.24456	4.14818	-1.33618
C	-5.31802	1.21923	0.27835
H	-4.82601	2.17855	0.14914
C	3.02545	2.47847	-0.80875
H	3.80988	1.73464	-0.90542
C	2.18544	4.70763	-0.93083
H	2.31562	5.7698	-1.11156
C	-8.85723	-0.08557	0.73977
H	-9.13184	0.01988	1.7961
H	-9.28134	-1.03161	0.39324
H	-9.35304	0.72696	0.2017
C	-6.69647	1.17254	0.41825
H	-7.2668	2.09891	0.40989
C	1.41812	-3.26689	-0.7409
C	-6.61312	-1.22041	0.54657
H	-7.11721	-2.17922	0.6484
C	-2.21413	-3.97832	-0.60041
H	-2.23714	-5.03353	-0.87856
H	-2.8332	-3.412	-1.30201
H	-2.68044	-3.86209	0.38217
C	-7.37249	-0.04502	0.5599
C	2.86358	-3.467	-0.98945

H	3.35294	-4.01478	-0.17608
H	3.34896	-2.49524	-1.11126
H	3.01396	-4.03895	-1.90877
O	1.63154	-0.02733	1.83283
Cl	1.904	-0.16166	-2.68247
H	-1.16682	3.18949	0.09323
C	2.89831	-0.26475	1.57272
C	3.88001	0.83993	1.95455
C	3.42381	-1.65468	1.91642
H	3.23777	-0.30544	0.0474
C	5.30562	0.57554	1.4904
H	3.8526	0.87818	3.05382
H	3.49892	1.80529	1.61017
C	4.85889	-1.8908	1.46307
H	3.36723	-1.72509	3.01317
H	2.7311	-2.40489	1.52378
C	5.7916	-0.79163	1.95675
H	5.97352	1.36929	1.84411
H	5.34112	0.60861	0.39046
H	5.20407	-2.87601	1.79872
H	4.8918	-1.91089	0.36448
H	6.81453	-0.97428	1.60933
H	5.82944	-0.80768	3.05599
O	-2.78487	4.0464	0.53327
H	-3.02148	3.10033	0.48008
H	-2.82855	4.24932	1.47174

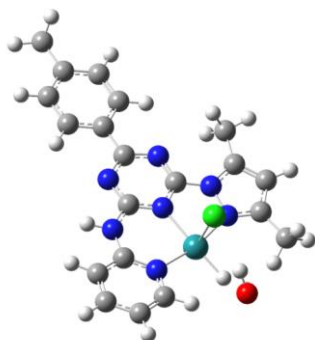
XI (dehydrogenation inner sphere MLC pathway for **2.2a**) Step 6:



Ru	1.71955	-0.0909	-0.32618
N	-0.36186	-2.19518	-0.40515
N	-0.40141	0.09106	-0.34128
N	1.93827	1.96948	-0.40834
N	-2.41112	1.26224	0.06758
N	-0.43047	2.41262	-0.0969
N	1.01859	-2.07204	-0.49931
N	-2.41876	-1.12119	-0.07139
C	-1.1129	-1.03668	-0.26586
C	0.88802	2.82103	-0.32728
C	-1.07713	1.22011	-0.12386
C	-5.19371	-1.14782	0.15376
H	-4.64925	-2.04975	-0.10601
C	-3.03188	0.07419	0.07757
C	-4.48436	0.05316	0.28504
C	-0.76546	-3.49079	-0.68118

C	1.04839	4.20805	-0.46689
H	0.17376	4.84533	-0.37214
C	0.38398	-4.18238	-0.95699
H	0.44344	-5.22867	-1.22025
C	3.37137	3.8611	-0.87099
H	4.37008	4.21298	-1.10329
C	-5.1945	1.21477	0.62449
H	-4.66387	2.15357	0.75219
C	3.14777	2.51047	-0.70714
H	3.94046	1.77751	-0.80686
C	2.29531	4.73766	-0.73274
H	2.42247	5.80966	-0.84384
C	-8.75596	-0.0682	0.92151
H	-8.99261	0.05474	1.98441
H	-9.19197	-1.01588	0.59691
H	-9.26993	0.73994	0.39227
C	-6.56481	1.16961	0.82217
H	-7.09756	2.07925	1.09074
C	1.46389	-3.273	-0.85054
C	-6.56638	-1.18251	0.34813
H	-7.10167	-2.12285	0.23563
C	-2.17208	-3.9502	-0.67277
H	-2.19932	-5.01119	-0.92799
H	-2.78417	-3.39961	-1.39306
H	-2.64179	-3.80822	0.30436
C	-7.2789	-0.02833	0.68807
C	2.90615	-3.50315	-1.08637
H	3.38562	-3.98096	-0.22418
H	3.40164	-2.54733	-1.27603
H	3.05301	-4.15708	-1.9495
O	1.30876	-0.03479	1.73795
H	3.30256	-0.33693	-0.5153
Cl	1.75388	-0.04484	-2.74718
H	-1.08486	3.19544	-0.00368
C	2.58578	-0.3067	1.66521
C	3.56155	0.7641	2.12796
C	3.04893	-1.70922	2.02174
C	5.01014	0.47654	1.75447
H	3.48051	0.78424	3.2281
H	3.23073	1.74956	1.79004
C	4.50513	-1.97449	1.65432
H	2.9366	-1.80017	3.11567
H	2.37132	-2.44816	1.58479
C	5.43051	-0.90931	2.22824
H	5.66971	1.24706	2.17132
H	5.11752	0.52432	0.66128
H	4.80514	-2.97364	1.99454
H	4.60271	-1.96856	0.56073
H	6.46988	-1.11335	1.94639
H	5.39501	-0.94409	3.32769
O	-2.75757	4.09384	-0.04997
H	-3.00726	4.35555	-0.94054
H	-2.99939	3.14984	-0.00109

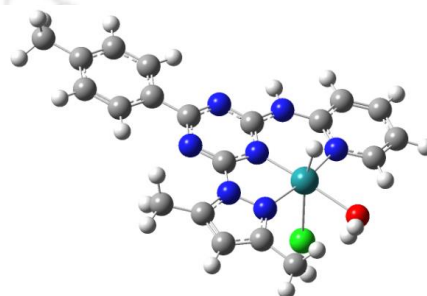
XII (dehydrogenation inner sphere MLC pathway for **2.2a**) Step 7:



C	-3.31158	3.65295	-0.32741
H	-3.49615	4.64318	0.09555
H	-3.90965	2.90422	0.1965
H	-3.65465	3.66088	-1.36783
H	-3.9154	0.55769	0.01514
Cl	-2.4398	0.22255	-2.45444
H	0.14249	-3.39122	0.04045
O	-5.71772	0.08635	-1.82752
H	-5.19096	0.49341	-1.12128
H	-5.03084	-0.04698	-2.49312

XIII (dehydrogenation inner sphere MLC pathway for 2.2a) Step 8:

Ru	-2.33957	0.12409	-0.10285
N	-0.11157	2.03672	-0.16341
N	-0.29755	-0.24417	-0.09615
N	-2.77109	-1.90875	-0.1785
N	1.63587	-1.61662	0.00272
N	-0.44675	-2.57177	0.00227
N	-1.50049	2.0302	-0.10394
N	1.85895	0.76139	-0.06837
C	0.54355	0.8121	-0.11326
C	-1.80943	-2.8655	-0.1268
C	0.31674	-1.43622	-0.03885
C	4.64782	0.52067	0.00371
H	4.18097	1.50039	-0.02335
C	2.37269	-0.49126	-0.01961
C	3.82865	-0.61933	0.01096
C	0.37028	3.31891	-0.33622
C	-2.11985	-4.23119	-0.18385
H	-1.3149	-4.95815	-0.12179
C	-0.73824	4.12578	-0.39958
H	-0.73134	5.19768	-0.53483
C	-4.41756	-3.6583	-0.45334
H	-5.4597	-3.91159	-0.61012
C	4.43731	-1.88137	0.04719
H	3.80736	-2.76486	0.05245
C	-4.05027	-2.32976	-0.37963
H	-4.7705	-1.52912	-0.52161
C	-3.43194	-4.63644	-0.33542
H	-3.67553	-5.6932	-0.38033
C	8.13226	-0.98454	0.09201
H	8.45193	-2.02321	0.20458
H	8.56962	-0.40819	0.91375
H	8.57979	-0.59917	-0.83076
C	5.81951	-1.99472	0.07422
H	6.27786	-2.98109	0.10133
C	-1.87657	3.29693	-0.26518
C	6.02652	0.39657	0.0326
H	6.6467	1.2905	0.02894
C	1.80594	3.66542	-0.42746
H	1.90326	4.74129	-0.58365
H	2.29783	3.14228	-1.25255
H	2.35063	3.38853	0.47955
C	6.64108	-0.8627	0.06787



Ru	2.27643	0.30349	-0.35926
N	0.06398	2.19373	-0.24698
N	0.3567	-0.08078	-0.22292
N	2.81152	-1.69973	-0.29795
N	-1.54622	-1.50706	-0.11064
N	0.53323	-2.4276	-0.18258
N	1.44249	2.21511	-0.30568
N	-1.84757	0.84838	-0.15588
C	-0.53819	0.9467	-0.20658
C	1.89879	-2.69229	-0.19405
C	-0.23663	-1.29861	-0.17002
C	-4.63497	0.51891	-0.0437
H	-4.20472	1.51461	-0.09042
C	-2.32671	-0.41257	-0.10628
C	-3.77554	-0.59071	-0.04468
C	-0.45599	3.46418	-0.1078
C	2.26393	-4.04162	-0.10567
H	1.48523	-4.79409	-0.02088
C	0.6331	4.3013	-0.07877
H	0.60232	5.37651	0.02254
C	4.54842	-3.3807	-0.22313
H	5.61131	-3.59272	-0.23629
C	-4.33911	-1.8727	0.0207
H	-3.6787	-2.73367	0.02559
C	4.1166	-2.0724	-0.30507
H	4.81777	-1.25251	-0.39294
C	3.59951	-4.39609	-0.12037
H	3.89145	-5.43887	-0.0502
C	-8.06226	-1.10945	0.12347
H	-8.34087	-2.11826	0.43848
H	-8.51161	-0.9418	-0.86228

H	-8.53573	-0.39875	0.80757
C	-5.71513	-2.03423	0.08326
H	-6.13684	-3.03581	0.13809
C	1.7866	3.49574	-0.19316
C	-6.00789	0.34659	0.01858
H	-6.65918	1.21822	0.02126
C	-1.89967	3.77195	-0.00786
H	-2.02676	4.85217	0.08514
H	-2.35984	3.28681	0.85781
H	-2.45337	3.42498	-0.8848
C	-6.57686	-0.93223	0.081
C	3.21316	3.89743	-0.16963
H	3.69963	3.7157	-1.13607
H	3.74663	3.34175	0.61039
H	3.31378	4.96231	0.0464
Cl	3.05702	0.68655	2.11241
H	-0.05071	-3.24935	-0.12472
H	2.13577	0.19704	-1.9514
O	4.4687	0.85867	-0.44546
H	4.56331	1.72887	-0.84485
H	4.4676	1.00387	0.53395

XIII...2.2a (molecular complex formation with 2.2a) Step 8:



Ru	-0.07819	-1.52149	-3.6309
Cl	-1.21202	-2.5576	-5.7235
N	-2.22018	-2.261	-1.79292
N	-1.47251	-0.37105	-2.85795
N	0.76239	0.01971	-4.73723
N	-2.5732	1.70521	-2.47299
N	-0.79761	1.63062	-3.89272
N	-1.20899	-2.87538	-2.50708
N	-3.32554	-0.24716	-1.34857
C	-2.37464	-0.89742	-1.98236
C	0.26878	1.27899	-4.71389
C	-1.63891	0.95923	-3.05108
C	-5.33553	1.24056	-0.06685
H	-5.22691	0.18048	0.1398
C	-3.40247	1.07118	-1.6263
C	-4.44987	1.84888	-0.96798
C	-3.03287	-3.18831	-1.1718
C	0.80341	2.30962	-5.49719
H	0.36176	3.30014	-5.43746
C	-2.511	-4.41258	-1.50899
H	-2.89682	-5.37286	-1.19828
C	2.38886	0.7611	-6.36702

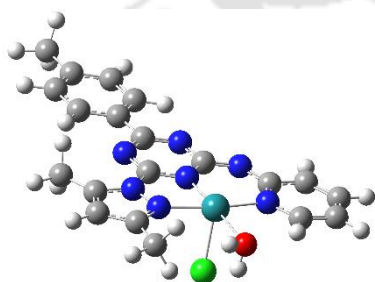
H	3.22407	0.49623	-7.00545
C	-4.59289	3.22115	-1.2222
H	-3.90656	3.69689	-1.91561
C	1.81105	-0.20673	-5.56973
H	2.17304	-1.22742	-5.55937
C	1.87434	2.05584	-6.33331
H	2.29254	2.84812	-6.94565
C	-7.57353	4.14096	0.94667
H	-7.9253	3.6688	1.86777
H	-8.4412	4.23615	0.28306
H	-7.25018	5.1577	1.18845
C	-5.58951	3.95313	-0.59682
H	-5.68468	5.01729	-0.80342
C	-1.39649	-4.18404	-2.34642
C	-6.32914	1.98214	0.55382
H	-7.00635	1.49487	1.25254
C	-4.21117	-2.84516	-0.3454
H	-4.6653	-3.76579	0.02631
H	-4.95755	-2.28671	-0.91769
H	-3.94392	-2.21393	0.50695
C	-6.47984	3.34991	0.30017
C	-0.54083	-5.16942	-3.04699
H	0.50541	-5.11319	-2.72905
H	-0.5844	-4.9828	-4.12708
H	-0.8955	-6.18471	-2.85986
O	1.44918	-2.91796	-4.48252
H	1.78085	-3.59152	-3.85339
H	0.81434	-3.33671	-5.09987
H	-1.06233	2.6036	-3.9476
H	0.85958	-1.10426	-2.39087
C	4.47045	-1.58252	-0.99839
C	3.85006	-2.38165	-2.15512
C	3.2783	-3.69234	-1.64011
C	2.08544	-3.4281	-0.73214
C	2.29089	-2.16768	0.12111
C	3.77104	-1.87362	0.33716
H	5.53981	-1.80841	-0.91092
H	3.02807	-1.81776	-2.6187
H	1.20782	-3.28417	-1.37617
H	1.82906	-1.31435	-0.39417
H	4.24235	-2.73754	0.8266
H	3.58883	-4.80043	-3.22628
H	4.06136	-4.23664	-1.08515
H	4.59064	-2.56542	-2.94407
H	4.40364	-0.5135	-1.22838
H	3.90499	-1.03248	1.02517
H	1.7674	-2.26796	1.07723
H	1.89336	-4.31216	-0.11316
O	2.81926	-4.54852	-2.7044

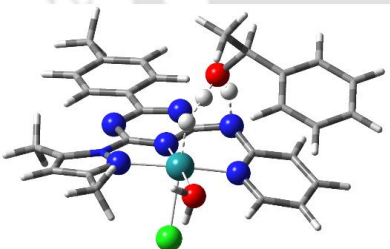
Annexure VIII

Table S2. The Cartesian coordinates (xyz) for all optimized structures (*Chapter 3*)

1-phenylethanol (3.1a)				C	0.55631	0.59827	0.68692
				C	-2.21577	-2.68366	0.63001
				C	-0.03771	-1.65273	0.76425
				C	4.56594	-0.27926	0.79754
				H	4.24819	0.75741	0.73351
				C	2.15984	-0.9535	0.74684
				C	3.5924	-1.28451	0.80326
				C	0.7772	3.11094	0.58087
				C	-2.79203	-3.97732	0.53256
				H	-2.1122	-4.81374	0.64907
				C	-0.17521	4.09217	0.72982
				H	-0.00351	5.15764	0.67425
				C	-4.93073	-3.02294	0.05644
				H	-5.98089	-3.09905	-0.20432
				C	4.00683	-2.62182	0.88157
				H	3.24439	-3.39483	0.88375
				C	-4.3493	-1.78126	0.20568
				H	-4.92155	-0.86881	0.07603
				C	-4.12704	-4.15362	0.24985
				H	-4.54063	-5.1542	0.15536
				C	7.78695	-2.28659	1.03809
				H	8.42059	-1.39605	1.03309
				H	8.09642	-2.91939	0.19926
				H	8.01125	-2.84931	1.95075
				C	5.35386	-2.93567	0.95524
				H	5.6606	-3.97825	1.01493
				C	-1.40334	3.44547	0.97445
				C	5.9144	-0.60357	0.87269
				H	6.66102	0.18832	0.86922
				C	2.23089	3.22698	0.33296
				H	2.48685	4.27872	0.18823
				H	2.54356	2.65661	-0.54547
				H	2.80739	2.82964	1.17425
				C	6.33442	-1.93407	0.95402
				C	-2.74229	4.04387	1.18958
				H	-3.26618	3.57187	2.02683
				H	-3.36593	3.93909	0.29349
				H	-2.65836	5.11141	1.40251
				O	-4.40158	1.14609	0.91118
				H	-4.47478	1.68425	1.73037
				H	-4.36695	1.73237	0.13993
				C	-5.65236	-1.6889	5.96374
				C	-5.7714	-0.32727	5.68446
				C	-5.72712	0.13936	4.36702
				C	-5.57384	-0.78662	3.32959
				C	-5.457	-2.14568	3.60457
				C	-5.49139	-2.59965	4.92282
				H	-5.68533	-2.0352	6.99322
				H	-5.89346	0.38815	6.49716
				H	-5.51864	-0.44036	2.29904
Ru	-2.31179	0.31712	0.83095				
Cl	-2.57608	0.8945	-1.44183				
N	0.10691	1.92155	0.73072				
N	-0.42624	-0.31656	0.72153				
N	-3.04924	-1.59005	0.53197				
N	1.29192	-1.94849	0.81035				
N	-0.87366	-2.66893	0.80043				
N	-1.22995	2.12536	0.98233				
N	1.85097	0.37172	0.66653				

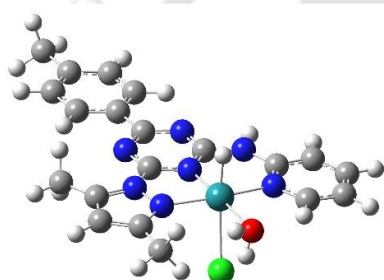
I (Dehydrogenation outer sphere MLC pathway for **3.1a**), step-1



H	-5.32037	-2.84578	2.78285	C	1.9334	1.14339	-1.2705
H	-5.39244	-3.66006	5.13665	C	3.33434	1.54852	-1.37681
C	-5.79121	1.62295	4.0802	C	-1.20985	3.82648	-0.06756
H	-5.91437	2.15152	5.03976	C	-0.86912	-3.9431	-1.7802
C	-6.92605	2.00237	3.15363	H	0.14402	-4.32615	-1.83698
H	-7.89015	1.73929	3.59465	C	-2.48566	4.10257	0.3625
H	-6.91413	3.0777	2.95773	H	-2.85045	5.06611	0.68782
H	-6.83607	1.47584	2.19813	C	-3.24383	-4.1843	-1.89875
O	-4.57738	2.08552	3.46284	H	-4.14118	-4.77185	-2.05614
H	-3.83618	1.76299	4.01408	C	4.32	0.59906	-1.68936
C	1.67998	1.61161	3.69907	H	4.01772	-0.43088	-1.85198
C	0.65691	0.70542	3.95878	C	-3.34812	-2.83432	-1.63778
C	-0.58368	1.14494	4.43081	H	-4.31063	-2.34083	-1.57515
C	-0.7863	2.51116	4.63159	C	-1.97083	-4.75743	-1.94325
C	0.23637	3.41906	4.36661	H	-1.84298	-5.8202	-2.12412
C	1.47051	2.97426	3.90323	C	7.49094	2.68301	-1.61482
H	2.63238	1.24861	3.31938	H	8.07881	2.17855	-0.84027
H	0.8286	-0.35892	3.79807	H	7.62937	3.75936	-1.48756
H	-1.74166	2.86176	5.00878	H	7.93293	2.3985	-2.57527
H	0.06451	4.48112	4.52221	C	5.65072	0.97117	-1.7686
H	2.26648	3.68612	3.69867	H	6.40402	0.2218	-2.00137
C	-1.66369	0.13305	4.71689	C	-3.21924	2.89884	0.29981
H	-1.27598	-0.588	5.45581	C	5.05996	3.23709	-1.23025
C	-2.08802	-0.63748	3.47688	H	5.35063	4.27004	-1.05037
H	-1.24711	-1.12906	2.98638	C	-0.02895	4.70961	-0.18291
H	-2.83983	-1.40073	3.70293	H	-0.32035	5.7306	0.07025
H	-2.60254	0.10215	2.81409	H	0.3931	4.70022	-1.19131
O	-2.78765	0.81175	5.28609	H	0.77397	4.39157	0.48886
H	-3.43149	0.138	5.5461	C	6.04774	2.29548	-1.53942
O-TS-3 (Dehydrogenation outer sphere MLC pathway for 3.1a), step-1				C	-4.63954	2.64905	0.64265
				H	-4.72374	2.05848	1.56421
Ru	-2.511	-0.09948	-0.714	H	-5.14119	2.12025	-0.17537
Cl	-3.87088	0.5604	-2.58958	H	-5.1695	3.58816	0.81044
N	-1.21184	2.48539	-0.38251	O	-4.57533	-0.63584	0.01066
N	-0.6458	0.40673	-1.17959	H	-4.78332	-0.09143	0.77987
N	-2.27935	-2.03337	-1.41359	H	-5.03508	-0.2181	-0.74656
N	1.6375	-0.13865	-1.49075	C	5.50223	-2.24063	2.95342
N	0.11948	-1.82631	-1.45757	C	4.49464	-3.04021	2.42325
N	-2.44181	1.91425	-0.14083	C	3.55761	-2.51725	1.5278
N	1.02852	2.0859	-0.90921	C	3.65221	-1.17043	1.17741
C	-0.20887	1.64948	-0.86274	C	4.65984	-0.36487	1.70267
C	-1.04127	-2.5678	-1.55051	C	5.58844	-0.89667	2.59361
C	0.35469	-0.49364	-1.39591	H	6.21861	-2.66338	3.65399
C	3.72338	2.87481	-1.14776	H	4.42517	-4.08965	2.71026
H	2.96442	3.61214	-0.90361	H	2.91789	-0.76716	0.48642
				H	4.71775	0.68293	1.4129
				H	6.37143	-0.26815	3.01073
				C	2.49176	-3.41451	0.91513
				H	2.23385	-4.16423	1.6953
				C	3.09694	-4.1842	-0.26089
				H	3.98954	-4.75183	0.02325
				H	2.36074	-4.88295	-0.67329
				H	3.37905	-3.47672	-1.05075
				O	1.35691	-2.74169	0.49513
				H	0.90113	-2.34721	-0.90667

C	-3.52919	0.99873	3.8312
C	-2.93588	-0.03264	3.10751
C	-1.63672	0.10266	2.60614
C	-0.94019	1.28768	2.84964
C	-1.53829	2.32376	3.56275
C	-2.83486	2.1872	4.05248
H	-4.53222	0.871	4.23221
H	-3.48443	-0.95906	2.94575
H	0.07334	1.37921	2.4686
H	-0.98649	3.24462	3.73713
H	-3.29799	2.99451	4.61323
C	-1.01254	-0.97358	1.74033
H	-1.5806	-0.8214	0.7107
C	-1.38778	-2.40961	2.08784
H	-2.45886	-2.59738	1.96764
H	-0.8301	-3.08795	1.43562
H	-1.1043	-2.62307	3.12306
O	0.30902	-0.76951	1.55783
H	0.81247	-1.65476	1.18303

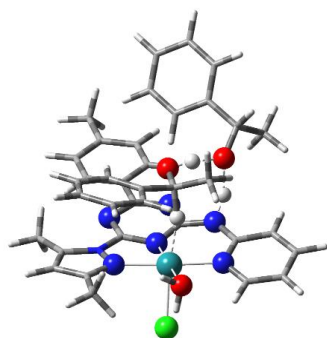
II (Dehydrogenation outer sphere MLC pathway for **3.1a**), step-2



Ru	-0.96818	0.02947	1.26532
Cl	-0.85041	0.25131	3.82358
N	1.28047	-1.81693	1.13026
N	0.86248	0.38646	0.64882
N	-1.56487	1.9966	1.03419
N	2.56802	1.7183	-0.34062
N	0.50864	2.62473	0.01453
N	-0.04857	-1.83295	1.50862
N	3.01743	-0.5502	0.20658
C	1.77778	-0.62204	0.6372
C	-0.77023	2.93354	0.46858
C	1.33529	1.53999	0.11932
C	5.65899	-0.27112	-0.69853
H	5.31454	-1.22168	-0.30378
C	3.38896	0.65581	-0.27295
C	4.7629	0.80667	-0.7479
C	1.90679	-3.00681	1.43853
C	-1.18237	4.26144	0.29986
H	-0.50488	4.96745	-0.17177
C	0.94038	-3.7836	2.02844
H	1.07668	-4.78785	2.40294
C	-3.23956	3.70892	1.36679
H	-4.21928	3.96115	1.75628

C	5.21601	2.02951	-1.2653
H	4.52489	2.8652	-1.30917
C	-2.77195	2.41575	1.49303
H	-3.36269	1.64171	1.96681
C	-2.42997	4.65812	0.74478
H	-2.75531	5.686	0.62076
C	8.83509	1.25326	-2.12414
H	9.26961	0.30155	-2.44124
H	9.47106	1.64314	-1.32055
H	8.91312	1.9568	-2.95781
C	6.51994	2.16366	-1.71521
H	6.85405	3.11843	-2.11639
C	-0.2504	-3.02498	2.06576
C	6.96103	-0.12645	-1.15111
H	7.642	-0.97406	-1.10823
C	3.33142	-3.29697	1.16334
H	3.56448	-4.30249	1.51873
H	3.99456	-2.58345	1.66088
H	3.56154	-3.23723	0.09577
C	7.41986	1.09199	-1.66537
C	-1.56471	-3.38179	2.64836
H	-2.35582	-3.35656	1.89216
H	-1.81816	-2.67681	3.44917
H	-1.53572	-4.38491	3.07716
O	-3.03803	-0.48527	1.97404
H	-3.27512	-1.31888	1.52137
H	-2.77544	-0.65772	2.89917
C	-4.13908	0.38199	-3.94759
C	-4.18541	-0.81466	-3.23738
C	-4.11201	-0.82144	-1.84411
C	-3.98782	0.3967	-1.16747
C	-3.92856	1.59252	-1.87521
C	-4.00666	1.58873	-3.26655
H	-4.1953	0.37054	-5.03289
H	-4.27404	-1.76099	-3.76902
H	-3.91295	0.4053	-0.08172
H	-3.81634	2.53018	-1.33449
H	-3.9606	2.52374	-3.81842
C	-4.18511	-2.12871	-1.09268
H	-4.03242	-2.94539	-1.81758
C	-5.52313	-2.32629	-0.40691
H	-6.33532	-2.33901	-1.1381
H	-5.53712	-3.26971	0.14587
H	-5.71198	-1.50867	0.29689
O	-3.18209	-2.23626	-0.07324
H	-2.39764	-1.71563	-0.3353
H	1.00528	3.40331	-0.39379
H	-1.32443	-0.22414	-0.29435

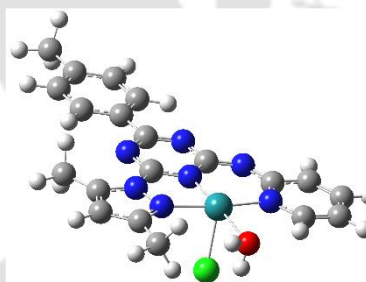
O-TS-4 (Dehydrogenation outer sphere MLC pathway for **3.1a**), step-2



Ru	-1.02313	-2.14297	-0.27073
Cl	-2.61238	-3.47155	-1.70699
N	-3.34557	-1.05368	1.09327
N	-1.80402	-0.32897	-0.44935
N	0.18455	-1.8318	-1.93016
N	-1.78509	1.94039	-1.12224
N	-0.04654	0.5915	-1.78268
N	-2.55911	-2.183	1.15812
N	-3.51084	1.14627	0.31837
C	-2.89797	-0.01695	0.2771
C	0.4273	-0.56506	-2.38098
C	-1.2381	0.7148	-1.1536
C	-4.72067	3.67516	0.27503
H	-5.16701	2.86578	0.84504
C	-2.91008	2.10594	-0.4233
C	-3.54166	3.42998	-0.43933
C	-4.47936	-1.18261	1.863
C	1.26493	-0.36909	-3.49399
H	1.45342	0.65683	-3.79081
C	-4.4012	-2.43713	2.42196
H	-5.12954	-2.88205	3.08474
C	1.45687	-2.73106	-3.76918
H	1.81196	-3.6137	-4.29069
C	-2.97364	4.47852	-1.17807
H	-2.06319	4.2826	-1.73557
C	0.66879	-2.87411	-2.64532
H	0.40668	-3.85569	-2.26807
C	1.78349	-1.44253	-4.19109
H	2.4183	-1.28076	-5.0578
C	-5.38119	7.33795	-0.50359
H	-6.32573	7.35331	0.04598
H	-5.58496	7.6695	-1.52731
H	-4.72601	8.09391	-0.05665
C	-3.56988	5.72871	-1.19481
H	-3.11821	6.53145	-1.77485
C	-3.20632	-3.02578	1.95912
C	-5.31089	4.93119	0.25124
H	-6.22779	5.10635	0.8105
C	-5.52118	-0.14063	2.00187
H	-6.33606	-0.53205	2.61417
H	-5.92203	0.16506	1.03176
H	-5.12974	0.76659	2.47044
C	-4.74875	5.9813	-0.48075

C	-2.66713	-4.38182	2.22025
H	-1.63138	-4.33524	2.57683
H	-2.69841	-4.98866	1.30734
H	-3.25398	-4.89817	2.98196
O	-0.26035	-4.28341	-0.12713
H	-0.41022	-4.60375	0.76817
H	-1.03565	-4.59379	-0.65089
C	5.00247	-0.25649	-2.1086
C	4.25322	0.41313	-1.14488
C	3.33083	-0.27742	-0.35797
C	3.15158	-1.65066	-0.5586
C	3.90096	-2.31833	-1.51959
C	4.83048	-1.62441	-2.29234
H	5.71747	0.29158	-2.71553
H	4.38514	1.48355	-0.99749
H	2.40343	-2.19441	0.0184
H	3.74644	-3.38227	-1.67602
H	5.41136	-2.15004	-3.04539
C	2.56726	0.45262	0.71038
H	2.82951	1.51592	0.68324
C	2.76516	-0.10146	2.10252
H	3.82014	-0.04167	2.37944
H	2.17693	0.45868	2.83283
H	2.46545	-1.15272	2.14813
O	1.11788	0.44318	0.45526
H	0.81384	0.69732	-0.54874
H	0.12911	-1.62434	0.83197
H	0.65737	-0.52902	0.59061

I (Dehydrogenation outer sphere MLC pathway for **3.1a**), releasing H₂, step-2.

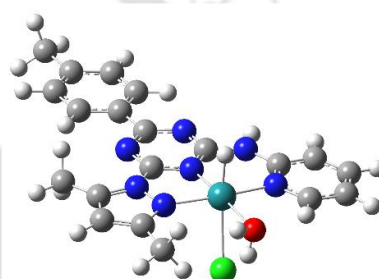


Ru	-2.22175	0.00187	1.34147
Cl	-2.51978	0.13941	-0.98395
N	0.00999	1.83578	1.02248
N	-0.27392	-0.43713	1.27382
N	-2.7477	-2.00622	1.39533
N	1.61909	-1.85914	1.41909
N	-0.44861	-2.79721	1.64331
N	-1.35308	1.91761	1.20213
N	1.90835	0.48268	1.03276
C	0.59988	0.56865	1.09781
C	-1.78925	-2.97931	1.56966
C	0.26243	-1.71042	1.43545
C	4.68068	0.14036	1.07058
H	4.24629	1.12807	0.94496

C	2.36499	-0.78932	1.21128
C	3.82694	-0.95958	1.21174
C	0.56435	3.07597	0.80949
C	-2.21075	-4.32991	1.68223
H	-1.42842	-5.06334	1.84138
C	-0.48965	3.95909	0.84074
H	-0.42561	5.02828	0.69817
C	-4.47891	-3.68305	1.31432
H	-5.53192	-3.90525	1.17633
C	4.39216	-2.23114	1.384
H	3.72399	-3.07948	1.49634
C	-4.04152	-2.3771	1.2422
H	-4.73175	-1.55863	1.06738
C	-3.53318	-4.68541	1.55735
H	-3.83106	-5.72782	1.63031
C	8.11484	-1.47956	1.28996
H	8.64334	-0.52798	1.19135
H	8.45022	-2.13048	0.47533
H	8.44795	-1.95106	2.22084
C	5.76827	-2.39065	1.41007
H	6.19196	-3.38462	1.5419
C	-1.65984	3.20692	1.07272
C	6.05918	-0.02897	1.09845
H	6.71097	0.83525	0.98537
C	2.00714	3.33167	0.60489
H	2.15906	4.4005	0.44035
H	2.40087	2.77898	-0.25194
H	2.59543	3.01126	1.47055
C	6.62944	-1.29406	1.2664
C	-3.06386	3.68315	1.11217
H	-3.60173	3.33071	1.99641
H	-3.60774	3.34068	0.2239
H	-3.09575	4.77413	1.11328
O	-4.38085	0.59243	1.33784
H	-4.53777	1.1951	2.09691
H	-4.46352	1.08643	0.51072
C	-8.29764	-0.18049	4.88206
C	-7.30036	0.75628	5.14766
C	-5.99753	0.5607	4.6871
C	-5.71698	-0.59854	3.95355
C	-6.70824	-1.53336	3.68589
C	-8.00583	-1.32695	4.15151
H	-9.30641	-0.00966	5.2482
H	-7.54623	1.6466	5.72033
H	-4.70947	-0.76601	3.57399
H	-6.46089	-2.42531	3.11517
H	-8.78402	-2.05657	3.9455
C	-4.87646	1.53336	4.96892
H	-4.11568	0.99954	5.56641
C	-5.27028	2.78822	5.72008
H	-5.68309	2.55725	6.70659
H	-4.39191	3.42264	5.86255
H	-6.01388	3.35991	5.1569
O	-4.26396	1.89091	3.71958
H	-3.31571	2.06803	3.90702

C	2.58774	-0.23847	4.33981
C	1.198	-0.2549	4.32621
C	0.47567	0.94638	4.26651
C	1.1756	2.16356	4.22946
C	2.56186	2.17514	4.23213
C	3.27075	0.9731	4.28181
H	3.13683	-1.17545	4.35751
H	0.68498	-1.21232	4.3522
H	0.59844	3.08308	4.17949
H	3.09675	3.12034	4.18823
H	4.35727	0.97946	4.26052
C	-0.99879	0.99233	4.22121
C	-1.78751	-0.27149	4.02141
H	-1.21511	-1.14771	3.71902
H	-2.33891	-0.52231	4.93638
H	-2.63676	-0.07267	3.31785
O	-1.59507	2.06934	4.34829

II (Alcoholysis segment, step-1)

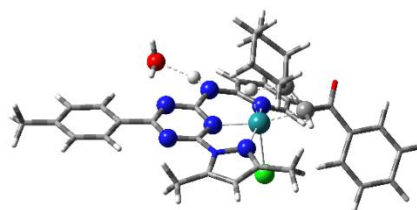


Ru	-0.60254	1.45585	1.226
Cl	-0.46153	1.98294	3.77048
N	0.49913	-1.23415	1.45585
N	1.14539	0.80106	0.61677
N	-0.17591	3.41526	0.75275
N	3.17888	0.97626	-0.60681
N	1.87145	2.82388	-0.33729
N	-0.66612	-0.56698	1.78519
N	2.54372	-1.1162	0.32397
C	1.46215	-0.51599	0.76908
C	0.95594	3.77514	0.10494
C	2.0695	1.49215	-0.09242
C	4.83853	-2.32035	-0.75155
H	4.12653	-2.91134	-0.18315
C	3.38796	-0.33286	-0.37725
C	4.58837	-0.95269	-0.93398
C	0.52509	-2.50272	1.99686
C	1.26383	5.11161	-0.17458
H	2.1891	5.34248	-0.69469
C	-0.65656	-2.62963	2.6839
H	-0.98345	-3.50217	3.23064
C	-0.75936	5.755	0.90859
H	-1.46956	6.49597	1.25735
C	5.51013	-0.19633	-1.67399
H	5.31787	0.86192	-1.81957
C	-0.99903	4.41749	1.15171

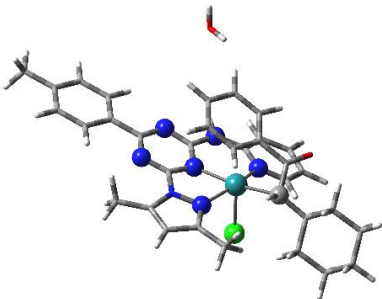
H	-1.88496	4.08768	1.67997
C	0.39999	6.11524	0.22416
H	0.63295	7.15413	0.0145
C	8.13675	-2.7853	-2.58475
H	8.06482	-3.87575	-2.60345
H	9.01733	-2.52917	-1.98405
H	8.34257	-2.44179	-3.60306
C	6.64074	-0.79195	-2.20913
H	7.34396	-0.19113	-2.78248
C	-1.36146	-1.41547	2.5447
C	5.97419	-2.90648	-1.29083
H	6.15351	-3.96921	-1.14133
C	1.64195	-3.45745	1.83001
H	1.41196	-4.37204	2.38016
H	2.58707	-3.04889	2.19911
H	1.79901	-3.70576	0.77598
C	6.89821	-2.15693	-2.02709
C	-2.65315	-1.02568	3.15719
H	-3.43744	-0.8926	2.40195
H	-2.52788	-0.09876	3.72917
H	-2.99946	-1.80486	3.83794
O	-2.70077	2.00722	1.86878
H	-3.22001	1.20134	1.73765
H	-2.4205	2.00937	2.81518
H	-1.0601	1.27226	-0.30053
H	2.65072	3.20469	-0.85423
C	-0.04022	-3.98429	-1.22795
C	0.71003	-3.0676	-1.96543
C	0.23298	-1.77144	-2.1448
C	-0.9801	-1.38676	-1.58304
C	-1.72905	-2.29157	-0.81543
C	-1.24333	-3.59649	-0.6532
H	0.32285	-5.00036	-1.09306
H	1.66564	-3.35973	-2.39444
H	0.81212	-1.0518	-2.71923
H	-1.32564	-0.36947	-1.73171
H	-1.83844	-4.28687	-0.06174
C	-3.01935	-1.94357	-0.14366
O	-3.61834	-2.8057	0.50554
C	-3.508	-0.55852	-0.27069
C	-4.77724	-0.12146	-0.0938
C	-5.97218	-0.97297	0.2159
C	-5.10193	1.33107	-0.30645
C	-7.06421	-0.78399	-0.84532
H	-6.37572	-0.64905	1.18886
H	-5.6899	-2.0196	0.32609
C	-6.17834	1.50248	-1.38222
H	-5.49337	1.74981	0.63491
H	-4.19882	1.89954	-0.55393
C	-7.41775	0.68323	-1.04752
H	-7.9498	-1.36387	-0.56389
H	-6.70818	-1.20619	-1.79506
H	-6.42631	2.56355	-1.49357
H	-5.77098	1.17355	-2.34829
H	-8.17207	0.79028	-1.83512

H	-7.87402	1.07808	-0.12775
H	-2.76668	0.19291	-0.53676

R-TS-1 (Alcoholysis segment, step-1)

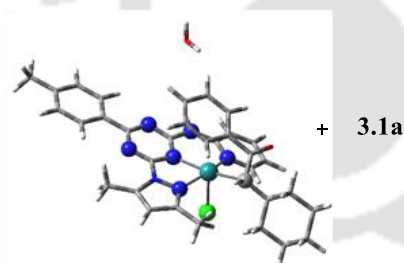


Ru	0.98032	-0.11712	0.00323
Cl	1.40589	-0.7093	-2.37402
N	-1.05049	-2.26733	-0.06757
N	-1.05641	0.00835	-0.32635
N	1.20578	1.86986	-0.58906
N	-3.10767	1.19684	-0.261
N	-1.12111	2.34863	-0.20645
N	0.31377	-2.14165	0.15997
N	-3.11584	-1.18033	-0.22632
C	-1.79719	-1.11112	-0.22939
C	0.16573	2.73225	-0.60413
C	-1.76861	1.15191	-0.28147
C	-5.90417	-1.21482	-0.29454
H	-5.34048	-2.13562	-0.18422
C	-3.74307	0.01095	-0.28361
C	-5.20528	0.00089	-0.35906
C	-1.42108	-3.59013	-0.21231
C	0.30261	4.05994	-1.02229
H	-0.56669	4.71034	-0.99608
C	-0.26206	-4.30815	-0.07951
H	-0.16959	-5.38254	-0.14608
C	2.56774	3.5859	-1.59663
H	3.53257	3.85589	-2.00961
C	-5.94313	1.18348	-0.51246
H	-5.42816	2.13594	-0.59293
C	2.36344	2.29518	-1.14893
H	3.13106	1.53906	-1.24134
C	1.52378	4.50097	-1.50157
H	1.64339	5.52878	-1.82974
C	-9.52203	-0.0962	-0.57982
H	-9.93248	0.82731	-0.99537
H	-9.95591	-0.22322	0.41871
H	-9.88242	-0.932	-1.18652
C	-7.32737	1.14694	-0.59173
H	-7.88062	2.07468	-0.72037
C	0.78713	-3.3868	0.13393
C	-7.28645	-1.24118	-0.37315
H	-7.80875	-2.19432	-0.3225
C	-2.80136	-4.05434	-0.47483
H	-2.78806	-5.13595	-0.62146
H	-3.22887	-3.58258	-1.36387
H	-3.47451	-3.81979	0.35439
C	-8.02777	-0.06169	-0.5192

C	2.23126	-3.69065	0.26878	N	1.06096	2.28133	-0.35149
H	2.59726	-3.53662	1.28943	N	1.00114	-0.00622	-0.5266
H	2.82023	-3.05099	-0.39478	N	-1.31488	-1.83131	-0.62928
H	2.42133	-4.73205	0.00277	N	3.01663	-1.24666	-0.304
H	3.15572	-1.38529	0.96321	N	1.00365	-2.34298	-0.26273
H	-1.78287	3.13065	-0.16848	N	-0.31015	2.18908	-0.18259
C	2.9316	-0.31941	0.9938	N	3.09865	1.12699	-0.35003
C	1.95342	0.05715	2.00305	C	1.78455	1.09695	-0.43031
C	1.57295	-1.0405	2.98943	C	-0.29657	-2.71872	-0.6106
C	2.01053	1.41991	2.68781	C	1.68702	-1.1664	-0.38482
H	0.50608	0.38411	1.45953	C	5.89465	1.0773	-0.29241
C	0.3018	-0.73806	3.76963	H	5.35636	2.01924	-0.25298
H	2.41373	-1.13462	3.69536	C	3.69722	-0.08061	-0.33855
H	1.49387	-2.00111	2.47065	C	5.15705	-0.11748	-0.34079
C	0.75544	1.71993	3.50224	C	1.46139	3.59379	-0.48969
H	2.89341	1.41592	3.34243	C	-0.48164	-4.07004	-0.92305
H	2.19978	2.20774	1.95794	H	0.37153	-4.7404	-0.87719
C	0.41127	0.60481	4.48226	C	0.30975	4.33843	-0.41546
H	0.0934	-1.5417	4.48518	H	0.24466	5.41388	-0.4957
H	-0.54877	-0.71683	3.0692	C	-2.75967	-3.58221	-1.43933
H	0.87877	2.67192	4.03108	H	-3.74873	-3.86029	-1.78368
H	-0.09063	1.86396	2.81041	C	5.86383	-1.32826	-0.40257
H	-0.51601	0.83501	5.02018	H	5.32289	-2.26734	-0.46878
H	1.20067	0.53869	5.24552	C	-2.50753	-2.26756	-1.09696
C	4.10332	0.49352	0.64347	H	-3.2651	-1.50043	-1.20083
O	4.33073	1.62474	1.08761	C	-1.7308	-4.51147	-1.32352
C	5.0874	-0.11662	-0.30718	H	-1.88703	-5.55711	-1.56998
C	4.72476	-1.09589	-1.23918	C	9.48327	-0.16851	-0.32119
C	6.40938	0.34435	-0.28121	H	9.88477	-1.10441	-0.71788
C	5.67228	-1.61389	-2.11728	H	9.86389	-0.06265	0.70164
H	3.682	-1.39312	-1.32699	H	9.90823	0.65615	-0.90078
C	7.35871	-0.18978	-1.14268	C	7.25034	-1.33885	-0.40624
H	6.66416	1.12528	0.43024	H	7.77776	-2.28871	-0.46336
C	6.99196	-1.17319	-2.06199	C	-0.76443	3.44028	-0.23895
H	5.37246	-2.3536	-2.85512	C	7.27916	1.0559	-0.29566
H	8.38667	0.16195	-1.10468	H	7.8303	1.99347	-0.25887
H	7.73282	-1.58446	-2.74303	C	2.86287	4.02368	-0.69104
O	-3.44125	4.02903	-0.09227	H	2.88356	5.10255	-0.85588
H	-3.66894	4.29097	0.804	H	3.32327	3.52641	-1.54927
H	-3.68334	3.08475	-0.13797	H	3.48866	3.78791	0.1741
III (Alcoholysis segment, step-2)				C	7.98757	-0.15141	-0.34748
				C	-2.21314	3.73851	-0.14831
Ru	-1.01468	0.19569	-0.2291	H	-2.56983	3.74074	0.88797
Cl	-1.64347	0.61225	-2.50963	H	-2.78535	2.98681	-0.69868
				H	-2.42729	4.72111	-0.57306
				H	-3.05405	1.46042	1.03561
				H	1.64352	-3.13774	-0.16489
				C	-2.76136	0.40865	1.06502
				C	-1.65696	0.13618	2.03701
				C	-1.29708	1.35597	2.89217
				C	-1.65851	-1.14284	2.88619
				H	-0.61654	-0.06767	1.47329
				C	0.02918	1.18061	3.6176
				H	-2.10767	1.49112	3.62282
				H	-1.2844	2.25384	2.26432

C	-0.33648	-1.30421	3.63125
H	-2.4978	-1.08487	3.5908
H	-1.86098	-2.01097	2.2583
C	0.01817	-0.08277	4.47046
H	0.2543	2.06262	4.22743
H	0.8355	1.11098	2.86777
H	-0.36716	-2.20521	4.25376
H	0.4661	-1.47341	2.89306
H	0.98475	-0.2223	4.96814
H	-0.72689	0.03438	5.27071
C	-3.91352	-0.48154	0.91589
O	-4.00944	-1.60348	1.42991
C	-5.04162	0.00054	0.05348
C	-4.87094	0.94564	-0.96484
C	-6.30547	-0.57007	0.24753
C	-5.94825	1.32294	-1.76141
H	-3.87496	1.3273	-1.17782
C	-7.38416	-0.17853	-0.53425
H	-6.40869	-1.32544	1.02163
C	-7.20786	0.7716	-1.54062
H	-5.79825	2.03852	-2.5656
H	-8.36464	-0.61739	-0.36765
H	-8.04963	1.07049	-2.16011
O	3.27749	-4.07298	-0.01486
H	3.48827	-4.28779	0.8979
H	3.53505	-3.13536	-0.10712

XIV (Alcoholysis segment, step-2, molecular complex formation with **3.1a**)

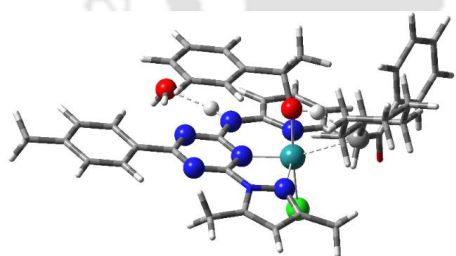


Ru	-2.10291	0.10168	-0.33155
Cl	-3.09423	0.86416	-2.3789
N	-0.1187	2.31537	-0.27252
N	-0.13321	0.13472	-1.0115
N	-2.33543	-1.81728	-1.17359
N	1.93342	-0.92034	-1.55438
N	0.018	-2.14799	-1.52083
N	-1.47321	2.15022	-0.04776
N	1.8912	1.39495	-1.00878
C	0.59792	1.24967	-0.79793
C	-1.30725	-2.5716	-1.61296
C	0.61409	-0.93199	-1.3553
C	4.5783	1.64152	-1.74597
H	3.96238	2.53376	-1.66213
C	2.52587	0.2749	-1.41385
C	3.95957	0.38282	-1.67815
C	0.28596	3.60515	0.01377

C	-1.50694	-3.83074	-2.18976
H	-0.64529	-4.40747	-2.51209
C	-0.85109	4.2634	0.40672
H	-0.91221	5.30162	0.69943
C	-3.85912	-3.49983	-1.98515
H	-4.88962	-3.80558	-2.12
C	4.75258	-0.76277	-1.83251
H	4.27985	-1.73812	-1.77244
C	-3.58489	-2.27682	-1.40139
H	-4.37425	-1.60828	-1.08788
C	-2.79412	-4.30639	-2.36685
H	-2.95767	-5.28136	-2.81514
C	8.23124	0.70708	-2.21746
H	8.62067	1.63824	-1.7965
H	8.5157	0.68852	-3.27594
H	8.74716	-0.12736	-1.73295
C	6.12172	-0.64958	-2.00841
H	6.72802	-1.54927	-2.08692
C	-1.91809	3.33923	0.34621
C	5.95027	1.74394	-1.92587
H	6.4165	2.7263	-1.96655
C	1.67886	4.09509	-0.07766
H	1.70608	5.13669	0.24825
H	2.06462	4.0352	-1.09918
H	2.35364	3.50374	0.55117
C	6.74931	0.60101	-2.047
C	-3.35227	3.56704	0.62073
H	-3.62206	3.31346	1.65215
H	-3.95143	2.94426	-0.04431
H	-3.61072	4.61597	0.46083
O	3.08592	-2.95663	3.54511
H	3.98373	-2.73316	3.80683
H	2.54997	-2.73249	4.3107
H	-3.75335	1.01976	1.56798
H	0.69727	-2.84251	-1.79652
C	0.03941	-2.39763	1.88736
C	0.77281	-1.20006	2.07436
C	0.12278	0.01197	2.11055
C	-1.28101	0.08526	1.90597
C	-2.01209	-1.11066	1.65939
C	-1.31598	-2.35383	1.68394
H	0.57019	-3.34682	1.91266
H	1.84375	-1.26527	2.24448
H	0.68053	0.92838	2.30622
H	-1.80175	0.99521	2.18939
H	-1.91935	-3.24737	1.53965
C	-3.48238	-1.11166	1.38524
O	-4.08556	-2.19737	1.30039
C	-3.99028	0.17209	0.91385
C	-5.45872	0.1623	0.52788
C	-6.33884	-0.07197	1.76725
C	-5.95345	1.40528	-0.20815
C	-7.8129	-0.19353	1.39799
H	-6.20118	0.77766	2.45673
H	-5.99809	-0.97012	2.29016

C	-7.41988	1.27357	-0.60373
H	-5.85744	2.27255	0.46475
H	-5.32619	1.59948	-1.08576
C	-8.2997	1.01964	0.61483
H	-8.42309	-0.34234	2.29738
H	-7.94866	-1.09637	0.78397
H	-7.75373	2.16987	-1.14019
H	-7.52668	0.43692	-1.31048
H	-9.34876	0.89521	0.31934
H	-8.2671	1.90466	1.26868
H	-5.63971	-0.70275	-0.1298
C	5.01048	-1.53325	1.38649
C	5.1438	-0.14642	1.51111
C	6.41089	0.42507	1.39936
C	7.52878	-0.37529	1.17394
C	7.39221	-1.756	1.06286
C	6.12723	-2.33442	1.17021
H	4.01964	-1.98195	1.4553
H	6.50868	1.50428	1.48789
H	8.51134	0.0829	1.08679
H	8.26524	-2.37968	0.88752
H	6.00928	-3.41095	1.07282
C	3.92802	0.70219	1.81662
H	3.06768	0.27184	1.27095
C	3.612	0.68091	3.30164
H	2.73261	1.29337	3.51939
H	3.41606	-0.34438	3.63094
H	4.45773	1.07805	3.87114
O	4.10029	2.06308	1.45534
H	4.29979	2.0732	0.5086

R-TS-5 (Alcoholysis segment, step-3)

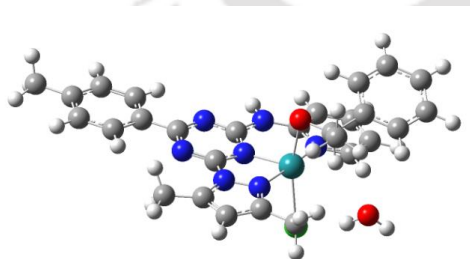


Ru	-0.73737	0.02163	-1.19689
Cl	-0.81483	-0.06804	-3.55255
N	1.14813	2.218	-1.09658
N	1.20573	-0.08805	-0.99692
N	-0.97408	-2.03626	-1.20351
N	3.2383	-1.18092	-0.43789
N	1.34959	-2.42745	-0.76202
N	-0.18133	2.02192	-1.41835
N	3.17693	1.18845	-0.56728
C	1.90576	1.07695	-0.87409
C	0.06117	-2.88222	-1.0186
C	1.93633	-1.20148	-0.73516
C	5.89627	1.34399	0.01105
H	5.32766	2.23507	-0.23503

C	3.82731	0.02509	-0.35923
C	5.24411	0.10115	-0.01118
C	1.5483	3.50614	-1.40663
C	-0.10601	-4.27328	-1.03801
H	0.75556	-4.90825	-0.8521
C	0.4412	4.1129	-1.94048
H	0.38809	5.13215	-2.29521
C	-2.41212	-3.93055	-1.5558
H	-3.40761	-4.28928	-1.7924
C	5.98734	-1.04069	0.32739
H	5.5029	-2.01241	0.34986
C	-2.18066	-2.56837	-1.51642
H	-2.96544	-1.84193	-1.7399
C	-1.3573	-4.80322	-1.29395
H	-1.50077	-5.87928	-1.30591
C	9.44213	0.39415	0.99572
H	10.05999	0.2121	0.10844
H	9.74002	-0.3456	1.74412
H	9.70859	1.38526	1.37215
C	7.32899	-0.93913	0.66074
H	7.88385	-1.83641	0.92656
C	-0.60529	3.15848	-1.96435
C	7.23884	1.43544	0.34294
H	7.72406	2.40932	0.35319
C	2.91502	4.02716	-1.18561
H	2.94743	5.07924	-1.4741
H	3.65702	3.4758	-1.77094
H	3.22056	3.93655	-0.13934
C	7.98546	0.29768	0.66887
C	-1.95674	3.28967	-2.5606
H	-2.68017	3.73078	-1.8664
H	-2.33294	2.31233	-2.87669
H	-1.90676	3.94006	-3.43737
H	2.01383	-3.1705	-0.52432
O	-0.79307	0.25961	1.04383
H	-1.76728	0.42655	0.87359
C	-0.63045	-0.63804	2.16434
H	-1.02607	-0.07378	3.02699
C	0.85081	-0.82377	2.39028
C	1.66858	0.3124	2.46101
C	1.43616	-2.07955	2.5634
C	3.02953	0.19487	2.71737
H	1.21949	1.29267	2.30778
C	2.80323	-2.20029	2.81242
H	0.82721	-2.97829	2.50132
C	3.60128	-1.06444	2.89725
H	3.65252	1.08522	2.75737
H	3.243	-3.18733	2.92437
H	4.66739	-1.15547	3.08815
C	-1.44216	-1.90938	2.03076
H	-2.46855	-1.67989	1.72858
H	-1.0241	-2.59794	1.29357
H	-1.48709	-2.43112	2.99171
C	-3.23282	1.02815	-0.10902
H	-2.90451	1.64295	-0.94854

C	-3.43576	1.8921	1.13552
C	-2.406	3.02815	1.19284
C	-4.84709	2.49466	1.21899
H	-3.28387	1.32248	2.07274
C	-2.57204	3.88289	2.44319
H	-2.53525	3.66217	0.30191
H	-1.38869	2.62132	1.13418
C	-5.0293	3.35274	2.46567
H	-5.00683	3.10302	0.31535
H	-5.59778	1.69691	1.18474
C	-3.98103	4.45603	2.54131
H	-1.82665	4.68726	2.46046
H	-2.37193	3.26136	3.3301
H	-6.03956	3.77769	2.49593
H	-4.94165	2.71005	3.35574
H	-4.09815	5.04023	3.46178
H	-4.13885	5.15801	1.70877
C	-4.09538	0.00767	-0.61929
O	-4.1009	-0.2609	-1.84947
C	-4.96258	-0.87514	0.2493
C	-5.80459	-1.77955	-0.41452
C	-4.97571	-0.88258	1.65146
C	-6.62955	-2.64812	0.28819
H	-5.78266	-1.76856	-1.50041
C	-5.79305	-1.75969	2.36002
H	-4.33916	-0.20191	2.20779
C	-6.62721	-2.64352	1.68174
H	-7.2797	-3.33277	-0.25146
H	-5.77969	-1.74769	3.44714
H	-7.27097	-3.32236	2.23532
O	3.62659	-3.97012	0.05954
H	4.11365	-4.31322	-0.69542
H	3.80249	-3.00909	0.03634

XV (Alcoholysis segment, step-4)

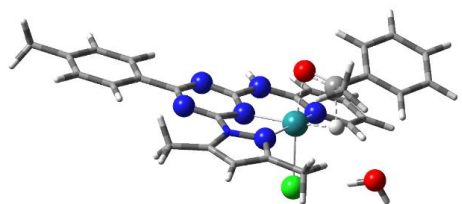


Ru	0.80615	-0.17754	-0.1266
Cl	0.60017	0.501	-2.41681
N	-1.36463	-1.95748	-0.99573
N	-1.21769	0.16566	-0.12003
N	1.18021	1.81181	0.42928
N	-3.1657	1.52349	-0.02788
N	-1.1563	2.38783	0.62343
N	-0.01914	-2.08487	-0.67503
N	-3.29984	-0.66323	-0.93514
C	-2.00696	-0.76887	-0.69424
C	0.19435	2.70497	0.70025

C	-1.85091	1.32422	0.12978
C	-6.05267	-0.36831	-1.33265
H	-5.52808	-1.22971	-1.73458
C	-3.85944	0.49327	-0.53947
C	-5.31032	0.62776	-0.67951
C	-1.91803	-3.16754	-1.36227
C	0.46153	4.02013	1.11439
H	-0.37905	4.6716	1.33632
C	-0.89812	-4.07556	-1.26551
H	-0.95957	-5.12988	-1.49489
C	2.78586	3.57509	0.89799
H	3.83311	3.85715	0.92654
C	-5.9969	1.73438	-0.15839
H	-5.45073	2.506	0.37631
C	2.44595	2.29631	0.50801
H	3.20115	1.591	0.20926
C	1.76422	4.46453	1.22633
H	1.97405	5.48084	1.54425
C	-9.59186	1.00102	-1.15365
H	-10.10612	0.04088	-1.05273
H	-9.82964	1.38143	-2.15404
H	-10.02771	1.69781	-0.43335
C	-7.37241	1.84327	-0.3014
H	-7.88746	2.70691	0.11409
C	0.25566	-3.38243	-0.83564
C	-7.42589	-0.24862	-1.47349
H	-7.98232	-1.02869	-1.98893
C	-3.32841	-3.38051	-1.75677
H	-3.45861	-4.42761	-2.03926
H	-3.61764	-2.74736	-2.59941
H	-4.01796	-3.14169	-0.94053
C	-8.11381	0.86131	-0.96705
C	1.57934	-3.99454	-0.57792
H	1.89438	-3.83422	0.45945
H	2.34445	-3.5533	-1.22898
H	1.52262	-5.07152	-0.75058
H	-1.76914	3.1941	0.77858
O	1.04179	-1.03124	1.95998
H	1.96562	-0.85327	2.18891
C	0.2312	-0.7569	3.13493
H	0.61342	-1.43377	3.91626
C	-1.179	-1.16899	2.7962
C	-1.39684	-2.45033	2.27712
C	-2.27258	-0.31858	2.96845
C	-2.67517	-2.8638	1.9196
H	-0.54728	-3.11338	2.1299
C	-3.55436	-0.72988	2.60665
H	-2.12868	0.68434	3.36292
C	-3.75874	-2.00046	2.0771
H	-2.82109	-3.85702	1.50192
H	-4.39177	-0.04644	2.72393
H	-4.75677	-2.30947	1.77528
C	0.4073	0.672	3.59441
H	1.46868	0.9021	3.73655
H	0.00395	1.37333	2.86016

H	-0.09908	0.84056	4.54912
C	2.97232	-0.89402	-0.18539
H	2.67316	-1.91564	0.05353
C	3.92792	-0.4813	0.97152
C	4.31117	-1.71763	1.81094
C	5.23042	0.25707	0.627
H	3.39616	0.20134	1.67221
C	5.08521	-1.35076	3.07205
H	4.9104	-2.38983	1.17852
H	3.41145	-2.29591	2.06948
C	5.99821	0.65649	1.88154
H	5.85413	-0.40405	0.00759
H	5.05843	1.14246	0.00636
C	6.33939	-0.55298	2.73995
H	5.33563	-2.25035	3.6465
H	4.43549	-0.74229	3.72349
H	6.90789	1.20395	1.60943
H	5.38291	1.35587	2.47059
H	6.85978	-0.25016	3.65605
H	7.03666	-1.19864	2.18685
C	3.47692	-0.99812	-1.57276
O	3.30311	-2.02001	-2.25045
C	4.25639	0.10479	-2.23346
C	3.82118	1.43081	-2.30813
C	5.48363	-0.2332	-2.81535
C	4.61746	2.40296	-2.90832
H	2.82985	1.6819	-1.94616
C	6.28858	0.73995	-3.3958
H	5.80028	-1.27313	-2.78938
C	5.861	2.0663	-3.43635
H	4.25744	3.42751	-2.97155
H	7.24957	0.4641	-3.8233
H	6.48703	2.82829	-3.89397
O	-3.32162	4.27669	0.6472
H	-3.30895	4.83316	-0.13647
H	-3.59458	3.39952	0.31333

R-TS-6 (Alcoholysis segment, step-5)

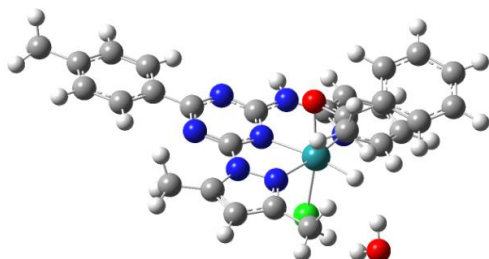


Ru	1.34798	0.66581	0.29184
N	-1.05853	2.29459	-0.08725
N	-0.61166	0.09443	0.36828
N	1.99867	-1.19778	0.88166
N	-2.31173	-1.54345	0.16297
N	-0.15908	-2.20091	0.55163
N	0.31631	2.45845	-0.03368
N	-2.83524	0.76145	-0.15874
C	-1.55618	1.00489	0.04699

C	1.18703	-2.27611	0.92172
C	-1.04591	-1.17808	0.35975
C	-5.55573	0.1117	-0.44262
H	-5.2356	1.14815	-0.48804
C	-3.17966	-0.54293	-0.05997
C	-4.59226	-0.88557	-0.2269
C	-1.70454	3.5165	-0.09286
C	1.64849	-3.53281	1.33084
H	0.96313	-4.37568	1.32809
C	-0.70973	4.45832	-0.03473
H	-0.85393	5.52894	-0.01651
C	3.77721	-2.55285	1.78337
H	4.80491	-2.60136	2.12494
C	-5.01127	-2.22107	-0.16749
H	-4.26882	-2.99388	0.00126
C	3.26341	-1.34731	1.35087
H	3.85468	-0.43436	1.35338
C	2.95792	-3.67984	1.75177
H	3.32299	-4.65152	2.06888
C	-8.75952	-1.90859	-0.7175
H	-9.07727	-1.76184	-1.75611
H	-9.40869	-1.27894	-0.10115
H	-8.95801	-2.95159	-0.45964
C	-6.35067	-2.54598	-0.3202
H	-6.66094	-3.58756	-0.27064
C	0.52601	3.76993	0.0194
C	-6.89177	-0.22329	-0.59209
H	-7.62778	0.56138	-0.7552
C	-3.17469	3.6764	-0.13859
H	-3.42121	4.7377	-0.07305
H	-3.66599	3.1462	0.68215
H	-3.59862	3.27173	-1.06222
C	-7.31633	-1.55727	-0.5362
C	1.89481	4.31282	0.17774
H	1.94272	4.95516	1.06184
H	2.20068	4.91489	-0.68418
H	2.61227	3.50055	0.31902
C	2.75963	0.70275	-1.45593
C	3.88993	-0.30357	-1.44467
C	3.65254	-1.59343	-1.92325
C	5.16254	0.02733	-0.96956
C	4.67055	-2.54234	-1.9241
H	2.65309	-1.83138	-2.27769
C	6.17807	-0.92368	-0.96676
H	5.33684	1.01366	-0.54488
C	5.93528	-2.21063	-1.44431
H	4.47679	-3.54418	-2.29996
H	7.16106	-0.66238	-0.58287
H	6.73033	-2.95211	-1.44182
C	3.10593	2.03005	-2.11134
H	2.24357	2.69756	-2.06059
H	3.97105	2.51723	-1.65219
H	3.33593	1.8431	-3.16555
O	1.56343	0.22071	-1.74628
H	2.90645	1.21003	-0.01545

Cl	1.42055	1.31711	2.66651
H	-0.63829	-3.08996	0.54924
O	4.47818	1.90299	1.74348
H	3.54845	1.80812	2.02283
H	4.95496	1.93808	2.57653

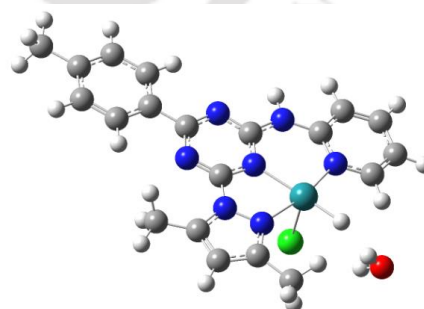
XVI (Alcohololysis segment, step-5, releasing 2.6a)



Ru	-1.38274	0.66093	-0.37925
N	0.96427	2.32602	0.01768
N	0.50312	0.12076	-0.41932
N	-2.06707	-1.20778	-0.87128
N	2.24302	-1.49157	-0.34283
N	0.09798	-2.1897	-0.66318
N	-0.40648	2.46956	-0.04731
N	2.75163	0.8061	0.00637
C	1.46693	1.04308	-0.13624
C	-1.26711	-2.29212	-0.91772
C	0.96751	-1.15032	-0.47432
C	5.48895	0.17832	0.22141
H	5.16416	1.21222	0.28762
C	3.11244	-0.48939	-0.12227
C	4.52933	-0.82138	0.00633
C	1.58898	3.55491	0.09936
C	-1.76476	-3.56441	-1.22234
H	-1.08542	-4.41187	-1.23254
C	0.5767	4.48197	0.07974
H	0.70218	5.55397	0.12776
C	-3.9267	-2.59224	-1.52649
H	-4.98275	-2.65299	-1.76278
C	4.95959	-2.15389	-0.0833
H	4.22071	-2.93007	-0.25308
C	-3.37113	-1.37082	-1.20536
H	-3.95706	-0.45365	-1.19128
C	-3.10747	-3.72053	-1.51818
H	-3.50267	-4.70377	-1.75267
C	8.70981	-1.83078	0.42465
H	8.90688	-2.25028	1.41813
H	9.35622	-0.95711	0.30915
H	9.02691	-2.58499	-0.30182
C	6.30184	-2.47076	0.04285
H	6.61783	-3.50955	-0.02945
C	-0.6457	3.77633	-0.02531
C	6.83109	-0.14986	0.34452
H	7.56435	0.63729	0.5076

C	3.05505	3.73422	0.18393
H	3.28273	4.80036	0.23762
H	3.56706	3.30779	-0.68366
H	3.47366	3.23657	1.0633
C	7.26484	-1.47716	0.26211
C	-2.02782	4.29244	-0.15578
H	-2.29491	4.95402	0.67401
H	-2.74792	3.47072	-0.19855
H	-2.1332	4.86551	-1.08219
C	-2.94416	0.74389	1.4862
C	-3.99177	-0.34886	1.63369
C	-3.61721	-1.60785	2.10321
C	-5.32389	-0.12202	1.27441
C	-4.55902	-2.62739	2.21107
H	-2.57262	-1.76542	2.35945
C	-6.2637	-1.1429	1.37581
H	-5.6109	0.85041	0.87863
C	-5.8833	-2.39975	1.84423
H	-4.25747	-3.60601	2.57728
H	-7.29555	-0.96036	1.08516
H	-6.61772	-3.19729	1.92399
C	-3.25552	1.98254	2.32533
H	-2.4715	2.72878	2.17376
H	-4.22552	2.42294	2.07272
H	-3.26457	1.70369	3.38266
O	-1.6615	0.30839	1.63507
H	-3.11263	1.129	0.38211
Cl	-1.65009	1.32423	-2.74036
H	0.59902	-3.06599	-0.69283
O	-4.47918	1.91865	-1.39657
H	-5.17954	1.8099	-2.0448
H	-3.66224	1.86472	-1.93028

XVII (Alcohololysis segment, step-6)

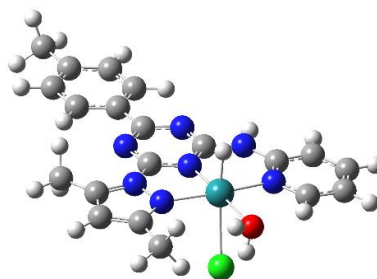


Ru	-1.572	0.70334	-0.22014
N	0.87291	2.31828	0.15775
N	0.45844	0.11037	-0.27315
N	-2.19097	-1.20226	-0.7808
N	2.17777	-1.50407	-0.18772
N	0.01455	-2.1666	-0.53269
N	-0.50616	2.49053	0.09628
N	2.67559	0.80943	0.16754
C	1.38183	1.0342	0.01606
C	-1.34734	-2.25543	-0.85299

C	0.89572	-1.14602	-0.32535
C	5.40261	0.19426	0.36111
H	5.06373	1.22078	0.45944
C	3.02844	-0.49149	0.03145
C	4.45419	-0.81316	0.1408
C	1.52499	3.53908	0.16253
C	-1.78566	-3.5257	-1.25014
H	-1.0732	-4.34522	-1.27988
C	0.53522	4.48385	0.10122
H	0.6815	5.55421	0.08524
C	-3.96491	-2.62361	-1.59616
H	-5.00658	-2.70659	-1.8841
C	4.89544	-2.13754	0.01032
H	4.16168	-2.91757	-0.1635
C	-3.47088	-1.40469	-1.18094
H	-4.09641	-0.52091	-1.13022
C	-3.10374	-3.71863	-1.61694
H	-3.44679	-4.7008	-1.92585
C	8.65124	-1.77586	0.43095
H	8.88436	-2.1891	1.41911
H	9.28467	-0.89655	0.29089
H	8.94925	-2.53049	-0.30268
C	6.24411	-2.43987	0.09711
H	6.57275	-3.47139	-0.0106
C	-0.70529	3.80343	0.04772
C	6.7513	-0.1186	0.44631
H	7.47843	0.67323	0.61234
C	2.99473	3.70137	0.21541
H	3.23624	4.76473	0.16792
H	3.49035	3.18717	-0.61257
H	3.41717	3.28398	1.1339
C	7.19834	-1.43787	0.31739
C	-2.06585	4.3755	-0.06723
H	-2.63339	4.23973	0.85913
H	-2.63705	3.89203	-0.8688
H	-2.01126	5.44617	-0.27206
C	-2.51786	0.56679	1.74352
C	-3.64653	-0.41679	1.78951
C	-3.37898	-1.75316	2.10712
C	-4.96945	-0.04237	1.52532
C	-4.40274	-2.69357	2.14536
H	-2.3482	-2.03249	2.31009
C	-5.99332	-0.98339	1.55642
H	-5.19192	0.98915	1.25886
C	-5.71416	-2.31371	1.8659
H	-4.17671	-3.72865	2.39036
H	-7.0128	-0.6786	1.33479
H	-6.51476	-3.04839	1.89049
C	-2.77662	1.89849	2.40868
H	-1.90003	2.54105	2.31339
H	-3.64634	2.41135	1.98963
H	-2.97114	1.73951	3.47746
O	-1.30116	0.08859	1.77956
H	-3.06078	1.31835	-0.33978
Cl	-1.41815	1.20805	-2.58946

H	0.50076	-3.05075	-0.57782
O	-4.24872	2.78384	-2.1693
H	-4.09993	2.28921	-1.35223
H	-3.49323	2.47521	-2.69144

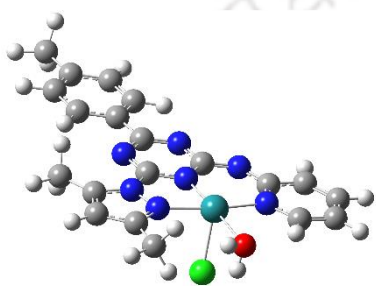
II (Alcoholysis segment, step-8)



Ru	2.27643	0.30349	-0.35926
N	0.06398	2.19373	-0.24698
N	0.3567	-0.08078	-0.22292
N	2.81152	-1.69973	-0.29795
N	-1.54622	-1.50706	-0.11064
N	0.53323	-2.4276	-0.18258
N	1.44249	2.21511	-0.30568
N	-1.84757	0.84838	-0.15588
C	-0.53819	0.9467	-0.20658
C	1.89879	-2.69229	-0.19405
C	-0.23663	-1.29861	-0.17002
C	-4.63497	0.51891	-0.0437
H	-4.20472	1.51461	-0.09042
C	-2.32671	-0.41257	-0.10628
C	-3.77554	-0.59071	-0.04468
C	-0.45599	3.46418	-0.1078
C	2.26393	-4.04162	-0.10567
H	1.48523	-4.79409	-0.02088
C	0.6331	4.3013	-0.07877
H	0.60232	5.37651	0.02254
C	4.54842	-3.3807	-0.22313
H	5.61131	-3.59272	-0.23629
C	-4.33911	-1.8727	0.0207
H	-3.6787	-2.73367	0.02559
C	4.1166	-2.0724	-0.30507
H	4.81777	-1.25251	-0.39294
C	3.59951	-4.39609	-0.12037
H	3.89145	-5.43887	-0.0502
C	-8.06226	-1.10945	0.12347
H	-8.34087	-2.11826	0.43848
H	-8.51161	-0.9418	-0.86228
H	-8.53573	-0.39875	0.80757
C	-5.71513	-2.03423	0.08326
H	-6.13684	-3.03581	0.13809
C	1.7866	3.49574	-0.19316
C	-6.00789	0.34659	0.01858
H	-6.65918	1.21822	0.02126
C	-1.89967	3.77195	-0.00786
H	-2.02676	4.85217	0.08514

H	-2.35984	3.28681	0.85781
H	-2.45337	3.42498	-0.8848
C	-6.57686	-0.93223	0.081
C	3.21316	3.89743	-0.16963
H	3.69963	3.7157	-1.13607
H	3.74663	3.34175	0.61039
H	3.31378	4.96231	0.0464
Cl	3.05702	0.68655	2.11241
H	-0.05071	-3.24935	-0.12472
H	2.13577	0.19704	-1.9514
O	4.4687	0.85867	-0.44546
H	4.56331	1.72887	-0.84485
H	4.4676	1.00387	0.53395

I (Dehydrogenation inner sphere MLC pathway for **3.1a**, step-1)

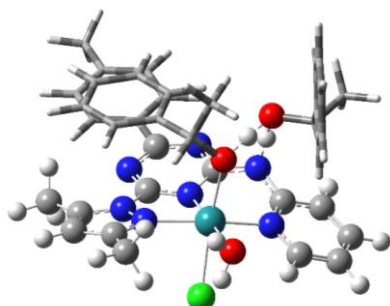


Ru	-2.31179	0.31712	0.83095
Cl	-2.57608	0.8945	-1.44183
N	0.10691	1.92155	0.73072
N	-0.42624	-0.31656	0.72153
N	-3.04924	-1.59005	0.53197
N	1.29192	-1.94849	0.81035
N	-0.87366	-2.66893	0.80043
N	-1.22995	2.12536	0.98233
N	1.85097	0.37172	0.66653
C	0.55631	0.59827	0.68692
C	-2.21577	-2.68366	0.63001
C	-0.03771	-1.65273	0.76425
C	4.56594	-0.27926	0.79754
H	4.24819	0.75741	0.73351
C	2.15984	-0.9535	0.74684
C	3.5924	-1.28451	0.80326
C	0.7772	3.11094	0.58087
C	-2.79203	-3.97732	0.53256
H	-2.1122	-4.81374	0.64907
C	-0.17521	4.09217	0.72982
H	-0.00351	5.15764	0.67425
C	-4.93073	-3.02294	0.05644
H	-5.98089	-3.09905	-0.20432
C	4.00683	-2.62182	0.88157
H	3.24439	-3.39483	0.88375
C	-4.3493	-1.78126	0.20568
H	-4.92155	-0.86881	0.07603
C	-4.12704	-4.15362	0.24985
H	-4.54063	-5.1542	0.15536

C	7.78695	-2.28659	1.03809
H	8.42059	-1.39605	1.03309
H	8.09642	-2.91939	0.19926
H	8.01125	-2.84931	1.95075
C	5.35386	-2.93567	0.95524
H	5.6606	-3.97825	1.01493
C	-1.40334	3.44547	0.97445
C	5.9144	-0.60357	0.87269
H	6.66102	0.18832	0.86922
C	2.23089	3.22698	0.33296
H	2.48685	4.27872	0.18823
H	2.54356	2.65661	-0.54547
H	2.80739	2.82964	1.17425
C	6.33442	-1.93407	0.95402
C	-2.74229	4.04387	1.18958
H	-3.26618	3.57187	2.02683
H	-3.36593	3.93909	0.29349
H	-2.65836	5.11141	1.40251
O	-4.40158	1.14609	0.91118
H	-4.47478	1.68425	1.73037
H	-4.36695	1.73237	0.13993
C	-5.65236	-1.6889	5.96374
C	-5.7714	-0.32727	5.68446
C	-5.72712	0.13936	4.36702
C	-5.57384	-0.78662	3.32959
C	-5.457	-2.14568	3.60457
C	-5.49139	-2.59965	4.92282
H	-5.68533	-2.0352	6.99322
H	-5.89346	0.38815	6.49716
H	-5.51864	-0.44036	2.29904
H	-5.32037	-2.84578	2.78285
H	-5.39244	-3.66006	5.13665
C	-5.79121	1.62295	4.0802
H	-5.91437	2.15152	5.03976
C	-6.92605	2.00237	3.15363
H	-7.89015	1.73929	3.59465
H	-6.91413	3.0777	2.95773
H	-6.83607	1.47584	2.19813
O	-4.57738	2.08552	3.46284
H	-3.83618	1.76299	4.01408
C	1.67998	1.61161	3.69907
C	0.65691	0.70542	3.95878
C	-0.58368	1.14494	4.43081
C	-0.7863	2.51116	4.63159
C	0.23637	3.41906	4.36661
C	1.47051	2.97426	3.90323
H	2.63238	1.24861	3.31938
H	0.8286	-0.35892	3.79807
H	-1.74166	2.86176	5.00878
H	0.06451	4.48112	4.52221
H	2.26648	3.68612	3.69867
C	-1.66369	0.13305	4.71689
H	-1.27598	-0.588	5.45581
C	-2.08802	-0.63748	3.47688
H	-1.24711	-1.12906	2.98638

H	-2.83983	-1.40073	3.70293
H	-2.60254	0.10215	2.81409
O	-2.78765	0.81175	5.28609
H	-3.43149	0.138	5.5461

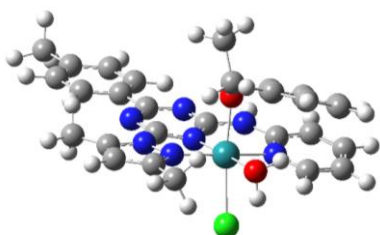
I-TS-3 (Dehydrogenation inner sphere MLC pathway for **3.1a**, step-1)



Ru	-1.17397	1.25373	-0.93251
Cl	-1.21828	2.7043	-2.89489
N	1.39867	2.42355	-0.26275
N	0.61616	0.4252	-1.07454
N	-2.02093	-0.24962	-2.07405
N	2.02021	-1.47828	-1.0188
N	-0.21294	-1.76321	-1.50394
N	0.06413	2.72172	-0.0932
N	2.92755	0.67593	-0.5543
C	1.699	1.12705	-0.6668
C	-1.33134	-1.40674	-2.26445
C	0.82566	-0.9229	-1.22636
C	5.46659	-0.46239	-0.19046
H	5.3187	0.60232	-0.03337
C	3.03976	-0.65844	-0.73269
C	4.36865	-1.24985	-0.562
C	2.20367	3.46105	0.14157
C	-1.79271	-2.37494	-3.16342
H	-1.19452	-3.27157	-3.28038
C	1.34313	4.45789	0.54214
H	1.62926	5.43287	0.90994
C	-3.6685	-0.98953	-3.6663
H	-4.59074	-0.77374	-4.19464
C	4.56045	-2.62661	-0.75027
H	3.7062	-3.23431	-1.03168
C	-3.15565	-0.05597	-2.78452
H	-3.65311	0.89156	-2.61393
C	-2.96847	-2.17672	-3.86741
H	-3.32783	-2.92721	-4.56524
C	8.27454	-3.02217	-0.05874
H	8.96672	-2.35115	0.45622
H	8.71741	-3.26127	-1.03251
H	8.23155	-3.96036	0.503
C	5.81444	-3.19013	-0.57754
H	5.94822	-4.25987	-0.72718
C	0.03183	3.96687	0.37752
C	6.71864	-1.03671	-0.02175
H	7.56306	-0.41392	0.26717

C	3.6822	3.41874	0.13113
H	4.07141	4.40223	0.40176
H	4.07813	3.13666	-0.84776
H	4.05722	2.6761	0.8432
C	6.91861	-2.40766	-0.21507
C	-1.2617	4.64324	0.63808
H	-1.89276	4.05048	1.31183
H	-1.80956	4.80684	-0.29747
H	-1.10653	5.61636	1.10717
O	-3.21212	2.21217	-0.74331
H	-3.29993	2.68643	0.09033
H	-3.03302	2.88618	-1.43038
C	-4.50682	-2.76566	3.66017
C	-3.60333	-3.13038	2.66753
C	-3.62958	-2.50899	1.41639
C	-4.57395	-1.50694	1.18397
C	-5.48474	-1.14215	2.17231
C	-5.45359	-1.77279	3.41352
H	-4.47531	-3.2578	4.62859
H	-2.85987	-3.89898	2.86862
H	-4.58082	-1.00365	0.21735
H	-6.21886	-0.36552	1.97336
H	-6.16407	-1.49284	4.18675
C	-2.63801	-2.86757	0.33518
H	-3.02339	-2.43029	-0.60268
C	-2.45951	-4.35811	0.12654
H	-3.41188	-4.8431	-0.10672
H	-1.76598	-4.54381	-0.69947
H	-2.04038	-4.82957	1.02012
O	-1.362	-2.29264	0.63348
H	-0.64792	-2.22181	-0.482
H	-1.47253	-1.09922	0.78476
O	-1.54847	0.1172	0.84715
C	-1.16088	0.65509	2.09984
H	-1.44398	1.72454	2.09587
C	-1.92413	-0.0526	3.21058
H	-1.6531	-1.11318	3.23872
H	-1.68237	0.38229	4.1853
H	-3.00386	0.01201	3.04606
C	0.33203	0.58509	2.35191
C	1.02873	1.70632	2.80358
C	1.02977	-0.61788	2.18926
C	2.39453	1.64174	3.07215
H	0.49425	2.64914	2.9229
C	2.39365	-0.68632	2.45646
H	0.49591	-1.50602	1.85478
C	3.08233	0.44439	2.89436
H	2.92126	2.53134	3.41129
H	2.92631	-1.62273	2.30509
H	4.1505	0.39051	3.09032

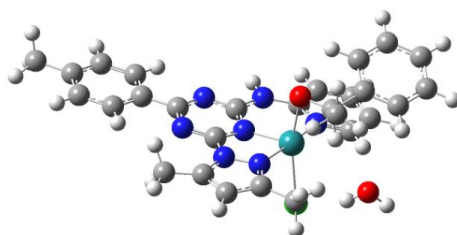
XVIII (Dehydrogenation inner sphere MLC pathway for **3.1a**, step-2)



Ru	-1.30928	0.32268	-0.53088
N	0.88796	2.11711	0.05102
N	0.60828	-0.11045	-0.43671
N	-1.83054	-1.6183	-1.0193
N	2.42514	-1.60943	-0.1233
N	0.3497	-2.45129	-0.51272
N	-0.48265	2.18141	-0.10474
N	2.76108	0.72375	0.17478
C	1.47735	0.87017	-0.06576
C	-0.9782	-2.65499	-0.8566
C	1.14314	-1.34934	-0.35297
C	5.515	0.29511	0.55512
H	5.11122	1.30183	0.59735
C	3.21554	-0.54607	0.09886
C	4.64392	-0.77444	0.30299
C	1.43034	3.37093	0.24855
C	-1.37895	-3.98394	-1.05042
H	-0.6619	-4.7814	-0.87826
C	0.36444	4.23634	0.21484
H	0.41694	5.30902	0.33342
C	-3.52496	-3.19196	-1.72566
H	-4.53316	-3.34191	-2.09475
C	5.1758	-2.07151	0.24287
H	4.5054	-2.90114	0.04331
C	-3.0648	-1.91232	-1.49446
H	-3.68926	-1.0488	-1.69138
C	-2.66552	-4.26144	-1.47276
H	-2.98315	-5.28773	-1.62388
C	8.86421	-1.46562	0.91796
H	9.05084	-1.83191	1.93432
H	9.45266	-0.55332	0.79128
H	9.26085	-2.22236	0.23454
C	6.53109	-2.28575	0.43193
H	6.92769	-3.29761	0.37881
C	-0.80155	3.47078	-0.01051
C	6.87037	0.06961	0.74339
H	7.53371	0.91052	0.93454
C	2.87273	3.63697	0.44144
H	3.02506	4.71313	0.54267
H	3.46983	3.27364	-0.40005
H	3.26294	3.1385	1.33335
C	7.40576	-1.22183	0.6885
C	-2.20301	3.92739	-0.15813
H	-2.27889	4.99969	0.03083
H	-2.86962	3.39558	0.52654
H	-2.56534	3.72592	-1.17165
C	-2.02	0.45757	2.33081

C	-3.50179	0.11903	2.22642
C	-3.90926	-1.10599	1.69059
C	-4.48306	1.03274	2.62036
C	-5.26339	-1.39923	1.52852
H	-3.13837	-1.80832	1.38144
C	-5.836	0.74189	2.47096
H	-4.17539	1.99586	3.02779
C	-6.23245	-0.47394	1.91469
H	-5.56128	-2.3532	1.09804
H	-6.58447	1.47033	2.77283
H	-7.28791	-0.69775	1.78449
C	-1.52349	0.19833	3.75345
H	-0.47517	0.49625	3.84142
H	-2.11172	0.74761	4.49645
H	-1.5943	-0.87021	3.98118
O	-1.23292	-0.26405	1.45103
H	-1.93866	1.55273	2.14289
Cl	-1.70334	0.97907	-2.89677
H	0.89603	-3.29512	-0.41927
O	-3.41963	1.08409	-0.51673
H	-3.51098	1.1809	-1.48587
H	-4.08699	0.46006	-0.19695

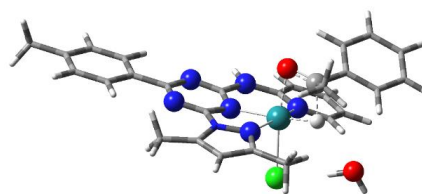
XIX (Dehydrogenation inner sphere MLC pathway for **3.1a**, step-2)



Ru	-1.38274	0.66093	-0.37925
N	0.96427	2.32602	0.01768
N	0.50312	0.12076	-0.41932
N	-2.06707	-1.20778	-0.87128
N	2.24302	-1.49157	-0.34283
N	0.09798	-2.1897	-0.66318
N	-0.40648	2.46956	-0.04731
N	2.75163	0.8061	0.00637
C	1.46693	1.04308	-0.13624
C	-1.26711	-2.29212	-0.91772
C	0.96751	-1.15032	-0.47432
C	5.48895	0.17832	0.22141
H	5.16416	1.21222	0.28762
C	3.11244	-0.48939	-0.12227
C	4.52933	-0.82138	0.00633
C	1.58898	3.55491	0.09936
C	-1.76476	-3.56441	-1.22234
H	-1.08542	-4.41187	-1.23254
C	0.5767	4.48197	0.07974
H	0.70218	5.55397	0.12776
C	-3.9267	-2.59224	-1.52649

H	-4.98275	-2.65299	-1.76278
C	4.95959	-2.15389	-0.0833
H	4.22071	-2.93007	-0.25308
C	-3.37113	-1.37082	-1.20536
H	-3.95706	-0.45365	-1.19128
C	-3.10747	-3.72053	-1.51818
H	-3.50267	-4.70377	-1.75267
C	8.70981	-1.83078	0.42465
H	8.90688	-2.25028	1.41813
H	9.35622	-0.95711	0.30915
H	9.02691	-2.58499	-0.30182
C	6.30184	-2.47076	0.04285
H	6.61783	-3.50955	-0.02945
C	-0.6457	3.77633	-0.02531
C	6.83109	-0.14986	0.34452
H	7.56435	0.63729	0.5076
C	3.05505	3.73422	0.18393
H	3.28273	4.80036	0.23762
H	3.56706	3.30779	-0.68366
H	3.47366	3.23657	1.0633
C	7.26484	-1.47716	0.26211
C	-2.02782	4.29244	-0.15578
H	-2.29491	4.95402	0.67401
H	-2.74792	3.47072	-0.19855
H	-2.1332	4.86551	-1.08219
C	-2.94416	0.74389	1.4862
C	-3.99177	-0.34886	1.63369
C	-3.61721	-1.60785	2.10321
C	-5.32389	-0.12202	1.27441
C	-4.55902	-2.62739	2.21107
H	-2.57262	-1.76542	2.35945
C	-6.2637	-1.1429	1.37581
H	-5.6109	0.85041	0.87863
C	-5.8833	-2.39975	1.84423
H	-4.25747	-3.60601	2.57728
H	-7.29555	-0.96036	1.08516
H	-6.61772	-3.19729	1.92399
C	-3.25552	1.98254	2.32533
H	-2.4715	2.72878	2.17376
H	-4.22552	2.42294	2.07272
H	-3.26457	1.70369	3.38266
O	-1.6615	0.30839	1.63507
H	-3.11263	1.129	0.38211
Cl	-1.65009	1.32423	-2.74036
H	0.59902	-3.06599	-0.69283
O	-4.47918	1.91865	-1.39657
H	-5.17954	1.8099	-2.0448
H	-3.66224	1.86472	-1.93028

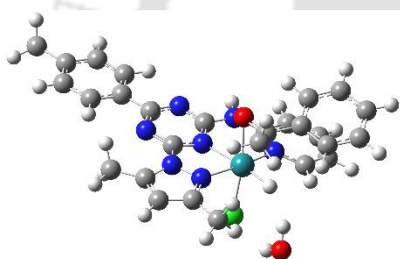
I-TS-4 (Dehydrogenation inner sphere MLC pathway for **3.1a**, step-2)



Ru	1.34798	0.66581	0.29184
N	-1.05853	2.29459	-0.08725
N	-0.61166	0.09443	0.36828
N	1.99867	-1.19778	0.88166
N	-2.31173	-1.54345	0.16297
N	-0.15908	-2.20091	0.55163
N	0.31631	2.45845	-0.03368
N	-2.83524	0.76145	-0.15874
C	-1.55618	1.00489	0.04699
C	1.18703	-2.27611	0.92172
C	-1.04591	-1.17808	0.35975
C	-5.55573	0.1117	-0.44262
H	-5.2356	1.14815	-0.48804
C	-3.17966	-0.54293	-0.05997
C	-4.59226	-0.88557	-0.2269
C	-1.70454	3.5165	-0.09286
C	1.64849	-3.53281	1.33084
H	0.96313	-4.37568	1.32809
C	-0.70973	4.45832	-0.03473
H	-0.85393	5.52894	-0.01651
C	3.77721	-2.55285	1.78337
H	4.80491	-2.60136	2.12494
C	-5.01127	-2.22107	-0.16749
H	-4.26882	-2.99388	0.00126
C	3.26341	-1.34731	1.35087
H	3.85468	-0.43436	1.35338
C	2.95792	-3.67984	1.75177
H	3.32299	-4.65152	2.06888
C	-8.75952	-1.90859	-0.7175
H	-9.07727	-1.76184	-1.75611
H	-9.40869	-1.27894	-0.10115
H	-8.95801	-2.95159	-0.45964
C	-6.35067	-2.54598	-0.3202
H	-6.66094	-3.58756	-0.27064
C	0.52601	3.76993	0.0194
C	-6.89177	-0.22329	-0.59209
H	-7.62778	0.56138	-0.7552
C	-3.17469	3.6764	-0.13859
H	-3.42121	4.7377	-0.07305
H	-3.66599	3.1462	0.68215
H	-3.59862	3.27173	-1.06222
C	-7.31633	-1.55727	-0.5362
C	1.89481	4.31282	0.17774
H	1.94272	4.95516	1.06184
H	2.20068	4.91489	-0.68418
H	2.61227	3.50055	0.31902
C	2.75963	0.70275	-1.45593
C	3.88993	-0.30357	-1.44467

C	3.65254	-1.59343	-1.92325
C	5.16254	0.02733	-0.96956
C	4.67055	-2.54234	-1.9241
H	2.65309	-1.83138	-2.27769
C	6.17807	-0.92368	-0.96676
H	5.33684	1.01366	-0.54488
C	5.93528	-2.21063	-1.44431
H	4.47679	-3.54418	-2.29996
H	7.16106	-0.66238	-0.58287
H	6.73033	-2.95211	-1.44182
C	3.10593	2.03005	-2.11134
H	2.24357	2.69756	-2.06059
H	3.97105	2.51723	-1.65219
H	3.33593	1.8431	-3.16555
O	1.56343	0.22071	-1.74628
H	2.90645	1.21003	-0.01545
Cl	1.42055	1.31711	2.66651
H	-0.63829	-3.08996	0.54924
O	4.47818	1.90299	1.74348
H	3.54845	1.80812	2.02283
H	4.95496	1.93808	2.57653

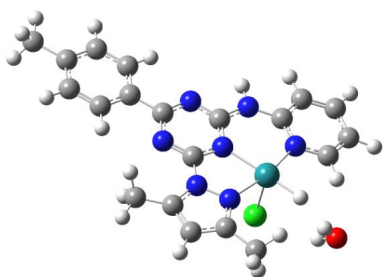
XX (Dehydrogenation inner sphere MLC pathway for **3.1a**, step-3)



Ru	-1.572	0.70334	-0.22014
N	0.87291	2.31828	0.15775
N	0.45844	0.11037	-0.27315
N	-2.19097	-1.20226	-0.7808
N	2.17777	-1.50407	-0.18772
N	0.01455	-2.1666	-0.53269
N	-0.50616	2.49053	0.09628
N	2.67559	0.80943	0.16754
C	1.38183	1.0342	0.01606
C	-1.34734	-2.25543	-0.85299
C	0.89572	-1.14602	-0.32535
C	5.40261	0.19426	0.36111
H	5.06373	1.22078	0.45944
C	3.02844	-0.49149	0.03145
C	4.45419	-0.81316	0.1408
C	1.52499	3.53908	0.16253
C	-1.78566	-3.5257	-1.25014
H	-1.0732	-4.34522	-1.27988
C	0.53522	4.48385	0.10122
H	0.6815	5.55421	0.08524
C	-3.96491	-2.62361	-1.59616
H	-5.00658	-2.70659	-1.8841

C	4.89544	-2.13754	0.01032
H	4.16168	-2.91757	-0.1635
C	-3.47088	-1.40469	-1.18094
H	-4.09641	-0.52091	-1.13022
C	-3.10374	-3.71863	-1.61694
H	-3.44679	-4.7008	-1.92585
C	8.65124	-1.77586	0.43095
H	8.88436	-2.1891	1.41911
H	9.28467	-0.89655	0.29089
H	8.94925	-2.53049	-0.30268
C	6.24411	-2.43987	0.09711
H	6.57275	-3.47139	-0.0106
C	-0.70529	3.80343	0.04772
C	6.7513	-0.1186	0.44631
H	7.47843	0.67323	0.61234
C	2.99473	3.70137	0.21541
H	3.23624	4.76473	0.16792
H	3.49035	3.18717	-0.61257
H	3.41717	3.28398	1.1339
C	7.19834	-1.43787	0.31739
C	-2.06585	4.3755	-0.06723
H	-2.63339	4.23973	0.85913
H	-2.63705	3.89203	-0.8688
H	-2.01126	5.44617	-0.27206
C	-2.51786	0.56679	1.74352
C	-3.64653	-0.41679	1.78951
C	-3.37898	-1.75316	2.10712
C	-4.96945	-0.04237	1.52532
C	-4.40274	-2.69357	2.14536
H	-2.3482	-2.03249	2.31009
C	-5.99332	-0.98339	1.55642
H	-5.19192	0.98915	1.25886
C	-5.71416	-2.31371	1.8659
H	-4.17671	-3.72865	2.39036
H	-7.0128	-0.6786	1.33479
H	-6.51476	-3.04839	1.89049
C	-2.77662	1.89849	2.40868
H	-1.90003	2.54105	2.31339
H	-3.64634	2.41135	1.98963
H	-2.97114	1.73951	3.47746
O	-1.30116	0.08859	1.77956
H	-3.06078	1.31835	-0.33978
Cl	-1.41815	1.20805	-2.58946
H	0.50076	-3.05075	-0.57782
O	-4.24872	2.78384	-2.1693
H	-4.09993	2.28921	-1.35223
H	-3.49323	2.47521	-2.69144

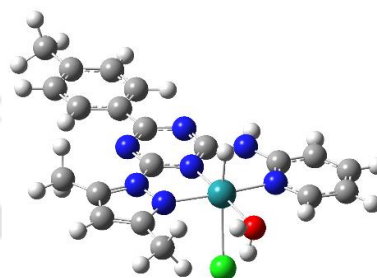
XXI (Dehydrogenation inner sphere MLC pathway for **3.1a**, step-4, releasing **3.1a'**)



H	-3.65465	3.66088	-1.36783
H	-3.9154	0.55769	0.01514
Cl	-2.4398	0.22255	-2.45444
H	0.14249	-3.39122	0.04045
O	-5.71772	0.08635	-1.82752
H	-5.19096	0.49341	-1.12128
H	-5.03084	-0.04698	-2.49312

XXII (Dehydrogenation inner sphere MLC pathway for **3.1a**, step-5)

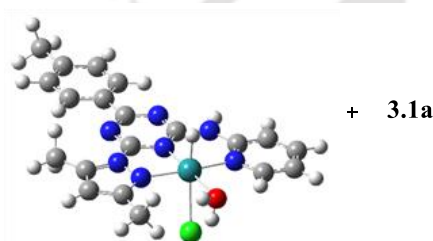
Ru	-2.33957	0.12409	-0.10285
N	-0.11157	2.03672	-0.16341
N	-0.29755	-0.24417	-0.09615
N	-2.77109	-1.90875	-0.1785
N	1.63587	-1.61662	0.00272
N	-0.44675	-2.57177	0.00227
N	-1.50049	2.0302	-0.10394
N	1.85895	0.76139	-0.06837
C	0.54355	0.8121	-0.11326
C	-1.80943	-2.8655	-0.1268
C	0.31674	-1.43622	-0.03885
C	4.64782	0.52067	0.00371
H	4.18097	1.50039	-0.02335
C	2.37269	-0.49126	-0.01961
C	3.82865	-0.61933	0.01096
C	0.37028	3.31891	-0.33622
C	-2.11985	-4.23119	-0.18385
H	-1.3149	-4.95815	-0.12179
C	-0.73824	4.12578	-0.39958
H	-0.73134	5.19768	-0.53483
C	-4.41756	-3.6583	-0.45334
H	-5.4597	-3.91159	-0.61012
C	4.43731	-1.88137	0.04719
H	3.80736	-2.76486	0.05245
C	-4.05027	-2.32976	-0.37963
H	-4.7705	-1.52912	-0.52161
C	-3.43194	-4.63644	-0.33542
H	-3.67553	-5.6932	-0.38033
C	8.13226	-0.98454	0.09201
H	8.45193	-2.02321	0.20458
H	8.56962	-0.40819	0.91375
H	8.57979	-0.59917	-0.83076
C	5.81951	-1.99472	0.07422
H	6.27786	-2.98109	0.10133
C	-1.87657	3.29693	-0.26518
C	6.02652	0.39657	0.0326
H	6.6467	1.2905	0.02894
C	1.80594	3.66542	-0.42746
H	1.90326	4.74129	-0.58365
H	2.29783	3.14228	-1.25255
H	2.35063	3.38853	0.47955
C	6.64108	-0.8627	0.06787
C	-3.31158	3.65295	-0.32741
H	-3.49615	4.64318	0.09555
H	-3.90965	2.90422	0.1965



Ru	2.27643	0.30349	-0.35926
N	0.06398	2.19373	-0.24698
N	0.3567	-0.08078	-0.22292
N	2.81152	-1.69973	-0.29795
N	-1.54622	-1.50706	-0.11064
N	0.53323	-2.4276	-0.18258
N	1.44249	2.21511	-0.30568
N	-1.84757	0.84838	-0.15588
C	-0.53819	0.9467	-0.20658
C	1.89879	-2.69229	-0.19405
C	-0.23663	-1.29861	-0.17002
C	-4.63497	0.51891	-0.0437
H	-4.20472	1.51461	-0.09042
C	-2.32671	-0.41257	-0.10628
C	-3.77554	-0.59071	-0.04468
C	-0.45599	3.46418	-0.1078
C	2.26393	-4.04162	-0.10567
H	1.48523	-4.79409	-0.02088
C	0.6331	4.3013	-0.07877
H	0.60232	5.37651	0.02254
C	4.54842	-3.3807	-0.22313
H	5.61131	-3.59272	-0.23629
C	-4.33911	-1.8727	0.0207
H	-3.6787	-2.73367	0.02559
C	4.1166	-2.0724	-0.30507
H	4.81777	-1.25251	-0.39294
C	3.59951	-4.39609	-0.12037
H	3.89145	-5.43887	-0.0502
C	-8.06226	-1.10945	0.12347
H	-8.34087	-2.11826	0.43848
H	-8.51161	-0.9418	-0.86228
H	-8.53573	-0.39875	0.80757
C	-5.71513	-2.03423	0.08326
H	-6.13684	-3.03581	0.13809
C	1.7866	3.49574	-0.19316

C	-6.00789	0.34659	0.01858
H	-6.65918	1.21822	0.02126
C	-1.89967	3.77195	-0.00786
H	-2.02676	4.85217	0.08514
H	-2.35984	3.28681	0.85781
H	-2.45337	3.42498	-0.8848
C	-6.57686	-0.93223	0.081
C	3.21316	3.89743	-0.16963
H	3.69963	3.7157	-1.13607
H	3.74663	3.34175	0.61039
H	3.31378	4.96231	0.0464
Cl	3.05702	0.68655	2.11241
H	-0.05071	-3.24935	-0.12472
H	2.13577	0.19704	-1.9514
O	4.4687	0.85867	-0.44546
H	4.56331	1.72887	-0.84485
H	4.4676	1.00387	0.53395

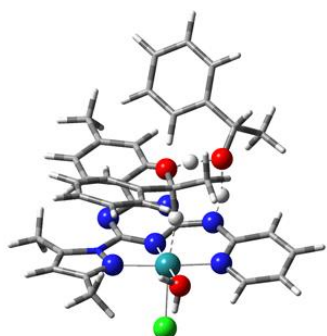
II (Dehydrogenation inner sphere MLC pathway for **3.1a**, molecular complex formation, step-6)



Ru	-0.96818	0.02947	1.26532
Cl	-0.85041	0.25131	3.82358
N	1.28047	-1.81693	1.13026
N	0.86248	0.38646	0.64882
N	-1.56487	1.9966	1.03419
N	2.56802	1.7183	-0.34062
N	0.50864	2.62473	0.01453
N	-0.04857	-1.83295	1.50862
N	3.01743	-0.5502	0.20658
C	1.77778	-0.62204	0.6372
C	-0.77023	2.93354	0.46858
C	1.33529	1.53999	0.11932
C	5.65899	-0.27112	-0.69853
H	5.31454	-1.22168	-0.30378
C	3.38896	0.65581	-0.27295
C	4.7629	0.80667	-0.7479
C	1.90679	-3.00681	1.43853
C	-1.18237	4.26144	0.29986
H	-0.50488	4.96745	-0.17177
C	0.94038	-3.7836	2.02844
H	1.07668	-4.78785	2.40294
C	-3.23956	3.70892	1.36679
H	-4.21928	3.96115	1.75628
C	5.21601	2.02951	-1.2653
H	4.52489	2.8652	-1.30917

C	-2.77195	2.41575	1.49303
H	-3.36269	1.64171	1.96681
C	-2.42997	4.65812	0.74478
H	-2.75531	5.686	0.62076
C	8.83509	1.25326	-2.12414
H	9.26961	0.30155	-2.44124
H	9.47106	1.64314	-1.32055
H	8.91312	1.9568	-2.95781
C	6.51994	2.16366	-1.71521
H	6.85405	3.11843	-2.11639
C	-0.2504	-3.02498	2.06576
C	6.96103	-0.12645	-1.15111
H	7.642	-0.97406	-1.10823
C	3.33142	-3.29697	1.16334
H	3.56448	-4.30249	1.51873
H	3.99456	-2.58345	1.66088
H	3.56154	-3.23723	0.09577
C	7.41986	1.09199	-1.66537
C	-1.56471	-3.38179	2.64836
H	-2.35582	-3.35656	1.89216
H	-1.81816	-2.67681	3.44917
H	-1.53572	-4.38491	3.07716
O	-3.03803	-0.48527	1.97404
H	-3.27512	-1.31888	1.52137
H	-2.77544	-0.65772	2.89917
C	-4.13908	0.38199	-3.94759
C	-4.18541	-0.81466	-3.23738
C	-4.11201	-0.82144	-1.84411
C	-3.98782	0.3967	-1.16747
C	-3.92856	1.59252	-1.87521
C	-4.00666	1.58873	-3.26655
H	-4.1953	0.37054	-5.03289
H	-4.27404	-1.76099	-3.76902
H	-3.91295	0.4053	-0.08172
H	-3.81634	2.53018	-1.33449
H	-3.9606	2.52374	-3.81842
C	-4.18511	-2.12871	-1.09268
H	-4.03242	-2.94539	-1.81758
C	-5.52313	-2.32629	-0.40691
H	-6.33532	-2.33901	-1.1381
H	-5.53712	-3.26971	0.14587
H	-5.71198	-1.50867	0.29689
O	-3.18209	-2.23626	-0.07324
H	-2.39764	-1.71563	-0.3353
H	1.00528	3.40331	-0.39379
H	-1.32443	-0.22414	-0.29435

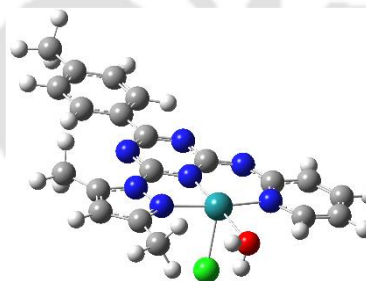
O-TS-4 (Dehydrogenation inner sphere MLC pathway for **3.1a**, step-7)



Ru	-1.02313	-2.14297	-0.27073
Cl	-2.61238	-3.47155	-1.70699
N	-3.34557	-1.05368	1.09327
N	-1.80402	-0.32897	-0.44935
N	0.18455	-1.8318	-1.93016
N	-1.78509	1.94039	-1.12224
N	-0.04654	0.5915	-1.78268
N	-2.55911	-2.183	1.15812
N	-3.51084	1.14627	0.31837
C	-2.89797	-0.01695	0.2771
C	0.4273	-0.56506	-2.38098
C	-1.2381	0.7148	-1.1536
C	-4.72067	3.67516	0.27503
H	-5.16701	2.86578	0.84504
C	-2.91008	2.10594	-0.4233
C	-3.54166	3.42998	-0.43933
C	-4.47936	-1.18261	1.863
C	1.26493	-0.36909	-3.49399
H	1.45342	0.65683	-3.79081
C	-4.4012	-2.43713	2.42196
H	-5.12954	-2.88205	3.08474
C	1.45687	-2.73106	-3.76918
H	1.81196	-3.6137	-4.29069
C	-2.97364	4.47852	-1.17807
H	-2.06319	4.2826	-1.73557
C	0.66879	-2.87411	-2.64532
H	0.40668	-3.85569	-2.26807
C	1.78349	-1.44253	-4.19109
H	2.4183	-1.28076	-5.0578
C	-5.38119	7.33795	-0.50359
H	-6.32573	7.35331	0.04598
H	-5.58496	7.6695	-1.52731
H	-4.72601	8.09391	-0.05665
C	-3.56988	5.72871	-1.19481
H	-3.11821	6.53145	-1.77485
C	-3.20632	-3.02578	1.95912
C	-5.31089	4.93119	0.25124
H	-6.22779	5.10635	0.8105
C	-5.52118	-0.14063	2.00187
H	-6.33606	-0.53205	2.61417
H	-5.92203	0.16506	1.03176
H	-5.12974	0.76659	2.47044
C	-4.74875	5.9813	-0.48075
C	-2.66713	-4.38182	2.22025
H	-1.63138	-4.33524	2.57683

H	-2.69841	-4.98866	1.30734
H	-3.25398	-4.89817	2.98196
O	-0.26035	-4.28341	-0.12713
H	-0.41022	-4.60375	0.76817
H	-1.03565	-4.59379	-0.65089
C	5.00247	-0.25649	-2.1086
C	4.25322	0.41313	-1.14488
C	3.33083	-0.27742	-0.35797
C	3.15158	-1.65066	-0.5586
C	3.90096	-2.31833	-1.51959
C	4.83048	-1.62441	-2.29234
H	5.71747	0.29158	-2.71553
H	4.38514	1.48355	-0.99749
H	2.40343	-2.19441	0.0184
H	3.74644	-3.38227	-1.67602
H	5.41136	-2.15004	-3.04539
C	2.56726	0.45262	0.71038
H	2.82951	1.51592	0.68324
C	2.76516	-0.10146	2.10252
H	3.82014	-0.04167	2.37944
H	2.17693	0.45868	2.83283
H	2.46545	-1.15272	2.14813
O	1.11788	0.44318	0.45526
H	0.81384	0.69732	-0.54874
H	0.12911	-1.62434	0.83197
H	0.65737	-0.52902	0.59061

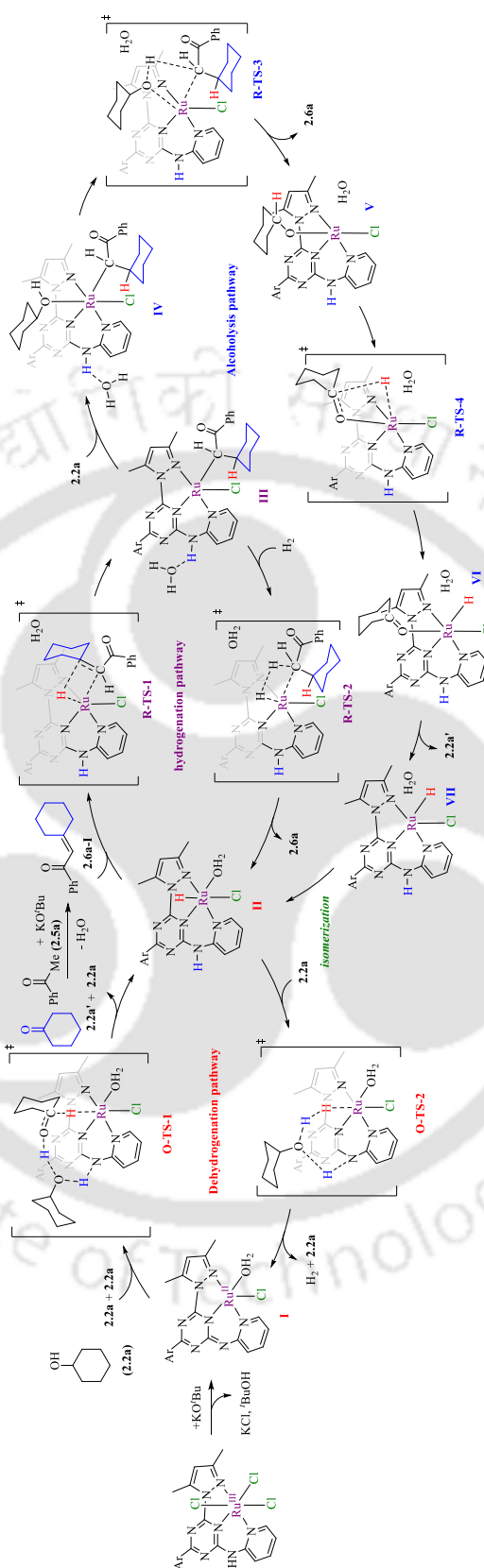
I (Dehydrogenation inner sphere MLC pathway for **3.1a**, liberating of H₂, step-7)



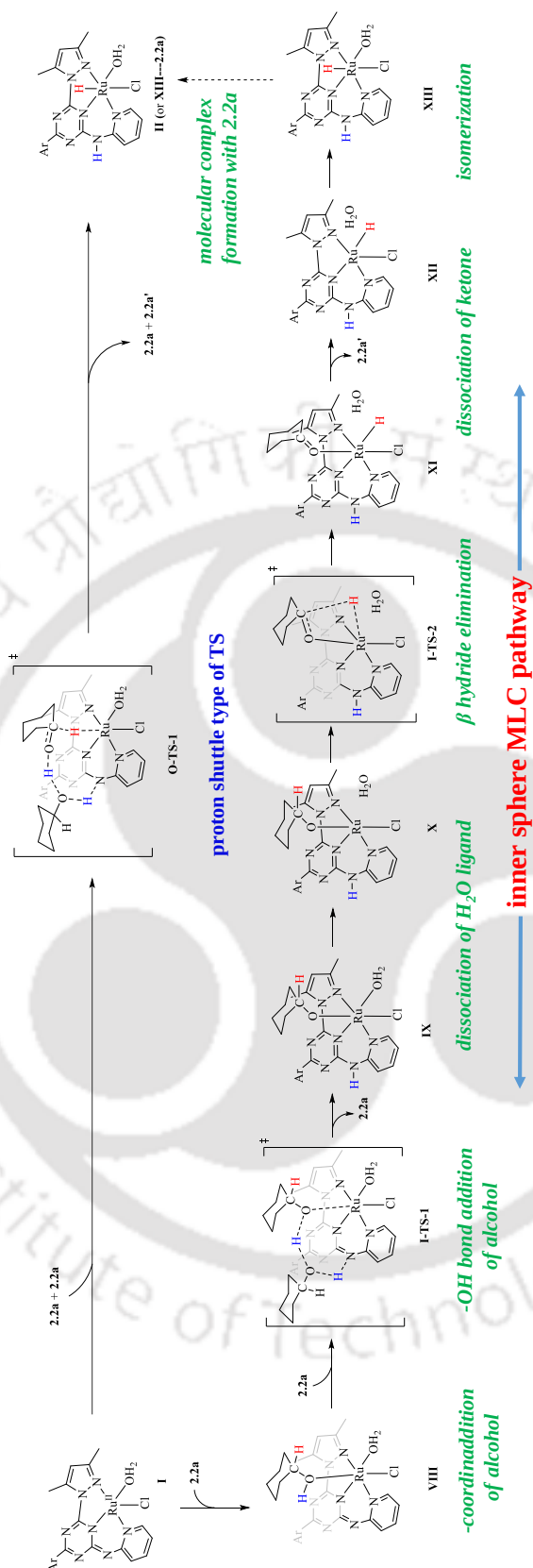
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N	-0.27392	-0.43713	1.27382
N	-2.7477	-2.00622	1.39533
N	1.61909	-1.85914	1.41909
N	-0.44861	-2.79721	1.64331
N	-1.35308	1.91761	1.20213
N	1.90835	0.48268	1.03276
C	0.59988	0.56865	1.09781
C	-1.78925	-2.97931	1.56966
C	0.26243	-1.71042	1.43545
C	4.68068	0.14036	1.07058
H	4.24629	1.12807	0.94496
C	2.36499	-0.78932	1.21128
C	3.82694	-0.95958	1.21174

C	0.56435	3.07597	0.80949	C	0.47567	0.94638	4.26651
C	-2.21075	-4.32991	1.68223	C	1.1756	2.16356	4.22946
H	-1.42842	-5.06334	1.84138	C	2.56186	2.17514	4.23213
C	-0.48965	3.95909	0.84074	C	3.27075	0.9731	4.28181
H	-0.42561	5.02828	0.69817	H	3.13683	-1.17545	4.35751
C	-4.47891	-3.68305	1.31432	H	0.68498	-1.21232	4.3522
H	-5.53192	-3.90525	1.17633	H	0.59844	3.08308	4.17949
C	4.39216	-2.23114	1.384	H	3.09675	3.12034	4.18823
H	3.72399	-3.07948	1.49634	H	4.35727	0.97946	4.26052
C	-4.04152	-2.3771	1.2422	C	-0.99879	0.99233	4.22121
H	-4.73175	-1.55863	1.06738	C	-1.78751	-0.27149	4.02141
C	-3.53318	-4.68541	1.55735	H	-1.21511	-1.14771	3.71902
H	-3.83106	-5.72782	1.63031	H	-2.33891	-0.52231	4.93638
C	8.11484	-1.47956	1.28996	H	-2.63676	-0.07267	3.31785
H	8.64334	-0.52798	1.19135	O	-1.59507	2.06934	4.34829
H	8.45022	-2.13048	0.47533				
H	8.44795	-1.95106	2.22084				
C	5.76827	-2.39065	1.41007				
H	6.19196	-3.38462	1.5419				
C	-1.65984	3.20692	1.07272				
C	6.05918	-0.02897	1.09845				
H	6.71097	0.83525	0.98537				
C	2.00714	3.33167	0.60489				
H	2.15906	4.4005	0.44035				
H	2.40087	2.77898	-0.25194				
H	2.59543	3.01126	1.47055				
C	6.62944	-1.29406	1.2664				
C	-3.06386	3.68315	1.11217				
H	-3.60173	3.33071	1.99641				
H	-3.60774	3.34068	0.2239				
H	-3.09575	4.77413	1.11328				
O	-4.38085	0.59243	1.33784				
H	-4.53777	1.1951	2.09691				
H	-4.46352	1.08643	0.51072				
C	-8.29764	-0.18049	4.88206				
C	-7.30036	0.75628	5.14766				
C	-5.99753	0.5607	4.6871				
C	-5.71698	-0.59854	3.95355				
C	-6.70824	-1.53336	3.68589				
C	-8.00583	-1.32695	4.15151				
H	-9.30641	-0.00966	5.2482				
H	-7.54623	1.6466	5.72033				
H	-4.70947	-0.76601	3.57399				
H	-6.46089	-2.42531	3.11517				
H	-8.78402	-2.05657	3.9455				
C	-4.87646	1.53336	4.96892				
H	-4.11568	0.99954	5.56641				
C	-5.27028	2.78822	5.72008				
H	-5.68309	2.55725	6.70659				
H	-4.39191	3.42264	5.86255				
H	-6.01388	3.35991	5.1569				
O	-4.26396	1.89091	3.71958				
H	-3.31571	2.06803	3.90702				
C	2.58774	-0.23847	4.33981				
C	1.198	-0.2549	4.32621				

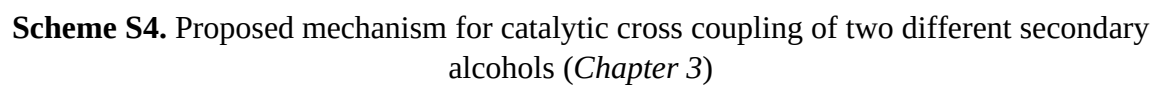
Appendix

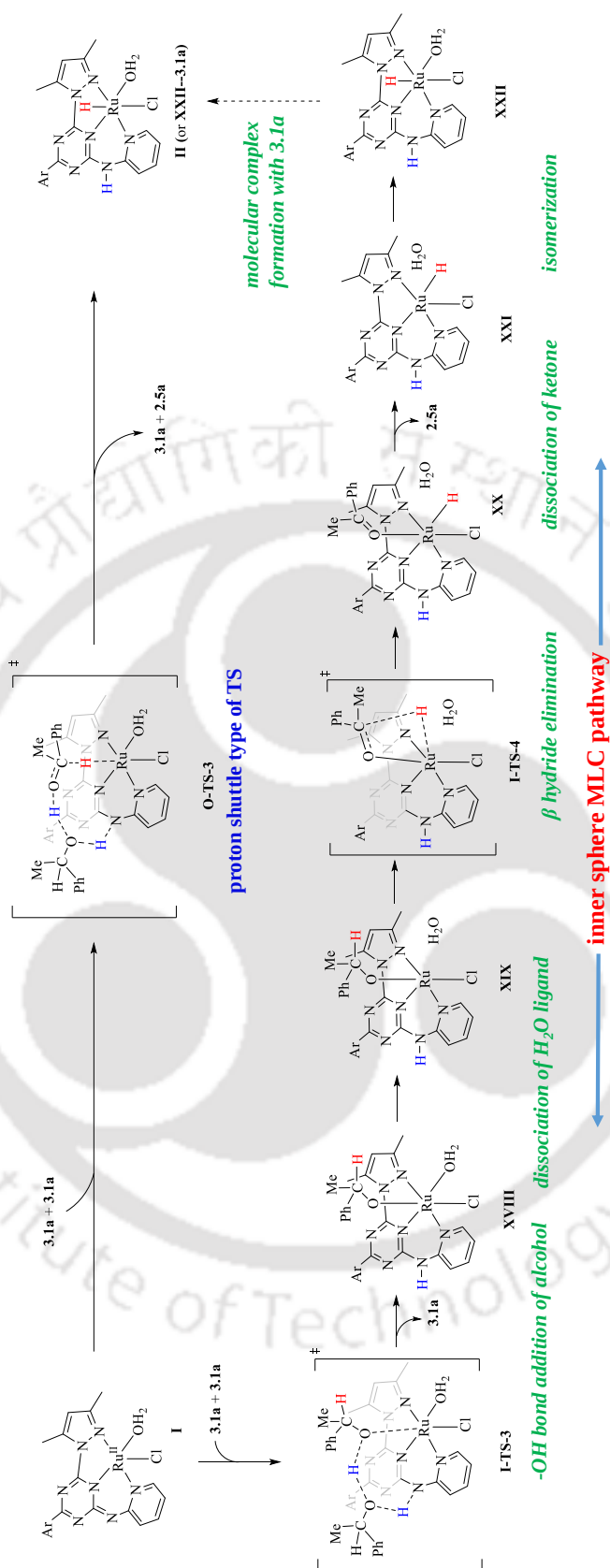


Scheme S2. Proposed mechanism for C-alkylation of ketones with secondary alcohols (Chapter 2)



Scheme S3. Proposed mechanism for dehydrogenation of cyclohexanol following inner sphere MLC pathway (Chapter 2)





Scheme S5. Proposed mechanism for dehydrogenation of 1-phenylethanol following inner sphere MLC pathway (Chapter 3)

List of publications

1. **Bhattacharyya, D.**; Sarmah, B. K.; Nandi, S.; Srivastava, H. K.; Das, A., Selective catalytic synthesis of α -alkylated ketones and β -disubstituted ketones via acceptorless dehydrogenative cross-coupling of alcohols. *Org. Lett.* **2021**, 23, 869-875.
2. **Bhattacharyya, D.**; Nandi, S.; Adhikari, P.; Sarmah, B. K.; Konwar, M.; Das, A., Boric acid catalyzed chemoselective reduction of quinolines. *Org. Biomol. Chem.* **2020**, 18, 1214-1220.
3. **Bhattacharyya, D.**; Adhikari, P.; Sarmah, B. K.; Das, A., Ruthenium(III)-catalyzed sustainable synthesis of β -disubstituted ketones via α -alkylation of ketones using secondary alcohols. *Manuscript under preparation*.
4. **Bhattacharyya, D.**; Adhikari, P.; Das, A., An efficient ruthenium(III) catalyzed sustainable synthesis of quinolines, and quinazolines via acceptorless dehydrogenative coupling of alcohols. *Manuscript under preparation*.
5. **Bhattacharyya, D.**; Senapati, S.; Das, A., Synthesis of biologically relevant *N*-aryl tetrahydroquinolines directly from quinoline, Hantzsch ester, and arylboronic acid under external base-free Chan-Lam-Evans *N*-arylation. *Manuscript under preparation*.
6. Adhikari, P.; **Bhattacharyya, D.**; Nandi, S.; Kancharla, P. K.; Das, A., Reductive alkylation of quinolines to *N*-alkyl tetrahydroquinolines catalyzed by arylboronic acid. *Org. Lett.* **2021**, 23, 2437-2442.
7. Sarmah, B. K.; Konwar, M.; **Bhattacharyya, D.**; Adhikari, P.; Das, A., Regioselective cyanation of six-membered *N*-heteroaromatic compounds under metal-, activator-, base- and solvent-free conditions. *Adv. Syn. Cat.* **2019**, 361, 5616-5625.

List of conferences attended

1. Research Conclave 2018 (IIT- Guwahati) - Poster presentation
2. Frontiers in Chemical Sciences 2018 (IIT- Guwahati) - Poster presentation
3. Modern Trends in Inorganic Chemistry XVIII 2019 (IIT- Guwahati) - Poster presentation
4. Recent Trends in Chemical Sciences 2020 - Poster presentation (Best poster award)
5. Frontiers in Organometallic and Catalysis 2021 - Poster presentation

