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SYNTHESIS AND CHARACTERIZATION OF TETRA(CARBOXYPHENYL)ETHENE DERIVATIVES AS LIGANDS FOR THE PREPARATION OF METAL ORGANIC FRAMEWORK MATERIALS

BY

KORAY OZHAN

A Thesis Submitted to the School of Graduate Studies
in Partial Fulfillment of the Requirements for the Degree of
Master of Science

Southern Connecticut State University
New Haven, Connecticut
January 2011

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TETRA(CARBOXYPHENYL)ETHENE DERIVATIVES
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KORAY OZHAN

This thesis was prepared under the direction of the candidate's thesis advisor, Dr. M. J. Gerald Lesley, Department of Chemistry, and it has been approved by the members of the candidate's thesis committee. It was submitted to the School of Graduate Studies and was accepted in partial fulfillment of the requirements for the degree of Master of Science.

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ABSTRACT

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Thesis Advisor: Dr. M. J. Gerald Lesley

Institution: Southern Connecticut State University

Year: 2010

The synthesis of two internal aryl acetylene derivatives (R-C_6H_4-C≡C-C_6H_4-R; R= 3-CO_2CH_3 or 4-CO_2CH_3) was accomplished using Pd catalyzed Heck reactions. Reaction of the internal alkynes with B_2Pin_2 in the presence of a Pt catalyst yielded the *cis-bis*(boryl)alkene derivatives in excellent yield. The *cis-bis*(boryl)alkene derivatives were investigated as precursors to *tetra*(carboxyphenyl)alkenes via double Suzuki coupling reactions. Reactions were studied that examined variation in catalyst (*cis*-[$PdCl_2$(dppf), $Pd(OAc)_2$), base (KOH, KOAc), refluxing solvent (DMSO, DMF), aryl halide (I-C_6H_4-R, Br-C_6H_4-R; where R= 3- or 4-CO_2CH_3), and duration of reflux (1–25 days). All reactions conditions resulted in the formation of *tris*(carboxyphenyl)alkene products, with none of the reactions leading to the desired *tetra*(carboxyphenyl)alkene products. Anhydrous reaction conditions resulted in the selective formation of *tris*(carboxyphenyl)(BPin)alkene products.

ACKNOWLEDGEMENTS

I would like to express the deepest appreciation to my thesis advisor, Dr. M. J. Gerald Lesley, for his support, expertise, valuable criticism and infinite patience throughout this project. The opportunity to conduct this research has truly been a defining experience of my educational career. I am also grateful to Dr. Adiel Coca for being the second reader. I remain indebted to my wife, teachers, and professors for providing me the means to learn and further my education.

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CHAPTER 1: INTRODUCTION

The purpose of this research was to investigate the multistep synthesis of ligands classified as *tetra*(carboxyphenyl)ethene derivatives using a variety of air sensitive transition metal catalyzed reactions. These novel ligands can be used in hydrothermal/solvothermal synthesis with stoichiometric amounts of transition metal compounds to generate novel hybrid organic-inorganic polymers, also known as metal-organic frameworks (MOFs).

Chapter 2 describes the background literature related to pertinent aspects of catalytic reactions of various transition metals that are employed in the synthesis of the desired multifunctional organic compounds. A brief description of the coupling reactions utilized in multistep syntheses is provided, with special attention given to the different mechanistic details of each reaction. Specific reaction conditions pertinent to this study are described in more detail. For example, details of prior studies related to the synthetic reaction conditions employed in the thesis are discussed. A brief description of the rapidly emerging field of MOF synthesis is provided, with attention given to the use of carboxylic acid derivatives.

Chapter 3 describes the experimental conditions that were employed in this research. These experimental conditions include the description of the compounds and solvents that were used and the specific additional reaction conditions employed for each

type of synthesis reaction. The products of the synthetic studies were characterized by melting point, ^{1}H NMR, ^{13}C NMR, IR spectroscopy, HRMS-FAB (where available) and elemental analysis. Reaction conditions for the attempted synthesis of *tetra*methyl-3,3',3",3"'-(ethene-1,1,2,2-*tetra*aryl)*tetra*benzoate and *tetra*methyl-4,4',4",4"'-(ethene-1,1,2,2-*tetra*aryl)*tetra*benzoate are also provided.

In chapter 4, variations to the methodology are explained and the experimental outcomes are discussed. This chapter compares similar experimental conditions and results reported in the literature with those of this research. Data that are consistent with those reported in the literature as well as data that deviates from those previously reported are identified and discussed.

Chapter 5 includes conclusions from this synthetic study and suggestions for future syntheses related to the goals of this research study. The bibliography for the literature cited is provided after this chapter.

The style used throughout the document follows American Chemical Society Guidelines[1] consistent with departmental standards for scientific writing.

CHAPTER 2: BACKGROUND

2.1 Introduction to Coupling Reactions

Cross-coupling is one of the most straightforward and general methods for the formation of carbon-carbon bonds. Transition metal catalyzed cross-coupling methods have enhanced synthetic organic chemistry since the first studies reported by Corriu and Masse[2] and Tamao and colleagues.[3] In a typical cross-coupling reaction, a halogenated alkyl or aryl derivative (R-X) reacts with a terminal metal-carbon or semimetal-carbon compound (R′-M) to form a new C-C bond, according to the general reaction shown in Equation 2.1.

(2.1) $$R{-}X \quad + \quad R'{-}M \xrightarrow{\text{Catalyst}} R'{-}R$$

Variations of this general reaction are prone to side reactions that lead to the formation of undesirable byproducts. These include the formation of R-R and R′-R′; reduction of R′X to give R′H; α elimination to give carbenoid compounds; β-elimination to give alkenes; stereoisomerization and regioisomerization reactions with certain functional groups; and other undesirable reactions of substrates, catalysts, ligands, solvents, added reagents, adventitious chemicals, etc.[4] Highly satisfactory cross-coupling reactions are those that are generally applicable and are capable of selectively providing the desired products in high yields, while avoiding all or most of these side reactions.

Coupling reactions have been evolving by substituting X, M, and catalysts with other compounds. A survey of the literature related to coupling reactions contains multiple variations to the general reaction involving X and M. Variants include those for X = I, Br, Cl, OTf (Tf = triflate), F, CN, OTs (Ts = tosylate), and OMs (Ms = mesylate) and M = Li, Mg, B, Si, Sn, Zn, Zr, Al, Cu, etc. Variation can also occur in the catalysts employed and includes a huge number of ligand complexes with Fe, Co, Ni, Cu, Pd, Ru, Rh, or Pt metal centers.

The identity of M serves as a basis for the different names applied to the coupling reactions. For example, M = Li (Murahashi), Mg (Kumada-Tamao, Corriu), B (Suzuki-Miyaura), Si (Tamao-Kumada, Hiyama-Hatanaka), Sn (Migita-Kosugi, Stille), Zn, Zr (Negishi), Al (Nozaki-Oshima, Negishi), Cu (Normant), etc.[5] The target compounds in this research proposal are 1,1′,2,2′-*tetra*(carboxyphenyl)ethene derivatives with variations in the substitution pattern of the carboxylic acid groups around the phenyl rings (3-or 4-substitution). The compounds will be prepared using combinations of Sonogashira coupling, catalyzed diboration reactions, and Suzuki-Miyaura coupling reactions. These reactions are described in the order in which they will be employed for the proposed synthesis.

2.2 Sonogashira Coupling

The palladium/copper catalyzed cross-coupling of terminal alkynes with aryl halides has become a very efficient way to prepare ethynylarenes and their derivatives. In 1975, Heck, Cassar, and Sonagashira independently reported the Pd-catalyzed cross-coupling reactions between C(sp^2)-halide compounds and terminal acetylenes.[6] The

Heck and Cassar methods had been developed as an extension of the original Heck reaction for olefin coupling.[7] A variety of amine solvents and catalysts have been employed in subsequent studies, and each has been found to be effective for the production of arylacetylene derivatives (Equation 2.2). The reaction is commonly performed in an organic solvent, such as an amine, tetrahydrofuran (THF), or dimethylformamide (DMF), with a complex palladium catalyst in conjugation with copper (I) iodide as a co-catalyst and a stoichiometric amount of base.[8] The catalyst

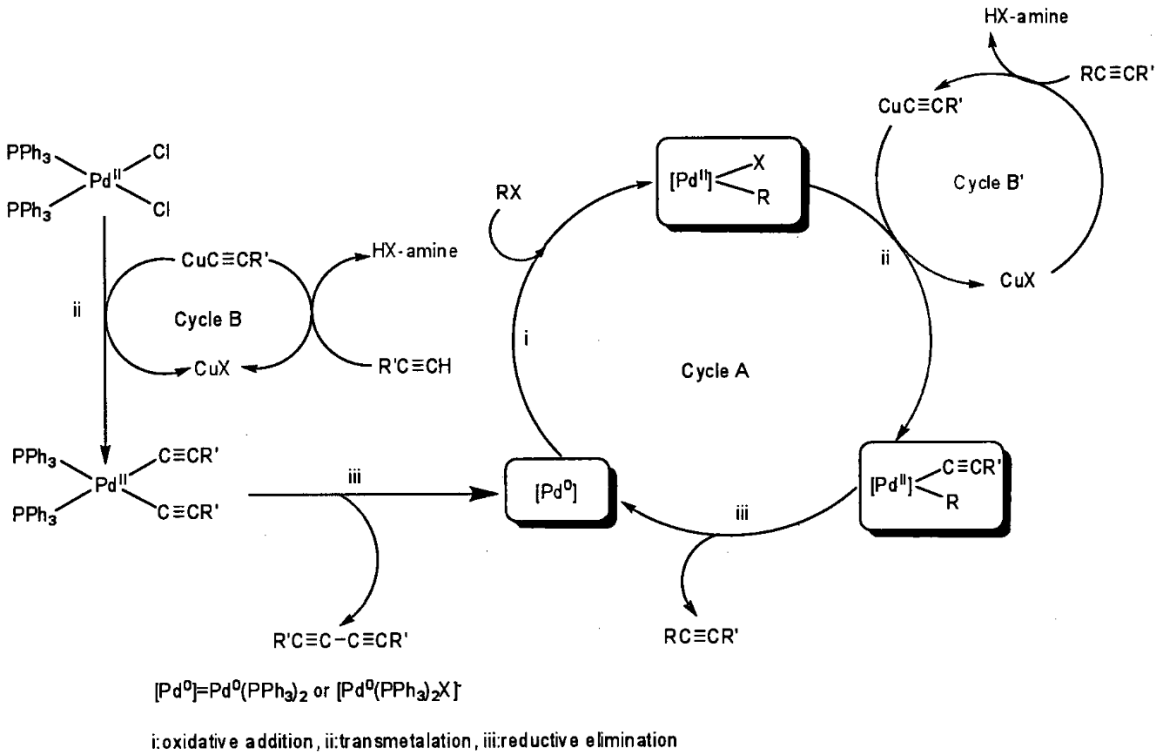
(2.2) $$R\text{-}X + HC\equiv C\text{-}R' \xrightarrow[NHEt_2,\ NEt_3 \text{ or piperidine}]{[PdCl_2(PPh_3)_2],\ CuI} R\text{-}C\equiv C\text{-}R'$$

R= Aryl, Alkenyl
X= Cl, Br, I, OTf

$[Pd_2(dba)_3]$ (dba = dibenzylideneacetone), $[Pd(PPh_3)_4]$, and $[PdCl_2(PPh_3)_2]$ are frequently employed with catalyst loadings of around 5 mol % for each reaction.[8]

The mechanism for the reaction developed by Sonogashira is shown in Scheme 1. The copper (I) halide combines with the alkyne reagent to form a copper (I) acetylide compound (Cycle B′). The amine solvent combines with the HX that forms, creating an amine salt (Cycle B; Step i). The copper (I) acetylide reacts with *cis*-$[PdCl_2(PPh_3)_2]$ (Cycle B; Step ii), a transmetalation in a 2:1 ratio, and reductive elimination of R′-C≡C-C≡C-R′, where R′= TMS, (step iii) generates the active catalyst, [Pd(0)]. This compound undergoes an oxidative addition with an aryl halide (Cycle A; Step i) to form a palladium(II) complex that then reacts with additional copper (I) acetylide (Cycle B′) to form the palladium (II) acetylide complex (Cycle A; Step ii). This complex then

undergoes reductive elimination of the arylacetylene product and regenerates the active catalyst (Cycle A; Step iii).[9]



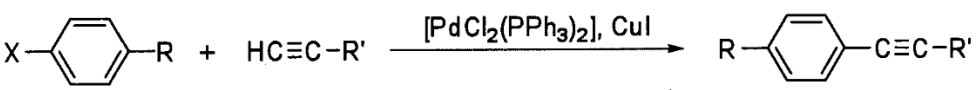
Scheme 1. Catalytic cycle for the Pd-Cu catalyzed coupling of C(sp^2)-halide compounds with terminal acetylenes.

This method can also be viewed as an application of palladium catalysts to the Stephens-Castro reaction (Equation 2.3).[10] Using copper as a co-catalyst rather than a stoichiometric reagent, the reaction proceeds under milder conditions and gives more satisfactory results for the direct synthesis of symmetrically disubstituted acetylenes pertinent to this proposal.[8] Notably, the reduction of copper concentration reduces the risk of explosion since copper acetylide derivatives are known to be explosive when heated.

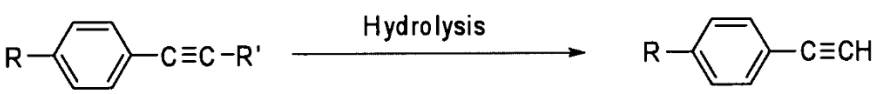
(2.3) $R-X + CuC\equiv C-R' \xrightarrow{\text{pyridine, reflux}} R-C\equiv C-R'$

No catalytic substitution of acetylenes occurred at room temperature in the absence of cuprous iodide, indicating that the role of cuprous iodide is important to facilitate the substitution reaction.[8] The reactions must all be performed in the absence of air since homo-coupling of the alkynes can occur in the presence of copper and oxygen, yielding TMS-C≡C-C≡C-TMS as the major product via the well-known Hay coupling reaction. This has been described in detail by Nguyen et al.[11]

It has been noted that when aryl iodides were reacted with a large excess of acetylene gas under similar conditions, the major product was a disubstituted acetylene derivative. Therefore, it was necessary to protect one end of the acetylene employed to ensure that only one end of acetylene coupled to a suitable aryl halide (Equation 2.4). The trimethylsilyl group (-TMS) was used as the protecting group since subsequent removal by treatment with dilute alkali is readily accomplished (Equation 2.5).[12] This modification gave satisfactory results in the preparation of ethynylarenes and diethynylarene derivatives.

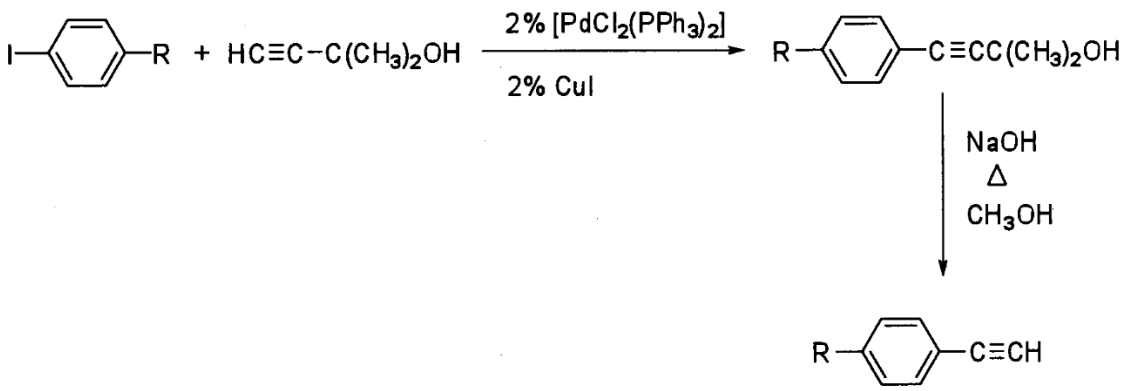
(2.4) 

X: Halide R': TMS(Trimethylsilyl) $-Si(CH_3)_3$

(2.5) 

R': TMS(Trimethylsilyl) $-Si(CH_3)_3$

Ethynylarenes and diethynylarene derivatives can also be prepared by coupling *p*-R-arylhalide derivatives with 2-methyl-3-butyn-2-ol (propargylacetylene) under similar reaction conditions. This protecting group requires treatment with NaOH in refluxing toluene (Scheme 2) to remove the protecting group.[13] Removal of the trimethylsilyl group however requires milder conditions (NaOH/ methanol/ room temperature) and this method will employed in the synthesis studied in this project.



Scheme 2. Preparation of terminal acetylene derivatives using propargylacetylene.

The direct synthesis of diarylacetylene derivatives has been reported by the dehydrohalogenation of dihalodibenzyl compounds, oxidation of the benzyl dihydrazone compounds with mercuric oxide, rearrangement of 1,1-diaryl-2-haloethene derivatives upon treatment with a base, and the action of a base upon 5,5-diaryl-3-nitroso-2-oxazolidones.[10] The scope of this reaction is limited by the violent reaction conditions and difficulties in handling of cuprous acetylides.[9] Sonogashira and coworkers have described the synthesis of internal acetylene derivatives via the reaction between iodoarenes and acetylene in the presence of a catalytic amount of dichloro*bis*(triphenylphosphine)palladium(II)/cuprous iodide in diethylamine under very mild conditions (Equation 2.6). While this route also provides direct access to internal

alkyne derivatives, the formation of copper (I) acetylide intermediates introduces potentially serious safety issues and will not be employed in the synthesis of diarylacetylene derivatives.[9] Instead, diarylacetylene derivatives will be prepared by the stepwise methodology utilizing two successive Sonogashira coupling reactions. In the second step, no protecting group is required and the reaction proceeds in high yields.

(2.6) $$2\ PhI + CH{\equiv}CH \xrightarrow[Et_2NH]{CuI\ /\ [PdCl_2(PPh_3)_2]} PhC{\equiv}CPh$$

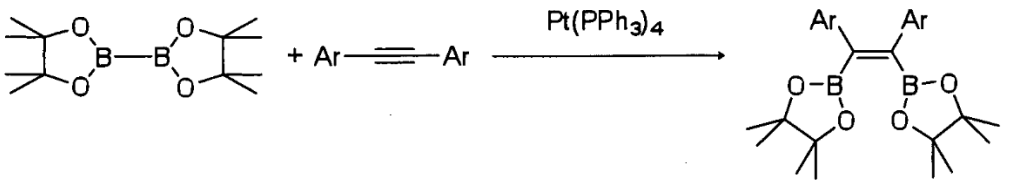
It has also been reported that a new catalyst system using a Pd/Mg La mixed oxide is very efficient for reactions involving aryl iodides, bromides, and even activated chlorides.[14] This catalyst system is effective for reactions in ionic liquids, reactions in aqueous media, and phase transfer catalytic reactions. The use of a variety of promoters, and microwave irradiation are other modifications that have been successful in the Sonogashira coupling procedure.

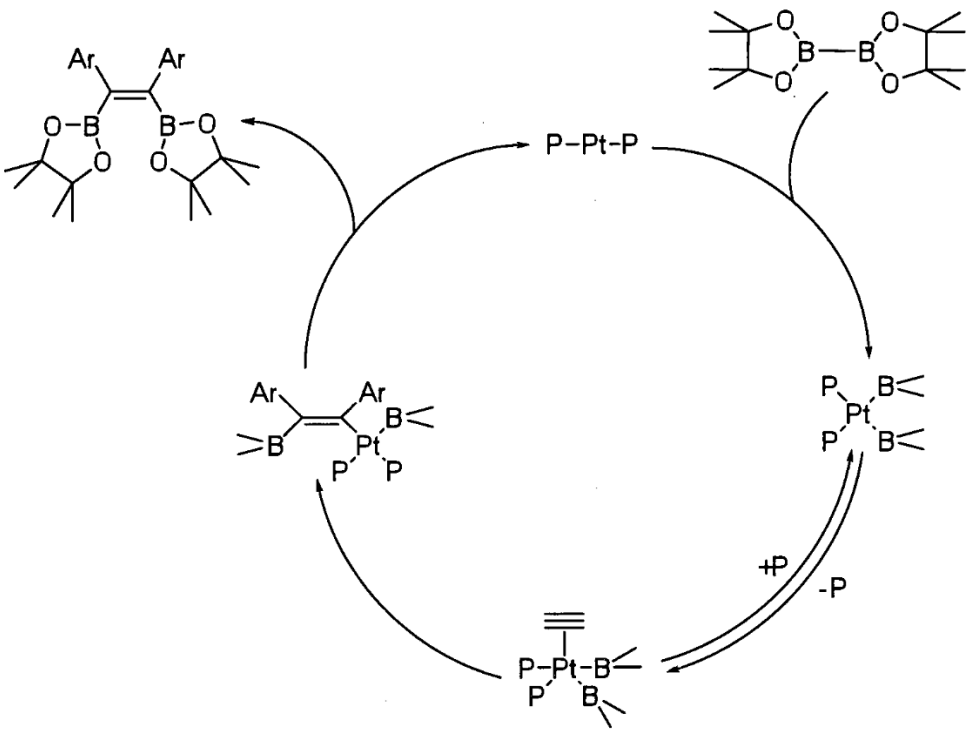
2.3 Catalyzed Diboration Reactions

Stock first synthesized colorless *tetra*chlorodiborane (4), B_2Cl_4, in 1925 by passing an electric discharge through liquid BCl_3. The yields obtained were so small that they were only sufficient to establish the identity of the product and to observe that it slowly decomposed into BCl_3 and yellow or brown boron chloride derivatives which may have been accompanied by elemental boron.[15] The addition of *tetra*halodiborane (4) compounds, (X_2B-BX_2), to unsaturated hydrocarbons was a significant discovery, as it presented the first example of the formation *bis*(borylated) organic products.[16] Schlesinger described a revised synthesis that produced 1 g/week of B_2Cl_4.[16] In the

following years, synthesis of B_2Br_4 by Schlesinger, and B_2I_4 by Schumb aided in the development of diborane (4) chemistry.[15] The diboron tetrahalides, B_2X_4 (X=F, Cl, Br, I), have since been added to C-C multiple bonds in the absence of catalyst, however difficulties with preparation, isolation, and storage of the reagents, their instability toward moisture, and availability limited the use of these derivatives on a routine basis.

Current examples of the catalyzed diboration reaction utilize *tetra*(alkoxy) diborane (4) derivatives.[17-21] These reactions have been demonstrated for a wide variety of unsaturated organic molecules including alkynes, alkenes, etc.[19] The *tetra*(alkoxy) diborane (4) derivatives, such as the structurally characterized $B_2(OR)_4$ ($(OR)_2$ = Cat = 1,2-O_2-C_6H_4; Pin = -$OCMe_2CMe_2O$-), are relatively easy to prepare via the reaction between $B_2(NMe_2)_4$ and the corresponding diol. The platinum(0)-catalyzed addition reaction of the pinacolate ester of diborane (4) (B_2Pin_2) to both terminal and internal alkynes to produce *cis-bis*(boryl)alkenes (Equation 2.7) was first reported by Suzuki and Miyaura.[22] The products can be isolated as pure solids with varying degrees of stability. For example, B_2Cat_2 is air sensitive, reacting with atmospheric moisture, while B_2Pin_2 is stable enough to be used in air for short periods of time. Both derivatives are considerably more stable than the halogenated analogues due to the electron donating ability of the oxygen atoms that stabilize the vacant *p*-orbital on boron. The extra stability of the boron atoms requires the use of a transition metal catalyst to invoke the cleavage of the B-B bond to enable addition reactions with unsaturated hydrocarbons. The accepted mechanism for the catalyzed diboration of an internal alkyne with B_2Pin_2 is given in Scheme 3 and is summarized in Equation 2.7.[18]

(2.7) 



Scheme 3. Catalytic cycle for the Pt-catalyzed diboration of internal alkynes.

The mechanism involves oxidative addition between the active platinum (0) catalyst and B_2Pin_2 to form a *cis-bis*(boryl)platinum (II) intermediate. The alkyne coordinates to the platinum and undergoes an insertion reaction with one of the Pt-B bonds to produce a Pt-vinylboronate intermediate that undergoes reductive elimination to give the *cis-bis*(borylated) olefin product.[20] The reaction conditions for the diboration of alkynes are given in Table 1 and are based on the reaction defined in Equation 2.7 for

1-octyne.[18] For the catalysts examined, only zerovalent platinum complexes exhibited excellent catalytic activity (Entries 2-3).

Table 1. The reaction conditions for diboration.

Entry	Catalyst	Solvent	temp/°C	yield/%
1	none	DMF	80	0
2	$Pt(PPh_3)_4$	DMF	80	92
3	$Pt(CO)_2(PPh_3)_2$	DMF	80	94
4	$PtCl_2(PPh_3)_2$	DMF	80	0
5	$Pd(PPh_3)_4$	DMF	80	8
6	$Pd(OAc)_2$/15 *t*-BuN=C:	DMF	80	1
7	$RhCl(PPh_3)_3$	DMF	80	1
8	$Ni(PPh_3)_4$	DMF	80	0
9	CuCN	DMF	80	0
10	$CoCl(PPh_3)_3$	DMF	80	0
11	$Pt(PPh_3)_4$	DMF	50	76
12	$Pt(PPh_3)_4$	CH_3CN	50	68
13	$Pt(PPh_3)_4$	THF	50	58
14	$Pt(PPh_3)_4$	Toluene	50	59
15	$Pt(PPh_3)_4$	Hexane	50	80

The solvents did not play an important role, but a comparison of the reaction rates at 50 °C using [$Pt(PPh_3)_4$] revealed that polar solvents accelerated the reaction (Entries

11-14). The reaction in hexane resulted in an exceptionally high yield. Although $[Pt(PPh_3)_4]$ was used as a suspension in hexane, the reaction rate was apparently faster than the reactions in other solvents (Entry 15).[18] Lesley and colleagues showed that $[(\eta^2\text{-}C_2H_4)Pt(PPh_3)_2]$ was a more efficient catalyst precursor than $[Pt(PPh_3)_4]$ for the diboration of alkynes.[17] In this case, direct access to the Pt(0) active catalyst via dissociation of ethene in solution, versus dissociation of two PPh_3 ligands, was proposed as a means to enhance the initial oxidative addition with diborane (4) compounds providing the active catalyst. In this study, $[(\eta^2\text{-}C_2H_4)Pt(PPh_3)_2]$ will be used as the active catalyst for the diboration reactions that will be examined.

In general, catalyzed diboration reactions involving $[Pt(PPh_3)_4]$ as the catalyst typically yield the corresponding *bis*(boryl)ethene derivatives in approximately 79% yield (Equation 2.7). Substitution of $[Pt(PPh_3)_4]$ with Pt(II)*bis*(boryl) compounds or Pt(0)-ethene complexes (*cis*-$[Pt(BPin)_2(PPh_3)_2]$ and $[(\eta^2\text{-}C_2H_4)Pt(PPh_3)_2]$, respectively), resulted in a quantitative yields for the same reaction.[17] Using $[(\eta^2\text{-}C_2H_4)Pt(PPh_3)_2]$ for preliminary studies (Ar = 3-MeO_2CPh , 4-MeO_2CPh in Equation 2.7) conducted in Dr. Lesley's laboratory have resulted in similar quantitative yields of the derivatives of *bis*(boryl)alkenes.

Recently, the formation of *trans-bis*(borylated) olefin products have also been reported using a cobalt catalyst.[21] In our research, $B_2(pin)_2$ will be used as a diboration reagent in platinum catalyzed diboration of alkynes to obtain *bis*(boryl)alkenes since this diborane (4) compound exhibits better air stability compared to the catechol derivatives.

2.4.1 Suzuki-Miyaura Coupling

The Suzuki-Miyaura coupling reaction (Equation 2.8) is a versatile synthetic method

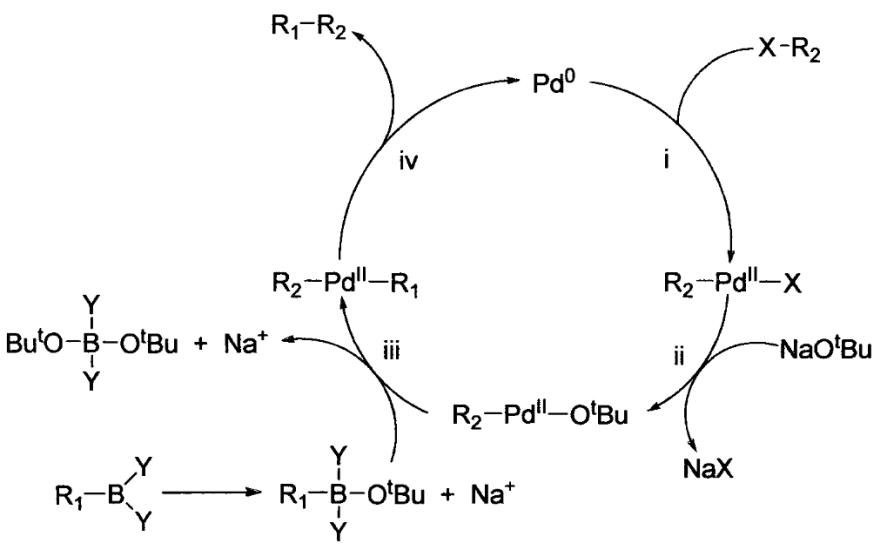
for the formation of carbon-carbon bonds.[23] The reaction occurs between an aryl- or vinyl-boronic acid with an aryl-, vinyl- or an alkyl-halide and is catalyzed by a palladium (0) complex. In a traditional palladium-catalyzed Suzuki-Miyaura coupling, C-X (X = Br, I, OTf; Tf = trifluoromethanesulfonyl) groups show the best results.[24] The reaction has been widely used to synthesize poly-olefin, styrene, and substituted biphenyl derivatives.[25]

(2.8) $$R_1{-}BY_2 + R_2{-}X \xrightarrow{\text{Pd catalyst}} R_1{-}R_2 + X{-}BY_2$$

The Suzuki-Miyaura coupling reaction, which is differentiated from other coupling reactions by the use of boron, has some advantages such as mild and versatile methods for synthesizing boranes, easy incorporation of non-transferable boron ligands, commercial availability of boronates and boronic acids, tolerance of a broad range of function groups, air-stability, non-toxic nature of starting materials and borate byproducts, etc.[26] Even though the reaction is often performed on a very large scale, the byproducts of the boronic acids are also very easy to remove from the solution.[27]

The organoboron reagents are restricted in use for ionic reactions because even organoboron compounds are highly electrophilic, but the organic groups on boron are weakly nucleophilic. The coordination of a negatively charged base to the boron atom has been recognized to be an efficient method of increasing its nucleophilicity to transfer the organic group on boron to the adjacent positive center.[23] The catalytic cycle of Suzuki-Miyaura coupling reaction involving oxidative addition, transmetalation, and reductive elimination sequences, is depicted in Scheme 4 in four steps.

Step i shows the oxidative addition of the aryl-halide to palladium to develop the organo-palladium (II) species. The zerovalent palladium is efficient for the activation of C-X bonds (X= Cl, Br, I, O) by an oxidative addition, which provides an organo-palladium(II) complex that tends to react with nucleophiles.[28] Different kinds of palladium (0) catalysts or precursors can be used for this reaction. Phosphine ligand substituted palladium complexes are commonly utilized due to the ability of these ligands to dissociate in solution to provide vacant coordination sites for reactivity at the metal center. This also provides a means for additional solution characterization via ^{31}P NMR spectroscopy even where the phosphine ligand complexes are air sensitive.[29]



Scheme 4. A general catalytic cycle for the Suzuki coupling reaction.

Oxidative addition proceeds with retention of stereochemistry with vinyl halides, while giving inversion of stereochemistry with allylic and benzylic halides.[30] The oxidative addition initially forms the *cis*-palladium complex, which rapidly isomerizes to the *trans*-complex and is often the rate determining step in the catalytic cycle.[31] The

relative reactivity decreases in the order of I > OTf > Br >> Cl.[27] The characterization of the intermediate can be accomplished by NMR spectroscopy as well as electrochemical techniques like cyclic, transient, steady state voltametry.[32]

Transmetalation is a type of general chemical reaction in organometallic chemistry, describing the exchange of ligands between two metal centers as described above for the Sonogashira coupling reaction. The transmetalation (Scheme 4; Step ii) for the Suzuki-Miyaura coupling reactions occurs between the organopalladium (II) complex and base. The organoboron compound also requires addition of a base because of the low nucleophilicity of the organic group on the boron atom.[33] The nucleophilicity of the organic group on the boron atom is enhanced by quarternization of the boron atom with negatively charged bases to give the corresponding "ate" complex. Such "ate" complexes undergo clean coupling reactions with organic halide derivatives.[33] The transmetalation of primary alkyl substituted boranes to palladium occurs with retention of stereochemistry. This was determined by hydroboration of diastereomeric dideuterioalkenes followed by coupling of the diastereomeric borane to α-iodocyclohexenone and examination of the spectral properties of the resulting cyclohexenones.[34] The first reaction with the base gives an R_2-Pd-O^{t}Bu intermediate, which reacts via transmetalation (Scheme 4; Step iii) with the boronate complex to form the R_2-Pd-R_1 organopalladium species.

Reductive elimination (Scheme 4; Step iv) of the desired product R_1-R_2 regenerates the original palladium (0) catalyst and completes the catalytic cycle. Reductive elimination takes place directly from the *cis*-(R_2-Pd-R_1) complex, and any *trans*-(R_2-Pd-R_1) compound present in solution reacts only after isomerization to the

corresponding *cis*-complex. The order of reactivity is diaryl- > (alkyl)aryl- > dipropyl- > diethyl- > dimethylpalladium(II).[32]

Although the mechanism of oxidative addition and reductive elimination sequences are reasonably well understood and are presumably, fundamentally common processes for all cross-coupling reactions of organometallics, less is known about the transmetalation step because the mechanism is highly dependent on the organometallic complexes or reaction conditions used for the couplings.[33]

Bis(boryl)alkenes are attractive starting materials and the reactivity of these compounds toward double Suzuki coupling reactions has been reported.[35-38] Initial reports of the diboration reaction by Miyaura and Suzuki reported the further substitution of the boryl groups to yield *tetra*(aryl)ethene derivatives however complete details were not furnished in these initial reports.[18] Subsequent studies have been reported as a means for the synthesis of the *tetra*-substituted ethene derivatives[36] including the anti-cancer compound Tamoxifen® (Figure 1; Compound a where $R_1 = R_4 = Ph$; $R_2 = CH_2CH_3$, $R_4 = Ph\text{-}OCH_2CH_2N(CH_3)_2$).[37,38] In this case, the stepwise substitution of the boryl group was examined as a means for the introduction of two different carbon-carbon bonds. The substitution of the first boryl group was reported to occur much faster than that for the second boryl group. The second substitution was accomplished using supported resin capture of an aryl group. The authors noted that hydrogenative deborylation could also

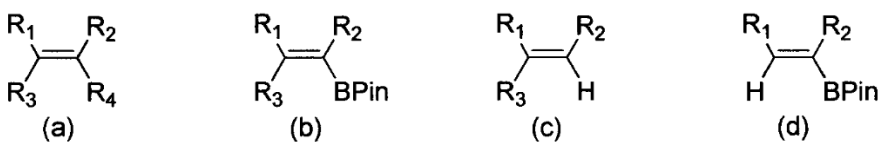
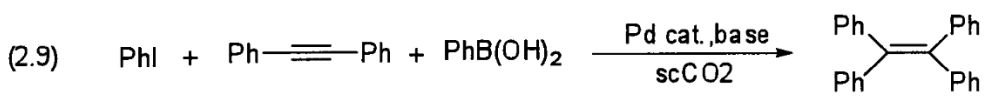


Figure 1. Products reported from *tetra*(aryl)ethene synthesis.

occur leading to a trisubstituted ethene byproduct (Figure 1; Compound b where $R_1 = R_4$ = Ph; R_2 = CH_2CH_3). Recent studies invoking microwave synthesis to form *tetra*(aryl)ethene derivatives have identified an additional byproduct related to the current proposed research.[35] The reactions were conducted with a variety of common catalysts in aqueous dioxane at 140 °C with KOH as the base. Incomplete reactions gave rise to the mono-substituted ethene derivative (Figure 1; Compound b where $R_1 = R_2 = R_3$ = Ph; R_4 = BPin) and the corresponding *tri*(aryl)ethene product (Figure 1; Compound c where $R_1 = R_2 = R_3$ = Ph) noted in prior studies as well as the unsubstituted product where hydrogenative deborylation has occurred (Figure 1; Compound d where $R_1 = R_2$ = Ph). The synthesis of the desired *tetra*(aryl)ethene product was achieved in 94% yield with 97% purity using 1-2 mol% of $Pd(OAc)_2$ with 2 equivalents of PPh_3 as the catalyst. In fact, increasing the mol% of catalysts in these reactions generally led to improvement of the yields of the desired product. A recent study that explains the another convenient way to the synthesis of tetrasubstituted olefins via Pd-catalyst showed that supercritical carbon dioxide ($ScCO_2$) can replace conventional solvents in organic synthesis since the $ScCO_2$ is environmentally friendly and its toxicological properties are much better than conventional solvents.[39] Different reaction conditions were examined including a variety of palladium catalysts, bases, temperature and pressure parameters as shown in Equation 2.9.

(2.9) 

Preliminary studies in Dr. Lesley's laboratory aimed at the formation of the *tetra*(carboxyphenyl)ethene derivatives have resulted in similar results to those reported

in the literature with some exceptions. The reaction of the *bis*(borylated)olefin derivatives has been studied in a temperature range of 85 °C – 110 °C using a variety of palladium catalysts. Reactions conducted in aqueous base resulted in a 83% yield of product that was found to contain the monosubstituted hydrogenative deborylation derivative (Figure 1; Compound c where $R_1 = R_2 = R_3 = o,p$-Ph-CO_2CH_3; 95%) as well as the corresponding biaryl derivative CH_3O_2C-Ph-Ph-CO_2CH_3 (5%). In the case of the *p*-Ph-CO_2CH_3 derivatives, both products were identified in the ^1H NMR spectra as well as by single crystal X-ray diffraction. When polar solvents such as DMF and DMSO were employed and water was excluded from the reaction, the products formed were mainly the monosubstituted derivative (Figure 1; Compound b where $R_1 = R_2 = R_3 = o,p$-Ph-CO_2CH_3). This indicates that the use of aqueous base may be responsible for the hydrogenative borylation side reaction. The formation of the biaryl derivative indicates that the side reaction involving unreacted aryl halides can also occur giving rise to byproducts in addition to those reported in the literature.

The result of these studies indicates that higher temperatures must be required to effect the formation of the desired *tetra*(aryl)ethene derivatives. Thus, reactions to be studied will involve higher temperatures (≥ 150 °C) that are accessible using the polar solvents DMF (bp = 153 °C) and DMSO (bp = 189 °C). Catalysts for these studies will include $[Pd(OAc)_2]$, $[Pd(OAc)_2]/PPh_3$, $[Pd(dppf)Cl_2]$, and $[PdCl_2 (PPh_3)_2]$. The reactions will be carried out under non-aqueous conditions using traditional inert atmosphere techniques.

The Suzuki-Miyaura coupling reaction continues to be used for applications in various fields of chemistry including nonlinear optics[40], biochemistry[41], *anti*-HIV

molecules[42], and solar cell fields.[43] In fact, online searches of the Suzuki reaction typically yield more than 3,500,000 hits.

2.5 Metal Organic Frameworks

A novel class of hybrid materials made from metals and organic compounds is changing the face of solid state chemistry and materials science just ten years after its discovery. The materials, termed MOFs (Metal Organic Frameworks), are also known as porous hybrid inorganic–organic solids and represent one of the biggest breakthroughs in solid state science, for which the potential applications are only just being realized. They can be formed in one-, two- or three-dimensional structures that mostly present massive flexibility and porosity with holes at molecular dimensions that resemble honeycombs. Ulrich Muller, a research director at BASF with a background in porous materials, came across a study on MOF compounds in which researchers reported measuring a surface area of some 3,000 m^2/g.[44] Muller's avowal, "the number was so unbelievably high, I thought it had to be a misprint," exemplifies the astounding properties of MOFs.

Gas molecules diffuse into the MOF solid and are contained within its pores. This property of having an astronomical number of tiny holes within a relatively small volume can be exploited in various ways, one of which is as a repository for gases. MOFs provide safe storage of highly flammable gases such as hydrogen and methane. MOFs offer the essential advantage of soaking up some of the gas pressure exerted by the molecules.

There is no doubt though that the first wide application of MOFs in gas storage will be highly vital, due to the urgency of developing alternatives to fossil fuels for

automobiles. Hydrogen has recently been forecasted to be a main source of clean energy. Hydrogen is a non-polluting fuel, but since it is a light gas it occupies too much volume, and it is flammable. Safe, effective, and practical hydrogen storage is a critical problem. The synthesis, characterization, and hydrogen storage capacity of MOFs were investigated as a potential solution. In fact, the use of MOFs is so promising that, according to Férey, prototypes of hydrogen-storing MOFs have already been created by car makers. The key difference between a conventional gas cylinder and MOF vessel is that the amount of gas stored in a conventional cylinder at, say, 200 atmospheres pressure could be accommodated in an MOF vessel of the same size at just 30 atmospheres, which is much safer.[45] This makes hydrogen derived from non-fossil energy sources such as fuel cells or even genetically engineered plants potentially viable as a fuel for cars while the alternative of pressurized canisters is not.

A study of six framework materials as selective adsorbents for various poisonous gases showed that CO, ammonia, sulfur dioxide, and chlorine can be trapped and filtered by MOFs.[45] In addition to storing valuable gases, MOF materials can be used to trap greenhouse gases, such as CO_2, and various poisons. MOFs represent a class of porous materials that offer a lot of advantages for CO_2 storage. The release of CO_2 from power plants, which is currently a major source of emission, is commonly controlled by chilling and pressurizing the exhaust or by passing the fumes through a fluidized bed of aqueous amine solution, both of which are costly and inefficient.[46] Other methods based on chemisorption of CO_2 on oxide surfaces or adsorption within porous silicates, carbons, and membranes have been pursued as means for CO_2 uptake.

Another potential area for MOF application is in the pharmaceutical industry. Two examples are the MIL-100 and MIL-101 (MIL=Materials of Institut Lavoisier), materials that showed remarkable ibuprofen adsorption (approx. 1.4 g ibuprofen/ g of MOF) and provided controlled release of the drug over 6 days. Enhanced pore sizes in MIL-101, which has a surface area of roughly 5,900 m^2/g, allow more absorption of drug and a longer controlled delivery, which may be advantageous for larger pharmacological molecules.[47]

MOFs have also started to show potential as selective catalysts. Researchers prepared a protonated form of a chiral copper aspartate-based MOF material and used it to catalyze an epoxide ring-opening reaction. It was observed that a manganese–based material can serve as a size-selective acid catalyst. A portion of the crystal structure of 1,3,5-benzenetristetrazol-5-yl showing the two different types of Mn(II) sites exposed within its three-dimensional pore system of 10 Å wide channels (Figure 2). Orange, green, gray and blue spheres represent Mn, Cl, C, and N atoms, respectively; Site I is five-coordinate, while site II is only two-coordinate; the separation between them is 3.420 Å.[48] They demonstrated that reactants small enough to enter the MOF's pores and reach the metal sites underwent cyanosilylation efficiently. However, molecules that were too large to enter the pores did not react.[49]

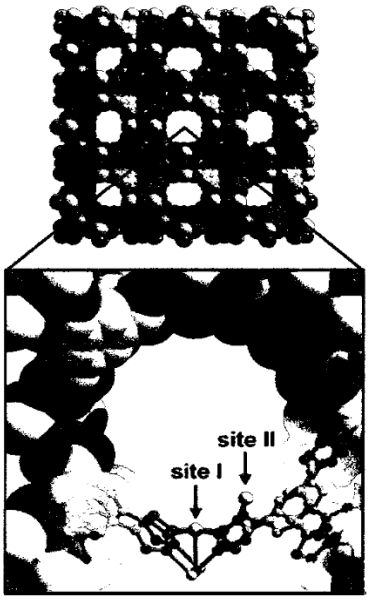


Figure 2. Representation of the Mn based size-selective acid catalyst.[48]

Additional studies have developed "organically doped metals" by using solution processing to trap small organic molecules or polymers inside a matrix of metal atoms. Immersing the organic molecules in the conducting metal framework's "sea of electrons" significantly alters the properties of both components.[50]

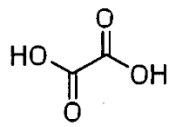
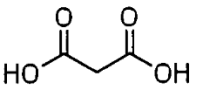
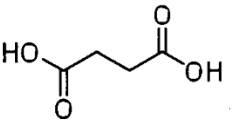
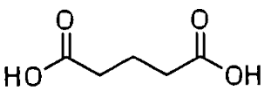
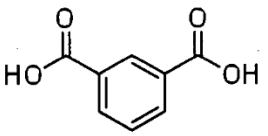
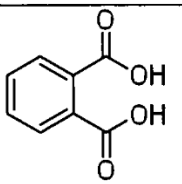
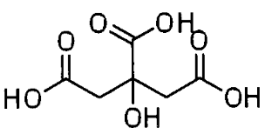
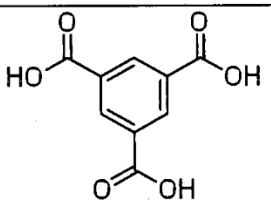
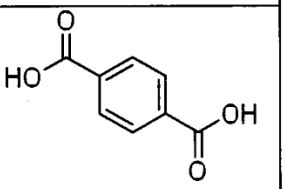
An important characteristic of MOFs is their ability to link together molecular building blocks that exhibit high porosity. The molecular scaffold in MOFs connects inorganic clusters that act as joints and rigid rod-like organic molecules. The chemical environment and size of the resulting void spaces are based on the length and functionalities of the organic units. Proper employment of this building strategy yields materials that exhibit selective adsorption of small molecules and inclusion of large molecules. In addition to the importance of the building blocks, the way in which they are connected is critical.[51] It is known that MOFs are crystalline materials composed of metal ions or clusters connected by way of organic linkages. The discrete metal organic

assemblies, which are termed metal organic polyhedra, have been studied and their linkage properties have been reviewed recently.[52] Yaghi and colleagues reported principles of reticular synthesis and design of MOFs that provide a level of predictive capability.[53] The ability to synthesize predetermined MOF structures allows extraordinary freedom to design porous materials for specific purposes.

Carboxylic acid based derivatives of ligands are commonly used in MOF synthesis. These linkers are very popular compared to other ligands due to their great ability to bind to metals and the thermal stability of the products obtained. These ligands provide excellent linkages for coordination polymers with varying 2-D and 3-D structures.[54] Some of the most commonly used carboxylic acid based derivatives of ligands are illustrated in Table 2.[55] The simplest member of this family, oxalic acid, has been used extensively. The majority of these are commercially available, however, trimesic acid has been synthesized and has been the focus of recent industrial scale preparation with MOFs.[49]

Metal carboxylates have been important for MOF synthesis for almost a decade. This group of derivatives includes not only mono- and dicarboxylates of transition, rare-earth, and main-group metals, but also a variety of hybrid structures. In terms of organic ligands, much of the recent focus has been on connectivity through oxygen atoms of carboxylic acid groups. Rao and his colleagues showed that the carboxylate unit provides an excellent means for designing novel materials by acting as a linker or by imparting unique structural features due to its functionalizability and flexibility.[56] Every year, around 1,000 new MOFs of various structures are reported, and 400 three-dimensional framework structures are known to exist.

Table 2. Commonly used carboxylic acid derivative ligands in MOFs

 Oxalic acid	 Malonic acid	 Succinic acid
 Glutaric acid	 Isophthalic acid	 Phthalic acid
 Citric Acid	 Trimesic acid	 Terephthalic acid

For example, the BASF pilot plant in Germany produces 100 kg/day of MOF compounds, which are sold by Sigma Aldrich.[49] New properties of MOFs are developed and existing features are fine-tuned by scientists everyday, showing that this area of research is still ongoing and is far from reaching its peak.

CHAPTER 3: EXPERIMENTAL

3.1 General Experimental Conditions

All experiments involving palladium catalysis were performed under a dry N_2 atmosphere using standard Schlenk line techniques, unless otherwise stated. The non-deuterated solvents were used as purchased and used under aerobic conditions except Et_2NH which was distilled over CaH_2 under a dry N_2 atmosphere prior to use and DMSO and DMF which were sealed under a dry N_2 atmosphere prior to purchase. Water was purified using Millipore water deionized ion exchange resin (18 mΩ). Deuterated solvents ($CDCl_3$, and DMSO-d_6) were dried over 4 Å molecular sieves prior to use.

Solid chemical reagents were used as purchased and prepared for anaerobic reactions by standard Schlenk line evacuation/refill techniques. Trimethylsilylacetylene (TMSA) was prepared using three freeze/pump/thaw degas cycles prior to use. The compounds *cis*-$[PdCl_2(NCPh)_2]$[57], *cis*-$[PdCl_2(PPh_3)_2]$[57], *cis*-$[PdCl_2(dppf)]\bullet CH_2Cl_2$[58] *cis*-$[PtCl_2(PPh_3)_2]$[57] and *cis*-$[Pt(\eta^2\text{-}C_2H_4)(PPh_3)_2]$[59] were prepared according to literature methods. All other chemical reagents were analyzed by ^1H NMR and used without further purification.[60] Nuclear magnetic resonance analyses were performed using a Bruker Avance III 300 MHz spectrometer at the following frequencies: ^1H – 300.130 MHz; ^{13}C – 75.468 MHz; ^{11}B – 96.294 MHz. The ^1H chemical shifts (δ) were referenced to the internal standard tetramethylsilane (TMS at 0.00 ppm) or to residual solvent resonances ($CHCl_3$, at 7.26 ppm; DMSO at 2.50 ppm). The ^{13}C chemical shifts

were referenced to the residual solvent resonance and ^{11}B chemical shifts were referenced to the external standard boron triflouride etherate F_3BOEt_2. The multiplicities of the resonances are reported as singlets (s), doublets (d), triplets (t), quartets (q) and multiplets (m). The IR analyses were performed using a Perkin-Elmer System 2000 FTIR spectrophotometer. Melting point determinations were obtained using a Thermo Scientific Mel-Temp equipped with a type K thermocouple adapted Fluke 51II digital thermometer. Elemental analyses were performed by Robertson Microlit Laboratories, Madison, NJ. HRMS-FAB ($M + H^+$) measurements were performed using an Applied Biosystem Co. QSTAR XL MS/MS system.

3.2 Synthesis of Aromatic Esters

3.2.1 Synthesis of Methyl-4-Iodobenzoate (**3**)

Solid 4-iodobenzoic acid (35.000 g; 0.1411 mol) was placed in a 500-mL round bottom flask equipped with a magnetic stir bar, and methanol (300 mL) was added. The flask was equipped with a reflux condenser and sulfuric acid (ca. 3 mL, conc.) was added via disposable pipette through the top of the condenser. The reaction mixture was heated to reflux for 4 days and cooled to room temperature. The solution was reduced *in vacuo* to approximately 150 mL and water (300 mL) and dichloromethane (DCM, 300 mL) were added to the flask. Solid sodium bicarbonate was added in portions until bubbling subsided. The DCM layer was isolated. The aqueous layer was extracted with additional DCM (2 x 50 mL) and the layers were combined and dried over $MgSO_4$. The suspension was filtered and reduced *in vacuo* yielding a white solid (34.692 g; 94%).

mp 119.9–120.4 °C; Anal. Calcd for $C_8H_7O_2I$: C, 36.67; H, 2.69. Found: C, 36.32; H, 2.60; HRMS-FAB (*m/z*): $[M+H]^+$ calcd for $C_8H_7O_2I$, 262.957; found, 262.9595; IR (Nujol mull) $\tilde{\nu}_{max}$: 2924–2854 (CH), 1709 (C=O), 1585 (C=C), 1285 (C–O), 755 (Ar–H) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$, δ): 7.80 (d, *J*= 8.7 Hz, 2H, $H_{2,6}$), 7.74 (d, *J*= 8.7 Hz, 2H, $H_{3,5}$), 3.91 (s, 3H, $-OCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$, δ): 166.4 (C=O), 137.6 (2C, $C_{2,6}$), 130.9 (2C, $C_{3,5}$), 129.4 (C_1), 100.7 (C_4), 52.3($-OCH_3$).

3.2.2 Synthesis of Methyl-3-Iodobenzoate (**4**)

Compound **4** was prepared in 97% yield using the same reaction conditions employed for the synthesis of **3**.

mp 56.8–58.6 °C; Anal. Calcd for $C_8H_7O_2I$: C, 36.67; H: 2.69. Found: C, 36.85; H, 2.66; HRMS-AB (*m/z*): $[M+H]^+$ calcd for $C_8H_7O_2I$, 262.957; found, 262.9618; IR (Nujol mull) $\tilde{\nu}_{max}$: 2925–2854 (CH), 1705 (C=O), 1566 (C=C), 1259 (C–O), 742 (Ar–H), 705 (Ar–H) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$, δ): 8.37 (s, 1H, H_2), 7.99 (d, *J*= 7.8 Hz, 1H, H_6), 7.87 (d, *J*= 7.8 Hz, 1H, H_4), 7.18 (dd, *J*= 7.9 Hz, 1H, H_5), 3.92 (s, 3H, $-OCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$, δ): 165.4 (C=O), 141.6 (C_4), 138.3 (C_2), 131.8 (C_1), 129.9 (C_5), 128.6 (C_6), 93.7 (C_3), 52.4 ($-OCH_3$).

3.3 Synthesis of Ethynyl Substituted Aromatic Esters

3.3.1 Synthesis of Methyl-3-(2-trimethylsilyl)ethynyl)benzoate (**5**)

A 250-mL round bottom Schlenk flask that was equipped with a magnetic stir bar was charged with methyl-3-iodobenzoate (10.000 g; 38.160 mmol), *cis*-dichloro*bis*(triphenyl phosphine)palladium(0) (0.803 g, 1.150 mmol, 5.000 mol%), and

copper (I) iodide (0.073 g, 0.380 mmol, 1.000 mol%) and the contents of the flask were degassed by evacuating the flask for 5-10 minutes and refilling with nitrogen gas three times. Diethylamine (50 mL) was added via syringe under nitrogen. Trimethylsilyl acetylene (TMSA) (6.470 mL, 45.79 mmol) was added dropwise via syringe, while the solution was stirring. The reaction mixture was stirred for 48 hours under a slight pressure of nitrogen. The suspension was reduced *in vacuo.* The amine salts were removed from the alkyne using a water/DCM extraction. The DCM layer was isolated and dried over magnesium sulfate, filtered and reduced on a rotary evaporator, yielding a crude red solid (9.118 g; 103%). The crude product was purified on neutral aluminum using hexane:acetone (60:40) as eluant. Samples were collected as fractions and reduced on a rotary evaporator forming a liquid that solidified over time. Each fraction was analyzed by NMR spectroscopy, and proper fractions were combined (4.543 g; 51%).

mp 50.1–51.1 °C; Anal. Calcd for $C_{13}H_{16}O_2Si$: C, 67.20; H: 6.94 Found: C, 66.72; H, 6.76; IR (neat) $\tilde{\nu}_{max}$: 2956 (CH), 2158 (C≡C), 1728 (C=O), 1289 (C–O), 1250 (C–Si), 844 (C–Si), 754(Ar–H) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$, δ): 8.14 (s, 1H, H_2), 7.97 (d, *J*= 7.9 Hz, 1H, H_6), 7.63 (d, *J*= 7.7 Hz, 1H, H_4), 7.38 (dd, *J*= 7.8 Hz, 1H, H_5), 3.92 (s, 3H, $-OCH_3$), 0.26 (s, 9H, $Si(CH_3)_3$); ^{13}C NMR (75 MHz, $CDCl_3$, δ): 166.5 (C=O), 136.2 (C_6), 133.3 (C_2), 130.4 (C_3), 129.6 (C_4), 128.5 (C_5), 123.7 (C_1), 104.0 (Ar<u>C</u>≡C), 95.5 (C≡<u>C</u>Si), 52.4 ($-OCH_3$), 0.0 ($Si(CH_3)_3$).

3.3.2 Synthesis of Methyl-4-(2-trimethylsilyl)ethynyl)benzoate (**6**)

Compound **6** was prepared in 74% yield using the same reaction conditions employed for the synthesis of **5**.

mp 56.9–57.8 °C; Anal. Calcd for $C_{13}H_{16}O_2Si$: C, 67.20; H: 6.94. Found: C, 66.47; H, 6.66; IR (Nujol mull) $\tilde{\nu}_{max}$: 2924-2854 (CH), 2160 (C≡C), 1720 (C=O), 1603 (C=C), 1275 (C–O), 1242 (C–Si), 771 (Ar–H), 760 (Ar–H) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$, δ): 7.97 (d, J= 8.6 Hz, 2H, $H_{2,6}$), 7.52 (d, J= 8.6 Hz, 2H, $H_{3,5}$), 3.91 (s, 3H, $-OCH_3$), 0.26 (s, 9H, $Si(CH_3)_3$); ^{13}C NMR (75 MHz, $CDCl_3$, δ): 166.4 (C=O), 131.8 (2C, $C_{3,5}$), 129.6 (C_1), 129.3 (2C, $C_{2,6}$), 127.7 (C_4), 104.0 (Ar<u>C</u>≡C), 97.6 (C≡<u>C</u>Si), 52.3 ($-OCH_3$), 0.0 ($Si(CH_3)_3$).

3.4 Synthesis of Terminal Alkyne Derivatives

3.4.1 Synthesis of Methyl-3-ethynylbenzoate (7)

A 250-mL round bottom Schlenk flask that was equipped with a magnetic stir bar was charged with methyl-3-(2-trimethylsilyl)ethynyl)benzoate (4.268 g; 18.33 mmol) and methanol (100 mL) and cooled in an ice water bath. An aqueous solution of potassium hydroxide (50 mL, 1.0 M) was added dropwise over a period of 1 hour and the reaction mixture was stirred for a period of 3.0 hours. The methanol was reduced on a rotary evaporator then extracted using DCM:water. The DCM layer was isolated and reduced *in vacuo* yielding methyl-3-ethynylbenzoate (1.945 g, 66%). The aqueous layer was acidified with dropwise addition of concentrated HCl until a pH of ca 2.0 was reached and diethylether (50 mL) was added. The diethylether layer was reduced *in vacuo* yielding a yellow precipitate of 3-ethynylbenzoic acid. The crude 3-ethynylbenzoic acid was transferred to a 250-mL round bottom flask equipped with a magnetic stir bar and methanol (60 mL) was added. The flask was equipped with a reflux condenser and sulfuric acid (ca. 0.5 mL, conc.) was added via disposable pipette through the top of the

condenser. The reaction mixture was heated to reflux for 4 hours and cooled to room temperature. The methanol was removed on a rotary evaporator and water (30 mL) was added. The suspension was neutralized by the addition of aqueous sodium bicarbonate (0.5 M) until all bubbling subsided. The solution was extracted with diethyl ether (50 mL) and the ether layer was isolated and reduced *in vacuo* yielding an additional fraction of methyl-3-ethynylbenzoate (0.621 g, 21%). The combined fractions of methyl-3 -ethynylbenzoate product (1.945 g; 87%) were used without further purification.

mp 52.3–53.8 °C; Anal. Calcd for $C_{10}H_8O_2$: C, 74.99; H: 5.03. Found: C, 70.70; H, 5.15; IR (Nujol mull) $\tilde{\nu}_{max}$: 3256 (C≡CH), 2922-2855 (CH), 1732 (C=O), 1294 (C–OCH_3), 753 (Ar–H), 716 (Ar–H) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$, δ): 8.16 (s, 1H, H_2), 8.02 (d, *J*=7.9 Hz, 1H, H_6), 7.67 (d, *J*=7.7 Hz, 1H, H_4), 7.41 (dd, *J*=7.7 Hz, 1H, H_5), 3.92 (s, 3H, –OCH_3), 3.13 (s, 1H, –CCH); ^{13}C NMR (75 MHz, $CDCl_3$, δ): 166.4 (C=O), 136.4 (2C, $C_{3,5}$), 133.4 (C_1), 129.9 (2C, $C_{2,6}$), 128.6 (C_4), 82.7 (Ar<u>C</u>≡C), 78.3 (C≡<u>C</u>H), 52.4 (–OCH_3).

3.4.2 Synthesis of Methyl-4-ethynylbenzoate (**8**)

Compound **8** was prepared in 95% yield using the same reaction conditions employed for the synthesis of **7**.

mp 90.8–92.2 °C; Anal. Calcd for $C_{10}H_8O_2$: C, 74.99; H: 5.03. Found: C, 73.83; H, 4.75; IR (Nujol mull) $\tilde{\nu}_{max}$: 3243 (CH), 2923-2854 (CH), 2101 (C≡C) 1704 (C=O), 1607 (C=C), 1280 (C–O), 773 (Ar–H) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$, δ): 8.06 (d, *J*= 8.6 Hz, 2H, $H_{2,6}$), 7.59 (d, *J*= 8.6 Hz, 2H, $H_{3,5}$), 3.94 (s, 3H, –OCH_3), 3.26 (s, 1H, –CCH);

^{13}C NMR (75 MHz, $CDCl_3$, δ): 166.6 (C=O), 132.2 (2C, $C_{2,6}$), 130.2 (C_4), 129.6 (2C, $C_{3,5}$), 126.9 (C_1), 82.9 (Ar<u>C</u>≡C), 80.2 (C≡<u>C</u>H), 52.4 (–OCH_3).

3.5 Synthesis of Internal Alkyne Derivatives

3.5.1 Synthesis of *Bis*(3-methylcarboxyphenyl)acetylene (**9**)

A 250-mL round bottom Schlenk flask that was equipped with a magnetic stir bar was charged with methyl-3-iodobenzoate (3.280 g; 12.50 mmol), crude methyl-3-ethynyl benzoate (2.000 g; 12.50 mmol), *cis*-dichloro*bis*(triphenylphosphine)palladium(0) (0.263 g, 0.380 mmol, 3.00 mol%), and copper(I)iodide (0.024 g, 0.125 mmol, 1.00 mol%) and the reaction mixture was degassed by evacuating the flask for 5-10 minutes and refilled with nitrogen gas three times. Diethylamine (150 mL) was added via syringe under nitrogen. The contents were stirred for 24 hours under a slight pressure of nitrogen. The solvent was removed *in vacuo* on the Schlenk line and water (100 mL) was added to the residue. The product was extracted using diethylether in a separatory funnel. After removal of diethylether, the residue was purified by column chromatography using neutral alumina. The crude product was eluted with DCM:hexane (80:20). The combined eluant was reduced in rotary evaporator to yield a white solid (3.467 g, 94%). mp 173.8–175.2 °C; Anal. Calcd for $C_{18}H_{14}O_4$: C, 73.46; H, 4.79. Found: C, 73.19; H, 4.71; HRMS-FAB (*m/z*): $[M+H]^+$ calcd for $C_{18}H_{14}O_4$, 295.0926; found, 295.0997; IR (Nujol mull) $\tilde{\nu}_{max}$: 2924-2854 (CH), 1730 (C=O), 1577-1599 (C=Ar), 1243 (C–O), 754 (Ar–H) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$, δ): 8.22 (s, 1H, H_2), 8.02 (d, *J*= 8.2 Hz, 1H, H_6), 7.72 (d, *J*= 8.1 Hz, 1H, H_4), 7.45 (dd, *J*= 7.7 Hz, 1H, H_5), 3.95 (s, 6H, –OCH_3); ^{13}C

NMR (75 MHz, $CDCl_3$, δ): 166.2 (2C, C=O), 135.6 (2C, C_6), 132.7 (2C, C_2), 130.4 (2C, C_3), 129.4 (2C, C_4), 128.5 (2C, C_5), 123.3 (2C, C_1), 89.1 (2C, C≡C), 52.3 (2C, $-OCH_3$).

3.5.2 Synthesis of *Bis*(4-methylcarboxyphenyl)acetylene (**10**)

Compound **10** was prepared in 79% yield using the same reaction conditions employed for the synthesis of **9**.

mp 222.9–224.2 °C; Anal. Calcd for $C_{18}H_{14}O_4$: C, 73.46; H, 4.79. Found: C, 73.70; H, 4.78; HRMS-FAB (*m/z*): $[M+H]^+$ calcd for $C_{18}H_{14}O_4$, 295.0926; found, 295.1057; IR (Nujol mull) $\tilde{\nu}_{max}$: 2924-2854 (CH), 1946 (C≡C), 1716 (C=O), 1607(C=Ar), 1279 (C–O), 771 (Ar–H) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$, δ): 8.04 (d, *J*= 8.6 Hz, 4H, $H_{2,2',6,6'}$), 7.61 (d, *J*= 8.6 Hz, 4H, $H_{3,3',5,5'}$), 3.94 (s, 6H, $-OCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$, δ): 166.3 (2C, C=O), 131.5 (4C, $C_{3,5}$), 132.7 (2C, C_2), 129.8 (2C, C_1), 129.5 (2C, C_6), 127.2 (2C, C_4), 91.3 (2C, C≡C), 52.3 (2C, $-OCH_3$).

3.6 Diboration of Alkynes

3.6.1 Diboration of *Bis*(3-methylcarboxyphenyl)acetylene (**11**)

Bis(3-methylcarboxyphenyl)acetylene (1.450 g, 5.000 mmol), *bis*(pinacolato) diborane (1.270 g, 5.000 mmol) and (η^2-ethylene)*bis*(triphenylphosphine)platinum(0) (0.112 g, 3.000 mol%) were added to a 100-mL Young's tap tube. The reaction vessel was evacuated for a period of 10 minutes and refilled with a dry N_2 (g) atmosphere in triplicate. Freshly distilled toluene (20 mL) was added via syringe and the tube was sealed and heated to 90 °C overnight. The toluene was removed *in vacuo* and the product was recrystallized from THF/hexane to give a white solid (2.239 g, 82%).

mp 122.8–123.8 °C; Anal. Calcd for $C_{30}H_{38}B_2O_8$; C: 65.72; H: 6.99. Found: C, 64.99; H, 6.99 HRMS-FAB (*m/z*): $[M+H]^+$ calcd for $C_{30}H_{38}B_2O_8$, 549.28; found, 549.2768; IR (Nujol mull) $\tilde{\nu}_{max}$: 2923-2855 (CH), 1723 (C=O), 1580 (C=C), 1295 (C–O), 765 (Ar–H), 734 (Ar–H) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$, δ): 7.75 (s, 1H, H_2), 7.73 (d, *J*= 7.5 Hz, 1H, H_4), 7.10 (dd, *J*= 7.6 Hz, 1H, H_5), 7.02 (d, *J*= 6.3 Hz, 1H, H_6), 3.83 (s, 6H, $-OCH_3$), 1.33 (s, 24H, $-CH_3$); ^{13}C NMR (75 MHz, $CDCl_3$, δ): 166.9 (2C, C=O), 140.9 (2C, C_1), 133.8 (2C, C_4), 130.3 (2C, C_2), 129.4 (2C, C_3), 127.6 (2C, C_5), 127.2 (2C, C_6), 84.3 (4C, $-O\underline{C}(CH_3)_2$), 51.9 (2C, $-OCH_3$), 24.9 (8C, $-OC(\underline{C}H_3)_2$), (C=C not observed); ^{11}B NMR (96 MHz, $CDCl_3$, δ): 30.3.

3.6.2 Diboration of *Bis*(4-methylcarboxyphenyl)acetylene (**12**)

Compound **12** was prepared in 82% yield using the same reaction conditions employed for the synthesis of **11**.

mp 223.8–225.2 °C; Anal. Calcd for $C_{30}H_{38}B_2O_8$; C: 65.72; H: 6.99. Found: C, 65.67; H, 6.83 HRMS-FAB (*m/z*): $[M+H]^+$ calcd for $C_{30}H_{38}B_2O_8$, 549.28; found, 549.2747; IR (Nujol mull) $\tilde{\nu}_{max}$: 2924-2854 (CH), 1721 (C=O), 1593 (C=C), 1271 (C–O), 728 (Ar–H) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$, δ): 7.75 (d, *J*= 8.5 Hz, 1H, H_3), 7.00 (d, *J*= 8.5 Hz, 1H, H_2), 3.84 (s, 6H, $-OCH_3$), 1.32 (s, 24H, $-CH_3$); ^{13}C NMR (75 MHz, $CDCl_3$, δ): 166.9 (2C, C=O), 145.9 (2C, C_1), 129.0 (4C, $C_{3,5}$), 128.9 (4C, $C_{2,6}$), 127.7 (2C, C_4), 84.4 (4C, $-O\underline{C}(CH_3)_2$), 51.9 (2C, $-OCH_3$), 24.9 (8C, $-OC(\underline{C}H_3)_2$), (C=C not observed); ^{11}B NMR (96 MHz, $CDCl_3$, δ): 30.8.

3.7 Synthesis of *tetra*(carboxyphenyl)ethene Derivatives

3.7.1 Method A: Synthesis of *tetra*methyl-4,4',4",4"'-(ethene-1,1,2,2-*tetra*aryl) *tetra*benzoate (**14**)

A 100-mL Young's tap tube was charged with **12** (ca. 250 mg), 2–2.2 equivalent of **3**, a base, and 3 mol% catalyst. The contents were evacuated for 15 minutes and refilled with N_2 (g) three times and the solvent was added via syringe under an inert atmosphere. The tube was sealed and the reaction was heated to a fixed temperature. The reaction conditions and specific reagents used in the synthesis of **14** are given in Table 3 (Entries 1 - 4).[61]

3.7.2 Method B: Synthesis of *tetra*methyl-4,4',4",4"'-(ethene-1,1,2,2-*tetra*aryl) *tetra*benzoate (**14**)

A 100-mL round bottom Schlenk flask equipped with a magnetic stir bar was charged with **12** (ca. 500 mg), 2–2.2 equivalent of **3** or methyl-4-bromobenzoate (**13**), a base, and 3 mol% catalyst. The contents of the flask were degassed by evacuating the flask for 15 minutes under a vacuum and refilled with nitrogen gas in triplicate. The ground glass stopper was replaced with a subseal, and solvent was added via syringe under nitrogen. A reflux condensor was purged with nitrogen for 15 minutes and attached to the flask. The contents were stirred and heated for a period of time under a slight pressure of nitrogen. The product was extracted using an organic solvent (DCM, ether, or ethyl acetate):water in a separatory funnel. The organic layer was isolated and dried over magnesium sulfate, filtered, and reduced on a rotary evaporator. The reaction

conditions for and specific reagents used in the synthesis of **14** are given in Table 3 (Entries 5 - 11).

Table 3. Reaction conditions for the attempted synthesis of *tetra*methyl-4,4',4",4'"-(ethene-1,1,2,2-*tetra*aryl)*tetra*benzoate.

Entry	Catalyst	Base	Solvent	X (I,Br)	T / °C	Time /d
1	$PdCl_2$(dppf)	10 eq. of KOH	Toluene	I	95	1
2	$PdCl_2$(dppf)	10 eq. of KOH	DMF	I	110	1
3	$PdCl_2$(dppf)	10 eq. of KOH	DMSO	I	189	1
4	$PdCl_2$(dppf)	10 eq. of KOH	DMSO	I	189	2
5	$PdCl_2$(dppf)	10 eq. of KOH	DMSO	I	189	5
6	$PdCl_2$(dppf)	10 eq. of KOAc	DMSO	Br	189	21
7	$Pd(OAc)_2$	10 eq. of KOAc	DMSO	Br	189	21
8	$PdCl_2$(dppf)	4.06 eq. of KOAc	DMSO	Br	189	25
9	$PdCl_2$(dppf)	4.06 eq. of KOAc	DMSO	I	189	25
10	$PdCl_2$(dppf)	10 eq. of KOAc	DMSO	Br	189	10
11	$PdCl_2$(dppf)	15 eq. of KOAc	DMSO	Br	189	21

3.7.3 Synthesis of *tetra*methyl-3,3',3",3"'-(ethene-1,1,2,2-*tetra*aryl)*tetra*benzoate (**15**)

Synthesis of compound **15** was attempted using the same experimental design employed for the synthesis of **14** (Method A) described in section 3.7.1. The reaction conditions and specific reagents used in the synthesis of **15** are given in Table 4.[61]

Table 4. Reaction conditions for the attempted synthesis of *tetra*methyl-3,3',3",3"'-(ethene-1,1,2,2-*tetra*aryl)*tetra*benzoate.

Entry	Catalyst	Base	Solvent	T / °C	Time /d
1	$PdCl_2$(dppf)	KOAc	DMF	95	1
2	$PdCl_2$(dppf)	KOAc	DMSO	110	2
3	$PdCl_2$(dppf)	KOH	DMSO	110	2
4	$Pd_2(dba)_3$ / 4 P-(*o*-tolyl)$_3$	KOAc	DMSO	110	2
5	$Pd_2(dba)_3$ / 4 P-(*o*-tolyl)$_3$	KOAc	DMF	110	2
6	$Pd_2(dba)_3$ / 4 P-(*o*-tolyl)$_3$	KOH	DMSO	110	2
7*	$Pd(OAc)_2$	KOH	H_2O	150	2
8	$Pd(OAc)_2$	KOAc	DMF	153	1

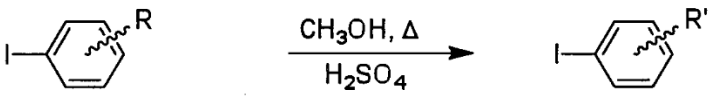
* Reaction involved hydrothermal synthesis.[61]

CHAPTER 4: DISCUSSION

The compounds prepared in this study were characterized by melting point, elemental analysis, IR spectroscopy, ^{1}H, $^{13}C\{^{1}H\}$ NMR spectroscopy and $^{11}B\{^{1}H\}$ NMR spectroscopy where appropriate. ^{1}H NMR and some ^{13}C NMR spectra are included in Appendix A and Appendix B, respectively. Other ^{13}C NMR spectra were obtained at The Hong Kong University of Science and Technology (HKUST) and are not reported herein. IR spectra are included in Appendix C. HRMS data were obtained at HKUST and are reported where available.

The synthesis of the aromatic esters **3** and **4** was based on the esterification of 4-iodobenzoic acid and 3-iodobenzoic acid using methanol (MeOH) and concentrated sulfuric acid (H_2SO_4), respectively (Equation 4.1). Even though the reactions seem very straightforward, extended periods of reflux (4-5 days) were required to ensure completion. The chemical shifts and coupling constants for the aromatic and ester functional groups are consistent with the reported values[62] for **3** and **4** within accepted experimental error. The reported[62] chemical shifts for **3** are 7.79 ppm and 7.73 ppm (d,*J*= 8.4 Hz) for the aromatic protons and 3.89 ppm for the protons of the methyl ester group and are consistent with the data obtained, with the exception of slight difference between the coupling constants. The data obtained from $^{13}C\{^{1}H\}$ NMR analysis are also in

agreement with literature values with slight chemical shifts differences attributed to the resolution of the instruments (166.6 ppm for C=O group, 137.7, 131.0, 129.5, 100.8 ppm for aromatic environments and 52.3 ppm for the $-OCH_3$ group).

(4.1) 

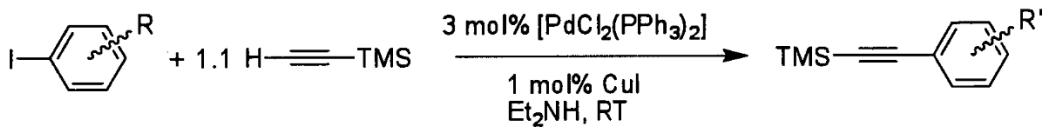
(**1**) R= 4- COOH
(**2**) R= 3- COOH
(**3**) R'= 4- CO_2CH_3
(**4**) R'= 3- CO_2CH_3

The syntheses of ethynyl substituted aromatic esters **5** and **6** have been reported by Sonogashira[8] using a trimethylsilyl (TMS) protecting group (Equation 4.2). Upon the completion of the reaction, the crude product was weighed, and the yield was determined. Since the crude solid contained traces of catalyst and amine salts, the yield were typically greater than the theoretical yield. The removal of these impurities was accomplished by chromatographic separation on neutral alumina. Spectral analysis of the crude product (^{1}H NMR) indicated that the reactions had reached completion. The low yield of compounds **5** and **6**, 51% and 74%, respectively, may be due to reaction with the column material during isolation, the reaction between the ester functionality with NEt_2H in the presence of water during isolation, or the presence of trace quantities of oxygen in the reaction mixture resulting in the formation of TMS-C≡C-C≡C-TMS via Hay coupling. A slight excess of trimethylsilyl acetylene (TMSA) was used to account for the 6 mol percent of TMSA required during catalyst activation.[11] These reactions are known to be highly air sensitive due to the homo-coupling of TMSA in the presence of copper and oxygen (Hay coupling) and it is possible that small amounts of air were introduced as these techniques were being learned.

The ^{13}C NMR spectra display singlet resonances at 104.0 ppm (Ar<u>C</u>≡C), 95.5 ppm (**5**) and 97.6 ppm (**6**) (ArC≡<u>C</u>), and 0.0 ppm indicative of the addition of TMSA to the aryl group for both derivatives. The ^{1}H NMR spectrum displayed one additional resonance when compared to those for **3** and **4** at 0.26 ppm (s, 9H, $Si(CH_3)_3$), indicative of the new TMS environment for both derivatives. The remaining chemical shifts and coupling constants for the aromatic and ester functional groups are also consistent with the reported values for **5** and **6** within accepted experimental error.[63] The reported ^{1}H NMR spectroscopy values for **6** are 8.00 ppm (d, J=8.0 Hz, 4H, aromatic H), 7.52 ppm (d, J=8.0 Hz, 4H, aromatic H), 3.90 ppm (s, 3H, $-OCH_3$), and 0.28 ppm (s, 9H, $Si(CH_3)_3$). With the exception of different coupling constant (J=8.6 Hz vs J=8.0 Hz[63]), the literature values for chemical shifts are consistent with our results.

The IR spectra display the presence of the C≡C group at 2158 cm^{-1} and 2160 cm^{-1} for **5** and **6**, respectively, and notable shifts for the C=O vibrations (1728 cm^{-1} (**5**) and 1720 cm^{-1} (**6**)). The literature values for **5** and **6** were 2160 cm^{-1} (C≡C), 1720 cm^{-1} (C=O), and 2160 cm^{-1} (C≡C), 1718 cm^{-1} (C=O), respectively.[63] The reported melting point for **6** is 55.0–55.5 °C and consistent with our results.[63]

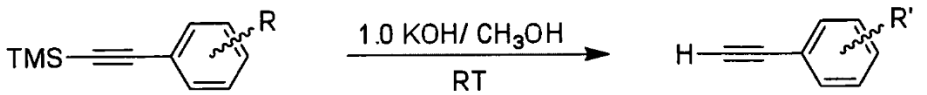
(4.2)



(**3**) R= 4- COOH
(**4**) R= 3- COOH

(**5**) R'= 3- CO_2CH_3
(**6**) R'= 4- CO_2CH_3

The removal of the TMS protecting group by treatment with a dilute alkali solution to generate the terminal arylacetylene derivatives was accomplished according to the literature (Equation 4.3).[12, 61] In a typical reaction the protected alkyne is treated with methanolic KOH at room temperature to form the terminal acetylene product. For the synthesis of **7**, further experimentation was needed to increase the yield for this reaction. Due to the different solubility of ester derivatives, loss of product as a carboxylate salt in the aqueous layer of the extraction seemed to be the most likely explanation. The addition of conc. HCl to the aqueous layer resulted in a large quantity of deprotected alkyne product, i.e. the ethynylbenzoic acid derivative. The addition of HCl into the aqueous layer, followed by extraction and isolation of the byproducts was not reported by Sonogashira et al. or Austin et al. in their studies. After the isolation of 3-ethynylbenzoic acid, it was esterified to reform the methyl ester. The overall yield increased from 66% to 87% using this method. The same procedure was employed in the synthesis of **8** and resulted in an overall yield of 95%. The vast improvement in yield coupled with the ease of removal of the ester functionality in the presence of base may be the cause of the lower yields obtained in the synthesis of **5** and **6** given that the solvent diethylamine is a base. Using a similar methodology for the synthesis of **5** and **6** has not been attempted as part of these studies since the yields obtained were sufficient to continue the synthesis of subsequent steps.

(4.3) 

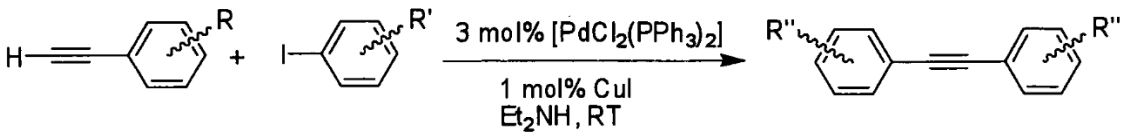
(**5**) R= 3- COOH
(**6**) R= 4- COOH
(**7**) R'= 3- CO_2CH_3
(**8**) R'= 4- CO_2CH_3

The IR spectra support the presence of terminal H at 3256 cm^{-1} and 3243 cm^{-1} in place of the TMS group for **7** and **8**, respectively. The ^1H NMR spectra also support the presence of the terminal H with the disappearance of the resonances due to the TMS group and new resonances at 3.13 ppm and 3.26 ppm (s, 1H, –CCH) for **7** and **8**, respectively. Aromatic resonances showed minor changes due to the change in the electronic environment resulting from the deprotection of the TMS group. The reported ^1H NMR chemical shifts (in ppm) for **7** and **8** are 8.17–7.33 (m, 4H, aromatic H), 3.91 (s, 3H, $–OCH_3$), 3.10 (s, 1H, –CCH) and 7.70 (q, J=8.0 Hz, 4H, aromatic H), 3.88 (s, 3H, $–OCH_3$), 3.19 (s, 1H, –CCH), respectively.[63]

The ^{13}C NMR spectrum displayed more significant changes in the alkyne resonances due to the deprotection of the TMS group. The alkyne resonances show an upfield shift from 104.0 ppm to 82.7 ppm and 82.9 ppm (Ar-C≡C) and from 95.5 and 97.6 ppm to 78.3 ppm and 80.2 ppm for **7** and **8**, respectively. The reported melting points for **7** and **8** are 48–50 °C and 92.5–93.5 °C, respectively and consistent with our results.[63]

The synthesis of the internal alkyne derivatives via the reaction between iodoarenes and the arylacetylene compounds was performed to prepare two *bis*(methyl-carboxyphenyl)acetylene derivatives (Equation 4.4). The reactions proceeded in excellent yield (94% and 79% for **9** and **10**, respectively). Given these yields and the similar conditions to those employed in the synthesis of **5** and **6**, it seems less likely that the low yields for compounds **5** and **6** would be due to interactions with the base, diethylamine.

(4.4)



(7) R= 3- CO_2CH_3 (3) R= 4- CO_2CH_3 (9) R'= 3- CO_2CH_3
(8) R= 4- CO_2CH_3 (4) R'= 3- CO_2CH_3 (10) R'= 4- CO_2CH_3

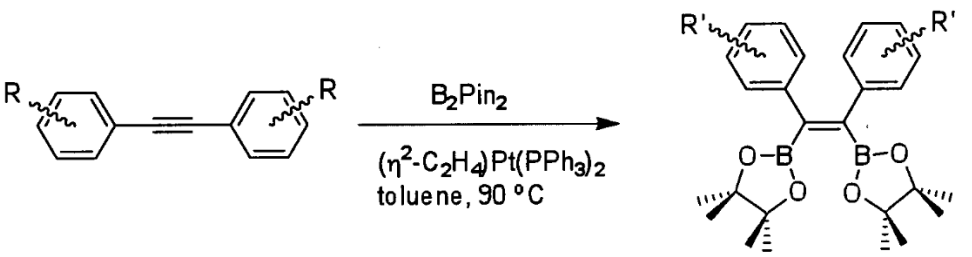
In the ^1H NMR spectra for **9** and **10** the resonances for the protons of the terminal acetylenes were no longer present. The aromatic proton environments changed slightly in chemical shift and minor changes were observed in the coupling constants for **9** versus those of the precursor, **7**. The $^{13}C\{^1H\}$ NMR spectrum also indicated the presence of a reaction to produce **9** and **10** notably with a change in the C≡C resonance (89.1 ppm and 91.3 ppm, respectively) consistent with the presence of two equivalent acetylene environments in each case.

The vibrations in the IR spectrum for **7** and **8** at 3256 and 3243 cm^{-1}, which are attributed to the presence of the terminal H, disappear in the spectra for **9** and **10**. The C≡C was not observed in the IR spectrum of **9** but a weak resonance at 1946 cm^{-1} in the spectrum for **10** may indicate resonance with the aromatic groups in these derivatives given the inherent weakening of the C≡C bond resulting in the lower value versus that for **8** (2101 cm^{-1}). Analytical data for compounds **9** and **10** are not reported in the literature but are consistent with the proposed structures and remaining data are consistent with previous studies conducted in this laboratory.[61] HRMS data were completed using products from the initial studies and are included for completion of the characterization.

Upon the successful synthesis of the internal alkynes, platinum catalyzed diboration of alkynes was performed to obtain the *cis-bis*(boryl)alkene derivatives

(Equations 4.5). These synthetic reactions have been performed previously in this laboratory however additional quantities were required to prepare samples for further reactions. The diboration of alkynes was initially reported by Ishiyama and colleagues to yield *cis-bis*(boryl)alkene derivatives using [$Pt(PPh_3)_4$] as a catalyst.[18] Subsequent studies demonstrated that *cis*-[$Pt(\eta^2\text{-}C_2H_4)(PPh_3)_2$] was also a suitable catalyst and was employed in the studies performed.[17] Derivatives **11** and **12** were obtained in 82% yield as pure white solids. Spectral and analytical data are consistent with the proposed structures.

(4.5)



(**9**) R= 3- CO_2CH_3
(**10**) R= 4- CO_2CH_3

(**11**) R= 3- CO_2CH_3
(**12**) R= 4- CO_2CH_3

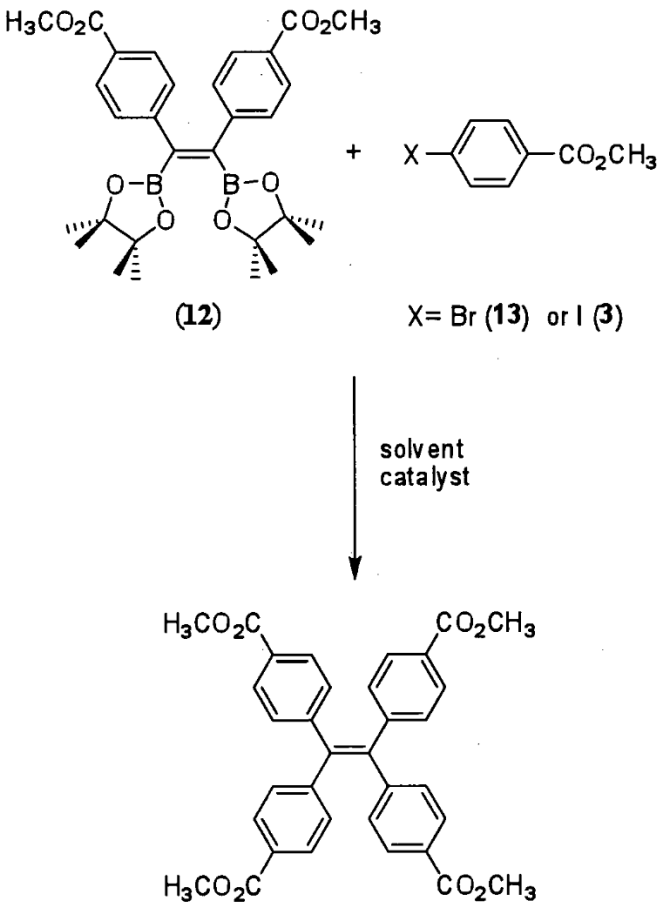
Multinuclear NMR analysis clearly indicates the presence of a reaction. The ^1H NMR spectra display resonances due to the methyl groups of the Bpin moiety at 1.33 ppm and 1.32 ppm for **11** and **12**, respectively. The chemical shifts and coupling constants for the aromatic protons in each derivative change significantly from those of the precursors **9** and **10**. For example, the resonances for **10** at 8.04 ppm and 7.61 ppm (J= 8.6 Hz) shift upfield to 7.75 ppm and 7.00 ppm (J= 8.5 Hz) in the spectrum for **12**. A significant shift in the $-OCH_3$ resonance also occurs from 3.94 ppm to 3.84 ppm.

The ^{13}C NMR spectra clearly indicate the methyl group on the BPin at 24.9 ppm for **11** and **12**. The ^{13}C NMR spectrum displayed one additional resonance at 84.3 ppm

and 84.4 ppm, indicative of the additional $O\underline{C}(CH_3)_2$ environment for **11** and **12**, respectively, when compared to the spectra for **9** and **10**. The reaction of the alkyne group is apparent with the disappearance of the resonances at 89.1 ppm and 91.3 ppm for **9** and **10**, respectively. The C=C environment is not observed in the spectra of **11** and **12** due to quadrupolar broadening of the BPin groups. The presence of the BPin groups was verified by the broad singlet resonance in the $^{11}B\{^1H\}$ NMR spectra at 30.3 ppm and 30.8 ppm for **11** and **12**, respectively.

Analytical data for compounds **11** and **12** are not reported in the literature but are consistent with the desired structures and previous studies in this laboratory.[61]

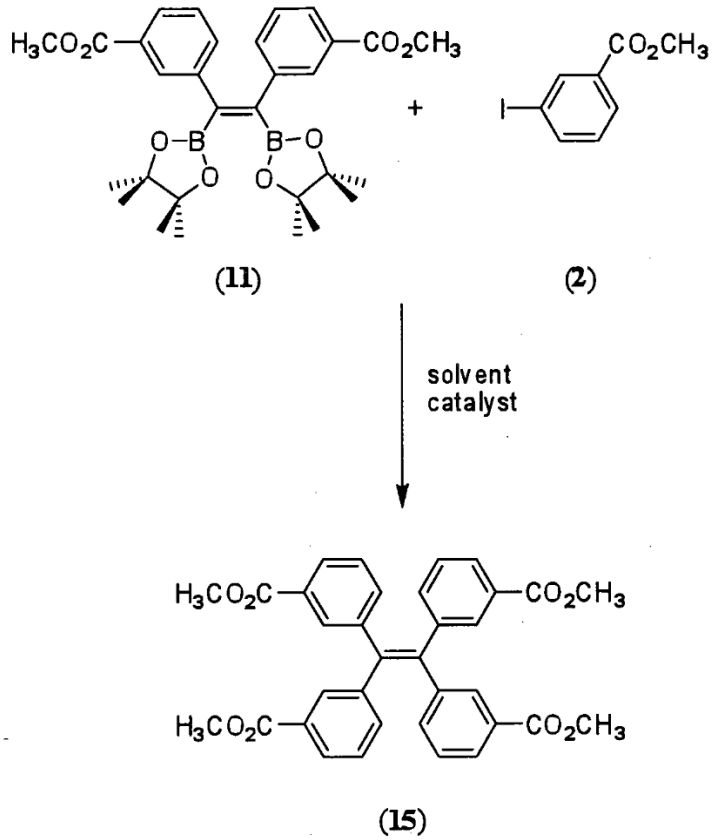
The synthesis of *tetra*(carboxyphenyl)ethene derivatives **14**, **15** relies on the sequential Suzuki coupling reaction (Equations 4.6 and 4.7). This methodology has been investigated by two different groups. Both reports[36, 37] examined the sequential coupling of each boryl group on diborated alkynes to form unsymmetrical alkene derivatives. We attempted to synthesize our desired products using various conditions, which are summarized in Table 3 and Table 4. The basic synthetic reactions are shown in Equations 4.6 and 4.7 for **14** and **15**, respectively.



(12) X= Br (13) or I (3)

(4.6)

(14)

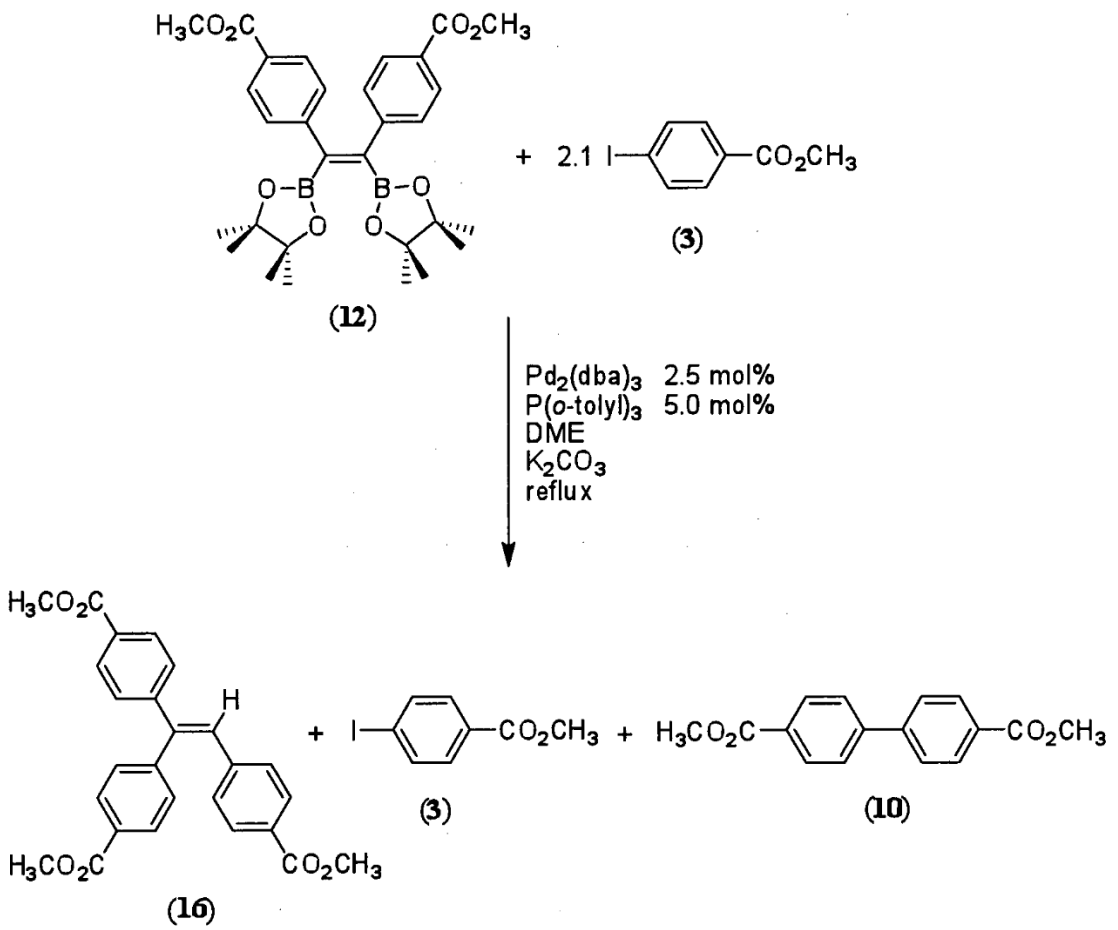


(4.7)

Our main goal was to obtain symmetrically substituted *tetra*-(carboxyphenyl)ethene derivatives by the sequential coupling of **11** and **12** with additional quantities of **3** and **4** or the corresponding bromide derivatives. Preliminary studies for the preparation of **15** were conducted by using $Pd_2(dba)_3$/2 P(*o*-tolyl)$_3$ as the catalyst in DME with aqueous K_2CO_3 as the base. This reaction yielded unexpected results as shown in Equation 4.8.[61] The *tri*(aryl) alkene derivative (**16**) was obtained as the major product likely due to the hydrolytic deboration noted by Brown and Armstrong.[37] Since water from the aqueous base solution was the only hydrogen source present to form a C–H bond in the reaction mixture, anhydrous DMF and DMSO were used to dissolve the base in further coupling reactions studied, in order to eliminate the unwanted side product. The preliminary reactions related to this study have not been

reported in the literature and are included (Table 3; Entries 1 - 4 and Table 4; Entries 1 - 8) to complete the discussion of the current results.[61] Anhydrous base (KOAc) stored in a dry glove box was used in the subsequent reactions (Table 3; Entries 6 - 11) since samples stored outside the glove box were noticeably hydrated. Reactions using KOH were studied to ascertain how the presence of a strong base would accelerate the coupling as noted by Ishiyama and colleagues.[18]

(4.8)



As far as the palladium catalyst is concerned, for the preparation of **15**, $PdCl_2$(dppf), $Pd(OAc)_2$ and $Pd_2(dba)_3$ / P-(*o*-tolyl)$_3$ were used as catalysts. The reactions

proceeded using KOH and KOAc as bases and DMF, H_2O, and DMSO as solvents. Table 4 summarizes all of the different attempts utilized in the synthesis of **15** based on the Equation 4.7. As shown in this table, temperature ranged between 95 °C and 153 °C. After each attempt, crude reaction mixtures were characterized by ^{1}H NMR spectroscopy. ^{1}H NMR spectra showed unreacted starting material and a 1:1:1 set of singlet resonances in the $-OCH_3$ region characteristic of the *tris*(aryl)alkene product in each individual reaction mixture, an indication of incomplete reactions. For Entries 1 - 8 (Table 4), the use of $PdCl_2$(dppf) provided better results than $Pd(OAc)_2$ and $Pd_2(dba)_3$ / P-(*o*-tolyl)$_3$, even though $Pd(OAc)_2$ was used at higher temperatures. The ^{1}H NMR spectra displayed less starting material when the catalyst was $PdCl_2$(dppf). Therefore, $PdCl_2$(dppf) was chosen to initiate the preparation of **14**.

As shown in Equation 4.6, in addition to compound **3**, methyl-4-bromobenzoate (**13**) was also prepared with the technique described in section 3.2.1. Three different solvents with varying boiling points were used to examine the reaction at different temperatures (Table 3; Entries 1 - 3). The reactions at 189 °C with DMSO provided the least amount of starting material when the ^{1}H NMR spectrum was analyzed; thus, DMSO was used as the solvent for the subsequent attempts. In the following attempts, the reaction mixture was prepared using $PdCl_2$(dppf) as the catalyst, KOH as the base, and DMSO as the solvent and the reaction mixtures were refluxed for successively longer time periods (Entries 4, 5). It was determined after these attempts that even a period of five days of reflux was insufficient to obtain completion. The ^{1}H NMR spectra indicated the presence of starting material and *tris*(aryl)alkene in the reaction mixture. The catalysts $PdCl_2$(dppf) and $Pd(OAc)_2$ were compared once more with **13** (assessing the

effect of Br vs I) in DMSO under reflux for a period of 3 weeks (Entries 6, 7). The ^{1}H NMR displayed multiple resonances in the methoxy and aromatic regions, however, none of the resonances could be assigned to the presence of any significant amount of the desired product.

Entries 8 and 9 were completed to compare the reactivity of **13** and **3** in DMSO with 4.06 equivalent of KOAc as the base. The reactions studied were often complicated by the presence of COOH groups derived from the reaction of strong base (KOH) with the ester function groups. The excess base (present in all other Entries) was therefore added to ensure the reaction was not reaching completion due to a lack of base. It should be noted that the presence of excess KOH was also shown to give sluggish reactions possibly due to deactivation of the catalyst. The reactions were refluxed for a period of 25 days. The reason 4.06 equivalent of KOAc was used instead of the large excess in other trials was to observe the effect of extended reaction times on the completion of the reaction. An ethyl acetate/water extraction was used in these and final trials since this was found to be more effective in terms of extracting all of the ester and carboxylic acid derivatives present in solution. During the isolation of the crude solid in the separatory funnel, some black precipitation was observed in the aqueous layer. This solid was characterized by ^{1}H NMR spectroscopy, and the resulting spectrum indicated the presence of a carboxylic acid derivative. This black solid was refluxed in MeOH with H_2SO_4 to reform the methyl ester. Then, it was characterized by ^{1}H NMR spectroscopy. Among all of the Entries, ^{1}H NMR results were the most promising for Entry 8. The ^{1}H NMR spectrum indicated that the reaction mixture contained a new product. The ^{1}H NMR spectrum of this minor fraction displayed two doublets in the aromatic region (8.11

and 7.70 ppm) and one singlet in methoxy region (at 3.95 ppm) consistent with a different reagent and different from the chemical shifts of the unreacted starting material. The integration of these resonances resulted in 1:1.5 ratio for aromatic and methoxy region, respectively. The yield was too low to perform further characterization and the new resonances could be attributed to the desired product but also additional derivatives such as CH_3O-C_6H_4-$B(OH)_2$ or a transition metal compound resulting from the oxidative addition of **13**. Using **13**, excess KOAc and reaction times of 10 days (Entry 10) or 21 days (Entry 11) resulted in similar results to the previous trials.

The required high activation energy for the formation of compounds **14** and **15** is consistent with the structure of the directing group on benzene. The activation or deactivation of the benzene ring toward electrophilic substitution correlated with the electron donating or electron withdrawing influence of the substituents, as measured by molecular dipole moments.[64] Our substituent, methyl benzoate, is highly electron deficient and has been characterized as a strong electron withdrawing group (EWG).[64] It is a known fact that a EWG will retard electrophilic substitution via deactivation of the benzene ring. When previous reports[35-39] were analyzed for the synthesis of tetrasubstituted olefins, the substituents were dominated by electron releasing groups (ERG), such as benzene, toluene, aniline, anisole, and (trifluoromethoxy)benzene. Jiang and colleagues[39] studied the formation of tetrasubstituted olefins using supercritical carbon dioxide as solvent. The authors showed that under the same reaction conditions, substantial yields of the tetrasubstituted olefins could be obtained when toluene (88%) and anisole (87%) were used. However, the use of ethoxybenzene, an EWG resulted in only a trace of the desired product under the same reaction conditions.

CHAPTER 5: CONCLUSION AND FUTURE RESEARCH

This research was carried out as part of an ongoing research project. This stage investigates the multistep synthesis of ligands classified as *tetra*(carboxyphenyl)ethene derivatives and their employment to generate MOFs. Though the precursor compounds were successfully synthesized, the synthesis of *tetra*methyl-4,4',4",4'"-(ethene-1,1,2,2 -*tetra*aryl)*tetra*benzoate and *tetra*methyl-3,3',3",3'"-(ethene-1,1,2,2-*tetra*aryl)*tetra* benzoate proved unsuccessful despite the multiple experimental conditions using a variety of catalysts, bases, solvents, temperatures and reaction times. The desired products needed to generate MOFs could not be synthesized with any certainty, even with extended periods of reflux at higher temperatures such as 189 °C, regardless of base (KOAC vs KOH), or halogen (Br vs I), or catalysts (dppf derivatives vs $Pd(OAc)_2$). This is likely due to the deactivation from the presence of the EWGs. In fact, it appears that the second Suzuki coupling reaction step did not occur to any significant extent in any of the reactions studied. It is unlikely that this may be attributed to the steric bulk of the *tri*(aryl)alkene derivatives since similar steric constraints are present in the synthesis of similar *tetra*-substituted derivatives using microwave conditions and supercritical carbon dioxide. Since time did not permit the set up of additional conditions for the synthesis of these compounds, generation of MOFs is waived in this research and is intended for future work.

Future research on the synthesis of ligands classified as *tetra*(carboxyphenyl) ethene derivatives will require modifications to the reaction conditions previously used and application of new synthetic routes.

As provided in chapter 3, reaction conditions for the attempted synthesis of *tetra*methyl-4,4',4",4"'-(ethene-1,1,2,2-*tetra*aryl)*tetra*benzoate and *tetra*methyl-3,3',3",3"'-(ethene-1,1,2,2-*tetra*aryl)*tetra*benzoate, utilized various catalysts, bases, solvents, temperatures and durations to achieve optimum reaction conditions. All of these experimental trials clearly indicate that conditions were not optimal, as the reactions did not reach completion. It is suggested that extended periods of reflux using a higher boiling solvent may help the reactions go to completion.

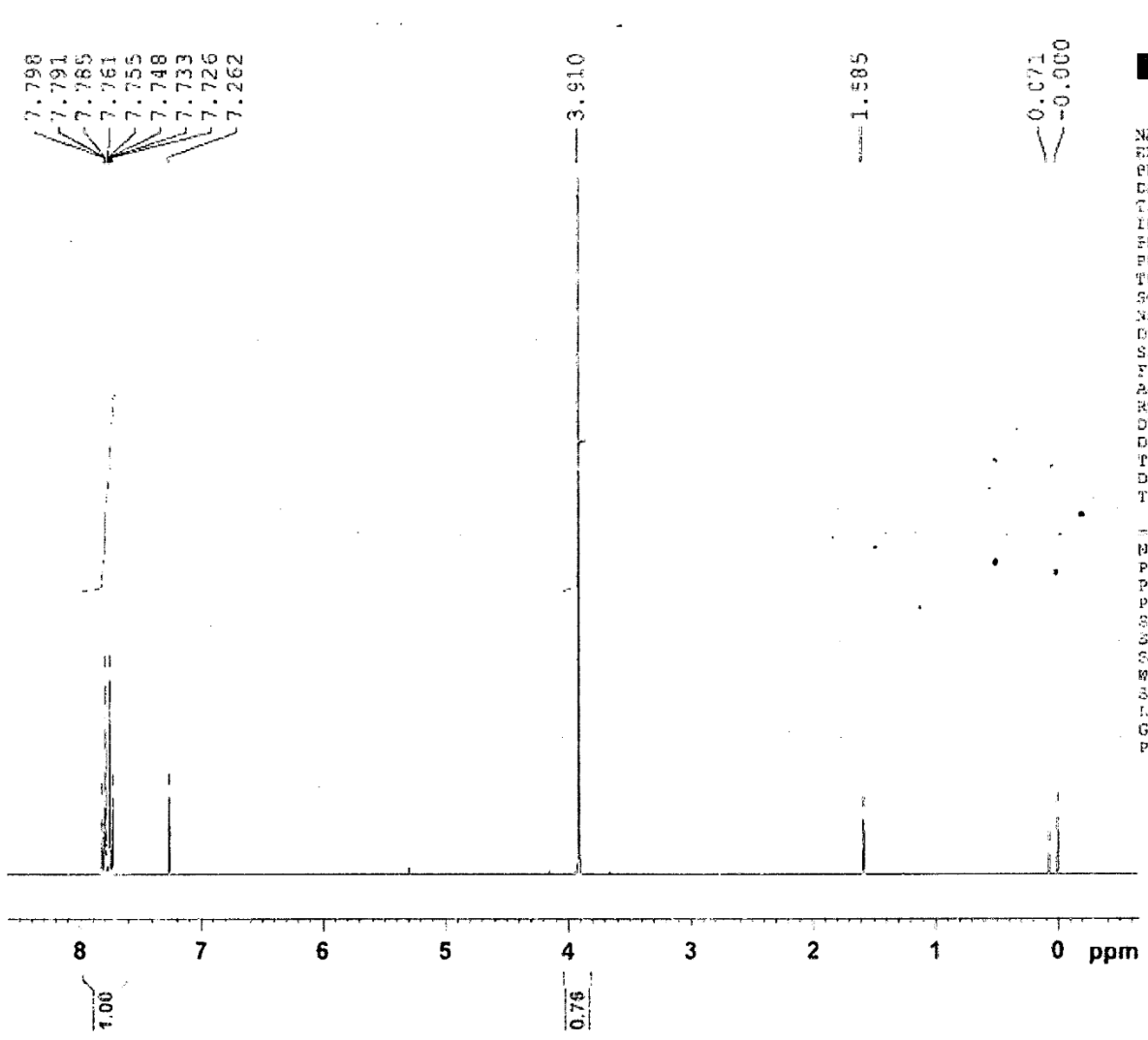
Recent literature suggests that other experimental designs, the use of microwave and supercritical carbon dioxide, rather than the conventional solvent techniques performed in this research would aid in the synthesis of *tetra*(carboxyphenyl)ethene derivatives.[35, 39] Since the typical 30-day duration is a very long time to conduct an experiment, these convenient techniques might facilitate synthesis and reduce the required time for the reactions go to completion.

It is proposed that the structure of the directing group on benzene should be chosen among electron releasing groups such as benzene, toluene, aniline, anisole instead of highly electron withdrawing groups. Particularly as an extension of this research, tolyl derivatives may be the most appropriate substituents. Once the *tetra*substituted olefins are prepared from tolyl derivatives, the pendant methyl groups can be oxidized using potassium permanganate $KMnO_4$ to convert the methyl groups to carboxylic acid

derivatives. The reactivity of the alkene moiety may or may not be oxidized during this process and is difficult to predict given the steric bulk of the four aryl groups.

APPENDIX A: ^{1}H NMR SPECTRA

Figure A.1: Methyl-4-Iodobenzoate in $CDCl_3$



NAME	1H SO1 E3 in CDCL3
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PROCNO	1
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TD	65536
SOLVENT	CDCl3
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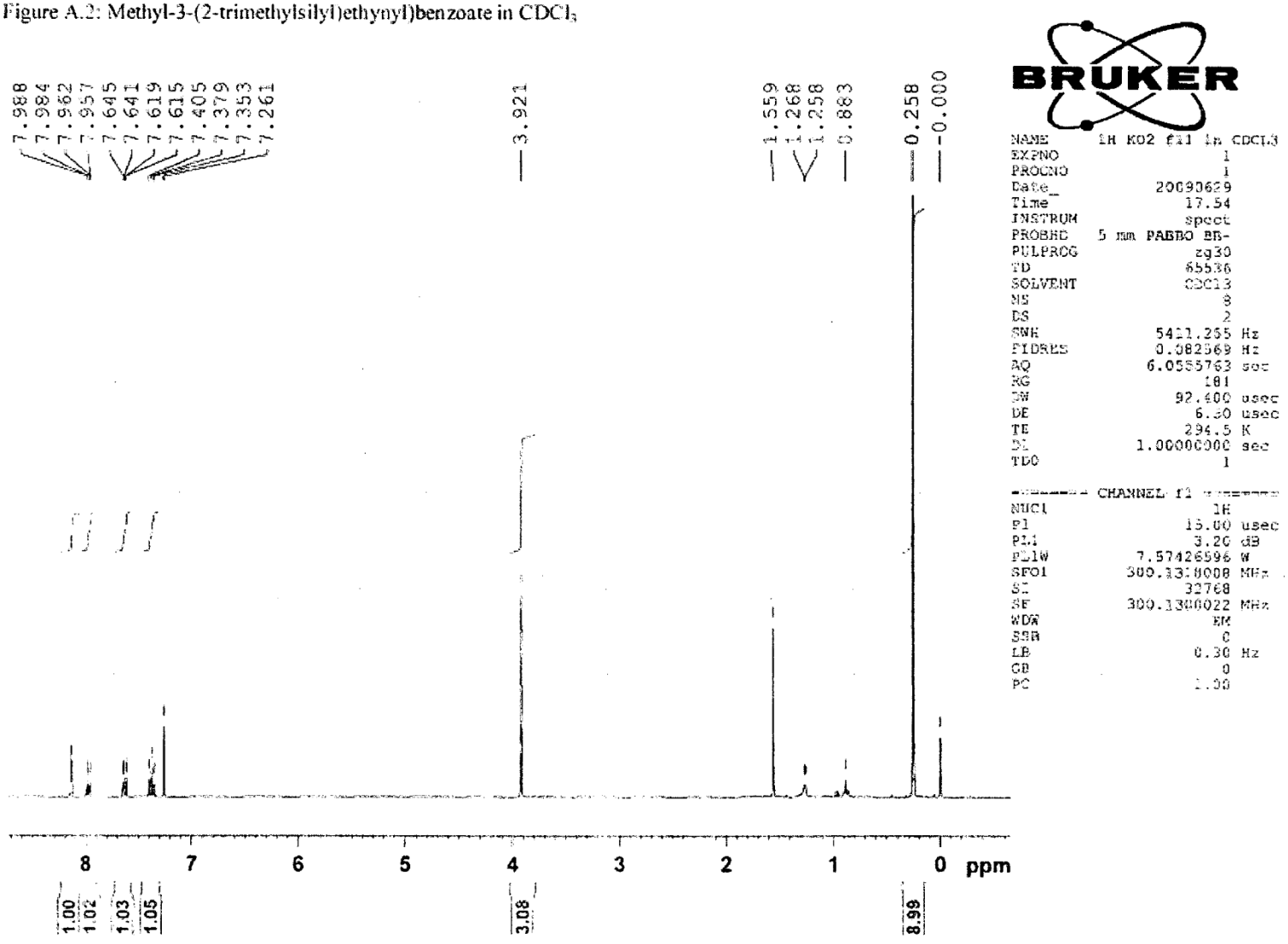
DS	2
SWH	5411.255 Hz
FIDRES	0.082569 Hz
AQ	6.0555763 sec
RG	181
DW	92.400 usec
DE	6.50 usec
TE	294.3 K
D1	1.00000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	1H
P1	15.00 usec
PL1	3.20 dB
PL1W	7.57426596 W
SFO1	300.1318000 MHz
SI	32768
SF	300.1300016 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

Figure A.2: Methyl-3-(2-trimethylsilyl)ethynyl)benzoate in $CDCl_3$



BRUKER

NAME	1H KO2 fil in CDCl3
EXPNO	1
PROCNO	1
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Time	17.54
INSTRUM	spect
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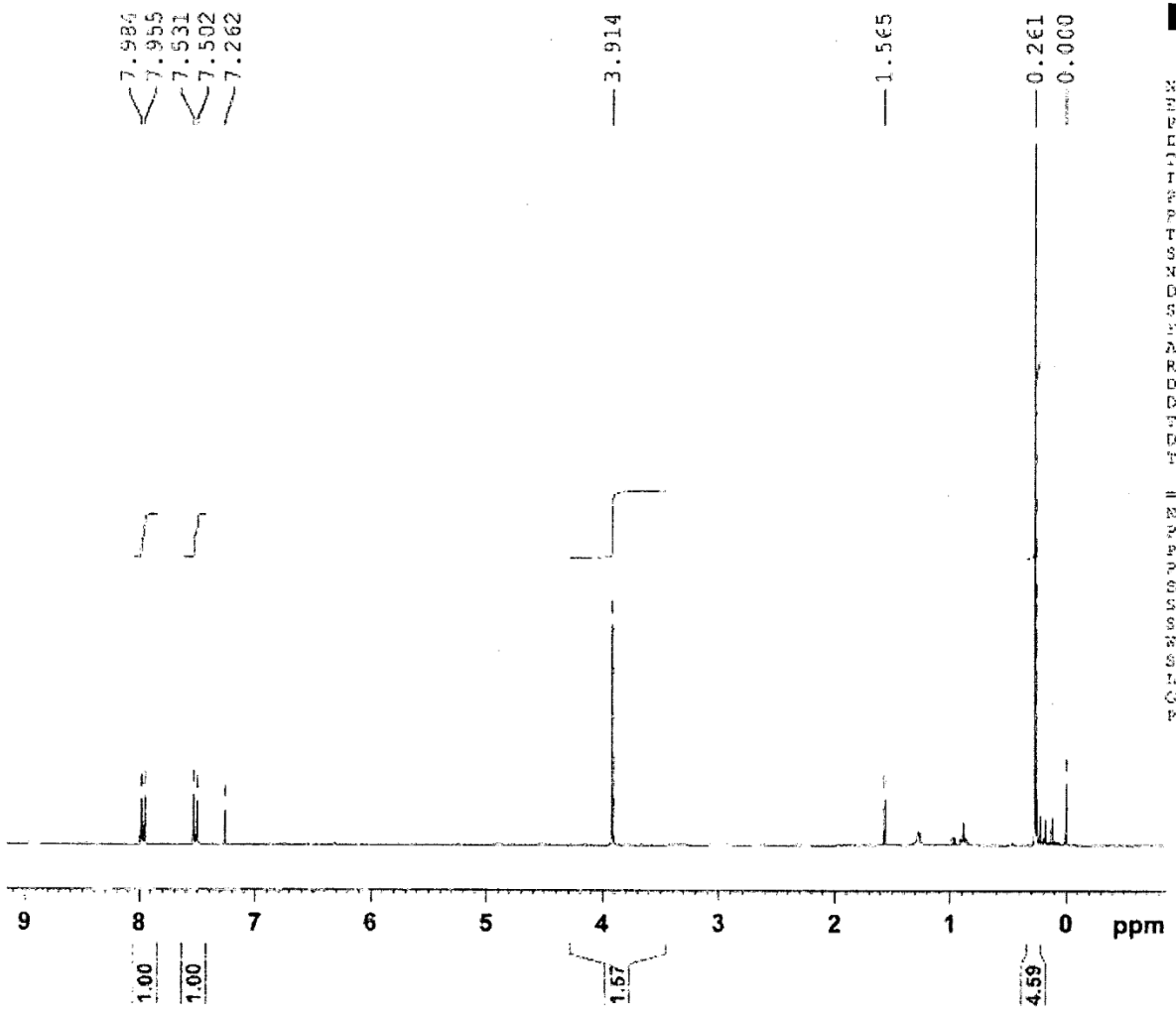
PULPROG	zg30
TD	65536
SOLVENT	CDCl3
NS	8
DS	2
SWH	5411.255 Hz
FIDRES	0.082569 Hz
AQ	6.0555763 sec
RG	181
DW	92.400 usec
DE	6.50 usec
TE	294.5 K
D1	1.00000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	1H
P1	15.00 usec
PL1	3.20 dB
PL1W	7.57426596 W
SFO1	300.1310008 MHz
SI	32768
SF	300.1300022 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

Figure A.3: Methyl-4-(2-trimethylsilyl)ethynyl)benzoate in $CDCl_3$



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PULPROG	zg30
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SOLVENT	CDCl3
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DS	2
SWH	6002.401 Hz
FIDRES	0.091589 Hz
AQ	5.4591990 sec
RG	161
DW	83.300 usec
DE	10.69 usec
TE	294.1 K
D1	1.00000000 sec
TD0	1
======== CHANNEL f1 ========	
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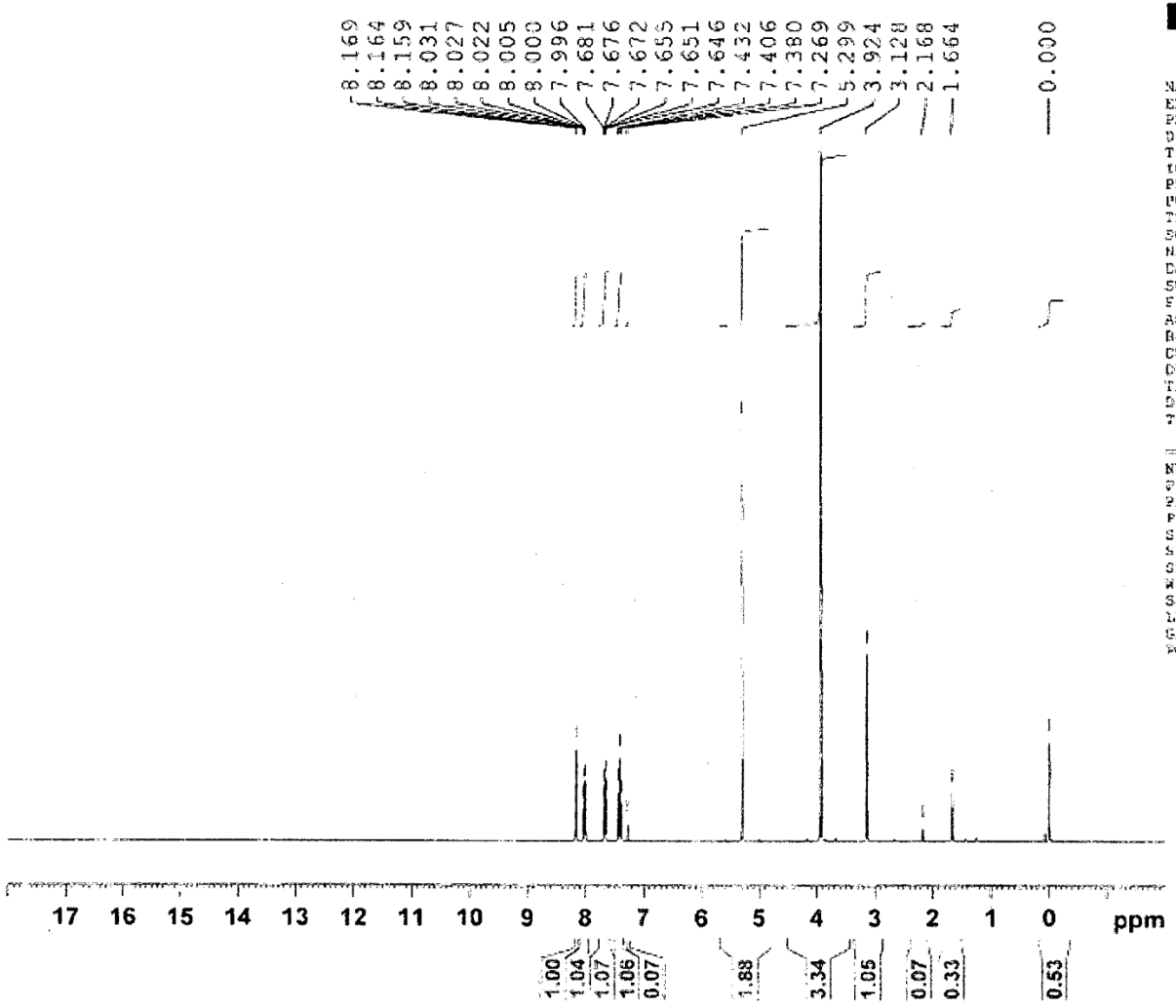
PL1	3.20 dB
PL1W	7.57426596 W
SFO1	300.2324010 MHz
SI	32768
SF	300.1300017 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

Figure A.4: Methyl-3-ethynylbenzoate in $CDCl_3$



BRUKER

NAME	1H ROS (final in CDCl3
EXPNO	1
PROCNO	1
Date_	20090711
Time	14.44
INSTRUM	spect
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PULPROG	zg30
TD	65536
SOLVENT	CDCl3
NS	8
DS	2
SWH	6002.401 Hz
FIDRES	0.091599 Hz
AQ	5.4591930 sec
RG	71.3
DW	83.300 usec
DE	12.09 usec
TE	298.9 K
D1	1.00000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	1H
P1	15.00 usec
PL1	3.20 dB
PLW1	7.57426596 W
SFO1	300.1324010 MHz
SI	32768
SF	300.1299996 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

Figure A.5: Methyl-4-ethynylbenzoate in $CDCl_3$

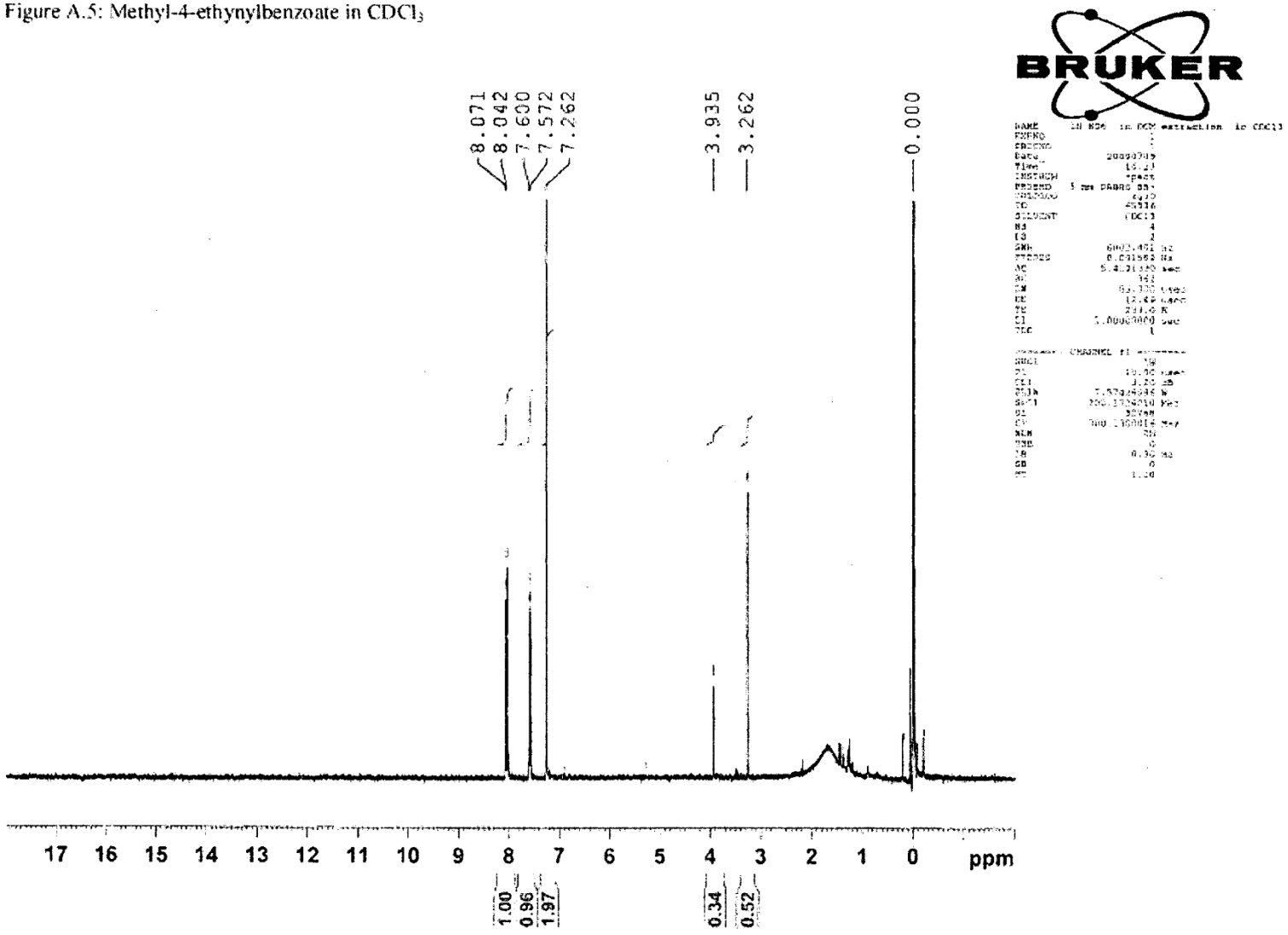


Figure A.6: *Bis*(3-methylcarboxyphenyl)acetylene in $CDCl_3$

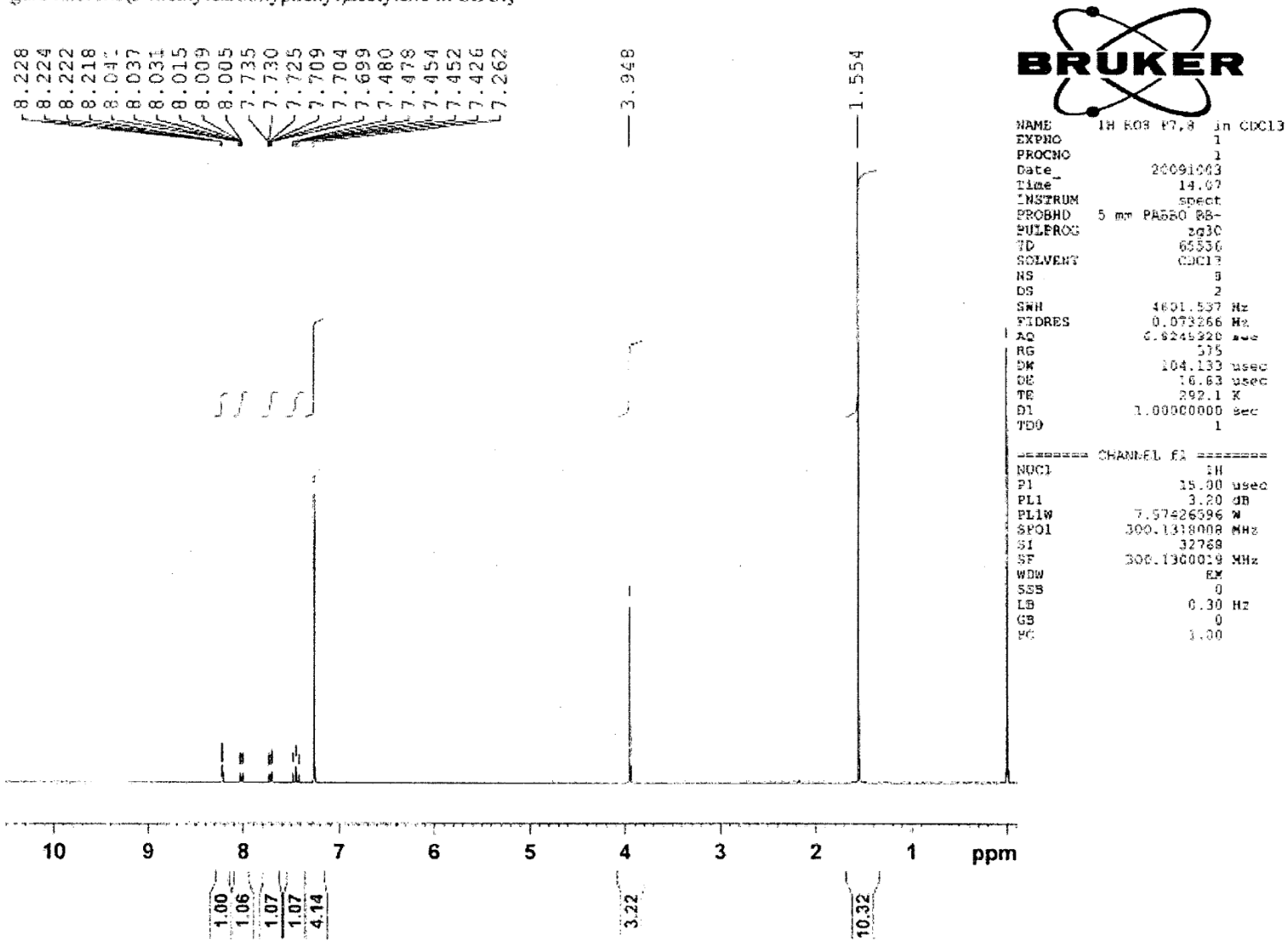
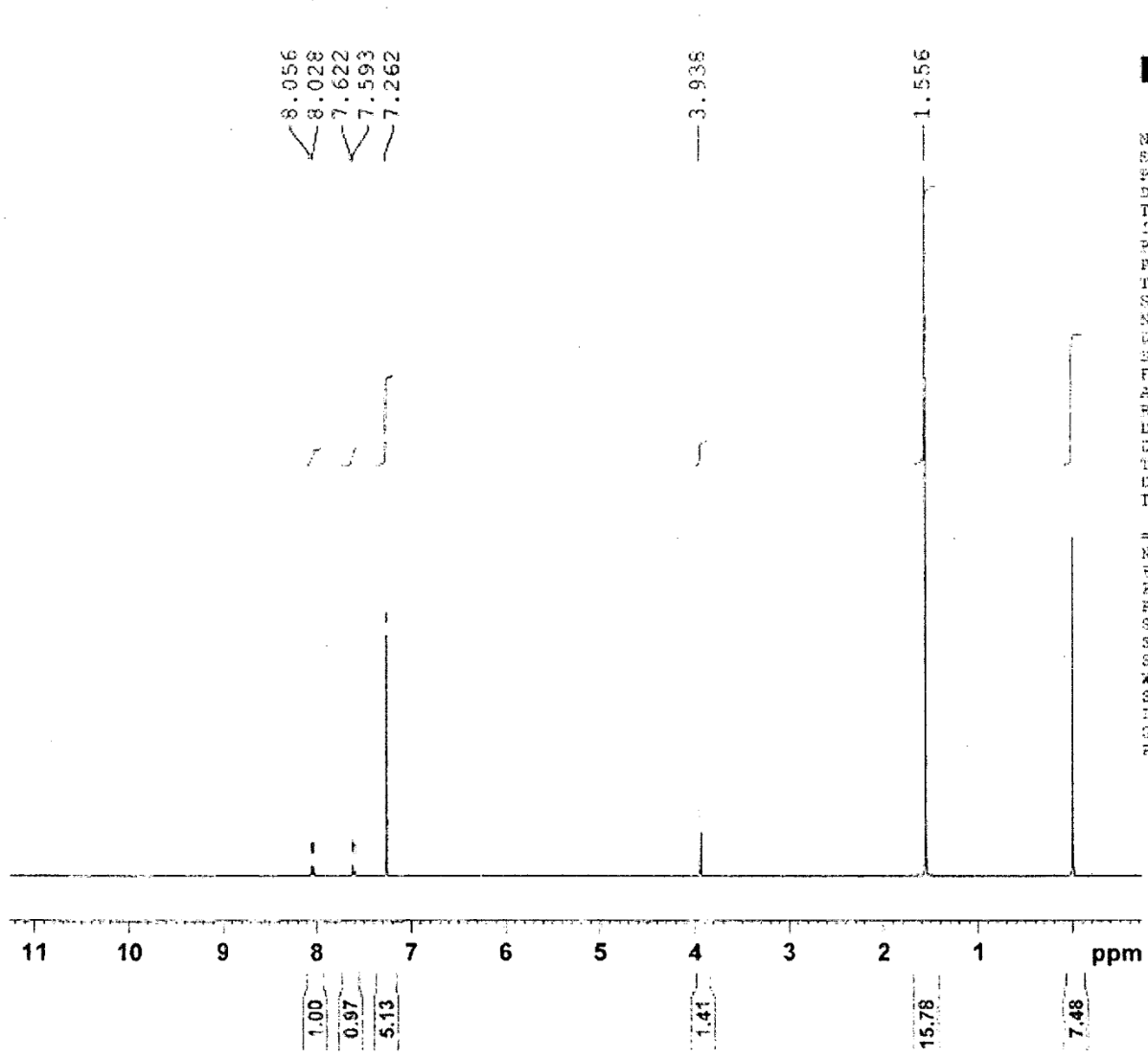


Figure A.7: *Bis*(4-methylcarboxyphenyl)acetylene in $CDCl_3$



BRUKER

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PROCNO            1
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Time_         14.30
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PULPROG        zg30
TD            65536
SOLVENT       CDCl3
NS                8
DS                2
SWH         4801.537 Hz
FIDRES      0.073266 Hz
AQ          6.8245320 sec
RG              575
DW            104.133 usec
DE             16.83 usec
TE             292.6 K
D1          1.00000000 sec
TD0               1

======== CHANNEL f1 ========
NUC1              1H
P1             15.60 usec
PL1             3.20 dB
PL1W       7.57426596 W
SFO1     300.1318008 MHz
SI            32768
SF       300.1300017 MHz
WDW              EM
SSB               0
LB             0.30 Hz
GB                0
PC             1.00
```

Figure A.8: Diborated *Bis*(3-methylcarboxyphenyl)acetylene in $CDCl_3$

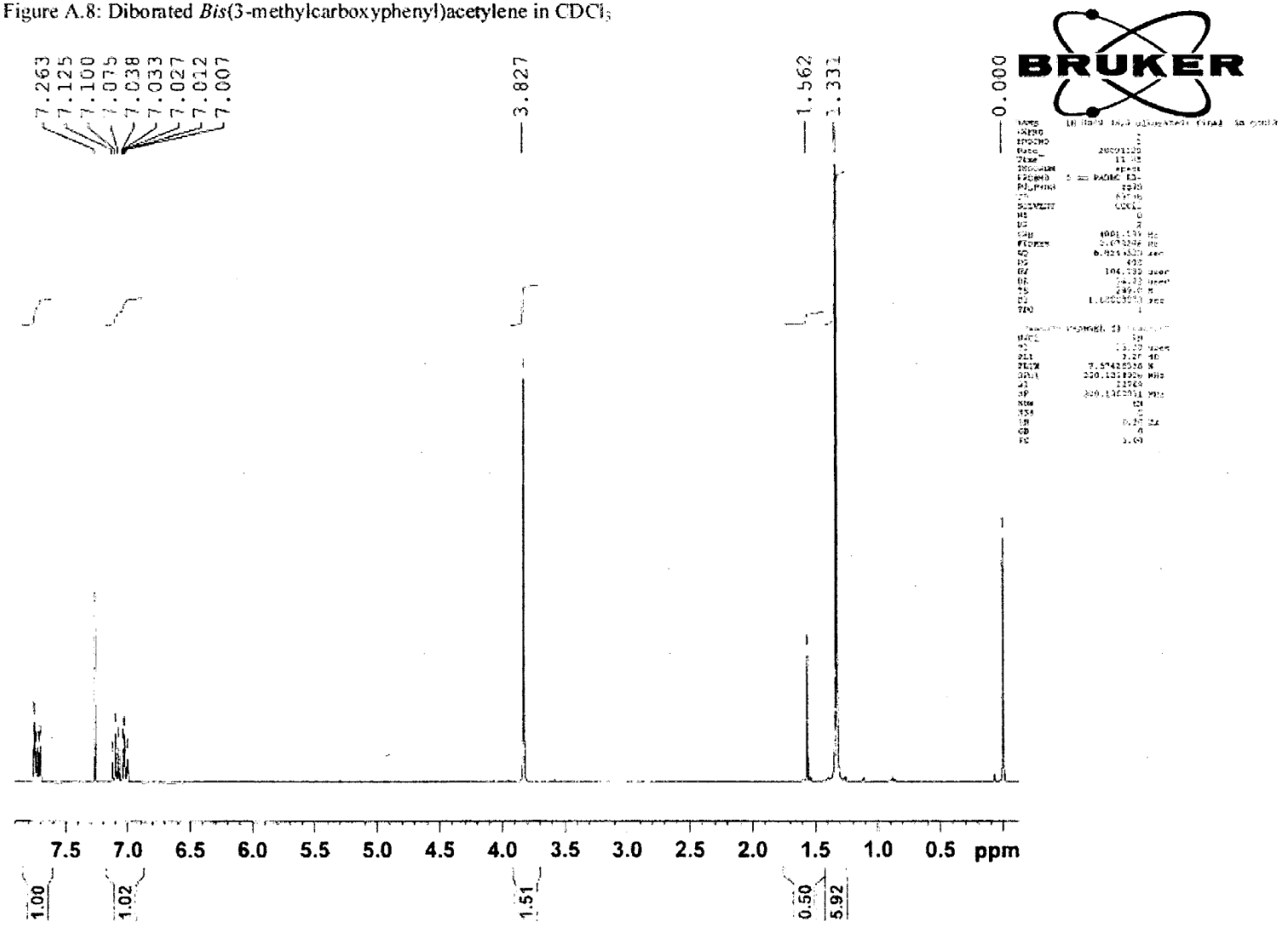


Figure A.9: Diborated *Bis*(4-methylcarboxyphenyl)acetylene in $CDCl_3$

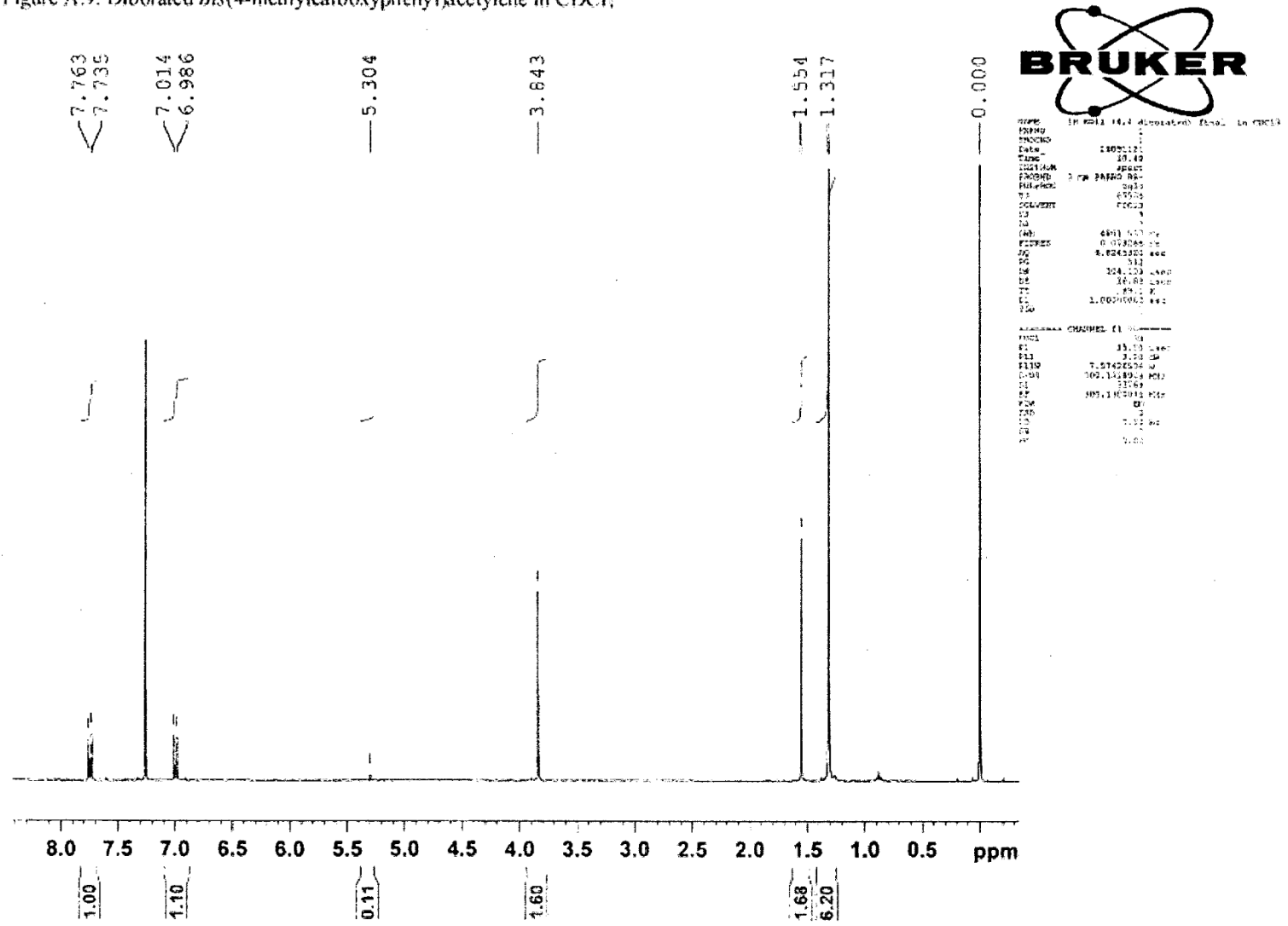
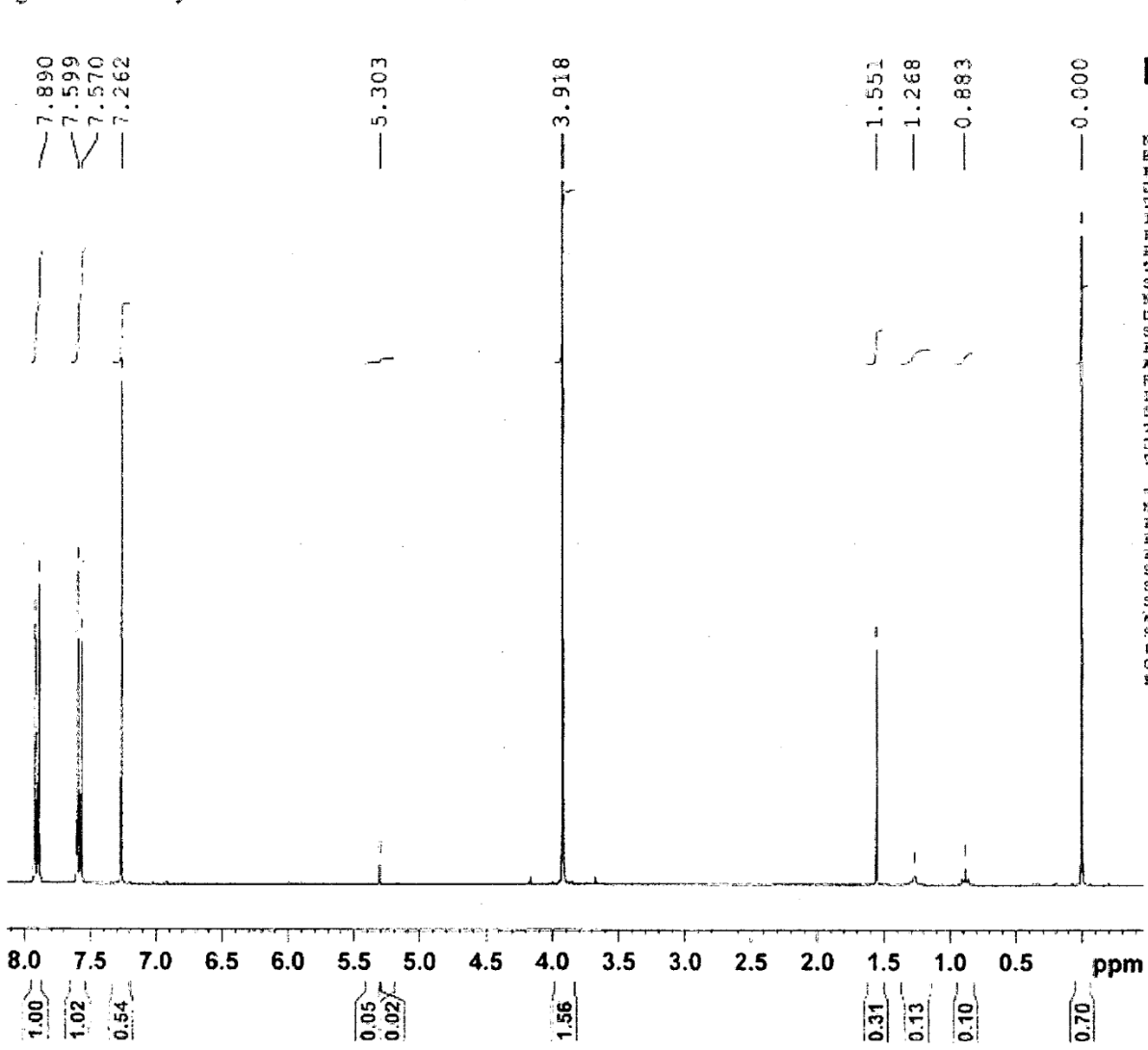


Figure A.10: Methyl-4-Bromobenzoate in $CDCl_3$



BRUKER

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SOLVENT	CDCl3	
NS	8	
DS	2	
SWH	4801.537	Hz
FIDRES	0.073266	Hz
AQ	6.8245320	sec
RG	575	
DW	104.133	usec
DE	16.83	usec
TE	291.3	K
D1	1.00000000	sec
TD0	1	
======== CHANNEL f1 ========		
NUC1	1H	
P1	15.00	usec
PL1	3.20	dB
PL1W	7.57426596	W
SFO1	300.1318008	MHz
SI	32768	
SF	300.1300016	MHz
WDW	EM	
SSB	0	
LB	0.30	Hz
GB	0	
PC	1.00	

APPENDIX B: ^{13}C NMR SPECTRA

Figure B.1: Methyl-3-(2-trimethylsilyl)ethynyl)benzoate in $CDCl_3$

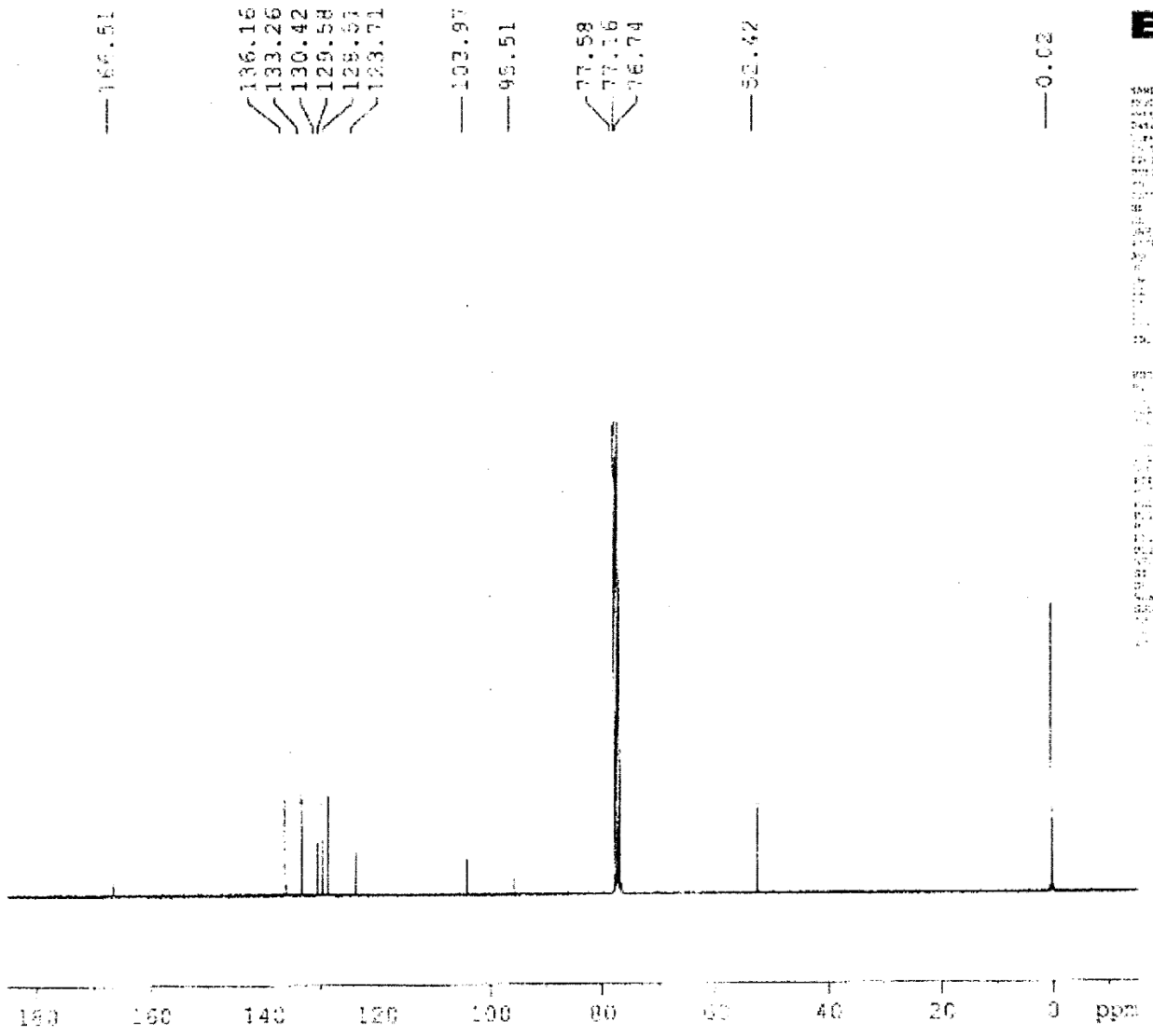


Figure B.2: Methyl-4-ethynylbenzoate in $CDCl_3$

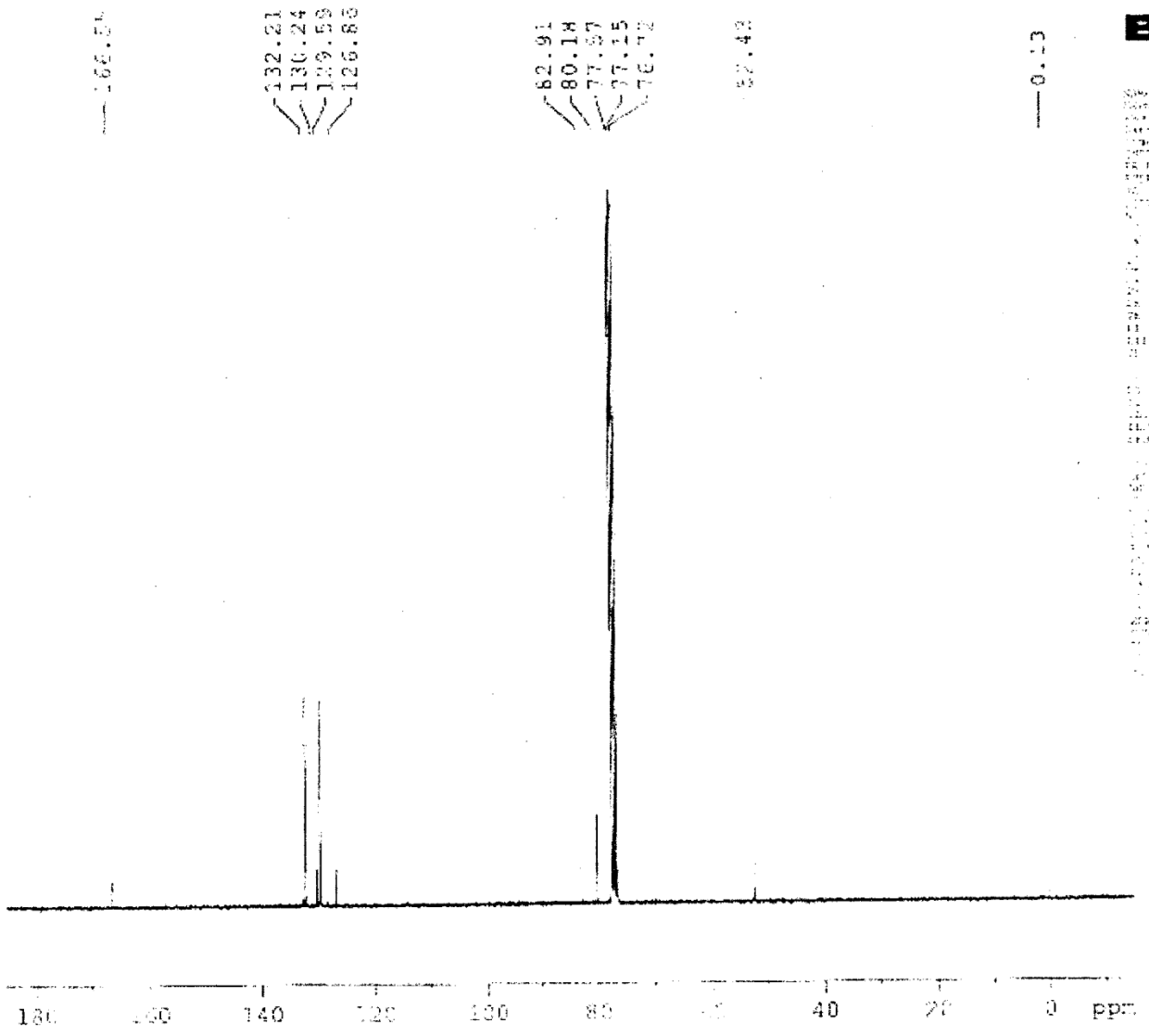
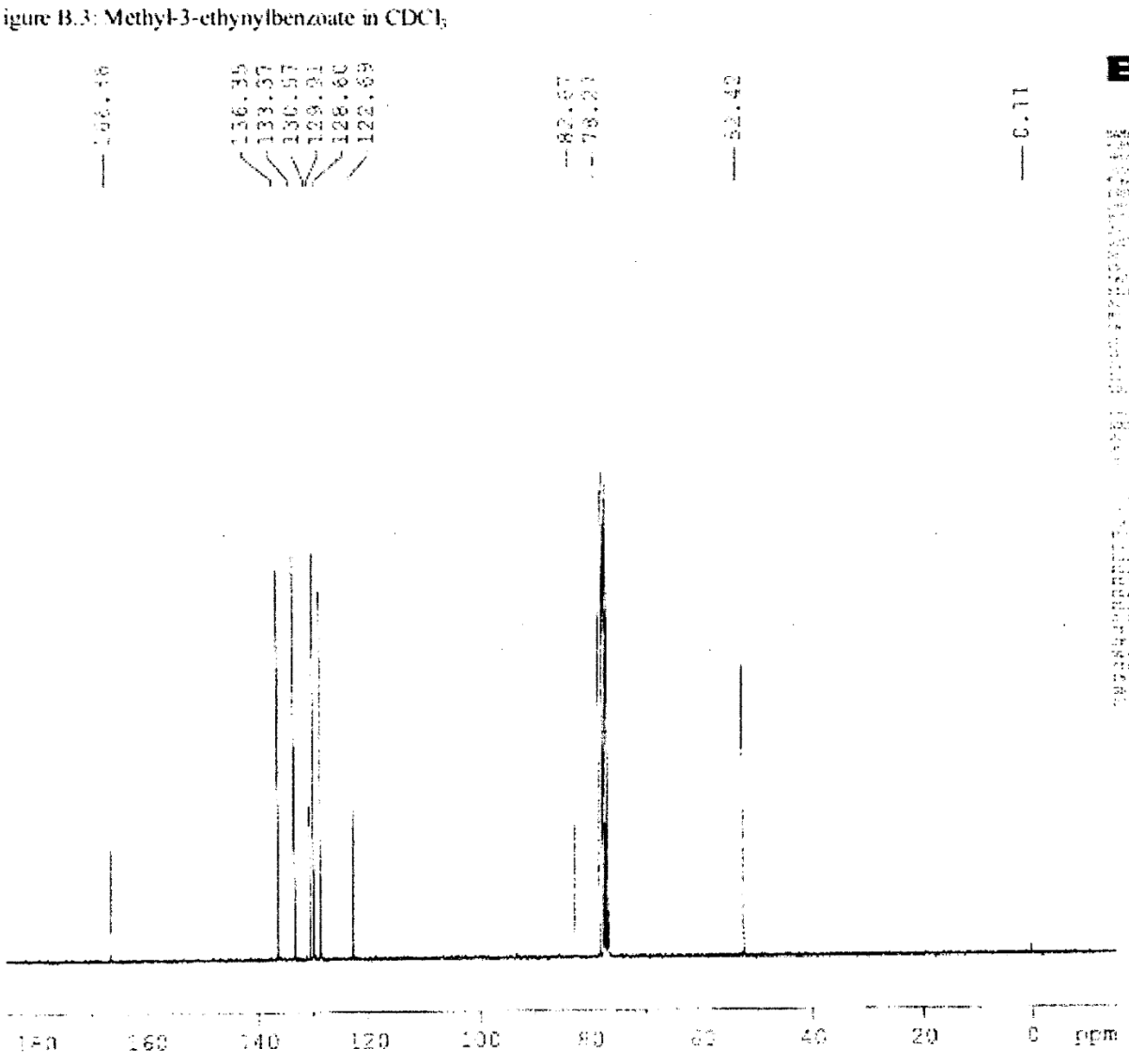
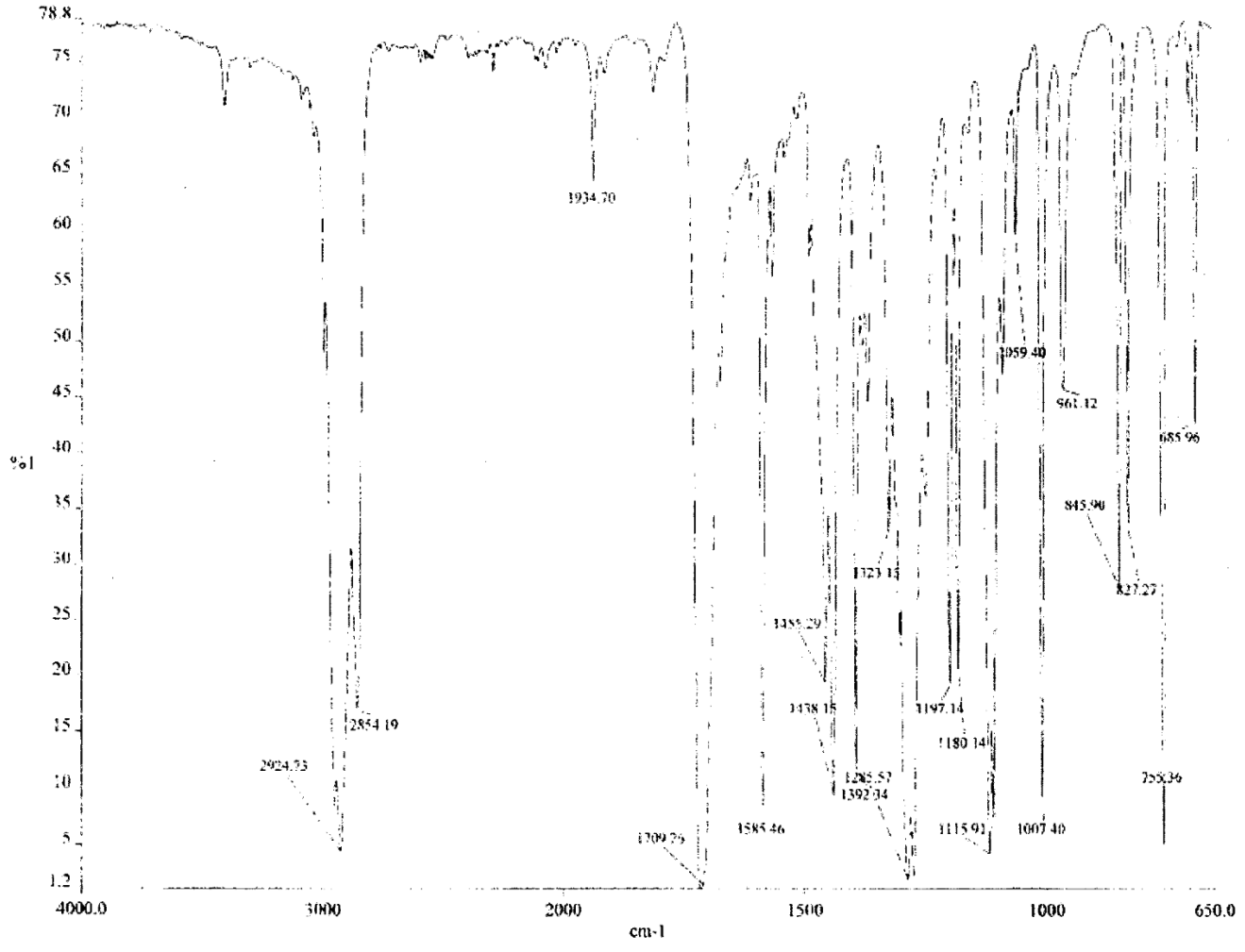


Figure B.3: Methyl-3-ethynylbenzoate in $CDCl_3$



APPENDIX C: IR SPECTRA

Figure C.1: nujol mull of 4 I-Ar-CO_2Me



c:\pei_data\spectra\4-iar-co2me.001 - nujol mull of 4 I-Ar-CO2Me

Figure C.2: nujol mull of 3 I-Ar-CO_2Me

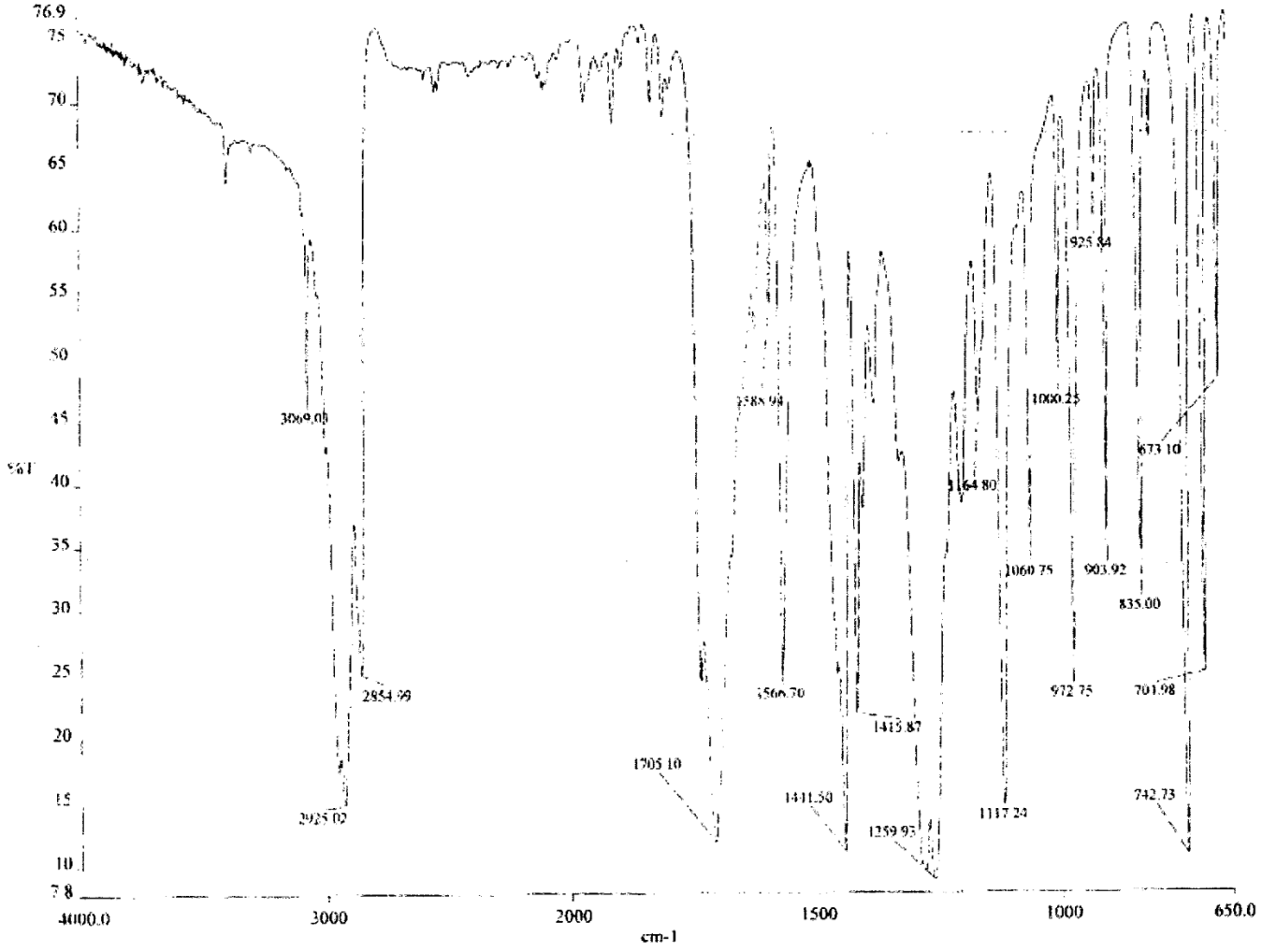
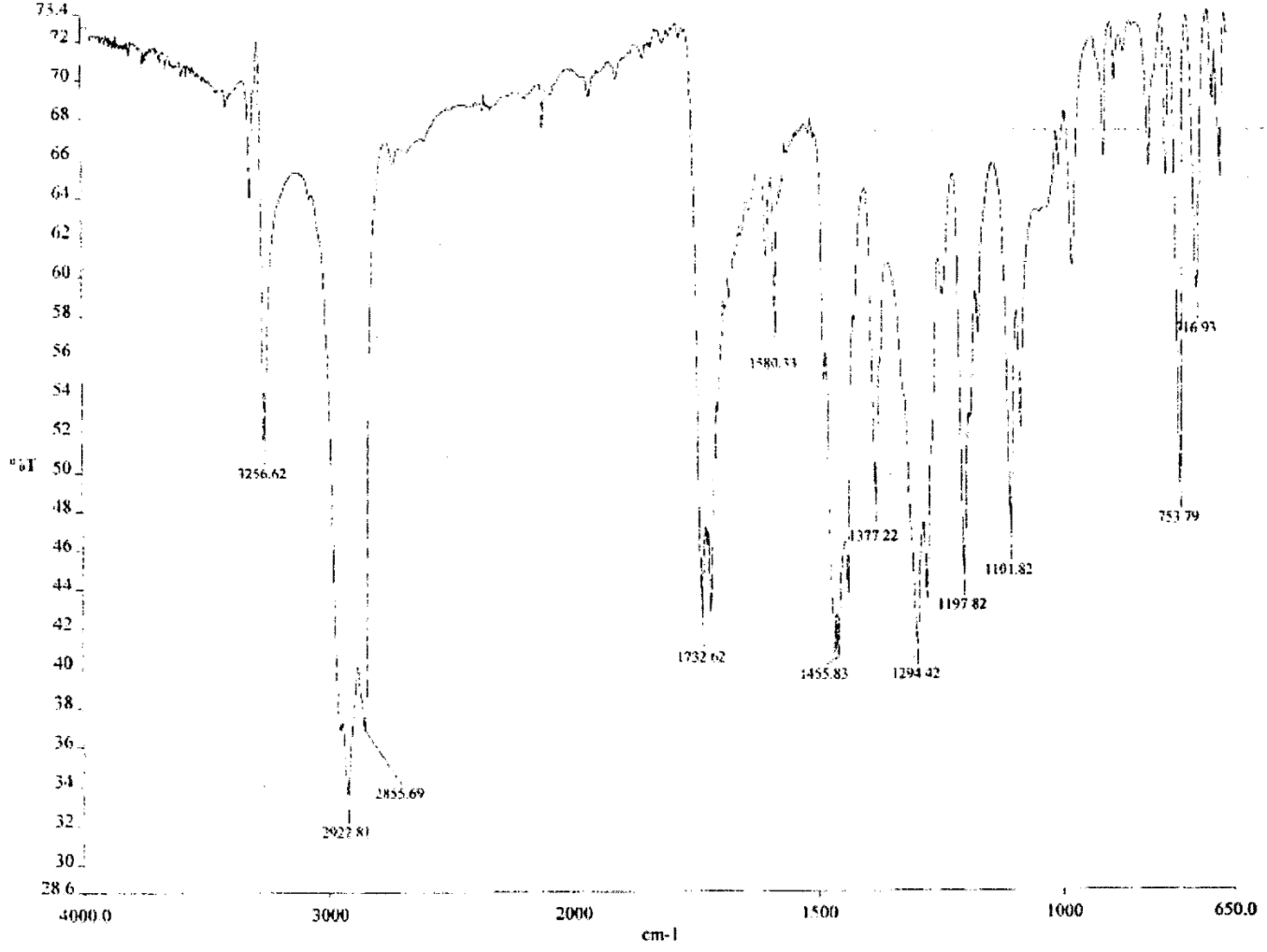


Figure C.3: nujol mull of 3 H-CC-Ar-CO_2Me



c:\pe_data\spectra\3 h-cc-ar-co2me 001 - nujol mull of 3 H-CC-Ar-CO2Me

Figure C.4: nujol mull of 4 H-CC-Ar-CO_2Me

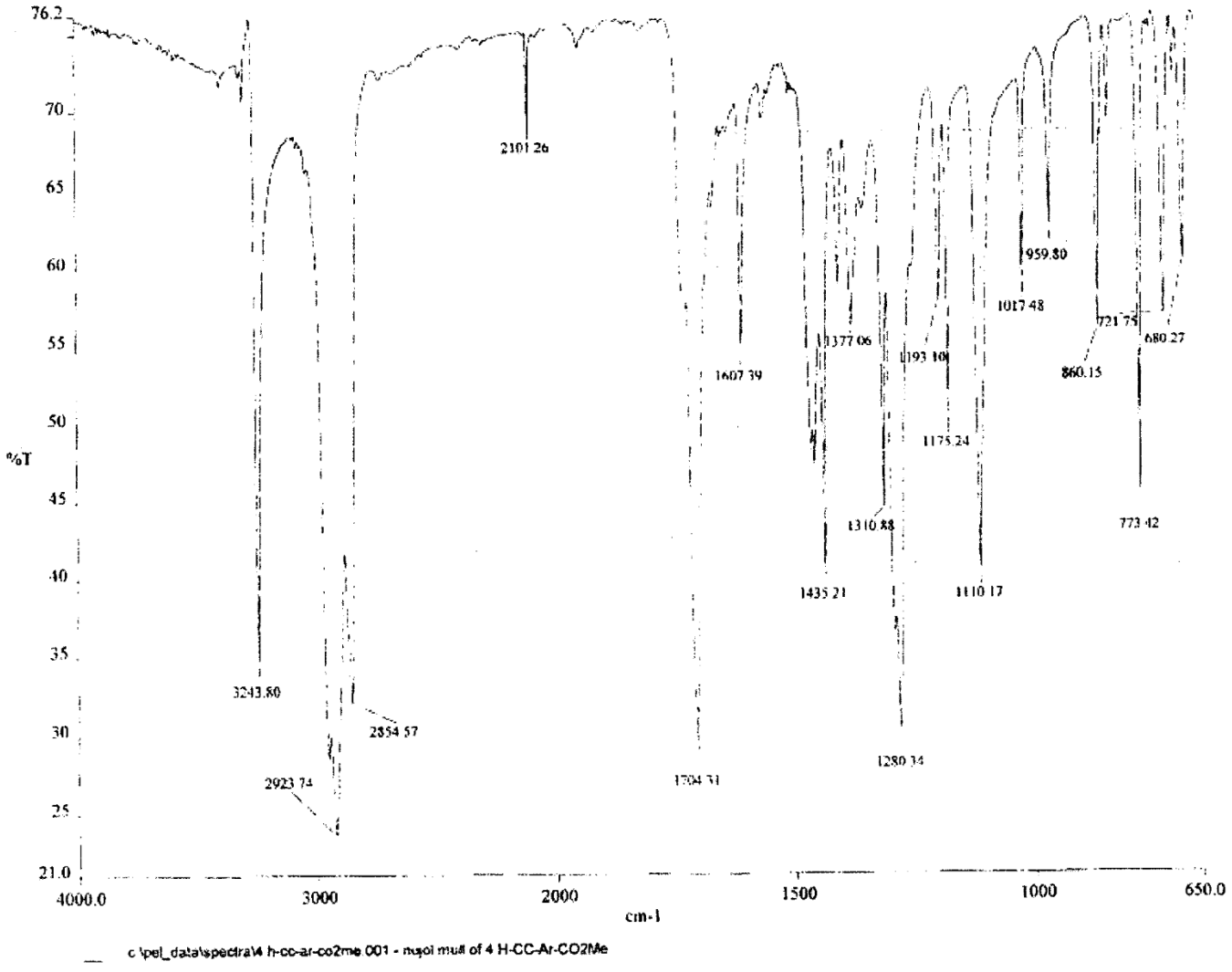


Figure C.5: nujol mull of 4-TMS-CC-Ar-CO_2Me

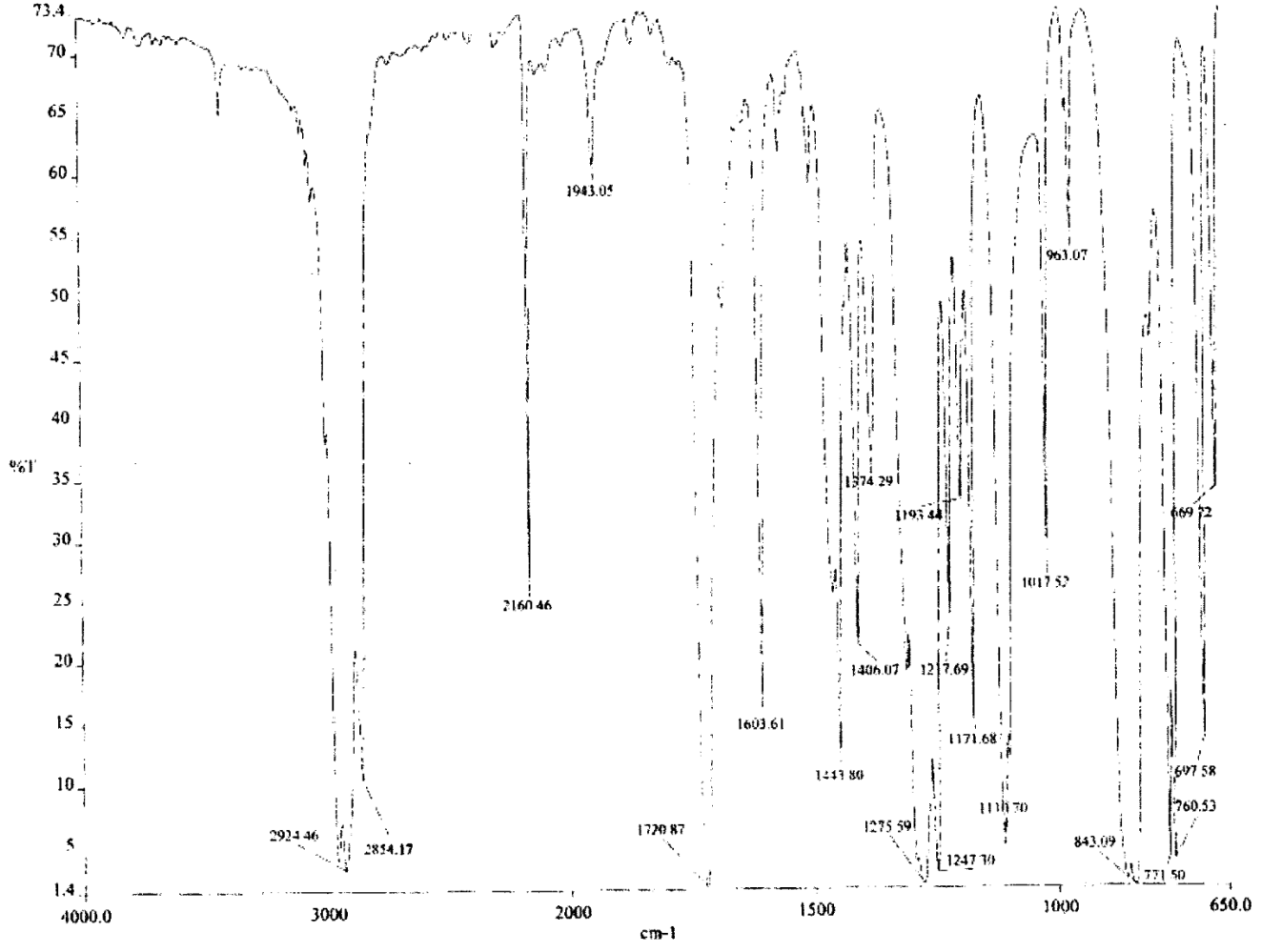


Figure C.6: neat 3 TMS-CC-Ar-CO2Me

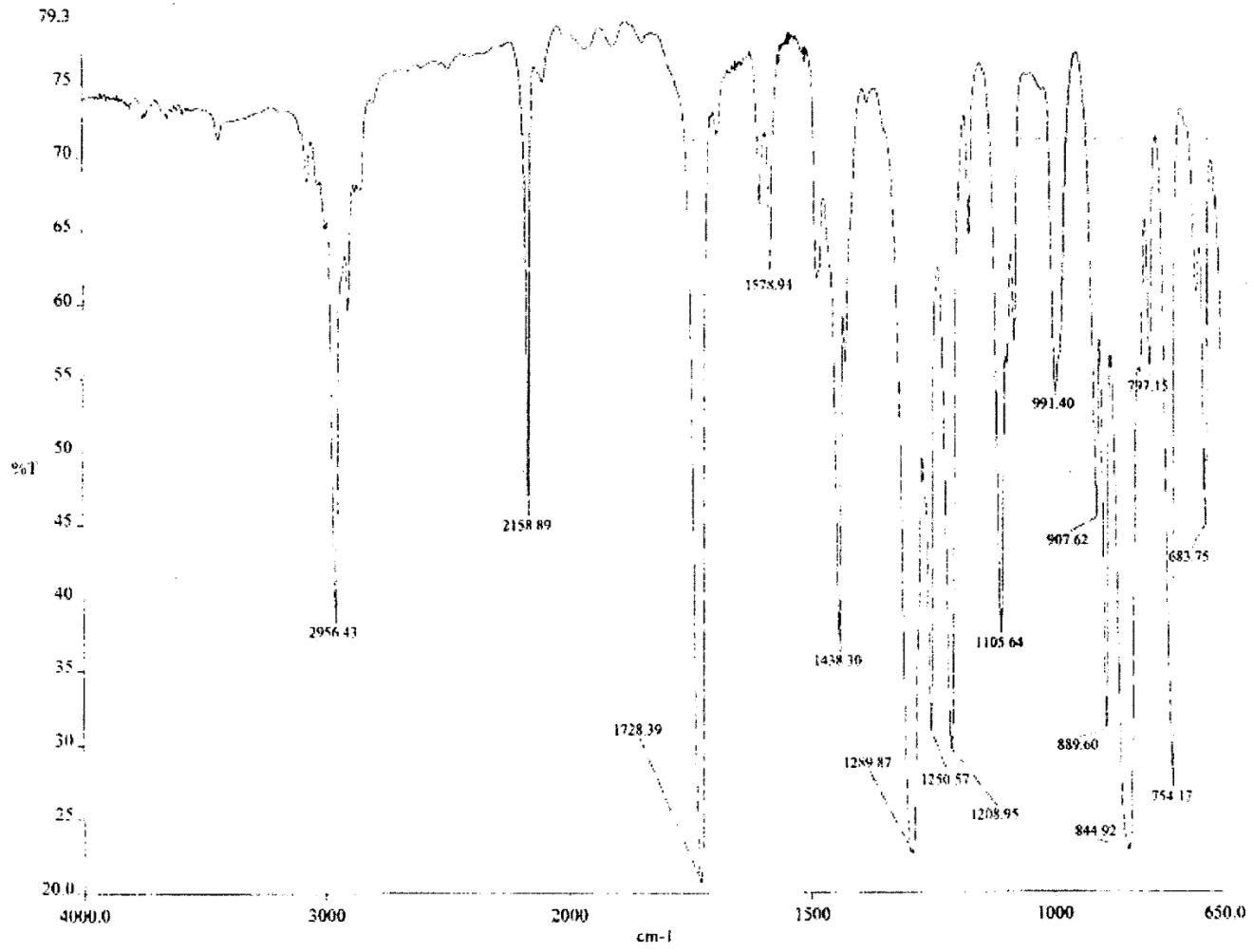


Figure C.7: nujol mull of 4,4' MeO_2C-Ar-CC-Ar-CO_2Me

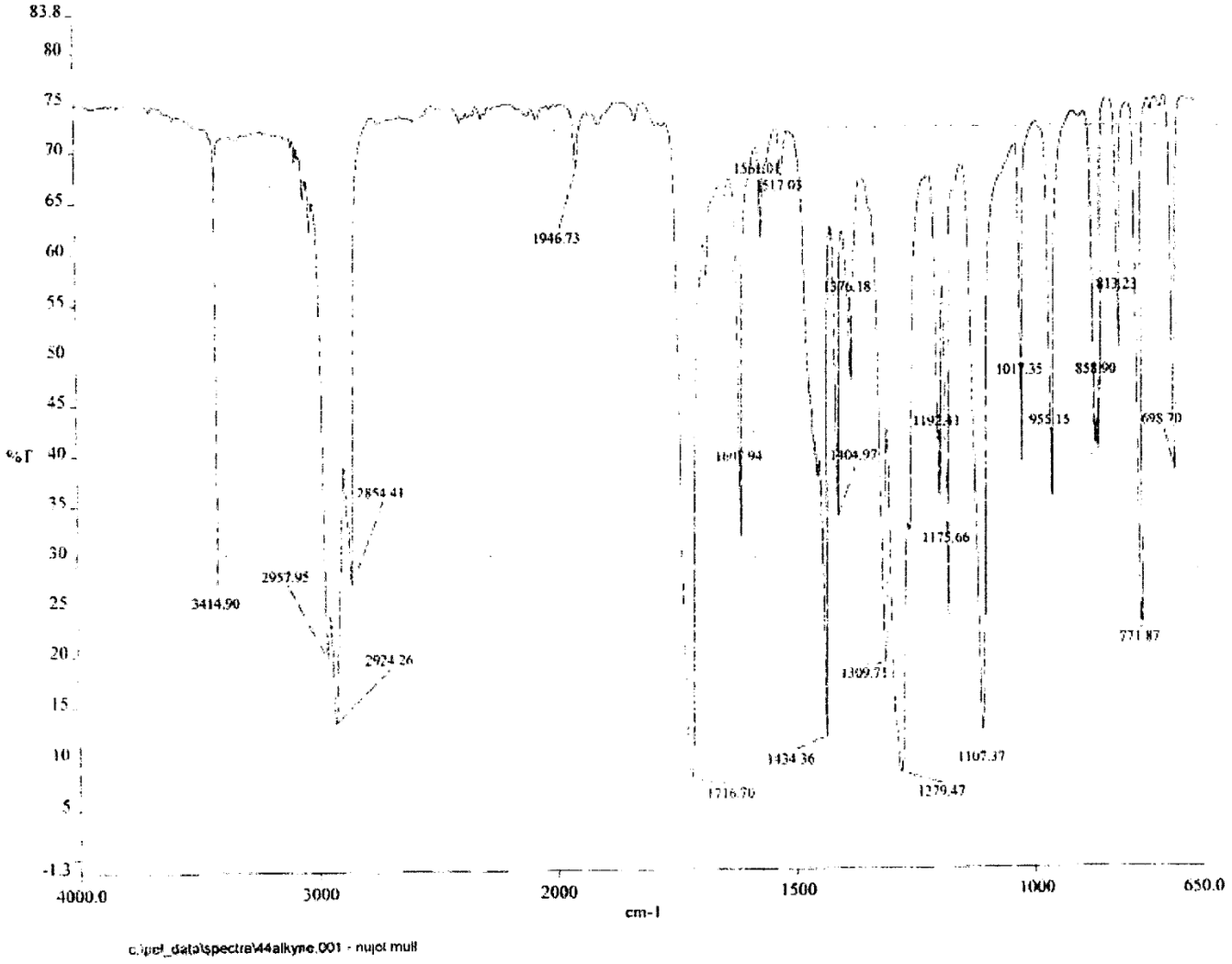


Figure C.8: nujol mull of 3,3' MeO_2C-Ar-CC-Ar-CO_2Me

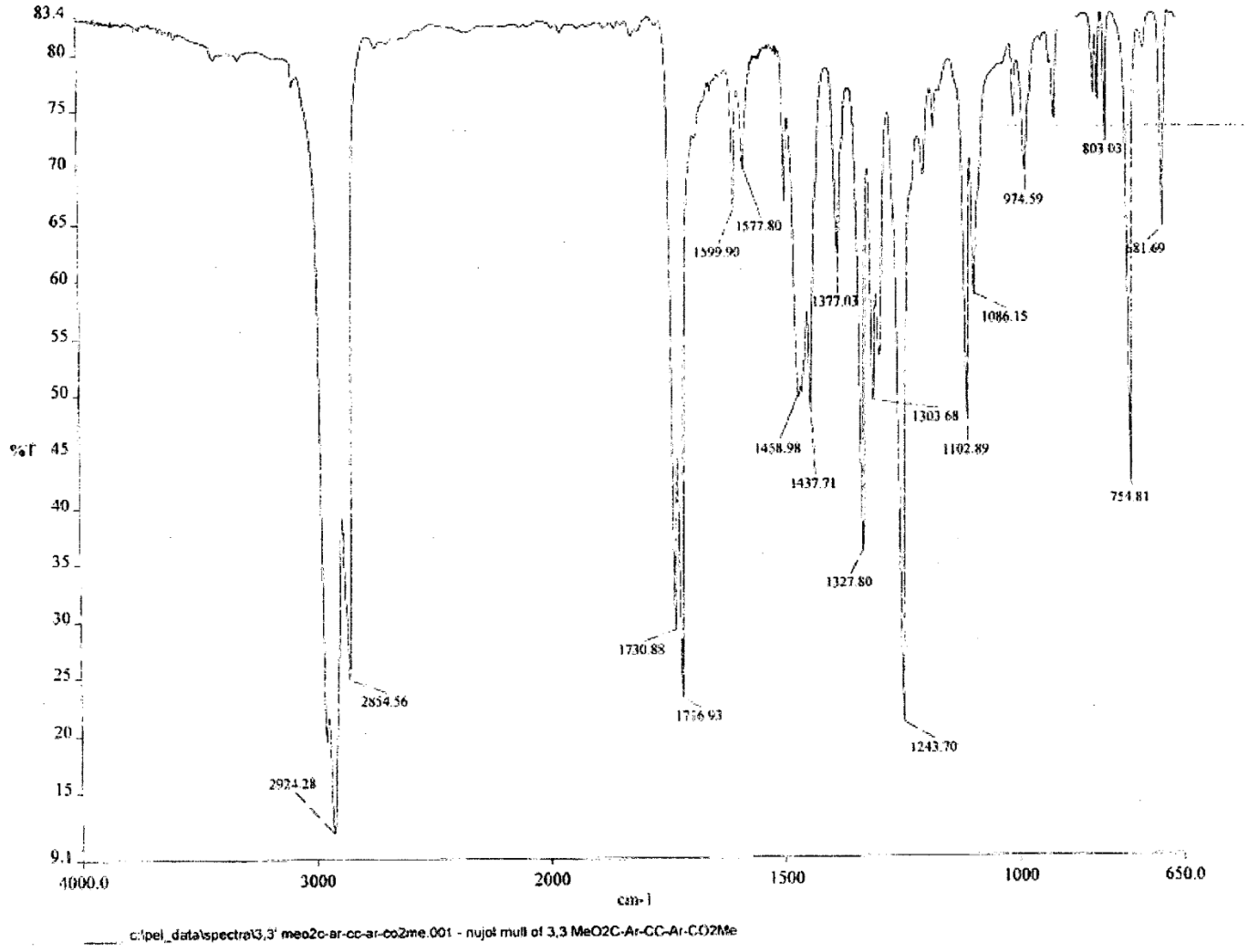


Figure C.9: nujol mull of 4,4 diborated alkyne

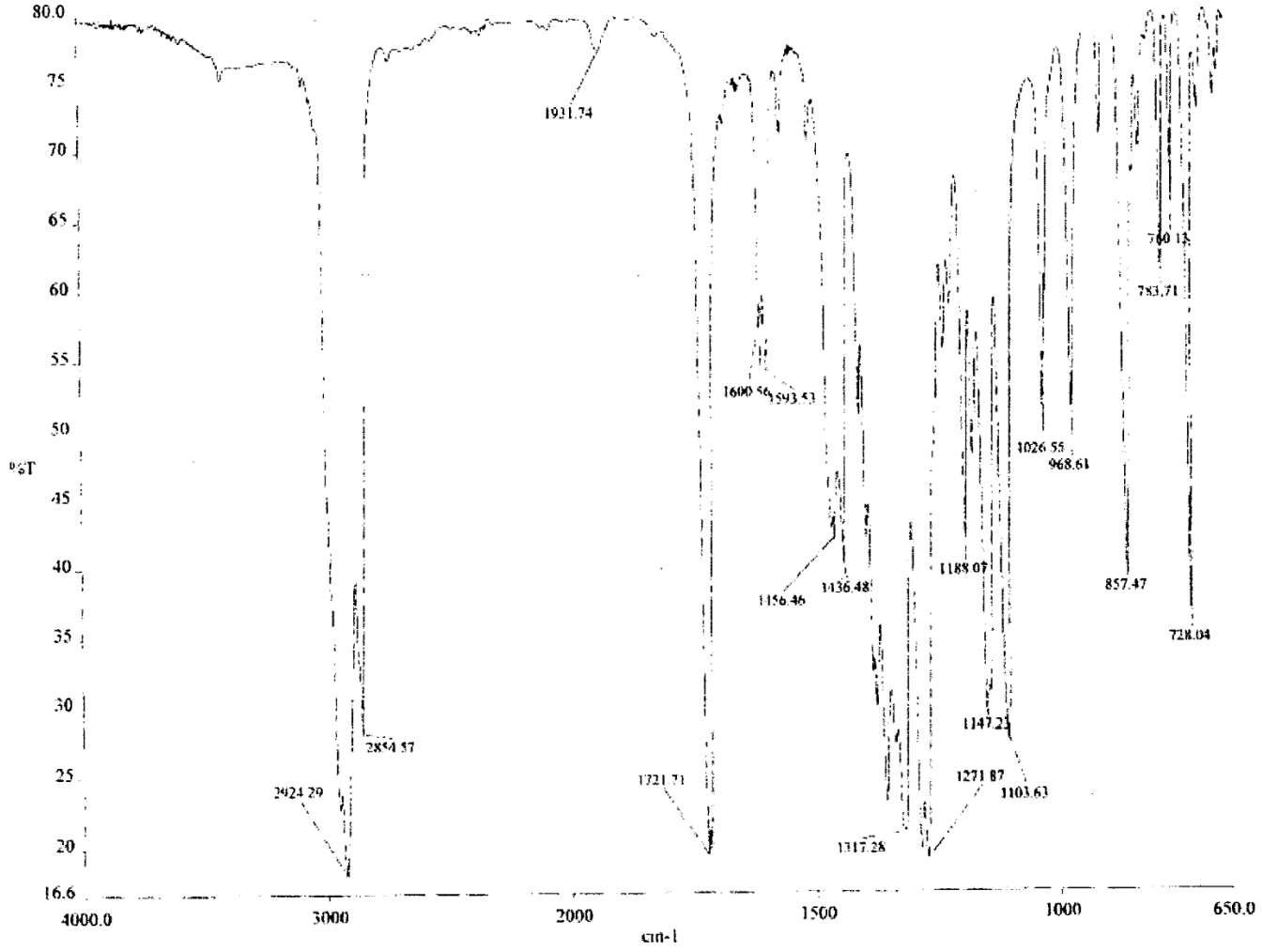
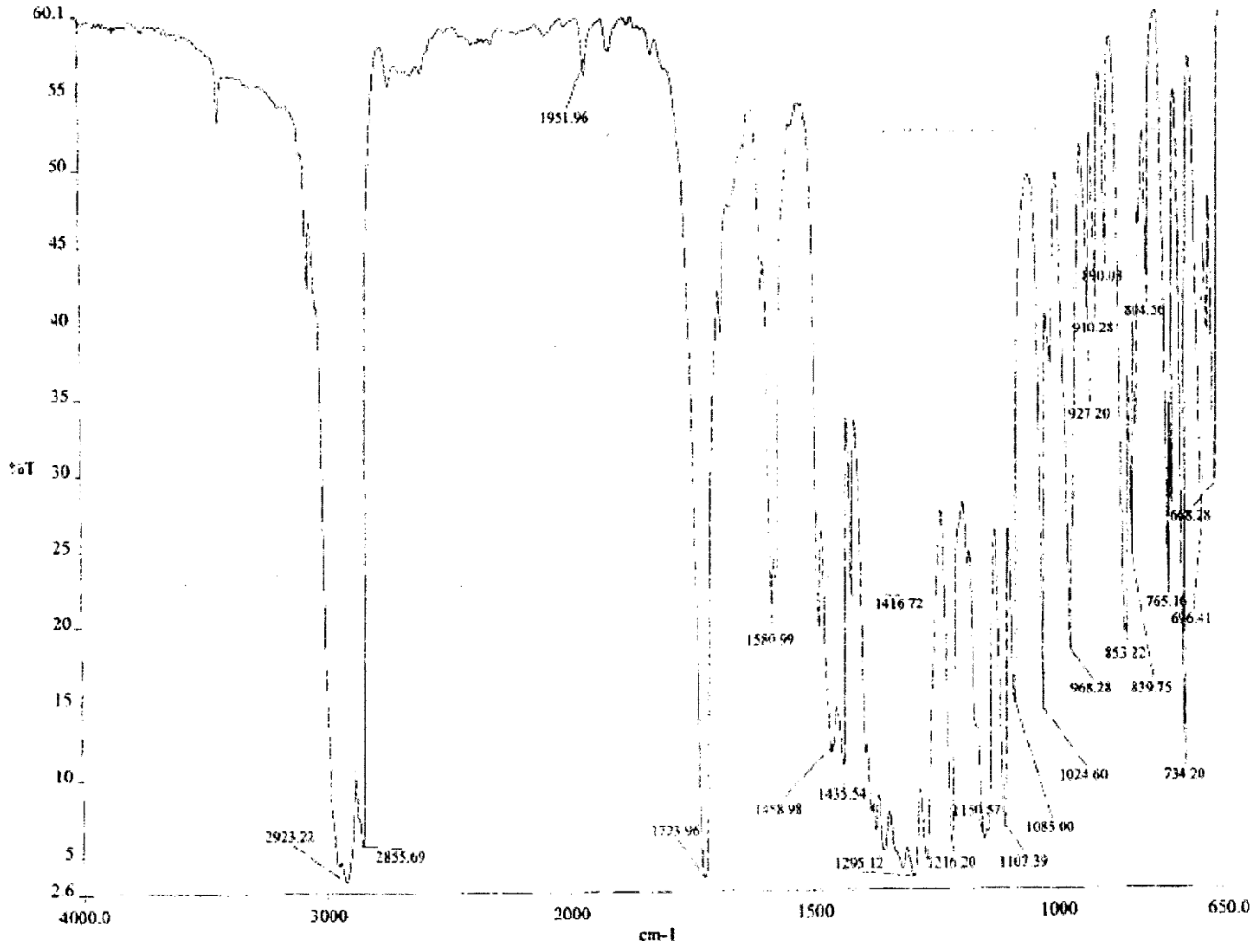


Figure C.10: nujol mull of 3,3 diborated alkyne



BIBLIOGRAPHY

1. *The ACS Style Guide: Effective Communication of Scientific Information;* Coghill, A. M.;Garson, L.R., Eds.; Oxford University Press: New York, NY, 2006.
2. Corriu, R. C. P.; Masse, J. P. *Chem. Commun.* **1972**, 144.
3. Tamao, K.; Sumutani, K.; Kumada, M. *J. Am. Chem. Soc.* **1972**, *94,* 4374.
4. Negishi, E. *J. Org. Chem.* **2002**, *653,* 34.
5. Steven, V. L.; Thomas, A. W. *Angew. Chem., Int. Ed.* **2003**, *42,* 5400.
6. Sonogashira, K. *J. Org. Chem.* **2002**, *653,* 46.
7. Heck, R. F.; Nolley, J. P. Jr. *J. Org. Chem.* **1972**, *37 (14),* 2320.
8. Sonogashira, K. *Comprehensive Organic Synthesis;* Pergamon Press: New York, 1991; Vol. 3, p 521.
9. Sonogashira, K.; Tohda, Y.; Hagihara, N. *Tetrahedron Lett.* **1975**, *16 (50),* 4467.
10. Stephens R. D.; Castro, C. E. *J. Org. Chem.* **1963**, *28,* 3313.
11. Nguyen, P.; Yuan, Z.; Agocs, L.; Lesley, G.; Marder, T. B. *Inorg. Chim. Acta.* **1994**, *220 (1-2)*, 289.
12. Takahashi, S.; Kuroyama, Y.; Sonogashira, K.; Hagihara, N. *Synthesis*, **1980**, *8,* 627.
13. Della Ciana, L.; Haim, A. *J. Heterocylic Chem.* **1984**, *21,* 607.
14. Cwik, A.; Hell, Z.; Figueras, F. *Tetrahedron Lett.* **2006**, *47 (18),* 3023.
15. Morrison, J. A. *Chem. Rev.* **1991**, *91 (1),* 35

16. Urry, G.; Wartik, T.; Moore, R. E.; Schlesinger, H. I. *J. Am. Chem. Soc.* **1954**, *76 (21),* 5293.

17. Lesley, G.; Nguyen, P.; Taylor, N. J.; Marder, T. B.; Scott, A. J.; Clegg, W.; Norman, N. C. *Organometallics* **1996**, *15 (24),* 5137.

18. Ishiyama, T.; Matsuda, N.; Murata, M.; Ozawa, F.; Suzuki, A.; Miyaura, N. *Organometallics* **1996**, *15 (2),* 713.

19. Irvine, G. J.; Lesley, M. J. G.; Marder, T. B.; Norman, N. C.; Rice, C. R.; Robins, E. G.; Roper, W. R.; Whittell, G. R.; Wright, L. J. *Chem. Rev.* **1998**, *98 (8),* 2685.

20. Iverson, C. N.; Smith, M. R. *Organometallics* **1996**, *15 (24),* 5155.

21. Adams, C. J.; Baber, R. A.; Batsanov, A. S.; Bramham, G.; Charmant, J. P. H.; Haddow, M. F.; Howard, J. A. K.; Lam, W. H.; Lin, Z.; Marder, T. B.; Norman, N. C.; Orpen, A. G. *Dalton Trans.* **2006**, 1370.

22. Ishiyama, T.; Matsuda, N.; Miyaura, N.; Suzuki, A. *J. Am. Chem. Soc.* **1993**, *115 (23),* 11018.

23. Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95 (7),* 2457.

24. Shi, B. L. Z.; Wan, X.; Cheng, J.; Fang, Z.; Cao, B.; Qin, C.; Wang,Y. *Angew. Chem. Int. Ed.* **2007**, *46 (29),* 5554.

25. Ijpeij, E. G.; Beijer, F. H.; Arts, H. J.; Newton, C.; de Vries, J. G.; Gruter, G. J. M. *J. Org. Chem.* **2002**, *67 (1),* 169.

26. Molander, G. A.; Katona, B. W.; Machrouhi, F. *J. Org. Chem.* **2002**, *67 (24),* 8416.

27. Cutertson, E. *Boronic Acids: Properties and Applications;* Alfa Aesar: Heysham UK, 2008; pp 1-2, 4-12.

28. Gillie, A.; Stille, J. K. *J. Am. Chem. Soc.* **1980**, *102,* 4933.

29. Ziegler, C. B.; Heck, R. F. *J. Org. Chem.* **1978**, *43 (15),* 2941.

30. Stille, J. K.; Lau, K. S. Y. *Acc. Chem. Res.* **1977**, *10 (12),* 434.

31. Casado, A. L.; Espinet, P. *Organometallics* **1998**, *17,* 954.

32. Amatore, C.; Jutand, A. *J. Organomet. Chem.* **1999**, *576,* 254.

33. Pelter, A.; Smith, K.; Brown, H. C. *Borane Reagents;* Academic: New York, 1988.

34. Ridgway, B. H.; Woerpel, K. A. *J. Org. Chem.* **1998**, *63,* 458.

35. Prokopcová, H.; Ramírez, J.; Fernández, E.; Kappe, C. O. *Tetrahedron Lett.* **2008**, *49,* 4831.

36. Ishiyama, T.; Masafumi, Y.; Miyaura, N. *Chem. Lett.***1996**, 1117.

37. Brown, S. D.; Armstrong, R. W. *J. Am. Chem. Soc.* **1996**, *118 (26)*, 6331.

38. Brown, S. D.; Armstrong, R. W. *J. Org. Chem.* **1997**, *62 (21)*, 7076.

39. Jiang, F. H.;Xu, X.Q.; Wang, A.Z. *J. of Supercritical Fluids* **2009**, *49*, 377.

40. Bahl, A.; Grahn, W.; Stadler, S.; Feiner, F.; Bourhill, G.; Brauchle, C.; Reisner, A.; Jones, P. G. *Angew. Chem., Int. Ed.* **1995**, *34,* 1485.

41. Sabat, M.; Johnson, C. R. *Org. Lett.* **2000**, *8,* 1089.

42. Bringmann, G.; Gotz, R.; Keller, P. A.; Walter, R.; Boyd, M. R.; Lang, F.; Garcia, A.; Walsh, J. J.; Tellitu, I.; Bhaskar, K. V.; Kelly, T. R. *J. Org. Chem.* **1998**, *63,* 1090.

43. Blouin, N.; Michaud, A.; Gendron, D.;Wakim, S.; Blair, E.; Neagu-Plesu, R.; Belletete, M.; Durocher, G.; Tao, Y.; Leclerc, M. *J. Am. Chem. Soc.* **2008**, *130,* 732.

44. Li, H.; Eddaoudi, M.; O'Keeffe, M.; Yaghi, O. M. *Nature* **1999**, *402,* 276.

45. Wong-Foy, A. G.; Matzger, A. J.; Yaghi, O. M. *J. Am. Chem. Soc.* **2006**, *128 (11),* 3494.

46. Millward, A. R.; Yaghi, O. M. *J. Am. Chem. Soc.* **2005**, *127 (51),* 17998.

47. Horcajada, P.; Serre C.; Vallet-Regí M.; Sebban M.; Taulelle F.; Férey G. *Angew. Chem., Int. Ed.* **2006**, *45 (36),* 5974.

48. Horike, S.; Dinca, M.; Tamaki, K.; Long, J. R. *J. Am. Chem. Soc.* **2008**, *130 (18),* 5854.

49. Jacoby, M. *Chem. & Eng. News.* **2008**, *86,* 13.

50. Yosef, I.; Abu-Reziq, R.; Avnir, D. *J. Am. Chem. Soc.* **2008**, *130 (36),* 11880.

51. Rowsell, J. L. C.; Yaghi, O. M. *Microporous and Mesoporous Materials* **2004**, *73 (1-2),* 3.

52. Tranchemontagne,D.J.; Ni, Z.; Yaghi, O. M.; O'Keeffe, M. *Angew. Chem., Int. Ed.* **2008**, *47 (28),* 5136.

53. Yaghi, O. M.; O'Keeffe, M.; Ockwig, N. W.; Chae, H. K.; Eddaoudi, M.; Kim, J. *Nature* **2003**, *423,* 705.

54. Cheetham A. K.; Rao, C. N. R.; Feller, R. K. *Chem. Commun.* **2006**, *46*, 4780.

55. Wikipedia. Metal-organic framework. http://en.wikipedia.org/wiki/Metal-organic_framework (accessed March 13, 2009).

56. Rao, C. N. R.; Natarajan, S.; Vaidhyanathan, R. *Angew. Chem., Int. Ed.* **2004**, *43 (12),* 1466.

57. Anderson, G. K.; Lin, M. *Inorg. Synth.* **1990**, *28*, 60.

58. Hayashi, T.; Konishi, M.; Kobori, Y.; Kumada, M.; Higuchi, T.; Hirotsu, K. *J. Am. Chem. Soc.* **1984**, *106*, 158.

59. Camalli, M.; Caruso, F.; Chaloupka, S.; Leber, E. M.; Rimml, H.; Venanzi, L. M. *Helv. Chim. Acta.* **1990**, *73*, 2263.

60. The author thanks Dr. Ian Williams, Department of Chemistry, Hong Kong University of Science and Technology, Clearwater Bay, Hong Kong for the generous gift of *bis*(pinacolato)diboron (B_2Pin_2).

61. Lesley, M. J. G. Personal communication.

62. Sieber, F.; Wentworth, P. J.; Janda, D.K. J. *Comb. Chem.* **1999**, *1*, 540.

63. Austin, W. B.; Bilow, N.; Kelleghan, W. J.; Lau, S. Y. *J. Org. Chem.* **1981**, *46*, 2280.

64. Carey, Francis. A.; Sundberg, Richard. J. *Advanced Organic Chemistry: Part A: Structure and Mechanisms*, 5th ed.; Springer: New York, 2008.