Exploring the Potential of Homogeneous Ru-SNS/NNS Complexes and Heterogeneous Ru-Hydrotalcite in De(hydrogenative) Transformations

A Dissertation

Submitted in partial fulfilment of the

Requirements for the Degree of

Doctor of Philosophy

by

Bitan Sardar

Department of Chemistry

Indian Institute of Technology Guwahati

Guwahati, 781039

Assam, India

Dedicated

to

My Parents

INDIAN INSTITUTE OF TECHNOLOGY GUWAHATI
ASSAM, INDIA, 781039
Department of Chemistry

Statement

I, hereby declare that the work comprised in this thesis entitled "***Exploring the Potential of Homogeneous Ru-SNS/NNS Complexes and Heterogeneous Ru-Hydrotalcite in De(hydrogenative) Transformations***" is the outcome of the research work carried out by me under the supervision of **Dr. Dipankar Srimani, 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 acknowledgments have been made if the work is established on the findings of other investigators.

Guwahati
July, 2023

Bitan Sardar
Roll no: 176122045
Department of Chemistry
IIT Guwahati, Assam
India, 781039

INDIAN INSTITUTE OF TECHNOLOGY GUWAHATI
ASSAM, INDIA, 781039
Department of Chemistry

Dr. Dipankar Srimani **Email: dsrimani@iitg.ac.in**
Associate Professor, Department of Chemistry

Certificate

This is to certify that the work incorporated in the thesis entitled **"*Exploring the Potential of Homogeneous Ru-SNS/NNS Complexes and Heterogeneous Ru-Hydrotalcite in De(hydrogenative) Transformations*"** which is being submitted to the Indian Institute of Technology Guwahati for the award of Doctor of Philosophy in Chemistry by **Mr. Bitan Sardar** (Roll No: **176122045**) was carried out by him under my supervision at this institute. The work presented in his thesis is original and has not been submitted elsewhere for a degree.

Guwahati
July, 2023

Dr. Dipankar Srimani
(Thesis Supervisor)
Associate Professor
Department of Chemistry
IIT Guwahati
Assam-781039
India

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Thank You

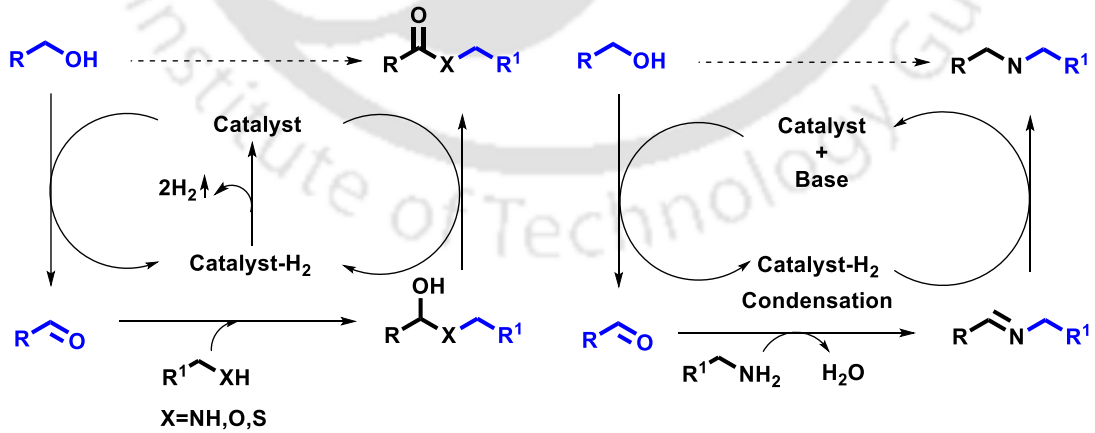
-Bitan

Context

Abstract

The contents of the present thesis entitled as "**Exploring the Potential of Homogeneous Ru-SNS/NNS Complexes and Heterogeneous Ru-Hydrotalcite in De(hydrogenative) Transformations**" have been divided into five chapters. The first chapter contains a brief literature study related to various de(hydrogenative transformations) and the last four chapters were based on the results achieved from the experimental works performed during the entire course of the PhD research programme.

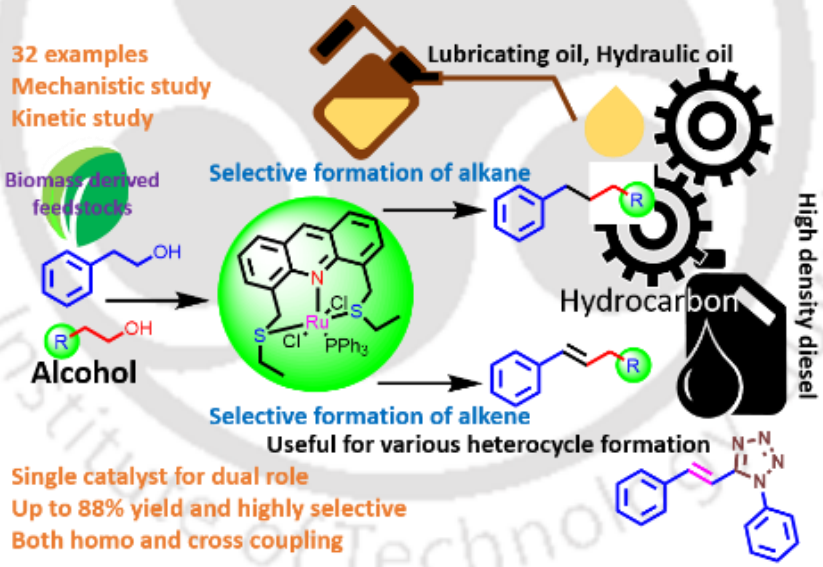
Chapter 1 contains a brief introduction about the literature review of acceptorless dehydrogenation and borrowing hydrogen reaction of alcohols via homogeneous catalysis and heterogeneous catalysis. In 21st century, the rapid depletion of fossil fuels and growing environmental concerns urges chemists and chemical industries to search for alternative raw materials and to develop new methodology to produce sustainable chemicals and important building blocks. In this regard, biomass derived alcohols was found to be best candidate, as they are non-toxic in nature. Moreover, alcohols are considered renewable starting materials that can be used in organic synthesis for various organic transformations and the preparation of commodity chemicals. In this context, "acceptorless dehydrogenation (AD)" and "borrowing hydrogen (BH)" catalysis play a key role. These approaches are sustainable because these process liberates water and in some cases (i.e., AD) molecular hydrogen as clean by-products. And, these type of reactions could be successfully performed by various types of homogeneous and heterogeneous catalysts.



Scheme 1: A schematic representation of acceptorless dehydrogenation and borrowing hydrogen

Publication: B. Sardar, D. Srimani, *Tetrahedron Letter*, **2023**, *138*, 133414

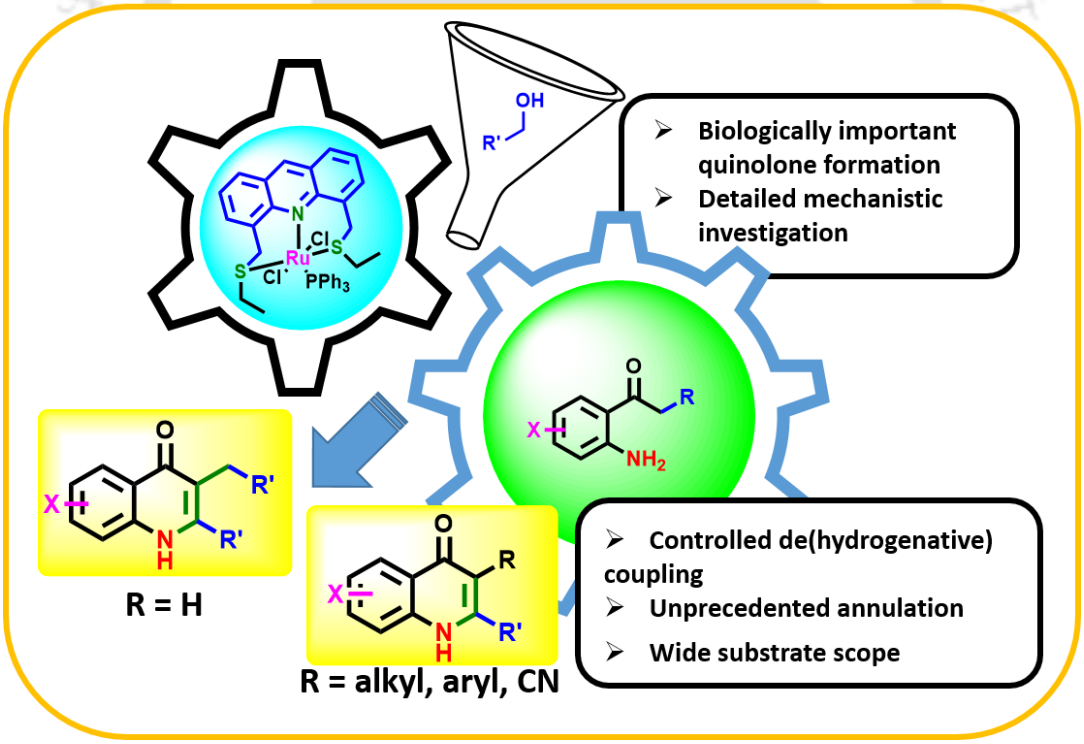
Chapter 2 highlights the selective conversion of alcohols to alkanes and alkenes. In this approach, the catalytic activity of various Ru complexes was thoroughly studied for deoxygenative coupling of primary alcohols to selectively synthesize both alkenes and alkanes. It is a captivating but extremely difficult process, as the success of the reaction primarily depends on multistep processes. Initially, dehydrogenation of primary alcohols produces aldehydes, which undergo aldol condensation to furnish unsaturated aldehydes. Deoxygenation of the formed unsaturated aldehydes leads to the formation of the corresponding alkenes. Finally, the hydrogenation of alkenes forms the desired alkanes. Delightfully, the activity of acridine-derived SNS-Ru pincer complex was found to be exemplary than the other complexes and the outcome of both homo- and cross-coupling reactions of primary alcohols was found to be moderate to excellent. Homo-coupled alkenes, alkanes, and cross-coupled alkanes were obtained in good yield with excellent selectivity. Various control experiments and mechanistic and kinetic studies were done to prove that the reaction sequence is dehydrogenation, aldol-condensation, deformylation, and hydrogenation. In addition, to demonstrate the synthetic utility of 1,3-diarylpropenes, various post-synthetic modifications were done.



Scheme 3: A schematic representation of the research work covered in **chapter 2**

Publication: B. Sardar, N. Biswas, D. Srimani, *Organometallics*, **2023**, *42*, 55 – 61.

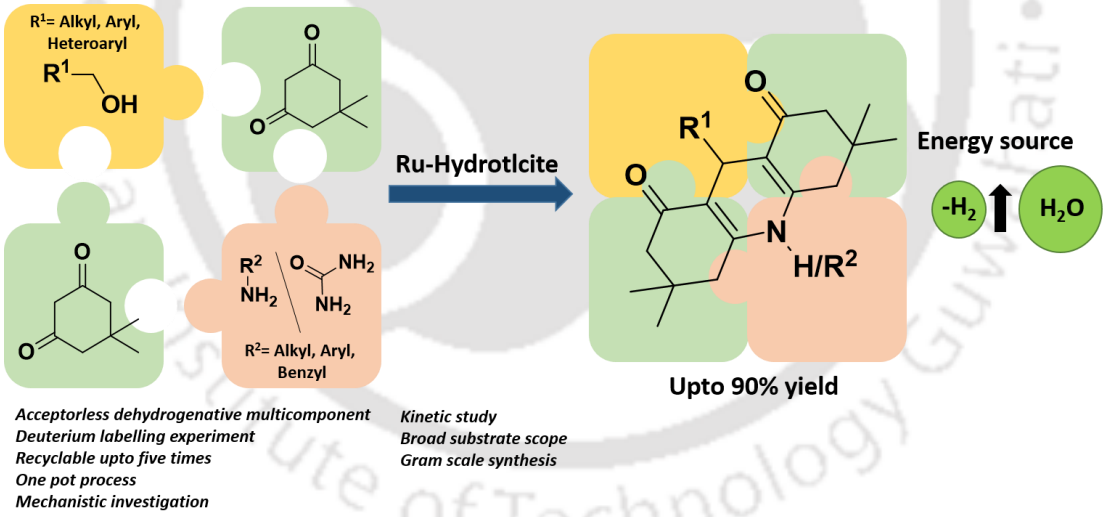
Chapter 3 highlights acridine based SNS-Ru complex catalysed oxidative coupling of alcohols with 2′-amino phenyl ketones to synthesize polysubstituted 4-quinolones. 4-quinolone analogues are well known for their wide range of bioactivities and prominent applications in medical science and pharmacology. The reported conventional methodologies were found to utilise harsh conditions, excessive amounts of oxidants and substrate prefunctionalization. In contrast, this methodology is based on de(hydrogenative) transformations. In addition, the reaction is selective towards 2,3-disubstituted-4-quinolone derivatives and barely formed *C/N*-alkylated products. Furthermore, the modified protocol could be utilized for a wide range of alcohols and diverse aminoacetophenones like *α*-alkylated 2'-aminoacetophenone. The synthetic utility of the methodology was highlighted by synthesising 4-quinolones with antibiotic properties. In order to understand the mechanism, various control experiments were performed, which showed that C-alkylation has an edge over *N*-alkylation and referred to the possibility of *in situ* alkenylation to branched ketones, which will eventually undergo oxidative annulation to polysubstituted 4 quinolones. Moreover, various post-synthetic modifications were done to synthesise polysubstituted quinolines.



Scheme 3: A schematic representation of the research work covered in **chapter 3**

Publication: B. Sardar, D. Pal, R. Sarmah, D. Srimani, *Chem Comm*, **2023**, *https://doi.org/10.1039/D3CC02426A*.

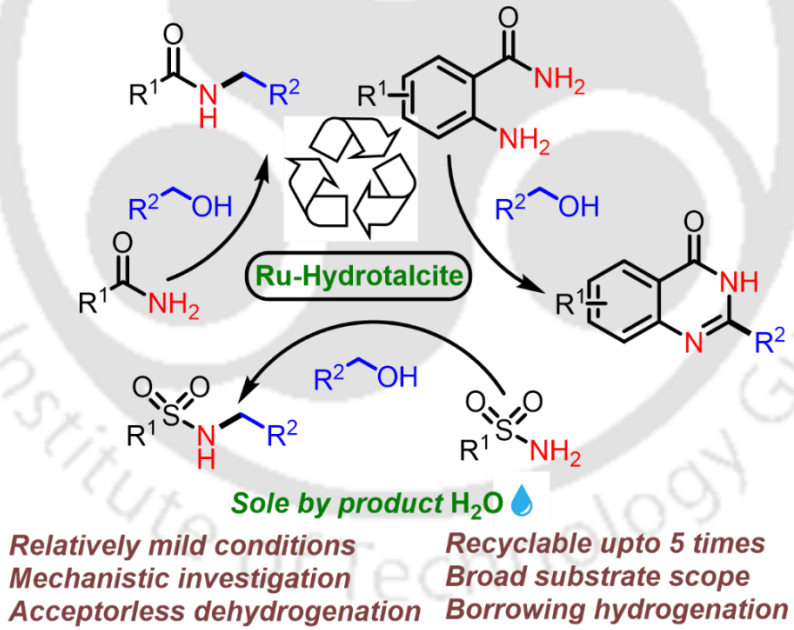
Chapter 4 highlights the usage of biomass-derived chemicals to synthesize pharmaceutically important heterocyclic scaffold via acceptorless dehydrogenation, which is an emerging trend in chemistry. Literature study shows, there are numerous reports on dehydrogenative multicomponent reactions but most of the reactions were reported with homogeneous catalysts. In contrast, heterogeneous catalysts have distinct advantages over homogeneous ones in terms of operational simplicity, cost-effectiveness and catalysts recycling. Therefore, in this report, Ru-grafted hydrotalcite was synthesised and thoroughly characterised with PXRD, FTIR, XPS, TGA, ICP AES, FETEM and EPR. In addition, the applicability of Ru-doped hydrotalcite (Ru-HT) in the dehydrogenative synthesis of structurally important acridine-1,8-dione derivatives was examined. It was observed that the catalyst successfully dehydrogenated a wide range of alcohols including aliphatic alcohols and delivered the expected product in good yield. Moreover, N-substituted acridine-1,8-dione was also synthesised. Various control experiments, mechanistic and kinetic studies were investigated to shed light on the proposed mechanistic pathway. To highlight the practical utility, the gram-scale synthesis of acridine-1,8-dione and successful recyclability of the catalyst were done.



Scheme 4: A schematic representation of the research work covered in **chapter 4**

Publication: B. Sardar, R. Jamatia, D. Pal, D. Srimani, *Asian J. Org. Chem.*, **2021**, *10*, 2195.

Chapter 5 contains an efficient Ru-doped hydrotalcite catalyzed *N*-alkylation of benzamides and sulfonamides with alcohols via borrowing hydrogen catalysis. Conventionally, aryl and alkyl halides were employed for the *N*-alkylation of amides. However, the stoichiometric equivalent of waste generation and involvement of multistep synthetic procedures lowers its practical applicability. In this regard, the usage of biomass-derived alcohols for the *N*-alkylation of amides was found to be sustainable. In this work, the scope of a newly developed Ru-grafted HT catalyst was explored for direct *N*-alkylation of amides, and various primary alcohols, including benzyl, heteroaryl, and aliphatic alcohols, were alkylated to various amides in good to excellent yields. To shed light on the mechanistic details, several control studies and deuterium labeling experiments were performed. Mechanistic studies underpin that the reaction is going via de(hydrogenative) pathway rather than an S_N1-type mechanism. The reaction could be easily scaled up without any detrimental effect on the yield. Moreover, the catalyst was found to be capable of synthesizing quinazolinone directly from 2′-amino benzamide and alcohols. In addition, successful recyclability and high reactivity highlight the practical applicability of the catalyst.



Scheme 5: A schematic representation of the research work covered in **chapter 5**

Publication: B. Sardar, R. Jamatia, A. Samanta, D. Srimani, *J. Org. Chem.*, **2022**, 87, 9, 5556–5567.

Abbreviations

Ac	Acetyl
α	Alpha
Å	Angstrom
Ar	Argon
ACN	Acetonitrile
AD	Acceptorless dehydrogenation
ADC	Acceptorless Dehydrogenative coupling
Br	Broad
β	Beta
Bn	Benzyl
Bu	Butyl
Cat	Catalyst
D	doublet
Dd	Doublet of doublet
δ	Chemical shift
DA	Donor-acceptor
DCE	Dichloroethane
DCM	Dichloromethane
DMSO	Dimethylsulfoxide
DMF	Dimethylformamide
DMA	Dimethyacetamide
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

Abbreviations

g	Grams
γ	Gamma
HA	Hydrogen-autotransfer
HRMS	High resolution mass spectrometry
Hz	Hertz
MHz	Mega Hertz
i	Iso
FT-IR	Fourier transform infrared sprectroscopy
J	Coupling constant
m	multiplet
mg	Milligram
mmol	Millimole
MS	Molecular seive
MLC	Metal-ligand cooperation
NMR	Nuclear magnetic resonance
Ts	Tosylate
o	*Ortho*
m	*Meta*
p	*Para*
PXRD	Powder X-ray diffraction
PNP	2,6-bis-(di-*tert*-butylphosphinomethyl)pyridine
ppb	Parts per billion
ppm	Parts per million
TGA	Thermogravimetric analysis
THF	Tetrahydrofuran
TEMPO	2,2,6,6-tetramethyl-1-piperidinyloxy
t	Tert
TMS	Tetramethylsilane
TS	Transition state
XPS	X-ray photo electron spectroscopy

Chapter 1

General Introduction

1.1. Introduction:

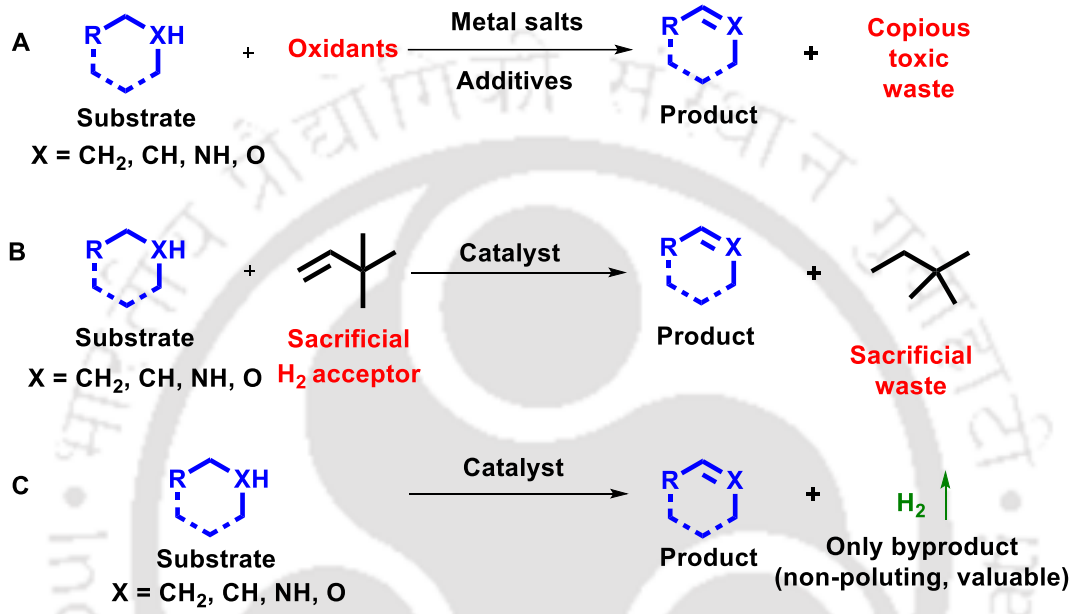
In the 21st century, the population of the world has increased dramatically due to advances in technology and economic prosperity. In addition, the consumption of energy and numerous chemical feedstocks has also intensified.[1] Every country is facing multiple complications in securing a sufficient supply of energy and essential chemicals to support its interest. Unfortunately, humanity paid a high price for this rapid progress by ignoring environmental issues. Humanity must own up to its actions and look for better options for the future. To address this issue, three things must be considered: alternative resources, catalysis, and sustainable transformations.[2] Currently, it is very desirable to utilize the natural resources of the world sustainably to meet demand while considering environmental constraints. Reports suggest fossil fuels are primarily utilized to manufacture the vast majority of the key chemicals needed for different chemical processes. The alarming point is that the use of fossil fuels has terrible effects on the earth's atmosphere. To address this problem, a hunt for alternatives to fossil fuels is currently going on. Considering, the number of by-products of present agricultural and food-processing units, the scientific community soon understood that agricultural waste could be the possible alternative. On the other hand, catalysis and sustainable reactions play a crucial role in the modern world. Catalysis, the process of accelerating chemical reactions, enables the production of desired products with higher efficiency and selectivity, minimizing waste and energy consumption. Sustainable reactions, on the other hand, focus on developing environmentally friendly and economically viable processes that utilize renewable resources, reduce toxic byproducts, and minimize the overall ecological footprint.

In this regard, reactions like acceptorless dehydrogenation and borrowing hydrogen is in demand. They are considered atom economical and environmentally friendly methods. With time several methodologies using homogeneous and heterogeneous catalyst systems have been developed and they have been utilized to perform various de(hydrogenative) transformations.

1.2. Acceptorless dehydrogenation:

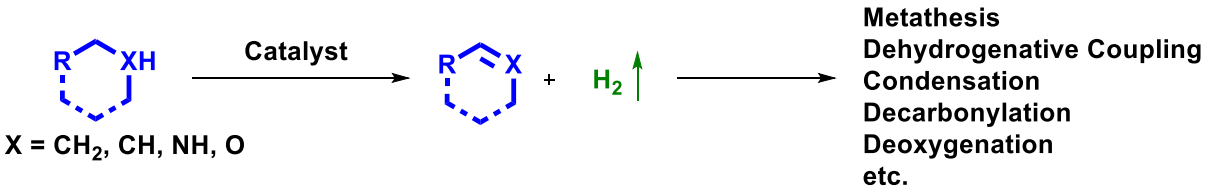
Acceptorless dehydrogenation[3] can efficiently oxidize small molecules like alcohols, amines, and alkanes by liberating molecular hydrogen and does not require any hydrogen acceptor, oxidants, or substrate pre functionalization. The catalytic dehydrogenation of organic molecules is a strained process and often requires relatively high temperature as the removal

of hydrogen atoms from adjacent atomic positions of an organic substrate is endothermic but it is widely considered as an environmentally benign and efficient approach for the synthesis of valuable products. Acceptorless dehydrogenation is superior to conventional methodologies (like the use of $Pb(OAc)_4$, $K_2Cr_2O_7$, $KMnO_4$, MnO_2, and H_2O_2) since it generates less waste. Another intriguing fact is, the acceptorless dehydrogenation strategy can perform well and shift the equilibrium of the reaction in the absence of sacrificial hydrogen acceptor[4] (Scheme **1.1**).



Scheme 1.1. (A) Conventional oxidation reactions. **(B)** Hydrogen-transfer reactions. **(C)** Acceptorless dehydrogenation reactions.

So, as a whole acceptorless dehydrogenation can convert less reactive substrates like alcohols, amines, alkanes, etc. into more reactive ones like carbonyls, imines, alkenes, etc. Later, the related highly active in-situ formed oxidized products can easily undergo tandem reactions to a variety of useful chemicals (Scheme **1.2**).



Scheme 1.2. Acceptorless dehydrogenative transformations.

1.2.1. Dehydrogenation of alcohols:

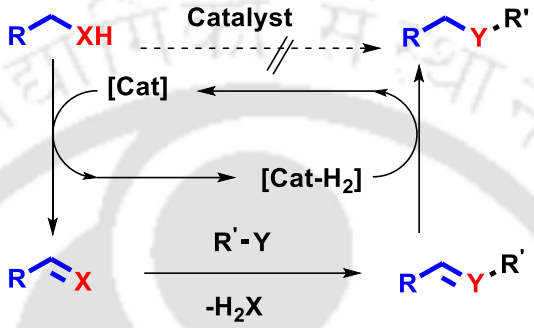
Fossil fuels, including coal, oil and natural gas are the three pillars for powering economies for over 150 years and are currently responsible to supply 80% of the world's energy.[5] They are a non-renewable source of energy and are widely used as fuel to generate electricity and power vehicles. But, burning fossil fuels releases greenhouse gases into the atmosphere, contributing to climate change. To minimize the damage related to the environment and control the release of greenhouse gas, the scientific community is actively researching and exploring alternative energy sources to fossil fuels. And among them, alcohol can be the most promising alternative. Alcohol is the most basic chemical for various organic synthesis and is renewably available from lignocellulosic biomass, agricultural waste, garbage, wood, and forestry. Biomass can also be converted into biofuels like ethanol and biodiesel. Nowadays, 90% of ethanol is produced from biomass mostly from the bagasse of sugarcane. Recently, various government organizations have launched the Ethanol Blended Petrol (EBP)[6] program to mix biofuel like ethanol with petrol to reduce the consumption of fossil fuel. Additionally, biomass is used in industrial processes as a feedstock or a fuel source. So, the source of alcohol is very promising, and acceptorless dehydrogenation is a rather encouraging alternative to the problem.

There is plenty of research going on to use the acceptorless dehydrogenation effectively to produce valuable products and fine chemicals. Reactions like C-C bond formation, esterification, and deoxygenation reactions have been developed to prepare synthetically useful chemicals. On the other hand, acids and some important heterocyclic compounds like quinoline, pyrrole, and benzimidazoles can also be synthesized directly from alcohol. Moreover, the liberated H_2 from the reaction can be easily harnessed to use as an alternative energy source. So, it became clear that alcohol and its source of renewable biomass are the most optimal choice for the near future.

1.3. Borrowing hydrogen approach:

The borrowing hydrogen (BH) catalysis[7] is also coined as hydrogen auto-transfer reaction, which is an important strategy in organic synthesis. In acceptorless dehydrogenation strategy, the catalyst dehydrogenates the organic compounds with the liberation of H_2. The catalyst in the (BH)-approach dehydrogenates the organic compounds, forming unsaturated organic species that can be converted to unsaturated intermediates (Scheme **1.3**) by the reaction

with nucleophiles (RY). In this case, the catalyst stores the hydrogen and transfers it to unsaturated intermediates to form the saturated product. As a result, H_2 is not liberated in the BH approach, and H_2O is the only by-product. The last step (hydrogenation) is thermodynamically privileged and hence it shifted the reaction equilibrium towards completion. Moreover, it drives the dehydrogenation step to form a more reactive intermediate from a less reactive donor molecule. And for these obvious reasons, BH reaction received much more attention in organic synthesis over the past few decades (Scheme **1.3**).



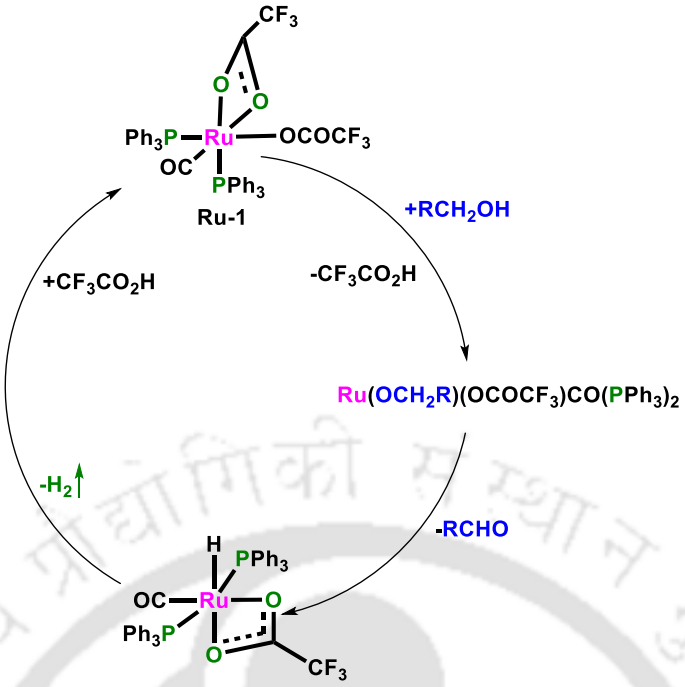
Scheme 1.3. Borrowing hydrogen.

These types of reactions have been reported both by heterogeneous and homogeneous catalysts and the introduction part has been divided into two parts. (i) Homogeneous Catalysis and (ii) Heterogeneous catalysis.

1.4. Homogeneous Catalysis:

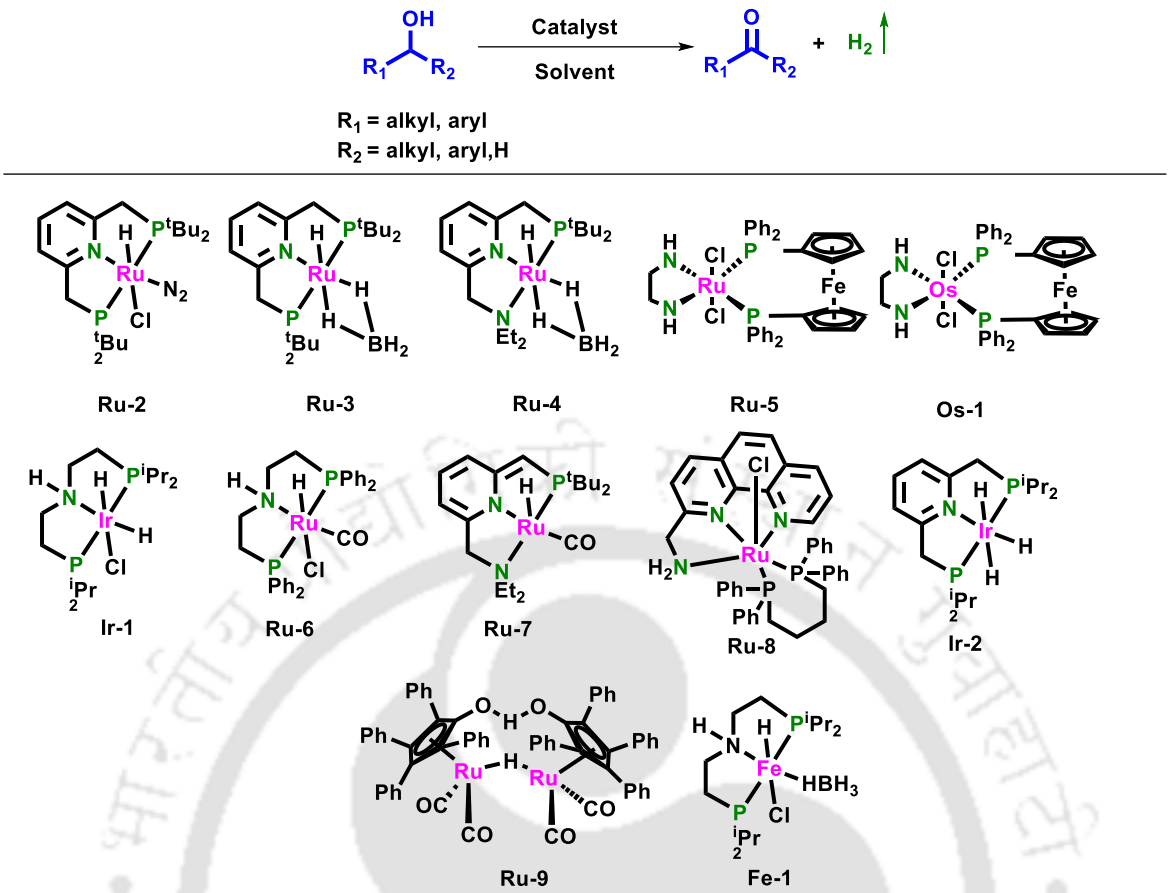
1.4.1. Dehydrogenation of alcohols to form aldehydes or ketones:

For decades, several oxidant-free catalytic acceptorless dehydrogenation was reported. The very first example is from 1975, when Dobson and Robinson[8] reported **[Ru(OCOCF$_3$)$_2$(CO)(PPh$_3$)$_2$]** catalyzed dehydrogenation of primary and secondary alcohols. Here, they proposed the formation of hydride complex **[RuH(OCOCF$_3$)$_2$(CO)(PPh$_3$)$_2$]**, **Ru-1** by β-hydride elimination, and subsequently, it leads to the formation of aldehydes and ketones. The mechanism was depicted in scheme **1.4**.



Scheme 1.4. Acceptorless dehydrogenation *via* Ru-hydride elimination pathway.

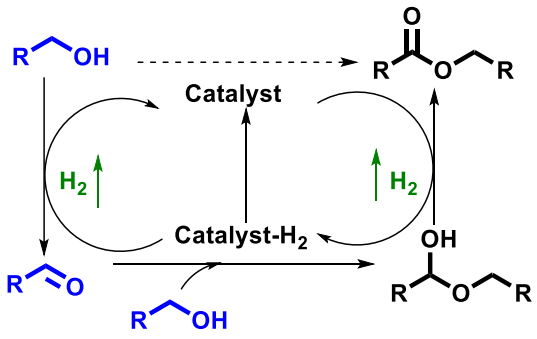
Later, various ligand-derived Ru,[9] Rh[10,] or Ir[11] metal complexes were also reported to be active in this type of reaction. In 2004, *Milstein* developed an electron-rich, bulky Ru PNP-type complex [2,6-bis-(di-tert-butylphosphinomethyl)pyridine] for efficient acceptorless catalytic alcohol dehydrogenation of both primary and secondary alcohols, which was found to be a significant improvement over the previous reports.[12a] Here, the base is required to activate the catalyst. Later, *Milstein* and *co-workers* further improved the catalyst and formed complex **Ru-3** and **Ru-4**.[12b] They can perform under neutral conditions and **Ru-3** is much superior to **Ru-4**. Next, *Baratta* and *co-workers*[13] reported a series of Ru and Os complexes for the dehydrogenation of secondary alcohols to ketones. Among them, diamine based *trans*-[MCl_2(dppf)(en)] (M = Ru, Os), dppf = 1,1'-bis(diphenyl-phosphino)ferrocene; en = ethylenediamine i.e.; **Ru-5**and **Os-1** was found to display high activity. Later, *Beller and co-worker*[14] introduced several known **Ru** and **Ir** complexes and applied those for the acceptorless dehydrogenation of secondary alcohols, with remarkable TONs and TOFs. Next, *Hong*[15] reported alcohol dehydrogenation with Shvo's catalysts, **Ru-9** and $RuH_2(CO)(PPh_3)_3$ (**1.2l**) in a neutral reaction medium. In recent times, dehydrogenation of secondary alcohols to ketones with earth-abundant transition metal complexes like **Fe-1** was also reported by *various groups*[16] (Scheme **1.5**).



Scheme 1.5. Dehydrogenation of alcohols to form aldehyde or ketone.

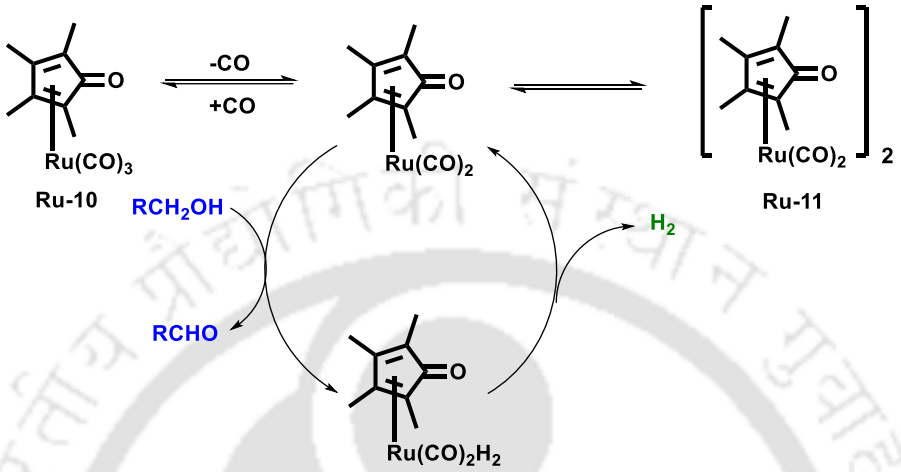
1.4.2. Dehydrogenative coupling of alcohols to form esters:

One of the most important chemical processes in synthetic organic chemistry is esterification, which finds use in the production of precise chemicals ranging from cosmetics to drugs. In conventional methodologies, esters were usually synthesized by reacting carboxylic acid (RCOOH) with the (ROH) hydroxyl group. But nowadays, esters were primarily synthesized via the dehydrogenative coupling of alcohols (Scheme **1.6**).



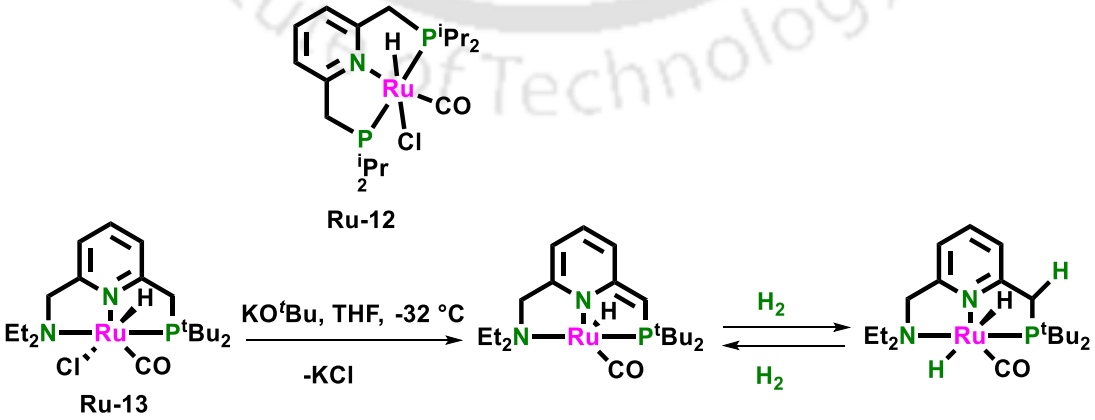
Scheme 1.6. Dehydrogenative coupling of alcohol to form ester.

In 1985, *Shvo and co-workers* reported (η^4-tetracyclone)$(CO)_3Ru$ and [(η^4-tetracyclone)$(CO)_2Ru]_2$ catalyzed acceptorless direct oxidation of primary alcohol to ester. Both the catalysts are involved in this transformation and the true catalytic species is the coordinatively unsaturated complex (Scheme **1.7**).[17]



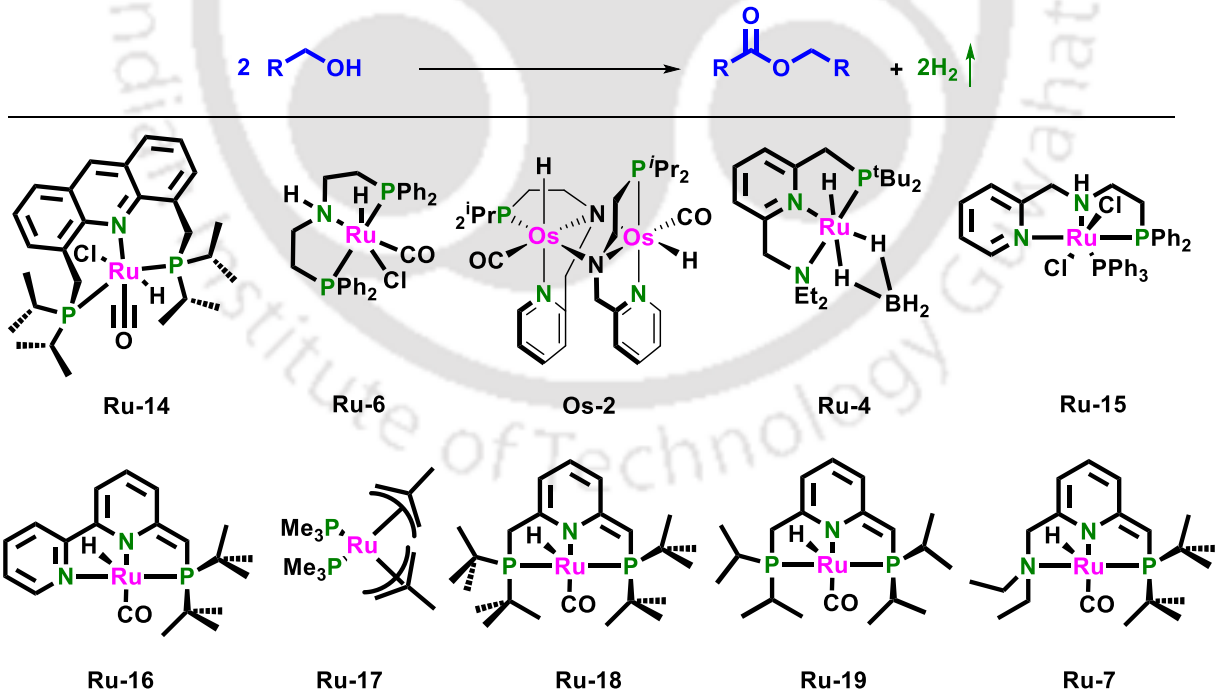
Scheme 1.7. Dehydrogenative coupling of alcohol to form ester presented by Shvo.

After 2 years, in 1987, *Murahashi and co-workers*[18] found both **$RuH_2(PPh_3)_3$** and **$RuH_2(CO)(PPh_3)_3$** were quite active for the effective transformation of alcohols to esters and lactams. Although, the methodology requires a high temperature (180 °C). In 2005, *Milstein*[19] prepared a ^{i}Pr-PNP (2,6-bis-(di-iso-propylphosphinomethyl)pyridine), **Ru-12** and PNN (2-(di-tert-butylphosphinomethyl)-6-diethylaminomethyl)pyridine, **Ru-13** ligand scaffold based two complexes. It was found that in the presence of base PNN ligand scaffold-based Ru complex acts at a much faster rate for esterification reaction (Scheme **1.8**).

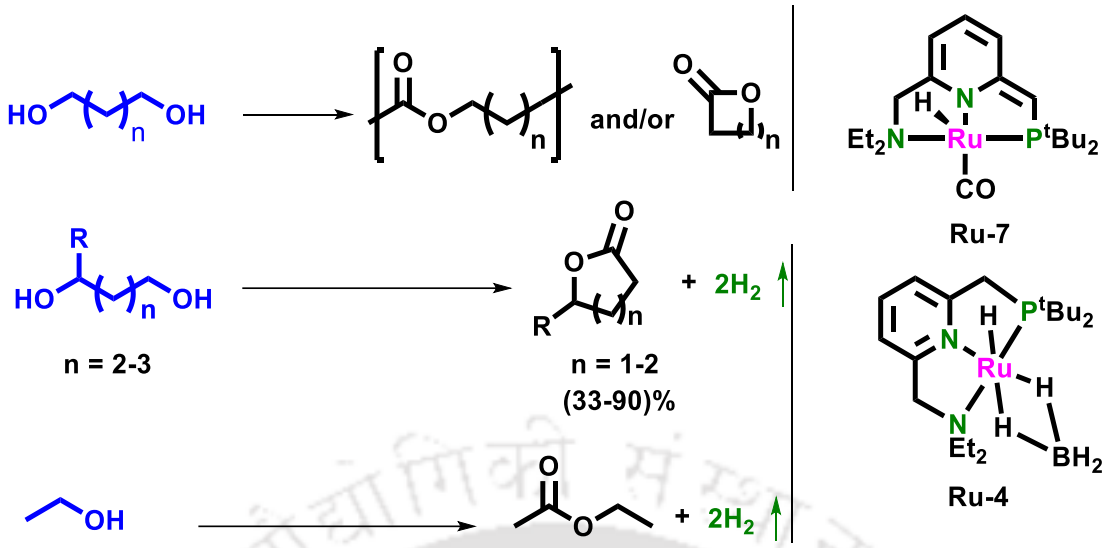


Scheme 1.8. MLC based on deprotonation/dearomatization-aromatization.

Again *Milstein* group[20] utilized a well-defined acridine-based ruthenium pincer complex RuHCl(CO)(A-^{i}Pr-PNP) Ru-14 [A-^{i}Pr-PNP = 4,5-bis-(diisopropylphosphinomethyl) acri dine] **Ru-14** for the direct conversion of alcohols into esters in presence of the catalytic amount of base. Later, the efficient conversion of bio-renewable ethanol to ethyl acetate was first reported with **Ru-MACHO**, **Ru-6**[21]and **Os-2**[21] dimer complex**.** A ruthenium hydrido borohydride complex, **Ru-4**[12b] based lactonization of primary-primary diol, as well as primary-secondary diol, have also been reported. In 2012, *Gusev* and *co-workers* developed a series of Ru and Os metal-based PN^{H}P, NN^{H}P, and NN^{H}N pincer complexes for the efficient acceptorless dehydrogenative coupling of ethanol to esters. Among them, $RuCl_2(PPh_3)$[NN^{H}P] was found to be superior.[21] Later, *Milstein* also designed a Bipy-PNN Ru pincer complex **Ru-16** to synthesize unsymmetrical esters, from the coupling of two distinct alcohols (primary and secondary alcohols)[22] (Scheme **1.9** and **1.10**). Here the catalyst can perform in neutral conditions. Previously, lactonization of 1,4- butanediol to γ-butyrolactone was reported with ruthenium-catalyst at 205 °C.[23] *Robertson and co-workers* demonstrated the synthesis of polyesters, by applying the dehydrogenative coupling strategy of alcohols.[24a] Some earth-abundant metals also developed for the effective transformation of alcohols to esters.[24b-f, 25]



Scheme 1.9. The dehydrogenative synthesis of ester by Ru and Os complexes.

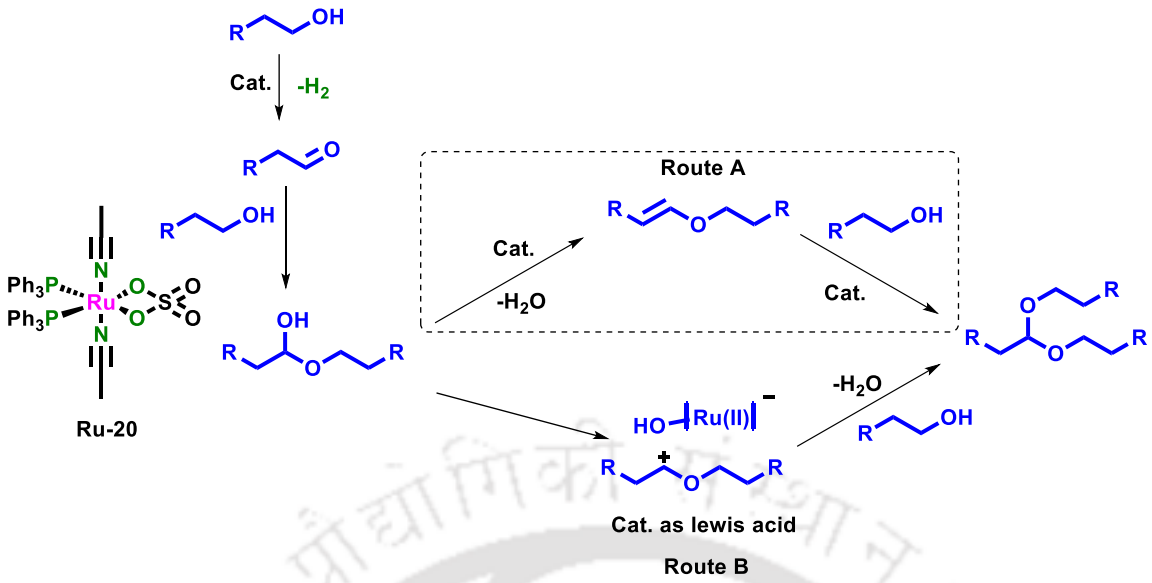


Scheme 1.10. The dehydrogenative coupling of alcohol to form ester

1.4.3. Dehydrogenative coupling of alcohols to form acetals:

In the dehydrogenative coupling reactions, alcohols reversibly combine with in-situ formed aldehyde to form hemiacetal. The addition of another alcohol to this reaction will eventually result in the formation of acetal. The first work related to this was reported by *Murahashi and co-workers*.[18] They used a whole variety of Ru precursors but it was found that $RuCl_2PPh_3$ was the most active one. Later, the Thorp group established an imidorhenium(V) complex, which successfully catalyzed the reaction with relatively higher TON[26]. Later in 2009, the *Milstein group*[20] introduced an acridine-PNP ruthenium pincer complex (0.1 mol %), **Ru-14**. The complex showed superior activity due to its unique "long-range" MLC.

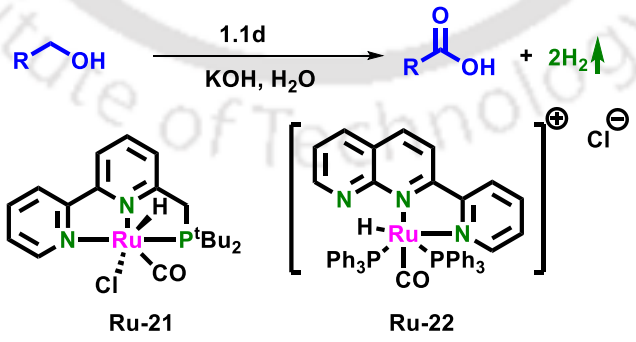
In 2012, the same group reported ruthenium sulfate complex [$Ru(\eta^2$-$SO_4)(PPh_3)_2(CH_3CN)_2$] **Ru-20** catalyzed acetal formation, efficiently at low temperature compared to the previously reported acridine-PNP ligand-derived Ru pincer complex.[27] This report is very much important as they proposed a new mechanism, which eliminates the necessity of β-hydrogen i.e.; the formation of vinyl ether intermediate, and established a new way of acetal formation. This new mechanism acknowledges the role of Lewis acidity influenced by the Ru metal complex (Scheme **1.11**).



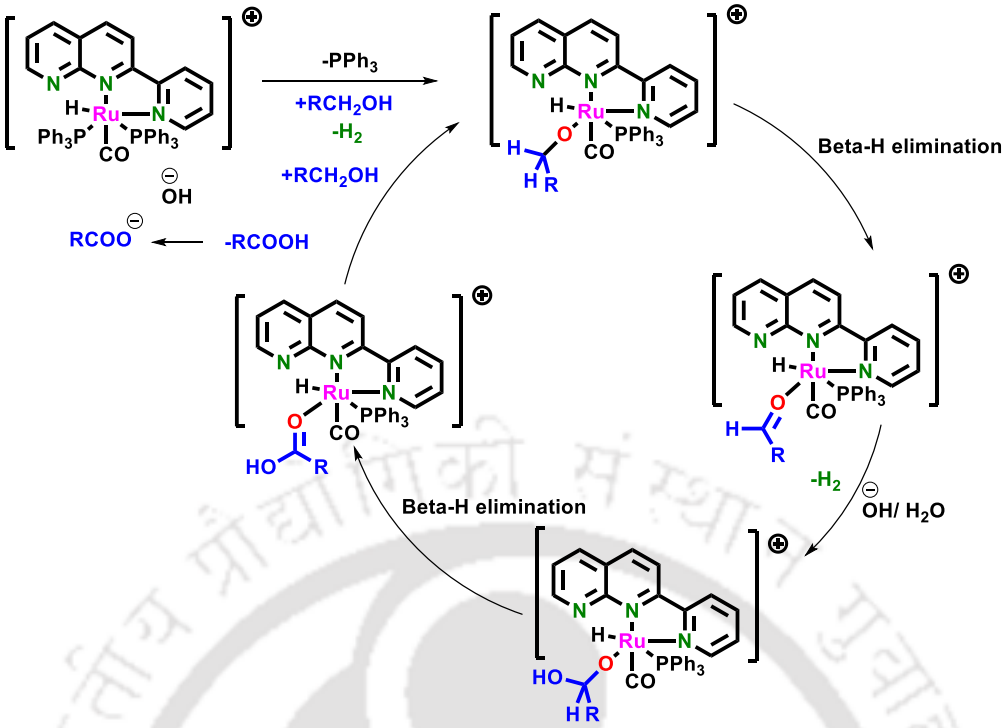
Scheme 1.11. Proposed pathways for acetalization

1.4.4. Dehydrogenative synthesis of acids from alcohols:

The most significant approach in organic synthesis is the direct conversion of alcohols in the presence of water to form carboxylate salts by the removal of H_2, which reduces the need for stoichiometric oxidants and chlorinated solvents.[28] Here, water serves as both an oxygen donor and a reaction medium. *Milstein* reported this transformation with complex **Ru-21**, with a very good yield, exhibiting excellent atom economy (Scheme **1.12**).[29] In the same year another group reported the conversion of alcohols to carboxylic acids with Ru-catalyst. J. K. Bera reported a **Ru-22** complex for the dehydrogenative synthesis of alcohols to acids. The mechanism of the reaction was depicted in scheme **1.13**.[30]



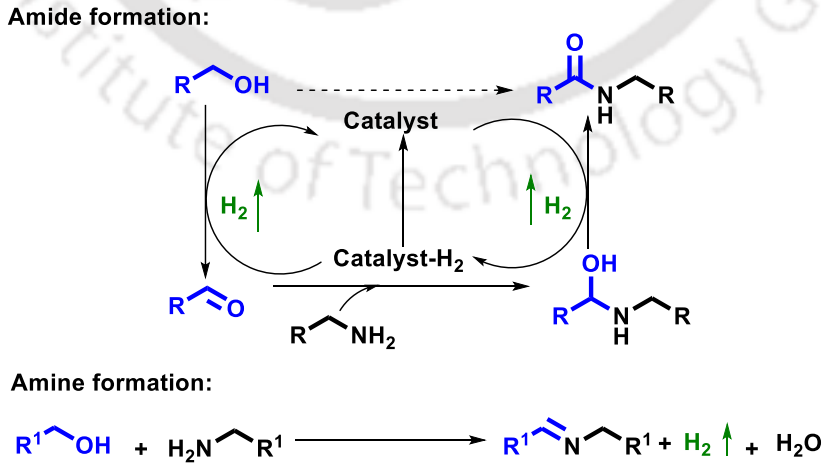
Scheme 1.12. The dehydrogenative synthesis of aids from alcohols.



Scheme 1.13. Proposed catalytic cycle converting alcohols to carboxylates.

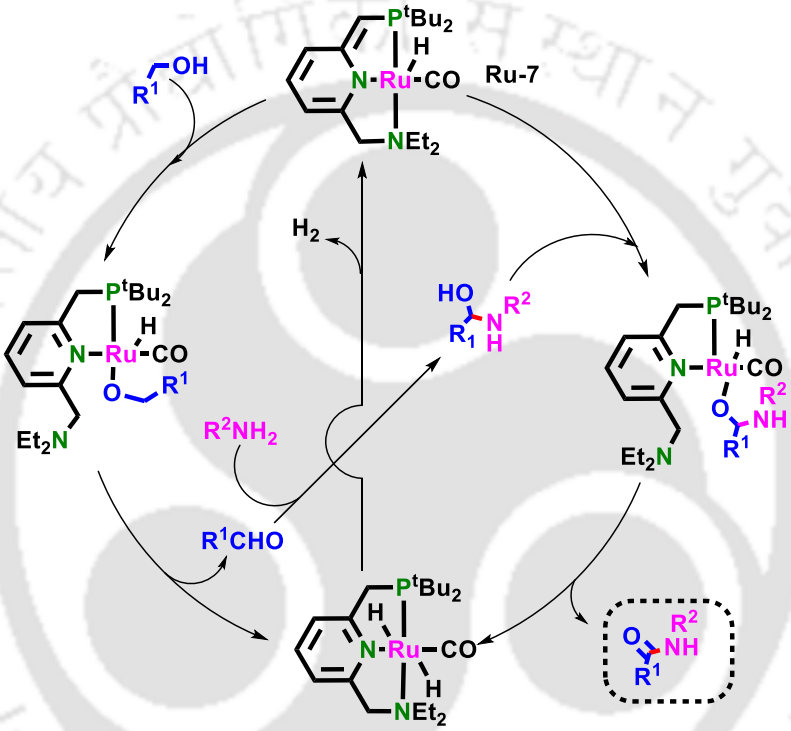
1.4.5. Dehydrogenative coupling of alcohols and amines to form imine and amides:

Alcohols and amines can be dehydrogenatively coupled to generate either amides or imines. The characteristics of the catalyst or ligand scaffold determine selectivity. Double dehydrogenation results in amide formation and dehydrogenation followed by elimination of H_2O *via* condensation furnished an imine formation (Scheme **1.14**).

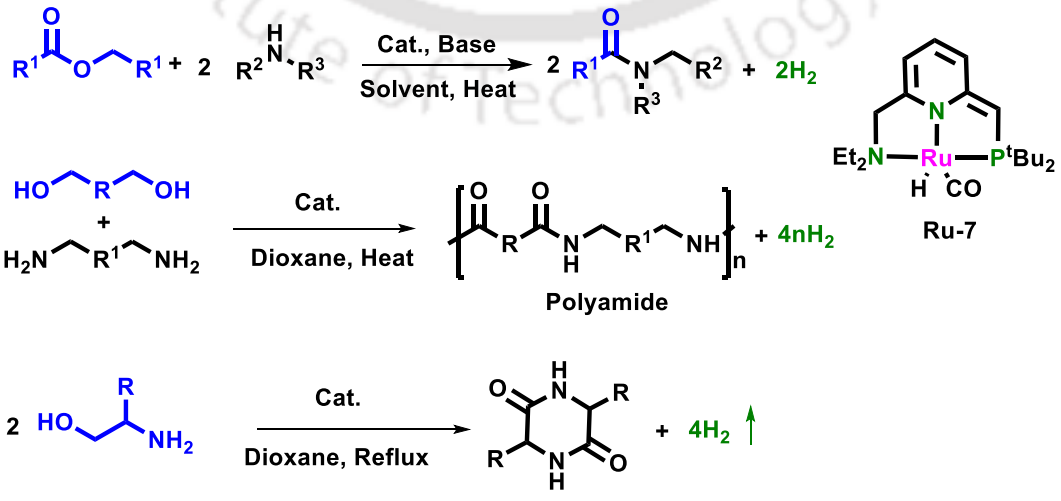


Scheme 1.14. Schematic representation of imines and amides via double dehydrogenation.

Milstein[31] introduced PNN ruthenium complex catalyzed selective synthesis of amide directly from alcohol and amine with the liberation of H_2. They proposed the mechanism of this reaction where the hemilability of the NEt_2 ligand is responsible for further dehydrogenating the hemiaminal intermediate **A**, which leads to the amide formation (Scheme **1.15**). They explored the strategy more and the strategy was further extended by the *Milstein* group to achieve the synthesis of polyamides and peptides directly from diols and diamines (Scheme **1.16**).[32] The same group also reported the dehydrogenative synthesis of amide by the reaction of ester and amine.[33]

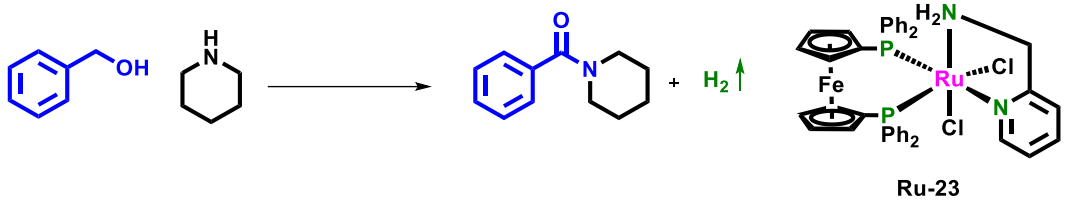


Scheme 1.15. Proposed catalytic cycle for the synthesis of amides from alcohols and amines.



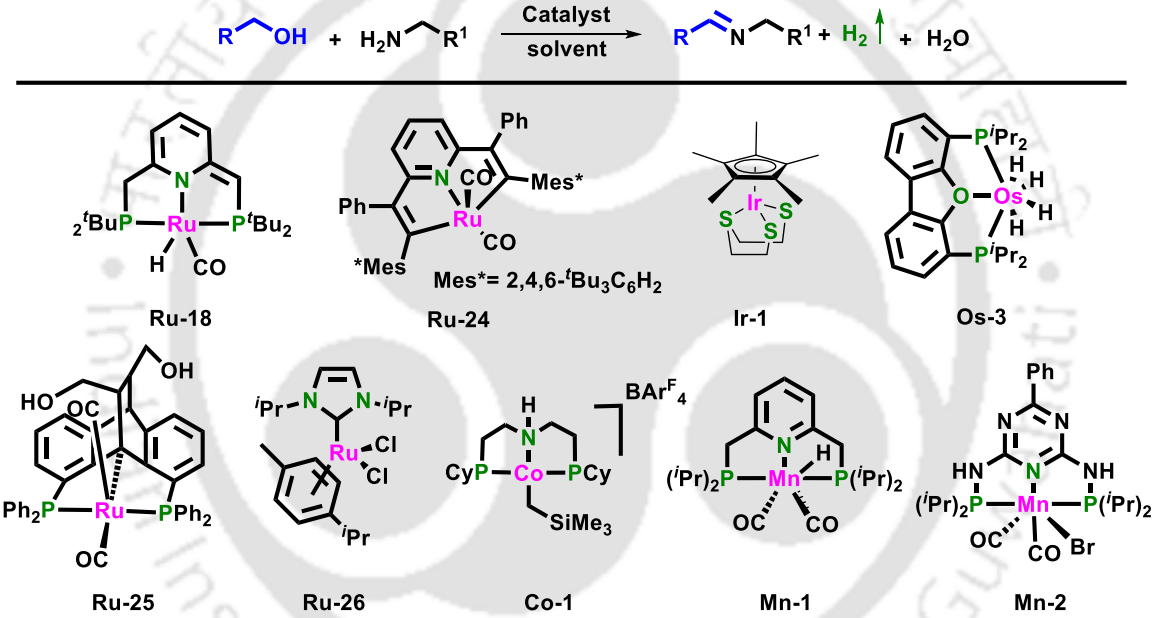
Scheme 1.16. Dehydrogenative coupling of alcohols and amines to form amides.

Later, Crabtree group also established **Ru-23** catalysed dehydrogenative coupling of alcohols and amines for the formation of amides (Scheme **1.17**).[34]



Scheme 1.17. Dehydrogenative coupling of alcohol and cyclic amine to form amides.

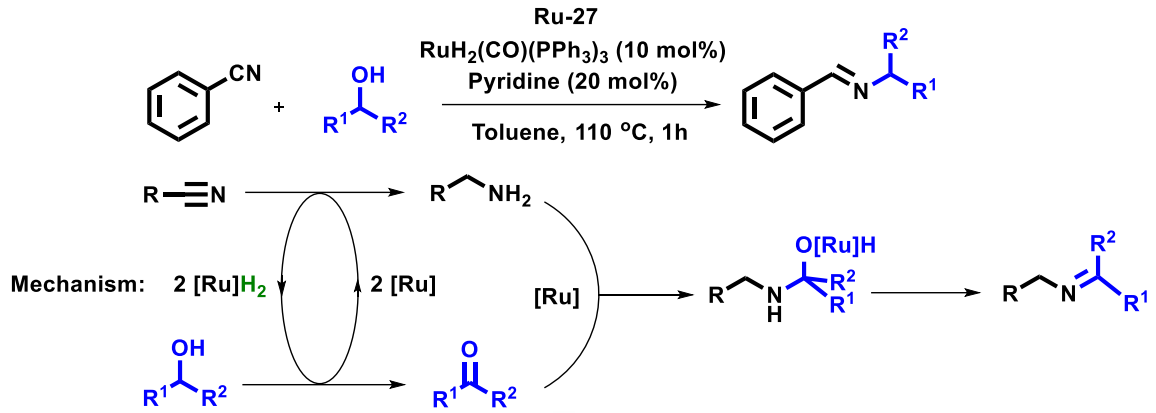
The PNP complexes **Ru-18** developed by the *Milstein* group[35] afforded the development of imines from alcohols and amines. After that, several imine formations have been reported with diverse catalysts (Scheme **1.18**).[36]



Scheme 1.18. Dehydrogenative coupling of alcohols and amines to form imines.

Very recently, Co-complex[37] and Mn-complexes[38] were shown catalytic activity. Aza –Wittig reaction can also be a possible alternative for the selective formation of imines via dehydrogenative coupling.[39]

Later, the Hong group established **Ru-27**[40] complex catalyzed selective imine synthesis from nitriles and secondary alcohols under hydrogen acceptor and base-free conditions. The complex is $RuH_2(CO)(PPh_3)_3$ and showed superior selectivity over the reaction. Following that, many heterogeneous and homogeneous catalytic methods for the synthesis of amides and imines from alcohols and amines were reported (Scheme **1.19**).

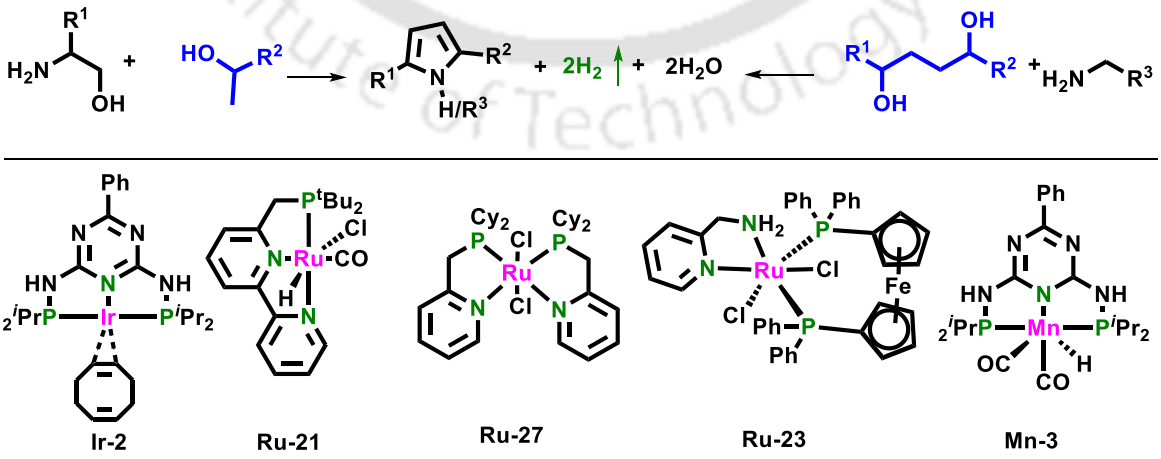


Scheme 1.19. Ruthenium-catalyzed selective imine synthesis from nitriles and secondary alcohols.

1.4.6. Dehydrogenative coupling of alcohols to form heterocyclic compounds:

1.4.6.1. Synthesis of pyrroles:

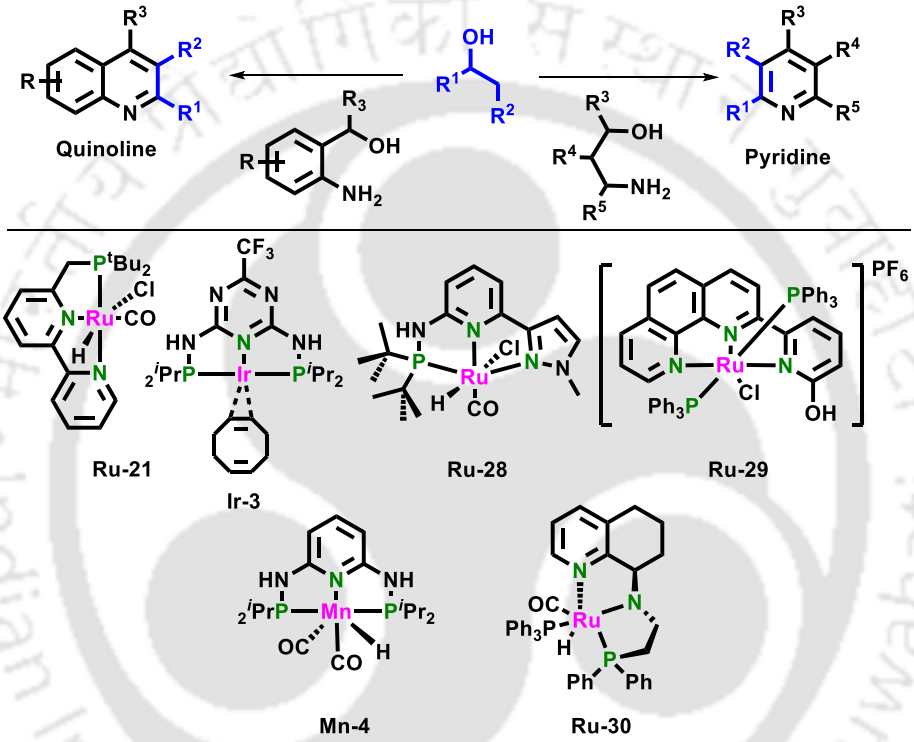
Pyrrole constitutes an important chemical analog for pharmaceuticals, agrochemicals, and advanced functional materials. In 2013, *Kempe*[41] first reported iridium **Ir-2** catalyzed pyrrole formation from secondary alcohols and *β*-amino alcohols *via* acceptorless dehydrogenation under very mild reaction conditions. During the process, two equivalents of hydrogen gas are eliminated. In the same year, the *Milstein* group[42] performed this efficient transformation with the bipyridine-derived Ru-PNN complex **Ru-21** with excellent yield. Later Saito **Ru-27**,[43] Beller[44,45] and Crabtree **Ru-23**[34] all synthesized pyrrole from the dehydrogenation of diol and amine (Scheme **1.20**).



Scheme 1.20. Pyrrole synthesis via dehydrogenative coupling.

1.4.6.2. Synthesis of pyridines and quinolines:

Pyridine and quinoline can be synthesised via reacting γ-amino alcohols with secondary alcohols/ketones. *Milstein* first reported the synthesis of quinolone direst from γ-amino alcohols and secondary alcohols in the presence of **Ru-21** complex.[46] In the same year, *Kempe*[47] also reported iridium-catalyzed **Ir-3** synthesis of pyridine with primary alcohols and γ-amino alcohols. Some earth-abundant transition metals-based reports are also published regarding this heterocyclic synthesis (Scheme **1.21**).[48]

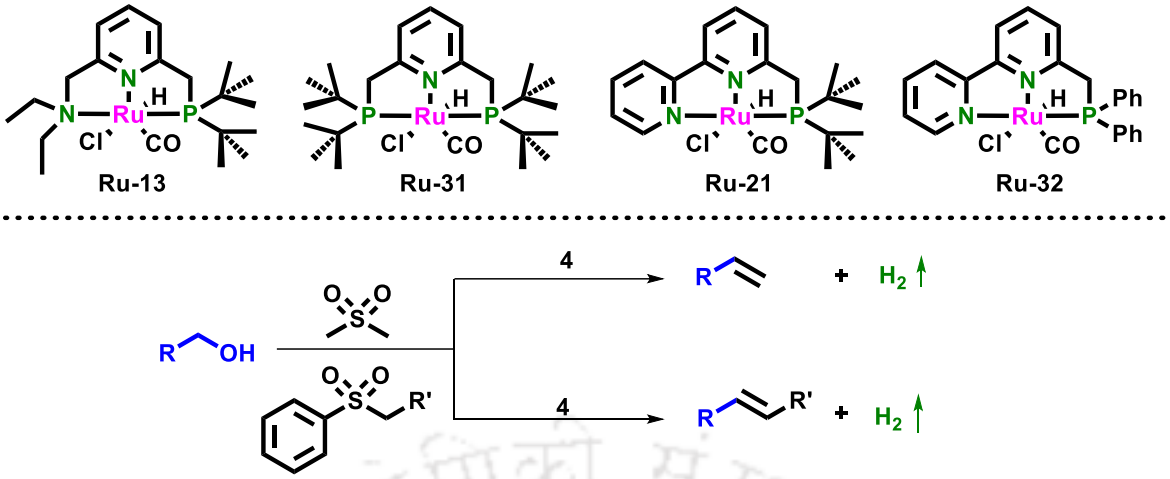


Scheme 1.21: Quinoline synthesis via dehydrogenative coupling.

1.4.7. C=C bond formation:

1.4.7.1. Julia type olefination:

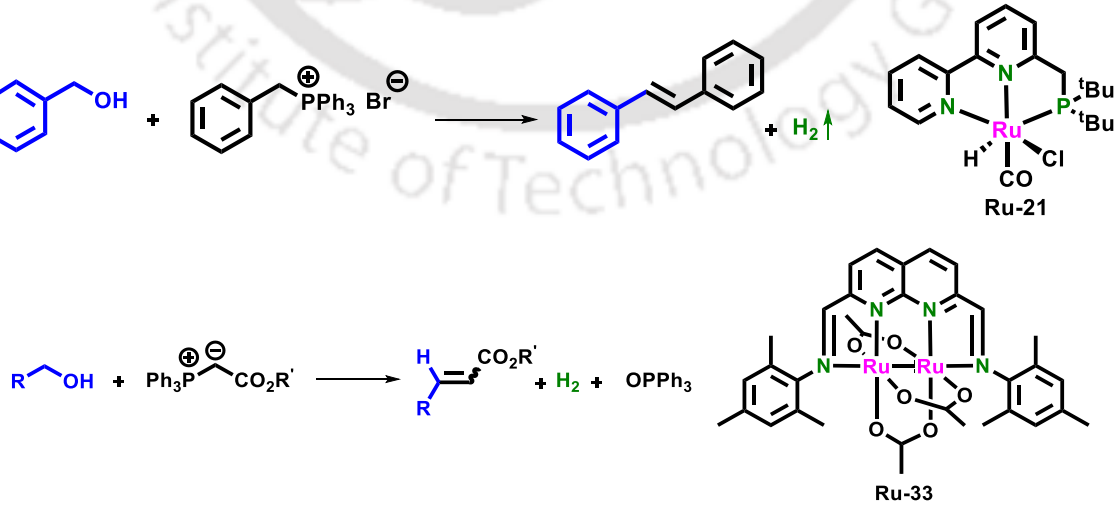
In 2014, *Milstein* and *co-workers*[49] first reported a catalytic Julia-type olefination reaction using a Ru-PNN pincer complex to form alkene directly from alcohols and sulfones. A series of primary alcohols such as aromatic alcohols and secondary alcohols were reacted with different sulfones such as dimethyl sulfone and benzyl phenyl sulfones in dioxane solvent to form styrene and stilbene (mostly *E*) derivatives. The sterically **less hindered bipyridyl-based Ru-PNN** catalyst (**Ru-32**) was found to be the most reactive (Scheme **1.22**).

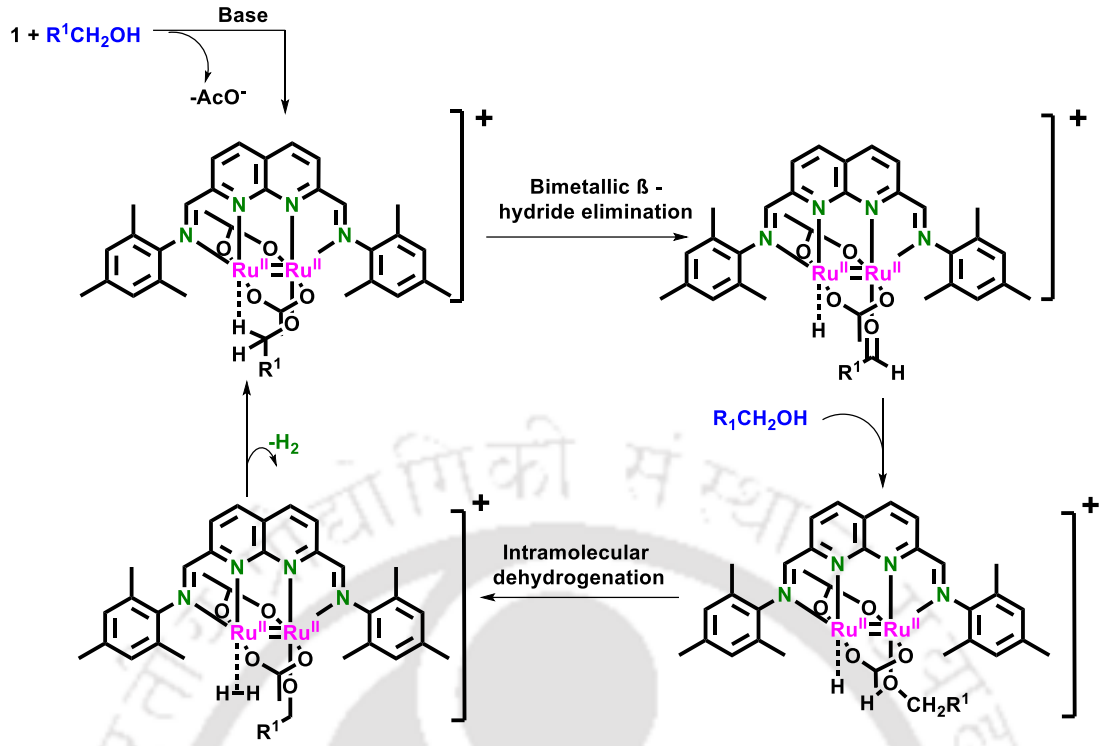


Scheme 1.22: Alkenylation and alkylation of sulfone with alcohols.

1.4.7.2. Wittig reaction:

The Wittig olefination reaction has gained recognition as one of the most useful processes for the formation of carbon– carbon bonds in organic chemistry. And In this regard, *Milstein*[50] and *co-workers* reported the Ru-PNN pincer-catalyzed, **Ru-21** olefination of alcohols using Wittig reagents under oxidant-free conditions. This method works well with both benzylic and aliphatic alcohols and the expected alkenes (*E*) were achieved in good yields. In 2016, Bera and *co-workers*[51] introduced a diruthenium complex $[Ru_2(L1)(OAc)_3]Cl$ **Ru-33**, which executed the Wittig reaction directly from alcohol. In this report, they used only triphenylphosphonium methoxycarbonylmethylide (Wittig reagent). The methodology is selective towards *E* alkene. The mechanism of the reaction is depicted here (Scheme **1.23**).



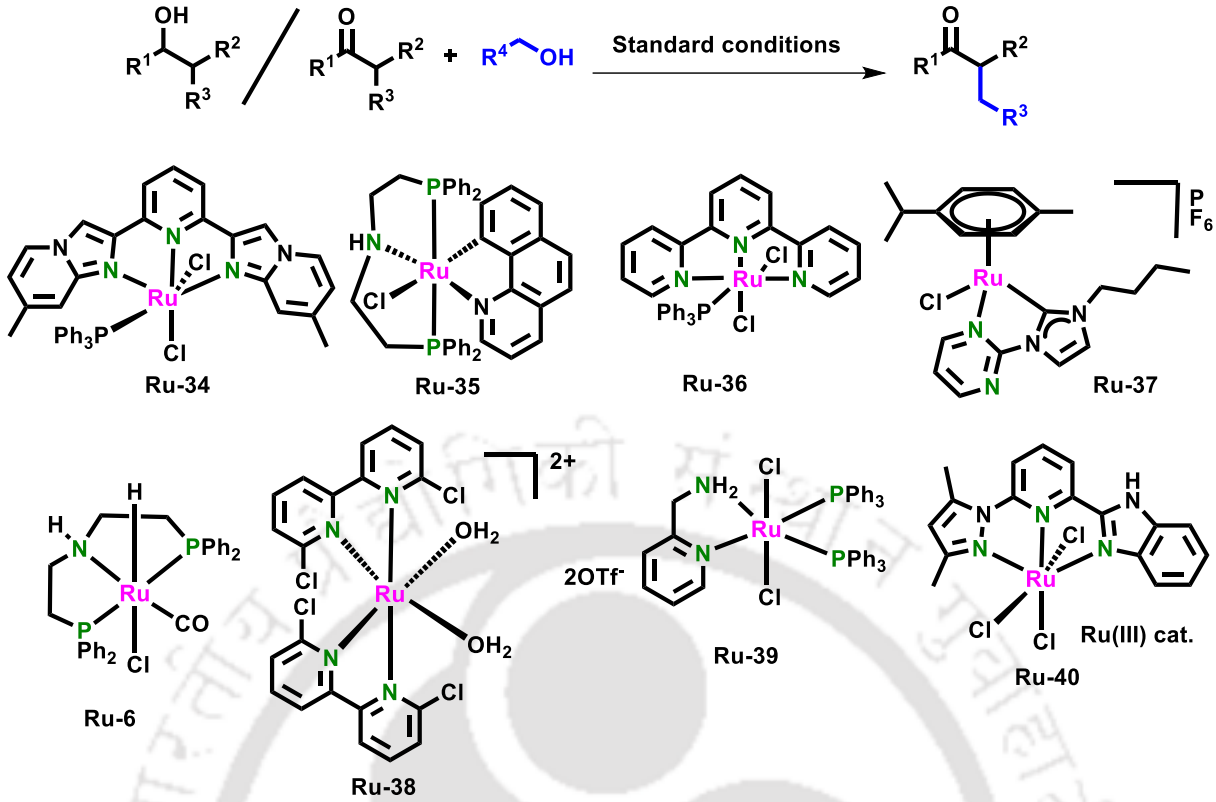


Scheme 1.23. Mechanistic pathway for bimetallic Ru-catalysed alcohol dehydrogenation.

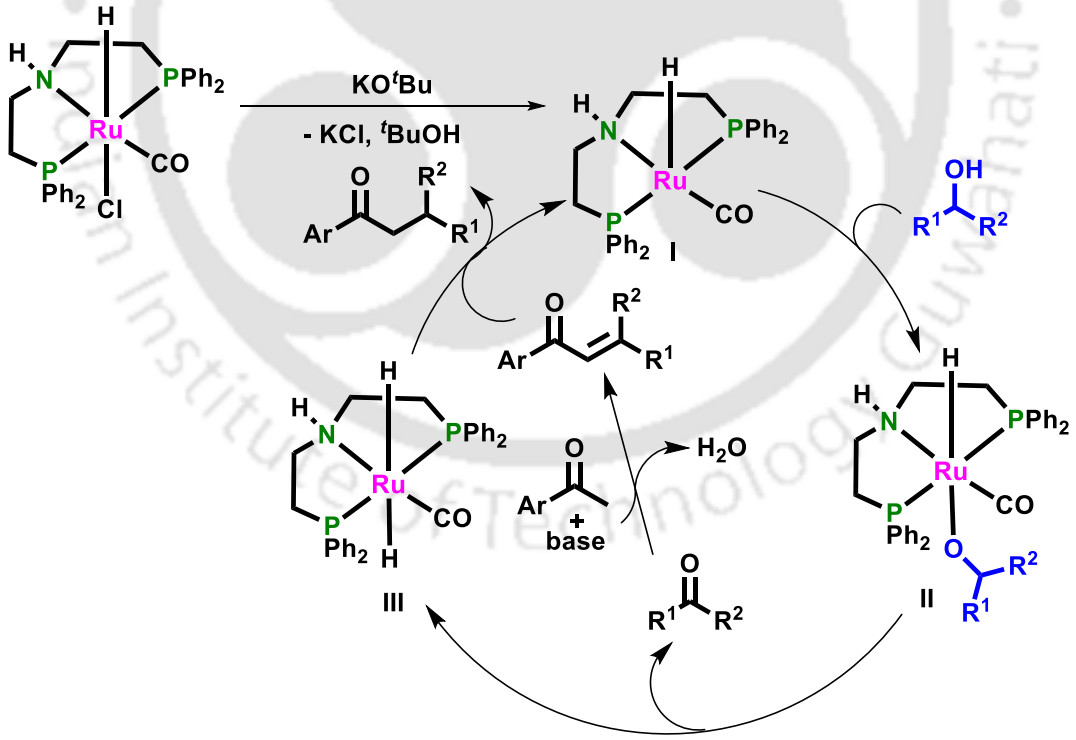
In 2019, *Srimani* and *co-workers* utilized a well-defined Ru-SNS pincer complex (Ru-16) to perform a similar transformation. Different benzylic or heteroaryl alcohols reacted well with Wittig-salt to form olefins, and in most cases, the E isomer was formed as the main product.[39]

1.4.8. C-C bond formation:

Strategically, by applying the BH method, ketones can be alkylated with alcohols to furnish α-alkylated ketones. There are numerous examples of complexes based on the C, N, and P-bound heterocyclic ligands to demonstrate the α-alkylation of ketones with alcohols as a green alkylating agent following a hydrogen auto-transfer protocol. In those reports, various benzylic/ aliphatic alcohols were efficiently alkylated with ketones containing aromatic, heteroaromatic, and cyclic ketones (Scheme **1.24** and **1.25**). [52]



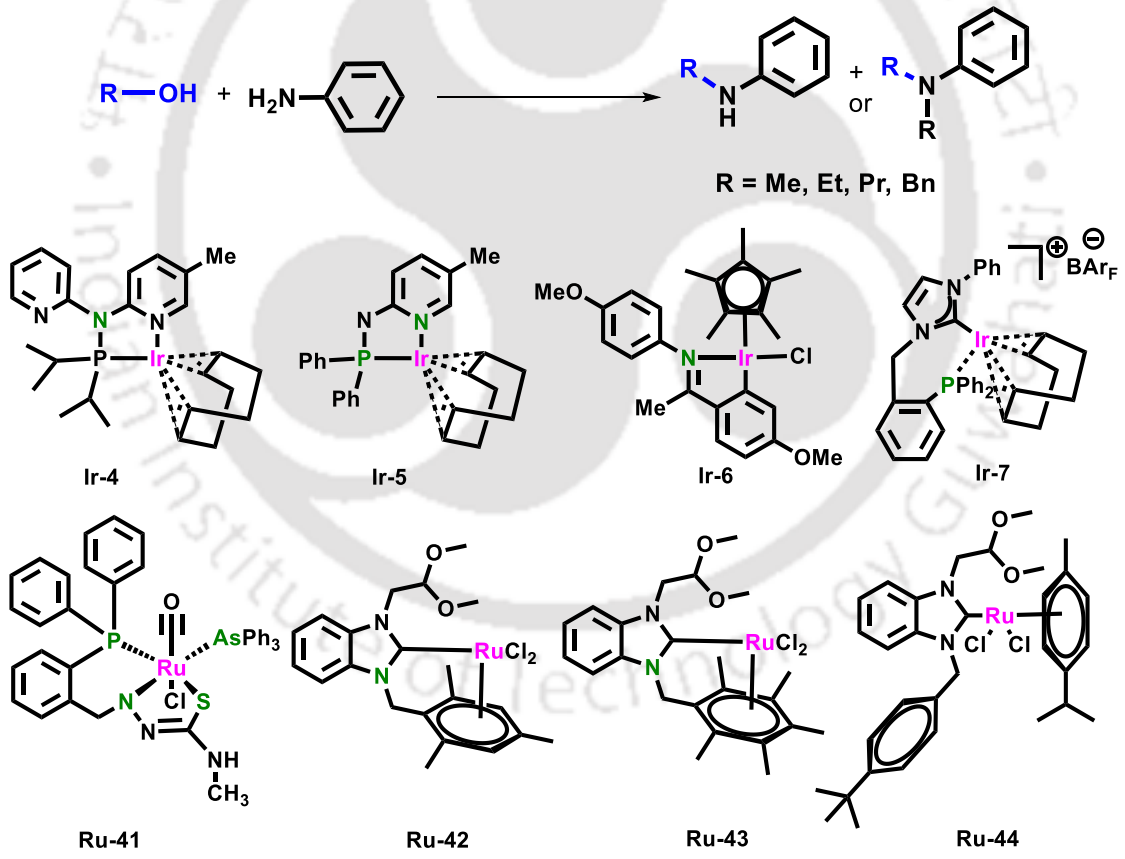
Scheme 1.24. Reports of C-C alkylation with various Ru-complexes.



Scheme 1.25. Mechanistic pathway of alkylation of ketone with secondary alcohol.

1.4.9. Amination of alcohols:

In 1981, *Grigg*[53] and *Watanable*[54] independently reported *N*-alkylation of amine with alcohol *via* BH strategy using **[RhH(PPh$_3$)$_4$]** and **[Ru(PPh$_3$)$_3$Cl$_2$]** catalysts respectively, and found great progress towards this reaction. Later, *Yamaguchi*[55] reported **[Cp*IrCl$_2$]$_2$** complex catalyzed efficient amination of alcohols. In 2010, *Kempe*[56] reported that different types of aniline have been mono-alkylated with alcohol in the presence of complex **Ir-5** and **Ir-6** under mild reaction conditions at 70 °C and a very low catalyst loading of 0.05% (Scheme **1.26**). *Xiao* and *co-workers*[57] also demonstrated *N*-alkylation of amine with iridium complex **Ir-6** by using a catalytic amount of a weaker base (5 mol% K_2CO_3). In 2013, *Andersson*[58] reported iridium-catalyzed **Ir-7** selective alkylation of anilines with alcohols at room temperature and without solvent. A ruthenium-phosphine-based catalyst **Ru-41** was active towards this transformation at very low catalyst loading and was reported by *Ramachandran et al.*[59]



Scheme 1.26: *N*-alkylation of amine with alcohol using Ir and Ru complexes

Ru-NHC complexes efficiently did the *N*-alkylation reaction of different cyclo-aliphatic amines like pyrrolidine and morpholine with different benzylic alcohols and were

reported by *Bruneau*.[60] In recent times, the capability of earth-abundant 3d transition metal complexes such as Mn,[61] Fe[62,] and Co[63] has been explored to catalyze such types of reactions.

1.5. Heterogeneous catalysis:

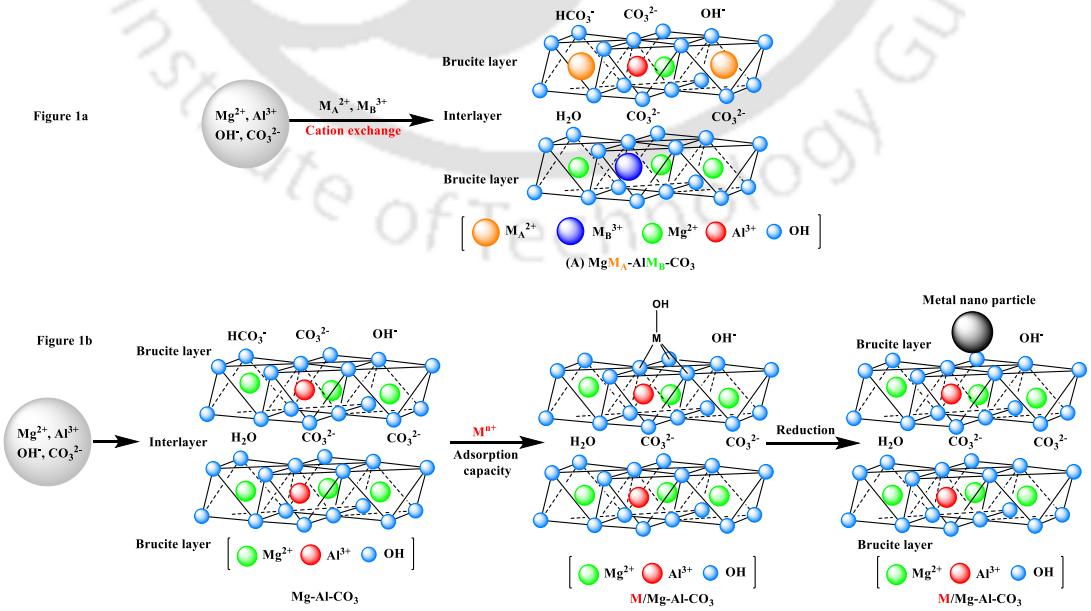
It is a fact that heterogeneous catalysts have several advantages over homogeneous ones. They can be easily separated, and recycled and the workup procedure is simple. There are several types of heterogeneous catalysts like graphene, MOFs, and other heterogeneous catalysts but among them, LDHs have gathered significant attention because of their robustness and tunable nature.

1.5.1. A quick introduction to Layered Double Hydroxide:

LDHs are a class of synthetic clays, often characterized by a layered structure, which is also known very often as hydrotalcite (HTs).[64-66] They deserved special recognition since these synthetic inorganic materials with well-organized alternate acidic/ basic sites and surfaces have beneficial features for solving today's environmental and industrial concerns. The first discovered LDH was the mineral hydrotalcite $[Mg_6Al_2(OH)_{16}](CO_3).4H_2O$. Because of its water content (hydro) and its talc-like appearance (talcite), it was given the name hydrotalcite. LDHs can be found in nature as minerals, but if necessary, they can be easily synthesized by using simple and inexpensive methods. The structure of most of LDHs is similar to that of naturally occurring hydrotalcite (HT), which is a natural magnesium-aluminum hydroxyl carbonate $[Mg_6Al_2(OH)_{16}](CO_3).4H_2O$. In natural hydrotalcite, Mg^{2+} ions coordinate with six OH^- in an octahedral way and form two-dimensional brucite sheets by sharing edges with surrounding atoms. The LDHs can be represented with the general formula $[M^{2+}_{1-x}\ M^{3+}_x(OH)_2]^{x+}A^{n-}_{x/n}.mH_2O$ $(0 < x < 1)$. Here M^{2+} denotes divalent metal cations, M^{3+} stands for trivalent metal cations, and A^{n-} is an n-valent anion. The Brucite-layers ($[Mg^{2+}_{1-x}Al^{3+}_x(OH)_2]^{x+}$), consist of Mg^{2+} ions which are isomorphically substituted by Al^{3+} ions. Interestingly, M^{2+} (M_A) and M^{3+} (M_B) ions having ionic radii close to Mg^{2+} and Al^{3+} can replace a portion of Mg^{2+} or Al^{3+} respectively in the brucite layer.[67] They can be substituted with Co, Zn, Fe, Ni, etc. This change often offers a distinct change in reactivity from the others. Between the two brucite layers, various organic and inorganic anions (A^{n-}) are positioned, along with water, to compensate for the positive charges of the brucite layers. The anions sandwiched between the layers of LDH can also be interchanged to bring in a variety of common organic

anions, inorganic anions such as NO_3^-, CO_3^{2-}, F^-, Cl^- etc.), and complex anions $Fe(CN)_6^{3-}$, $Fe(CN)_6^{4-}$ and polyoxometalates as catalytically active species. Notably, a wide variety of LDHs can also be synthesized by altering M^{2+}/M^{3+} molar ratios. The catalytic reactivity of these LDHs also varied with the M^{2+}/M^{3+} molar ratios. Other noticeable advantages of hydrotalcite are, (i) Memory effect: The memory effect of hydrotalcite refers to its ability to retain a structural memory of its previous state even after changing high temperature. This memory effect has been observed in hydrotalcite's reversible dehydration and rehydration. When hydrotalcite is dehydrated at high temperatures, it loses its water molecules and forms mixed metal oxides. However, when the dehydrated hydrotalcite is rehydrated, it returns to its original structure with the same crystallographic orientation as before,[68,69] (ii) Adsorption capacity: Hydrotalcite has excellent adsorption and catalytic properties, making it useful in a wide range of applications such as wastewater treatment,[70] gas purification, and catalysis. They can adsorb various organic and inorganic species like arsenates,[71] chromates,[72] and anionic surfactants[73] on their external surface as well as interlayer space, (iii) High thermal stability: Hydrotalcite is widely used as a flame retardant in plastics, rubbers, and other materials due to its high thermal potential[74,75] and (iv) Non-Toxicity: It is non-toxic, making it safe for use in various applications, including pharmaceuticals and food additives.[76] Overall, hydrotalcite has a unique combination of properties, making it a versatile and valuable material in many fields. In the context of catalysis, metal-fabricated hydrotalcite catalysts also have attracted significant attention (Scheme **1.27**).

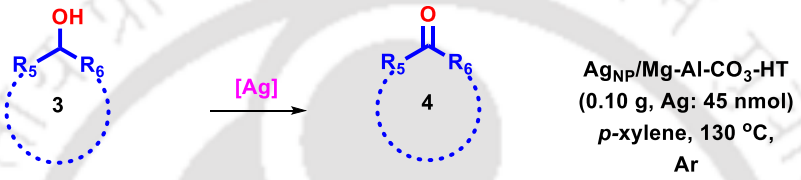
General formula: $[(MgM_A)^{2+}_{1-x}(AlM_B)^{3+}_{X}(OH)_2]^{X+}$



Scheme 1.27: Strategies for the preparation of hydrotalcite-based catalysts

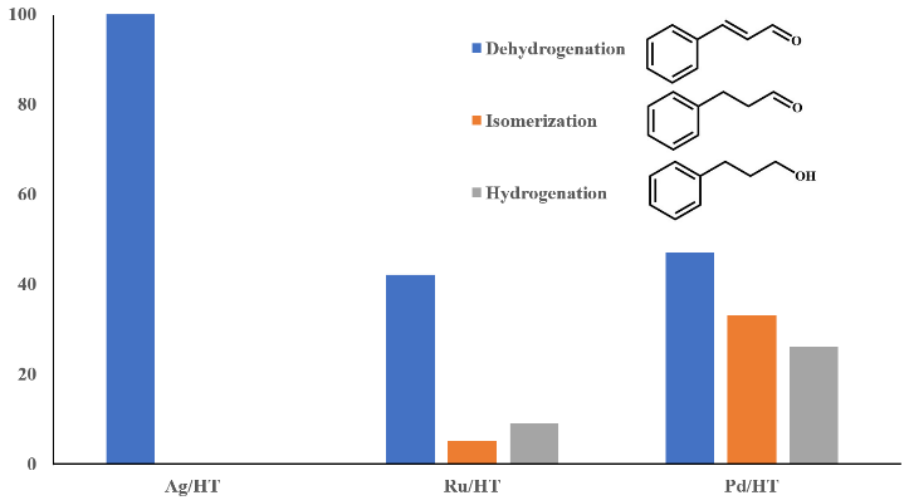
1.5.2. Dehydrogenation of Alcohols to form aldehydes and ketones:

In 2008, the group of Kaneda first introduced **Ag NP fabricated HT (Ag/Mg-Al-CO_3 HT)**, which was capable of dehydrogenating alcohols with the simultaneous liberation of molecular H_2 (Scheme **1.28**). The Ag-nanoparticle having a 3.3 nm mean diameter was found highly effective for this process. **Ag/Mg-Al-CO_3 HT** showed high TON (220 000) and TOF(1375 h^{-1}) for the oxidation of 1-phenyl ethanol to acetophenone at 130 °C in the *p*-xylene solvent under Ar atmosphere. The surface adsorption of H_2 is weak for **Ag/Mg-Al-CO_3** HT which promotes the release of equivalent molar amounts of H_2 during the acceptorless dehydrogenation of alcohols.[77]



Scheme 1.28. Ag/Mg-Al-CO_3 HT catalyzed acceptorless dehydrogenation of alcohols.

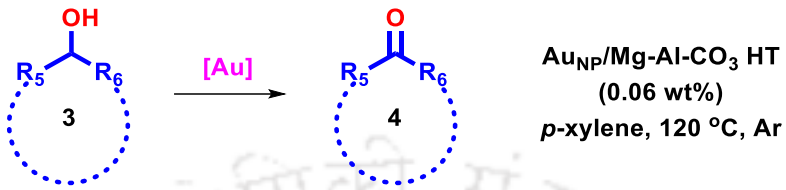
This weak adsorption of H_2 over the **Ag/Mg-Al-CO_3 HT** surface leads to a distinctive chemoselective property (Scheme **1.29**) e.g. when cinnamyl alcohol is dehydrogenated, it just produces cinnamaldehyde, neither hydrogen transfer nor isomerization occurs.



Scheme 1.29. Comparison of chemoselectivity among Ag/HT, Ru/HT, and Pd/HT.

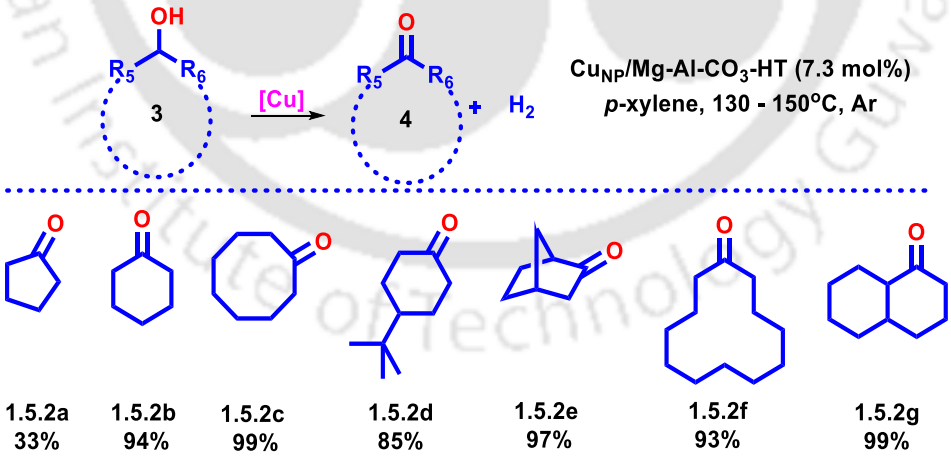
Two years later, the potential of another noble metal fabricated HT was also explored (Scheme **1.30**). Hung synthesized hydrotalcite-supported **Au nano particles** (mean diameter 2.8 nm), which are capable enough to dehydrogenate alcohol to their corresponding carbonyl

compounds and liberate hydrogen. It was prepared via the impregnation method, followed by H_2 reduction. It outperforms the previously reported Ag_{NP}/Mg-Al-CO_3 HT. It can even dehydrogenate less reactive alicyclic, aliphatic primary, and aliphatic secondary alcohols also. The rate of the reaction is comparatively slow in the case of aliphatic primary.[78]



Scheme 1.30. Au_{NP}/Mg-Al-CO_3 HT catalyzed acceptorless dehydrogenation of alcohols.

The applicability of less expensive base metal catalyst-supported HT for acceptorless dehydrogenation was introduced by *Kaneda* and *co-workers* (Scheme **1.31**). Cu NPs (7.5 nm mean diameter) were successfully grafted onto HT (Cu_{NP}/Mg-Al-CO_3 HT) which displayed an excellent dehydrogenation ability towards various alcohols.[79] The catalyst was well characterized by XAFS. The Cu_{NP}/Mg-Al-CO_3 HT could perform in acceptorless dehydrogenation reactions under both solvent and neat conditions. Although it failed to dehydrogenate primary aliphatic alcohols, its catalytic reactivity towards the dehydrogenation of alicyclic alcohols is admirable.

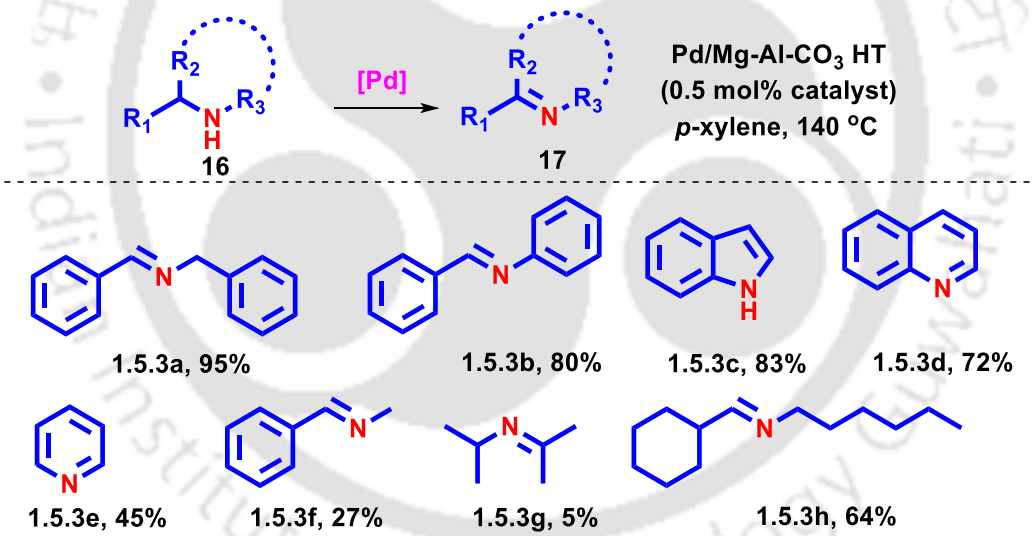


Scheme 1.31. Cu_{NP}/Mg-Al-CO_3 HT catalysed oxidation of secondary alcohols.

1.5.3. Dehydrogenation of Amines to Imines:

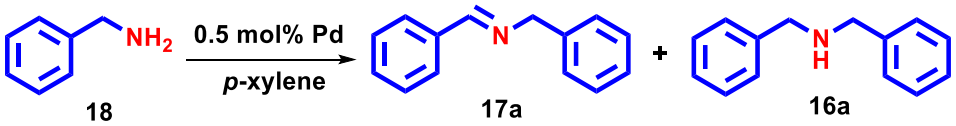
In 2019, *Kostal* and *co-workers* reported acceptorless dehydrogenation of primary and secondary amines using Pd-doped hydrotalcite (Scheme **1.32**).[80] In this report, they developed

two types of Pd-doped hydrotalcite. A catalyst with high Pd (5%) loading **5%Pd/Mg-Al-CO_3 HT** and another with low Pd (0.5%) loading **0.5Pd%/Mg-Al-CO_3 HT** was created *via* coprecipitation approach under continuous flow condition. Catalysts **5%Pd/Mg-Al-CO_3 HT** and **0.5Pd%/Mg-Al-CO_3 HT** have the same layered double hydroxide structure but their XPS speciation is different, showing proof of dispersed Pd^0, $Pd^{2+,}$ and Pd^{4+} species. XPS analysis also suggests that catalyst 5%Pd/Mg-Al-CO_3 HT contains Pd (0) nanoparticles and Pd^{2+} clusters. On the other hand, catalyst 0.5%Pd/Mg-Al-CO_3 HT mainly contains Pd^{2+} and Pd^{4+}. For the dehydrogenation of secondary amines and oxidative transamination process, catalyst 5%Pd/Mg-Al-CO_3 HT showed higher activity and selectivity compared to 0.5%Pd/Mg-Al-CO_3 HT. Substrate scope variation suggested that catalyst 5%Pd/Mg-Al-CO_3 HT was very much active to secondary benzyl, and alkyl amines. Notably, various N-heterocyclic compounds such as 1,2,3,4-tetrahydroquinoline, piperidine, and indoline could be easily dehydrogenated. Moreover, the developed catalyst could also perform the oxidative transamination of primary amines to form secondary imines in excellent yields.



Scheme 1.32. Pd/Mg-Al-CO_3 HT catalysed dehydrogenation of amines.

Under standard reaction conditions, when catalyst, 5%Pd/Mg-Al-CO_3 HT was treated with benzyl amine, it afforded 93% imine and catalyst 0.5%Pd/Mg-Al-CO_3 HT gave 56% (Scheme **1.33**). The superior activity of 5%Pd/Mg-Al-CO_3 HT over catalyst 0.5%Pd/Mg-Al-CO_3 HT suggests that Pd^0 might be the most effective Pd species for this process. Similar outcomes were achieved under inert conditions, which negates the involvement of residual oxygen and confirms acceptorless dehydrogenation. The catalyst was also recycled up to six times.

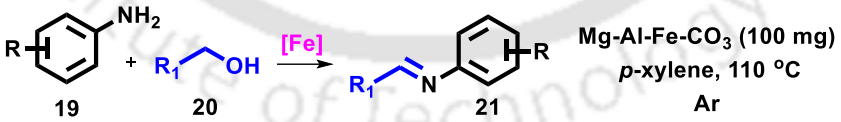


Catalyst	Imine	Amine	Conversion %
5% Pd-HT	96 (+/- 3)	<5	>98
0.5% Pd-HT	56 (+/- 4)	<5	>98
Mg-Al-CO_3 HT	<5	0	<5

Scheme 1.33. Selectivity of the catalyst.

1.5.4. Dehydrogenative Coupling of alcohol and amine:

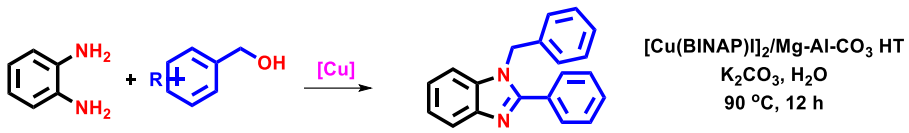
In 2015, *Kostal* and *co-workers* presented the Mg-Al-Fe-CO_3 catalyzed dehydrogenative synthesis imines by reaction alcohols and amines.[81] In this report, six modified Mg-Al-CO_3 HTs were prepared via the coprecipitation method with first-row transition metal ions (Cu^{2+}, Cr^{3+}, Fe^{3+}, $Zn^{2+,}$ and Ni^{2+}). Though the structures of all six HTs are similar, they differ in acid-base, redox properties, adsorption capacity, and surface area. Among these Mg-Al-Fe-CO_3 HT resulted in the highest yield (92%) for the synthesis imine (Scheme **1.34**). Notably, the reaction does not require any external base. The immobilization of Pd (0) on Mg-Al-Fe-CO3 leads to the enhancement in the catalytic activity further. Increased Pd (5%) results in a loss of catalytic activity. The catalyst was found to be effective in the coupling of benzylic alcohols with primary amines. However, it failed to activate aliphatic and alicyclic alcohols. Furthermore, the catalyst was reused up to for imination reaction.



Scheme 1.34. Mg-Al-Fe-CO_3 catalyzed synthesis of imines.

In 2018, *Wang* and *co-workers*[82] illustrated a hydrotacite-supported **BINAP-Cu** system for the acceptorless dehydrogenative synthesis of benzimidazoles in water (Scheme **1.35**). Characterization of the catalyst was done via TEM, PXRD, SEM, FT-IR, etc. The reaction is not facile with $[Cu(binap)I]_2$ and CuI, which indicates the influence of support in this process. The synergistic effect of the HT and BINAP results in an enhancement in the catalytic activity of **$[Cu(binap)I]_2$@HT** over **$[Cu(binap)I]_2$**. Later, substrate scope analysis showed that various

substituted diamines and aromatic alcohols responded well to deliver the targeted heterocycles in high yield.

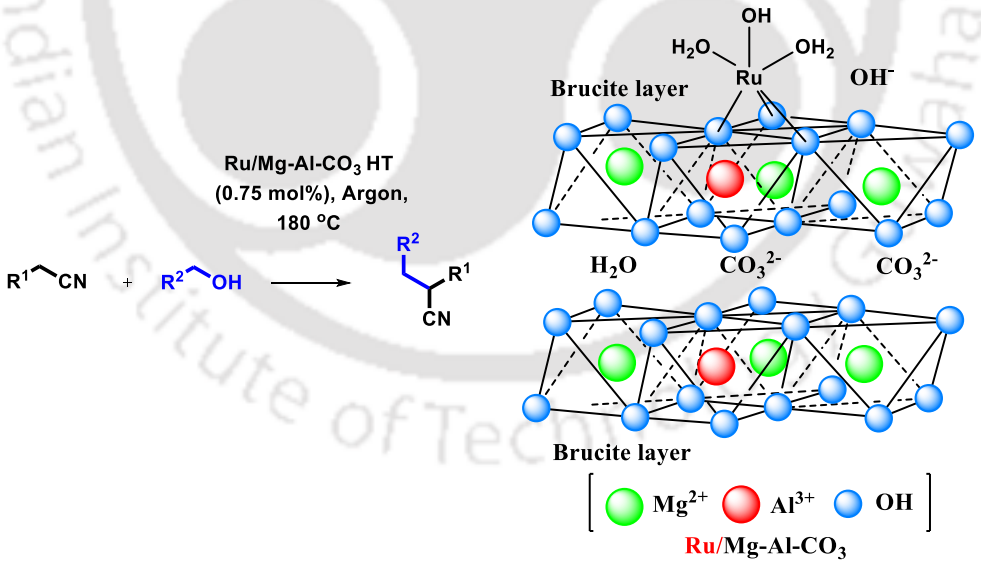


Scheme 1.35. Benzimidazole synthesis.

1.5.5. C-C bond formation:

1.5.5.1. Nitrile alkylation:

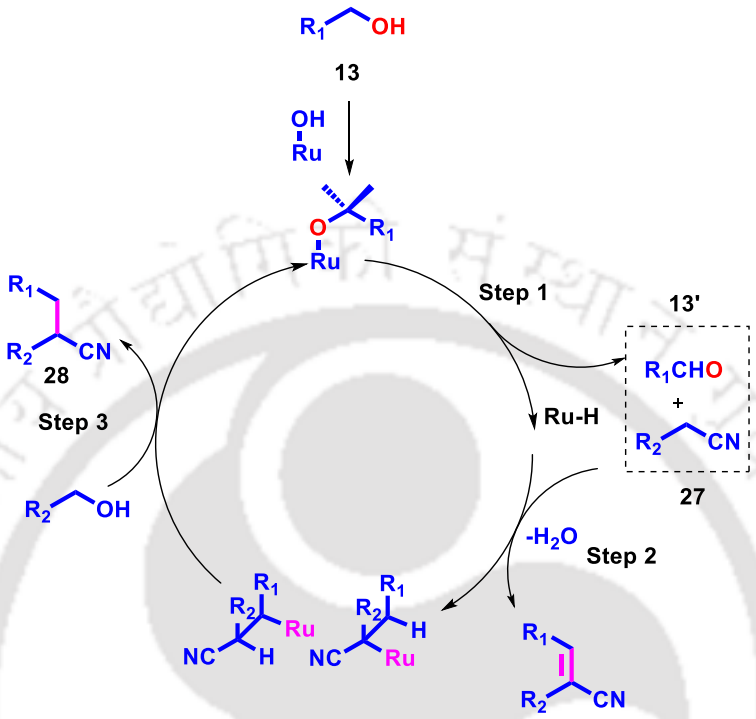
In 2004, Kaneda introduced the first additive-free Ru/Mg-Al-CO_3 HT for the *α*-alkylation of nitrile *via* BH approach. Characterization data revealed that Ru is in a +4 oxidation state within the catalyst. This Ru/Mg–Al–CO_3 HT can alkylate a variety of arylacetonitriles with diverse alcohols. The catalyst can even activate ethanol in the presence of phenyl acetonitrile to deliver an excellent yield (98%) of *α*-ethylated phenyl acetonitrile (Scheme **1.36**).[83]



Scheme 1.36. Ru/Mg-Al-CO_3 HT cataysed *α*-alkylation of nitrile.

The mechanism of the reaction can be explained easily. It consists of three steps. Dehydrogenation of alcohols to aldehydes (Step 1). The next step involves, base promoted aldol condensation of nitriles with aldehydes, (Step 2) followed by reduction of *α,β*-unsaturated nitriles with a Ru–H species (Step 3) (Scheme **1.37**). Moreover, via borrowing the hydrogen

approach, *α*-alkylation of carbonyl compounds was first introduced by Kaneda. The Ru/HT catalyst system effectively performs *α*-alkylation of a ketone with alcohol without any base additive.[84]



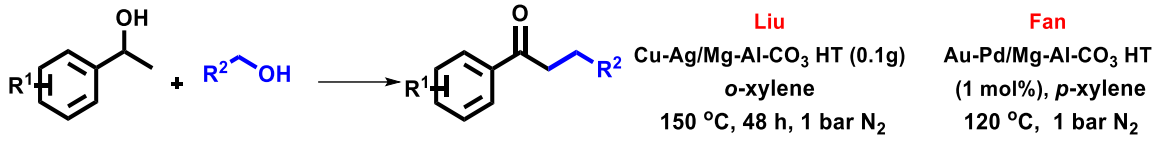
Scheme 1.37. A proposed catalytic cycle of Ru/Mg-Al-CO_3 HT in *α*-alkylation of nitrile.

1.5.5.2. *α*-alkylation of ketones:

Later, in 2013, *Fan* and *co-workers* reported an HT-supported Au-Pd bimetallic catalyst (Au:Pd = 13:1), which performed C–C cross-coupling of primary and secondary benzylic alcohols in the absence of any additives under an inert atmosphere in *p*-xylene. The catalyst was prepared by allowing HT in an aqueous solution of $HAuCl_4$ and $PdCl_2$ with varying Au/Pd molar ratios. Later, the filtered material was dried and heated at 300 ºC under 5% H_2/Ar for 2 hours. This report is a unique example of bimetallic interaction over the support of hydrotalcite. The optimal ratio of Au:Pd was illustrated as 13:1. The activity of the catalyst was greatly affected by the decreasing ratio and led to unnecessary side products.[84]

Later, in 2016 *Liu et al.* developed another bimetallic Cu-Ag/HT catalyst.[84] The catalyst was prepared via the co-impregnation method by mixing the support with an aqueous solution of aqueous solution of Ag(I) and Cu(II) nitrates. The catalyst responded well to various substituted benzyl alcohols and 1-phenyl ethanol, including both electron-rich and electron-

withdrawing substituents. The catalyst is reusable up to 5 times, which promotes the heterogeneity of the catalyst (Scheme **1.38**).



Scheme 1.38. Cu-Ag/Mg-Al-CO_3 HT catalysed dehydrogenative C-C cross-coupling of alcohols

1.5.6. Amine alkylation:

Wang and *co-workers* used their well-characterized hydrotalcite supported **[Cu(binap)I]**$_2$ for the N-alkylation of amines *via* the BH approach.[82] The reaction can proceed under solvent-free conditions. The protocol showed a range of substrate scope related to benzylic alcohols with electron-donating and electron-withdrawing substituents but it failed to dehydrogenate aliphatic alcohols. The catalyst also effectively catalyzes the α-alkylation of ketones.

1.6. Concluding remarks:

The above discussion shows that acceptorless dehydrogenation and borrowing hydrogen principle have attracted significant attention because of their significant contribution to the creation of atom-economical, environmentally benign sustainable methodologies for the synthesis of important building blocks. The number of reports in terms of heterogeneous and homogeneous catalysts is quite significant and it inspires us for further development. In homogeneous catalysis, various ligand frameworks like PNP, NNP, and NHC carbene-based ligands have been used to form these complexes. However, the synthesis of these complexes is frequently found to be challenging. In addition, these complexes are often found to be moisture sensitive and quite expensive. Moreover, it has been observed that different types of catalysts can lead to different products from the same set of reactions. This underpins that there is growing interest in the development of new catalysts in various de(hydrogenative) transformations. So, here air stable Ru-SNS/NNS complexes have been synthesized and utilized in a much simpler way. On the other hand in terms of cost effectiveness and recyclability, heterogeneous catalysts are much more superior to homogeneous catalysts.

Consequently, Ru-grafted hydrotalcite was utilized in various de(hydrogenative) transformations.

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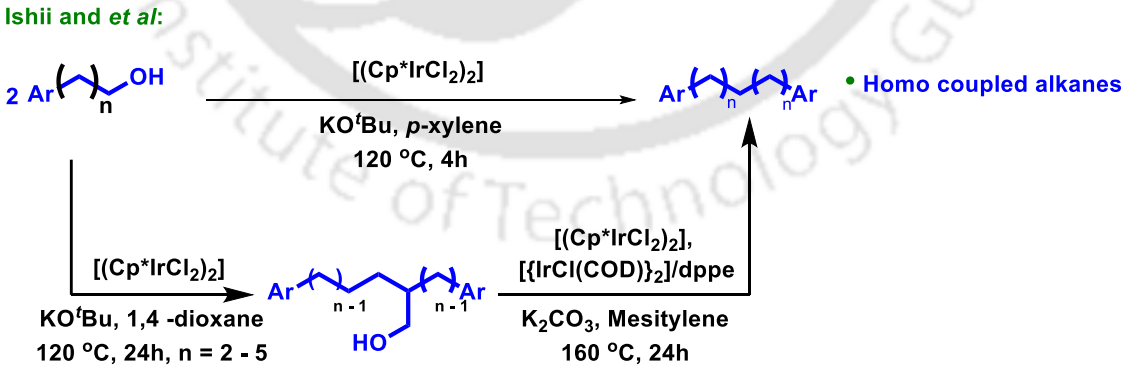
Chapter 2

Ruthenium Pincer Catalyzed Selective Synthesis of Alkanes and Alkenes via Deoxygenative Coupling of Primary Alcohols

2.1. Introduction:

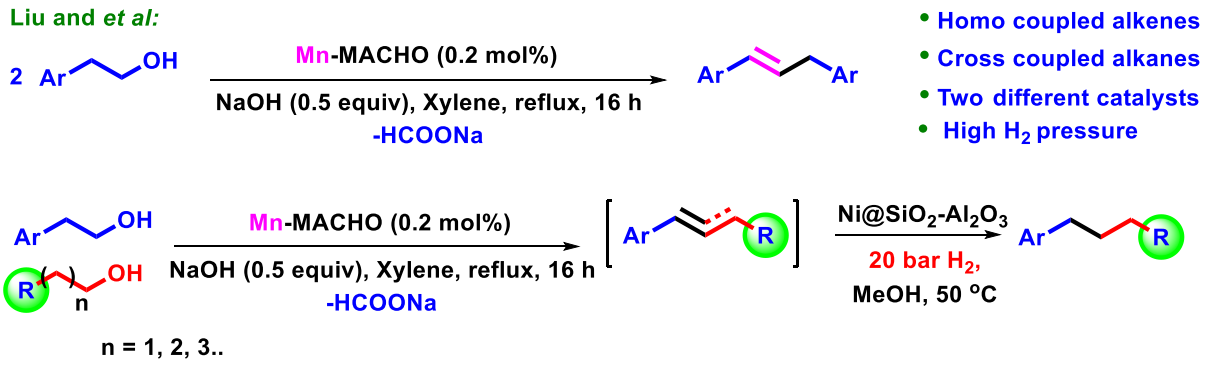
In light of the rapid depletion of fossil fuels and increasing awareness of environmental protection and economic benefits, the sustainable conversion of low-cost biomass into biofuels and various chemical feedstocks is an important goal.[1] In this context, recently, significant efforts have been contributed towards borrowing hydrogen-mediated upgradation of short-chain alcohols into long-chain alcohols.[2] Compared to oxygenated fuels, hydrocarbon fuels have higher energy density and are more compatible with the existing engines and infrastructure.[3] Therefore, the catalytic conversion of alcohols to hydrocarbons is highly captivating.[4] However, the access of alkanes via direct coupling of alcohols is rare[5] because the success of the reaction depends on the selective multistep reaction sequence. Initially, dehydrogenation of primary alcohols[6] produces aldehydes, which undergo aldol condensation to furnish unsaturated aldehydes. Deoxygenation of the formed unsaturated aldehydes leads to the formation of the corresponding alkenes. Finally, the hydrogenation of alkenes forms the desired alkanes. A highly active catalyst with a high degree of selectivity is critical for achieving such a challenging process.

In 2011, *Obora* and *co-workers* described an Ir-catalyzed homocoupling of 2-aryl ethanols to produce 1,3-diarylpropanes. They also demonstrated that the higher *ω*-aryl alcohols furnishes *β*-methyl hydroxyl-*α,ω*-diaryl alkanes which can be further converted to *α,ω*–diaryl alkanes in the presence of $[(Cp^*IrCl_2)_2]$/$[\{IrCl(cod)\}_2]$ /dppe (dppe: 1,2-bis(diphenylphosphino) ethane) catalytic systems (Scheme **2.1**). [5a]



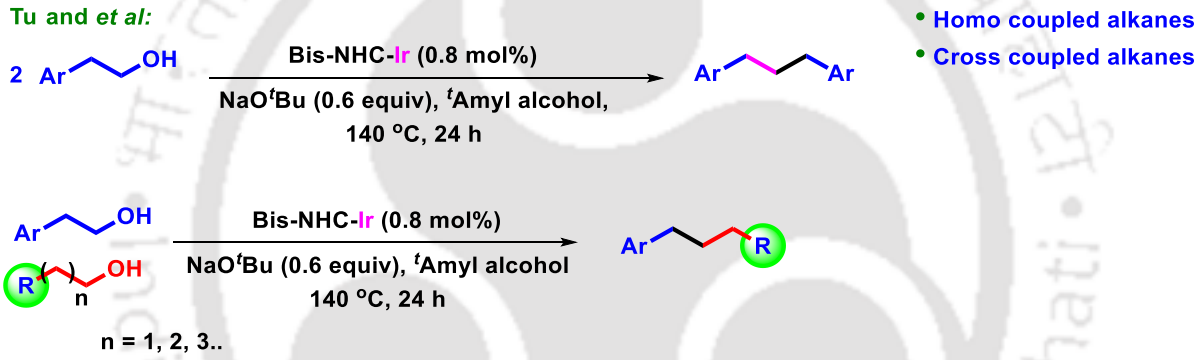
Scheme 2.1. Preparation of *α,ω*-diarylalkanes by Obora.

In 2018, Wang and his group first established manganese catalyzed deoxygenative coupling of various aryl alcohols to their corresponding olefins. Finally, the alkenes were hydrogenated by employing $Ni@SiO_2{-}Al_2O_3$ under 20 bar H_2 to furnish the desired alkanes (Scheme **2.2**). [5b]



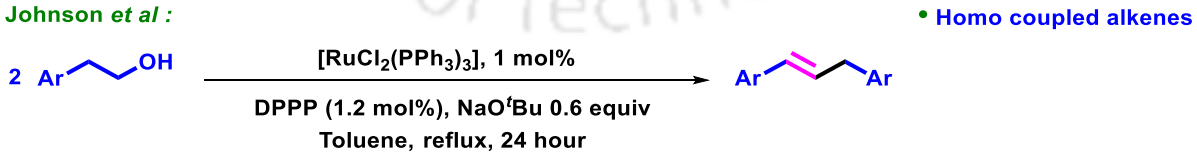
Scheme 2.2. Selective alkene and alkane preparation by Wang

Recently, Tu and *co-workers* utilized a bis-*N*-heterocyclic carbene-derived Ir-complex for synthesizing alkanes via direct deoxygenative coupling of alcohols (Scheme **2.3**).[5c]

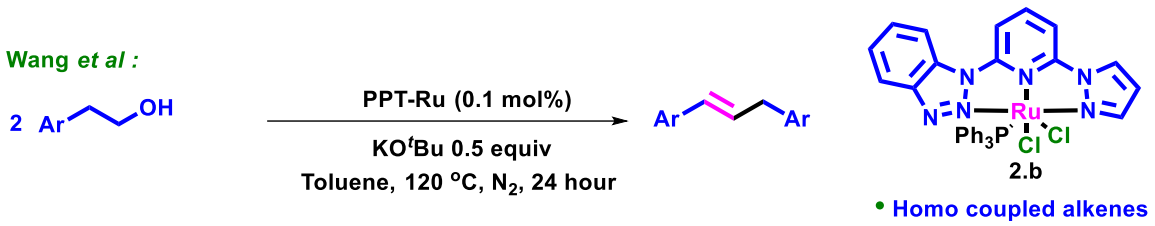


Scheme 2.3: Selective alkane preparation by Tu

Interestingly, the selective synthesis of 1,3-diarylpropenes from the coupling of alcohols[7] is also important as these can be further utilized to synthesize important building blocks (Scheme **2.4** and **2.5**).[8]



Scheme 2.4: Previous work by Johnson



Scheme 2.5: Previous work by Wang

From the above discussion, it was observed that the outcome of the reaction (alkene/alkane) was very much dependent on the design of the catalysts. Tuning the ligand framework can alter the electronic environment of the metal center and the outcome may vary between an alkene or alkane, which eventually limits the scope of the methodology. Thus, we envisioned that a single catalyst capable of selectively synthesizing 1,3-diaryl propenes from alcohols and also having the ability to hydrogenate them under mild conditions to produce the desired alkanes would be appealing, as both alkenes and alkanes are synthetically important. For instance, alkenes could be used for heterocycle formation and alkanes have numerous applications.

2.2. Our work:

Here in this chapter, the activity of various well-defined Ru[9] complexes was explored in the selective conversion of primary alcohols into both long-chain alkenes and alkanes. Both homo- and cross-coupling reactions provide good yields of the desired products with excellent selectivity. Various control experiments, mechanistic and kinetic studies were performed to detect the pathway of the reaction.

2.3. Results and discussions:

In our initial experiments, NNS/SNS ligand-derived Ru complexes were synthesized according to the literature procedure and Ru-MACHO was obtained commercially. Next, the deoxygenative coupling of 2-phenyl ethanol **2.1.1a** was thoroughly investigated. After rigorous screening (**Table 2.1**), the optimal reaction conditions were found to obtain 1,3-aryl propene, **2.1.2a**. When a toluene solution containing 2-phenyl ethanol **2.1.1a** (2 mmol), **Cat. 1** (0.5 mol%), and NaOH (0.6 equiv) was refluxed for 24 h in a 10 mL Schlenk tube under argon; 1,3-diphenyl propene was isolated in 85% yield. Notably, the hydrogenated product of 1,3-diphenyl propene was not detected. NaOH was found to be significantly better compared to KOH,

KO^{t}Bu, NaO^{t}Bu, and carbonates. (**Table 2.1**, **entries 1** to **7**). For this process, 0.6 equivalent of NaOH was found to be optimal. (**Table 2.1**, **entries 8** and **9**). **Cat. 2** and **cat. 3** were quite active towards the reaction but were inferior compared to **Cat. 1**. Ru-MACHO failed to give the desired product; however, the formation of ester phenyl ethyl 2-phenylacetate (10%) was noticed (**Table 2.1**, **entry 20**).

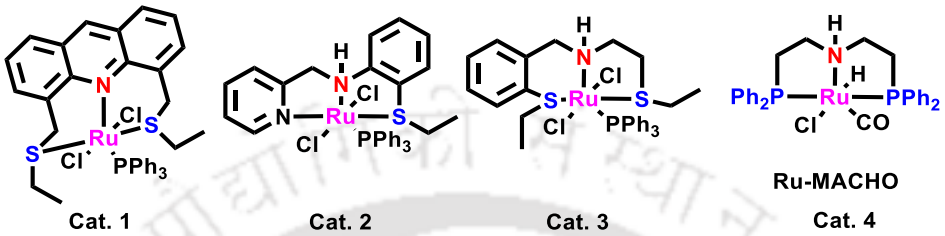
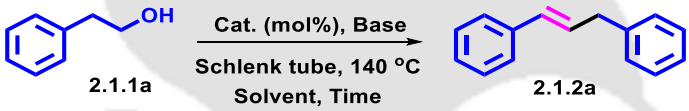


Figure 2.1: Ruthenium complexes

2.3.1. Optimization of the reaction condition for the selective synthesis of alkenes:

Table 2.1. Screening table:



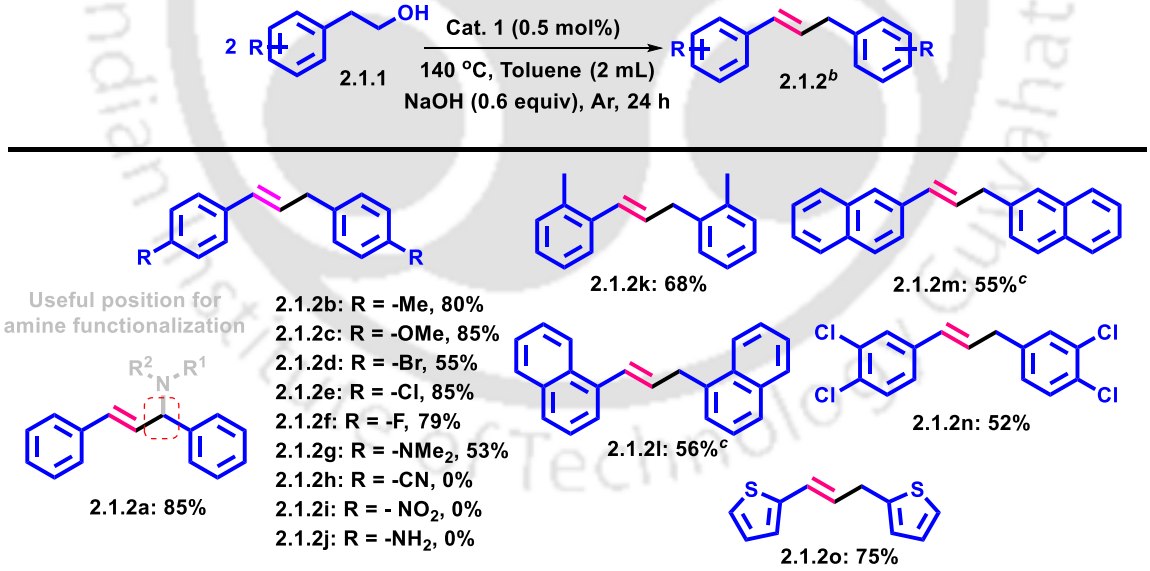
Entry	Cat. (mol%)	Base (equiv)	Solvent (2 mL)	Conversion of alcohol	Yield (%)[b]
1	Cat. 1 (1.0)	KOH (1.0)	Toluene	62	34 (25)
2	Cat. 1 (1.0)	CsOH.H_2O (1.0)	Toluene	58	42 (30)
3	Cat. 1 (1.0)	NaO^{t}Bu (1.0)	Toluene	89	61 (60)
4	Cat. 1 (1.0)	KO^{t}Bu (1.0)	Toluene	91	85 (72)
5	Cat. 1 (1.0)	Na_2CO_3 (1.0)	Toluene	25	20 (18)
6	Cat. 1 (1.0)	Cs_2CO_3 (1.0)	Toluene	32	24 (15)
7	Cat. 1 (1.0)	NaOH (1.0)	Toluene	97	86 (88)
8	Cat. 1 (1.0)	NaOH (0.6)	Toluene	100	88 (85)
9	Cat. 1 (1.0)	NaOH (0.4)	Toluene	65	60 (52)
10	**Cat. 1 (0.5)**	**NaOH (0.6)**	**Toluene**	**100**	**88 (85)**
11	Cat. 1 (0.3)	NaOH (0.6)	Toluene	75	66 (65)
12	Cat. 1 (0.5)	NaOH (0.6)	Neat	100	14 (12)
13[c]	Cat. 1 (0.5)	NaOH (0.6)	Toluene	35	20 (15)
14	Cat. 1 (0.5)	NaOH (0.6)	Dioxane	40	30 (38)
15	Cat. 1 (0.5)	NaOH (0.6)	^{t}Amyl alcohol	62	60 (55)

16	Cat. 2 (0.5)	NaOH (0.6)	Toluene	83	52 (40)
17	Cat. 3 (0.5)	NaOH (0.6)	Toluene	90	74 (65)
18	Cat. 1 (0.5)	-	Toluene	-	-
19	-	NaOH (0.6)	Toluene	-	-
20[d]	Cat. 4 (0.5)	NaOH (0.6)	Toluene	50	-

[a] Reaction conditions: **2.1.1a** (2 mmol), **Cat.** (0.3 – 1.0 mol%), base (0.3 – 1.0 equiv), solvent (2 mL), at 140 °C (bath temperature) for 24 h, Ar. [b] NMR yield (Yield in parenthesis is the isolated yield). [c] Pressure tube. [d] 10% percent formation of ester phenylethyl 2-phenylacetate.

2.3.2. Homocoupling of 2-arylethanols:

To explore the applicability of the protocol, different 2-aryl ethanols were reacted under optimal conditions. Homo-coupled alkene products with high selectivity were obtained in good to excellent yields (64-85% for **2.1.2a-2g**) (**Scheme 2.6**). Different functional groups with varying electronic and steric properties were well tolerated at the *ortho*-, *meta*-, and *para*-positions. The 1-(naphthalenyl)- and 2-(naphthalenyl) ethanols (**2.1.2l** and **2.1.2m**) also furnished a moderate yield of the desired alkenes.



[a]Standard reaction conditions: **2.1.1** (2 mmol), NaOH (0.6 equiv), **Cat. 1** (0.5 mol%), 2 mL toluene, Ar, 140 °C (bath temperature) for 24 h. [b]Isolated yield, [c]36 h.

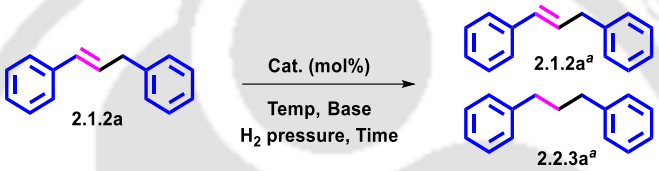
Scheme 2.6. Substrate Scope for Alkenes[a]

The electronic properties of the substituents on the phenyl ring were found to have a negligible effect on the deoxygenative coupling process. Under optimal conditions, the heterocyclic

alcohol 2-(thiophenyl)ethanol undergoes a smooth reaction and furnished desired **2.1.2o** in an excellent yield (75%). However, 2-pyridine-ethanol failed to give the desired product. Encouraged by this finding, it was thought whether the developed catalyst could hydrogenate 1,3-diaryl propenes to the corresponding alkanes under the mild pressure of hydrogen. (**Table 2.2**) Thus, when 1,3-diphenylpropene **2.1.2a** (1 mmol), KO^{t}Bu (0.5 equiv), **Cat. 1** (0.5 mol%) were reacted under 3 bar hydrogen at 100 ºC for 24 hours, 1,3-diphenylpropane **2.1.3a** was isolated exclusively (99%). Notably, the H_2 pressure used in our method (**Scheme 2.7**, **A**) is substantially lower than the previously reported protocol.[5b]

2.3.3. Optimization of the reaction conditions for the synthesis of alkanes:

Table 2.2. Optimization of the Reaction Conditions:



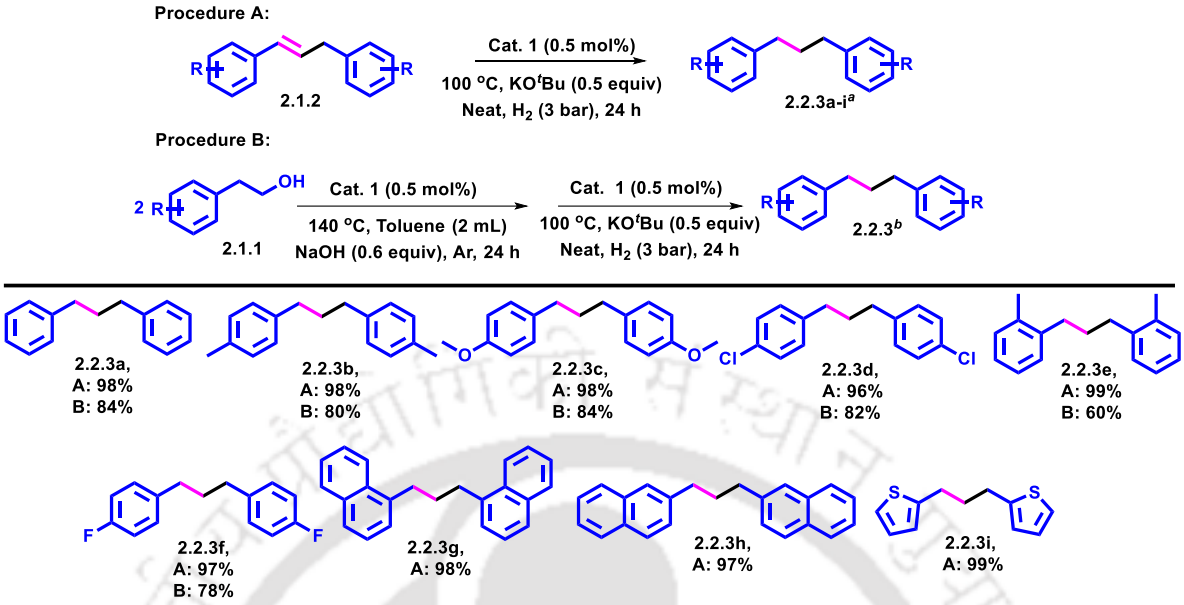
entry	cat. (mol%)	base (mmol)	solvent (2 mL)	Temp.	H_2 Pressure (bar)	time (h)	yield (%)[b] 2a:3a
Solvent and base variation:							
1	1 (1.0)	KOH (1)	Toluene	140 ºC	30	30	99:1
2	1 (1.0)	CsOH.H_2O(1)	Toluene	140 ºC	30	30	99:1
3	1 (1.0)	NaO^{t}Bu (1)	Toluene	140 ºC	30	30	99:1
4	1 (1.0)	KO^{t}Bu (1)	Toluene	140 ºC	30	30	90:10
5	1 (1.0)	K_2CO_3 (1)	Toluene	140 ºC	30	30	99:1
6	1 (1.0)	Na_2CO_3 (1)	Toluene	140 ºC	30	30	99:1
7	1 (1.0)	Cs_2CO_3 (1)	Toluene	140 ºC	30	30	85:15
8	1 (1.0)	NaOH (1)	Toluene	140 ºC	30	24	99:1
9	1 (1.0)	KO^{t}Bu (1)	^{t}amyl alcohol	140 ºC	30	24	85:15
10	1 (1.0)	KO^{t}Bu (1)	Dioxane	140 ºC	30	24	95:5
Base variation and neat condition:							
11	1 (1.0)	KOH (1)	Neat	140 ºC	30	24	40:60
12	1 (1.0)	CsOH.H_2O(1)	Neat	140 ºC	30	30	15:85
13	1 (1.0)	NaO^{t}Bu (1)	Neat	140 ºC	30	30	30:70

14	1 (1.0)	KO^{t}Bu (1)	Neat	140 ºC	30	30	0:100
15	1 (1.0)	K_2CO_3 (1)	Neat	140 ºC	30	30	20:80
16	1 (1.0)	Na_2CO_3 (1)	Neat	140 ºC	30	30	10:90
17	1 (1.0)	Cs_2CO_3 (1)	Neat	140 ºC	30	30	35:65
Temperature variation:							
18	1 (1.0)	KO^{t}Bu (1)	Neat	100 ºC	30	30	0:100
19	1 (1.0)	KO^{t}Bu (1)	Neat	80 ºC	30	30	30:70
Pressure variation:							
20	1 (1.0)	KO^{t}Bu (1)	Neat	100 ºC	3	30	0:100
21	1 (1.0)	KO^{t}Bu (1)	Neat	100 ºC	1	30	5:95
Loading of catalyst, base and time variation:							
22	1 (1.0)	KO^{t}Bu (1)	Neat	100 ºC	3	24	0:100
23	1 (1.0)	KO^{t}Bu (1)	Neat	100 ºC	3	18	20:80
24	1 (0.5)	KO^{t}Bu (1)	Neat	100 ºC	3	24	0:100
25	1 (0.5)	KO^{t}Bu (0.5)	Neat	100 ºC	3	24	0:100
26	1 (0.4)	KO^{t}Bu (0.5)	Neat	100 ºC	3	24	10:90
27	1 (0.5)	KO^{t}Bu (0.5)	Neat	100 ºC	3	24	30:70
28	2 (0.5)	KO^{t}Bu (0.5)	Neat	100 ºC	3	24	10:90
29	3 (0.5)	KO^{t}Bu (0.5)	Neat	100 ºC	3	24	30:70

[a]Reaction conditions: **2.1.2a** (1 mmol), **Cat.** (0.3 – 1.0 mol%), base (0.3 – 1.0 equiv), at 100 - 140 °C (bath temperature), H_2 pressure, 18 – 24h.

Next, it was decided to explore the scope of this protocol towards other 1,3-diaryl propenes. Gratifyingly, for all the cases, desired 1,3-diaryl propane (**2.2.3a** – **3i**) were obtained in a quantitative yield. Then, the synthesis of 1,3-diaryl propane directly from alcohol by sequential manner was examined. Therefore, after the deoxygenative coupling of alcohol, the crude mixture was subjected to hydrogenation without further purification. Delightfully, excellent yields were also obtained in this sequential strategy (**Scheme 2.7**, **B**).

2.3.4. Selective synthesis of alkanes:



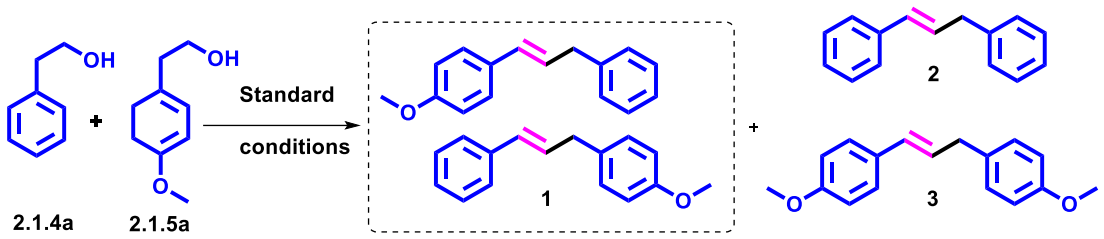
^{a}Standard reaction conditions: **Procedure A:** alkene **2.1.2** (1 mmol), **Cat. 1** (0.5 mol%), KO^{t}Bu (0.5 equiv) at 100 ºC (bath temperature), neat, 3 bar H_2, 24 h, isolated yield.
Procedure B: Step 1 includes alcohol **2.1.1** (2 mmol), NaOH (0.6 equiv), **Cat. 1** (0.5 mol%), 2 mL toluene, Ar, 140 °C (bath temperature) for 24 h. **Step 2** is performed without purification and similar to procedure A. ^{b}Overall yield of the isolated product for two reaction steps.

Scheme 2.7. Substrate scope for homo-coupled alkanes

Furthermore, the deoxygenative cross-coupling of 2-aryl ethanols (**2.1.1a**) with different primary alcohols was investigated (**Scheme 2.8**). Homo coupling side-reactions is the primary obstacle to this reaction. It is important to note that the ratio of two alcohol substrates was found critical for effectively obtaining the desired cross-coupled product. The yield of cross-coupling products increases when the stoichiometric ratio of **2.1.4a** and **2.1.5a** is changed from 1:1 to 4:1 (**Table 2.3**).

2.3.5. Optimization of the ratio of two alcohols for cross-coupling of 2-aryl ethanols:

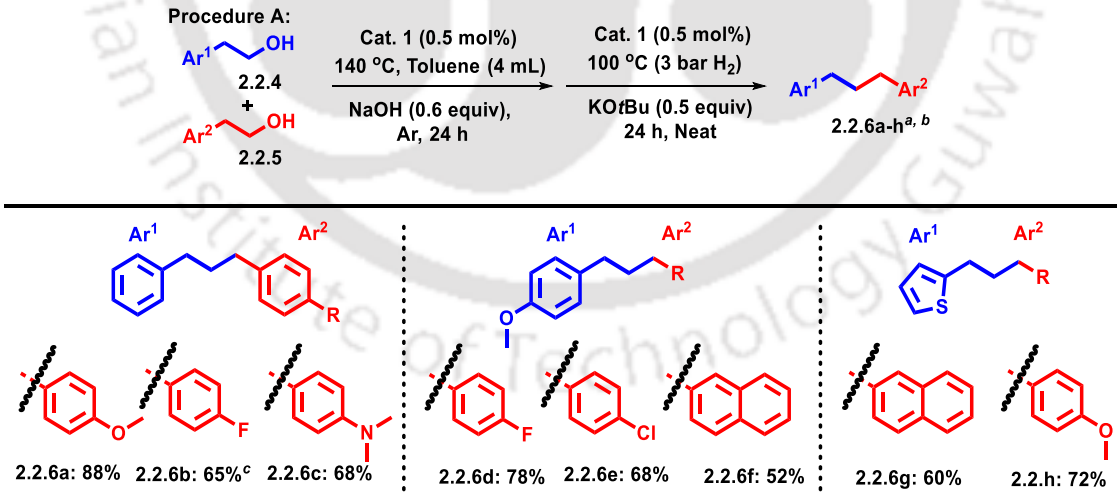
Table 2.3. Screening Table:



Entry	Ratio of 4a:5a	Yield of 1	Yield of 2	Yield of 3
1	**1:1**	62	18	20
2	**3:1**	78	36	8
3	**4:1**	85	44	N.D

A broad scope of 2-aryl ethanols was compatible under the optimal reaction conditions. 2-aryl ethanols containing electron-donating, electron-withdrawing, or heterocyclic groups resulted in moderate to good yield (**2.2.6a** – **6h**). A mixture of alkene products was first produced by the non-selective cross-aldol condensation of the two aldehyde intermediates formed by alcohol dehydrogenation. Nevertheless, hydrogenation of the mixture with **Cat. 1** produced only the hydrogenated alkane products **2.2.6** (**Scheme 2.8**).

2.3.6. Deoxygenative cross-coupling of various 2-arylethanols:

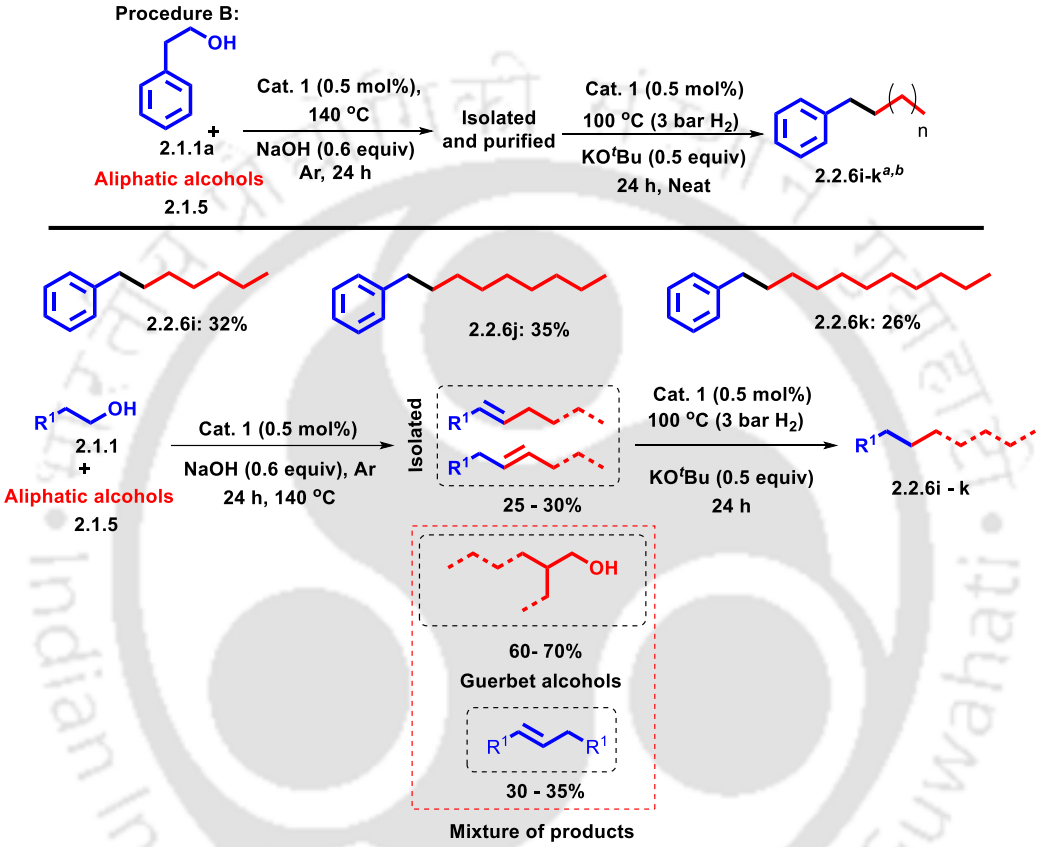


[a] Standard reaction conditions: **2.1.4** (4 mmol) and **2.1.5** (1 mmol) with NaOH (0.6 equiv), Cat. 1 (0.5 mol% w.r.t to total amount of alcohol), 4 mL toluene, Ar, 140 °C (bath temperature), 24 h. [b]The overall yield of the isolated product, [c] **2.1.4** (1 mmol) and **2.1.5** (4 mmol),

Scheme 2.8. Substrate Scope of Cross-Alkanes

This method was also extended to the cross-coupling reactions with more challenging long-chain aliphatic alcohols (**2.2.6i**, **2.2.6j,** and **2.2.6k**). However, the yields of crossed alkanes are moderate as long-chain aliphatic alcohols tend to form Guerbet alcohols, which are also considered valuable products (**Scheme 2.9**).[10]

2.3.7. Deoxygenative cross-coupling of various 2-aryl ethanols with primary alcohols:



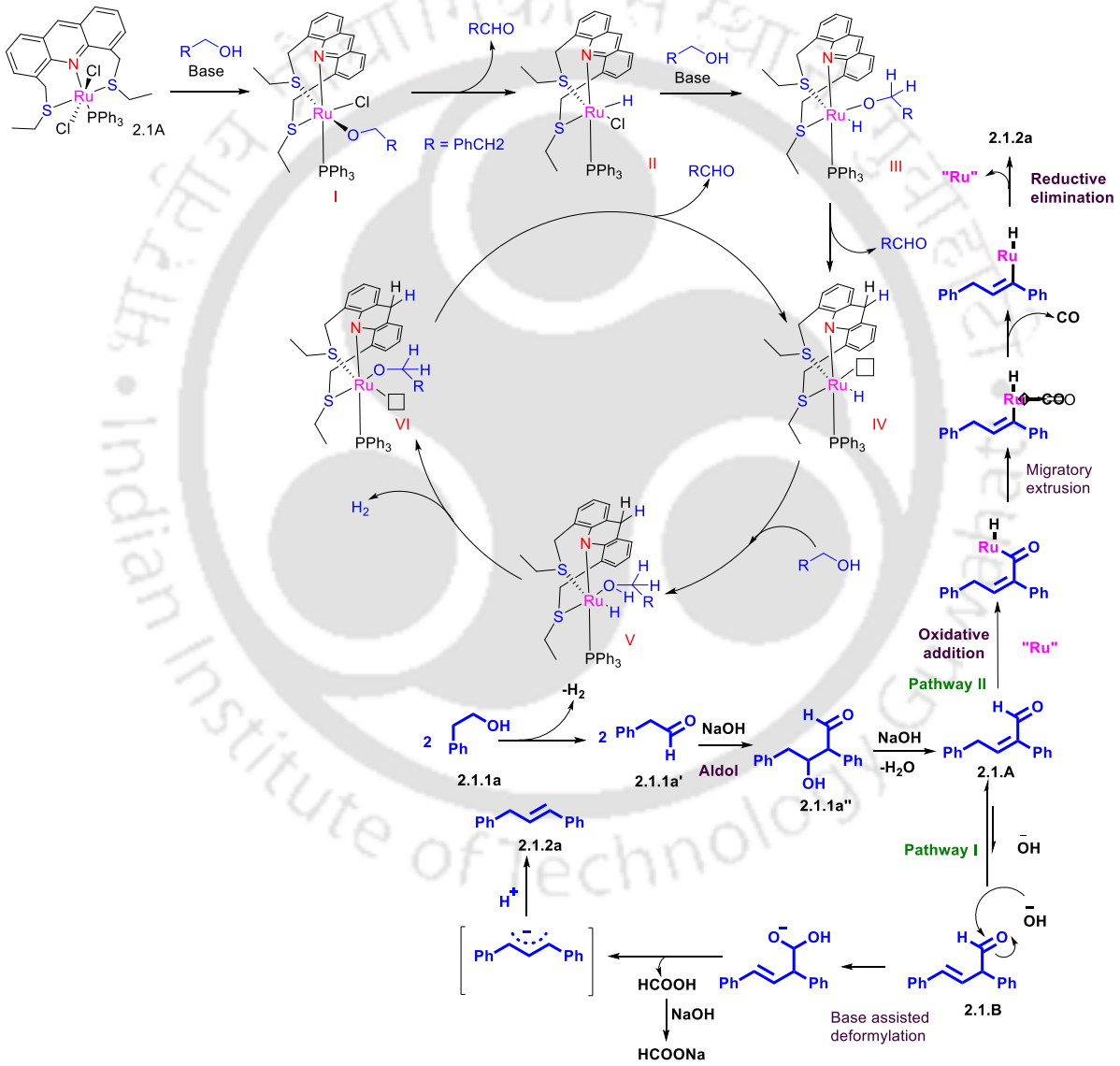
[a] Standard reaction conditions: **2.1.5** (4 mmol) and **2.1.1a** (1 mmol) with NaOH (0.6 equiv), **Cat. 1** (0.5 mol% w.r.t to total amount of alcohol), Ar, 140 °C (bath temperature), [b] In neat condition.

Scheme 2.9. Substrate Scope of Cross-Alkanes

2.4. Reaction mechanism for dehydrogenation:

For this deoxygenative synthesis of olefins, two possible mechanistic pathways are proposed (**Scheme 2.10**). Initially, Ru-catalyzed dehydrogenation of 2-phenyl ethanol furnishes 2-phenylacetaldehyde which can further undergo a base-mediated aldol reaction to form β-hydroxyaldehyde (**2.1.1a''**). Dehydration of *β*-hydroxyaldehyde under the reaction condition

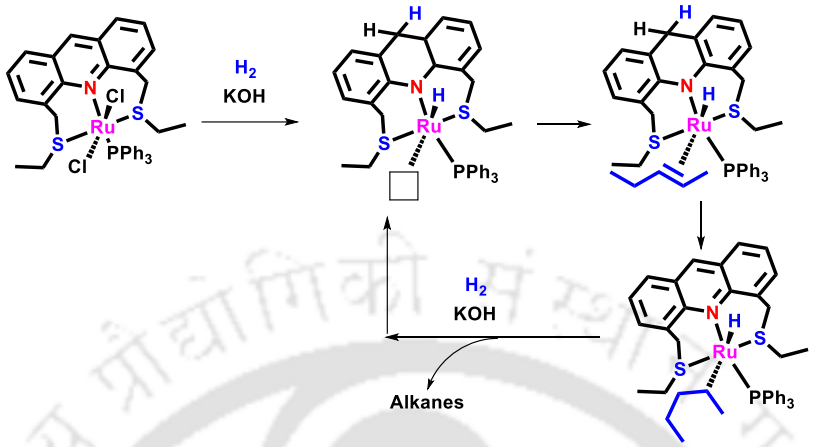
leads to the formation of *α,β*-unsaturated aldehyde (**2.1.A**). Under the reaction conditions, *α, β*-unsaturated aldehyde (**2.1.A**) is in equilibrium with the *β,γ*-unsaturated aldehyde (**2.1.B**). Nucleophilic attack by hydroxide ion on the carbonyl group of *β,γ*-unsaturated aldehyde and subsequent liberation of sodium formate generates the allyl anionic species that can be protonated to form the 1,3-diphenyl propane (**Pathway I**). Another possibility is the Ru-catalyzed decarbonylation and reductive elimination of *α,β*-unsaturated aldehyde (**1.1.A**) to form **2.1.2a** (**Pathway II**). In addition we have also proposed the catalytic cycle with the Ru catalyst in scheme **2.10A** based on previous literature studies.[6]



Scheme 2.10A. Plausible Mechanism

2.5 Reaction mechanism for hydrogenation:

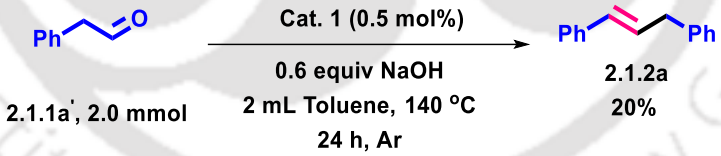
Bassed on previos literature study, a long range metal-ligand cooperation could be ascertained for H_2 activation (Scheme 2.10B).[6]



Scheme 2.10B. Plausible Mechanism

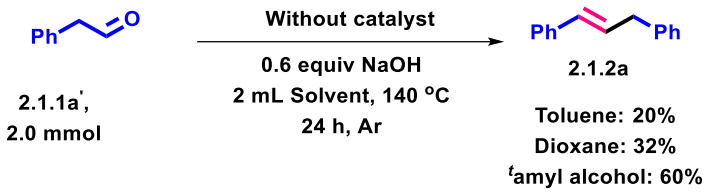
2.6. Mechanistic investigation:

To understand the plausible mechanistic pathway various control experiments were performed (**Scheme 2.10**). Initially, dehydrogenation of alcohol forms the aldehyde **2.1.1a′**. To shed light on the reactivity of **2.1.1a′** to form **2.1.2a**, first, 2-phenyl acetaldehyde was reacted under the standard conditions which furnish the desired 1,3 diphenyl propene, **2.1.2a** in 20% yield (**control experiment 1**).



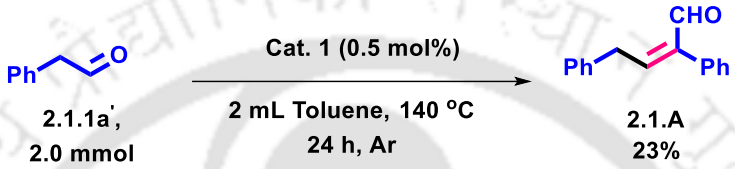
Scheme 2.10.1 Control experiment 1

Even in the absence of **cat. 1,** a similar yield of **2a** was isolated (**control experiment 2**) in toluene. The lower yield might be due to the initial high concentration of 2-phenyl acetaldehyde, which can lead to several side reactions[11] under the reaction conditions before converting to the desired 1,3-diphenyl propene. Low solubility of NaOH in toluene might be another important factor.[11] Thus, when the reaction was performed in ^{t}amyl alcohol, 60% of **2.1.2a** was formed (**control experiment 2**).



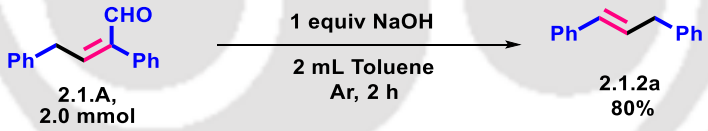
Scheme 2.10.2. Control experiment 2

The proposed intermediate aldehyde (*E*)-2,4-diphenylbut-3-enal (**2.1.A**) was not detected under the standard reaction conditions. However, in the absence of NaOH only **cat. 1** is capable of converting 2-phenyl acetaldehyde to **2.1.A** (**control experiment 3**).



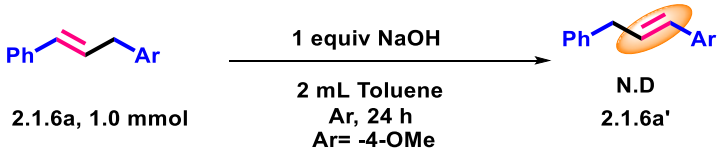
Scheme 2.10.3. Control experiment 3

This underpins the conversion of **2.1.A** to **2.1.2a** is very fast under basic conditions, which was further proved by reacting **2.1.A** in the presence of NaOH to afford **2.1.2a** in 80% yield within just 2 hours. (**control experiment 4**). This indicates that **2.1.A** is the key intermediate for this transformation.



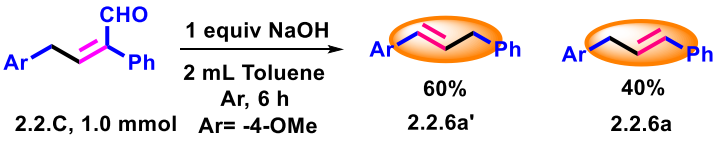
Scheme 2.10.4. Control experiment 4

Moreover, in the presence of a base, **2.1.6a** did not isomerize to **2.1.6a'** (**control experiment 5**), which indicates that the isomerization of alkenes under the reaction condition is not possible.



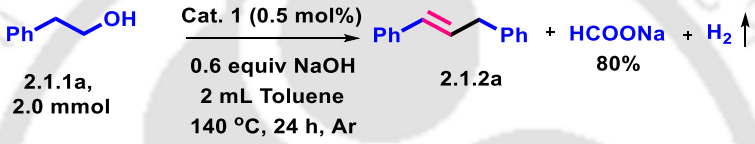
Scheme 2.10.5. Control experiment 5

Interestingly, when **2.2.C** was treated under similar conditions, a mixture of two isomers (**2.2.6a'** and **2.2.6a)** was isolated (**control experiment 6**). This suggests the formation of an allyl-anionic intermediate (**Pathway I**).

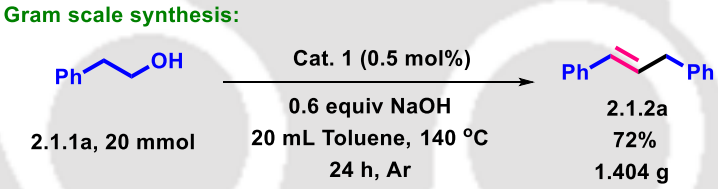


Scheme 2.10.6. Control experiment 6

Furthermore, the isolation of HCOONa (77%) under the reaction conditions confirms that the reaction follows pathway I (**control experiment 7**).



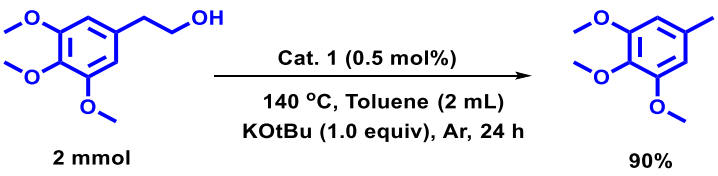
Scheme 2.10.7. Control experiment 7



Scheme 2.10.8. Control experiment 8

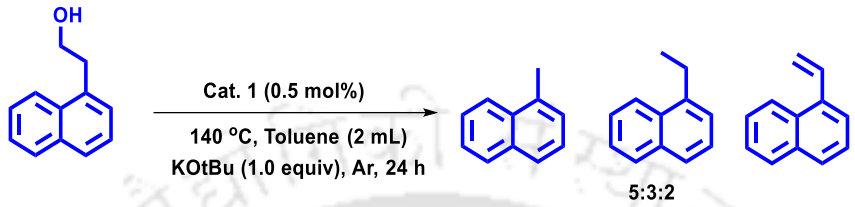
During our mechanistic investigation, it was found the base has a vital role in the progress of the reaction. Also, substrate-specific reactivity in the presence of different bases was detected (**Scheme 2.11**).

Case 1: When the reaction was performed with KO^{t}Bu in toluene with 2-(3,4,5-trimethoxyphenyl)ethan-1-ol, 1,2,3-trimethoxy-5-methylbenzene was obtained as the final product (**Scheme 2.11.1)**.



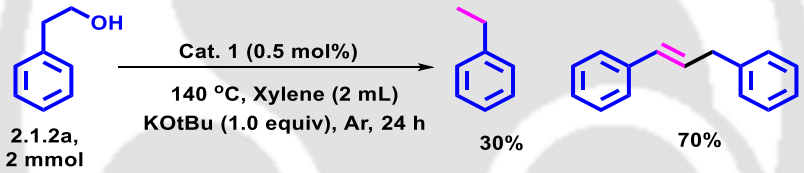
Scheme 2.11.1. Selective conversion to 1,2,3-trimethoxy-5-methylbenzene.

Case 2: When the reaction was performed with KO^{t}Bu in toluene with 2-(naphthalene-1-yl)ethan-1-ol, a mixture of 1-methylnaphthalene, 1-ethyl naphthalene, and 1-vinyl naphthalene was obtained in 5:3:2 manner (**Scheme 2.11.2)**.



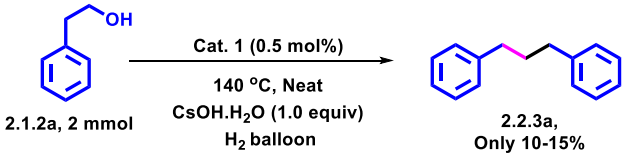
Scheme 2.11.2. The selective case related to 2-(naphthalene-1-yl)ethan-1-ol.

Case 3: When the reaction was performed with KO^{t}Bu in xylene, a mixture of product of our target product and styrene was obtained. (**Scheme 2.11.3**).



Scheme 2.11.3. Selective transformation of 2-phenyl ethanol.

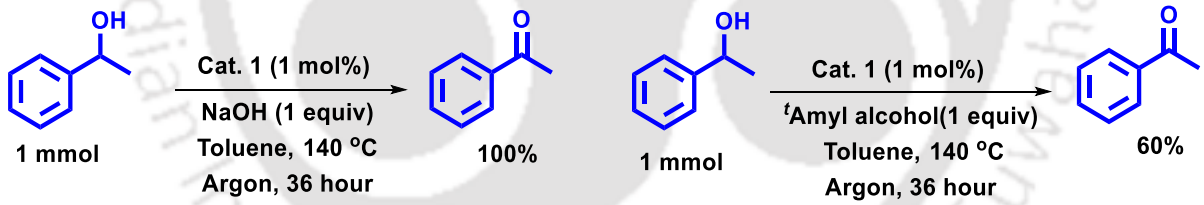
Case 4: To a Schlenk tube (10 mL), acridine-based Ru-SNS catalyst, **Cat. 1** (0.5 mol%, 7 mg), $CsOH.H_2O$ (1.0 equiv, 336 mg), 2-aryl ethanol (2 mmol) were added under hydrogen atmosphere. The reaction was conducted in neat condition at 140 °C for 24 h. After cooling to room temperature, EtOAc (5 mL) was added and the reaction mixture was passed through a small pad of celite filter and was transferred into another flask. The filtrate was then evaporated and the crude product was purified by column chromatography (typically petroleum ether as an eluent) using silica to afford a pure product (**Scheme 2.11.4**).



Scheme 2.11.4. Direct approach from alcohol to 1,3-diphenylpropane in presence of hydrogen

2.7. Kinetic study:

Thus, it was decided to study the reaction kinetics at various base loading. The optimum amount of the NaOH was found to be 0.6 equivalent to 2-phenyl ethanol. Lowering of base loading to 0.4 or 0.3 equivalent leads to a significant decrease in the rate of the reaction. However, when 0.8 or even 1.0 equiv base was used instead of the optimal base loading (0.6 equiv), there was no significant change in reaction rate. To check the optimal catalyst loading in the reaction, the initial rate of the reaction to various catalyst loading was studied. A sharp increase in the initial rate of the reaction was observed when catalyst loading was increased from 0.25 mol% to 0.5 mol%. However, a further increase in loading has no positive impact on the initial reaction rate. So, the catalyst loading of 0.5 mol% is the ideal loading. Next, the rate of the reaction to various solvents was explored. From the mechanistic studies (**control experiment 3**), it was found that ^{t}amyl alcohol is a good solvent for the conversion of phenylacetaldehyde **2.1.1a'** to compound **2.1.2a** in high yield (60%). So, the reaction profile diagram to solvent was explored, which revealed that the reaction is faster in toluene compared to ^{t}amyl alcohol or dioxane (**Scheme 2.12**).



Scheme 2.12. Kinetic profile at different solvent.

This suggests that, while the formation of product **2.1.2a** from phenylacetaldehyde is faster in ^{t}amyl alcohol, the alcohol dehydrogenation step might be slower in ^{t}amyl alcohol compared to toluene (**Scheme 2.12**). The temperature-dependent product formation was also checked. At low temperatures like 110 ºC or 125 ºC, the progress of the reaction was found to be slow. It is also necessary to mention, that other than the product and reactant we failed to detect any intermediate at any hour of the reaction (**Figure 2.3**). This also suggests that the dehydrogenation step is significantly slower compared to the subsequent aldol condensation and deformylation step.

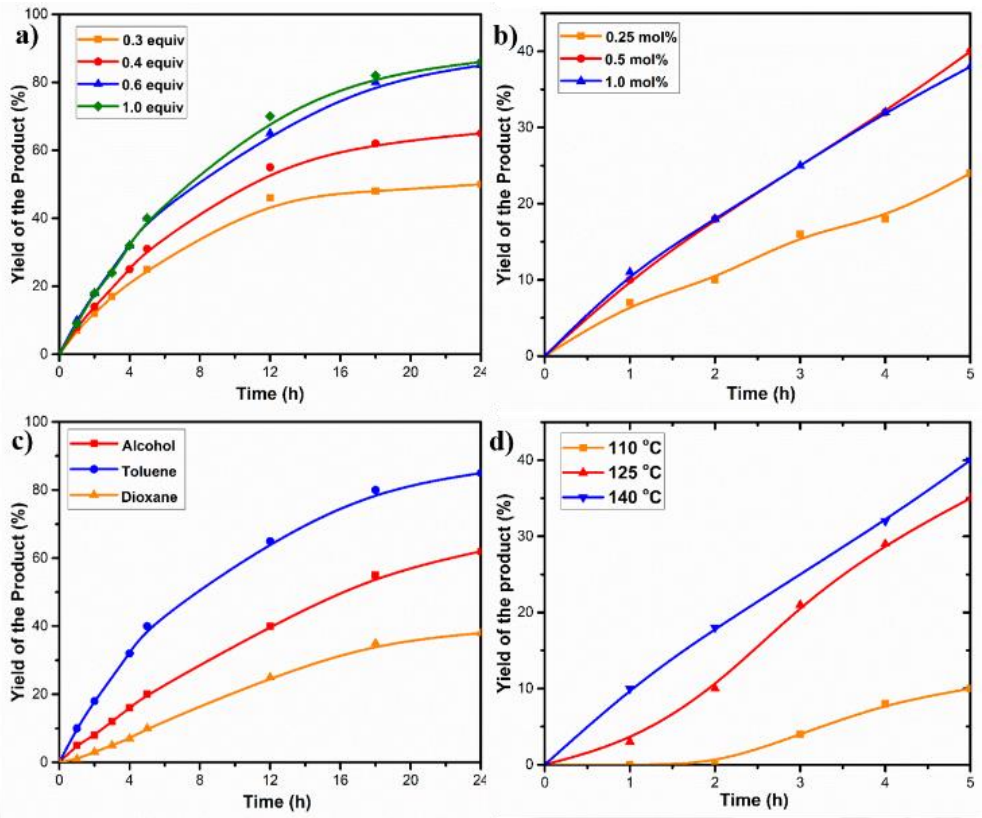


Figure 2.2. Conversion-time profile of the homocoupling of 2-phenylethanol with respect to (a) base (NaOH) loading, (b) catalyst loading, (c) solvent and (d) bath temperature.

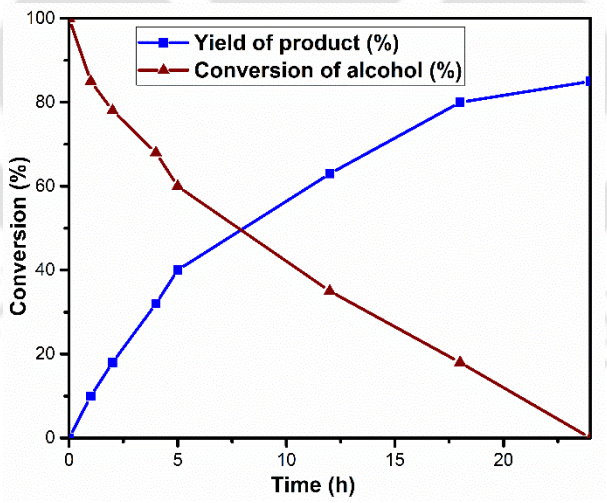
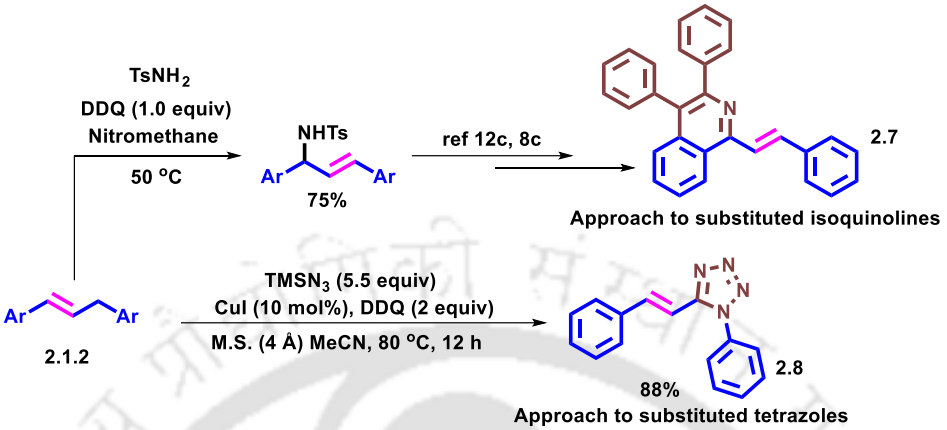


Figure 2.3: Kinetic profile of the reaction with respect to alcohol (**2.1.1a**) and product (**2.1.2a**)

2.8. Post-synthetic modification:

To demonstrate the utility of 1,3-diaryl propenes, strategies that can easily convert them into synthetically important heterocycles such as isoquinolines and tetrazoles were illustrated. (**Scheme 2.14**).



Scheme 2.14: Derivatization of Alkenes

2.9. Conclusion:

In conclusion, the coupling of primary alcohols to synthesize selectively alkenes and alkanes is achieved by a single Ru-catalyst. The protocol is applicable for both homo and cross-coupling reactions of primary alcohols and is highly selective. Mechanistic studies reveal that deformylation of intermediate *α,β*-unsaturated aldehyde with simultaneous formation of sodium formate is an important step to produce olefin. This selective dehydrogenation and hydrogenation reaction with a single catalyst not only proves the versatility and tunability of the catalyst but also elucidates future applications in upgrading of bio alcohols to chemicals.

2.10. Experimental Section:

2.10.1. General Information:

Unless otherwise mentioned, all chemicals were purchased from common commercial sources and used as received. $RuCl_2(PPh_3)_3$ was purchased from Sigma-Aldrich. All solvents were dried by standard procedure.[13] Solvents such as toluene were pre-dried using CaH_2 over Na with a benzophenone indicator. The catalyst preparation was carried out under an argon atmosphere with freshly distilled dry THF or dichloromethane. All catalytic reactions were carried out under an argon atmosphere using dry glassware and standard syringe/septa

techniques. Bruker Avance III 600, 500, and 400 spectrometers were used to record ^{1}H, ^{13}C NMR, and ^{31}P NMR, respectively. Chemical shifts (δ) are reported in ppm downfield from tetramethylsilane; spin-spin coupling constants (*J*) are expressed in Hz and other data are reported as follows: s = singlet, d = doublet, t = triplet, m = multiplet, q = quartet, and br s = broad singlet. Column chromatography was done with SRL silica gel 100-200 mesh. Analytical thin layer chromatography (TLC) was carried out on silica gel plates (silica gel 60 F254), that were visualized by exposure to ultraviolet light and an aqueous solution of *p*-anisaldehyde.

2.10.2. Experimental Procedure:

2.10.2a. General procedure for deoxygenative homo-coupling of different aryl ethanols:

To a round bottom flask (10 mL) fitted with a condenser, 2-aryl ethanol, **1** (2 mmol), acridine-based Ru-SNS[9a] catalyst, **Cat. 1** (0.5 mol%, 7 mg), NaOH (0.6 equiv, 48 mg), and toluene (2.0 mL) were added under argon atmosphere. The solution was heated at 140 °C for 24 h. After cooling to room temperature, EtOAc (5 mL) was added and the reaction mixture was passed through a small pad of celite filter and was transferred into another flask. The filtrate was then evaporated and the crude product was purified by column chromatography (typically petroleum ether as an eluent) using silica to afford a pure product (**Scheme 2.6**).

2.10.2b. General procedure for hydrogenation of olefins to alkane products:

Procedure A: The purified homo-coupled alkene, **2** (1.0 mmol), Cat. **1** (0.5 mol%), and KO^{t}Bu (0.5 equiv) were added sequentially to a 5 mL Teflon vial, inserted within a Parr reactor system and was stirred for 24 hours at 100 °C under 3 bar hydrogen pressure. After cooling to room temperature and gas releasing, the resulting solution was diluted by 5 mL of EtOAc. The product can be easily extracted just via celite filtration without any further purification (**Scheme 2.7A**).

Procedure B: Sequential conversion of alcohol to alkane. To a round bottom flask (10 mL) fitted with a condenser, 2-aryl ethanol, **2.1.1a** (2 mmol), acridine-based Ru-SNS catalyst, **Cat. 1** (0.5 mol%, 7 mg), NaOH (0.6 equiv, 48 mg) and toluene (2.0 mL) were added under argon atmosphere. The solution was heated at 140 °C for 24 h. After cooling to room temperature,

EtOAc (5 mL) was added and the reaction mixture was passed through a small pad of celite filter and was transferred into another flask. The filtrate was then evaporated and the crude mixture was transferred to the Parr reactor without further purification. The crude mixture, **Cat. 1** (0.5 mol%) and KO^{t}Bu (0.5 equiv) were added sequentially to a 5 mL Teflon vial, inserted within a Parr reactor system, and was stirred for 24 hours at 100 ºC under 2 - 3 bar hydrogen pressure. After cooling to room temperature and gas releasing, the resulting solution was diluted by 5 mL of EtOAc. The filtrate was then evaporated and the crude product was purified by column chromatography (typically petroleum ether as an eluent) using silica to afford a pure product (**Scheme 2.7B**).

2.10.2c. General procedure for deoxygenative cross-coupling of different aryl ethanols:

Under the protection of argon, 2-aryl ethanols, **2.1.4** (1.00 mmol), primary alcohols, **2.1.5** (4.0 mmol), **Cat. 1** (19 mg, 0.5 mol%), NaOH (120 mg, 0.6 equiv) and toluene (4.0 mL) were added sequentially to a 10 mL round bottom flask fitted with a condenser. The reaction was stirred for 24 hours at reflux temperature. After cooling to room temperature, the resulting solution was diluted by 5 mL of EtOAc. The mixed olefin products were obtained by flash column chromatography. Under the protection of argon, the mixed olefins, **Cat. 1** (0.5 mol%) and KO^{t}Bu (0.5 equiv) were added sequentially to a 5 mL Teflon vial, inserted within a Parr reactor system and were stirred for 24 hours at 100 ºC under 3 bar hydrogen pressure. After cooling to room temperature and gas releasing, the resulting solution was diluted by 5 mL of EtOAc. The product can be easily extracted just via celite filtration and later the reaction mixture was charged into column chromatography to obtain the desired alkane (**Scheme 2.8**).

2.10.2d. General procedure for deoxygenative cross-coupling of aryl ethanol and aliphatic alcohols:

Under the protection of argon, 2-aryl ethanols, **1** (1.00 mmol), aliphatic alcohols, **5** (4.0 mmol), complex Ru-SNS catalyst, **Cat. 1** (19 mg, 0.5 mol%), NaOH (120 mg, 0.6 equiv) were added sequentially to a 10 mL Schlenk tube. The reaction was stirred for 24 hours at 140 ºC. After cooling to room temperature, the resulting solution was diluted by 5 mL of EtOAc. The reaction mixture was extracted just via celite filtration and it was charged into column chromatography to obtain the desired alkene. Later, the desired alkene, Cat. **1** (0.5 mol%) and KO^{t}Bu (0.5 equiv) were sequentially charged to a 5 mL Teflon vial, inserted within a Parr reactor system, and stirred for 24 hours at 100 ºC under 3 bar hydrogen pressure. After cooling to room temperature

and gas releasing, the resulting solution was diluted by 5 mL of EtOAc. The product can be easily extracted just via celite filtration (**Scheme 2.9**).

2.10.3. Mechanistic Investigation:

Control Experiment 1:

To a round bottom flask (10 mL) fitted with a condenser, acridine-based Ru-SNS catalyst, **Cat. 1** (0.5 mol%, 7 mg), NaOH (0.6 equiv, 48 mg), phenylacetaldehyde (2 mmol) and toluene (2.0 mL) were added under argon atmosphere. The solution was heated at 140 °C for 24 h. After cooling to room temperature, EtOAc (5 mL) was added and the reaction mixture was passed through a small pad of celite filter and was transferred into another flask. The filtrate was then evaporated and the NMR of the crude mixture was recorded using CH_3CN as an external standard (**Scheme 2.10.1**).

Control Experiment 2a:

To a round bottom flask (10 mL) fitted with a condenser, NaOH (0.6 equiv, 48 mg), phenylacetaldehyde (2.0 mmol), and toluene (2.0 mL) were added under an argon atmosphere. The solution was heated at 140 °C for 24 h. After cooling to room temperature, EtOAc (5 mL) was added and the reaction mixture was passed through a small pad of celite filter and was transferred into another flask. The filtrate was then evaporated and the NMR of the crude mixture was recorded using CH_3CN as an external standard (**Scheme 2.10.2**).

Control Experiment 2b:

To a round bottom flask (10 mL) fitted with a condenser, acridine-based Ru-SNS catalyst, **Cat. 1** (0.5 mol%, 7 mg), NaOH (0.6 equiv, 48 mg), phenylacetaldehyde (2 mmol) and ^{t}amyl alcohol (2.0 mL) were added under argon atmosphere. The solution was heated at 140 °C for 24 h. After cooling to room temperature, EtOAc (5 mL) was added and the reaction mixture was passed through a small pad of celite filter and was transferred into another flask. The filtrate was then evaporated and the NMR of the crude mixture was recorded using CH_3CN as an external standard (**Scheme 2.10.2**).

Control Experiment 2c:

To a round bottom flask (10 mL) fitted with a condenser, acridine-based Ru-SNS catalyst, **Cat. 1** (0.5 mol%, 7 mg), NaOH (0.6 equiv, 48 mg), phenylacetaldehyde (2 mmol) and dioxane (2.0

mL) were added under argon atmosphere. The solution was heated at 140 °C for 24 h. After cooling to room temperature, EtOAc (5 mL) was added and the reaction mixture was passed through a small pad of celite filter and was transferred into another flask. The filtrate was then evaporated and the NMR of the crude mixture was recorded using CH_3CN as an external standard (**Scheme 2.10.2**).

Control Experiment 3:

To a round bottom flask (10 mL) fitted with a condenser, acridine-based Ru-SNS catalyst, **Cat. 1** (0.5 mol%, 7 mg), phenylacetaldehyde (2 mmol), and toluene (2.0 mL) were added under argon atmosphere. The solution was heated at 140 °C for 24 h. After cooling to room temperature, EtOAc (5 mL) was added and the reaction mixture was passed through a small pad of celite filter and was transferred into another flask. The filtrate was then evaporated and the NMR of the crude mixture was recorded using CH_3CN as an external standard (**Scheme 2.10.3**).

Control Experiment 4:

To a round bottom flask (10 mL) fitted with a condenser, *(Z)*-2,4-diphenylbut-2-enal (1.0 mmol), NaOH (1.0 mmol), and toluene (2.0 mL) were added under argon atmosphere. The solution was heated at 140 °C for 2 h. After cooling to room temperature, EtOAc (5 mL) was added and the reaction mixture was passed through a small pad of celite filter and was transferred into another flask. The filtrate was then evaporated and the NMR of the crude mixture was recorded using CH_3CN as an external standard (**Scheme 2.10.4**).

Control Experiment 5:

Under the protection of argon, 1-cinnamyl-4-methoxybenzene, **2.1.6a** (1.0 mmol), toluene (2.0 mL), **Cat. 1** (0.5 mol%), NaOH (1.0 mmol) was added to a round bottom flask (10 mL) fitted with a condenser. The solution was heated at 140 °C for 24 h. After cooling to room temperature, EtOAc (5 mL) was added and the reaction mixture was passed through a small pad of celite filter and was transferred into another flask. The filtrate was then evaporated and the NMR of the crude mixture was recorded (**Scheme 2.10.5**).

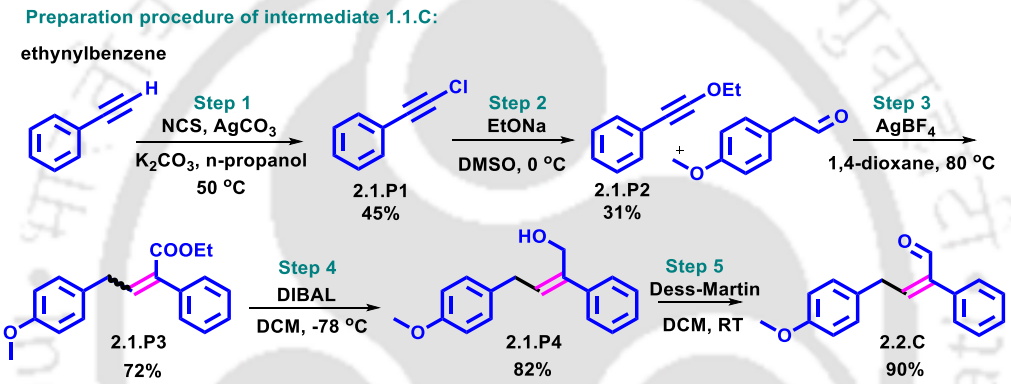
Preparation procedure 2.1.6a.

A mixture of cinnamyl alcohol (0.30 mmol), (4-methoxyphenyl)boronic acid (0.36 mmol), $Pd(PPh_3)_4$ (0.015 mmol), and dry dichloromethane (1 mL) was heated at 80 °C in a sealed tube

under argon atmosphere. After being stirred at the same temperature for 8 h, the reaction mixture was evaporated and purified by column chromatography to give the product.[14]

Control Experiment 6:

To a round bottom flask (10 mL) fitted with a condenser, **2.2.C**, (*E*)-4-(4-methoxyphenyl)-2-phenylbut-3-enal (1.0 mmol), NaOH (1.0 mmol) and toluene (2.0 mL) were added under argon atmosphere. The solution was heated at 140 °C for 3 h. After cooling to room temperature, EtOAc (5 mL) was added and the reaction mixture was passed through a small pad of celite filter and was transferred into another flask. The filtrate was then evaporated and the NMR of the crude mixture was recorded using CH_3CN as an external standard (**Scheme 2.11.6**).



Scheme 2.15. Step wise synthesis of **2.2.C.**

Preparation procedure of 2.2.C:

Step 1: K_2CO_3 (523 mg, 3.79 mmol), NCS (2.02 g, 15.15 mmol), Ag_2CO_3 (209 mg, 0.758 mmol), and ethynylbenzene (775 g, 7.575 mmol) were added into a dry schlenk flask. The reaction flask was evacuated and backfilled with argon (three cycles). Then 20 mL of *n*-propanol was added to the reaction system, and the reaction mixture was stirred at 50 ºC overnight. After that, the mixture was cooled to room temperature, and brine was added to the mixture at 0 ºC. The resulting mixture was extracted by ethyl ether, and the combined organic phase was washed with water, then dried over sodium sulfate. The resulting mixture was kept in a beaker for 2-3 days for slow evaporation as the resulting compound is highly volatile. Later, the resulting compound **2.1.P1** was used for step 2, without further purification (464 mg, 3.40 mmol, 45%). [5b]

Step 2: EtONa (1360 mg, 20 mmol) was added into a dry schlenk flask. The reaction flask was evacuated and backfilled with argon (three cycles). After that, a solution of **2.1.P1** (1.36 g, 10 mmol) in 5 mL of dry DMSO was added dropwise at 0 °C and the reaction was conducted at 0 ºC. The progress of the reaction was monitored by TLC. Around 1 hour later, water was added at 0 °C to quench the reaction. The mixture was then extracted with ether (3 × 25 mL) and the combined organic layer was dried over MgSO4, filtered, and concentrated in a vacuum. The residue was purified by flash chromatography on silica gel to afford the product (452 mg, 2.37 mmol, 31%)[14]

Step 3: 2-(4-methoxyphenyl)acetaldehyde (132 mg, 1.1 mmol), $AgBF_4$ (21 mg, 0.11 mmol), **2.1.P2** (192 mg, 1.32 mmol) and 4 mL of 1,4-dioxane was added into a sealed tube. After stirring at 80 ºC for 2 h, the reaction mixture was quenched with water, extracted with EtOAc, washed with brine, dried over anhydrous Na_2SO_4, and concentrated. Column chromatography on silica gel gave the product (268 mg, 0.9 mmol, 82%) as mixed isomers, which can be isolated as single isomers after reduction by DIBAL.[16]

Step 4: 2.1.P3 (268 mg, 0.9 mmol) was dissolved in 5 mL of DCM in a dry schlenk tube. The reaction system was cooled to -78 ºC and then DIBAL (1 mmol, 1.5 M in toluene, 0.66 mL) was added dropwise to the solution. The reaction mixture was maintained at -78 ºC for 1.5 h. After that it was allowed to warm to room temperature and 10 mL water was added to quench the reaction. The reaction mixture was extracted with DCM, washed with brine, dried over anhydrous Na_2SO_4, and concentrated. Column chromatography on silica gel gave the product **2.1.P4**[5b] (187 mg, 0.74 mmol, 82%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.39 (t, *J* = 7.6 Hz, 2H), 7.32 (d, *J* = 7.3 Hz, 1H), 7.28 – 7.26 (m, 2H), 7.05 (d, *J* = 8.5 Hz, 2H), 6.82 (d, *J* = 8.6 Hz, 2H), 5.89 (t, *J* = 7.5 Hz, 1H), 4.36 (d, *J* = 4.4 Hz, 2H), 3.78 (s, 3H), 3.29 (d, *J* = 7.5 Hz, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 157.9, 140.9, 138.1, 132.8, 129.2, 128.7, 128.5, 127.4, 127.3, 113.9, 68.0, 55.3, 33.8.

Step 5: Dess-Martin oxidant (220 mg, 0.52 mmol) was added to a solution of **2.1.P4** (170 mg, 0.5 mmol) in DCM (5 mL) at 0 ºC. The reaction mixture was stirred at 0ºC for 30 minutes and at room temperature for 1.5 hours, the reaction mixture was quenched with water. Then the reaction mixture was washed with sodium thiosulfate 10% in water (25 mL) and sodium hydroxide 1M (25 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The title compound, *(Z)*-4-(4-methoxyphenyl)-2-phenylbut-2-enal, **2.2.C** was extracted with

DCM, obtained in quantitative yield and can be used in the next step without further purification (114 mg, 0.45 mmol, 90%).[5b] ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.64 (s, 1H), 7.43 (t, *J* = 7.3 Hz, 1H)), 7.38, d, J = 7.2 Hz, 1H), 7.22 (7.22, d, *J* = 7.1 Hz, 2H), 7.07 (d, *J* = 8.5 Hz, 2H), 6.87 – 6.85 (m, 2H), 6.82 (d, *J* = 7.6 Hz, 1H), 3.79 (s, 3H), 3.63 (d, *J* = 7.6 Hz, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 193.6, 158.5, 153.9, 143.8, 132.3, 130.0, 129.5, 129.5, 128.4, 128.2, 114.3, 55.3, 35.0.

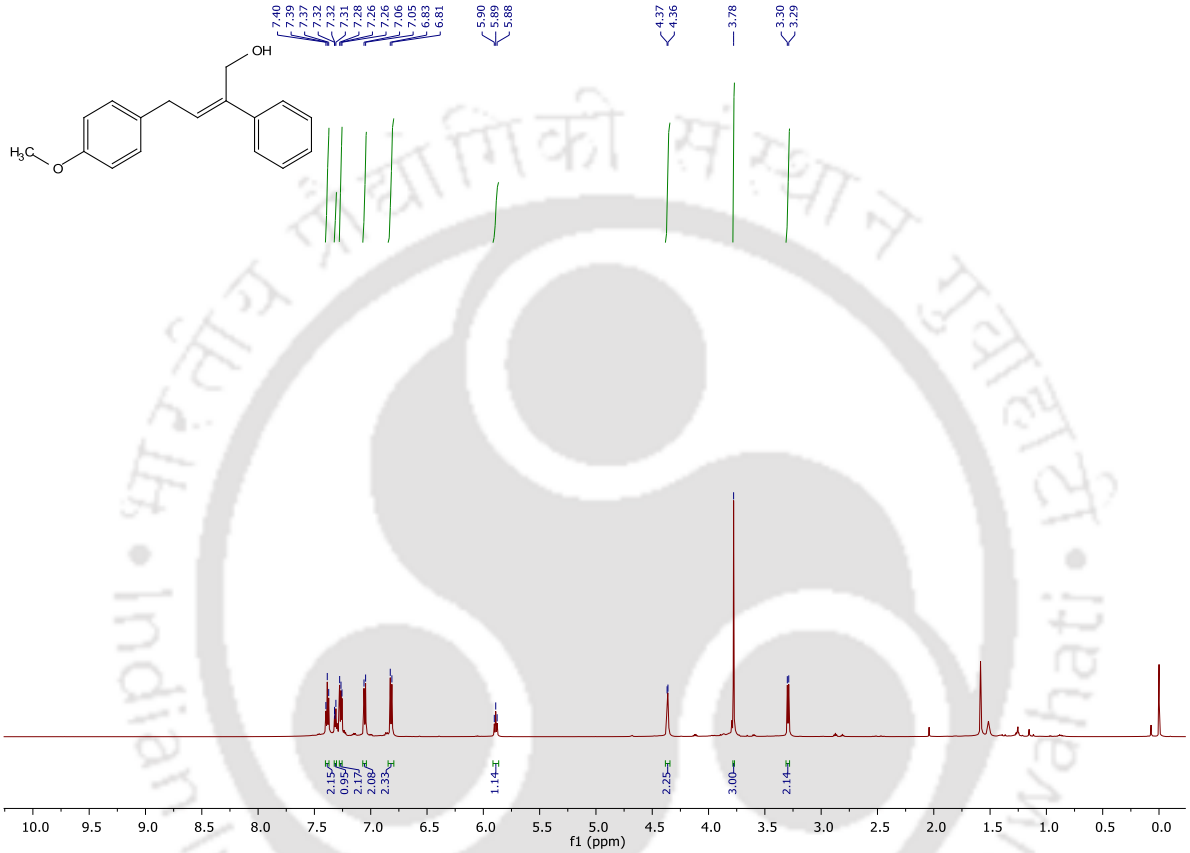


Figure 2.3: ^{1}H NMR (600 MHz) spectra of compound **2.1.P4** in $CDCl_3$

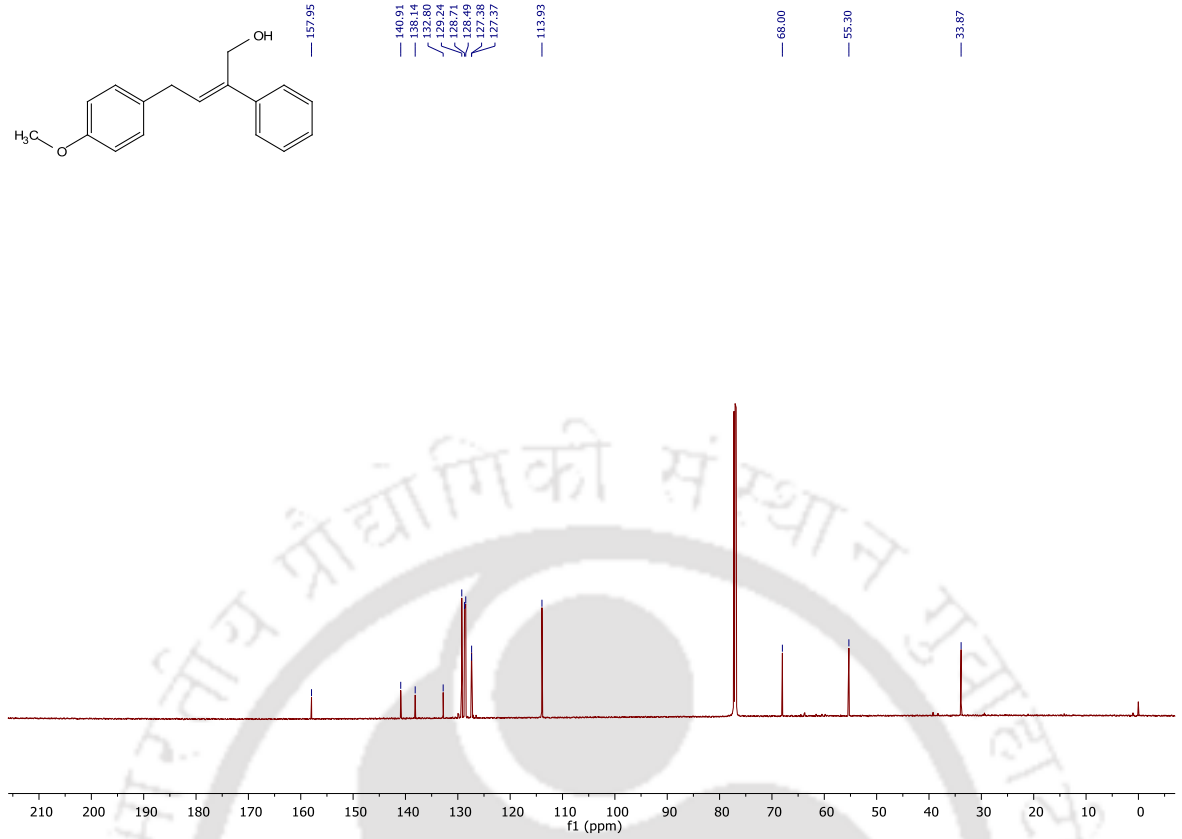


Figure 2.4: $^{13}C\{^{1}H\}$ NMR (150 MHz) spectra of compound **2.1.P4** in $CDCl_3$

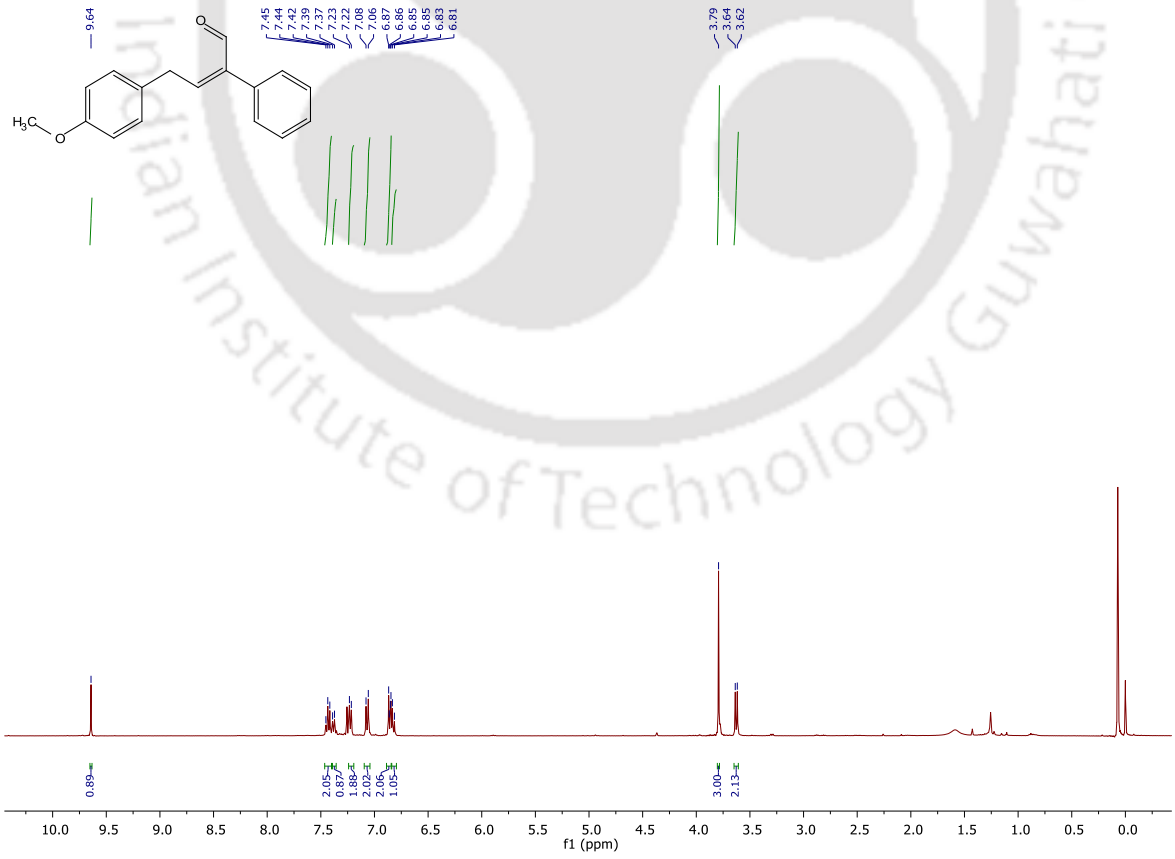


Figure 2.5: ^{1}H NMR (400 MHz) spectra of compound **2.1.C** in $CDCl_3$

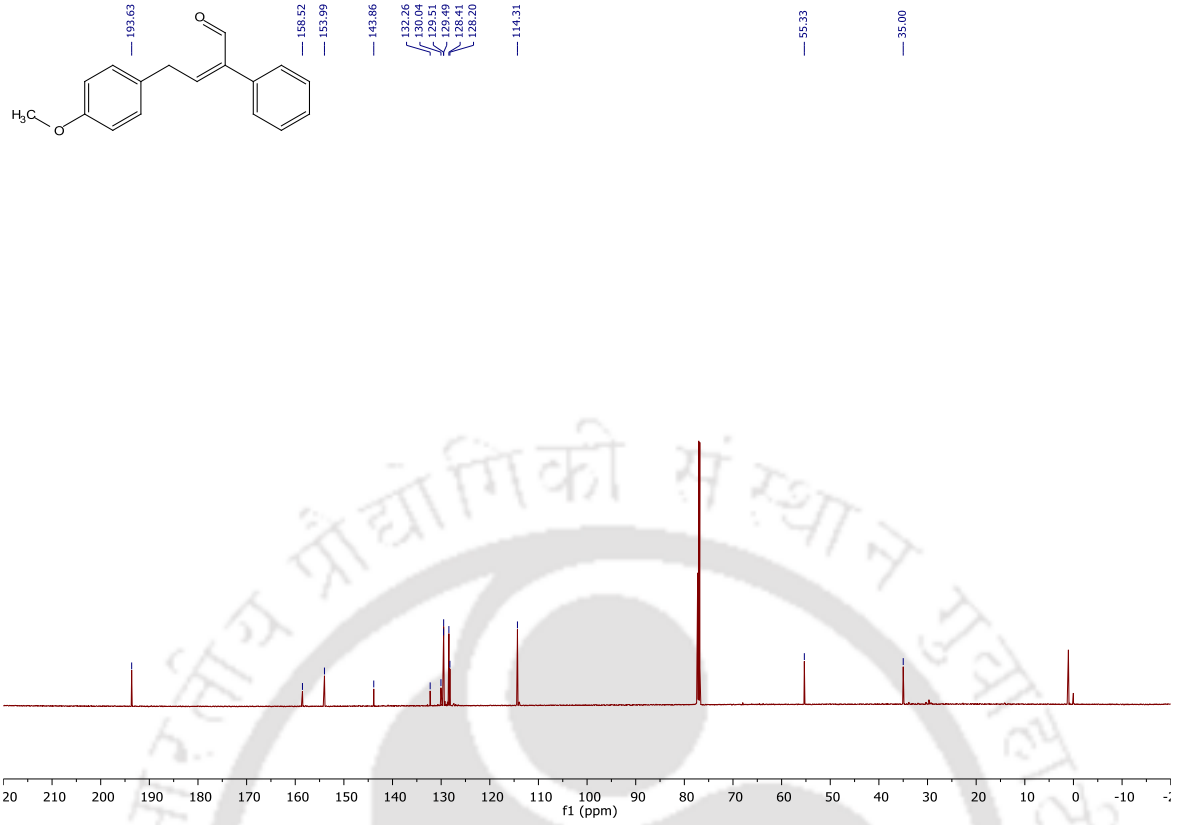


Figure 2.6: $^{13}C\{^{1}H\}$ NMR (150 MHz) spectra of compound **2.1.C** in $CDCl_3$

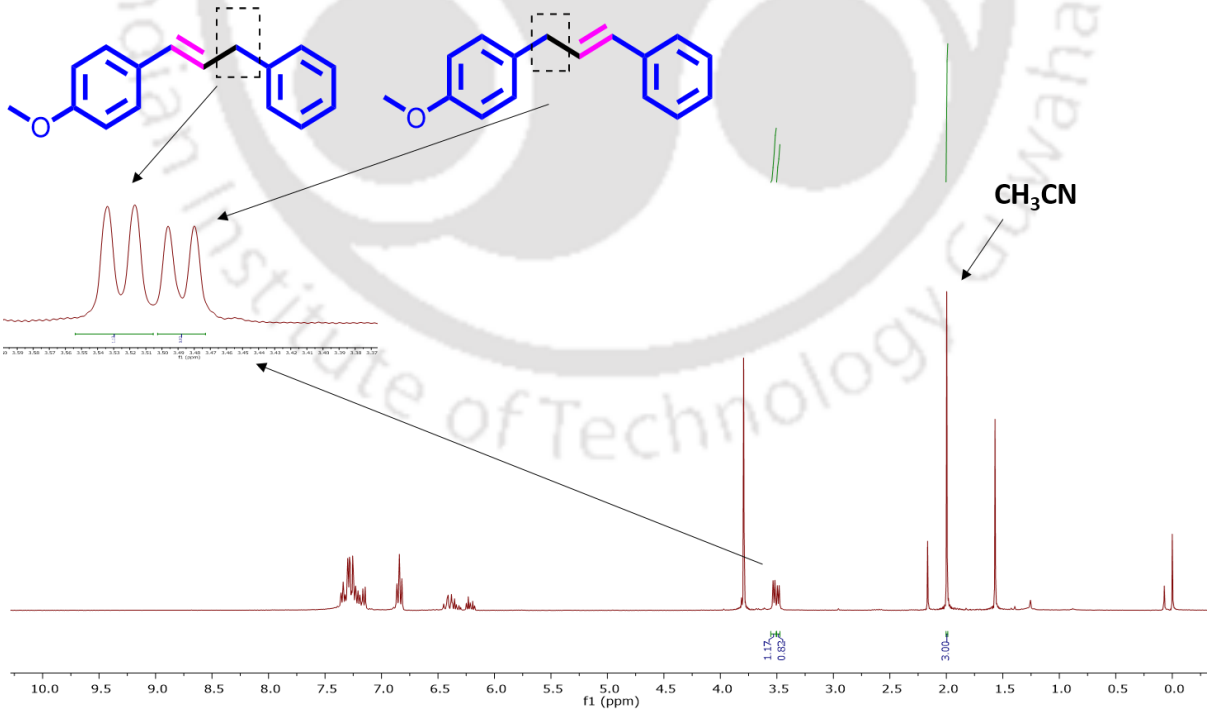


Figure 2.7: Mixture of alkenes.

Control Experiment 7:

Under the protection of argon, 2-aryl ethanol, **1** (2.0 mmol), Cat. **1** (0.5 mol%), NaOH (0.6 equiv), and toluene (2.0 mL) were added sequentially to a 10 mL round bottom flask fitted with a condenser (**Scheme 2.11.7**). The reaction was stirred for 24 hours at reflux temperature. After cooling to room temperature, the resulting solution was diluted by 5 mL of EtOAc. The mixed olefin products were obtained by flash column chromatography. After the reaction, the resulting reaction mixture was diluted by 5 mL of CH_2Cl_2 and 5 mL of water. Then the aqueous phase was separated and subjected to NMR analysis (D_2O as solvent) using DMSO (1 mmol) as the external standard. It was found that HCOONa was produced an 80% yield (**Figure 2.8**).

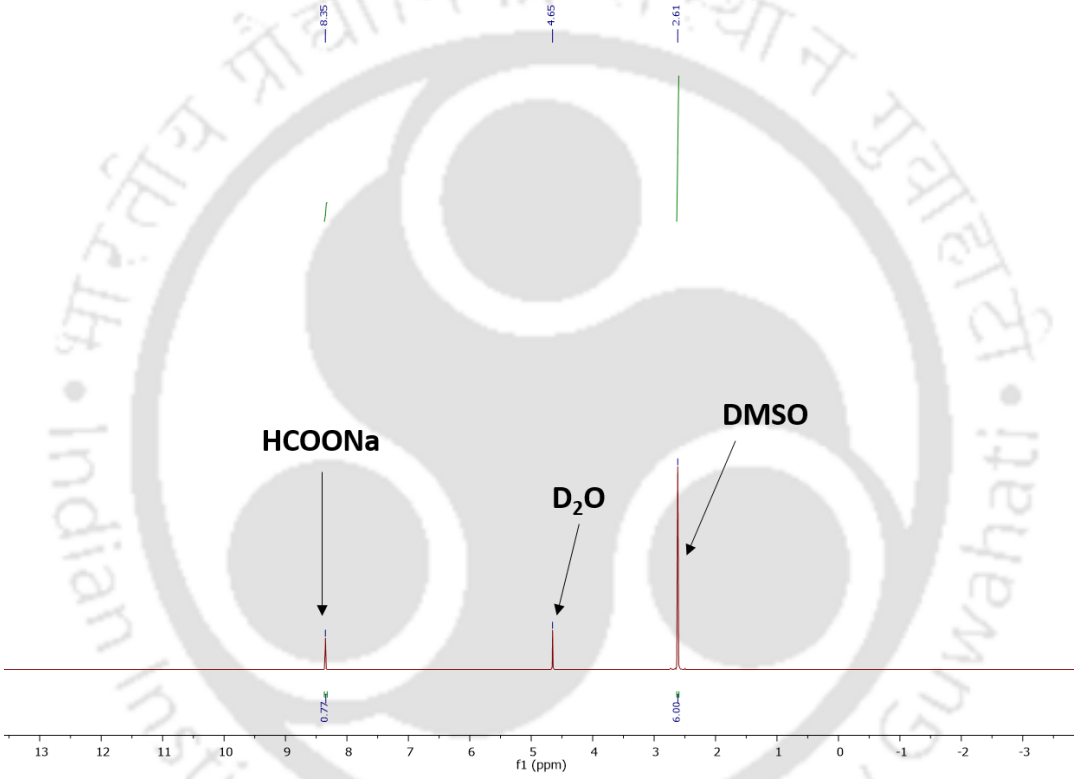


Figure 2.8: Aqueous phase NMR analysis

2.9.4. Gram Scale Synthesis:

To a round bottom flask (50 mL) fitted with a condenser, acridine-based Ru-SNS catalyst, Cat. **1** (0.5 mol%, 7 mg), NaOH (0.6 equiv, 480 mg), 2-aryl ethanol, **1a** (20 mmol) and toluene (20 mL) were added under argon atmosphere. The solution was heated at 140 °C for 24 h. After cooling to room temperature, EtOAc (50 mL) was added and the reaction mixture was passed through a small pad of celite filter and was transferred into another flask. The filtrate was then

evaporated and the crude product was purified by column chromatography (typically petroleum ether as an eluent) using silica to afford a pure product. The obtained yield was 72% (1.404 g).

2.9.5. Kinetic Study:

2.9.5a. Rate of the reaction in different solvents:

To a round bottom flask (10 mL) fitted with a condenser, acridine-based Ru-SNS catalyst, Cat. **1** (0.5 mol%, 7 mg), NaOH (1.0 equiv, 40 mg), 1-phenyl ethanol, **1a** (1 mmol) and toluene (1.0 mL) were added under argon atmosphere. The solution was heated at 140 °C for 36 h. After cooling to room temperature, EtOAc (5 mL) was added and the reaction mixture was passed through a small pad of celite filter and was transferred into another flask. The filtrate was then evaporated and the NMR of the crude mixture was recorded using CH_3CN as an external standard. It proves that the initial rate of the reaction is faster in toluene compared to ^{t}amyl alcohol (**Scheme 2.12**).

2.9.5b. Reaction with respect to various amount of base loading:

Eight different reactions were set up under the standard reaction condition for each specific loading of base and the reaction mixtures were analyzed by ^{1}H NMR after 1h, 2h, 3h, 4h, 5h, 1 2h, 18h, and 24h respectively using CH_3CN as external standard. Erroneous points have been discarded (**Figure 2.2**).

2.9.5c. Reaction to various amounts of catalyst loading:

Five different reactions were set up under the standard reaction condition for each specific loading of catalyst and the reaction mixture was analyzed by ^{1}H NMR after 1h, 2h, 3h, 4h, and 5h respectively using CH_3CN as external standard. Erroneous points have been discarded (**Figure 2.2**).

2.9.5d. Reaction with respect to various solvent:

Eight different reactions were set up under the standard reaction condition for each solvent and the reaction mixture was analyzed by ^{1}H NMR after 1h, 2h, 3h, 4h, 5h, 12 h, 18h and 24h

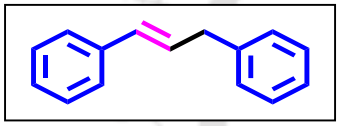
respectively using CH_3CN as external standard. Erroneous points have been discarded (**Figure 2.2**).

2.9.5e. Reaction to temperature:

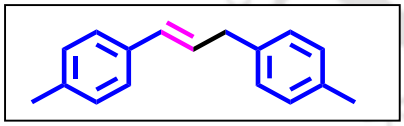
Five different reactions were set up under the standard reaction condition for specific temperatures and the reaction mixture was analyzed by ^1H NMR after 1h, 2h, 3h, 4h, and 5h respectively using CH_3CN as the external standard. Erroneous points have been discarded (**Figure 2.2**)

2.10. Spectroscopic data of the newly synthesized compounds in the present study:

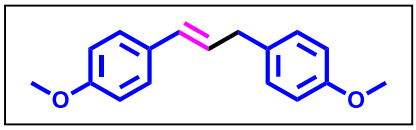
(E)-prop-1-ene-1,3-diyldibenzeneProduct (2.1.2a): Product was isolated via column chromatography (PE/EA = 99:1) as a colorless liquid. (Yield: 85%) ^1H NMR (600 MHz, $CDCl_3$) δ 7.35 (d, J = 7.5 Hz, 2H), 7.30 (dt, *J* = 13.6, 7.7 Hz, 4H), 7.25 – 7.18 (m, 4H), 6.45 (d, *J* = 15.8 Hz, 1H), 6.38 - 6.33 (m, 1H), 3.54 (d, *J* = 6.9 Hz, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 140.2, 137.4, 131.0, 129.2, 128.7, 128.5, 128.5, 127.1, 126.2, 126.1, 39.4.[5b]



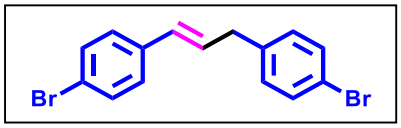
(E)-4,4'-(prop-1-ene-1,3-diyl)bis(methylbenzene)(2.1.2b): Product was isolated *via* column chromatography (PE/EA = 99:1) as colourless liquid. (Yield: 80%) ^1H NMR (600 MHz, $CDCl_3$) δ 7.24 (d, *J* = 7.2 Hz, 3H), 7.13 – 7.08 (m, 5H), 6.41 (d, *J* = 15.7 Hz, 1H), 6.31– 6.26 (m, 1H), 3.49 (d, J = 6.8 Hz, 2H), 2.33 (s, 3H), 2.32 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 137.26, 136.78, 135.63, 134.78, 130.70, 129.19, 129.16, 128.56, 128.49, 126.02, 38.94, 21.16, 21.04.[5b]



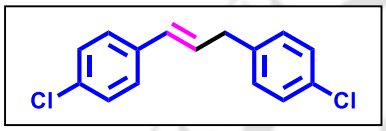
(E)-4,4'-(prop-1-ene-1,3-diyl)bis(methoxybenzene) (2.1.2c): Product was isolated *via* column chromatography (PE/EA = 99:1) as yellow oil. (Yield: 85%) ^1H NMR (600 MHz, $CDCl_3$) δ 7.28 (d, *J* = 8.6 Hz, 2H), 7.15 (d, J = 8.5 Hz, 2H), 6.84 (dd, *J* = 12.0, 8.7 Hz, 4H), 6.37 (d, *J* = 15.7 Hz, 1H), 6.22 – 6.17 (m, 1H), 3.79 (s, 6H), 3.46 (d, *J* = 6.8 Hz, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 158.8, 158.0, 132.5, 130.4, 130.1, 129.5, 127.5, 127.2, 113.9, 113.8, 55.3, 38.4.[5b]



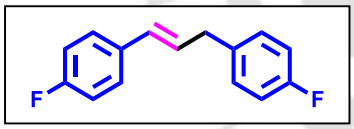
(E)-4,4'-(prop-1-ene-1,3-diyl)bis(bromobenzene) (2.1.2d): Product was isolated *via* column chromatography (PE/EA = 99:1) as yellow oil. (Yield: 55%) ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.42 (t, *J* = 8.8 Hz, 4H), 7.20 (d, *J* = 8.5 Hz, 2H), 7.09 (d, *J* = 8.2 Hz, 2H), 6.35 (d, *J* = 15.0 Hz, 1H), 6.31 – 6.26 (m, 1H), 3.47 (d, *J* = 6.6 Hz, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 138.7, 136.2, 131.6, 131.6, 130.4, 130.3, 129.3, 127.7, 120.9, 120.1, 38.6.[5b]



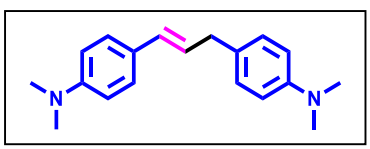
(E)-4,4'-(prop-1-ene-1,3-diyl)bis(chlorobenzene) (2.1.2e): Product was isolated *via* column chromatography (PE/EA = 99:1) as yellow oil. (Yield: 85%) ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28 – 7.26 (m, 6H), 7.15 (d, *J* = 8.4 Hz, 2H), 6.37 (d, *J* = 15.8 Hz, 1H), 6.27 (dt, *J* = 15.8, 6.7 Hz, 1H), 3.49 (d, *J* = 6.6 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.31, 135.80, 132.89, 132.13, 130.31, 130.03, 129.36, 128.71, 128.67, 127.37, 38.59.[5b]



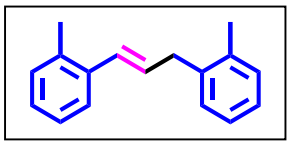
(E)-4,4'-(prop-1-ene-1,3-diyl)bis(fluorobenzene) (2.1.2f): Product was isolated *via* column chromatography (PE/EA = 99:1) as yellow oil. (Yield: 79%) ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.23 (dd, *J* = 8.6, 5.5 Hz, 2H), 7.10 (dd, *J* = 8.5, 5.5 Hz, 2H), 6.91 (td, *J* = 8.7, 6.4 Hz, 4H), 6.32 (d, *J* = 15.8 Hz, 1H), 6.15 (dt, *J* = 15.8, 6.8 Hz, 1H), 3.43 (d, *J* = 6.8 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.0 (d, *J* = 58.6 Hz), 160.6 (d, *J* = 56.3 Hz), 135.6 (d, *J* = 3.2 Hz), 133.5 (d, *J* = 3.4 Hz), 130.0 (d, *J* = 2.6 Hz), 129.9, 128.8, 128.7, 127.5 (d, *J* = 8.0 Hz), 115.5, 115.3 (d, *J* = 7.5 Hz), 115.2, 38.4.[5b]



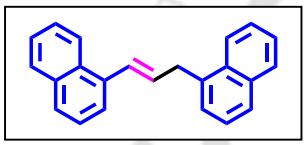
(E)-4,4'-(prop-1-ene-1,3-diyl)bis(N,N-dimethylaniline) (2.1.2g): Product was isolated *via* column chromatography (PE/EA = 99:1) as yellow oil. (Yield: 53%) ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.25 (d, *J* = 9.8 Hz, 2H), 7.12 (d, *J* = 8.6 Hz, 2H), 6.72 (d, *J* = 8.6 Hz, 2H), 6.67 (d, *J* = 8.8 Hz, 2H), 6.35 (d, *J* = 15.7 Hz, 1H), 6.13 (dt, *J* = 15.8, 7.0 Hz, 1H), 3.43 (d, J = 6.9 Hz, 2H), 2.93 (s, 6H), 2.91 (s, 6H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 149.72, 149.18, 130.18, 129.76, 129.31, 126.98, 126.48, 125.98, 113.19, 112.65, 41.08, 40.73, 38.47.[17]



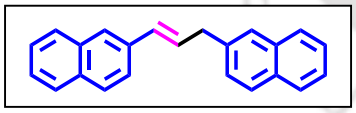
(E)-2,2'-(prop-1-ene-1,3-diyl)bis(methylbenzene) (2.1.2k): Product was isolated *via* column chromatography (PE/EA = 99:1) as yellow oil. (Yield: 68%) ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 (d, *J* = 6.1 Hz, 1H), 7.20 (d, *J* = 6.6 Hz, 1H), 7.16 – 7.11 (m, 6H), 6.58 (d, *J* = 15.7 Hz, 1H), 6.19 (dt, *J* = 13.6, 6.6 Hz, 1H), 3.55 (d, *J* = 6.5 Hz, 2H), 2.34 (s, 3H), 2.30 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 138.4, 136.7, 136.4, 135.0, 130.2, 130.2, 129.9, 129.1, 128.9, 127.0, 126.4, 126.1, 126.0, 125.5, 37.2, 19.8, 19.4.[5b]



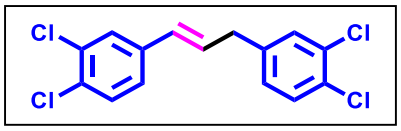
(E)-1,1'-(prop-1-ene-1,3-diyl)dinaphthalene (2.1.2l): Product was isolated *via* column chromatography (PE/EA = 99:1) as white solid. (Yield: 56%) ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.13 (d, *J* = 8.3 Hz, 1H), 7.99 (d, *J* = 5.4 Hz, 1H), 7.85 (d, *J* = 7.9 Hz, 1H), 7.80 – 7.76 (m, 1H), 7.76 – 7.72 (m, 1H), 7.69 (d, *J* = 7.9 Hz, 1H), 7.51 (t, *J* = 7.1 Hz, 2H), 7.48 – 7.45 (m, 1H), 7.44 – 7.41 (m, 4H), 7.35 (t, *J* = 7.7 Hz, 1H), 7.17 (d, J = 15.9 Hz, 1H), 6.48 (dt, *J* = 15.5, 6.5 Hz, 1H), 4.07 (d, *J* = 6.5 Hz, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 136.34, 135.40, 134.02, 133.68, 132.17, 131.22, 128.86, 128.84, 128.55, 127.60, 127.24, 126.52, 126.07, 125.96, 125.80, 125.75, 125.72, 124.17, 123.96, 123.78, 36.93.[5b]



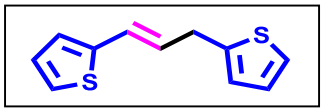
(E)-2,2'-(prop-1-ene-1,3-diyl)dinaphthalene (2.1.2m): Product was isolated *via* column chromatography (PE/EA = 99:1) as white solid. (Yield: 55%) ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 – 7.66 (m, 6H), 7.62 (s, 2H), 7.51 (d, *J* = 8.6 Hz, 1H), 7.38 – 7.32 (m, 5H), 6.58 (d, *J* = 15.8 Hz 1H), 6.52 – 6.46 (m, 1H), 3.68 (d, *J* = 6.6 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 136.5, 133.8, 132.6, 132.6, 131.7, 131.1, 130.3, 128.5, 127.0, 127.0, 126.8, 126.6, 126.6, 126.5, 126.4, 125.7, 125.1, 124.9, 124.7, 124.5, 124.3, 122.5, 38.55.[5b]



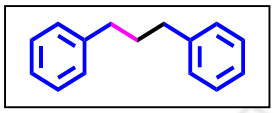
(E)-4,4'-(prop-1-ene-1,3-diyl)bis(1,2-dichlorobenzene) (2.1.2n): Product was isolated *via* column chromatography (PE/EA = 99:1) as a yellowish liquid. (Yield: 52%) ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 (d, *J* = 2.1 Hz, 1H), 7.29 (dd, *J* = 9.8, 8.3 Hz, 2H), 7.23 (d, *J* = 2.1 Hz, 1H), 7.08 (dd, *J* = 8.4, 2.1 Hz, 1H), 6.98 (dd, *J* = 8.1, 2.1 Hz, 1H), 6.28 – 6.17 (m, 2H), 3.41 (d, *J* = 6.2 Hz, 2H). 13C NMR (100 MHz, $CDCl_3$) δ 138.65, 136.08, 131.65, 131.48, 130.01, 129.54, 129.45, 129.42, 129.41, 128.85, 128.69, 127.07, 126.87, 124.36, 37.21.[7a]



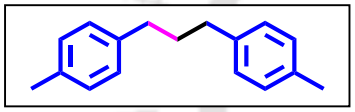
(E)-2,2'-(prop-1-ene-1,3-diyl)dithiophene (2.1.2o): Product was isolated *via* column chromatography (PE/EA = 99:1) as yellow oil. (Yield: 75%) ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.16 (d, *J* = 5.1 Hz, 1H), 7.11 (d, *J* = 4.9 Hz, 1H), 6.95 – 6.91 (m, 3H), 6.85 (d, *J* = 2.6 Hz, 1H), 6.60 (d, *J* = 15.6 Hz, 1H), 6.23 – 6.18 (m, 1H), 3.69 (d, *J* = 6.8 Hz, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 142.72, 142.29, 128.02, 127.32, 127.00, 125.17, 124.89, 124.59, 123.89, 123.83, 33.12.[5b]



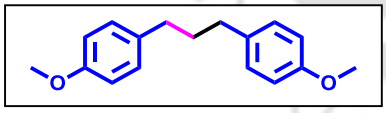
(E)-prop-1-ene-1,3-diyldibenzene (2.2.3a): Product was isolated *via* column chromatography (PE/EA = 99:1) as yellow oil. (Yield: 98%) ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.28 – 7.26 (m, 4H), 7.17 (d, *J* = 6.9 Hz, 6H), 2.64 (t, *J* = 7.2 Hz, 4H), 1.95 (p, *J* = 7.7 Hz, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 142.3, 128.5, 128.3, 125.8, 35.5, 33.0.[8]



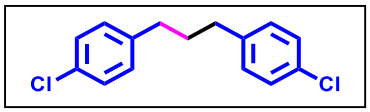
1,3-di-p-tolylpropane (2.2.3b): Product was isolated *via* column chromatography (PE/EA = 99:1) as colourless oil. (Yield: 98%) ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.08 (s, 8H), 2.60 (t, *J* = 7.7 Hz, 4H), 2.31 (s, 6H), 1.91 (p, *J* = 7.7 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.3, 135.1, 128.9, 128.3, 35.0, 33.2, 21.0.[8]



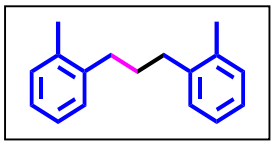
(E)-4,4'-(prop-1-ene-1,3-diyl)bis(methoxybenzene) (2.2.3c): Product was isolated *via* column chromatography (PE/EA = 99:1) as yellow oil. (Yield: 98%) ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.09 (d, *J* = 8.6 Hz, 4H), 6.82 (d, *J* = 8.6 Hz, 4H), 3.79 (s, 6H), 2.58 (t, *J* = 7.7 Hz, 4H), 1.89 (p, *J* = 7.7 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.71, 134.47, 129.31, 113.73, 55.27, 34.45, 33.42.[8]



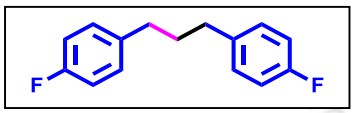
1,3-bis(4-chlorophenyl)propane (2.2.3d): Product was isolated *via* column chromatography (PE/EA = 99:1) as yellow oil. (Yield: 96%) ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.17 (d, *J* = 8.4 Hz, 4H), 7.02 (d, *J* = 8.4 Hz, 4H), 2.52 (t, *J* = 7.7 Hz, 4H), 1.82 (p, *J* = 7.7 Hz, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 140.44, 131.52, 129.80, 128.47, 34.60, 32.82.[8]



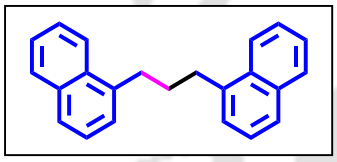
(E)-2,2'-(prop-1-ene-1,3-diyl)bis(methylbenzene) (2.2.3e): Product was isolated *via* column chromatography (PE/EA = 99:1) as yellow oil. (Yield: 99%) ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.15 – 7.08 (m, 8H), 2.68 (t, *J* = 7.7 Hz, 4H), 2.28 (s, 6H), 1.86 (p, *J* = 7.9 Hz, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 140.5, 135.8, 130.2, 128.7, 125.9, 33.2, 30.5, 19.3.[5c]



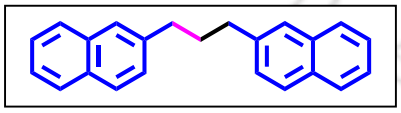
1,3-bis(4-fluorophenyl)propane (2.2.3f): Product was isolated *via* column chromatography (PE/EA = 99:1) as a yellow oil. (Yield: 97%) ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.15 (dd, *J* = 8.4, 5.5 Hz, 4H), 6.99 (t, *J* = 8.7 Hz, 4H), 2.63 (t, *J* = 7.7 Hz, 4H), 1.92 (p, *J* = 7.7 Hz, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 162.0, 160.4, 137.7 (d, *J* = 3.3 Hz), 129.7 (d, *J* = 7.7 Hz), 115.0 (d, *J* = 21.0 Hz), 34.4, 33.3.[5c]



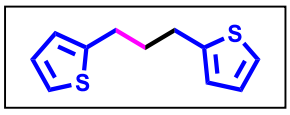
1,3-di(naphthalen-1-yl)propane (2.2.3g): Product was isolated *via* column chromatography (PE/EA = 99:1) as a yellow oil. (Yield: 98%) ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.96 – 7.94 (m, 2H), 7.87 – 7.84 (m, 2H), 7.71 (d, *J* = 8.0 Hz, 2H), 7.47 – 7.43 (m, 4H), 7.43 – 7.35 (m, 4H), 3.23 – 3.20 (m, 4H), 2.28 – 2.21 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.2, 133.9, 131.8, 128.7, 126.6, 125.9, 125.7, 125.5, 125.4, 123.7, 32.9, 31.5.[5c]



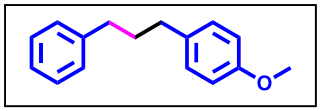
1,3-di(naphthalen-2-yl)propane (2.2.3h): Product was isolated *via* column chromatography (PE/EA = 99:1) as a yellow oil. (Yield: 97%) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 – 7.77 (m, 5H), 7.63 (s, 2H), 7.43 (pd, *J* = 6.8, 1.4 Hz, 4H), 7.36 (d, *J* = 1.7 Hz, 1H), 7.26 (s, 2H), 2.85 (t, J= 7.6 Hz, 4H), 2.15 (p, *J* = 7.7 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.7, 133.6, 132.0, 127.8, 127.6, 127.4, 127.4, 126.5, 125.9, 125.1, 35.5, 32.7.[5c]



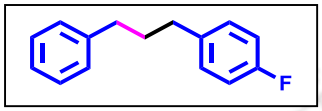
1,3-di(thiophen-2-yl)propane (2.2.3i)*:* Product was isolated *via* column chromatography (PE/EA = 99:1) as a yellow oil. (Yield: 99%) ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.12 (dd, *J* = 5.2, 1.2 Hz, 2H), 6.92 (dd, *J* = 5.1, 3.5 Hz, 2H), 6.80 (d, *J* = 3.4 Hz, 2H), 2.89 (t, *J* = 7.5 Hz, 4H), 2.06 (p, *J* = 7.5 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.7, 126.7, 124.3, 123.1, 33.5, 29.1.[5c]



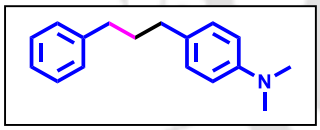
1-methoxy-4-(3-phenylpropyl)benzene (2.2.6a): Product was isolated *via* column chromatography (PE/EA = 98:2) as a yellow oil. (Yield: 88%) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 – 7.23 (m, 2H), 7.17 (d, *J* = 7.8 Hz, 3H), 7.08 (d, *J* = 8.5 Hz, 2H), 6.82 (d, *J* = 8.6 Hz, 2H), 3.76 (s, 3H), 2.60 (dt, *J* = 16.9, 7.7 Hz, 4H), 1.91 (p, *J* = 7.7 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.8, 142.4, 134.4, 129.3, 128.5, 128.3, 125.7, 113.8, 55.3, 35.4, 34.5, 33.2. [5b]



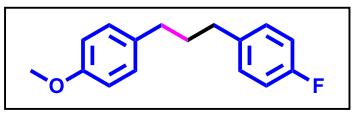
1-fluoro-4-(3-phenylpropyl)benzene (2.2.6b): Product was isolated *via* column chromatography (PE/EA = 99:1) as a yellow oil. (Yield: 65%) ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 – 7.25 (m, 2H), 7.17 (t, J = 7.7 Hz, 3H), 7.15 – 7.11 (m, 2H), 6.96 (t, *J* = 8.5 Hz, 2H), 2.63 (q, *J* = 8.5 Hz, 4H), 1.93 (p, *J* = 7.7 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.1, 160.2, 142.1, 137.84 (d, *J* = 3.2 Hz), 129.71 (d, *J* = 7.8 Hz), 128.38 (d, *J* = 10.6 Hz), 128.3, 125.8, 115.01 (d, J = 21.1 Hz), 114.9, 35.3, 34.5, 33.0.[18]



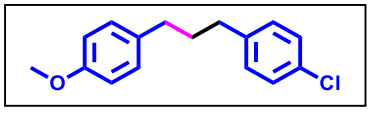
N,N-dimethyl-4-(3-phenylpropyl)aniline (2.2.6c): Product was isolated *via* column chromatography (PE/EA = 90:10) as yellow oil. (Yield: 68%) ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28 – 7.24 (m, 1H), 7.18 (d, *J* = 7.9 Hz, 2H), 7.06 (d, *J* = 8.6 Hz, 1H), 6.70 (d, *J* = 8.6 Hz, 1H), 2.91 (s, 3H), 2.70 – 2.61 (m, 1H), 2.60 – 2.52 (m, 1H), 1.92 (p, *J* = 7.7 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.0, 142.6, 130.5, 129.0, 128.4, 128.2, 125.6, 113.0, 40.9, 35.5, 34.4, 33.2.[5b]



1-fluoro-4-(3-(4-methoxyphenyl)propyl)benzene (2.2.6d): Product was isolated *via* column chromatography (PE/EA = 98:2) as yellow oil. (Yield: 78%), ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.14 – 7.08 (m, 4H), 6.95 (t, *J* = 8.7 Hz, 2H), 6.83 (d, *J* = 8.6 Hz, 2H), 3.78 (s, 3H), 2.59 (dt, *J* = 11.4, 7.7 Hz, 4H), 1.89 (p, *J* = 7.7 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.4, 160.0, 157.7, 137.9 (d, *J* = 3.2 Hz), 134.2, 129.7 (d, J = 7.7 Hz), 129.6, 129.3, 115.0 (d, J = 21.1 Hz), 114.9, 113.7, 55.3, 34.5, 34.4, 33.3.[5b]

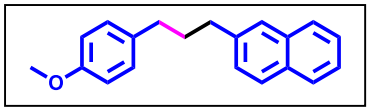


1-chloro-4-(3-(4-methoxyphenyl)propyl)benzene (2.2.6e): Product was isolated *via* column chromatography (PE/EA = 99:1) as yellow oil. (Yield: 68%), R_f = 0.9. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.17 (d, *J* = 8.3 Hz, 2H), 7.02 (t, *J* = 7.9 Hz, 4H), 6.76 (d, *J* = 8.6 Hz, 2H), 3.72 (s, 3H),

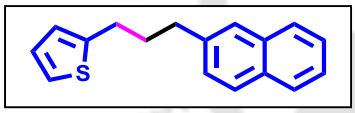


2.52 (dt, *J* = 10.4, 7.8 Hz, 4H), 1.83 (p, *J* = 7.7 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.7, 140.7, 134.1, 131.4, 129.8, 129.3, 128.3, 113.7, 55.2, 34.6, 34.3, 33.0.[5b]

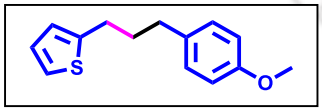
2-(3-(4-methoxyphenyl)propyl)naphthalene (2.2.6f): Product was isolated *via* column chromatography (PE/EA = 99:1) as yellow oil. (Yield: 52%), R_f = 0.9. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.84 (d, *J* = 1.4 Hz, 1H), 7.80 (d, *J* = 8.4 Hz, 2H), 7.64 (s, 1H), 7.50 – 7.42 (m, 2H), 7.36 (dd, *J* = 8.4, 1.7 Hz, 1H), 7.14 (d, *J* = 8.6 Hz, 2H), 6.87 (d, *J* = 8.6 Hz, 2H), 3.82 (s, 3H), 2.83 (t, *J* = 7.7 Hz, 2H), 2.66 (t, 2H), 2.04 (p, *J* = 7.7 Hz, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 157.6, 139.9, 134.3, 133.6, 131.9, 129.3, 127.8, 127.6, 127.4, 126.4, 125.9, 125.1, 113.7, 55.3, 35.5, 34.5, 33.1.[5b]



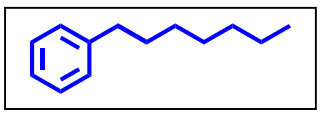
2-(3-(naphthalen-2-yl)propyl)thiophene (2.2.6g): Product was isolated *via* column chromatography (PE/EA = 99:1) as a yellow oil. (Yield: 60%), R_f = 0.9. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (dd, *J* = 11.2, 8.6 Hz, 3H), 7.66 (s, 1H), 7.46-7.41 (m, 2H), 7.34 (d, *J* = 9.8 Hz, 1H), 7.13 (d, *J* = 5.8 Hz, 1H), 6.93 (dd, *J* = 5.2, 3.4 Hz, 1H), 6.81 (s, 1H), 2.90 (t, *J* = 7.6 Hz, 2H), 2.85 (t, *J* = 7.6 Hz, 2H), 2.10 (p, *J* = 7.6 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.1, 139.4, 133.6, 132.0, 127.9, 127.6, 127.4, 127.3, 126.7, 126.5, 125.9, 125.2, 124.2, 123.0, 35.3, 33.1, 29.4.[5b]



2-(3-(4-methoxyphenyl)propyl)thiophene (2.2.6h): Product was isolated *via* column chromatography (PE:EA = 99:1) as a yellow oil. (Yield: 72%) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.11 – 7.09 (m, 3H), 6.91 (dd, *J* = 5.1, 3.4 Hz, 1H), 6.83 (d, *J* = 8.6 Hz, 2H), 6.80 – 6.78 (m, 1H), 3.78 (s, 3H) 2.84 (t, *J* = 7.5 Hz, 2H), 2.62 (t, *J* = 7.6 Hz, 2H), 1.98 (p, *J* = 7.6 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.8, 145.2, 134.0, 129.4, 126.7, 124.2, 122.9, 113.7, 55.3, 34.2, 33.5, 29.3.[5b]



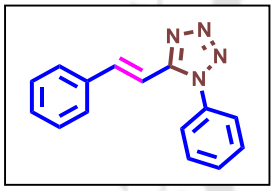
Heptylbenzene (2.2.6i): Product was isolated *via* column chromatography (only petroleum ether) as a yellow oil. (Yield: 32%), R_f = 0.9, ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.20 (t, *J* = 7.7 Hz, 2H), 7.10 (d, *J* = 7.7 Hz, 3H), 2.53 (t, *J* = 7.9 Hz, 2H), 1.54 (t, *J* = 7.5 Hz, 2H), 1.32 – 1.12 (m, 8H), 0.81 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 142.9, 128.4, 128.2, 125.5, 36.0, 31.8, 31.5, 29.3, 29.2, 22.6, 14.1.[5c]



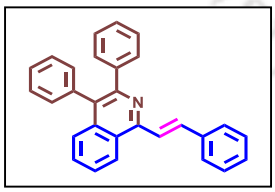
Nonylbenzene (2.2.6j): Product was isolated *via* column chromatography (only petroleum ether) as a yellow oil. (Yield: 35%), R_f = 0.9, ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.19 – 7.15 (m, 2H), 7.06 (d, *J* = 7.5 Hz, 3H), 2.49 (t, *J* = 7.8 Hz, 2H), 1.27 – 1.06 (m, 14H), 0.77 (t, *J* = 6.7 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.97, 128.39, 128.20, 125.53, 35.99, 31.89, 31.50, 29.55, 29.51, 29.34, 29.31, 22.66, 14.08.[5c]

Undecylbenzene (2.2.6k): Product was isolated *via* column chromatography (only petroleum ether) as a yellow oil. (Yield: 26%), ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.19 (q, *J* = 6.6, 5.5 Hz, 2H), 7.10 (d, *J* = 7.6 Hz, 3H), 2.52 (t, *J* = 7.8 Hz, 2H), 1.53 (p, *J* = 7.4 Hz, 2H), 1.33 – 1.07 (m, 16H), 0.81 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 143.0, 128.4, 128.2, 125.5, 36.0, 31.9, 31.5, 29.7, 29.6, 29.6, 29.5, 29.3, 22.7, 14.1.[19]

(E)-1-phenyl-5-styryl-1H-tetrazole (2.7): ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.00 (d, *J* = 16.1 Hz, 1H), 7.64 (d, *J* = 6.6 Hz, 3H), 7.52 (dd, *J* = 15.1, 7.7 Hz, 4H), 7.39 (d, *J* = 5.3 Hz, 3H), 6.82 (d, *J* = 16.1 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 152.3, 141.3, 134.7, 133.7, 130.5, 130.1, 130.0, 129.0, 127.7, 125.2, 107.4.[12a]



(E)-N-(1,3-diphenylallyl)-4-methylbenzenesulfonamide (2.8): ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.69 (d, *J* = 8.0 Hz, 2H), 7.33 – 7.06 (m, 12H), 6.38 (d, *J* = 15.8 Hz, 1H), 6.11 (dd, *J* = 15.8, 6.8 Hz, 1H), 5.15 (t, *J* = 6.9 Hz, 1H), 5.00 (s, 1H), 2.36 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 143.32, 139.66, 137.75, 136.07, 132.20, 129.47, 128.76, 128.49, 128.18, 127.94, 127.92, 127.36, 127.08, 126.55, 59.79, 21.44.[12b]



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2.12. Copies of ^{1}H and ^{13}C spectra of newly synthesised compounds:

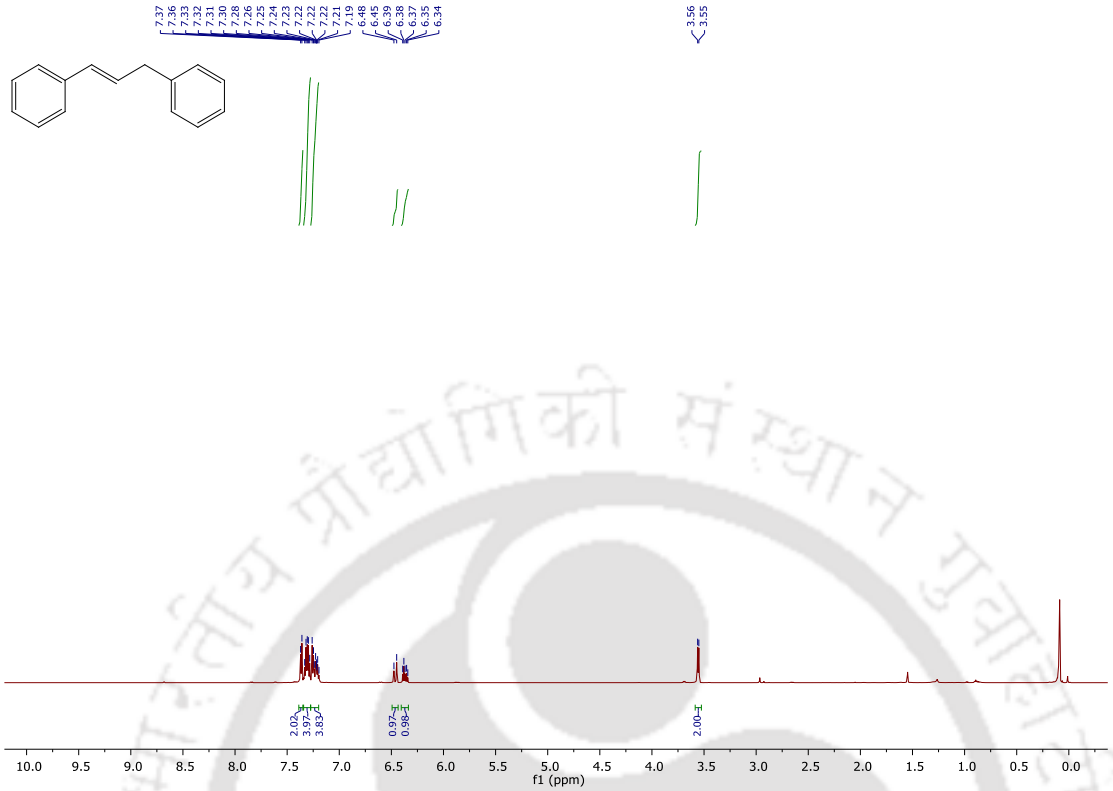


Figure 2.9: ^{1}H NMR (600 MHz) spectra of compound **2.1.2a** in $CDCl_3$

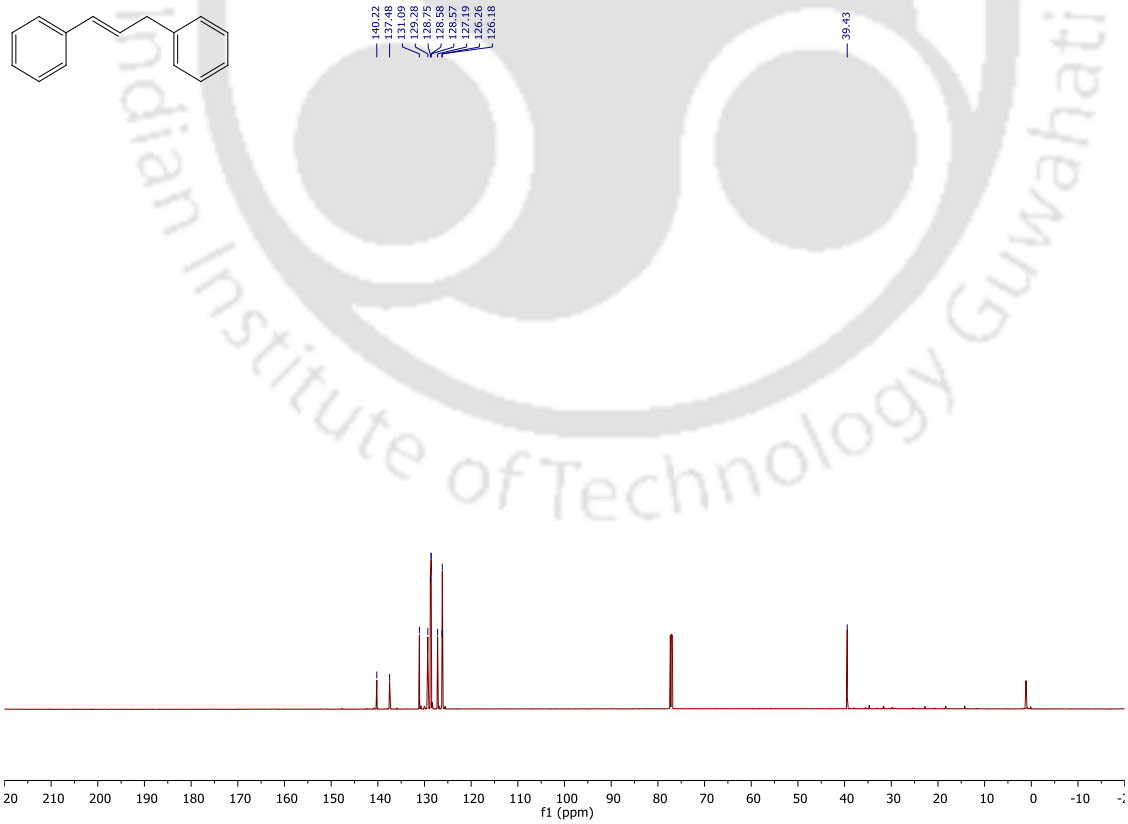


Figure 2.10. $^{13}C\{^{1}H\}$ NMR (150 MHz) spectra of compound **2.1.2a** in $CDCl_3$

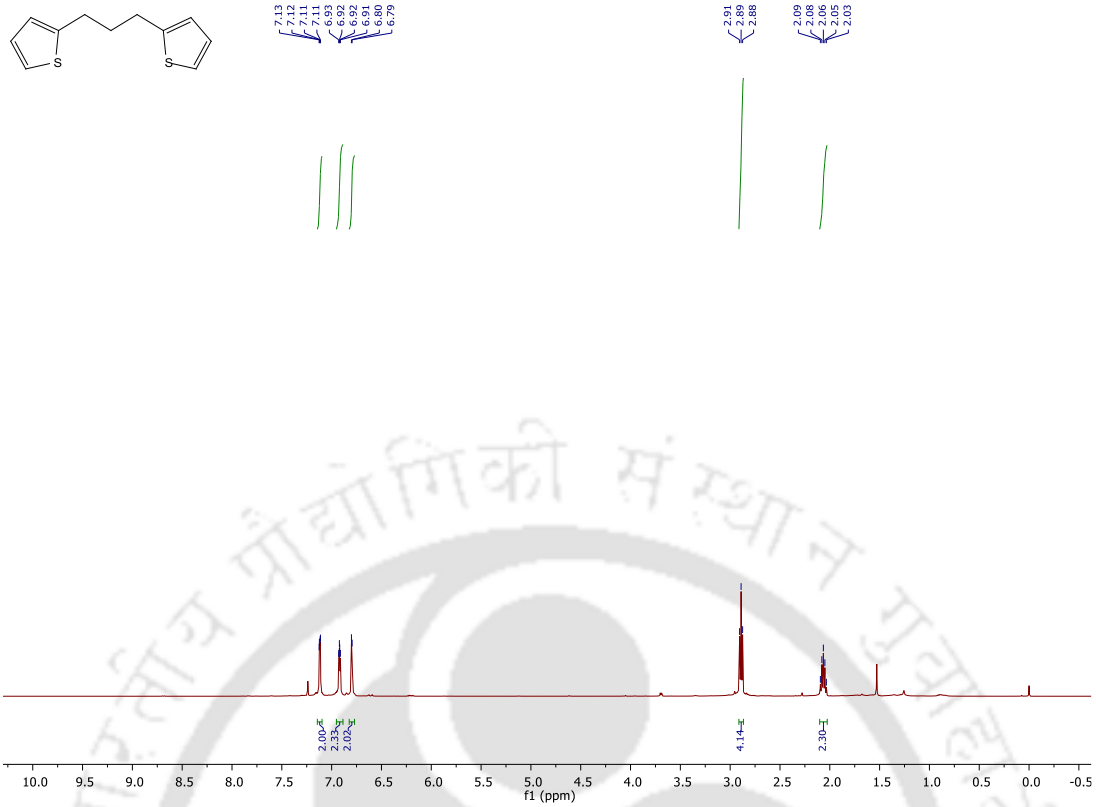


Figure 2.11. ^{1}H NMR (500 MHz) spectra of compound **2.2.3i** in $CDCl_3$

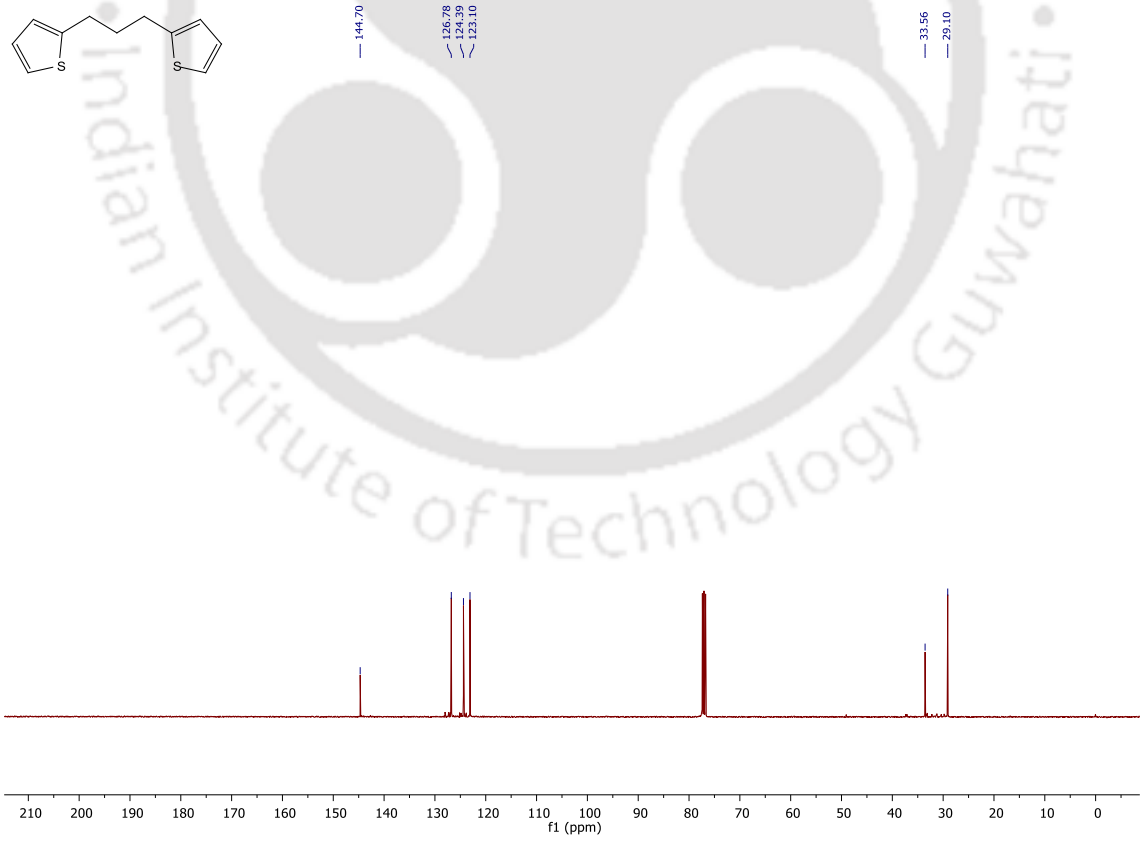


Figure 2.12. ^{13}C{1H} NMR (100 MHz) spectra of compound **2.2.3i** in CDCl

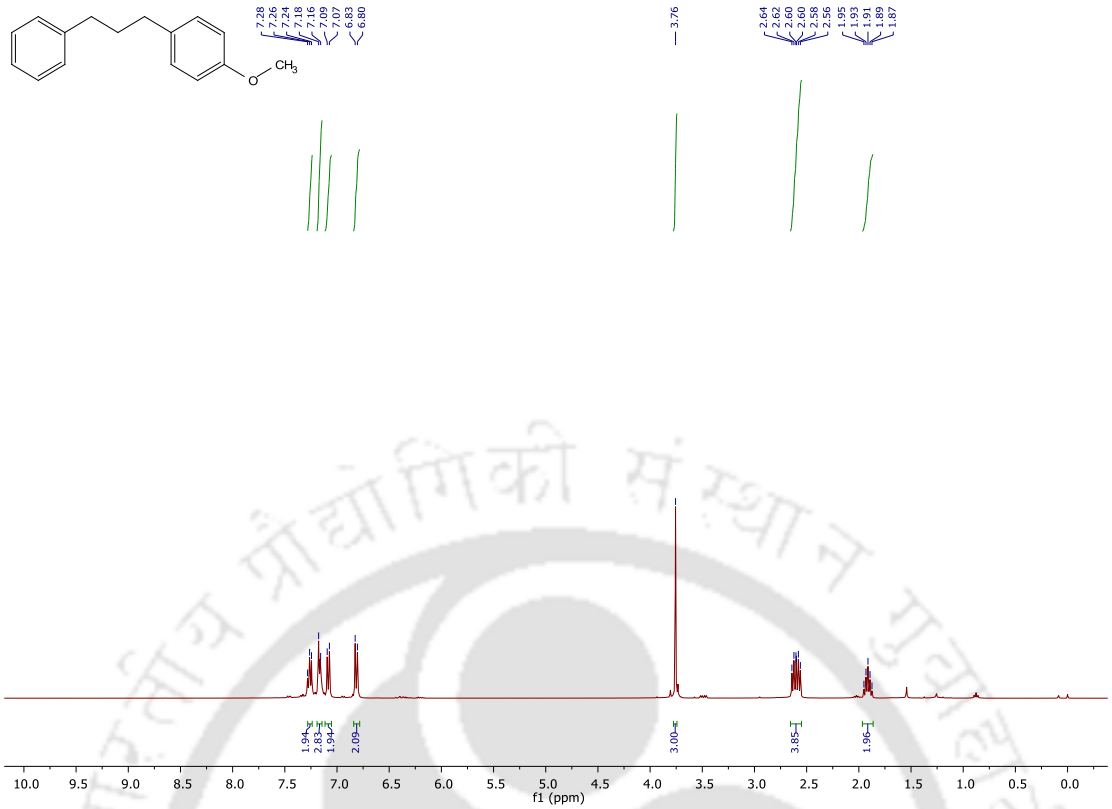


Figure 2.13. ^{1}H NMR (400 MHz) of spectra of compound **2.2.6a** in $CDCl_3$

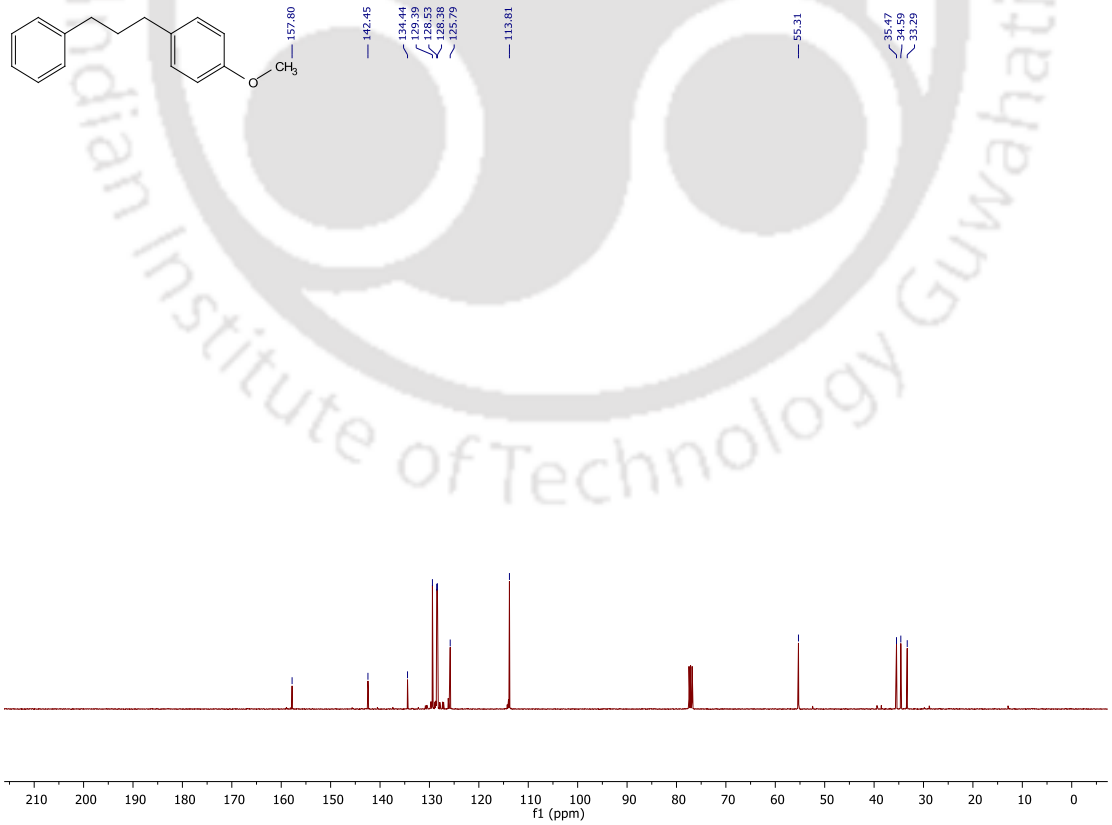


Figure 2.14. $^{13}C\{^{1}H\}$ NMR (100 MHz) spectra of compound **2.2.6a** in $CDCl_3$

Chapter 3

Ruthenium Catalysed Dehydrogenative Cyclization to Synthesize Polysubstituted 4-quinolones under Solvent-Free Conditions

3.1. Introduction:

N-heterocyclic compounds are a ubiquitous structural framework of various biologically active compounds, natural products, and pharmaceuticals. According to FDA (Food and Drug Administration) databases, *N*-containing heterocycles exist in approximately 60% of unique small-molecule drugs.[1] Specifically, 4-quinolone derivatives have gained prominence due to their wide range of bioactivities[2] and prominent applications in medical science and pharmacology.[3] Several quinolones such as nalidixic acid,[4a] ciprofloxacin,[4b] norfloxacin[4a,] and fleroxacin have emerged as extremely effective antibiotics. These engaging biological profiles have lured researchers to develop various synthetic methods for this scaffold (Figure **3.1**).

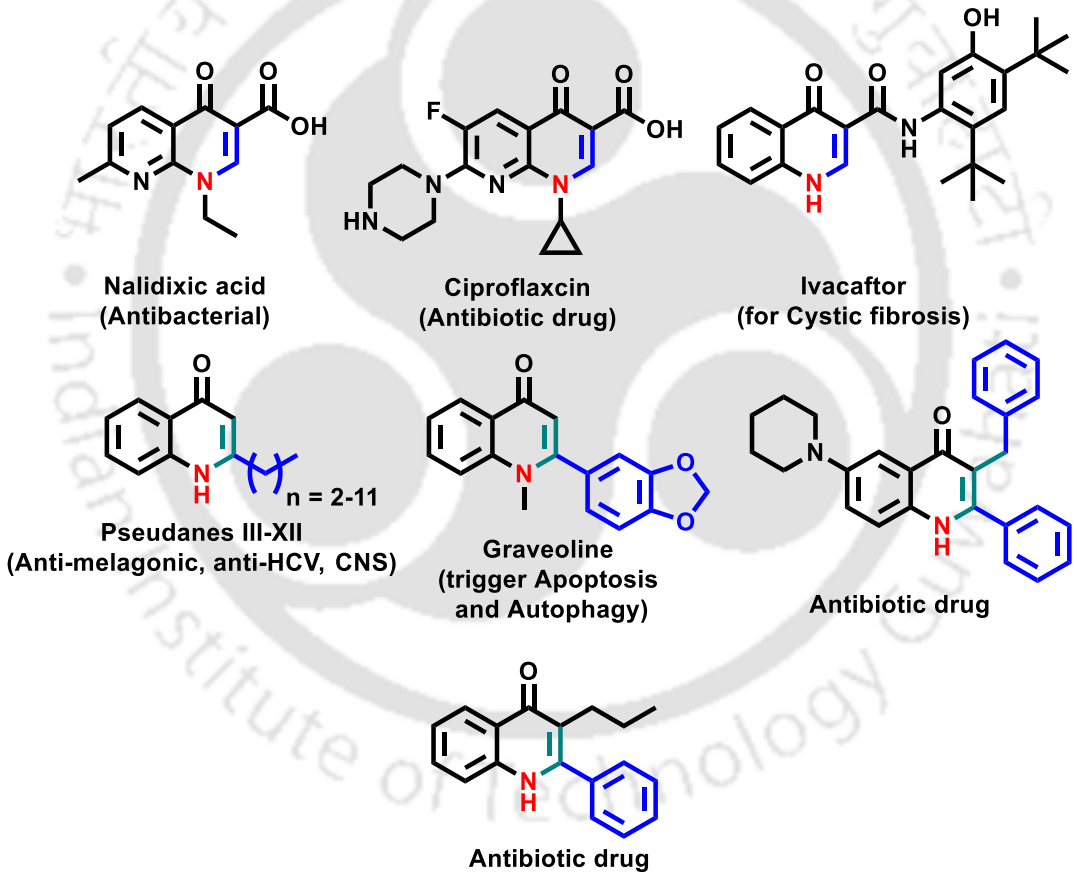
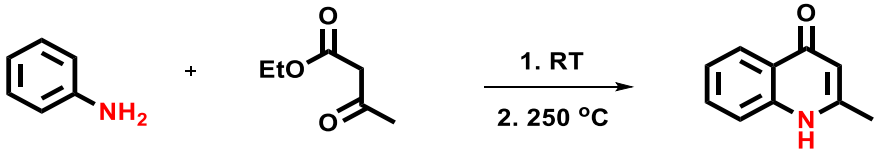


Figure 3.1. Biologically important molecules

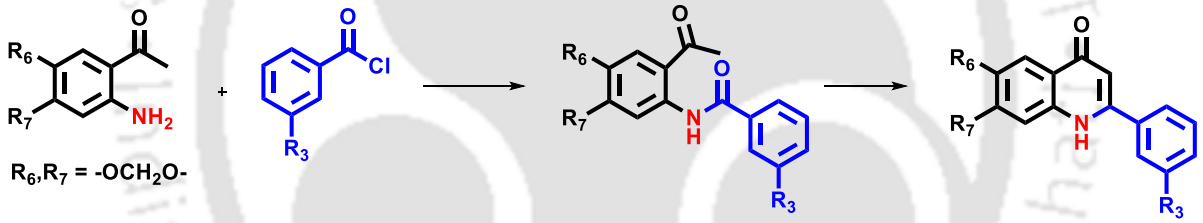
Conventionally, the Conrad−Limpach[5] and Niementowski reactions[6] have been employed to construct various scaffolds related to 4-quionolones. These classical approaches are based on the idea of a generic condensation reaction between aromatic amine and a carbonyl

group (like ethyl acetoacetate), followed by cyclization. But these processes suffer from limited substrate scope and harsh conditions (Scheme **3.1**).



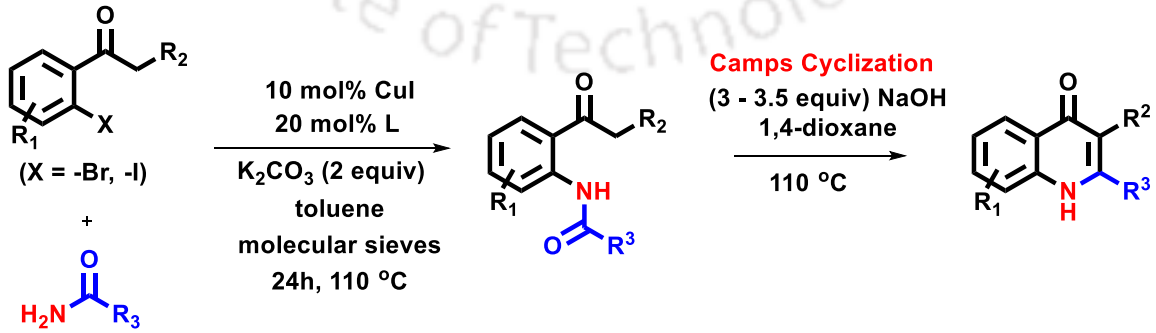
Scheme 3.1. Quinolone synthesis: Conrad-Limpach-Knorr

Later Camps cyclization,[7a] a base-assisted cyclocondensation reaction of *N*-(2-ketoaryl)amides, received considerable attention to construct this heterocycle.[7b] Previously, these Camps precursors were made by condensation of *o*-aminoacetophenones and carboxylic acids or acid chlorides, Friedel-Crafts acylation of anilides (which often result in a complex mixture of products) or synthesis and subsequent opening of a benzoxazinone with the dianion of an N-substituted acetamide (Scheme **3.2**).



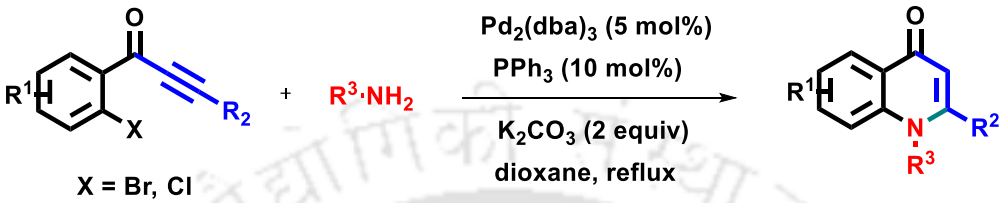
Scheme 3.2. Conventional synthetic route to *N*-(2-ketoaryl)amides and quinolones.

Based on this, Buchwald demonstrated a CuI-catalysed amidation of *o*-halo acetophenones with amide to deliver 2-aryl-4-quinolnes[7c] (Scheme **3.3**).



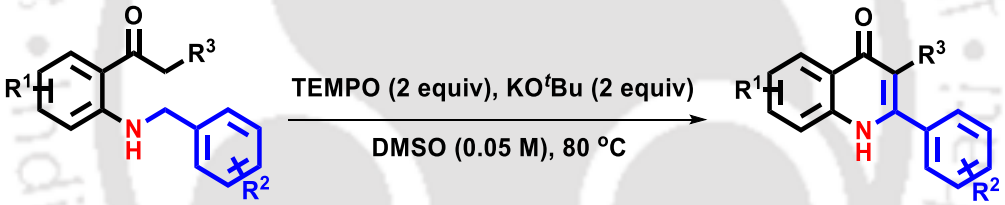
Scheme 3.3. Sequential Cu-catalyzed amidation, base mediated Camps cyclization to synthesise 2-aryl-4-quinolones (Scheme **3.3**)

Recently, transition metal catalyzed tandem reactions of substrates such as *o*-haloaryl acetylenic ketones/amines[8] and *o*-amino aryl acetylenic ketones[9] were developed to afford 2-aryl-4-quinolones. Synthesis of 2,3-disubstituted quinolones was also demonstrated by *Huang* and *co-workers*.[10] However, many of these methods require complex substrate prefunctionalization (Scheme **3.4**).



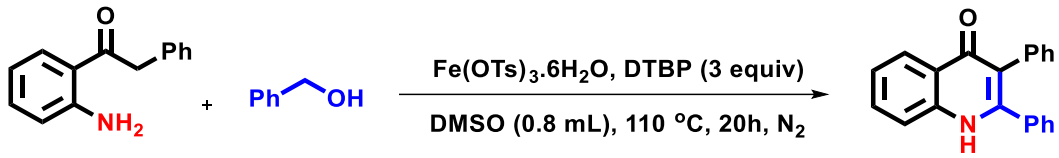
Scheme 3.4. Pd-catalyzed tandem amination reaction for the synthesis of 4-quinolones.

In 2015, Long reported TEMPO-promoted oxidative annulation of *N*-benzyl-2′-aminoacetophenone to afford quinolones (Scheme **3.5**).[11]



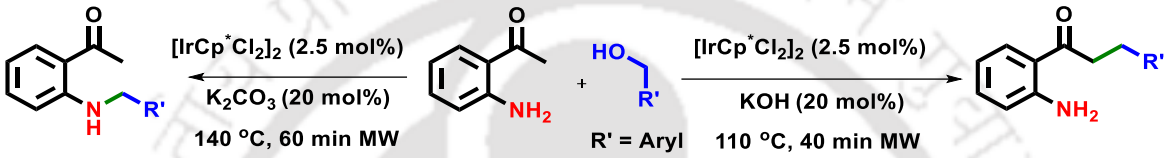
Scheme 3.5. Direct synthesis of 2-Aryl-4-quinolones via transition metal-free intramolecular oxidative C(sp^3)-H/C(sp^3)-H coupling.

Most recently, Hong's group reported a one-step synthesis of 4-quinolones but at the expense of an excessive amount of strong oxidants and reactants.[12] Thus, there is an increasing demand for atom-economical, environmentally benign, and sustainable routes for synthesizing quinolones (Scheme **3.6**).



Scheme 3.6. One-pot synthesis of 4-quinolone via Fe-catalyzed oxidative coupling of alcohol.

Catalytic de(hydrogenative) reactions have recently sparked interest in green and sustainable catalysis.[13] This approach gives a unique opportunity to construct diverse heterocyclic scaffolds from the similar/same set of starting materials by switching the catalyst systems or tuning the reaction parameters.[14] So, the synthesis of 2-quinolones/ 2,3-disubstituted quinolones, directly from 2′-aminoacetophenones and alcohols was planned and tried out. But there are other possibilities also. Like recently, Ir-catalyzed chemoselective alkylation of 2′-aminoacetophenone was accomplished to selectively deliver the corresponding *C*- or *N*-alkylated products.[15] So, here catalytic dehydrogenative approaches were performed to construct 4-quinolones directly from 2′-aminoacetophenones and alcohols (Scheme **3.7**).



Scheme 3.7. Chemoselective alkylation of 2′-aminoacetophenones.

This work prompted us to investigate two critical issues. First, 2′-aminoacetophenone will undergo rapid C-C alkylation, followed by a condensation reaction with aldehyde formed *in situ* from alcohol. Second, the strategy is to halt the reaction at the alkene stage and whether an annulation reaction is possible under the reaction conditions. Thus, we envisioned 4-quinolone derivatives could be synthesized via dehydrogenative annulation of 2′-aminoacetophenone and primary alcohols using a suitable catalytic system, which can control this selectivity.

3.2. Our work:

Here in this chapter, the activity of various well-defined Ru-complexes[9] was explored to synthesize 2,3-disubtituted-4-quinolones *via* dehydrogenative annulation of alcohols with 2′-aminoacetophenones. Here, the developed protocol was utilized for a wide range of alcohols, including diverse aminoacetophenones. To expand the synthetic utility, 4-quinolones with antibiotic properties were synthesized and post-synthetic modifications were performed. Apart from that, various control experiments were done to understand the mechanism of the reaction.

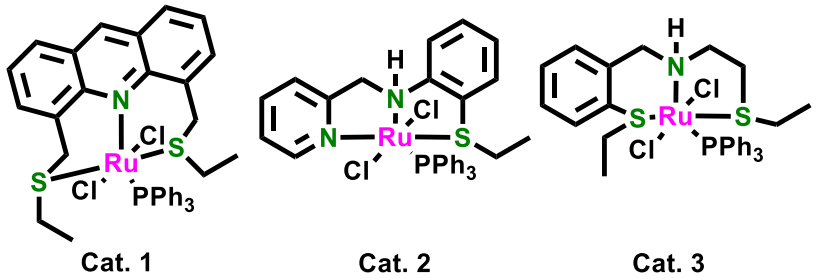
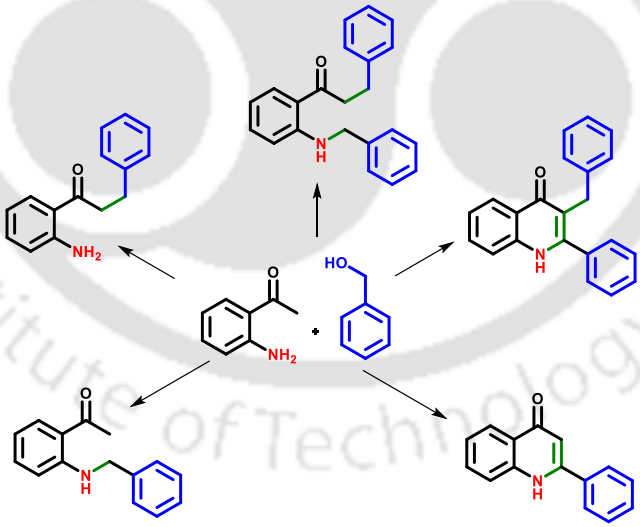


Figure 3.2. Ruthenium complexes

3.3. Results and discussions:

3.3.1. Optimization for the reaction between 2′-aminoacetophenone (3.1.1a) and benzyl alcohol (3.1.2a):

To materialize our synthetic hypothesis, the feasibility of our developed air-stable Ru-complexes[16] towards dehydrogenative annulation of 2′-aminoacetophenones and benzyl alcohol was investigated. The reaction of 2′-aminoacetophenones and alcohols can lead to various possibilities but it was found that our developed methodology is highly selective towards 3-benzyl-2-phenylquinolin-4*(1H)*-ones and C/N-alkylated products were barely detected (Scheme **3.8**).

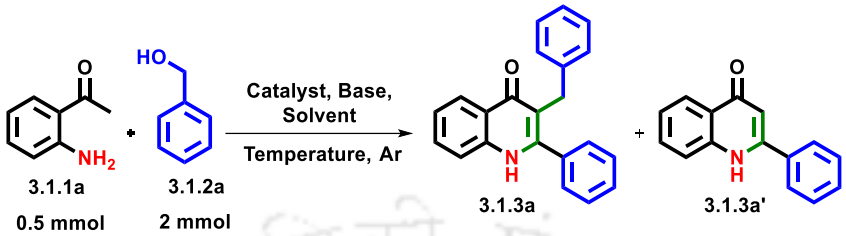


Scheme 3.8. Possible outcomes of the reaction.

Except for KOH, bases like KO^{t}Bu, NaO^{t}Bu, and NaOH lead to the formation of the 3-benzyl-2-phenylquinolin-4(1*H*)-one in lower yield. Surprisingly in the presence of K_2CO_3 **3.1.3a** was not formed, instead 2-phenylquinolin-4*(1H)*-one, **3.1.3a′** was isolated in 55% yield **(Table 1, entry 5)**. Later, various other screening conditions were performed but failed to increase the

yield of 2-phenylquinolin-4*(1H)*-one. In addition, Cat. **2** and Cat. **3** gave a lower yield of **3.1.3a** in

Table 3.1. Screening table:



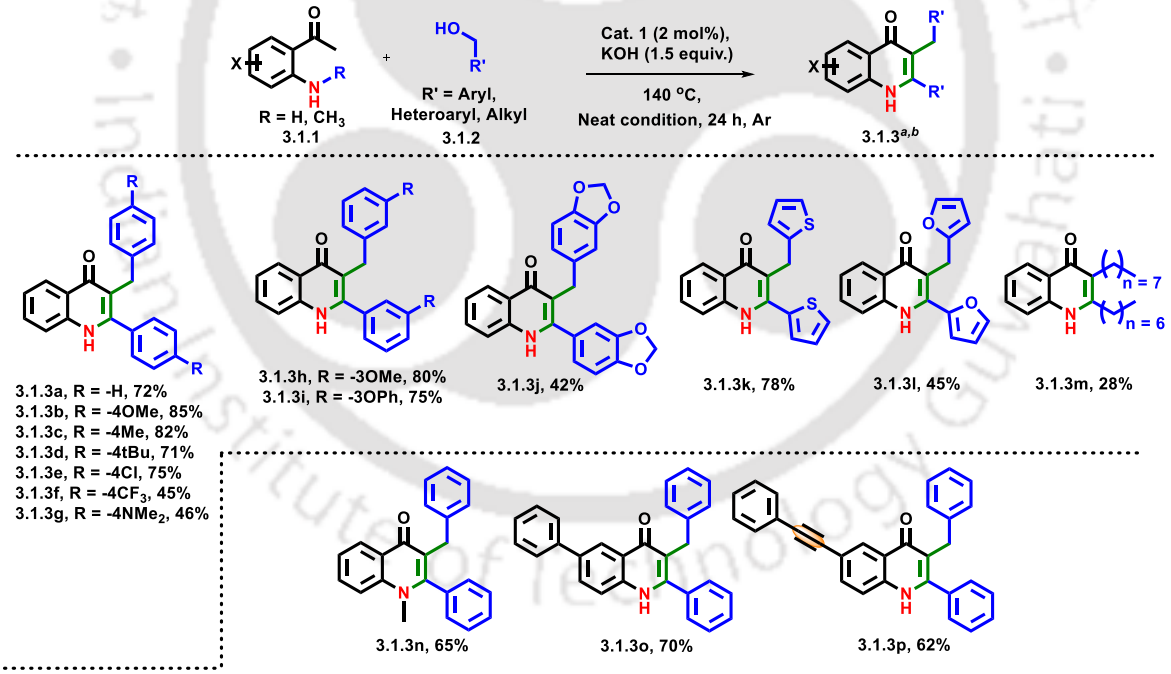
Sl No.	Cat. (mol%)	Base (mmol)	Solvent	Yield of 3a[a,b](%)	Yield of 3a′(%)
1	**Cat. 1**, 2 mol%	KO^{t}Bu (0.5)	Neat	52	-
2	**Cat. 1**, 2 mol%	KOH (0.5)	Neat	65	-
3	**Cat. 1**, 2 mol%	NaOH (0.5)	Neat	25	-
4	**Cat. 1**, 2 mol%	NaO^{t}Bu (0.5)	Neat	32	-
5[c]	**Cat. 1**, 2 mol%	K_2CO_3 (0.5)	Neat	-	55
6	**Cat. 1**, 2 mol%	Cs_2CO_3 (0.5)	Neat	41	-
7	**Cat. 1**, 2 mol%	**KOH (0.75)**	**Neat**	**72**	-
8	**Cat. 1**, 2 mol%	KOH (1.0)	Neat	73	-
9[d]	**Cat. 1**, 2 mol%	KOH (0.75)	Neat	45	-
10	**Cat. 1**, 1 mol%	KOH (0.75)	Neat	45	-
11	**Cat. 1**, 2 mol%	KOH (0.75)	Toluene	35	-
12	**Cat. 1**, 2 mol%	KOH (0.75)	Dioxane	17	-
13	**Cat. 1**, 2 mol%	KOH (0.75)	Xylene	33	-
14	**Cat. 1**, 2 mol%	KOH (0.75)	^{t}Amyl alcohol	55	-
15	-	KOH (0.75)	Neat	15	-
16	**Cat. 2**, 2 mol%	KOH (0.75)	Neat	32	-
17	**Cat. 3**, 2 mol%	KOH (0.75)	Neat	55	-
18[e]	**Cat. 1**, 2 mol%	KOH (0.75)	Neat	42	-

[a] Reaction conditions: **1a** (0.5 mmol), **2a** (2.0 mmol), **Cat.** (1 - 2 mol%), KOH (0.5 - 1.0 mmol), solvent (0 - 2 mL), at 140 °C of a preheated oil bath for 24 h in a 15 mL Schlenk tube under Ar. [b] Isolated yield. [c] **1a** (0.5 mmol), **2a** (1.0 mmol). [d] Under O_2.

comparison to **Cat. 1 (Table 1, entries 16 and 17)**. In the absence of a catalyst, the conversion towards **3.1.3a** is insignificant (**Table 1**, **entry 15**).

3.3.2. Substrate scope of 2, 3-disubstituted 4-quinolones:

After optimization, the developed protocol was applied to various 2′-aminoacetophenones and primary alcohols to afford a wide range of 2,3 disubstituted 4-quinolone derivatives. The reactions of 4-substituted and 3-substituted benzyl alcohols with varying electron donating (-OMe, -Me, -NMe_2, etc.) and electron-withdrawing (-Cl, -CF_3) functional groups gave the desired product selectively **3.1.3a-3.1.3i** in good to excellent yield (45 - 85%) (Scheme **3.9**). Heterocyclic alcohols like 2-thiophene methanol (**3.1.3k**, Scheme **3.9**) responded well, delivering the final product with a 78% yield. In contrast, furfural alcohol (**3.1.3l**, Scheme **3.9**) resulted in a moderate yield. Aliphatic alcohols gave only 28% yield of **3.1.3m** as this tends to form 3-substituted quinoline.[17] Various functionally diverse 2′-aminoacetophenones also furnish good yields of the desired heterocycle (**3.1.3n-3.1.3p**).

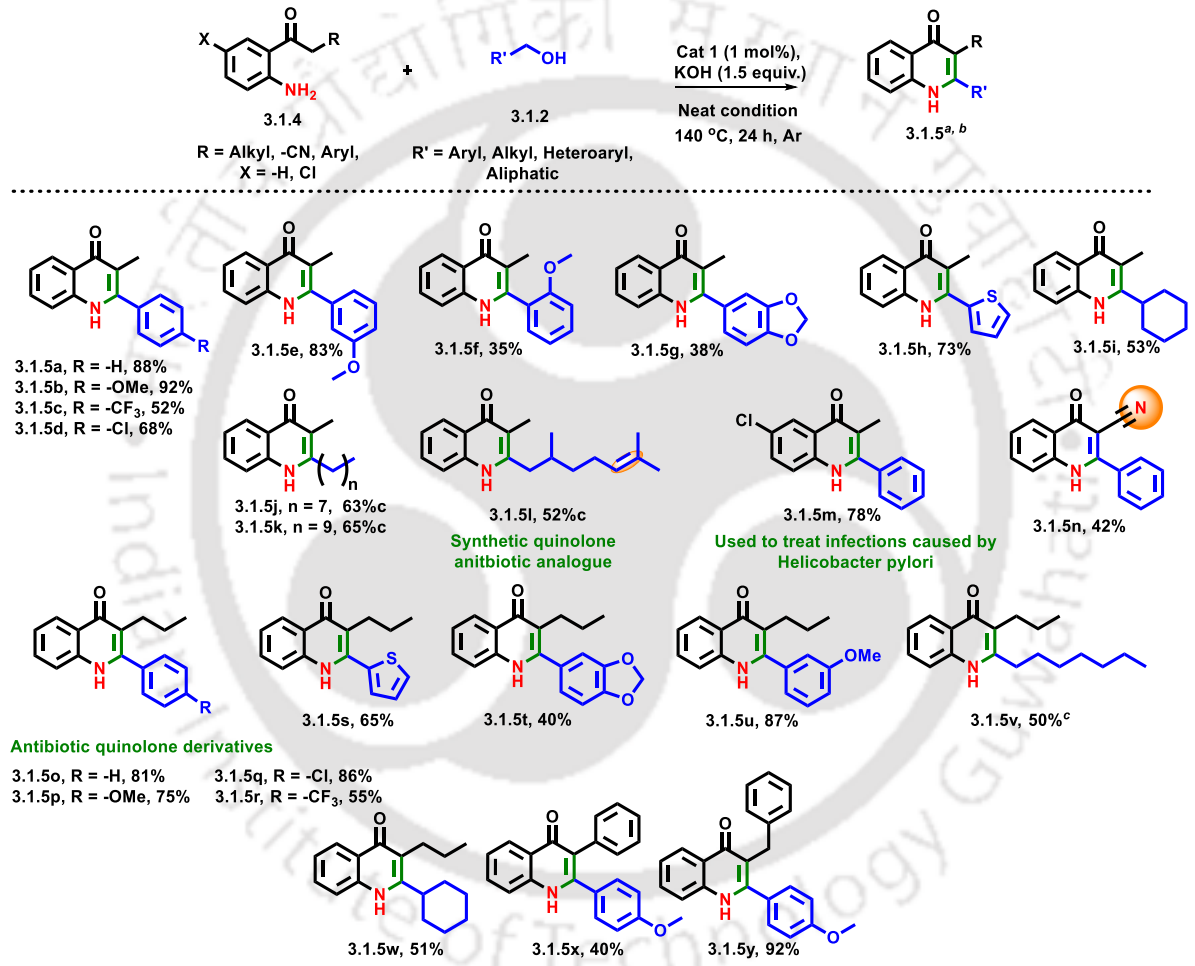


[a]Reaction conditions: 2'-Aminoacetophenone, **3.1.1** (0.5 mmol), alcohol, **3.1.2** (2.0 mmol). Cat. **1** (2 mol%), KOH (1.5 equiv), Neat condition, 140 °C, Ar, 24h. [b]Isolated yield.

Scheme 3.9. Synthesis of 4-quinolones from various alcohols and substituted 2′-aminoacetophenones.

3.3.3. Scope of 2′-amino aryl ketones:

To expand the applicability of our reaction, functionally diverse α-alkylated 2'-aminoacetophenone-based derivatives were employed (**Scheme 3.10**). Apart from evaluating the scope of traditional benzylic alcohols with groups like -OMe, -Me, and halide functionalities (-CF_3, -Cl), here we primarily focused on evaluating thermodynamically more challenging aliphatic alcohols.



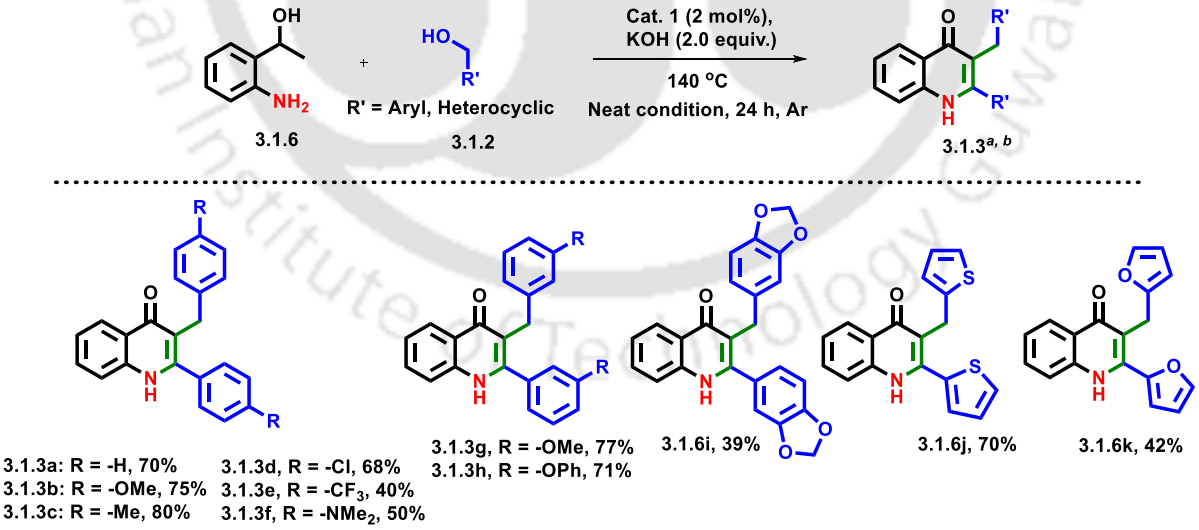
[a] Reaction conditions: 2'-amino aryl ketone, **3.1.4** (0.5 mmol), alcohol, **3.1.2** (1.0 mmol). Cat. 1 (1 mol%), KOH (1.5 equiv.), Neat condition, 140 °C, Ar, 24 h. [b]Isolated yield. [c]Alcohol (2 mmol), Cat. 1 (2 mol%), KOH (2.0 equiv.)

Scheme 3.10. Synthesis of 2,3-disubstituted 4-quinolones from various alcohols and α-alkylated 2'-aminoacetophenones

Interestingly, cyclohexyl methanol (**3.1.5i**), octanol (**3.1.5j**) and decanol (**3.1.5k**) went through smooth dehydrogenative transformations and delivered the expected product in moderate yield. However, an excess amount of alcohol is required in these cases. A natural monoterpenoid, citronellol was chemoselectively converted and gave the targeted product in good yield (**3.1.5l**). In addition, we synthesized a biologically active compound (**3.1.5m),** which is used to treat infections in the stomach caused by the bacteria Helicobacter pylori.[18] Apart from that, functional group like –CN (**3.1.5n**) is well tolerated in our reaction system and afforded the expected product in modest yield. Next, we explored 2'-aminobutyrophenone moiety-based 4-quinolone derivatives, which are potent antibiotics.[2] Unfortunately, our methodology failed to utilize thermodynamically more challenging substrates like MeOH and EtOH. Nevertheless, with 1-(2-aminophenyl)-3-phenylpropan-1-one (**5, R = -CH_2CH_2Ph**), we successfully prepared a differently substituted quinolone and the yield was excellent (**3.1.5y, Scheme 3.10**).

3.3.4. Substrate scope of 2, 3-disubstituted 4-quinolones from 2'-amino phenylethan-1-ols:

Next, we were curious to investigate the applicability of our synthetic methodology towards the coupling of 2'-amino phenylethan-1-ol, **3.1.6,** and various functionally diverse



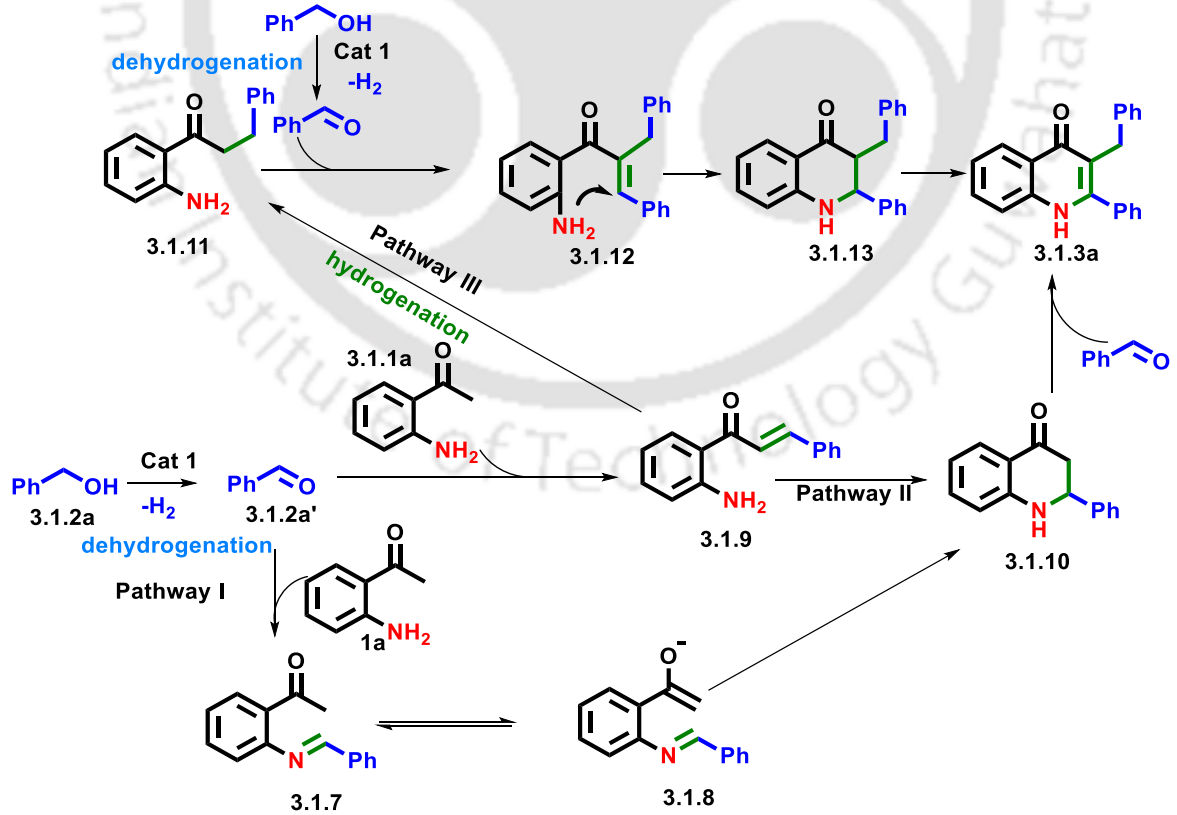
[a]Reaction conditions: 2'-aminophenylethan-1-ol, **3.1.6** (0.5 mmol), alcohol, **3.1.2** (2.0 mmol). Cat. 1 (2 mol%), KOH (2.0 equiv), Neat condition, 140 °C, Ar, 24h. [b]Isolated yield.

Scheme 3.11. Synthesis of 4-quinolones from substituted benzyl alcohols and 1-(2-aminophenyl)ethan-1-ol

benzyl alcohols, which necessitates dehydrogenation of both substrates and is hence challenging. A slight increase in base loading is necessary to get the best result (**Scheme 3.11**).

3.4. Mechanism of the reaction:

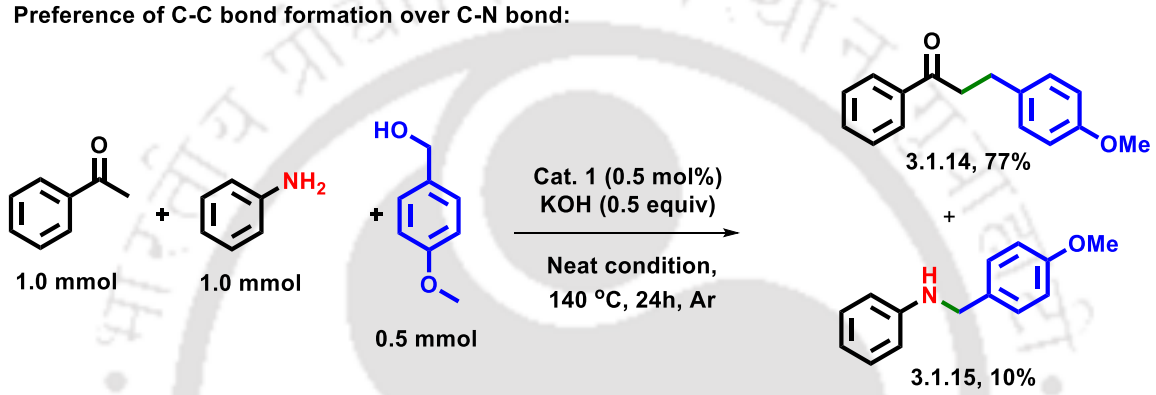
For this multistep dehydrogenative synthesis of 2,3-disubstituted 4-quinolones, three possible mechanistic pathways are proposed, which are depicted in scheme **3.12**. At the outset, the catalyst dehydrogenates benzyl alcohol to benzaldehyde (Scheme **3.12**). In pathway **I**, first benzaldehyde undergoes condensation with the amine to form imine, which via Mannich-type cyclization and further condensation with aldehyde lead to the formation of 2,3-disubstituted 4-quinolones. In pathway **II**, the formed aldehyde will undergo base catalyzed Claisen-Schmidt condensation to form the chalcone intermediate **3.1.9**, which on further cyclization produces 2- substituted 2,3-dihydro-4-quinolones, **3.1.10**. This intermediate **3.1.10** may undergo a condensation reaction with benzaldehyde to form the target product. Another possibility is the transformation of chalcone intermediate **3.1.9** to form intermediate **3.1.11,** via transfer hydrogenation, which upon condensation with *in situ* formed aldehyde and Aza-Michael type reaction eventually can form product **3.1.3a** (Scheme **3.12**).



Scheme 3.12. Plausible Mechanism

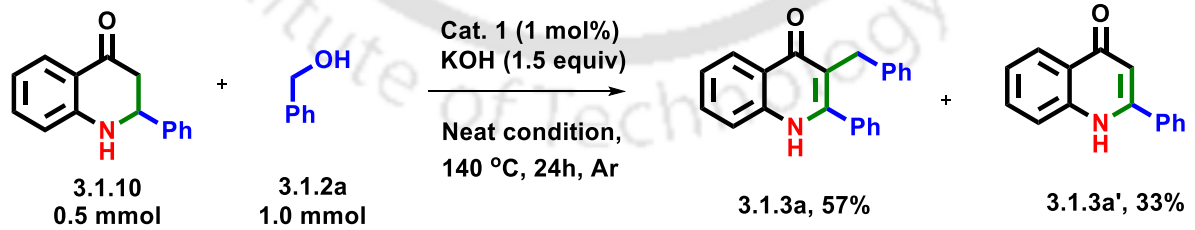
3.5. Mechanistic investigation:

To prove the mechanism, several control experiments were carried out (Scheme 3.12). Initially, the selectivity towards borrowing hydrogen-mediated C-N and C-C bond formation was examined. Thus, when 4-methoxy benzyl alcohol was reacted with the equimolar mixture of aniline and acetophenone, high selectivity was observed toward C-C bond formation and **3.1.14** was obtained in 77% yield (**Scheme 3.12.1**). This underpins the pathway **I** via carbon-nitrogen bond formation is less favorable under the optimum reaction condition.



Scheme 3.12.1. Control experiment 1.

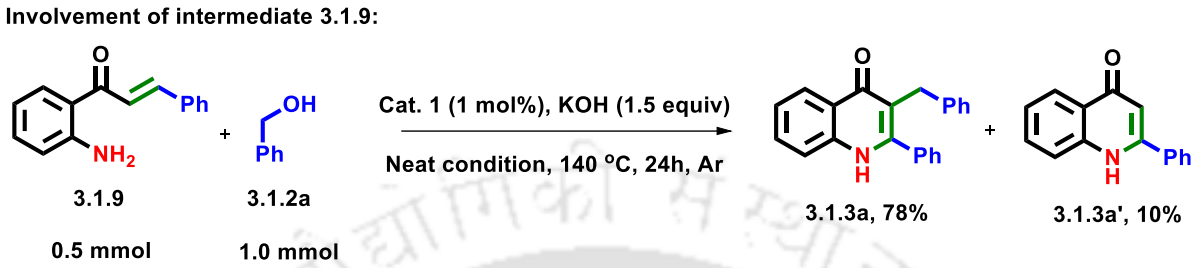
When 2-substituted dihydro quinolone intermediate **3.1.10** was reacted with benzyl alcohol **3.1.2a**, a mixture of 2,3-disubstituted quinolone **3.1.3a** (57%) and 2-substituted quinolone **3.1.3a′** (33%) was formed (**Scheme 3.12.2).** However, under the optimized reaction conditions formation of **3.1.3a′** was not detected. From this result, we can conclude that intermediate **3.1.10** is not involved in the reaction system.



Scheme 3.12.2. Control experiment 2.

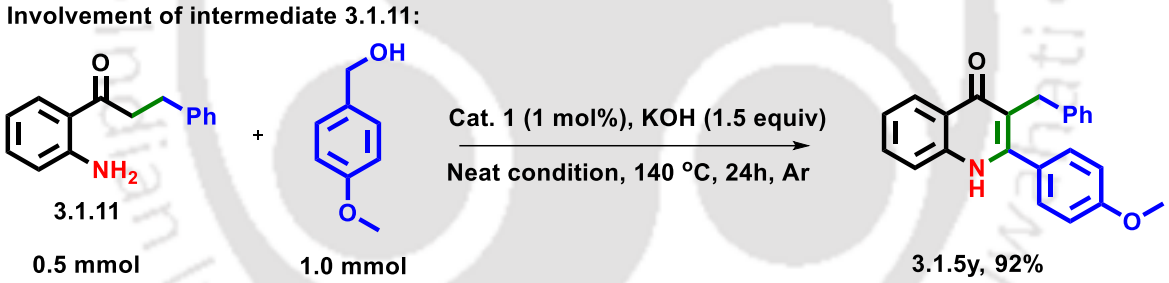
When intermediate chalcone **3.1.9** (**Scheme 3.12.3**) was reacted with primary alcohols **3.1.2a**, the desired 2,3-disubstituted quinolone **3.1.3a** was isolated in a 78% yield**.** Apart from that, a slight amount of compound **3.1.3a′** was also detected. This underpins that intermediate **3.1.9** could be one of the key intermediates of the reaction. The slight production of compound

3.1.3a′ i.e., 2-substituted quinolone might be due to the initial high concentration of the chalcone intermediate, which undergoes annulation to form intermediate **3.1.10** and eventually converts into **3.1.3a′**. So, the rapid conversion of chalcone **3.1.9** to intermediate **3.1.11** i.e., rapid C-C alkylation is very much important for the successful production of compound **3.1.3a**.



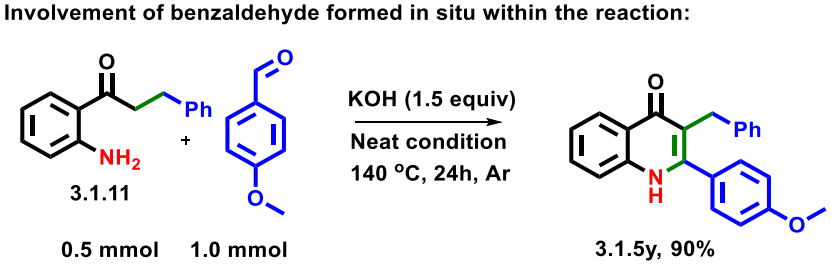
Scheme 3.12.3. Control experiment 3.

Next, when *α*-alkylated 2′-aminoacetophone was treated with (**Scheme 3.13**) benzylic alcohol under our standard reaction condition, it results in the formation of compound **3.1.5y** selectively, which proves that only reaction pathway **III** is feasible.



Scheme 3.12.4. Control experiment 4.

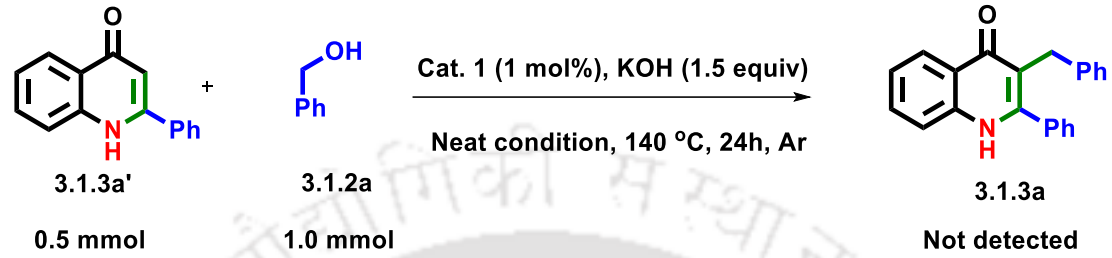
Later, when intermediate **3.1.11** was treated with benzaldehyde **3.1.2a′**, in the absence of catalyst the target product **3.1.5y** was obtained in 90% yield. Finally, the evolved H_2 was detected by GC analysis.



Scheme 3.12.5. Control experiment 5.

In control experiment 6, compound **3.1.3a′** was treated with benzyl alcohol in our optimized reaction condition and the target product was not detected (Control experiment 6).

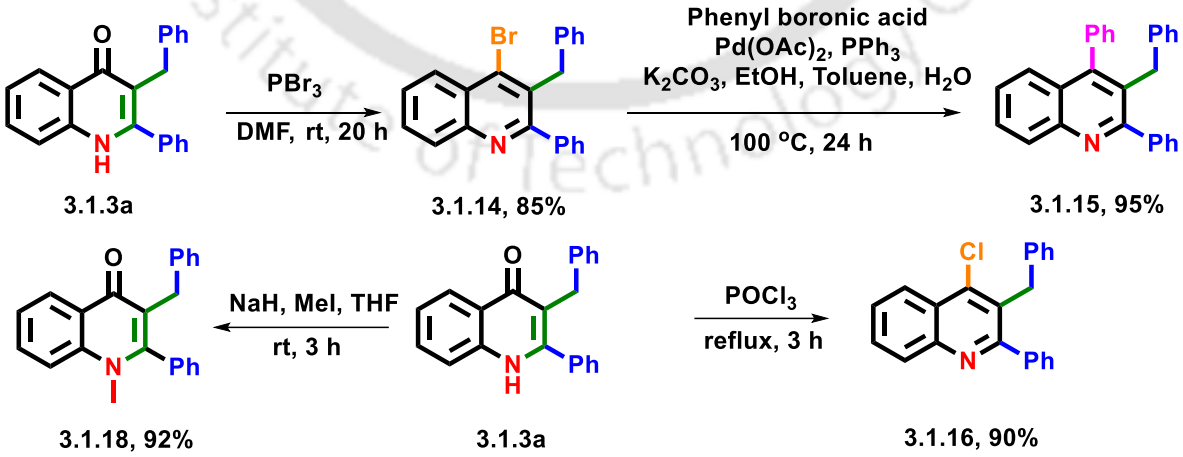
Eliminating the involvement of intermediate 3.1.3a':



Scheme 3.12.6. Control experiment 6.

3.6. Post-synthetic modification:

To demonstrate the synthetic potential of the developed method, we tried to convert 4-quinolone products **3.1.3a** to various quinoline derivatives via functionalization of the ketone moiety at position **3.1.4** (**Scheme 3.14**). Halogenation with PBr_3 and $POCl_3$ provided the corresponding 4-haloquinolones **3.1.14** and **3.1.16**, respectively. Suzuki coupling introduced a phenyl group at position **3.1.4**, and 4-phenyl quinoline **3.1.15** was synthesized. In addition, the position of N - H was substituted directly with iodomethane in the presence of NaH as a base and resulted in N-Methylated quinolones in high yield **3.1.16**.



Scheme 3.13. Post synthetic modification.

3.7. Conclusion:

In conclusion, we have demonstrated the first dehydrogenative annulation between alcohol and 2-amino phenyl ketone/alcohol for the synthesis of 4-quinolone. A wide range of substrate scope and diverse chemical transformation of 3-benzyl-2-phenylquinolin-4*(1H)*-one and related analogs were demonstrated to highlight the synthetic potential of the developed method. A systematic mechanistic investigation revealed that the reaction proceed via a C-alkylation-Aldol condensation-annulation sequence.

3.8. Experimental sections:

3.8.1. General Information:

Unless otherwise mentioned, all chemicals were purchased from common commercial sources and used as received. $RuCl_2(PPh_3)_3$ was purchased from Sigma-Aldrich. All solvents were dried by standard procedure.[19] Solvents such as toluene were pre-dried using CaH_2 over Na with a benzophenone indicator. The catalyst preparation was carried out under an argon atmosphere with freshly distilled dry THF or dichloromethane. All catalytic reactions were carried out under an argon atmosphere using dry glassware and standard syringe/septa techniques. Bruker Avance III 600, 500, and 400 spectrometers were used to record ^{1}H, ^{13}C NMR, and ^{31}P NMR respectively. Chemical shifts (δ) are reported in ppm downfield from tetramethylsilane; spin-spin coupling constants (*J*) are expressed in Hz and other data are reported as follows: s = singlet, d = doublet, t = triplet, m = multiplet, q = quartet, and br s = broad singlet. Column chromatography was done with SRL silica gel 100-200 mesh. Analytical thin layer chromatography (TLC) was carried out on silica gel plates (silica gel 60 F254), that were visualized by exposure to ultraviolet light and an aqueous solution of *p*-anisaldehyde.

3.8.2. Experimental procedures:

3.8.2.1. General procedure for the synthesis of 4-quinolones from various alcohols and 2′-aminoacetophenones:

To a 15 ml schelnk tube, 2′-Aminoacetophenone analogue, **3.1.1** (0.5 mmol, 1 equiv.), alcohol, **3.1.2** (2 mmol, 4 equiv.), acridine-based Ru-SNS^2 catalyst, **Cat. 1** (2 mol%), KOH (42 mg, 0.75 mmol, 1.5 equiv.) were added under argon atmosphere. The reaction mixture was heated at 140 °C for 24 h. After cooling to room temperature, ethyl acetate (15 mL) was added and the reaction mixture was passed through a small pad of celite filter and transferred into another flask. The filtrate was then evaporated and the crude product was purified by column chromatography (typically ethyl acetate/petroleum ether as an eluent) using silica to afford a pure product (Scheme **3.9**).

3.8.2.2. General procedure for the synthesis of 4-quinolones from alcohols and functionally diverse 2′-amino aryl ketones-based derivatives:

To a 15 mL schelnk tube, 2'-amino aryl ketones, **3.1.4** (0.5 mmol, 1 equiv.), aryl alcohols, **3.1.2** (1 mmol, 2 equiv.), acridine-based Ru-SNS^2 catalyst, **Cat. 1** (1 mol%), KOH (42 mg, 0.75 mmol, 1.5 equiv.) were added under argon atmosphere. The reaction mixture was heated at 140 °C for 24 h. After cooling to room temperature, ethyl acetate (15 mL) was added and the reaction mixture was passed through a small pad of celite filter and transferred into another flask. The filtrate was then evaporated and the crude product was purified by column chromatography (typically ethyl acetate/petroleum ether as an eluent) using silica to afford a pure product (Scheme **3.10**).

3.8.2.3. General procedure for the synthesis of quinolones from aliphatic alcohols and functionally diverse *α*-alkylated 2'-amino acetophenone based derivatives:

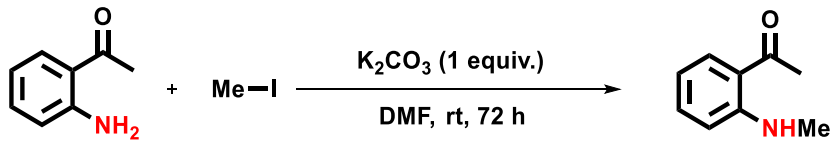
To a 15 mL schelnk tube, 2'-amino aryl ketones, **3.1.4** (0.5 mmol, 1 equiv.), aliphatic alcohols, **3.1.2** (2 mmol, 4 equiv.), acridine-based Ru-SNS^2 catalyst, **Cat. 1** (2 mol%), KOH (56 mg, 1 mmol, 2.0 equiv.) were added under argon atmosphere. The reaction mixture was heated at 140 °C for 24 h. After cooling to room temperature, ethyl acetate (15 mL) was added and the reaction mixture was passed through a small pad of celite filter and transferred into another flask. The filtrate was then evaporated and the crude product was purified by column chromatography (typically ethyl acetate/petroleum ether as an eluent) using silica to afford a pure product (Scheme **3.10**).

3.8.2.4. General procedure for the synthesis of 4-quinolones from substituted benzyl alcohols and 1-(2-aminophenyl)ethan-1-ol:

To a 15 mL schelnk tube, 1-(2-aminophenyl)ethan-1-ol, **3.1.6** (0.5 mmol, 1 equiv.), benzyl alcohol, **3.1.2** (2 mmol, 4 equiv.), acridine-based Ru-SNS[16a] catalyst, **Cat. 1** (2 mol%), KOH (56 mg, 1 mmol, 2.0 equiv.) were added under argon atmosphere. The reaction mixture was heated at 140 °C for 24 h. After cooling to room temperature, ethyl acetate (15 mL) was added and the reaction mixture was passed through a small pad of celite filter and transferred into another flask. The filtrate was then evaporated and the crude product was purified by column chromatography (typically ethyl acetate/petroleum ether as an eluent) using silica to afford a pure product (Scheme **3.11**).

3.8.2.5. Preparation of various starting materials:

3.8.2.5a. Procedure for the synthesis of 1-(2′-(methylamino)phenyl)ethan-1-one (3.1.1n): In a flame-dried 100 mL round bottom flask, 2′-aminoacetophenone (608 mg, 4.5 mmol, 1.0 equiv.) was dissolved in 10 mL dry DMF and K_2CO_3 (622 mg, 4.5 mmol, 1 equiv.) was added to it, and the mixture was stirred for 15 minutes at room temperature (23 °C). Next, methyl iodide (0.28 mL, 4.5 mmol, 1 equiv.) was added dropwise via syringe and the reaction mixture was stirred for 3 days at room temperature (23 °C). After completion of the reaction as monitored by thin-layer chromatography, water was added (15 mL) and the reaction mixture was extracted with ethyl acetate. The combined organic layer was washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by silica gel flash column chromatography to give the expected product in 60% yield (403 mg) using ethyl acetate/petroleum ether as the eluent. The analytical data of the prepared compound matched with reported literature data.[20]

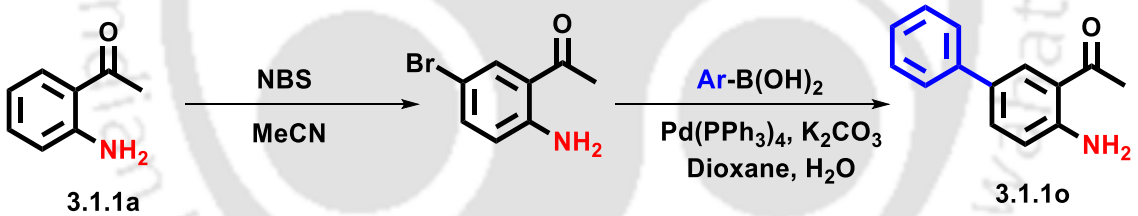


3.1.1a 3.1.1n

3.8.2.5b. Preparation procedure of 1-(4-amino-[1,1'-biphenyl]-3-yl)ethan-1-one (1.1.1o):

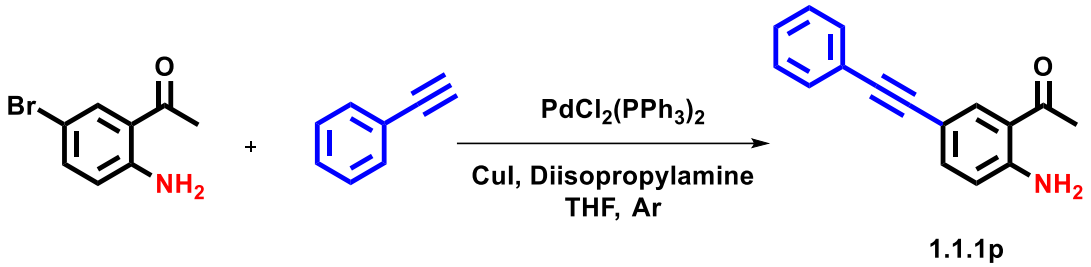
To a 50 mL round-bottom flask was added 1-(2-aminophenyl)ethanone (1.35 g, 10.0 mmol, 10 equiv.) and 10 mL MeCN. N-bromosuccinimide (1.77 g, 10.0 mmol, 10 equiv.) in 10 mL MeCN was added to the solution at 0 °C over 3 min under stirring. The mixture was allowed to warm to room temperature and stirred for 3 h. The solvent was removed in a vacuum and the crude residue was filtered through a short plug of silica (washed with petroleum ether: ethyl acetate = 5: 1). The filtrate was concentrated in a vacuum to afford 1-(2-amino-5-bromophenyl)ethanone as a dark yellow solid (2.08 g, 97 % yield). The product was utilized for the next step without further purification.

To a 100 mL round-bottom, Schlenk bottle was added 1-(2-amino-5-bromophenyl)ethanone (1.07 g, 5.0 mmol, 1.0 equiv.), aryl boronic acid (5.5 mmol, 670 mg, 1.1 equiv.), K_2CO_3 (2.28 g, 16.5 mmol, 3.3 mmol), $Pd(PPh_3)_4$ (58 mg, 0.05 mmol), 14 mL dioxane and 14 mL H_2O. The bottle was evacuated and backfilled with Ar three times. The mixture was stirred at 100 °C for 3 h. Upon the completion of the reaction, the mixture was poured into 50 mL ethyl acetate and the organic layer was separated. The organics were washed with 1 M HCl and brine dried over Na_2SO_4 and concentrated. The residue was purified by flash column chromatography to afford the coupling product (824 mg, 78 % yield).[21]



3.8.2.5c. Preparation procedure of 1-(2-Amino-5-(phenylethynyl)phenyl)ethanone (1p):

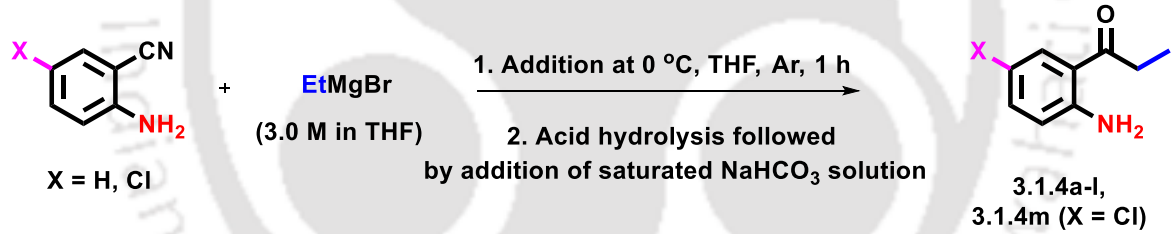
To a round-bottom flask was added 1-(2-amino-5-bromophenyl)ethanone (2.13 g, 10.0 mmol, 1.0 equiv.), ethynylbenzene (1.12 g, 11.0 mmol, 1.1 equiv.), bis(triphenylphosphine)palladium(II) dichloride (281 mg, 0.4 mmol), copper iodide (380 mg, 2.0 mmol), diisopropylamine (5.7 mL, 40 mmol, 4.0 equiv.) and 20 mL THF. The bottle was evacuated and backfilled with Ar three times. The reaction mixture was stirred at room temperature overnight and was allowed to pass through a short plug of silica gel (washed with ethyl acetate/petroleum ether = 1: 1). The filtrate was concentrated in a vacuum and the residue was further purified by flash column chromatography with ethyl acetate/petroleum ether (1:15) to yield the target product as a yellow solid (1.79 g, 76 % yield).[21]



1.1.1p

3.8.2.5d. Preparation procedure of 1-(2-(methylamino)phenyl)ethan-1-one (4a-l, 4m):

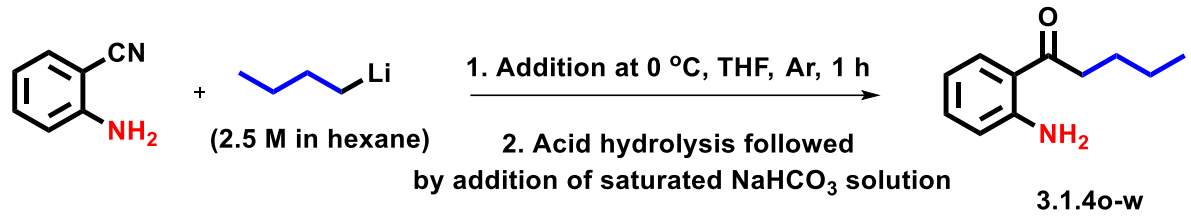
A solution of substituted 2-amino benzonitrile in THF (0.3 M) was stirred at 0 °C. Next, the Grignard reagent (3.0 M, 3.0 equiv.) was slowly added to the mixture. After the completion of the reaction (monitored by TLC), the temperature of the reaction mixture was promoted to room temperature. Later, the reaction mixture was slowly quenched with 6 M HCl and left for overnight imine hydrolysis at room temperature. Next, it was treated with excess saturated aqueous $NaHCO_3$ solution to remove the traces of HCl and extracted three times with ethyl acetate. The combined extracts was washed by brine. The organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Finally, the residue was purified by silica gel column chromatography in ethyl acetate/petroleum ether (1:9).[21]



3.1.4a-l,
3.1.4m (X = Cl)

3.8.2.5e. Preparation procedure of 1-(2-aminophenyl)pentan-1-one (4o-w):

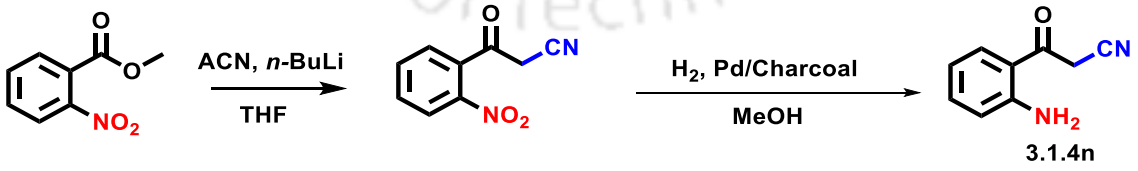
^{n}BuLi (2.5 M in hexane, 30 mmol, 3.0 equiv.) was added slowly to a solution of 2-amino benzonitrile (10 mmol, 1.0 equiv.) in THF (50 mL) at 0 °C under Ar. Afterward, the mixture was stirred for 1 h at 0 °C. After the reaction completion, the reaction mixture was quenched with 1M aqueous HCl at 0 °C. The mixture was extracted with ethyl acetate (3×20 mL) and the combined organic extracts were washed with saturated $NaHCO_3$ solution and brine. Later, it was dried over Na_2SO_4, filtered, and concentrated. It was later purified by flash column chromatography on silica gel with ethyl acetate/petroleum ether (1:15).[21]



3.8.2.5f. Synthesis of 3-(2-aminophenyl)-3-oxopropanenitrile (4n):

Acetonitrile (0.9 mL, 16.6 mmol, 2.0 equiv.) and dry THF (10.0 mL) were added to an oven-dried round bottom flask under argon gas. The mixture was cooled to -78 ℃ and then, 2.0 M ^{n}BuLi in hexane (8.5 mL, 16.6 mmol, 2.0 equiv.) was added to a stirred mixture. After 1 h, methyl-2-nitrobenzoate (1.2 mL, 8.3 mmol, 1.0 equiv.) in THF (5.0 mL) was added dropwise for 15 min by a syringe pump. The reaction mixture was stirred for 1 h, and then stirred for a further 2 h at -45 ℃. Upon the completion of the reaction, the mixture was quenched saturated solution of NH_4Cl (25 mL). The mixture was extracted with ethyl acetate (4 x 40 mL). The organic layer was washed with brine (40 mL), dried over anhydrous Na_2SO_4, concentrated, and then, purified by flash column chromatography on silica gel using hexane and ethyl acetate (5:1 to 3:1). 3-(2-nitrophenyl)-3-oxopropanenitrile was obtained as a red solid (1.1 g, 55% yield).

3-(2-nitrophenyl)-3-oxopropanenitrile (800 mg, 4.2 mmol, 1.0 equiv.), 10% Pd/C (156 mg, 1.5 mmol, 0.35 equiv.) and ethyl acetate (18.0 mL) were added to an oven-dried round bottom flask under argon gas. A reaction vessel was charged with H_2 balloon and stirred for 3 h at room temperature. Upon the completion of the reaction, the mixture was filtered on celite using DCM. A mixture was concentrated and then, purified by flash column chromatography on silica gel using ethyl acetate/petroleum ether (1:3). The target product was obtained as pale yellow solid (560 mg, 64% yield).[12]

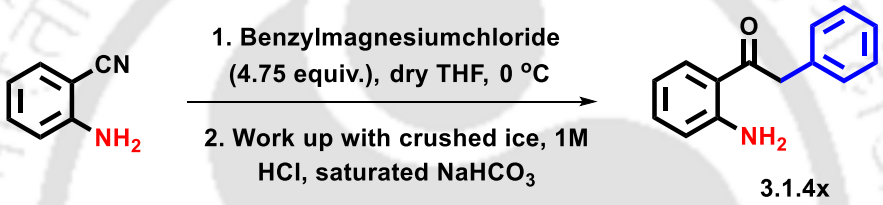


3.8.2.5g. Preparation procedure of 2-phenyl-2,3-dihydroquinolin-4*(1H)*-one (4x):

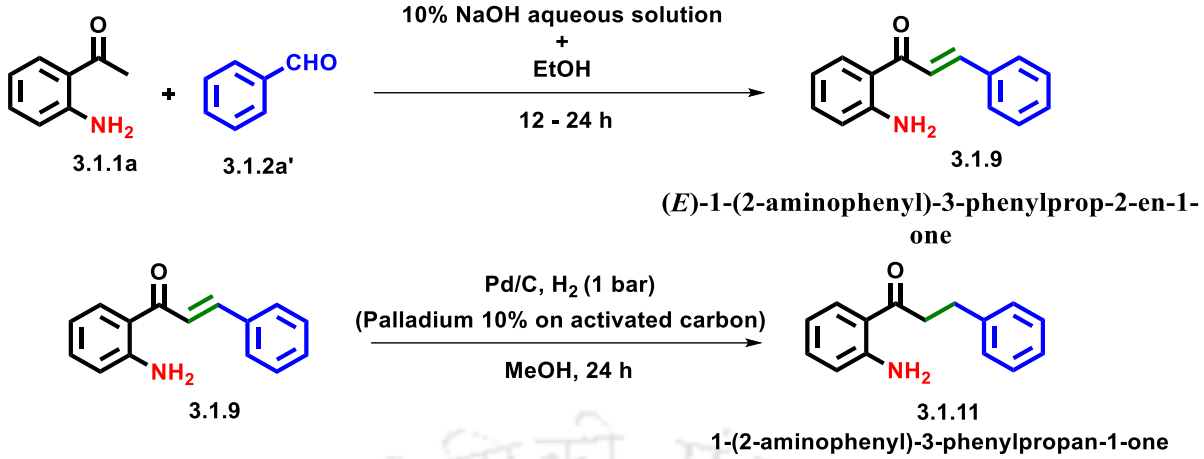
Magnesium turnings (4.75 equiv.), iodine crystalline (1 piece, catalytic amount), and dry THF

(1.0 M) were added to an oven-dried 2-necked round bottom flask under argon gas. Benzyl halide (4.75 equiv.) was added to a stirred mixture and then, the reaction mixture was heated to 60 °C using an oil bath and stirred for 1.5 h. After the reaction mixture was warmed to room temperature, a freshly prepared Grignard was directly used in the next reaction.

Next, 1.4 M benzylmagnesium chloride in THF (47.0 mL, 66.5 mmol, 4.75 equiv.) was added drop wise to a solution of 2-aminobenzonitrile (1.6 g, 14.0 mmol, 1.0 equiv.) in dry THF (0.5 M) for 1 h using syringe pump. The reaction was allowed to stir overnight at room temperature. Upon the completion of the reaction, the mixture was poured into crushed ice and 1 M HCl was added (adjusted with pH 1). After neutralization using sat. $NaHCO_3$, the mixture was extracted with ethyl acetate (2 x 40 mL). The organic layer was washed with brine (40 mL), dried over anhydrous Na_2SO_4, concentrated and then, it was purified by silica gel column chromatography, obtained as a white solid (1.48 g, 50% yield).[21]

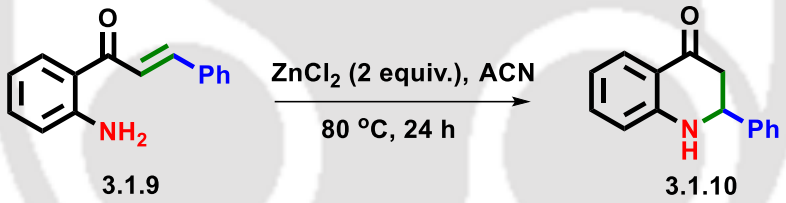


3.8.2.5h. Preparation procedure of (*E*)-1-(2-aminophenyl)-3-phenylprop-2-en-1-one 1-(2-aminophenyl)-3-phenylpropan-1-one (9 and 11): To a 100 mL round-bottom flask were added 2′-amino acetophenone (1.2 mL, 10 mmol, 1.0 equiv.), benzaldehyde (1.1 mL, 11 mmol, 1.1 equiv.), 10% NaOH aqueous solution (40 mL), and EtOH (10 mL). The reaction mixture was stirred for another 12−24 h at room temperature. After the reaction was completed, the mixture was solid recrystallized in EtOH and afforded **(*E*)-1-(2-aminophenyl)-3-phenylprop-2-en-1-one** in good yield. Later, it was reduced by H_2 (balloon) and Pd/C (Palladium 10% on activated carbon, 100 mg) in methanol to afford 1-**(2-aminophenyl)-3-phenylpropan-1-one.**[22,23]



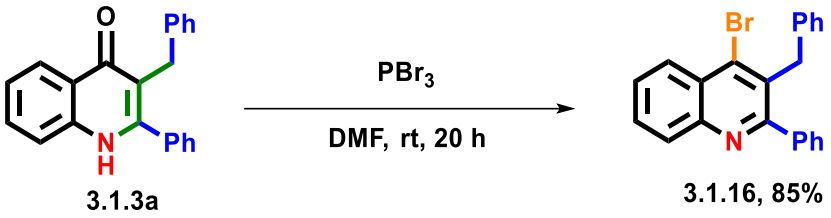
3.8.2.5i. Preparation procedure of 2-phenyl-2,3-dihydroquinolin-4*(1H)*-one (10):

(*E*)-1-(2-aminophenyl)-3-phenylprop-2-en-1-one **9** (446 mg, 2 mmol, 1.0 equiv.) was taken in a 15 mL schlenk tube and was refluxed with 2 equiv. of $ZnCl_2$ (545 mg, 4 mmol) in ACN solvent for 24 h. Later, the crude reaction mixture was purified by silica gel column chromatography using ethyl acetate/petroleum ether (3:7). The target product was obtained as a yellow solid (312 mg, 70% yield). [24]



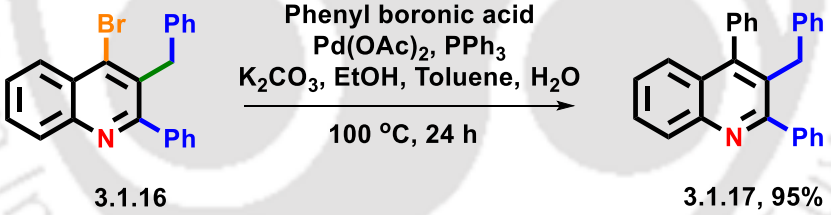
3.8.6. Post synthetic modification:

3.8.6a. Preparation procedure of 3-benzyl-4-bromo-2-phenylquinoline: 3.1.3a (311 mg, 1.0 mmol, 1.0 equiv.) and dry DMF (5 mL) was added to an oven-dried round bottom flask under argon gas. A mixture was cooled to 0 °C and then, PBr_3 (0.192 mL, 2.0 mmol, 2.0 equiv.) was added slowly to a stirred mixture. The reaction mixture was warmed to room temperature and stirred overnight. The mixture was monitored by TLC and quenched with sat. $NaHCO_3$ to make a mixture neutral. The mixture was extracted with DCM (2 x 15 mL). The organic layer was washed with H_2O (2 x 15 mL) and brine (15 mL), dried over anhydrous Na_2SO_4, concentrated, and then residues were purified by flash column chromatography on silica gel, using ethyl acetate/petroleum ether (1:9). **3.1.16** was obtained as a white solid (318 mg, 85% yield).[12]



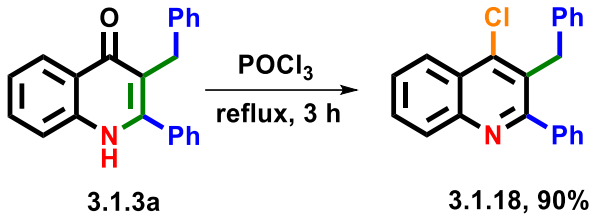
3.8.6b. Preparation procedure of 3-benzyl-4-bromo-2-phenylquinoline:

3.1.16 (186 mg, 0.5 mmol, 1.0 equiv.), phenyl boronic acid (92 mg, 8.0 mmol, 8.0 equiv.), anhydrous K_2CO_3 (298 mg, 2.0 mmol, 4.0 equiv.), PPh_3 (19 mg, 0.075 mmol, 15 mol%), $Pd(OAc)_2$ (6 mg, 0.025 mmol, 5 mol%), H_2O (1.0 mL), EtOH (0.5 mL) and toluene (2.0 mL) were added to an oven-dried Borosilicate Glass Tube. The reaction vessel was charged with argon and sealed. The mixture was heated to 100 °C using an oil bath and stirred for 24 h. The mixture was diluted with DCM (5.0 mL) and H_2O (5.0 mL), and extracted with DCM (2 x 15.0 mL). The organic layer was washed with H_2O (10.0 mL) and brine (10.0 mL), dried over anhydrous Na_2SO_4, concentrated, and then residues were purified by flash column chromatography on silica gel using ethyl acetate/petroleum ether (1:9). **3.1.17** was obtained as a white solid (176 mg, 95% yield).[12]



3.8.6c. Preparation procedure of 3-benzyl-4-bromo-2-phenyl quinoline:

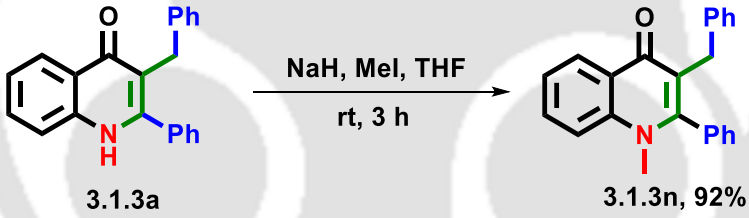
3.1.3a (311 mg, 1.0 mmol, 1.0 equiv.) and $POCl_3$ (0.753 mL, 8.0 mmol, 8.0 equiv.) were added to an oven-dried round bottom flask. The reaction vessel was equipped with a reflux condenser, charged with argon gas, and stirred for 3 h at 80 °C using an oil bath. The mixture was monitored by TLC and quenched with sat. $NaHCO_3$ to make a mixture neutral. The mixture was extracted with DCM (2 x 15 mL). The organic layer was washed with H_2O (2 x 15 mL) and brine (15 mL), dried over anhydrous Mg_2SO_4, concentrated, and then residues were purified by flash column chromatography on silica gel, using ethyl acetate/petroleum ether (1:9). **3.1.18** was obtained as a yellow solid (296 mg, 90% yield).[12]



3.1.3a 3.1.18, 90%

3.8.6d. Preparation procedure of 3-benzyl-4-bromo-2-phenyl quinoline:

3.1.3a (155 mg, 0.5 mmol, 1.0 equiv.) and dry THF (10.0 mL) were added to an oven-dried round bottom flask. The mixture was cooled to 0 ℃ and stirred for 10 min, and then NaH (40 mg, 1.0 mmol, 2.0 equiv.) was added portion-wise for 15 min. Iodomethane (94.0 µL, 1.5 mmol, 3.0 equiv.) was added to the mixture and the mixture was stirred for 3 h at room temperature. The mixture was quenched with H_2O (10 mL) and extracted with ethyl acetate (2 x 20 mL). The organic layer was washed with brine (10 mL), dried over anhydrous Na_2SO_4, concentrated, and then residues were purified by flash column chromatography on silica gel using ethyl acetate/petroleum ether (1:1). **3.1.3n** was obtained as a yellow solid (149 mg, 92% yield).[12]



3.1.3a 3.1.3n, 92%

3.8.3. Mechanistic investigation:

Control experiment 1:

To a 15 mL schlenk tube, acetophenone (120 mg, 1.0 mmol, 2.0 equiv.), aniline (93 mg, 1.0 mmol, 2.0 equiv.), 4-methoxybenzyl alcohol (69 mg, 0.5 mmol, 1.0 equiv.), acridine based Ru-SNS catalyst (0.5 mol%) and KOH (28 mg, 0.5 mmol, 1.0 equiv.) was added under an atmosphere of Ar. The reaction mixture was then heated at 140 °C with stirring for 24 h. After cooling, ethyl acetate (5 mL) was added and the crude mixture was passed through a short plug of celite filter. The filtrate was then evaporated and the crude product was purified by column chromatography using ethyl acetate/petroleum ether. **3.1.14** was obtained as a colourless liquid (185 mg, 77%) and **3.1.15** was obtained as a yellow solid (21 mg, 10% yield). (Scheme **3.12.1**)

Control experiment 2:

To a 15 mL schlenk tube, 2-phenyl-2,3-dihydroquinolin-4*(1H)*-one, **3.1.10** (111 mg, 0.5 mmol, 1.0 equiv.), benzyl alcohol (108 mg, 1 mmol, 2.0 equiv.), acridine based Ru-SNS catalyst (1 mol%) and KOH (42 mg, 0.75 mmol, 1.5 equiv.) were added under an atmosphere of Ar. The reaction mixture was then heated at 140 °C with stirring for 24 h. After cooling, ethyl acetate (5 mL) was added and the crude mixture was passed through a short plug of celite filter. The filtrate was then evaporated and the crude product was purified by column chromatography using ethyl acetate/petroleum ether (ranging from 2:3 to 9:1). **3.1.3a** was obtained as a white solid (88 mg, 57% yield) and **3.1.3a′** was obtained as a grey solid (36 mg, 33% yield). (Scheme **3.12.2**)

Control experiment 3:

To a 15 mL schlenk tube, (*E*)-1-(2-aminophenyl)-3-phenylprop-2-en-1-one, **3.1.9** (111 mg, 0.5 mmol, 1.0 equiv.), benzyl alcohol (108 mg, 1 mmol, 2.0 equiv.), acridine based Ru-SNS catalyst (1 mol%) and KOH (42 mg, 0.75 mmol, 1.5 equiv.) were added under an atmosphere of Ar. The reaction mixture was then heated at 140 °C with stirring for 24 h. After cooling, ethyl acetate (5 mL) was added and the crude mixture was passed through a short plug of celite filter. The filtrate was then evaporated and the crude product was purified by column chromatography using ethyl acetate/petroleum ether (ranging from 2:3 to 9:1). **3.1.3a** was obtained as a white solid (121 mg, 78% yield) and **3.1.3a′** was obtained as a grey solid (11 mg, 10% yield). (Scheme **3.12.3**)

Control experiment 4:

To a 15 mL schlenk tube, 1-(2-aminophenyl)-3-phenylpropan-1-one, **3.1.11** (112 mg, 0.5 mmol, 1.0 equiv.), 4-methoxybenzyl alcohol (138 mg, 1 mmol, 2.0 equiv.), acridine based Ru-SNS catalyst (1 mol%) and KOH (42 mg, 0.75 mmol, 1.5 equiv.) were added under an atmosphere of Ar. The reaction mixture was then heated at 140 °C with stirring for 24 h. After cooling, ethyl acetate (5 mL) was added and the crude mixture was passed through a short plug of celite filter. The filtrate was then evaporated and the crude product was purified by column chromatography using ethyl acetate/petroleum ether (4:1). **3.1.5y** was obtained as a white solid (157 mg, 92% yield). (Scheme **3.12.4**)

Control experiment 5:

To a 15 mL schlenk tube, 1-(2-aminophenyl)-3-phenylpropan-1-one, **3.1.11** (112 mg, 0.5 mmol, 1.0 equiv.), 4-methoxy benzaldehyde (136 mg, 1 mmol, 2.0 equiv.) and KOH (42 mg,

0.75 mmol, 1.5 equiv.) were added under an atmosphere of Ar. The reaction mixture was then heated at 140 °C with stirring for 24 h. After cooling, ethyl acetate (5 mL) was added and the crude mixture was passed through a short plug of celite filter. The filtrate was then evaporated and the crude product was purified by column chromatography using ethyl acetate/petroleum ether (4:1). **3.1.5y** was obtained as a white solid (153 mg, 90% yield). (Scheme **3.12.5**)

Control experiment 6:

To a 15 mL schlenk tube, 2-phenyl quinolin-4*(1H)*-one (110 mg, 0.5 mmol, 1.0 equiv.), benzyl alcohol (108 mg, 1 mmol, 2.0 equiv.), **Cat. 1** (1 mol%) and KOH (42 mg, 0.75 mmol, 1.5 equiv.) were added under an atmosphere of Ar. The reaction mixture was then heated at 140 °C with stirring for 24 h. After cooling, ethyl acetate (5 mL) was added and the crude mixture was passed through a short plug of celite filter and analyzed with TLC. The target product was not detected (Scheme **3.12.6**).

Control experiment 7:

Ruthenium catalyzed dehydrogenation of alcohol and detection of evolved hydrogen gas:

To an oven-dried 100 mL seal tube, benzyl alcohol (2.0 mmol), 2'-amino acetophenone (0.5 mmol), Cat 1 (2 mol%), and KOH (0.75 mmol) were added under argon. Then the reaction mixture was kept for stirring in a preheated oil bath at 140 °C for the next 24 h. After completion of the reaction, the sealed tube was cooled at 0 °C. Then the evolved gas was syringed out and detected from PerkinElmer Clarus-590 GC instrument using Elite Plot-Q column (30 m length x 530 µm x 20 µm ID) employing the following method:

TCD starting temperature: 40 °C

Oven temperature: 60 °C

Time at starting temperature: 0 min

Hold time: 5 min

Ramp: 28 °C/ min up to 200 °C

Flow rate: 5 mL / min (N_2)

Split ration: 20

Inlet temperature: 40 °C

Detector temperature TCD: 200 °C

The detected gas chromatogram was shown in figure S2 (right).

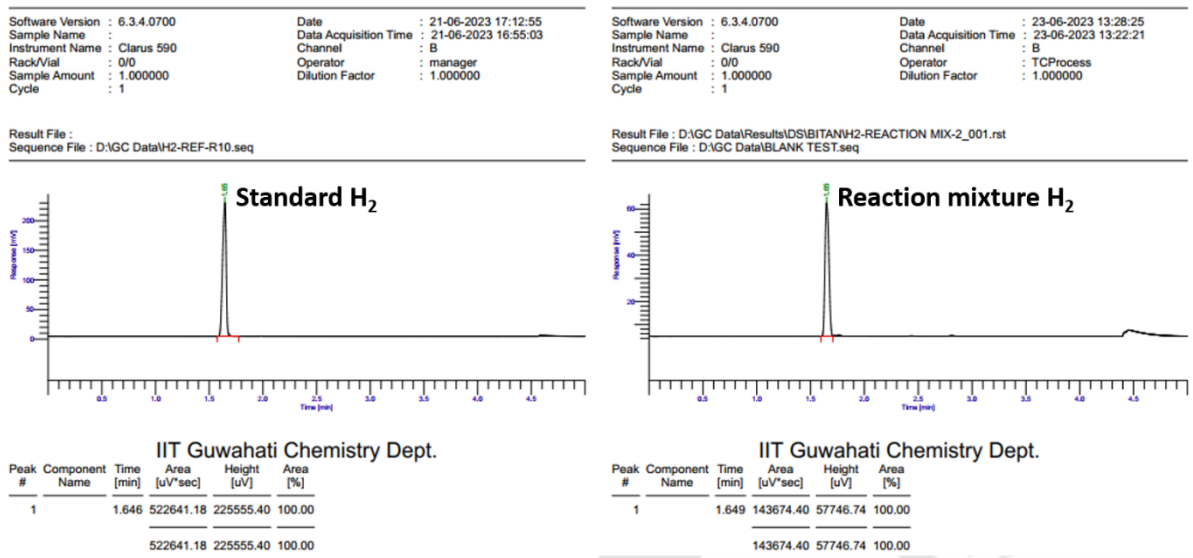
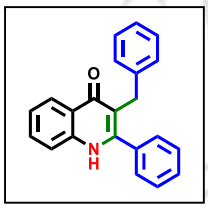


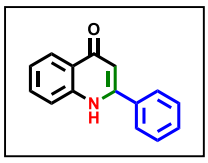
Figure S2. Chromatogram of standard hydrogen gas (left) and evolved hydrogen gas during catalysis (right).

3.9. Characterization data and reports:

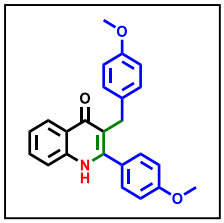
***3-benzyl-2-phenylquinolin-4(1H)-one (3.1.3a)*:** The title compound was isolated as a white solid using silica-gel column chromatography eluting with ethyl acetate/ petroleum ether (2:3), (Yield: 72%), ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.72 (s, 1H), 8.13 (d, J = 8.1 Hz, 1H), 7.66 – 7.62 (m, 2H), 7.54 – 7.50 (m, 3H), 7.44 (d, J = 7.4 Hz, 2H), 7.34 – 7.31 (m, 1H), 7.13 (t, J = 7.4 Hz, 2H), 7.06 (t, J = 7.2 Hz, 1H), 6.95 (d, J = 7.4 Hz, 2H), 3.74 (s, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 181.5, 154.3, 146.7, 144.7, 140.0, 136.7, 134.7, 133.9, 133.7, 133.1, 133.0, 130.5, 130.3, 128.9, 128.1, 123.5, 122.8, 36.3.[25]



2-phenylquinolin-4(1H)-one (3.1.3a'): The title compound was isolated as a grey solid using silica-gel column chromatography eluting with ethyl acetate/petroleum ether (4:1), (Yield: 55%), ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.79 (s, 1H), 8.15 (d, J = 7.6 Hz, 1H), 7.88 – 7.85 (m, 2H), 7.81 (d, J = 8.3 Hz, 1H), 7.70 (t, J = 8.2 Hz, 1H), 7.62 – 7.60 (m, 3H), 7.37 (t, J = 7.5 Hz, 1H), 6.38 (s, 1H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 177.5, 150.5, 141.0, 134.7, 132.3, 130.9, 129.5, 127.9, 125.4, 125.2, 123.7, 119.2, 107.8.[12]

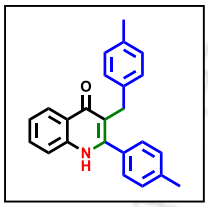


3-(4-methoxybenzyl)-2-(4-methoxyphenyl)quinolin-4(1H)-one (3.1.3b): The title compound



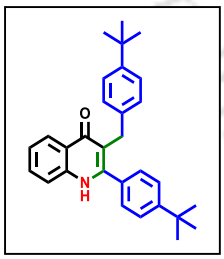
was isolated as a white solid using silica-gel column chromatography eluting with ethyl acetate/ petroleum ether (2:3), (Yield: 85%), ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.55 (s, 1H), 8.05 (d, J = 8.0 Hz, 1H), 7.58 – 7.53 (m, 2H), 7.31 (d, J = 8.6 Hz, 2H), 7.23 (t, J = 7.9 Hz, 1H), 7.00 (d, J = 8.6 Hz, 2H), 6.82 (d, J = 8.5 Hz, 2H), 6.64 (d, J = 8.6 Hz, 2H), 3.75 (s, 3H), 3.62 (s, 2H), 3.59 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 176.8, 160.5, 157.5, 149.3, 140.0, 134.0, 131.8, 130.6, 129.2, 127.6, 125.5, 124.2, 123.2, 118.7, 118.5, 114.3, 113.8, 55.8, 55.3, 30.7. [25]

3-(4-methylbenzyl)-2-(p-tolyl)quinolin-4(1H)-one (3.1.3c): The title compound was isolated



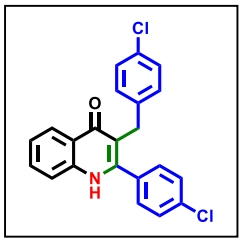
as a white solid using silica-gel column chromatography eluting with ethyl acetate/ petroleum ether (2:3), (Yield: 82%), ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.68 (s, 1H), 8.16 (d, J = 8.1 Hz, 1H), 7.67 (d, J = 3.8 Hz, 2H), 7.37 (s, 5H), 6.99 (d, J = 7.7 Hz, 2H), 6.91 (d, J = 7.7 Hz, 2H), 3.73 (s, 2H), 2.43 (s, 3H), 2.24 (s, 3H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 176.7, 149.5, 140.0, 139.5, 138.9, 134.5, 132.5, 131.8, 129.4, 129.0, 128.9, 128.2, 125.5, 124.2, 123.3, 118.7, 118.2, 31.2, 21.4, 21.0. [25]

3-(4-(tert-butyl)benzyl)-2-(4-(tert-butyl)phenyl)quinolin-4(1H)-one (3.1.3d): The title



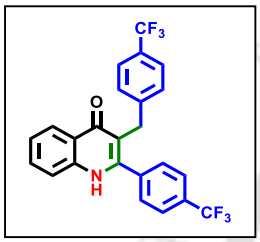
compound was isolated as a white solid using silica-gel column chromatography eluting with ethyl acetate/ petroleum ether (2:3), (Yield: 71%), ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.68 (s, 1H), 8.10 (d, J = 8.0 Hz, 1H), 7.63 (s, 2H), 7.56 (d, J = 8.2 Hz, 2H), 7.43 (d, J = 8.1 Hz, 2H), 7.32 (dd, J = 9.3, 6.5 Hz, 1H), 7.16 (d, J = 8.2 Hz, 2H), 6.92 (d, J = 8.0 Hz, 2H), 3.71 (s, 2H), 1.34 (s, 9H), 1.22 (s, 9H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 181.5, 157.4, 154.3, 152.7, 144.8, 143.5, 137.3, 136.7, 133.6, 132.7, 130.6, 130.2, 129.8, 128.9, 128.1, 123.5, 122.8, 39.7, 39.1, 36.4, 36.2. HRMS (ESI-TOF) m/z $[M+H]^+$ calculated for $C_{30}H_{33}NO$ is 425.2674. Found 425.2674.

3-(4-chlorobenzyl)-2-(4-chlorophenyl)quinolin-4(1H)-one (3.1.3e): The title compound was



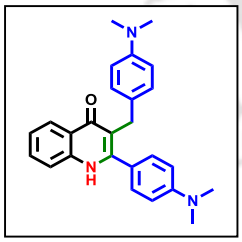
isolated as a white solid using silica-gel column chromatography eluting with ethyl acetate/ petroleum ether (2:3), (Yield: 75%), ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.82 (s, 1H), 8.15 (d, J = 8.1 Hz, 1H), 7.68 – 7.63 (m, 2H), 7.59 (d, J = 8.4 Hz, 2H), 7.46 (d, J = 8.4 Hz, 2H), 7.34 (t, J = 7.3 Hz, 1H), 7.19 (d, J = 8.4 Hz, 2H), 6.99 (d, J = 8.3 Hz, 2H), 3.71 (s, 2H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 176.7, 148.7, 140.8, 140.0, 134.9, 133.8, 132.2, 131.0, 130.0, 129.1, 128.3, 125.6, 124.2, 123.6, 118.8, 117.9, 30.9. [25]

3-(4-(trifluoromethyl)benzyl)-2-(4-(trifluoromethyl)phenyl)quinolin-4(1H)-one (3.1.3f):



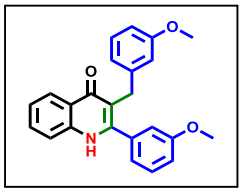
The title compound was isolated as a white solid using silica-gel column chromatography eluting with ethyl acetate/ petroleum ether (2:3), (Yield: 45%), ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.92 (s, 1H), 8.16 (d, J = 8.1 Hz, 1H), 7.90 (d, J = 7.9 Hz, 2H), 7.72 – 7.68 (m, 3H), 7.64 (d, J = 8.6 Hz, 1H), 7.50 (d, J = 8.1 Hz, 2H), 7.38 – 7.35 (m, 1H), 7.20 (d, J = 8.0 Hz, 2H), 3.82 (s, 2H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 176.6, 148.5, 146.6, 140.0, 138.9, 132.4, 130.4 (q, J = 31.9 Hz), 130.2, 128.9, 126.7 (q, J = 31.3 Hz), 126.0 (q, J = 3.9 Hz), 125.5, 125.4, 125.2 (q, J = 3.9 Hz), 124.4 (q, J = 270 Hz), 118.8, 117.4, 31.4.[25]

3-(4-(dimethylamino)benzyl)-2-(4-(dimethylamino)phenyl)quinolin-4(1H)-one (3.1.3g): The



title compound was isolated as a white solid using silica-gel column chromatography eluting with ethyl acetate/ petroleum ether (2:3), (Yield: 45%), ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.44 (s, 1H), 8.09 (d, J = 8.1 Hz, 1H), 7.65 – 7.58 (m, 2H), 7.31 – 7.26 (m, 3H), 6.83 (dd, J = 17.7, 8.3 Hz, 4H), 6.56 (d, J = 8.2 Hz, 2H), 3.69 (s, 2H), 2.97 (s, 6H), 2.79 (s, 6H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 176.8, 151.4, 149.7, 148.9, 140.1, 131.6, 130.2, 130.0, 128.8, 125.5, 124.1, 122.9, 122.6, 118.6, 118.4, 112.9, 111.9, 40.9, 40.4, 30.8. HRMS (ESI-TOF) m/z [M+H]$^{+}$ calculated for $C_{26}H_{27}N_3O$ 398.2232. Found 398.2291.

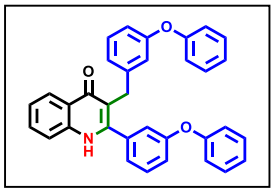
3-(3-methoxybenzyl)-2-(3-methoxyphenyl)quinolin-4(1H)-one (3.1.3h): The title compound



was isolated as a white solid using silica-gel column chromatography eluting with ethyl acetate/ petroleum ether (2:3), (Yield: 80%), ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.76 (s, 1H), 8.16 (d, J = 8.1 Hz, 1H), 7.65 – 7.64 (m, 2H), 7.44 (t, J = 7.9 Hz, 1H), 7.35 – 7.31 (m, 1H), 7.12 – 7.05 (m,

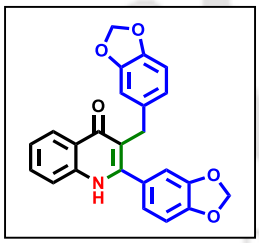
3H), 6.97 (s, 1H), 6.66 (dd, *J* = 8.1, 2.2 Hz, 1H), 6.60 (d, *J* = 7.6 Hz, 1H), 6.53 (s, 1H), 3.74 (s, 2H), 3.69 (s, 3H), 3.63 (s, 3H). ^{13}C NMR (150 MHz, DMSO-*d*$_6$) δ 176.8, 159.5, 159.4, 149.4, 143.7, 140.0, 136.4, 131.9, 130.2, 129.3, 125.5, 124.2, 123.4, 121.2, 120.6, 118.7, 117.9, 115.7, 114.5, 114.1, 111.1, 55.5, 55.2, 31.6. [25]

3-(3-phenoxybenzyl)-2-(3-phenoxyphenyl)quinolin-4(1H)-one (3.1.3i): The title compound



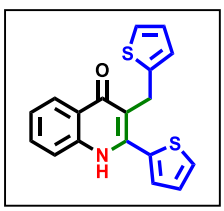
was isolated as a white solid using silica-gel column chromatography eluting with ethyl acetate/ petroleum ether (2:3), (Yield: 75%), ^{1}H NMR (600 MHz, DMSO-*d*$_6$) δ 11.77 (s, 1H), 8.13 (d, *J* = 8.1 Hz, 1H), 7.65 – 7.60 (m, 2H), 7.51 (t, *J* = 7.9 Hz, 1H), 7.36 (t, *J* = 7.9 Hz, 2H), 7.34 – 7.31 (m, 3H), 7.19 (d, *J* = 7.6 Hz, 1H), 7.16 – 7.13 (m, 3H), 7.07 (t, *J* = 7.3 Hz, 1H), 6.98 (d, *J* = 7.8 Hz, 3H), 6.88 (d, *J* = 7.9 Hz, 2H), 6.74 – 6.70 (m, 2H), 6.58 (s, 1H), 3.76 (s, 2H). ^{13}C NMR (150 MHz, DMSO-*d*$_6$) δ 176.7, 157.2, 157.1, 156.7, 156.5, 148.9, 144.2, 139.9, 136.8, 132.1, 130.9, 130.6, 130.3, 129.9, 125.5, 124.3, 124.2, 124.1, 123.6, 123.5, 119.9, 119.3, 118.9, 118.7, 118.6, 117.8, 116.1, 31.2. HRMS (ESI-TOF) m/z $[M+H]^+$ calculated for $C_{34}H_{25}NO_3$ is 496.1913. Found 496.1914.

2-(benzo[d][1,3]dioxol-5-yl)-3-(benzo[d][1,3]dioxol-5-ylmethyl)quinolin-4(1H)-one (3.1.3j):



The title compound was isolated as a white solid using silica-gel column chromatography eluting with ethyl acetate/ petroleum ether (1:1), (Yield: 42%), ^{1}H NMR (600 MHz, DMSO-*d*$_6$) δ 11.66 (s, 1H), 8.13 (d, *J* = 8.1 Hz, 1H), 7.64 (s, 2H), 7.32 (dt, *J* = 8.1, 3.7 Hz, 1H), 7.08 – 7.05 (m, 2H), 6.94 (dd, *J* = 7.9, 1.9 Hz, 1H), 6.69 (d, *J* = 7.9 Hz, 1H), 6.59 (s, 1H), 6.42 (dd, *J* = 8.0, 1.9 Hz, 1H), 6.13 (s, 2H), 5.91 (s, 2H), 3.70 (s, 2H). ^{13}C NMR (150 MHz, DMSO-*d*$_6$) δ 176.7, 149.2, 148.6, 147.7, 147.4, 145.3, 139.9, 135.9, 131.9, 128.8, 125.5, 124.2, 123.3, 123.3, 120.9, 118.7, 118.3, 109.7, 108.9, 108.8, 108.2, 102.0, 100.9, 31.3. [25]

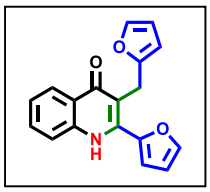
2-(thiophen-2-yl)-3-(thiophen-2-ylmethyl)quinolin-4(1H)-one (3.1.3k): The title compound



was isolated as a white solid using silica-gel column chromatography eluting with ethyl acetate/ petroleum ether (1:1), (Yield: 78%), ^{1}H NMR (600 MHz, DMSO-*d*$_6$) δ 11.80 (s, 1H), 8.15 (d, *J* = 8.0 Hz, 1H), 7.89 (d, *J* = 5.0 Hz, 1H), 7.68 (d, *J* = 3.4 Hz, 2H), 7.45 (d, *J* = 2.7 Hz, 1H), 7.36 (dt, *J* = 8.0, 4.2 Hz, 1H), 7.29 (dd, *J* = 5.1, 3.5 Hz, 1H), 7.20 (d, *J* = 4.3 Hz, 1H), 6.86 (dd, *J* = 5.1, 3.4 Hz, 1H), 6.65 (d, *J* = 4.3 Hz, 1H), 4.05 (s, 2H). ^{13}C NMR (150 MHz, DMSO-*d*$_6$) δ 176.3,

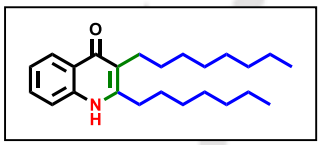
144.6, 142.5, 140.0, 134.5, 132.3, 130.3, 129.5, 128.0, 126.9, 125.5, 124.7, 124.1, 123.9, 123.7, 119.3, 118.8, 26.7. [25]

2-(furan-2-yl)-3-(furan-2-ylmethyl)quinolin-4(1H)-one (3.1.3l): The title compound was



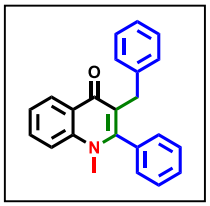
isolated as a white solid using silica-gel column chromatography eluting with ethyl acetate/ petroleum ether (1:1), (Yield: 45%), ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.63 (s, 1H), 8.12 (d, J = 8.0 Hz, 1H), 8.05 (s, 1H), 7.80 (d, J = 8.3 Hz, 1H), 7.67 (t, J = 7.6 Hz, 1H), 7.47 (s, 1H), 7.33 (t, J = 7.5 Hz, 1H), 7.01 (d, J = 3.1 Hz, 1H), 6.78 (s, 1H), 6.28 (s, 1H), 5.87 (s, 1H), 4.08 (s, 2H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 176.5, 154.6, 146.6, 145.6, 141.5, 140.1, 138.2, 125.5, 123.8, 123.6, 118.9, 114.6, 114.3, 112.8, 110.9, 105.6, 24.8. HRMS (ESI-TOF) m/z $[M+H]^+$ calculated for $C_{18}H_{13}NO_3$ 292.0974. Found 292.0975.

2-heptyl-3-octylquinolin-4(1H)-one (3.1.3m): The title compound was isolated as a brown



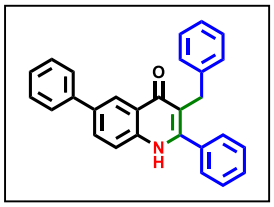
solid using silica-gel column chromatography eluting with ethyl acetate/ petroleum ether (2:3), (Yield: 28%), ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.54 (s, 1H), 8.27 (d, J = 8.1 Hz, 1H), 7.64 (d, J = 8.3 Hz, 1H), 7.41 (t, J = 7.4 Hz, 1H), 7.16 (t, J = 7.3 Hz, 1H), 2.65 (t, J = 8.1 Hz, 2H), 2.57 (t, J = 7.9 Hz, 2H), 1.59 – 1.54 (m, 2H), 1.47 – 1.43 (m, 2H), 1.22 – 1.10 (m, 16H), 0.85 – 0.66 (m, 8H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 172.9, 146.6, 134.9, 126.2, 120.7, 119.2, 118.1, 115.4, 113.4, 27.6, 27.2, 26.9, 25.4, 25.1, 25.1, 24.9, 24.9, 24.6, 24.4, 24.3, 24.2, 20.9, 17.9, 17.8, 9.34, 9.29. HRMS (ESI-TOF) m/z $[M+H]^+$ calculated for $C_{23}H_{19}NO$ is 356.2953. Found 356.2926.

3-benzyl-1-methyl-2-phenylquinolin-4(1H)-one (3.1.3n): The title compound was isolated as

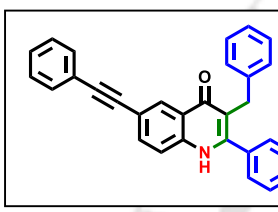


a brown solid using silica-gel column chromatography eluting with ethyl acetate/ petroleum ether (1:1), (Yield: 65%), ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.30 (d, J = 7.8 Hz, 1H), 7.78 (d, J = 4.2 Hz, 2H), 7.53 – 7.49 (m, 3H), 7.46 – 7.43 (m, 1H), 7.27 (dd, J = 7.6, 1.7 Hz, 2H), 7.09 (t, J = 7.3 Hz, 2H), 7.04 (t, J = 7.2 Hz, 1H), 6.86 (d, J = 7.1 Hz, 2H), 3.57 (s, 2H), 3.42 (s, 3H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 175.9, 153.0, 141.6, 141.3, 134.9, 132.6, 129.6, 129.3, 128.9, 128.3, 128.2, 126.2, 125.7, 125.5, 123.7, 120.1, 117.5, 37.7, 32.7. HRMS (ESI-TOF) m/z $[M+H]^+$ calculated for $C_{23}H_{19}NO$ is 326.1545. Found 326.1524.

3-benzyl-2,6-diphenylquinolin-4(1H)-one (3.1.3o): The title compound was isolated as a brown solid using silica-gel column chromatography eluting with ethyl acetate/ petroleum ether (1:1), (Yield: 70%), ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.84 (s, 1H), 8.38 (d, *J* = 2.0 Hz, 1H), 8.01 (dd, *J* = 8.7, 2.2 Hz, 1H), 7.75 (t, *J* = 8.0 Hz, 3H), 7.56 – 7.47 (m, 7H), 7.39 (t, *J* = 7.8 Hz, 1H), 7.15 (t, *J* = 7.5 Hz, 2H), 7.08 (t, *J* = 7.3 Hz, 1H), 6.98 (d, *J* = 7.4 Hz, 2H), 3.77 (s, 2H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 176.8, 149.5, 141.9, 140.0, 139.4, 135.3, 135.2, 130.7, 130.0, 129.6, 129.2, 129.0, 128.4, 128.3, 127.9, 127.0, 125.8, 124.4, 122.9, 119.6, 118.3, 31.6. HRMS (ESI-TOF) m/z $[M+H]^+$ calculated for $C_{28}H_{21}NO$ is 388.1701. Found 388.1699.

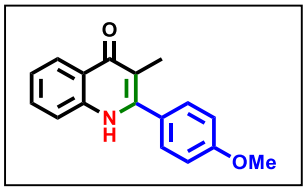


3-benzyl-2-phenyl-6-(phenylethynyl)quinolin-4(1H)-one (3.1.3p): The title compound was isolated as a brown solid using silica-gel column chromatography eluting with ethyl acetate/ petroleum ether (1:1), (Yield: 62%), ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.81 (s, 1H), 8.28 (d, *J* = 1.6 Hz, 1H), 7.99 (dd, *J* = 8.7, 1.9 Hz, 1H), 7.65 (dd, *J* = 8.1, 3.3 Hz, 2H), 7.55 – 7.51 (m, 3H), 7.46 – 7.43 (m, 2H), 7.41 – 7.38 (m, 2H), 7.32 (s, 1H), 7.28 (d, *J* = 7.1 Hz, 1H), 7.14 (t, *J* = 7.5 Hz, 2H), 7.08 (t, *J* = 7.2 Hz, 1H), 6.98 (d, *J* = 7.4 Hz, 2H), 3.77 (s, 2H). ^{13}C NMR (150 MHz, DMSO- d_6) δ 176.7, 149.3, 141.9, 139.6, 137.6, 135.2, 132.4, 129.9, 129.7, 129.2, 129.1, 129.0, 128.9, 128.7, 128.6, 128.5, 128.4, 128.3, 128.1, 126.9, 125.8, 124.4, 123.9, 119.3, 118.4, 31.5. HRMS (ESI-TOF) m/z $[M+H]^+$ calculated for $C_{30}H_{21}NO$ is 412.1701. Found 412.1702.

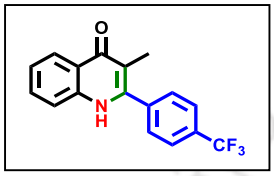


3-methyl-2-phenylquinolin-4(1H)-one (3.1.5a): The title compound was isolated as a white solid using silica-gel column chromatography eluting with ethyl acetate/ petroleum ether (3:2), (Yield: 88%), ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.65 (s, 1H), 8.15 (d, *J* = 8.1 Hz, 1H), 7.63 (d, *J* = 5.52 Hz, 2H), 7.57 (d, *J* = 5.2 Hz, 5H), 7.31(t, *J* = 7.8 Hz, 1H), 1.90 (s, 3H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 178.3, 149.3, 140.9, 136.5, 132.8, 130.9, 130.4, 130.1, 126.4, 124.5, 124.2, 119.6, 115.9, 13.6.[12]

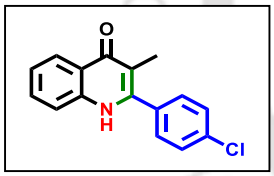
2-(4-methoxyphenyl)-3-methylquinolin-4(1H)-one (3.1.5b): The title compound was isolated as a white solid using silica-gel column chromatography eluting with ethyl acetate/ petroleum ether (3:2), (Yield: 92%), ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.53 (s, 1H), 8.13 (d, *J* = 8.0 Hz, 1H), 7.63 (t, *J* = 7.9 Hz, 2H), 7.51 (d, *J* = 8.5 Hz, 2H), 7.30 (t, *J* = 7.2 Hz, 1H), 7.13 (d, *J* = 8.5 Hz, 2H), 3.86 (s, 3H), 1.92 (s, 3H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 177.2, 160.4, 148.0, 139.9, 131.6, 130.9, 127.7, 125.4, 123.4, 123.0, 118.5, 114.7, 114.3, 55.8, 12.7.[26]



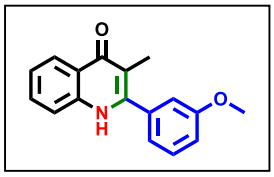
3-methyl-2-(4-(trifluoromethyl)phenyl)quinolin-4(1H)-one (3.1.5c): The title compound was isolated as a white solid using silica-gel column chromatography eluting with ethyl acetate/ petroleum ether (3:2), (Yield: 52%), ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.74 (s, 1H), 8.15 (d, *J* = 8.1 Hz, 1H), 7.96 (d, *J* = 8.0 Hz, 2H), 7.82 (d, *J* = 7.9 Hz, 2H), 7.65 (t, *J* = 7.6 Hz, 1H), 7.60 (d, *J* = 8.3 Hz, 1H), 7.34 (t, *J* = 7.5 Hz, 1H), 1.89 (s, 3H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 177.2, 146.8, 139.9, 139.4, 132.0, 130.5, 130.2 (q, *J* = 32.1 Hz) , 125.9 (q, *J* = 3.9 Hz), 125.5, 124.5 (q, *J* = 271 Hz), 123.5, 123.4, 118.6, 115.1, 12.4.[26]



2-(4-chlorophenyl)-3-methylquinolin-4(1H)-one (3.1.5d): The title compound was isolated as a white solid using silica-gel column chromatography eluting with ethyl acetate/ petroleum ether (3:2), (Yield: 68%), ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.74 (s, 1H), 8.14 (d, *J* = 8.1 Hz, 1H), 7.63 (d, *J* = 8.8 Hz, 4H), 7.58 (d, *J* = 8.2 Hz, 2H), 7.33 (t, *J* = 7.3 Hz, 1H), 1.88 (s, 3H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 177.4, 147.2, 139.8, 134.7, 134.0, 132.0, 131.3, 129.1, 125.4, 123.5, 123.4, 118.6, 115.1, 12.5. [26]



2-(3-methoxyphenyl)-3-methylquinolin-4(1H)-one (3.1.5e): The title compound was isolated as a white solid using silica-gel column chromatography eluting with ethyl acetate/ petroleum ether (3:2), (Yield: 83%), ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.62 (s, 1H), 8.15 (d, *J* = 7.7 Hz, 1H), 7.63 (s, 2H), 7.50 (t, *J* = 6.2 Hz, 1H), 7.30 (t, *J* = 7.9 Hz, 1H), 7.13 (s, 3H), 3.84 (s, 3H), 1.92 (s, 3H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 177.2, 159.6, 147.9, 139.9, 136.8, 131.7, 130.2, 125.4, 123.5, 123.1, 121.6, 118.6, 115.4, 114.9, 114.8, 55.8, 12.6.[27]



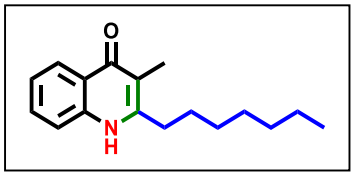
2-(2-methoxyphenyl)-3-methylquinolin-4(1H)-one (3.1.5f): The title compound was isolated as a white solid using silica-gel column chromatography eluting with ethyl acetate/ petroleum ether (4:1), (Yield: 35%), ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.60 (s, 1H), 8.14 (d, J = 8.0 Hz, 1H), 7.62 (q, J = 7.9 Hz, 2H), 7.49 (d, J = 8.6 Hz, 2H), 7.30 (t, J = 7.3 Hz, 1H), 7.11 (d, J = 8.6 Hz, 2H), 3.84 (s, 3H), 1.92 (s, 3H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 177.3, 160.4, 148.2, 139.8, 131.7, 130.8, 127.6, 125.3, 123.4, 123.1, 118.5, 114.8, 114.3, 55.8, 12.7. HRMS (ESI-TOF) m/z $[M+H]^+$ calculated for $C_{17}H_{15}NO_2$ is 266.1181. Found 266.1178.

2-(benzo[d][1,3]dioxol-5-yl)-3-methylquinolin-4(1H)-one (3.1.5g): The title compound was isolated as a white solid using silica-gel column chromatography eluting with ethyl acetate/ petroleum ether (4:1), (Yield: 38%), ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.56 (s, 1H), 8.12 (d, J = 8.1 Hz, 1H), 7.62 (s, 2H), 7.30 (t, J = 6.8 Hz, 1H), 7.16 (s, 1H), 7.11 (d, J = 7.9 Hz, 1H), 7.05 (d, J = 7.9 Hz, 1H), 6.14 (s, 2H), 1.93 (s, 3H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 177.2, 148.4, 147.8, 147.7, 139.8, 131.7, 129.1, 125.3, 123.5, 123.4, 123.1, 118.5, 114.8, 109.9, 108.8, 102.0, 12.7. HRMS (ESI-TOF) m/z $[M+H]^+$ calculated for $C_{17}H_{13}NO_3$ is 280.0974. Found 280.0974.

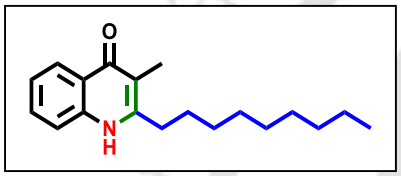
3-methyl-2-(thiophen-2-yl)quinolin-4(1H)-one (3.1.5h): The title compound was isolated as a white solid using silica-gel column chromatography eluting with ethyl acetate/ petroleum ether (4:1), (Yield: 73%), ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.61 (s, 1H), 8.13 (d, J = 8.1 Hz, 1H), 7.90 (d, J = 5.1 Hz, 1H), 7.67 – 7.62 (m, 2H), 7.52 (d, J = 3.6 Hz, 1H), 7.31 (d, J = 5.4 Hz, 2H), 2.06 (s, 3H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 177.0, 141.3, 139.9, 135.4, 131.9, 130.3, 129.3, 128.0, 125.4, 123.4, 123.3, 118.6, 116.0, 12.8.[28]

2-cyclohexyl-3-methylquinolin-4(1H)-one (3.1.5i): The title compound was isolated as a white solid using silica-gel column chromatography eluting with ethyl acetate/ petroleum ether (4:1), (Yield: 53%), ^{1}H NMR (600 MHz, DMSO-d_6) δ 10.73 (s, 1H), 8.07 (d, J = 8.0 Hz, 1H), 7.73 (d, J = 8.4 Hz, 1H), 7.58 (t, J = 7.6 Hz, 1H), 7.25 (t, J = 7.5 Hz, 1H), 2.97 (t, J = 11.7 Hz, 1H), 2.06 (s, 3H), 1.86 (d, J = 12.8 Hz, 2H), 1.80 – 1.75 (m, 5H), 1.43 (q, J = 13.6, 12.1 Hz, 2H), 1.33 (t, J = 10.3 Hz, 1H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 176.9, 153.5, 139.8, 131.3, 125.3, 123.2, 122.8, 118.4, 113.4, 30.2, 26.4, 25.8, 10.5.[26]

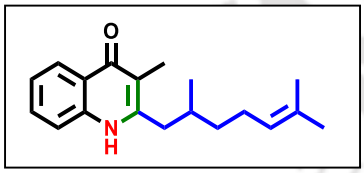
2-heptyl-3-methylquinolin-4(1H)-one (3.1.5j): The title compound was isolated as a white solid using silica-gel column chromatography eluting with ethyl acetate/ petroleum ether (1:1), (Yield: 63%), ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.35 (s, 1H), 8.06 (d, *J* = 7.8 Hz, 1H), 7.58 (t, *J* = 7.4 Hz, 1H), 7.50 (d, *J* = 8.2 Hz, 1H), 7.24 (t, *J* = 7.2 Hz, 1H), 2.68 (t, *J* = 7.8 Hz, 2H), 2.00 (s, 3H), 1.63 (t, *J* = 7.1 Hz, 2H), 1.37 – 1.27 (m, 8H), 0.86 (t, *J* = 6.3 Hz, 3H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 176.7, 150.2, 139.6, 131.4, 125.5, 123.3, 122.7, 118.0, 114.2, 32.1, 31.7, 29.3, 28.9, 28.8, 22.5, 14.4, 10.8.[28]



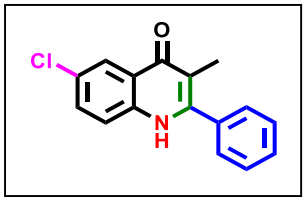
3-methyl-2-nonylquinolin-4(1H)-one (3.1.5k): The title compound was isolated as a white solid using silica-gel column chromatography eluting with ethyl acetate/ petroleum ether (1:1), (Yield: 65%), , ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.39 (s, 1H), 8.05 (d, *J* = 8.0 Hz, 1H), 7.57 (t, *J* = 8.2 Hz, 1H), 7.50 (d, *J* = 8.1 Hz, 1H), 7.24 (t, *J* = 7.5 Hz, 1H), 2.67(t, *J* = 7.9 Hz, 2H), 1.98 (s, 3H), 1.61 (p, *J* = 7.6 Hz, 2H), 1.35 – 1.23 (m, 12H), 0.83 (t, *J* = 6.7 Hz, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 176.8, 150.3, 139.6, 131.4, 125.4, 123.3, 122.8, 118.0, 114.2, 32.1, 31.7, 29.4, 29.3, 29.2, 29.1, 28.7, 22.5, 14.4, 10.7.[29]



2-(2,6-dimethylhept-5-en-1-yl)-3-methylquinolin-4(1H)-one (3.1.5l): The title compound was isolated as a white solid using silica-gel column chromatography eluting with ethyl acetate/ petroleum ether (1:1), (Yield: 52%), ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.96 (s, 1H), 8.39 (d, *J* = 8.2 Hz, 1H), 7.54 (q, *J* = 8.6 Hz, 2H), 7.29 (t, *J* = 7.8 Hz, 1H), 5.02 (t, *J* = 7.0 Hz, 1H), 2.81 (dd, *J* = 13.8, 6.4 Hz, 1H), 2.56 (dd, *J* = 13.8, 8.7 Hz, 1H), 2.20 (s, 3H), 2.05 (dq, *J* = 14.8, 6.9, 6.4 Hz, 1H), 1.96 (dq, *J* = 16.4, 7.1 Hz, 2H), 1.68 (s, 3H), 1.58 (s, 3H), 1.42 – 1.37 (m, 1H), 1.28 (ddd, *J* = 22.6, 13.9, 8.3 Hz, 1H), 0.94 (d, *J* = 6.6 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 178.1, 148.8, 139.1, 131.7, 131.2, 126.0, 124.1, 123.6, 122.9, 117.3, 116.3, 40.2, 36.9, 32.8, 25.7, 25.5, 19.3, 17.7, 11.2. HRMS (ESI-TOF) m/z $[M+Na]^+$ calculated for $C_{19}H_{25}NO$ 284.2014. Found 284.2027.

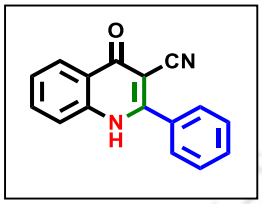


6-chloro-3-methyl-2-phenylquinolin-4(1H)-one (3.1.5m): The title compound was isolated as



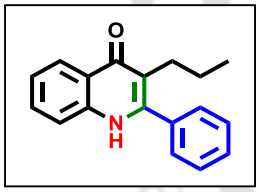
a white solid using silica-gel column chromatography eluting with ethyl acetate/ petroleum ether (1:1), (Yield: 78%), ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.79 (s, 1H), 8.06 (s, 1H), 7.65 (s, 2H), 7.59 – 7.56 (m, 5H), 1.89 (s, 3H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 176.0, 148.5, 138.5, 135.2, 131.8, 130.0, 129.3, 129.0, 127.7, 124.4, 124.2, 121.1, 115.3, 12.6.[18]

4-oxo-2-phenyl-1,4-dihydroquinoline-3-carbonitrile (3.1.5n): The title compound was



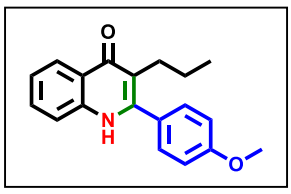
isolated as a white solid using silica-gel column chromatography eluting with ethyl acetate/ petroleum ether (9:1), (Yield: 42%), ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.79 (brs, 1H), 8.16 (d, J = 7.7 Hz, 1H), 7.82 – 7.79 (m, 3H), 7.76 (d, J = 8.1 Hz, 1H), 7.70 – 7.65 (m, 3H), 7.51 (t, J = 7.9 Hz, 1H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 175.6, 157.7, 139.8, 133.9, 132.8, 131.9, 129.3, 129.2, 126.0, 125.3, 124.4, 120.0, 117.4, 93.9. [12]

2-phenyl-3-propylquinolin-4(1H)-one (3.1.5o): The title compound was isolated as a white



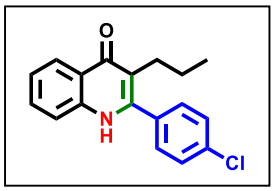
solid using silica-gel column chromatography eluting with ethyl acetate/ petroleum ether (4:1), (Yield: 81%), ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.58 (s, 1H), 8.14 (d, J = 7.4 Hz, 1H), 7.61-7.53 (m, 7H), 7.31 (t, J = 7.0 Hz, 1H), 2.31 (t, J = 7.4 Hz, 2H), 1.41 – 1.37 (m, 2H), 0.73 (t, J = 7.4 Hz, 3H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 176.8, 148.6, 139.8, 135.7, 131.7, 129.7, 129.2, 129.0, 125.5, 124.1, 123.1, 119.6, 118.6, 28.4, 22.5, 14.7. HRMS (ESI-TOF) m/z $[M+Na]^+$ calculated for $C_{18}H_{17}NO$ 286.1208. Found 286.1219.

2-(4-methoxyphenyl)-3-propylquinolin-4(1H)-one (3.1.5p): The title compound was isolated



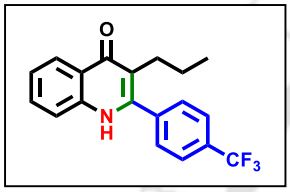
as a white solid using silica-gel column chromatography eluting with ethyl acetate/ petroleum ether (4:1), (Yield: 75%), ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.49 (s, 1H), 8.12 (d, J = 8.1 Hz, 1H), 7.62 -7.59 (m, 2H), 7.46 (d, J = 8.3 Hz, 2H), 7.29 (t, J = 6.9 Hz, 1H), 7.13 (d, J = 8.4 Hz, 2H), 3.86 (s, 3H), 2.34 (t, J = 7.8 Hz, 2H), 1.42 - 1.38 (m, 2H), 0.75 (t, J = 7.3 Hz, 3H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 176.9, 160.3, 148.5, 139.9, 131.7, 130.6, 127.9, 125.4, 123.9, 123.0, 119.7, 118.5, 114.3, 55.8, 28.5, 22.5, 14.6. HRMS (ESI-TOF) m/z $[M+Na]^+$ calculated for $C_{19}H_{19}NO_2$ 316.1313. Found 316.1322.

2-(4-chlorophenyl)-3-propylquinolin-4(1H)-one (3.1.5q): The title compound was isolated as



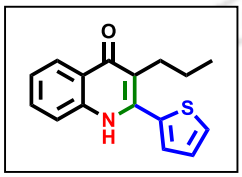
a white solid using silica-gel column chromatography eluting with ethyl acetate/ petroleum ether (4:1), (Yield: 86%), ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.60 (s, 1H), 8.13 (d, J = 8.1 Hz, 1H), 7.65 – 7.62 (m, 1H), 7.57 (d, J = 8.3 Hz, 3H), 7.32 (t, J = 7.5 Hz, 1H), 2.30 (t, J = 7.7 Hz, 2H), 1.38 (q, J = 7.5 Hz, 2H), 0.74 (t, J = 7.3 Hz, 3H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 176.8, 147.4, 139.8, 134.6, 134.4, 131.9, 131.2, 129.1, 125.5, 124.0, 123.2, 119.7, 118.6, 28.3, 22.4, 14.6. HRMS (ESI-TOF) m/z $[M+Na]^+$ calculated for $C_{18}H_{16}ClNO$ 320.0818. Found 320.0824.

3-propyl-2-(4-(trifluoromethyl)phenyl)quinolin-4(1H)-one (3.1.5r): The title compound was



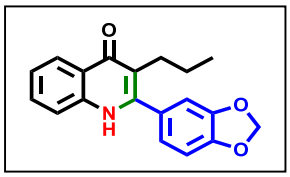
isolated as a white solid using silica-gel column chromatography eluting with ethyl acetate/ petroleum ether (4:1), (Yield: 55%), ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.65 (s, 1H), 8.15 (d, J = 8.0 Hz, 1H), 7.96 (d, J = 8.0 Hz, 3H), 7.79 (d, J = 7.9 Hz, 3H), 7.64 (t, J = 7.1 Hz, 1H), 7.57 (d, J = 8.3 Hz, 1H), 7.33 (t, J = 7.4 Hz, 1H), 2.30 (t, J = 7.7 Hz, 2H), 1.40 (q, J = 7.5 Hz, 2H), 0.73 (t, J = 7.3 Hz, 3H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 176.8, 147.1, 139.9, 139.6, 131.9, 130.4, 130.1 (q, J = 32.0 Hz), 125.9 (q, J = 3.8 Hz), 125.5, 124.5 (q, J= 271.5 Hz), 124.1, 123.3, 119.7, 118.6, 28.3, 22.4, 14.5. HRMS (ESI-TOF) m/z $[M+H]^+$ calculated for $C_{19}H_{16}F_3NO$ is 332.1262. Found 332.1209.

3-propyl-2-(thiophen-2-yl)quinolin-4(1H)-one (3.1.5s): The title compound was isolated as a



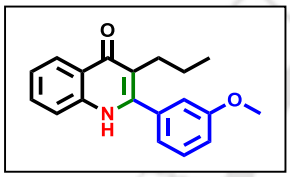
white solid using silica-gel column chromatography eluting with ethyl acetate/ petroleum ether (4:1), (Yield: 65%), ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.61 (s, 1H), 8.12 (d, J = 8.0 Hz, 1H), 7.87 (d, J = 5.0 Hz, 1H), 7.63 (s, 2H), 7.46 (d, J = 3.3 Hz, 1H), 7.32 – 7.28 (m, 2H), 2.47 (t, J = 7.8 Hz, 2H), 1.40 (q, J = 7.5 Hz, 2H), 0.83 (t, J = 7.3 Hz, 3H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 176.7, 141.4, 139.9, 135.3, 132.0, 129.9, 129.1, 127.9, 125.5, 123.9, 123.3, 121.2, 118.6, 28.7, 22.9, 14.6. HRMS (ESI-TOF) m/z $[M+H]^+$ calculated for $C_{16}H_{15}NOS$ is 270.0953. Found 270.0976.

2-(benzo[d][1,3]dioxol-5-yl)-3-methylquinolin-4(1H)-one (3.1.5t): The title compound was



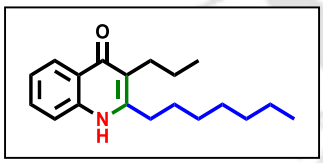
isolated as a white solid using silica-gel column chromatography eluting with ethyl acetate/ petroleum ether (9:1), (Yield: 40%), ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.50 (s, 1H), 8.12 (d, J = 8.0 Hz, 1H), 7.60 (q, J = 8.0 Hz, 2H), 7.29 (t, J = 7.2 Hz, 1H), 7.11 (d, J = 9.2 Hz, 2H), 7.01 (d, J = 7.8 Hz, 1H), 6.15 (s, 2H), 2.47 (t, J = 7.8 Hz, 2H), 1.40 (q, J = 7.5 Hz, 2H), 0.76 (t, J = 7.3 Hz, 3H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 176.9, 148.4, 148.2, 147.7, 139.8, 131.7, 129.3, 125.5, 123.9, 123.2, 123.0, 119.7, 118.5, 109.7, 108.8, 101.9, 28.4, 22.4, 14.7. HRMS (ESI-TOF) m/z calculated for $C_{19}H_{17}NO_3$ is 330.1106. Found 330.1108.

2-(3-methoxyphenyl)-3-propylquinolin-4(1H)-one (3.1.5u): The title compound was isolated



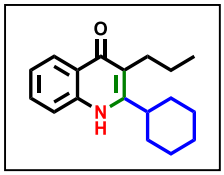
as a white solid using silica-gel column chromatography eluting with ethyl acetate/ petroleum ether (9:1), (Yield: 87%), ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.08 (d, J = 8.0 Hz, 1H), 7.57 – 7.54 (m, 2H), 7.44 (t, J = 8.1 Hz, 1H), 7.24 (ddd, J = 8.0, 5.8, 2.1 Hz, 1H), 7.08 (dd, J = 9.1, 1.8 Hz, 1H), 7.04 – 7.03 (m, 2H), 3.78 (s, 3H), 2.30 (t, J = 7.8 Hz, 2H), 1.36 (q, J = 7.9 Hz, 2H), 0.70 (t, J = 7.4 Hz, 3H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 181.6, 164.3, 153.1, 144.6, 141.7, 136.4, 134.9, 130.2, 128.7, 127.8, 126.1, 124.2, 123.3, 120.0, 119.4, 60.5, 33.2, 27.2, 19.4. HRMS (ESI-TOF) m/z calculated for $C_{19}H_{19}NO_2$ is 294.1494. Found 294.1492.

2-heptyl-3-propylquinolin-4(1H)-one (3.1.5v): The title compound was isolated as a white

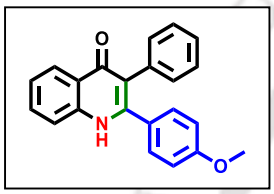


solid using silica-gel column chromatography eluting with ethyl acetate/ petroleum ether (1:1), (Yield: 50%), ^{1}H NMR (500 MHz, $CDCl_3$) δ 11.35 (s, 1H), 8.25 (d, J = 8.1 Hz, 1H), 7.59 – 7.57 (m, 1H), 7.40 (t, J = 7.6 Hz, 1H), 7.15 (t, J = 7.6 Hz, 1H), 2.62 (t, J = 7.6 Hz, 2H), 2.53 (t, J = 7.6 Hz, 2H), 2.30 (t, J = 7.5 Hz, 1H), 1.57 (q, J = 7.2 Hz, 2H), 1.48 (q, J = 7.2 Hz, 2H), 1.27 – 1.07 (m, 6H), 0.85 (t, J = 7.3 Hz, 2H), 0.80 (t, J = 6.9 Hz, 2H), 0.75 (t, J = 7.0 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.6, 139.5, 131.0, 125.5, 123.8, 123.0, 120.0, 118.0, 34.4, 34.3, 32.3, 31.7, 29.8, 29.7, 29.6, 29.1, 28.9, 28.9, 27.7, 24.9, 22.9, 22.6, 22.6, 14.4, 14.1, 14.0. HRMS (ESI-TOF) m/z $[M+H]^+$ calculated for $C_{19}H_{27}NO$ is 286.2171. Found 286.2133.

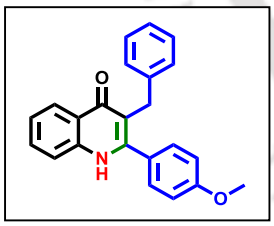
2-cyclohexyl-3-propylquinolin-4(1H)-one (3.1.5w): The title compound was isolated as a white solid using silica-gel column chromatography eluting with ethyl acetate/ petroleum ether (1:1), (Yield: 51%), ^{1}H NMR (600 MHz, DMSO-d_6) δ 10.70 (s, 1H), 8.04 (d, *J* = 8.0 Hz, 1H), 7.70 (d, *J* = 8.3 Hz, 1H), 7.57 (t, *J* = 7.6 Hz, 1H), 7.23 (t, *J* = 7.5 Hz, 1H), 2.93 (t, *J* = 12.1 Hz, 1H), 2.55 (t, *J* = 7.6 Hz, 2H), 1.86 – 1.80 (m, 4H), 1.76 – 1.68 (m, 3H), 1.45 – 1.33 (m, 5H), 0.91 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 176.7, 153.6, 139.9, 131.4, 125.4, 123.5, 122.7, 118.2, 118.2, 30.8, 26.8, 26.4, 25.7, 23.4, 14.5. HRMS (ESI-TOF) m/z $[M+H]^+$ calculated for $C_{18}H_{23}NO$ is 270.1858. Found 270.1565.



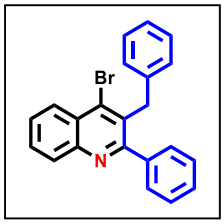
2-(4-methoxyphenyl)-3-phenylquinolin-4(1H)-one (3.1.5x): The title compound was isolated as a white solid using silica-gel column chromatography eluting with ethyl acetate/ petroleum ether (4:1), (Yield: 40%), ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.64 (s, 1H), 8.15 (d, *J* = 8.1 Hz, 1H), 7.71 – 7.65 (m, 2H), 7.34 (t, *J* = 6.9 Hz, 1H), 7.24 (d, *J* = 8.7 Hz, 2H), 7.19 (t, *J* = 7.4 Hz, 2H), 7.13 (d, J = 7.2 Hz, 1H), 7.08 (d, *J* = 7.9 Hz, 2H), 6.88 (d, *J* = 8.7 Hz, 2H), 3.75 (s, 3H).^{13}C NMR (150 MHz, DMSO-d_6) δ 175.8, 160.0, 148.7, 140.1, 136.4, 132.2, 132.1, 131.4, 127.8, 127.7, 126.3, 125.7, 125.0, 123.5, 120.7, 118.8, 113.9, 55.7.[12]



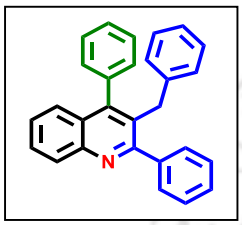
3-benzyl-2-(4-methoxyphenyl)quinolin-4(1H)-one (3.1.5y): The title compound was isolated as a white solid using silica-gel column chromatography eluting with ethyl acetate/ petroleum ether (4:1), (Yield: 92%), ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.64 (s, 1H), 8.13 (d, *J* = 8.1 Hz, 1H), 7.65 (d, *J* = 3.6 Hz, 2H), 7.40 (d, *J* = 8.3 Hz, 2H), 7.33 (dt, *J* = 7.9, 3.9 Hz, 1H), 7.16 (t, *J* = 7.4 Hz, 2H), 7.09 (t, *J* = 7.0 Hz, 3H), 7.0 (d, *J* = 7.5 Hz, 2H), 3.83 (s, 3H), 3.78 (s, 2H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 176.7, 160.5, 149.4, 142.1, 140.1, 131.9, 130.6, 128.4, 128.3, 127.5, 125.7, 125.5, 124.2, 123.3, 118.7, 118.1, 114.4, 55.8, 31.6. HRMS (ESI-TOF) m/z $[M+Na]^+$ calculated for $C_{23}H_{19}NO_2$ 364.1313. Found 364.1316.



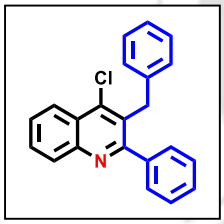
3-benzyl-4-bromo-2-phenylquinoline (3.1.16): ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.32 (d, *J* = 8.4 Hz, 1H), 8.19 (d, *J* = 8.4 Hz, 1H), 7.79 (t, *J* = 7.6 Hz, 1H), 7.69 (t, *J* = 7.6 Hz, 1H), 7.42 – 7.38 (m, 5H), 7.21 (dt, *J* = 13.6, 6.9 Hz, 3H), 6.95 (d, *J* = 7.3 Hz, 2H), 4.45 (s, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 161.4, 147.1, 140.6, 138.8, 137.9, 132.3, 130.0, 129.8, 128.6, 128.5, 128.4, 128.2, 128.1, 127.9, 127.6, 127.2, 126.1, 39.6. HRMS (ESI-TOF) m/z $[M+H]^+$ calculated for $C_{22}H_{16}BrN$ 374.0544. Found 374.0528.



3-benzyl-2,4-diphenylquinoline (3.1.17): ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.23 (d, *J* = 8.4 Hz, 1H), 7.72 (t, *J* = 7.4 Hz, 1H), 7.46 – 7.41 (m, 7H), 7.36 (s, 3H), 7.24 (d, *J* = 3.9 Hz, 2H), 7.03 (d, *J* = 5.5 Hz, 3H), 6.60 (d, *J* = 5.9 Hz, 2H), 4.05 (s, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 161.6, 148.8, 146.6, 141.3, 140.7, 137.0, 129.6, 129.5, 129.4, 129.0, 128.7, 128.3, 128.2, 128.1, 127.9, 127.8, 127.4, 126.4, 126.3, 125.5, 36.1. HRMS (ESI-TOF) m/z $[M+H]^+$ calculated for $C_{28}H_{21}NO$ 372.1752. Found 372.1764.



3-benzyl-4-chloro-2-phenylquinoline (3.1.18): ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.33 (d, *J* = 8.4 Hz, 1H), 8.20 (d, *J* = 8.4 Hz, 1H), 7.80 (t, *J* = 7.6 Hz, 1H), 7.69 (t, *J* = 7.6 Hz, 1H), 7.43 – 7.41 (m 5H), 7.24 – 7.19 (m, 3H), 6.95 (d, *J* = 7.4 Hz, 2H), 4.40 (s, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 161.5, 147.1, 143.4, 140.4, 138.9, 130.0, 129.9, 129.8, 128.6, 128.5, 128.3, 128.2, 128.1, 127.5, 126.1, 125.8, 124.3, 36.6. HRMS (ESI-TOF) m/z $[M+H]^+$ calculated for $C_{22}H_{16}ClN$ 330.1050. Found 330.1025.



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3.11. Copies of ^{1}H and ^{13}C spectra of newly synthesised compounds:

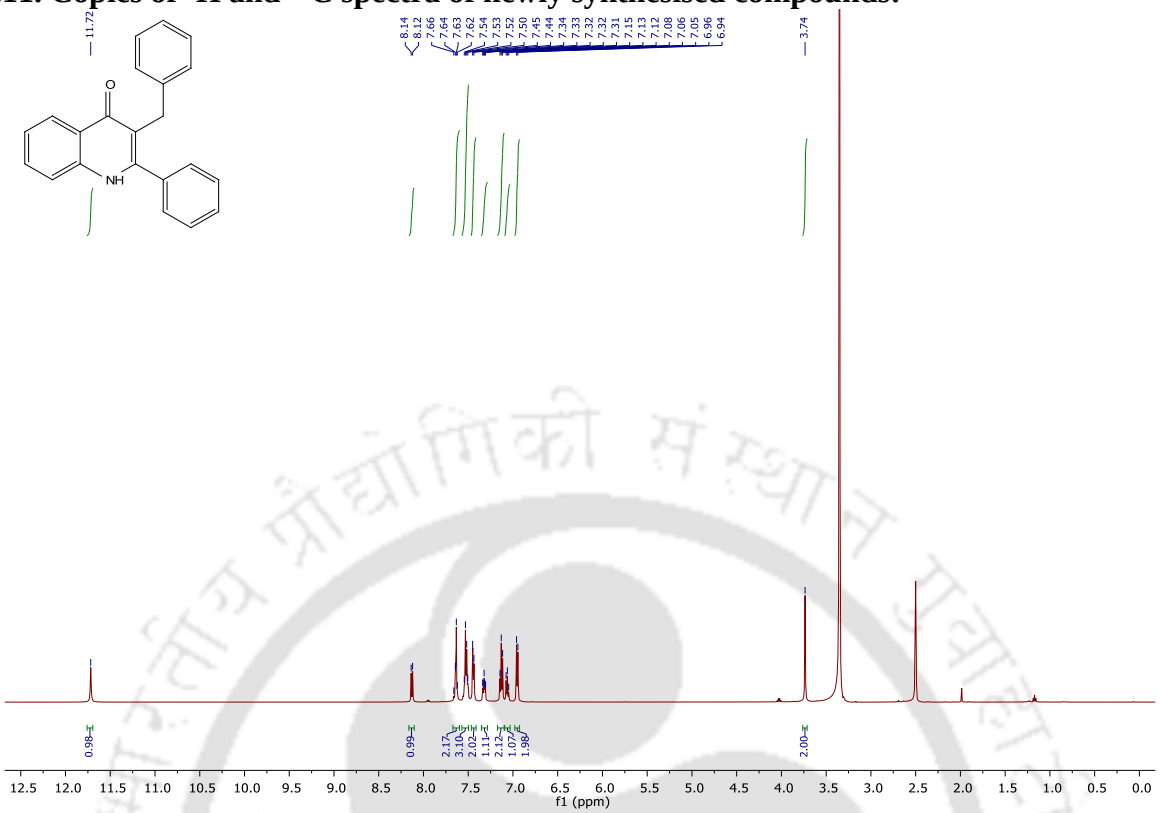


Figure 3.3.^{1}H NMR (500 MHz) spectra of compound **3.1.3a** in DMSO-d_6

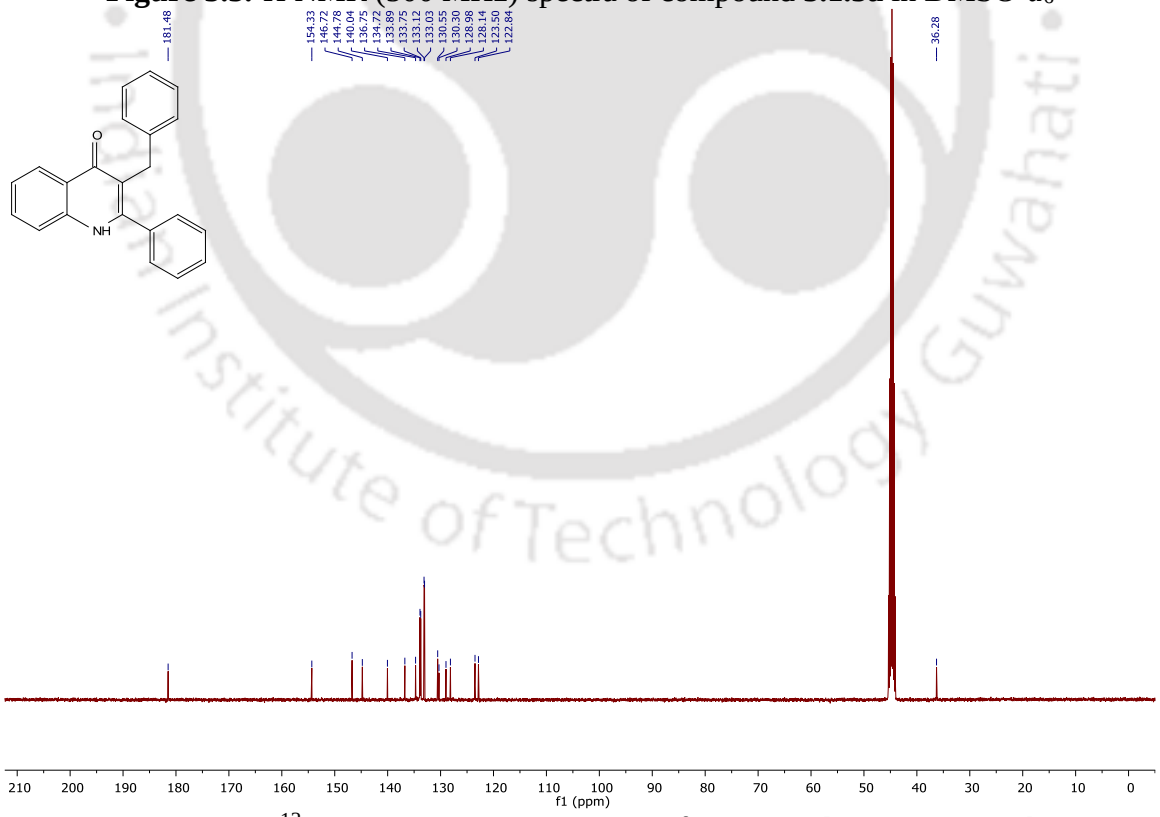


Figure 3.4. ^{13}C NMR (100 MHz) spectra of compound **3a** in DMSO-d_6

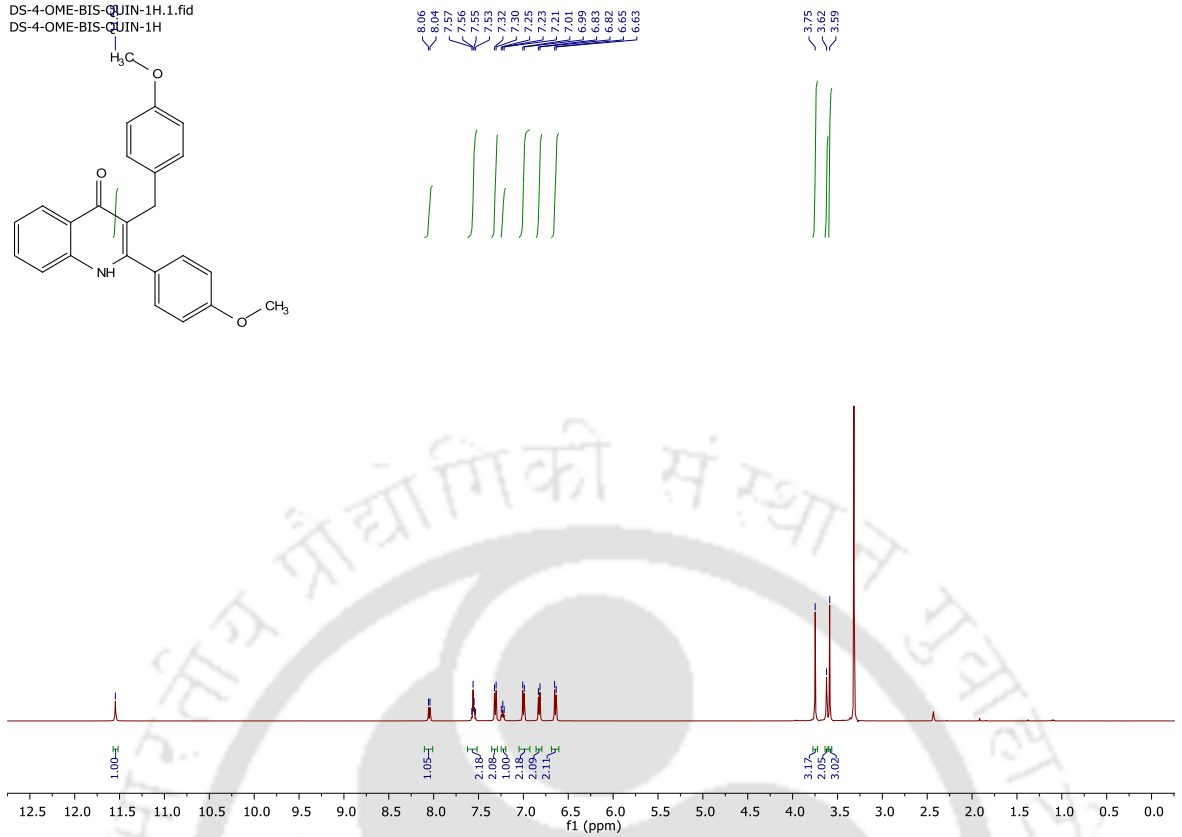


Figure 3.5. ^{1}H NMR (500 MHz) spectra of compound **3b** in DMSO-d_6

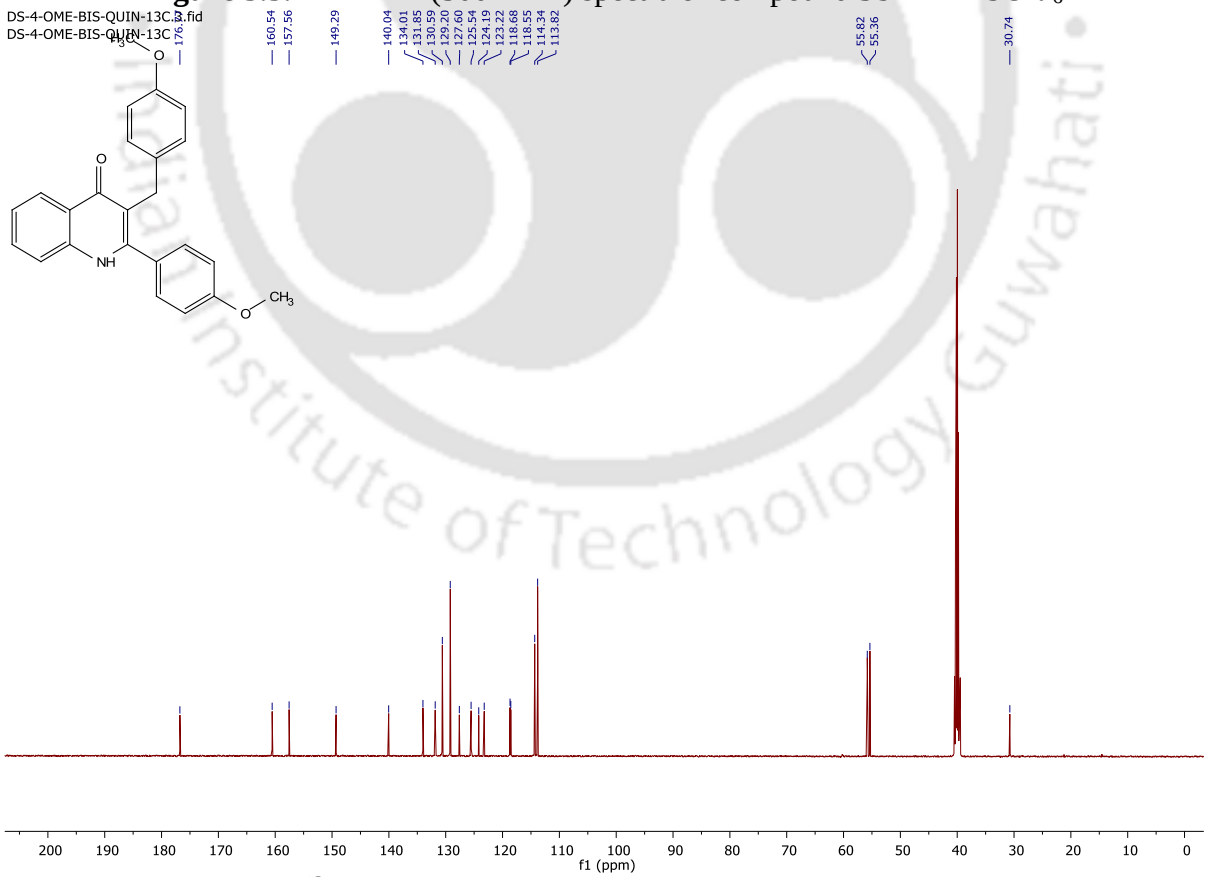


Figure 3.6. ^{13}C NMR (100 MHz) spectra of compound **3b** in DMSO-d_6

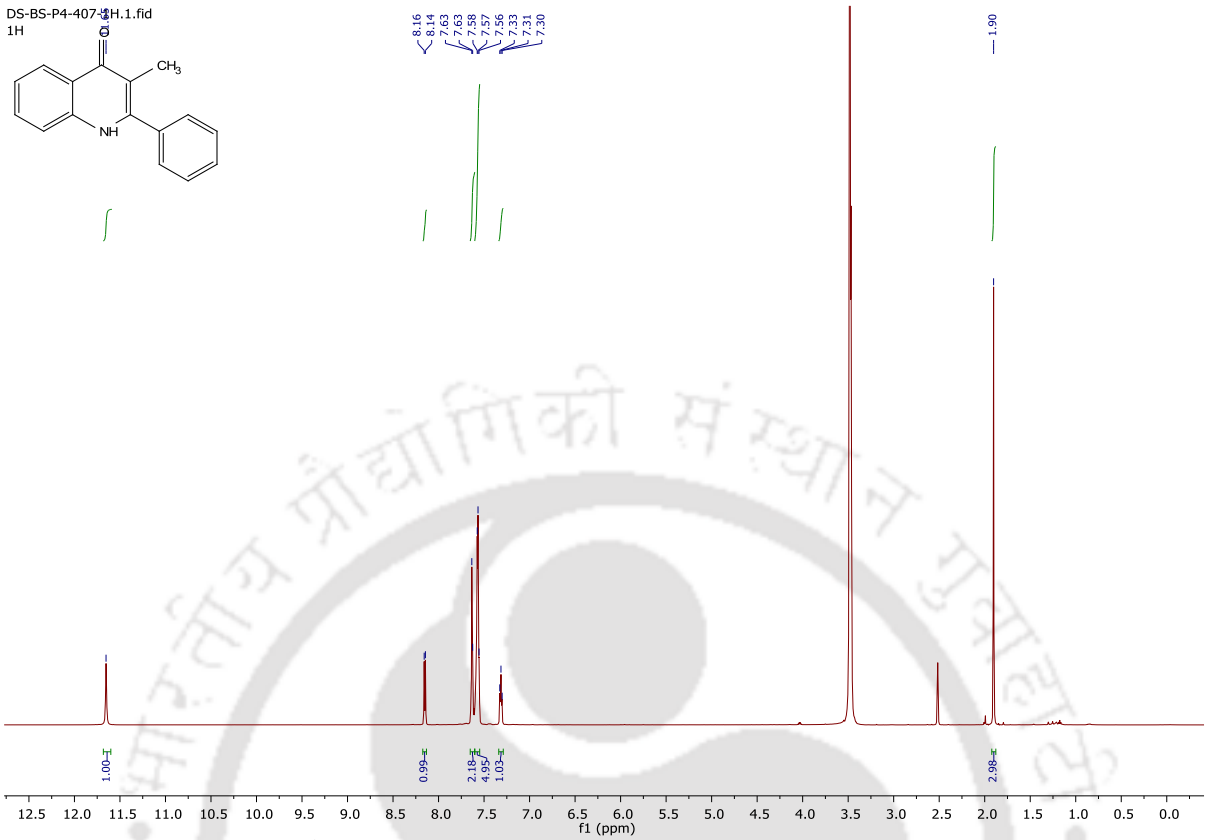


Figure 3.7. ^{1}H NMR (600 MHz) spectra of compound **5a** in DMSO-d_6

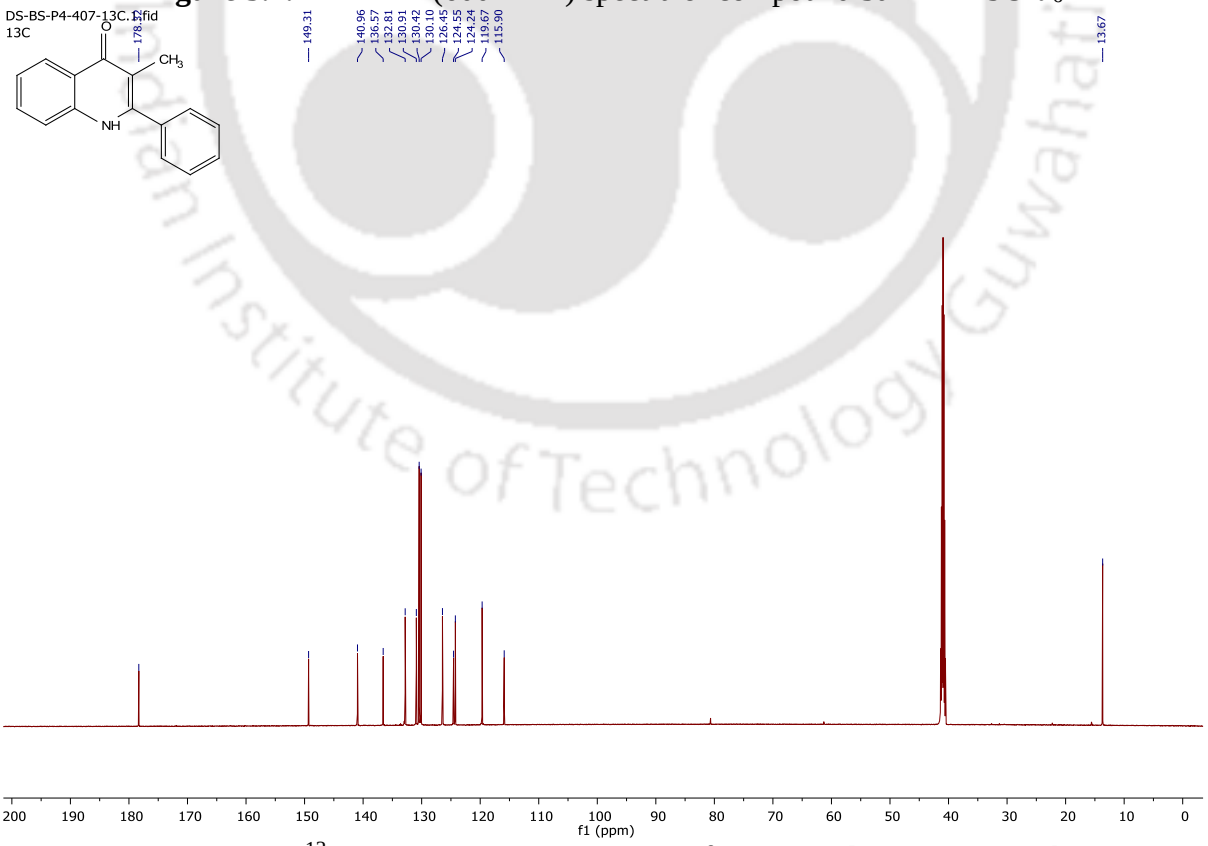


Figure 3.8. ^{13}C NMR (150 MHz) spectra of compound **5a** in DMSO-d_6

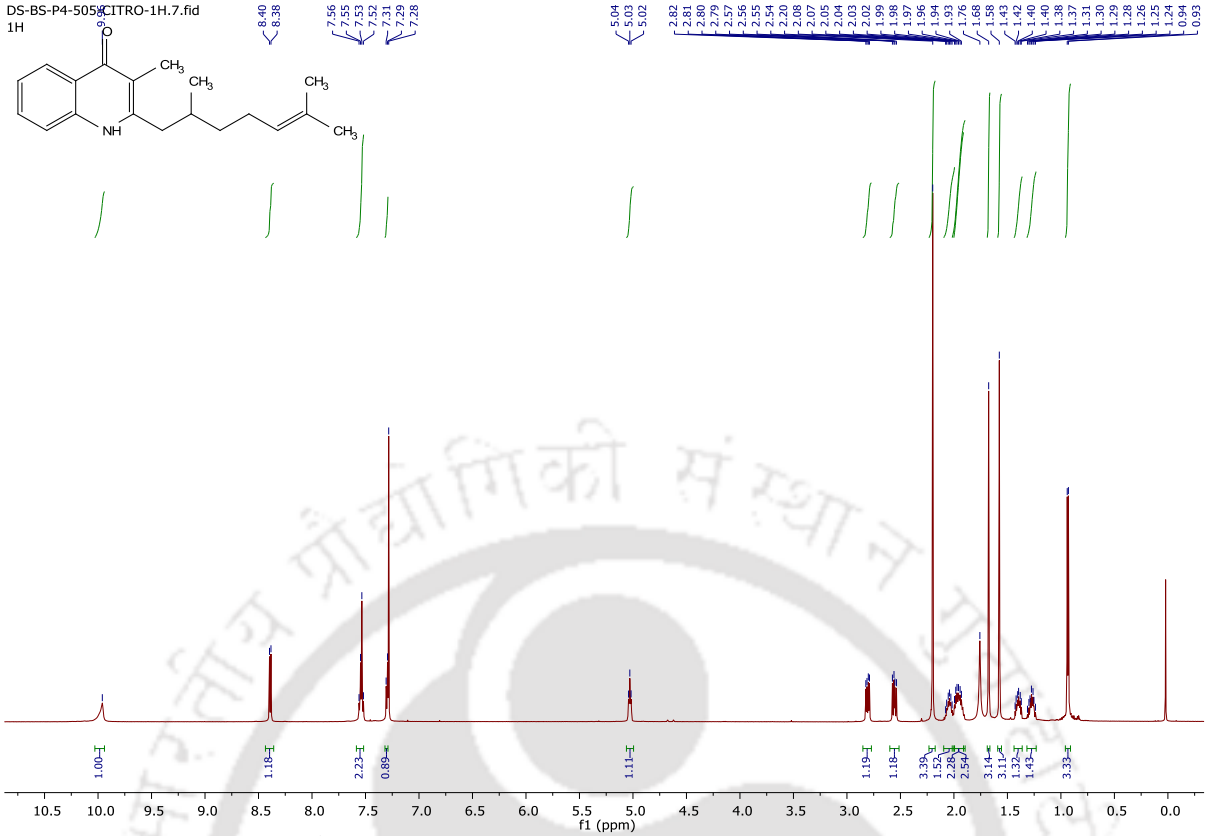


Figure 3.9. ^{1}H NMR (600 MHz) spectra of compound **5l** in DMSO-d_6

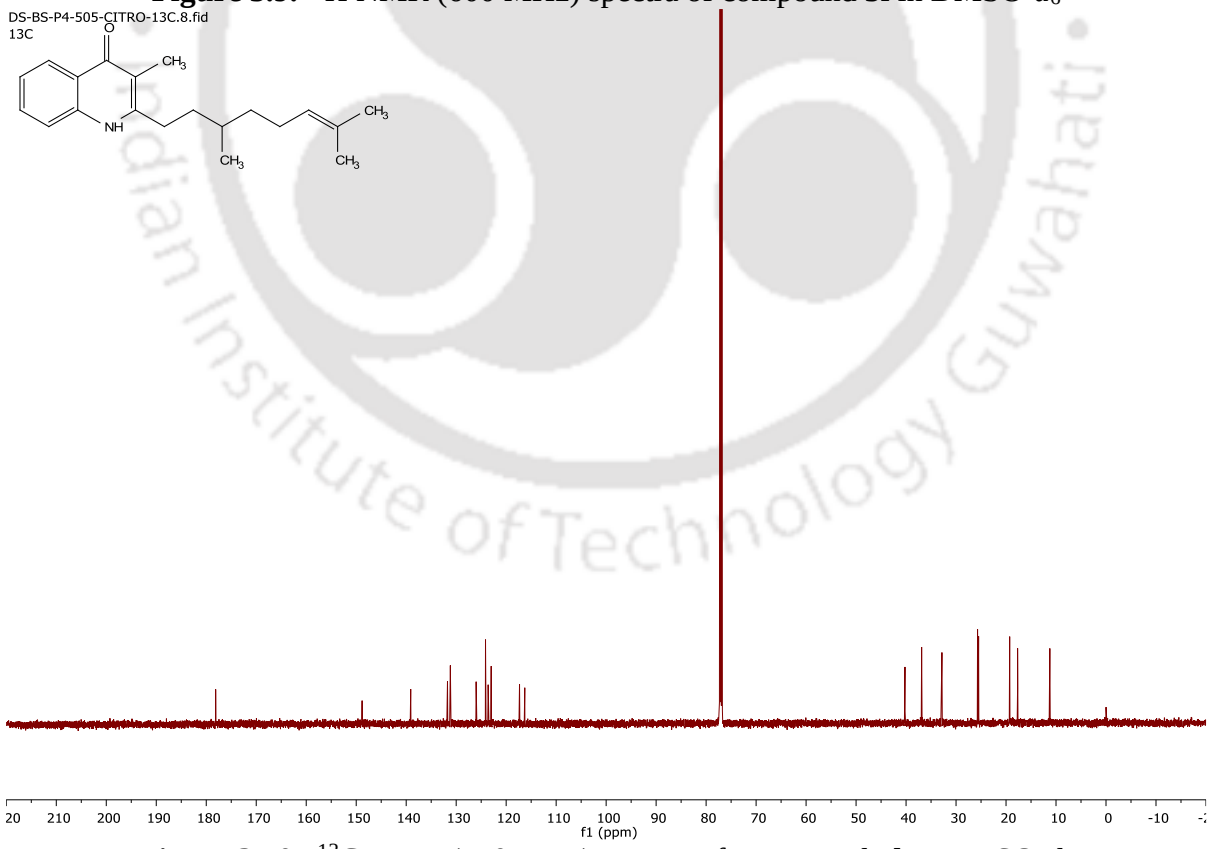


Figure 3.10. ^{13}C NMR (150 MHz) spectra of compound **5l** in DMSO-d_6

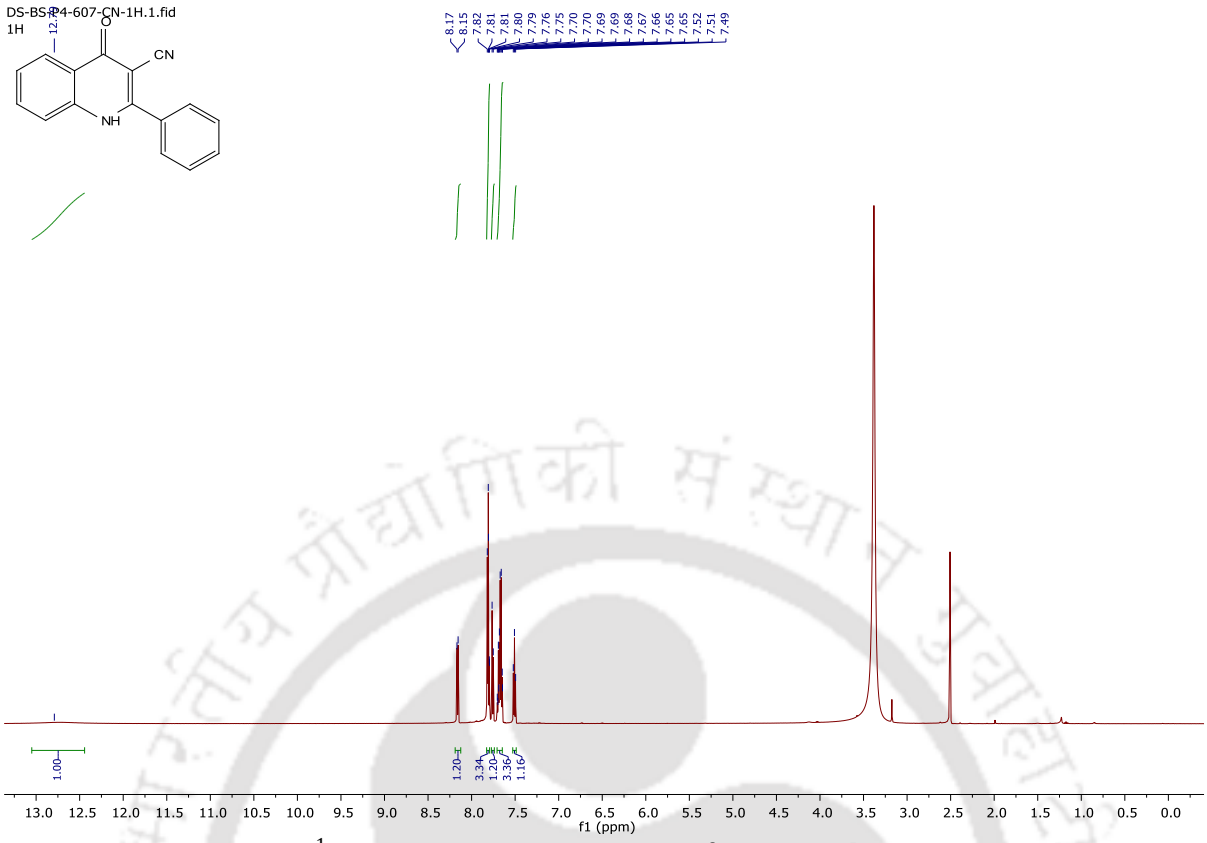


Figure 3.11. ^{1}H NMR (600 MHz) spectra of compound **5n** in DMSO-d_6

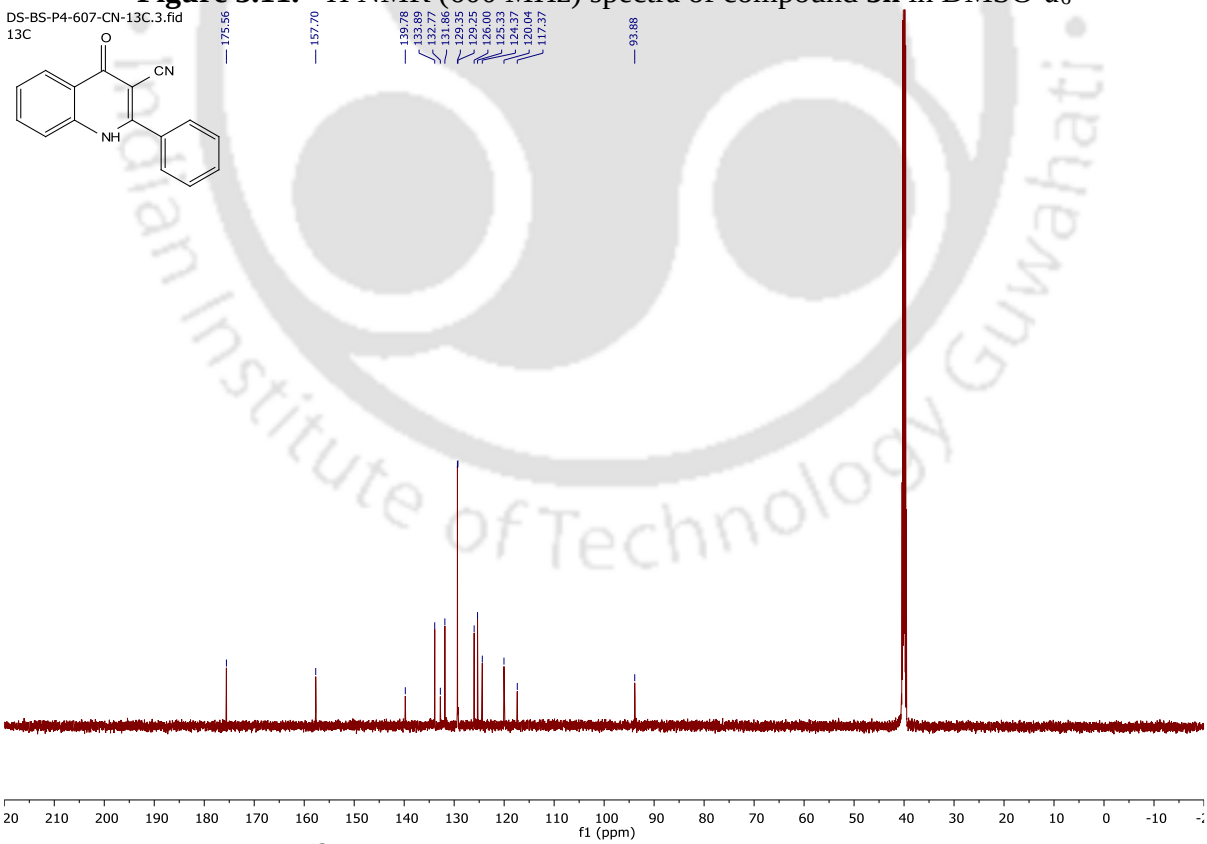


Figure 3.12. ^{13}C NMR (150 MHz) spectra of compound **5n** in DMSO- d_6

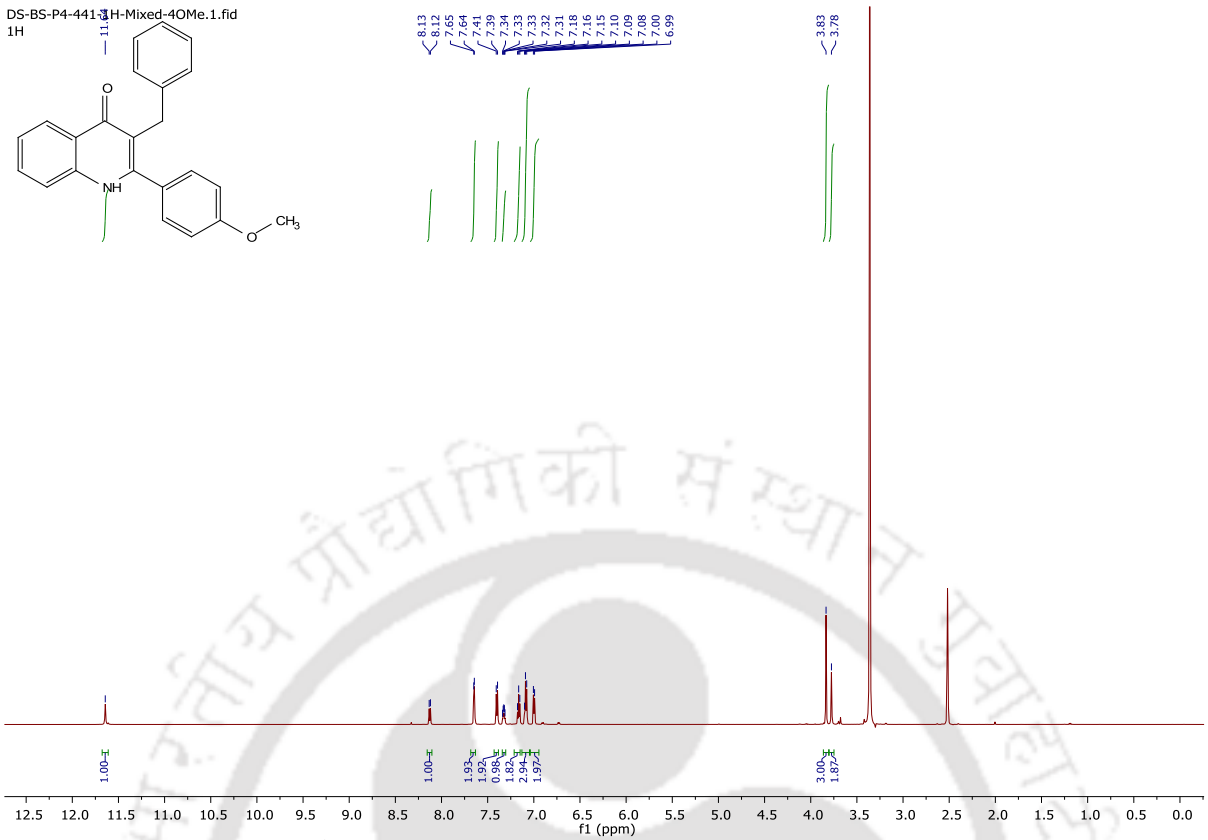


Figure 3.13. ^{1}H NMR (600 MHz) spectra of compound **5y** in DMSO-d_6

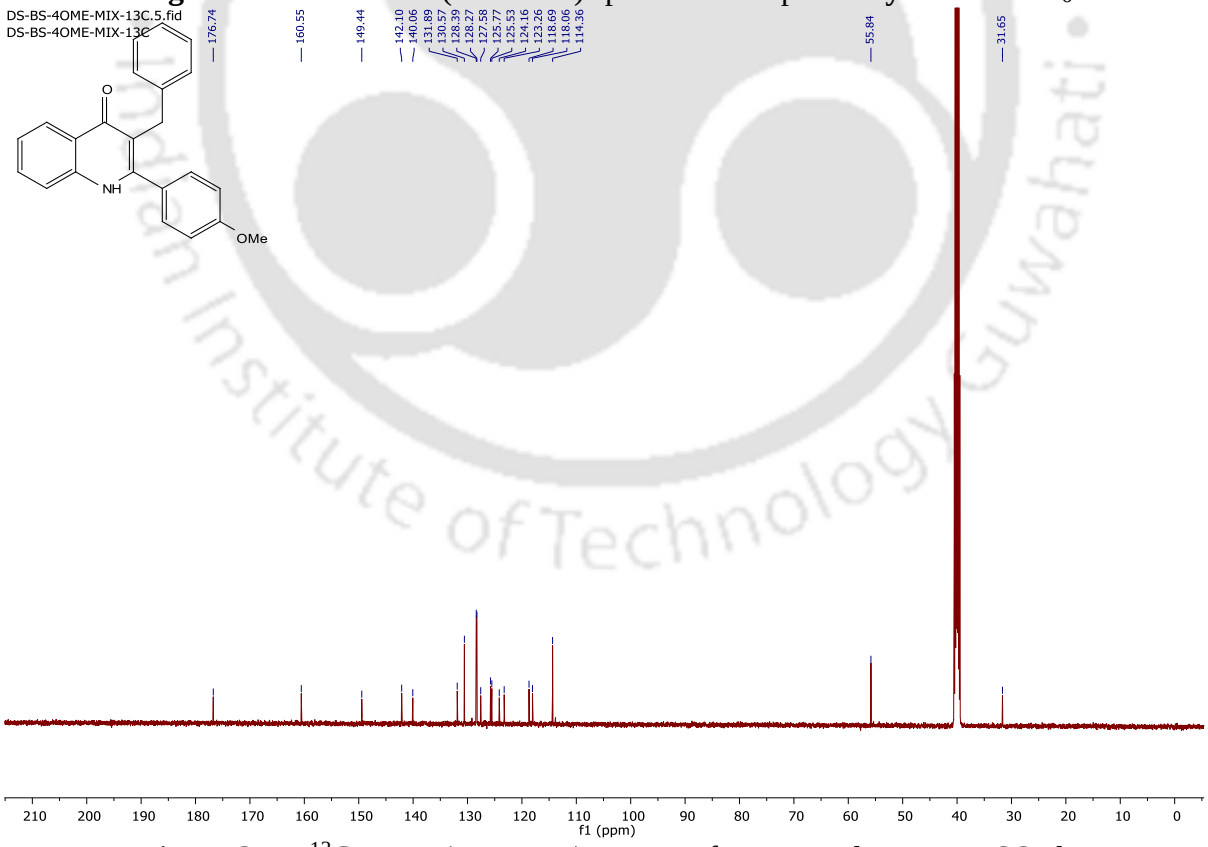


Figure 3.14. ^{13}C NMR (125 MHz) spectra of compound **5y** in DMSO-d_6

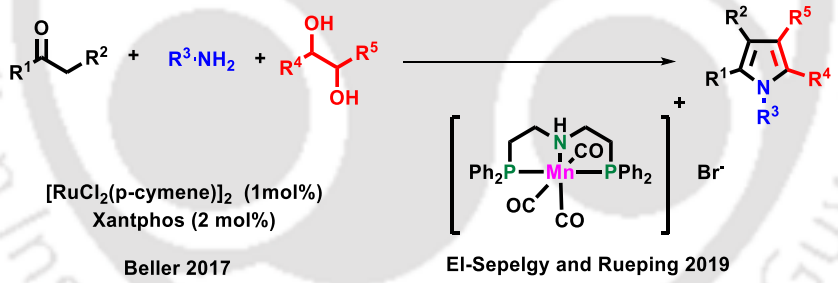
Chapter 4

Multicomponent Dehydrogenative Synthesis of Acridine-1,8-diones Catalyzed by Ru-doped Hydrotalcite

4.1. Introduction:

Nitrogen-containing heterocycles have found profound applications as drugs,[1a] flavors,[1b] vitamins,[1c] agrochemicals[1d,] and dyes.[1e] Thus, the development of new atom-economical and environmentally benign synthetic routes for the heterocycles is always demanding. The past decade witnessed explosive growth in catalytic (de)hydrogenative utilization of renewable alcohols by homogeneous transition metal complexes.[2,3] These de(hydrogenative) transformations have proven to be extremely useful for the synthesis of a wide range of heterocycles in a sustainable manner. Multicomponent reactions have several advantages, as these types of reactions are considered to be green in terms of productivity, energy saving, and step-economy. Thus, the one-pot multicomponent dehydrogenative synthesis of *N*-heterocycle is considered highly sustainable and economically viable.[4,5]

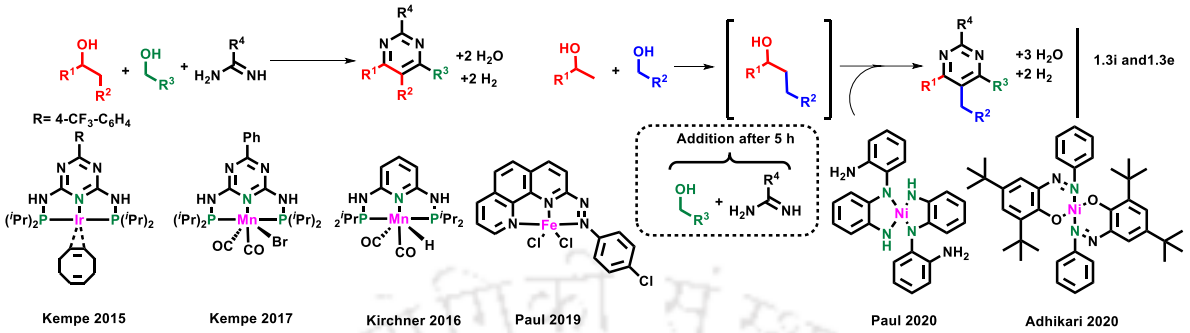
In this regard, a few examples are noteworthy to mention, as *Beller* and *co-workers* reported a unique ADMCR strategy to prepare pyrroles *via* one-pot three-component (ketones, amines, and 1,2-diols) coupling. In 2019, *Rueping* and *co-workers* also published the same reaction with manganese catalyst (Scheme **4.1**).



Scheme 4.1. Synthesis of pyrroles *via* one-pot three-component

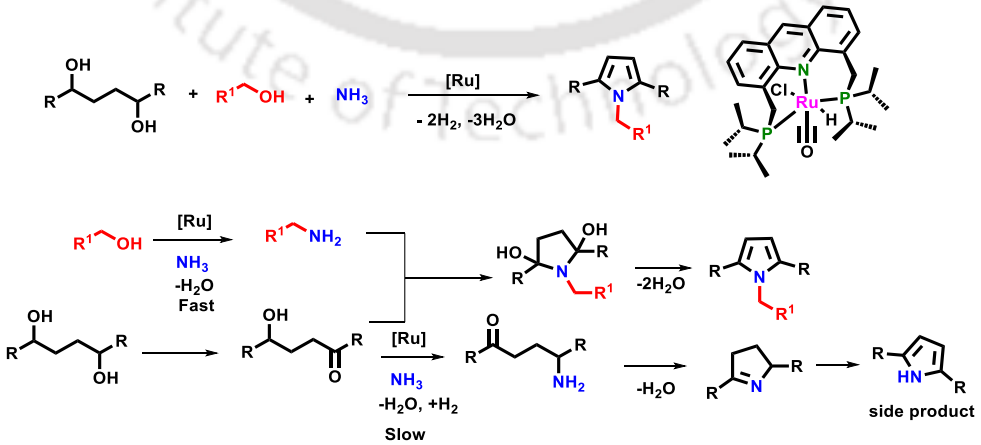
Later, in 2015, *Kempe* reported Ir-complex catalyzed multicomponent pyrimidine synthesis from a combination of amidine, primary alcohol, and secondary alcohol. Two equivalents of hydrogen and water were released during this sustainable three-component coupling process. Later, they extended their methodology and reported consecutive four-component reactions for pyrimidine synthesis. The reaction involves a series of dehydrogenation, borrowing hydrogen, and condensation reaction, which leads to the formation of selective C-C and C-N bonds. Condensation step results in deoxygenation of alcohols and dehydrogenation gives rise to aromatization. Later in 2017, *Kempe* introduced a manganese catalyst to illustrate three and four-component pyrimidine synthesis (Scheme **4.2**). Later, other reports were also published

with various transition metal-based complexes that were also found suitable for this transformation.[4,5]



Scheme 4.2. Synthesis of pyrimidines *via* ADMCR strategy using Ir, Mn, Fe and Ni complex

Milstein and *co-workers* reported the synthesis of *N*-substituted pyrroles *via* one-pot synthesis of NH-pyrroles followed by *N*-alkylation with acridine-derived Ru complex (Scheme **4.3**). First, a reaction between alcohol and ammonia creates a benzyl amine derivative. After that, benzyl amine reacted with *in situ* formed 1,4-diketone *via* dehydrogenation of 1,4-diol to afford the *N*-alkylated pyrrole product. If the ammonia directly reacts with the *in situ* formed 1,4-diketone, then it will give NH-pyrrole derivative which is the small side product of this reaction. Therefore, two competitive reactions can take place in this approach and it was observed that the primary alcohols are more reactive towards ammonia than secondary ones and quickly affords the *N*-substituted pyrroles. Increasing the amount of primary alcohol to 1,4-diol derivative increases the concentration of the primary amine and favors its attack to form the desired *N*-substituted pyrrole product (Scheme **4.3**).[4]



Scheme 4.3. Synthesis of *N*-alkylated pyrrole *via* ADMCR

In the above section, important examples related to multicomponent reactions by homogeneous complexes were discussed. Although homogeneous catalysts are well known for their remarkable reactivity, they have significant drawbacks, including high cost, low recovery, complicated synthetic procedures for ligand preparation, and average scalability. In comparison, heterogeneous catalysts have distinct advantages in terms of operational simplicity, cost-effectiveness, catalyst recycling, and reusability.[6,7,8]

So, keeping in mind the convenience of multicomponent reactions and heterogeneous catalysts, it was therefore envisioned that a heterogeneous catalyst could be utilized for ADMCR reaction to create biologically important *N*-heterocycles like acridine-1,8-dione, as they are known for their wide range of pharmacological properties like antitumor,[9a] cytotoxic,[9b] anticancer,[9c] anti-fungal,[9d] antimicrobial,[9e] antimalarial,[9f] and GCN5 inhibiton[9g] (**Figure 4.1**).

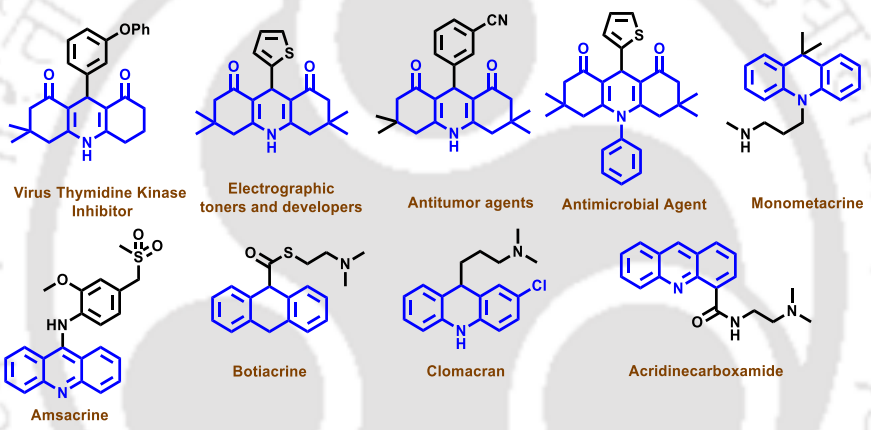


Figure 4.1. Biologically active 1,8-dioxodecahydroacridines derivatives

4.2 Our work:

In this chapter, Ru-fabricated hydrotalcite has been synthesized and well-characterized with FETEM, XPS, PXRD, TGA, ICP-AES, etc. In addition, the scope and limitations of the developed catalysts were explored in the ADMCR reaction. In chapter 1, we have thoroughly discussed the catalytic applicability of Ru-fabricated hydrotalcite in acceptorless dehydrogenation and borrowing the hydrogen approach. The catalyst is quite versatile, tunable, and easy to synthesize. In addition, the present protocol offers three-fold advantages: the use of renewable starting materials, the formation of environmentally benign by-products (H_2 and H_2O), and the recyclability of the catalyst. To highlight the practical utility, the gram-scale synthesis of acridine-1,8-dione was also performed. In addition, detailed mechanistic investigations and kinetic studies were also carried out.

4.3. Results and discussions:

4.3.1. Material characterization:

Ru-grafted hydrotalcite was prepared by the literature procedure[10, 3a] with slight variation. In previous studies, HT, $Mg_6Al_2(OH)_{16}CO_3$ was generally treated with an aqueous solution of $RuCl_3.nH_2O$ at room temperature, which later afforded the Ru/HT as a gray powder. Here, the modification is the use of 1M NaOH solution.

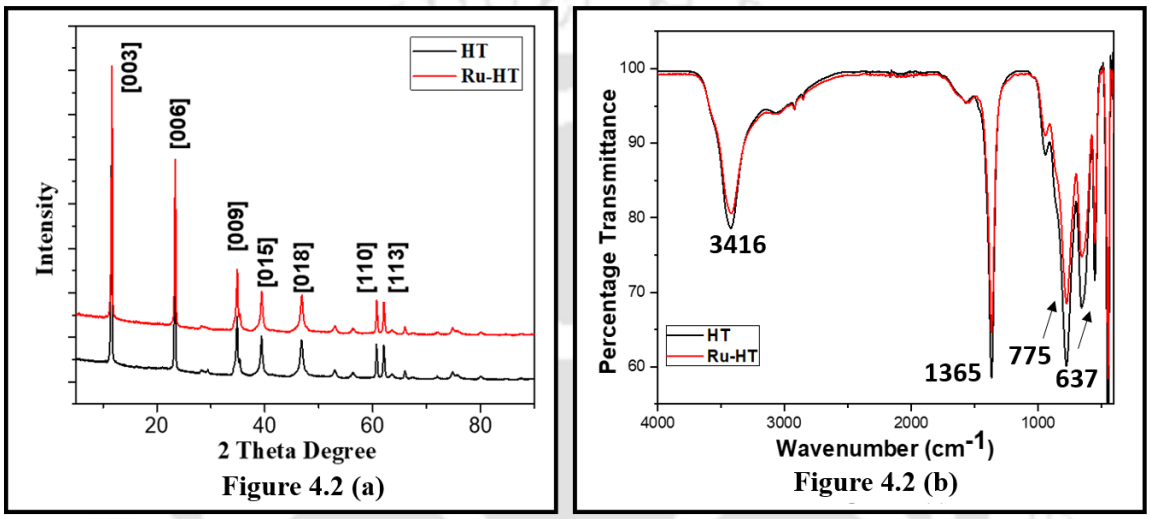


Figure 4.2. (a) PXRD and (b) FTIR pattern of HT and Ru-HT.

Inductively coupled atomic emission spectroscopy (ICP-AES) analysis indicated that the Ru content is 0.918%. Analysis of PXRD patterns and FT-IR of both Ru-HT and hydrotalcite underpins that the original hydrotalcite structure is retained in the prepared Ru-HT (Figure **4.2**). TEM images of the prepared Ru-HT was also taken, which showed uniform distribution of Ru metal particles over the support (Figure **4.3** and **4.4**).

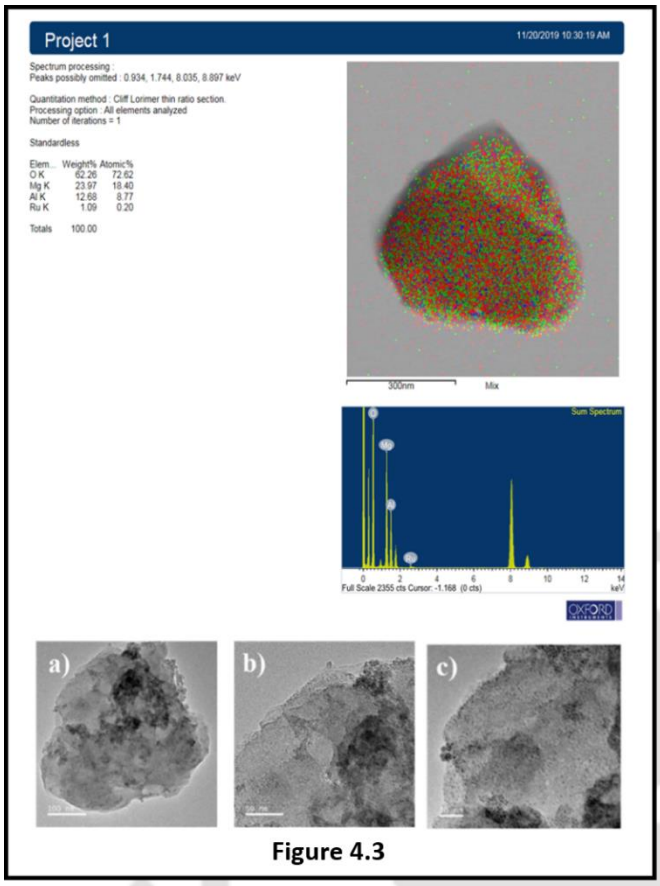


Figure 4.3

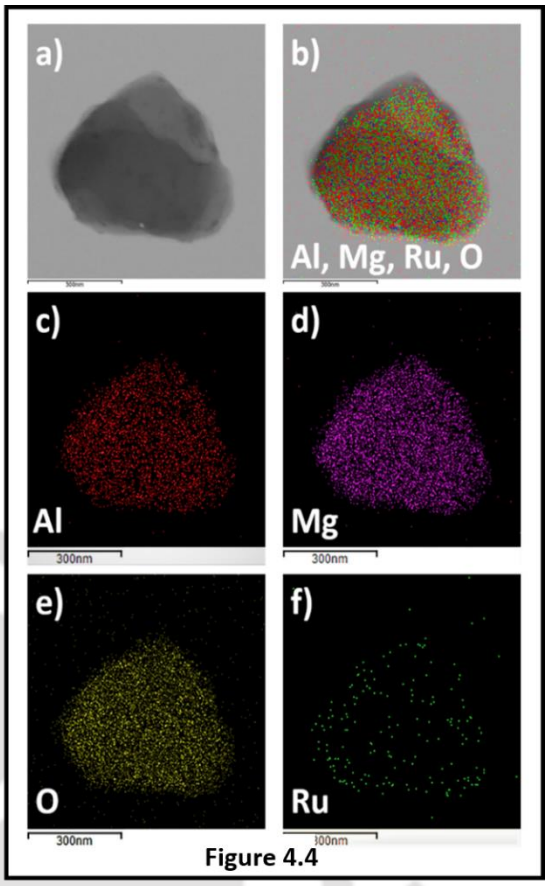


Figure 4.4

Figure 4.3. TEM images of Ru-HT and **Figure 4.4.** TEM-EDS mapping images: (a) FETEM image of Ru-HT, (b) overlap, (c) Al, (d) Mg, (e) O, (f) Ru.

TGA profile reflects that the pattern of weight loss for both Ru-HT and the hydrotalcite support is similar. The steady loss of mass below 100 °C is due to physisorbed water. The next rapid depletion of mass (9.25%) within the region (~180 °C to 240 °C) is associated with the loss of interlayer water; and the weight loss between ~300 °C to 580 °C, reflects dehydroxylation and decarbonation (**Figure 4.5**). In the XPS study, a high magnification Ru 3p scan of Ru-HT shows the binding energy of Ru $3p_{3/2}$ and $3p_{1/2}$ at 462.8 and 485.2 eV respectively, [11d,10] which indicate that the Ru existing in +4 oxidation state. The deconvoluted Ru 3d spectrum shows two closely separated peaks corresponding to Ru $3d_{5/2}$ and Ru $3d_{3/2}$, located at 281.3 and 285.8 eV respectively. The 287.7 eV curve belongs to sp^2 C 1s (CO_3^{2-}) of HT (**Figure 4.6**). Moreover, the absence of Cl in elemental mapping as well as in XPS analysis also validates the successful anchoring of Ru into the support. XPS analysis indicates that the Ru exists in +4 oxidation state. This is further supported by a silent EPR spectrum.[11]

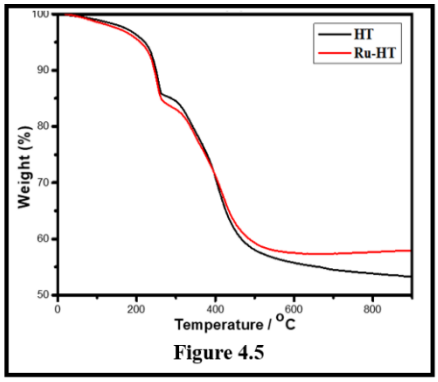


Figure 4.5

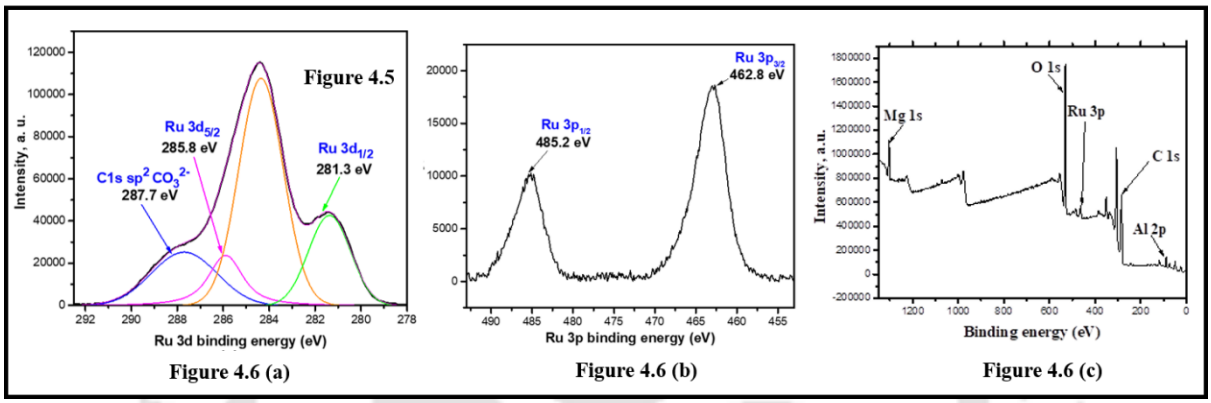


Figure 4.6 (a) Figure 4.6 (b) Figure 4.6 (c)

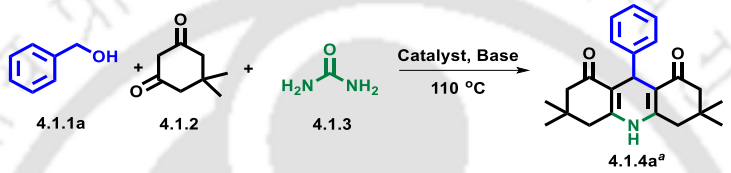
Figure 4.5. TGA curves of Ru-HT and HT, **Figure 4.6.** (a) XPS pattern of Ru 3p at Ru-H, (b) XPS pattern of Ru 3d at Ru-HT and (c) XPS survey spectrum of Ru-HT.

4.3.2. Optimization of the reaction condition for the synthesis of acridine-1,8-diones:

Next, the scope and limitation of the prepared catalyst were investigated in the dehydrogenative multicomponent synthesis of acridine-1,8-dione derivatives. Here urea has been used as a nitrogen source[12] to synthesize acridine-1,8-diones. To find out the optimum reaction conditions, various reaction parameters were screened employing benzyl alcohol **4.1.1a**, dimedone **4.1.2**, and urea **4.1.3**, as our model substrates (**Table 4.1**). When a mixture of benzyl alcohol (1 mmol), dimedone (0.5 mmol), and urea (1 mmol) was heated at 110 °C under the neat condition for 36 h in the presence of 50 mg Ru-HT catalyst under argon (**Table 4.1**, **Entry 1**), 54% of 3,3,6,6-tetramethyl-9-phenyl-3,4,6,7,9,10-hexahydroacridine-1,8(2H,5H)-dione **4.1.4a** was obtained. For further improvement of the yield of the desired product, ratios of the reactants were varied. Interestingly, it was observed that on increasing the amount of benzyl alcohol to 2 mmol, an enhancement in the yield (64%) of the product was attained **(Table 4.1**, **Entry 2**). Varying the concentration of urea (2 mmol) along with the alcohol did not improve the yield (**Table 4.1**, **Entries 3-5**). The yield of the desired product was further improved by the addition of 20 mol% KO^{t}Bu. Bases like KOH and K_2CO_3 were found inferior compared to

KO^{t}Bu (**Table 4.1**, **Entries 8-11**). Under the identical condition, solvents like ^{t}amyl alcohol, toluene, and dioxane afforded lower yield (**Table 4.1**, **Entries 12 to 14**), and the applicability of ammonium acetate, ammonium formate, and thiourea was found inferior compared to urea (**Entries 15,16** and **17**). Notably, support HT without any Ru-doping failed to activate alcohol. Similarly, only KO^{t}Bu resulted in a trace amount of the product (**Table 4.1**, **Entries 18** & **20**). Interestingly, when the reaction was performed under identical conditions in a 30 mL Ace pressure tube under argon, the yield of **4.1.4a** was further improved to 85% (**Table 4.1**, **Entry 23**).

Table 4.1. Screening table:



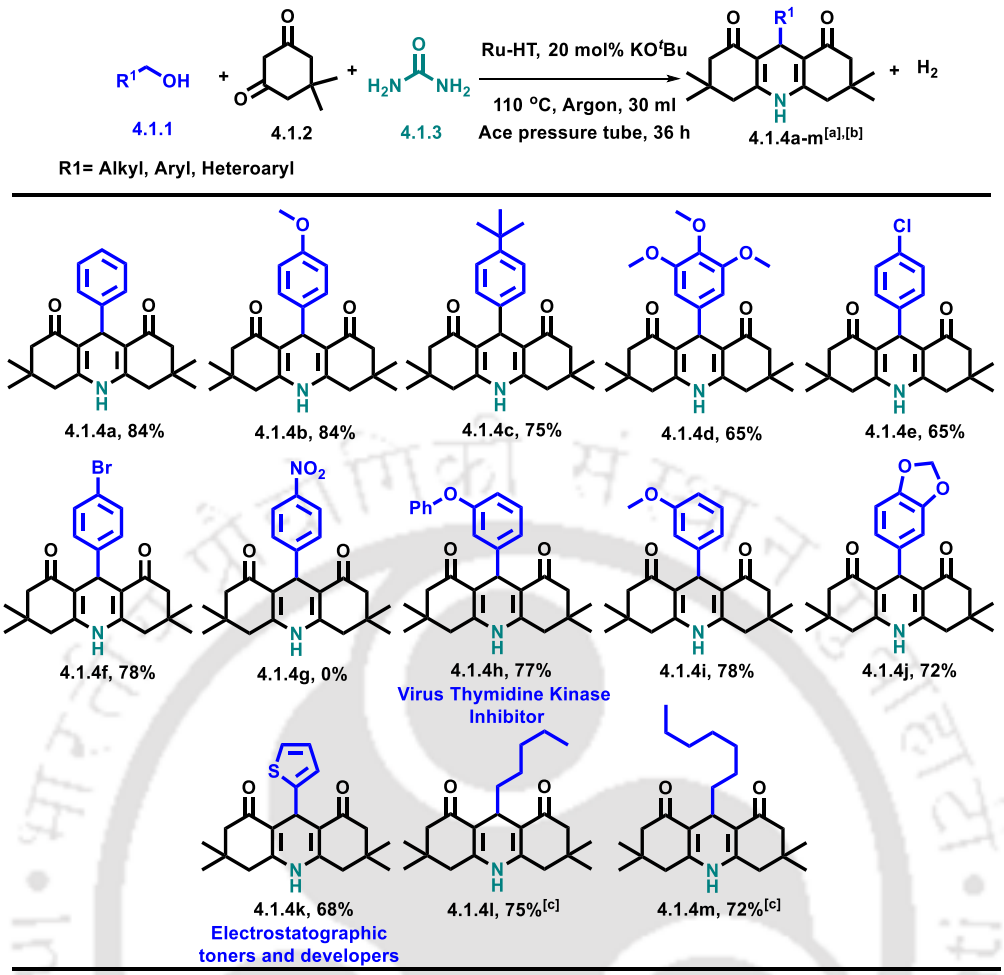
Entry	Catalyst	Stoichiometric ratio (1a:2:3)	Base (20 mol%)	Solvent	Yield (%)[b]
1	Ru-HT	1:0.5:1	-	-	54
2	Ru-HT	2:0.5:1	-	-	64
3	Ru-HT	2:0.5:2	-	-	62
4	Ru-HT	3:0.5:1	-	-	68
5	Ru-HT	3:0.5:2	-	-	67
6[c]	Ru-HT	2:0.5:1	-	-	68
7[d]	Ru-HT	2:0.5:1	-	-	58
8	Ru-HT	2:0.5:1	KO^{t}Bu	-	78
9	Ru-HT	2:0.5:1	KO^{t}Bu (1 equiv)	-	75
10	Ru-HT	2:0.5:1	KOH	-	72
11	Ru-HT	2:0.5:1	K_2CO_3	-	62
12	Ru-HT	2:0.5:1	KO^{t}Bu	^{t}Amyl alc.	46
13	Ru-HT	2:0.5:1	KO^{t}Bu	Toluene	32
14	Ru-HT	2:0.5:1	KO^{t}Bu	Dioxane	25
15	Ru-HT	2:0.5:1	KO^{t}Bu	-	32
16	Ru-HT	2:0.5:1	KO^{t}Bu	-	28
17	Ru-HT	2:0.5:1	KO^{t}Bu	-	35

18	-	2:0.5:1	KO^{t}Bu	-	Trace
19	$RuCl_3.nH_2O$	2:0.5:1	KO^{t}Bu	-	Trace
20	HT	2:0.5:1	KO^{t}Bu	-	Trace
21[e]	Ru-HT	2:0.5:1	KO^{t}Bu	-	44
22[f]	Ru-HT	2:0.5:1	KO^{t}Bu	-	35
23[g]	Ru-HT	2:0.5:1	KO^{t}Bu	-	85
24[h]	Ru-HT	2:0.5:1	KO^{t}Bu	-	80
25	Ru-HT	2:0.5:1	-	-	65

[a]Reaction conditions: 110 °C (Oil bath temperature), 36 h, under Ar. [b]Isolated yield. [c]80 mg Ru-HT. [d]40 mg Ru-HT. [e]Oil bath temperature 140 °C. [f]Oil bath temperature, 80 °C. [g]30 mL Ace pressure tube packed with Ar. [h]30 mL Ace pressure tube in air.

4.3.3. Substrate scope acridine-1,8-dione derivatives:

After optimizing the reaction conditions, it was sought to explore the versatility and limitations of our developed protocol. Under the optimized conditions, various alcohols have been employed to synthesize a diverse range of hexahydroacridine-1,8-diones. Aromatic ring containing electron-donating or electron-withdrawing functional groups at various positions of the aryl rings efficiently produced the corresponding acridine-1,8-diones. The halogen group was well survived under the reaction condition and no dehalogenated product was observed. (**Scheme 4.4**, **entries 4.1.4e** and **4.1.4f**). Unfortunately, 4-nitrobenzyl alcohol unable to afford any desired product. Our protocol provides a route to synthesize compound **4.1.4h**, which is used to treat infections caused by herpes simplex virus.[13a] Compound **4.1.4k** is used in electrophotographic toners and developers.[13b] To our delight, **4.1.4k** was isolated in 68% yield using heteroaromatic alcohol such as 2-thiophene methanol as substrate. Encouraged by this, our attention was turned toward aliphatic alcohols as these are considered challenging substrates for dehydrogenation reactions. However, it was observed that under the optimum condition, the yield was poor. Increasing the temperature to 140 °C also did not furnish the desired acridine-1,8-dione in good yield. Therefore, the reaction was carried out consecutively via dehydrogenation of alcohol at 140 °C followed by the addition of dimedone and urea. Delightfully, the sequential addition resulted in excellent yield for aliphatic alcohols (**Scheme 4.4**, **entries 4.1.4l** and **4.1.4m**).



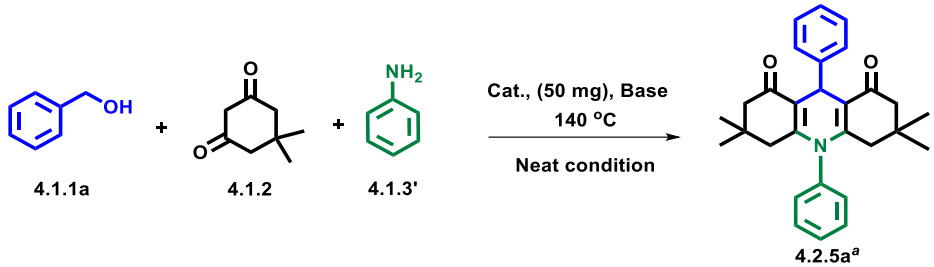
[a]Reaction conditions: **4.1.1** (2 mmol), dimedone (0.5 mmol), urea (1 mmol) heated at 110 °C (oil bath temperature) for 36 h in 30 mL Ace pressure tube in Ar, [b]Isolated yield, [c]Primary alcohol (2 mmol), 50 mg Ru- HT (Ru content ~ 0.5 mg) was treated at 140 °C (oil bath temperature) for 18 h, followed by addition of 20 mol% KO^{t}Bu, dimedone (0.5 mmol) and urea (1.0 mmol) heated at 110 °C for 12 h.

Scheme 4.4. Synthesis of hexahydroacridine-1,8-dione derivatives

4.3.4. Optimization of the reaction condition for the synthesis of *N*-substituted acridine-1,8-diones:

Next, the scope of various amines to synthesize N-substituted acridine-1,8-dione was investigated. The screening for the optimum condition of the reaction was discussed in **Table 4.2.**

Table 4.2. Optimization of the reaction conditions.

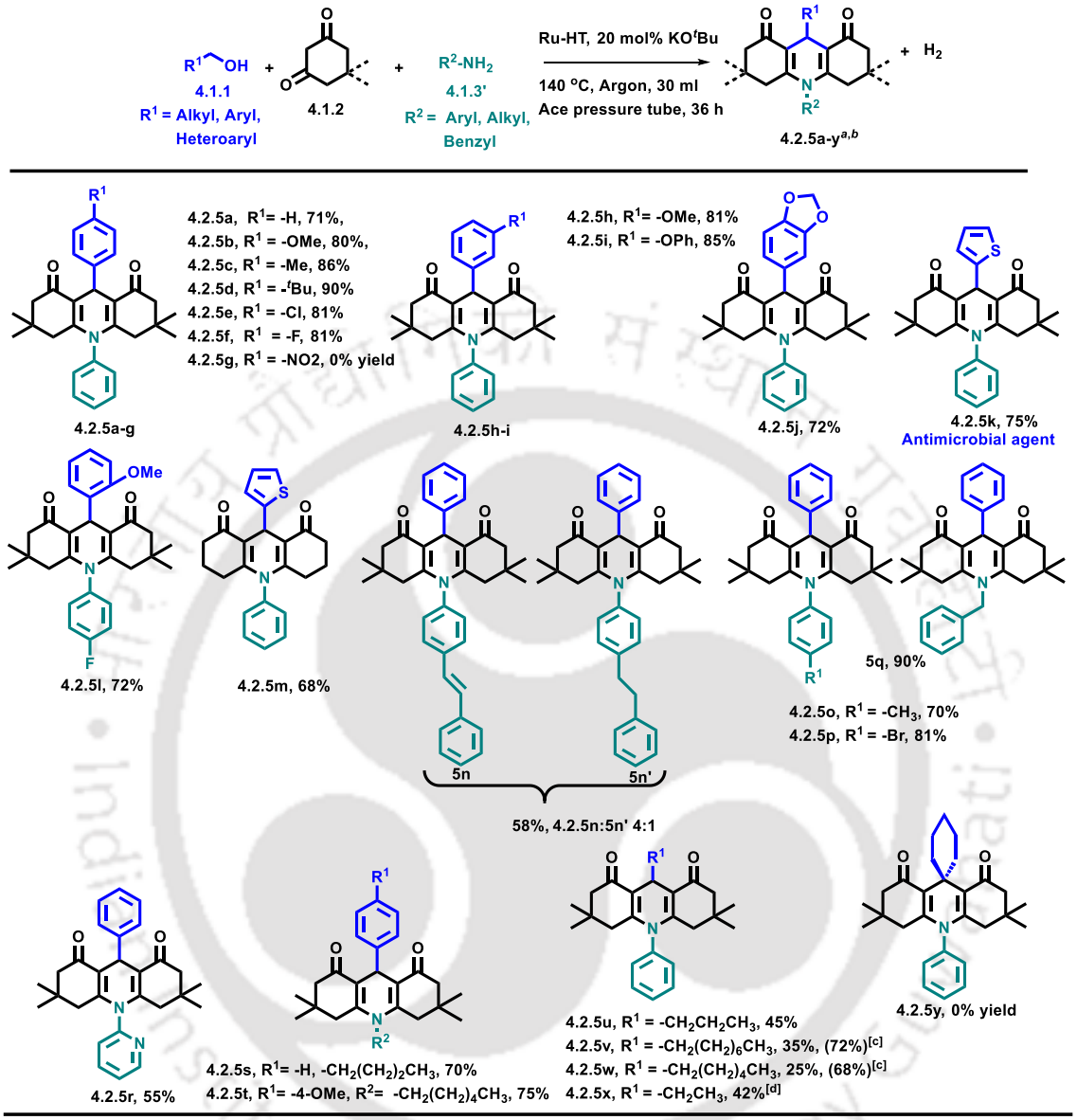


4.1.1a + 4.1.2 + 4.1.3' → 4.2.5a[a]

Entry	Cat.	Stoichiometric Ratio (mmol) 1a:2:3	Base (20 mol%)	Solvent	Yield[b] (%)
1	Ru-HT	0.5:1:0.5	-	-	30
2	Ru-HT	1:1:0.5	-	-	42
3	Ru-HT	2:1:0.5	-	-	50
4	Ru-HT	3:1:0.5	-	-	55
5	Ru-HT	4:1:0.5	-	-	58
6	Ru-HT	3:1:0.5	-	-	56
7	Ru-HT	3:1:0.5	-	-	48
8	**Ru-HT**	**3:1:0.5**	**KO^{t}Bu**	-	**71**
9	Ru-HT	3:1:0.5	KO^{t}Bu (1equiv)	-	70
10	Ru-HT	3:1:0.5	KOH	-	68
11	Ru-HT	3:1:0.5	K_2CO_3	-	54
12	Ru-HT	3:1:0.5	KO^{t}Bu	^{t}Amyl alcohol	40
13	Ru-HT	3:1:0.5	KO^{t}Bu	Toluene	35
14	Ru-HT	3:1:0.5	KO^{t}Bu	Dioxane	25
15	-	3:1:0.5	KO^{t}Bu	-	Trace
16	$RuCl_3.nH_2O$	3:1:0.5	KO^{t}Bu	-	Trace
17	HT	3:1:0.5	KO^{t}Bu	-	Trace
18	Ru-HT	3:1:0.5	KO^{t}Bu	-	55
19	Ru-HT	3:1:0.5	KO^{t}Bu	-	78
20	Ru-HT	1.5:1:0.5	KO^{t}Bu	-	54

[a]Reaction conditions: 50 mg Cat 0.918% Ru-HT, 140 °C, Ar for 36 hour, [b]Isolated yield. [c]Catalyst loading (80 mg). [d]Catalyst loading (40 mg). [e]Temperature 110 °C. [f]30 mL Pressure tube.

4.3.5. Substrate scope *N*-substituted acridine-1,8-dione derivatives:



[a]Reaction conditions: **4.1.1** (3 mmol), dimedone (1.0 mmol), **4.1.3′** (0.5 mmol), 50 mg Ru-HT (Ru content ~ 0.5 mg), 20 mol% KO^{t}Bu, 140 °C, Ar, 30 mL Ace pressure tube for 36 h. [b]Isolated yield. [c]Yield in parenthesis is for consecutive addition. [d]Ethanol (0.5 mL), 160 °C.

Scheme 4.5. Synthesis of N-substituted acridine-1,8-dione derivatives.

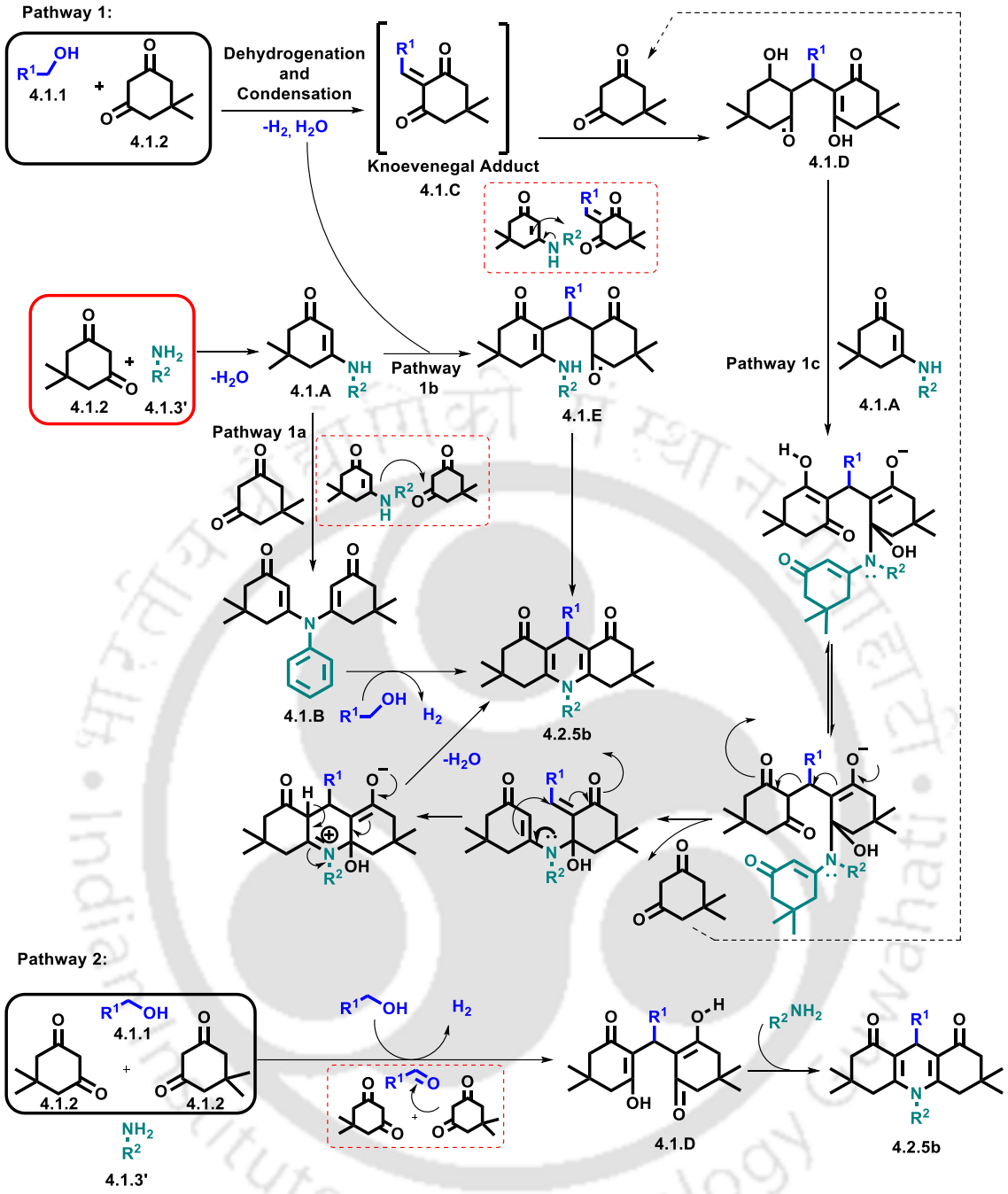
Upon heating various aromatic alcohols (3.0 mmol), dimedone (1.0 mmol), aniline (0.5 mmol) at 140 °C in the presence of 50 mg Cat and 20 mol% KO^{t}Bu under argon atmosphere led to the formation of the corresponding products in good isolated yields after 36 h (**Scheme 4.5**, **4.2.5a-5g, 5h-i, 5m**). Anilines containing electron-withdrawing and electron-donating substituents at the *para* position were compatible with different alcohols and dimedone to form corresponding

hexahydroacridine-1,8-diones. Our methodology offers a route to synthesize antimicrobial agent **4.2.5k**[13c] in 75% yield. When (E)-4-styrylaniline was used, desired **5n** was formed in moderate yield together with small amount of C=C reduction product **4.2.5n´(5n**:**5n´** 4:1).(**Scheme 4.5**, **Entry 4.2.5n** and **4.2.5n´**). Benzyl amine, heterocyclic amine or aliphatic amines such as butyl amine, 2-aminopyridine, and hexylamine responded well to give the desired product (**4.2.5q-5t**) in good yield.

Anilines reacting with different aliphatic alcohols and dimedone afforded the desired heterocycles in moderate yields whereas ethanol failed to give any product. However, **4.2.5x** was isolated in 42% yield just by increasing the temperature to 160 °C. Unfortunately, in the case of cyclohexanol, no product formation was observed even at 160 °C. A gram-scale synthesis was also performed to check the scalability of our developed catalytic protocol. Of note, an excellent yield of **4.2.5a** (70%, 1.190 gm) was obtained even with a lower amount of alcohol.

4.4. Reaction mechanism:

Two possible mechanistic pathways are proposed for this dehydrogenative multicomponent reaction, which is depicted in **Scheme 4.6**. An equimolar amount of dimedone and aniline can react to form *β*-enaminone **4.1.A**, which upon condensation with another molecule of dimedone (**pathway 1a**) would generate intermediate **4.1.B**. Intermediate **4.1.B** can react further with the aldehyde formed by the dehydrogenation of alcohol to furnish the final product, **4.2.5b**. Another possibility is the condensation of dimedone with the *in situ* formed aldehyde to furnish Knoevenagel adduct **4.1.C**. This Knoevenagel adduct can eventually react with intermediate **4.1.A** (*β*-enaminone) and may generate the target product **4.2.5b** (**pathway 1b**). Another proposed pathway is **pathway 1c**.

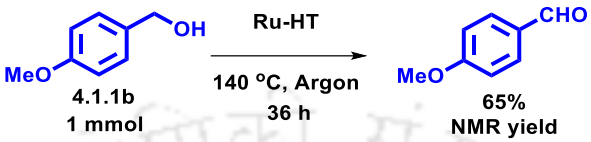


Scheme 4.6. Plausible Mechanism

The intermediate **4.1.C** also can react with dimedone to furnish **4.1.D**, which eventually reacts with *β*-enaminone **4.1.A** to give the final product **4.2.5b** (**pathway 1c**). Furthermore, in **pathway 2**, the formed aldehyde would first undergo condensation with 2 equivalents of dimedone to form intermediate **4.1.D** which can lead to the formation of acridine 1,8 dione, **4.2.5b** via condensation with the aniline.

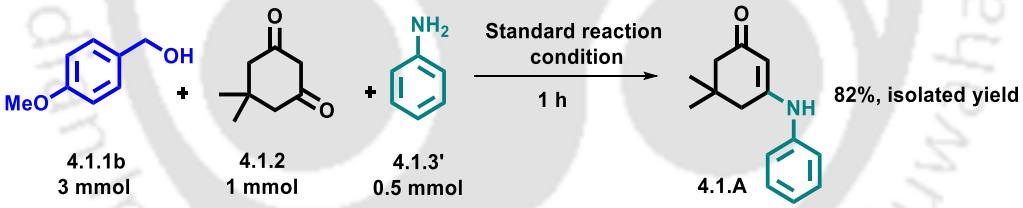
4.5. Mechanistic investigation:

To shed light on the preferred pathway, some control experiments have been performed. At first, the dehydrogenative property of our catalyst was examined. Delightfully, the 4-methoxy benzaldehyde was formed in 65% yield even in the absence of a traditional inorganic base (**Scheme 4.6.1**).



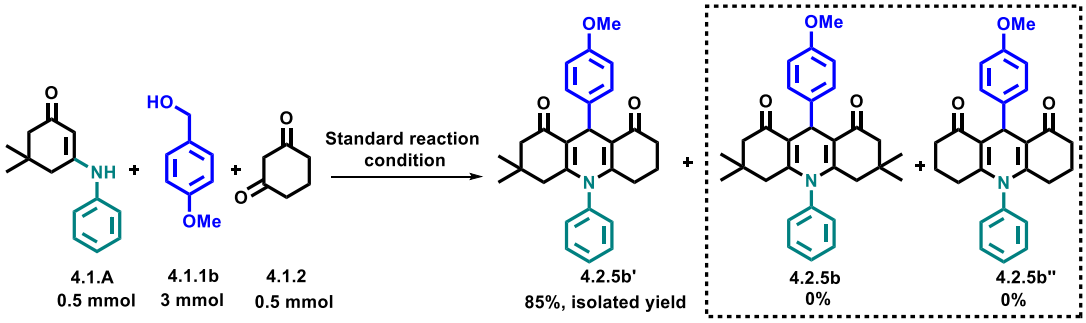
Scheme 4.6.1. Control experiment 1

When, the reaction of aniline, dimedone, and 4-methoxybenzyl alcohol was stopped after 1 h, *β*-enaminone **4.1.A** was isolated in 82% yield (**experiment 2**). After 1 h the conversion of alcohol to aldehyde was not observed which was also confirmed as **4.1.B**, **4.1.C,** or **4.1.D** was not detected. This result suggests that the rate of formation of **4.1.A** is much faster than the conversion of alcohol to aldehyde. This confirms that **pathway 2** is not possible, as it does not involve *β*-enaminone intermediate (**Scheme 4.6.2**).



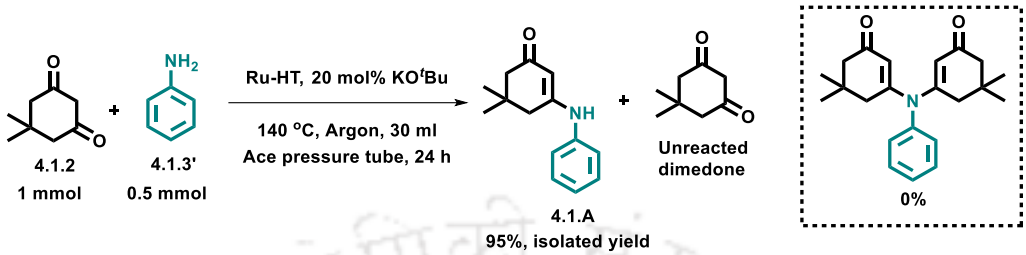
Scheme 4.6.2. Control experiment 2

Furthermore, when performed **4.1.A** was treated with 1,3- cyclohexanedione and alcohol, and the product, **4.2.5b'** was formed exclusively which indicates that the *β*-enaminone formation is not reversible (**experiment 3**).



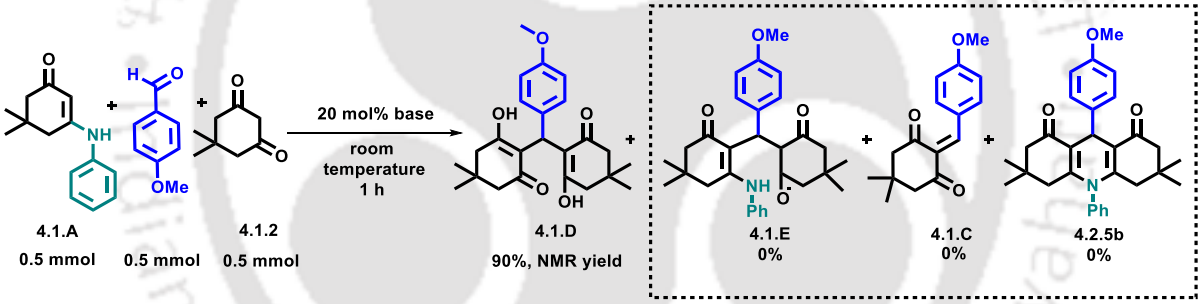
Scheme 4.6.3. Control experiment 3

Interestingly, reacting aniline with 2 equivalent of dimedone for a prolonged time (24 h) does not lead to the formation of **4.1.B** (**experiment 4**), which underpins that **pathway 1a** is not possible (**Scheme 4.6.4**).



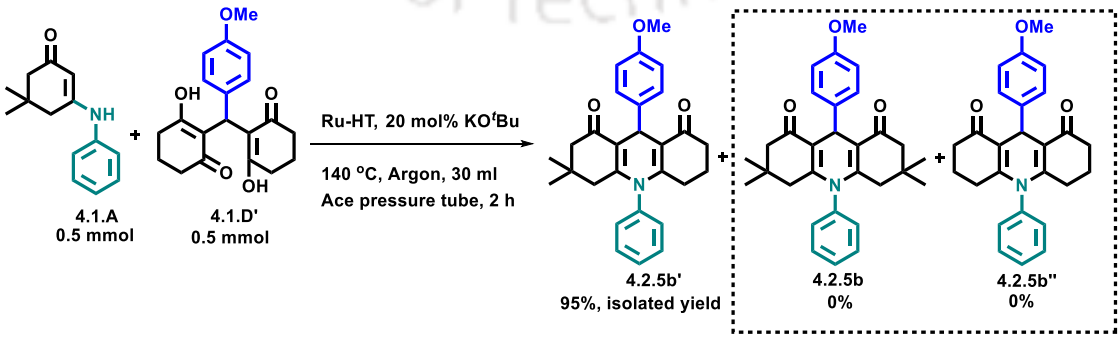
Scheme 4.6.4. Control experiment 4

Moreover, it was also observed that the Knoevenegal adduct **4.1.C** is highly reactive to form **4.1.D**, even in the presence of *β*-enaminone (**experiment 5**) which reflects that the formation of **4.1.D** more viable than the formation of **4.1.E** (**Scheme 4.6.5**).



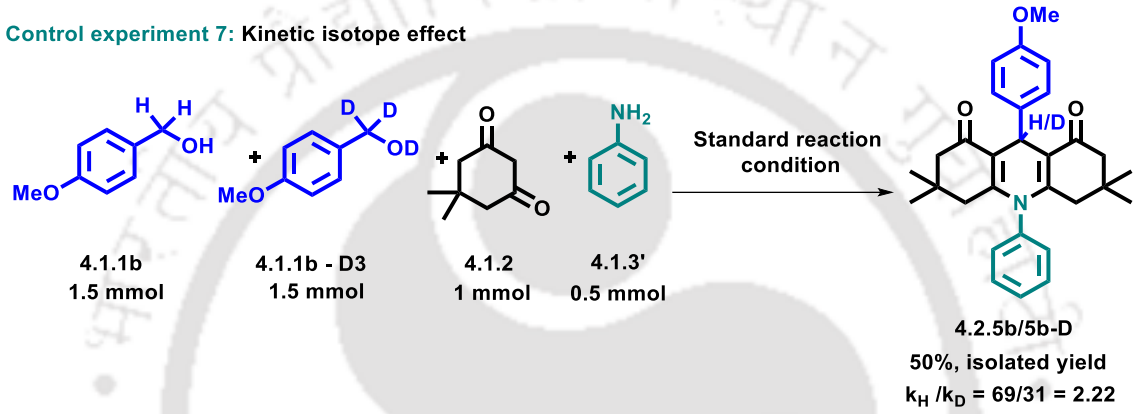
Scheme 4.6.5. Control experiment 5

Furthermore, the reaction of **4.1.D´** with the *β*-enaminone gave **4.2.5b´** within 2 h (**experiment 6**) which reveals that **pathway 1c** is more feasible (**Scheme 4.6.6**).



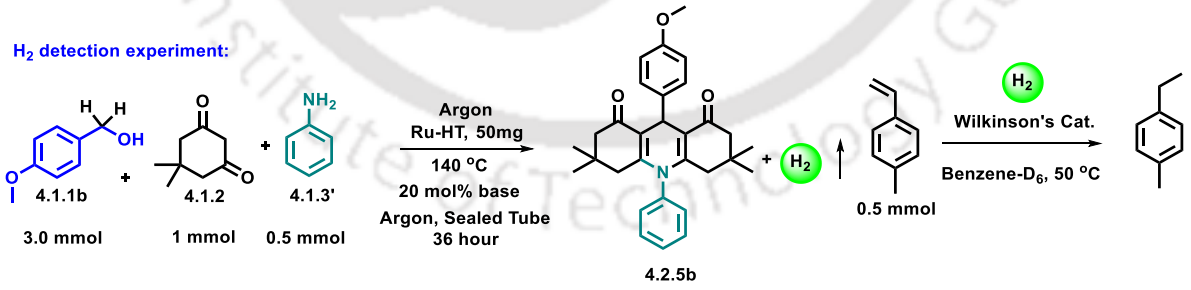
Scheme 4.6.6. Control experiment 6

Next, the kinetic isotope effect (KIE) was investigated. First, a competition reaction (**Scheme 4.6.7**, **experiment 7**) was performed using both **4.1.1b** and **4.1.1b-D3** under the standard reaction condition. The observed product ratio of the deuterated and non-deuterated products was determined by ^{1}H NMR which indicates the KIE value ~2.22. Further, the parallel reaction with **4.1.1b** and **4.1.1b-D3** afforded nondeuterated and deuterated products in 80% and 38% yield respectively. The calculated k_H/k_D value (~2.10) from the parallel reaction is in close agreement with that of the competitive reaction. This strongly underpins that the C-H bond cleavage occurs in the rate-determining step (RDS) (**Scheme 4.6.7**).



Scheme 4.6.7. Control experiment 7

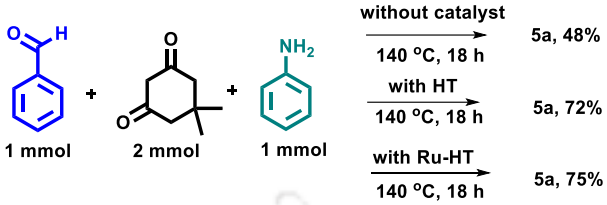
To confirm the H_2 evolution in this multicomponent reaction, hydrogenation of 4-methyl styrene was executed with the evolved H_2 employing Wilkinson's catalyst, which resulted in the formation of 4-ethyltoluene (**Scheme 4.6.8**)



Scheme 4.6.8. H_2 detection experiment

Next, the role of Ru-doped hydrotalcite in these reactions has also been investigated; whether it only promotes alcohol dehydrogenation (**Scheme 4.6.9**) or hydrotalcite also catalyzes the condensation steps. A comparative study was carried out by conducting three successive experiments among aldehyde, dimedone, and aniline: i) in the absence of any catalyst, ii) with

HT, and ii) in the presence of Ru-HT. The results strongly support that hydrotalcite has a clear role to catalyze the reaction. The Lewis acidic[14] site of hydrotalcite helps to activate the carbonyl compound whereas Brønsted basic sites[14] assists condensation steps.



Scheme 4.6.9. Role of HT and Ru-HT.

4.6. Kinetic study:

The study of the time course of the reaction (**Figure 4.7**) confirmed that the reaction between dimedone and aniline is much faster compared to the dehydrogenative conversion of alcohol to aldehyde. Within 3 h quantitative conversion of aniline to intermediate **4.1.A** was observed. The formation of the **4.2.5b** was started at 6 h and gradually increased with simultaneous consumption of intermediate **4.1.A**. At any given time concentration of the formed aldehyde was very less indicating the rapid consumption of formed aldehyde by dimedone to form **4.1.D** under the reaction condition which ultimately leads to the formation of acridine1,8-dione by reacting with **4.1.A**.

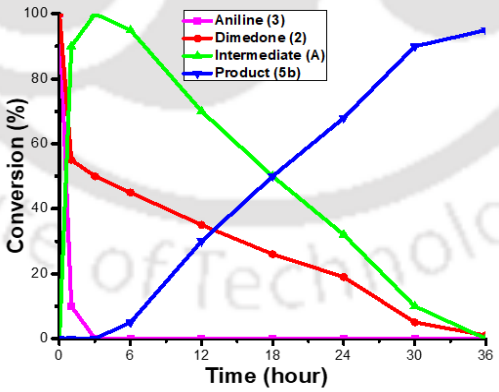


Figure 4.7. Time course of the reaction during the formation of **4.2.5b** from 4-methoxybenzyl alcohol, dimedone and aniline compared to the reaction

The reaction also proceeds smoothly in the presence of one equivalent radical scavenger, 2,6-di-*tert*-butyl-4-methylphenol (BHT). This ruled out the involvement of any radical species in the reaction. Next, the reaction was performed in the presence of an equimolar amount of

TEMPO. In the presence of TEMPO, the rate of the reaction was increased compared to the reaction without any TEMPO. This suggests that the abstraction of hydrogen atoms from the ruthenium hydride species[15] by the TEMPO is much easier than the formation of molecular H_2 (**Figure 4.8**).

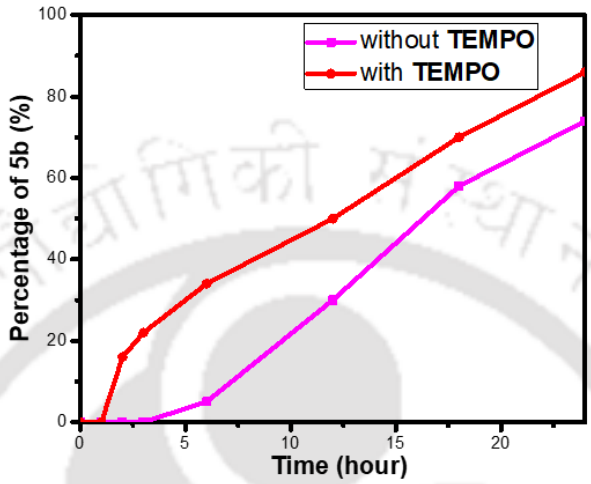


Figure 4.8. The effect of radical scavengers (TEMPO, 1 equivalent to 3) on the Ru-HT catalyzed one-pot multicomponent reaction.

After the reaction negligible leaching (< 10 ppb) of Ru was confirmed by ICP-AES. The developed Ru-HT was reused at least five cycles without considerable loss in the yield. In addition, both the FT- IR and PXRD data of the reused catalyst were analyzed and compared with the fresh Ru-HT. A slight decrease in average crystallite size after the fifth consecutive run was observed. However, the decrease is not significant enough to ascertain any structural changes within the catalyst (**Figure 4.9**).

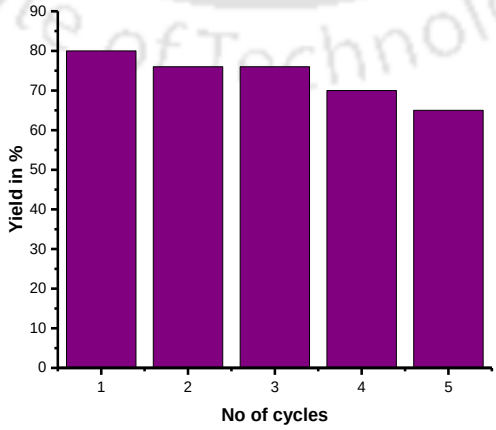


Figure 4.9. Recovery and reuse of the Ru-HT catalyst.

4.7. Conclusion:

In conclusion, the first dehydrogenative synthesis of functionalized hexahydroacridine-1,8-diones has been demonstrated. In this Ru-doped hydrotalcite-catalyzed multicomponent reaction, the selective formation of the C-C and C-N bonds is achieved via dehydrogenation and selective condensation. Mechanistic investigation and kinetic studies help to understand the reactivity and selectivity pattern of the substrates and reveal the suitable reaction sequences to furnish the desired product. The kinetic isotope effect is indicative of the involvement of C-H bond cleavage in the rate-determining step. The synthesis of structurally important medicinal compounds was also demonstrated. Easy scalability and successful recyclability of the developed catalyst make this protocol attractive and practical.

4.8. Experimental Section:

4.8.1. General Information: All catalytic experiments were carried out using standard Schlenk techniques and pressure tubes according to their respective condition. All solvents were dried using standard procedure.[16] Deuterated solvents were used as received without any additional purification. Most of the chemicals used in catalysis reactions were purified according to standard procedure (or by vacuum distillation/sublimation). Thin layer chromatography (TLC) on silica-gel 60 F254 plates (from Merck Company) and SRL silica gel (100-200 mesh) for column chromatography was used. NMR (400 and 600 MHz) spectra were recorded on the BRUKER NMR spectrometer. Deuterated chloroform was used as the solvent, and chemical shift values (δ) are reported in parts per million relatives to the residual signals of this solvent [δ 7.27 for 1 H (chloroform-d), δ 77.16 for ^{13}C {^{1}H} (chloroform-d). Abbreviations used in the NMR follow-up experiments: br, broad; s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. Q-Tof ESIMS instrument (model HAB 273) was used for recording mass spectra. Powder X-ray diffraction analysis was carried out on Rigaku using a Cu source with Kα =1.5406 Å with a 9 kW power. The samples were scanned in a 2θ range from 10° to 90° with a scan rate of 20° per minute. The morphology of the material and energy-dispersive X-ray elemental mapping were analyzed with field emission transmission electron microscopy using a JEOL (JEM 2100F) instrument with an operating voltage of 200 kV. Inductively coupled plasma atomic emission spectroscopy (ICP-AES) was acquired for the elemental analysis of Ru content within the sample by SPECTRO analytical instruments GmbH, model ARCOS simultaneous ICP spectrometer. Thermogravimetric analysis (TGA)

was carried out on an SDT Q600 thermogravimetric analyzer in the temperature range of 25-900 °C under argon at a heating rate of 10 °C min^{-1}. Fourier transform infrared spectroscopy was performed on a KBr pellet in the spectral range of 400-4000 cm^{-1} using a Perkin Elmer Spectrum Two FT-IR spectrometer. X-ray Photoelectron spectroscopy analysis was done on an X-ray photoelectron spectrometer, Thermo Fisher Scientific, UK (ESCALAB Xi^{+}) using Au4f as a reference. A JES-FA200 electron paramagnetic resonance spectrometer was used to record the EPR spectra at liquid nitrogen temperature with microwave power, 0.998 mW; microwave frequency, 9.14 GHz; and modulation amplitude, ^{2}.

4.8.2. Experimental procedures and characterization data:

4.8.2a. Synthesis of Ru-doped hydrotalcite (Ru-HT): Commercially available hydrotalcite (HT) was used for the preparation of Ru-doped hydrotalcite. First, 475 mg hydrotalcite was slowly added to 100 mL of aqueous $RuCl_3.nH_2O$ (52 mg) solution with stirring. The resulting suspension was then tailored to pH~13 by dropwise addition of NaOH (1 M), which was then vigorously stirred, at room temperature for 24 h. The suspension was then centrifuged and washed three times with deionized water and three times with ethanol consecutively. The solid sample obtained was dried at 60 °C overnight. Then, it was ground to a fine powder to perform a catalytic reaction.

4.8.2b. General procedure for the preparation of 9, 10 -diaryl/ alkyl hexahydroacridine-1,8- dione using urea: To an oven-dried Ace pressure tube (30 mL), Ru-HT (50 mg), KO^{t}Bu (0.1 mmol), alcohol (2 mmol), dimedone (0.5 mmol) and urea (1 mmol) were added under argon. The reaction mixture was then heated at 110 °C with stirring for 36 h. After cooling, $CHCl_3$ (5 mL) was added and the catalyst was separated by filtration whereas the filtrate was transferred into another flask. The filtrate was then evaporated and the crude product was purified by column chromatography (typically using EtOAc/Hexane = 50/50 containing 1% triethyl amine as eluent) using silica to afford a pure product (**Scheme 4.5**).

4.8.2c. Synthesis of compound 4.1.4l and 4.1.4m via sequential addition: To an oven-dried Ace pressure tube (30 mL), Ru-HT (50 mg) and aliphatic alcohol (2 mmol) were added under argon. Then, the reaction mixture was heated at 140 °C with stirring for 18 h. After 18 h, the reaction mixture was cooled to room temperature, and KO^{t}Bu (0.1 mmol), dimedone (0.5 mmol), and urea (1 mmol) were added to it under argon. Then it was heated at 110 °C, for

another 12 h. After that, $CHCl_3$ (5 mL) was added and the catalyst was separated by filtration whereas the filtrate was transferred into another flask. The filtrate was then evaporated and the crude product was purified by column chromatography (typically using EtOAc/Hexane = 50/50 containing 1% triethyl amine as eluent) using silica to afford a pure product (**Scheme 4.5**).

4.8.2d. General procedure for the preparation of 9, 10 -diaryl/ alkyl hexahydroacridine-1,8- dione: To an oven-dried Ace pressure tube (30 mL), Ru-HT (50 mg), KO^{t}Bu (0.1 mmol), alcohol (3 mmol), dimedone (1.0 mmol) and aniline (0.5 mmol) were added under argon. The reaction mixture was stirred at 140 °C, for 36 h. After cooling, $CHCl_3$ (5 mL) was added and the catalyst was separated by filtration whereas the filtrate was transferred into another flask. The filtrate was then evaporated and the crude product was purified by column chromatography (typically using EtOAc/Hexane = 50/50) using silica to afford a pure product (**Scheme 4.6**).

4.8.2e. Synthesis of compound 4.2.5u and 4.2.5v via sequential addition: To an oven-dried Ace pressure tube (30 mL), Ru-HT (50 mg), and aliphatic alcohol (3 mmol) were added under argon. The reaction mixture was stirred at 140 °C for 24 h. After cooling, KO^{t}Bu (0.1 mmol), dimedone (1 mmol), and aniline (0.5 mmol) were added under argon and stirred at 140 °C for another 12 h. Next, $CHCl_3$ (5 mL) was added after cooling the reaction mixture, and the catalyst was separated by filtration whereas the filtrate was transferred into another flask. The filtrate was then evaporated and the crude product was purified by column chromatography (typically using EtOAc/Hexane = 50/50) using silica to afford a pure product (**Scheme 4.6**).

4.8.3 Mechanistic studies:

Control Experiment 1:

To an oven-dried two-neck round bottom flask (10 mL) attached to Schlenk line, Ru-HT (50 mg) and 4-methoxybenzyl alcohol (1 mmol) were added under argon flow. The mixture was heated at 140 °C for 36 h. After completion of the reaction, the reaction mixture was cooled down to room temperature, and $CHCl_3$ (5 mL) was added. Next, the catalyst was separated by filtration whereas the filtrate was transferred into another flask. The filtrate was then evaporated and the NMR of the crude mixture was recorded using CH_3CN as an internal standard (**Scheme 4.6.1**).

Control Experiment 2:

To an oven-dried Ace pressure tube (30 mL), Ru-HT (50 mg), KO^{t}Bu (0.1 mmol), 4-methoxybenzyl alcohol (3 mmol), dimedone (1.0 mmol), and aniline (0.5 mmol) were added argon. The reaction mixture was stirred at 140 °C for 1 h. Then, the reaction mixture was allowed to cool to room temperature and $CHCl_3$ (5 mL) was added. Next, the catalyst was separated by filtration whereas the filtrate was transferred into another flask. The filtrate was then evaporated and a NMR of the crude mixture was recorded using CH_3CN as an internal standard. Alcohol-to-aldehyde conversion was not observed. Formation of intermediate **A** was observed. Next, the crude mixture was subjected to silica gel column chromatography (using EtOAc/Hexane = 50/50) to afford pure *β*-enaminone**, 4.1.A** in 82% yield (**Scheme 4.6.2**).

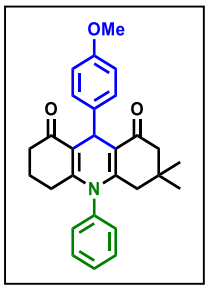
Control Experiment 3:

To an oven-dried Ace pressure tube (30 mL), Ru-HT (50 mg), KO^{t}Bu (0.1 mmol), dimedone (1.0 mmol) and aniline (0.5 mmol) were added under argon. The reaction mixture was stirred at 140 °C for 24 h. Then the reaction mixture was allowed to cool to room temperature and $CHCl_3$ (5 mL) was added. Then, the catalyst was separated by filtration whereas the filtrate was transferred into another flask. The filtrate was then evaporated and a NMR of the crude mixture was taken. Formation of intermediate **4.1.A** was observed. Later, the crude mixture was purified by column chromatography (typically using EtOAc/Hexane = 50/50) using silica to afford pure intermediate **4.1.A** in 95% yield (**Scheme 4.6.3**).

Control Experiment 4:

To an oven-dried Ace pressure tube (30 mL), Ru-HT (50 mg), KO^{t}Bu (0.1 mmol), 4-methoxybenzyl alcohol (3 mmol), *β*-enaminone, **4.1.A** (0.5 mmol), cyclohexane -1,3- dione (0.5 mmol) were added under Ar. The reaction mixture was heated at 140 °C for 36 h. After cooling, $CHCl_3$ (5 mL) was added and the catalyst was separated by filtration whereas the filtrate was transferred into another flask. The filtrate was then evaporated and the crude product was purified by column chromatography (typically using EtOAc/Hexane = 40/60 as eluent) using silica to afford a pure product, **4.2.5b'** in 85% yield (**Scheme 4.6.4**).

9-(4-methoxyphenyl)-3,3-dimethyl-10-phenyl-3,4,6,7,9,10-hexahydroacridine -1,8(2H,5H)-dione (4.2.5b′): ^{1}H NMR (600 MHz, $CDCl_3$)[3] δ 7.57-7.53 (m, 3H), 7.36 (d, *J* = 8.6 Hz, 2H), 7.27 (d, *J* = 6.8 Hz, 2H) ,6.82 (d, *J* = 8.6 Hz, 2H), 5.29 (s, 1H), 3.77 (s, 3H), 2.39-2.35 (m, 1H), 2.30-2.15 (m, 4H), 2.10-2.07 (m, 1H), 2.05-2.01 (m, 1H), 1.91- 1.86 (m, 1H), 1.83 (s, 1H), 1.81-1.75 (m, 1H), 0.96 (s, 3H), 0.84 (s, 3H).^{13}C NMR (150 MHz, $CDCl_3$) δ 196.3, 196.2, 157.8, 151.5, 149.6, 139.2, 139, 130.1,129.5, 128.9, 115.9, 115, 113.6, 55.3, 50.4, 41.9, 36.9, 32.5, 31.7, 29.8, 28.5, 27, 21.3.



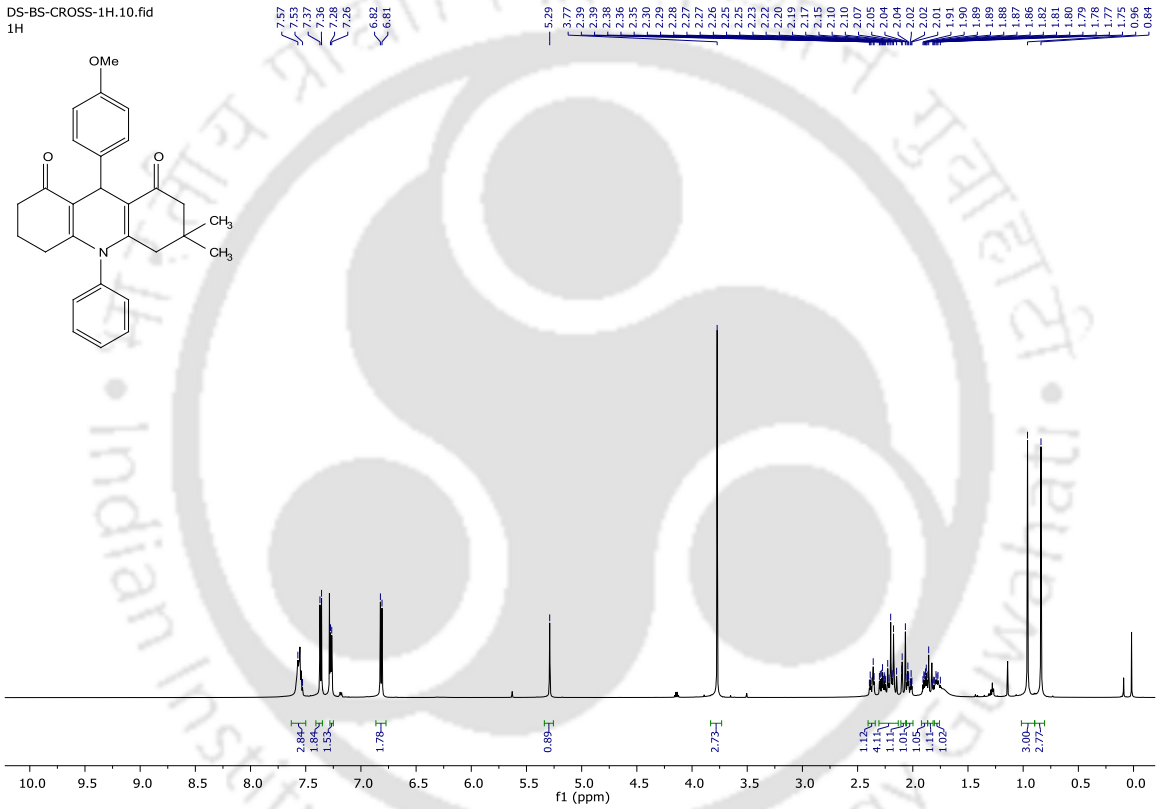


Figure 4.10. ^{1}H NMR (600 MHz, $CDCl_3$) of compound **4.2.5b′**

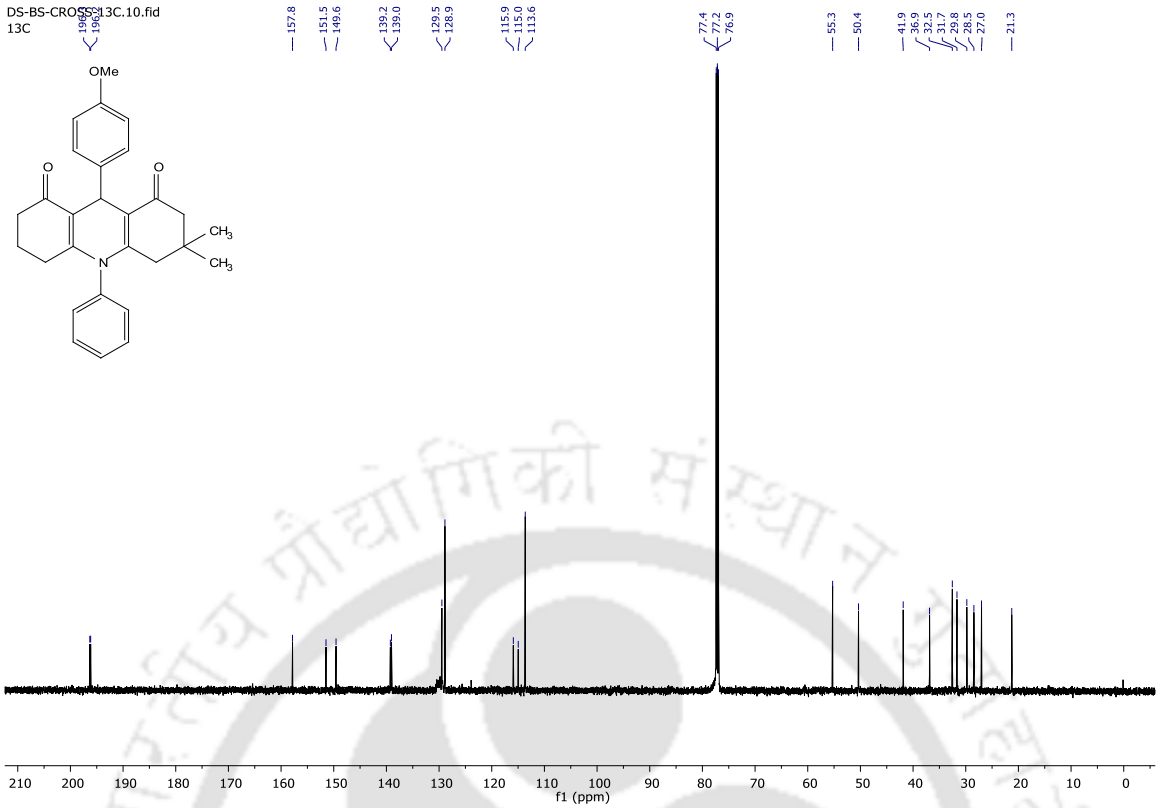


Figure 4.11. ^{13}C {^{1}H} NMR (150 MHz, $CDCl_3$) of compound **4.2.5b′**

Control Experiment 5:

In an oven-dried 10 mL round bottom flask, KO^{t}Bu (0.1 mmol), *β*- enaminone, **4.1.A** (0.5 mmol), 4- methoxy benzaldehyde (0.5 mmol), dimedone (0.5 mmol), and 1 mL ethanol were added. The reaction mixture was stirred at room temperature for 0.5 h. Next, ethanol was evaporated from the reaction mixture and a NMR of the crude was recorded using CH_3CN as an internal standard. **4.1.D** was formed 90% yield whereas the formation of **4.1.C**, **4.2.5b**, and 4.1.**E** were not detected (**Scheme 4.6.5**).

Control Experiment 6:

To an oven-dried Ace pressure tube (30 mL), Ru-HT (50 mg), KO^{t}Bu (0.1 mmol), 4-methoxybenzyl alcohol (3 mmol), *β*-enaminone **4.1.A** (0.5 mmol), intermediate **4.1.D´** (0.5 mmol), KO^{t}Bu (0.1 mmol) were added under argon. The reaction mixture was heated at 140 °C for 2 h. Then, after cooling the reaction mixture, $CHCl_3$ (5 mL) was added and the catalyst was separated by filtration whereas the filtrate was transferred into another flask. The filtrate was then evaporated and the crude product was purified by column chromatography (typically using EtOAc/Hexane = 50/50) using silica to afford a pure product, **4.2.5b'** in 95% yield (**Scheme 4.6.6**).

Control Experiment 7: Kinetic isotope study:

Competition reaction: To an oven-dried Ace pressure tube (30 mL), Ru-HT (50 mg), KO^{t}Bu (20 mol%), 4-methoxybenzyl alcohol, (1.5 mmol, **4.1.1b**), deuterated 4-methoxybenzyl alcohol, (1.5 mmol, **4.1.1b-D3**), dimedone (1.0 mmol) and aniline (0.5 mmol) were added under argon. The reaction mixture was heated at 140 °C for 36 h. Then, cooling the reaction mixture, $CHCl_3$ (5 mL) was added and the catalyst was separated by filtration whereas the filtrate was transferred into another flask. The filtrate was then evaporated and the crude product was purified by column chromatography (typically using EtOAc/Hexane = 50/50) using silica to afford a mixture of **4.2.5b** and **4.2.5b-D** in 50% yield (**Scheme 4.6.7**).

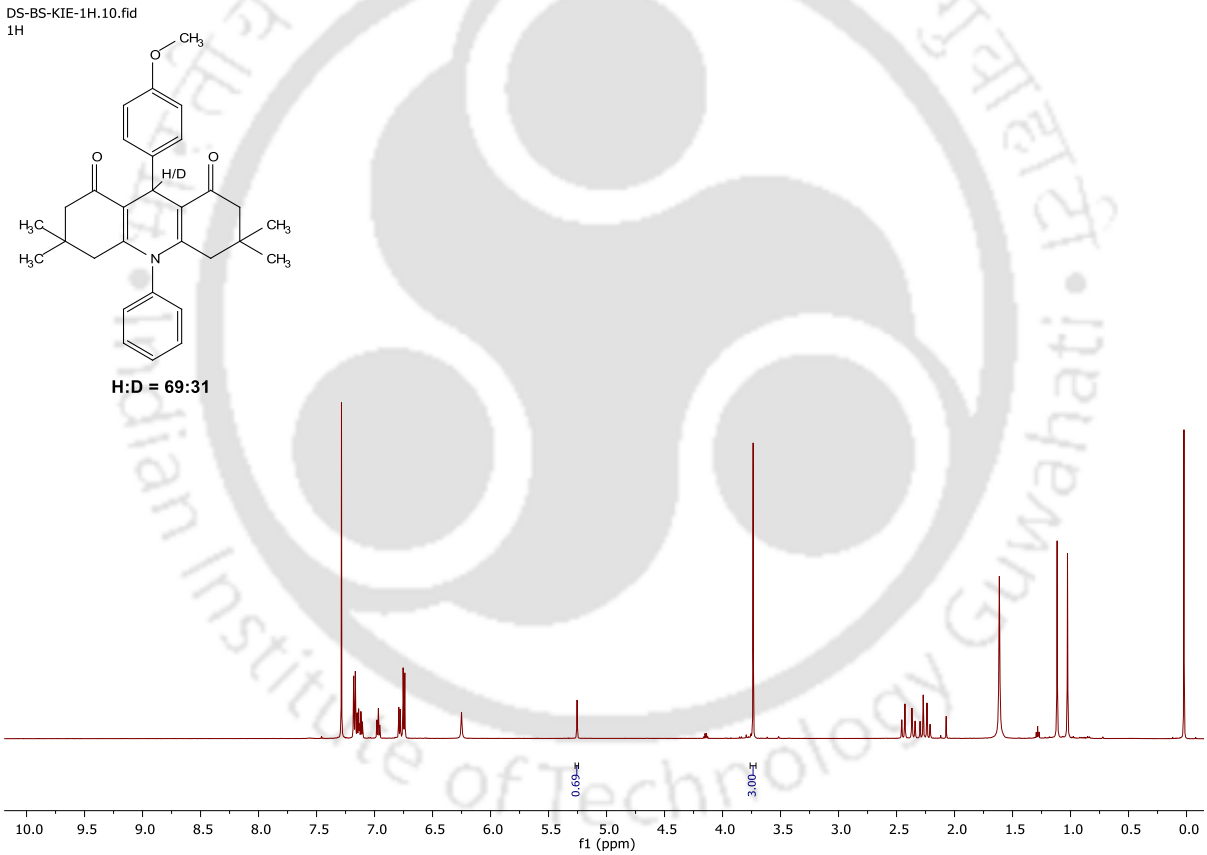


Figure 4.12. Competition reaction

Parallel reaction: To an oven-dried Ace pressure tube (30 mL), Ru-HT (50 mg), KO^{t}Bu (20 mol%), 4-methoxybenzyl alcohol, (3.0 mmol, **4.1.1b**) or deuterated 4-methoxybenzyl alcohol, (3.0 mmol, **4.1.1b-D$_3$**), dimedone (1.0 mmol) and aniline (0.5 mmol) were added under argon. The reaction mixture was heated at 140 °C for 36 h. After 36 h, the reaction mixture was cooled, $CHCl_3$ (5 mL) was added and the catalyst was separated by filtration whereas the filtrate was

transferred into another flask. The filtrate was then evaporated and the crude product was purified by column chromatography (typically using EtOAc/Hexane = 40/60) using silica to afford pure product **4.2.5b** and **4.2.5b-D** in 80% and 38% yield respectively (**Scheme 4.6.7**).

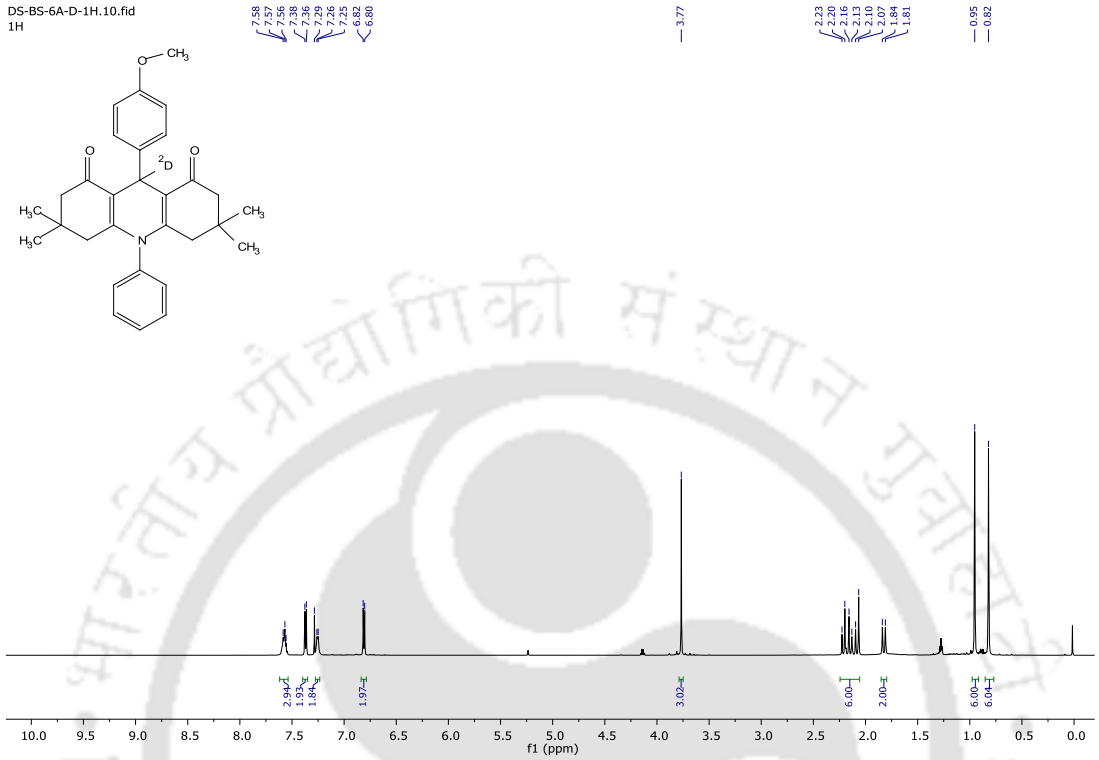


Figure Figure 4.13. ^{1}H NMR (600 MHz, $CDCl_3$) of compound **4.2.5b′**

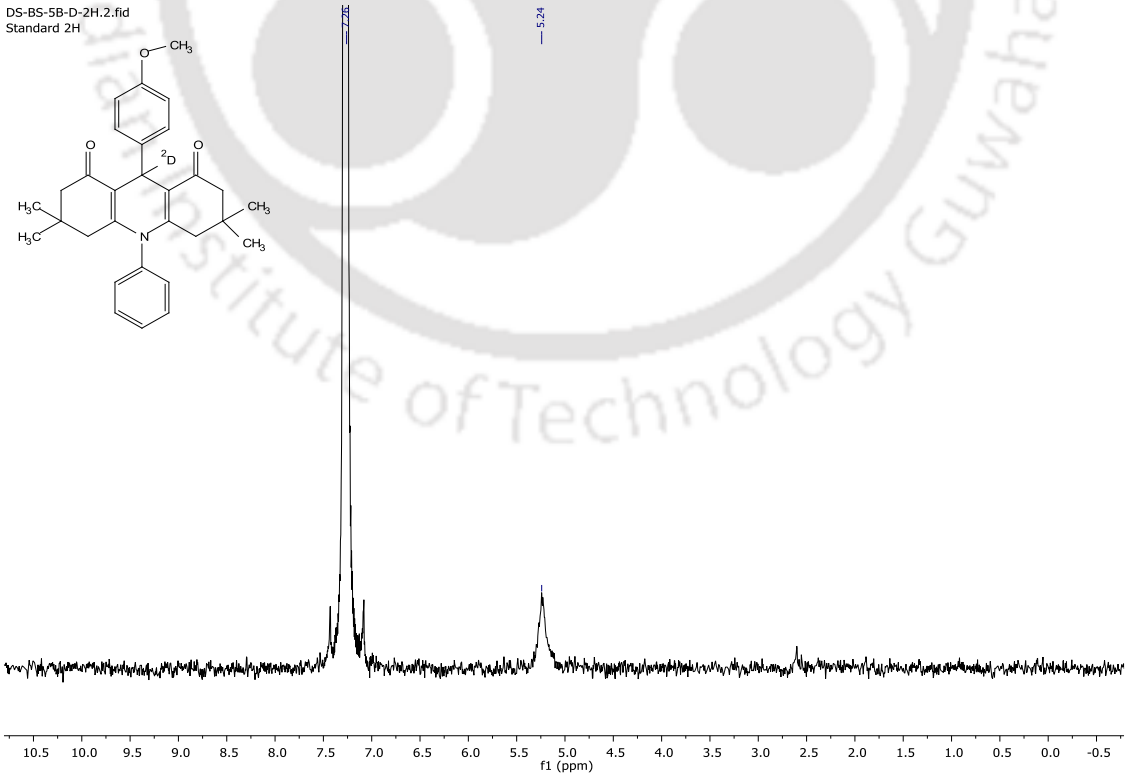


Figure 4.14. ^{2}H (600 MHz, $CDCl_3$) spectra of compund of **4.2.5b-D**

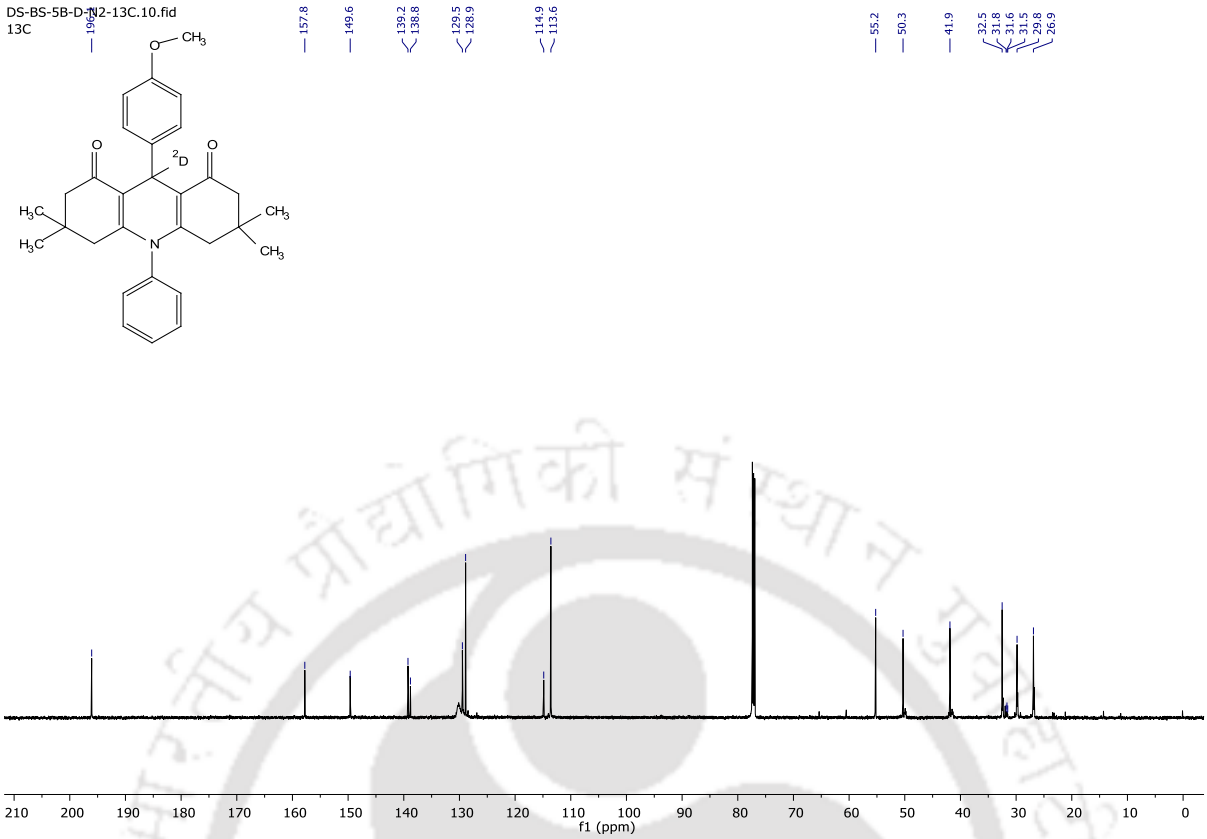


Figure 4.15. $^{13}C\{^{1}H\}$ NMR spectra of compund of **4.2.5b-D**

9-(4-methoxyphenyl)-3,3,6,6-tetramethyl-10-phenyl-3,4,6,7,9,10-hexahydroacridine-1,8(2H,5H)-dione-9-d (4.2.5b-D): White solid, ^{1}H NMR (600 MHz, $CDCl_3$) 7.57 (t, *J* = 8.4 Hz, 3H), 7.37 (d, J = 8.6 Hz, 2H), 7.26 (d, *J* = 7.3 Hz, 2H), 6.81 (d, *J* = 8.6 Hz, 2H), 3.77 (s, 3H), 2.23-2.07 (m, 6H), 1.82 (d, *J* =17.3 Hz, 2H), 0.95 (s, 6H), 0.82 (s, 6H). ^{2}H NMR 5.24 (s, 1D), ^{13}C NMR (150 MHz, $CDCl_3$) δ 196.2, 157.8, 149.6, 139.2, 138.8, 129.5, 128.9, 114.6, 113.6, 55.2, 50.3, 41.9, 32.5, 31.6 (t, *J* = 22 Hz), 29.8, 26.9. HRMS calculated for $C_{30}H_{32}DNO_3$: 457.2601. Found: 457.2622

4.8.4. H_2 detection experiment (Scheme 4.6.8):

[RhCl(PPh$_3$)$_3$] Catalysed hydrogenation of 4-methyl styrene involving hydrogen formed through the dehydrogenation process: To an oven-dried round bottom flask (5 mL), Ru-HT catalyst (50 mg), KO^{t}Bu (0.1 mmol), 4-methoxybenzyl alcohol (3 mmol), dimedone (1 mmol) and aniline (0.5 mmol) were added under argon. Then the entire system was degassed and flushed with argon for 5 minutes (three times) and packed 14 joints with rubber septum. In

another 5 mL round bottom flask, $RhCl(PPh_3)_3$ (10 mol%) catalyst, and 4-methyl styrene (0.5 mmol) were dissolved in benzene-d_6 (2 mL). Both the flasks were connected through a double-headed syringe and allowed to equilibrate for 5 minutes. The mixture in the former flask was heated at 140 °C while the mixture in the latter flask was stirred at 50 °C. After 24 hours, the organic entities present in the latter flask were analyzed by analytical HPLC and NMR.

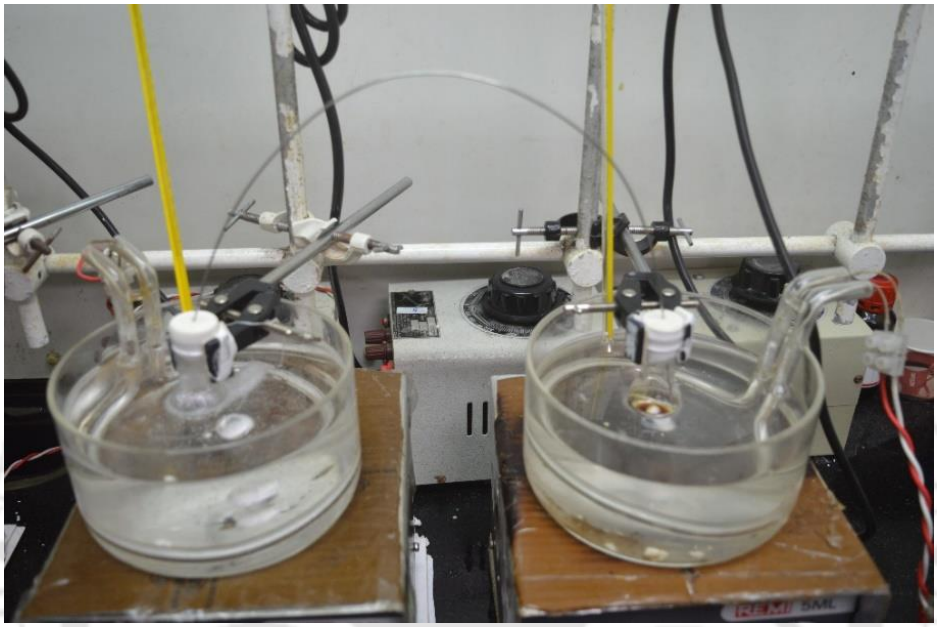


Figure 4.16. Dehydrogenation setup

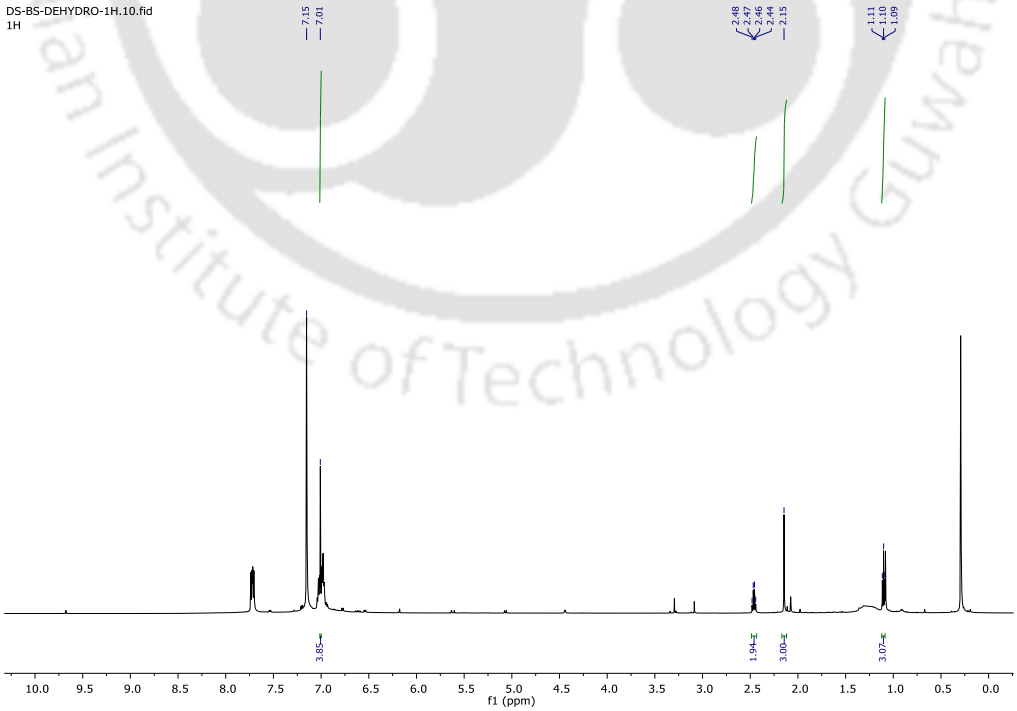


Figure 4.17. ^1H NMR of compound ethyl benzene

4.8.5. Kinetic studies: Eight different reactions were set up under the standard reaction condition and the reaction mixture were analyzed by ^{1}H NMR after 1 h, 3 h, 6 h, 12 h, 18 h, 24 h, 30 h, and 36 h respectively using CH_3CN as internal standard (**Figure 4.1**).

4.8.6. Radical scavenger experiment: To a 30 mL oven-dried Ace Pressure Tube (30 mL), Ru-HT catalyst (50 mg), KO^{t}Bu (0.1 mmol), 4-methoxybenzyl alcohol (3 mmol), dimedone (1 mmol), aniline (0.5 mmol), and 2,6-di-tert-butyl-4-methylphenol (BHT) (0.5 mmol) was added under argon. The reaction mixture was heated at 140 °C. After 36 h, $CHCl_3$ (5 mL) was added and the catalyst was separated by filtration whereas the filtrate was transferred into another flask. The filtrate was then evaporated and the crude product was purified by column chromatography (typically using EtOAc/Hexane = 40/60) using silica to afford a pure product, **4.2.5b** in 85% yield.

4.8.7. TEMPO study: Seven different reactions were set up under the standard reaction condition with 1 equivalent of TEMPO and the reaction mixture was analyzed by 1H NMR after 1 h, 2h, 3 h, 6 h, 12 h, 18 h, and 24 h respectively using CH_3CN as internal standard. The rate of the reaction increases compared to the reaction without any TEMPO. Mass spectral analysis confirms the formation of 2, 2, 6, 6-tetramethylpipiridine (TEMPH) and TEMPOH. TEMPOH is known to form TEMPH under inert conditions (**Figure 4.2**).[15]

4.8.8. Reusability of the catalyst: To an oven-dried Ace pressure tube (30 mL) Ru-HT catalyst (50 mg, 0.918%), KO^{t}Bu (0.1 mmol), 4-methoxybenzyl alcohol (3 mmol), dimedone (1.0 mmol), aniline (0.5 mmol) were added under argon. The reaction mixture was heated at 140 °C with stirring under argon for 36 h. After cooling, $CHCl_3$ (5 mL) was added and the catalyst was separated by centrifugation whereas the filtrate was transferred into another flask. While the separated catalyst was then washed with deionized water (2 x 5 mL) and ethanol (2 x 5 mL), dried, and used again for consecutive runs. The transferred solvent was evaporated from the reaction mixture and the crude mixture was subjected to silica gel column chromatography. It was established that no deactivation of the material was observed up to three cycles (**Figure 4.9**) and a slight decrease in yield was observed in 4th and 5th cycle. All of the yields are isolated yields. The catalyst was characterized with FT-IR and PXRD after 5th recycle.

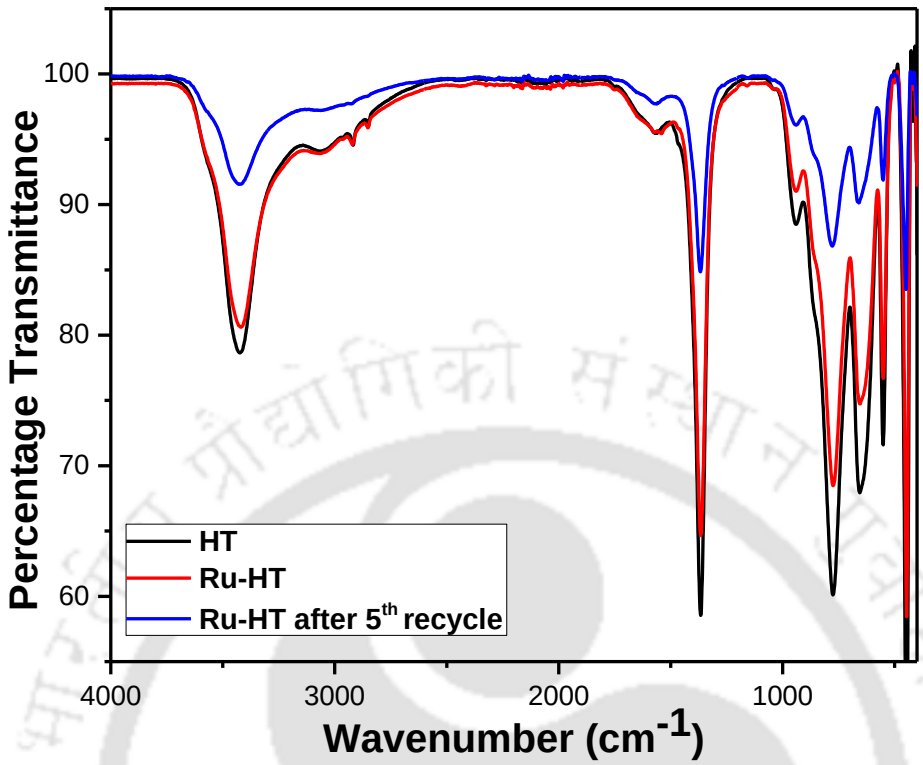


Figure 4.18. FT-IR spectrum of HT, Ru-HT and Ru-HT after 5th recycle.

Catalyst	Crystallographic Parameters							
	$d_{(003)}$	$d_{(006)}$	$d_{(009)}$	$d_{(110)}$	$d_{(113)}$	a (Å)	c (Å)	L (nm)
Commercially available hydrotalcite(HT)	7.62	3.81	2.57	1.52	1.49	3.04	22.86	22.25
Ru-HT	7.65	3.82	2.58	1.52	1.49	3.04	22.94	23.32
Ru – HT recovered after 5th cycle	7.67	3.82	2.58	1.52	1.49	3.04	22.96	21.89
*a, the average cation-cation distance; *c, three times the distance from the center of one brucite like layer to the next layer; L, the average crystalline size (using the Scherrer's formula)								

Table 4.3. Characterization data of commercially available HT, Ru-HT, reused Ru-HT: PXRD crystallographic parameters (a, c and L).

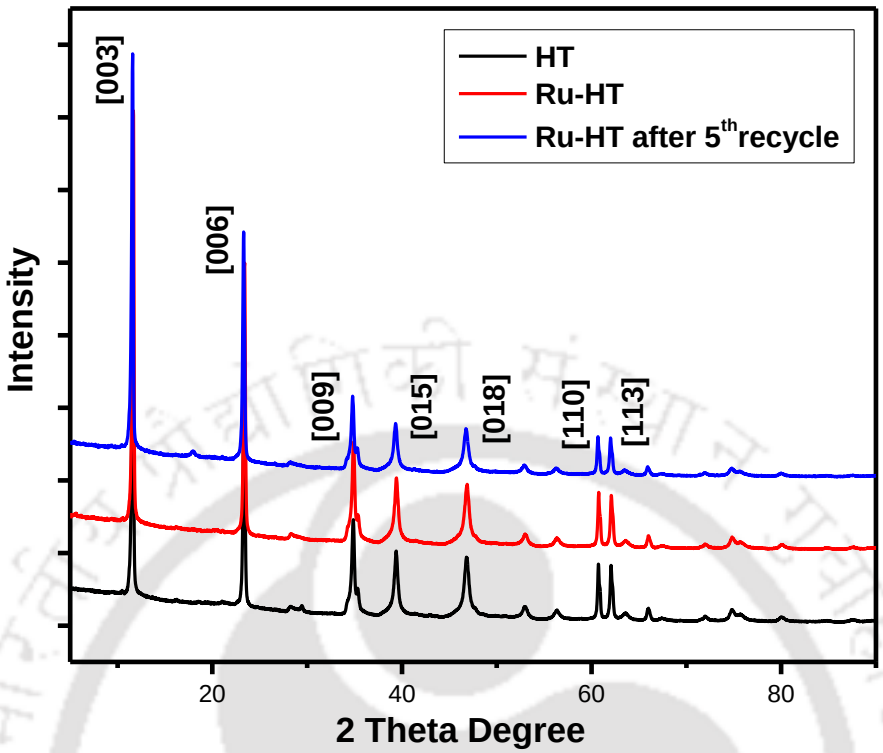


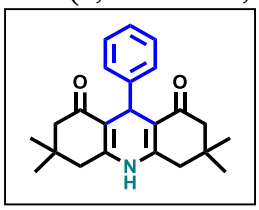
Figure 4.19. PXRD pattern of HT, Ru-HT and Ru-HT after 5th recycle.

4.8.9. Gram Scale synthesis: To an oven-dried Ace pressure tube (30 mL), Ru-HT (400 mg), 20 mol % KO^{t}Bu, benzyl alcohol (12 mmol), dimedone (8 mmol), aniline (4 mmol) was added under argon atmosphere. The reaction mixture was heated at 140 °C with stirring for 36 hours. The reaction mixture was allowed to cool to room temperature. After cooling, $CHCl_3$ (50 mL) was added and the catalyst was separated by filtration whereas the filtrate was transferred into another flask. The filtrate was then evaporated and the crude product was purified by column chromatography (typically using EtOAc/Hexane = 50/50) using silica to afford the 70% isolated yield (1.190 gm) of the desired product. While the separated catalyst was then washed with ethanol (2 x 20 mL) and stored.

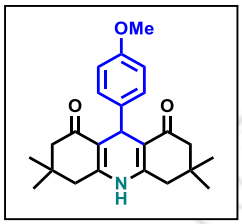
4.9. Spectroscopic data of the newly synthesized compounds in the present study:

3,3,6,6-tetramethyl-9-phenyl-3,4,6,7,9,10-hexahydroacridine -1,8(2H,5H)-dione (4.1.4a).[8b]
The compound 4a was synthesized by the procedure as described above and obtained as white solid: 84% yield (74 mg); R_f = 0.3 (40% EtOAc + pet ether); ^{1}H NMR (600 MHz, $CDCl_3$) δ

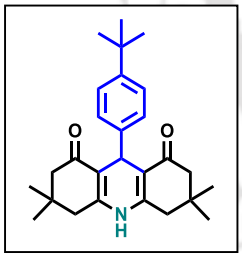
7.35 (d, J = 7.3 Hz, 2H), 7.21 (t, J = 7.6 Hz, 2H), 7.08 (t, J = 7.4 Hz, 1H), 6.42 (s, 1H), 5.09 (s, 1H), 2.37 (d, J = 16.4 Hz, 2H), 2.27-2.24 (m, 4H), 2.18 (d, J = 16.4 Hz, 2H), 1.10 (s, 6H), 0.98 (s, 6H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 195.8, 148.7, 146.7, 128.2, 128.1, 126.1, 113.6, 51.0, 41.0, 33.8, 32.8, 29.7, 27.3.



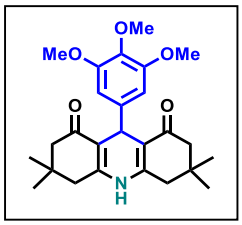
9-(4-methoxyphenyl)-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydroacridine-1,8(2H,5H)-dione (4.1.4b).[8b] The compound 4b was synthesized by the procedure as described above and obtained as a white solid: 84% yield (80 mg), R_f = 0.2 (40% EtOAc + pet ether); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.26 (d, *J* = 8.3 Hz, 2H), 6.74 (d, *J* = 8.3 Hz, 2H), 6.37 (s, 1H), 5.04 (s, 1H), 3.73 (s, 3H), 2.36 (d, *J* = 16.6 Hz, 2H), 2.25-2.16 (m, 6H), 1.10 (s, 6H), 0.99 (s, 6H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 195.6, 157.8, 147.7, 139.1, 129.1, 114, 113.5, 55.2, 50.9, 41.3, 32.9, 32.8, 29.6, 27.3.



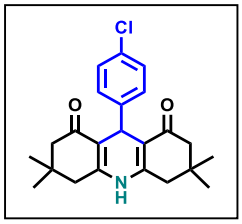
9-(4-(tert-butyl)phenyl)-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydroacridine-1,8(2H,5H)-dione (4.1.4c).[17] The compound 4c was synthesized by the procedure as described above and obtained as a yellow solid: 75% yield (76 mg), R_f = 0.3 (40% EtOAc + pet ether); ^{1}H NMR (400 MHz, $CDCl_3$) 7.22 (d, *J* = 8.5 Hz, 2H), 7.18 (d, *J* = 8.5 Hz, 2H), 6.40 (s, 1H), 5.07 (s, 1H), 2.36 (d, *J* = 16.6 Hz, 2H), 2.30-2.16 (m, 6H), 1.23 (s, 9H), 1.08 (s, 6H), 0.99 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.0, 148.6, 148.4, 143.4, 127.5, 125.0, 113.7, 51.0, 41.1, 34.4, 32.9, 32.8, 31.5, 29.5, 27.5.



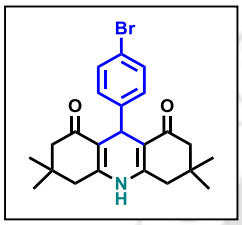
3,3,6,6-tetramethyl-9-(3,4,5-trimethoxyphenyl)-3,4,6,7,9,10-hexa hydroacridine-1,8(2H,5H)-dione (4.1.4d).[8b] The compound 4d was synthesized by the procedure as described above and obtained as a white solid: 84% yield (74 mg); R_f = 0.3 (40% EtOAc + pet ether) White solid, Yield: 65%, ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.59 (s, 2H), 6.00 (s, 1H), 5.06 (s, 1H), 3.81 (s, 6H), 3.78 (s, 3H), 2.43 (d, *J* = 16.5 Hz, 2H), 2.28-2.24 (m, 6H), 1.12 (s, 6H), 1.04 (s, 6H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 195.5, 152.8, 147.4, 142.2, 136.3, 113.8, 105.5, 60.8, 56.2, 50.8, 41.5, 33.7, 32.8, 29.7, 27.2



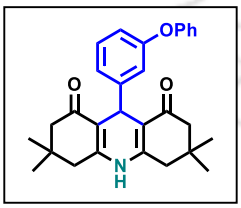
9-(4-chlorophenyl)-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydroacridine-1, 8(2H,5H)- dione (4.1.4e).[8b] The compound 4e was synthesized by the procedure as described and obtained as a yellow crystal: 65% yield (62 mg); R_f = 0.2 (40% EtOAc + pet ether), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 (d, *J* = 8.4 Hz, 2H), 7.16 (d, *J* = 8.4 Hz, 2H), 5.05 (s, 1H), 2.33-2.13 (m, 8H), 1.07 (s, 6H), 0.95 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 196, 149, 145.2, 131.7, 129.6, 128.2, 113.1, 50.9, 40.9, 33.5, 32.8, 29.7, 27.2.



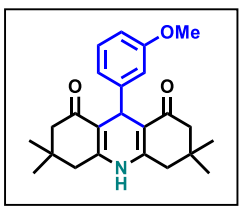
9-(4-bromophenyl)-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydroacridine-1,8(2H, 5H)-dione (4.1.4f).[8b] The compound 4f was synthesized by the procedure as described above and obtained as a white crystal: 78% yield (84 mg), R_f = 0.2 (40% EtOAc + pet ether), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (d, *J* = 8.4 Hz, 2H), 7.21 (d, *J* = 8.4 Hz, 2H), 6.34 (s, 1H), 5.03 (s, 1H), 2.36 (d, *J* = 16.6 Hz, 2H), 2.26-2.14 (m, 6H), 1.08 (s, 6H), 0.97 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.5, 147.9, 145.6, 131.1, 130, 119.9, 113.5, 50.8, 41.3, 33.6, 32.8, 29.6, 27.3.



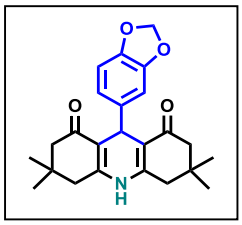
3,3,6,6-tetramethyl-9-(3-phenoxyphenyl)-3,4,6,7,9,10 -hexahydroacridine -1,8(2H,5H)-dione (4.1.4h).[13a] The compound 4h was synthesized by the procedure as described above and obtained as yellow solid: 77% yield (84 mg), R_f = 0.3 (40% EtOAc + pet ether), ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.25-7.23 (m, 1H), 7.20 (s, 1H), 7.14 (t, *J* = 7.7 Hz, 1H), 7.01 (t, *J* = 7.2 Hz, 1H), 6.93 (s, 1H), 6.89 (d, *J* = 7.8 Hz, 2H), 6.81 (brs, 1H), 6.70 (d, *J* = 7.7 Hz, 1H), 5.08 (s, 1H), 2.33 (d, *J* = 16.8 Hz, 2H), 2.24-2.14 (m, 6H), 1.06 (s, 6H), 0.94 (s, 6H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 195.9, 157.7, 156.8, 148.7, 129.7, 129.2, 124, 122.8, 118.8, 118.4, 116.9, 113.3, 50.9, 41, 33.7, 32.7, 29.7, 27.2. (Eclipsed)



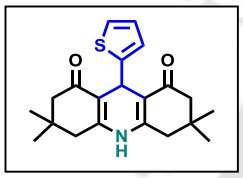
9-(3-methoxyphenyl)-3,3,6,6-tetramethyl-3,4,6,7,9,10 -hexahydroacridine -1,8 (2H,5H)-dione (4.1.4i).[18] The compound 4i was synthesized by the procedure as described above and obtained as white solid: 78% yield (74 mg), R_f = 0.3 (40% EtOAc + pet ether); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.09 (t, *J*= 6.54 Hz, 1H), 6.93-6.90 (m, 2H), 6.63- 6.61 (m, 1H), 5.07 (s, 1H), 3.73 (s, 3H), 2.32 (d, *J* = 16.8 Hz, 2H), 2.25-2.15 (m, 6H), 1.07 (s, 6H), 0.97 (s, 6H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 195.6, 159.5, 148.2, 128.9, 120.8, 114.3, 113.6, 111.4, 55.2, 50.9, 41.2, 33.7, 32.8, 29.6, 27.4.



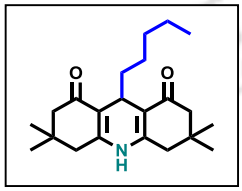
9-(benzo[d][1,3]dioxol-5-yl)-3,3,6,6-tetramethyl-3,4, 6,7,9,10-hexahydroacridine -1,8(2H,5H)-dione (4.1.4j).[8b] The compound 4j was synthesized by the procedure as described above and obtained as a white solid, 72% yield (66 mg), R_f = 0.3 (40% EtOAc + pet ether); ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.87 (s, 1H), 6.81 (d, *J* = 7.9 Hz, 1H), 6.66-6.64 (m, 2H), 5.86 (s, 2H), 5.01 (s, 1H), 2.36 (d, *J* = 16.7 Hz, 2H), 2.27-2.18 (m, 6H), 1.10 (s, 6H), 1.00 (s, 6H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 195.7, 147.9, 147.3, 145.7, 140.9, 121.2, 113.9, 109, 107.9, 100.8, 50.9, 41.2, 33.5, 32.8, 29.6, 27.4.



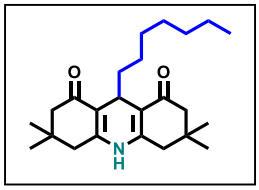
3,3,6,6-tetramethyl-9-(thiophen-2-yl)-3,4,6,7,9,10-hexahydroacridine-1,8 (2H,5H)-dione (4.1.4k). [8b] The compound 4k was synthesized by the procedure as described above and obtained as white crystal, 68% yield (60 mg), R_f = 0.1 (40% EtOAc + pet ether); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.01-7.00 (m, 1H), 6.95 (d, *J* = 3.4 Hz, 1H), 6.85-6.83 (m, 1H), 6.05 (s, 1H), 5.50 (s, 1H), 2.41 (d, *J* = 16.6 Hz, 1H), 2.31-2.26 (m, 6H), 1.12 (s, 6H), 1.07 (s, 6H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 194.5, 151, 149.8, 126.3, 123.1, 122.9, 110.9, 50.2, 32.1, 29.2, 27.3, 26.5.



3,3,6,6-tetramethyl-9-pentyl-3,4,6,7,9,10-hexahydroacridine-1,8(2H, 5H)-dione (4.1.4l). The compound 4l was synthesized by the procedure as described above and obtained as white solid, 65% yield, (55 mg), R_f = 0.3 (40% EtOAc + pet ether); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18 (s, 1H), 4.01 (t, J = 4.9 Hz, 1H), 2.31 (d, J = 17.0 Hz, 2H), 2.26-2.15 (m, 6H), 1.38-1.33 (m, 2H), 1.22-1.17 (m, 1H), 1.13-1.08 (m, 5H), 1.04 (s, 6H), 1.03 (m, 6H), 0.74 (t, J = 6.9 Hz, 3H). 13C NMR (150 MHz, CDCl3) δ 196.4, 150, 112.8, 51.1, 41.1, 35.2, 32.6, 32.3, 29.9, 27.3, 27.2, 25.1, 22.8, 14.2. HRMS calculated for $C_{22}H_{34}NO_2$ $[M+H]^+$:: 345.2623. Found: 345.2605

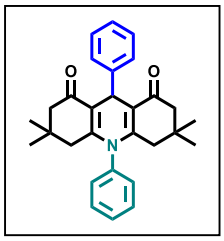


9-heptyl-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydroacridine-1,8(2H,5H)-dione (4.1.4m).[18]



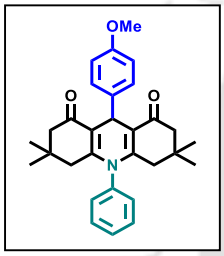
The compound 4m was synthesized by the procedure as described above and obtained as white solid: 72% yield (67 mg), R_f = 0.3 (40% EtOAc + pet ether); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.44 (s, 1H), 4.08 (t, *J* = 5.0 Hz, 1H), 2.50-2.45 (m, 1H), 2.41-2.37 (m, 2H), 2.31-2.30 (m, 1H), 2.28-2.24 (m, 4H), 1.45-1.41 (m, 2H), 1.30-1.22 (m, 3H), 1.21-1.15 (m, 7H), 1.12 (s, 6H), 1.11 (s, 6H), 0.84 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 196.5, 150.3, 112.7, 51.1, 41.1, 35.3, 32.6, 32.0, 30.1, 29.9, 29.5, 28.3, 27.2, 25.5, 22.7, 14.2.

3,3,6,6-tetramethyl-9,10-diphenyl-3,4,6,7,9,10-hexahydroacridine-1,8 (2H, 5H)-dione (4.2.5a).[20] The compound 5a was synthesized by the procedure as described above and obtained as white solid: 71% yield (150 mg), ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.59-7.55 (m, 3H),



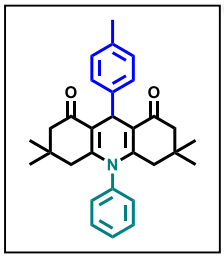
7.46 (d, *J* = 7.2 Hz, 2H), 7.28-7.25 (m, 4H), 7.12 (t, *J* = 7.3 Hz, 1H), 5.30 (s, 1H), 2.18 (ABq, *J* = 20.6 Hz, 4H), 2.09 (d, *J* = 17.5 Hz, 2H), 1.83 (d, *J* = 17.5 Hz, 2H), 0.96 (s, 6H), 0.81 (s, 6H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 196, 149.8, 146.3, 139.2, 129.5, 128.2, 128, 126.1, 114.8, 50.3, 41.9, 32.8, 32.5, 29.9, 26.9.

9-(4-methoxyphenyl)-3,3,6,6-tetramethyl-10-phenyl-3,4,6,7,9,10-hexahydroanthracene-1,8(2H,5H)-dione (4.2.5b).[20] The compound 5b was synthesized by the procedure as described above and obtained as yellow solid: 80% yield (182 mg), ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.58-



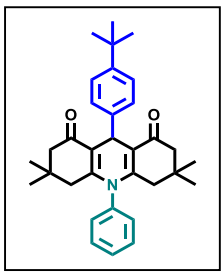
7.54 (m, 3H), 7.35 (d, *J* = 8.6 Hz, 2H), 7.24 (d, J = 7.2 Hz, 2H), 6.79 (d, *J* = 8.6 Hz, 2H), 5.22 (s, 1H), 3.75 (s, 3H), 2.16 (ABq, *J* = 19.5 Hz, 4H), 2.06 (d, *J* = 17.4 Hz, 2H), 1.81 (d, *J* = 17.4 Hz, 2H), 0.94 (s, 6H), 0.81 (s, 6H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 196.1, 157.8, 149.6, 139.3, 138.9, 130.5, 129.5, 128.9, 115, 113.6, 55.3, 50.3, 41.9, 32.5, 32, 29.9, 26.9.

3,3,6,6-tetramethyl-10-phenyl-9-(p-tolyl)-3,4,6,7,9, 10-hexahydroacridine-1,8(2H,5H)-dione (4.2.5c).[21] The compound 5c was synthesized by the procedure as described above and obtained as white solid: 86% yield (190 mg), ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.59-7.55 (m, 3H),

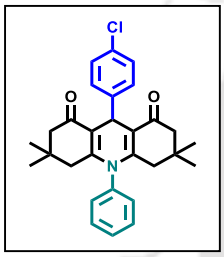


7.34 (d, *J* = 8.0 Hz, 2H), 7.26 (d, *J* = 7.2 Hz, 2H), 7.07 (d, *J* = 7.7 Hz, 2H), 5.26 (s, 1H), 2.28 (s, 3H), 2.21 (ABq, *J* = 21.8 Hz, 4H), 2.08 (d, *J* = 17.4 Hz, 2H), 1.82 (d, *J* = 17.4 Hz, 2H), 0.96 (s, 6H), 0.82 (s, 6H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 196, 149.7, 143.4, 139.3, 135.4, 130.2, 129.5, 128.9, 127.9, 114.9, 50.3, 41.9, 32.5, 32.4, 29.8, 27, 21.2.

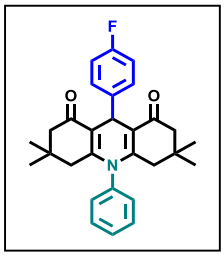
9-(4-(tert-butyl)phenyl)-3,3,6,6-tetramethyl-10-phenyl-3,4,6,7,9,10-hexah ydroacridine-1,8(2H,5H)-dione (4.2.5d). The compound 5d was synthesized by the procedure as described above and obtained as white solid: 90% yield (216 mg), ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.60-7.56 (m, 3H), 7.35 (d, *J* = 8.3 Hz, 2H), 7.26-7.25 (m, 4H), 5.27 (s, 1H), 2.19 (ABq, *J* = 17.5 Hz, 4H), 2.08 (d, *J* = 17.4 Hz, 2H), 1.84 (d, *J* = 17.4 Hz, 2H), 1.27 (s, 9H), 0.96 (s, 6H), 0.83 (s, 6H). ^{13}C NMR (150 MHz, CDCl3) δ 196, 149.6, 148.3, 143, 139.2, 129.4, 127.4, 125, 114.8, 50.2, 41.8, 34.3, 32.4, 32.1, 31.4, 29.7, 27. (Eclipsed) HRMS calculated for $C_{33}H_{40}NO_2$ $[M+H]^+$:: 482.3059 Found: 482.3029



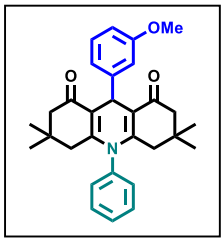
9-(4-chlorophenyl)-3,3,6,6-tetramethyl-10-phenyl-3,4,6,7,9,10-hexahy droacridine 1,8 (2H,5H)-dione (4.2.5e).[20] The compound 5e was synthesized by the procedure as described above and obtained as yellow solid: 81% yield (186 mg), ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.59-7.57 (m, 3H), 7.39 (d, *J* = 6.3 Hz, 2H), 7.25-7.23 (m, 4H), 5.26 (s, 1H), 2.19 (ABq, *J* = 16.8 Hz, 4H), 2.09 (d, *J* = 17.6 Hz, 2H), 1.83 (d, *J* = 17.6 Hz, 2H), 0.96 (s, 6H), 0.82 (s, 6H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 195.9, 150, 144.9, 139.1, 131.7, 129.6, 129.4, 128.3, 114.4, 50.3, 42, 32.6, 32.5, 29.9, 26.9. (Eclipsed)



9-(4-fluorophenyl)-3,3,6,6-tetramethyl-10-phenyl-3,4,6,7,9,10-hexahydro acridine-1,8(2H,5H)-dione (4.2.5f).[22] The compound 5f was synthesized by the procedure as described above and obtained as white solid: 81% yield (180 mg), ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.59-7.57 (m, 3H), 7.43-7.40 (m, 2H), 7.25 (d, *J* = 6.9 Hz, 2H), 6.95 (t, J = 8.7 Hz, 2H), 5.27 (s, 1H), 2.18 (ABq, *J* = 20.9 Hz, 4H), 2.09 (d, *J* = 17.5 Hz, 2H), 1.83 (d, *J* = 17.5 Hz, 2H), 0.96 (s, 6H), 0.82 (s, 6H). 13C NMR (150 MHz, CDCl3) δ 196, 161.3 (d, *J* = 243.2 Hz), 149.9, 142.2 (d, *J* = 3.2 Hz), 139.1, 130.2, 129.6, 129.4 (d, *J* = 7.9 Hz), 114.9 (d, *J* =21.2 Hz), 114.6, 50.3, 41.9, 32.5, 32.3, 29.8, 26.8. (Eclipsed)

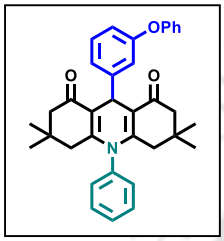


9-(3-methoxyphenyl)-3,3,6,6-tetramethyl-10-phenyl-3,4,6,7,9,10-hexahydroacridine-1,8(2H,5H)-dione (4.2.5h).[23] The compound 5h was synthesized by the procedure as described above and obtained as white solid: 81% yield (184 mg), ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.59-7.54 (m, 3H), 7.25 (d, *J* = 6.7 Hz, 2H), 7.18 (t, *J* = 7.8 Hz, 1H), 7.05-7.03 (m, 2H), 6.69-6.68

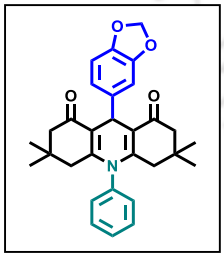


(m, 1H), 5.30 (s, 1H), 3.82 (s, 3H), 2.20 (ABq, *J* = 16.3 Hz, 4H), 2.09 (d, *J* = 17.5 Hz, 2H), 1.83 (d, *J* = 17.5 Hz, 2H), 0.96 (s, 6H), 0.84 (s, 6H). 13C NMR (150 MHz, $CDCl_3$) δ 196, 159.5, 149.8, 147.8, 139.2, 129.5, 129, 120.3, 114.7, 113.7, 111.9, 55.3, 50.3, 42, 32.8, 32.5, 29.8, 27.

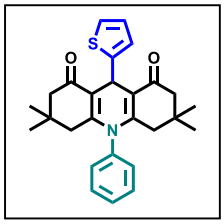
3,3,6,6-tetramethyl-9-(3-phenoxyphenyl)-10-phenyl-3,4,6,7,9,10-hexahydroacridine-1,8(2H,5H)-dione (4.2.5i). The compound 5i was synthesized by the procedure as described above and obtained as white solid: 85% yield (220 mg), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52-7.43 (m, 3H), 7.34-7.29 (m, 3H), 7.25-7.21 (m, 1H), 7.13-7.10 (m, 2H), 6.99-6.97 (m, 2H), 6.91-6.90 (m, 1H), 6.84-6.82 (m, 1H), 6.72-6.60 (m, 1H), 5.26 (s, 1H), 2.16 (ABq, *J* = 13.9 Hz, 4H), 2.01 (d, *J* = 17.5 Hz, 2H), 1.68 (d, *J* = 17.5 Hz, 2H), 0.92 (s, 6H), 0.77 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.9, 157.7, 157.6, 149.9, 148.2, 138.9, 129.8, 129.4, 124, 123.1, 119.4, 117, 116.9, 114.4, 50.3, 41.8, 32.7, 32.4, 29.9, 26.7. HRMS calculated for $C_{35}H_{36}NO_3[M+H]^+$:: 518.2695. Found: 518.2713



9-(benzo[d][1,3]dioxol-5-yl)-3,3,6,6-tetramethyl-10-phenyl-3,4,6,7,9,10-hexahydroacridine-1,8(2H,5H)-dione (4.2.5j).[22] The compound 5j was synthesized by the procedure as described above and obtained as black solid: 72% yield (168 mg), ^{1}H NMR (600 MHz, $CDCl_3$) 7.57-7.54 (m, 3H), 7.23 (d, *J* = 6.8 Hz, 2H), 6.96 (d, *J* = 1.7 Hz, 1H), 6.92-6.89 (m, 1H), 6.70 (d, *J* = 7.9 Hz, 1H), 5.88 (s, 2H), 5.19 (s, 1H), 2.17 (ABq, *J* = 18.6 Hz, 4H), 2.06 (d, *J* = 17.4 Hz, 2H), 1.81 (d, *J* = 17.4 Hz, 2H), 0.94 (s, 6H), 0.83 (s, 6H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 196.1, 149.7, 147.4, 145.7, 140.7, 139.2, 130.2 129.5, 121, 114.8, 108.9, 108, 100.7, 66, 50.3, 41.9, 32.5, 29.8, 27, 15.4. HRMS calculated for $C_{22}H_{31}NO_4$ $[M+H]^+$:: 470.2331. Found: 470.2334

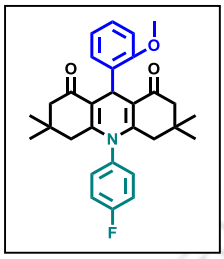


3,3,6,6-tetramethyl-10-phenyl-9-(thiophen-2-yl)-3,4,6,7,9,10-hexahydro acridine-1,8(2H,5H)-dione (4.2.5k).[13c] The compound 5k was synthesized by the procedure as described above and obtained as yellow solid: 75% yield (162 mg), R_f = 0.3 (30% EtOAc + pet ether); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.55-7.54 (m, 3H), 7.32-7.23 (m, 2H), 7.03-7.01 (m, 2H), 6.87-6.86 (m, 1H), 5.67 (s, 1H), 2.22 (ABq, *J* = 11.6 Hz, 4H), 2.10 (d, *J* = 17.5 Hz, 2H), 1.80 (d, *J* = 17.5 Hz, 2H), 0.96 (s, 6H), 0.86 (s, 6H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 195.8,

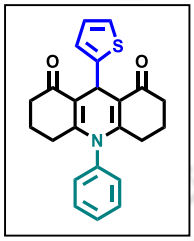


150.5, 150.2, 130.6, 130.2 139.1, 129.7, 129.5, 127.1, 124.3, 122.5, 114.3, 50.3, 41.8, 32.5, 30, 27.4, 26.9.

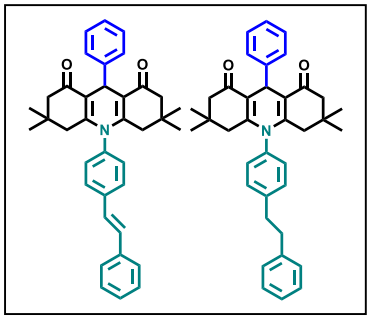
10-(4-fluorophenyl)-9-(2-methoxyphenyl)-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydroacridine-1,8(2H,5H)-dione (4.2.5l). The compound 5l was synthesized by the procedure as described above and obtained as yellow solid: 72% yield (170 mg), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53-7.50 (m, 1H), 7.34-7.23 (m, 4H), 7.12-7.07 (m, 1H), 6.91-6.87 (m, 1H), 6.83-6.81 (m, 1H), 5.39 (s, 1H), 3.89 (s, 3H), 2.11 (ABq, *J* = 14.8 Hz, 4H), 1.97 (d, *J* = 17.2 Hz, 2H), 1.78 (d, *J* = 17.2 Hz, 2H), 0.92 (s, 6H), 0.80 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.9, 162.5 (d, *J* = 250.8 Hz), 157.8, 149.8, 135.7 (d, *J* = 3.5 Hz), 133.1, 132.2, 127.4, 120.4, 117.2 (d, J = 22.8 Hz), 113.8, 111.3, 55.9, 50.3, 42.4, 32.5, 31.3, 29.9, 26.6. HRMS calculated for $C_{30}H_{32}FNO_3$ $[M+H]^+$:: 474.2400. Found: 474.2451



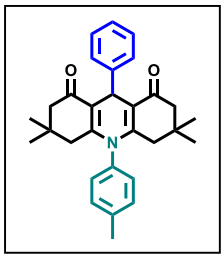
10-phenyl-9-(thiophen-2-yl)-3,4,6,7,9,10-hexahydroacridine-1,8(2H,5H)-dione (4.2.5m).[24] The compound 5m was synthesized by the procedure as described above and obtained as yellow solid: 68% yield (188 mg), ^{1}H NMR (600 MHz, CDCl3)δ 7.53-7.50 (m, 3H), 7.29-7.27 (m, 2H), 7.05-7.04 (m, 1H), 6.99 (d, *J* = 3.3 Hz, 1H), 6.89-6.88 (m, 1H), 5.72 (s, 1H), 2.44 (dt, *J* = 16.5, 4.5 Hz, 2H), 2.32-2.26 (m, 2H), 2.23-2.17 (m, 2H), 2.03 (dt, *J* = 17.3, 4.7 Hz, 2H), 1.93-1.89 (m, 2H), 1.85-1.81 (m, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 196.1, 151.8, 151.2, 139.1, 130.5, 129.9, 129.7, 129.5, 127.3, 123.9, 122.8, 115.3, 36.9, 28.3, 27.2, 21.3.



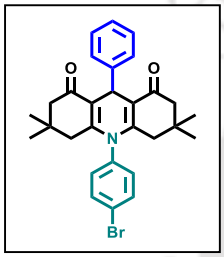
(E)-3,3,6,6-tetramethyl-9-phenyl-10-(4-styrylphenyl) -3,4,6,7,9,10-hexahydro acridine-1,8(2H,5H)-dione (4.2.5n). The compound 5n was synthesized by the procedure as described above and obtained as white solid: 58% yield (153 mg), ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.71 (d, *J* = 8.0 Hz, 2H), 7.59 (d, *J* = 7.6 Hz, 2H), 7.48-7.42 (m, 4H), 7.35 (t, *J* = 7.3 Hz, 1H), 7.29-7.20 (m, 6H), 7.13 (t, *J* = 7.3 Hz, 1H), 5.31 (s, 1H), 2.24-2.12 (m, 6H), 1.91 (d, *J* = 17.5 Hz, 2H), 0.98 (s, 6H), 0.84 (s, 6H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 195.9, 149.8, 146.2, 138.5, 138, 136.6, 131.1, 128.9, 128.4, 128.1, 127.9, 126.9, 126.8, 126, 114.7, 50.2, 41.8, 32.7, 32.5, 29.8, 26.8. HRMS calculated for $C_{37}H_{37}NO_2$ $[M+H]^+$ :: 528.2903 Found: 528.2943



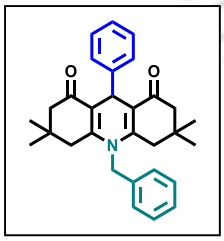
3,3,6,6-tetramethyl-9-phenyl-10-(p-tolyl)-3,4,6,7, 9, 10-hexahydroacridine-1,8(2H,5H)-dione (4.2.5o).[20] The compound 5o was synthesized by the procedure as described above and obtained as white solid: 70% yield (154 mg), ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.45 (d, *J* = 7.2 Hz, 2H), 7.36 (d, *J* = 7.2 Hz, 2H), 7.26 (t, *J* = 7.6 Hz, 2H), 7.12 (t, *J* = 7.1 Hz, 3H), 5.29 (s, 1H), 2.50 (s, 3H), 2.18 (ABq, *J* = 20.4 Hz, 4H), 2.09 (d, J = 17.5 Hz, 2H), 1.86 (d, *J* = 17.5 Hz, 2H), 0.96 (s, 6H), 0.82 (s, 6H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 196, 150.1, 146.3, 139.6, 136.5, 128.2, 128, 126.1, 114.7, 50.3, 41.9, 32.8, 32.5, 29.9, 26.9, 21.4.



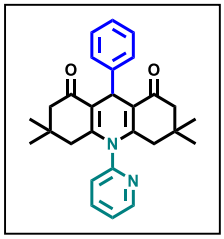
10-(4-bromophenyl)-3,3,6,6-tetramethyl-9-phenyl-3,4,6,7,9,10-hexahydro acridine-1,8(2H,5H)-dione (4.2.5p).[20] The compound 5p was synthesized by the procedure as described above and obtained as yellow solid: 81% yield (204 mg), ^{1}H NMR (600 MHz, CDCl3) δ 7.70 (d, J = 8.0 Hz, 2H), 7.40 (d, *J* = 7.2 Hz, 2H), 7.26 (t, *J* = 7.7 Hz, 2H), 7.16-7.13 (m, 3H), 5.27 (s, 1H), 2.19 (ABq, *J* = 18.4 Hz, 4H), 2.06 (d, *J* = 17.5 Hz, 2H), 1.82 (d, *J* = 17.5 Hz, 2H), 0.96 (s, 6H), 0.81 (s, 6H). ^{13}C NMR (150 MHz, CDCl3) δ 195.9, 149.3, 146, 138.3,133.6 128.3, 128, 126.2, 123.6, 115.1, 50.3, 42, 32.8, 32.6, 29.9, 27.



10-benzyl-3,3,6,6-tetramethyl-9-phenyl-3,4,6,7,9,10-hexahydroacridine-1,8(2H,5H)-dione *(4.2.5q).*[25] The compound 5q was synthesized by the procedure as described above and obtained as white solid: 90% yield (198 mg), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42-7.34 (m, 3H), 7.30-7.28 (m, 2H), 7.21-7.15 (m, 4H), 7.11-7.06 (m, 1H), 5.33 (s, 1H), 4.90 (s, 2H), 2.49 (d, *J* = 16.6 Hz, 2H), 2.30 (*J* = 16.6 Hz, 2H), 2.20 (ABq, *J* = 9.5 Hz, 4H), 0.99 (s, 6H), 0.89 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.9, 150.7, 146, 137.2, 129.4, 128.1, 128.1, 126.1, 125.5, 115.5, 50.2, 48.9, 40.4, 32.9, 32.3, 28.6, 28.4.

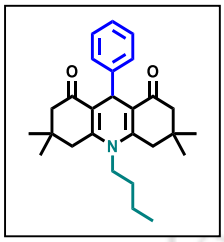


3,3,6,6-tetramethyl-9-phenyl-10-(pyridin-2-yl)-3,4,6,7,9,10-hexa hydro acridine-1,8(2H,5H)-dione *(4.2.5r).*[26] The compound 5r was synthesized by the procedure as described above and obtained as white solid: 55% yield (117 mg), ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.72 (s, 1H), 7.95 (t, *J* = 7.6 Hz, 1H), 7.50-7.45 (m, 3H), 7.32 (d, *J* = 7.8 Hz, 1H), 7.26-7.22 (m, 2H), 7.10 (t, *J* = 7.3 Hz, 1H), 5.27 (s, 1H), 2.23-2.11 (m, 6H), 2.21 (d, *J* = 16.2 Hz, 2H), 0.95 (s, 6H), 0.81 (s, 6H). ^{13}C

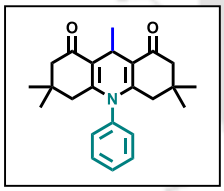


NMR (125 MHz, $CDCl_3$) δ 195.8, 152.7, 150.5, 149.0, 146.1, 139.2, 128.2, 128.1, 126.1, 124.8, 124.5, 115.1, 50.4, 41.4, 33.1, 32.6, 29.7, 27.1.

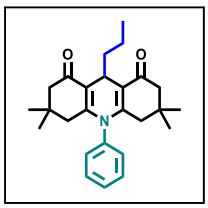
10-butyl-3,3,6,6-tetramethyl-9-phenyl-3,4,6,7,9,10-hexahydroacridine-1,8(2H,5H)-dione (4.2.5s). The compound 5s was synthesized by the procedure as described above and obtained as white solid: 70% yield (198 mg), ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.25-7.23 (m, 2H), 7.16 (t, *J*= 7.7 Hz, 2H), 7.05 (t, *J*= 7.3 Hz, 1H), 5.26 (s, 1H), 3.64 (t, *J*= 7.6 Hz, 2H), 2.53 (d, J = 16.6 Hz, 2H), 2.39 (d, *J* = 16.6 Hz, 2H), 2.22 (s, 4H), 1.61-1.59 (m, 2H), 1.40-1.36 (m, 2H), 1.09 (s, 6H), 1.00 (s, 6H), 0.98 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 195.6, 150.2, 145.7, 127.9, 127.6, 125.8, 115.4, 49.9, 44.6, 40.4, 33.5, 32.5, 31.8, 29.3, 27.9, 19.9, 13.8. HRMS calculated for $C_{27}H_{35}NO_2$ $[M+H]^+$ :: 406.2746. Found: 406.2760



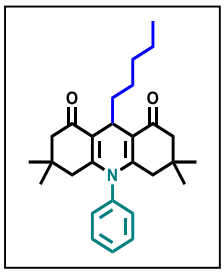
10-hexyl-9-(4-methoxyphenyl)-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydroacridine-1,8(2H,5H)-dione (4.2.5t). The compound 5t was synthesized by the procedure as described above and obtained as white solid: 75% yield (173 mg), ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.17 (d, *J* = 8.7 Hz, 2H), 6.72 (d, *J* = 8.7 Hz, 2H), 5.21 (s, 1H), 3.73 (s, 3H), 3.65 (t, *J* = 7.6 Hz, 2H), 2.53(d, *J* = 16.6 Hz, 2H), 2.40 (d, *J* = 16.6 Hz, 2H), 2.23 (s, 4H), 1.62 (t, *J* = 7.3 Hz, 2H), 1.35-1.33 (m, 6H), 1.10 (s, 6H), 1.01 (s, 6H), 0.93 (t, *J* = 6.7 Hz, 3H). 13C NMR (150 MHz, $CDCl_3$) δ 195.8, 157.7, 150.1, 138.4, 128.6, 115.7, 113.4, 55.2, 50, 44.9, 40.5, 32.6, 31.6, 31.5, 31.1, 29.5, 28, 26.5, 22.7, 14.1. HRMS calculated for $C_{30}H_{41}NO_3$ $[M+H]^+$:: 464.3165. Found: 464.3145



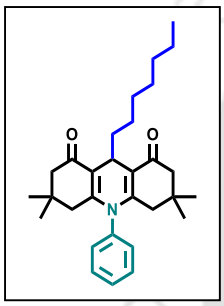
3,3,6,6-tetramethyl-10-phenyl-9-propyl-3,4,6,7,9,10-hexahydroacridine-1,8(2H,5H)-dione (3.1.5u). The compound 5u was synthesized by the procedure as described above and obtained as white solid: 45% yield (88 mg), ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.54-7.53 (m, 3H), 7.17-7.15 (m, 2H), 4.25 (t, *J* = 5.1 Hz, 1H), 2.22 (ABq, *J* = 10.4, 4H), 2.03 (d, *J* = 17.5 Hz, 2H), 1.73 (d, *J* = 17.5 Hz, 2H), 1.47-1.44 (m, 2H), 1.35-1.28 (m, 2H), 0.96 (s, 6H), 0.95 (s, 6H), 0.89 (t, J = 7.3 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 196.5, 151.0, 139.3, 130.0, 129.3, 114.1, 50.5, 41.9, 38.2, 32.3, 30.2, 26.7, 26.1, 18.9, 14.6. HRMS calculated for $C_{26}H_{33}NO_2$ $[M+H]^+$:: 392.2590. Found: 392.2596.



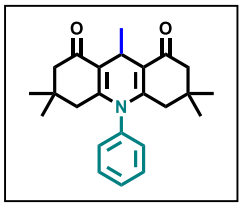
3,3,6,6-tetramethyl-9-pentyl-10-phenyl-3,4,6,7,9,10-hexahydroacridine- 1,8(2H,5H)-dione (4.2.5v). The compound 5v was synthesized by the procedure as described above and obtained as white solid: 72% yield (151 mg), ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.54-7.52 (m, 3H), 7.16 (d, *J* = 7.0 Hz, 2H), 4.26 (t, *J* = 5.0 Hz, 1H), 2.24 (ABq, *J* = 10.6 Hz, 4H), 2.05 (d, *J* = 17.4 Hz, 2H), 1.75 (d, *J* = 17.4 Hz, 2H), 1.50-1.46 (m, 2H), 1.33-1.26 (m, 6H), 0.97 (s, 6H), 0.96 (s, 6H), 0.88 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 196.5, 151.0, 139.4, 130.2, 129.3, 114.1, 50.6, 41.9, 35.6, 32.4, 32.3, 30.2, 26.7, 26.2, 25.3, 22.9, 14.2. HRMS calculated for $C_{28}H_{37}NO_2$ $[M+H]^+$:: 420.2903. Found: 420.2947



9-heptyl-3,3,6,6-tetramethyl-10-phenyl-3,4,6,7,9,10-hexahydroacridine-1,8(2H,5H)-dione (4.2.5w).[27] The compound 5w was synthesized by the procedure as described above and obtained as white solid: 68% yield (152 mg), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56-7.51 (m , 3H), 7.16 (d, *J* = 6.9 Hz, 2H), 4.26 (t, *J* = 4.9 Hz, 1H), 2.24 (ABq, *J* = 10.6 Hz, 4H), 2.05 (d, *J* = 17.5 Hz, 2H), 1.75 (d, *J* = 17.5 Hz, 2H), 1.50-1.47 (m, 2H), 1.32-1.26 (m, 10H), 0.97 (s, 6H), 0.96 (s, 6H), 0.88 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 196.6, 151.1, 139.4, 130.1, 129.3, 114.1, 50.6, 41.9, 35.6, 32.3, 32, 30.2, 30, 29.5, 26.7, 26.2, 25.6, 22.8, 14.3.



***3,3,6,6,9-pentamethyl-10-phenyl-3,4,6,7,9,10-hexahydroacridine-1,8(2H,5H)*-dione (4.2.5x).**[28] The compound 5x was synthesized by the procedure as described above and obtained as white solid: 42% yield (76 mg), ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.54-7.52 (m, 3H), 7.19-7.17 (m, 2H), 4.16 (q, *J* = 6.2 Hz, 1H), 2.23 (s, 4H), 2.02 (d, *J* = 17.4 Hz, 2H), 1.74 (d, *J* = 17.4 Hz, 2H), 1.08 (d, *J* = 6.5 Hz, 3H), 0.96 (s, 6H), 0.95 (s, 6H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 196.3, 150.2, 139.2, 129.9, 129.2, 115.8, 50.4, 41.7, 32.4, 29.8, 26.5, 22, 21.7.



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4.11. Figures reproducing ^{1}H and ^{13}C NMR spectra:

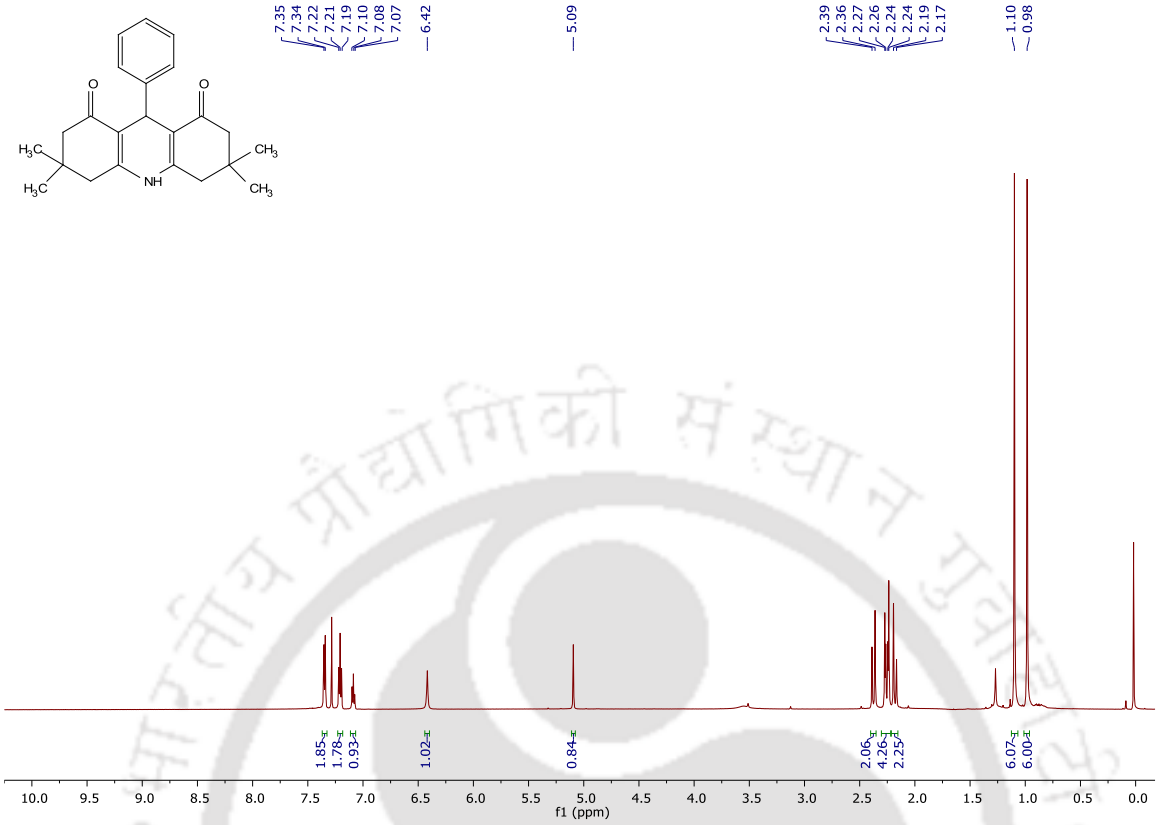


Figure 4.19. ^{1}H NMR (600 MHz) spectra of compound **4.1.4a** in $CDCl_3$

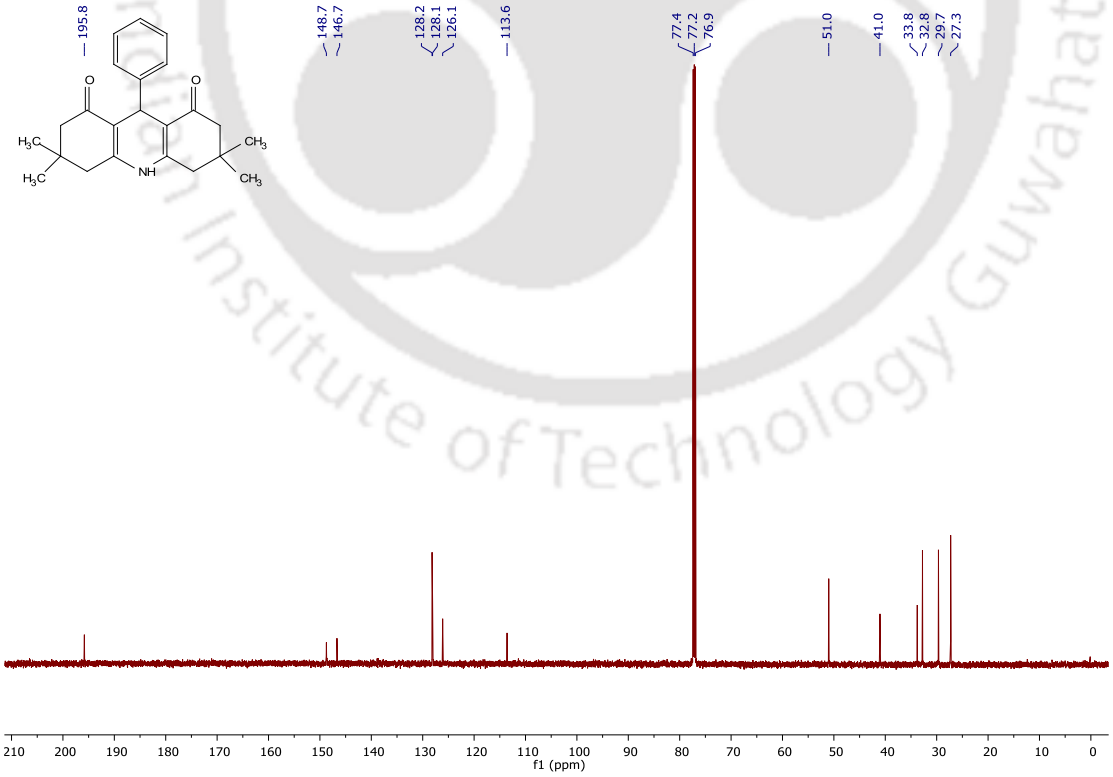


Figure 4.20. $^{13}C\{^{1}H\}$ NMR (150 MHz) spectra of compound **4.1.4a** in $CDCl_3$

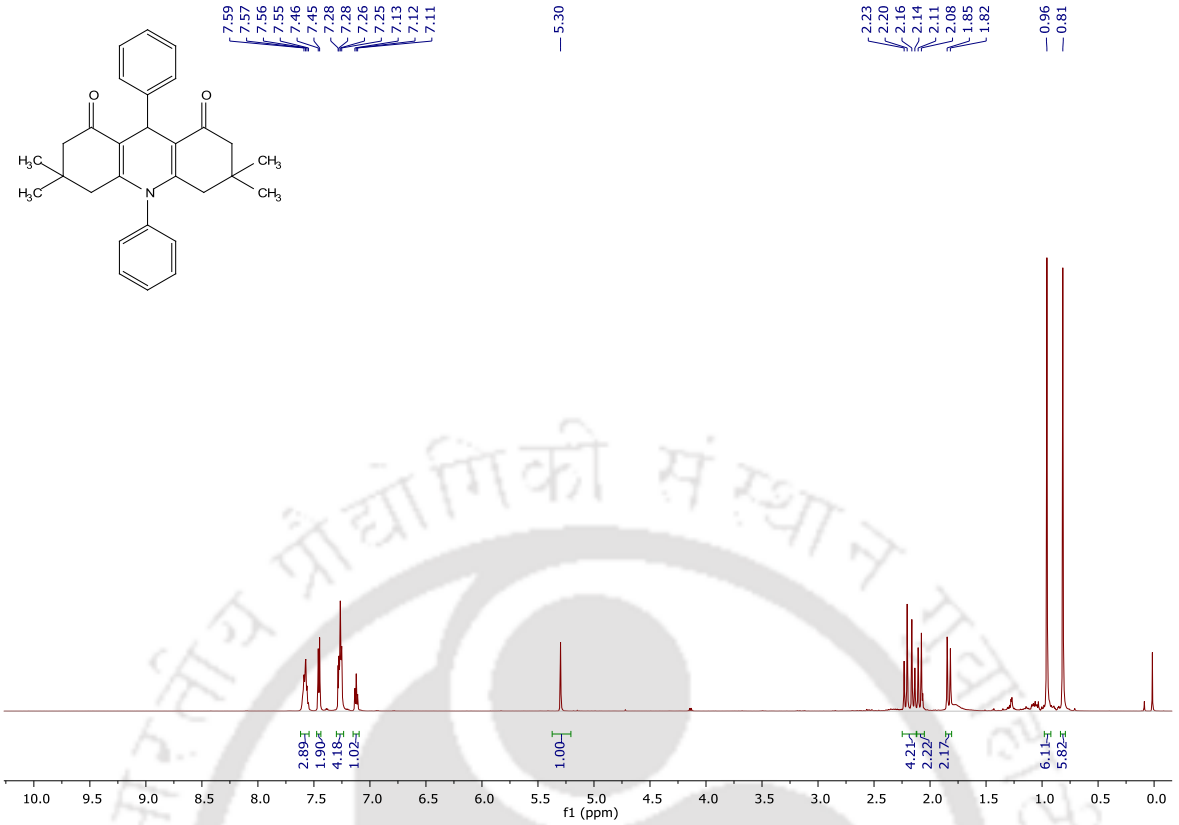


Figure 4.21. ^{1}H NMR (600 MHz) spectra of compound **4.2.5a** in $CDCl_3$

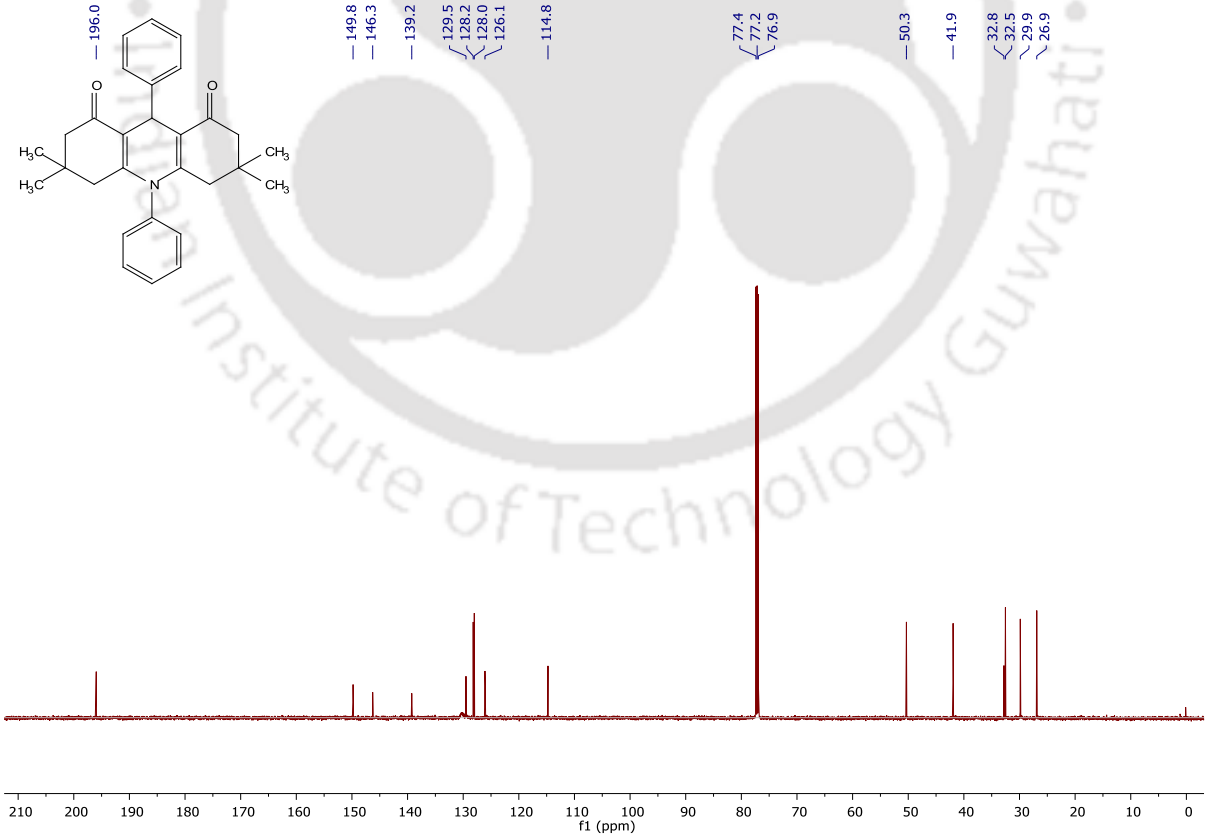


Figure 4.22. ^{13}C{^{1}H} NMR (150 MHz) spectra of compound **4.2.5a** in $CDCl_3$

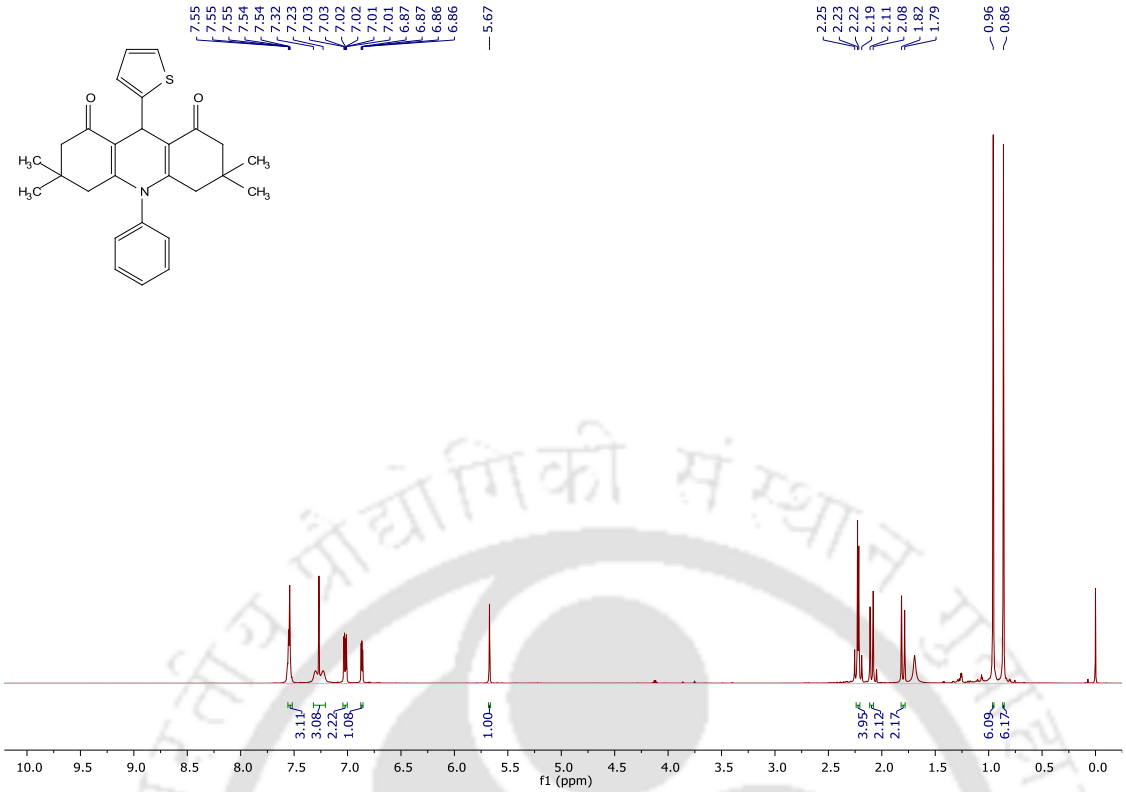


Figure 4.23. ^{1}H NMR (600 MHz) spectra of compound **4.2.5k** in $CDCl_3$

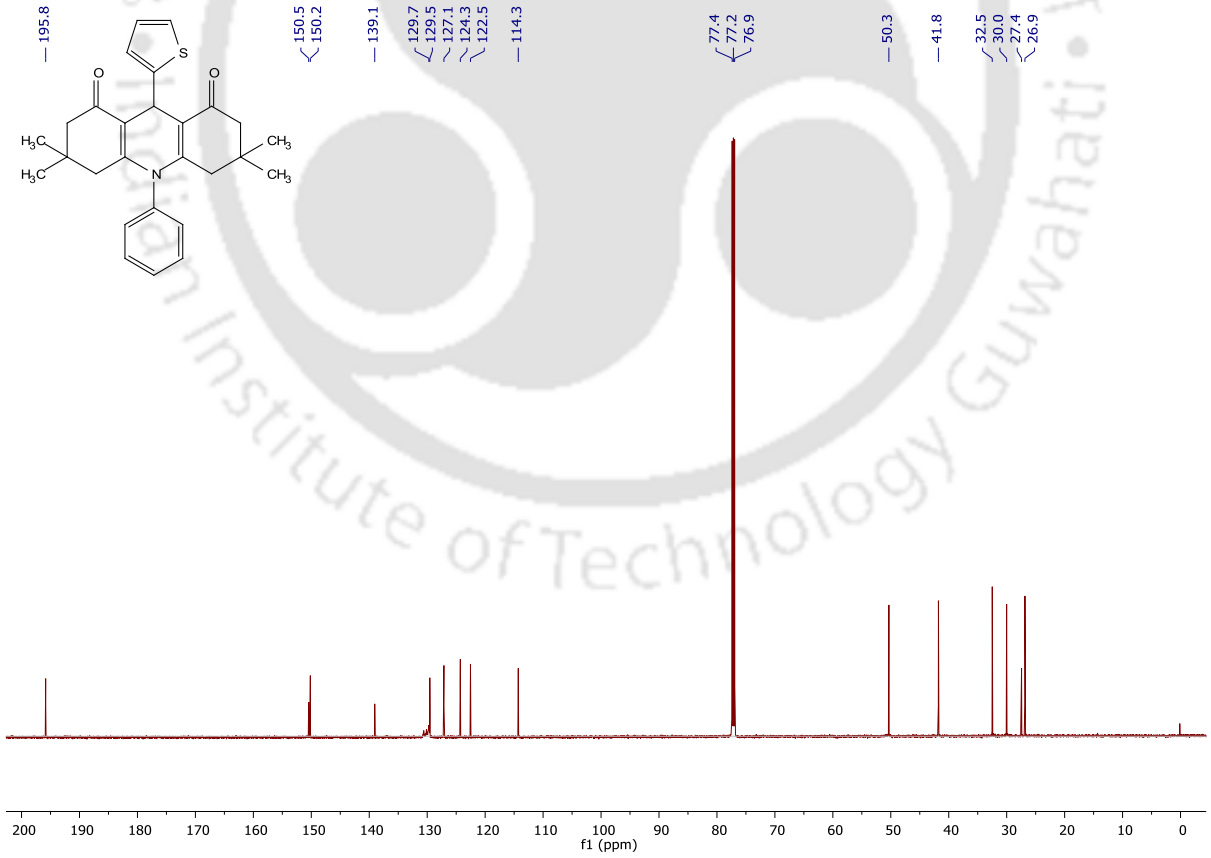


Figure 4.24. $^{13}C\{^{1}H\}$ NMR (150 MHz) spectra of compound **4.2.5k** in $CDCl_3$

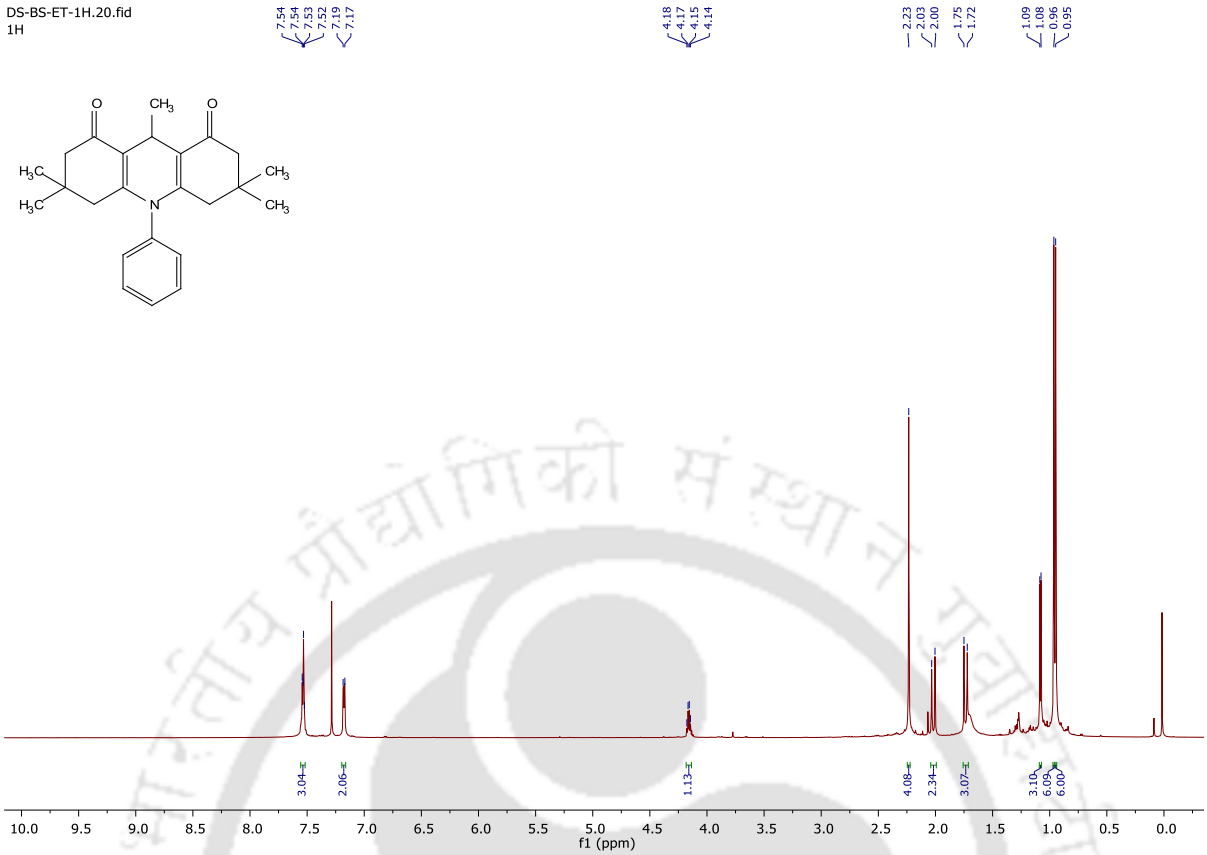


Figure 4.25. ^{1}H NMR (600 MHz) spectra of compound **4.2.5x** in $CDCl_3$

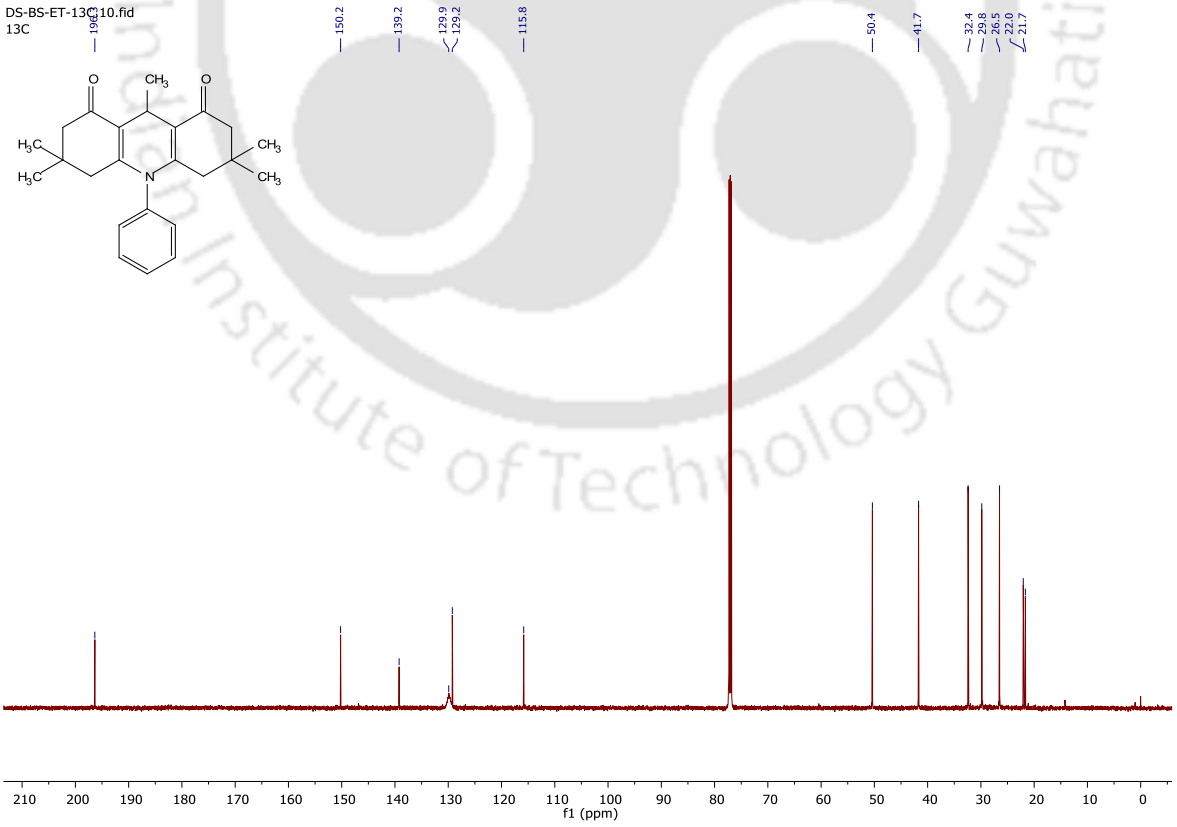


Figure 4.26. $^{13}C\{^{1}H\}$ NMR (150 MHz) spectra of compound **4.2.5x** in $CDCl_3$

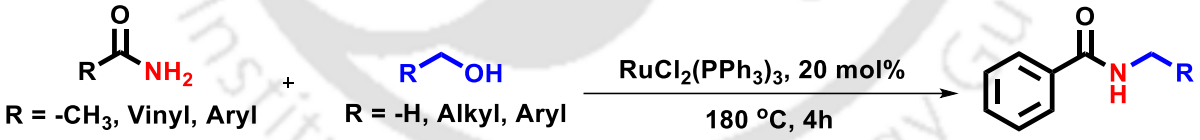
Chapter 5

Ru doped Hydrotalcite Catalyzed Borrowing Hydrogen Mediated N-Alkylation of Benzamides, Sulfonamides and Dehydrogenative Synthesis of Quinazolines

Chapter 5

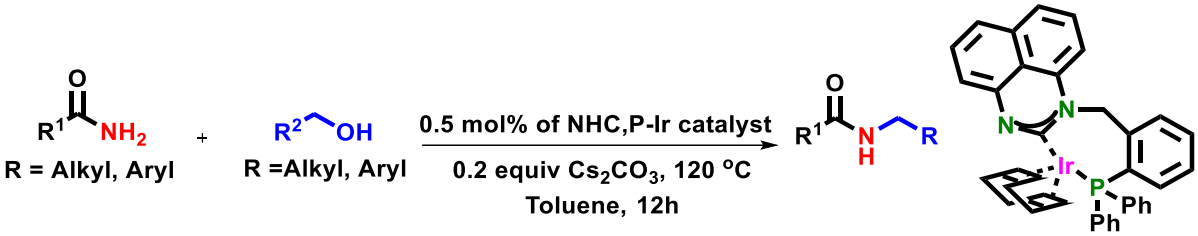
5.1. Introduction:

Construction of C-N bond is a fundamental reaction in chemistry and C-N bond acts as a major building block for various biological systems.[1] From a synthetic and pharmacological standpoint, the derivatization of amide motifs is highly important as amide analog represents various synthetically and biologically useful compounds and drugs.[3,4]. *N*-alkylation of amides is one of the most widely used strategies for the diversification of amide motifs. Conventionally, aryl and alkyl halides were employed for the *N*-alkylation of amides.[5] However, the stoichiometric equivalent of waste generation and involvement of multistep synthetic procedures lowers its practicable applicability.[6] Therefore, the derivatization of amides in a sustainable and eco-friendly manner is highly demanding.[2] In this regard, the use of biomass-derived alcohols for the *N*-alkylation of amides is notable as alcohols are less toxic, highly stable, and readily available. The borrowing hydrogen (BH)[7] approach for the N alkylation of amides has attracted significant focus as it uses renewable alcohols and generates water as a sole by-product which makes this process highly atom economical, sustainable, and economically viable. The BH N alkylation of amides is less explored compared to amines. This might be due to the less nucleophilic nature of amides compared to amine, which imposes harsher reaction conditions and/or high catalyst loading to achieve *N*-alkylation of amides with alcohols[8] via BH. *Watanabe et al*. first illustrated $RuCl_2(PPh_3)_3$ catalyzed borrowing hydrogen approach for the *N*-alkylation of carboxamides at 180 °C (**Scheme 5.1**).[8a]



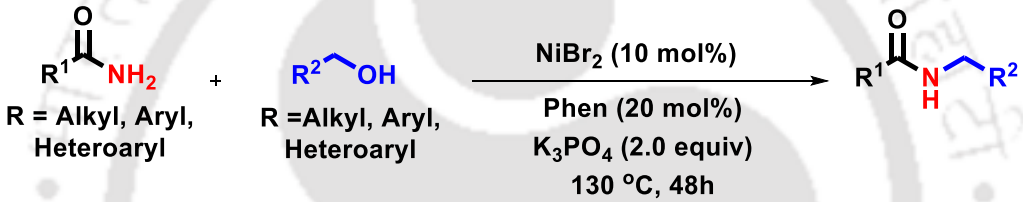
Scheme 5.1. *N*-alkylation of amides catalyzed by $RuCl_2(PPh_3)_3$

Afterward, *Jenner* and *co-workers* demonstrated the applicability of $RuCl_2(PBu_3)_3$ to enhance the yields and versatility of the reaction by activating various alcohols at very high reaction temperatures.[8a] Subsequently several efforts have been attributed to achieve the N alkylation of carboxamide under milder reaction conditions using various homogenous catalysts.[8a] In this context, the group of Andersson illustrated the efficacy of N-heterocyclic carbene-phosphine-derived iridium complexes to catalyze the *N*-alkylation of carboxamide with alcohols at 120 °C (**Scheme 5.2**).[8b]



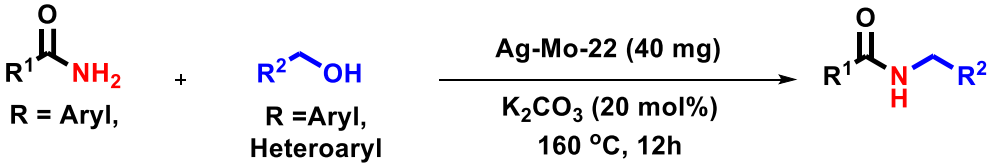
Scheme 5.2. *N*-alkylation of amides catalyzed by NHC,P-Ir catalyst

The use of earth-abundant and nontoxic/less toxic first-row transition metals replacing costly noble metals has attracted significant attention in recent years. In this perspective, Banerjee and his group applied a combination of $NiBr_2$ (10 mol%) and 1,10-phenanthroline (20 mol%) to catalyze *N*-alkylation of amide in the presence of an excess amount of alcohols (4 eq. to carboxamide) and 2 equivalent K_3PO_4 (**Scheme 5.3**).[8d]



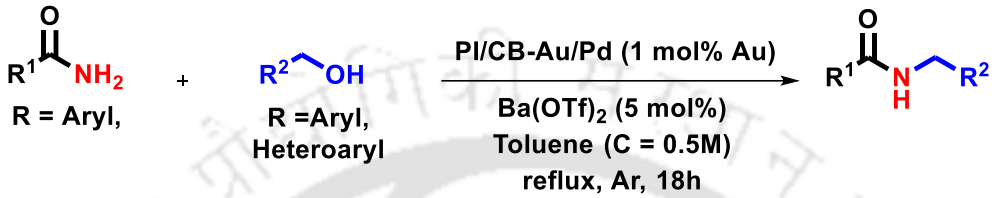
Scheme 5.3. *N*-alkylation of amides catalyzed by $NiBr_2$

The major disadvantage of homogeneous catalysis lies in the difficulties of separating metal impurities from the desired product and reusing the catalyst. Heterogeneous catalysts[9] are well known to solve these problems, however, the major disadvantages are the lower reactivity and selectivity compared to the homogeneous catalyst. Thus, the development of a heterogeneous catalyst to afford selectively mono *N*-alkylated amide from alcohol and carboxamide under relatively milder conditions would be cost-effective and highly sustainable. In this context, *Shi* and *co-workers* described the efficacy of Ag/Mo oxide ($Ag_6Mo_{10}O_{33}$) for such a process.[8e] However, their protocol relies only on the use of excess alcohols (5eq) and failed to activate aliphatic alcohols (**Scheme 5.4**).



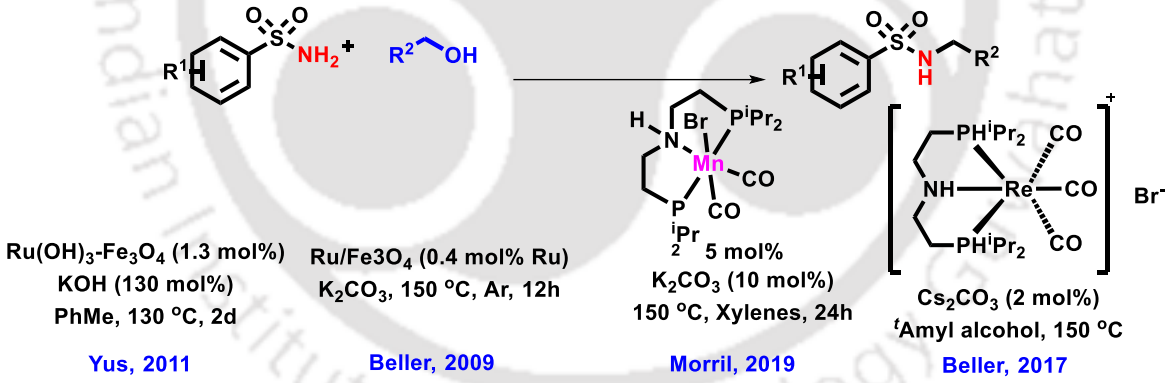
Scheme 5.4. *N*-alkylation of amides catalyzed by Ag/Mo oxide ($Ag_6Mo_{10}O_{33}$)

The group of Kobyashi developed polymer-encapsulated Au/Pd nanoparticles with carbon black as a secondary support to catalyze such reactions.[8f] They also successfully demonstrated the recyclability of the catalyst. However, the use of excess alcohols (3-5eq) and $Ba(OTf)_2$ as an additive is essential to afford the good yield of desired *N*-alkylated amide. Thus, the development of reactive heterogeneous catalysts to perform various de(hydrogenative) transformations, using less/stoichiometric amounts of alcohols is advantageous.



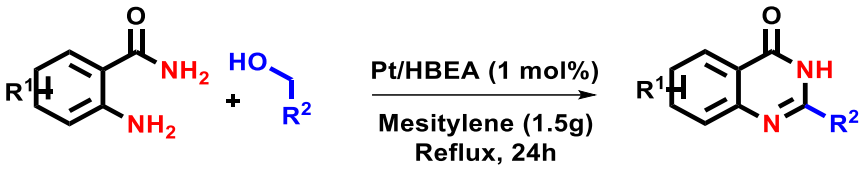
Scheme 5.5. *N*-alkylation of amides catalyzed by PI/CB-Au/Pd catalyst

Apart from benzamide, various reports related to sulfonamide alkylation were also published recently. Here some selected examples were presented in (**Scheme 5.6**). Sulfonamide alkylation is also important.[10]



Scheme 5.6. *N* -alkylation of sulphonamides

Synthesis of heterocycle quinazolinones can be possible by dehydrogenative reaction between 2-amino benzamide and benzyl alcohols via C-N bond formation. However, the use of heterogeneous catalysts in this process is less explored.[15] In 2014, *Shimizu* and *co-workers* described the applicability of heterogeneous Pt catalysts for this reaction.[18d]



Scheme 5.6. *N*-alkylation of amides catalyzed by PI/CB-Au/Pd catalyst

The B-H alkylation of amide/ sulfonamide and the synthesis of quinazolinones are less explored with heterogeneous catalysts. The preceding discussion also revealed that the heterogeneous catalysts used for these transformations frequently necessitate harsh conditions and an excess of alcohol. In addition, the developed catalysts are particularly effective in the *N*-alkylation of either benzamide or sulphonamide. Therefore the development of a new versatile heterogeneous catalyst capable of *N*-alkylation of both carboxamides and sulfonamides as well as quinazoline synthesis via de(hydrogenative) pathway is captivating.

5.2. Our work:

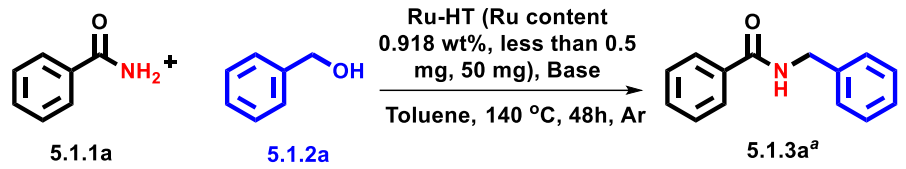
Here, we have utilized Ru-fabricated hydrotalcite[9a-9e, 9h], which was previously (in Chapter 4) explored and characterized. Here, the *N*-alkylation of benzamides and sulphonamides via borrowing hydrogen catalysis is illustrated. Various primary alcohols, including benzyl, heteroaryl, and aliphatic alcohols, were alkylated and the yield is promising. To shed light on the mechanistic details, several control studies and deuterium labeling experiments were performed. Mechanistic studies underpin that the reaction is going via a borrowing hydrogen pathway rather than an S_N1-type mechanism. The reaction can be easily scaled up without any detrimental effect on the yield. The catalyst is also capable of synthesizing quinazolinone directly from 2-aminobenzamide and alcohols. Successful recyclability and high reactivity highlight the practical applicability of the catalyst.

5.3. Results and discussions:

5.3.1. Optimization of the reactions conditions:

First, commercially available hydrotalcite, $Mg_6Al_2CO_3(OH)_{16}.4H_2O$ was added to the aqueous $RuCl_3 \cdot nH_2O$ solution. The resulting suspension was then treated with 1M NaOH until it reaches ~ pH 13 and vigorously stirred for 24 h to afford Ru-HT as grey powder.

Table 5.1. Screening table:



5.1.1a 5.1.2a 5.1.3a[a]

Entry	Catalyst	Base (equiv.)	Solvent	Yield (%)[b]
1	Ru-HT	-	Neat	n.d.
2	Ru-HT	-	Toluene	n.d.
3	Ru-HT	K_2CO_3 (0.5)	Toluene	38
4	Ru-HT	K_3PO_4 (0.5)	Toluene	55
5	Ru-HT	NaO^{t}Bu (0.5)	Toluene	74
6	Ru-HT	KO^{t}Bu (0.5)	Toluene	64
7	**Ru-HT**	**Cs_2CO_3 (0.5)**	**Toluene**	**87**
8	Ru-HT	Cs_2CO_3 (0.25)	Toluene	68
9[c]	Ru-HT	Cs_2CO_3 (0.5)	Toluene	60
10[d]	Ru-HT	Cs_2CO_3 (0.5)	Toluene	62
11	Ru-HT	Cs_2CO_3 (0.5)	Xylene	37
12	Ru-HT	Cs_2CO_3 (0.5)	Dioxane	24
13[e]	Ru-HT	Cs_2CO_3 (0.5)	Toluene	70
14[f]	Ru-HT	Cs_2CO_3 (0.5)	Toluene	51
15[g]	Ru-HT	Cs_2CO_3 (0.5)	Toluene	82
16[h]	Ru-HT	Cs_2CO_3 (0.5)	Toluene	74
17	-	Cs_2CO_3 (0.5)	Toluene	n.d
18	HT	Cs_2CO_3 (0.5)	Toluene	12

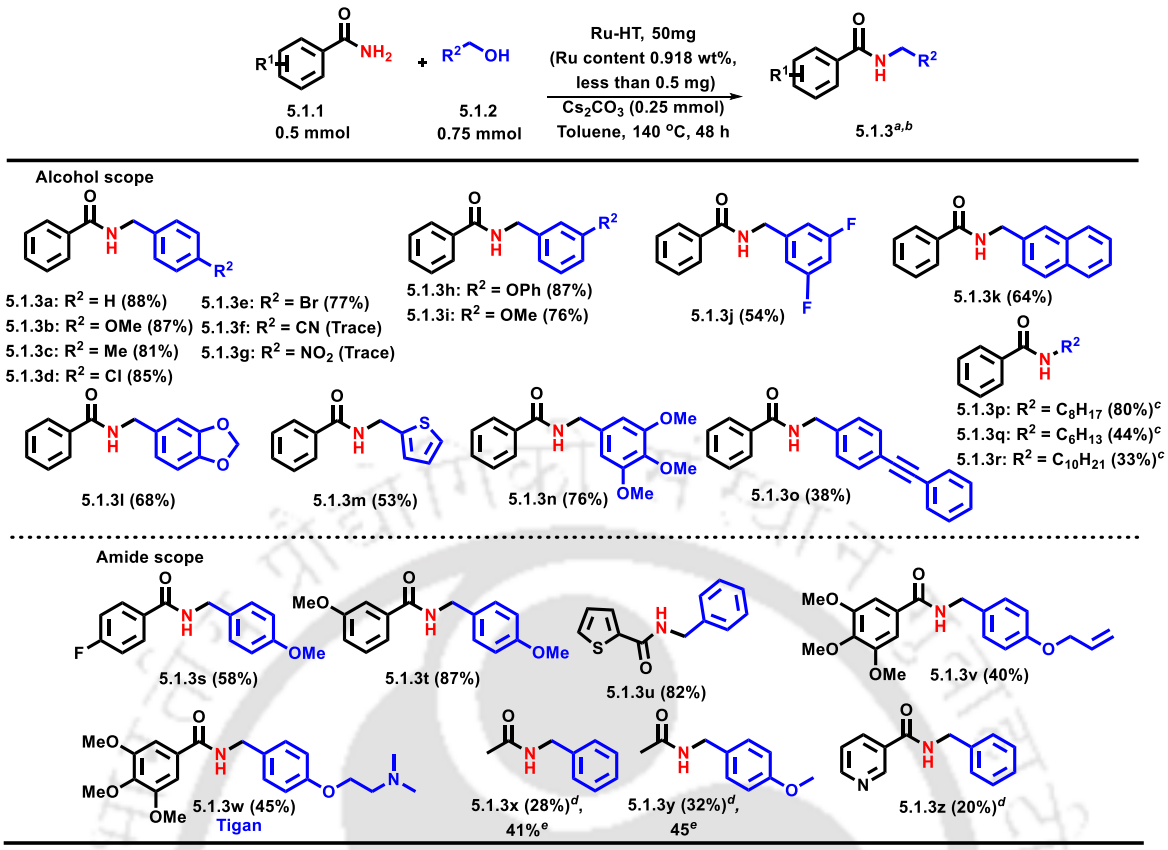
[a] Standard reaction conditions: **5.1.1a** (0.5 mmol), **5.1.2a** (0.75 mmol), Ru-HT (50 mg, Ru content 0.918 wt%, less than 0.5 mg) and Cs_2CO_3 (0.25 mmol) in toluene (2 mL), at 140 °C of a preheated oil bath for 48 h in a 60 mL pressure tube under Ar. [b]Isolated yield. [c]Low catalyst loading (30 mg). [d]**5.1.1a** (0.5 mmol) and **5.1.2a** (0.5 mmol), [e]36 h, [f]160 °C, [g]30 mL pressure tube. [h]100 mL pressure tube. n.d = Not detected.

Initially, the scope of Ru-HT was explored for direct *N*-alkylation of amides by taking benzamide (**5.1.1a**, 0.5 mmol) and benzyl alcohol (**5.1.2a,** 0.75 mmol) as a model system. At first, benzamide (**5.1.1a**, 0.5 mmol) and benzyl alcohol (**5.1.2a**, 0.75 mmol) were heated at

140 °C in a 60 mL pressure tube in the presence of Ru-HT (50 mg, Ru content 0.5 mg, 0.918 wt%) in neat condition (**Table 5.1**, **entry 1**). Unfortunately, the formation of benzaldehyde was observed, but no *N*-alkylated amide was formed. The reaction in toluene solvent also did not proceed (**Table 5.1**, **entry 2**). Next, the reaction was executed in the presence of various bases like KO^{t}Bu, K_2CO_3, K_3PO_4, NaO^{t}Bu, and Cs_2CO_3. To our delight, in the presence of Cs_2CO_3, the desired *N*-alkylated amide **5.1.3a** was isolated in excellent yield (87%) (**Table 1**, entry 7). The solvents like xylene or dioxane gave inferior results compared to toluene (**Table 5.1**, **entries 11** and **12**). Further, the effect of temperature and the volume of the pressure tube was also inspected (**Table 5.1**, **entries 13-16**). From these studies, it was established that 140 ºC and 60 mL pressure furnished the best result. In the absence of a catalyst, the reaction did not proceed (**Table 5.1**, **entry 17**).

5.3.2. N-Alkylation of diverse benzamides with various alcohols:

Next, the full scope of the Ru-HT-catalyzed *N*-alkylation of carboxamide with various alcohols was examined (**Scheme 5.6**). At the outset, alcohols having various functional groups have been employed as alkylating agents. Delightfully, the aryl unit containing both electron-donating substituents and electron-withdrawing substituents afforded good to excellent yield of the corresponding mono-alkylated product (**Scheme 5.6**, entries **5.1.3a-3e**). However, 4-CN, 4-NO_2 benzyl alcohols remain unreactive. Heterocyclic alcohols like piperonyl alcohol (**Scheme 5.6**, **entry 5.1.3l**), and 2-thiophene methanol (**Scheme 5.6**, **entry 5.1.3m**) gave moderate yields. It is important to note that even primary aliphatic alcohols gave moderate to good yield at higher temperatures 160 °C (**Scheme 5.6**, **entries 5.1.3p-3r**). This is quite a significant improvement over the earlier reports.[8e,8f] However, the catalytic system failed to dehydrogenate thermodynamically more challenging substrates like MeOH, EtOH, or cyclohexanol. Next, the focus was changed to various functionally diverse benzamides. When the optimized reaction conditions were employed, various benzamides were smoothly *N*-alkylated with benzyl alcohols. 4-fluoro benzamide, 3-methoxy benzamide, and thio carboxamide gave excellent yields in our standard reaction condition (**Scheme 5.6**, **entries 5.1.3s-3u**). The developed methodology successfully synthesized the drug molecule Tigan **5.1.3w**, which is used to treat nausea and vomiting. Aliphatic amides and nicotinamide gave moderate yields under more stringent conditions (**5.1.3x-3z**).]

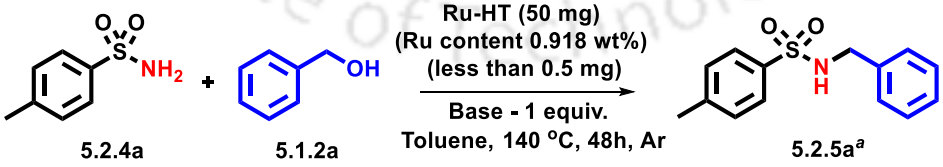


[a]Standard reaction conditions: **5.1.1** (0.5 mmol), **5.1.2** (0.75 mmol), Ru-HT (50 mg, Ru content 0.918 wt%, Ru is less than 0.5mg) and Cs_2CO_3 (0.25 mmol) in toluene (2 mL), at 140 °C of a preheated oil bath for 48 h in a 60 mL pressure tube under Ar. [b]Isolated yield. [c]High temperature (160 °C). [d]NaO^{t}Bu (0.5 mmol). [e]Alcohol (2.5 mmol).

Scheme 5.6. Scope of Ru-HT catalyzed BH mediated *N*-alkylation of benzamide

5.3.3. Optimization of the reaction condition for *N*-alkylation of sulfonamide:

5.2. Screening table:



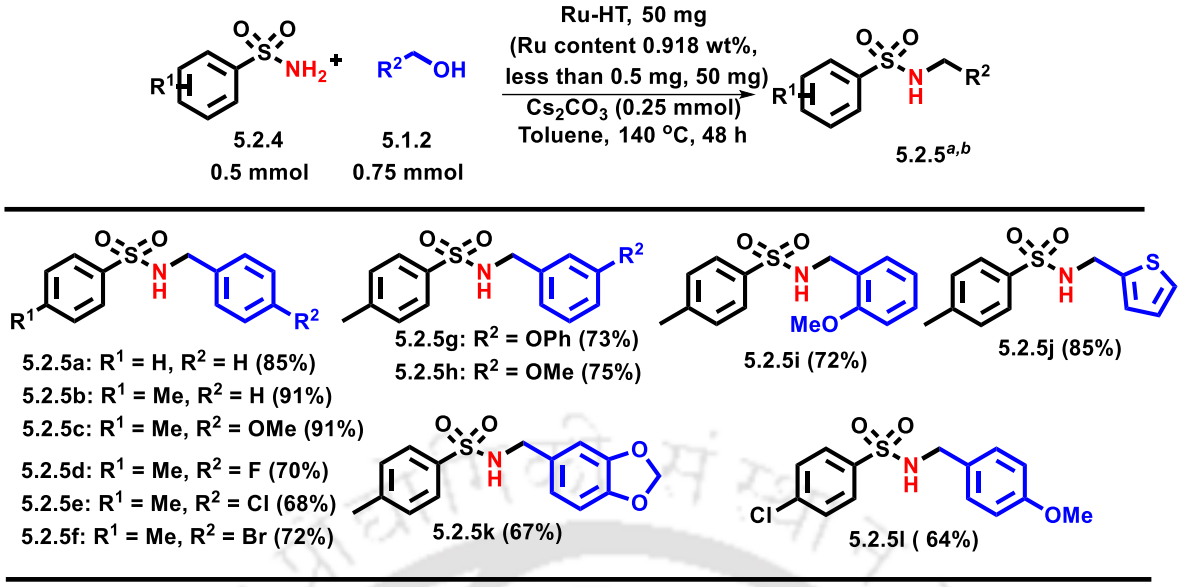
Entry	Catalyst (mg)	Base (equiv)	Yield (%)[b]
1	**Ru-HT**	**Cs_2CO_3 (0.5)**	**85**
2	-	Cs_2CO_3 (0.5)	n.d
3	Ru-HT	-	n.d
4	Ru-HT	Cs_2CO_3 (0.5)	12

5	Ru-HT	Cs_2CO_3 (0.5)	73
6	Ru-HT	Cs_2CO_3 (0.5)	63
7	Ru-HT	Cs_2CO_3 (0.5)	65
8	Ru-HT	Cs_2CO_3 (0.5)	55
9	Ru-HT	Cs_2CO_3 (0.5)	78
10	Ru-HT	Cs_2CO_3 (0.5)	73
11	Ru-HT	Cs_2CO_3 (0.5)	63
12	Ru-HT	Cs_2CO_3 (0.5)	58
13	Ru-HT	Cs_2CO_3 (0.5)	45
14	Ru-HT	Cs_2CO_3 (0.5)	59
15	Ru-HT	K_2CO_3 (0.5)	38
16	Ru-HT	K_3PO_4 (0.5)	45
17	Ru-HT	NaO^tBu (0.5)	55
18	Ru-HT	KO^tBu (0.5)	80
19	Ru-HT	Cs_2CO_3 (0.25)	68
20	Ru-HT	Cs_2CO_3 (1.0)	91

[a]Standard reaction conditions: **5.2.4a** (0.5 mmol), **5.1.2a** (0.75 mmol), Ru-HT (50 mg) and Cs_2CO_3 (0.25 mmol) in toluene (2 mL) of a preheated oil bath at 140 °C for 48 h in a 60 mL pressure tube under Ar, [b]Isolated yield, [c]Low catalyst loading (30 mg), [d]**5.2.4a** (0.5 mmol) and **5.1.2a** (0.5 mmol), [e]36h, [f]120 °C, [g]30 mL pressure tube. [h]100 mL pressure tube. [i]25 mL rb. [j]Xylene. [k]Dioxane. [l]tertAmyl alcohol. n.d. stands for not detected.

5.3.4. N-Alkylation of diverse sulfonamides with various alcohols:

Both electron-donating substituents (4-OMe, 3-OMe, 2-OMe) and electron-withdrawing (4-Cl, 4-Br, 4-F) substituents (**Scheme 5.9**, **entries 5.2.5a-5f**) gave excellent yields of the respective *N*-alkylated sulfonamides. Heterocyclic alcohols can be employed in the reaction to afford the desired product in good to excellent yield (**Scheme 5.9**, **entries 5.2.5j** and **5.2.5k**). Unfortunately, the *N*-alkylation of sulfonamides with aliphatic alcohols was not achieved under optimized conditions. Even, a rise in temperature up to 160 °C, leads to the decomposition of the sulfonamide and hence alkylation remains unresponsive.



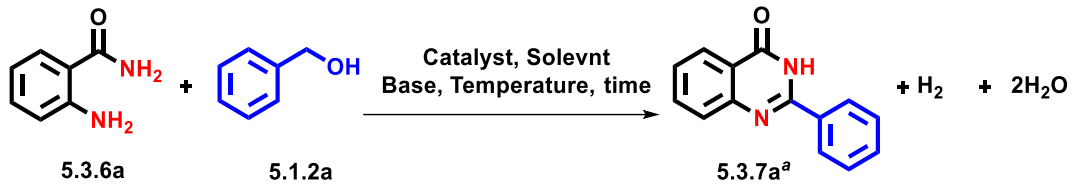
[a]Standard reaction conditions: **5.2.4** (0.5 mmol), **5.1.2** (0.75 mmol), Ru-HT (50 mg, Ru content 0.918 wt%, Ru is less than 0.5 mg) and Cs_2CO_3 (0.25 mmol) in toluene (2 mL), at 140 °C of a preheated oil bath for 48 h in a 60 mL pressure tube under Ar. [b]Isolated yield.

Scheme 5.9. Scope of Ru-HT Catalysed BH *N*-Alkylation of Sulfonamides

5.3.5. Optimization of the reaction condition for the synthesis of quinazolin-4(3H)-ones:

Encouraged by the catalytic activity of the Ru-doped hydrotalcite, the scope to synthesize quinazolinones from 2- amino benzamides and alcohols (**Scheme 5.10**) was examined as this heterocyclic motif is known for their remarkable importance in pharmaceutical chemistry.[14, 15] Initially different reaction parameters were screened to accomplish the optimized reaction conditions for the synthesis of quinazolinone (**Table 5.3**). It is worth mentioning that only a catalytic amount (5 mol%) of KO^{t}Bu is sufficient to afford the desired quinazolin-4(3H)-ones in high yield. Next, the scope of different alcohols and differently substituted 2-amino benzamide was tested. Benzyl alcohols having various electron donating or withdrawing groups (**Scheme 5.10**, **entries 5.3.7a-7f**) in the aromatic ring afforded excellent yield of the corresponding products. Halogen groups are well-survived which creates further scope for functionalization of these scaffolds (**Scheme 5.10**, **entries 5.3.7k-7n**). Of note, challenging aliphatic alcohols also furnished a good yield (70-75%) of the corresponding quinazolinone derivatives (**Scheme 5.10**, entries **5.3.7h-7j**).

Table 5.3. Optimization of the reaction condition:

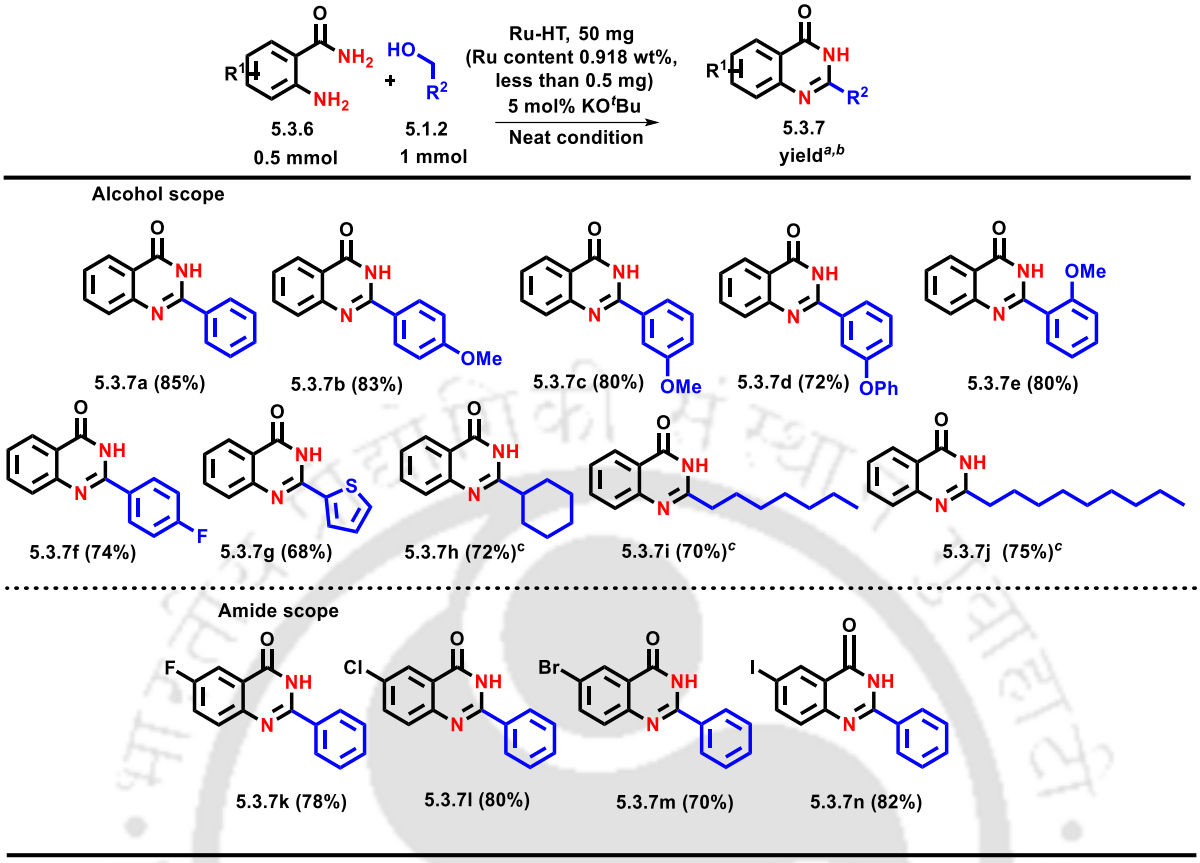


5.3.6a 5.1.2a 5.3.7a[a]

Entry	Catalyst (50 mg)	Solvent (2 mL)	Base (mmol)	Yield[b] (%)
1	Ru-HT	-	-	78
2	Ru-HT	Toluene	-	42
3[c]	Ru-HT	Toluene	-	60
4[d]	Ru-HT	Toluene	-	58
5	Ru-HT	-	KO^{t}Bu (0.5)	88
6	Ru-HT	Toluene	KO^{t}Bu (0.5)	64
7	**Ru-HT**	**-**	**KO^{t}Bu (0.05)**	**85**
8[e]	Ru-HT	-	KO^{t}Bu (0.05)	70
9	Ru-HT	Dioxane	KO^{t}Bu (0.5)	24
10	Ru-HT	Xylene	KO^{t}Bu (0.5)	32
11	$RuCl_3$	-	-	38
12	-	-	-	n.d
13	HT	-	-	8

[a]Standard reaction conditions: **5.1.2a** (1 mmol), **5.3.6a** (0.5 mmol), Ru-HT (50 mg, Ru content 0.918 wt%, less than 0.5 mg) and KO^{t}Bu (0.025 mmol) in neat condition, at 140 °C of a preheated oil bath 24 h in a 10 mL round bottom flusk under Ar. [b]Isolated yield. [c]Low catalyst loading (30 mg). [d]**5.3.6a** (0.5 mmol) and **5.1.2a** (0.5 mmol), [e]Low temperature (120 ^{o}C). n.d stands for not detected.

5.3.6. Substrate scope of Quinazolin-4(3H)-ones:

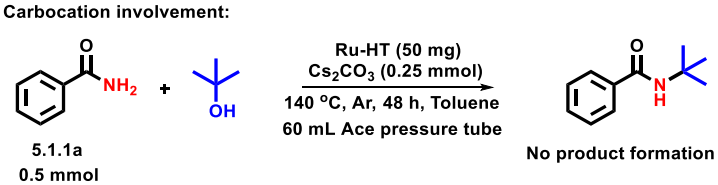


^{a} Standard reaction conditions: **5.3.6** (0.5 mmol), **5.1.2** (1.00 mmol), Ru-HT (50 mg, Ru content 0.918 wt%, Ru is less than 0.5 mg) and KO^{t}Bu (5 mol%) in neat condition at 140 °C of a preheated oil bath for 24 h in a schlenk tube under Ar, ^{b} Isolated yield, ^{c}36 h.

Scheme 5.10. Scope of Ru-HT Catalysed Quinazolin-4(3H)-ones

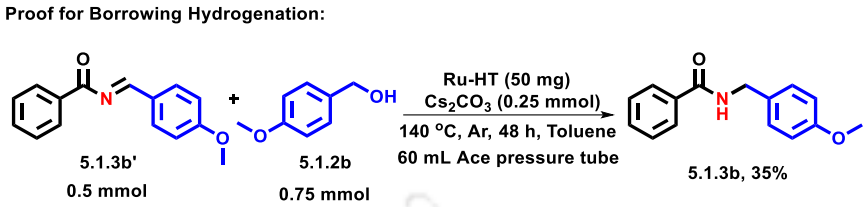
5.4. Mechanistic investigation:

In order to explore mechanistic details several control experiments were performed (**Scheme 5.7**). At first, tertiary alcohol was used in the reaction conditions to furnish the N-alkylated product. This confirms that the reaction does not proceed via carbocation formation (**Scheme 5.7.1**).



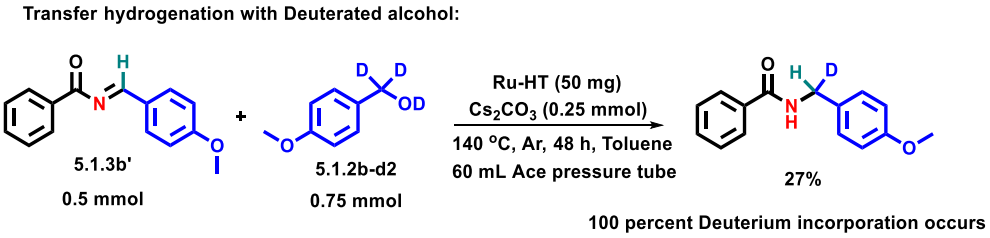
Scheme 5.7.1: Control experiment 1

To study whether the reaction is going via borrowing hydrogen pathway, N-acyl imine intermediate **5.1.3b′** was reacted with the benzyl alcohol **5.1.2b** (**Scheme 5.7.2**), which led to the formation of desired *N*-alkylated product **5.1.3b** (**Scheme 5.7.2**).



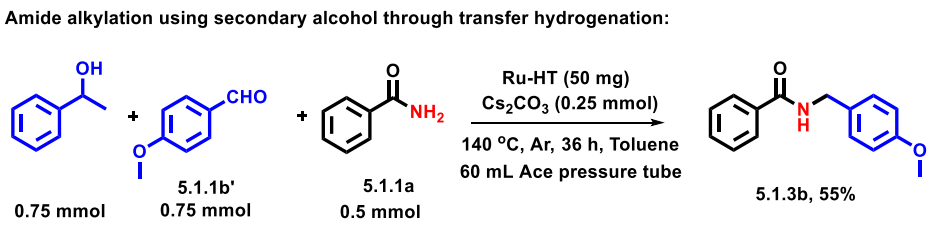
Scheme 5.7.2: Control experiment 2

Furthermore, when **5.1.3b′** was treated with deuterated benzyl alcohol (**5.1.2b-d2)** incorporation of deuterium to the desired product validates the involvement of borrowing hydrogen method (**Scheme 5.7.3**).



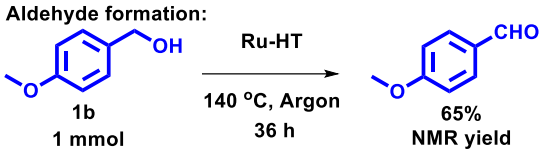
Scheme 5.7.3. Control experiment 3

The reaction of 4-methoxy benzaldehyde (**5.1.1b′)** with benzamide (**5.1.1a)** in the presence of 1-phenyl ethanol as a reductant under the reaction condition afforded the desired product (**5.1.3b)** in 55% yield in 36 h and which was further increased to 85% just by increasing reaction time to 60 h (**Scheme 5.7.4**). This further confirms the BH pathway. This study also reflects that the dehydrogenation of secondary alcohol is relatively slower than the primary alcohol and coupling amide with aldehyde is much easier than ketone (**Scheme 5.7.4**).



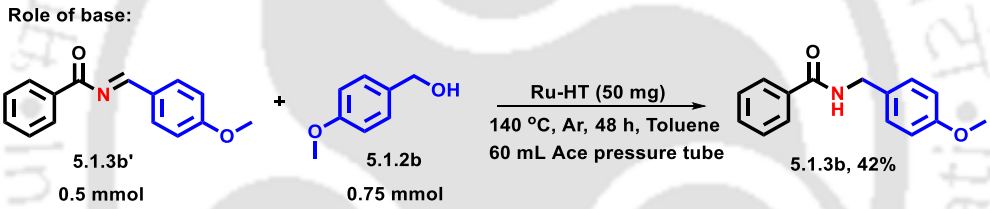
Scheme 5.7.4. Control experiment 4

Later, the dehydrogenative property of the catalyst was examined. Delightfully, the 4-methoxy benzaldehyde was formed in 65% yield even in the absence of a traditional inorganic base (**Scheme 5.7.5**).



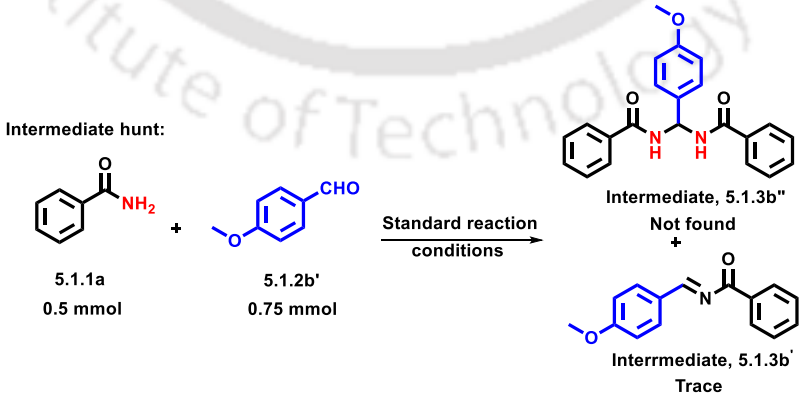
Scheme 5.7.5. Control experiment 5

It is worth mentioning that the hydrogenation of the N-acyl intermediate proceeds without Cs_2CO_3 (**Scheme 5.7.6**). However, the BH *N*-alkylation of amide failed to proceed without Cs_2CO_3 (**Table 5.1, entry 2**). This indicates that Cs_2CO_3 might help the aldehyde-amide coupling step.



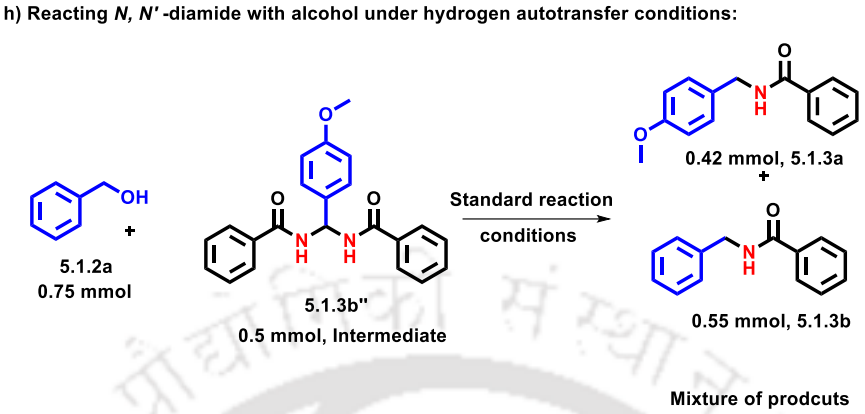
Scheme 5.7.6. Control experiment 6

Surprisingly, the reaction of 4-methoxy benzaldehyde and benzamide failed to furnish either N-acyl intermediate **5.1.3b′** or intermediate **5.1.3b′′** (**Scheme 5.7.7**).



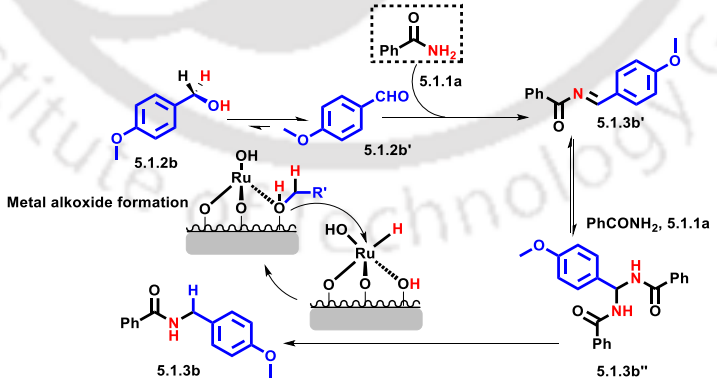
Scheme 5.7.7. Control experiment 7

However, intermediate **5.1.3b′′** under the standard condition in presence of benzyl alcohol gave *N*-alkylated product (**5.1.3a)** and (**5.1.3b)** (**Scheme 5.7.8**).



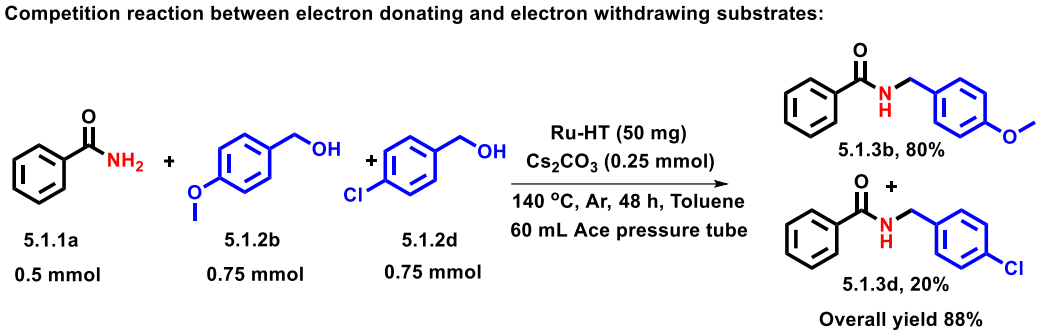
Scheme 5.7.8. Control experiment 8

This underpins that intermediate **5.1.3b′** and **5.1.3b′′** are in equilibrium under the reaction conditions and the failure to isolate the intermediates is probably related to their lower stability under the reaction conditions (**Scheme 5.7.8**). (**Scheme 5.8**) Thus, the slow generation of intermediate **5.1.3b′** and its quick hydrogenation to the corresponding stable *N*-alkylated product **5.1.3b** is the key factor in achieving the high yield. At first the basic site of the catalyst promotes the formation of metal alkoxide species. Later, β-hydride elimination leads to the formation of metal hydride species which promotes borrowing hydrogen mediated functionalization of amide.



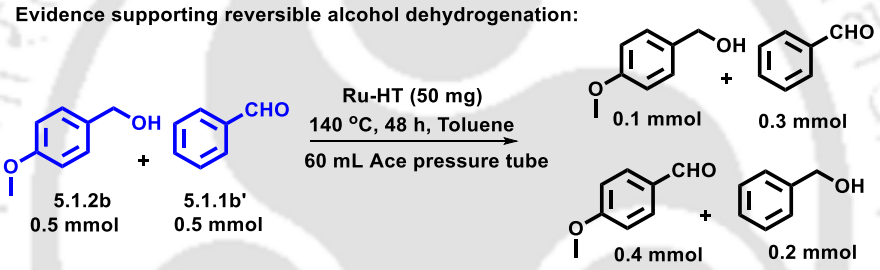
Scheme 5.8. Reaction mechanism for the synthesis of **5.1.3a**

A competition experiment between 4-chlorobenzyl alcohol (**5.1.3d**) and 4-methoxybenzyl alcohol (**5.1.3b**) was also performed and it was observed for an electron-rich substituent, amidation occurred at faster rates (**Scheme 5.7.9**).



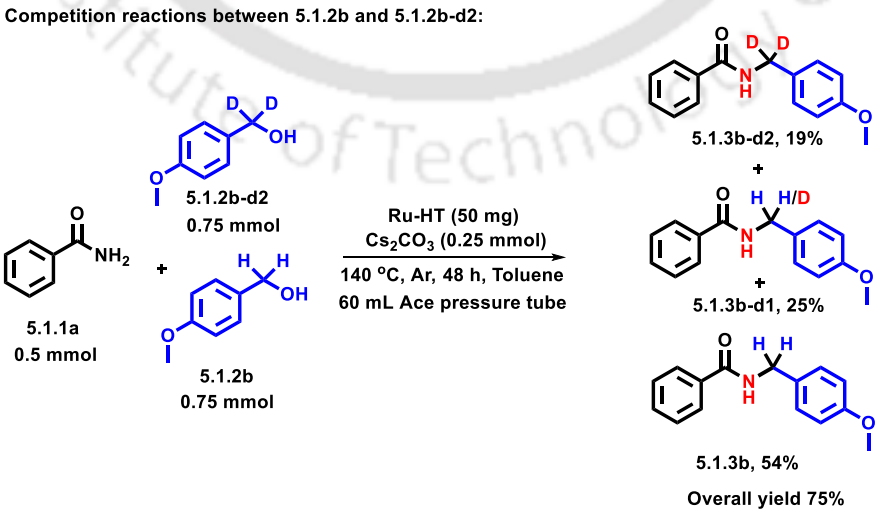
Scheme 5.7.9. Control experiment 9

The reversibility of the dehydrogenation of alcohol was also confirmed cross de(hydrogenative) reaction of 4-methoxybenzyl alcohol (**5.1.2b**) and benzaldehyde (**5.1.1b′**) (**Scheme 5.7.10**)

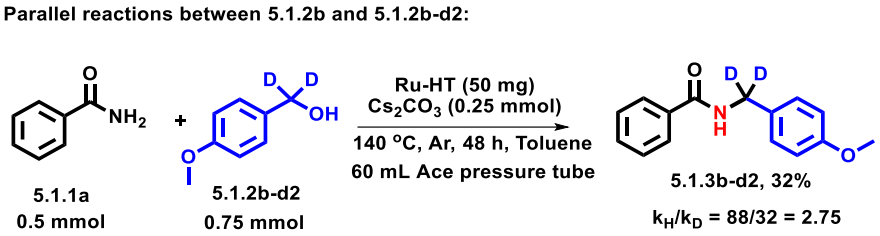


Scheme 5.7.10. Control experiment 10

In addition, an intermolecular competition reaction was performed, which showed the kinetic isotope effect **(Scheme 5.7.11** and **5.7.12**).

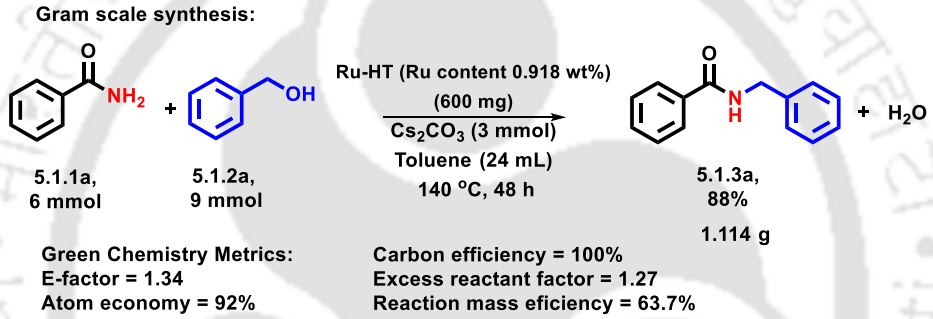


Scheme 5.7.11. Control experiment 11



Scheme 5.7.12. Control experiment 12

A gram scale synthesis was performed taking benzamide and benzyl alcohol as model substrates. The desired product was isolated in 88% yield which highlights the practical usefulness of our catalytic protocol. The green chemistry matrix has also been calculated. (**Scheme 5.7.13**)



Scheme 5.7.13. Green chemistry matrix calculation

The catalyst has been recycled after five times. But a gradual loss in yield has been observed after 3rd cycle. (**Figure 5.1**) ICP MS experiment has been carried out after the third cycle and leaching of Ru metal was observed. PXRD of the recovered catalyst was also performed. The support is almost intact. So, the Ru leaching could be the possible reason for the yield loss.

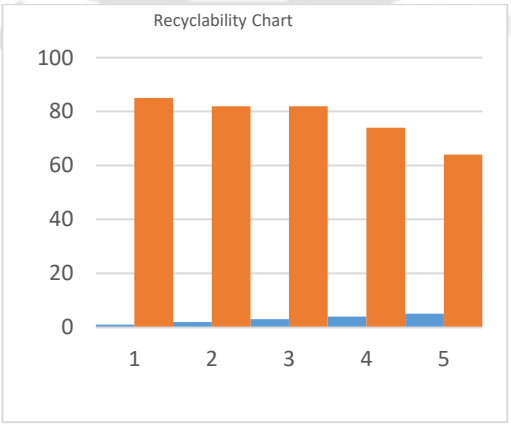


Figure 5.1 Recyclability test

To check the versatility of our protocol, next it was decided to investigate the possibility of BH *N*-alkylation of sulfonamides with alcohols,[10, 11, 12] as *N*-alkylated sulfonamide are highly important for their medicinal application.[13]

5.5. Kinetic profile:

Next, the kinetic profile of the reaction between 2-aminobenzamide (**5.3.6a**) and benzyl alcohol (**5.1.2a**) (**Figure 5.2**) was explored. The dehydrogenative oxidation of benzyl alcohol (**5.1.2a**) to benzaldehyde (**5.1.2b**) was found to be steady. A small uniform concentration of benzaldehyde and the intermediate, (**5.3.7a′**) was observed throughout the reaction. This indicates that the condensation of 2-aminobenzamide with the formed aldehyde and the conversion of intermediate (**5.3.7a′**) to quinazolinone (**5.3.7a)** is relatively faster compared to dehydrogenation of alcohols. This was further confirmed by studying the kinetic profile of the reaction of the aldehyde and 2-aminobenzamide. Within 6 h 84% of product, formation was observed. (**Figure 5.2 and 5.3**)

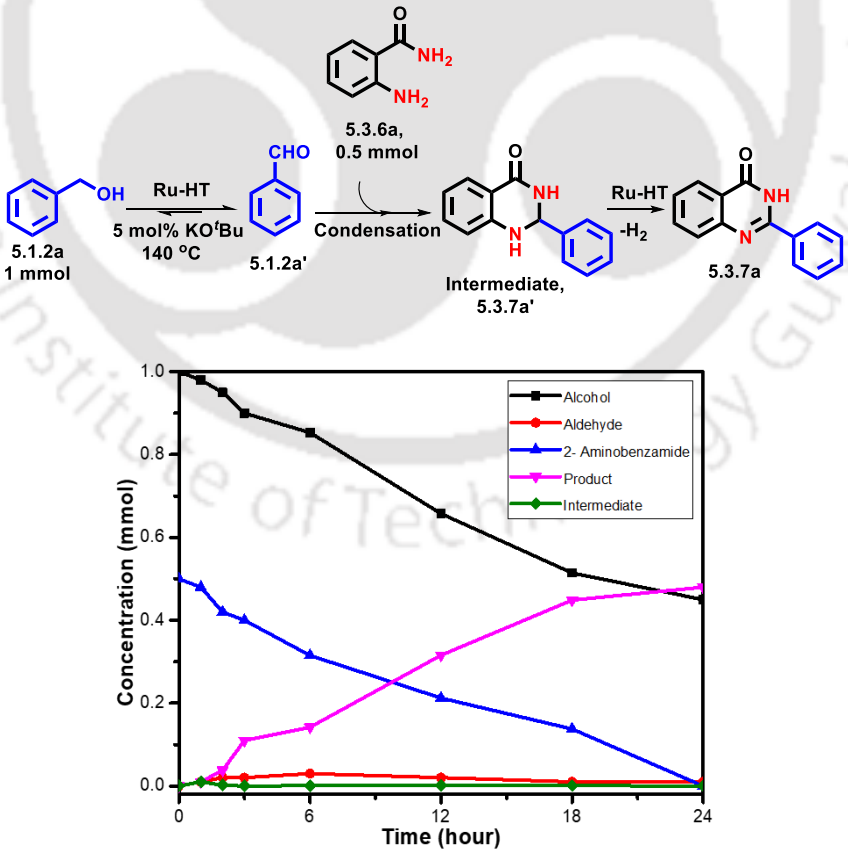
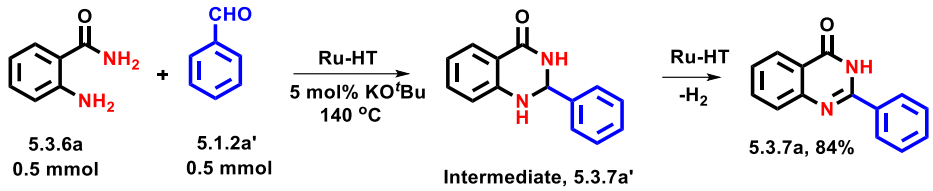


Figure 5.2. Time course of the reaction during the formation of 2-phenylquinazolin-4(3H)-one from 4-methoxybenzyl alcohol and 2-aminobenzamide.



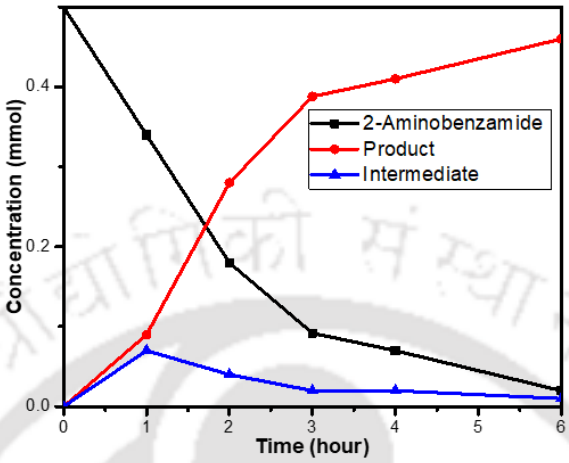


Figure 5.3. Time course of the reaction during the formation of 2-phenylquinazolin-4(3H)-one from benzaldehyde and 2-aminobenzamide.

5.6. Conclusion:

In conclusion, an efficient Ru-HT-catalyzed BH *N*-alkylation of various carboxamide with a diverse range of alcohols has been developed. Mechanistic studies were performed to understand the reaction pathway. This indicates the reaction proceeds via the BH pathway rather than the involvement of the carbocation intermediate. Of note, for the dehydrogenation of alcohol and hydrogenation of N-acyl intermediate, Cs_2CO_3 is not required, which underpins the assistance of Cs_2CO_3 in the condensation step of amide and aldehyde. The protocol was further extended to alkylate sulfonamides. Moreover, dehydrogenative condensation 2-amino benzamides with various primary alcohols to achieve quinazolinone was demonstrated. Successful recyclability, easy scalability, and calculated green chemistry metrics highlight the practical applicability of the current protocol.

5.7. Experimental Section:

5.7.1. General Information: All catalytic experiments were carried out using standard Schlenk techniques and pressure tubes according to their respective condition. All solvents were dried using standard procedure. Deuterated solvents were used as received without any

additional purification. Most of the chemicals used in catalysis reactions were purified according to standard procedure (or by vacuum distillation/sublimation). Thin layer chromatography (TLC) on silica-gel 60 F254 plates (from Merck Company) and SRL silica gel (100-200 mesh) for column chromatography was used. NMR (400 and 600 MHz) spectra were recorded on the BRUKER NMR spectrometer. Deuterated chloroform was used as the solvent, and chemical shift values (δ) are reported in parts per million relatives to the residual signals of this solvent [δ 7.26 for 1 H ($CDCl_3$), δ 77.16 for ^{13}C {^1H} ($CDCl_3$). Abbreviations used in the NMR follow-up experiments: br, broad; s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. Q-Tof ESIMS instrument (model HAB 273) was used for recording mass spectra. Powder X-ray diffraction analysis was carried out on Rigaku using a Cu source with Kα =1.5406 Å with a 9 kW power. The samples were scanned in a 2θ range from 10° to 90° with a scan rate of 20° per minute. The morphology of the material and energy-dispersive X-ray elemental mapping were analyzed with field emission transmission electron microscopy using a JEOL (JEM 2100F) instrument with an operating voltage of 200 kV. Inductively coupled plasma atomic emission spectroscopy (ICP-AES) was acquired for the elemental analysis of Ru content within the sample by SPECTRO analytical instruments GmbH, model ARCOS simultaneous ICP spectrometer. X-ray Photoelectron spectroscopy analysis was done on an X-ray photoelectron spectrometer, Thermo Fisher Scientific, UK (ESCALAB Xi^+) using Au4f as a reference.

5.7.2. Experimental procedures:

5.7.2a. Synthesis of Ru-doped hydrotalcite (Ru-HT): Commercially available hydrotalcite (HT) was used for the preparation of Ru-doped hydrotalcite. First, 475 mg hydrotalcite was slowly added to 100 mL of aqueous $RuCl_3.nH_2O$ (52 mg) solution with stirring. The resulting suspension was then tailored to pH~13 by dropwise addition of NaOH (1 M), which was then vigorously stirred, at room temperature for 24 h. The suspension was then centrifuged and washed three times with deionized water and three times with ethanol consecutively. The solid sample obtained was dried at 60 °C overnight. Then, it was ground to a fine powder to perform a catalytic reaction.

5.7.2b. General procedure for Ru-HT catalysed amidation of alcohols: To an oven-dried Ace pressure tube (60 mL), Ru-HT (50 mg), Cs_2CO_3 (0.25 mmol, 1.0 equiv, 81 mg), alcohol (0.75 mmol, 3.0 equiv, 81 mg)) and benzamide (0.5 mmol, 2.0 equiv, 61 mg) were added,

followed by toluene (2 mL, 18.82 mmol, 75 equiv) under an atmosphere of Ar. The reaction mixture was then heated at 140 °C with stirring for 48 h. After cooling, EtOAc (5 mL) was added and the catalyst was separated by filtration whereas the filtrate was transferred into another flask. The filtrate was then evaporated and the crude product was purified by column chromatography (typically using EtOAc/Hexane = 20/80) using silica to afford a pure product (**Scheme 5.6**).

5.7.2c General procedure for Ru-HT catalysed amidation of alcohols: To an oven-dried Ace schlenk tube (60 mL), Ru-HT (50 mg), Cs_2CO_3 (0.25 mmol, 1.0 equiv, 81 mg), alcohol (0.75 mmol, 3.0 equiv, 81 mg) and sulfonamide (0.5 mmol, 2.0 equiv, 85.5 mg) were added, followed by toluene (2 mL, 18.82 mmol, 75 equiv) under an atmosphere of Ar. The reaction mixture was then heated at 140 °C with stirring for 48 h. After cooling, EtOAc (5 mL) was added and the catalyst was separated by filtration whereas the filtrate was transferred into another flask. The filtrate was then evaporated and the crude product was purified by column chromatography (typically using EtOAc/Hexane = 25/75) using silica to afford a pure product (**Scheme 5.9**)

5.7.2d. General procedure for Ru-HT catalysed quinazolin -3(3H)-one preparation: To an oven-dried Schlenk tube (60 mL), Ru-HT (50 mg), KO^{t}Bu (0.025 mmol, 3 mg), alcohol (1 mmol, 40 equiv, 54 mg) and 2-amino benzamide (0.5 mmol, 20 equiv, 68 mg) were added under an atmosphere of Ar. The reaction mixture was then heated at 140 °C with stirring for 24 h. After cooling, EtOAc (5 mL) was added and the catalyst was separated by filtration whereas the filtrate was transferred into another flask. The filtrate was then evaporated and the crude product was purified by column chromatography (typically using EtOAc/Hexane = 25/75) using silica to afford a pure product (**Scheme 5.10**).

5.7.3. Mechanistic Studies:

Control Experiment 1:

To an oven-dried Ace pressure tube (60 mL), Ru-HT (50 mg), Cs_2CO_3 (0.25 mmol), alcohol (0.75 mmol), and benzamide (0.5 mmol) were added, followed by toluene (2 mL) under an atmosphere of Ar (**Scheme 5.7.1**). The reaction mixture was then heated at 140 °C with stirring for 48 h. After cooling, EtOAc (5 mL) was added and the catalyst was separated by filtration

whereas the filtrate was transferred into another flask. The filtrate was then analyzed through TLC, which confirmed that no product formation had taken place.

Control Experiment 2 & 3:

To an oven-dried Ace pressure tube (60 mL), Ru-HT (50 mg), Cs_2CO_3 (0.25 mmol), 4-methoxybenzyl alcohol, **5.1.2b** (0.75 mmol) or, deuterated 4-methoxybenzyl alcohol, **5.1.2b-d2** and acylimine, **5.1.3b'** (0.5 mmol) were added, followed by toluene (2 mL) under an atmosphere of Ar.

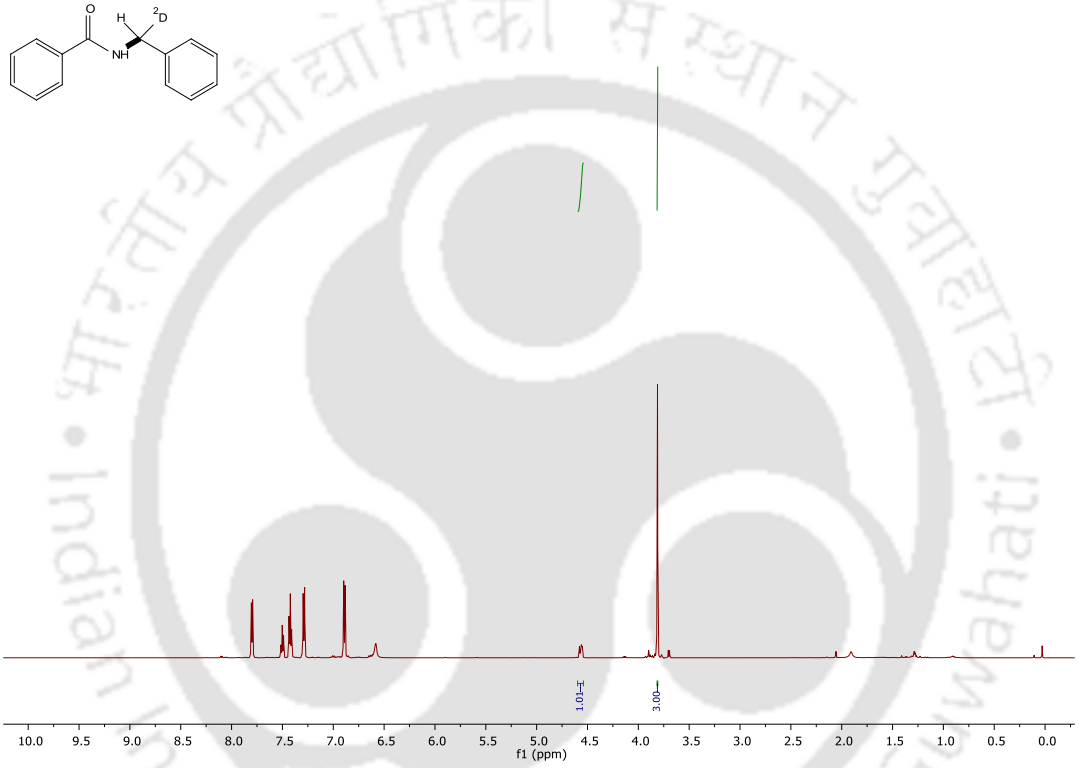


Figure 5.4: ^1H spectra of **5.1.3b** and **5.1.3b-D** in $CDCl_3$ in 600 MHz

The reaction mixture was then heated at 140 °C with stirring for 48 h. After cooling, EtOAc (5 mL) was added and the catalyst was separated by filtration whereas the filtrate was transferred into another flask. The filtrate was then evaporated and the crude product was purified by column chromatography (typically using EtOAc/Hexane = 20/80) using silica to afford pure product **3b** and **3b-d** in **35%** and **27%** yield respectively (**Scheme 5.7.2 and 5.7.3**).

Control Experiment 4:

To an oven-dried Ace pressure tube (60 mL), Ru-HT (50 mg), Cs_2CO_3 (0.25 mmol), 4-methoxy benzaldehyde, **5.1.1b'** (0.75 mmol), 1-phenyl ethanol and benzamide, **5.1.1a** (0.5 mmol) were

added, followed by toluene under an atmosphere under Ar (**Scheme 5.7.4**). The reaction mixture was then heated at 140 °C with stirring for 48 h. After cooling, EtOAc (5 mL) was added and the catalyst was separated by filtration whereas the filtrate was transferred into another flask. The filtrate was then evaporated and the crude product was purified by column chromatography (typically using EtOAc/Hexane = 20/80) using silica to afford the pure product, **5.1.3b** in 55% yield.

Control Experiment 5: Reference Alcohol to aldehyde (Scheme 5.7.6)[9i]

Control Experiment 6:

To an oven-dried Ace pressure tube (60 mL), Ru-HT (50 mg), 4-methoxybenzyl alcohol**, 5.1.2b** (0.75 mmol), and acylimine**, 5.1.3b'** (0.5 mmol) were added, followed by toluene (2 mL) under an atmosphere of Ar (**Scheme 5.7.5**). The reaction mixture was then heated at 140 °C with stirring for 48 h. After cooling, EtOAc (5 mL) was added and the catalyst was separated by filtration whereas the filtrate was transferred into another flask. The filtrate was then evaporated and the crude product was purified by column chromatography (typically using EtOAc/Hexane = 20/80) using silica to afford pure product **5.1.3b** in **42%** yield exclusively.

Control Experiment 7:

To an oven-dried Ace pressure tube (60 mL), Ru-HT (50 mg), 4-methoxybenzaldehyde, **5.1.2b**' (0.75 mmol), and benzamide, **5.1.1a** (0.5 mmol) were added, followed by toluene (2 mL) under an atmosphere of Ar (**Scheme 5.7.7**). The reaction mixture was then heated at 140 °C with stirring for 48 h. After cooling, EtOAc (5 mL) was added and the catalyst was separated by filtration whereas the filtrate was transferred into another flask. The filtrate was then evaporated and a NMR of the crude mixture was recorded.

Control Experiment 8:

Intermediate **3b"** was separately synthesised according to the literature procedure. To an oven-dried Ace pressure tube (60 mL), Ru-HT (50 mg), 4-methoxybenzyl alcohol, **2b** (0.75 mmol) and intermediate, **3b**" (0.5 mmol) were added, followed by toluene (2 mL) under an atmosphere of Ar (**Scheme 5.7.8**). The reaction mixture was then heated at 140 °C with stirring for 48 h. After cooling, EtOAc (5 mL) was added and the catalyst was separated by filtration whereas the filtrate was transferred into another flask. The filtrate was then evaporated and the crude

product was purified by column chromatography (typically using EtOAc/Hexane = 20/80) using silica to afford pure product **3a** and **3b** in **45%** and **55%** yield respectively.

Control Experiment 9:

To an oven-dried Ace pressure tube (60 mL), Ru-HT (50 mg), Cs_2CO_3 (0.25 mmol), 4-methoxybenzyl alcohol, **2b** (0.75 mmol), and 4-chlorobenzyl alcohol, **2d** (0.75 mmol), benzamide, **1a** (0.5 mmol) were added, followed by toluene (2 mL) under an atmosphere of Ar. The reaction mixture was then heated at 140 °C with stirring for 48 h (**Scheme 5.7.9**). After cooling, EtOAc (5 mL) was added and the catalyst was separated by filtration whereas the filtrate was transferred into another flask. The filtrate was then evaporated and the crude product was purified by column chromatography (typically using EtOAc/Hexane = 20/80) using silica to afford pure product **3b** and **3d** in **80%** and **20%** yield respectively.

Control Experiment 10:

To an oven-dried Ace pressure tube (60 mL), Ru-HT (50 mg), Cs_2CO_3 (0.25 mmol), 4-methoxybenzyl alcohol, **5.1.2b** (0.5 mmol), benzaldehyde, **1b'** (0.5 mmol) were added, followed by toluene under an atmosphere of Ar (**Scheme 5.7.10**). The reaction mixture was then heated at 140 °C with stirring for 48 h. After cooling, EtOAc (5 mL) was added and the catalyst was separated by filtration whereas the filtrate was transferred into another flask. The filtrate was then evaporated and a NMR of the crude mixture was recorded.

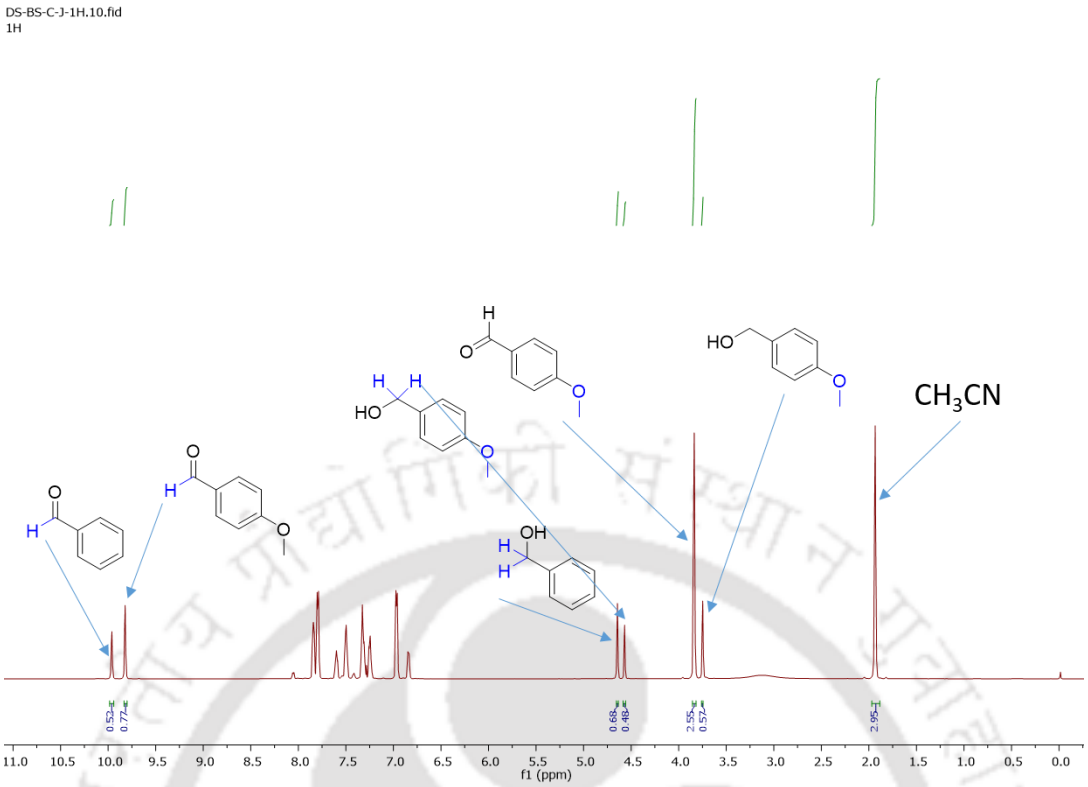


Figure 5.5. ^{1}H spectra of crossover experiment with respect CH_3CN as an internal standard

Control Experiment 11 & 12:

To an oven-dried Ace pressure tube (60 mL), Ru-HT (50 mg), Cs_2CO_3 (0.25 mmol), 4-methoxybenzyl alcohol, **5.1.2b** (0.75 mmol) or, deuterated 4-methoxybenzyl alcohol, **5.1.2b-d2** and benzamide, **5.1.1a** (0.5 mmol) were added, followed by toluene (2 mL) under an atmosphere of Ar (**Scheme 5.7.11**). The reaction mixture was then heated at 140 °C with stirring for 48 h. After cooling, EtOAc (5 mL) was added and the catalyst was separated by filtration whereas the filtrate was transferred into another flask. The filtrate was then evaporated and a NMR of the crude mixture was recorded, which yields **5.1.3b-d2**, **5.1.3b-d1** and **5.1.3b** in **19%**, **25%** and **54%** yield respectively.

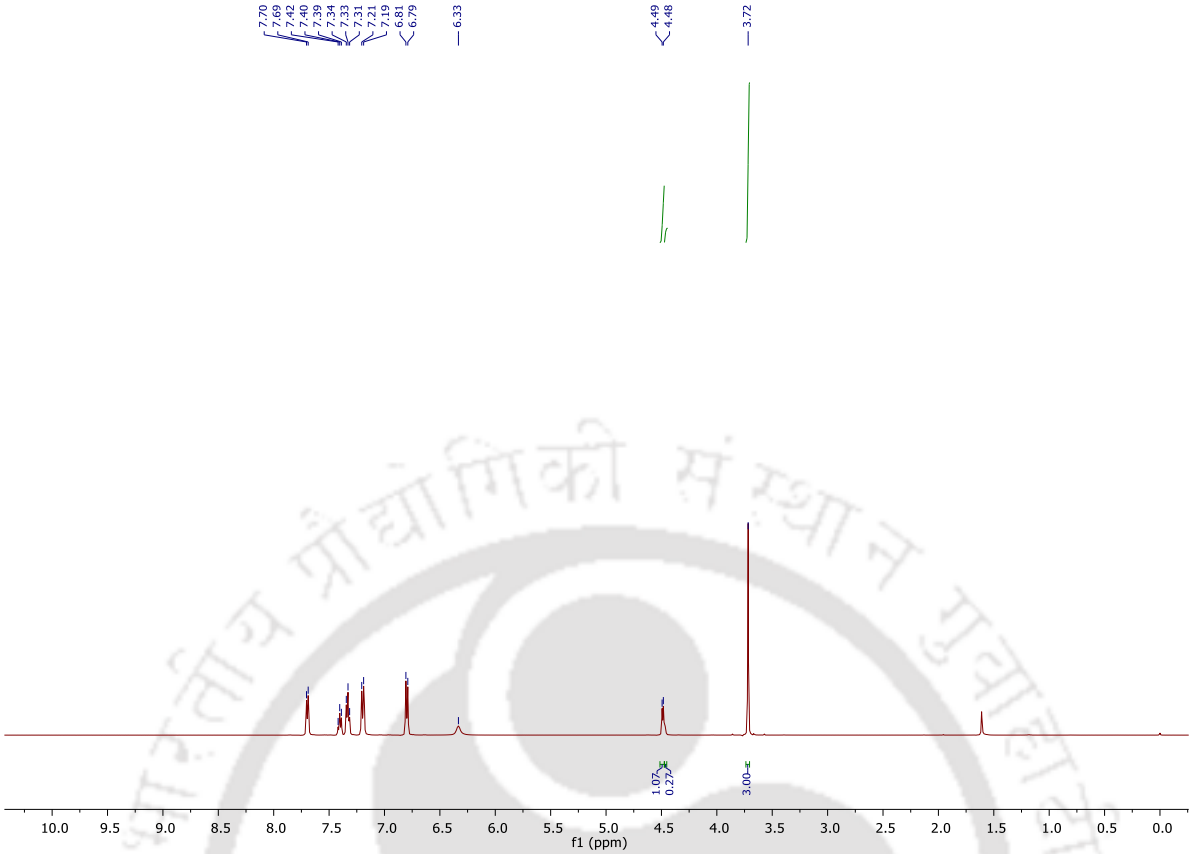


Figure 5.6. ^{1}H spectra of competition reaction between **2b** and **2b-d2**

Parallel reaction: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, *J* = 7.6 Hz, 2H), 7.40 (t, *J* = 7.3 Hz, 1H), 7.32 (t, *J* = 7.5 Hz, 1H), 7.19 (d, *J* = 8.7 Hz, 1H), 6.79 (d, *J* = 8.6 Hz, 1H), 6.37 (s, 1H), 3.71 (s, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 167.30, 159.17, 134.52, 131.47, 130.24, 129.30, 128.56, 126.96, 114.19, 55.32, 43.64-43.04 (m, deuterium splitting)

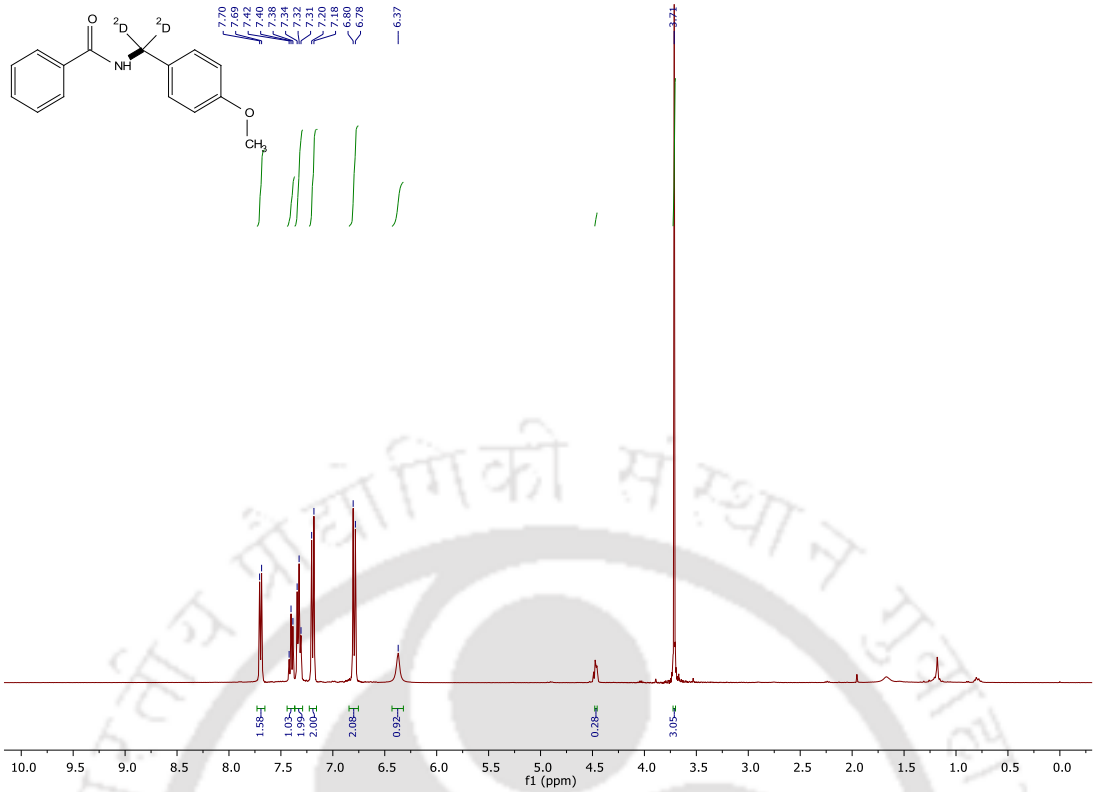


Figure 5.7. ^{1}H (400 MHz) NMR spectra of **5.1.3b-d2** in $CDCl_3$ (400 MHz)

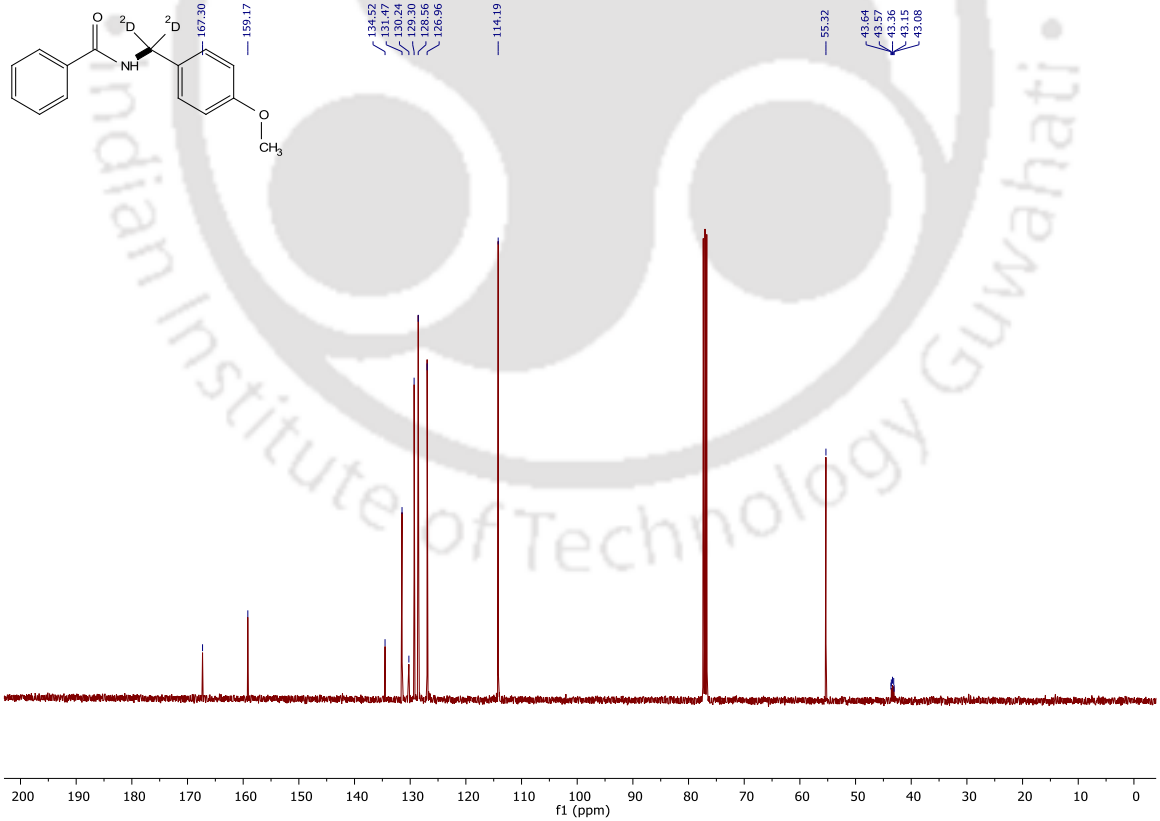
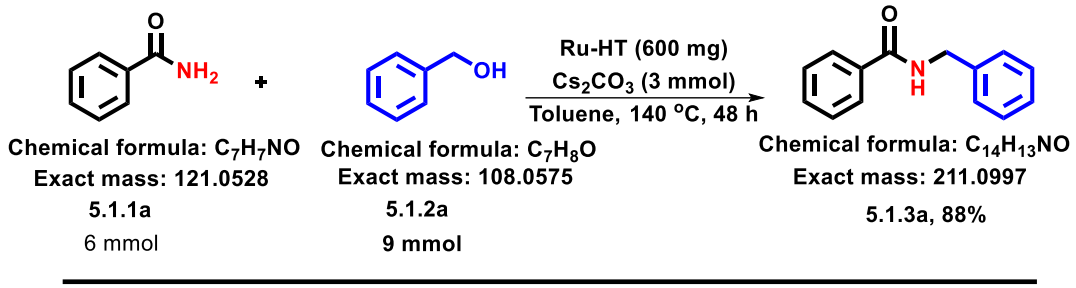


Figure 5.8. $^{13}C\{^{1}H\}$(100 MHz) NMR spectra of **5.1.3b-d2** in $CDCl_3$ (400 MHz)

5.7.4. Green chemistry matrix calculation:



1a 726.3168 mg **2a** 972.5175 mg Recycle **Toluene** **3a** 1.114 g

Cs_2CO_3 977.46 mg

Total weight: 2,676.2943 mg

1. E factor = (2.6 g - 1.11 g) / 1.11 g = 1.34 kg waste per 1 kg of product

2. Atom economy = [211.0997 / (121.0528 + 108.0575)] = 92%

3. Atom efficiency = 88 x (92 / 100) = 80.96%

4. Carbon efficiency = (14 / 14) x 100 = 100%

5. Reaction mass efficiency = [1.114 / (.726 + .972)] x 100 = 65.6%

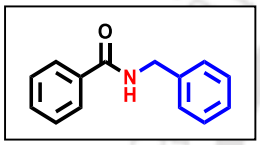
5.7.5. Gram Scale synthesis: To an oven-dried Ace pressure tube (60 mL), Ru-HT (600 mg), benzyl alcohol (9 mmol), benzamide (6 mmol), and Cs_2CO_3 (3 mmol) were added followed by 10 mL of toluene under an atmosphere of Ar. The reaction mixture was heated at 140 °C with stirring for 36 hours. The reaction mixture was allowed to cool to room temperature. After cooling, EtOAc (50 mL) was added and the catalyst was separated by filtration whereas the filtrate was transferred into another flask. The filtrate was then evaporated and the crude product was purified by column chromatography (typically using EtOAc/Hexane = 50/50) using silica to afford the 70% isolated yield (1.190 gm) of the desired product. While the separated catalyst was then washed with ethanol (2 x 20 mL) and stored.

5.7.6. Reusability of the catalyst: To an oven-dried Ace pressure tube (60 mL), Ru-HT (50 mg, Ru content 0.918 wt%), Cs_2CO_3 (0.25 mmol), alcohol (0.75 mmol) and benzamide (0.5 mmol) were added, followed by toluene (2 mL) under an atmosphere of Ar. The reaction mixture was then heated at 140 °C with stirring for 48 h. After cooling, EtOAc (5 mL) was added and the catalyst was separated by centrifugation whereas the filtrate was transferred into

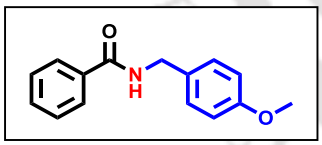
another flask. While the separated catalyst was then washed with deionized water (2 x 5 mL) and ethanol (2 x 5 mL), dried, and used again for consecutive runs. The transferred solvent was evaporated from the reaction mixture and the crude mixture was subjected to silica gel column chromatography. It was established that no deactivation of the material was observed up to three cycles (**Figure 5.1**) and a slight decrease in yield was observed in 4th and 5th cycle. All of the yields are isolated yields.

5.8. Spectroscopic data of the newly synthesized compounds in the present study:

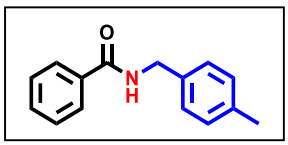
N-Benzylbenzamide (5.1.3a). The title compound was isolated as a white solid using silica-gel column chromatography eluting with ethyl acetate/hexane (1:4), (93 mg, Yield: 88%); R_f = 0.35, ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.79 (d, *J* = 7.1 Hz, 2H), 7.51 (t, *J* = 6.9 Hz, 1H), 7.43 (t, *J* = 7.7 Hz, 2H), 7.33-7.27 (m, 5H), 6.49 (brs, 1H), 4.61 (d, *J* = 5.8 Hz, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 168.3, 137.6, 135.0, 134.3, 132.5, 130.0, 129.7, 129.5, 127.7, 44.2.[8d]



N-(4-Methoxybenzyl)benzamide (5.1.3b). The title compound was isolated as a white solid using silica-gel column chromatography eluting with ethyl acetate/hexane (1:3), (105 mg, Yield: 87%); R_f = 0.30, ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.80 (d, *J* = 7.0 Hz, 2H), 7.50 (t, *J* = 7.4 Hz, 1H), 7.42 (t, *J* = 7.7 Hz, 2H), 7.28 (d, *J* = 8.6 Hz, 2H), 6.88 (d, *J* = 8.6 Hz, 2H), 6.67 (brs, 1H), 4.56 (d, *J* = 5.6 Hz, 2H), 3.81 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 168.1, 159.8, 135.2, 132.3, 131.1, 130.1, 129.3, 127.8, 114.9, 56.1, 44.3.[8d]

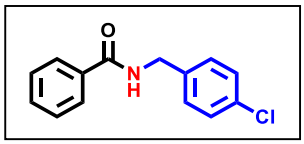


N-(4-methylbenzyl)benzamide (5.1.3c). The title compound was isolated as a white solid using silica-gel column chromatography eluting with ethyl acetate/hexane (1:3), (91 mg, Yield: 81%); R_f = 0.35, ^{1}H NMR (400 MHz, $CDCl_3$), 7.77 (d, *J* = 7.1 Hz, 2H), 7.48 (t, *J* = 7.4 Hz, 1H), 7.40 (t, *J* = 7.4 Hz, 2H), 7.23 (d, *J* = 8.0 Hz, 2H), 7.15 (d, *J* = 7.9 Hz, 2H), 6.52 (brs, 1H), 4.58 (d, *J* = 5.6 Hz, 2H), 2.34 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 168.1, 138.2, 135.9, 135.2, 132.3, 130.2, 129.4, 128.7, 127.7, 44.7, 21.9.[8d]

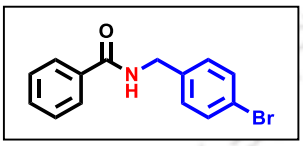


N-(4-Chlorobenzyl)benzamide (5.1.3d). The title compound was isolated as a white solid using silica-gel column chromatography eluting with ethyl acetate/hexane (1:4), (104 mg, Yield:

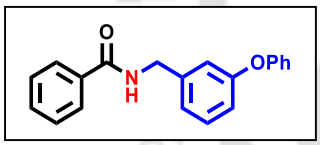
85%); R_f = 0.30, ^{1}H NMR (400 MHz, $CDCl_3$), 7.79 (d, *J* = 7.0 Hz, 2H), 7.49 (d, *J* = 7.4 Hz, 1H), 7.43 (t, *J* = 7.4 Hz, 2H), 7.36 (d, *J* = 4.4 Hz, 3H), 7.33-7.29 (m, 1H), 6.44 (brs, 1H), 4.65 (d, *J* = 5.6 Hz, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 168.2, 139.0, 135.2, 132.4, 129.6, 129.5, 128.7, 128.5, 127.7, 44.9.[8d]



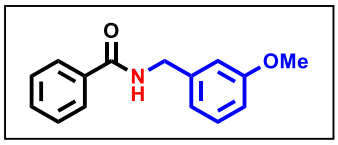
N-(4-Bromobenzyl)benzamide (5.1.3e). The title compound was isolated as a white solid using silica-gel column chromatography eluting with ethyl acetate/hexane (1:4), (111 mg, Yield: 77%); R_f = 0.35, ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.80 (d, *J* = 7.7 Hz, 2H), 7.53 (t, *J* = 7.4 Hz, 1H), 7.48-7.44 (m, 4H), 7.23 (d, *J* = 8.0 Hz, 2H), 6.66 (brs, 1H), 4.60 (d, *J* = 5.9 Hz, 2H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 167.5, 137.3, 134.1, 131.8, 131.7, 129.5, 128.6, 127.0, 121.5, 43.4.[8c]



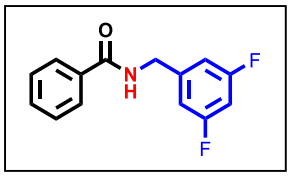
N-(3-Phenoxybenzyl)benzamide (5.1.3h). The title compound was isolated as a white solid using silica-gel column chromatography eluting with ethyl acetate/hexane (1:4), (131 mg, Yield: 87%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 7.0 Hz, 2H), 7.53-7.49 (m, 1H), 7.45-7.41 (m, 2H), 7.36-7.28 (m, 3H), 7.13-7.08 (m, 2H), 7.02-7.00 (m, 3H), 6.91 (dd, *J* = 8.2, 1.8 Hz, 1H), 6.48 (brs, 1H), 4.63 (d, *J* = 5.8 Hz, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 168.2, 158.6, 157.7, 141.1, 135.1, 132.5, 130.9, 130.6, 129.5, 127.8, 124.3, 123.3, 119.9, 118.8, 118.5, 44.6.[16e]



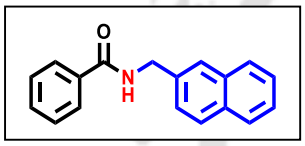
N-(3-Methoxybenzyl)benzamide (5.1.3i). The title compound was isolated as a white crystal using silica-gel column chromatography eluting with ethyl acetate/hexane (1:3), (92 mg, Yield: 76%); R_f = 0.35, ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.81 (d, *J* = 7.3 Hz, 2H), 7.51 (t, *J* = 7.3 Hz, 1H), 7.43 (t, *J* = 7.6 Hz, 2H), 7.28 (t, *J* = 7.9 Hz, 1H), 6.94 (d, *J* = 7.5 Hz, 1H), 6.90 (s, 1H), 6.85 (d, *J* = 8.2 Hz, 1H), 6.66 (brs, 1H), 4.62 (d, *J* = 5.6 Hz, 2H), 3.80 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 168.2, 160.6, 140.6, 135.1, 132.30, 130.6, 129.3, 127.8, 120.9, 114.2, 113.7, 56.0, 44.8.[8c]



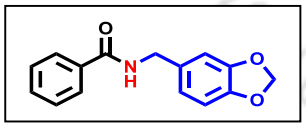
N-(3,5-Difluorobenzyl)benzamide(5.1.3j). The title compound was isolated as a white solid using silica-gel column chromatography eluting with ethyl acetate/hexane (1:3), (66 mg, Yield: 54%); R_f = 0.30, ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.82 (d, *J* = 8.4 Hz, 2H), 7.54 (t, *J* = 7.4 Hz, 1H), 7.45 (t, *J* = 7.7 Hz, 2H), 6.86 (d, *J* = 6.2 Hz, 2H), 6.72 (t, *J* = 8.9 Hz, 1H), 4.61 (d, *J* = 6.0 Hz, 2H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 167.6, 164.1 (d_{C-F}, *J* = 12.7 Hz), 162.4 (d_{C-F}, *J* = 12.7 Hz), 142.41 (t_{C-F}, *J* = 8.8 Hz), 133.8, 131.8, 128.7, 127.0, 110.31 (dd_{C-F}, *J* = 20.1, 5.2 Hz), 103.0, 102.89 (t_{C-F}, *J* = 25.2 Hz), 43.1. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{14}H_{11}F_2NO$ 248.0887; Found 248.0886.



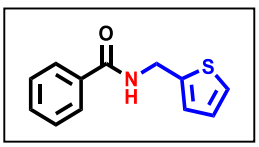
N-(Naphthalen-2-ylmethyl)benzamide (5.1.3k). The title compound was isolated as a white solid using silica-gel column chromatography eluting with ethyl acetate/hexane (1:4), (83.62 mg, Yield: 64%); R_f = 0.40, ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.87 – 7.81 (m, 5H), 7.79 (s, 1H), 7.54 – 7.47 (m, 4H), 7.45 (t, *J* = 7.7 Hz, 2H), 6.66 (brs, 1H), 4.81 (d, *J* = 5.7 Hz, 2H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 167.5, 135.7, 134.3, 133.4, 132.8, 131.6, 128.6, 127.7, 127.7, 127.0, 126.5, 126.3, 126.0, 126.0, 44.2.[8c]



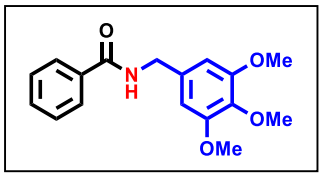
N-(Benzo[d][1,3]dioxol-5-ylmethyl)benzamide (5.1.3l). The title compound was isolated as a white solid using silica-gel column chromatography eluting with ethyl acetate/hexane (1:4), (87 mg, Yield: 68%); R_f = 0.35, ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.80 (d, *J* = 7.0 Hz, 2H), 7.52 (t, *J* = 7.4 Hz, 1H), 7.44 (t, *J* = 7.6 Hz, 2H), 6.86 (s, 1H), 6.83 – 6.78 (m, 2H), 6.51 (brs, 1H), 5.97 (s, 2H), 4.55 (d, *J* = 5.6 Hz, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 168.1, 148.8, 147.9, 135.2, 132.8, 132.4, 129.4, 127.8, 122.1, 109.3, 109.2, 101.9, 44.8.[16a]



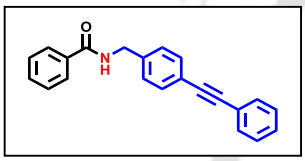
N-(Thiophen-2-ylmethyl)benzamide (5.1.3m). The title compound was isolated as a white crystal using silica-gel column chromatography eluting with ethyl acetate/hexane (1:4), (58 mg, Yield: 53%); R_f = 0.25. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.81 (d, J = 7.4 Hz, 2H), 7.57 – 7.49 (m, 1H), 7.45 (dd, J = 8.4, 6.9 Hz, 2H), 7.30 – 7.20 (m, 1H), 7.07 (d, J = 3.4 Hz, 1H), 7.00 (dd, J = 5.2, 3.4 Hz, 1H), 6.50 (s, 1H), 4.84 (d, J = 5.5 Hz, 2H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 167.1, 140.7, 134.1, 131.6, 128.6, 127.0, 126.2, 125.4, 38.8.[8b]



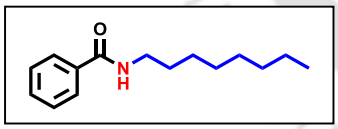
N-(3,4,5-Trimethoxybenzyl)benzamide (5.1.3n): The title compound was isolated as a colorless liquid using silica-gel column chromatography eluting with ethyl acetate/hexane (1:5), (114 mg, Yield: 76%); R_f = 0.35, ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.74 (d, *J* = 7.5 Hz, 2H), 7.39 (d, *J* = 6.9 Hz, 1H), 7.31 (t, *J* = 6.8 Hz, 2H), 6.87 (s, 1H), 6.44 (s, 2H), 4.44 (d, *J* = 4.3 Hz, 2H), 3.70 (s, 9H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 167.5, 153.3, 137.1, 134.3, 134.1, 131.5, 128.5, 127.0, 104.8, 60.8, 56.0, 44.3.[8d]



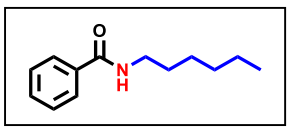
N-(4-(Phenylethynyl)benzyl)benzamide (5.1.3o): The title compound was isolated as a white crystal using silica-gel column chromatography eluting with ethyl acetate/hexane (1:5), (60 mg, Yield: 38%); R_f = 0.35, ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80 (d, *J* = 7.3 Hz, 2H), 7.52 (q, *J* = 5.6, 4.2 Hz, 5H), 7.44 (t, *J* = 7.5 Hz, 2H), 7.34 (d, *J* = 7.1 Hz, 5H), 6.42 (s, 1H), 4.67 (d, *J* = 5.8 Hz, 2H), ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 167.4, 138.4, 134.3, 132.0, 131.6, 131.6, 128.6, 128.3, 128.3, 127.8, 126.9, 123.2, 122.6, 89.6, 89.0, 43.8. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{22}H_{17}NO$ 312.1388; Found 312.1383.



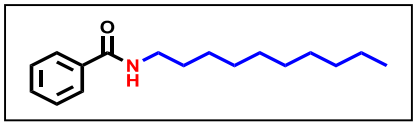
N-Octylbenzamide (5.1.3p). The title compound was isolated as a colourless liquid using silica-gel column chromatography eluting with ethyl acetate/hexane (1:5), (87 mg, Yield: 80%); R_f = 0.40 ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.5 Hz, 2H), 7.50 (t, *J* = 7.4 Hz, 1H), 7.44 (t, *J* = 7.3 Hz, 2H), 6.24 (brs, 1H), 3.46 (q, *J* = 6.5 Hz, 2H), 1.63 (p, *J* = 7.1 Hz, 2H), 1.39 – 1.29 (m, 10H), 0.90 (t, *J* = 6.9 Hz, 3H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 168.4, 135.6, 132.1, 129.3, 127.6, 40.9, 32.6, 30.5, 30.1, 30.0, 27.8, 23.5, 14.9.[16b]



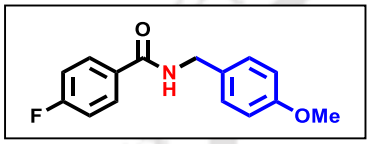
N-Hexylbenzamide (5.1.3q). The title compound was isolated as a yellow solid using silica-gel column chromatography eluting with ethyl acetate/hexane (1:5), (45.16 mg, Yield: 44%); R_f = 0.40, ^{1}H NMR (400 MHz,$CDCl_3$) δ 7.69 (d, *J* = 7.3 Hz, 2H), 7.41 (t, *J* = 7.2 Hz, 1H), 7.34 (t, *J* = 7.4 Hz, 2H), 6.19 (brs, 1H), 3.37 (q, *J* = 7.0 Hz, 2H), 1.52 (p, *J* = 7.2 Hz, 2H), 1.32 – 1.18 (m, 6H), 0.82 (t, *J* = 6.8 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 168.4, 135.7, 132.1, 129.3, 127.7, 41.0, 32.3, 30.5, 27.5, 23.4, 14.8.[16c]



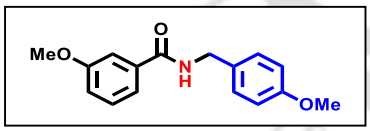
N-Decylbenzamide (5.1.3r): The title compound was isolated as a white crystal using silica-gel column chromatography eluting with ethyl acetate/hexane (1:5), (43 mg, Yield: 33%); R_f = 0.40, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 7.2 Hz, 2H), 7.48 (t, *J* = 7.3 Hz, 1H), 7.42 (t, *J* = 7.4 Hz, 2H), 6.19 (brs, 1H), 3.44 (q, *J* = 7.0 Hz, 2H), 1.61 (p, *J* = 7.2 Hz, 2H), 1.39 – 1.25 (m, 14H), 0.88 (t, *J* = 6.8 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 168.3, 135.7, 132.1, 129.3, 127.6, 40.9, 32.7, 30.5, 30.3, 30.2, 30.1, 27.8, 23.5, 14.9.[8d]



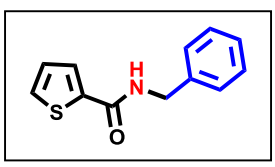
***4-Fluoro-N-(4-methoxybenzyl)benzamide (5.1.3s)*:** The title compound was isolated as a white crystal using silica-gel column chromatography eluting with ethyl acetate/hexane (1:3), (75 mg, Yield: 58%); R_f = 0.30, ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78 (dd, *J* = 8.7, 5.3 Hz, 2H), 7.27 (d, *J* = 8.9 Hz, 2H), 7.08 (t, *J* = 8.6 Hz, 2H), 6.88 (d, *J* = 8.6 Hz, 2H), 6.33 (brs, 1H), 4.55 (d, *J* = 5.5 Hz, 2H), 3.80 (s, 3H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 167.0, 166.4, 164.7, 160.0, 131.4, (d, *J* = 3.3 Hz), 130.9, 130.2, 130.1 (d_{C-F}, *J* = 8.9 Hz), 116.5 (d_{C-F}, *J* = 21.7 Hz). 115.0, 56.2, 44.5.[16d]



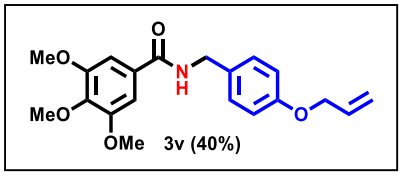
3-Methoxy-N-(4-methoxybenzyl)benzamide (5.1.3t): The title compound was isolated as a white crystal using silica-gel column chromatography eluting with ethyl acetate/hexane (1:3), (118 mg, Yield: 87%); R_f = 0.35, ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.40 (s, 1H), 7.35 – 7.29 (m, 4H), 7.05 (dt, *J* = 8.1, 1.7 Hz, 1H), 6.91 (d, *J* = 8.5 Hz, 2H), 6.38 (brs, 1H), 4.59 (d, *J* = 5.5 Hz, 2H), 3.86 (s, 3H), 3.83 (s, 3H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 167.1, 160.6, 159.9, 136.7, 130.1, 130.4, 130.2, 119.4, 118.5, 115.0, 113.1, 56.3, 56.2, 44.5.[16d]



N-Benzylthiophene-2-carboxamide (5.1.3u): The title compound was isolated as a white crystal using silica-gel column chromatography eluting with ethyl acetate/hexane (1:4), (89 mg, Yield: 82%); R_f = 0.35, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (d, *J* = 3.5 Hz, 1H), 7.47 (d, *J* = 4.9 Hz, 1H), 7.35 (d, *J* = 4.1 Hz, 4H), 7.33 – 7.28 (m, 1H), 7.06 (t, *J* = 4.2 Hz, 1H), 6.37 (brs, 1H), 4.61 (d, *J* = 5.7 Hz, 2H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 162.6, 139.6, 138.9, 130.8, 129.6, 129.0, 128.7, 128.5, 128.3, 44.9.[8b]

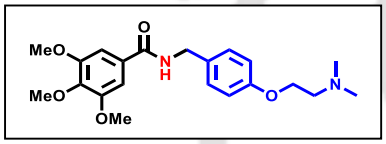


3,4,5-Trimethoxy-N-(4-(vinyloxy)benzyl)benzamide (5.1.3v): The title compound was isolated as a white crystal using silica-gel column chromatography eluting with ethyl acetate/hexane (1:2), (68 mg, Yield: 40%); R_f = 0.15, ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27 (d, *J* = 7.6 Hz, 2H), 7.01 (s, 2H), 6.90 (d, *J* = 7.7 Hz, 2H), 6.36 (brs, 1H), 6.05 – 6.04 (dt, m, 1H), 5.41 (d, J = 17.2 Hz, 1H), 5.28 (d, *J* = 10.5 Hz, 1H), 4.57 – 4.53 (m, 4H), 3.88 (s, 9H). δ ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 167.0, 158.2, 153.2, 141.1, 133.2, 130.5, 129.3, 117.7, 115.0, 107.5, 104.6, 68.9, 60.8, 56.4, 43.8.[8d]

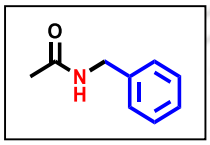


3v (40%)

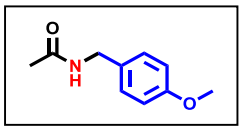
N-(4-(2-(Dimethylamino)ethoxy)benzyl)-3,4,5-trimethoxybenzamide (5.1.3w): The title compound was isolated as a white solid using silica-gel column chromatography eluting with ethyl acetate/methanol (99:1), (87 mg, Yield: 45%); R_f = 0.20, ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.29 (d, *J* = 8.3 Hz, 2H), 7.03 (s, 2H), 6.92 (d, *J* = 8.5 Hz, 2H), 6.41 (s, 1H), 4.57 (d, *J* = 5.5 Hz, 2H), 4.08 (t, *J* = 5.6 Hz, 2H), 3.90 (s, 6H), 3.88 (s, 3H), 2.76 (t, *J* = 5.6 Hz, 2H), 2.36 (s, 6H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 166.9, 158.3, 153.2, 140.9, 130.3, 129.8, 129.3, 114.8, 104.4, 65.9, 60.9, 58.2, 56.3, 45.8, 43.7.[8d]



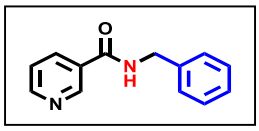
N-Benzylacetamide (5.1.3x): The title compound was isolated as a white crystal using silica-gel column chromatography eluting with ethyl acetate/hexane (1:3), (20 mg, Yield: 28%); R_f = 0.35, ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.33 (t, *J* = 7.3 Hz, 2H), 7.28 (t, *J* = 7.4 Hz, 3H), 6.22 (brs, 1H), 4.40 (d, *J* = 5.7 Hz, 2H), 2.00 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 170.2, 138.2, 128.7, 127.8, 127.5, 43.7, 23.2.[8d]



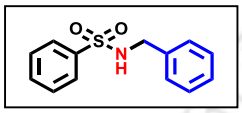
N-(4-Methoxybenzyl)acetamide (5.1.3y): The title compound was isolated as a white crystal using silica-gel column chromatography eluting with ethyl acetate/hexane (1:3), (28 mg, Yield: 32%) R_f = 0.35, ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.19 (d, *J* = 8.6 Hz, 2H), 6.85 (d, *J* = 8.6 Hz, 2H), 6.02 (s, 1H), 4.32 (d, *J* = 5.6 Hz, 2H), 3.78 (s, 3H), 1.97 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 170.0, 159.0, 130.4, 129.2, 114.05, 55.3, 43.1, 23.2.[8d]



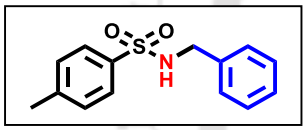
N-Benzylnicotinamide (5.1.3z): The title compound was isolated as a white solid using silica-gel column chromatography eluting with ethyl acetate/hexane (6:4), (21 mg, Yield: 20%), R_f = 0.25, ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.93 (s, 1H), 8.61 (d, *J* = 4.6 Hz, 1H), 8.12 (d, *J* = 7.9 Hz, 1H), 7.32 (t, *J* = 6.0 Hz, 4H), 7.27 (d, *J* = 4.8 Hz, 2H), 4.61 (d, *J* = 5.7 Hz, 2H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 165.6, 152.0, 147.9, 137.9, 135.3, 130.1, 128.7, 127.9, 127.6, 123.5, 44.1.[8d]



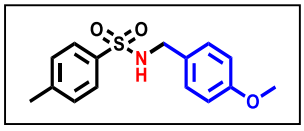
N-Benzylbenzenesulfonamide (5.2.5a): The title compound was isolated as a white crystal using silica-gel column chromatography eluting with ethyl acetate/hexane (3:7), (105 mg, Yield: 85%); R_f = 0.35, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 7.6 Hz, 2H), 7.55 (d, *J* = 7.3 Hz, 1H), 7.48 (t, *J* = 7.6 Hz, 2H), 7.25-7.23 (m, 3H), 7.18 – 7.16 (m, 2H), 5.06 (s, 1H), 4.13 (d, *J* = 6.2 Hz, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 139.9, 136.2, 132.6, 129.1, 128.6, 127.9, 127.8, 127.1, 47.2.[10f]



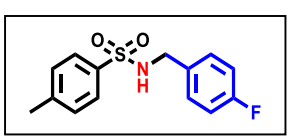
N-Benzyl-4-methylbenzenesulfonamide (5.2.5b): The title compound was isolated as a white crystal using silica-gel column chromatography eluting with ethyl acetate/hexane (3:7), (118 mg, Yield: 91%); R_f = 0.35 ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.3 Hz, 2H), 7.30 – 7.24 (m, 5H), 7.20 – 7.18 (m, 2H), 4.78 (t, *J* = 5.7 Hz, 1H), 4.11 (d, *J* = 6.2 Hz, 2H), 2.43 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 143.6, 137.1, 136.4, 129.8, 128.8, 128.0, 128.0, 127.3, 47.4, 21.6.[10f]



N-(4-Methoxybenzyl)-4-methylbenzenesulfonamide (5.2.5c): The title compound was isolated as a white crystal using silica-gel column chromatography eluting with ethyl acetate/hexane (3:7), R_f = 0.35, (132 mg, Yield: 91%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.2 Hz, 2H), 7.30 (d, *J* = 8.2 Hz, 2H), 7.10 (d, *J* = 8.5 Hz, 2H), 6.79 (d, *J* = 8.6 Hz, 2H), 4.66 (t, *J* = 5.7 Hz, 1H), 4.05 (d, *J* = 6.1 Hz, 2H), 3.77 (s, 3H), 2.43 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 159.5, 143.5, 137.2, 129.8, 129.4, 128.5, 127.3, 114.2, 55.4, 46.9, 21.6.[10f]

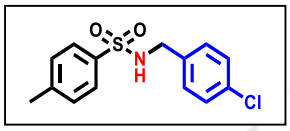


N-(4-Fluorobenzyl)-4-methylbenzenesulfonamide (5.2.5d): The title compound was isolated as a white crystal using silica-gel column chromatography eluting with ethyl acetate/hexane (4:6), (98 mg, Yield: 70%); R_f = 0.35, ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.3 Hz, 2H), 7.32 (d, *J* = 8.2 Hz, 2H), 7.19 (dd, *J* = 8.4, 5.4 Hz, 2H), 6.97 (t, *J* = 8.6 Hz, 2H), 4.94 (t, *J* = 5.6 Hz, 1H), 4.10 (d, *J* =

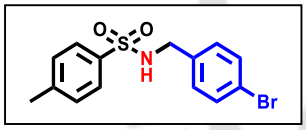


6.3 Hz, 2H), 2.46 (s, 3H). $^{13}C\{^{1}H\}$ NMR (150 MHz, $CDCl_3$) δ 163.2, 161.5, 143.6, 136.8, 132.1 (d, J_{C-F} = 3.2 Hz), 129.8, 129.6 (d, J = 8.2 Hz), 129.6, 127.2, 115.6, 115.5 (d, J_{C-F} = 21.6 Hz), 46.5, 21.5. [17a]

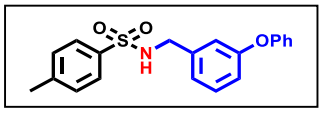
N-(4-Chlorobenzyl)-4-methylbenzenesulfonamide (5.2.5e): The title compound was isolated as a white crystal using silica-gel column chromatography eluting with ethyl acetate/hexane (4:6), (101 mg, Yield: 68%); R_f = 0.35, ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72 (d, J = 8.2 Hz, 2H), 7.29 (d, J = 7.8 Hz, 2H), 7.23 (d, J = 8.4 Hz, 2H), 7.13 (d, J = 8.3 Hz, 2H), 4.89 (t, J = 6.0 Hz, 1H), 4.08 (d, J = 6.3 Hz, 2H), 2.43 (s, 3H). $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 143.6, 136.8, 134.9, 133.7, 129.7, 129.2, 128.8, 127.1, 46.5, 21.5.[17a]



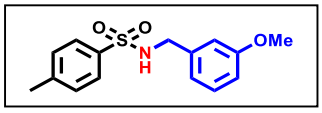
N-(4-Bromobenzyl)-4-methylbenzenesulfonamide (5.2.5f): The title compound was isolated as a white crystal using silica-gel column chromatography eluting with ethyl acetate/hexane (4:6), (122 mg, Yield: 72%); R_f = 0.35, ^{1}H NMR (400 MHz,$CDCl_3$) δ 7.74 (d, J = 8.3 Hz, 2H), 7.40 (d, J = 8.4 Hz, 2H), 7.31 (d, J = 8.0 Hz, 2H), 7.08 (d, J = 8.4 Hz, 2H), 4.67 (t, J = 5.8 Hz, 1H), 4.08 (d, J = 6.3 Hz, 2H), 2.45 (s, 3H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 143.7, 136.7, 135.3, 131.8, 129.8, 129.5, 127.1, 121.9, 46.6, 21.5.[17a]



4-Methyl-N-(3-phenoxybenzyl)benzenesulfonamide (5.2.5g): The title compound was isolated as a white crystal using silica-gel column chromatography eluting with ethyl acetate/hexane (3:7), (129 mg, Yield: 73%); R_f = 0.35, ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.76 (d, J = 8.3 Hz, 2H), 7.36 (t, J = 8.0 Hz, 2H), 7.31 (d, J = 8.0 Hz, 2H), 7.26 (t, J = 7.9 Hz, 1H), 7.14 (t, J = 7.4 Hz, 1H), 6.97 (d, J = 7.9 Hz, 3H), 6.91 (dd, J = 8.3, 2.4 Hz, 1H), 6.83 (s, 1H), 4.75 (t, J = 6.3 Hz, 1H), 4.12 (d, J = 6.2 Hz, 2H), 2.45 (s, 3H). $^{13}C\{^{1}H\}$ NMR (150 MHz, $CDCl_3$) δ 157.5, 156.8, 143.6, 138.3, 136.8, 130.0, 129.8, 129.7, 127.1, 123.5, 122.5, 118.9, 118.1, 118.0, 46.9, 21.5. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for 354.1164; Found 354.1160.

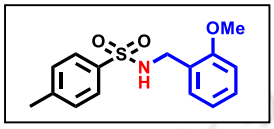


N-(3-Methoxybenzyl)-4-methylbenzenesulfonamide (5.2.5h): The title compound was isolated as a white crystal using silica-gel column chromatography eluting with ethyl acetate/hexane (3:7), (109 mg, Yield: 75%); R_f = 0.35, ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.78 (d, J = 8.0 Hz, 2H), 7.33

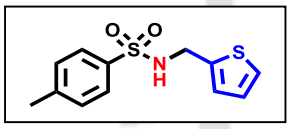


(d, *J* = 7.9 Hz, 2H), 7.21 (t, *J* = 7.9 Hz, 1H), 6.85 – 6.77 (m, 2H), 6.75 (d, *J* = 2.1 Hz, 1H), 4.69 (t, *J* = 6.3 Hz, 1H), 4.12 (d, *J* = 5.6 Hz, 2H), 3.77 (s, 3H), 2.46 (s, 3H). $^{13}C\{^{1}H\}$ NMR (150 MHz, $CDCl_3$) δ 159.8, 143.5, 137.9, 136.8, 129.7, 127.1, 120.0, 113.6, 113.1, 55.2, 47.2, 21.5.[17a]

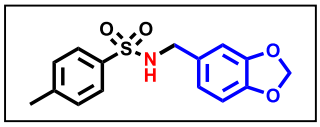
N-(2-Methoxybenzyl)-4-methylbenzenesulfonamide (5.2.5i): The title compound was isolated as a white crystal using silica-gel column chromatography eluting with ethyl acetate/hexane (3:7), (104 mg, Yield: 72%); R_f = 0.35, ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.68 (d, *J* = 8.3 Hz, 2H), 7.21 (d, *J* = 7.9 Hz, 3H), 7.08 (dd, *J* = 7.4, 1.7 Hz, 1H), 6.81 (t, *J* = 7.4 Hz, 1H), 6.74 (d, *J* = 8.2 Hz, 1H), 5.27 (s, 1H), 4.15 (d, *J* = 6.3 Hz, 2H), 3.74 (s, 3H), 2.40 (s, 3H). $^{13}C\{^{1}H\}$ NMR (150 MHz, $CDCl_3$) δ 157.2, 143.0, 137.2, 129.7, 129.4, 129.2, 127.0, 124.3, 120.5, 55.1, 43.9, 21.5.[17d]



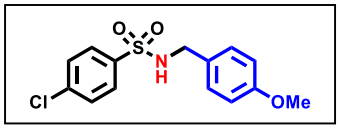
4-Methyl-N-(thiophen-2-ylmethyl)benzenesulfonamide (5.2.5j): The title compound was isolated as a white crystal using silica-gel column chromatography eluting with ethyl acetate/hexane (3:7), (113 mg, Yield: 85%); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.2 Hz, 2H), 7.33 (d, *J* = 7.9 Hz, 2H), 7.22 (dd, *J* = 5.0, 1.3 Hz, 1H), 6.90 (t, *J* = 6.5 Hz, 1H), 6.87 (d, *J* = 2.5 Hz, 1H), 4.84 (t, *J* = 6.1 Hz, 1H), 4.35 (d, *J* = 6.1 Hz, 2H), 2.46 (s, 3H). $^{13}C\{^{1}H\}$ NMR (150 MHz, $CDCl_3$) δ 143.7, 138.9, 136.7, 129.8, 127.2, 126.9, 126.5, 125.8, 42.1, 21.6.[17b]



N-(Benzo[d][1,3]dioxol-5-ylmethyl)-4-methylbenzenesulfonamide (5.2.5k): The title compound was isolated as a white crystal using silica-gel column chromatography eluting with ethyl acetate/hexane (3:7), (102 mg, Yield: 67%); R_f = 0.35, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 8.3 Hz, 2H), 7.30 (d, *J* = 8.1 Hz, 2H), 6.69 – 6.62 (m, 3H), 5.91 (s, 2H), 4.80 (t, *J* = 5.9 Hz, 1H), 4.01 (d, *J* = 6.2 Hz, 2H), 2.43 (s, 3H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 147.9, 147.3, 143.5, 136.9, 130.1, 129.7, 127.2, 121.4, 108.5, 108.2, 101.1, 47.1, 21.5.[17c]

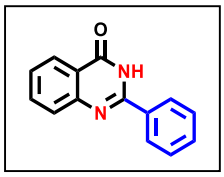


4-Chloro-N-(4-methoxybenzyl)benzenesulfonamide (5.2.5l): The title compound was isolated as a white crystal using silica-gel column chromatography eluting with ethyl acetate/hexane (3:7), (99 mg, Yield: 64%); R_f = 0.35, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.6 Hz, 2H), 7.44 (d, *J* = 8.6 Hz, 2H), 7.07 (d, *J* = 8.6 Hz, 2H), 6.77 (d, *J* = 8.6 Hz, 2H), 4.98 (s, 1H), 4.06 (d, *J* = 6.0

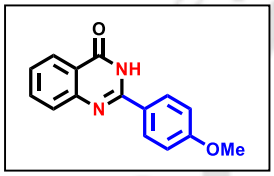


Hz, 2H), 3.76 (s, 3H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 159.4, 139.0, 138.6, 129.3, 129.3, 128.5, 127.9, 114.1, 55.3, 46.8.[17d]

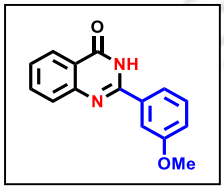
2-Phenylquinazolin-4(3H)-one (5.3.7a): The title compound was isolated as a white powder using silica-gel column chromatography eluting with ethyl acetate/hexane (2:8), (94 mg, Yield: 85%); R_f = 0.40, ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.94 (s, 1H), 8.33 (d, *J* = 7.9 Hz, 1H), 8.20 (dd, *J* = 6.7, 2.9 Hz, 2H), 7.85 – 7.79 (m, 2H), 7.60 – 7.58 (m, 3H), 7.51(t, *J* = 7.32 Hz, 1H). $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 163.6, 151.6, 149.5, 134.8, 132.8, 131.6, 129.1, 128.0, 127.3, 126.8, 126.4, 120.9.[15f]

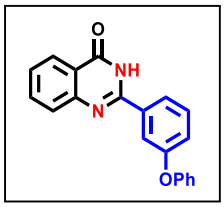


2-(4-Methoxyphenyl)quinazolin-4(3H)-one(5.3.7b): The title compound was isolated as a white powder using silica-gel column chromatography eluting with ethyl acetate/hexane (2:8), (104 mg, Yield: 83%); R_f = 0.35, ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.38 (s, 1H), 8.20 (d, *J* = 8.8 Hz, 2H), 8.14 (d, *J* = 7.9 Hz, 1H), 7.82 (t, *J* = 7.6 Hz, 1H), 7.71 (d, *J* = 8.1 Hz, 1H), 7.49 (t, *J* = 7.5 Hz, 1H), 7.10 (d, *J* = 8.2 Hz, 2H), 3.86 (s, 3H). $^{13}C\{^{1}H\}$ NMR (150 MHz, DMSO-d_6) δ 162.7, 162.3, 152.3, 149.39, 135.0, 129.9, 127.7, 126.6, 126.3, 125.2, 121.1, 114.4, 55.9.[15f]



2-(3-Methoxyphenyl)quinazolin-4(3H)-one (5.3.7c): The title compound was isolated as a white powder using silica-gel column chromatography eluting with ethyl acetate/hexane (2:8), (100 mg, Yield: 80%); R_f = 0.35, ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.45 (s, 1H), 8.16 (d, *J* = 7.5 Hz, 1H), 7.84 (t, *J* = 7.6 Hz, 1H), 7.80 (d, *J* = 7.8 Hz, 1H), 7.76 – 7.74 (m, 2H), 7.53 (t, *J* = 7.4 Hz, 1H), 7.46 (t, *J* = 8.0 Hz, 1H), 7.15 (dd, *J* = 8.2, 2.2 Hz, 1H), 3.87 (s, 3H). $^{13}C\{^{1}H\}$ NMR (100 MHz, DMSO) δ 162.8, 159.8, 152.6, 149.1, 135.0, 134.6, 130.2, 127.9, 127.0, 126.3, 121.4, 120.6, 118.0, 113.0, 55.8.[15f]

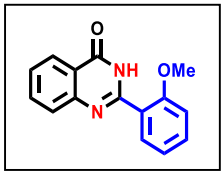




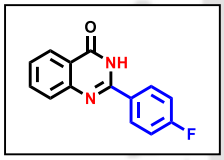
2-(3-Phenoxyphenyl)quinazolin-4(3H)-one (5.3.7d): The title compound was isolated as a white powder using silica-gel column chromatography eluting with ethyl acetate/hexane (2:8), (113 mg, Yield: 72%); R_f = 0.35, ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.59 (s, 1H), 8.20 (d, *J* = 7.9 Hz, 1H), 8.02 (d, *J* = 7.8 Hz, 1H), 7.91 – 7.86 (m, 2H), 7.77 (d, *J* = 8.1 Hz, 1H), 7.60 (dt, *J* = 21.2, 8.0 Hz, 2H), 7.49 (t, *J* = 8.0 Hz, 2H), 7.29 – 7.27 (m, 1H), 7.24 (t, *J* = 7.4 Hz, 1H), 7.14 (d, *J* = 8.5 Hz,

2H). $^{13}C\{^{1}H\}$ NMR (150 MHz, DMSO) δ 162.6, 157.3, 156.8, 152.0, 149.0, 135.1, 130.8, 130.6, 128.0, 127.2, 126.3, 124.2, 123.3, 122.1, 121.5, 119.3, 118.3.[18a]

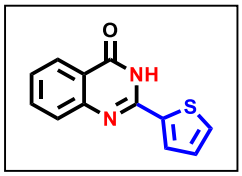
2-(2-Methoxyphenyl)quinazolin-4(3H)-one (5.3.7e): The title compound was isolated as a white powder using silica-gel column chromatography eluting with ethyl acetate/hexane (2:8), (100 mg, Yield: 80%); R_f = 0.40, ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.10 (s, 1H), 8.16 (d, *J* = 7.9 Hz, 1H), 7.83 (t, *J* = 7.6 Hz, 1H), 7.72 (t, *J* = 7.2 Hz, 2H), 7.54 (q, *J* = 7.7, 7.1 Hz, 2H), 7.20 (d, *J* = 8.4 Hz, 1H), 7.11 (d, *J* = 7.5 Hz, 1H), 3.87 (s, 3H). $^{13}C\{^{1}H\}$ NMR (150 MHz, DMSO) δ 161.6, 157.6, 152.7, 149.5, 134.8, 132.7, 130.9, 127.8, 127.0 126.2, 123.1, 121.5, 120.9, 112.4, 56.3.[18b]



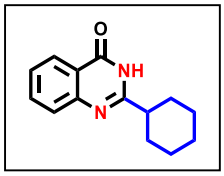
***2-(4-Fluorophenyl)quinazolin-4(3H)-one (5.3.7f)*:** The title compound was isolated as a white powder using silica-gel column chromatography eluting with ethyl acetate/hexane (2:8), (88 mg, Yield: 74%); R_f = 0.35, ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.57 (s, 1H), 8.26 (dd, *J* = 8.9, 5.5 Hz, 2H), 8.16 (d, *J* = 8.5 Hz, 1H), 7.86 – 7.82 (m, 1H), 7.74 (d, *J* = 8.0 Hz, 1H), 7.53 (t, *J* = 7.4 Hz, 1H), 7.39 (t, *J* = 8.9 Hz, 2H). $^{13}C\{^{1}H\}$ NMR (100 MHz, DMSO-d_6) δ 165.7, 163.3, 162.6, 151.8, 149.1, 135.1, 130.8 (d, $J_{C\text{-}F}$ =8.9 Hz), 129.7 (d, *J* = 3.0 Hz), 127.9, 127.0, 126.3, 121.3, 116.1 (d, $J_{C\text{-}F}$ = 21.9 Hz).[15f]



2-(Thiophen-2-yl)quinazolin-4(3H)-one (5.3.7g): The title compound was isolated as a white powder using silica-gel column chromatography eluting with ethyl acetate/hexane (2:8), (77 mg, Yield: 68%); R_f = 0.30, ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.63 (s, 1H), 8.23 (d, *J* = 2.9 Hz, 1H), 8.13 (d, *J* = 7.7 Hz, 1H), 7.86 (d, *J* = 4.6 Hz, 1H), 7.81 (t, *J* = 7.4 Hz, 1H), 7.66 (d, *J* = 8.0 Hz, 1H), 7.49 (t, *J* = 7.3 Hz, 1H), 7.24 (s, 1H). $^{13}C\{^{1}H\}$ NMR (150 MHz, DMSO) δ 162.3, 149.1, 148.3, 137.8, 135.2, 132.6, 129.8, 128.9, 127.4, 126.8, 126.4, 121.3.[15f]

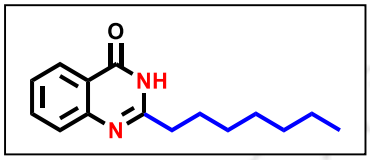


2-Cyclohexylquinazolin-4(3H)-one (5.3.7h): The title compound was isolated as a white powder using silica-gel column chromatography eluting with ethyl acetate/hexane (2:8), (82 mg, Yield: 72%); R_f = 0.40, ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.08 (s, 1H), 8.08 (d, *J* = 8.8 Hz, 1H), 7.77 (t, *J* = 8.3 Hz, 1H), 7.60 (d, *J* = 8.1 Hz, 1H), 7.45 (t, *J* = 7.9 Hz, 1H), 2.58 (tt, *J* = 11.7, 3.2 Hz, 1H), 1.91 (d, *J* = 12.0 Hz, 2H), 1.80 (d, *J* = 12.9 Hz, 2H), 1.69 (d, *J* = 12.2 Hz, 1H), 1.59 (qd,



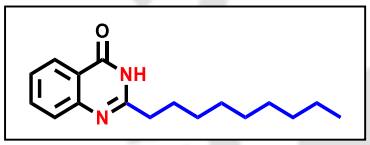
J = 12.5, 2.8 Hz, 2H), 1.34 – 1.20 (m, 4H). $^{13}C\{^{1}H\}$ NMR (150 MHz, DMSO-d_6) δ 162.3, 161.2, 149.4, 134.7, 127.4, 126.4, 126.1, 121.4, 43.3, 30.6, 25.9, 25.8.[15b]

2-Heptylquinazolin-4(3H)-one (5.3.7i): The title compound was isolated as a white powder using silica-gel column chromatography eluting with ethyl acetate/hexane (2:8), (85 mg, Yield: 70%); R_f = 0.40, ^{1}H NMR (500 MHz, $CDCl_3$) δ 11.97 (s, 1H), 8.22 (d, *J* = 7.4 Hz, 1H), 7.77 – 7.58 (m, 2H), 7.40 (t, *J* = 7.8 Hz, 1H), 2.74 (t, *J* = 7.8 Hz, 2H), 1.82 (p, *J* = 7.6 Hz, 2H) 1.45 – 1.35 (m, 2H), 1.31 (dt, *J* = 14.8, 6.8 Hz, 2H), 1.25 – 1.17 (m, 4H), 0.87 (t, *J* = 6.6 Hz, 3H).



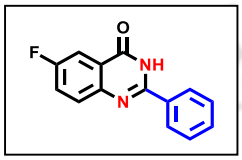
$^{13}C\{^{1}H\}$ NMR (150 MHz, $CDCl_3$) δ 164.4, 157.7, 149.3, 134.8, 127.2, 126.3, 125.2, 120.5, 35.9, 31.6, 29.2, 28.9, 27.6, 22.6, 14.0. [18c]

2-Nonylquinazolin-4(3H)-one (5.3.7j): The title compound was isolated as a white powder using silica-gel column chromatography eluting with ethyl acetate/hexane (2:8), (102 mg, Yield: 75%); R_f = 0.40, ^{1}H NMR (500 MHz, $CDCl_3$) δ 12.27 (s, 1H), 8.19 (d, *J* = 7.9 Hz, 1H), 7.68 – 7.61 (m, 2H), 7.36 (t, *J* = 7.2 Hz, 1H), 2.71 (t, 2H), 1.80 (p, *J* = 7.8 Hz, 2H), 1.37 (p, *J* = 7.7 Hz, 2H), 1.28 – 1.17 (m, 10H), 0.77 (t, *J* = 6.8 Hz, 3H).

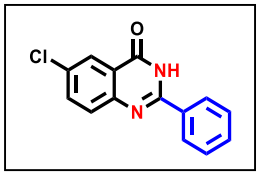


$^{13}C\{^{1}H\}$ NMR (150 MHz, $CDCl_3$) δ 164.2, 156.9, 149.5, 134.7, 127.2, 126.2, 120.5, 36.0, 31.8, 29.4, 29.2, 27.5, 22.6, 14.1. [18d]

6-Fluoro-2-phenylquinazolin-4(3H)-one (5.3.7k): The title compound was isolated as a white powder using silica-gel column chromatography eluting with ethyl acetate/hexane (2:8), (93 mg, Yield: 78%); R_f = 0.30, ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.69 (s, 1H), 8.22 (d, *J* = 7.2 Hz, 2H), 7.88 (d, *J* = 7.9 Hz, 2H), 7.77 (t, *J* = 8.4 Hz, 1H), 7.65 – 7.59 (m, 3H). $^{13}C\{^{1}H\}$ NMR (125 MHz, DMSO-d_6) δ 162.2, 161.4, 159.5, 152.4, 146.1, 133.1, 131.8, 130.7 (d, $J_{C\text{-}F}$ = 7.1 Hz), 129.1, 128.2, 123.5 (d, $J_{C\text{-}F}$ = 24.0 Hz), 122.6 (d, $J_{C\text{-}F}$ = 8.2 Hz), 110.9 (d, $J_{C\text{-}F}$ = 23.4 Hz).[15b]

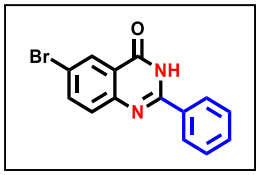


6-Chloro-2-phenylquinazolin-4(3H)-one (5.3.7l): The title compound was isolated as a white powder using silica-gel column chromatography eluting with ethyl acetate/hexane (2:8), (108 mg, Yield: 80%); R_f = 0.35, ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.62 (s, 1H), 8.11 (d, *J* = 7.3 Hz, 2H), 8.03 (d, *J* = 2.4 Hz, 1H), 7.80 (dd, *J* = 8.7, 2.5 Hz, 1H), 7.71 (d, *J* = 8.7 Hz, 1H), 7.56 – 7.53 (m, 1H), 7.51 – 7.48

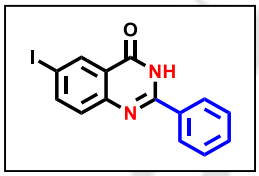


(m, 2H). $^{13}C\{^{1}H\}$ NMR (125 MHz, DMSO-d_6) δ 161.7, 153.3, 147.9, 135.2, 132.9, 132.1, 131.2, 130.2, 129.1, 128.3, 125.3, 122.7.[15a]

6-Bromo-2-phenylquinazolin-4(3H)-one (5.3.7m): The title compound was isolated as a white powder using silica-gel column chromatography eluting with ethyl acetate/hexane (2:8), (105 mg, Yield: 70%); R_f = 0.35, ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.69 (s, 1H), 8.23 (s, 2H), 8.18 (d, *J* = 7.3 Hz, 2H), 7.97 (d, *J* = 6.8 Hz, 1H), 7.69 (d, *J* = 8.6 Hz, 1H), 7.62 – 7.54 (m, 2H). $^{13}C\{^{1}H\}$ NMR (125 MHz, DMSO) δ 161.6, 153.4, 148.2, 137.8, 132.9, 132.1, 130.3, 129.1, 128.5, 128.3, 123.1, 119.3.[17b]



6-Iodo-2-phenylquinazolin-4(3H)-one (5.3.7n): The title compound was isolated as a white powder using silica-gel column chromatography eluting with ethyl acetate/hexane (2:8), (142 mg, Yield: 82%); R_f = 0.35, ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.52 (s, 1H), 8.17 (t, *J* = 8.4 Hz, 3H), 7.84 (t, *J* = 7.2 Hz, 1H), 7.75 (d, *J* = 7.9 Hz, 1H), 7.55 (tt, *J* = 14.1, 7.0 Hz, 3H). $^{13}C\{^{1}H\}$ NMR (150 MHz, DMSO-d_6) δ 162.7, 152.7, 149.2, 135.1, 133.2, 131.8, 129.1, 128.2, 127.9, 127.1, 126.3, 121.4.[18e]



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5.10. Figures reproducing ^{1}H and ^{13}C NMR spectra:

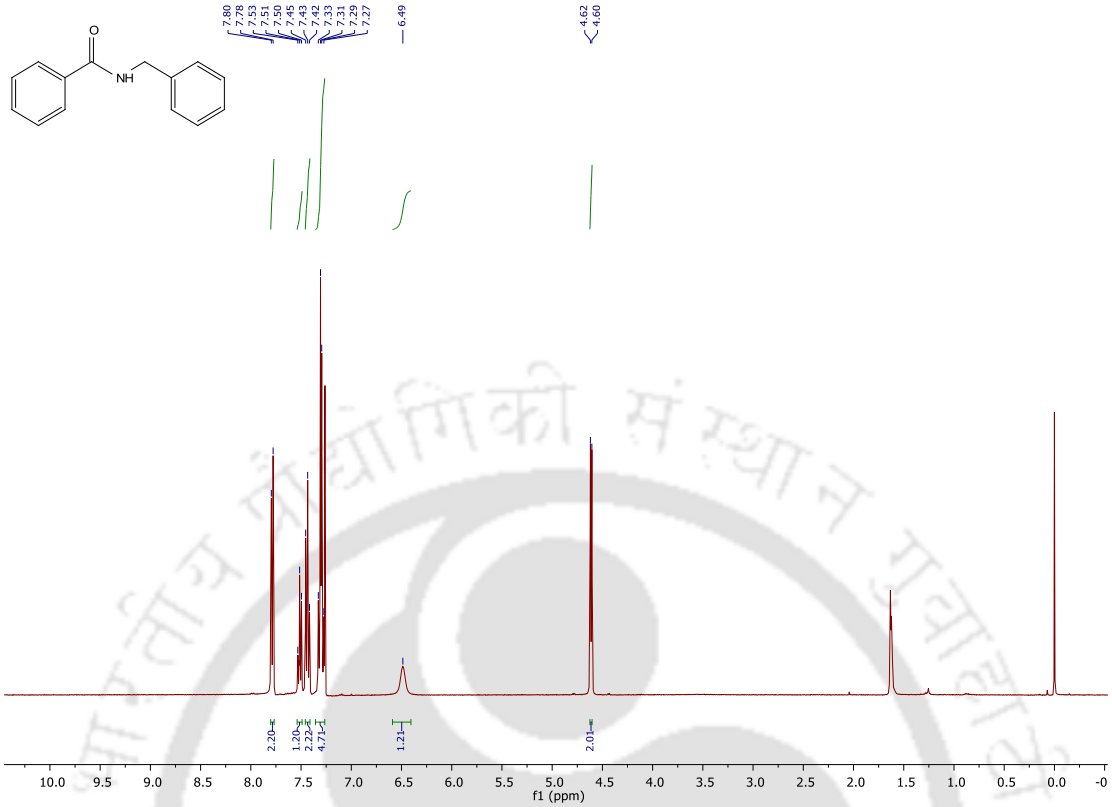

Figure 5.9: ^{1}H (600 MHz) spectra of compound **5.1.3a** in $CDCl_3$

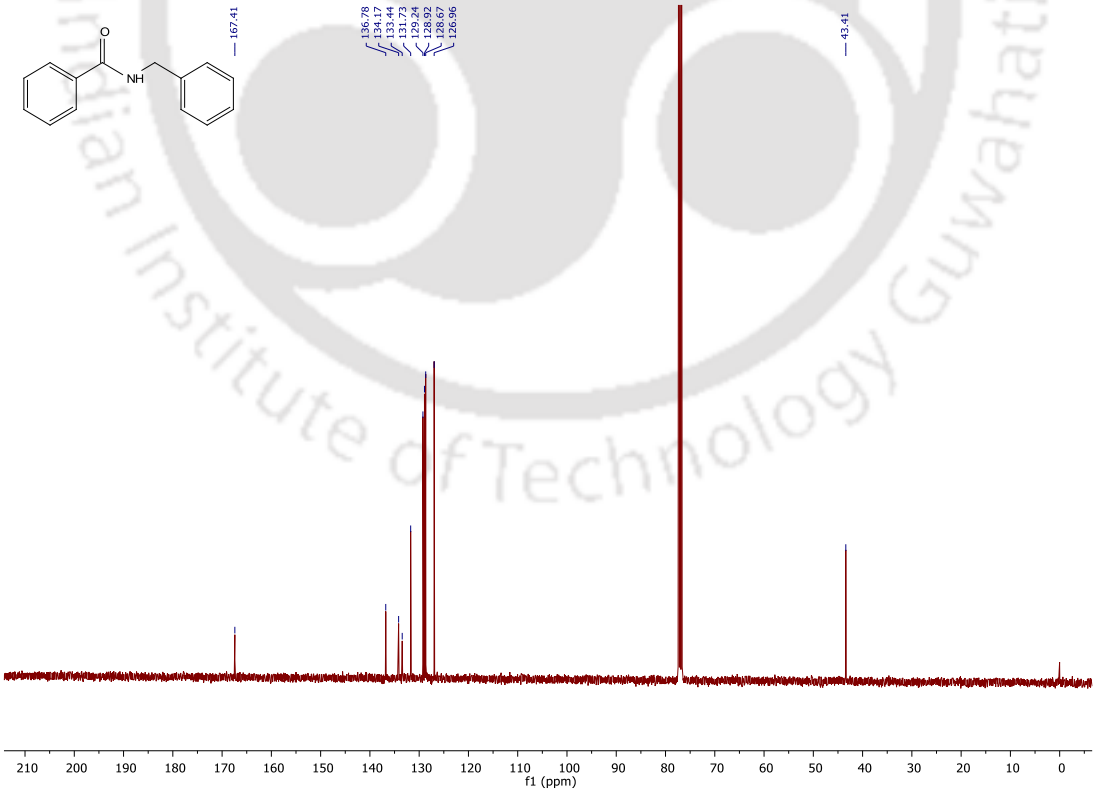

Figure 5.10: $^{13}C\{^{1}H\}$ NMR (100 MHz) spectra of compound **5.1.3a** in $CDCl_3$

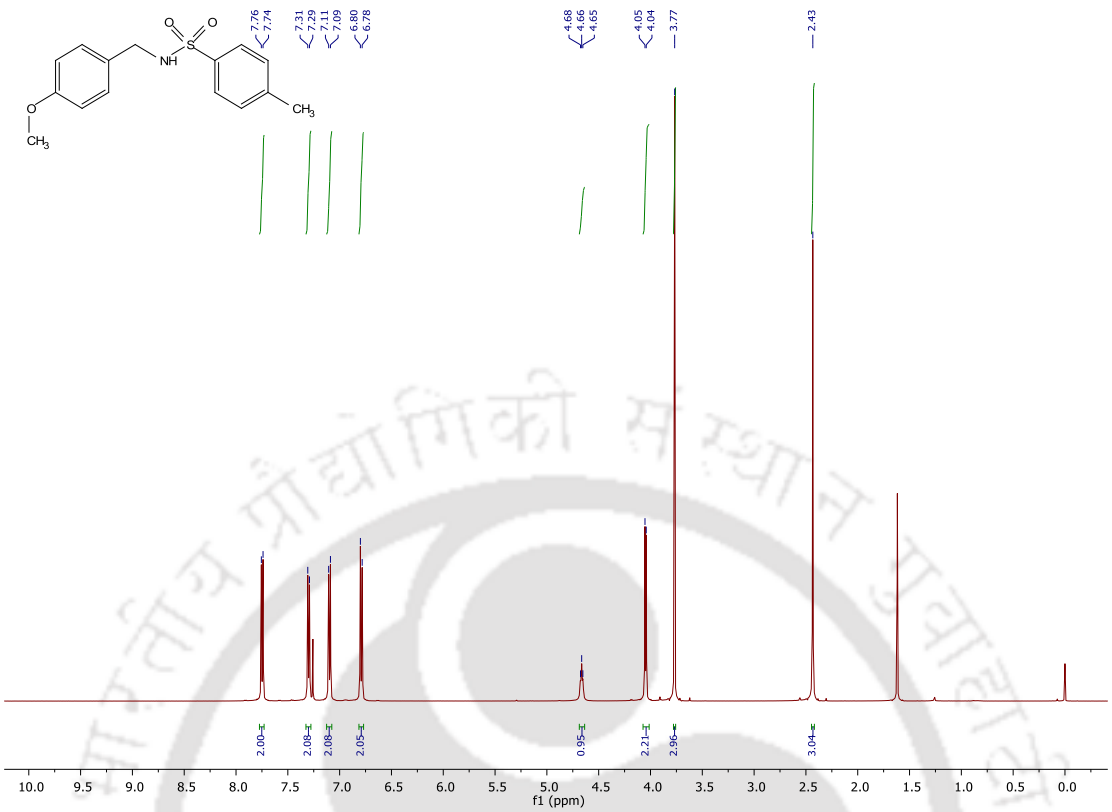

Figure 5.11. ^{1}H NMR (500 MHz) spectra of compound **5.2.5c** in $CDCl_3$

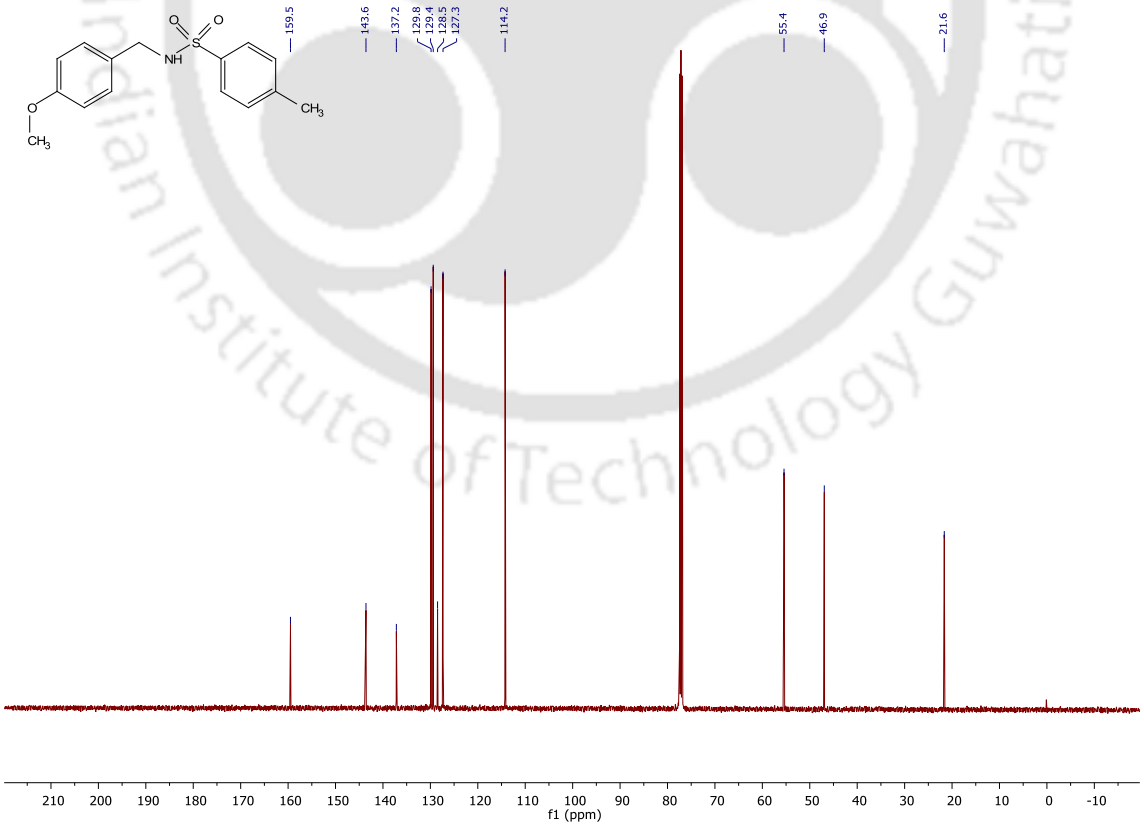

Figure 5.12. $^{13}C\{^{1}H\}$ NMR (125 MHz) spectra of compound **5.2.5c** in $CDCl_3$

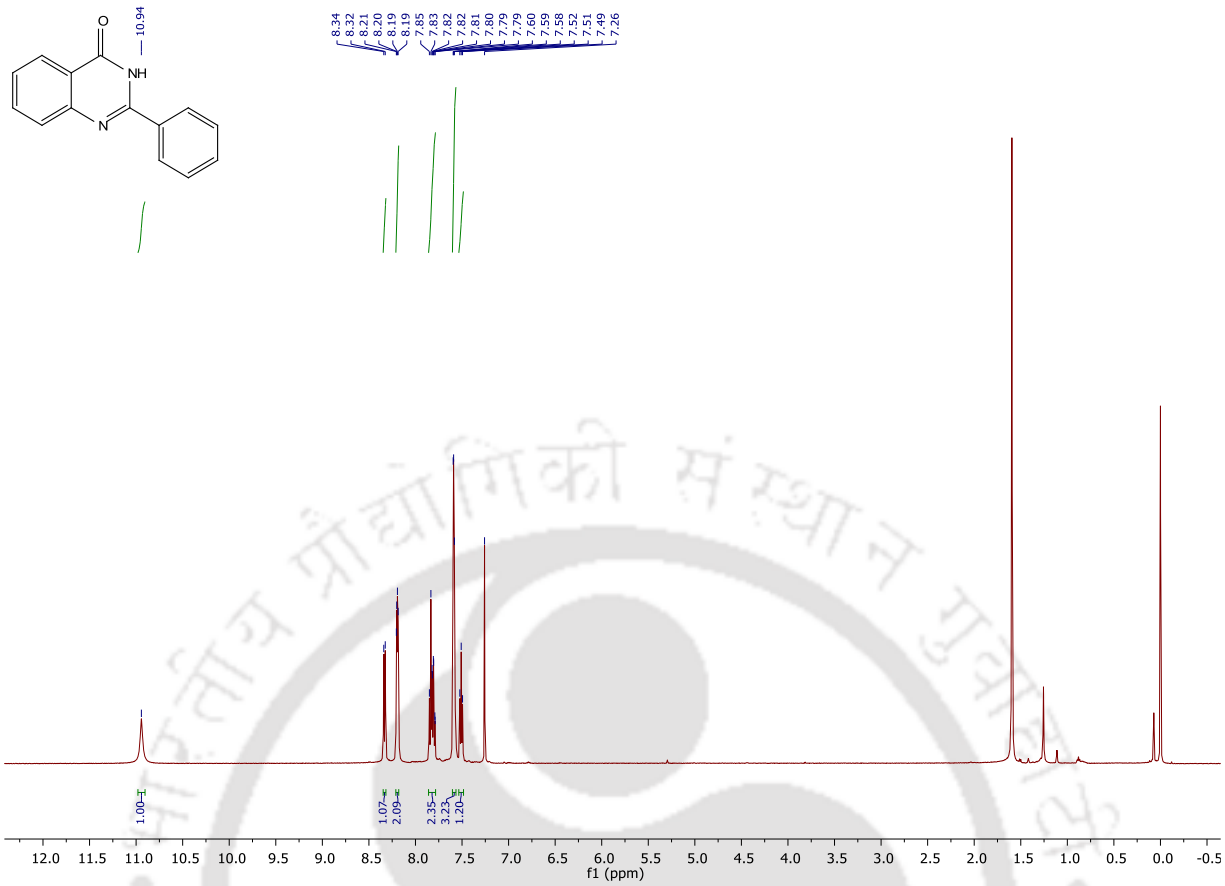

Figure 5.13. ^{1}H NMR (500 MHz) spectra of compound **5.3.7a** in $CDCl_3$

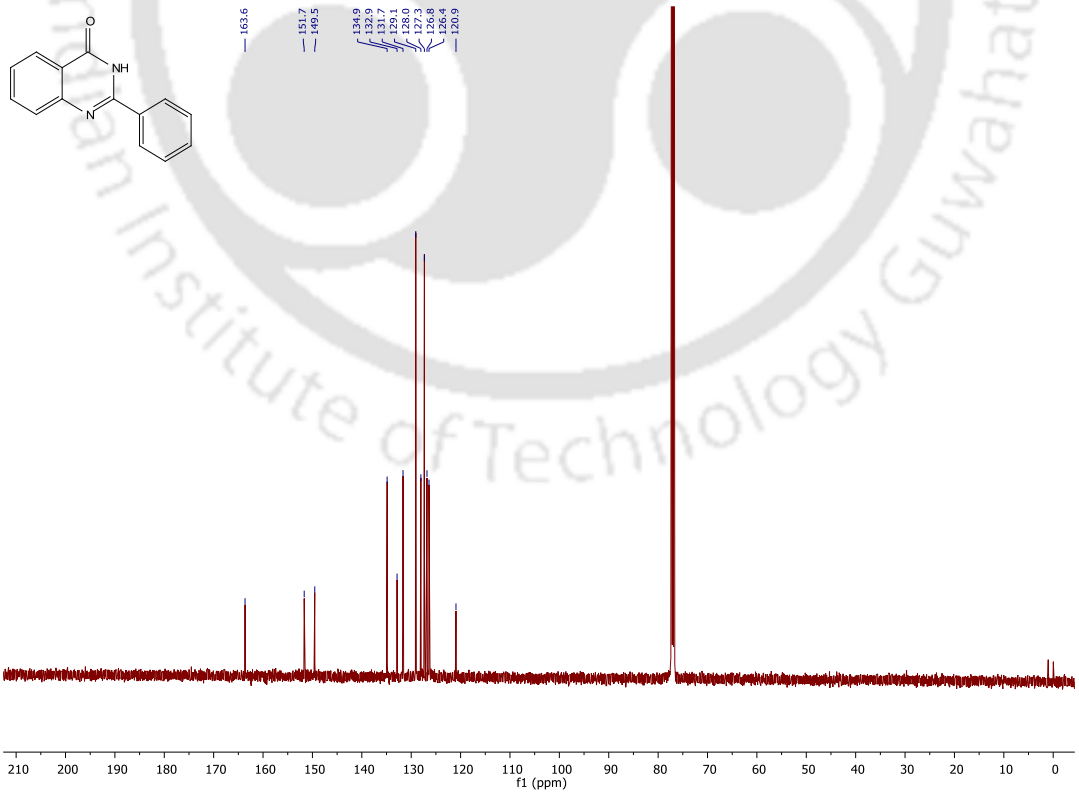

Figure 5.14. $^{13}C\{^{1}H\}$ NMR (125 MHz) spectra of compound **5.3.7a** in $CDCl_3$

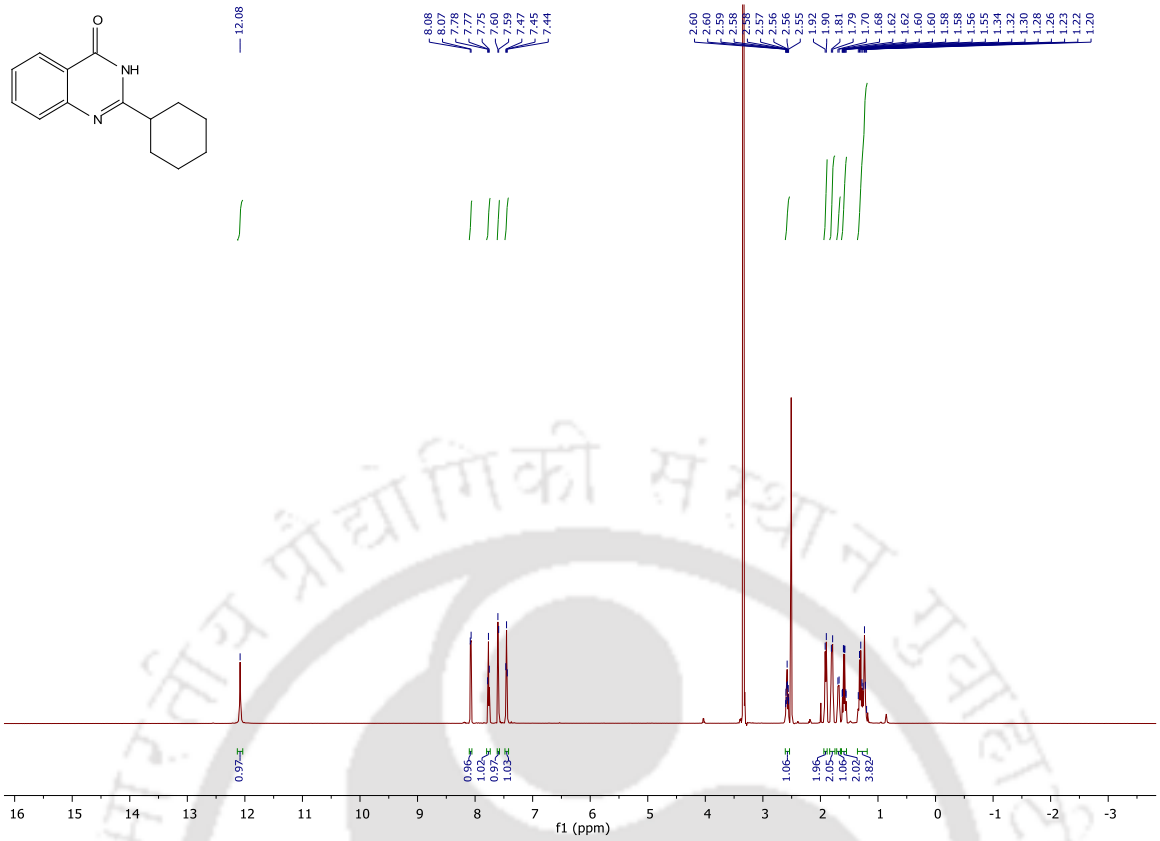

Figure 5.15. ^{1}H NMR (600 MHz) spectra of compound **5.3.7h** in DMSO-d_6

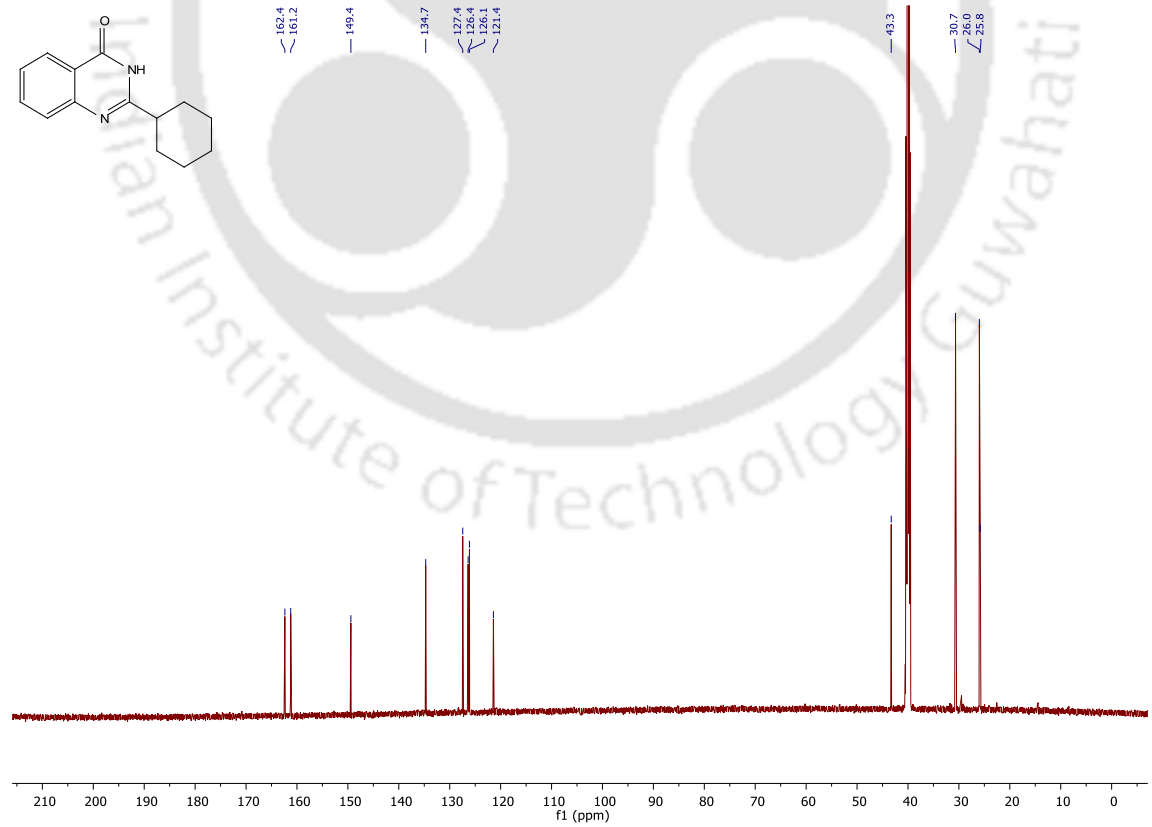

Figure 5.16. ^{13}C{^{1}H} NMR (150 MHz) spectra of compound **5.3.7h** in DMSO-d_6

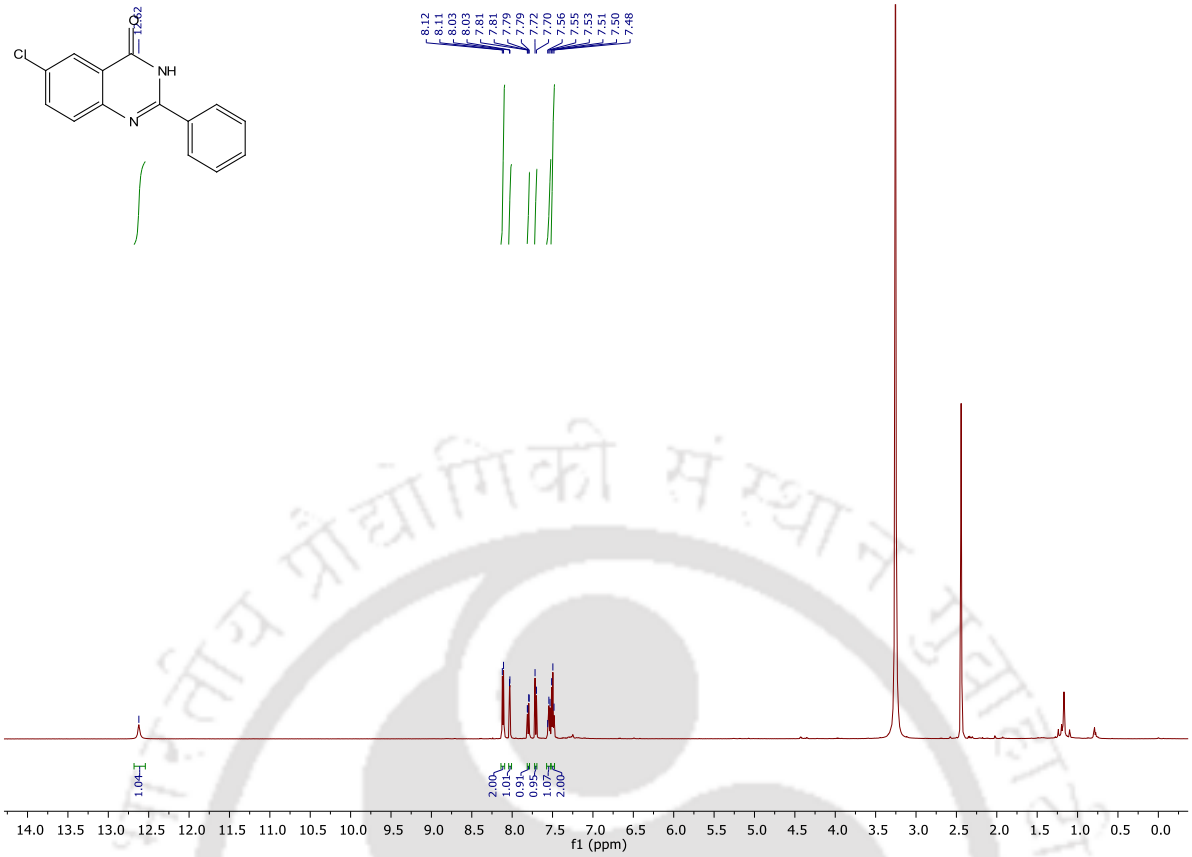

Figure 5.17. ^{1}H NMR (500 MHz) spectra of compound **5.3.7l** in DMSO-d_6

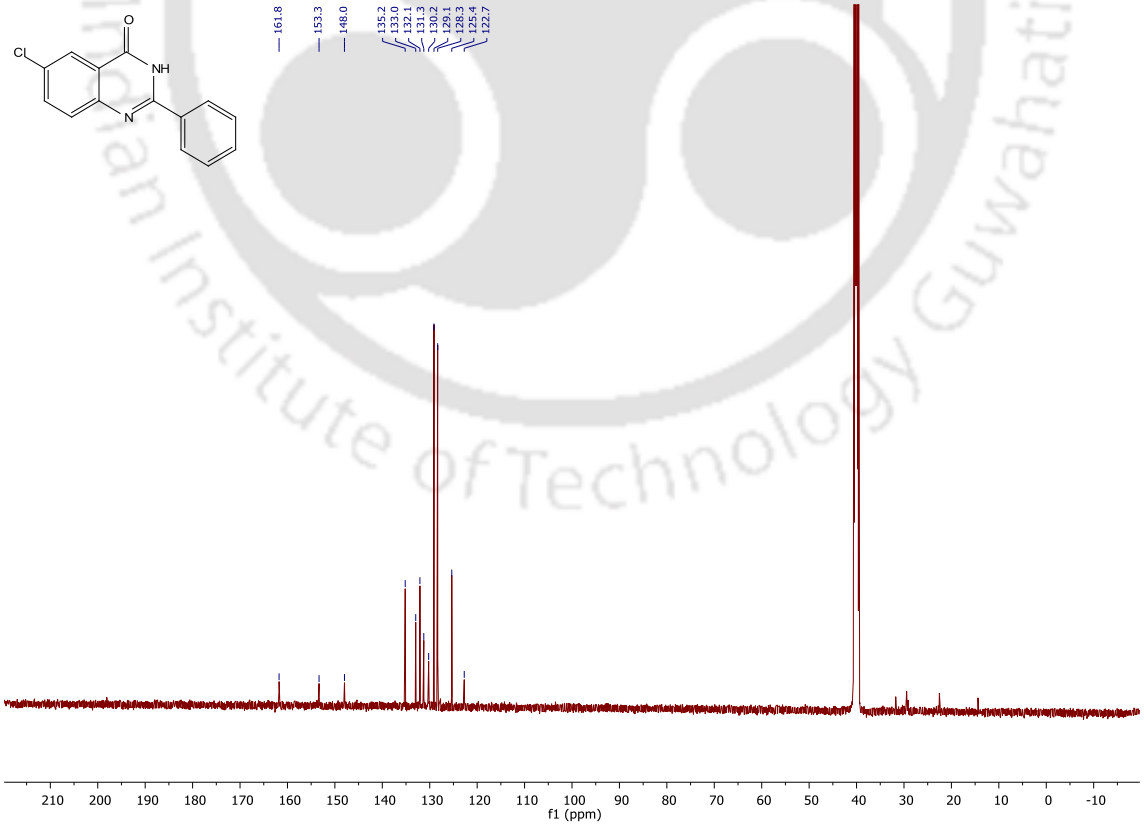

Figure 5.18. ^{13}C{^{1}H} NMR (125 MHz) spectra of compound **5.3.7l** in DMSO-d_6

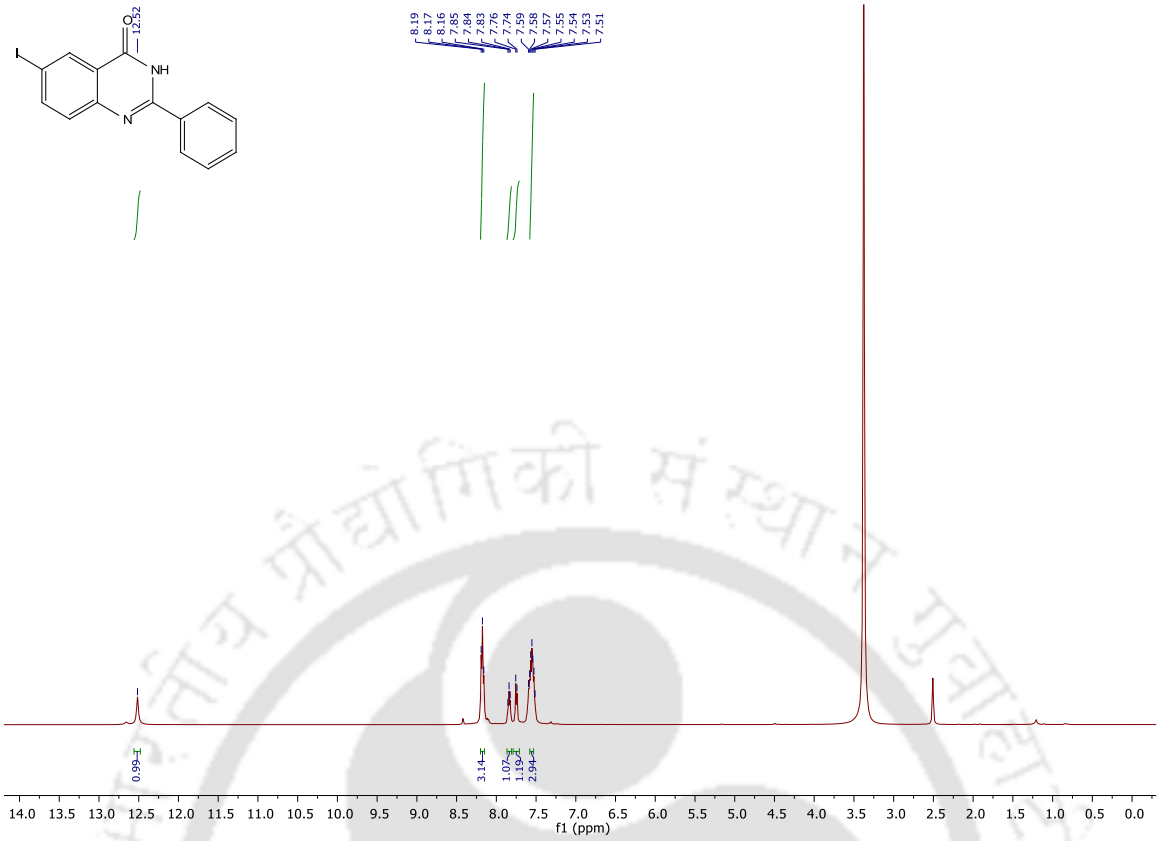

Figure 5.19. ^{1}H NMR (500 MHz) spectra of compound **5.3.7n** in DMSO-d_6

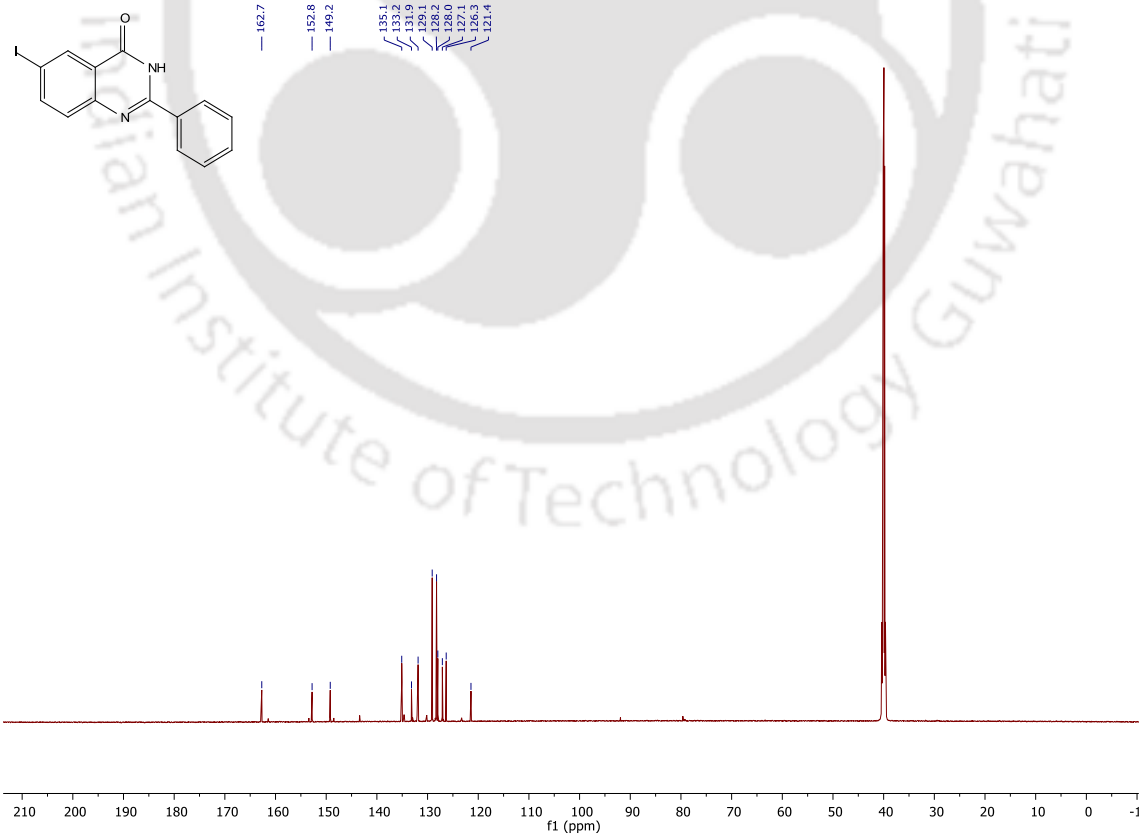

Figure 5.20. ^{13}C{^{1}H} NMR (150 MHz) spectra of compound **5.3.7n** in DMSO-d_6

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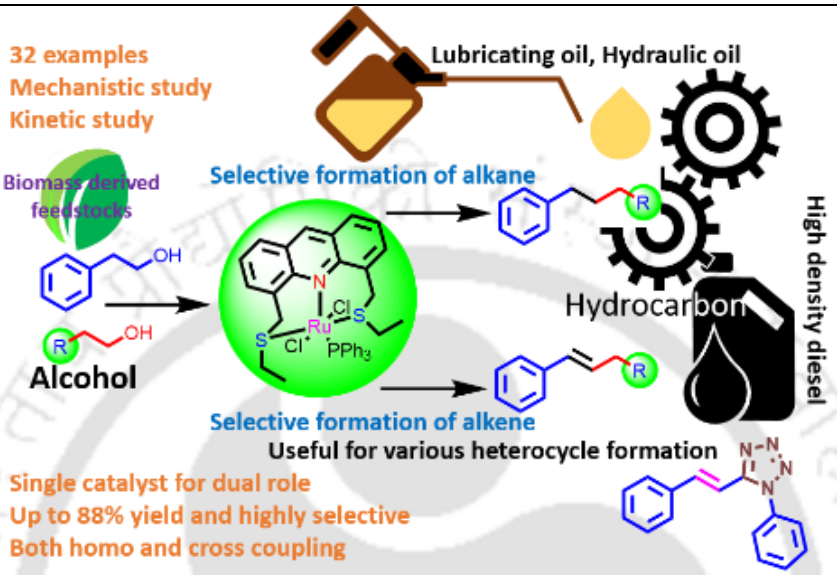
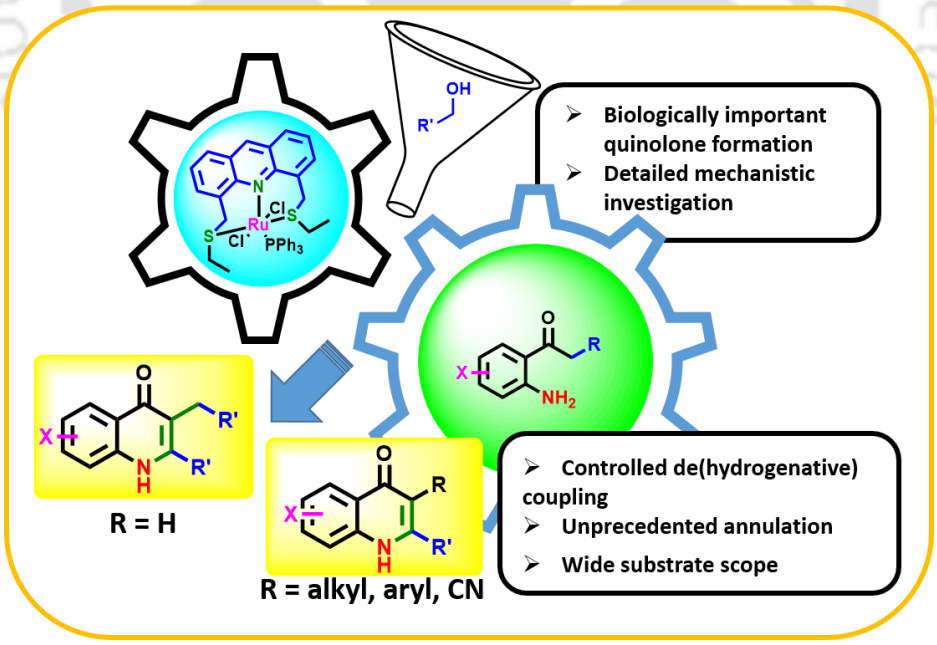
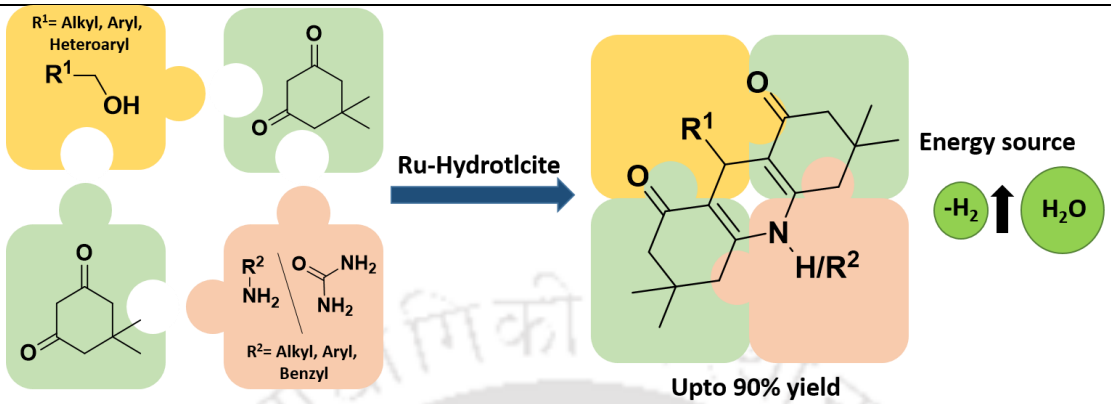
Chapter 2



Chapter 3



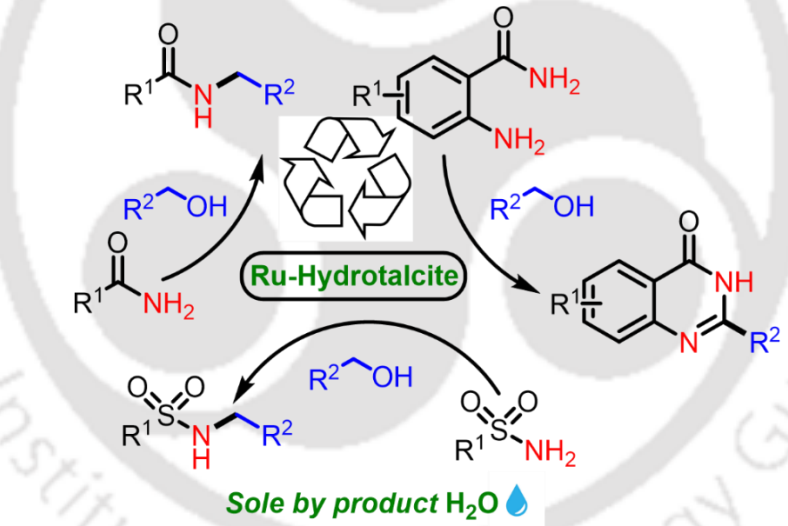
Chapter 4



Acceptorless dehydrogenative multicomponent
Deuterium labelling experiment
Recyclable upto five times
One pot process
Mechanistic investigation

Kinetic study
Broad substrate scope
Gram scale synthesis

Chapter 5



Sole by product H_2O

Relatively mild conditions
Mechanistic investigation
Acceptorless dehydrogenation

Recyclable upto 5 times
Broad substrate scope
Borrowing hydrogenation

Publications

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1. N. Biswas, K. Das, **B. Sardar**, D. Srimani, Acceptorless Dehydrogenative Construction of C=N and C=C Bonds through Catalytic Aza-Wittig and Wittig reactions in the presence of an Air-stable Ruthenium Pincer Complex, *Dalton Trans*., **2019**, *48*, 6501–6512.

2. B. Sardar, R. Jamatia, D. Pal, D. Srimani, Multicomponent Dehydrogenative Synthesis of Acridine-1,8-diones Catalyzed by Ru-doped Hydrotalcite, *Asian J. Org. Chem.*, **2021**, *10*, 2195.

3. B. Sardar, R. Jamatia, A. Samanta, D. Srimani Ru Doped Hydrotalcite Catalyzed Borrowing Hydrogen-Mediated *N*-Alkylation of Benzamides, Sulfonamides, and Dehydrogenative Synthesis of Quinazolinones, *J. Org. Chem.*, **2022**, 87, 9, 5556–5567.

4. R. Sharma, A. Samanta, **B. Sardar**, M. Roy, D. Srimani, Progressive Study on Ruthenium Catalysis for De(hydrogenative) Alkylation and Alkenylation using Alcohols as a Sustainable Source, *Org. Biomol. Chem.*, **2022**, *20*, 7998.

5. N. Biswas, R. Sharma, **B. Sardar**, D. Srimani, Acridine Based SNS-Ruthenium Pincer Complex Catalysed Borrowing Hydrogen Mediated C-C Alkylation Reaction: Application Towards Guerbet Reaction, *Synlett*, **2022**, *33*, 10.1055/a-1874-2406.

6. B. Sardar, N. Biswas, D. Srimani, Ruthenium Pincer-Catalyzed Selective Synthesis of Alkanes and Alkenes via Deoxygenative Coupling of Primary Alcohols, *Organometallics*, **2023**, *42*, 55 – 61.

7. B. Sardar, D. Srimani, Concept and Progress on the De(hydrogenation) and Hydrogenation Reactions using Transition Metal Integrated Layered Double Hydroxides (LDHs), *Tetrahedron Letter.*, **2023**, *138*, 133414.

8. B. Sardar, D. Pal, R. Sarmah, D. Srimani, Ruthenium Catalysed Dehydrogenative Cyclization to Synthesize Polysubstituted 4-quinolones under Solvent-Free Condition, *Chem Comm*, **2023**, *https://doi.org/10.1039/D3CC02426A*.

Conference

1. *Research conclave,* 2022, Poster: Ruthenium Pincer-Catalyzed Selective Synthesis of Alkanes and Alkenes via Deoxygenative Coupling of Primary Alcohols.

2. *Frontiers in Chemical Sciences*, 2022, Poster: Ruthenium Pincer-Catalyzed Selective Synthesis of Alkanes and Alkenes via Deoxygenative Coupling of Primary Alcohols, *Organometallics*, **2023**, 42, 55 – 61.

Workshop attended

Process Chemistry Workshop at Dr. Reddy's Institute of Life Sciences

Hyderabad, Telangana

[12 Jun 2023 – 23 Jun 2023]

Introduction and in hand experience to flow chemistry, electro chemistry and scale up chemistry.

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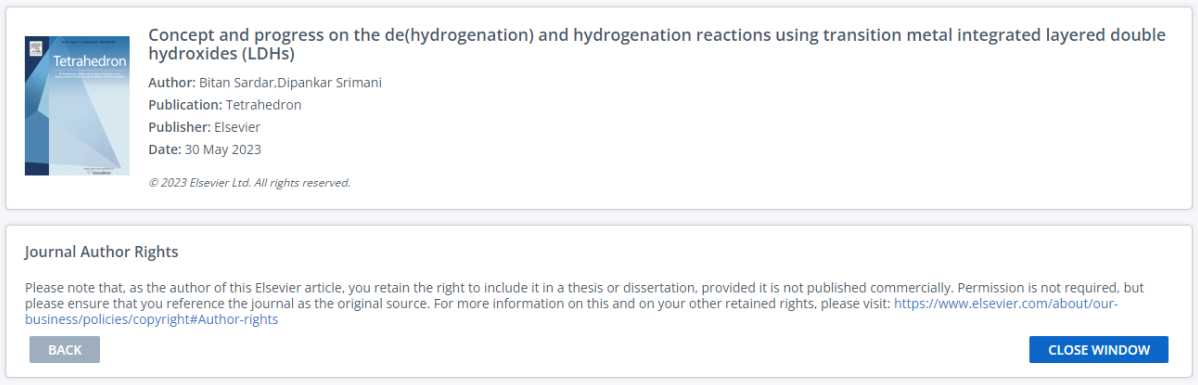

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Publication: Tetrahedron
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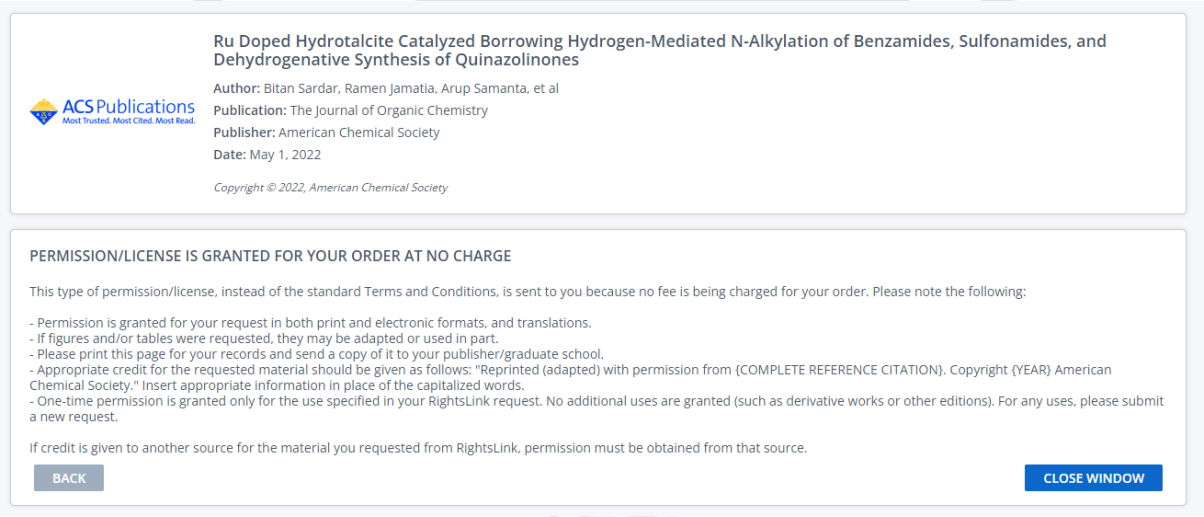

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Publication: The Journal of Organic Chemistry
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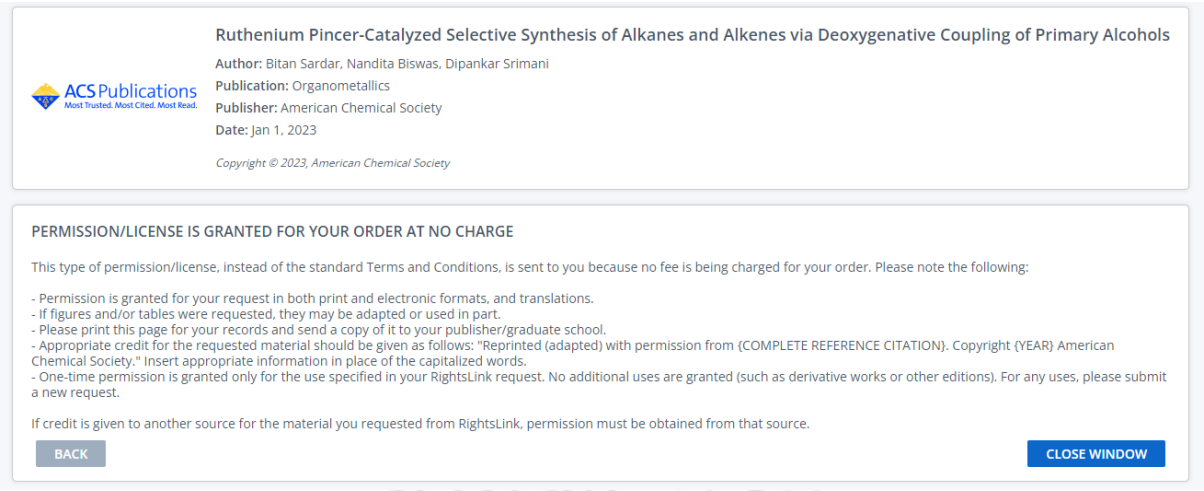

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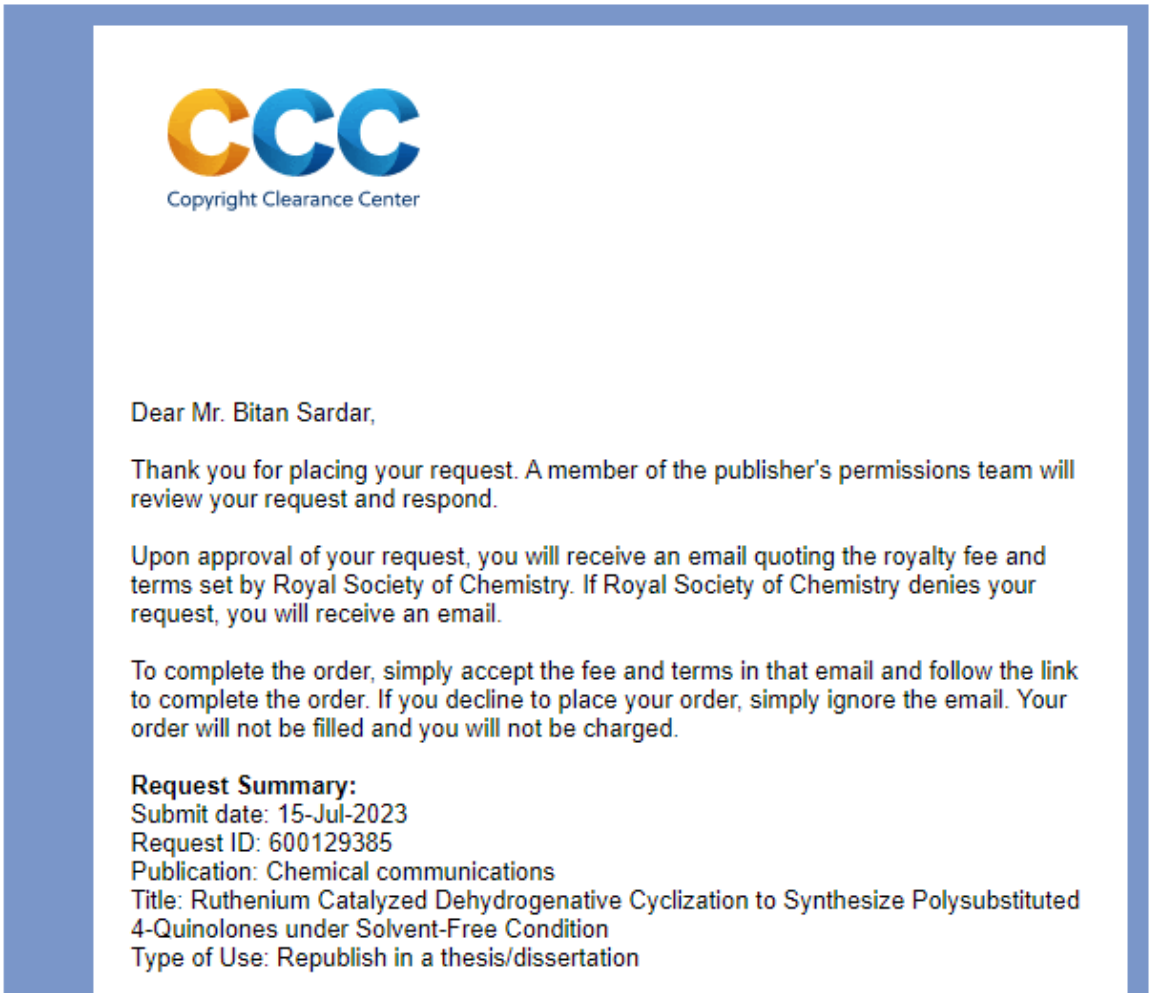

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