DEVELOPMENT OF A COBALT COMPLEX CATALYZED GREEN APPROACH FOR SUSTAINABLE N-ALKYLATION OF AMINES

By

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ABSTRACT

The N-alkylation of amines is a fundamental transformation in organic synthesis, particularly in pharmaceutical manufacturing. However, conventional methods often pose economic and environmental challenges due to their dependence on toxic reagents and precious metals. In this study, a phosphine oxide pincer ligand was synthesized to construct a cobalt-based catalytic complex for the N-alkylation of amines using structurally diverse alcohol substrates. This approach aligns with green chemistry principles, enabling efficient alkylation while minimizing chemical waste. The method represents a significant step toward more sustainable pharmaceutical synthesis.

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LIST OF ABBREVIATIONS

VOCs	**Volatile Organic Solvents**
CO_2	**Carbon dioxide**
BH	**Borrowing Hydrogen**
HA	**Hydrogen Autotransfer**
Ru	**Ruthenium**
Ir	**Iridium**
Rh	**Rhodium**
Pd	**Palladium**
Pt	**Platinum**
PdCl2	**Palladium chloride**
Co	**Cobalt**
ADC	**Acceptorless Dehydrogenative Coupling**
MPV	**Meerwein-Ponndorf-Verley**
KOtBu	**Potassiun tert-butoxide**
NaOtBu	**Sodium tert-butoxide**
KOH	**Potassium hydroxide**
K_2CO_3	**Potassium Carbonate**

TMS	**Trimethylsilane**
NMR	**Nuclear Magnetic Resonance**
C_6D_6	**Deuterated benzene**
$CDCl_3$	**Deuterated chloroform**
NEt3	**Triethylamine**
HCl	**Hydrogen Chloride**
DCM	**Dichloromethane**
$CoCl_2$	**Cobalt Chloride**
EWG	**Electron Withdrawing Group**
EDG	**Electron Donating Group**

CHAPTER I

INTRODUCTION

1.1 Green Chemistry

Green chemistry, also known as sustainable chemistry, focuses on designing chemical products and processes that minimize or eliminate the generation of hazardous substances. Its primary objective is to reduce the environmental impact of the chemical industry by adopting cleaner reactions, safer materials, and sustainable resources.[1]

Green chemistry is defined as the application of principles that mitigate environmental risks by developing production processes that avoid or significantly reduce hazardous substances in the manufacture and use of chemical products. Additionally, it aims to advance green chemical reactions and materials, providing long-term, cost-effective solutions for environmental protection. In essence, green chemistry serves as a framework for designing industrial processes and products that safeguard both human health and the environment.[2]

The field is guided by **12 principles of green chemistry**, which collectively help chemists develop sustainable processes that reduce or eliminate harmful substances, thereby promoting ecological and human well-being.[3]

1.1.1 Principles of Green Chemistry

1. **Prevention**

It is more effective to prevent waste generation than to treat or dispose of waste after its creation. *Proactive waste reduction minimizes environmental pollution and lowers costs associated with waste management. For example, optimizing reaction yields reduces byproducts at the source.*

2. **Atom Economy**

Synthetic methods should maximize the incorporation of all starting materials into the final product. *High atom economy means fewer wasted atoms, as seen in addition reactions (e.g., Diels-Alder) versus substitutions, which generate stoichiometric byproducts.*

3. **Less Hazardous Chemical Syntheses**

Whenever possible, synthetic routes should utilize and produce substances with minimal toxicity to humans and the environment. *For instance, replacing phosgene (toxic) with dimethyl carbonate (safer) in polycarbonate synthesis reduces risks.*

4. **Designing Safer Chemicals**

Chemical products should be designed to achieve their desired function while minimizing toxicity. *Biodegradable pesticides that target pests without harming pollinators exemplify this principle.*

5. **Safer Solvents and Auxiliaries**

Auxiliary substances (e.g., solvents, separation agents) should be avoided where possible; if necessary, non-hazardous alternatives should be used. *Water or supercritical* CO_2 *can replace volatile organic solvents (VOCs) in many processes.*

6. **Design for Energy Efficiency**

Energy requirements should be minimized, prioritizing reactions at ambient temperature and pressure when feasible. *Microwave-assisted or photocatalytic reactions often reduce energy use compared to traditional heating methods.*

7. **Use of Renewable Feedstocks**

Raw materials should be derived from renewable (rather than depletable) sources whenever technically and economically viable. *Plant-based ethanol or lignin-derived chemicals are sustainable alternatives to petroleum feedstocks.*

8. **Reduce Derivatives**

Unnecessary derivatization (e.g., protecting groups, temporary modifications) should be avoided to reduce reagent use and waste generation. *Solid-phase peptide synthesis minimizes protecting groups by anchoring reactants to a resin.*

9. **Catalysis**

Catalytic reagents (preferably selective) are preferable to stoichiometric reagents. *Enzymes or transition-metal catalysts (e.g., Pd in cross-coupling) enable efficient, low-waste transformations.*

10. **Design for Degradation**

Chemical products should break down into harmless substances after use, avoiding environmental persistence. *Biodegradable plastics (e.g., polylactic acid) decompose naturally, unlike conventional plastics.*

11. **Real-Time Analysis for Pollution Prevention**

Analytical methods should enable real-time monitoring to prevent hazardous substance formation. *In-line spectroscopy can detect impurities early, allowing immediate process adjustments.*

12. **Inherently Safer Chemistry for Accident Prevention**

Chemicals and their forms should be selected to minimize risks such as leaks, explosions, and fires. *Using dilute hydrogen peroxide instead of concentrated solutions reduces storage hazards.*

1.2 Amines: Versatile Building Blocks in Organic Synthesis, Pharmaceuticals, and Materials Science

Amines are a fundamental class of organic compounds distinguished by the presence of nitrogen atoms bonded to carbon, typically forming one or more carbon-nitrogen (C–N) linkages. Their broad chemical reactivity and structural variety make them highly valuable across numerous scientific and industrial domains. Due to their functional versatility, amines serve as essential building blocks in fields such as organic synthesis, pharmaceutical development, and materials science.

Historically, amines have been central to the advancement of organic chemistry, functioning as pivotal intermediates in many synthetic routes. Traditional techniques for amine synthesis such as nucleophilic substitution and reductive amination have gradually evolved, with modern approaches incorporating transition metal-catalyzed transformations.

These innovations have greatly enhanced the ability to synthesize complex molecules with increased precision and efficiency.

In medicinal chemistry, amines play a prominent role as key structural features in pharmaceutical compounds, biologically active molecules, and drug delivery platforms. Their capacity to form hydrogen bonds, engage in electrostatic interactions, and coordinate with metal ions enables effective targeting of biological systems. As a result, amines are present in a wide range of therapeutic agents, including antibiotics, antiviral medications, antihypertensives, and anticancer drugs.

Beyond pharmaceuticals, amines also possess diverse physical and chemical characteristics that make them indispensable in materials science. They contribute to the development of polymers, catalysts, sensors, and other functional materials, thereby driving innovations in organic electronics, solar energy devices, and biomaterials. More recently, research into amines has expanded to include sustainable chemistry, renewable energy technologies, and environmental remediation strategies-underscoring their growing significance in addressing global challenges.[4]

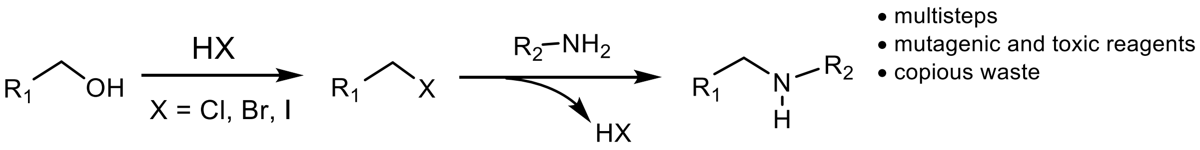
1.3 Green Synthesis of Amines: N-Alkylation via Borrowing Hydrogen Methodology Using Earth-Abundant Metal Catalysts

The N-alkylation of amines with alcohol represents an important class of organic transformations where primary amines are converted to secondary and tertiary amines using alcohol as alkylating agents. This reaction provides a valuable route for constructing C-N bonds in organic synthesis.[5]

Conventional amine alkylation typically employs alkyl halides as electrophilic partners in nucleophilic substitution reactions with amines. While effective, this classical approach presents several significant drawbacks:

1. Generation of stoichiometric amounts of halide salts as byproducts
2. Frequent formation of overalkylated side products
3. Production of environmentally hazardous waste streams
4. Requirement for strong bases in many cases

These limitations not only reduce the atom economy of the process but also create substantial waste management challenges, making traditional alkyl halide-based methods less desirable from both environmental and practical perspectives.



Scheme 1.1: Traditional method for Amine synthesis

To eliminate this drawback, catalytic N-alkylation of amines with alcohols is carried out via BH (Borrowing Hydrogen)/ HA (Hydrogen Autotransfer) mechanism which is an efficient and green process.[6,7]

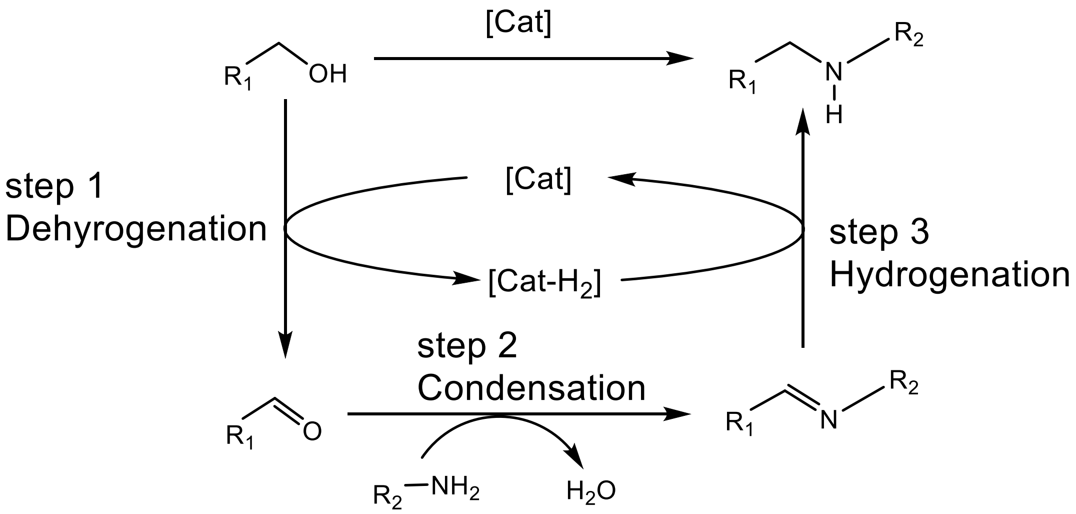
1.3.1 Borrowing Hydrogen (BH)

The borrowing hydrogen method is referred to as hydrogen auto transfer, is a recently developed strategy in organic synthesis which extends the usefulness of alcohols by employing them as alkylating agents. This process involves the use of a catalytic system in which one of the equivalent alcohol functions of an alcohol substrate is removed in a reversible fashion, to create a carbonyl compound: aldehyde or ketone or an imine in the case of amines. This reactive intermediate then undergoes other transformations including condensations with amines before the final hydrogenation step, which re-forms the active catalyst thus ending the catalytic cycle with water as the only appreciable byproduct.[6]

The goals of the BH/HA mechanism for green N-alkylation of amines with alcohol include an efficient, selective alternative to hazardous alkyl halides and unwanted byproducts with environmentally safe reagents and water as the only byproduct.[8–10]

The key steps in a typical borrowing hydrogen reaction involving amine and alcohol are:

1. Dehydrogenation of Alcohol: The catalyst helps to strip off hydrogen from the alcohol to give a carbonyl compound.
2. Condensation: The carbonyl compound reacts with an amine by forming an imine intermediate.
3. Hydrogenation of the imine intermediate: The imine intermediate formed is hydrogenated with the help of the hydrogen which was “borrowed” in the first step to give an N-alkylated amine.



Scheme 1.2: Borrowing Hydrogen: A Green Approach to Sustainable Amine Synthesis

1.3.2 Advantages of Borrowing Hydrogen Method

1. Atom Economy: The method employs alcohol as alkylating agents directly, eliminating the steps of converting alcohol into more reactive species which often create stoichiometric waste.

2. Environmental Friendliness: The only product which is formed as a byproduct is water making this method conform to the principles of green chemistry.

3. Versatility: The methodology is versatile in terms of transformation with application to both C-N and C-C bond forming reactions, thereby providing excellent scope for synthesis.

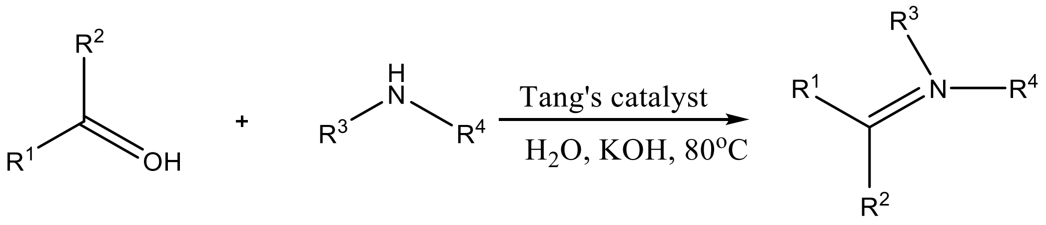
4. Selectivity: The process is also selective for monoalkylation, which is very beneficial when synthesizing multi-component systems.

1.3.3 N-Alkylation of amines with Precious Metals

The catalytic N-alkylation of amines with alcohol has traditionally employed precious metal catalysts due to their superior performance characteristics. Precious metals (Ru, Ir, Rh, Pd, Pt) are defined by their low natural abundance and exceptional catalytic properties, including high d-electron density and optimal orbital energetics that facilitate oxidative addition/reductive elimination steps in catalytic cycles. These transition metals exhibit several advantages in catalytic applications: (1) high turnover frequencies enabled by favorable metal-ligand cooperativity, (2) excellent functional group tolerance due to their moderate Lewis acidity, and (3) remarkable stability under both thermal and oxidative conditions.

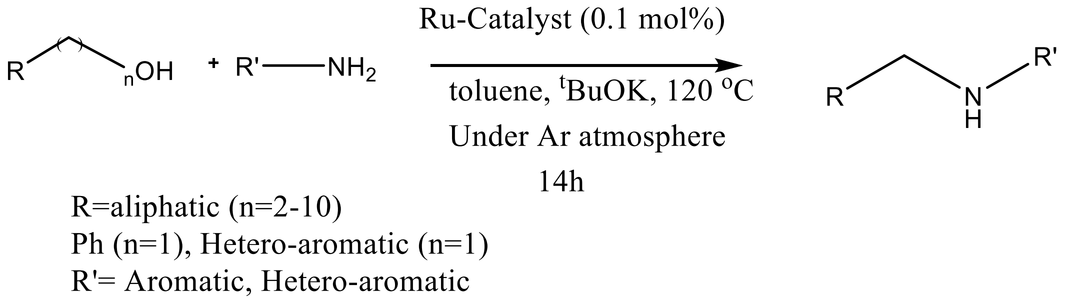
The literature documents extensive use of Group 8-10 metals, particularly in pincer-type ligand architectures (e.g., PNP and NNN frameworks), where their d^8 electron configuration promotes formation of stable, 18-electron complexes. These pincer complexes demonstrate exceptional catalytic performance in borrowing hydrogen mechanisms due to: (i) strong metal-ligand σ-donation/π-backdonation characteristics, (ii) rigid meridional coordination geometry that prevents catalyst decomposition, and (iii) tunable steric and electronic parameters through ligand modification. The stability of these complexes under harsh conditions (elevated temperatures, protic solvents) has enabled their application in both homogeneous and heterogenized catalytic systems.[11]

The article by Luo et al. presents a comprehensive study on the N-alkylation of amines with alcohol using a cyclometalated iridium complex as a catalyst. This process was highly efficient, achieving substrate-to-catalyst ratios up to 10,000 and yields up to 96%.[9]



Scheme 1.3: Iridium-catalyzed N-alkylation of amines

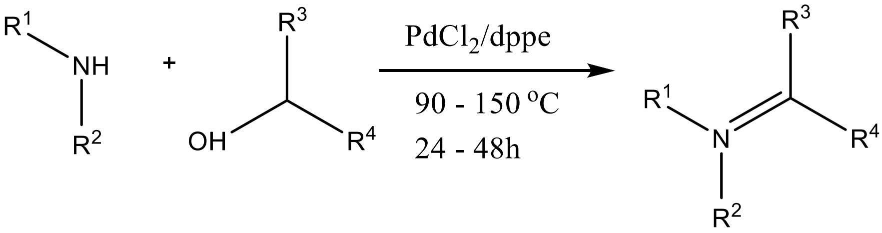
Ruthenium pincer complexes find versatile applications in catalysis, including hydrogen transfer and oxidation coupling processes. These complexes are usually described as having a certain degree of tunability, in large part due to changes within the ligands, which can affect the electronic characteristics and reactivity of the complexes. Guin et al. group developed a ruthenium (II) based catalyst which exhibited remarkable efficiency and selectivity in the N-alkylation of amines using a broad range of aliphatic alcohols, from methanol to decanol.[8]



R=aliphatic (n=2-10)
Ph (n=1), Hetero-aromatic (n=1)
R'= Aromatic, Hetero-aromatic

Scheme 1.4: N-Alkylation with Ruthenium based catalyst

Palladium pincer complexes are indispensable for cross-coupling reactions that are fundamental in forming bonds that are necessary in the synthesis of drugs. A research group introduced a palladium-based catalyst system, specifically $PdCl_2$ in combination with various phosphine ligands, which proved highly effective under relatively mild conditions. This catalyst system enabled the N-alkylation of primary and cyclic secondary amines using alcohol as alkylating agents.[11]



Scheme 1.5: N-Alkylation with Palladium based catalyst

This method has received recognition as one of the green, atom-economical reactions for the synthesis of substituted amines.[12] These advanced methods need catalysts constructed from noble metal complex-based systems. However, noble metals are expensive and there is a high risk of extinction with continuous use, hence, there is rising use of earth abundant metals that are cheap.[4]

1.3.4 N-Alkylation of amines with Base Metals

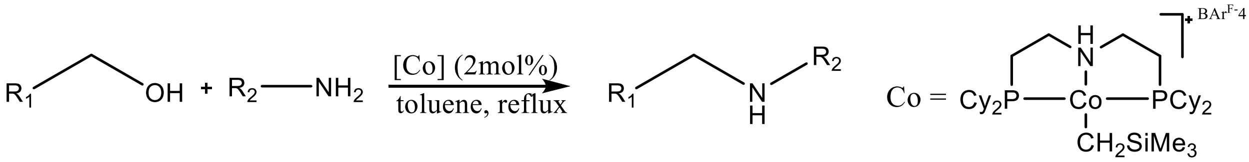
Recent studies have established that first-row transition metals, particularly nickel and cobalt, can serve as effective catalysts for N-alkylation reactions, though their catalytic behavior differs fundamentally from precious metal systems. While they generally exhibit lower turnover frequencies (10^2-10^3 h^{-1}) compared to precious metal catalysts (10^4-10^5 h^{-1}), their development represents a significant advance in sustainable catalysis.

The implementation of base metal catalysts presents unique synthetic challenges but offers compelling advantages in terms of sustainability and economics. With crustal abundances orders of magnitude higher than precious metals (nickel at 84 ppm versus palladium at 0.015

ppm) and significantly lower costs (cobalt at approximately $30/kg compared to rhodium at $15,000/kg), these systems address critical limitations of traditional catalysts. Recent progress in ligand design, particularly through the development of redox-active pincer frameworks and hemilabile donors, has yielded base metal catalysts demonstrating competitive performance metrics. Optimized nickel systems now achieve turnover numbers exceeding 1,000 while showing improved functional group tolerance and novel selectivity patterns.

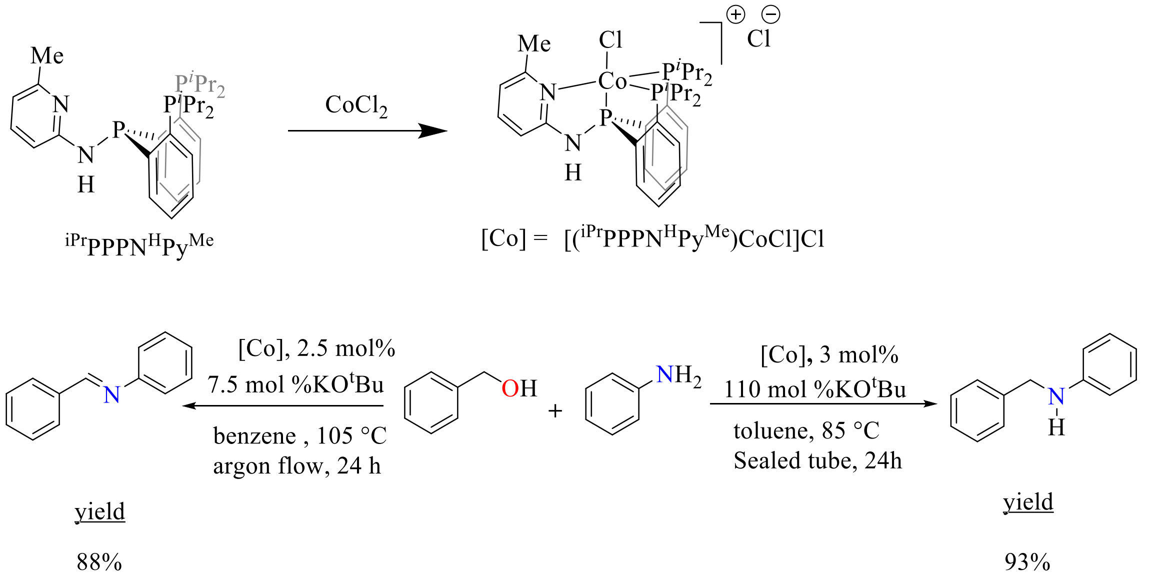
Mechanistically, these base metal catalysts often operate through unique pathways involving metal-ligand cooperative catalysis, radical intermediates in nickel and cobalt systems, and dinuclear activation mechanisms. Beyond their economic and abundance advantages, base metal catalysts offer environmental benefits including lower energy requirements, reduced risks of heavy metal contamination, and improved compatibility with biorenewable solvents. These characteristics position base metal systems as promising alternatives for sustainable industrial applications, though further research is needed to fully match the efficiency and robustness of precious metal catalysts in all transformations.

Cobalt-based pincer complexes have been shown to work efficiently in the N-alkylation of amines with alcohols whereby it produced secondary amines with high selectivity and yield. It has been shown to enhance the ready conversion of both aromatic and aliphatic amines and alcohols at comparatively low temperatures, revealing the capability of cobalt to substitute more costly metals in prevailing chemical transformations.[9,10]



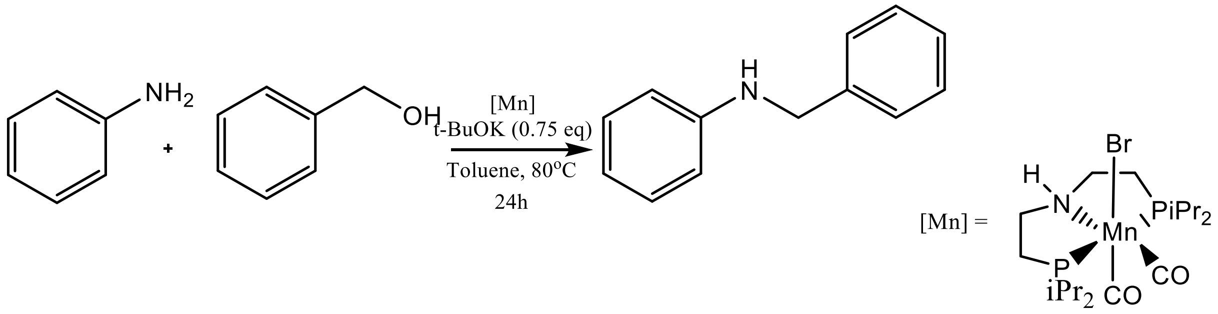
Scheme 1.6: N-Alkylation with Cobalt based catalyst[12]

In our lab, we have recently reported a cobalt-catalyzed, base-mediated strategy for selective N-alkylation of amines with alcohols to synthesize either imines or amines via acceptorless dehydrogenative coupling (ADC) or borrowing hydrogen (BH) pathways. It was found that the base loading acts as a "switch" for product selectivity—catalytic KO*ᵗ*Bu favors imines, while large excess of base promote amines through a Meerwein-Ponndorf-Verley (MPV) reduction mechanism. The cobalt pincer complex demonstrates broad substrate scope and functional group tolerance, achieving high yields (up to 99%) for both aromatic and aliphatic substrates. Notably, this selectivity control extends to C-alkylation of alcohols, marking the first base-metal-catalyzed method for switchable ketone/alcohol synthesis, offering a sustainable alternative to precious-metal systems.[6]



Scheme 1.7: Selective N-Alkylation with Cobalt based catalyst for amine and imine synthesis

Other base metals such as Manganese in pincer complexes have been used to catalyze N-alkylation of amines [7] and Hydrogen borrowing reactions catalyzed by Iron catalysts has also been shown to form C-N bonds.[13]



Scheme 1.8: N-Alkylation with Manganese based catalyst[7]

1.4 Formation of Imine as a Byproduct During Amine Synthesis

In borrowing hydrogen (BH) catalysis for N-alkylation, imines form as key intermediates through a three-step sequence: (1) metal-catalyzed alcohol dehydrogenation to aldehydes, (2) nucleophilic attack by the amine to generate a hemiaminal, and (3) dehydration to yield the imine. The fate of this intermediate—whether it persists or undergoes further reduction to the amine—is governed by reaction conditions, particularly base stoichiometry.

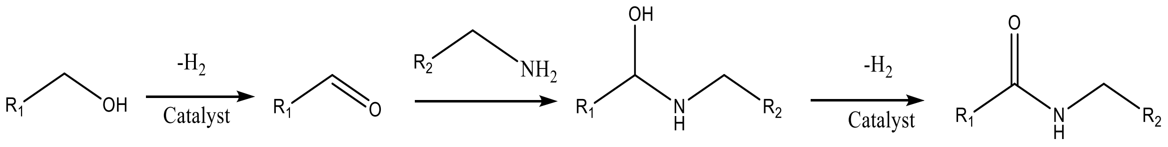
In our previous work on selective N-alkylation with cobalt based catalytic system (Scheme 7),[6] the catalytic base quantities (e.g., 7.5 mol% KOtBu) favor imine accumulation by limiting the hydrogenation step, as the metal-hydride intermediate preferentially releases H_2 (acceptorless dehydrogenation). In contrast, stoichiometric base (e.g., 110 mol% KOtBu) shifts equilibrium toward amine formation via two pathways: (i) metal-hydride reduction of the imine or (ii) base-mediated Meerwein-Ponndorf-Verley (MPV) hydrogen transfer from the alcohol donor. This highlights the dual role of base—as both catalyst activator (at low loadings) and reductant promoter (at high loadings)—in steering selectivity.

1.5 Amide Formation as an Alternative Pathway in Amine Alcohol Coupling Reactions

While N-alkylation of amines with alcohol predominantly yields secondary or tertiary amines through borrowing hydrogen (BH) or hydrogen autotransfer mechanisms, certain catalytic systems can selectively promote direct amide formation. A significant advancement in this area demonstrated the use of a ruthenium pincer complex to catalyze the direct synthesis of amides from primary amines and alcohols via acceptorless dehydrogenative coupling (ADC), with hydrogen gas as the sole byproduct. This atom-economical transformation proceeds through a well-defined sequence beginning with alcohol dehydrogenation to form an aldehyde, followed by condensation with the amine to generate a hemiaminal intermediate, which subsequently undergoes dehydrogenation to yield the amide product.[14]

The competition between amide and amine formation stems from the dual reactivity of the hemiaminal intermediate. Under neutral conditions with full dehydrogenation, the pathway favors amide production, while hydrogen retention promotes imine formation and subsequent reduction to amines. This delicate balance underscores the critical importance of hydrogen management in these transformations, where subtle changes in reaction conditions can switch the outcome between oxidative amide formation and reductive amine production.

For selective amine synthesis, catalyst design must either suppress over-dehydrogenation to prevent amide byproducts or maintain sufficient hydrogenation activity to ensure complete reduction of imine intermediates. This requires careful optimization of metal center choice, ligand environment, and reaction parameters such as temperature and hydrogen partial pressure. The ruthenium pincer system exemplifies how precise control of these factors can divert the reaction pathway toward exclusive amide formation, while other catalytic systems may be tuned to favor amine products through selective hydrogenation capabilities. These insights highlight the importance of understanding intermediate reactivity and hydrogen transfer processes when developing catalysts for selective transformations in amine-alcohol coupling reactions.



Scheme 1.9: Amide formation

1.6 Pincer Ligands

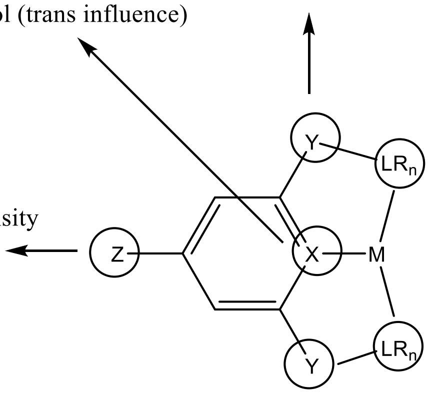
While our previous work has focused on tetradentate phosphine ligands, we are now investigating pincer ligand systems due to their unique advantages in organometallic chemistry and catalysis. Pincer ligands are tridentate frameworks that form well-defined, stable complexes with metals, offering exceptional control over steric and electronic properties at the metal center. These ligands typically feature a central aromatic ring flanked by two coordinating arms, creating a rigid meridional geometry that precisely tunes the metal's reactivity.[15]

The defining features of pincer ligands include: (1) Structural Rigidity: The constrained geometry enhances thermal stability, making them ideal for high-temperature catalytic processes; (2) Electronic Tunability: The aromatic backbone and donor groups (e.g., P, N, or S) allow fine-tuning of the metal's electron density, enabling selective reactivity unattainable with conventional ligands; (3) Metal-Ligand Cooperativity: Some pincer systems participate directly in catalysis through bond activation or redox processes, expanding their utility in green chemistry applications.

Pincer ligands are highly versatile, supporting both precious and base metals across oxidation states, and have become indispensable in designing efficient, sustainable catalytic systems. Their potential remains underexplored, particularly in emerging areas such as earth-abundant metal catalysis and asymmetric transformations.

Determines ringsize and bite angle effect
Also useful for introduction of chirality

Electronic control (trans influence)



Typical groups
X= C,N
Y= $(CH_2)_n$, O, NH
L= P,N,O
Z= Halogen, R, RO

Determines electron density
of central donor
Useful for anchoring

Steric control by modification of R
Introduction of chirality
Electronic control by modification of L
The nature of L determines the hemilability of the pincer

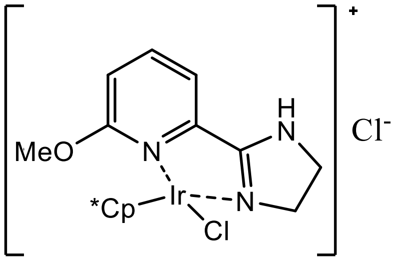
Scheme 1.10: Generic Structure of Pincer Ligands

1.6.1 Examples of Pincer Ligands with Precious Metal Center

Pincer ligands have proven particularly effective in stabilizing and activating precious metal catalysts, including platinum (Pt), palladium (Pd), and iridium (Ir) complexes, for selective transformations. The rigid meridional coordination geometry of pincer architectures creates an ideal electronic environment for these metals, enabling efficient catalytic cycles in hydrogen transfer reactions.

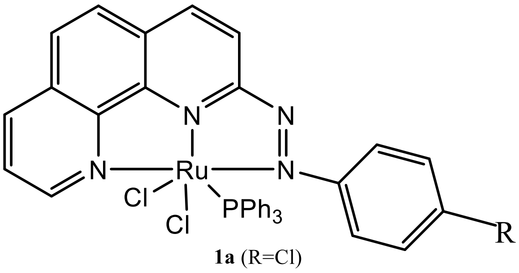
A notable example is the use of cyclometalated iridium pincer complexes in the N-alkylation of amines with alcohol under mild, sustainable conditions. Iridium demonstrates exceptional catalytic performance in borrowing hydrogen (BH) reactions due to facile oxidative addition/reductive elimination kinetics at the metal center and stable hydride intermediates crucial for hydrogen transfer.

The Tang catalyst exemplifies these advantages, achieving high yields (>90%) and selectivity across diverse substrates. Iridium's d^6 electron configuration and optimal metal-ligand bond strengths contribute to its superior activity in BH processes compared to other precious metals. This system highlights how pincer ligand design, combined with iridium's intrinsic properties, can enable efficient, atom-economical transformations under green conditions.[9]



Scheme 1.11: Tang's catalyst

It is noted that the catalytic performance of many metal catalysts is strongly influenced by ligand design, where subtle structural modifications can significantly alter reactivity and selectivity. In an example of ruthenium catalyzed N-alkylation work, the redox-active azo-aromatic pincer ligand (L1a) in complex **1a** features a 4-chlorophenyl substituent, which introduces electron-withdrawing effects and stabilizes the metal center. In contrast, the related ligand L1b lacks this chlorine substituent, leading to differences in electronic properties and coordination geometry around ruthenium. These structural variations directly impact catalytic efficiency—**1a** demonstrates superior activity due to its optimized ligand framework, which facilitates hydrogen borrowing through reversible azo/hydrazo redox transitions.



1a (R=Cl)
1b (R=H)

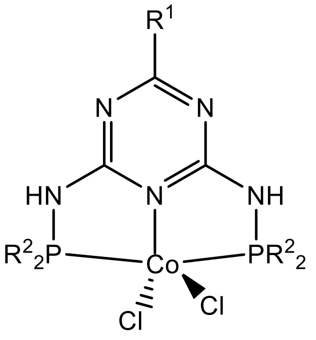
Scheme 1.12: Ruthenium Catalyzed N-Alkylation[8]

1.6.2 Examples of Pincer Ligands with Base Metal center

Recent research has shifted focus from precious metals to base metals like nickel and cobalt for catalytic N-alkylation reactions, driven by sustainability and cost considerations. While these base metals historically exhibited lower efficiency and stability compared to noble metals, advances in pincer complex design have significantly improved their performance.

Cobalt-based pincer complexes demonstrates remarkable efficiency in the N-alkylation of amines with alcohol, achieving high selectivity and yield for secondary amines. These catalysts operate effectively at mild temperatures and accommodate both aromatic and aliphatic substrates, rivaling traditional noble metal systems. Their abundance, low cost, and reduced environmental impact make them attractive alternatives for sustainable industrial applications.

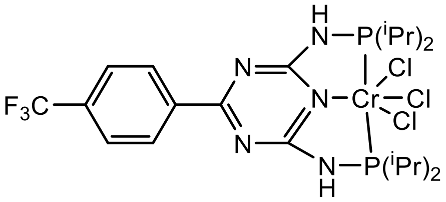
This progress highlights the potential of base metals to replace precious metals in catalytic transformations, though further optimization is needed to match the robustness of noble metal catalysts fully. The development of well-designed ligand frameworks will be crucial in enhancing their reactivity and broadening their synthetic utility. [6,12,16]



1a: R^1= 4-CF_3-C_6H_4; R^2= iPr
1b: R^1=Ph; R^2= iPr
1c: R^1=Me; R^2= iPr
1d: R^1=NH-C_3H_5; R^2= iPr
1e:R^1=Me; R^2= Cy
1f: R^1=H; R^2= iPr

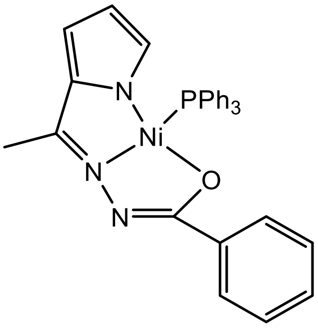
Scheme 1.13: Cobalt metal complex[16]

In another example, chromium was selected as the catalytic metal for the N-alkylation of amines with alcohols due to its earth-abundant nature and favorable redox properties that facilitate efficient borrowing hydrogen (BH) catalysis. The developed chromium complex demonstrated high catalytic activity, achieving yields up to 94% under mild conditions while maintaining excellent functional group tolerance. Notably, the system required only sub-stoichiometric amounts of base, enhancing its practicality and sustainability. These results highlight chromium's potential as a cost-effective and environmentally benign alternative to precious metal catalysts for BH-mediated N-alkylation reactions, offering comparable efficiency with improved economic and ecological benefits. The findings suggest that further development of chromium-based catalysts could expand their utility in sustainable organic transformations.



Scheme 1.14: Chromium metal complex[17]

Nickel also represents an attractive catalytic metal for N-alkylation reactions due to its earth-abundant character, economic viability, and demonstrated competence in borrowing hydrogen (BH) transformations. When incorporated into an NNO pincer-type ligand framework, the resulting nickel complex exhibits enhanced catalytic performance, achieving both high efficiency and selectivity in the N-alkylation of amines with alcohols. This system capitalizes on nickel's versatile redox chemistry while benefiting from the pincer ligand's ability to stabilize the metal center and modulate its reactivity. The combination of nickel's inherent catalytic properties with the structural control offered by the NNO pincer architecture enables effective C-N bond formation under mild conditions, positioning nickel-based catalysts as sustainable alternatives to traditional precious metal systems.[18]



Scheme 1.15: Nickel metal complex

1.7 Objective of the study

The study aims to:

1. Design and synthesize a novel phosphine-based pincer ligand to serve as a robust scaffold for metal coordination.
2. Develop a base metal (e.g., cobalt) complex by chelating the synthesized ligand, optimizing its catalytic properties for sustainable applications.
3. Evaluate the catalytic efficiency of the resulting complex in the N-alkylation of amines with alcohol, assessing its viability as an alternative to precious metal catalysts.
4. Investigate the reaction mechanism, focusing on substrate activation and key intermediates, to elucidate the catalytic pathway and guide further optimization.

This systematic approach seeks to establish a cost-effective and environmentally benign catalytic system for selective C–N bond formation.

CHAPTER II

EXPERIMENTAL METHODOLOGY

2.1 General Methods

All reactions and manipulations were conducted using standard air-free techniques under a dry nitrogen atmosphere within an MBraun glovebox, unless stated otherwise. Anhydrous solvents were obtained by purification through a Pure Solv solvent purification system equipped with activated alumina columns.

Organic substrates were purchased from commercial suppliers and used as received if supplied in intact SURE/SEAL packaging. Substrates lacking air-free seals were dried over activated 4 Å molecular sieves prior to use. Strong bases, including potassium tert-butoxide (KOtBu), sodium tert-butoxide (NaOtBu), potassium hydroxide (KOH), and potassium carbonate (K_2CO_3), were purified by vacuum sublimation before use.

Solvent removal during reaction work-up was carried out using a Büchi Rotavapor R-200 rotary evaporator. Nuclear magnetic resonance (NMR) spectrum was recorded on JEOL Unity 500 MHz or 300 MHz spectrometers. Tetramethylsilane (TMS, $\delta = 0.00$ ppm) was used as the internal standard for chemical shift calibration in C_6D_6 and $CDCl_3$ solvents for ^1H NMR spectra. The NMR data obtained for known compounds were consistent with previously reported literature values.

2.2 Experimental Methods

2.2.1 Synthesis of Tridentate PPP Pincer Ligand and Cobalt Complex

2.2.1.1 Synthesis of ^{iPr}PPPOH Ligand

The synthesis of the ^{iPr}PPPOH ligand was carried out under an inert nitrogen atmosphere in a glovebox to prevent moisture or air sensitivity during the reaction. In a 10 mL reaction vial equipped with a magnetic stir bar, bis(2-diisopropylphosphinophenyl) chlorophosphine (^{iPr}PPPCl, 0.500 g, 1.106 mmol) was combined with deionized water (2.0 mL) and stirred for 1 hour to initiate hydrolysis. Following this, triethylamine (NEt_3, 0.14 mL) was added dropwise using a microsyringe to neutralize the generated HCl and facilitate the conversion to the hydroxyl-substituted phosphine.

Stirring continued until a homogeneous white suspension was observed. The excess water was removed via vacuum filtration, yielding a solid product. This solid was then subjected to a liquid-liquid extraction process by dissolving it in a biphasic mixture of toluene/pentane and water. The resulting mixture was transferred into a separatory funnel, and the organic phase, containing the desired product, was carefully isolated. The organic solvents were removed under reduced pressure using a rotary evaporator, affording the target ligand as a white powder.

The identity and purity of the product were confirmed via ^{31}P NMR spectroscopy, recorded in $CDCl_3$. The white powder was collected (yield = 87%) and stored in the glovebox under an inert atmosphere for future use. ^{1}H NMR (500 MHz, C_6D_6) δ 9.86 (dt, J = 3.8 Hz, 1H), 8.09 –

8.00 (m, 2H), 7.29 – 7.22 (m, 2H), 7.11 – 7.06 (m, 2H), 7.03 (t, *J* = 7.5 Hz, 2H), 1.90 (dq, *J* = 13.5, 6.8 Hz, 2H), 1.81 (dt, *J* = 14.0, 7.0 Hz, 2H), 1.07 (dt, *J* = 15.7, 7.9 Hz, 6H), 1.03 – 0.94 (m, 6H), 0.81 (dt, *J* = 13.2, 6.6 Hz, 6H), 0.72 (dd, *J* = 13.5, 7.0 Hz, 6H). ^{31}P {^{1}H} NMR (121 MHz, C_6D_6) 9.61 (t, J = 85.0 Hz), 6.62 (d, J = 83.2 Hz)

2.2.1.2 Coordination of ^{iPr}PPPOH ligand with $CoCl_2$

Under an inert nitrogen atmosphere within a glovebox, cobalt (II) chloride ($CoCl_2$, 25 mg, 0.195 mmol) was weighed into a 4 mL vial and dissolved in 1 mL of dichloromethane (DCM). In a separate 4 mL vial, bis(2-diisopropylphosphinophenyl) hydroxyphosphine ([iPrPPPOH], 85 mg, 0.195 mmol) was dissolved in 1 mL of DCM.

The ligand solution was added dropwise to the $CoCl_2$ solution with vigorous stirring. During the addition, a visible color change from blue to red was observed, indicating complex formation. The reaction mixture was then capped and allowed to stir overnight inside the glovebox.

The following day, the resulting solution was filtered through a celite pad to remove any insoluble impurities. The filtrate was transferred to a 20 mL scintillation vial containing a layered solution of diethyl ether and DCM to promote slow crystallization. After 1–2 days, red crystals of the cobalt complex were obtained. These crystals were collected and dried under vacuum for 3 hours.

The product, a red crystalline powder, was further stirred overnight to ensure complete drying and subsequently stored in the glovebox under an inert atmosphere. The isolated yield was 65%.

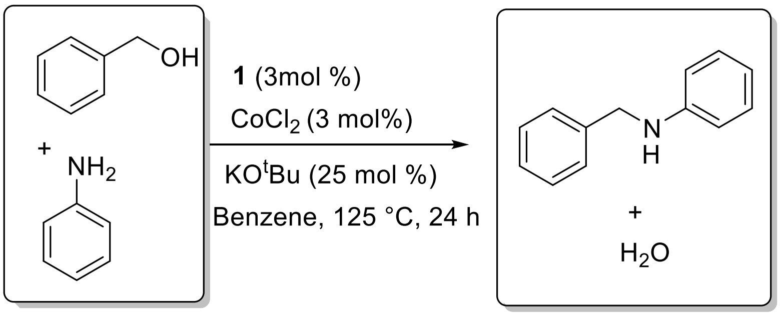
2.3 N-Alkylation Reaction Optimization Using Aniline as an Analogue for Aromatic Amines

2..3.1 General Considerations for Optimization

All reactions were performed inside an MBraun glovebox under a dry nitrogen atmosphere to maintain air- and moisture-free conditions. Initial optimization studies employed aniline as the model substrate to explore conditions for the N-alkylation of aromatic amines using benzyl alcohol as the alkylating agent.

A series of screening experiments were conducted to evaluate the effects of different bases, solvents, and reaction temperatures on the efficiency of N-benzylamine formation. These experiments aimed to identify the optimal conditions for high conversion and selectivity.

The catalytic system employed in this study is based on a metal–ligand cooperative framework, which facilitates substrate activation in the presence of a base. The transformation proceeds via a borrowing hydrogen (BH) mechanism, wherein temporary oxidation of the alcohol generates an intermediate that undergoes nucleophilic attack by the amine, followed by in situ hydrogen transfer to furnish the desired N-alkylated product.



Scheme 2.1: N-Alkylation of N-benzylamine

2.3.2 N-Alkylation of N-benzylamine: Condition 1

An oven-dried 10 mL reaction vial equipped with a magnetic stir bar was transferred into an MBraun glovebox operating under a nitrogen atmosphere. Into the vial were added the following reagents in the specified stoichiometric amounts: ligand **1** (3.3 mg, 0.0075 mmol), cobalt(II) chloride ($CoCl_2$, 0.97 mg, 0.0075 mmol), potassium tert-butoxide (KOtBu, 7.0 mg, 0.0625 mmol), benzyl alcohol (52 µL, 0.5 mmol), aniline (23 µL, 0.25 mmol), and toluene (1.0 mL) as solvent.

The vial was sealed with a screw cap and removed from the glovebox. The reaction mixture was then heated at 85 °C in an oil bath under continuous stirring for 24 hours. After completion of the reaction, the vessel was allowed to cool to room temperature before being opened.

The reaction mixture was filtered through a celite pad to remove any insoluble residues, and the filtrate was extracted with diethyl ether. The organic solvent was removed under reduced pressure using a rotary evaporator.

For quantitative analysis, 1,3,5-trimethoxybenzene (8.4 mg, 0.05 mmol) was added to the crude product mixture as an internal standard. The residue was dissolved in deuterated chloroform ($CDCl_3$) and transferred to a clean NMR tube. The product composition was analyzed using proton nuclear magnetic resonance (^1H NMR) spectroscopy.

2.3.3 N-Alkylation of N-benzylamine: Condition 2

An oven-dried 10 mL reaction vial equipped with a magnetic stir bar was introduced into an MBraun glovebox under a nitrogen atmosphere. The following reagents were quantitatively added to the vial: ligand **1** (3.3 mg, 0.0075 mmol), cobalt (II) chloride ($CoCl_2$, 0.97 mg, 0.0075 mmol), potassium tert-butoxide (KOtBu, 7.0 mg, 0.0075 mmol), benzyl alcohol (52 µL, 0.5 mmol), aniline (23 µL, 0.25 mmol), and toluene (1.0 mL) as the solvent.

The vial was sealed with a cap and removed from the glovebox. The reaction mixture was stirred in an oil bath preheated to 105 °C for 24 hours. After completion of the reaction, the vessel was allowed to cool to room temperature before being opened.

The reaction mixture was filtered through a celite pad to remove any solid residues, and the filtrate was extracted with diethyl ether. The organic layer was concentrated under reduced pressure using a rotary evaporator. For quantitative analysis, 1,3,5-trimethoxybenzene (8.4 mg, 0.05 mmol) was added as an internal standard. The residue was dissolved in deuterated chloroform ($CDCl_3$) and transferred to a clean NMR tube.

Product analysis was performed using proton nuclear magnetic resonance (^{1}H NMR) spectroscopy.

2.3.4 N-Alkylation of N-benzylamine: Condition 3

An oven-dried 10 mL reaction vial equipped with a magnetic stir bar was transferred into an MBraun glovebox maintained under a dry nitrogen atmosphere. The following reagents were quantitatively added: ligand **1** (3.3 mg, 0.0075 mmol), cobalt (II) chloride ($CoCl_2$, 0.97 mg, 0.0075 mmol), potassium tert-butoxide (KOtBu, 7.0 mg, 0.0075 mmol), benzyl alcohol (52 μL, 0.5 mmol), aniline (23 μL, 0.25 mmol), and toluene (1.0 mL) as the reaction solvent.

The vial was sealed with a screw cap and removed from the glovebox. The reaction mixture was heated in a 125 °C oil bath and stirred continuously for 24 hours. After completion, the reaction vessel was allowed to cool to room temperature before being opened.

The mixture was filtered through a celite plug to remove any particulate matter. The filtrate was extracted with diethyl ether, and the combined organic layers were concentrated under reduced pressure using a rotary evaporator. For quantitative NMR analysis, 1,3,5-trimethoxybenzene (8.4 mg, 0.05 mmol) was added as an internal standard. The residue was dissolved in deuterated chloroform ($CDCl_3$), transferred into a clean NMR tube, and analyzed using proton nuclear magnetic resonance (^{1}H NMR) spectroscopy.

2.3.5 N-Alkylation of N-benzylamine: Condition 4

An oven-dried 10 mL reaction vial equipped with a magnetic stir bar was introduced into an MBraun glovebox under a dry nitrogen atmosphere. The following reagents were accurately measured and added to the vial: ligand **1** (3.3 mg, 0.0075 mmol), cobalt(II) chloride ($CoCl_2$, 0.97 mg, 0.0075 mmol), potassium tert-butoxide (KOtBu, 7.0 mg, 0.0075 mmol), benzyl alcohol (52 µL, 0.5 mmol), aniline (23 µL, 0.25 mmol), and benzene (1.0 mL) as the reaction solvent.

The vial was sealed with a screw cap and removed from the glovebox. The reaction mixture was stirred in an oil bath maintained at 125 °C for 24 hours. After the completion of the reaction, the vessel was cooled to room temperature before being opened.

The mixture was filtered through a celite pad to remove insoluble materials, and the filtrate was extracted with diethyl ether. The combined organic layers were concentrated under reduced pressure using a rotary evaporator. For quantitative nuclear magnetic resonance (NMR) analysis, 1,3,5-trimethoxybenzene (8.4 mg, 0.05 mmol) was added as an internal standard. The residue was dissolved in deuterated chloroform ($CDCl_3$), transferred to a clean NMR tube, and analyzed using proton nuclear magnetic resonance (^1H NMR) spectroscopy.

2.3.6 N-Alkylation of N-benzylamine: Condition 5

An oven-dried 10 mL reaction vial equipped with a magnetic stir bar was transferred into an MBraun glovebox under a nitrogen atmosphere. The following reagents were quantitatively added: ligand **1** (3.3 mg, 0.0075 mmol), cobalt (II) chloride ($CoCl_2$, 0.97 mg, 0.0075 mmol), sodium tert-butoxide (NaOtBu, 6.0 mg, 0.0075 mmol), benzyl alcohol (52 μL, 0.5 mmol), aniline (23 μL, 0.25 mmol), and benzene (1.0 mL) as the reaction solvent.

The reaction vial was sealed with a screw cap and removed from the glovebox. The mixture was stirred in an oil bath maintained at 125 °C for 24 hours. After the completion of the reaction, the vessel was cooled to room temperature before being opened.

The reaction mixture was filtered through a celite pad to remove any insoluble materials. The resulting filtrate was extracted with diethyl ether, and the solvent was removed under reduced pressure using a rotary evaporator. For quantitative nuclear magnetic resonance (NMR) analysis, 1,3,5-trimethoxybenzene (8.4 mg, 0.05 mmol) was added as an internal standard. The residue was dissolved in deuterated chloroform ($CDCl_3$), transferred into a clean NMR tube, and analyzed by proton nuclear magnetic resonance (^1H NMR) spectroscopy.

2.3.7 N-Alkylation of N-benzylamine: Condition 6

An oven-dried 10 mL reaction vial equipped with a magnetic stir bar was introduced into an MBraun glovebox under a nitrogen atmosphere. The following reagents were accurately measured and added to the vial: ligand **1** (3.3 mg, 0.0075 mmol), cobalt (II) chloride ($CoCl_2$, 0.97 mg, 0.0075 mmol), potassium hydroxide (KOH, 3.5 mg, 0.0075 mmol), benzyl alcohol (52 μL, 0.5 mmol), aniline (23 μL, 0.25 mmol), and benzene (1.0 mL) as the solvent.

The vial was sealed with a screw cap and removed from the glovebox. The reaction mixture was stirred in an oil bath preheated to 125 °C for 24 hours. Upon completion, the vessel was allowed to cool to room temperature before being opened.

The reaction mixture was filtered through a celite pad to remove insoluble material, and the filtrate was extracted with diethyl ether. The combined organic layers were concentrated under reduced pressure using a rotary evaporator. For quantitative analysis by nuclear magnetic resonance (NMR) spectroscopy, 1,3,5-trimethoxybenzene (8.4 mg, 0.05 mmol) was added as an internal standard. The crude product was dissolved in deuterated chloroform ($CDCl_3$), transferred into a clean NMR tube, and analyzed using proton nuclear magnetic resonance (^{1}H NMR) spectroscopy.

2.3.8 N-Alkylation of N-benzylamine: Condition 7

An oven-dried 10 mL reaction vial equipped with a magnetic stir bar was transferred into an MBraun glovebox maintained under a nitrogen atmosphere. The following reagents were accurately weighed and added to the vial: ligand **1** (3.3 mg, 0.0075 mmol), cobalt(II) chloride ($CoCl_2$, 0.97 mg, 0.0075 mmol), potassium carbonate (K_2CO_3, 6.0 mg, 0.0075 mmol), benzyl alcohol (52 µL, 0.5 mmol), aniline (23 µL, 0.25 mmol), and benzene (1.0 mL) as the reaction solvent.

The vial was sealed with a screw cap and removed from the glovebox. The reaction mixture was stirred in an oil bath maintained at 125 °C for 24 hours. After the reaction period, the vessel was allowed to cool to room temperature before opening.

The resulting mixture was filtered through a celite pad to remove any solid particulates. The filtrate was extracted with diethyl ether, and the combined organic layers were concentrated under reduced pressure using a rotary evaporator. For quantitative analysis, 1,3,5-trimethoxybenzene (8.4 mg, 0.05 mmol) was added as an internal standard. The crude residue was dissolved in deuterated chloroform ($CDCl_3$), transferred into a clean NMR tube, and analyzed by proton nuclear magnetic resonance (^1H NMR) spectroscopy.

2.3.9 N-Alkylation of N-benzylamine: Condition 8

An oven-dried 10 mL reaction vial equipped with a magnetic stir bar was transferred into an MBraun glovebox maintained under a nitrogen atmosphere. The following reagents were accurately weighed and added to the vial: ligand **1** (3.3 mg, 0.0075 mmol), cobalt(II) chloride ($CoCl_2$, 0.97 mg, 0.0075 mmol), benzyl alcohol (52 µL, 0.5 mmol), aniline (23 µL, 0.25 mmol), and benzene (1.0 mL) as the reaction solvent.

The vial was sealed with a screw cap and removed from the glovebox. The reaction mixture was stirred in an oil bath maintained at 125 °C for 24 hours. After the reaction period, the vessel was allowed to cool to room temperature before opening.

The resulting mixture was filtered through a celite pad to remove any solid particulates. The filtrate was extracted with diethyl ether, and the combined organic layers were concentrated under reduced pressure using a rotary evaporator. For quantitative analysis, 1,3,5-trimethoxybenzene (8.4 mg, 0.05 mmol) was added as an internal standard. The crude residue was dissolved in deuterated chloroform ($CDCl_3$), transferred into a clean NMR tube, and analyzed by proton nuclear magnetic resonance (^1H NMR) spectroscopy.

2.3.10 N-Alkylation of N-benzylamine: Condition 9

An oven-dried 10 mL reaction vial equipped with a magnetic stir bar was transferred into an MBraun glovebox maintained under a nitrogen atmosphere. The following reagents were accurately weighed and added to the vial: potassium tert-butoxide (KOtBu, 7.0 mg, 0.0625 mmol), benzyl alcohol (52 µL, 0.5 mmol), aniline (23 µL, 0.25 mmol), and benzene (1.0 mL) as the reaction solvent.

The vial was sealed with a screw cap and removed from the glovebox. The reaction mixture was stirred in an oil bath maintained at 125 °C for 24 hours. After the reaction period, the vessel was allowed to cool to room temperature before opening.

The resulting mixture was filtered through a celite pad to remove any solid particulates. The filtrate was extracted with diethyl ether, and the combined organic layers were concentrated under reduced pressure using a rotary evaporator. For quantitative analysis, 1,3,5-trimethoxybenzene (8.4 mg, 0.05 mmol) was added as an internal standard. The crude residue was dissolved in deuterated chloroform ($CDCl_3$), transferred into a clean NMR tube, and analyzed by proton nuclear magnetic resonance (^1H NMR) spectroscopy.

2.3.11 N-Alkylation of N-benzylamine: Condition 10

An oven-dried 10 mL reaction vial equipped with a magnetic stir bar was transferred into an MBraun glovebox maintained under a nitrogen atmosphere. The following reagents were accurately weighed and added to the vial: ligand **1** (3.3 mg, 0.0075 mmol), cobalt(II) chloride ($CoCl_2$, 0.97 mg, 0.0075 mmol), potassium tert-butoxide (KOtBu, 3.6 mg, 0.00325 mmol), benzyl alcohol (52 μL, 0.5 mmol), aniline (23 μL, 0.25 mmol), and benzene (1.0 mL) as the reaction solvent.

The vial was sealed with a screw cap and removed from the glovebox. The reaction mixture was stirred in an oil bath maintained at 125 °C for 24 hours. After the reaction period, the vessel was allowed to cool to room temperature before opening.

The resulting mixture was filtered through a celite pad to remove any solid particulates. The filtrate was extracted with diethyl ether, and the combined organic layers were concentrated under reduced pressure using a rotary evaporator. For quantitative analysis, 1,3,5-trimethoxybenzene (8.4 mg, 0.05 mmol) was added as an internal standard. The crude residue was dissolved in deuterated chloroform ($CDCl_3$), transferred into a clean NMR tube, and analyzed by proton nuclear magnetic resonance (^1H NMR) spectroscopy.

2.3.12 N-Alkylation of N-benzylamine: Condition 11

An oven-dried 10 mL reaction vial equipped with a magnetic stir bar was transferred into an MBraun glovebox maintained under a nitrogen atmosphere. The following reagents were accurately weighed and added to the vial: ligand **1** (0.9 mg, 0.002 mmol), cobalt(II) chloride ($CoCl_2$, 0.3 mg, 0.002 mmol), potassium tert-butoxide (KOtBu, 7 mg, 0.0625 mmol), benzyl alcohol (52 µL, 0.5 mmol), aniline (23 µL, 0.25 mmol), and benzene (1.0 mL) as the reaction solvent.

The vial was sealed with a screw cap and removed from the glovebox. The reaction mixture was stirred in an oil bath maintained at 125 °C for 24 hours. After the reaction period, the vessel was allowed to cool to room temperature before opening.

The resulting mixture was filtered through a celite pad to remove any solid particulates. The filtrate was extracted with diethyl ether, and the combined organic layers were concentrated under reduced pressure using a rotary evaporator. For quantitative analysis, 1,3,5-trimethoxybenzene (8.4 mg, 0.05 mmol) was added as an internal standard. The crude residue was dissolved in deuterated chloroform ($CDCl_3$), transferred into a clean NMR tube, and analyzed by proton nuclear magnetic resonance (^1H NMR) spectroscopy.

2.3.13 N-Alkylation of N-benzylamine: Condition 12

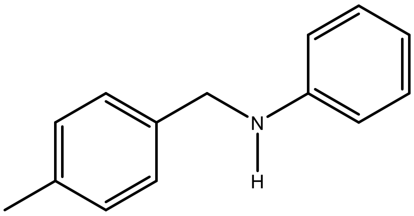
An oven-dried 10 mL reaction vial equipped with a magnetic stir bar was transferred into an MBraun glovebox maintained under a nitrogen atmosphere. The following reagents were accurately weighed and added to the vial: ligand **1** (3.3 mg, 0.0075 mmol), cobalt(II) chloride ($CoCl_2$, 0.97 mg, 0.0075 mmol), potassium tert-butoxide (KOtBu, 14 mg, 0.125 mmol), benzyl alcohol (52 µL, 0.5 mmol), aniline (23 µL, 0.25 mmol), and benzene (1.0 mL) as the reaction solvent.

The vial was sealed with a screw cap and removed from the glovebox. The reaction mixture was stirred in an oil bath maintained at 125 °C for 24 hours. After the reaction period, the vessel was allowed to cool to room temperature before opening.

The resulting mixture was filtered through a celite pad to remove any solid particulates. The filtrate was extracted with diethyl ether, and the combined organic layers were concentrated under reduced pressure using a rotary evaporator. For quantitative analysis, 1,3,5-trimethoxybenzene (8.4 mg, 0.05 mmol) was added as an internal standard. The crude residue was dissolved in deuterated chloroform ($CDCl_3$), transferred into a clean NMR tube, and analyzed by proton nuclear magnetic resonance (^1H NMR) spectroscopy.

2.4 Synthesis Details and Characterization of Products

2.4.1 Synthesis of N-[4-methylphenyl) methyl] aniline (Product 1)



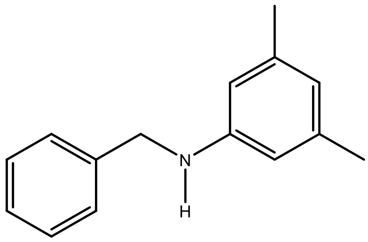
An oven-dried 10 mL reaction vial equipped with a magnetic stir bar was transferred into an MBraun glovebox under a nitrogen atmosphere. The following reagents were quantitatively measured and added to the vial: ligand **1** (3.3 mg, 0.0075 mmol), cobalt(II) chloride ($CoCl_2$, 0.97 mg, 0.0075 mmol), potassium tert-butoxide (KOtBu, 7.0 mg, 0.0075 mmol), 4-

methylphenylmethanol (61 mg, 0.5 mmol), aniline (23 μL, 0.25 mmol), and benzene (1.0 mL) as the reaction solvent.

The vial was sealed with a cap and removed from the glovebox. The reaction mixture was stirred in an oil bath maintained at 125 °C for 24 hours. Upon completion, the vial was cooled to room temperature before being opened.

The reaction mixture was filtered through a celite pad to remove insoluble materials. The filtrate was extracted with diethyl ether, and the solvent was removed under reduced pressure using a rotary evaporator. For quantitative nuclear magnetic resonance (NMR) analysis, 1,3,5-trimethoxybenzene (8.4 mg, 0.05 mmol) was added as an internal standard. The residue was dissolved in deuterated chloroform ($CDCl_3$), transferred to a clean NMR tube, and analyzed using proton nuclear magnetic resonance (^1H NMR) spectroscopy. NMR yield: 86%. In another experiment, 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 amine product. ^1H NMR (500 MHz, $CDCl_3$) δ 7.28 (d, J = 8.0 Hz, 2H), 7.20–7.16 (m, 4H), 6.74 (t, J = 7.3 Hz, 1H), 6.64 (dd, J = 8.6, 1.0 Hz, 2H), 4.29 (s, 2H), 2.36 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 148.3, 137.0, 136.4, 129.4, 129.3, 127.6, 117.6, 112.9, 48.2, 21.2.

2.4.2 Synthesis of N-benzyl-3,5-dimethylaniline (Product 2)

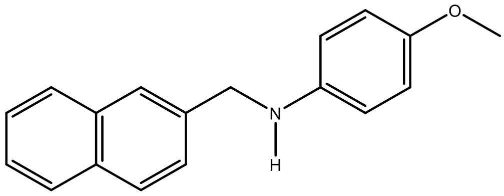


An oven-dried 10 mL reaction vial equipped with a magnetic stir bar was transferred into an MBraun glovebox under a nitrogen atmosphere. The following reagents were accurately measured and added to the vial: ligand **1** (3.3 mg, 0.0075 mmol), cobalt(II) chloride ($CoCl_2$, 0.97 mg, 0.0075 mmol), potassium tert-butoxide (KOtBu, 7.0 mg, 0.0625 mmol), benzyl alcohol (52 mg, 0.5 mmol), 3,5-dimethylaniline (30.3 mg, 0.25 mmol), and benzene (1.0 mL) as the reaction solvent.

The vial was sealed with a screw cap and removed from the glovebox. The reaction mixture was stirred in an oil bath maintained at 125 °C for 24 hours. After completion, the vessel was cooled to room temperature before being opened.

The reaction mixture was filtered through a celite pad to remove any insoluble materials. The filtrate was extracted with diethyl ether, and the solvent was removed under reduced pressure using a rotary evaporator. For quantitative nuclear magnetic resonance (NMR) analysis, 1,3,5-trimethoxybenzene (8.4 mg, 0.05 mmol) was added as an internal standard. The residue was dissolved in deuterated chloroform ($CDCl_3$), transferred into a clean NMR tube, and analyzed by proton nuclear magnetic resonance (^1H NMR) spectroscopy. NMR yield: 68%. In another experiment, 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 amine product. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50 – 7.43 (m, 4H), 7.42 – 7.39 (m, 1H), 6.53 (s, 1H), 6.40 (s, 2H), 4.41 (s, 2H), 3.98 (s (broad), 1H), 2.37 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 147.4 (s), 138.8 (s), 138.0 (s), 127.7 (s), 126.6 (s), 126.2 (s), 118.7 (s), 109.8 (s), 47.4 (s), 20.6 (s).

2.4.3 Synthesis of 4-methoxy-N-(naphthalen-2-ylmethyl) aniline (Product 3)

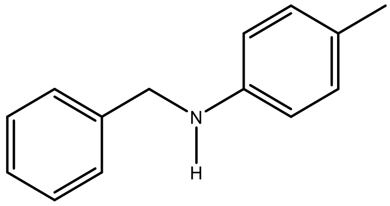


An oven-dried 10 mL reaction vial equipped with a magnetic stir bar was transferred into an MBraun glovebox maintained under a nitrogen atmosphere. The following reagents were accurately measured and added to the vial: ligand **1** (3.3 mg, 0.0075 mmol), cobalt(II) chloride ($CoCl_2$, 0.97 mg, 0.0075 mmol), potassium tert-butoxide (KOtBu, 7.0 mg, 0.0075 mmol), naphthalen-2-ylmethanol (79 mg, 0.5 mmol), 4-methoxyaniline (30.8 mg, 0.25 mmol), and benzene (1.0 mL) as the reaction solvent.

The vial was sealed with a screw cap and removed from the glovebox. The reaction mixture was stirred in an oil bath preheated to 125 °C for 24 hours. Upon completion, the vessel was cooled to room temperature before being opened.

The mixture was filtered through a celite pad to remove any insoluble material. The filtrate was extracted with diethyl ether, and the organic solvents were removed under reduced pressure using a rotary evaporator. For quantitative nuclear magnetic resonance (NMR) analysis, 1,3,5-trimethoxybenzene (8.4 mg, 0.05 mmol) was added as an internal standard. The crude residue was dissolved in deuterated chloroform ($CDCl_3$), transferred to a clean NMR tube, and analyzed by proton nuclear magnetic resonance (^1H NMR) spectroscopy. NMR yield: 72%. In another experiment, 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 amine product. ^{1}H NMR (500 MHz, $CDCl_3$) δ7.83-7.79 (m, 4H), 7.50-7.45 (m, 3H), 6.79 (d, J=7.4 Hz, 2H), 6.65 (d, J=7.4 Hz, 2H), 4.45 (s, 2H), 3.72 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 152.3, 142.5, 137.3, 133.6, 132.8, 128.4, 127.8, 127.8, 126.2, 126.0, 125.9, 125.8, 115.0, 114.3, 55.9, 49.5.

2.4.4 Synthesis of N-benzyl-4-methylaniline (Product 4)

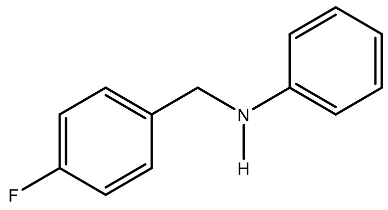


An oven-dried 10 mL reaction vial equipped with a magnetic stir bar was introduced into an MBraun glovebox under a nitrogen atmosphere. The following reagents were accurately measured and loaded into the vial: ligand **1** (3.3 mg, 0.0075 mmol), cobalt(II) chloride ($CoCl_2$, 0.97 mg, 0.0075 mmol), potassium tert-butoxide (KOtBu, 7.0 mg, 0.0075 mmol), benzyl alcohol (52 μL, 0.5 mmol), 4-methylaniline (30.8 mg, 0.25 mmol), and benzene (1.0 mL) as the reaction solvent.

The vial was sealed with a screw cap and removed from the glovebox. The reaction mixture was stirred in an oil bath maintained at 125 °C for 24 hours. Upon completion, the reaction vessel was allowed to cool to room temperature before being opened.

The reaction mixture was filtered through a celite pad to remove any insoluble material, and the filtrate was extracted with diethyl ether. The organic phase was concentrated under reduced pressure using a rotary evaporator. For quantitative analysis by nuclear magnetic resonance (NMR) spectroscopy, 1,3,5-trimethoxybenzene (8.4 mg, 0.05 mmol) was added as an internal standard. The crude product was dissolved in deuterated chloroform ($CDCl_3$), transferred into a clean NMR tube, and analyzed using proton nuclear magnetic resonance (^1H NMR) spectroscopy. NMR yield: 80%. In another experiment, 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 amine product. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.43 – 7.37 (m, 4H), 7.36 – 7.30 (m, 1H), 7.02 (d, 3JHH = 7.1 Hz, 2H), 6.62 (d, 3JHH = 6.7 Hz, 2H), 4.35 (s, 2H), 3.94 (s (broad), 1H), 2.340(s, 3H). ^{13}C NMR (126 MHz, CDCl$_3$): δ 146.1, 139.8, 129.9, 128.8, 127.6, 127.3, 126.9, 113.1, 48.8, 20.6.

2.4.5 Synthesis of N-[(4-fluorophenyl) methyl] aniline (Product 5)

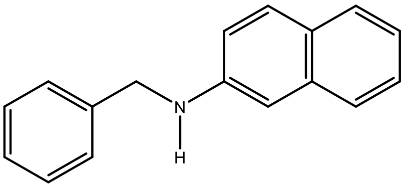


An oven-dried 10 mL reaction vial equipped with a magnetic stir bar was transferred into an MBraun glovebox under a nitrogen atmosphere. The following reagents were quantitatively measured and added to the vial: ligand **1** (3.3 mg, 0.0075 mmol), cobalt(II) chloride ($CoCl_2$, 0.97 mg, 0.0075 mmol), potassium tert-butoxide (KOtBu, 7.0 mg, 0.0625 mmol), 4-fluorobenzyl alcohol (63.1 mg, 0.5 mmol), aniline (23 µL, 0.25 mmol), and benzene (1.0 mL) as the reaction solvent.

The vial was sealed with a screw cap and removed from the glovebox. The reaction mixture was stirred in an oil bath maintained at 125 °C for 24 hours. Upon completion, the vessel was allowed to cool to room temperature before being opened.

The reaction mixture was filtered through a celite pad to remove any insoluble material. The filtrate was extracted with diethyl ether, and the organic layer was concentrated under reduced pressure using a rotary evaporator. For quantitative nuclear magnetic resonance (NMR) analysis, 1,3,5-trimethoxybenzene (8.4 mg, 0.05 mmol) was added as an internal standard. The residue was dissolved in deuterated chloroform ($CDCl_3$), transferred to a clean NMR tube, and analyzed using proton nuclear magnetic resonance (^1H NMR) spectroscopy. NMR yield: 77%. In another experiment, 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 amine product. ^{1}H NMR (500 MHz, $CDCl_3$) 7.35–7.33 (m, 2H), 7.19-7.16 (m, 2H), 7.05-7.00 (m, 2H), 6.74-6.71 (m, 1H), 6.63-6.61 (m, 2H), 4.30 (s, 2H), 4.01 (br s, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 163.1, 161.2, 148.2, 135.2, 129.4, 129.1, 129.1, 117.8, 115.6, 115.5, 112.9, 47.7.

2.4.6 Synthesis of N-benzylnaphthalen-2-amine (Product 6)

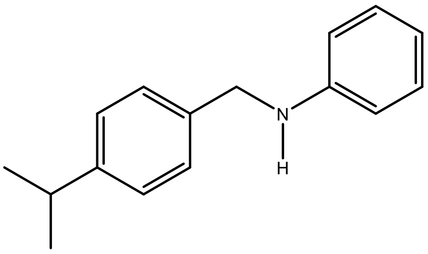


An oven-dried 10 mL reaction vial equipped with a magnetic stir bar was transferred into an MBraun glovebox under a nitrogen atmosphere. The following reagents were accurately measured and added to the vial: ligand **1** (3.3 mg, 0.0075 mmol), cobalt(II) chloride ($CoCl_2$, 0.97 mg, 0.0075 mmol), potassium tert-butoxide (KOtBu, 7.0 mg, 0.0625 mmol), benzyl alcohol (52 μL, 0.5 mmol), naphthalen-2-amine (35.8 mg, 0.25 mmol), and benzene (1.0 mL) as the reaction solvent.

The vial was sealed with a screw cap and removed from the glovebox. The reaction mixture was stirred in a heated oil bath at 125 °C for 24 hours. After completion of the reaction, the vessel was allowed to cool to room temperature before being opened.

The reaction mixture was filtered through a celite pad to remove insoluble materials, and the resulting solution was extracted with diethyl ether. The organic layer was concentrated under reduced pressure using a rotary evaporator. For quantitative nuclear magnetic resonance (NMR) analysis, 1,3,5-trimethoxybenzene (8.4 mg, 0.05 mmol) was added as an internal standard. The crude product was dissolved in deuterated chloroform ($CDCl_3$), transferred into a clean NMR tube, and analyzed using proton nuclear magnetic resonance (^1H NMR) spectroscopy. NMR yield: 72%. In another experiment, 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 amine product. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69 (d, J = 8.1 Hz, 1H), 7.65 (d, J = 8.8 Hz, 1H), 7.61 (d, J = 8.1 Hz, 1H), 7.46-7.41 (m, 2H), 7.41-7.34 (m, 3H), 7.34-7.28 (m, 1H), 7.24-7.18 (m, 1H), 6.93 (dd, J = 8.8, 2.3 Hz, 1H), 6.86 (d, J = 2.3 Hz, 1H), 4.45 (s, 2H), 4.20 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 145.9, 139.3, 135.3, 129.1, 128.8, 127.7, 127.4, 126.4, 126.1, 122.1, 118.0, 104.7, 48.5.

2.4.7 Synthesis of N-[(4-propan-2-ylphenyl) methyl] aniline (Product 7)

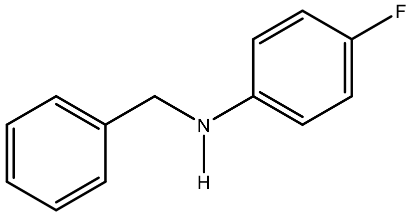


An oven-dried 10 mL reaction vial equipped with a magnetic stir bar was transferred into an MBraun glovebox under a nitrogen atmosphere. The following reagents were quantitatively measured and added to the vial: ligand **1** (3.3 mg, 0.0075 mmol), cobalt(II) chloride ($CoCl_2$, 0.97 mg, 0.0075 mmol), potassium tert-butoxide (KOtBu, 7.0 mg, 0.0625 mmol), 4-(propan-2-yl)benzyl alcohol (75.11 mg, 0.5 mmol), aniline (23 µL, 0.25 mmol), and benzene (1.0 mL) as the reaction solvent.

The vial was sealed with a screw cap and removed from the glovebox. The reaction mixture was stirred in a heated oil bath at 125 °C for 24 hours. After completion, the vessel was allowed to cool to room temperature before being opened.

The mixture was filtered through a celite pad to remove any insoluble materials, and the filtrate was extracted using diethyl ether. The organic solvents were removed under reduced pressure using a rotary evaporator. For quantitative nuclear magnetic resonance (NMR) analysis, 1,3,5-trimethoxybenzene (8.4 mg, 0.05 mmol) was added as an internal standard. The crude product was dissolved in deuterated chloroform ($CDCl_3$), transferred to a clean NMR tube, and analyzed by proton nuclear magnetic resonance (^1H NMR) spectroscopy. NMR yield: 80%. In another experiment, 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 amine product. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28 (d, J = 8.1 Hz, 2 H), 7.14–7.04 (m, 4 H), 6.62 (t, J = 7.3 Hz, 1 H), 6.55 (d, J = 7.6 Hz, 2 H), 4.18 (s, 2 H), 3.86 (s, 1 H), 2.81 (m, 1H), 1.17 (d, J = 6.9 Hz, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 148.5, 148.1, 137.0, 129.5, 127.9, 126.9, 117.7, 113.0, 48.3, 34.0, 24.3.

2.4.8 Synthesis of N-benzyl-4-fluoroaniline (Product 8)

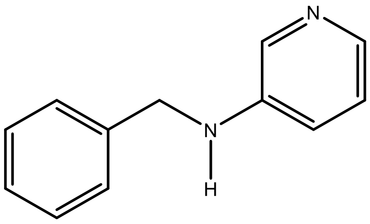


An oven-dried 10 mL reaction vial equipped with a magnetic stir bar was transferred into an MBraun glovebox under a nitrogen atmosphere. The following reagents were accurately measured and added to the vial: ligand **1** (3.3 mg, 0.0075 mmol), cobalt(II) chloride ($CoCl_2$, 0.97 mg, 0.0075 mmol), potassium tert-butoxide (KOtBu, 7.0 mg, 0.0625 mmol), benzyl alcohol (52 µL, 0.5 mmol), 4-fluoroaniline (27.8 mg, 0.25 mmol), and benzene (1.0 mL) as the reaction solvent.

The vial was sealed with a screw cap and removed from the glovebox. The reaction mixture was stirred in a preheated oil bath at 125 °C for 24 hours. After completion, the vessel was cooled to room temperature before being opened.

The reaction mixture was filtered through a celite pad to remove insoluble material, and the filtrate was extracted with diethyl ether. The combined organic layers were concentrated under reduced pressure using a rotary evaporator. For quantitative nuclear magnetic resonance (NMR) analysis, 1,3,5-trimethoxybenzene (8.4 mg, 0.05 mmol) was added as an internal standard. The crude product was dissolved in deuterated chloroform ($CDCl_3$), transferred to a clean NMR tube, and analyzed using proton nuclear magnetic resonance (^1H NMR) spectroscopy. NMR yield: 76%. In another experiment, 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 amine product. ^{1}H NMR (500 MHz, $CDCl_3$) 7.37–7.33 (m, 4H), 7.28-7.25 (m, 1H), 6.89–6.82 (m, 2H), 6.57–6.55 (m, 2H), 4.30 (s, 1H), 3.92 (br s, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 156.9, 155.0, 144.56, 139.31, 128.75, 127.57, 127.40, 115.84, 115.66, 113.74, 113.68, 49.02.

2.4.9 Synthesis of N-benzylpyridin-3-amine (Product 9)

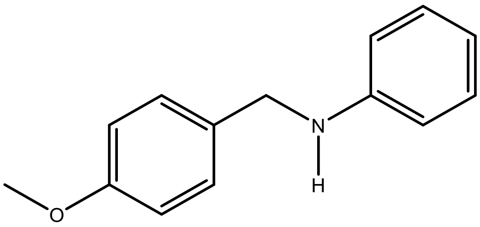


An oven-dried 10 mL reaction vial equipped with a magnetic stir bar was transferred into an MBraun glovebox maintained under a nitrogen atmosphere. The following reagents were accurately weighed and added to the vial: ligand **1** (3.3 mg, 0.0075 mmol), cobalt(II) chloride ($CoCl_2$, 0.97 mg, 0.0075 mmol), potassium tert-butoxide (KOtBu, 7.0 mg, 0.0625 mmol), benzyl alcohol (52 µL, 0.5 mmol), pyridin-3-amine (23.5 mg, 0.25 mmol), and benzene (1.0 mL) as the reaction solvent.

The vial was sealed with a screw cap and removed from the glovebox. The reaction mixture was stirred in a preheated oil bath at 125 °C for 24 hours. After completion, the vial was allowed to cool to room temperature before being opened.

The mixture was then filtered through a celite pad to remove insoluble material, and the filtrate was extracted with diethyl ether. The organic solvent was removed under reduced pressure using a rotary evaporator. For quantitative analysis by nuclear magnetic resonance (NMR) spectroscopy, 1,3,5-trimethoxybenzene (8.4 mg, 0.05 mmol) was added as an internal standard. The residue was dissolved in deuterated chloroform ($CDCl_3$), transferred into a clean NMR tube, and analyzed using proton nuclear magnetic resonance (^1H NMR) spectroscopy. NMR yield: 78%. In another experiment, 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 amine product. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.06 (d, J = 2.9 Hz, 1H), 8.02-7.90 (m, 1H), 7.35 (d, J = 4.4 Hz, 4H), 7.32-7.26 (m, 1H), 7.11-7.01 (m, 1H), 6.91-6.81 (m, 1H), 4.34 (d, J = 4.8 Hz, 2H), 4.19 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 144.1, 138.8, 138.6, 136.2, 128.8, 127.5, 127.4, 123.8, 118.6, 47.9.

2.4.10 Synthesis of N-[(4-methoxyphenyl) methyl] aniline (Product 10)



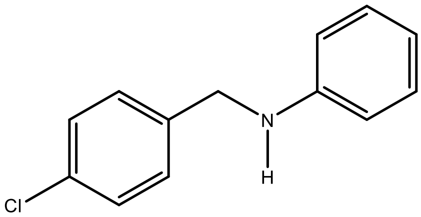
An oven-dried 10 mL reaction vial equipped with a magnetic stir bar was transferred into an MBraun glovebox maintained under a nitrogen atmosphere. The following reagents were quantitatively measured and added to the vial: ligand **1** (3.3 mg, 0.0075 mmol), cobalt(II) chloride ($CoCl_2$, 0.97 mg, 0.0075 mmol), potassium tert-butoxide (KOtBu, 7.0 mg, 0.0625 mmol), 4-methoxyphenylmethanol (69.1 mg, 0.5 mmol), aniline (23 μL, 0.25 mmol), and benzene (1.0 mL) as the reaction solvent.

The vial was sealed with a screw cap and removed from the glovebox. The reaction mixture was stirred in an oil bath maintained at 125 °C for 24 hours. After the reaction was complete, the vial was cooled to room temperature before being opened.

The mixture was filtered through a celite pad to remove insoluble materials, and the filtrate was extracted with diethyl ether. The organic solvent was removed under reduced pressure using a rotary evaporator. For quantitative nuclear magnetic resonance (NMR) analysis, 1,3,5-trimethoxybenzene (8.4 mg, 0.05 mmol) was added as an internal standard. The resulting residue was dissolved in deuterated chloroform ($CDCl_3$), transferred into a clean NMR tube, and analyzed by proton nuclear magnetic resonance (^1H NMR) spectroscopy. NMR yield: 97%.

In another experiment, 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 amine product. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33 (d, J = 8.4 Hz, 2H), 7.20–7.16 (m, 2H,), 6.88 (d, J = 8.4 Hz, 2H), 6.71 (t, J = 7.4 Hz, 1H,), 6.66 (d, J = 7.6 Hz, 2H), 4.28 (s, 2H), 3.83 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.98, 148.35, 131.55, 129.39, 128.94, 117.62, 114.15, 112.97, 77.45, 77.20, 76.95, 55.42, 47.90.

2.4.11 Synthesis of N-[(4-chlorophenyl) methyl] aniline (Product 11)

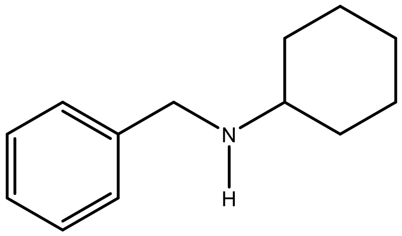


An oven-dried 10 mL reaction vial equipped with a magnetic stir bar was transferred into an MBraun glovebox under a nitrogen atmosphere. The following reagents were accurately measured and added to the vial: ligand **1** (3.3 mg, 0.0075 mmol), cobalt(II) chloride ($CoCl_2$, 0.97 mg, 0.0075 mmol), potassium tert-butoxide (KOtBu, 7.0 mg, 0.0625 mmol), 4-chlorobenzyl alcohol (71.3 mg, 0.5 mmol), aniline (23 µL, 0.25 mmol), and benzene (1.0 mL) as the reaction solvent.

The reaction vial was sealed with a screw cap and removed from the glovebox. The mixture was stirred in a heated oil bath at 125 °C for 24 hours. Upon completion, the vessel was allowed to cool to room temperature before being opened.

The reaction mixture was filtered through celite to remove insoluble material, and the filtrate was extracted using diethyl ether. The solvent was removed under reduced pressure using a rotary evaporator. For quantitative nuclear magnetic resonance (NMR) analysis, 1,3,5-trimethoxybenzene (8.4 mg, 0.05 mmol) was added as an internal standard. The crude product was dissolved in deuterated chloroform ($CDCl_3$), transferred into a clean NMR tube, and analyzed by proton nuclear magnetic resonance (^1H NMR) spectroscopy. NMR yield: 72%.

2.4.12 Synthesis of N-benzylcyclohexanamine (Product 12)

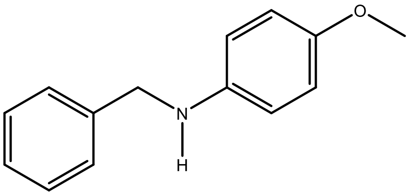


An oven-dried 10 mL reaction vial equipped with a magnetic stir bar was transferred into an MBraun glovebox under a nitrogen atmosphere. The following reagents were accurately measured and added to the vial: ligand **1** (3.3 mg, 0.0075 mmol), cobalt(II) chloride ($CoCl_2$, 0.97 mg, 0.0075 mmol), potassium tert-butoxide (KOtBu, 7.0 mg, 0.0625 mmol), benzyl alcohol (52 μL, 0.5 mmol), cyclohexanamine (28.8 μL, 0.25 mmol), and benzene (1.0 mL) as the reaction solvent.

The vial was sealed with a screw cap and removed from the glovebox. It was then placed in an oil bath set to 125 °C and stirred for 24 hours. After the reaction time elapsed, the vessel was removed from the oil bath and allowed to cool to room temperature before being opened.

The mixture was filtered through a celite pad to remove insoluble materials, and the filtrate was extracted with diethyl ether. The solvent was removed under reduced pressure using a rotary evaporator. For quantitative nuclear magnetic resonance (NMR) analysis, 1,3,5-trimethoxybenzene (8.4 mg, 0.05 mmol) was added as an internal standard. The residue was dissolved in deuterated chloroform ($CDCl_3$), transferred into a clean NMR tube, and analyzed using proton nuclear magnetic resonance (^1H NMR) spectroscopy. NMR yield: trace amount.

2.4.13 Synthesis of N-benzyl-4-methoxyaniline (Product 13)

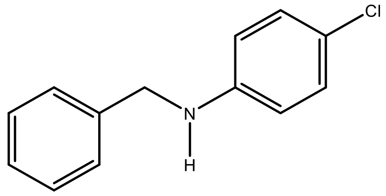


An oven-dried 10 mL reaction vial equipped with a magnetic stir bar was transferred into an MBraun glovebox under a nitrogen atmosphere. The following reagents were accurately measured and added to the vial: ligand **1** (3.3 mg, 0.0075 mmol), cobalt(II) chloride ($CoCl_2$, 0.97 mg, 0.0075 mmol), potassium tert-butoxide (KOtBu, 7.0 mg, 0.0625 mmol), benzyl alcohol (52 µL, 0.5 mmol), 4-methoxyaniline (30.8 mg, 0.25 mmol), and benzene (1.0 mL) as the reaction solvent.

The reaction vial was sealed with a screw cap and removed from the glovebox. It was placed into an oil bath set to 125 °C and stirred continuously for 24 hours. After the reaction time had elapsed, the vessel was removed from the oil bath and allowed to cool to room temperature before being opened.

The reaction mixture was filtered through a celite pad to remove any insoluble material. The filtrate was extracted with diethyl ether, and the organic solvent was removed under reduced pressure using a rotary evaporator. For quantitative nuclear magnetic resonance (NMR) analysis, 1,3,5-trimethoxybenzene (8.4 mg, 0.05 mmol) was added as an internal standard. The crude product was dissolved in deuterated chloroform ($CDCl_3$), transferred to a clean NMR tube, and analyzed using proton nuclear magnetic resonance (^1H NMR) spectroscopy. NMR yield: 91%. In another experiment, 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 amine product. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40- 7.31 (m, 4H), 7.28-7.26 (m, 1H), 6.78 (d, J = 8.9 Hz, 2H), 6.61 (d, J = 8.9 Hz, 2H), 4.30 (s, 2H), 3.75 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.3, 142.6, 139.8, 128.7, 127.7, 127.3, 115.1, 114.2, 56.0, 49.4

2.4.14 Synthesis of N-benzyl-4-chloroaniline (Product 14)

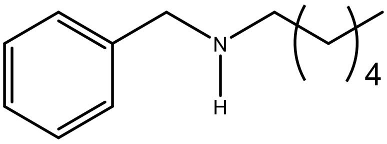


An oven-dried 10 mL reaction vial equipped with a magnetic stir bar was transferred into an MBraun glovebox under a nitrogen atmosphere. The following reagents were quantitatively measured and added to the vial: ligand **1** (3.3 mg, 0.0075 mmol), cobalt(II) chloride ($CoCl_2$, 0.97 mg, 0.0075 mmol), potassium tert-butoxide (KOtBu, 7.0 mg, 0.0625 mmol), benzyl alcohol (52 μL, 0.5 mmol), 4-chloroaniline (31.9 mg, 0.25 mmol), and benzene (1.0 mL) as the reaction solvent.

The vial was sealed with a screw cap and removed from the glovebox. It was then placed into an oil bath set to 125 °C and stirred for 24 hours. After completion of the reaction, the vial was removed from the oil bath and allowed to cool to room temperature before being opened.

The mixture was filtered through a celite pad to remove insoluble material, and the filtrate was extracted with diethyl ether. The organic layer was concentrated under reduced pressure using a rotary evaporator. For quantitative nuclear magnetic resonance (NMR) analysis, 1,3,5-trimethoxybenzene (8.4 mg, 0.05 mmol) was added as an internal standard. The crude product was dissolved in deuterated chloroform ($CDCl_3$), transferred into a clean NMR tube, and analyzed by proton nuclear magnetic resonance (^1H NMR) spectroscopy. NMR yield: 84%. In another experiment, 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 amine product. ^{1}H NMR (500 MHz, $CDCl_3$) δ7.35-7.34 (d, 4H), 7.32-7.24 (m, 1H), 7.14-7.08 (m, 2H), 6.56-6.52 (m, 2H), 4.29 (s, 2H), 4.20 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 146.7, 139.0, 129.2, 128.8, 127.5, 127.5, 122.2, 122.2, 114.0, 48.4, 29.8.

2.4.15 Synthesis of N-benzylpentan-1-amine (Product 15)

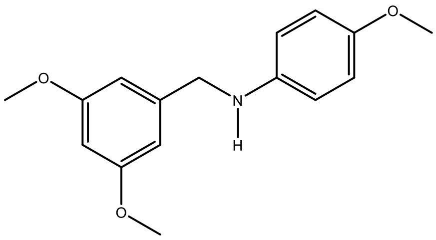


An oven-dried 10 mL reaction vial equipped with a magnetic stir bar was transferred into an MBraun glovebox under a nitrogen atmosphere. The following reagents were quantitatively measured and added to the vial: ligand **1** (3.3 mg, 0.0075 mmol), cobalt(II) chloride ($CoCl_2$, 0.97 mg, 0.0075 mmol), potassium tert-butoxide (KOtBu, 7.0 mg, 0.0625 mmol), benzyl alcohol (52 μL, 0.5 mmol), pentan-1-amine (21.8 mg, 0.25 mmol), and benzene (1.0 mL) as the reaction solvent.

The vial was sealed with a screw cap and removed from the glovebox. It was then placed into an oil bath set to 125 °C and stirred for 24 hours. After completion of the reaction, the vial was removed from the oil bath and allowed to cool to room temperature before being opened.

The mixture was filtered through a celite pad to remove insoluble material, and the filtrate was extracted with diethyl ether. The organic layer was concentrated under reduced pressure using a rotary evaporator. For quantitative nuclear magnetic resonance (NMR) analysis, 1,3,5-trimethoxybenzene (8.4 mg, 0.05 mmol) was added as an internal standard. The crude product was dissolved in deuterated chloroform ($CDCl_3$), transferred into a clean NMR tube, and analyzed by proton nuclear magnetic resonance (^1H NMR) spectroscopy. NMR yield: trace.

2.4.16 Synthesis of N-[(3,5-dimethoxyphenyl) methyl]-4-methoxyaniline (Product 16)

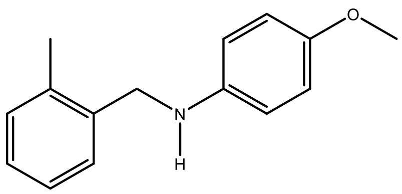


An oven-dried 10 mL reaction vial equipped with a magnetic stir bar was transferred into an MBraun glovebox under a nitrogen atmosphere. The following reagents were accurately measured and added to the vial: ligand **1** (3.3 mg, 0.0075 mmol), cobalt(II) chloride ($CoCl_2$, 0.97 mg, 0.0075 mmol), potassium tert-butoxide (KOtBu, 7.0 mg, 0.0625 mmol), 3,5-dimethoxyphenylmethanol (84.1 mg, 0.5 mmol), 4-methoxyaniline (30.8 mg, 0.25 mmol), and benzene (1.0 mL) as the reaction solvent.

The vial was sealed with a screw cap and removed from the glovebox. It was then placed in an oil bath set to 125 °C and stirred for 24 hours. After the reaction time elapsed, the vial was removed from the oil bath and allowed to cool to room temperature before being opened.

The reaction mixture was filtered through a celite pad to remove any insoluble material, and the filtrate was extracted with diethyl ether. The solvent was evaporated under reduced pressure using a rotary evaporator. For quantitative nuclear magnetic resonance (NMR) analysis, 1,3,5-trimethoxybenzene (8.4 mg, 0.05 mmol) was added as an internal standard. The residue was dissolved in deuterated chloroform ($CDCl_3$), transferred into a clean NMR tube, and analyzed using proton nuclear magnetic resonance (^1H NMR) spectroscopy. NMR yield: 91%. In another experiment, 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 amine product. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.78–6.76 (m, 2H), 6.57 (d, 2H), 6.40 (t, 1H), 4.22 (s, 2H), 3.77 (s, 6H), 3.74 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.1, 152.3, 142.5, 142.4, 114.9, 114.2, 105.4, 99.2, 55.6, 55.9, 49.5

2.4.17 Synthesis of 4-methoxy-N-[(2-methylphenyl) methyl] aniline (Product 17)

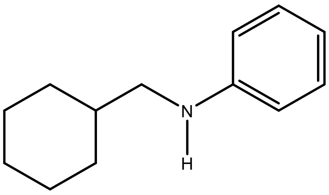


An oven-dried 10 mL reaction vial equipped with a magnetic stir bar was transferred into an MBraun glovebox under a nitrogen atmosphere. The following reagents were accurately measured and loaded into the vial: ligand **1** (3.3 mg, 0.0075 mmol), cobalt(II) chloride ($CoCl_2$, 0.97 mg, 0.0075 mmol), potassium tert-butoxide (KOtBu, 7.0 mg, 0.0625 mmol), 2-methylphenylmethanol (61.0 mg, 0.5 mmol), 4-methoxyaniline (30.8 mg, 0.25 mmol), and benzene (1.0 mL) as the reaction solvent.

The vial was sealed with a screw cap and removed from the glovebox. It was placed in an oil bath set to 125 °C and stirred continuously for 24 hours. After the reaction period, the vial was removed from the oil bath and allowed to cool to room temperature before being opened.

The reaction mixture was filtered through a celite pad to remove any insoluble material, and the resulting solution was extracted with diethyl ether. The organic layer was concentrated under reduced pressure using a rotary evaporator. For quantitative analysis by nuclear magnetic resonance (NMR) spectroscopy, 1,3,5-trimethoxybenzene (8.4 mg, 0.05 mmol) was added as an internal standard. The crude product was dissolved in deuterated chloroform ($CDCl_3$), transferred into a clean NMR tube, and analyzed by proton nuclear magnetic resonance (^1H NMR) spectroscopy. NMR yield: 99%. In another experiment, 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 amine product. ^{1}H NMR (500 MHz, $CDCl_3$) 7.34-7.33 (m, 1H), 7.20-7.19 (m, 2H), 7.18 (m, 1H), 7.17 (m, 1H), 6.79 (m, 2H), 6.60 (m, 2H), 4.23 (s, 2H), 3.75 (s, 3H), 2.37 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.21, 142.73, 137.35, 136.41, 130.45, 128.30, 127.42, 126.21, 115.02, 113.99, 77.35, 77.10, 76.85, 55.94, 47.34, 19.02.

2.4.18 Synthesis of N-(cyclohexylmethyl) aniline (Product 18)



An oven-dried 10 mL reaction vial equipped with a magnetic stir bar was transferred into an MBraun glovebox under a nitrogen atmosphere. The following reagents were accurately measured and added to the vial: ligand **1** (3.3 mg, 0.0075 mmol), cobalt(II) chloride ($CoCl_2$, 0.97 mg, 0.0075 mmol), potassium tert-butoxide (KOtBu, 7.0 mg, 0.0625 mmol), cyclohexyl methanol (57.1 mg, 0.5 mmol), aniline (23 µL, 0.25 mmol), and benzene (1.0 mL) as the reaction solvent.

The vial was sealed with a screw cap and removed from the glovebox. It was then placed into an oil bath set to 125 °C and stirred for 24 hours. After completion of the reaction, the vial was removed from the oil bath and allowed to cool to room temperature before being opened.

The reaction mixture was filtered through a celite pad to remove any insoluble material. The filtrate was extracted with diethyl ether, and the organic layer was concentrated under reduced pressure using a rotary evaporator. For quantitative analysis by nuclear magnetic resonance (NMR) spectroscopy, 1,3,5-trimethoxybenzene (8.4 mg, 0.05 mmol) was added as an internal standard. The resulting residue was dissolved in deuterated chloroform ($CDCl_3$), transferred into a clean NMR tube, and analyzed using proton nuclear magnetic resonance (^1H NMR) spectroscopy. NMR yield: 99%. In another experiment, 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 amine product. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.23 – 7.19 (m, 2H), 6.75 (tt, J = 7.3, 1.1 Hz, 1H), 6.70 – 6.63 (m, 2H), 3.84 (br, 1H), 3.03 (d, 2H), 1.95 – 1.72 (m, 5H), 1.66 (dddt, 1H), 1.43–1.16 (m, 3H), 1.13–0.96 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.7, 129.3, 117.0, 112.7, 50.7, 37.6, 31.4, 26.7, 26.0.

CHAPTER III

RESULTS AND DISCUSSION

3.1 Synthesis of Ligand 1 and Complex 1a

Transition metals possess vacant d-orbitals and variable oxidation states, which enable them to act as central atoms in coordination complexes. Ligands with donor atom(s) coordinate to these metal centers through the donation of electron pairs, typically via lone pairs from heteroatoms like nitrogen, oxygen, sulfur, or phosphorus. The resulting metal complexes often exhibit enhanced chemical reactivity, stability, and selectivity compared to the free metal ion or ligand alone. A rigid tridentate binding mode that provides excellent thermal and oxidative stability to the metal center which supports catalytic activity is enforced. Metal complexes formed from transition metals are particularly valuable in homogeneous catalysis. They can facilitate a wide range of transformations including C–C, C–H, and C–N bond formation through well-defined mechanisms.

Scheme 3.1: Synthesis of ^{iPr}PPPOH Pincer Ligand from ^{iPr}PPPCl

The synthesis of the tridentate phosphine ligand **1** was successfully carried out under inert atmosphere conditions using standard glovebox techniques, as the starting material (^{iPr}PPPCl) was expected to be highly sensitive to air and moisture. Characterization of the ligand by $^{31}P\{^{1}H\}$ NMR spectroscopy in C_6D_6 or $CDCl_3$ revealed a well-defined doublet and triplet, consistent with the distinct chemical environments of the phosphorus atoms in the ligand backbone. The compound is a secondary phosphine oxide featuring a central phosphinous acid moiety (P–H, P=O) flanked by two diisopropylphosphino-substituted phenyl rings. The $^{31}P\{^{1}H\}$ NMR spectrum displays a triplet at 9.61 ppm, corresponding to the central phosphorus atom coupled to two equivalent terminal phosphine groups. A doublet at 6.62 ppm arises from the terminal diisopropylphosphino groups, each coupled to the central phosphorus. This AX_2 spin system is consistent with a P–P–P framework and confirms the presence of a P–H bond at the central site.

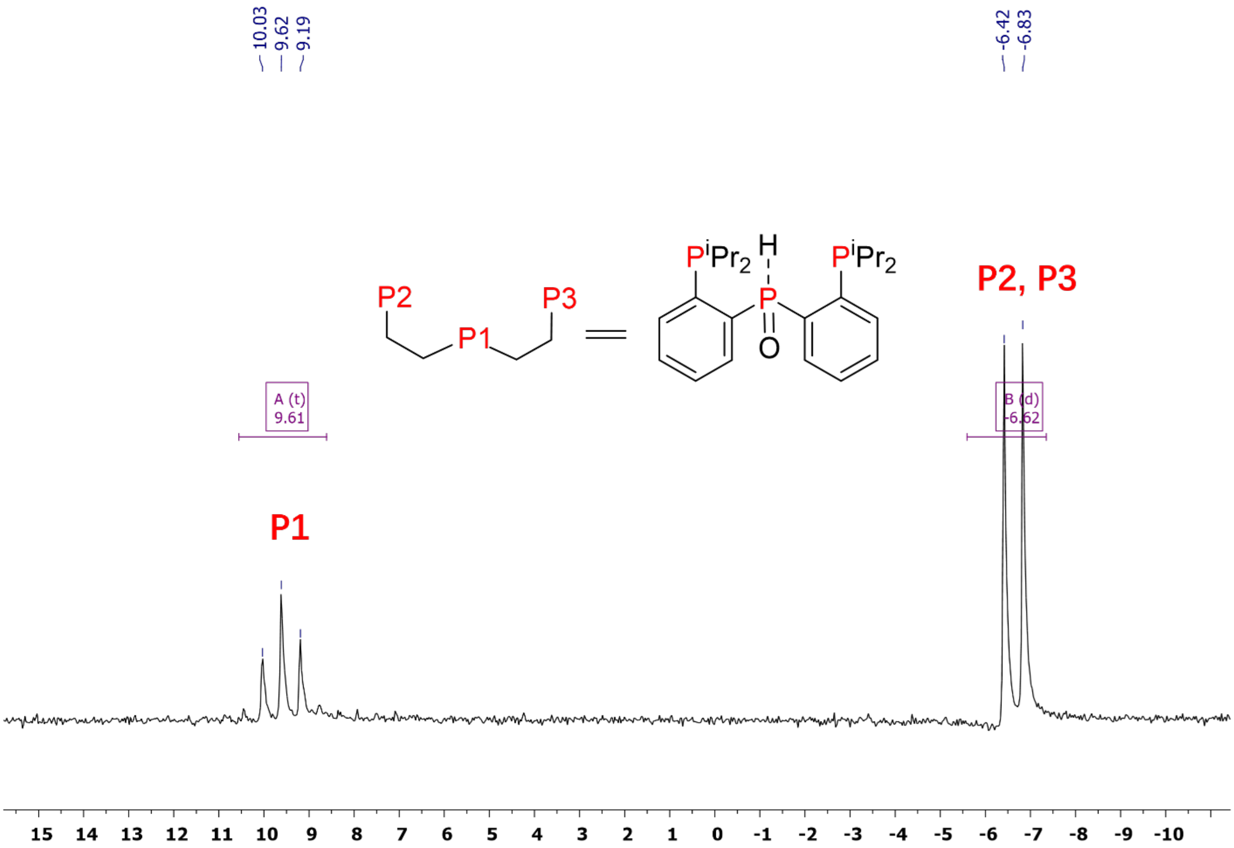


Figure 3.1. ^{31}P{^{1}H} NMR spectrum (121 MHz, C_6D_6) of ligand **1**, showing a triplet at 9.61 ppm (P1, central phosphorus) and a doublet at 6.62 ppm (P2, P3, terminal diisopropylphosphino groups), consistent with a P–P–P spin system.

The ^{1}H NMR spectrum displays a signal at 9.86 ppm integrating for one proton, which appears as a well-resolved doublet of triplets (dt, J = 522.2, 3.8 Hz). This splitting pattern is characteristic of a proton directly bonded to a phosphorus atom (P–H), where the large coupling constant (522.2 Hz) corresponds to the one-bond coupling ($^{1}J_{\text{P-H}}$) with the central phosphorus atom (P1). The smaller coupling constant (3.8 Hz) arises from three-bond couplings ($^{3}J_{\text{P-H}}$) to two equivalent terminal phosphorus atoms (P2 and P3) located on either side of the central phosphorus. This pattern supports a three-phosphorus spin system (P–P–P), with the central phosphorus bearing both the P=O group and the directly bonded hydrogen, flanked by two aryl-substituted diisopropylphosphine groups. The clear resolution of both couplings in the proton NMR further corroborates the connectivity deduced from the ^{31}P{^{1}H} NMR data and confirms the presence of a phosphinous acid motif with a defined P–H bond. Ligand **1** design features a tridentate phosphine scaffold comprising two isopropyl-substituted diphenylphosphino arms and a central phosphine oxide moiety. This configuration promotes a rigid, electron-rich coordination environment around the metal center, offering both steric protection and electronic tunability. The central phosphine group is hydrolyzed in situ and oxidized to form a P=O unit, which helps stabilize the ligand backbone and enforce a well-defined bite angle for metal coordination.

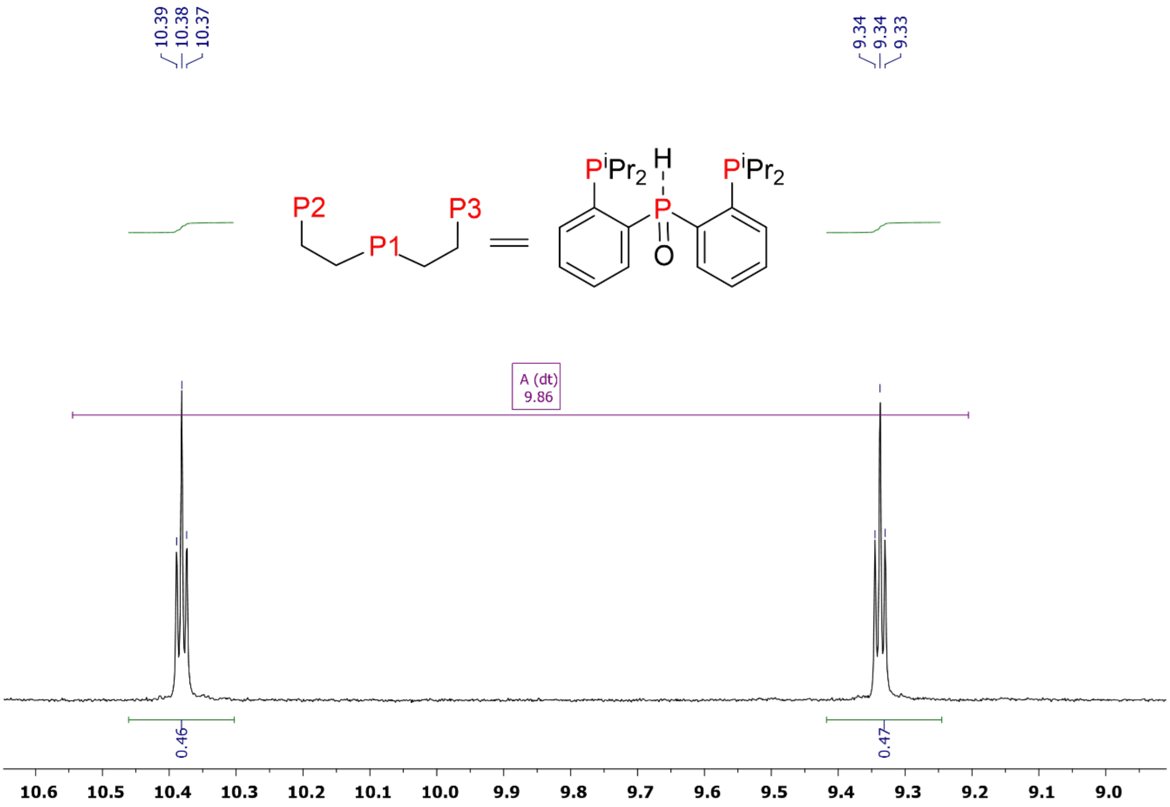


Figure 3.2. ^{1}H NMR spectrum (500 MHz, C$_6$D$_6$) showing the P–H resonance at 9.86 ppm as a doublet of triplets (dt, J = 522.2, 3.8 Hz, 1H), consistent with one-bond coupling to the central

phosphorus atom (P1) and three-bond coupling to two equivalent terminal phosphorus atoms (P2 and P3) in a P–P–P spin system.

Initially, ligand **1** was presumed to be air-sensitive due to the presence of reactive phosphine functionalities. To evaluate this, a portion of the isolated **1** was exposed to ambient atmosphere for further observation. After 24 hours outside the glovebox, ^{31}P NMR analysis revealed no change in the spectral features, both the doublet and triplet remain unaltered. Remarkably, the same sample was analyzed again after one week of exposure to air, and the NMR spectrum showed no evidence of degradation or oxidation. These observations confirm that the ligand is air-stable, despite initial assumptions to the contrary. In conclusion, the synthesis of 1 was achieved with high efficiency and purity.

Scheme 3.2: Coordination of ligand **1** (^{iPr}PPPOH) with $CoCl_2$

Under an inert nitrogen atmosphere within a glovebox, stoichiometric amount of cobalt (II) chloride was mixed with the DCM solution of ligand at room temperature. The reaction mixture immediately changed color to red, indicating a successful complex formation. The reaction mixture was allowed to stir overnight, followed by filtration and concentration under vacuum. Red crystal of complex **1a** was grown by layering diethyl ether over a crude solution of **1a** in DCM.

In most of the following catalytic studies, ligand **1** and cobalt chloride were combined in a 1:1 ratio to generate the active catalytic precursor in situ. Alternatively, the pre-formed complex **1a** was employed directly and provided comparable results.

3.2 Reaction Optimizations for Cobalt Catalyzed N-Alkylation using Aniline and Benzyl Alcohol

Reaction optimization was carried out using aniline and benzyl alcohol as model substrates to investigate the catalytic efficiency of ligand **1**/$CoCl_2$ for N-alkylation via the borrowing hydrogen (BH) methodology. Key reaction variables including catalytic loading, base selection, solvent, and temperature were systematically evaluated to maximize the conversion of benzyl alcohol to N-benzylaniline (Table 3.1).

Initial trials began with the use of ligand **1**/$CoCl_2$ (3 mol %), potassium tert-butoxide (25 mol %), and toluene (1 mL) at 85 °C for 24 hours. Under these conditions, NMR analysis indicated a moderate yield of 44% for the desired N-benzylaniline product (Table 3.1, Condition 1). Raising the reaction temperature to 105 °C led to an improved yield of 56% (Condition 2), and further elevation to 125 °C resulted in a substantial increase in product yield to 88% (Condition 3).

Encouraged by this trend, the solvent was switched from toluene to benzene, which provided a more favorable environment due to its lower polarity and higher stability under heating.

Remarkably, a quantitative yield (100%) was achieved when the reaction was conducted in benzene at 125 °C (Condition 4), marking a major improvement in catalytic performance. This condition was thus identified as optimal for subsequent substrate scope studies.

The role of the base was then evaluated. While KOtBu proved highly effective, substitution with sodium tert-butoxide (NaOtBu) under identical conditions led to a significant drop in yield to 25% (Condition 5), suggesting that electropositivity plays crucial role in catalyst activation. Further testing with potassium hydroxide (KOH) maintained high reactivity, affording a 97% yield (Condition 6), which demonstrates that strong, non-nucleophilic bases are generally suitable for this transformation.

Conversely, the use of potassium carbonate (K_2CO_3) a weaker base resulted in complete inhibition of the reaction, with 0% yield observed even at an elevated temperature of 140 °C (Condition 7). This finding confirmed that strong base is essential not only for deprotonating the alcohol but also for maintaining the activity of the cobalt catalyst.

Next, one reaction was carried out in the absence of base, and 0 % yield was observed (Condition 8). Conversely, the reaction was carried out in the absence of **1a** (Condition 9).0% yield was observed. When less amount of 13 mol% of KOtBu is used, the yield is significantly reduced (Condition 10). Likewise, when less metal catalyst 1a is used (Condition 11), the yield is significantly suppressed to 50%.

The optimized condition (Condition 4) was selected for further substrate scope evaluation and mechanistic studies described in the subsequent sections.

Table 3.1: Reaction Optimization of N-Alkylation using Aniline and Benzyl Alcohol [a,b]

Condition	Catalyst	Base	Solvent	Temp (°C)	Yield (%)
1	**1 + $CoCl_2$**	KO^tBu	Toluene	85	44
2	**1 + $CoCl_2$**	KO^tBu	Toluene	105	56
3	**1 + $CoCl_2$**	KO^tBu	Toluene	125	88
4	**1 + $CoCl_2$**	KO^tBu	Benzene	125	100
5	**1 + $CoCl_2$**	NaO^tBu	Benzene	125	25
6	**1 + $CoCl_2$**	KOH	Benzene	125	97
7	**1 + $CoCl_2$**	K_2CO_3	Benzene	140	0
8[c]	**1 + $CoCl_2$**	-	Benzene	125	0
9[d]	**-**	KO^tBu	Benzene	125	0
10[e]	**1 + $CoCl_2$**	KO^tBu	Benzene	125	55
11[f]	**1 + $CoCl_2$**	KO^tBu	Benzene	125	50
12[g]	**1 + $CoCl_2$**	KO^tBu	Benzene	125	82

[a]Reaction conditions: **1** (3 mol%), $CoCl_2$ (3 mol%), base (KOtBu = 25 mol%), alcohol (0.5 mmol), amine (0.25 mmol), and benzene (0.75 ml) were heated in a 15 ml sealed reaction tube for 24 h. [b]Yields were determined by ^1H NMR analysis of the crude reaction mixture with 1,3,5 trimethoxybenzene as an internal standard. [c]Reaction was carried out in the absence of base. [d]Reaction was carried out in the absence of **1** and $CoCl_2$. [e]13 mol% of KOtBu was used. [f]**1** and $CoCl_2$ (0.8 mol% was used). [g]50 mol% of KOtBu was used.

Table 3.2: Dehydrogenative Coupling of Primary Alcohol and Aniline Catalyzed by 1/$CoCl_2$ and KO^tBu[a,b]

[a]Reaction conditions: **1** (3 mol%), $CoCl_2$ (3 mol%), base (KOtBu = 25 mol%), Alcohol (0.5 mmol), Amine (0.25 mmol), and benzene (0.75 ml) were heated at 125°C in a 15 ml sealed reaction tube for 24 h. [b]Yields were determined by 1H NMR analysis of the crude reaction mixture with 1,3,5 trimethoxybenzene as an internal standard.

3.3 Catalytic N-Alkylation of Aromatic Amines and Aromatic Alcohol

The catalytic N-alkylation of aromatic amines with benzylic alcohol derivatives was successfully achieved using the borrowing hydrogen (BH) methodology. Aromatic amines such as aniline and its substituted derivatives, including 4-chloroaniline and 3,5-dimethylaniline, participated effectively in the transformation. The nature of the substituents on the aromatic ring played a notable role in determining reactivity. Electron-donating groups (EDGs) tended to enhance the nucleophilicity of amine nitrogen, while electron-withdrawing groups (EWGs) had a comparatively modest effect. Nevertheless, both classes of substituents were generally well-tolerated under the reaction conditions, leading to high product yields.

In contrast, the use of aliphatic amines under identical conditions proved challenging. For example, pentan-1-amine resulted in only trace amounts of the corresponding secondary amine product, indicating the unsuitability of non-aromatic amines for this protocol. This limitation is consistent with literature reports, which highlight the difficulty of imine formation and hydrogenation when aliphatic amines are employed under BH conditions.

A diverse range of aromatic alcohols was also investigated, including benzyl alcohol, 4-methylbenzyl alcohol, 4-methoxybenzyl alcohol, 4-chlorobenzyl alcohol, 2-methylbenzyl alcohol, and 3,5-dimethoxybenzyl alcohol. Electron-donating substituents on alcohol generally improved reactivity and yield, especially when positioned at the ortho position. Notably, 2-methylbenzyl alcohol afforded the N-alkylated amine in a yield of 99%. Electron-withdrawing substituents were also effective, with meta-substituted derivatives such as 4-chlorobenzyl alcohol delivering excellent yields (up to 91%). These results collectively demonstrate that the BH method is robust and amenable to a wide variety of electronically diverse aromatic substrates, though it is clearly optimized for aromatic amines.

3.4 Catalytic N-alkylation of Aromatic Amines and Aliphatic Alcohol

The reaction of aromatic amines with aliphatic alcohol was successful with great yields as in the case of the reaction between aniline and cyclohexylmethanol, affording the corresponding N-cyclohexyl methyl aniline product in 99% yield (Product 18). This result highlights the adaptability of the catalytic system toward less activated alcohols. The success of the transformation is attributed to the unhindered nature of the primary alcohol, cyclohexylmethanol, which facilitates dehydrogenation to the corresponding aldehyde intermediate. The subsequent imine formation and hydrogenation steps also proceeded smoothly under the optimized reaction conditions. These findings demonstrate the potential of this methodology to extend beyond benzylic systems and accommodate aliphatic alcohols for the N-alkylation of aromatic amines with high efficiency.

3.5 Catalytic N-alkylation of Aliphatic Amines and Aromatic Alcohol

The reaction between aliphatic amines and aromatic alcohol was not successful as only trace amount of yield was recovered. This is because of aliphatic imines being less stable and readily hydrolyzing back to starting material in the presence of water which is a byproduct in the condensation step in borrowing hydrogen method which is being employed.

CHAPTER IV

CONCLUSION

In summary, this study reports the synthesis and application of a novel cobalt–ligand complex featuring a hydroxyl-functionalized pincer ligand (iPrPPPOH). The ligand was synthesized under inert conditions and its identity confirmed by ^{31}P NMR spectroscopy. Although initially presumed to be air-sensitive, the free ligand demonstrated remarkable stability, retaining its integrity for over a week upon exposure to air, which enhances its practical utility.

Reaction of $CoCl_2$ with the ligand yielded a dark red, air-sensitive crystalline complex in moderate yield. The immediate color change upon ligand addition provided visual evidence of complex formation.

The resulting cobalt complex proved to be an efficient catalyst for the N-alkylation of aromatic amines with both benzylic and aliphatic alcohols under borrowing hydrogen (BH) conditions.

Optimization studies revealed that reaction performance was highly dependent on temperature, base, and solvent. Among the bases tested, KOtBu and KOH were the most effective, while benzene emerged as the optimal solvent, enabling reactions to proceed with yields up to 100%. It is noteworthy that only 25 mol% of KOtBu was required in these reactions, in contrast to previously reported catalytic systems that rely on a stoichiometric or excess amount of KOtBu.

The substrate scope was thoroughly investigated by varying the electronic nature and positional substitution on both amines and alcohols. Electron-donating groups—especially at the ortho position of benzylic alcohols—enhanced reactivity and afforded excellent yields. Electron-withdrawing groups were also well tolerated, albeit with slightly reduced efficiency. Substituted anilines, such as 4-chloroaniline and 4-fluoroaniline, reacted smoothly, underscoring the broad functional group compatibility of the catalytic system.

In contrast, aliphatic amines such as cyclohexylamine were ineffective with benzylic alcohol under the applied BH conditions, likely due to the inherent instability of the resulting aliphatic imines. However, aromatic amines like aniline reacted efficiently with aliphatic alcohols, such as cyclohexylmethanol, achieving yields as high as 99%. This demonstrates the catalyst's competence in activating unactivated aliphatic alcohols.

Collectively, these findings highlight the potential of cobalt–pincer complexes in sustainable N-alkylation chemistry via the borrowing hydrogen strategy. Their catalytic efficiency, functional group tolerance, and air stability position them as promising candidates for green amine synthesis and broader applications in organic transformations.

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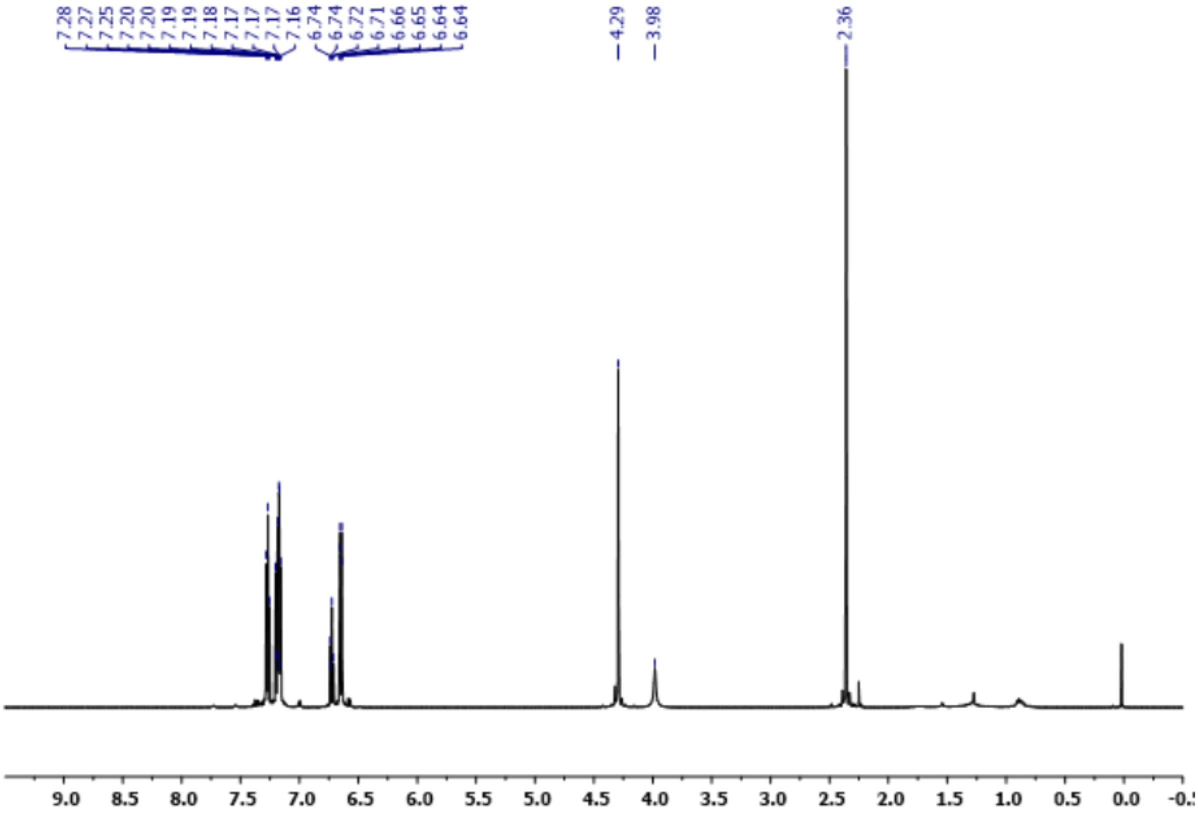

Figure 4.1: ^{1}H NMR (500 MHz, $CDCl_3$) of product 1.

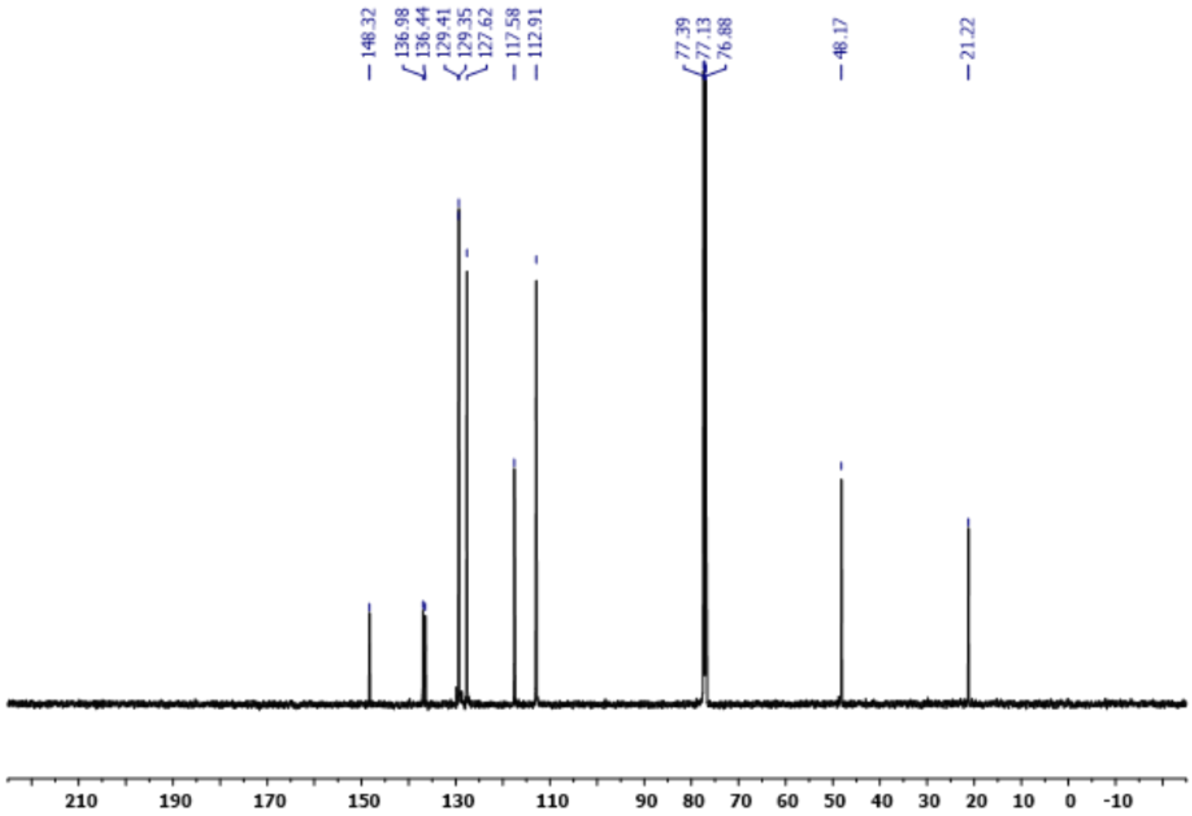

Figure 4.2: ^{13}C NMR (125 MHz, $CDCl_3$) of product 1.

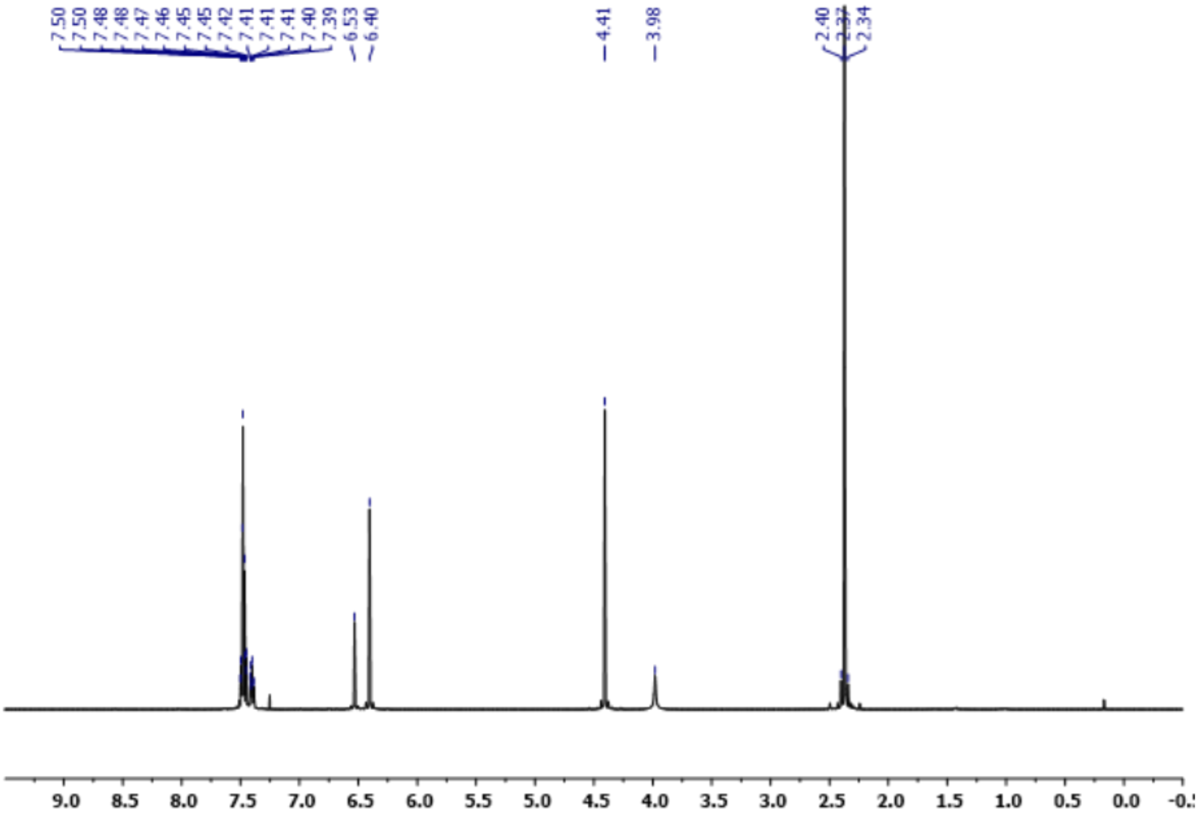

Figure 4.3: ^{1}H NMR (500 MHz, $CDCl_3$) of product 2.

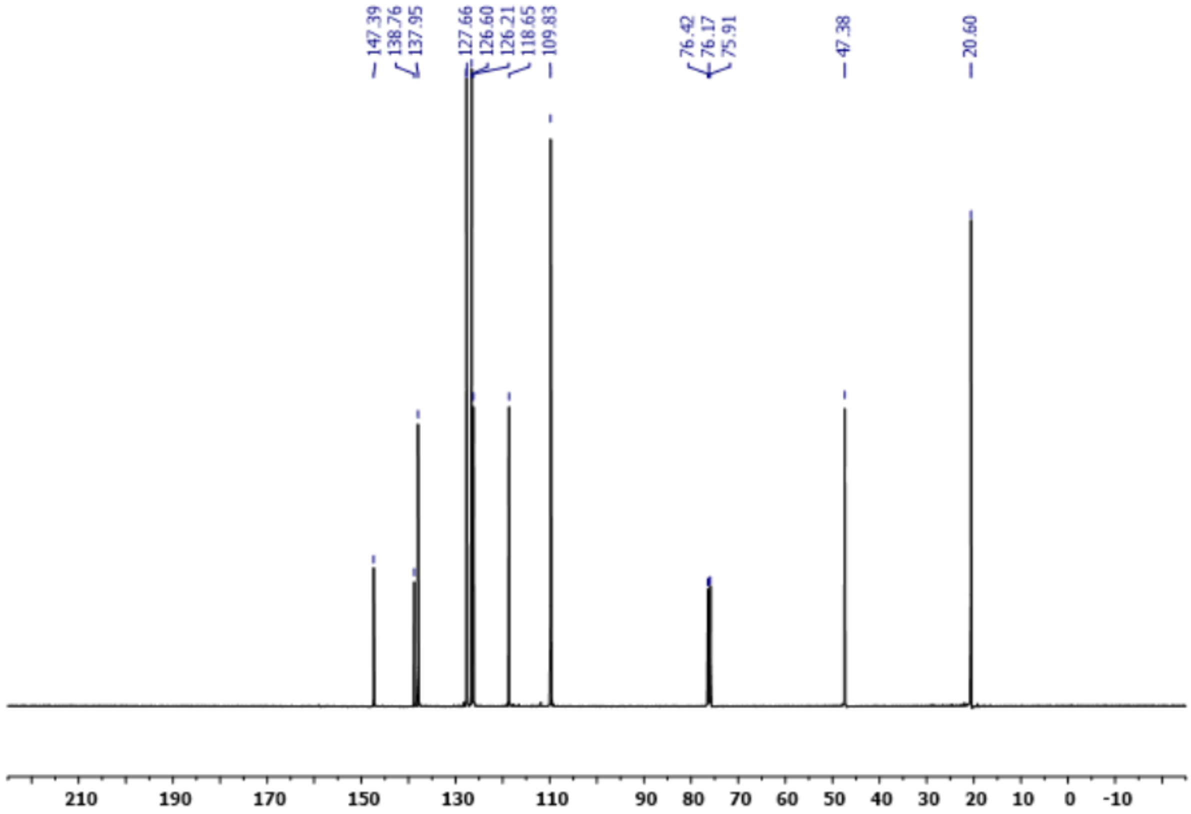

Figure 4.4: ^{13}C NMR (125 MHz, $CDCl_3$) of product 2.

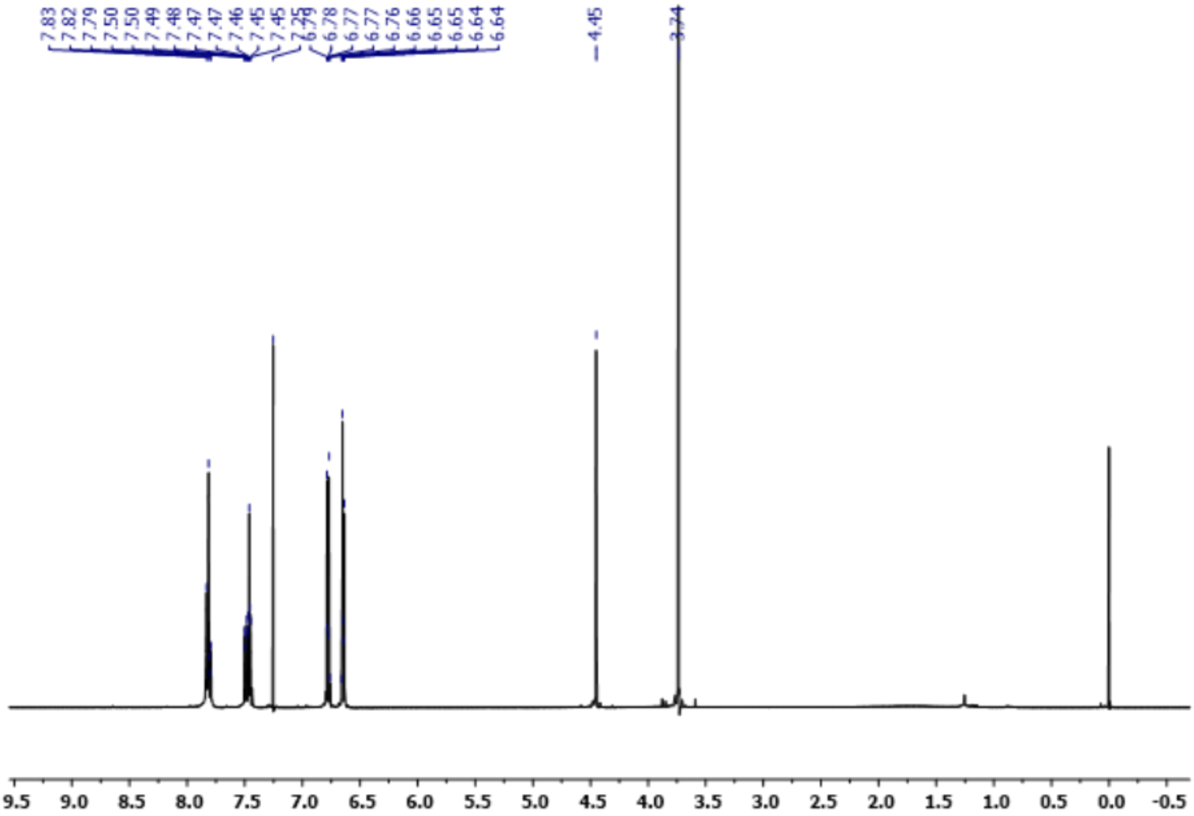

Figure 4.5: ^{1}H NMR (500 MHz, $CDCl_3$) of product 3.

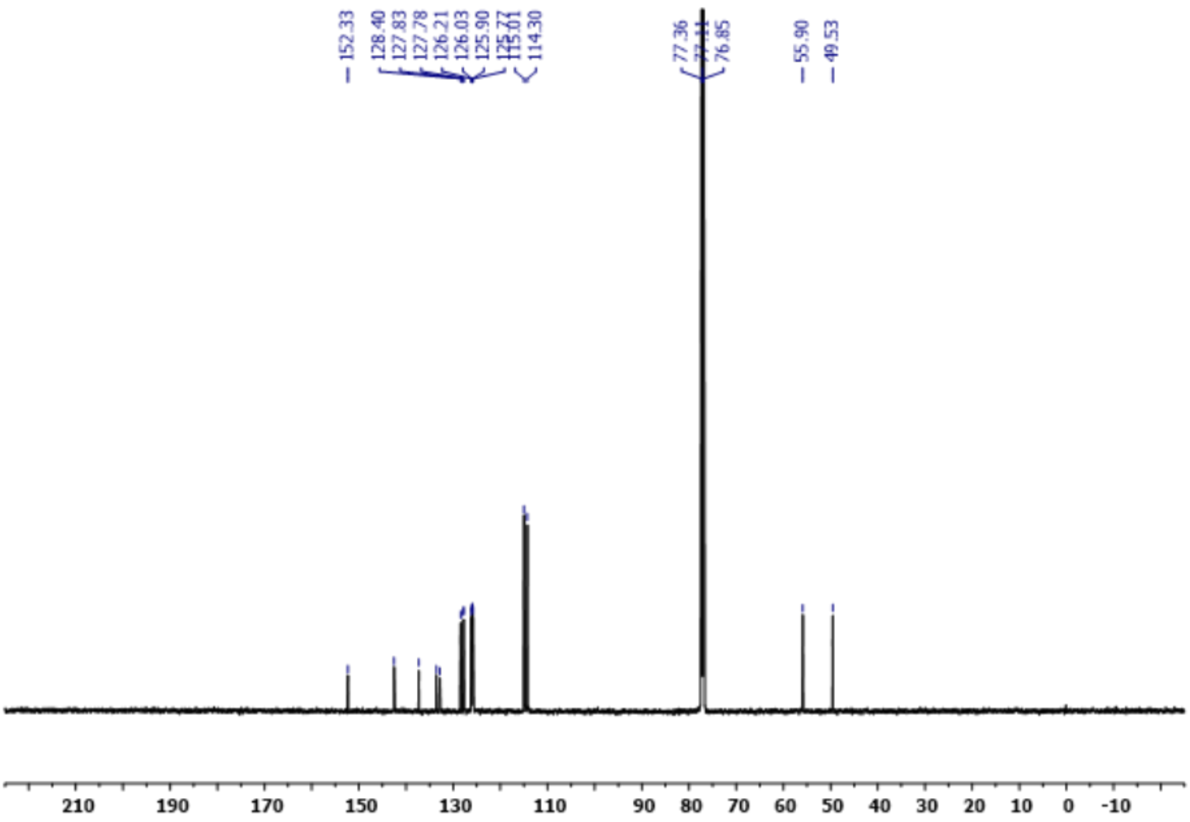

Figure 4.6: ^{13}C NMR (125 MHz, $CDCl_3$) of product 3.

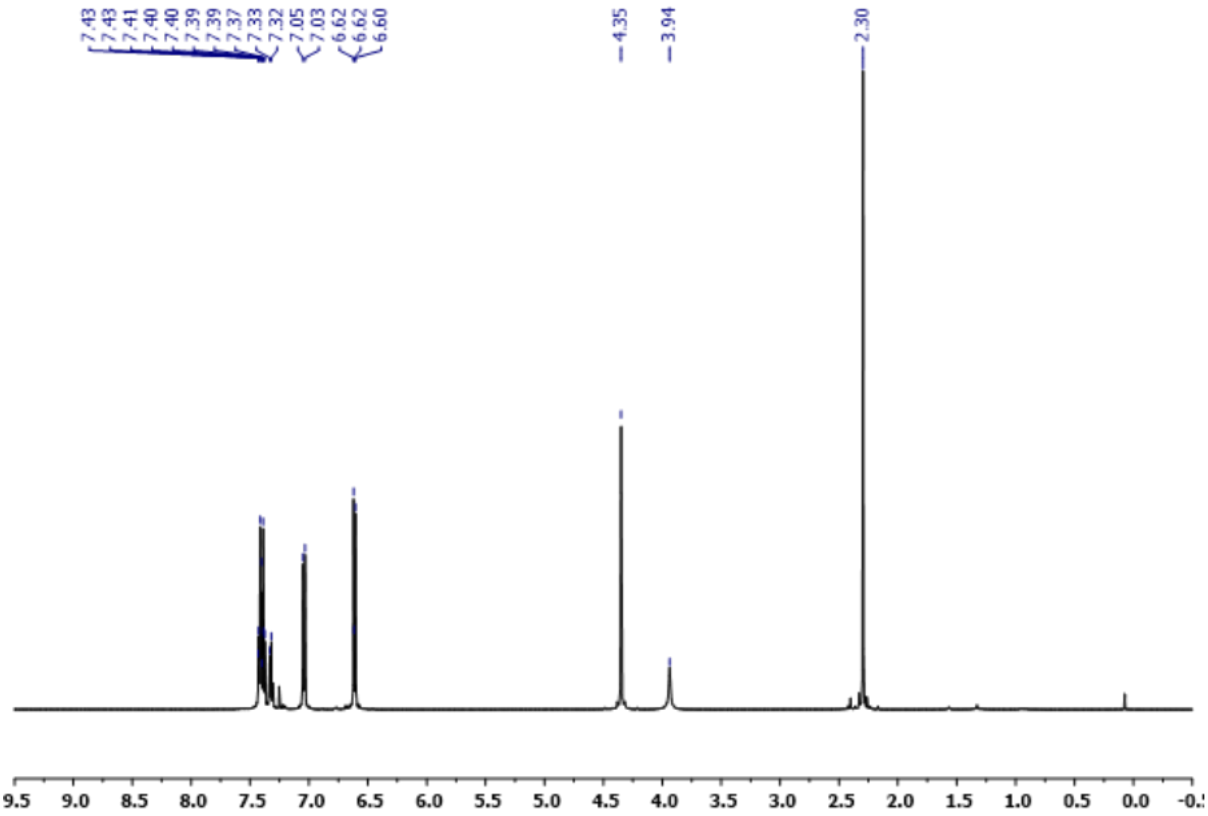

Figure 4.7: ^{1}H NMR (500 MHz, $CDCl_3$) of product 4.

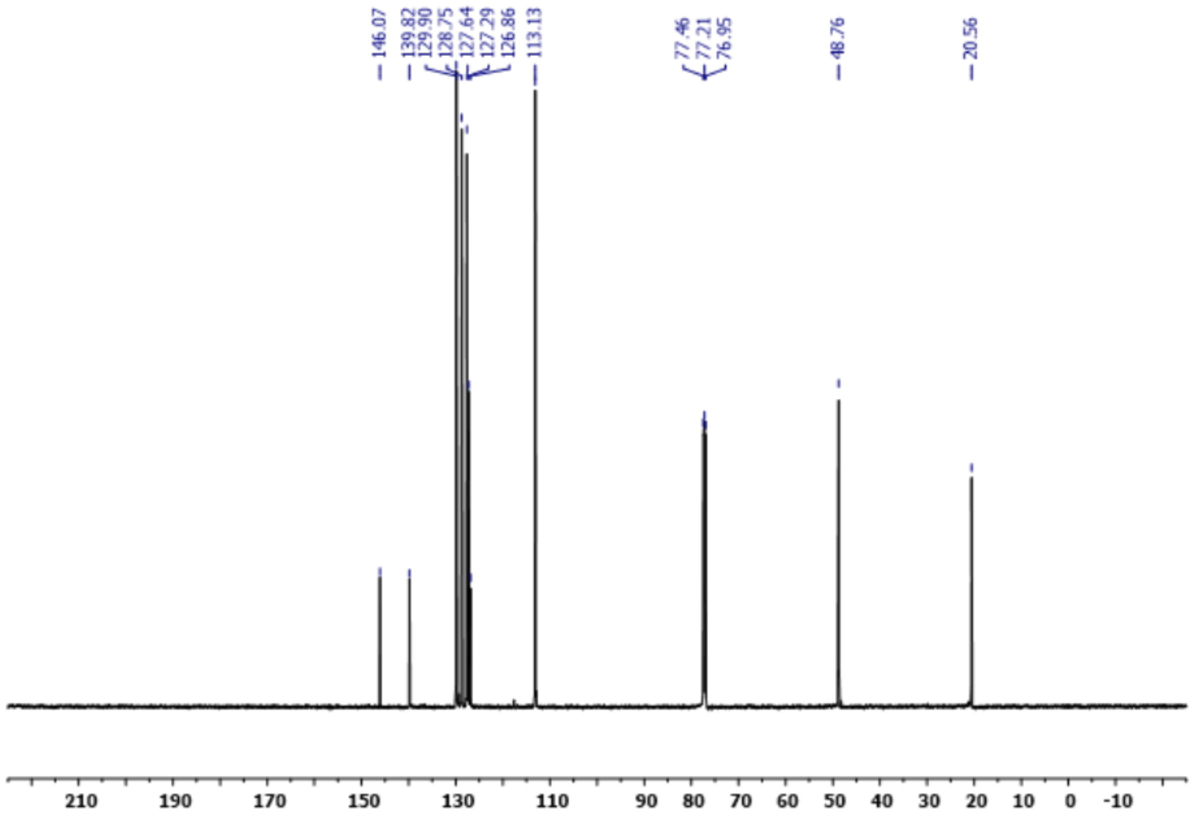

Figure 4.8: ^{13}C NMR (125 MHz, $CDCl_3$) of product 4.

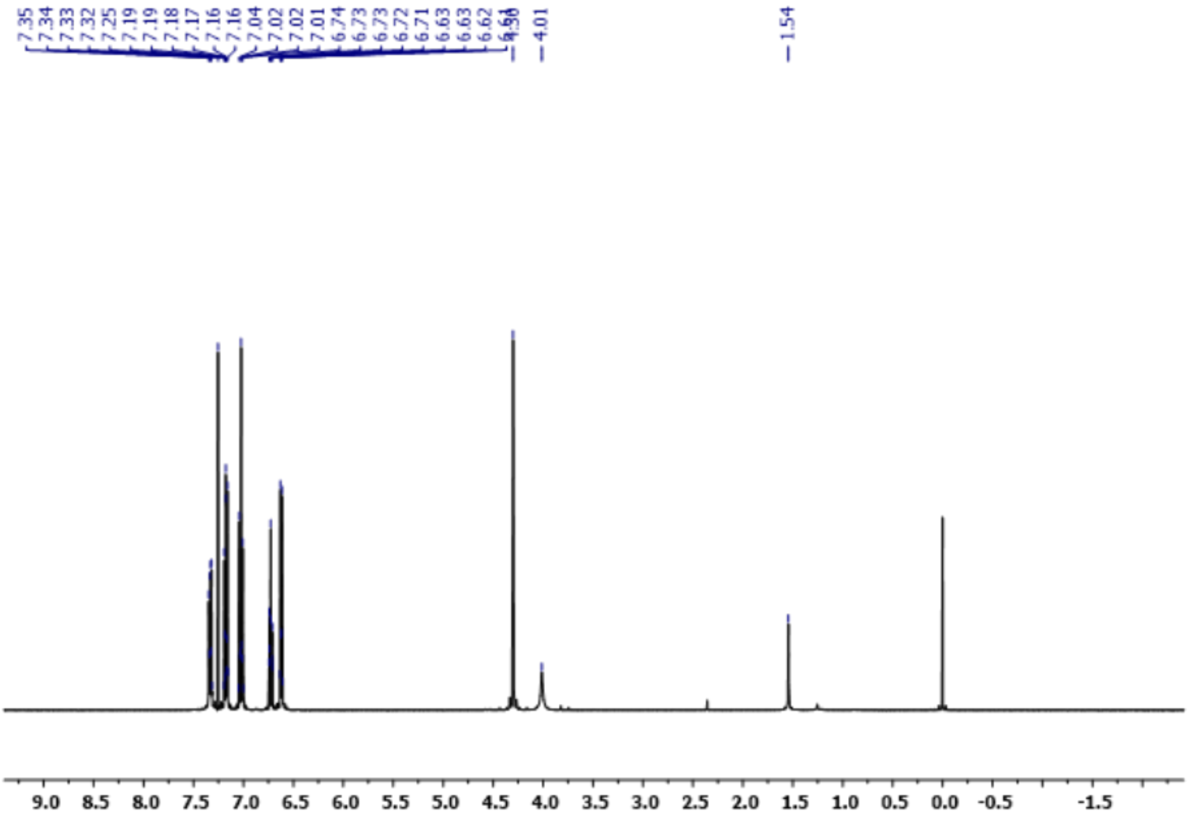

Figure 4.9: ^{1}H NMR (500 MHz, $CDCl_3$) of product 5.

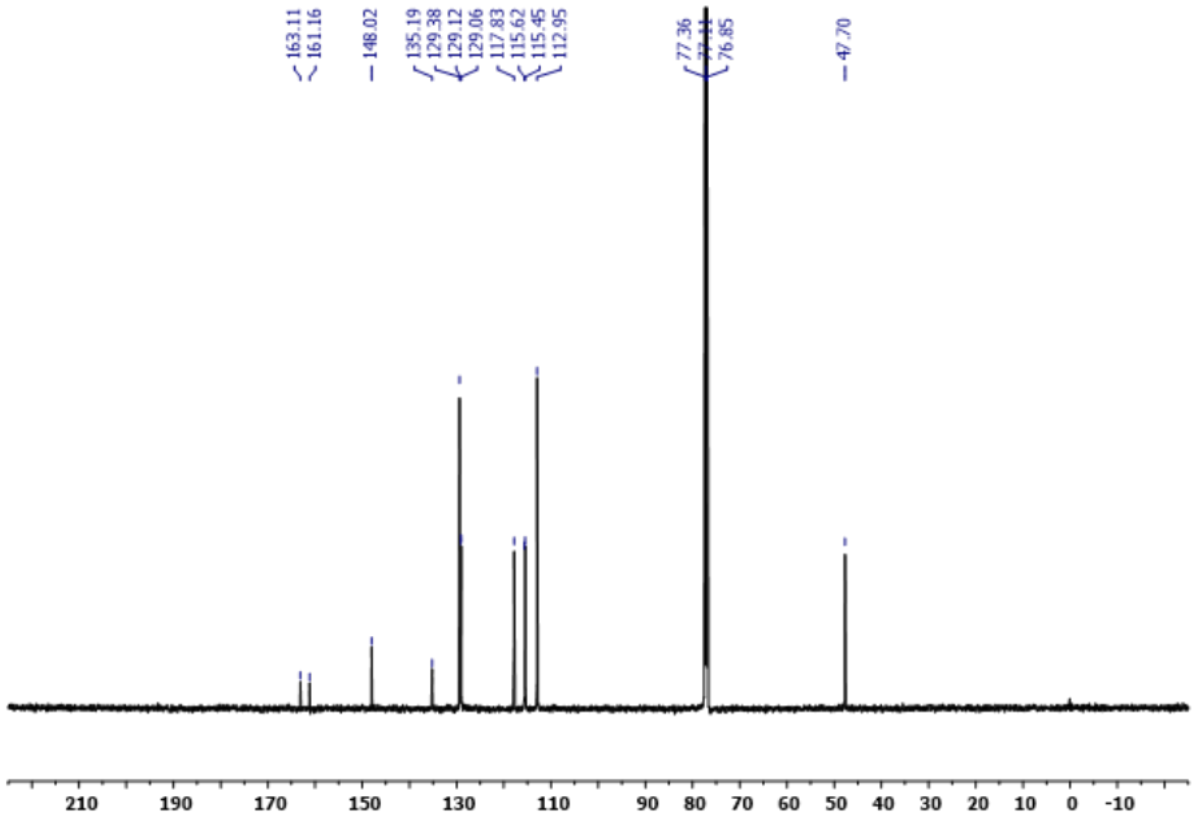

Figure 4.10: ^{13}C NMR (125 MHz, $CDCl_3$) of product 5.

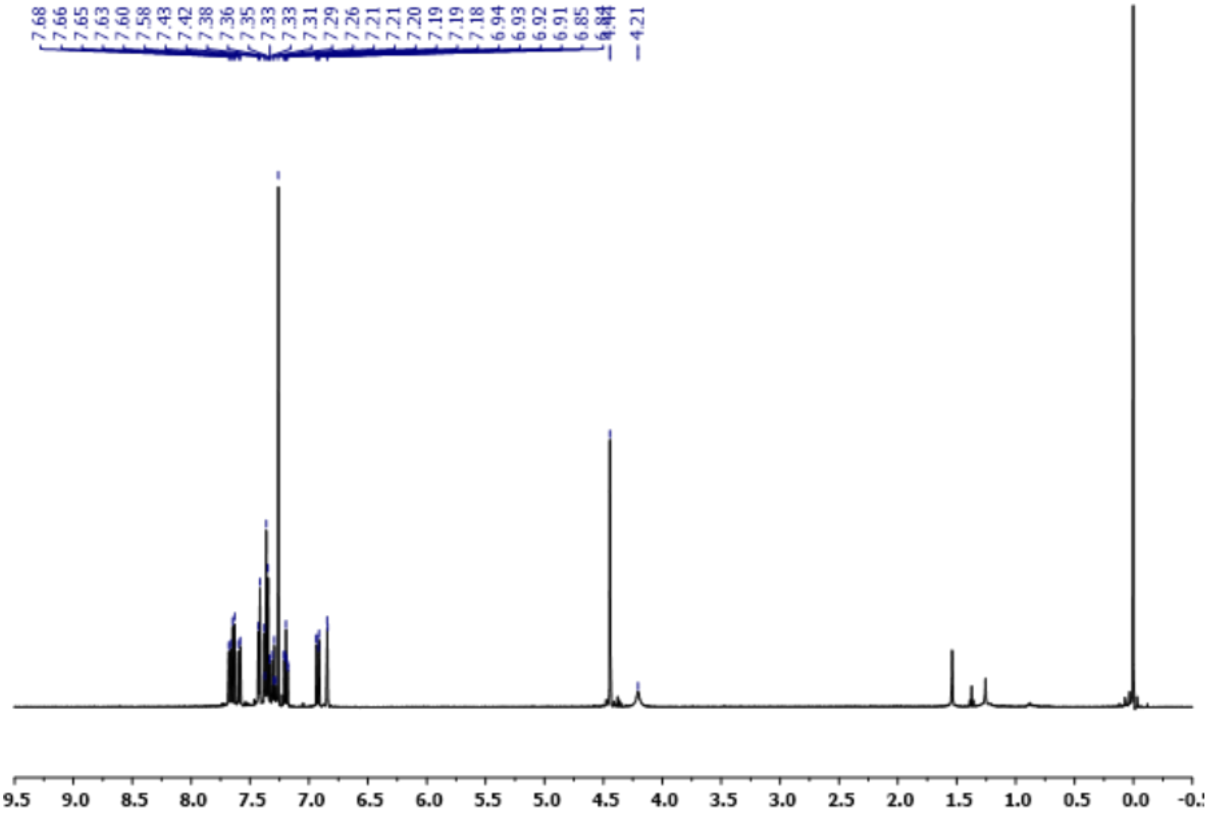

Figure 4.11: ^{1}H NMR (500 MHz, $CDCl_3$) of product 6.

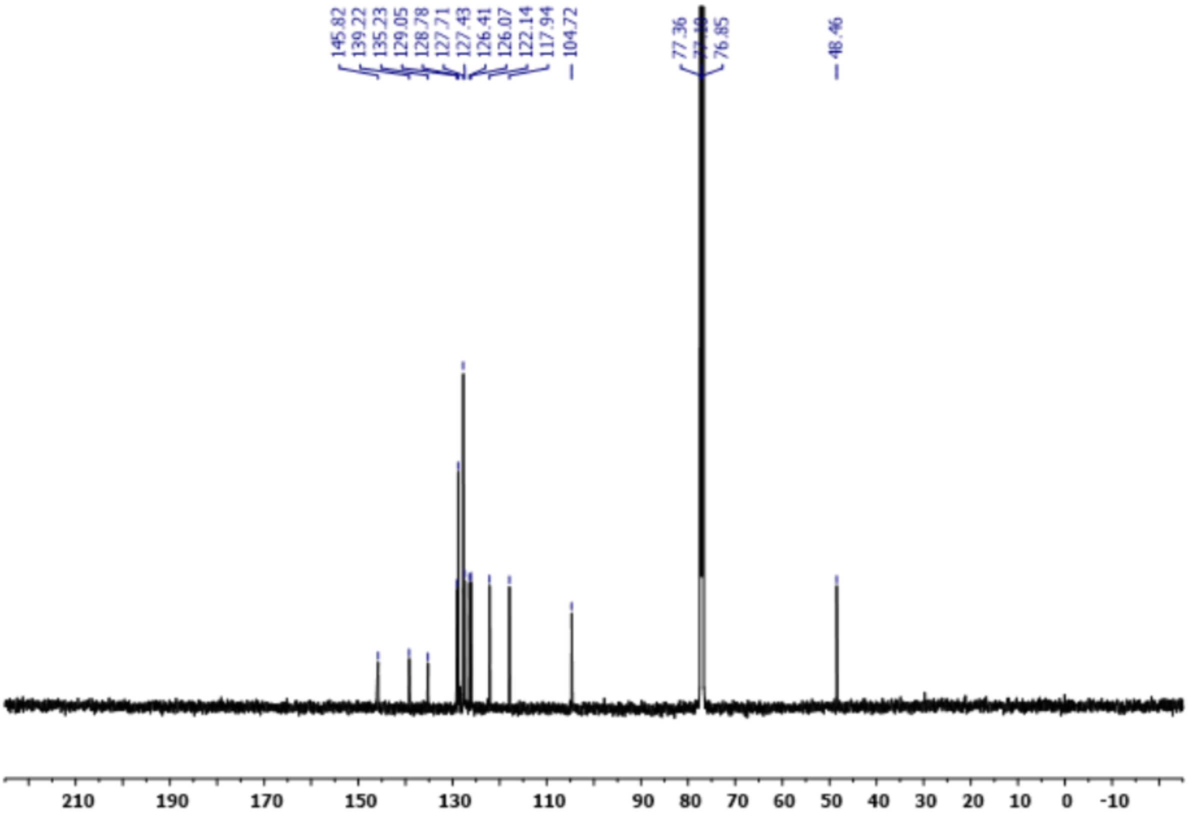

Figure 4.12: ^{1}H NMR (500 MHz, CDCl$_3$) of product 6.

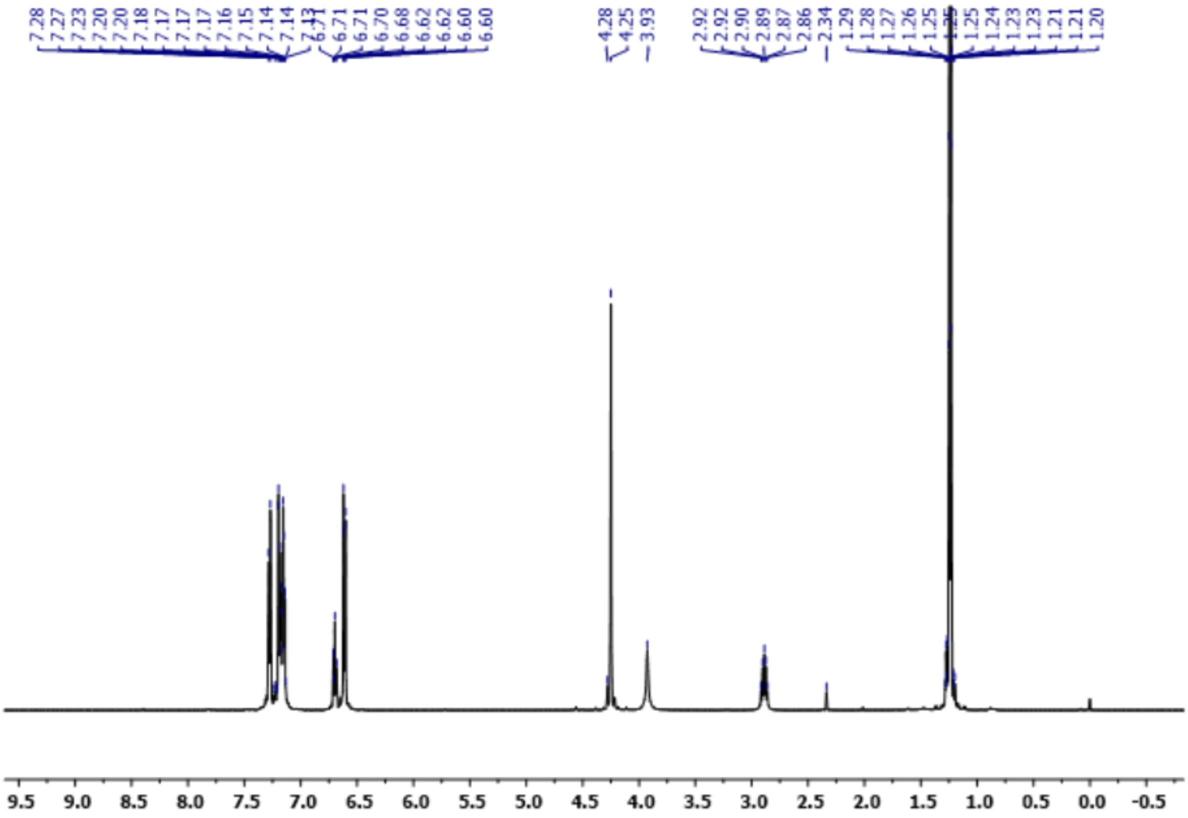

Figure 4.13: ^{1}H NMR (500 MHz, $CDCl_3$) of product 7.

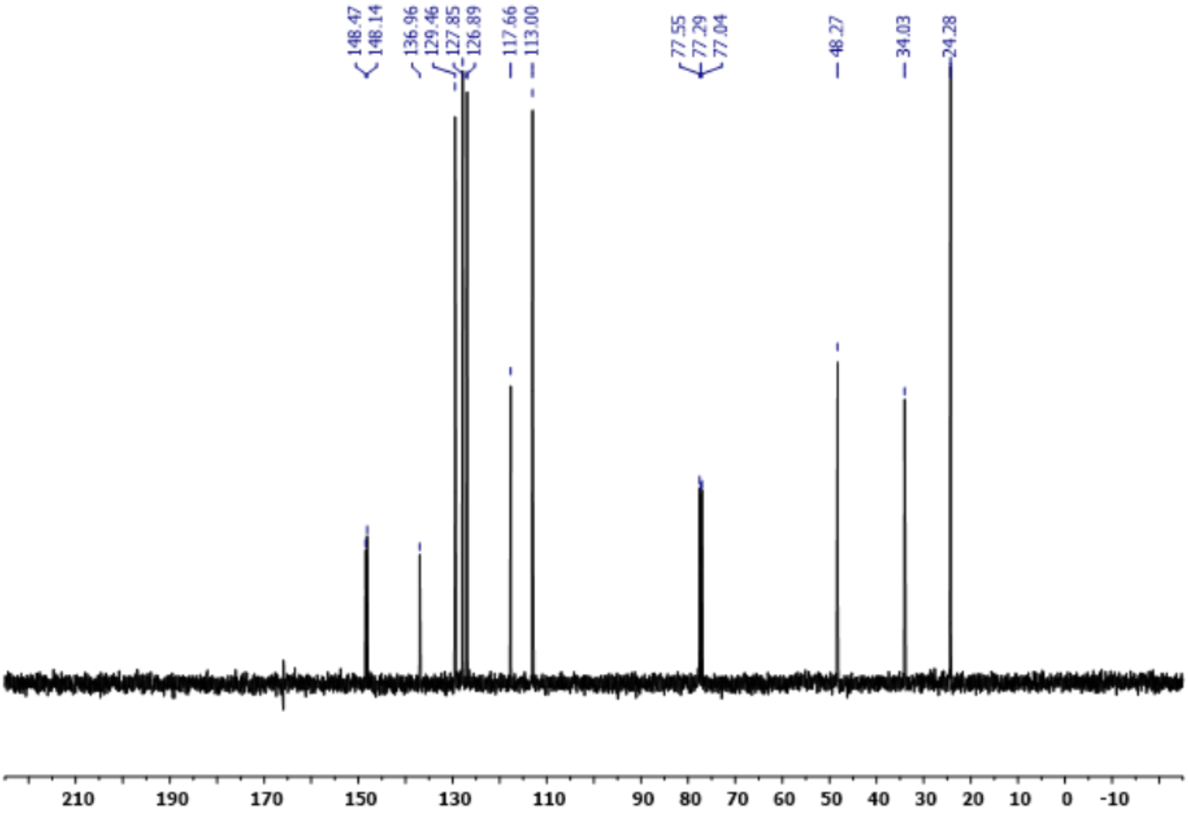

Figure 4.14: ^{13}C NMR (125 MHz, $CDCl_3$) of product 7.

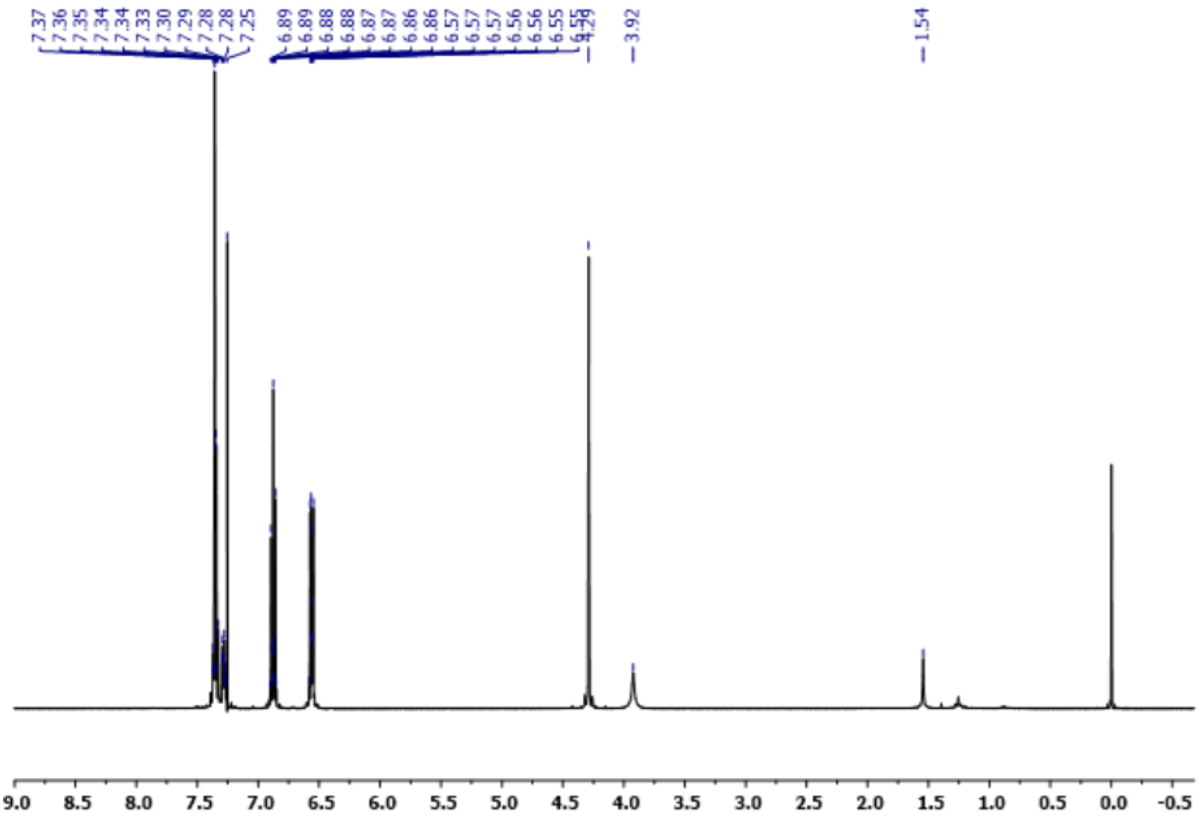

Figure 4.15: ^{1}H NMR (500 MHz, $CDCl_3$) of product 8.

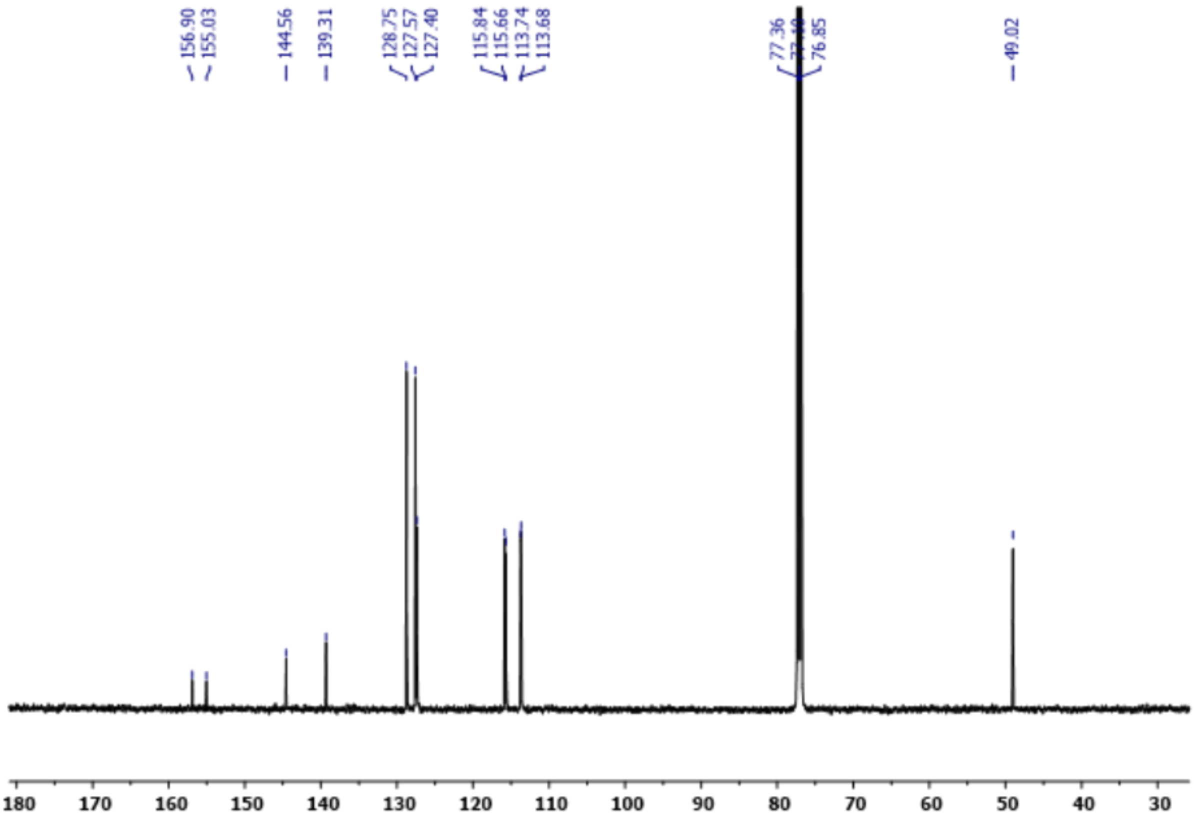

Figure 4.16: ^{13}C NMR (125 MHz, CDCl$_3$) of product 8.

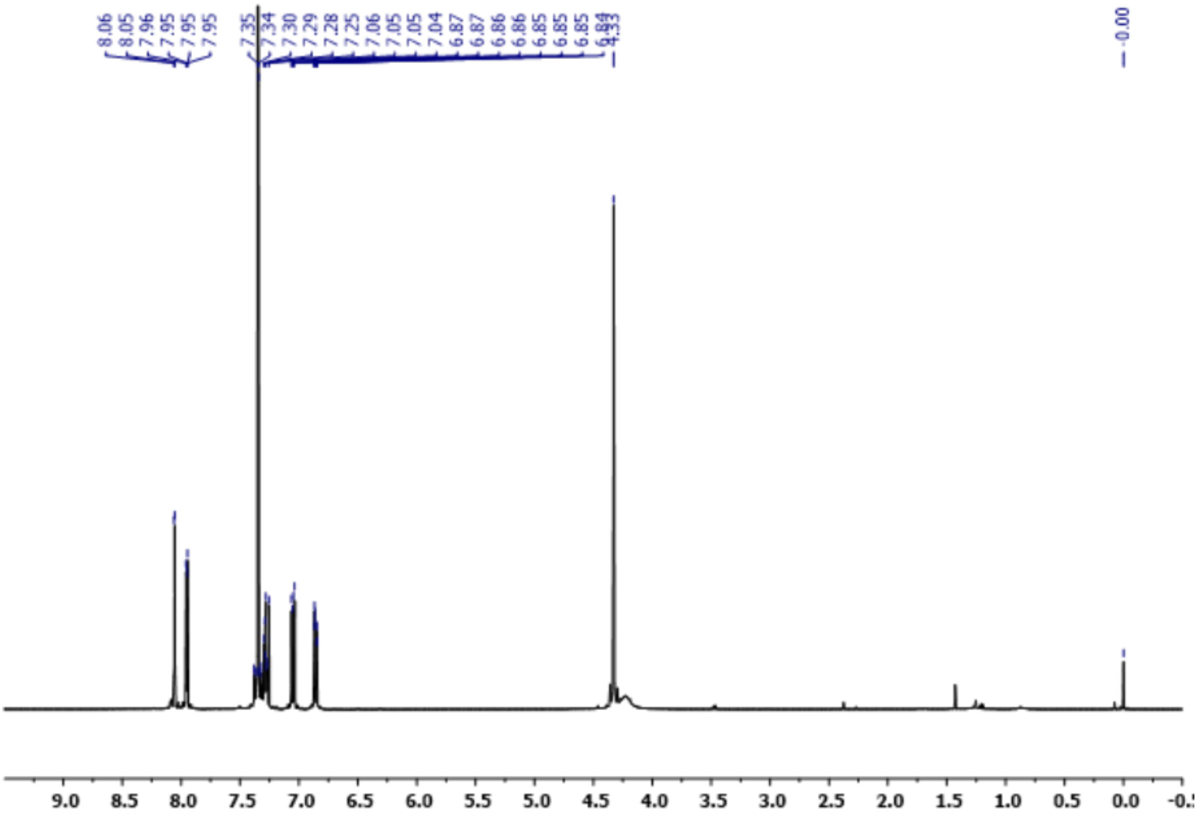

Figure 4.17: ^{1}H NMR (500 MHz, $CDCl_3$) of product 9.

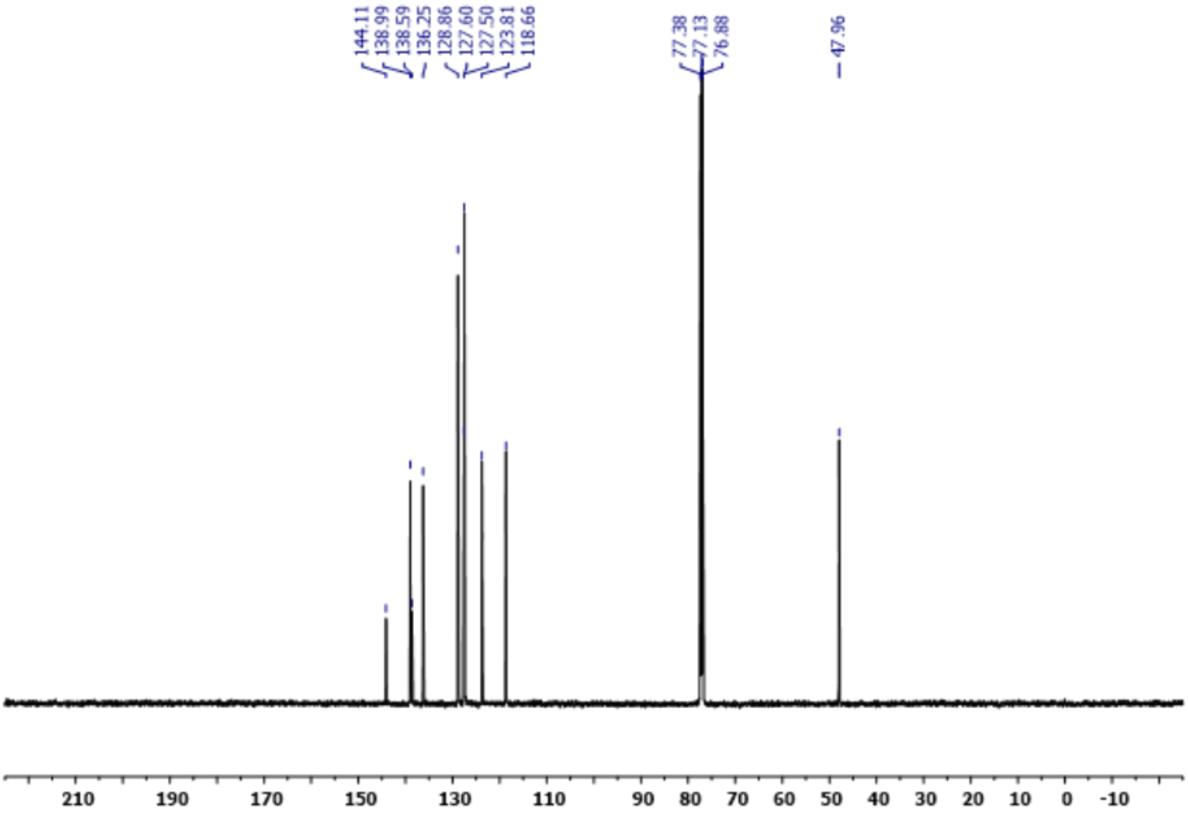

Figure 4.18: ^{13}C NMR (125 MHz, $CDCl_3$) of product 9.

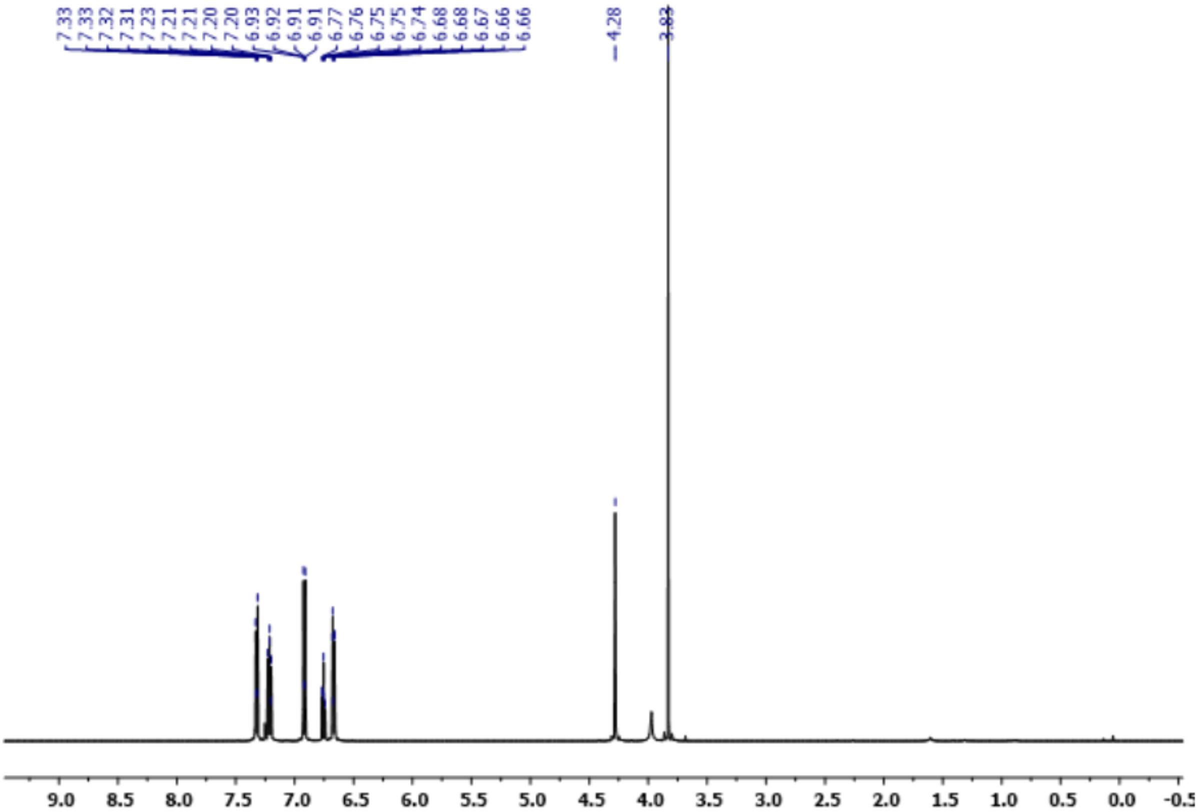

Figure 4.19: ^{1}H NMR (500 MHz, $CDCl_3$) of product 10.

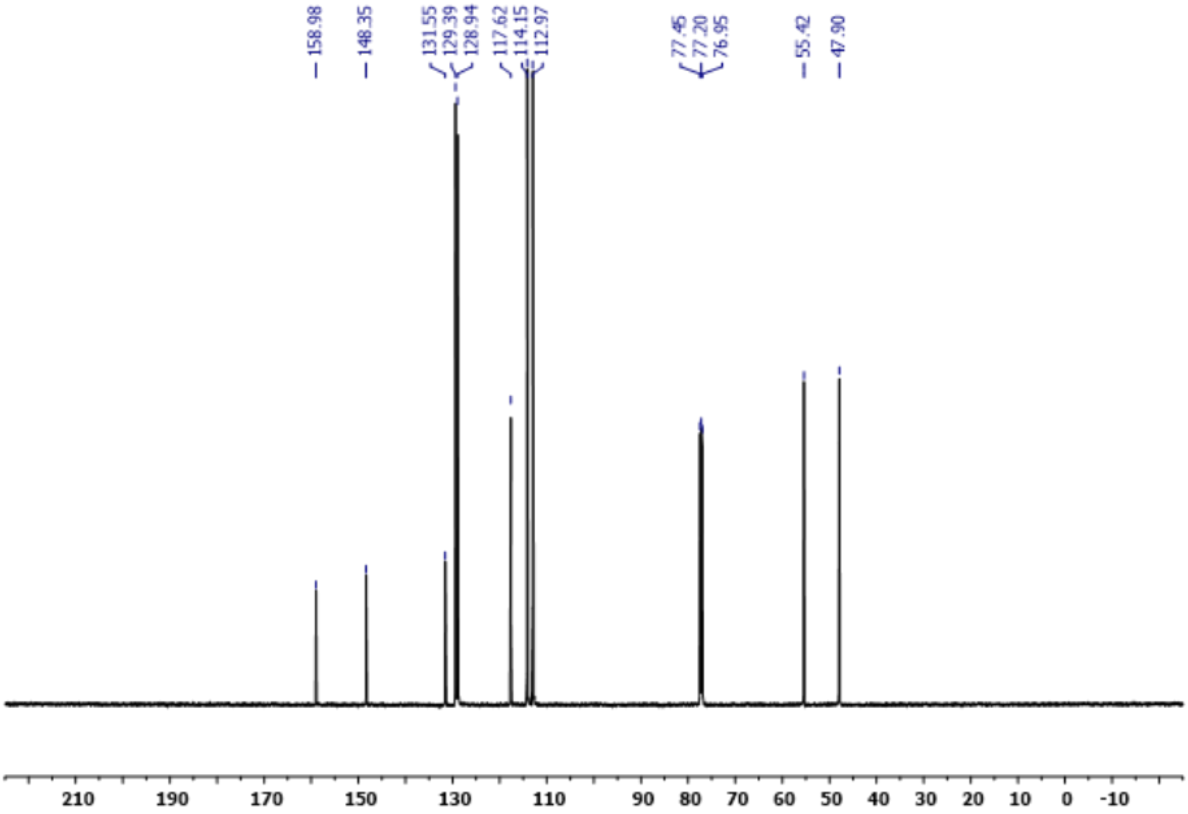

Figure 4.20: ^{13}C NMR (125 MHz, CDCl$_3$) of product 10.

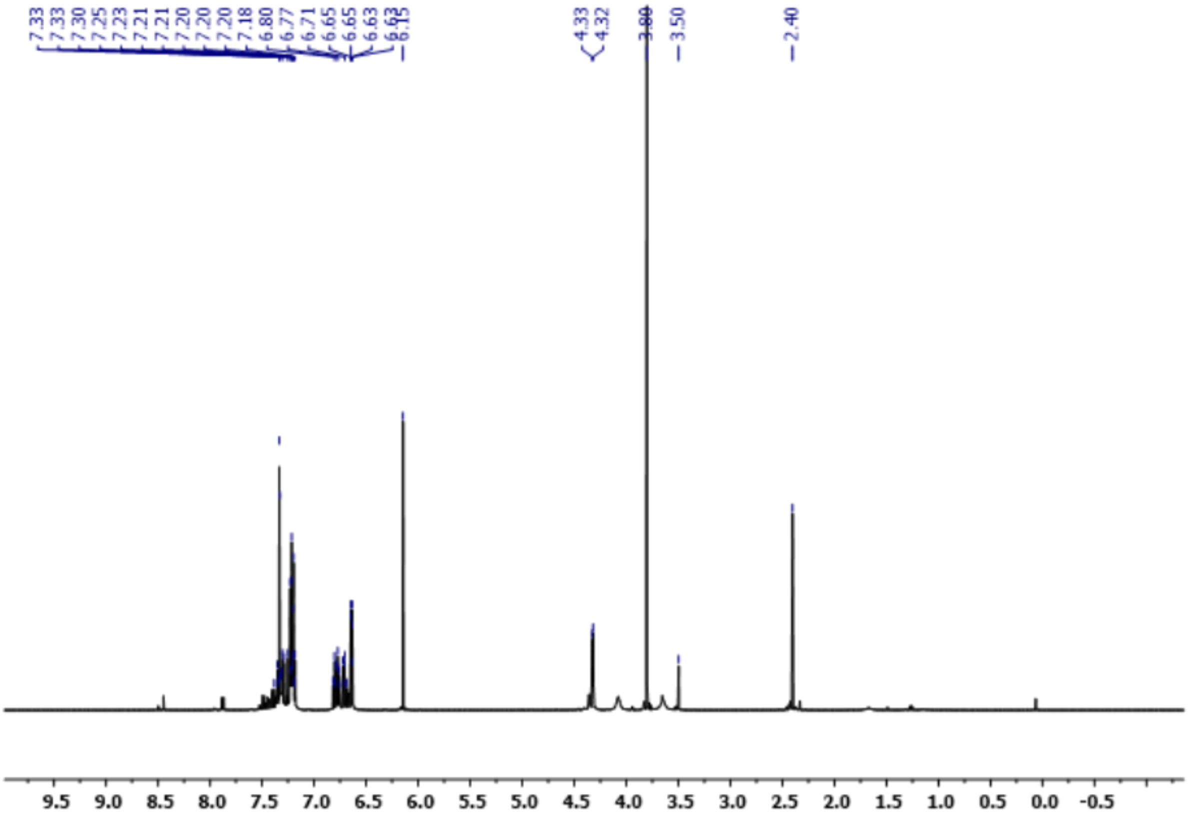

Figure 4.21: ^{1}H NMR (500 MHz, $CDCl_3$) of product 11.

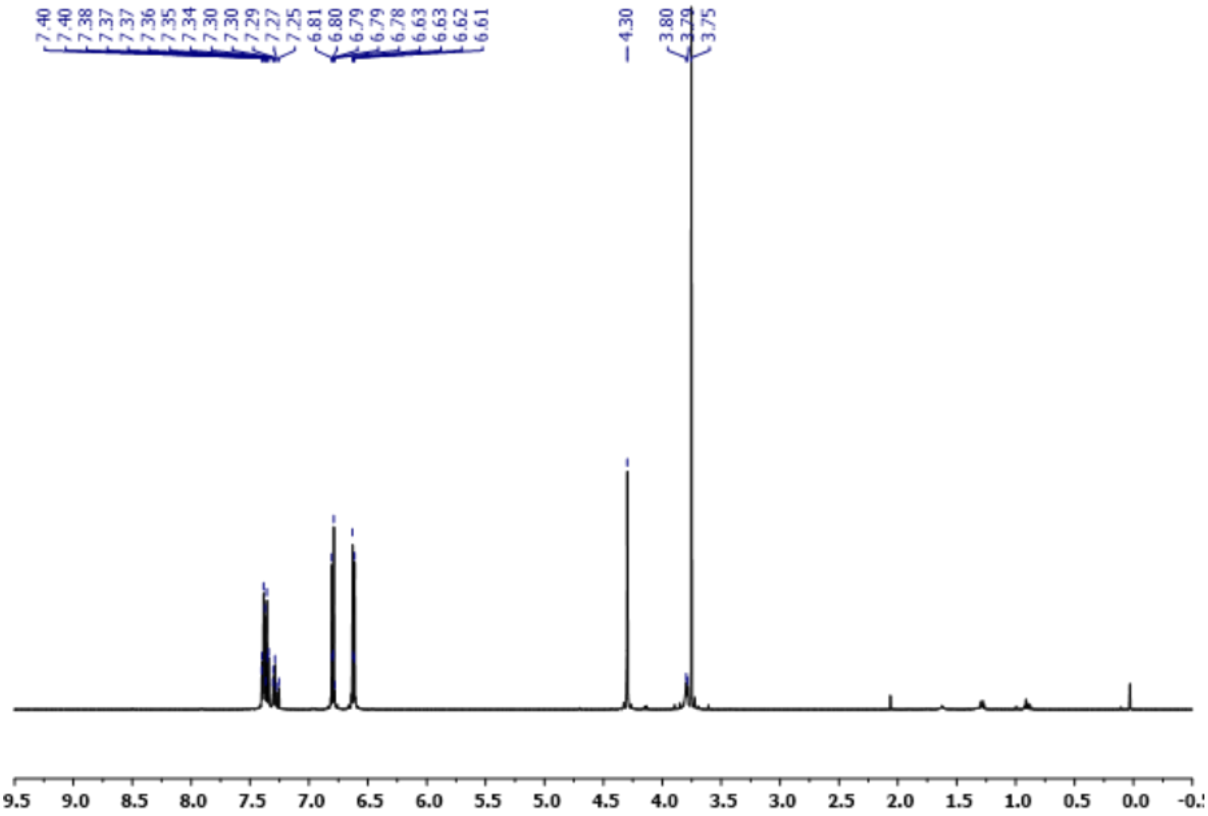

Figure 4.22: ^{1}H NMR (500 MHz, $CDCl_3$) of product 13.

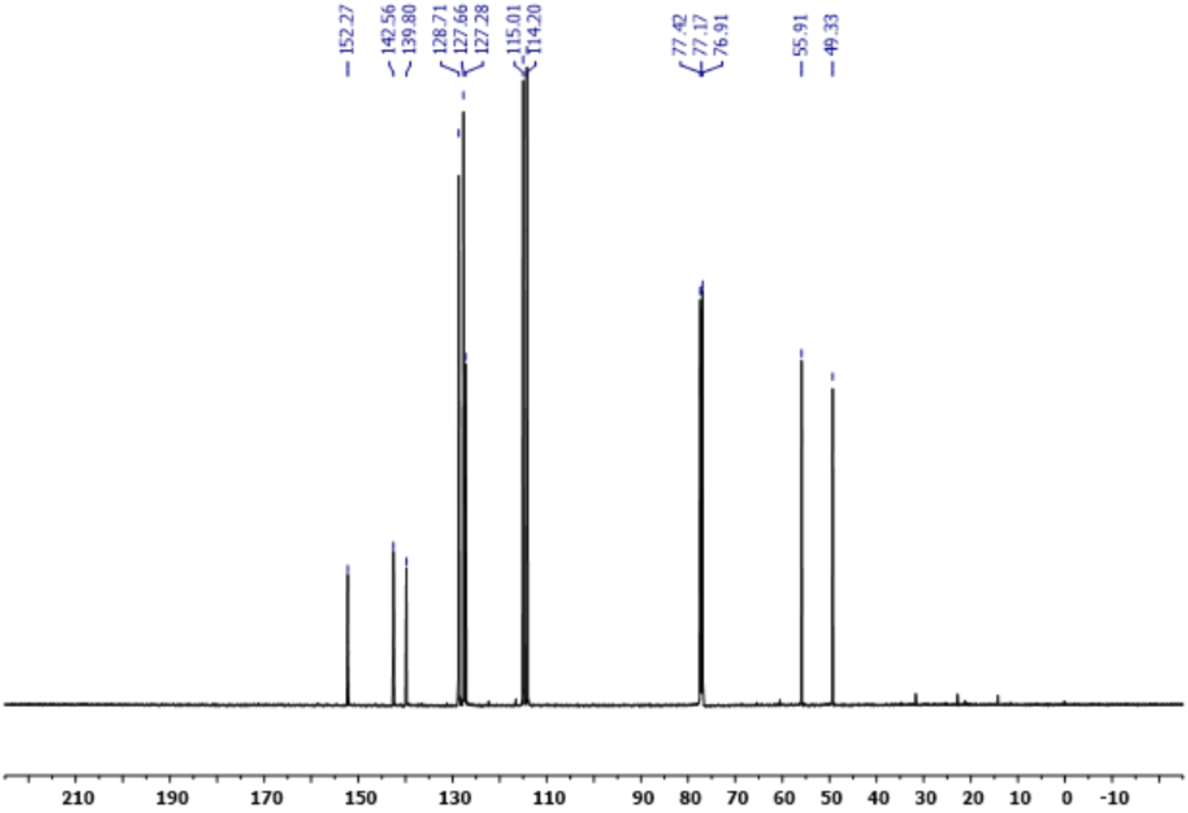

Figure 4.23: ^{13}C NMR (125 MHz, $CDCl_3$) of product 13.

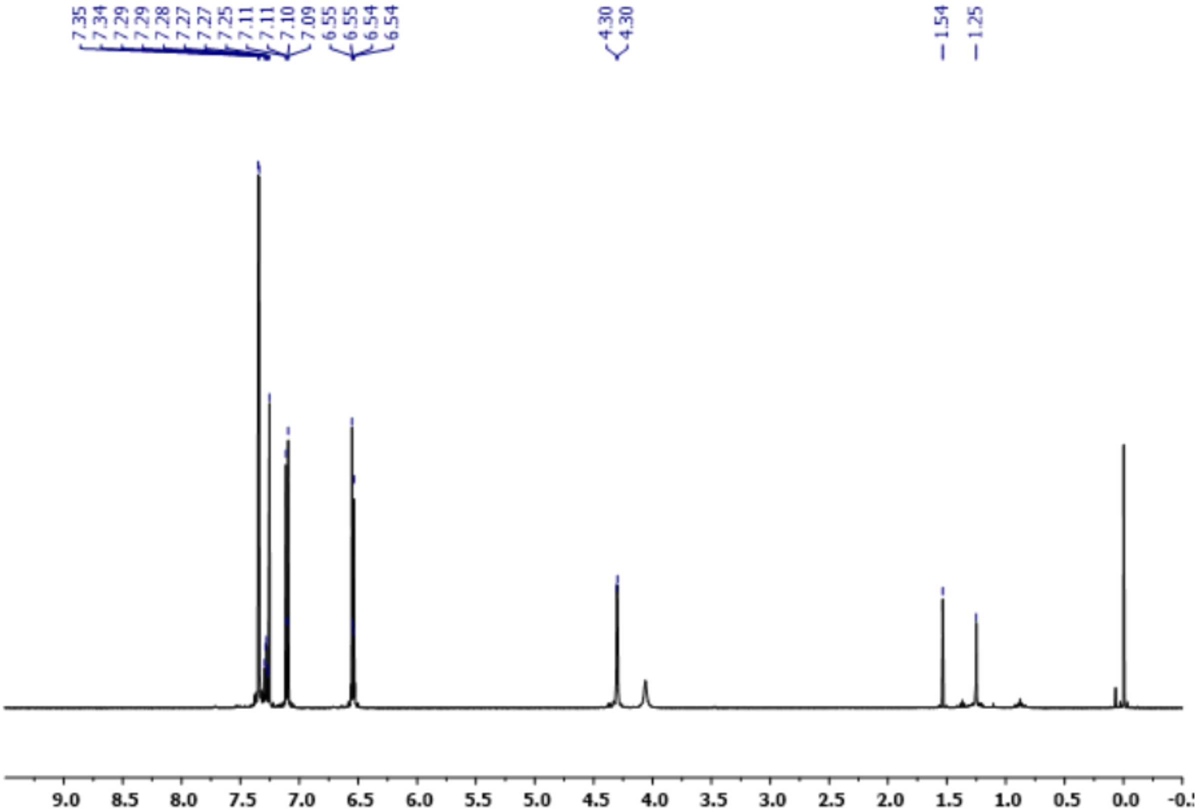

Figure 4.24: ^{1}H NMR (500 MHz, $CDCl_3$) of product 14.

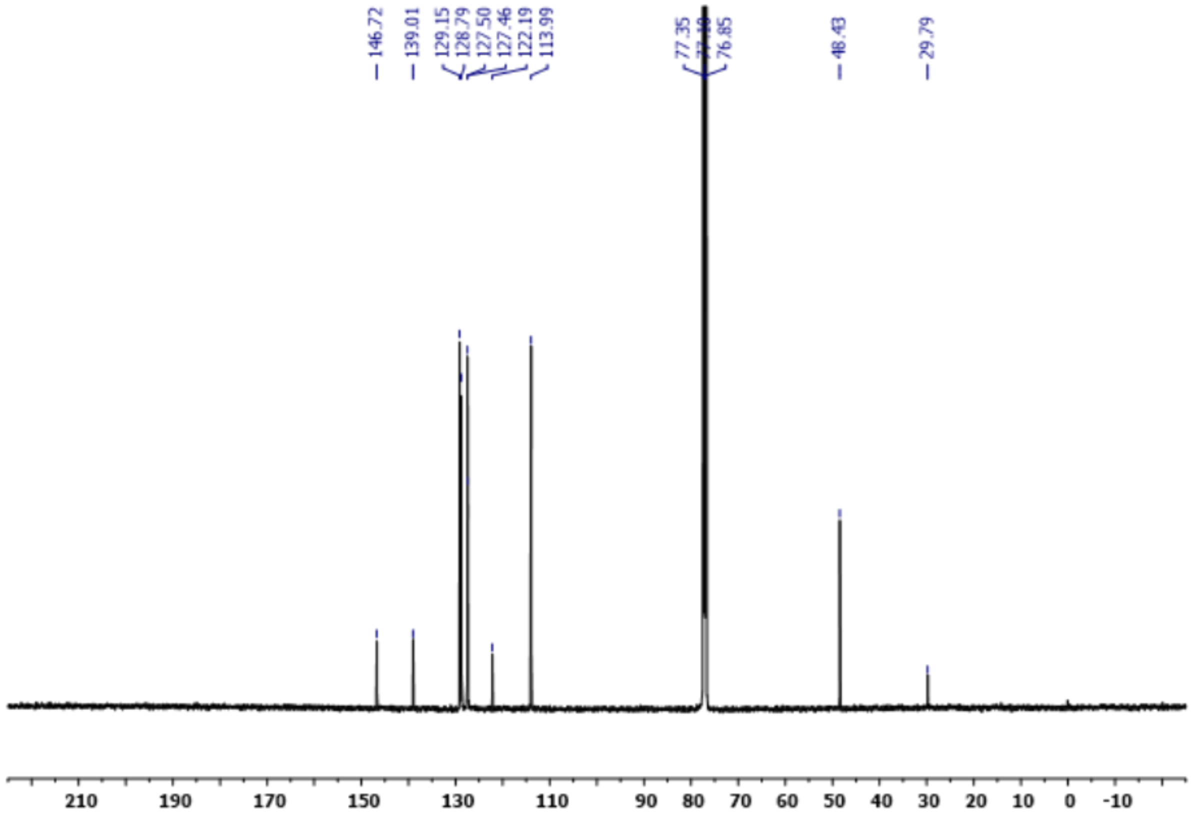

Figure 4.25: ^{13}C NMR (125 MHz, CDCl$_3$) of product 14.

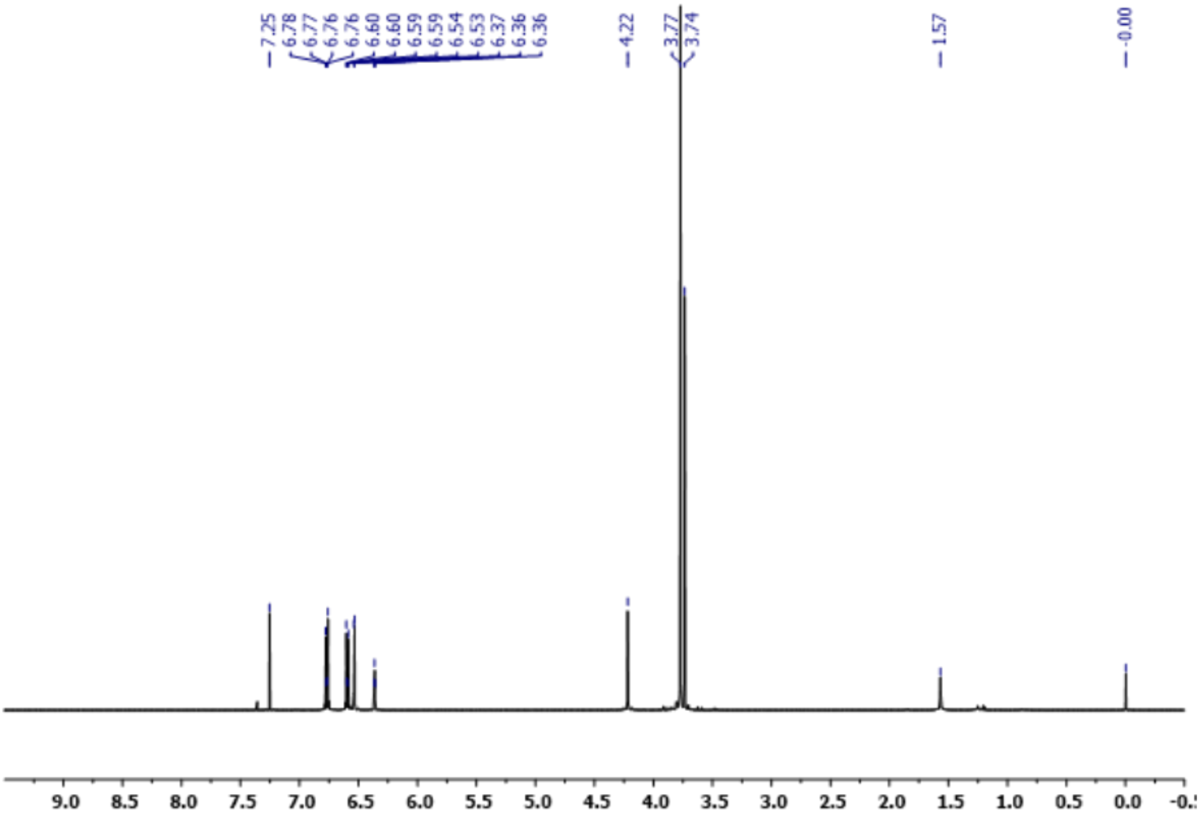

Figure 4.26: ^{1}H NMR (500 MHz, $CDCl_3$) of product 16.

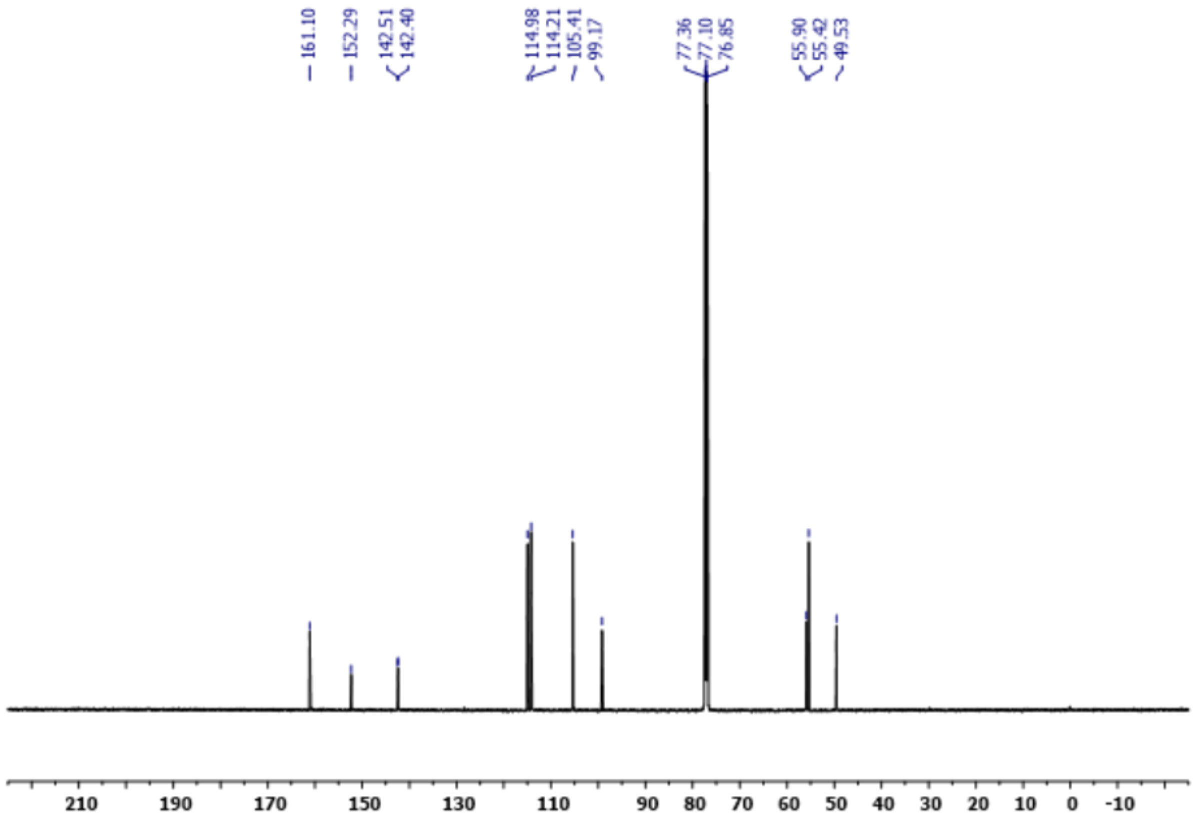

Figure 4.27: ^{13}C NMR (125 MHz, CDCl$_3$) of product 16.

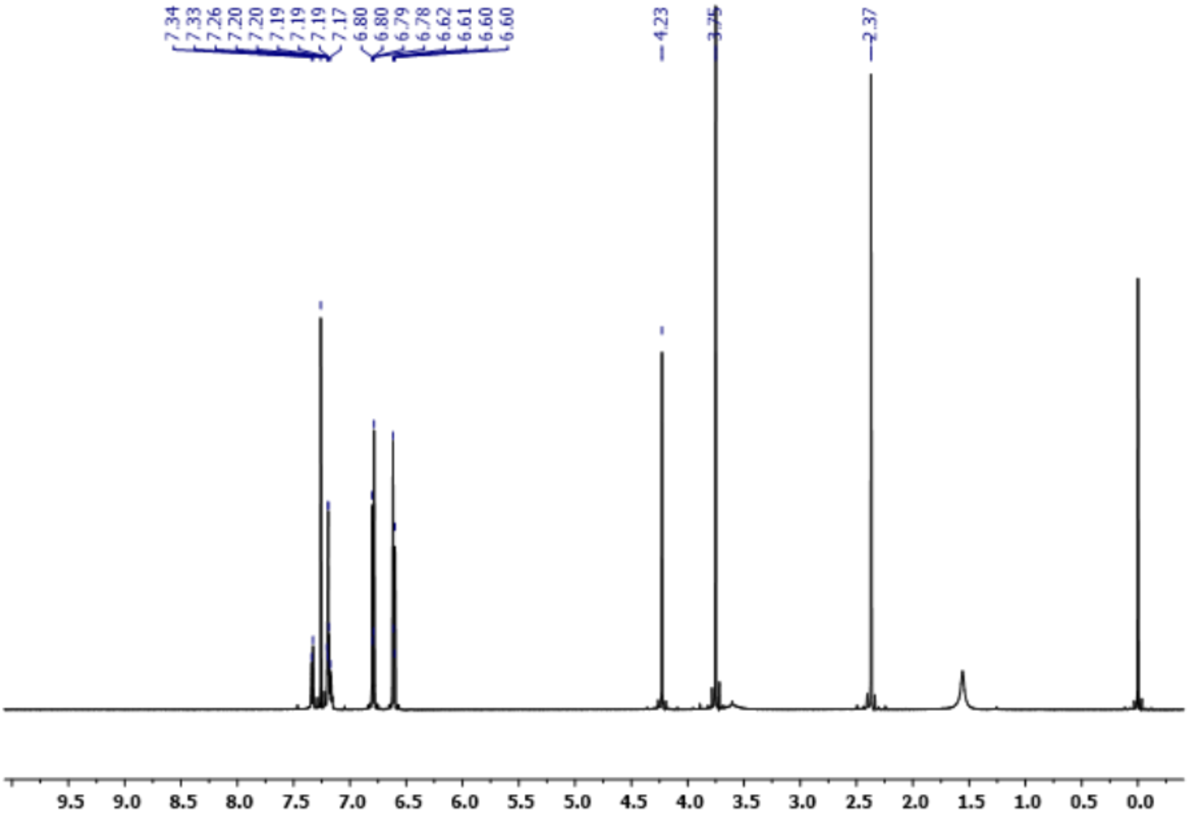

Figure 4.28: ^{1}H NMR (500 MHz, $CDCl_3$) of product 17.

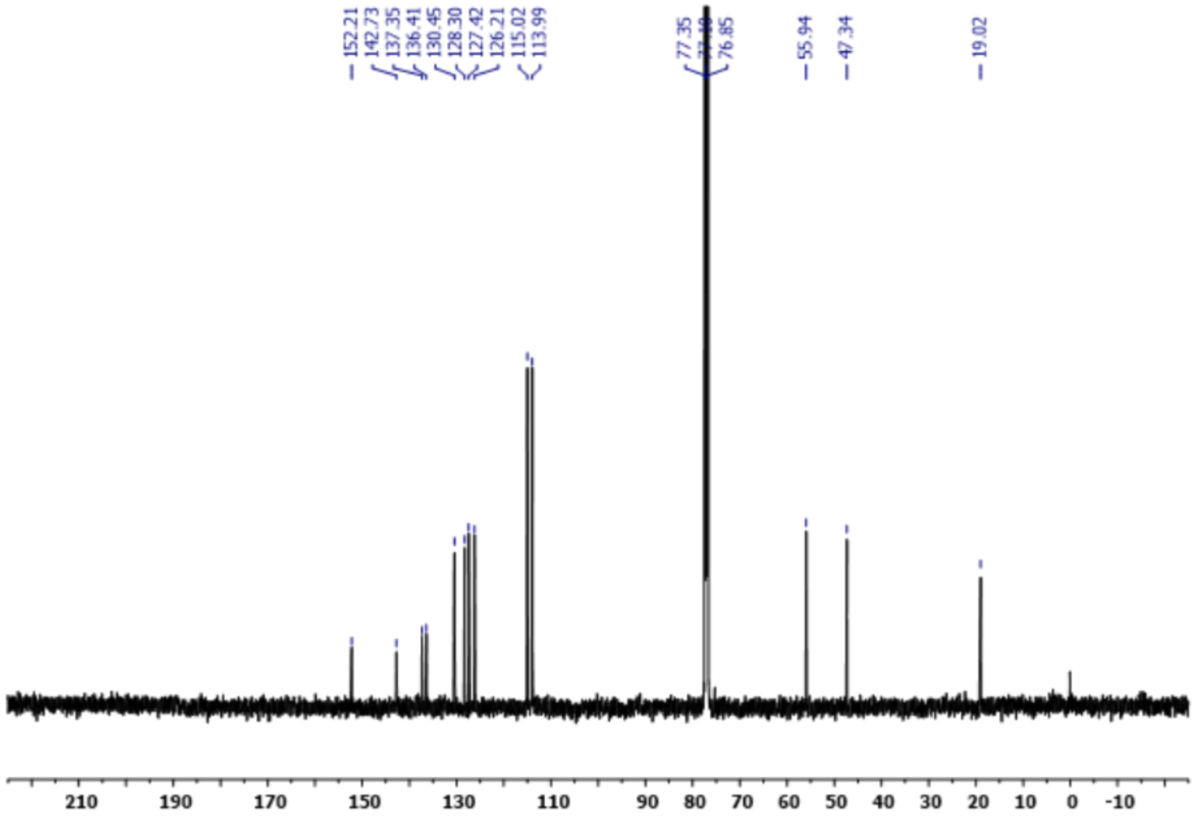

Figure 4.29: ^{13}C NMR (125 MHz, $CDCl_3$) of product 17.

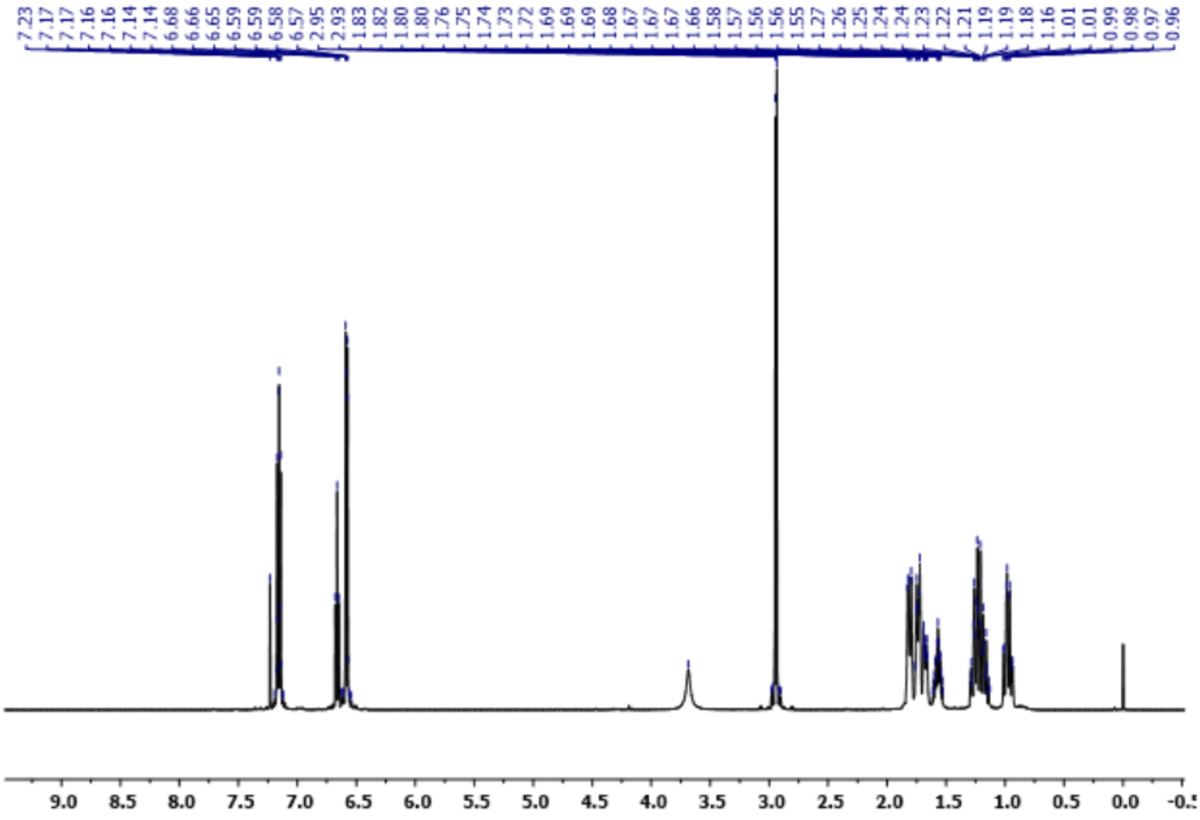

Figure 4.30: ^{1}H NMR (500 MHz, CDCl$_3$) of product 18.

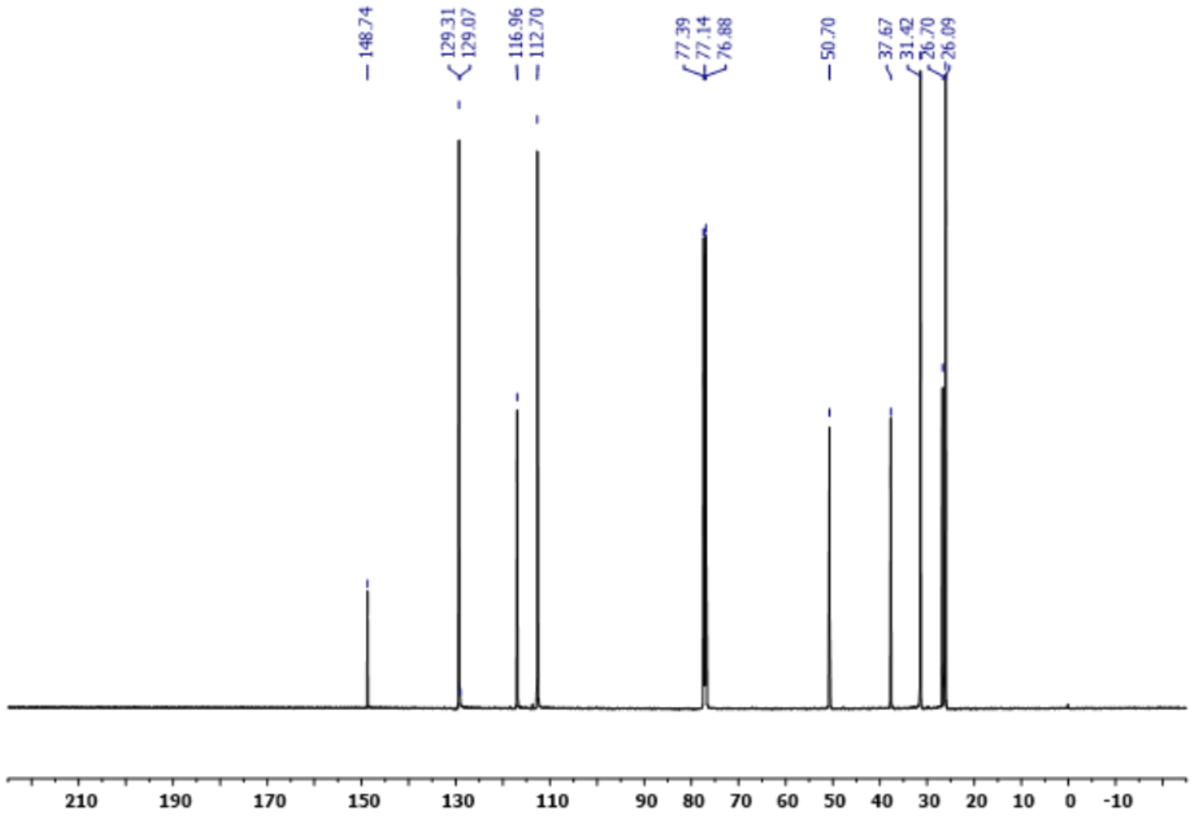

Figure 4.31: ^{13}C NMR (125 MHz, CDCl$_3$) of product 18.