Catalytic Applications of Transition Metal Complex With N-Heterocyclic Carbene Ligands

M.Sc. Thesis

by

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DEPARTMENT OF CHEMISTRY

INDIAN INSTITUTE OF TECHNOLOGY INDORE

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A THESIS

Submitted in partial fulfilment of the requirements for the award of the degree

of

Master of Science

by

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CANDIDATE'S DECLARATION

I hereby certify that the work presented in the thesis entitled **Catalytic Applications of Transition Metal Complex With N-Heterocyclic Carbene Ligands**, which was submitted to the **DEPARTMENT of CHEMISTRY**, Indian Institute of Technology Indore, is an authentic record of my own work completed during the time period from July 2022 to May 2023. This thesis is being submitted in partial fulfilment of the requirement for the award of the degree of **MASTER of SCIENCE** under the supervision of **Dr. Amrendra Kumar Singh**, Department of Chemistry, IIT Indore.

16-05-2023

Signature of the student with the date

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This is to certify that the above statement made by the candidate is correct to the best of my/our knowledge.

16/5/2023

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Dedicated to.....

My Parents

For their unwavering belief in my potential

ABSTRACT

A Ru (II) pNHC metal complex, $[Ru(NNC^{H})(PPh_3)_2Cl]Cl$, has been synthesized by transmetallation reaction of silver complex bearing NHC ligand precursor, 6-(1H-benzo[d]imidazol-1-yl)-N-(pyridin-2-yl)-N-(p- tolyl)pyridin-2-amine as reported in previous research article of our lab. Metal precursor $[RuCl_2(PPh_3)_3]$ was synthesized by $RuCl_3 \cdot 3H_2O$ using literature procedure. This complex was previously reported in our lab. All the structures of the synthesized ligand and the complex have been characterized by mass spectrometry, ^{1}H, and ^{13}C NMR, which clearly matches with the previous data. The catalytic activity of NHC−Ru(II) complex was investigated in the N-alkylation reaction of aniline derivatives with benzyl alcohols to form N-benzyl amine. In this report, Ru(II) complex in N-alkylation reactions was optimized with different substrates, and considerable results were obtained. All obtained products were synthesized under optimized conditions and characterized by ^{1}H and ^{13}C NMR data. Conversion percentages have been determined by NMR spectroscopy.

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ABBREVIATIONS

℃	Degree celsius
g	Gram
h	Hours
Min	Minutes
Mol	Mole
mg	Milligram
mL	Millilitre
%	Percentage
RT	Room temperature

ACRONYMS

DCM	Dichloromethane
DMSO	Dimethyl sulfoxide
GCMS	Gas chromatography
HCl	Hydrochloric acid
MS	Mass spectroscopy
MeOH	Methanol
NMR	Nuclear magnetic resonance
NHC	N-Heterocyclic carbene
N	nitrogen
NaO^tBu	Sodium tert-butoxide
Na_2SO_4	Sodium sulphate
$NaHCO_3$	Sodium bicarbonate
Ru	Ruthenium
PPh_3	Triphenylphosphine

Chapter 1

INTRODUCTION

1.1 Aim of the project:

The aim of the project is to study the nature of an N-heterocyclic carbene-based CNC ruthenium pincer complex, which has already been synthesized in our lab and check their different type of catalytic activities towards various applications like hydrogenation, acceptorless dehydrogenation, hydroboration, hydrosilylation, N-formylation of amine, N-methylation of amine and N-alkylation of amines, etc. Due to the strong ability of σ donation of an electron pair by NHC, an electron-rich complex is formed. It can be useful for activating small molecules, such as oxidation of ammonia, water oxidation, and CO_2 reduction.

1.2 General Introduction:

Transition metal complexes featuring pincer ligands encompass a broad spectrum of applications within the realm of transition-metal catalysis, spanning diverse areas such as hydrogenation and transfer hydrogenation reactions.[1] Pincer ligands, known for their distinctive tridentate coordination around the metal center, play a pivotal role in enhancing the efficiency and selectivity of these catalytic processes.[2] Transition metal complexes incorporating N-heterocyclic carbenes (NHCs) are highly versatile in organometallic chemistry and catalysis due to their exceptional stereoelectronic diversity and ability to form stable compounds.[3]The unique electronic properties and structural characteristics of NHCs provide a wide array of options for fine-tuning reactivity and selectivity in various chemical transformations. These complexes have found applications in diverse catalytic processes. A well-known example of such a reaction is the cross-coupling reaction by the Heck, Sonogashira, and Suzuki, hydrogenation, C-H activation, and olefin metathesis. The stability of NHC-based transition metal complexes allows for their efficient use as catalysts, enabling the development of new synthetic methodologies and the synthesis of complex organic molecules.[4–6] Wilkinson and his colleagues

significantly contributed to catalytic research in 1964 by introducing Wilkinson's catalyst, which served as a catalyst model, leading to numerous breakthroughs in the scientific community.

N-alkylated amines are widely used compounds with numerous applications in pharmaceuticals, agrochemicals, polymer materials, and synthetic industries.[7] Grigg and Watanabe independently published pioneering studies introducing homogeneous catalysts for alkylating amines with alcohols. In 1982, Murahashi and his colleagues demonstrated that aliphatic amines could undergo high-efficiency N-alkylation reactions when a catalyst containing $[RuH_2(PPh_3)_4]$ is employed. This research revealed that these amines possess the necessary reactivity and can serve as suitable substrates for this particular type of chemical transformation. Van Koten and his team published a study describing N-heterocycles' formation through the N-alkylation of aromatic amines with diols. They utilized pincer ruthenium complexes as catalysts for this reaction.[8] In 2002, Fujita and Yamaguchi conducted a study demonstrating multiple alcohol activation reactions using CpIr complexes. They specifically reported an Oppenauer-type oxidation of primary and secondary alcohols using catalytic quantities of $[CpIrCl_2]_2$ in the presence of a base, carried out in acetone as the solvent.[9] An N-alkylation reaction was carried out by Tejeda, Peris, Royo, and their colleagues, utilizing an iridium complex that incorporated a Cp*-functionalized N-heterocyclic carbene (NHC).[10] Milstein and co-workers developed a convenient and potentially important method for generating primary amines from primary alcohols and ammonia. (Fig.1)[11]

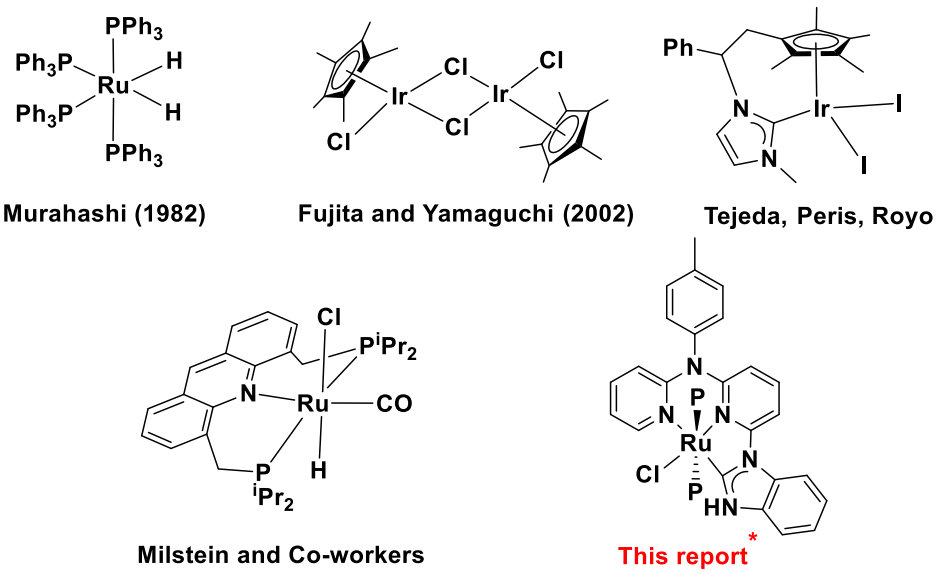


Fig.1: Previously reported catalyst

1.3 N-Heterocyclic carbene (NHC):

N-Heterocyclic carbenes (NHCs) are organic compounds containing a carbon atom with two heteroatoms (usually nitrogen) attached, giving it a heterocyclic structure. They are highly versatile and widely used as ligands in organometallic chemistry and catalysis. NHCs are carbene analogs, where a divalent carbon atom carries two lone pairs of electrons instead of two substituents. The carbon atom in NHCs is often part of a five-membered or six-membered heterocyclic ring, which provides stability to the compound. The most common NHC is the imidazolium-based NHC, which features a five-membered imidazole ring. Other examples include the triazolylidene NHC with a five-membered triazole ring and the benzimidazolylidene NHC with a six-membered benzimidazole ring. NHCs are strong σ-donor ligands and can form stable complexes with transition metals. They have remarkable stability and can stabilize highly reactive metal species. NHC ligands are often used in various catalytic reactions, including cross-coupling, hydrogenation, and olefin metathesis.[13] Carbenes have been extensively studied as one of the most investigated reactive species in the field of organic chemistry. These reactive intermediates are characterized by their neutral nature and the presence of a bivalent carbon atom possessing an electron sextet. The existence of carbenes was first suggested by the groundbreaking research of Buchner and Curtius and

Staudinger and Kupfer during the late 19th and early 20th centuries. Following the pioneering work of Bertrand and colleagues and Arduengo[14] and co-workers[15] in the late 1980s and early 1990s, stable nucleophilic carbenes, specifically N-heterocyclic carbenes (NHCs), have proven to be highly versatile and widely applicable in the field of organic synthesis. In addition to their exceptional performance as ligands in various metal-based catalytic reactions, these carbenes have demonstrated impressive potential as synthetic building blocks for a diverse range of organic compounds.[16] The field of synthetic organic chemistry has seen a significant boost in recent years with the emergence of organocatalytic carbene catalysis as an exceptionally productive research area. This innovative approach to catalysis has proven to be highly effective, offering a multitude of opportunities for the development of novel synthetic pathways and the creation of structurally complex organic molecules.

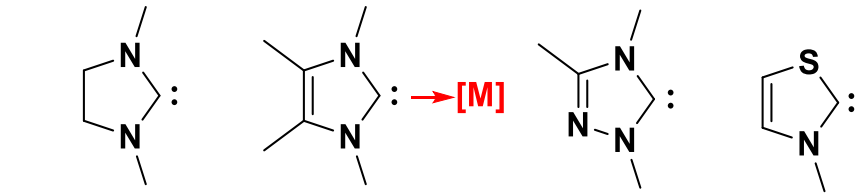


Fig.2: N-Heterocyclic Carbenes

1) The NHC is a stronger σ-donor and weaker π-acceptor than the most electron-rich phosphine.
2) The NHC can be useful spectator ligands because they are sterically and electronically tunable.
3) The NHC can promote a wide series of catalytic reactions like phosphine.
4) The NHC has advantages over phosphines and offers catalysts with better air stability

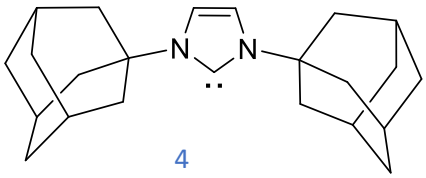
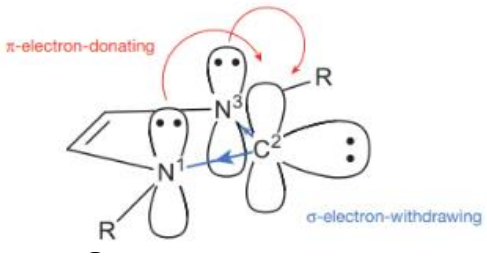


Fig.3: First stable N-Heterocyclic carbene[17]



1.4 Ru Metal Precursor:

Dichlorotris(triphenylphosphine)ruthenium, also known as $[Ru(Cl)_2(PPh_3)_3]$, is a coordination compound having a chocolate-brown color. It promotes oxidation, reduction, cross-coupling, cyclization, and isomerization and is employed as an active hydrogenation catalyst. It forms a square pyramidal crystal structure with an agnostic C-H.....Ru interaction involving one of the PPh_3 ligands.[18]

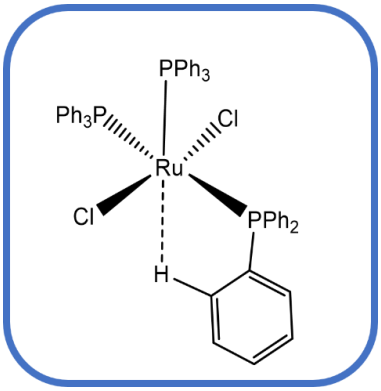


Fig.5: Dichlorotris(triphenylphosphine)ruthenium (Square planar structure)

1.5 N-alkylation of amines with alcohols:

The N-alkylation of amine was first introduced by Grigg and Watanabe in 1981 for homogeneous catalysts. Amines hold significant importance due to their extensive use as synthetic intermediates in various fields, including pharmaceuticals, agrochemicals, paints, dyes, drugs, polymers, and more. Numerous catalytic reactions have been documented for the N-alkylation process, which involves metal complexes containing elements such as Ru, Ir, Fe, Co, Mn, Cu, Pd, Ni,

and Cr as catalysts for the reaction between amines and alcohols. Among the various catalysts employed in the N-alkylation reaction, Ru complexes featuring NHC ligands have been recognized as highly productive.[19]

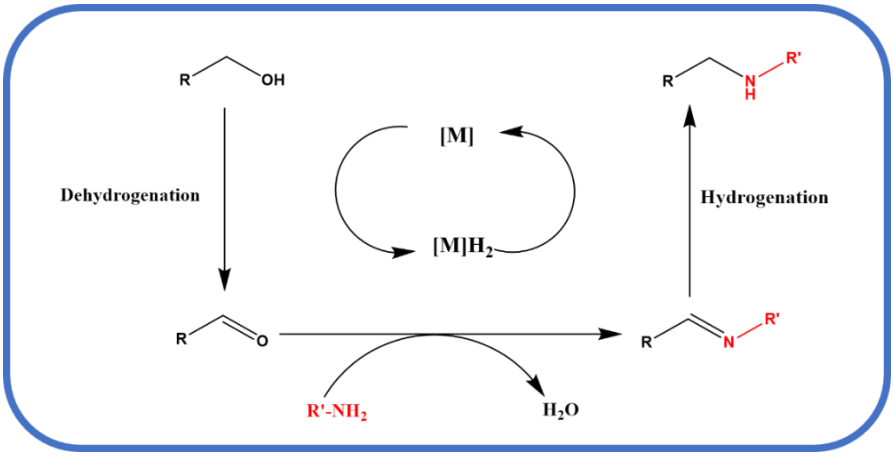


Fig.6: General mechanism for N-alkylation via dehydrogenative coupling of alcohol with primary amine[20]

Numerous research papers have focused on investigating a particular reaction utilizing benzyl alcohol and aniline as the standard substrates for optimizing reaction conditions. The process involves the hydrogenation of benzyl alcohol to produce benzaldehyde, followed by a hydration reaction with aniline to form a secondary imine, wherein water is eliminated from the system. The subsequent step relies on the reactivity of the system, which was later shown to be influenced by the hydrogen pressure. Eventually, the reaction undergoes hydrogenation to yield the desired secondary amine. Notably, this reaction is typically catalyzed by precious metals, such as ruthenium, rhodium, and iridium, as demonstrated in a study conducted by Velarga et al. in 2012.

Chapter 2

EXPERIMENTAL SECTION

2.1 General consideration:

The commercially available reagents and solvents were used without any purification. Toluene and DMSO were distilled before use. All the reactions were performed by the Schlenk line techniques under a nitrogen atmosphere and monitored by thin-layer chromatography (TLC) of Merck 60 F_{254} precoated silica gel plates. Purification of the synthesized products was performed by Column Chromatography filled with silica gel (100-200 mesh).

2.2 Chemicals and reagents:

All the chemicals were purchased and used as received without further purification. These chemicals include imidazole (SRL, 99%), 2,6-dibromo pyridine (Alfa Aesar, 98%), potassium carbonate (SRL, 99.5%), sodium bicarbonate (SRL, 99.5%), sodium chloride (SRL, 99.9%), ruthenium trichloride trihydrate (SRL), magnesium sulphate (SRL, 99%), potassium hydroxide (Emplura, 85%), Isopropyl bromide (Spectrochem, 99%) and tertiary Butylamine (Spectrochem, 99%)

2.3 Instrumentation:

At ambient temperature, NMR spectra were recorded on an ADVANCE III 400 and 500MHz Ascend Bruker BioSpin machine. Mass spectrometric analyses were done on Bruker-Daltonics, a micro to-Q II mass spectrometer.

2.4. Synthesis of dichlorotris(triphenylphosphine)ruthenium:

Experimental procedure:

In two necked round bottom flask, 200 mg (0.766 mmol) of ruthenium trichloride trihydrate ($RuCl_3 \cdot 3H_2O$) was taken and dissolved in (250 mL) methanol, and this solution was refluxed under an N_2 atmosphere. Cooled the reaction mixture after 1h. After cooling, PPh_3 was added, and the solution was again refluxed under the N_2 atmosphere for 3-4 h. A precipitate formed in the hot solution as a tiny black crystal on completion. On cooling, it filtered under the N_2 atmosphere. Washed

with diethyl ether and dried under a vacuum. The obtained product was 600 mg, i.e.,81.74% yield.

2.5. Synthesis of Ru Complex (C1):

Experimental procedure:

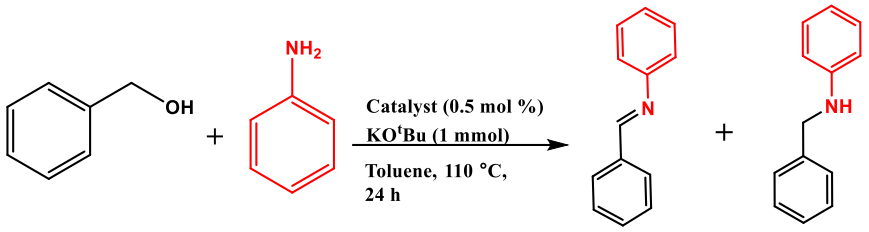
In a schlenk tube, ligand (37.74 mg) and Ag_2O (23.1 mg) were added and stirred at room temperature for 45 min-1 h. After that, $RuCl_2(PPh_3)_3$ (95.88 mg) was added and refluxed overnight (12-18h). Stopped the reaction and filtered it via celite. The filtrate was ppt out with ether. Then the ppt was filtered, and a yellow powder was obtained. Then the ppt was filtered, and a yellow powder was obtained with 57 % yield, i.e., 62 mg. The characterization data exactly matched the previously synthesized complex **C1**.

LCMS (ESI): calculated $[M\text{-}Cl]^+$ = 1038.2203, observed $[M\text{-}Cl]^+$ = 1038.1709. **^{1}H NMR** (500 MHz, DMSO) δ 14.15 (s, 1H), 13.97 (s, 1H), 9.35 (d, *J* = 6.0 Hz, 1H), 9.07 (d, *J* = 5.8 Hz, 2H), 8.13 (d, *J* = 8.2 Hz, 1H), 7.86 (d, *J* = 8.2 Hz, 2H), 7.75 (d, *J* = 8.1 Hz, 1H), 7.72 – 7.65 (m, 2H), 7.60 (d, *J* = 7.0 Hz, 2H), 7.52 (t, *J* = 7.9 Hz, 6H), 7.36 (d, *J* = 8.9 Hz, 10H), 7.25 (d, *J* = 7.9 Hz, 6H), 7.20 (q, *J* = 9.1 Hz, 9H), 7.12 (d, *J* = 8.1 Hz, 7H), 7.08 (d, *J* = 17.1 Hz, 19H), 6.84 (t, *J* = 6.5 Hz, 1H), 6.75 (d, *J* = 7.6 Hz, 3H), 6.52 (d, *J* = 8.9 Hz, 1H), 6.25 (d, *J* = 9.6 Hz, 2H), 6.12 (d, *J* = 8.9 Hz, 2H), 5.75 (d, *J* = 7.6 Hz, 2H), 2.45 (s, 6H). **^{31}P{^{1}H} NMR** (202 MHz, DMSO-d_6) δ 33.68 (s), 25.14(s), 5.97(s, PPh_3).**^{13}C{^{1}H} NMR** (126 MHz, DMSO-d_6) δ 205.14 (d, *J* = 12.7 Hz), 203.33 (d, *J* = 12.9 Hz), 154.52, 154.06, 153.53, 153.30 (d, *J* = 9.2 Hz), 152.35, 140.88, 140.13 (d, *J* = 7.4 Hz), 139.23, 138.38, 137.99, 136.89, 136.54 (d, *J* = 6.4 Hz), 136.38, 133.84, 133.69, 133.33 – 133.02 (m), 132.79, 131.77, 131.62, 131.47, 131.38, 131.16, 131.05, 130.77, 130.35, 130.21, 129.85, 129.62, 129.23 (d, *J* = 7.4 Hz), 128.60 (d, *J* = 8.7 Hz), 128.47 (t, *J* = 4.1 Hz), 124.99, 124.64, 123.93, 123.33, 118.17, 117.83, 117.57, 116.36, 113.76, 112.84, 112.50, 112.23, 111.69, 106.11, 21.27 (d, *J* = 4.1 Hz)., 128.81 – 128.48 (m), 125.79, 125.00, 123.94, 118.18, 117.57, 113.75, 112.50, 112.24, 106.12, 21.54, 21.32.

2.6: N-Alkylation of alcohol with primary amine:

General procedure:

2.6.1 General procedure for imine synthesis and characterization data:



1 eq **1 eq**

In a Schlenk tube, Ruthenium complex (5.36 mg, 0.005 mmol) and the base (KO^tBu) were added. Then, 5 mL of the toluene was added and stirred till the reaction mixture became homogeneous. Then, benzyl alcohol (103.98 µL) was added. After that, the aniline (91.17 µL) was added and heated at 110 ℃ for 24 h. Then stopped the reaction and cooled it. Next, the reaction mixture was filtered. The amount of toluene present in the filtrate was dried under rota vapor to obtain a liquid product. The product was characterized by ^1H and ^{13}C NMR.

2.6.2 NMR Data

2.6.2.1 (E)-N,1-Diphenylmethanimine:

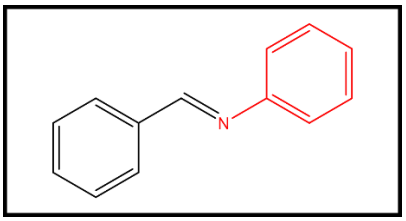


Fig.7: (E)-N,1-Diphenylmethanimine

Black liquid, Conversion: 85 %. LCMS (ESI): calculated $[M+H]^+$ = 182.0964, observed $[M+H]^+$ = 182.0934. ^1H NMR (400 MHz, $CDCl_3$) δ 8.48 (s, 1H, CH=N), 7.94 (dd, J = 6.8, 2.6 H_Z, 2H, Ar-H), 7.51 (d, J = 5.3 H_Z, 3H Ar-H), 7.43 (t, J = 7.8 H_Z, 2H, Ar-H), 7.26 (t, J = 9.2 H_Z, 3H, Ar-H), ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.5 (C=N), 152.2 (Ar-C), 136.3 (Ar-C), 131.5 (Ar-C), 129.2 (Ar-C), 128.9 (Ar-C), 126.0 (Ar-C), 123.0 (Ar-C), 121.0 (Ar-C).

2.6.2.2 (E)-N-Benzyl-1-phenylmethanimine:

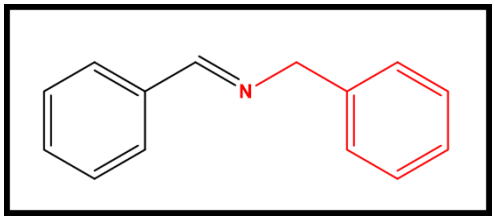


Fig.8: (E)-N-Benzyl-1-phenylmethanimine

Black liquid, Conversion: 83 %. LCMS (ESI): calculated $[M+H]^+$ = 182.1121, observed $[M+H]^+$ = 182.1368. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (s, 1H, CH=N), 7.70 (d, J = 1.5 Hz, 2H, Ar-H), 7.34 (d, J = 5.3 Hz, 3H, Ar-H), 7.28-7.26 (m, 5H), 7.19-7.17 (m, 2H),4.75 (d, J = 1.1 Hz, 2H, Ar-H), ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.9 (C=N), 139.1 (Ar-C), 136.0 (Ar-C), 130.7 (Ar-C), 128.4 (Ar-C), 128.3 (Ar-C), 128.2 (Ar-C), 127.9 (Ar-C), 126.9 (Ar-C), 65.0 (CH_2).

2.6.2.3 (E)-N-Cyclohexyl-1-phenylmethanimine:

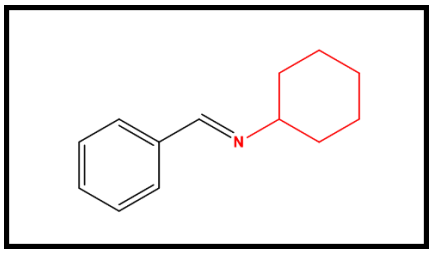


Fig.9: (E)-N-Cyclohexyl-1-phenylmethanimine

Black liquid, Conversion: 82 %. LCMS (ESI): calculated $[M+H]^+$ = 188.1434, observed $[M+H]^+$ = 182.1352. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (s, 1H, CH=N), 7.73 (d, J = 3.9 Hz, 2H, Ar-H), 7.43-7.38(m, 3H), 3.21 (s, 1H), 1.84 (d, J = 16.3 Hz, 2H, Ar-H), 1.74 (d, J = 15.8 Hz, 2H, Ar-H), 1.60 (d, J = 13.4 Hz, 2H, Ar-H), 1.39-1.25 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.8 (C=N), 136.8 (Ar-C), 130.4 (Ar-C), 128.7 (Ar-C), 128.1 (Ar-C), 70.1 (Ar-C), 34.8 (Ar-C), 25.8 (Ar-C), 25.0 (Ar-C).

2.6.2.4 (E)-1-Phenyl-N-(p-tolyl)methanimine

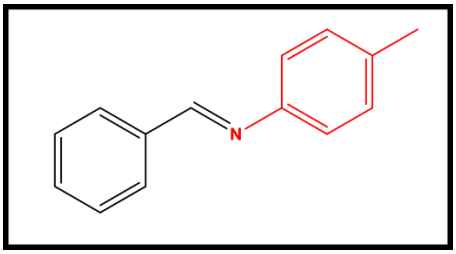


Fig.10: (E)-1-Phenyl-N-(p-tolyl)methanimine

Black liquid, Conversion: 84 %. LCMS (ESI): calculated $[M+H]^+$ = 196.1121, observed $[M+H]^+$ = 196.1029. ^1H NMR (400 MHz, $CDCl_3$) δ 8.25 (s, 1H, CH=N), 7.70 (d, J = 2.3 H_Z, 2H, Ar-H), 7.27-7.24 (m, 3H), 7.00 (d, J = 14.1 H_Z, 2H, Ar-H), 6.95 (d, J = 8.3 H_Z, 2H, Ar-H), 2.17 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.7 (C=N), 149.5 (Ar-C), 136.4 (Ar-C), 135.9 (Ar-C), 131.2 (Ar-C), 129.9 (Ar-C), 128.9 (Ar-C), 123.0 (Ar-C), 121.0 (Ar-C), 21.0 (CH_3).

2.6.2.5 (E)-N-(4-Fluorophenyl)-1-phenylmethanimine:

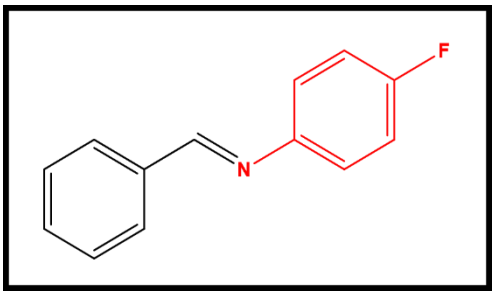


Fig.11: (E)-N-(4-Fluorophenyl)-1-phenylmethanimine

Black Solid, Conversion: 80 %. LCMS (ESI): calculated $[M+H]^+$ = 200.0870, observed $[M+H]^+$ = 200.0827. ^1H NMR (400 MHz, $CDCl_3$) δ 8.21 (s, 1H, CH=N), 7.68 (d, J = 9.5 H_Z, 2H, Ar-H), 7.28-7.22 (m, 2H), 6.97 (d, J = 5.0 H_Z, 2H, Ar-H), 6.87 (d, J = 8.6 H_Z, 2H, Ar-H), ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.29 (C=N), 160.2 (Ar-C), 148.1 (Ar-C), 136.1 (Ar-C), 131.5 (Ar-C), 128.9 (Ar-C), 124.9 (Ar-C), 122.4 (Ar-C), 116.0 (Ar-C), 155.9 (Ar-C).

2.6.2.6 (E)-N-(4-Bromophenyl)-1-phenylmethanimine:

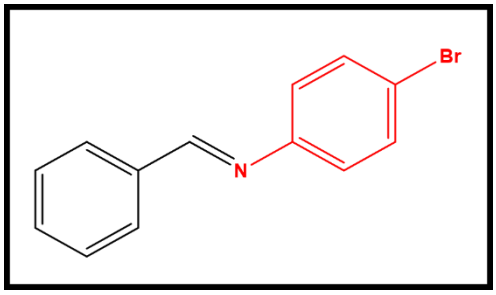


Fig.12: (E)-N-(4-Bromophenyl)-1-phenylmethanimine

Black Solid, Conversion: 82 %. LCMS (ESI): calculated $[M+H]^+$ = 262.0050, observed $[M+H]^+$ = 261.9996. ^1H NMR (400 MHz, $CDCl_3$) δ 8.17 (s, 1H, CH=N), 7.67 (d, J = 7.5 Hz, 2H, Ar-H), 7.26 (d, J = 7.7 Hz, 3H, Ar-H), 6.99 (d, J = 8.8 Hz, 2H, Ar-H), 6.86 (d, J = 8.7 Hz, 2H, Ar-H), ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.8 (C=N), 151.0 (Ar-C), 136.0 (Ar-C), 132.2 (Ar-C), 132.0 (Ar-C), 131.7 (Ar-C), 129.0 (Ar-C), 128.9 (Ar-C), 122.5 (Ar-C), 199.3 (Ar-C).

2.6.2.7 (E)-N-(4-Iodophenyl)-1-phenylmethanimine:

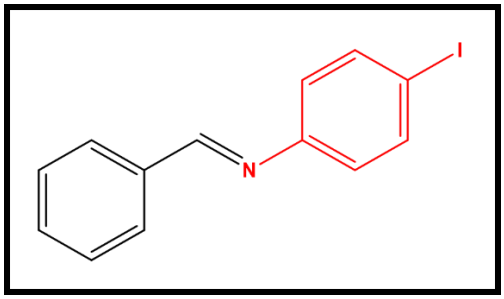


Fig.13: (E)-N-(4-Iodophenyl)-1-phenylmethanimine

Black liquid, Conversion: 65 %. LCMS (ESI): calculated $[M+H]^+$ = 306.9996, observed $[M+H]^+$ = 306.9996. ^1H NMR (400 MHz, $CDCl_3$) δ 8.35 (s, 1H, CH=N), 7.82 (d, J = 7.8 Hz, 2H, Ar-H),7.42 (t, J = 6.8 Hz, 3H, Ar-H),7.33 (d, J = 7.4 Hz, 2H, Ar-H), 6.89 (d, J = 7.8 Hz, 2H, Ar-H), ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.91 (C=N), 151.8 (Ar-C), 138.2 (Ar-C), 138.0 (Ar-C), 137.9 (Ar-C), 131.8 (Ar-C), 129.0 (Ar-C), 129.0 (Ar-C), 128.78 (Ar-C), 123.0 (Ar-C), 90.4 (Ar-C).

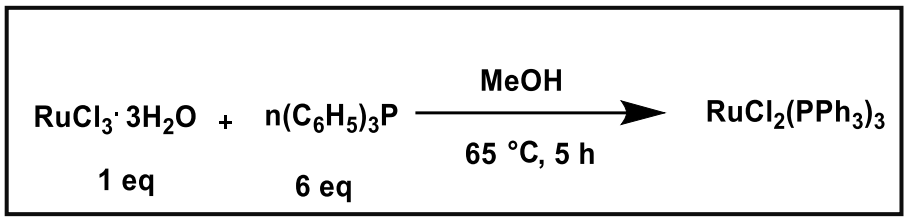
Chapter 3

RESULTS AND DISCUSSION

To investigate the different catalytic activities for the NHC-based ruthenium complexes, we have performed the N-alkylation of amines with alcohols by using previously synthesized complex **C1** and tried to obtain better selectivity for the imine products.

3.1 Synthesis of Metal precursor dichlorotris(triphenylphosphine)ruthenium:

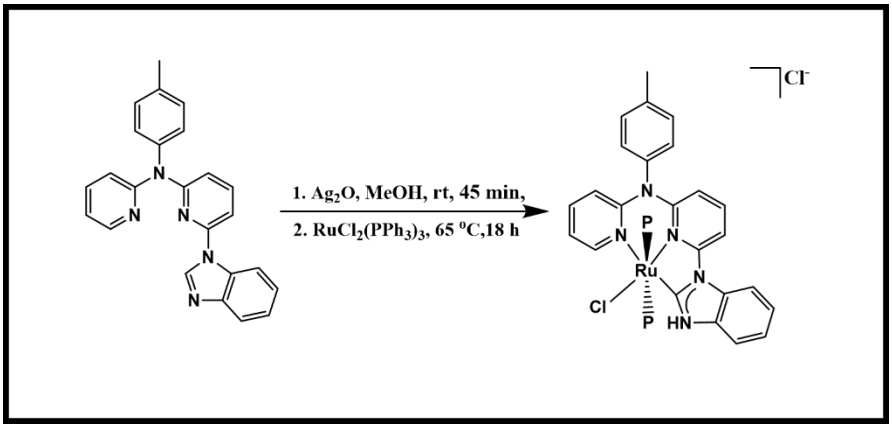
$RuCl_2(PPh_3)_3$ metal precursor was synthesized to carry out the ligand metalation. It was prepared by the commercially available $RuCl_3 \cdot 3H_2O$ and triphenylphosphine under suitable conditions.



Scheme 1: Synthesis of dichlorotris(triphenylphosphine)ruthenium

3. 2 Synthesis of Ru Complex (C1) and Characterization[12]

Ligand and silver oxide were added, and the mixture was stirred continuously under N_2 at rt for 45 min to 1h to generate a silver carbene complex. After that, $RuCl_2(PPh_3)_3$ was added and refluxed overnight to obtain the desired ruthenium complex (**C1**) by transmetallation of the silver complex. Reaction conditions are shown in **Scheme 2** as already mentioned in previous report of our lab.[12] The product was obtained as a yellow powder with a 57 % yield.



Scheme 2: Synthesis of Ru Complex (C1)

Mass data of Ru Complex (C1)[12]:

The LCMS of complex **1** displayed a signal at m/z 1038.17 (z =1) assigned to $[M\text{-}Cl]^+$ that could be seen from **Fig.14.** No other peak is higher than that of 1038.17. Observed mass $[M\text{-}Cl]^+$ = 1038.1709, Calculated mass $[M\text{-}Cl]^+$ =1038.2203.

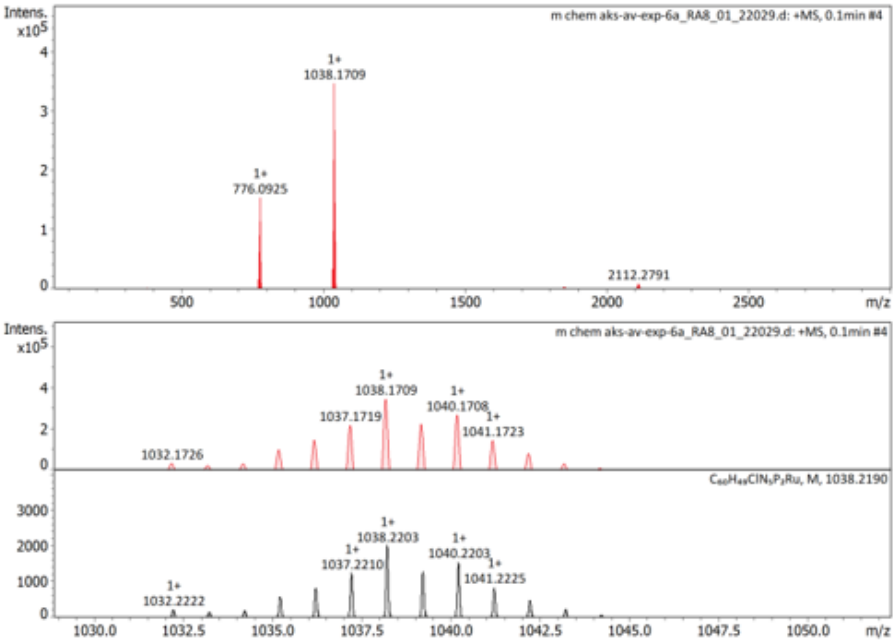


Fig.14: LCMS of Ru complex **(C1)**

NMR data of Ru Complex (C1)[12]

The ^{1}H NMR data clearly showed the existence of NH proton and confirmed the formation of the Ru-pNHC complex. The ^{1}H, ^{13}C, ^{31}P NMR data clearly resembles the previous data.[12] The peak at δ 14.15 and δ 13.97 are for protic NH protons.

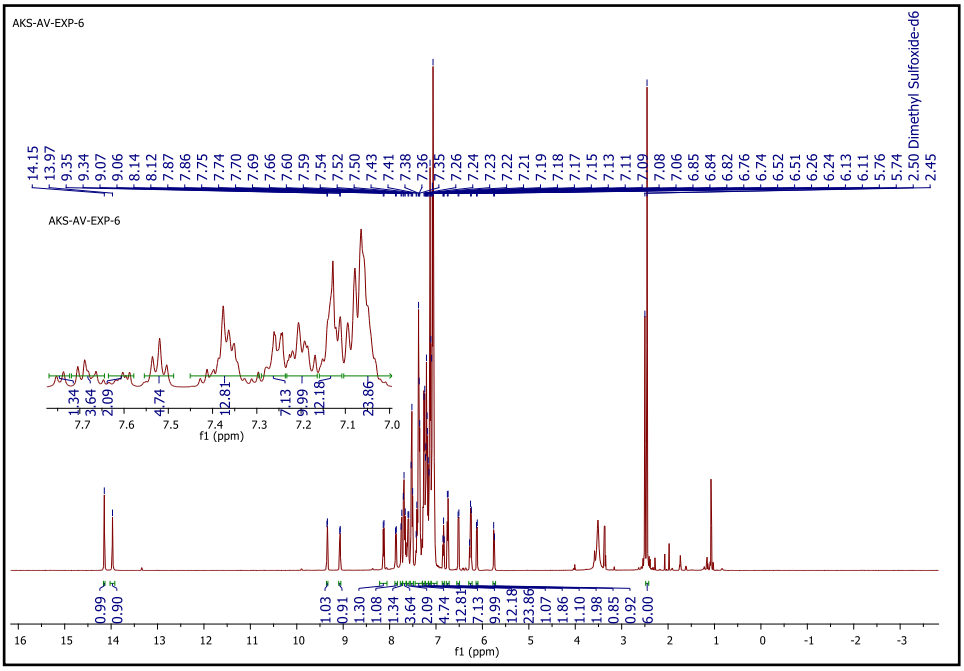


Fig.15: ^{1}H NMR Spectrum of Ru Complex C1

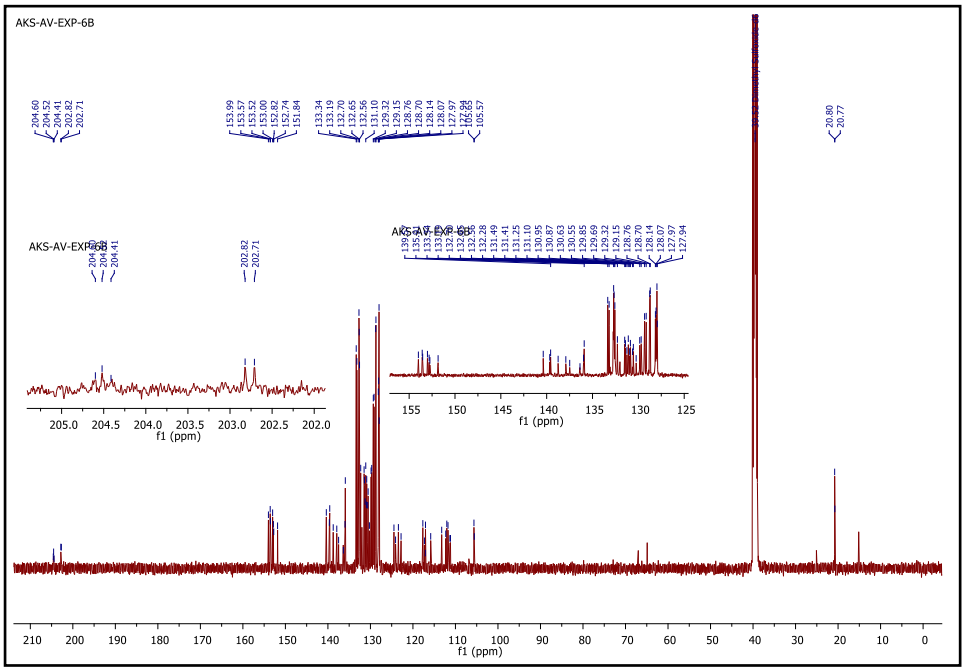


Fig.16: ^{13}C NMR Spectrum of **Ru** Complex C1

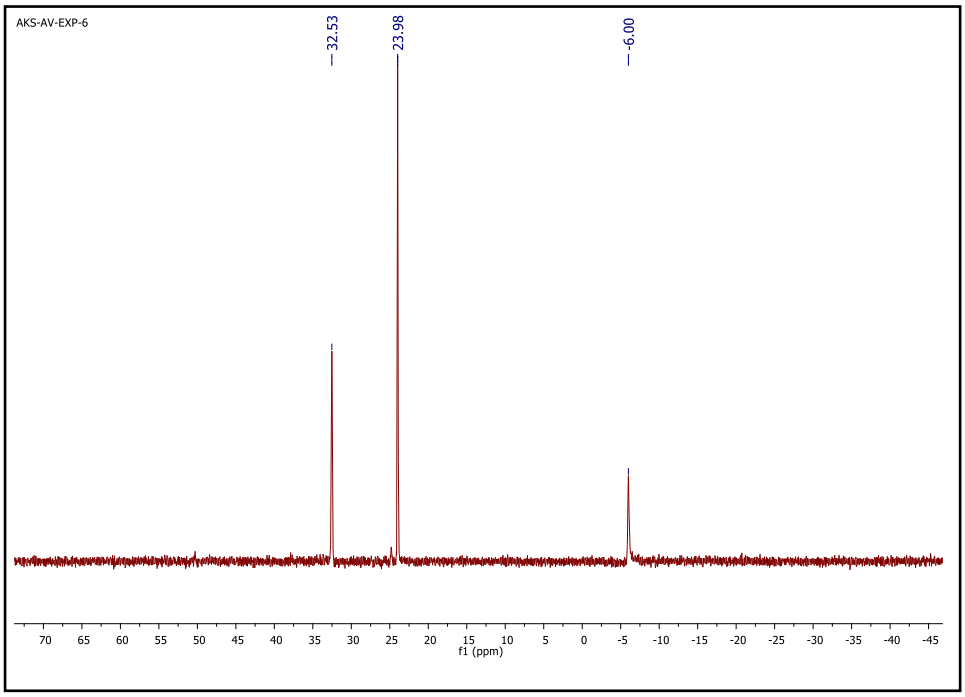
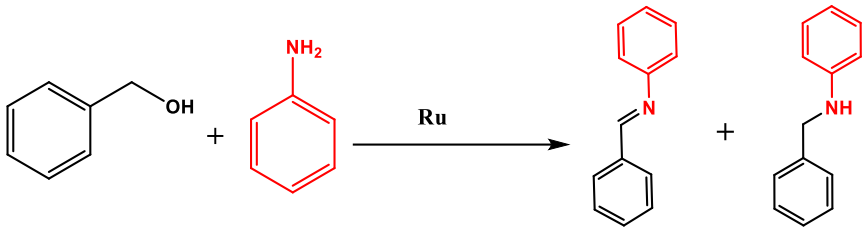


Fig.17: ^{31}P NMR Spectrum of Ru Complex C1

3.3 N-alkylation of primary amines with alcohol:

Optimization of the reaction:



1 eq **1 eq**

Table 1: Optimization of the catalyst loading(%)

Entry	Base mol (%)	Cat mol (%)	Solvent	Temp (℃)	Time (h)	Conversion (%)
1	KO^{t}Bu (100)	1	Toluene	110	24	52
2	KO^{t}Bu (100)	0.5	Toluene	110	24	85
3	KO^{t}Bu (10)	2	Toluene	110	24	7

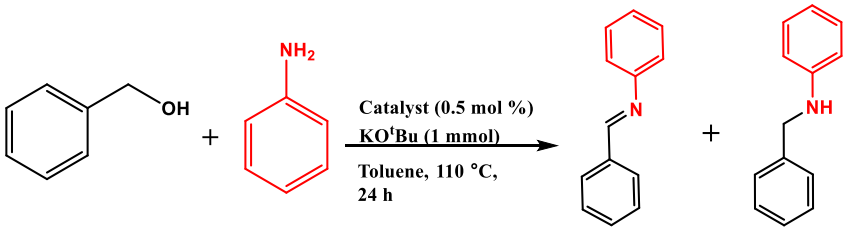
In the above table, the catalyst's effectivity was tested at different mol %; it demonstrated the highest conversion at 0.5 mol % and lowest at 2 mol %. On increasing the catalyst loadings, the conversion % decreases.

Table 2: Optimization of the catalyst and the base loading

Entry	Base mol (%)	Cat mol (%)	Solvent	Temp (℃)	Time (h)	Conversion (%)
1	KO^{t}Bu (10)	1	Toluene	110	24	17
2	KO^{t}Bu (100)	1	Toluene	110	24	52

3	KO^{t}Bu (100)	0.5	Toluene	110	24	85
4	KOH (100)	0.5	Toluene	110	24	51
5	NaO^{t}Bu (100)	0.5	Toluene	110	24	74

In the above table, the different bases and base loading were examined to decide the optimal base to be chosen. KOH was the least performing base, with a conversion of 51 %. Bases like KO^{t}Bu (85 %) and NaO^{t}Bu (74 %) have performed well.



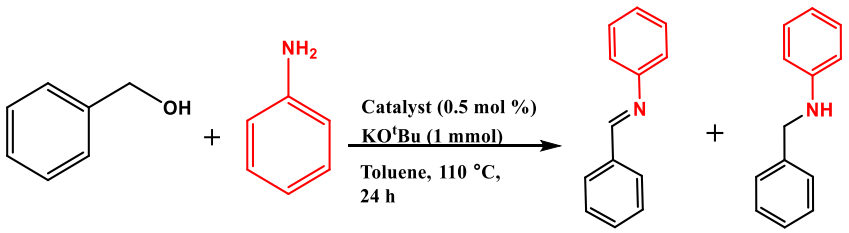
1 eq **1 eq** **85 %**

In this report, we have achieved a greater than 85% conversion. The reaction condition used for obtaining the full reaction conversion was 1 mmol of aniline and 1 mmol of benzyl alcohol, and 100 mol% of KO^{t}Bu. Then, 0.5 mol % catalyst was used in 5 mL of toluene at 100 °C for 24 h. The reaction selectivity to imine was altered by increasing the base amount to 100 mole %, which led to greater than 85% selectivity towards the imines instead of the amine.

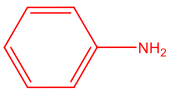
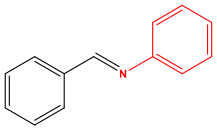
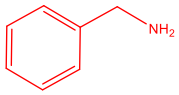
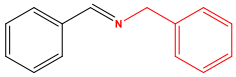
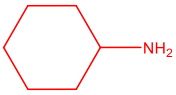
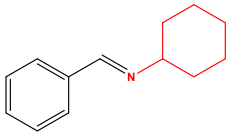
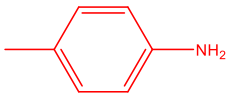
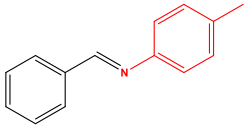
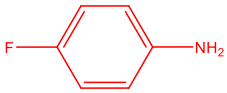
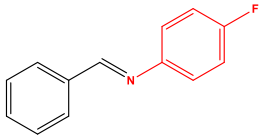
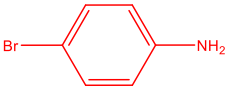
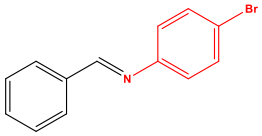
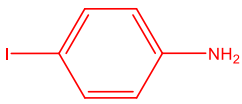
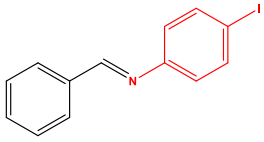
Table 3: Summary of the optimization:

Entry	Base mol (%)	Cat mol (%)	Solvent	Temp (℃)	Time (h)	Conversion (%)
1	KO^tBu (100)	1	Toluene	110	24	52
2	KO^tBu (100)	0.5	Toluene	110	24	85
3	KO^tBu (10)	2	Toluene	110	24	7
4	KO^tBu (10)	1	Toluene	110	24	17
5	KO^tBu (100)	1	Toluene	110	24	52
6	KOH (100)	0.5	Toluene	110	24	51
7	NaO^tBu (100)	0.5	Toluene	110	24	74

Reaction conditions: Benzyl alcohol (1 mmol), Aniline (1 mmol), Ru Catalyst:(0.5 mol %), KO^tBu (1.0 mmol), toluene (5 mL), 110℃, 24 h.



Optimization of the substrate

Entry	Substrate	Product	Conversion (%)	TON/TOF (h)
1			85	170/7.083
2			83	166/6.916
3			82	164/6.833
4			84	168/7
5			80	160/6.666
6			82	164/6.833
7			65	130/5.41

Note: TON = (Number of moles of substrate converted)/(Number of moles of catalyst) at the end of the reaction. TOF = [(TON)/h]

Reaction conditions: Benzyl alcohol (1 mmol), Aniline (1 mmol), KO^{t}Bu (1 mmol), Ru catalyst (0.5 % mol), toluene (5 mL) 24 h, 110 °C

NMR Data

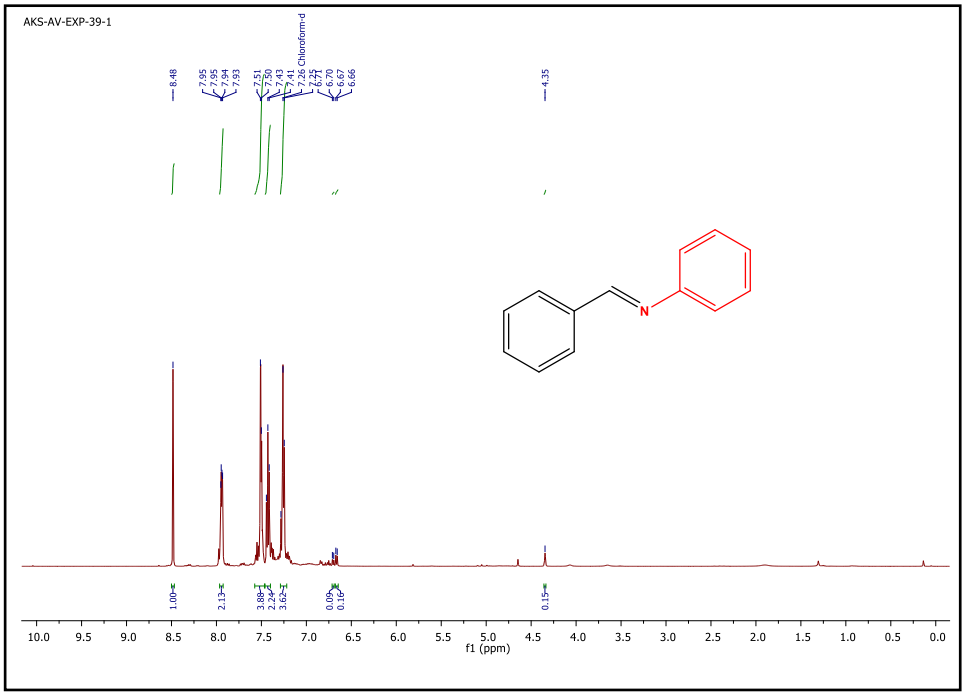


Fig.18: ^{1}H NMR Spectrum of (E)-N,1-Diphenylmethanimine

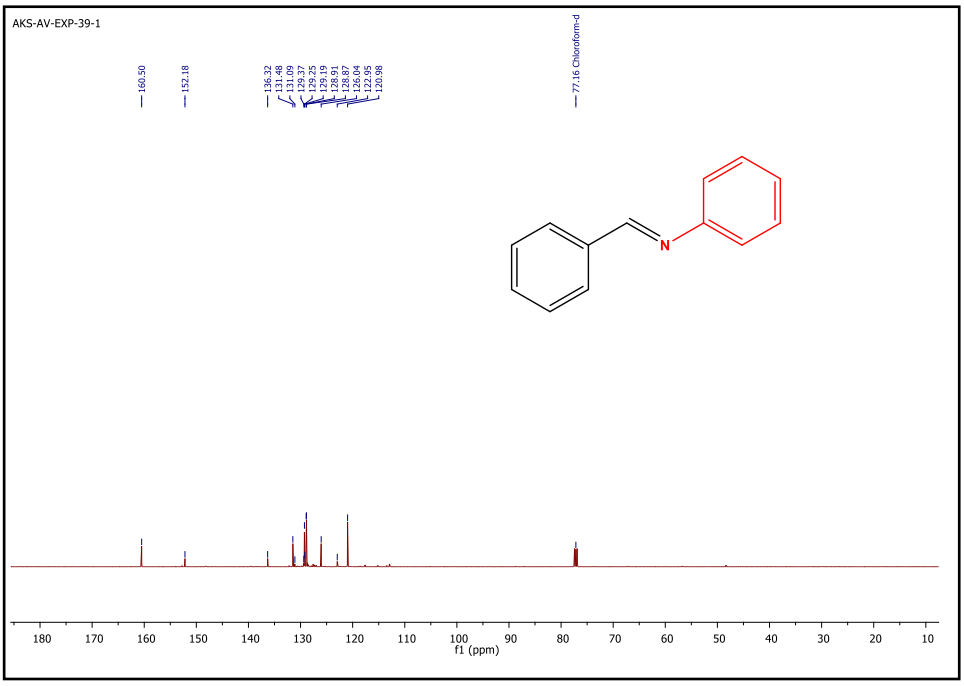


Fig.19: ^{13}C NMR Spectrum of (E)-N,1-Diphenylmethanimine

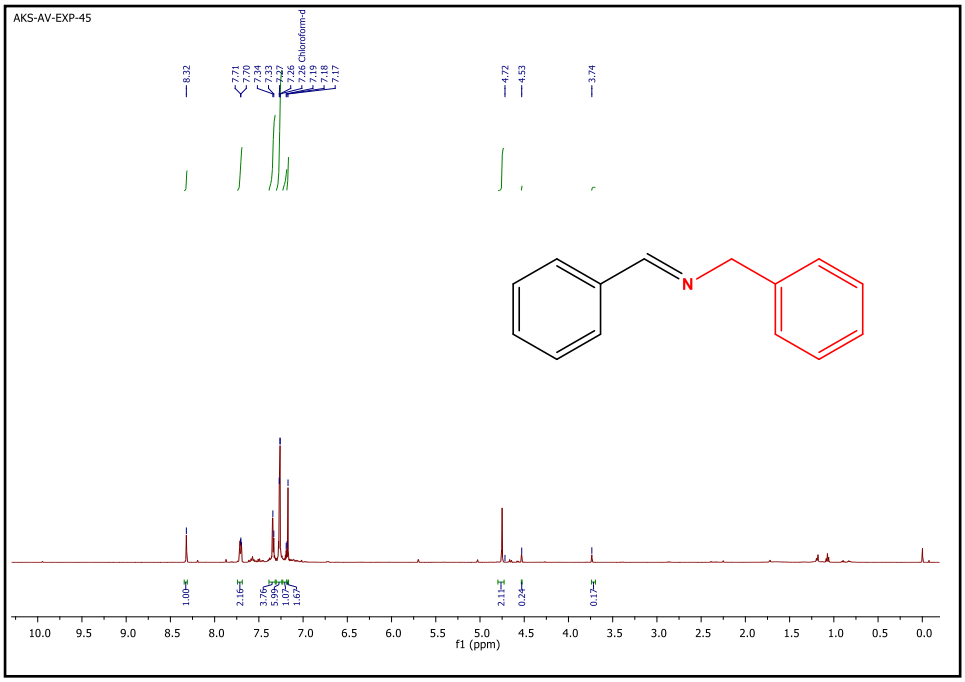


Fig.20: ^{1}H NMR Spectrum of (E)-N-Benzyl-1-phenylmethanimine

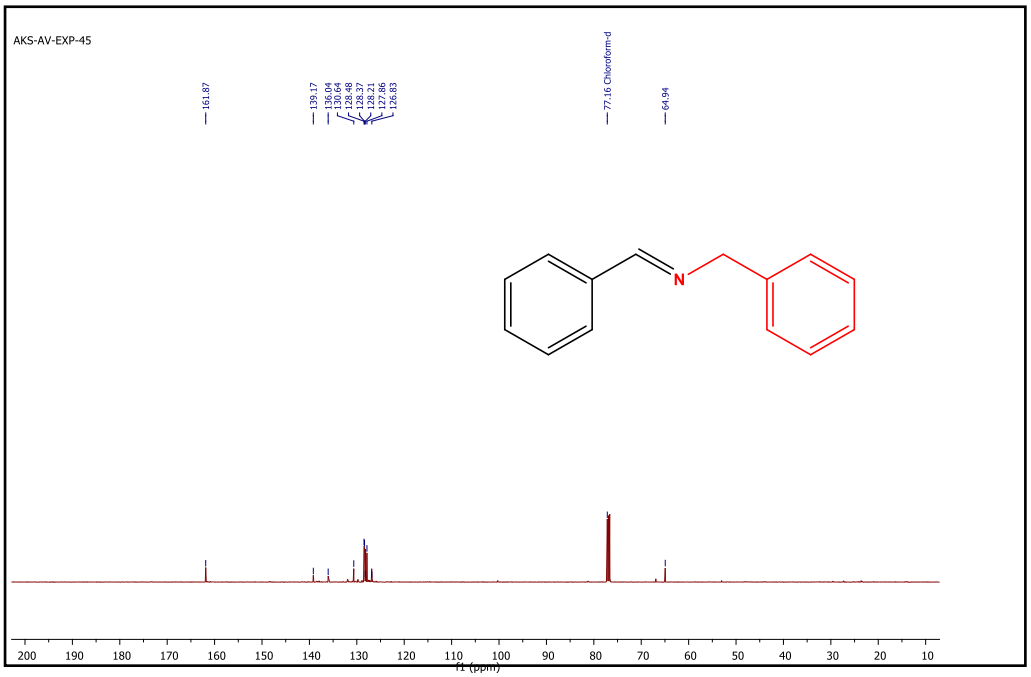


Fig.21: ^{13}C NMR Spectrum of (E)-N-Benzyl-1-phenylmethanimine

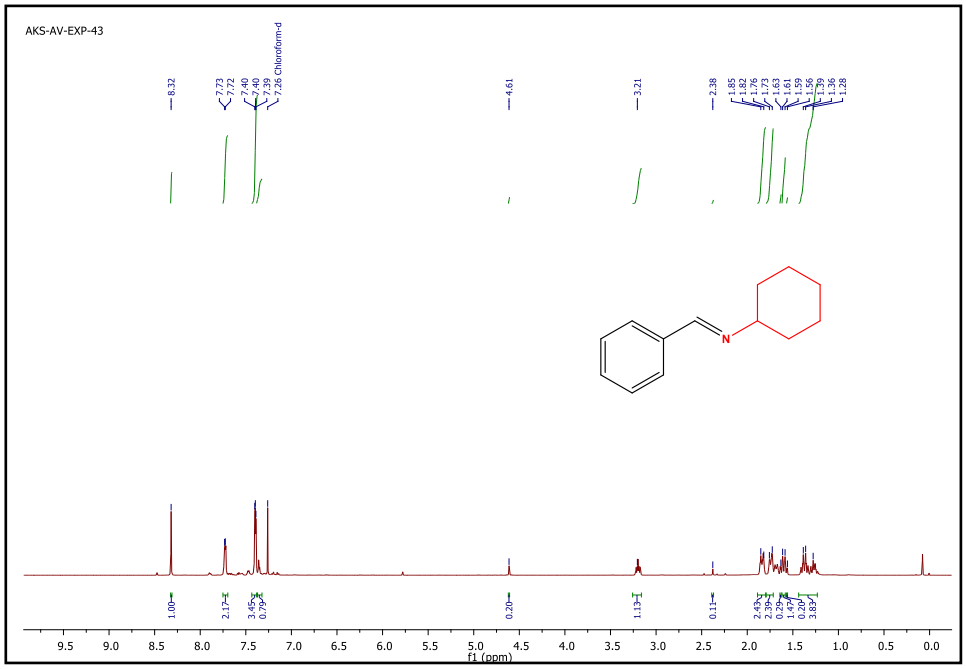


Fig.22: ^{1}H NMR Spectrum of (E)-N-Cyclohexyl-1-phenylmethanimine

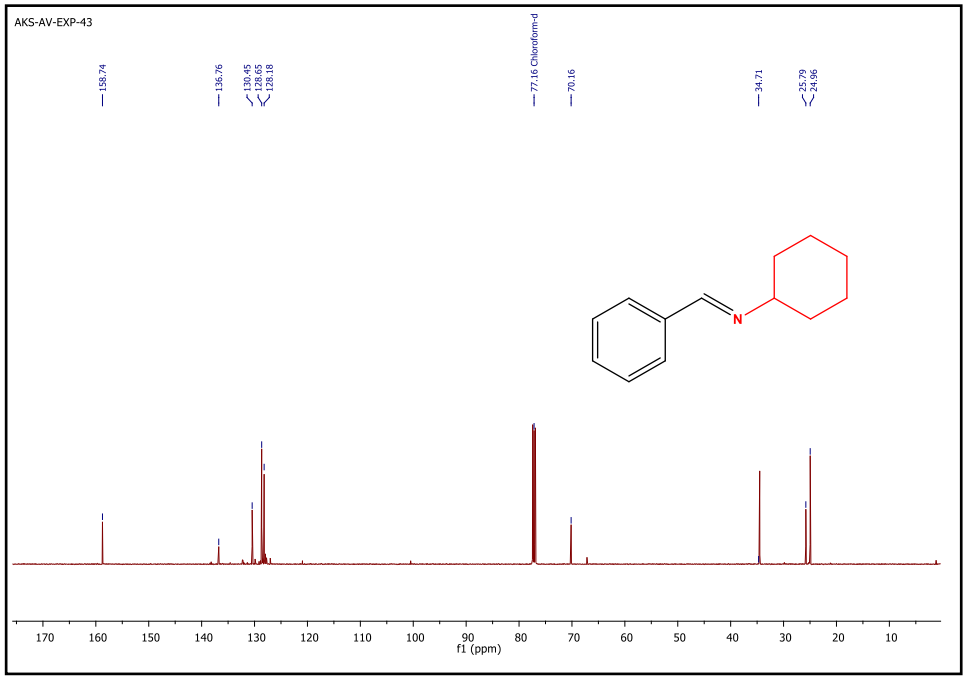


Fig.23: ^{13}C NMR Spectrum of (E)-N-Cyclohexyl-1-phenylmethanimine

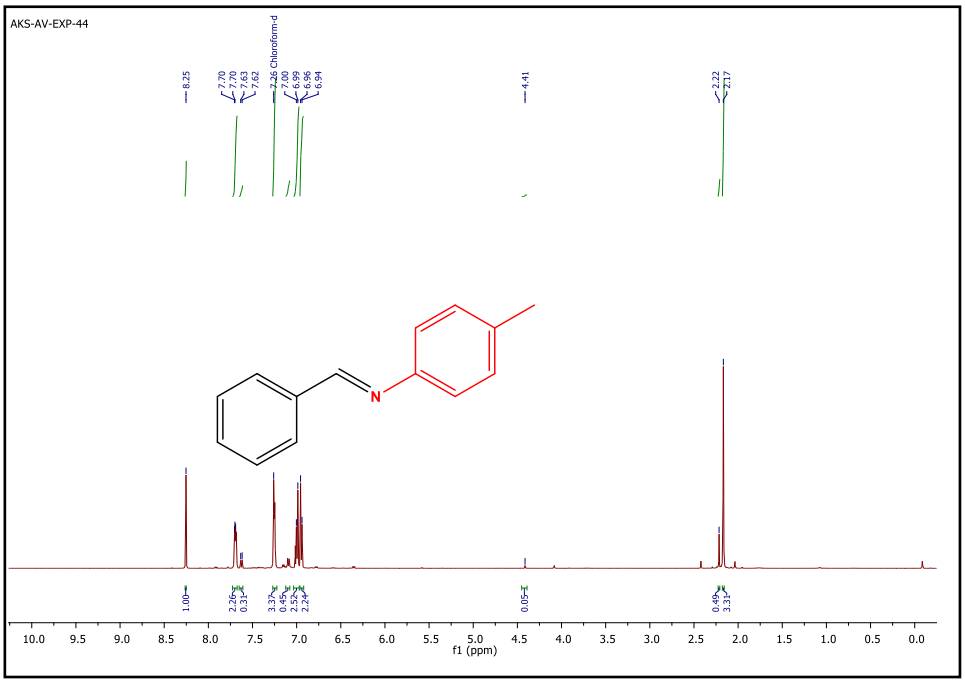


Fig.24: ^{1}H NMR Spectrum of (E)-1-Phenyl-N-(p-tolyl)methanimine

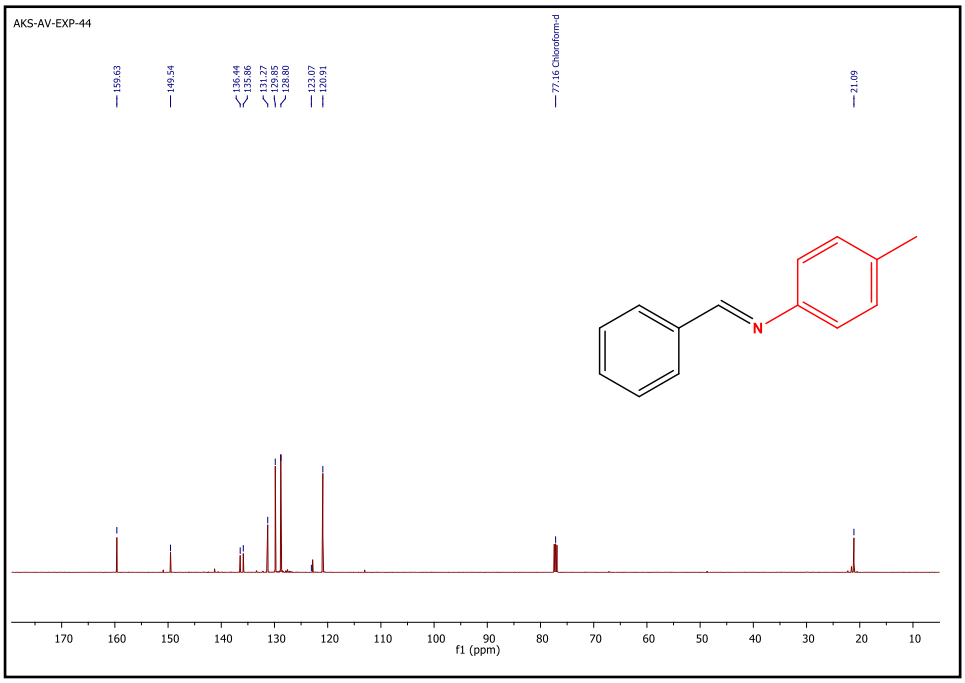


Fig.25: ^{13}C NMR Spectrum of (E)-1-Phenyl-N-(p-tolyl)methanimine

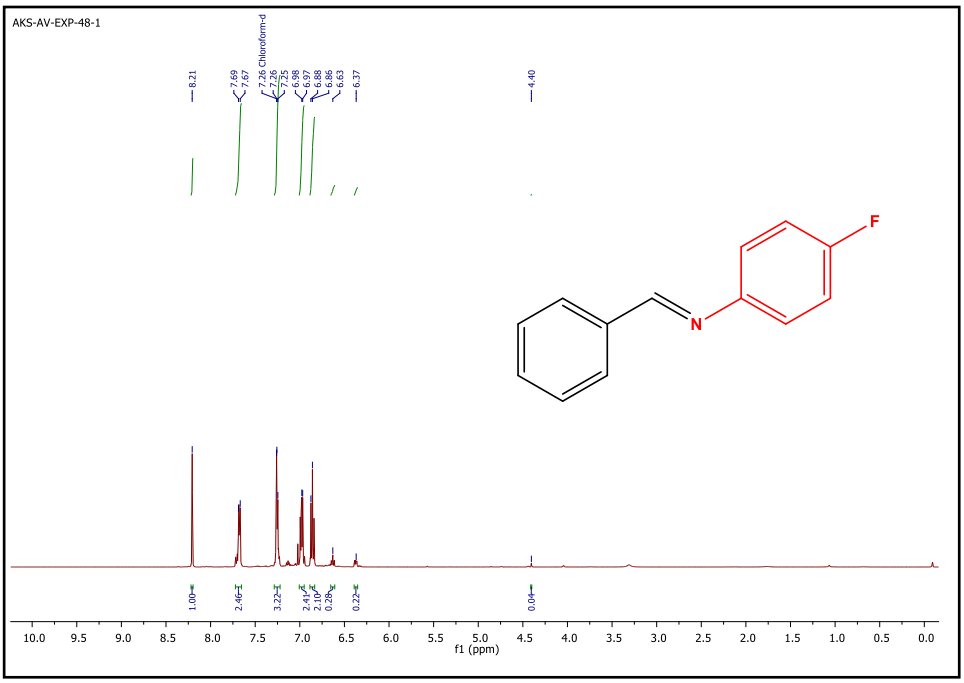


Fig.26: ^{1}H NMR Spectrum of (E)-N-(4-Fluorophenyl)-1-phenylmethanimine

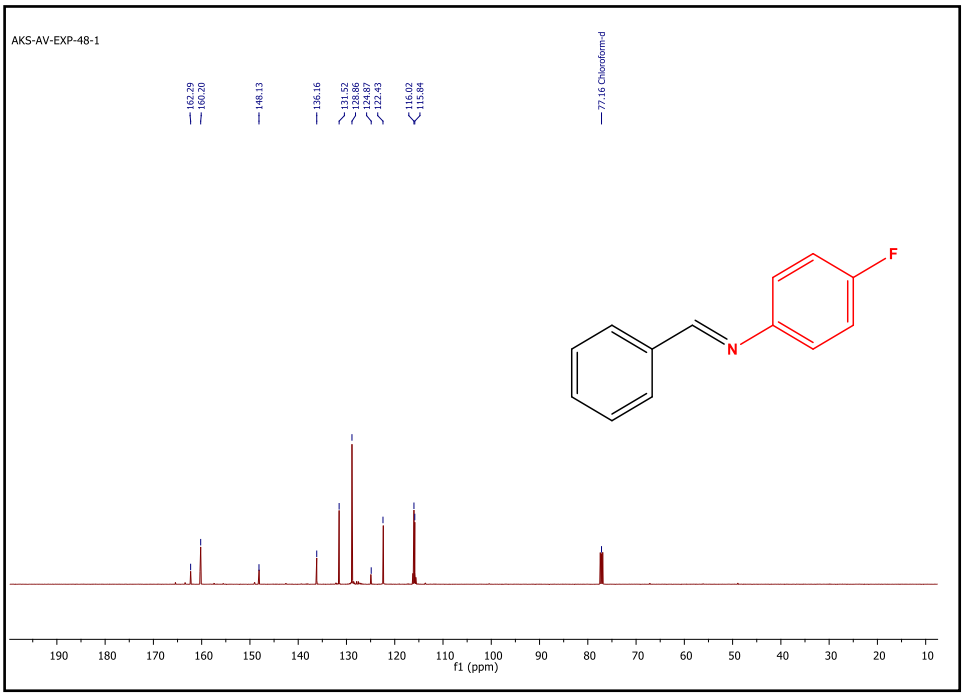


Fig.27: ^{13}C NMR Spectrum of (E)-N-(4-Fluorophenyl)-1-phenylmethanimine

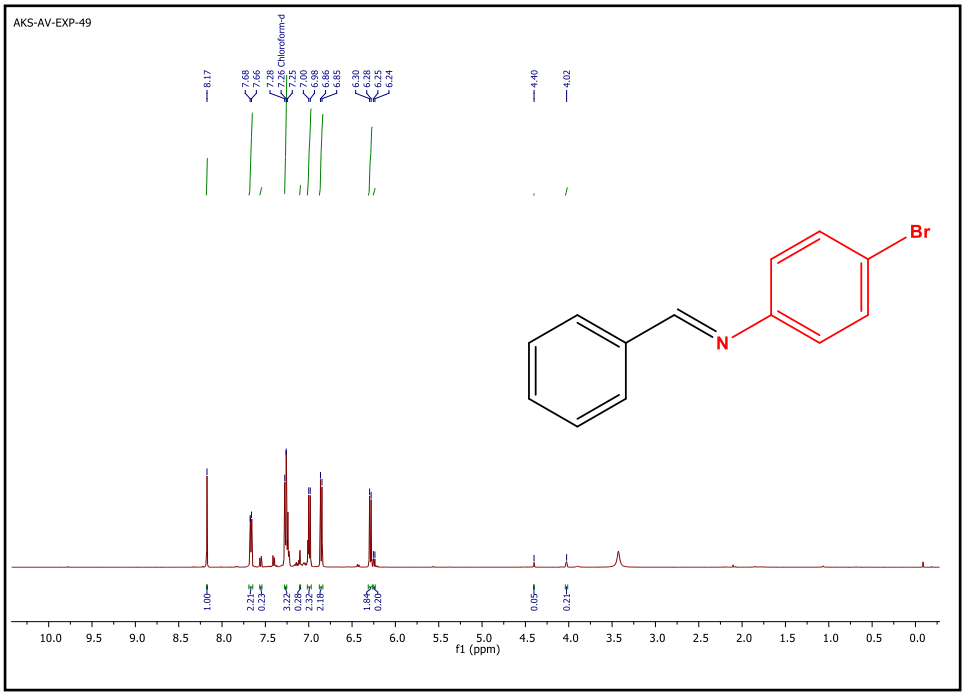


Fig.28: ^{1}H NMR Spectrum of (E)-N-(4-Bromophenyl)-1-phenylmethanimine

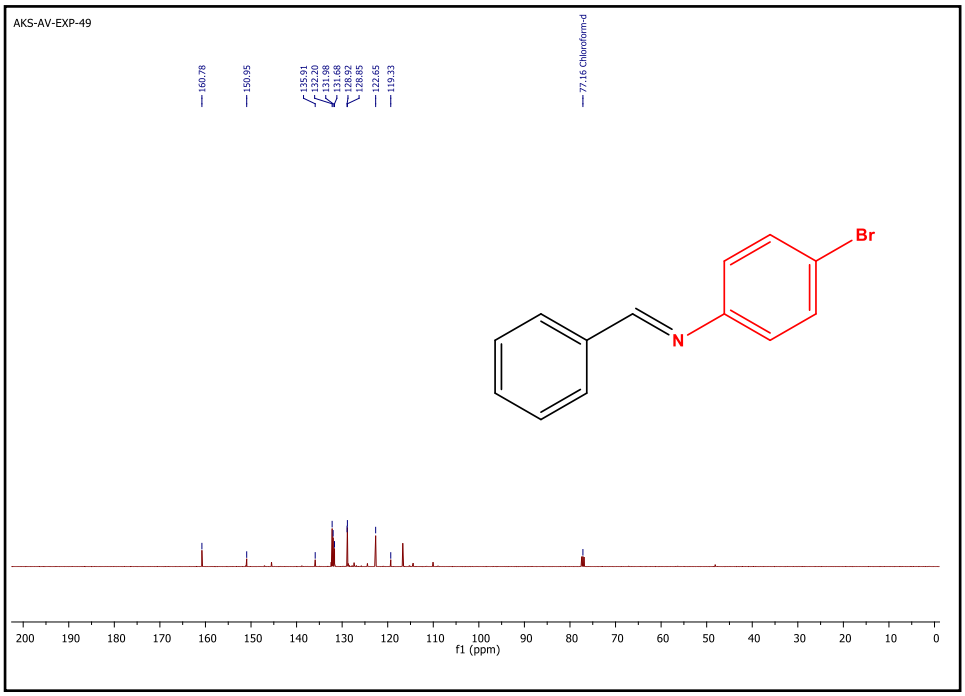


Fig.29: ^{13}C NMR Spectrum of (E)-N-(4-Bromophenyl)-1-phenylmethanimine

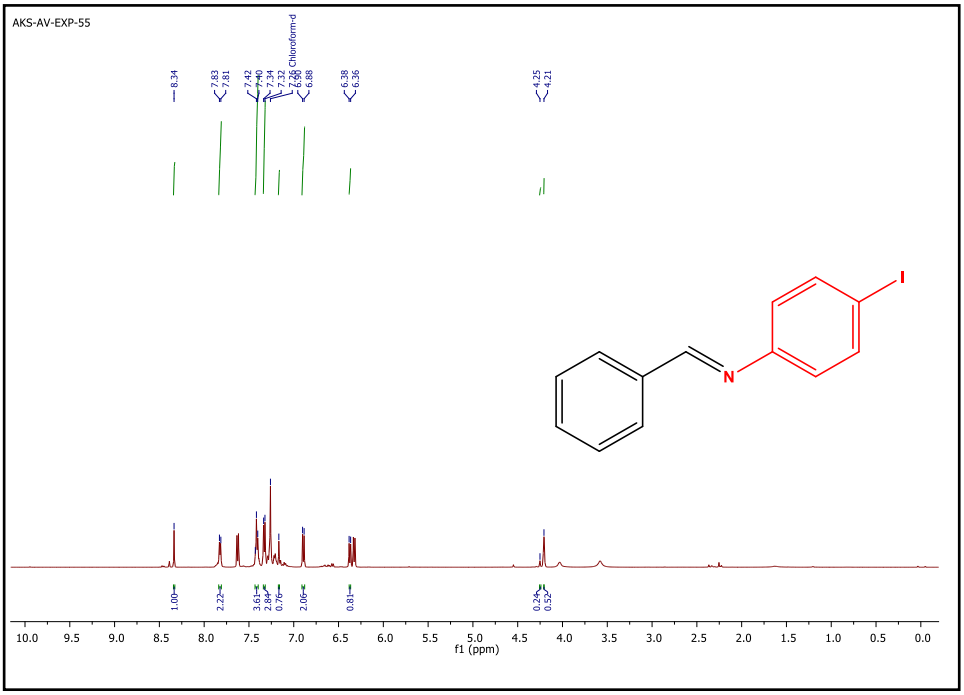


Fig.30: ^{1}H NMR Spectrum of (E)-N-(4-Iodophenyl)-1-phenylmethanimine

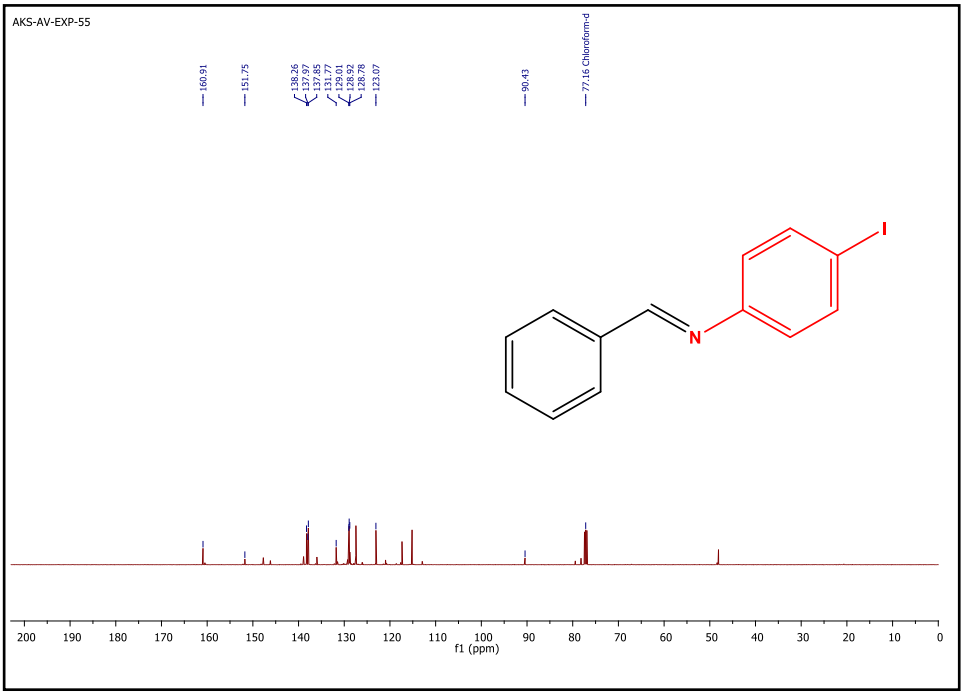


Fig.31: ^{13}C NMR Spectrum of (E)-N-(4-Iodophenyl)-1-phenylmethanimine

Chapter 4

CONCLUSION AND FUTURE PROSPECTIVE

4.1 Conclusion:

In summary, we have performed the N-alkylation of amines with alcohol using the previously synthesized Ruthenium pNHC complex **C1**. All the products obtained by treating various derivatives of amines with alcohol were characterized by ^{1}H and ^{13}C NMR with NMR yield. It was found that the complex **C1** is showing selectivity towards forming imines instead of the amine.

4.2 Future Prospectives:

The N-alkylation of amines with alcohols is one of the many useful applications of ruthenium pNHC complexes. The complex C1 can be used for many applications like hydrogenation-dehydrogenation, hydrogenation of internal and external alkynes, oxidation of water, reduction of CO_2, etc.

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