HETEROGENEOUS COPPER AND PALLADIUM CATALYSTS FOR CROSS-COUPLING REACTIONS

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บทคัดย่อ

ชื่อเรื่อง : ตัวเร่งปฏิกิริยาวิวิธพันธุ์ทองแดงและแพลเลเดียมสำหรับปฏิกิริยาคู่ควบ
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ศัพท์สำคัญ : ตัวเร่งปฏิกิริยาวิวิธพันธุ์ ปฏิกิริยาคู่ควบ เฟอร์ไรต์ ซูซูกิ-มิยาอูระ โซโนกาชิระ

งานวิจัยนี้มีวัตถุประสงค์เพื่อเตรียมตัวเร่งปฏิกิริยาแบบวิวิธพันธุ์คอปเปอร์และแพลเลเดียมและประยุกต์ใช้สำหรับเร่งปฏิกิริยาคู่ควบ ตัวเร่งนาโนคอปเปอร์และนาโนคอปเปอร์ (I) ออกไซด์ (**CuNPs** และ **Cu_2ONPs**) สังเคราะห์ขึ้นโดยปฏิกิริยารีดักชันอย่างง่าย และสำหรับตัวเร่งแพลเลเดียม (II) (**Fe_3O_4-DOPA-Pd** และ **CAT1**) เตรียมโดยซัพพอร์ตแพลเลเดียม (II) บนอนุภาคนาโนเฟอร์ไรต์ที่ปรับผิวหน้าด้วยโดพามีนและลิแกนด์คาร์บีนตามลำดับ การทดลองพบว่า **CuNPs** และ **Cu_2ONPs** มีประสิทธิภาพในการเร่งปฏิกิริยาสร้างพันธะคาร์บอน-ออกซิเจนและ คาร์บอนไนโตรเจนเพื่อสังเคราะห์สารประกอบไดเอริลอีเทอร์และเอริลอิมมิดาโซล นอกจากนั้นงานวิจัยนี้ยังประสบผลสำเร็จในการพัฒนาปฏิกิริยาซูซูกิ-มิยาอูระและปฏิกิริยาโซโนกาชิระซึ่งใช้ตัวเร่งแบบวิวิธพันธุ์ของแพลเลเดียมเพื่อสังเคราะห์สารประกอบไบเอริลและไดเอริลอะเซทิลีนที่หลากหลายโดยใช้ตัวเร่ง **Fe_3O_4-DOPA-Pd** และ **CAT1** ตามลำดับ ข้อได้เปรียบของปฏิกิริยาเหล่านี้ซึ่งใช้ตัวเร่งปฏิกิริยาแบบวิวิธพันธุ์ที่เหนือกว่าการใช้ตัวเร่งปฏิกิริยาแบบเอกพันธุ์คือการแยกตัวเร่งปฏิกิริยาสามารถทำได้ง่ายโดยการกรองหรือใช้แม่เหล็กภายนอก รวมทั้งความสามารถในการนำตัวเร่งกลับมาใช้ใหม่ได้ ซึ่งเป็นสิ่งสำคัญในการพัฒนาวิธีการสังเคราะห์ทางเคมีอินทรีย์ที่ประหยัดและเป็นมิตรกับสิ่งแวดล้อม

ABSTRACT

TITLE : HETEROGENEOUS COPPER AND PALLADIUM CATALYSTS
FOR CROSS-COUPLING REACTIONS
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The purpose of this research was to prepare heterogeneous copper and palladium catalysts and apply for catalyzing cross-coupling reactions. Copper and copper(I) oxide nanoparticle catalysts (**CuNPs** and **Cu_2ONPs**) were synthesized by simple chemical reduction, while palladium(II) catalysts (**Fe_3O_4-DOPA-Pd** and **CAT1**) were prepared by supporting palladium(II) chloride on the surface of dopamine and carbene complex modified nanoferrite, respectively. We demonstrated that **CuNPs** and **Cu_2ONPs** effectively catalyzed C-O and C-N bond formations to synthesize corresponding diarylethers and arylimidazoles. In addition, heterogeneous Pd-catalyzed Suzuki-Miyaura and Sonogashira reactions were successfully developed to synthesize various kinds of biaryls and diarylacetylenes using **Fe_3O_4-DOPA-Pd** and **CAT1** catalyst, respectively. The advantages of these heterogeneous catalysis protocols over the traditional homogeneous catalysis are their simple catalyst separation by filtration or external magnet and reusability that are important for developing economic and green organic synthesis methods.

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LIST OF ABBREVIATIONS

ABBREVIATIONS	**FULL WORD**
Bipy	2,2'-bipyridine
DMF	*N,N*-dimethylformamide
XRD	X-ray diffraction spectroscopy
DMSO	Dimethyl sulfoxide
NMP	*N*-methyl-2-pyrrolidone
THF	Tetrahydrofuran
EtOH	Ethanol
MeOH	Methanol
H_2O	Water
Phen	1,10-phenanthroline
PPh_3	Triphenyl phosphine
BSC	Benzenesulfonyl chloride
SDS	Sodium dodecyl sulfate
PEG	Polyethylene glycol
NHCs	*N*-heterocyclic carbenes ligand
GC	Gas chromatography
SEM	Scanning electron microscopy
NMR	Nuclear magnetic resonance spectroscopy
g	Gram
^{o}C	Degree Celsius
Lig	Ligand
mol%	Percent by mole
l	Liter
cm	Centimeter
eq	Equivalent
JCPDS	Joint Committee on Powder Diffraction Standards

LIST OF ABBREVIATIONS (CONTINUED)

ABBREVIATIONS	**FULL WORD**
mmol	Millimole
NPs	Nanopaticles
h	Hours
RT	Room temperature
PMMA	Poly(methyl methacrylate)
DOPA, DA	Dopamine
ZnO	Zine oxide
Fe_3O_4	Ferrite
Cu	Copper
CuI	Copper(I) iodide
CuO	Copper(II) oxide
Cu_2O	Copper(I) oxide
CuNPs	Copper(0) nanoparticle
Cu_2ONPs	Copper(I) oxide nanoparticle
Fe_3O_4-DOPA-Pd	Ferrite - dopamine - palladium(II)
CAT1	Ferrite - *N*-heterocarbenecycle-palladium(II)

CHAPTER 1

INTRODUCTION

Metal-catalyzed cross-coupling reactions have been an important tool for organic chemists and are now widely utilized in both academic and industrial applications allowing the syntheses of various kinds of compounds through the C-C and C-heteroatom bond formations as shown in Figure 1.1 [1-2].

$$R{-}m + R'{-}X \xrightarrow{\text{catalyst [M]}} R{-}R'$$

m = Li (Murahashi)
Mg (Kumada-Tamao, Corriu)
B (Suzuki-Miyaura)
Al (Nozaki-Oshima, Negishi)
Si (Tamao-Kumada, Hiyama-Hatanaka)
Zn (Negishi)
Cu (Normant)
Zr (Negishi)
Sn (Migita-Kosugi, Stille), etc.

[M]= Fe, Ni, Cu, Pd, Rh, etc.
X = I, Br, Cl, OTf

Figure 1.1 Definition of cross-coupling reaction [3]

During the last decade, the development of cross-coupling chemistry has shown significant growth as can be seen from the greatly increasing numbers of publications and patents. After decades of intensive research, Heck, Negishi, and Suzuki reactions are the most well-known palladium-catalyzed reactions that led to their Nobel Prize in Chemistry in 2010 [4]. A key reason for the impressive development of palladium-catalyzed reactions is the feasibility that a wide range of substrates and many functional groups are highly ensured due to the mild reaction conditions which is convenient for the total synthesis of complex drug molecules. Furthermore, the starting materials are absolutely available, stable and sustainable [5].

The catalytic processes are essential for the efficient and sustainable synthesis of organic compounds and represent one of the economically and ecologically impacting technologies for laboratory and industrial scale synthesis [6]. Recently, it has been an important issue for chemists to develop the more environmentally friendly methods under green chemistry

Table 1.1 Comparison of homogeneous and heterogeneous catalysts properties

Properties	Homogeneous	Heterogeneous
catalyst recovery	difficult and expensive	easy and cheap
thermal stability	poor	good
selectivity	excellent/good-single active site	good/poor-multiple active sites

Traditional catalysts are mostly homogeneous which has major drawback in terms of separation and reusability. In contrast, heterogeneous catalysis has increasingly attracted attention especially in the pharmaceutical and medicinal materials syntheses [7]. Many strategies have been designed and developed to synthesize heterogeneous catalysts [8-14].

Our group has been interested in preparation of heterogeneous catalysts such as metal and metal oxide nanoparticles and catalysts supported on magnetic materials and testing their catalytic activities to the selected cross-coupling reactions. The catalysts of interest are palladium and copper. Palladium catalyst is highly efficient catalyst, while copper has lower catalytic activity but due to its economic cost, copper is still being used in many large scale industrial syntheses. Therefore, in this research we reported the synthesis of heterogeneous copper and copper(I) oxide catalysts and their applications in C-O and C-N bond formations. In addition, palladium catalysts supported on magnetic materials were prepared and applied as reusable catalyst for Suzuki-Miyaura and Sonogashira coupling reaction.

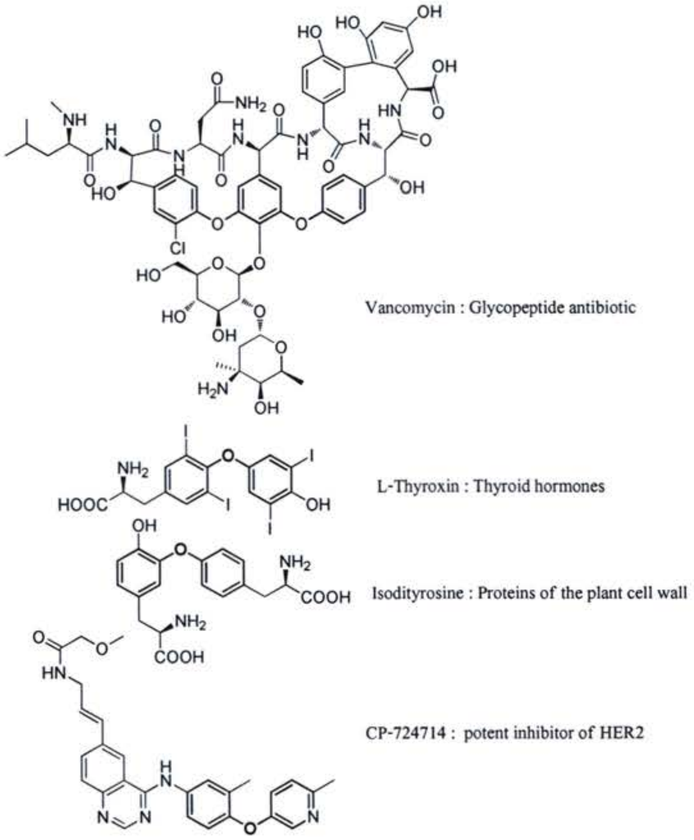
In this thesis, the research work has been derived in the following sequence. Chapter 2 and Chapter 3 reported the preparation and application of heterogeneous copper catalysts. Copper nanoparticle (CuNPs) and copper oxide nanoparticle (Cu_2ONPs) syntheses and their applications in catalyzing of C-O and C-N bond formations to synthesize diarylethers and arylimidazoles, were illustrated in Chapter 2 and 3, respectively. Next, in Chapter 4 and Chapter 5, heterogeneous palladium catalysts supported on Fe_3O_4 magnetic nanoparticles syntheses and applications in cross-coupling reactions were presented. In Chapter 4, palladium catalyst supported on the surface of dopamine-modified Fe_3O_4 nanoparticles was prepared and applied as catalyst for the Suzuki-Miyaura coupling reaction in aqueous system that the catalyst can be simply separated and reused with only slightly loss of activity. Then, in Chapter 5, *N*-heterocyclic carbene ligand (NHCs) modified-Fe_3O_4 nanoparticles was synthesized and used for the Sonogashira cross-coupling reaction. The catalyst complex exhibited high stability, easy handling, and recyclability. Finally, Chapter 6 concluded all the work that has been done in this thesis.

CHAPTER 2

SYNTHESIS OF DIARYLETHERS USING HETEROGENEOUS COPPER-CATALYZED REACTION

2.1 Introduction

Diarylethers are important moieties found in many biologically active compounds such as vancomycin, perrottetines [15], L-thyroxine, afatinib (BIBW-2992), CP-724714 [16], pulcherosine and isodityrosine [17] as shown in Figure 2.1. Therefore, during the last few decades, a number of protocols to synthesize diarylethers unit have been reported [15].



Vancomycin : Glycopeptide antibiotic

L-Thyroxin : Thyroid hormones

Isodityrosine : Proteins of the plant cell wall

CP-724714 : potent inhibitor of HER2

Figure 2.1 Examples of diarylethers moieties found in biologically active compounds

2.2 Background

A large number of methods have been developed for C-O bond formations such as alkyl and aryl halide substituted by alkoxy ion, dehydration of alcohols, addition of alcohol to alkene, and cross-coupling reaction [18-20]. Among those protocols, palladium-catalyzed cross-coupling reaction of phenols to aryl halides is effective method that offers good to excellent yields, tolerates various functional groups on substrates, and could easily couple low reactivity substrates such as aryl bromides and chlorides [21-23] (Figure 2.2). However, for the large industrial scale applications, the use of expensive and air-sensitive palladium catalysts and phosphine ligands limit the attractiveness of this method.

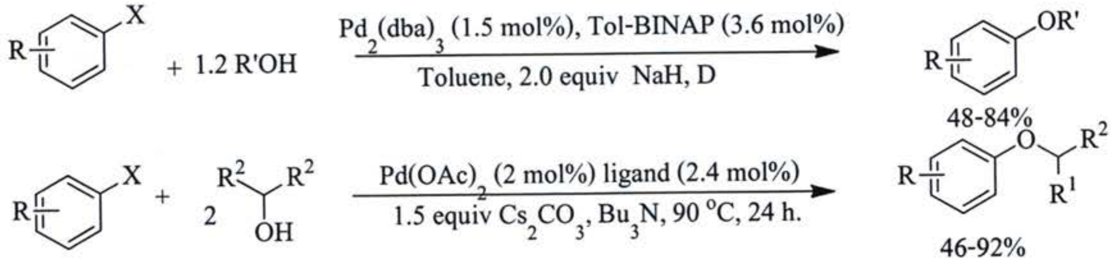


Figure 2.2 Examples of palladium-catalyzed C-O bond formations [21-23]

Copper is one of the attractive catalysts of choice as an alternative to palladium due to its economic point of view. Various kinds of copper catalysts have been used to form carbon-carbonand carbon-heteroatom bonds such as C-O, C-N, and C-S bonds [19, 24]. Examples of copper-catalyzed C-O bond formation reactions as shown in Figure 2.3.

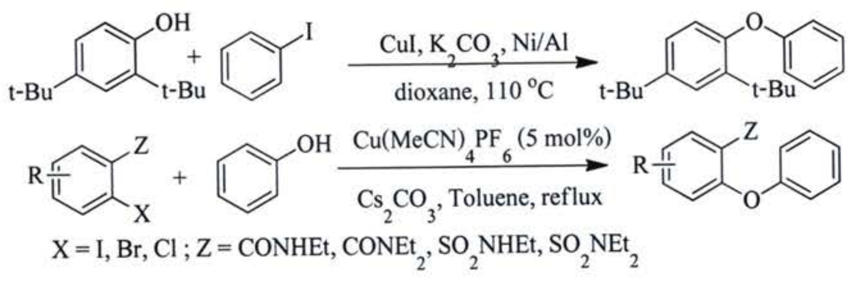


Figure 2.3 Examples of copper-catalyzed C-O bond formations [19, 24]

Since the use of homogeneous catalysts has some drawbacks such as the difficulty to separate heavy metal catalyst and the contamination of the metal in product especially medical and pharmaceutical materials, therefore the search for effective heterogeneous catalysts is still challenging [25]. Many heterogeneous catalysts based on copper have been developed for applications in synthesis of diarylethers such as copper, copper(II) oxide, and copper(II) oxide supported on magnetite and alumina as shown Figure 2.4 [26-33].

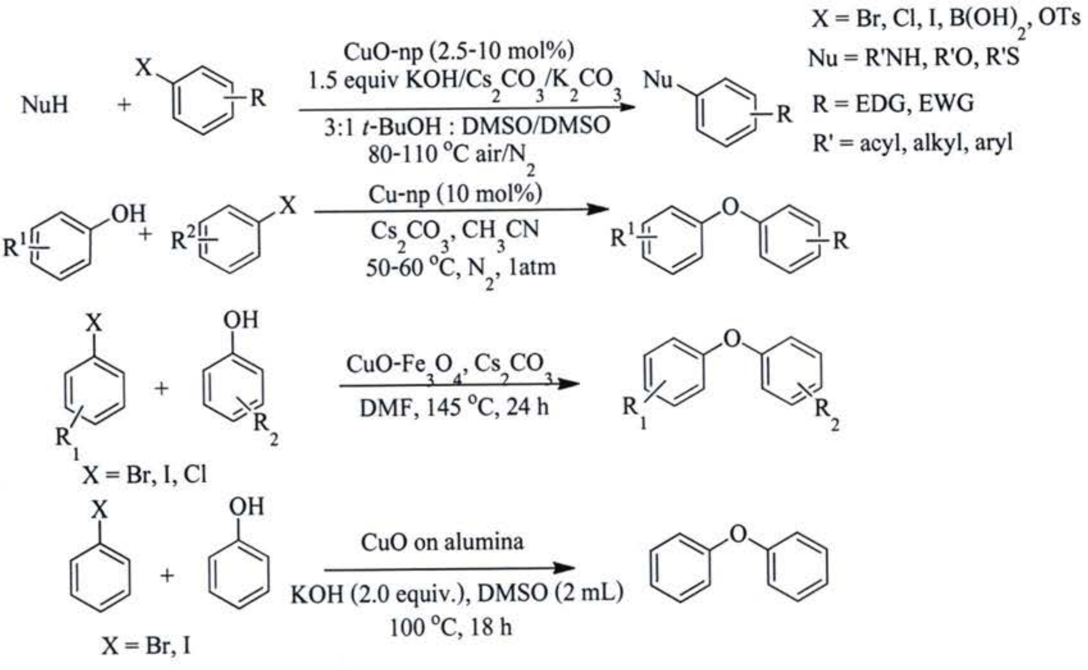


Figure 2.4 Examples of heterogeneous copper-catalyzed C-O bond formation [26, 29, 33]

In this work, we reported the preparation and application of copper nanoparticle to catalyze cross-coupling reaction of phenol and aryl halides for the synthesis of diarylethers.

2.3 Results and discussions

2.3.1 Synthesis and characterization of catalysts

Copper nanoparticle (**CuNPs**) used in this experiment was simply prepared by chemical reduction of copper(II) chloride with sodium borohydride in water/methanol mixed solvent having sodium stearate as protecting group at 70°C under ambient atmosphere. Copper(I) oxide nanoparticle (**Cu_2ONPs**) was also prepared by chemical reduction but with milder reducing agent using glucose under basic condition (Figure 2.5).

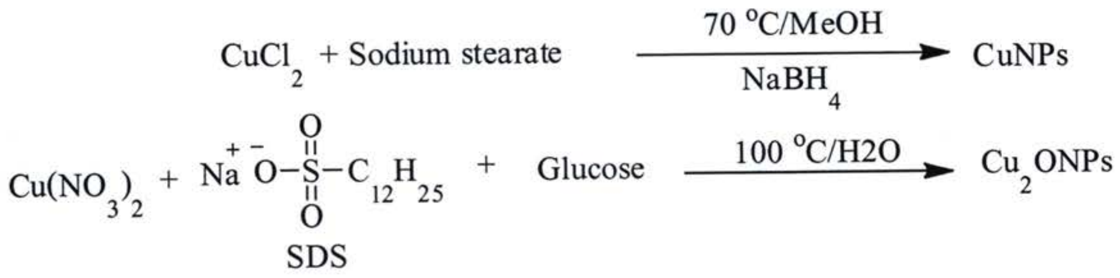


Figure 2.5 Preparations of copper nanoparticle and copper(I) oxide nanoparticle

The synthesized materials were characterized by X-ray diffraction technique. The preferred orientation of the X-ray diffraction patterns of **CuNPs** and **Cu_2ONPs** were illustrated in Figure 2.6. The XRD analysis showed that the major component of synthesized **CuNPs** is Cu with only small amount of Cu_2O, while **Cu_2ONPs** is a mixture of Cu_2O and Cu.

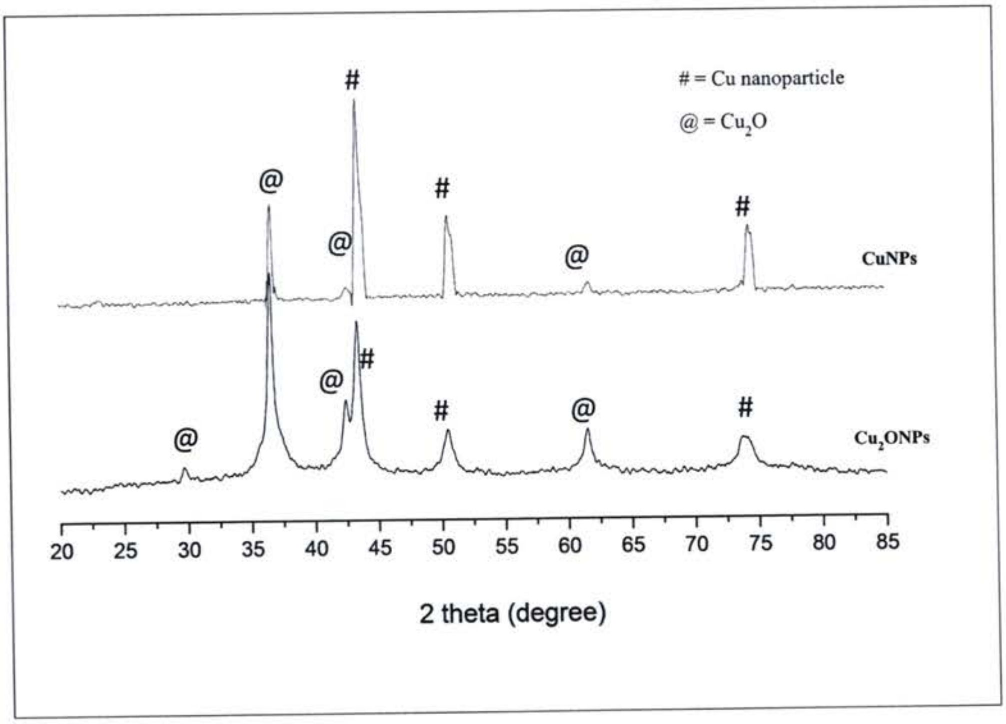
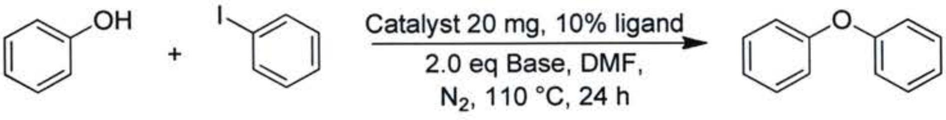


Figure 2.6 X-ray diffractograms of **CuNPs** and **Cu_2ONPs**

2.3.2 Optimizations of the reaction

We started with optimization of the reaction in which iodobenzene and phenol were chosen as model compounds and the results are shown in Table 2.1.

Table 2.1 Optimizations of phenol coupling using copper catalyst



Entry	Catalyst	Base	Ligand	%Yield[a,b]
1	-	Cs_2CO_3	Phen	0
2	**Cu_2ONPs**	Cs_2CO_3	Phen	58
3	**CuNPs**	Cs_2CO_3	Phen	66
4	**CuNPs**	-	Phen	2
5	**CuNPs**	Na_2CO_3	Phen	35
6	**CuNPs**	K_2CO_3	Phen	48
7	**CuNPs**	Cs_2CO_3	Bipy	44
8	**CuNPs**	Cs_2CO_3	PPh_3	41
9	**CuNPs**	Cs_2CO_3	Phen/PPh_3	67
10[c]	**CuNPs**	Cs_2CO_3	Phen	0
11[d]	**CuNPs**	Cs_2CO_3	Phen	24

[a] GC yield with dodecane as an internal standard; [b] conditions: 1.1 mmol phenol, 1.0 mmol iodobenzene, 20 mg **CuNPs**, 10% Phen, 2.0 mmol base, 3 mL dry DMF, 110°C for 24 h, [c] Under air, [d] Toluene as solvent

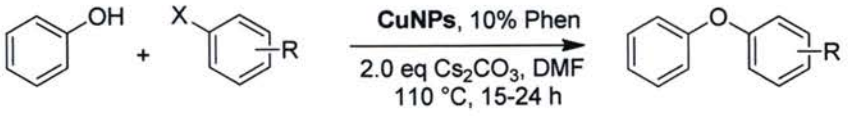
Through the optimizations, we found that copper catalyst is necessary for the cross-coupling of iodobenzene with phenol to synthesize diphenylether. Without catalyst, the reaction could not proceed to give the desired product (entry 1). A comparison between nanocopper(I) oxide (**Cu_2ONPs**) and nanocopper (**CuNPs**) as catalyst has shown that nanocopper (**CuNPs**) is a better catalyst (entries 2 and 3). With **CuNPs** catalyst, it was found that cesium carbonate is essential for the reaction, as can be seen in entry 4 that without cesium carbonate the reaction underwent with very low yield. Using Na_2CO_3 or K_2CO_3 resulted in lower yields than Cs_2CO_3 as base (entries 4-6). In this case, Cs_2CO_3 was especially effective as a base because it is indeed more dissociated and more soluble in organic solvents than other kinds of carbonate base. In addition, Cs_2CO_3 is stronger base than Na_2CO_3 and K_2CO_3, therefore it could effectively generate phenoxide ion as nucleophile to react with iodobenzene and resulted in higher yield. In this work, ligand 1,10-phenanthroline (Phen) was chosen as the most suitable ligand compared with 2,2'-bipyridine (Bipy) and mixed ligand of Phen and triphenyl phosphine (PPh_3) (entries 3 and 7-9). The result in entry 10 was evident that this reaction is air sensitive and dry N,N dimethylformamide (DMF) was found to be better solvent than toluene and was used as appropriate solvent for the next study under nitrogen atmosphere (entry 11).

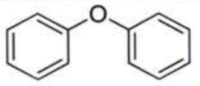
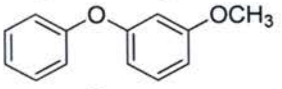
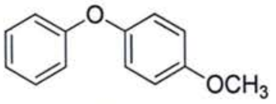
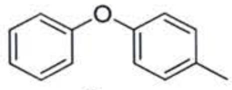
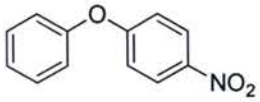
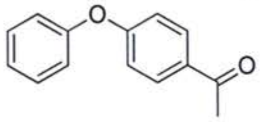
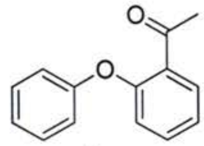
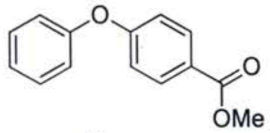
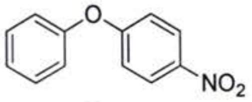
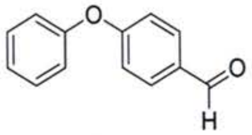
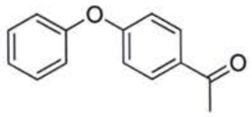
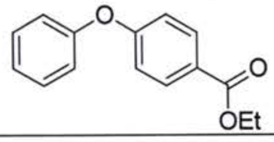
Therefore, the optimum conditions to synthesize diphenylether are 20 mg nanocopper as catalyst, 1,10-phenanthroline as a ligand, cesium carbonate as a base, in DMF at 110°C under nitrogen atmosphere.

2.3.3 CuNPs-catalyzed cross-coupling reaction for the synthesis of diarylethers

To determine the scope of the reaction, we then examined the cross-coupling reactions of phenol with varieties of aryl halides as shown in Table 2.2.

Table 2.2 Copper nanoparticle catalyzed cross-coupling reaction of phenol and aryl halides



Entry	X	Product	Time (h)	Isolated Yields (%)
1	I		15	55
2	I		24	56
3	I		24	45
4	I		24	57
5	I		24	37
6	I		15	76
7	I		24	46
8	I		15	12
9	Br		24	64
10	Br		24	71
11	Br		24	82
12	Br		24	21

As shown in Table 2.1, both electron rich and electron poor aryl iodides and aryl bromide were coupled with phenol to provide the corresponding diarylethers in moderate to good yields. When electron rich substrates such as iodoanisole and iodotoluene (entries 2-4) were used, the reactions gave moderate yields after 24 hours. The poor yield was observed in the coupling of 4-iodonitrobenzene (entry 5) due to the homocoupling of substrate. However, using electron poor substrate as 4-acetyliodobenzene (entry 6), the cross-coupling reaction afforded considerably higher yield after 15 hours and 2-acetyliodobenzene (entry 7) could be coupled in moderate yield due to the steric hindrance of this *ortho*-substituted aryl halide. Base-sensitive functional groups such as methyl ester and ethyl ester (entries 8 and 12) gave relatively low yields possibly due to the hydrolysis. Furthermore, with this protocol, we found that various aryl bromides (entries 10-11) with electron poor functional groups could also successfully be coupled in good yields using longer reaction time. Similar to the aryl iodides, high yields of diarylethers were obtained for aryl bromides with electron-withdrawing group such as ketone and aldehyde (entries 10 and 11). These results are comparable with other groups that Cu, Cu_2O, or CuO were used as catalysts to couple aryl halides with electron rich phenols.

The possible mechanism of C-O formation by cross-coupling of phenol and aryl halides is represented in Figure 2.7. Starting from Cu^0 species in **CuNPs** catalyst **I**, the aryl halide is oxidatively added to the catalyst resulted in $[Cu^{II}]$ complex **II**. Then the phenoxide ion, forming in the presence of base, replaces with X in complex **II** to form complex **III**. Reductive elimination from complex **III** affords the desired product and the catalyst **I** returns to the catalytic cycle.

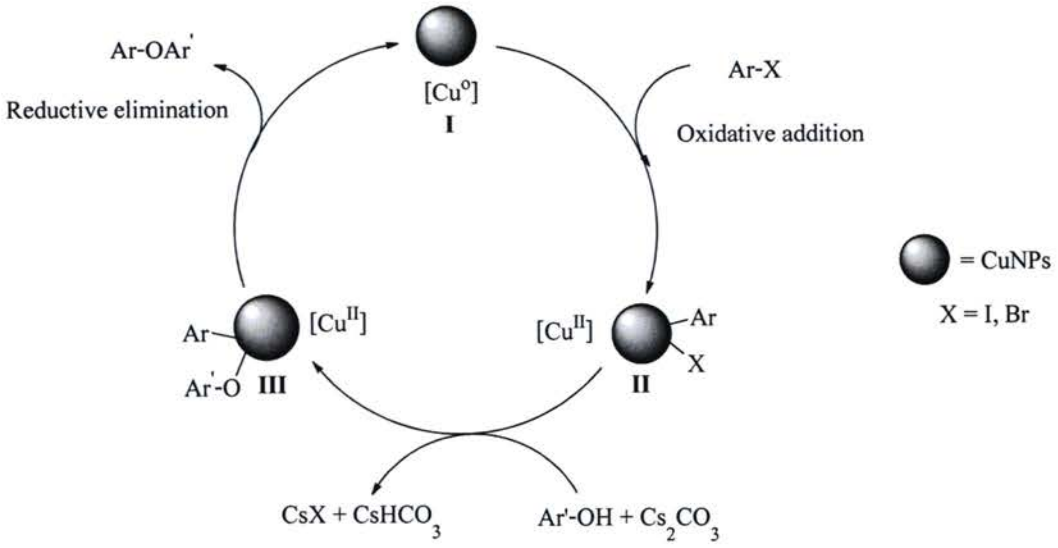


Figure 2.7 Possible reaction pathway for **CuNPs** catalyzed C-O bond formation [16]

2.4 Conclusion

In conclusion, copper and copper(I) oxide nanoparticle were synthesized by simple chemical reduction method and then examined the catalytic activities as heterogeneous catalyst for C-O bond formation. Through the optimization, we developed a cross-coupling method of phenol to aryl halides for the synthesis of diarylethers using nanocopper as catalyst. This protocol tolerates a wide range of functional groups and the reaction avoids the use of palladium and/or expensive additives. Varieties of diarylethers were synthesized at moderate to good yields.

CHAPTER 3

SYNTHESIS OF PHENYLIMIDAZOLE USING HETEROGENEOUS COPPER-CATALYZED REACTION

3.1 Introduction

Ullmann coupling reaction, which has been widely used since 1903 for building of the C–N bond, has been done using copper metal to mediate the reaction [19, 34]. However, this type of reaction generally suffered from high temperatures (around 200 °C) and the use of stoichiometric amounts of copper reagents, which make the further applications limited. In recent years, significant improvements have been achieved in the C-N bond formation using catalytic amount of various copper salts in the presence of various ligands as shown in Figure 3.1 [34]. C-N bond construction of aromatic compounds is particularly important and proved to be challenging especially to medicinal chemists. This unit has been found in many natural products that have shown interesting biological activities such thromboxane synthase inhibitors [35], AMP phosphodiesterase inhibitors [36], AMP receptor antagonists [37] and anti-glaucoma agents [38]. Among those biologically active compounds, N-containing heterocyles such as substituted imidazole derivatives are found prevalently in many important natural products such as quizartinib [39] and nilotinib [40] as shown in Figure 3.2.

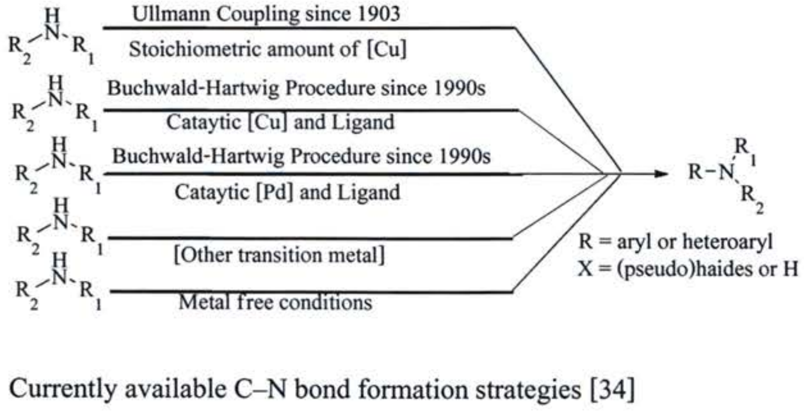
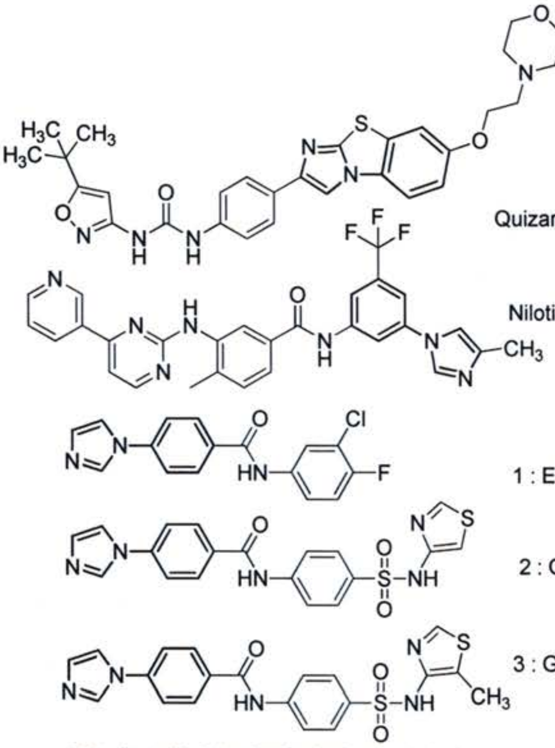


Figure 3.1 Currently available C–N bond formation strategies [34]

In the field of five membered heterocyclic structures, imidazole nucleus appears to be high therapeutic unit that many related drugs and chemotherapeutic agents have been synthesized and studied by medicinal chemists [41-42].



Quizartinib : protein kinases inhibitors

Nilotinib : Bcr-Abl tyrosine kinase inhibitor

1 : Exhibited highest activity against cervical cancer

2 : Good antibacterial activity

3 : Good antifungal activity

Substituted Imidazole Derivatives : 1, 2, 3

Figure 3.2 Examples of biologically active compounds containing aryl-imidazole unit

3.2 Background

The keys to the success of developing methods for certain cross-coupling reactions are simple organic derivatives substrates, and inexpensive and readily available catalyst and ligand. As mentioned above, one of the most significant organic transformation reactions is the aromatic C-N bond formation. Although excellent progress has been made, it is still a challenge to organic chemists to develop milder and cheaper methodologies to construct this particular bond [43].

The discovery of C-N coupling reaction using Pd-catalyzed amination [20, 34] by Buchwald and Hartwig has finished a major advance in the chemistry of amines, opening access to huge numbers of previously inaccessible compounds. However, with copper as catalyst appropriate ligands can be used to modulate the reactivity of the catalyst [19, 44]. For example, Patil, N. M. and coworker reported a simple and efficient methodology for the synthesis of triarylamines from aryl chlorides in a single step with high activity and selectivity using a CuI/tributyl phosphine catalyst system as shown in Figure 3.3 [45].

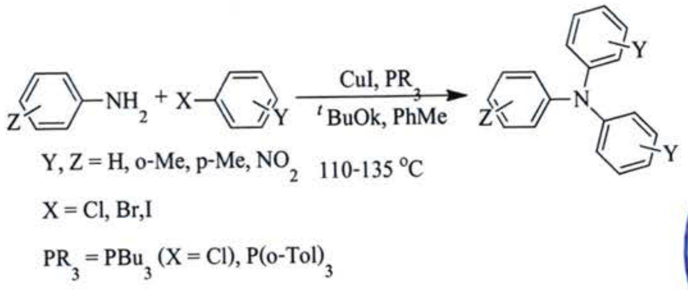


Figure 3.3 Synthesis of triarylamines using copper catalyst [45]

Buchwald, S. L. and coworker constructed C-N bonds using $(CuOTf)_2$-catalyzed N-arylation of imidazoles in xylenes at 110-125 °C (Figure 3.4) [46]. Addition of two ligands; 1,10-phenanthroline (Phen) and *trans,trans*-dibenzylideneacetone (dba), was essential to the proceed the reaction.

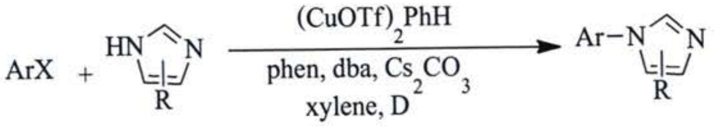


Figure 3.4 Copper-catalyzed synthesis of N-arylimidazoles [46]

Liu, Y. and coworker developed air and moisture stable copper-salen complexes as catalysts for effective N-arylation of imidazoles [47]. Various aryl imidazoles were synthesized in moderate to excellent yields without the protection by an inert gas (Figure 3.5).

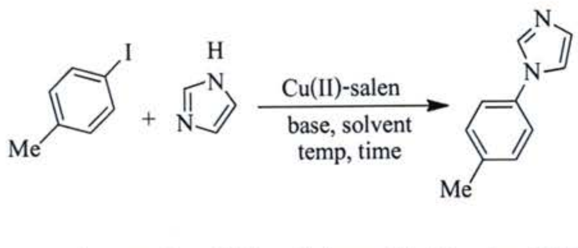


Figure 3.5 Cu(II)-salen complex catalyzed N-arylation of imidazoles [47]

Recently, heterogeneous copper and copper oxide nanoparticles have been reported as catalysts for cross-coupling reactions [48-50]. Jammi, S. and coworker used CuO nanoparticle for C-N bond formations as shown in Figure 3.6 [30]. The procedure was simple, general, ligand-free, and efficient to afford the cross-coupled products in high yields.

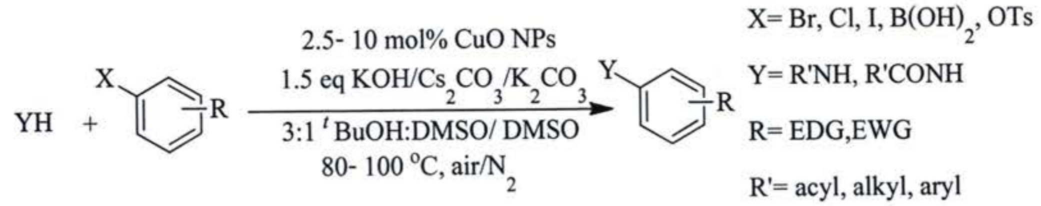


Figure 3.6 CuO nanoparticles catalyzed C-N bond formation [30]

The heterogeneous catalyst of nanocopper series for the N-arylation of heterocycles with aryl halides demonstrated by Kim, A. Y., et al. and Xu, Y., et al. were prepared. CuO and Cu_2O nanoparticles were used for cross-coupling reactions of aryl halide with N-heterocycles and the desired products were obtained in excellent yields (Figure 3.7) [51-52].

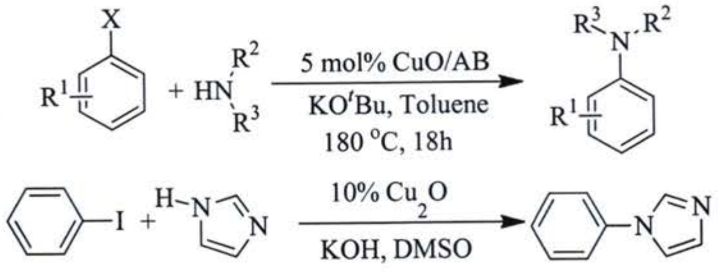
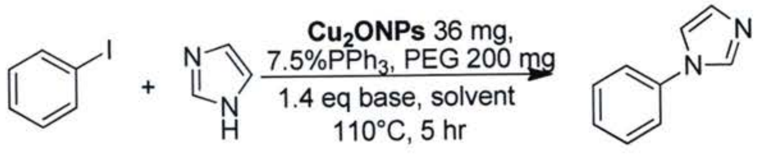


Figure 3.7 Heterogeneous copper catalysts for C-N bond formations [51-52]

3.3 Optimization of the reaction

In this work, **Cu_2ONPs** catalyst was prepared by chemical reduction using glucose under basic condition and used for catalyzing cross-coupling reaction of imidazole and aryl halides for the synthesis of arylimidazoles. The optimization as shown in Table 3.1.

Table 3.1 Optimization of imidazole coupling using nanocopper(I) oxide as catalyst



Entry	Solvents	Ligands	Bases	% Yield [a]
1[b]	DMF	Phen	Cs_2CO_3	0
2	DMF	-	Cs_2CO_3	40
3	DMF	Phen	-	0
4[c]	DMF	Phen	Cs_2CO_3	0
5	DMF	Phen	Cs_2CO_3	45
6	DMF	Bipy	Cs_2CO_3	19
7	DMF	PPh_3	Cs_2CO_3	50
8	DMF	PPh_3	KOH	0
9	DMF	PPh_3	K_2CO_3	0
10	DMF	PPh_3	Na_2CO_3	0
11	Toluene	PPh_3	Cs_2CO_3	0
12	NMP	PPh_3	Cs_2CO_3	0
13	DMSO	PPh_3	Cs_2CO_3	65
14[d]	DMSO	PPh_3	Cs_2CO_3	46

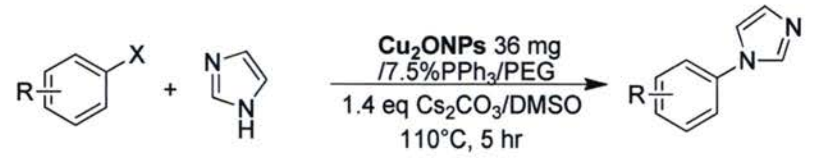
[a] GC yield with dodecane as internal standard, [b] no catalyst, [c] no PEG [d] 5% PPh_3

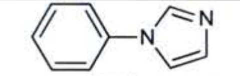
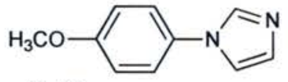
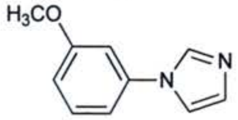
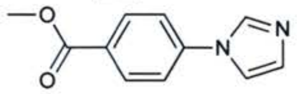
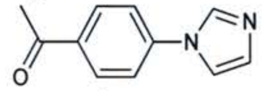
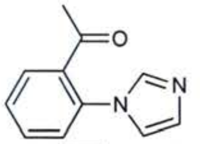
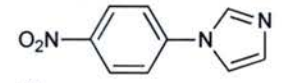
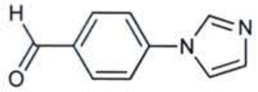
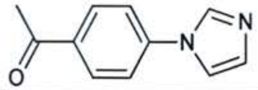
In order to optimize the reaction conditions, the reaction was performed with dry DMF as solvent and the influence of the catalyst, ligand, base and PEG as an additive in the imidazole coupling reaction was investigated. As can be seen in entries 1-4, without catalyst, base, and PEG additive, the reaction did not proceed to give the phenyl imidazole at all. However, without Phen ligand, moderate yield of product was obtained (entry 2) but slightly lowered than the reaction with Phen as a ligand (entry 5). Therefore, in the next reactions, we examined the effect of different ligands by changing to Bipy and PPh_3 ligand. The results have shown that PPh_3 was the most appropriate ligand (entries 5-7). Furthermore, various kinds of bases were investigated (entries 8-10) and found that Cs_2CO_3 was the most efficient base. Reactions in toluene and NMP as solvent were unsuccessful (entries 11-12), however slightly better yield was obtained when DMSO was used (entry 13). Finally, decreasing amount of PPh_3 ligand from 7.5% to 5% resulted in fairly lower yield (entry 14). Therefore, the optimum conditions were 36 mg Cu_2O, 7.5% PPh_3, 200 mg PEG, 1.4 eq Cs_2CO_3, in DMSO at 110 $^{\circ}C$ for 5 hours.

3.4 Cu_2ONPs catalyzed cross-coupling of imidazole and aryl halides

The developed protocol was then used to couple imidazole with variety aryl halides as shown in Table 3.2.

Table 3.2 Cross-coupling of imidazole and aryl halides using Cu_2O catalyst



Entry	X	Product	Time (h)	Isolated Yields (%)
1	I		5	94
2	I		5	64
3	I		5	75
4	I		5	24
5	I		5	68
6	I		5	57
7	Br		5	96
8	Br		10	11
9	Br		5	27

To examine the scope of the developed protocol, various kinds of substituted aryl halides were coupled to imidazole and the results as illustrated in Table 3.2. Using our protocol, aryl iodides with electron donating and electron withdrawing groups reacted with imidazole in moderated to excellent yields (entries 1-6). However, aryl iodide with strong electron donating group, $-OCH_3$, and steric hindrance at ortho position, resulted in lower yields of the corresponding aryl imidazoles. Coupling of base-sensitive functional group as methyl-4-iodobenzoate (entry 4) afforded very low yield due to hydrolysis. Aryl bromide with strong electron-withdrawing group, $-NO_2$, gave a good yield (entry 7). In contrast, electron poor aryl bromides with aldehyde and ketone as substituents were coupled in lower yields even with longer reaction time (entries 8 and 9).

The possible mechanism of C-N formation by heterogeneous Cu_2O catalyzed reaction of imidazole and aryl halides is shown in Figure 3.8. The reaction is assumed to occur via oxidation addition of aryl halide to **Cu_2ONPs** catalyst **I** to form [Cu^{III}] complex **II,** followed by replacement of X in complex **II** with imidazolide anion, which is generated from imidazole under basic condition. Upon reductive elimination from complex **III**, the desired product is obtained and the catalyst **I** returns to the catalytic cycle.

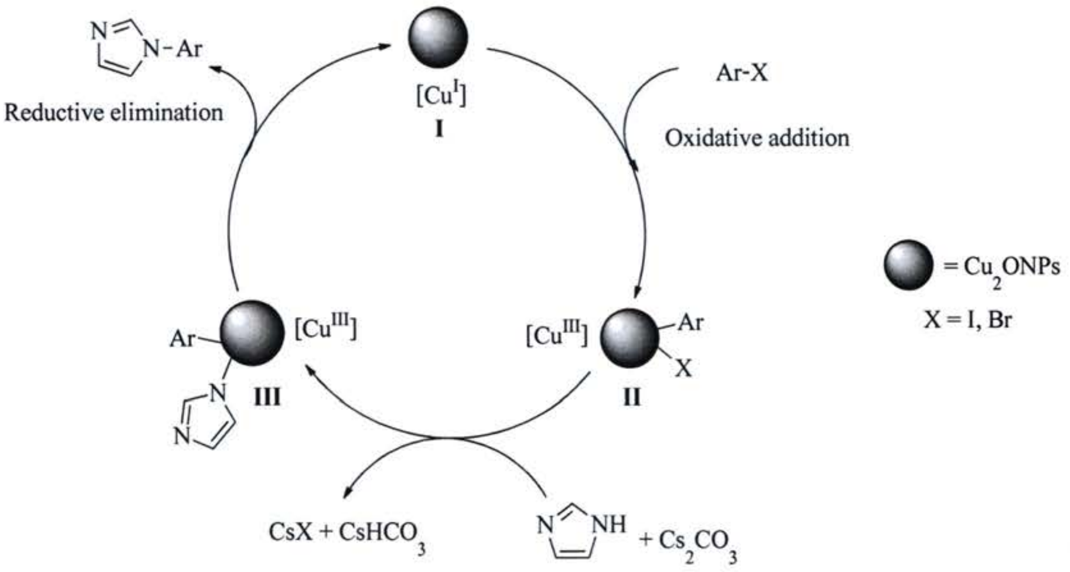


Figure 3.8 Possible reaction pathway for **Cu_2ONPs** catalyzed C-N bond formation [16]

3.5 Conclusion

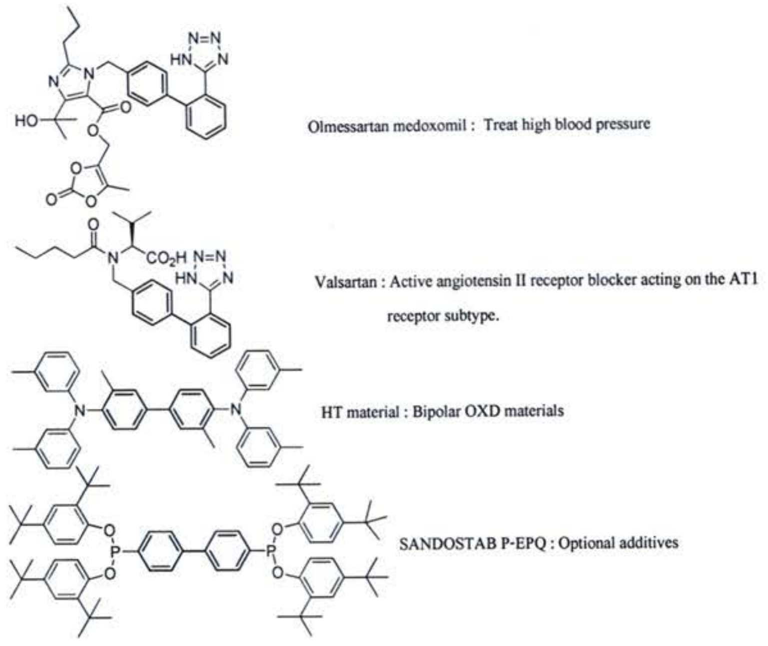
In conclusion, we developed an *N*-arylation reaction of imidazole using heterogeneous copper catalyst. This mothod offered a simple and effective catalyst system to carry out C-N bond formation of heterocycle. It is an alternative to the expensive palladium-catalyzed protocol and the catalyst can be separated from the reaction by simple filtration.

CHAPTER 4

HETEROGENEOUS PALLADIUM-CATALYZED SUZUKI-MIYAURA CROSS-COUPLING REACTION

4.1 Introduction

Suzuki-Miyaura cross-coupling reaction under transition metal-catalyzed of aryl, vinyl, or alkyl halides or pseudohalides with organoboron reagents is one of the most efficient methods for the formation of C-C bond [20, 53-56]. This reaction can be carried out under mild reaction conditions and tolerates a wide range of functionalities, therefore has been found prevalent uses in many organic syntheses. The Suzuki-Miyaura reaction is nowadays of great industrial significance since many kinds of materials such as drugs [57], materials [58-59], and optical devices [60-62], commercialized or in the development have diaryl moiety which can be assembled by Suzuki-Miyaura cross-coupling reaction [63-65] as shown in Figure 4.1



Olmessartan medoxomil : Treat high blood pressure

Valsartan : Active angiotensin II receptor blocker acting on the AT1 receptor subtype.

HT material : Bipolar OXD materials

SANDOSTAB P-EPQ : Optional additives

Figure 4.1 Structures of some diaryl-containing compounds

4.2 Background

Heterogeneous palladium catalysts for C-C bond formation reactions have made considerable progress in the past few decades [66]. There are many kinds of heterogeneous palladium catalysts, such as Pd on carbon, Pd on metal oxides, Pd on porous aluminosilicate, Pd on clay and Pd on organic polymers. Among those, palladium on carbon (Pd/C) is the most common heterogeneous source of palladium catalyst and has been applied to catalyze many cross-coupling reactions.

Suzuki-Miyaura reaction for C-C bond formation using heterogeneous palladium catalyst has been reported and some examples are shown in Figure 4.2 [66-67].

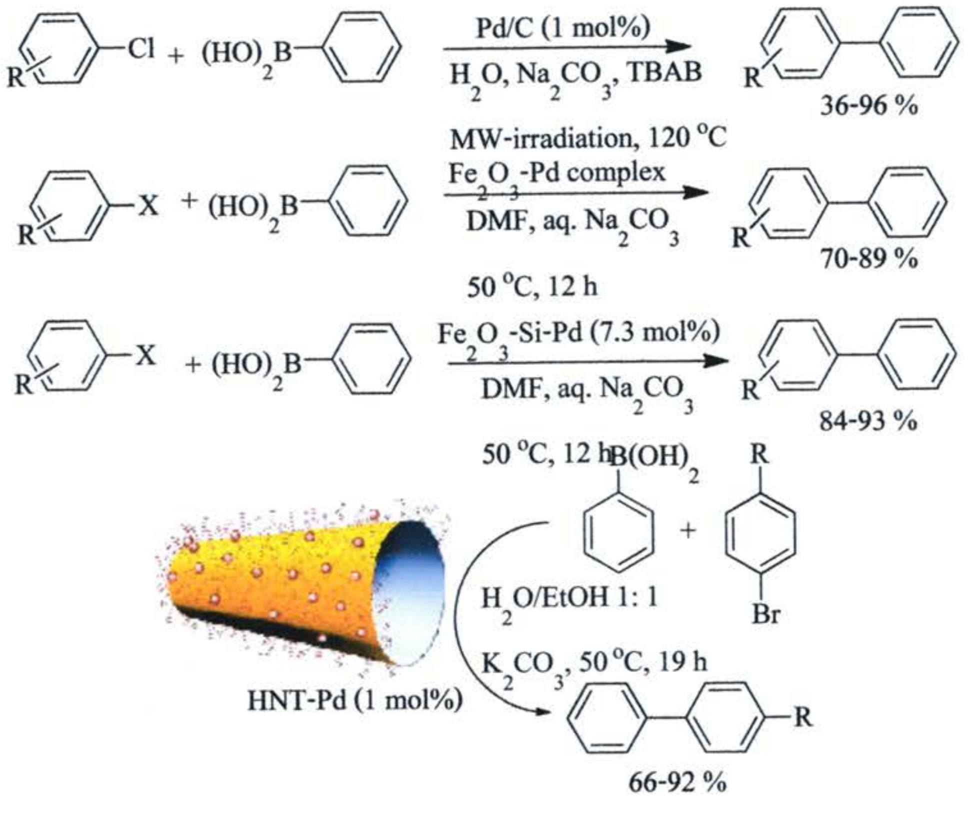


Figure 4.2 Examples of heterogeneous palladium-catalyzed Suzuki-Miyaura reaction [66-67]

Among the heterogeneous catalysts developed, magnetically recoverable catalyst is one of the most attractive catalysts due to its easy separation and reusability [68]. Recently, magnetic nanoparticles have attracted great interest in many fields of chemistry with potential applications such as drug delivery, supporter, removal of toxic metal ions, and antimicrobial applications [69-72]. Various methods have been used to immobilize metal catalyst onto the magnetic support. One of the methods to stabilize the catalyst on the magnetic material surface is to functionalize its surface with linker or ligand. To increase the stability of catalysts on nanoparticles, many strategies have been employed such as modifying of the surface of ferrite with dopamine or coating the surface with certain materials such as silica and chitosan. For example, Zhou, Z. and coworker prepared nanoscaled magnetic chitosan particles by two-step route, which resulted in narrow size distribution nanoparticles. X-ray diffraction patterns showed that the chitosan coating process did not change the spinal structure of ferrite as shown in Figure 4.3 [73].

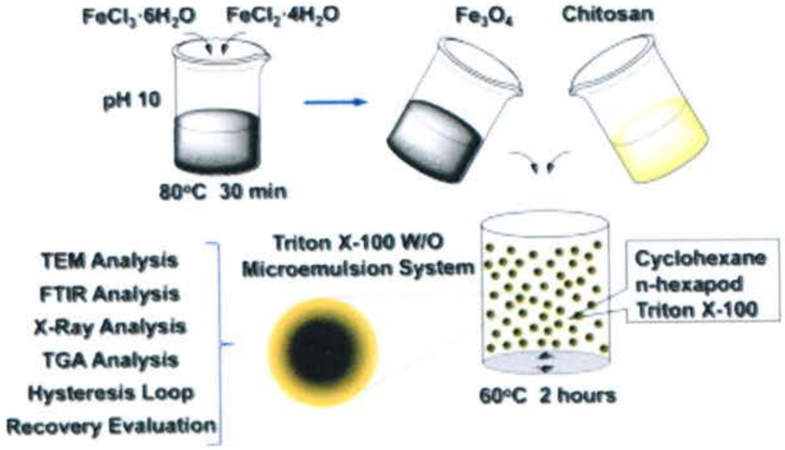


Figure 4.3 Preparation of Fe_3O_4/chitosan nanoparticles [73]

Due to the inertness and high thermal stability of silica, it has been used to coat on the surface of magnetic nanoparticles with modification on the silica surface by polymer and dendron [74-77]. For instance, Abu-Reziq, R. and coworker reported the synthesis of silica-coated magnetic nanoparticles which was based on growing Poly(methyl methacrylate) (PMMA) dendrons on silica-coated magnetic nanoparticle as presented in Figure 4.4 [78]. Hong, R. Y. and coworker modified the surface of ZnO and Fe_3O_4 nanoparticles by grafting polymethyl methacrylate (PMMA) polymer using free radical polymerization process and approach based on thiol-lactam initated radical polymerization as shown in Figure 4.5.[78-79]

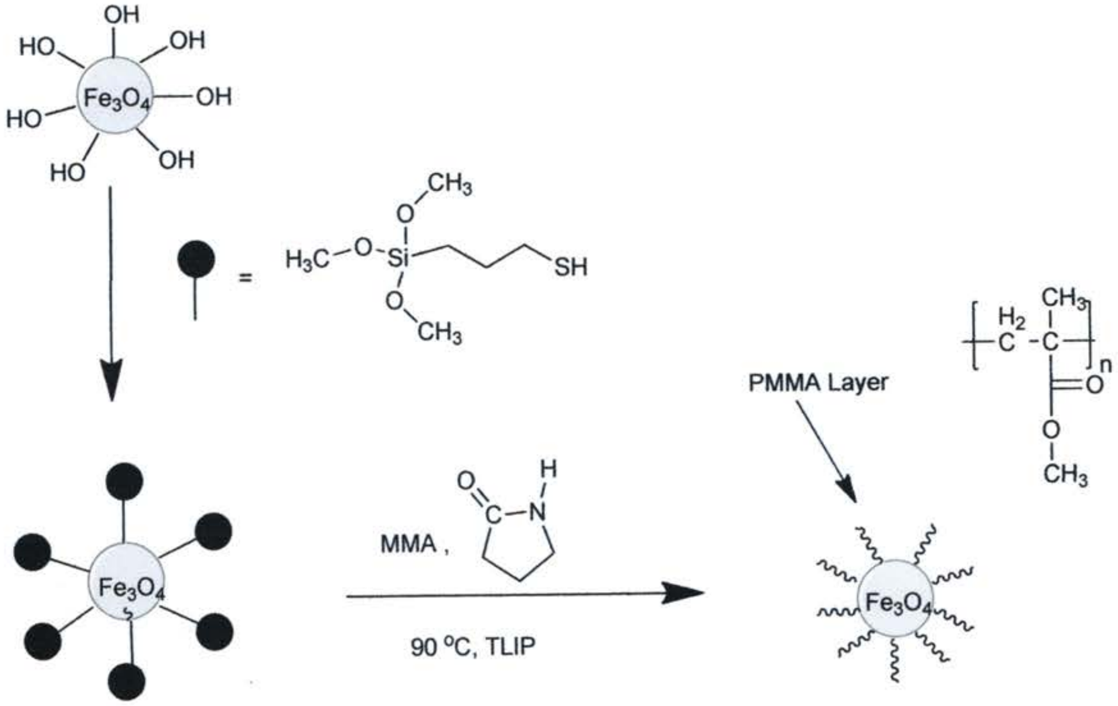


Figure 4.4 Surface modification of metal nanoparticles using PMMA [78]

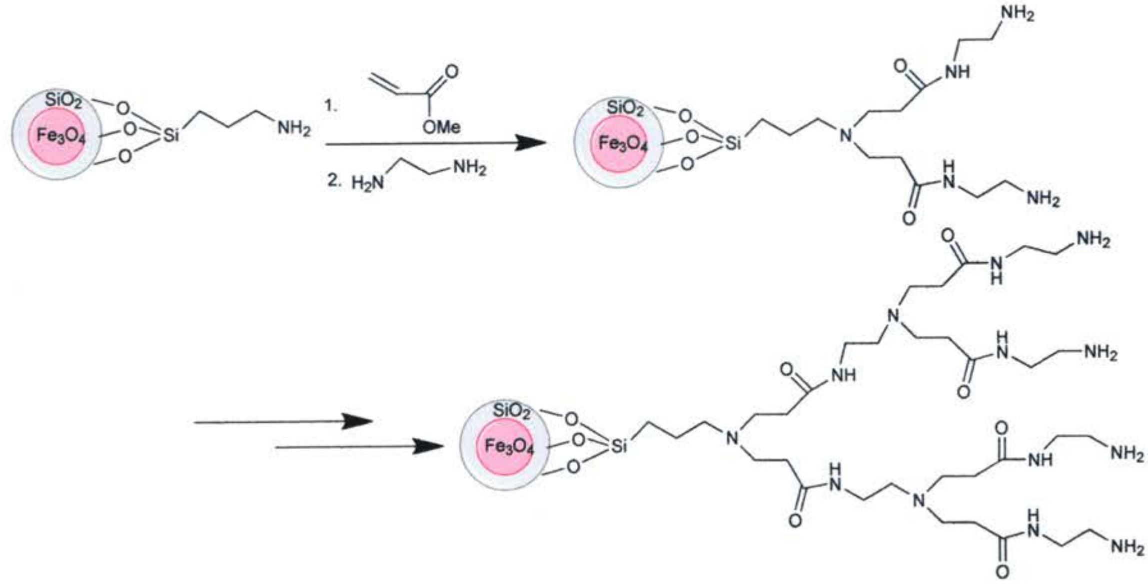


Figure 4.5 Synthesis of dendron-modified silica-coated magnetic nanoparticles [79]

Wang, Z. and coworker used bottom-up approach to synthesize palladium catalyst supported on silica-coated magnetic nanoparticles as shown in Figure 4.5 [80]. The catalyst was tested in Heck cross-coupling of acrylic acid with iodobenzene. However, the activity in reuse was poor and highly influenced by the base used in the reaction. In this case, the activity loss due to the leaching of Pd nanoparticle from the surface of magnetic nanoparticle was confirmed by TEM images.

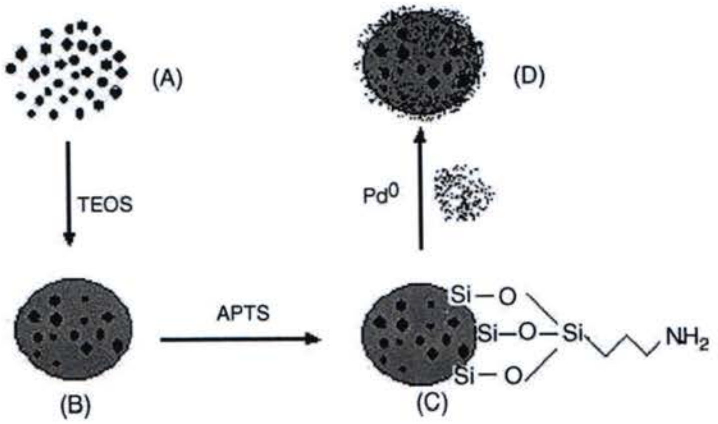


Figure 4.6 Preparation of Pd catalyst supported on silica-coated magnetic nanoparticle (A)Fe_3O_4; (B) SiO_2/Fe_3O_4; (C) APTS coated SiO_2/Fe_3O_4; (D) Pd/(SiO_2/Fe_3O_4) [80]

A metal nanoparticle dispersed on the surface of metal oxide composite has been reported as an efficient catalyst for a wide variety of reactions compared to bulk catalyst. For example, Singh, A. S. and coworker synthesized palladium nanoparticle supported on zinc ferrite magnetic nanoparticle (Zn-Fe_2O_4) and applied as catalyst for Suzuki-Miyaura and Heck coupling reactions [81]. The catalyst has shown excellent performance for Suzuki-Miyaura and Heck reactions under ligand-free condition as shown in Figure 4.6.

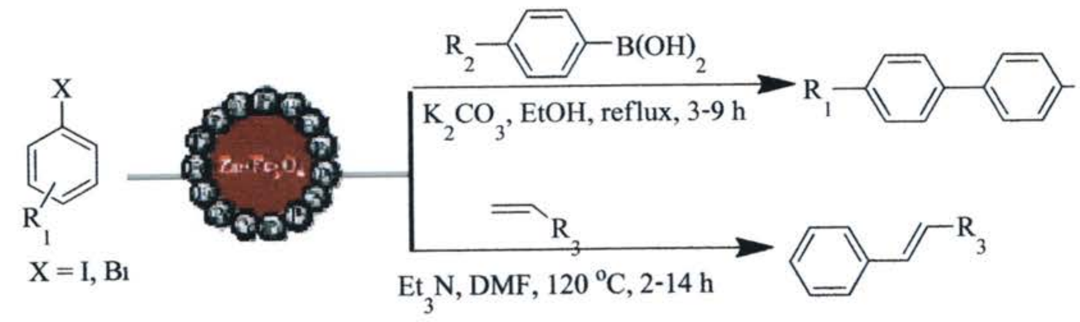


Figure 4.7 Suzuki-Miyaura and Heck reaction catalyzed by Pd-$ZnFe_2O_4$ catalyst [81]

Nanoferrites, post-synthetically modified by ligand, were also used to immobilize nanometals and metal ions catalysts. Dopamine is widely used ligand to modify nanoferrite surface by simple sonicating nanoferrite with dopamine followed by metal adsorption. Yung, E. S. and coworker prepared catalyst by immobilizing palladium(II) acetate onto the surface of dopamine-modified ferrite and then used as catalyst for Suzuki-Miyaura reaction and reduction of nitrobenzene [82]. It was found that the developed protocol resulted in good to excellent yields of products as shown in Figure 4.7 and the catalyst can be reused for six cycles with only slightly loss of activity.

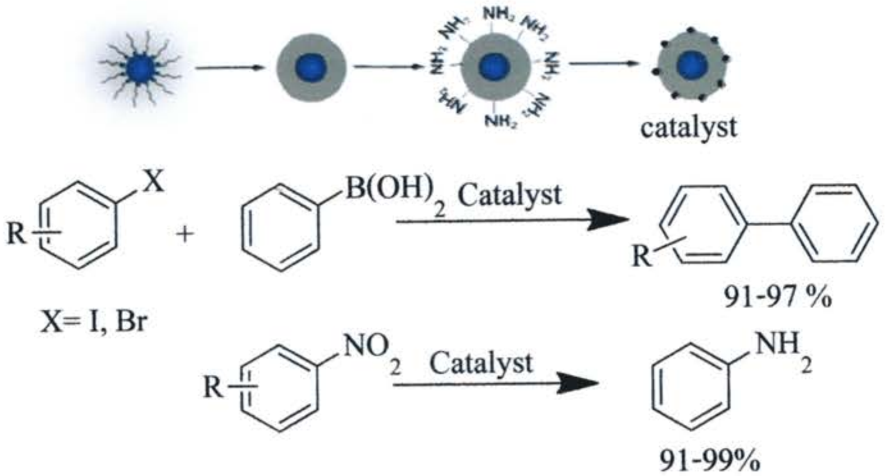


Figure 4.8 Synthesis of magnetically recyclable nanocatalyst and its applications [82]

Baruwati, B. and coworker reported the synthesis of $NiFe_2O_4$-DA-Pd as heterogeneous magnetically separable catalyst that is highly active toward Suzuki-Miyaura and Heck coupling reactions. The catalyst was highly efficient for the cross-coupling of inactive aryl chloride substrates as shown in Figure 4.8. The catalytic efficiency remains unaltered even after three repeated cycles [83].

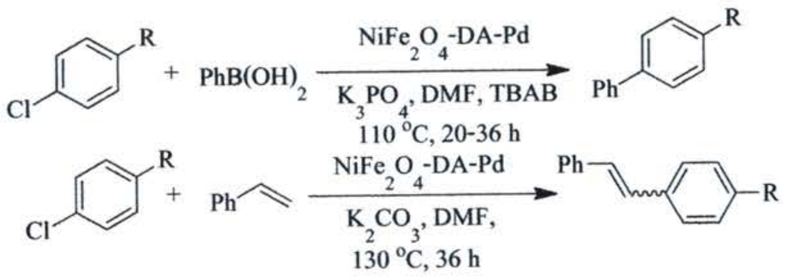


Figure 4.9 The $NiFe_2O_4$-DA-Pd recoverable catalyst for Suzuki-Miyaura and Heck reactions [83]

The simple process of Pd(0) immobilization on the surface of amine terminated Fe_3O_4 and $NiFe_2O_4$ nanoparticles are presented in Figure 4.9 [84]. These catalysts could be simply recovered using external magnet and the efficiency of the catalyst was found to be unaltered even after many repeated cycles.

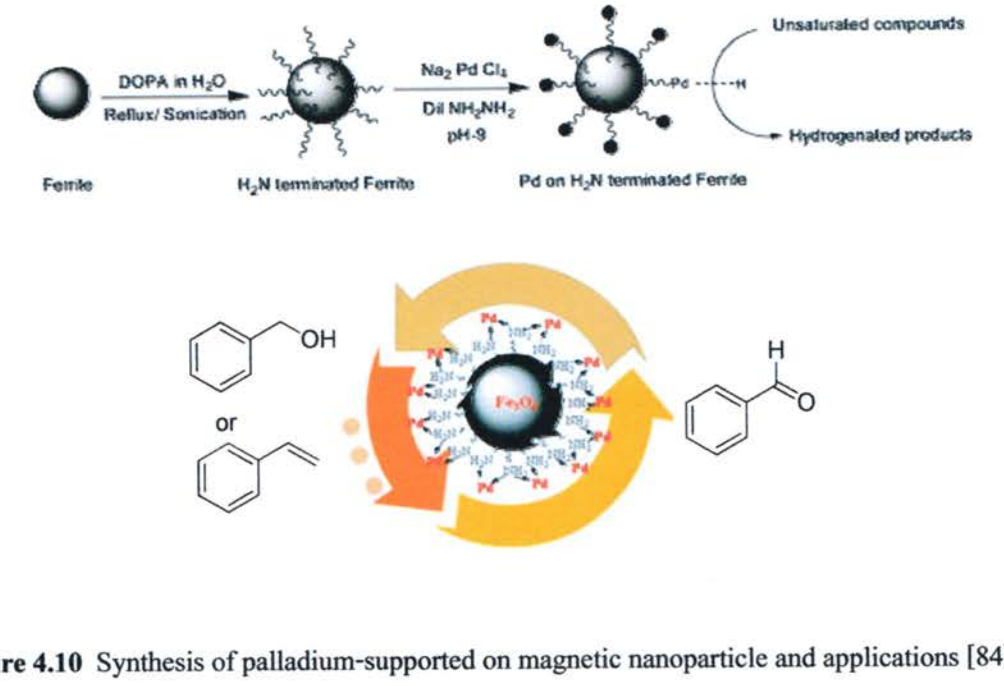
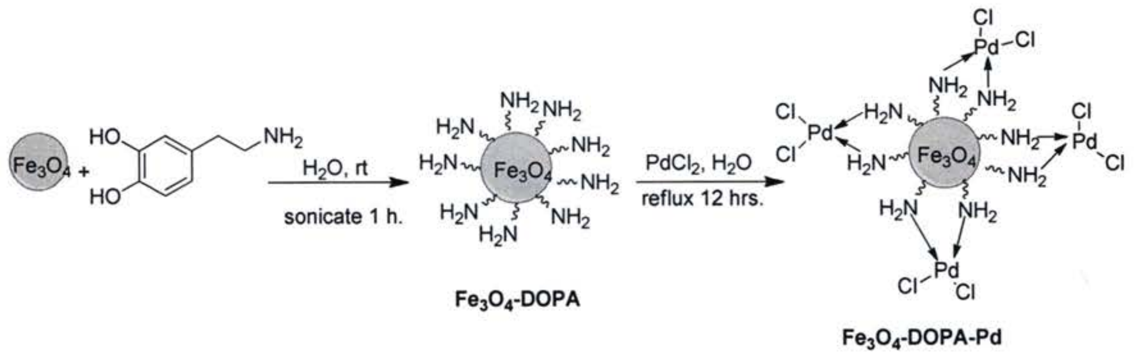


Figure 4.10 Synthesis of palladium-supported on magnetic nanoparticle and applications [84]

In this work, palladium catalyst for Suzuki-Miyaura reaction has been immobilized on ferrite (Fe_3O_4) modified by dopamine. This catalyst can be used to catalyze Suzuki-Miyaura coupling reaction in aqueous system and simply separated and reused with only slightly loss of activity.

4.3 Results and discussions

4.3.1 Synthesis and characterization of catalyst (**Fe_3O_4-DOPA-Pd**)



We synthesized **Fe_3O_4-DOPA-Pd** catalyst from dopamine-modified nanoferrite (**Fe_3O_4-DOPA**) which was prepared by mixing nanoferrite (Fe_3O_4) with dopamine hydrochloride in water under ultrasonication. Palladium(II) chloride was adsorbed onto the **Fe_3O_4-DOPA** surface by stirring the mixture overnight at room temperature. The resulting catalyst **Fe_3O_4-DOPA-Pd** was obtained as black powder and characterized by XRD and SEM technique as illustrated in Figure 4.7 and 4.8.

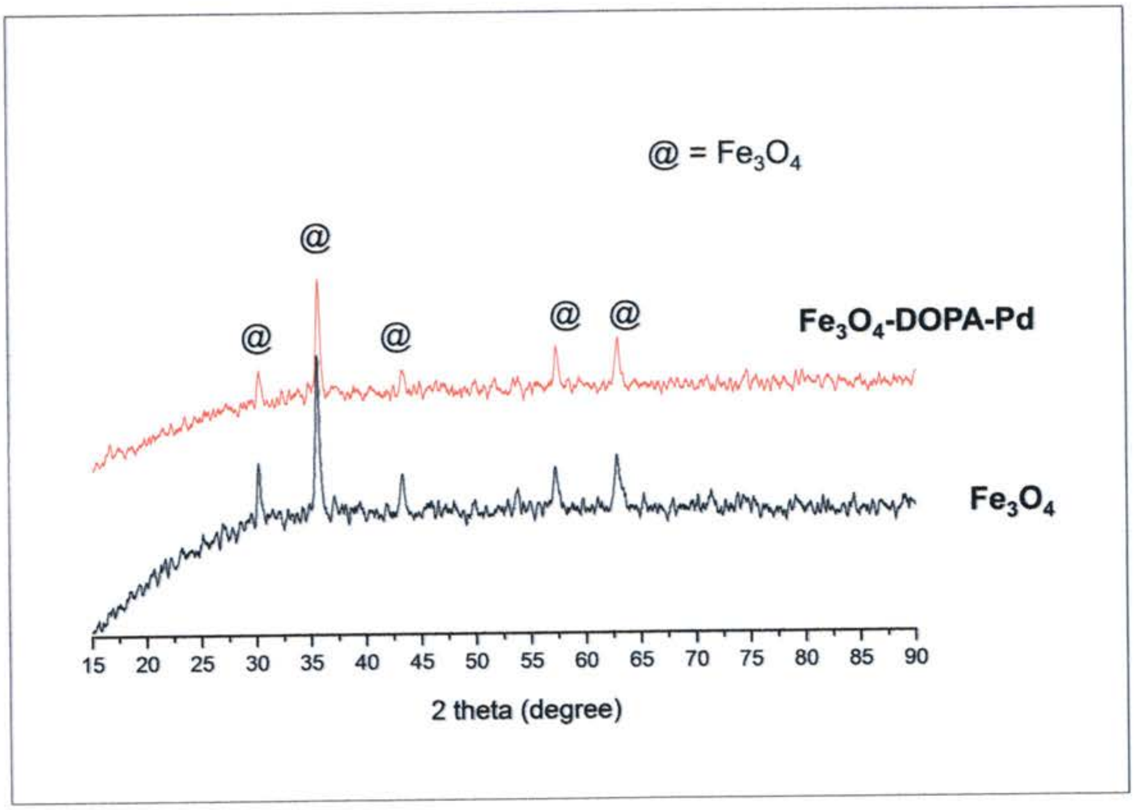


Figure 4.11 X-ray diffractograms of **Fe_3O_4** and **Fe_3O_4-DOPA-Pd**

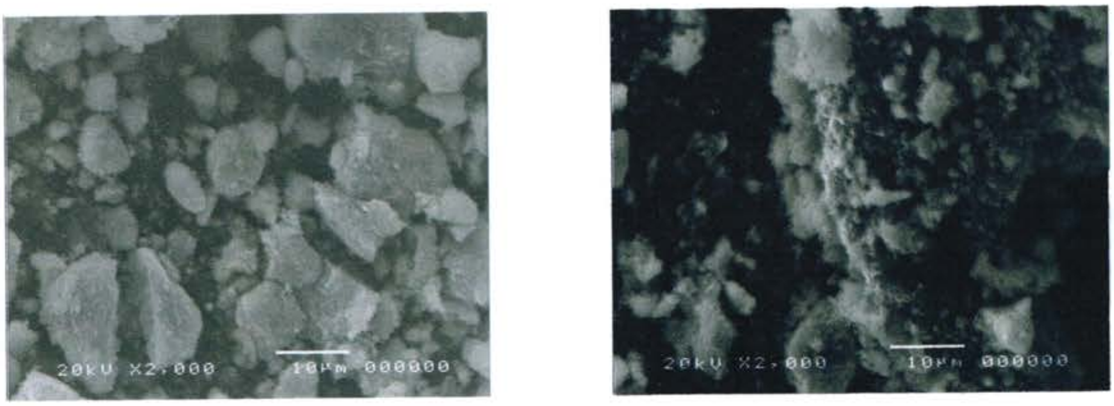


Figure 4.12 SEM images of **Fe_3O_4** (left) and **Fe_3O_4-DOPA-Pd** (right)

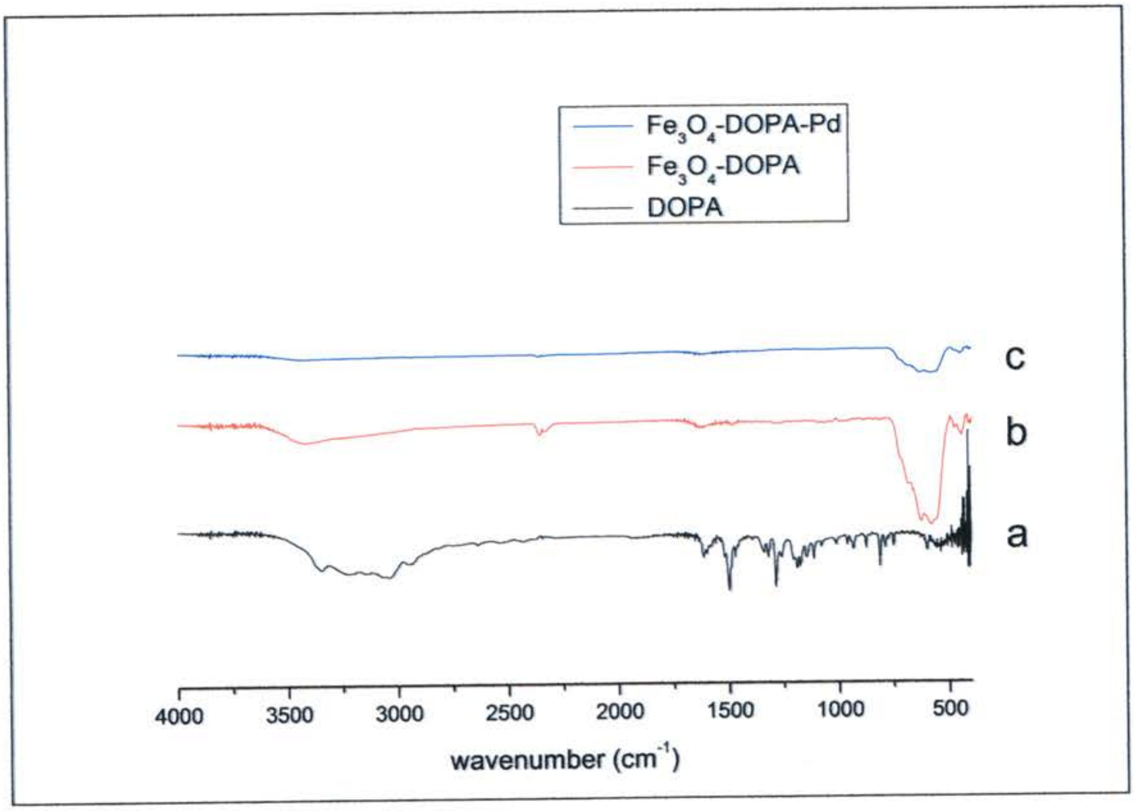


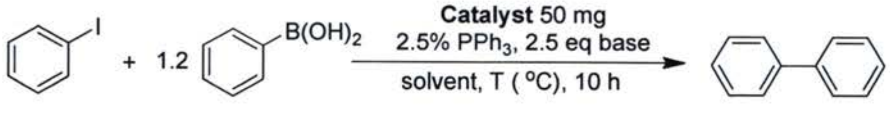
Figure 4.13 FT- IR spectra of (a) **DOPA,** (b) **Fe_3O_4-DOPA** and (c) **Fe_3O_4-DOPA-Pd**

As can be seen from the XRD patterns, the modification of Fe_3O_4 surface with dopamine and deposition of palladium catalyst did not change the structure of Fe_3O_4. However, from SEM images and FT- IR spectra, it can be clearly observed the difference of the Fe_3O_4 surface before and after deposition of palladium catalyst. The synthesized **Fe_3O_4-DOPA-Pd** catalyst was then examined for catalytic activity in Suzuki-Miyaura reaction.

4.3.2 Optimization of the reaction

We first optimized the Suzuki-Miyaura reaction of phenylboronic acid and iodobenzene using **Fe_3O_4-DOPA-Pd** catalyst to synthesize biphenyl in water as shown in Table 4.1.

Table 4.1 Optimization of Suzuki-Miyaura reaction using **Fe_3O_4-DOPA-Pd** catalyst



Entry	Catalysts	Base	PPh_3	Solvent	Temp (°C)	% Yield[a,b]
1	**Fe_3O_4-DOPA-Pd**	Cs_2CO_3	5%	H_2O	100	81
2	**Fe_3O_4-DOPA-Pd**	Cs_2CO_3	-	H_2O	100	27
3	**Fe_3O_4-DOPA-Pd**	KOH	5%	H_2O	100	79
4	**Fe_3O_4-DOPA-Pd**	NaOH	5%	H_2O	100	79
5	**Fe_3O_4-DOPA-Pd**	K_2CO_3	5%	H_2O	100	72
6	**Fe_3O_4-DOPA-Pd**	Na_2CO_3	5%	H_2O	100	89
7	**Fe_3O_4-DOPA-Pd**	Na_2CO_3	5%	H_2O	60	94
8	**Fe_3O_4-DOPA-Pd**	Na_2CO_3	5%	H_2O	RT	2
9	**Fe_3O_4-DOPA-Pd**	Na_2CO_3	2.5%	H_2O	60	98(79)[c]
10	**Fe_3O_4-DOPA-Pd**	Na_2CO_3	2.5%	Toluene	60	9
11	**Fe_3O_4-DOPA-Pd**	Na_2CO_3	2.5%	DMF	60	15
12	**Fe_3O_4-DOPA-Pd**	Na_2CO_3	2.5%	EtOH	60	33
13	**Fe_3O_4**	Na_2CO_3	2.5%	H_2O	100	18
14	**Fe_3O_4-DOPA**	Na_2CO_3	2.5%	H_2O	100	0
15	**CuNPs**	Na_2CO_3	2.5%	H_2O	60	0
16	**Cu_2ONPs**	Na_2CO_3	2.5%	H_2O	60	0
17[d]	**CAT1**	Na_2CO_3	2.5%	H_2O	60	30

[a] GC yield with dodecane as internal standard, [b] conditions: 1.2 mmol phenylboronic acid, 1.0 mmol iodobenzene, 50 mg **Fe_3O_4-DOPA-Pd**, PPh_3, 2.5 mmol base, 3 mL solvent, heated for 10 hrs, [c] %yield after 4th run, [d] **CAT1 = Fe_3O_4-AMA-PI-$PdCl_2$**

From Table 4.1, throughout the optimization, it was found that ligand PPh_3 is essential for the reaction and without PPh_3 the reaction proceeded with only low yield (entries 1-2). Various hydroxide (entries 3-4) and carbonate (entries 5-6) bases were investigated and it was found that the optimum base is Na_2CO_3 (entry 6). Although NaOH and KOH gave similar yields to Na_2CO_3, these two bases were not chosen due to their strong basic character that could affect certain base-sensitive function groups. Next, in order to develop milder conditions, the lower reaction temperatures were examined. Decreasing the temperature to 60 °C (entry 7), slightly better yield was obtained, but running reaction at room temperature was unsuccessful (entry 8). The amount of ligand is also important factor, so decreasing ligand from 5% to 2.5% was studied (entry 9). We have found that using 2.5% PPh_3 ligand resulted in higher yield than 5% PPh_3. Moreover, H_2O was found to be the most suitable solvent compared to toluene, DMF and EtOH (entries 9-12) and this could be explained by solubility of aryl boronic acid in aqueous solution [85]. As control reactions, Fe_3O_4 and Fe_3O_4-DOPA as the catalyst supporters were tested activities and found that without palladium catalyst, Fe_3O_4 and Fe_3O_4-DOPA were ineffective in catalyzing the reaction (entries 13-14). Other catalysts prepared in our group were also studied and the results revealed that they are not as effective as **Fe_3O_4-DOPA-Pd** catalyst (entries 15-17).

Therefore, the optimum conditions are 50 mg Fe_3O_4-DOPA-Pd as a catalyst, 2.5% PPh_3 as ligand, 2.5 eq. Na_2CO_3 as base, water as a solvent at 60°C for 10 hours. After reuse the catalyst for 4 times, only slightly decrease of %yield was observed as shown in Figure 4.14.

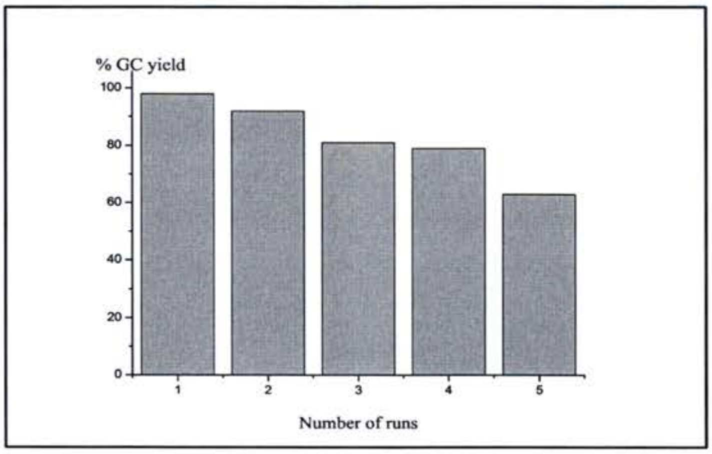
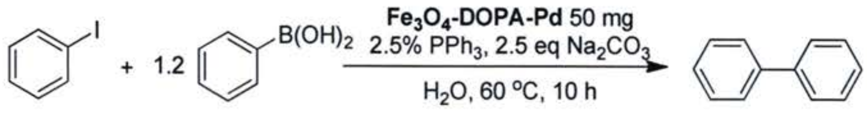


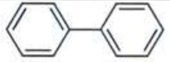
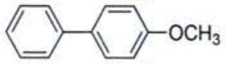
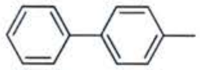
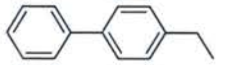
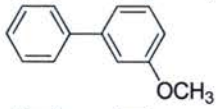
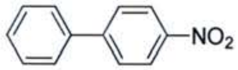
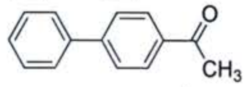
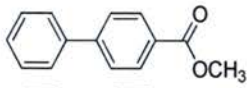
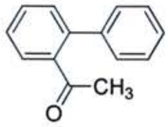
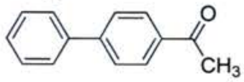
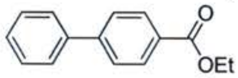
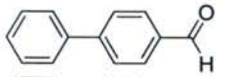
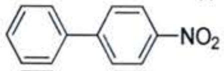
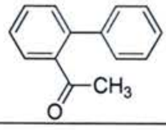
Figure 4.14 Recycling of **Fe_3O_4-DOPA-Pd** in Suzuki-Miyaura reaction

4.3.3 Fe_3O_4-DOPA-Pd catalyzed Suzuki-Miyaura cross-coupling reaction

With the optimum conditions, we then examined the scopes of the developed protocol to couple phenylboronic acid with various aryl halides as shown in Table 4.2.

Table 4.2 Suzuki-Miyaura cross-coupling reaction of using **Fe_3O_4-DOPA-Pd** catalyst



Entry	X	Product	Time (h)	Isolated Yields (%)
1	I		10	98
2	I		15	77
3	I		10	95
4	I		10	99
5	I		10	99
6	I		10	88
7	I		10	99
8	I		10	99
9	I		10	40
10	Br		15	94
11	Br		10	60
12	Br		15	91
13	Br		15	72
14	Br		10	30

From Table 4.2, with the optimum protocol, varieties of aryl halides with electron rich (entries 1-5) and electron poor (entries 6-14) functional groups were coupled in good to excellent yields within 10-15 h. With strong electron donating group, 4-iodoanisole (entry 2) coupled to phenyl boronic acid in good yield after longer reaction time than other electron donating groups (entries 3-5). Electron poor aryl halides with nitro, acetyl, methyl ester, and aldehyde were coupled in good yields (entries 6-8 and 10-13) although aryl bromides need longer reaction time to give comparable yields as the iodides (entries 10-13). The sensitive aryl halides bearing ethyl ester functional group gave the corresponding coupled product in moderate yield due to the hydrolysis (entry 11). However, both aryl iodide and aryl bromide substrates with electron withdrawing group suffered from sterically hindrance at *ortho* position resulted in lower yields (entries 9 and 14).

The possible mechanism of C-C formation by heterogeneous **Fe_3O_4-DOPA-Pd** catalyzed reaction of imidazole and aryl halides is shown in Figure 4.15. The reaction is assumed to occur via oxidation addition of aryl halide to **Fe_3O_4-DOPA-Pd** catalyst **II** to form [Pd^{II}]complex **III,** followed by replacement of X in complex **III** with aryl anion, which is generated from arylboronic acid under basic condition. Upon reductive elimination from complex **IV**, the desired product is obtained and the catalyst **II** returns to the catalytic cycle.

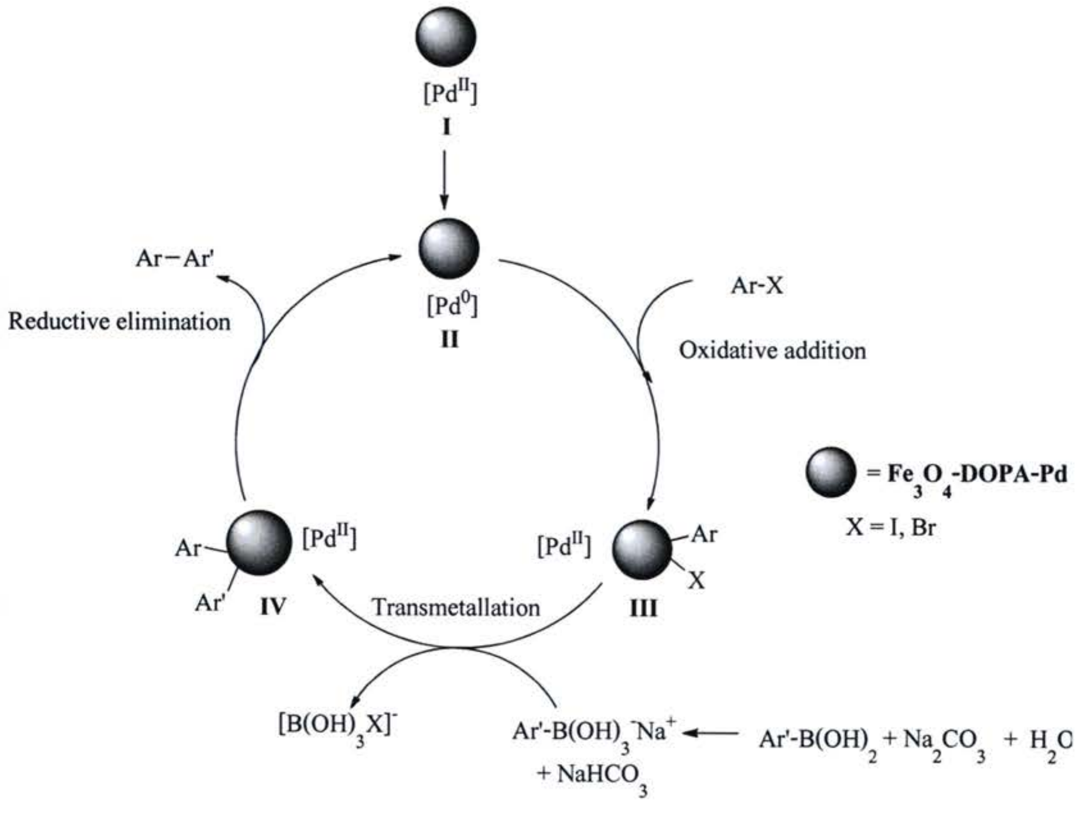


Figure 4.15 Possible mechanism for **Fe_3O_4-DOPA-Pd** catalyzed Suzuki-Miyaura reaction

4.4 Conclusion

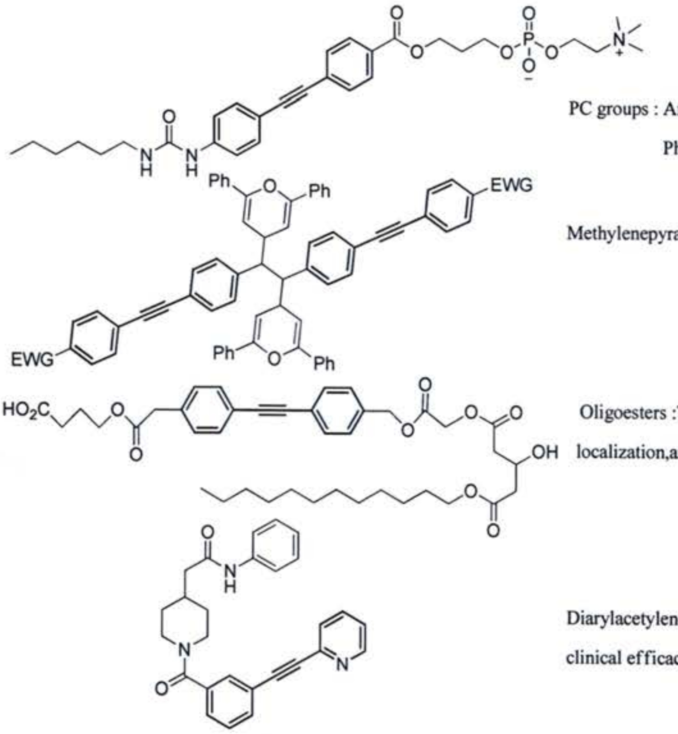
In conclusion, we prepared **Fe_3O_4-DOPA-Pd** catalyst and developed a mild and efficient protocol for the synthesis of biaryls using Suzuki-Miyaura reaction in aqueous system. Varieties of biaryls were synthesized in good to excellent yields. Facile magnetic recycling of the catalyst is another remarkable feature of this reaction as simple work-up procedure for catalyst separation and recovery after completion of the reaction. The catalysts could be reused for 4 consecutive cycles that only slightly decrease of product were observed.

CHAPTER 5

HETEROGENEOUS PALLADIUM-CATALYZED SONOGASHIRA CROSS-COUPLING REACTION

5.1 Introduction

Alkyne is an important moiety found in various kinds of materials such as natural products and precursors for pharmaceuticals and molecular organic materials [86]. Recently, diarylacetylene has been extensively utilized for the preparation of many conjugated poly(arylacetylenes) in an emerging area of molecular electronics and nanotechnology [87]. Examples of compound containing diarylacetylene unit in structure are shown in Figure 5.1 [88-90].



PC groups : Anion binding of Fluorescent Phospholipid

Methylenepyran : Reversible redox system Increase of the m*b* values

Oligoesters :Transport activity, membrane localization,and dynamics of oligoester ion

Diarylacetylene piperidinyl amides : Activity of clinical efficacy for the treatment of anxiety

Figure 5.1 Examples of diarylacetylene containing compounds

5.2 Background

During the last few decades, a large number of research have been dedicated to develop transition metal catalyzed methods to effect C–C and C–heteroatom bond forming reactions. The most powerful method for construction of sp^2C-spC bonds is Sonogashira reaction which is a versatile tool for varieties of alkynes synthesis [91]. The most common catalyst system for this reaction involves the use of palladium-phosphine complexes such as $PdCl_2(PPh_3)$ and $Pd(PPh_3)_4$ with CuI as co-catalyst in a large amount of amine as solvents or co-solvents [92-93]. The method has been modified and improved to expand the scope and overcome limitations of the reaction. For example, $PdCl_2(CH_3CN)_2$ complex has been found to be the optimal catalyst to effect the Sonogashira reaction under copper-free [94-95] and phosphine-free condition [96]. With $Pd(OAc)_2$ catalyst, homocoupling of terminal alkynes in the synthesis of symmetric diynes has shown to be effective methods under mild reaction condition (Figure 5.2). The similar protocol has been used to catalyze cross-coupling of 1-iodo-4-nitrobenzene with phenylacetylene. The reactions were carried out smoothly in good yields. However, in this case the presence of CuI disfavor the cross-coupling reaction of the less reactive aryl iodides and bromides [97].

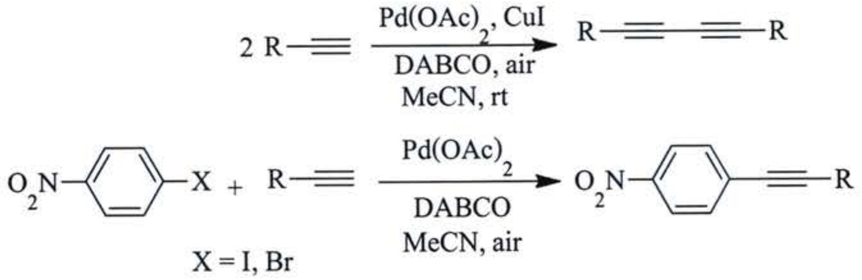


Figure 5.2 Palladium-catalyzed homocoupling and cross-coupling of Sonogashira reaction

The goal of many researches is to develop effective, copper-free, easily available catalyst and starting aryl chlorides, and mild condition reactions. Microwave irradiation has been used to shorten the reaction time and in many cases has shown to improve the yields of the reactions [98]. For example, palladacycle/Xphos has been successfully used to deacetonative Sonogashira reaction of electron-poor, electron-neutral, and even inactive sterically hindered electron-rich aryl chlorides such as aryl propargyl alcohols as shown in Figure 5.3 [99].

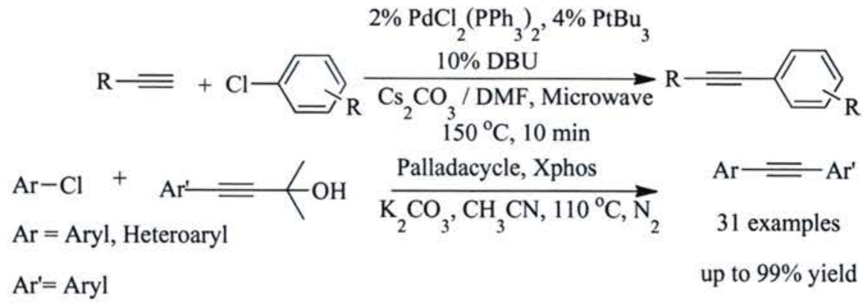


Figure 5.3 Pd-catalyzed Sonogashira coupling of aryl chlorides [98]

Although homogeneous catalysts have many advantages [100], heterogeneous catalyst is a well-known methodology to allow efficient catalyst separation and to obtain metal-free products. Several types of solid materials such as zeolites [101], alumina [102], silica [103] and polymers [104] have been used to support transition-metal species. The separation of the catalysts from the reaction mixture is essential for returnable of catalyst. Compare to heterogeneous catalyst, the separation of homogeneous catalyst is more difficult, therefore many strategies have been utilized to isolate the catalyst.

Magnetic nanoparticles or magnetic-supported catalysts have attracted many interests due to their insoluble and paramagnetic nature that empowers easy and efficient separation of the catalysts from the reaction mixture with an external magnet [12, 105-106]. For example, Pd catalyst supported on nanoferrite composites were used as catalyst for Suzuki and Heck coupling reactions. The catalyst is completely recoverable using external magnet as presented in Figure 5.4 and Figure 5.5 [107].

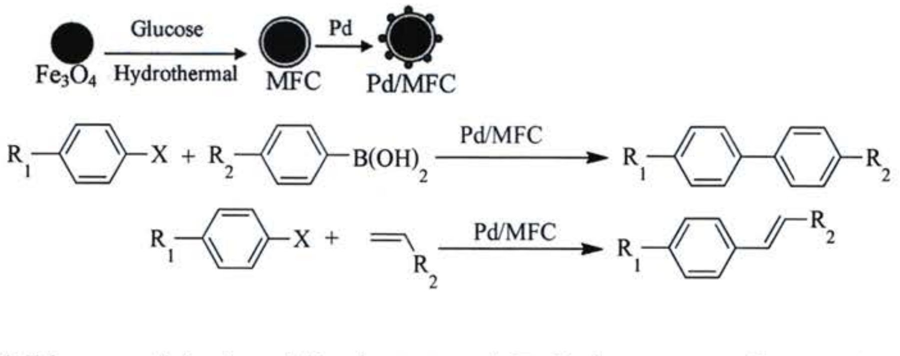


Figure 5.4 Pd nanoparticles immobilized on magnetic Fe_3O_4 for cross-coupling reactions [108]

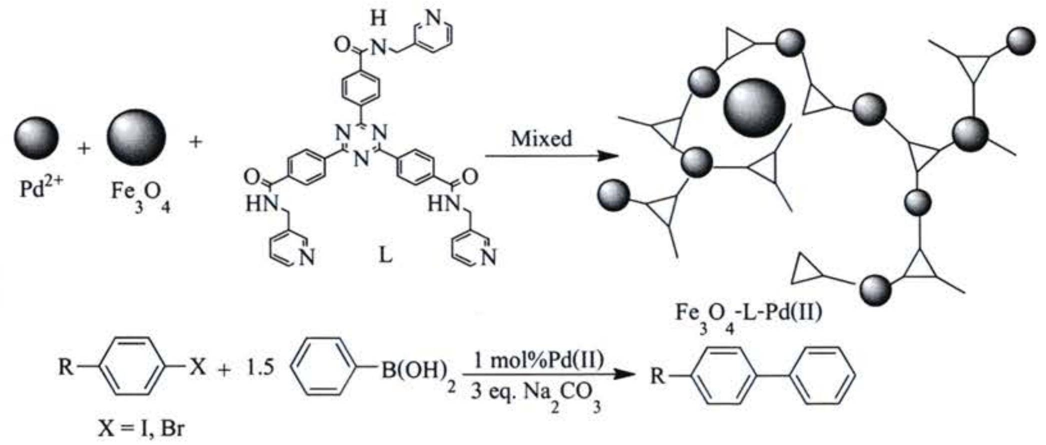


Figure 5.5 Pd(II) supported on magnetic gel nanofibers for Suzuki reaction [107]

In order to increase the stability of metal catalyst supported on magnetic materials, the desired ligand has to be attached to the surface of the magnetic nanoparticle. One of the methods to modify of the surface of supporting medium with ligand is to covalently attach them together. Griffete, N. and coworker reported the preparation of water-soluble magnetic nanocrystal using aryl diazonium salt chemistry as shown in Figure 5.6 [109]. This method results in strong Fe_3O_4 and aryl bonds, therefore the material is suitable for further applications.

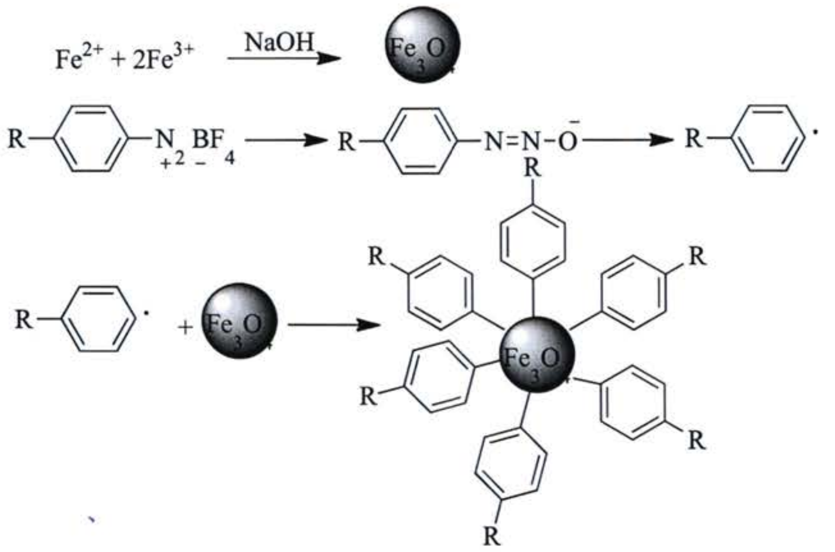


Figure 5.6 Surface fictionalization of Fe_3O_4 using aryl diazonium salt chemistry [109]

In this work, we synthesized *N*-heterocyclic carbenes ligand (NHCs) which was covalently attached on the surface of Fe_3O_4 nanoparticles. Then supported palladium(II) catalyst and used for Sonogashira cross-coupling reaction. The catalyst complexes exhibit high stability, allowing for long term storage, easy handling, and recyclability.

5.3 Results and discussions

5.3.1 Synthesis and characterization of catalyst

We prepared **CAT1** from N-heterocyclic carbenes ligand (NHCs) modified Fe_3O_4 nanoparticle and then supported $PdCl_2$ using four steps as reported in Figure 5.7.

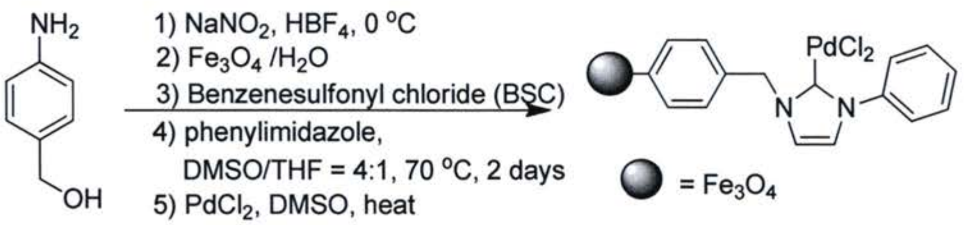


Figure 5.7 Synthesis of **CAT1** using diazonium chemistry

The **CAT1** catalyst was characterized by XRD, SEM and FT-IR and the results as shown in Figure 5.8, 5.9 and 5.10 respectively. As can be seen from the XRD patterns, the modification of Fe_3O_4 surface with 4-aminobenzyl alcohol (AMA) and deposition of phenyl immidazole (PI) and palladium catalyst did not change the structure of Fe_3O_4. However, from SEM images and FT- IR spectra, it can be clearly observed the difference of the Fe_3O_4 surface before and after deposition of palladium catalyst. The synthesized **CAT1** catalyst was then examined for catalytic activity in Sonogashira reaction.

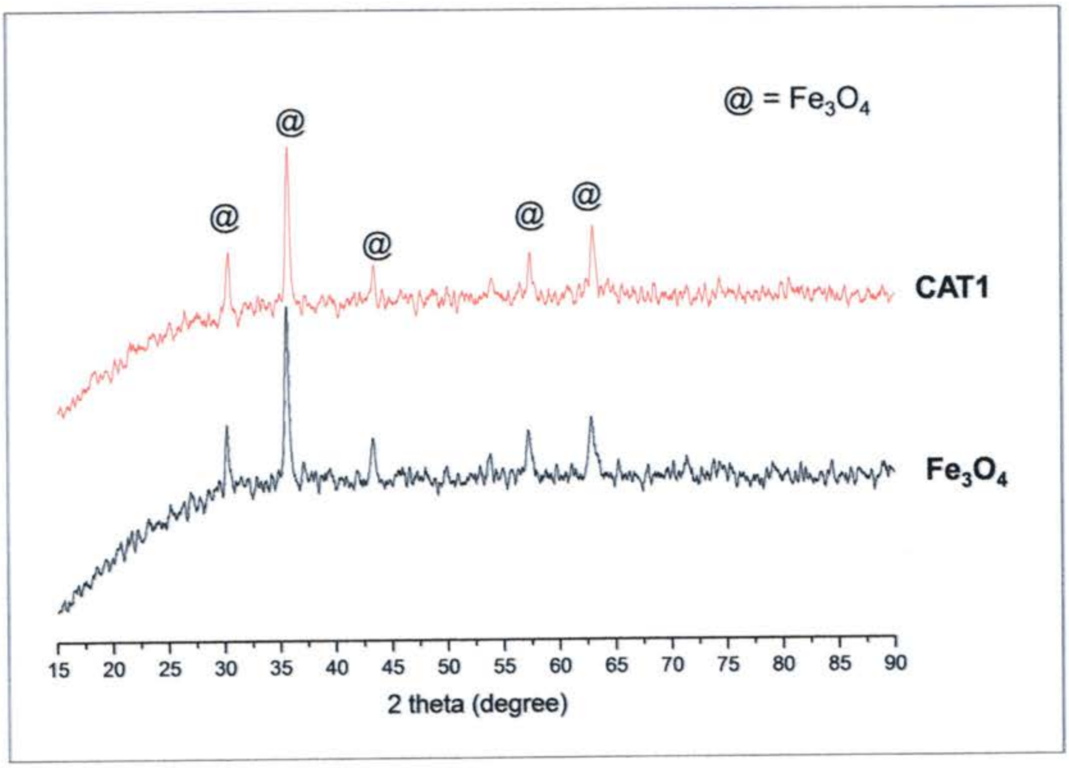


Figure 5.8 X-ray diffractograms of **Fe_3O_4** and **CAT1**

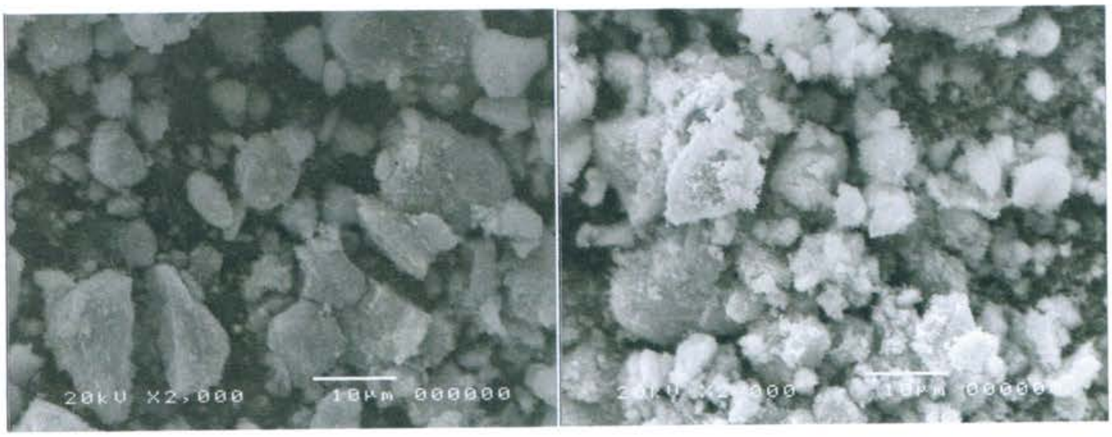


Figure 5.9 SEM images of **Fe_3O_4** (left) and **CAT1** (right)

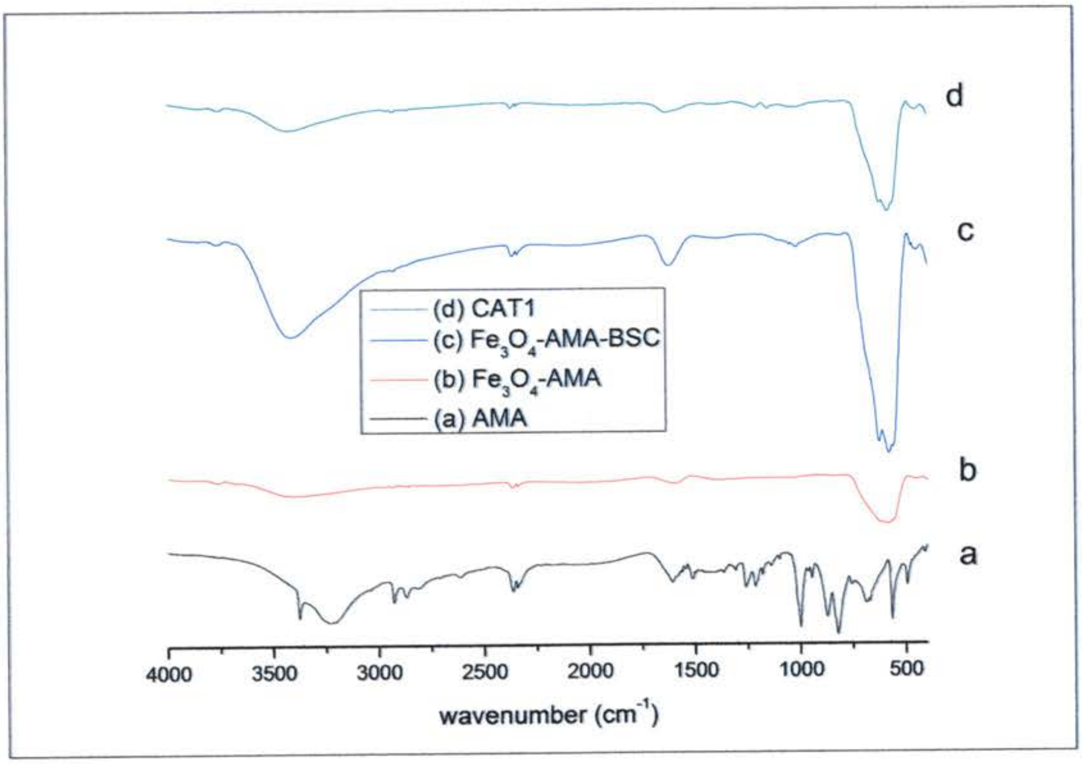
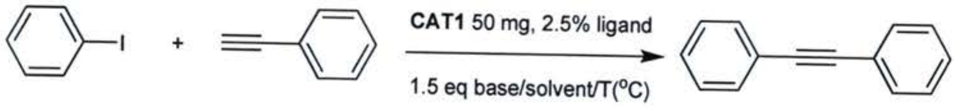


Figure 5.10 FT- IR spectra of (a) **AMA**, (b) **Fe_3O_4-AMA**, (c) **Fe_3O_4-AMA-BSC** and (d) **CAT1**

5.3.2 Optimization of the reaction

We started with optimization the reaction in which iodobenzene and phenylacetylene were chosen as model compounds and the results as shown in Table 5.1.

Table 5.1 Optimization of Sonogashira reaction using **CAT1** catalyst



Entry	Solvents	2.5%Ligand	Base	T(°C)	% GC yields[a]
1	DMF	PPh_3	KOH	100	59
2	DMF	PPh_3	Na_2CO_3	100	23
3	DMF	PPh_3	K_2CO_3	100	3
4	DMF	PPh_3	Cs_2CO_3	100	76
5	DMF	Bipy	Cs_2CO_3	100	71
6	DMF	Phen	Cs_2CO_3	100	45
7	Toluene	PPh_3	Cs_2CO_3	100	6
8	DMSO	PPh_3	Cs_2CO_3	100	22
9	Ethanol	PPh_3	Cs_2CO_3	100	88
10	Ethanol	PPh_3	Cs_2CO_3	90	100[b]
11	Ethanol	PPh_3	Cs_2CO_3	70	62
12	Ethanol	PPh_3	Cs_2CO_3	50	0
13[c]	Ethanol	PPh_3	Cs_2CO_3	90	0

[a] % GC yield with dodecane as internal standard, [b] conditions: 1.0 mmol phenylacetylene, 1.0 mmol iodobenzene, 50 mg **CAT1**, 2.5% ligand, 1.5 mmol base, 3 mL solvent, heated for 20 h 90 °C, [c] no catalyst

First, we started to optimize the base with DMSO and PPh_3 as solvent and ligand, respectively. Various bases such as KOH, Na_2CO_3, K_2CO_3, and Cs_2CO_3 were examined as shown in entries 1-4. The results revealed that strong bases (KOH and Cs_2CO_3, entries 1 and 4) were more effective than weak bases (Na_2CO_3 and K_2CO_3, entries 2 and 3), therefore Cs_2CO_3 was chosen as a base for this Sonogashira reaction. Next, two common ligands such as 2,2'-bipyridine (Bipy) and 1,10-phenanthroline (Phen) were used instead of PPh_3 ligand. It can be seen that PPh_3 is the most effective ligand in stabilizing the palladium species resulted in better yield (entry 4) than other ligands (entries 5 and 6) [110]. Solvents also affect the yield of the reaction. From the previous work, it was found that polar solvents increase the reaction rate [111], and in this case it was found that the product yields increased in the order of toluene < DMSO < DMF < EtOH as solvent (entries 4 and 7-9). With EtOH as the best solvent, we then examined the possibility of decreasing reaction temperature from 100° to 50 °C (entries 10-12). It is evident that at 90 °C (entry 10) the yield was higher than 100 °C. However, the temperature lower than 90 °C resulted in much lower yield (entries 11-12); therefore optimal reaction temperature is 90°C. Finally, we found that catalyst is essential to the reaction and without catalyst, the reaction could not proceed to give the desired product (entry 13).

In the recycling experiments, the catalyst separated from reaction mixture using external magnet was used without any modification. The results as shown in Figure 5.6 revealed that the catalyst can be used up to four runs with only slightly decrease of product yields.

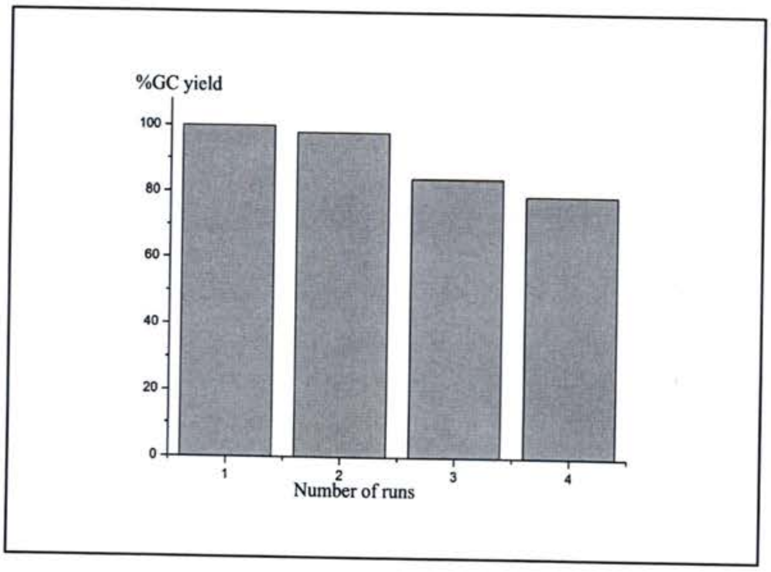
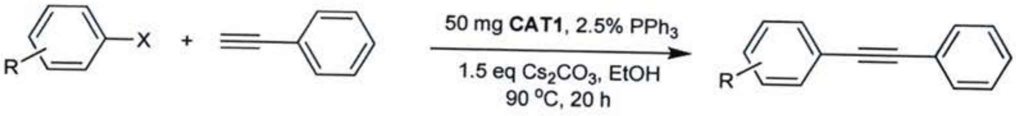


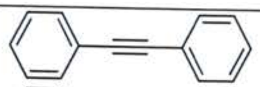
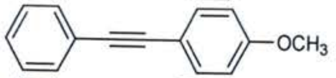
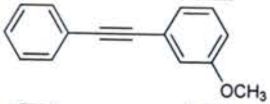
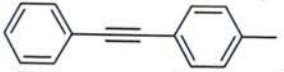
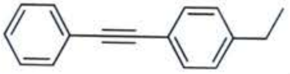
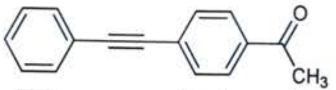
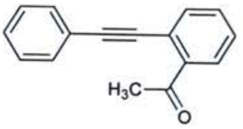
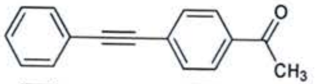
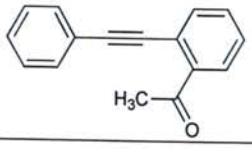
Figure 5.11 Recycling of **CAT1** for Sonogashira reaction

5.3.3 CAT1 catalyzed Sonogashira reaction of phenylacetylene and aryl halides

With the optimal reaction conditions using 50 mg **CAT1** as catalyst, 2.5% PPh_3 as ligand, 1.5 eq Cs_2CO_3 as base, and ethanol as solvent, at 90°C for 20 hours, various kinds of aryl halides were coupled to phenylacetylene in moderate to excellent yields as shown in Table 5.2.

Table 5.2 Sonogashira reaction of phenylacetylene and aryl halides using **CAT1** catalyst



Entry	X	Products	Isolated Yields (%)
1	I		86
2	I		95
3	I		81
4	I		90
5	I		96
6	I		98
7	I		68
8	Br		96
9	Br		60

With the optimum conditions, we then examined the scopes of the developed protocol to couple phenylacetylene with various aryl halides as shown in Table 5.2. Both electron rich (entries 1-5) and electron poor (entries 6-9) aryl iodides were coupled in good to excellent yields within 20 h. Aryl bromide substrates (entries 8-9) gave comparable yields as the aryl iodides with the acetyl as functional group. In addition, substrates with sterically hindrance at *ortho* position resulted in lower yields (entries 7 and 9).

Finally, various catalysts that have been prepared in our group were tested for their catalytic activities to the Sonogashira coupling reaction. Under the optimal conditions, it was found that **CuNPs, Cu$_2$ONPs, Fe$_3$O$_4$-DOPA-Pd** were effective catalysts for Sonogashira reaction.

In this case, **Fe_3O_4-DOPA-Pd** gave comparable yield to the **CAT1**, and surprisingly **CuNPs** gave excellent yield under the same conditions.

The possible mechanism of **CAT1** catalyzed Sonogashira reaction is represented in Figure 5.12. The Pd(II) complex **I** is converted to active [Pd^0]catalyst **II** which then undergoes oxidation addition by inserting into C-X bond of aryl halides forming complex **III**. Aryl acetylene coordinated to the complex **III** resulted in complex **IV** and facilitates deprotonation of the terminal alkyne proton. After reacts with base, the acetylide ion exchanges with halide X to form complex **V**, which is upon reductive elimination gives desired diaryl acetylene product and the [Pd^0] catalyst **II** back to the catalytic cycle.

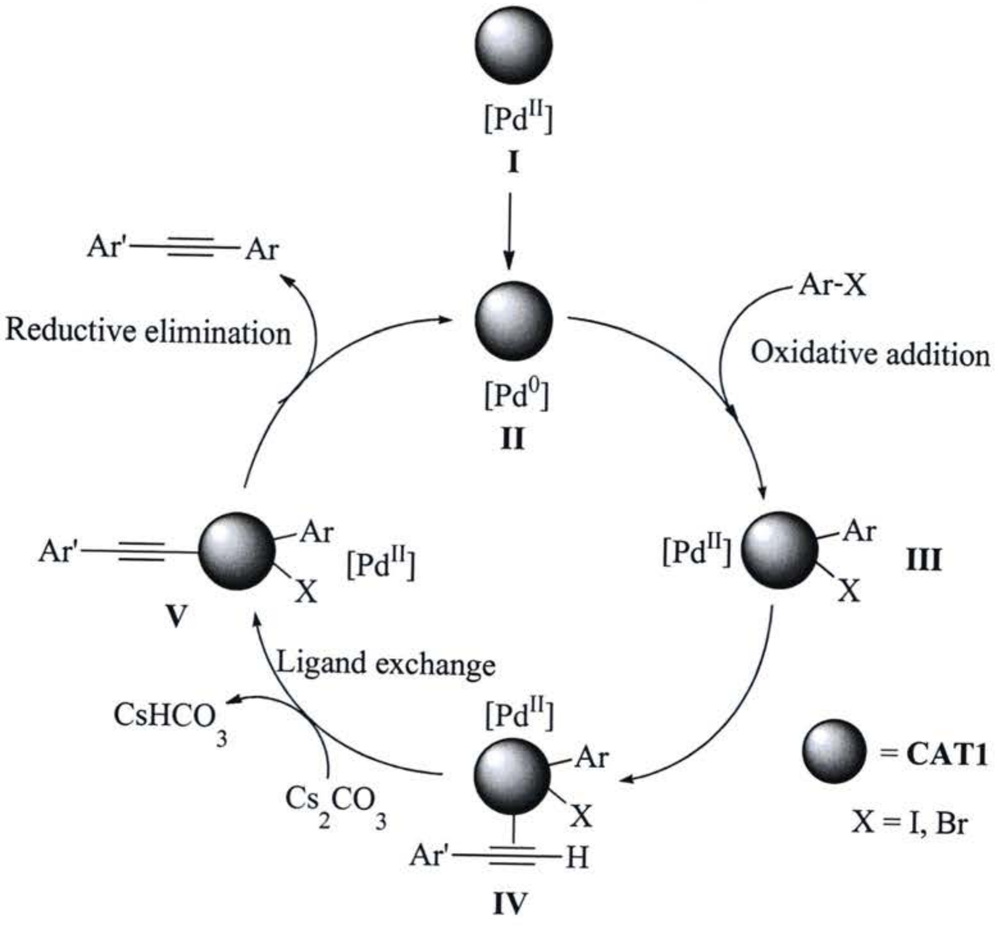


Figure 5.12 Possible mechanism for **CAT1** catalyzed Sonogashira reaction

5.4 Conclusion

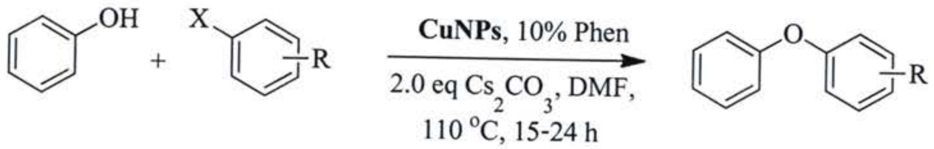
In conclusion, we have prepared **CAT1** catalyst which has Pd(II)-carbene complex covalently attached to the surface of Fe_3O_4 nanoparticles using diazonium chemistry. The **CAT1** catalyst was used to develop a protocol for the synthesis of diarylacetylene using Sonogashira coupling reaction. Varieties of diarylacetylenes were synthesized in good to excellent yields. The catalyst can be separated from the reaction mixture using external magnet and reused without any special treatment. The catalysts could be reused 4 times with only slightly decreased of product yield in Sonogashira coupling of iodobenzene with phenylacetylene.

CHAPTER 6

CONCLUSION

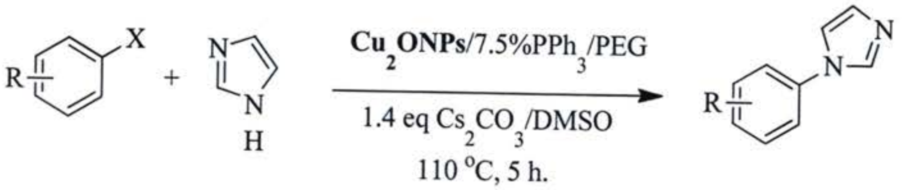
The aim of this thesis work has been focused on preparation of heterogeneous copper and palladium catalysts and applications for cross-coupling reactions. These catalysts include of **CuNPs**, **Cu_2ONPs**, **Fe_3O_4-DOPA-Pd** and **CAT1** catalyst which have been shown to be effective catalysts for C-O, C-N, and C-C bond formations.

Firstly, we prepare copper and copper(I) oxide nanoparticles (**CuNPs** and **Cu_2ONPs**) by simple chemical reduction method and then examined the catalytic activities as heterogeneous catalyst for cross-coupling reactions. Through the optimization, we developed a method for C-O bond formation using phenol coupled to aryl halides for the synthesis of diarylethers with **CuNPs** as catalyst as shown in equation (1). Varieties of diarylethers were synthesized at moderate to good yields.



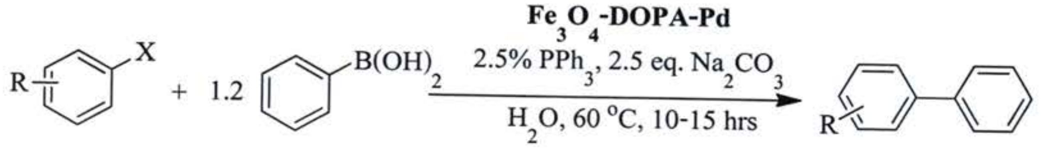
(1)

Cu_2ONPs has been found to be effective catalyst for C-N bond formation through cross-coupling reaction of imidazole to aryl halides as shown in equation (2). This method offered a simple and effective catalyst system to carry out C-N bond formation of heterocycle.



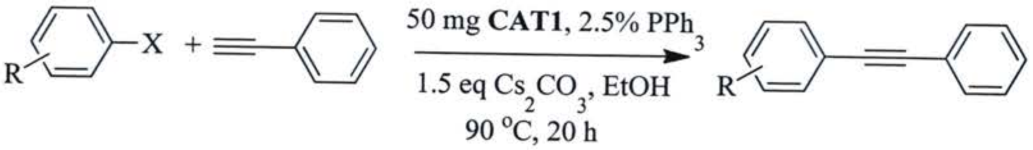
(2)

We also prepared palladium catalysts supported on nanoferrite magnetic material (Fe_3O_4).The **Fe_3O_4-DOPA-Pd** catalyst was prepared by simple method and used as reusable catalyst for the synthesis of biaryl using Suzuki-Miyaura reaction (equation (3)). Varieties of biaryls were synthesized in good to excellent yields. The catalysts could be reused for 4 consecutive cycles that only slightly decrease of product yields was observed.



(3)

Finally, we have prepared **CAT1** catalyst in which the Pd(II)-carbene complex was covalently attached the Fe_3O_4. The catalyst was applied for the synthesis of diarylacetylene using Sonograshira coupling reaction as shown in equation (4). Varieties of diarylacetylene were synthesized in good to excellent yields. The catalyst was found to be effective and only slightly decrease for product yield was obtained after the 4th run.



(4)

These heterogeneous catalysis protocols offered a simple separation of the catalysts and therefore the reuse of the catalyst is achievable. These are important for developing economic and green organic synthesis methods.

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APPENDIX

A. Chemicals and instruments

Table A-1 Chemicals

Chemicals	Formula	Assay (%)	Manufacturer
Iron (II,III) oxide nanopowder	Fe_3O_4	98.0 %	SIGMA ALDRICH
Palladium(II) chloride	$PdCl_2$	59.9 %	SIGMA ALDRICH
Hydrochloric acid	HCl	37.0 %	CARLO ERBA
Potassium hydroxide	KOH	-	AKZO NOBEL
Acetone	C_3H_6O	99.8%	CARLO ERBA
Sodium hydroxide	NaOH	97.0%	CARLO ERBA
Methanol	CH_3OH	99.9%	CARLO ERBA
Acetic acid	CH_3COOH	-	CARLO ERBA
Sodium dodecyl sulfate (SDS)	$NaC_{12}H_{25}SO_4$		CARLO ERBA
1,10-Phenanthroline	$C_{12}H_8N_2$	-	CARLO ERBA
Dichloromethane	CH_2Cl_2	99.5%	CARLO ERBA
Tetrahydrofuran	C_4H_8O	99.5%	CARLO ERBA
Diethyl ether	$C_4O_{10}O$	99.7%	CARLO ERBA
Dimethylsulfoxide	C_2H_6OS	99.9%	CARLO ERBA
Toluene	C_7H_8	99.5%	CARLO ERBA
Ethyl alcohol	CH_3CH_2OH	99.9 %	MERCK
Chloroform-D	CCl_3D	99.8 %	ACROS
Celite	-	-	ACROS
Cesium Carbonate	Cs_2CO_3	99.5%	ACROS
Sodium stearate	$C_{18}H_{35}NaO_2$	-	ACROS
Potassium carbonate	K_2CO_3	-	ACROS
Phenylacetylene	C_8H_6	98.0%	ACROS
N,N'-Dimethylformamide	C_3H_7NO	99.8%	ACROS
Iodobenzene	C_6H_5I	98.0%	ACROS
Dodecane	$C_{12}H_{26}$	99.0%	ACROS
Sodium carbonate	Na_2CO_3	99.5%	ACROS

Phenol	C_6H_5OH	-	ACROS
Imidazole	$C_3H_4N_2$	99.0%	ACROS
Triphenylphosphine	$C_{18}H_{15}P$	99.0%	ACROS
Dopamine	$C_8H_{11}NO_2.HCl$	99.0%	ACROS
4-Bromobenzaldehyde	C_7H_5BrO	99.0%	ACROS
Sodium borohydride	$NaBH_4$	98.0%	ACROS
4-Iodotoluene	C_7H_7I	98.0%	ACROS
3-Iodoanisole	C_7H7IO	97.0%	ACROS
4-Iodoanisole	C_7H_7IO	98.0%	ACROS
2-Iodoacetophenone	C_8H_7IO	99.0%	ACROS
4-Iodoacetophenone	C_8H_7IO	98.0%	ACROS
Methyl-4-iodobenzoate	C_8H_7IO	98.0%	ACROS
2-Bromoacetophenone	C_8H_7BrO	98.0%	ACROS
4-Bromoacetophenone	C_8H_7BrO	98.0%	ACROS
1-Ethyl-4-iodobenzene	C_8H_9I	-	ACROS
Ethyl-4-bromobenzoate	$C_9H_9BrO_2$	99%	ACROS
2,2'-Dipyridine	$C_{10}H_8N_2$	99.0%	ACROS
1-Iodo-4-nitrobenzene	$C_6H_4INO_2$	99.0%	ACROS
1-Bromo-4-nitrobenzene	$C_6H_4BrNO_2$	99.0%	ACROS
Fluoroboric acid	HBF_4	50.0%	ACROS

Table A-2 Instruments

Instruments	**Model**	**Company**
X-ray diffractometer (XRD)	Philips X 'pert MPD	Philips
Scanning electron microscope (SEM)	JSM 5410-LV	JEOL
Fourier transform infrared spectrometer (FT-IR)	Spectrum RX 1	Perkin Elmer
Gas chromatography (GC)	GC-17 A	Shimadzu
Nuclear magnetic resonance spectrometer (NMR)	AVANCE 300 MHz	Bruker

B. Experimental detail

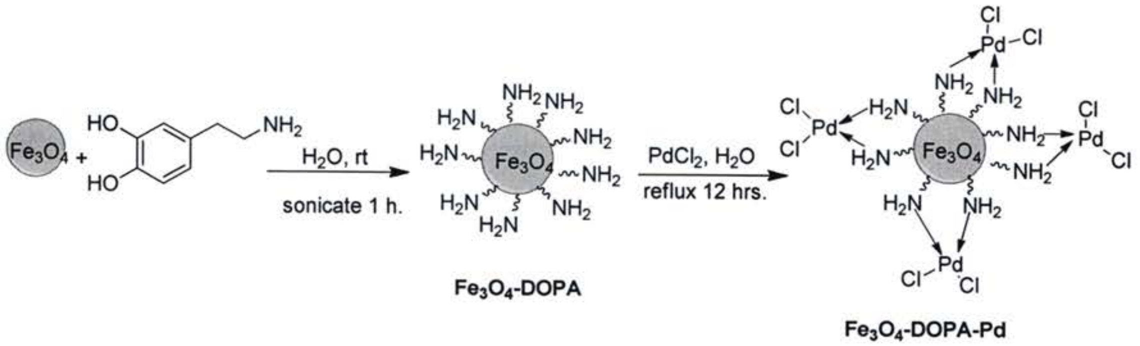
General information: All of the reactions reported herein were conducted under nitrogen atmosphere unless otherwise noted. All chemicals and solvents were obtained from commercial suppliers and used as received without further purification. The optimizations were reported as GC yields using dodecane as an internal standard and gas chromatograph used was a Shimadzu GC-17 A series with a 30-meter 100% dimethylpolysiloxane capillary column. Analytically pure samples were obtained by chromatography on silica gel using an ethyl acetate-hexanes mixture as the eluent unless specified otherwise. The yields given refer to isolated yields of the characterized compounds. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AVANCE 300 MHz spectrometer. Chemical shifts (δ) were reported in parts per million (ppm) and TMS was used as the internal reference. Melting points were uncorrected. Power X-ray diffraction (XRD) was performed on a Philips X 'pert MPD X-ray diffractometer with Cu K_{α} (λ = 0.154 nm) radiation. The FT-IR spectra were recorded on Perkin Elmer Spectrum RX 1 FT-IR spectrophotometer. The morphology of were determined by using JEOL JSM 5410 scanning electron microscope (SEM).

B-1 Preparation of the catalysts

Preparation of copper nanoparticle catalyst (CuNPs): Copper(II) chloride (3.57 g, 20.99 mmol) dissolved in 100 mL of distilled water was added 50 mL methanolic solution of sodium stearate (1.14 g, 3.75 mmol) and stirred constantly at room temperature for 30 minutes. Then the mixture was heated at 70 ° C for an hour. Sodium borohydride (2.26 g, 59.82 mmol) solution in ethanol 50 mL was slowly dropped and stirred at 70 °C for 2 hours. Cooled down the reaction mixture to room temperature, then centrifuged and washed with ethanol 3 times. The reaction mixture was filtered, washed with excess hot water and dried at 70-80 °C. The copper nanoparticle was obtained as black powder 3.01 g.

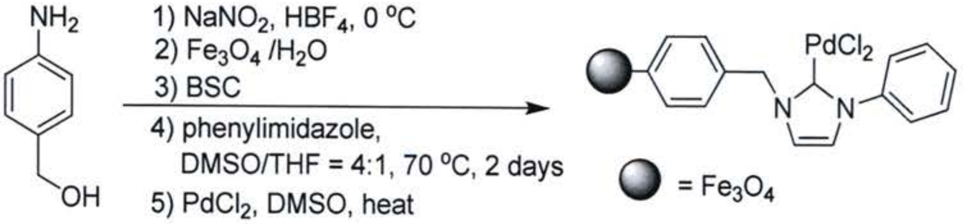
Preparation of copper (I) oxide nanoparticle catalyst (Cu_2ONPs): Glucose (3.17 g, 17.63 mmol), sodium hydroxide solution (100 ml, 1.29 g, 32.50 mmol) and sodium dodecyl sulfate (SDS) (3.43 g, 11.92 mmol) were added in a round bottom flask and stirred constantly until completely dissolved. After that, solution of copper(II) nitrate (3.88 g, 16.08 mmol) was added and the mixed solution was refluxed for 24 hours. The reaction mixture was cooled down, filtered, and washed with excess hot water and dried at 100 °C. The copper(I) oxide nanoparticle was obtained as dark red powder 2.18 g.

Preparation of the Fe_3O_4-DOPA-Pd(II) catalyst:



Dopamine-modified nanoferrite (Fe_3O_4-DOPA) was prepared by mixing nanoferrite (Fe_3O_4, 2.00 g) with dopamine hydrochloride (3.00 g) in 50 mL water under ultrasonication for 1.5 h. After that Fe_3O_4-DOPA (0.3 g) and $PdCl_2$ (0.1 g) in 30 mL water mixture was stirred overnight at room temperature. Finally, the **Fe_3O_4-DOPA-Pd(II)** was separated, washed with water and acetone, and dried at 60°C for 2 h. The resulting **Fe_3O_4-DOPA-Pd(II)** was obtained as black powder 0.27 g.

Preparation of the CAT1 catalyst

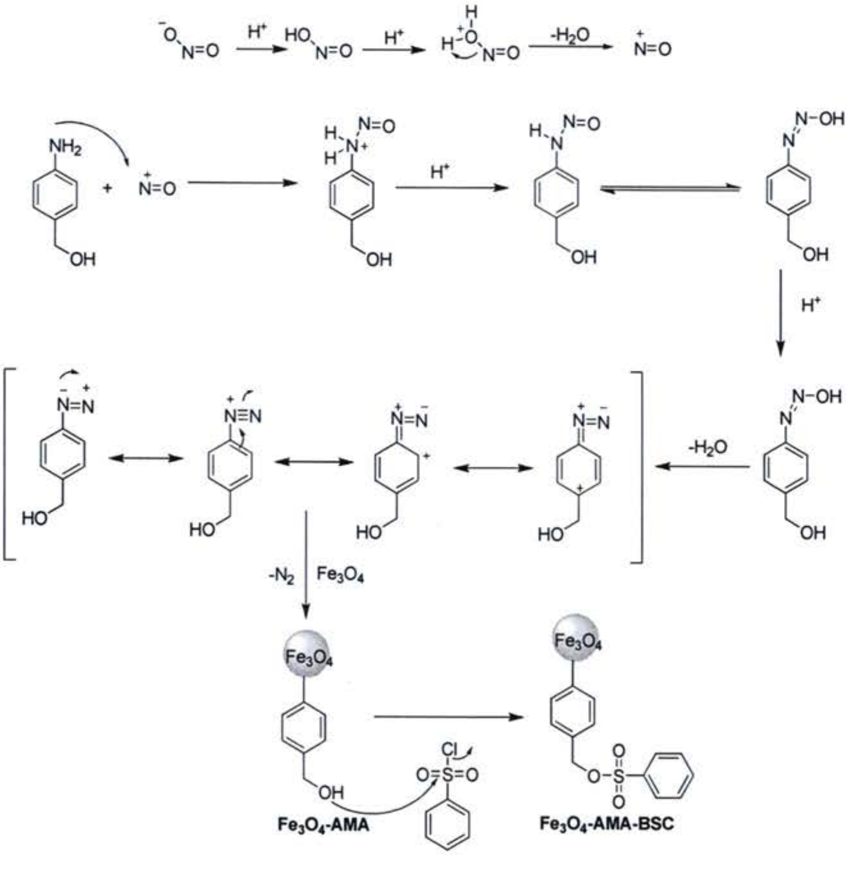


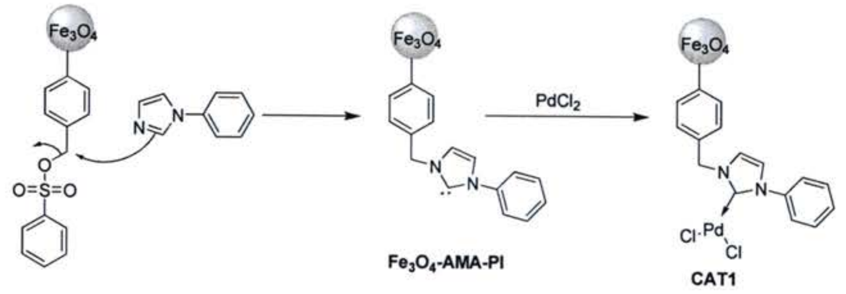
Fe_3O_4 supported 4-aminobenzyl alcohol (Fe_3O_4-AMA): Typically a solution of $NaNO_2$ (0.63 g, 6 mmol) in DI water (3 mL) was added dropwise to a cold solution (in an ice bath) composed of 4-aminobenzyl alcohol (0.09 g, 0.75 mmol) and HBF_4 (0.3 mL) in DI water (15 mL). The reaction was conducted at 0 °C for 1 h. The slightly turbid pale grey solution of benzene diazonium salt solution was obtained. Fe_3O_4 particles (1.5 g) were dispersed in 20 mL water by ultrasonicating and then the diazonium salt solution was added and sonicated for another hour. The particles were washed by 5 cycles of water and ethanol and dried at 50 °C.

Fe_3O_4-AMA-benzyl chloride (Fe_3O_4-AMA-BSC): A mixture of Fe_3O_4-AMA (0.34 g), Benzenesulfonyl chloride (BSC) (0.36 g, 2.0 mmol) was stirred in THF (15 mL) at room temperature for 1 h, then added 50% NaOH (10 mL) and refluxed for 5 h. Cooled down the reaction mixture to room temperature, added 2 N HCl (40 mL) and then washed with excess water and ethanol, and dried at 60 °C.

Fe_3O_4-AMA-Bz-phenyl imidazole (Fe_3O_4-AMA-PI): The **Fe_3O_4-AMA-BSC** (0.1 g) and phenylimidazole (0.15 g) were mixed and stirred in DMSO/THF (15:5 mL) at 70 °C for 2 days. After cooling to room temperature, the reaction was washed with DMF (3x20 mL), DCM (3x20 mL) and methanol (3x20 mL). The **Fe_3O_4-AMA-PI** product was dried at 60 °C.

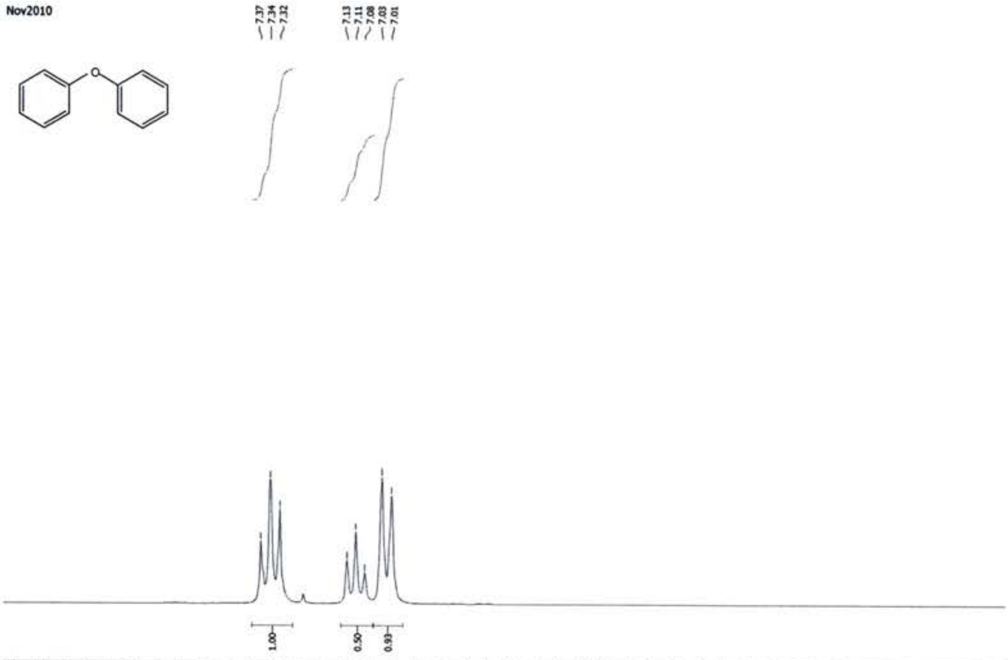
Fe_3O_4-AMA-PI-$PdCl_2$ (CAT1) : A mixture of **Fe_3O_4-AMA-PI** (1.2 g), $PdCl_2$ (0.08 g) was stirred in DMSO (20 mL) at 50 °C for 4 h. After increasing the temperature to 100 °C, the mixture was stirred further for an hour and then washed thoroughly with DMSO (5x10 mL), distilled water (5x10 mL) and MeOH (5x10 mL). The product was then dried at 60 °C.

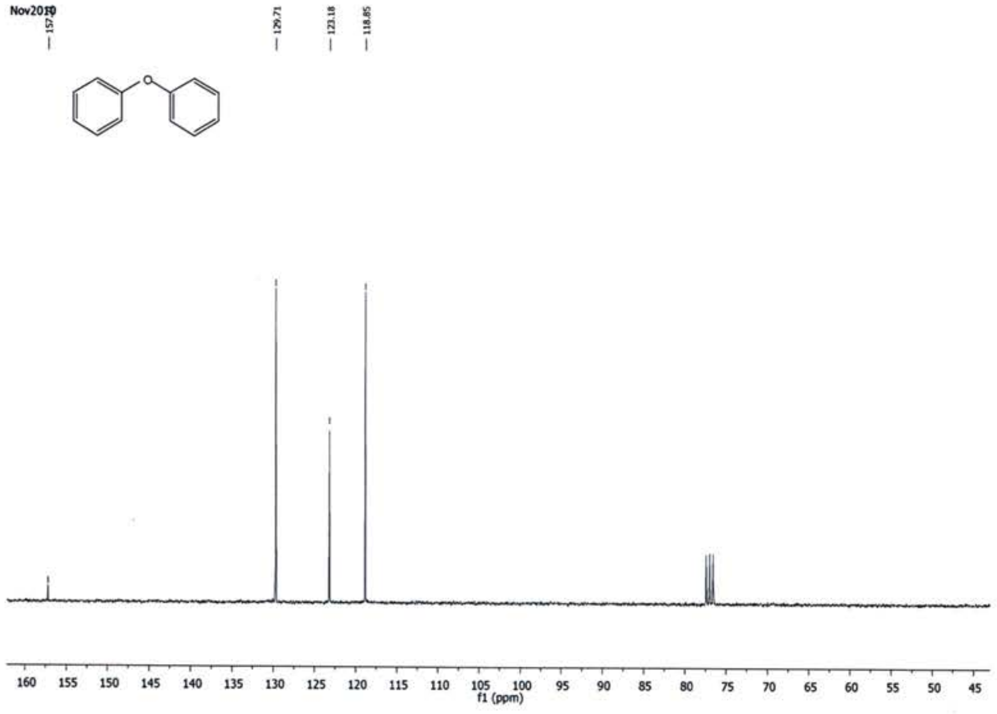




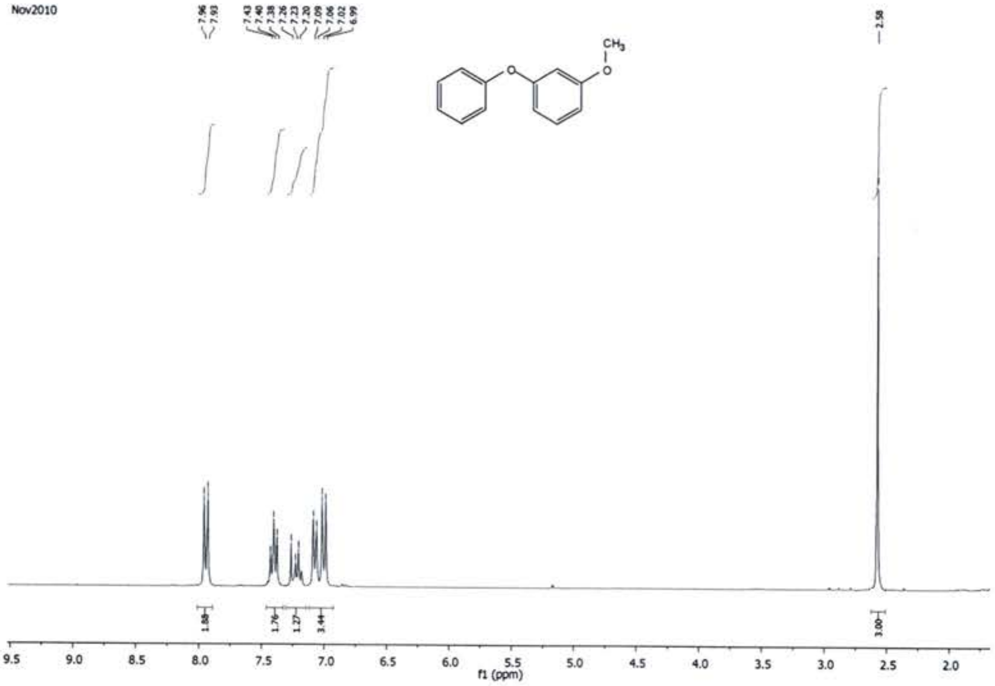
B-2 General experimental procedure for phenol coupling: A flamed-dried Pyrex glass tube equipped with a stir bar was charged with copper nanoparticle (20 mg), phenol (0.10 g, 1.1 mmol), cesium carbonate (0.48 g, 1.5 mmol), 1,10-phenanthroline (0.02 g, 10%), and the appropriate aryl halide (1.0 mmol). The tube was then sealed with a rubber septum and evacuated and backfilled with nitrogen gas 5 times. *N,N*-dimethylformamide 3 mL was injected through the septum. The contents were then stirred at 110 °C for 15 h. Cooled down the reaction mixture to room temperature, then added dodecane (1.0 mmol) as an internal standard and extracted with ethyl acetate for gas chromatography analysis of %yield. To determine the isolated yield, the reaction mixture was filtered through celite to remove any insoluble residues. The filtrate was then extracted with ethyl acetate (3x10 mL), washed with brine, dried with anhydrous sodium sulfate, filtered and concentrated in vacuo. The residue was purified by column chromatography on silica gel to obtain the pure product.

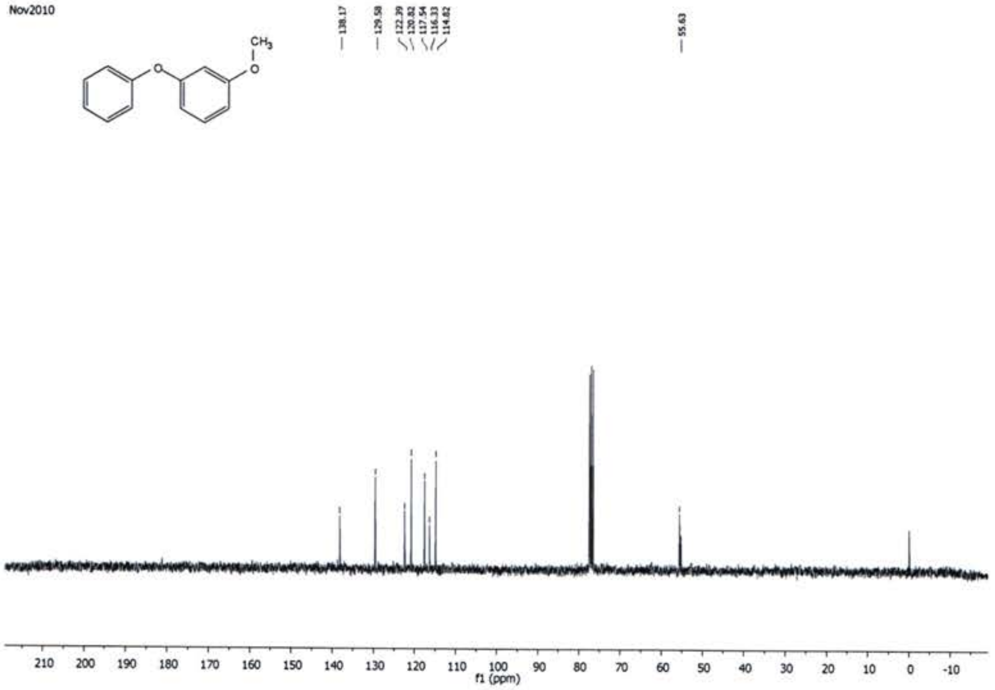
Diphenyl ether : The general procedure was used to afford the title product. (55% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34 (t, *J* = 7.9 Hz, 4H), 7.11 (t, *J* = 7.4 Hz, 2H), 7.02 (d, *J* = 7.8 Hz, 4H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.21, 129.71, 123.18, 118.85.



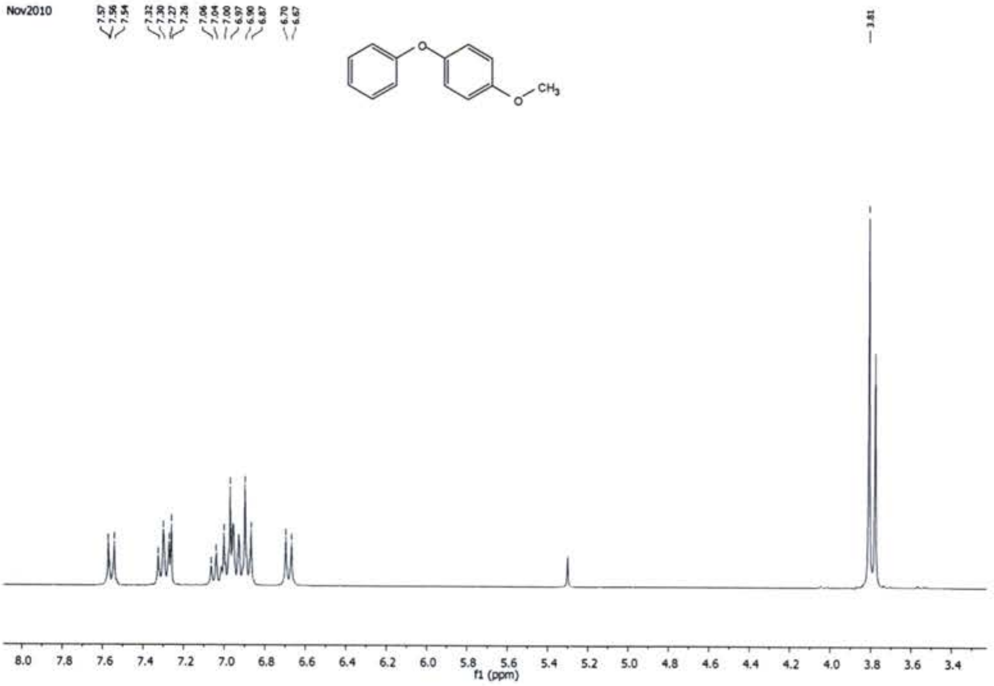


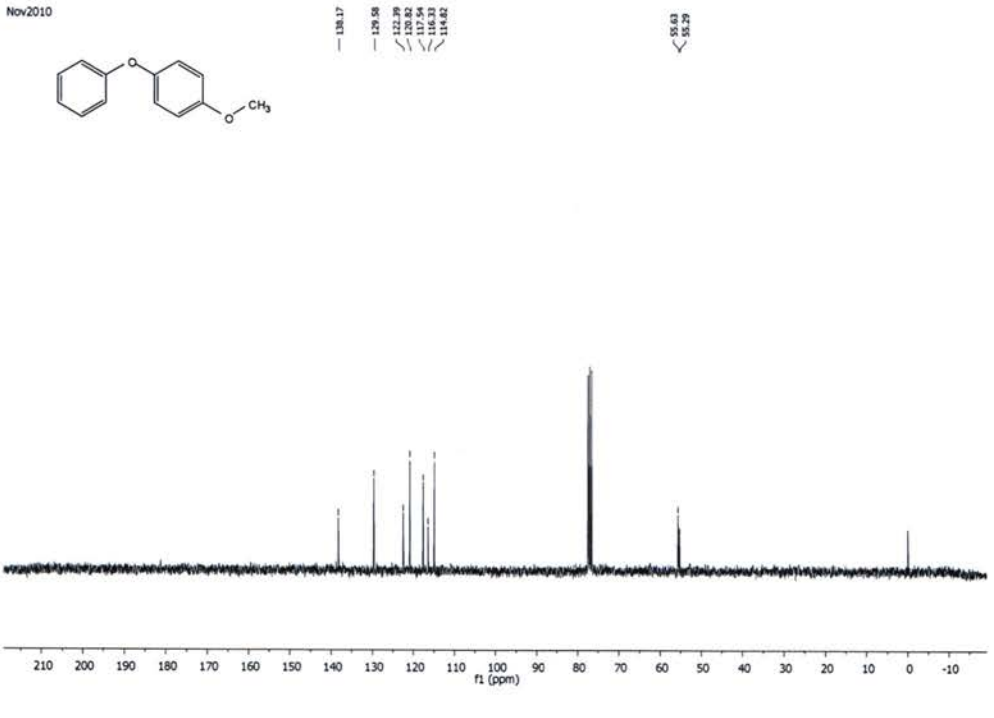
1-methoxy-3-phenoxybenzene: The general procedure was used to afford the title product. (56% yield) ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35 – 7.30 (m, 2H), 7.23 – 7.18 (m, 1H), 7.11 – 7.06 (m, 1H),7.01 – 6.99 (m, 2H), 6.92 – 6.90 (m, 1H), 6.83 – 6.80 (m, 2H), 2.58 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.5, 157.4, 140.1, 129.8, 129.6, 124.2, 123.2, 119.7, 119.0, 116.1, 55.50.



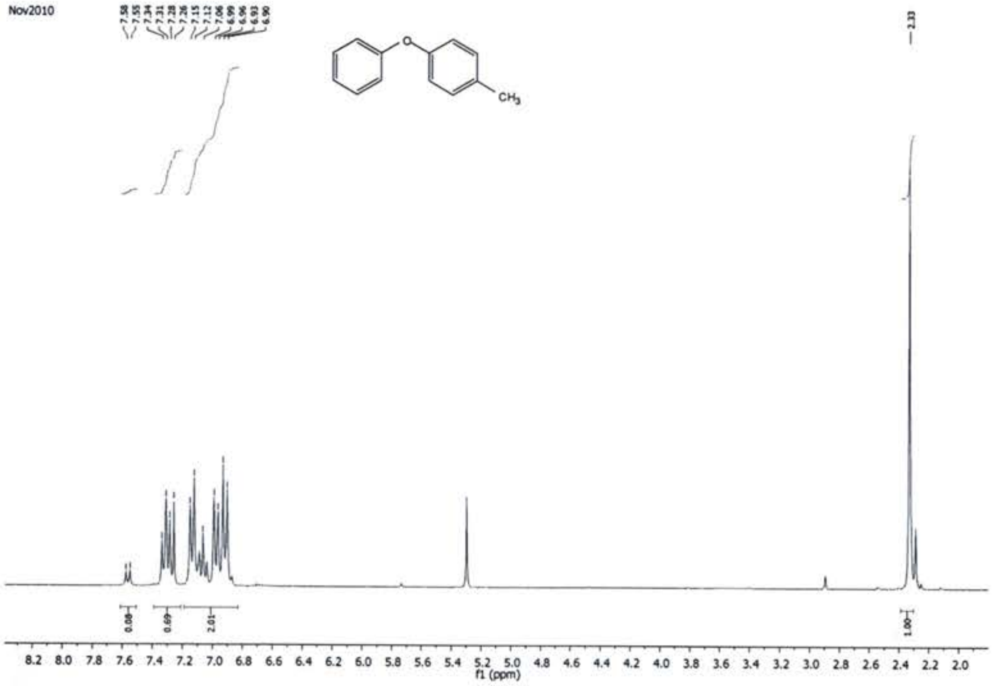


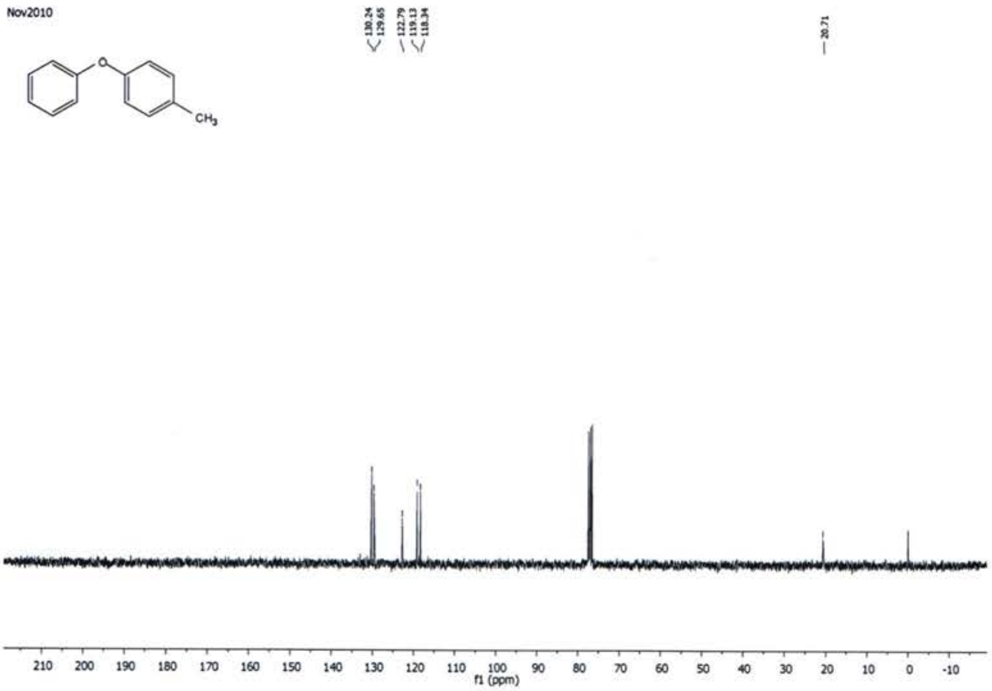
1-methoxy-4-phenoxybenzene: The general procedure was used to afford the title product. (45% yield) ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.56 (d, J = 8.9 Hz, 1H), 7.32 – 7.26 (m, 2H), 6.97 – 6.87 (m, 5H), 6.68 (d, J = 8.9 Hz, 1H), 3.81 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.09, 129.58, 122.39, 120.82, 117.50, 116.33, 55.63.



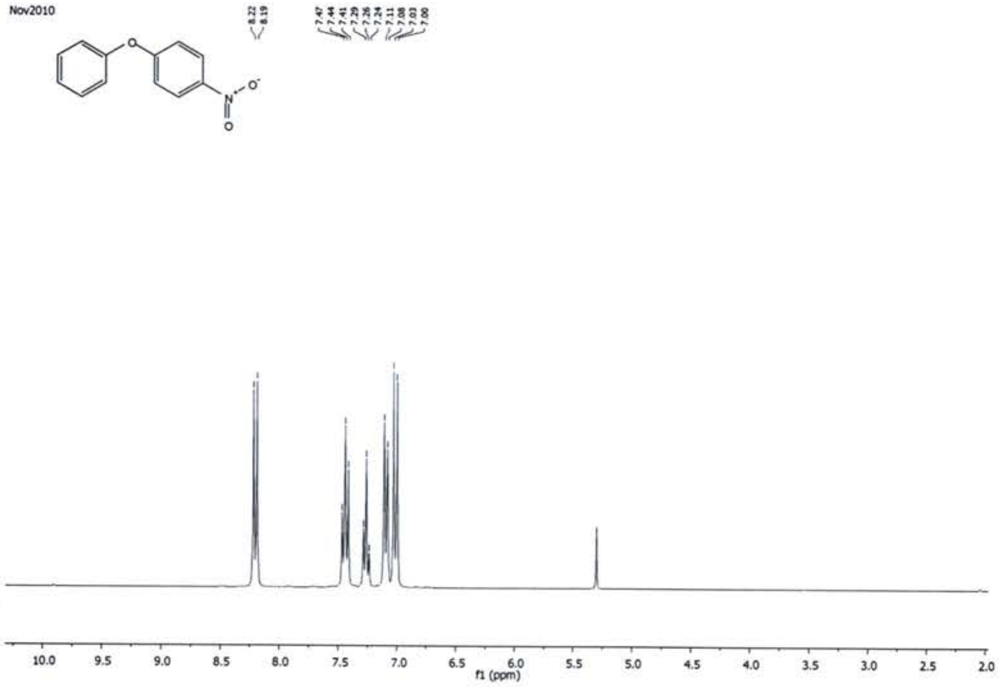


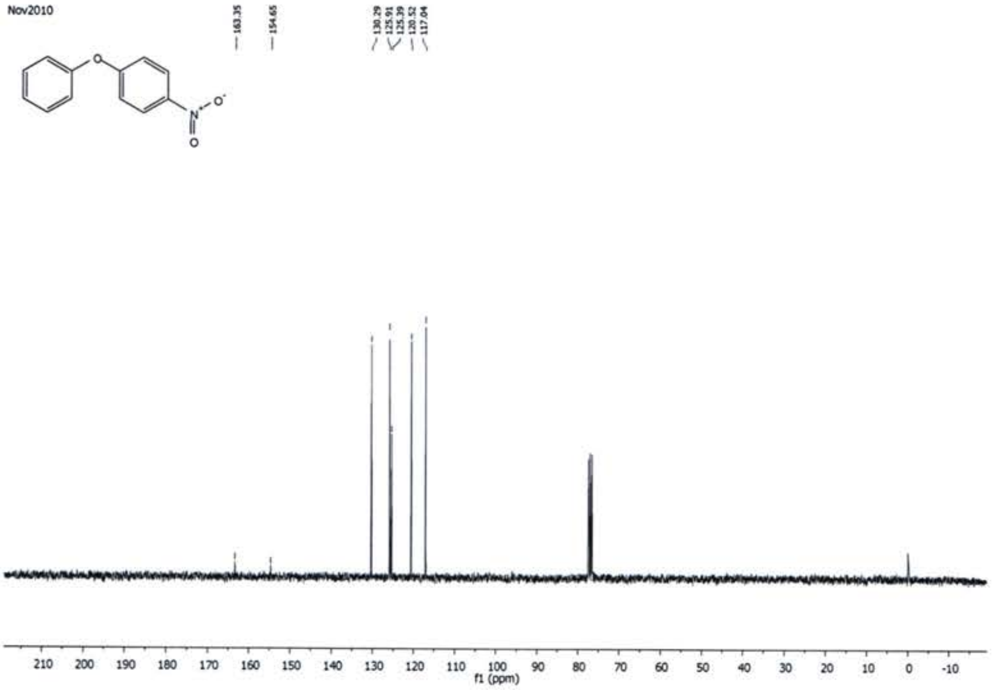
1-methyl-4-phenoxybenzene : The general procedure was used to afford the title product. (57% yield) ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34 – 7.25 (m, 2H), 7.15 – 7.07 (m, 3H), 7.01 – 6.86 (m, 4H), 2.33 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 130.24, 129.65, 122.79, 119.13, 118.34, 20.71.



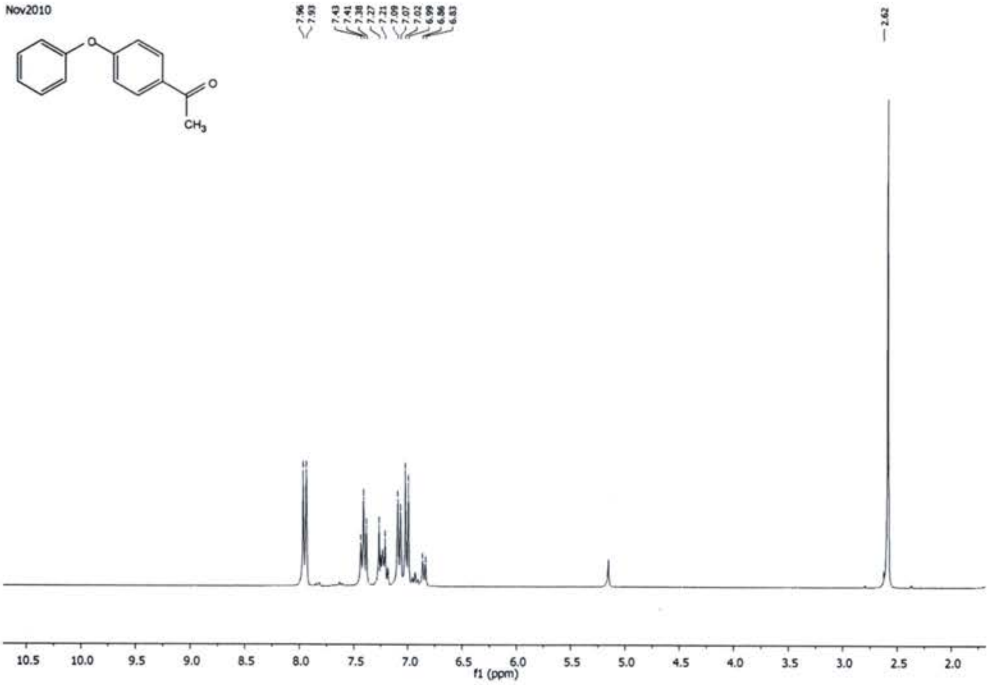


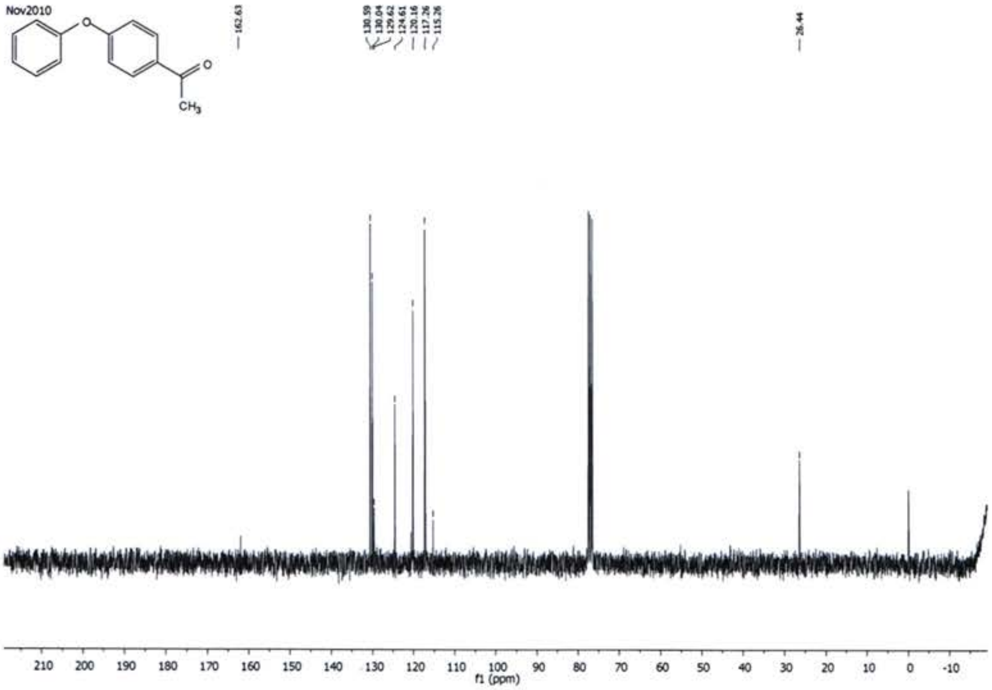
1-nitro-4-phenoxybenzene : The general procedure was used to afford the title product. (55% yield) ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.20 (d, J = 9.2 Hz, 2H), 7.44 (t, J = 7.9 Hz, 2H), 7.26 (t, J = 7.4 Hz, 1H), 7.10 (d, J = 7.7 Hz, 2H), 7.01 (d, J = 9.2 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.35, 154.59, 130.29, 125.91, 125.39, 120.52, 117.04.



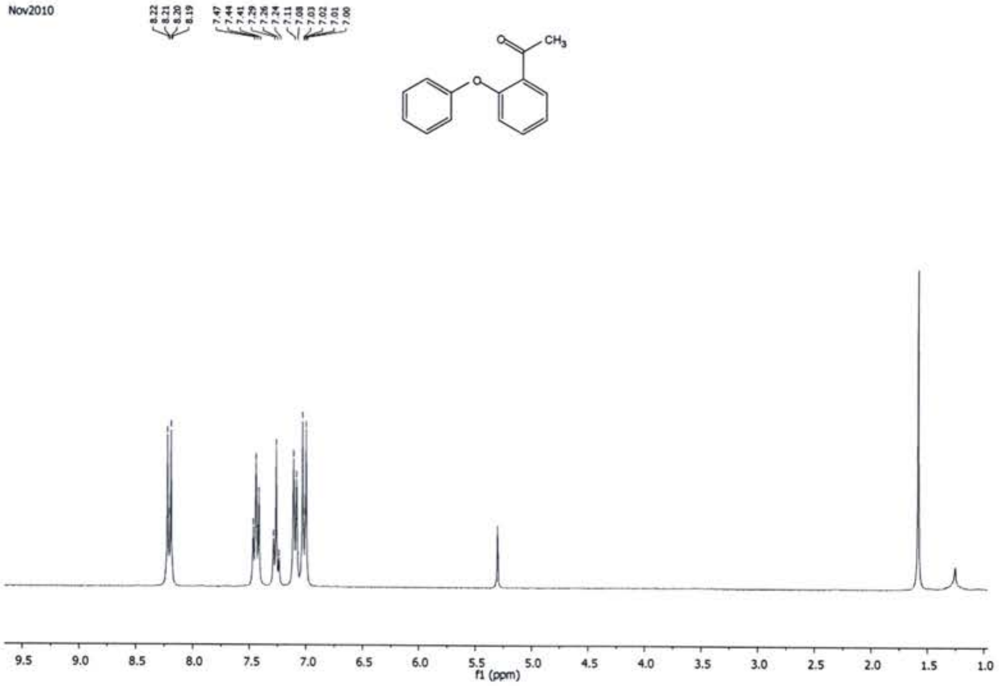


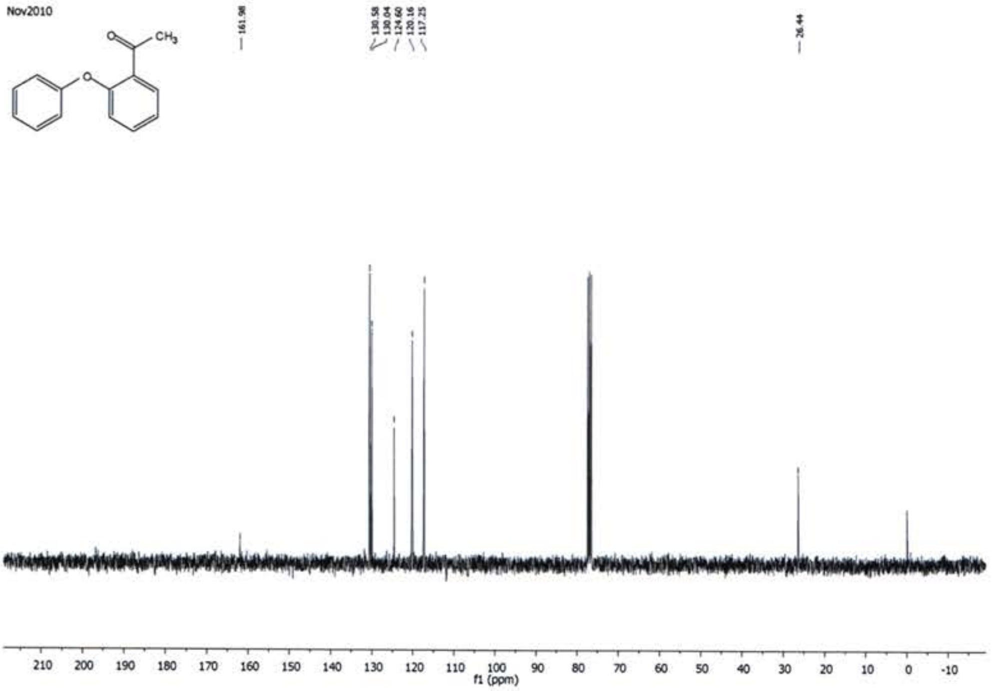
1-(4-phenoxyphenyl)ethanone : The general procedure was used to afford the title product .(82% yield) ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.94 (d, *J* = 8.8 Hz, 2H), 7.40 (t, *J* = 7.9 Hz, 2H), 7.20 (t, *J* = 7.4 Hz, 1H), 7.07 (d, *J* = 7.8 Hz, 2H), 7.00 (d, *J* = 8.8 Hz, 2H), 2.58 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.63, 130.58, 130.04, 124.60, 120.16, 117.25, 26.44.



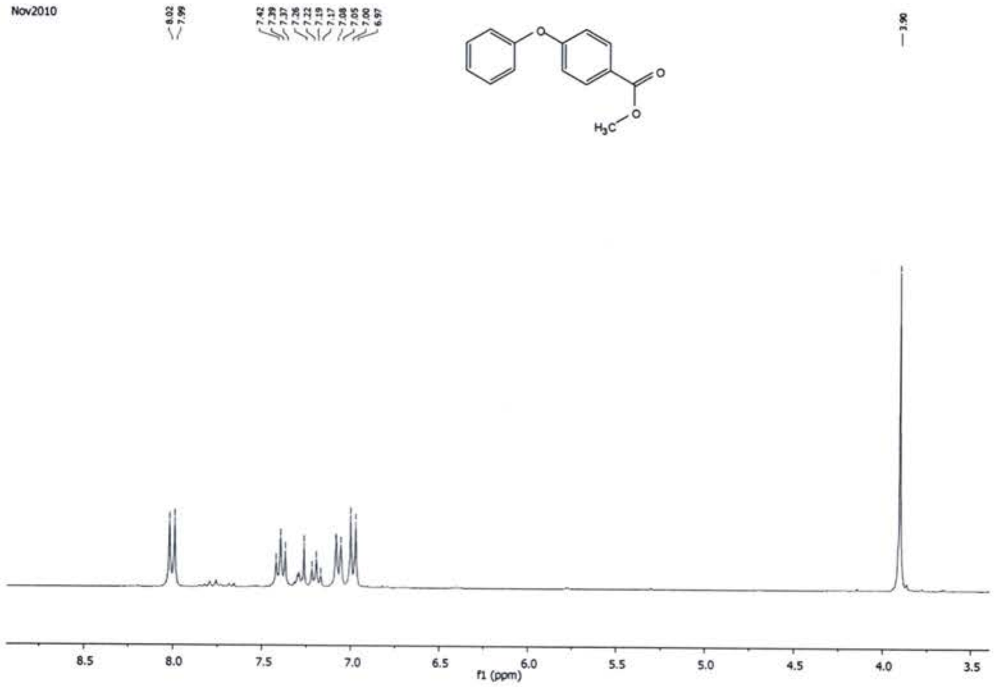


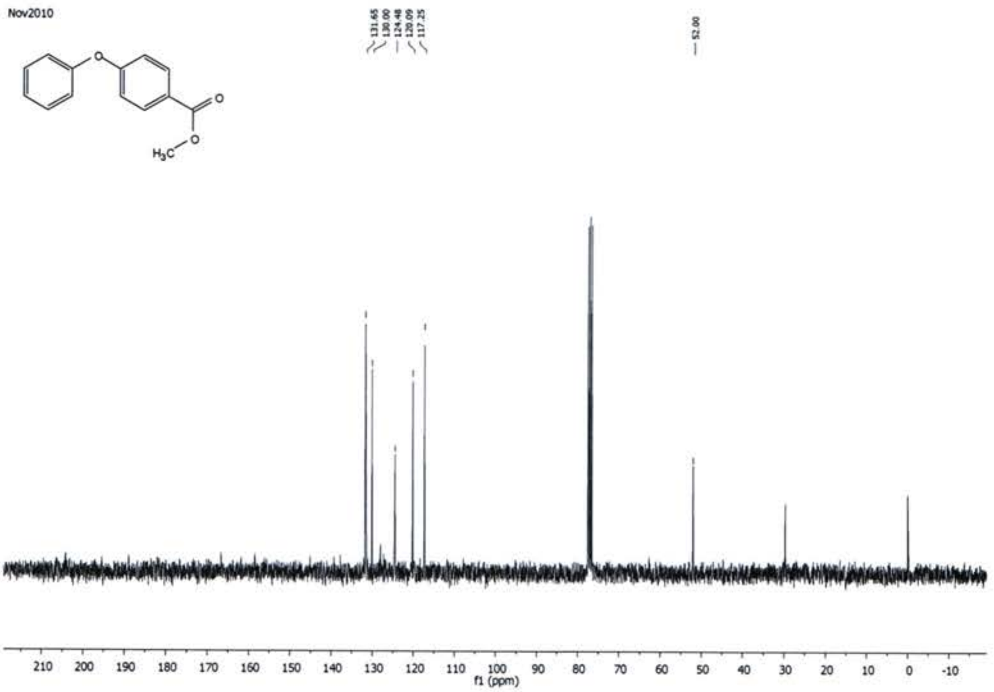
1-(2-phenoxyphenyl)ethanone : The general procedure was used to afford the title product. (46% yield) ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34 – 7.26 (m, 2H), 7.19 – 7.02 (m, 3H), 6.99 – 6.90 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.00, 130.59, 130.04, 129.62, 124.61, 120.16, 117.26, 115.26, 26.44.



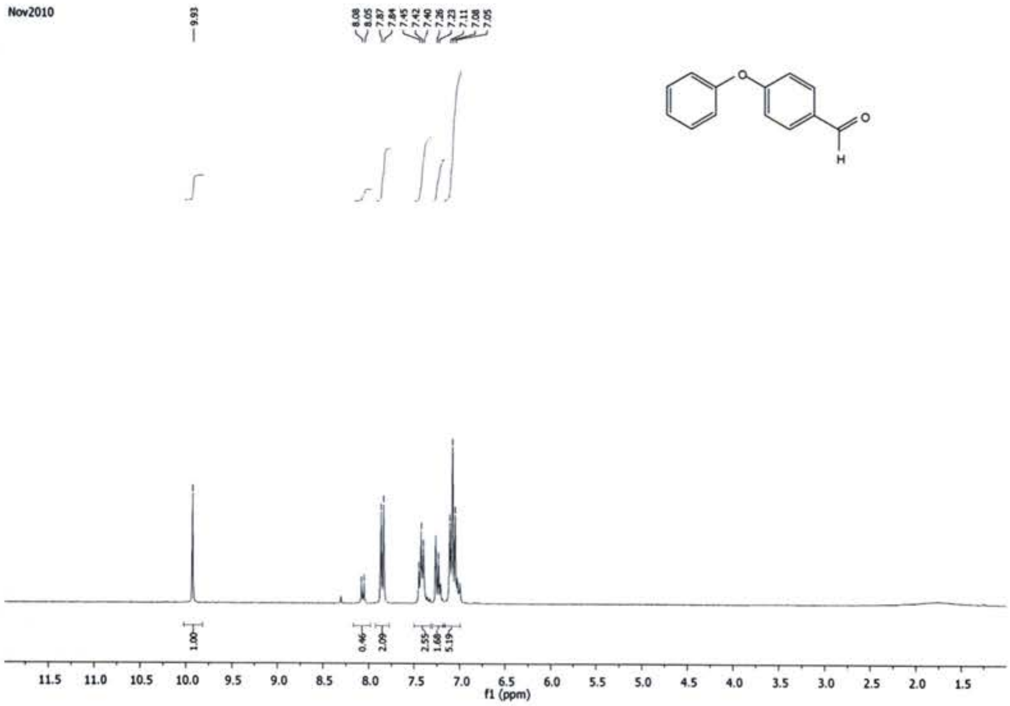


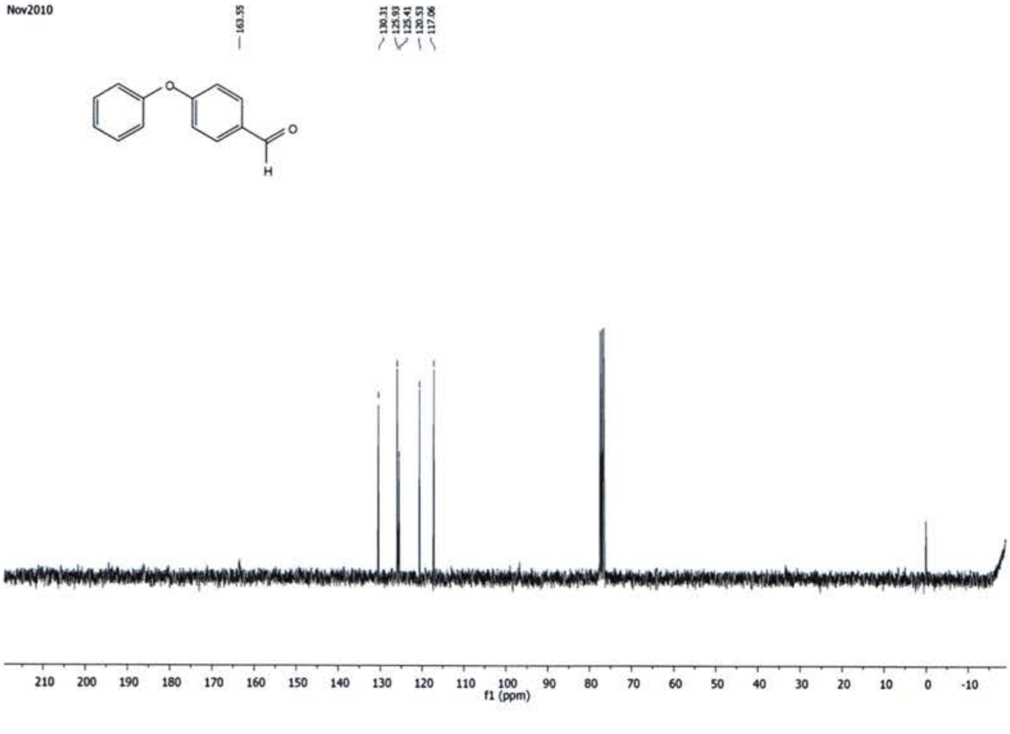
Methyl 4-phenoxybenzoate : The general procedure was used to afford the title product. (12% yield) ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.00 (d, J = 8.8 Hz, 2H), 7.39 (t, J = 7.9 Hz, 2H), 7.19 (t, J = 7.4 Hz, 1H), 7.07 (d, J = 8.6 Hz, 2H), 6.99 (d, J = 8.8 Hz, 2H), 3.90 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 131.65, 130.00, 124.48, 121.45, 120.09, 117.25, 102.45, 52.00.



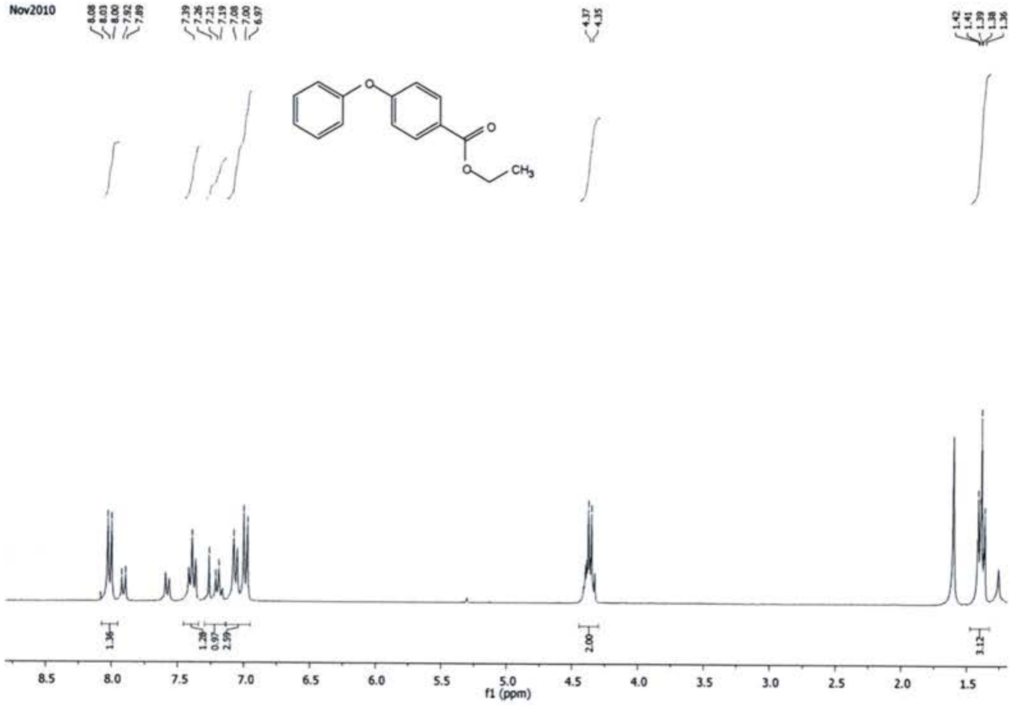


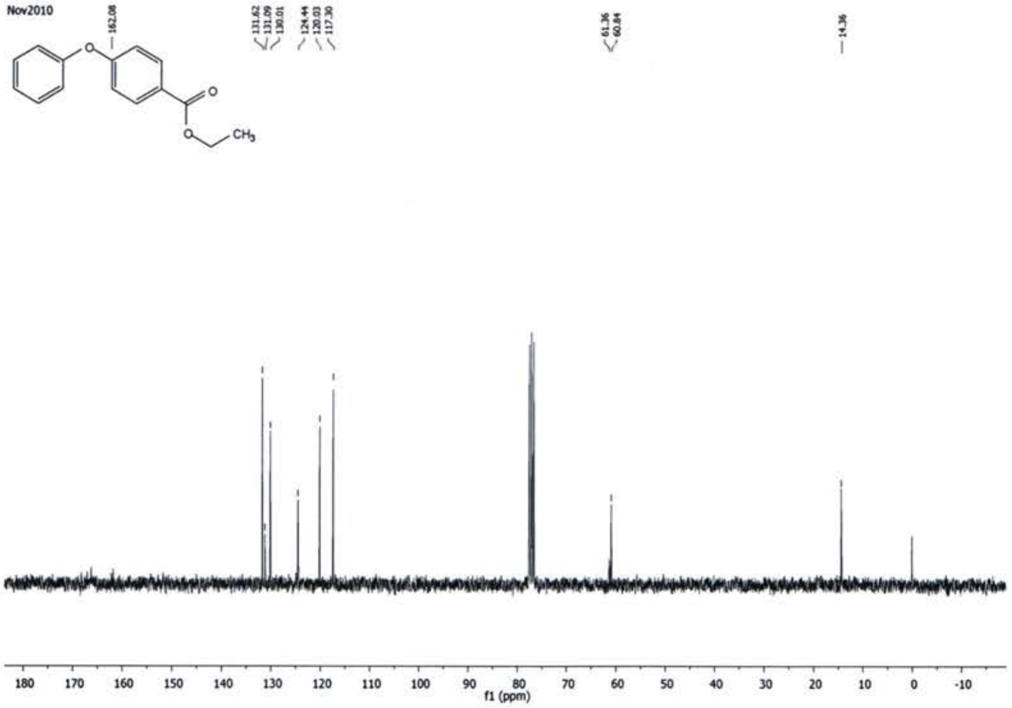
4-Phenoxybenzaldehyde : The general procedure was used to afford the title product (71% yield) ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.93 (s, 1H), 7.85 (d, *J* = 8.7 Hz, 2H), 7.42 (t, *J* = 7.9 Hz, 2H), 7.28 – 7.20 (m, 1H), 7.08 (t, *J* = 8.5 Hz, 4H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.55, 132.31, 125.53, 125.41, 120.53, 117.06.





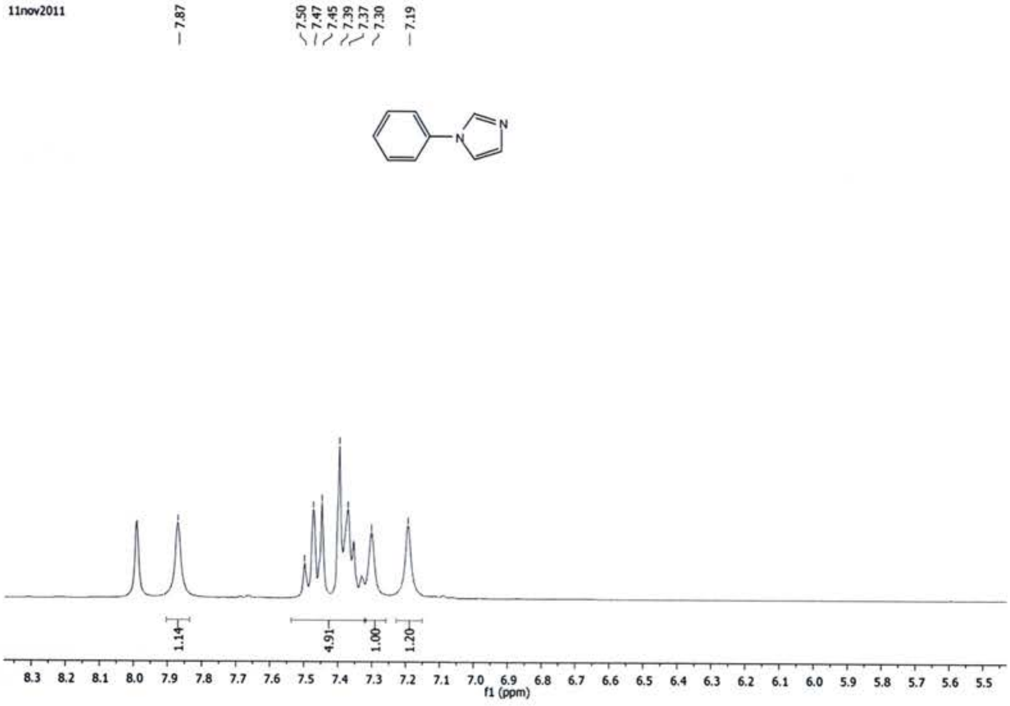
Ethyl 4-phenoxybenzoate : The general procedure was used to afford the title product (21% yield) ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.01 (d, *J* = 8.8 Hz, 2H), 7.39 (t, *J* = 7.9 Hz, 2H), 7.19 (t, *J* = 7.4 Hz, 1H), 7.06 (d, *J* = 7.7 Hz, 2H), 6.99 (d, *J* = 8.8 Hz, 2H), 4.40 – 4.34 (m, 2H), 1.42 – 1.36 (m, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.08, 131.62, 131.09, 130.01, 124.44, 120.03, 117.30,61.36, 60.84,

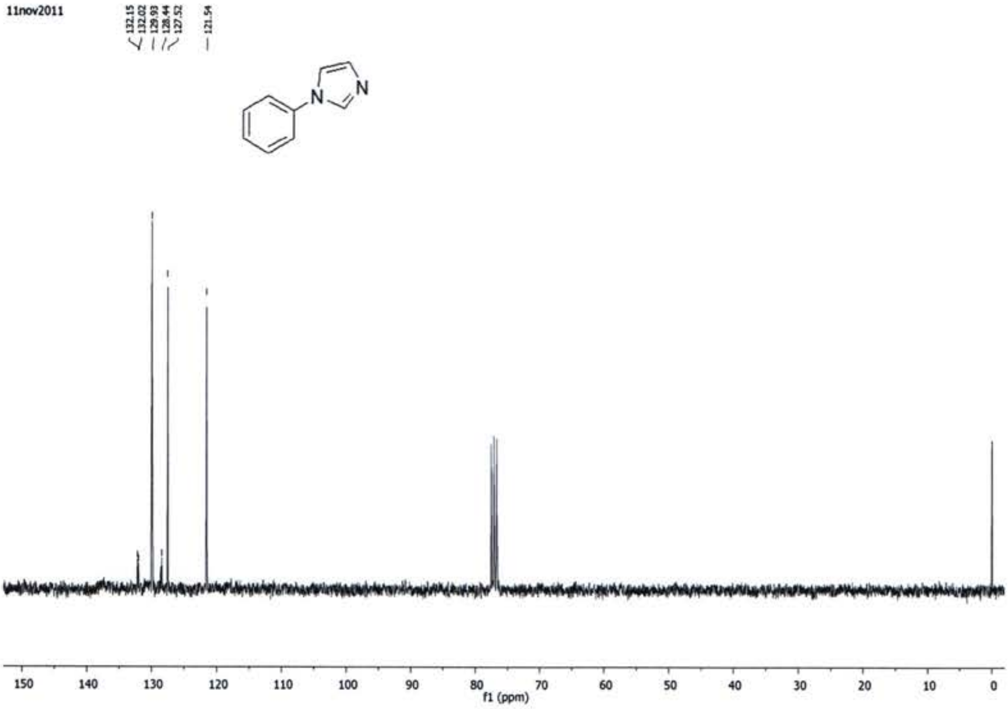




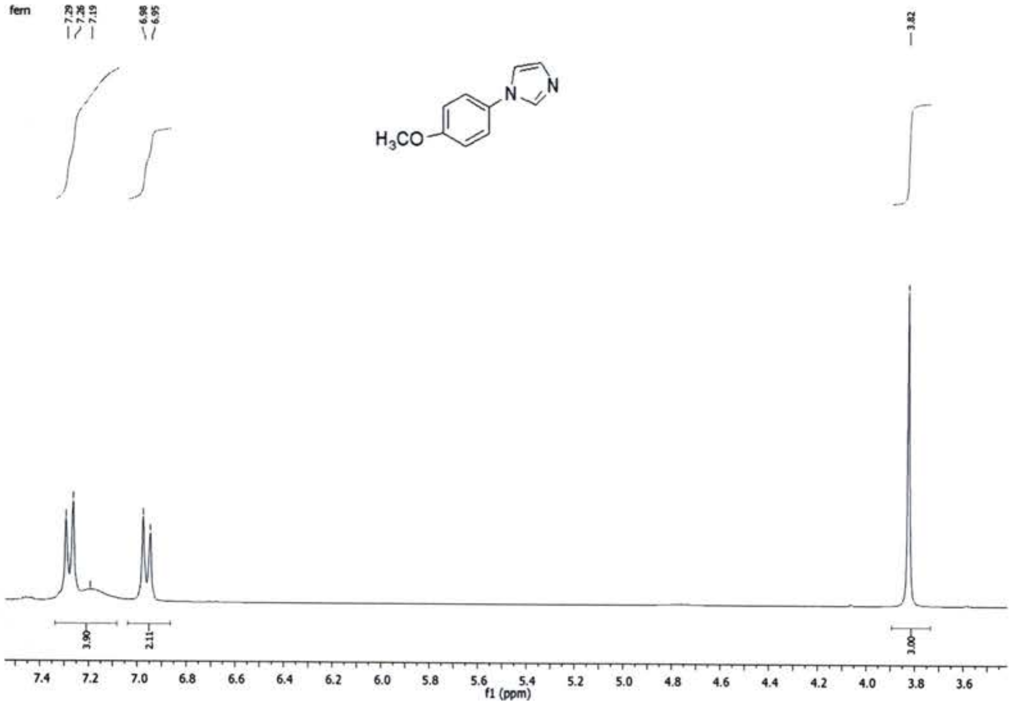
B-3 General experimental procedure for imidazole coupling: Imidazole (0.08 g, 1.2 mmol), aryl halide (1.0 mmol), triphenylphosphine (0.02 g, 0.075 mmol), cesium carbonate (0.45g, 1.4 mmol), polyethylene glycol (200 mg), and copper(I) oxide (3.6 mg) were added into flamed-dried Pyrex glass tube equipped with a stir bar and sealed with a rubber septum. Evacuated and backfilled with nitrogen gas 5 times and then added DMSO (4 mL) through rubber septum. The mixture was stirred at 110 °C for 5 h. Cooled down the reaction mixture to room temperature, added dodecane (1.0 mmol, internal standard), and extracted with ethyl acetate for gas chromatography analysis. To determine the isolated yield, the reaction mixture was filtered through celite to remove any insoluble residues. The filtrate was then extracted with ethyl acetate (3x10 mL), washed with water (5x10 mL), dried with sodium sulfate, filtered and concentrated in vacuo. The residue was purified by column chromatography on silica gel to obtain the analytically pure product.

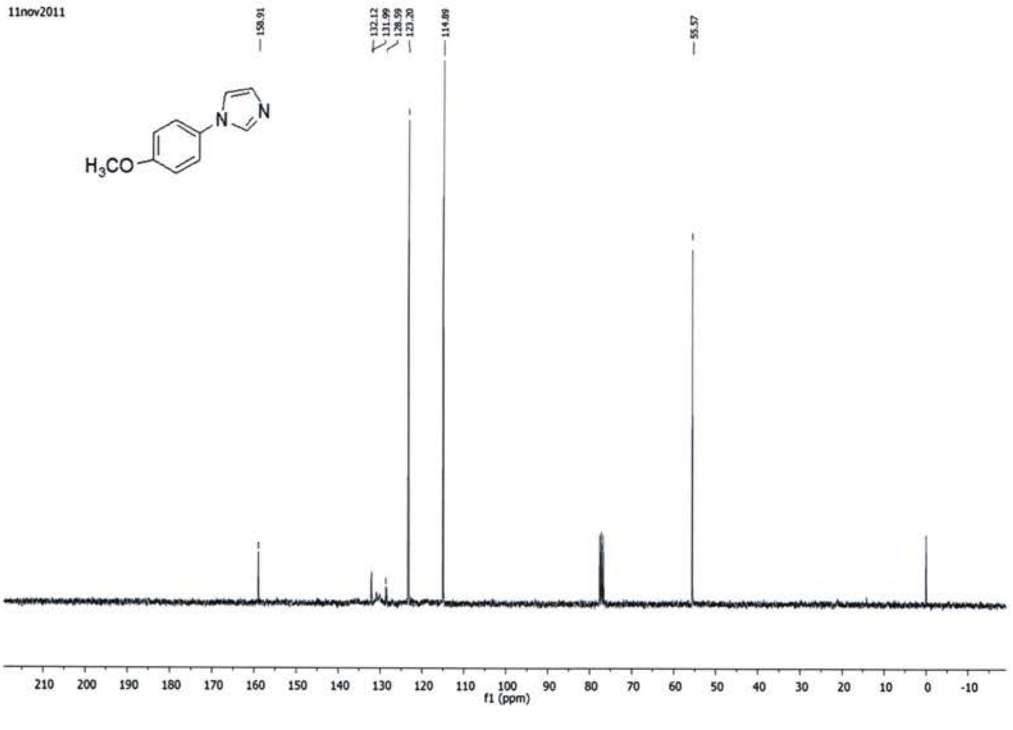
1-phenyl-1H-imidazole : The general procedure was used to afford the title product as colorless oil (94% yield) ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.91 (s, 1H), 7.41 (dt, J = 18.4, 9.0 Hz, 7H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 132.15, 132.02 129.93, 128.44, 127.52, 121.54.



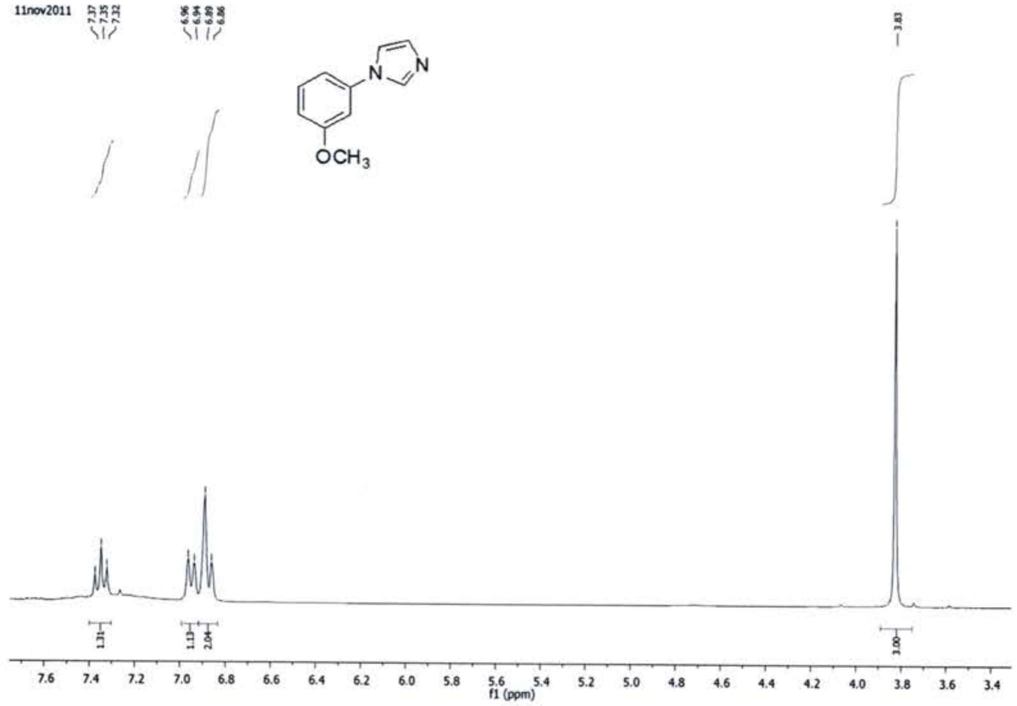


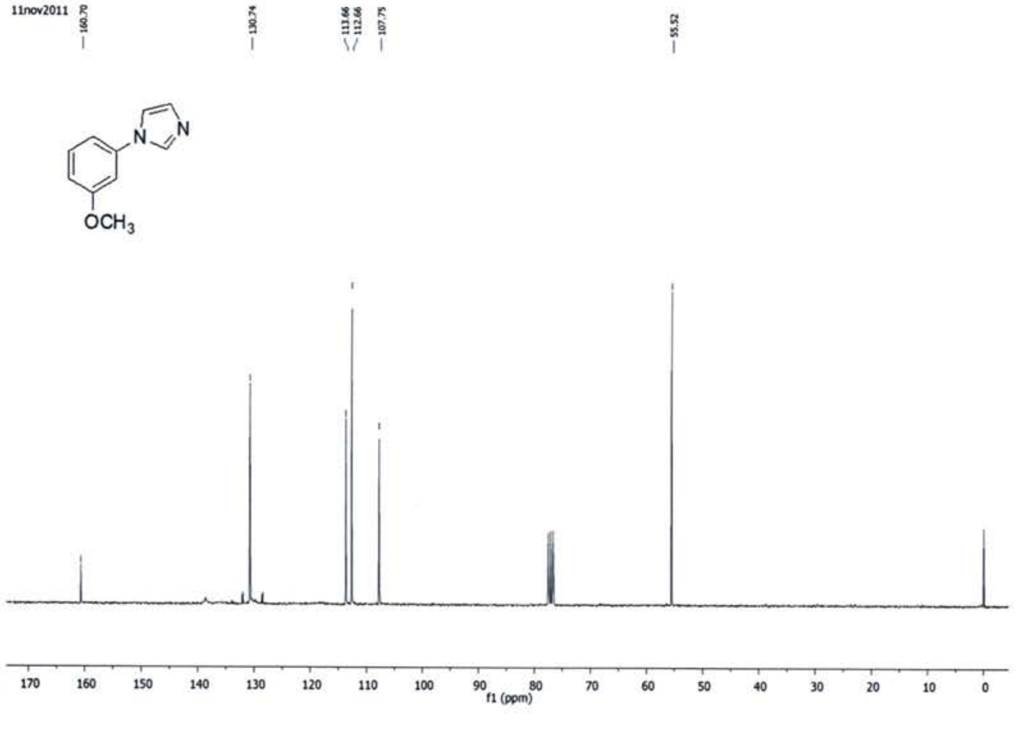
1-(4-methoxyphenyl)-1H-imidazole : The general procedure was used to afford the title product as yellow solid (64% yield) ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.24 (d, J = 29.9 Hz, 4H), 6.96 (d, J = 8.7 Hz, 2H), 3.82 (s, 3H). ^{13}C NMR (75 MHz, CDCl$_3$) δ 158.93, 133.98, 133.76, 132.00, 128.57, 128.44, 123.23, 114.90, 55.59.



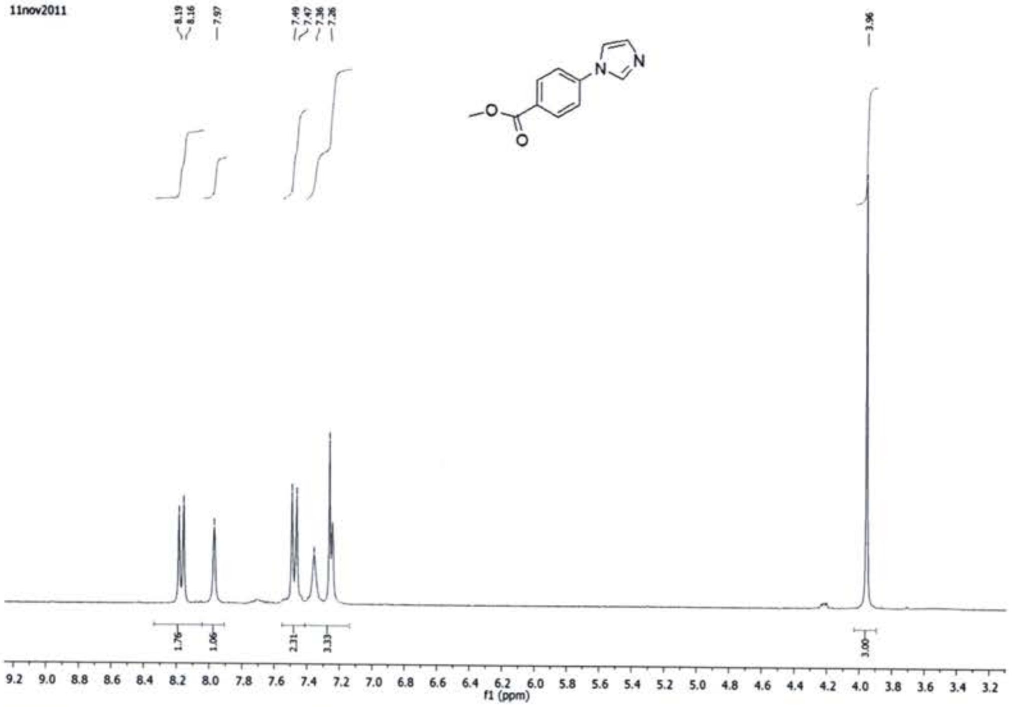


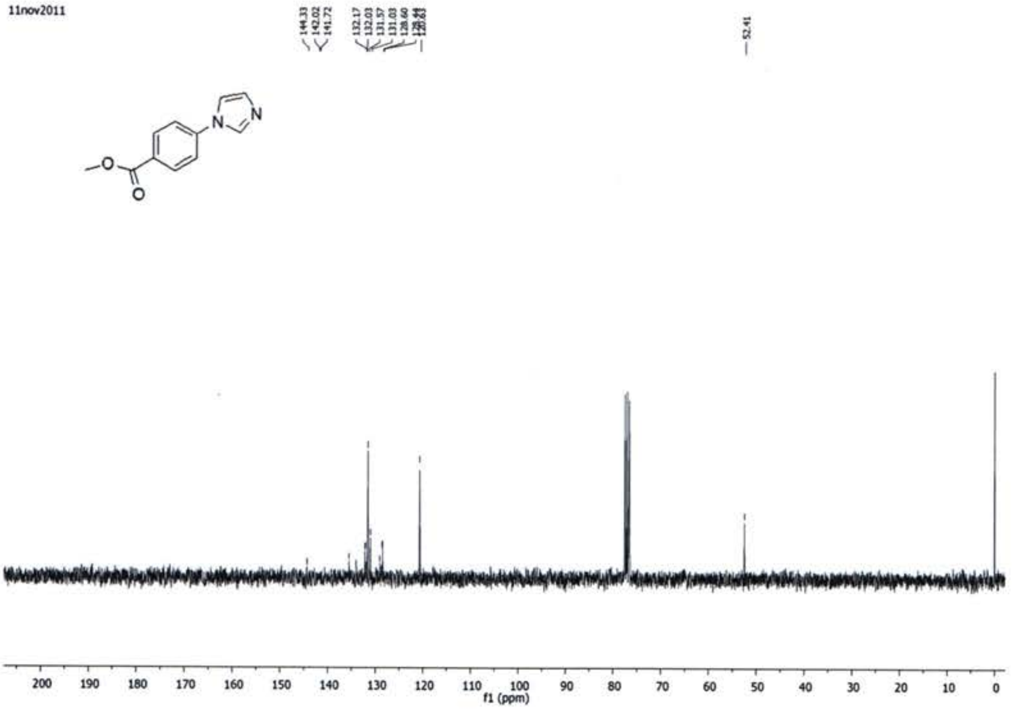
1-(3-methoxyphenyl)-1H-imidazole : The general procedure was used to afford the title product product as yellow solid (75% yield) ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35 (t, *J* = 8.0 Hz, 1H), 6.95 (d, *J* = 8.0 Hz, 1H), 6.88 (d, *J* = 8.7 Hz, 1H), 3.83 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.70, 130.74, 113.66, 112.66, 107.75, 55.52.



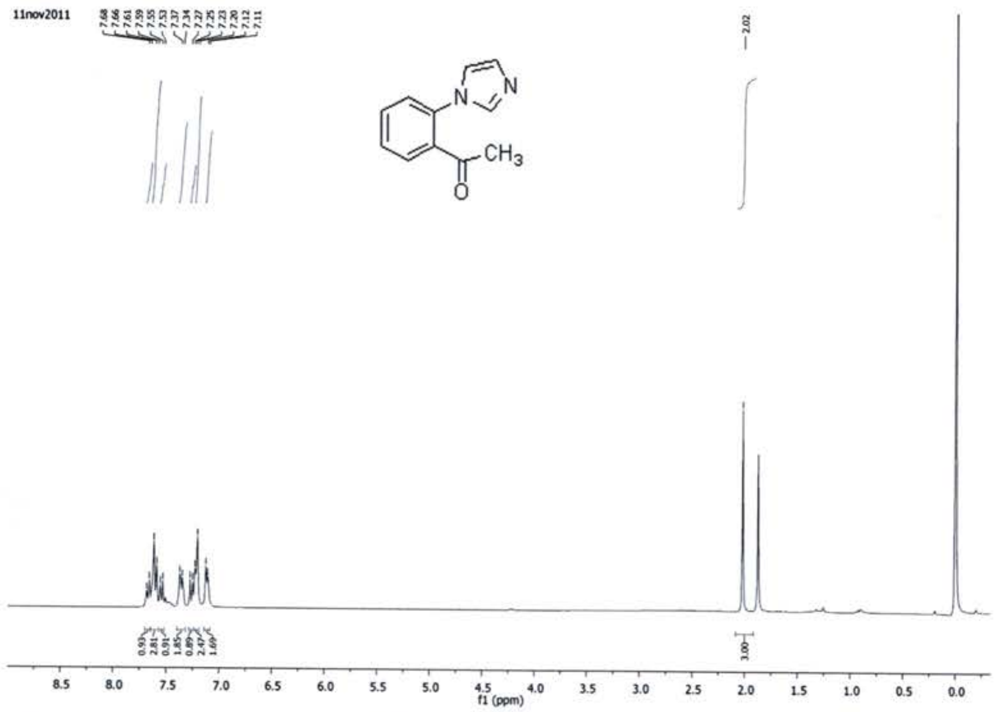


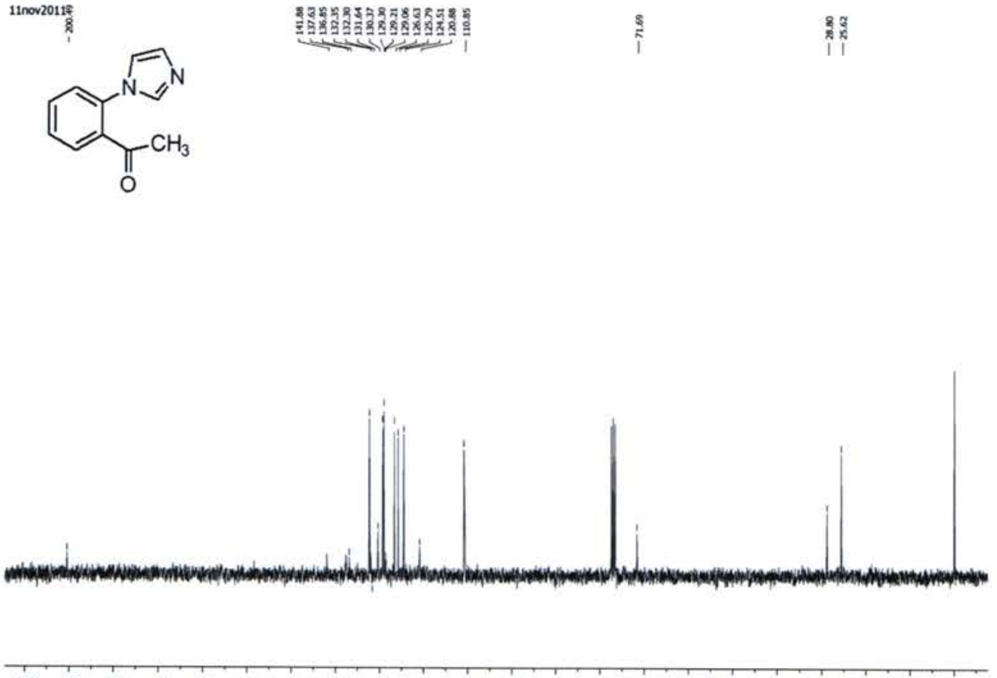
Methyl 4-(1H-imidazol-1-yl)benzoate : The general procedure was used to afford the title product as pale yellow solid (24% yield) ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.17 (d, J = 8.6 Hz, 1H), 7.97 (s, 1H), 7.48 (d, J = 8.6 Hz, 1H), 7.31 (d, J = 28.3 Hz, 1H), 3.96 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.33, 135.48, 134.02, 132.17, 132.03, 131.57, 131.03, 129.05, 128.60, 128.44, 120.63, 52.41.



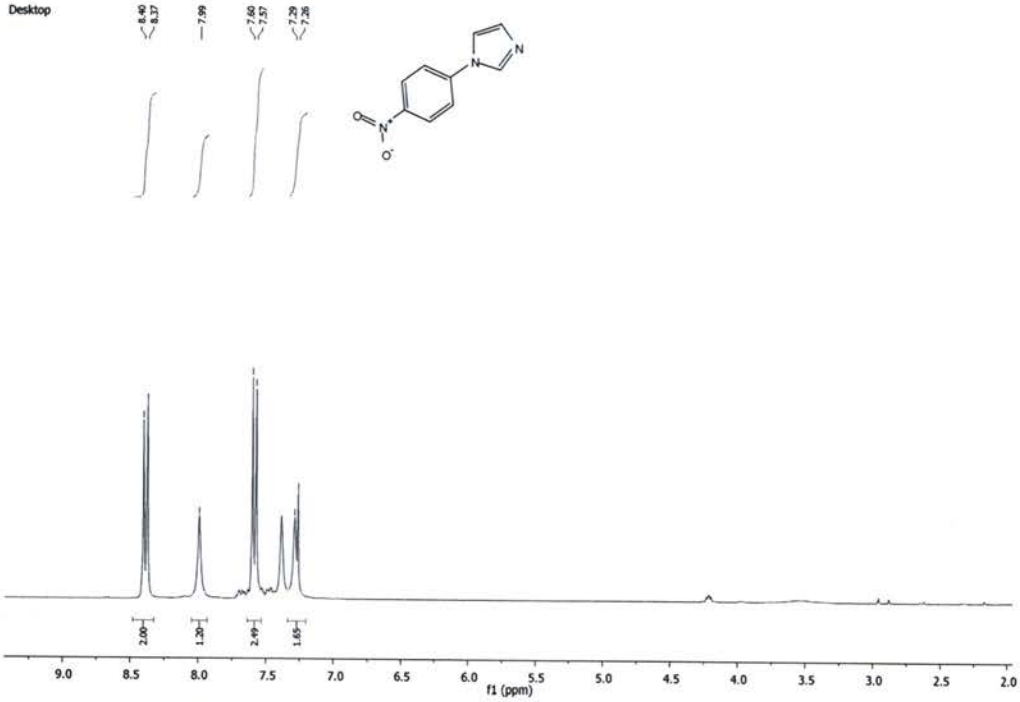


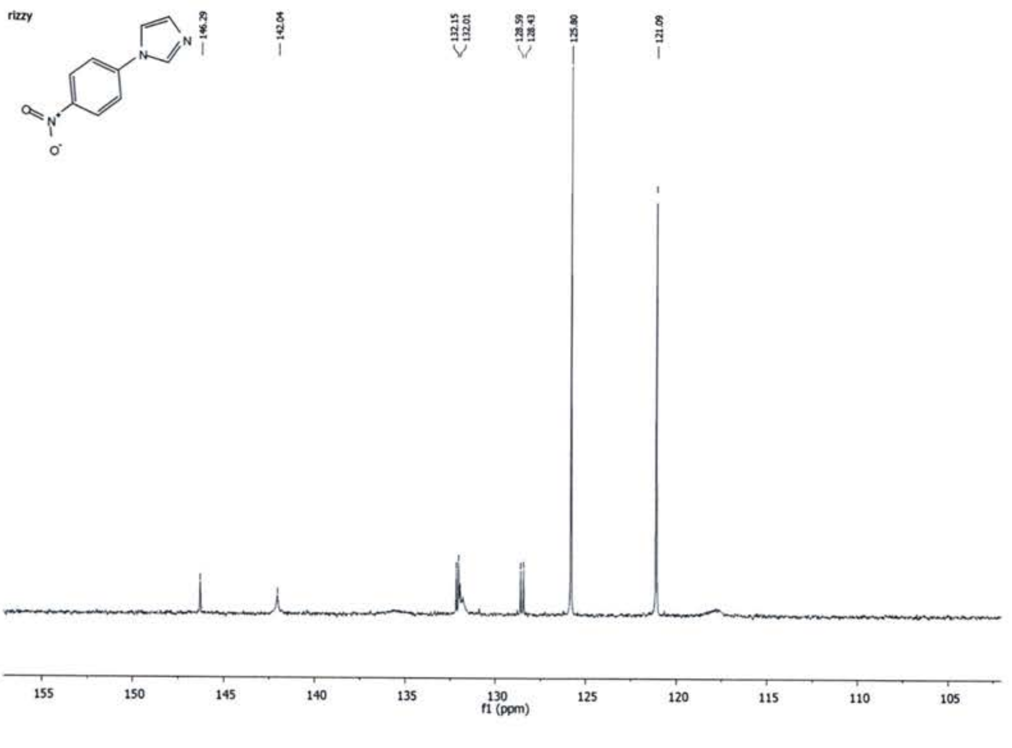
1-(2-(1H-imidazol-1-yl)phenyl)ethanone : The general procedure was used to afford the title product as yellow oil (57% yield) ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.67 (d, *J* = 7.9 Hz, 1H), 7.60 (d, *J* = 7.7 Hz, 2H), 7.54 (d, *J* = 7.4 Hz, 1H), 7.36 (d, *J* = 7.6 Hz, 1H), 7.26 (d, *J* = 7.5 Hz, 1H), 7.22 (d, *J* = 7.2 Hz, 1H), 7.11 (d, *J* = 5.6 Hz, 1H), 2.02 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 200.49, 141.88, 137.63, 136.85, 132.35, 132.30, 131.64, 130.37, 129.30, 129.21, 129.06, 126.63, 125.79, 124.51, 120.88, 110.85, 71.69, 28.80, 25.62.



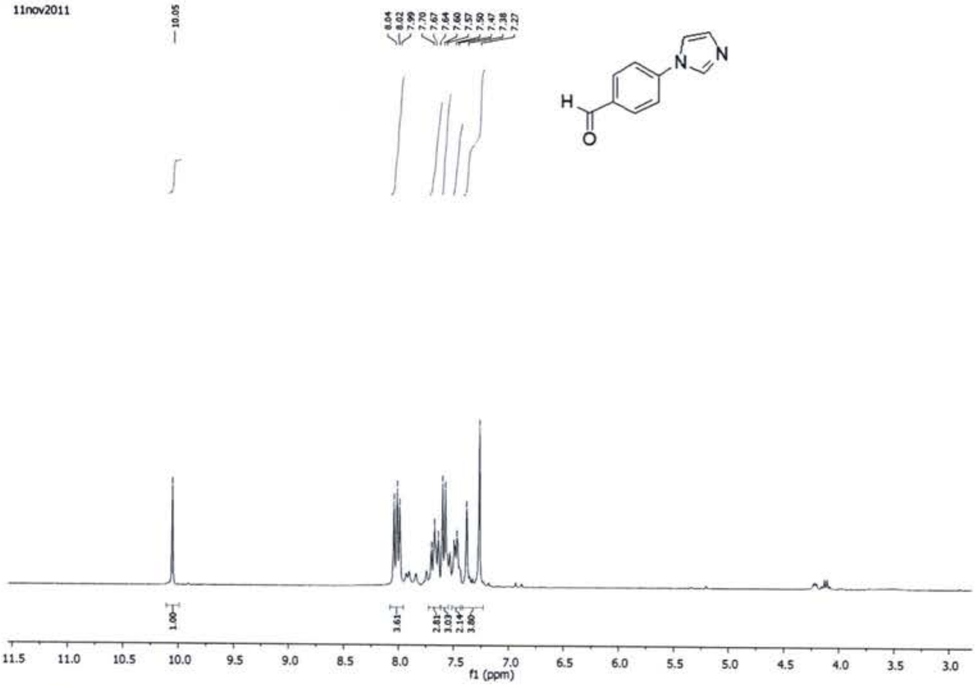


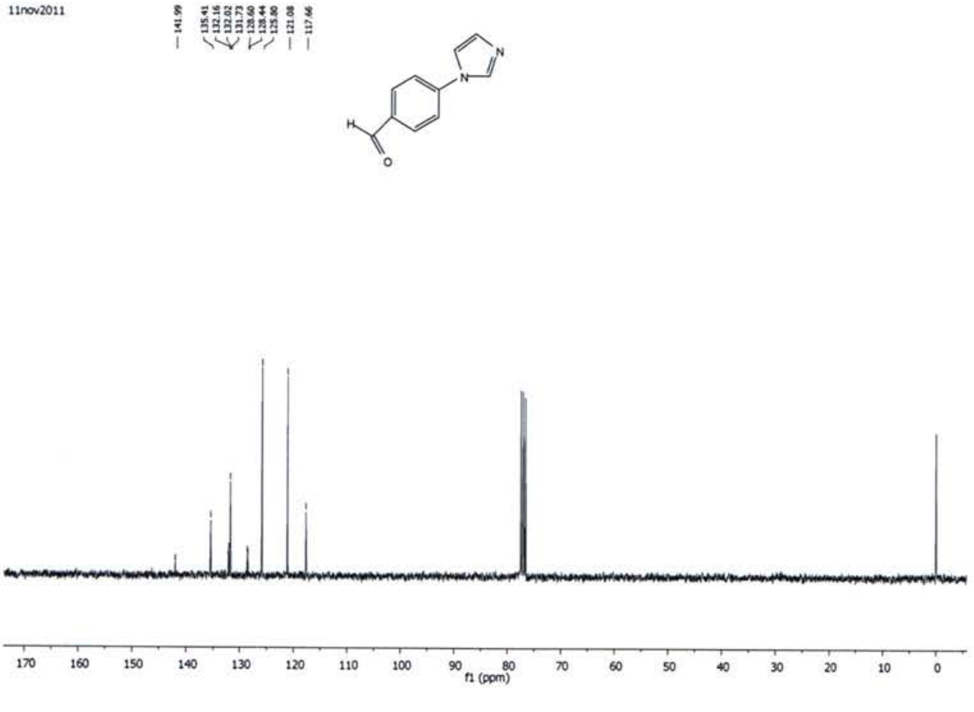
1-(4-nitrophenyl)-1H-imidazole : The general procedure was used to afford the title product as yellow solid (96% yield) ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.39 (d, *J* = 9.0 Hz, 2H), 7.93 (s, 1H)7.59 (d, *J* = 9.0 Hz, 2H), 7.27 (d, *J* = 7.3 Hz, 1H). ^{13}C NMR (75 MHz, CDCl3) δ 146.29, 142.04, 132.15, 132.01, 128.59, 128.43, 125.80, 121.09.



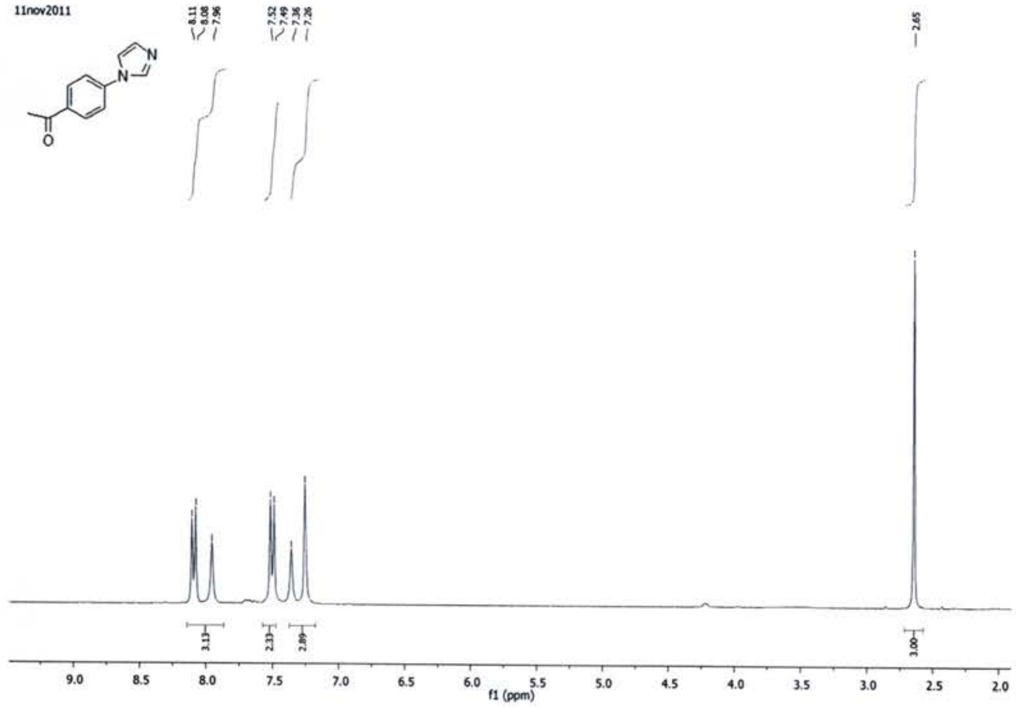


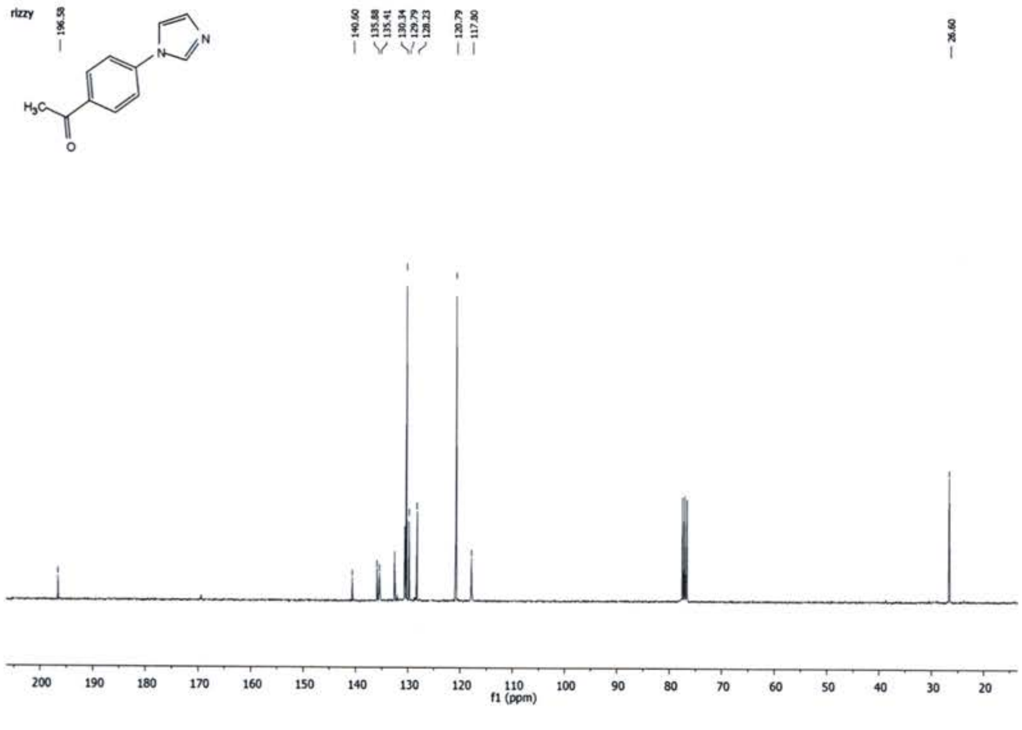
4-(1H-imidazol-1-yl)benzaldehyde : The general procedure was used to afford the title product as yellow oil (11% yield) ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.05 (s, 1H), 8.08 – 7.96 (m, 1H), 7.73 – 7.63 (m, 1H), 7.59 (d, J = 8.3 Hz, 1H), 7.48 (d, J = 7.7 Hz, 1H), 7.32 (d, J = 34.8 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 141.99, 135.41, 132.16, 132.02, 131.73, 128.60, 128.44, 125.80, 121.08, 117.66.





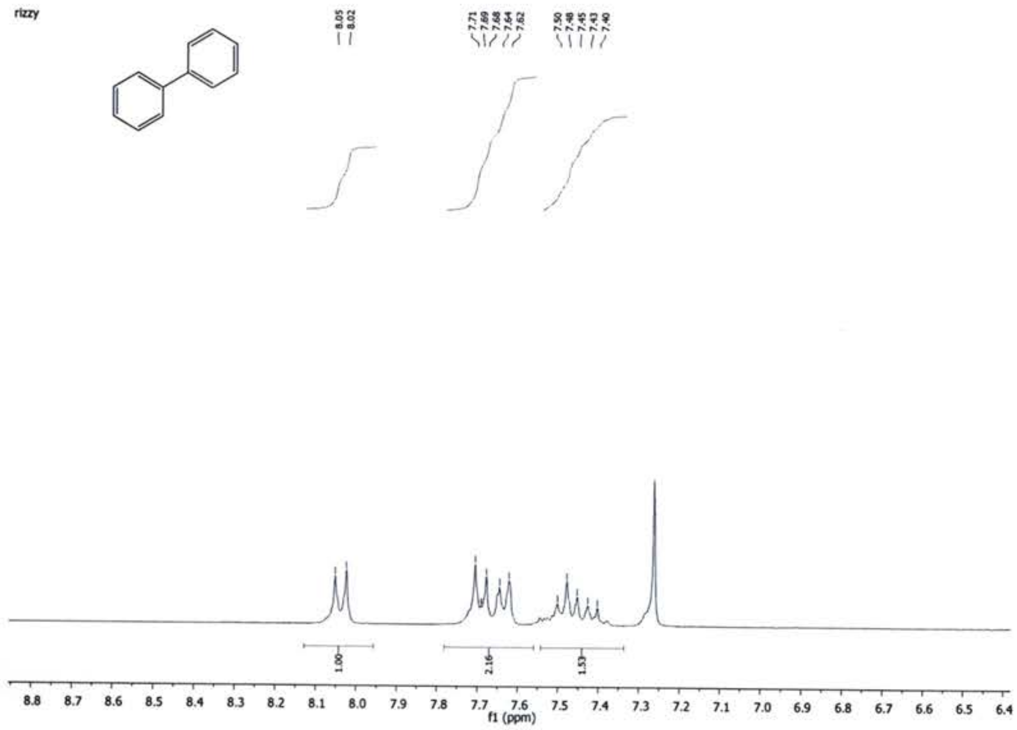
1-(4-(1H-imidazol-1-yl)phenyl)ethanone : The general procedure was used to afford the title product as yellow solid (68% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.22 – 7.83 (m, 3H), 7.50 (d, *J* = 8.5 Hz, 2H), 7.31 (d, *J* = 32.5 Hz, 2H), 2.64 (s, 3H). ^{13}C NMR (75 MHz, CDCl3) δ 196.58, 140.60, 135.88, 135.41, 130.34, 129.79, 128.23, 120.79, 117.80, 26.60.

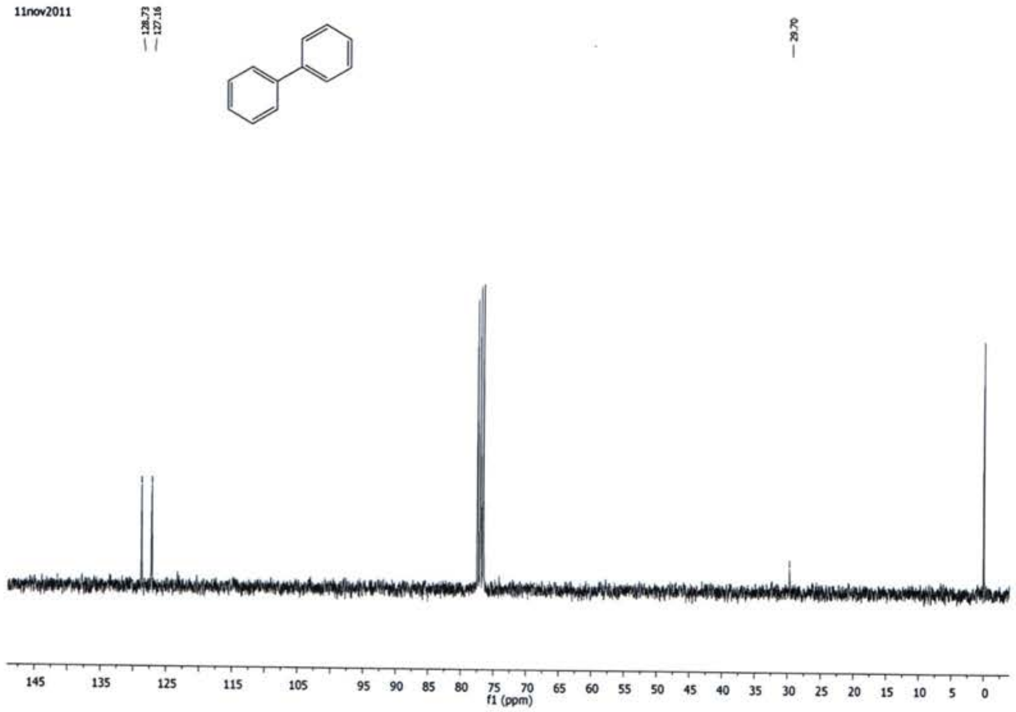




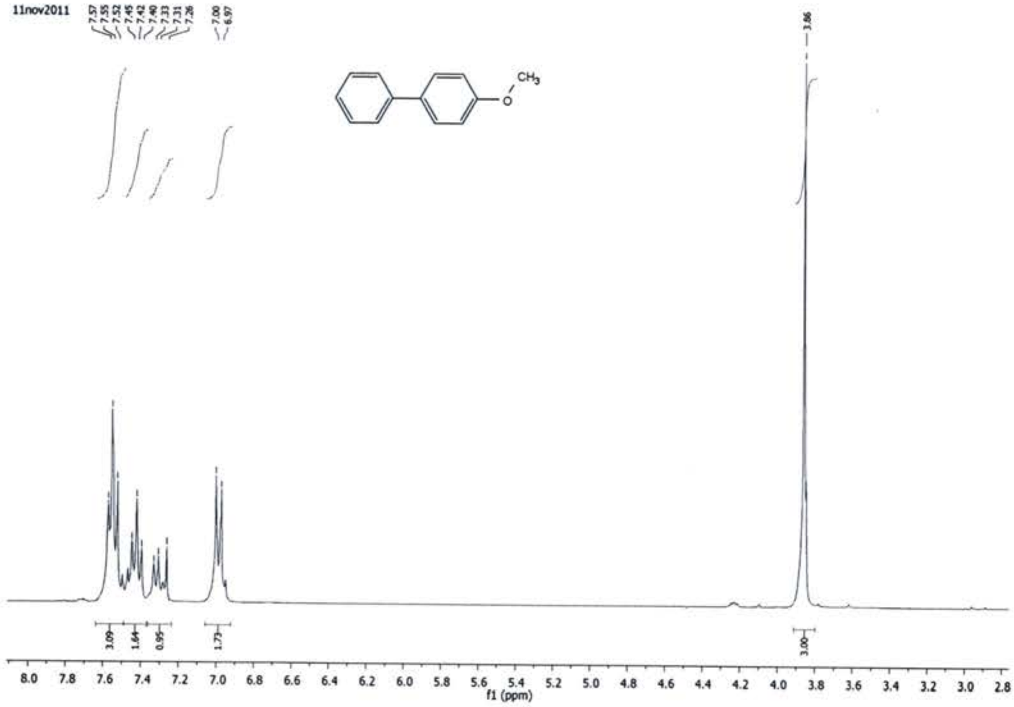
B-4 General experimental procedure for Suzuki-Miyaura coupling: Phenylboronic acid (1.4 g, 1.2 mmol), aryl halide (1.0 mmol), sodium carbonate (2.5 mmol), triphenylphosphine ligand (6.5 mg, 0.025 mmol), dodecane (1.0 mmol, an internal standard), **Fe_3O_4-DOPA-Pd(II)** catalyst (50 mg) and H_2O (3 mL) were added into a test tube equipped with a stir bar. Then the mixture was stirred at 60 °C for 10 h. After magnetic separation of the catalyst, the mixture was extracted with ethyl acetate and then injected to gas chromatography for %yield analysis. To obtain the isolated yield, the reaction mixture was extracted with ethyl acetate (3x10 mL), dried over anhydrous sodium sulfate and evaporated solvent under reduced pressure. The product was purified by column chromatography using silica gel as stationary phase. In the recycling experiments, the separated catalyst was successively reused for the next run without any pretreatment.

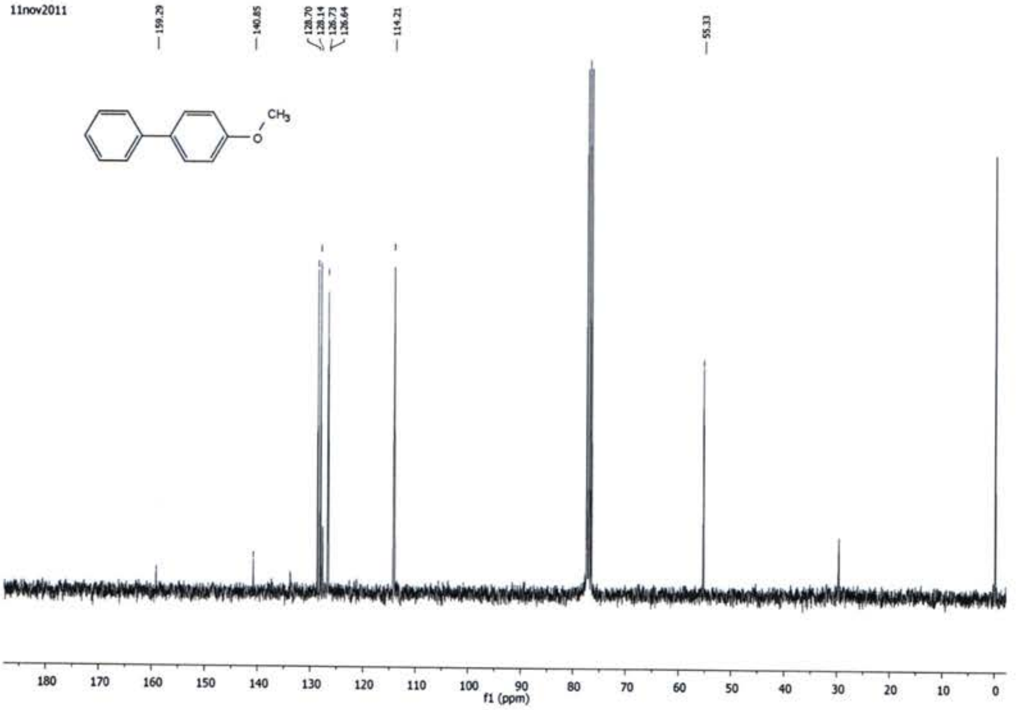
1,1'-biphenyl : The general procedure was used to afford the title product as white solid (98% yield) ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.05, 8.02, 7.71, 7.69, 7.68, 7.64, 7.62, 7.50, 7.48, 7.45, 7.43, 7.40.



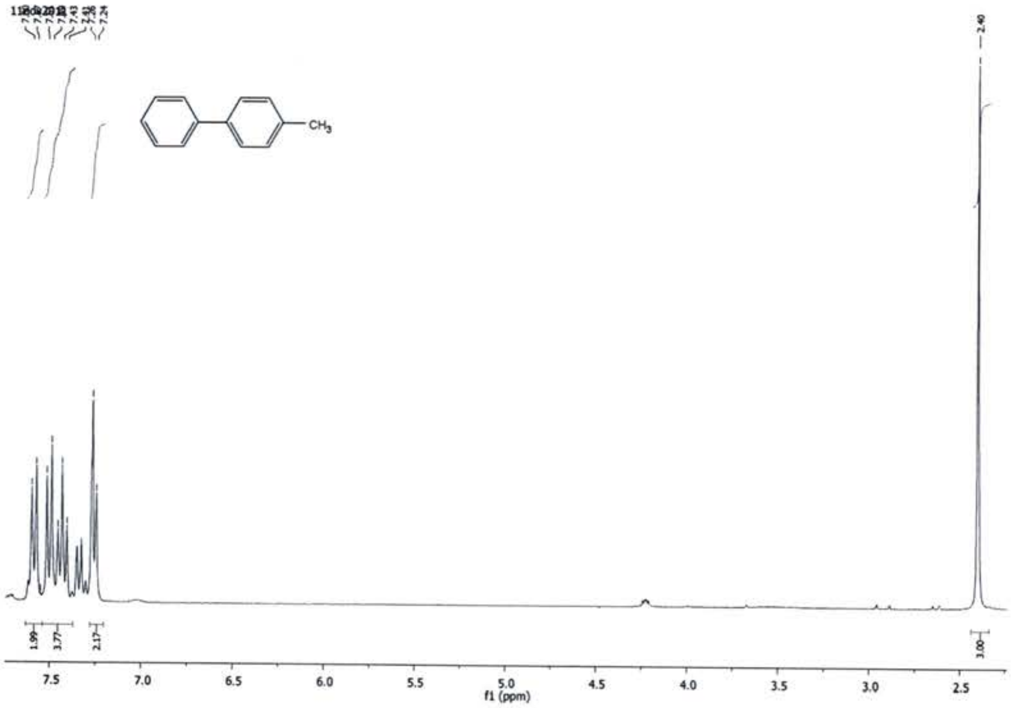


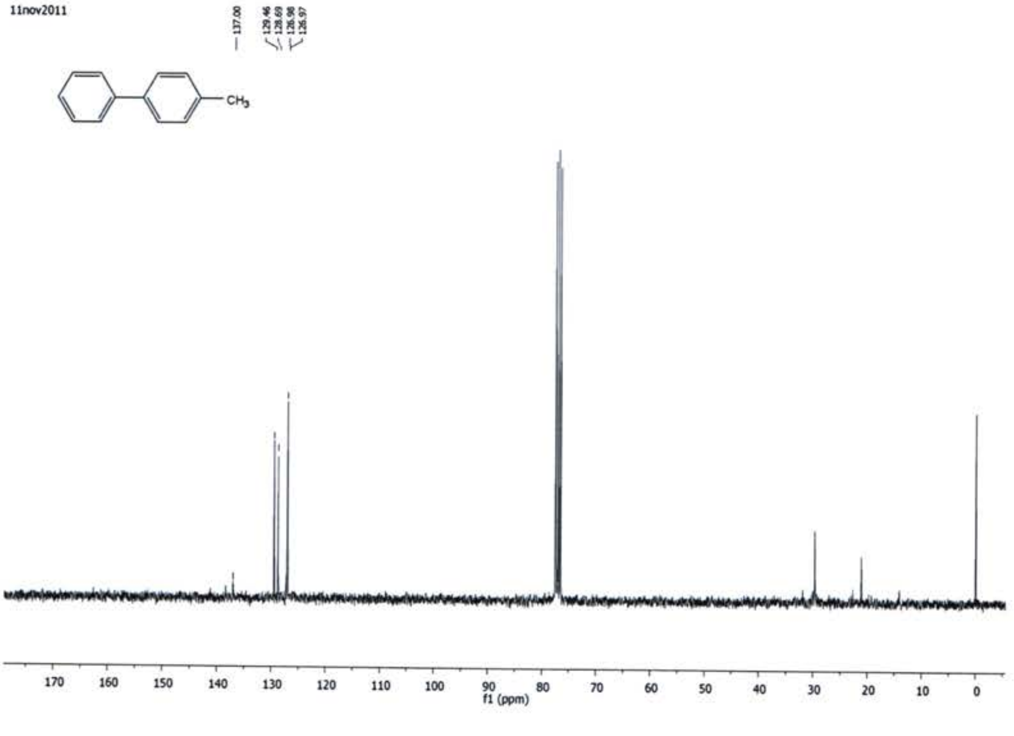
4-methoxy-1,1'-biphenyl: The general procedure was used to afford the title product as white solid (77% yield) ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.55 (t, J = 7.2 Hz, 2H), 7.42 (t, J = 7.5 Hz, 1H), 7.36 – 7.22 (m, 1H), 6.99 (d, J = 8.7 Hz, 1H), 3.85 (s, 3H). ^{13}C- NMR (75 MHz, $CDCl_3$) δ 140.85, 128.70, 128.14, 126.73, 126.64, 114.21, 55.33.



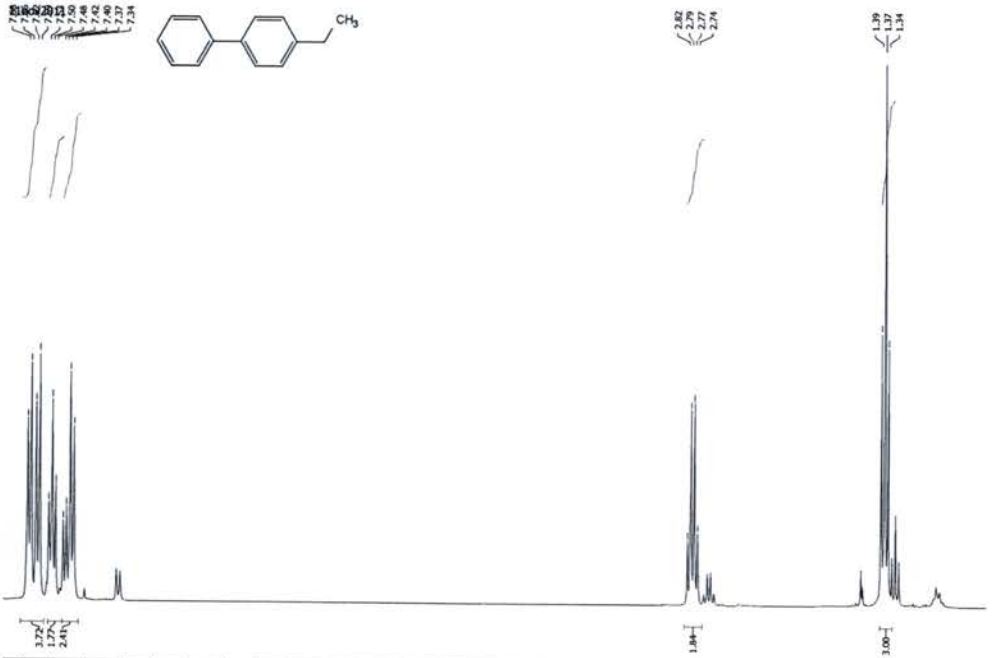


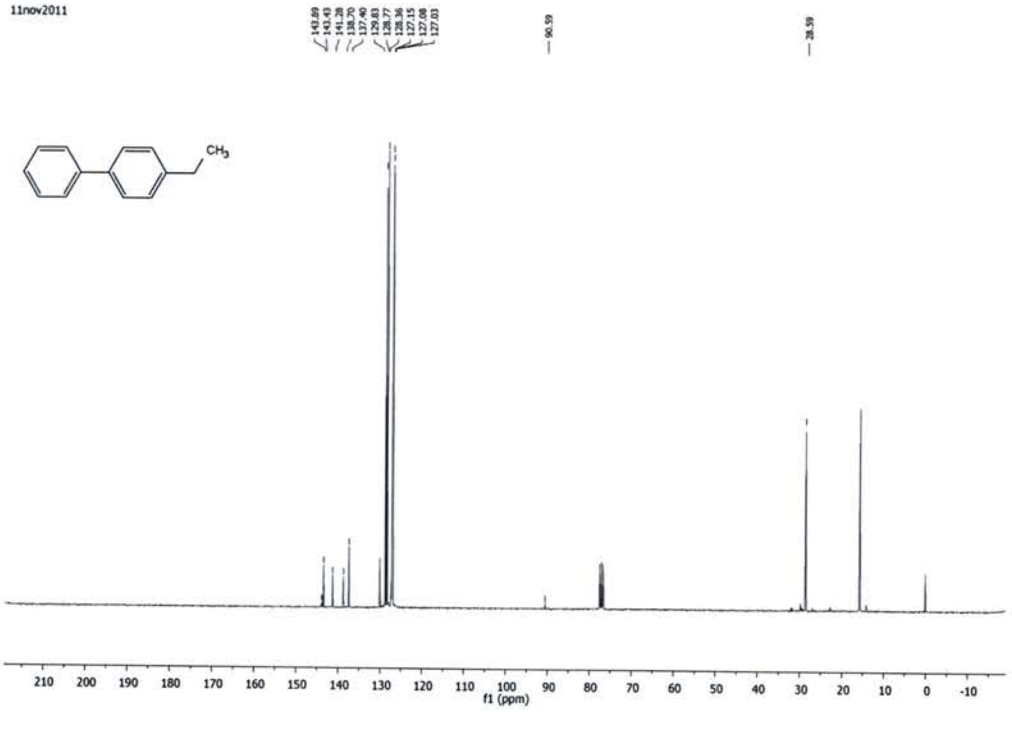
4-methyl-1,1'-biphenyl: The general procedure was used to afford the title product as white solid (95% yield) ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.57 (t, *J* = 7.1 Hz, 1H), 7.54 – 7.39 (m, 2H), 7.25 (d, *J* = 5.7 Hz, 1H), 2.40 (s, 3H). ^{13}C -NMR (75 MHz, $CDCl_3$) δ 137.00, 129.46, 128.69, 126.98, 126.97.



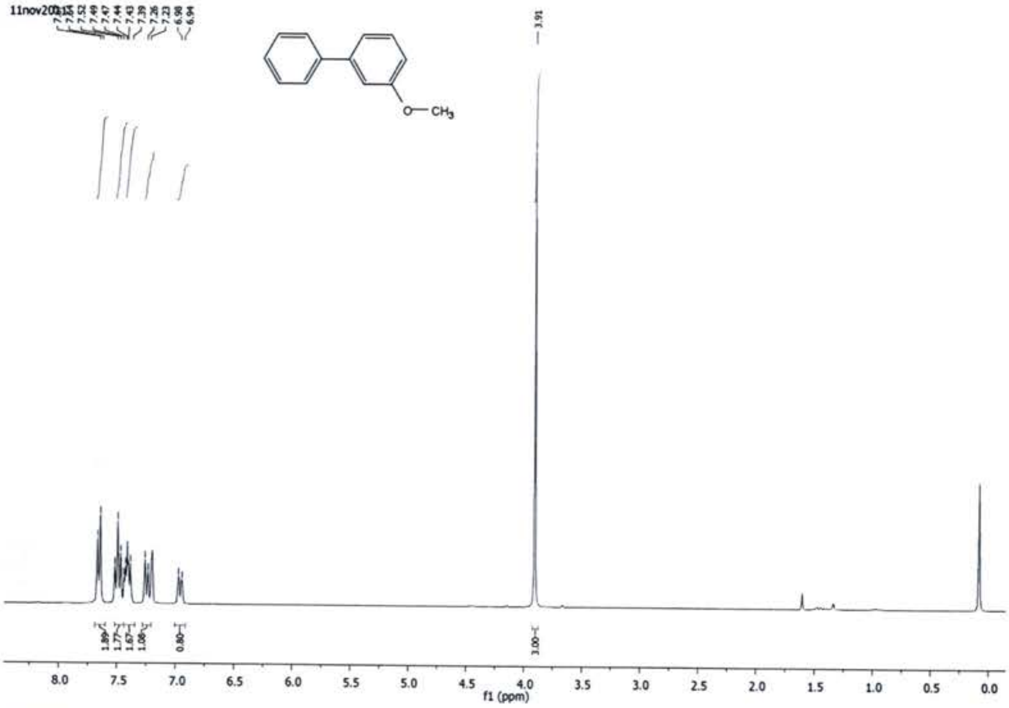


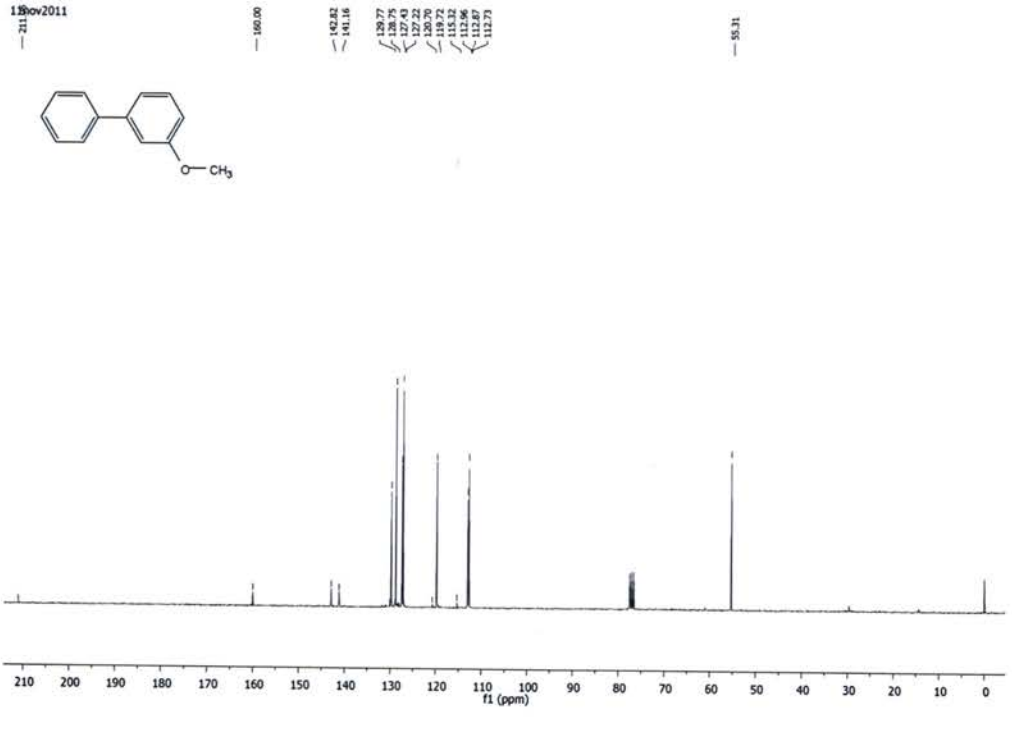
4-ethyl-1,1'-biphenyl: The general procedure was used to afford the title product as colorless oil (99% yield) ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.64 (dd, *J* = 18.5, 7.7 Hz, 2H), 7.50 (t, *J* = 7.5 Hz, 1H), 7.38 (dd, *J* = 16.2, 7.7 Hz, 1H), 2.78 (q, *J* = 7.6 Hz, 1H), 1.37 (t, *J* = 7.6 Hz, 2H). ^{13}C- NMR (75 MHz, $CDCl_3$) δ 143.89, 143.43, 141.28, 138.70, 137.40, 129.83, 128.77, 128.36, 127.15, 127.08, 127.03, 90.59, 28.59.



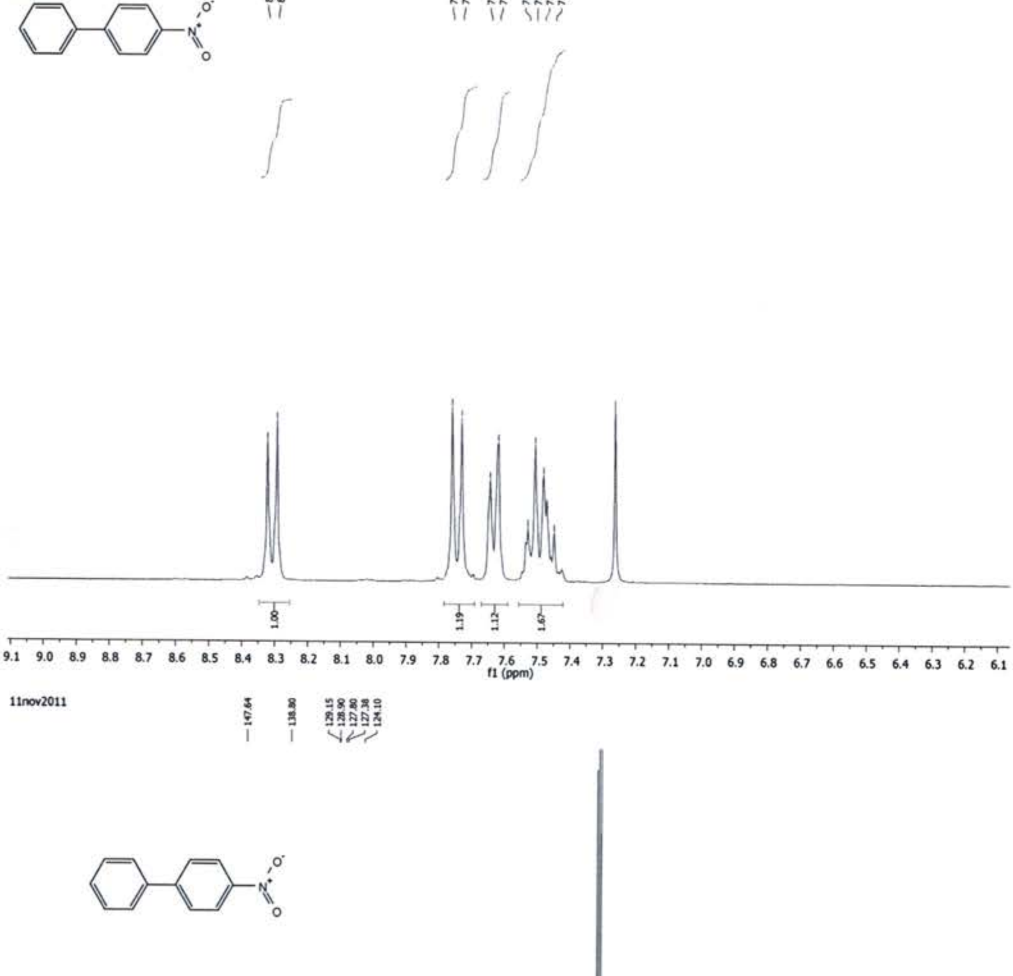


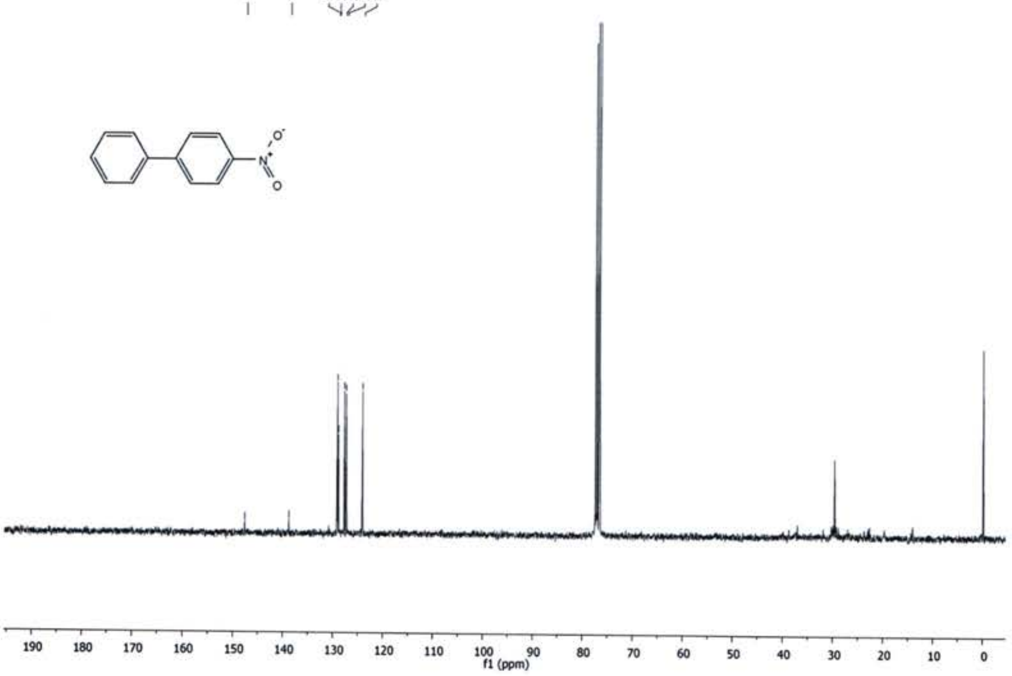
3-methoxy-1,1'-biphenyl: The general procedure was used to afford the title product as white solid (99% yield) ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.65 (d, *J* = 7.1 Hz, 1H), 7.49 (t, *J* = 7.3 Hz, 1H), 7.44 – 7.36 (m, 1H), 7.25 (d, *J* = 7.8 Hz, 1H), 6.96 (d, *J* = 9.7 Hz, 1H), 3.91 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.00, 142.82, 141.16, 129.77, 128.75, 127.43, 127.22, 120.70, 119.72, 115.32, 112.96, 112.87, 112.73, 55.31.



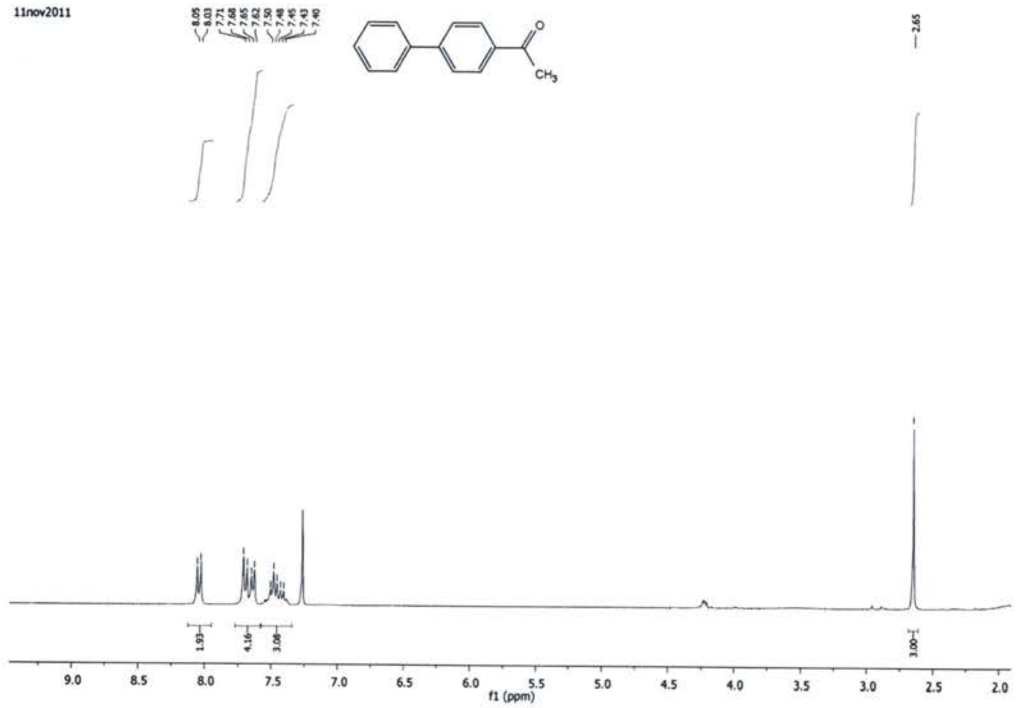


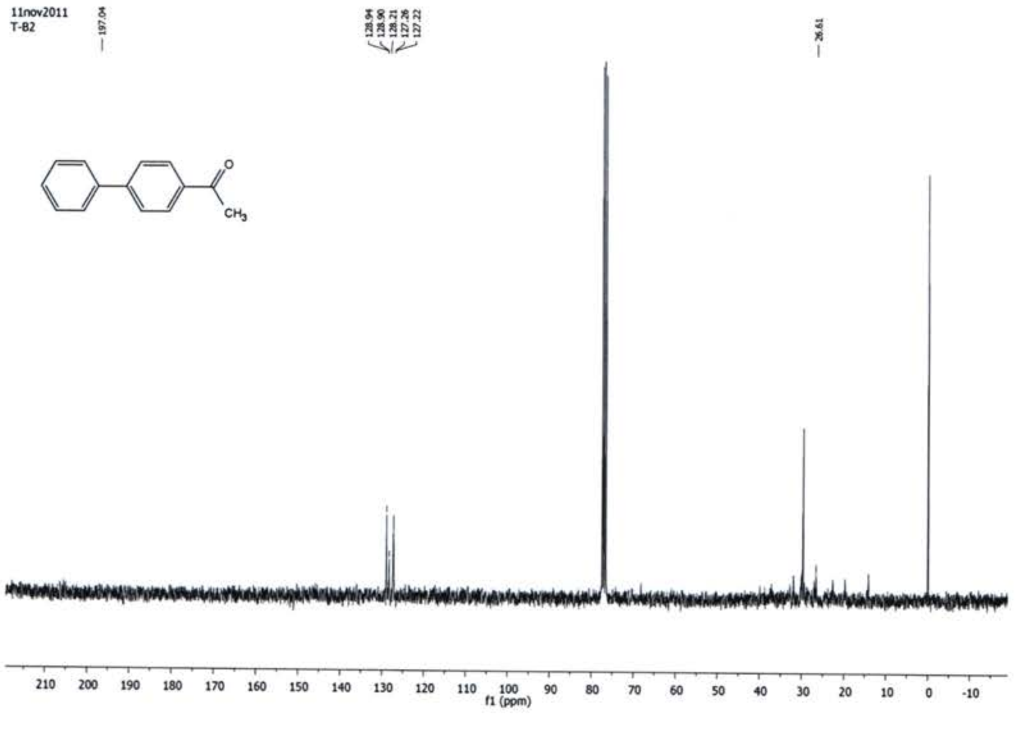
4-nitro-1,1'-biphenyl: The general procedure was used to afford the title product as white solid (88% yield) ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.31 (d, J = 8.8 Hz, 1H), 7.75 (d, J = 8.8 Hz, 1H), 7.63 (d, J = 7.6 Hz, 1H), 7.49 (dd, J = 15.9, 8.2 Hz, 2H). ^{13}C -NMR (75 MHz, $CDCl_3$) δ 147.64, 138.80, 129.15, 128.90, 127.80, 127.38, 124.10.



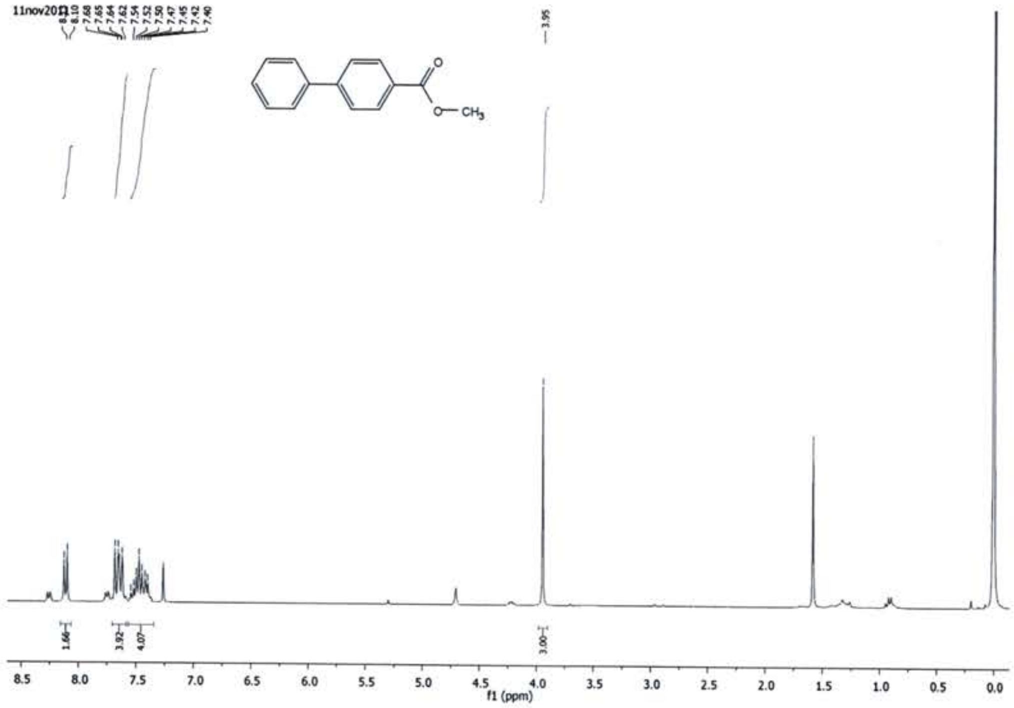


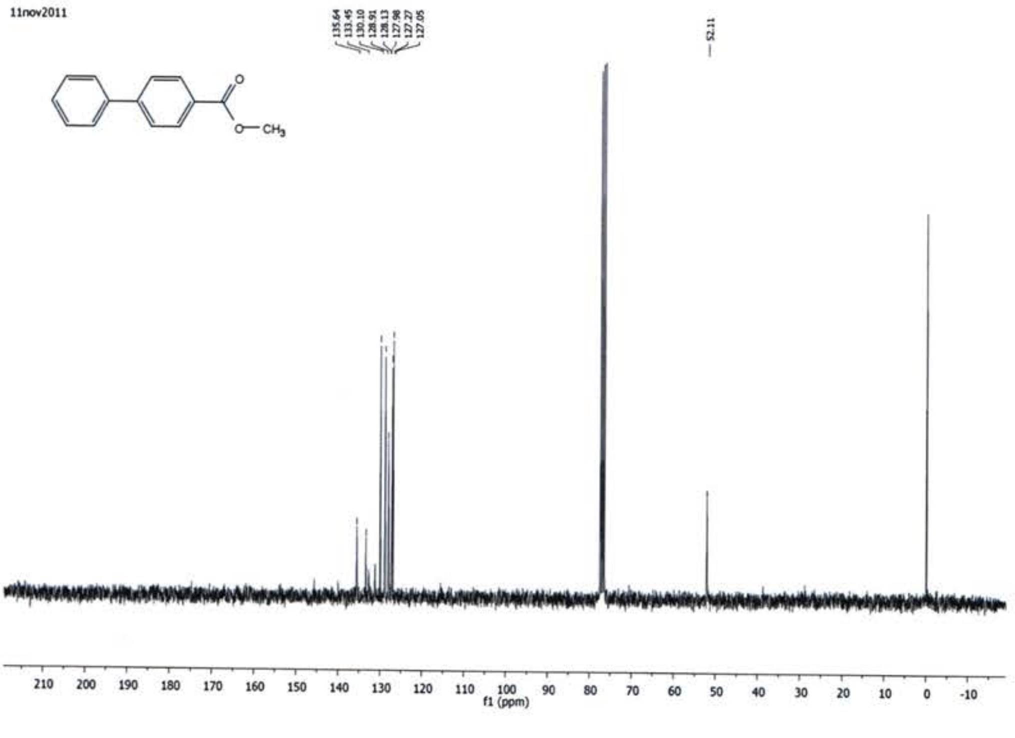
1-([1,1'-biphenyl]-4-yl)ethanone: The general procedure was used to afford the title product as pale yellow solid (99% yield) ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.04 (d, *J* = 8.4 Hz, 1H), 7.66 (dd, *J* = 17.6, 7.7 Hz, 2H), 7.56 – 7.36 (m, 2H),.2.65 (s, 3H). ^{13}C- NMR (75 MHz, $CDCl_3$) δ 197.04, 128.94, 128.90, 128.21, 127.26, 127.22, 26.61.



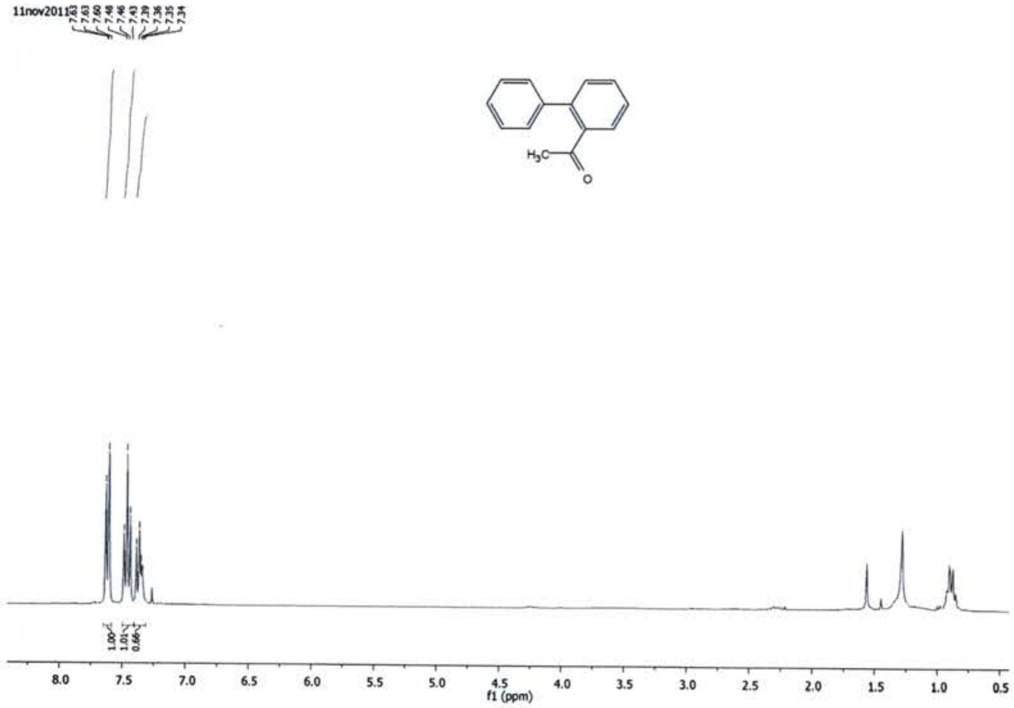


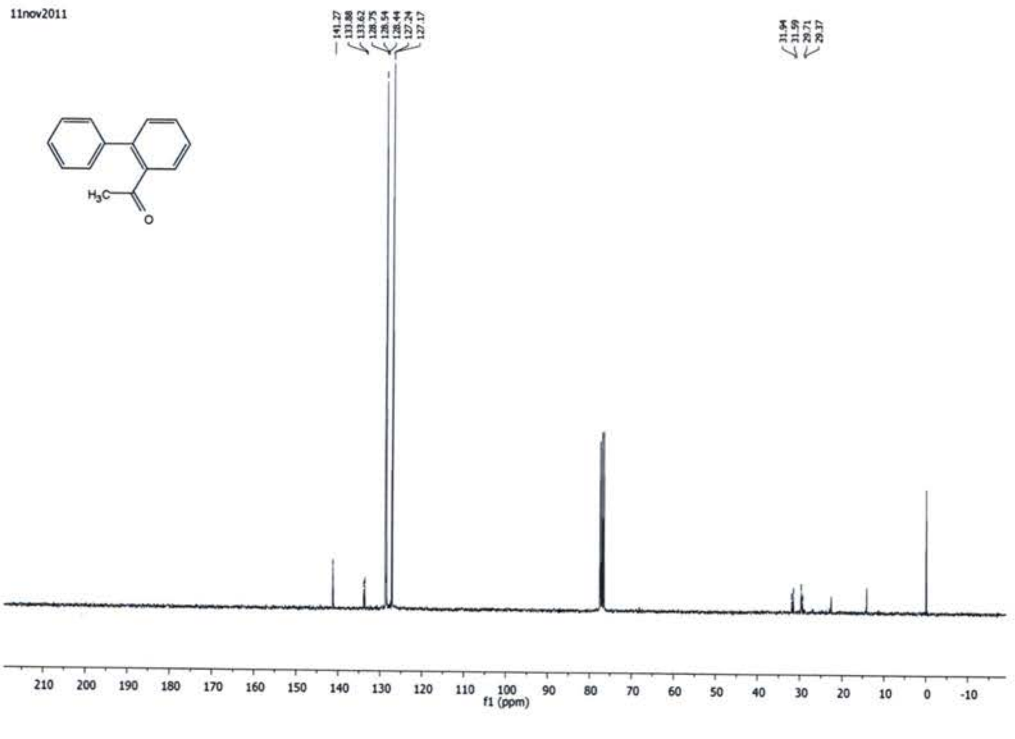
1-([1,1'-biphenyl]-4-yl)ethanoate: The general procedure was used to afford the title product as yellow solid (99% yield) ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.11 (d, J = 8.3 Hz, 1H), 7.65 (dd, J = 11.2, 7.9 Hz, 1H), 7.56 – 7.35 (m, 1H), 3.95 (s, 3H). ^{13}C -NMR (75 MHz, $CDCl_3$) δ 135.64, 133.45, 130.10, 128.91, 128.13, 127.98, 127.27, 127.05, 52.11.



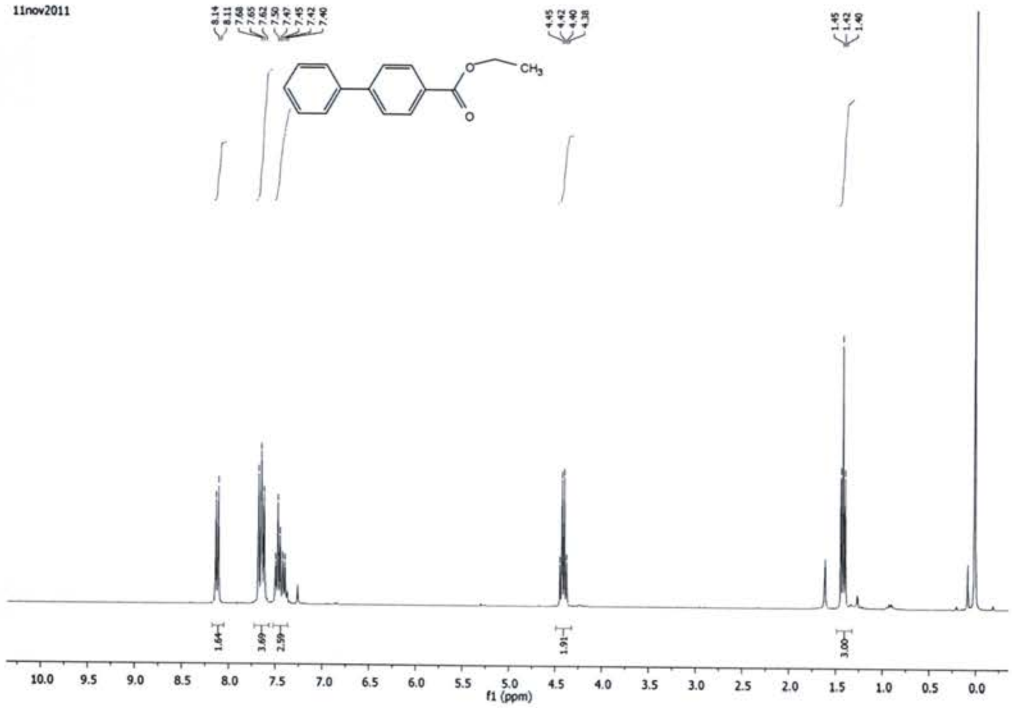


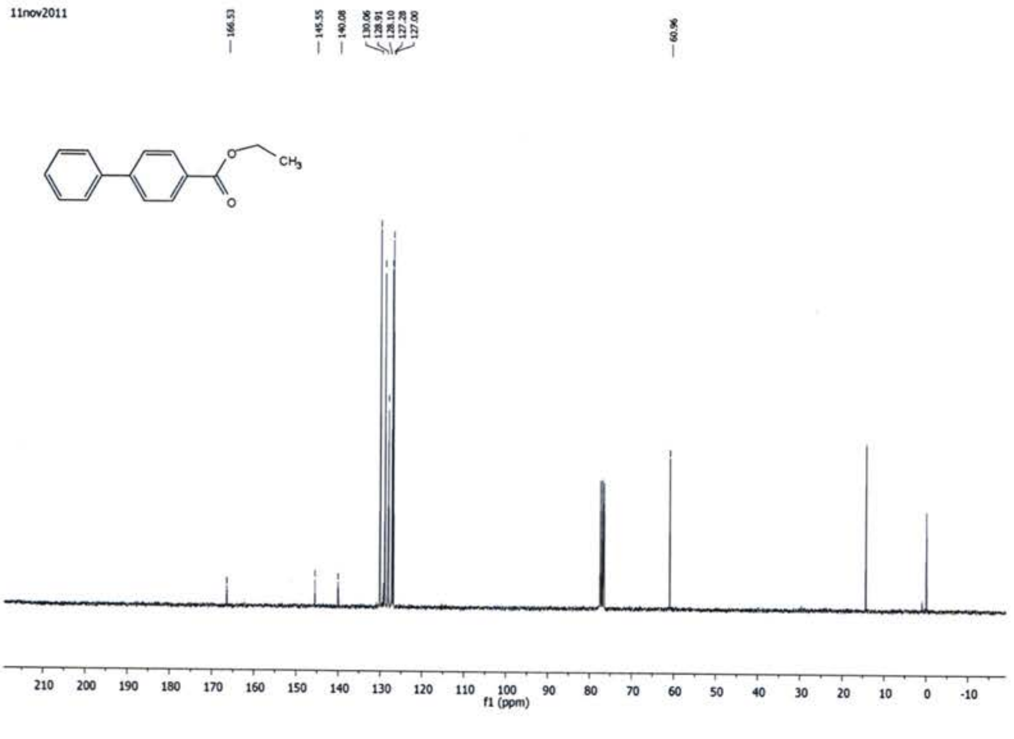
1-([1,1'-biphenyl]-2-yl)ethanone: The general procedure was used to afford the title product as yellow oil (40% yield) ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.64 – 7.58 (m, 2H), 7.46 (t, J = 7.5 Hz, 2H), 7.36 (dd, J = 8.9, 5.6 Hz, 1H). ^{13}C -NMR (75 MHz, CDCl$_3$) δ 141.27, 133.88, 133.62, 128.75, 128.54, 128.44, 127.24, 127.17, 31.94, 31.59, 29.71, 29.37.



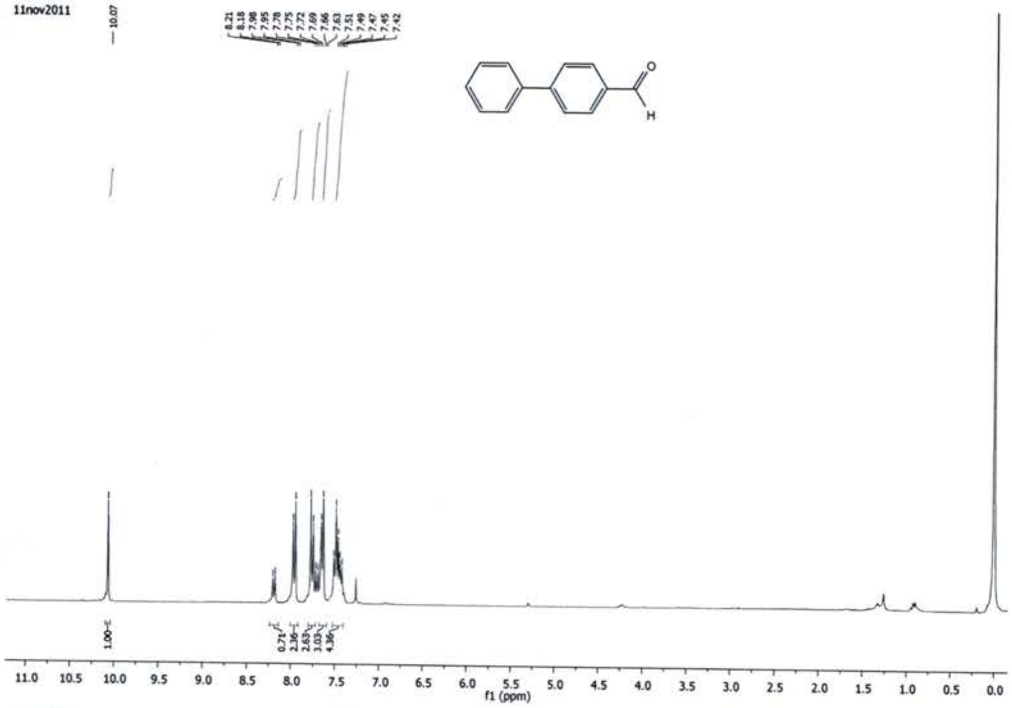


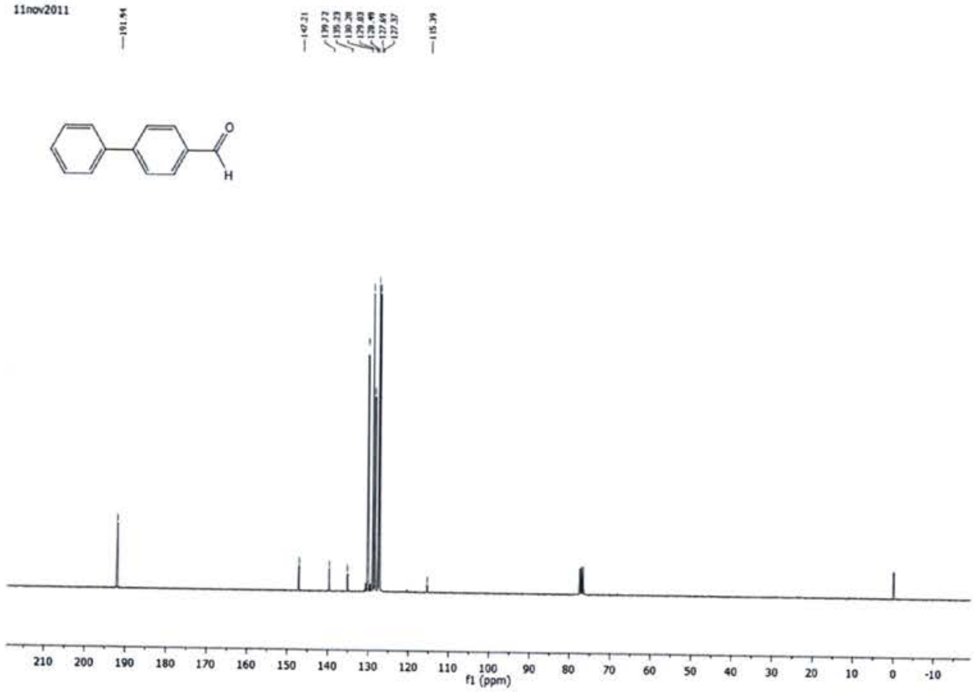
Ethyl [1,1'-biphenyl]-4-carboxylate: The general procedure was used to afford the title product as white solid (60% yield) ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.12 (d, J = 8.4 Hz, 1H), 7.71 – 7.58 (m, 2H), 7.54 – 7.38 (m, 1H), 4.41 (q, J = 7.1 Hz, 2H), 1.42 (t, J = 7.1 Hz, 3H). ^{13}C- NMR (75 MHz, $CDCl_3$) δ 166.53, 145.55, 140.08, 130.06, 128.91, 128.10, 127.28, 127.00, 60.96.





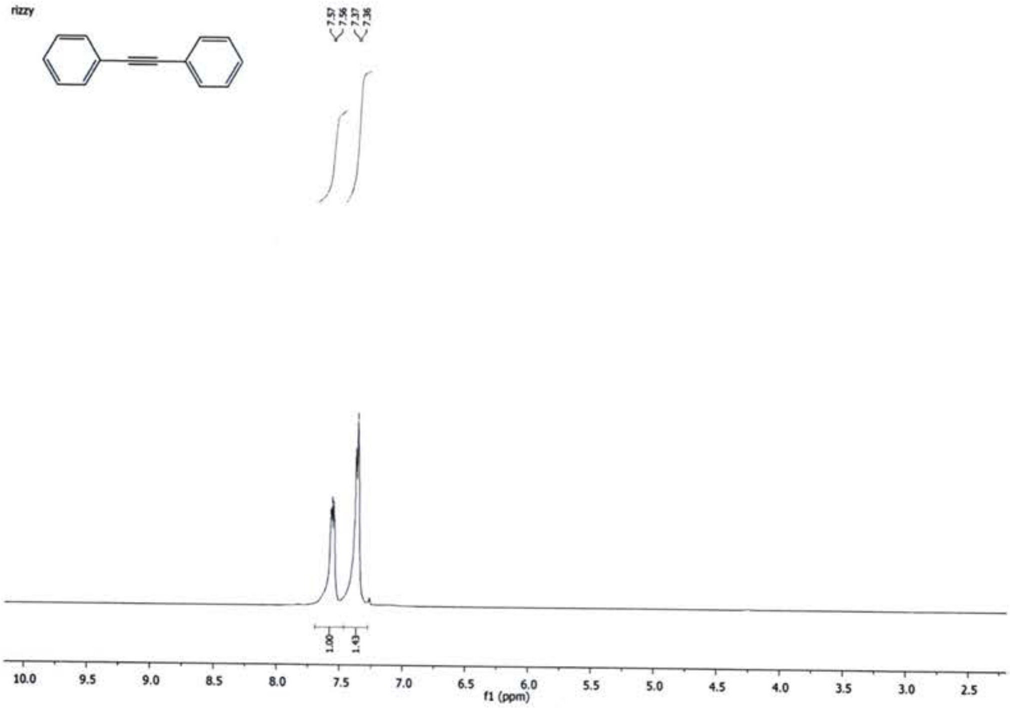
[1,1'-biphenyl]-4-carbaldehyde: The general procedure was used to afford the title product as yellow oil (91% yield) ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.07 (s, 1H), 8.19 (d, J = 8.3 Hz, 1H), 7.96 (d, J = 8.2 Hz, 1H), 7.76 (d, J = 8.2 Hz, 1H), 7.65 (d, J = 7.1 Hz, 1H), 7.55 – 7.39 (m, 2H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 191.94, 147.21, 139.72, 135.23, 130.28, 129.03, 128.49, 127.69, 127.37, 115.39.

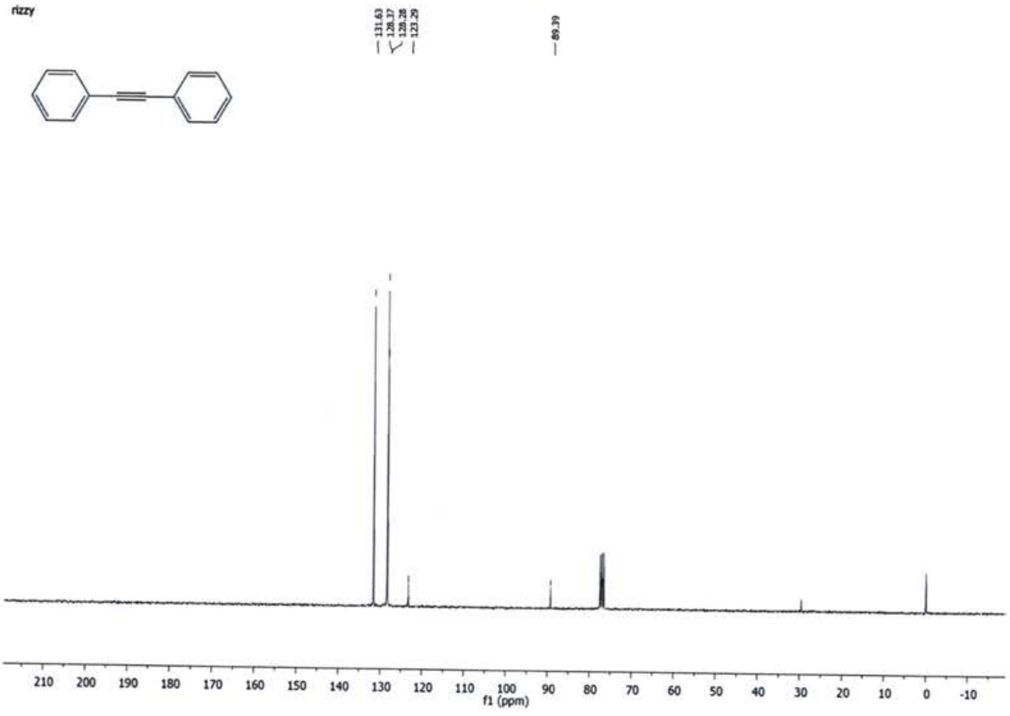




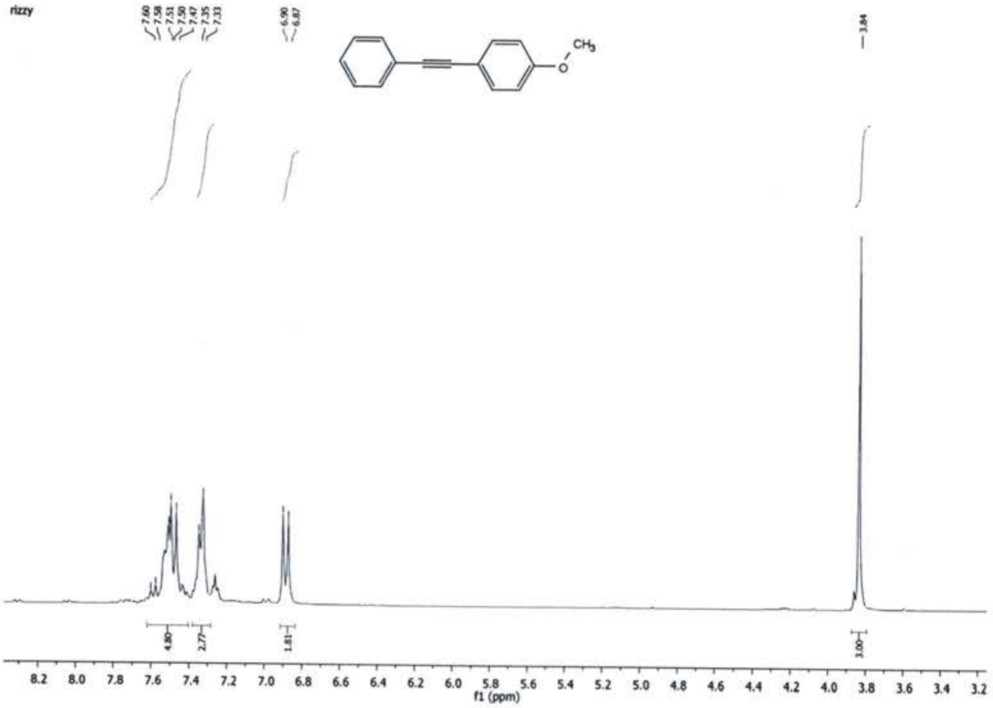
B-5 General experimental procedure for Sonogashira coupling: Phenylacetylene (1.0 mmol), aryl halide (1.0 mmol), triphenylphosphine ligand (0.0065 g, 0.025 mmol), cesium carbonate (0.49 g, 1.5 mmol), and **CAT1** (50 mg) were added into flamed-dried Pyrex glass tube equipped with a stir bar and sealed with a rubber septum and then added ethanol (3 mL) through rubber septum. The mixture was stirred at 90 °C for 20 h. Cooled down the reaction mixture to room temperature, added dodecane (1.0 mmol, an internal standard), separated magnetic catalyst and then extracted with ethyl acetate for gas chromatography analysis. To determine the isolated yield, after magnetic separation of the catalyst, the reaction mixture was filtered through celite to remove any insoluble residues. The filtrate was then extracted with ethyl acetate (3x10 mL), washed with water (5x10 mL), dried with sodium sulfate, filtered and concentrated in vacuo. The residue was purified by column chromatography on silica gel to obtain the analytically pure product.

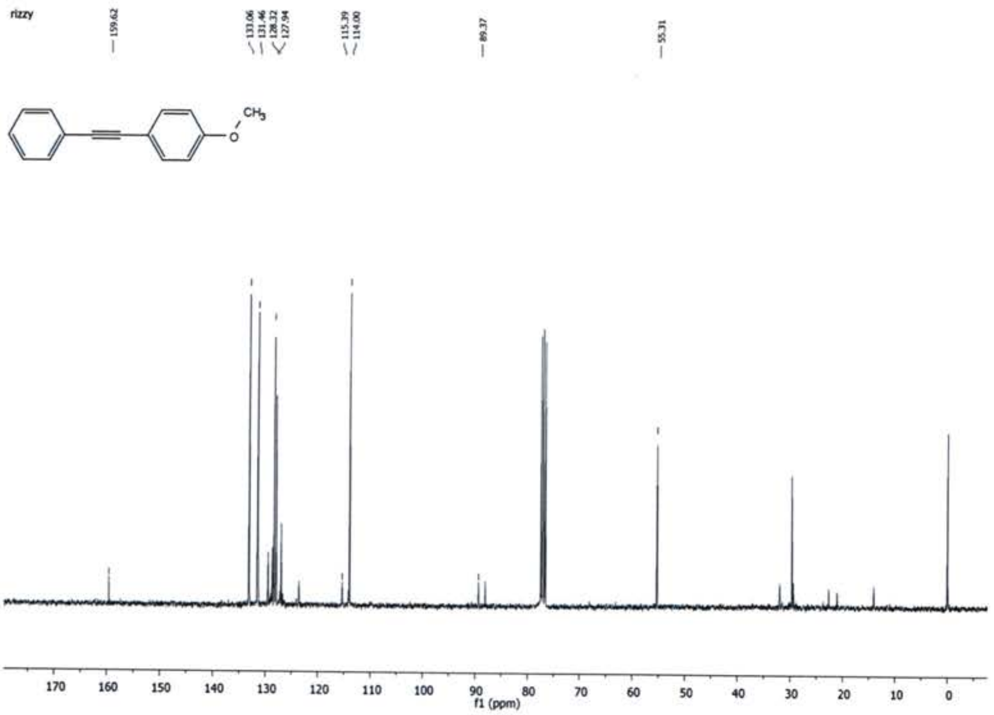
1,2-diphenylethyne: The general procedure was used to afford the title product as white solid (86% yield) ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.57 (d, J = 3.9 Hz, 1H), 7.36 (d, J = 4.6 Hz, 2H). ^{13}C NMR (75 MHz, CDCl$_3$) δ 131.63, 128.37, 128.28, 123.29, 89.39.



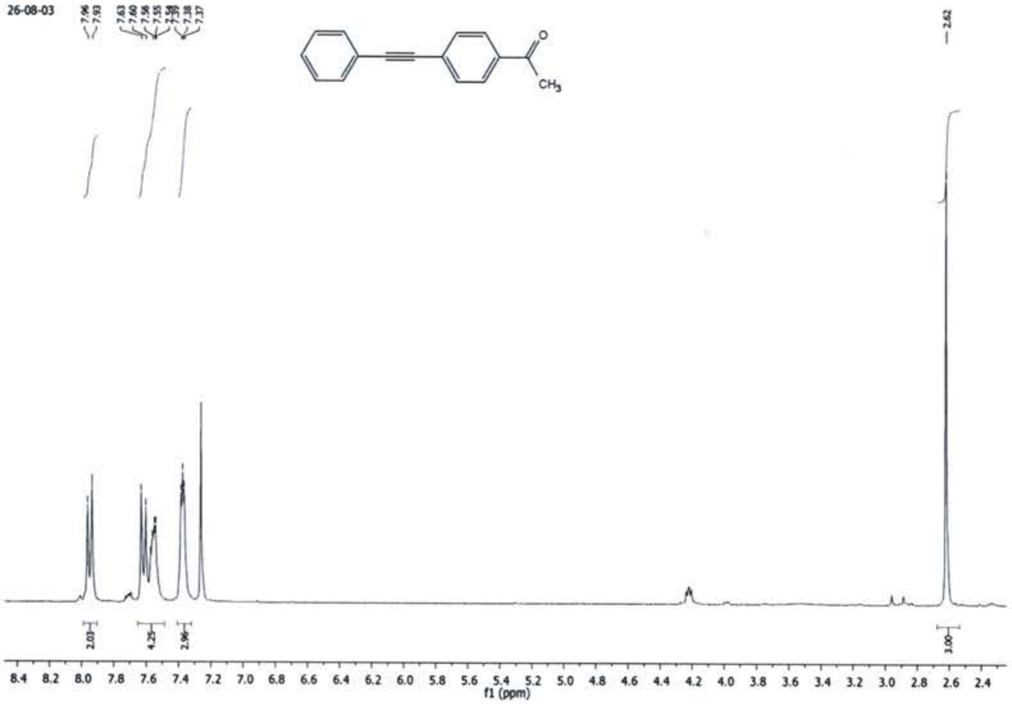


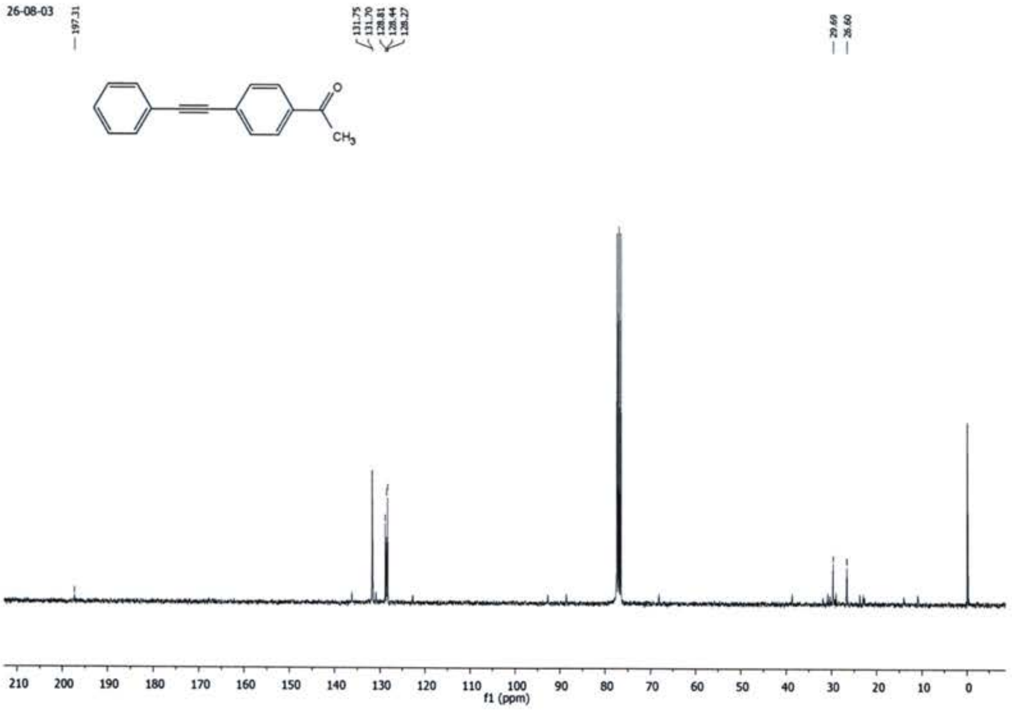
1-methoxy-4-(phenylethynyl)benzene: The general procedure was used to afford the title product product as a pale yellow solid (95% yield) ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.61 – 7.42 (m, 2H), 7.34 (d, *J* = 6.6 Hz, 1H), 6.89 (d, *J* = 8.6 Hz, 1H), 3.84 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.62, 133.06, 131.46, 128.32, 127.94, 115.39, 114.00, 89.37, 55.31.



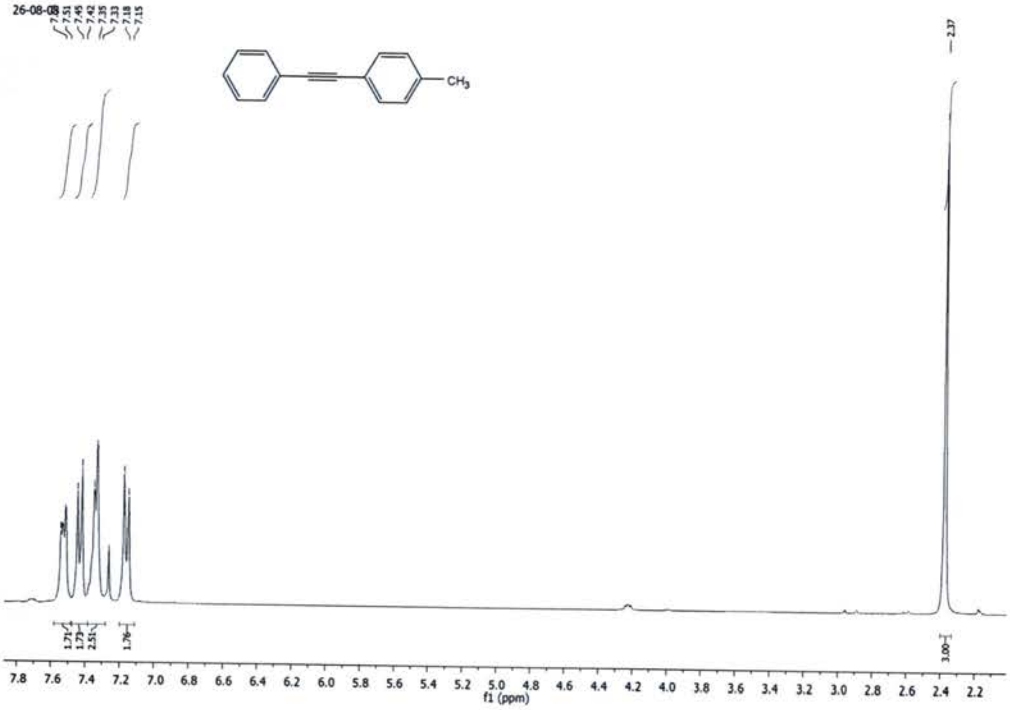


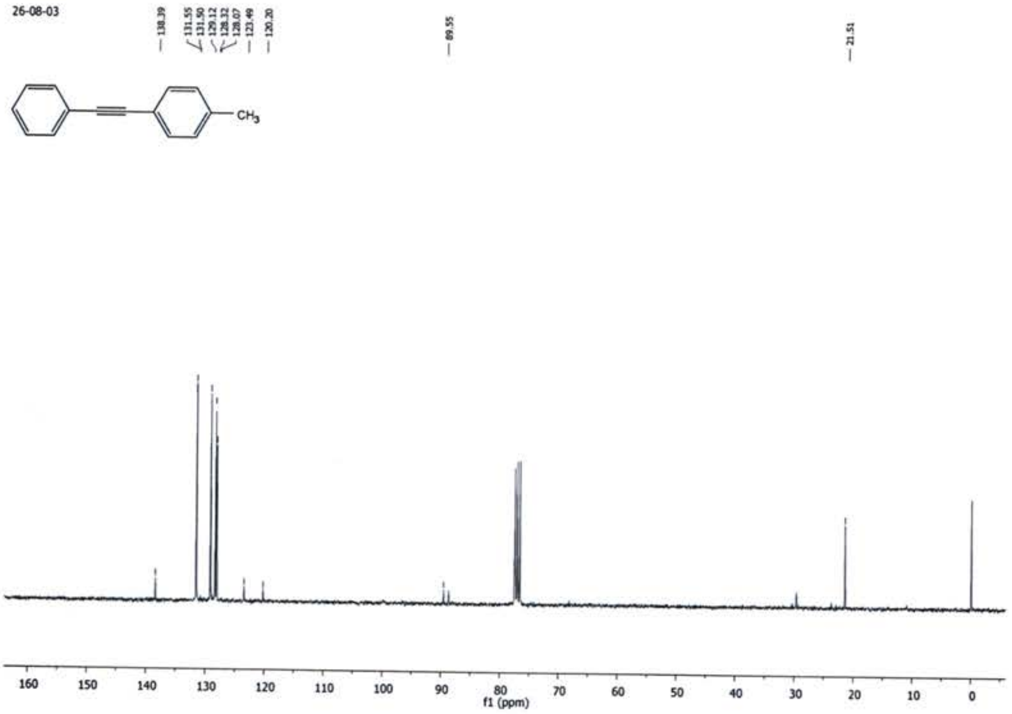
1-(4-(phenylethynyl)phenyl)ethanone: The general procedure was used to afford the title product as a pale yellow solid (98% yield) ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.95 (d, J = 8.3 Hz, 1H), 7.66 – 7.48 (m, 1H), 7.42 – 7.30 (m, 1H), 2.62 (s, 3H). ^{13}C NMR (75 MHz, CDCl$_3$) δ 197.31, 131.75, 131.70, 128.81, 128.44, 128.27, 29.69, 26.60.



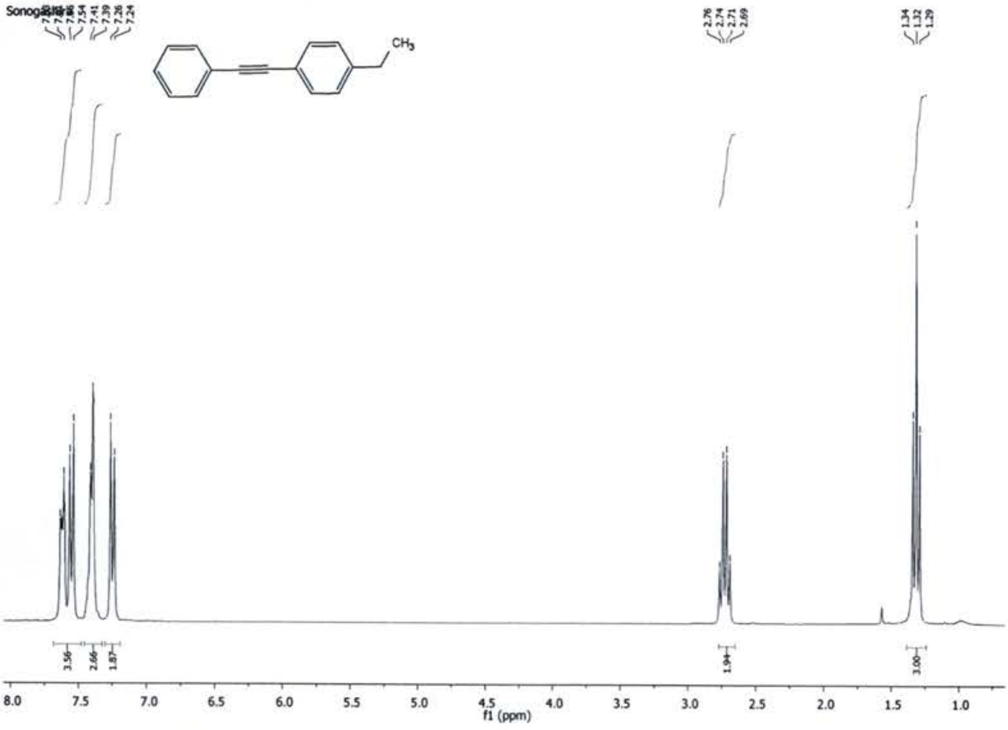


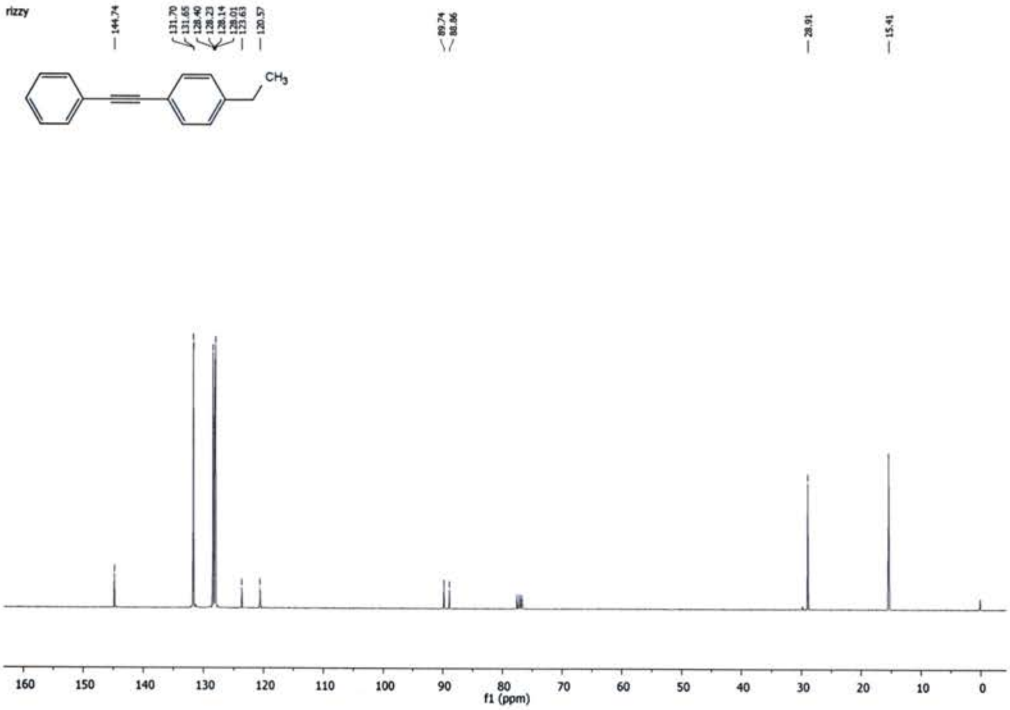
1-methyl-4-(phenylethynyl)benzene: The general procedure was used to afford the title product as a white solid (90% yield) ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.53 (d, J = 9.2 Hz, 1H), 7.43 (d, J = 8.0 Hz, 1H), 7.34 (d, J = 6.6 Hz, 1H), 7.16 (d, J = 7.9 Hz, 1H), 2.37 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.39, 131.55, 131.50, 129.12, 128.32, 128.07, 123.49, 120.20, 89.55, 21.51.



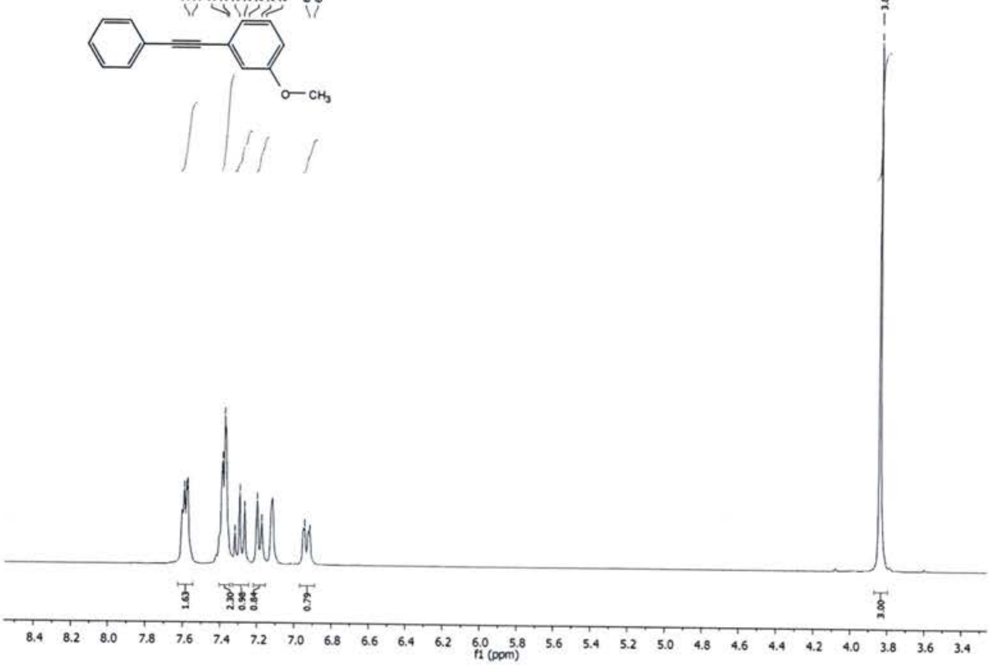


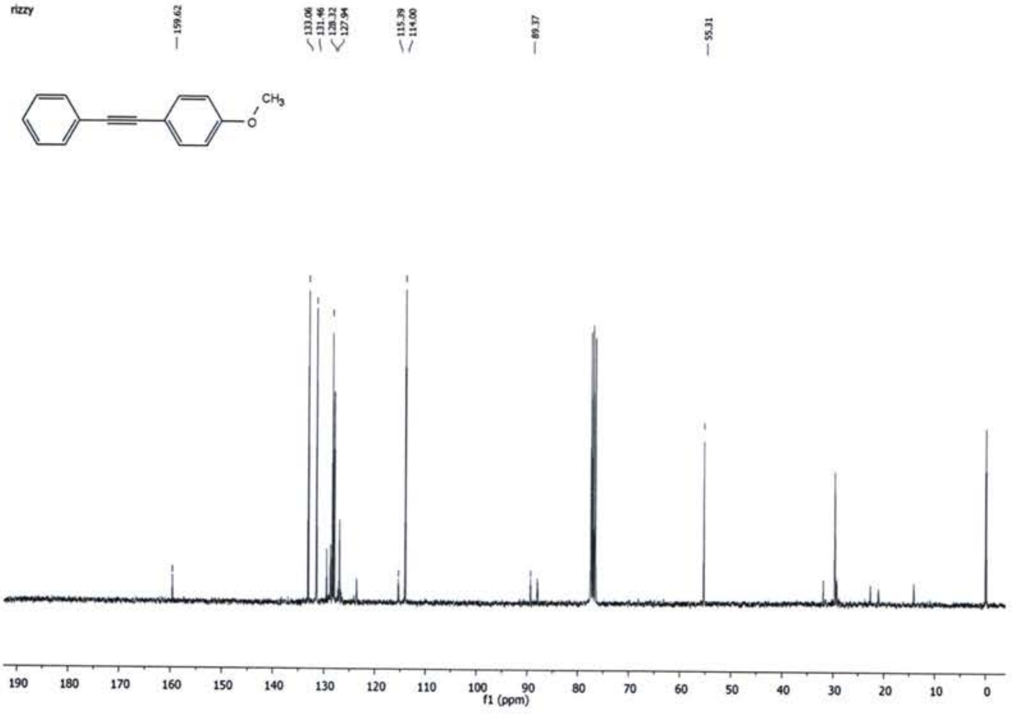
1-ethyl-4-(phenylethynyl)benzene: The general procedure was used to afford the title product as a colourless liquid (96% yield) ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.59 (dd, *J* = 21.1, 7.9 Hz, 1H), 7.40 (d, *J* = 7.0 Hz, 1H), 7.25 (d, *J* = 8.0 Hz, 1H), 2.73 (q, *J* = 7.6 Hz, 2H), 1.32 (t, *J* = 7.6 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.74, 131.70, 131.65, 128.40, 128.23, 128.14, 128.01, 123.63, 120.57, 89.74, 88.86, 28.91, 15.41.



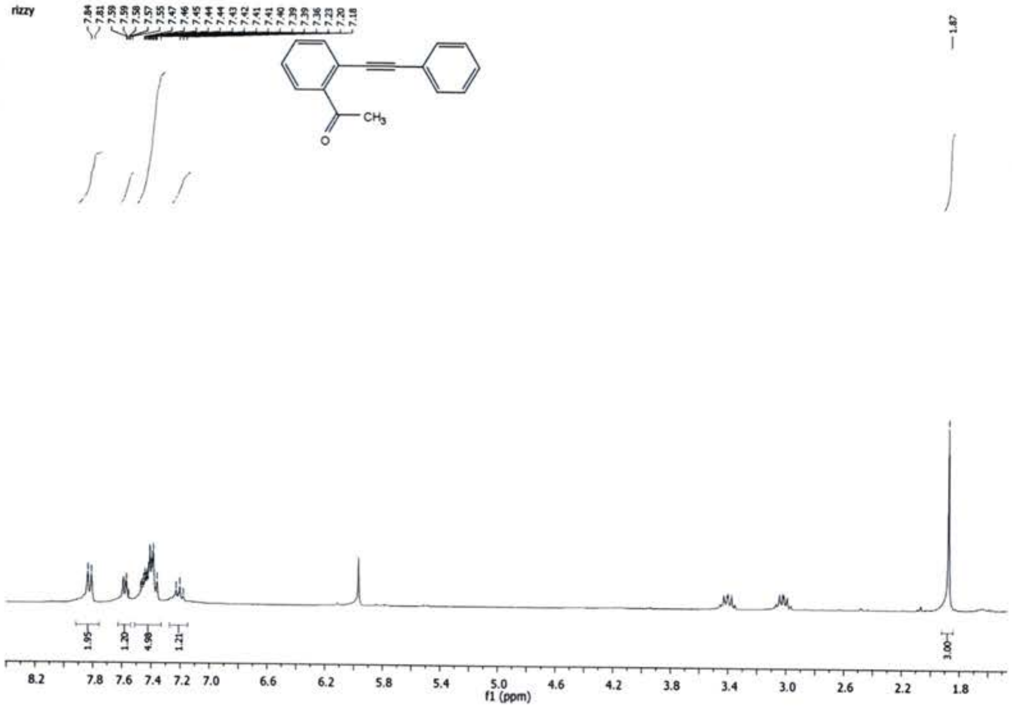


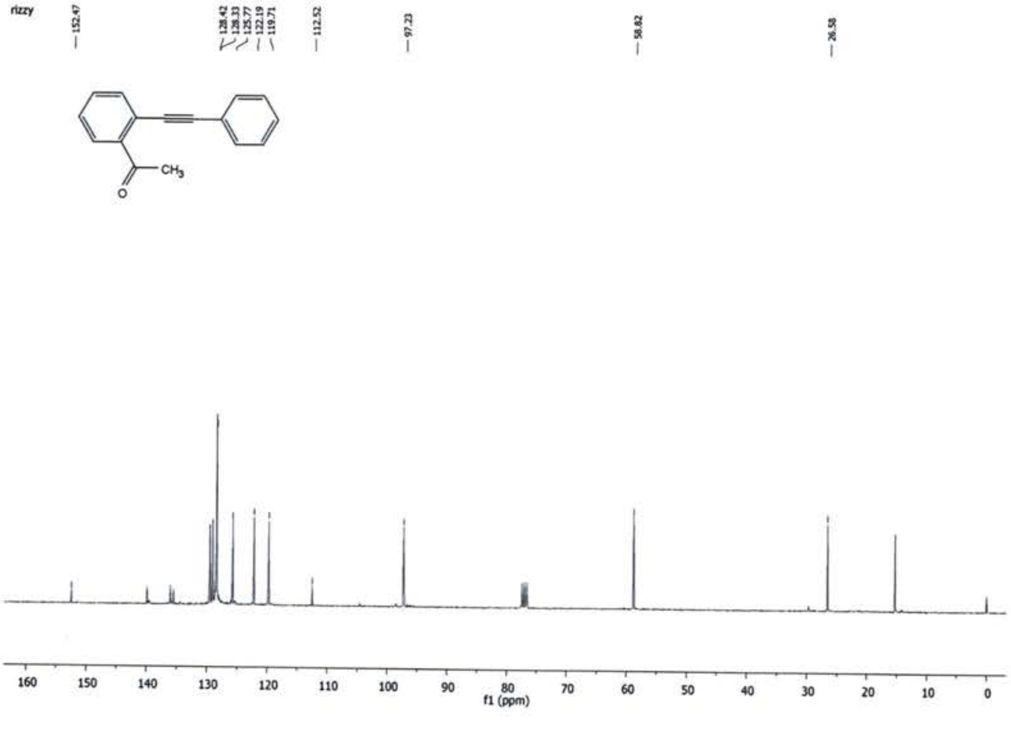
1-methoxy-3-(phenylethynyl)benzene: The general procedure was used to afford the title product as a yellow oil (81% yield) ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.58 (d, J = 5.3 Hz, 2H), 7.36 (t, J = 10.0 Hz, 3H), 7.29 (t, J = 7.9 Hz, 1H), 7.19 (d, J = 7.5 Hz, 1H), 6.93 (d, J = 8.2 Hz, 1H), 3.84 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.62, 133.06, 131.46, 128.32, 127.94, 115.39, 114.00, 89.37, 55.31.





1-([1,1'-biphenyl]-2-yl)ethanone : The general procedure was used to afford the title product as a yellow oil (60% yield) ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.82 (d, *J* = 7.4 Hz, 1H), 7.61 – 7.54 (m, 1H), 7.49 – 7.34 (m, 2H), 7.20 (t, *J* = 7.4 Hz, 1H), 1.87 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.47, 128.42, 128.33, 125.77, 122.19, 119.71, 122.52, 97.23, 58.82, 26.58.





C. FT-IR spectra of products

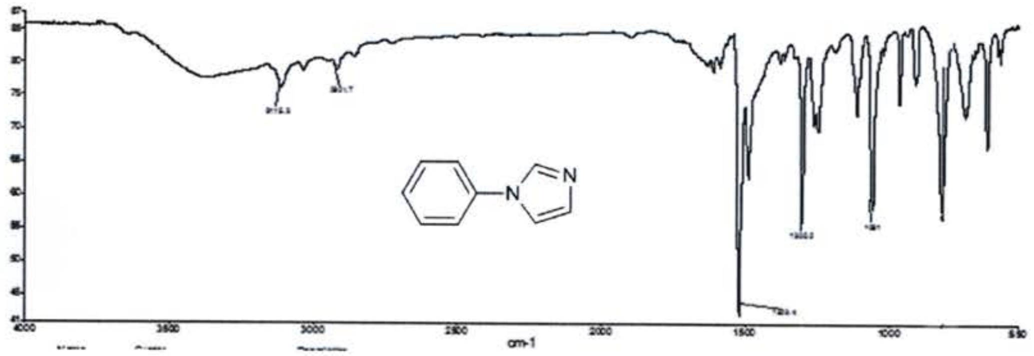


Figure C.1 FT-IR spectrum of 1-phenyl-1H-imidazole

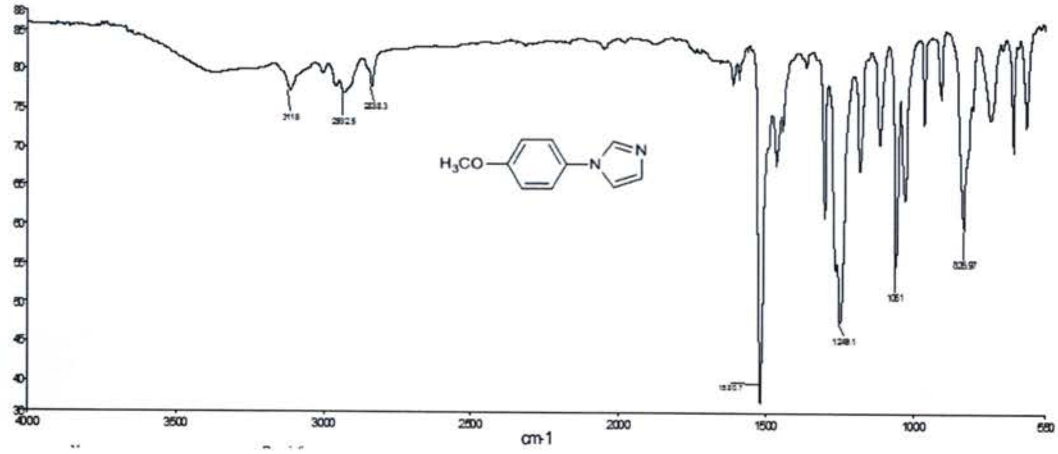


Figure C.2 FT-IR spectrum of 1-(4-methoxyphenyl)-1H-imidazole

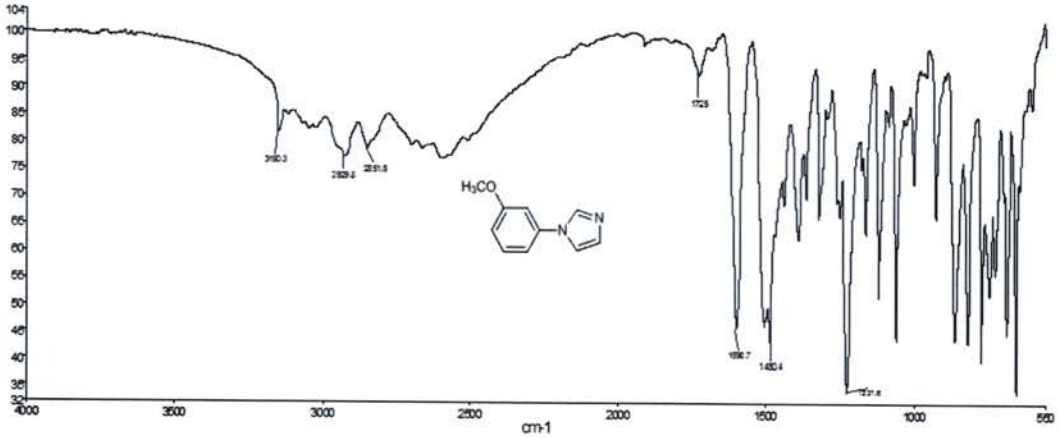


Figure C.3 FT-IR spectrum of 1-(3-methoxyphenyl)-1H-imidazole

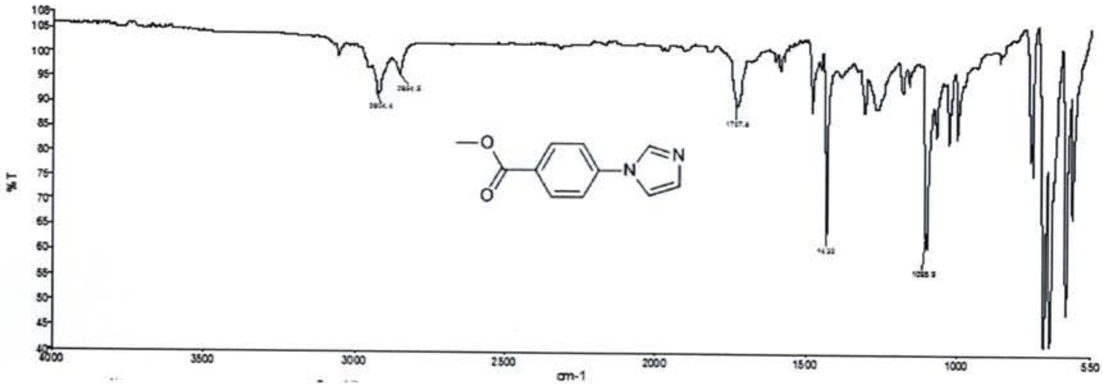


Figure C.4 FT-IR spectrum of Methyl 4-(1H-imidazol-1-yl)benzoate

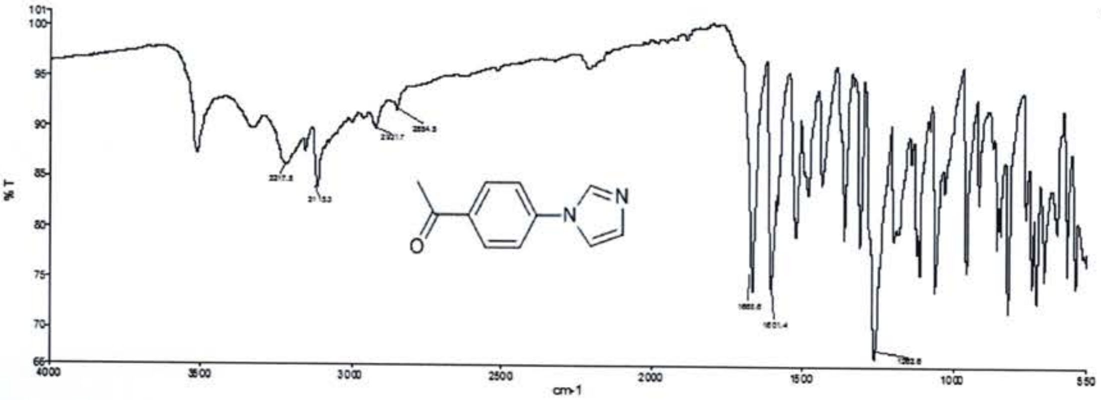


Figure C.5 FT-IR spectrum of 1-(4-(1H-imidazol-1-yl)phenyl)ethanone

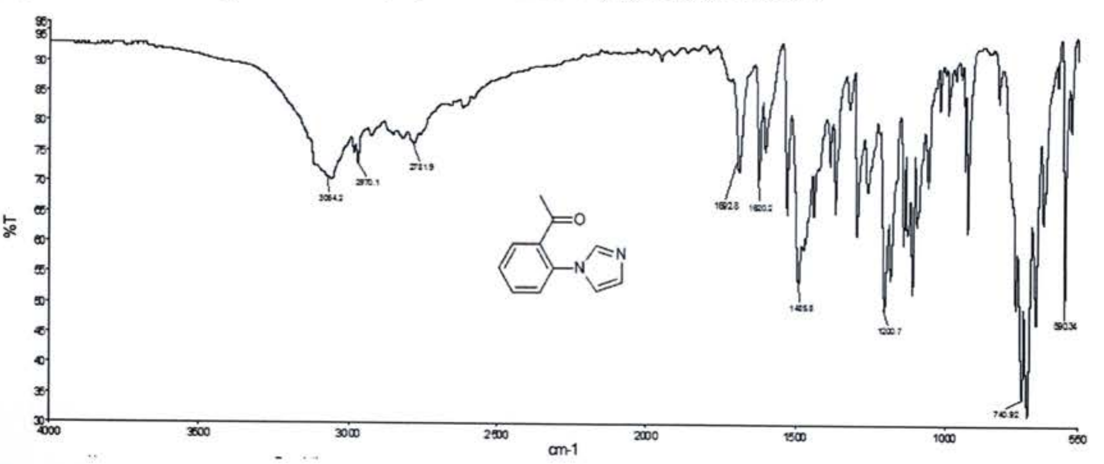


Figure C.6 FT-IR spectrum of 1-(2-(1H-imidazol-1-yl)phenyl)ethanone

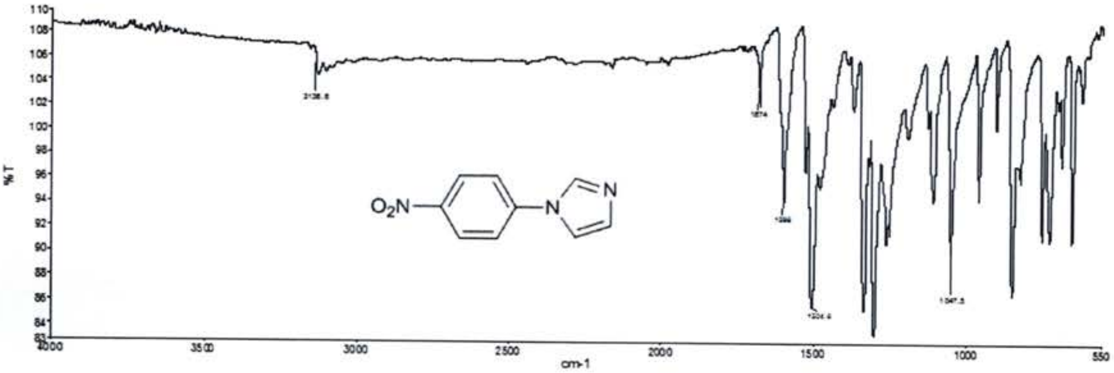


Figure C.7 FT-IR spectrum of 1-(4-nitrophenyl)-1H-imidazole

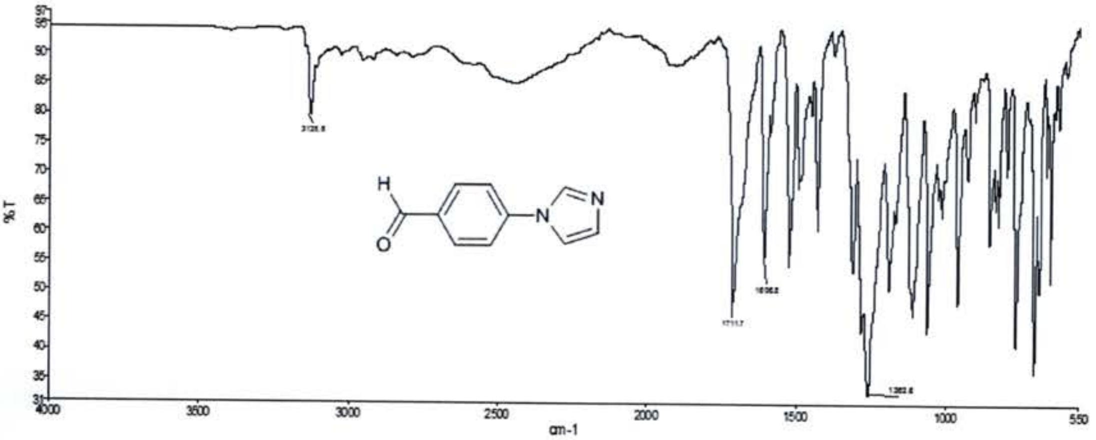


Figure C.8 FT-IR spectrum of 4-(1H-imidazol-1-yl)benzaldehyde

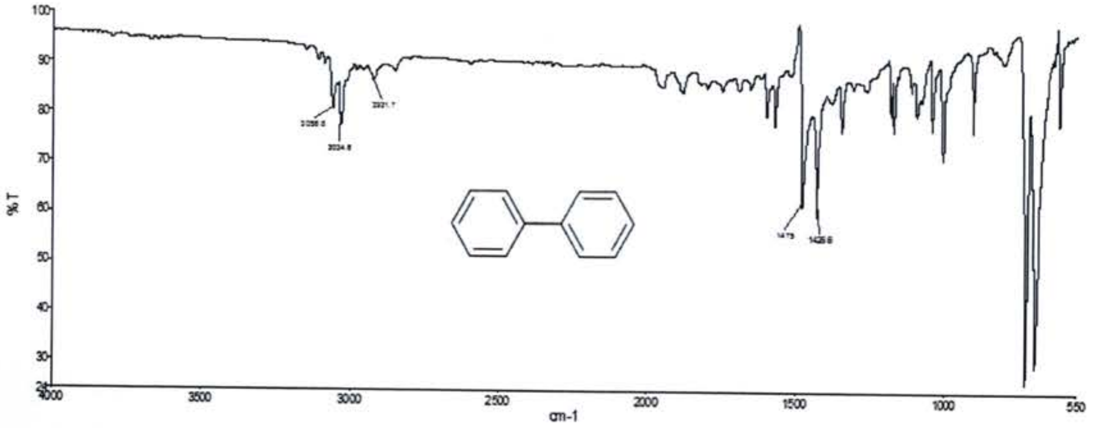


Figure C.9 FT-IR spectrum of 1,1'-biphenyl

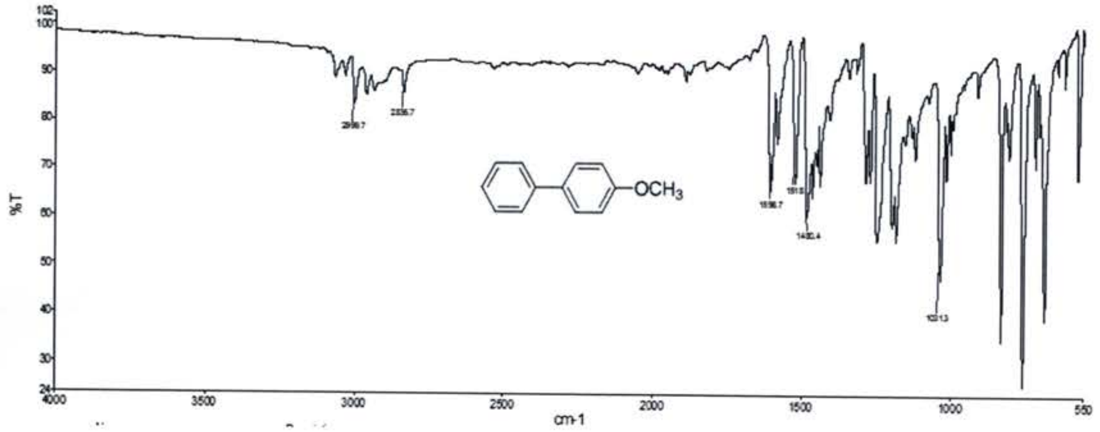


Figure C.10 FT-IR spectrum of 4-methoxy-1,1'-biphenyl

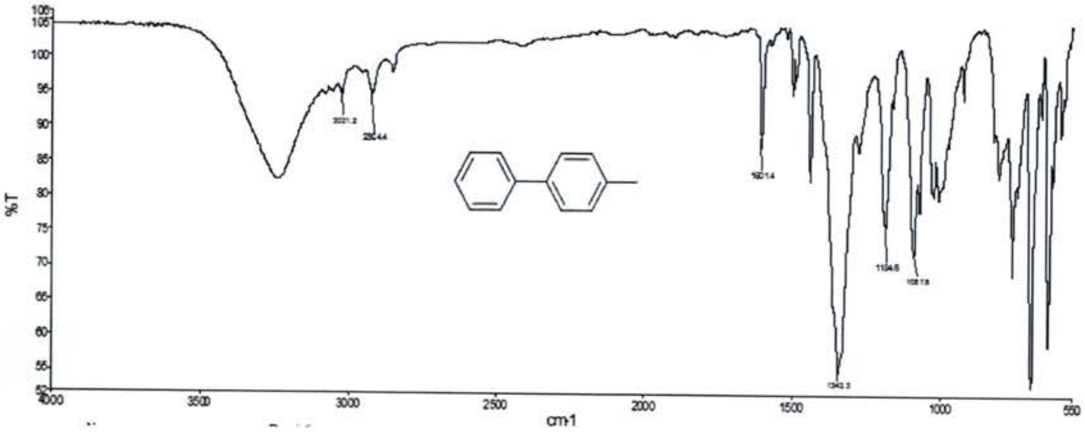


Figure C.11 FT-IR spectrum of 4-methyl-1,1'-biphenyl

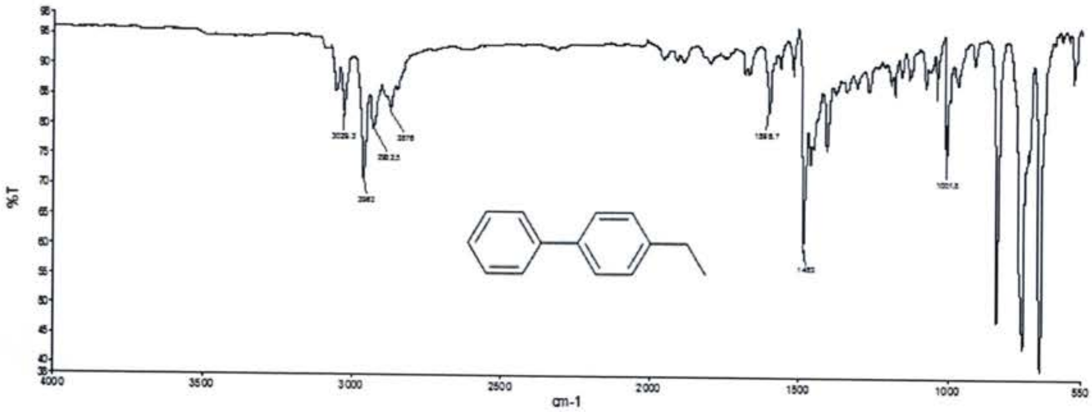


Figure C.12 FT-IR spectrum of 4-ethyl-1,1'-biphenyl

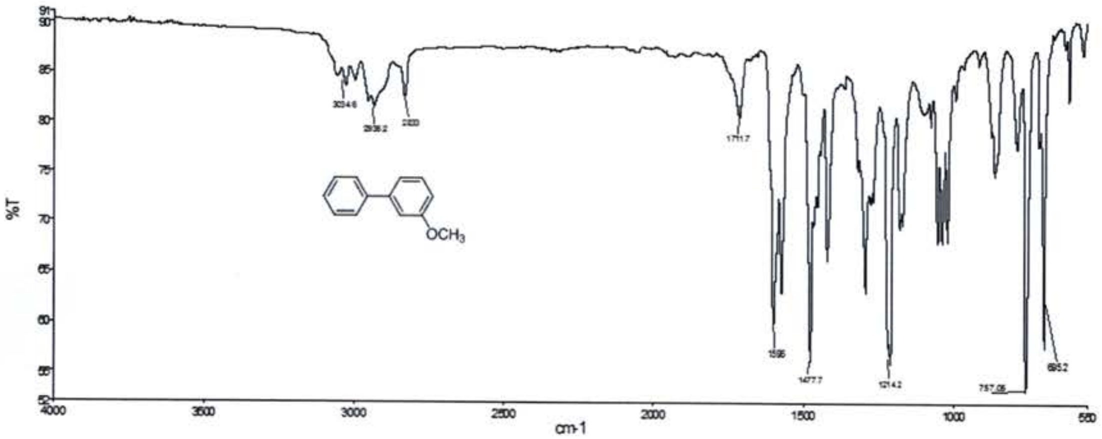


Figure C.13 FT-IR spectrum of 3-methoxy-1,1'-biphenyl

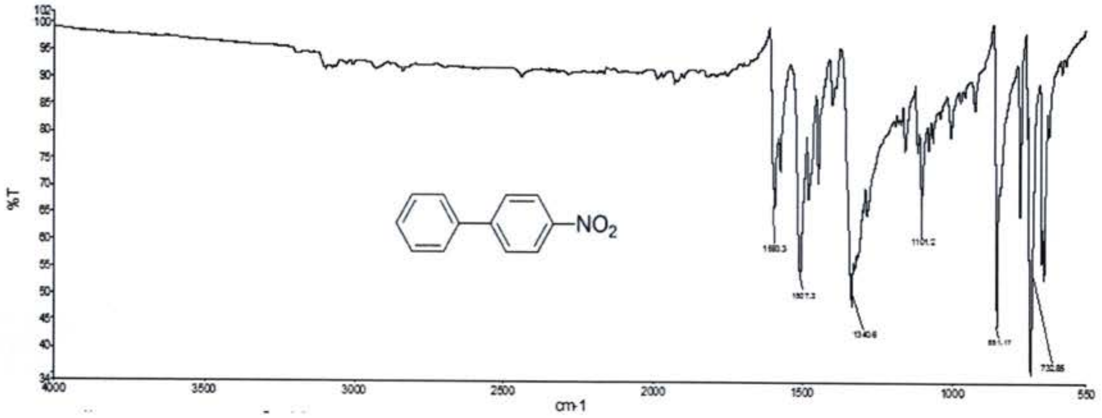


Figure C.14 FT-IR spectrum of 4-nitro-1,1'-biphenyl

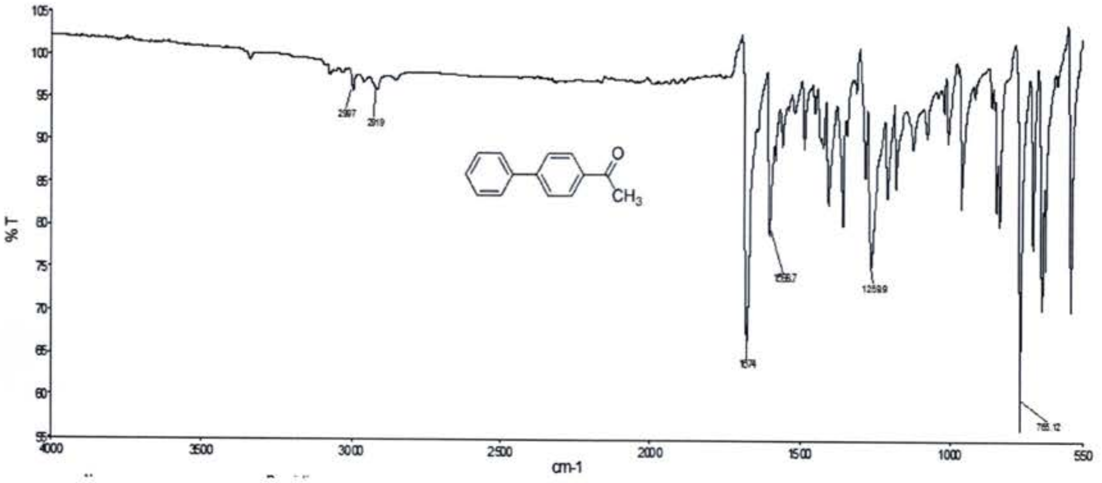


Figure C.15 FT-IR spectrum of 1-([1,1'-biphenyl]-4-yl)ethanone

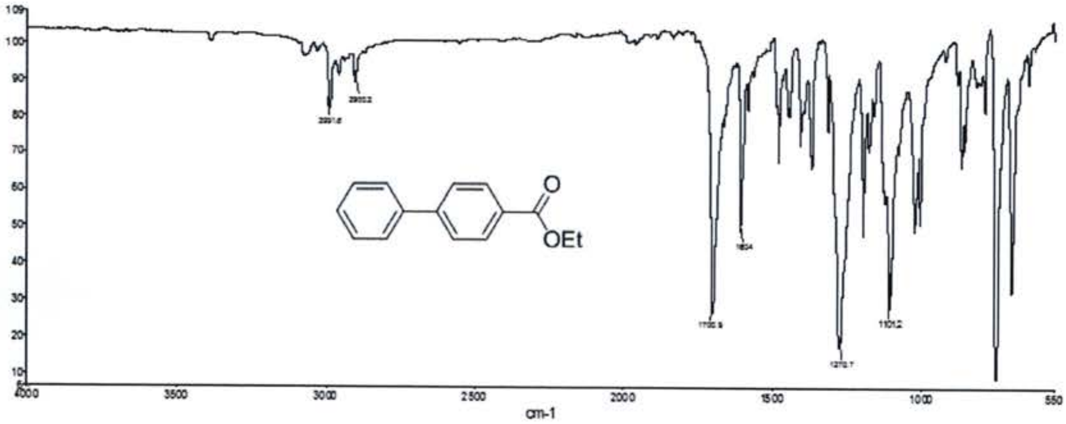


Figure C.16 FT-IR spectrum of Ethyl [1,1'-biphenyl]-4-carboxylate

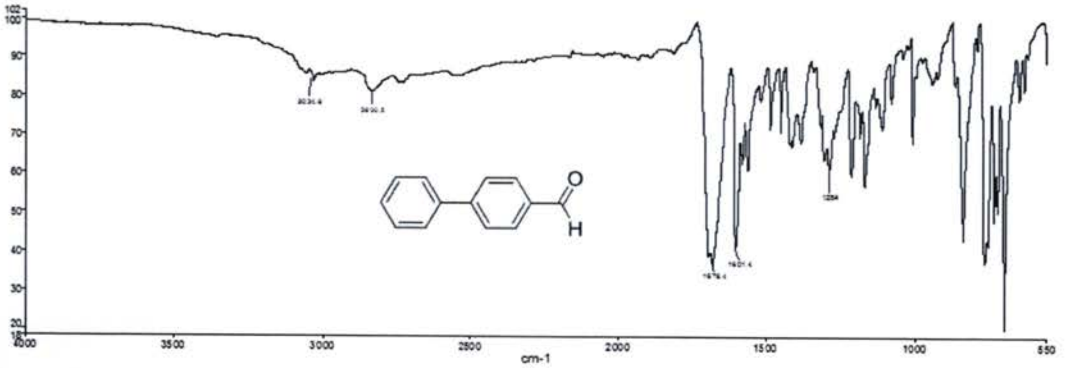


Figure C.17 FT-IR spectrum of [1,1'-biphenyl]-4-carbaldehyde

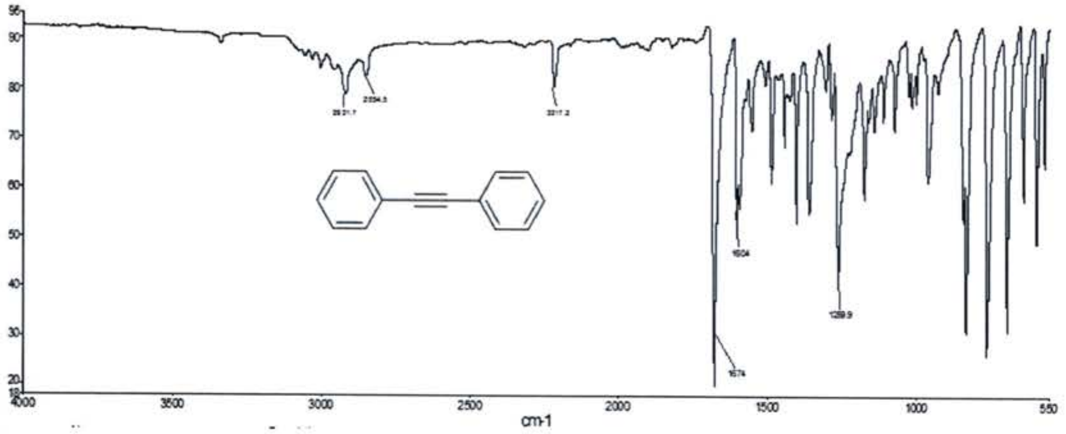


Figure C.18 FT-IR spectrum of 1,2-diphenylethyne

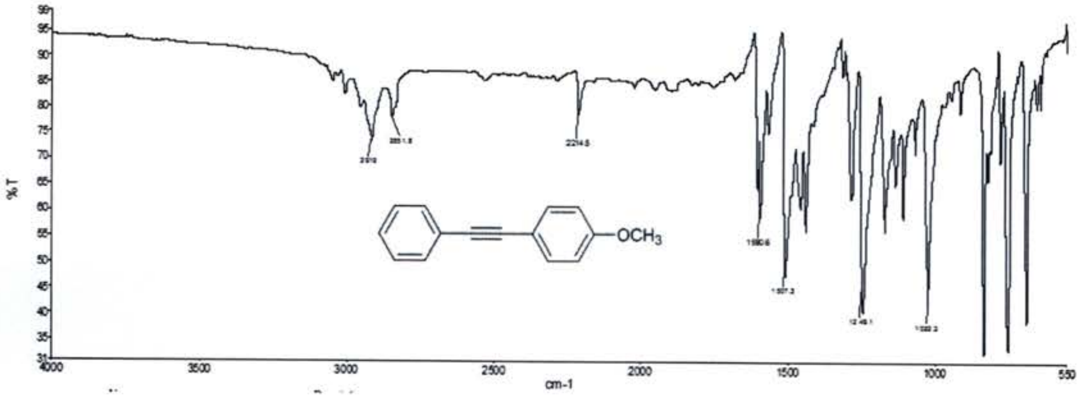


Figure C.19 FT-IR spectrum of 1-methoxy-4-(phenylethynyl)benzene

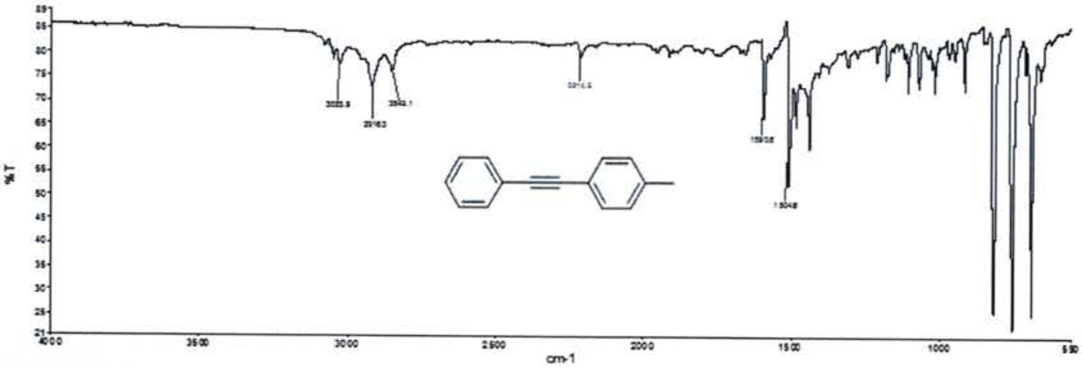


Figure C.20 FT-IR spectrum of 1-methyl-4-(phenylethynyl)benzene

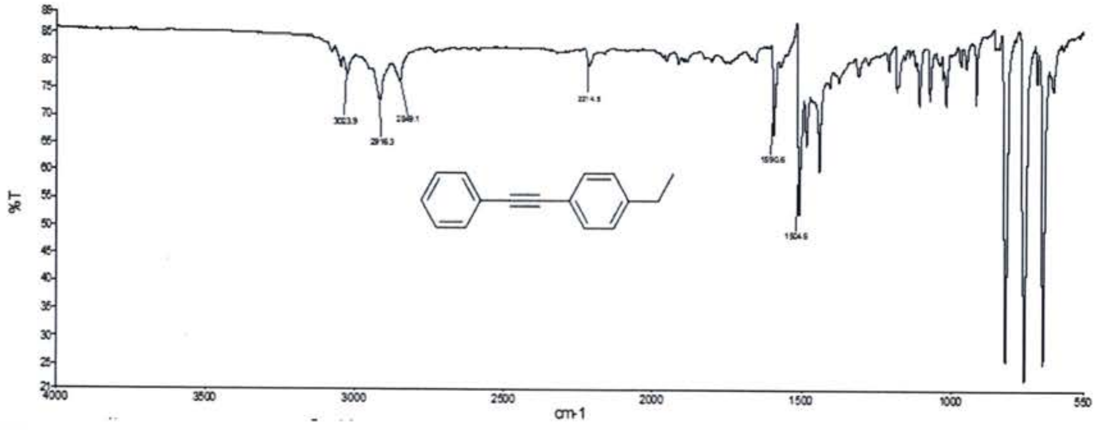


Figure C.21 FT-IR spectrum of 1-ethyl-4-(phenylethynyl)benzene

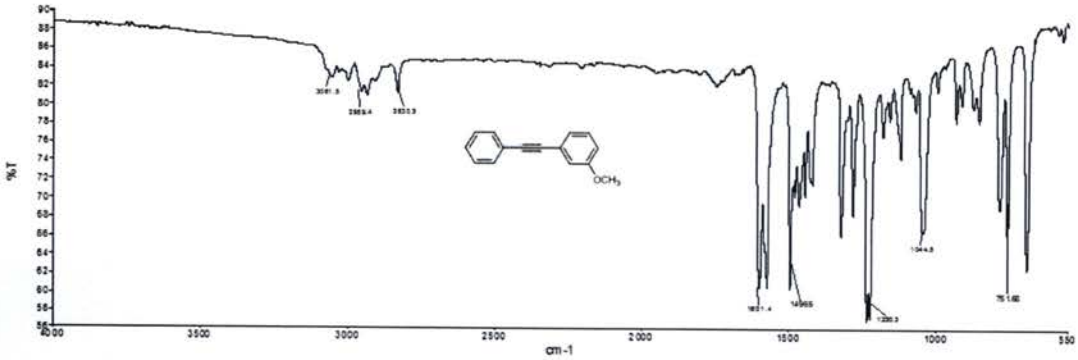


Figure C.22 FT-IR spectrum of 1-methoxy-3-(phenylethynyl)benze

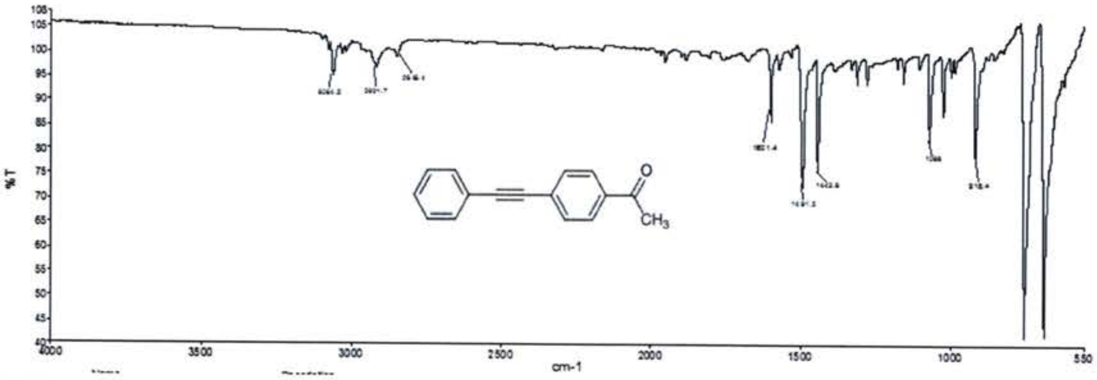


Figure C.23 FT-IR spectrum of 1-(4-(phenylethynyl)phenyl)ethanone