SELECTIVE SYNTHESIS OF AMINES, IMINES AND NITRILES BY A WELL-DEFINED COBALT CATALYST

by

Keshav Paudel

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Dissertation Committee:

Dr. Keying Ding, Research Advisor

Dr. Scott Handy

Dr. Chengshan Wang

Dr. Kevin Bicker

Dr. Justin M. Miller

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ABSTRACT

The chemistry of amine, imine and nitrile-containing compounds plays a central role in synthesizing high-value products, e.g., drugs, fertilizer, and fine chemicals. The unquestionable benefits from these products to our society have prompted pharmaceutical and agricultural industries to develop better protocols for their synthesis. The traditional synthetic methods for these chemicals depend on toxic and mutagenic reagents and release huge waste. Hence, it is desirable to find an alternative way that circumvents these issues. Catalytic dehydrogenative coupling of alcohols provides an appealing approach since only water, or hydrogen gas are the possible byproducts, and alcohols are environmentally benign. So far, this research field has been predominated by catalysts containing noble metals, e.g., Pd, Ir, Rh, and Ru. These metals are rare, expensive, and toxic. So, it is highly desirable to search for more sustainable metal alternatives. In recent years, there have been a few breakthroughs on non-precious metal (Fe, Co, Mn, and Ni) based catalysts. However, the pincer ligand-supported catalyst dominates this field, and chemo selectivity control strategies are missing in most studies. Recently, our group developed an air and moisture-stable cobalt molecular catalyst stabilized by a tripodal mixed P/N donor ligand. The cobalt metal is earth-abundant, cheap, and less toxic. This cobalt catalyst showed excellent activities for the dehydrogenation of secondary alcohol into ketone, dehydrogenative homocoupling of primary alcohol into ester, and coupling of a secondary alcohol and primary alcohol into corresponding alcohol and ketone products. In my projects, I further explore the catalytic activities into a dehydrogenative hetero couple of primary alcohol and amine to secondary imine and amine. Also, the hetero couple of primary alcohol and nitrile

into α-olefinic and α-alkylated nitrile product with water and/or hydrogen as byproducts. It is discovered that the product's selectivity strongly depends on the amount of base used in the reaction. A catalytic amount of base leads to an imine and α-olefinic nitrile product, while an excess base loading results in an amine and α-alkylated nitrile product. We expect that this study could provide helpful insight into selective organic synthesis and catalyst design.

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ABBREVIATIONS

ADC	**Acceptorless dehydrogenative coupling**
BH	**Borrowing hydrogen**
Nuc	**Nucleophile**
Ru	**Ruthenium**
Ir	**Iridium**
Os	**Osmium**
Pd	**Palladium**
DABCO	**(1,4-diazabicyclo[2.2.2]octane)**
^{i}Pr	**Isopropyl**
KO^{t}Bu	**Potassium tert-butoxide**
NaO^{i}Pr	**Sodium propan-2-olate**
COD	**Cyclooctadiene**
OAC	**Acetate**
PPh_3	**Triphenylphosphine**
KOH	**Potassium hydroxide**
HT	**Hydrotalcite**
MgO	**Magnesium oxide**
MLC	**Metal ligand cooperation**
MS	**Molecular seives**
Mn	**Manganese**
Fe	**Iron**

Co	**Cobalt**
NaO^tBu	**Sodium tert-butoxide**
^nBuLi	**n-Butyllithium**
ClP^iPr_2	**Chlorodiphenylphosphine**
PCl_3	**Phosphorous trichloride**
NEt_3	**Triethyl amine**
$NaHCO_3$	**Sodium bicarbonate**
K_2CO_3	**Potassium carbonate**
Cs_2CO_3	**Cesium carbonate**
$KHBEt_3$	**Potasium triethylborohydride**
$CDCl_3$	**Deuterated chloroform**
H_3PO_4	**Phosphoric acid**
MeOH	**Methanol**
MPV	**Meerwein-Ponndorf-Verley**
KIE	**Kinetic isotope effect**
DCM	**Dichloro methane**

CHAPTER I: INTRODUCTION

1.1 Aim of the project

This project aims to develop a homogeneous earth-abundant metal catalyst for carbon-carbon and carbon-nitrogen bond formation reactions.

1.2 Sustainability challenges

In the last 40 years, the consumption of the earth's natural resources has tripled.[1] According to the report published on Earth Overshoot Day in 2018, natural resources are overdrawn at an alarming rate. The data showed that it requires nearly two Earths to supply the resources needed to meet the annual global needs.[2] The increasing rates at which the natural resources are extracted will cause a potential clash between the present and future generations to meet their demands. This problem needs to be addressed urgently before the irreversible depletion of natural resources.

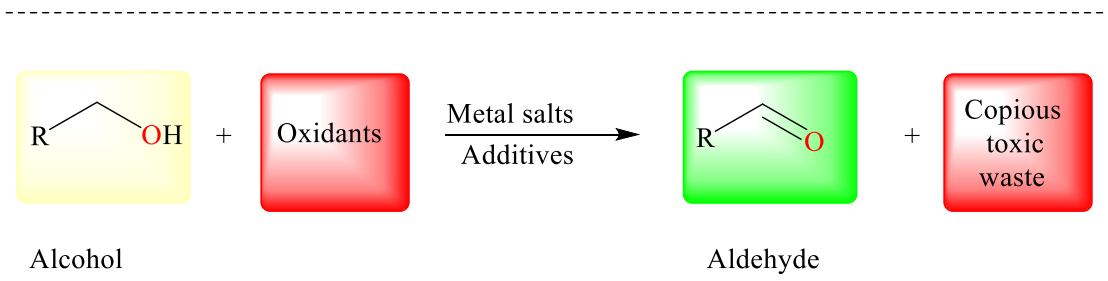
One approach to address this issue is to look for renewable alternatives and reduce the dependency on non-renewable natural resources. In this regard, biomass is one such alternative, and it can be converted into many valuable chemicals. The use of biomass to produce chemicals has many advantages, such as 1) it is barely used waste material, 2) indigestible, i.e., it does not alter the food chain, and 3) abundantly available. In this respect, biomass-derived lignocellulose can be a potential candidate to meet the increasing demand for chemicals.[1] Lignocellulose can be processed to alcohols which can further be converted into the diversity of bulk and fine chemicals containing carbon.[1] This approach using alcohol as a carbon source will cut down on the dependency on the limited fossil

resources, such as oil or coal. However, the limited reactivity of alcohol narrows its scope to be used directly as a starting material. Hence, it is desirable to find a suitable method to activate the alcohol into its more reactive form, i.e., carbonyl form. The carbonyl form usually has a much broader range of reactivity than alcohol because it is suitable for nucleophilic addition reactions and can also act as a nucleophile themselves via enol or enolate.[3]

1.3 Common methods for alcohol activation

1.3.1 Dehydrogenation/oxidation by using conventional oxidants

In this method, alcohol is activated into aldehyde or ketone by employing a stoichiometric amount of inorganic oxidants such as chromium (IV) reagents, peroxide, and other metal salt additives (scheme 1.1). This method generates a massive amount of undesirable waste that could directly harm the environment and human health.

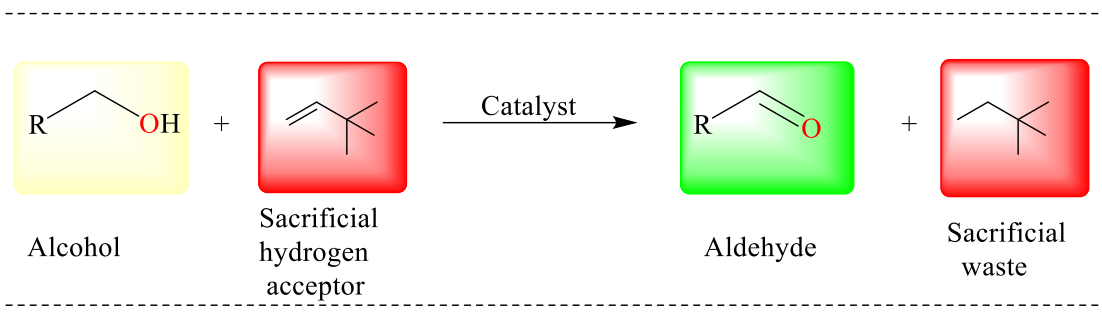


Scheme 1.1 Oxidation of alcohol by a conventional method

1.3.2 Hydrogen transfer method

This method requires a catalyst that removes hydrogen from the alcohol to give a carbonyl compound (scheme 1.2). This method is more environmentally benign than the

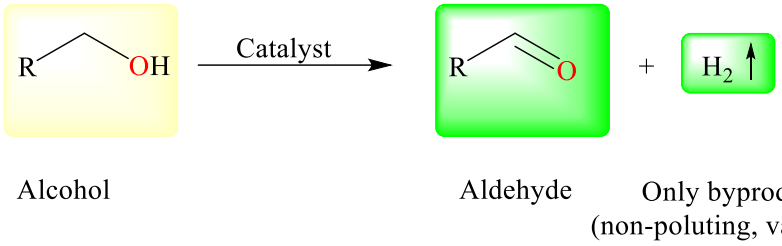
conventional method; however, it requires a sacrificial hydrogen acceptor, resulting in the release of sacrificial waste.[3]



Scheme 1.2 Oxidation of alcohol by a hydrogen transfer method

1.3.3 Acceptorless dehydrogenation method

In this method, the catalyst takes hydrogen from the alcohol to give its more reactive carbonyl form without any oxidants and hydrogen acceptors.[3] In a one-pot reaction, the so-formed carbonyl compound can further couple with a nucleophile to give an unsaturated compound. Finally, the hydrogenated catalyst liberates the hydrogen gas, and the catalyst regenerates. This process is called acceptorless dehydrogenative coupling Scheme (1.3) (ADC).[3–6] Alternatively, the hydrogenated catalyst can reduce the unsaturated intermediate to give the saturated product. This process is recognized as borrowing hydrogen (BH).[3–6] Both ADC and BH are environmentally benign methods for synthesizing carbon-carbon (C-C) and carbon-nitrogen (C-N) bonds, releasing only water or hydrogen gas as the only possible byproducts. Hence, developing a catalyst that can use alcohol as a starting material and undergoes ADC/BH (Figure 1.1) process to synthesize C-C and C-N bonds is the primary goal in the Ding research group..



Scheme 1.3 Oxidation of alcohol by an acceptorless dehydrogenation method

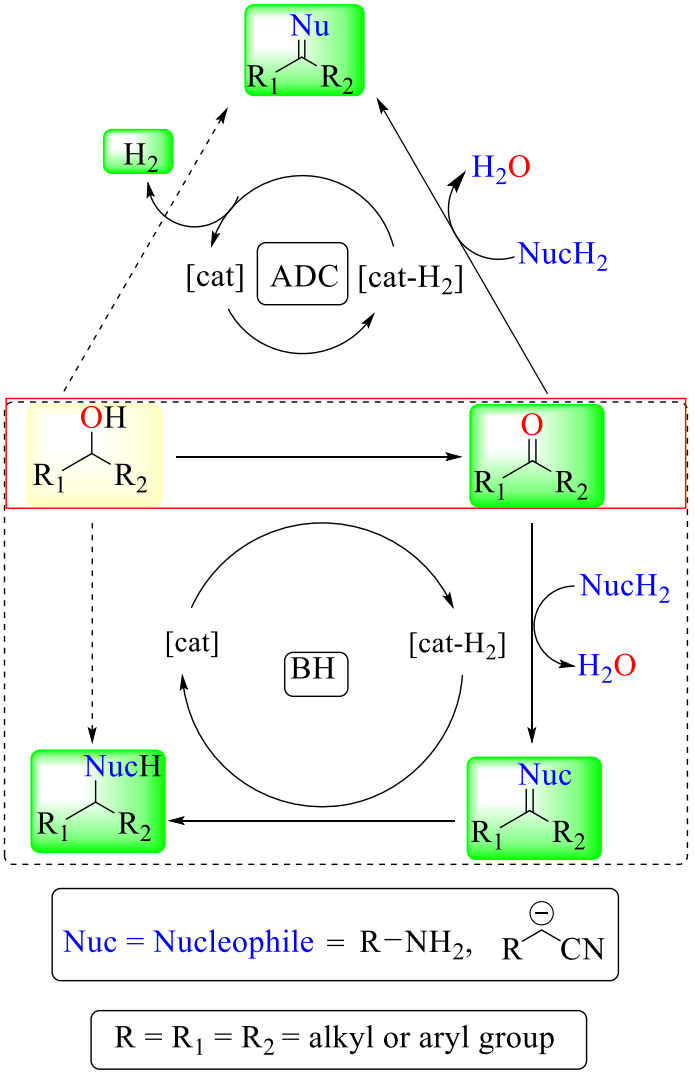


Fig. 1.0 ADC/BH process for C-C and C-N bonds synthesis from alcohol

1.4 Transition metal-catalyzed acceptorless dehydrogenative coupling of alcohols with amines/nitriles

1.4.1 Catalysis using transition metal complexes

Transition metals, situated at the middle of the periodic table, have an excellent ability to lend and take electrons from other molecules. This property makes transition metals suitable catalytic tools in modern synthetic organic[7–10] and organometallic chemistry.[7–10] After the discovery of organometallic reagents and coordination complexes in the late 1960s, transition metals became implemented in the catalytic process.[11] Five years later, Wilkinson and Coffey first reported a homogeneous organometallic catalyst for hydrogenation and opened the door for organometallic catalysis in the industry.[12,13] Since then, the chemistry of these metals has contributed to growing along with the development of supporting ligands. The ligands that bind with metals provide stability and tune the reactivity of the metal complexes (Figure 1.1). In some cases, ligand also participates in the substrate activation along with the metal and such a process is called metal-ligand cooperation.[14]

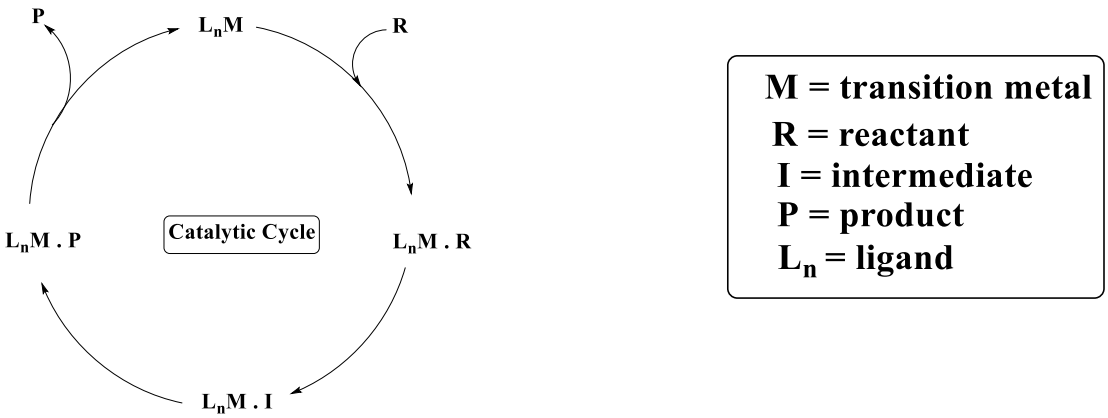


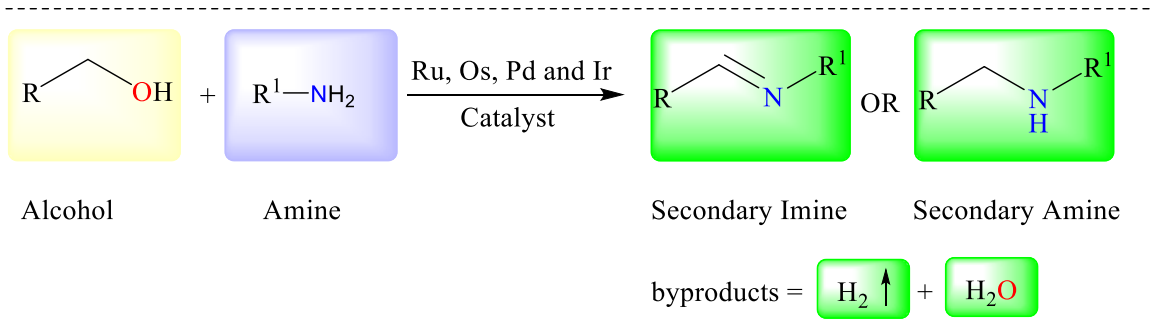
Figure 1.1. Catalytic cycle by transition metal catalysts

1.4.2 Acceptorless dehydrogenative coupling of alcohols with amines/nitriles

Acceptorless dehydrogenative coupling of alcohols with amines/nitriles is an environmentally benign approach to synthesize substituted amine/imine or *α,β*-unsaturated or saturated nitrile products. Amines and imines have broad applications as pharmaceuticals[15,16], agrochemicals[17], detergents, lubricants, dyes, and other commodity products.[18] The *α,β*-unsaturated or saturated nitrile products serve as valuable intermediates in pharmaceuticals and natural products.[19] They are also key structural motifs in many synthetic transformations.[20]

1.4.3 Precious transition metal-based catalysts for alcohol amine coupling

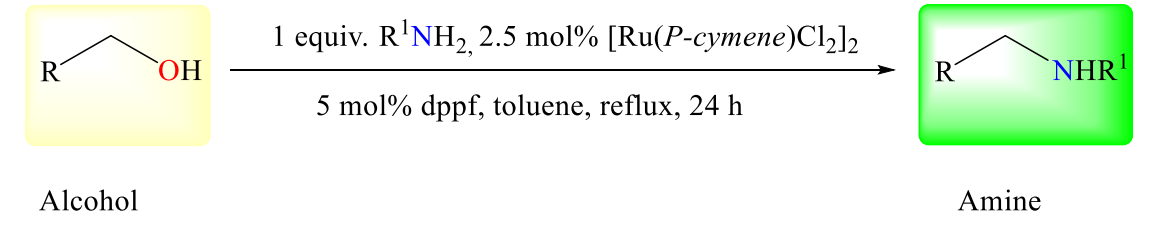
Grigg[21] and Watanabe's[22] groups were the first to report the alkylation of amines using alcohols by homogeneous transition metal-based catalysts. The commonly used noble transition metals for such reactions are Ru[21–27], Ir[28–31], Os[32], and Pd (Scheme 1.4).[33,34]



Scheme 1.4 Alkylation of amine with alcohol by precious-metal-based catalysts

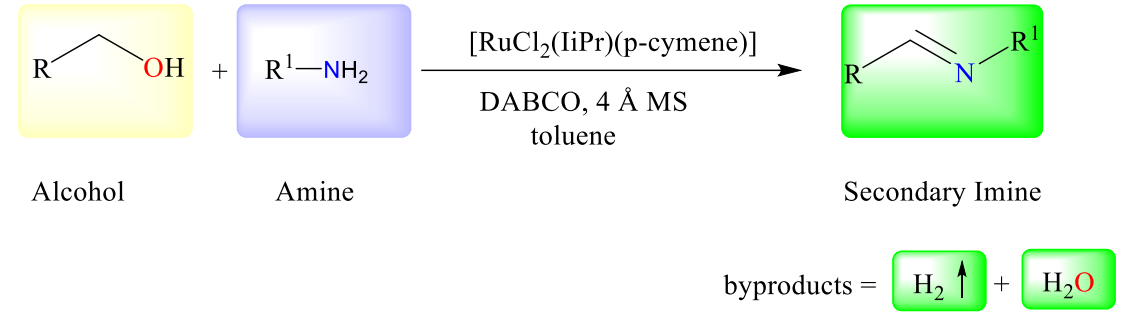
Williams group[23] in 2009 used bidentate phosphine dppf, or DPEphos supported ruthenium complex to synthesize secondary and tertiary amines including some pharmaceuticals such

as Piribedil, Antergan, Tripelennamine, Pheniramine, and Chlorpheniramine. They proposed their mechanism under the framework of BH, where alcohol first undergoes oxidative addition to ruthenium complex to form ruthenium hydride and release of aldehyde from ruthenium complex. After that, imine is generated from the condensation of aldehyde and amine. At last, ruthenium hydride hydrogenates imine into amine and water is released as a byproduct.



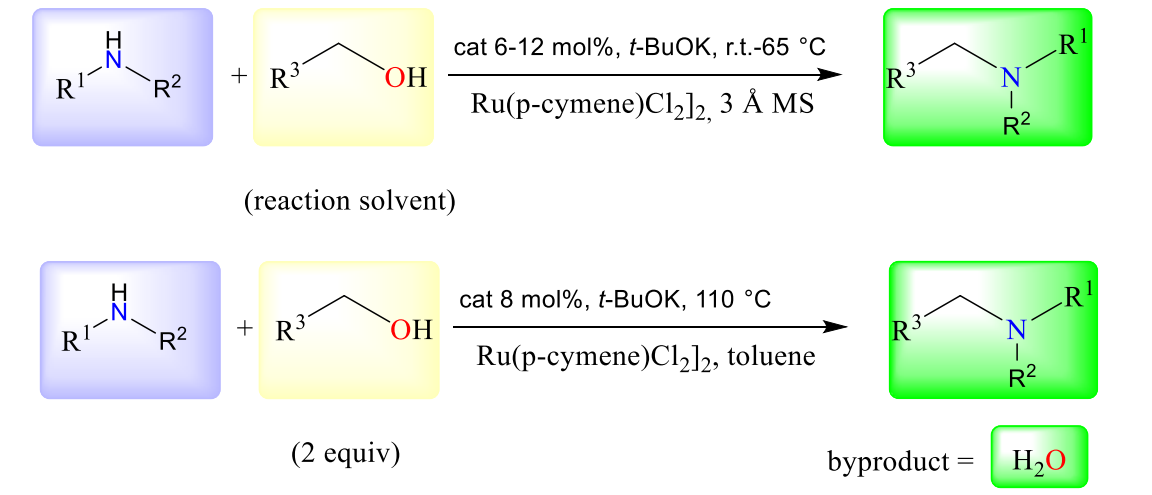
Scheme 1.5. Ruthenium-catalyzed N-alkylation of amines

In 2012, the Maggi and Madsen group[27] employed ruthenium N-heterocyclic carbene complex [$RuCl_2$(Iipr)(*p-cymene*)] along with DABCO ligand and molecular sieves for the synthesis of imines (Scheme 1.6). They believed that the reaction proceeds by initial dehydrogenation of alcohol to aldehyde, which stays coordinated to ruthenium. After that, substrate amine attacks the aldehyde to afford the hemiaminal. Eventually, the hemiaminal departs from the ruthenium and is converted to an imine.



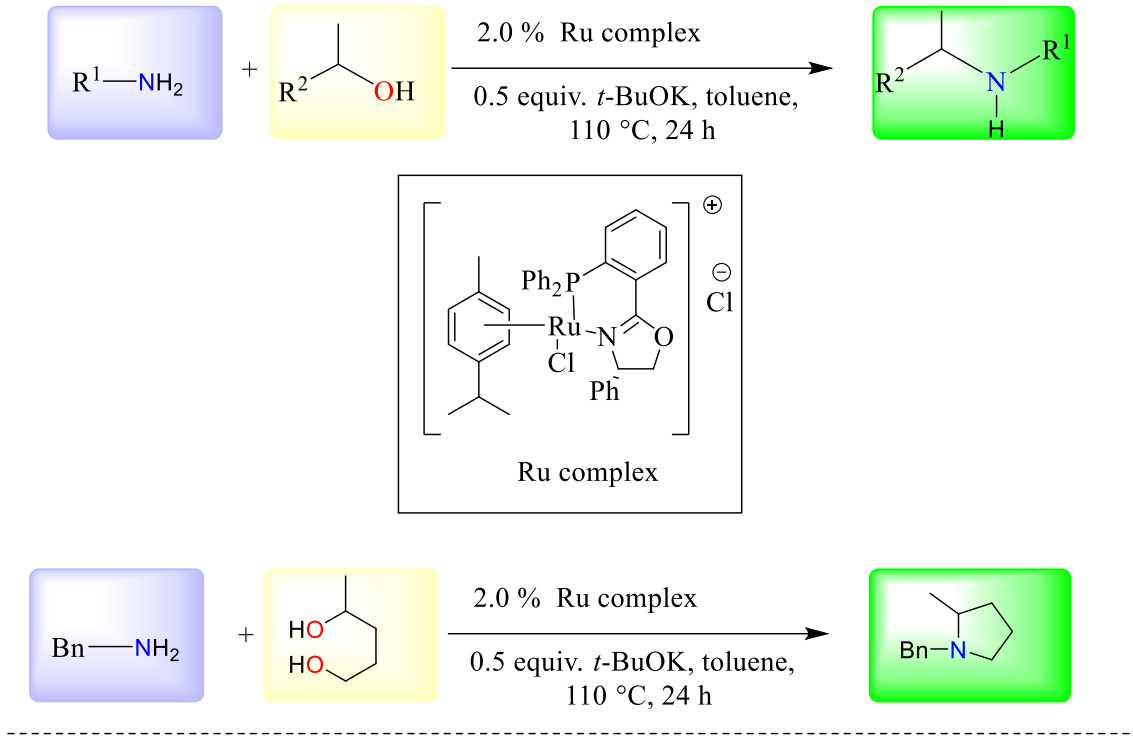
Scheme 1.6. Synthesis of imine by ruthenium N-hetorocyclic carbene complex

Moasser and Enyong[25] in 2014 used amino amide ligand supported ruthenium complex [Ru(*p-cymene*)Cl_2]Cl_2 to synthesize secondary and tertiary amine from the coupling of a primary alcohol with a primary and secondary amine, respectively (Scheme 1.7). In their reaction, they used alcohol as a solvent, and the alkylation reaction was taking place at a lower temperature of 45-65 °C. The reaction was also feasible in an organic solvent but required a high temperature. The authors mentioned that reaction follows the BH pathway.



Scheme 1.7. N-alkylation of amine by ruthenium complex under mild conditions

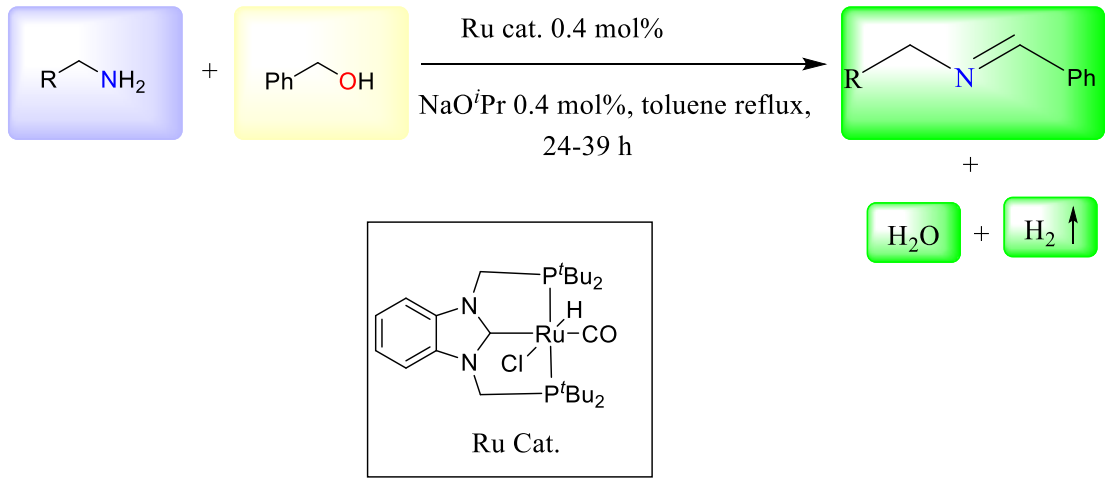
Takacs et al.[24] developed a new ruthenium complex in 2016 for the amination of primary and secondary alcohols to give secondary and tertiary amines, respectively. They used their ruthenium catalyst to synthesize heterocyclic rings from diols and a primary amine. Also, their catalyst was able to do regioselective mono- and sequential diamination of diols. They reported that the products were formed via the BH pathway (Scheme 1.8).



Scheme 1.8. Ruthenium-catalyzed amination of secondary alcohols

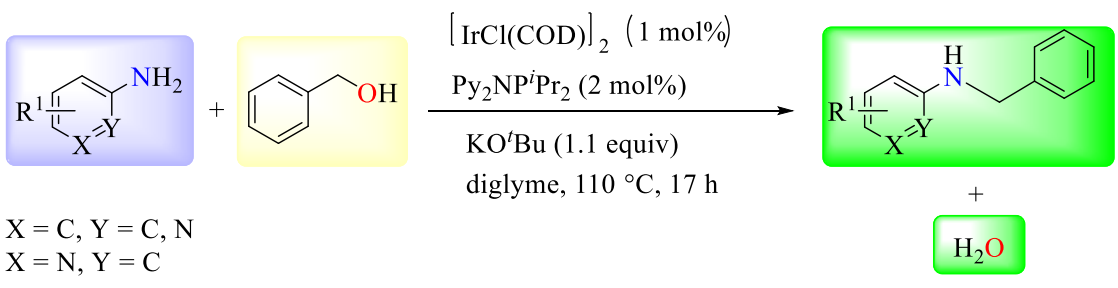
Nishibayashi et al.[26], in 2018, synthesized ruthenium complex supported by N-heterocyclic carbene and phosphine-based PCP-type pincer ligands for the synthesis of secondary imines from amines and benzyl alcohol (Scheme 1.9). They proposed an ADC pathway for imine formation where the first catalyst reacted with 1 eq. of $NaO^{i}Pr$ to give Ru(0) complex. After that, it undergoes oxidative addition of alcohol to give corresponding

alkoxide and hydride complex. Then, *β*-hydride elimination gives aldehyde complex. The dissociation of aldehyde from the ruthenium complex gives ruthenium hydride and free aldehyde. The free aldehyde reacts with 1 eq. of amine to give secondary imine as a final product. Finally, the catalyst was regenerated by the extrusion of hydrogen gas.



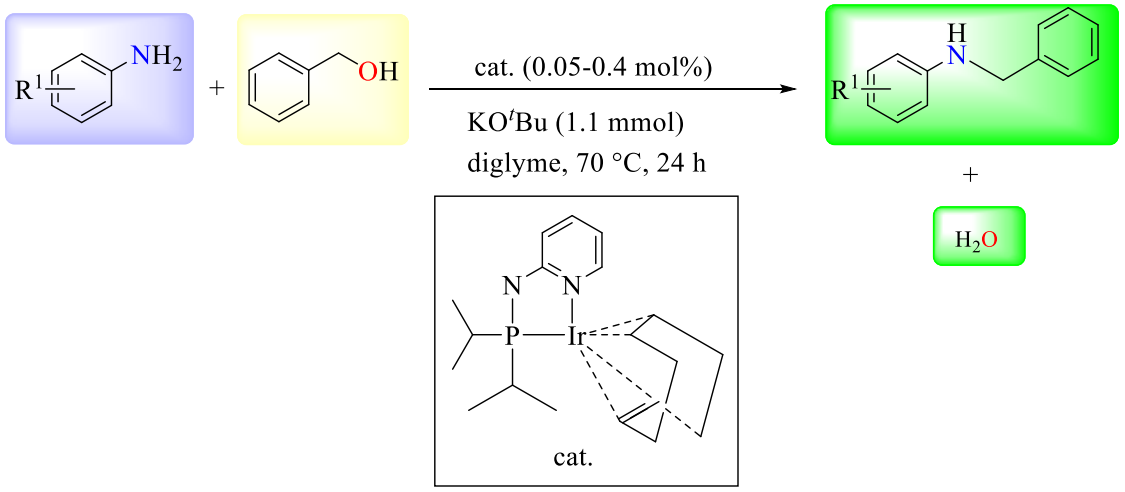
Scheme 1.9 Ruthenium complex bearing PCP-type ligand for the synthesis of imine

Kempe group[28] in 2008 used iridium-P,N complexes for the N-alkylation reaction with primary alcohols (Scheme 1.10). Under their optimized reaction conditions, primary and secondary amine were coupled with primary alcohol to give secondary and tertiary amine.



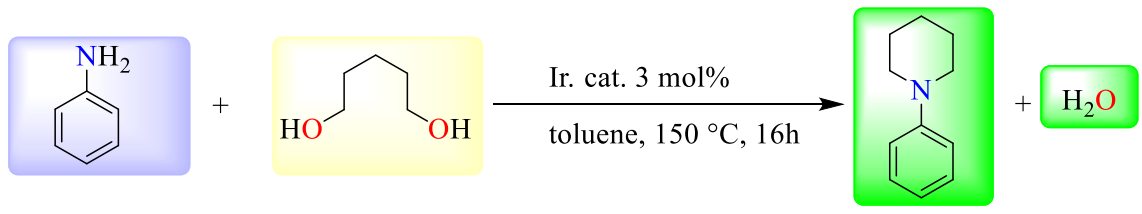
Scheme 1.10. Iridium-catalyzed synthesis of (hetero)aromatic amines

Two years later, Kempe group[29] synthesized a new iridium complex supported by anionic P,N ligands for the alkylation of anilines by alcohol. They synthesized a new iridium complex by treating the previously reported iridium complex in 2008 with 2-amino pyridine in the presence of KO^{t}Bu. They employed the new iridium catalyst to synthesize secondary amine at lower reaction temperatures with the BH mechanism (Scheme 1.11).



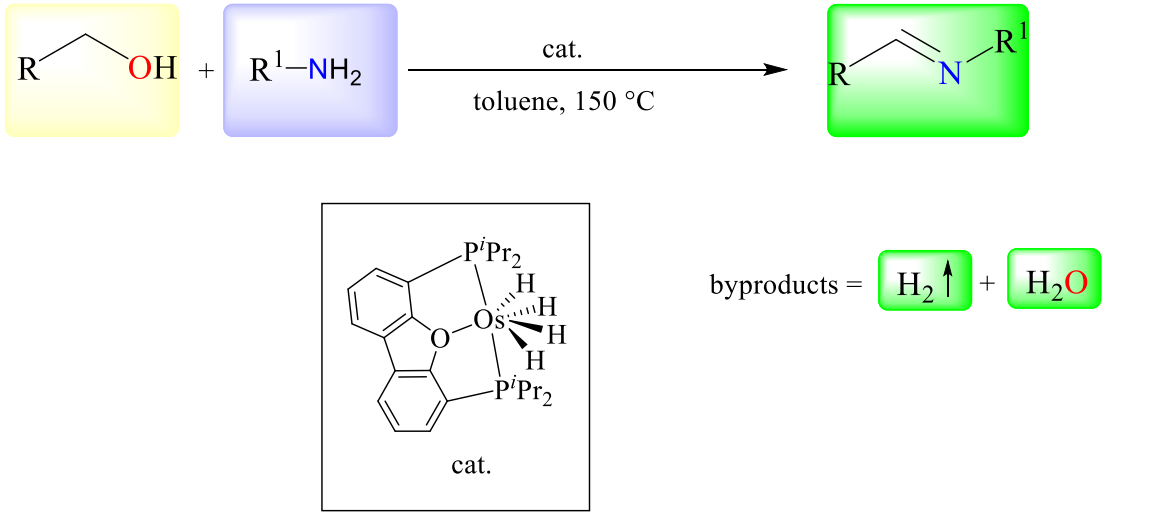
Scheme 1.11 P, N-ligand-stabilized iridium complex for the synthesis of amine

In 2012, the Bruneau group[31] developed a new iridium complex featuring phosphanesulfonate ligand for the selective synthesis of N-arylpiperidines via the BH mechanism. This group used their iridium catalyst for the synthesis of tertiary amine by coupling diols and aniline (Scheme 1.12).



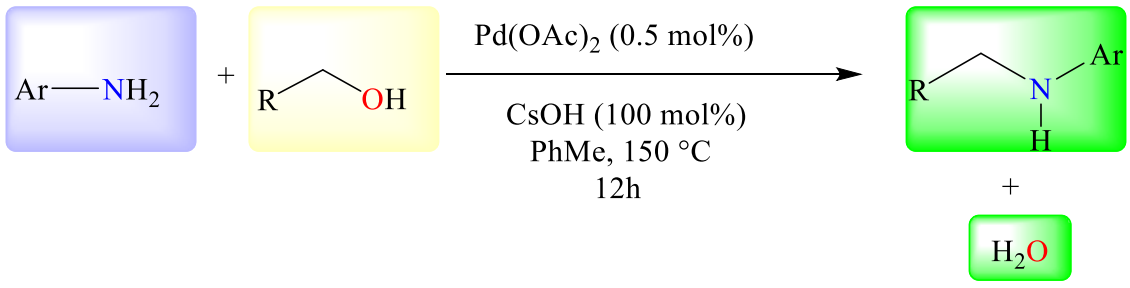
Scheme 1.12 Coupling of diols and aniline by iridium catalyst

Esteruelas group[32] in 2011 reported POP-type osmium (II) and (IV) complexes. They mentioned that the tetrahydride osmium complex is an efficient catalyst for synthesizing imines from alcohols and primary amines (Scheme 1.13).



Scheme 1.13 Synthesis of imine by osmium complex

In 2011 Ramón group[33] used palladium(II) acetate as a catalyst for the N-alkylation of nitrogenated compounds with alcohols to give secondary amine, carboxamides, and sulfonamides by BH approach (Scheme 1.14).

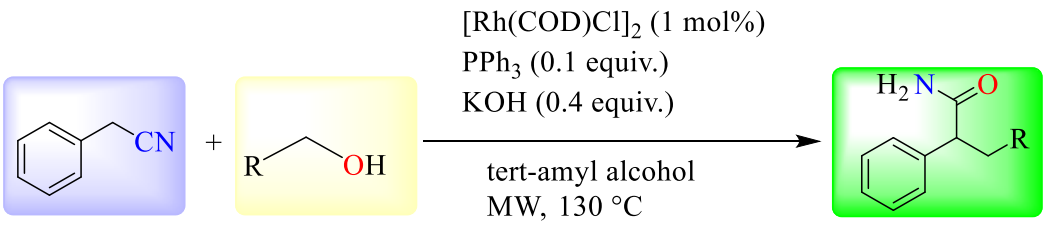


Scheme 1.14 Palladium(II) acetate catalyst for the synthesis of amine

1.4.4 Precious transition metal-based catalysts for alcohol nitrile coupling

The coupling of alcohols with nitriles to form *α,β*-saturated nitriles has been dominated by precious metals such as Rh[35,36], Ir[37,38], Ru[39], Pd[40] based catalysts. The traditional method for synthesis of *α,β*-unsaturated nitriles involves the condensation reaction between aldehyde with arylacetonitriles in the presence of bases.[41–43]

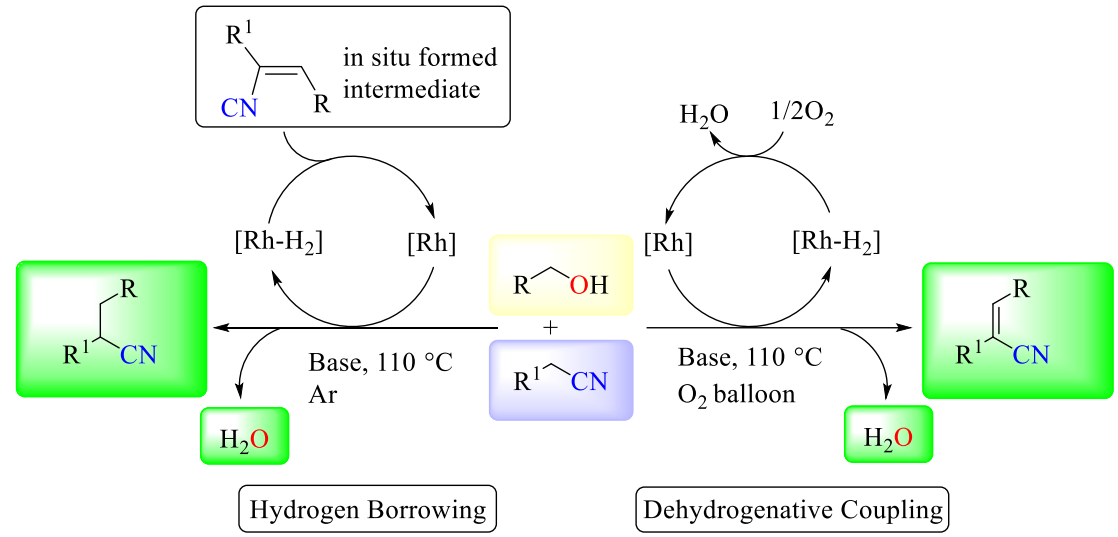
In 2015, the Wang group[35] used a rhodium complex supported by a triphenylphosphine ligand to synthesize arylacetamides from arylacetonitriles and primary alcohols (Scheme 1.15). Their mechanistic studies show that the product arylacetamides results from the hydration of α-alkylated arylacetonitriles. They report the BH approach for product formation.



Scheme 1.15 Rhodium complex for the synthesis of α-alkylated arylacetamide

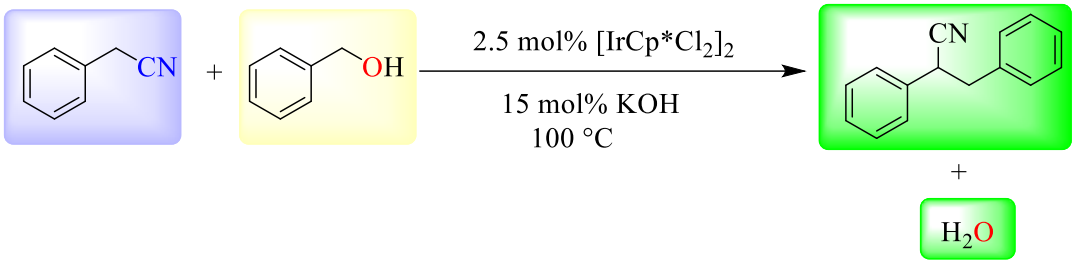
Wang et al.[36], in 2017, used the binuclear rhodium catalyst for the selective synthesis of olefinic and alkylated nitrile products (Scheme 1.16). Here, they controlled the selectivity of the reaction by altering the reaction atmosphere. For alkylated nitrile product, the

reaction was carried out under argon gas, and for olefinic nitrile product, the reaction was performed under oxygen.



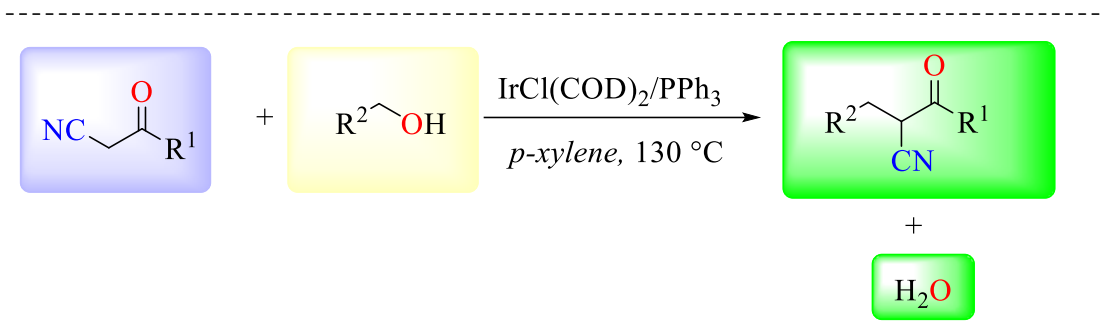
Scheme 1.16 Synthesis of α-olefinic and alkylated nitrile by rhodium complex

In 2006, the Derrick group[37] used iridium catalyst to synthesize substituted acetonitriles in a solvent-free condition via the BH mechanism (Scheme 1.17). In their finding, they report that the rate of the reaction was accelerated by irradiation with a microwave source.



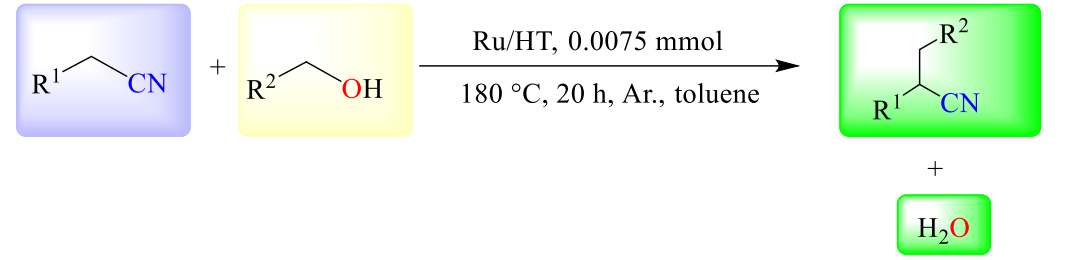
Scheme 1.17 Synthesis of α-alkylated nitrile by iridium complex

Ishii group[38] in 2007 developed a base-free iridium complex supported by PPh_3 ligand for the synthesis of saturated α-alkylated nitrile products (Scheme 1.18). Since their reaction is base-free, the aldol type of condensation reaction is catalyzed by the iridium catalyst.



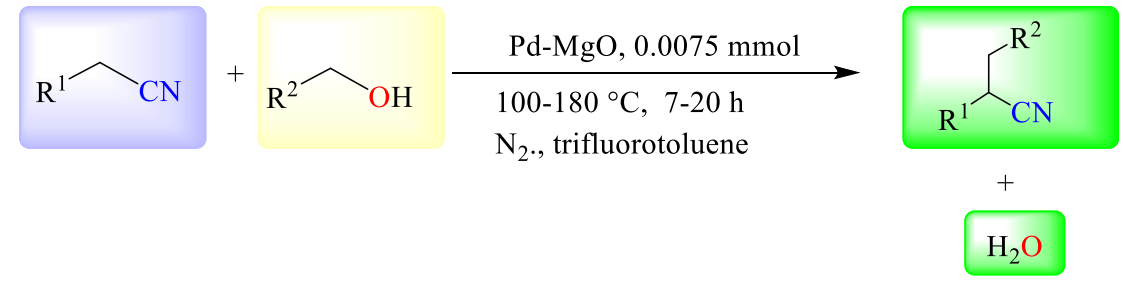
Scheme 1.18 Alkylation of active methylene compound with alcohol by iridium complex

Kaneda et al.[39] in 2004 used ruthenium nanostructured heterogeneous catalysts for the coupling of nitriles with the alcohol to give α-alkylated nitriles product. From the controlled experiment, they found that α-alkylation of nitriles with alcohol takes place in three consecutive reaction steps (i) the ruthenium complex dehydrogenates the alcohol into an aldehyde, (ii) HT (hydrotalcite) catalyzed aldol type condensation reaction between aldehyde and nitrile to give olefinic nitrile intermediate and (iii) ruthenium hydride hydrogenates the olefinic intermediate into alkylated nitrile product (Scheme 1.19).



Scheme 1.19 Synthesis of α-alkylated nitrile by Ruthenium nanostructured catalyst

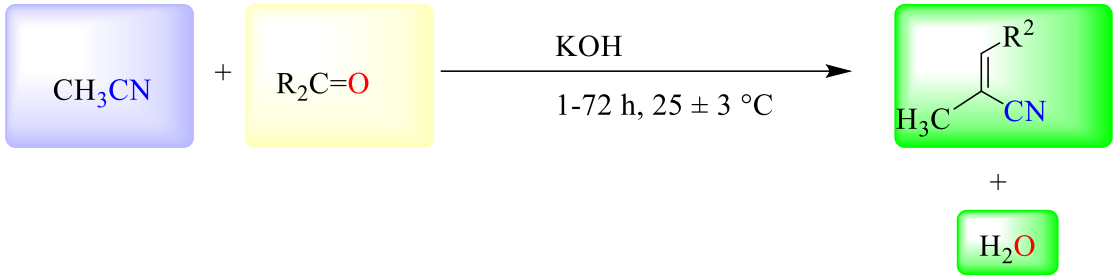
In 2011, the Sabater group[40] used a Pd-MgO bifunctional catalyst for the alkylation of nitriles with alcohol (Scheme 1.20). The reaction mechanism is on par with the Kaneda group mentioned above.



Scheme 1.20 Synthesis of α-alkylated nitrile by Pd-MgO bifunctional catalyst

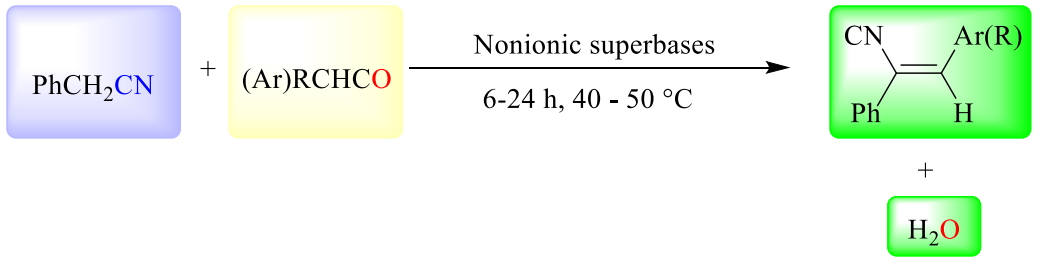
1.5 Base catalyzed synthesis of *α,β*-unsaturated nitriles

The condensation of carbonyl compounds with acetonitrile in the presence of a base to synthesize *α,β*-unsaturated nitriles was done by Gokel et al.[41] in 1979. They mentioned that aliphatic aldehyde did not condense satisfactorily, and base-sensitive functional groups are incompatible in their reaction (Scheme 1.21). The reaction time varies with the type of substrates.



Scheme 1.21 Synthesis of α,β-unsaturated nitrile by a KOH

Verkade group[42] in 1998 used strong nonionic Lewis bases $P(MeNCH_2CH_2)_3N$ and $P(HNCH_2CH_2)(i\text{-}PrNCH_2CH_2)_2N$ to synthesize a variety of functionalized *α,β* unsaturated nitrile (Scheme 1.22). In their mechanistic study, polar protic and nonpolar aprotic solvent were tested for the condensation reaction. It was found that primary and secondary aliphatic aldehydes do not condense satisfactorily with acetonitrile, and ketones are incompatible substrates in the condensation reaction.



Scheme 1.22 Synthesis of *α,β*-unsaturated nitrile by nonionic superbases

1.6 Challenges of precious-metal-based catalysts

Precious metals have played an excellent role in catalysis. However, their high price[44], limited quantity[45], and toxicity[46,47] make them challenging to use as catalysts in the

agrochemical and pharmaceutical industries. In this regard, 3d-transition metal-based catalysts are appealing alternatives because they are less toxic[46,47], earth-abundant[45], and cheap. [44] However, the challenge is to design an earth-abundant metal-based catalyst with comparable catalytic activities as precious metals. Achieving this goal requires the development of novel structured ligand that can bind with the metal and participate in substrate activation steps. The approach that involves the direct participation of both metal and ligand for bond activation is called metal-ligand cooperation (MLC). In this approach, it is hoped that the nonprecious metals may achieve comparable catalytic activities with those precious metals.

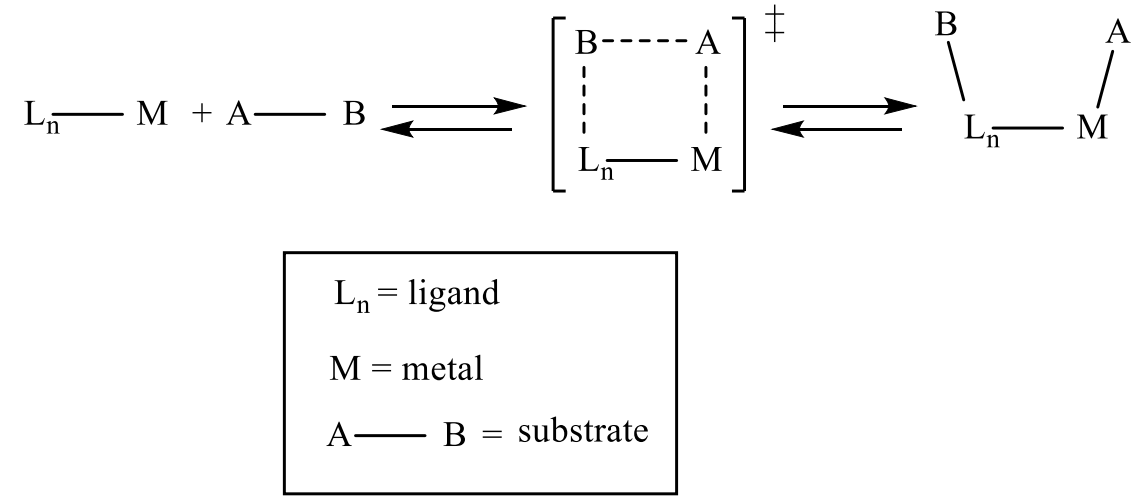


Fig.1.2 Bond activation by metal-ligand cooperation

1.7 Objectives of my research

(1) To synthesize organic ligands with potential metal-ligand cooperativities.

(2) To develop a molecular metal catalyst based on an earth-abundant metal (e.g. cobalt) supported by the above cooperative ligands.

(3) To employ the developed metal complex as an alternative to precious metal catalysts in acceptorless dehydrogenative coupling of alcohols with amines/nitriles.

(4) To perform a mechanistic study of the above-developed catalyst in substrate activation.

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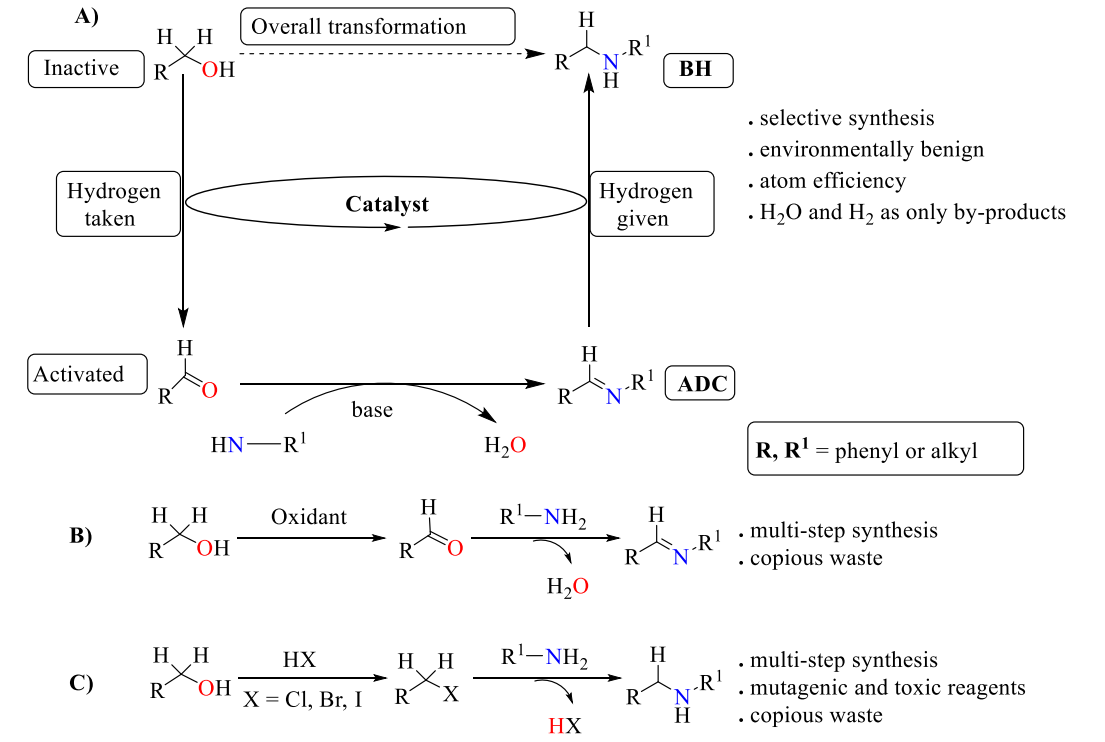
CHAPTER II

Switchable Imine and Amine Synthesis Catalyzed by a Well-Defined Cobalt Complex

2.1 Introduction

Homogeneous transition metal-catalyzed carbon-carbon and carbon-heteroatom bond forming reactions are among the preeminent organic synthetic methods for high value products.[1] One such prominent synthetic strategy is acceptorless dehydrogenative coupling (ADC) which has recently attracted enormous interest in academia and fine-chemical industries.[2-5] In a typical ADC pathway, a substrate is first dehydrogenated with the catalyst taking one hydride and one proton (Scheme 1A, step 1 and 2). The dehydrogenated intermediate is then attacked by a nucleophile, e.g., an amine, leading to an unsaturated product with loss of a water molecule. In the final step, the hydrogen gas is liberated, regenerating the catalyst. Alternatively, the catalyst bearing a hydride and a proton could reduce the unsaturated product at the final step to afford the saturated product. This is known as the borrowing hydrogen (BH) process (Scheme 1A, steps 1 to 3).[2-5] Both ADC and BH offer great advantages over conventional methods (Scheme 1B and 1C), as: a) no hydrogen acceptor or oxidant is required; b) less waste is generated with water and hydrogen as the only possible byproducts; c) high atom efficiency can be achieved; and d) challenging reactants such as normally unreactive alcohols can be directly used.[5] In addition, alcohols are inexpensive, less toxic, readily available, and obtainable from biomass feedstock.[6] In the past decades, precious metal catalysts have been studied intensively for the ADC and BH processes, significantly promoting this field. Due to the

increasing economic and environmental concerns, earth-abundant metal catalysts as desirable alternative to the precious metal catalysts have emerged in a surge of recent discoveries.[7-14]

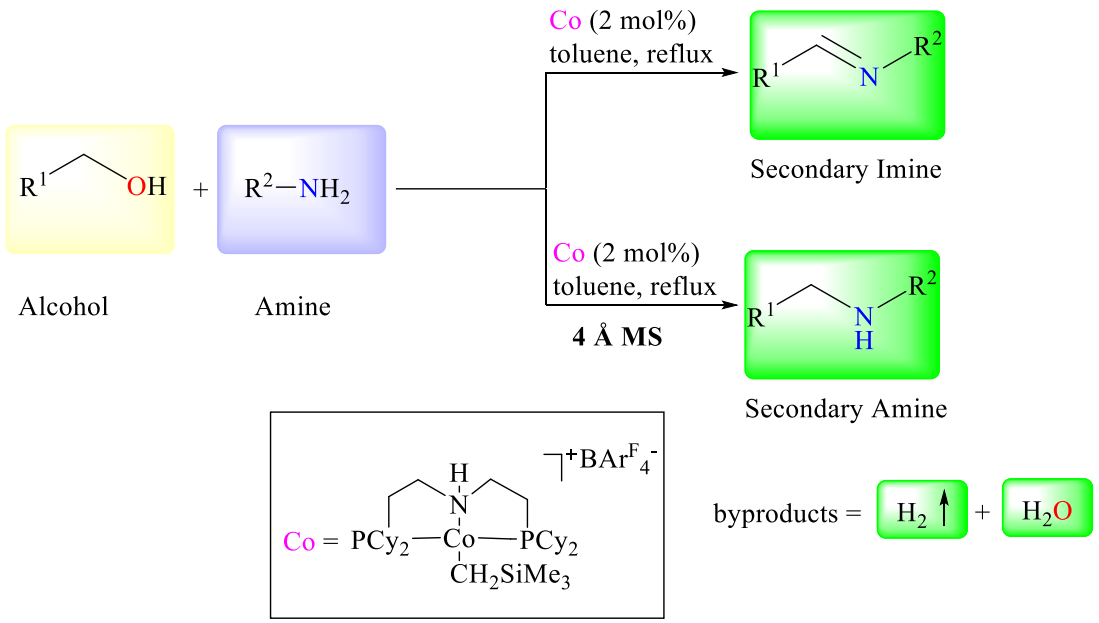


Scheme 2.1 Comparison of ADC/BH with conventional methods for imine/amine synthesis. **A),** More sustainable ADC/BH pathways for imine/amine synthesis, **B)** conventional method for imine synthesis, and **C),** The conventional method for amine synthesis

Imines and amines are important classes of compounds that have found ubiquitous applications in pharmaceutical, chemical, and agricultural industries.[15,16] N-alkylation of amines with alcohols catalyzed by earth-abundant metal catalysts to access secondary

imines or amines via ADC or BH, respectively, is a promising and environmentally-friendly process.[7-14, 17-38] However, there remains a great challenge to efficiently tune the selectivity, e.g., imine is normally identified as a major side product in amine synthesis and *vice versa*. Thus, it is highly desirable to explore the factors that favor either imine or amine product from both practical and mechanistic points of view. Toward this end, new synthetic methods and catalyst design are required. Unfortunately, current understanding of the selectivity control over imine or amine synthesis via ADC or BH is still limited.

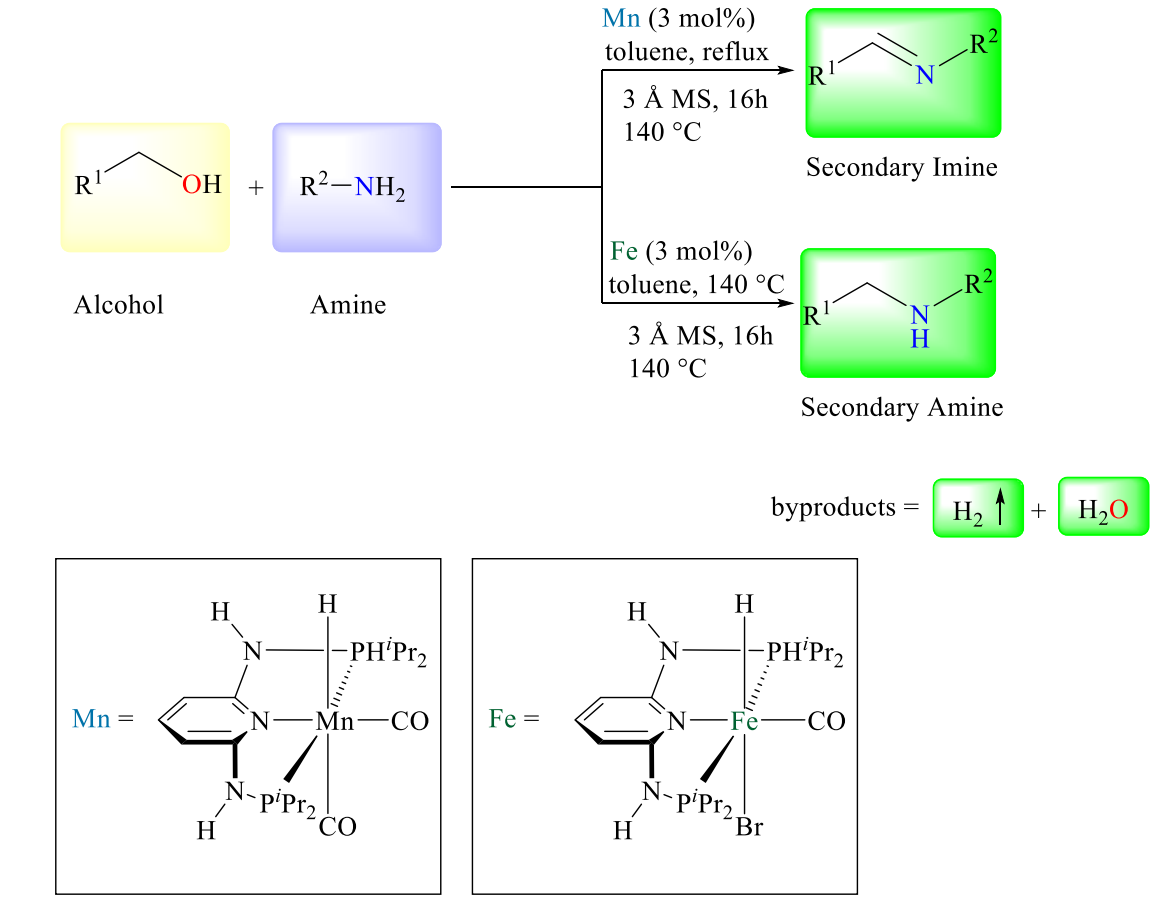
In their pioneering work, Hanson, Zhang, and co-workers reported that in a cobalt-catalyzed amine/imine synthesis, addition of molecular sieves shifts the product from imine to



Scheme 2.2 Cobalt catalyzed imine and amine synthesis by Hanson, Zang and co-workers

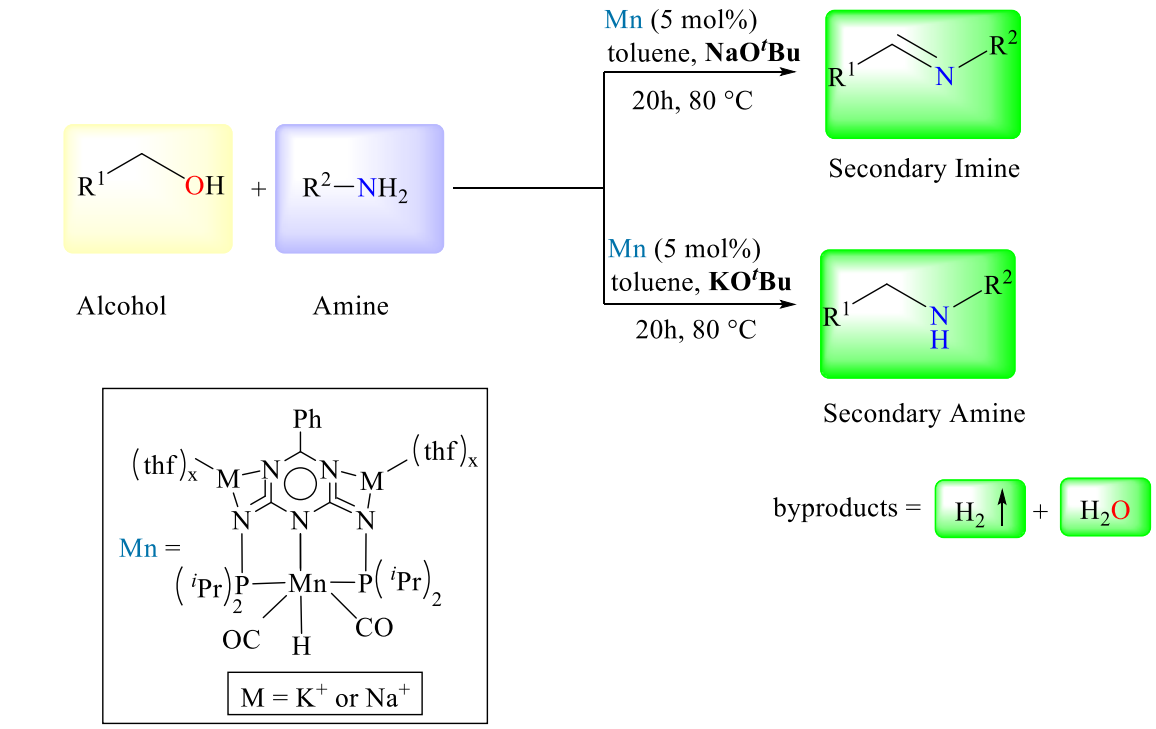
amine.[17,18] However, this method does not seem to be a general one and contradictory results are known, as molecular sieves were also reported to promote imine product instead.[19,20] Furthermore, the heterogeneous nature of molecular sieves exerts challenges to understanding the mechanism.

Kirchner and coworkers presented that the choice of metal leads to different products, in which iron and manganese catalysts afford amine and imine, respectively, in the presence of molecular sieves.[21]



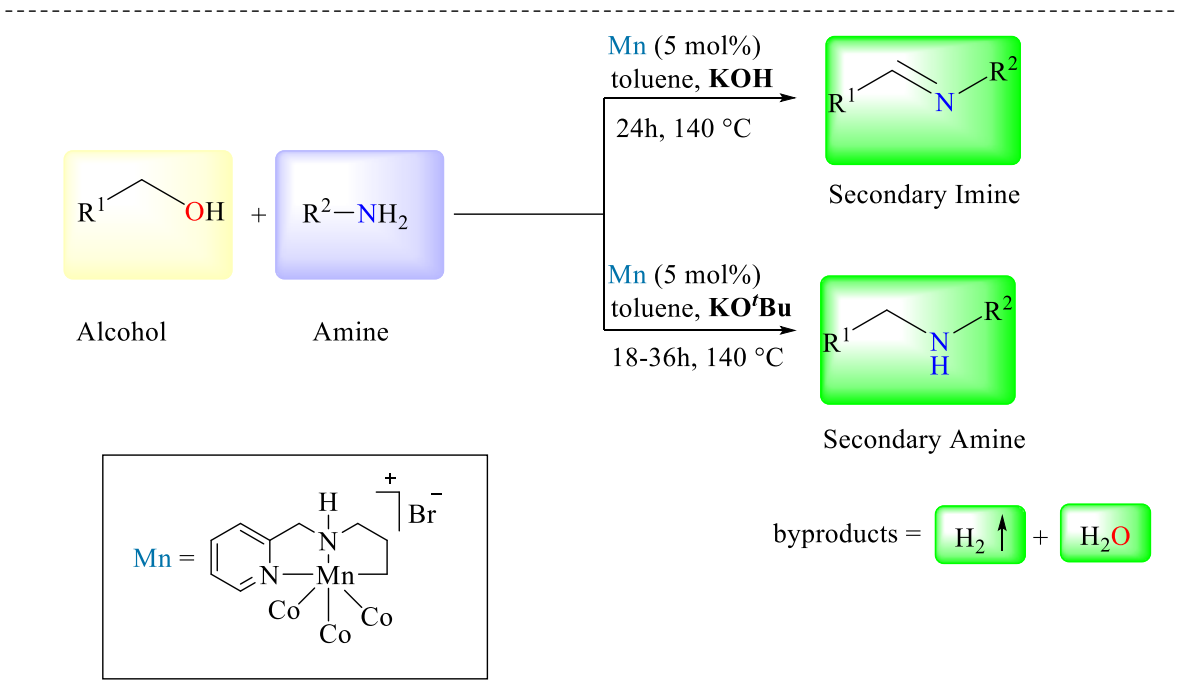
Scheme 2.3 Krichner's manganese and iron catalyst for the selective synthesis of imine and amine

Kempe and co-workers reported an interesting synthetic method that the change of base type, i.e., KO^{t}Bu or NaO^{t}Bu, can result in switchable amine/imine synthesis mediated by a manganese catalyst.[22] A large amount of base, i.e., 1.0 and 1.5 equiv. with respect to the substrate is mandatory for amine and imine synthesis, respectively. It is noted that this method is not applicable to the cobalt- and iridium-based analogues.



Scheme 2.4 Switchable synthesis of imine and amine by Kemp's manganese catalyst using different bases i.e. NaO^{t}Bu for imine and KO^{t}Bu for amine

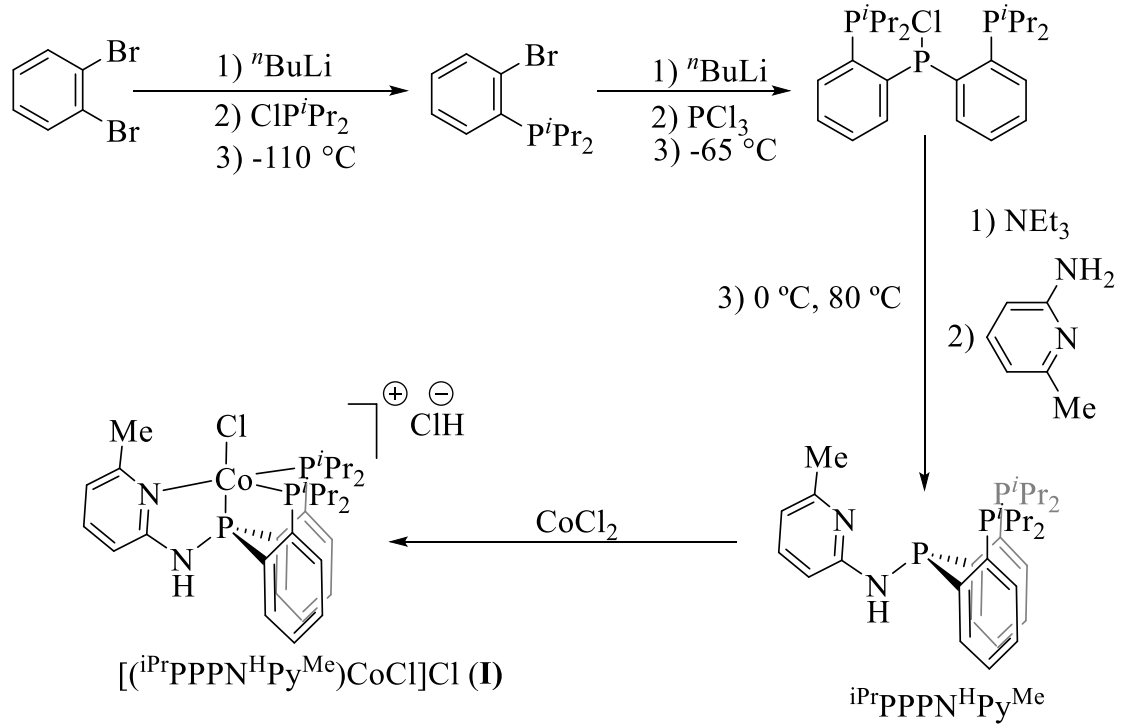
Recently, Srivastava, Srimani, and co-workers reported a similar strategy by changing the type of bases using a manganese catalyst.[38] Harsh reaction conditions, such as 30 mol % base and 140 °C, are required for imine synthesis. Heterogeneous catalysts based on precious metals are also known for selective imine/amine formations.[39-40] Thus, it is highly desirable to develop more general and sustainable strategies to manipulate the ADC or BH process for efficient selectivity control under milder conditions employing base transition metal catalysts.



Scheme 2.5 Selective synthesis of imine and amine by srivastava's manganese catalyst using different bases i.e KOH for imine and KO^{t}Bu for amine

Recently, we have developed a novel ^{iPr}PPPN^{H}Py^{Me} tetradentate ligand which is designed to offer extraordinary stability to base transition metal centers and may actively participate

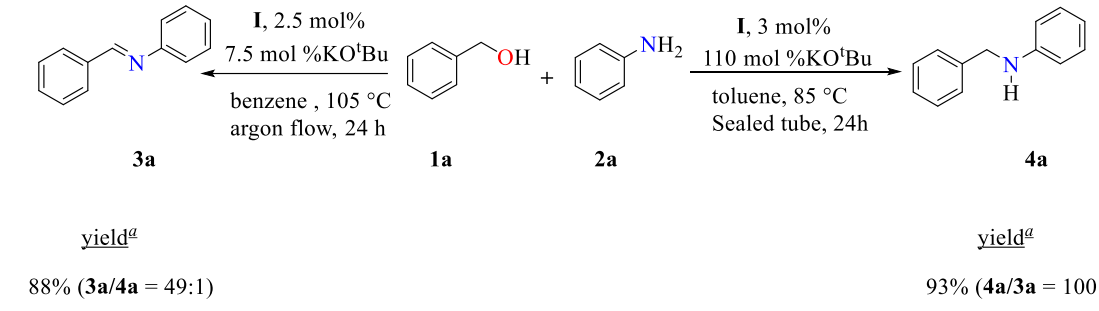
in catalysis by metal-ligand cooperativity (MLC).[41] We are interested in this tetradentate tripodal ligand for the following reasons: (1) It may provide extra stability to the reactive intermediates by enforcing five or six coordination on the metal center. (2) Because of the different coordination environments, metal complexes by such ligands may have different from those of tridentate pincer ligand systems, which currently dominate the dehydrogenation of alcohols.



Scheme 2.6 Synthesis of tripodal ligand by Ding's group

The air- and moisture stable cobalt complex **I** (Scheme 2) has shown great reactivity in dehydrogenation of secondary alcohols to ketones,[41] dehydrogenative self-coupling of primary alcohols to esters,[42] and dehydrogenative cross-coupling of primary and secondary alcohols to ketones.[43] Herein, we describe an unprecedented and convenient method using

I for the highly selective imine/amine synthesis by simply adjusting the base loadings. We expect to provide useful insights that could enable new strategies in selective organic synthesis and catalyst design.



Scheme 2.7 Switchable synthesis of imine and amine by tripodal ligand supported cobalt catalyst

2.2 Results and Discussion

In the ADC/BH route for the imine/amine formation, amine is afforded from the imine hydrogenation step (Scheme 1A, step 3), the imine/amine selectivity determining step. We initiated our study by probing any strategy that could favor or disfavor this key step. In our previous studies, a base such as KO^{t}Bu is required to activate the cobalt pre-catalyst.[41-43] Since base is known to promote transition metal-catalyzed hydrogenation reactions,[44-46] our initial speculation is that by adjusting the amount of base the amine/imine selectivity might be achieved. Toward this end, we examined our cobalt catalyst in response to the base loadings in transfer hydrogenation of imine. In the model reaction of N-benzylideneaniline with benzyl alcohol, an 82% yield of N-benzylaniline was obtained using 2.5 mol % **I** and 110 mol % KO^{t}Bu at 85 °C after 24 h. However, when the KO^{t}Bu loading was reduced to a catalytic amount of 7.5 mol %, only 1% of N-benzylideneaniline was converted to

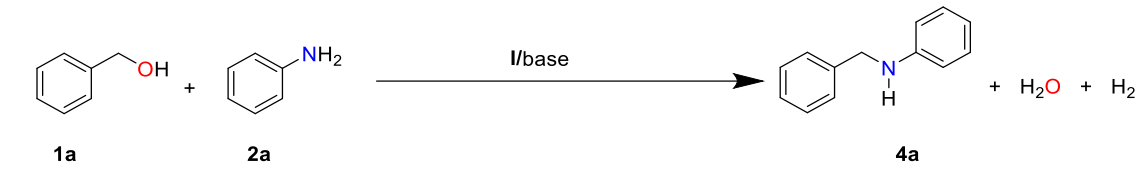
Nbenzylaniline. These results suggest a key role the base, serving as a "switch" for the imine/amine selectivity with our cobalt catalytic system. Following this hypothesis, we explored the reaction conditions for switchable imine/amine synthesis (Table 2.1 and Table 2.2).

Table 2.1 Optimization of the Reaction Conditions for Imine Synthesis

entry[a]	base	base (mol%)	temp (°C)	solvent	Yield (%)[b]
1	KO^{t}Bu	0	105	benzene	0
2	KO^{t}Bu	2.5	105	benzene	29
3	KO^{t}Bu	5	105	benzene	74
4	KO^{t}Bu	7.5	105	benzene	88, 0[c], 79[d], 74[e]
5	KO^{t}Bu	10	105	benzene	86
6	NaO^{t}Bu	7.5	105	benzene	82
7	KOH	7.5	105	benzene	72
8	$NaHCO_3$	7.5	105	benzene	2
9	K_2CO_3	7.5	105	benzene	4
10	Cs_2CO_3	7.5	105	benzene	9
11	KO^{t}Bu	7.5	105	toluene	72
12	KO^{t}Bu	7.5	105	THF	51
13	KO^{t}Bu	7.5	105	1,4-dioxane	24
14	KO^{t}Bu	7.5	85	benzene	15
15	KO^{t}Bu	7.5	115	benzene	86

[a]Reaction conditions: Benzyl alcohol (0.25 mmol), aniline (0.275 mmol), **I** (2.5 mol%), base, and solvent (1.2 mL) were heated in a 15 mL reaction tube under Ar flow for 24 h. [b]NMR yield using 1,3,5 trimethoxybenzene as internal standard. [c]Without **I**. [d]Isolated yield on 1 mmol scale. [e]Mercury (125 mg) was added to the reaction.

Table 2.2 Optimization of the Reaction Conditions for Amine Synthesis



entry[a]	base	base (mol%)	temp (°C)	solvent	Yield (%)[b]
1	KO^{t}Bu	0	85	toluene	0
2	KO^{t}Bu	7.5	85	toluene	4
3	KO^{t}Bu	25	85	toluene	47
4	KO^{t}Bu	75	85	toluene	78
5	KO^{t}Bu	110	85	toluene	93, 4,[c] 89,[d] 77[e]
6	KO^{t}Bu	125	85	toluene	93
7	NaO^{t}Bu	110	85	toluene	89
8	KOH	110	85	toluene	78
9	NaOH	110	85	toluene	79
10	K_2CO_3	110	85	toluene	2
11	KO^{t}Bu	110	85	benzene	72
12	KO^{t}Bu	110	85	THF	48
13	KO^{t}Bu	110	85	1,4-dioxane	35
14	KO^{t}Bu	110	65	toluene	22
15	KO^{t}Bu	110	105	toluene	85

[a]Reaction conditions: Benzyl alcohol (0.25 mmol), aniline (0.275 mmol), **I** (3 mol%), base, and solvent (0.75 mL) were heated in a sealed 15 mL reaction tube for 24 h. [b]NMR yield using 1,3,5 trimethoxybenzene as internal standard. [c]Without **I**. [d]Isolated yield on 1 mmol scale. [e]Mercury (125 mg) was added to the reaction.

Gratifyingly, we found that for efficient imine formation, 2.5 mol % **I** with 7.5 mol % of KO^{t}Bu at 105 °C under argon flow is required. Alternatively, for selective amine

generation, 3 mol % **I** with 110 mol % of KO^{t}Bu at 85 °C in a small, closed reaction vessel is needed (Scheme 2). Notably, excellent **3a**/**4a** selectivity was observed and *vice versa*. Both **I** and KO^{t}Bu are crucial for the imine/amine formations. 1 mmol scale reaction was also performed, leading to very good 79% and 89% isolated yields of **3a** and **4a**, respectively (Scheme 2). H_2 was confirmed by GC from the gas phase after the imine forming reaction, suggesting an ADC process. Mercury tests indicated homogeneous catalytic processes for both imine and amine formations.

We then examined a comprehensive list of alcohol and amine substrates to explore the scope of this method (Table 2.3). The presence of electron-donating groups such as –OMe, –Me, –^{i}Pr, etc. attached to *meta* or *para* positions of benzyl alcohol or aniline substrates gave good-to-excellent yields of amine or imine products (Table 2.3, **3b-3k**; **4b-4k**). The analogous substrates with electron-withdrawing groups like –F and –Cl, also proceeded smoothly to furnish the corresponding products (Table 2.3, **3l-3q**; **4l-4q**). *Ortho*-substituted substrates also displayed good-to-excellent activity (Table 2.3, **3r-3s**; **4r-4s**). The substrates bearing naphthalene and pyridine rings were well-tolerant with this method (Table 2.3, **3t-3w**; **4t-4w**). In addition, amines and imines with alkyl groups could also be accessed. Interestingly, aliphatic amines reacted with both benzyl and alkyl alcohol substrates affording the corresponding imines with excellent yields but failed for amine formation (Table 2.3, **3x3ab**; **4x-4ab**). This might be due to the hindrance by the bulky KO^{t}Bu group at the last hydrogenation step in MPV reduction (Figure 2.0). It is noted that the proposed transition state shown on the mechanism is simplified model, as the identity of KO^{t}Bu is unclear to us.[47] On the contrary, anilines underwent the catalytic reactions smoothly with alkyl alcohols to give amine products, but not for imine generation (Table

2.3, **3ac-3ai**; **4ac-4ai**). The substrates with nitrile, nitro, and furfuryl groups were not compatible. Also, note that our strategy can be employed to selectively synthesize diimine **3aj** or diamine **4aj** from alkylation of 1,3-diaminobenzene (0.275 mmol) with benzyl alcohol (0.5 mmol) in the yields of 83% and 91%, respectively.

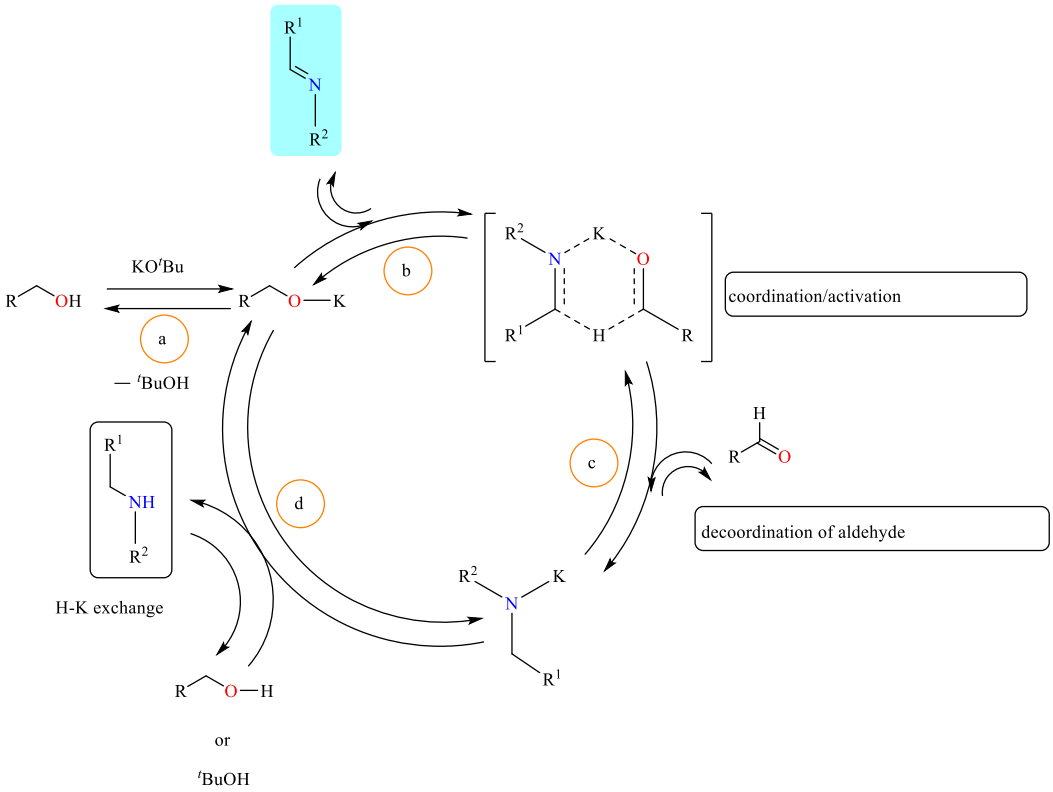
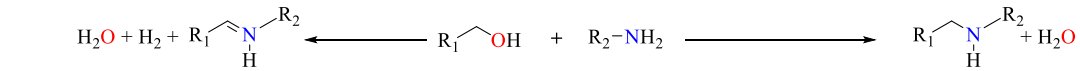
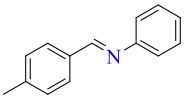
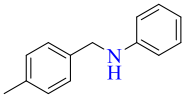
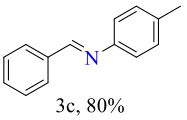
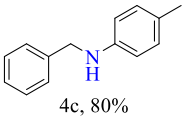
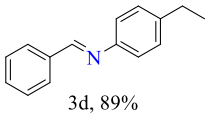
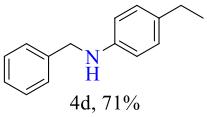
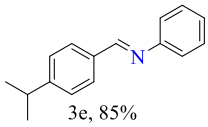
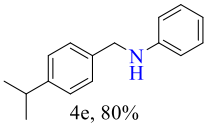
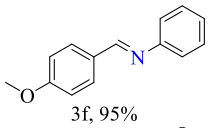
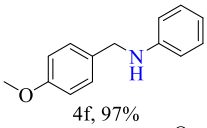
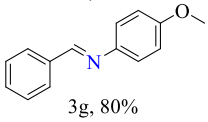
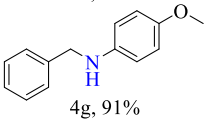
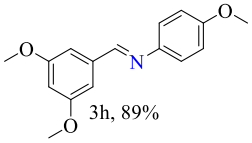
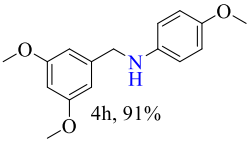
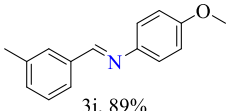
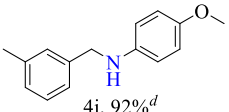
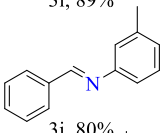
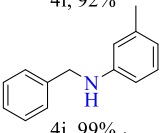
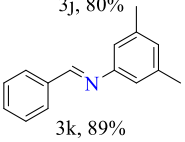
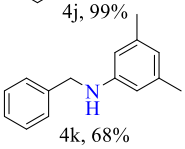


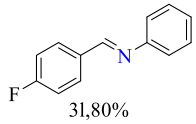
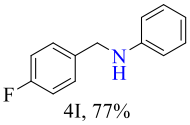
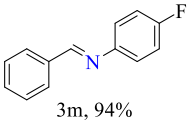
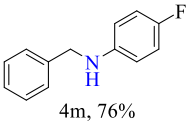
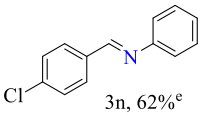
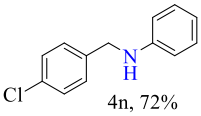
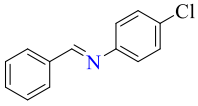
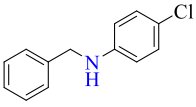
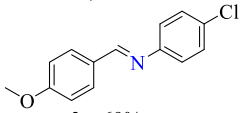
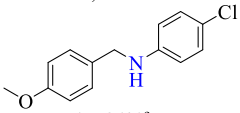
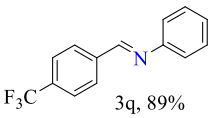
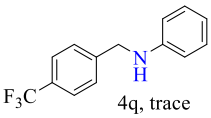
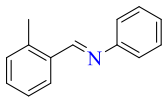
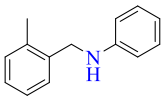
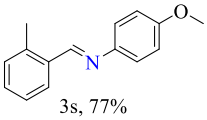
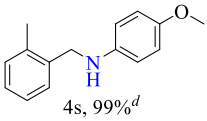
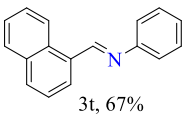
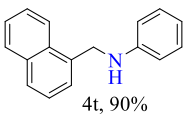
Figure 2.0 Meerwein-Ponndorf-Verley reduction cycle for amine synthesis

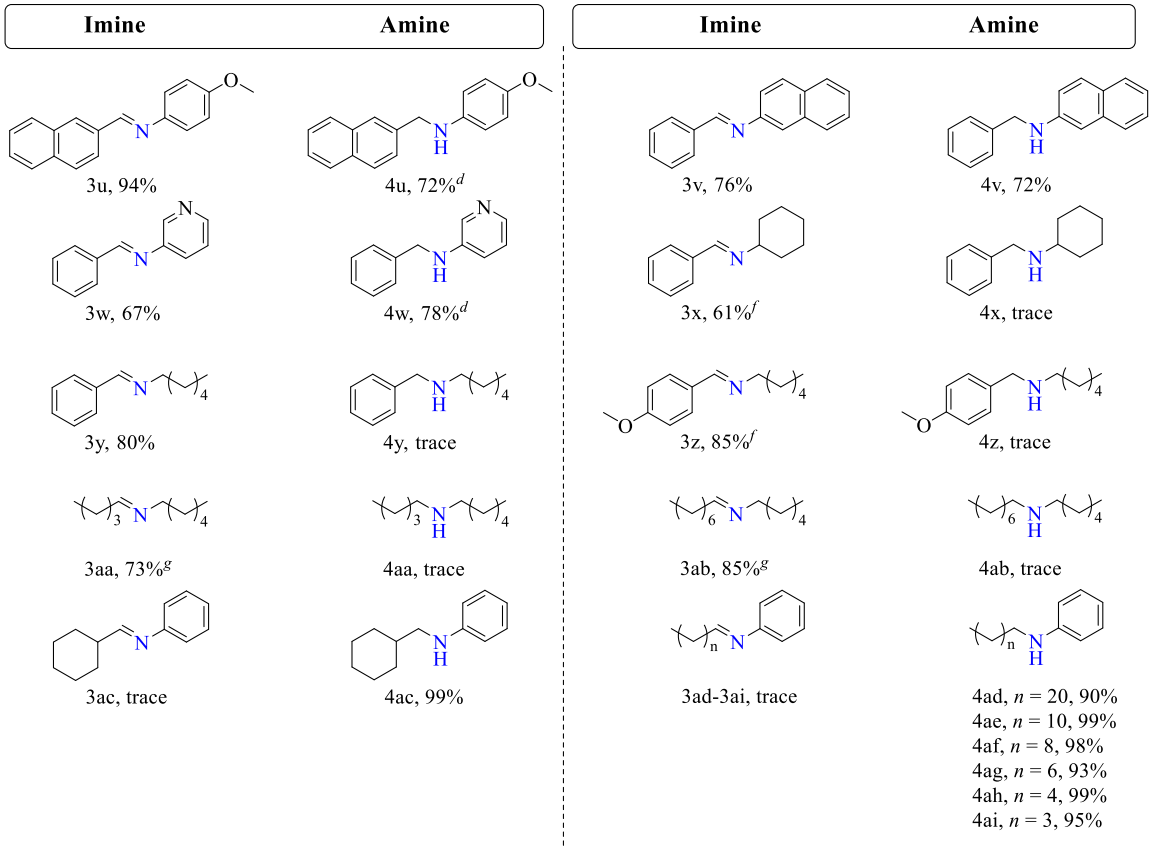
Table 2.3 Switchable Synthesis of Imines 3b – 3ai and Amines 4b – 4ai from Various Alcohol and Amine Substrates[a,b,c]



3 **1** **2** **4**

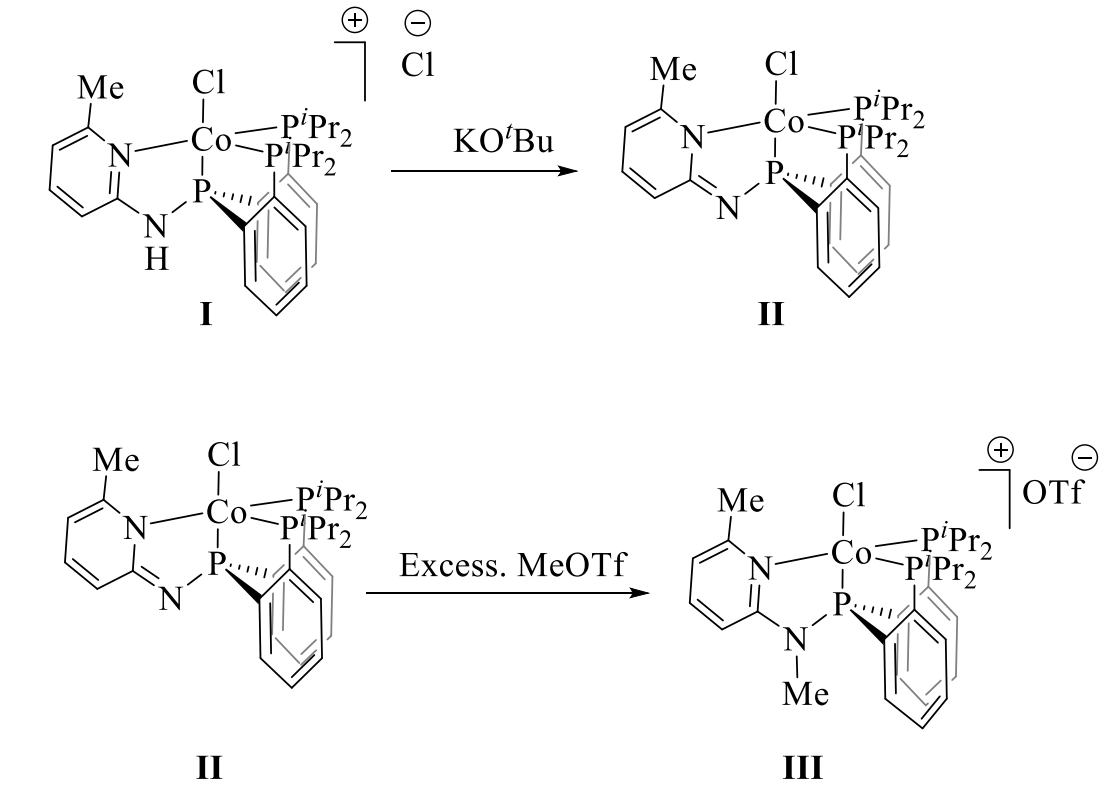
Imine	Amine
 3b,89%	 4b, 86%
 3c, 80%	 4c, 80%
 3d, 89%	 4d, 71%
 3e, 85%	 4e, 80%
 3f, 95%	 4f, 97%
 3g, 80%	 4g, 91%
 3h, 89%	 4h, 91%
 3i, 89%	 4i, 92%[d]
 3j, 80%	 4j, 99%
 3k, 89%	 4k, 68%

Imine	Amine
 3l,80%	 4I, 77%
 3m, 94%	 4m, 76%
 3n, 62%[e]	 4n, 72%
 3o, 82%	 4o, 84%[e]
 3p, 69%	 4p, 84%[e]
 3q, 89%	 4q, trace
 3r, 73%	 4r, 93%
 3s, 77%	 4s, 99%[d]
 3t, 67%	 4t, 90%



[a]General reaction conditions for imine synthesis: alcohol **1** (0.25 mmol), amine **2** (0.275 mmol), **I** (2.5 mol%), KO^{t}Bu (7.5 mol%), benzene (1.2 mL), Ar flow, 105 °C, 24h. [b]General reaction conditions for amine synthesis: **1** (0.25 mmol), amine **2** (0.275 mmol), **I** (3 mol%), KO^{t}Bu (110 mol%), toluene (0.75 mL), 15 mL reaction tube, 85 °C, 24h. [c]NMR yield using 1,3,5-trimethoxybenzene or nitromethane as internal standard. [d]Alcohol (o.3mmol) and amine (0.25 mmol) were used. [e]**1** (0.25 mmol) and **2** (0.35 mmol) were used. [f]Reactions were run in a 100 mL pressure vessel for 48 h. [g]Reaction were run in a 100 mL pressure vessel for 24 h.

Next, we performed a mechanistic study to understand these reactions. Three derivatives of **I** (**II** – **IV**, Scheme 3B) were investigated for the amine alcohol coupling reactions. Derivative **II** bearing a dearomatized pyridine arm is synthesized by reacting **I** with one equiv. of KO^{t}Bu or KHBEt$_3$.[41] **II** shows comparable activity to **I** in both imine and amine formation reactions with 85% and 79% yields, respectively, demonstrating **II** could also be an efficient pre-catalyst.



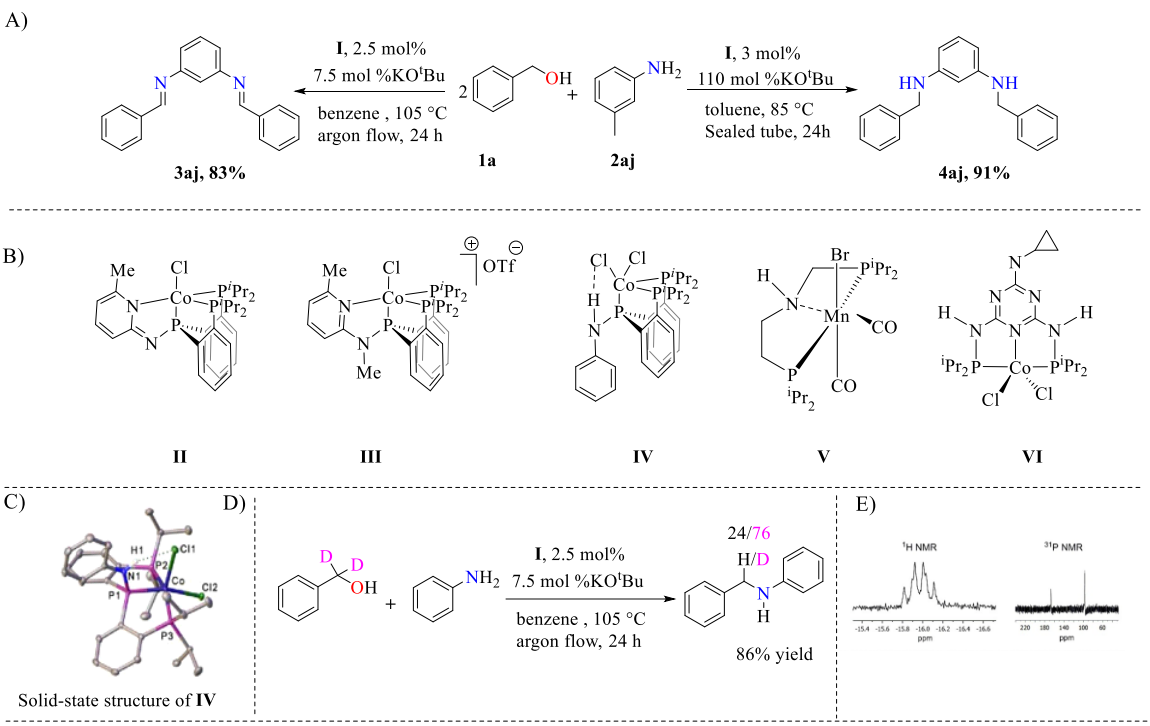
Scheme 2.8 Dearomatization and methylation of Ding's catalyt

In order to test if MLC from the N–H linker on the ligand plays a role, the [(^{iPr}PPPN^{Me}Py^{Me})]CoCl$_2$ complex **III**[41] with the N–Me linker was employed. An amine

yield of 80% was observed which is comparable with **I**, suggesting MLC may not have a crucial effect in amine formation. However, **III** showed dramatically reduced activity toward imine formation leading to only 1% yield. Instead, a large amount of amine (29% yield) and ester(20% yield) side products were generated, indicating poor reactivity and selectivity using **III** as the pre-catalyst for imine synthesis. To investigate the role of the coordinating pyridine arm, we synthesized **IV** bearing a benzene pendant arm instead. The solid-state structure of **IV** featured a distorted trigonal bipyramidal geometry on the cobalt center (Scheme 3C). As expected, the –NH–Ph arm does not coordinate to the cobalt. The interaction between one Cl and H on the N–H linker suggests a potential function of MLC. The IR spectrum displays a ν(N–H) peak at 3365 cm^{-1}. **IV** showed superior activity towards amine formation with an excellent 93% yield but performed poorly in the imine synthesis without any imine product detected. Interestingly, an amine yield of 75% was observed under the imine forming conditions using **IV**. Taking together, these results indicate the critical roles of both the pyridyl ring and the N–H linker of **I** for the switchable imine/amine synthesis.

When the optimized imine reaction was conducted with benzyl alcohol-α,α-d_2 and aniline, H/D scrambling was detected with a Ph–CH=N–Ph/Ph–CD=N–Ph ratio of about 1:3 (Scheme 3D), suggesting that the alcohol dehydrogenation step is reversible and involves cobalt hydride species as the intermediate. The amine formation was monitored using a *J-Young* NMR tube. A triplet of doublets at –15.99 ppm (J = 53.8 Hz (t) and 40.3 Hz (d)) was observed in the ^{1}H NMR spectrum (Scheme 3E). Although **I** is a paramagnetic Co(II) complex, the diamagnetic hydride signal indicates the generation of a Co(I) or Co(III) hydride in the presence of KO^{t}Bu and alcohol/amine substrates, which is analogous to other

reported Co-based catalytic systems.[48-50] Attempts to isolate the hydride species were unsuccessful. In addition, no product was observed from dehydrogenation of aniline or benzyl amine in the absence of alcohol under the standard conditions, suggesting the amine dehydrogenation pathway could be excluded. To explore the generality of our method in selective amine/imine synthesis, two representative base transition metal catalysts **V** and **VI** (Scheme 3B) originally reported for amine synthesis were examined by our strategy to form imines. Note that both catalytic systems require excess amount of KO^{t}Bu for amine synthesis.[25,28] **V** and **VI** were prepared according to the published procedures.[51,52] Benzyl alcohol and aniline were chosen as the model substrates. Beller's manganese pincer complex **V** gave a N-benzylideneaniline yield of 80% under the analogous imine synthesis conditions with 3.5 mol % **V** and 6 mol % KO^{t}Bu. This demonstrates our strategy is amenable for Beller's catalytic system, although more extensive reaction condition optimization is required to further enhance the productivity. On the other hand, Kempe's cobalt pincer complex **VI** with the triazine backbone showed poor activity (3% yield) when subjected to the standard imine synthesis conditions. The stability of the reactive complexes could play a pivotal role, as catalyst degradation was observed during the reaction. Kempe and coworkers proposed a possible stabilization effect from the coordination of the potassium or sodium cation to the nitrogen atoms of the triazine backbone.[22] Under our conditions for imine synthesis, the catalytic amount of KO^{t}Bu may be insufficient to stabilize the catalyst, leading to catalyst degradation. Collectively, considering other known catalytic systems that require otherwise a large amount of base for the imine formation,[22,38] we conclude that our switchable imine/amine synthetic strategy is strongly dependent on the choice of the metal catalysts.



[a](A) Switchable synthesis of diamine and diimine using benzyl alcohol and benzenediamine. (B) Base transition metal complexes examined for switchable imine/amine synthesis. (C) Solid state structure of **IV.** Hydrogen atoms are omitted except the N-H proton. (D) Deuterium labeling experiment of the imine forming reaction using (benzyl alcohol)-α,α-d_2. (E) Cobalt hydride species detected by ^{1}H NMR (left) and ^{31}P NMR (right) from the *in situ* amine forming reaction in a J. Young NMR tube.

Scheme2.9 Studies on the switchable imine/amine formation by Ding's catalyst

2.3 Conclusion

In summary, we reported the couplings of primary alcohols and amines to selectively synthesize imines or amines catalyzed by a well-defined cobalt catalyst. Intriguingly, the product selectivity can be simply controlled by the base loadings and strongly depends on

the catalysts used. Moreover, the imine forming reaction is environmentally benign with hydrogen and water as the only byproducts. We anticipate that this study could provide insights that lead for more efficient base transition metal catalysts, potentially opening new avenues of research on selective transformations in catalysis.

2.4 Experimental Section

2.4.1 General Methods.

Unless specified, all reactions were performed in a MBraun glovebox under an atmosphere of N_2 or using standard Schlenk techniques with Ar atmosphere. Anhydrous solvents were deoxygenated by sparging with dinitrogen and dried by passing through activated alumina columns of a Pure Solv solvent purification system. $CDCl_3$ was purchased from Cambridge Isotope Lab and dried over molecular sieves (4 Å). Benzyl alcohol-α,α-d_2 was purchased from Sigma Aldrich and used as received. All organic substrates were purchased from Sigma Aldrich or Fisher Scientific and used as received. KO^{t}Bu (≥98%) was purchased from Sigma Aldrich and vacuum sublimed before use. Comparable results were obtained as using KO^{t}Bu (99.99%, Aldrich). All other chemicals were purchased and used as received. NMR spectra were recorded on a JEOL Unity 500 MHz or 300 MHz spectrometer. ^{1}H NMR spectra were referenced to tetramethylsilane (0.00 ppm) using $CDCl_3$ as solvent. ^{13}C NMR were referenced to solvent carbons at 77.0 ppm for $CDCl_3$. ^{31}P NMR spectra were referenced to 85% H_3PO_4 at 0 ppm. Metal complexes (**I-III, V, VI**) were prepared according to the previously published procedures,[41,51,52] and recrystallized before use. All other reagents were purchased from common suppliers and used without further purification.

2.5 Synthesis of ^{iPr}PPPN^{H}Ph Ligand (IV-L). In a N_2 filled glovebox, aniline (50 μL, 0.55 mmol) and toluene (4 mL) was loaded into a 100 mL Schlenk flask. NEt_3 (76.2 μL, 0.55 mmol) was added to the solution dropwise over 5 min. The flask was sealed with a rubber septum, taken out of glovebox and cooled at 0 °C with an ice bath. In the glovebox, *bis*(2-diisopropylphosphinophenyl)chlorophosphine (247.5 mg, 0.55 mmol) was measured and dissolved in 3 mL toluene. The solution was charged into a 5 mL syringe and added to the Schlenk flask under Ar flow dropwise over 10 min. After the addition was complete, the ice bath was removed and allowed the mixture to warm to room temperature. The rubber septum was switched with a glass stopper and reaction mixture was heated to 80 °C for 24 h. After that, the solvent was removed under vacuum and the Schlenk flask was taken inside the glovebox. Diethyl ether (15 mL) was added into the Schlenk flask to dissolve the powder and the mixture was filtered through Celite. Colorless crystals were obtained from the concentrated at room temperature (229 mg, 82% yield). ^{1}H NMR (500 MHz, 298 K, C_6D_6): δ (ppm) 7.14-7.11 (m, 2H), 7.06-7.04 (m, 2H), 6.84-6.83 (m, 1 H), 6.82 (dd, J = 2.4 and 1.3 Hz, 2H), 6.81-6.80 (m, 1H), 6.77 (t, J = 7.4 Hz, 2H), 6.68-6.65 (m, 2H), 6.44-6.41 (m, 1H), 3.62 (d, $^2J_{HP}$ = 6.1 Hz, N-H, 1H), 1.81-1.73 (m, 2H), 1.65-1.57 (m, 2H), 0.87-0.77 (m , 12H), 0.64-0.56 (m, 12H). ^{31}P {^{1}H} NMR (121 MHz, 298 K, C_6D_6): δ (ppm) 18.59 (dd, J = 164.4 and 156.7 Hz, 1P), −2.23 (d, J = 4.5 Hz, 1P), −3.56 (d, J = 5.2 Hz). ^{13}C{^{1}H} NMR (126 MHz, 298K, C_6D_6): δ (ppm) 150.6 (dd, J = 11.9, 5.0 Hz), 150.3 (dd, J = 13.9 and 5.2 Hz), 147.3 (d, J = 18.4 Hz), 141.1 (dd, J = 29.6 and 19.2 Hz) 132.2 (s), 131.5 (d, J = 7.6 Hz), 129.0 (s), 128.7 (s), 128.0 (s), 118.6 (s), 115.9 (d, J = 13.1 Hz), 25.4 (d, J = 16.3 Hz), 23.9 (dd, J = 14.6, 5.8 Hz), 20.3 (dd, J = 17.2, 9.8 Hz), 19.9 (d, J = 20.4 Hz), 19.2 (d, J =

8.3 Hz). ESI-HRMS-TOF m/z: $[M + H]^+$ calc. for $C_{30}H_{42}NP_3$, 509.2512; found, 509.2518.

2.6 Synthesis of [(^{iPr}PPPN^{H}Ph)CoCl]Cl Complex (IV). ^{iPr}PPPN^{H}Ph (34 mg, 0.066 mmol) solution in THF was added dropwise to the slurry of $CoCl_2$ (8.5 mg, 0.065 mmol) in THF, and the mixture was stirred for overnight at room temperature. The resulted dark-red slurry was filtered via Celite and the filtrate was dried under vacuum to give a red powder. Red-orange crystals were grown overnight by slow diffusion of ether into the dichloromethane solution of the complex. ^{1}H NMR (500 MHz, 298 K, CD_2Cl_2): δ (ppm) 9.92, 8.61, 7.96, 7.10, 6.24, 4.99, 4.80, 3.19, 1.43, 1.23, 1.12, 0.85, 0.05, −1.08, −2.69, −5.15. μ_{eff} (B.M.): 1.95. UV-vis [CH_2Cl_2; λ, nm (ε, $M^{-1}cm^{-1}$)]: 472 (71.1). Anal. Calcd. for C, 56.35; H, 6.62; N, 2.19. Found: C, 56.21; H, 6.60; N, 2.18.

2.7 Transfer Hydrogenation of Imine.

2.7.1 Condition A: Inside a N_2 filled glovebox, an oven-dried 15 mL reaction tube was charged with *N*-benzylideneaniline (45 mg, 0.25 mmol), benzyl alcohol (30 μL, 0.275 mmol), **I** (4.1 mg, 2.5 mol %), KO^{t}Bu (31 mg, 110 mol %), and toluene (0.75 mL). The tube was sealed by a screw cap fitted with a PTFE septa, and heated at 85 °C for 24 h. The reaction mixture was filtered through a silica gel plug and analyzed by ^{1}H NMR spectroscopy. N-benzylaniline was observed with 82 % yield.

2.7.2 Condition B: Inside a N_2 filled glovebox, an oven-dried 15 mL reaction tube was charged with *N*-benzylideneaniline (45 mg, 0.25 mmol), benzyl alcohol (30 μL, 0.275 mmol), **I** (4.1 mg, 2.5 mol %), KO^{t}Bu (2.1 mg, 7.5 mol %), and toluene (0.75 mL). The tube was sealed by a screw cap fitted with a PTFE septa, and heated at 85 °C for 24 h. The

reaction mixture was filtered through silica gel plug and analyzed by ^{1}H NMR spectroscopy. Trace amount (<1%) of N-benzylaniline was observed.

2.8 Synthesis of N-Benzylideneaniline 3a.

2.8.1 Condition A: Inside a N_2 filled glovebox, an oven-dried 15 mL reaction tube was charged with **I** (4.1 mg, 2.5 mol %), KO^{t}Bu (2.1 mg, 7.5 mol %), benzyl alcohol (0.25 mmol), aniline (0.275 mmol) and benzene (1.2 mL). The tube was then sealed by a screw cap fitted with a PTFE septa, and attached to argon flow through a needle. The reaction was carried out at 105 °C for 24 h. 1,3,5-Trimethoxybenzene (8.4 mg, 0.05 mmol) was added to the reaction mixture as internal standard. The mixture was diluted with $CDCl_3$ and filtered through Celite and subjected to NMR analysis. NMR yield: 88%.

2.8.2 Condition B: Inside a N_2 filled glovebox, an oven-dried 100 mL pressure vessel was charged with **I** (4.1 mg, 2.5 mol %), KO^{t}Bu (2.1 mg, 7.5 mol %), benzyl alcohol (0.25 mmol), aniline (0.275 mmol), and benzene (1.2 mL). The vessel was sealed by a PTFE valve and heated to 105°C for 24 h. 1,3,5-Trimethoxybenzene (8.4 mg, 0.05 mmol) was added to the reaction mixture as internal standard. An aliquot of mixture was filtered through Celite, rinsed with $CDCl_3$, and subjected to NMR analysis. NMR yield: 82%.

2.8.3 Condition C (1 mmol scale): Inside a N_2 filled glovebox, an oven-dried 15 mL reaction tube was charged with **I** (16.4 mg, 2.5 mol %), KO^{t}Bu (8.4 mg, 7.5 mol %), benzyl alcohol (1 mmol), aniline (1.1 mmol) and benzene (3 mL). The tube was then sealed by a screw cap fitted with a PTFE septa, and attached to argon flow through a needle. The reaction was carried out at 105 °C for 24 h. At the end of the reaction, the solvent was removed under reduced pressure and the crude mixture was purified by short-

path vacuum distillation. Light yellow powder of **3a** was isolated. Yield: 143 mg (79%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.47 (s, 1H), 7.93-7.91 (m, 2H), 7.51-7.49 (m, 2H), 7.50-7.48 (m, 1H), 7.43-7.39 (m, 2H), 7.27 (m, 1H), 7.25-7.22 (m, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.5, 152.2, 136.3, 131.5, 129.3, 129.0, 128.9, 126.0, 121.0 ppm.

2.8.4 Condition D: Inside a N_2 filled glovebox, an oven-dried 15 mL reaction tube was charged with **II** (3.9 mg, 2.5 mol %), KO^{t}Bu (1.4 mg, 5 mol %), benzyl alcohol (0.25 mmol), aniline (0.275 mmol) and benzene (1.2 mL). The tube was then sealed by a screw cap fitted with a PTFE septa, and attached to argon flow through a needle. The reaction was carried out at 105 °C for 24 h. 1,3,5-Trimethoxybenzene (8.4 mg, 0.05 mmol) was added to the reaction mixture as internal standard. The mixture was diluted with $CDCl_3$ and filtered through Celite and subjected to NMR analysis. NMR yield: 85%.

2.8.5 Condition E: Inside a N_2 filled glovebox, an oven-dried 15 mL reaction tube was charged with **III** (4.9 mg, 2.5 mol %), KO^{t}Bu (2.1 mg, 7.5 mol %), benzyl alcohol (0.25 mmol), aniline (0.275 mmol) and benzene (1.2 mL). The tube was then sealed by a screw cap fitted with a PTFE septa, and attached to argon flow through a needle. The reaction was carried out at 105 °C for 24 h. 1,3,5-Trimethoxybenzene (8.4 mg, 0.05 mmol) was added to the reaction mixture as internal standard. The mixture was diluted with $CDCl_3$ and filtered through Celite and subjected to NMR analysis. NMR yield: 1%.

2.8.6 Condition F: Inside a N_2 filled glovebox, an oven-dried 15 mL reaction tube was charged with **IV** (3.9 mg, 2.5 mol %), KO^{t}Bu (2.1 mg, 7.5 mol %), benzyl alcohol (0.25 mmol), aniline (0.275 mmol) and benzene (1.2 mL). The tube was then sealed by a screw cap fitted with a PTFE septa, and attached to argon flow through a needle. The reaction

was carried out at 105 °C for 24 h. 1,3,5-Trimethoxybenzene (8.4 mg, 0.05 mmol) was added to the reaction mixture as internal standard. The mixture was diluted with $CDCl_3$ and filtered through Celite and subjected to NMR analysis. NMR yield: 0%.

2.8.7 Condition G: Inside a N_2 filled glovebox, an oven-dried 15 mL reaction tube was charged with **V** (4.4 mg, 3.5 mol %), KO^{t}Bu (1.7 mg, 6 mol %), benzyl alcohol (0.3 mmol), aniline (0.25 mmol) and benzene (1.2 mL). The tube was then sealed by a screw cap fitted with a PTFE septa, and attached to argon flow through a needle. The reaction was carried out at 105 °C for 24 h. 1,3,5-Trimethoxybenzene (8.4 mg, 0.05 mmol) was added to the reaction mixture as internal standard. The mixture was diluted with $CDCl_3$ and filtered through Celite and subjected to NMR analysis. NMR yield: 80%.

2.8.8 Condition H: Inside a N_2 filled glovebox, an oven-dried 15 mL reaction tube was charged with **VI** (3.3 mg, 2.5 mol %), KO^{t}Bu (2.1 mg, 7.5 mol %), benzyl alcohol (0.25 mmol), aniline (0.275 mmol) and benzene (1.2 mL). The tube was then sealed by a screw cap fitted with a PTFE septa, and attached to argon flow through a needle. The reaction was carried out at 105 °C for 24 h. 1,3,5-Trimethoxybenzene (8.4 mg, 0.05 mmol) was added to the reaction mixture as internal standard. The mixture was diluted with $CDCl_3$ and filtered through Celite and subjected to NMR analysis. NMR yield: 3%.

2.9 Synthesis of N-Benzylaniline 4a.

2.9.1 Condition A: Inside a N_2 filled glovebox, an oven-dried 15 mL reaction tube was charged with **I** (4.9 mg, 3 mol %), KO^{t}Bu (31 mg, 110 mol %), benzyl alcohol (0.25 mmol), aniline (0.275 mmol) and toluene (0.75 mL). The tube was then sealed by a screw cap fitted with a PTFE septa, taken out of the box and heated at 85 °C for 24 h. 1,3,5-Trimethoxy

benzene (8.4 mg, 0.05 mmol) was added to the reaction mixture as internal standard. An aliquot of mixture was filtered through silica gel and rinsed with diethyl ether (5 mL). The solvent was removed under reduced pressure and the crude mixture was subjected to NMR analysis to identify the products and determine product yields. NMR yield: 93%.

2.9.2 Condition B (1 mmol scale): Inside a N_2 filled glovebox, an oven-dried 15 mL reaction tube was charged with **I** (19.6 mg, 3 mol %), KO^{t}Bu (124 mg, 110 mol %), benzyl alcohol (1 mmol), aniline (1.1 mmol) and toluene (2 mL). The tube was then sealed by a screw cap fitted with a PTFE septa, taken out of the box and heated at 85 °C for 24 h. At the end of the reaction, the solvent was removed under reduced pressure and the crude mixture was passed through a silica gel column using ethyl acetate/hexane (1:10, v/v) as an eluent. Pale yellow oil of **4a** was isolated. Yield: 163 mg (89%). ^{1}H NMR (500 MHz, CDCl3) δ 7.47−7.52 (m, 4 H), 7.40−7.43 (m, 1 H), 7.31−7.34 (m, 2 H), 6.86–6.89 (m, 1 H), 6.75–6.77 (m, 2 H), 4.43 (s, 2 H), 4.11 (s, 1 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.4, 139.7, 129.5, 128.9, 127.7, 127.4, 117.7, 113.1, 48.5 ppm.

2.9.3 Condition C: Inside a N_2 filled glovebox, an oven-dried 15 mL reaction tube was charged with **II** (4.6 mg, 3 mol %), KO^{t}Bu (31 mg, 110 mol %), benzyl alcohol (0.25 mmol), aniline (0.275 mmol) and toluene (0.75 mL). The tube was then sealed by a screw cap fitted with a PTFE septa, taken out of the box and heated at 85 °C for 24 h. 1,3,5-Trimethoxy benzene (8.4 mg, 0.05 mmol) was added to the reaction mixture as internal standard. An aliquot of mixture was filtered through silica gel and rinsed with diethyl ether (5 mL). The solvent was removed under reduced pressure and the crude mixture was

subjected to NMR analysis to identify the products and determine product yields. NMR yield: 79%.

2.9.4 Condition D: Inside a N_2 filled glovebox, an oven-dried 15 mL reaction tube was charged with **III** (5.9 mg, 3 mol %), KO^{t}Bu (31 mg, 110 mol %), benzyl alcohol (0.25 mmol), aniline (0.275 mmol) and toluene (0.75 mL). The tube was then sealed by a screw cap fitted with a PTFE septa, taken out of the box and heated at 85 °C for 24 h. 1,3,5-Trimethoxy benzene (8.4 mg, 0.05 mmol) was added to the reaction mixture as internal standard. An aliquot of mixture was filtered through silica gel and rinsed with diethyl ether (5 mL). The solvent was removed under reduced pressure and the crude mixture was subjected to NMR analysis to identify the products and determine product yields. NMR yield: 80%.

2.9.5 Condition E: Inside a N_2 filled glovebox, an oven-dried 15 mL reaction tube was charged with **IV** (4.6 mg, 3 mol %), KO^{t}Bu (31 mg, 110 mol %), benzyl alcohol (0.25 mmol), aniline (0.275 mmol) and toluene (0.75 mL). The tube was then sealed by a screw cap fitted with a PTFE septa, taken out of the box and heated at 85 °C for 24 h. 1,3,5-Trimethoxy benzene (8.4 mg, 0.05 mmol) was added to the reaction mixture as internal standard. An aliquot of mixture was filtered through silica gel and rinsed with diethyl ether (5 mL). The solvent was removed under reduced pressure and the crude mixture was subjected to NMR analysis to identify the products and determine product yields. NMR yield: 93%.

2.9.6 Condition F: Inside a N_2 filled glovebox, an oven-dried 15 mL reaction tube was charged with **V** (3.7 mg, 3 mol %), KO^{t}Bu (21 mg, 75 mol %), benzyl alcohol (0.25 mmol),

aniline (0.275 mmol) and toluene (0.75 mL). The tube was then sealed by a screw cap fitted with a PTFE septa, taken out of the box and heated at 85 °C for 24 h. 1,3,5-Trimethoxy benzene (8.4 mg, 0.05 mmol) was added to the reaction mixture as internal standard. An aliquot of mixture was filtered through silica gel and rinsed with diethyl ether (5 mL). The solvent was removed under reduced pressure and the crude mixture was subjected to NMR analysis to identify the products and determine product yields. NMR yield: 74%.

2.9.7 Condition G: Inside a N_2 filled glovebox, an oven-dried 15 mL reaction tube was charged with **VI** (4.0 mg, 3 mol %), KO^{t}Bu (31 mg, 110 mol %), benzyl alcohol (0.25 mmol), aniline (0.275 mmol) and toluene (0.75 mL). The tube was then sealed by a screw cap fitted with a PTFE septa, taken out of the box and heated at 85 °C for 24 h. 1,3,5-Trimethoxy benzene (8.4 mg, 0.05 mmol) was added to the reaction mixture as internal standard. An aliquot of mixture was filtered through silica gel and rinsed with diethyl ether (5 mL). The solvent was removed under reduced pressure and the crude mixture was subjected to NMR analysis to identify the products and determine product yields. NMR yield: 86%.

2.10 Hydrogen Detection. Inside a N_2 filled glovebox, an ovendried 100 mL pressure vessel was charged with **I** (16.4 mg, 2.5 mol %), KO^{t}Bu (8.4 mg, 7.5 mol %), benzyl alcohol (1 mmol), aniline (1.1 mmol), and benzene (2 mL). The vessel was sealed by a PTFE valve and heated to 105°C for 24 h. The headspace gas sample was taken by a needle syringe from the side arm and detected by SRI 8610C Gas Chromatograph with a 5 Å molecular sieves column (Restek CP753415) with N_2 carrier gas.

2.11 Homogeneity Test of the Reaction System for Imine Synthesis. Inside a N_2 filled glovebox, an oven-dried 15 mL reaction tube was charged with **I** (4.1 mg, 2.5 mol %), KO^{t}Bu (2.1 mg, 7.5 mol %), benzyl alcohol (0.25 mmol), aniline (0.275 mmol) and benzene (1.2 mL). Mercury (125 mg, 0.625 mmol) was added to the tube which was then sealed by a screw cap fitted with a PTFE septa, and attached to argon flow through a needle. The reaction was carried out at 105 °C for 24 h. 1,3,5Trimethoxybenzene (8.4 mg, 0.05 mmol) was added to the reaction mixture as internal standard. The mixture was diluted with $CDCl_3$ and filtered through Celite and subjected to NMR analysis. NMR yield: 74%.

2.12 Homogeneity Test of the Reaction System for Amine Synthesis. Inside a N_2 filled glovebox, an oven-dried 15 mL reaction tube was charged with **I** (4.9 mg, 3 mol %), KO^{t}Bu (31 mg, 110 mol %), benzyl alcohol (0.25 mmol), aniline (0.275 mmol) and toluene (0.75 mL). Mercury (125 mg, 0.625 mmol) was added to the tube which was then sealed by a screw cap fitted with a PTFE septa and heated at 85 °C for 24 h. 1,3,5-Trimethoxy benzene (8.4 mg, 0.05 mmol) was added to the reaction mixture as internal standard. An aliquot of mixture was filtered through silica gel and rinsed with diethyl ether (5 mL). The solvent was removed under reduced pressure and the crude mixture was subjected to NMR analysis to identify the products and determine product yields. NMR yield: 77%.

2.13 Deuterium Labeling Study of Benzyl Alcohol and Aniline Coupling to N-Benzylideneaniline. Inside a N_2 filled glovebox, an oven-dried 15 mL reaction tube was charged with benzyl alcohol-α,α-d_2 (0.25 mmol), aniline (0.275 mmol), **I** (4.1 mg, 2.5 mol %), KO^{t}Bu (2.1 mg, 7.5 mol %), and benzene (1.2 mL). The tube was sealed by a screw cap fitted with a PTFE septa, and attached to argon flow through a needle. The reaction

was carried out at 105 °C for 24 h. 1,3,5-Trimethoxybenzene (8.4 mg, 0.05 mmol) was added to the reaction mixture as internal standard. The mixture was diluted with $CDCl_3$, filtered through Celite and subjected to NMR analysis. H/D scrambling was detected with a Ph–CH=N–Ph/Ph–CD=N–Ph ratio of 1:3.

2.14 Study of the Cobalt Hydride in the Coupling of Benzyl Alcohol and Aniline to N-Benzylaniline. Inside a N_2 filled glovebox, an oven-dried J-Young NMR tube was charged with benzyl alcohol (0.125 mmol), aniline (0.125 mmol), **I** (8.2 mg, 10 mol %), KO^{t}Bu (11.2 mg, 80 mol %), and toluene-d8 (0.5 mL). The tube was sealed with PTFE cap, and the reaction was monitored by ^{1}H NMR (500 MHz) at 85 °C.

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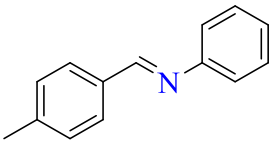
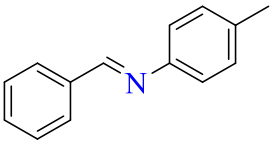
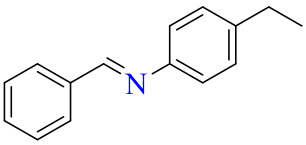
2.16 Synthetic details for imine 3b-3ai and amines 4b-4ai.



3b[1]: Inside a N_2 filled glovebox, an oven-dried 15 mL reaction tube was charged with **I** (4.1 mg, 2.5 mol %), KO^{t}Bu (2.1 mg, 7.5 mol %), 4methylbenzyl alcohol (0.25 mmol), aniline (0.275 mmol) and benzene (1.2 mL). The tube was sealed by a screw cap fitted with a PTFE septa, and attached to argon flow through a needle. The reaction was carried out at 105 °C for 24 h. Nitromethane (20 µL, 373 µmol) was added to the reaction mixture as internal standard. The mixture was diluted with $CDCl_3$, filtered through Celite and subjected to NMR analysis. NMR yield: 89%.

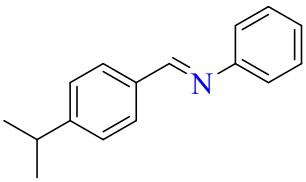


3c[2]: Inside a N_2 filled glovebox, an oven-dried 15 mL reaction tube was charged with **I** (4.1 mg, 2.5 mol %), KO^{t}Bu (2.1 mg, 7.5 mol %), benzyl alcohol (0.25 mmol), 4-methyl aniline (0.275 mmol) and benzene (1.2 mL). The tube was sealed by a screw cap fitted with a PTFE septa, and attached to argon flow through a needle. The reaction was carried out at 105 °C for 24 h. 1,3,5-Trimethoxybenzene (8.4 mg, 0.05 mmol) was added to the reaction mixture as internal standard. The mixture was diluted with $CDCl_3$, filtered through Celite and subjected to NMR analysis. NMR yield: 80%.

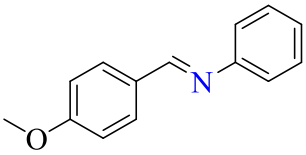


3d[3]: Inside a N_2 filled glovebox, an oven-dried 15 mL reaction tube was charged with **I** (4.1 mg, 2.5 mol %), KO^{t}Bu (2.1 mg, 7.5 mol %), benzyl alcohol (0.25 mmol), 4-ethylaniline (0.275 mmol) and benzene (1.2 mL). The tube was sealed by a screw cap fitted with a PTFE septa, and attached to argon flow through a needle. The reaction was carried out at 105 °C for 24 h. Nitromethane (20 µL, 373 µmol) was added to the reaction mixture as internal standard. The mixture was

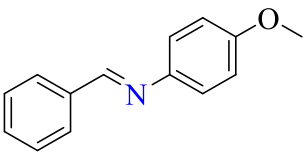
diluted with $CDCl_3$, filtered through Celite and subjected to NMR analysis. NMR yield: 89%.



3e[4]: Inside a N_2 filled glovebox, an ovenwas charged with **I** (4.1 mg, 2.5 mol %), KO^{t}Bu (2.1 mg, 7.5 mol %), 4-isopropylbenzyl alcohol (0.25 mmol), aniline (0.275 mmol) and benzene (1.2 mL). The tube was sealed by a screw cap fitted with a PTFE septa, and attached to argon flow through a needle. The reaction was carried out at 105 °C for 24 h. Nitromethane (20 µL, 373 µmol) was added to the reaction mixture as internal standard. The mixture was diluted with $CDCl_3$, filtered through Celite and subjected to NMR analysis. NMR yield: 85%.

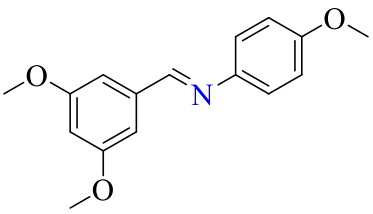


3f[5]: Inside a N_2 filled glovebox, an oven-dried 15 mL reaction tube was charged with **I** (4.1 mg, 2.5 mol %), KO^{t}Bu (2.1 mg, 7.5 mol %), 4-methoxybenzyl alcohol (0.25 mmol), aniline (0.275 mmol) and benzene (1.2 mL). The tube was sealed by a screw cap fitted with a PTFE septa, and attached to argon flow through a needle. The reaction was carried out at 105 °C for 24 h. 1,3,5-Trimethoxybenzene (8.4 mg, 0.05 mmol) was added to the reaction mixture as internal standard. The mixture was diluted with $CDCl_3$, filtered through Celite and subjected to NMR analysis. NMR yield: 95%.

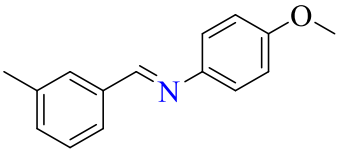


3g[6]: Inside a N_2 filled glovebox, an oven-dried 15 mL reaction tube was charged with **I** (4.1 mg, 2.5 mol %), KO^{t}Bu (2.1 mg, 7.5 mol %), benzyl alcohol (0.25 mmol), 4-methoxyaniline (0.275 mmol) and benzene (1.2 mL). The tube was sealed by a screw cap fitted with a

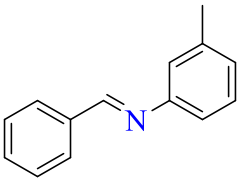
PTFE septa, and attached to argon flow through a needle. The reaction was carried out at 105 °C for 24 h. Nitromethane (20 µL, 373 µmol) was added to the reaction mixture as internal standard. The mixture was diluted with $CDCl_3$, filtered through Celite and subjected to NMR analysis. NMR yield: 80%.



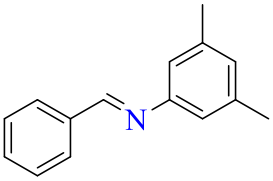
3h[7]: Inside a N_2 filled glovebox, an oven-dried 15 mL reaction tube was charged with **I** (4.1 mg, 2.5 mol %), KO^{t}Bu (2.1 mg, 7.5 mol %), 3,5-dimethoxy benzyl alcohol (0.25 mmol), 4methoxyaniline (0.275 mmol) and benzene (1.2 mL). The tube was sealed by a screw cap fitted with a PTFE septa, and attached to argon flow through a needle. The reaction was carried out at 105 °C for 24 h. Nitromethane (20 µL, 373 µmol) was added to the reaction mixture as internal standard. The mixture was diluted with $CDCl_3$, filtered through Celite and subjected to NMR analysis. NMR yield: 89%.



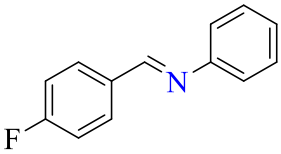
3i[8]: Inside a N_2 filled glovebox, an oven-dried 15 mL reaction tube was charged with **I** (4.1 mg, 2.5 mol %), KO^{t}Bu (2.1 mg, 7.5 mol %), 3-methyl benzyl alcohol (0.25 mmol), 4-methoxy aniline (0.275 mmol) and benzene (1.2 mL). The tube was sealed by a screw cap fitted with a PTFE septa, and attached to argon flow through a needle. The reaction was carried out at 105 °C for 24 h. Nitromethane (20 µL, 373 µmol) was added to the reaction mixture as internal standard. The mixture was diluted with $CDCl_3$, filtered through Celite and subjected to NMR analysis. NMR yield: 89%.



3j[9]: Inside a N_2 filled glovebox, an oven was charged with **I** (4.1 mg, 2.5 mol %), KO^{t}Bu (2.1 mg, 7.5 mol %), benzyl alcohol (0.25 mmol), 3-methyl aniline (0.275 mmol) and benzene (1.2 mL). The tube was sealed by a screw cap fitted with a PTFE septa, and attached to argon flow through a needle. The reaction was carried out at 105 °C for 24 h. Nitromethane (20 µL, 373 µmol) was added to the reaction mixture as internal standard. The mixture was diluted with $CDCl_3$, filtered through Celite and subjected to NMR analysis. NMR yield: 80%.

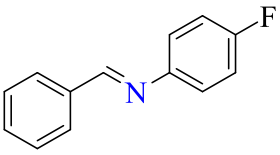


3k[3]: Inside a N_2 filled glovebox, an oven-dried 15 mL reaction tube was charged with **I** (4.1 mg, 2.5 mol %), KO^{t}Bu (2.1 mg, 7.5 mol %), benzyl alcohol (0.25 mmol), 3,5-dimethyl aniline (0.275 mmol) and benzene (1.2 mL). The tube was sealed by a screw cap fitted with a PTFE septa, and attached to argon flow through a needle. The reaction was carried out at 105 °C for 24 h. Nitromethane (20 µL, 373 µmol) was added to the reaction mixture as internal standard. The mixture was diluted with $CDCl_3$, filtered through Celite and subjected to NMR analysis. NMR yield: 89%.

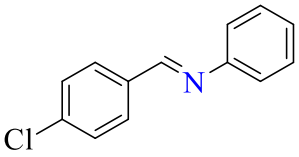


3l[10]: Inside a N_2 filled glovebox, an oven-dried 15 mL reaction tube was charged with **I** (4.1 mg, 2.5 mol %), KO^{t}Bu (2.1 mg, 7.5 mol %), 4-fluoro benzyl alcohol (0.25 mmol), aniline (0.275 mmol) and benzene (1.2 mL). The tube was sealed by a screw cap fitted with a PTFE septa and taken out of the box. An argon balloon was attached on the top. The reaction was carried out at 105 °C for 24 h. 1,3,5-Trimethoxybenzene (8.4 mg, 0.05 mmol) was

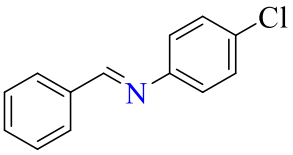
added to the reaction mixture as internal standard. The mixture was diluted with $CDCl_3$, filtered through Celite and subjected to NMR analysis. NMR yield: 80%.



3m[1]: Inside a N_2 filled glovebox, an oven-dried 15 mL reaction tube was charged with **I** (4.1 mg, 2.5 mol %), KO^{t}Bu (2.1 mg, 7.5 mol %), benzyl alcohol (0.25 mmol), 4-fluoro aniline (0.275 mmol) and benzene (1.2 mL). The tube was sealed by a screw cap fitted with a PTFE septa and taken out of the box. An argon balloon was attached on the top. The reaction was carried out at 105 °C for 24 h. Nitromethane (20 µL, 373 µmol) was added to the reaction mixture as internal standard. The mixture was diluted with $CDCl_3$, filtered through Celite and subjected to NMR analysis. NMR yield: 94%.

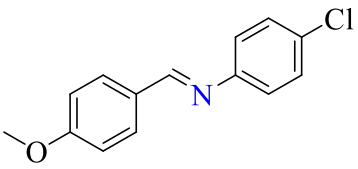


3n[9]: Inside a N_2 filled glovebox, an oven-dried 15 mL reaction tube was charged with **I** (4.1 mg, 2.5 mol %), KO^{t}Bu (2.1 mg, 7.5 mol %), 4-chloro benzyl alcohol (0.25 mmol), aniline (0.35 mmol) and benzene (1.2 mL). The tube was sealed by a screw cap fitted with a PTFE septa and taken out of the box. An argon balloon was attached on the top. The reaction was carried out at 105 °C for 24 h. 1,3,5-Trimethoxybenzene (8.4 mg, 0.05 mmol) was added to the reaction mixture as internal standard. The mixture was diluted with $CDCl_3$, filtered through Celite and subjected to NMR analysis. NMR yield: 62%.

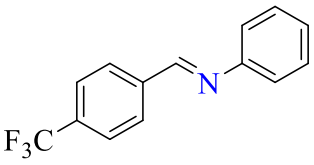


3o[11]: Inside a N_2 filled glovebox, an ovenwas charged with **I** (4.1 mg, 2.5 mol %), KO^{t}Bu (2.1 mg, 7.5 mol %), benzyl alcohol (0.25 mmol), 4-chloro aniline (0.275 mmol) and benzene (1.2 mL). The tube was sealed by a screw cap fitted with a PTFE septa, and attached to argon flow through

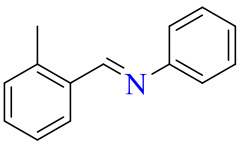
a needle. The reaction was carried out at 105 °C for 24 h. 1,3,5-Trimethoxybenzene (8.4 mg, 0.05 mmol) was added to the reaction mixture as internal standard. The mixture was diluted with $CDCl_3$, filtered through Celite and subjected to NMR analysis. NMR yield: 82%.



3p[12]: Inside a N_2 filled glovebox, an oven-dried 15 mL reaction tube was charged with **I** (4.1 mg, 2.5 mol %), KO^{t}Bu (2.1 mg, 7.5 mol %), 4-methoxy benzyl alcohol (0.25 mmol), 4-chloro aniline (0.275 mmol) and benzene (1.2 mL). The tube was sealed by a screw cap fitted with a PTFE septa, and attached to argon flow through a needle. The reaction was carried out at 105 °C for 24 h. 1,3,5-Trimethoxybenzene (8.4 mg, 0.05 mmol) was added to the reaction mixture as internal standard. The mixture was diluted with $CDCl_3$, filtered through Celite and subjected to NMR analysis. NMR yield: 69%.

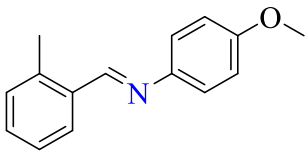


3q[13]: Inside a N_2 filled glovebox, an oven-dried 15 mL reaction tube was charged with **I** (4.1 mg, 2.5 mol %), KO^{t}Bu (2.1 mg, 7.5 mol %), 4-trifluoro methyl benzyl alcohol (0.25 mmol), aniline (0.275 mmol) and benzene (1.2 mL). The tube was sealed by a screw cap fitted with a PTFE septa, and attached to argon flow through a needle. The reaction was carried out at 105 °C for 24 h. Nitromethane (20 µL, 373 µmol) was added to the reaction mixture as internal standard. The mixture was diluted with $CDCl_3$, filtered through Celite and subjected to NMR analysis. NMR yield: 89%.

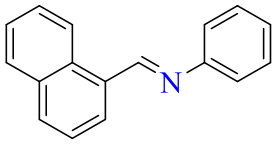


3r[14]: Inside a N_2 filled glovebox, an oven-dried 15 mL reaction tube was charged with **I** (4.1 mg, 2.5 mol %), KO^{t}Bu (2.1 mg, 7.5 mol %),

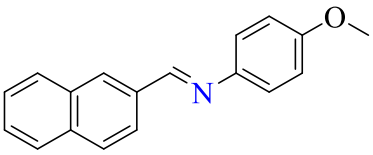
2-methyl benzyl alcohol (0.25 mmol), aniline (0.275 mmol) and benzene (1.2 mL). The tube was sealed by a screw cap fitted with a PTFE septa, and attached to argon flow through a needle. The reaction was carried out at 105 °C for 24 h. 1,3,5-Trimethoxybenzene (8.4 mg, 0.05 mmol) was added to the reaction mixture as internal standard. The mixture was diluted with $CDCl_3$, filtered through Celite and subjected to NMR analysis. NMR yield: 73%.



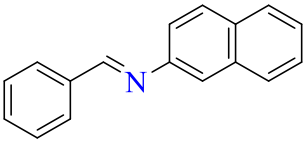
3s[15]: Inside a N_2 filled glovebox, an oven-dried 15 mL reaction tube was charged with **I** (4.1 mg, 2.5 mol %), KO^{t}Bu (2.1 mg, 7.5 mol %), 2-methyl benzyl alcohol (0.25 mmol), 4-methoxy aniline (0.275 mmol) and benzene (1.2 mL). The tube was sealed by a screw cap fitted with a PTFE septa, and attached to argon flow through a needle. The reaction was carried out at 105 °C for 24 h. 1,3,5-Trimethoxybenzene (8.4 mg, 0.05 mmol) was added to the reaction mixture as internal standard. The mixture was diluted with $CDCl_3$, filtered through Celite and subjected to NMR analysis. NMR yield: 77%.



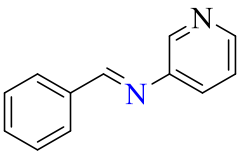
3t[16]: Inside a N_2 filled glovebox, an oven-dried 15 mL reaction tube was charged with **I** (4.1 mg, 2.5 mol %), KO^{t}Bu (2.1 mg, 7.5 mol %), 1napthalene methanol (0.25 mmol), aniline (0.275 mmol) and benzene (1.2 mL). The tube was sealed by a screw cap fitted with a PTFE septa, and attached to argon flow through a needle. The reaction was carried out at 105 °C for 24 h. 1,3,5-Trimethoxybenzene (8.4 mg, 0.05 mmol) was added to the reaction mixture as internal standard. The mixture was diluted with $CDCl_3$, filtered through Celite and subjected to NMR analysis. NMR yield: 67%.



3u[15]: Inside a N_2 filled glovebox, an oven-dried 15 mL reaction tube was charged with **I** (4.1 mg, 2.5 mol %), KO^{t}Bu (2.1 mg, 7.5 mol %), 2-napthalene methanol (0.25 mmol), 4-methoxy aniline (0.275 mmol) and benzene (1.2 mL). The tube was sealed by a screw cap fitted with a PTFE septa, and attached to argon flow through a needle. The reaction was carried out at 105 °C for 24 h. Nitromethane (20 µL, 373 µmol) was added to the reaction mixture as internal standard. The mixture was diluted with $CDCl_3$, filtered through Celite and subjected to NMR analysis. NMR yield: 94%.

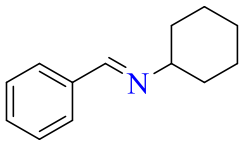


3v[17]: Inside a N_2 filled glovebox, an oven-dried 15 mL reaction tube was charged with **I** (4.1 mg, 2.5 mol %), KO^{t}Bu (2.1 mg, 7.5 mol %), benzyl alcohol (0.25 mmol), 2-naphthylamine (0.275 mmol) and benzene (1.2 mL). The tube was sealed by a screw cap fitted with a PTFE septa, and attached to argon flow through a needle. The reaction was carried out at 105 °C for 24 h. Nitromethane (20 µL, 373 µmol) was added to the reaction mixture as internal standard. The mixture was diluted with $CDCl_3$, filtered through Celite and subjected to NMR analysis. NMR yield: 76%.

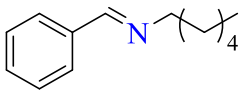


3w[17]: Inside a N_2 filled glovebox, an oven-dried 15 mL reaction tube was charged with **I** (4.1 mg, 2.5 mol %), KO^{t}Bu (2.1 mg, 7.5 mol %), benzyl alcohol (0.25 mmol), 3-amino pyridine (0.275 mmol) and benzene (1.2 mL). The tube was sealed by a screw cap fitted with a PTFE septa, and attached to argon flow through a needle. The reaction was carried out at 105 °C for 24 h. Nitromethane (20 µL, 373 µmol) was added to the reaction mixture as internal standard.

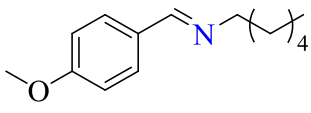
The mixture was diluted with $CDCl_3$, filtered through Celite and subjected to NMR analysis. NMR yield: 67%.



3x[18]: Inside a N_2 filled glovebox, an oven-dried 100 mL pressure vessel was charged with **I** (4.1 mg, 2.5 mol %), KO^{t}Bu (2.1 mg, 7.5 mol %), benzyl alcohol (0.25 mmol), cyclohexyl amine (0.275 mmol) and benzene (1.2mL). The vessel was closed with a PTFE screw cap and heated at 105 °C for 48 h. 1,3,5-Trimethoxybenzene (8.4 mg, 0.05 mmol) was added to the reaction mixture as internal standard. The mixture was diluted with $CDCl_3$, filtered through Celite and subjected to NMR analysis. NMR yield: 61%.

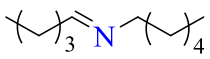


3y[19]: Inside a N_2 filled glovebox, an oven-dried 100 mL pressure vessel was charged with **I** (4.1 mg, 2.5 mol %), KO^{t}Bu (2.1 mg, 7.5 mol %), benzyl alcohol (0.25 mmol), n-hexyl amine (0.275 mmol) and benzene (1.2 mL). The vessel was closed with a PTFE screw cap and heated at 105 °C for 48 h. Nitromethane (20 µL, 373 µmol) was added to the reaction mixture as internal standard. The mixture was diluted with $CDCl_3$, filtered through Celite and subjected to NMR analysis. NMR yield: 80%.

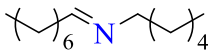


3z[20] : Inside a N_2 filled glovebox, an oven-dried 100 mL pressure vessel was charged with **I** (4.1 mg, 2.5 mol %), KO^{t}Bu (2.1 mg, 7.5 mol %), 4-methoxy benzyl alcohol (0.25 mmol), n-hexyl amine (0.275 mmol) and benzene (1.2 mL). The vessel was closed with a PTFE screw cap and heated at 105 °C for 48 h. Nitromethane (20 µL, 373 µmol) was added to the reaction mixture as internal

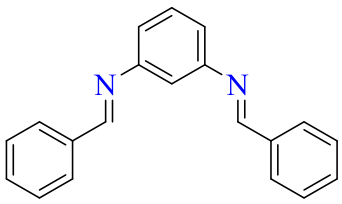
standard. The mixture was diluted with $CDCl_3$, filtered through Celite and subjected to NMR analysis. NMR yield: 85%.



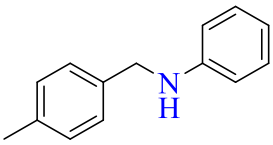
3aa[21]: Inside a N_2 filled glovebox, an oven-dried 100 mL pressure vessel was charged with **I** (4.1 mg, 2.5 mol %), KO^{t}Bu (2.1 mg, 7.5 mol %), 1-pentanol (0.25 mmol), hexyl amine (0.275 mmol) and benzene (1.2 mL). The vessel was closed with a PTFE screw cap and heated at 105 °C for 24 h. 1,3,5-Trimethoxybenzene (8.4 mg, 0.05 mmol) was added to the reaction mixture as internal standard. The mixture was diluted with $CDCl_3$, filtered through Celite and subjected to NMR analysis. NMR yield: 73%.



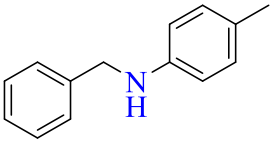
3ab[21]: Inside a N_2 filled glovebox, an oven-dried 100 mL pressure vessel was charged with **I** (4.1 mg, 2.5 mol %), KO^{t}Bu (2.1 mg, 7.5 mol %), 1-octanol (0.25 mmol), n-hexyl amine (0.275 mmol) and benzene (1.2 mL). The vessel was closed with a PTFE screw cap and heated at 105 °C for 24 h. Nitromethane (20 µL, 373 µmol) was added to the reaction mixture as internal standard. The mixture was diluted with $CDCl_3$, filtered through Celite and subjected to NMR analysis. NMR yield: 85%.



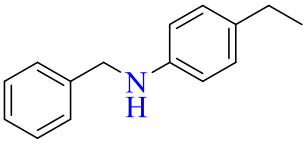
3aj [22] : Inside a N_2 filled glovebox, an oven-dried 15 mL reaction tube was charged with **I** (8.2 mg, 2.5 mol %), KO^{t}Bu (4.2 mg, 7.5 mol %), benzyl alcohol (0.5 mmol), mphenylenediamine (0.275 mmol) and benzene (1.2 mL). The tube was sealed by a screw cap fitted with a PTFE septa, and attached to argon flow through a needle. The reaction was carried out at 105 °C for 48 h. 1,3,5Trimethoxybenzene (8.4 mg, 0.05 mmol) was added to the reaction mixture as internal standard. The mixture was diluted with $CDCl_3$, filtered through Celite and subjected to NMR analysis. NMR yield: 83%.



4b[23]: Inside a N_2 filled glovebox, an oven-dried 15 mL reaction tube was charged with **I** (4.9 mg, 3 mol %), KO^{t}Bu (31 mg, 110 mol %), 4methylbenzyl alcohol (0.25 mmol), aniline (0.275 mmol) and toluene (0.75 mL). The tube was sealed with a screw cap fitted with a PTFE septa, taken out of the box and heated at 85 °C for 24 h. To the reaction mixture was added 1,3,5-trimethoxy benzene (8.4 mg, 0.05 mmol) as internal standard. The reaction mixture was then filtered through silica gel plug and rinsed with diethyl ether (5 mL).

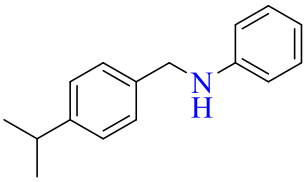


4c[24]: Inside a N_2 filled glovebox, an oven-dried 15 mL reaction tube was charged with **I** (4.9 mg, 3 mol %), KO^{t}Bu (31 mg, 110 mol %), benzyl alcohol (0.25 mmol), 4-methyl aniline (0.275 mmol) and toluene (0.75 mL). The tube was sealed with a screw cap fitted with a PTFE septa, taken out of the box and heated at 85 °C for 24 h. To the reaction mixture was added 1,3,5-trimethoxy benzene (8.4 mg, 0.05 mmol) as internal standard. The reaction mixture was then filtered through silica gel plug and rinsed with diethyl ether (5 mL). The filtrate was concentrated under reduced pressure and subjected to NMR analysis to identify the product and determine its yield. NMR yield: 80%.

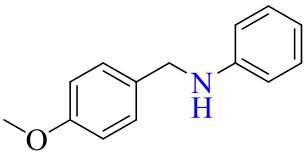


4d[25]: Inside a N_2 filled glovebox, an oven-dried 15 mL reaction tube was charged with **I** (4.9 mg, 3 mol %), KO^{t}Bu (31 mg, 110 mol %), benzyl alcohol (0.25 mmol), 4-ethyl aniline (0.275 mmol) and toluene (0.75 mL). The tube was sealed with a screw cap fitted with a PTFE septa, taken out of the box and heated at 85 °C for 24 h. To the reaction mixture was added 1,3,5-trimethoxy

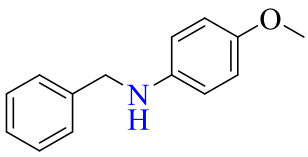
benzene (8.4 mg, 0.05 mmol) as internal standard. The reaction mixture was then filtered through silica gel plug and rinsed with diethyl ether (5 mL). The filtrate was concentrated under reduced pressure and subjected to NMR analysis to identify the product and determine its yield. NMR yield: 71%.



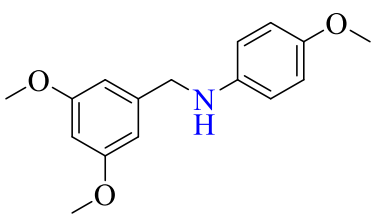
4e[26]: Inside a N_2 filled glovebox, an oven-dried 15 mL reaction tube was charged with **I** (4.9 mg, 3 mol %), KO^{t}Bu (31 mg, 110 mol %), 4-isopropyl benzyl alcohol (0.25 mmol), aniline (0.275 mmol) and toluene (0.75 mL). The tube was sealed with a screw cap fitted with a PTFE septa, taken out of the box and heated at 85 °C for 24 h. To the reaction mixture was added 1,3,5-trimethoxy benzene (8.4 mg, 0.05 mmol) as internal standard. The reaction mixture was then filtered through silica gel plug and rinsed with diethyl ether (5 mL). The filtrate was concentrated under reduced pressure and subjected to NMR analysis to identify the product and determine its yield. NMR yield: 80%.



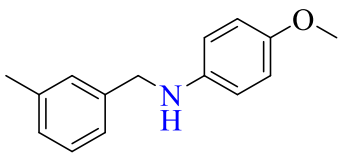
4f[27]: Inside a N_2 filled glovebox, an oven-dried 15 mL reaction tube was charged with **I** (4.9 mg, 3 mol %), KO^{t}Bu (31 mg, 110 mol %), 4-methoxy benzyl alcohol (0.25 mmol), aniline (0.275 mmol) and toluene (0.75 mL). The tube was sealed with a screw cap fitted with a PTFE septa, taken out of the box and heated at 85 °C for 24 h. To the reaction mixture was added 1,3,5-trimethoxy benzene (8.4 mg, 0.05 mmol) as internal standard. The reaction mixture was then filtered through silica gel plug and rinsed with diethyl ether (5 mL). The filtrate was concentrated under reduced pressure and subjected to NMR analysis to identify the product and determine its yield. NMR yield: 97%.



4g[28]: Inside a N_2 filled glovebox, an oven-dried 15 mL reaction tube was charged with **I** (4.9 mg, 3 mol %), KO^{t}Bu (31 mg, 110 mol %), benzyl alcohol (0.25 mmol), 4-methoxy aniline (0.275 mmol) and toluene (0.75 mL). The tube was sealed with a screw cap fitted with a PTFE septa, taken out of the box and heated at 85 °C for 24 h. To the reaction mixture was added 1,3,5-trimethoxy benzene (8.4 mg, 0.05 mmol) as internal standard. The reaction mixture was then filtered through silica gel plug and rinsed with diethyl ether (5 mL). The filtrate was concentrated under reduced pressure and subjected to NMR analysis to identify the product and determine its yield. NMR yield: 91%.

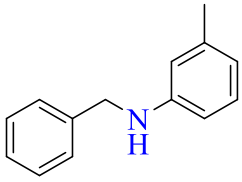


4h[29]: Inside a N_2 filled glovebox, an oven-dried 15 mL reaction tube was charged with **I** (4.9 mg, 3 mol %), KO^{t}Bu (31 mg, 110 mol %), 3,5-dimethoxy benzyl alcohol (0.25 mmol), 4-methoxy aniline (0.275 mmol) and toluene (0.75 mL). The tube was sealed with a screw cap fitted with a PTFE septa, taken out of the box and heated at 85 °C for 24 h. To the reaction mixture was added 1,3,5-trimethoxy benzene (8.4 mg, 0.05 mmol) as internal standard. The reaction mixture was then filtered through silica gel plug and rinsed with diethyl ether (5 mL). The filtrate was concentrated under reduced pressure and subjected to NMR analysis to identify the product and determine its yield. NMR yield: 91%.

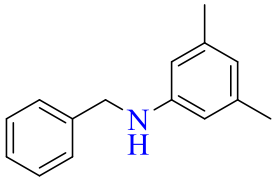


4i[30]: Inside a N_2 filled glovebox, an oven-dried 15 mL reaction tube was charged with **I** (4.9 mg, 3 mol %), KO^{t}Bu (31 mg, 110 mol %), 3-methyl benzyl alcohol (0.3 mmol), 4-methoxy aniline (0.25 mmol) and toluene (0.75 mL). The tube was sealed with a screw cap fitted

with a PTFE septa, taken out of the box and heated at 85 °C for 24 h. To the reaction mixture was added 1,3,5-trimethoxy benzene (8.4 mg, 0.05 mmol) as internal standard. The reaction mixture was then filtered through silica gel plug and rinsed with diethyl ether (5 mL). The filtrate was concentrated under reduced pressure and subjected to NMR analysis to identify the product and determine its yield. NMR yield: 92%.

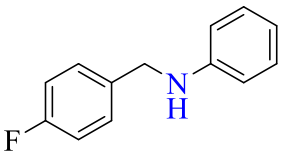


4j[31]: Inside a N_2 filled glovebox, an oven-dried 15 mL reaction tube was charged with **I** (4.9 mg, 3 mol %), KO^{t}Bu (31 mg, 110 mol %), benzyl alcohol (0.25 mmol), 3-methyl aniline (0.275 mmol) and toluene (0.75 mL). The tube was sealed with a screw cap fitted with a PTFE septa, taken out of the box and heated at 85 °C for 24 h. To the reaction mixture was added 1,3,5-trimethoxy benzene (8.4 mg, 0.05 mmol) as internal standard. The reaction mixture was then filtered through silica gel plug and rinsed with diethyl ether (5 mL). The filtrate was concentrated under reduced pressure and subjected to NMR analysis to identify the product and determine its yield. NMR yield: 99%.

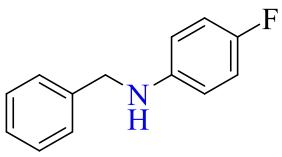


4k[32]: Inside a N_2 filled glovebox, an oven-dried 15 mL reaction tube was charged with **I** (4.9 mg, 3 mol %), KO^{t}Bu (31 mg, 110 mol %), benzyl alcohol (0.25 mmol), 3,5-dimethyl aniline (0.275 mmol) and toluene (0.75 mL). The tube was sealed with a screw cap fitted with a PTFE septa, taken out of the box and heated at 85 °C for 24 h. To the reaction mixture was added 1,3,5-trimethoxy benzene (8.4 mg, 0.05 mmol) as internal standard. The reaction mixture was then filtered through silica gel plug and rinsed with diethyl ether (5 mL). The filtrate

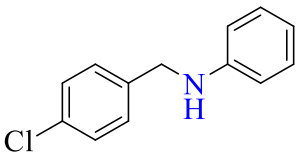
was concentrated under reduced pressure and subjected to NMR analysis to identify the product and determine its yield. NMR yield: 68%.



4l[33]: Inside a N_2 filled glovebox, an oven-dried 15 mL reaction tube was charged with **I** (4.9 mg, 3 mol %), KO^{t}Bu (31 mg, 110 mol %), 4fluorobenzyl alcohol (0.25 mmol), aniline (0.275 mmol) and toluene (0.75 mL) The tube was sealed with a screw cap fitted with a PTFE septa, taken out of the box and heated at 85 °C for 24 h. To the reaction mixture was added 1,3,5-trimethoxy benzene (8.4 mg, 0.05 mmol) as internal standard. The reaction mixture was then filtered through silica gel plug and rinsed with diethyl ether (5 mL). The filtrate was concentrated under reduced pressure and subjected to NMR analysis to identify the product and determine its yield. NMR yield: 77%.

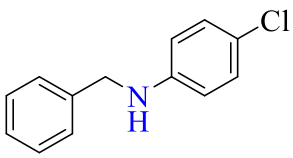


4m[34]: Inside a N_2 filled glovebox, an oven-dried 15 mL reaction tube was charged with **I** (4.9 mg, 3 mol %), KO^{t}Bu (31 mg, 110 mol %), benzyl alcohol (0.25 mmol), 4-fluoroaniline (0.275 mmol) and toluene (0.75 mL). The tube was sealed with a screw cap fitted with a PTFE septa, taken out of the box and heated at 85 °C for 24 h. To the reaction mixture was added 1,3,5-trimethoxy benzene (8.4 mg, 0.05 mmol) as internal standard. The reaction mixture was then filtered through silica gel plug and rinsed with diethyl ether (5 mL). The filtrate was concentrated under reduced pressure and subjected to NMR analysis to identify the product and determine its yield. NMR yield: 76%.

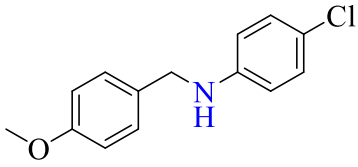


4n[35]: Inside a N_2 filled glovebox, an oven-dried 15 mL reaction tube was charged with **I** (4.9 mg, 3 mol %), KO^{t}Bu (31 mg, 110

mol %), 4chlorobenzyl alcohol (0.25 mmol), aniline (0.275 mmol) and toluene (0.75 mL). The tube was sealed with a screw cap fitted with a PTFE septa, taken out of the box and heated at 85 °C for 24 h. To the reaction mixture was added 1,3,5-trimethoxy benzene (8.4 mg, 0.05 mmol) as internal standard. The reaction mixture was then filtered through silica gel plug and rinsed with diethyl ether (5 mL). The filtrate was concentrated under reduced pressure and subjected to NMR analysis to identify the product and determine its yield. NMR yield: 72%.

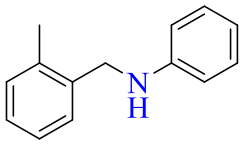


4o[36]: Inside a N_2 filled glovebox, an oven-dried 15 mL reaction tube was charged with **I** (4.9 mg, 3 mol %), KO^{t}Bu (31 mg, 110 mol %), benzyl alcohol (0.25 mmol), 4-chloroaniline (0.35 mmol) and toluene (0.75 mL). The tube was sealed with a screw cap fitted with a PTFE septa, taken out of the box and heated at 85 °C for 24 h. To the reaction mixture was added 1,3,5-trimethoxy benzene (8.4 mg, 0.05 mmol) as internal standard. The reaction mixture was then filtered through silica gel plug and rinsed with diethyl ether (5 mL). The filtrate was concentrated under reduced pressure and subjected to NMR analysis to identify the product and determine its yield. NMR yield: 84%.

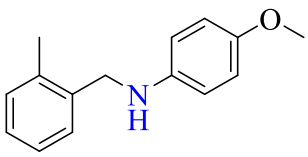


4p[11]: Inside a N_2 filled glovebox, an oven-dried 15 mL reaction tube was charged with **I** (4.9 mg, 3 mol %), KO^{t}Bu (31 mg, 110 mol %), 4-methoxybenzyl alcohol (0.25 mmol), 4-chloroaniline (0.35 mmol) and toluene (0.75 mL). The tube was sealed with a screw cap fitted with a PTFE septa, taken out of the box and heated at 85 °C for 24 h. To the reaction mixture was added 1,3,5- trimethoxy benzene (8.4 mg, 0.05 mmol) as internal standard.

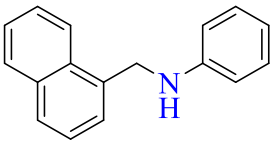
The reaction mixture was then filtered through silica gel plug and rinsed with diethyl ether (5 mL). The filtrate was concentrated under reduced pressure and subjected to NMR analysis to identify the product and determine its yield. NMR yield: 84%.



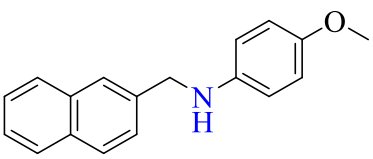
4r[3]: Inside a N_2 filled glovebox, an oven-dried 15 mL reaction tube was charged with **I** (4.9 mg, 3 mol %), KO^{t}Bu (31 mg, 110 mol %), 2methylbenzyl alcohol (0.25 mmol), aniline (0.275 mmol) and toluene (0.75 mL). The tube was sealed with a screw cap fitted with a PTFE septa, taken out of the box and heated at 85 °C for 24 h. To the reaction mixture was added 1,3,5-trimethoxy benzene (8.4 mg, 0.05 mmol) as internal standard. The reaction mixture was then filtered through silica gel plug and rinsed with diethyl ether (5 mL). The filtrate was concentrated under reduced pressure and subjected to NMR analysis to identify the product and determine its yield. NMR yield: 93%.



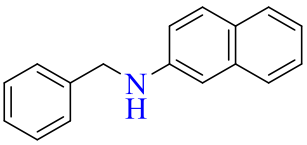
4s[37]: Inside a N_2 filled glovebox, an oven-dried 15 mL reaction tube was charged with **I** (4.9 mg, 3 mol %), KO^{t}Bu (31 mg, 110 mol %), 2-methylbenzyl alcohol (0.3 mmol), 4-methoxyaniline (0.25 mmol) and toluene (0.75 mL). The tube was sealed with a screw cap fitted with a PTFE septa, taken out of the box and heated at 85 °C for 24 h. To the reaction mixture was added 1,3,5-trimethoxy benzene (8.4 mg, 0.05 mmol) as internal standard. The reaction mixture was then filtered through silica gel plug and rinsed with diethyl ether (5 mL). The filtrate was concentrated under reduced pressure and subjected to NMR analysis to identify the product and determine its yield. NMR yield: 99%.



4t[3]: Inside a N_2 filled glovebox, an oven-dried 15 mL reaction tube was charged with **I** (4.9 mg, 3 mol %), KO^{t}Bu (31 mg, 110 mol %), 1naphthalenemethanol (0.25 mmol), aniline (0.275 mmol) and toluene (0.75 mL). The tube was sealed with a screw cap fitted with a PTFE septa, taken out of the box and heated at 85 °C for 24 h. To the reaction mixture was added 1,3,5-trimethoxy benzene (8.4 mg, 0.05 mmol) as internal standard. The reaction mixture was then filtered through silica gel plug and rinsed with diethyl ether (5 mL). The filtrate was concentrated under reduced pressure and subjected to NMR analysis to identify the product and determine its yield. NMR yield: 90%.

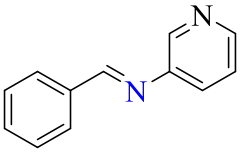


4u[38]: Inside a N_2 filled glovebox, an oven-dried 15 mL reaction tube was charged with **I** (4.9 mg, 3 mol %), KO^{t}Bu (31 mg, 110 mol %), 2-naphthalenemethanol (0.3 mmol), 4-methoxyaniline (0.25 mmol) and toluene (0.75 mL). The tube was sealed with a screw cap fitted with a PTFE septa, taken out of the box and heated at 85 °C for 24 h. To the reaction mixture was added 1,3,5-trimethoxy benzene (8.4 mg, 0.05 mmol) as internal standard. The reaction mixture was then filtered through silica gel plug and rinsed with diethyl ether (5 mL). The filtrate was concentrated under reduced pressure and subjected to NMR analysis to identify the product and determine its yield. NMR yield: 72%.

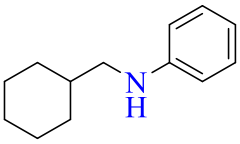


4v[17]: Inside a N_2 filled glovebox, an oven-dried 15 mL reaction tube was charged with **I** (4.9 mg, 3 mol %), KO^{t}Bu (31 mg, 110 mol %), benzyl alcohol (0.25 mmol), 2-naphthylamine (0.275 mmol) and toluene (0.75 mL). The tube was sealed with a screw cap fitted with a PTFE septa, taken out of the box

and heated at 85 °C for 24 h. To the reaction mixture was added 1,3,5-trimethoxy benzene (8.4 mg, 0.05 mmol) as internal standard. The reaction mixture was then filtered through silica gel plug and rinsed with diethyl ether (5 mL). The filtrate was concentrated under reduced pressure and subjected to NMR analysis to identify the product and determine its yield. NMR yield: 72%.

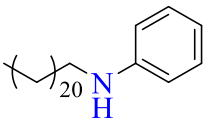


4w[39]: Inside a N_2 filled glovebox, an oven-dried 15 mL reaction tube was charged with **I** (4.9 mg, 3 mol %), KO^{t}Bu (31 mg, 110 mol %), benzyl alcohol (0.25 mmol), 3-aminopyridine (0.275 mmol) and toluene (0.75 mL The tube was sealed with a screw cap fitted with a PTFE septa, taken out of the box and heated at 85 °C for 24 h. To the reaction mixture was added 1,3,5-trimethoxy benzene (8.4 mg, 0.05 mmol) as internal standard. The reaction mixture was then filtered through silica gel plug and rinsed with diethyl ether (5 mL). The filtrate was concentrated under reduced pressure and subjected to NMR analysis to identify the product and determine its yield. NMR yield: 78%.

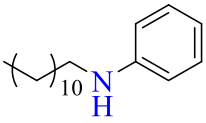


4ac[40]: Inside a N_2 filled glovebox, an oven-dried 15 mL reaction tube was charged with **I** (4.9 mg, 3 mol %), KO^{t}Bu (31 mg, 110 mol %), cyclohexyl methanol (0.25 mmol), aniline (0.275 mmol) and toluene (0.75 mL). The tube was sealed with a screw cap fitted with a PTFE septa, taken out of the box and heated at 85 °C for 24 h. To the reaction mixture was added 1,3,5- trimethoxy benzene (8.4 mg, 0.05 mmol) as internal standard. The reaction mixture was then filtered through silica gel plug and rinsed with diethyl ether (5 mL). The filtrate was concentrated under reduced pressure

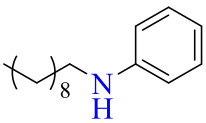
and subjected to NMR analysis to identify the product and determine its yield. NMR yield: 99%.



4ad[24]: Inside a N_2 filled glovebox, an oven-dried 15 mL reaction tube was charged with **I** (4.9 mg, 3 mol %), KO^{t}Bu (31 mg, 110 mol %), 1-docosanol (0.25 mmol), aniline (0.275 mmol) and toluene (0.75 mL). The tube was sealed with a screw cap fitted with a PTFE septa, taken out of the box and heated at 85 °C for 24 h. To the reaction mixture was added 1,3,5- trimethoxy benzene (8.4 mg, 0.05 mmol) as internal standard. The reaction mixture was then filtered through silica gel plug and rinsed with diethyl ether (5 mL). The filtrate was concentrated under reduced pressure and subjected to NMR analysis to identify the product and determine its yield. NMR yield: 90%.

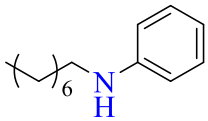


4ae[41]: Inside a N_2 filled glovebox, an oven-dried 15 mL reaction tube was charged with **I** (4.9 mg, 3 mol %), KO^{t}Bu (31 mg, 110 mol %), 1-dodecanol (0.25 mmol), aniline (0.275 mmol) and toluene (0.75 mL). The tube was sealed with a screw cap fitted with a PTFE septa, taken out of the box and heated at 85 °C for 24 h. To the reaction mixture was added 1,3,5- trimethoxy benzene (8.4 mg, 0.05 mmol) as internal standard. The reaction mixture was then filtered through silica gel plug and rinsed with diethyl ether (5 mL). The filtrate was concentrated under reduced pressure and subjected to NMR analysis to identify the product and determine its yield. NMR yield: 99%.

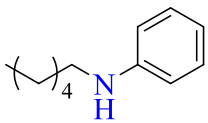


4af[42]: Inside a N_2 filled glovebox, an oven-dried 15 mL reaction tube was charged with **I** (4.9 mg, 3 mol %), KO^{t}Bu (31 mg, 110 mol

%),decanol (0.25 mmol), aniline (0.275 mmol) and toluene (0.75 mL). The tube was sealed with a screw cap fitted with a PTFE septa, taken out of the box and heated at 85 °C for 24 h. To the reaction mixture was added 1,3,5- trimethoxy benzene (8.4 mg, 0.05 mmol) as internal standard. The reaction mixture was then filtered through silica gel plug and rinsed with diethyl ether (5 mL). The filtrate was concentrated under reduced pressure and subjected to NMR analysis to identify the product and determine its yield. NMR yield: 98%.

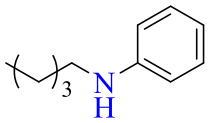


4ag[41]: Inside a N_2 filled glovebox, an oven-dried 15 mL reaction tube was charged with **I** (4.9 mg, 3 mol %), KO^{t}Bu (31 mg, 110 mol %), 1-octanol (0.25 mmol), aniline (0.275 mmol) and toluene (0.75 mL). The tube was sealed with a screw cap fitted with a PTFE septa, taken out of the box and heated at 85 °C for 24 h. To the reaction mixture was added 1,3,5- trimethoxy benzene (8.4 mg, 0.05 mmol) as internal standard. The reaction mixture was then filtered through silica gel plug and rinsed with diethyl ether (5 mL). The filtrate was concentrated under reduced pressure and subjected to NMR analysis to identify the product and determine its yield. NMR yield: 93%.

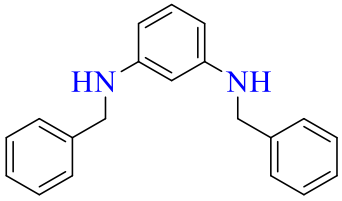


4ah[41]: Inside a N_2 filled glovebox, an oven-dried 15 mL reaction tube was charged with **I** (4.9 mg, 3 mol %), KO^{t}Bu (31 mg, 110 mol %), 1-hexanol (0.25 mmol), aniline (0.275 mmol) and toluene (0.75 mL). The tube was sealed with a screw cap fitted with a PTFE septa, taken out of the box and heated at 85 °C for 24 h. To the reaction mixture was added 1,3,5- trimethoxy benzene (8.4 mg, 0.05 mmol) as internal standard. The reaction mixture was then filtered through silica gel plug and rinsed

with diethyl ether (5 mL). The filtrate was concentrated under reduced pressure and subjected to NMR analysis to identify the product and determine its yield. NMR yield: 99%.



4ai[43]: Inside a N_2 filled glovebox, an oven-dried 15 mL reaction tube was charged with **I** (4.9 mg, 3 mol %), KO^{t}Bu (31 mg, 110 mol %), 1-pentanol (0.25 mmol), aniline (0.275 mmol) and toluene (0.75 mL). The tube was sealed with a screw cap fitted with a PTFE septa, taken out of the box and heated at 85 °C for 24 h. To the reaction mixture was added 1,3,5- trimethoxy benzene (8.4 mg, 0.05 mmol) as internal standard. The reaction mixture was then filtered through silica gel plug and rinsed with diethyl ether (5 mL). The filtrate was concentrated under reduced pressure and subjected to NMR analysis to identify the product and determine its yield. NMR yield: 95%.



4aj[25]: Inside a N_2 filled glovebox, an oven-dried 15 mL reaction tube was charged with **I** (9.8 mg, 3 mol %), KO^{t}Bu (62 mg, 110 mol %), benzyl alcohol (0.5 mmol), m-phenylenediamine (0.275 mmol) and toluene (1.2 mL). The tube was sealed with a screw cap fitted with a PTFE septa, taken out of the box and heated at 85 °C for 48 h. To the reaction mixture was added 1,3,5-trimethoxy benzene (8.4 mg, 0.05 mmol) as internal standard. The reaction mixture was then filtered through silica gel plug and rinsed with diethyl ether (5 mL). The filtrate was concentrated under reduced pressure and subjected to NMR analysis to identify the product and determine its yield. NMR yield: 90%.

2.17 Supplementary figures

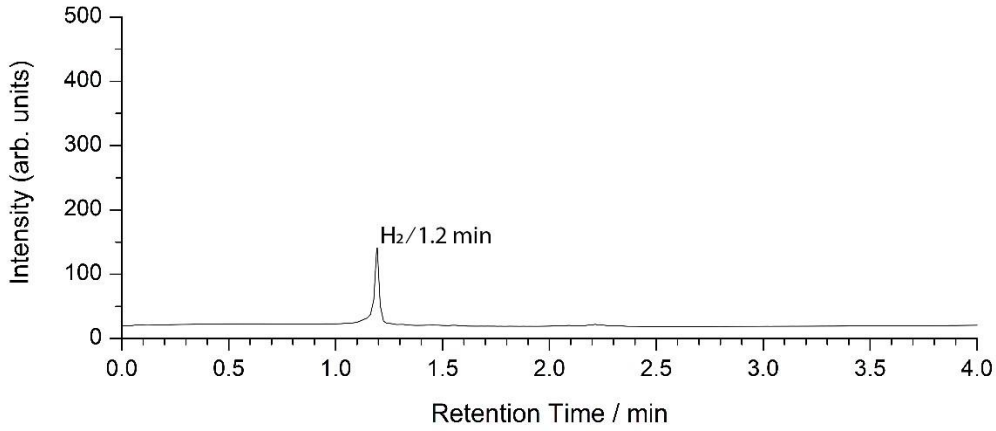


Figure 2.1 H_2 detection by GC chromatography.

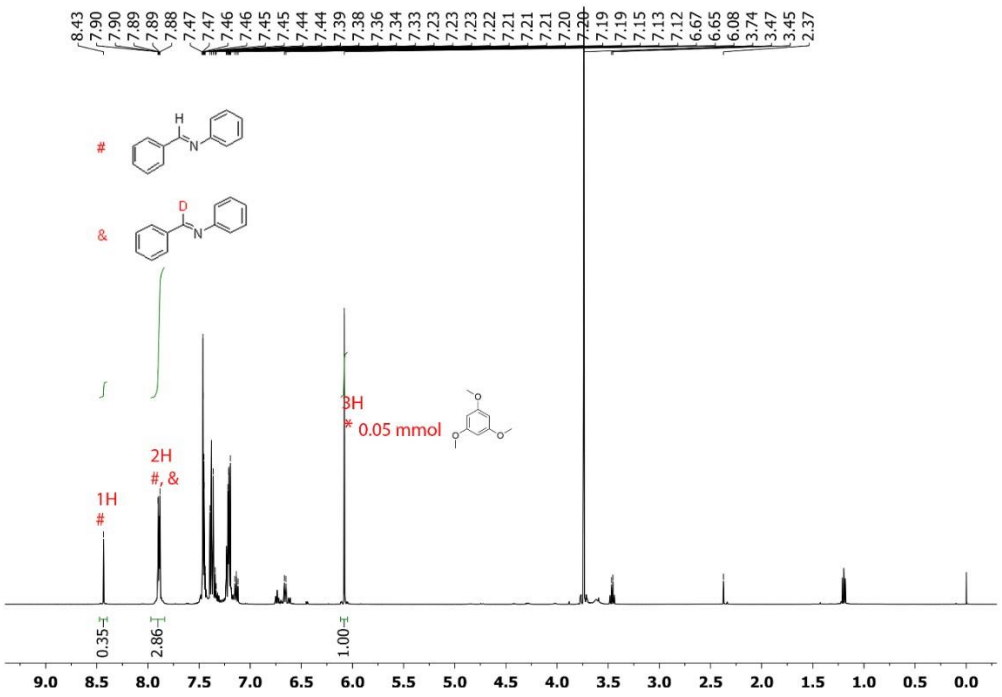


Figure 2.2 ^{1}H NMR (500 MHz, $CDCl_3$) of the coupling reaction of benzyl alcohol-α,α-d_2 and aniline to N-benzylideneaniline.

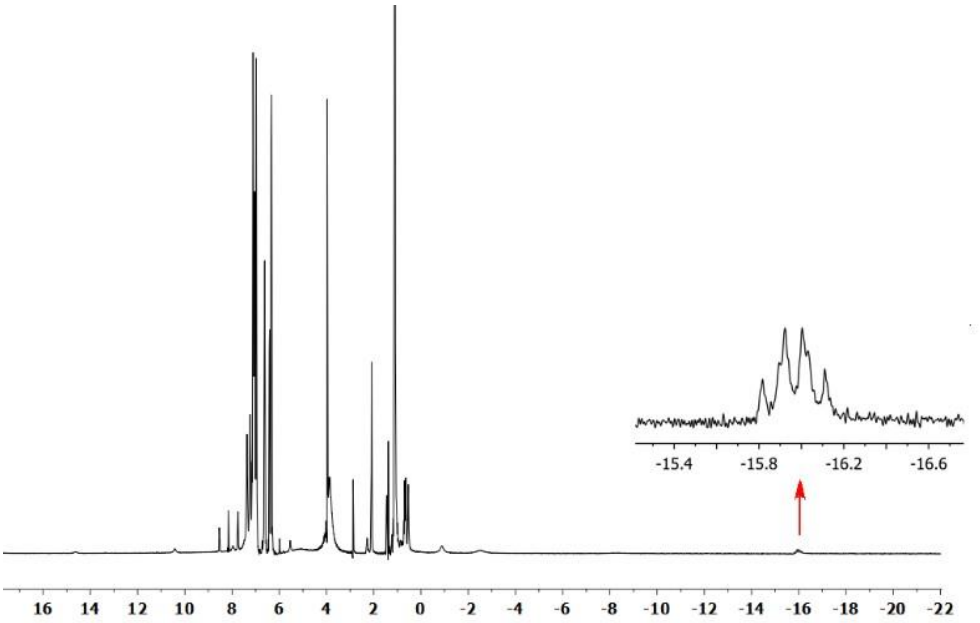


Figure 2.3 ^{1}H NMR (500 MHz, toluene-d8) of the reaction mixture of benzyl alcohol and aniline coupling to N-benzylaniline. A cobalt hydride species was observed at – 15.99 ppm.

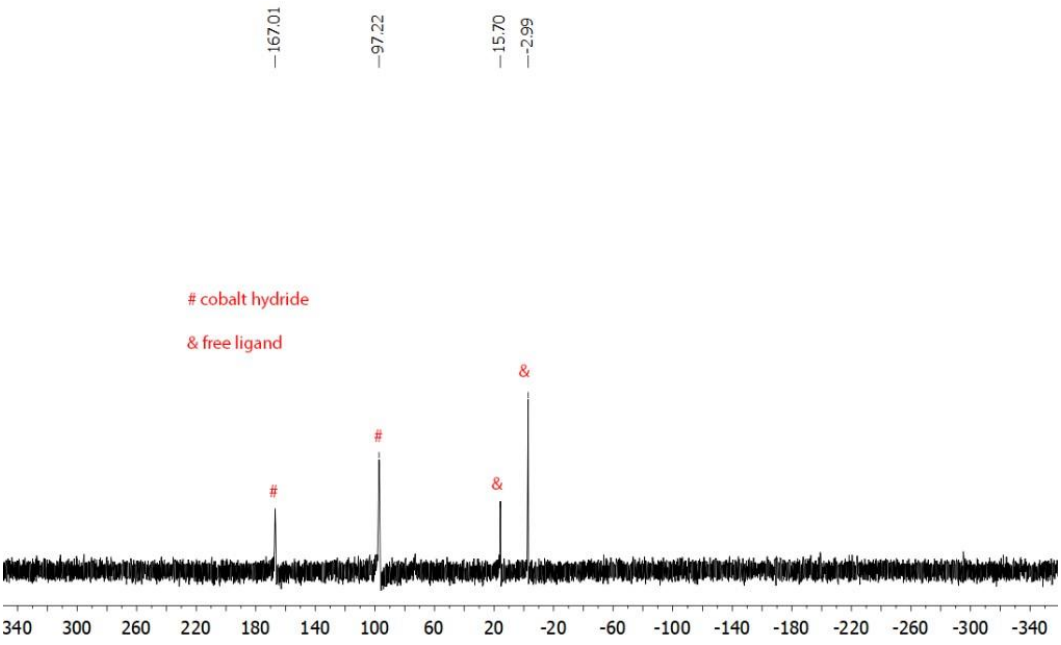


Figure 2.4 ^{31}P NMR (122 MHz, toluene-d8) of the reaction mixture of benzyl alcohol and aniline coupling to N-benzylaniline.

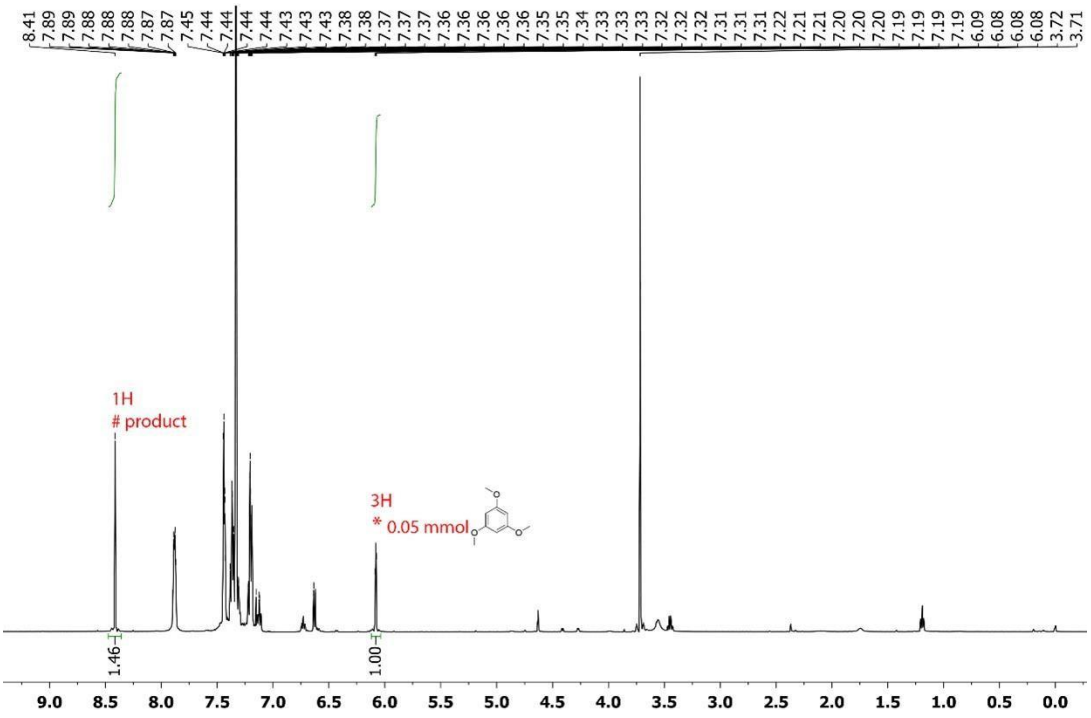


Figure 2.5 ^{1}H NMR (500 MHz, $CDCl_3$) of the reaction mixture of 3a.

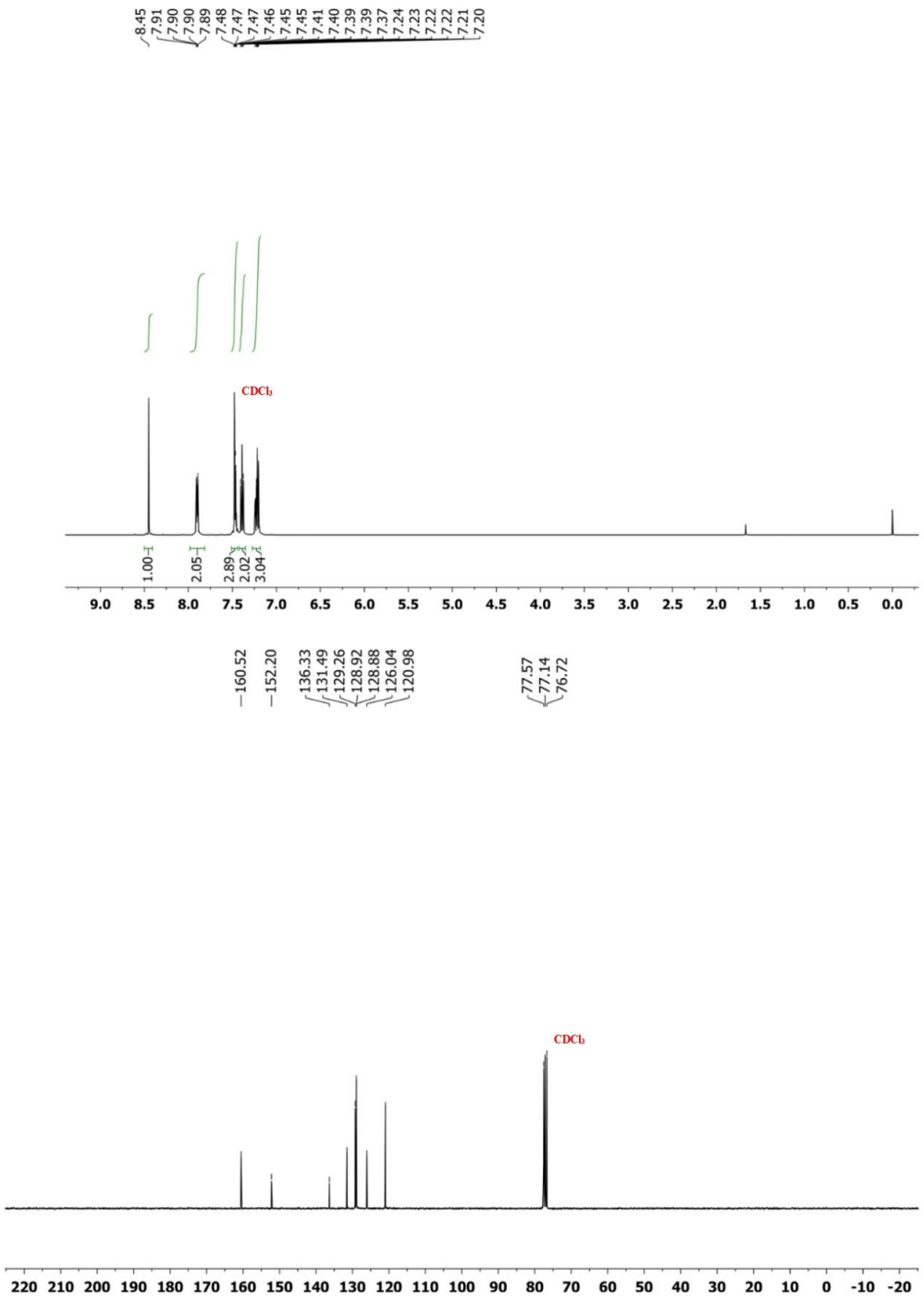


Figure 2.6 ^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) of the isolated 3a.

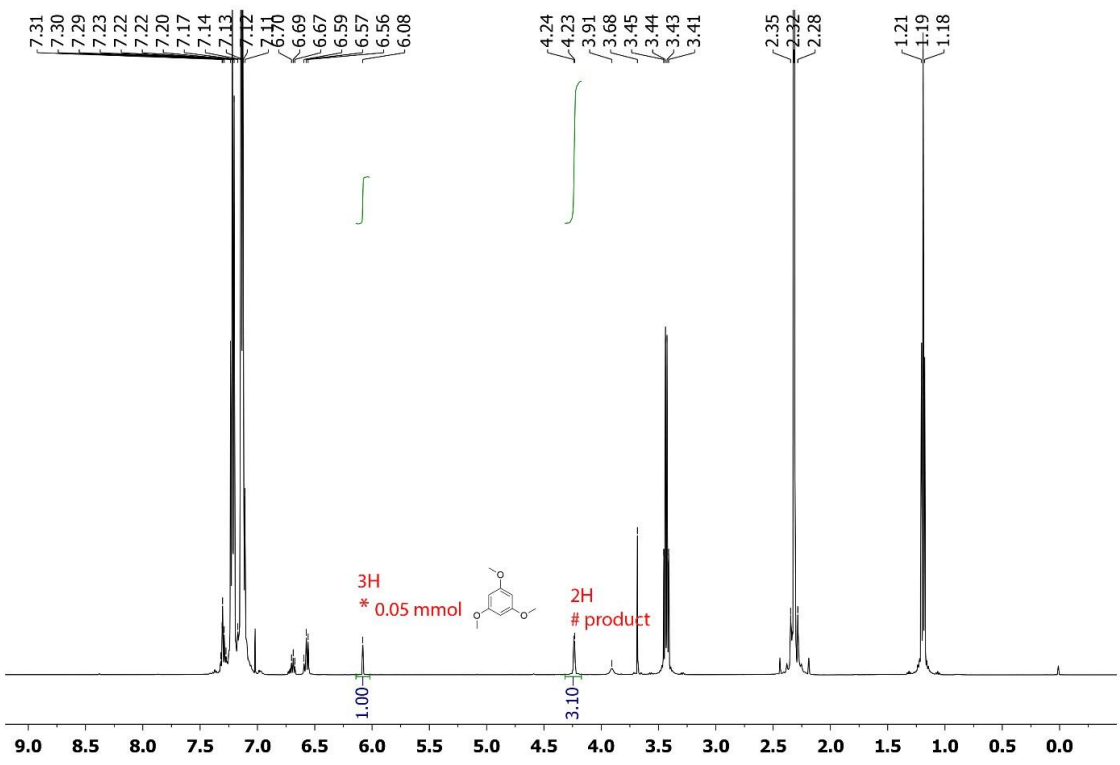


Figure 2.7 ^{1}H NMR (500 MHz, $CDCl_3$) of the reaction mixture of 4a.

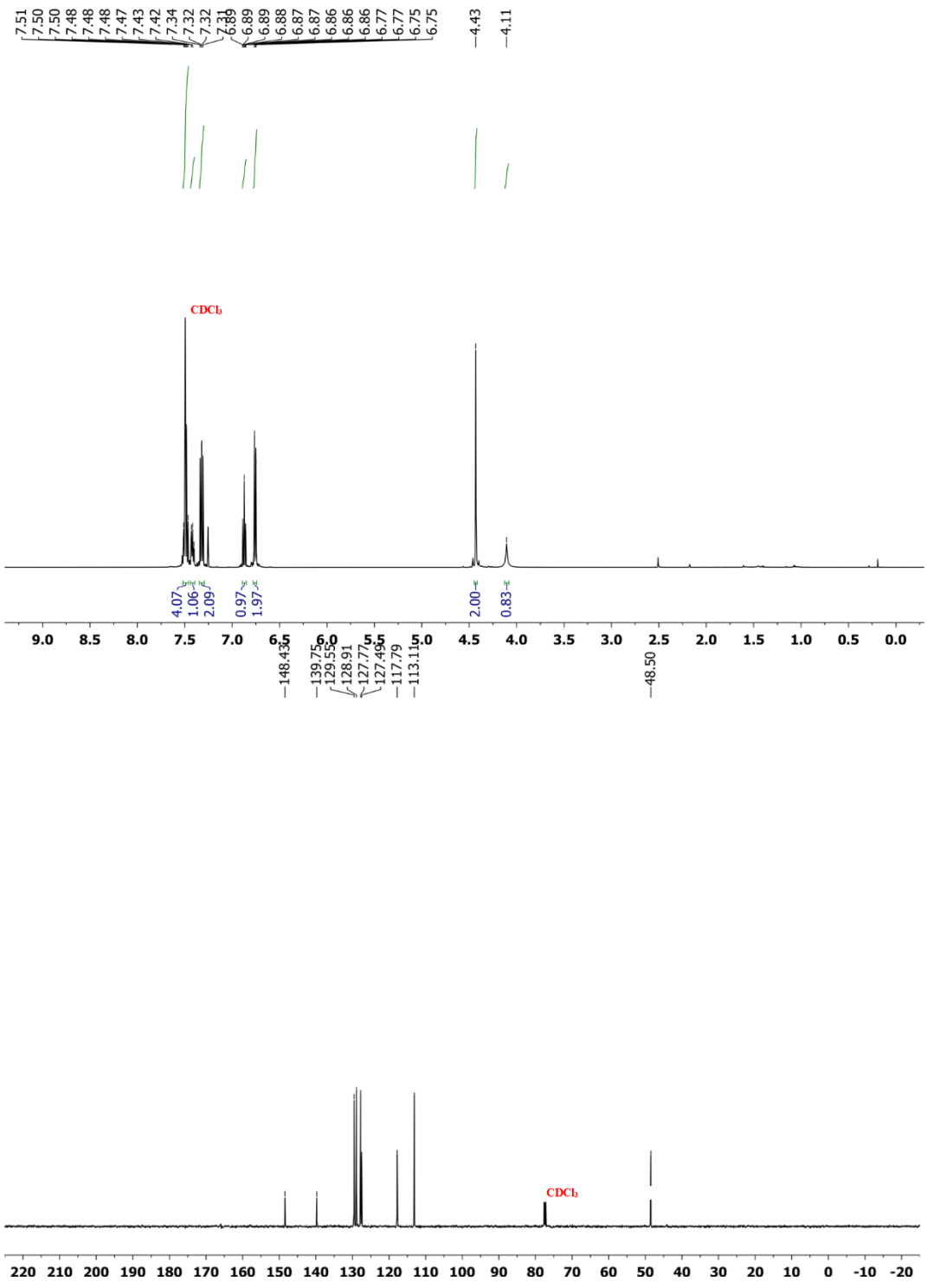


Figure 2.8 ^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) of the isolated 4a**.**

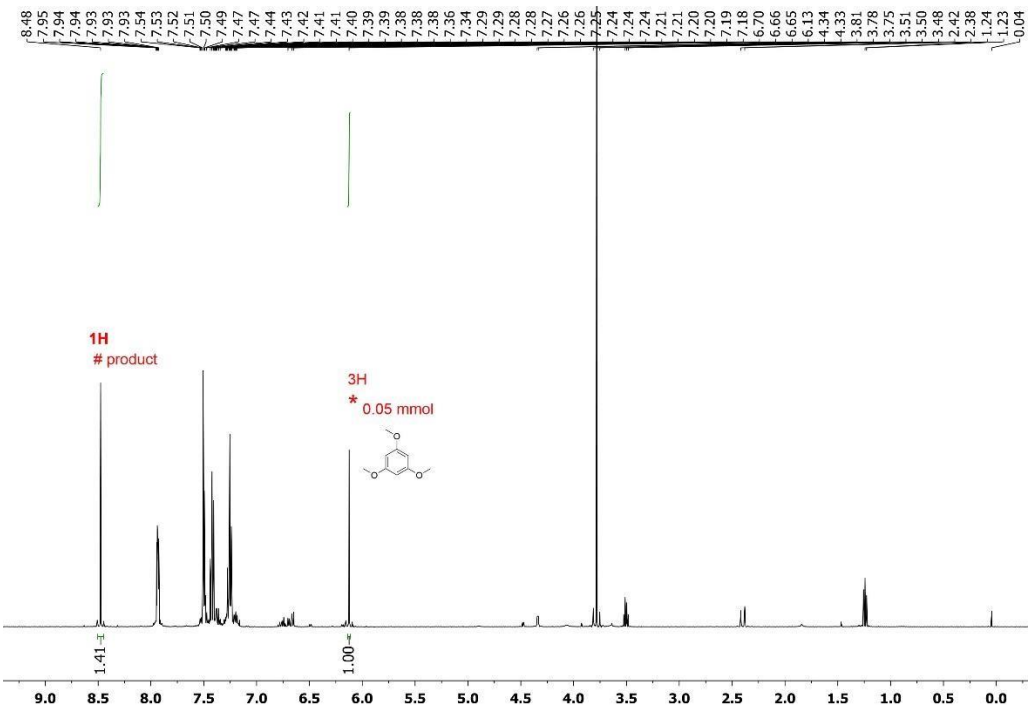


Figure 2.9 ^{1}H NMR (500 MHz, $CDCl_3$) of the reaction mixture of imine synthesis by II and KO^{t}Bu.

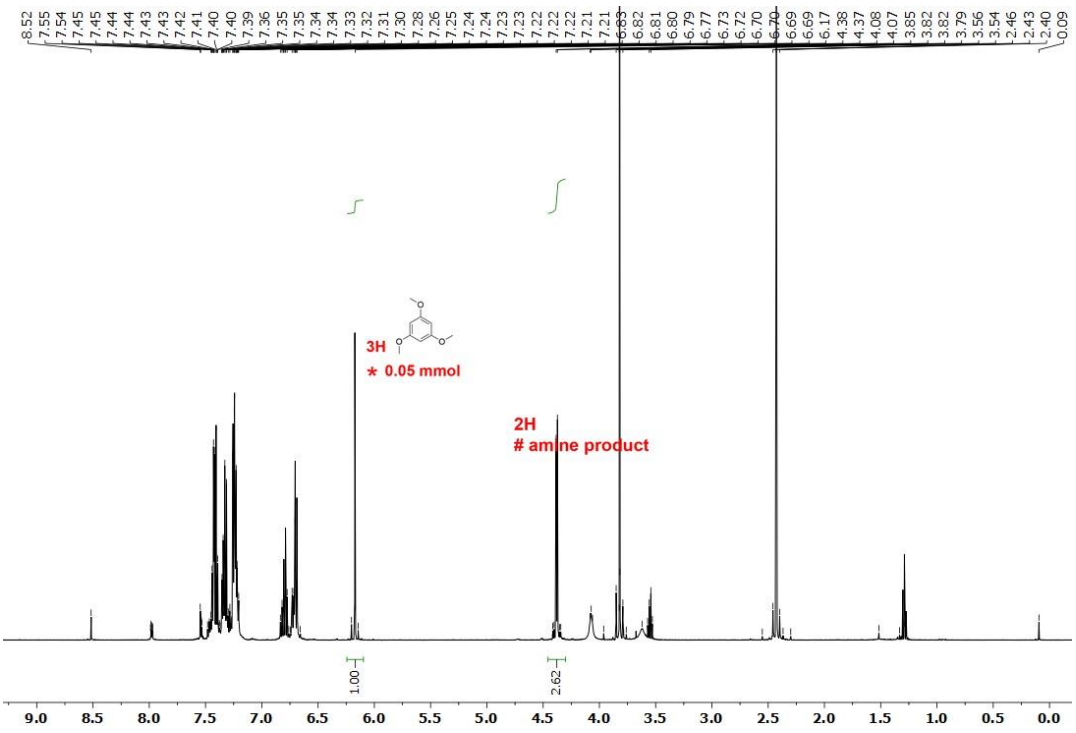


Figure 2.10 ^{1}H NMR (500 MHz, $CDCl_3$) of the reaction mixture of amine synthesis by II and $KO^{t}Bu$.

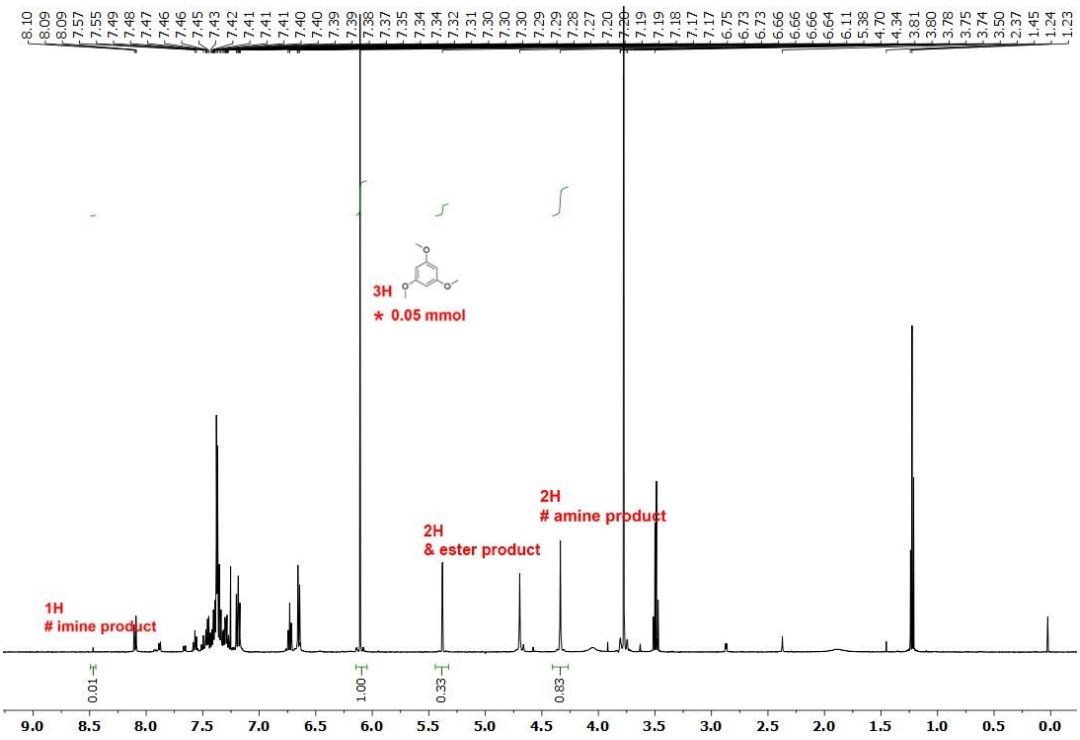


Figure 2.11 ^{1}H NMR (500 MHz, $CDCl_3$) of the reaction mixture of imine synthesis by III and $KO^{t}Bu$.

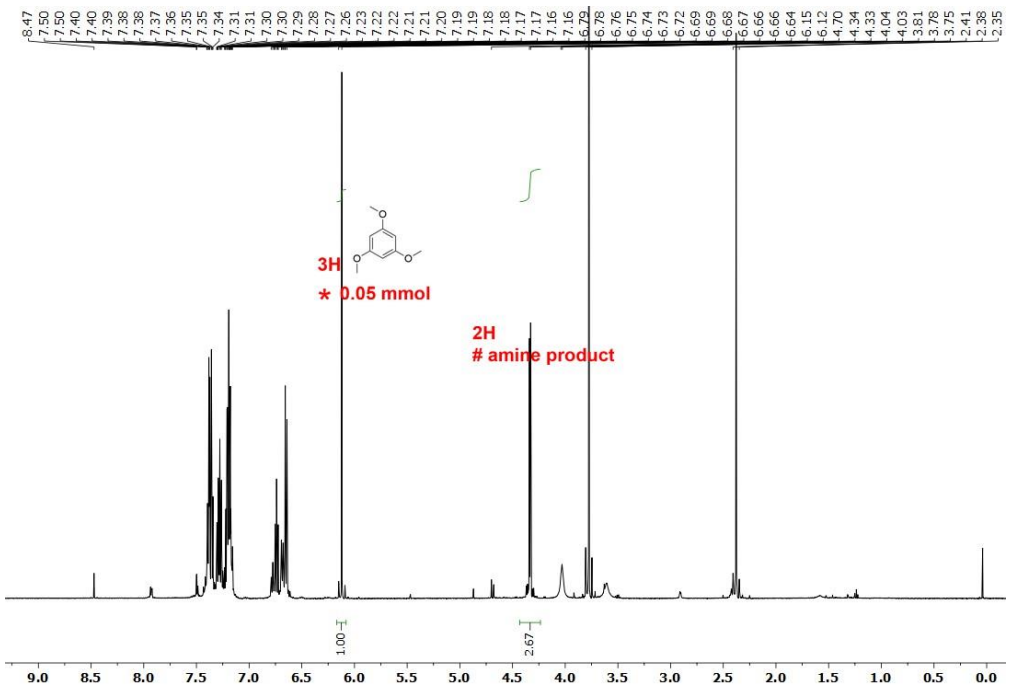


Figure 2.12 ^{1}H NMR (500 MHz, $CDCl_3$) of the reaction mixture of amine synthesis by III and KO^{t}Bu.

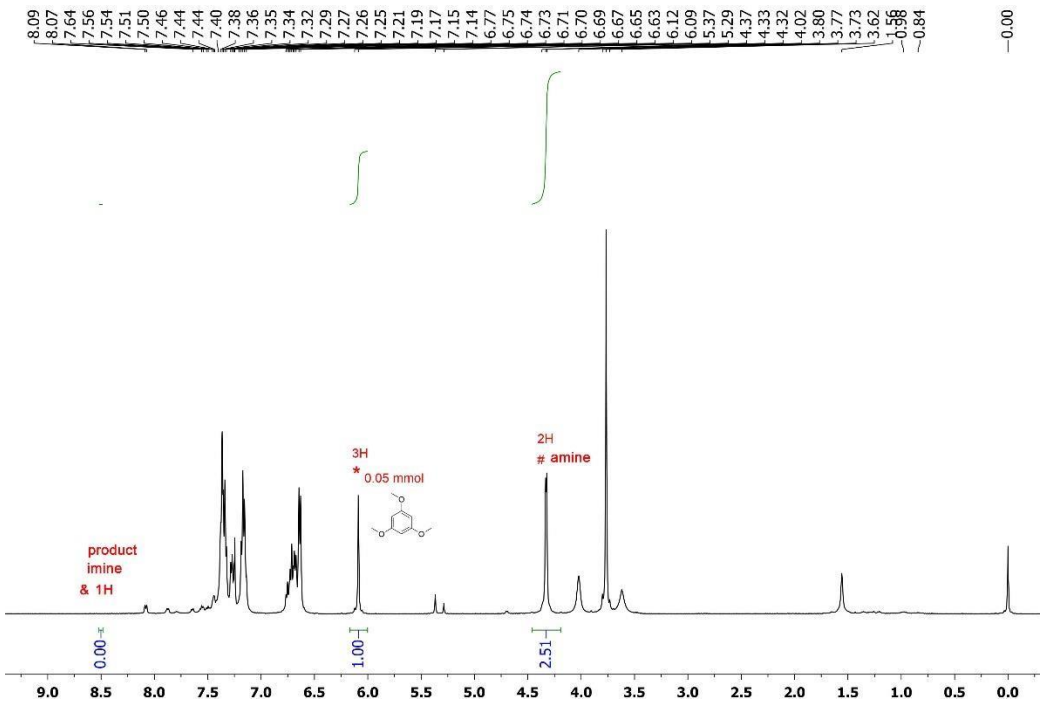


Figure 2.13 ^{1}H NMR (500 MHz, $CDCl_3$) of the reaction mixture of imine synthesis by IV and KO^{t}Bu.

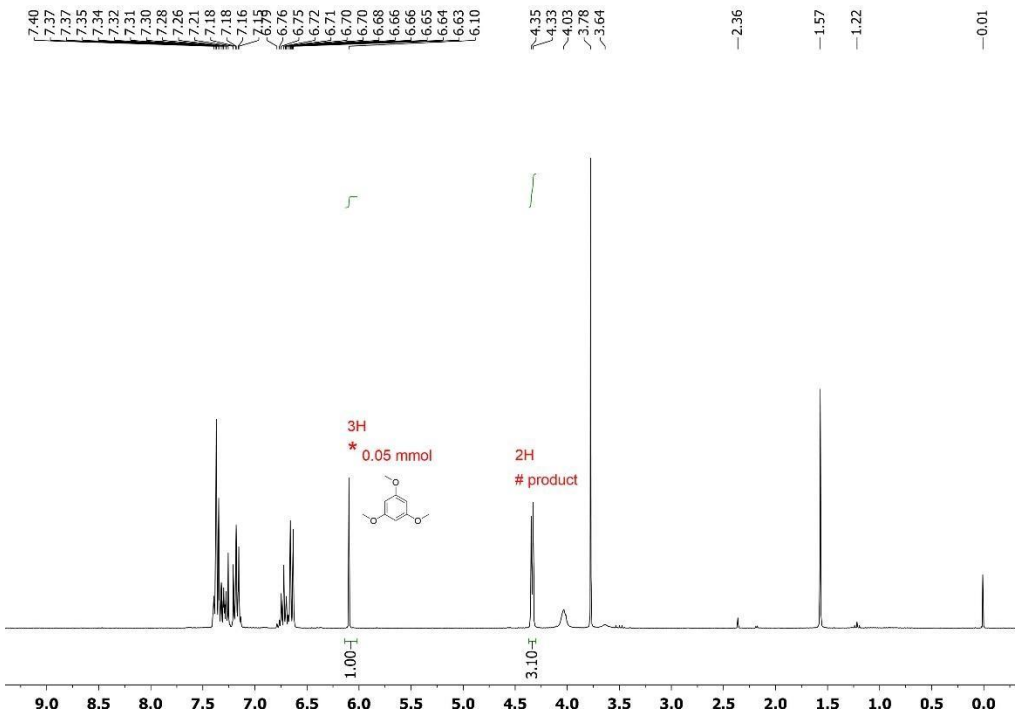


Figure 2.14 ^{1}H NMR (500 MHz, $CDCl_3$) of the reaction mixture of amine synthesis by IV and KO^{t}Bu.

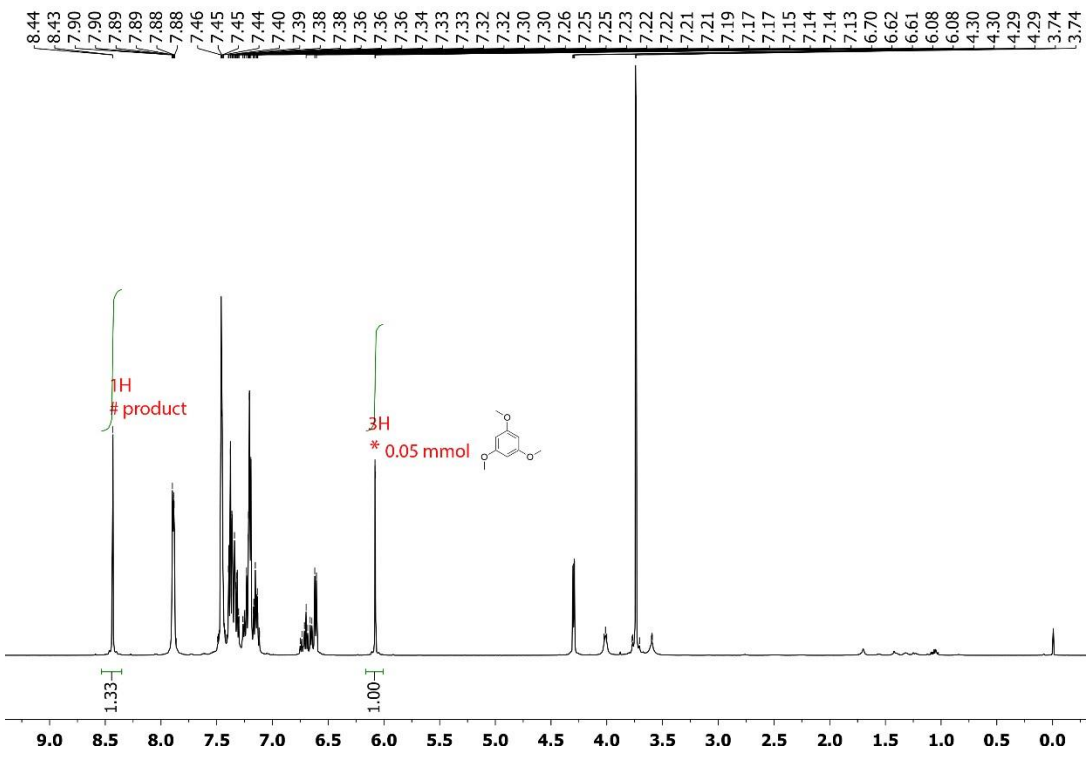


Figure 2.15 ^{1}H NMR (500 MHz, $CDCl_3$) of the reaction mixture of imine synthesis by V and KO^{t}Bu.

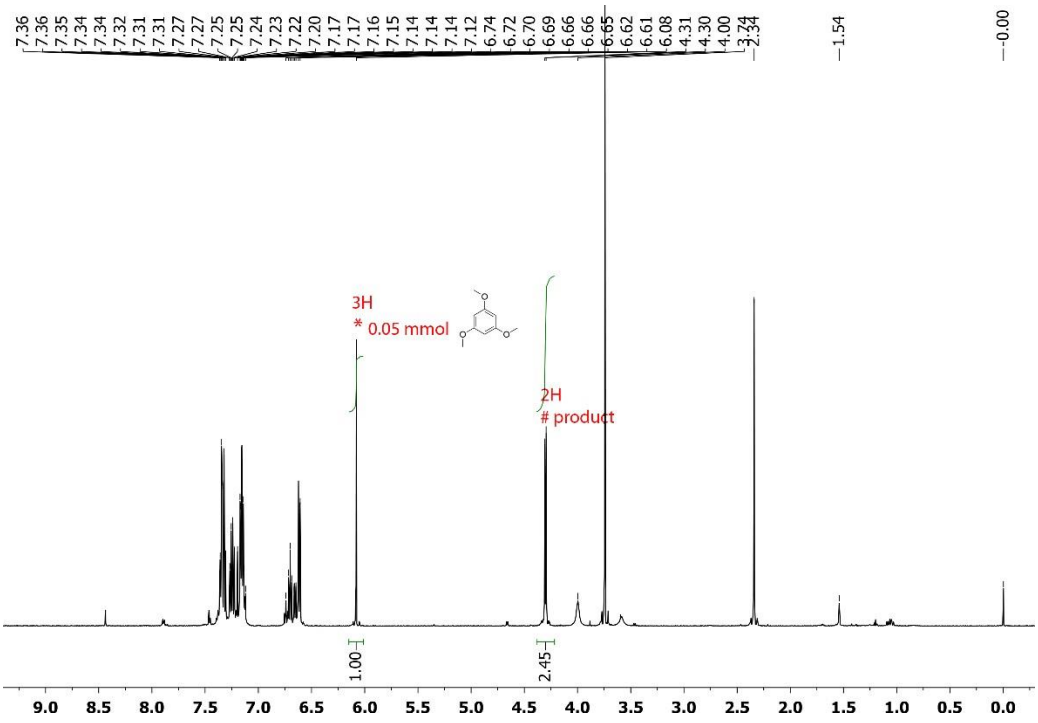


Figure 2.16 ^{1}H NMR (500 MHz, $CDCl_3$) of the reaction mixture of amine synthesis by VI and KO^{t}Bu.

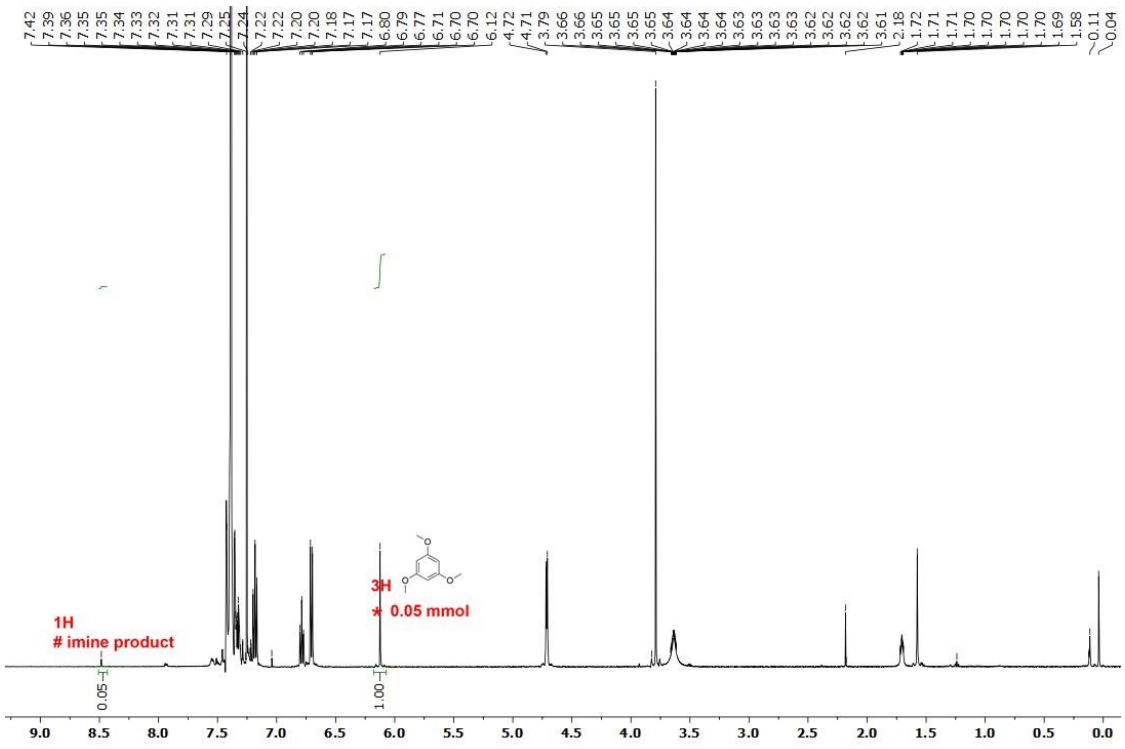


Figure 2.17 ^{1}H NMR (500 MHz, $CDCl_3$) of the reaction mixture of imine synthesis by VI and KO^{t}Bu.

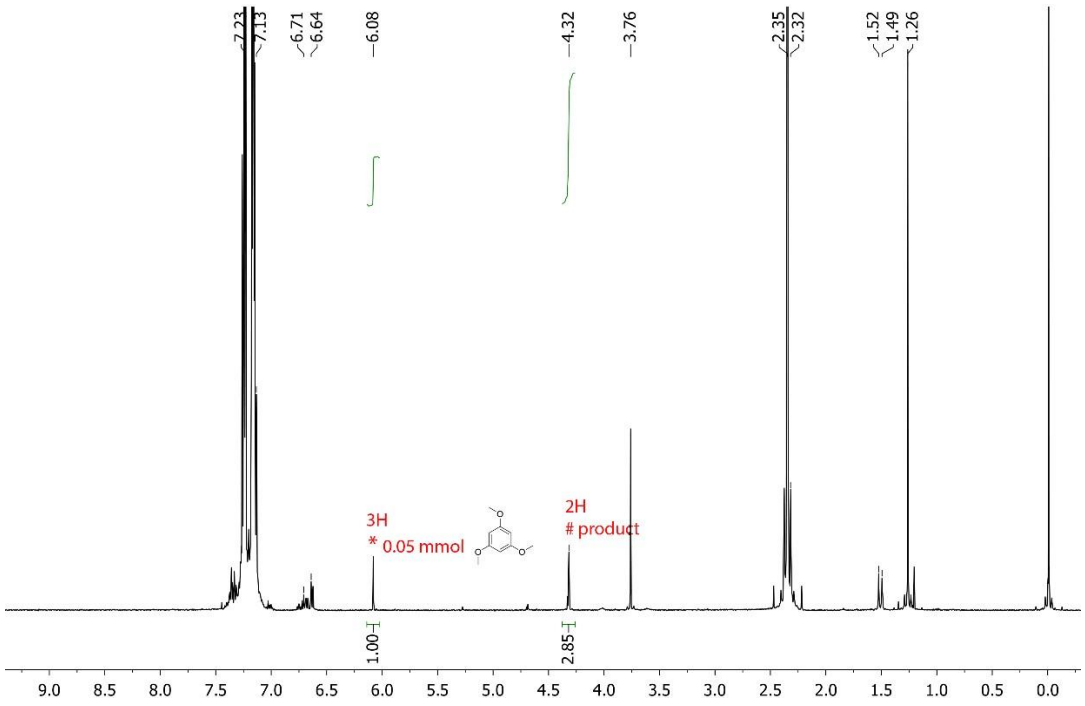


Figure 2.18 ^{1}H NMR (500 MHz, $CDCl_3$) of the reaction mixture of amine synthesis by VI and KO^{t}Bu.

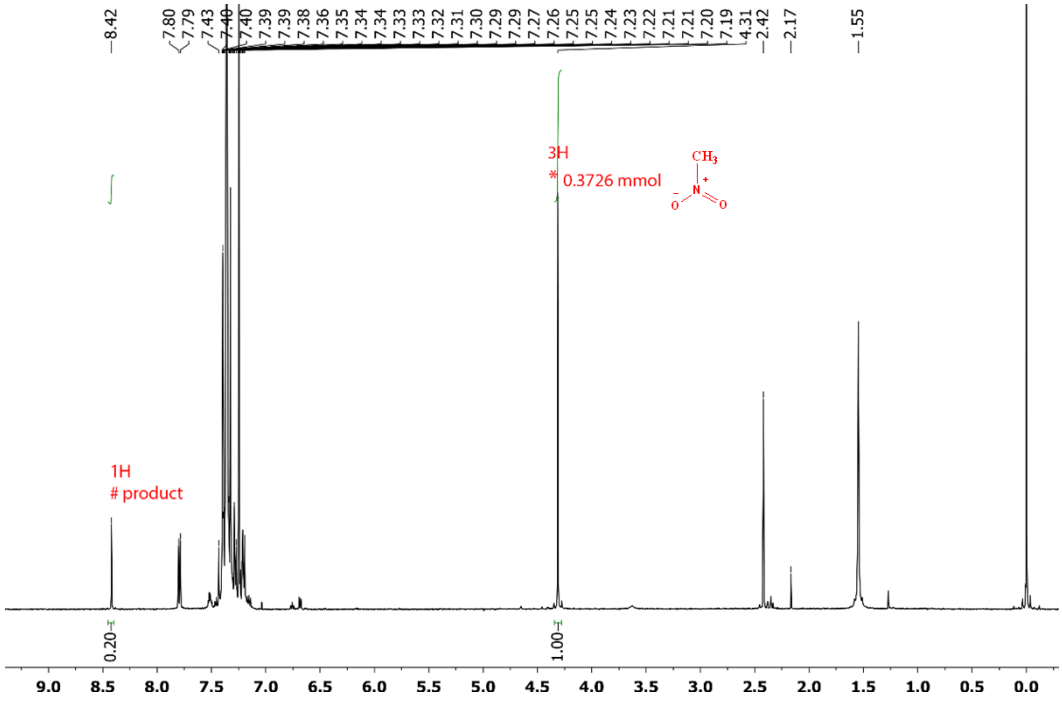


Figure 2.19 ^{1}H NMR (500 MHz, $CDCl_3$) of the reaction mixture of 3b.

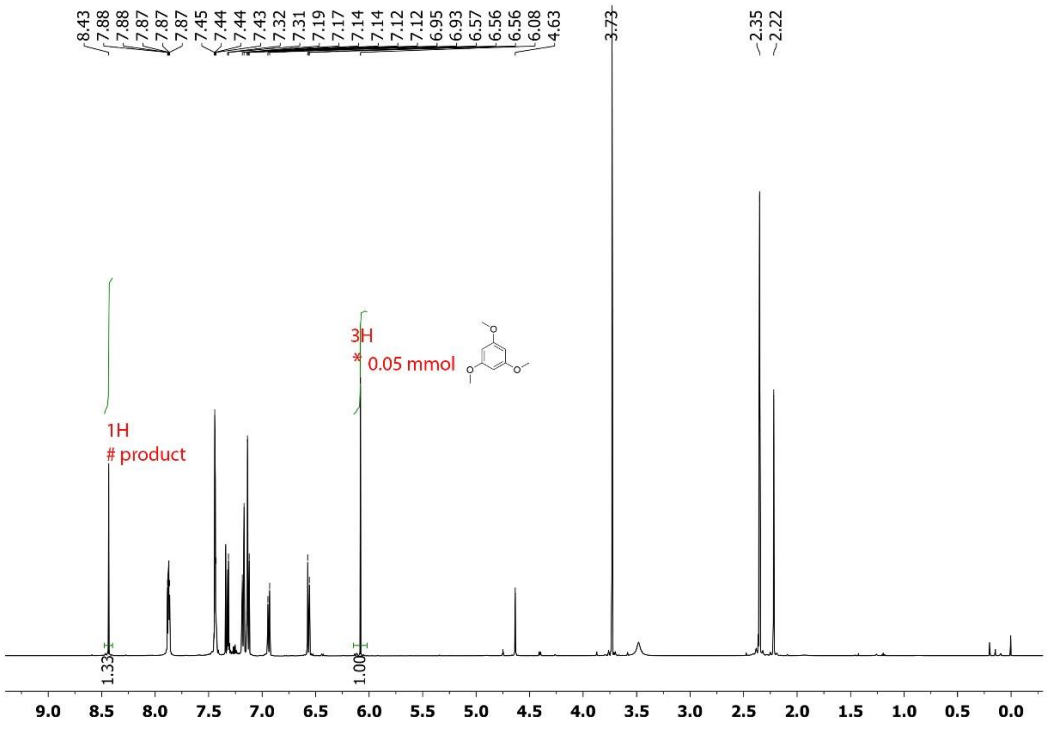


Figure 2.20. ^{1}H NMR (500 MHz, $CDCl_3$) of the reaction mixture of 3c.

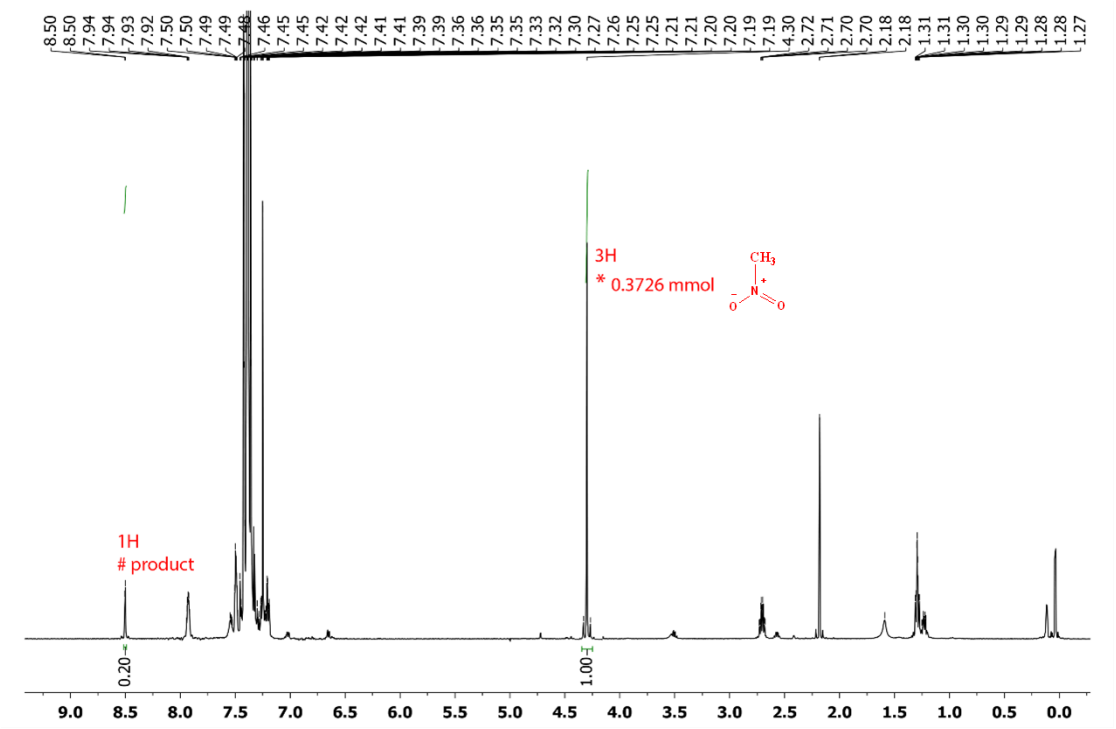


Figure 2.21 ^{1}H NMR (500 MHz, $CDCl_3$) of the reaction mixture of 3d.

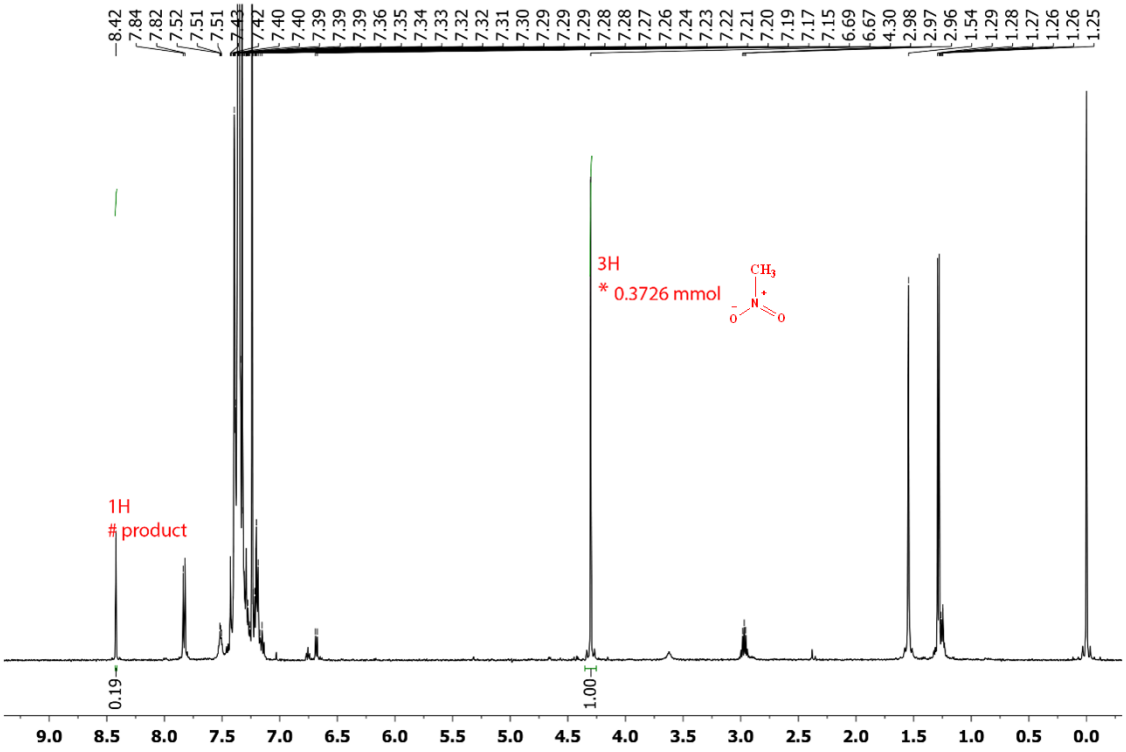


Figure 2.22 ^{1}H NMR (500 MHz, $CDCl_3$) of the reaction mixture of 3e.

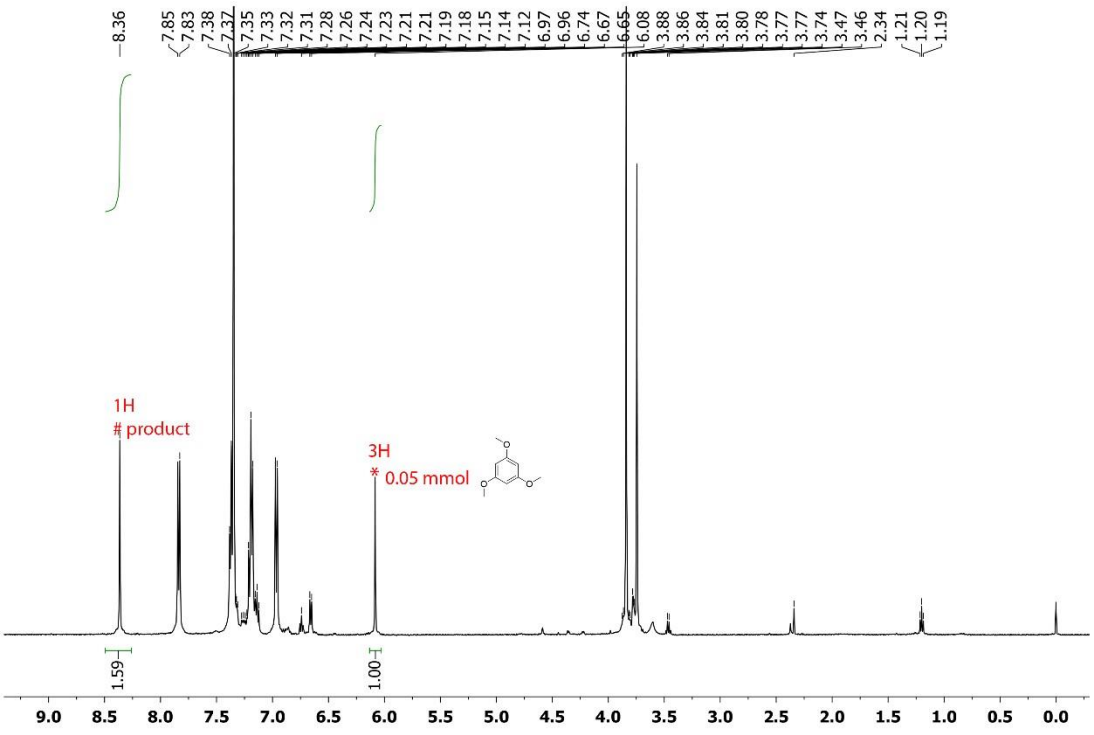


Figure 2.23 ^{1}H NMR (500 MHz, $CDCl_3$) of the reaction mixture of 3f.

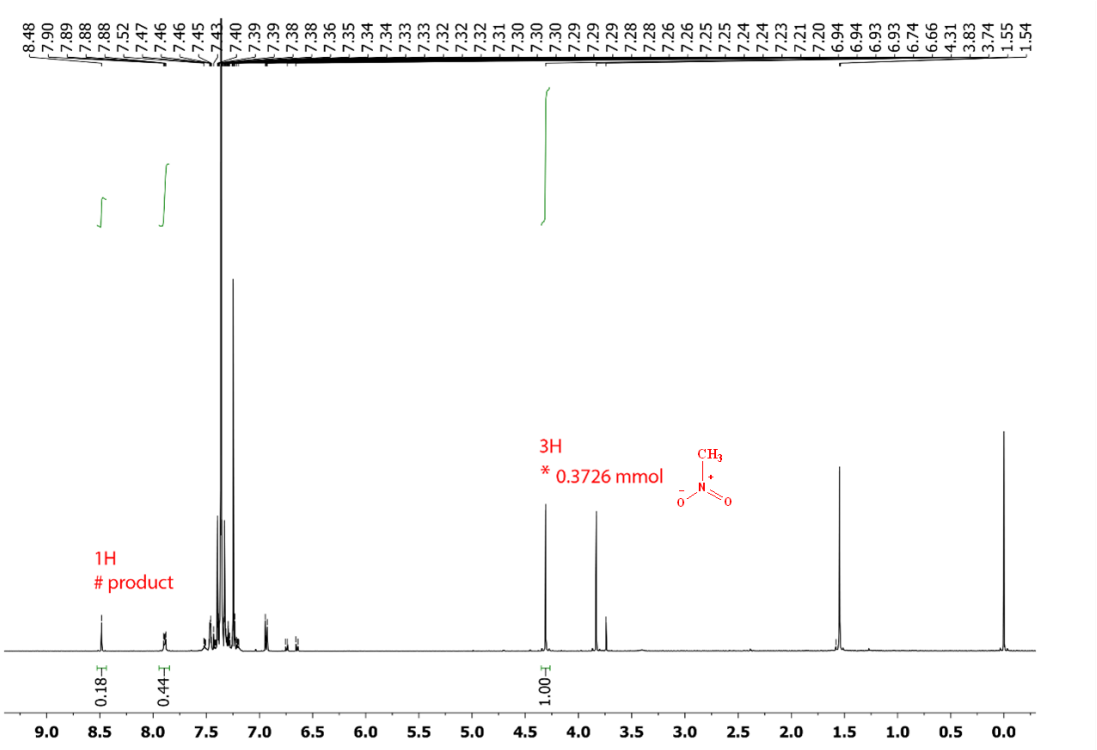


Figure 2.24 ^{1}H NMR (500 MHz, $CDCl_3$) of the reaction mixture of 3g.

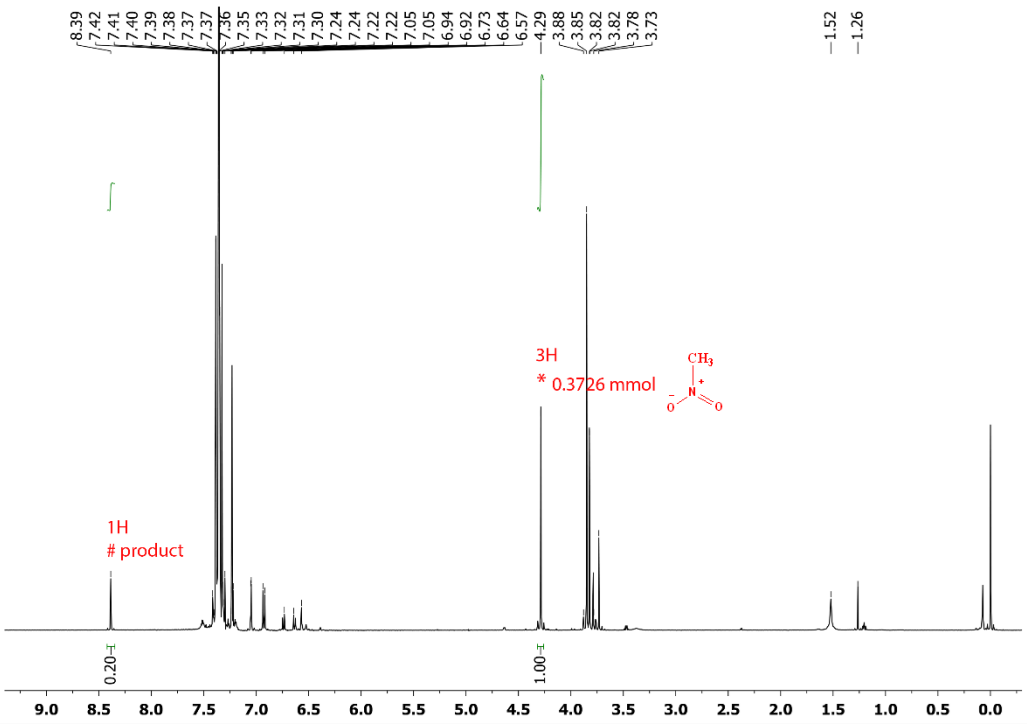


Figure 2.25 ^{1}H NMR (500 MHz, $CDCl_3$) of the reaction mixture of 3h.

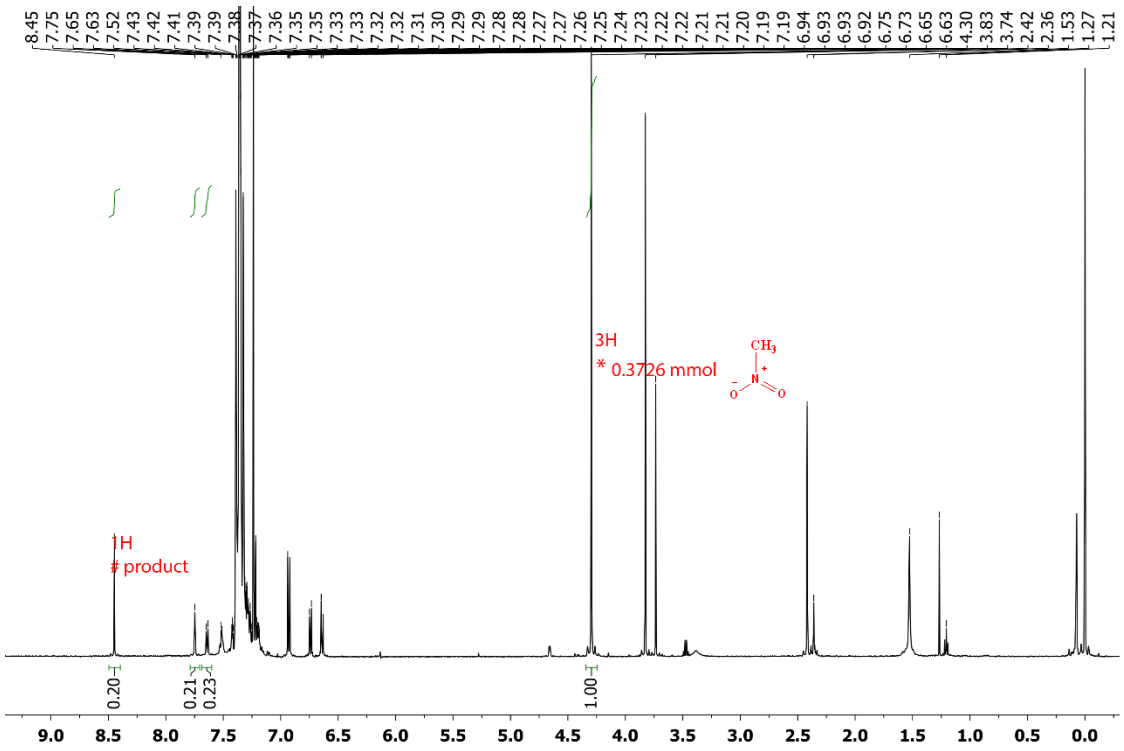


Figure 2.26. ^{1}H NMR (500 MHz, $CDCl_3$) of the reaction mixture of 3i.

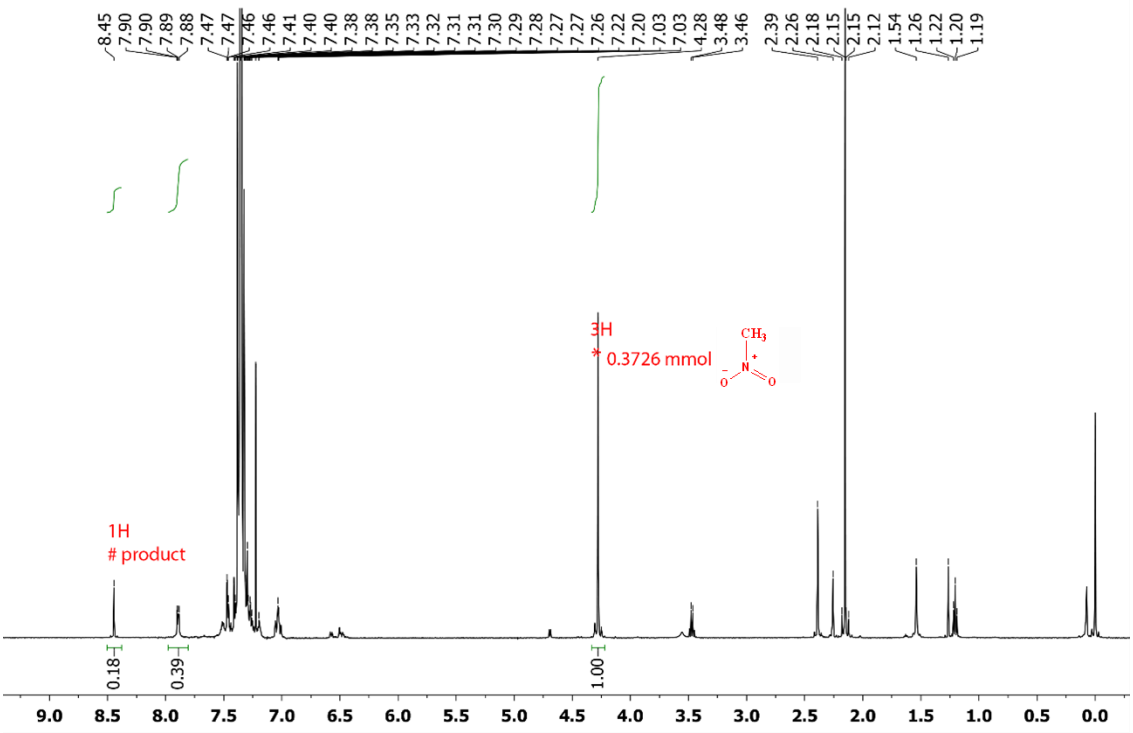


Figure 2.27 ^{1}H NMR (500 MHz, $CDCl_3$) of the reaction mixture of 3j.

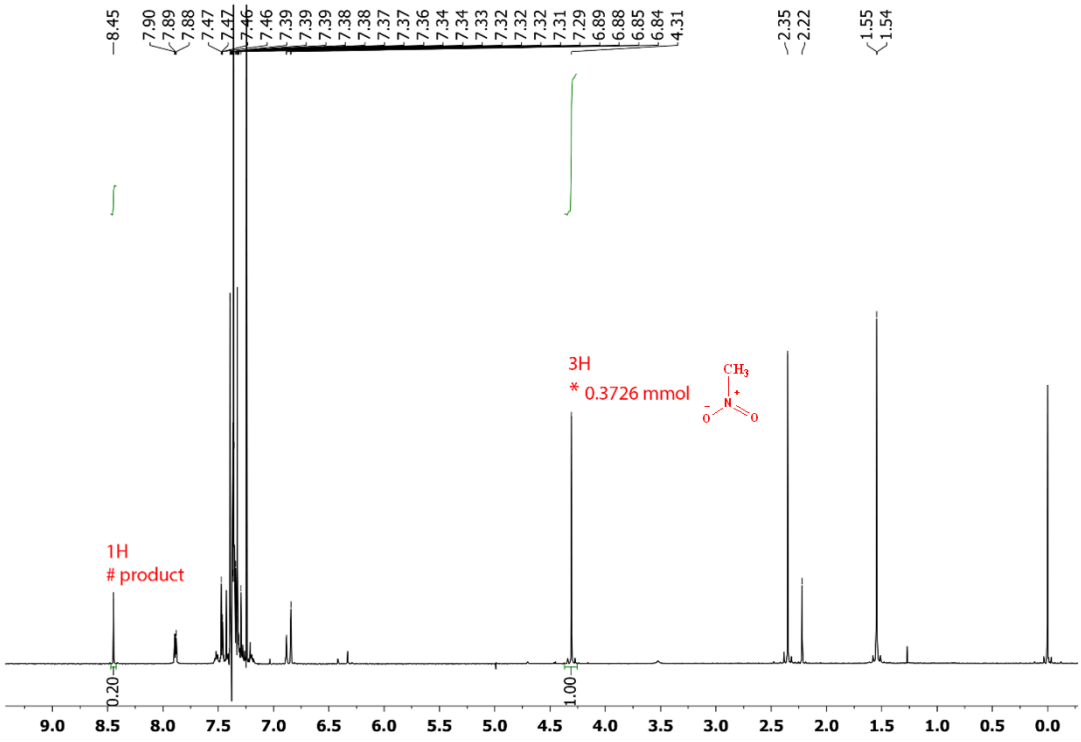


Figure 2.28 ^{1}H NMR (500 MHz, $CDCl_3$) of the reaction mixture of 3k.

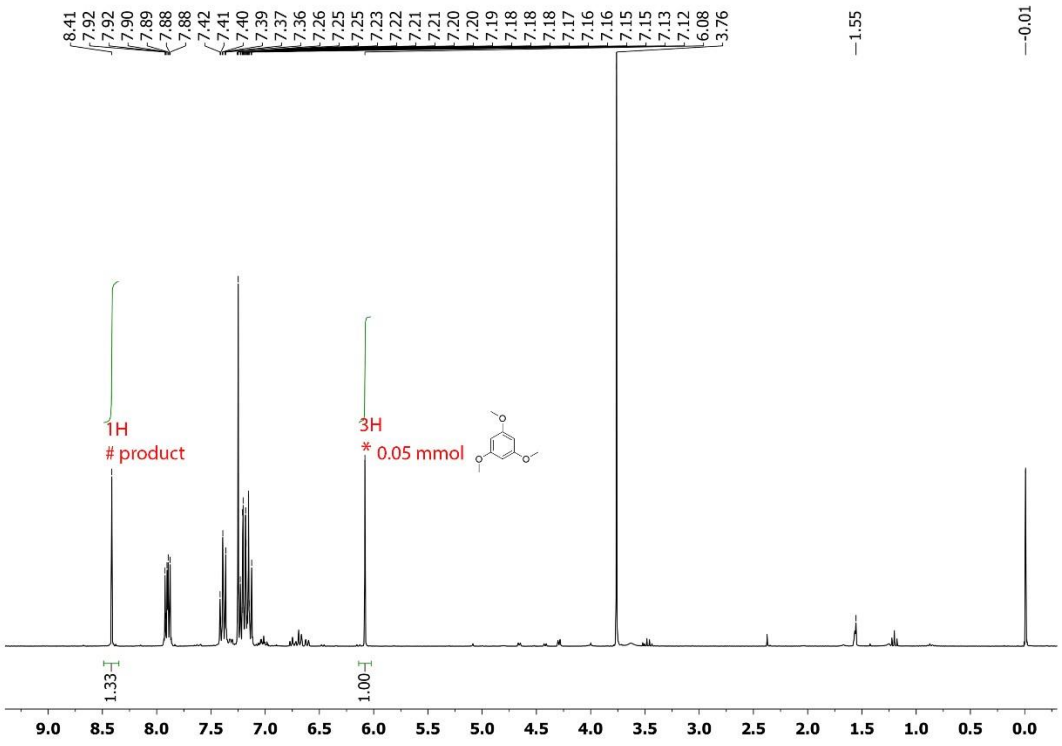


Figure 2.29 ^{1}H NMR (500 MHz, $CDCl_3$) of the reaction mixture of 3l.

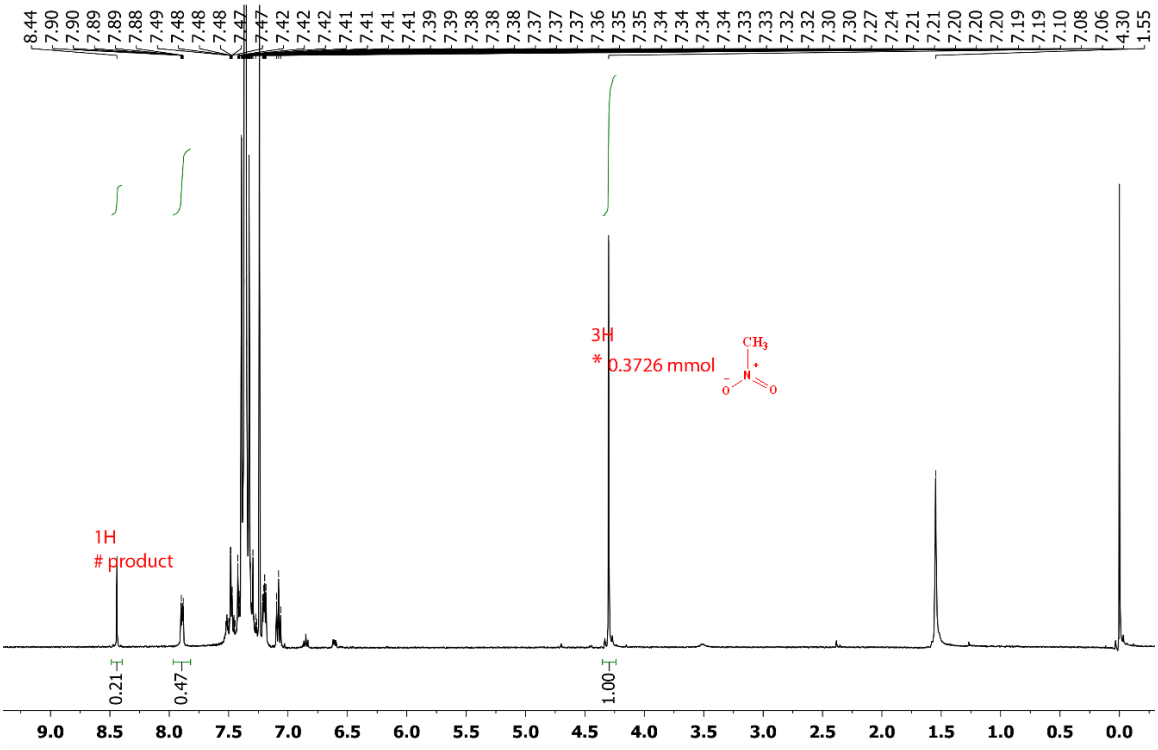


Figure 2.30. ^{1}H NMR (500 MHz, $CDCl_3$) of the reaction mixture of 3m.

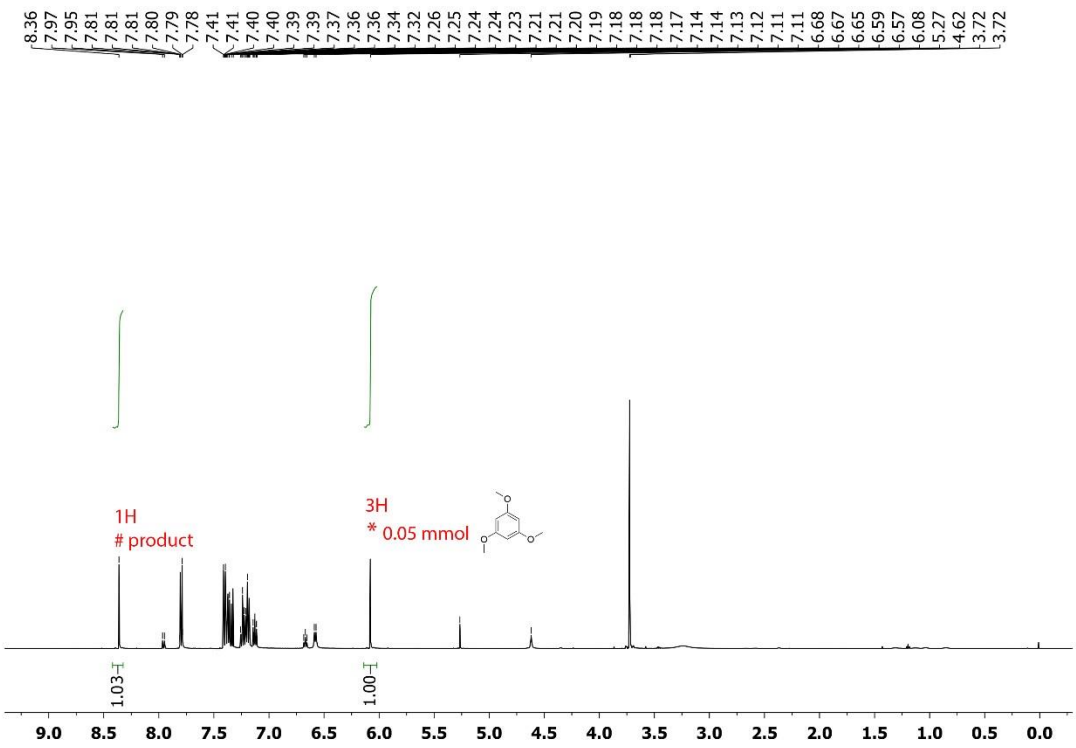


Figure 2.31 ^{1}H NMR (500 MHz, $CDCl_3$) of the reaction mixture of 3n**.**

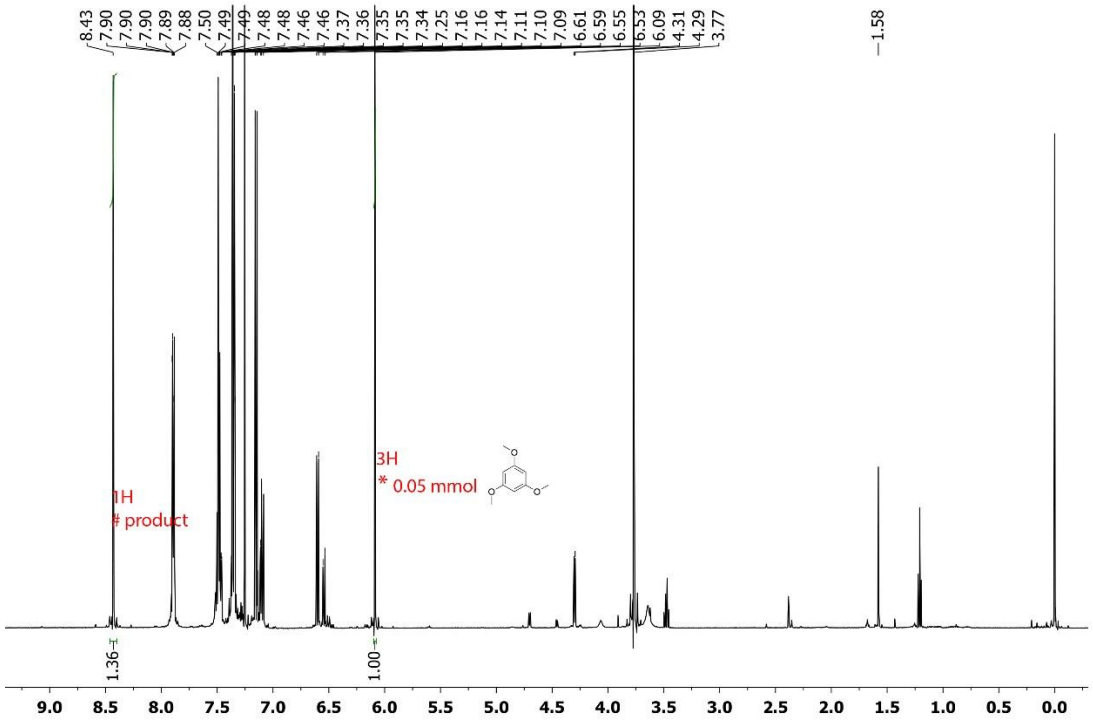


Figure 2.32 ^{1}H NMR (500 MHz, $CDCl_3$) of the reaction mixture of 3o.

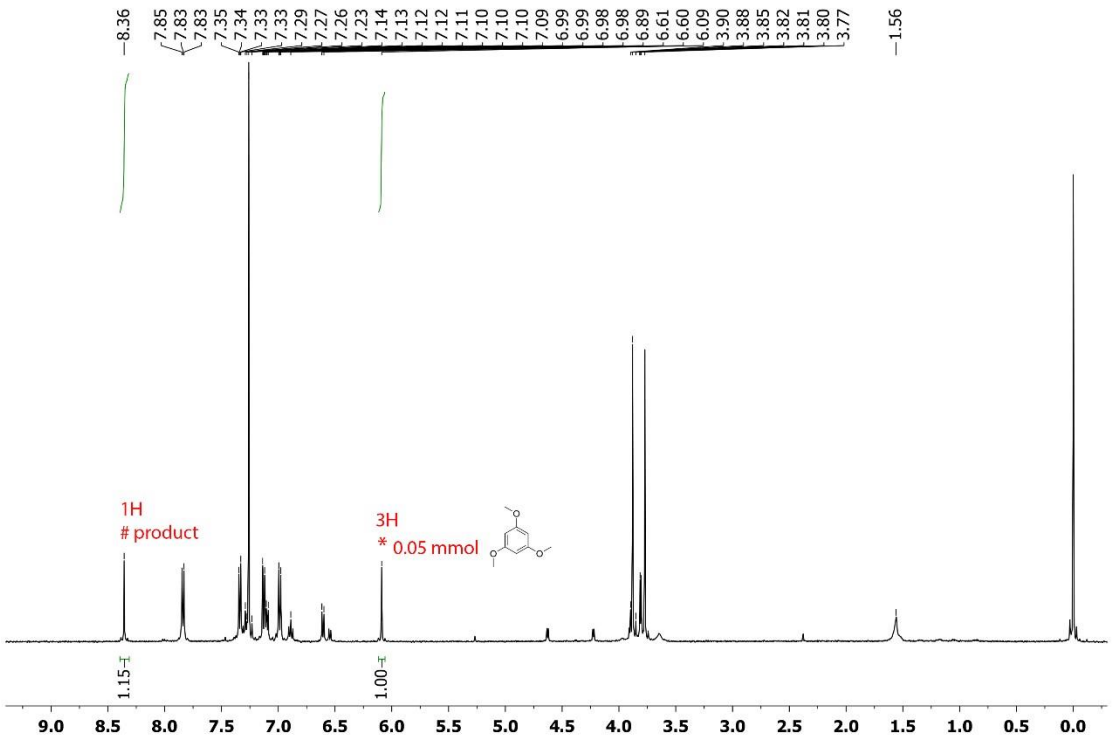


Figure 2.33 ^{1}H NMR (500 MHz, $CDCl_3$) of the reaction mixture of 3p.

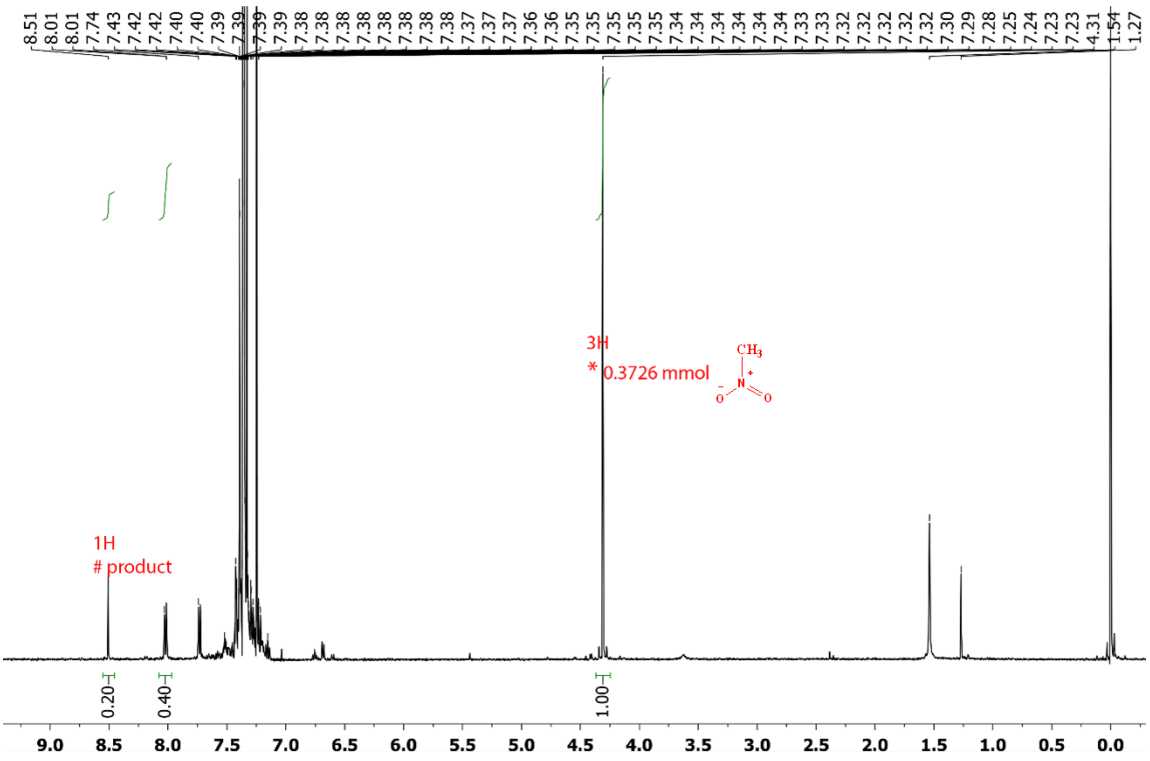


Figure 2.34 ^{1}H NMR (500 MHz, $CDCl_3$) of the reaction mixture of 3q.

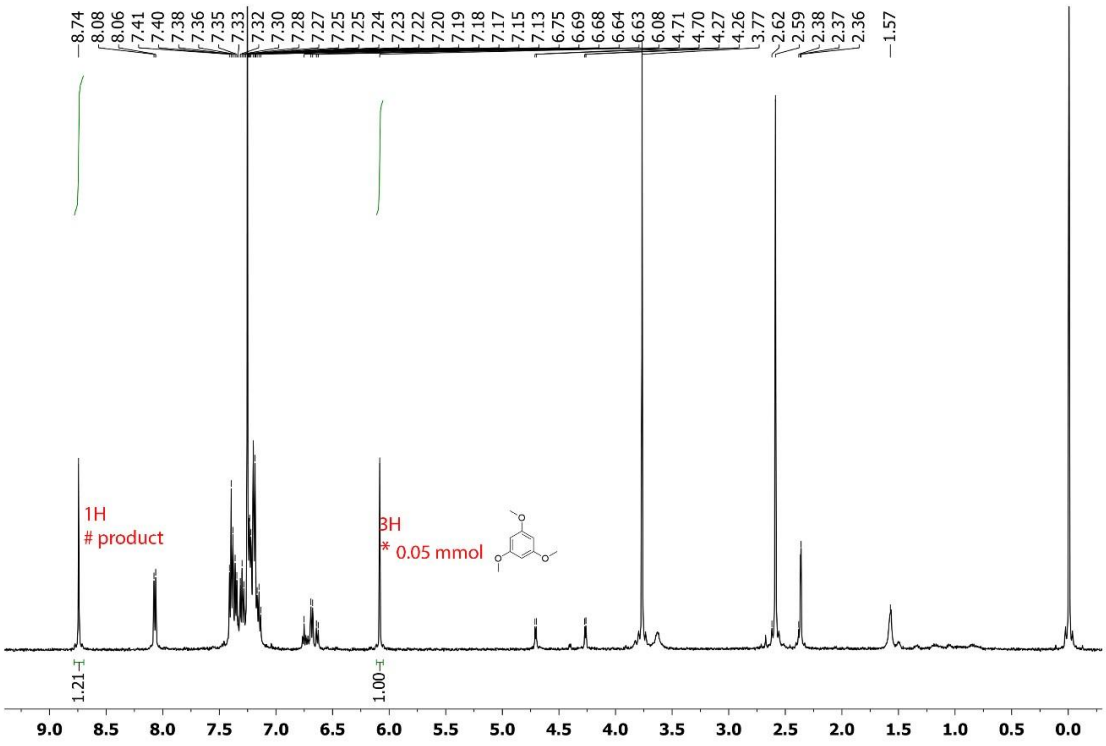


Figure 2.35 ^{1}H NMR (500 MHz, $CDCl_3$) of the reaction mixture of 3r.

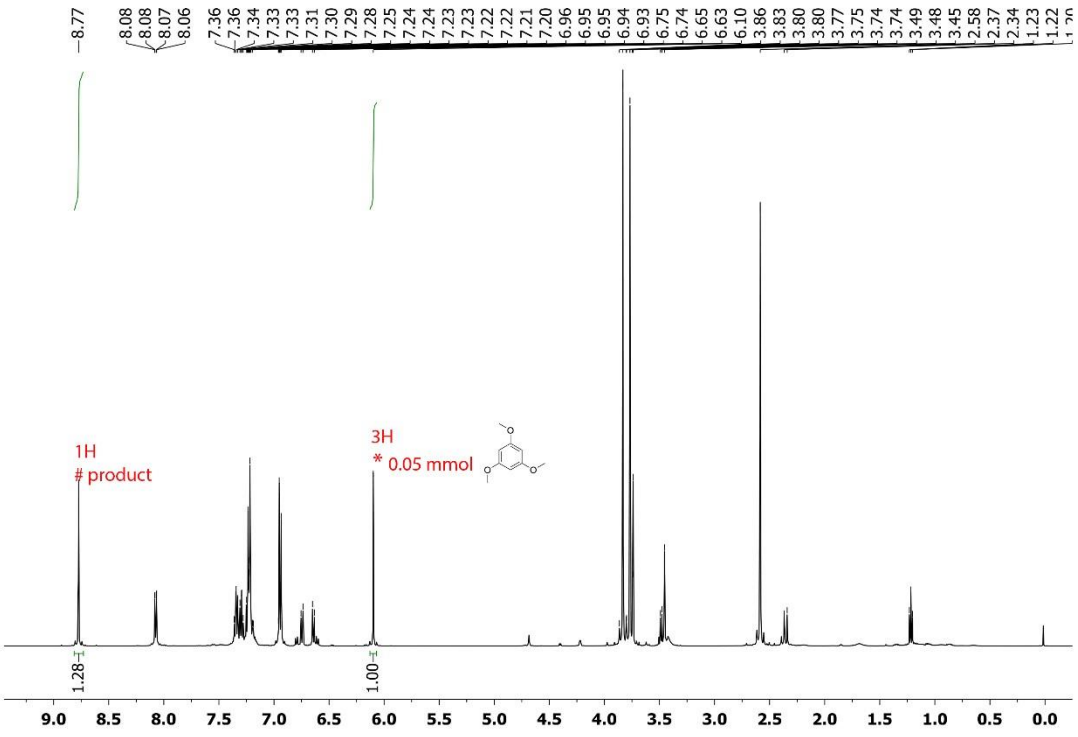


Figure 2.36 ^{1}H NMR (500 MHz, $CDCl_3$) of the reaction mixture of 3s

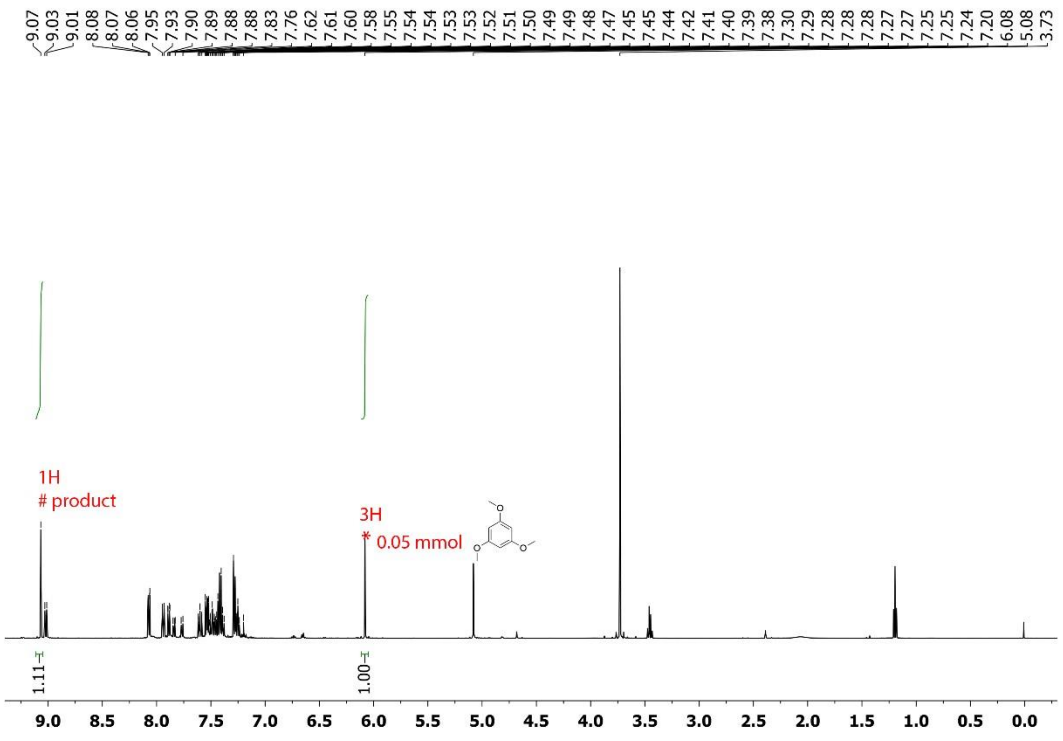


Figure 2.37 ^{1}H NMR (500 MHz, $CDCl_3$) of the reaction mixture of 3t.

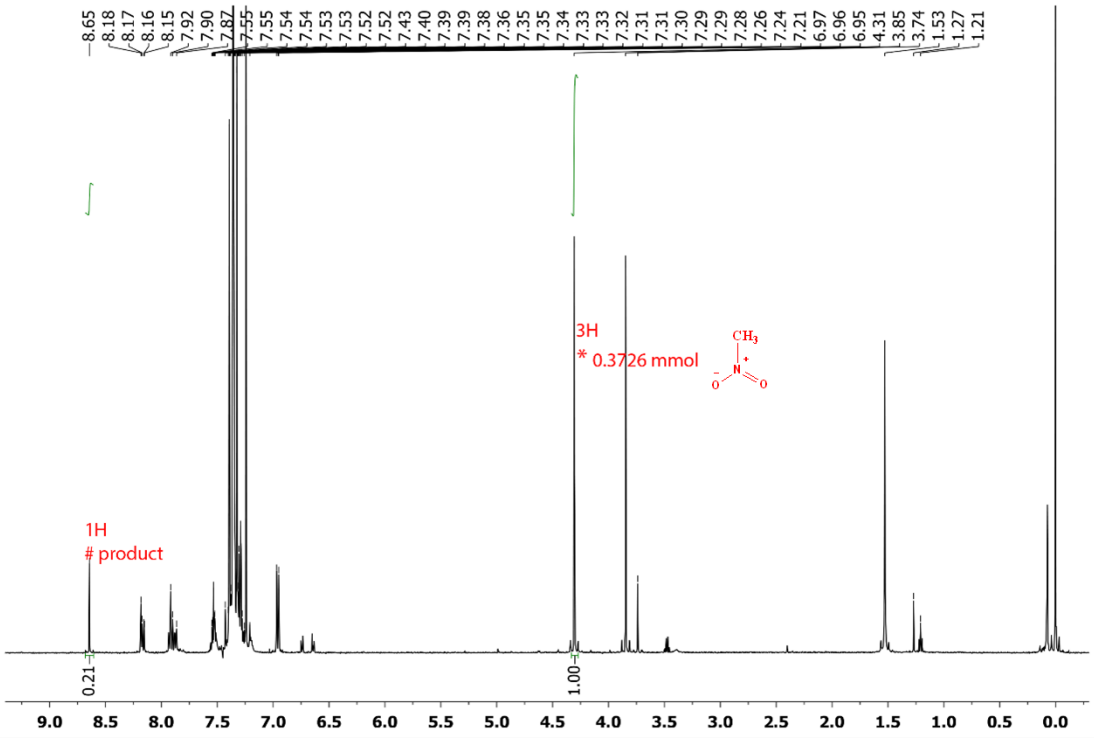


Figure 2.38 ^{1}H NMR (500 MHz, $CDCl_3$) of the reaction mixture of 3u.

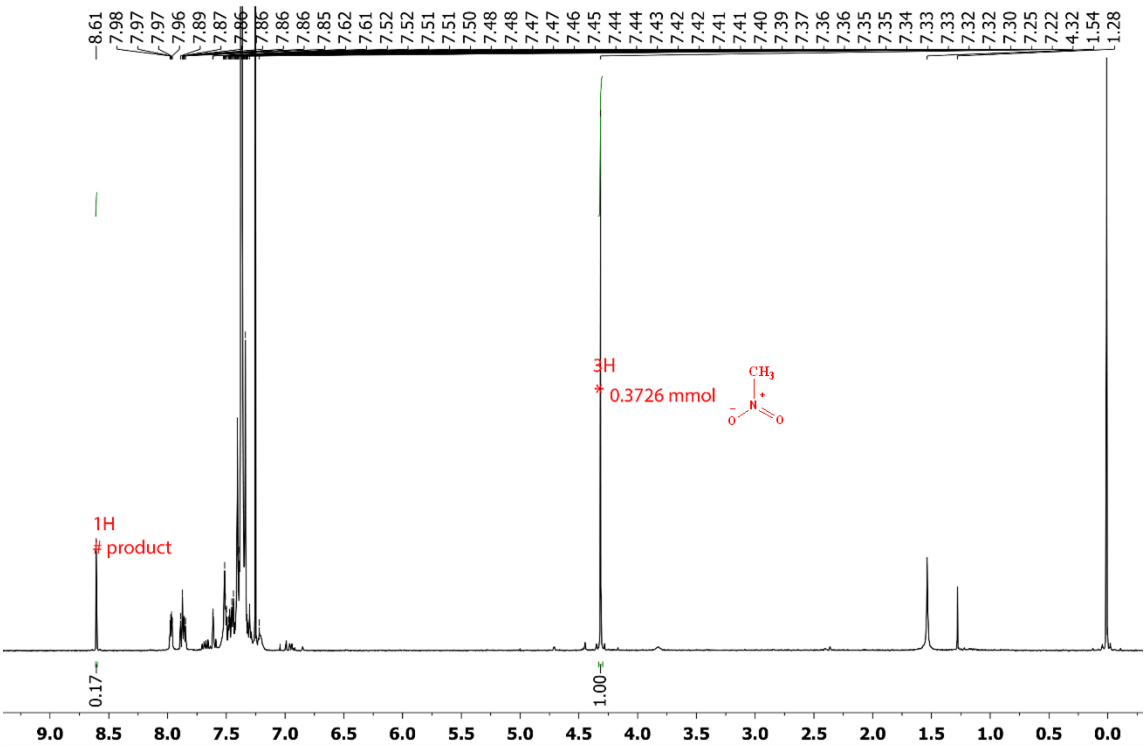


Figure 2.39 ^{1}H NMR (500 MHz, $CDCl_3$) of the reaction mixture of 3v.

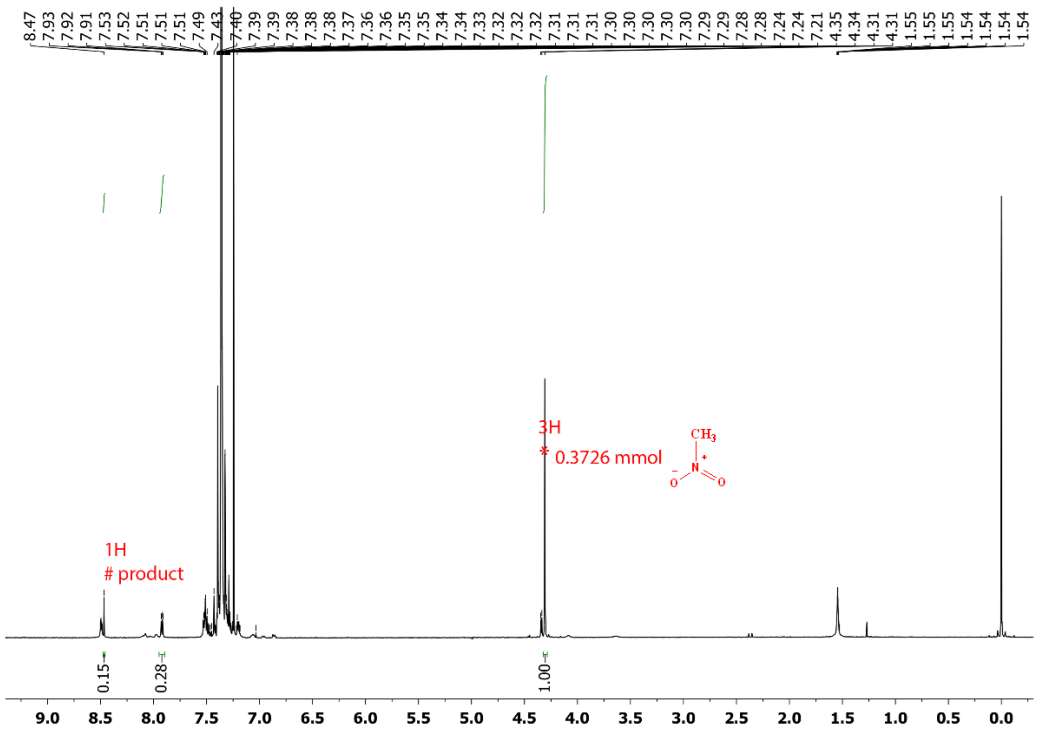


Figure 2.40 ^{1}H NMR (500 MHz, $CDCl_3$) of the reaction mixture of 3w.

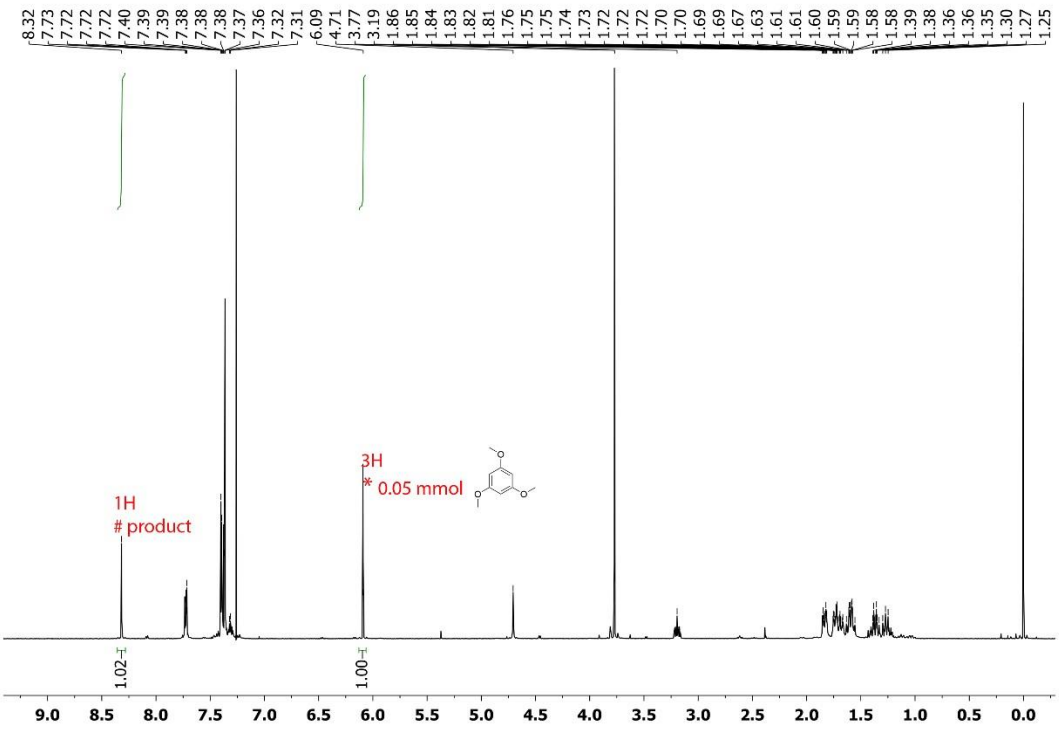


Figure 2.41 ^{1}H NMR (500 MHz, $CDCl_3$) of the reaction mixture of 3x.

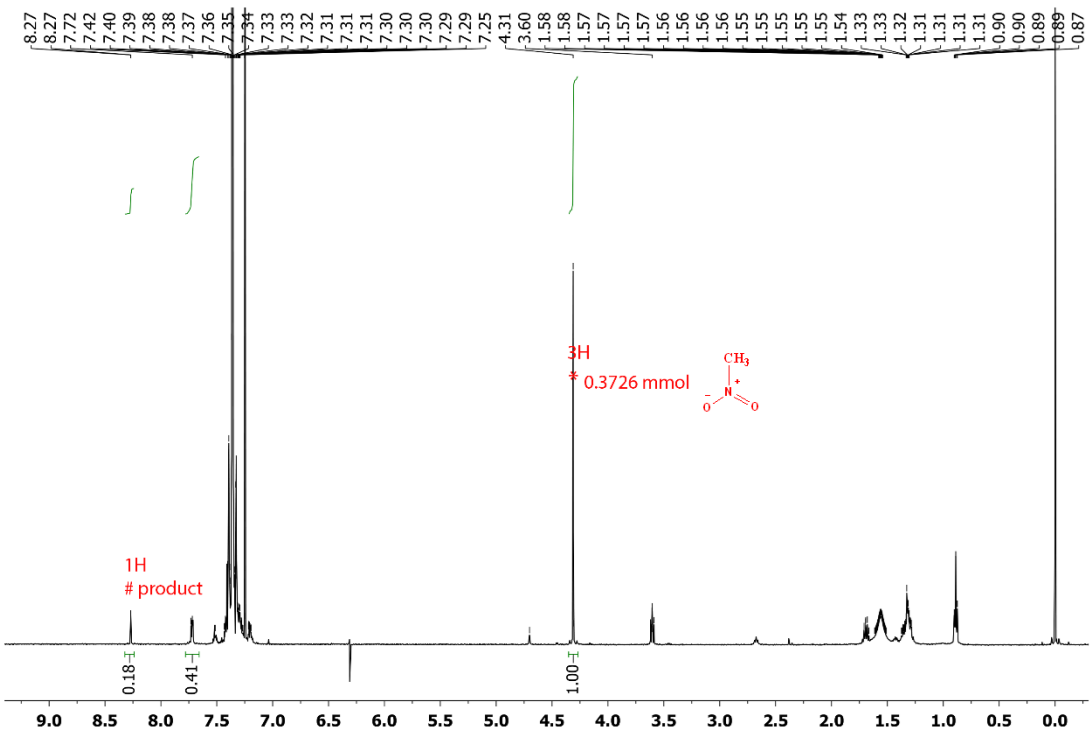


Figure 2.42 ^{1}H NMR (500 MHz, $CDCl_3$) of the reaction mixture of 3y.

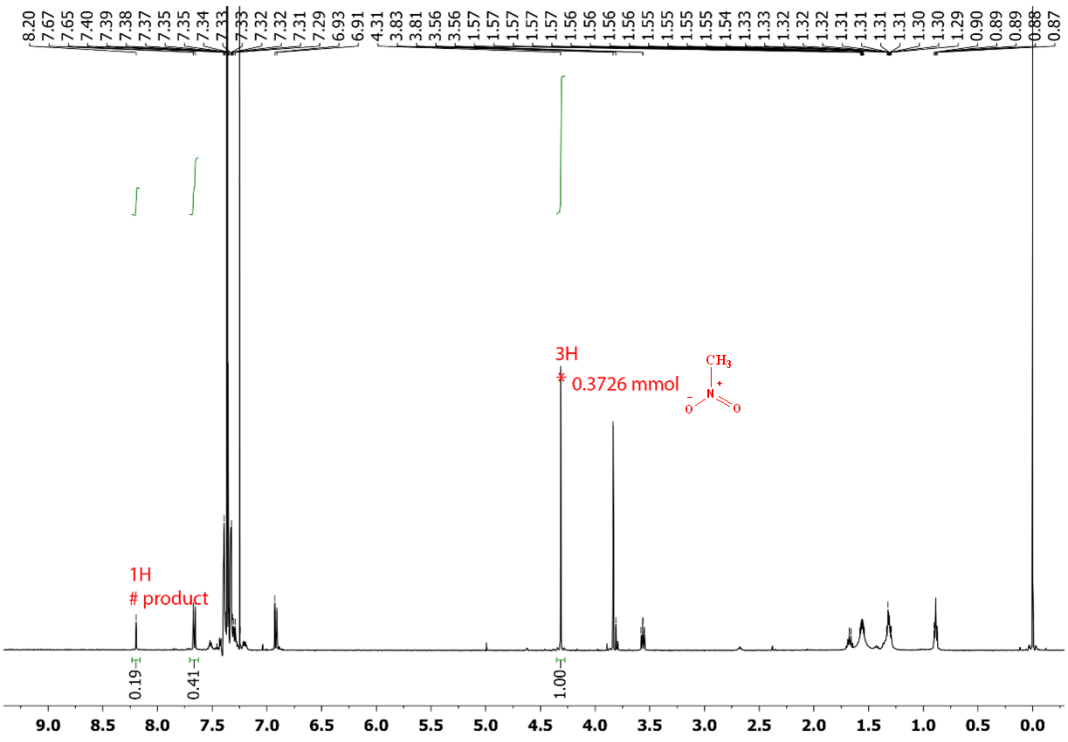


Figure 2.43 ^{1}H NMR (500 MHz, $CDCl_3$) of the reaction mixture of 3z.

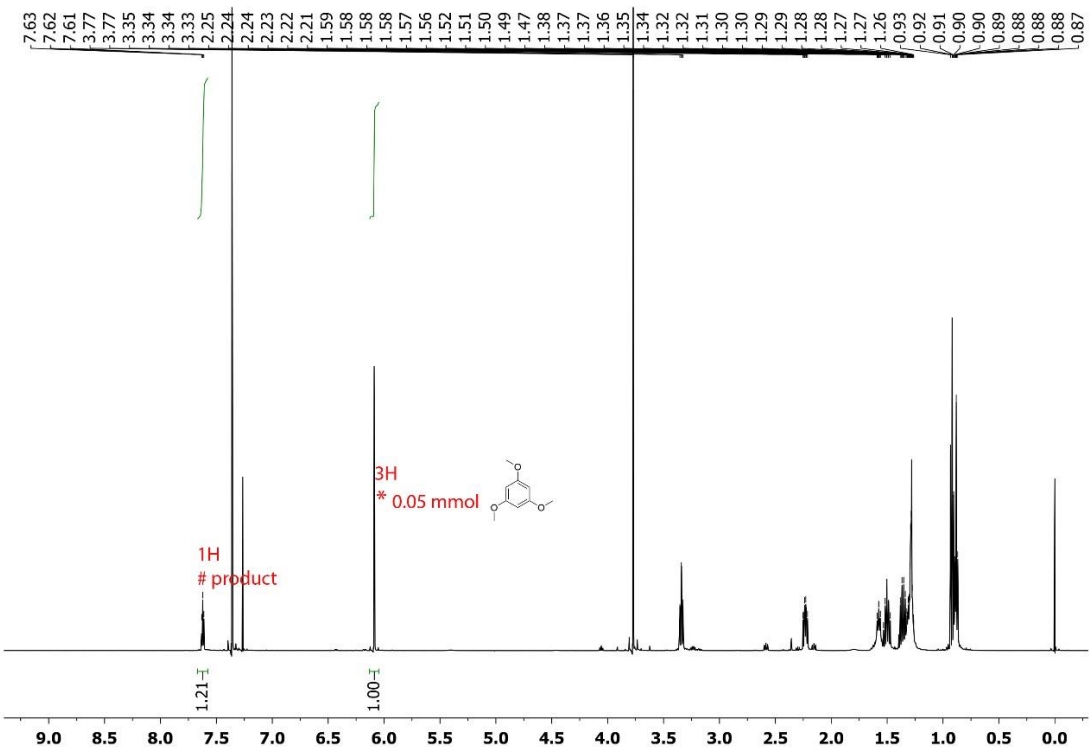


Figure 2.44 ^{1}H NMR (500 MHz, $CDCl_3$) of the reaction mixture of 3aa.

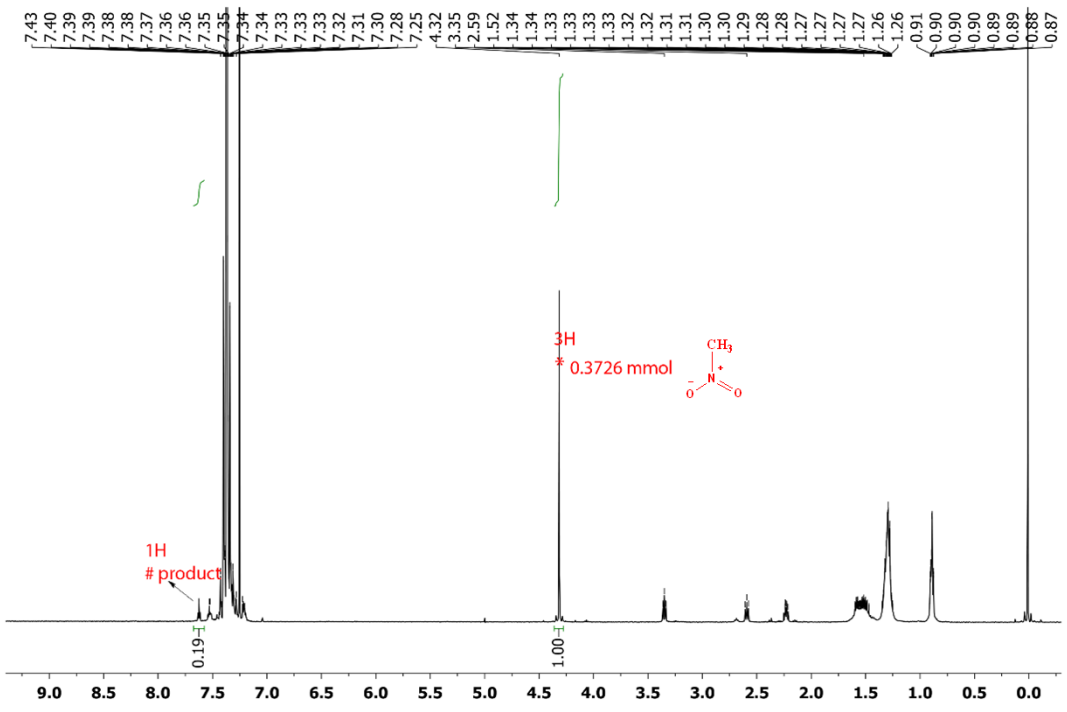


Figure 2.45 ^{1}H NMR (500 MHz, $CDCl_3$) of the reaction mixture of 3ab.

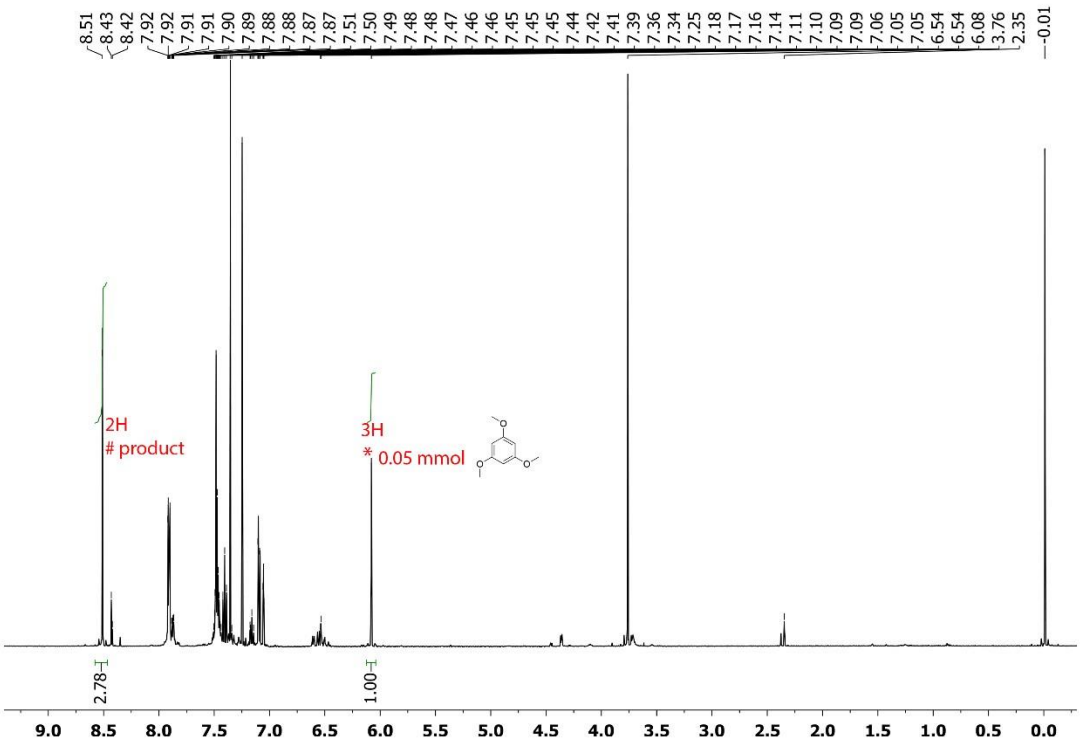


Figure 2.46 ^{1}H NMR (500 MHz, $CDCl_3$) of the reaction mixture of 3aj**.**

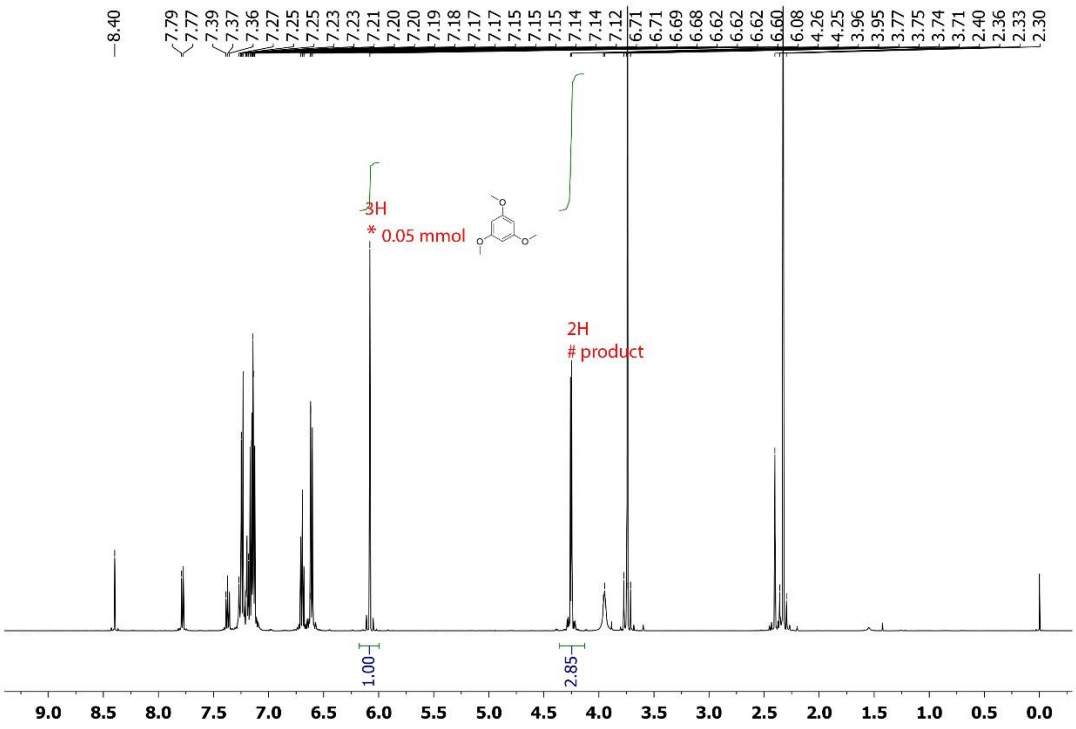


Figure 2.47 ^{1}H NMR (500 MHz, $CDCl_3$) of the reaction mixture of 4b.

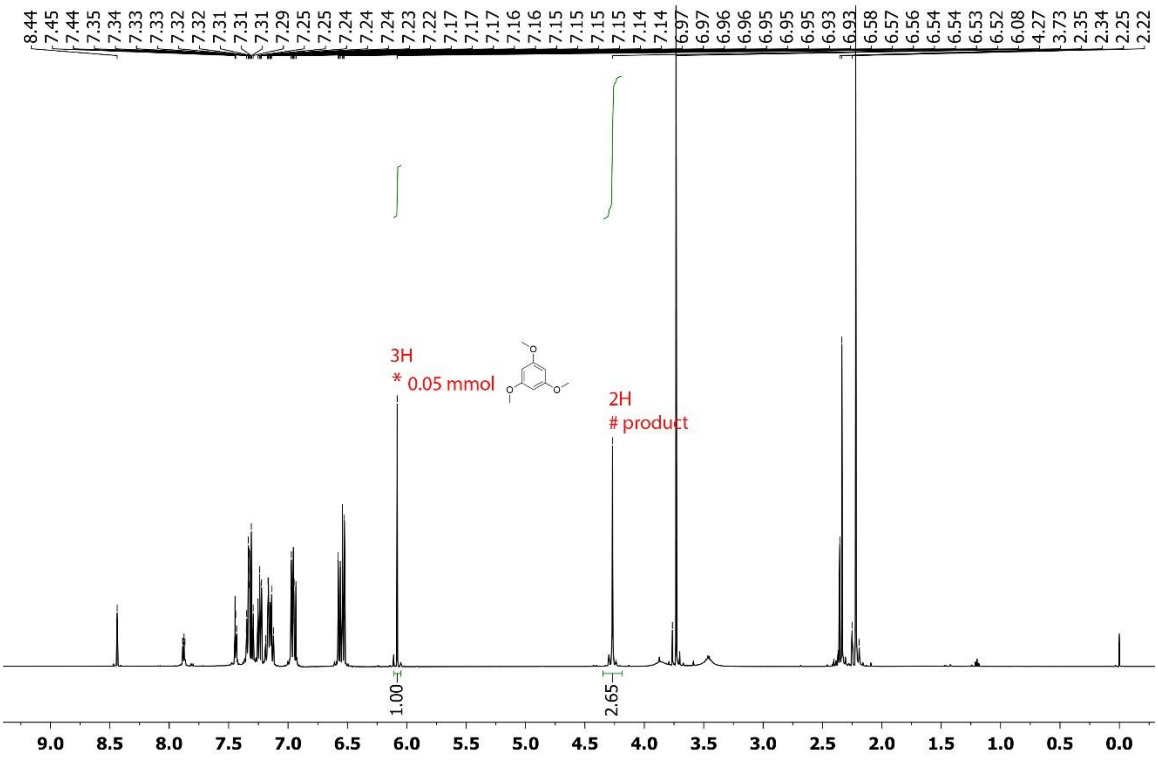


Figure 2.48 ^{1}H NMR (500 MHz, $CDCl_3$) of the reaction mixture of 4c

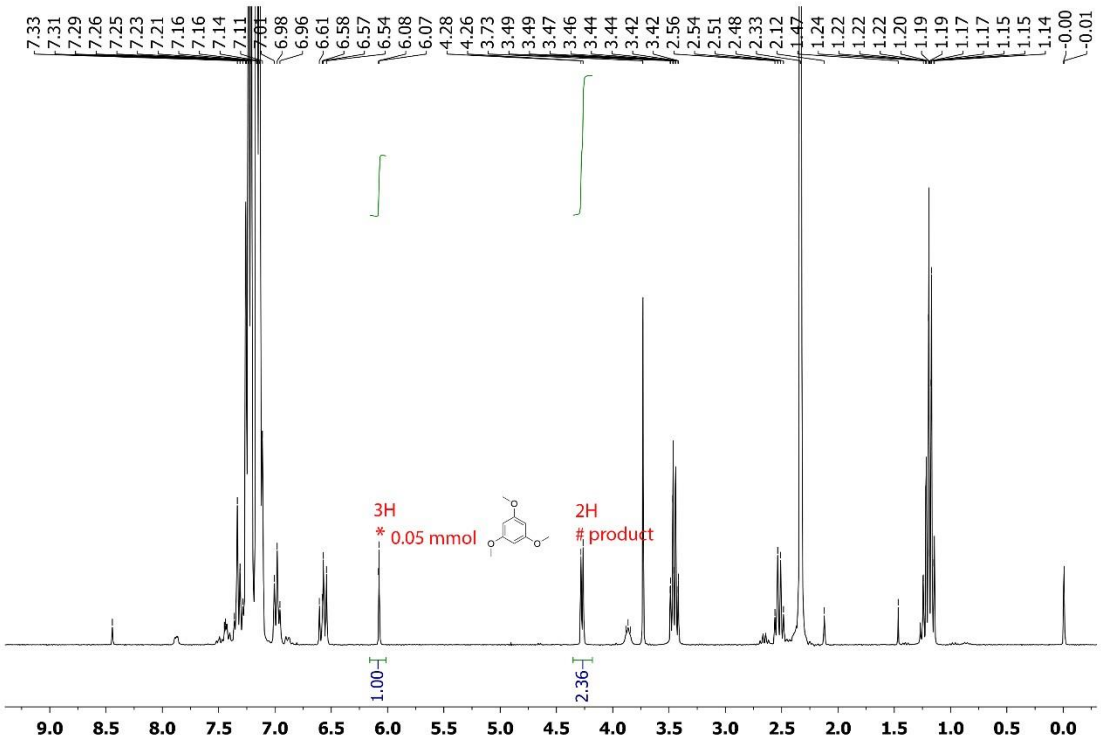


Figure 2.49. ^{1}H NMR (500 MHz, $CDCl_3$) of the reaction mixture of 4d.

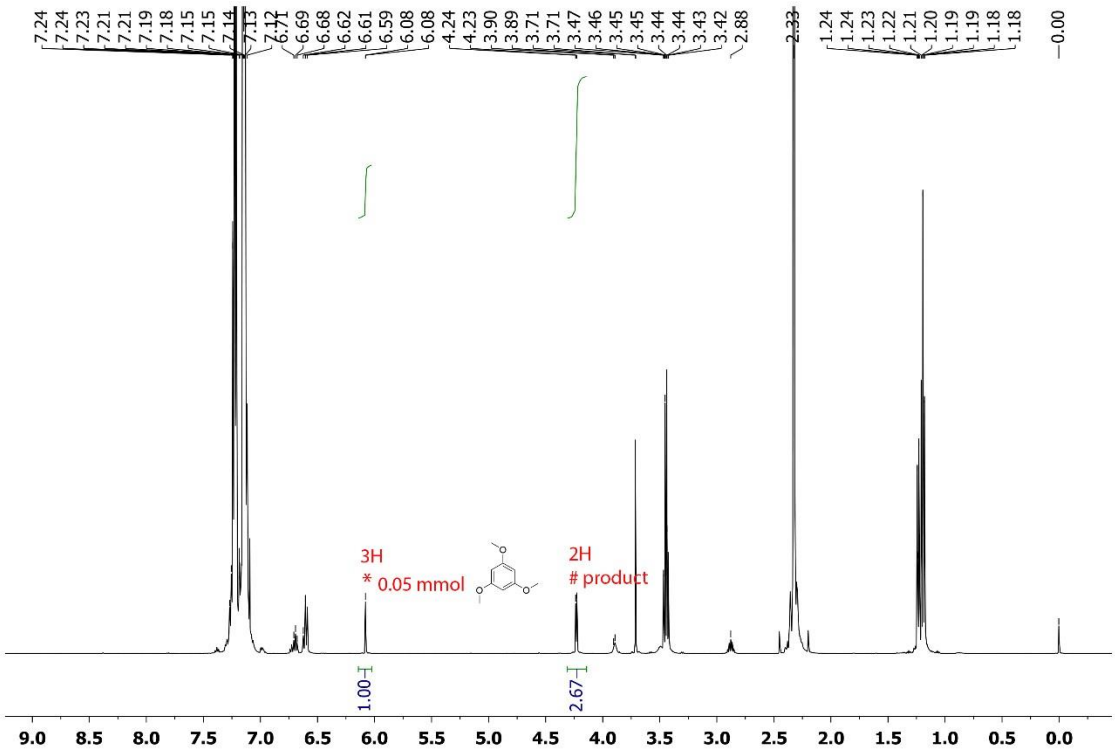


Figure 2.50 ^{1}H NMR (500 MHz, $CDCl_3$) of the reaction mixture of 4e.

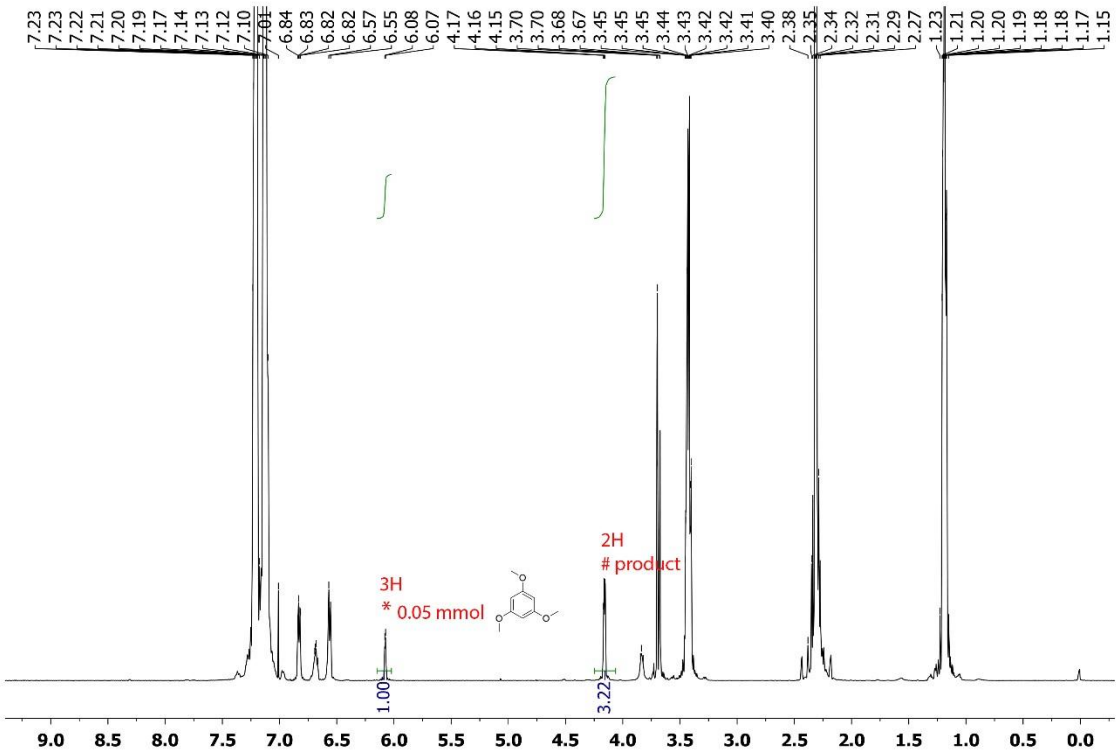


Figure 2.51 ^{1}H NMR (500 MHz, $CDCl_3$) of the reaction mixture of 4f.

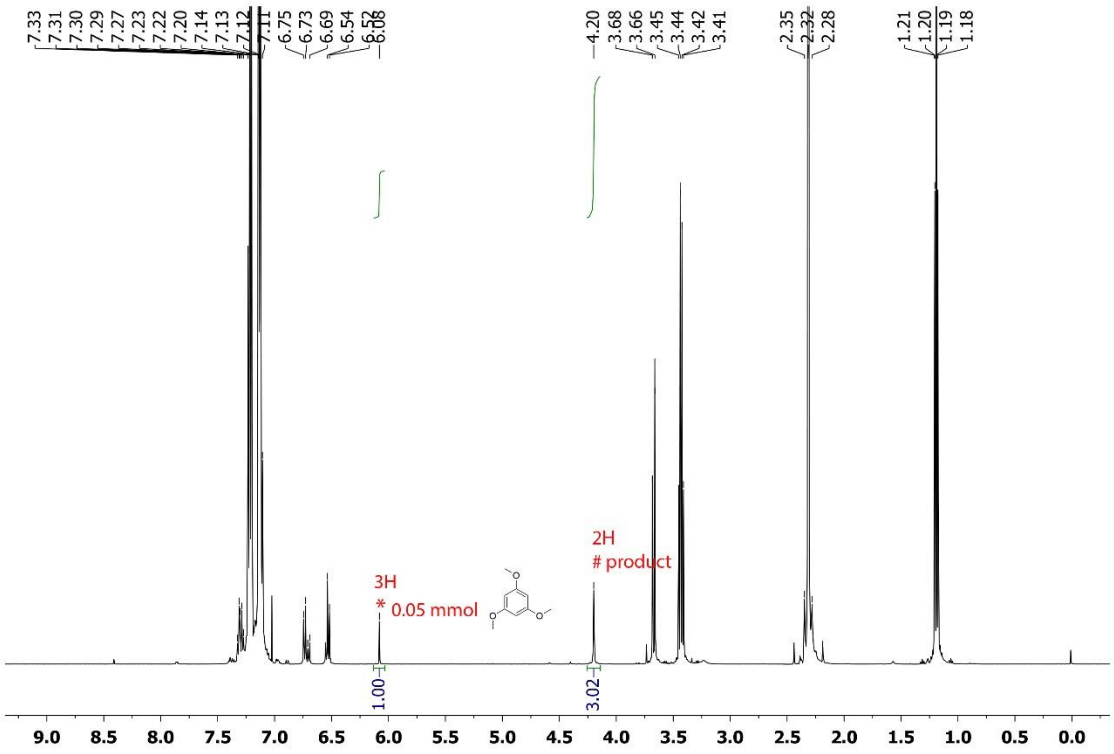


Figure 2.52 ^{1}H NMR (500 MHz, $CDCl_3$) of the reaction mixture of 4g.

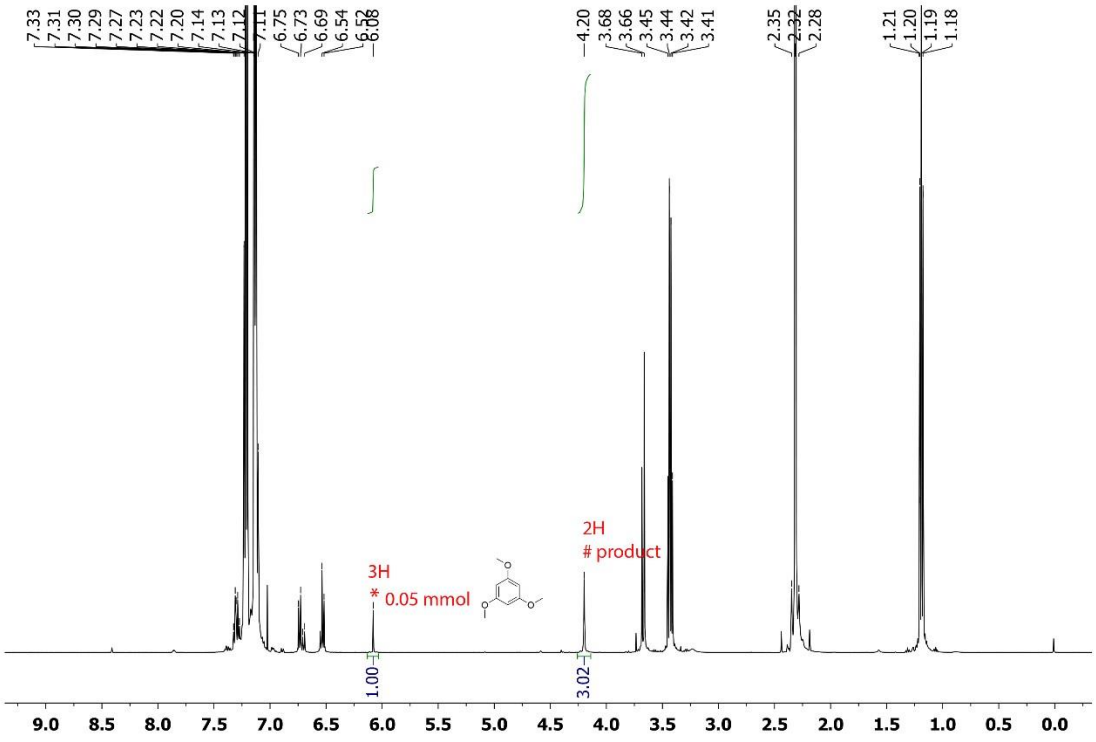


Figure 2.53 ^{1}H NMR (500 MHz, $CDCl_3$) of the reaction mixture of 4h.

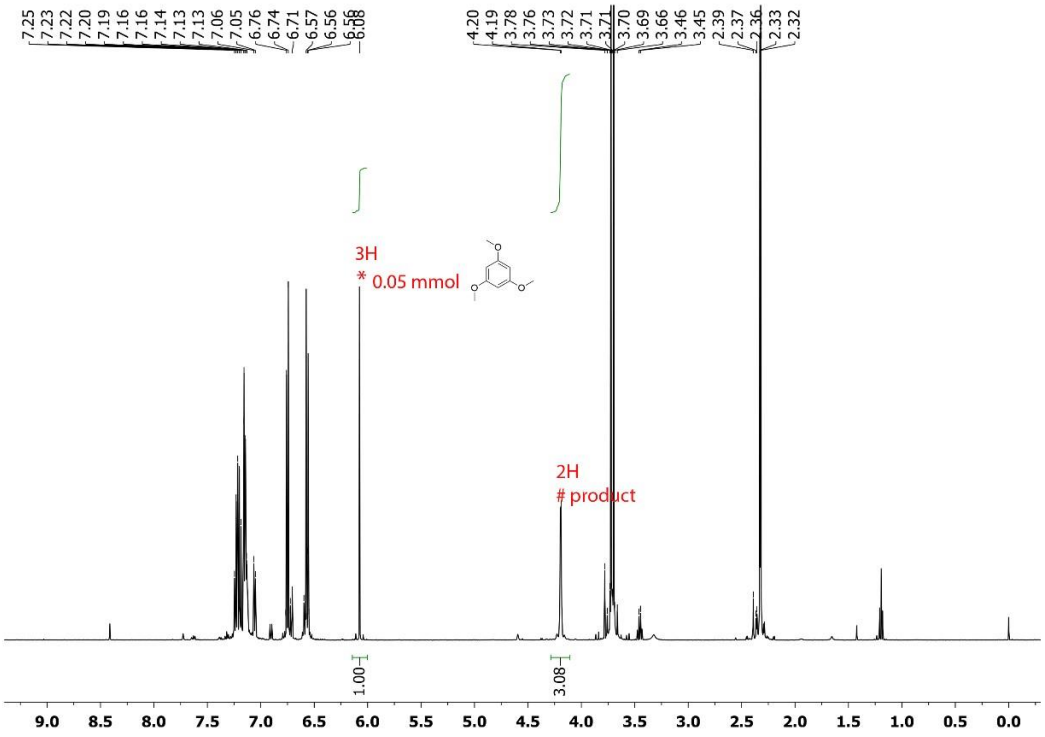


Figure 2.54 ^{1}H NMR (500 MHz, $CDCl_3$) of the reaction mixture of 4i.

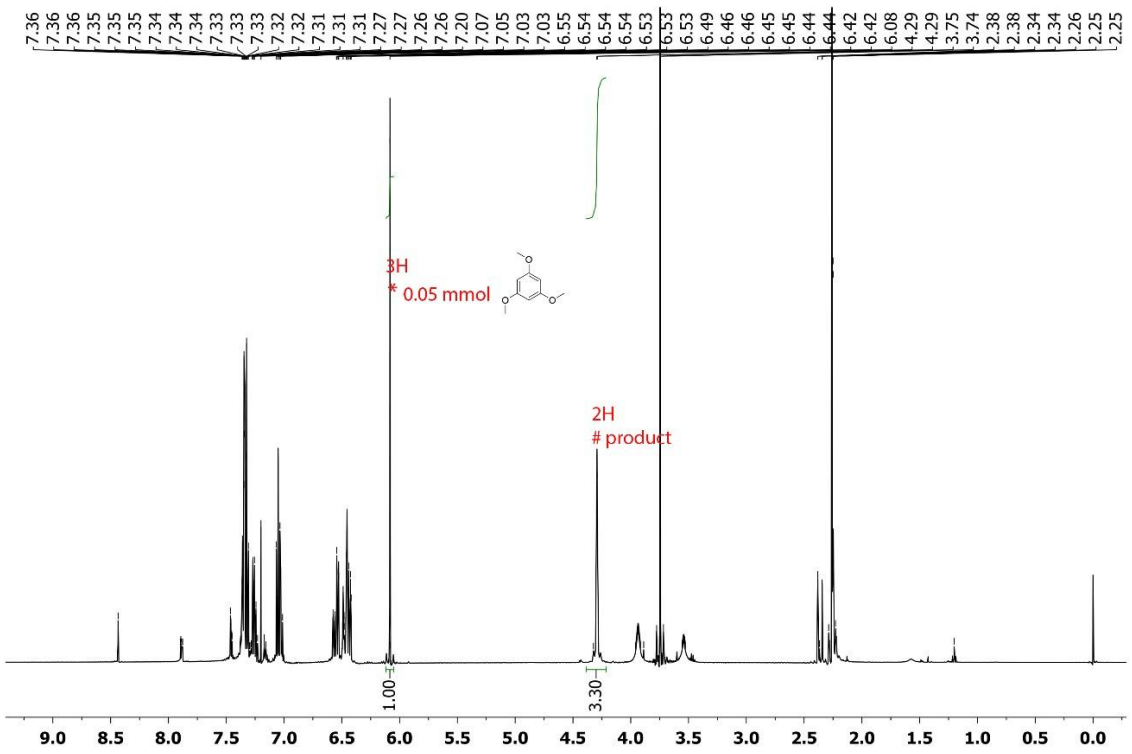


Figure 2.55 ^{1}H NMR (500 MHz, $CDCl_3$) of the reaction mixture of 4j.

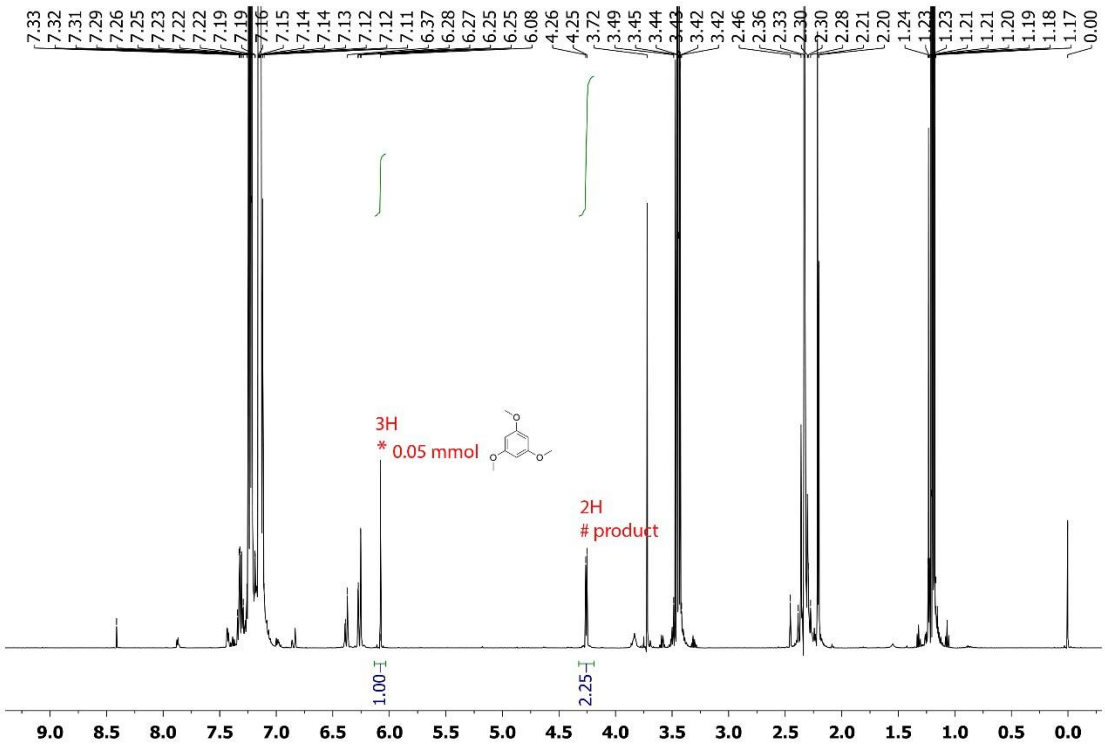


Figure 2.56 ^{1}H NMR (500 MHz, $CDCl_3$) of the reaction mixture of 4k.

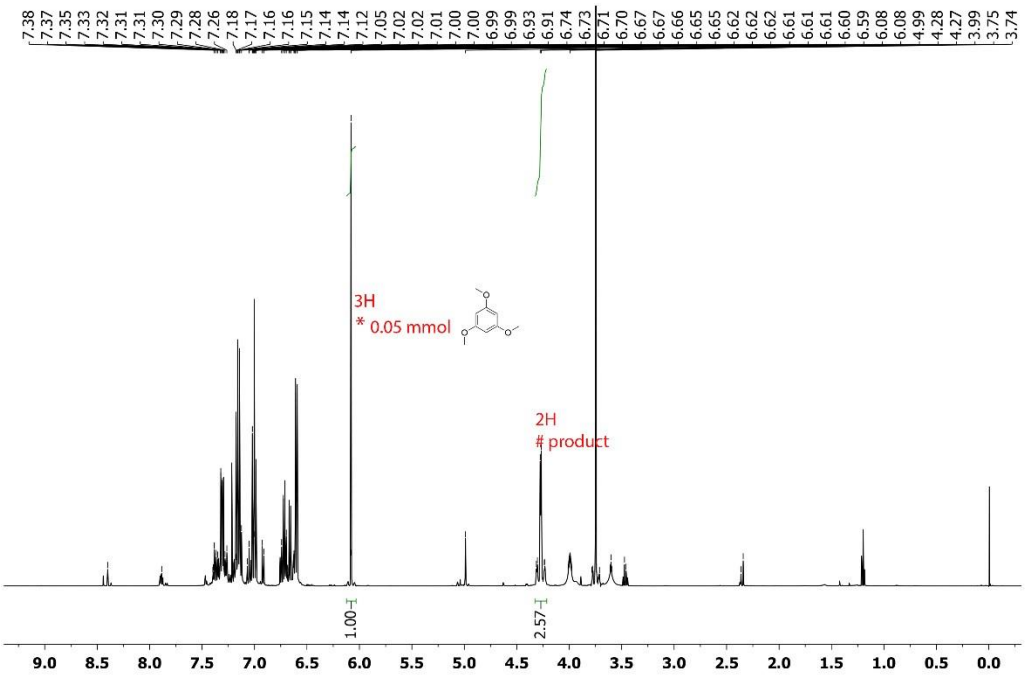


Figure 2.57 ^{1}H NMR (500 MHz, $CDCl_3$) of the reaction mixture of 4l.

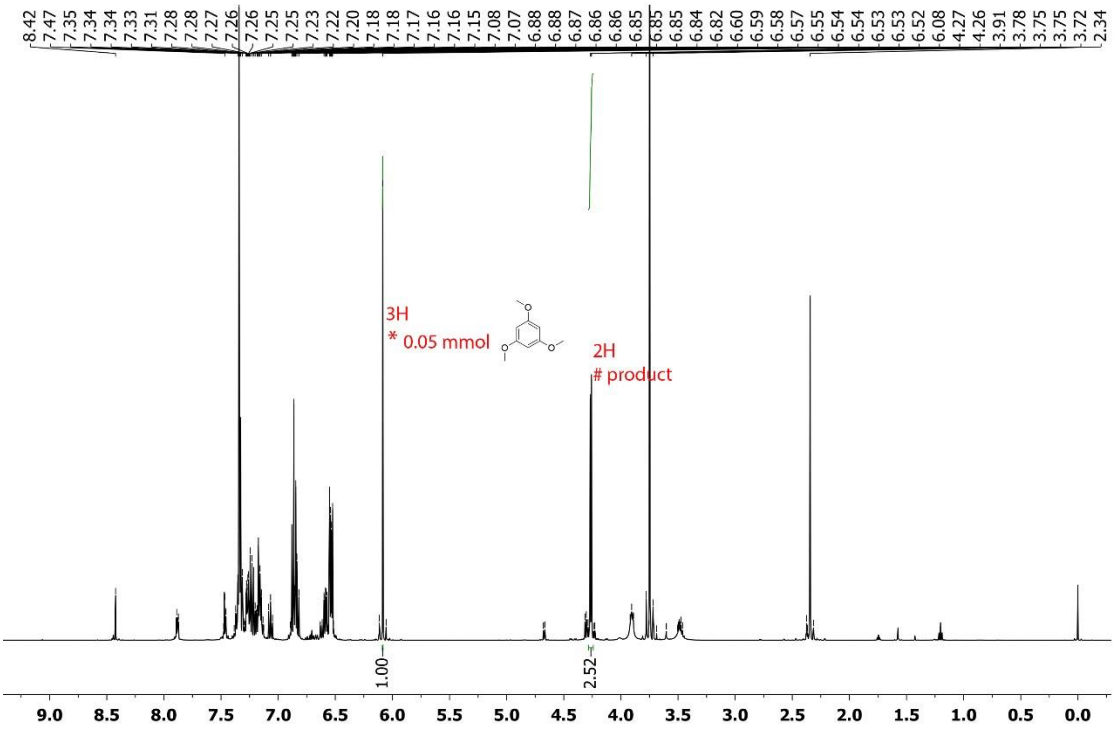


Figure 2.58. ^{1}H NMR (500 MHz, $CDCl_3$) of the reaction mixture of 4m.

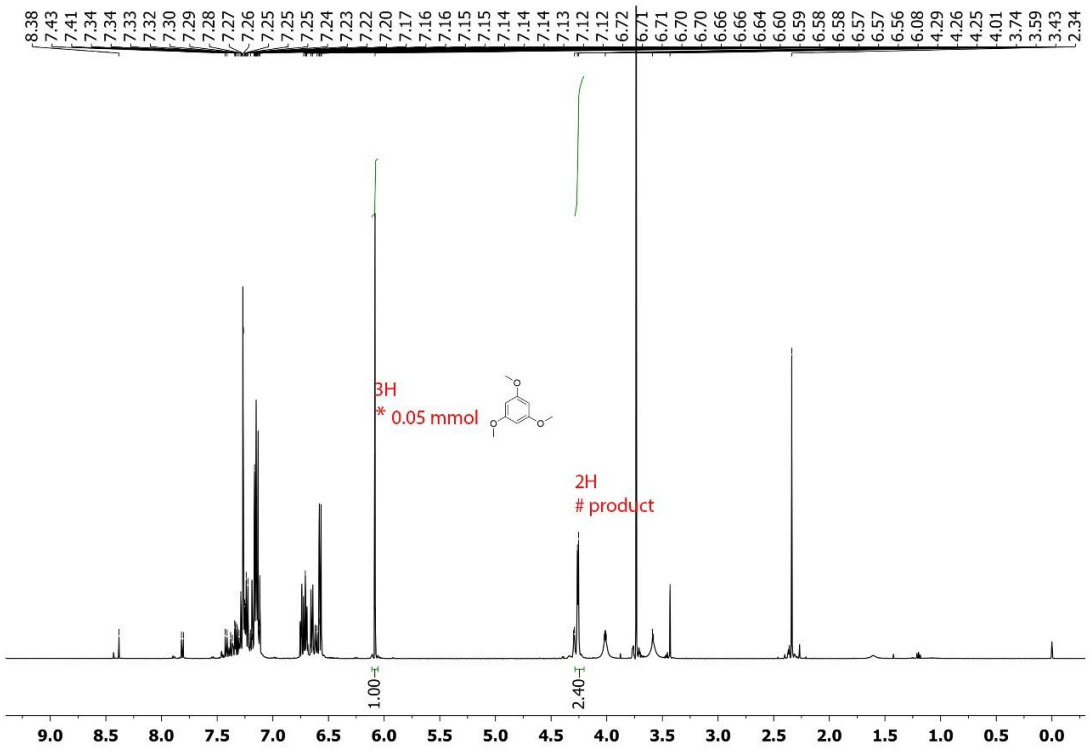


Figure 2.59 ^{1}H NMR (500 MHz, $CDCl_3$) of the reaction mixture of 4n.

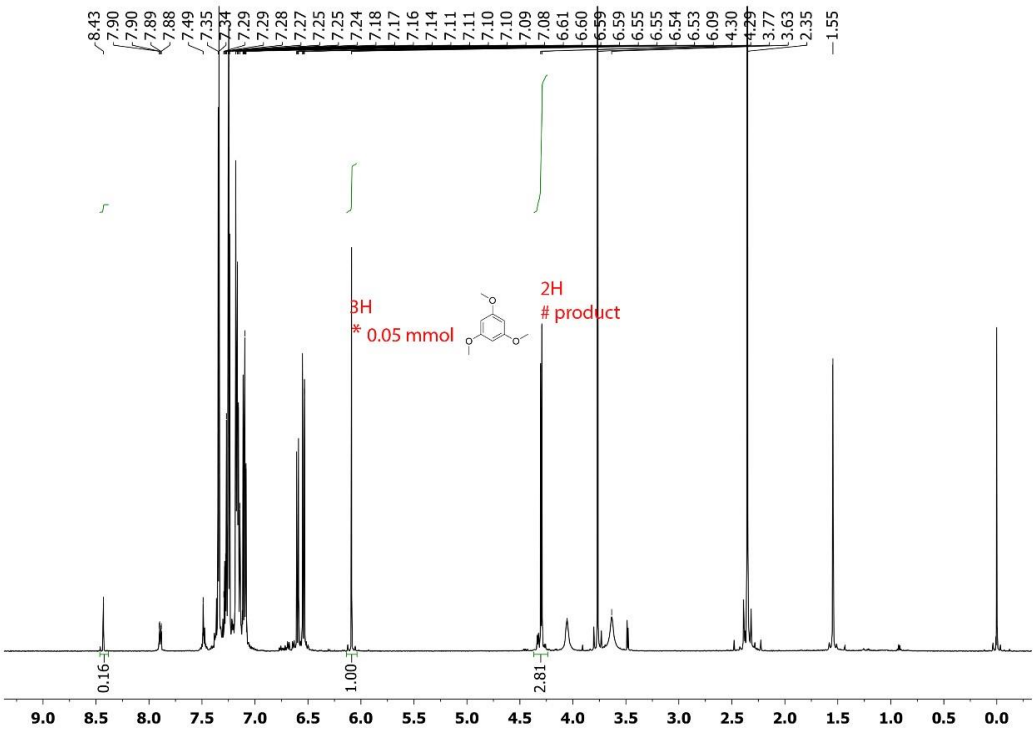


Figure 2.60 ^{1}H NMR (500 MHz, $CDCl_3$) of the reaction mixture of 4o.

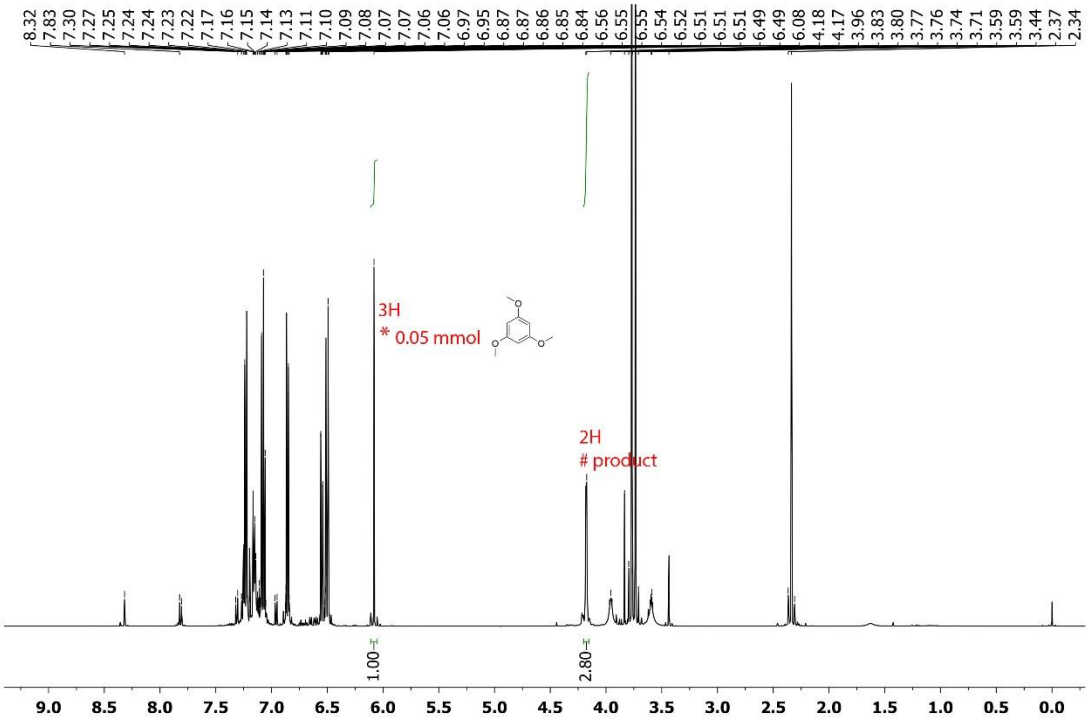


Figure 2.61 ^{1}H NMR (500 MHz, $CDCl_3$) of the reaction mixture of 4p.

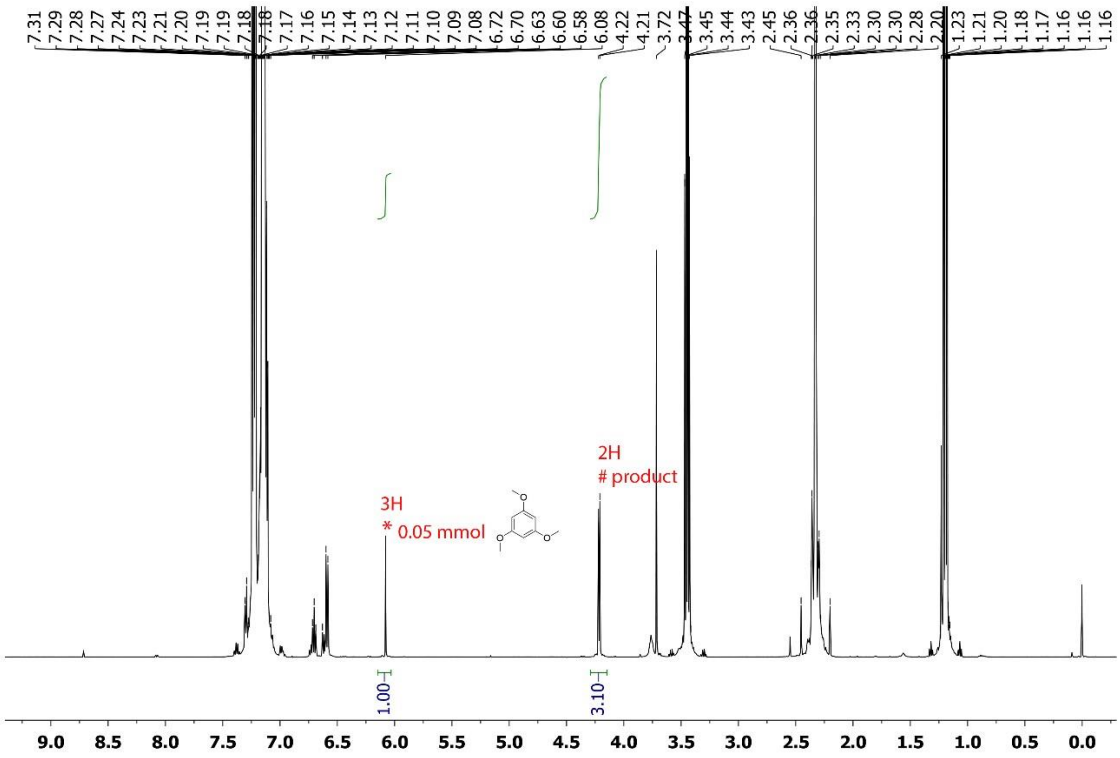


Figure 2.62 ^{1}H NMR (500 MHz, $CDCl_3$) of the reaction mixture of 4r.

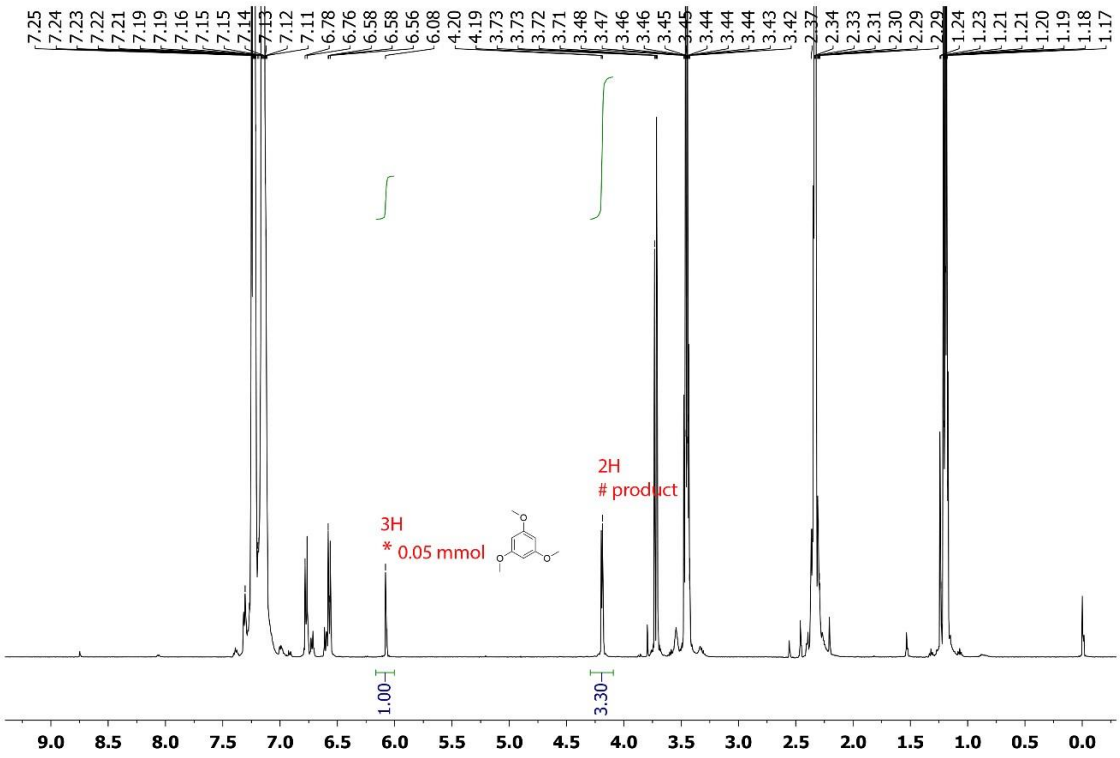


Figure 2.63 ^{1}H NMR (500 MHz, $CDCl_3$) of the reaction mixture of 4s.

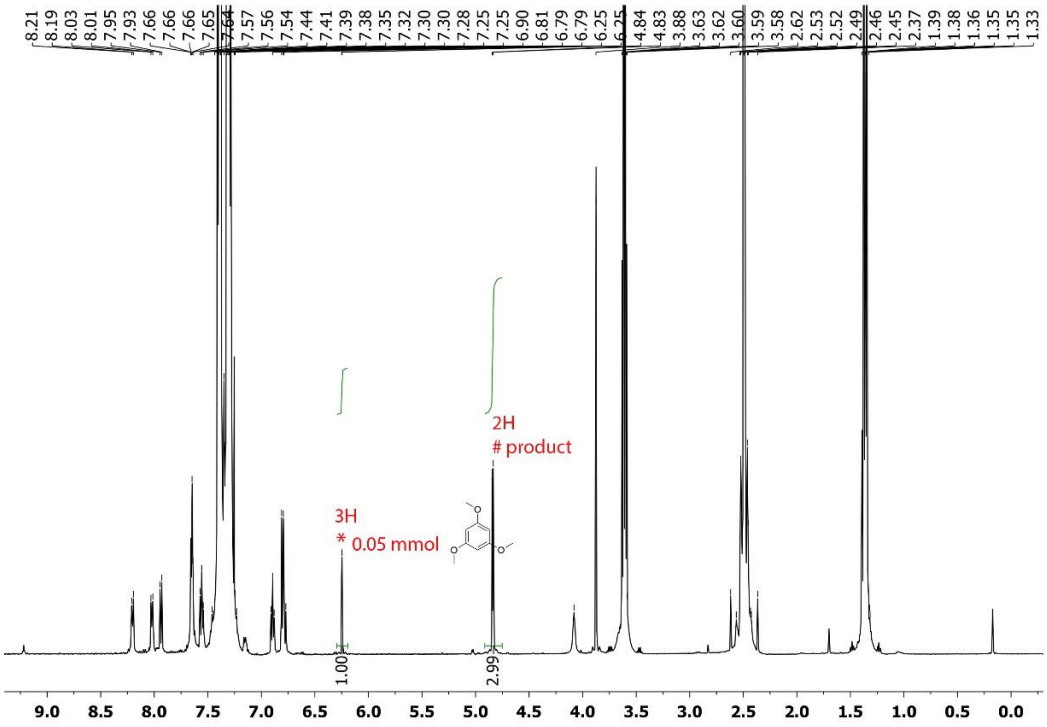


Figure 2.64 ^{1}H NMR (500 MHz, $CDCl_3$) of the reaction mixture of 4t.

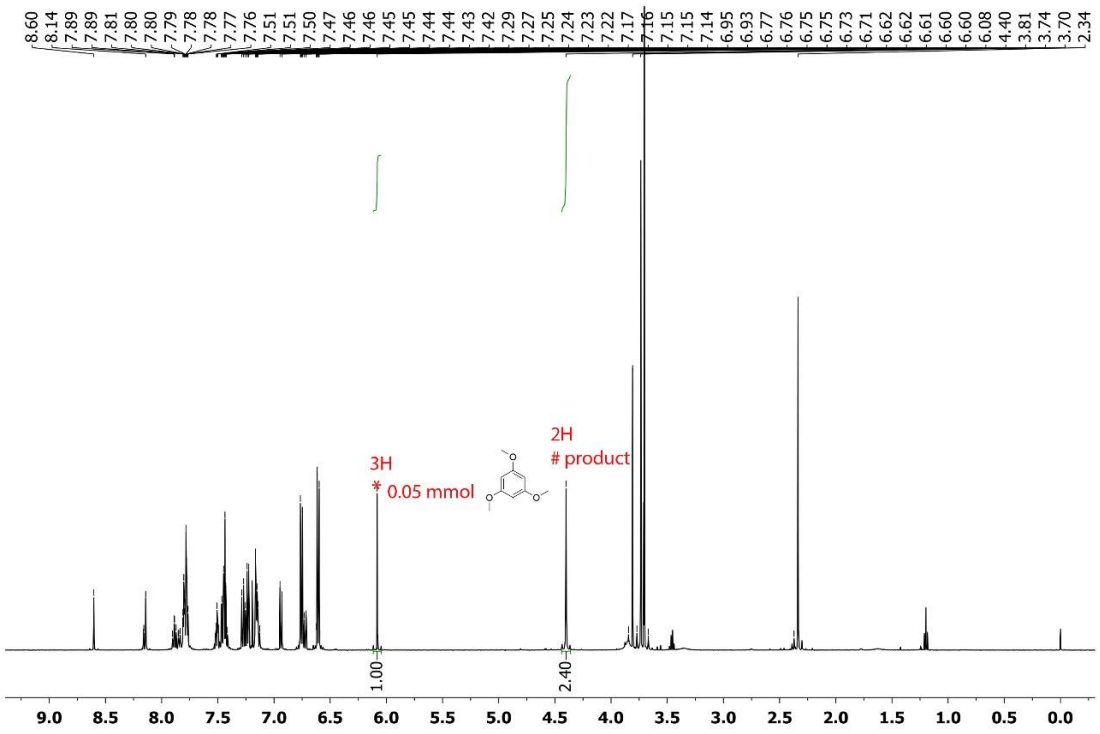


Figure 2.65 ^{1}H NMR (500 MHz, $CDCl_3$) of the reaction mixture of 4u**.**

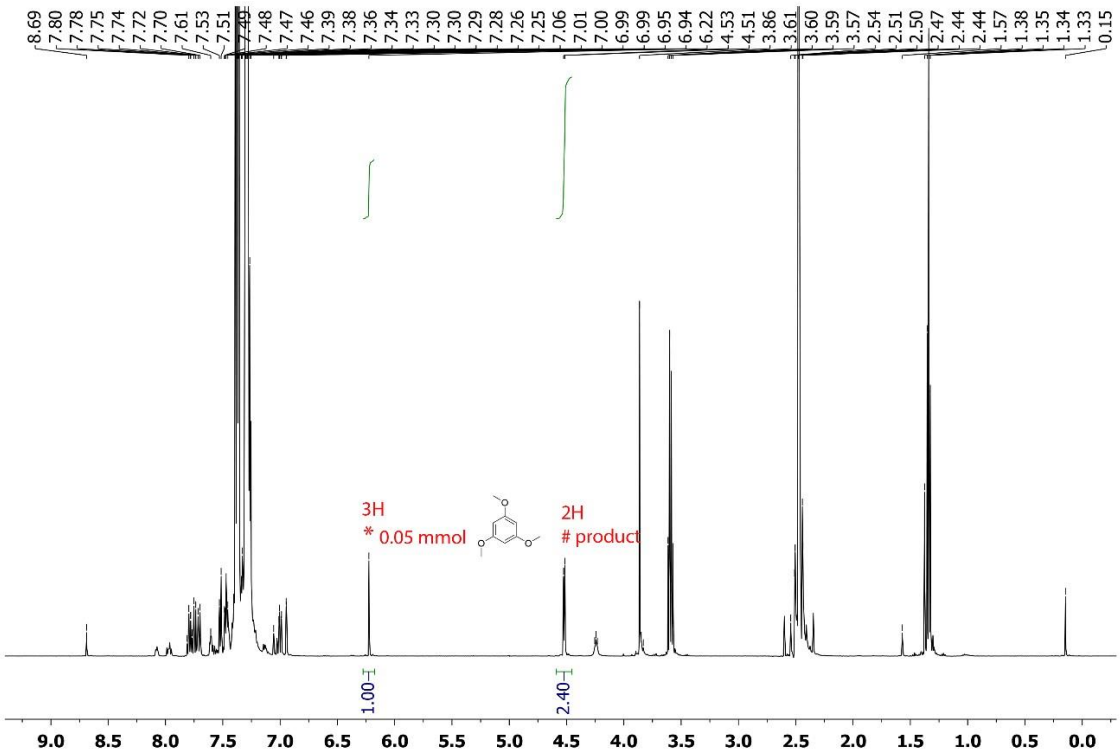


Figure 2.66 ^{1}H NMR (500 MHz, $CDCl_3$) of the reaction mixture of 4v**.**

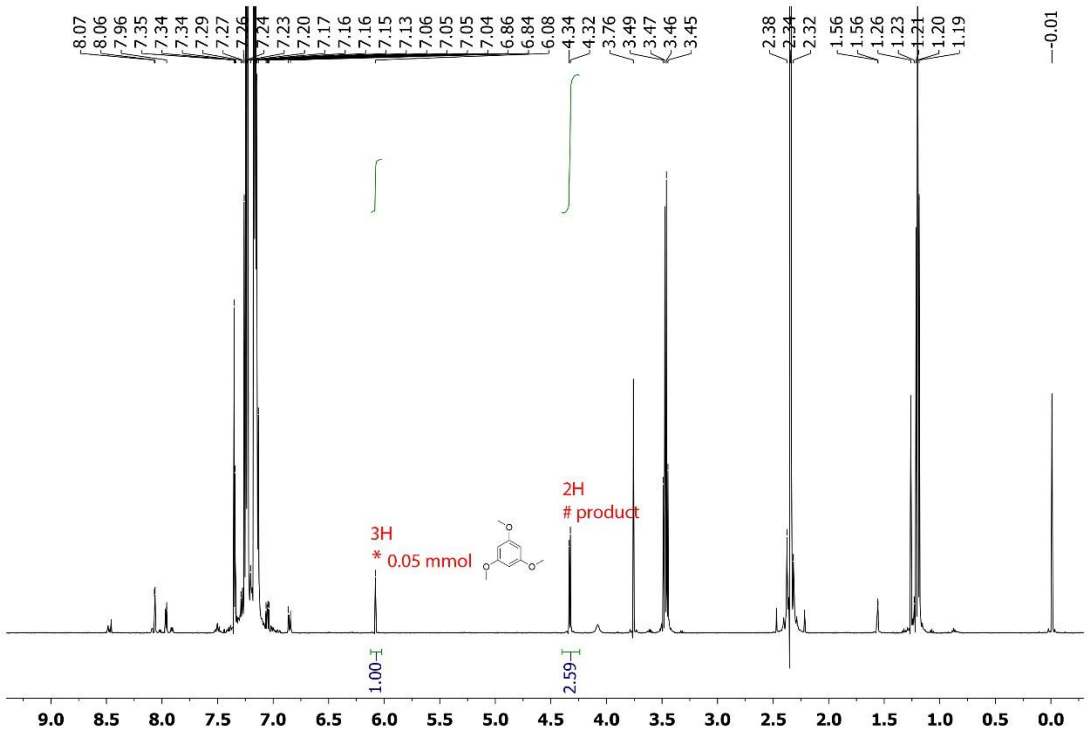


Figure 2.67 ^{1}H NMR (500 MHz, $CDCl_3$) of the reaction mixture of 4w.

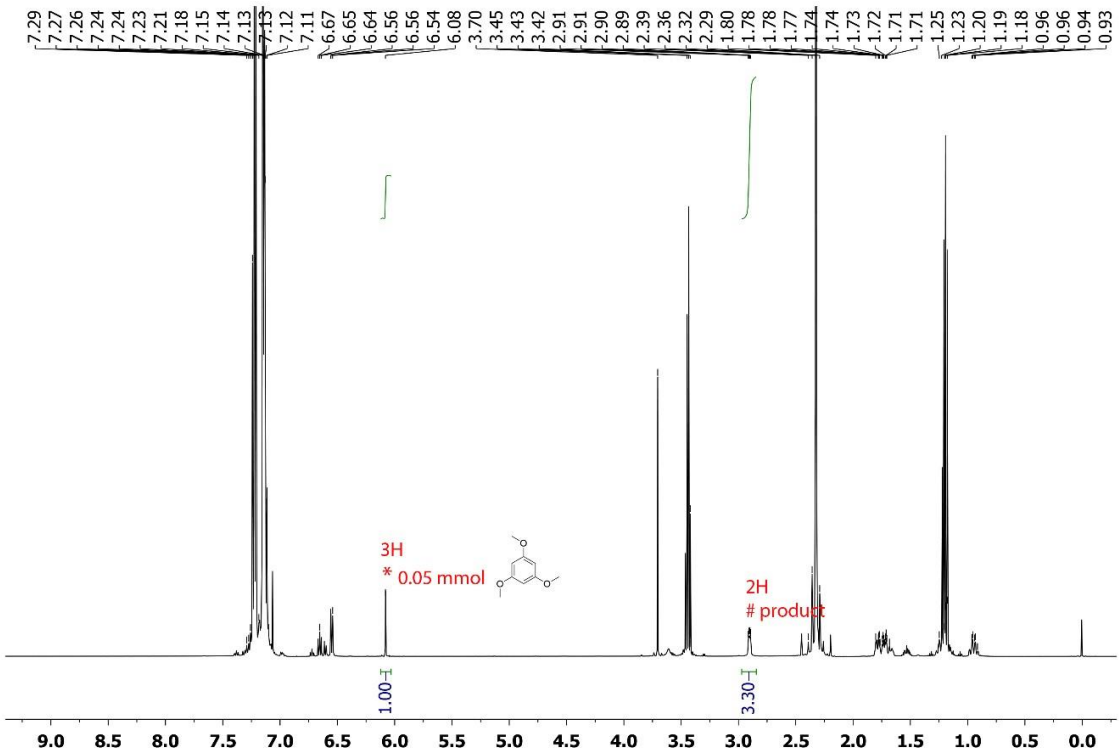


Figure 2.68. ^{1}H NMR (500 MHz, $CDCl_3$) of the reaction mixture of 4ac.

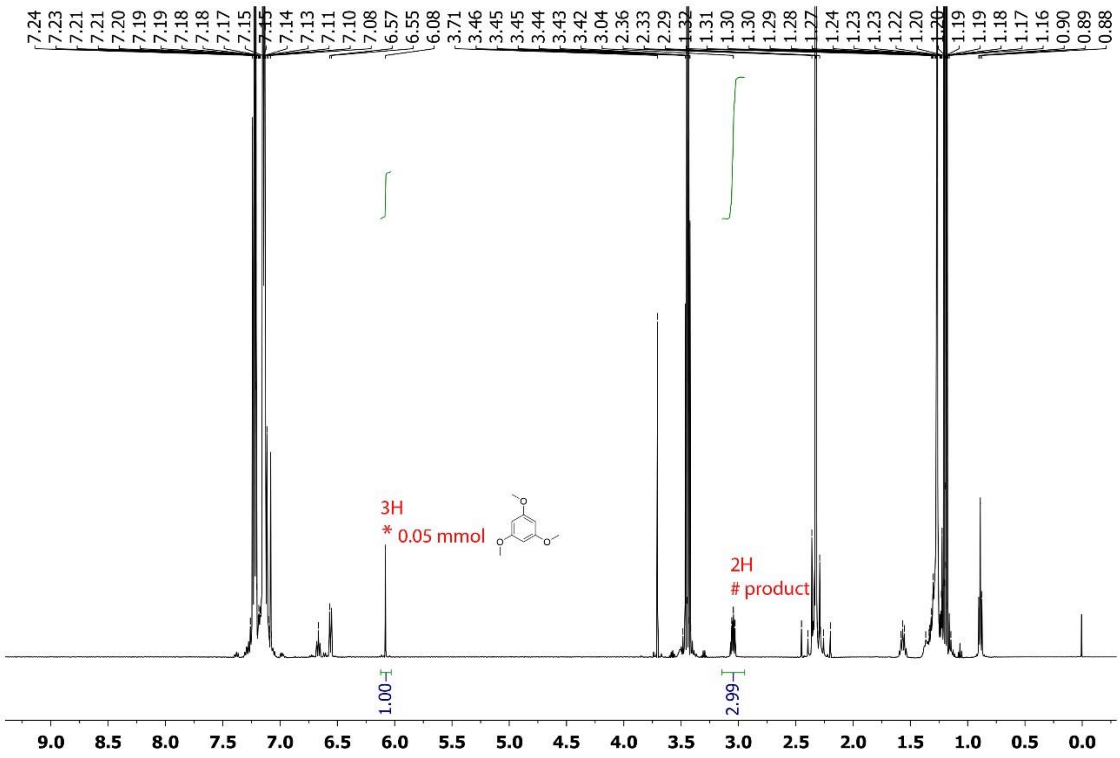


Figure 2.69 ^{1}H NMR (500 MHz, $CDCl_3$) of the reaction mixture of 4ad.

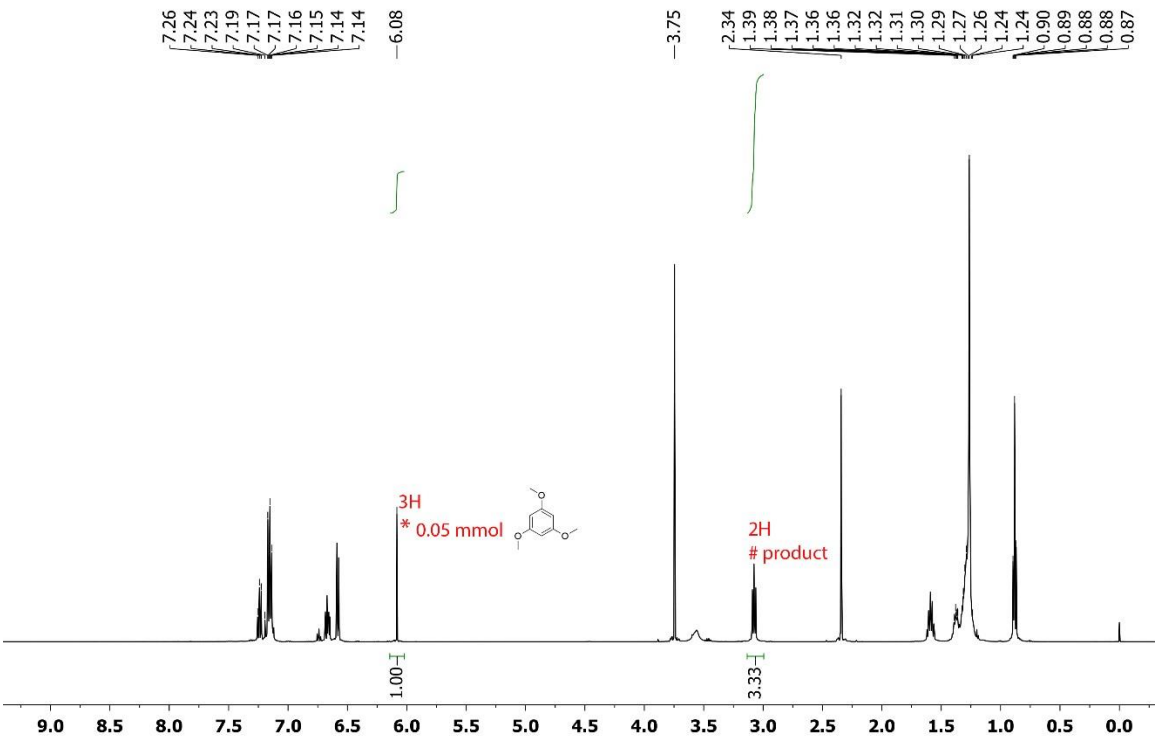


Figure 70. ^{1}H NMR (500 MHz, $CDCl_3$) of the reaction mixture of 4ae.

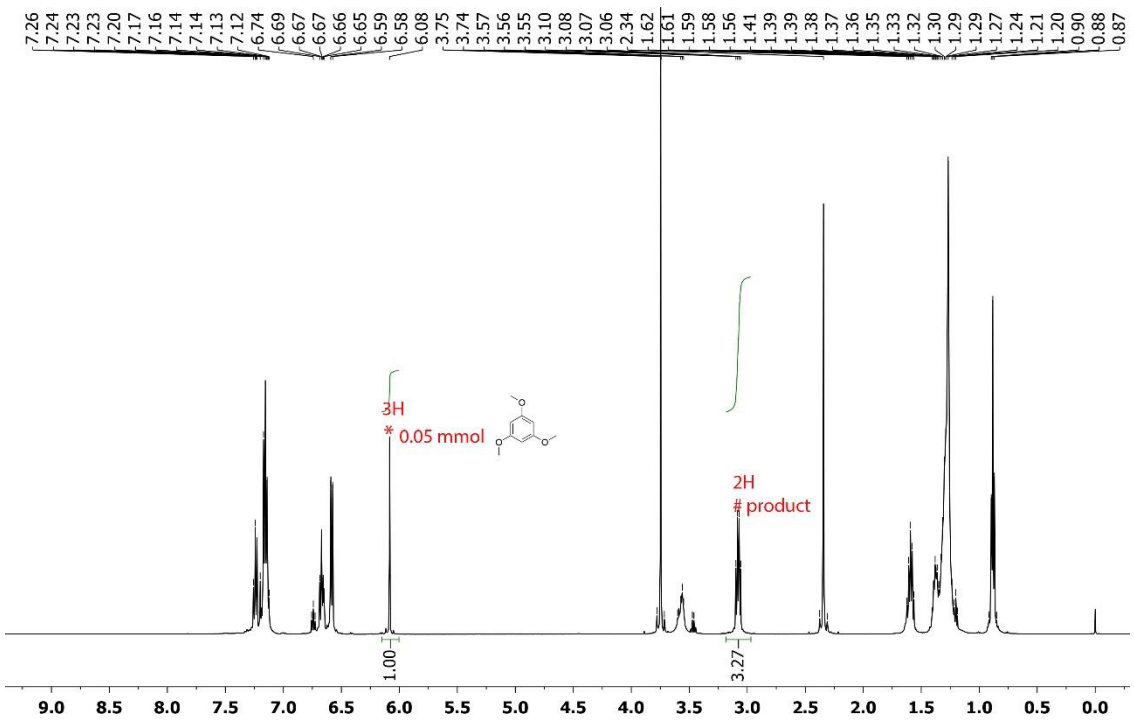


Figure 2.71 ^{1}H NMR (500 MHz, $CDCl_3$) of the reaction mixture of 4af.

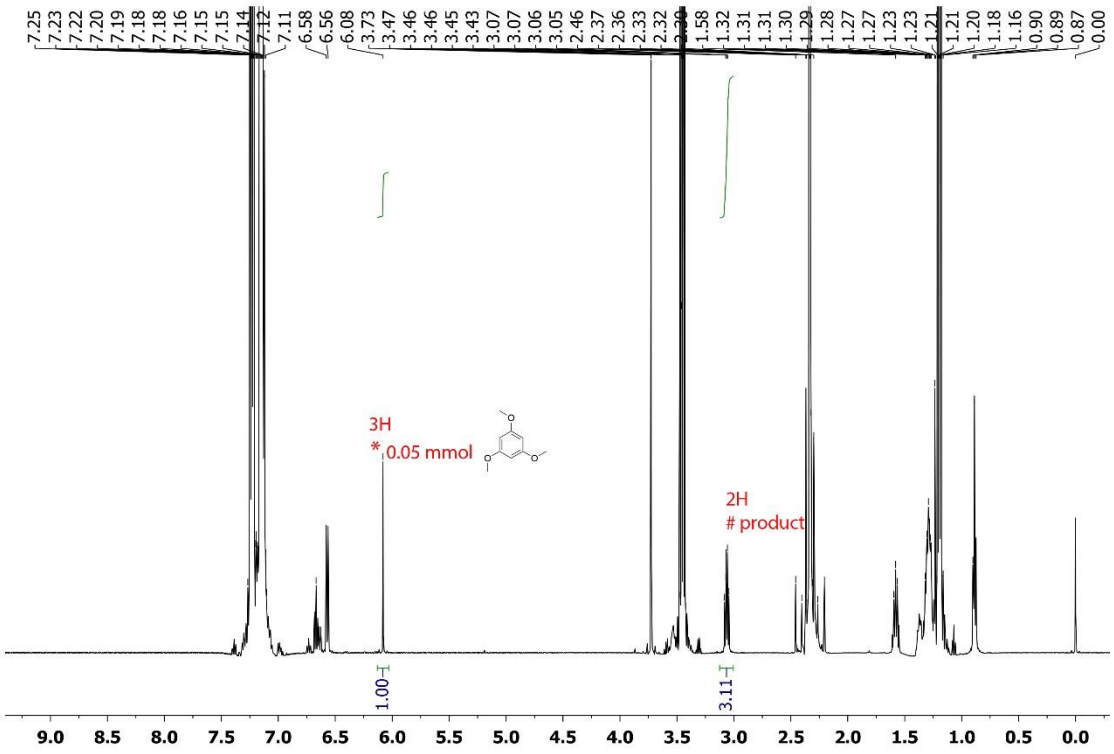


Figure 2.72 ^{1}H NMR (500 MHz, $CDCl_3$) of the reaction mixture of 4ag**.**

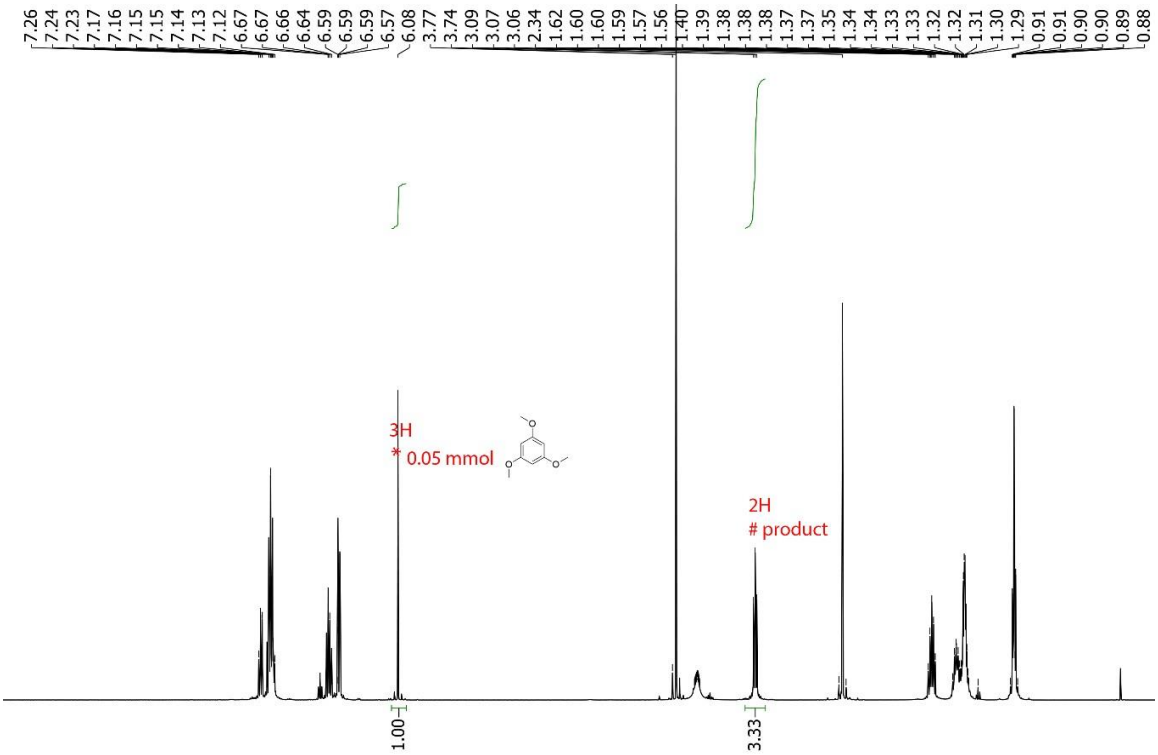


Figure 2.73. ^{1}H NMR (500 MHz, $CDCl_3$) of the reaction mixture of 4ah.

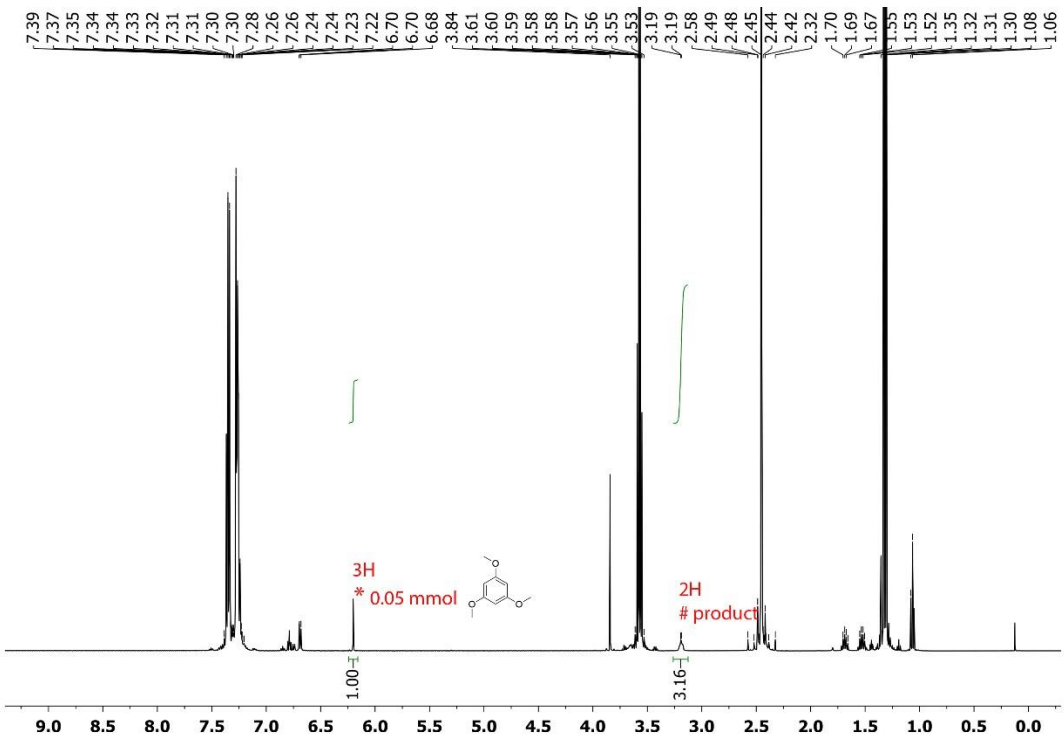


Figure 2.74 ^{1}H NMR (500 MHz, $CDCl_3$) of the reaction mixture of 4ai.

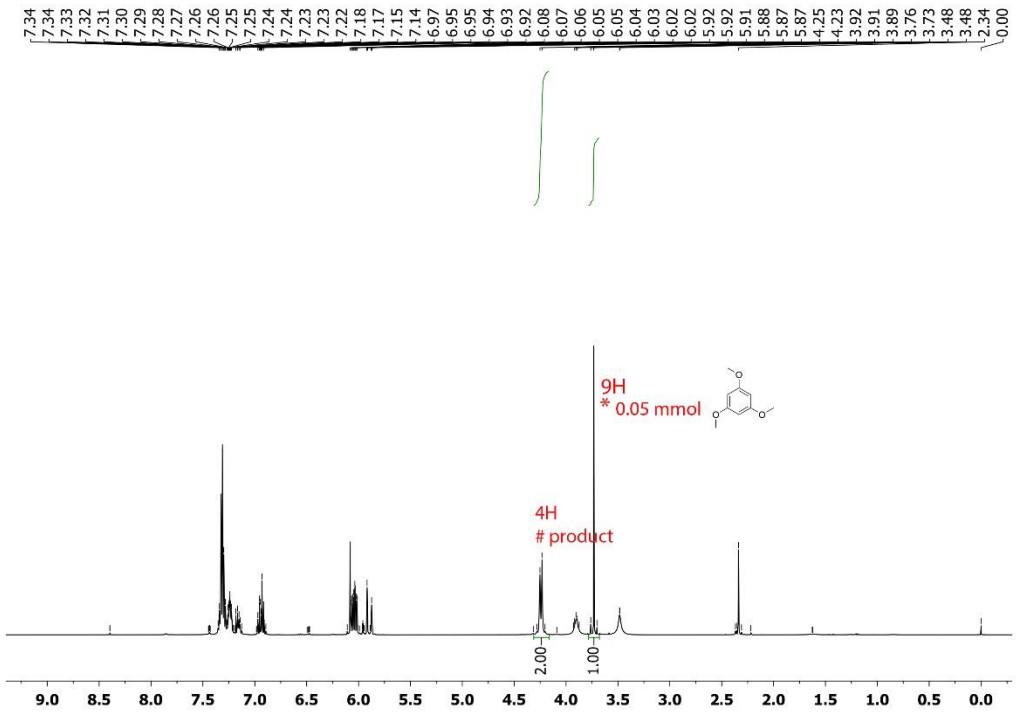


Figure 2.75 ^{1}H NMR (500 MHz, $CDCl_3$) of the reaction mixture of 4aj.

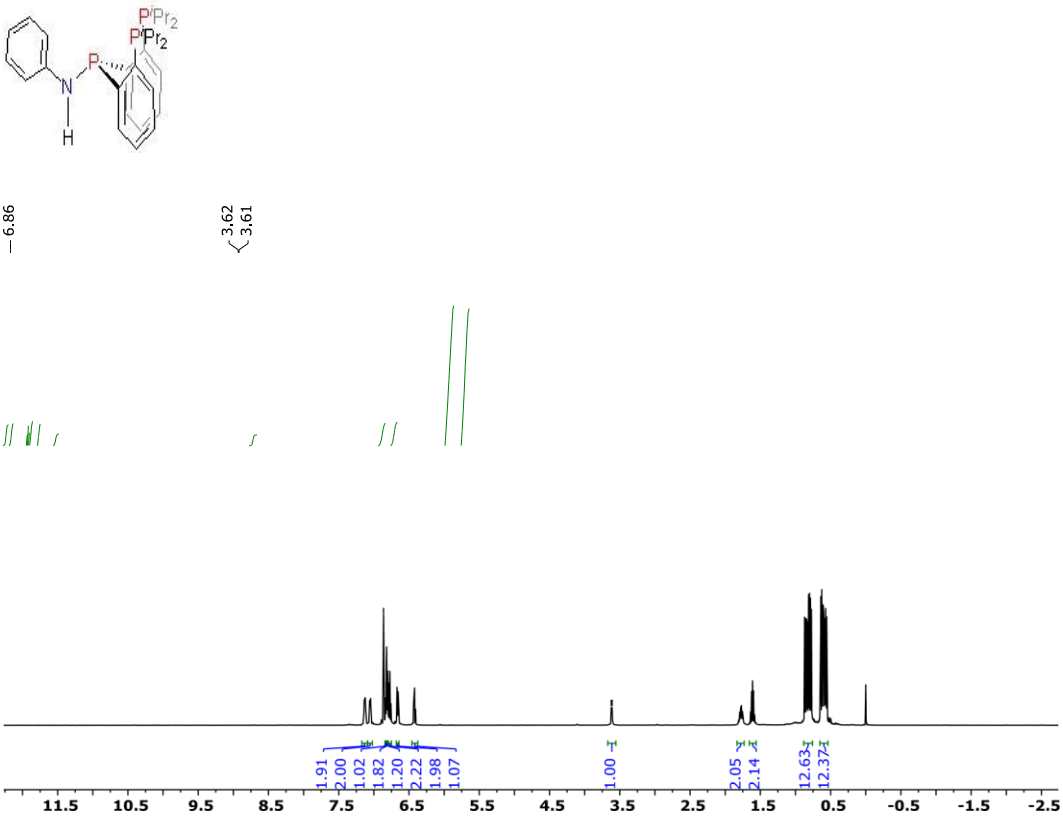


Figure 2.76 ^{1}H NMR (500 MHz, C_6D_6) of IV ligand.

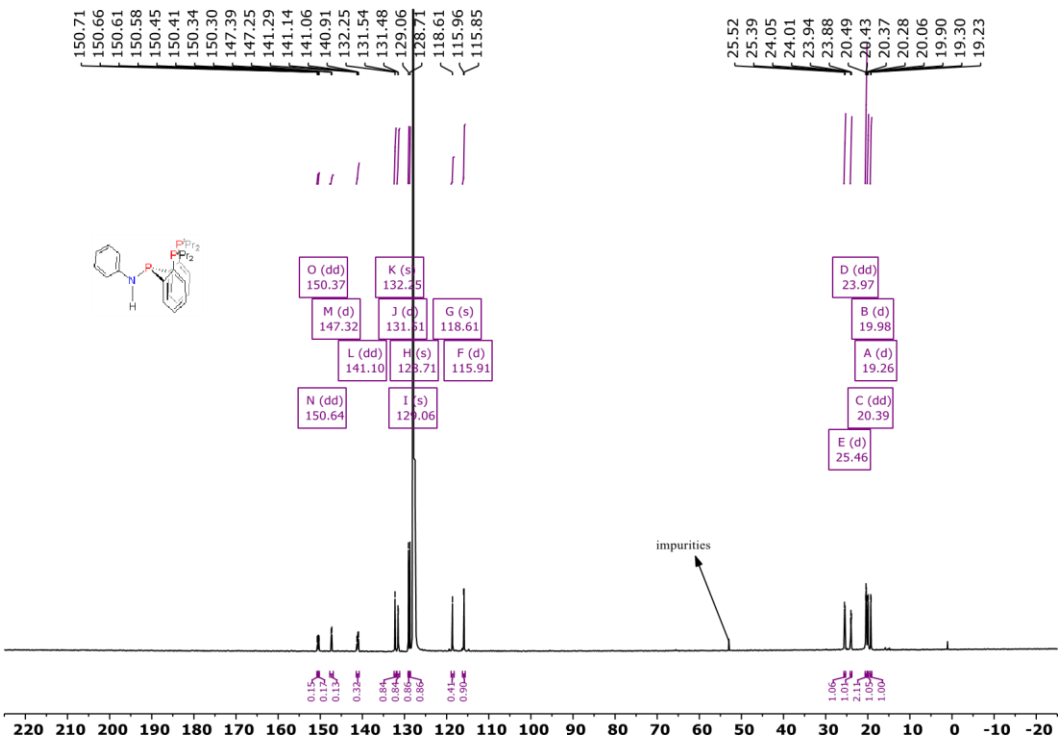


Figure 2.77 $^{13}C\{^{1}H\}$ NMR (126 MHz, C_6D_6) of IV ligand.

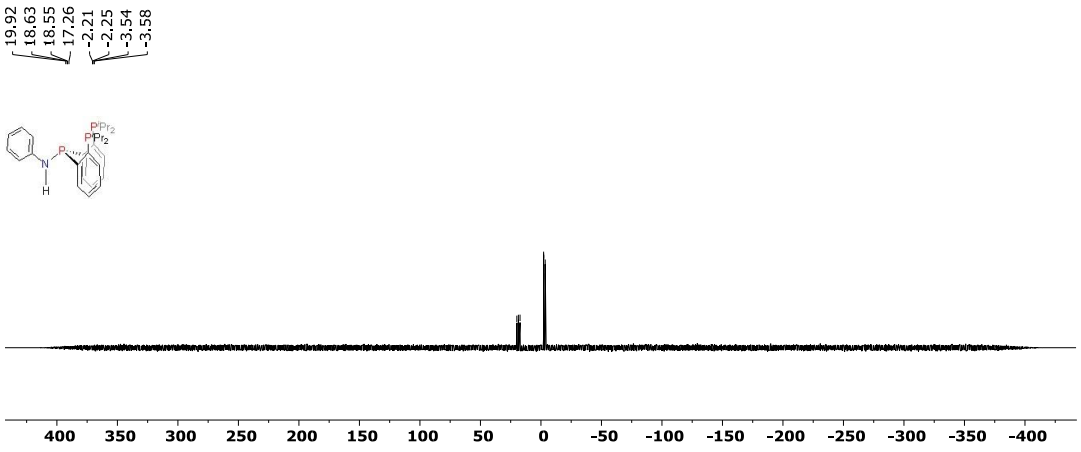


Figure 2.78 ^{31}P {^{1}H} NMR (121 MHz, C_6D_6) of IV ligand.

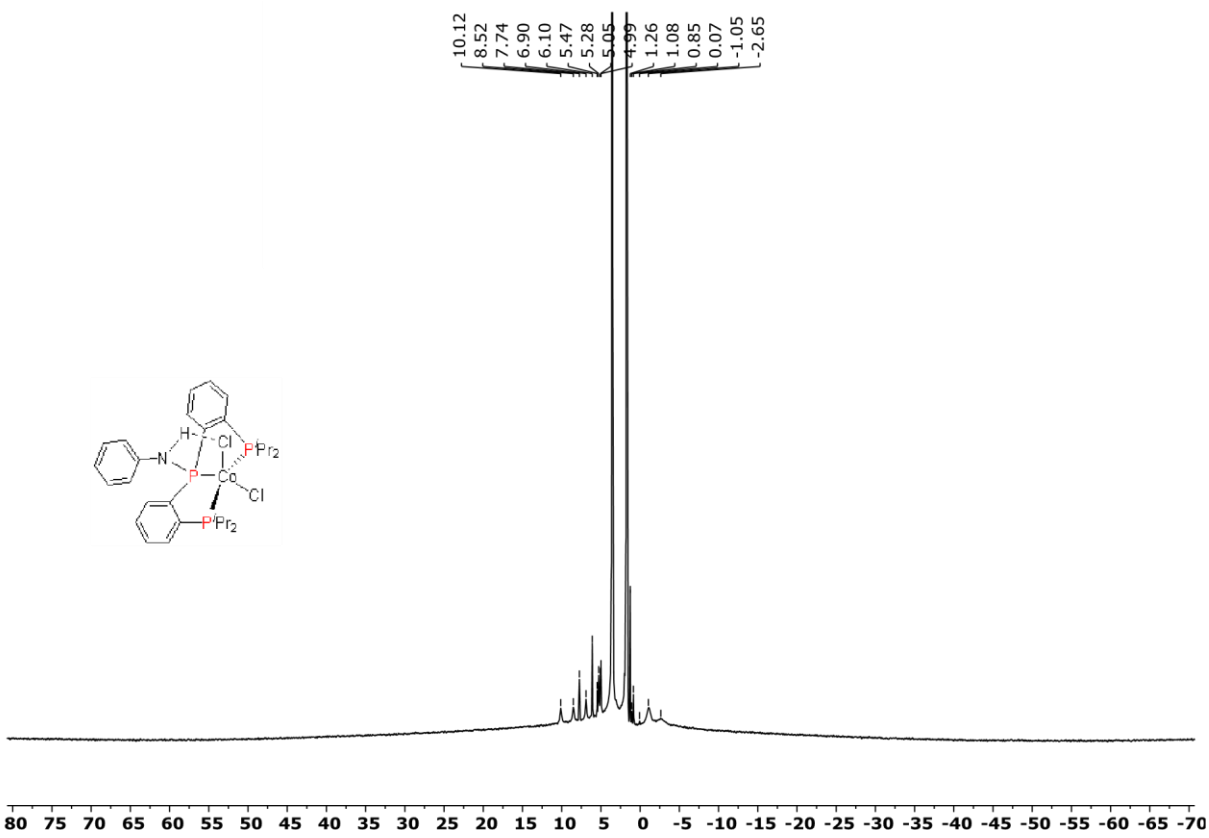


Figure 2.79 ^{1}H NMR (500 MHz, CD_2Cl_2) of IV.

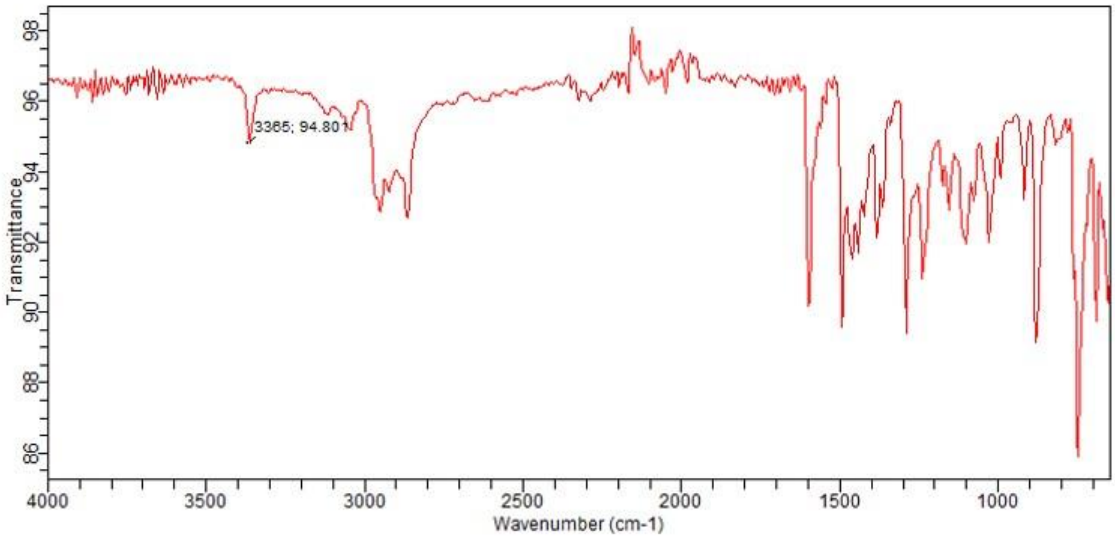


Figure 2.80 IR spectrum of IV.

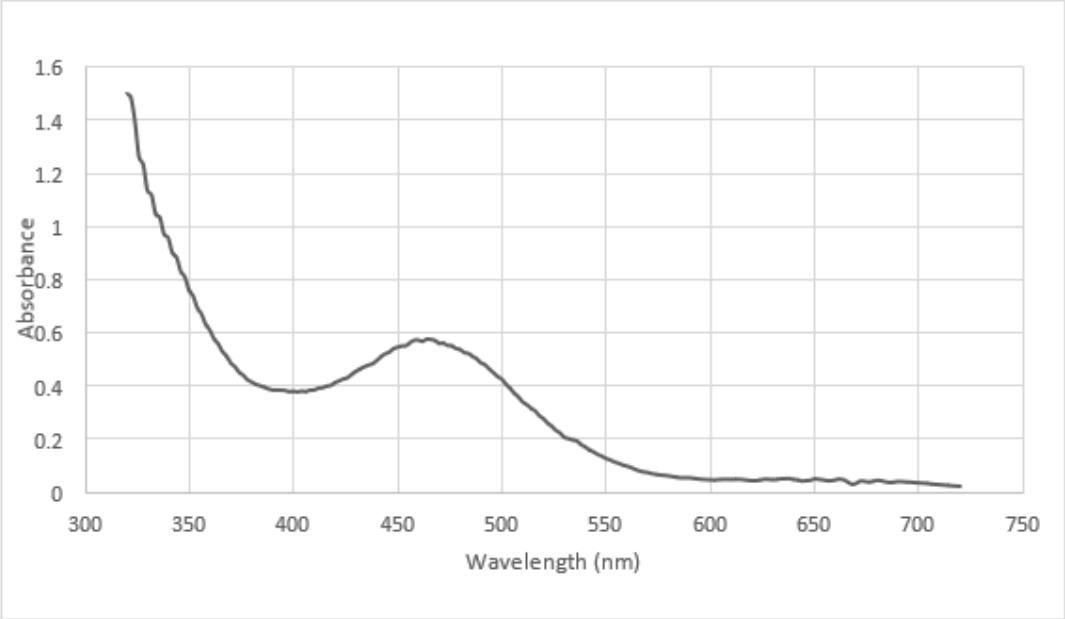


Figure 2.81 UV-Vis spectrum of IV.

2.18 Supplementary references

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CHAPTER III

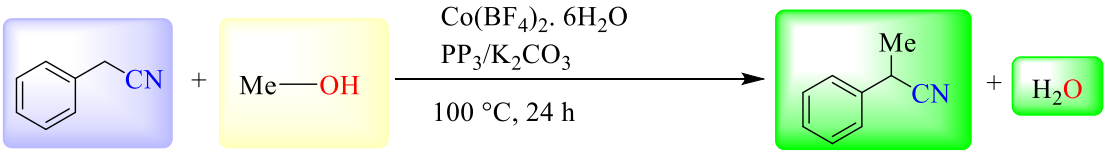
α-Alkylation of Nitriles with Primary Alcohols by a Well-Defined Molecular Catalyst

3.1 Introduction

With a unique -CN functional group, nitriles are a class of organic compounds that have found ubiquitous applications in chemical and pharmaceutical industries.[1-3] α-Alkylated nitriles are key building blocks for the synthesis of various compounds such as carboxylic acids, amides, amines, ketones, etc.[1-3] Homogeneous transition-metal-mediated construction of the carbon−carbon bond belongs to one of the most imperative synthetic strategies for the products of added value.[4] Traditional alkylation requires toxic alkyl halides and stoichiometric amounts of bases, generating the copious amount of waste.[5,6] An attractive alternative is to utilize alcohol as the alkylating agent via a borrowing hydrogen (BH) process.[7-19] In a typical BH process to α-alkylated nitriles, a primary alcohol is first dehydrogenated to an aldehyde with the catalyst "borrowing" a hydride and a proton. The aldehyde undergoes a nucleophilic attack by the nitrile in the presence of a base to generate an α,β-unsaturated nitrile, which is subsequently hydrogenated to the α-alkylated nitrile product by the catalyst "returning" the hydride and the proton. The BH strategy is more sustainable, environmentally friendly, and atom-efficient, with water as the only byproduct.[7-19]

In this regard, catalysts based on precious transition metals, such as Rh,[20,21] Ir,[22,23] Os,[24] Ru,[25] and Pd,[26] have significantly promoted this field (Scheme 3.1). With increasing

concerns on sustainability and economy, base transition-metal surrogates like Fe, Co, Mn, Ni, and Cu are becoming more appealing.[27] It is just recently that such base transition-metal-catalyzed transformations are revealed.[28-34]



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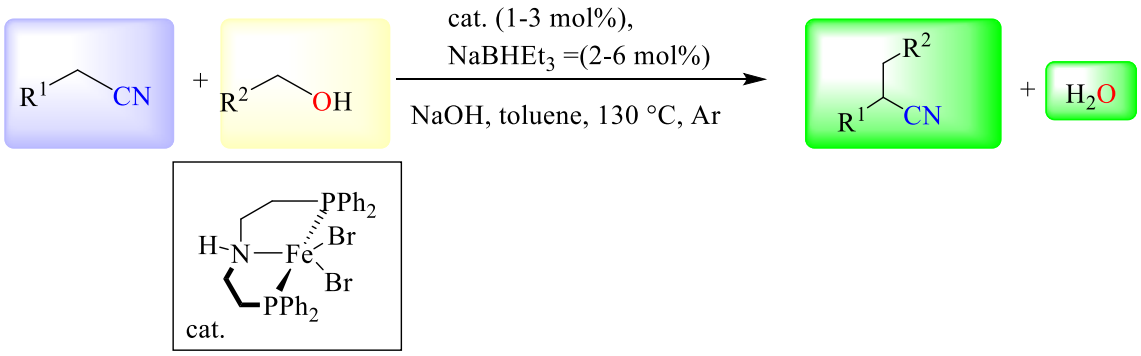

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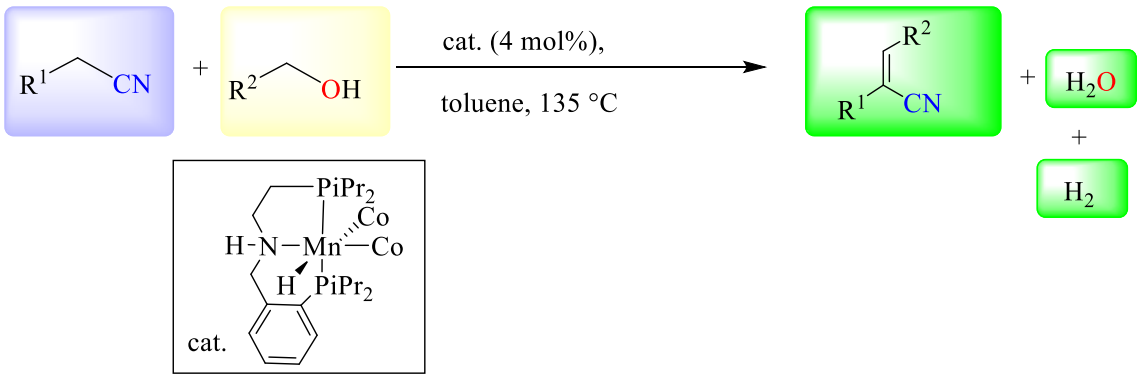

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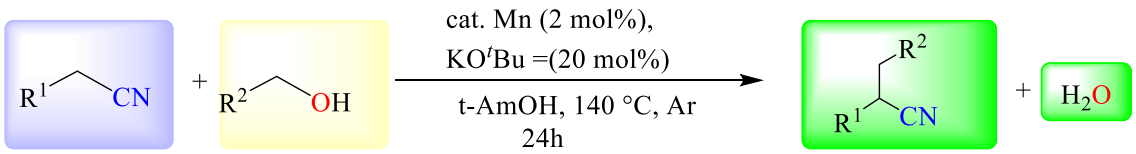

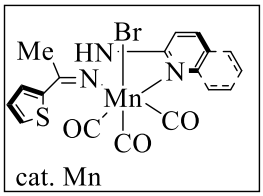

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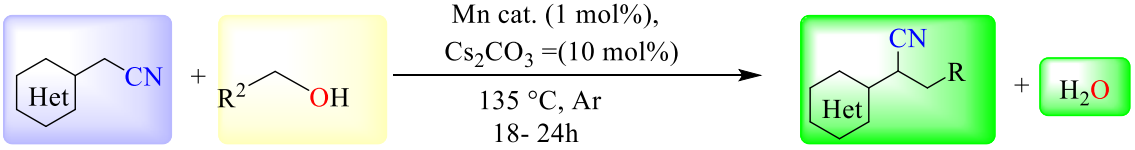

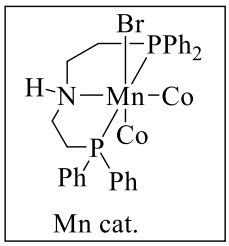

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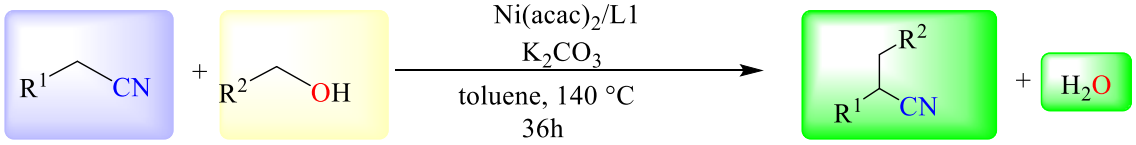

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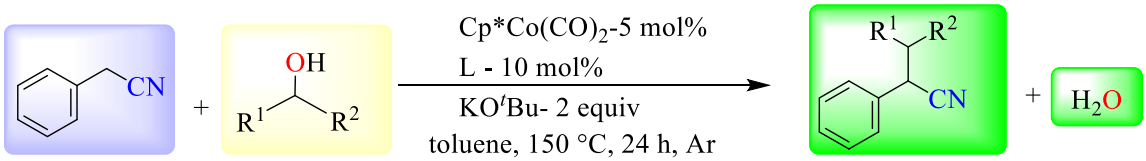
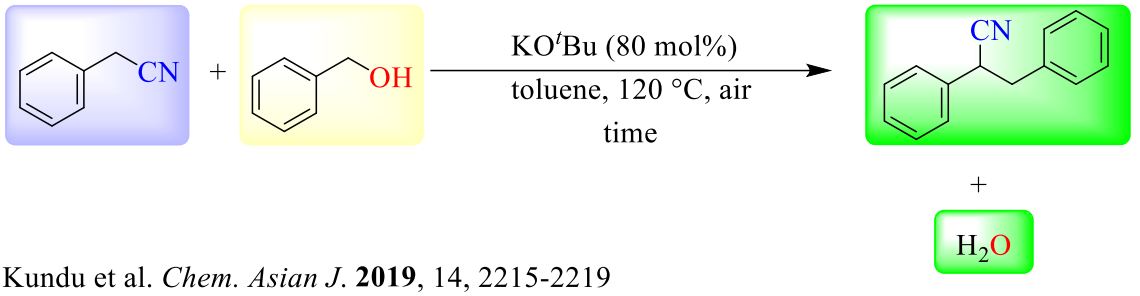


Sundararaju et al., *ACS Catal*. **2020**, 10, 8023-8031

Scheme 3.1 Synthesis of α-alkylated nitriles by different groups

A transition-metal-free method was recently reported using 80 mol % KO^{t}Bu under aerobic conditions (Scheme 3.2).[35]



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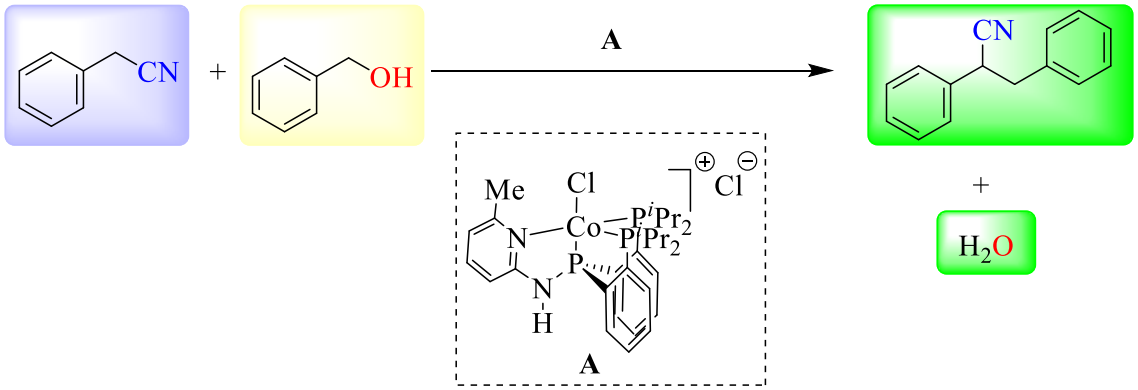
Scheme 3.2 Synthesis of α-alkylated nitriles by a KO^{t}Bu under aerobic condition

As part of the study on methylation of C(sp^3)−H/C(sp^2)−H bonds, Liu and co-workers reported their seminal work on the nitrile alkylation by a cobalt salt $Co(BF_4)_2{\cdot}6H_2O$, $P(CH_2CH_2PPh_2)_3$ (PP_3) ligand, and a stoichiometric amount of base, which is the only known cobalt example in literature.[28] However, the reported substrates were very limited, and methanol was the only alcohol used.[28] In addition, no mechanistic study on the α-alkylation of nitrile was disclosed.[28] Herein, we present a systematic study on the selective nitrile alkylation with primary alcohols mediated by a well-defined molecular cobalt catalyst **A** (Scheme 3.3).



Scheme 3.3 Ding's cobalt catalyst for the synthesis of *α*-alkylated nitriles

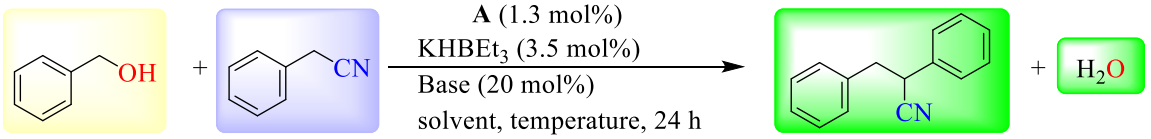
We have recently developed a new tetradentate mixed P/N donor ligand ^{iPr}PPPN^{H}Py^{Me}.[36] The air-stable cobalt complex **A** is an efficient precatalyst for dehydrogenation of secondary alcohols to ketones,[36] dehydrogenative self-coupling of primary alcohols to esters,[37] and β-alkylation of secondary alcohols with primary alcohols to ketones.[38] We envision that the **A**-based catalytic system has potential for the selective nitrile alkylation with primary alcohols to α-alkylated nitriles.

3.2 Results and discussion

We initiated the work to explore the reaction of the model substrates benzyl alcohol (0.5 mmol) and phenylacetonitrile (0.25 mmol) under various conditions. A temperature of 140 °C was required to obtain an optimized yield (Table 3.1, entries 1−3). After investigating various bases for the reaction, KOH turned out to be the most suitable base (Table 3.1, entries 3−6). It was shown that **A**, base, and $KHBEt_3$ were essential for this reaction (Table

3.1, entries 7−9). The $KHBEt_3$ is necessary for the reaction because it could regenerate the inactive cobalt catalyst by providing hydrides to form an activated cobalt catalyst, i.e., cobalt hydride (Table 3.1, entries 7[c]). Twenty-mole percent KOH was needed to optimize the yield (Table 3.1, entries 5 and 10). Interestingly, doubling **A** and $KHBEt_3$ loading gave a comparable yield (Table 3.1, entry 11). Solvents were also screened, and toluene was found to be the most suitable one (Table 3.1, entries 5, 12−14). Notably, a good 83% yield was observed in only 6 h, demonstrating the great reactivity of the catalytic system (Table 3.1, entry 16). Thus, the optimized conditions were obtained (Table 3.1 entry 5). Mercury test suggested a homogeneous catalytic process (Table 3.1, entry 17).

Table 3.1 Optimization of the Reaction Conditions[a]



1a **2a** **3a**

entry[a]	Cat.	base	solvent	temp (°C)	Yield (%)[b]
1	A	KO^{t}Bu	toluene	105	15
2	A	KO^{t}Bu	toluene	125	65
3	A	KO^{t}Bu	toluene	140	68
4	A	NaO^{t}Bu	toluene	140	74
5	A	KOH	toluene	140	88 (85)
6	A	K_2CO_3	toluene	140	13
7[c]	A	KOH	toluene	140	65
8	A		toluene	140	16
9		KOH	toluene	140	11
10[d]	A	KOH	toluene	140	68
11	A	KOH	toluene	140	85
12	A	KOH	benzene	140	74
13	A	KOH	THF	140	66
14	A	KOH	*t*-AmOH	140	50

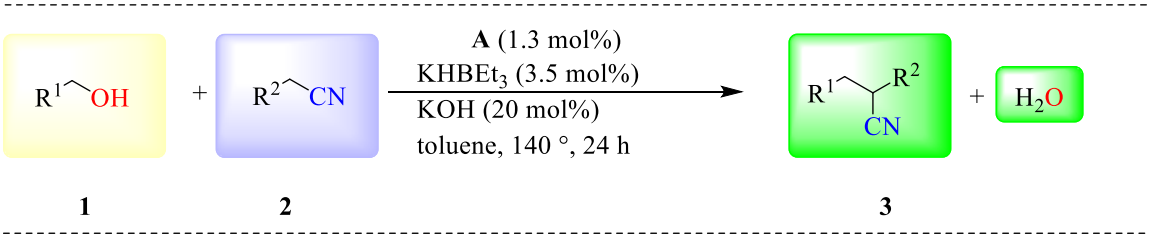
15[f]	A	KOH	toluene	140	82
16[g]	A	KOH	toluene	140	83
17[h]	A	KOH	toluene	140	83

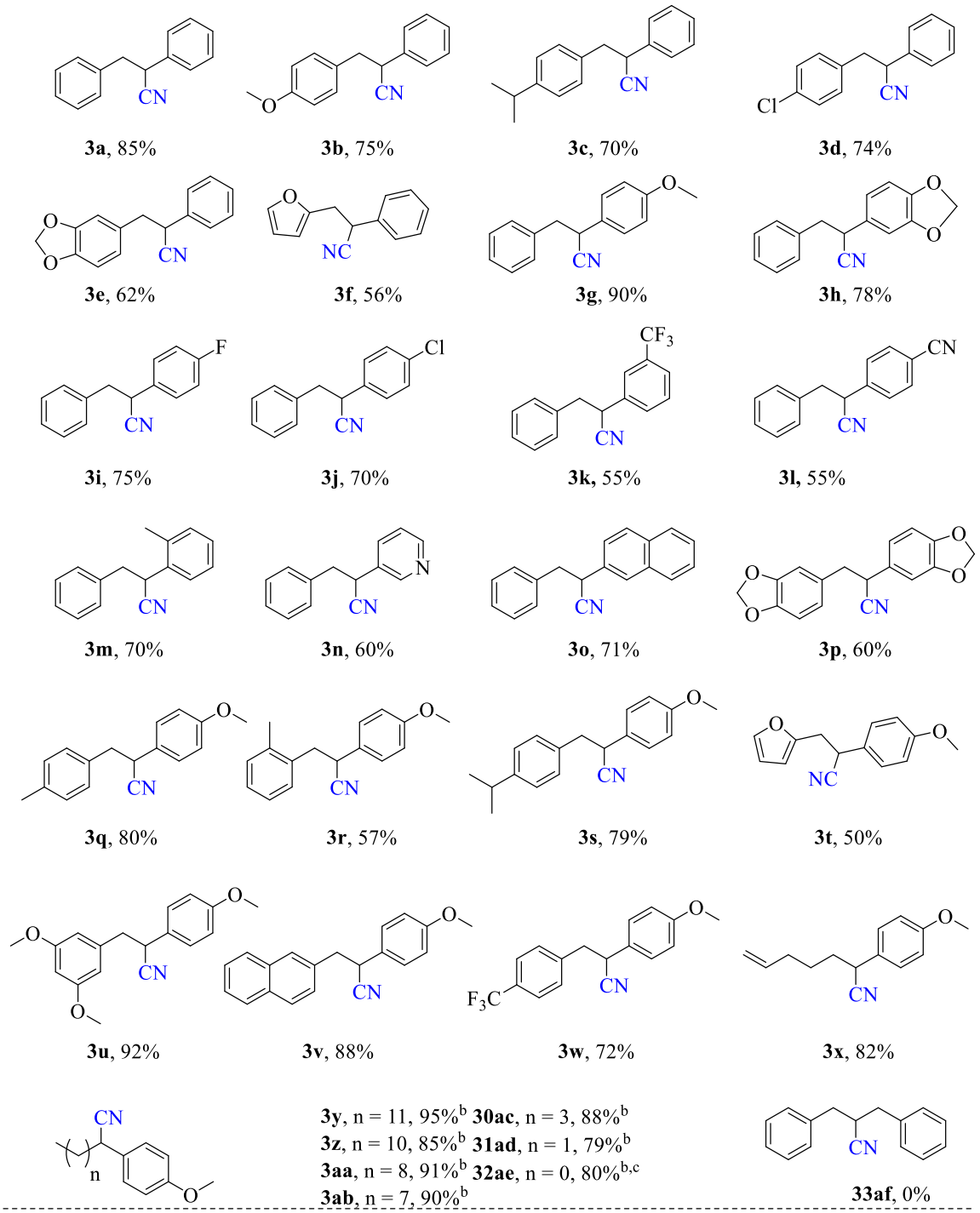
[a]Reaction conditions: **A** (1.3 mol %), KHBEt3 (3.5 mol %), base (20 mol%), **1a** (0.5 mmol), **2a** (0.25 mmol), and solvent (1.25 mL) were heated in a sealed 15 mL reaction tube for 24 h. [b]Yields were determined by ^{1}H NMR analysis of the crude reaction mixture with 1,3,5-trimethoxybenzene as an internal standard. Isolated yield is in parenthesis. [c]Reaction was carried out in the absence of $KHBEt_3$. [d]KOH (10 mol%) was used. [e]**A** (2.6 mol%) and $KHBEt_3$ (7 mol%) were used. [f]**1a** (2.0 mmol) and **2a** (1.0 mmol) were used. [g]6 h. [h]Mercury (125 mg) was added to the reaction.

With the optimized conditions in hand, we then probed the scope of the reaction by examining a wide range of primary alcohols and nitriles. First, we explored the scope of primary alcohols. Aromatic primary alcohols bearing electron-donating groups such as −OMe, $-^iPr$, and −Me at the para position afforded the desired nitriles in good 70−80% yields (Table 3.2, entries 3b, 3c, and 3q). Aromatic primary alcohols with electron-withdrawing groups like −Cl and $-CF_3$ at the para position also transformed smoothly (Table 3.2, entries 3d and 3w). 2-Methyl benzyl alcohol showed a diminished activity in a 57% yield probably due to the steric hindrance (Table 3.2, entry 3r). Notably, 2-naphthyl methanol proceeds successfully in a very good 88% yield (Table 3.2, entry 3v). Heteroaryl alcohols, such as piperonyl alcohol and 2-furyl methanol, furnished the corresponding nitriles in moderate yields (Table 3.2, entries 3e, 3f, 3p, and 3t). Moreover, aliphatic primary alcohols could also be applied to give the desired nitrile products in good to

excellent yields (80−95%) using 2.6 mol % **A** and 15 mol % KO^{t}Bu (Table 3.2, entries 3x−3ae). It is worth noting that the alkene functional group is intact (Table 3.2, entries 3x). A methanol/4-methoxybenzonitrile ratio of 10 was required to reach an 80% yield of 2-(4-methoxyphenyl)propanenitrile (Table 3.2, entry 3ae). Next, we investigated the scope of nitriles. Similarly, a variety of aromatic nitriles with electron donating or -withdrawing groups at different positions could be utilized for the alkylation reactions with 50−90% yields (Table 3.2, entries 3g−3ae). Importantly, nitriles bearing pyridyl and naphthyl ring delivered the corresponding products in 60 and 71% yields, respectively (Table 3.2, entries 3n and 3o). Unfortunately, benzenepropanenitrile and aliphatic nitriles did not work under these conditions (Table 3.2, entry 3af).

Table 3.2 α-Alkylation of Nitriles with Primary Alcohols[a,b,c]





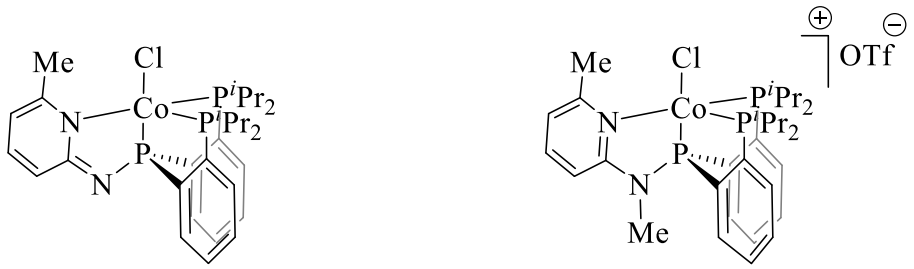
[a]Reaction conditions: **A** (1.3 mol%), $KHBEt_3$ (3.5 mol%), KOH (20 mol%), alcohol (0.5 mmol), nitrile (0.25 mmol), and toluene (1.25 mL), were heated in a 15 mL reaction tube

for 24 h. Isolated yields are given. [b]Reaction was carried out using **A** (2.6 mol%) and KO^{t}Bu (15 mol%). [c]Reaction was carried out using MeOH (2.5 mmol) for 60 h.

Next, we performed a mechanistic study to understand the nitrile alkylation reaction. We first explored the reactivity of **A** derivatives **B** and **C** using the model substrates[36] (Figure 1). **B** is air-sensitive, but **C** is air-stable. **B**, with a dearomatized pyridine arm, demonstrated a slightly diminished activity compared to **A** (73% yield), indicating **B** is also a precatalyst. **C** that bears a N−Me linker on the pyridine arm efficiently mediated the reaction leading to an 82% yield, suggesting metal−ligand cooperativity (MLC) that might originate from the N−H linker on **A** did not play an essential role.

We have shown that **A** can mediate the self-coupling of primary alcohols to esters.[37] Mechanistic study suggests a pathway that involves dehydrogenation of primary alcohols to aldehydes followed by the Tishchenko reaction to esters. We also reported dehydrogenation of secondary alcohols to ketones catalyzed by **A**.[36] Thus, aldehyde is likely an intermediate in the α-alkylation of nitriles with primary alcohols. The condensation of benzaldehyde and phenylacetonitrile under the optimal of 88% was also obtained (Scheme 2B). These results suggest that α,β-unsaturated nitrile is a possible intermediate,[39] and its formation can be mediated by base alone. Interestingly, the transfer hydrogenation of 2,3-diphenylacrylonitrile with benzyl alcohol (2 equiv) proceeded to completion by 20 mol % KOH in the standard conditions, with or without **A**/KHBEt$_3$. This

unexpected result supports a base mediated Meerwein-Ponndorf-Verley (MPV) hydrogenation pathway.[39-44]

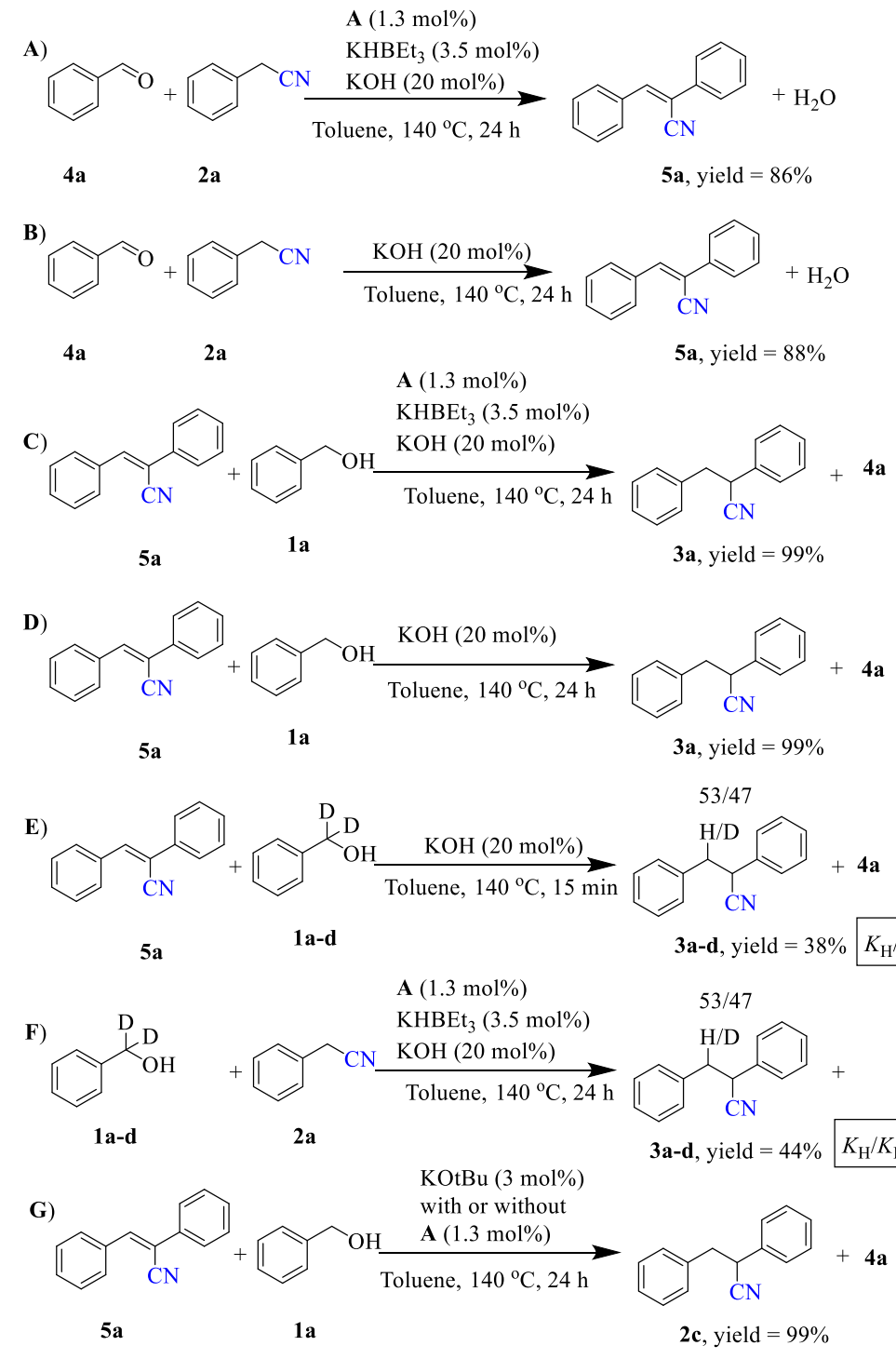


B **C**

Figure 3.1. **A** derivatives **B** and **C** examined.

Further investigations showed that the transfer hydrogenation can be finished in an hour by 20 mol % KOH. The deuterium labeling experiment utilizing benzyl alcohol-α,α-d_2 in the 2,3-diphenylacrylonitrile transfer hydrogenation resulted in a k_H/k_D ratio of 2.16 (Scheme 3.4), indicating that the cleavage of the α-C−H bond of benzyl alcohol is a slow step. The H/D ratio is close to unit, which suggests that the deuterium at the benzyl position transfers to the β position of the nitrile group in the MPV process. However, a H/D ratio close to 1:4 was obtained in the α-alkylation of phenylacetonitrile with benzyl alcohol-α,α-d_2 (Scheme 3.4). The incorporation of hydrogen infers that A-mediated dehydrogenation of primary alcohol may be reversible. A k_H/k_D ratio of 1.88 was acquired, which is in line with the result from the 2,3diphenylacrylonitrile transfer hydrogenation. Different bases were also examined. Employing only 3 mol % KO^{t}Bu with or without **A** both gave a full

conversion of 2,3-diphenylacrylonitrile in 24 h (Scheme 3.4), suggesting that A might not play a crucial role in the α,β-unsaturated nitrile hydrogenation step.



Scheme 3.4 Control experiments for the synthesis of α-alkylated nitriles

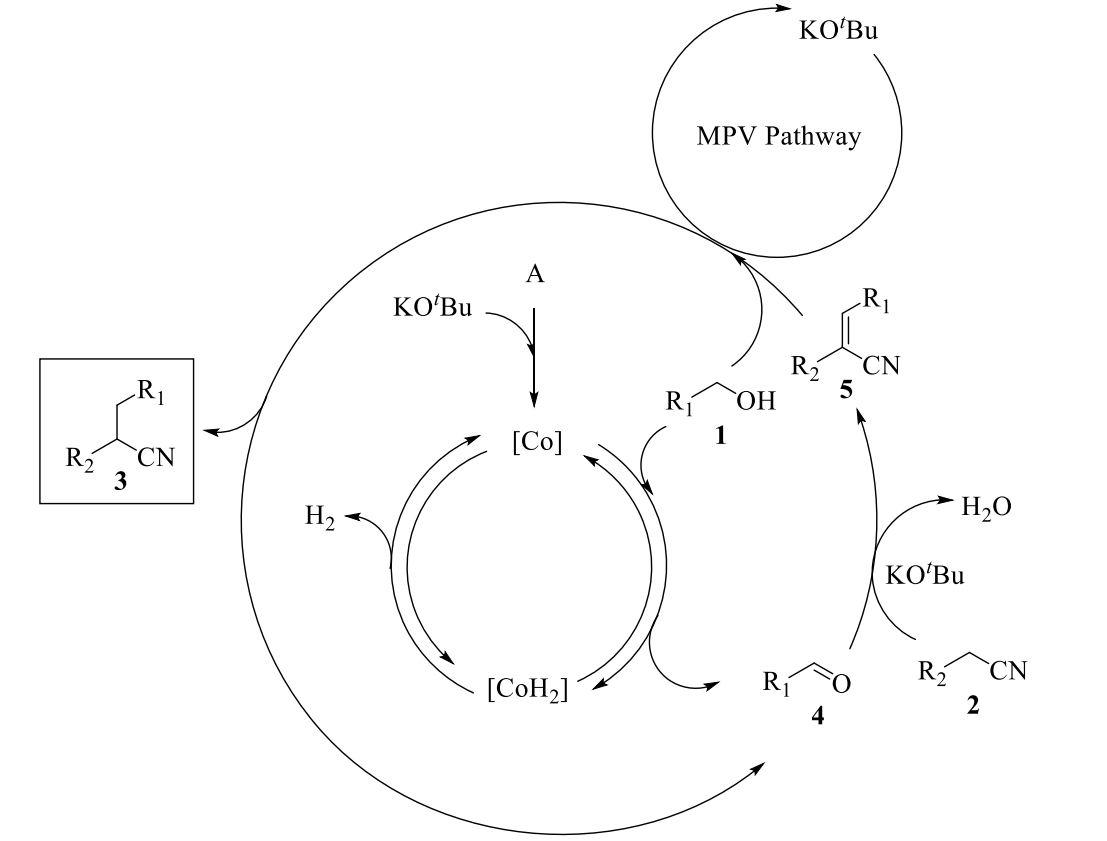


Fig. 3.2 Proposed reaction mechanism

Based on the mechanistic study, a plausible catalytic cycle is proposed as depicted in Scheme 3.2. Initial **A**-mediated primary alcohol dehydrogenation leads to aldehyde, which undergoes a nucleophilic attack by the nitrile substrate affording α,β unsaturated nitrile in the presence of base. Finally, the α,β unsaturated nitrile is reduced to the nitrile product via a base mediated MPV pathway. To the best of our knowledge, such a mechanism has not yet been revealed for the α-alkylation of nitriles. A more in-depth mechanistic investigation is ongoing in our laboratory.

3.3 Conclusion

In summary, we disclosed a well-defined molecular cobalt catalyst for the selective nitrile alkylation with primary alcohols to α-alkylated nitriles. Notably, this method is atom-efficient and environmentally friendly with water as the only byproduct. We expect this work will contribute to the development of base transition-metal catalysts in green synthesis.

3.4 Experimental Section

3.4.1 General Methods.

Unless otherwise is stated, all reactions were set up in an MBraun glovebox under an atmosphere of N_2. Anhydrous solvents were deoxygenated by sparging with N_2 and dried by passing through activated alumina columns of a Pure Solv solvent purification system. $CDCl_3$ was purchased from Cambridge Isotope Lab and dried over molecular sieves (4 Å). Cobalt complexes (A−C) were prepared according to our published procedures.[10a] Chemicals used in this paper were purchased from Sigma-Aldrich, Oakwood Chemical, or Fisher Scientific and used as received. NMR spectra were recorded on a JEOL Unity 500 or 300 MHz spectrometer. ^{1}H NMR spectra were referenced to tetramethyl silane (0.00 ppm) using $CDCl_3$ as a solvent. ^{13}C NMR were referenced to solvent carbons at 77.0 ppm for $CDCl_3$. ^{19}F NMR spectra were referenced to fluorobenzene at −113.15 ppm. HRMS were acquired from the Mass Spectrometry and Proteomics Facility at University of Notre Dame.

3.5 General Procedure for the α-Alkylation of Nitriles with Aryl Primary Alcohols Using A.

Inside a N_2-filled glovebox, a mixture of **A** (1.3 mol %), $KHBEt_3$ (3.5 mol %), KOH (20 mol %), nitrile (0.25 mmol), primary alcohol (0.5 mmol), and toluene (1.25 mL) was loaded into a 15 mL reaction vessel. The reaction vessel was sealed by a screw cap and brought out of the glovebox. The reaction tube was placed in a preheated oil bath at 140 °C for 24 h. After the reaction was finished and cooled down, the reaction mixture was

filtered through a silica gel plug and the collected filtrate was concentrated by a rotavap. The obtained residue was purified by a silica gel column using ethyl acetate/hexane (1:20, v/v) as an eluent, giving the pure alkylated nitrile product.

3.6 General Procedure for the α-Alkylation of Nitriles with Aliphatic Primary Alcohols Using A.

Inside a N_2-filled glovebox, a mixture of **A** (2.6 mol %), KO^{t}Bu (15 mol %), nitrile (0.25 mmol), primary alcohol (0.5 mmol), and toluene (1.25 mL) was loaded into a 15 mL reaction vessel. The reaction vessel was sealed by a screw cap and brought out of the glovebox. The reaction tube was placed in a preheated oil bath at 140 °C for 24 h. After the reaction was finished and cooled down, the reaction mixture was filtered through a silica gel plug and the collected filtrate was concentrated by a rotavap. The obtained residue was purified by a silica gel column using ethyl acetate/hexane (1:20, v/v) as an eluent, giving the pure alkylated nitrile product.

3.7 Procedure for the α-Alkylation of 4-Methoxybenzonitrile with Methanol Using A.

Inside a N_2-filled glovebox, a mixture of **A** (2.6 mol %), KO^{t}Bu (15 mol %), 4-methoxybenzonitrile (0.25 mmol), methanol (2.5 mmol), and toluene (1.25 mL) was loaded into a 15 mL reaction vessel. The reaction vessel was sealed by a screw cap and brought out of the glovebox. The reaction tube was placed in a preheated oil bath at 140 °C for 60 h. After the reaction was finished and cooled down, the reaction mixture was filtered through a silica gel plug and the collected filtrate was concentrated by a rotavap. The

obtained residue was purified by a silica gel column using ethyl acetate/hexane (1:20, v/v) as an eluent, giving the pure alkylated nitrile product.

3.8 Procedure for the α-Alkylation of Phenylacetonitrile with Benzyl Alcohols Using B.

Inside a N_2-filled glovebox, a mixture of **B** (1.3 mol %), $KHBEt_3$ (3.5 mol %), KOH (20 mol %), phenylacetonitrile (0.25 mmol), benzyl alcohol (0.5 mmol), and toluene (1.25 mL) was loaded into a 15 mL reaction vessel. The reaction vessel was sealed by a screw cap and brought out of the glovebox. The reaction tube was placed in a preheated oil bath at 140 °C for 24 h. After the reaction was finished and cooled down, the reaction mixture was filtered through a silica gel plug and the collected filtrate was concentrated by a rotavap. The obtained residue was purified by a silica gel column using ethyl acetate/hexane (1:20, v/v) as an eluent, giving the pure alkylated nitrile product.

3.9 Procedure for the α-Alkylation of Phenylacetonitrile with Benzyl Alcohols Using C.

Inside a N_2-filled glovebox, a mixture of **C** (1.3 mol %), $KHBEt_3$ (3.5 mol %), KOH (20 mol %), phenylacetonitrile (0.25 mmol), benzyl alcohol (0.5 mmol), and toluene (1.25 mL) was loaded into a 15 mL reaction vessel. The reaction vessel was sealed by a screw cap and brought out of the glovebox. The reaction tube was placed in a preheated oil bath at 140 °C for 24 h. After the reaction was finished and cooled down, the reaction mixture was filtered through a silica gel plug and the collected filtrate was concentrated by a rotavap.

The obtained residue was purified by a silica gel column using ethyl acetate/hexane (1:20, v/v) as an eluent, giving the pure alkylated nitrile product.

3.10 Procedure for the α-Alkylation of Phenylacetonitrile with Benzyl Alcohols Using A in 1.0 mmol Scale.

Inside a N_2-filled glovebox, a mixture of **A** (1.3 mol %), $KHBEt_3$ (3.5 mol %), KOH (20 mol %), phenylacetonitrile (1.0 mmol), benzyl alcohol (2.0 mmol), and toluene (2.0 mL) was loaded into a 15 mL reaction vessel. The reaction vessel was sealed by a screw cap and brought out of the glovebox. The reaction tube was placed in a preheated oil bath at 140 °C for 24 h. After the reaction was finished and cooled down, the reaction mixture was filtered through a silica gel plug and the collected filtrate was concentrated by a rotavap. The obtained residue was purified by a silica gel column using ethyl acetate/hexane (1:20, v/v) as an eluent, giving the pure alkylated nitrile product: 166 mg (80%).

3.11 Procedure for Homogeneity Test.

Inside a N_2-filled glovebox, a mixture of **A** (1.3 mol %), $KHBEt_3$ (3.5 mol %), KOH (20 mol %), phenylacetonitrile (0.25 mmol), benzyl alcohol (0.5 mmol), and toluene (1.25 mL) was loaded into a 15 mL reaction vessel and stirred at room temperature for 10 min. Mercury (125 mg, 0.625 mmol) was added to the vessel. The reaction vessel was sealed by a screw cap and brought out of the glovebox. The reaction tube was placed in a preheated oil bath at 140 °C for 24 h. After the reaction was finished and cooled down, the reaction mixture was filtered through a silica gel plug and the collected filtrate was concentrated by

a rotavap. The obtained residue was purified by a silica gel column using ethyl acetate/hexane (1:20, v/v) as an eluent, giving the pure alkylated nitrile product.

3.12 Procedure for Condensation of Benzaldehyde and Phenylacetonitrile by KOH or A/KHBEt$_3$/KOH.

Inside a N_2-filled glovebox, a mixture of **A** (0 or 1.3 mol %), KHBEt$_3$ (0 or 3.5 mol %), KOH (20 mol %), phenylacetonitrile (0.25 mmol), benzaldehyde (0.25 mmol), and toluene (1.25 mL) was loaded into a 15 mL reaction vessel. The reaction vessel was sealed by a screw cap and brought out of the glovebox. The reaction tube was placed in a preheated oil bath at 140 °C for 24 h. After the reaction was finished and cooled down, 1,3,5-trimethoxybenzene (8.4 mg, 0.05 mmol) dissolved in diethyl ether was added to the reaction mixture, stirred, and filtered through a silica gel plug. The plug was washed with diethyl ether, and the collected filtrate was concentrated under vacuum using a rotavapor. The obtained residue was dissolved in $CDCl_3$ and subjected to NMR analysis.

3.13 Procedure for Transfer Hydrogenation of 2,3-Diphenylacrylonitrile with Benzyl Alcohol by A/KO^{t}Bu or KO^{t}Bu.

Inside a N_2-filled glovebox, a mixture of **A** (1.3 mol %), KO^{t}Bu (3 mol %), 2,3diphenylacrylonitrile (0.25 mmol), benzyl alcohol (0.5 mmol), and toluene (1.25 mL) was loaded into a 15 mL reaction vessel. The reaction vessel was sealed by a screw cap and brought out of the glovebox. The reaction tube was placed in a preheated oil bath at 140 °C for 24 h. After the reaction was finished and cooled down, 1,3,5trimethoxybenzene (8.4 mg, 0.05 mmol) dissolved in diethyl ether was added to the reaction mixture, stirred,

and filtered through a silica gel plug. The plug was washed with diethyl ether, and the collected filtrate was concentrated under vacuum using a rotavapor. The obtained residue was dissolved in $CDCl_3$ and subjected to NMR analysis.

3.14 Procedure for Transfer Hydrogenation of 2,3-Diphenylacrylonitrile with Benzyl Alcohol by KOH or A/KHBEt$_3$/KOH.

Inside a N_2-filled glovebox, a mixture of **A** (0 or 1.3 mol%), $KHBEt_3$ (0 or 3.5 mol %), KOH (20 mol %), 2,3-diphenylacrylonitrile (0.25 mmol), benzyl alcohol (0.5 mmol), and toluene (1.25 mL) was loaded into a 15 mL reaction vessel. The reaction vessel was sealed by a screw cap and brought out of the glovebox. The reaction tube was placed in a preheated oil bath at 140 °C for 24 h. After the reaction was finished and cooled down, 1,3,5-trimethoxybenzene (8.4 mg, 0.05 mmol) dissolved in diethyl ether was added to the reaction mixture, stirred, and filtered through a silica gel plug. The plug was washed with diethyl ether, and the collected filtrate was concentrated under vacuum using a rotavapor. The obtained residue was dissolved in $CDCl_3$ and subjected to NMR analysis

3.15 Deuterium Labeling Experiment for the Transfer Hydrogenation of 2,3-Diphenylacrylonitrile with Benzyl Alcohol or Benzyl Alcohol-α,α-d$_2$ by KOH.

Inside a N_2-filled glovebox, a mixture of KOH (20 mol %), 2,3-diphenylacrylonitrile (0.25 mmol), benzyl alcohol or benzyl alcohol-α,α-d_2 (0.5 mmol), and toluene (1.25 mL) was loaded into a 15 mL reaction vessel. The reaction vessel was sealed by a screw cap and brought out of the glovebox. The reaction tube was placed in a preheated oil bath at 140 °C for 15 min. After the reaction was finished and cooled down, 1,3,5-trimethoxybenzene

(8.4 mg, 0.05 mmol) dissolved in diethyl ether was added to the reaction mixture, stirred, and filtered through a silica gel plug. The plug was washed with diethyl ether, and the collected filtrate was concentrated under vacuum using a rotavapor. The obtained residue was dissolved in $CDCl_3$ and subjected to NMR analysis.

3.16 Deuterium Labeling Experiment for the α-Alkylation of Phenylacetonitrile with Benzyl Alcohols or Benzyl Alcoholα,α-d_2 by A/KHBEt_3/KOH.

Inside a N_2-filled glovebox, a mixture of A (1.3 mol %), KHBEt_3 (3.5 mol %), KOH (20 mol %), phenylacetonitrile (0.25 mmol), benzyl alcohol or benzyl alcoholα,α-d_2 (0.5 mmol), and toluene (1.25 mL) was loaded into a 15 mL reaction vessel. The reaction vessel was sealed by a screw cap and brought out of the glovebox. The reaction tube was placed in a preheated oil bath at 140 °C for 6 h. After the reaction was finished and cooled down, 1,3,5-trimethoxybenzene (8.4 mg, 0.05 mmol) dissolved in diethyl ether was added to the reaction mixture, stirred, and filtered through a silica gel plug. The plug was washed with diethyl ether, and the collected filtrate was concentrated under vacuum using a rotavapor. The obtained residue was dissolved in $CDCl_3$ and subjected to NMR analysis.

3.17 Characterization data

2,3-Diphenylpropanenitrile[31] (3a): White solid; 44 mg (85%); ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.37−7.25 (m, 8H), 7.14−7.13 (m, 2H), 3.99 (dd, 1H, J = 8.4, 6.4 Hz), and 3.21−3.11 (m, 2H); and $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ 136.3, 135.3, 129.2, 129.1, 128.7, 128.2, 127.5, 127.4, 120.4, 42.2, and 39.8.

3-(4-Methoxyphenyl)-2-phenylpropanenitrile[31] (3b): White solid; 45 mg (75%); ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.37−7.31 (m, 3H), 7.26−7.25 (m, 2H), 7.04 (d, 2H, J = 10.5 Hz), 6.82 (d, 2H, J = 10.9 Hz), 3.96 (t, 1H, J = 7.7 Hz), 3.79 (s, 3H), and 3.16−3.07 (m, 2H); and $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 125 MHz): δ 158.9, 135.3, 130.3, 129.0, 128.4, 128.2, 127.5, 120.5, 114.0, 55.3, 41.5, and 40.1.

3-(4-Isopropylphenyl)-2-phenylpropanenitrile[33] (3c): White solid; 44 mg (70%); m.p. 65−67 °C; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.38− 7.33 (m, 3H), 7.30−7.28 (m, 2H), 7.16 (d, 2H, J = 8.1 Hz), 7.09 (d, 2H, J = 8.1 Hz), 3.97 (dd, 1H, J = 8.7, 6.2 Hz), 3.18−3.07 (m, 2H), 2.93−2.84 (m, 1H), and 1.24 (d, 6H, J = 6.9 Hz); and $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 125 MHz): δ 148.1, 135.5, 133.7, 129.1, 129.0, 128.2, 127.5, 126.7, 120.5, 41.9, 40.0, 33.8, and 24.0.

3-(4-Chlorophenyl)-2-phenylpropanenitrile[29] (3d): White solid; 45 mg (74%); ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.38−7.33 (m, 3H),7.27−7.23 (m, 4H), 7.04 (d, 2H, J = 8.4 Hz), 3.99 (dd, 1H, J = 7.9, 6.5 Hz), and 3.18−3.10 (m, 2H); and $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 125 MHz): δ 134.8, 134.6, 133.4, 130.6, 129.1, 128.8, 128.4, 127.5, 120.1, 41.5, and 39.6.

3-(Benzo[d][1,3]dioxol-5-yl)-2-phenylpropanenitrile[33] (3e): Colorless oil; 39 mg (62%); ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.37−7.33 (m, 3H), 7.27−7.26 (m, 2H), 6.73 (d, 1H, J = 7.9 Hz), 6.62−6.60 (m, 2H), 5.94 (s, 2H), 3.95 (dd, 1H, J = 8.3, 6.5 Hz), and 3.13−3.03 (m, 2H); and $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 125 MHz): δ 147.8, 146.9, 135.2, 130.0, 129.1, 128.3, 127.5, 122.5, 120.4, 109.5, 108.4, 101.1, 42.0, and 40.1.

3-(Furan-2-yl)-phenylpropanenitrile[29] (3f): Pale yellow oil; 28 mg (56%); ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.40−7.31 (m, 4H), 7.30−7.27 (m, 2H), 6.29 (dd, 1H, J = 3.1, 2.0

Hz), 6.11 (d, 1H, J = 3.4 Hz), 4.15 (dd, 1H, J = 8.5, 6.6 Hz), and 3.30−3.13 (m, 2H); and $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 125 MHz): δ 150.0, 142.2, 134.9, 129.1, 128.4, 127.3, 120.1, 110.5, 108.2, 37.1, and 34.7.

2-(4-Methoxyphenyl)-3-phenylpropanenitrile[31] (3g): White Solid; 53 mg (90%); ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.29−7.25 (m, 3H), 7.17−7.12 (m, 4H), 6.87 (d, 2H, J = 8.6 Hz), 3.95 (dd, 1H, J = 8.2, 6.6 Hz), 3.80 (s, 3H), and 3.19−3.08 (m, 2H); and $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 125 MHz): δ 159.5, 136.4, 129.3, 128.7, 128.6, 127.3, 127.3, 120.6, 114.4, 55.4, 42.3, and 39.0.

2-(Benzo[d][1,3]dioxol-5-yl)-3-phenylpropanenitrile[33] (3h): Colorless oil; 49 mg (78%); ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.32−7.26 (m, 3H), 7.15−7.13 (m, 2H), 6.76−6.75 (m, 2H), 6.69 (dd, 1H, J = 8.1, 1.7 Hz), 5.98 (s, 2H), 3.90 (dd, 1H, J = 8.2, 6.5 Hz), and 3.19− 3.07 (m, 2H); and $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 125 MHz): δ 148.2, 147.6, 136.3, 129.2, 128.9, 128.7, 127.4, 121.0, 120.4, 108.6, 107.9, 101.4, 42.3, and 39.5.

2-(4-Fluorophenyl)-3-phenylpropanenitrile[33] (3i): White solid; 42 mg (75%); ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.31−7.26 (m, 3H), 7.21−7.19 (m, 2H), 7.10 (dd, 2H, J = 7.6, 1.5 Hz), 7.03 (t, 2H, J = 8.6 Hz), 3.99 (dd, 1H, J = 7.8, 6.9 Hz), and 3.21−3.09 (m, 2H); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 125 MHz): δ 162.5 (d, J_{C-F} = 247.5 Hz), 135.9, 131.0 (d, J_{C-F} = 6.0 Hz), 129.3 (d, J_{C-F} = 6.0 Hz), 129.2, 128.7, 127.5, 120.2, 116.0 (d, J_{C-F} = 21.8 Hz), 42.2, and 39.0; and ^{19}F NMR (283 MHz, $CDCl_3$): δ −113.4.

2-(4-Chlorophenyl)-3-phenylpropanenitrile[31] (3j): White Solid; 42 mg (70%); ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.33−7.25 (m, 5H), 7.16 (d, 2H, J = 8.5 Hz), 7.10 (dd, 2H, J = 7.6,

1.7 Hz), 3.99 (dd, 1H, J = 7.8, 6.8 Hz), and 3.21−3.08 (m, 2H); and $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 125 MHz): δ 134.7, 133.2, 132.5, 128.1, 128.1, 127.8, 127.6, 126.4, 118.8, 40.9, and 38.1.

3-Phenyl-2-(3-(trifluoromethyl)phenyl)propanenitrile (3k): Colorless oil; 38 mg (55%); ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.60 (d, 1H, J = 7.7 Hz), 7.49(t, 1H, J = 8.0 Hz), 7.46−7.44 (m, 2H), 7.32−7.28 (m, 3H), 7.11 (dd, 2H, J = 7.4, 1.8 Hz), 4.08 (dd, 1H, J = 8.1, 6.5 Hz), and 3.25−3.13 (m, 2H); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 125 MHz): δ 136.2, 135.5, 131.5 (q, J_{C-F} = 33.1 Hz), 130.9, 129.6, 129.2, 128.8, 127.7, 125.9 (q, J_{C-F} = 272.0 Hz), 125.2 (d, J_{C-F} = 3.7 Hz), 124.5 (d, J_{C-F} = 3.7 Hz), 119.6, 42.0, and 39.6; ^{19}F NMR (283 MHz, $CDCl_3$): δ −62.6; HRMS (ESI+): m/z $[M]^+$ calcd for $C_{16}H_{12}NF_3$, 275.0922; found 275.0912.

4-(Benzyl-cyano-methyl)-benzonitrile (3l): White solid; 33 mg (57%); m.p. 84 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.65 (d, 2H, J = 8.4 Hz), 7.34 (d, 2H, J = 8.4 Hz), 7.30-7.27 (m, 3H,), 7.07 (dd, 2H, J = 7.0, 2.3 Hz), 4.08 (t, 1H, J = 7.2 Hz), and 3.19 (ddd, 2H, J = 20.3, 13.6, 7.2 Hz); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 125 MHz): 140.2, 135.2, 132.8, 129.2, 128.8, 128.5, 127.8, 119.2, 118.1, 112.6, 41.8, and 39.7; HRMS (ESI+): m/z $[M]^+$ calcd for $C_{16}H_{13}N_2$, 233.1073; found 233.1077.

3-Phenyl-2-(o-tolyl)propanenitrile[24] (3m): Colorless oil; 39 mg (70%); ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.44−7.42 (m, 1H), 7.33− 7.27 (m, 3H), 7.25−7.22 (m, 2H), 7.18−7.16 (m, 3H), 4.15 (dd, 1H, J = 8.9, 6.0 Hz), 3.18−3.06 (m, 2H), and 2.26 (s, 3H); and $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 125 MHz): δ 136.6, 135.1, 133.7, 131.0, 129.1, 128.7, 128.3, 127.7, 127.4, 126.9, 120.7, 41.0, 36.6, and 19.0.

3-Phenyl-2-(pyridin-3-yl)propanenitrile[22] (3n): Colorless solid; 31 mg (60%); ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.59 (dd, 1H, J = 4.9, 1.5 Hz), 8.46 (d, 1H, J = 2.4 Hz), 7.61−7.55 (m, 1H), 7.35−7.27 (m, 4H), 7.11 (dd, 2H, J = 7.4, 1.8 Hz), 4.06 (t, 1H, J = 7.2 Hz), and 3.26−3.13 (m, 2H); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 125 MHz): δ 149.7, 148.9, 135.4, 135.0, 131.0, 129.3, 128.8, 127.8, 123.7, 119.4, 41.9, and 37.3.

2-(Naphthalen-2-yl)-3-phenylpropanenitrile (3o): White solid; 46 mg (71%); m.p. 95−96 °C; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.86− 7.83 (m, 2H), 7.81−7.79 (m, 1H), 7.73 (d, 1H, J = 1.3 Hz), 7.51 (dd, 2H, J = 6.1, 3.2 Hz), 7.35 (dd, 1H, J = 8.5, 1.8 Hz), 7.31-7.26 (m, 3H), 7.16 (dd, 2H, J = 7.6, 1.8 Hz), 4.17 (dd, 1H, J = 8.2, 6.5 Hz), and 3.30−3.21 (m, 2H); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 125 MHz): δ 136.3, 133.3, 132.9, 132.5, 129.3, 129.0, 128.7, 127.9, 127.8, 127.5, 126.7, 126.7, 126.6, 125.0, 120.4, 42.2, and 40.0; HRMS (ESI+): m/z $[M]^+$ calcd for $C_{19}H_{15}N$, 257.1204; found 257.1212.

2,3-bis(Benzo[d][1,3]dioxol-5-yl)propanenitrile (3p): Colorless oil; 44 mg (60%); m.p. 64−66 °C; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 6.69 (dd, 3H), 6.62−6.58 (m, 2H), 5.98 (s, 2H), 5.95 (s, 2H), 3.85 (dd, 1H, J = 8.2, 6.6 Hz), and 3.09−2.99 (m, 2H); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 125 MHz): δ 148.2, 147.8, 147.6, 146.9, 129.9, 128.8, 122.5, 121.0, 120.4, 109.5, 108.6, 108.4, 107.9, 101.4, 101.1, 42.0, and 39.7; HRMS (ESI+): m/z $[M + Na]^+$ calcd for $C_{17}H_{13}NNaO_4$, 318.0737; found 318.0735.

2-(4-Methoxyphenyl)-3-(p-tolyl)propanenitrile[31] (3q): Colorless oil; 50 mg (80%); ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.17 (d, 2H, J = 8.7 Hz), 7.10 (d, 2H, J = 7.9 Hz), 7.02 (d, 2H, J = 8.0 Hz), 6.87 (d, 2H, J = 8.6 Hz), 3.92 (dd, 1H, J = 8.3, 6.5 Hz), 3.81 (s, 3H), 3.15−

3.04 (m, 2H), and 2.32 (s, 3H); and $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 125 MHz): δ 159.4, 137.0, 133.4, 129.3, 129.1, 128.7, 127.4, 120.7, 114.4, 55.4, 41.9, 39.2, and 21.1.

2-(4-Methoxyphenyl)-3-(o-tolyl)propanenitrile (3r): Colorless oil; 36 mg (57%); ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.22−7.08 (m, 6H), 6.87 (d, 2H, J = 8.6 Hz), 3.91 (dd, 1H, J = 8.5, 6.6 Hz), 3.81 (s, 3H), 3.23−3.07 (m, 2H), and 2.22 (s, 3H); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 125 MHz): δ 159.5, 136.3, 134.8, 130.6, 130.1, 128.6, 127.5, 126.3, 120.8, 114.4, 55.4, 39.6, 38.0, and 19.3; HRMS (ESI+): m/z $[M + H]^+$ calcd for $C_{17}H_{18}NO$, 252.1382; found 252.1374.

3-(4-Isopropylphenyl)-2-(4-methoxyphenyl) phenylpropanenitrile[31] (3s): White solid; 55 mg (79%); m.p. 67−69 °C; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.19 (d, 2H, J = 8.7 Hz), 7.16 (d, 2H, J = 8.1 Hz), 7.08 (d, 2H, J = 8.1 Hz), 6.88 (d, 2H, J = 8.7 Hz), 3.92 (dd, 1H, J = 8.7, 6.2 Hz), 3.81 (s, 3H), 3.15−3.04 (m, 2H), 2.93−2.84 (m, 1H), and 1.24 (d, 6H, J = 6.9 Hz); and $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 125 MHz): δ 159.4, 148.0, 133.8, 129.1, 128.6, 127.5, 126.7, 120.8, 114.4, 55.4, 42.0, 39.2, 33.8, and 24.0.

3-(Furan-2-yl)-2-(4-methoxyphen-yl)propanenitrile (3t): Colorless oil; 28 mg (50%); ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.38−7.32 (m, 1H), 7.19 (d, 2H, J = 8.7 Hz), 6.88 (d, 2H, J = 8.6 Hz), 6.29 (dd, 1H, J = 3.1, 1.9 Hz), 6.11 (d, 1H, J = 3.7 Hz), 4.09 (dd, 1H, J = 8.3, 6.7 Hz), 3.81 (s, 3H), and 3.27−3.10 (m, 2H); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 125 MHz): δ 159.6, 150.1, 142.1, 128.4, 126.9, 120.4, 114.5, 110.5, 108.2, 55.4, 36.3, and 34.8; HRMS (ESI+): m/z $[M + Na]^+$ calcd for $C_{14}H_{13}NNaO_2$, 250.0838; found 250.0840.

3-(3,5-Dimethoxyphenyl)-2-(4-methoxyphenyl)propanenitrile (3u): Pale yellow oil; 68 mg (92%); ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.18(d, 2H, J = 8.7 Hz), 6.88 (d, 2H, J = 8.6 Hz), 6.36 (t, 2H, J = 2.2 Hz), 6.28 (d, 2H, J = 2.3 Hz), 3.94 (dd, 1H, J = 8.3, 6.5 Hz), 3.81 (s, 3H), 3.74 (s, 6H), and 3.13−3.01 (m, 2H); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 125 MHz): δ 160.9, 159.5, 138.7, 128.7, 127.3, 120.7, 114.4, 107.3, 99.49, 55.4, 55.3, 42.6, and 38.8; HRMS (ESI+): m/z $[M + Na]^+$ calcd for $C_{18}H_{19}NNaO_3$, 320.1257; found 320.1256.

2-(4-Methoxyphenyl)-3-(naphthal-en-2-yl)propanenitrile[31] (3v): Pale yellow oil; 63 mg (88%); ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.84− 7.80 (m, 1H), 7.77 (d, 2H, J = 8.0 Hz), 7.60 (s, 1H), 7.49−7.43 (m, 2H), 7.23 (dd, 1H, J = 8.3, 1.8 Hz), 7.18 (d, 2H, J = 8.7 Hz), 6.86 (d, 2H, J = 8.6 Hz), 4.05 (dd, 1H, J = 8.1, 6.7 Hz), 3.80 (s, 3H), and 3.36−3.24 (m, 2H); and $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 125 MHz): δ 159.5, 133.9, 133.4, 132.6, 128.7, 128.3, 128.2, 127.8, 127.7, 127.2, 126.2, 125.9, 120.7, 114.4, 55.4, 42.5, and 39.0.

2-(4-Methoxyphenyl)-3-(4-(trifluoromethyl)phenyl)propanenitrile[31] (3w): Colorless oil; 55 mg (72%); ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.55 (d, 2H, J = 8.1 Hz), 7.23 (d, 2H, J = 8.1 Hz), 7.15 (d, 2H, J = 8.7 Hz), 6.88 (d, 2H, J = 8.6 Hz), 3.9 (t, 1H, J = 7.5 Hz), 3.81 (s, 3H), and 3.24−3.15 (m, 2H); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 125 MHz): δ 159.6, 140.2, 129.7, 128.6, 126.5, 125.6 (q, J_{C-F} = 3.7 Hz), 124.1 (q, J_{C-F} = 270.0 Hz), 120.2, 114.5, 55.4, 41.9, and 38.6; and ^{19}F NMR (283 MHz, $CDCl_3$): δ −62.4.

2-(4-Methoxyphenyl)hept-6-enenitrile (3x): Colorless oil; 44 mg (82%); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.23 (d, 2H, J = 8.6 Hz), 6.90 (d, 2H, J = 8.6 Hz), 5.75 (ddt, 1H, J = 16.9, 10.1, 6.7 Hz), 5.07−4.89 (m, 2H), 3.81 (s, 3H) 3.73 (dd, 1H, J = 8.2, 6.5 Hz), 2.09 (q,

2H, J = 7.1 Hz), 1.96−1.76 (m, 2H), and 1.63−1.45 (m, 2H); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 125 MHz): 159.4, 137.6, 128.4, 127.9, 121.1, 115.4, 114.5, 55.4, 36.5, 35.3, 33.0, and 26.1; HRMS (ESI+): m/z $[M]^+$ calcd for $C_{14}H_{18}NO$, 216.1383; found 216.1388.

2-(4-Methoxyphenyl)tetradecanenitrile (3y): Colorless oil; 75 mg (95%); ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.23 (d, 2H, J = 8.7 Hz), 6.90 (d, 2H, J = 8.6 Hz), 3.81 (s, 3H), 3.71 (dd, 1H, J = 8.5, 6.3 Hz), 1.93−1.78 (m, 2H), 1.50−1.37 (m, 2H), 1.30−1.25 (m, 18H), and 0.88 (t, 3H, J = 6.9 Hz); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 125 MHz): δ 158.4, 127.5, 127.3, 120.3, 113.5, 54.5, 35.7, 35.1, 31.0, 28.8, 28.7, 28.6, 28.5, 28.5, 28.1, 26.1, 21.8, and 13.2; HRMS (ESI+): m/z $[M + H]^+$ calcd for $C_{21}H_{34}NO$, 316.2635; found 316.2631.

2-(4-Methoxyphenyl)tridecanenitrile (3z): Colorless oil; 64 mg (85%); ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.23 (d, 2H, J = 8.7 Hz), 6.90 (d, 2H, J = 8.8 Hz), 3.81 (s, 3H), 3.71 (dd, 1H, J = 8.5, 6.4 Hz), 1.93−1.78 (m, 2H), 1.50−1.37 (m, 2H), 1.31−1.25 (m, 16H), and 0.88 (t, 3H, J = 6.9 Hz); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 125 MHz): δ 159.4, 128.4, 128.2, 121.3, 114.5, 55.4, 36.7, 36.0, 32.0, 29.7, 29.7, 29.6, 29.4, 29.0, 29.0, 27.1, 22.8, and 14.2; HRMS (ESI+): m/z $[M + Na]^+$ calcd for $C_{20}H_{31}NNaO$, 324.2297; found 324.2289.

2-(4-Methoxyphenyl)undecanenitrile[31] (3aa): Colorless oil; 62 mg (91%); ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.23 (d, 2H, J = 8.7 Hz), 6.90 (d, 2H, J = 8.8 Hz), 3.81 (s, 3H), 3.71 (dd, 1H, J = 8.5, 6.3 Hz), 1.93−1.78 (m, 2H), 1.50−1.37 (m, 2H), 1.30−1.25 (m, 12H), and 0.88 (t, 3H, J = 6.9 Hz); and $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 125 MHz): δ 159.3, 128.4, 128.1, 121.2, 114.4, 55.4, 36.6, 36.0, 31.9, 29.5, 29.3, 29.3, 29.0, 27.0, 22.7, and 14.1.

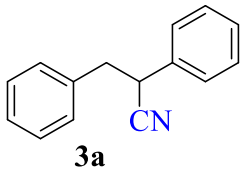
2-(4-Methoxyphenyl)decanenitrile (3ab): Colorless oil; 58 mg (90%); ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.23 (d, 2H, J = 8.7 Hz), 6.90 (d, 2H, J = 8.7 Hz), 3.81 (s, 3H), 3.71 (dd, 1H, J = 8.3, 6.5 Hz), 1.93−1.78 (m, 2H), 1.51−1.38 (m, 2H), 1.30−1.25 (m, 10H), and 0.87 (t, 3H, J = 6.8 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz): δ 159.3, 128.4, 128.1, 121.2, 114.4, 55.4, 36.6, 36.0, 31.8, 29.3, 29.2, 29.0, 27.0, 22.6, and 14.1; HRMS (ESI+): m/z $[M + Na]^+$ calcd for $C_{17}H_{25}NNaO$, 282.1828; found 282.1824.

2-(4-Methoxyphenyl)hexanenitrile[31] (3ac): Colorless oil; 45 mg (88%); ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.24 (d, 2H, J = 8.7 Hz), 6.90 (d, 2H, J = 8.8 Hz), 3.81 (s, 3H), 3.71 (dd, 1H, J = 8.5, 6.4 Hz), 1.94−1.79 (m, 2H), 1.47−1.31 (m, 4H), and 0.90 (t, 3H, J = 7.2 Hz); and ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz): δ 158.2, 127.3, 127.0, 120.1, 113.3, 54.3, 35.5, 34.6, 28.0, 21.0, and 12.7.

2-(4-Methoxyphenyl)butanenitrile[31] (3ad): Colorless oil; 35 mg (79%); ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.24 (d, 2H, J = 8.5 Hz), 6.90 (d, 2H, J = 8.8 Hz), 3.81 (s, 3H), 3.68 (dd, 1H, J = 7.8, 6.6 Hz), 1.95−1.87 (m, 2H), and 1.06 (t, 3H, J = 7.4 Hz); and ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz): δ 159.3, 128.4, 127.8, 121.0, 114.4, 55.4, 38.2, 29.3, and 11.5.

2-(4-Methoxyphenyl)propanenitrile[28] (3ae): Yellowish oil; 33 mg (80%); ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.28−7.25 (m, 2H), 6.93− 6.88 (m, 2H), 3.85 (q, 1H, J = 7.3 Hz), 3.81 (s, 3H), and 1.62 (d, 3H, J = 7.1 Hz); and ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz): δ 159.4, 129.1, 127.9, 121.8, 114.5, 55.4, 30.5, and 21.5.

3.18 Supplementary figures



3a

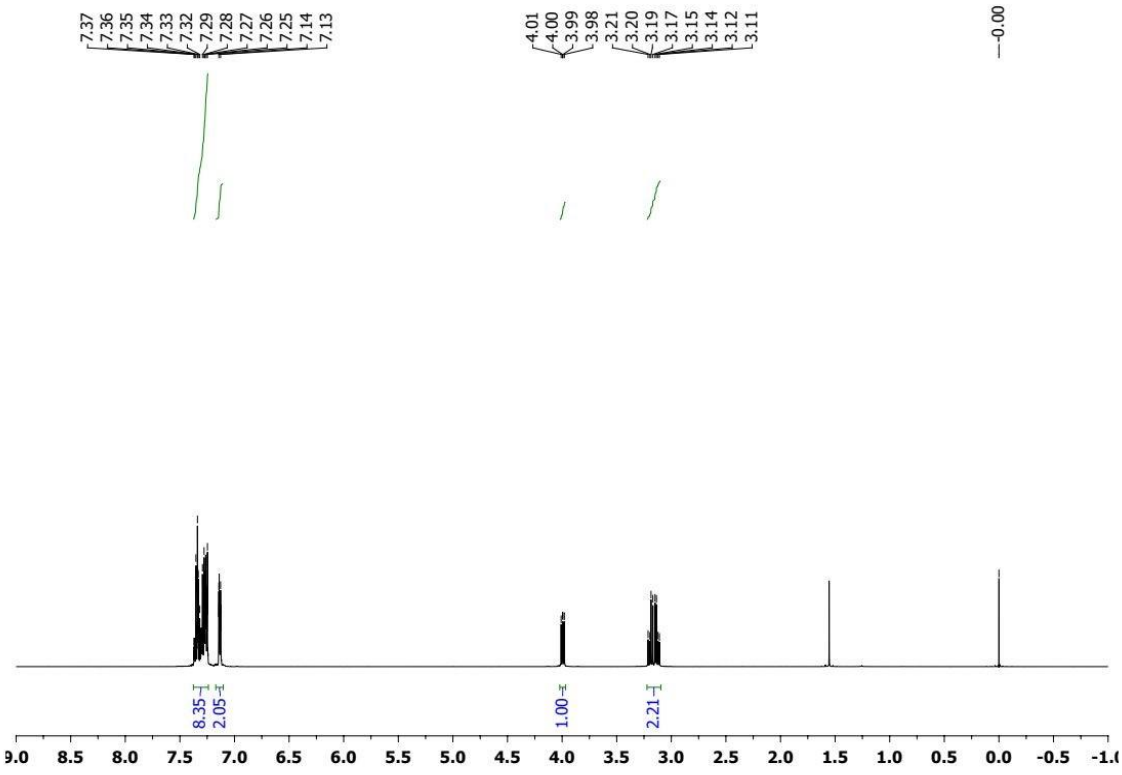


Figure 3.3 ^{1}H NMR ($CDCl_3$, 500 MHz) of 3a

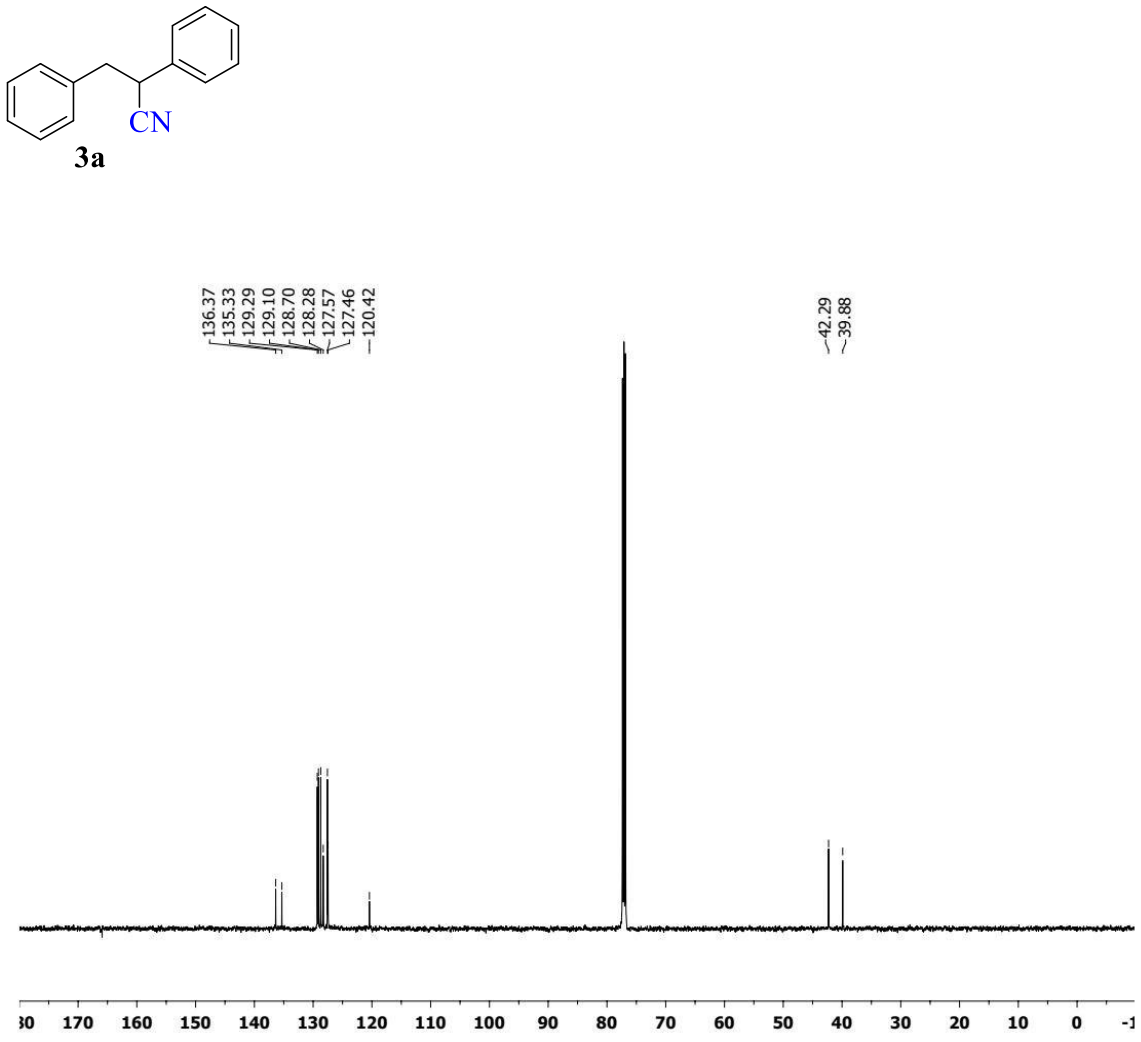
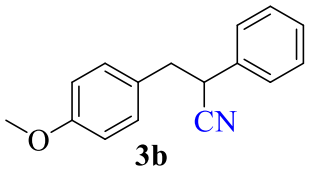


Figure 3.4 ^{13}C NMR ($CDCl_3$, 125 MHz) of 3a



3b

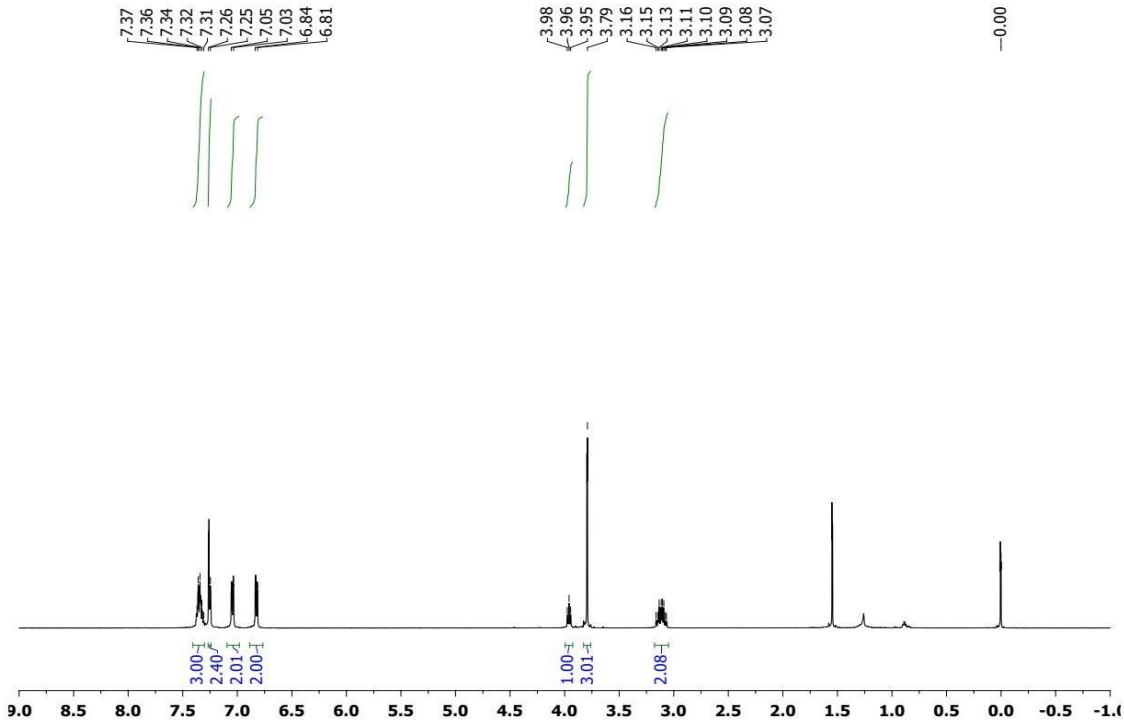


Figure 3.5 ^{1}H NMR ($CDCl_3$, 500 MHz) of 3b

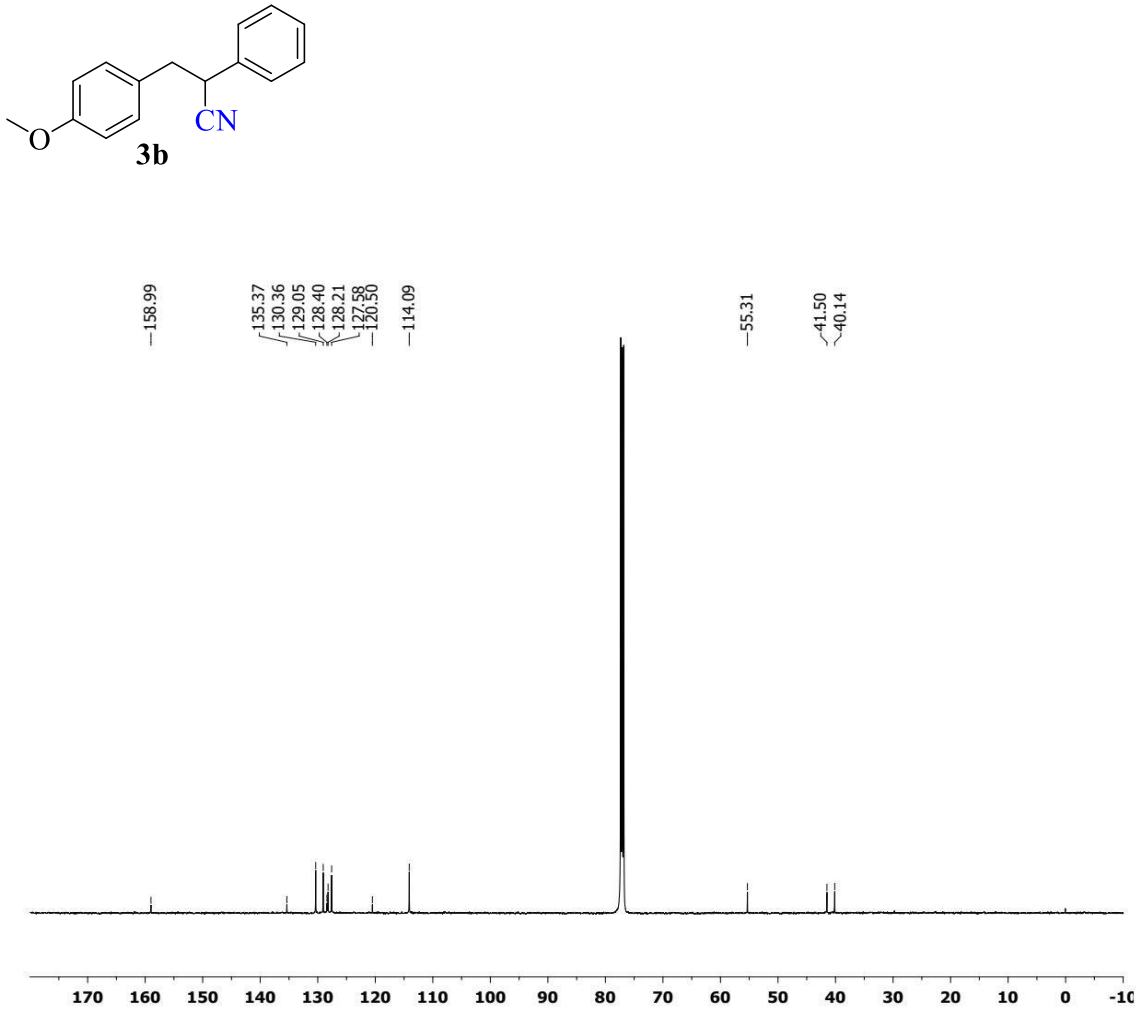


Figure 3.6 ^{13}C NMR ($CDCl_3$, 125 MHz) of 3b

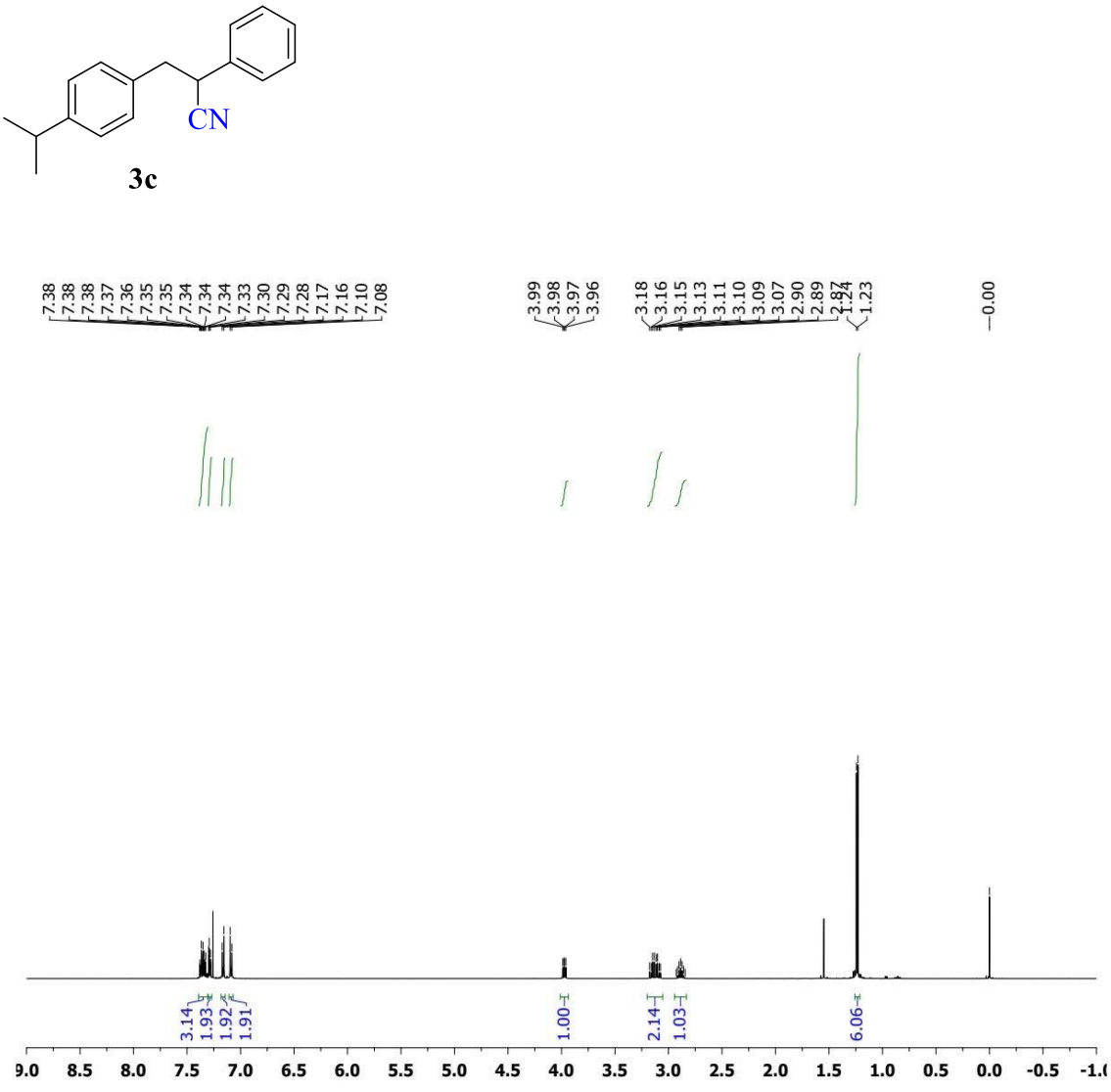


Figure 3.7 ^{1}H NMR ($CDCl_3$, 500 MHz) of 3c

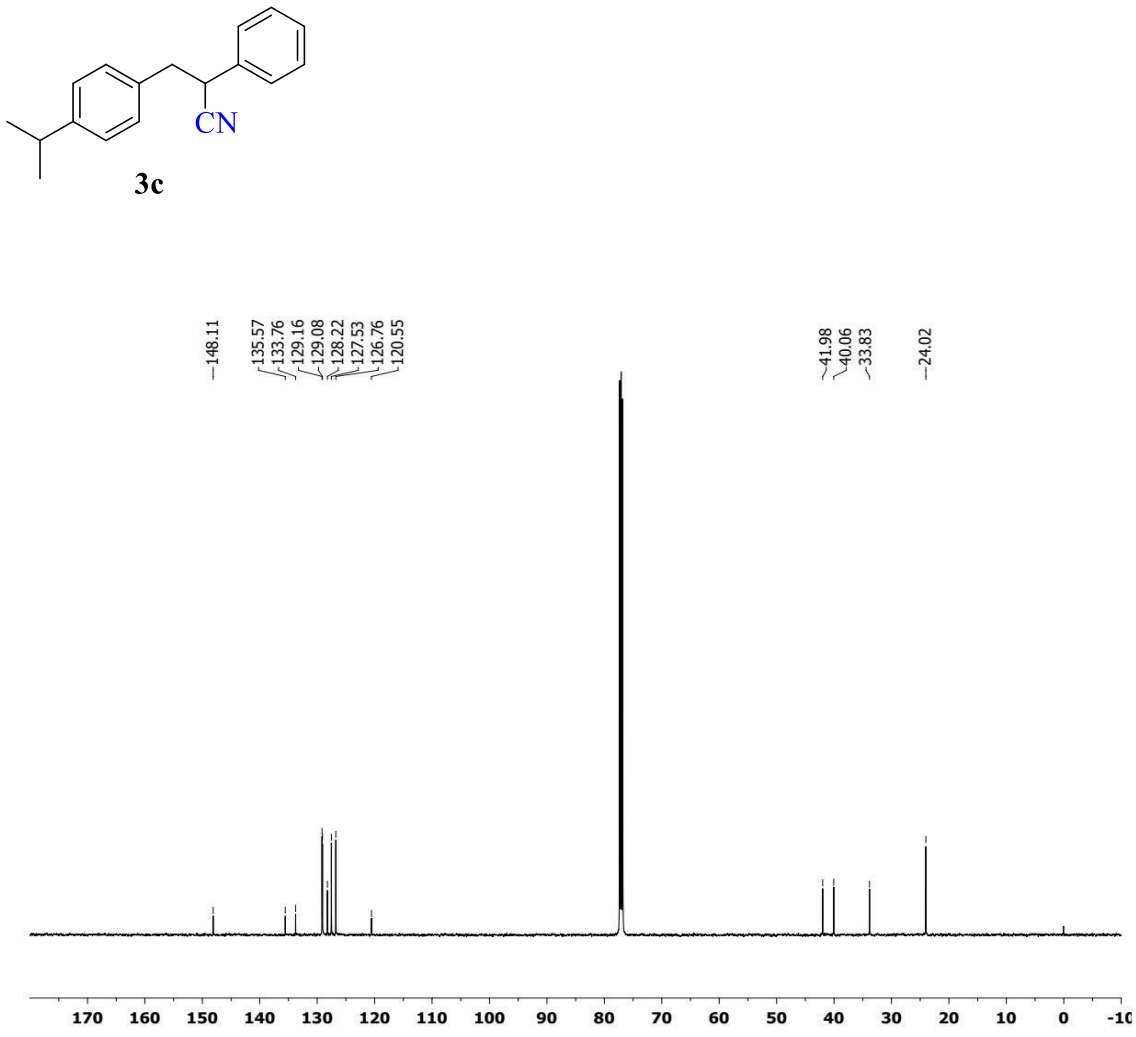


Figure 3.8 ^{13}C NMR ($CDCl_3$, 125 MHz) of 3c

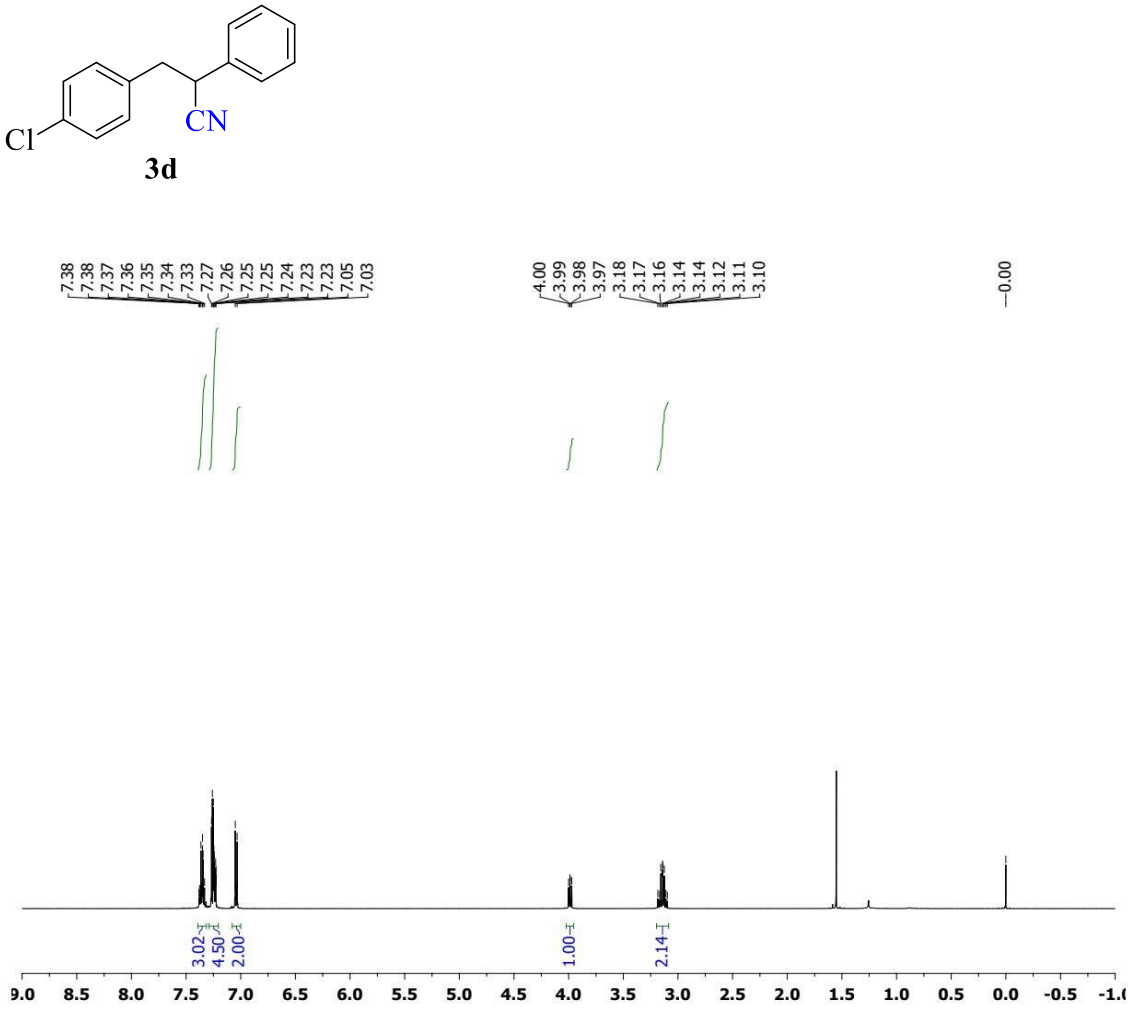
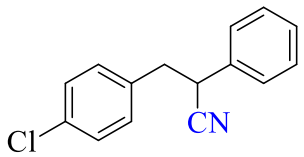


Figure 3.9 ^{1}H NMR ($CDCl_3$, 500 MHz) of 3d



3d

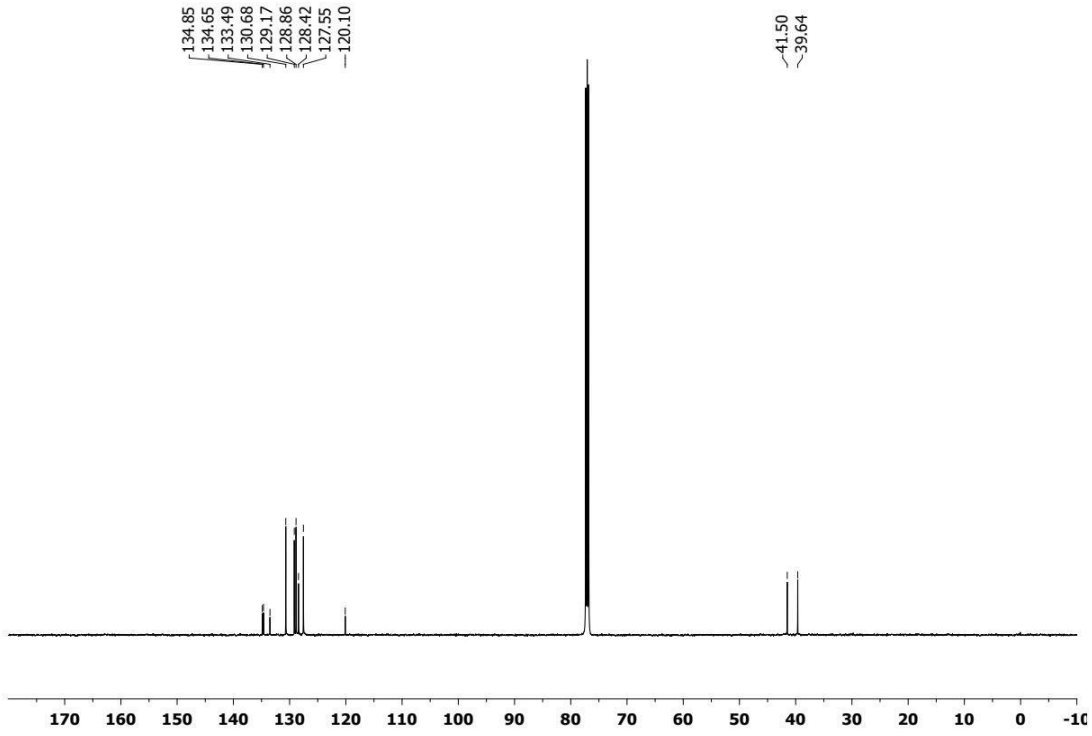
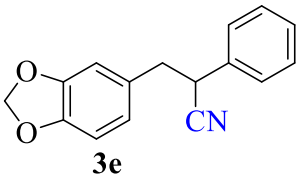


Figure 3.10 ^{13}C NMR ($CDCl_3$, 125 MHz) of 3d



3e

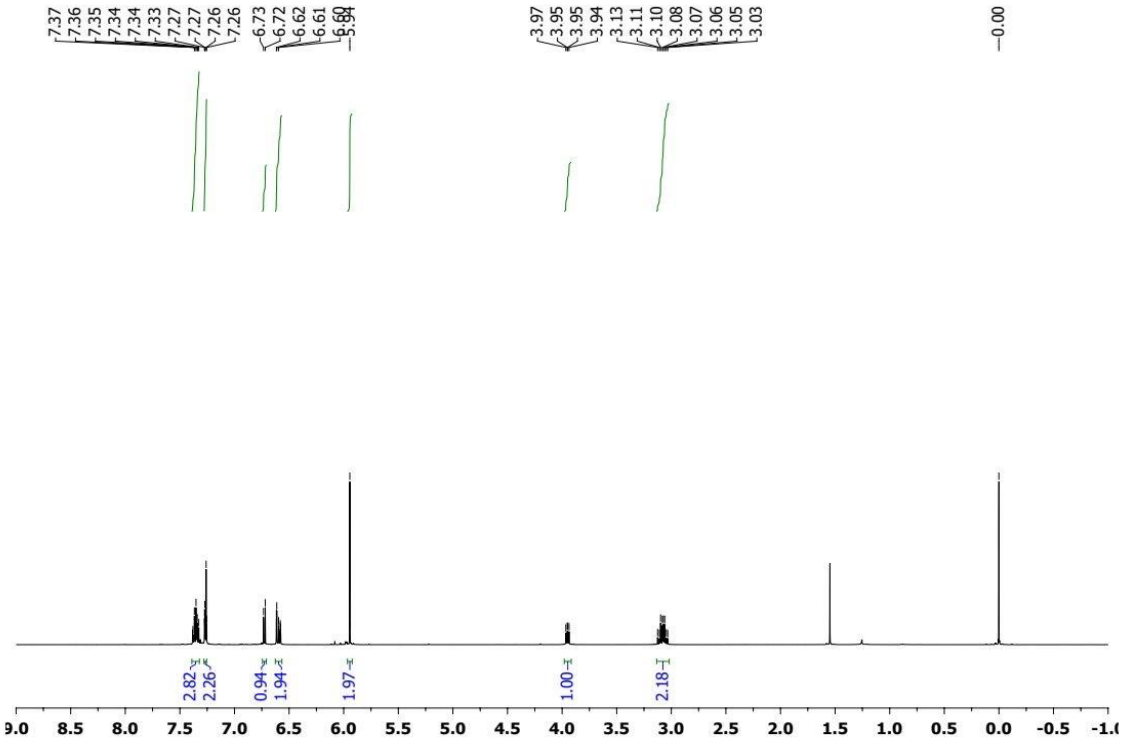


Figure 3.11 ^{1}H NMR ($CDCl_3$, 500 MHz) of 3e

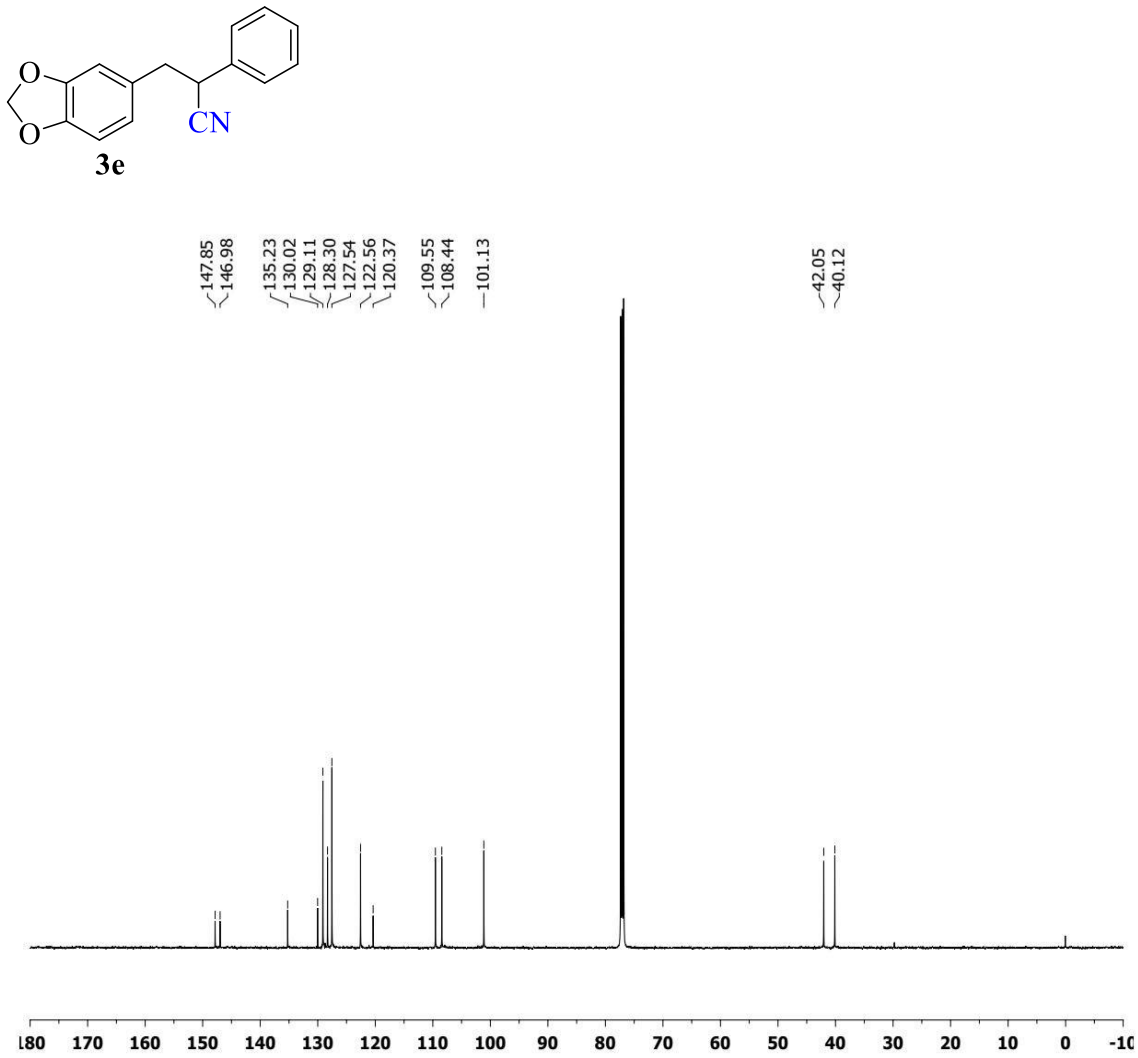
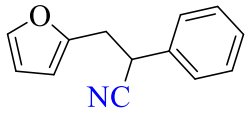


Figure 3.12 ^{13}C NMR ($CDCl_3$, 125 MHz) of 3e



3f

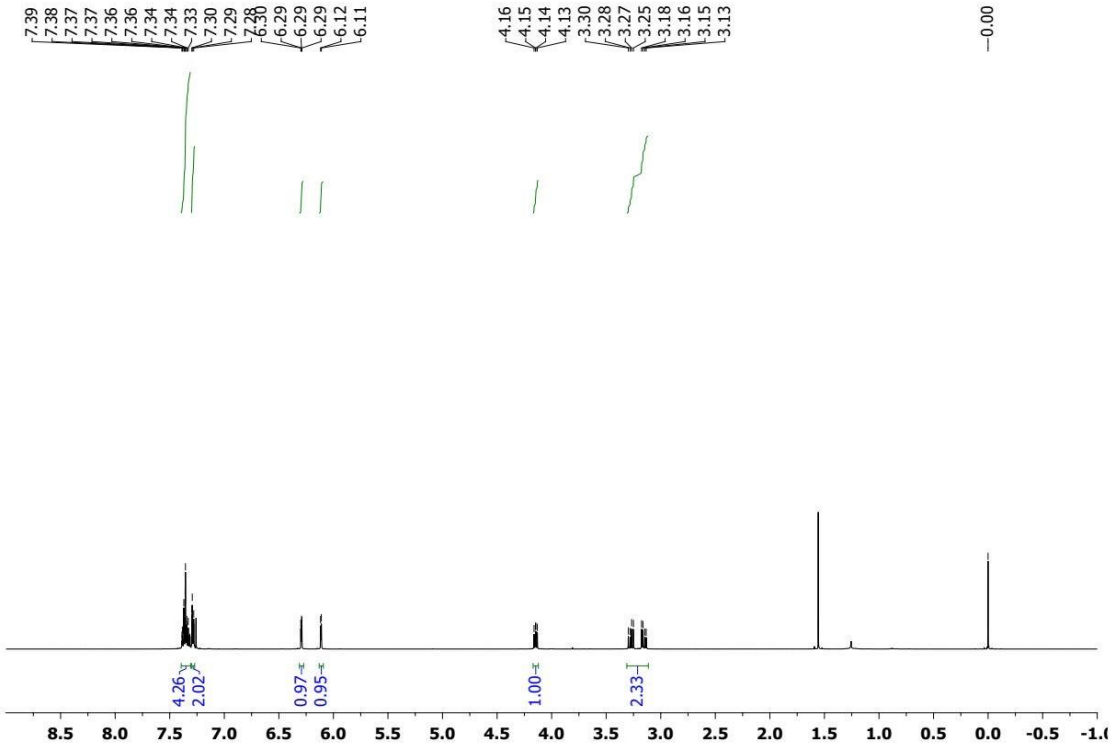
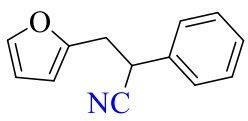


Figure 3.13 ^{1}H NMR ($CDCl_3$, 500 MHz) of 3f



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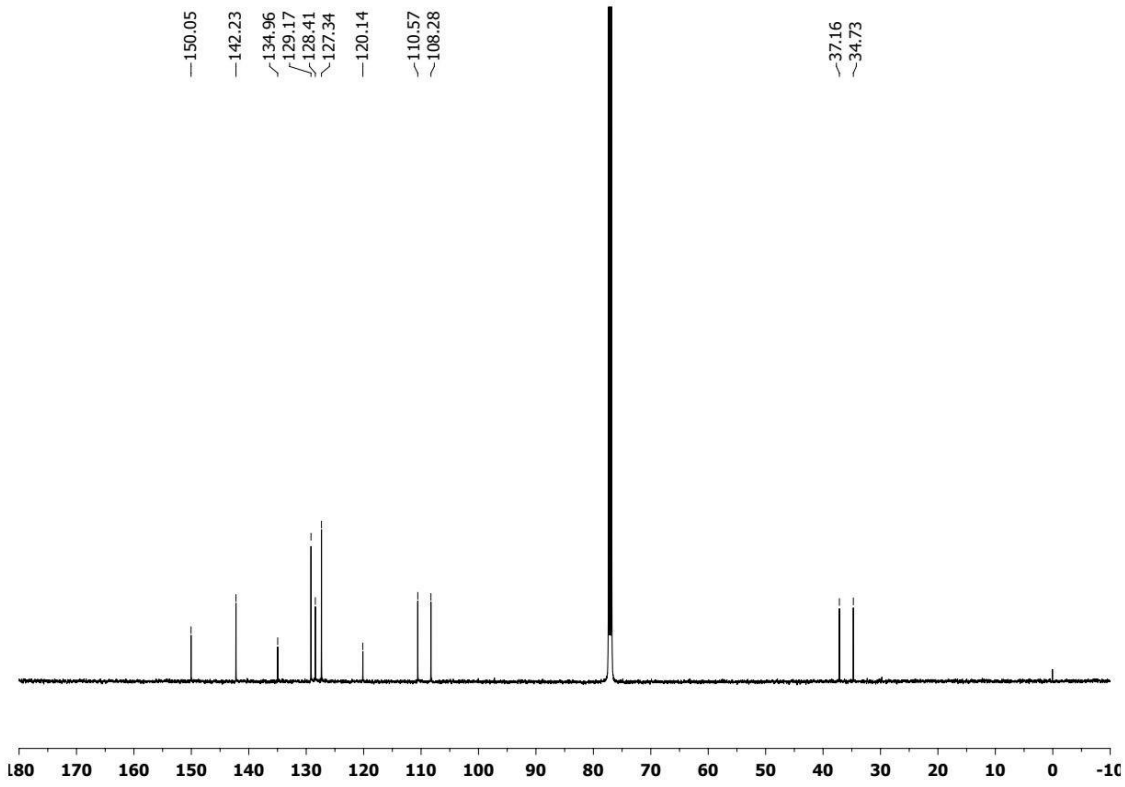
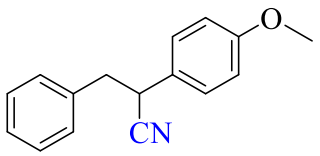


Figure 3.14 ^{13}C NMR ($CDCl_3$, 125 MHz) of 3f



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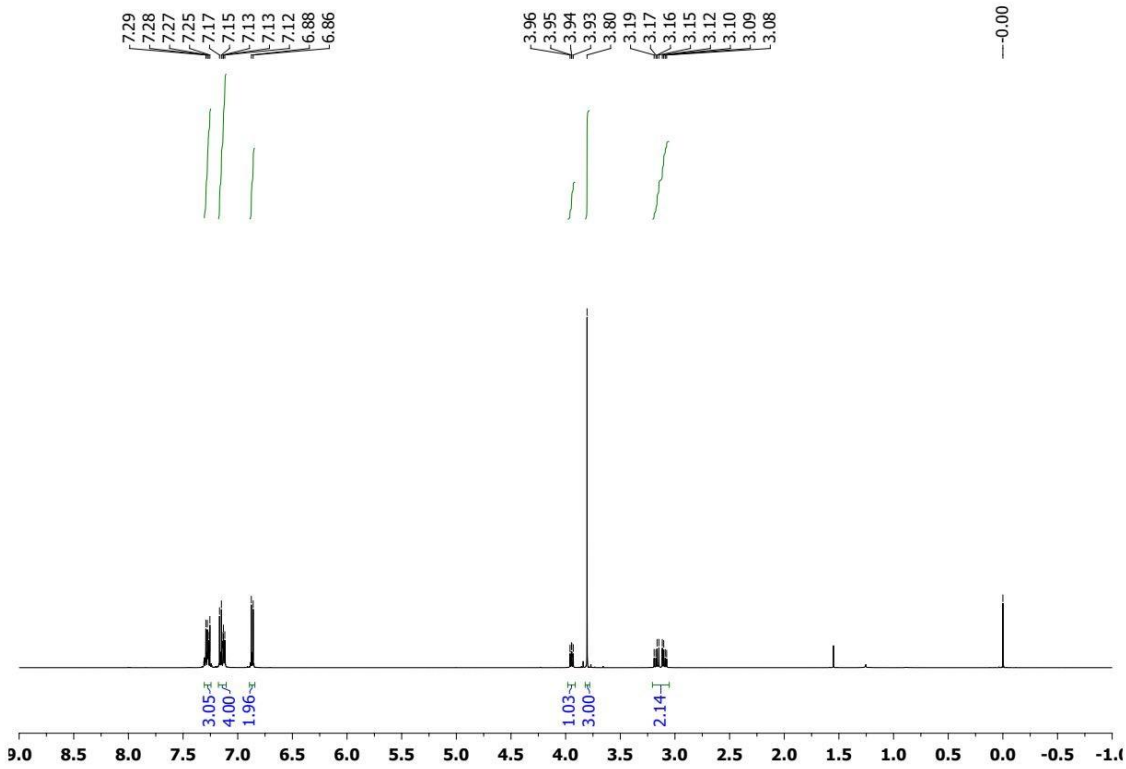
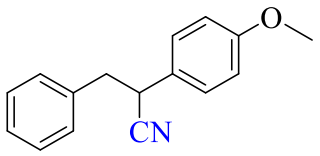


Figure 3.15 ^{1}H NMR ($CDCl_3$, 500 MHz) of 3g



3g

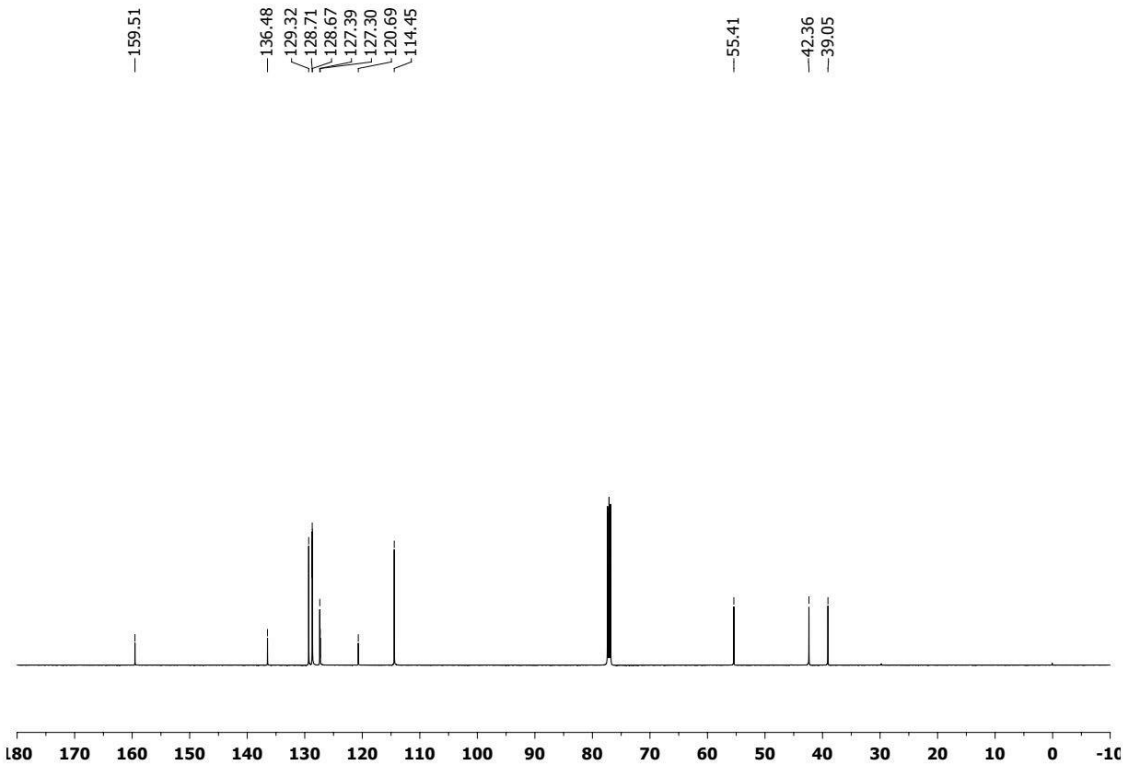
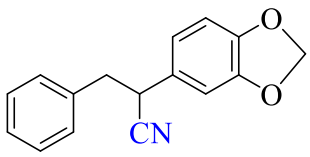


Figure 3.16 ^{13}C NMR ($CDCl_3$, 125 MHz) of 3g



3h

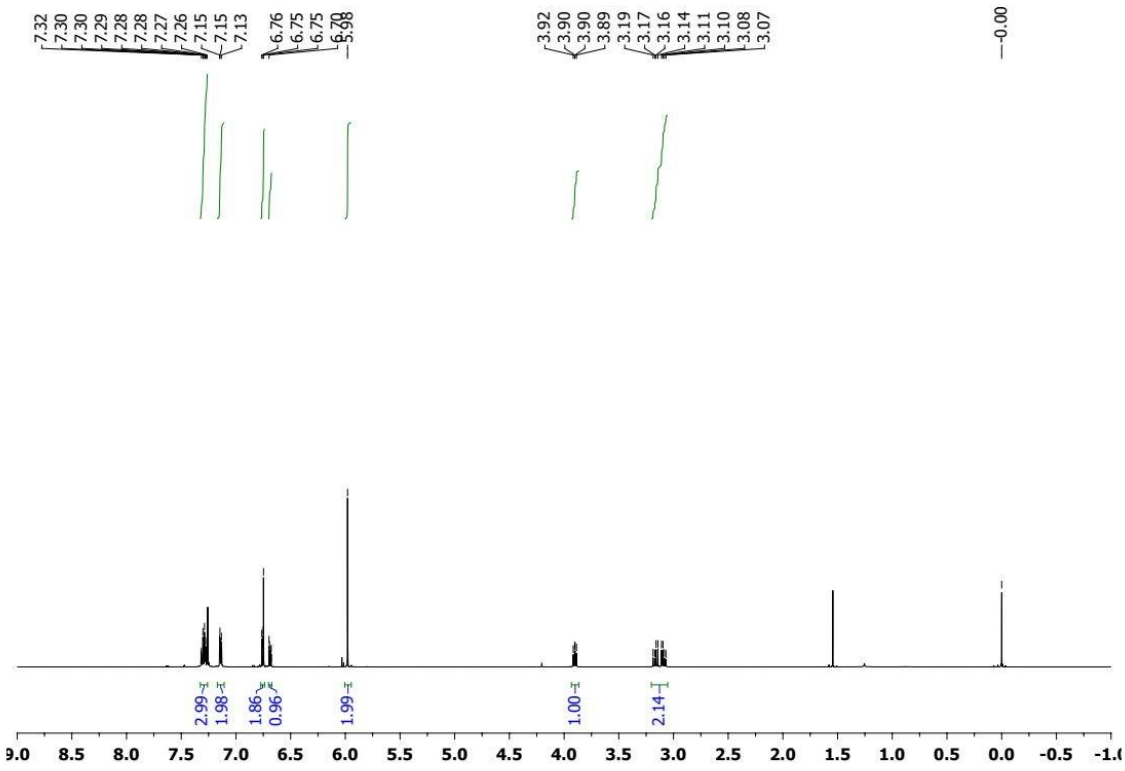
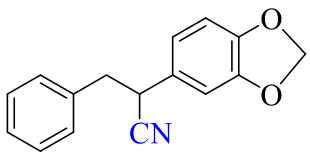


Figure 3.17 ^{1}H NMR ($CDCl_3$, 500 MHz) of 3h



3h

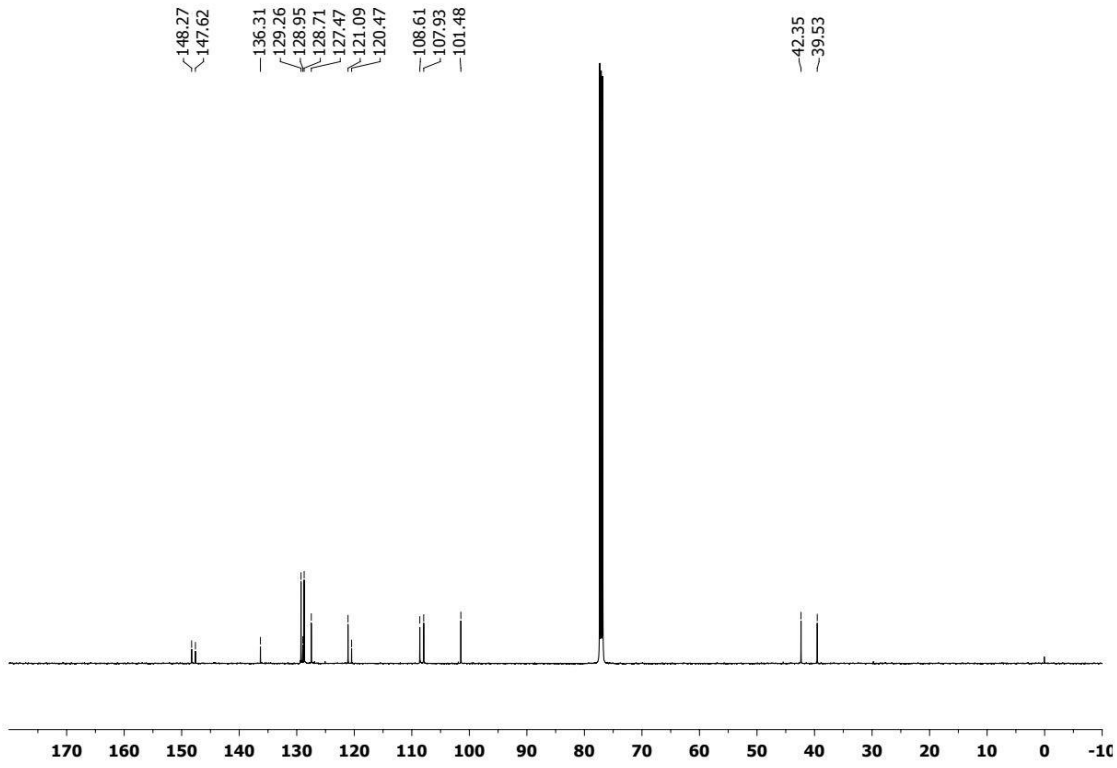
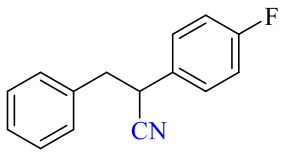


Figure 3.18 ^{13}C NMR ($CDCl_3$, 125 MHz) of 3h



3i

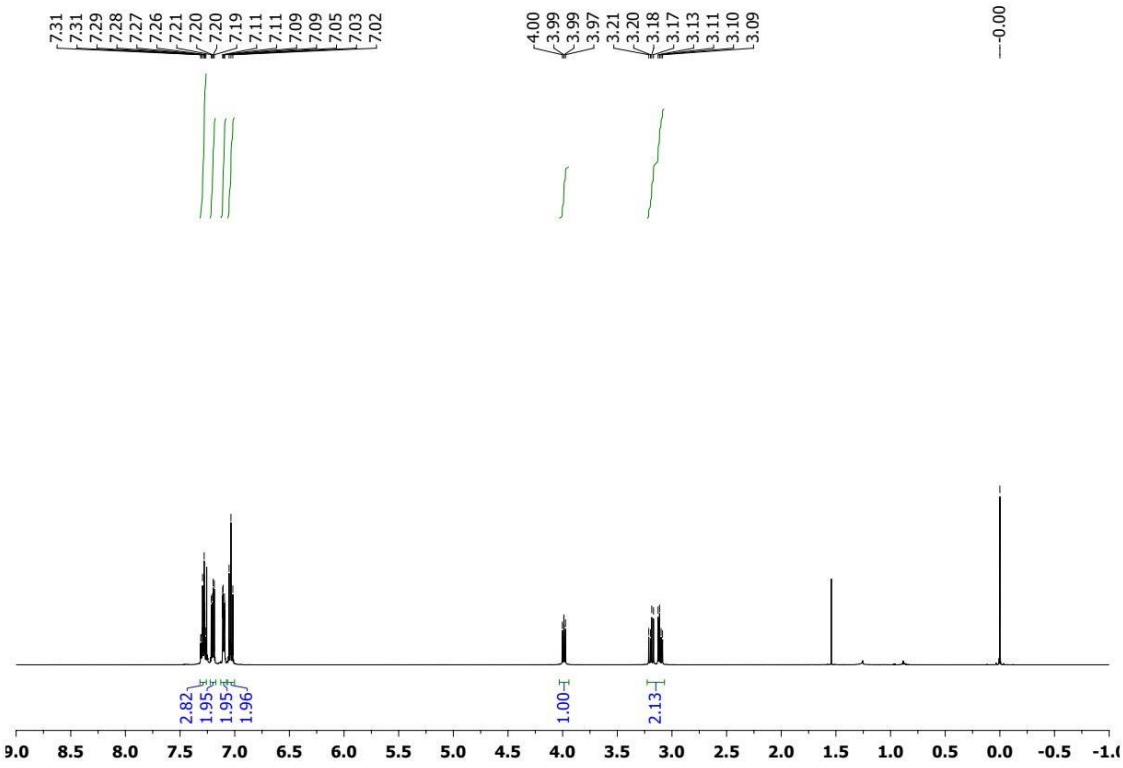
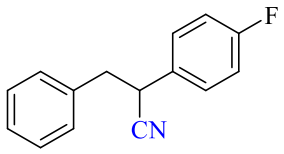


Figure 3.19 ^{1}H NMR ($CDCl_3$, 500 MHz) of 3i



3i

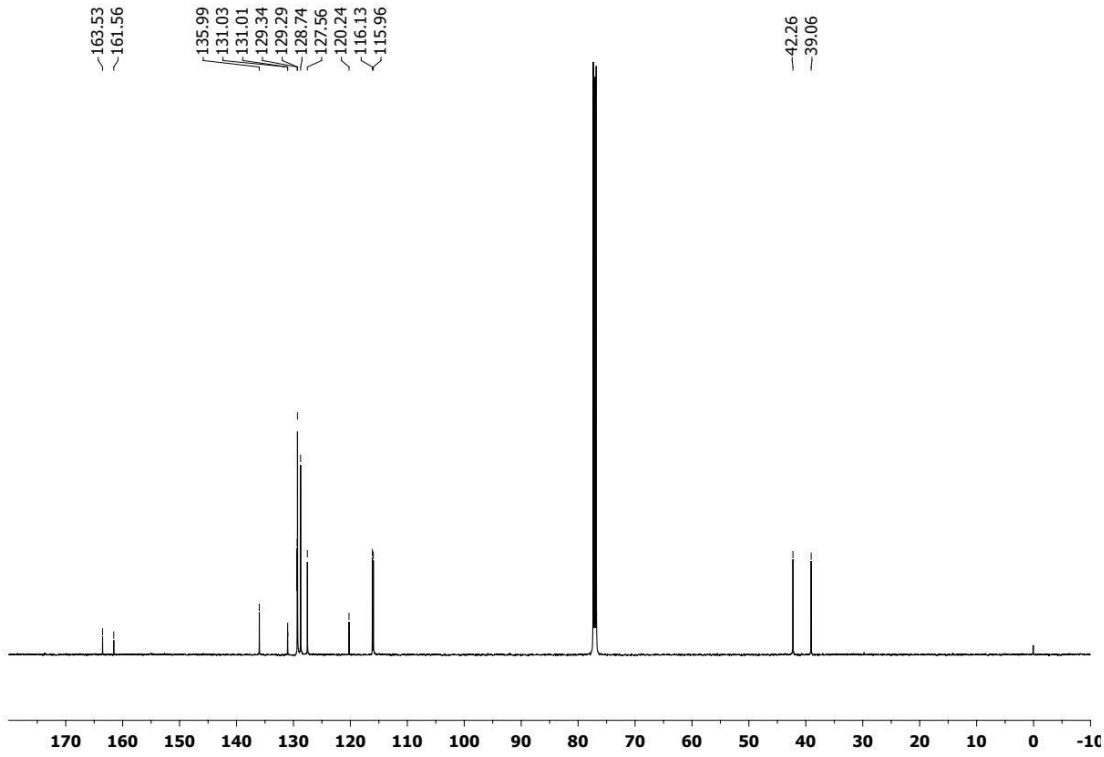
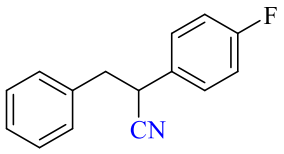


Figure 3.20 ^{13}C NMR ($CDCl_3$, 125 MHz) of 3i



3i

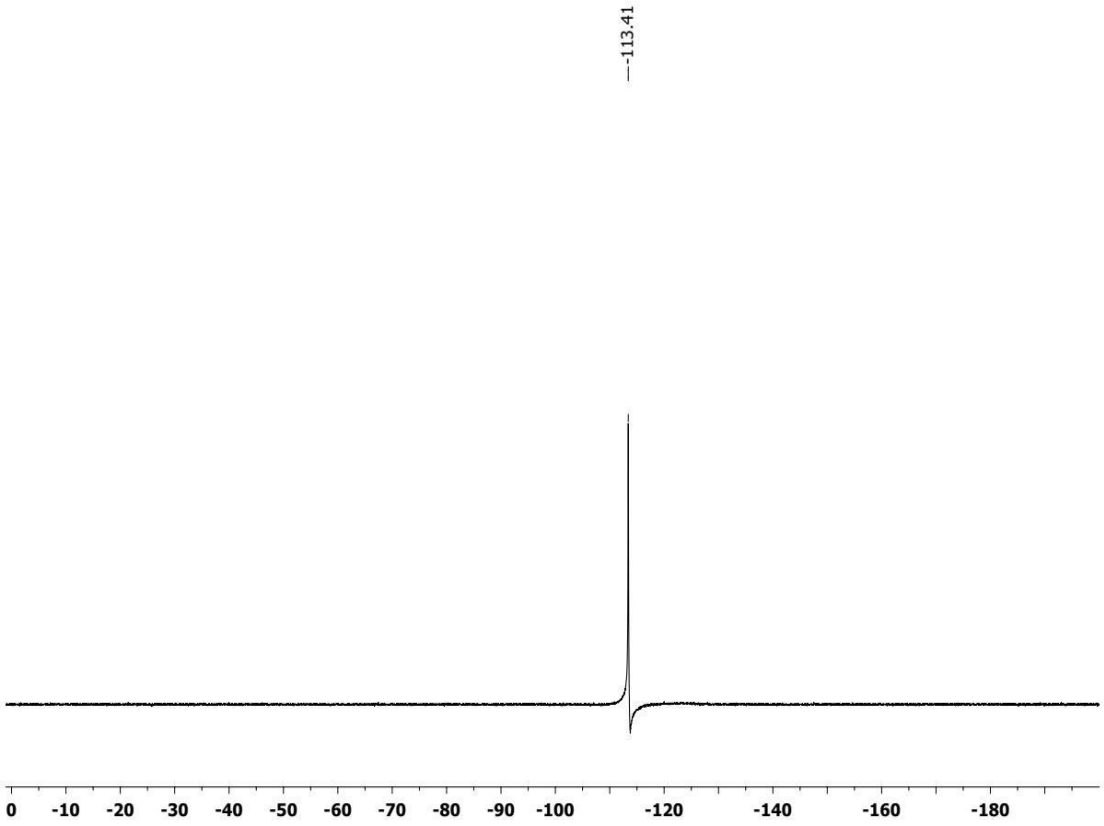
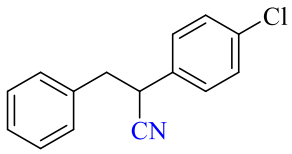


Figure 3.21 ^{19}F NMR (CDCl3, 283 MHz) of 3i



3j

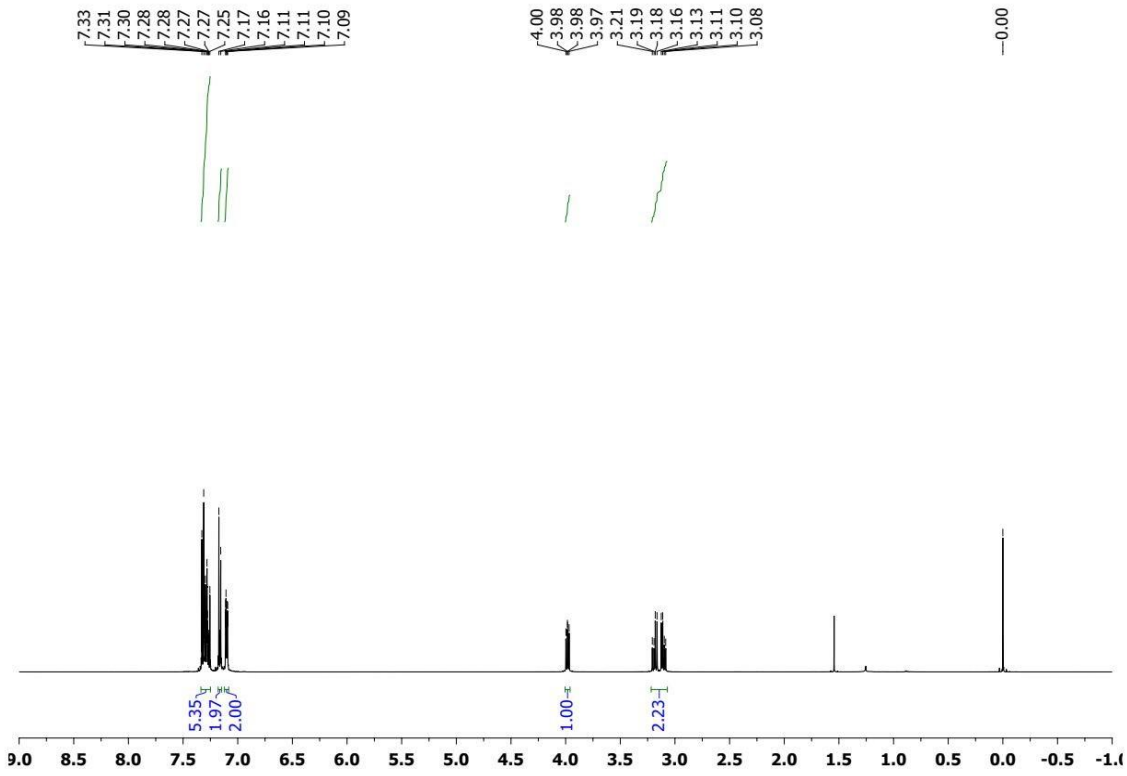
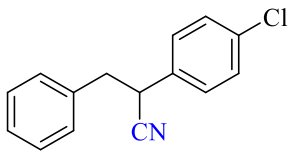


Figure 3.22 ^{1}H NMR ($CDCl_3$, 500 MHz) of 3j



3j

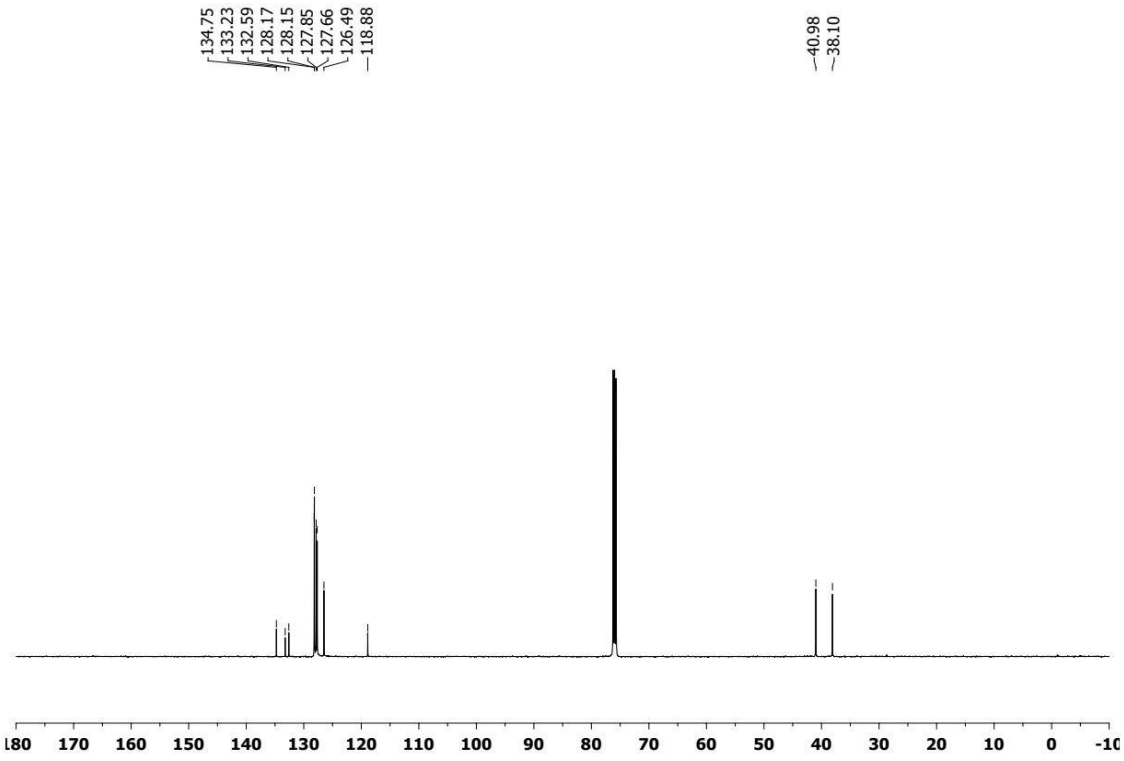
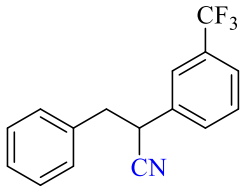


Figure 3.23 ^{13}C NMR ($CDCl_3$, 125 MHz) of 3j



3k

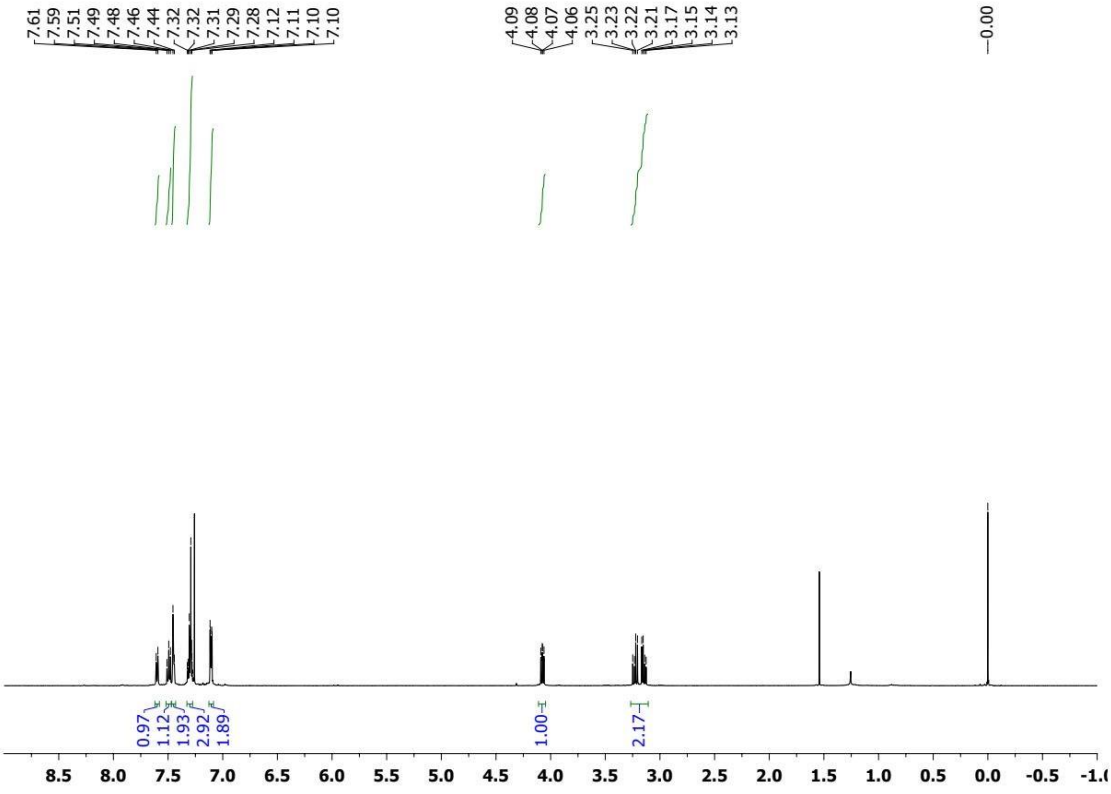
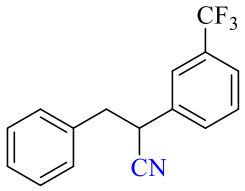


Figure 3.24 ^{1}H NMR ($CDCl_3$, 500 MHz) of 3k



3k

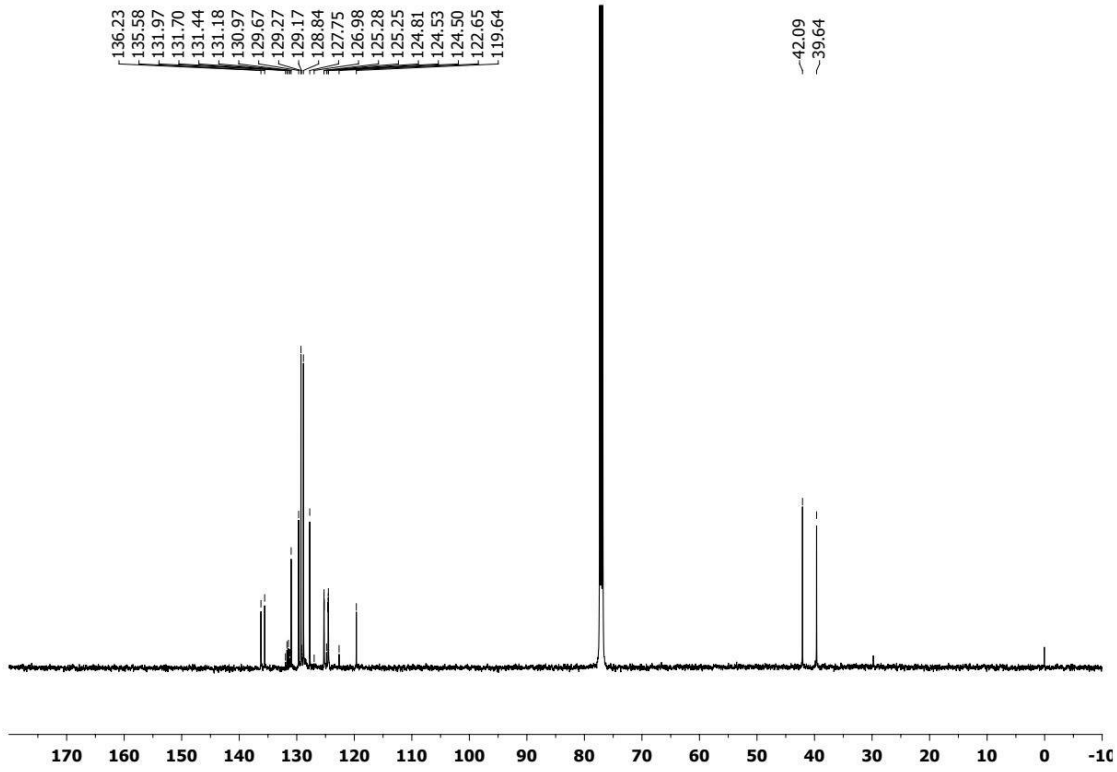
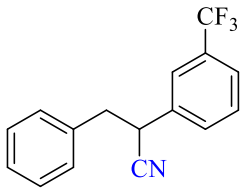


Figure 3.25 ^{13}C NMR ($CDCl_3$, 125 MHz) of 3k



3k

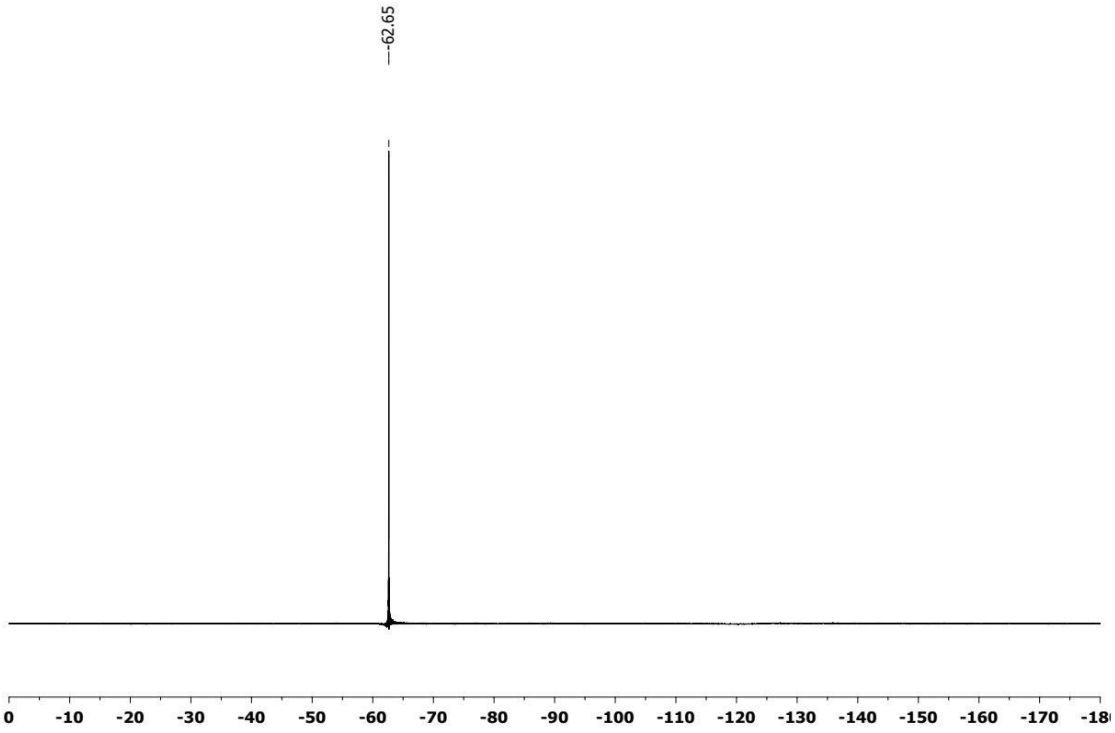
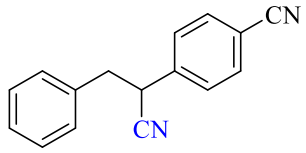


Figure 3.26 ^{19}F NMR ($CDCl_3$, 283 MHz) of 3k



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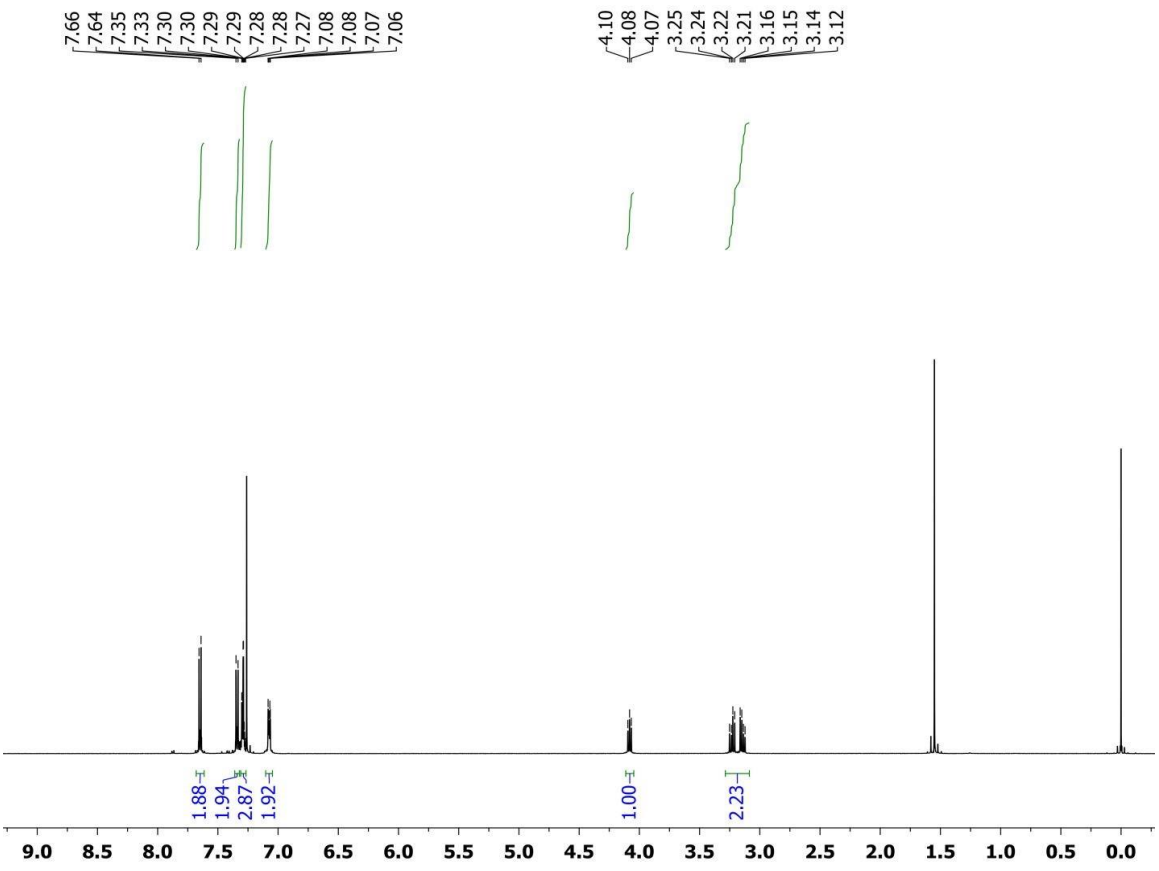
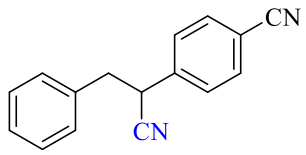


Figure 3.27 ^{1}H NMR ($CDCl_3$, 500 MHz) of 3l



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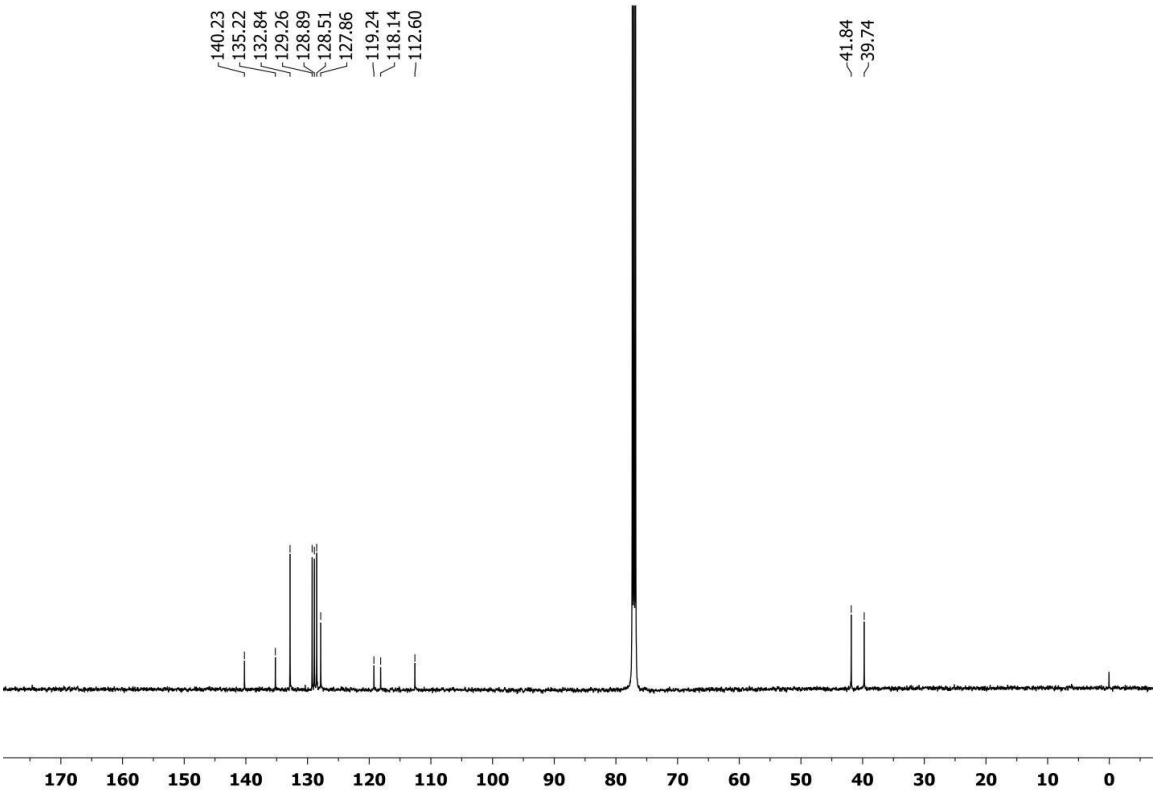
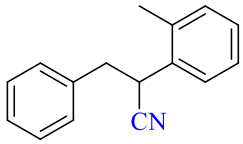


Figure 3.28 ^{13}C NMR ($CDCl_3$, 125 MHz) 3l



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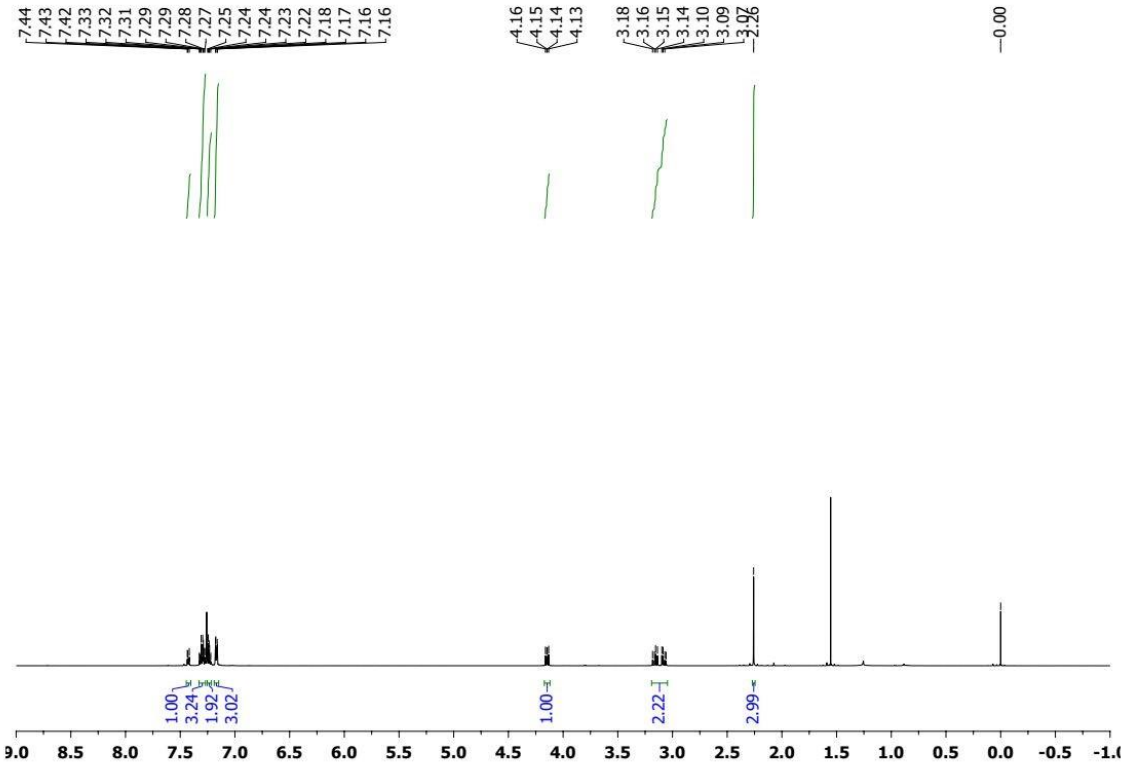
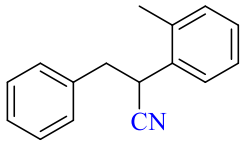


Figure 3.29 ^{1}H NMR ($CDCl_3$, 500 MHz) of 3m



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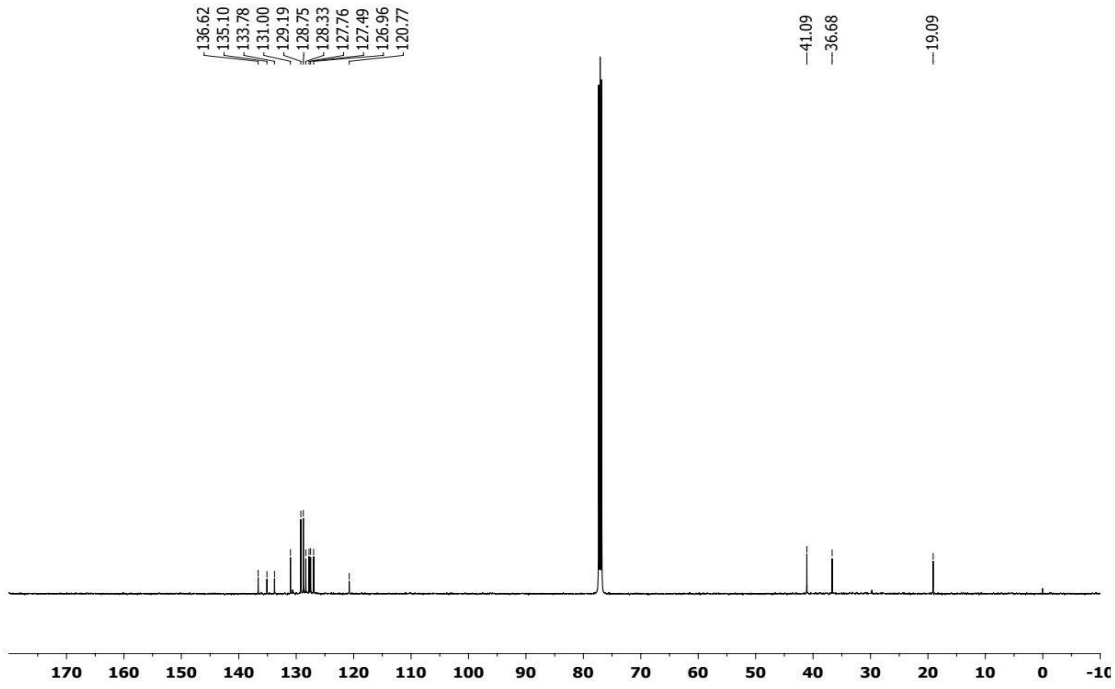
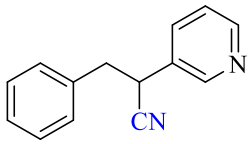


Figure 3.30 ^{13}C NMR (CDCl3, 125 MHz) of 3m



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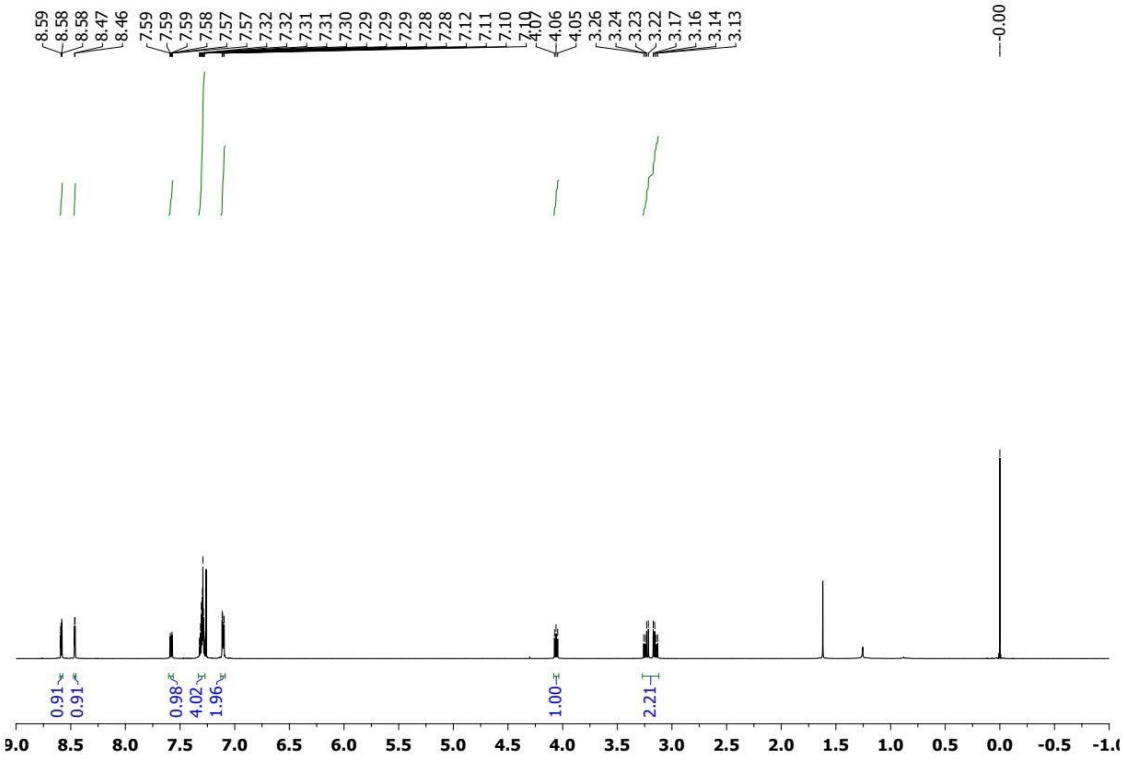
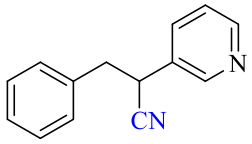


Figure 3.31 ^{1}H NMR ($CDCl_3$, 500 MHz) of 3n



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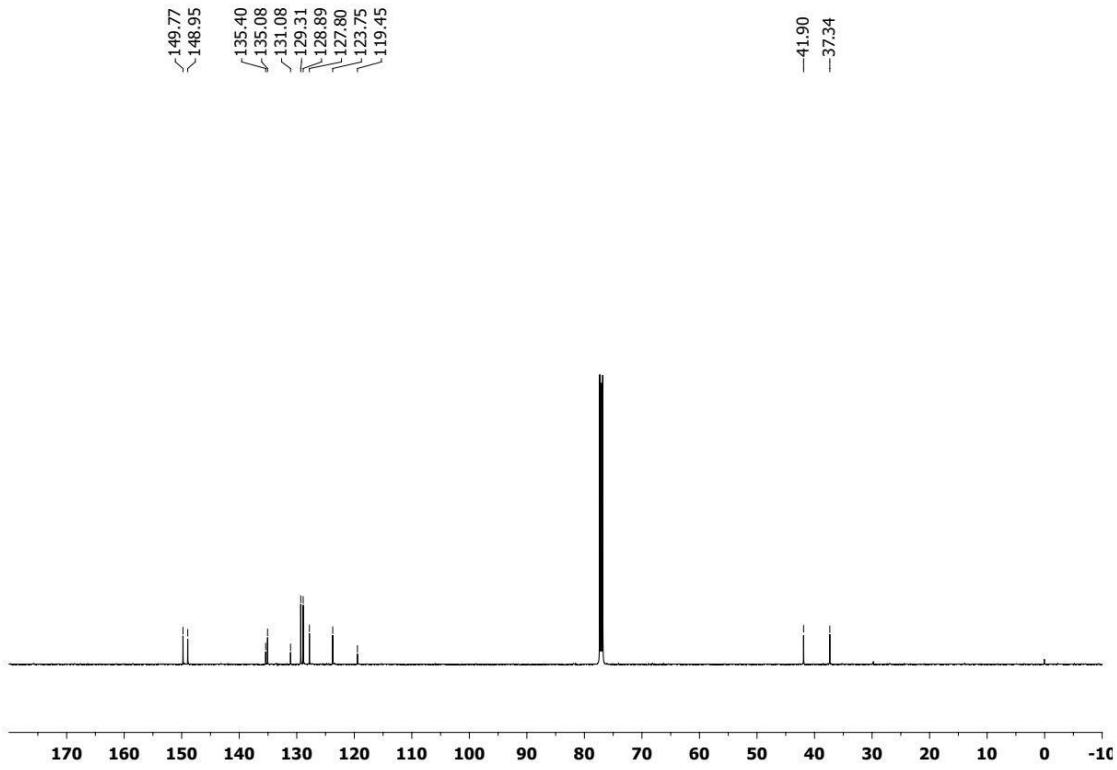
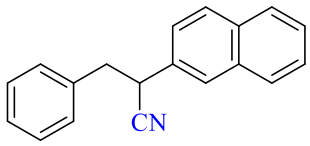


Figure 3.32 ^{13}C NMR ($CDCl_3$, 125 MHz) of 3n



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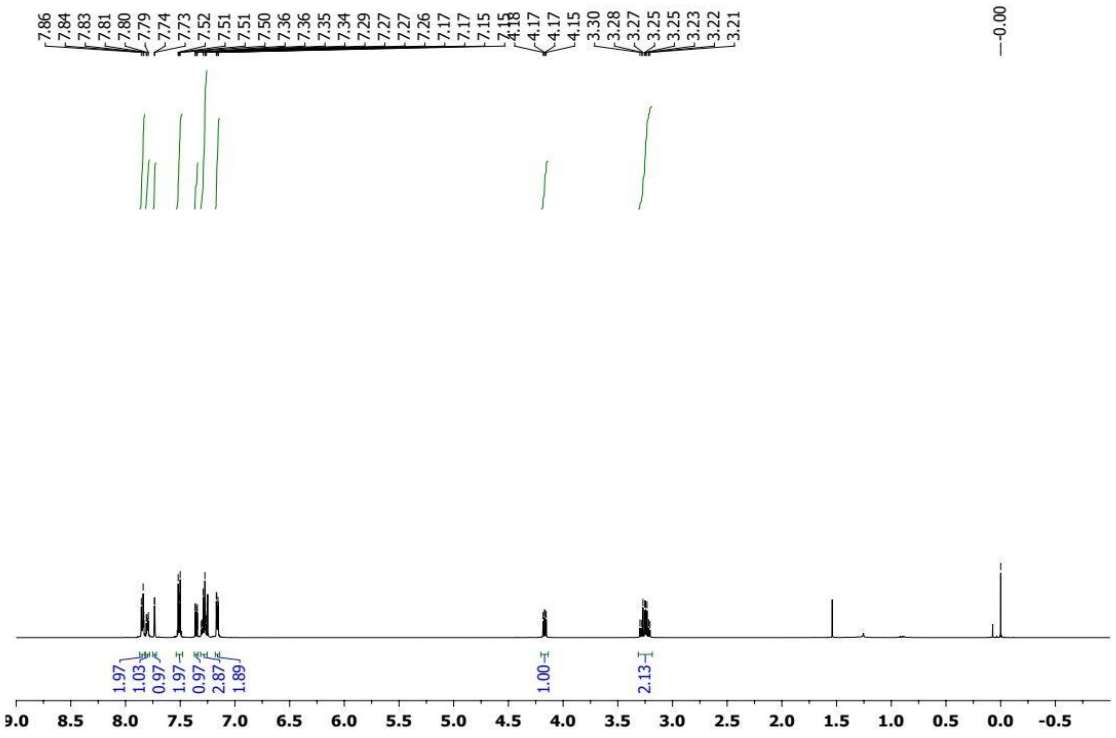
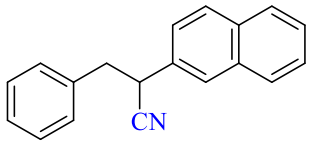


Figure 3.33 ^{1}H NMR ($CDCl_3$, 500 MHz) of 3o



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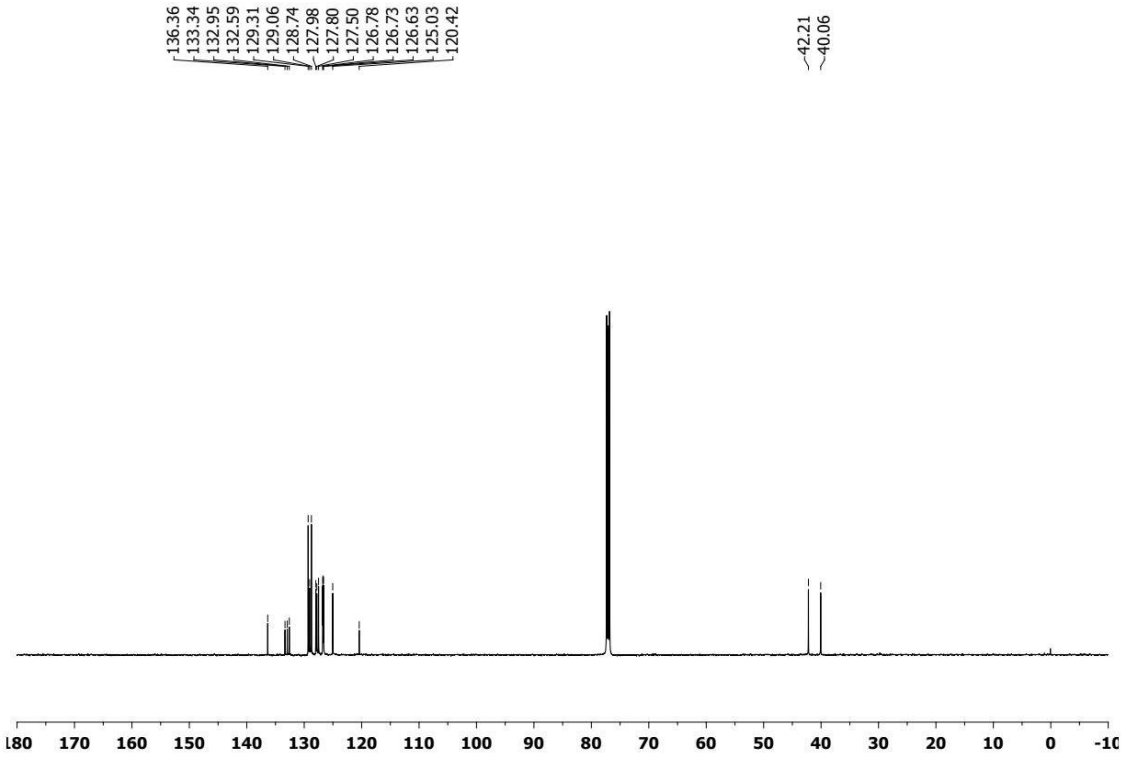
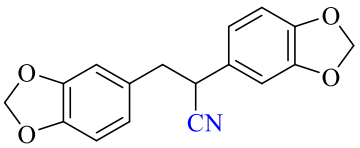


Figure 3.34 ^{13}C NMR ($CDCl_3$, 125 MHz) of 3o



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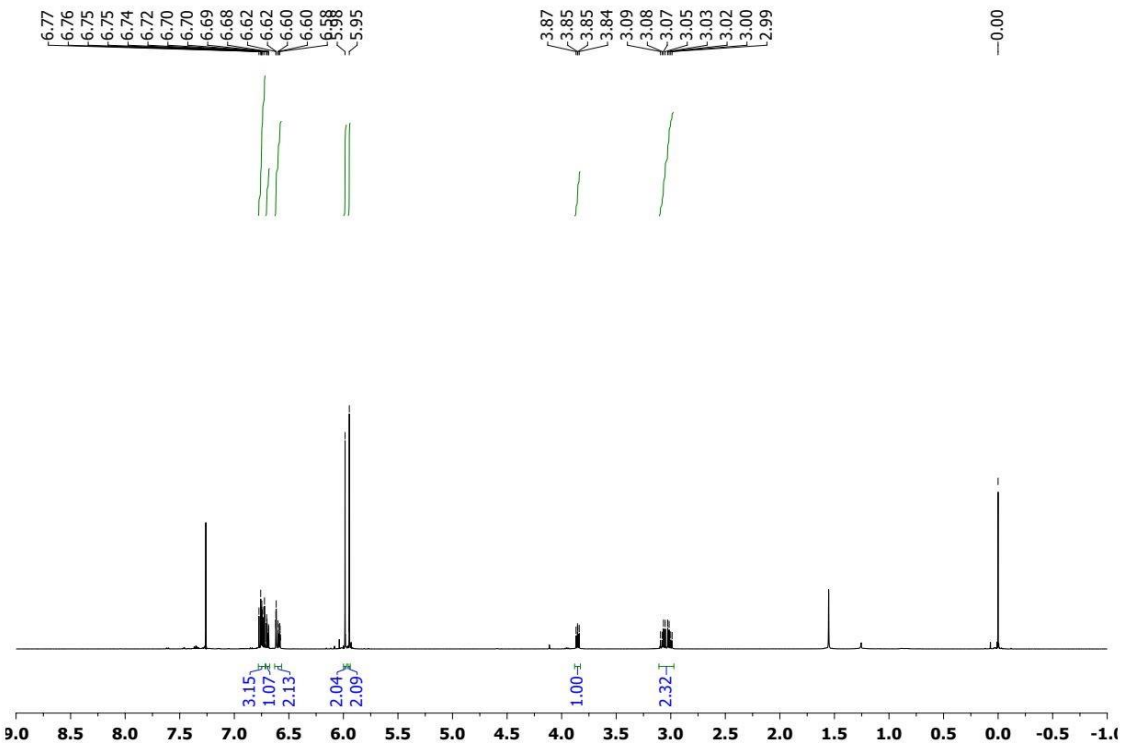
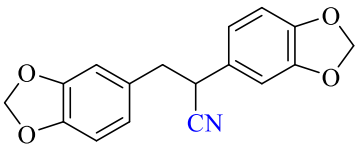


Figure 3.35 ^{1}H NMR ($CDCl_3$, 500 MHz) of 3p



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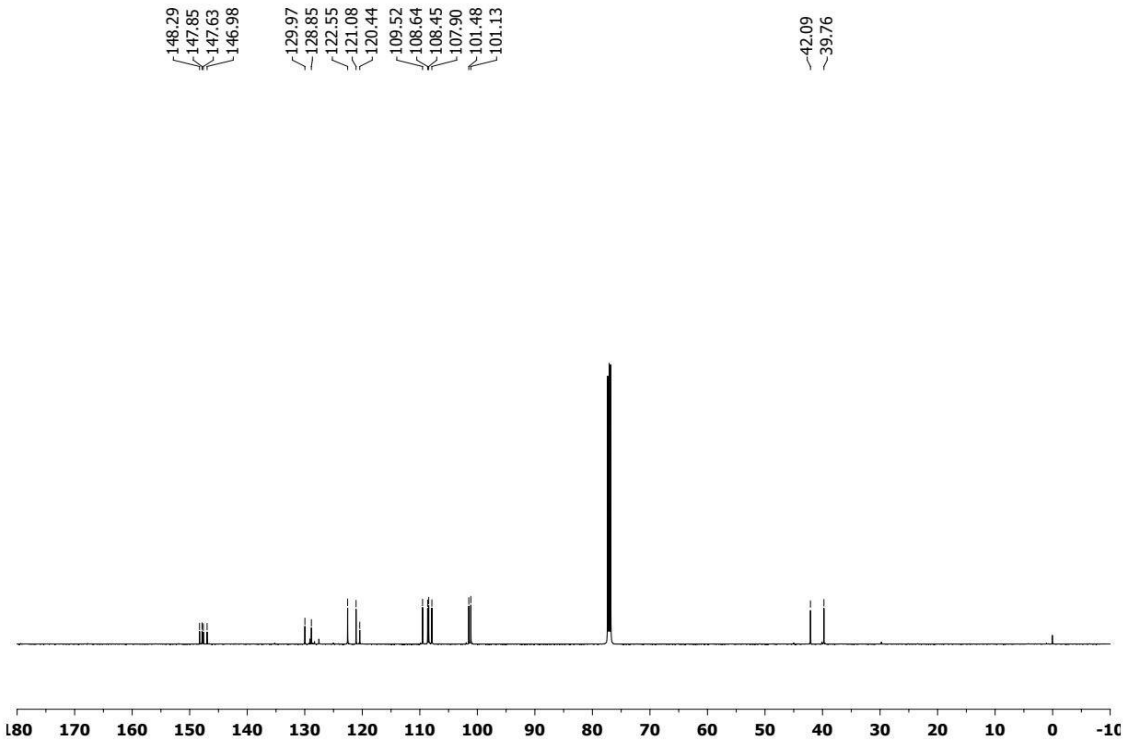
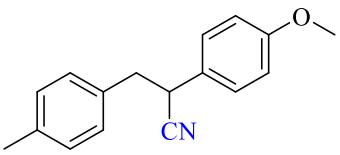


Figure 3.36 ^{13}C NMR ($CDCl_3$, 125 MHz) of 3p



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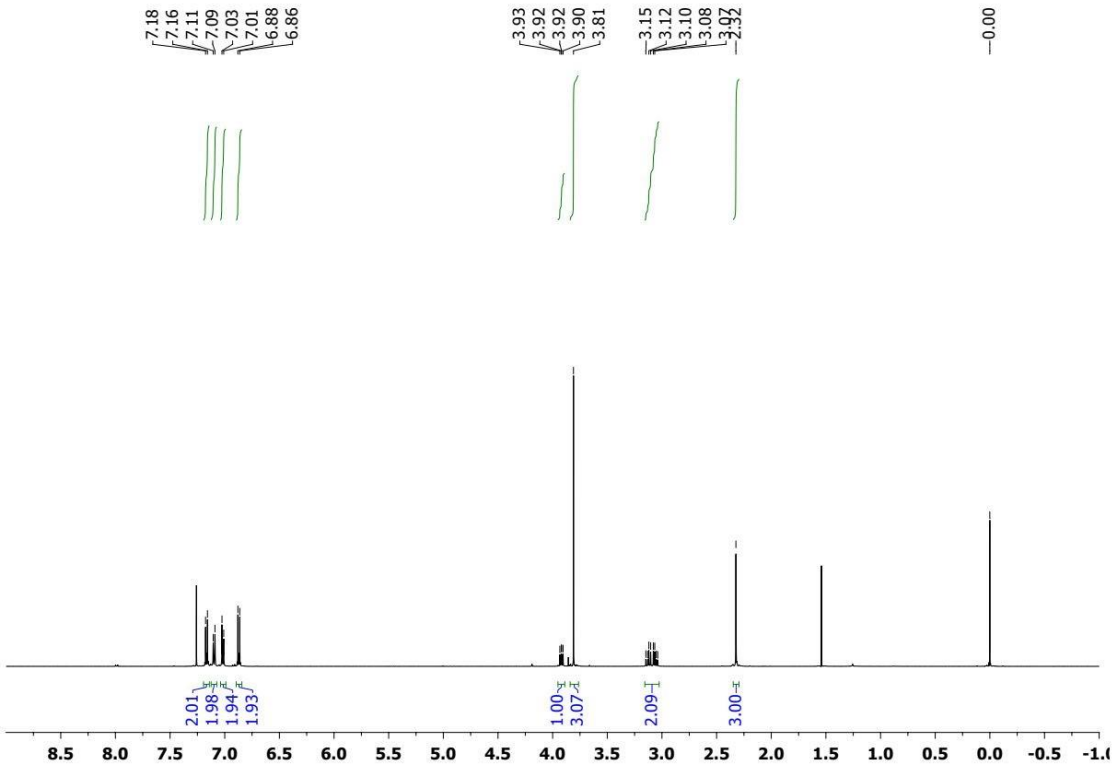
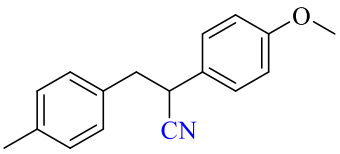


Figure 3.37 ^{1}H NMR ($CDCl_3$, 500 MHz) of 3q



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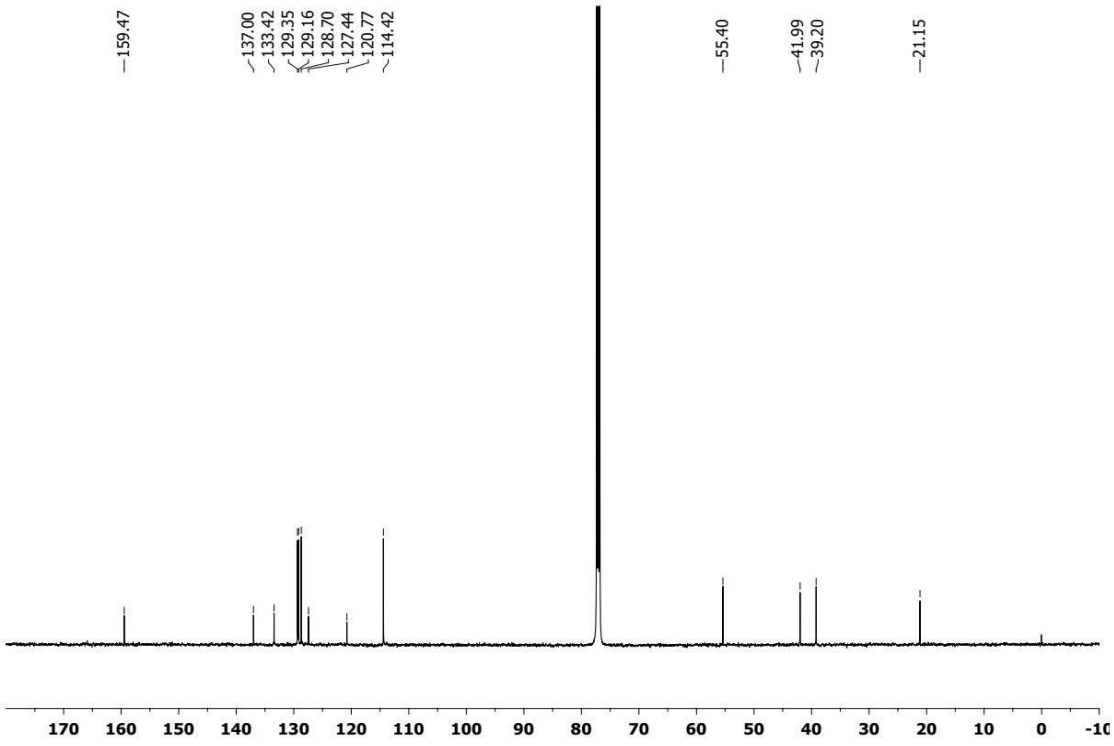
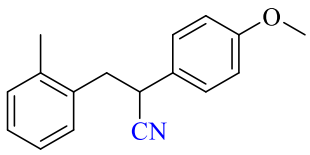


Figure 3.38 ^{13}C NMR ($CDCl_3$, 125 MHz) of 3q



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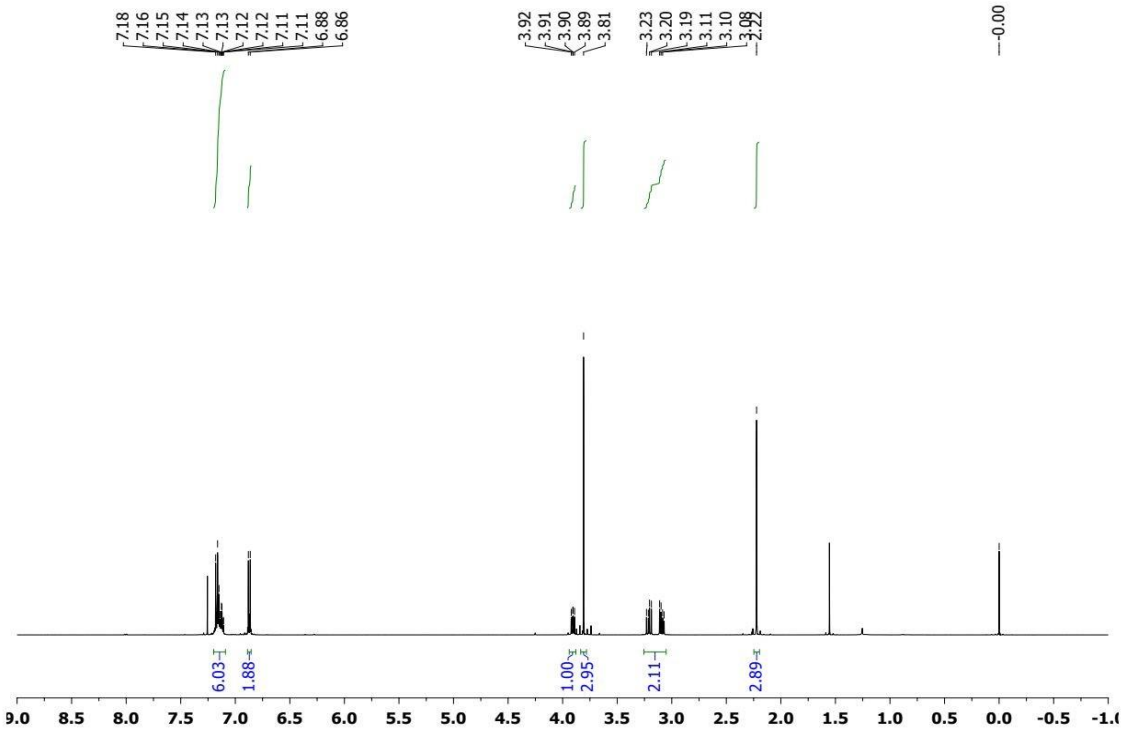
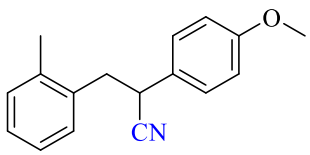


Figure 3.39 ^{1}H NMR ($CDCl_3$, 500 MHz) or 3r



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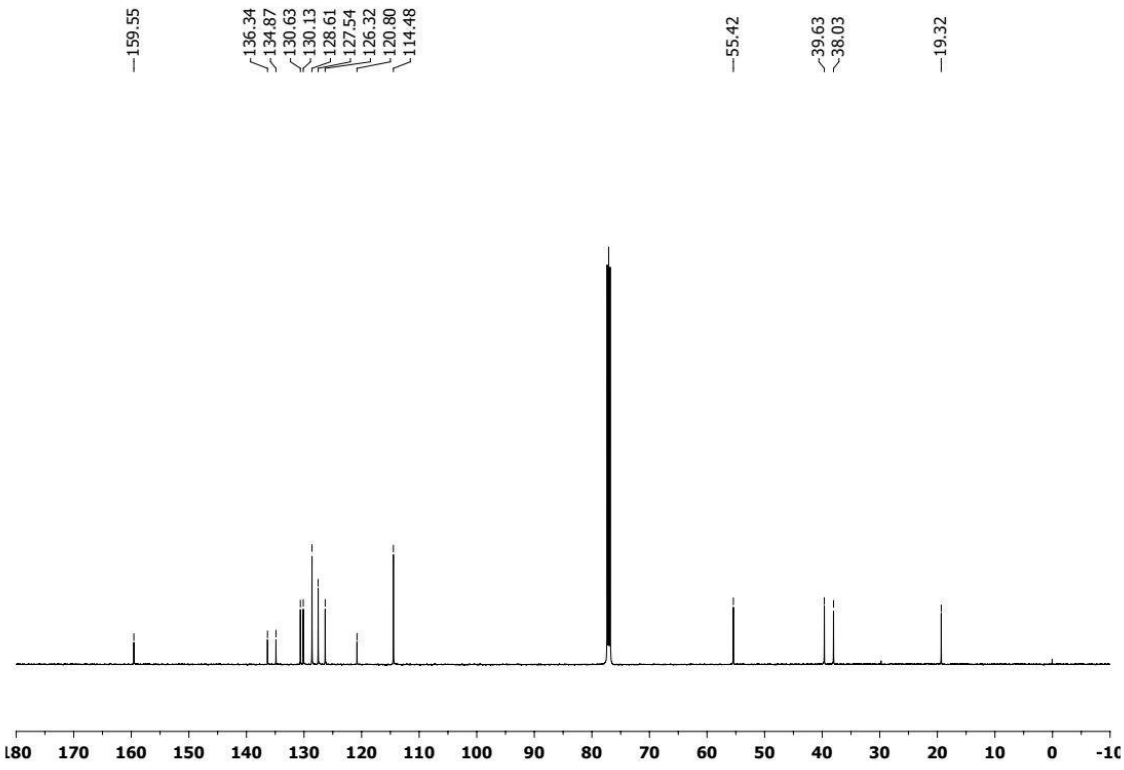
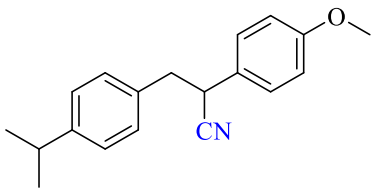


Figure 3.40 ^{13}C NMR ($CDCl_3$, 125 MHz) of 3r



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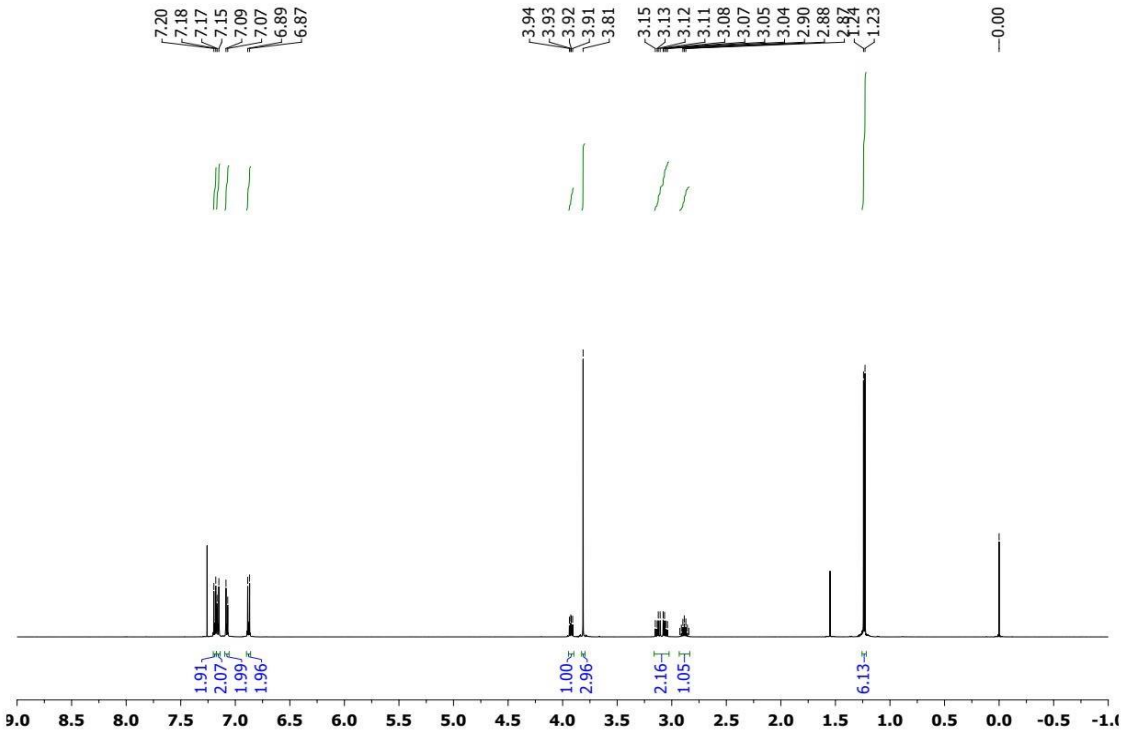
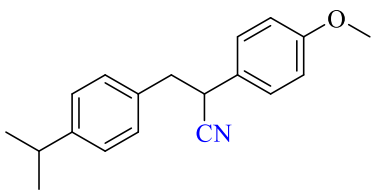


Figure 3.41 ^{1}H NMR ($CDCl_3$, 500 MHz) of 3s



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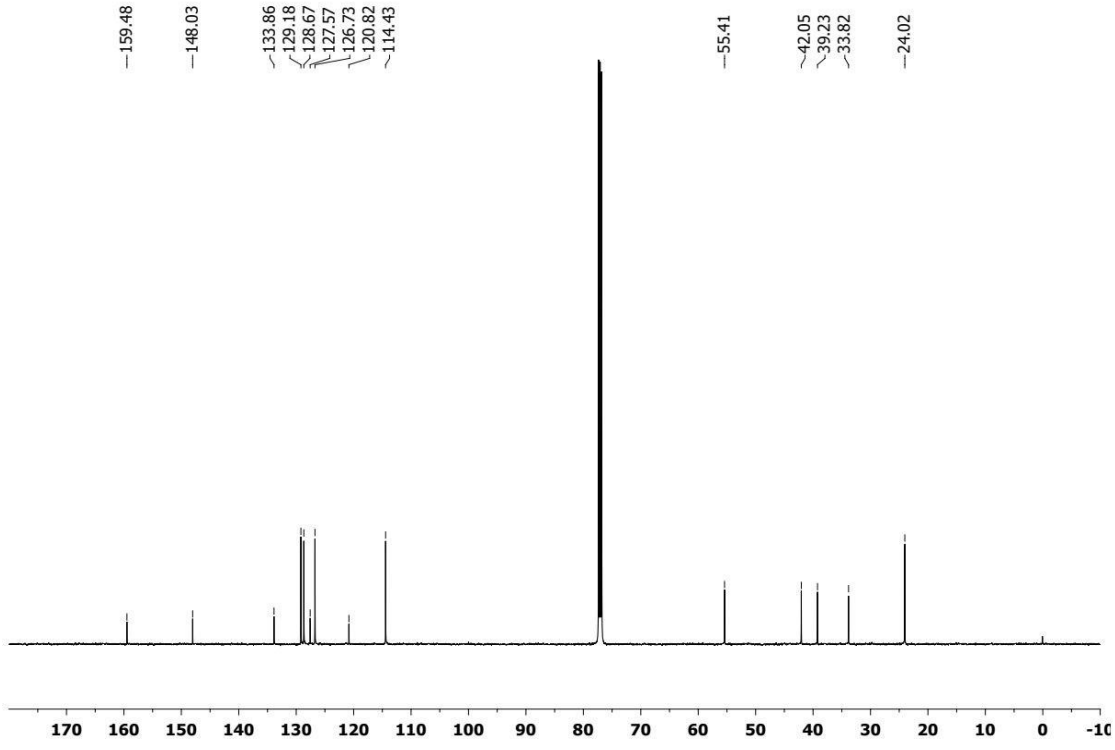
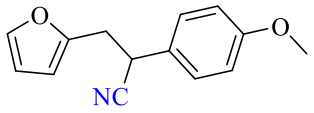


Figure 3.42 ^{13}C NMR ($CDCl_3$, 125 MHz) of 3s



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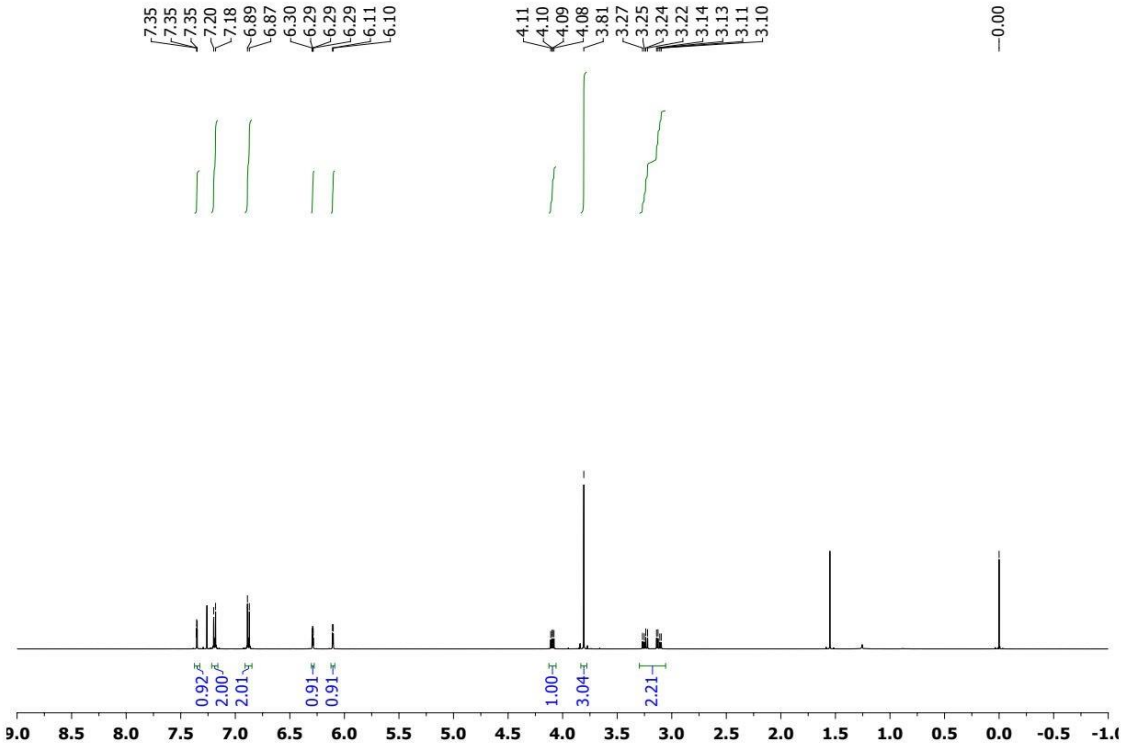
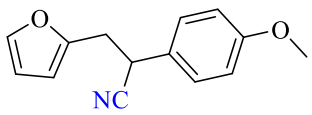


Figure 3.43 ^{1}H NMR ($CDCl_3$, 500 MHz) of 3t



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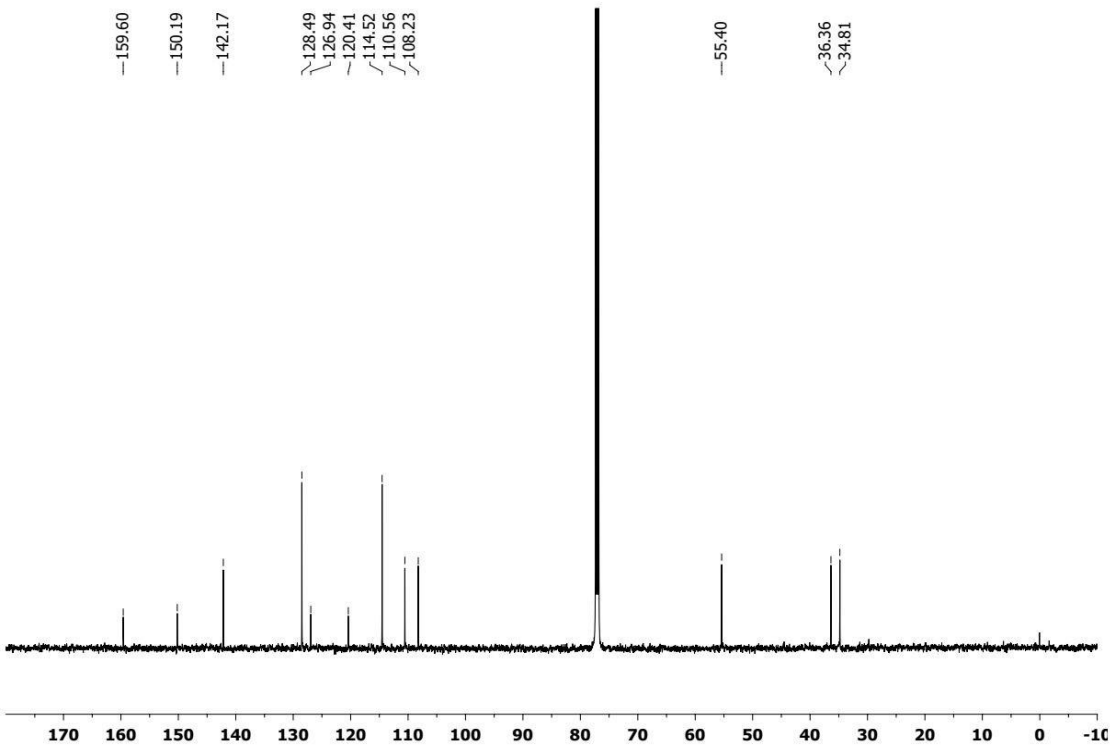
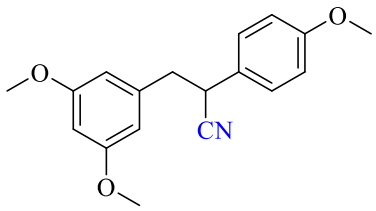


Figure 3.44 ^{13}C NMR ($CDCl_3$, 125 MHz) of 3t



3u

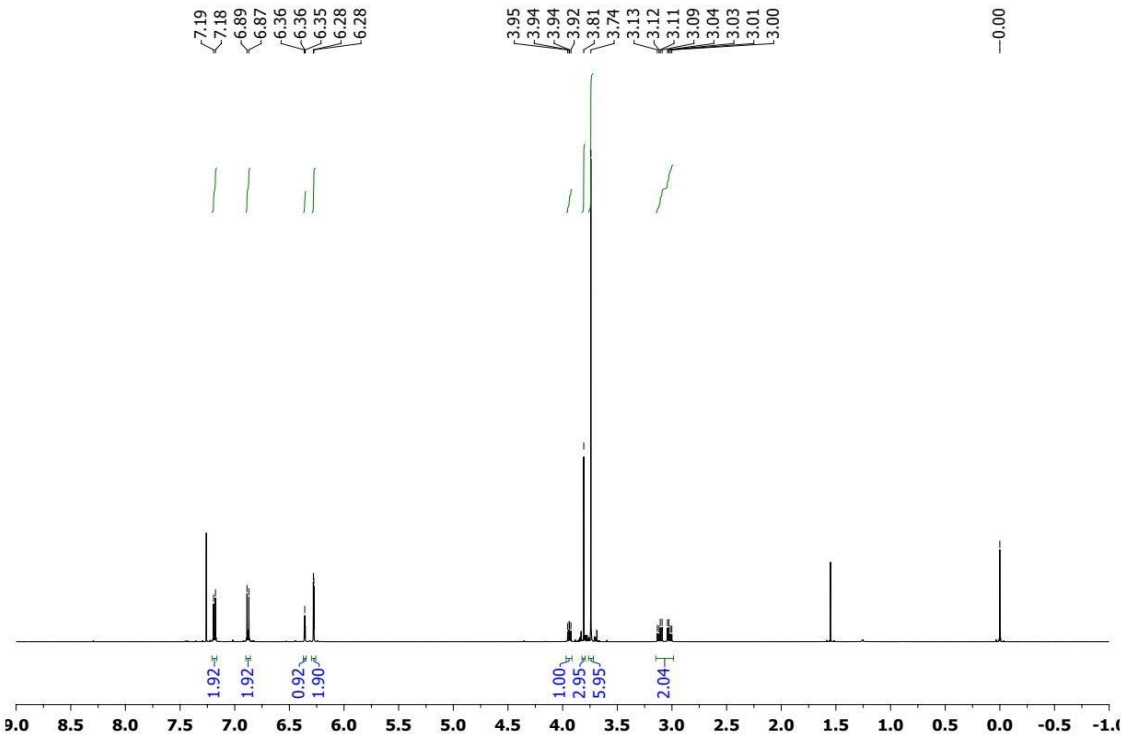
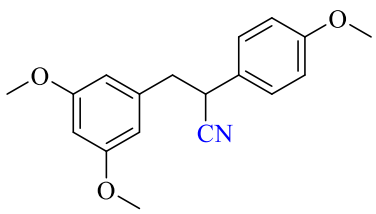


Figure 3.45 ^{1}H NMR ($CDCl_3$, 500 MHz) of 3u



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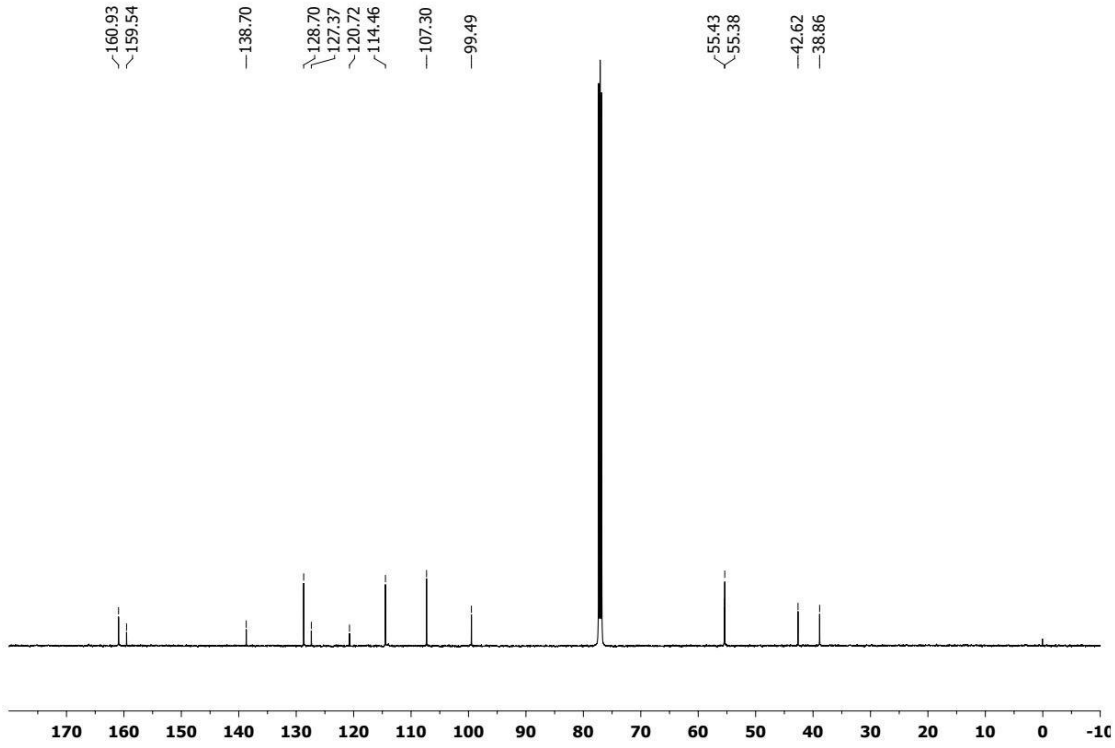
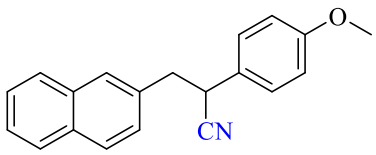


Figure 3.46 ^{13}C NMR ($CDCl_3$, 125 MHz) of 3u



3v

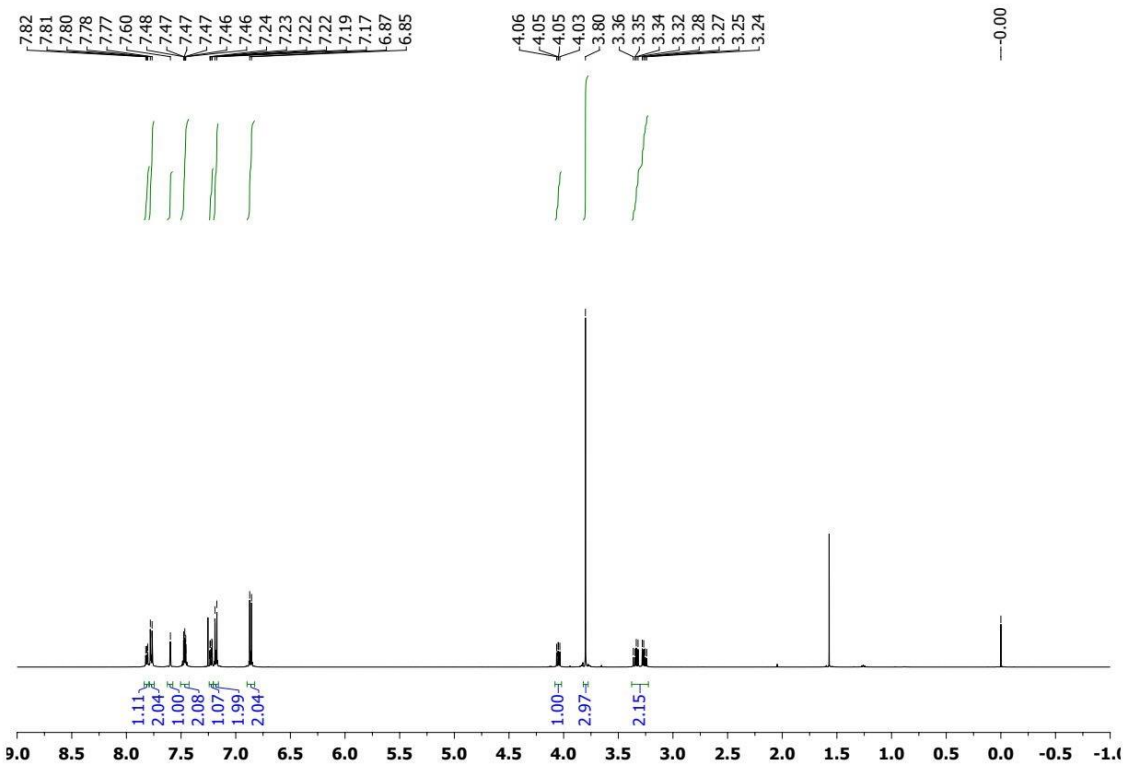
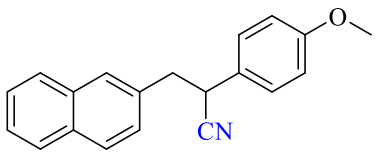


Figure 3.47 ^{1}H NMR ($CDCl_3$, 500 MHz) of 3v



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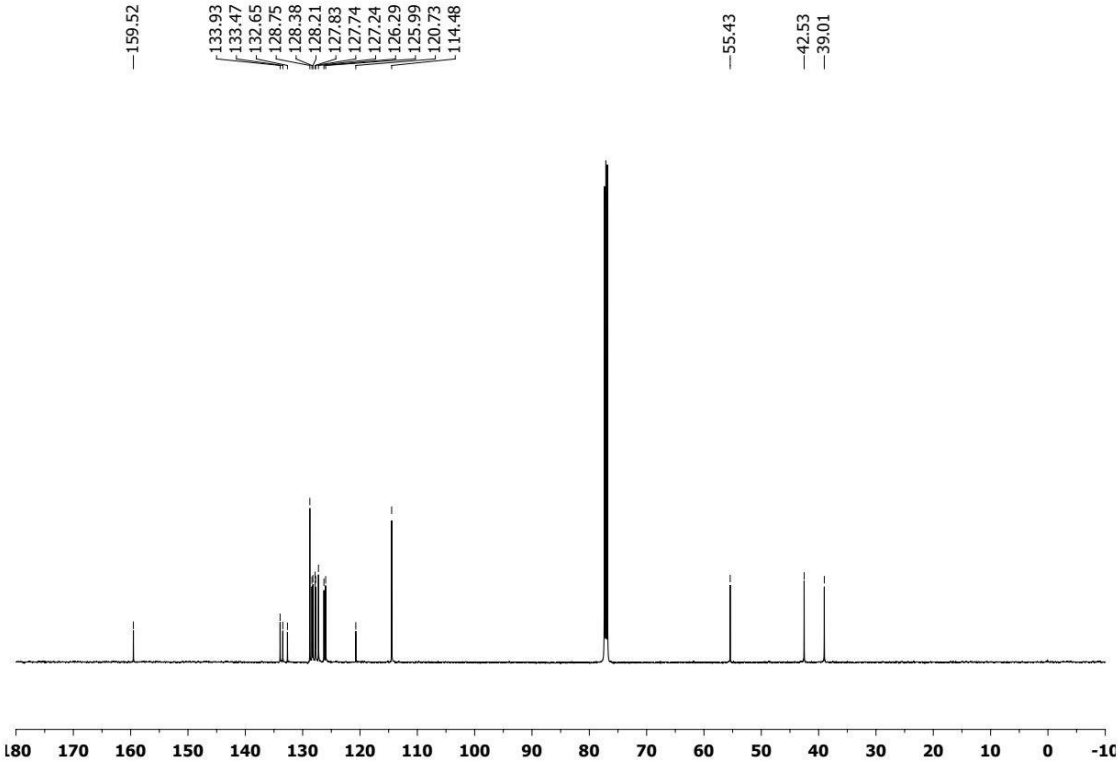
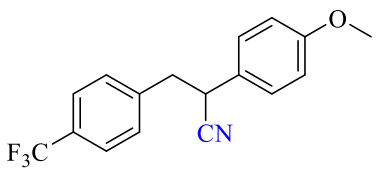


Figure 3.48 ^{13}C NMR ($CDCl_3$, 125 MHz) of 3v



3w

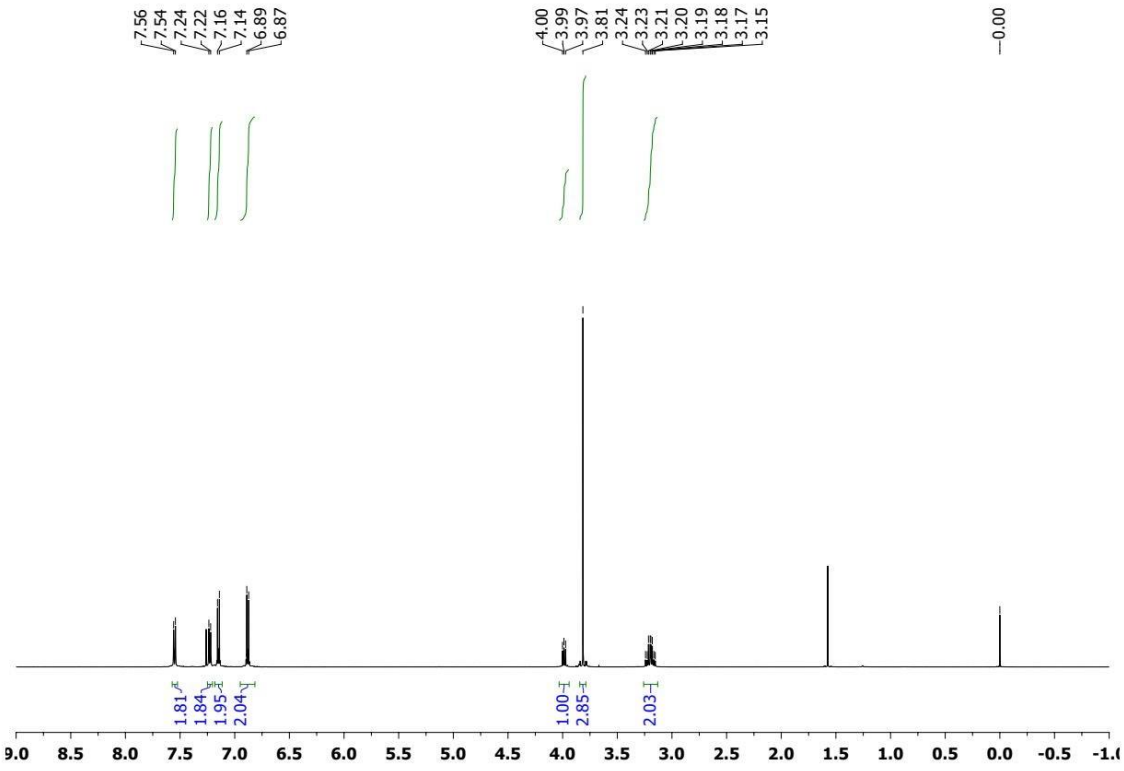
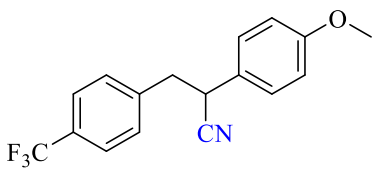


Figure 3.49 ^{1}H NMR ($CDCl_3$, 500 MHz) of 3w



3w

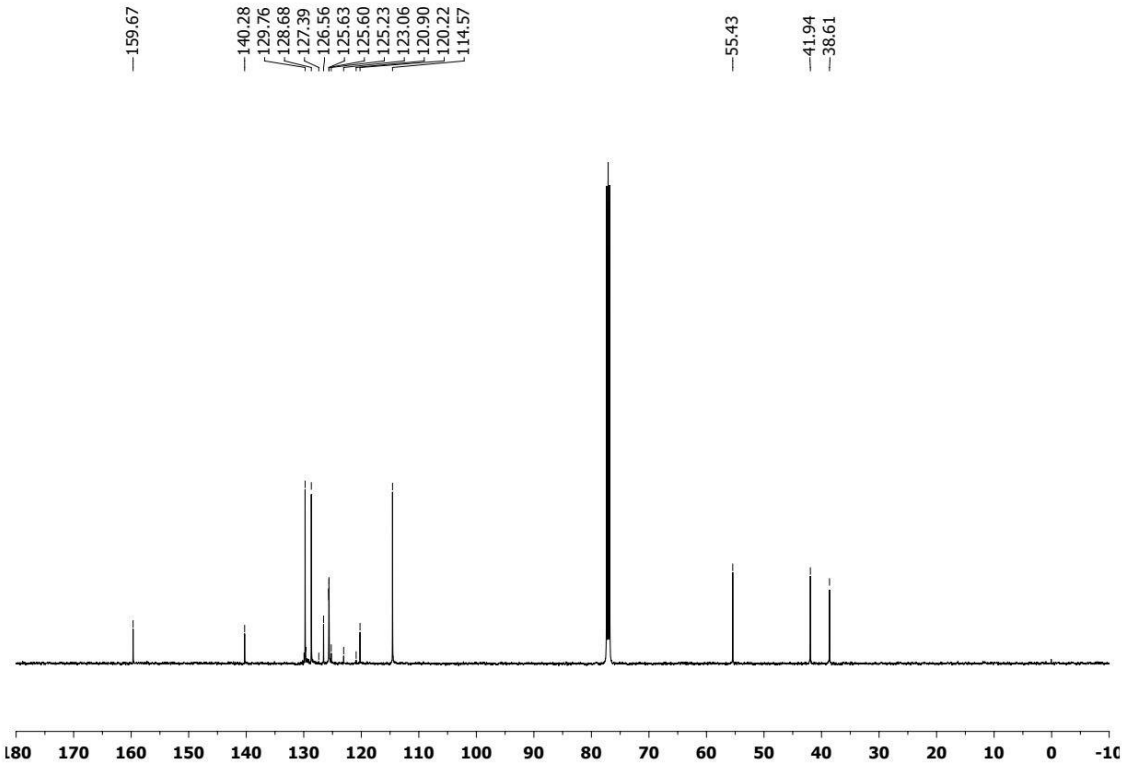
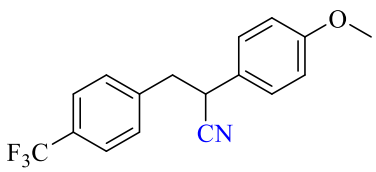


Figure 3.50 ^{13}C NMR ($CDCl_3$, 125 MHz) of 3w



3w

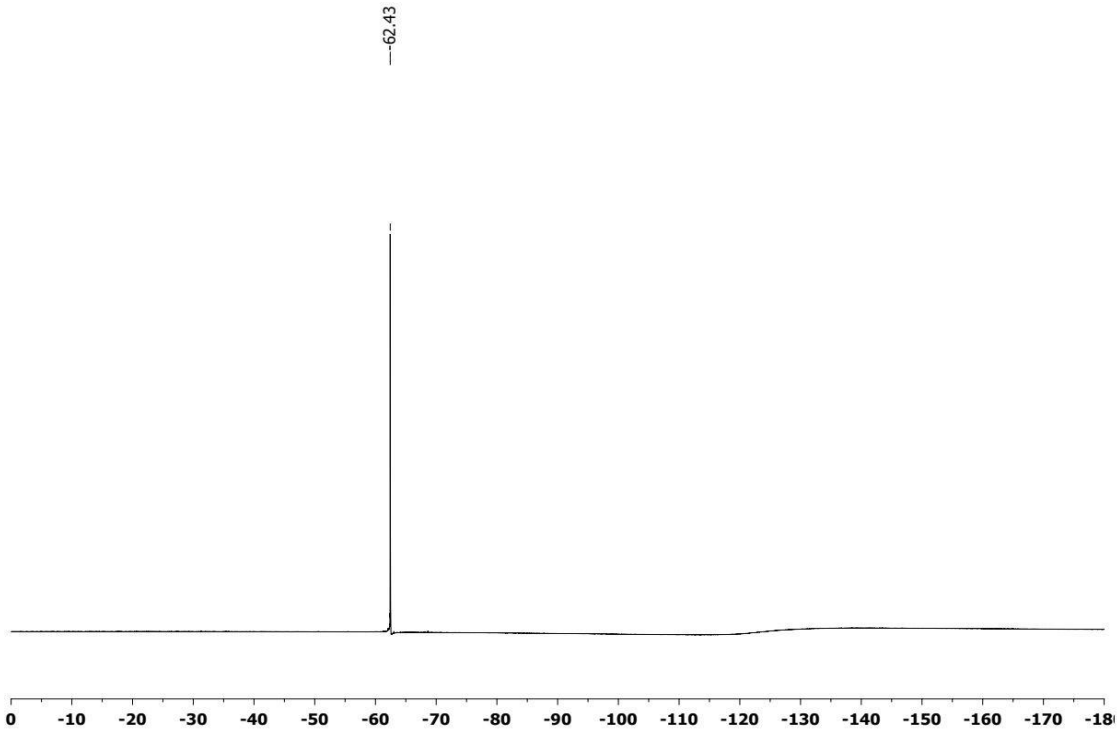
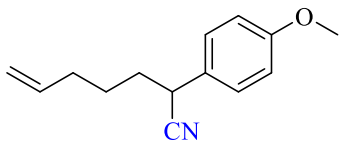


Figure 3.51 ^{19}F NMR ($CDCl_3$, 283 MHz) of 3w



3x

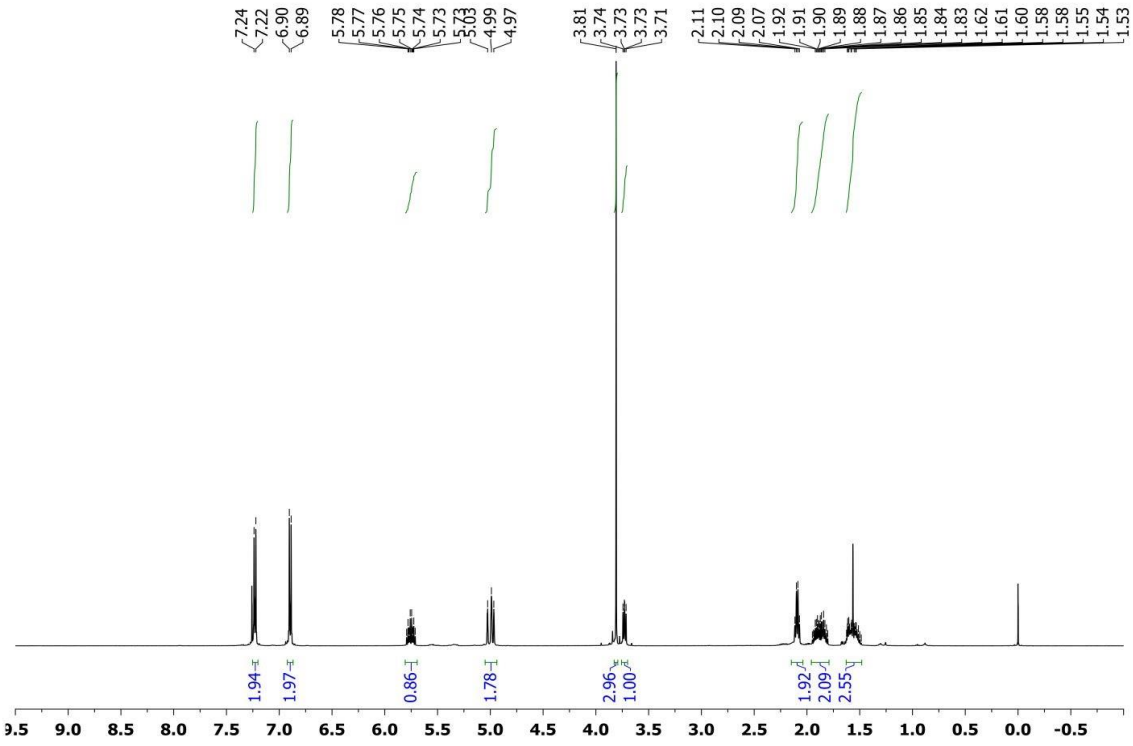
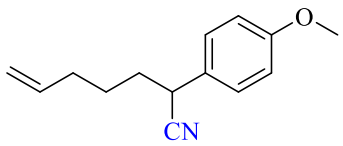


Figure 3.52 ^{1}H NMR ($CDCl_3$, 500 MHz) of 3x



3x

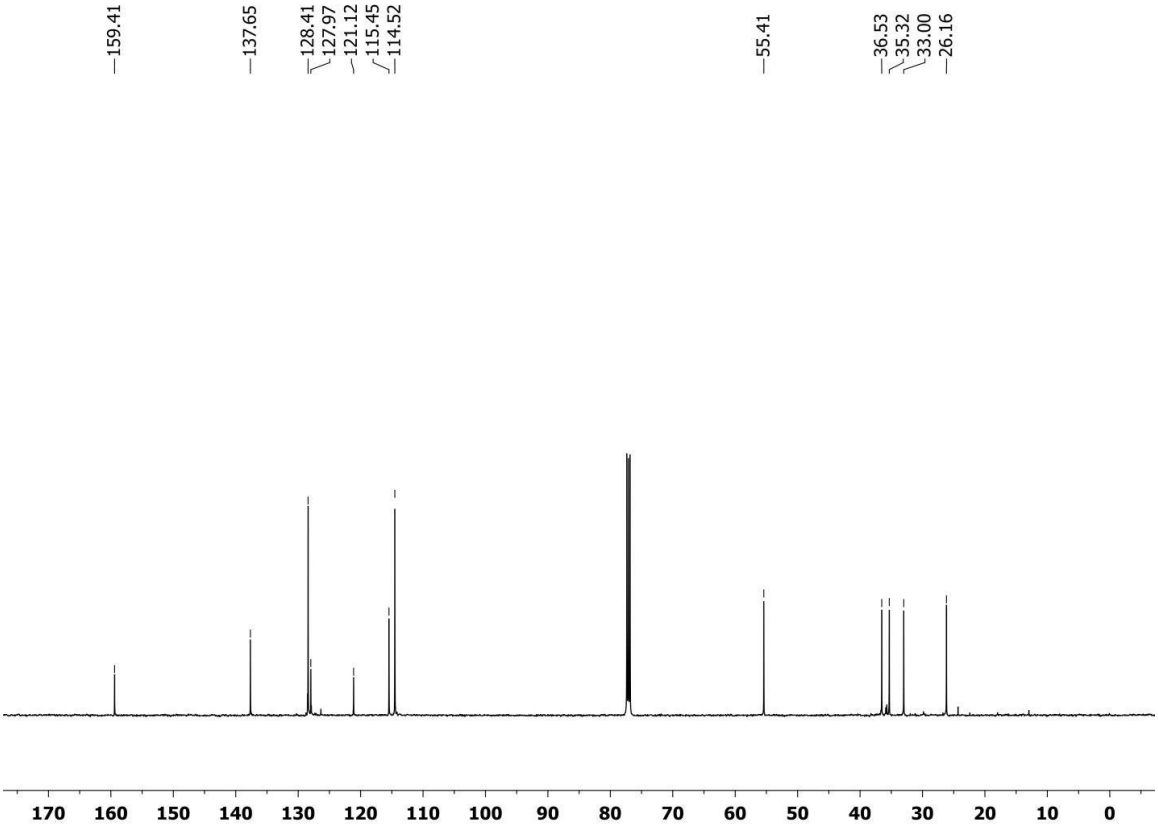
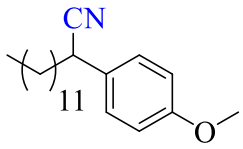


Figure 3.53 ^{13}C NMR (CDCl3, 125 MHz) of 3x



3y

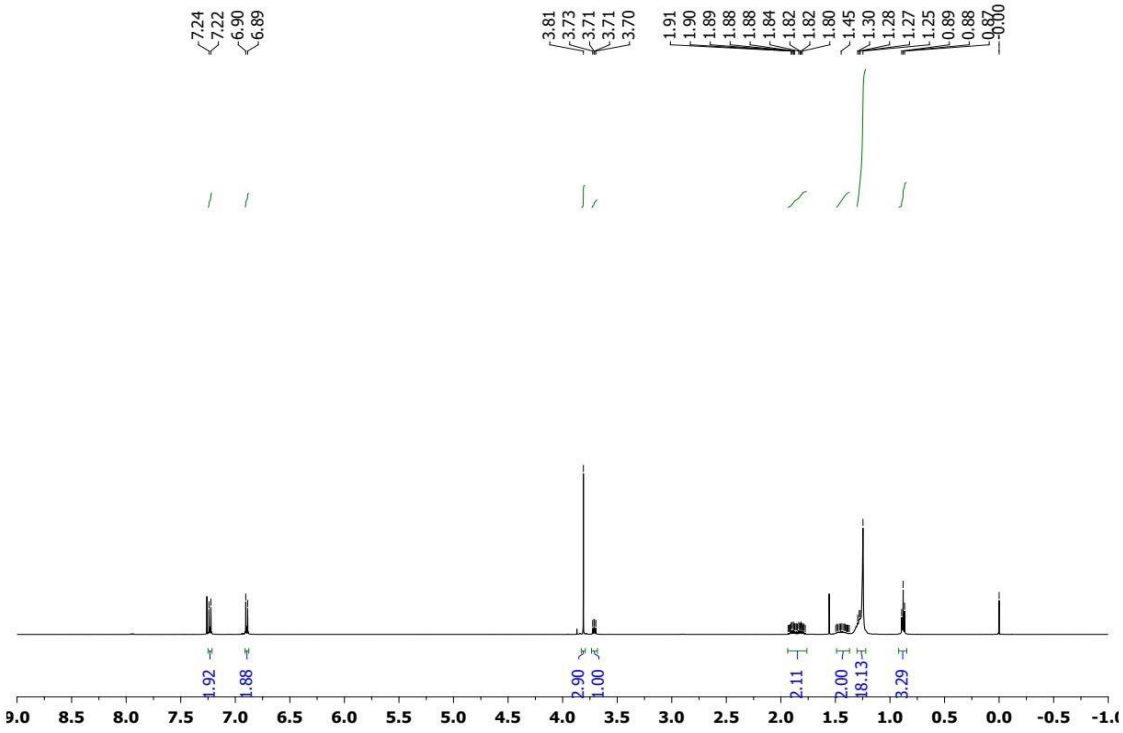


Figure 3.54 ^{1}H NMR ($CDCl_3$, 500 MHz) of 3y

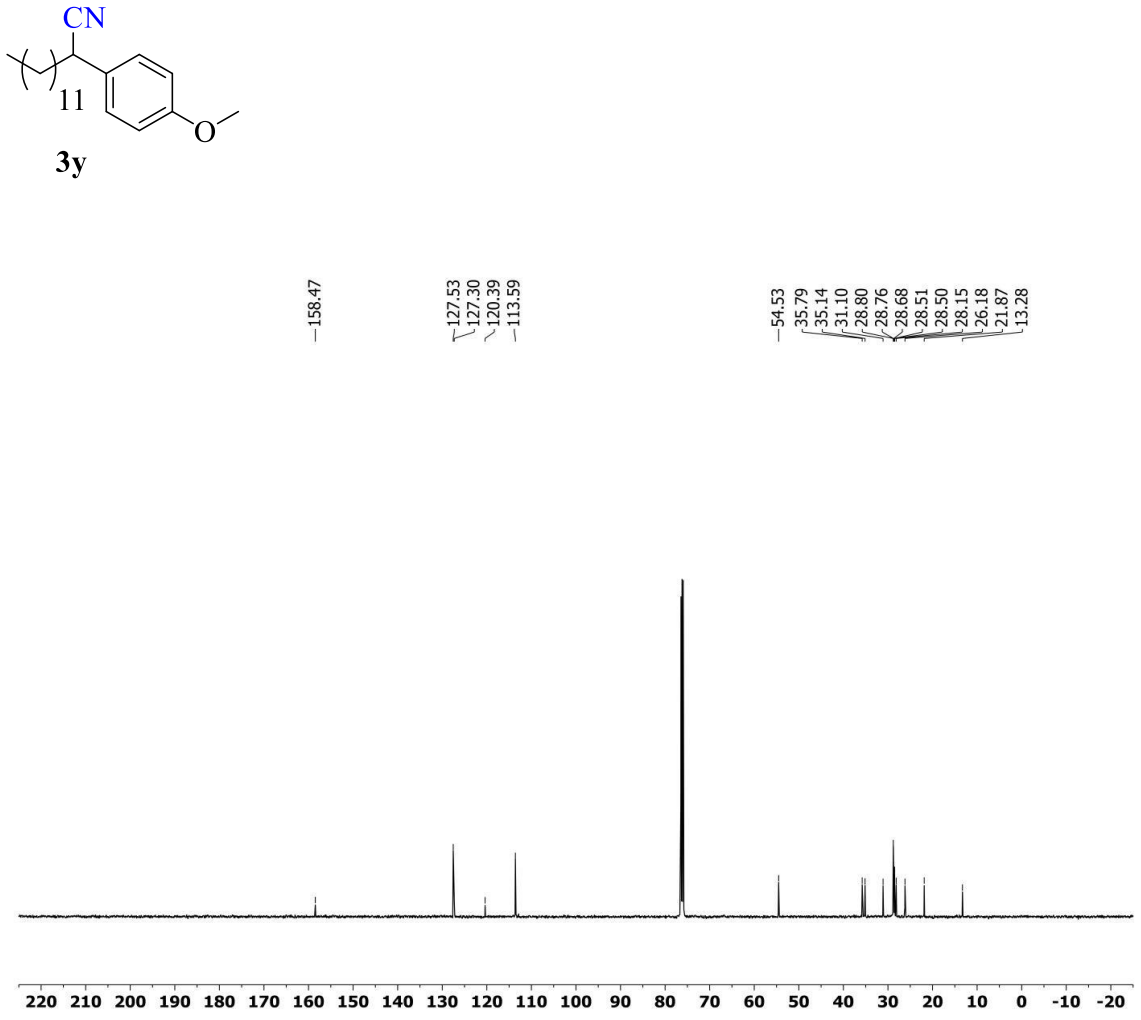
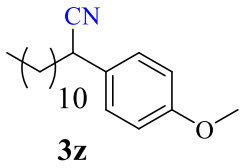


Figure 3.55 ^{13}C NMR ($CDCl_3$, 125 MHz) of 3y



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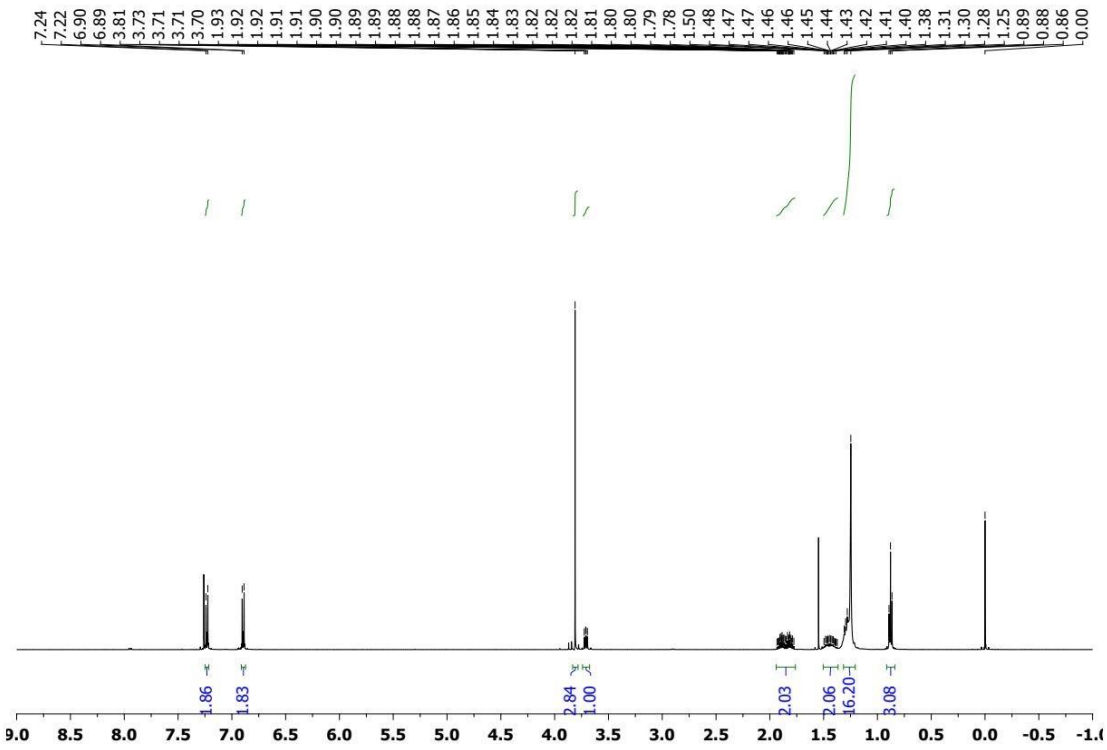
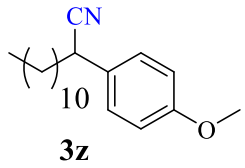


Figure 3.56 ^{1}H NMR ($CDCl_3$, 500 MHz) of 3z



3z

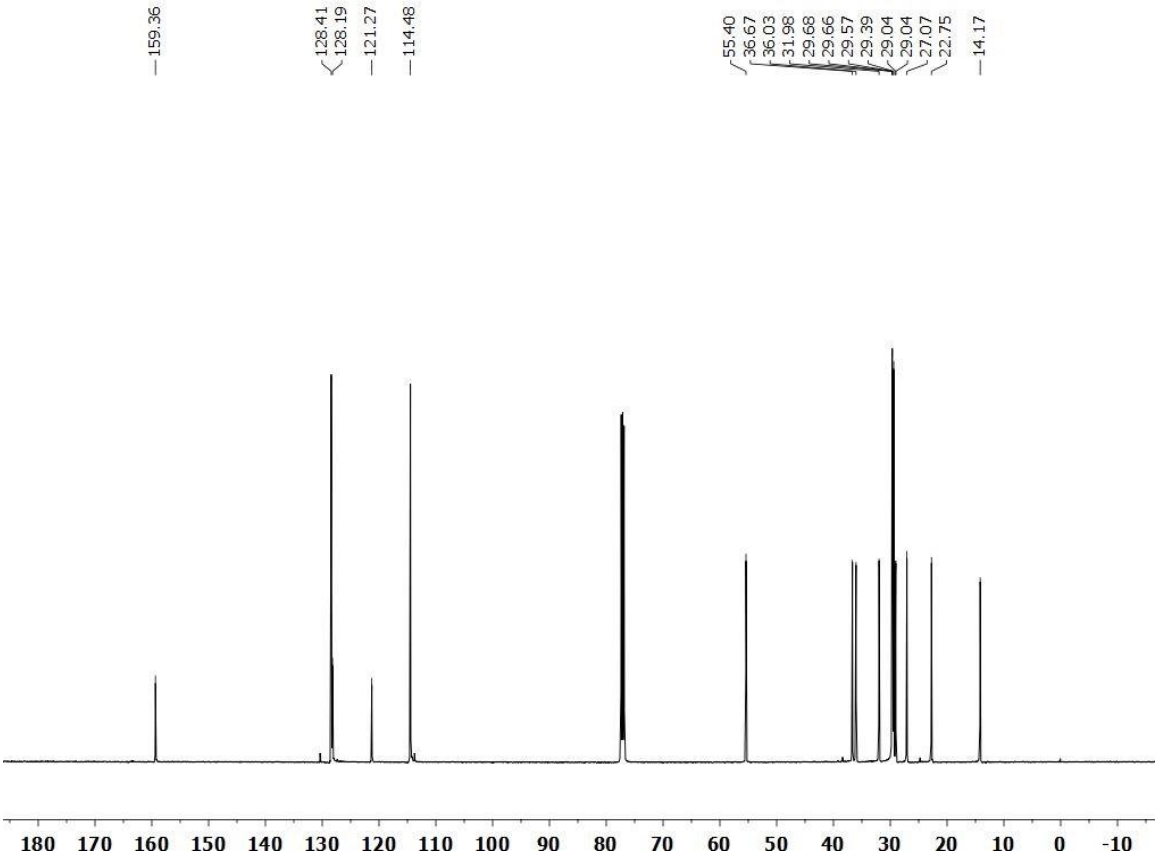
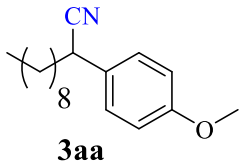


Figure 3.57 ^{13}C NMR ($CDCl_3$, 500 MHz) of 3z



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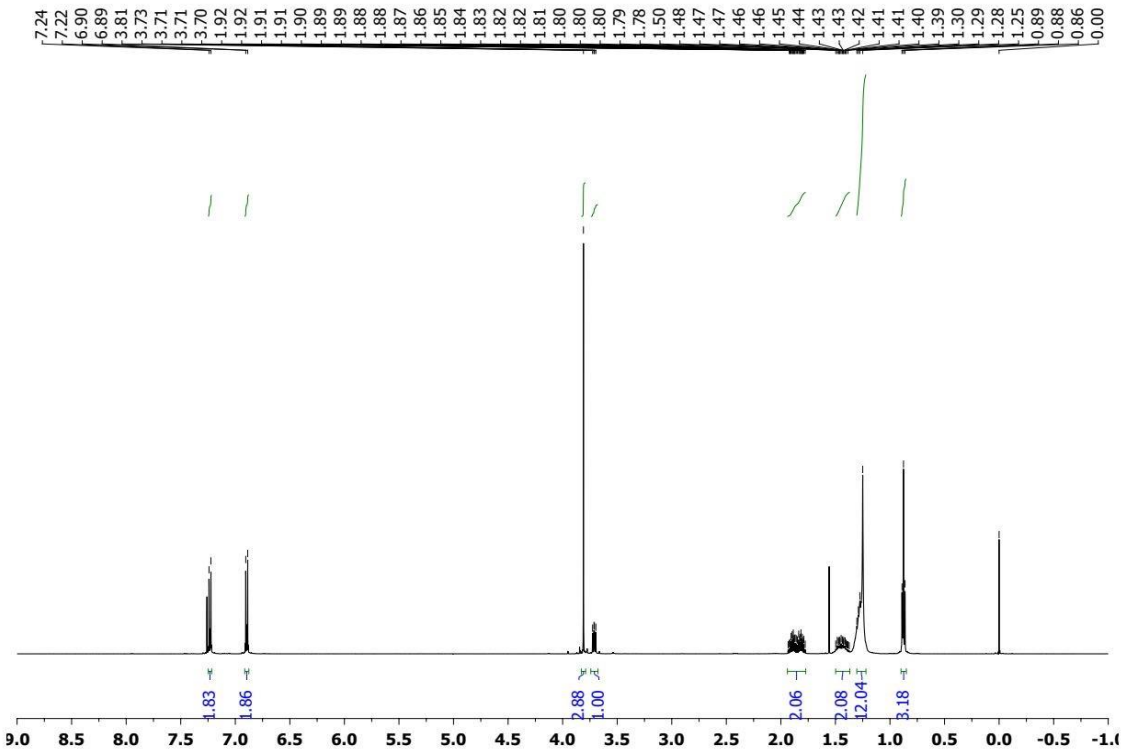
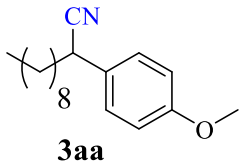


Figure 3.58 ^{1}H NMR ($CDCl_3$, 500 MHz) of 3aa



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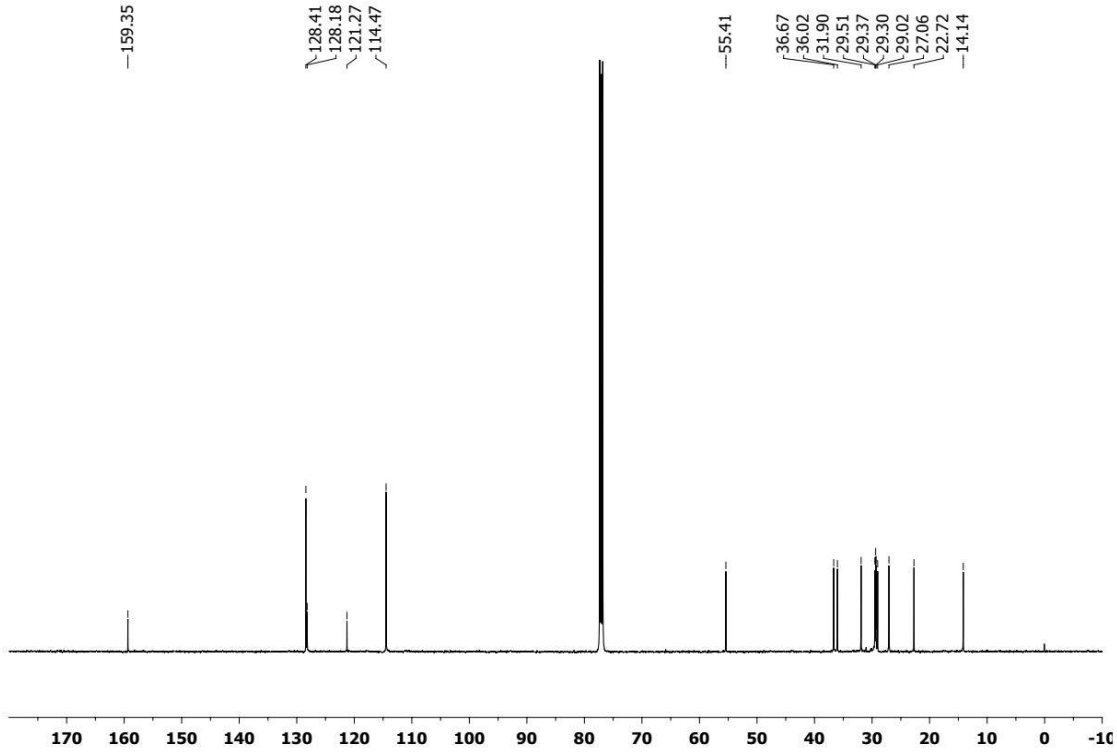
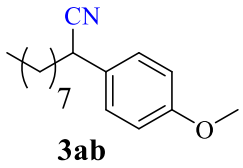


Figure 3.59 ^{13}C NMR ($CDCl_3$, 125 MHz) of 3aa



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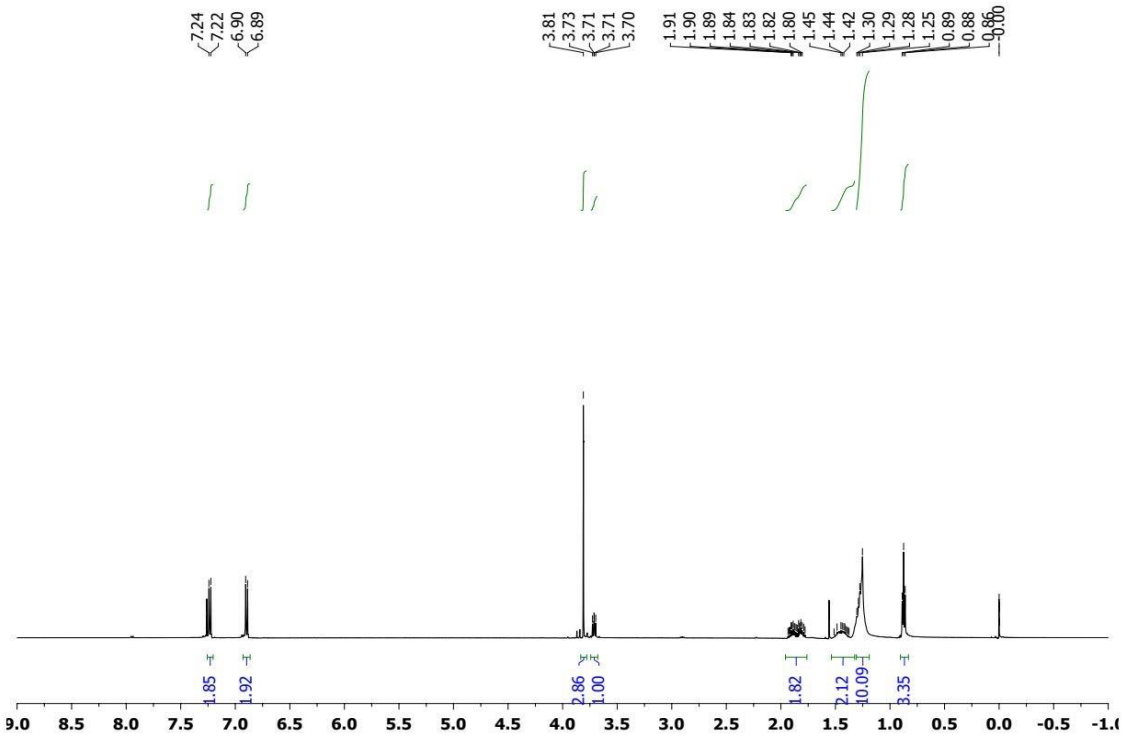
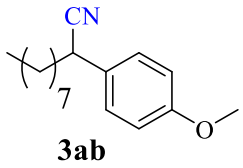


Figure 3.60 ^{1}H NMR ($CDCl_3$, 500 MHz) of 3ab



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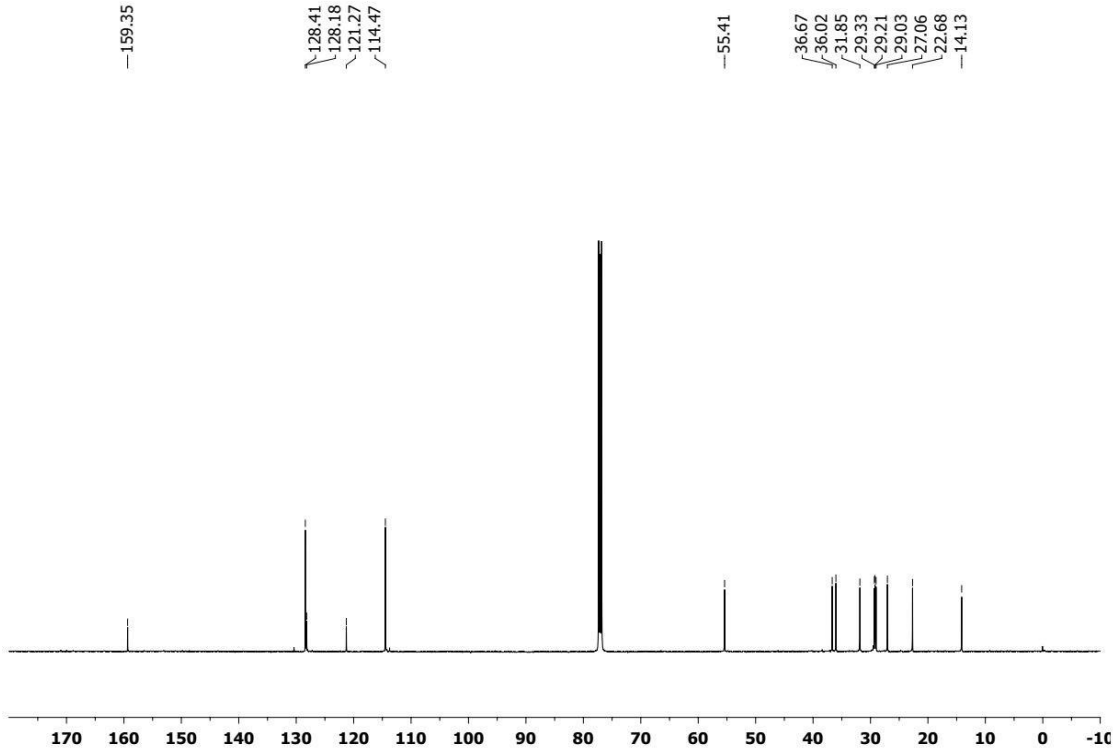
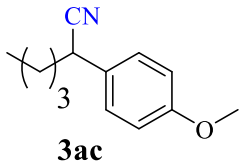


Figure 3.61 ^{13}C NMR ($CDCl_3$, 125 MHz) of 3ab



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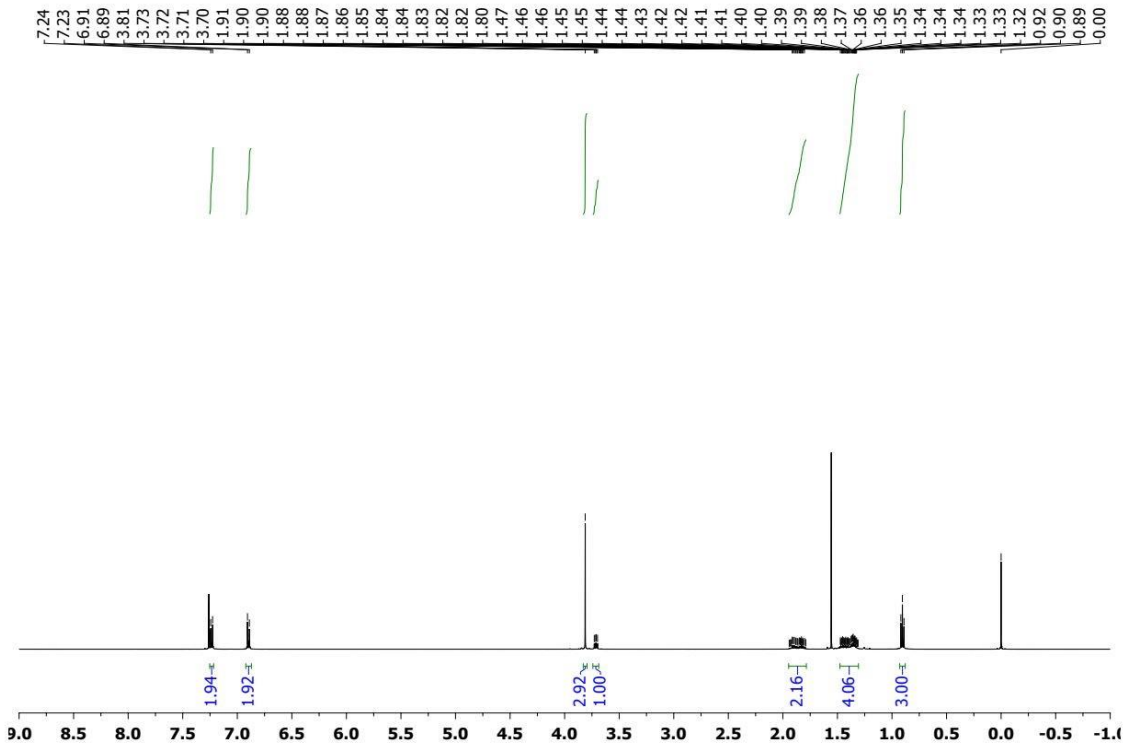
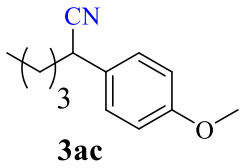


Figure 3.62 ^{1}H NMR ($CDCl_3$, 500 MHz) of 3ac



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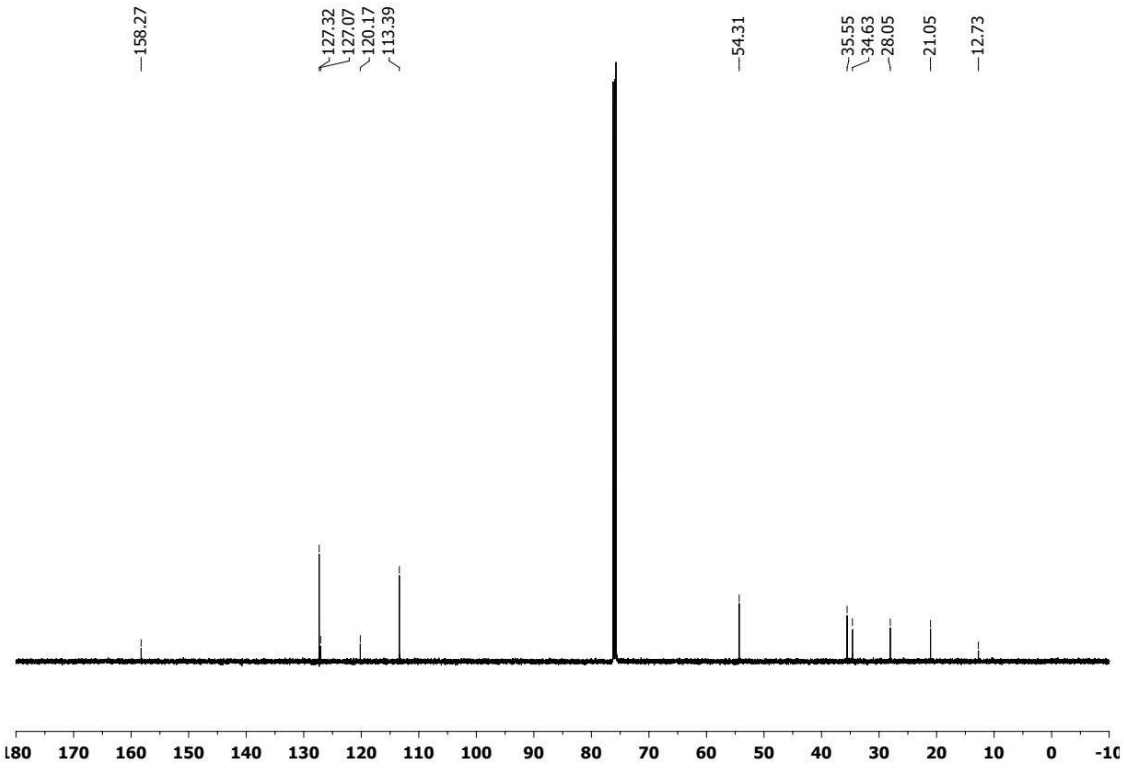
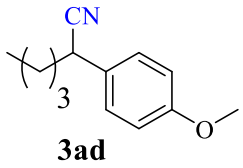


Figure 3.63 ^{13}C NMR ($CDCl_3$, 125 MHz) of 3ac



3ad

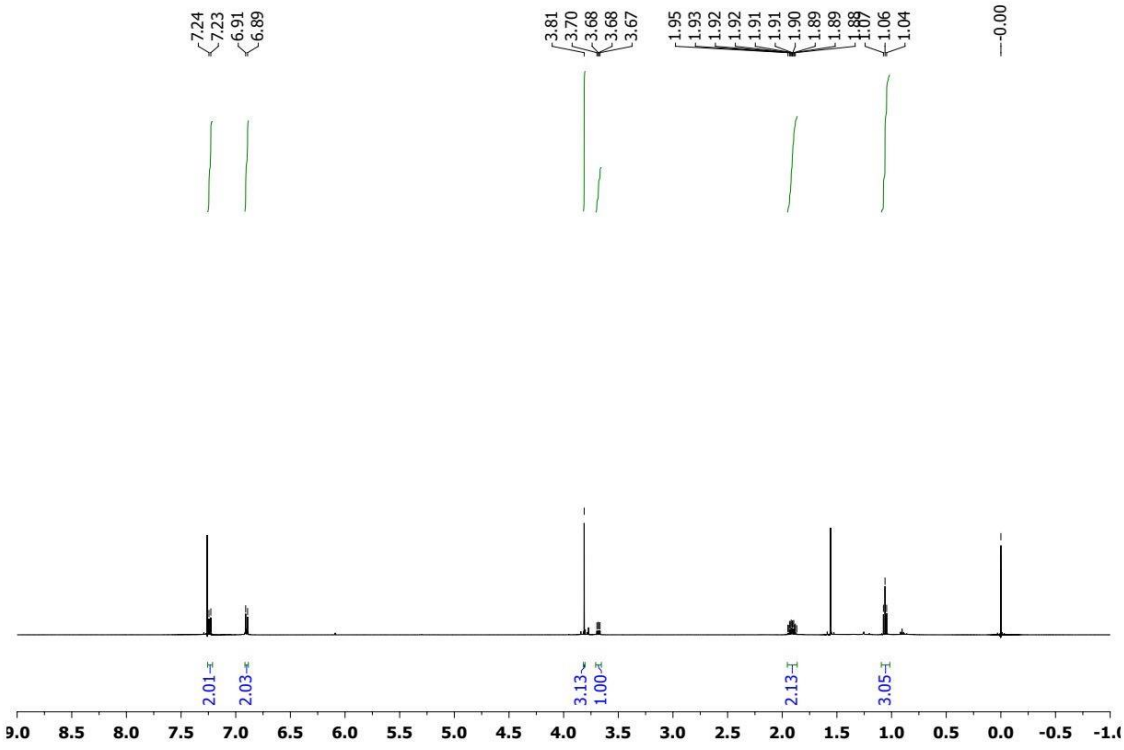


Figure 3.64 ^{1}H NMR ($CDCl_3$, 500 MHz) of 3ad

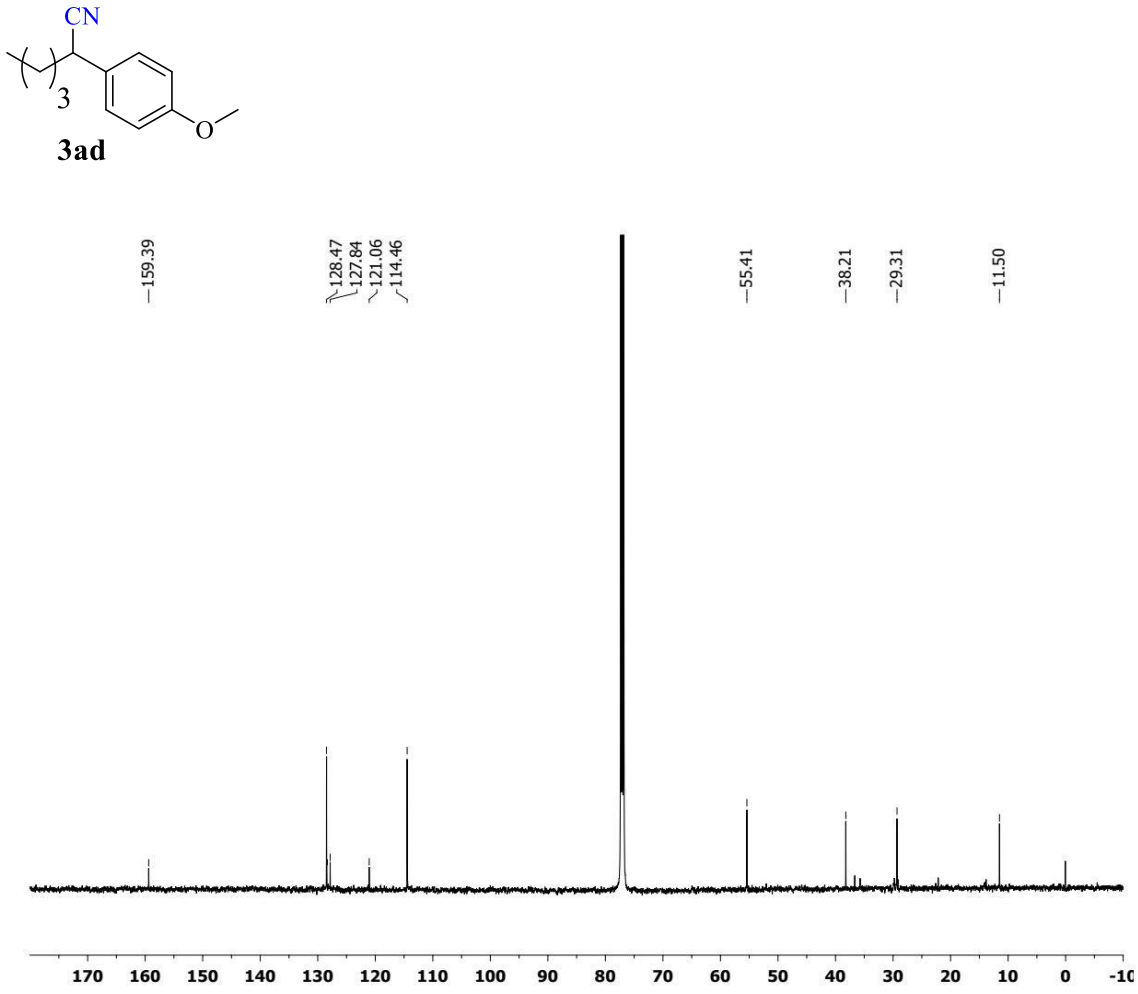


Figure 3.65 ^{13}C NMR ($CDCl_3$, 125 MHz) of 3ad

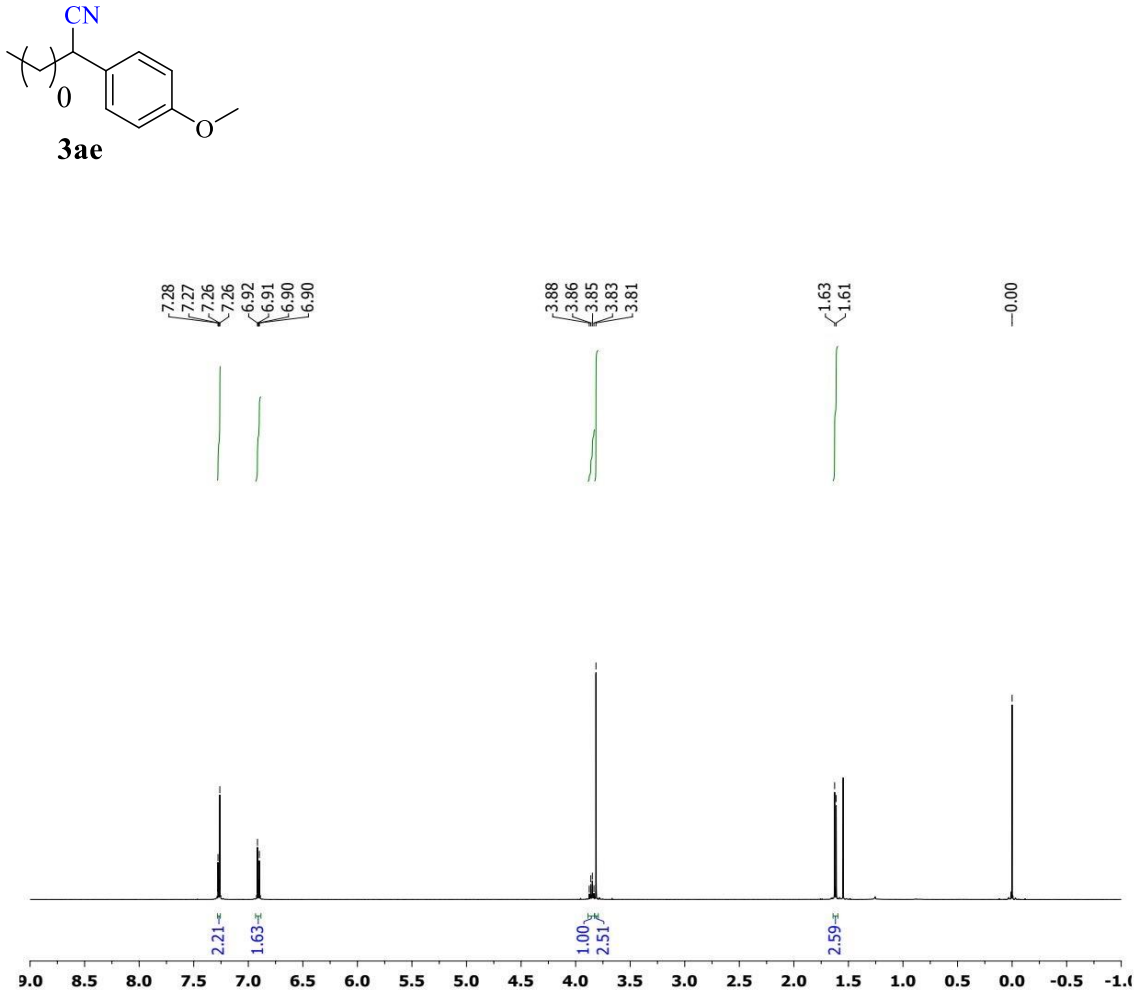


Figure 3.66 ^{1}H NMR ($CDCl_3$, 500 MHz) of 3ae

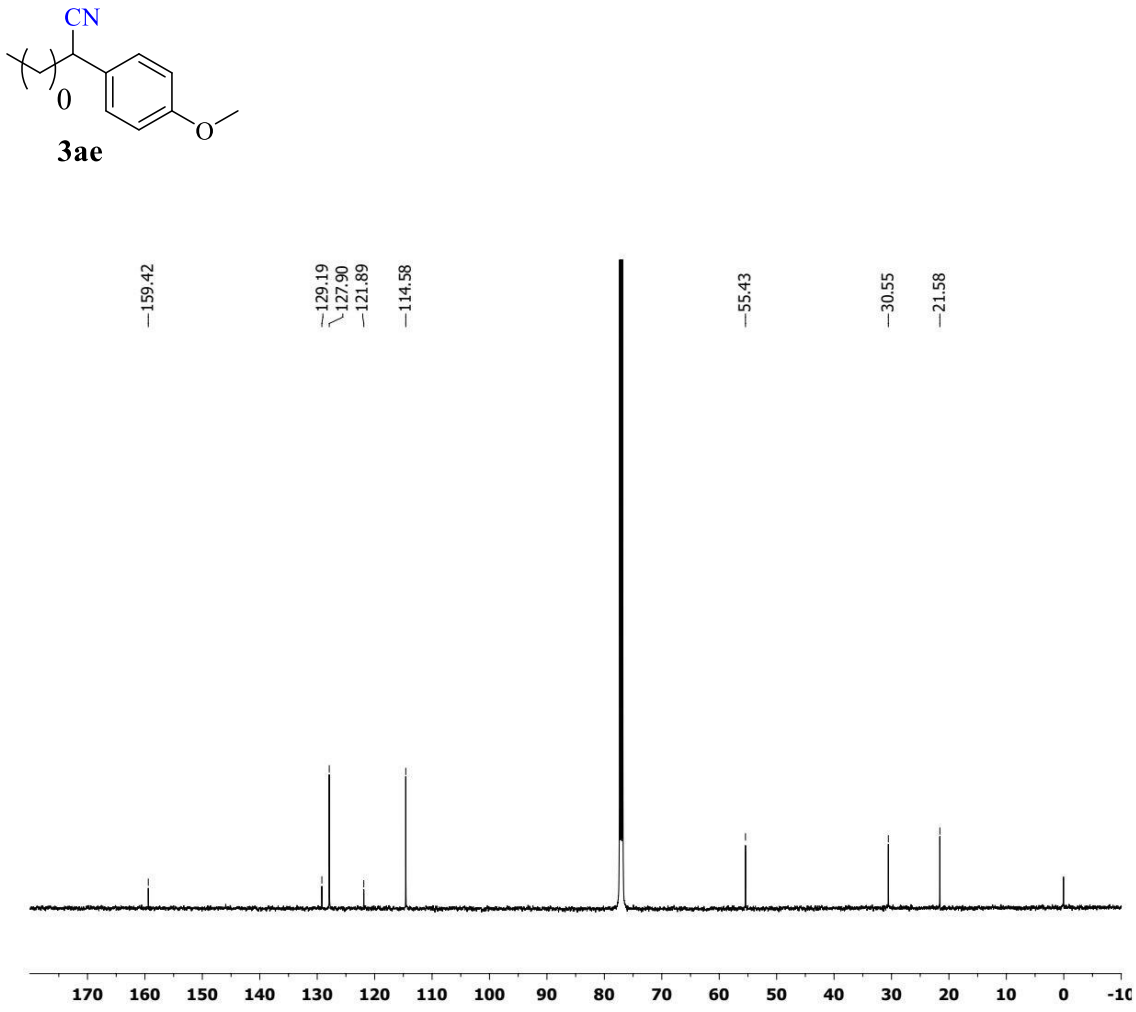


Figure 3.67 ^{13}C NMR ($CDCl_3$, 125 MHz) of 3ae

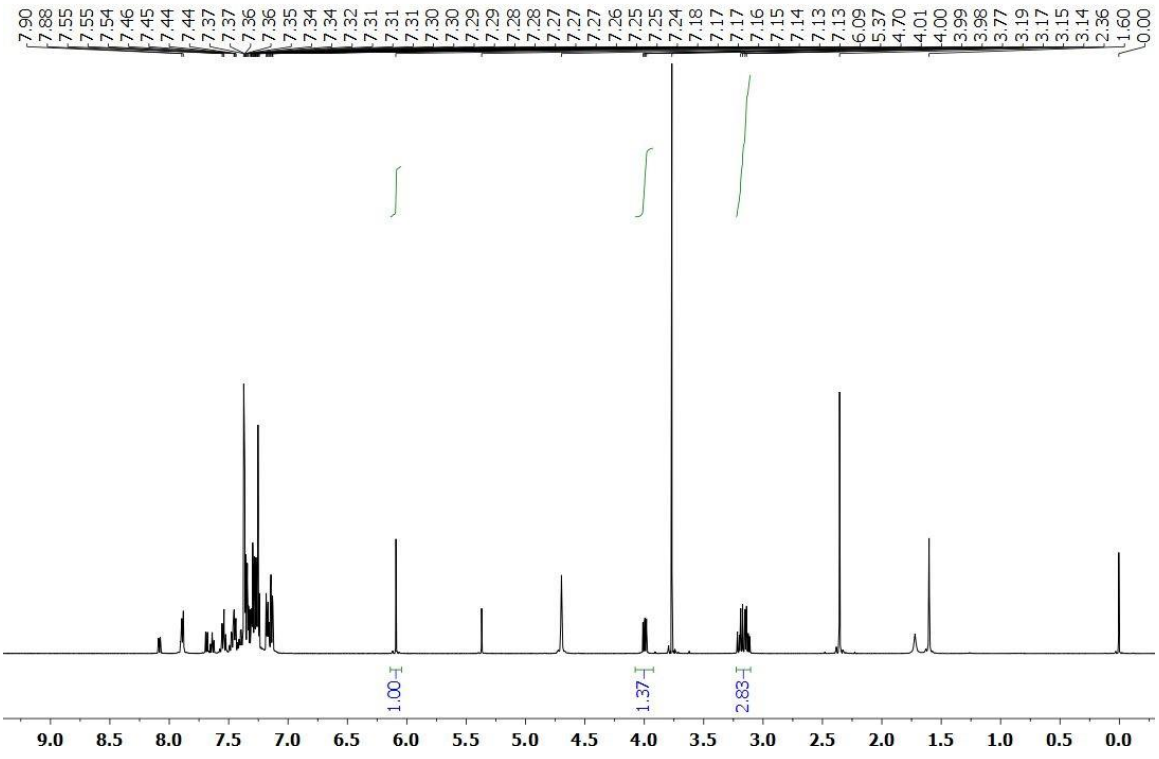


Figure 3.68 ^{1}H NMR Spectra ($CDCl_3$, 500 MHz) of the deuterium labeling experiment for the 2,3-diphenylacrylonitrile transfer hydrogenation using benzyl alcohol.

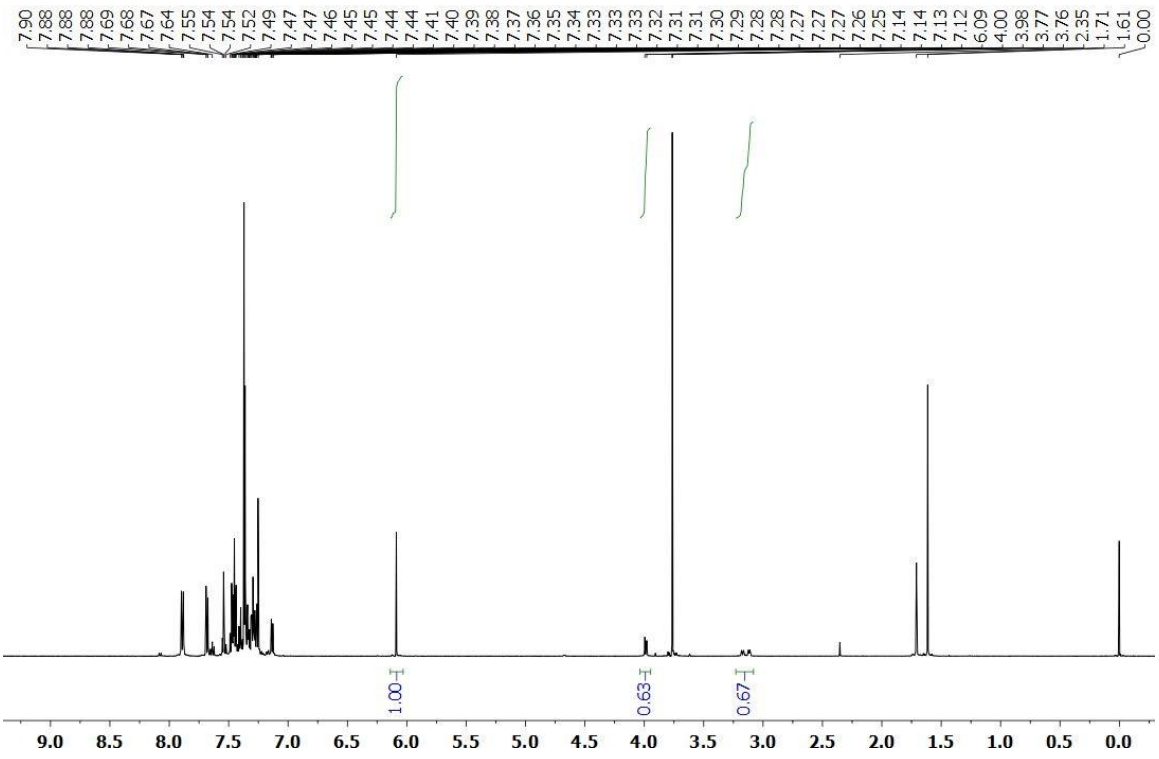


Figure 3.69 ^{1}H NMR Spectra ($CDCl_3$, 500 MHz) of the deuterium labeling experiment for the 2,3-diphenylacrylonitrile transfer hydrogenation using benzyl alcohol-α,α-d_2.

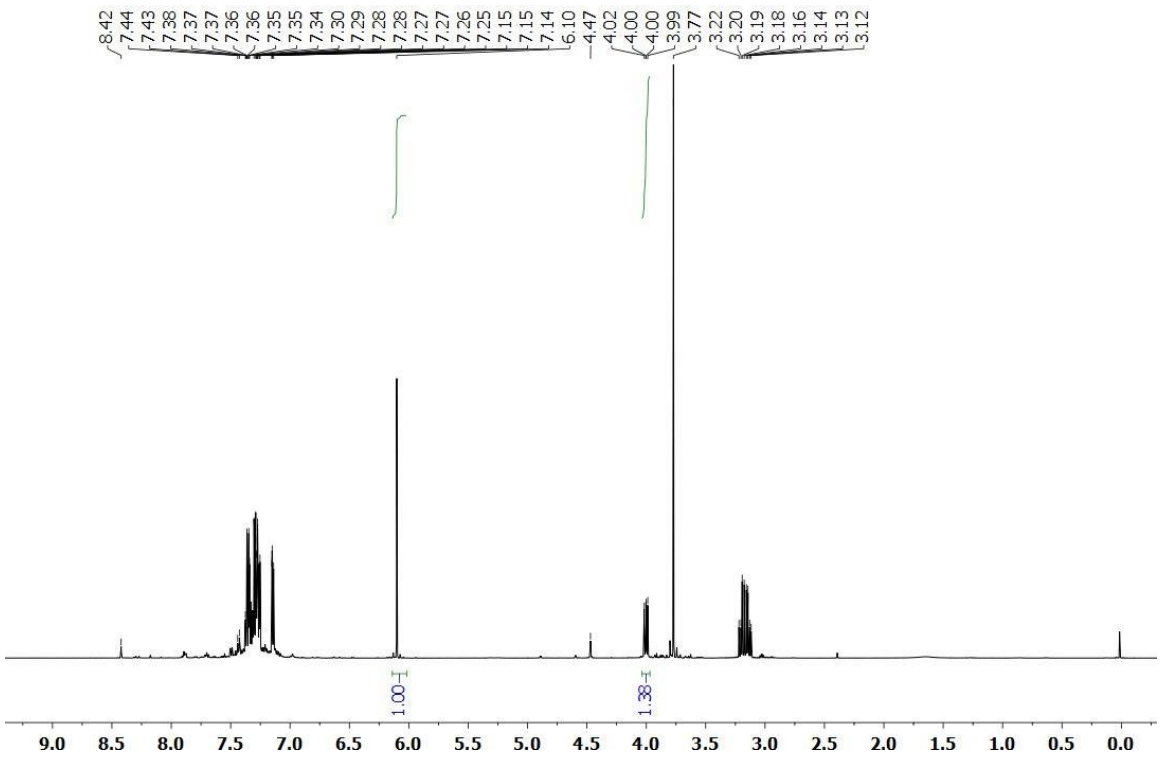


Figure 3.70 ^{1}H NMR Spectra ($CDCl_3$, 500 MHz) of the deuterium labeling experiment for the α-alkylation of phenylacetonitrile with benzyl alcohol.

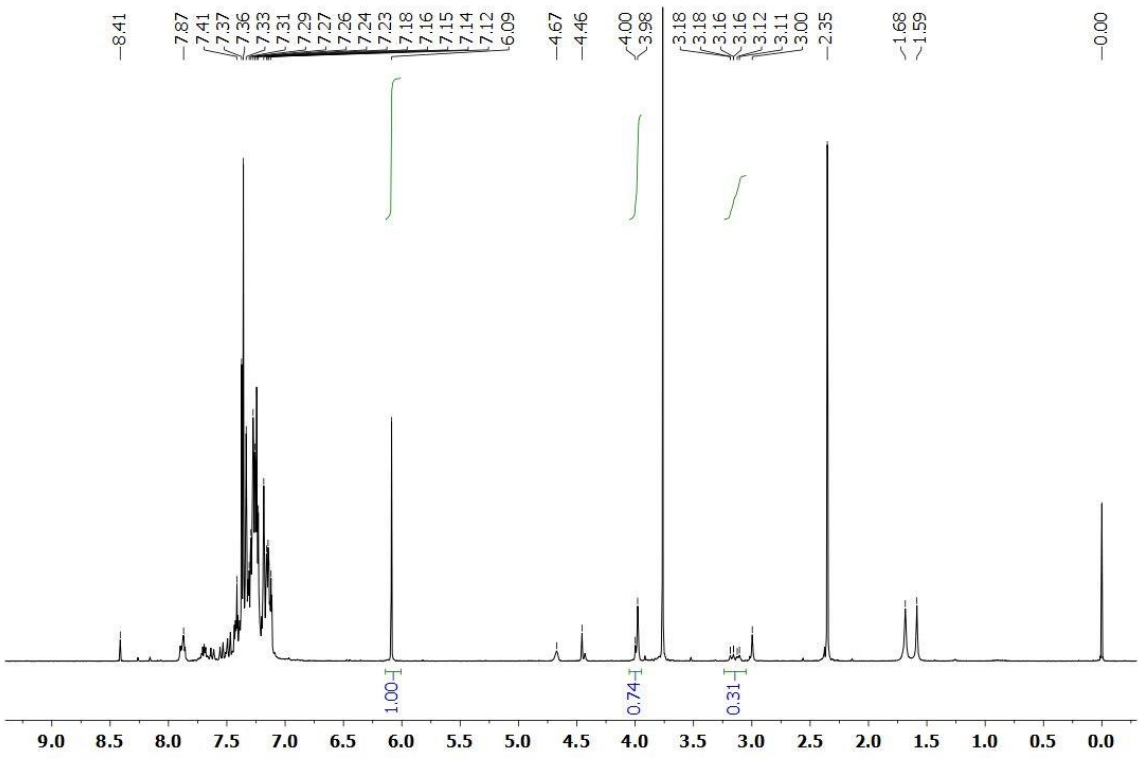


Figure 3.71 ^{1}H NMR Spectra ($CDCl_3$, 500 MHz) of the deuterium labeling experiment for the α-alkylation of phenylacetonitrile with benzyl alcohol-α,α-d_2.

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CHAPTER IV

Switchable Cobalt-Catalyzed α-Olefination and α-Alkylation of Nitriles with Primary Alcohols

4.1 Introduction

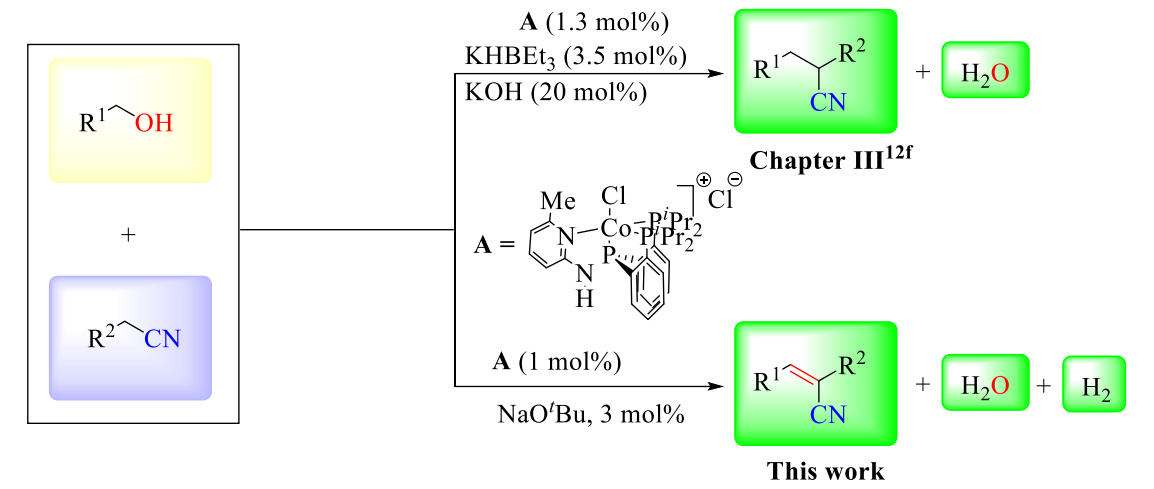
α,β-Substituted acrylonitriles are a family of organic compounds that are primarily applied as important building blocks, intermediates, and functional molecules for a range of products such as fragrances, dyes, polymeric materials, pharmaceuticals, natural products, etc.[1-7] Traditionally, the synthesis of the α,βsubstituted acrylonitriles involves base-mediated condensation of carbonyl compounds and nitriles, which is normally accompanied by several competitive side-reactions, e.g., aldol reaction of aldehydes, self-condensation of nitriles, hydrolysis of nitriles to amides, etc.[8-13] Alternative synthetic methods of the condensation of nitriles and carbonyl compounds toward the α,β-substituted acrylonitriles have been disclosed, which, however, suffer from several issues such as low yields, the involvement of toxic reagents, generation of plentiful wastes, limited availability of the substrates, and tedious procedures.[14-22] Thus, there is an emerging need to develop new synthetic methods to address these challenges.

Homogeneous transition-metal-catalyzed carbon−carbon bond formation belongs to one imperative synthetic strategy for value-added products.[23] An attractive method is to utilize the cheap, low-toxic, and readily available alcohols as the alkylating agents through an acceptorless dehydrogenative coupling (ADC) process.[24-36] The typical procedure of ADC toward α,β-substituted acrylonitriles involves the dehydrogenation of primary alcohols to

aldehydes, liberating H_2 to regenerate the catalytically active species. Then, the *in situ* formed aldehydes undergo condensation with the nitriles, furnishing the α,β-unsaturated acrylonitrile products and H_2O. Alternatively, the α,β-substituted acrylonitriles can be hydrogenated by the catalyst, leading to the saturated nitrile products. This process is recognized as the borrowing hydrogen (BH).[24-36]

There are a few examples of the synthesis of α,β-substituted acrylonitriles via the ADC process, the majority of which are based on precious transition-metal catalysts.[37-42] With the growing concerns on sustainability and economy, replacements of these precious metals with earth-abundant alternatives, e.g., Mn, Fe, Co, etc., are becoming more appealing.[43,44] To the best of our knowledge, there is just a single case disclosed by Milstein and co-workers using primary alcohols as the alkylating agents by a pincer Mn complex.[45] However, the reaction is sluggish with an average reaction time of over 40 h. Very recently, Balaraman and co-workers reported a Mn-catalyzed α-olefination of nitriles with secondary alcohols.[46] Examples of α-alkylation of nitriles with primary alcohols to saturated nitriles by base transition-metal catalysts are also limited.[47-52]

We have established a bench-stable Co complex (**A**) supported by a tetradentate N,P mixed-donor ligand iPrPPPNHPyMe. [53] **A** has proven to be an efficient and versatile precatalyst for secondary alcohol dehydrogenation to ketones,[53] primary alcohol dehydrogenative self-coupling to esters,[54] switchable couplings of primary and secondary alcohols to ketones and alcohols,[55,56] and switchable couplings of alcohols and amines to imines and amines.[57] We recently demonstrated that **A** can efficiently catalyze couplings of primary alcohols and nitriles to selectively form saturated nitriles[58] (Scheme 1, top).



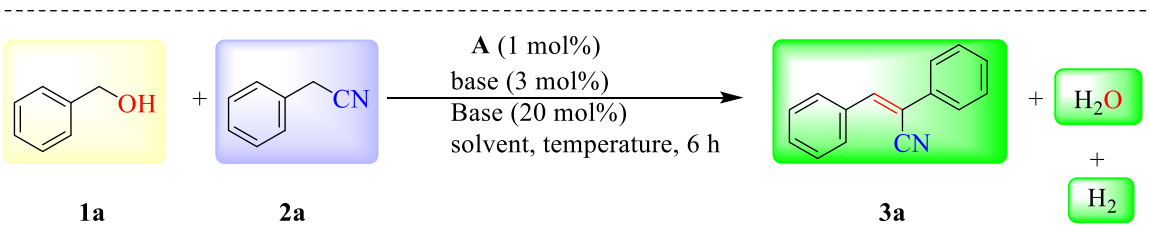
Scheme 4.1 Switchable α-Alkylation and α-olefinatiom of Nitriles with Primary Alcohols Catalyzed by Ding's cobalt catalyst

Encouraged by our recent studies, we herein present the cobalt-based catalytic system for the selective synthesis of α,β-substituted acrylonitriles via the ADC process with H_2 and H_2O as the only byproducts (Scheme 1, bottom). To the best of our knowledge, Co-catalyzed α-olefination of nitriles with primary alcohols has not been known so far. It is noteworthy that a short reaction time of 6 h suffices. This work also represents the first switchable α-olefination and α-alkylation of nitriles with primary alcohols to α,β-substituted acrylonitriles and nitriles, respectively, catalyzed by any base transition-metal catalyst.

4.2 Results and Discussion

Previously, we disclosed that **A** can catalyze α-alkylation of nitriles using primary alcohols to nitriles in the presence of 20 mol % KOH and 3.5 mol % KHBEt3.[58] Mechanistic study

showed that KOH plays a crucial role in the hydrogenation of the acrylonitrile intermediate to nitrile via the Meerwein− Ponndorf−Verley (MPV) pathway.[59-65] We surmise that at the reduced base loading, whereas the MPV process is efficiently suppressed, the reaction could be delicately controlled at the acrylonitrile level. Indeed, the reaction of benzyl alcohol (0.25 mmol) and benzyl cyanide (0.35 mmol) in the presence of 1 mol % A and 3 mol % KOH without KHBEt3 resulted in a 67% yield of 2,3-diphenylacrylonitrile in 6 h at 140 °C (Table 1, entry 1).



Scheme 4.2 Selective synthesis of olefinic nitrile product by Ding's catalyst

Table 4.1 Reaction Screening[a]

entry	Cat.	base	solvent	temp (°C)	Yield (%)[b]
1	A	KOH	toluene	140	67
2	A	KO^{t}Bu	toluene	140	82
3	A	KO^{t}Bu	toluene	125	52
4	A	NaO^{t}Bu	toluene	140	90, 85[c]
5	A	NaO^{t}Bu	toluene	140	90,[d] 85[e]
6	A	K_2CO_3	toluene	140	0
7	A	$KHBEt_3$	toluene	140	83
8	A	$LiHBEt_3$	toluene	140	63
9	A	–	toluene	140	0
10	–	NaO^{t}Bu	toluene	140	0
11	A	NaO^{t}Bu	benzene	140	90
12	A	NaO^{t}Bu	THF	140	44
13[f]	A	NaO^{t}Bu	toluene	140	87
14[g]	A	NaO^{t}Bu	toluene	140	83

[a]Reaction conditions: **1a** (0.25 mmol), **2a** (0.35 mmol), **A** (1 mol %), base (3 mol%), and solvent (1.2 mL) were heated in a reaction vessel (15 mL) with an argon balloon on top for 6 h. [b]Yields were determined by ^{1}H NMR analysis of the crude reaction mixture with 1,3,5-trimethoxybenzene as an internal standard. [c]Isolated yield of **3a**. [d]15 h. [e]5 h. [f]Isolated yield of 3a on a 1 mmol scale reaction. [g]Mercury (125 mg) was added to the reaction.

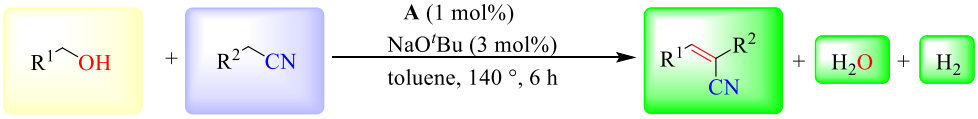
Intrigued by this result, we performed the optimization of the reactions. Among various types of bases, NaO^{t}Bu was proven to be more suitable, leading to an excellent 90% NMR yield and 85% isolated yield after purification by column chromatography (Table 4.1, entries 1, 2, 4, and 6−8). Control experiments showed that both **A** and base are essential for the reaction (Table 4.1, entries 9 and 10). A temperature of 140 °C and solvents such as toluene and benzene are more favorable for the reaction (Table 4.1, entries 2−4, 11, and

12). Remarkably, 6 h is sufficient for the completion of the reaction (Table 4.1, entries 4 and 5), which is in stark contrast to the reported Mn case, where a long reaction time of about 40 h is required.[45] The ^{1}H NMR indicates the product is the Z-isomer. An 87% isolated yield was obtained on the 1 mmol scale reaction (Table 4.1, entry 13). Mercury testing suggested a homogeneous catalytic system[66] (Table 4.1, entry 14). H_2 was confirmed by the analysis of gas phase by GC, indicating an ADC pathway (see experimental section).

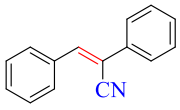
After obtaining the optimized reaction conditions, we then explored the substrate scope of the reaction. First, we focused on the scope of aromatic primary alcohols. Aromatic primary alcohols bearing electron-donating groups such as −OMe, −Me, −i Pr at the para position transformed smoothly to give the corresponding products in good to very good 60%−87% yields with Z-selectivity (Table 4.2, entries 3b−3d, 3s, and 3t). Here, we believe that the reason for getting Z-selective product is due to the thermodynamic of the reaction. Similarly, aromatic primary alcohols with electron-withdrawing groups such as −Cl, −F, $-CF_3$ at the para position afforded desired products in good to excellent 76−92% yields (Table 4.2, entries 3f−3h). Pleasingly, sterically hindered 2-methyl benzyl alcohol and 2-naphthyl methanol also proceeded well, leading to 81% and 82% yields, respectively (Table 4.2, 3e and 3k). Heteroaryl alcohols like piperonyl alcohol and 2-furfuryl methanol rendered the olefinic nitrile products in moderate to very good yields (Table4. 2, entries 3i, 3j, and 3u). Next, we investigated the scope of nitriles. Pleasingly, various aromatic nitriles with various electronic properties gave the corresponding products with 60−87% yields (Table 4.2, entries 3h, 3l, 3m, 3q, 3r, and 3s). Interestingly, nitriles with pyridyl and naphthyl ring delivered the desired acrylonitriles in 73% and 89% yields, respectively

(Table 4.2, entries 3o and 3p). It is noteworthy that the cyanide functionality is well tolerated (Table 4.2, entry 3t). With regards to the aliphatic primary alcohols, such as 1-hexanol and 1-dodecanol, the reactions turned out to be sluggish under the standard conditions. Gratifyingly, upon doubling the loadings of A and NaO^{t}Bu and prolonging the reaction time to 24 h, the reactions were significantly enhanced, revealing excellent 95% and 90% yields, respectively (Table 4.2, entries 3v and 3w). Notably, unsaturated aliphatic primary alcohols are also viable substrates with the C=C bond remaining intact (Table 4.2, entry 3x). Unfortunately, benzenepropanenitrile and aliphatic nitrile were not compatible with this method (Table 4.2, entry 3y).

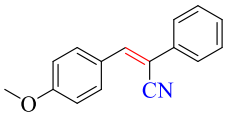
Table 4.2 α-Olefination of Nitriles with Primary Alcohols[a,b]



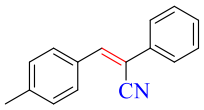
1 **2** **3**



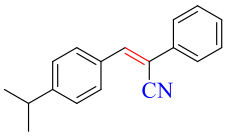
3a, 85%



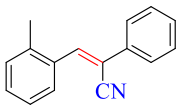
3b, 87%



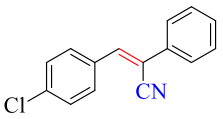
3c, 85%



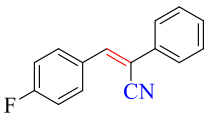
3d, 79%



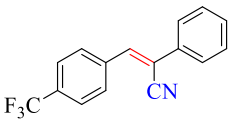
3e, 81%



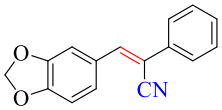
3f, 88%



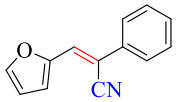
3g, 76%



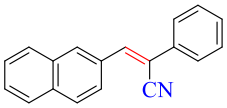
3h, 92%



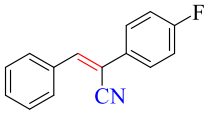
3i, 81%



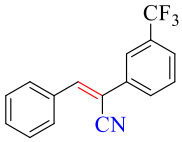
3j, 52 %



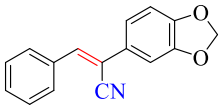
3k, 82 %



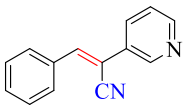
3l, 87 %



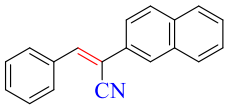
3m, 78 %



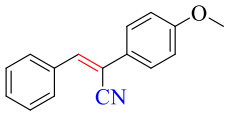
3n, 65 %



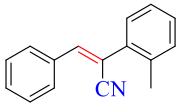
3o, 73 %



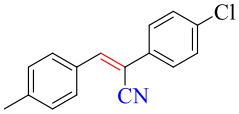
3p, 89 %



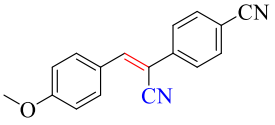
3q, 78 %



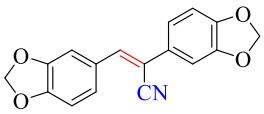
3r, 78 %



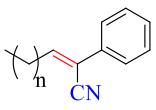
3s, 60 %



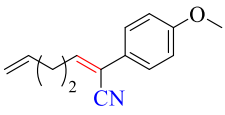
3t, 76 %



3u, 76 %



3v,n = 4, 95 %[c]
3w, n = 10, 90 %[c]

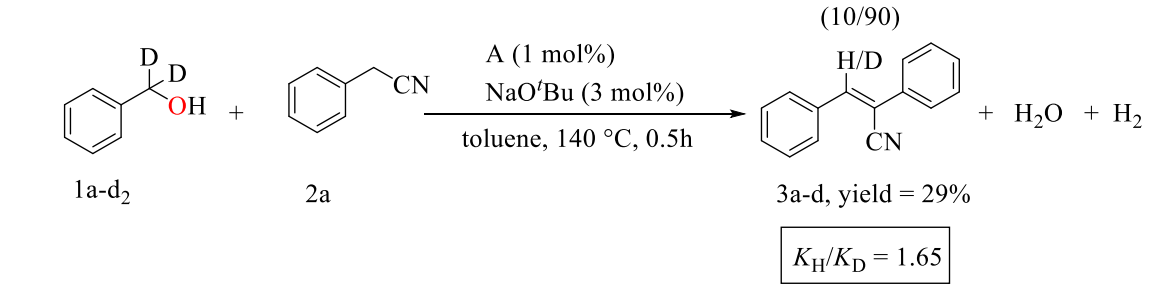


3x, 68 %[c]

3y,0 %

[a]Reaction conditions: primary alcohol (0.25 mmol), nitrile (0.35 mmol), **A** (1 mol%), NaOtBu (3 mol%), and toluene (1.2 mL) were heated at 140 °C in a reaction vessel (15 mL) with an argon balloon on top for 6 h. bIsolated yields. [c]**A** (2 mol%) and NaOtBu (6 mol%) for 24 h.

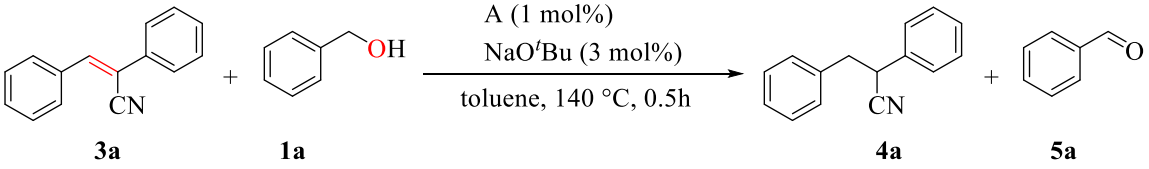
Next, we performed a mechanistic exploration to understand this reaction. A deuterium labeling experiment using 1a-d_2 and 2a resulted in 90% D-incorporation at the β position of the nitrile group, indicating the alcohol dehydrogenation step is reversible (Scheme 2). The kinetic isotope effect (KIE) of 1.65 was obtained, which indicates that the breakage of the α-C−H bond of 1a is moderately slow. The KIE number echoes the one from our prior study on the selective nitrile forming reaction, which is 1.88.[58]



Scheme 4.3 Deuterium labeling experiment using 1a- d_2

In the switchable acrylonitrile and nitrile synthesis, the base loadings play a critical and unique role in the selectivity determination. High base loadings that facilitate the MPV hydrogenation process result in the saturated nitrile products;[58] on the contrary, acrylonitriles are selectively formed employing a catalytic amount of base as revealed in

the present work. We have successfully leveraged this strategy to achieve switchable imine/amine and ketone/alcohol synthesis based on **A**.[55-57] The series of studies apparently demonstrate the high efficiency, selectivity, and versatility of our Co catalytic system affording a range of valuable products. In addition to the effects of the base loadings, the lack of hydrogenation ability of **A** at low base loadings is crucial for the product-switching. To test this hypothesis, the transfer hydrogenation of 2,3-diphenylacrylonitrile by benzyl alcohol was performed in the presence of 1 mol % **A** and 3 mol % of NaO^{t}Bu at 140 °C for 6 h (Scheme 3). A poor 12% yield of 2,3-diphenylpropanenitrile resulted. In stark contrast, with 20 mol % base alone, a significantly enhanced 82% yield was reached in just 15 min.[58] These results shed light on the roles of base loadings on the selectivity. **A** comprehensive mechanistic study is currently underway in our laboratory.

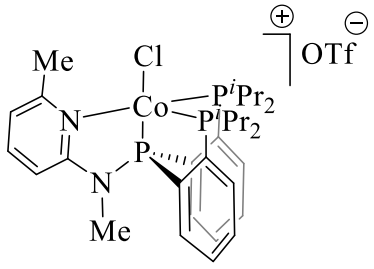


Scheme 4.4. Transfer hydrogenation of 2,3 Diphenylacrylonitrile

To explore if the metal−ligand cooperativity (MLC) participates through the N−H linker on A, we employed complex B as the precatalyst, which bears an N−Me moiety[12a] (Figure 1). Interestingly, a comparable 84% yield of 3a was obtained, suggesting that MLC may not play a crucial role.

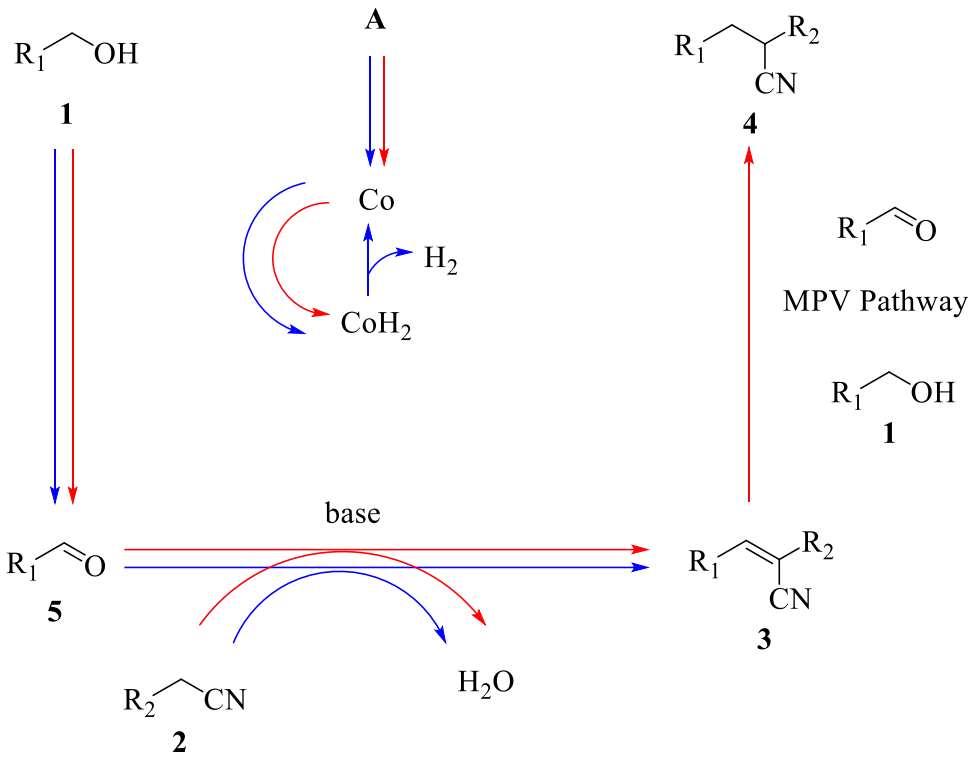
Previously, we have shown that **A** is capable of dehydrogenation of alcohols,[53,54] and base alone can mediate the condensation of aldehydes and nitriles.[58] Benzaldehydes were

observed in the α-olefination of benzyl cyanide with benzyl alcohol, suggesting that the condensation is a relatively slow step. Based on the literature,[24-36] and our studies, a plausible reaction mechanism is given (Scheme 4). Initially, the Co precatalyst **A** is activated by a base through the salt elimination.[53] The catalytically active Co species mediates the dehydrogenation of primary alcohols to form the aldehyde intermediates, which subsequently undergo the base-mediated condensation with the nitriles to yield the acrylonitriles and H_2O. Finally, the liberation of H_2 regenerates the catalyst. Alternatively, at high base loadings, the base mediated MPV process further reduces the acrylonitriles to the nitrile products.[58]



B

Fig. 4.1 Complex B examined.



Scheme 4.5 Proposed mechanism (α-Olefination in Blue and α-alkylation in Red)

4.3 Conclusions

We present the first Co-catalyzed switchable formations of α,βsubstituted acrylonitriles and nitriles. A large variety of nitriles and primary alcohols are viable substrates with this protocol. Notably, this reaction is environmentally friendly and atom efficient with H_2 and H_2O being the sole byproducts. We anticipate that this study will contribute to the catalyst designs, especially the ones that take advantage of the earth-abundant transition metals.

4.4 Experimental Section

4.4.1 General Methods.

Unless otherwise is stated, all reactions were set up in an MBraun glovebox under an atm of N_2. Anhydrous solvents were deoxygenated by sparging with N_2 and dried by passing through activated alumina columns of a Pure Solv solvent purification system. $CDCl_3$ was purchased from Cambridge Isotope Lab and dried over molecular sieves (4 Å). Cobalt complexes (**A** and **B**) were prepared according to our published procedures.[53] The alcohol and nitrile substrates were purchased from Sigma Aldrich and used as received. All other chemicals were purchased from Fisher Scientific. Bases such as KO^{t}Bu and NaO^{t}Bu were vacuum sublimed before use. Comparable results were obtained as using >99.9% commercial ones. NMR spectra were recorded on a JEOL Unity 500 MHz or 300 MHz spectrometer. ^{1}H NMR spectra were referenced to tetramethyl silane (0.00 ppm) using $CDCl_3$ as solvent. ^{13}C NMR were referenced to solvent carbons at 77.0 ppm for $CDCl_3$. ^{19}F NMR spectra were referenced to fluorobenzene at –113.15 ppm. The NMR spectra for the known compounds are comparable with the previously reported ones.[22,45, 67-72] High resolution mass spectrometry (HRMS) analyses were performed on Waters GCT Premier orthogonal acceleration time of flight (oa-TOF) mass spectrometer in positive EI method using MassLynx Software control.

4.5 General procedures for α-olefination of nitriles with primary alcohols:

Inside the N_2 filled glove box, an oven-dry 15 mL reaction tube was charged with the mixture of **A** (1.6 mg, 2.44 µmol, 1 mol%), NaO^{t}Bu (0.7 mg, 7.3 µmol, 3 mol%), nitrile (0.35 mmol), primary alcohol (0.25 mmol), and toluene (1 mL). The reaction tube was sealed by a screw cap fitted with PTFE septa and taken out from the box. An argon filled balloon was fitted on the top of the reaction tube and placed in a pre-heated oil bath at 140 °C for 6 h. After the reaction was finished and cooled down, the reaction mixture was filtered through a silica gel plug and washed with DCM. The collected filtrate was concentrated under reduced pressure. The obtained crude mixture was purified by a silica gel column using ethyl acetate /hexane (1:50, v/v) as an eluent to obtain the isolated yield.

4.5.1 Procedures for α-olefination of nitriles with primary alcohols by complex B:

Inside the N_2 filled glove box, an oven-dry 15 mL reaction tube was charged with the mixture of **B** (1.9 mg, 2.44 µmol, 1 mol%), NaO^{t}Bu (0.7 mg, 7.3 µmol, 3 mol%), nitrile (0.35 mmol), primary alcohol (0.25 mmol), and toluene (1 mL). The reaction tube was sealed by a screw cap fitted with PTFE septa and taken out from the box. An argon filled balloon was fitted on the top of the reaction tube and placed in a pre-heated oil bath at 140 °C for 6 h. After the reaction was finished and cooled down, the reaction mixture was filtered through a silica gel plug and washed with DCM. The collected filtrate was concentrated under reduced pressure. The obtained crude mixture was purified by a silica gel column using ethyl acetate /hexane (1:50, v/v) as an eluent to obtain the isolated yield.

4.6 Procedures for α-olefination of benzyl nitrile with benzyl alcohol at 1 mmol scale:

Inside the N_2 filled glove box, an oven-dry 15 mL reaction tube was charged with the mixture of **A** (6.4 mg, 9.76 µmol, 1 mol%), NaOtBu (2.8 mg, 29.2 µmol, 3 mol%), benzyl nitrile (1.4 mmol), benzyl alcohol (1.0 mmol), and toluene (1 mL). The reaction tube was sealed by a screw cap fitted with PTFE septa and taken out from the box. An argon filled balloon was fitted on the top of the S3 reaction tube and placed in a pre-heated oil bath at 140 °C for 6 h. After the reaction was finished and cooled down, the reaction mixture was filtered through a silica gel plug and washed with DCM. The collected filtrate was concentrated under reduced pressure. The obtained crude mixture was purified by a silica gel column using ethyl acetate /hexane (1:50, v/v) as an eluent to obtain the isolated yield.

4.7 Mercury test:

Inside the N_2 filled glove box, an oven-dry 15 mL reaction tube was charged with the mixture of **A** (1.6 mg, 2.44 µmol, 1 mol%), NaO^{t}Bu (0.7 mg, 7.3 µmol, 3 mol%), nitrile (0.35 mmol), primary alcohol (0.25 mmol), Hg (125 mg), and toluene (1 mL). The reaction tube was sealed by a screw cap fitted with PTFE septa and taken out from the box. An argon filled balloon was fitted on the top of the reaction tube and placed in a pre-heated oil bath at 140 °C for 6 h. After the reaction was finished and cooled down, 1,3,5-trimethoxybenzene (8.4 mg, 0.05 mmol) dissolved in diethyl ether was added to the reaction mixture, stirred, and filtered through silica gel plug. The plug was washed with diethyl ether and the collected filtrate was concentrated under vacuum using rotavapor. The obtained residue was dissolved in $CDCl_3$ and subjected for NMR analysis.

4.8 Filtration experiment:

Inside the N_2 filled glove box, an oven-dry 15 mL reaction tube was charged with the mixture of **A** (1.6 mg, 2.44 µmol, 1 mol%), NaO^{t}Bu (0.7 mg, 7.3 µmol, 3 mol%), nitrile (0.35 mmol), primary alcohol (0.25 mmol), and toluene (1 mL). The reaction tube was sealed by a screw cap fitted with PTFE septa and taken out from the box. An argon filled balloon was fitted on the top of the reaction tube and placed in a pre-heated oil bath at 140 °C for 10 min. The reaction tube was cooled down and taken back to the glove box. The solution was filtered through a PTFE filtering disc and loaded into a new reaction vessel (to avoid possible nanoparticles sticked on the wall) and allowed to run for 6 h. After the reaction was finished and cooled down, 1,3,5-trimethoxybenzene (8.4 mg, 0.05 mmol) dissolved in diethyl ether was added to the reaction mixture, stirred, and filtered through silica gel plug. The plug was washed with diethyl ether and the collected filtrate was concentrated under vacuum using rotavapor. The obtained residue was dissolved in $CDCl_3$ and subjected for NMR analysis. A good 78% yield was recorded. In the control experiment for 10 min, only 19% yield was obtained. These results suggest that the reaction is not mediated by nanomaterials.

4.9 Hydrogen gas detection:

Inside the N_2 filled glove box, an oven-dry 100 mL pressure vessel was charged with the mixture of **A** (6.4 mg, 9.76 µmol, 1 mol%), NaO^{t}Bu (2.8 mg, 29.2 µmol, 3 mol%), benzeneacetonitrile (1.4 mmol), benzyl alcohol (1 mmol), and toluene (1.5 mL). The pressure vessel was sealed and taken out from the box and placed in a pre-heated oil bath at 140 °C for 6 h. The headspace gas sample was taken by a needle syringe from the side

arm and detected by SRI 8610C Gas Chromatograph with a 5 Å molecular sieves column (Restek CP753415) with N_2 carrier gas.

4.10 Deuterium labeling experiments for α-olefination of nitriles with primary alcohols:

Inside the N_2 filled glove box, an oven-dry 15 mL reaction tube was charged with the mixture of **A** (1.6 mg, 2.44 μmol, 1 mol%), NaO^{t}Bu (0.7 mg, 7.3 μmol, 3 mol%), benzeneacetonitrile (0.35 mmol), benzyl alcohol or benzyl alcohol-α,α-d2 (0.25 mmol), and toluene (1 mL). The reaction tube was S4 sealed by a screw cap fitted with PTFE septa and taken out from the box. An argon filled balloon was fitted on the top of the reaction tube and placed in a pre-heated oil bath at 140 °C for 0.5 h. After the reaction was finished and cooled down, 1,3,5-trimethoxybenzene (8.4 mg, 0.05 mmol) dissolved in diethyl ether was added to the reaction mixture, stirred, and filtered through silica gel plug. The plug was washed with diethyl ether and the collected filtrate was concentrated under vacuum using rotavapor. The obtained residue was dissolved in $CDCl_3$ and subjected for NMR analysis.

4.11 Transfer hydrogenation of 2,3-diphenylacrylonitrile by NaO^{t}Bu:

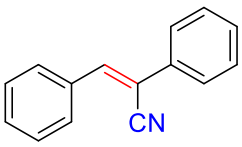
Inside the N_2 filled glove box, an oven-dry 100 mL reaction tube was charged with the mixture of NaO^{t}Bu (0.7 mg, 1 mol%), 2,3-diphenylacrylonitrile (0.75 mmol), benzyl alcohol (1.5 mmol) and toluene (2 mL). The reaction tube was sealed, taken out from the box, and placed in a pre-heated oil bath at 140 °C for 6 h. After the reaction was finished and cooled down, 1,3,5-trimethoxybenzene (8.4 mg, 0.05 mmol) dissolved in diethyl ether

was added to the reaction mixture, stirred, and filtered through silica gel plug. The plug was washed with diethyl ether and the collected filtrate was concentrated under vacuum using rotavapor. The obtained residue was dissolved in $CDCl_3$ and subjected for NMR analysis.

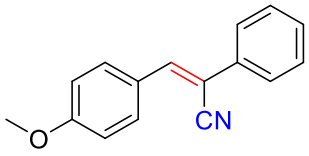
4.12 Transfer hydrogenation of 2,3-diphenylacrylonitrile in the presence of NaO^{t}Bu and A:

Inside the N_2 filled glove box, an oven-dry 100 mL reaction tube was charged with the mixture of **A** (1.6 mg, 1 mol%), NaO^{t}Bu (0.7 mg, 3 mol%), benzyl alcohol (0.5 mmol) and toluene (2 mL). The reaction tube was sealed, taken out from the box, and placed in a pre-heated oil bath at 140 °C for 1 min, and the color changed from dark red to light yellow. The tube was taken back to the box, and 2,3-diphenylacrylonitrile (0.25 mmol) was added. After heating for 6 h at 140 °C and cooling down, 1,3,5-trimethoxybenzene (8.4 mg, 0.05 mmol) dissolved in diethyl ether was added to the reaction mixture, stirred, and filtered through silica gel plug. The plug was washed with diethyl ether and the collected filtrate was concentrated under vacuum using rotavapor. The obtained residue was dissolved in $CDCl_3$ and subjected for NMR analysis.

4.13 Synthetic Details for α-Olefinic Nitriles 3a – 3x

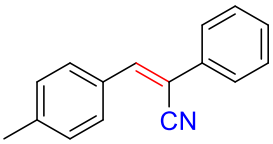


3a[67]. Inside the N_2 filled glove box, an oven-dry 15 mL reaction tube was charged with the mixture of **A** (1.6 mg, 2.44 µmol, 1 mol%), NaO^{t}Bu (0.7 mg, 7.3 µmol, 3 mol%), benzeneacetonitrile (0.35 mmol, 40 µL), benzyl alcohol (0.25 mmol, 26 µL), and toluene (1 mL). The reaction tube was sealed by a screw cap fitted with PTFE septa and taken out from the box. An argon filled balloon was fitted on the top of the reaction tube and placed in a pre-heated oil bath at 140 °C for 6 h. After the reaction was finished and cooled down, the reaction mixture was filtered through a silica gel plug and washed with DCM. The collected filtrate was concentrated under reduced pressure. The obtained crude mixture was purified by a silica gel column using ethyl acetate/hexane (1:50, v/v) as an eluent. White solid of 3a was isolated. Yield: 43.6 mg (85%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.89 (d, J = 7.2 Hz, 2H), 7.68 (d, J = 7.4 Hz, 2H), 7.54 (s, 1H), 7.49 - 7.37 (m, 6H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.4, 134.6, 133.8, 130.6, 129.4, 129.3, 129.2, 129.1, 126.1, 118.1, 111.8 ppm.

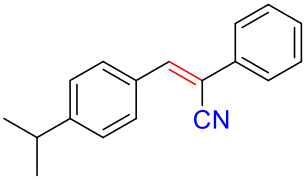


3b[67]. Inside the N_2 filled glove box, an oven-dry 15 mL reaction tube was charged with the mixture of **A** (1.6 mg, 2.44 µmol, 1 mol%), NaO^{t}Bu (0.7 mg, 7.3 µmol, 3 mol%), benzeneacetonitrile (0.35 mmol, 40 µL), 4-methoxybenzyl alcohol (0.25 mmol, 31 µL), and toluene (1 mL). The reaction tube was sealed by a screw cap fitted with PTFE septa and taken out from the box. An argon filled balloon was fitted on the top of the reaction tube and placed in a pre-heated oil bath at 140 °C for 6 h. After the reaction was finished

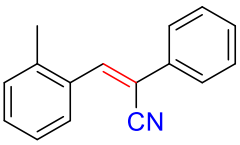
and cooled down, the reaction mixture was filtered through a silica gel plug and washed with DCM. The collected filtrate was concentrated under reduced pressure. The obtained crude mixture was purified by a silica gel column using ethyl acetate/hexane (1:50, v/v) as an eluent. White solid of 3b was isolated. Yield: 51.2 mg (87%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.89 (d, J = 8.8 Hz, 2H), 7.65 (d, J = 7.6 Hz, 2H), 7.50 - 7.32 (m, 4H), 6.98 (d, J = 8.8 Hz, 2H), 3.87 (s, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.4, 140.9, 133.9, 130.2, 128.0, 127.8, 125.6, 124.8, 117.6, 113.4, 107.7, 54.5 ppm.



3c[67]. Inside the N_2 filled glove box, an oven-dry 15 mL reaction tube was charged with the mixture of **A** (1.6 mg, 2.44 µmol, 1 mol%), NaO^{t}Bu (0.7 mg, 7.3 µmol, 3 mol%), benzeneacetonitrile (0.35 mmol, 40 µL), 4- methylbenzyl alcohol (0.25 mmol, 30.5 mg), and toluene (1 mL). The reaction tube was sealed by a screw cap fitted with PTFE septa and taken out from the box. An argon filled balloon was fitted on the top of the reaction tube and placed in a pre-heated oil bath at 140 °C for 6 h. After the reaction was finished and cooled down, the reaction mixture was filtered through a silica gel plug and washed with DCM. The collected filtrate was concentrated under reduced pressure. The obtained crude mixture was purified by a silica gel column using ethyl acetate/hexane (1:50, v/v) as an eluent. White solid of 3c was isolated. Yield: 46.5 mg (85%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80 (d, J = 8.1 Hz, 2H), 7.67 (d, J = 8.8 Hz, 2H), 7.51 (s, 1H), 7.44 (t, J = 7.5 Hz, 2H), 7.38 (t, J = 7.3 Hz, 1H), 7.28 (d, J = 8.1 Hz, 2H), 2.42 (s, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 141.2, 140.0, 133.6, 129.9, 128.6, 128.2, 127.9, 127.9, 124.8, 117.1, 109.3, 20.5 ppm.

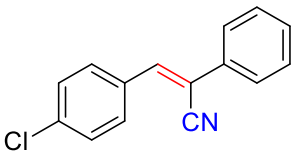


3d. Inside the N_2 filled glove box, an oven-dry 15 mL reaction tube was charged with the mixture of **A** (1.6 mg, 2.44 µmol, 1 mol%), NaO^{t}Bu (0.7 mg, 7.3 µmol, 3 mol%), benzeneacetonitrile (0.35 mmol, 40 µL), 4-isopropylbenzyl alcohol (0.25 mmol, 38 µL), and toluene (1 mL). The reaction tube was sealed by a screw cap fitted with PTFE septa and taken out from the box. An argon filled balloon was fitted on the top of the reaction tube and placed in a pre-heated oil bath at 140 °C for 6 h. After the reaction was finished and cooled down, the reaction mixture was filtered through a silica gel plug and washed with DCM. The collected filtrate was concentrated under reduced pressure. The obtained crude mixture was purified by a silica gel column using ethyl acetate/hexane (1:50, v/v) as an eluent. Colorless liquid of 3d was isolated. Yield: 49 mg (79%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84 (d, J = 8.2 Hz, 2H), 7.67 (d, J = 7.3 Hz, 2H), 7.52 (s, 1H), 7.47 - 7.42 (m, 2H), 7.38 (t, J = 6.8 Hz, 1H), 7.33 (d, J = 8.2 Hz, 2H), 3.03 – 2.89 (m, 1H), 1.28 (d, J = 6.9 Hz, 6H) ppm; ^{13}C NMR δ 152.0, 142.3, 131.4, 129.4, 129.0, 127.0, 125.9, 118.2, 110.5, 34.2, 23.7 ppm; HRMS (ESI+): m/z [M+H]+calcd for C18H17NNa, 270.1258; found 270.1253.

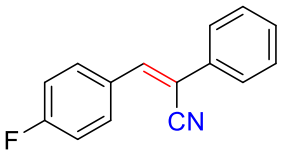


3e[67]. Inside the N_2 filled glove box, an oven-dry 15 mL reaction tube was charged with the mixture of **A** (1.6 mg, 2.44 µmol, 1 mol%), NaO^{t}Bu (0.7 mg, 7.3 µmol, 3 mol%), benzeneacetonitrile (0.35 mmol, 40 µL), 2- methylbenzyl alcohol (0.25 mmol, 30 µL), and toluene (1 mL). The reaction tube was sealed by a screw cap fitted with PTFE septa and taken out from the box. An argon filled balloon was fitted on the top of the reaction tube and placed in a pre-heated oil bath at 140 °C for 6 h. After the reaction was finished and cooled down, the reaction

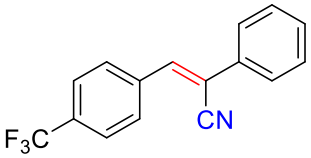
mixture was filtered through a silica gel plug and washed with DCM. The collected filtrate was concentrated under reduced pressure. The obtained crude mixture was purified by a silica gel column using ethyl acetate/hexane (1:50, v/v) as an eluent. White solid of 3e was isolated. Yield: 44.4 mg (81%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 (d, J = 7.0 Hz, 1H), 7.86 (d, J = 7.4 Hz, 1H), 7.76 (s, 1H), 7.69 (d, J = 8.2 Hz, 2H), 7.44 (dt, J = 14.7, 7.8 Hz, 3H), 7.34 (dd, J = 11.3, 7.4 Hz, 2H), 2.40 (s, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 114.2, 137.6, 134.4, 133.3, 130.6, 130.3, 129.4, 129.2, 128.2, 126.5, 126.2, 117.8, 114.0, 20.1 ppm.



3f[67] . Inside the N_2 filled glove box, an oven-dry 15 mL reaction tube was charged with the mixture of **A** (1.6 mg, 2.44 µmol, 1 mol%), NaO^{t}Bu (0.7 mg, 7.3 µmol, 3 mol%), benzeneacetonitrile (0.35 mmol, 40 µL), 4- chlorobenzyl alcohol (0.25 mmol, 36 mg), and toluene (1 mL). The reaction tube was sealed by a screw cap fitted with PTFE septa and taken out from the box. An argon filled balloon was fitted on the top of the reaction tube and placed in a pre-heated oil bath at 140 °C for 6 h. After the reaction was finished and cooled down, the reaction mixture was filtered through a silica gel plug and washed with DCM. The collected filtrate was concentrated under reduced pressure. The obtained crude mixture was purified by a silica gel column using ethyl acetate/hexane (1:50, v/v) as an eluent. White solid of 3f was isolated. Yield: 52.7 mg (88%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.83 (d, J = 8.5 Hz, 2H), 7.68 (d, J = 8.7 Hz, 2H), 7.51 - 7.37 (m, 6H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 140.8, 136.5, 134.3, 132.3, 130.6, 129.5, 129.4, 129.2, 126.1, 117.8, 112.4 ppm.

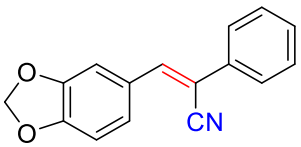


3g[68]. Inside the N_2 filled glove box, an oven-dry 15 mL reaction tube was charged with the mixture of **A** (1.6 mg, 2.44 µmol, 1 mol%), NaO^{t}Bu (0.7 mg, 7.3 µmol, 3 mol%), benzeneacetonitrile (0.35 mmol, 40 µL), 4- fluorobenzyl alcohol (0.25 mmol, 27 µL), and toluene (1 mL). The reaction tube was sealed by a screw cap fitted with PTFE septa and taken out from the box. An argon filled balloon was fitted on the top of the reaction tube and placed in a preheated oil bath at 140 °C for 6 h. After the reaction was finished and cooled down, the reaction mixture was filtered through a silica gel plug and washed with DCM. The collected filtrate was concentrated under reduced pressure. The obtained crude mixture was purified by a silica gel column using ethyl acetate/hexane (1:50, v/v) as an eluent. White solid of 3g was isolated. Yield: 42.4 mg (76%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90 (dd, J = 8.8, 5.3 Hz, 2H), 7.67 (d, J = 7.2 Hz, 2H), 7.50 (s, 1H), 7.43 (dt, J = 25.7, 7.2 Hz, 3H), 7.16 (t, J = 8.6 Hz, 2H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.8 (d, 1J C-F = 253 Hz), 141.0, 134.4, 131.4 (d, 3J C-F = 8.6 Hz), 130.1, 129.4, 129.2, 126.0, 118.0, 116.3 (d, 2J C-F = 21.9 Hz), 115.6 ppm. 19F NMR (283 MHz, CDCl3) δ -108.1 ppm

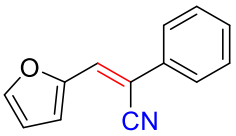


3h[68] . Inside the N_2 filled glove box, an oven-dry 15 mL reaction tube was charged with the mixture of **A** (1.6 mg, 2.44 µmol, 1 mol%), NaO^{t}Bu (0.7 mg, 7.3 µmol, 3 mol%), benzeneacetonitrile (0.35 mmol, 40 µL), 4-trifluoromethylbenzyl alcohol (0.25 mmol, 34 µL), and toluene (1 mL). The reaction tube was sealed by a screw cap fitted with PTFE septa and taken out from the box. An argon filled balloon was fitted on the top of the reaction tube and placed in a pre-heated oil

bath at 140 °C for 6 h. After the reaction was finished and cooled down, the reaction mixture was filtered through a silica gel plug and washed with DCM. The collected filtrate was concentrated under reduced pressure. The obtained crude mixture was purified by a silica gel column using ethyl acetate/hexane (1:50, v/v) as an eluent. White solid of 3h was isolated. Yield: 63 mg (92%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (d, J = 8.4 Hz, 2H), 7.79 – 7.65 (m, 4H), 7.57 (s, 1H), 7.53 – 7.40 (m, 3H) ppm; ^{13}C NMR (126 MHz, CDCl3) δ 140.2, 137.1, 133.9, 132.0 (q, 2JC-F = 33.3 Hz), 129.9, 129.3 (d, 3JC-F = 22.5 Hz), 126.3, 126.0, 123.7 (d, 1JC-F = 272.5 Hz), 117.5, 114.6 ppm. ^{19}F NMR (283 MHz, $CDCl_3$) δ -62.9 ppm.

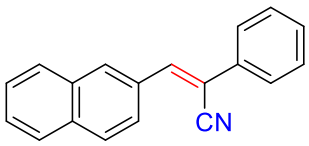


3i[68] . Inside the N_2 filled glove box, an oven-dry 15 mL reaction tube was charged with the mixture of **A** (1.6 mg, 2.44 µmol, 1 mol%), NaO^{t}Bu (0.7 mg, 7.3 µmol, 3 mol%), benzeneacetonitrile (0.35 mmol, 40 µL), 3,4 methylenedioxybenzyl alcohol (0.25 mmol, 38 mg), and toluene (1 mL). The reaction tube was sealed by a screw cap fitted with PTFE septa and taken out from the box. An argon filled balloon was fitted on the top of the reaction tube and placed in a pre-heated oil bath at 140 °C for 6 h. After the reaction was finished and cooled down, the reaction mixture was filtered through a silica gel plug and washed with DCM. The collected filtrate was concentrated under reduced pressure. The obtained crude mixture was purified by a silica gel column using ethyl acetate/hexane (1:50, v/v) as an eluent. Yellow solid of 3i was isolated. Yield: 50.4 mg (81%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64 (d, J = 7.6 Hz, 2H), 7.60 (d, J = 7.6 Hz, 1H), 7.48 – 7.35 (m, 4H), 7.30 (d, J = 9.4 Hz, 1H), 6.89 (d, J = 8.1 Hz, 1H), 6.05 (s, 2H) ppm; ^{13}C NMR (126



MHz, $CDCl_3$) δ 149.8, 148.4, 141.9, 134.8, 129.1, 129.0, 128.2, 125.9, 118.4, 109.3, 108.7, 108.2, 101.9 ppm.

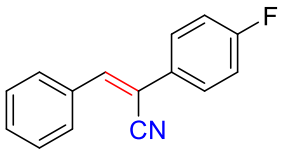
3j[69]. Inside the N_2 filled glove box, an oven-dry 15 mL reaction tube was charged with the mixture of **A** (1.6 mg, 2.44 µmol, 1 mol%), NaO^{t}Bu (0.7 mg, 7.3 µmol, 3 mol%), benzeneacetonitrile (0.35 mmol, 40 µL), 2-furfuryl alcohol (0.25 mmol, 22 µL), and toluene (1 mL). The reaction tube was sealed by a screw cap fitted with PTFE septa and taken out from the box. An argon filled balloon was fitted on the top of the reaction tube and placed in a pre-heated oil bath at 140 °C for 6 h. After the reaction was finished and cooled down, the reaction mixture was filtered through a silica gel plug and washed with DCM. The collected filtrate was concentrated under reduced pressure. The obtained crude mixture was purified by a silica gel column using ethyl acetate/hexane (1:50, v/v) as an eluent. Yellow liquid of 3j was isolated. Yield: 25.3 mg (52%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65 (dd, J = 7.6, 1.8 Hz, 2H), 7.60 (d, J = 1.6 Hz, 1H), 7.43 (t, J = 7.6 Hz, 2H), 7.40 - 7.34 (m, 2H), 7.21 (d, J = 3.5 Hz, 1H), 6.59 (dd, J = 3.5, 1.7 Hz, 1H) ppm; ^{13}C NMR



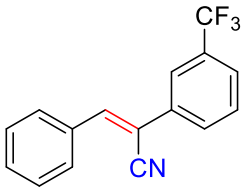
(126 MHz, $CDCl_3$) δ 149.1, 143.8, 132.6, 128.0, 128.0, 127.0, 124.5, 116.7, 114.1, 111.7, 106.6 ppm.

3k[70]. Inside the N_2 filled glove box, an oven-dry 15 mL reaction tube was charged with the mixture of **A** (1.6 mg, 2.44 µmol, 1 mol%), NaO^{t}Bu (0.7 mg, 7.3 µmol, 3 mol%), benzeneacetonitrile (0.35 mmol, 40 µL), 2-naphthylmethyl alcohol (0.25 mmol, 34 µL), and toluene (1 mL). The reaction tube was sealed by a screw cap fitted with PTFE septa and taken out from the box. An argon filled balloon was fitted on the top of the reaction tube and placed in a pre-heated oil bath at 140 °C for 6 h. After the reaction

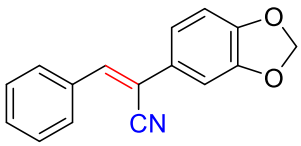
was finished and cooled down, the reaction mixture was filtered through a silica gel plug and washed with DCM. The collected filtrate was concentrated under reduced pressure. The obtained crude mixture was purified by a silica gel column using ethyl acetate/hexane (1:50, v/v) as an eluent. White solid of 3k was isolated. Yield: 52.3 mg (82%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.30 (s, 1H), 8.09 (dd, J = 8.6, 1.7 Hz, 1H), 7.92 (d, J = 8.5 Hz, 2H), 7.86 (d, J = 7.4 Hz, 1H), 7.73 (d, J = 7.1 Hz, 2H), 7.69 (s, 1H), 7.59 - 7.51 (m, 2H), 7.47 (t, J = 7.5 Hz, 2H), 7.44 - 7.38 (m, 1H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.3, 134.7, 134.2, 133.2, 131.4, 130.5, 129.3, 129.2, 128.9, 128.8, 127.9, 127.8, 126.9, 126.1, 125.4, 118.3, 111.8 ppm.



3l[45] . Inside the N_2 filled glove box, an oven-dry 15 mL reaction tube was charged with the mixture of **A** (1.6 mg, 2.44 µmol, 1 mol%), NaO^{t}Bu (0.7 mg, 7.3 µmol, 3 mol%), 4-fluorobenzeneacetonitrile (0.35 mmol, 42 µL), benzyl alcohol (0.25 mmol, 26 µL), and toluene (1 mL). The reaction tube was sealed by a screw cap fitted with PTFE septa and taken out from the box. An argon filled balloon was fitted on the top of the reaction tube and placed in a pre-heated oil bath at 140 °C for 6 h. After the reaction was finished and cooled down, the reaction mixture was filtered through a silica gel plug and washed with DCM. The collected filtrate was concentrated under reduced pressure. The obtained crude mixture was purified by a silica gel column using ethyl acetate/hexane (1:50, v/v) as an eluent. White solid of 3l was isolated. Yield: 48.5 mg (87%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88 (d, J = 6.9 Hz, 2H), 7.67 – 7.64 (m, 2H), 7.57 – 7.36 (m, 4H), 7.23 – 7.08 (m, 2H) ppm; 13C NMR (126 MHz, $CDCl_3$) δ 163.3 (d, 1J C-F = 250.1 Hz), 142.3, 133.6, 130.7, 129.3, 129.1, 128.0 (d, 3J C-F = 8.2 Hz), 118.0, 116.2 (d, 2J C-F = 21.9 Hz), 110.7 ppm. ^{19}F NMR (283 MHz, $CDCl_3$) δ -112.9 ppm.

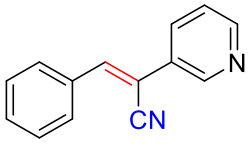


3m. Inside the N_2 filled glove box, an oven-dry 15 mL reaction tube was charged with the mixture of **A** (1.6 mg, 2.44 µmol, 1 mol%), NaO^{t}Bu (0.7mg, 7.3 µmol, 3 mol%), 3-trifluoromethylbenzeneacetonitrile (0.35 mmol, 52 µL), benzyl alcohol (0.25 mmol, 26 µL), and toluene (1 mL). The reaction tube was sealed by a screw cap fitted with PTFE septa and taken out from the box. An argon filled balloon was fitted on the top of the reaction tube and placed in a pre-heated oil bath at 140 °C for 6 h. After the reaction was finished and cooled down, the reaction mixture was filtered through a silica gel plug and washed with DCM. The collected filtrate was concentrated under reduced pressure. The obtained crude mixture was purified by a silica gel column using ethyl acetate/hexane (1:50, v/v) as an eluent. White solid of **3m** was isolated. Yield: 53 mg (78%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.87 – 7.92 (m, 4H), 7.66 (d, J = 7.1 Hz, 1H), 7.60 (s, 2H), 7.49 (s, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.9, 135.5, 133.3, 131.7 (q, J C – F = 33.5 Hz), 131.2, 129.8, 129.6, 129.5, 129.1, 125.9 (q, J C – F = 272.0 Hz), 125.8 (d, J C – F = 3.7 Hz), 122.7 (d, J C – F = 3.7 Hz), 117.6, 110.4 ppm. ^{19}F NMR (283 MHz, $CDCl_3$) δ -62.7 ppm; HRMS (ESI+): m/z [M+H]+calcd for C16H10F3NNa, 296.0666; found 296.0658.



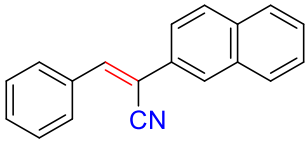
3n. Inside the N_2 filled glove box, an oven-dry 15 mL reaction tube was charged with the mixture of **A** (1.6 mg, 2.44 µmol, 1 mol%), NaO^{t}Bu (0.7 mg, 7.3 µmol, 3 mol%), (benzodioxol-5-yl)acetonitrile (0.35 mmol, 40 mg), benzyl alcohol (0.25 mmol, 26 µL), and toluene (1 mL). The reaction tube was sealed by a screw cap fitted with PTFE septa and taken out from the box. An argon filled balloon was fitted on the top

of the reaction tube and placed in a pre-heated oil bath at 140 °C for 6 h. After the reaction was finished and cooled down, the reaction mixture was filtered through a silica gel plug and washed with DCM. The collected filtrate was concentrated under reduced pressure. The obtained crude mixture was purified by a silica gel column using ethyl acetate/hexane (1:50, v/v) as an eluent. White solid of 3n was isolated. Yield: 40.5 mg (65%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.85 (d, J = 6.9 Hz, 2H), 7.56 – 7.34 (m, 4H), 7.21 (dd, J = 8.1, 1.9 Hz, 1H), 7.14 (d, J = 2.0 Hz, 1H), 6.87 (d, J = 8.1 Hz, 1H), 6.03 (s, 2H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) 148.7, 148.6, 140.8, 133.9, 130.4, 129.2, 129.0, 128.9, 120.8, 118.1, 111.5, 108.7, 106.0, 101.8 ppm; HRMS (ESI+): m/z [M+H]+calcd for C16H11NNaO2, 272.0690; found 272.0682.

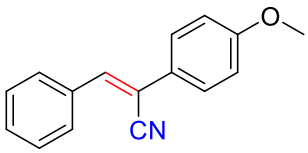


3o[45]. Inside the N_2 filled glove box, an oven-dry 15 mL reaction tube was charged with the mixture of **A** (1.6 mg, 2.44 µmol, 1 mol%), NaO^{t}Bu (0.7 mg, 7.3 µmol, 3 mol%), 3-pyridylacetonitrile (0.35 mmol, 38 µL), benzyl alcohol (0.25 mmol, 26 µL), and toluene (1 mL). The reaction tube was sealed by a screw cap fitted with PTFE septa and taken out from the box. An argon filled balloon was fitted on the top of the reaction tube and placed in a pre-heated oil bath at 140 °C for 6 h. After the reaction was finished and cooled down, the reaction mixture was filtered through a silica gel plug and washed with DCM. The collected filtrate was concentrated under reduced pressure. The obtained crude mixture was purified by a silica gel column using ethyl acetate/hexane (1:50, v/v) as an eluent. White solid of 3o was isolated. Yield: 37.6 mg (73%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.94 (s, 1H), 8.65 (d, J = 4.6 Hz, 1H), 7.99 – 7.97 (m, 1H), 7.95 – 7.87 (m, 2H), 7.58 (s, 1H), 7.55 – 7.45 (m, 3H), 7.40 (dd, J = 8.3, 4.7 Hz, 1H) ppm; ^{13}C

NMR (126 MHz, $CDCl_3$) 150.2, 147.2, 143.9, 133.6, 133.3, 131.3, 130.7, 129.5, 129.2, 123.7, 117.3, 108.6 ppm.

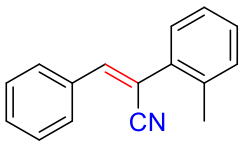


3p[71] . Inside the N_2 filled glove box, an oven-dry 15 mL reaction tube was charged with the mixture of **A** (1.6 mg, 2.44 µmol, 1 mol%), NaO^{t}Bu (0.7 mg, 7.3 µmol, 3 mol%), 2-naphthylacetonitrile (0.35 mmol, 59 mg), benzyl alcohol (0.25 mmol, 26 µL), and toluene (1 mL). The reaction tube was sealed by a screw cap fitted with PTFE septa and taken out from the box. An argon filled balloon was fitted on the top of the reaction tube and placed in a pre-heated oil bath at 140 °C for 6 h. After the reaction was finished and cooled down, the reaction mixture was filtered through a silica gel plug and washed with DCM. The collected filtrate was concentrated under reduced pressure. The obtained crude mixture was purified by a silica gel column using ethyl acetate/hexane (1:50, v/v) as an eluent. White solid of 3p was isolated. Yield: 56.8 mg (89%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.18 (s, 1H), 8.06 – 7.82 (m, 5H), 7.77 (d, J = 8.6 Hz, 1H), 7.69 (s, 1H), 7.62 – 7.41 (m, 5H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.3, 133.9, 133.5, 133.4, 131.7, 130.7, 129.4, 129.1, 129.0, 128.6, 127.8, 127.2, 127.1, 126.4, 122.6, 118.2, 111.9 ppm.

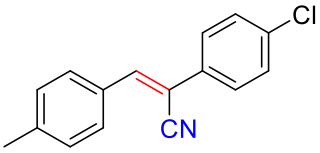


3q[22]. Inside the N_2 filled glove box, an oven-dry 15 mL reaction tube was charged with the mixture of **A** (1.6 mg, 2.44 µmol, 1 mol%), NaO^{t}Bu (0.7 mg, 7.3 µmol, 3 mol%), 4-methoxybenzeneacetonitrile (0.35 mmol, 46 µL), benzyl alcohol (0.25 mmol, 26 µL), and toluene (1 mL). The reaction tube was sealed by a screw cap fitted with PTFE septa and taken out from the box. An argon filled balloon was fitted on the top of the reaction tube

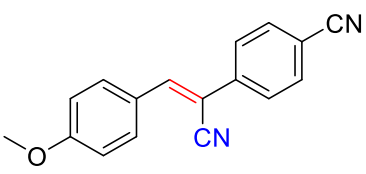
and placed in a pre-heated oil bath at 140 °C for 6 h. After the reaction was finished and cooled down, the reaction mixture was filtered through a silica gel plug and washed with DCM. The collected filtrate was concentrated under reduced pressure. The obtained crude mixture was purified by a silica gel column using ethyl acetate/hexane (1:50, v/v) as an eluent. Colorless liquid of 3q was isolated. Yield: 43.0 mg (78%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.86 (d, J = 8.8 Hz, 2H), 7.62 (d, J = 9.0 Hz, 2H), 7.45 (dt, J = 14.9, 7.6Hz, 4H), 6.97 (d, J = 7.1 Hz, 2H), 3.85 (s, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.5, 140.2, 134.1, 130.2, 129.1, 129.0, 127.4, 127.1, 118.2, 114.5, 111.4, 55.5 ppm.



3r. Inside the N_2 filled glove box, an oven-dry 15 mL reaction tube was charged with the mixture of **A** (1.6 mg, 2.44 µmol, 1 mol%), NaO^{t}Bu (0.7 mg, 7.3 µmol, 3 mol%), 2-methylbenzeneacetonitrile (0.35 mmol, 46 µL), benzyl alcohol (0.25 mmol, 26 µL), and toluene (1 mL). The reaction tube was sealed by a screw cap fitted with PTFE septa and taken out from the box. An argon filled balloon was fitted on the top of the reaction tube and placed in a pre-heated oil bath at 140 °C for 6 h. After the reaction was finished and cooled down, the reaction mixture was filtered through a silica gel plug and washed with DCM. The collected filtrate was concentrated under reduced pressure. The obtained crude mixture was purified by a silica gel column using ethyl acetate/hexane (1:50, v/v) as an eluent. Colorless liquid of 3r was isolated. Yield: 43.2 mg (78%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88 (d, J = 7.6 Hz, 2H), 7.47 (d, J = 7.0 Hz, 4H), 7.31 (d, J = 6.8Hz, 3H), 7.15 (s, 1H), 2.49 (s, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 147.0, 136.4, 135.5, 133.7, 131.0, 130.7, 129.5, 129.3, 129.2, 129.1, 126.6, 118.0, 111.3, 20.2 ppm; HRMS (ESI+): m/z [M+H]+calcd for C16H13NNa, 242.0939; found 242.0940.

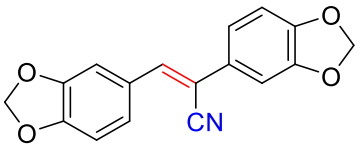


3s[68] . Inside the N_2 filled glove box, an oven-dry 15 mL reaction tube was charged with the mixture of **A** (1.6 mg, 2.44 µmol, 1 mol%), NaO^{t}Bu (0.7 mg, 7.3 µmol, 3 mol%), 4-chlorobenzeneacetonitrile (0.35 mmol, 44 µL), 4-methylbenzyl alcohol (0.25 mmol, 30 µL), and toluene (1 mL). The reaction tube was sealed by a screw cap fitted with PTFE septa and taken out from the box. An argon filled balloon was fitted on the top of the reaction tube and placed in a pre-heated oil bath at 140 °C for 6 h. After the reaction was finished and cooled down, the reaction mixture was filtered through a silica gel plug and washed with DCM. The collected filtrate was concentrated under reduced pressure. The obtained crude mixture was purified by a silica gel column using ethyl acetate/hexane (1:50, v/v) as an eluent. White solid of 3s was isolated. Yield: 38.0 mg (60%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.79 (d, J = 8.1 Hz, 2H), 7.59 (d, J = 9.6 Hz, 2H), 7.47 (s, 1H), 7.42 – 7.39 (m, 2H), 7.27 (d, J = 8.0 Hz, 2H), 2.41 (s, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) 142.7, 141.6, 135.1, 133.3, 130.8, 129.8, 129.5, 129.3, 127.2, 118.0, 109.3, 21.7 ppm.

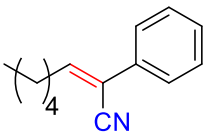


3t[72]. Inside the N_2 filled glove box, an oven-dry 15 mL reaction tube was charged with the mixture of **A** (1.6 mg, 2.44 µmol, 1 mol%), NaO^{t}Bu (0.7 mg, 7.3 µmol, 3 mol%), 4-cyanobenzeneacetonitrile (0.35 mmol, 50mg), 4-methoxylbenzyl alcohol (0.25 mmol, 32 µL), and toluene (1 mL). The reaction tube was sealed by a screw cap fitted with PTFE septa and taken out from the box. An argon filled balloon was fitted on the top of the reaction tube and placed in a pre-heated oil bath at 140 °C for 6 h. After the reaction was finished and cooled down, the reaction mixture was filtered through a silica gel plug and washed with DCM. The collected filtrate was concentrated under reduced pressure. The

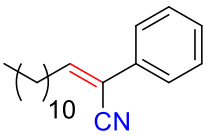
obtained 11crude mixture was purified by a silica gel column using ethyl acetate/hexane (1:50, v/v) as an eluent. Yellow solid of 3t was isolated. Yield: 49.5 mg (76%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.93 (d, J = 8.7 Hz, 2H), 7.77 (d, J = 8.7 Hz, 2H), 7.72 (d, J = 8.2 Hz, 2H), 7.56 (s, 1H), 7.01 (d, J = 8.9 Hz, 2H), 3.90 (s, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) 162.4, 144.5, 139.4, 132.9, 131.9, 126.3, 125.8, 118.4, 117.8, 114.7, 112.2, 106.7, 55.6 ppm.



3u. Inside the N_2 filled glove box, an oven-dry 15 mL reaction tube was charged with the mixture of **A** (1.6 mg, 2.44 µmol, 1 mol%), NaO^{t}Bu (0.7 mg, 7.3 µmol, 3 mol%), (benzodioxol-5-yl)acetonitrile (0.35 mmol, 38 mg), 3,4-methylenedioxybenzyl alcohol (0.25 mmol, 40 mg), and toluene (1 mL). The reaction tube was sealed by a screw cap fitted with PTFE septa and taken out from the box. An argon filled balloon was fitted on the top of the reaction tube and placed in a pre-heated oil bath at 140 °C for 6 h. After the reaction was finished and cooled down, the reaction mixture was filtered through a silica gel plug and washed with DCM. The collected filtrate was concentrated under reduced pressure. The obtained crude mixture was purified by a silica gel column using ethyl acetate/hexane (1:50, v/v) as an eluent. White solid of 3u was isolated. Yield: 56.0 mg (76%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55 (d, J = 1.7 Hz, 1H), 7.16 (dd, J = 8.2, 1.9 Hz, 2H), 7.10 (d, J = 1.8 Hz, 1H), 6.87 (t, J = 1.7 Hz, 3H), 6.04 (s, 2H), 6.02 (s, 2H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.5, 148.5, 148.4, 148.3, 140.4, 129.1, 128.2, 125.6, 121.3, 120.5, 118.4, 108.9, 108.7, 108.1, 105.8, 101.8, 101.7 ppm. HRMS (ESI+): m/z [M+H]+calcd for C17H11NNaO4, 316.0575; found 316.0580.

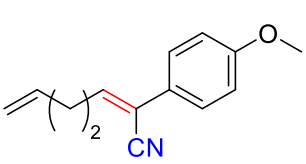


3v[45]. Inside the N_2 filled glove box, an oven-dry 15 mL reaction tube was charged with the mixture of **A** (3.2 mg, 4.88 µmol, 2 mol%), NaO^{t}Bu (1.4 mg, 14.6 µmol, 6 mol%), benzeneacetonitrile (0.35 mmol, 40 µL), 1-hexyl alcohol (0.25 mmol, 31 µL), and toluene (1 mL). The reaction tube was sealed by a screw cap fitted with PTFE septa and taken out from the box. An argon filled balloon was fitted on the top of the reaction tube and placed in a pre-heated oil bath at 140 °C for 24 h. After the reaction was finished and cooled down, the reaction mixture was filtered through a silica gel plug and washed with DCM. The collected filtrate was concentrated under reduced pressure. The obtained crude mixture was purified by a silica gel column using ethyl acetate/hexane (1:50, v/v) as an eluent. Colorless liquid of 3v was isolated. Yield: 47.3 mg (95%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53 (d, J = 7.3 Hz, 2H), 7.45 - 7.30 (m, 3H), 6.83 (t, J = 7.8 Hz, 1H), 2.59 (dd, J = 15.1, 7.7 Hz, 2H), 1.62 – 1.54 (m, 2H), 1.39 – 1.36 (m, 4H), 0.92 (t, J = 7.0 Hz, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 147.4, 133.4, 129.0, 128.9, 125.7, 116.8, 115.9, 32.3, 31.4, 28.5, 22.5, 14.0 ppm.



3w. Inside the N_2 filled glove box, an oven-dry 15 mL reaction tube was charged with the mixture of **A** (3.2 mg, 4.88 µmol, 2 mol%), NaO^{t}Bu (1.4 mg, 14.6 µmol, 6 mol%), benzeneacetonitrile (0.35 mmol, 40 µL), 1-dodecyl alcohol (0.25 mmol, 56 µL), and toluene (1 mL). The reaction tube was sealed by a screw cap fitted with PTFE septa and taken out from the box. An argon filled balloon was fitted on the top of the reaction tube and placed in a pre-heated oil bath at 140 °C for 24 h. After the reaction was finished and cooled down, the reaction mixture was filtered through a silica gel plug and washed with DCM. The collected filtrate was concentrated under reduced pressure. The obtained crude mixture was purified by a silica gel column

using ethyl acetate/hexane (1:50, v/v) as an eluent. Colorless liquid of 3w was isolated. Yield: 63.7 mg (90%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53 (dd, J = 7.2, 1.5 Hz, 2H), 7.41 - 7.34 (m, 3H), 6.83 (t, J = 7.8 Hz, 1H), 2.58 (dd, J = 15.0, 7.5 Hz, 2H), 1.59 – 1.53 (m, 2H), 1.40 – 1.26 (m, 16H), 0.88 (t, J = 7.0 Hz, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 147.4, 133.4, 129.0, 128.9, 125.7, 116.8, 115.9, 32.3, 32.0, 29.7, 29.6, 29.5, 29.4, 29.3, 29.3, 28.8, 22.8, 14.2 ppm; HRMS (ESI+): m/z [M+H]+calcd for C20H29NNa, 306.2183; found 306.2192.



3x. Inside the N_2 filled glove box, an oven-dry 15 mL reaction tube was charged with the mixture of **A** (3.2 mg, 4.88 µmol, 2 mol%), NaO^{t}Bu (1.4 mg, 14.6 µmol, 6 mol%), 4-methoxybenzeneacetonitrile (0.35 mmol, 49 µL), 4-pentenol (0.25 mmol, 26 µL), and toluene (1 mL). The reaction tube was sealed by a screw cap fitted with PTFE septa and taken out from the box. An argon filled balloon was fitted on the top of the reaction tube and placed in a pre-heated oil bath at 140 °C for 12 h. After the reaction was finished and cooled down, the reaction mixture was filtered through a silica gel plug and washed with DCM. The collected filtrate was concentrated under reduced pressure. The obtained crude mixture was purified by a silica gel column using ethyl acetate/hexane (1:50, v/v) as an eluent. Colorless liquid of **3x** was isolated. Yield: 36.0 mg (68%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45 (d, J = 8.9 Hz, 2H), 6.91 (d, J = 8.9 Hz, 2H), 6.68 (t, J = 7.7 Hz, 1H), 5.89 – 5.81 (m, 1H), 5.12 – 5.05 (m, 2H), 3.83 (s, 3H), 2.67 (dd, J = 14.8, 7.4 Hz, 2H), 2.31 (dd, J = 14.0, 7.1 Hz, 2H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) 160.2, 143.8, 136.7, 127.0, 125.9, 116.8, 116.2, 115.9, 114.4, 55.5, 32.8, 31.3 ppm; HRMS (ESI+): m/z [M+H]+calcd for C14H15NNao, 236.1043; found 236.1046.

4.14 Supplementary Figures

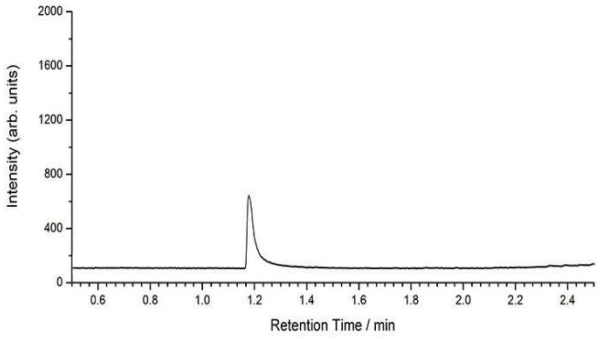
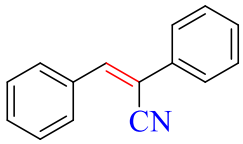


Figure 4.2 H_2 detection by GC chromatography.



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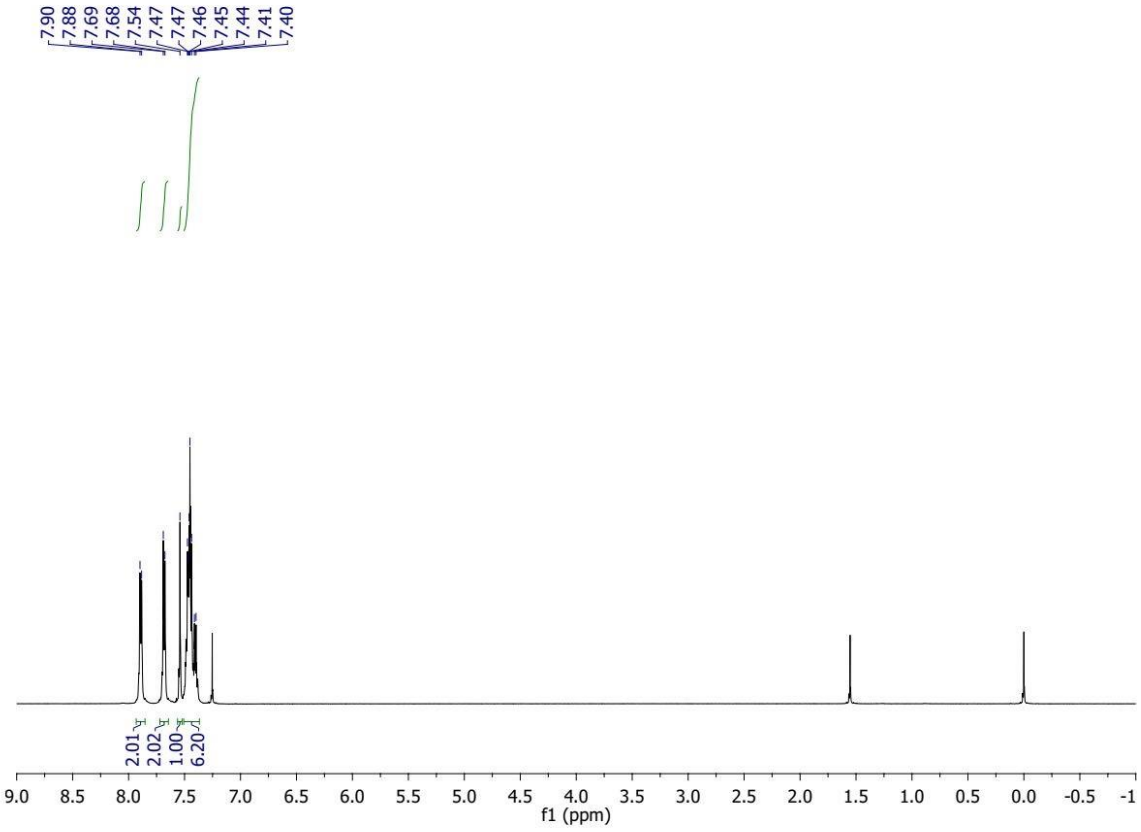
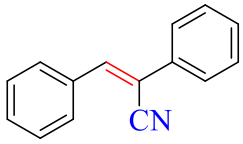


Figure 4.3 ^{1}H NMR ($CDCl_3$, 500 MHz) of 3a



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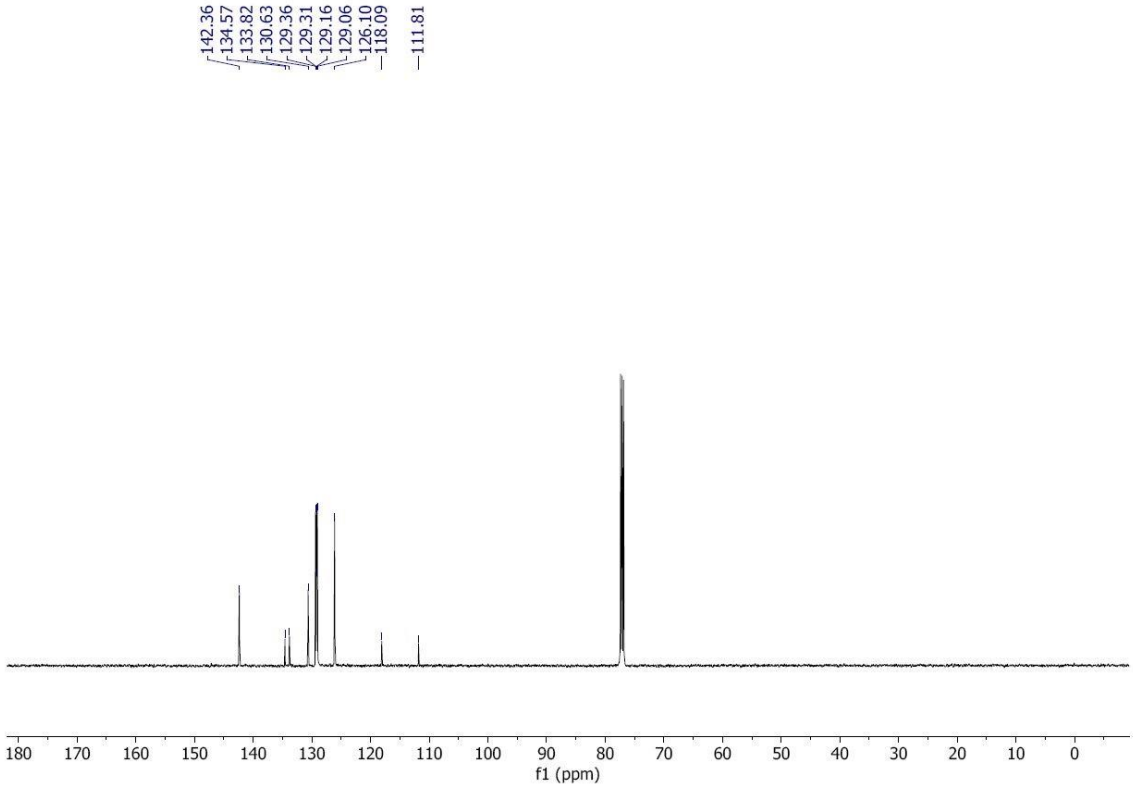
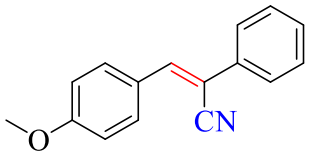


Figure 4.4 ^{13}C NMR ($CDCl_3$, 125 MHz) of 3a



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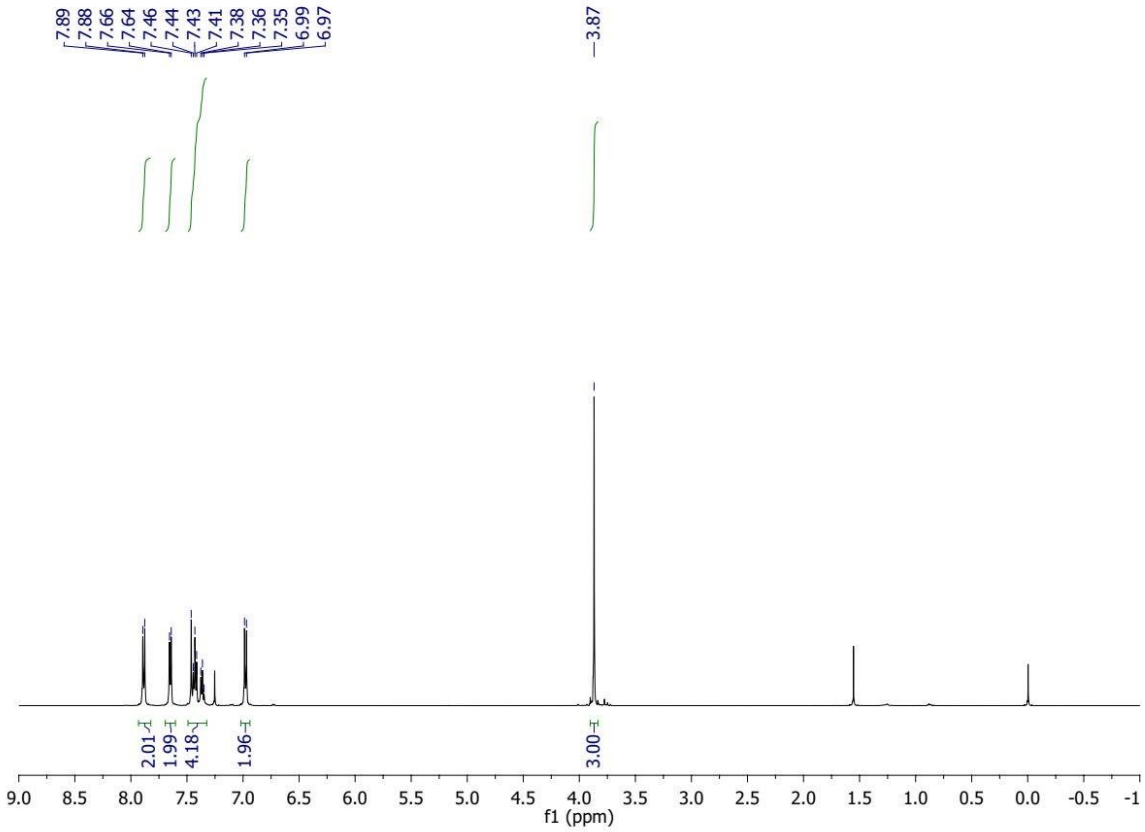
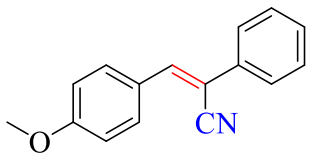


Figure 4.5 ^{1}H NMR ($CDCl_3$, 500 MHz) of 3b



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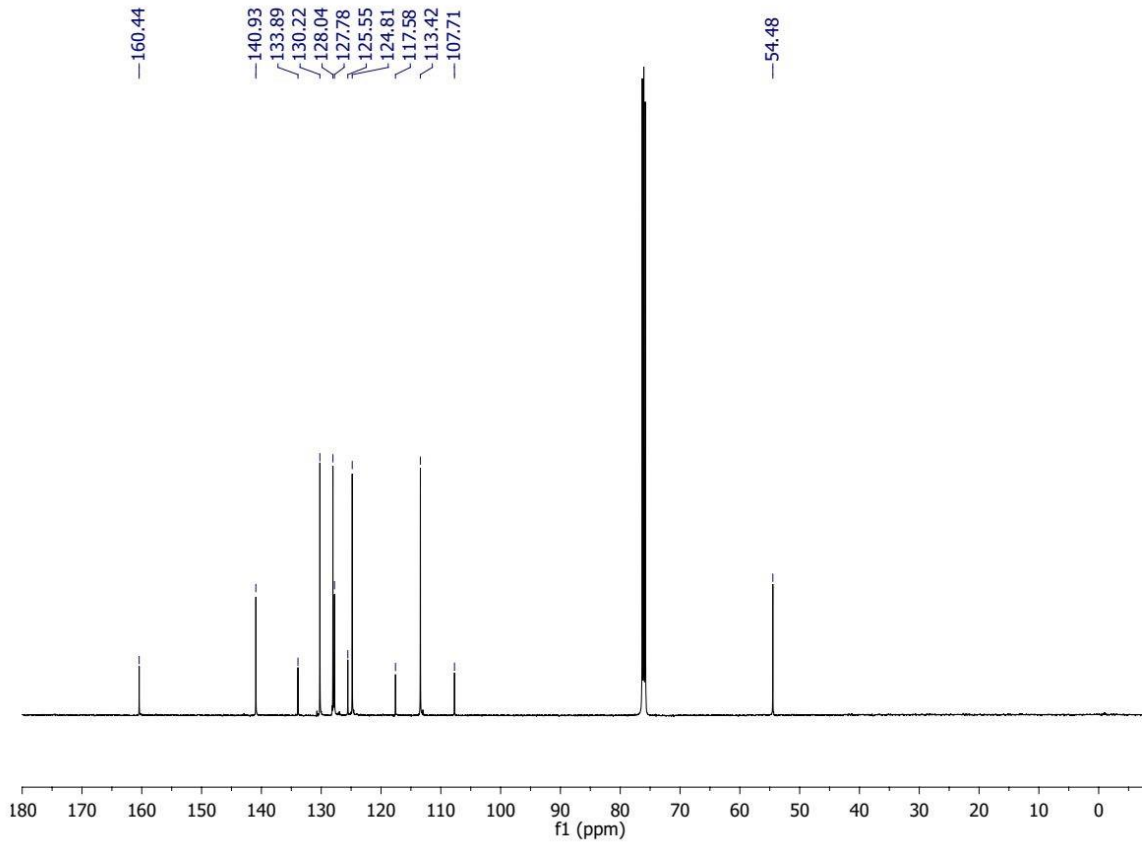
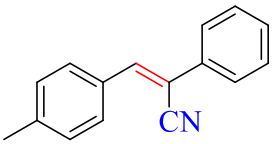


Figure 4.6 ^{13}C NMR ($CDCl_3$, 125 MHz) 3b



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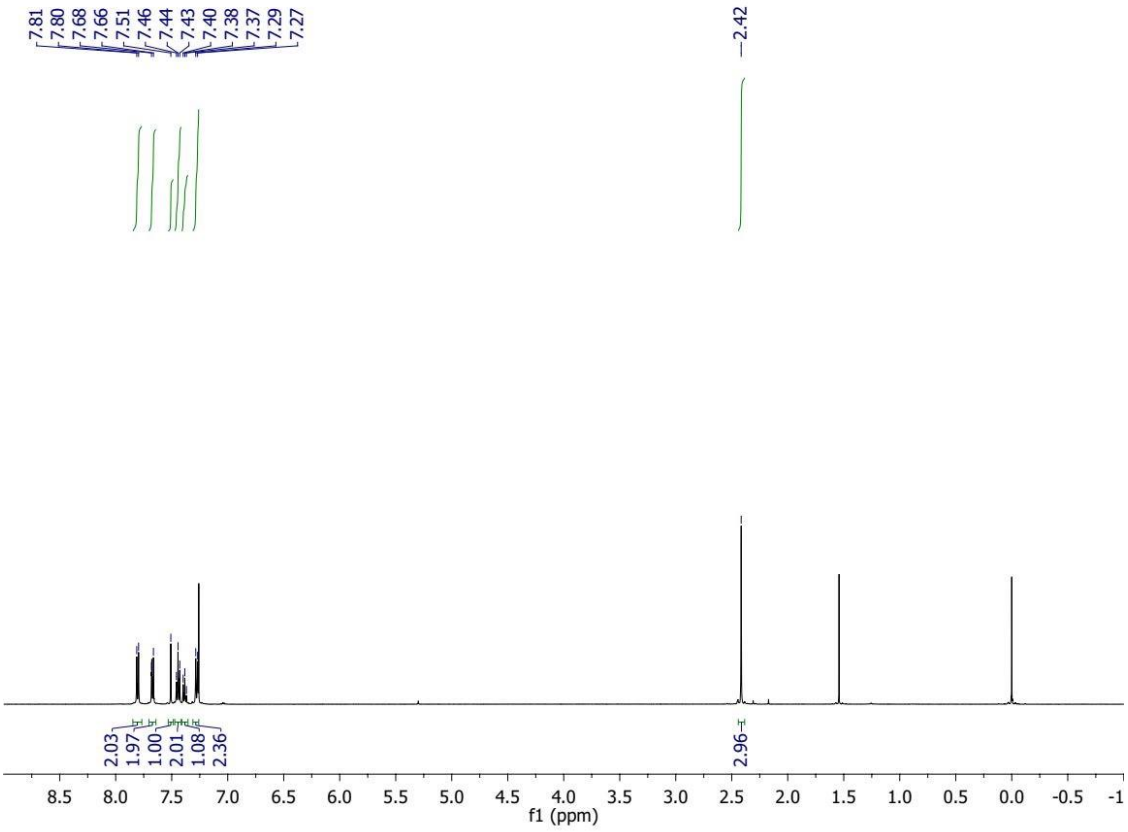
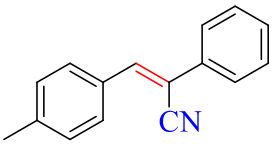


Figure 4.7 ^{1}H NMR ($CDCl_3$, 500 MHz) of 3c



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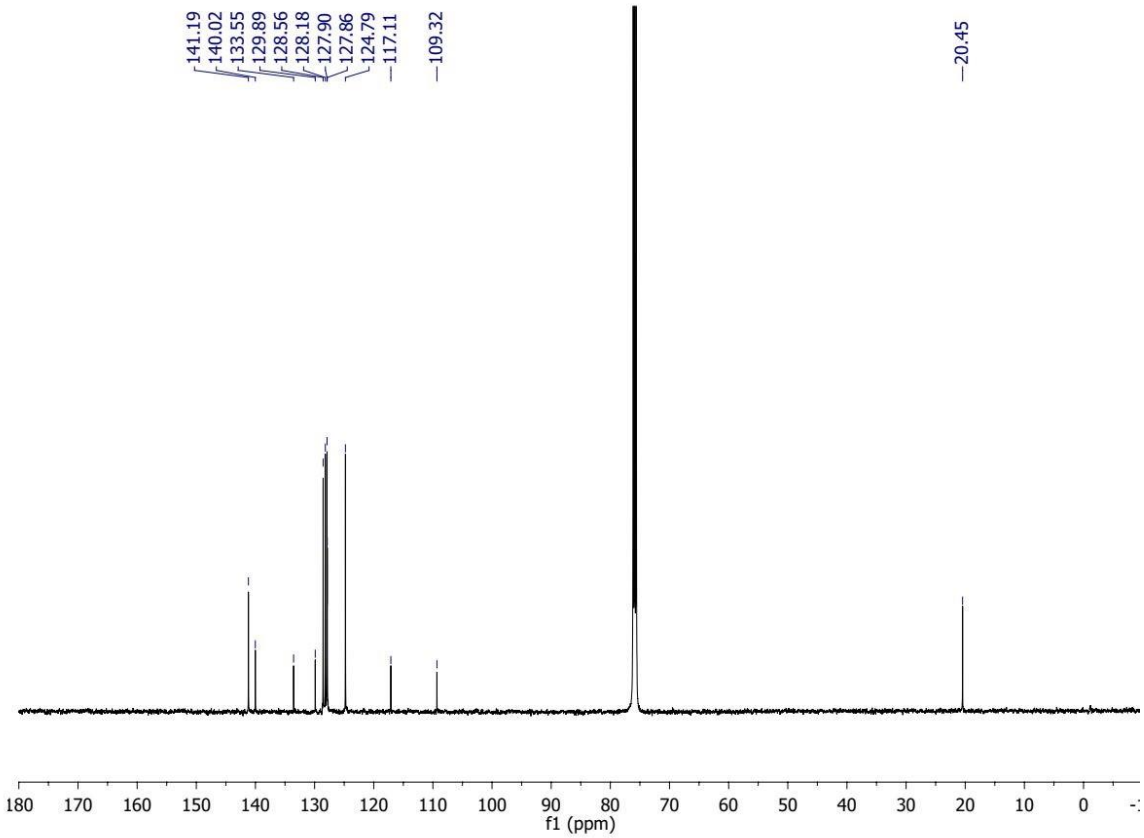
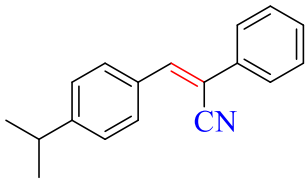


Figure 4.8 ^{13}C NMR ($CDCl_3$, 125 MHz) of 3c



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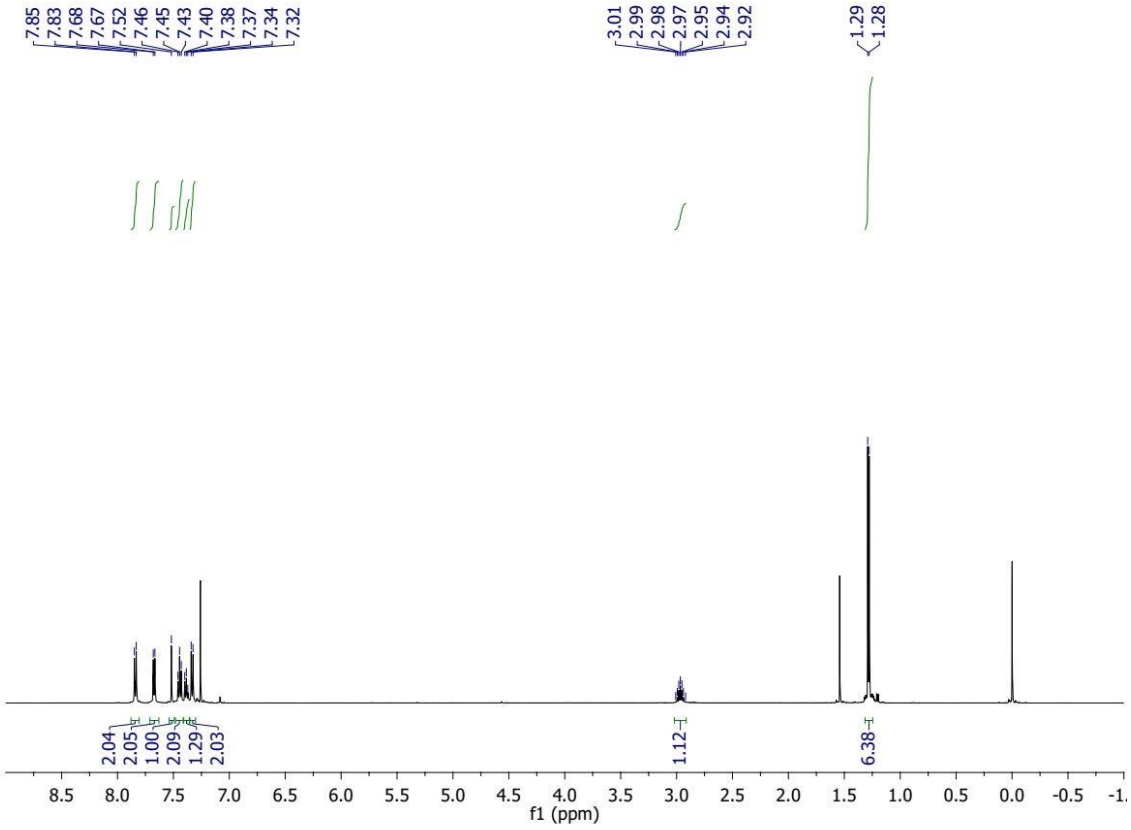
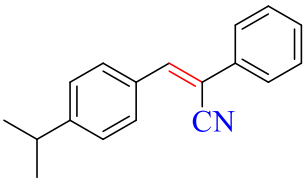


Figure 4.9 ^{1}H NMR ($CDCl_3$, 500 MHz) of 3d



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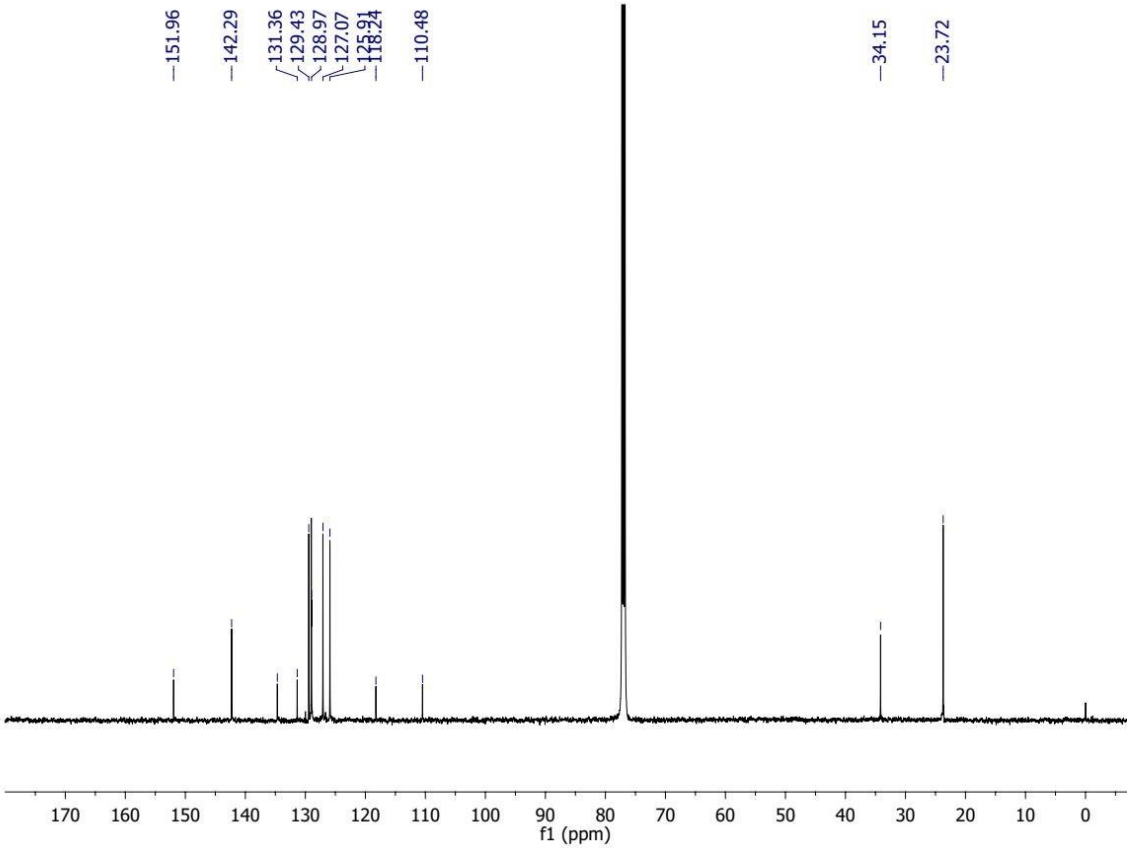
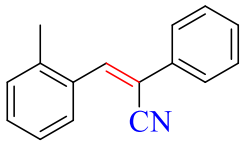


Figure 4.10 ^{13}C NMR ($CDCl_3$, 125 MHz) of 3d



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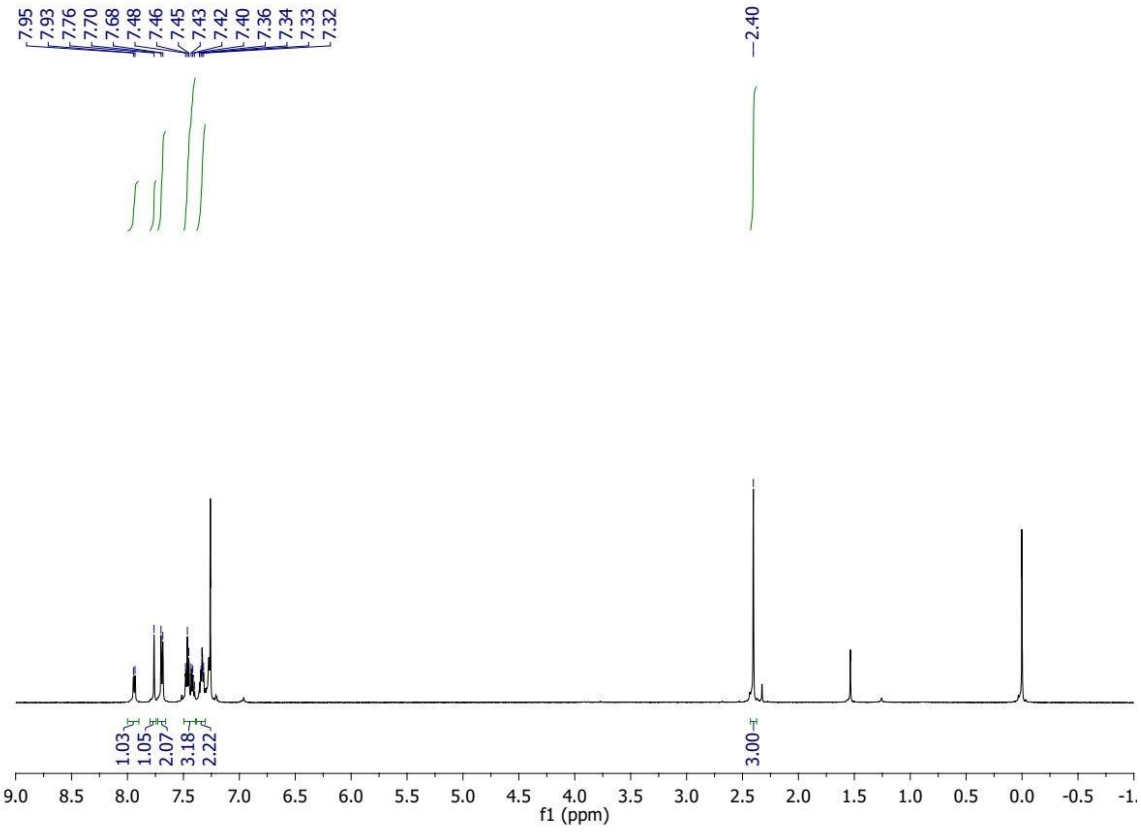
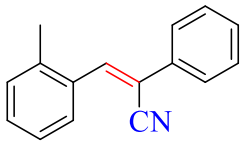


Figure 4.11 ^{1}H NMR ($CDCl_3$, 500 MHz) of 3e



3e

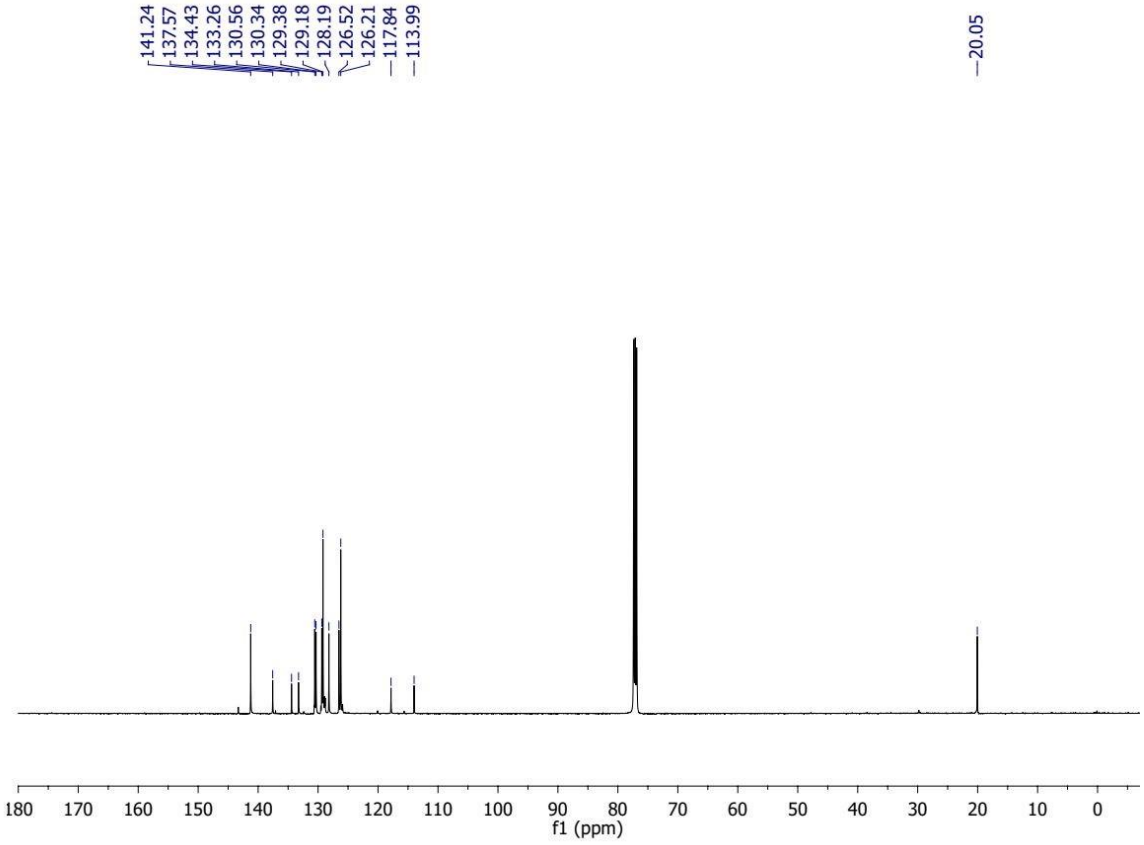
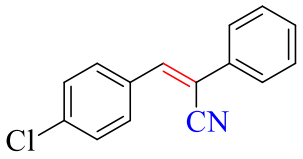


Figure 4.12 ^{13}C NMR ($CDCl_3$, 125 MHz) of 3e



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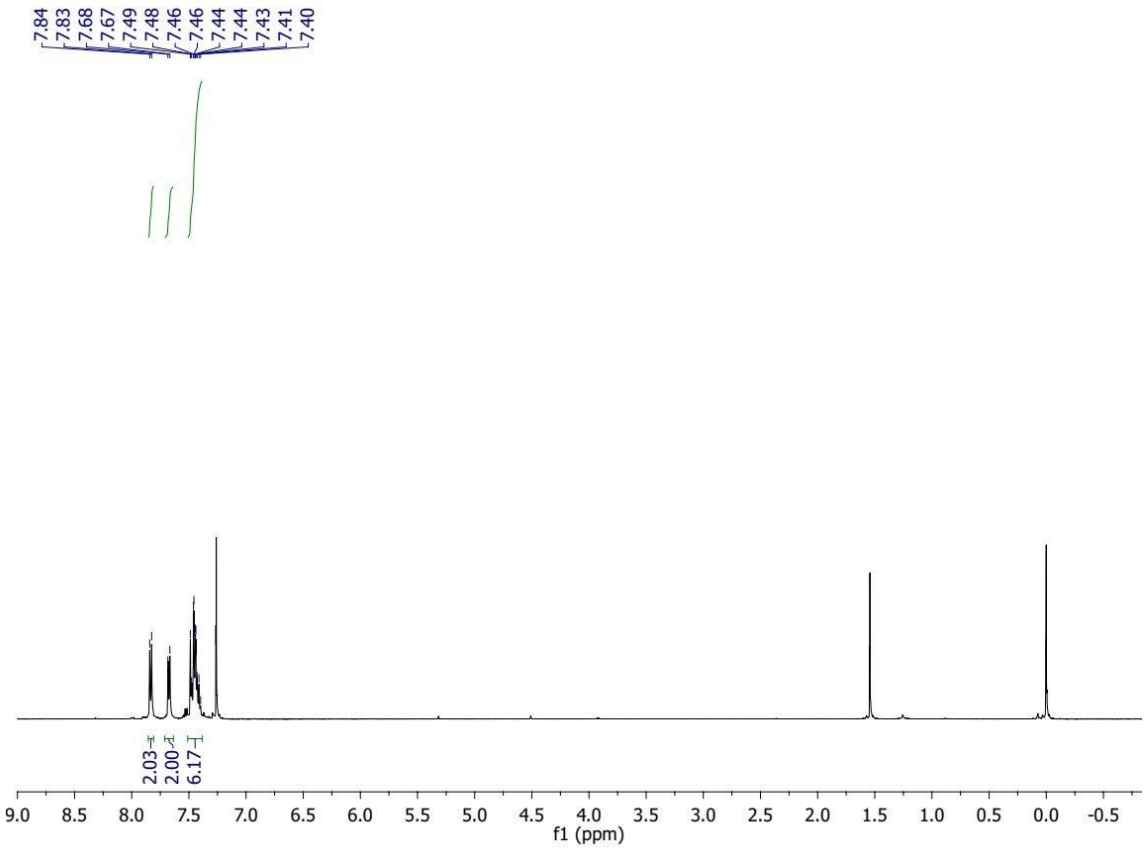
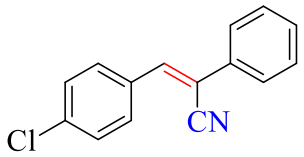


Figure 4.13 ^{1}H NMR ($CDCl_3$, 500 MHz) of 3f



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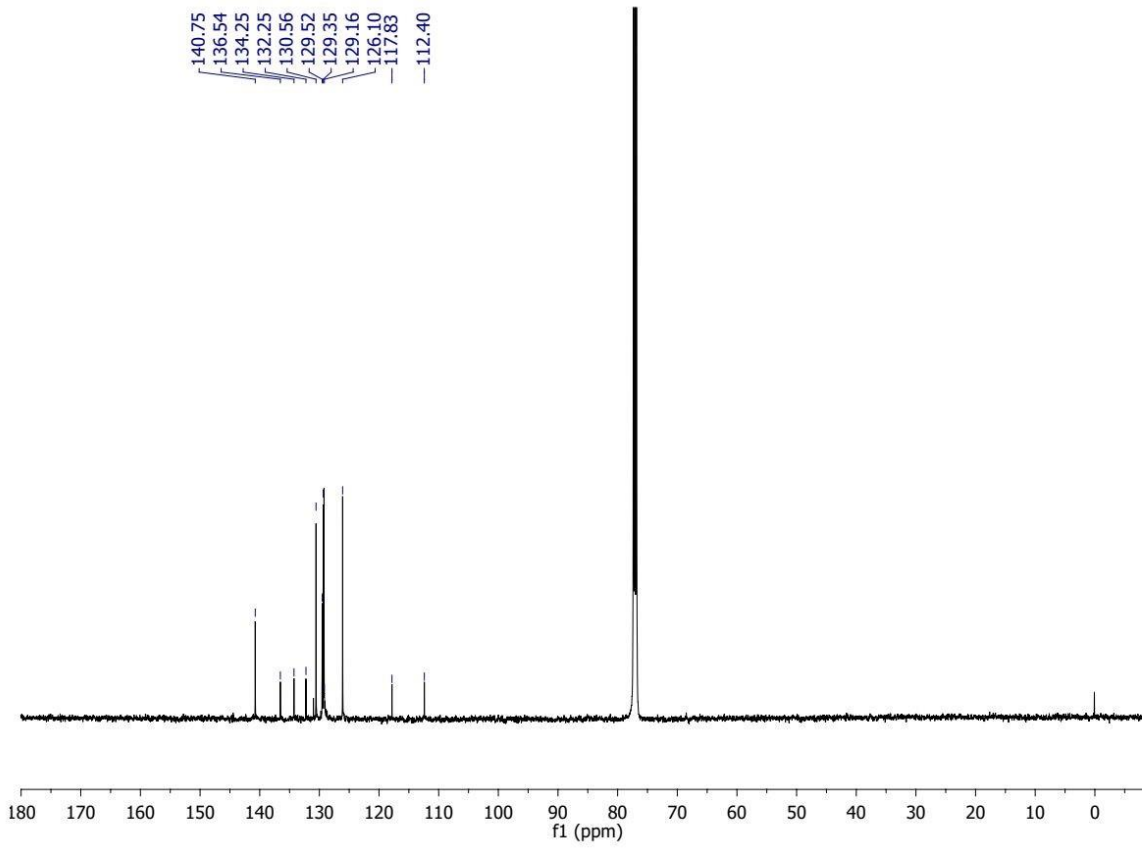
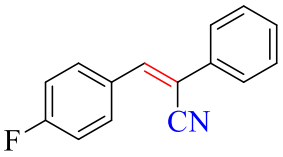


Figure 4.14 ^{13}C NMR ($CDCl_3$, 125 MHz) of 3f



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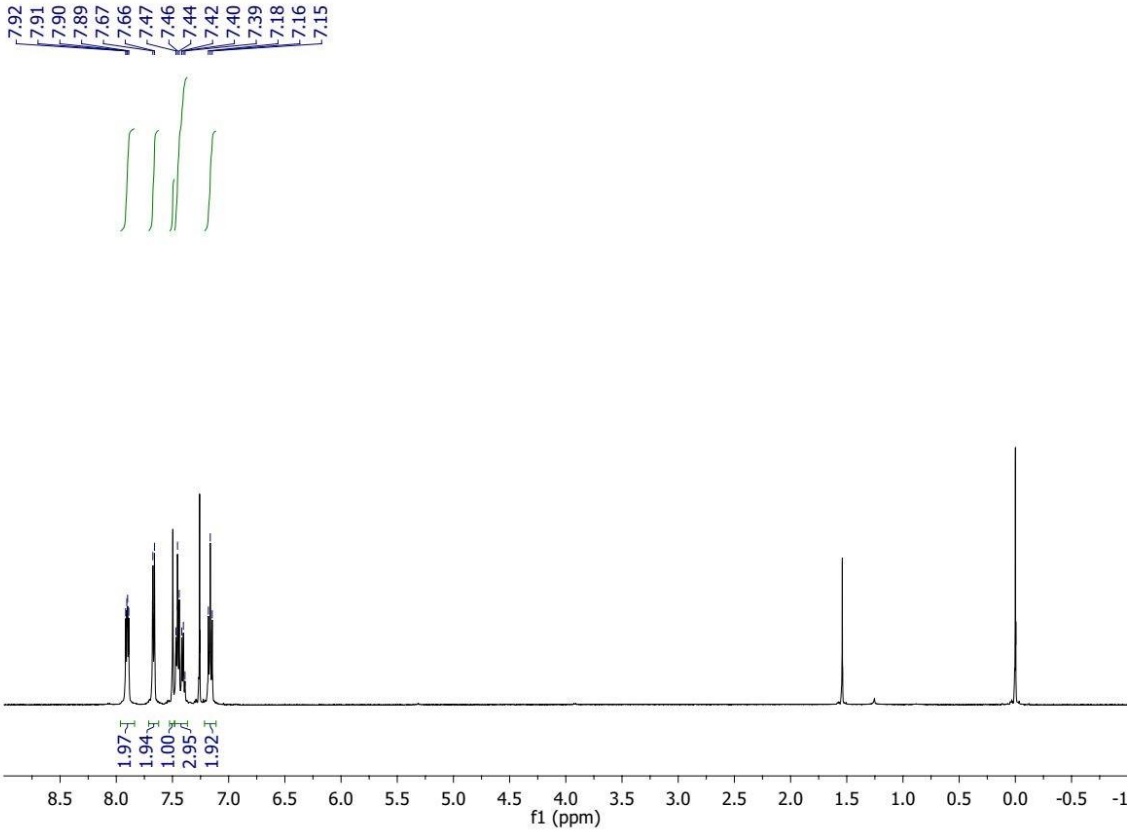


Figure 4.15 ^{1}H NMR ($CDCl_3$, 500 MHz) of 3g

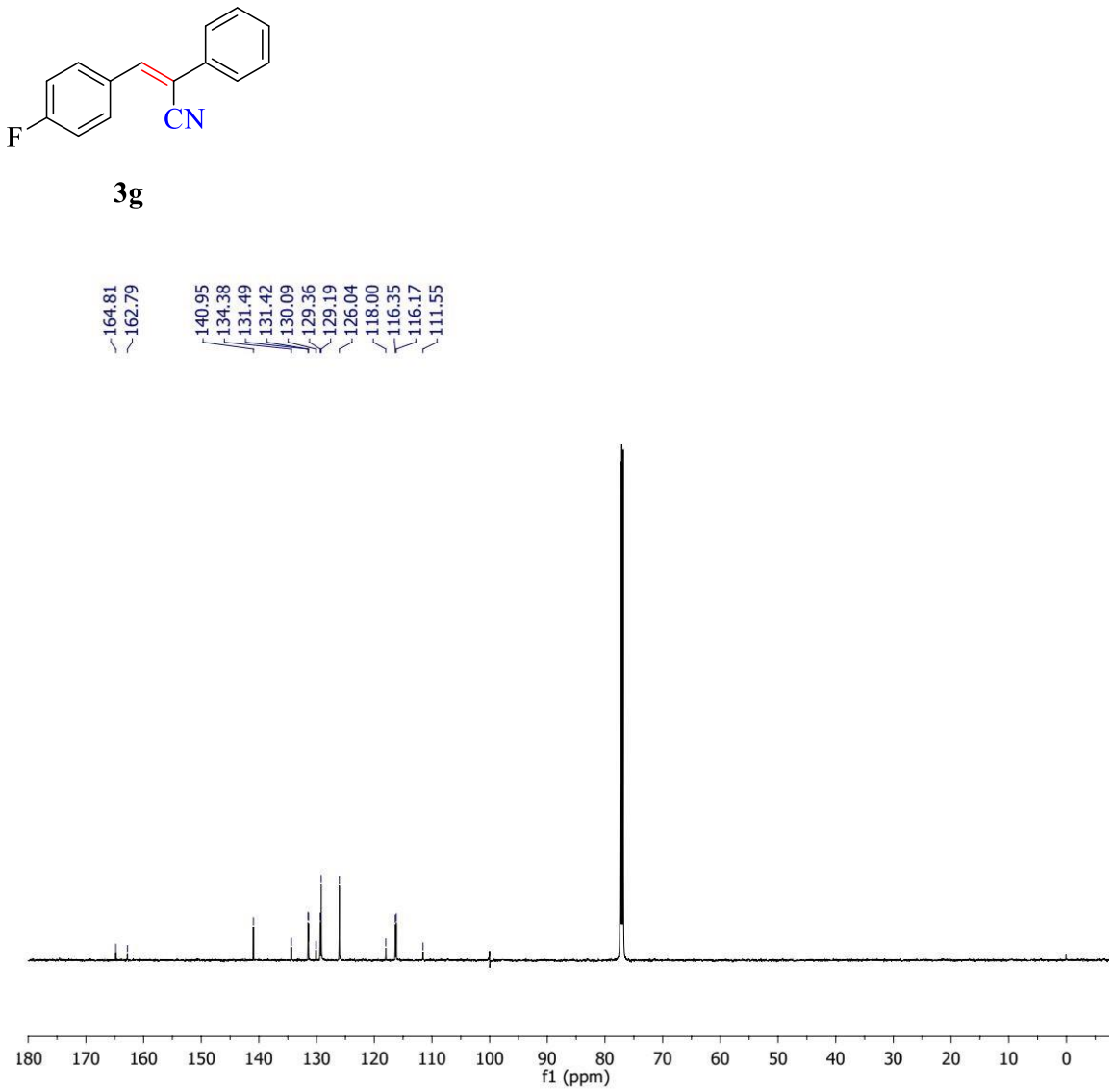
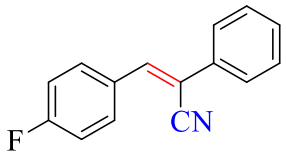


Figure 4.16 ^{13}C NMR ($CDCl_3$, 125 MHz) of 3g



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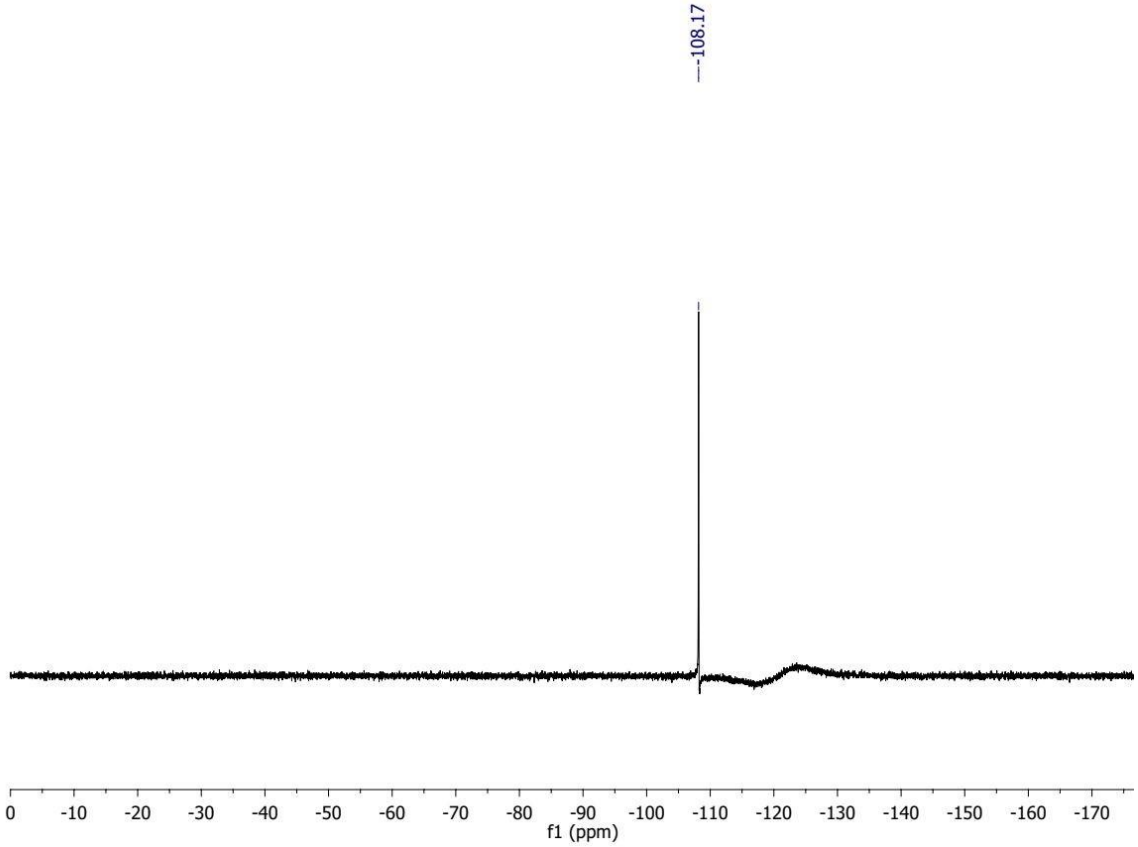
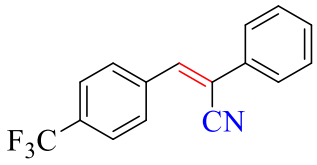


Figure 4.17 ^{19}F NMR ($CDCl_3$, 283 MHz) of 3g



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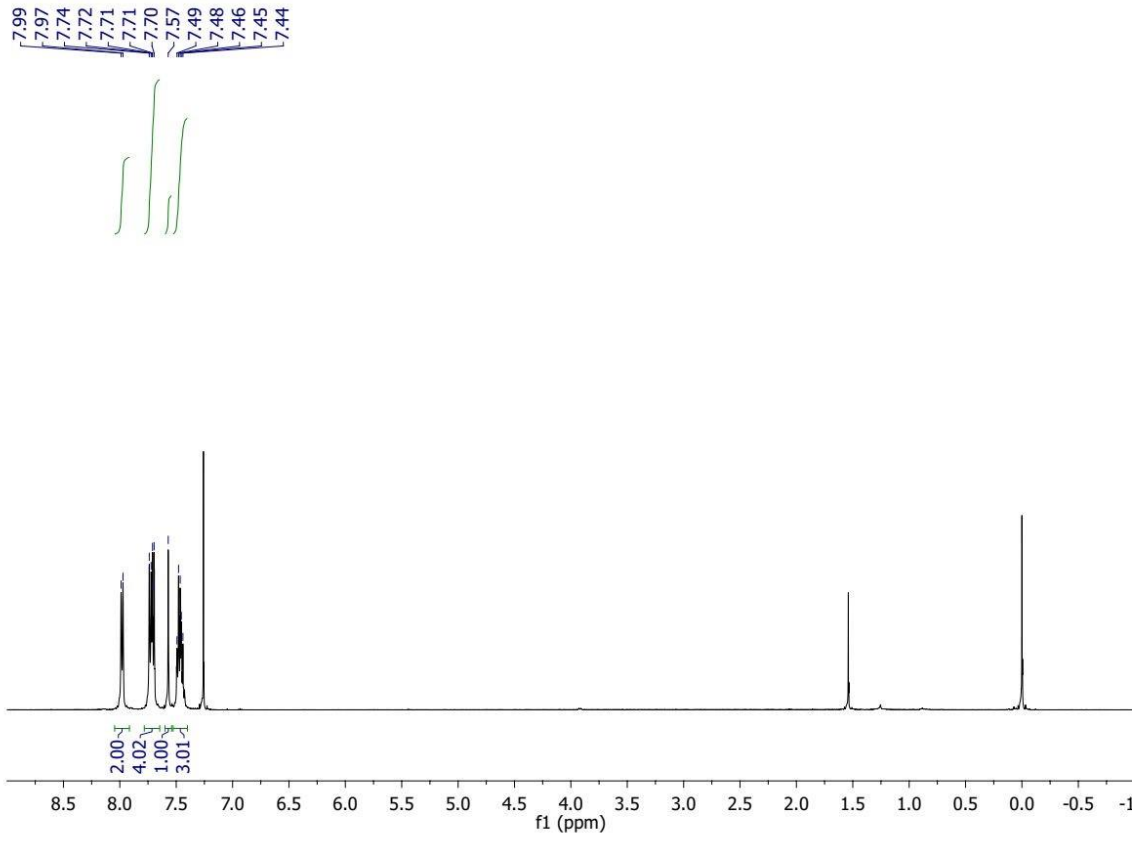
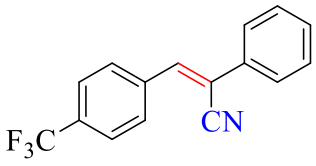


Figure 4.18 ^{1}H NMR ($CDCl_3$, 500 MHz) of 3h



3h

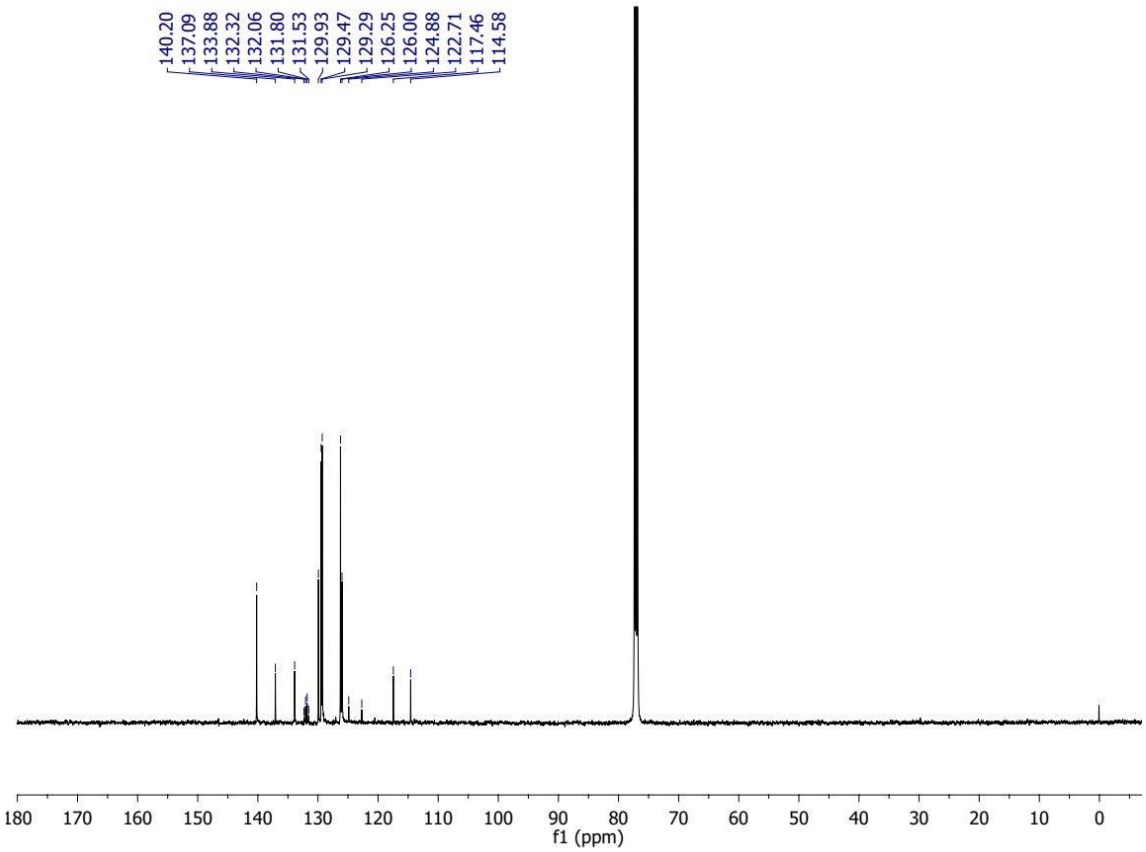
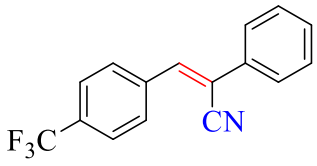


Figure 4.19 ^{13}C NMR ($CDCl_3$, 125 MHz) of 3h



3h

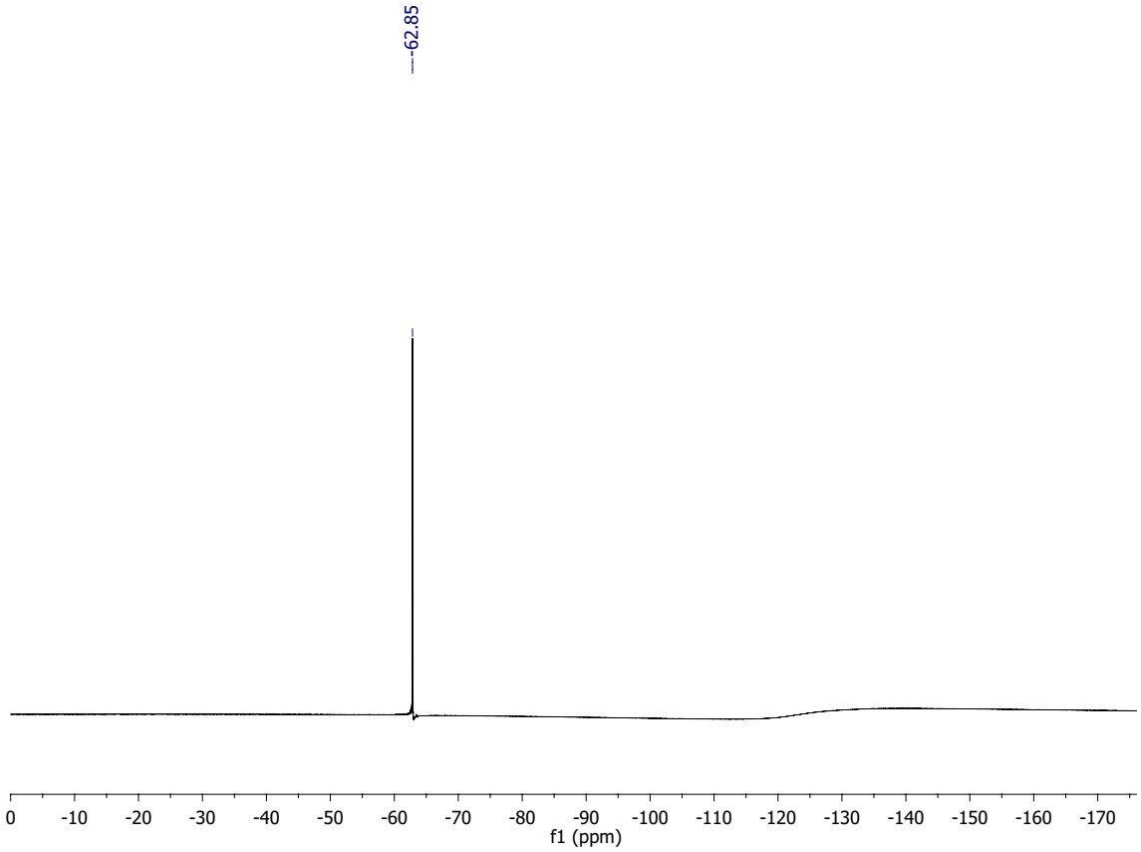
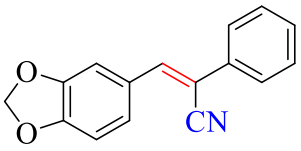


Figure 4.20 ^{19}F NMR ($CDCl_3$, 283 MHz) of 3h



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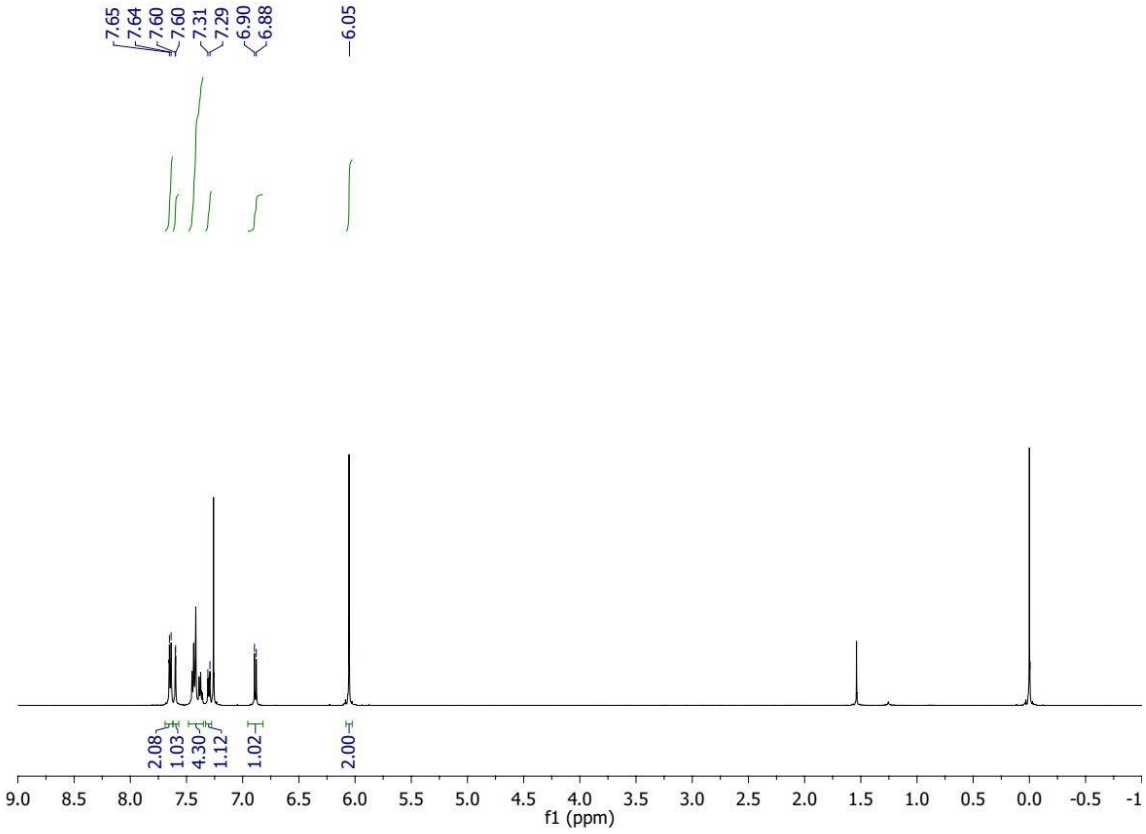
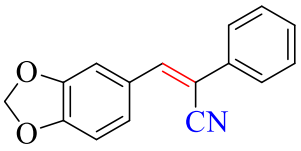


Figure 4.21 ^{1}H NMR ($CDCl_3$, 500 MHz) of 3i



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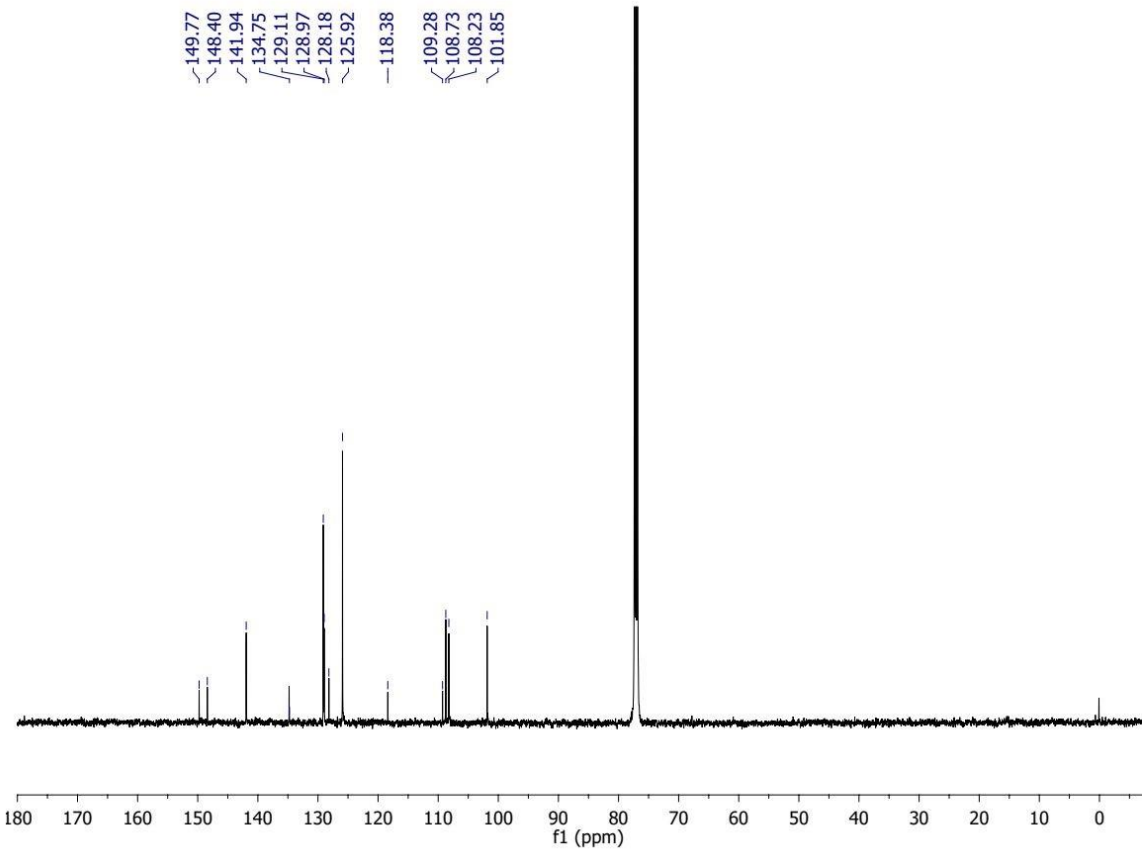
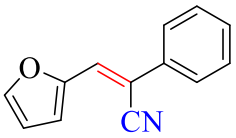


Figure 4.22 ^{13}C NMR ($CDCl_3$, 125 MHz) of 3i



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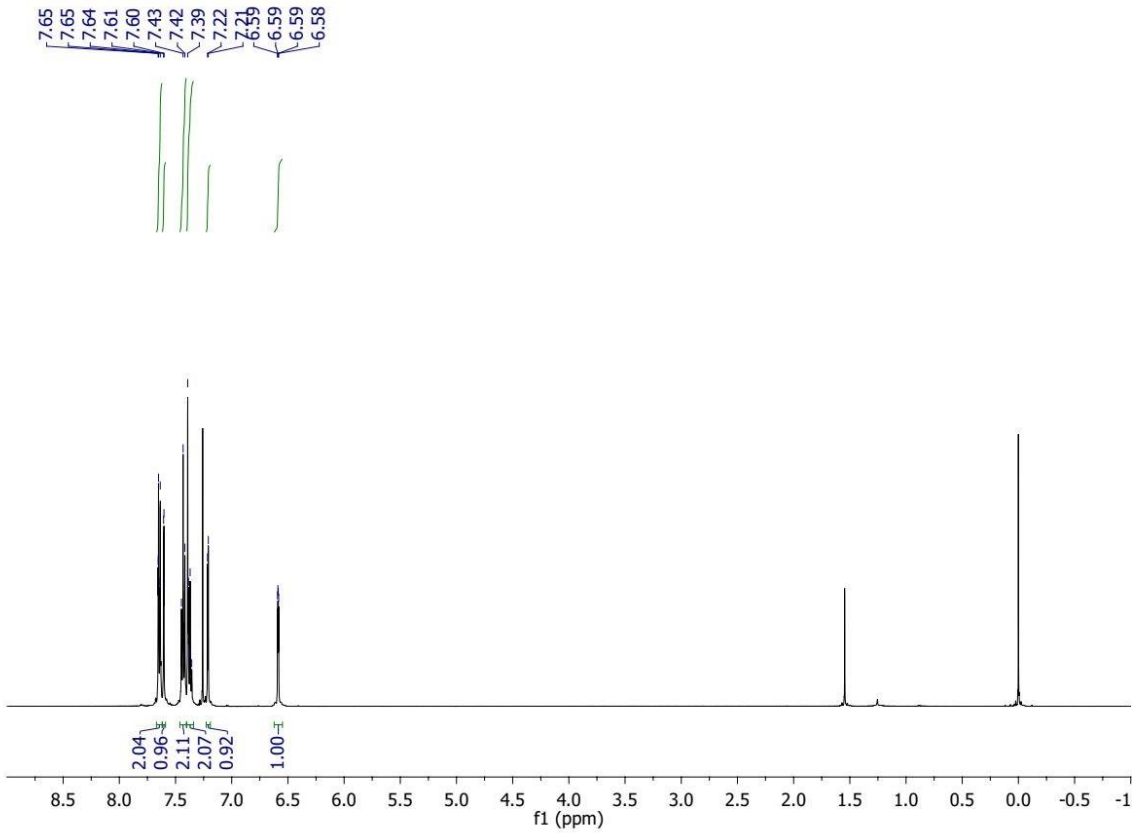
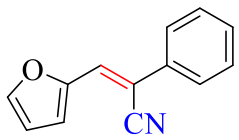


Figure 4.23 ^{1}H NMR ($CDCl_3$, 500 MHz) of 3j



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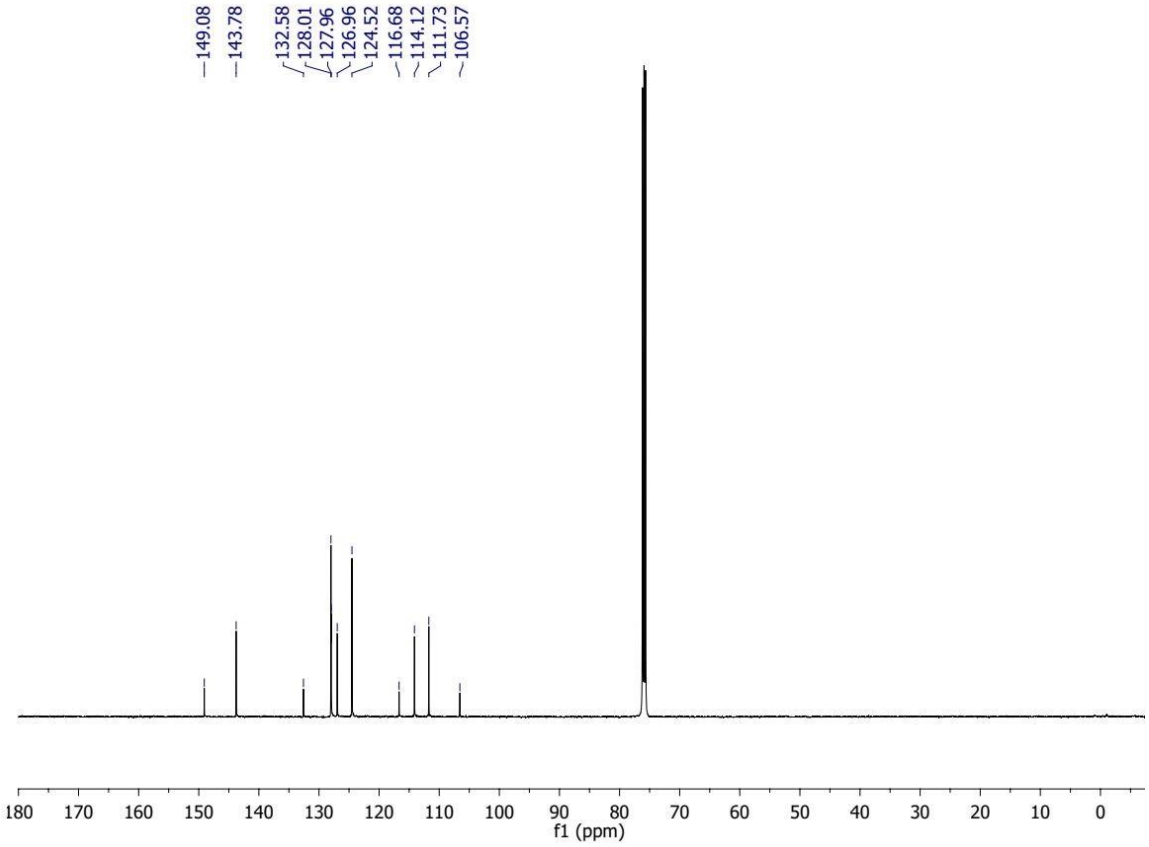
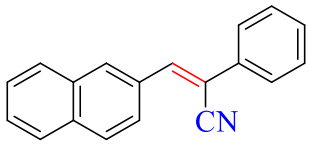


Figure 4.24 ^{13}C NMR ($CDCl_3$, 125 MHz) of 3j



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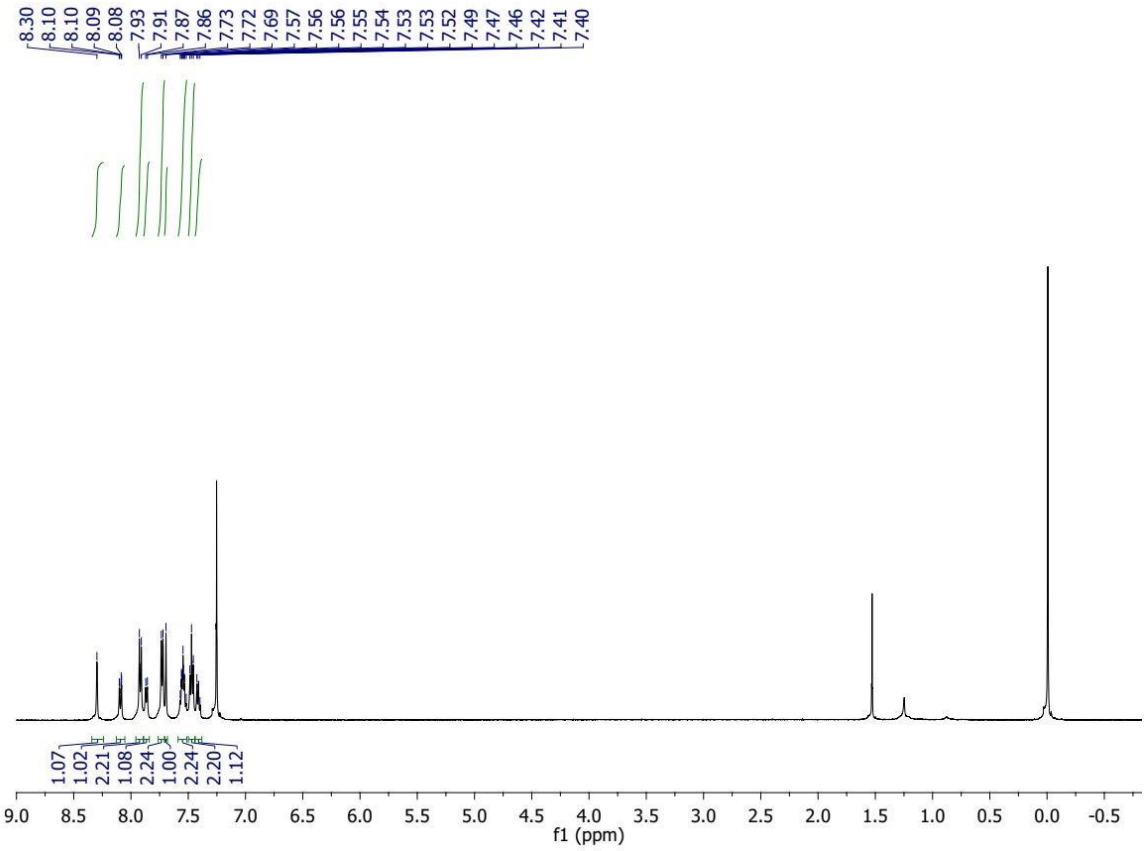
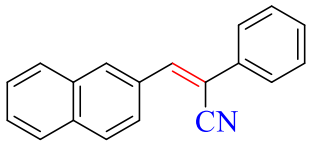


Figure 4.25 ^{1}H NMR ($CDCl_3$, 500 MHz) of 3k



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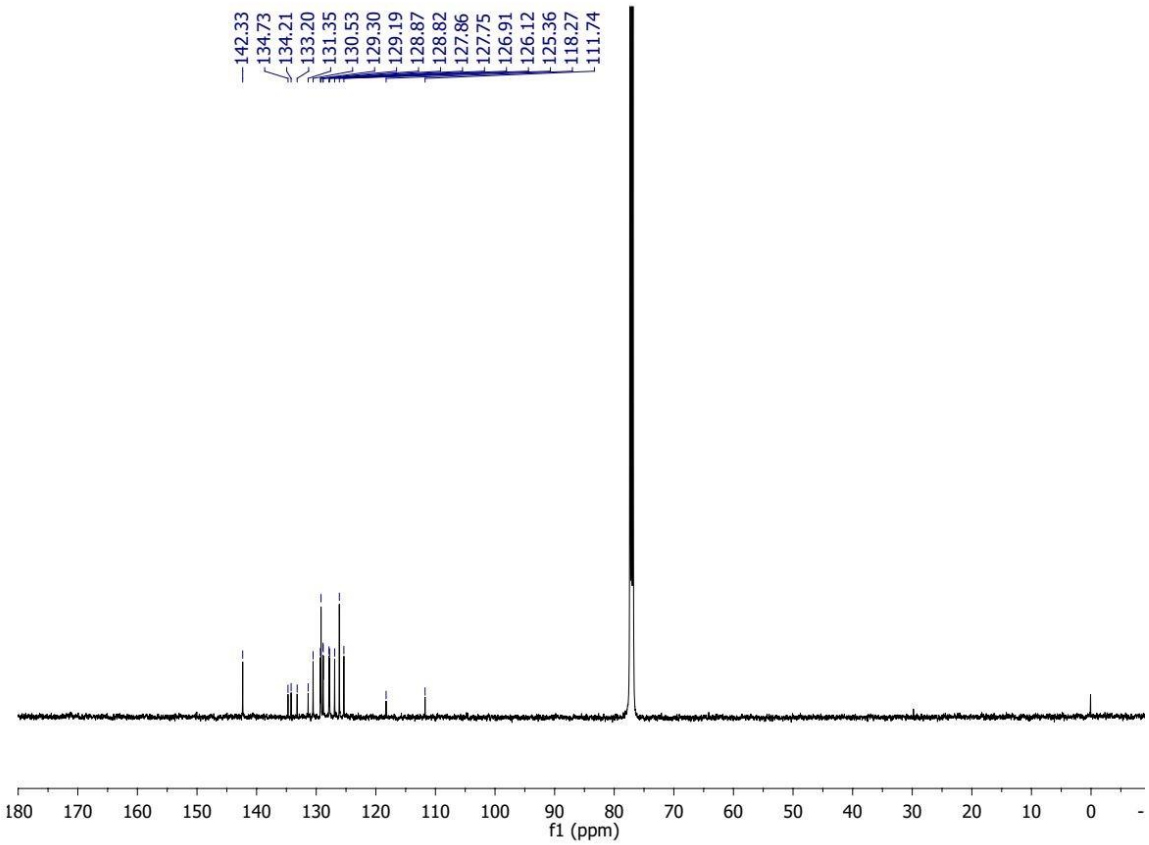
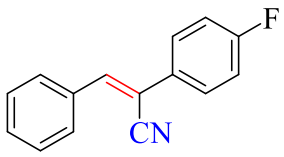


Figure 4.26 ^{13}C NMR ($CDCl_3$, 125 MHz) of 3k



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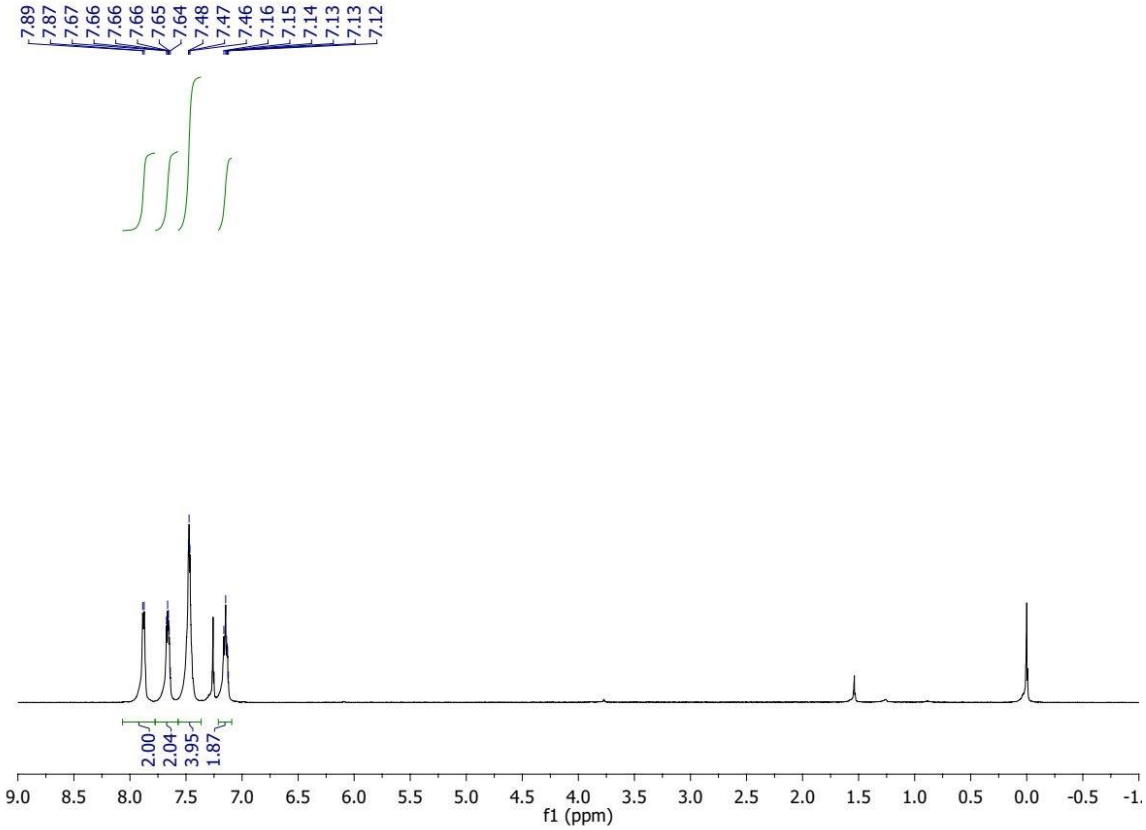
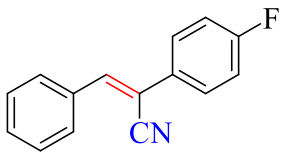


Figure 4.27 ^{1}H NMR ($CDCl_3$, 500 MHz) of 3l



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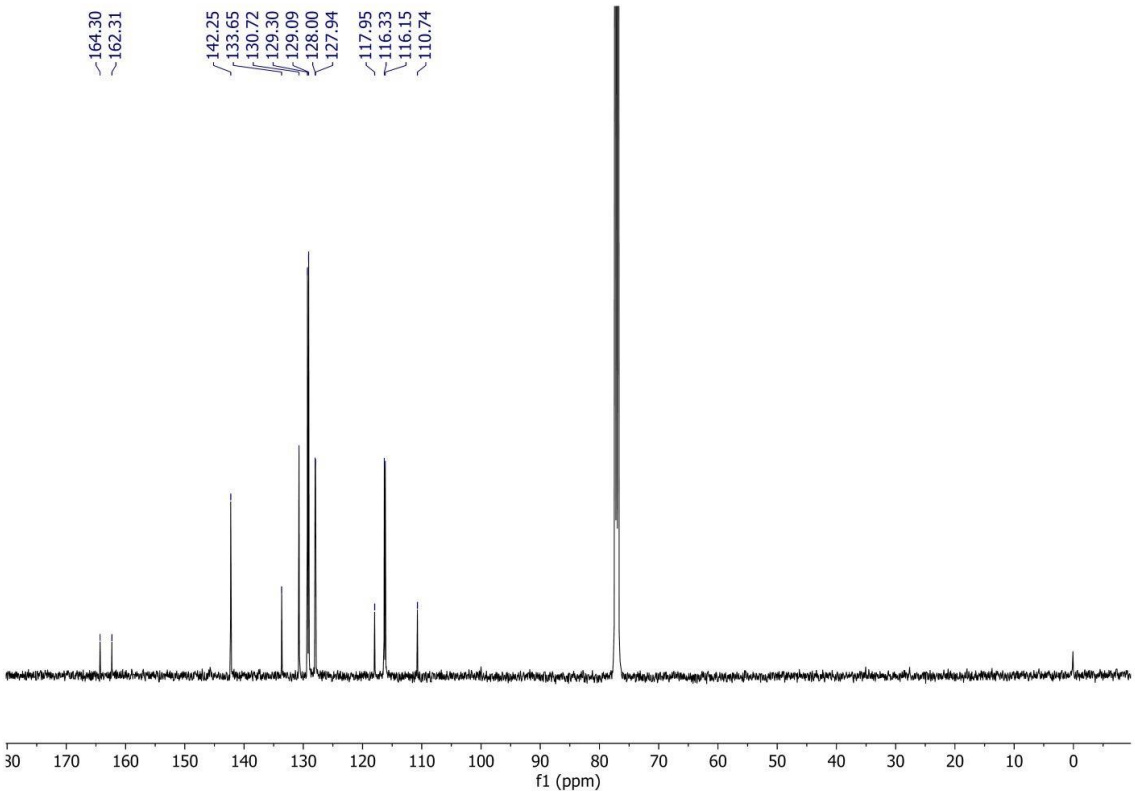
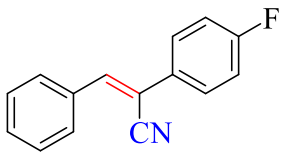


Figure 4.28 ^{13}C NMR ($CDCl_3$, 125 MHz) of 3l



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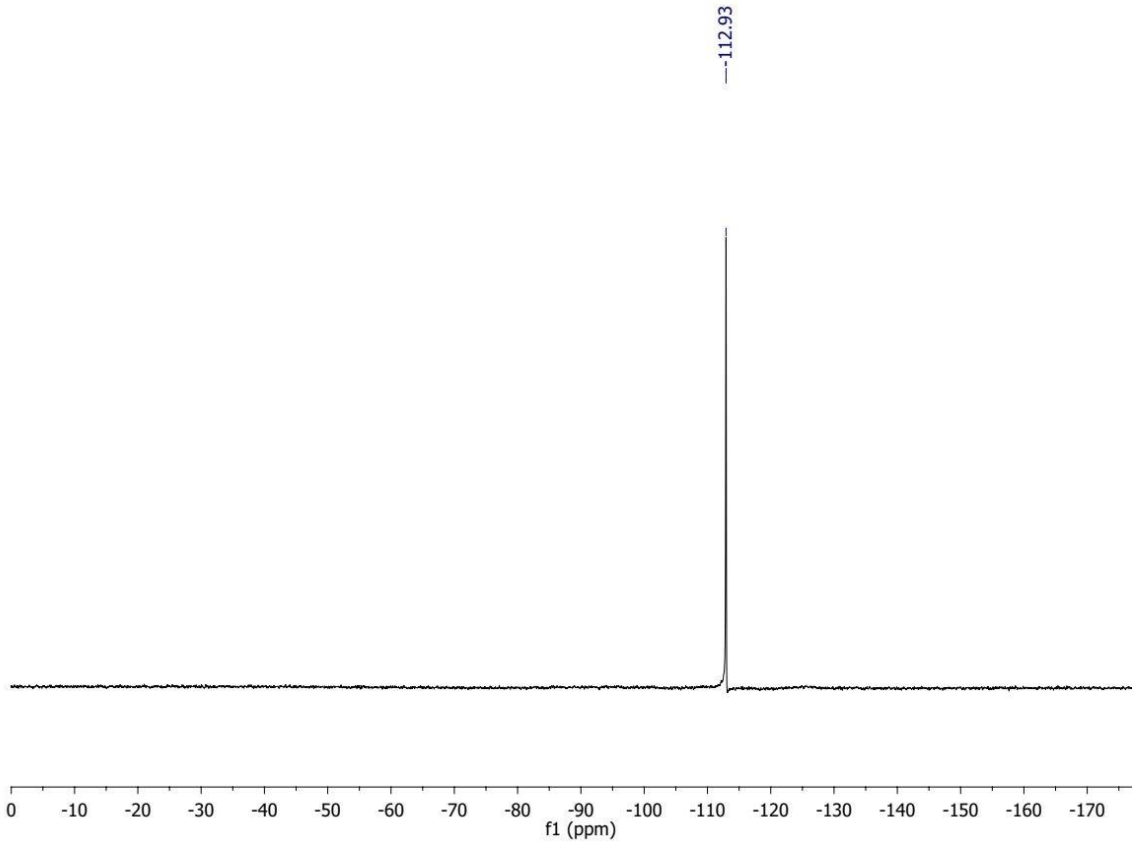
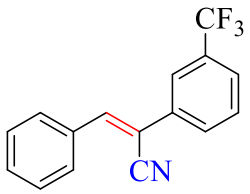


Figure 4.29 ^{19}F NMR ($CDCl_3$, 283 MHz) of 3l



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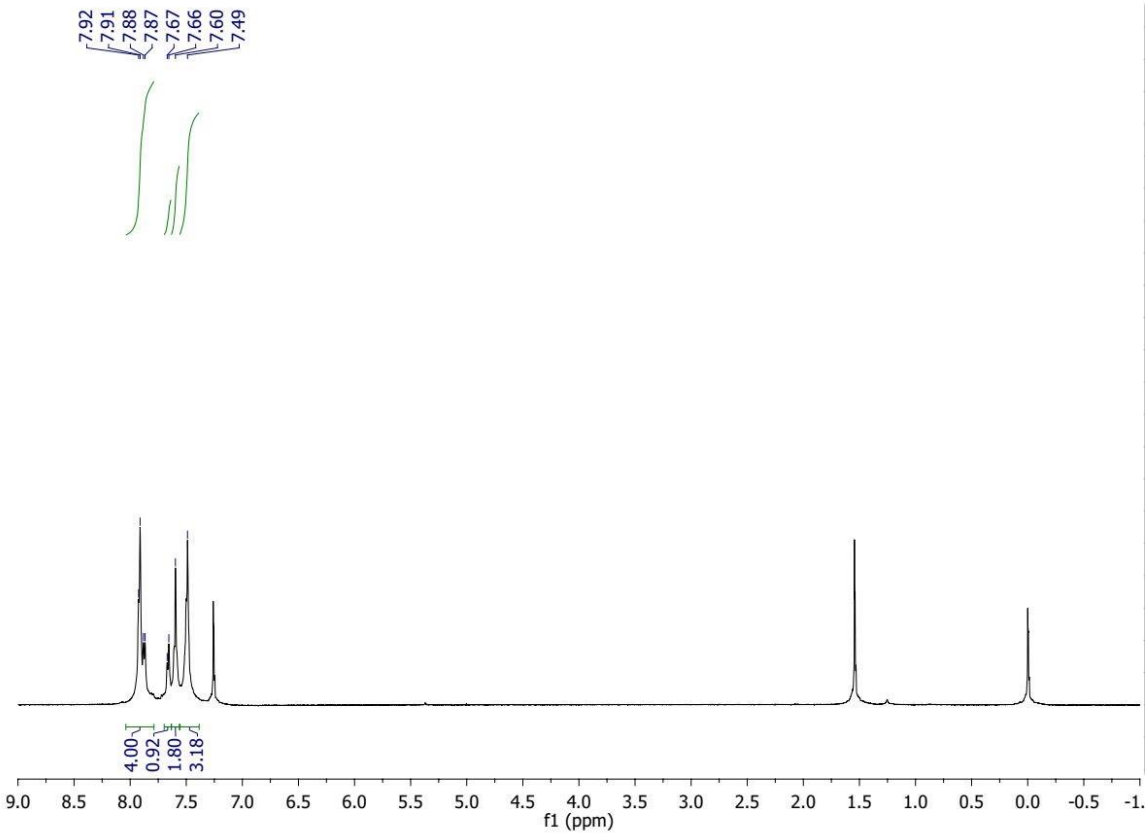
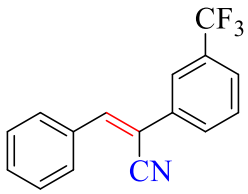


Figure 4.30 ^{1}H NMR ($CDCl_3$, 500 MHz) of 3m



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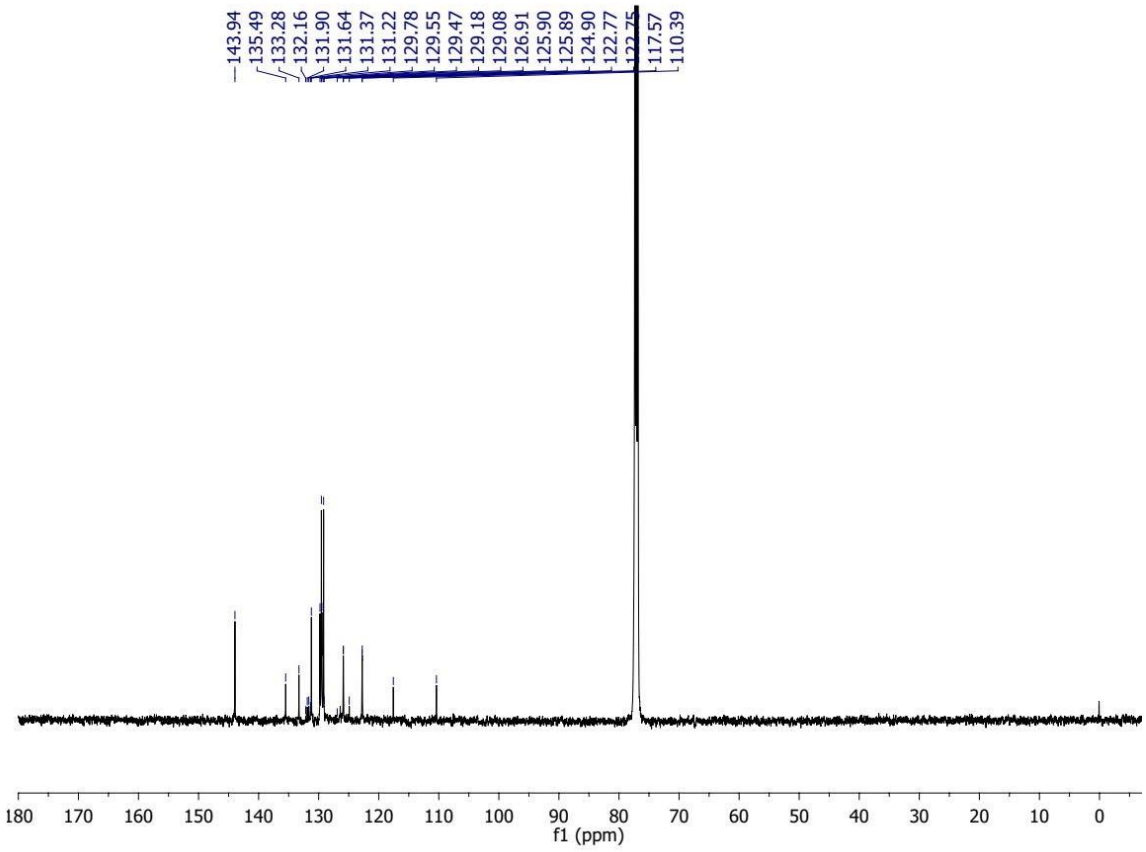
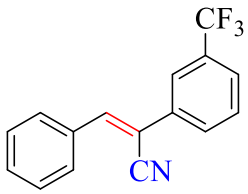


Figure 4.31 ^{13}C NMR ($CDCl_3$, 125 MHz) of 3m



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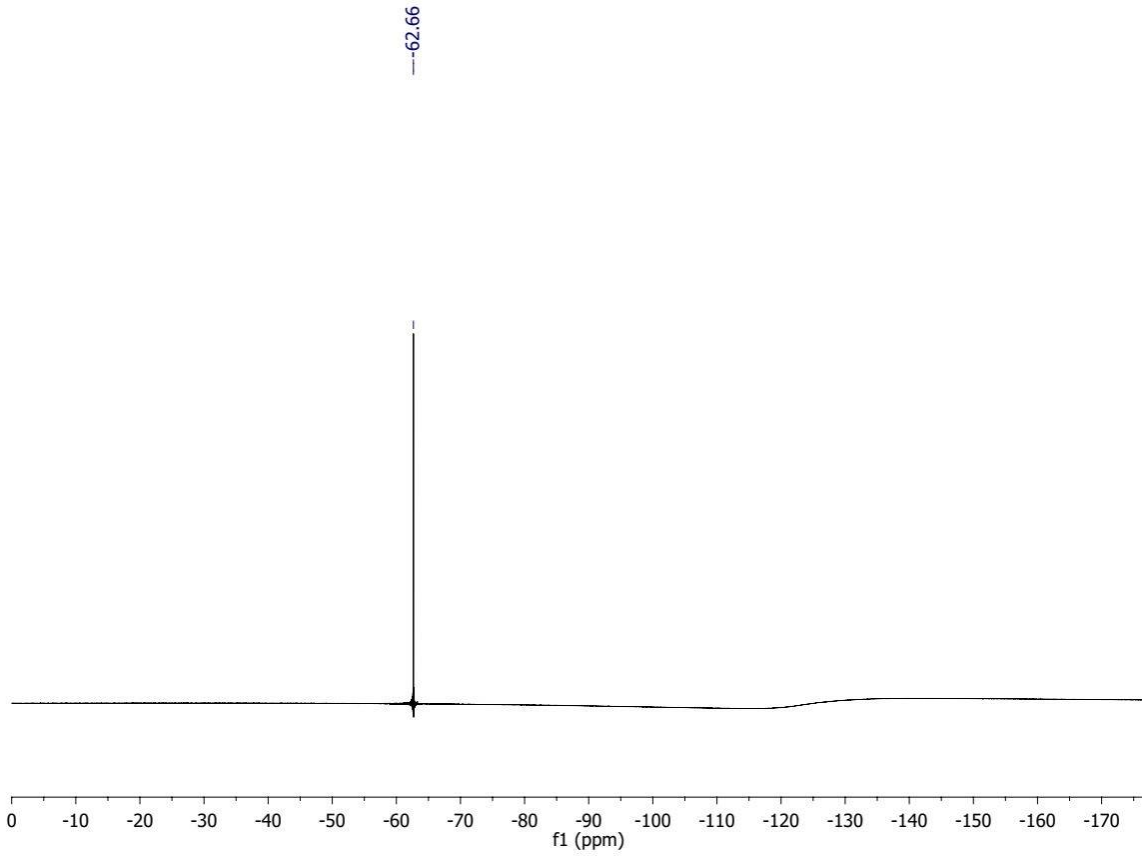
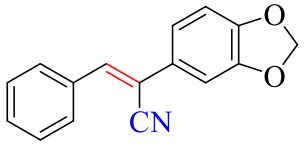


Figure 4.32 ^{19}F NMR ($CDCl_3$, 283 MHz) of 3m



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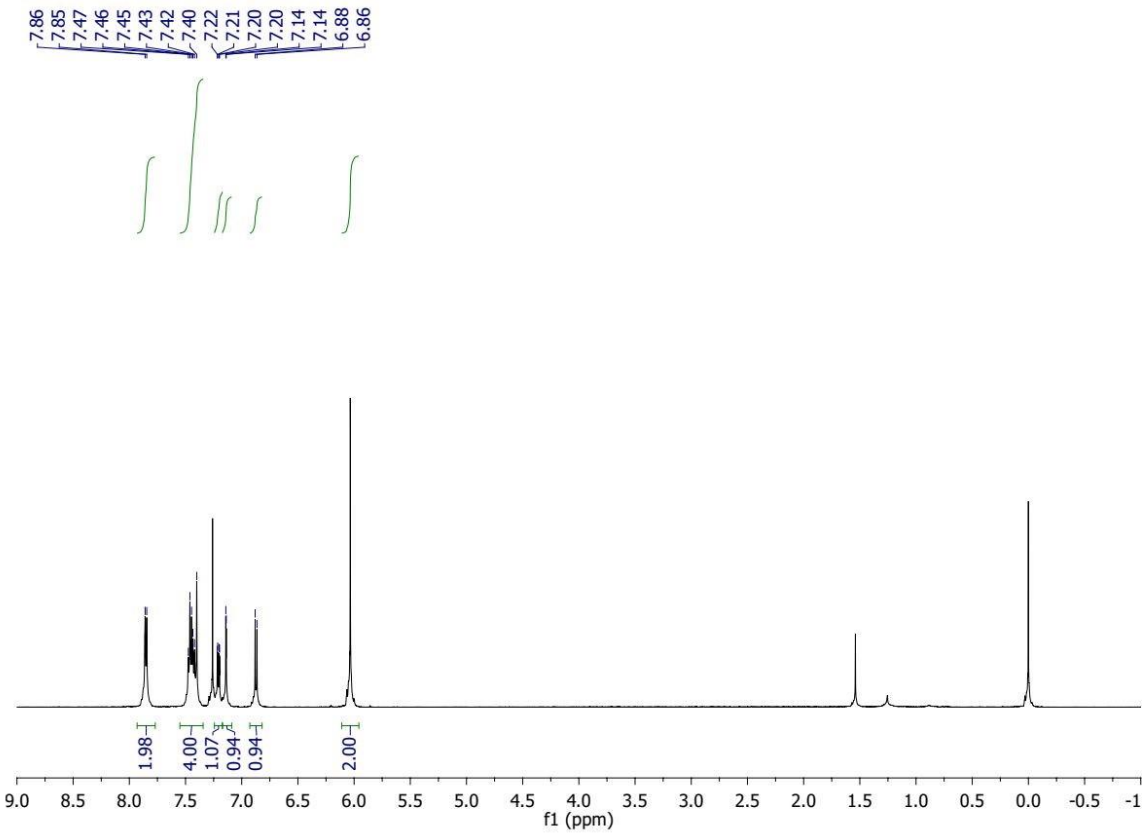
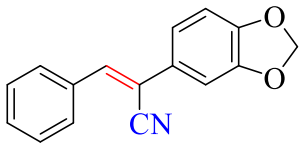


Figure 4.33 ^{1}H NMR ($CDCl_3$, 500 MHz) of 3n



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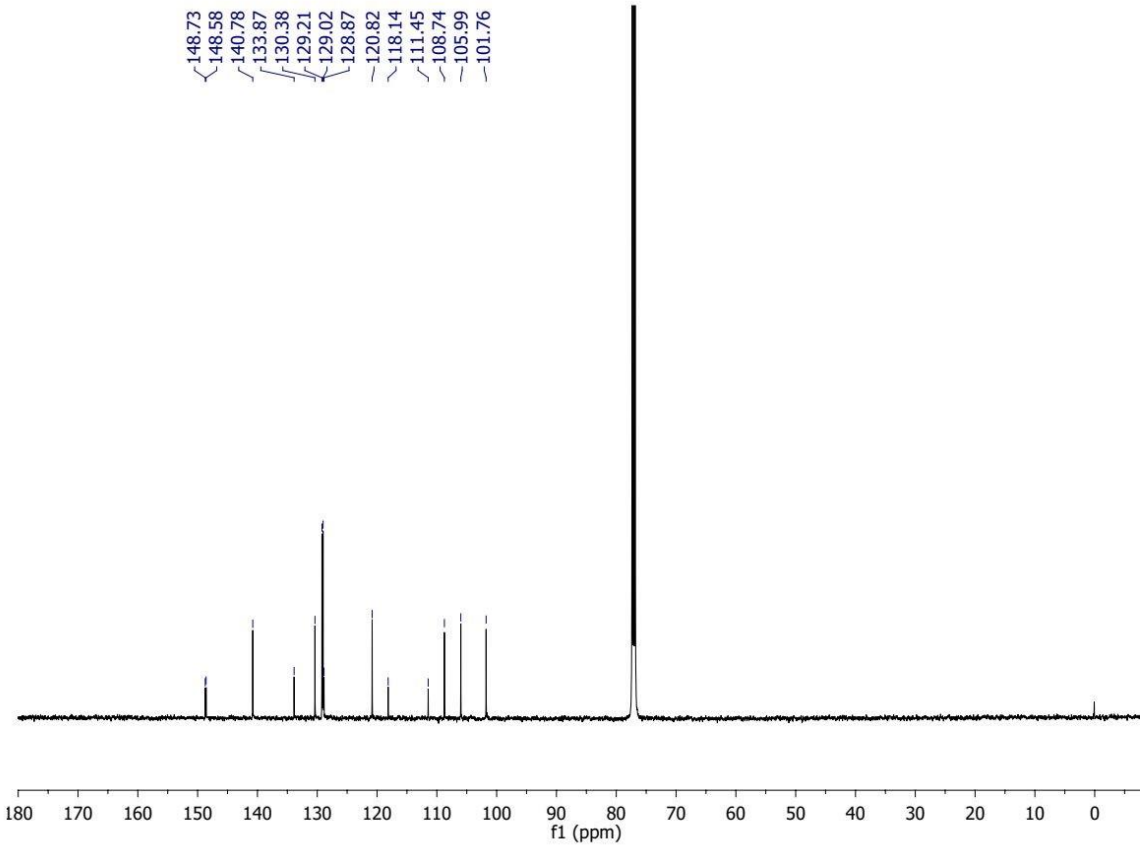
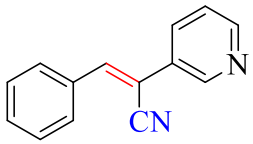


Figure 4.34 ^{13}C NMR ($CDCl_3$, 125 MHz) of 3n



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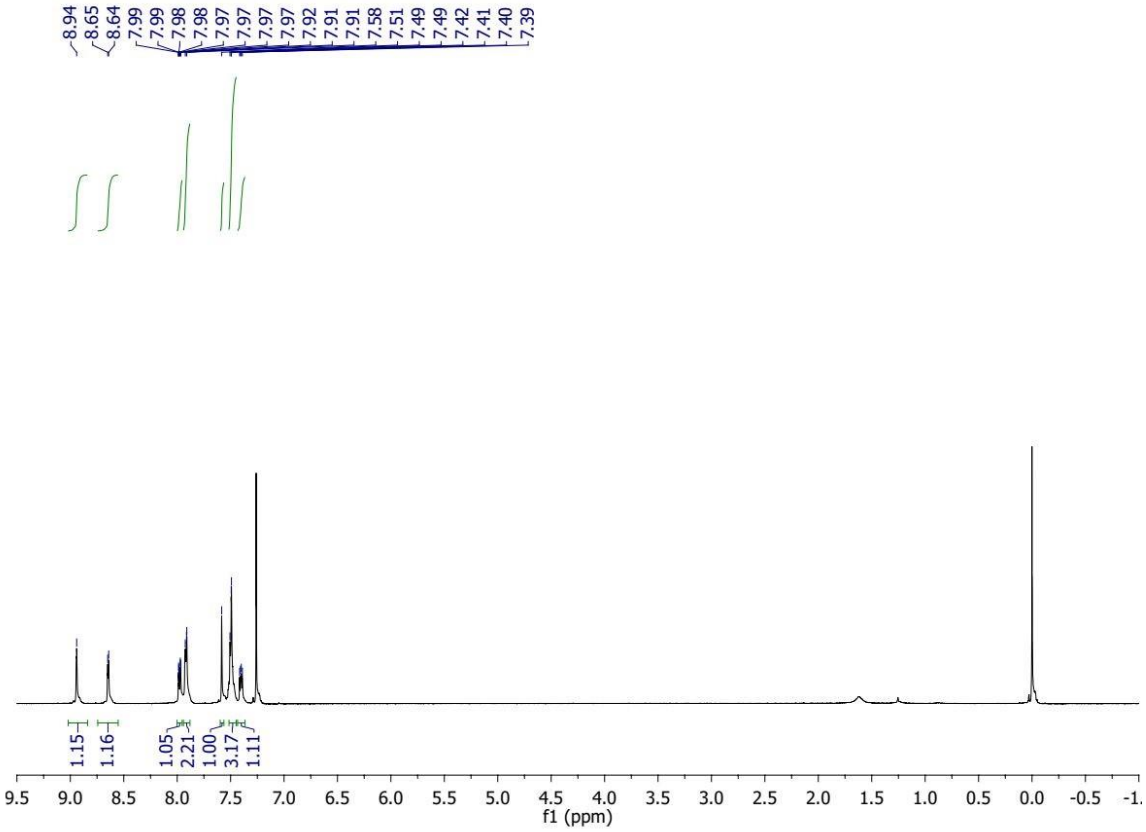
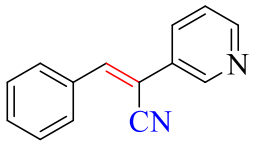


Figure 4.35 ^{1}H NMR ($CDCl_3$, 500 MHz) of 3o



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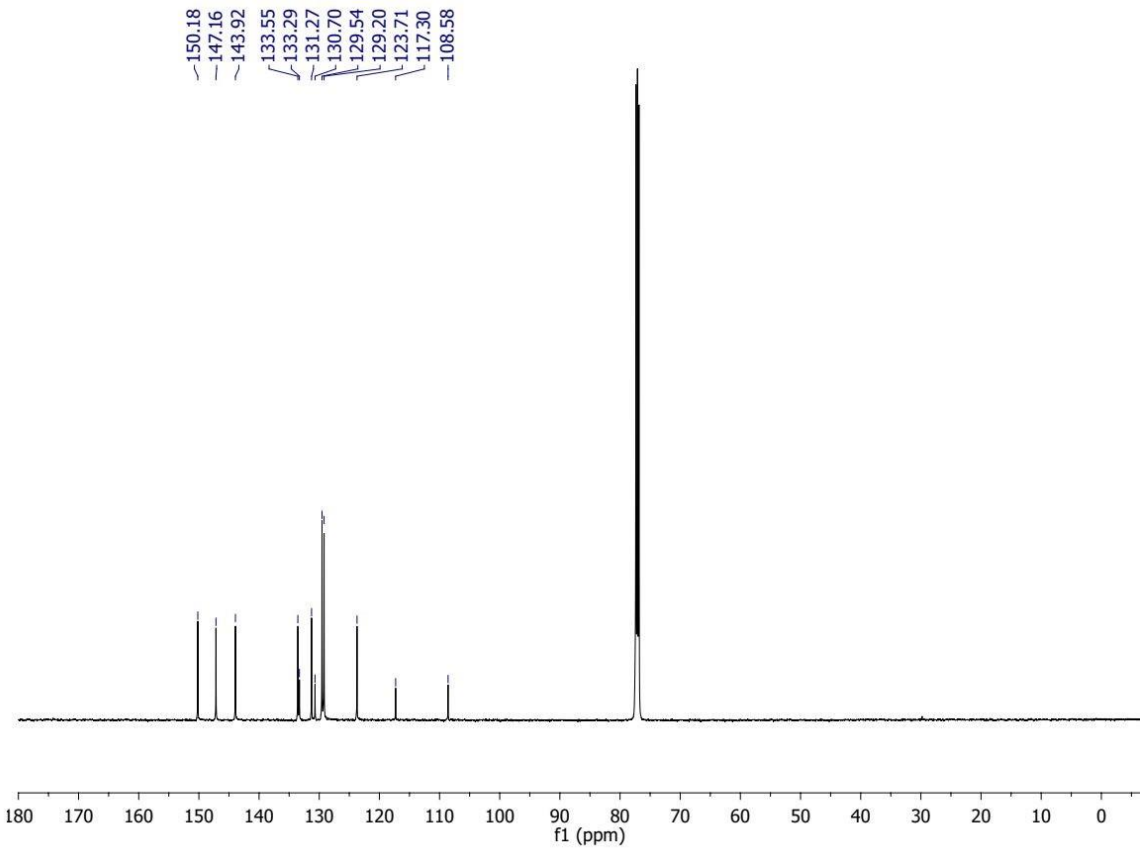
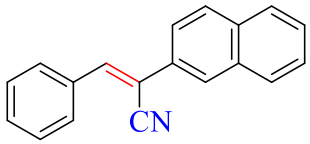


Figure 4.36 ^{13}C NMR ($CDCl_3$, 125 MHz) 3o



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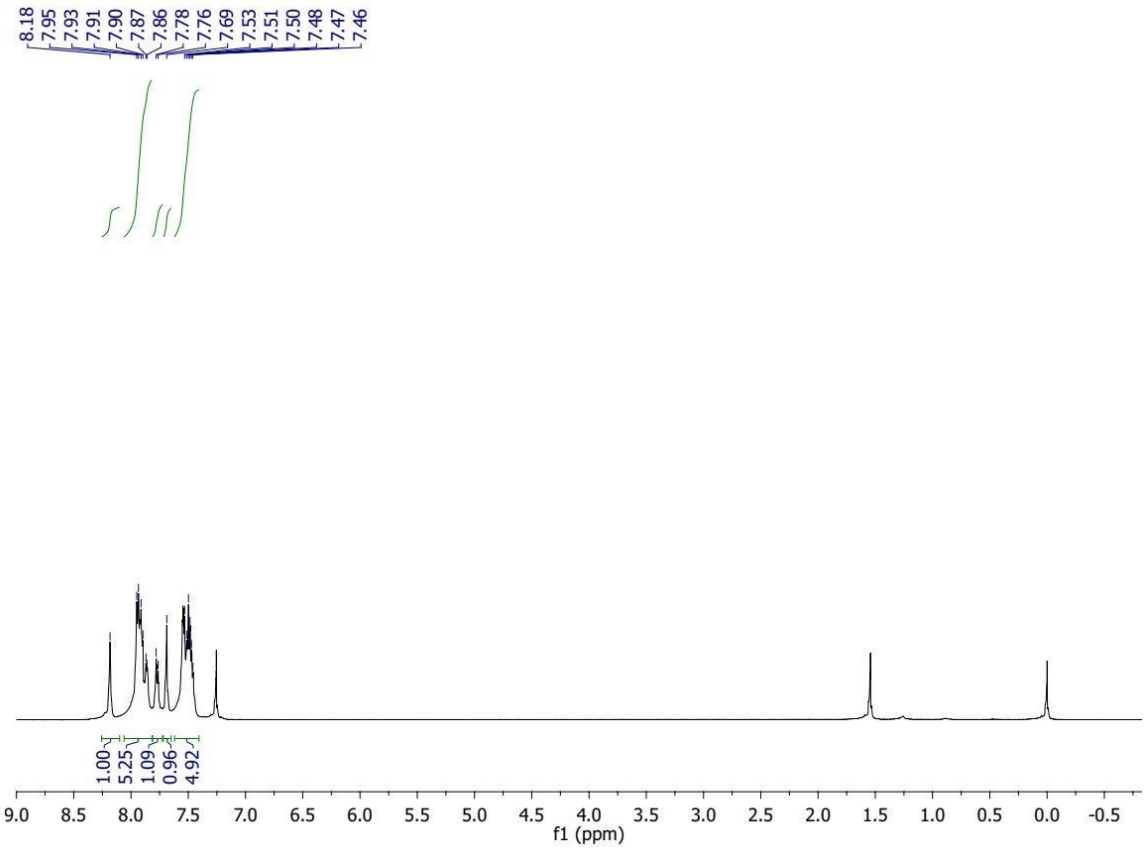
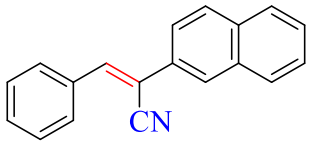


Figure 4.37 ^{1}H NMR ($CDCl_3$, 500 MHz) of 3p



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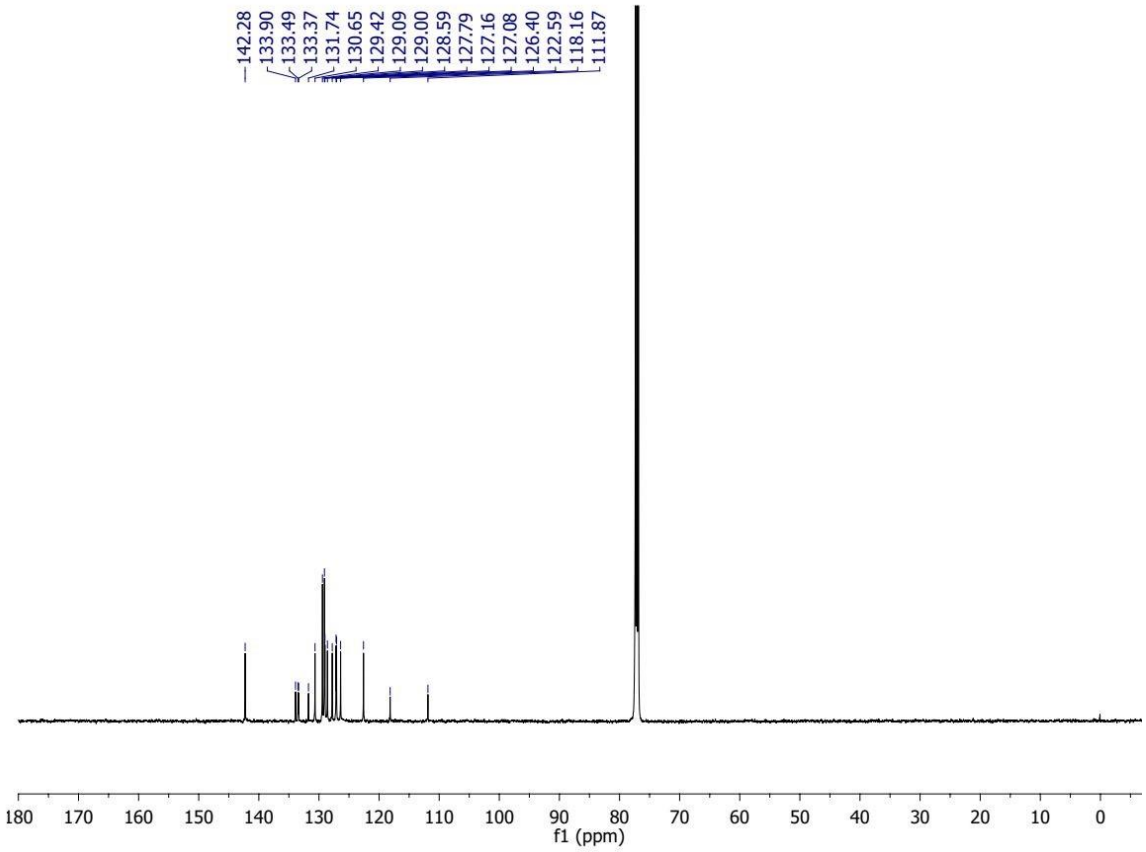
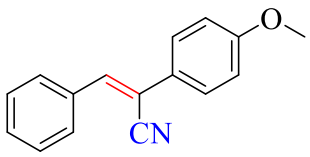


Figure 4.38 ^{13}C NMR ($CDCl_3$, 125 MHz) of 3p



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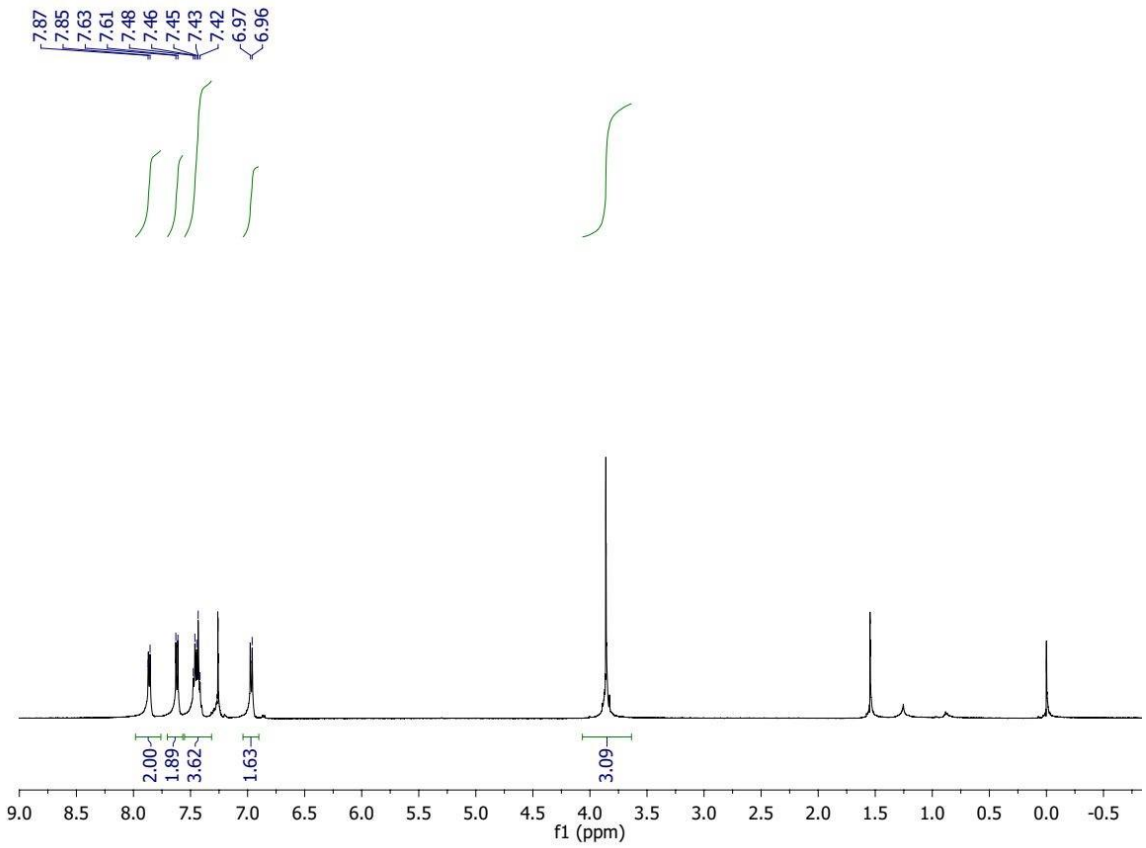
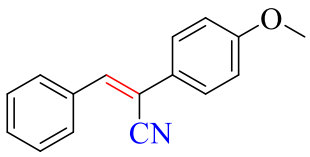


Figure 4.39 ^{1}H NMR ($CDCl_3$, 500 MHz) of 3q



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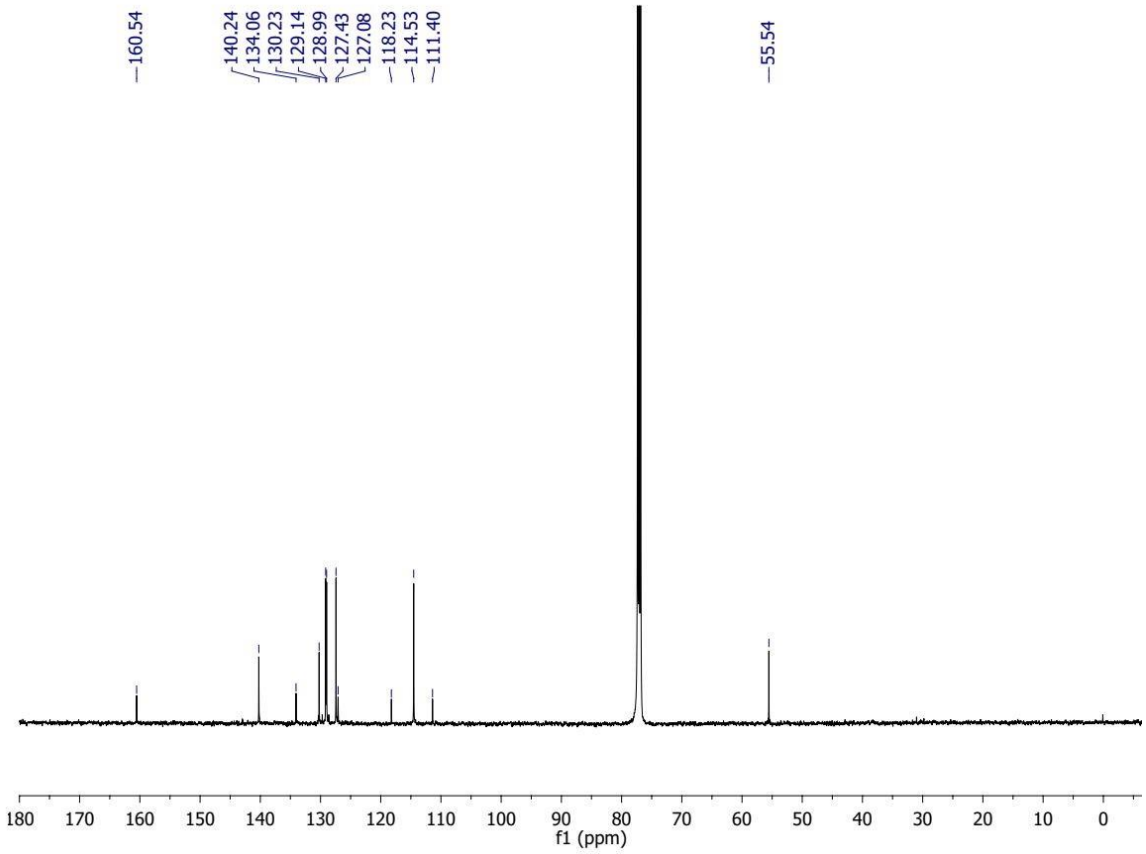
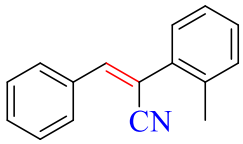


Figure 4.40 ^{13}C NMR ($CDCl_3$, 125 MHz) of 3q



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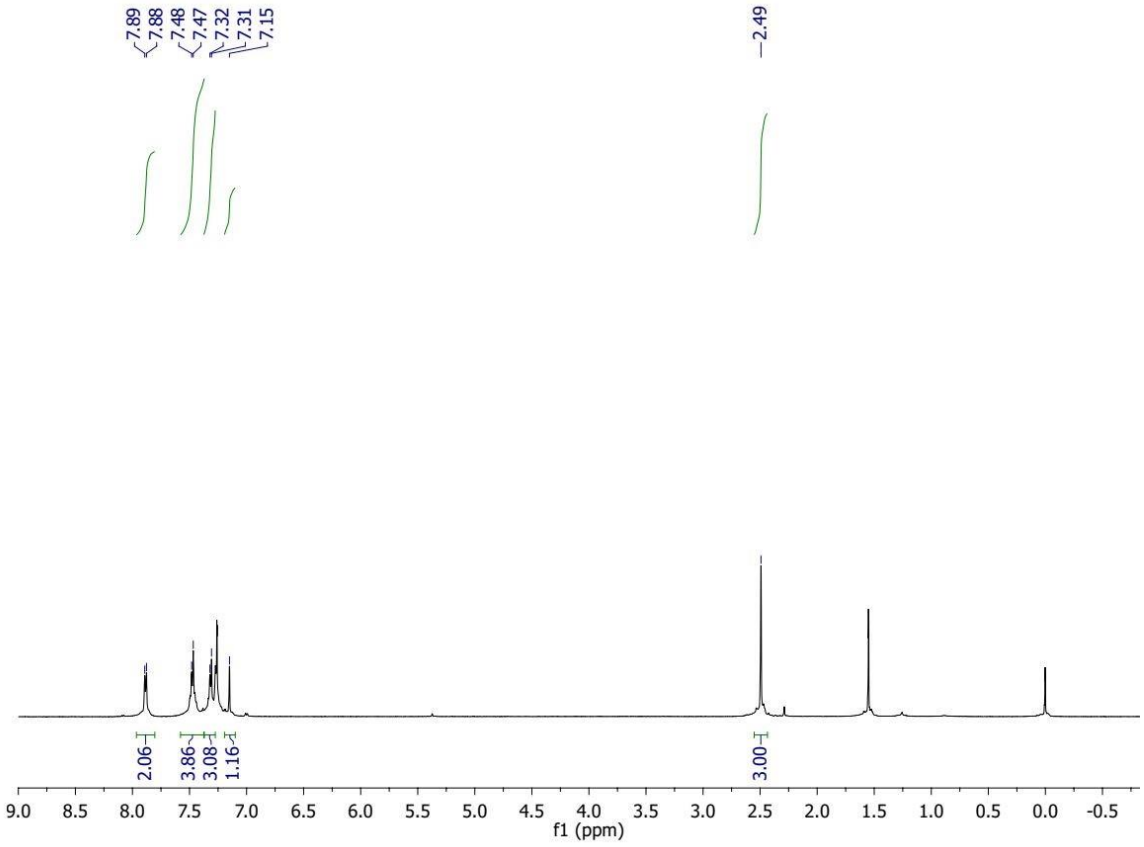
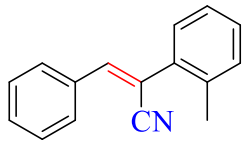


Figure 4.41 ^{1}H NMR ($CDCl_3$, 500 MHz) of 3r



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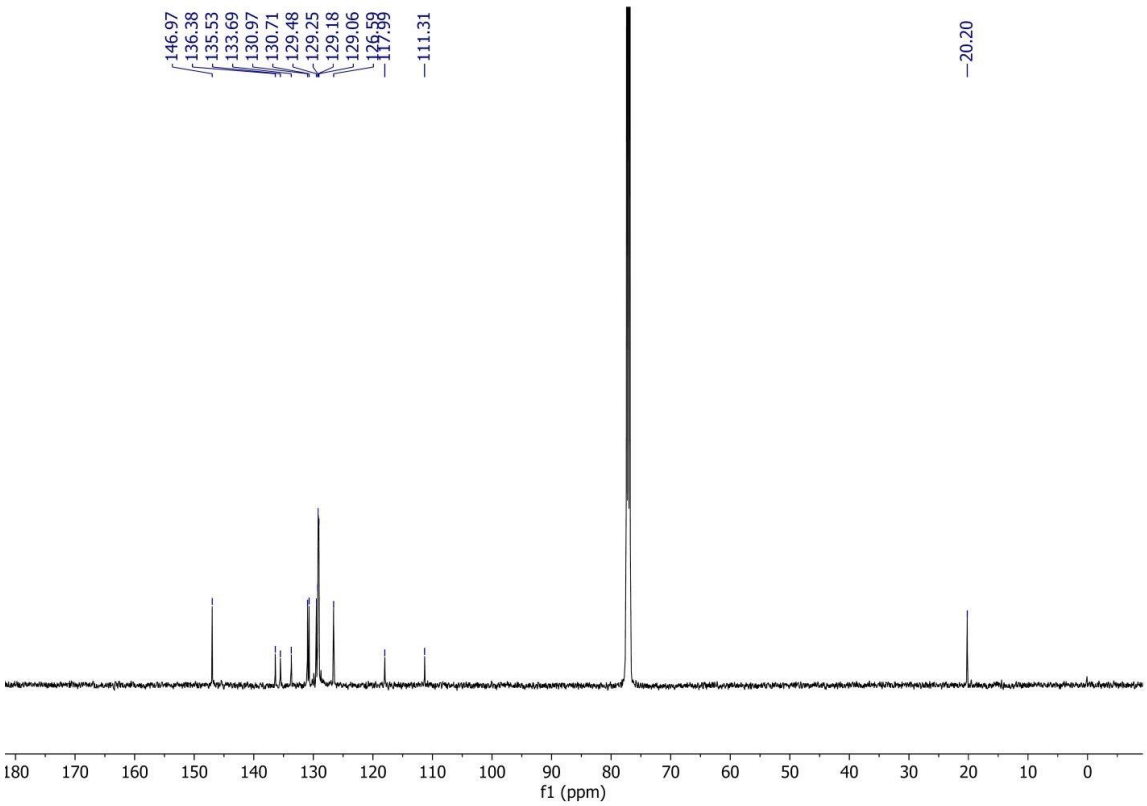
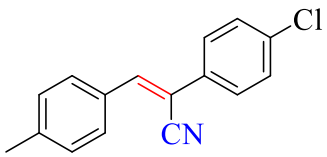


Figure 4.42 ^{13}C NMR ($CDCl_3$, 125 MHz) of 3r



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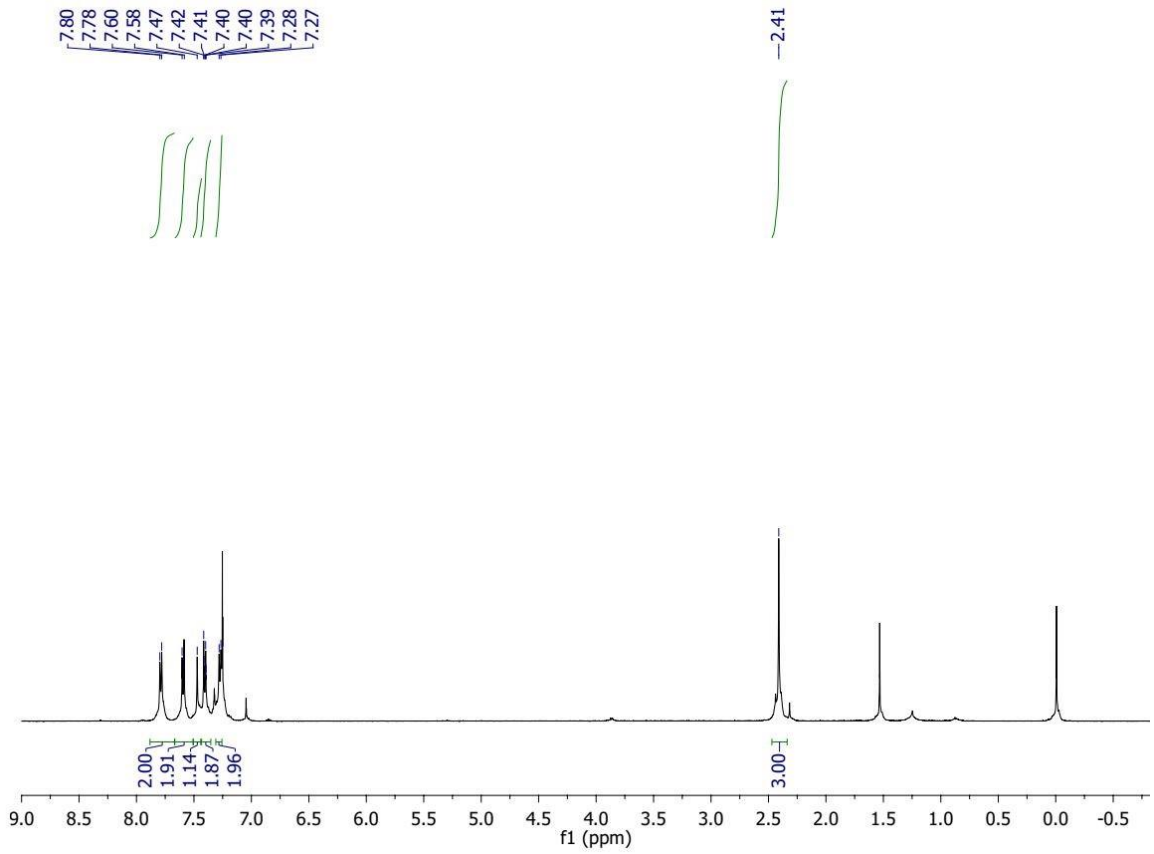
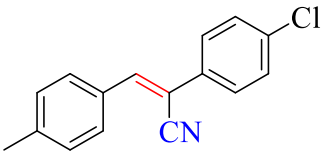


Figure 4.43 ^{1}H NMR ($CDCl_3$, 500 MHz) of 3s



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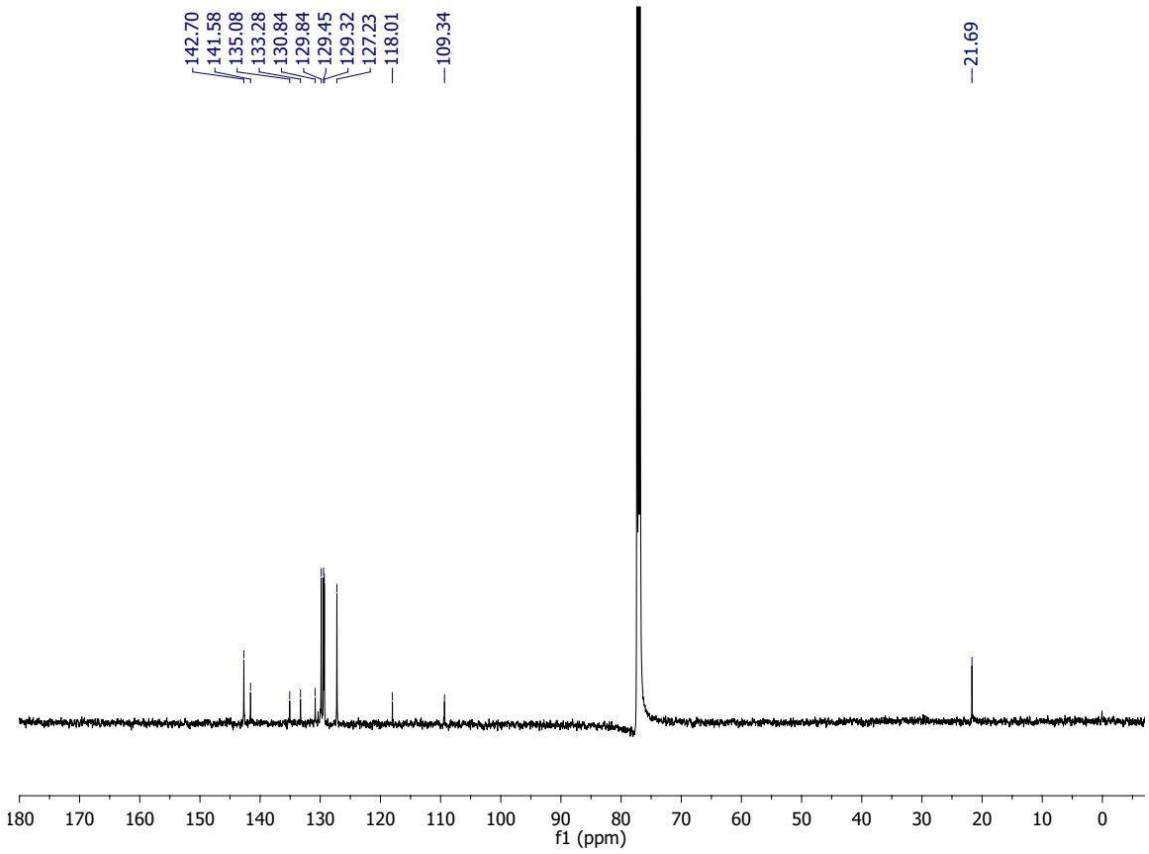
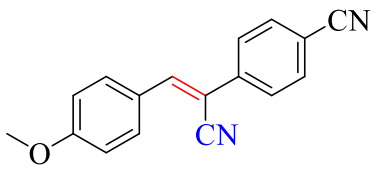


Figure 4.44 ^{13}C NMR ($CDCl_3$, 125 MHz) of 3s



3t

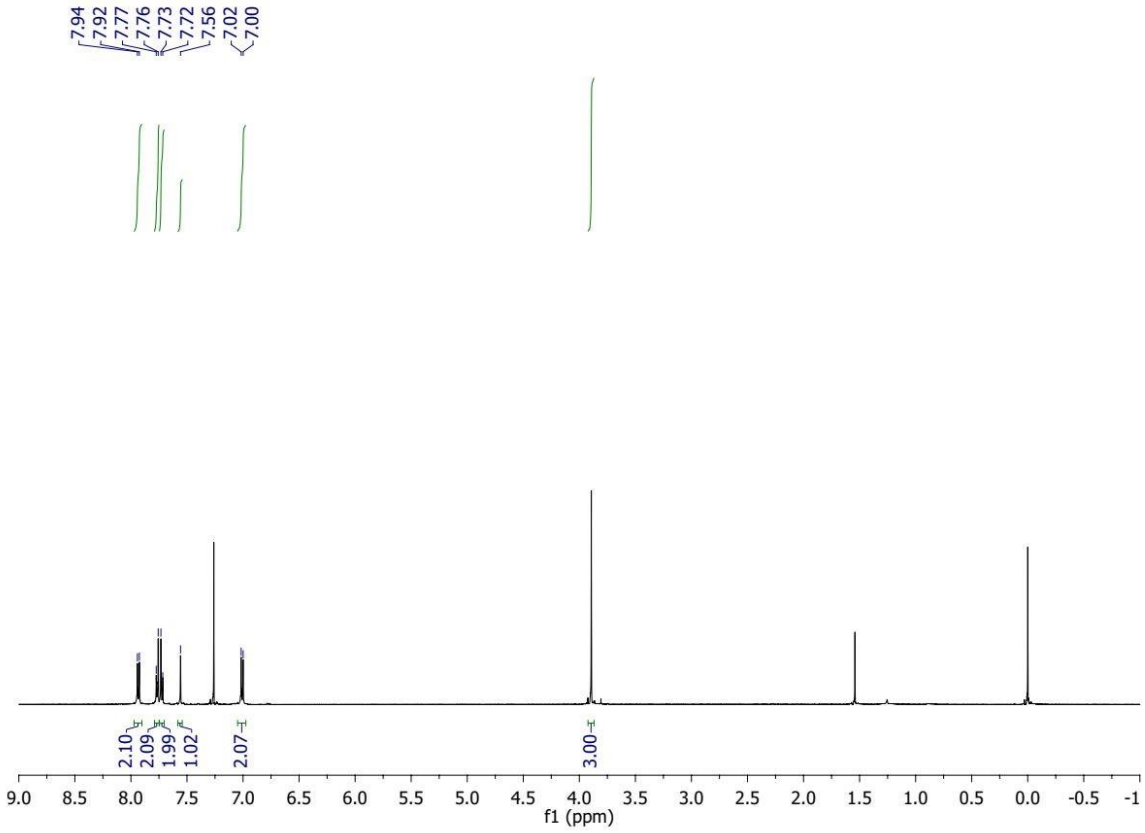
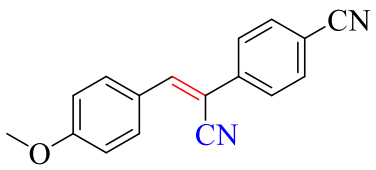


Figure 3.53 ^{1}H NMR ($CDCl_3$, 500 MHz) of 3t



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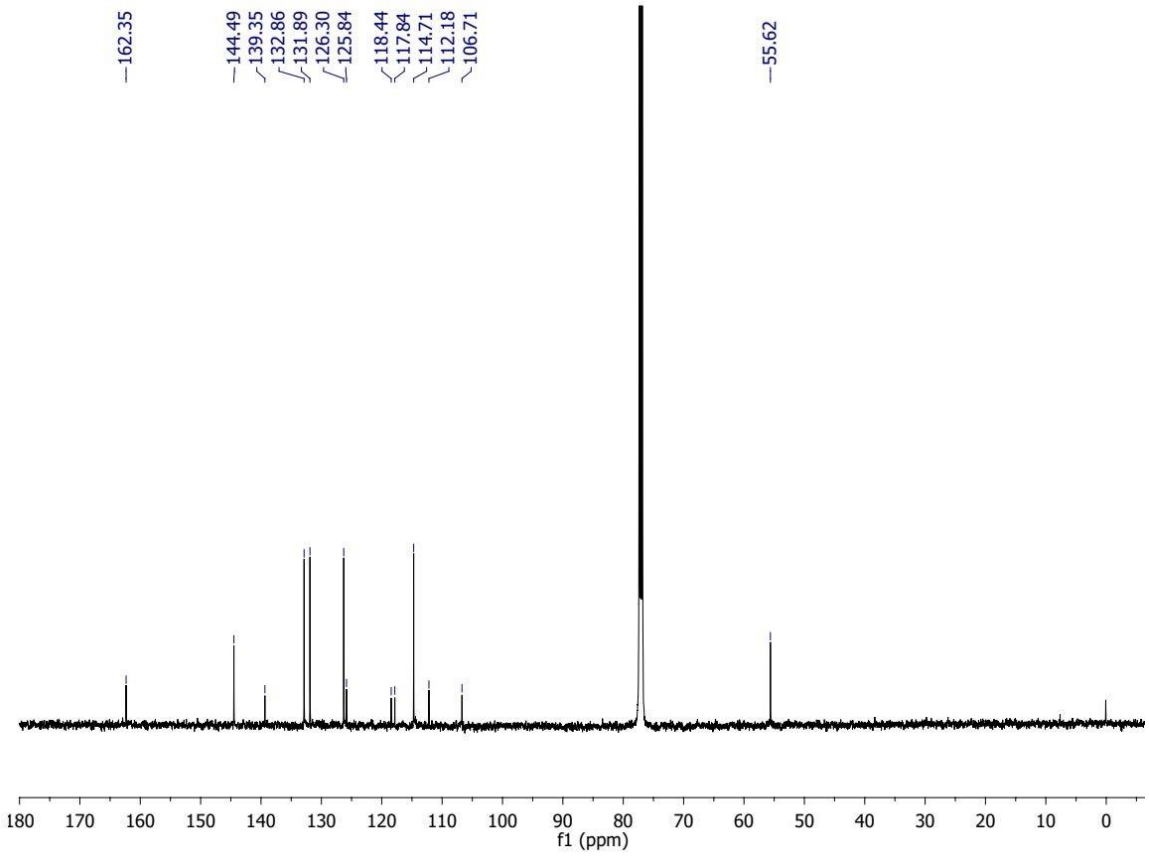
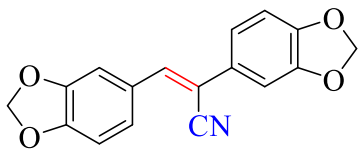


Figure 4.46 ^{13}C NMR ($CDCl_3$, 125 MHz) of 3t



3u

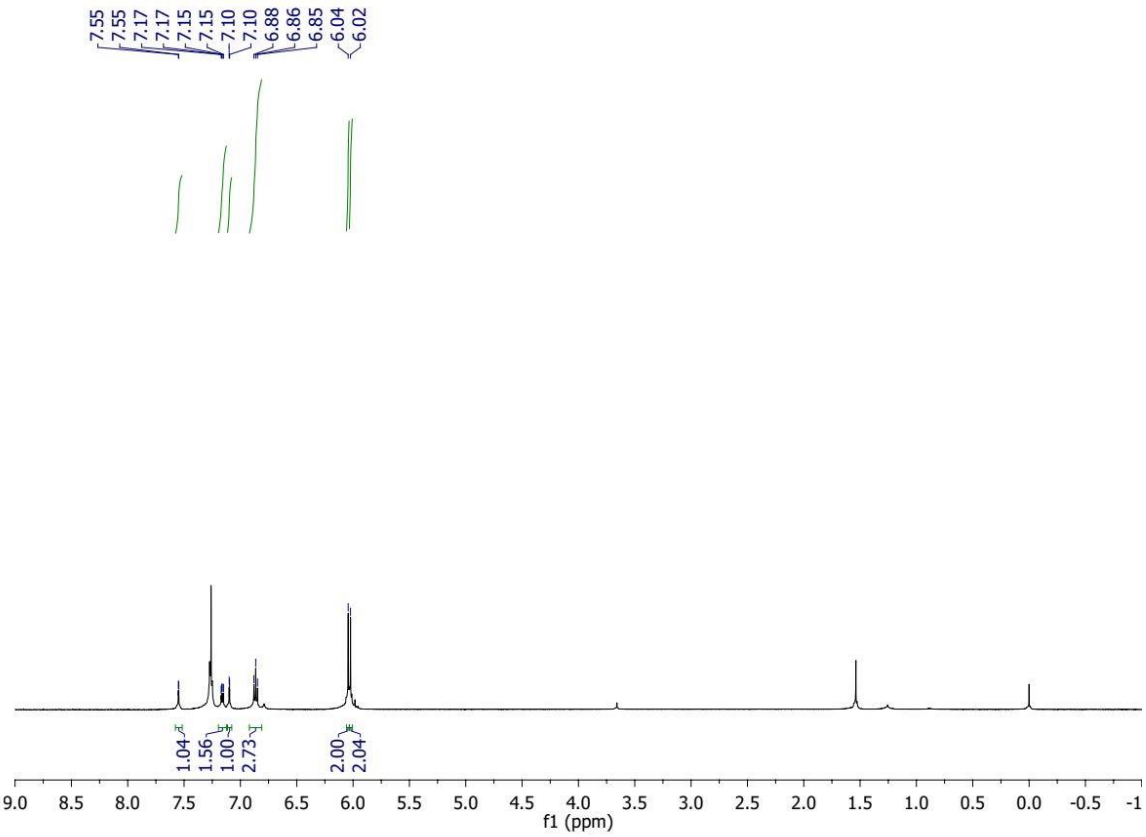
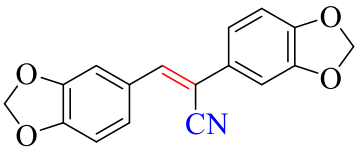


Figure 4.47 ^{1}H NMR ($CDCl_3$, 500 MHz) of 3u



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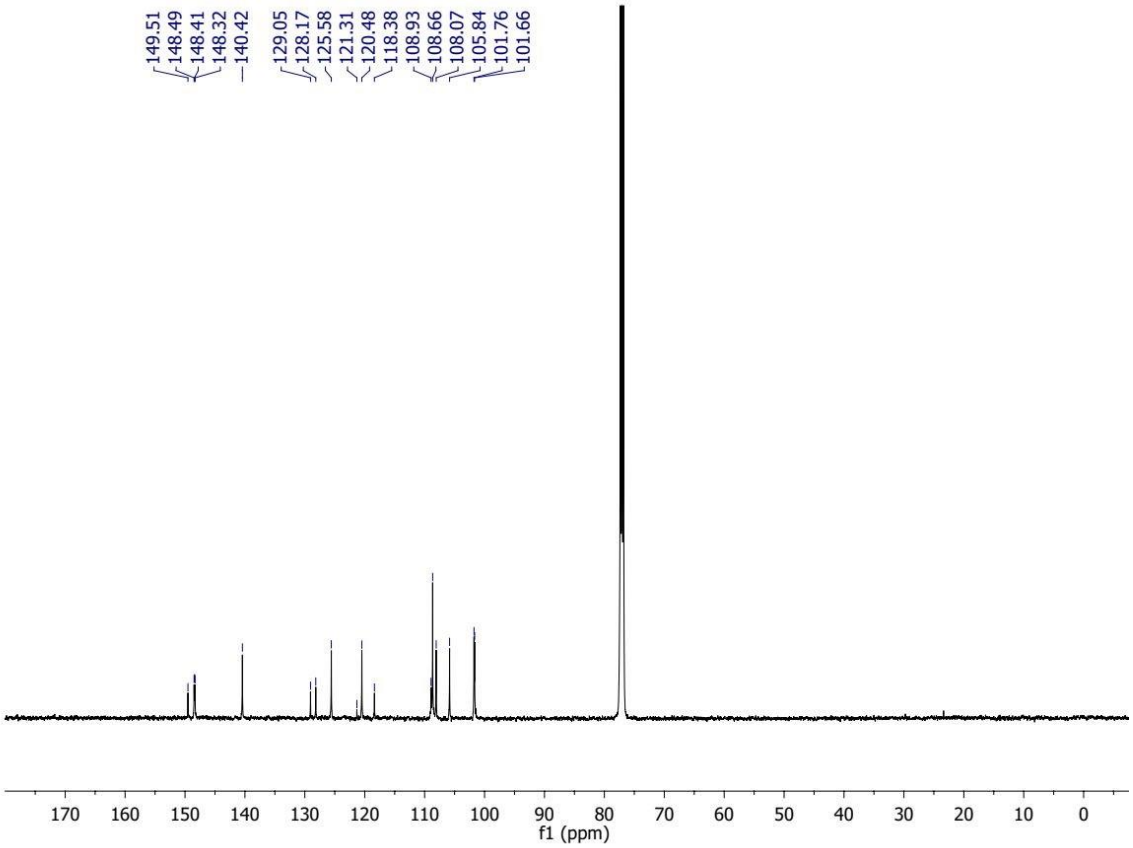
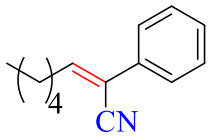


Figure 4.48 ^{13}C NMR ($CDCl_3$, 125 MHz) of 3u



3v

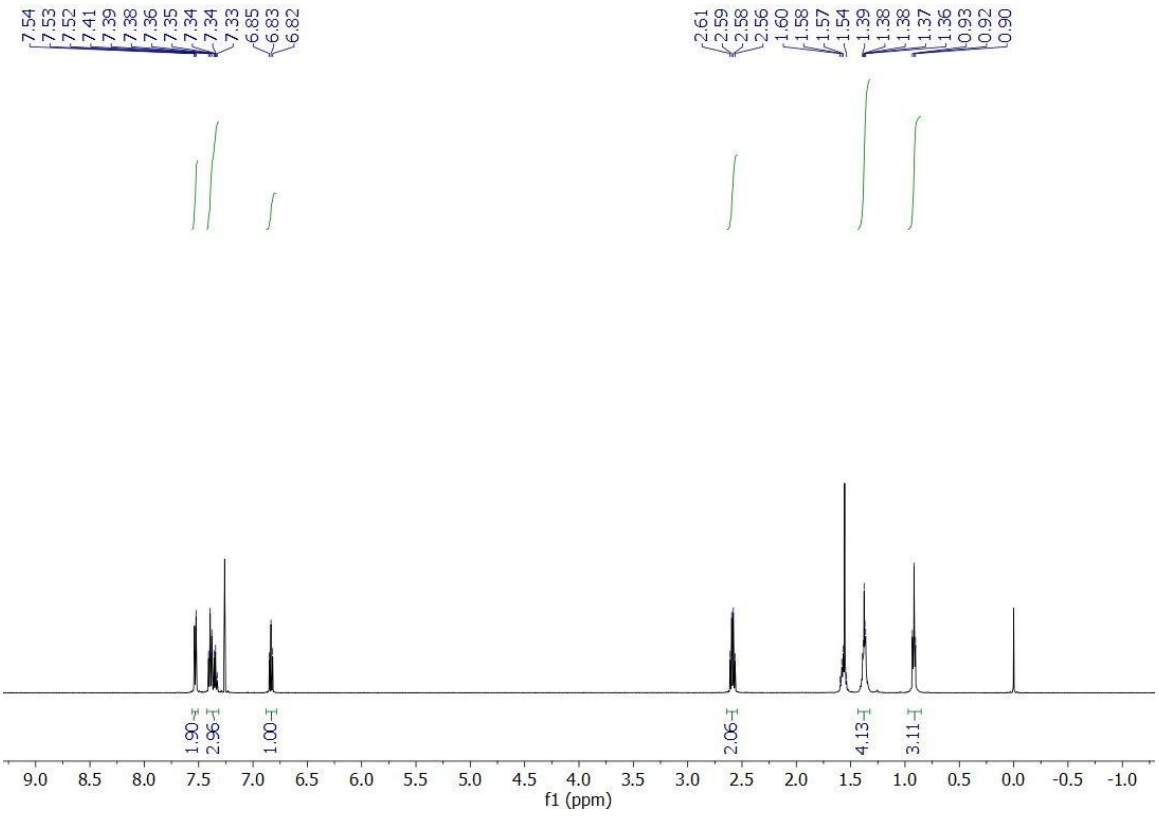
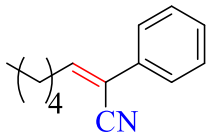


Figure 4.49 ^{1}H NMR ($CDCl_3$, 500 MHz) of 3v



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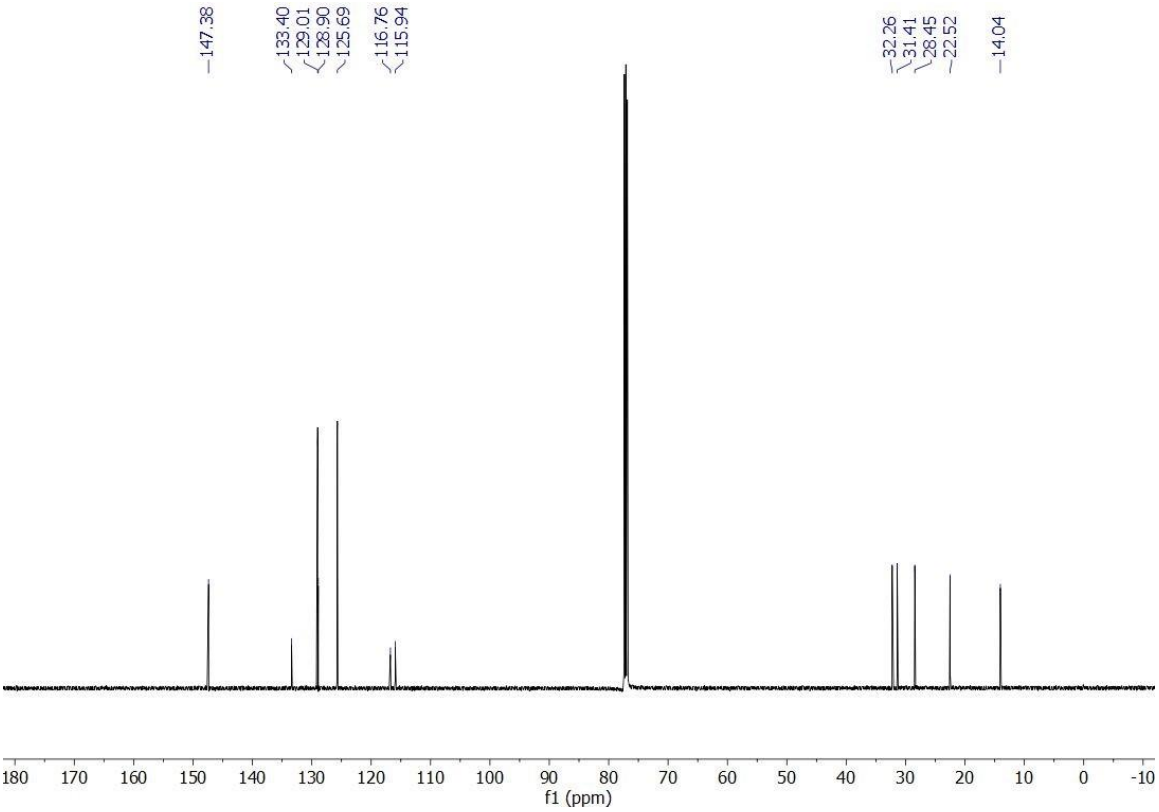
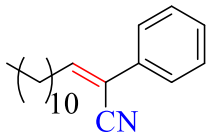


Figure 4.50 ^{13}C NMR ($CDCl_3$, 125 MHz) of 3v



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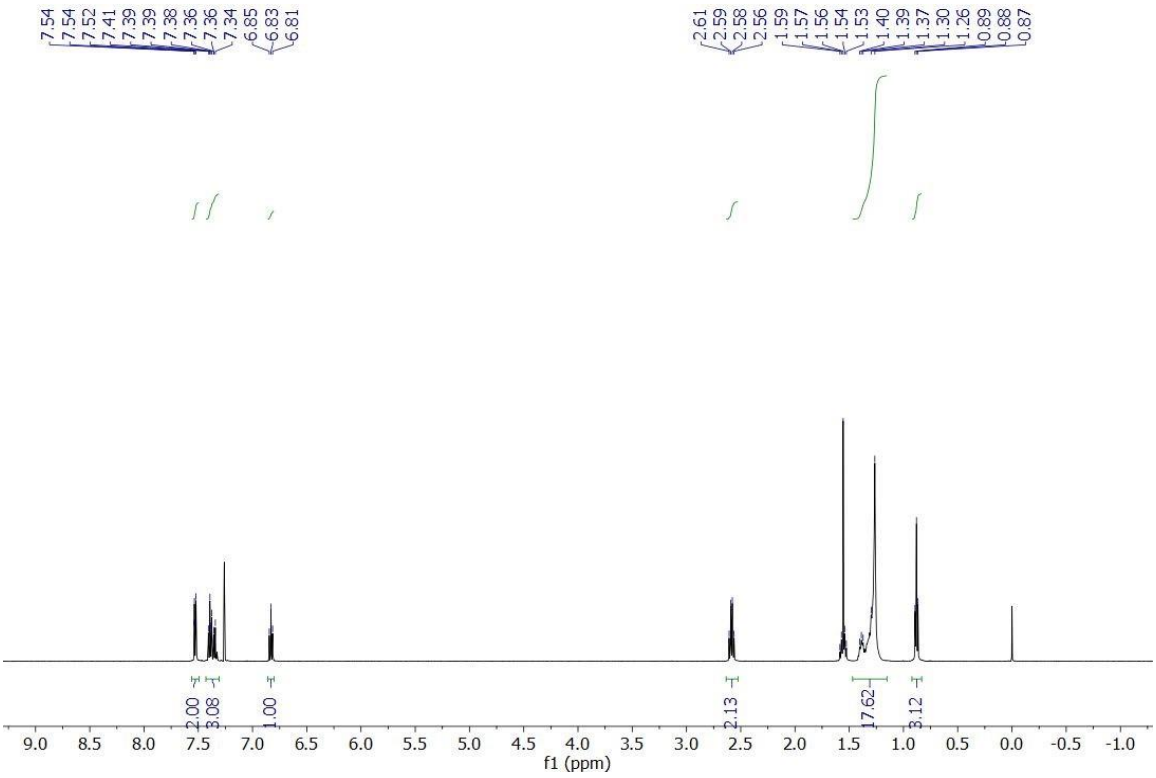
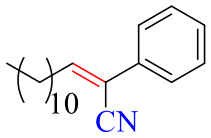


Figure 4.51 ^{1}H NMR ($CDCl_3$, 500 MHz) of 3w



3w

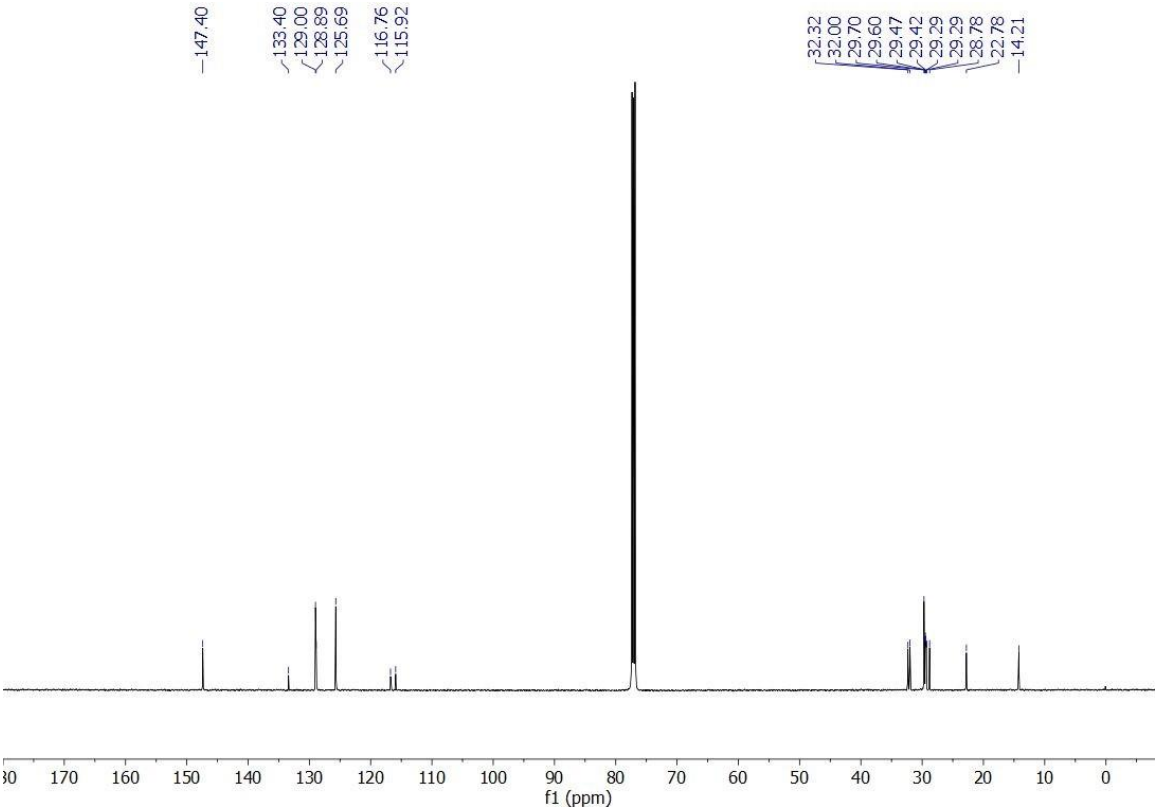
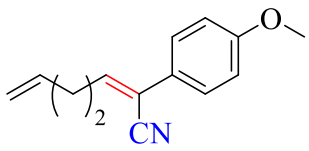


Figure 4.52 ^{13}C NMR ($CDCl_3$, 125 MHz) of 3w



3x

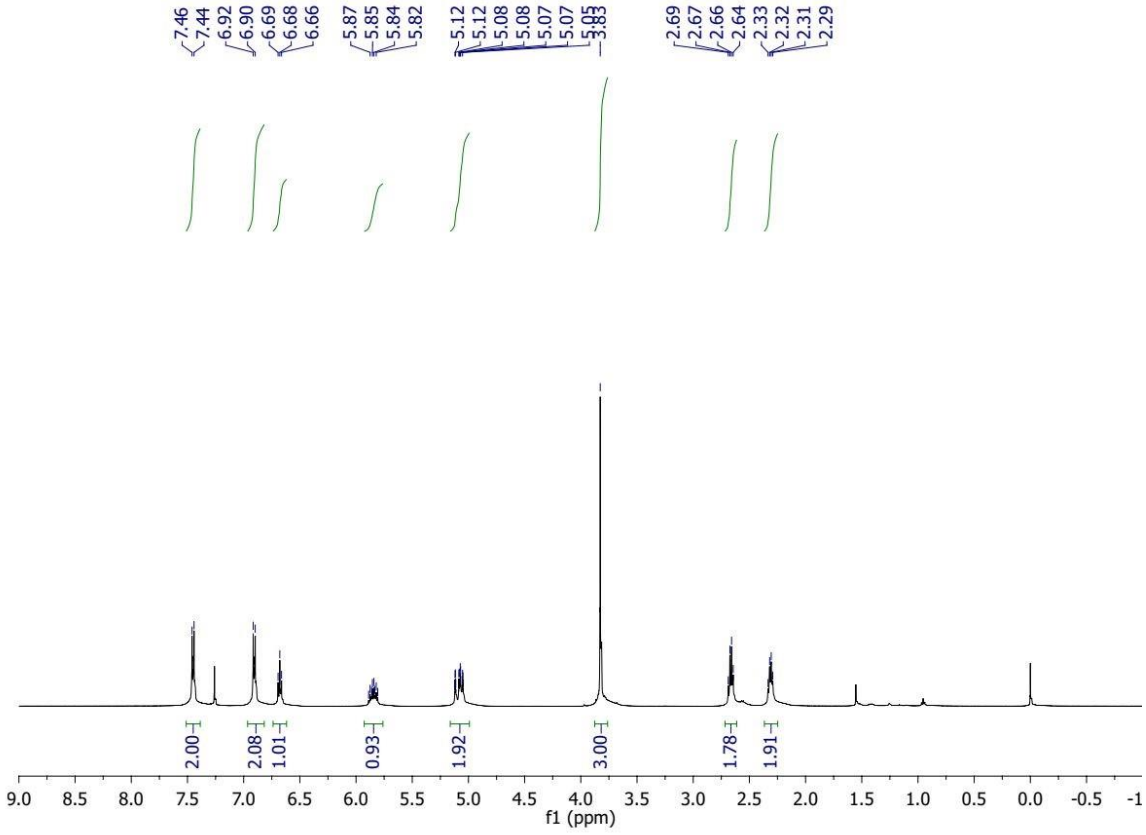
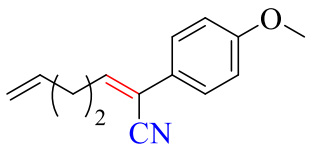


Figure 4.53 ^{1}H NMR ($CDCl_3$, 500 MHz) of 3x



3x

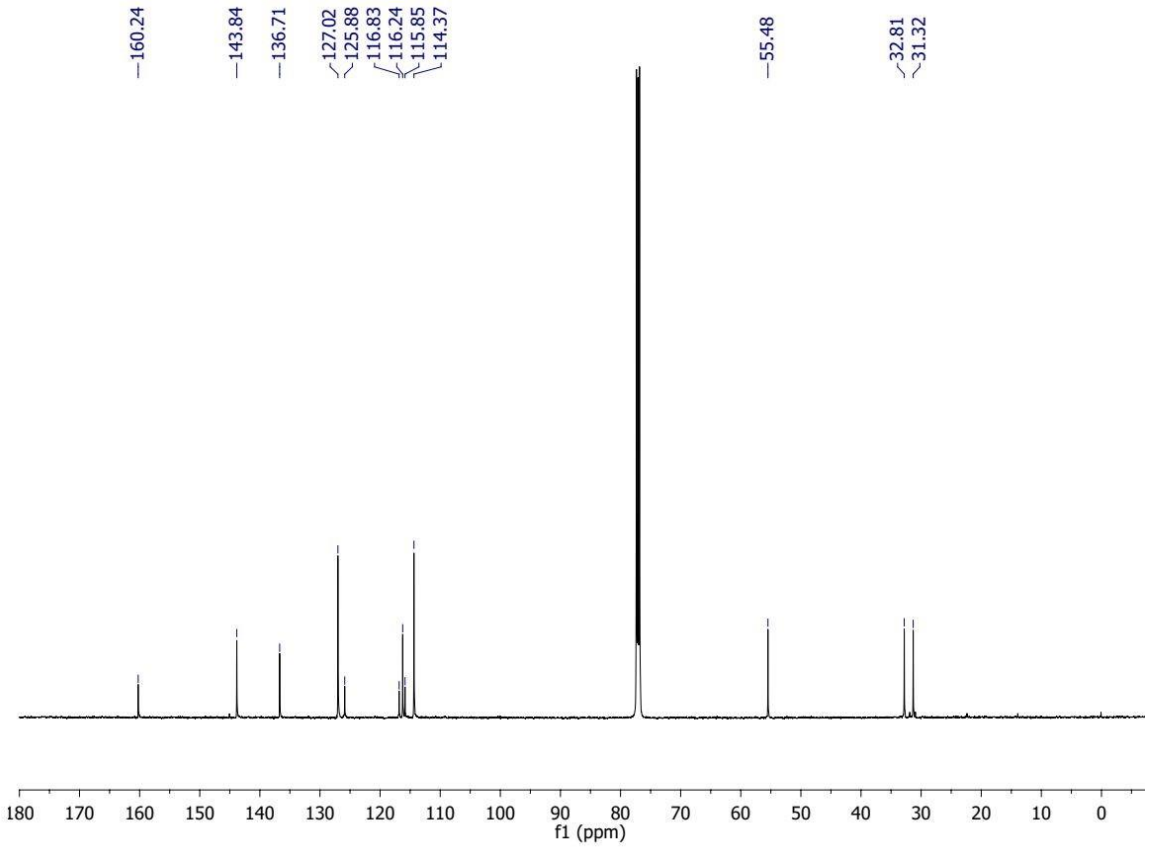


Figure 4.54 ^{13}C NMR ($CDCl_3$, 125 MHz) of 3x

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CHAPTER V

5.1 Conclusions

In summary, we developed N, P mixed-donor ligands and their cobalt complexes. These air and moisture-stable cobalt complexes are great pre-catalysts for the acceptorless dehydrogenative coupling reactions to synthesize substituted amine, imine, α-alkylated, and olefinic nitriles.

Chapter II presented the selective synthesis of amine and imine by tripodal ligand-supported cobalt complexes. In this work, we coupled a large variety of primary alcohols and amines to get secondary imines and amines in good to excellent yields. The product selectivity was controlled by the amount of an external base used in the reaction. The catalytic amount of a base is sufficient to activate the cobalt pre-catalyst into a cobalt catalyst. The cobalt catalyst then dehydrogenates the alcohol into an aldehyde. The aldehyde and aniline undergo condensation reactions *in situ* to give imine products. In the presence of excess loading of a base and alcohol, it undergoes MPV type of reduction to give amine product exclusively. The mechanistic study showed that the alcohol dehydrogenation step is reversible and involves cobalt hydride species as the intermediate. Moreover, the amine/imine forming reaction is environmentally benign, with only hydrogen or/and water as byproducts.

Chapter III presented the selective synthesis of *α*-alkylated nitriles from alcohols and nitriles using the same cobalt molecular catalyst mentioned in chapter II. Different types of α-alkylated nitriles were synthesized in good to excellent yields by coupling various alcohols and nitriles. We used the same strategy developed in chapter II for the product

selectivity, i.e., excess amount of base for the saturated product. The mechanistic study showed that first, alcohol is converted into aldehyde and then undergoes condensation reaction with nitrile in the presence of a base to give *α,β* unsaturated nitrile as an intermediate. Finally, the intermediate is reduced to the nitrile product via the MPV pathway. Remarkably, this transformation is environmentally friendly and atom economical with water as the only byproduct.

Chapter IV presented the selective synthesis of *α,β*-substituted acrylonitriles by our well-defined cobalt catalyst mentioned in chapter II. This chapter introduced the coupling of a wide variety of nitriles and primary alcohols to their corresponding products. It is noteworthy that the transformation is environmentally benign and atom efficient, with H_2O and H_2 being the only byproducts.

5.2 Future Outlook

This research has demonstrated the versatile catalytic activities of our cobalt catalyst in the synthesis of C-C and C-N bonds. Although this catalyst has excellent catalytic properties, it lacks the MLC properties and requires external base additives for activation. As a future perspective, the developed ligand can be modified by introducing MLC modes having higher basicity than the current pendant arm. This can be done by installing more basic imidazole or Benzimidazole moiety in the pendant arm.

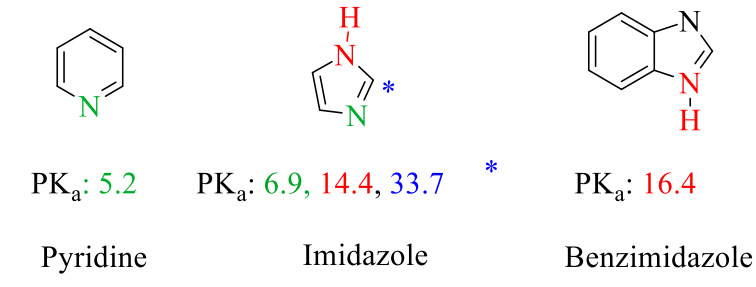
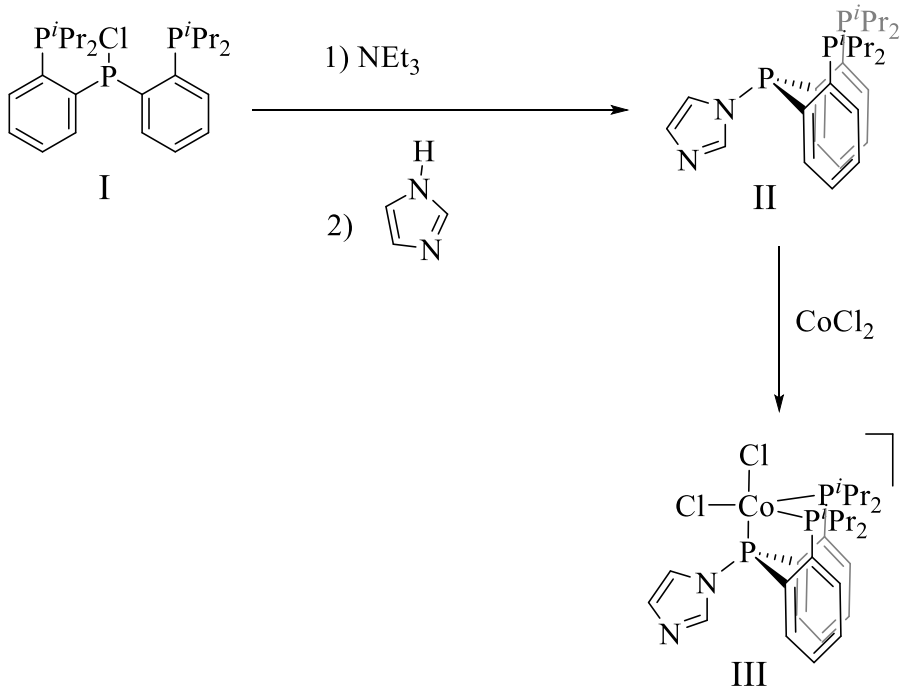


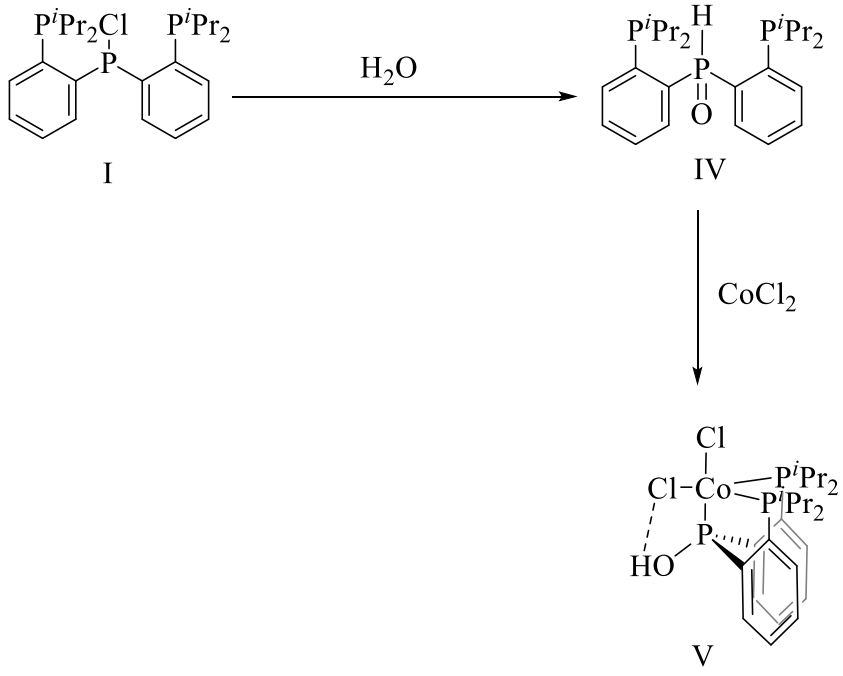
Figure 5.1 PK_a Value of Heterocycles



Scheme 5.1 Synthesis of a new cobalt complex III

We were able to synthesize the cobalt complex III (Scheme 5.1). The cobalt complex III showed promising results towards amine synthesis with a reduced base loading than the current cobalt catalyst. However, we saw the decomposition of the metal complex during the reaction. We hypothesize that the imidazole pendant arm may be broken due to a weak

phosphorous nitrogen bond. To support this hypothesis, we exposed our ligand to the air and took the NMR. Indeed, we saw the ligand decomposition into imidazole, and phosphine oxide peak was also observed in NMR. To synthesize the oxidized version of the ligand, we add water to the **I** from scheme 5.1. As expected, we obtained the phosphine oxide containing ligand (Scheme 5.2). After that, we made a cobalt complex by using ligand IV and used it in the catalysis. The preliminary study showed that complex V requires 85 mol% less added base than the current cobalt catalyst reported in chapter III for amine synthesis. Further exploration of the catalytic activities of this new cobalt catalyst and the iron catalyst development is ongoing in our lab.



Scheme 5.2 Synthesis of cobalt complex V