การสังเคราะห์ไดแอริลเอไทน์จากแคลเซียมคาร์ไบด์

นาย ปฏูล ชื่นตระกูล

วิทยานิพนธ์นี้เป็นส่วนหนึ่งของการศึกษาตามหลักสูตรปริญญาวิทยาศาสตรมหาบัณฑิต
สาขาวิชาเคมี ภาควิชาเคมี
คณะวิทยาศาสตร์   จุฬาลงกรณ์มหาวิทยาลัย
ปีการศึกษา 2554
ลิขสิทธิ์ของจุฬาลงกรณ์มหาวิทยาลัย

SYNTHESIS OF DIARYL ETHYNES FROM CALCIUM CARBIDE

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A Thesis Submitted in Partial Fulfillment of the Requirements
for the Degree of Master of Science Program in Chemistry
Department of Chemistry
Faculty of Science
Chulalongkorn University
Academic Year 2011

Thesis Title	SYNTHESIS OF DIARYL ETHYNES FROM CALCIUM CARBIDE
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Field of Study	Chemistry
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Accepted by the Faculty of Science, Chulalongkorn University in Partial Fulfillment of the Requirements for the Master's Degree

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ปฎล ชื่นตระกูล   :   การสังเคราะห์ไดแอริลเอไทน์จากแคลเซียมคาร์ไบด์
(SYNTHESIS OF DIARYL ETHYNES FROM CALCIUM CARBIDE)
อ. ที่ปรึกษาวิทยานิพนธ์หลัก : ผศ. ดร. สัมฤทธิ์ วัชรสินธุ์, อ. ที่ปรึกษาวิทยานิพนธ์ร่วม :
รศ. ดร. มงคล สุขวัฒนาสินิทธิ์, 86 หน้า.

การสังเคราะห์ไดแอริลเอไทน์จากแคลเซียมคาร์ไบด์โดยปฏิกิริยาคับปลิงด้วยแพลลาเดียม
ได้ถูกพัฒนาขึ้น ปฏิกิริยานี้ให้ร้อยละผลได้ของไดแอริลเอไทน์ที่สูงและสามารถประยุกต์กับแอริล
ไอโอไดด์ที่มีหมู่ฟังก์ชันหลากหลายชนิด จำนวน ยี่สิบเอ็ดชนิด ทั้งชนิดที่มีความเข้มของ
อิเล็กตรอนสูงและต่ำ ทั้งชนิดที่มีเฮโทรอะตอม ทั้งสารตั้งต้นที่ทำปฏิกิริยาได้ยาก และหมู่ฟังก์ชัน
ที่มีความว่องไวต่อปฏิกิริยาสูงก็สามารถทนต่อปฏิกิริยาได้ดี โดยแคลเซียมคาร์ไบด์เลือกทำปฏิกิริยา
กับหมู่ไอโอไดด์เท่านั้น ภาวะของการเกิดปฏิกิริยาไม่รุนแรงและใช้สารตั้งต้นที่สามารถหาซื้อได้
ง่ายและมีราคาถูก เช่น แพลลาเดียมอะซิเทต คอปเปอร์ไอโอไดด์ ไทรเอทิลเอมีน ในแอซิโทไนทริล
ที่ไม่ได้ทำให้แห้งก่อน ให้ร้อยละผลได้ของปฏิกิริยาสูง อีกทั้งวิธีการแยกสารก็ยังทำได้ง่ายด้วยการ
กรองผ่านชั้นของซิลิกาเจลเท่านั้น นอกจากนี้สารที่มีหมู่ฟังชันมากและมีความเกะกะสูงอย่างฟีนิลีน
เอไทน์นิลีนยังสามารถเกิดปฏิกิริยาได้ดี จากการศึกษากลไกการเกิดปฏิกิริยาพบว่าน้ำมีผลต่อการ
เกิดปฏิกิริยาดังนั้นปฏิกิริยาเกิดผ่านการเกิดโมเลกุลของแก๊สอะเซทิลีนอย่างช้าๆ จากการไฮโดรไล
ซิสของแคลเซียมคาร์ไบด์และน้ำ

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ภาควิชา ......เคมี...... .	ลายมือชื่อนิสิต	
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ปีการศึกษา ......2554......	ลายมือชื่อ อ.ที่ปรึกษาวิทยานิพนธ์ร่วม	

5272396023: MAJOR CHEMISTRY

KEYWORDS : DIARYL E THYNE / CALCIUM C ARBIDE / PALLADIUM / SONOGASHIRA

PADON CHUENTRAGOOL : SYNTHESIS OF DIARYL ETHYNES FROM CALCIUM CARBIDE. ADVISOR: A SST. PROF. SUMRIT WACHARASINDHU, Ph.D., CO-ADVISOR: ASSOC. PROF. MONGKOL SUKWATTANASINITT, Ph.D., 86 pp.

The synthesis of diaryl ethynes from an inexpensive calcium c arbide as acetylene s urrogate via p alladium c atalyzed coupling r eaction with a ryl i odides was developed. A number of symmetrical diaryl ethynes were synthesized from various substituted aryl iodides including electron donating, e lectron withdrawing, heteroatoms, and labile f unctional g roups. T he r eaction proceeded smoothly in mild conditions with commercially inexpensive reagents such as $Pd(OAc)_2$, CuI a nd triethylamine in the presence of undried acetonitrile as s olvent to g enerate t he coupling products in good to high yields. Moreover, highly functionalized oligo(phenyleneethynylenes) were prepared in good y ields demonstrating t he h igh functional group compatibility of our methodology. The reaction mechanism w as a lso investigated. The presence of water is r equired i n o rder t o d rive t he r eaction completely suggesting t he s low r elease o f a cetylene g as i n t he reaction condition from the h ydrolysis of c alcium carbide with wa ter.
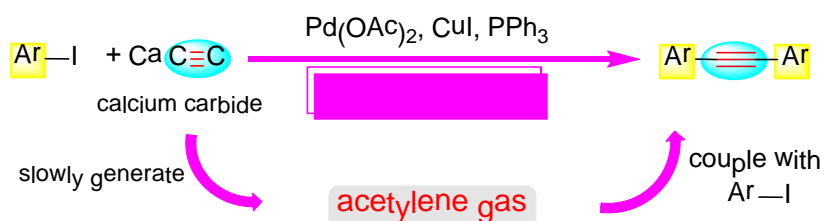
Department: _____Chemistry_____.   Student's Signature _____

Field of Study : _____Chemistry_____.   Advisor's Signature _____

Academic Year : _____2011_____.   Co-advisor's Signature _____

ACKNOWLEDGEMENTS

First of a ll, I would like to express my sincere gratitude to my thesis advisor, Assistant Professor Sumrit Wacharasindhu, Ph.D. and my co-advisor, Associate Professor Mongkol Sukwattanasinitt, Ph.D., for v aluable a dvice, g uidance a nd kindness t hroughout t his r esearch. Sincere thanks are also extended to Assistant Professor Warinthorn Chavasiri, Ph.D., Assistant Professor Yongsak S ritana-Anant, Ph.D. and Jutatip B oonsombat, Ph.D., attending as the c ommittee m embers, f or t heir valuable comments and suggestions.

I w ould l ike t o especially thank Associate Professor Dr. Paitoon Rashatasakhon, Ph.D. and Miss Kunnigar V ongnam for generous supply of various chemicals, synthesis of starting material for oligo (phenyleneethynylenes), and their helpful advice.

In particular, I am thankful to The National Center of Excellence for Petroleum, Petrochemicals, and Advanced Materials, The T hailand R esearch F und, The N ational Nanotechnology C enter, NSTDA (NN-B-22-FN9-10-52-06), the 100th Anniversary of C hulalongkorn U niversity Fund, Asahi G lass F oundation, the National R esearch U niversity o f C HE a nd t he TKK2555, S P2. for supporting my thesis. Gratitude i s a lso e xtended t o t he m embers o f m y r esearch g roup f or their helpful discussion.

Finally, I would l ike t o specially t hank m y f amily a nd f riends f or t heir encouragement a nd u nderstanding t hroughout. I would not be able to reach this success w ithout them.

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LIST OF ABBREVIATIONS

°C	Degree celsius
$CDCl_3$	Deuterated chloroform
CH_2Cl_2	Methylene chloride
CuI	Copper iodide
d	Doublet
DBU	1,8-Diazabicycloundec-7-ene
dd	Doublet of doublet
DMSO	Dimethyl sulfoxide
DMSO-$d6$	Deuterated dimethyl sulfoxide
EtOAc	Ethyl acetate
g	Gram(s)
h	Hour
H_2SO_4	Sulfuric acid
Hz	Hertz
J	Coupling constant
K_2CO_3	Potassium carbonate
KI	Potassium iodide
KIO_3	Potassium iodate
m	Multiplet
MeCN	Acetonitrile
MeOH	Methanol
mg	Milligram (s)
min	Minute (s)
mL	Milliliter (s)
mmol	Millimole
M	Molar
MS	Mass spectrometry
$NaSO_4$	Sodium sulfate
NMR	Nuclear magnetic resonance
Pd	Palladium

PdCl$_2$(PPh$_3$)$_2$ Bis(triphenylphosphine)palladium(II) chloride

ppm   Parts per million

s   Singlet

t   Triplet

THF   Tetrahydrofuran

TLC   Thin layer chromatography
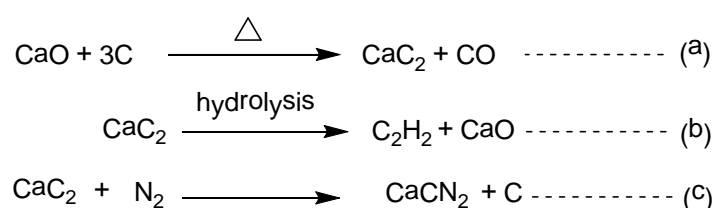
%   Percent

δ   Chemical shift

CHAPTER I
INTRODUCTION

1.1 Introduction

Over t he p ast t wo d ecades, P d-catalyzed c ross-coupling reactions such as Heck, Suzuki, Nigishi, S tille, and Sonogashira reactions had been the most powerful tools for C-C bond construction [1-7]. A mong t hese, t he S onogashira cross-coupling reaction was the most efficient m ethod t o c onnect s p-C to s p^2-C i n t he s ynthesis o f diaryl alkynes and areneethynylene polymers due to the simplicity of the reaction process [8-18]. T hese compounds had caught much attention r ecently i n t he f ields of bi oactive compounds a nd functional m aterials [19-22]. Historically, the Sonogashira reaction utilized terminal acetylene, usually obtained from protected acetylene, as a sp-C s ource, a nd l ater, acetylene gas has also been used [8-18, 23-26]. Acetylene gas is appreciably more e conomical t han t he terminal acetylenes for the synthesis of symmetrical diaryl ethyne that can be accomplished within one step. Due t o c omplicated h andling a nd c lose a ttention r equired f or a n a pplication of h ighly f lammable a cetylene g as, t he t hree-step s ynthesis o f d iaryl ethynes from terminal acetylene is currently a more favorable route. Recently, a number of reports demonstrated the use of inexpensive and readily available calcium carbide, as the acetylene surrogate in the preparation of carbon nanotubes [27], poly-ynes [28], and aryltriazoles [29]. The u tilization of c alcium c arbide f or P d-catalyzed coupling reaction was pioneered by Zhang [30] using aryl bromides for p reparation o f s ymmetrical d iaryl ethynes. E ven t hough i t w as t he f irst report on the u se o f c alcium c arbide f or t he s ynthesis o f d iaryl alkynes, a n on-commercially available amino phosphine ligand and elevated reaction temperature were required to obtain reasonable yields of the desired products. We found that this inspiring work worth further exploring as a general and economical s ynthetic a pproach f or s ymmetrical d iary l ethynes. Thus, this w ork a ims to develop a convenient synthetic method for symmetrical diaryl ethynes from c alcium c arbide a nd a ryl i odides in m ild c ondition using commercially available and inexpensive reagents. Furthermore, variety of functionalized aryl iodides are being tested in t he r eport.

1.2 Introduction to calcium carbide

Calcium c arbide (CaC_2) i s a f lammable s olid t hat w as f ound since 1888. It is easily generated from h eating low-price lime (CaO) and c oke (C) at 2000 $^{\circ}$C (Scheme 1.1a). Due t o its inexpensive price and domestically available, it has been widely used, mainly for producing a cetylene g as or c alcium c yanamide [31-32] (Scheme 1.1b, 1.1c), and others such as incubation of agricultural p roducts [33], pr oducing of P VC [34-35], u se as a l ow-priced fuel, a nd u se i n c hemical synthesis [27-29, 36]. The p ure m aterial o f c alcium c arbide i s colorless; however t he t echnical g rade c alcium c arbide i s grey or brown and consists of only 80-85% of CaC_2, and the rest are CaO, Ca_3P_2, CaS, Ca_3N_2, SiC, PH_3, NH_3, and H_2S [31].

$$CaO + 3C \xrightarrow{\triangle} CaC_2 + CO \quad\text{-----------}\quad (a)$$

$$CaC_2 \xrightarrow{hydrolysis} C_2H_2 + CaO \quad\text{-----------}\quad (b)$$

$$CaC_2 + N_2 \longrightarrow CaCN_2 + C \quad\text{----------}\quad (c)$$

Scheme 1.1 a) production of c alcium carbide, b) hydrolysis of c alcium carbide, c) production of calcium cyanamide

1.3 Introduction to diaryl ethynes

Diaryl ethynes have caught much attention recently in the fields of bioactive compounds and functional m aterials [19-22]. Synthetically, there are two processes for preparing diaryl alkyne (Scheme 1.2) [8-18, 23 -26]. The f irst o ne i nvolves t he u tilization o f a cetylene g as to serve a s C -C t riple bon d. T his on e pot r oute can synthesize diaryl ethynes efficiently in m ild conditions. I n a ddition, t he r eaction g ives e xcellent y ields f rom b oth e lectron r ich a nd electron poor a ryl i odides. However, t he a pplication o f a cetylene g as i n t he r eal reaction set up for lab work and industrial work are complicated, r equired e xpensive r eactor, a nd n eed close attention due to the h ighly f lammable p roperty o f a cetylene g as. T he s econd p rocess involve three-step s ynthesis o f d iaryl a lkynes, involving coupling r eaction, de protection a nd coupling reaction, w hich i s commonly u sed i n l aboratory w orks. The t hree s tep s ynthesis results in a lower of overall yields and difficulty in purification of product from byproducts [12, 16, 25, 26]. Recently, the synthesis through protected acetylene has been developed to a one pot procedure, but the r eaction s till n eed e xpensive p rotected a cetylene s uch a s trimethysilyl acetylene and 2-methyl-3-butyn-2-ol, a nd p roduct y ields a re b etween m oderated to high yields [12, 16].
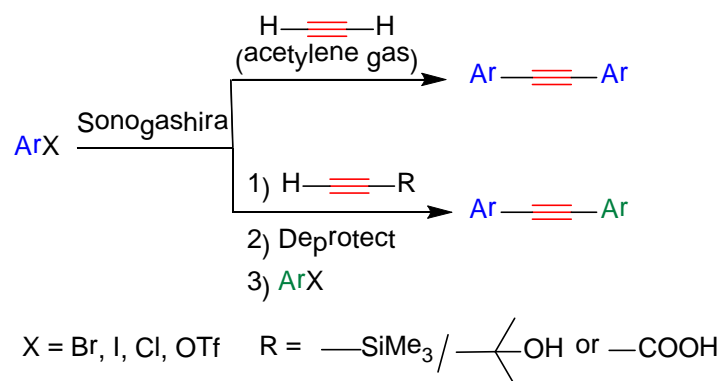
Scheme 1.2 Typical methods for synthesis of diarly ethynes

Furthermore, calcium carbide is reported to be an acetylene sources in the synthesis of diaryl ethynes (Scheme 1.3). The reaction required noncommercial aminophosphine ligand to give high yields on electron-rich aryl bromides, but very low yield or no reaction in the case of electron-deficient aryl iodides [30].
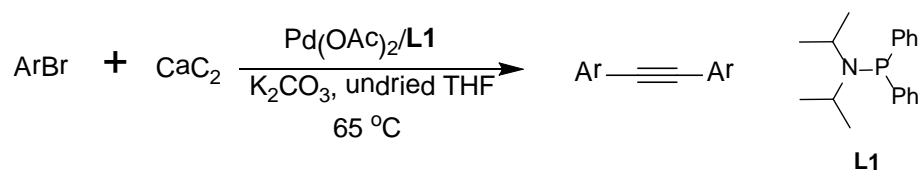
Scheme 1.3 The previous use of calcium carbide in diaryl ethynes synthesis

The major reaction used in the synthesis of diaryl ethynes is the Sonogashira coupling reaction. Sonogashira coupling is the palladium catalyzed sp^2-sp coupling reaction between aryl halides and terminal alkynes with or without copper(I) co-catalyst (Scheme 1.4) that was discovered by Kenkichi Sonogashira in 1975 [5].

X = Cl, Br, I, OTf
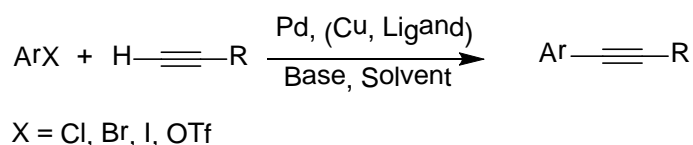
Scheme 1.4 General Scheme of Sonogashira coupling

The exact mechanism for this type of coupling is still in an open discussion [8]. However, it is believed to take place through two independent catalytic cycles shown in Scheme 1.5, where a tertiary amine is represented as base, with other amines or inorganic bases performing similarly. The reaction start with oxidative addition of palladium(0) to palladium(II) species (Pd-cycle). Then it connects with the Cu-cycle through the

transmetalation with copper acetylides, and followed by reductive elimination to diarylethyne and regeneration of palladium(0) catalyst. Copper is believed to involve in formation of copper acetylide, because amine is generally not basic enough to deprotonate the alkyne in order to generate the anionic nucleophile.
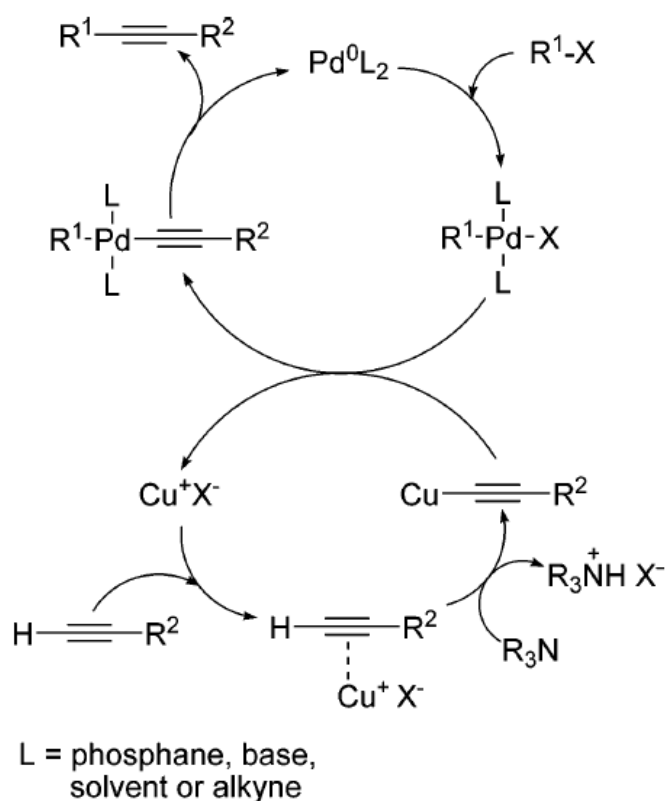
Scheme 1.5 Mechanism of Sonogashira coupling

1.4 Literature reviews

1.4.1   Synthesis of diaryl ethynes from acetylene gas

Acetylene gas is an economic reagent to insert the alkyne to target organic molecules. The synthesis of diaryl ethynes from acetylene gas is generally an effective reaction resulted in good yields of product and high compatibility of aryl halides tarting materials. However, the dangerous gas involved reaction is not favored in both laboratory and industry work.

In 1995, Pal and Kundu developed the use of acetylene gas for diaryl ethynes synthesis (Scheme 1.6) [24]. Varieties of diaryl ethynes have been coupled in moderate to good yields in mild condition using DMF as a solvent. The selectivity of this reaction could be controlled by switching from DMF to chloroform and using continuous flow of acetylene gas. Aryl

acetylenes (**3**) have been isolated from the c rude m ixture in 2 0-30% y ields. Chloroform slowed reaction rate along with large excess amount of acetylene gas supported by the formation of aryl acetylenes (**3**), diaryl e thynes (**2**) still major products, however.
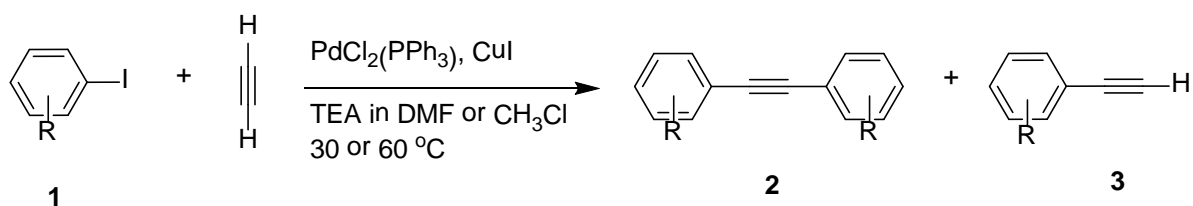
Scheme 1.6 Synthesis of diaryl ethynes from a ryl halides and acetylene g as.

In 1997, L i a nd c o-workers demonstrated the convenient synthesis of diaryl ethynes having v arious s ubstituents f rom Sonogashira coupling reaction between aryl halides and ethylene gas i n a m ixture o f acetonitrile and w ater (Scheme 1.7) [23]. The desired products diaryl e thynes were obtained in fair to good yield.
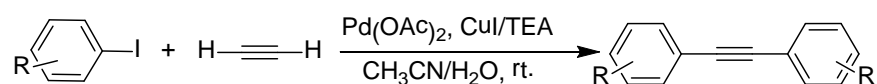

Scheme 1.7 Synthesis of diaryl ethynes from a ryl halides and acetylene g as.

In 2010, Yum and co-workers reported synthesis of diaryl ethynes from acetylene gas over n ano-sized c arbon ba ll s upported pa lladium catalyst (Scheme 1.8) [37]. This catalyst works w ell f or a variety o f a ryl i odides i n m ild c onditions; especially for 4-iodophenol which is known to be difficult substrate for this type of coupling. The catalyst also showed high degree of reusability and considerable to be used in a variety of organic reactions.
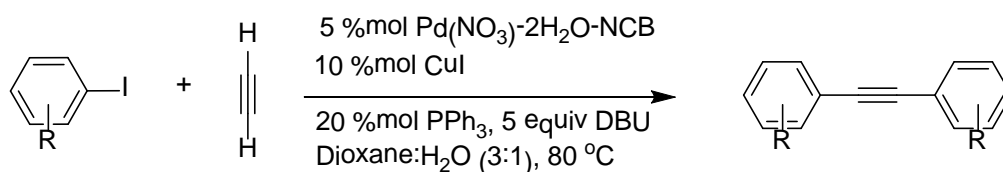
Scheme 1.8 Synthesis of diaryl ethynes from a ryl halides and acetylene g as.

1.4.2   Synthesis of diaryl ethynes from protected acetylene

Protected acetylene is preferred route to the synthesis of diaryl e thynes in l aboratory. The three-step synthesis results in a lower overall yield, even the improved one-pot procedure still g ives diaryl ethynes in moderate yield together with formation o f byproduct that is difficult to separated. However, this process provides the solution to prepare the

unsymmetrical diarylethylenes, which is hardly prepared under acetylene gas. The below is the highlighted examples describing the synthesis of unsymmetrical diaryl ethynes.

In 2002, Mio and co-workers reported the synthesis of symmetrical and unsymmetrical diaryl ethynes in one-pot using combination of DBU as base and a substoichiometric amount of water which is critical to the mediated the reaction (Scheme 1.9) [16]. Aryl halides were couple with trimethysilyl acetylene resulting in monodiarylethylene which underwent desilylation with water and DBU. The resulting alkyne intermediate reacted with other aryl halide to form 22 symmetrical diaryl ethynes and 8 unsymmetrical diaryl ethynes in 48% to 99% yields.
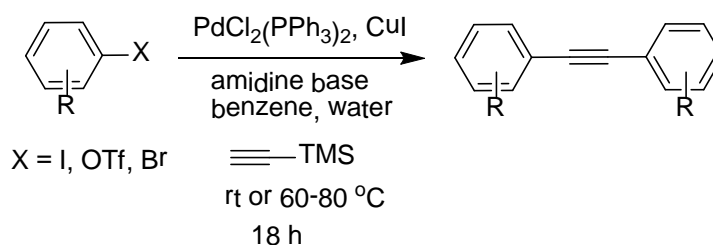
Scheme 1.9 Synthesis of diaryl ethynes through trimethysilyl acetylene.

Later in 2004, Novak and co-workers showed the one-pot synthesis of unsymmetrical diarly ethynes (Scheme 1.10) [12]. Aryl halides were coupled first with 2-methyl-3-butyn-2-ol (**4**) and the coupling products were further reacted with other aryl halides in the presence of strong base. This method p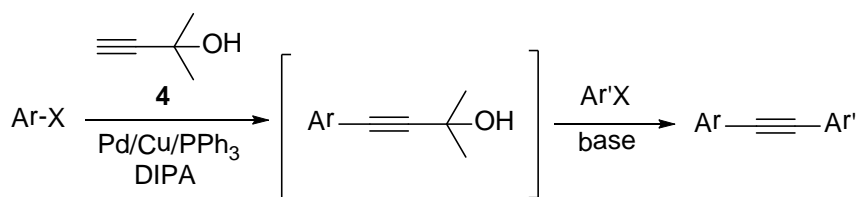rovides the convenience route for synthesis of unsymmetrical diarly ethynes. Twenty different diaryl ethynes were synthesized in 17% to 84% yields.

Scheme 1.10 Synthesis of diaryl ethynes through 2-methyl-3-butyn-2-ol.

In 2008, the same research group developed the use of 1-ethynyl-cyclohexanol as an acetylene surrogate in the synthesis of diaryl ethynes via Sonogashira coupling (Scheme 1.11) [26]. This reagent can be used either in a sequential manner or in a one-pot procedure to synthesize diaryl ethynes. In comparison with **4**, this reagent is more efficient giving higher reaction yields and wider generality. More than 40 substrates were tested and the corresponding diaryl ethynes were synthesized in 24% to 95% yields.

Later in 2005, Cataldo reported the synthesis of polyynes from calcium carbide in ammonium chloride solution (Scheme 1.14) [28]. The reaction resulted in high concentration of polyynes, mainly C_6H_2 or C_8H_2. The reaction started with the hydrolysis of calcium carbide to acetylene gas, which was reacted with cuprous ion to form copper acetylide and immediately oxidized by cupric ion or oxygen to afford polyynes.

$$CaC_2 \xrightarrow[\text{NH}_4\text{Cl}_{(aq)}]{\text{Cu}^+,\ \text{Cu}^{2+}} \text{Polyynes}$$
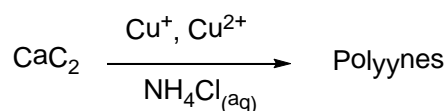
Scheme 1.14 The synthesis of polyynes from calcium carbide.
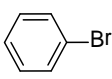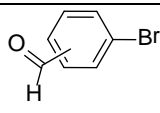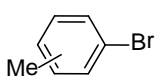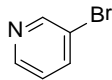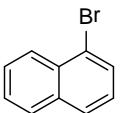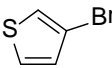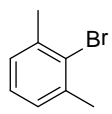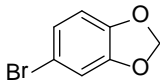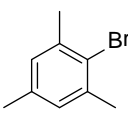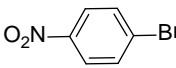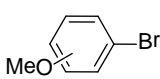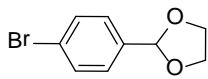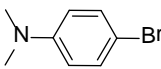
In 2009, Jiang and co-workers were successfully prepared aryltriazoles (**7**) and related compounds directly from calcium carbide with the corresponding azide via click chemistry as shown in Scheme 1.15 [29]. This is the first report in calcium carbide participated in 1, 3-dipolarcycloaddition by copper catalyst in MeCN-H$_2$O mixture. The yields ranged from moderate to excellent yields.

$$\text{Ar}-\text{N}_3 + CaC_2 \xrightarrow[\text{MeCN-H}_2\text{O}]{\text{Cu(I), Na ascorbate}} \text{Ar}-\text{N} \begin{smallmatrix} N \diagdown N \\ \diagdown \diagdown \end{smallmatrix}$$

7
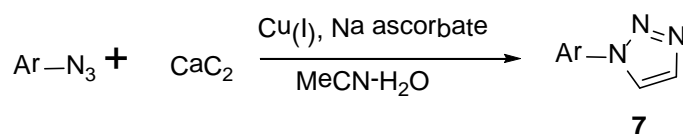
Scheme 1.15 The use of calcium carbide in Click chemistry.

In 2006, Zhang reported the synthesis of diaryl ethynes via copper free Pd-catalyzed coupling reaction of aryl bromides from calcium carbide (Table 1.1) [30]. The reaction gave moderate to high yields for aryl bromide containing electron-donating substituents (Table 1.1 entries 3, 6). The steric hindrance effects the reaction slightly as shown in Table 1.1 entries 2, 4, 5. The author described that sulfur could coordinated to palladium atom resulted in decreasing of yield on 3-bromothiophene (entry 12). The aryl bromide containing electron-withdrawing substituents such as 4-bromobenzaldehyde and 3-bromobenzaldehyde afforded the product in lower yields 14% and 56% respectively. No reaction took place in the case of 1-bromo-4-nitrobenzene (entries 10, 14). This hypothesis was confirmed when the carbonyl group in 4-bromobenzaldehyde was protected by ethylene glycol, the product yield dramatically increased to 56% (entry 15).

Table 1.1 synthesis of diaryl ethynes from calcium carbide in the presence of ligand L1
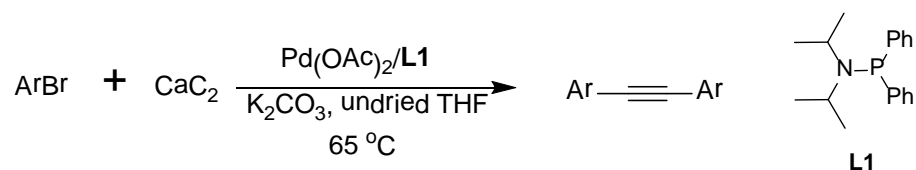
entry	aryl bromide	yield(%)[b]	entry	aryl bromide	yield(%)[b]
1		83	10		*p, 14* *m, 56*
2		*p, 78* *m, 76* *o, 75*	11		72
3		97	12		44
4		69	13		56
5		62	14		N.R.
6		*p, 79* *m, 67*	15		56
7		65			

[a] General conditions: a mixture of aryl bromide (2 mmol), CaC_2 (4 mmol), $Pd(OAc)_2$ (0.05 mmol), **L1** (0.15 mmol), and K_2CO_3 (4 mmol) in 5 mL of undried THF was stirred at 65 °C for 12 hours.

Although, this was the first report on the use of calcium carbide for synthesizing diaryl alkynes, the requirement for amino phosphine ligand is inconvenient in laboratory and industry because the compound is not commercially available and required multistep synthesis. Furthermore, this condition works only with electron-rich aryl bromide at high temperature, while electron-poor species were reported in low to zero percent yields.

1.5 Objective of this Research

From the literature reviewed above, there was no report that has the combination of mild condition, cost-effective, wide range of substrate compatibility, and easy reaction set up and purification of product in the synthesis of diaryl ethynes. Calcium carbide has a very good potential for that challenge, since it's the most low-price material, and it's reported to be used in place of acetylene gas. Thus, this work aim to use calcium carbide as an acetylene source in the synthesis of diaryl ethynes, focusing on milder condition, using low-price commercial available reagents to synthesize symmetrical diaryl ethynes. This work is going to study the reaction optimization based on effects of palladium sources, copper sources, catalyst loading, bases, solvents, addition methods, and effects of water.

CHAPTER II

EXPERIMENTAL

Unless otherwise indicated, all starting materials were obtained from commercial suppliers, and were used without further purification. Analytical thin-layer chromatography (TLC) was performed on Kieselgel F-254 pre-coated plastic TLC plates from EM Science. Visualization was performed with a 254 nm ultraviolet lamp. Silica gel column chromatography was carried out with silica gel (60, 230-400 mesh) from ICN Silitech. The ^{1}H and ^{13}C NMR spectra were recorded on a Varian or Bruker 400 MHz for ^{1}H NMR and 100 MHz for ^{13}C NMR in CDCl$_3$, (CD$_3$)$_2$SO or (CD$_3$)$_2$CO. ^{1}H and ^{13}C NMR chemical shifts were referenced to CDCl$_3$ (δ 7.26 for ^{1}H, δ 77.00 for ^{13}C), (CD$_3$)$_2$SO (δ 39.43 for ^{13}C) or (CD$_3$)$_2$CO (δ 2.09 for ^{1}H, δ 30.60 for ^{13}C). Coupling constants (J) are reported in Hertz (Hz). Splitting patterns are designated as s (singlet), d (doublet), t (triple), q (quartet), bs (broad singlet), m (multiplet).

2.1 Initial observation

Table 3.1 Initial observation using 4-bromoanisole: A 100 mL round bottom flask with a magnetic stir bar was charged with 200.0 mg of 4-bromoanisole (2 or 1 equiv), calcium carbide (1 or 3 equiv), copper iodide (0.025 equiv), palladium sources (0.05 equiv), and triphenylphosphine (0.05 equiv) in 4 mL of solvents. The solution was degassed with nitrogen for 20 minutes. Then, base (equiv equals to calcium carbide) were added. The mixture was stirred at room temperature or reflux condition for 12-20 hrs. The reaction mixture was then filtrated through a filter paper and washed with dichloromethane. The filtered was evaporated under vacuum and separated by column chromatography using 5 % EtOAc in hexane as the eluent to give 1,2-bis(4-methoxyphenyl)ethyne (**2f**) in a trace amount or 8% yield.

phenyl 4-methylbenzenesulfonate: phenol 300.0 mg (3.19 mmol), 4-toluenesulfonyl chloride (2.9 mmol), and potassium carbonate (5.8 mmol) were charge in an 150 mL Erlenmeyer flask. The flask was heated with heat gun while shaking it by hand, until all of the phenol is melted and the compounds were mixed. The reaction mixture was irradiated with 250 MW for 5 min. After cooling to room temperature, the remaining mixture was dissolved in 10 mL of water and stirred for several minutes. The pure product was easily obtained by filtration, wash with a

0.1 N aqueous sodium hydroxide solution, water, and dried in vacuum to afford 619.0 mg (2.5 mmol, 86%) of phenyl 4-methylbenzenesulfonate as a white solid. ^{1}H NMR (400 MHz, *CDCl₃*): δ ppm 7.73 (2H, d, *J* = 7.8 Hz), 7.27-7.34 (5H, m), 7.01 (2H, d, *J* = 7.3 Hz), 2.47 (3H, s).

phenyl trifluoromethanesulfonate: A solution of trifluoromethanesulfonic anhydride (456 μL, 2.7 mmol) in CH_2Cl_2 (5 mL) was added drop wise to a solution of pyridine (369 μL, 4.6 mmol) and the phenol (500.0 mg, 2.3 mmol) in anhydrous CH_2Cl_2 (5 mL) at 0 °C. After complete addition, the mixture was warmed to room temperature and allowed to stir for 1 hour. The mixture was then diluted with ether, quenched with 10% aq HCl and washed successively with sat. $NaHCO_3$, and brine. After drying (anhydrous $NaSO_4$), the solvent was removed under reduced pressure and the residue was purified by Kugelrohr distillation to give the phenyl triflates 95% yield as a clear liquid. ^{1}H NMR (400 MHz, *CDCl₃*): δ ppm 7.43-7.50 (2H, m), 7.43-7.36 (1H, m), 7.25-7.31 (2H, m)**.**

Table 3.2 Screened reactions for types of aryl compounds: A 100 mL round bottom flask with a magnetic stir bar was charged with 200.0 mg of phenyl derivatives (1 equiv), calcium carbide (3 equiv), copper iodide (0.05 equiv), palladium acetate (0.025 equiv), and triphenylphosphine (0.05 equiv) in 4 mL of acetonitrile. The solution was degassed with nitrogen for 20 minutes. Then, triethylamine (3 equiv) were added. The mixture was stirred at room temperature 10 h. The reaction mixture was then filtered through a filter paper and washed with dichloromethane. The filtrate was evaporated under vacuum and separated by column chromatography. In the case of bromobenzene and phenyl triflate, trace amount of diphenylacetylene was produce, small amount of aryl starting materials were recover, while the complex mixtures were mainly formed. For phenyl tosylated, 90% of phenyl tosylated was recovered, and trace amount of product was observed.

2.2 Synthesis of aryl iodides

Synthesis of 4-iodotoluene (1b) and 2-iodotolune (1d) from iodinemonochloride; ICl (1.09 mL, 21.7 mmol) was added dropwise to a solution of 20 mL dichloromethane and toluene (1.15 mL, 10.9 mmol) below 15 °C in a 100 mL round bottom flask equipped with a magnetic stir bar. After the addition, the reaction was then heated under refluxing conditions for 4 h and allowed to cool to room temperature. The solvent was evaporated and the residue was extracted

with CH_2Cl_2 (50 mL × 2). The combined organic phase was washed with a saturated solution of $Na_2S_2O_3$ until the brown color disappeared. The resulting solution was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure to give 4-iodotoluene and 2-iodotolune in 1:1 ratio in the total of 70% yield.

Synthesis of 4-iodotoluene (1b) from 4-toluidine: A 500 mL round bottom flask with a magnetic stir bar was charged with 4-toluidine (10,000.0 mg, 93.5 mmol), 10 M H_2SO_4 (1.3 mol), and cool to 0 °C. Then 4 M $NaNO_2$ (102 mmol) solution was added dropwise to the reaction. After stir the reaction for 1 hour KI 4 M (140 mmol) was added, and stir at 0 °C for 30 minutes. The reaction then allowed to cool to room temperature, and stir for further 15 minutes. The reaction was extracted with CH_2Cl_2 (200 mL × 3). The combined organic phase was washed with a saturated solution of $Na_2S_2O_3$ until the brown color disappeared. The resulting solution was dried over anhydrous Na_2SO_4, and filtered. The solvent was removed under reduced pressure and the residue was purified by passing through a short plug of silica gel using hexane as an eluent to afford 4-iodotoluene **1b** in 72% yield as a white solid. ^{1}H NMR (400 MHz, *CDCl₃*): δ ppm 7.56 (2H, d, *J* = 7.3 Hz), 6.93 (2H, d, *J* = 7.8 Hz), 2.29 (3H, s).

Synthesis of 2-iodotoluene (1d) from 2-toluidine: A 100 mL round bottom flask with a magnetic stir bar was charged with 2-toluidine (1,000.0 mg, 9.35 mmol), 10 M H_2SO_4 (130 mmol), and cool to 0 °C. Then 4 M $NaNO_2$ (10.2 mmol) solution was added dropwise to the reaction. After stir the reaction for 1 hour KI 4 M (14.0 mmol) was added, and stir at 0 °C for 30 minutes. The reaction then allowed to cool to room temperature, and stir for further 15 minutes. The reaction was extracted with CH_2Cl_2 (50 mL × 3). The combined organic phase was washed with a saturated solution of $Na_2S_2O_3$ until the brown color disappeared. The resulting solution was dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to afford 2-iodotoluene **1d** in 63% yield as a clear liquid. ^{1}H NMR (400 MHz, *CDCl3*): δ ppm 7.81 (1H, d, *J* = 7.8 Hz), 7.23 (2H, t, *J* = 6.3 Hz), 6.91 -6.82 (1H, m), 2.43 (3 H, s).

(4-iodophenyl)methanol (1i): A 100 mL round bottom flask equipped with a magnetic stir bar was charged with 4 -iodobenzoic acid (2500.0 mg, 10.1 mmol) and 20 mL tetrahydrofuran under nitrogen atmosphere. Then, 1 M borane tetrahydrofuran complex solution was slowly added to the solution, and the reaction was stirred for 16 hours. The reaction was

extracted with 2 N HCl, CH₂Cl₂, NaHCO₃, and brine. The organic layer was separated, dried over anhydrous Na₂SO₄, and filtered. The solvent was removed under reduced pressure and the residue was purified by column chromatography using 20% EtOAc in hexane as the eluent to afford (4-iodophenyl)methanol **1i** in 64% yield as a white solid. ¹H NMR (400 MHz, *CDCl₃*): δ ppm 7.69 (2H, d, *J* = 8.4 Hz), 7.12 (2H, d, *J* = 8.4 Hz), 4.65 (2H, d, *J* = 5.6 Hz)

1-iodo-4-(methoxymethyl)benzene (1h): A 100 mL round bottom flask with a magnetic stir bar was charged with (4-iodophenyl)methanol **1i** (300.0 mg, 1.37 mmol), NaH (1.65 mmol), and MeI (2.74 mmol) in 15 mL THF, and heated at 70 °C for overnight. TLC indicated remaining of (4-iodophenyl)methanol, so MeI (6.85 mmol) was further added, and stirred for another night. The reaction was quenched with methanol, extract with water, dichloromethane, brine, The organic layer was filtered, and concentrated under reduced pressure to give 1-iodo-4-(methoxymethyl)benzene **1h** in 75% yield as a white solid. ¹H NMR (400 MHz, *CDCl₃*): δ ppm 7.68 (2H, d, *J* = 7.6 Hz), 7.08 (2H, d, *J* = 7.6 Hz), 4.40 (2H, s), 3.38 (3H, s).

4-iodo-N,N-dimethylaniline (1l): *N*, *N*-dimethylaniline (5,000.0 g, 0.041 mol) was dissolved in dioxane (40 mL) and pyridine (40 mL) and the solution was cooled to 0 °C. Then, I₂ (2090.0 g, 0.17 mol) was added. The solution progressively took a dark brown color. After 1 h, the ice bath was removed. The solution was further stirred for 3 h at room temperature, the resulting dark brown mixture was extracted with CH₂Cl₂ (3 × 50 mL). The combined extracts were washed with a saturated solution of Na₂S₂O₃. The organic phase was dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. The crude product was purified by recrystallization from methanol and water to give **1l** as a flaky colorless solid (7,500.0 g, 73%). ¹H NMR (400 MHz, *CDCl₃*): δ ppm 7.47 (2H, d, *J* = 8.9 Hz), 6.51 (2H, d, *J* = 7.4 Hz), 2.92 (6H, s).

4-iodobenzaldehyde (1o): A 100 mL round bottom flask with a magnetic stir bar was charged with oxalyl dichloride (5.8 mmol) in 10 mL of CH₂Cl₂, and cooled to -78 °C with dry ice and acetone bath. Then, the solution of DMSO (11.0 mmol) in 2 mL of CH₂Cl₂ was slowly added to the reaction. After stirred the reaction at -78 °C for 20 minutes, the reaction temperature was changed to -50 to -60 °C, and the solution of (4-iodophenyl)methanol **1i** (300.0 mg, 3.65 mmol) in 8 mL of CH₂Cl₂ was slowly added to the reaction. Next, DIPEA (21.6 mmol) solution

in 1 mL of CH_2Cl_2 was added dropwise to the reaction, and stirred at -45 °C for 30 minutes, and stirred at 0 °C for additional 10 minutes. The reaction was quenched with cold 1 M HCl, and extract with CH_2Cl_2. The organic layer was separated, washed with brine, dried over anhydrous Na_2SO_4, and filtered. The solvent was removed under reduced pressure and the residue was purified by column chromatography using 30% EtOAc in hexane as the eluent to afford 4-iodobenzaldehyde **1o** in 59% yield as a yellow solid. ^{1}H NMR (400 MHz, *CDCl3*): δ ppm 9.96 (1 H, s), 7.92 (2H, d, *J* = 8.0 Hz), 7.59 (2H, d, *J* = 8.0 Hz).

N-(2-iodophenyl)acetamide (1p): A 100 mL round bottom flask with a magnetic stir bar was charged with *o*-iodoaniline (300.0 mg, 1.37 mmol) and DIPEA (1.37 mmol) in 15 mL THF, and heated to 60 °C. Then, acetic anhydride (2.0 mmol) was slowly added to the reaction, and stirred for 16 h. The reaction was extract with 1 N HCl and ethy acetate. The organic layer was separated, washed with brine, dried over anhydrous Na_2SO_4, and filtered. The solvent was removed under reduced pressure and the residue was purified by column chromatography using 30% EtOAc in hexane as the eluent to afford N-(2-iodophenyl)acetamide **1p** in 76% yield as a brown solid. ^{1}H NMR (400 MHz, *CDCl3*): δ ppm 8.20 (1H, d, J = 7.8 Hz), 7.77 (1H, d, *J* = 7.8 Hz), 7.42 (1H, s), 7.34 (1H, t, *J* = 7.8 Hz), 6.84 (1H, t, *J* = 7.6 Hz), 2.25 (3H, s).

methyl 4-iodobenzoate (1q): To a 250 mL round bottom flask containing methyl-4-iodobenzoic acid (5000.0 mg, 0.02 mol) and methanol (50 mL) was added concentrated sulfuric acid (1.07 mL, 0.02 mmol) slowly. The reaction mixture was heated under refluxing conditions for 24 h. The solvent was evaporated, and the residue was diluted with CH_2Cl_2 (50 mL) and $NaHCO_3$ (50 mL). The organic layer was separated and extracted with CH_2Cl_2 (25 mL × 2), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure to give methyl 4-iodobenzoate **1q** as a white solid (4.96 g, 94%). ^{1}H NMR (400 MHz, *CDCl3*): δ ppm 7.80 (2H, d, *J* = 8.5 Hz), 7.74 (2H, d, *J* = 8.5 Hz), 3.91 (3H, s). ^{13}C NMR (101 MHz, *CDCl3*): δ ppm 166.5, 137.7, 130.9, 129.6, 100.6, 52.2.

((4-iodophenyl)ethynyl)trimethylsilane (1t): A 100 mL round bottom flask with a magnetic stir bar was charged with diiodobenzene (2,000.0 g, 7.63 mmol), $PdCl_2(PPh_3)_2$ (26.7 mg, 0.038 mmol) and CuI (14.5 mg, 0.076 mmol) in PhMe (20 mL), and stirred in nitrogen balloon for 20 minutes. The DBU (1.26 mL, 8.39 mmol) was added slowly to the reaction, and

trimethylsilyl acetylene (1.18 mL, 8.39 mmol) was added in small portions and the mixture was stirred at room temperature for 4 h under N_2 atmosphere. The organic layer was separated and the residue was extracted with EtOAc (3 x 50 mL) and dried over anhydrous Na_2SO_4. The combined filtrate was evaporated and the residue was purified by column chromatography using hexane as the eluent to afford ((4-iodophenyl)ethynyl)trimethylsilane **1t** in 33% yield as a yellow solid, along with 15% recovery of diiodobenzene, and 22% of 1,4-bis((trimethylsilyl)ethynyl)benzene. ^{1}H NMR (400 MHz, *CDCl₃*): δ ppm 7.48 (2H, d, *J* = 8.5 Hz), 7.03 (2H, d, *J* = 8.5 Hz), 0.09 (9H, s).

4-iodophenyl 4-methylbenzenesulfonate (1u): 4-iodophenol 500.0 mg (2.27 mmol), *p*-toluenesulfonyl chloride (2.1 mmol), and potassium carbonate (4.1 mmol) were charge in an 150 mL Erlenmeyer flask. The reaction mixture was irradiated with 250 MW for 5 min. After cooling to room temperature, the remaining mixture was dissolved in 10 mL of water and stirred for several minutes. The pure product was easily obtained by filtration, wash with a 0.1 N aqueous sodium hydroxide solution, water, and then dried in vacuum to afford of 4-iodophenyl 4-methylbenzenesulfonate **1u** in a 63% yield as a white solid. : ^{1}H NMR (400 MHz, *CDCl₃*): δ ppm 7.70 (2H, d, *J* = 7.6 Hz), 7.60 (2H, d, *J* = 7.6 Hz) , 7.32 (2H, d, *J* = 7.6 Hz) 6.74 (2H, d, *J* = 7.6 Hz), 2.46 (3H, s).

2-iodopyridine (1k): A 100 mL round bottom flask with a magnetic stir bar was charged with 2-chloropyridine (300.0 mg, 2.6 mmol) and NaI (7.93 mmol) in 15 mL of MeCN, and cooled to 0 °C. Acetyl chloride (6.6 mmol) was slowly added to the reaction; followed by stirring at 80 °C for 24 h. The reaction was diluted with CH_2Cl_2 and extracted with 10% K_2CO_3, 5% Na_2SO_3, and $Na_2S_2O_8$, The organic layer was separated, filtered, and concentrated under reduced pressure to give 2-iodopyridine **1k** in 86% yield as a yellow liquid. ^{1}H NMR (400 MHz, *CDCl₃*): δ ppm 8.37 (1H, d, *J* = 4.1 Hz), 7.73 (1H, d, *J* = 7.8 Hz), 7.33 (1H, t, *J* = 7.8 Hz), 7.30-7.21 (1H, m).

2.3 Pd-catalyst coupling reaction using calcium carbide as a starting material.

2.3.1 Optimization conditions

Table 3.3 Optimization using 4-iodotoluene: A 100 mL round bottom flask with a magnetic stir bar was charged with 200.0 mg of 4-iodotoluene (1 equiv), calcium carbide (3 equiv), copper sources (0.05 equiv), palladium sources (0.025 equiv), and triphenylphosphine (0.05 equiv) in 5 mL of solvents. The solution was degassed with nitrogen for 20 minutes. Then, bases (3 equiv) were added. The mixture was stirred at room temperature for 12-20 hrs. The reaction mixture was then filtered through a filter paper and washed with dichloromethane. The filtrate was evaporated under vacuum and separated by column chromatography using hexane as the eluent to give 1,2-Di-4-tolylethyne in corresponding yields.

Table 3.4 Scale up to 200-600 mg with constant amount of catalysts: A 100 mL round bottom flask with a magnetic stir bar was charged with 200 to 600 mg of 4-iodotoluene (1 equiv), calcium carbide (3 equiv), copper sources (0.023 mmol), palladium sources (0.046 mmol), and triphenylphosphine (0.046 mmol) in 5 mL of MeCN. The solution was degassed with nitrogen for 20 minutes. Then, triethylamine (3 equiv) was added. The mixture was stirred at room temperature for 12-20 hrs. The reaction mixture was then filtered through a filter paper and washed with dichloromethane. The filtrate was evaporated under vacuum and the crudes were analyzed by NMR spectroscopy, or separated by column chromatography using hexane as the eluent to give 1,2-Di-4-tolylethyne in corresponding yields. The ratio of product: starting material refers to the ratio of 1,2-Di-4-tolylethyne:4-iodotoluene, by observing ratio of -CH$_3$ ^{1}H NMR of 1,2-Di-4-tolylethyne ^{1}H NMR (400 MHz, *CDCl$_3$*): δ 2.37 (6H, s); and 4-iodotoluene δ 2.29 (3H, s); in the crude mixture.

Table 3.5 Effect of catalysts loading: A 100 mL round bottom flask with a magnetic stir bar was charged with 100.0 mg of 4-iodotoluene (1 equiv), calcium carbide (3 equiv), copper iodide, palladium acetate, and triphenylphosphine in 3 mL of MeCN. The solution was degassed with nitrogen for 20 minutes. Then, triethylamine (3 equiv) was added. The mixture was stirred at room temperature for 12-20 hrs. The reaction mixture was then filtrated through a filter paper and washed with dichloromethane. The filtrate was evaporated under vacuum and the crudes were analyzed by NMR spectroscopy. The ratio of product: starting material refers to the ratio of

1,2-Di-4-tolylethyne:4-iodotoluene, by observing ratio of -CH$_3$ ^{1}H NMR of 1,2-Di-4-tolylethyne ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.37 (6H, s); and 4-iodotoluene δ 2.29 (3H, s); in the crude mixture.

Table 3.6 Final optimization conditions: A 100 mL round bottom flask with a magnetic stir bar was charged with copper sources (0.025 equiv), palladium sources (0.05 equiv), and triphenylphosphine (0.05 equiv) in 3 mL of solvents. The solution was degassed with nitrogen for 20 minutes. Then, bases (3 equiv), 4-iodotoluene (100.0 mg, 1 equiv), and calcium carbide (3 equiv) were added. The mixture was stirred at room temperature for 10 h. The reaction mixture was then filtered through a filter paper and washed with dichloromethane. The filtrate was evaporated under vacuum and separated by column chromatography using hexane as the eluent to give 1,2-Di-4-tolylethyne in corresponding yields.

2.3.2 Screening of aryl iodides and synthesis of oligo (phenyleneethynylenes)

General procedure for screening of aryl iodides and synthesis of oligo (phenyleneethynylenes): A 100 mL round bottom flask with a magnetic stir bar was charged with copper iodide (0.1 equiv), palladium acetate (0.05 equiv), and triphenylphosphine (0.1 equiv) in acetonitrile. The solution was degassed with nitrogen for 20 minutes. Then, triethylamine (3 equiv), aryl iodides (1 equiv), and calcium carbide (3 equiv) were added. The mixture was stirred at room temperature overnight. The reaction mixture was then filtered through a short plug of silica gel and washed with hexane. The filtrate was evaporated under vacuum to give the desired compounds.

1,2-Diphenylethyne (2a): Synthesized according to general procedure from iodobenzene (200.0 mg, 0.98 mmol), calcium carbide (188.5 mg, 2.94 mmol), copper iodide (18.7 mg, 0.098 mmol), palladium(II)acetate (11.0 mg, 0.049 mmol), triphenylphosphine (25.7 mg, 0.098 mmol), and triethylamine (297.6 mg, 2.94 mmol) to afford 83.9 mg (0.47 mmol, 96%) of **2a** as a white solid: mp 57–59 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 7.63-7.56 (4H, m), 7.43-7.35 (6H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 131.6, 128.3, 128.2, 123.2, 89.4; IR (neat, cm^{-1}) 3065, 3027.

1,2-Di-4-tolylethyne (2b): Synthesized according to general procedure from 4-iodotoluene (200.0 mg, 0.917 mmol), calcium carbide (176.4 mg, 2.75 mmol), copper iodide (17.5 mg, 0.092 mmol), palladium(II)acetate (10.3 mg, 0.046 mol), triphenylphosphine (24.0 mg, 0.092 mmol), and triethylamine (278.4 mg, 2.752 mmol) to afford 94.2 mg (0.456 mmol, 99.6%) of **2b** as a white solid: mp 135–139 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 7.42 (4H, d, J = 7.8 Hz), 7.15 (4H, d, J = 7.8 Hz), 2.37 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.1, 131.4, 129.1, 120.4, 88.9, 21.5; IR (neat, cm^{-1}) 3018, 2917, 2843.

1,2-Di-3-tolylethyne (2c): Synthesized according to general procedure from 3-iodotoluene (200.0 mg, 0.917 mmol), calcium carbide (176.4 mg, 2.75 mmol), copper iodide (17.5 mg, 0.092 mmol), palladium(II)acetate (10.3 mg, 0.046 mol), triphenylphosphine (24.0 mg, 0.092 mmol), and triethylamine (278.4 mg, 2.752 mmol) to afford 93.7 mg (0.454 mmol, 99.1%) of **2c** as a white solid: mp 71–73 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 7.36-7.33 (4H, m), 7.23 (2H, d, J = 7.6 Hz), 7.15 (2H, d, J = 7.6 Hz), 2.36 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.0, 132.2, 129.1, 128.7, 128.2, 123.2, 89.2, 21.3; IR (neat, cm^{-1}) 3050, 2917.

1,2-Di-2-tolylethyne (2d): Synthesized according to general procedure from 2-iodotoluene (200.0 mg, 0.917 mmol), calcium carbide (176.4 mg, 2.75 mmol), copper iodide (17.5 mg, 0.092 mmol), palladium(II)acetate (10.3 mg, 0.046 mol), triphenylphosphine (24.0 mg, 0.092 mmol), and triethylamine (278.4 mg, 2.752 mmol) to afford 91.2 mg (0.442 mmol, 96.4%) of **2d** as a brown liquid: ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 7.54-7.52 (2H, m), 7.27-7.19 (6H, m), 2.55 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.0, 131.9, 129.5, 128.2, 125.6, 123.3, 92.3, 21.0; IR (neat, cm^{-1}) 3056, 3009.

1,2-Di(naphthalen-1-yl)ethyne (2e): Synthesized according to general procedure from 1-iodonaphthalene (200.0 mg, 0.787 mmol), calcium carbide (151.4 mg, 2.36 mmol), copper iodide (15.0 mg, 0.079 mmol), palladium(II)acetate (8.8 mg, 0.039 mol), triphenylphosphine (20.6 mg, 0.079 mmol), and triethylamine (278.5 mg, 2.752 mmol) to afford 104.5 mg (0.376 mmol, 96.3%) of **2e** as a white solid: mp 117–119 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 8.62 (2H, d, J = 8.0 Hz), 7.92 (6H, m), 7.68 (2H, t, J = 7.6 Hz), 7.59 (2H, t, J = 7.4 Hz), 7.54 (2H, t J = 7.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 133.2, 130.6, 128.9, 128.4, 126.9, 126.5, 126.3, 125.3, 121.0, 92.4; IR (neat, cm^{-1}) 3056, 3009.

1,2-Bis(4-methoxyphenyl)ethyne (2f): Synthesized according to general procedure from 4-iodoanisole (200.0 mg, 0.855 mmol), calcium carbide (164.4 mg, 2.56 mmol), copper iodide (16.3 mg, 0.086 mmol), palladium(II)acetate (9.6 mg, 0.043 mol), triphenylphosphine (22.4 mg, 0.086 mmol), and triethylamine (278.3 mg, 2.56 mmol) to afford 98.1 mg (0.412 mmol, 96.4%) of **2f** as a white solid: mp 135–137 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 7.45 (4H, d, $J = 8.8$ Hz), 6.87 (4H, d, $J = 8.8$ Hz), 3.83 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.4, 132.9, 115.7, 114.0, 87.9, 55.3; IR (neat, cm^{-1}) 3000, 2968, 2832.

4,4'-(Ethyne-1,2-diyl)diphenol (2g): Synthesized according to general procedure from 4-iodophenol (200.0 mg, 0.91 mmol), calcium carbide (174.8 mg, 2.73 mmol), copper iodide (17.3 mg, 0.091 mmol), palladium(II)acetate (10.2 mg, 0.045 mol), triphenylphosphine (23.0 mg, 0.091 mmol), and triethylamine (275.9 mg, 2.73 mmol) to afford 76.4 mg (0.364 mmol, 80.4%) of **2g** as a brown solid: ^{1}H NMR (400 MHz, $(CD_3)_2CO$): δ ppm 8.76 (2H, s), 7.31 (4H, d, $J = 8.4$ Hz), 6.81 (4H, d, $J = 8.4$ Hz); ^{13}C NMR (100 MHz, $(CD_3)_2CO$): δ 159.4, 134.6, 117.4, 116.5, 89.4

1,2-Bis(4-(methoxymethyl)phenyl)ethyne (2h): Synthesized according to general procedure from 1-iodo-4-(methoxymethyl)benzene (200.0 mg, 0.86 mmol), calcium carbide (165.0 mg, 2.57 mmol), copper iodide (16.4 mg, 0.086 mmol), palladium(II)acetate (9.6 mg, 0.043 mol), triphenylphosphine (22.5 mg, 0.086 mmol), and triethylamine (260.6 mg, 2.57 mmol) to afford 101.1 mg (0.428 mmol, 99.8%) of **2h** as a white solid: mp 59–61 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 7.52 (4H, d, $J = 7.7$ Hz), 7.32 (4H, d, $J = 7.7$ Hz), 4.47 (4H, s), 3.40 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.4, 132.5, 131.6, 127.5, 122.4, 89.2, 74.2, 58.1; IR (neat, cm^{-1}) 3003, 2923, 2864.

(4,4'-(Ethyne-1,2-diyl)bis(4,1-phenylene))dimethanol (2i): Synthesized according to general procedure from (4-iodophenyl)methanol (200.0 mg, 0.855 mmol), calcium carbide (164.4 mg, 2.56 mmol), copper iodide (16.3 mg, 0.086 mmol), palladium(II)acetate (9.6 mg, 0.043 mol), triphenylphosphine (22.4 mg, 0.086 mmol), and triethylamine (259.5 mg, 2.56 mmol) and purified by flash chromatography to afford 41.6 mg (0.175 mmol, 40.8%) of **2i** as a brown solid: ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 7.53 (4H, d, $J = 8.4$ Hz), 7.35 (4H, d, $J = 8.4$

Hz), 4.72 (4H, s), 3.41 (1H, s); ^{13}C NMR (100 MHz, $(CD_3)_2SO$): δ 143.4, 132.6, 131.5, 127.1, 127.1, 120.9, 89.4, 62.9

1,2-Di(thiophen-2-yl)ethyne (2m): Synthesized according to general procedure from 2-iodothiophene (200.0 mg, 0.952 m mol), c alcium c arbide (183.0 mg, 2.86 m mol), c opper iodide (18.2 mg, 0.095 mmol), palladium(II)acetate (10.7 mg, 0.048 mol), triphenylphosphine (25.0 mg, 0.095 mmol), and triethylamine (289.1 mg, 2.86 mmol) to afford 89.6 mg (0.472 mmol, 99.6%) of **2m** as a w hite s olid: mp 96–97 °C; ^{1}H N MR (400 M Hz, $CDCl_3$): δ ppm 7.33-7.26 (4H, m), 7.05-6.99 (2H, m); ^{13}C N MR (100 MHz, $CDCl_3$): δ 132.1, 127.6, 127.1, 122.9, 86.2 ; IR (neat, cm^{-1}) 3101, 3080.

1,1'-(4,4'-(Ethyne-1,2-diyl)bis(4,1-phenylene))diethanone (2n): Synthesized according to general procedure f rom 1-(4-iodophenyl)ethanone (200.0 mg, 0.81 3 m mol), c alcium c arbide (156.3 mg, 2.44 mmol), copper iodide (11.6 mg, 0.081 mmol), palladium(II)acetate (9.1 mg, 0.041 mol), triphenylphosphine (23.3 mg, 0.081 mmol), and triethylamine (246.8 mg, 2.44 mmol) t o a fford 105.0 m g (0.400 mmol, 98.6%) of **2n** as a w hite s olid: ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 7.96 (4H, d, J = 8.3 Hz), 7.63 (4H, d, J = 8.3 Hz), 2.62 (6H, s); ^{13}C NMR (101 MHz, $CDCl_3$): δ 197.2, 136.6, 131.9, 128.3, 127.46, 91.6, 26.6

4,4'-(Ethyne-1,2-diyl)dibenzaldehyde (2o): Synthesized according to general procedure f rom 4-iodobenzaldehyde (200.0 mg, 0.858 mmol), calcium carbide (165.1 mg, 2.57 mmol), copper iodide (16.4 m g, 0.086 m mol), pa lladium(II)acetate (9.6 m g, 0.043 m ol), triphenylphosphine (22.5 mg, 0.086 mmol), and triethylamine (261.4 mg, 2.57 mmol) to a fford 87.7 mg (0.372 m mol, 86.7%) of **2o** as a y ellow s olid: ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 10.04 (1H, s), 7.90 (2H, d, J = 8.4 Hz), 7.71 (2H, d, J = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.3, 135.9, 132.3, 129.6, 128.7, 92.1; IR (neat, cm^{-1}) 3080, 1687.

N,N'-(4,4'-(Ethyne-1,2-diyl)bis(4,1-phenylene))diacetamide (2p): Synthesized according to general procedure from N-(2-iodophenyl)acetamide (200.0 mg, 0.766 mmol), calcium carbide (147.3 mg, 2.36 mmol), copper iodide (14.6 mg, 0.077 mmol), palladium(II)acetate (8.6 mg, 0.034 m ol), t riphenylphosphine (20.1 m g, 0.077 m mol), a nd triethylamine (232.6 mg, 2.36 m mol) t o a fford 105.7 m g (0.362 m mol, 94.5 %) of **2p** as a brown solid: : mp 240–242 °C; ^{1}H N MR (400 M Hz, $CDCl_3$): δ ppm 8.31 (2H, d, J = 8.2 Hz), 7.90

(2H, s), 7.50 (2H, d, J = 7.5 Hz), 7.41 (2H, t, J = 7.9 Hz), 7.13 (2H, t, J = 7.5 Hz), 2.25 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.5, 139.0, 132.0, 130.4, 123.92, 120.5, 91.1, 24.8 ; IR (neat, cm^{-1}) 3293, 2959, 2920, 1729; HRMS (ESI) Cacld for $C_{18}H_{16}N_2O_2Na$, 315.1104; Found, 315.1107.

Dimethyl 4,4'-(ethyne-1,2-diyl)dibenzoate (2q): Synthesized according to general procedure f rom 4-iodobenzoate (200.0 mg, 0.76 mmol), calcium carbide (146.8 mg, 2.29 mmol), copper iodide (14.5 m g, 0.076 m mol), pa lladium(II)acetate (8.6 m g, 0.038 m ol), triphenylphosphine (20.0 mg, 0.076 mmol), and triethylamine (230.9 mg, 2.29 mmol) to a fford 83.2 mg (0.278 m mol, 73.8%) of **2q** as a br own solid: : mp 220–222 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 8.03 (4H, d, J = 8.2 Hz), 7.60 (4H, d, J = 8.2 Hz), 3.93 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.4, 131.6, 130.0, 129.6, 127.4, 91.4, 52.3; IR (neat, cm^{-1}) 3012, 2959, 1711.

1,2-Bis(4-nitrophenyl)ethyne (2r): Synthesized according to general procedure from 4-iodonitrobenzene (200.0 mg, 0.80 mmol), calcium carbide (154.5 mg, 2.41 mmol), copper iodide (15.3 mg, 0.080 m mol), pa lladium(II)acetate (9.0 m g, 0.040 m ol), t riphenylphosphine (21.0 m g, 0.080 mmol), and triethylamine (243.8 mg, 2.4 mmol) to afford 102.7 mg (0.400 m mol, 95.7%) of **2r** as a y ellow s olid: ^{1}H N MR (400 M Hz, $CDCl_3$): δ ppm 8.26 (4H, d, J = 8.7 Hz), 7.72 (4H, d, J = 8.7 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.7, 132.6, 128.9, 127.7, 92.0

1,2-Bis(4-bromophenyl)ethyne (2q) : Synthesized according to general procedure from 1-bromo-4-iodobenzene (200.0 mg, 0.71 mmol), calcium carbide (136.0 mg, 2.12 mmol), copper i odide (13.5 m g, 0.071 m mol), pa lladium(II)acetate (7.9 mg, 0.035 mol), triphenylphosphine (18.5 mg, 0.071 mmol), and triethylamine (214.6 mg, 2.12 mmol) to a fford 115.3 mg (0.34 m mol, 97.1%) of **2q** as a w hite s olid: : mp 180–183 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 7.49 (4H, d, J = 8.5 Hz), 7.38 (4H, d, J = 8.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 133.0, 131.7, 122.8, 121.8, 89.4; IR (neat, cm^{-1}) 3104, 3071, 2926, 1593; IR (neat, cm^{-1}) 3074, 3071, 2926, 1593.

1,2-Bis(4-((trimethylsilyl)ethynyl)phenyl)ethyne (2t): Synthesized a ccording t o general p rocedure f rom ((4-iodophenyl)ethynyl)trimethylsilane (200.0 mg, 0.667 mmol), calcium carbide (128.2 mg, 2.00 mmol), copper iodide (12.7 mg, 0.067 mmol), palladium(II)acetate (7.5 mg, 0.033 m ol), t riphenylphosphine (17.5 m g, 0.067 m mol), and

triethylamine (202.4 mg, 2.00 mmol) to afford 118.8 mg (0.321 mmol, 96.6%) of **2t** as a yellow solid: ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 7.46 (4H, s), 7.44 (4H, s), 0.26 (18H, s); ^{13}C NMR (101 MHz, $CDCl_3$): δ 131.9, 131.4, 123.0, 104.5, 96.5, 91.0, -0.1

4,4'-(Ethyne-1,2-diyl)bis(4,1-phenylene) bis(4-methylbenzenesulfonate) (2u): Synthesized according to general procedure from 4-iodophenyl 4-methylbenzenesulfonate (200.0 mg, 0.536 mmol), calcium carbide (103.0 mg, 1.63 mmol), copper iodide (10.2 mg, 0.05 mmol), palladium(II)acetate (6.0 mg, 0.027 mol), triphenylphosphine (14.0 mg, 0.05 mmol), and triethylamine (162.2 mg, 1.63 mmol) to afford 137.7 mg (0.266 mmol, 99.4%) of **2u** as a brown solid: ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 7.70 (4H, d, J = 7.5 Hz), 7.41 (4H, d, J = 7.7 Hz), 7.32 (4H, d, J = 7.5 Hz), 6.97 (4H, d, J = 7.7 Hz), 2.45 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.4, 145.6, 132.9, 129.8, 128.5, 122.6, 121.9, 90.0, 21.7; IR (neat, cm^{-1}) 3039, 2920, 1590; HRMS (ESI) Cacld for $C_{28}H_{22}O_6S_2Na$, 541.0750; Found, 541.0756.

Dimethyl 4,4'-(4,4'-(ethyne-1,2-diyl)bis(2,5-dibutoxy-4,1-phenylene))bis(ethyne-2,1-diyl)dibenzoate (2w): Synthesized according to general procedure from methyl 4-((2,5-dibutoxy-4-iodophenyl)ethynyl)benzoate (200.0 mg, 0.407 mol), calcium carbide (78.3 mg, 1.22 mol), copper iodide (7.8 mg, 0.041 mmol), palladium(II)acetate (4.6 mg, 0.020 mol), triphenylphosphine (10.7 mg, 0.041 mmol), and triethylamine (123.0 mg, 1.22 mol) and purified by flash chromatography to afford 133.4 mg (0.171 mmol, 87.1%) of **2w** as a yellow solid: ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 8.03 (4H, d, J = 8.2 Hz), 7.58 (4H, d, J = 8.2 Hz), 7.02 (4H, s), 4.05 (8H, dd, J = 14.8, 6.6 Hz), 3.93 (6H, s), 1.89-1.78 (8H, m), 1.62-1.53 (9H, m), 1.05-0.95 (12H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.6, 153.8, 153.5, 131.4, 131.4, 129.5, 129.4, 128.2, 117.1, 117.1, 114.9, 113.4, 94.1, 91.7, 89.1, 69.5, 69.3, 52.2, 31.4, 31.4, 19.3, 13.9, 13.9; IR (neat, cm^{-1}) 2956, 2864, 2205; HRMS (ESI) Cacld for $C_{50}H_{54}O_8Na$, 805.3711 Found; 805.3713.

Dimethyl 4,4'-(4,4'-(ethyne-1,2-diyl)bis(2,5-dibutoxy-4,1-phenylene))bis(ethyne-2,1-diyl)dibenzoate (2x): Synthesized according to general procedure from using 3,3'-(2-iodo-5-((4-(methoxycarbonyl)phenyl)ethynyl-1,4-phenylene)bis(oxy)bis(propane-3,1-diyl) diacetate (100.0 mg, 0.166 mmol), calcium carbide (32.4 mg, 0.50 mmol), copper iodide (3.2 mg, 0.017 mmol), palladium(II)acetate (1.9 mg, 0.009 mol), triphenylphosphine (4.4 mg, 0.017 mmol), and

triethylamine (50.1 mg, 0.5 mmol) and p urified b y f lash c hromatography to a fford 17.8 m g (0.019 mmol, 50.8%) of **2x** as a yellow solid: ^{1}H NMR (400 MHz, *CDCl$_3$*): δ ppm 8.03 (4H, d, *J* = 8.2 Hz), 7.60 (4H, d, *J* = 8.2 Hz), 7.04 (4H, d, *J* = 6.9 Hz), 4.38-4.31 (8H, m), 4.18-4.11 (8H, m), 3.93 (6H, s), 2.23-2.14 (8H, m), 2.07-2.03 (12H, m); ^{13}C NMR (100 MHz, *CDCl$_3$*): δ 171.0, 170.9, 166.5, 153.6, 153.2, 131.5, 131.5, 129.6, 127.9, 117.2, 117.1, 114.7, 113.7, 94.5, 91.5, 88.5, 66.1, 66.0, 61.3, 61.2, 61.2, 61.1, 52.2, 28.75, 28.7, 20.9, 20.9; IR (neat, cm^{-1}) 3059, 2205, 1702; HRMS (ESI) C acld for C$_{50}$H$_{54}$O$_{16}$Na, 981.3304; Found, 981.3308.

2.3.3 Effect of moisture

Acetonitrile w as distilled a nd k ept over m olecular s ieve 4 ^{o}A (Sigma Aldrich) for two days prior t o use.

Table 3.8 effect of moisture: A 100 mL round b ottom flask w ith a magnetic s tir b ar w as charged with copper iodide (0.1 equiv), palladium acetate (0.05 equiv), and triphenylphosphine (0.1 e quiv) i n 3 mL of acetonitrile. The solution was degassed with nitrogen for 20 minutes. Then, triethylamine (3 equiv), 4-iodotoluene (100 mg, 1 e quiv), c alcium c arbide (3 e quiv), a nd water (0, 10, 30 μL; 0% , 0.3% , 1% f or e ach r eaction) w as added. The mixture was stirred at room temperature overnight. The r eaction m ixture w as t hen f iltrated t hrough a s hort p lug o f silica gel and washed with hexane, or purified by column chromatography in the case of 0% water. The filtrate was evaporated under vacuum to give 1,2-Di-4-tolylethyne (**2b**) in 52%, 99%, and 99% respectively.

2.3.4 Synthesis of aryl acetylene

Table 3.9 Synthesis of 4-toluenenyl acetylene: A 100 mL round bottom flask with a magnetic s tir b ar w as c harged w ith c opper iodide (0.05 equiv), palladium acetate (0.025 equiv), and t riphenylphosphine (0.05 e quiv) i n 5 mL of chloroform. The solution was degassed with nitrogen for 20 minutes. Then, triethylamine (3 equiv), 4-iodotoluene (100.0 mg, 1 e quiv), a nd calcium c arbide (10 e quiv) w ere a dded. T he m ixture w as s tirred a t r oom temperature for 12 h. The reaction mixture was then filtered through a f ilter p aper a nd w ashed w ith d ichloromethane.

The filtrate was evaporated under vacuum and yields were calculated from the crude mixture by NMR ratio of 1,2-Di-4-tolylethyne and *p*-iodotoluene.

2.3.5 Pd-Free reactions

Table 3.10 Screening for Pd-Free reactions: A 100 mL round bottom flask with a magnetic stir bar was charged with copper iodide (0.05 to 0.1 equiv), potassium or cesium carbonate (0.15-0.30 equiv), additives (0.15-0.30 equiv), 4-iodotoluene (100 mg, 1 equiv), and calcium carbide (3 equiv) in 3 mL of solvents. The solution was degassed with nitrogen for 20 minutes. The mixture was stirred at 80 °C for 12 h. The reactions were followed by TLC indicated that no formation of 1,2-Di-4-tolylethyne ($R_f = 0.3$ in hexane), but only *I*-iodotoluene remained in the reactions.

2.3.6 Three components Click chemistry

Table 3.11 Three components Click chemistry using calcium carbide: A 100 mL round bottom flask with a magnetic stir bar was charged with copper iodide (0.3 to 0.5 equiv), palladium acetate (0.5 equiv), and triphenylphosphine (0.1 equiv), sodium azide (1.5 equiv), sodium ascorbate (0.30 equiv), 4-iodotoluene (100.0 mg, 1 equiv), triethylamine (3 equiv), and calcium carbide (3 equiv) in 3 mL of acetonitrile with one drop of water. The solution was degassed with nitrogen for 20 minutes. The mixture was stirred at room temperature of 90 °C for 12 h. Microwave irradiation was set at 125 °C for 10-15 minutes. . The reaction mixture was then filtered through a short plug of silica gel and washed with hexane to afford 1,2-Di-4-tolylethyne in corresponding yields by never observing of other products.

2.3.7 Synthesis of unsymmetrical diaryl ethynes

Coupling of *p*-nitro iodobenzene, 4-iodotoluene, and calcium carbide: A 100 mL round bottom flask with a magnetic stir bar was charged with copper iodide (0.2 equiv), palladium acetate (0.1 equiv), and triphenylphosphine (0.2 equiv), 4-iodotoluene (1 equiv), *p*-nitro iodobenzene (100.0 mg, 1 equiv) and calcium carbide (6 equiv) in 5 mL of acetonitrile. The solution was degassed with nitrogen for 20 minutes. Then, triethylamine (6 equiv) was added. The mixture was stirred at room temperature overnight. The reaction mixture was then filtered through a filter paper and washed with dichloromethane. The filtrate was evaporated under

vacuum a nd s eparated b y c olumn c hromatography u sing hexane/ethyl a cetate as the eluent to give 1,2-Di-4-tolylethyne (**2b**), 1-methyl-4-((4-nitrophenyl)ethynyl)benzene (**2y**), and 1,2-bis(4-nitrophenyl)ethyne (**2r**) in 30%, 18% a nd 42% yields respectively. Yields b ase o n N MR integal ratio c alculation of the mixture of **2y** and **2b**.

Coupling of 4-iodoanisole, 4-nitro iodobenzene, and calcium carbide: A 100 mL round bottom flask with a magnetic stir bar was charged with copper iodide (0.2 equiv), palladium acetate (0.1 equiv), and triphenylphosphine (0.2 equiv), 4- iodoanisole (1 equiv), 4-nitro iodobenzene (100.0 mg, 1 equiv) and calcium carbide (6 equiv) in 5 mL of a cetonitrile. The solution was degassed with nitrogen for 20 minutes. Then, triethylamine (6 equiv) was added. The mixture was stirred at room temperature overnight. The reaction mixture was then filtered through a filter paper and washed with dichloromethane. The filtrate was evaporated under vacuum a nd s eparated b y c olumn c hromatography u sing hexane/ethyl a cetate as the eluent to give 1,2-bis(4-methoxyphenyl)ethyne) (**2f**), and 1,2-bis(4-nitrophenyl)ethyne (**2r**) in 38% a nd 32% y ields r espectively, a long w ith 11% r ecovery of 4- iodoanisole. Yields base on NMR ratio calculation of the mixture of **2f** and **2r**.
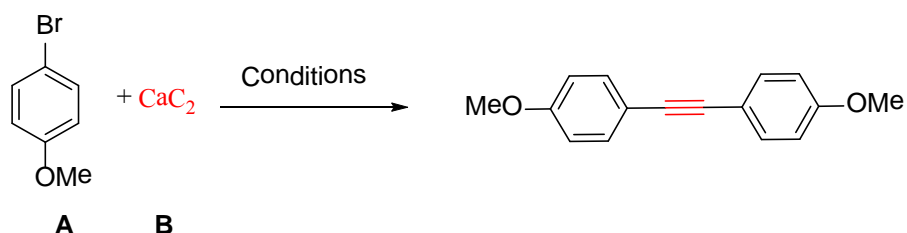
CHAPTER III

RESULTS AND DISCUSSION

3.1 Initial observation

Firstly, coupling reactions of 4-bromoanisole and calcium carbide have been screened under mild conditions using commercially available reagents. The results are summarized in

Table 3.1 Initial observation[a]

entry	catalyst	base	ligand	solvent	temp.	**A:B**	yield (%)
1	$PdCl_2(PPh_3)_2$, CuI	DBU	-	toluene	rt	2:1	trace
2	$PdCl_2(PPh_3)_2$, CuI	DBU	-	THF/MeCN 1:1	rt	2:1	trace
3	$Pd(OAc)_2$, CuI	TEA	PPh_3	MeCN	reflux	2:1	trace
4	$Pd(OAc)_2$, CuI	TEA	PPh_3	MeCN	reflux	1:3	8
5	$Pd(OAc)_2$, CuI	TEA	PPh_3	toluene	reflux	1:3	trace
6	$Pd(OAc)_2$, CuI	TEA	PPh_3	THF	reflux	1:3	trace
7	$Pd(OAc)_2$, CuI	TEA	PPh_3	MeOH	Reflux	1:3	trace

[a]Unless otherwise noted, calcium carbide, Pd, Cu, ligand = 5, 2.5, 5 (mol%), and solvent was stirred in N_2 for 30 min. Then 4-bromoanisole (1 equiv) and base (3 equiv) was added to the reaction mixture and stirred under N_2 overnight.

Table 3.1. Most conditions resulted in only trace amount of product yield with significant recovery of starting material or decomposition, in the case of reflux conditions. The best results were obtained with Pd(OAc)$_2$, CuI, PPh$_3$, triethylamine (TEA) in acetonitrile (MeCN), but only eight percent yield was achieved. We hypothesized that poor yield is caused by failure of aryl bromide to react under mild conditions. Thus, we switched to other types of aryl compounds.

To enhance the reaction yield, we decided to use four phenyl derivatives in our screening: bromobenzene, iodobenzene, phenyl 4-methylbenzenesulfonate, and phenyl trifluoromethanesulfonate. Phenyl 4-methylbenzenesulfonate was prepared by reacting phenol with *p*-toluenesulfonyl chloride (TsCl) under microwave treatment. Similar reaction was used to prepare phenyl trifluoromethanesulfonate but heat was used instead of microwave radiation (Scheme 3.1).
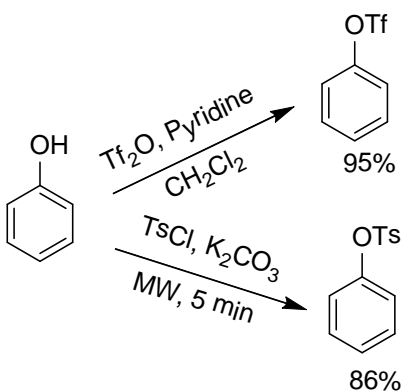
Scheme 3.1 Preparation of phenyl sulfonate esters

With all starting materials in hand, we first attempted the coupling reaction by treatment of calcium carbide with the four phenyl derivatives in acetonitrile at room temperature in the presence of Pd(OAc)$_2$ (2.5 mol%), triphenylphosphine (PPh$_3$, 5 mol%), CuI (5 mol%) and triethylamine (Table 3.2). Unfortunately, the reaction of phenyl bromide or triflate gave no desired product and only a small amount of starting material could be recovered along with unidentified complex mixtures. In the case of the tosylate, only a trace amount of the targeted product **2a** was isolated along with an almost 90% recovery of starting material.

It is well known that the reactivity of aryl iodides in oxidative addition to palladium is much greater than aryl bromides and the oxidative addition is believed to be the rate determining

steps in most Sonogashira c oupling [8]. T herefore, a ryl iodides would e nhance t he f ormation o f the desired product under these conditions. To our delight, switching from bromide to iodide analogues, d iphenylethyne **2a** was obtained in 68% yield along with recovery of iodobenzene (15%).

**Table 3.2** Screened r eactions for types of aryl compounds[a]
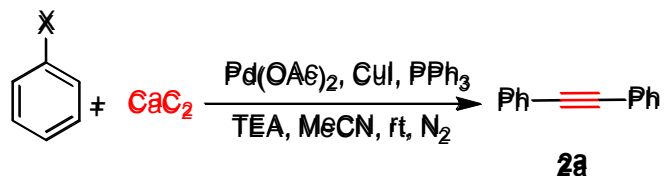
X	yield (%)[b]
Br	complex m ixtures
OTs	0[c]
OTf	complex m ixtures
I	68

[a] All reactions were carried out with phenyl derivatives (1 equiv), CaC_2 (3 equiv), $Pd(OAc)_2$ (2.5%), CuI (5%), PPh_3 (5%), a nd t riethylamine (3 e quiv) at rt for 10 h,.[b]Isolated y ield, [c]A q uantitative amount o f phenyl derivatives was recovered.

After we found the best type of aryl compound for coupling reaction with calcium carbide, w e then p repared a stock of a ryl iodides.

3.2 Preparation of aryl iodides

Twenty t wo a ryl i odides will be tested in this work (Scheme 3.2). Iodobenzene (**1a**), iodotoluene (**1b-1d**), 1 -iodonaphthalene (**1e**), 4-iodoanisole (**1f**), 4-iodophenol (**1g**), 2-iodoaniline (**1j**), 2 -iodothiophene (**1m**), 1 -(4-iodophenyl)ethanone (**1n**), 4-nitroiodobenzene (**1r**), and 1-bromo-4-iodobenzene (**2s**) were obtained from commercial sources, a nd w ere u sed without further purification. Aryl iodides **1h, 1i, 1o-1q, 1t, 1u**, on the other hands were p repared according to literatures. The synthesis of such compounds will be discussed in t his section.
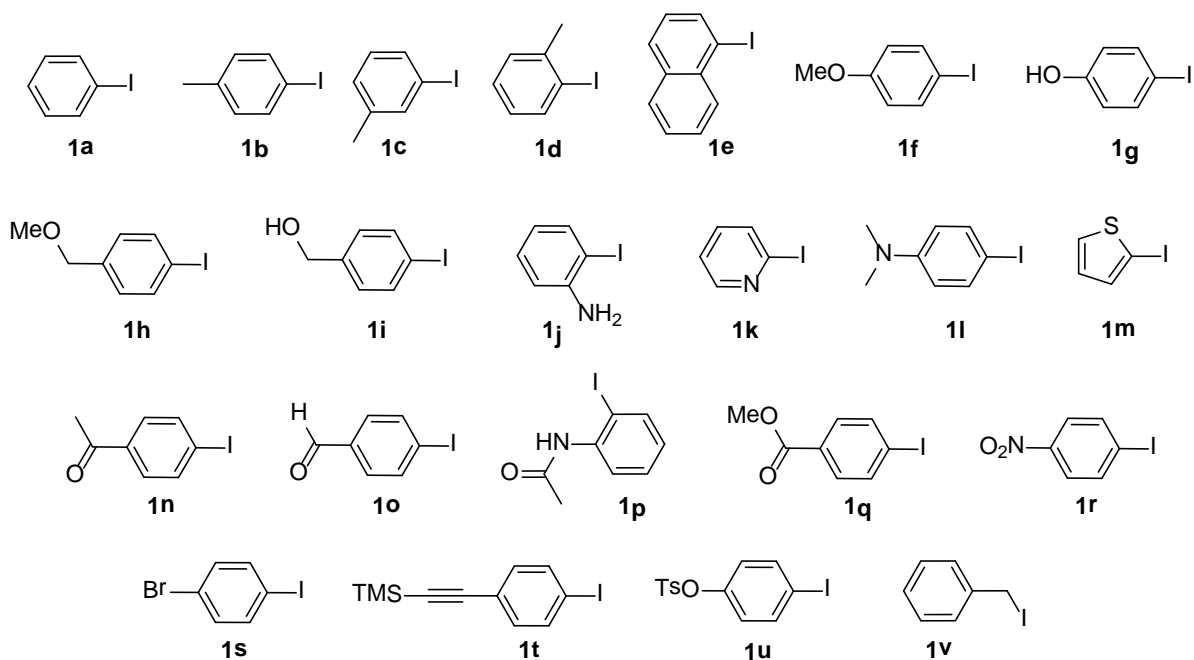
Scheme 3.2 aryl iodides used in this work

4-iodotoluene (1b) and o-iodotoluene (1d)

To synthesized compounds **1b** and **1d**, we reacted iodinemonochloride (ICl) with toluene (Scheme 3.3). The 1:1 mixture of para and otho iodotoluene (**1b** and **1d**) was formed in 70% combine yield, which cannot be separated.
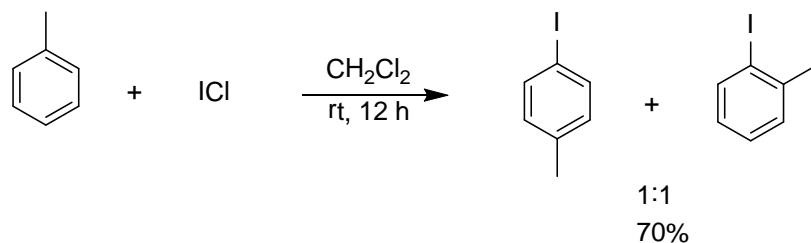

Scheme 3.3 Reaction of ICl with toluene

Then, we moved to the iodination of corresponding diazo arenes. Compounds **1b** and **1d** were formed in 72 and 63% yields, respectively (Scheme 3.4). However, the synthesized compounds gave lower yield and lower reproducibility when used in subsequent reactions as compared to the commercial ones from Sigma-Aldrich Company, so we decided to use the commercial compound in our reaction (for more detail see 3.3.1 optimization conditions).
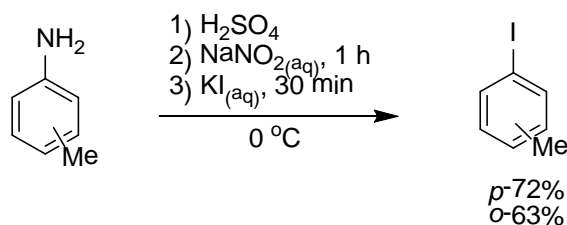
Scheme 3.4 Synthesis of compounds **1b** and **1d** from corresponding amines

1-iodo-4-(methoxymethyl)benzene (1h), (4-iodophenyl)methanol (1i), 4-iodobenzaldehyde (1o) and methyl 4-iodobenzoate (1q)

Compound **1i** was synthesized by reduction of 4-iodobenzoicacid using borane in THF in 64% yield (Scheme 3.5). Then, the methylation of **1i** by methy iodide and sodium hydride gave compound **1h** in 75% yield. Furthermore, using Swern oxidation reaction to compound **1i** gave aldehyde **1o** in 59% yield. On the other hand, ester **1q** was easily generated from esterification of 4-iodobenzoic acid in 97% yield.
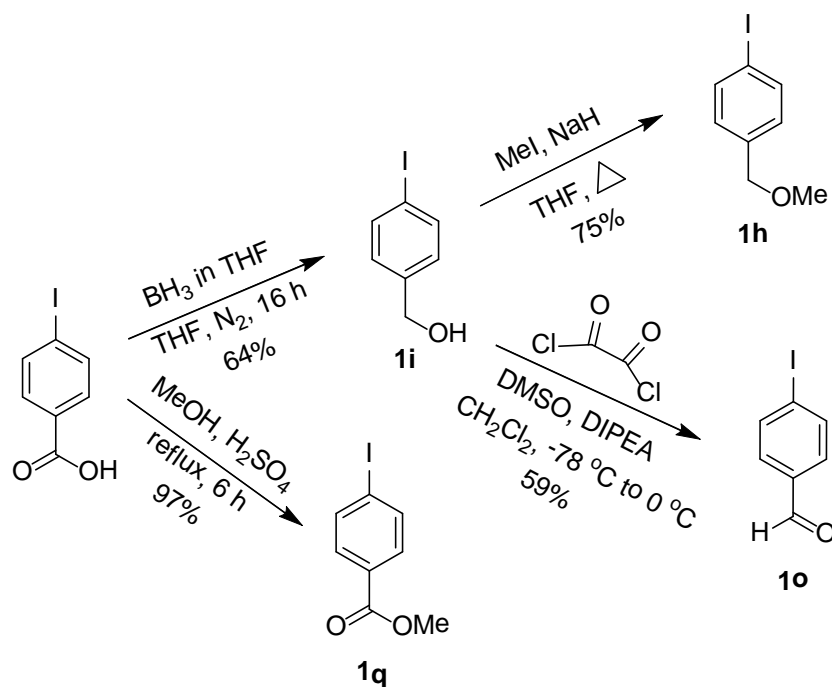
Scheme 3.5 Synthesis of compounds **1h**, **1i**, **1o** and **1q**

N-(2-iodophenyl)acetamide (1p)

Reaction o f 2-iodoaniline with acetic anhydride in THF and diisopropylethylamine at 60 °C gave aromatic amide **1p** in 76% yield (Scheme 3.6).
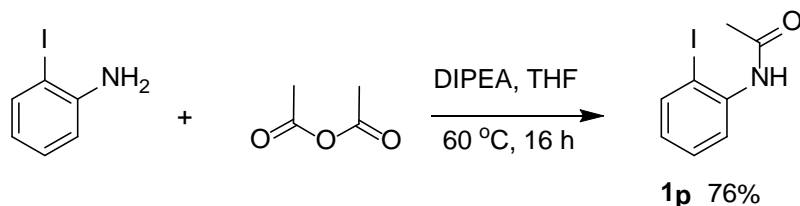
Scheme 3.6 Synthesis of compound **1p**

((4-iodophenyl)ethynyl)trimethylsilane (1t)

Sonogashira coupling of diiodobenzene with trimethysilyl acetylene gave compound **1t** in 33% yield (Scheme 3.7). The low yield was caused by formation of di-substituted product, unreacted iodobenzene, and difficulty in product purification.
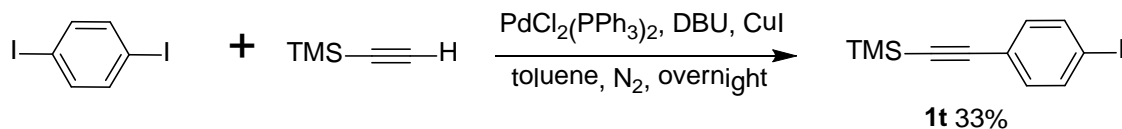
Scheme 3.7 Synthesis of compound **1t**

4-iodophenyl 4-methylbenzenesulfonate (1u)

Reaction of 4-iodophenol to compound **1u** did not proceed as well a s in the case of phenyl 4-methylbenzenesulfonate (Scheme 3.8 and 3.1) because 4-iodophenol is a s olid, u nlike phenol, so the reactants were not homogeneously mixed together. This led to a lower yield.
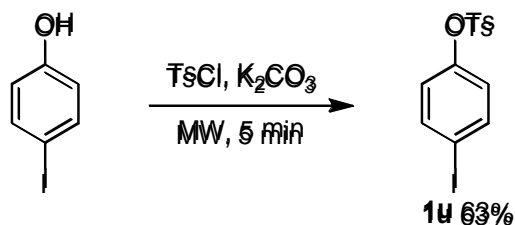
Scheme 3.8 Synthesis of compound **1u**

2-iodopyridine (1k)

Iodination of 2-chloropyridine using acetyl chloride and sodium iodide in acetonitrile gave corresponding iodide in 86% yield (Scheme 3.9).
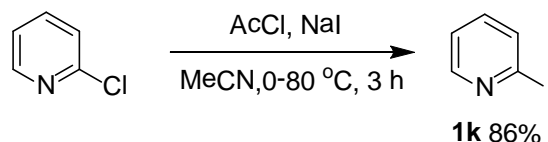
Scheme 3.9 Synthesis of compound **1k**

**3.3 Pd-catalyst coupling reaction using calcium carbide as a starting material.**

3.3.1 Optimization conditions

For all conditions screening experiments, 4-iodotoluene was selected, due to a clear difference between the methyl group ^{1}H NMR signal of the starting material and that of its di-4-tolylethyne product.

Part I: Initial study and problems solving

1) Optimization conditions with 4-iodotoluene

In this section, we used 4-iodotoluene 200 mg, calcium carbide 3 equiv, Pd source 5%, Cu source 2.5%, triphenylphosphine 5% and base 3 equivalent and the reactions were performed under nitrogen atmosphere in 5 mL of solvent. The results were summarized in Table 3.3 The optimization condition indicated that copper iodide is the best copper source in this reaction as well as the combination of acetonitrile and triethylamine (Table 3.3, entries 1-13)

Table 3.3 Optimization condition with 4-iodotoluene
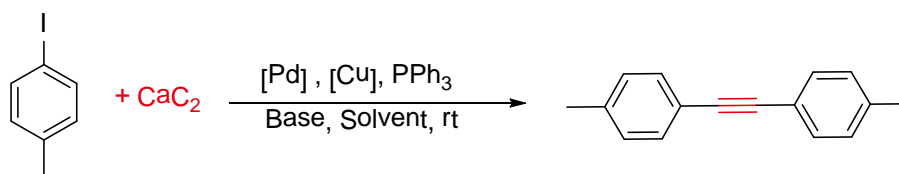
entry	Pd/Cu source	base	solvent	yield[a]
1	Pd(OAc)$_2$/CuI	TEA	MeCN	84%
2	Pd(OAc)$_2$/ CuOAc	TEA	MeCN	55%
3	Pd(OAc)$_2$/ Cu(OAc)$_2$	TEA	MeCN	64%
4	Pd(OAc)$_2$/--	TEA	MeCN	22%
5	PdCl$_2$(PPh$_3$)$_2$/CuI	TEA	MeCN	24%
6	PdCl$_2$(MeCN)$_2$/CuI	TEA	MeCN	25%
7	Pd(OAc)$_2$/CuI	TEA	MeOH	34%
8	Pd(OAc)$_2$/CuI	TEA	THF	19%
9	Pd(OAc)$_2$/CuI	TEA	DMF	43%
10	Pd(OAc)$_2$/CuI	K$_2$CO$_3$	THF	trace[b]
11	Pd(OAc)$_2$/CuI	K$_2$CO$_3$	MeOH	14%
12	Pd(OAc)$_2$/CuI	--	MeCN	6%
13	Pd(OAc)$_2$/CuI	TEA	MeCN	trace[c]

[a] Isolated yield, [b] 88% recovery starting material, [c] air open 90% recovery starting material

2) Scale up to 200-600 mg with constant amount of catalysts

In this section, we used 4-iodotoluene 1 equiv, calcium carbide 3 equiv, triethylamine 3 equiv, by fix the amount of Pd(OAc)$_2$ at 10.3 mg, CuI 4.4 mg and triphenylphosphine 12.0 mg, and the reactions were carried out under nitrogen atmosphere in 5 mL of acetonitrile (%mol Pd, Cu, PPh$_3$ = 5%, 2.5%, 5%, respectively; base on 200 mg of 4-iodotoluene). The results were illustrated in Table 3.4

**Table 3.4** Scale up to 200-600 mg with the same amount of catalysts
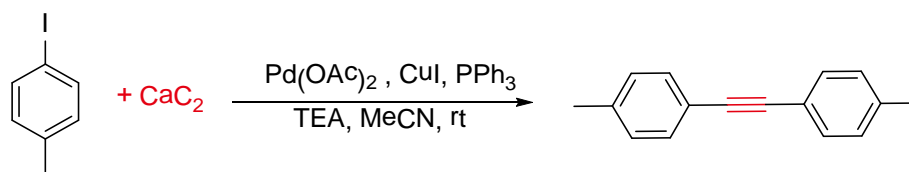
entry	*4-iodotoluene* (mg)	result[a]
1	200	21% NMR yield
2	400	26% Isolated yield
3	600	32% Isolated yield

[a,] Copper iodide 0.046 mmol, palladium acetate 0.023 mmol, triphenylphosphine, 0.046 mmol

200, 400 and 600 mg of iodotoluene were subjected to the coupling reaction b y u sing the same amount of catalyst (Pd(OAc)$_2$ and CuI) in order to see the scalability and process efficiency. H owever, t he r esults w ere disappointed. Reaction y ields were dropped when scale up to 400 a nd 600 m g s cale (Table 3.4 entries 2 , 3) c ompared to pr evious r esults of 84% a t 200 m g scale (Table 3.3, entry 1). Even 200 mg scale was failed t o reproduce p revious r esult (Table 3.4, entry 1). However, this problem w as f ixed w hen c hanging n umber o f c atalysts, a nd u p catalyst loading to 5% Pd, 10% Cu, and 10% PPh$_3$. The result is shown in the next topic.

3) Catalysts loading

Base c onditions: 4-iodotoluene 100.0 mg, calcium carbide 3 equiv, Pd(OAc)$_2$, CuI, triphenylphosphine, triethylamine 3 equiv under nitrogen atmosphere in 3 mL of acetonitrile. The r esults i n T able 3.5 indicate that changing catalyst ratio (%mol Pd/Cu/PPh$_3$) from 5/2.5/5 to 2.5/5/5, gave better results. The best result was achieved with 5/10/10 ratio. However, the result in entry 1 was n ot r eproducible (Table 3.3, e ntry 1) , because this r eaction i s e xceptionally sensitive t o c atalyst l oading, b ut t he b alance w as i nconsistent a t m illigram s cale. T his m ay c ause the low reproducibility o f t he r eaction, s o l ater o n, h igh c onsciousness o n w eighting o f c atalysts was applied to the reaction set up.

Table 3.5 Effect o f catalysts l oading
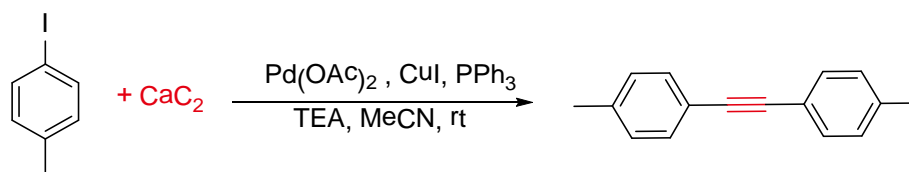
entry	% molPd/Cu/PPh$_3$	result
1	5/2.5/5	32% NMR yield
2	2.5/5/5	41% NMR yield
3	5/10/10	99% I solated yield

[a] obtained from NMR calculation

Part II: Final optimization conditions

The optimization results showed that Pd(OAc)$_2$ was t he m ost e ffective p alladium s ource for this reaction in comparison with bis(triphenylphosphine)palladium(II)dichloride and palladium tetrakis (Table 3.6, entries 1-4). Cleary, CuI is needed in the reaction, and its absence resulted in a lower yield (22%, entry 5). The formation of copper acetylide is significant to drive trans-metalation with palladium, better than hydride-metal transfer form acetylene gas. In addition, a lternative c opper s ources, s uch a s C uOAc a nd C u(OAc)$_2$, or CuCl could be used in this transformation (entries 6-8), CuI is more s table a nd lower-price, h owever.

Base screening indicated that TEA was the most effective base in comparison with others, although diisopropylethylamine gave s atisfactory r esults (entry 9). W hen t he r eaction w as c arried out at 60 °C, 40% of ditolylethyne product (2b) was isolated without the recovery of any starting material. This is likely due to the instability o ft he p alladium c omplex i ntermediates u nder t hese conditions (entry 12).

Under atmospheric condition, a lower yield of the desired product was isolated (30%, entry 1 3) i n c omparison w itht hat u nder i nert n itrogen environment. In addition, the reactions went t o c ompletion w ith a n i ncreased a mount of catalyst as the mentioned result (Table 3.5,

entry 3 or Table 3.6, entry 14). Reaction proceeded smoothly at room temperature. Moreover, this also fixes the problem on low reproducibility from catalyst loading.

Table 3.6 Final optimization conditions[a]
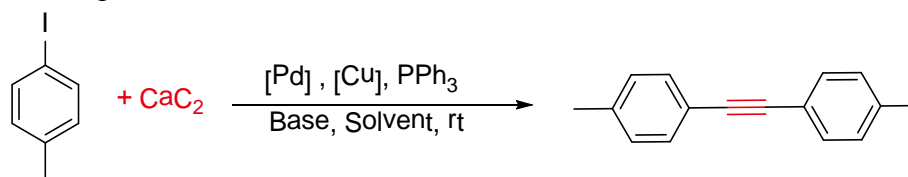
entry	Pd/Cu source	base	solvent	yield[b]
1	Pd(OAc)$_2$/CuI	TEA	MeCN	50%
2	PdCl$_2$(PPh$_3$)$_2$/CuI	TEA	MeCN	24%
3	Pd(PPh$_3$)$_4$/CuI	TEA	MeCN	24%
4	Pd on C/CuI	TEA	MeCN	5%
5	Pd(OAc)$_2$/--	TEA	MeCN	22%
6	Pd(OAc)$_2$/CuOAc	TEA	MeCN	50%
7	Pd(OAc)$_2$/ (CuOAc)$_2$	TEA	MeCN	50%
8	Pd(OAc)$_2$/ CuCl	TEA	MeCN	45%
9	Pd(OAc)$_2$/CuI	DIPEA	MeCN	41%
10	Pd(OAc)$_2$/CuI	K$_2$CO$_3$	THF	0%[c]
11	Pd(OAc)$_2$/CuI	K$_2$CO$_3$	MeOH	16%
12	Pd(OAc)$_2$/CuI	TEA	MeCN	40%[d]
13	Pd(OAc)$_2$/CuI	TEA	MeCN	30%[e]
14	Pd(OAc)$_2$/CuI	TEA	MeCN	99%[f]

[a]Unless otherwise noted, a mixture of 4-iodotoluene (1 equiv), CaC$_2$ (3 equiv), Pd catalyst (2.5%), PPh$_3$ (5%), Cu catalyst. (5%) and base (3 equiv) room temperature for 10 h, [b] Isolated yield, [c] 90% of *4-iodotoluene* was recovered. [d] Heated at 60 °C, [e] Reaction was carried out under air, [f] 5% of Pd(OAc)$_2$, 10% CuI and 10% of PPh$_3$ were used.
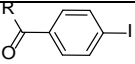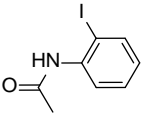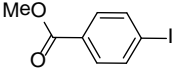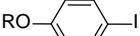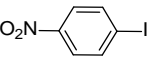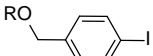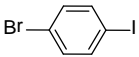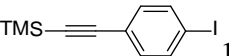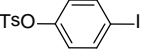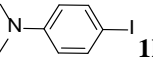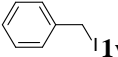
Thus, the optimized conditions involved the treatment of 4-iodotoluene (1 equiv), CaC$_2$ (3 equiv), Pd(OAc)$_2$ (5%), PPh$_3$ (10%), CuI (10%) and triethylamine (3 equiv) in MeCN at room temperature under a nitrogen atmosphere. Under these optimized conditions, the coupling product **2b** was isolated in 99% yield (Table 3.6, entry 14) with more than 5 times reproducibility. It must be noted that under these conditions, complete conversion to **2b** was confirmed by NMR spectroscopic analysis and TLC. To the best of our knowledge, formation of

diaryl ethynes under these efficient and mild conditions have not been reported in the literature [12, 16, 17, 25, 37-40].

3.3.2 Functional group compatibility of the reaction

We intend to demonstrate the high compatibility of various functional groups in our methods. Therefore, a series of aryl iodides either commercially available or prepared according to section 3.2 were subjected to the coupling reaction with CaC_2 under the optimized reaction conditions (Table 3.7). The aryl iodides bearing a nelectron donating groups uch as methyl, naphthyl, and, methoxy (entries 2-4) yielded the desired bisarylacetylenes in good to excellent yields. Notably, the substituent position effect was found to be minimal in our study, as seen in the case of three isomers of iodotoluenes (1b, 1c and 1d), providing the coupling products 2b, 2c and 2d in 99%, 99% and 96% yields, respectively (entry 2). However, 4-iodobenzyl alcohol (1i), high electron density nitrogen containing compound (1k-1l), and benzyl iodide (1v) were not suitable for this transformation as they afforded the target compounds, 2i in only 41% yield, while complex mixtures were obtained in the case of 1k-1l, and decomposition of starting material in the case of 1v (entries 5, 7, 8, 11). Surprisingly, compound 1j was successfully coupling in 74% yields (entry 6). In addition, compound 1g and 1j are known as the difficult substrate in Sonogashira coupling [37], but this work resulted in high yields of the desired products (entries 4, 6). These results may be due to the chelation of the palladium catalyst with the high electron density oxygen or nitrogen atoms. The yield was significantly increased when the hydroxyl moiety in 1i was methylated. The product 2h was isolated in much higher yield. Interestingly, the presence of a sulfur atom gave no effect in this reaction, as shown in the coupling reaction of 2-iodothiophene (1m). The product 2m was isolated in 99% yield. The substrates bearing electron-withdrawing groups such as the aldehyde, ketone, amido, ester, and nitro moieties reacted efficiently to obtain the coupled products in good to high yields (entries 10-13). In contrast to previous report, our experiment resulted in good yields of product 2o and 2r [30]. This outcome suggests that the rate determining step of this reaction may not be the same as the reactions investigated by Zhang [30]. Moreover, other leaving groups such as bromo, tosyl, and methoxy as well as trimethylsilyl protecting groups were able to tolerate the reaction conditions well and iodo group were reacted selectively, giving the desired products in excellent yields (entries 14-16). We attributed the wide range of functional group tolerance to the

Table 3.7 Screening of aryl iodides[a]

$$\text{ArI} + \text{CaC}_2 \xrightarrow[\text{TEA, MeCN, rt, N}_2]{\text{Pd(OAc)}_2,\ \text{CuI, PPh}_3} \text{Ar}\equiv\equiv\text{Ar}$$

entry	aryl iodide	product	yield(%)[b]	entry	aryl iodide	product	yield(%)[b]
1	**1a**	**2a**	96(86)	10	R=Me ; **1n** / R=H ; **1o**	**2n** / **2o**	99(99) / 87
2	Me, p;**1b**, m;**1c**, o;**1d**	**2b** / **2c** / **2d**	99(84) / 99(64) / 96(24)	11	**1p**	**2p**	94(74)
3	**1e**	**2e**	96(75)	12	MeO **1q**	**2q**	74(5)
4	RO, R=Me; **1f** / R=H ; **1g**	**2f** / **2g**	96(45) / 80[c]	13	O₂N **1r**	**2r**	96
5	RO, R=Me; **1h** / R=H ; **1i**	**2h** / **2i**	99 / 41[c](38)	14	Br **1s**	**2s**	97(33)
6	NH₂ **1j**	**2j**	74%	15	TMS **1t**	**2t**	97(35)
7	**1k**	**2k**	(complex mixture)	16	TsO **1u**	**2u**	99
8	**1l**	**2l**	(complex mixture)	17	**1v**	**2v**	(0)
9	S **1m**	**2m**	99(79)				

[a] General conditions: a mixture of aryl iodides (1 equiv), CaC₂ (3 equiv), Pd(OAc)₂ (5%), PPh₃ (10%), CuI (10%) and TEA (3 equiv) was stirred in 5 mL of acetonitrile for 12 hours, and purified by filtration through a short plug of siliga gel, [b] Isolated yield, [c] Purified by column chromatography, yields in parenthesis indicated the results when using Pd/Cu/PPh₃ = 5/2.5/5 mol%

heterogeneous nature of calcium carbide and proper concentration of gradually generated acetylene gas under the reaction condition. These high functional group selectivity and compatibility should expand the scope of this reaction in the synthesis of more complex π-conjugated molecules whilst further modification at the remaining reactive groups should be explored.

3.3.3 Synthesis of oligo (phenyleneethynylenes)

The success of this Pd-catalyzed reaction turned our attention to the synthesis of oligo-(aryleneethynylenes). Such compounds attracted considerable interest due to their electronic and photonic properties, which have been applied widely in chemo- and biosensors and electronic devices [41-45]. The oligo-(aryleneethynylenes) **2w** and **2x** were prepared according to Scheme 3.10. Compound **1w** and **1x** were prepared form previous work by Vongnam [46] according to described methods a, b, c, and d. The coupling of highly functionalize and highly steric molecules **1w** and **1x** with calcium carbide under the optimized conditions gave compound **2w** and **2x** bearing three phenyleneethynylene units in 87 and 51% yields, respectively.
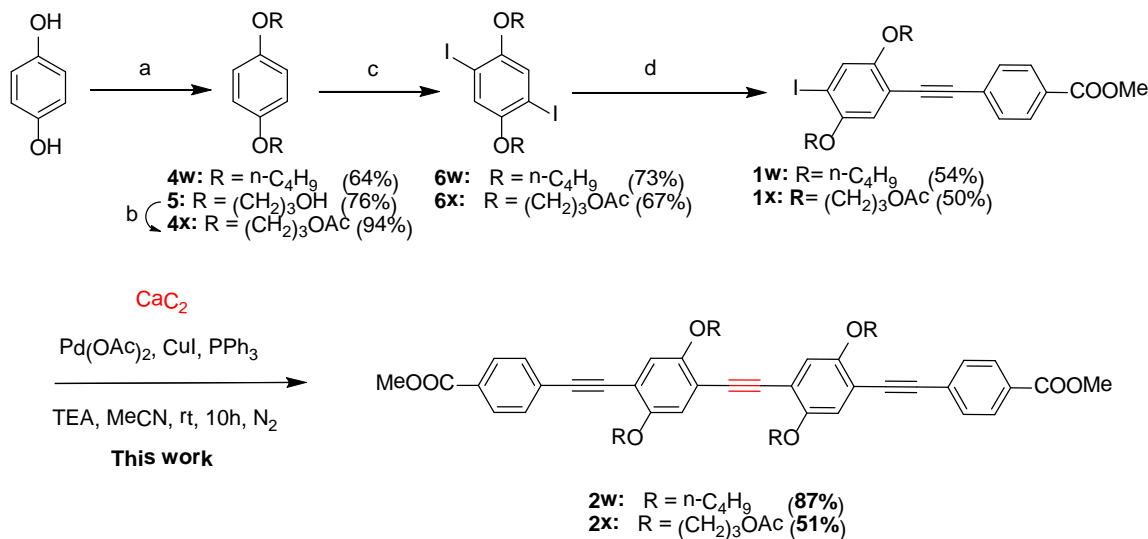

Scheme 3.10 Synthesis of Oligo-(aryleneethynylenes) **2w** and **2x**

Reagents and conditions: (a) *n*-BuBr, KOH DMF for **4w** or ClC$_3$H$_6$OH, K$_2$CO$_3$, MeCN for **5**; (b) AcCl, DMAP, py, CH$_2$Cl$_2$; (c) ICl, MeOH for **6w** or I$_2$, KIO$_3$, AcOH, H$_2$O, H$_2$SO$_4$ for **6x**; (d) Methyl 4-ethynyl benzoate, PdCl$_2$(PPh$_3$)$_2$, CuI, DBU, PhMe for **1w, 1x**

3.3.4 Mechanistic Investigation

The mechanism of coupling reaction between aryl iodide and calcium carbide would probably followed t he s imple Sonogashira c oupling m echanism. However, there are two possibilities. First, the reaction proceed through hydrolysis of calcium carbide to acetylene gas, and t hen react with copper, or second, copper is directly transmetalated with calcium carbide to copper a cetylide t hat c an d rive t o c atalytic c ycle i n S onogashira c oupling m echanism. Therefore, the role of water will b e i nvestigated i n o rder t o g ain m ore m echanistic i nformation o ft his reaction. The reaction were then performed in the various amount of water in acetonitrile and the results were described in Table 3.8

Table 3.8 Effect o f water[a]
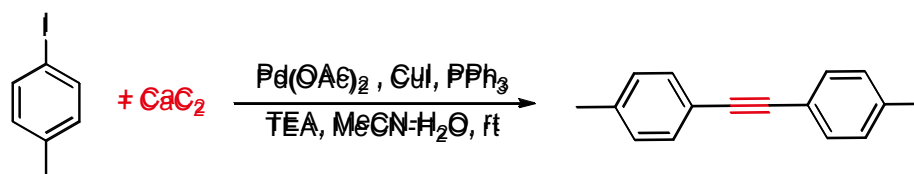
entry	equiv of water	yield (%)[b]
1	0	52
2	1.2	99
3	3.6	99

[a] General conditions: a mixture o f 4-iodotoluene (1 e quiv), CaC_2 (3 e quiv), $Pd(OAc)_2$ (5%), PPh_3 (10%), CuI (10%) and TEA (3 e quiv) was stirred in 3 mL of acetonitrile for 12 hours, [b] Isolated yield

When the reaction were carried in freshly distilled acetonitrile and kept over molecular sieve f or 2 d ays, the yield w as s ignificantly dr opped t o 52 % (Table 3.10, entry 1). It was confirmed that 1.2 equiv of water is enough for driving the reaction, even 3.6 e quiv gave t he same results (Table 3.10, entries 2-3). Thus, water is needed in the reaction in order t o dr ive the reaction c ompletely.

3.3.5 Synthesis of aryl acetylene

In 1995, Pal and Kundu had successfully synthesized 2:1 mixture of diphenyl acetylene and phenyl acetylene in 61% yield from the coupling reaction from phenyl iodide, under simple Sonogashira coupling reaction when chloroform was used together with a continuous flow of acetylene gas [24]. This is a motivation to the synthesis of unsymmetrical diaryl ethynes. Thus their conditions reaction were used in our reaction with calcium carbide, focusing on observing terminal alkyne peak. The results are showed in Table 3.9.

Table 3.9 Synthesis of *p*-toluenenyl acetylene[a]

| entry	catalysts	yield (%)[b]	A:B
1	Pd(OAc)$_2$ 3%, CuI 6%, PPh$_3$ 6%	35	1:0
2	Pd(OAc)$_2$ 5%, CuI 10%, PPh$_3$ 10%	42	1:0
3	PdCl$_2$(PPh$_3$)$_2$ 3.5%, CuI 11.5%	33	1:0

[a] General conditions: a mixture of 4-iodotoluene (1 equiv), CaC$_2$ (10 equiv), catalysts, and TEA (5 equiv) was stirred in 5 mL of chloroform for 12 hours, [b] obtained by NMR

The first entry was the conditions that lower the catalyst loading were used in the hope that a lower reaction rate would favor the formation of 4-toluenenyl acetylene (**B**). However, the reaction resulted in no yield of the desired product **B** (Table 3.9, entry 1). Increasing the catalyst loading resulted in increasing of product yield, but still no formation of a mono-sub product. Then the exactly same condition to Pal and K undu conditions were tried by using calcium carbide instead of acetylene gas, di-sub product **A** was the only product observed in 33% yield. Hypothesizingly, the slow release of acetylene from calcium carbide is not excess enough compare to Kundu's conditions which using the continuous flow of acetylene gas.

3.3.6 Pd-Free reactions

Copper is known to be a catalyst in cross coupling reaction between aryl halide and terminal alkyne without palladium facilitation when the l igand s uch a s L-proline, *N,N*-dimethylglycine or ascorbate were used [47]. Therefore, those additives were tried in the reaction of a ryl i odide a nd c alcium c arbide w ithout p alladium c atalyst. T he r esults a re s ummarized i n Table 3.10.

Table 3.10 Screening for P d-Free reactions[a]
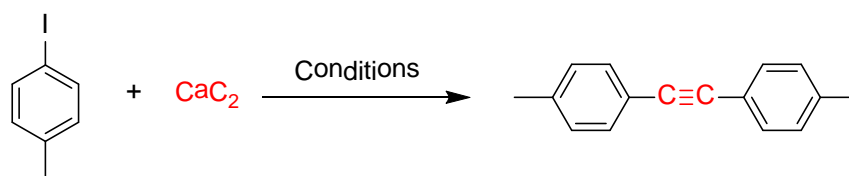
entry	conditions	yield
1	CuI 10%, , *N,N*-dimethylglycine 30%, CsCO$_3$, dioxane, 80 ^{o}C	N.R.
2	CuI 5%, , L-proline 15%, K$_2$CO$_3$, DMF, 80 ^{o}C	N.R.
3	CuI 10%, , Sodium a scorbate 30%, CsCO$_3$, dioxane, 80 ^{o}C	N.R.

[a] General conditions: a mixture of 4-iodotoluene (1 equiv), CaC$_2$ (3 equiv), copper iodide, additives, and base was stirred in 3 mL of solvent for 12 hours,

Unfortunately, t here w ere n o r eaction o ccur e ven h igh a mount of copper and three types of additives were applied to the reactions (Table 3.10, e ntries 1 -3). T hese r esults i ndicate that o ur system i s n ot r eactive e nough t o f orm the desired product under these conditions, and palladium is required in t he r eaction.

3.3.7 Three components Click chemistry

Jiang a nd c o-worker reported t he preparation of aryltriazole via Click chemistry from the coupling o f organic azide a nd c alcium c arbide i n 2 009 [29]. T he r eaction p roceed v ery w ell t o form 1 1 d ifferent a ryltriazole i n g ood y ields. T his r eport c onfirmed the possibility of applying

calcium carbide in Click chemistry. Another report was pu blished i n 2004; Appukkuttan successfully a rchived t hree c omponents c oupling o f b enzyl halides, sodium azide, and terminal alkynes. They were a ble t o s ynthesize 14 different 1,4-disubstituted 1,2,3-triazoles in good yields [48].

Table 3.11 Three c omponents Click chemistry using c alcium carbide[a]
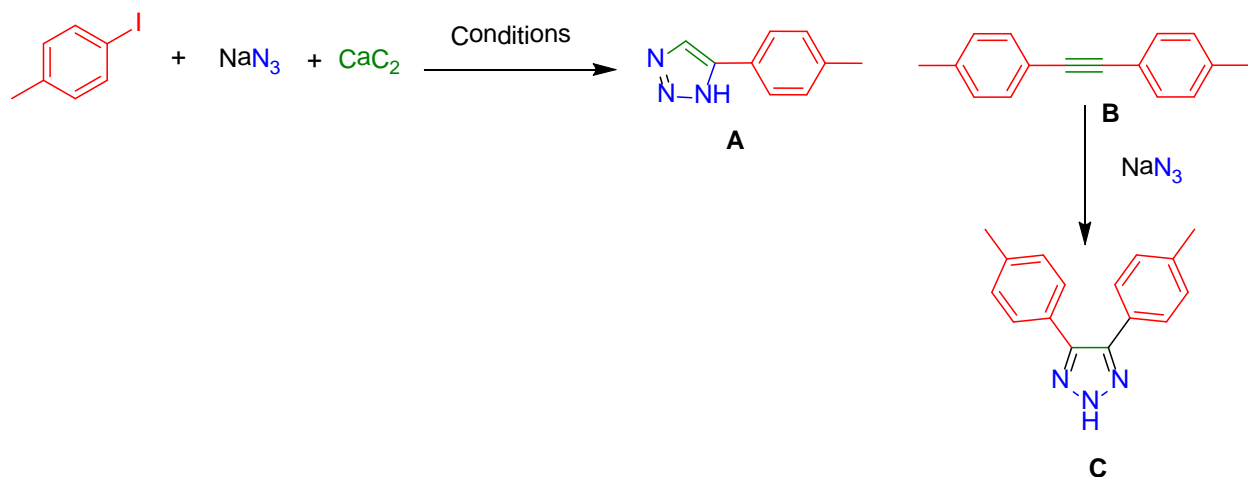
| entry	catalysts	additives	solvent, h eat	yield[b]	A:B:C
1	Pd(OAc)$_2$ 5%, CuI 30%, PPh$_3$ 10%	Na ascorbate 30%, TEA	MeCN/H$_2$O	82%	0:1:0
2	Pd(OAc)$_2$ 5%, CuI 30%, PPh$_3$ 10%	Na ascorbate 30%, TEA	MeCN/H$_2$O, 90 ^{o}C	89%	0:1:0
3	Pd(OAc)$_2$ 5%, CuI 30%, PPh$_3$ 10%	Na ascorbate 30%, TEA	MeCN/H$_2$O MW 125 ^{o}C	85%	0:1:0
4	CuI 50%	Na ascorbate 50%,	MeCN/H$_2$O MW 125 ^{o}C	N.R.	0:1:0

[a] General conditions: a mixture of 4-iodotoluene (1 equiv), CaC$_2$ (3 equiv), catalysts, additives were stirred in 3 mL of solvents for 12 hours, [b] Isolated yield

The results from these reports suggested that the three components coupling of a ryl iodides, sodium azide, and calcium carbide could be possible. Based on the previous mentioned reactions, the three click component coupling reactions using calcium carbide were tested and the results were summarized in Table 3.11.

According to Jiang's report [29], ascorbate and 30% copper iodide were placed in the reaction to increase rate of azide-alkyne cyclo-addition. However, three conditions of room temperature, heat at 90 $^{\circ}$C, or use of 15 minutes Microwaves irradiation gave similar results. The reactions resulted in the formation of 1,2-di-4-tolylethyne **B** in 82% -89% yields, without formation of cycloaddition product **A** or **C** (Table 3.11, entries 1-3). There was no reaction occurred, if palladium catalyst was not present (entry 4). The results indicated that a ryl iodide-alkyne coupling is faster than azide-alkyne cyclo-addition, and 1,2 -di-4-tolylethyne product is not reactive enough to react with sodium azide under these conditions.

3.3.8 Synthesis of unsymmetrical diaryl ethynes

The synthesis of unsymmetrical diaryl ethynes is one of the challenging tasks. Here are the preliminary results using an electron-deficient 4-nitroiodobenzene with the electron-rich 4-iodoanisole or 4-iodotoluene. The cross coupling results under the optimized condition of 4-nitro iodobenzene with 4-iodotoluene is show in Scheme 3.11. The unsymmetrical 1 -methyl-4-((4-nitrophenyl)ethynyl)benzene (**2y**) was found in 9% yield along with 30% of 1,2 -di-4-tolylethyne (**2b**) and 42% of 1,2 -bis(4-nitrophenyl)ethyne (**2r**). On the other hand, when the same reaction was used with *p*-iodoanisole (Scheme 3.12), The unsymmetrical product **2z** was not observed in this reaction, but two symmetrical products **2r** and **2f** were afforded in moderate yields.
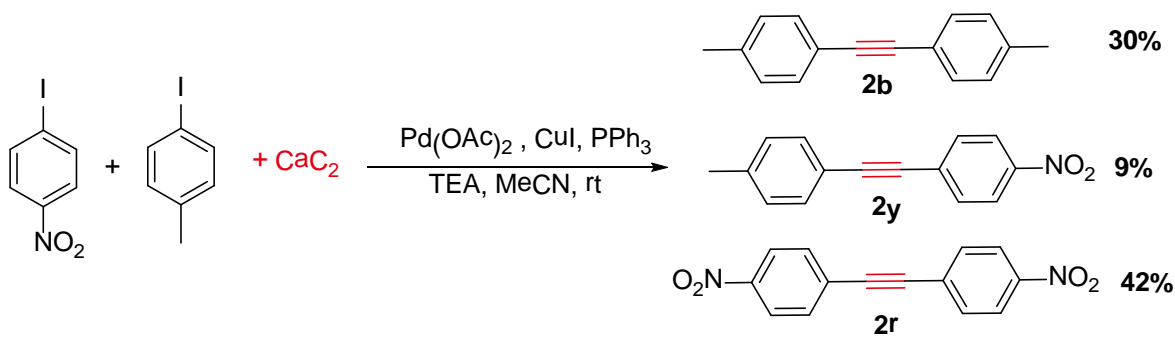

Scheme 3.11 Coupling of 4-nitro iodobenzene, 4-iodotoluene, and calcium carbide
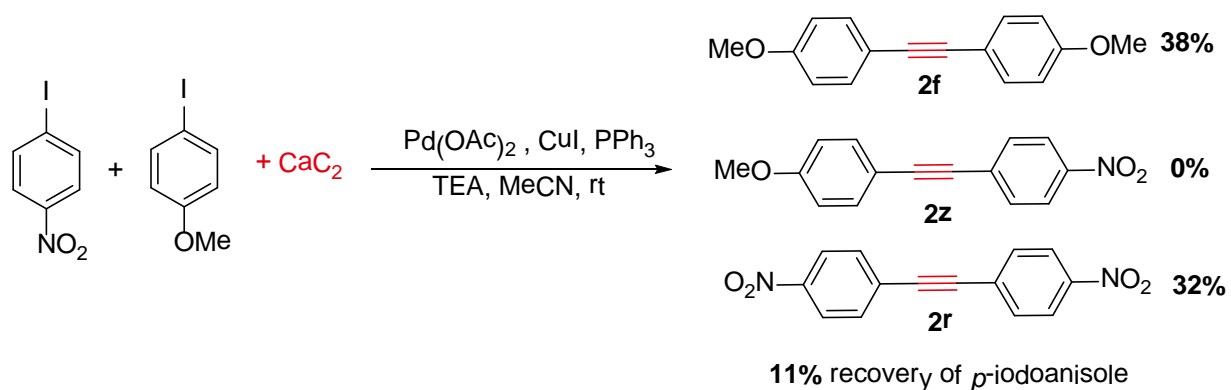
Scheme 3.12 Coupling of 4-nitro iodobenzene, 4-iodoanisole, and calcium carbide

Based on our study on effect of moisture we would like to propose a mechanism for palladium catalyst coupling reaction of calcium carbide and aryl iodide. The mechanism is illustrated in Scheme 3.13. We hypothesized that the reaction mechanism starts with a first molecule of acetylene gas, produced from calcium carbide and moisture, reacting with copper iodide to give copper acetylide. It then releases hydrogen iodide (HI), which can continuously generate more acetylene by reacting with calcium carbide. Next, the copper acetylide is trans- metalated with the palladium complex species formed by the oxidative addition between palladium(0) and aryl iodide. The resulting palladium-aryl-alkyne complex undergoes reductive elimination to form aryl acetylene. The aryl acetylene is again driven through reaction cycles and transformed into the desired product, diaryl ethynes.

The greater yield of **2r** in Scheme 3.11 is an opposite results compared to Zhang's work in 2006 [30], since the rate determining step may be difference. In Zhang's work, the rate determining step is transmetalation of aryl acetylide to palladium complex. However, in this work, rate determining step is the oxidative addition, which is known as general RDS in Sonogashira coupling (Scheme 3.13). Therefore, electron withdrawing groups substituent is a weak nucleophile and cannot transmetalate in Zhang works, but greater ability to oxidative addition of palladium due to weak Ar-I bond. However, in our work, even electron donating groups substituent containing compounds give lower rate compare to electron withdrawing one, product yields great for the both cases. For the results in section 3.4.4, unsymmetrical diaryl ethyne **2z** in Scheme 3.12 cannot be observed. This due to the much higher rate of oxidative addition of nitro compound and **2r** is rapidly formed. Thus, when anisole compound undergo
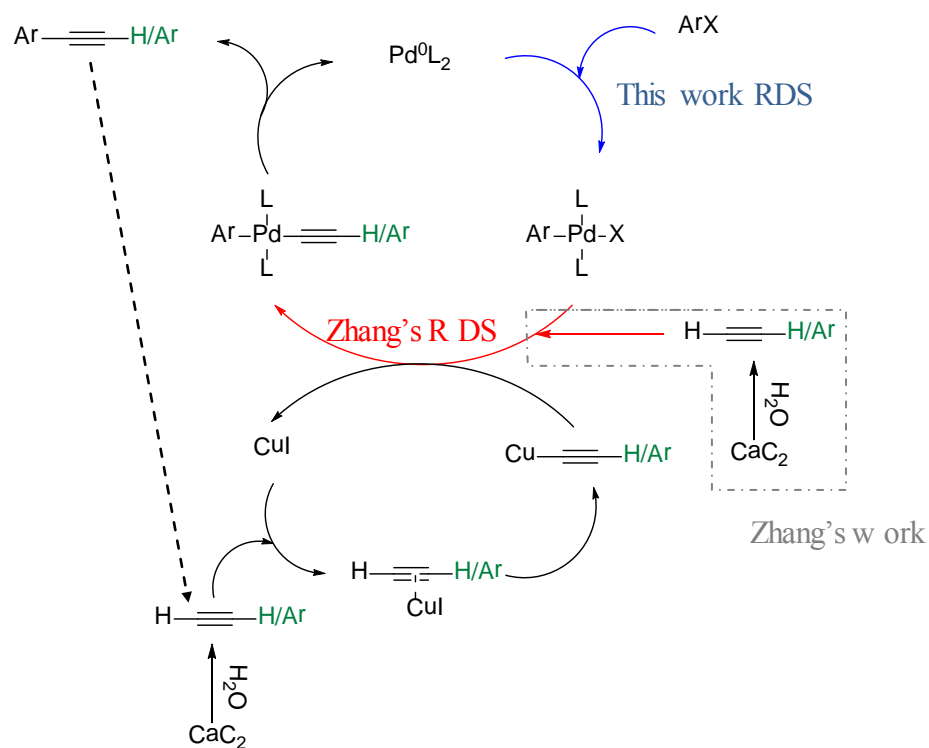
Scheme 3.13 Reaction mechanism and rate determining steps

oxidative addition, no nitro compound left in the reaction to form unsymmetrical diaryl ethynes. When using 4-iodotoluene with nitro compound in Scheme 3.11, rate of oxidative addition is not much difference. Some iodotoluene can undergo oxidative addition with palladium while that **2r** is not completely formed. Thus some **2y** could be observed.

CHAPTER IV
CONCLUSION

In conclusion, we have demonstrated a synthetic method to synthesize symmetrical diaryl ethynes directly from basic chemical feedstock, calcium carbide, via a Pd-catalyzed coupling reaction. The reactions were carried out under mild conditions in undried solvent, and the product can be purified by a simple filtration through a bed of silica gel. Also, inexpensive and commercially available reagents were used in the reaction. Aryl bromide, phenyl 4-methylbenzenesulfonate, and phenyl 4-methylbenzenesulfonate were not suitable for the reaction under these conditions. However, the synthesized or commercial aryl iodides have been subjected to the coupling reaction with calcium carbide under the optimized condition. The aryl iodide containing either electron-donating or electron-withdrawing group, as well as highly conjugated steric moeity were successfully proceeded in this reaction to afford the symmetrical diaryl ethynes in excellent yields. In addition, we demonstrated that the aryl iodides bearing the reactive functional groups such as bromo, tosyl, or trimethylsilyl can be tolerate in this reaction to produce the target products in good yields. Mechanistically, we found that water is necessary for the reaction. The reaction may initiate with a slow release of acetylene from the hydrolysis of calcium carbide with water. Then the acetylene gas will drive through the known Sonogashira coupling process. Thus, this transformation is proven to be an efficient process for the preparation of symmetrical diaryl ethynes.

REFERENCES

[1] King, A. O.; Okukado, N.; Negishi, E. Highly General Stereo-, Regio- and Chemoselective Synthesis of Terminal and Internal Conjugated Enynes by the Pd-Catalyzed Reactions of Alkynylzinc Reagents with Alkenyl Halides. *J. Chem. Soc. Chem. Comm*. **1977**, *19*, 683-684.

[2] Heck, R. F. Acylation, Methylation, and Carboxyalkylation of Olefins by Group VIII Metal Derivatives. *J. Am. Chem. Soc*. **1968**, *90*, 5518-5526.

[3] Miyaura, N.; Suzuki, A. Stereoselective Synthesis of Arylated (E)-alkenes by the Reaction of alk-1-enylboranes with Aryl Halides in the Presence of Palladium Catalyst. *J. Chem. Soc., Chem. Commun*. **1979**, 866-867.

[4] Milstein, D.; Stille, J. K. A General, Selective, and Facile Method for Ketone Synthesis from Acid Chlorides and Organotin Compounds Catalyzed by Palladium. *J. Am. Chem. Soc*. **1978**, *100*, 3636.

[5] Sonogashira, K.; Tohda, Y.; Hagihara, N. A Convenient Synthesis of Acetylenes: Catalytic Substitutions of Acetylenic Hydrogen with Bromoalkenes, Iodoarenes and Bromopyridines. *Tetrahedron Lett*. **1975**, *16*, 4467-4470.

[6] Nicolaou, K. C.; Bulger, P. G.; Sarla, D. Palldaium- Catlayzed Cross- Coupling Reaction in Total Synthesis. *Angew. Chem. Int. Ed*. **2005**, *44*, 4442-4489.

[7] Torborga, C.; Bellera, M. Recent Applications of Palladium-Catalyzed Coupling Reactions in the Pharmaceutical, Agrochemical, and Fine Chemical Industries. *Adv. Synth. Catal*. **2009**, *351*, 3027-3043.

[8] Chinchilla, R.; Najera, C. The Sonogashira Reaction: A Booming Methodology in Synthetic Organic Chemistry. *Chem. Rev*. **2007**, *107,* 874-922.

[9] Eckhardt, M.; Fu G. C. The First Applications of Carbene Ligands in Cross-Couplings of Alkyl Electrophiles: Sonogashira Reactions of Unactivated Alkyl Bromides and Iodides. *J. Am. Chem. Soc*. **2003***, 125,* 13642-13643.

[10] Yasuhara, A.; Kanamori, Y.; Kaneko, M.; Numata, A.; Kondo, Y.; Sakamoto, T. Convenient Synthesis of 2-substituted Indoles from 2-ethynylanilines
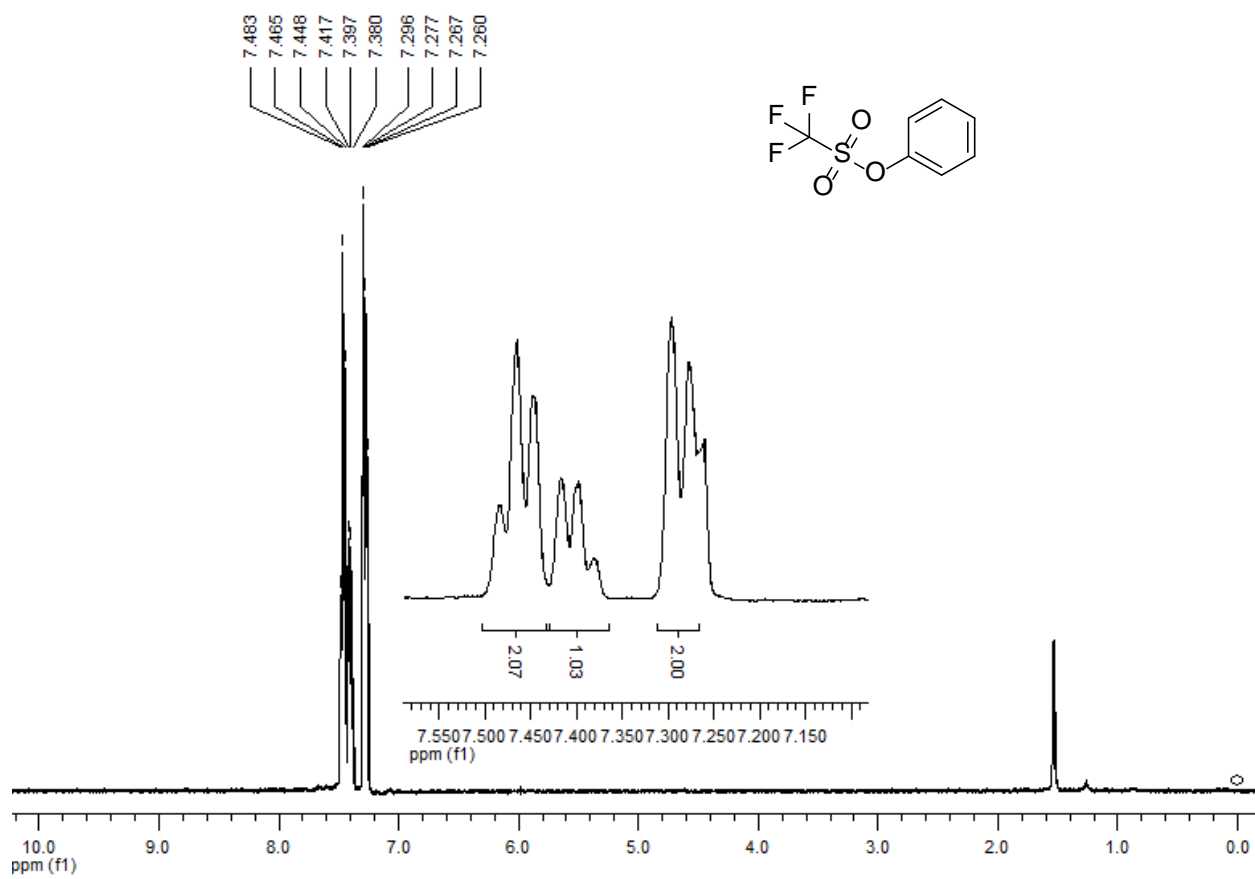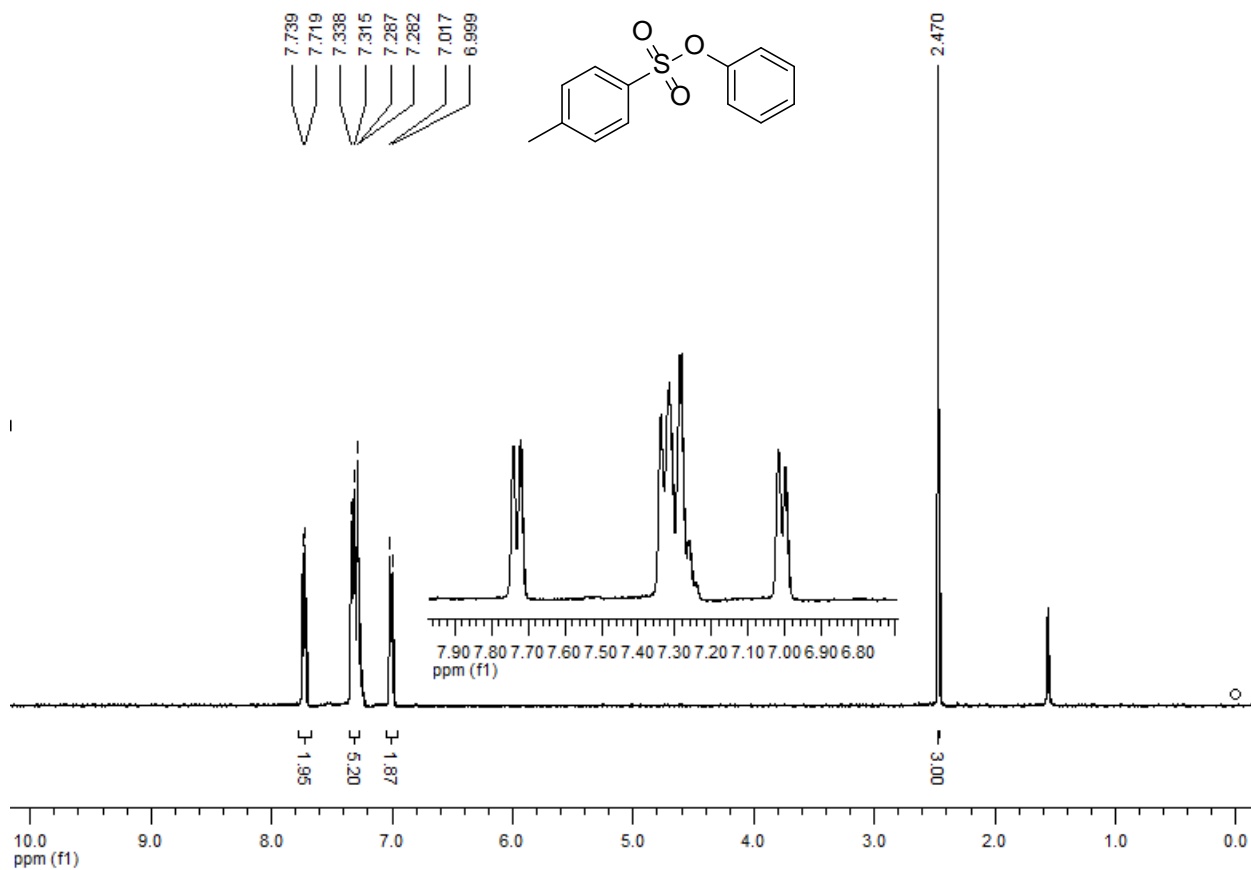
with Tetrabutylammonium Fluoride. *J. Chem. Soc, Perkin T rans. 1* **1999**, 529-534.

[11] Fiandanese, V .; B ottalico, D .; M archese, G .; P unzi, A . A Straightforward Synthesis of Indole and Benzofuran Derivatives. *Tetrahedron* **2008**, *64*, 53-60.

[12] Novak, Z.; Nemes, P.; Kotschy, A. Tandem Sonogashira Coupling: An Efficient Tool for the Synthesis of Diarylalkynes. *Org. Lett.* **2004**, *6*, 4917-4920.

[13] Siemsen, P.; Livingston, R.C.; Diederich, F. Acetylenic C oupling: A P owerful T ool in M olecular Construction. *Angew. Chem. Int. Ed.* **2000**, *39*, 2632-2657.

[14] Fusano, A .; F ukuyama, T .; N ishitani, S .; I nouye, T .; R yu, I . Synthesis of Alkyl Alkynyl K etones b y Pd/Light-Induced Three-Component Coupling Reactions of I odoalkanes, C O, and 1-Alkynes. *Org. Lett.* **2010,** *12*, 2410-2413.

[15] Liu, J .; Lam, J. Y.; Tang, B. Z. Acetylenic Polymers: Syntheses, Structures, and Functions. *Chem. Rev.* **2009,** *109,* 5799-5867.

[16] Mio, M . J.; K opel, L. C.; B raun, J. B.; G adzikwa, T. L.; H ull, K . L.; Brisbois, R. G.; Markworth, C . J .; G rieco, P . A . One-Pot S ynthesis o f S ymmetrical a nd Unsymmetrical Bisarylethynes by a M odification o f t he S onogashira Coupling Reaction. *Org. Lett.* **2002,** *4*, 3199-3202.

[17] Liang, Y.; Xie, Y. X .; L i, J . H . Modified P alladium-Catalyzed S onogashira C ross-Coupling R eactions u nder C opper-, A mine-, and Solvent-Free Conditions. *J. Org. Chem.* **2006**, *71*, 379-381.

[18] Severin, R.; Reimer, J.; Doye, S. One-Pot Procedure for the Synthesis of Unsymmetrical Diarylalkynes. *J. Org. Chem.* **2010**, *75*, 3518-3521.

[19] Yamashita, M .; H origuchi, H .; H irano, K . Fused R ing C onstruction a round P yrrole, Indole, a nd R elated C ompounds v ia P alladium-Catalyzed O xidative Coupling with Alkynes. *J. Org. Chem.* **2009**, *74*, 7481-7488.

[20] Li, C .; S alaven, W .; J ohn, V . Palladium Catalysed Polymerization o f Aryl Diodides with Acetylene gas i n Aqueous Medium: a Novel Synthesis of
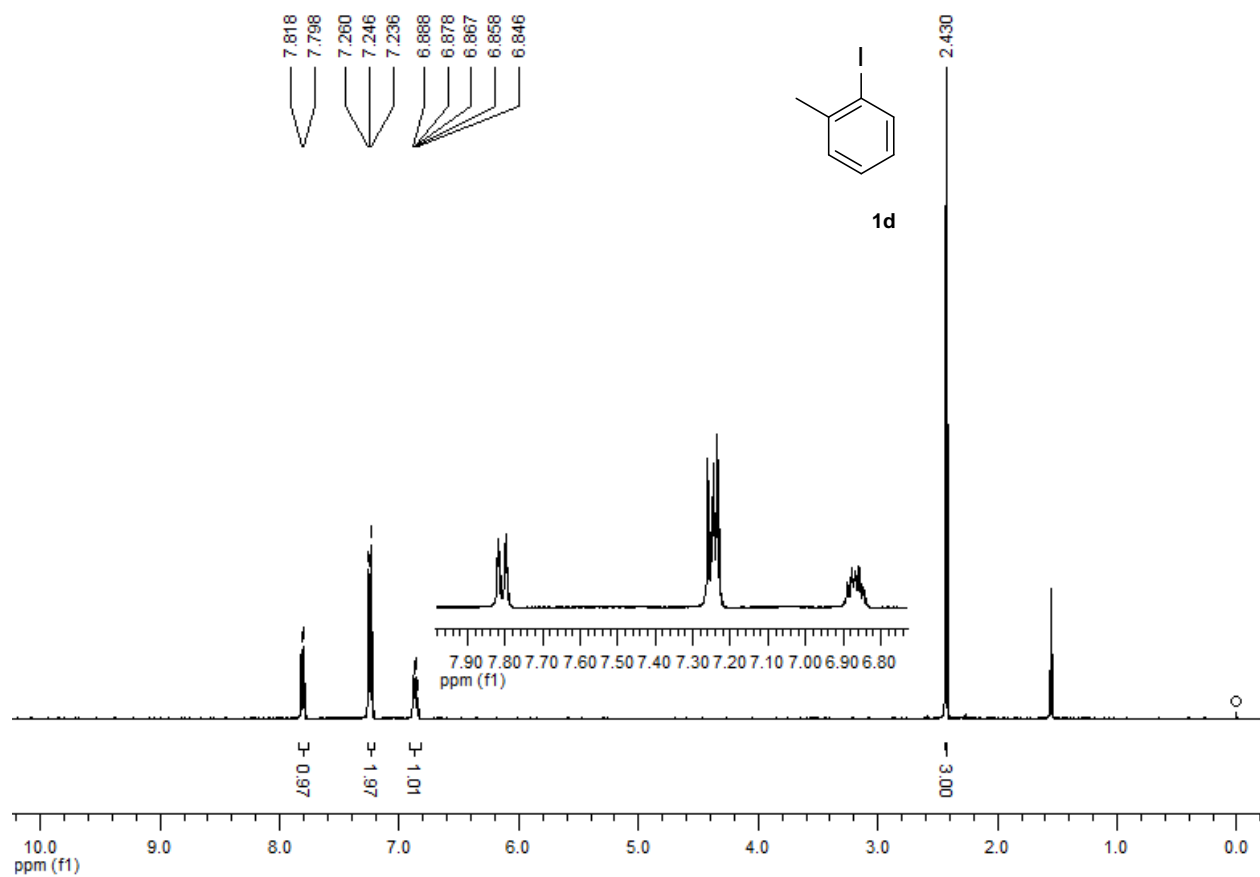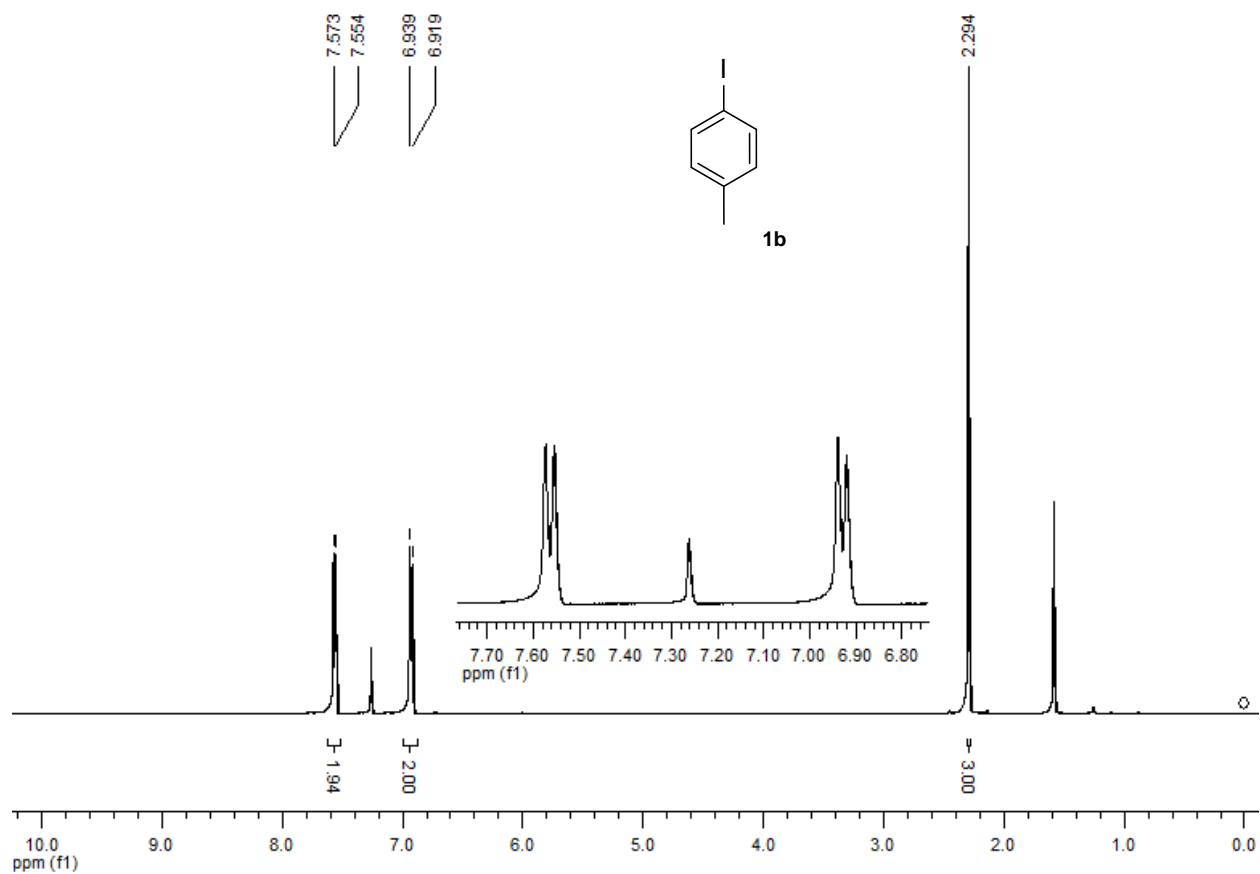
Areneethynylene Polymers Andoligomers. *Chem. Commun.* **1997**, 1569-1570.

[21] Iyoda, M.; Vorasingha, A.; Kuwatani, Y. A One-step Synthesis of Dehydro[12]annulenes Using Palladium-catalyzed Reaction of o-diiodoarenes with Acetylene Gas. *Tetrahedron Lett.* **1998**, *39*, 4701-4704.

[22] Bunz, U. H. F. Poly(aryleneethynylene)s. *Macromol. Rapid Commun.* **2009**, *30*, 772-805.

[23] Li, C.; Li, D.; Costello, C. Highly Efficient Palladium-Catalyzed Coupling of Acetylene Gas with Aryl Iodides in Aqueous Medium. *Org. Process Res. Dev.* **1997**, *1*, 325-327.

[24] Pal, M.; Kundu, N. An Improved Procedure for the Synthesis of Substituted Acetylenes from the Reaction of Acetylene Gas with Aryl Iodides under Palladium-copper Catalysis. *J. Chem. Soc, Perkin Trans 1* **1995**, 449-451.

[25] Moon, J.; Jeong, M.; Nam, H.; Ju, J.; Moon, J. H.; Jung, H. M.; Lee, S. One-Pot Synthesis of Diarylalkynes Using Palladium-Catalyzed Sonogashira Reaction and Decarboxylative Coupling of sp Carbon and sp2 Carbon. *Org. Lett.* **2008**, *10*, 945-948.

[26] Csekei, M.; Novak, Z.; Kotschy, A. Ethynyl-cyclohexanol: an Efficient Acetylene Surrogate in Sonogashira Coupling. *Tetrahedron*, **2008**, *64*, 975–982.

[27] Pang, L. L.; Bi, J. Q.; Bai, Y. J.; Zhu, H. L.; Qi, Y. Z.; Wang, C. G.; Han, F. D.; Li, S. J. Synthesis of Carbon Spheres via a Low-Temperature Metathesis Reaction. *J. Phys. Chem. C.* **2008**, *112*, 12134-12137.

[28] Cataldo, F. A Method for Synthesizing Polyynes in Solution. *Carbon* **2005**, *43*, 2792-2800.

[29] Jiang, Y.; Kuang, C.; Yang, Q. The Use of Calcium Carbide in the Synthesis of 1-Monosubstituted Aryl 1,2,3-Triazole via Click Chemistry. *Synlett* **2009**, *19*, 3163-3166.
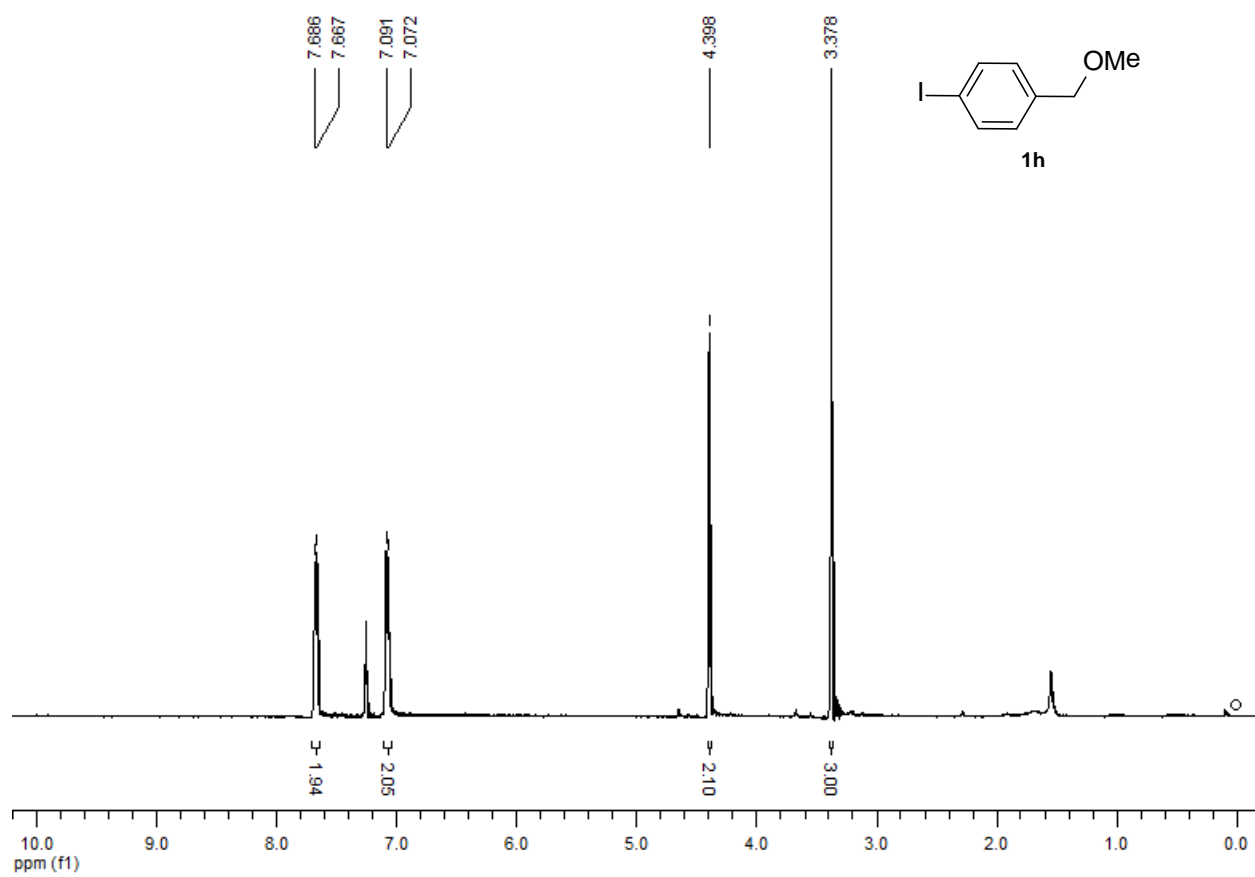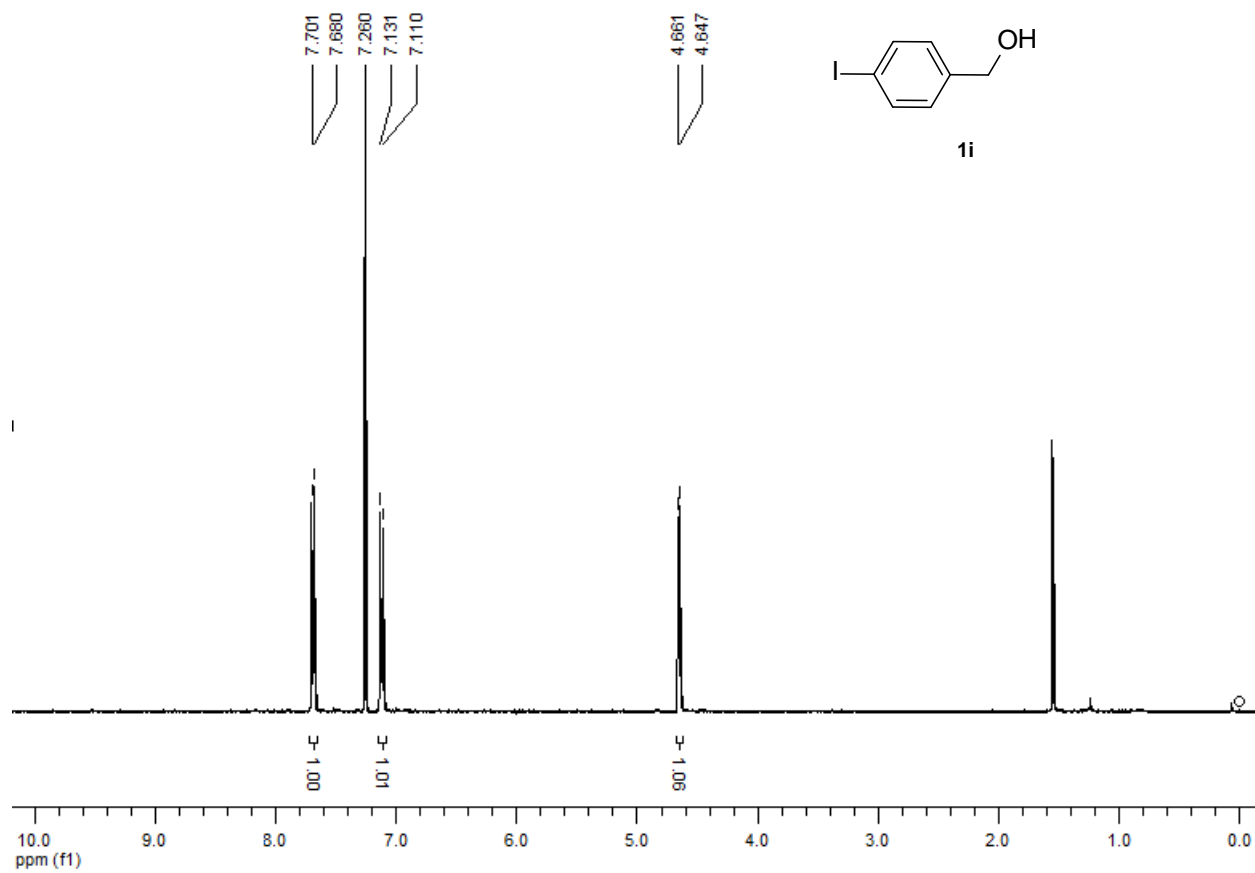
[30] Zhang, W.; Wu, H.; Liu, Z.; Zhong, P.; Zhang, L.; Huang, X.; Cheng, J. <u>The Use o f Calcium Carbide i n One-pot Synthesis o f Symmetric Diaryl Ethynes.</u> *Chem. Commun.* **2006**, *46*, 4826-4828.

[31] Patnaik, Pradyot (2003). <u>Handbook of Inorganic Chemical Compounds</u> *McGraw-Hill.* ISBN 0070494398. Retrieved 2009-06-06.

[32] L anghammer, B . <u>Calcium C arbide Ullmann's E ncyclopedia o f I ndustrial Chemistry</u> *Wiley Interscience*, **2006**.

[33] Abeles, F. B .; G ahagan, H . E . I II. <u>Abscission: T he R ole o f E thylene, E thylene Analogues, C arbon D ioxide, a nd O xygen</u> *Plant P hysiol.,* **1968,** *43*, 1255 – 1258.

[34] Dun, Y. <u>Troubles in t he P VC i ndustry</u> *Hong K ong T rade D evelopment C ouncil,* **2006**.

[35] Greenwood, Norman N.; Earnshaw, A. <u>Chemistry of the Elements</u> *Oxford: Butterworth-Heinemann*, **1997,** (2nd ed.)

[36] Ray, F . E .; S awicki, E .; Borum, O.H. *Cancer research laboratory, university of Florida*, **1952**, *74*, 1247-1249.

[37] Y um, E. K .; S on, J. W .; K im, S. K .; K im, S. N .; Kim, K. M.; Lee, C. W. <u>Synthesis of Functionalized Bisarylacetylene D erivatives f rom A cetylene G as O ver Nano-sized Carbon Ball Supported Palladium Catalyst.</u> *Bull. K orean C hem. Soc.* **2010**, *31,* 2097-2099.

[38] Severin, R.; Reimer, J.; Doye, S. <u>One-Pot Procedure for the Synthesis of Unsymmetrical Diarylalkynes.</u> *J. Org. Chem.* **2010**, *75*, 3518–3521.

[39] Shirakawa, E .; K itabata, T .; O tsuka, H .; T suchimoto, T . <u>A Simple Catalyst System for t he Palladium-catalyzed Coupling of Aryl Halides with Terminal Alkynes.</u> *Tetrahedron* **2005**, *61*, 9878-9885.

[40] Novak, Z.; S zabo, A .; R epasi, J.; K otschy, A. <u>Sonogashira C oupling o f A ryl H alides Catalyzed by Palladium on Charcoal.</u> *J. Org. Chem.* **2003**, *68*, 3327-3329.
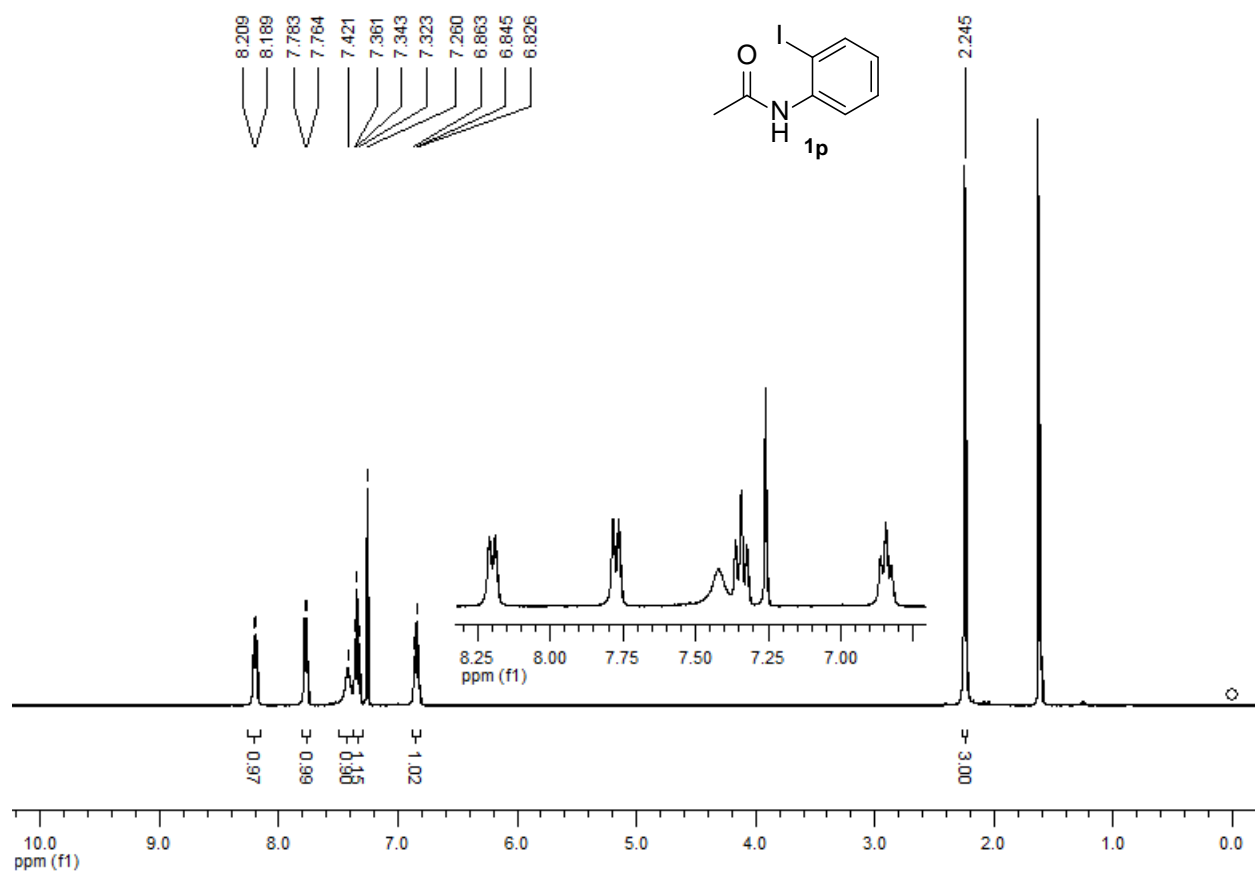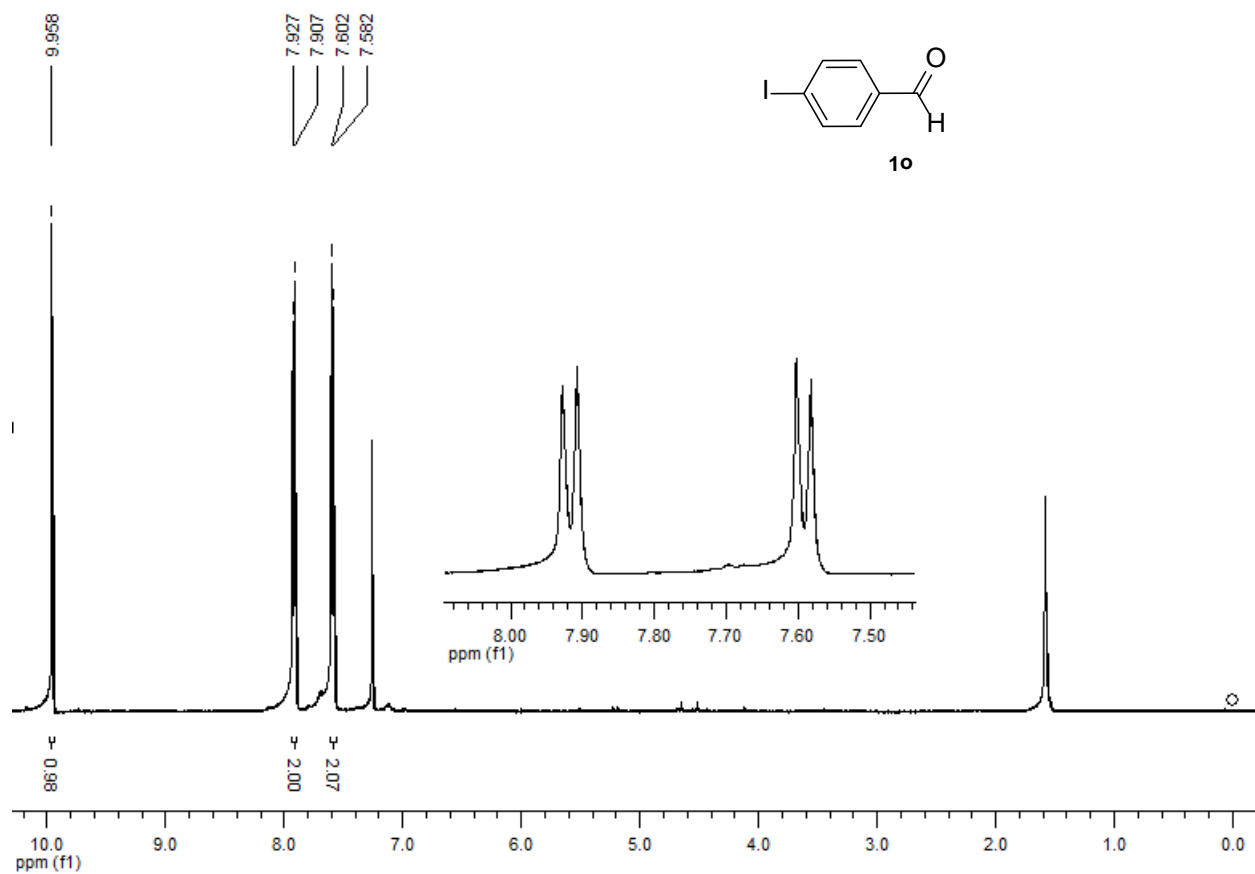
[41] Wackerly, J. M .; M oore, J . S . <u>Cooperative Self-Assembly of Oligo(m-phenyleneethynylenes) into Supramolecular Coordination Polymers.</u> *Macromolecules* **2006**, *39*, 7269–7276.

[42] Tour, J. M. Molecular Electronics. <u>Synthesis and T esting o fC omponents.</u> *Acc. Chem. Res.* **2000**, *33*, 791-804.

[43] Martin, R. E.; Diederich, F. <u>Linear Monodisperse π-Conjugated O ligomers:M odel Compounds for Polymers and More.</u> *Angew. Chem. Int. Ed.* **1999**, *38*, 1350-1377.

[44] Bunz, U . H . F . <u>Poly(aryleneethynylene)s: Syntheses, Properties, Structures, and Applications.</u> *Chem. Rev.* **2000**, *100*, 1605-1644.

[45] Weder, C. <u>Synthesis, Processing a nd Properties of Conjugated Polymer Networks.</u> *Chem. Commun.* **2005**, 5378-5389.

[46] Vongnam, K . <u>Phenylene Ethynelene Dendrimer for Fluorescent DNA Sensor</u> *Program i n P etrochemistry and P olymer Sc ience, C hulalongkorn University,* **2010**.

[47] M a, D .; L ui, F. <u>CuI-catalyzed Coupling Reaction o f Aryl Halides with Terminal Alkynes in the Absence of Palladium and Phosphine.</u> *Chem. C ommun.* **2004**, 1934-1935.

[48] Appukkuttan, P.; Dehaen, W.; F okin, V.V.; E ycken, E. V. D. A <u>Microwave-Assisted Click C hemistry S ynthesis o f 1 ,4-Disubstituted 1,2,3 -Triazoles via a Copper(I)-Catalyzed Three-Component Reaction.</u> *Org. Lett.* **2004,** *6*, 4223-4225.
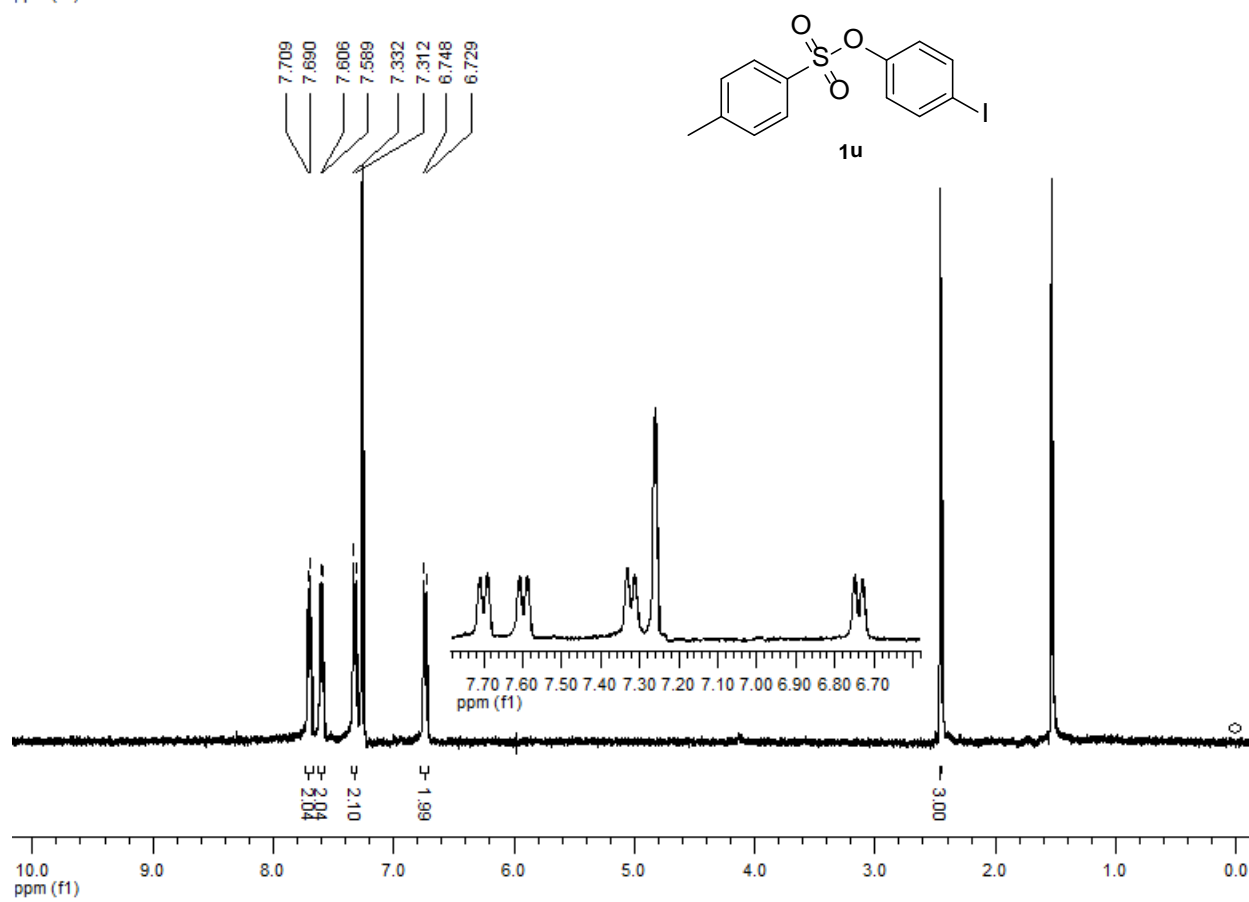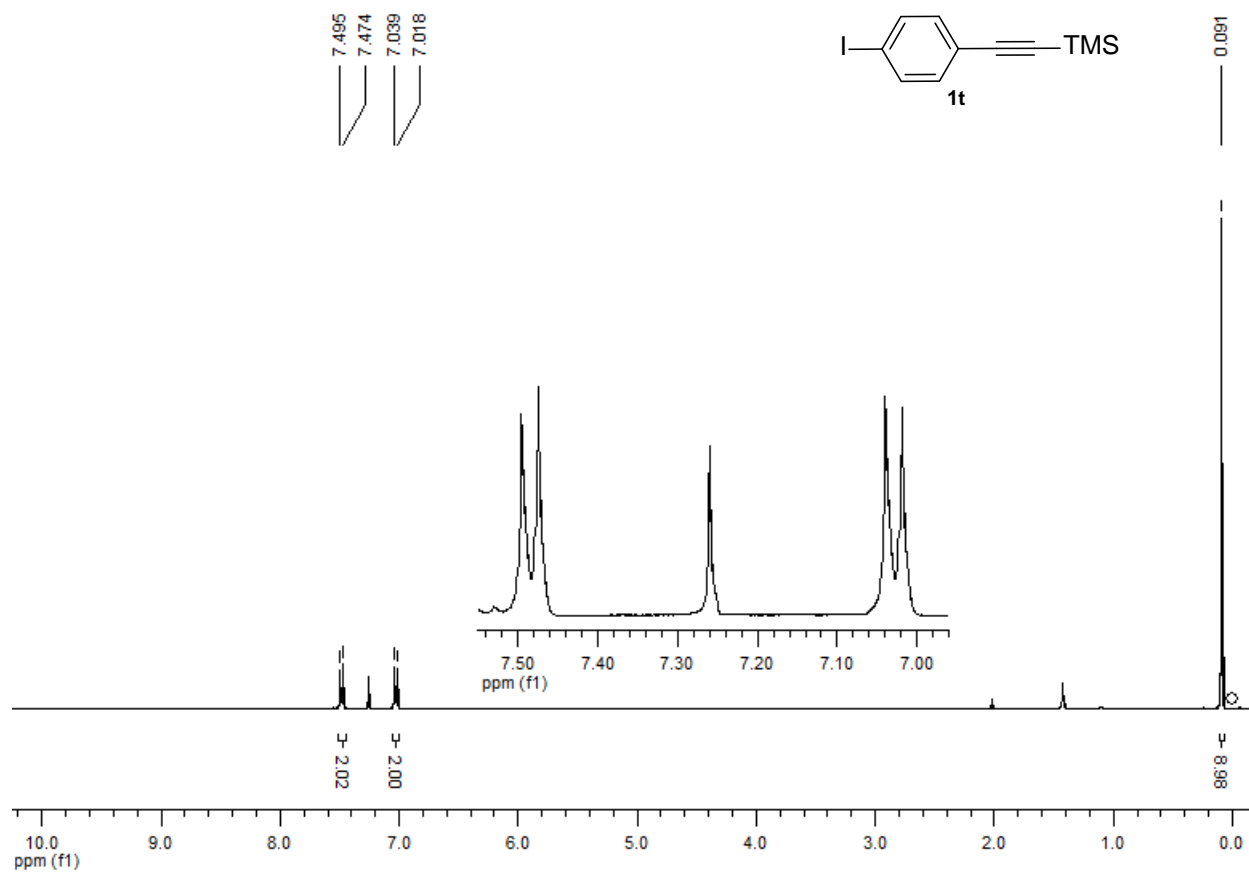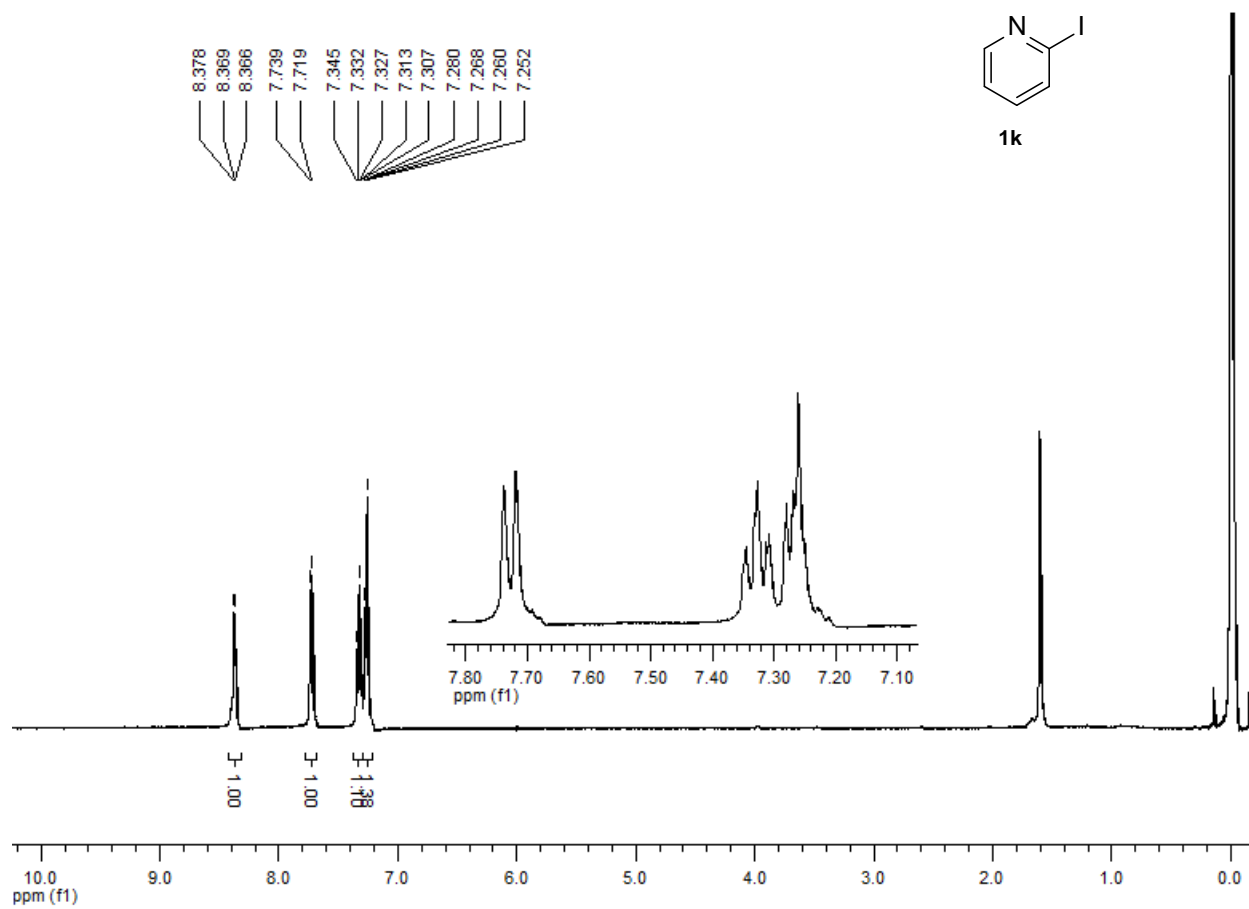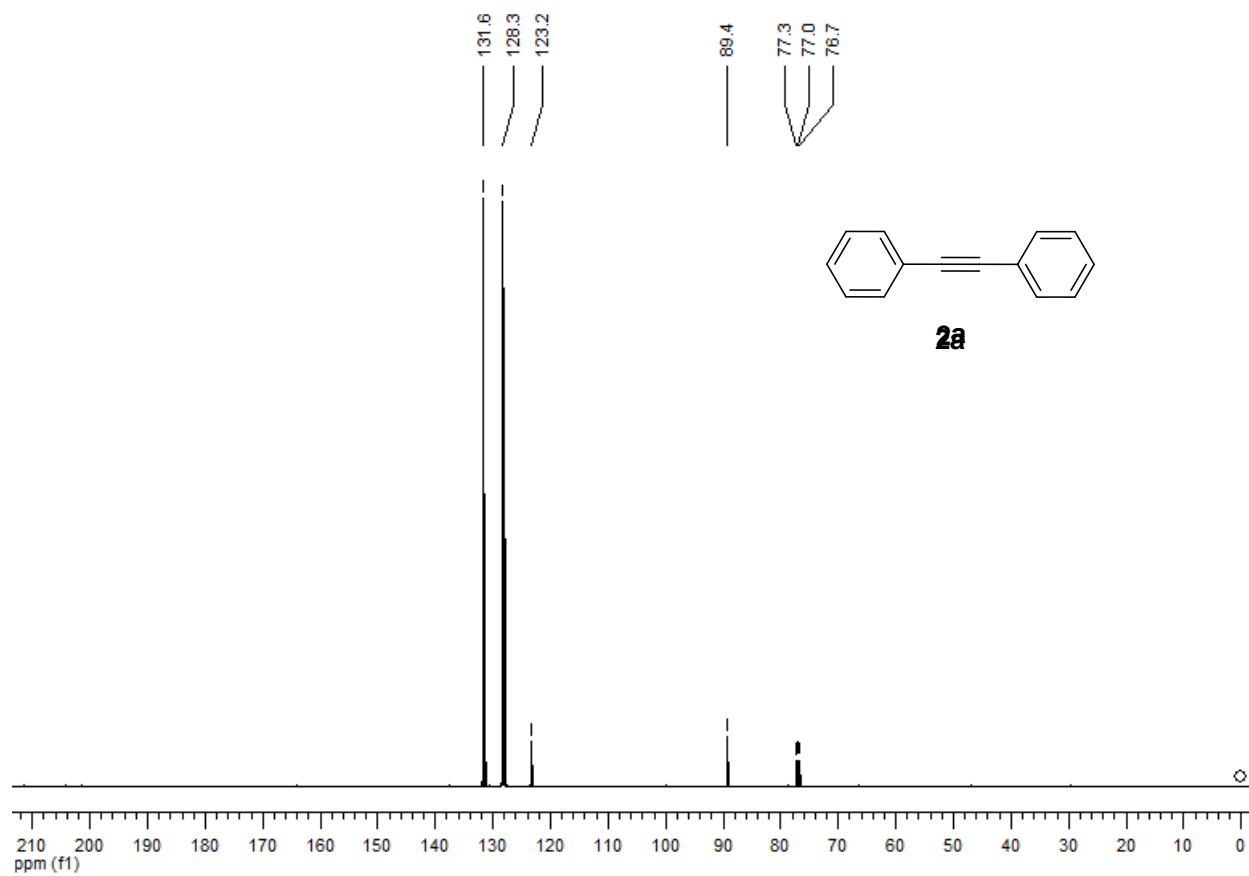
Appendix

7.739
7.719
7.338
7.315
7.287
7.282
7.017
6.999

2.470

7.90 7.80 7.70 7.60 7.50 7.40 7.30 7.20 7.10 7.00 6.90 6.80
ppm (f1)

1.95
5.20
1.87

3.00

10.0
ppm (f1)
9.0   8.0   7.0   6.0   5.0   4.0   3.0   2.0   1.0   0.0

7.483
7.465
7.448
7.417
7.397
7.380
7.296
7.277
7.267
7.260

7.550 7.500 7.450 7.400 7.350 7.300 7.250 7.200 7.150
ppm (f1)

2.07
1.03
2.00

10.0
ppm (f1)
9.0   8.0   7.0   6.0   5.0   4.0   3.0   2.0   1.0   0.0

1b

1d

7.701
7.680
7.260
7.131
7.110

4.661
4.647

OH

I

1i

10.0   9.0   8.0   7.0   6.0   5.0   4.0   3.0   2.0   1.0   0.0
ppm (f1)

1.00   1.01   1.06

7.688
7.667
7.091
7.072

4.398

3.378

OMe

I

1h

10.0   9.0   8.0   7.0   6.0   5.0   4.0   3.0   2.0   1.0   0.0
ppm (f1)

1.94   2.05   2.10   3.00

9.958

7.927
7.907
7.602
7.582

1o

8.00   7.90   7.80   7.70   7.60   7.50
ppm (f1)

0.98

2.00

2.07

10.0   9.0   8.0   7.0   6.0   5.0   4.0   3.0   2.0   1.0   0.0
ppm (f1)

8.209
8.189
7.783
7.764
7.421
7.361
7.343
7.323
7.260
6.863
6.845
6.826

2.245

1p

8.25   8.00   7.75   7.50   7.25   7.00
ppm (f1)

0.97

0.99

1.15
0.96

1.02

3.00

10.0   9.0   8.0   7.0   6.0   5.0   4.0   3.0   2.0   1.0   0.0
ppm (f1)

7.495
7.474
7.039
7.018

0.091

1t

I — ⬡ — ≡ — TMS

7.50 7.40 7.30 7.20 7.10 7.00
ppm (f1)

2.02
2.00
8.98

10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0.0
ppm (f1)

7.709
7.690
7.606
7.589
7.332
7.312
6.748
6.729

1u

7.70 7.60 7.50 7.40 7.30 7.20 7.10 7.00 6.90 6.80 6.70
ppm (f1)

2.84
2.04
2.10
1.99
3.00

10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0.0
ppm (f1)

8.378
8.369
8.366
7.739
7.719
7.345
7.332
7.327
7.313
7.307
7.280
7.268
7.260
7.252

1k

7.80 7.70 7.60 7.50 7.40 7.30 7.20 7.10
ppm (f1)

1.00 1.00 1.38

10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0.0
ppm (f1)

7.611
7.603
7.597
7.591
7.587
7.395
7.384
7.381

2a

7.650 7.600 7.550 7.500 7.450 7.400 7.350
ppm (f1)

4.00
6.03

10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0.0
ppm (f1)

131.6
128.3
123.2
89.4
77.3
77.0
76.7

2a

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
ppm (f1)

2a

2b

138.2
131.4
129.1
120.4
88.9
77.3
77.0
76.7
21.5

2b

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
ppm (f1)

%Reflectance

3018.41
2917.88
2843.95

2b

4000 3500 3000 2500 2000 1500 1000
Wavenumbers (cm-1)

¹H NMR peaks: 7.539, 7.521, 7.260, 7.248, 7.212, 7.192, 7.171, 2.547

26

Integrations: 2.00, 6.19, 5.95

ppm (f1): 10.0, 9.0, 8.0, 7.0, 6.0, 5.0, 4.0, 3.0, 2.0, 1.0, 0.0

Inset ppm (f1): 7.50, 7.40, 7.30, 7.20, 7.10

¹³C NMR peaks: 139.9, 131.9, 129.5, 128.2, 125.6, 123.3, 92.3, 77.3, 77.0, 76.7, 20.9

26

ppm (f1): 210, 200, 190, 180, 170, 160, 150, 140, 130, 120, 110, 100, 90, 80, 70, 60, 50, 40, 30, 20, 10, 0

%Reflectance

3050.94

2917.88

Wavenumbers (cm-1)

2e

7.369
7.354
7.334
7.260
7.242
7.223
7.158
7.139

2.361

2d

7.400 7.350 7.300 7.250 7.200 7.150 7.100 7.050
ppm (f1)

10.0   9.0   8.0   7.0   6.0   5.0   4.0   3.0   2.0   1.0   0.0
ppm (f1)

2d

8.630
8.610
7.636
7.620
7.669
7.692
7.676
7.658
7.655
7.611
7.593
7.576
7.558
7.537
7.519

2e

8.708.608.508.408.308.208.108.007.907.807.707.607.507.40
ppm (f1)

2.00   6.12   3.18
              2.08

10.0   9.0   8.0   7.0   6.0   5.0   4.0   3.0   2.0   1.0   0.0
ppm (f1)

133.2
130.6
128.9
128.4
126.9
126.5
126.3
125.3
121.0

92.4

77.3
77.0
76.7

2e

133.2   130.6   128.9   128.4   126.9   126.5   126.3   125.3

133.8 132.5 131.3 130.0 128.8 127.5 126.3 125.0
ppm (f1)

210   200   190   180   170   160   150   140   130   120   110   100   90   80   70   60   50   40   30   20   10   0
ppm (f1)

2e

2f

8.757

7.321
7.300
6.824
6.803

HO—⟨ ⟩—≡≡—⟨ ⟩—OH

2g

7.30 7.20 7.10 7.00 6.90 6.80
ppm (f1)

0.34

1.00

1.04

10.0   9.0   8.0   7.0   6.0   5.0   4.0   3.0   2.0   1.0   0.0
ppm (f1)

207.2

159.4

134.6

117.4
117.3
116.5

89.4

31.4
31.2
31.0
30.8
30.6
30.4
30.3

HO—⟨ ⟩—≡≡—⟨ ⟩—OH

2g

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
ppm (f1)

7.528
7.508
7.329
7.313
7.260

4.467

3.400

MeO — OMe

2h

7.60 7.50 7.40 7.30 7.20
ppm (f1)

3.98 4.00   9.05   5.83

10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0.0
ppm (f1)

138.4
132.5
131.6
127.5
122.4

89.2

77.3
77.0
76.7
74.2

58.1

MeO — OMe

2h

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
ppm (f1)

2h

Peaks labeled: 3003.63, 2923.79, 2864.65

2i

Peaks labeled: 7.537, 7.521, 7.366, 7.356, 4.724, 3.414, 3.411

Integrations: 3.97, 4.00, 3.82, 0.85

10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0.0
ppm (f1)

143.4 132.6 131.5 127.1 127.1 120.9 89.4 62.9 40.1 39.8 39.6 39.4 39.2 39.0 38.8

HO

OH

2i

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
ppm (f1)

7.311 7.309 7.299 7.282 7.260 7.021 7.013

2k

7.30 7.20 7.10 7.00 6.90
ppm (f1)

3.96 2.00

10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0.0
ppm (f1)

132.1
127.6
127.1
122.9

86.2
77.3
77.0
76.7

2k

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
ppm (f1)

3101.21
3080.51

%Reflectance

2k

4000 3500 3000 2500 2000 1500 1000
Wavenumbers (cm-1)

7.970
7.949
7.643
7.622
7.260

2.624

2l

4.00
3.97
6.00

10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (f1)

8.00
7.90
7.80
7.70
7.60
ppm (f1)

197.2
136.6
131.8
128.3
127.5
91.6
77.3
77.0
76.7
26.6

2l

210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm (f1)

IR spectrum with peaks labeled: 3080.51, 2843.95, 2740.46, 1687.78. Structure labeled **2m**.

^{1}H NMR spectrum with peaks at 8.325, 8.323, 8.310, 8.306, 7.893, 7.889, 7.884, 7.517, 7.469, 7.430, 7.410, 7.390, 7.260, 7.153, 7.133, 7.115, 2.249. Structure labeled **2n**.

8.043
8.023
7.609
7.589
7.260

3.929

4.00
4.20
5.96

166.4

131.6
129.9
129.6
127.3

91.4

77.3
77.0
76.7

52.2

2θ

2o

2p

2p

2p

7.497
7.476
7.387
7.366
7.260

Br—⬡—≡—⬡—Br
2q

7.550 7.500 7.450 7.400 7.350
ppm (f1)

10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0.0
ppm (f1)

133.0
131.7
122.8
121.8
89.4
77.3
77.0
76.7

Br—⬡—≡—⬡—Br
2q

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
ppm (f1)

2q

3074.60
2923.79

7.451
7.440

0.256

Me₃Si—————————SiMe₃

2f

7.4600 7.4550 7.4500 7.4450 7.4400 7.4350
ppm (f1)

8.00

17.94

10.0   9.0   8.0   7.0   6.0   5.0   4.0   3.0   2.0   1.0   0.0
ppm (f1)

131.9
131.4
123.0

104.5

96.5
91.0

77.3
77.0
76.7

-0.1

Me₃Si—≡—⟨benzene⟩—≡—⟨benzene⟩—≡—SiMe₃

2F

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
ppm (f1)

7.714
7.695
7.419
7.400
7.325
7.306
7.260
6.983
6.964

2.450

TsO—⟨benzene⟩—≡—⟨benzene⟩—OTs

2S

7.70 7.60 7.50 7.40 7.30 7.20 7.10 7.00
ppm (f1)

4.00
4.08
4.08
4.12

6.00

10.0   9.0   8.0   7.0   6.0   5.0   4.0   3.0   2.0   1.0   0.0
ppm (f1)

149.4
145.6
132.9
129.8
128.5
122.6
121.9
89.0
77.3
77.0
76.7
21.7

TsO—⬡—≡≡—⬡—OTs

2§

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
ppm (f1)

%Reflectance

3039.11
2920.83
1590.20

TsO—⬡—≡≡—⬡—OTs

2§

4000 3500 3000 2500 2000 1500 1000
Wavenumbers (cm-1)

¹H NMR and ¹³C NMR spectra of compound **2t**.

IR spectrum of **2t** with peaks at 2956.32, 2864.65, 2205.25, 1708.48 cm⁻¹.

¹H NMR spectrum of **2u**. Peaks: 8.042, 8.022, 7.605, 7.585, 7.260, 7.052, 7.035, 4.357, 4.351, 4.341, 4.335, 4.162, 4.147, 4.132, 3.930, 2.194, 2.178, 2.056, 2.048. Integrations: 3.99, 4.00, 3.88, 7.99, 8.02, 6.12, 8.13, 12.01.
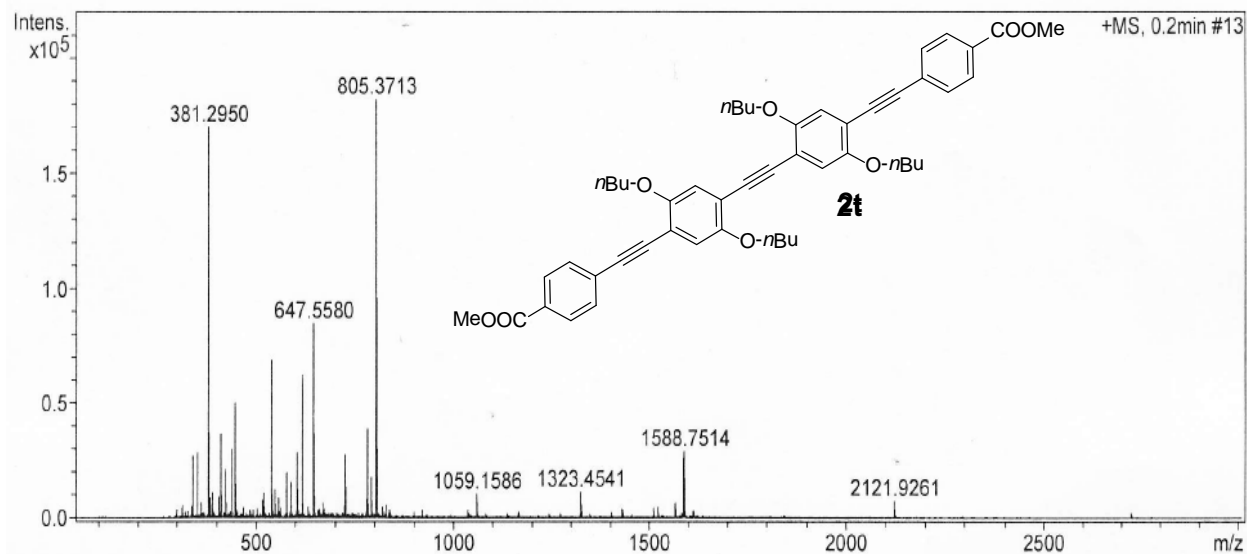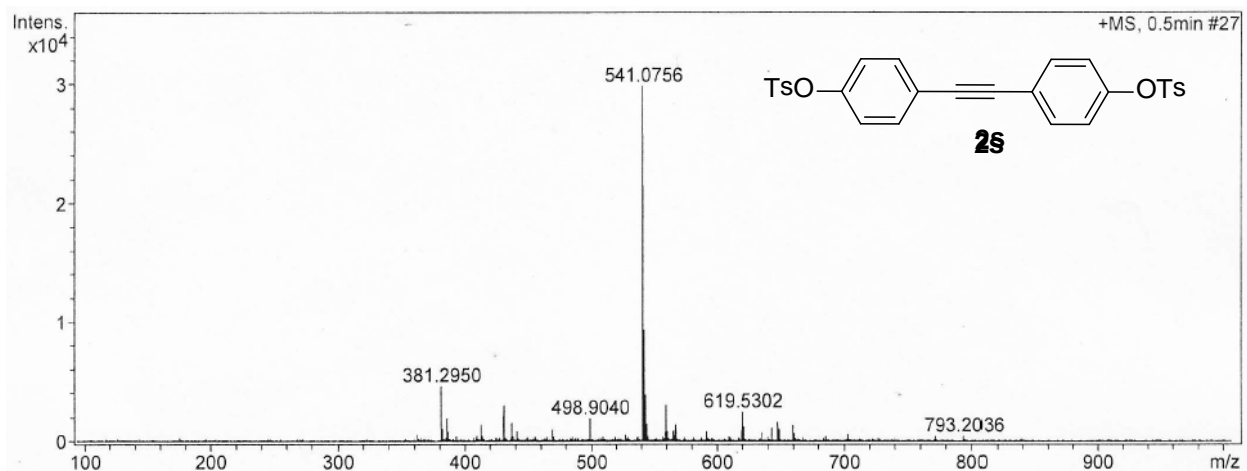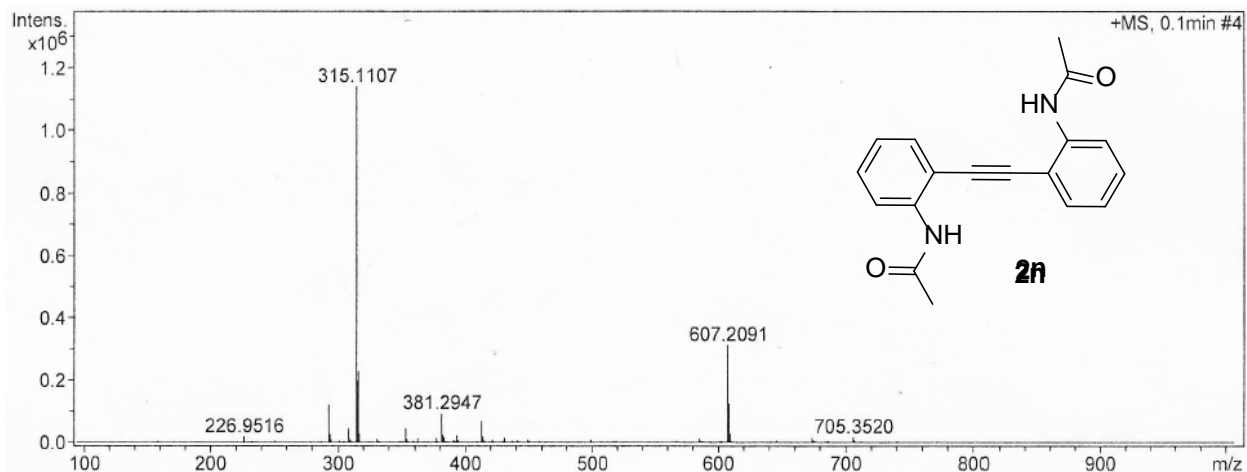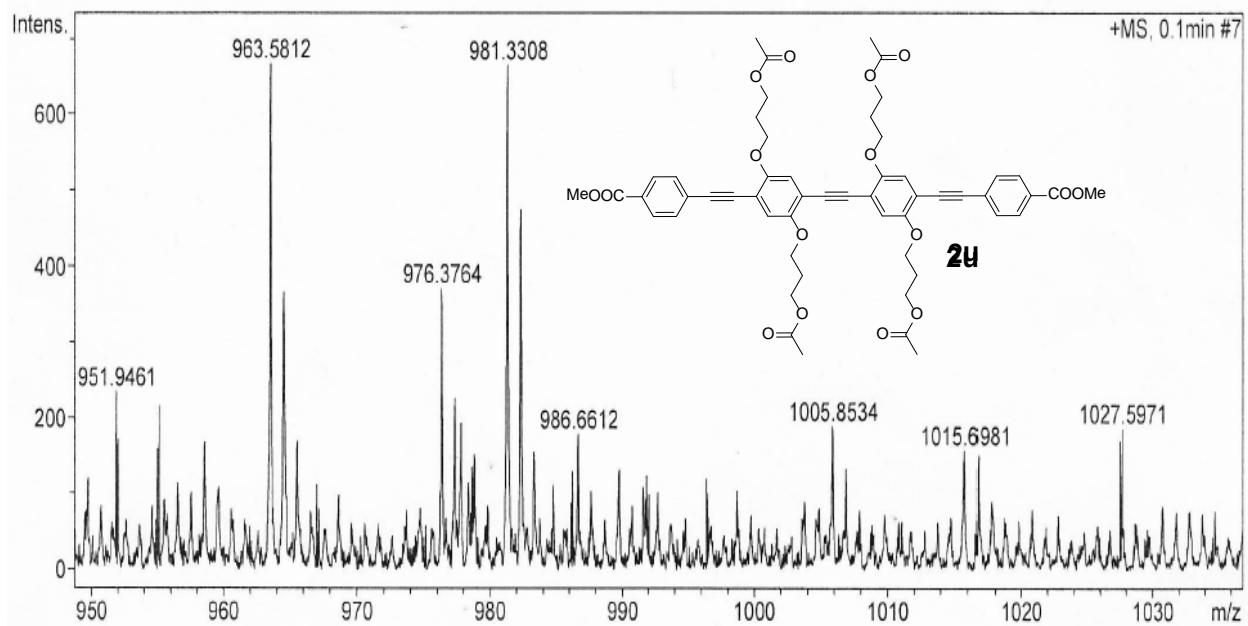
VITAE

Mister Padon Chuentragool was born on November 13, 1984 in Bangkok, Thailand. He got a Bachelor's Degree of Science in Chemical Engineering from Chulalongkorn University in 2007. Then, he went to U.S. to study an English language at University of Illinois at Chicago to the high advance level, and study more English, and general chemistry at Truman College. After that, he came back to Bangkok and enrolled a non-degree study at Mahidol University. He took causes of organic chemistry III and IV, spectroscopy, heterocyclic chemistry etc. Then, he started his a Master's Degree in chemistry program at Chulalongkorn University. He had presented his research on "Synthesis of Diaryl Ethynes from Calcium Carbide" in The Inaugural CU-IMS Joint Symposium, The Winter School of Sokendai/Asian CORE Program, and 14th Asian Chemical Congress 2011 (14 ACC). Part of this work also accepted to be published in the international journal, Tetrahedron.

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