Nickel-Based Catalysis for Carbonyl and Imine Hydrosilylation

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Certificate of Examination

This is to certify that the dissertation titled *"Nickel Based Catalysis for Carbonyl and Imine Hydrosilylation"* submitted by Mr. Md Misbahur Rahman (Reg. No. MS14056) for the partial fulfillment of BS-MS dual degree programme of the Institute, has been examined by the thesis committee duly appointed by the Institute. The committee finds the work done by the candidate satisfactory and recommends that the report be accepted.

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Declaration

The work presented in this dissertation has been carried out by me under the guidance of Dr. Debashis Adhikari at the Indian Institute of Science Education and Research Mohali.

This work has not been submitted in part or in full for a degree, a diploma, or a fellowship to any other university or institute. Whenever contributions of others are involved, every effort is made to indicate this clearly, with due acknowledgment of collaborative research and discussions. This thesis is a bonafide record of original work done by me and all sources listed within have been detailed in the bibliography.

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In my capacity as the supervisor of the candidate's project work, I certify that the above statements by the candidate are true to the best of my knowledge.

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Notations and Abbreviations

NMR	Nuclear Magnetic Resonance
δ	Chemical Shift
^{o}	Degree
acac	acetyl acetonate
Ar	Aryl
aq.	Aqueous
br	broad
Bu	butyl
d	doublet
DCM	dichloromethane
dd	doublet of doublet
eq.	equation
equiv.	equivalent
^{i}Pr	isopropyl
KO^{t}Bu	Potassium tert-butoxide
m	milli/mutiplet
µ	micro
Me	methyl
mg	milli-gram
mL	milli-litre
µL	micro-litre
mmol	millimole
mol	mole
Ph	phenyl
Ppm	parts per million
q	quartet
rt	room temperature
rxn	reaction
s	singlet
t	triplet
^{t}Bu	tert-butyl
td	triplet of doublets

Table of Contents

Abstract

The amine functional group constitutes an essential component of agrochemical, biological and pharmaceutical compounds: amino acids, vitamins and commonly used analgesics. Various methods have been reported in the literature for the synthesis of amines which includes reductive amination of carbonyl derivatives with primary amines, but it often requires extreme reaction conditions to carry out the conversion. Another method to make amines is metal catalyzed reduction of the amide group, but it bears limited scope due to lower electrophilicity at the carbonyl group. An easy, direct and efficient method is metal catalyzed reduction of imines. This includes hydrosilylation as an efficient method which creates a convenient pathway for hydrogen transfer from readily available silanes via the metal catalyst to the substrate.

The effective one-step reduction of carbonyl, as well as protection of alcohol, can be achieved by metal-catalyzed hydrosilylation rather than conventional tedious two-step method of first reducing the carbonyl and then protecting the alcohol.

In chapter 1, a short overview of different methods for amine and alcohol synthesis from respective imines and carbonyl, hydrosilylation and its advantage, synthesis of NacNac ligand, and its Ni complex has been discussed.

In chapter 2, Hydrosilylation of carbonyl and imine using Ni- NacNac catalyst, plausible mechanism and substrate sope have been discussed. Also, Alcohol dehydrogenation using $Ni(Azo)_2$ and other attempted projects which includes, C–H activation via single electron transfer using PLY ligand; pyridine catalyzed C–H activation has been discussed.

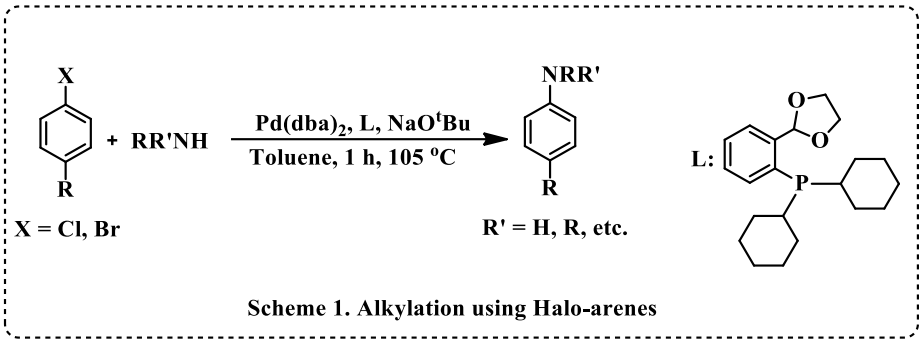
Key words: hydrosilylation, carbonyl, imine, silane, nickel, NacNac ligand.

Chapter 1

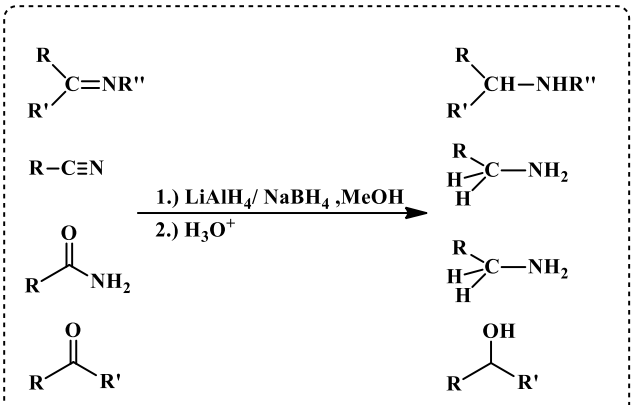
Introduction

1.1 General

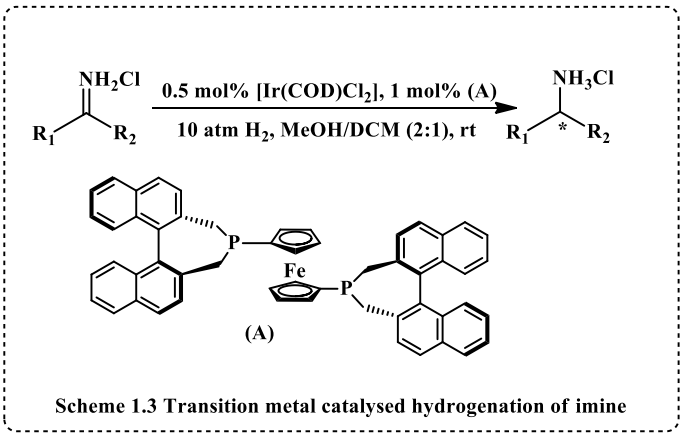
Amines are regarded as an essential functional group in synthetic chemistry due to its applications in biological, pharmaceutical and medicinal chemistry, agrochemical industry.[1] Numerous methods are reported in the literature for the synthesis of amines. It includes alkylation using alcohols or haloalkanes to prepare amines. However, the limitation here is to control the degree of alkylation with alkyl iodide and bromide (Scheme 1).[2,3] An alternative route is reductive amination of carbonyl derivatives. However, the drawback is the harsh reaction condition required to carry out the conversion.[4] Another method for the preparation of amine derivatives is the reduction of amides, imines or nitriles. For this method, the stoichiometric amount of reactive alkali hydrides, such as lithium aluminium hydride and boron hydrides are used as a reducing agent to prepare amines. However, this method still raises concern, due to the waste generation of metallic salt by-product when reactions are performed on a large scale, the lack of functional group tolerance and sensitivity of reducing agents (Scheme 1.2).[5]



Scheme 1. Alkylation using Halo-arenes



Scheme 1.2 Reduction using reactive Alkali hydrides: $NaBH_4$ or $LiAlH_4$



Scheme 1.3 Transition metal catalysed hydrogenation of imine

In this area transition metal catalyzed hydrogenation (Scheme 1.3)[6] or hydrosilylation are being regarded as the straightforward way in the synthesis of amines. If hydrogenation is considered, high temperature and pressure required for the reaction, lack of chemoselectivity still makes this process challenging.[7,8] If hydrosilanes are

considered, they are being regarded as a good alternative to alkali hydrides and hydrogen due to their ability to easily get activated under mild conditions, ease of handling and their stability.[9]

1.2 Hydrosilylation

The hydrosilylation reaction is considered as one of the most crucial methods to form silicon-carbon, silicon-oxygen, silicon-nitrogen bond, which can be further utilized for many organic transformations. In organic synthesis, the number of multiple bonds may be involved, where the hydrosilylation reaction can be regarded as a convenient method for the synthesis of numerous silicon-containing organic compounds and a suitable way of reducing organic molecules. It proceeds via the addition of hydride source i.e. silicon hydrides (Et_3SiH, Ph_3SiH, Ph_2SiH_2, $PhSiH_3$, PMHS, etc.) to the multiple bonds such as carbon-carbon, carbon-oxygen, carbon-nitrogen, nitrogen-nitrogen, nitrogen-oxygen as presented in Fig. 1.

Transition metal-catalyzed hydrosilylation is an attractive process. Because, a sequence of hydrosilylation and hydrolysis leads to the formation of alcohols and amines respectively from carbonyls and imines. During this transformation, silyl group may also be retained as a protecting group, a process that can be of great interest in organic synthesis. This method appeals from a synthetic point of view if the substrate is being used for multi-step synthesis. Thus, both the reduction and protection are carried out in a single, atom-efficient fashion.

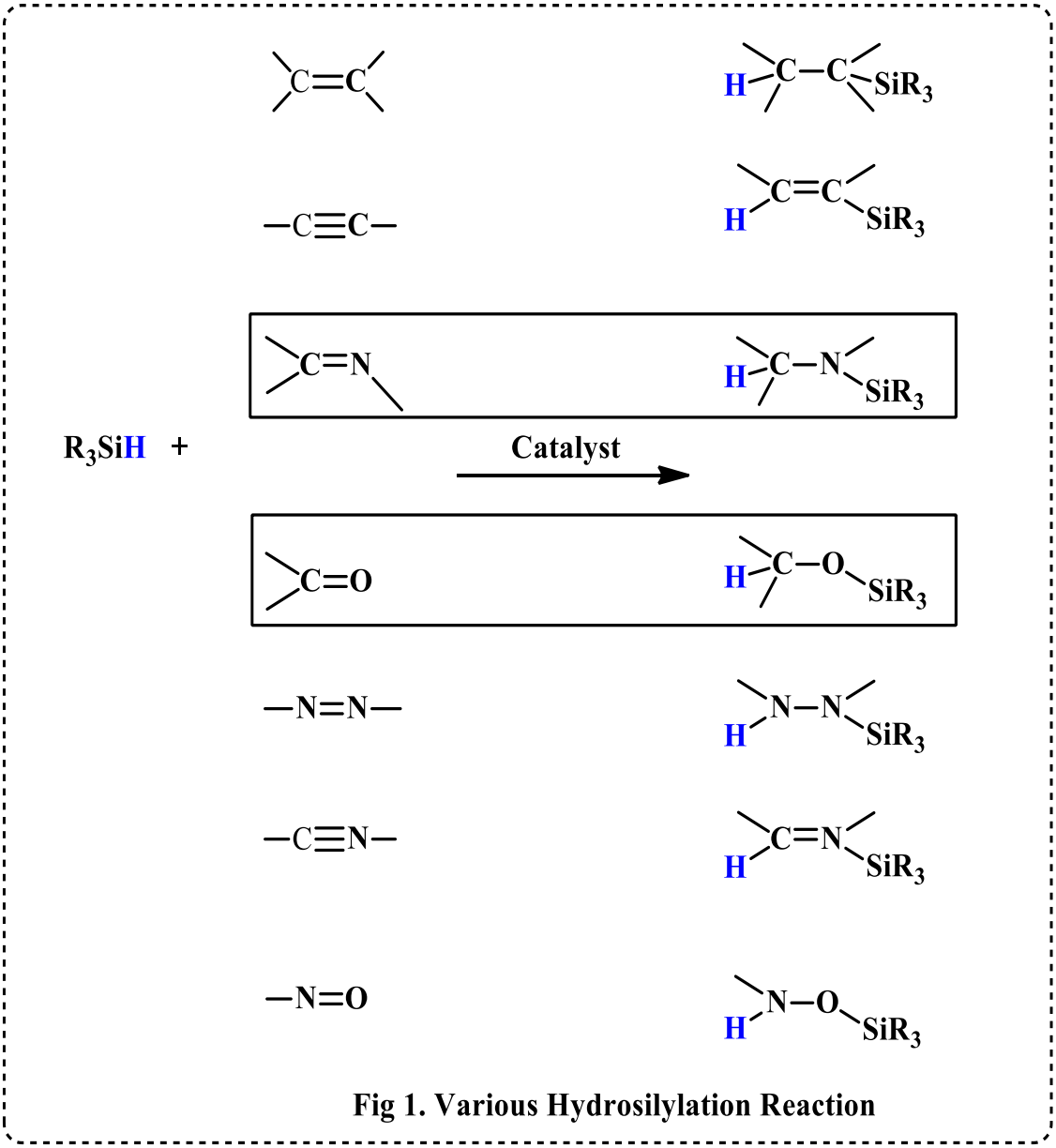
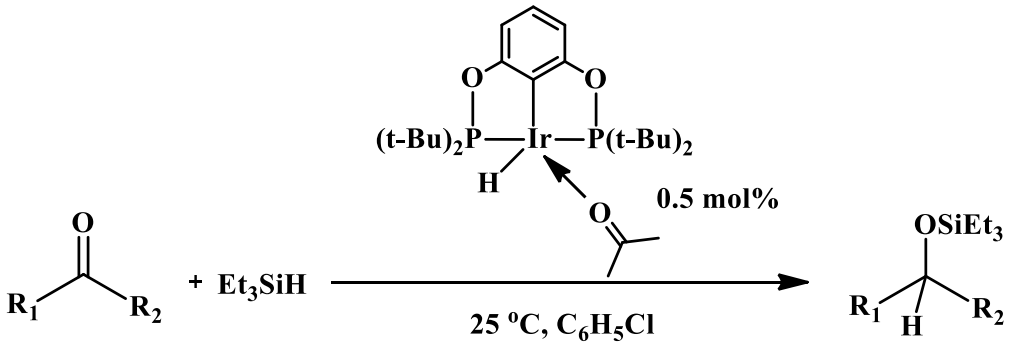


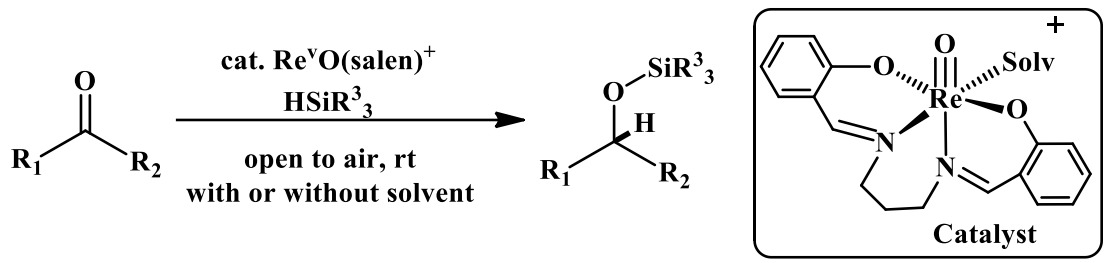
Fig 1. Various Hydrosilylation Reaction

1.3 Noble metal catalyst

Many metal complex, especially noble metals like iridium, rhenium, rhodium and ruthenium are well known to catalyze hydrosilylation. Some of the recent work on them are discussed here (Scheme 1.4) and (Scheme 1.5). [10,11]

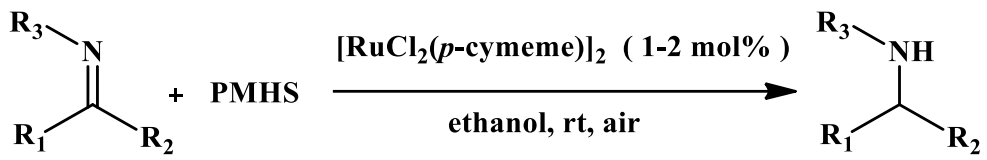


Scheme 1.4 Hydrosilylation of carbonyl using Iridium Catalyst



Scheme 1.5 Hydrosilylation of carbonyl using Rhenium Catalyst

Similarly, various work on hydrosilylation of imine to produce amine has been reported and one of them is discussed here (Scheme 1.6) using ruthenium catalyst with inexpensive, easily available, stable reducing silane such as PMHS.[12]



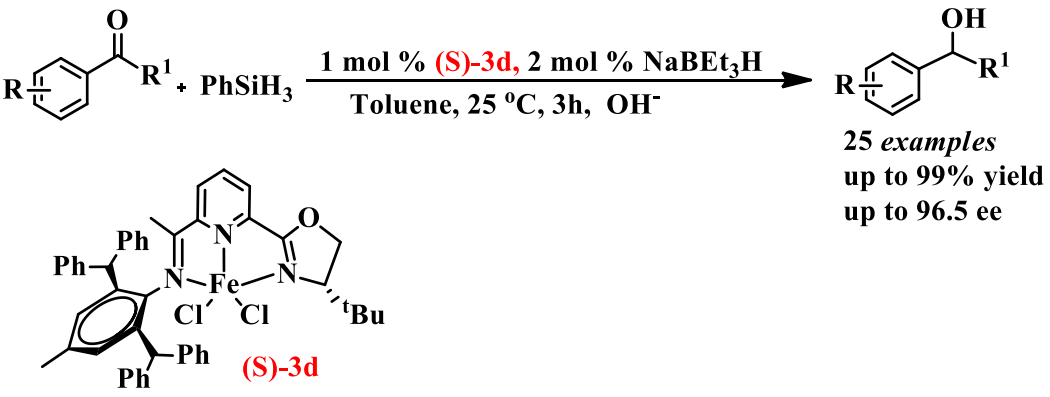
Scheme 1.6 Hydrosilylation of imine using Ruthenium Catalyst

owever, the limited availability, higher cost and toxicity associated with heavy metals prompt scientists to search for a base metal laternatives. The demand for non-precious metal-based hydrosilylation catalyst has led to the development of inexpensive, environmentally benign and earth-abundant metals such as Ni, Co, Cu, Fe and Mn for such transformations.

1.4 Base metal catalyst

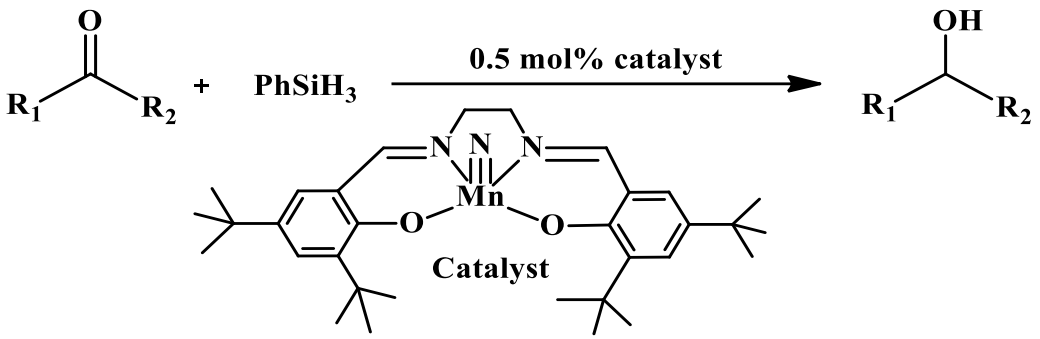
-

Various studies on hydrosilylation using base metal catalyst has been done in recent years. Iminopyridine-oxazoline (IPO) iron complex is used as a catalyst with diphenylsilane (Ph_2SiH_2) as a hydride source for hydrosilylation of carbonyl which is discussed in (Scheme 1.7).[13]



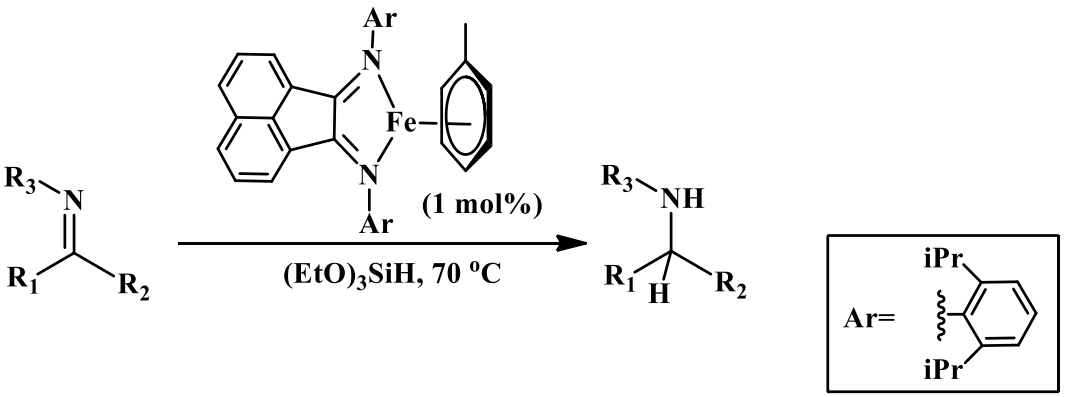
Scheme 1.7 Hydrosilylation of carbonyl using Iminopyridine-oxazoline (IPO) iron complex and diphenylsilane

Another example of earth-abundant, and inexpensive base metal, low catalyst loading, and functional group tolerance is shown by manganese salen complex which acts as precatalyst and phenylsilane as hydride source (scheme 1.8).[14]



Scheme 1.8 Hydrosilylation of carbonyl using Manganese salen Precatalyst

Imine to amine conversion through Fe-BIAN (full form of BIAN needs mention) catalyzed hydrosilylation reaction have been recently reported (Scheme 1.9).[15]



Scheme 1.9 Iron catalyzed hydrosilylation of imine

1.5 β-diketiminate (NacNac) ligand

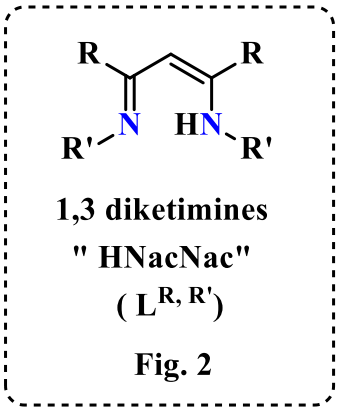


Fig. 2

β-diketimines is among the most ubiquitous chelating ligand in coordination chemistry.[16] β-diketiminate, commonly known as "**NacNac, (L$^{R, R'}$)**" is analogous to acatylacetonate (acac) ligand. The oxygen atoms in acac is replaced by NR moieties in NacNac. The variation of R group on nitrogen can be hydrogen, alkyl, aryl or silyl. The substituent at N atom provides steric protection at metal centre that the oxygen in case acac is unable to offer.[16,17]

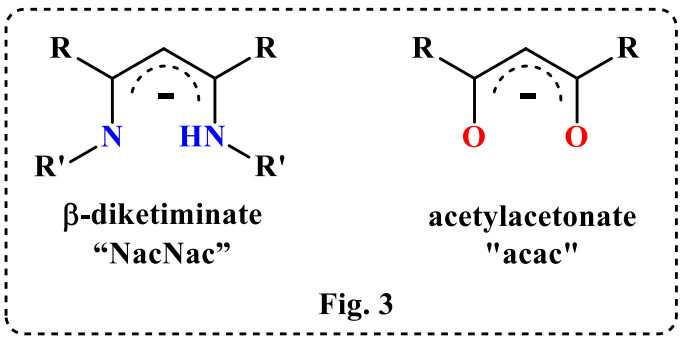


Fig. 3

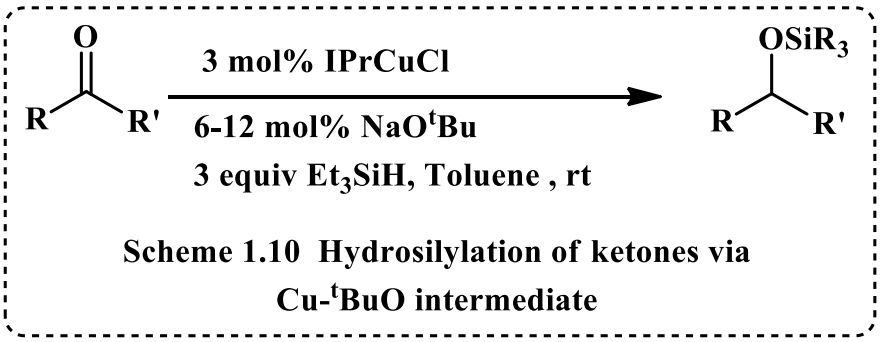
NacNac hs been shown enormous promise as a good ancillary ligand, which in turn helps to stabilize or generate unique coordination environment and stabilizes high as well as low oxidation states.[17] It can also support reactive organometallic reagents or catalysts. NacNac is more popular among chemists due to its ease in preparation, monoionic and chelating nature, with the variable mode of hapticity. This class of ligand draws significant interest due to its ability to tune the electronic as well as steric properties.[16–18] β-diketiminates have been discovered long back at 1960s, but only in late 1990s chemists did incorporate

diisopropylphenyl ligand that surrounds the metal ion, and start using it for multiple purposes.[16,19,20]

The first β-diketiminates metal complex was reported in 1968,[19,20] since then enormous amount of work has been accomplished using this ligand in small molecule activation, catalysis, polymerization, materials etc. .[21,22] Recently, β-Diketiminato manganese(II) complex have been used for hydrosilylation of alkene.[23]

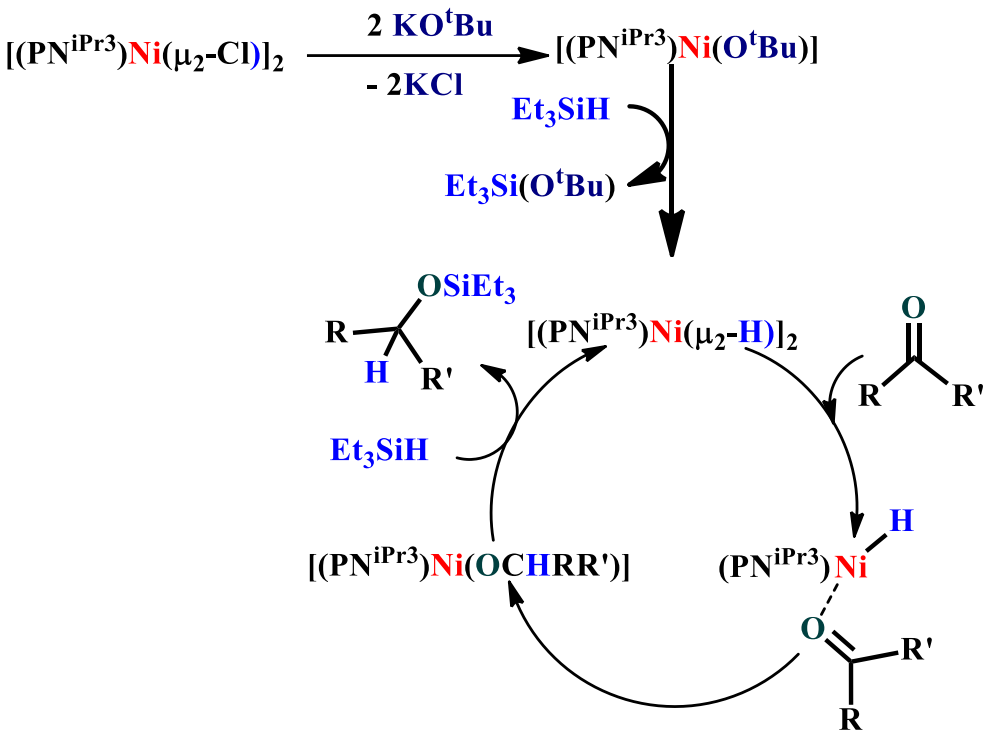
1.6 Ni-NacNac Complex

A number of catalysts are reported for hydrosilylation of the carbonyl. Cu(I) in the form of (IPr)CuO^{t}Bu (IPr) *N*,*N*′-bis(2,6-diisopropylphenyl)imidazol-2-ylidene) are reported to show hydrosilylation with various silanes (Scheme 1.10). On reacting the precursor complex (IPr)Cu(O^{t}Bu) with stoichiometric triethoxysilane, $(EtO)_3SiH$, $[(IPr)Cu(\mu_2\text{-}H)]_2$ dimer was formed via alkoxide-silyl σ-bond metathesis reaction. In addition, the byproduct, $(EtO)_3SiO^tBu$, was observed by ^1H NMR spectroscopy when the reaction was conducted in a stoichiometric fashion, therefore confirming the role of the silane in the σ-bond metathesis step.[24,25]



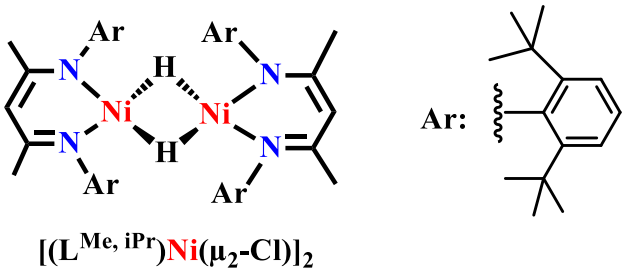
Scheme 1.10 Hydrosilylation of ketones via Cu-^{t}BuO intermediate

A similar protocol had been reported using Ni (II) precursor capable of conducting the hydrosilylation of ketones and aldehydes, utilizing Et_3SiH as the hydride source. In these reactions, reactive transient nickel hydride mediates the catalytic hydrosilylation (Scheme 1.11).[26]



Scheme 1.11 Hydrosilylation of carbonyl functionality mediated by $[(PN^{iPr3})Ni(\mu_2\text{-}Cl)]_2$ with KO^tBu and Et_3SiH

Various bis(*β*-diketiminato)nickel complexes have been reported earlier.[19] Ni(II) with neutral *β*-diketimine ligand have been synthesized and reported in the literature. Ni(II) with *β*-diketiminate ligand, $[(L^{Me,\ iPr})Ni(\mu_2\text{-}H)]_2$ (Fig.4) have been synthesized and reported.[27,28] It has also been used for H_2 and N_2 activation.[21] However, it has not been reported for hydrosilylation of carbonyl and imine.



$[(L^{Me,\ iPr})Ni(\mu_2\text{-}Cl)]_2$

Fig. 4

As discussed earlier, hydrosilylation of carbonyl and imine functionalities are considered as very important reactions.. Nickel being a base metal has attracted significant attention as a surrogate to expensive, yet toxic 4d, 5d heavy metals in catalysis. A lot of fascinating chemistry is found for the combination of hydride ligands with nickel since insertion of a substarte is prevalent in the reactive Ni-H bond.Use of transiently generated nickel-hydride spans a wide range including this activation of N_2 and H_2 to hydrogenase enzymes where hydride bridges between nickel and iron are proposed to be central to the reactivity. We surmised that the nickel with β-diketiminates ligand in the backbone can be used for hydrosilylation of carbonyl and imine. There have been few reports on nickel mediated hydrosilylation of carbonyl,[29] olefins,[23] alkynes.[30] However, Nickel catalyzed hydrosilylation of imine are yet to be reported.. This work is focused on the use of $[(L^{Me,\ iPr})Ni(\mu_2\text{-}Cl)]_2$ (Fig.5) as precatalyst with KO^{t}Bu and diphenylsilane (Ph_2SiH_2, as hydride source) for hydrosilylation of carbonyl and imine.[27,29,31] This will follow the same mechanism as discussed in (Scheme 1.11), generating the catalyst $[(L^{Me,\ iPr})Ni(\mu_2\text{-}H)]_2$ in the intermediate step.[29]

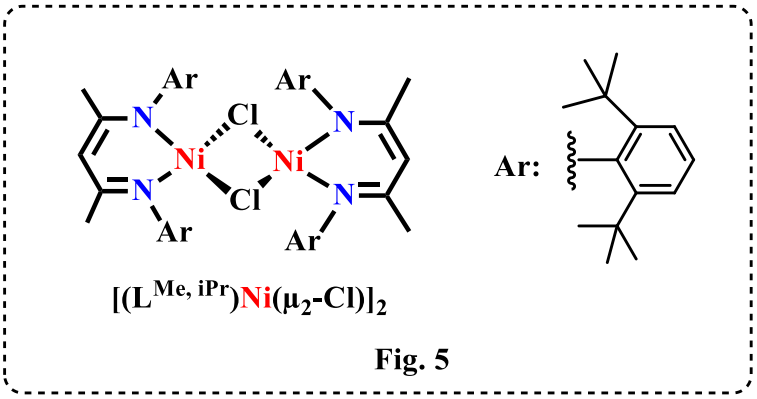
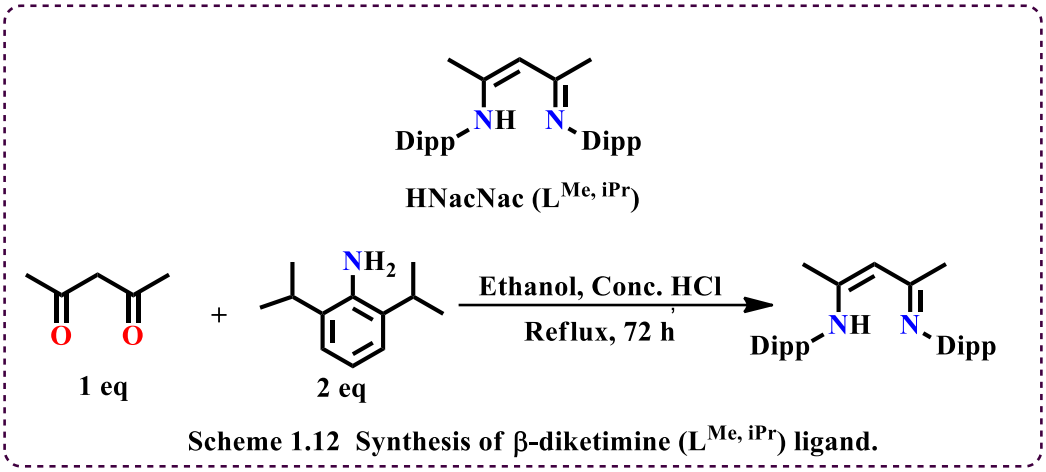


Fig. 5

1.7 Experimental Section

1.7.1 Ligand Synthesis

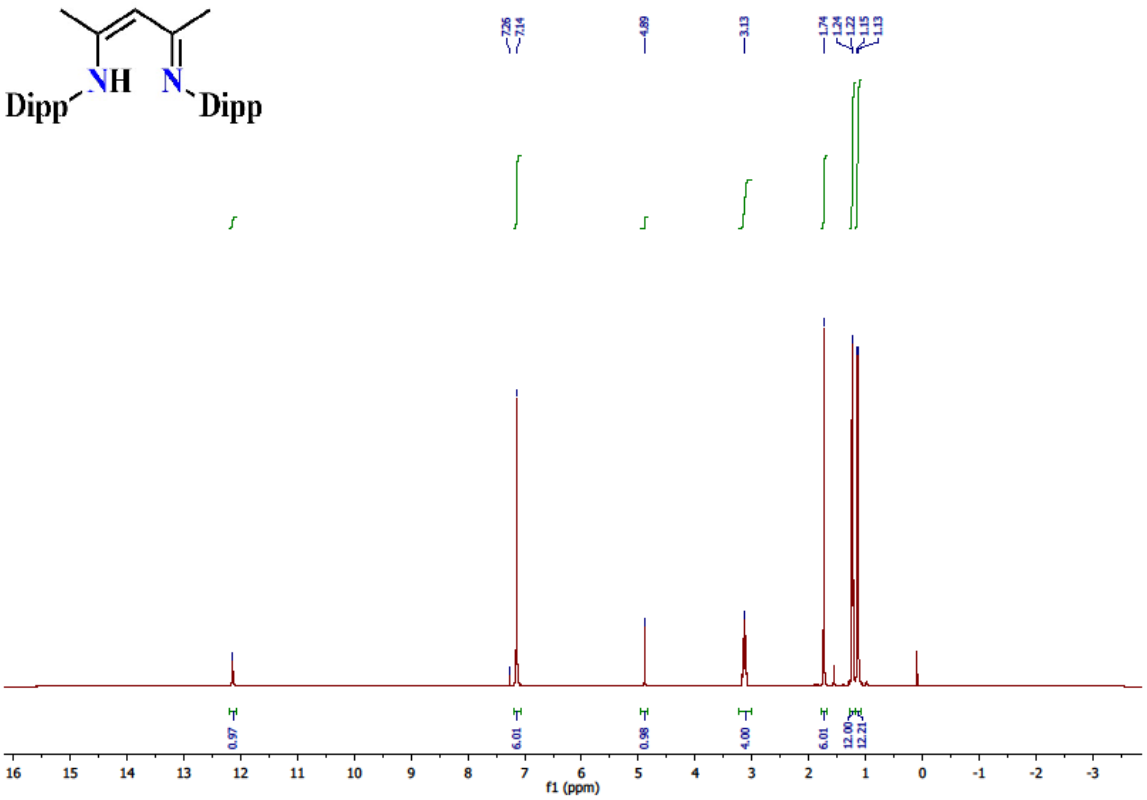


Scheme 1.12 Synthesis of β-diketimine ($L^{Me, iPr}$) ligand.

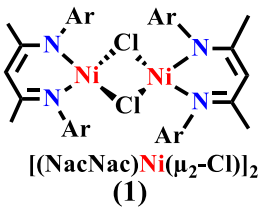
Procedure:

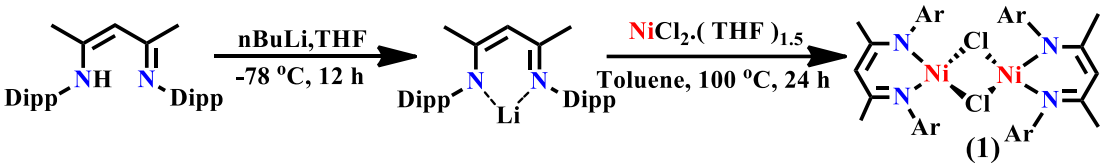
1,4 pentanedione (6.71g, 0.067mol) is mixed with 300 mL of ethanol and 2,6-diisopropylaniline (28.72g, 0.162mol). To the mixture is added 7.5 mL of conc. HCl (~12 M) and the solution is refluxed with vigorous stirring at 100 ^{o}C for three days. After 6 hours a white precipitate starts to form, but the reaction must be continued for full 3 days for complete conversion. The slurry is allowed to cool to room temperature and then filtered. The filtered solid is dried under reduced pressure, and the filtrate is evaporated on a rotary evaporator. The dried mass is mixed with filtrate residue and the mixture is refluxed in 250mL hexane at 80 ^{o}C for 1 hour. After cooling the mixture, the slurry is filtered, and the solid residue is treated with 300 mL of a saturated aqueous solution of Na_2CO_3 and 500 ml DCM. The slurry is stirred until the solid dissolves, giving a yellowish orange solution and a pale yellow aqueous layer. The orange layer is separated using separating funnel and the solution is dried over $MgSO_4$. The solution is filtered again and dried under reduced pressure to yield a slightly yellow residue that upon washing with 50 mL of methanol (-20 ^{o}C) yields white HNacNac as a fluffy powder.

^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 12.14(s, 1H, N-H), 7.14(m, 6H, Ar-H), 4.89(s, 1H, CH), 3.13s(m, 4H, $CH(CH_3)_2$), 1.74(s, 6H, $NC(CH_3)$), 1.24-122(d, 12H, $CH(CH_3)_2$), 1.15-1.13(d, 12H, $CH(CH_3)_2$)



1.7.2 Metal Complex Synthesis





Scheme 1.13 Synthesis of Ni-NacNac metal complex, Precatalyst.

Procedure:

$NiCl_2.(THF)_x$ prepared by refluxing anhydrous $NiCl_2$ in dry THF under a nitrogen atmosphere for 24 hours. The amount of THF coordinated to Ni varies from 0.1 to 0.7.

$NiCl_2.(THF)_{0.7}$ (432mg, 2.4 mmol) and $L^{Me,\ iPr}Li$ (1g, 2.4 mmol) are placed in a 50 mL schlenk flask and toluene (~30 mL) is added to produce a tan coloured slurry under a nitrogen atmosphere. The reaction mixture is heated and stirred at 100 ^oC. After 24 h, the dark blue reaction mixture is cooled to room temperature, and the solvent is removed under reduced pressure. Under nitrogen, DCM (30 mL) is added to the residue, and the mixture is filtered through 3 cm of Celite. DCM is evaporated under vacuum and the green precipitate left is the desired nickel catalyst.

Chapter 2

2.1 Hydrosilylation of aldehydes and ketones

2.1.1 Catalytic Hydrosilylation Studies with Complex 1

When pre-catalyst (**1)** is combined with 2 equiv. of KO^tBu, the mixture can mediate the catalytic hydrosilylation of carbonyl functionalities such as aldehydes and ketones to the silyl ether products at 100 °C when Ph_2SiH_2 is used as a reductant. Hydrosilylation catalysis of benzaldehyde with 4 mol % of **1** in benzene or toluene at 100 °C and in the presence of KO^tBu (8 mol %) and diphenylsilane (1.2 equiv.) and carbonyl (1 equiv.) to afford the desired silyl ether product $PhCH_2OSiEt_3$. The silyl ether product is further hydrolyzed to yield the respective alcohol.

The successful hydrosilylations of 4-fluorobenzaldehyde, 4-chlorobenzaldehyde, 4-nitrobenzaldehyde and 4-methylbenzaldehyde indicate that the catalyst, under the above reaction conditions, can toler-ate these functional groups on the aromatic ring.

2.2 Hydrosilylation of aldimine and ketimine

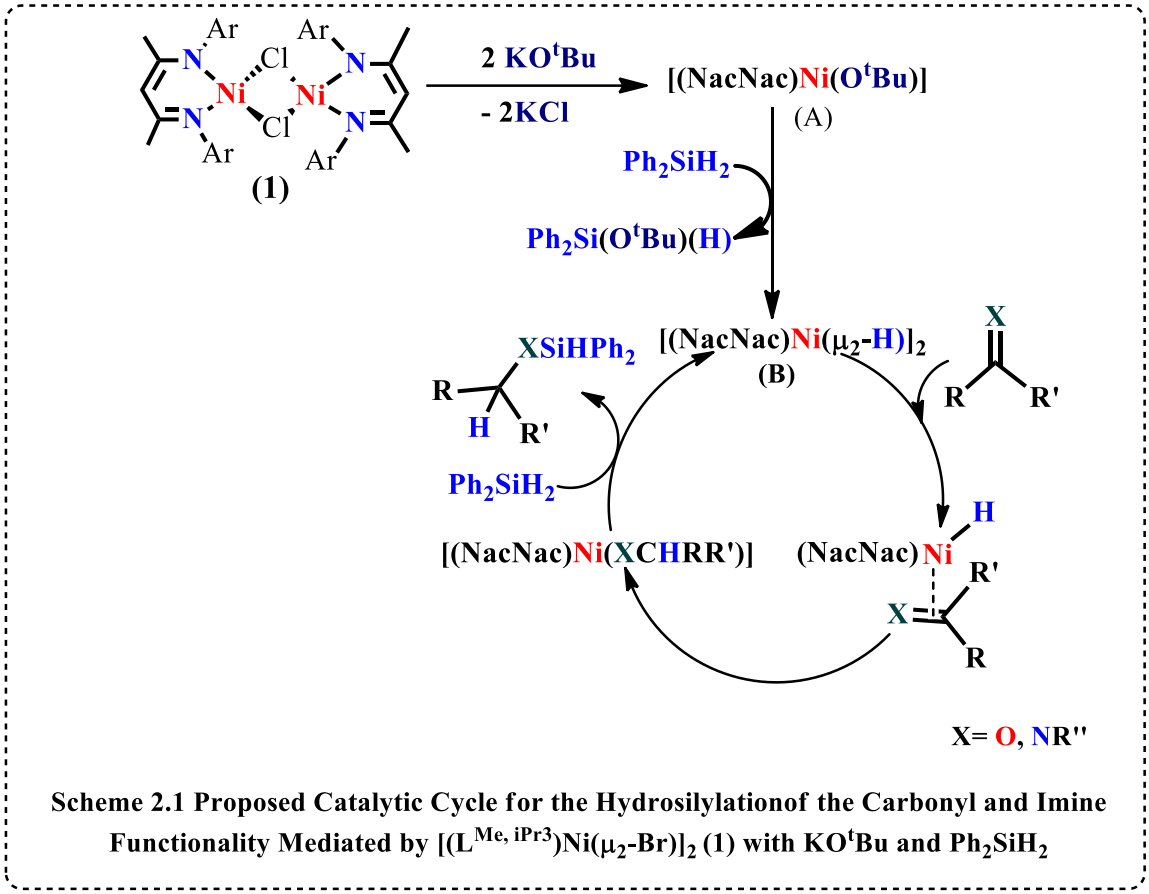
2.2.1 Catalytic Hydrosilylation Studies with Complex 1

When pre-catalyst (**1)** is combined with 2 equiv. of KO^{t}Bu, the mixture can execute the catalytic hydrosilylation of imine to the silylated amine products at 100 °C in presence of Ph_2SiH_2 . Hydrosilylation catalysis with 7 mol % of (**1)** in toluene at 100 °C and in the presence of KO^{t}Bu (14 mol %) and diphenylsilane (1.2 equiv.) and imine (1 equiv.) to afford the desired silylated product ($PhCH_2N$)Si(H)Ph_2. The silylated product is further hydrolyzed to yield the respective amine

The successful hydrosilylations of N-[(4-fluorophenyl)methylene]benzenamine and 4-methoxy-N-(phenylmethylene)benzamine indicate that the catalyst, under the above reaction conditions, can tolerate these functional groups on the aromatic ring.

2.3 Proposed Mechanism for Catalytic Hydrosilylation of Aldehyde, Ketone and Imine by Precursor (1)

Catalytic Hydrosilylation is not observed in the absence of complex **1**,thus, implying that nickel complex is is the required catalyst for the reaction. The role of KO^{t}Bu is essential as an alkoxide source. It is being proposed that transient ($L^{Me,\ iPr}$)Ni(O^{t}Bu) is generated, followed by exchange by exchange of alkoxide for hydride with diphenyl silane. This proposal is further corroborated by the observation that green **1** undergoes a rapid color change to red when treated with 2 equiv. of KO^{t}Bu. Ni(II)-mediated hydrosilylation of the carbonyl or imine with **1** as a precatalyst, using of KO^{t}Bu and Ph_2SiH_2, involves the in situ generations of a nickel alkoxide intermediate. This complex **(A)** converts to the **(B)** hydride by σ-bond metathesis with Ph_2SiH_2 and elimination of the silyl ether Ph_2Si(O^{t}Bu)(H). Coordination of the carbonyl group of O=CRR′ or R″N=CRR′ into the nickel-hydride bond in **(B)** forms the transient adduct ($L^{Me,\ iPr3}$)Ni(H)(O=CRR′) or ($L^{Me,\ iPr3}$)Ni(H)(R″N=CRR′), which then undergoes migratory insertion to produce an alkoxide intermediate complex ($L^{Me,\ iPr3}$)Ni(OCHRR′) or ($L^{Me,\ iPr3}$)Ni(N(R″)(CHRR′)). The latter would then undergo a σ-bond metathesis reaction with diphenylsilane to close the catalytic hydrosilylation cycle by reforming **(B)** and the silylated product (Scheme 2.1).[29]



Scheme 2.1 Proposed Catalytic Cycle for the Hydrosilylationof the Carbonyl and Imine Functionality Mediated by [(L$^{Me, iPr3}$)Ni(μ$_2$-Br)]$_2$ (1) with KO^{t}Bu and Ph$_2$SiH$_2$

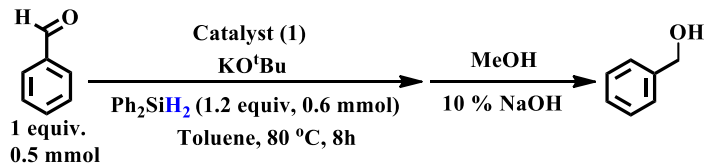
2.4 Results and Discussions

2.4.1 Hydrosilylation of Aldehyde and Ketone

To optimize the reaction condition of carbonyl reduction (Table 2.1), benzaldehyde (1 equiv., 0.5 mmol) in the presence of (1) as a precatalyst (2 mol%) and KO^{t}Bu (4 mol%) and diphenylsilane (1.2 equiv., 0.6 mmol) reaction was carried out for 12 hours. The yield was calculated using a NMR standard to reveal 70%. On increasing the catalyst loading to pre-catalyst (7 mol%) and KO^{t}Bu (14 mol%) and decreasing the time to 8 h the NMR yield was quantitative. On decreasing the catalyst loading to pre-catalyst (4 mol%) and

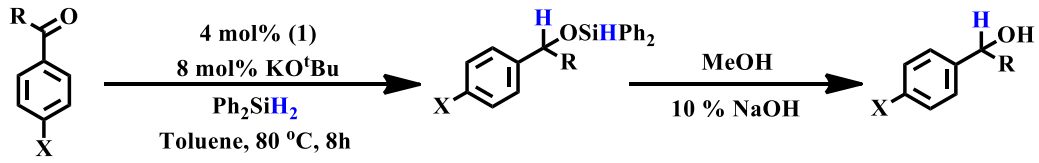
KO^{t}Bu (8 mol%) and keeping the time for reaction same (8 h) the NMR yield was around 99%. Following the optimized experimental conditions, a wide range of carbonyl hydrosilylation with nickel were tetsed, which offered moderate to excellent yields of alcohol (Table 2.2). The library of substrates had shown for the degree of functional group tolerance, for halogen, nitro, hydroxyl, methoxy and methyl group on the aryl. Functional gourps with different steric and electronic requirements survive well the synthetic protocol. The successful hydrosilylations of 4-fluorobenzaldehyde, 4-chlorobenzaldehyde, 4-nitrobenzaldehyde and 4-methoxyacetophenone indicate that the catalyst, under our reaction conditions, can tolerate these functional groups on the aromatic ring. However, placing an electron-donating group in the para position of the aryl ring, 4-methylbenzaldehyde slowed the reduction significantly. 4-methoxyacetophenone, due to electron-donating nature of methoxy group, the yield is significantly reduced as well.

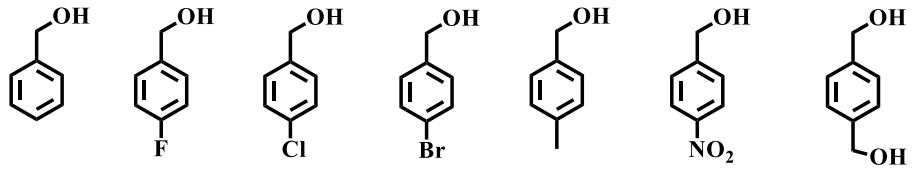
Table 2.1 Optimization of Carbonyl Hydrosilylation



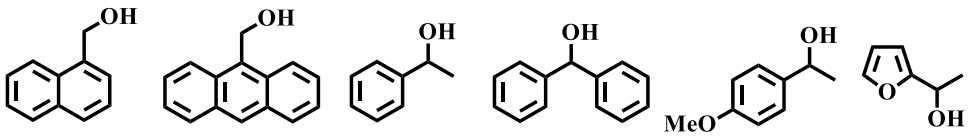
Catalyst loading	KO^{t}Bu	Time	Conversion
2 mol%	4 mol%	12 h	70%
7 mol %	14 mol %	8 h	99%
4 mol %	8 mol%	8 h	99%

Table 2.2 Nickel Catalyzed Hydrosilylation of Aldehydes and Ketones





(99%) 90% | (99%) 92% | (95%) 90% | (95%) 88% | (83%) 80% | (97%) | (90%)



(70%) 67% | (85%) 82% | (70%) 63% | (90%) | (60%) | (40%)

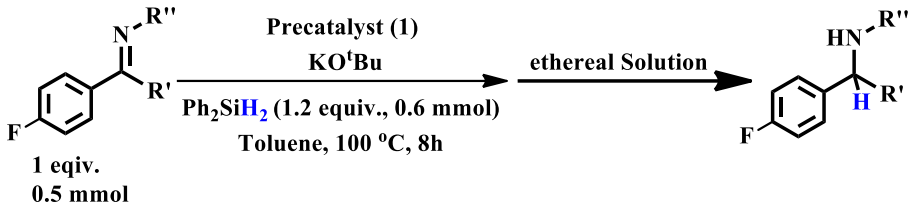
Conversions were determined by NMR yield using ferrocene as NMR standard and are given in parentheses. Yields with parantheses correspond to isolated pure products.

2.4.2 Hydrosilylation of Imine

To optimize the reaction condition (Table 2.3), imine (1 equiv., 0.5 mmol) in the presence of (1) as a pre-catalyst (10 mol%) and KO^{t}Bu (20 mol%) and diphenylsilane (1.2 equiv., 0.6 mmol) reaction was carried out for 24 hours. The yield was calculated using NMR yield which was around 99%. On decreasing the catalyst loading to pre-catalyst (7 mol%) and KO^{t}Bu (14 mol%) and decreasing the time to 12 h the NMR yield was around 99%. Following the optimized experimental conditions, a wide range of imine to nickel-catalyzed hydrosilylation was subjected, which offered moderate to excellent yields of amines (Table 2.4). The library of substrates had shown for the degree of tolerance, for halogen and methoxy group on the aryl, as well as differences in an electronic and steric factor. The successful hydrosilylation and presence of an electron withdrawing group at the para position of N-[(fluorophenyl)methylene]benzenamine have shown the reduction

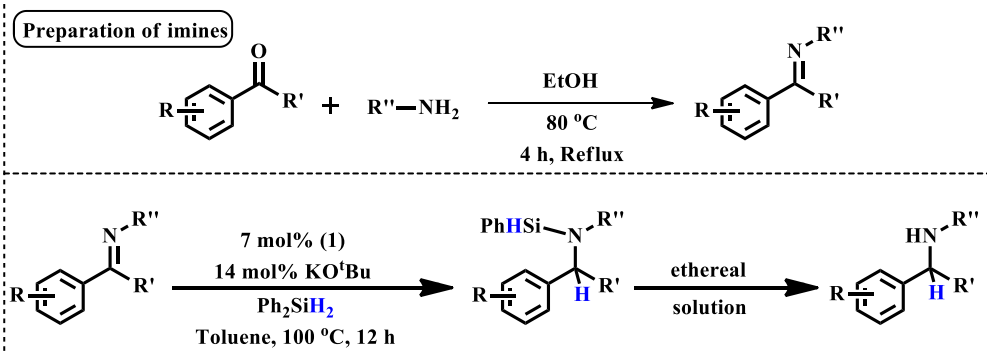
significantly. However, when the substituent is replaced by an electron-donating group like methoxy and methyl, the reduction is decreased.

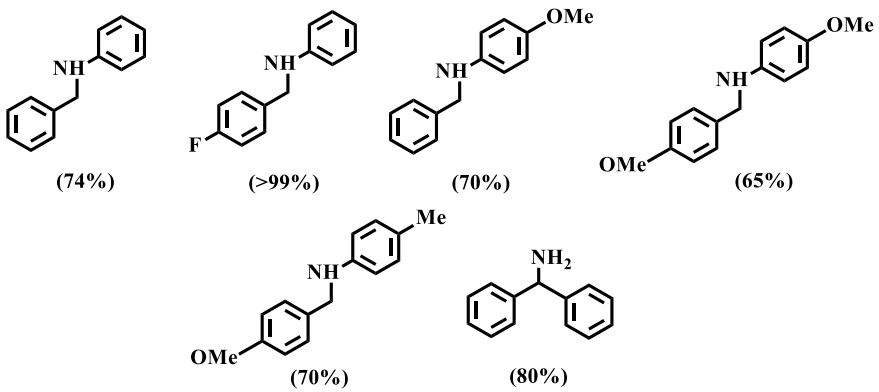
Table 2.3 Optimization of Imine Hydrosilylation



Catalyst loading	KO^{t}Bu	Time	Conversion
10 mol%	20 mol%	24 h	>99%
7 mol %	14 mol %	12 h	>99%

Table 2.4 Nickel Catalyzed Hydrosilylation of Imines





Conversions were determined by NMR yield using mesitylene as standard and are given in parentheses.

2.5 Experimental Procedure:

2.5.1 Hydrosilylation of Aldehyde and Ketone

In a glovebox, schlenk flask was charged with 4 mol % of **1** (21 mg, 0.02 mmol), 8 mol % of KO^{t}Bu (11 mg, 0.04 mmol), and triethylsilane (93 μL, 0.6 mmol). The schlenk flask was removed from the glovebox, and the carbonyl compound (0.5 mmol) was added to it via syringe under the nitrogen atmosphere . The sample was placed into a preheated oil bath kept at 100 °C.

Hydrolytic Workup and Purification of Alcohols. Upon completion, the reaction mixture was quenched with 3 mL NaOH in 2 mL MeOH, allowed to stir at 60 ^{o}C for 3 hours. After this, a NMR standard ferrocene (0.5 mmol) was added to the solution so that a yield can be conveniently calculated. The solvent was evaporated, and the residue was dissolved in diethyl ether (30 mL and washed with water (2 × 20 mL). The organic phase was separated, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The NMR was recorded and yield was calculated with respect to the added standard. Hydrolyzed products were purified by a short silica gel column and washed with n-hexane/ethyl acetate (3:2).

2.5.2 Hydrosilylation of Imine

In a glovebox, schlenk flask was charged with 7 mol % of **(1)** (37 mg, 0.035 mmol), 14 mol % of KO^{t}Bu (15 mg, 0.14 mmol), and triethylsilane (93 μL, 0.6 mmol). The schlenk flask was removed from the glovebox, and the imine compound (0.5 mmol) was added to the schlenk flask via syringe under a nitrogen atmosphere at schlenk line. The sample was placed into a preheated 100 °C oil bath.

Hydrolytic Workup: Upon completion, the reaction mixture was quenched with 10 mL-ethereal solution, allowed to stir at room temperature for 3 hours. After this, NMR standard, mesitylene (0.5 mmol) was added to the solution. The olvent was evaporated, and the residue was dissolved in diethyl ether (30 mL and washed with water (2 × 20 mL). The organic phase was separated, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The NMR was recorded and the NMR yield was calculated.

2.6 Other Works

2.6.1 Azo: Potential Redox Backbone

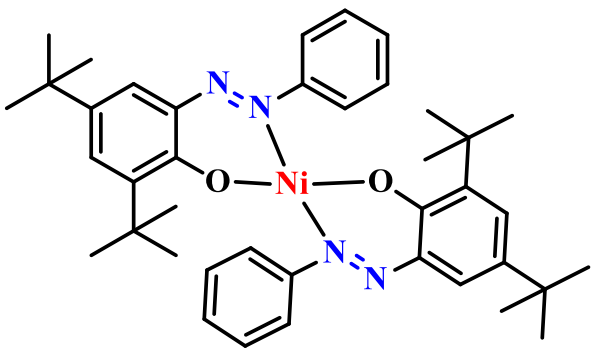


Figure 6. Ni(Azo)$_2$

Nickel catalyst containing bis-azo aromatic ligand was synthesized with a potential goal to N-alkylate a variety of amines starting from alcohols as the alkyl source. The low-lying π* orbitals of the coordinated azo function acts as a dominant electron sink and helps in multiple electron and proton transfer. Thus, azo ligand helps in the dehydrogenation of alcohol while metal ion remains as spectator helping in holding the ligands and substrate. Few substrates have been tried on the conversion of alcohol to the N-alkylated product. The synthetic protocol results the final product in good yield.[32,33]

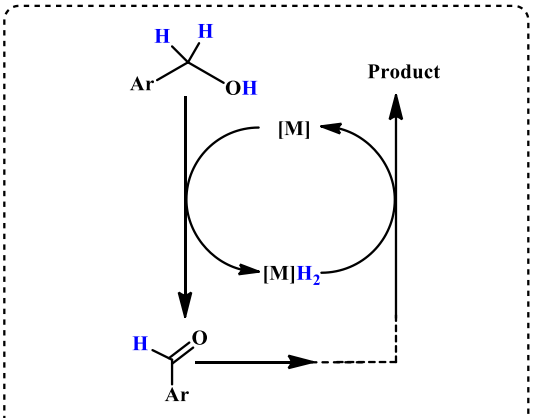
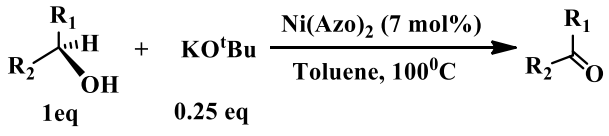
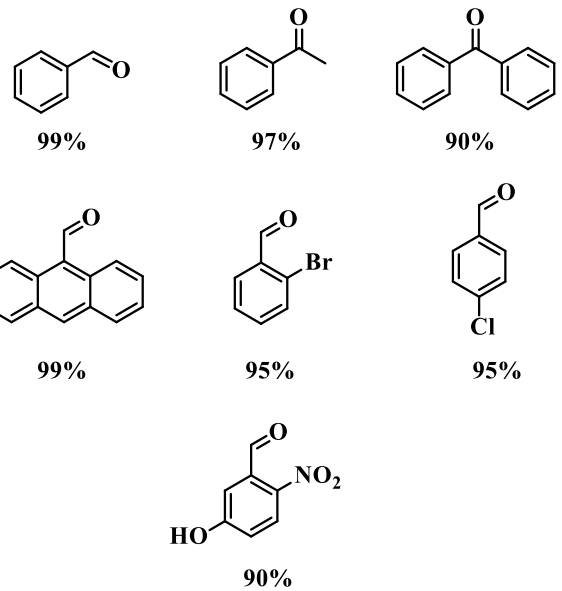


Figure 7. Alcohol dehydrogenation using $Ni(Azo)_2$ catalyst

Table 2.5 Dehydrogenation of Alcohol using $Ni(Azo)_2$ catalyst



1eq 0.25 eq



Experimental Procedure: A mixture of 1 mmol alcohol, 7 mmol catalyst, 0.25 mmol KO^tBu (11.2 mg) was stirred in 10 mL of dry toluene in a round-bottom flask fitted with a condenser at 100 ^oC. The stirring was continued for 24 h. The crude oxidized products ran

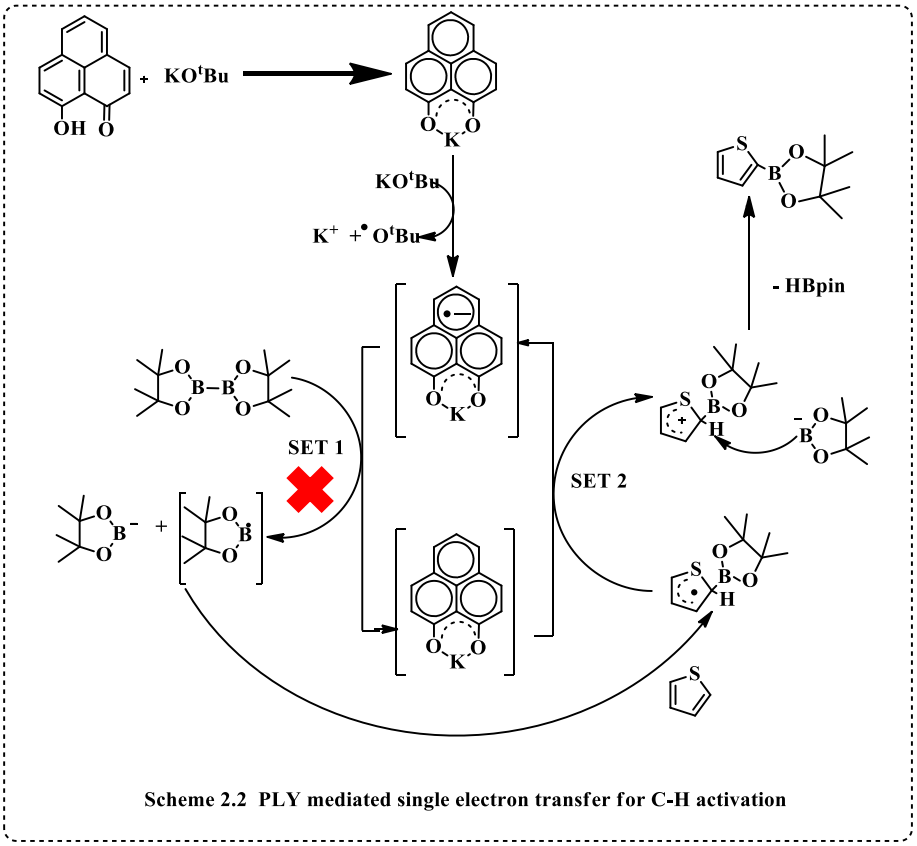
on TLC to confirm the formation of product and purified using column chromatography hexane/ ethylacetate (10:1) as eluent.

2.6.2 Single Electron Transfer Mediated C-H activation

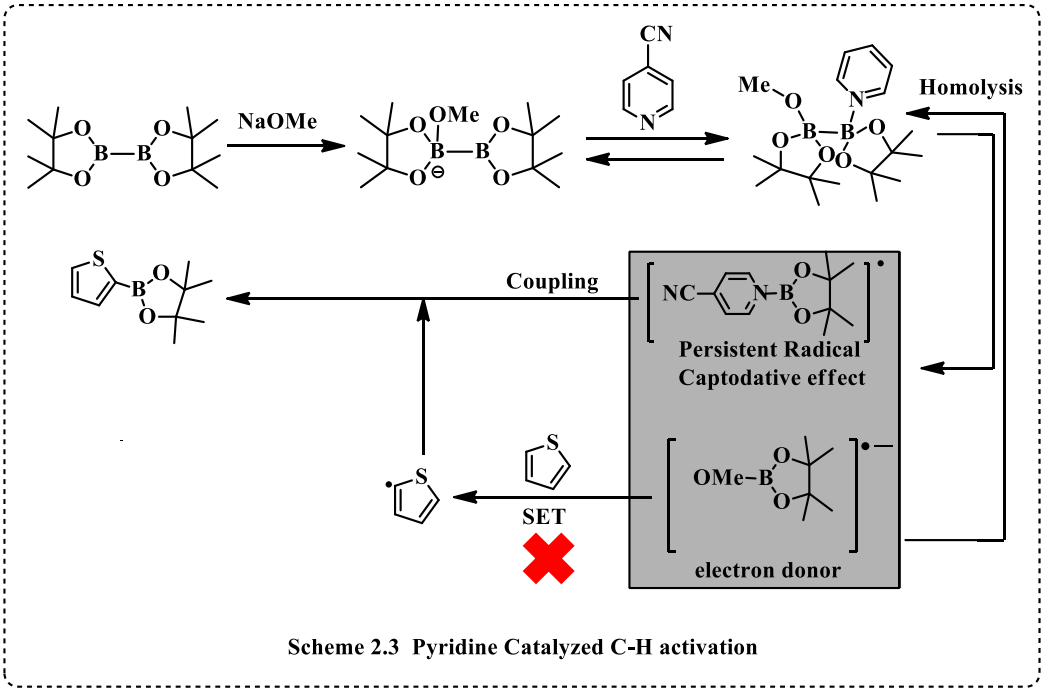
Phenylenyl (PLY) has a non-bonding molecular orbital (NBMO) that can switch between redox active closed shell and open shell. Thus, PLY can act as an electron reservoir. The open shell state is unstable. Therefore, the advantage is taken by in-situ generation of the radical through external electron transfer into the NBMO of closed-shell phenalenyl unit. Here, C-H activation for heteroarenes was tried using B_2pin_2, KO^tBu and PLY. It had also been tried on different heteroarenes includingthiophene, imidazole and 1-methylimidazole. Unfortunately the reactions failed (Scheme 2.2). The reason may be that the reduction potential of open shell PLY might not match the reduction potential to cleave B_2pin_2.[34]

2.6.3 Pyridine Catalyzed C-H activation

B_2pin_2 in the presence of nucleophile sodium methoxide and Lewis base 4-cyanopyridine leads to cleavage of B_2pin_2 and generates stable radical i.e. cyanopyridine boryl radical and another reactive radical as had been reported in the literature. Here, C-H activation had been tried as shown in (Scheme 2.3). However, the reaction failed, possibly stemming from the mismatch of the reduction potential to cleave C-H bond. is.[35]



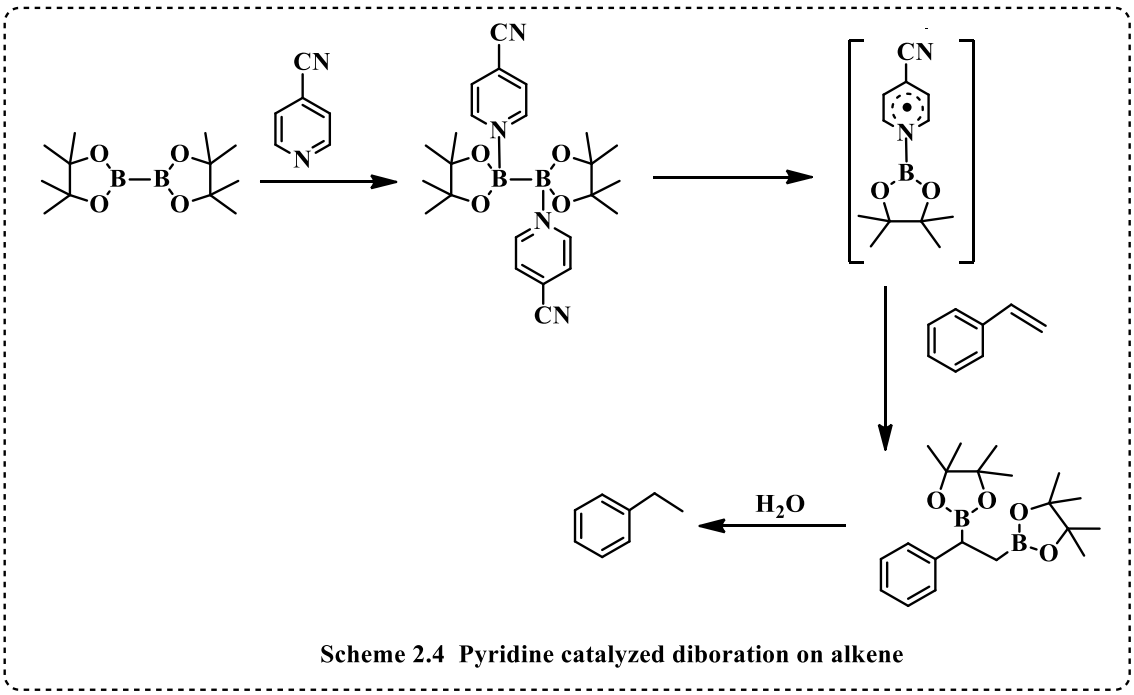
Scheme 2.2 PLY mediated single electron transfer for C-H activation



Scheme 2.3 Pyridine Catalyzed C-H activation

2.6.4 Pyridine Catalyzed diboration of alkene

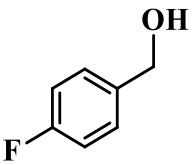
B_2pin_2 in the presence of Lewis base 4-cyanopyridine leads to cleavage of B_2pin_2 and generates two stable radical, i.e. cyanopyridine boryl radical. This persistent radical couples with alkene and diboration on alkene happen as shown in (Scheme 2.4). The reaction went successfully but in between the same work was published by another group.[36]



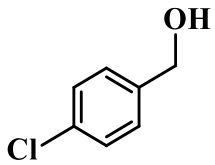
Scheme 2.4 Pyridine catalyzed diboration on alkene

2.7 Supplementary Information

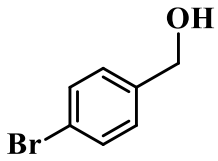
2.7.1 Spectroscopic Data



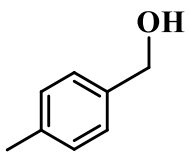
Following general procedure, ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ 7.35-7.32 (m, 2H, ArH), 7.06- 7.02 (m, 2H, ArH), 4.66 (s, 2H, CH_2), 1.77 (br, 1H, OH). ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 161.31, 136.92, 128.56, 64.71.



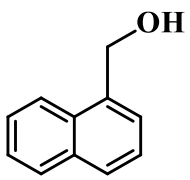
Following general procedure, ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ 7.34-7.32 (m, 2H, ArH), 7.30-7.28 (m, 2H, ArH), 4.67 (s, 2H, CH_2), 1.78 (s, 1H, OH). ^{13}C NMR (400 MHz, $CDCl_3$, ppm): δ 139.23, 131.36, 128.68, 128.28, 64.58



Following general procedure, ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ 7.50-7.48 (m, 2H, ArH), 7.25-7.23 (m, 2H, ArH), 4.65 (s, 2H, CH_2), 2.08 (br s, 1H, OH). ^{13}C NMR (400 MHz, $CDCl_3$, ppm): δ 139.76, 131.61, 128.59, 121.49, 64.53.

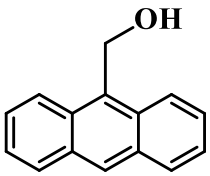


Following general procedure, 1H NMR (400 MHz, $CDCl_3$, ppm): δ 7.29-7.27 (d, 2H, ArH), 7.21-7.19 (d, 2H, ArH), 4.65 (s, 2H, OCH_2), 1.93 (br s, 1H, OH), 2.39 (s, 3H, CH_3). 13C NMR (100 MHz, CDCl3, ppm): δ 137.96, 137.39, 129.24, 127.13, 65.23, 21.18.

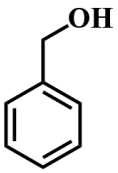


Following general procedure, 1H NMR (400 MHz, $CDCl_3$, ppm): δ 8.17–8.15 (m, 1H, ArH), 7.92 - 7.90(m, 1H, ArH), 7.86 - 7.84 (m, 1H, ArH), 7.60- 7.46 (m, 4H, ArH), 5.18

(s, 2H, CH_2), 1.79 (br s, 1H, OH). 13C NMR (400 MHz, $CDCl_3$, ppm): δ 136.24, 133.84, 131.23, 128.68, 128.62, 126.37, 125.90, 125.37, 123.65, 63.77.

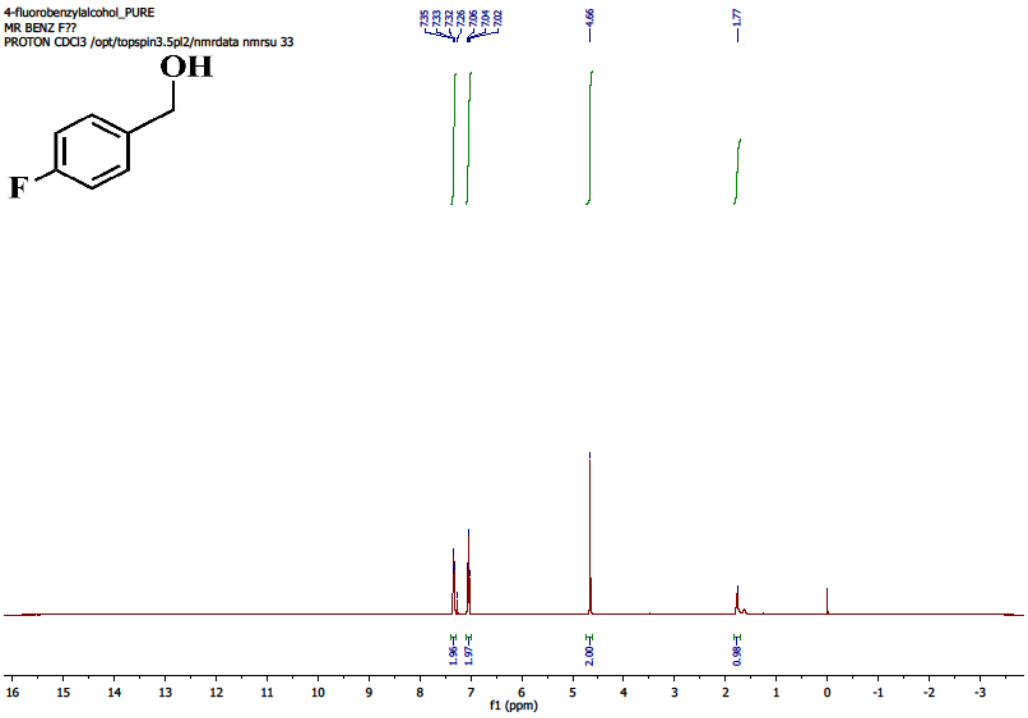


Following general procedure, 1H NMR (400 MHz, $CDCl_3$, ppm): δ 8.50 (s, 1H, ArH), 8.46–8.44 (d, 2H, ArH), 8.07-8.05 (d, 2H, ArH), 7.62- 7.58 (m, 2H, ArH), 7.54- 7.50 (m, 2H, ArH), 5.71 (s, 2H, CH_2), 1.78 (br s, 1H, OH). 13C NMR (400 MHz, $CDCl_3$, ppm): δ 131.54, 130.99, 130.24, 129.16, 128.42, 126.49, 125.12, 123.88, 57.45

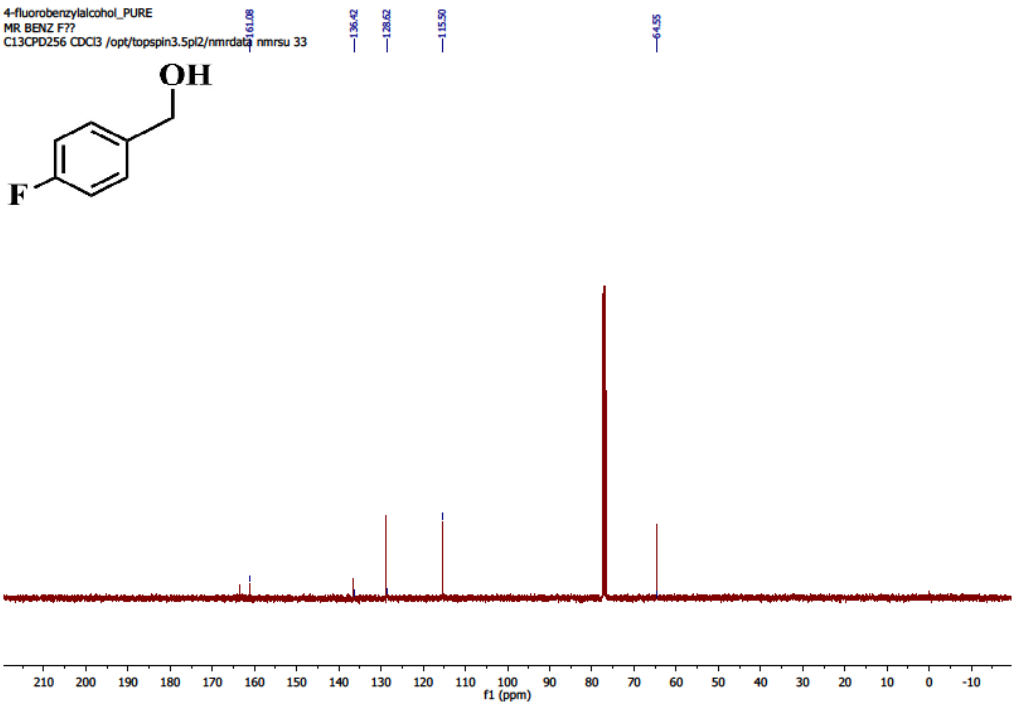


Following general procedure, 1H NMR (400 MHz, $CDCl_3$, ppm): δ 7.41-733 (m, 5H, ArH), 2.75 (br s, 1H, OH). 13C NMR (400 MHz, $CDCl_3$, ppm): δ 140.90, 128.55, 127.60, 127.04, 65.11

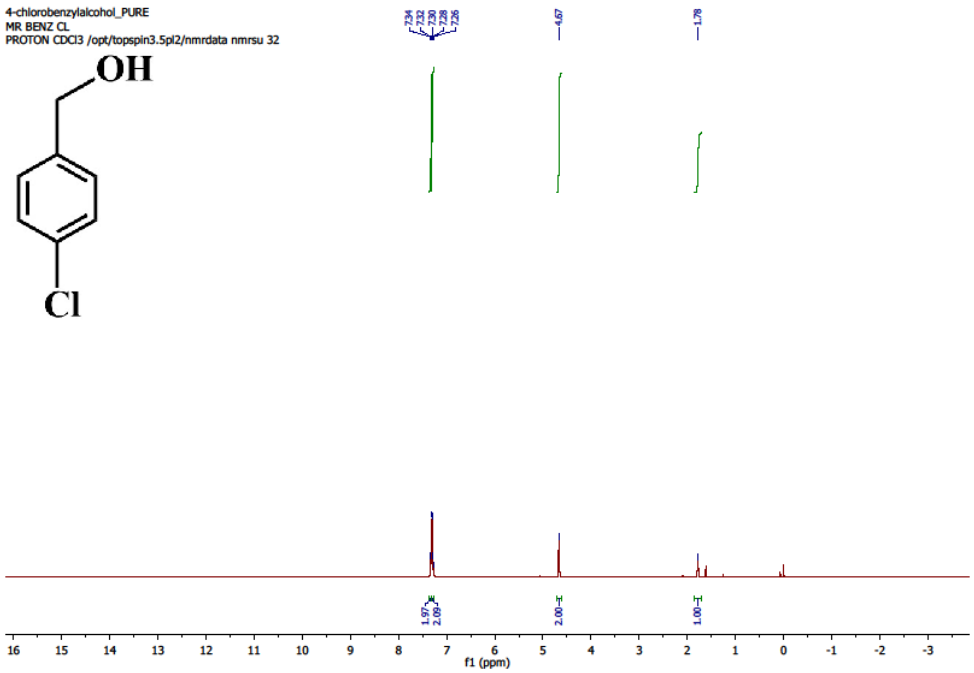
1H NMR (400MHz, $CDCl_3$)



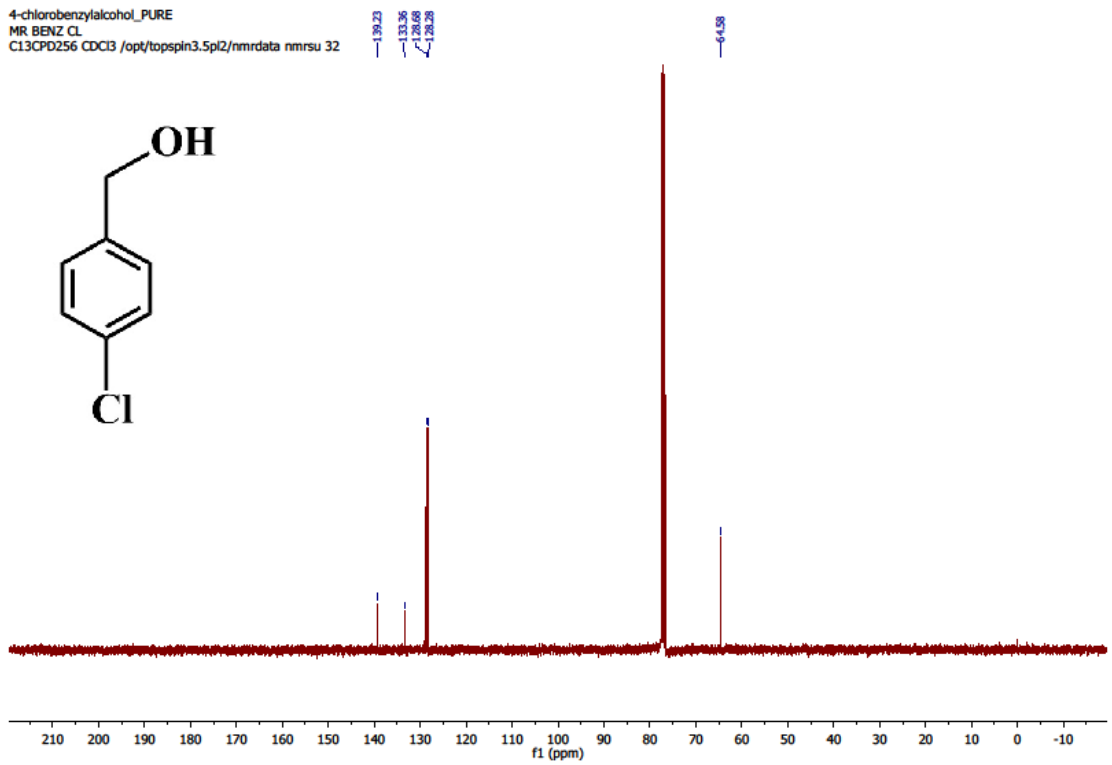
13C NMR (125MHz, $CDCl_3$)



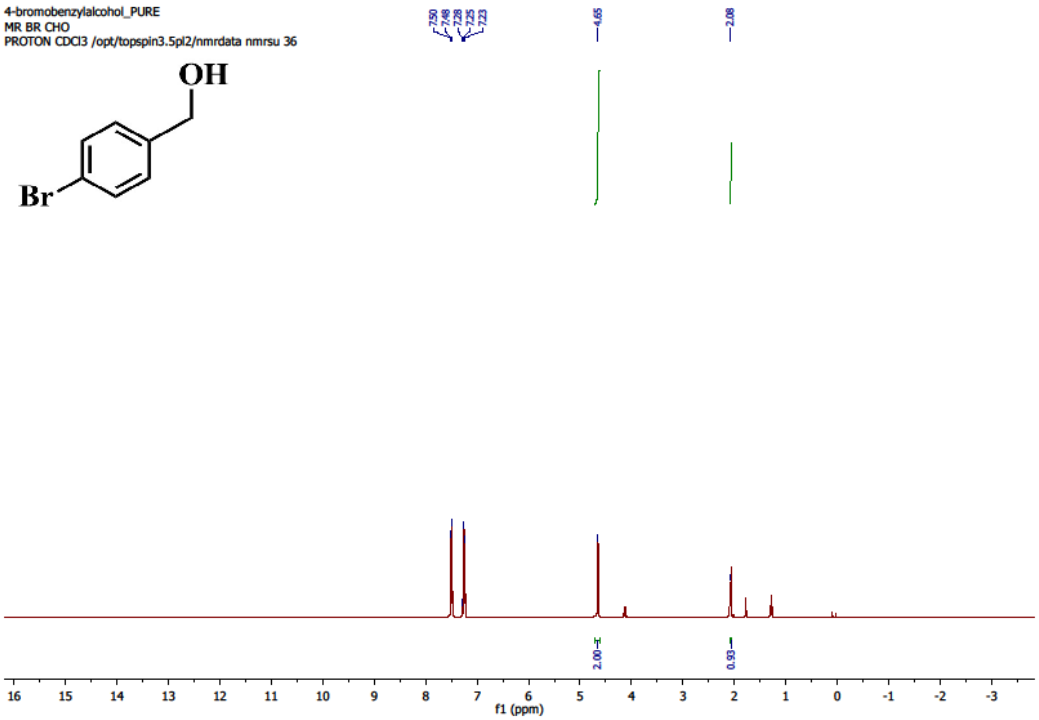
^{1}H NMR (400MHz, $CDCl_3$)



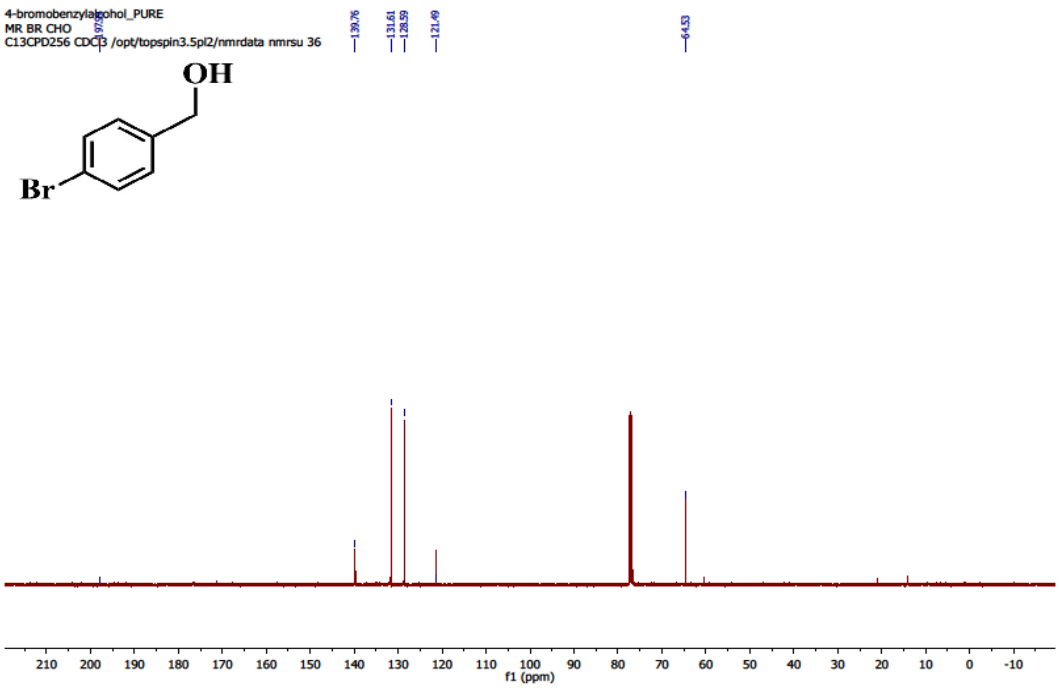
^{13}C NMR (400MHz, $CDCl_3$)



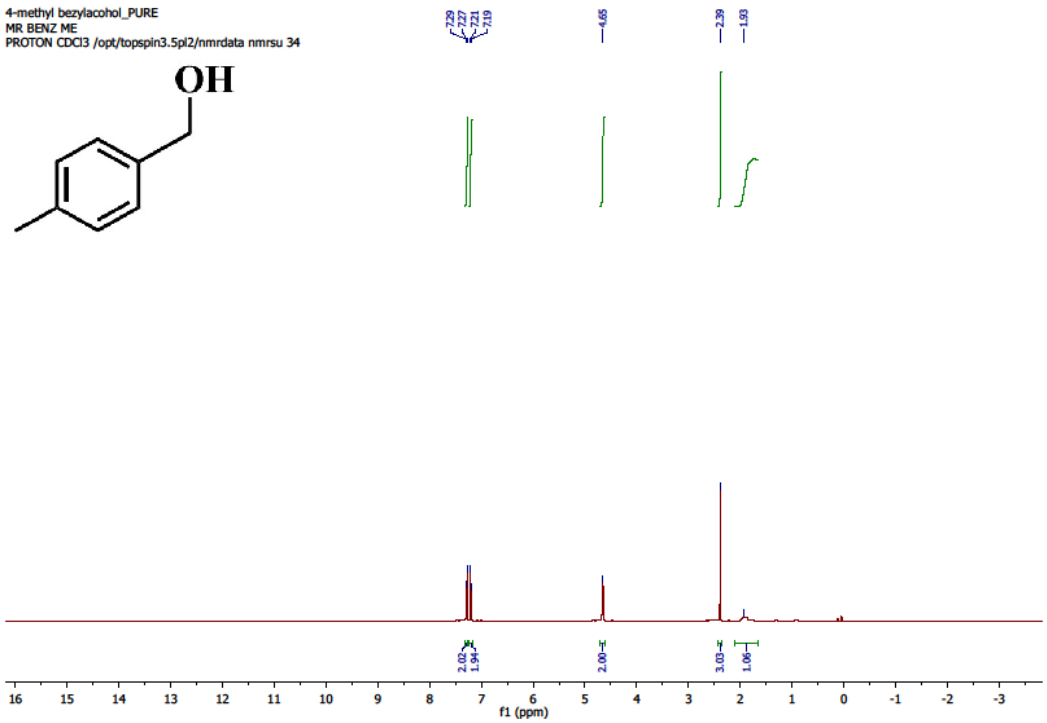
1H NMR (400MHz, $CDCl_3$)



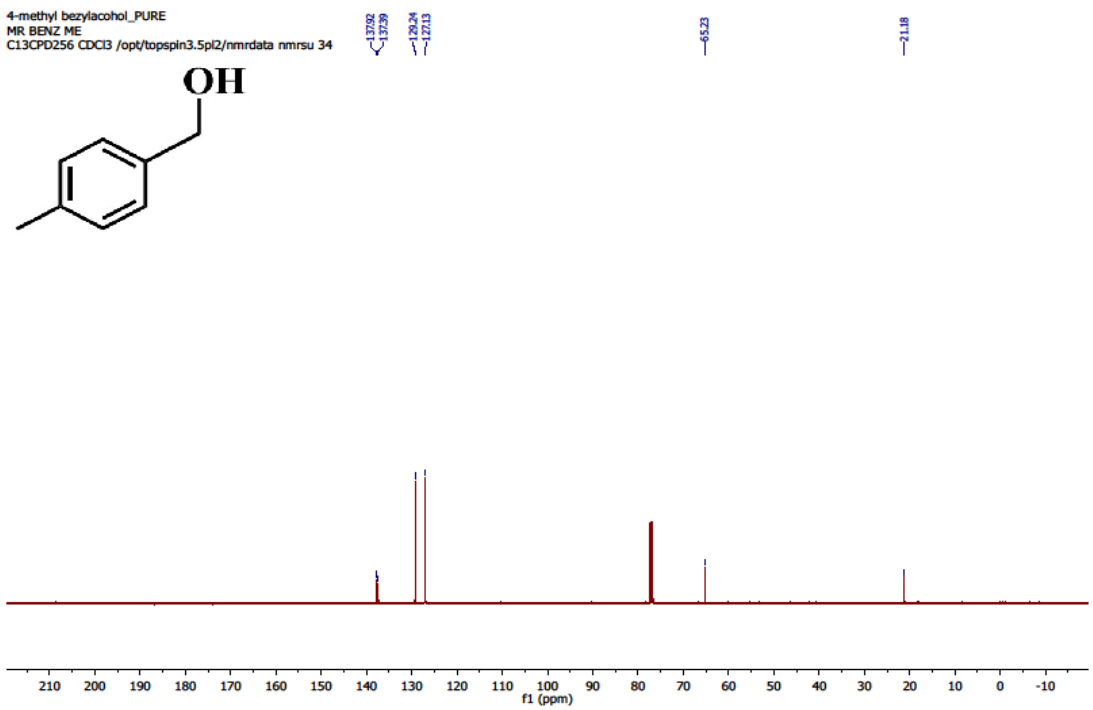
13C NMR (400MHz, $CDCl_3$)



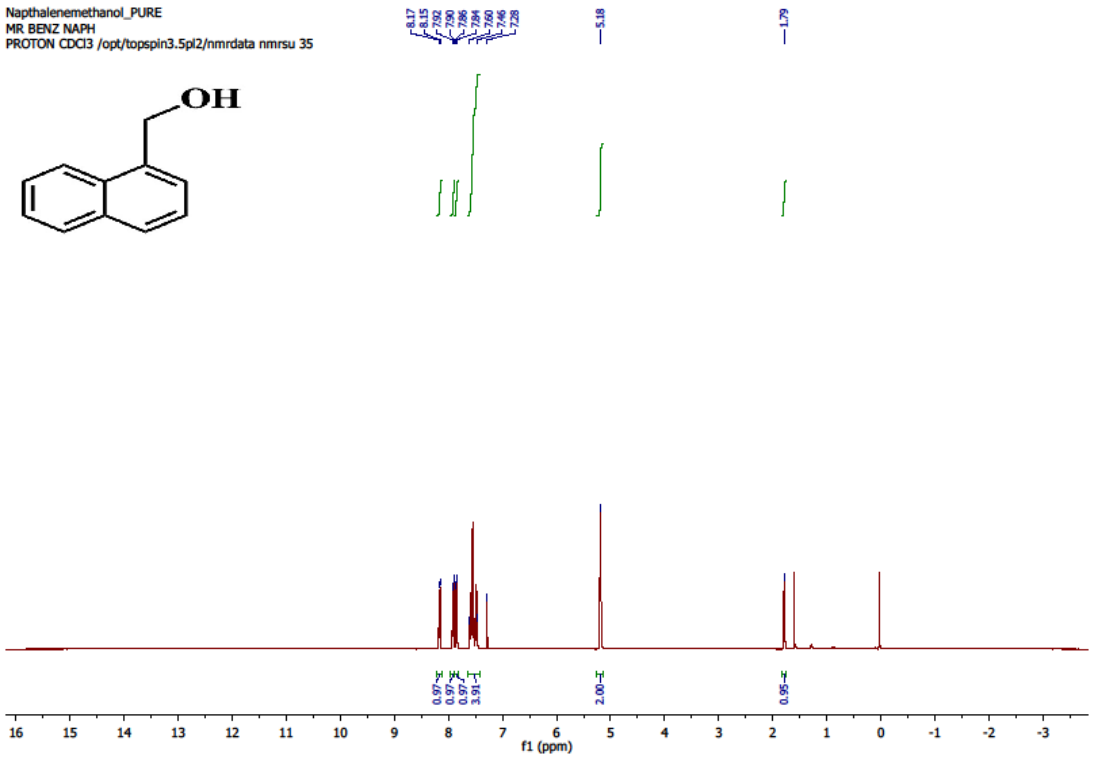
1H NMR (400MHz, $CDCl_3$)



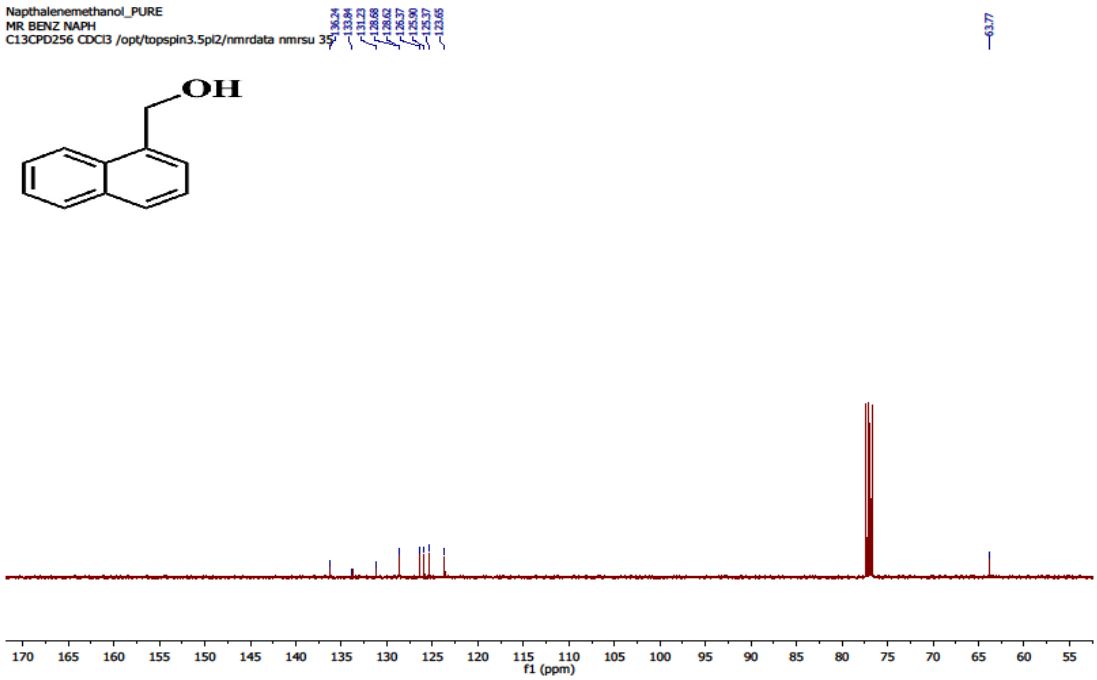
13C NMR (400MHz, $CDCl_3$)



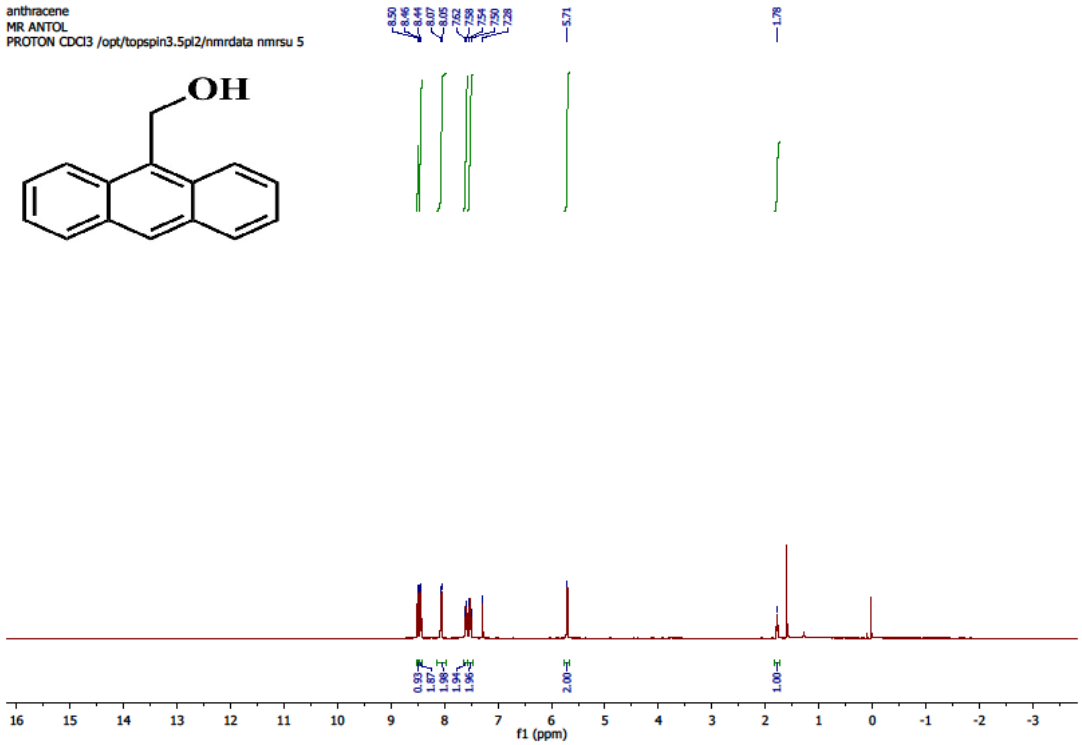
1H NMR (400MHz, $CDCl_3$)



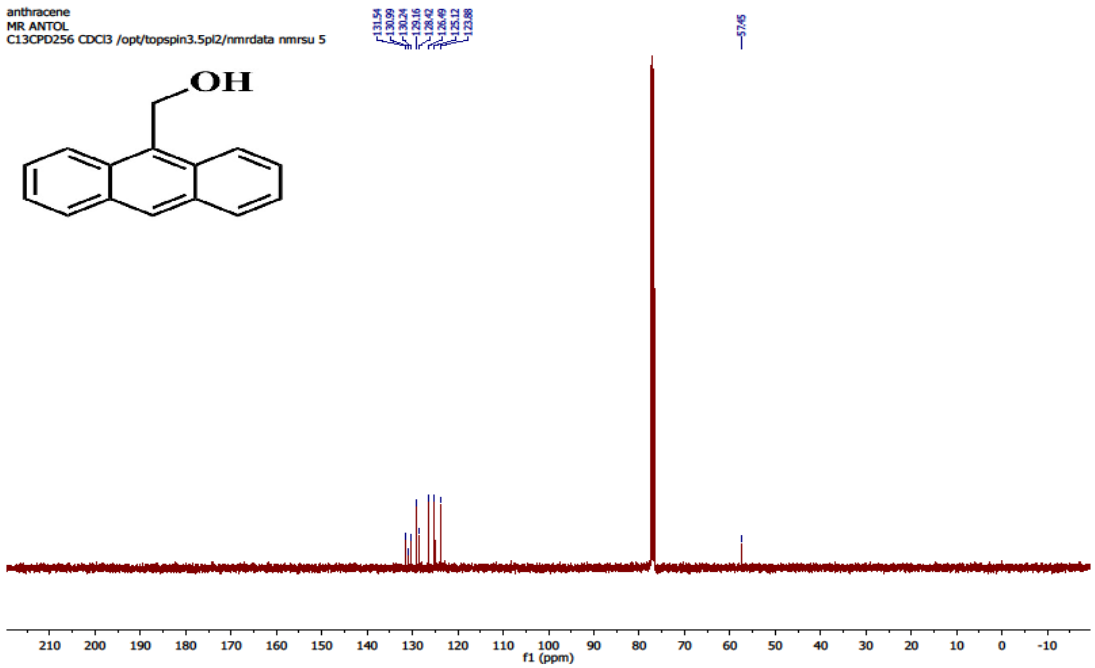
13C NMR (400MHz, $CDCl_3$)



1H NMR (400MHz, $CDCl_3$)



13C NMR (400MHz, $CDCl_3$)



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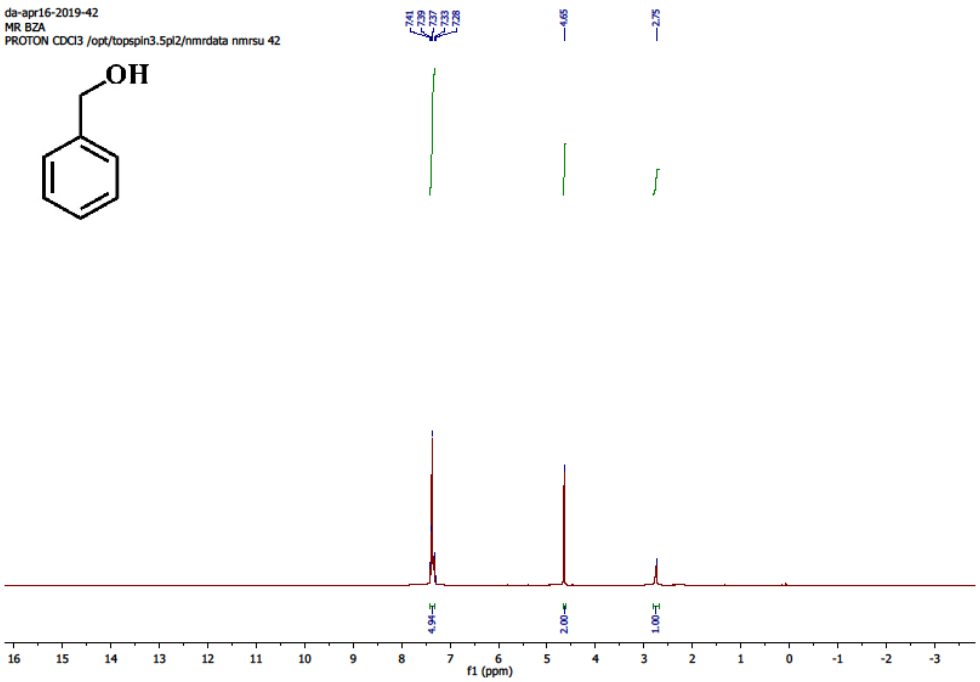
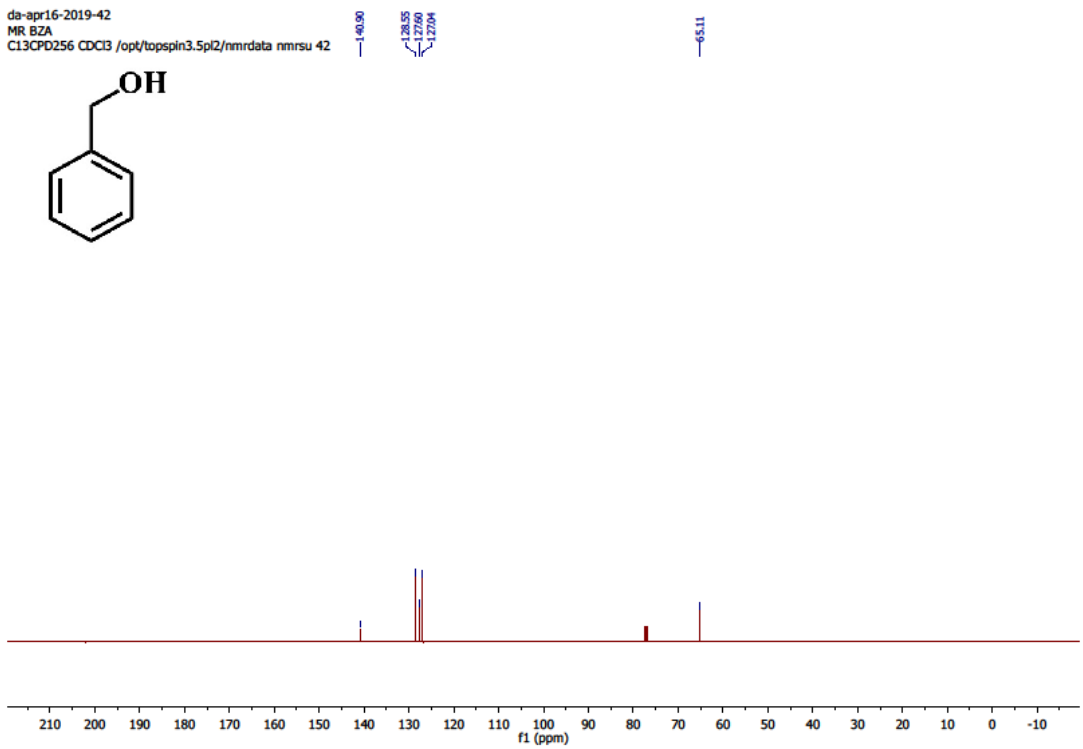


13C NMR (400MHz, $CDCl_3$)



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