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I am submitting herewith a dissertation written by Travis R. Quick entitled "New Carbon-Carbon Bond Forming Reactions Mediated by Boron and Transition Metal Halides." I have examined the final electronic copy of the dissertation for form and content and recommend that it be accepted in partial fulfillment of the requirements for the degree of Doctor of Philosophy, with a major in Chemistry.

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NEW CARBON-CARBON BOND FORMING REACTIONS MEDIATED BY BORON AND TRANSITION METAL HALIDES

A Dissertation

Presented for

the Doctor of Philosophy

Degree

The University of Tennessee, Knoxville

Travis R. Quick
December 2008

DEDICATION

To my wife, Dana,

You have been there throughout the good and the bad.

Thank you for your love through all of it.

To my parents,

Without the love, support, and encouragement you showed

Through our darkest hour, I might not have furthered my education.

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ABSTRACT

This dissertation summarizes the recent use of boron and transition metal halides to form new carbon-carbon bonds. Several novel reactions have been discovered. These include the haloallylation of aryl aldehydes with boron trihalide; alkyne-aldehyde couplings mediated by boron trihalide to give either (*Z*,*Z*)-1,5-dihaloalkenes or (*Z*,*E*)-1,5-dihaloalkenes; dehydroxylation of benzylic alcohols and *in situ* generated benzylic alcohol salts with iron(III) chloride and triethylsilane to afford diarylmethanes; and, the alkenylation of allylic, benzylic, and propargylic alcohols with phenylacetylenes and titanium(IV) halide. The results of these studies strongly imply a cationic mechanism. The reaction methodology of the research described herein can be characterized as atom-efficient, environmentally friendly, and capable of generating the desired products in good to excellent yields.

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LIST OF SYMBOLS AND ABBREVIATIONS

OAc	Acetate
α	Alpha
Anal. Calcd	Analytical Calculated
Å	Angstrom
Bn	Benzyl
β	Beta
9-BBN	9-Borabicyclo[3.3.1]nonane
n-Bu_4NI	Tetrabutylammonium iodide
n-BuLi	Butyllithium
Cat.	Catalyst
C	Celsius
DCM	Dichloromethane
J	Coupling constant
°	degrees
$CDCl_3$	Deuterochloroform
d	doublet
dd	doublet of doublets
dt	doublet of triplets
Equiv.	Equivalents
Et	Ethyl
Et_2O	Diethyl ether
OTf	Trifluoromethanesulfonate

g	grams
Hz	Hertz
n-C_6H_{13}, *n*-Hx	hexyl
h	hours
THF	Tetrahydrofuran
MHz	Megahertz
Me	Methyl
OTs	4-Methylbenzenesulfonate
TMS	Tetramethylsilane
μm	micrometer
mg	milligram
mL	milliliter
mmol	millimole
min	minutes
M	Molar
m	multiplet
NMR	Nuclear Magnetic Resonance
Ph	Phenyl
PhLi	Phenyllithium
n-Pr	Propyl
q	quartet
s	singlet
t	triplet

Chapter 1. Lewis Acids in Organic Synthesis

1.1 Scope of This Dissertation

This dissertation is focused on the reactions of alcohols and aldehydes with boron Lewis acids, or Lewis acids containing transition metals. Several novel reactions have been developed. These include: (1) haloallylation of aryl aldehydes with boron trihalides; (2) alkyne-aldehyde coupling with boron trihalides; (3) dehydroxylation of benzylic alcohols and *in situ* generated benzylic alcohol salts with triethylsilane and iron(III) chloride; and, (4) alkenylation of allylic, benzylic and propargylic alcohols with phenylacetylenes and titanium(IV) halides. Each chapter will illustrate the synthetic utility of the newly discovered reactions, relationships with the published literature, and, when relevant, propose a potential mechanism responsible for the newly discovered reactions. This chapter will serve to provide pertinent background information necessary to understand the chemistry presented in this dissertation.

1.1.1 Historical Aspects of Boron and Transition Metal Halides in Organic Synthesis

J. L. Gay-Lussac described[1] the boron-trifluoride-ammonia complex (BF_3•NH_3) in 1809. This was the first published report of a boron trihalide complex in the literature. Boron halides, iron halides and titanium halides are all Lewis acids; a concept named for American physical chemist Gilbert Norton Lewis. It is a based on the fact that a molecule can be either an electron pair acceptor (Lewis acid) or an electron pair donor (Lewis base).[2] In valence bond formalism, boron complexes are Lewis acids due to being

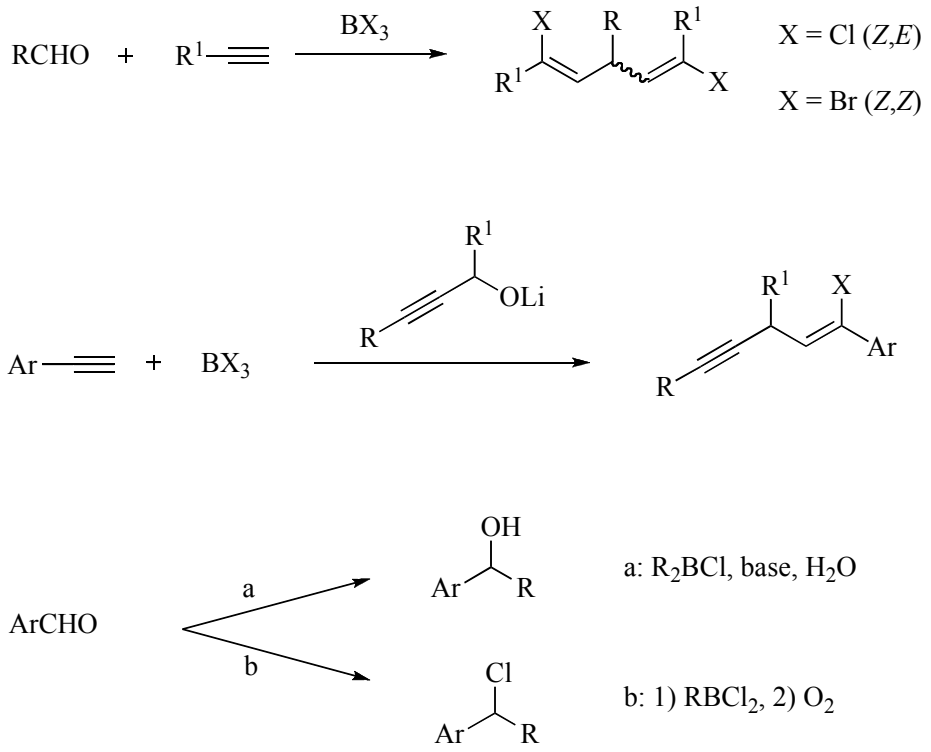
electron deficient in the valence shell. The Lewis base (electron pair donor) contains filled p-orbitals, while the boron complex can accept those p-orbital electrons to formally complete a full octet of electrons in the outer valence shell. This results in the formation of a new σ-bond. The Lewis acidities of boron trihalides have been measured and found to be in the order $BI_3 > BBr_3 > BCl_3 > BF_3$,[3] exactly the reverse of the order expected on the basis of the relative σ-donor strengths of the halide ions.

In transition metal Lewis acids, those with small d^n configurations are stronger Lewis acids than those with higher d^n configurations. In this dissertation, iron(III) chloride and titanium(IV) chloride and bromide are used. On the basis of d^n configurations, iron(III) chloride is a d^5 complex, while titanium(IV) chloride and bromide are d^0 complexes. The titanium(IV) chloride and bromide are much more electron deficient, thereby making them stronger Lewis acids.

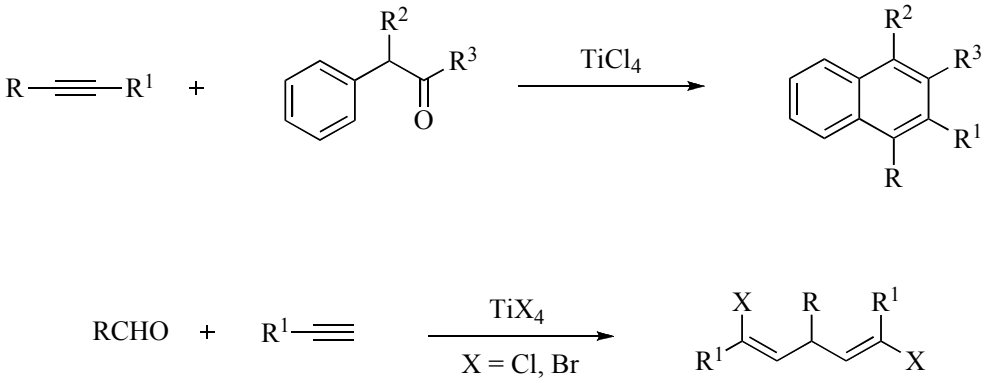
1.1.2 Reactions of Boron Trihalides in Organic Chemistry

The synthetic applications of boron halide Lewis acids, such as boron trichloride, has been known for nearly fifty years.[4,5] These applications include the cleavage of ethers, acetals and esters,[6] stereoselective glycosidation of glycols under mild conditions,[7] Aldol reactions,[8] Friedel-Crafts reactions[9] and other acid-induced reactions.

In recent years, the Kabalka group has developed several novel reactions using boron[10-13] and transition metal halide[14,15] Lewis acids (**Schemes 1-1** and **1-2**). These reactions serve as the background for the research presented in this dissertation.



Scheme 1-1 Kabalka group boron trihalide reactions

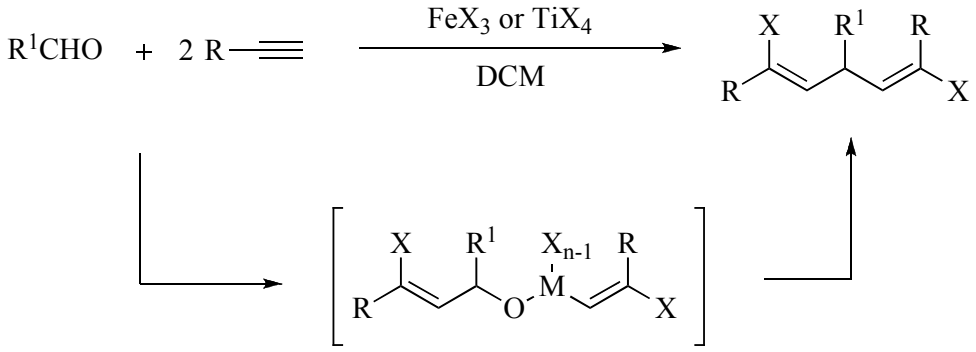


Scheme 1-2 Kabalka group transition metal halide reactions

1.1.3 Reactions of Iron(III) Halides in Organic Chemistry

Within the Lewis acid catalog, iron halide reagents are inexpensive, environmentally friendly, and stable. They are described in the literature as effective agents for the cleavage[16] and formation[17] of ethers, as oxidizing agents,[18] for cross coupling of alkenyl or aryl derivatives with Grignard reagents,[19] for carbometalation of olefins,[20] in the synthesis of 2-aryl-tetrahydrofurans,[21] for Nazarov cyclizations,[22] in the allylation of aldehydes,[23] and a number of other applications.[24,25]

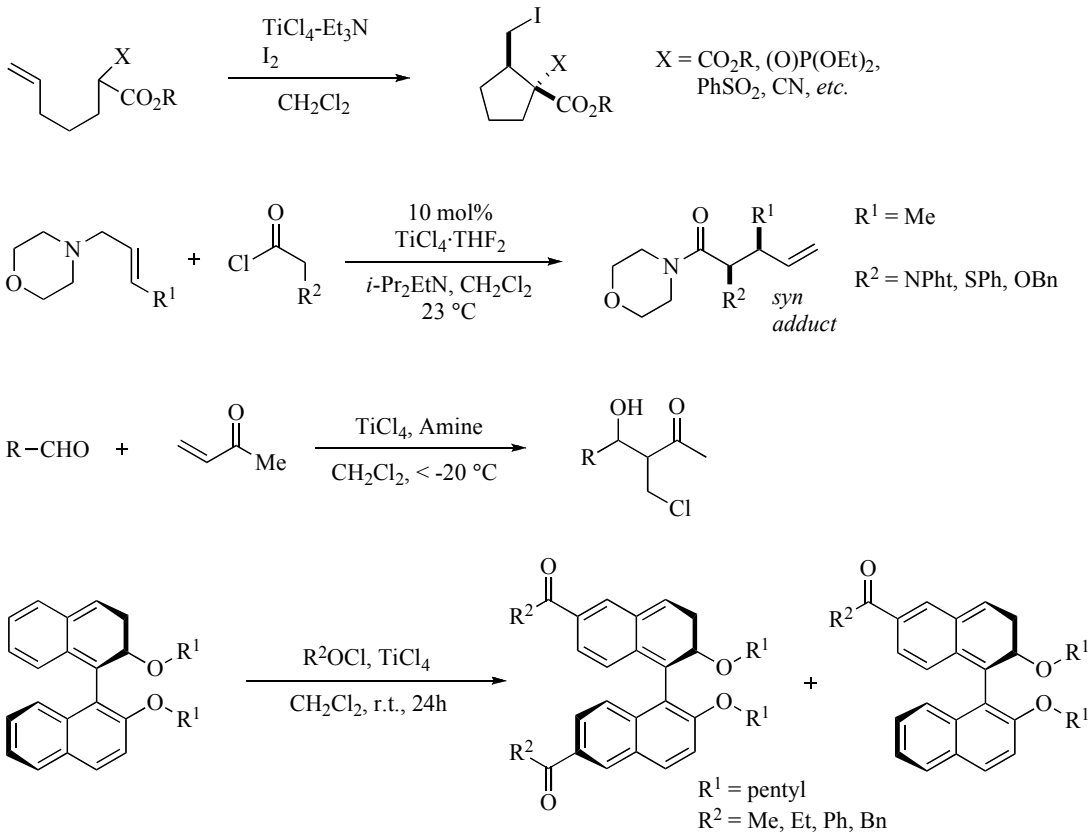
In recent years, the $FeCl_3$[26] and $TiCl_4$[15] mediated coupling reactions of aldehydes and alkynes to generate halogenated (*Z,E*)-1,4-pentadienes have been reported (**Scheme 1-3**). A stereodefined (*Z,E*)-intermediate, which will readily undergo a vinyl migration and a C-O bond cleavage, was proposed to explain the reaction stereoselectivity. However, the mechanism (concerted or cationic) is not clear.



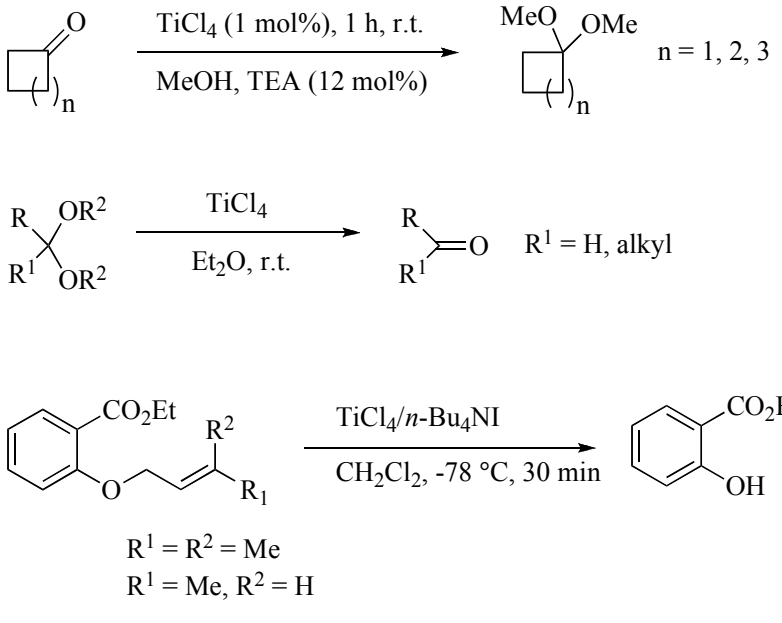
Scheme 1-3 Titanium or iron halide mediated coupling of aldehydes and alkynes

1.1.4 Reactions of Titanium(IV) Halides in Organic Chemistry

Titanium(IV) halides are very versatile reagents in organic synthesis.[27] $TiCl_4$ is widely used in many carbon-carbon bond-forming reactions, including the coupling of carbonyl and aldimine compounds,[28] aldol condensations,[29] Claisen condensations,[30] and alkynylations of carbonyl compounds.[31] Other syntheses involve the additions of allylsilane,[32] allyltin,[33] propargylsilane,[34] and 2,4-pentadienylsilane[35] reagents to aldehydes, ketones, α-keto esters, and ketals. Titanium(IV) chloride is also used in the carbocyclization of active methane compounds with alkyne groups,[36] Claisen rearrangements,[37] as well as Baylis-Hillman[38] and Friedel-Crafts[39] reactions (**Scheme 1-4**). In addition, numerous organic functional group transformations have been achieved using $TiCl_4$. Examples include conversion of propargylic alcohols to α,β-acetylenic aldehydes,[40] alkyl azides and ketones to amides,[41] *α*-nitro ketones to *anti*-β-nitro alcohols,[42] ketamines to pyrroles,[43] carbonyl compounds to acetals,[44] and ketals to carbonyl compounds,[45] ethers to alcohols[46] and enamines to anilines[47] (**Scheme 1-5**).



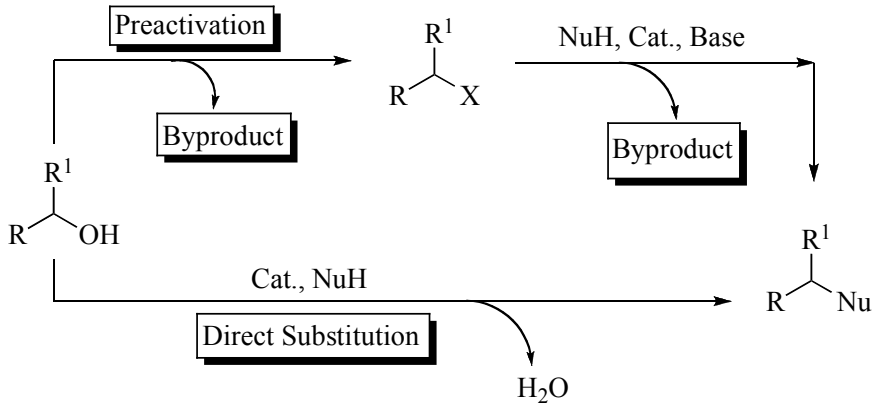
Scheme 1-4 Titanium(IV) chloride in various organic syntheses



Scheme 1-5 Organic functional group transformations mediated by titanium(IV) chloride

1.2 Alcohol Functional Group Conversion

Alcohols are key precursors to other functionalized compounds, such as carbonyls, ethers, and alkenes. Carbon-carbon bond formation by direct substitution of hydroxyl groups has been regarded as a quite important process in organic syntheses. However, the poor leaving ability of the hydroxyl group often retards direct substitution reactions; preactivation of the hydroxyl groups by converting them to more reactive leaving groups (X, OAc, OTf, OTs, etc.) is generally required. In terms of atom-efficiency and environmental concerns, the direct substitution of hydroxyl groups by nucleophiles is highly desirable because only water is generated as byproduct (**Scheme 1-6**). Although encouraging results have been achieved,[48-50] and some of these results have already been applied successfully in the total synthesis of natural products, the direct substitution of the hydroxyl group in alcohols is far from being fully developed. For example, 3-5 equivalents of the nucleophile are often required and no general method has been developed which works for all types of alcohols. In summary, the development of an efficient and practical method for the catalytic substitution of alcohols remains a challenging goal.



Scheme 1-6 Activation/substitution vs. direct substitution of an aliphatic alcohol

1.3 Alkylation of Carbonyls with Organoboron Compounds

Aldehydes and ketones are ideal starting materials in synthesis due to the polarization of the carbon-oxygen double bond. Because of this, their reactions are regioselective, and take place at either the carbon or oxygen center. In turn, many reactions have been developed to control the regio-, chemo-, and stereoselectivity of the resulting products.

The Grignard reaction is one of the most common reactions involving carbonyl compounds, which generally give alcohols.[51] The organic portion of the Grignard reagent is nucleophilic, and can thus attack the carbon center of the carbon-oxygen double bond. Evidence shows that both a concerted pathway and radical pathway (single electron transfer) are possible.[52]

Other organometallic reagents have been used in the alkylation of carbonyl compounds. Organometallic compounds giving products similar to Grignard reagents include organolithium,[53] and organozinc[54].

Organoboranes can also alkylate carbonyl compounds, however their reactivity is not consistent with Grignard or other organometallic reagents; exceptions include allyl-,[55] alkenyl-,[56,57] and alkynylboranes.[58] The final two entries of **Scheme 1-1** highlight the ability of organoboron halides to halogenate and alkylate carbonyl compounds.[10-12,15,59]

Finally, organoboranes also have significant reducing ability.[60] Diisopinocampheylboron chloride is an important organoboron reducing agent (Ipc_2BCl). Aldehydes and ketones are reduced in near quantitative yield, with high enantiomeric excess. Further, both enantiomeric forms are available commercially and no side reactions are usually observed.

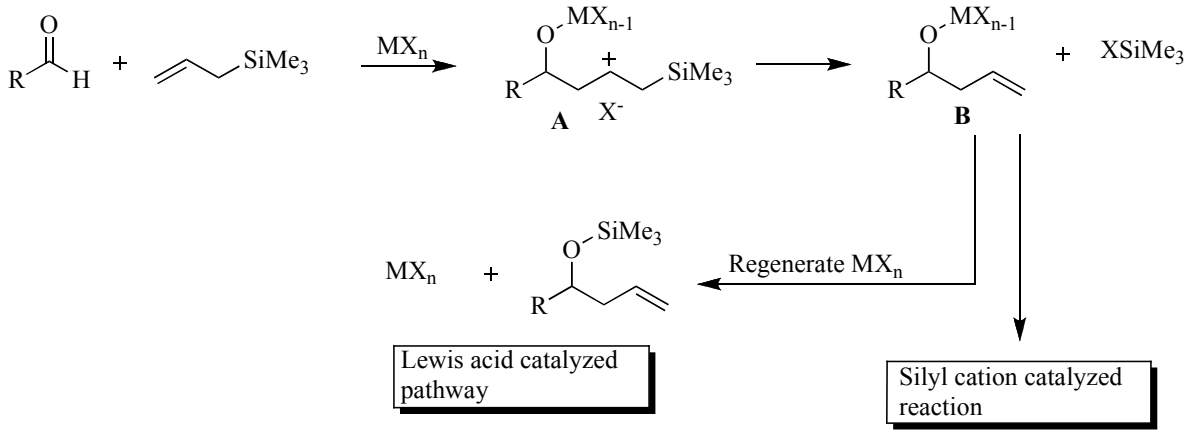
1.4 Statement of Problem

Lewis acids such as boron trihalides, iron(III) halides, and titanium(IV) halides can mediate reactions involving aldehydes or alcohols to give compounds containing new carbon-carbon and new carbon-halogen bonds. This dissertation is focused on the reactions of boron halides and transition metal halides with carbonyl and hydroxy compounds. Haloallylation of aromatic aldehydes by boron trihalides and allyltrimethylsilanes was investigated (Chapter 2). Dialkenylation of aromatic aldehydes to generate 1,3,5-triaryl-1,5-dihalo-1,4-dienes brings two haloalkenyl groups to the carbonyl center (Chapter 3). Also, the effects of the sequence of reactant addition and reaction temperature were studied to try to explain why boron tribromide only produces the (*Z*,*Z*)-1,5-dihaloalkene isomer, while boron trichloride produces the (*Z*,*E*)-1,5-dihaloalkene isomer. Dehydroxylations of benzylic alcohols and corresponding *in situ* generated benzylic alcohol salts with triethylsilane and iron(III) chloride to give diarylmethane products was also investigated (Chapter 4). Finally, the alkenylation of allylic, benzylic, and propargylic alcohols with phenylacetylenes and titanium(IV) halides to afford high (*E*,*Z*) ratios of alkenylated products was investigated (Chapter 5).

Chapter 2. Boron Trihalide Mediated Haloallylation of Aryl Aldehydes: Reactions and Mechanistic Insight

2.1 Introduction

The Lewis acid mediated allylation of carbonyl compounds leading to homoallylic alcohols constitutes one of the most important synthetic reactions.[61] Numerous allylic organometallic reagents and Lewis acids have been investigated. In recent years, asymmetric allylation reactions have also been studied extensively due to their importance in medicinal and natural product chemistry. Lewis acid mediated allylations have been shown to be stepwise processes, as in **Scheme 2-1.**

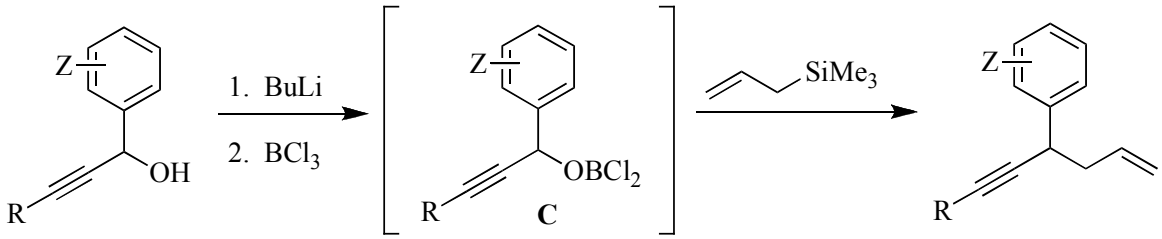


Scheme 2-1 Process of Lewis acid addition to allyltrimethylsilane and an aldehyde

The addition of allylsilane to an activated aldehyde forms intermediate **A**. The silyl electrofuge cleavage then produces the metal homoallyloxide **B** and Me_3SiX. If the metal exchange between **B** and Me_3SiX occurs, Lewis acid MX_n is regenerated and the reaction is catalytic in nature. However, if the metal exchange does not occur, Me_3SiX could also

induce further allylations (silyl cation catalyzed pathway). To achieve high enantioselectivity in chiral Lewis acid catalyzed allylations, minimizing the contribution from the silyl cation catalyzed pathway is required.

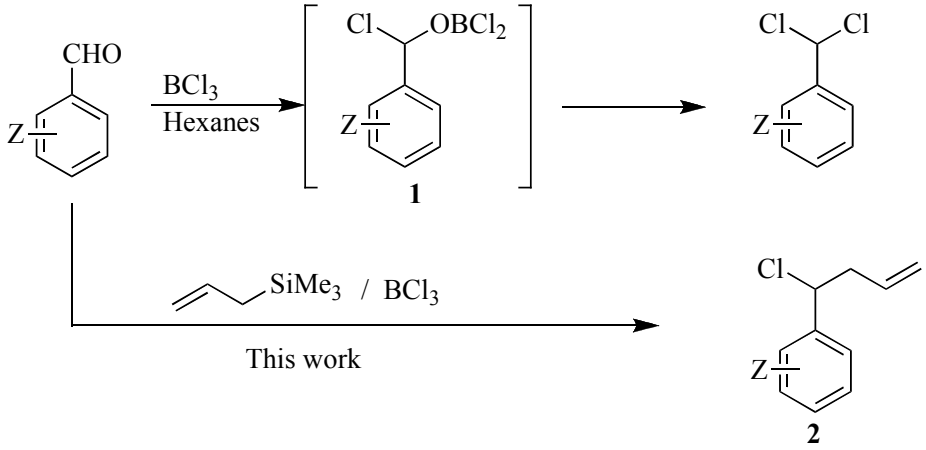
In the last decade, our group has developed a number of novel reactions using the chemistry of boron halide derivatives. These include, for example, the dialkenylation of aryl aldehydes by divinylboron halides,[62] a reaction that appears to occur *via* an unprecedented process: C—O bond cleavage in the alkoxyboron monohalide intermediate. This discovery led us to develop reactions in which the hydroxyl groups were substituted with stereodefined alkenyl[12,63,64] and alkynyl[65] moieties using boron dihalides. Very recently we found that C—O bond cleavage also occurs smoothly (**Scheme 2-2**) in propargyloxyboron dihalide **C**.[66,67]



Scheme 2-2 Allyltrimethylsilane addition to a propargyloxyboron dihalide

In an earlier study, we reported a novel method for dihalogenating aryl aldehydes (**Scheme 2-3**).[68] NMR study revealed that the reaction proceeds through the alkoxyboron dihalide intermediate **1**. The similarity between intermediates **C** and **1** led us to investigate the feasibility of capturing intermediate **1** with allyltrimethylsilane.

The mechanism shown in **Scheme 2-3** led us to postulate that the reaction of aryl aldehydes with allylsilane in the presence of a stoichiometric quantity of a boron halide would lead to haloallylated product **2** rather than the homoallylic alcohol. In fact, during a kinetic study of the reaction between a carbocation and allylsilane, Mayr and Gorath noted chloroallylation of aryl aldehydes in the presence of 2—4 equivalents of BCl_3.[69] The sentence, "In the BCl_3-promoted reaction of aldehydes with allyltrimethylsilanes, further halogeneration by excess BCl_3 took place, and consecutive products were isolated instead of the corresponding alcohols" was used to describe the reaction mechanism. Herein are reported the results of a detailed study of this reaction, including a mechanistic discussion.



Scheme 2-3 Formation of di- and haloallylated compounds from aryl aldehydes

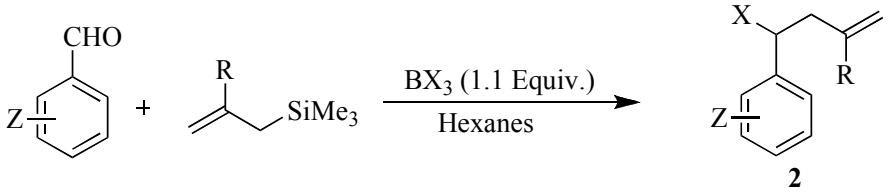
2.2 Results and Discussion

Due to its air and moisture sensitivity, 1.1 equivalents of BCl_3 were utilized for the reaction of benzaldehyde with allyltrimethylsilane. We found that the reaction proceeded readily in hexanes and gave the expected haloallylated product **2a** in 85% yield. A series

of aryl aldehydes were subjected to the reaction, shown in **Table 2-1**. Essentially all of the aryl aldehydes investigated were successfully converted to the haloallylated products with the exception of *p*-anisaldehyde (the cleavage of the methoxy ether by BCl_3 and BBr_3 is well known). Generally, reactions with BBr_3 are faster than those using BCl_3. Bromoallylated product **2k** formed exclusively when a mixture of BBr_3 and BCl_3 (1.1 equivalents each) was added to the *p*-chlorobenzaldehyde reaction, demonstrating a high chemoselectivity.

Several control experiments were performed to probe the reaction mechanism. First, the reaction of allyltrimethylsilane with *p*-chlorobenzaldehyde using a substoichiometric amount of boron trihalide (0.8 equivalent) was carried out to determine whether the reaction was catalytic (**Scheme 2-4**). *p*-Chlorobenzaldehyde was not completely consumed after 24 hours, clearly indicating that the reaction is not catalytic. Remarkably, the Me_3SiX (X = Cl, Br) generated in the reaction did not initiate a silyl cation catalyzed allylation. The discovery that Me_3SiX (X = Cl, Br) was not a catalyst in the non-polar solvent hexane could be significant for allylation reactions involving chiral Lewis acid catalysts. Hydrolysis of the reaction mixture at this stage revealed products **4** and **2**. Homoallylic alcohol **4** was isolated as the major product (70% yield) along with chloroallylated product **2c** (8% yield) when BCl_3 was employed. In contrast, bromoallylated product **2k** was the main product if boron tribromide was used; the yields of **4** and **2k** were 26% and 41%, respectively. In a separate experiment, an additional 0.3 equivalents of boron trihalide was added to the substoichiometric (0.8 equivalents) mediated reactions after they had been allowed to react for 24 hours

Table 2-1 Haloallylation of Aryl Aldehydes[a]

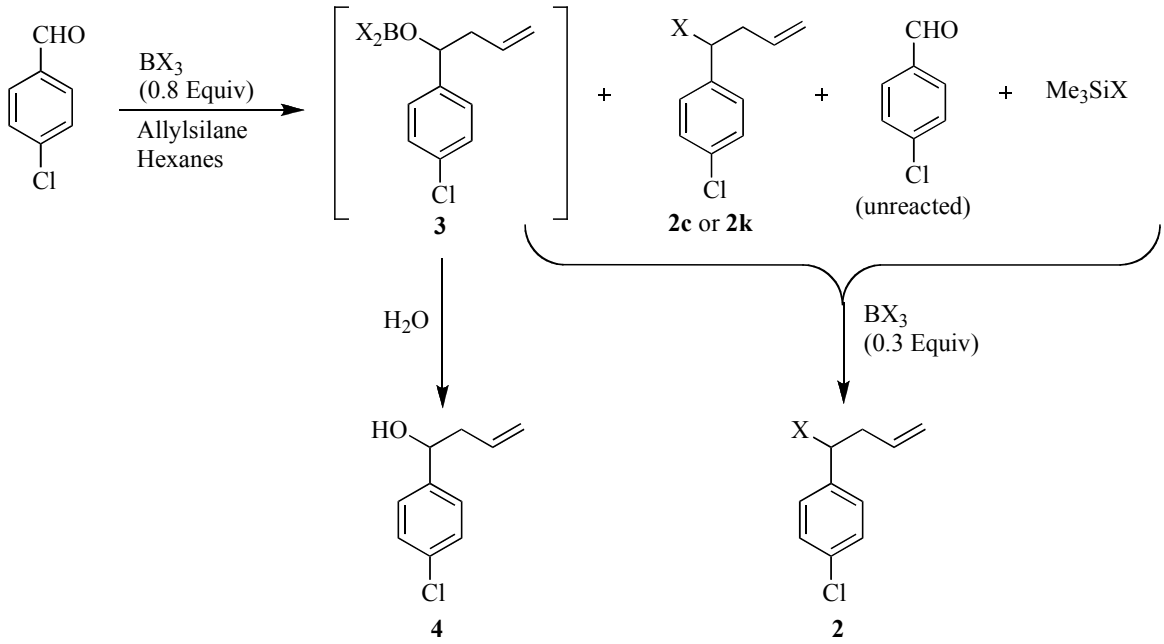


Entry	Z	R	X	Time/min	Product	Yield[b] (%)
1	H	H	Cl	30	**2a**	85
2	4-F	H	Cl	30	**2b**	62
3	4-Cl	H	Cl	20	**2c**	90
4	4-Br	H	Cl	30	**2d**	87
5	2-Me	H	Cl	20	**2e**	73
6	3,5-Br_2	H	Cl	120	**2f**	61
7	4-Cl	Me	Cl	60	**2g**	92
8	2-Me	Me	Cl	60	**2h**	69
9	2,3,4,5,6-F_5	Me	Cl	180	**2i**[c]	67
10	4-CF_3	Me	Cl	120	**2j**	89
11	4-Cl	H	Br	10	**2k**	81
12	4-Cl	Me	Br	10	**2l**	72
13	4-Br	Me	Br	10	**2m**	78
14	3-Cl	Me	Br	20	**2n**	63

[a] Boron halide was added at 0 °C and then the reaction mixture was warmed to room temperature until complete (see Experimental for details).

[b] Isolated yield based on aldehyde.

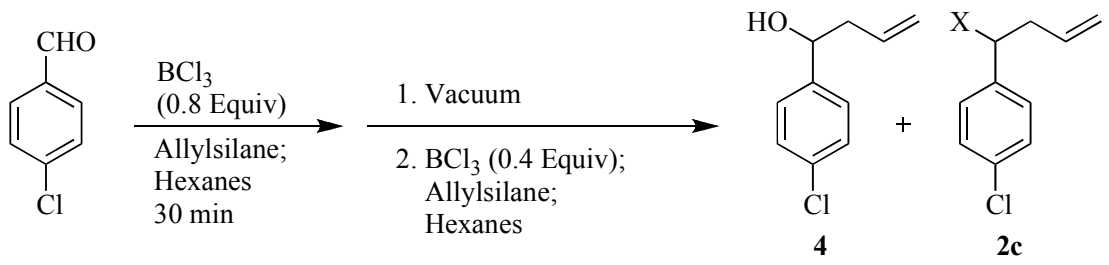
[c] Refluxing is required for completion.



Scheme 2-4 Determination of catalytic nature of reaction by addition of substoichiometric amount of BX_3

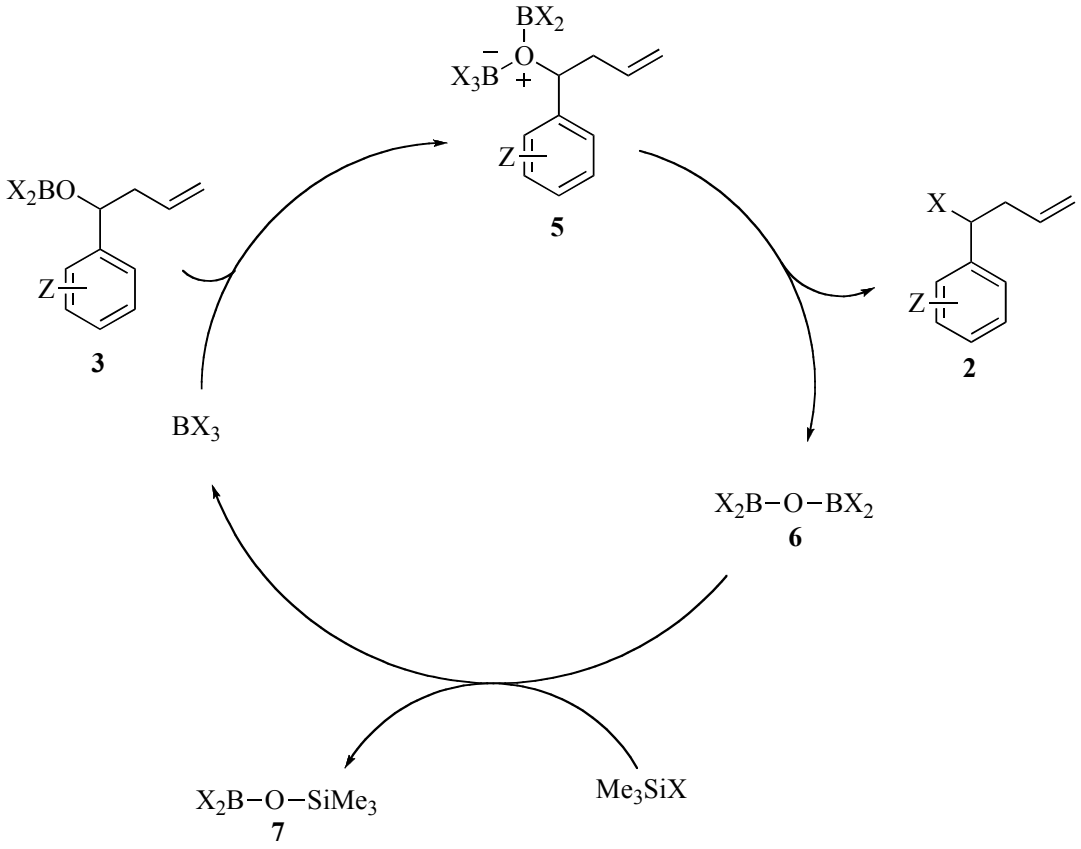
Both intermediate **3** and the unreacted *p*-chlorobenzaldehyde disappeared (no homoallylic alcohol **4** detected). Clearly the conversion of intermediate **3** to haloallylated product **2** occurred.

The complete conversion of intermediate **3** and unreacted *p*-chlorobenzaldehyde to haloallylated product **2** using only an additional 0.3 equivalent of boron trihalide (**Scheme 2-4**) was somewhat surprising. The isolation of homoallylic alcohol **4** in 53% yield from a modified reaction (**Scheme 2-5**) helps explain the earlier observation. Removal of the Me_3SiCl prior to addition of the extra BCl_3 inhibits the conversion of intermediate **3** to product **2c**.



Scheme 2-5 Experimental illustration of Me_3SiCl removal

Based on these experiments, a tentative mechanism was proposed to explain the boron trihalide catalyzed transformation of **3** to **2** (**Scheme 2-6**). Boron trihalide coordinates with the oxygen in intermediate **3** to form **5**. Rearrangement of **5** generates the desired product **2** along with $X_2B—O—BX_2$ (**6**). Exchange between **6** and Me_3SiX regenerates boron trihalide and mixed anhydride **7**.



Scheme 2-6 Proposed mechanistic pathway for formation of haloallylated product (**2**) from intermediate **3**

2.3 Conclusions

In summary, a facile haloallylation of aryl aldehydes using boron trihalide is reported. A mechanistic study revealed the reaction involves two-steps: i) conversion of aldehydes to homoallyloxide borates in the presence of a stoichiometric amount of boron trihalides; ii) a boron trihalide catalyzed conversion of homoallyloxide borates into halogenated products in the presence of Me_3SiX (X = Cl, Br).

2.4 Experimental

2.4.1 General Methods

All reagents were used as received. Column chromatography was performed using silica gel (60 Å, 230–400 mesh, ICN Biomedicals GmbH, Eschwege, Germany). Analytical thin-layer chromatography was performed using 250 μm silica plates (Analtech, Inc., Newark, DE).

^{1}H NMR and ^{13}C NMR spectra were recorded at 250.13 and 62.89 MHz, respectively. Chemical shifts for ^{1}H NMR and ^{13}C NMR spectra were referenced to TMS and measured with respect to the residual protons in the deuterated solvents. Atlantic Microlab, Inc., Norcross, Georgia, performed microanalysis.

2.4.2 Typical Reaction Procedure

Finely ground 4-chlorobenzaldehyde (210 mg, 1.5 mmol), allyltrimethylsilane (256 mg, 2.25 mmol) and dry hexanes (16 mL) were placed in a dry argon-flushed, 50 mL round-bottomed flask equipped with a magnetic stirring bar. The solution was cooled to 0 °C, and boron trichloride (1.65 mmol, 1.65 mL of a 1.0 *M* CH_2Cl_2 solution) was added *via* syringe. After completion of the addition, the ice-bath was removed and the resulting solution was allowed to warm to room temperature. The reaction mixture was hydrolyzed with water and extracted with hexanes. The organic layer was separated, dried over anhydrous $MgSO_4$, the solvent removed under reduced pressure, and the product isolated by flash column chromatography.

2.4.3 Characterization of Compounds 2a-2n

(1-Chlorobut-3-enyl)benzene (2a)[69]**:** ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.25-7.38 (m, 2H), 7.00–7.08 (m, 2H), 5.62-5.77 (m, 1H), 5.06-5.16 (m, 2H), 4.82 (t, J = 7.22 Hz, 1H), 2.72-2.85 (m, 2H). ^{13}C NMR ($CDCl_3$): δ 138.1, 134.4, 129.0, 128.8, 128.6, 116.3, 56.7, 43.2.

1-(1-Chlorobut-3-enyl)-4-fluorobenzene (2b): ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.25-7.38 (m, 2H), 7.00–7.08 (m, 2H), 5.65-5.79 (m, 1H), 5.08-5.15 (m, 2H), 4.83 (t, J = 7.27 Hz, 1H), 2.73-2.86 (m, 2H). ^{13}C NMR ($CDCl_3$): δ 162.5, ($^{1}J_{CF}$= 246.5 Hz), 160.5, 137.4, 133.6, 128.8, ($^{3}J_{CF}$= 7.7 Hz), 118.4, 115.5, ($^{2}J_{CF}$= 21.2 Hz), 61.3, 44.2. Anal. Calcd for $C_{10}H_{10}ClF$: C, 65.05; H, 5.46. Found: C, 65.48; H, 5.61.

1-(1-Chlorobut-3-enyl)-4-chlorobenzene (2c)[69]**:** ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.29-7.33 (m, 4H), 5.63-5.77 (m, 1H), 5.06-5.14 (m, 2H), 4.86 (t, J = 7.33 Hz, 1H), 2.71-2.86 (m, 2H). ^{13}C NMR ($CDCl_3$): δ 139.7, 134.0, 133.5, 128.7, 128.4, 116.5, 61.7, 44.0.

1-(1-Chlorobut-3-enyl)-4-bromobenzene (2d)[70]**:** ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.44-7.47 (m, 2H), 7.21–7.25 (m, 2H), 5.63-5.76 (m, 1H), 5.06-5.13 (m, 2H), 4.81 (t, J = 7.21 Hz, 1H), 2.70-2.85 (m, 2H). ^{13}C NMR ($CDCl_3$): δ 140.1, 133.4, 131.7, 128.7, 118.5, 61.6, 43.9.

1-(1-Chlorobut-3-enyl)-2-methylbenzene (2e): ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.14-7.50 (m, 4H), 5.74-5.80 (m, 1H), 5.07-5.17 (m, 3H), 2.81-2.91 (m, 2H), 2.38 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 139.1, 135.3, 134.2, 130.5, 128.1, 126.5, 118.1, 58.7, 43.0, 19.1. Anal. Calcd for $C_{11}H_{13}Cl$: C, 73.12; H, 7.25. Found: C, 73.54; H, 7.37.

1,3-Dibromo-(1-chlorobut-3-enyl)benzene (2f): ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.45-7.61 (m, 3H), 5.67-5.77 (m, 1H), 5.09-5.16 (m, 2H), 4.72-4.77 (m, 1H), 2.73-2.81 (m, 2H). ^{13}C NMR ($CDCl_3$): δ 133.9, 132.9, 129.0, 123.0, 119.1, 60.6, 43.9. HR-MS for $C_{10}H_9Br_2Cl$: 321.8760. Found: 321.8757.

1-Chloro-4-(1-chloro-3-methylbut-3-enyl)benzene (2g): ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.23-7.37 (m, 4H), 4.97 (dd, J = 7.21, 7.19 Hz, 1H), 4.83 (s, 1H), 4.73 (s, 1H), 2.71-2.83 (m, 2H), 1.69 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 140.7, 140.0, 134.0, 128.7, 128.4, 114.4, 60.3, 47.9, 22.1. Anal. Calcd for $C_{11}H_{12}Cl_2$: C, 61.42; H, 5.62. Found: C, 61.19; H, 5.25.

1-(1-Chloro-3-methylbut-3-enyl)-2-methylbenzene (2h): ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.14-7.51 (m, 4H), 5.30 (dd, J = 6.43, 6.41 Hz, 1H), 4.85 (s, 1H), 4.78 (s, 1H), 2.77-2.85 (m, 2H), 2.39 (s, 3H), 1.73 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 141.2, 139.4, 135.0, 130.5, 128.0, 126.6, 126.5, 114.0, 57.3, 46.7, 22.2, 19.1. HR-MS for $C_{12}H_{15}Cl$: 194.0862. Found: 194.0874.

1-(1-Chloro-3-methylbut-3-enyl)-2,3,4,5,6-pentafluorobenzene (2i): ^{1}H NMR (250 MHz, CDCl3): δ 5.35 (t, J = 8.08 Hz, 1H), 4.81 (s, 1H), 4.74 (s, 1H), 2.95 (d, J = 8.08 Hz, 2H), 1.73 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 147.0, 143.0, 140.2, 135.7, 120.8, 114.8, 112.7, 48.5, 45.0, 21.8. HR-MS for $C_{11}H_8ClF_5$: 270.0235. Found: 270.0237.

1-(1-Chloro-3-methylbut-3-enyl)-4-(trifluoromethyl)benzene (2j): ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.35-7.50 (m, 4H), 4.90 (t, J = 7.47 Hz, 1H), 4.72 (s, 1H), 4.62 (s, 1H), 2.60-2.70 (m, 2H), 1.58 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 145.4, 140.5, 130.7, 130.2, 127.4, 126.1, 125.6, 125.5, 114.6, 60.1, 48.0, 22.1. Anal. Calcd for $C_{12}H_{12}ClF_3$: C, 57.96; H, 4.86. Found: C, 58.04; H, 4.91.

1-(1-Bromobut-3-enyl)-4-chlorobenzene (2k)[70]**:** ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.29 (s, 4H), 5.61-5.78 (m, 1H), 5.07-5.14 (m, 2H), 4.90 (t, J = 7.25 Hz, 1H), 2.81-3.04 (m, 2H). ^{13}C NMR ($CDCl_3$): δ 140.0, 134.2, 128.8, 128.7, 127.8, 118.4, 52.6, 43.9.

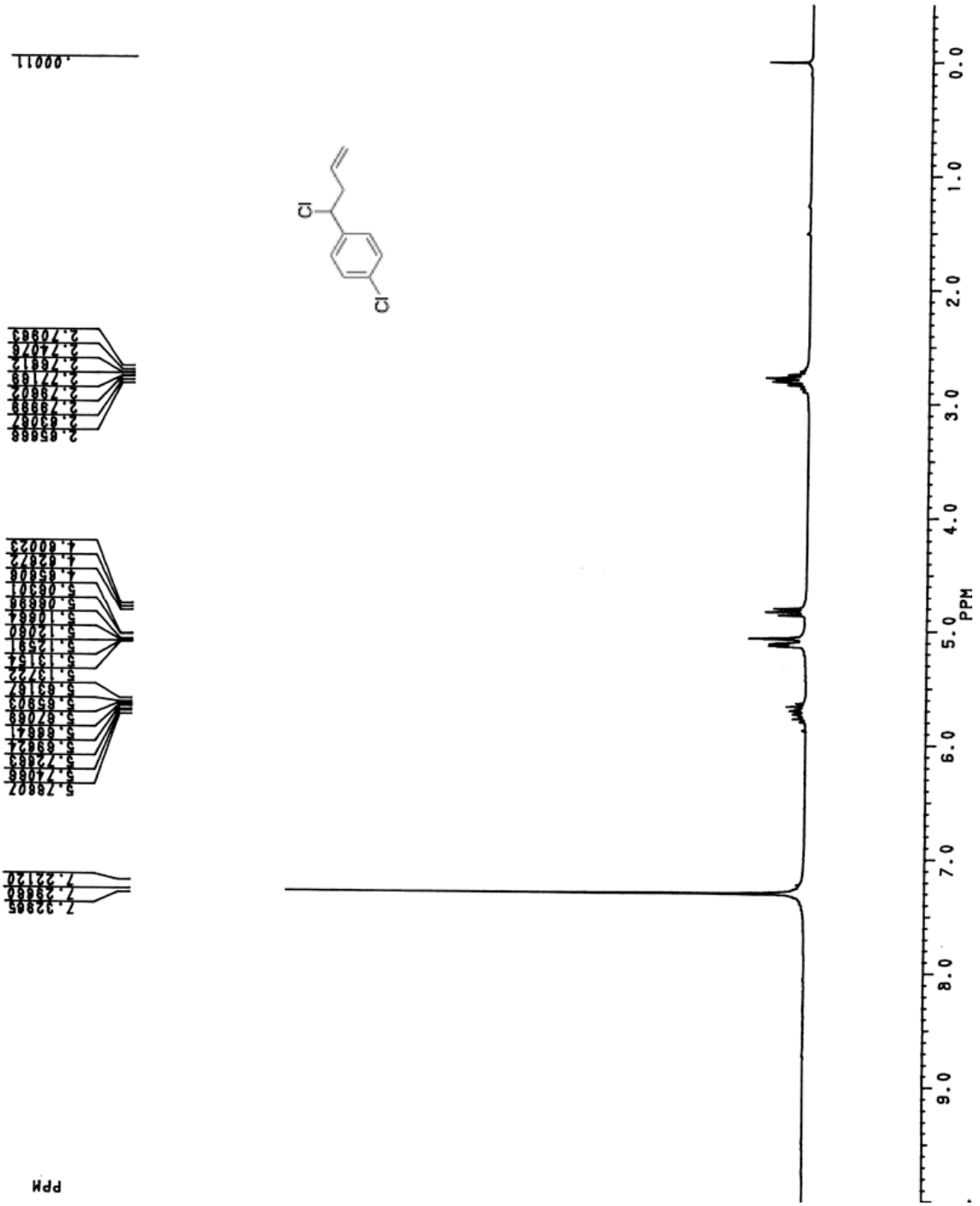
1-(1-Bromo-3-methylbut-3-enyl)-4-chlorobenzene (2l): ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.26-7.34 (m, 4H), 5.06 (t, J = 7.76 Hz, 1H), 4.82 (s, 1H), 4.72 (s, 1H), 2.86-2.97 (m, 2H), 1.68 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 141.2, 140.3, 134.0, 128.7, 128.6, 114.3, 51.3, 47.9, 22.0. Anal. Calcd for $C_{11}H_{12}BrCl$: C, 50.90; H, 4.66. Found: C, 50.67; H, 4.32.

1-Bromo-4-(1-bromo-3-methylbut-3-enyl)benzene (2m): ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.23-7.39 (m, 4H), 5.03 (t, J = 7.72 Hz, 1H), 4.84 (s, 1H), 4.74 (s, 1H), 2.80-3.02 (m, 2H), 1.70 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 143.7, 141.1, 134.3, 129.9, 128.5, 127.5, 125.5, 114.4, 51.1, 47.8, 22.0. HR-MS for $C_{11}H_{12}Br_2$: C, 301.9306. Found: 301.9312.

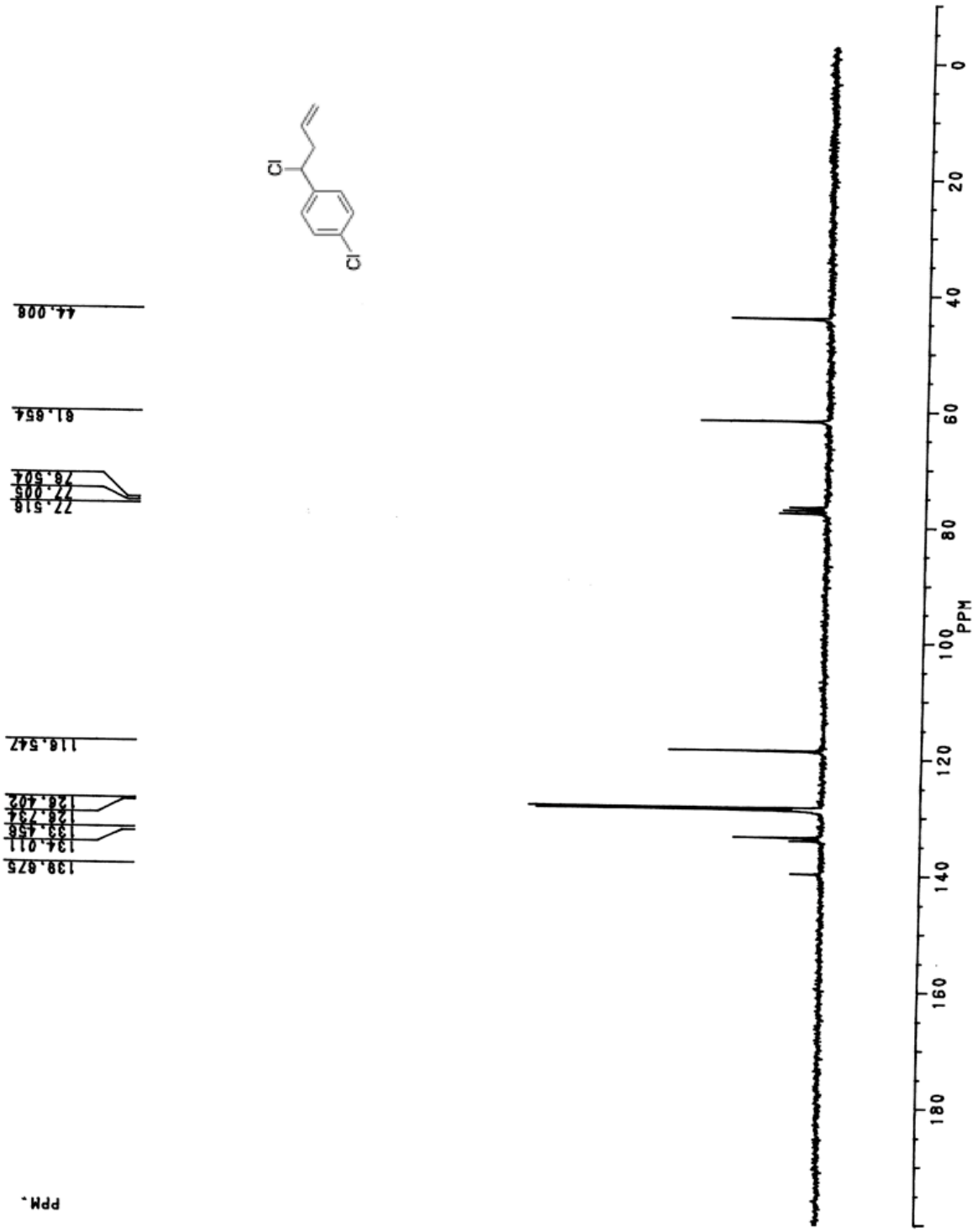
1-(1-Bromo-3-methylbut-3-enyl)-3-chlorobenzene (2n): ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.45 (d, J = 8.48 Hz, 2H), 7.26 (d, J = 8.48 Hz, 2H), 5.05 (t, J = 7.73 Hz, 1H), 4.82 (s, 1H), 4.72 (s, 1H), 2.81-3.04 (m, 2H), 1.68 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 141.2, 140.8, 131.8, 129.0, 122.2, 114.4, 51.3, 47.8, 22.0. Anal. Calcd for $C_{11}H_{12}BrCl$: C, 50.90; H, 4.66. Found: C, 51.07; H, 4.73.

2.4.4 Representative NMR Spectra

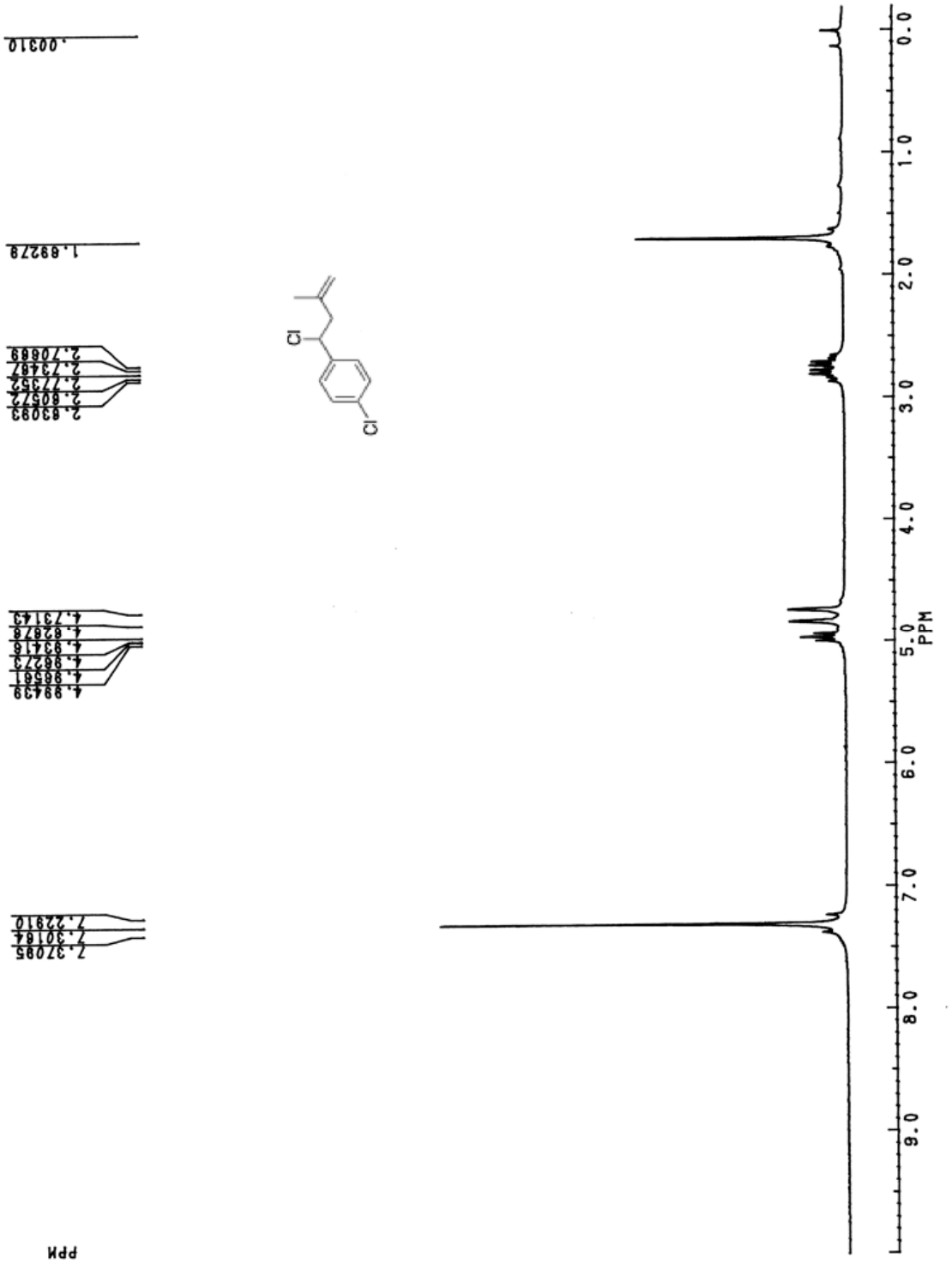
^{1}H spectrum of 2c



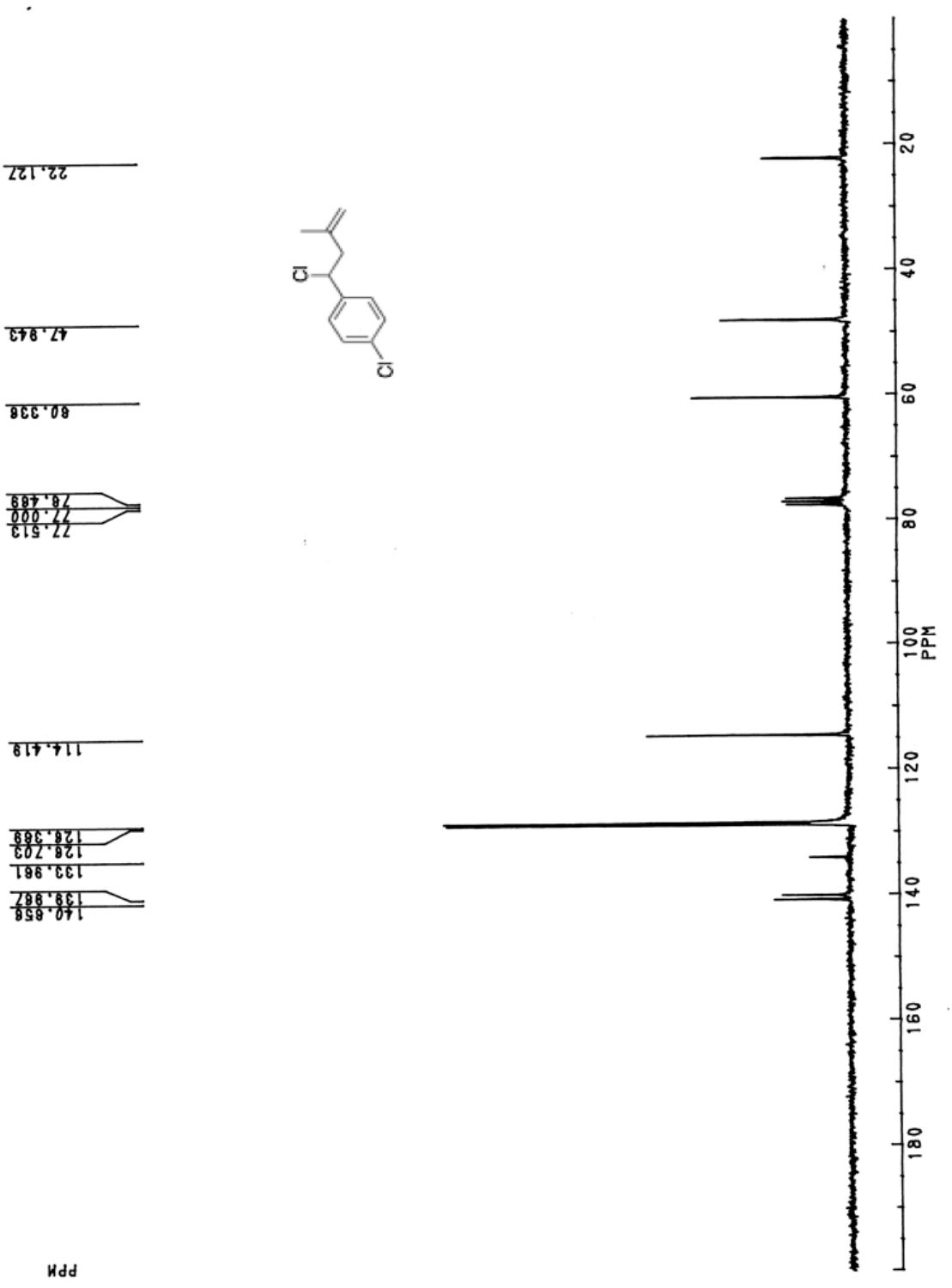
^{13}C spectrum of 2c



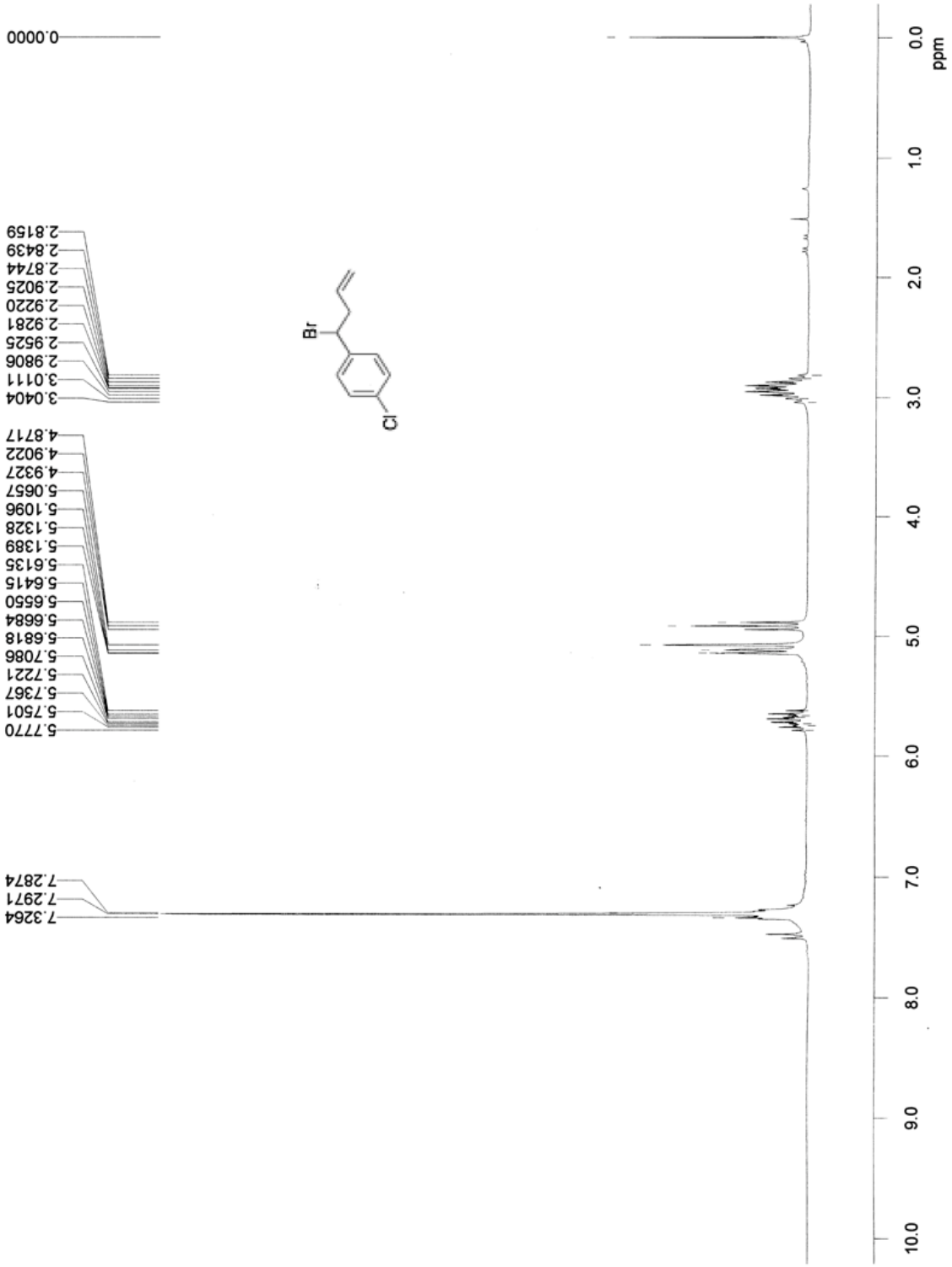
^{1}H spectrum of 2g



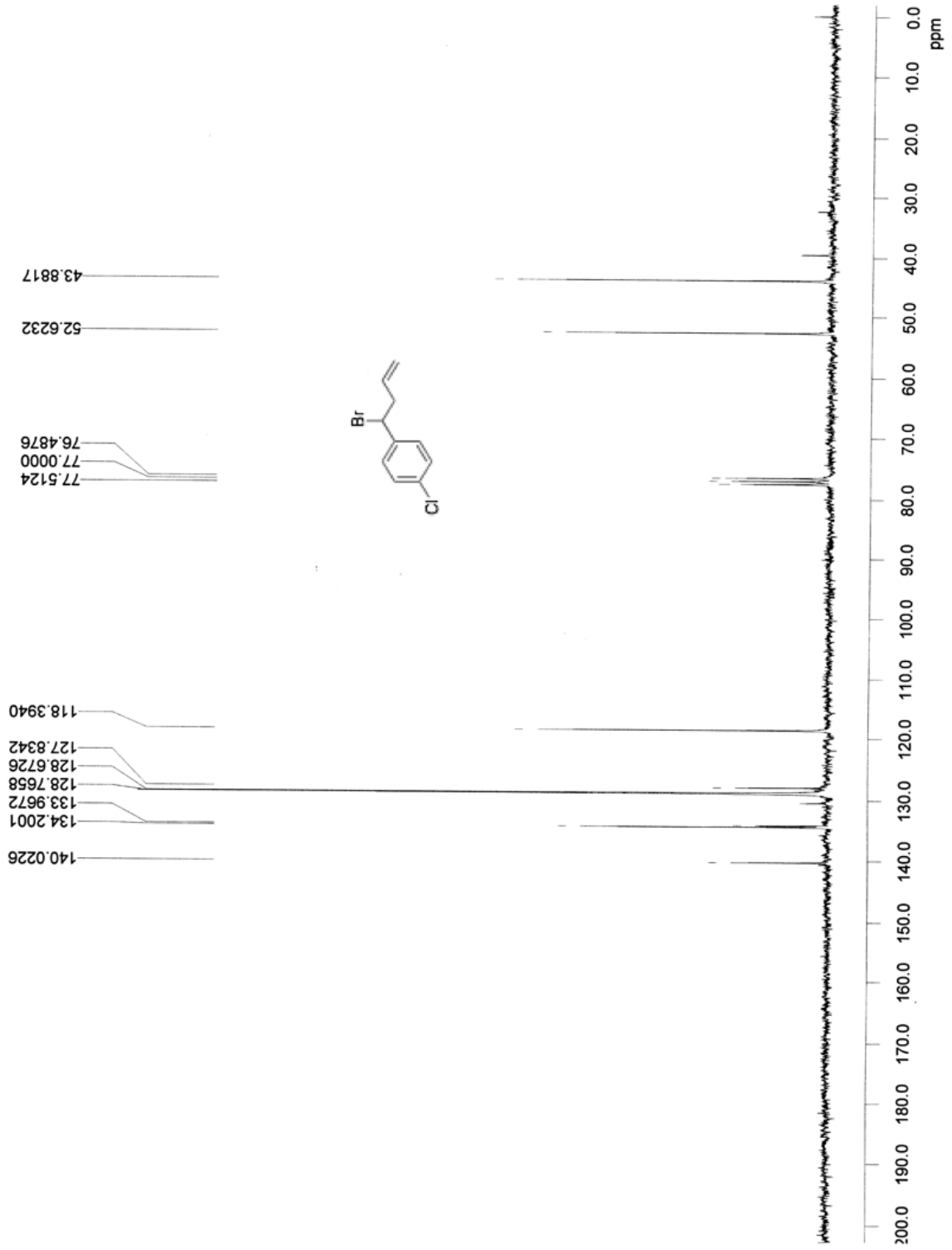
^{13}C spectrum of 2g



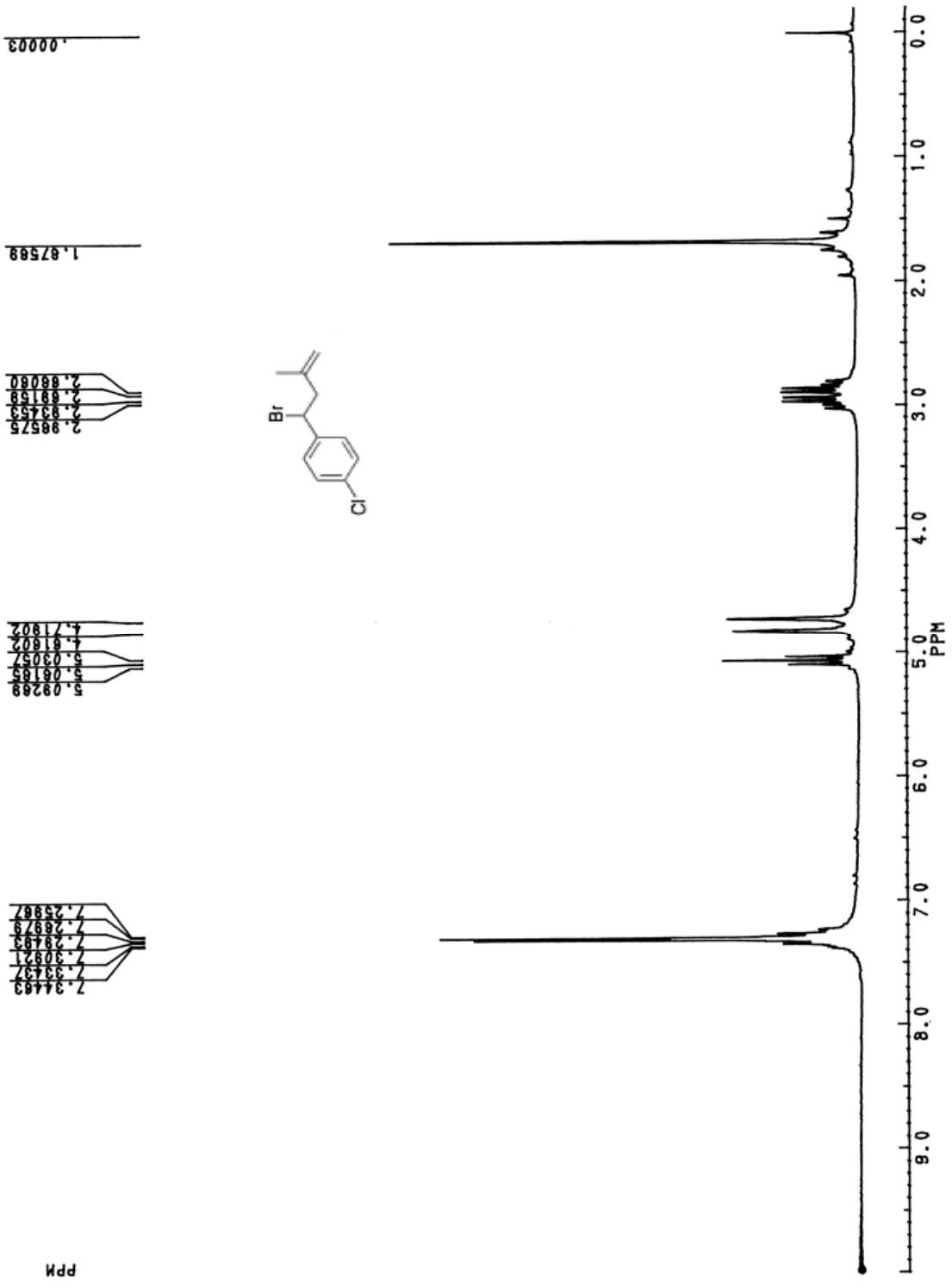
^{1}H spectrum of 2k



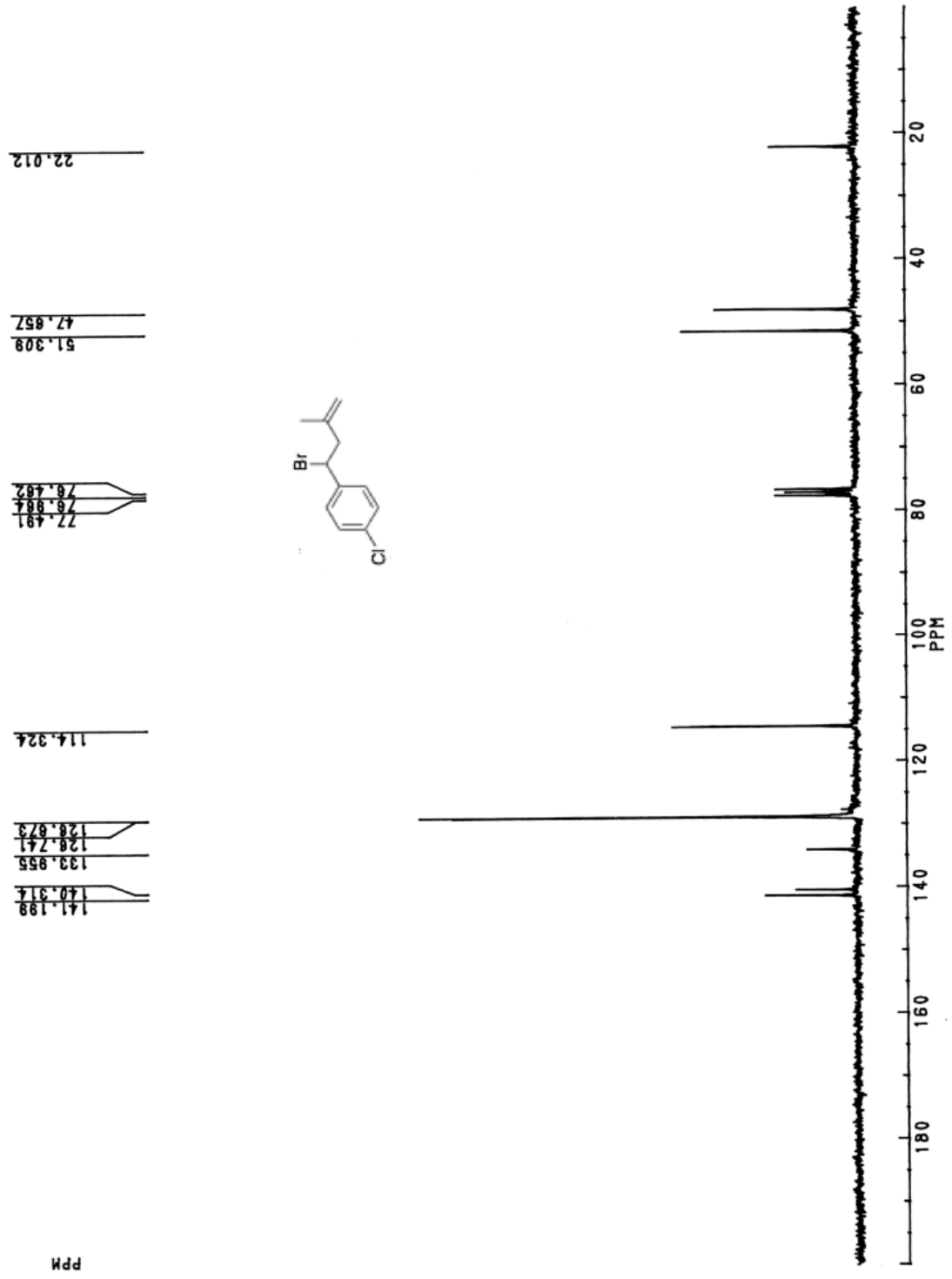
^{13}C spectrum of 2k



^{1}H spectrum of 2l



^{13}C spectrum of 2l

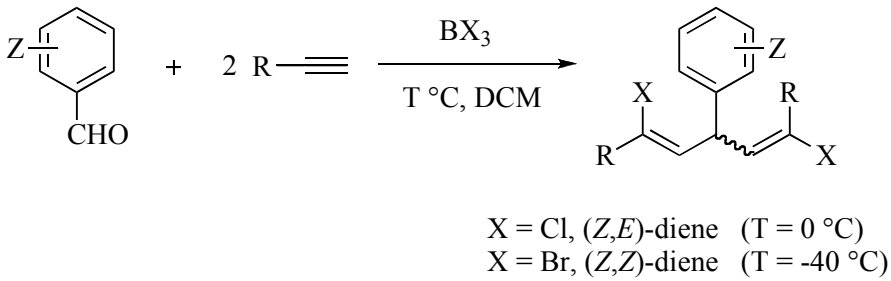


Chapter 3. Boron Trihalide Mediated Alkyne-Aldehyde Coupling Reactions: A Mechanistic Investigation

3.1 Introduction

Efficient one-pot syntheses of complex molecules from readily available starting materials are always desirable. Especially attractive are reactions affording multifunctionalized molecules.[71] The alkyne-aldehyde coupling reaction is a prime example. A variety of molecules can be generated from this coupling reaction by varying the Lewis acids and transition metal complexes employed. Synthons afforded by this coupling reaction include propargylic alcohols,[72] α,β-unsaturated ketones,[73] allylic alcohols,[74] stereodefined enynols[75] and naphthalene derivatives.[14,76] When carried out in an intramolecular fashion, the reaction provides for the efficient route to α-alkylidenecycloalkanones[77] and cycloalkenones.[78] Using transition metal complexes, additional products can be generated through either carbon—carbon triple bond cleavage in alkynes[79] or decarbonylation of aldehydes.[80]

A new alkyne-aldehyde coupling reaction was recently discovered.[62] In the presence of a stoichiometric amount of boron trihalide, aryl aldehydes were found to couple with two equivalents of aryl alkynes to provide stereodefined 1,3,5-triaryl-1,5-dihalo-1,4-pentadienes (**Scheme 3-1**). Interestingly, the stereochemistry of the diene products is dependent on the boron halide employed. If boron trichloride is used, the reactions afford (*Z*,*E*)-1,4-pentadienes as major products along with minor quantities of the (*Z*,*Z*)-1,4-pentadienes. However, (*Z*,*Z*)-1,4-pentadienes are the products formed if



X = Cl, (*Z*,*E*)-diene (T = 0 °C)
X = Br, (*Z*,*Z*)-diene (T = -40 °C)

Scheme 3-1 Boron halide mediated coupling of aryl aldehydes and alkynes

boron tribromide is used. In view of the potential value of these halodiene products in organic synthesis, the study led to the use of other Lewis acids, including TiX_4,[15] $FeCl_3$[26] and GaX_3.[81] A tentative reaction mechanism for these coupling reactions was proposed.[15,26,62] With this work, we describe an investigation initially designed to validate the originally proposed mechanism. A modified reaction mechanism was subsequently put forward and led to the discovery of the dramatic influence of temperature on the stereochemistry of the boron trichloride mediated alkyne-aldehyde coupling reaction. In addition, it was found that the mode of reagent addition greatly affects the stereochemistry of the products formed in these three-component reactions (allyloxide, boron trihalide and alkyne).

3.2 Results and Discussion

3.2.1 Boron Trihalide Mediated Alkyne-Aldehyde Coupling Reaction

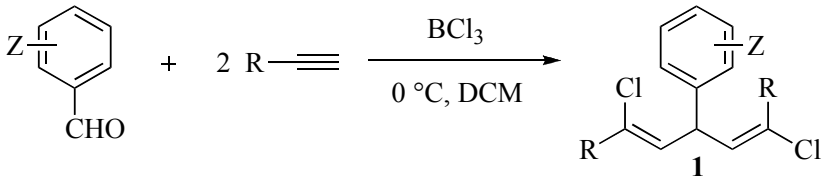
We have been investigating the chemistry of boron halide derivatives for many years, and a number of novel reactions have been developed.[11,13,68,82] In a continuation of a study focused on Grignard-like alkylation of aryl aldehydes using dialkylboron halides, we investigated the addition of alkenylboron dihalide reagents to aldehydes. Brown[57] and

Soderquist[83] had earlier reported the successful 1,2-addition of *B*-alkenyl-9-BBN derivatives to aldehydes. The rigid nature of the 9-BBN ring prohibits reduction of the aldehyde *via* β-hydride transfer.[84] The low reactivity of *B*-alkenyl-9-BBN derivatives and the limited availability of functionally substituted *B*-alkenyl-9-BBN derivatives restrict the scope of the 9-BBN reactions. Alkenylboron dihalides exhibit high reactivity and are not prone to β-hydride transfer; these chemical features led us to investigate the reaction of aldehydes with (*Z*)-2-halo-1-alkenylboron dihalides.

It has been reported that boron trihalides add to terminal alkynes readily at –78 °C.[5] Therefore, we examined the possibility of a one-pot reaction by mixing boron trichloride, phenylacetylene and benzaldehyde at 0 °C. The diene product formed. The (*Z*,*E*)-1,4-pentadiene was isolated as the major product along with minor amounts of the expected (*Z*,*Z*)-1,4-pentadiene. None of the (*E*,*E*)-1,4-pentadiene isomer was detected. A series of aldehydes and alkynes were then subjected to the new reaction. The results are presented in **Table 3-1**. Generally, reactions involving aryl aldehydes bearing electron-withdrawing groups tend to proceed more slowly. The ^{1}H and ^{13}C NMR spectra of each 1,5-dichloro-1,4-diene derivative displayed two sets of vinyl hydrogen resonances, indicating that all were (*Z*,*E*)-1,4-pentadienes.

(*Z*,*Z*)-1,5-dibromo-1,4-pentadienes (rather than (*Z*,*E*)-1,5-dibromo-1,4-pentadienes) were obtained as the major products from the one-pot BBr_3-mediated alkyne-aldehyde coupling reaction. Since the bromination of aryl aldehydes by boron tribromide has been reported to be quite facile, the boron tribromide mediated reactions were carried out at –40 °C.

Table 3-1 Boron Trichloride Mediated Coupling of Aryl Aldehydes and Alkynes[a]



Entry	Z	R	Product	Yield[b] (%)
1	H	Ph	**1a**	65
2	4-F	Ph	**1b**	73
3	4-Br	Ph	**1c**	68
4	4-Me	Ph	**1d**	65
5	4-CN	Ph	**1e**	27[c,d]
6	H	4-Me-Ph	**1f**	67
7	4-F	4-Me-Ph	**1g**	63
8	4-Me	4-Me-Ph	**1h**	62
9	4-F	4-F-Ph	**1i**	76
10	4-Me	4-F-Ph	**1j**	62

[a] Reaction carried out at 0 °C for 2 h and then maintained at room temperature (see Experimental for details).

[b] Isolated yields based on the starting aldehyde.

[c] (*Z*,*Z*)-isomer (41%) was isolated as the major product.

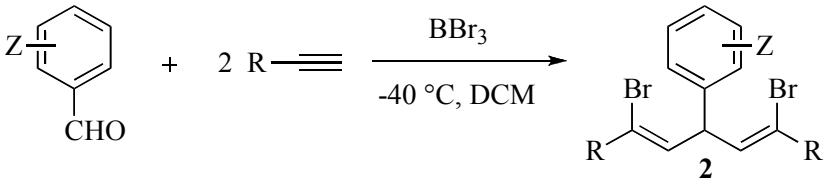
[d] (*Z*,*E*)-isomer was obtained in 66% isolated yield when the reaction was kept at 0 °C for 5 h while using excess alkyne (3.0 equivalents).

Consistent with the fact that the haloboration of alkynes is faster with boron tribromide than boron trichloride, coupling reactions involving boron tribromide are also faster than those using boron trichloride. The results are summarized in **Table 3-2**. As anticipated, the ^{1}H and ^{13}C NMR spectra of the symmetrical (*Z*,*Z*)-1,5-dibromide-1,4-pentadiene derivatives exhibited only one set of vinyl resonances.

3.2.2 Tentative Reaction Mechanism

Due to the facile nature of the haloboration reaction, the boron trihalide mediated alkyne-aldehyde coupling reactions were initially postulated to occur as outlined in **Scheme 3-2**. Haloboration of the alkyne first generates di(halovinyl)boron halide **3**, which then adds to the aldehyde in a Grignard-like fashion to form **4**. The migration of the second halovinyl group from boron to the carbon center then affords the final product. The retention of the vinyl group configuration during migration leads to high stereoselectivity. (The *E*,*Z* stereochemistry of the vinyl groups was believed to have been established during the formation of the divinylboron halide intermediate; a postulation that was later shown to be incorrect.) This tentative mechanism was based on the following two factors: isolation of the anticipated 1,4-pentadiene from the reaction of preformed dialkenylboron bromides with aldehydes and isolation of (*Z*)-3-halo-1,3-diarylprop-2-en-1-ol, the expected product from intermediate **4**, when the reactions were quenched with water prior to completion.

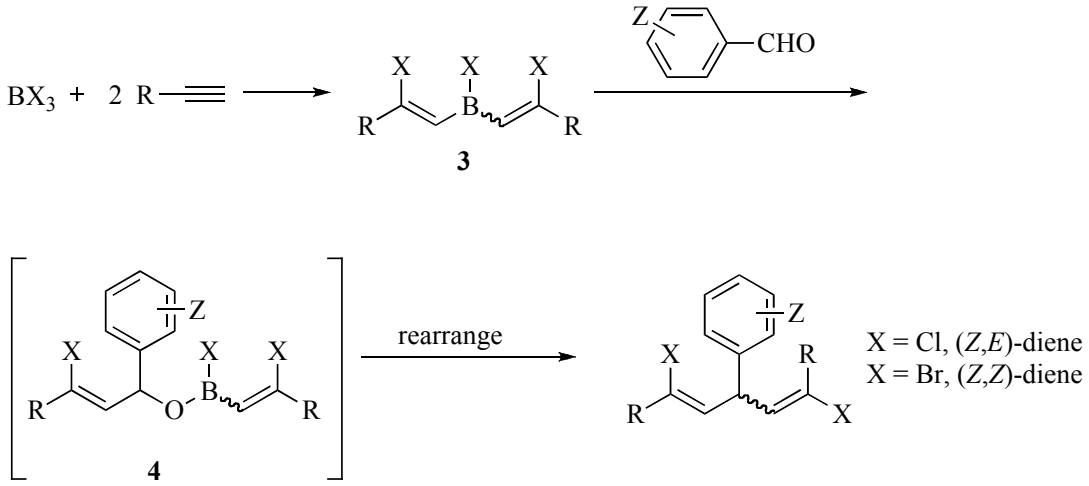
Table 3-2 Boron Tribromide Mediated Coupling of Aryl Aldehydes and Alkynes[a]



Entry	Z	R	Product	Yield[b] (%)
1	4-F	Ph	**2a**	91
2	4-Cl	Ph	**2b**	95
3	4-Me	Ph	**2c**	80
4	2-Me	Ph	**2d**	83
5	4-NO_2	Ph	**2e**	80
6	4-F	4-Me-Ph	**2f**	80
7	4-Br	4-Me-Ph	**2g**	70
8	4-F	4-Cl-Ph	**2h**	83
9	4-Br	4-Cl-Ph	**2i**	74
10	2-Me	4-Cl-Ph	**2j**	89

[a] Reaction carried out at –40 °C (see Experimental for details).

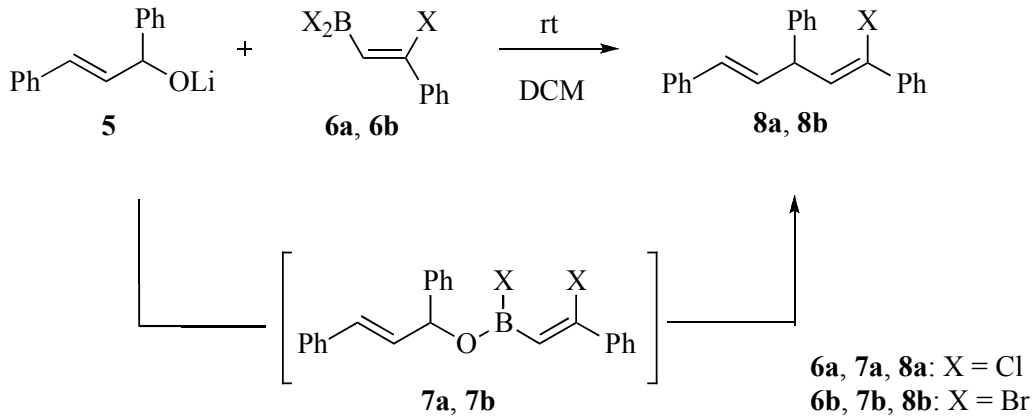
[b] Isolated yields based on the starting aldehyde.



Scheme 3-2 Tentative reaction mechanism for boron halide mediated coupling reaction

To examine the feasibility of a halovinyl group migration from boron to carbon, the reaction in **Scheme 3-3** was carried out. The reaction of allyloxide **5** and alkenylboron dihalide **6** would be expected to generate intermediate **7**, which is similar to the proposed reaction intermediate **4**. If the migration outlined in **Scheme 3-2** occurred, intermediate **7** should be expected to rearrange to the desired product **8**. Indeed, reactions of allyloxides with alkenylboron dihalides proceed efficiently at room temperature and generate **8** in good yields. Thus, the proposed migration appeared reasonable since the stereochemistry of the vinyl group was also retained. The reaction shown in **Scheme 3-3** provides a formal, transition metal free Suzuki reaction.

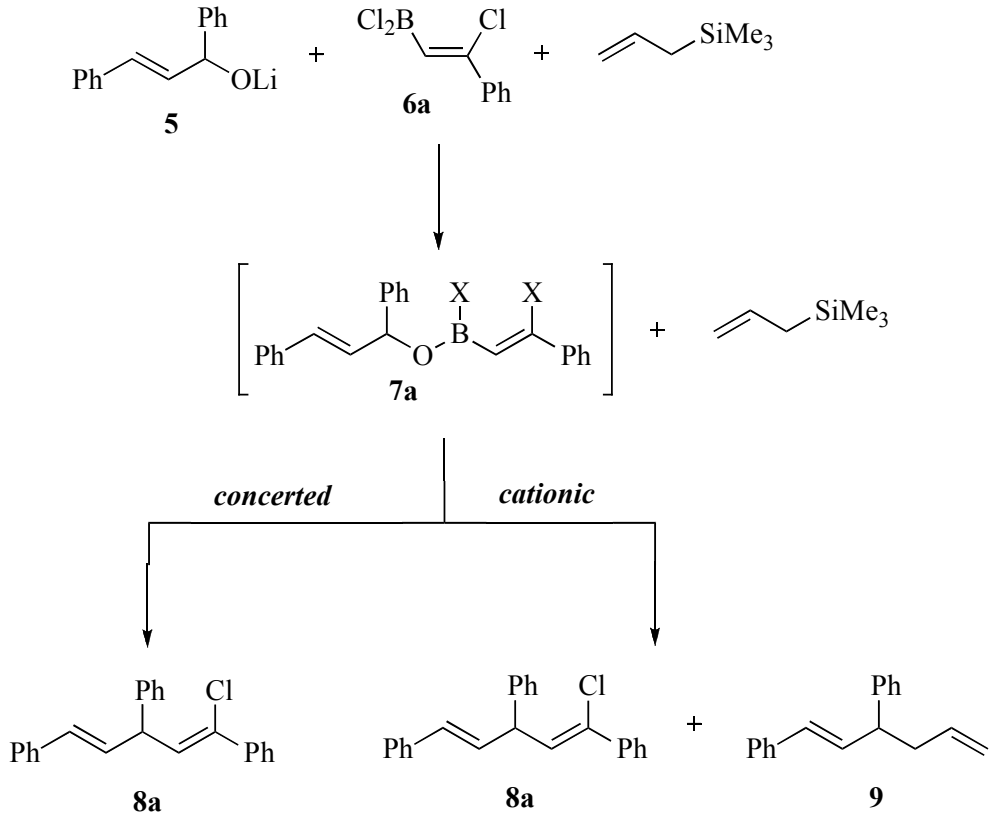
Upon confirmation of vinyl group migration, we attempted to ascertain whether the vinyl group migration proceeded *via* a cationic or concerted pathway. It is known that allylmethylsilane readily captures cationic intermediates. Therefore, a competition reaction involving vinylboron dihalide, allylsilane and an allyloxide was designed to probe the vinyl group migration (**Scheme 3-4**). To a mixture of preformed alkenylboron



Scheme 3-3 Direct evidence supporting alkenyl group migration

dichloride **6a** and allyltrimethylsilane, one equivalent of allyloxide **5** was added to generate intermediate **7a**. If the vinyl group migration proceeds in a concerted fashion, only product **8a** should form. In contrast, if the vinyl group migration proceeds through a cationic intermediate, allyltrimethylsilane should capture a percentage of the cation intermediate, generating **9** in addition to the desired product **8a**. When the reaction was carried out, a mixture of allylated product **9** and **8a** formed in a ratio of 5:2 (isolated yields of **9** and **8a** are 62% and 25%, respectively, based on **5**).

The identification of a cationic intermediate[64] raises questions relating to the stereochemistry of products isolated from this reaction. The postulated intermediacy of the (*Z*,*E*)-di(chlorovinyl) boron chloride was probably incorrect.



Scheme 3-4 Competitive reaction designed to distinguish concerted and cationic mechanisms

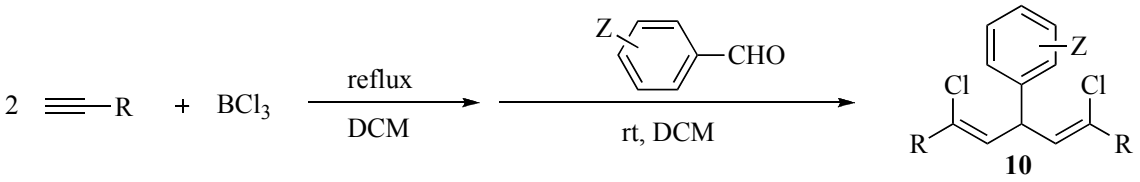
3.2.3 Reinvestigation of the Boron Trichloride Mediated Alkyne-Aldehyde Coupling Reaction.

The intermediacy of a (*Z*,*E*)-di(chlorovinyl)boron chloride was initially postulated to explain the *Z*,*E*-stereochemistry of the product dienes. However, the reaction of boron halides with two equivalents of alkyne has been reported to afford only (*Z*,*Z*)-di(halovinyl)boron halides. Upon reexamining the initial report, we noted that the (*Z*,*Z*)-di(2-chloro-2-phenylvinyl)boron chloride used for product characterization was obtained by distillation and in relatively low yield (the reaction of alkynes with BBr_3 gives quantitative yields). Therefore, it is reasonable to postulate that, at low temperatures, the reaction of two equivalents of phenylacetylene with one equivalent of boron trichloride might produce the monovinylboron dichloride product and that the divinylboron chloride product would be formed only during distillation.

To support the postulation that (*Z*,*Z*)-di(vinylchlorophenyl)boron chloride formed only during distillation, phenylacetylene and boron trichloride (2:1) were refluxed in dichloromethane for 3 h and the reaction mixture then allowed to cool to 0 °C. Addition of *p*-chlorobenzaldehyde to the mixture produced (*Z*,*Z*)-diene **10a** in 78% isolated yield (**Scheme 3-5**). This strongly supports the postulation that the observed (*Z*,*Z*)-diene products arise from divinylboron halide intermediates (the reaction of aldehyde with preformed dialkenylboron bromide also produces (*Z*,*Z*)-dienes).

Reactions of preformed (*Z*,*Z*)-di(chlorovinyl)boron chlorides with various aryl aldehydes were then carried out. The results are summarized in **Table 3-3**. The ^{1}H and ^{13}C NMR spectra of each product revealed only one set of vinyl group resonances due to

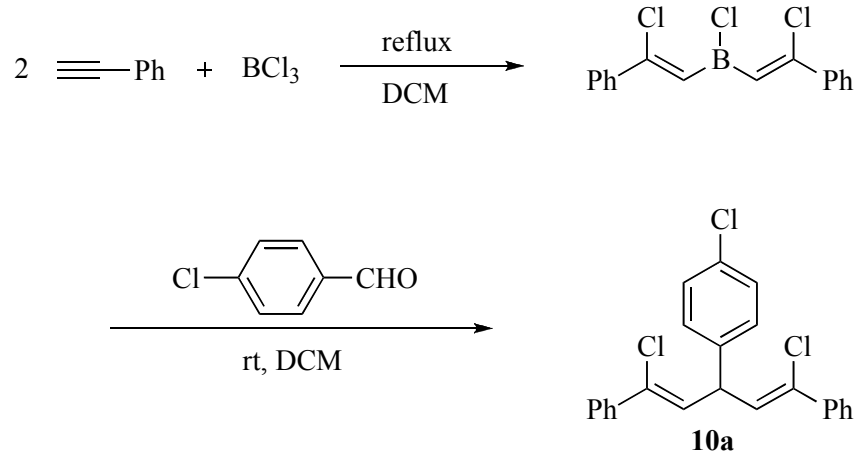
Table 3-3 Reaction of Preformed (*Z*,*Z*)-Dialkenylboron Chloride with Aryl Aldehydes[a]



Entry	Z	R	Product	Yield[b] (%)
1	4-Cl	Ph	**10a**	78
2	4-Br	Ph	**10b**	83
3	4-CN	Ph	**10c**	82
4	2-Me	Ph	**10d**	76
5	H	Ph	**10e**	60
6	4-Cl	4-Me-Ph	**10f**	81
7	4-NO_2	4-Me-Ph	**10g**	82
8	3,4-*di*-OMe	4-Me-Ph	**10h**	34
9	4-Cl	4-Br-Ph	**10i**	75
10	4-CF_3	3-OMe-Ph	**10j**	48
11	4-Cl	3-F-Ph	**10k**	76

[a] Reaction carried out at 0 °C and then maintained at room temperature (see Experimental for details).

[b] Isolated yields based on the starting aldehyde.



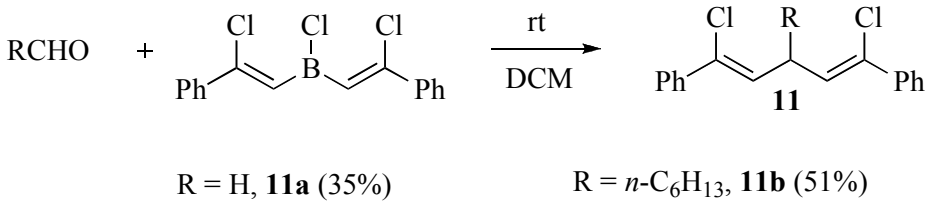
Scheme 3-5 Reaction of (*Z*,*Z*)-dialkenylboron chloride with 4-chlorobenzaldehyde

a single vinyl group, supporting the formation of (*Z*,*Z*)-1,5-dichloro-1,4-pentadienes.

Thus, by changing the reaction sequence, and the temperature at which the reaction is conducted, either (*Z*,*E*)-dichloro-1,4-pentadienes **1** or (*Z*,*Z*)-dichloro-1,4-pentadienes **10** can be prepared from the same starting materials (alkynes, aldehydes and boron trichloride).

We also investigated the reactions of preformed divinylboron halides with aliphatic aldehydes. The reactions afford the desired dialkenylation products **11** in moderate yields (**Scheme 3-6**). The use of preformed divinylboron halide reagents minimizes enolization reactions leading to aldol products.

To summarize, the formation of (*Z*,*Z*)-1,5-dihalo-1,4-pentadienes from mixtures of alkynes with boron tribromide at –40 °C and from mixtures of alkynes refluxed with boron trichloride, *both* involve (*Z*,*Z*)-di(halovinyl)boron halide intermediates.



Scheme 3-6 Dialkenylation of aliphatic aldehydes using preformed divinylboron halides

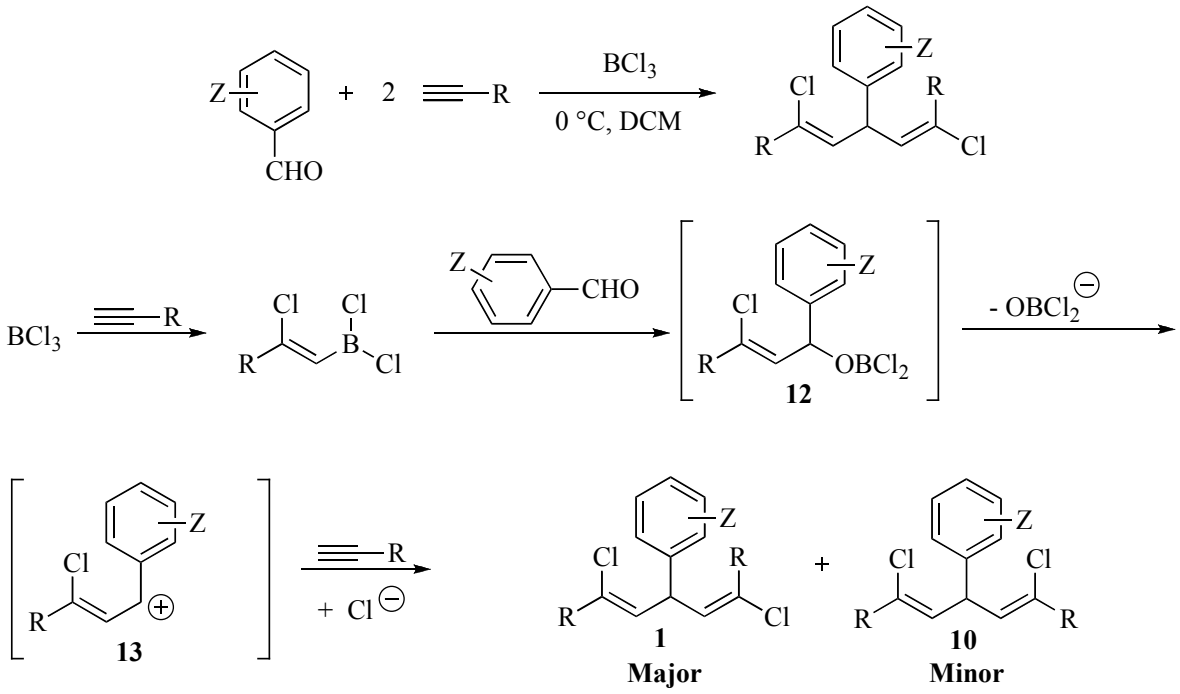
Grignard-like addition of the divinylboron halide intermediate to the aryl aldehyde, followed by migration of the second vinyl group proceeds with retention of olefin configuration, leads to high stereoselectivity in the alkyne-aldehyde coupling.

3.2.4 A Modified Reaction Mechanism for the Boron Trichloride Mediated Alkyne-Aldehyde Coupling Reaction at 0 °C

Since the reaction of boron trichloride with alkynes at 0 °C generates only the (*Z*)-chlorovinylboron dichloride species, a modified reaction mechanism is now proposed for the boron trichloride mediated reaction at 0 °C (**Scheme 3-7**). The Grignard-like addition of (*Z*)-halovinylboron dichloride to the aldehyde forms intermediate **12**. The subsequent cleavage of the carbon-oxygen bond affords carbocation intermediate **13**. Addition of cation **13** to the second alkyne then generates the more thermodynamically stable (*Z*,*E*)-diene product **1** with high stereoselectivity.[85] The isolation of pure (*Z*)-3-chloro-1,3-diarylprop-2-en-1-ol from experiments in which incomplete reactions were quenched with water is thus readily explained.

The modified mechanism (**Scheme 3-7**) involves an unusual carbon-oxygen bond cleavage to generate a cation intermediate **13**.[86]

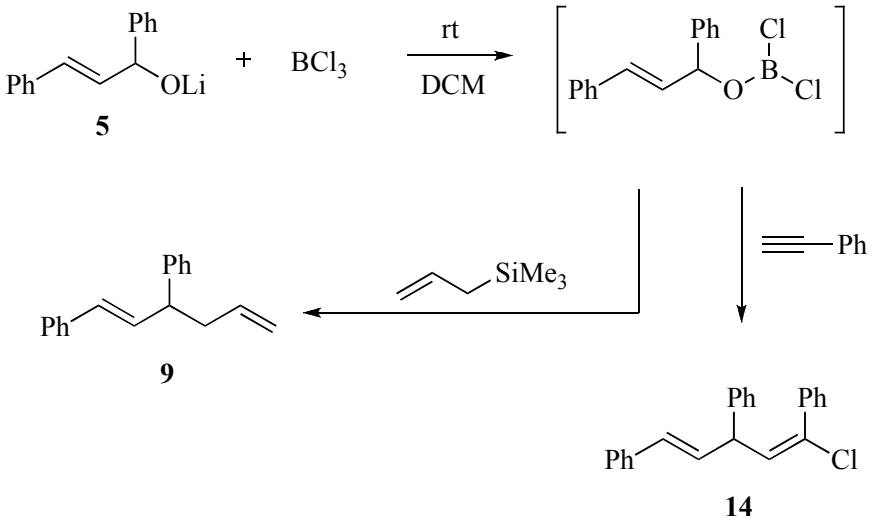
To validate the formation of **13**, the reaction of allyloxide **5** with phenylacetylene in the presence of boron trichloride was examined at room temperature (**Scheme 3-8**). The (*E*,*E*)-1-chloro-1,3,5-triphenyl-1,4-pentadiene (**14**) was isolated in 78% yield, with only 4% of (*Z*,*E*)-1-chloro-1,3,5-triphenyl-1,4-pentadiene formed.



Scheme 3-7 Modified mechanism for boron trichloride mediated coupling of aryl aldehydes and alkynes at 0 °C

The isolation of diene **9** when allyltrimethylsilane is present in the reaction mixture provides further support for the intermediacy of a carbocation. The generation of cations from alkoxides with the assistance of a Lewis acid is unprecedented. This unusual carbon-oxygen bond cleavage reaction led to the discovery of the straightforward allylation of propargyl alcohols.[66,67]

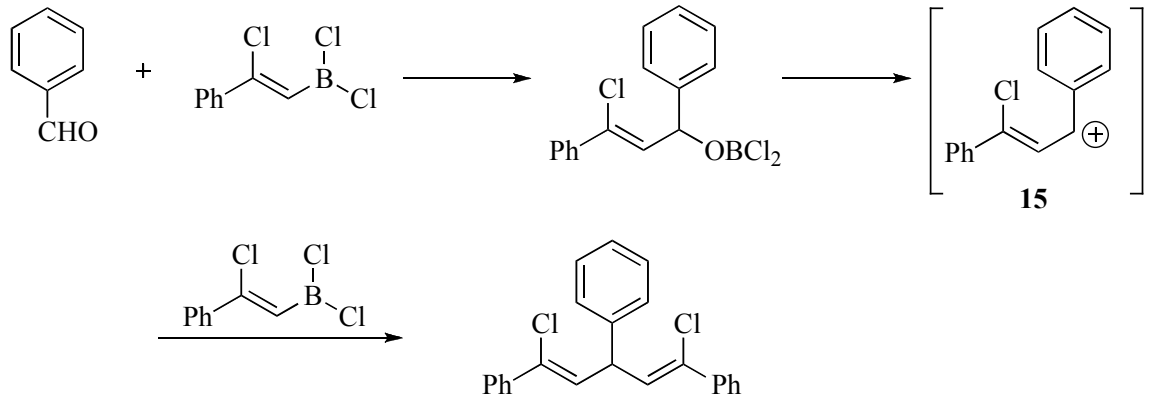
Significantly, the stereochemistry of the 1,4-diene product obtained (**Scheme 3-8**) is opposite to that of the products from the reaction shown in **Scheme 3-3**. Thus, by changing the mode of addition of the reactants, both (*Z*,*E*)-1-halo-1,3,5-triphenyl-1,4-pentadienes **8** and (*E*,*E*)-1-halo-1,3,5-triphenyl-1,4-pentadienes **14** can be prepared from the same starting materials (alkynes, boron trihalide and allyloxides).



Scheme 3-8 Evidence supporting the cleavage of the C—O bond *via* boron trichloride

Since the *syn*-addition of TiX_4[87] and $FeCl_3$[26,88] to terminal alkynes are known, the TiX_4- and $FeCl_3$-mediated alkyne-aldehyde coupling reactions to form (*Z*,*E*)-dienes most likely proceed through the pathway similar to that in **Scheme 3-7**.

The intermediacy of a carbocation intermediate such as **13** (**Scheme 3-7**) also explains the formation of (*Z*,*Z*)-diene products from preformed (*Z*)-2-chloro-2-phenylvinylboron dichloride (**Scheme 3-8**). It is well known that electrophiles can add to vinylboron reagents stereoselectively with retention of configuration of the vinyl group.[89] Thus, an intermediate cation would add to a second equivalent of the monovinylboron dihalide to generate the observed *Z*,*Z*-diene product as illustrated for the formation of (*Z*,*Z*)-1,5-dichloro-1,3,5-triphenyl-1,4-pentadiene (**Scheme 3-9**). In fact, the reaction of benzaldehyde with preformed (*Z*)-2-chloro-phenylvinylboron dichloride (in DCM at room temperature) afforded the (*Z*,*Z*)-1,5-dichloro-1,3,5,-triphenyl-1,4-pentadiene along with the expected allylic alcohol, (*Z*)-3-chloro-1,3-diphenylprop-2-en-1-ol.



Scheme 3-9 Reaction of *Z*-chlorovinylboron dichloride with aldehyde

3.3 Conclusions

The effects of the sequence of reactant addition and temperature on the boron trihalide mediated alkyne-aldehyde coupling reaction are described. It is now possible, by controlling the sequence of reactant addition and the reaction temperature, to generate either (*Z*,*Z*)-1,5-dichloro-1,4-pentadienes or the corresponding (*Z*,*E*)-isomers. The (*Z*,*Z*)-1,5-dibromo-1,4-pentadienes are the primary products under all reaction conditions. It was discovered that, at room temperature, the reaction of boron trichloride with two equivalents of alkynes actually generates only the monovinylboron dichloride products and not the originally reported divinylboron chloride. Several novel carbon—carbon bond-forming reactions were developed, including a direct substitution of a hydroxyl group with a stereodefined alkenyl moiety.

3.4 Experimental

3.4.1 General Methods

All glassware was dried in an oven at 120 °C and flushed with dry argon. All reactions were carried out under argon atmosphere. CH_2Cl_2 was distilled over CaH_2. All aldehydes and alkynes were purchased from commercial sources and used as received. Boron trichloride (1 *M* hexane solution) diluted to a 1 *M* CH_2Cl_2 solution. Products were purified by flash chromatography using silica gel (60 D, 230-400 mesh). ^{1}H NMR and ^{13}C NMR were recorded in $CDCl_3$ at 250 MHz or 300 MHz with chemical shifts reported relative to TMS.

3.4.2 Syntheses and Characterizations of (Z,E)-1,5-Dichloro-1,3,5-triaryl-1,4-Pentadienes (1a-1j)

Benzaldehyde (0.42g, 4.0 mmol) and phenylacetylene (0.82 g, 8.0 mmol) were placed in a dry, argon-flushed, 50 mL round-bottomed flask equipped with a magnetic stirring bar and dissolved in 20 mL dry CH_2Cl_2. The solution was cooled to 0 °C in an ice bath, and boron trichloride (4.4 mmol, 4.4 mL of a 1.0 *M* CH_2Cl_2 solution) was added via syringe. The solution was allowed to stir for 2 hrs at 0 °C and then for 4 hrs at room temperature. The reaction solution gradually turned dark purple. The resulting mixture was hydrolyzed with water (20 mL) and extracted with hexanes (3 x 30 mL). The organic layer was separated and dried over anhydrous $MgSO_4$. Product **1a** (0.95 g, 65% yield) was isolated by flash column chromatography.

(*Z*,*E*)- 1,5-Dichloro-1,3,5-triphenyl-1,4-pentadiene (1a): ^{1}H NMR (250 MHz): δ 7.57-7.21 (m, 15H), 6.26 (d, 1H, *J* = 9.2 Hz), 6.19 (d, 1H, *J* = 10.6 Hz), 4.88 (dd, 1H, *J* = 10.6 and 9.2 Hz). ^{13}C NMR: δ 141.5, 137.6, 136.7, 133.7, 129.0, 128.9, 128.8, 128.3, 127.6, 127.2, 126.9, 126.5, 45.6. Anal. Calcd for $C_{23}H_{18}Cl_2$: C, 75.62; H, 4.97. Found: C, 75.48; H, 4.88.

(*Z*,*E*)-1,5-Dichloro-3-(4-fluorophenyl)-1,5-diphenyl-1,4-pentadiene (1b): ^{1}H NMR (250 MHz): δ 7.58- 6.99 (m, 14H), 6.22 (d, 1H, *J* = 9.1 Hz), 6.15 (d, 1H, *J* = 10.4 Hz), 4.85 (dd, 1H, *J* = 10.4 and 9.1 Hz). ^{13}C NMR: δ 163.7, 159.8, 137.4, 137.1, 136.6, 133.9, 133.3, 129.0, 128.9, 128.8, 128.7, 128.4, 127.3, 126.6, 115.8, 115.5, 44.9. Anal. Calcd for $C_{23}H_{17}Cl_2F$: C, 72.07; H, 4.47. Found: C, 72.32; H, 4.52.

(*Z*,*E*)-1,5-Dichloro-3-(4-bromophenyl)-1,5-diphenyl-1,4-pentadiene (1c): ^{1}H NMR (250 MHz): δ 7.56- 7.09 (m, 14H), 6.21 (d, 1H, *J* = 9.1 Hz), 6.13 (d, 1H, *J* = 10.5 Hz), 4.81 (dd, 1H, *J* = 10.5 and 9.1 Hz). ^{13}C NMR: 140.4, 137.3, 136.5, 134.1, 133.5, 131.9, 129.1, 129.0, 128.7, 128.4, 126.9, 126.5, 120.8, 45.0. Anal. Calcd for $C_{23}H_{17}BrCl_2$: C, 62.19; H, 3.86. Found: C, 62.35; H, 3.84.

(*Z*,*E*)-1,5-Dichloro-1,5-diphenyl-3-(4-methylphenyl)-1,4-pentadiene (1d): ^{1}H NMR (250 MHz): δ 7.58-7.15 (m, 14H), 6.26 (d, 1H, *J* = 9.2 Hz), 6.18 (d, 1H, *J* = 10.6 Hz), 4.84 (dd, 1H, *J* = 10.6 and 9.2 Hz), 2.33 (s, 3H). ^{13}C NMR: δ 138.5, 137.6, 136.7, 136.6, 133.5, 132.8, 129.5, 129.2, 128.9, 128.8, 128.3, 127.8, 127.1, 126.5, 45.2, 21.0. Anal. Calcd for $C_{24}H_{20}Cl_2$: C, 75.99; H, 5.31. Found: C, 76.10; H, 5.40.

(*Z*,*E*)-1,5-Dichloro-3-(4-cyanophenyl)-1,5-diphenyl-1,4-pentadiene (1e): ^{1}H NMR (250 MHz): δ 7.62-7.23 (m, 14H), 6.23 (d, 1H, *J* = 9.0 Hz), 6.15 (d, 1H, *J* = 10.4 Hz), 4.91 (dd, 1H, *J* = 10.4 and 9.0 Hz). ^{13}C NMR: δ 146.8, 137.0, 136.3, 134.9, 134.3, 132.6, 129.2, 128.5, 128.4, 128.0, 127.5, 126.5, 125.9, 118.6, 110.8, 45.6. Anal. Calcd for $C_{24}H_{17}Cl_2N$: C, 73.85; H, 4.39; N, 3.59. Found: C, 73.63; H, 4.42; N, 3.72.

(*Z*,*E*)-1,5-Dichloro-3-phenyl-1,5-di(4-methylphenyl)-1,4-pentadiene (1f): ^{1}H NMR (250 MHz): δ 7.48-7.12 (m, 13H), 6.22 (d, 1H, *J* = 9.2 Hz), 6.14 (d, 1H, *J* = 10.6 Hz), 4.87 (dd, 1H, *J* = 10.6 and 9.2 Hz), 2.36 (s, 3H), 2.34(s, 3H). ^{13}C NMR: δ 141.7, 138.8, 134.9, 133.7, 133.1, 129.0, 128.8, 128.7, 127.3, 126.8, 126.5, 45.6, 21.3, 21.1. Anal. Calcd for $C_{25}H_{22}Cl_2$: C, 76.34; H, 5.64. Found: C, 76.16; H, 5.71.

(*Z*,*E*)-1,5-Dichloro-3-(4-fluorophenyl)-1,5-di(4-methylphenyl)-1,4-pentadiene (1g): ^{1}H NMR (250 MHz): δ 7.46 (d, 2H, *J* = 8.1 Hz), 7.31 (d, 2H, *J* = 8.1 Hz), 7.22-6.95 (m, 8H), 6.19 (d, 1H, *J* = 9.0 Hz), 6.10 (d, 1H, *J* = 10.5 Hz), 4.84 (dd, 1H, *J* = 10.5 and 9.0 Hz), 2.36 (s, 3H), 2.35 (s, 3H). ^{13}C NMR: δ 163.7, 159.8, 139.0, 137.4, 134.7, 133.9, 133.7, 133.3, 129.0, 128.8, 128.6, 126.5, 126.4, 115.7, 44.9, 21.3, 21.1. Anal. Calcd for $C_{25}H_{21}Cl_2F$: C, 73.00; H, 5.15. Found: C, 72.83; H, 5.29.

(*Z*,*E*)-1,5-Dichloro-1,3,5-tri(4-methylphenyl)-1,4-pentadiene (1h): ^{1}H NMR (250 MHz): δ 7.45(d, 2H, *J* = 8.2 Hz), 7.33 (d, 2H, *J* = 8.2 Hz), 7.18-7.11 (m, 8H), 6.21 (d, 1H, *J* = 9.1 Hz), 6.13 (d, 1H, *J* =10.5 Hz), 4.84 (dd, 1H, *J* = 10.5 and 9.1 Hz), 2.35- 2.31 (overlap, 9H). ^{13}C NMR: δ 138.8, 138.7, 136.4, 134.9, 133.9, 133.5, 132.8, 129.5, 128.9, 128.7, 127.1, 127.0, 126.4, 45.2, 21.3, 21.0. Anal. Calcd for $C_{26}H_{24}Cl_2$: C, 76.66; H, 5.94. Found: C, 76.62; H, 6.08.

(*Z*,*E*)-1,5-Dichloro-1,3,5-tri(4-fluorophenyl)-1,4-pentadiene (1i): ^{1}H NMR (250 MHz): δ 7.55-7.00 (m, 12H), 6.15 (m, 2H), 4.78 (m, 1H). ^{13}C NMR: 165.0, 164.9, 163.8, 161.1, 160.9, 159.9, 138.9, 133.5, 132.9, 132.7, 132.3, 130.7, 130.6, 128.9, 128.7, 128.5, 128.3, 127.2, 115.9, 115.6, 115.5, 115.3, 115.2, 44.9. Anal. Calcd for $C_{23}H_{15}Cl_2F_3$: C, 65.89; H, 3.61. Found: C, 66.13; H, 3.74.

(*Z*,*E*)-1,5-Dichloro-1,5-di(4-fluorophenyl)-3-(4-methylphenyl)-1,4-pentadiene (1j): ^{1}H NMR (250 MHz): δ 7.55- 6.99 (m, 12H), 6.17 (m, 2H), 4.76 (m, 1H), 2.33 (s, 3H). ^{13}C NMR: δ 165.0, 164.8, 161.0, 160.8, 138.2, 136.8, 133.8, 132.8, 132.4, 131.8, 130.8, 130.7, 129.6, 129.3, 128.5, 128.3, 127.7, 127.0, 115.5, 115.4, 115.2, 115.1, 45.3, 21.0. Anal. Calcd for $C_{24}H_{18}Cl_2F_2$: C, 69.41; H, 4.37. Found: C, 69.64; H, 4.49.

3.4.3 Syntheses and Characterizations of (Z,Z)-1,5-Dibromo-1,3,5-triaryl-1,4-Pentadienes (2a-2j)

4-Fluorobenzaldehyde (0.52 g, 4.2 mmol) and phenylacetylene (0.86 g, 8.4 mmol) were placed in a dry, argon-flushed, 50 mL round-bottomed flask equipped with a stirring bar and dissolved in 20 mL dry CH_2Cl_2. The solution was cooled to -40 °C, and boron tribromide (4.5 mmol, 4.5mL of a 1.0 *M* CH_2Cl_2 solution) was added via syringe. The reaction solution turned purple immediately. The solution was allowed to stir at -40 °C for 4 hrs. The resulting mixture was hydrolyzed with water (20 mL) and extracted with hexanes (3 x 25 mL). The organic layer was separated and dried over anhydrous $MgSO_4$. Product **2a** (1.80 g, 91% yield) was isolated by flash column chromatography.

(*Z*,*Z*)-1,5-Dibromo-1,5-diphenyl-3-(4-fluorophenyl)-1,4-pentadiene (2a): ^{1}H NMR (250 MHz): δ 7.58- 7.00 (m, 14H), 6.40 (d, 2H, *J* = 8.9 Hz), 5.31 (t, 1H, *J* = 8.9 Hz). ^{13}C NMR: δ 163.8, 159.8, 139.4, 136.5, 130.7, 129.0, 128.9, 128.3, 127.7, 127.3, 115.8, 115.5, 50.7. Anal. Calcd for $C_{23}H_{17}Br_2F$: C, 58.50; H, 3.63. Found: C, 58.41; H, 3.73.

(*Z*,*Z*)-1,5-Dibromo-1,5-diphenyl-3-(4-chlorophenyl)-1,4-pentadiene (2b): ^{1}H NMR (250 MHz): δ 7.57-7.23 (m, 14H), 6.38 (d, 2H, *J* = 8.8 Hz), 5.30 (t, 1H, *J* = 8.8 Hz). ^{13}C NMR: δ 139.3, 132.7, 130.4, 128.9, 128.8, 128.3, 127.8, 127.7, 127.6, 50.8. Anal. Calcd for $C_{23}H_{17}Br_2Cl$: C, 56.53; H, 3.51. Found: C, 56.18; H, 3.50.

(*Z*,*Z*)-1,5-Dibromo-1,5-diphenyl-3-(4-methylphenyl)-1,4-pentadiene (2c): ^{1}H NMR (250 MHz): δ 7.58-7.14 (m, 14H), 6.43 (d, 2H, *J* = 8.9 Hz), 5.30 (t, 1H, *J* = 8.9 Hz), 2.33 (s, 3H). ^{13}C NMR: δ 139.6, 137.8, 136.5, 131.2, 129.5, 128.7, 128.2, 127.7, 127.3, 126.8, 51.0, 21.0. Anal. Calcd for $C_{24}H_{20}Br_2$: C, 61.56; H, 4.31. Found: C, 61.83; H, 4.35.

(*Z*,*Z*)-1,5-Dibromo-1,5-diphenyl-3-(4-methylphenyl)-1,4-pentadiene (2d): ^{1}H NMR (250 MHz): δ 7.55-7.14 (m, 14H), 6.44 (d, 2H, *J* = 8.7 Hz), 5.34 (t, 1H, *J* = 8.7 Hz), 2.52 (s, 3H). ^{13}C NMR: δ 140.2, 139.4, 136.5, 131.5, 130.8, 128.7, 128.2, 127.7, 127.0, 126.8, 126.5, 126.4, 48.8, 20.2. Anal. Calcd for $C_{24}H_{20}Br_2$: C, 61.56; H, 4.31. Found: C, 61.27; H, 4.42.

(*Z*,*Z*)-1,5-Dibromo-1,5-diphenyl-3-(4-nitrophenyl)-1,4-pentadiene (2e): ^{1}H NMR (250 MHz): δ 8.18- 7.31 (m, 14H), 6.44 (d, 2H, J = 8.8 Hz), 5.42 (t, 1H, J = 8.8 Hz). ^{13}C NMR: δ 148.2, 146.8, 138.9, 129.3, 129.1, 128.6, 128.4, 127.7, 124.0, 51.3. Anal. Calcd for $C_{23}H_{17}Br_2NO_2$: C, 55.34; H, 3.43; N, 2.81. Found: C, 55.60; H, 3.53; N, 2.87.

(*Z*,*Z*)-1,5-Dibromo-1,5-di(4-methylphenyl)-3-(4-fluorophenyl)-1,4-pentadiene (2f): ^{1}H NMR (250 MHz): δ 7.46- 6.96 (m, 12H), 6.35 (d, 2H, *J* = 8.9 Hz), 5.30 (t, 1H, *J* = 8.9 Hz), 2.31 (s, 6H). ^{13}C NMR: δ 163.6, 159.7, 138.8, 136.5, 129.8, 129.5, 129.3, 128.9, 128.8, 128.2, 127.5, 127.3, 127.1, 115.7, 115.3, 50.6, 21.1. Anal. Calcd for $C_{25}H_{21}Br_2F$: C, 60.02; H, 4.23. Found: C, 60.33; H, 4.52.

(*Z*,*Z*)-1,5-Dibromo-1,5-di(4-methylphenyl)-3-(4-bromophenyl)-1,4-pentadiene (2g): ^{1}H NMR (250 MHz): δ 7.45-7.06 (m, 12H), 6.33 (d, 2H, *J* = 8.9 Hz), 5.26 (t, 1H, *J* = 8.9 Hz), 2.32 (s, 6H). ^{13}C NMR: δ 139.9, 138.9, 136.5, 131.8, 129.5, 128.9, 127.5, 120.7, 50.8, 21.1. Anal. Calcd for $C_{25}H_{21}Br_3$: C, 53.51; H, 3.77. Found: C, 53.21; H, 3.99.

(*Z*,*Z*)-1,5-Dibromo-1,5-di(4-chlorophenyl)-3-(4-fluorophenyl)-1,4-pentadiene (2h): ^{1}H NMR (250 MHz): δ 7.51-7.00 (m, 12H), 6.39 (d, 2H, *J* = 8.9 Hz), 5.26 (t, 1H, *J* = 8.9 Hz). ^{13}C NMR: δ 163.8, 159.9, 137.7, 136.1, 134.8, 131.0, 128.9, 128.8, 128.4, 126.1, 115.9, 115.6, 50.7. Anal. Calcd for $C_23H_{15}Br_2Cl_2F$: C, 51.05; H, 2.79. Found: C, 51.37; H, 2.65.

(*Z*,*Z*)-1,5-Dibromo-1,5-di(4-chlorophenyl)-3-(4-bromophenyl)-1,4-pentadiene (2i): ^{1}H NMR (250 MHz): δ 7.49-7.20 (m, 12H), 6.37 (d, 2H, *J* = 8.9 Hz), 5.23 (t, 1H, *J* = 8.9 Hz). ^{13}C NMR: δ 139.4, 137.6, 134.8, 131.9, 130.5, 129.1, 128.9, 128.4, 126.4, 121.0, 50.9. Anal. Calcd for $C_{23}H_{15}Br_3Cl_2$: C, 45.89; H, 2.51. Found: C, 46.11; H, 2.66.

(*Z*,*Z*)-1,5-Dibromo-1,5-di(4-chlorophenyl)-3-(4-methylphenyl)-1,4-pentadiene (2j): ^{1}H NMR (250 MHz): δ 7.46-7.16 (m, 12H), 6.43 (d, 2H, *J* = 8.7 Hz), 5.31 (t, 1H, *J* = 8.7 Hz), 2.51 (s, 3H). ^{13}C NMR: δ 139.7, 137.8, 136.4, 134.6, 131.8, 130.9, 128.9, 128.3, 126.9, 126.5, 125.3, 48.8, 20.2. Anal. Calcd for $C_{24}H_{18}Br_2Cl_2$: C, 53.67; H, 3.38. Found: C, 53.92; H, 3.45.

3.4.4 The Coupling of Alkoxides with Vinylboron Dihalides to afford Dienes 8 (Evidence Supporting the Migration of Halovinyl Group from Boron to Carbon Center)

Boron trihalide (1.5 mmol, 1.5mL of a 1.0 *M* CH_2Cl_2 solution), phenylacetylene (0.15g, 1.5 mmol) and dry dichloromethane (8 mL) were combined in a 50 mL flask and stirred for 1 hour under a nitrogen atmosphere. Alkoxide **5** (generated in situ by treating 315 mg, 1.5 mmol of (*Z*)-1,3-diphenylprop-2-en-1-ol with 1 mL of 1.6 *M* *n*-BuLi) was

added at 0 °C and allowed to stir at room temperature overnight. Water (20 mL) was added and the reaction mixture was extracted with ethyl acetate (3 x 20 mL) and dried over anhydrous $MgSO_4$. The product was isolated by flash column chromatography using hexane as an eluent.

((1*Z*,4*E*)-1-Chloropenta-1,4-diene-1,3,5-triyl)tribenzene (**8a)** (yield: 83%)**:** ^{1}H NMR (250 MHz): δ 7.60-7.57 (m, 2H), 7.37-7.15 (m, 13H), 6.58-6.34 (m, 3H), 4.94 (dd, 1H, *J*= 9.0 and 8.9 Hz). ^{13}C NMR: δ 142.1, 137.9, 137.1, 133.4, 130.9, 130.3, 128.7, 128.5, 128.3, 127.8, 127.4, 126.9, 126.6, 126.3, 48.5. Anal. Calcd for $C_{23}H_{19}Cl$: C, 83.50; H, 5.79. Found: C, 83.57; H, 5.65.

((1*Z*,4*E*)-1-Bromopenta-1,4-diene-1,3,5-triyl)tribenzene (**8b)** (yield: 71%)**:** ^{1}H NMR (250 MHz): δ 7.59–7.54 (m, 2H), 7.41–7.21 (m, 13H), 6.55–6.37 (m, 3H), 4.90 (dd, 1H, *J*= 8.94 and 8.88 Hz). ^{13}C NMR: δ 141.9, 139.7, 137.1, 132.1, 131.0, 130.0,128.7, 128.5, 128.3, 127.8, 127.4, 126.8, 126.3, 126.1, 51.3. Anal. Calcd for $C_{23}H_{19}Br$: C, 73.61; H, 5.10. Found: C, 73.57; H, 5.22.

3.4.5 The Competition Reaction between Vinylboron Dihalides and Allyltrimethylsilane (Evidence Supporting a Cationic Mechanism)

Boron trihalide (1.5 mmol, 1.5mL of a 1.0 *M* CH_2Cl_2 solution), phenylacetylene (153 mg, 1.5 mmol) and dry dichloromethane (8 mL) were combined in a 50 mL flask and stirred for 1 hour under a nitrogen atmosphere. The reaction mixture was cooled to 0 °C, allyltrimethylsilane (171 mg, 1.5 mmol) and alkoxide **5** (generated in situ by treating 315 mg, 1.5 mmol of (*Z*)-1,3-diphenylprop-2-en-1-ol with 1 mL of 1.6 *M n*-

BuLi) were added. The resulted reaction mixture was stirred at room temperature overnight. Water (20 mL) was added and the reaction mixture was extracted with ethyl acetate (3 x 20 mL) and dried over anhydrous $MgSO_4$. The product **8a** (125 mg, 25% yield) and **9** (218 mg, 62% yield) were isolated by flash column chromatography using hexane as an eluent. Compound **9** is a known compound.[90]

3.4.6 Syntheses and Characterizations of (Z,Z)-1,5-Dichloro-1,4-Pentadienes (10a-k and 11a,b)

Phenylacetylene (306 mg, 3.0 mmol) and boron trichloride (1.5 mm0l, 1.5mL of a 1.0 *M* CH_2Cl_2 solution) were placed in a dry, argon-flushed, 50 mL round-bottomed flask equipped with a magnetic stirring bar and dissolved in 20 mL dry CH_2Cl_2. The solution was refluxed for 3 hrs and then cooled down to 0 °C using an ice-bath. To this solution, 4-chlorobenzaldehyde (210 mg, 1.5 mmol) was added. The solution was allowed to stir for 2 hrs at 0 °C and then 6 hrs at room temperature. The resulting mixture was hydrolyzed with water (20 mL) and extracted with hexanes (3 x 20 mL). The organic layer was separated and dried over anhydrous $MgSO_4$. Product **10a** (471 mg, 78% yield) was isolated by flash column chromatography.

(*Z*,*Z*)-1,5-Dichloro-1,5-diphenyl-3-(4-chlorophenyl)-1,4-pentadiene (10a): ^{1}H NMR (300 MHz): δ 7.62-7.29 (m, 14H), 6.29 (dd, 2H, *J* = 9.00 and 0.9 Hz), 5.42 (t, 1H, *J* = 9.00 Hz). ^{13}C NMR: δ 139.8, 137.5, 134.8, 132.6, 128.9, 128.8, 128.4, 126.8, 126.6, 45.2. IR (Neat, max/cm^{-1}): 3032, 1596, 1491, 1445, 1093, 827, 759, 693. Anal. Calcd for $C_{23}H_{17}Cl_3$: C, 69.11; H, 4.29. Found: C, 69.27; H, 4.31.

(*Z*,*Z*)-1,5-Dichloro-1,5-diphenyl-3-(4-bromophenyl)-1,4-pentadiene (10b): ^{1}H NMR (250 MHz): δ 7.78-7.23 (m, 14H), 6.30 (d, 2H, *J* = 8.97 Hz), 5.39 (t, 1H, *J* = 8.97 Hz). ^{13}C NMR: δ 140.3, 137.6, 134.8, 131.8, 129.1, 126.7, 126.3, 126.7, 126.6, 120.7, 45.3. Anal.Calcd for $C_{23}H_{17}BrCl_2$: C: 62.19; H: 3.86. Found: C: 62.16; H: 3.99.

(*Z*,*Z*)-1,5-Dichloro-1,5-diphenyl-3-(4-cyanophenyl)-1,4-pentadiene (10c): ^{1}H NMR (300 MHz): δ 7.65-7.25 (m, 14H), 6.31 (dd, 2H, *J* = 9.0 and 1.5 Hz), 5.49 (t, 1H, *J* = 9.0 Hz). ^{13}C NMR: δ 146.8, 137.8, 137.6, 137.3, 135.7, 132.6, 129.1, 128.4, 128.3, 126.6, 125.8, 118.7, 110.8, 45.8. Anal. Calcd for $C_{24}H_{17}Cl_2N$: C, 73.85; H, 4.39; N, 3.59. Found: C, 73.55; H, 4.52; N, 3.56.

(*Z*,*Z*)-1,5-Dichloro-1,5-diphenyl-3-(2-methylphenyl)-1,4-pentadiene (10d): ^{1}H NMR (300 MHz): δ 7.59-7.18 (m, 14H), 6.35 (m, 2H), 5.51 (m, 1H), 2.52 (s, 3H). ^{13}C NMR: δ 140.5, 137.7, 136.4, 133.7, 130.8, 128.7, 128.3, 128.0, 127.8, 126.9, 126.8, 126.5, 126.4, 43.1, 19.9. HR-MS Calcd for $C_{24}H_{20}Cl_2$: 378.0942. Found: 378.0944.

(*Z*,*Z*)-1,5-Dichloro-1,3,5-triphenyl-1,4-pentadiene (10e): ^{1}H NMR (300 MHz): δ 7.63- 7.24 (m, 15H), 6.34 (d, 2H, *J* = 9.0 Hz), 5.47 (t, 1H, *J* = 9.0 Hz). ^{13}C NMR: δ 141.3, 137.7, 134.3, 128.8, 128.7, 128.3, 127.4, 127.3, 126.9, 126.6, 45.7. Anal. Calcd for $C_{23}H_{18}Cl_2$: C: 75.62; H: 4.97. Found: C: 75.33; H: 4.80.

(*Z*,*Z*)-1,5-Dichloro-1,5-di(4-methylphenyl)-3-(4-chlorophenyl)-1,4-pentadiene (10f): ^{1}H NMR (300 MHz): δ 7.50-7.12 (m, 12H), 6.24 (d, 2H, *J* = 9.0 Hz), 5.39 (t, 1H, *J* = 9.0 Hz), 2.33 (s, 6 H). ^{13}C NMR: δ 140.0, 138.9, 134.7, 132.5, 129.0, 128.8, 128.7, 128.6, 126.5, 126.0, 45.1, 21.1. HR-MS Calcd for $C_{25}H_{21}Cl_3$: 426.0709. Found: 426.0703.

(*Z*,*Z*)-1,5-Dichloro-1,5-di(4-methylphenyl)-3-(4-nitrophenyl)-1,4-pentadiene (10g): ^{1}H NMR (300 MHz): δ 8.10-7.06 (m, 12H), 6.19 (d, 2H, *J* = 9.0 Hz), 5.42 (t, 1H, *J* = 9.0 Hz), 2.26 (s, 6H). ^{13}C NMR: 149.1, 146.7, 139.2, 135.7, 134.4, 129.1, 128.3, 126.5, 124.9, 124.0, 53.4, 45.6, 21.1. HR-MS Calcd for $C_{25}H_{21}Cl_2NO_2$: 437.0949. Found: 437.0957.

(*Z*,*Z*)-1,5-Dichloro-1,5-di(4-methylphenyl)-3-(3,4-dimethoxyphenyl)-1,4-pentadiene (10h): ^{1}H NMR (300 MHz): δ 7.55-6.82 (m, 11H), 6.27 (dd, 2H, *J* = 9.0 and 1.5 Hz), 5.37 (t, 1H, *J* = 9.0 Hz), 3.87 (s, 3H), 3.86 (s, 3H), 2.35 (s, 6H). ^{13}C NMR: δ 149.1, 147.9, 138.8, 138.2, 138.1, 138.0, 137.9, 137.7, 135.0, 134.1, 129.0, 126.7, 126.5, 119.1, 111.3, 110.8, 55.9, 45.3, 21.1. Anal. Calcd for $C_{27}H_{26}Cl_2O_2$: C: 71.52; H: 5.78. Found: C: 70.61; H: 5.80. HR-MS Calcd for $C_{27}H_{26}Cl_2O_2$: 452.1310. Found: 452.1318.

(*Z*,*Z*)-1,5-Dichloro-1,5-di(4-bromophenyl)-3-(4-chlorophenyl)-1,4-pentadiene (10i): ^{1}H NMR (300 MHz): δ 7.44-7.24 (m, 12H), 6.28 (d, 2H, *J* = 9.0 Hz), 5.36 (t, 1H, *J* = 9.0 Hz). ^{13}C NMR: δ 139.2, 136.3, 133.8, 132.8, 131.4, 129.0, 128.7, 128.0, 127.0, 123.1, 45.2. IR (Neat, max/cm^{-1}): 3029, 1586, 1486, 1395, 1093, 1073, 1010, 818. Anal. Calcd for $C_{23}H_{15}Cl_3Br_2$: C: 49.55; H: 2.71. Found: C: 49.23; H: 2.67.

(*Z*,*Z*)-1,5-Dichloro-1,5-di(3-methoxyphenyl)-3-(4-trifluoromethylphenyl)-1,4-pentadiene (10j): ^{1}H NMR (300 MHz): δ 7.61-6.87 (m, 12H), 6.33 (dd, 2H, *J* = 9.0 and 0.6 Hz), 5.50 (t, 1H, *J* = 9.0 Hz), 3.82 (s, 6H). ^{13}C NMR: δ 159.5, 145.3, 138.9, 135.0, 129.4, 127.8, 126.6, 125.8, 125.7, 119.0, 114.5, 112.5, 55.3, 45.6. HR-MS Calcd for $C_{26}H_{21}Cl_2F_3O_2$: 492.0871. Found: 492.0879.

(*Z*,*Z*)-1,5-Dichloro-1,5-di(3-fluorophenyl)-3-(4-chlorophenyl)-1,4-pentadiene (10k): ^{1}H NMR (300 MHz): δ 7.41-7.00 (m, 12H), 6.33 (d, 2H, *J* = 9.0 Hz), 5.39 (t, 1H, *J* = 9.0 Hz). ^{13}C NMR: δ 164.2, 161.0, 139.6, 139.2, 138.2, 138.0, 137.9, 133.6, 133.5, 132.9, 129.9, 129.8, 129.0, 128.7, 127.6, 122.2, 122.1, 116.0, 115.7, 113.9, 113.6, 45.2. Anal. Calcd for $C_{23}H_{15}Cl_2F_2$: C, 63.40; H, 3.47. Found: C, 63.51; H, 3.29.

(*Z*,*Z*)-1,5-Dichloro-1,5-diphenyl-1,4-pentadiene (11a): ^{1}H NMR (250 MHz): δ 7.61-7.25 (m, 10H), 6.21 (t, 2H, *J* = 7.2 Hz), 3.50 (t, 2H, *J* = 7.2 Hz). ^{13}C NMR: δ 137.9, 134.4, 128.6, 128.3, 126.5, 123.8, 30.2. HR-MS Calcd for $C_{17}H_{14}Cl_2$: 288.0473. Found: 288.0477.

(*Z*,*Z*)-1,5-Dichloro-1,5-diphenyl-3-hexyl-1,4-pentadiene (11b): ^{1}H NMR (300 MHz): δ 7.60-7.29 (m, 10H), 6.01 (dd, 2H, *J*=9.0 and 1.2 Hz), 4.13 (m, 1H), 1.63-1.58 (m, 2H), 1.34-1.26 (m, 8H), 0.88 (t, 3H, *J*=6.2 Hz). ^{13}C NMR: δ 138.1, 133.3, 128.8, 128.5, 128.2, 126.5, 40.9, 34.9, 31.8, 29.3, 26.9, 22.6, 14.1. HR-MS Calcd for $C_{23}H_{26}Cl_2$: 372.1412. Found: 372.1420.

3.4.7 The BCl_3-mediated Coupling Reaction of Allyloxide 5 with Phenylacetylene (Evidence Supporting the C-O Bond Cleavage in Alkoxide).

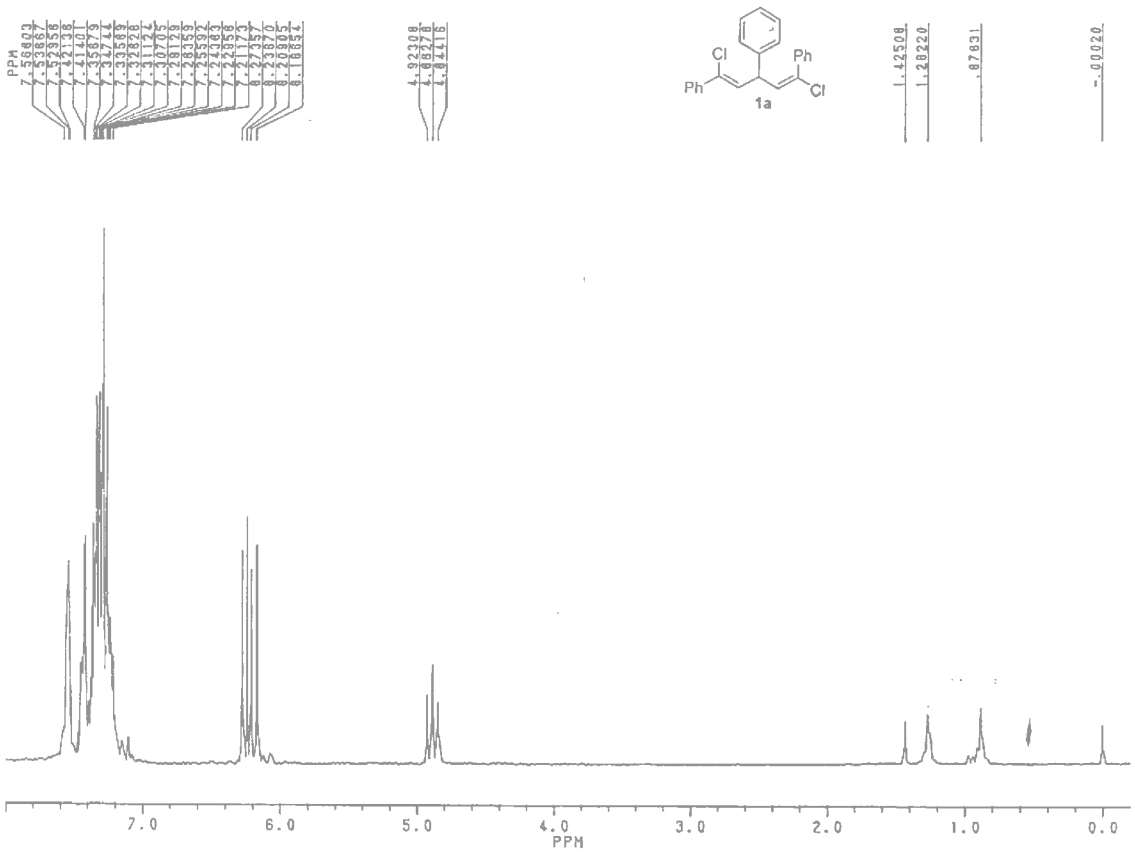
Alkoxide **5** (generated in situ by treating 315 mg, 1.5 mmol of (*Z*)-1,3-diphenylprop-2-en-1-ol with 1 mL of 1.6 *M* *n*-BuLi), phenylacetylene (153 mg, 1.5 mmol) and dry dichloromethane (8 mL) were combined in a 50 mL flask under a nitrogen atmosphere at 0 °C. Boron trihalide (1.5 mmol, 1.5mL of a 1.0 *M* CH_2Cl_2 solution) was

added and stirred at room temperature overnight. Water (20 mL) was added and the reaction mixture was extracted with ethyl acetate (3 x 20 mL) and dried over anhydrous $MgSO_4$. Product **14** (275 mg, 78% yield) was isolated by flash column chromatography using hexane as an eluent.

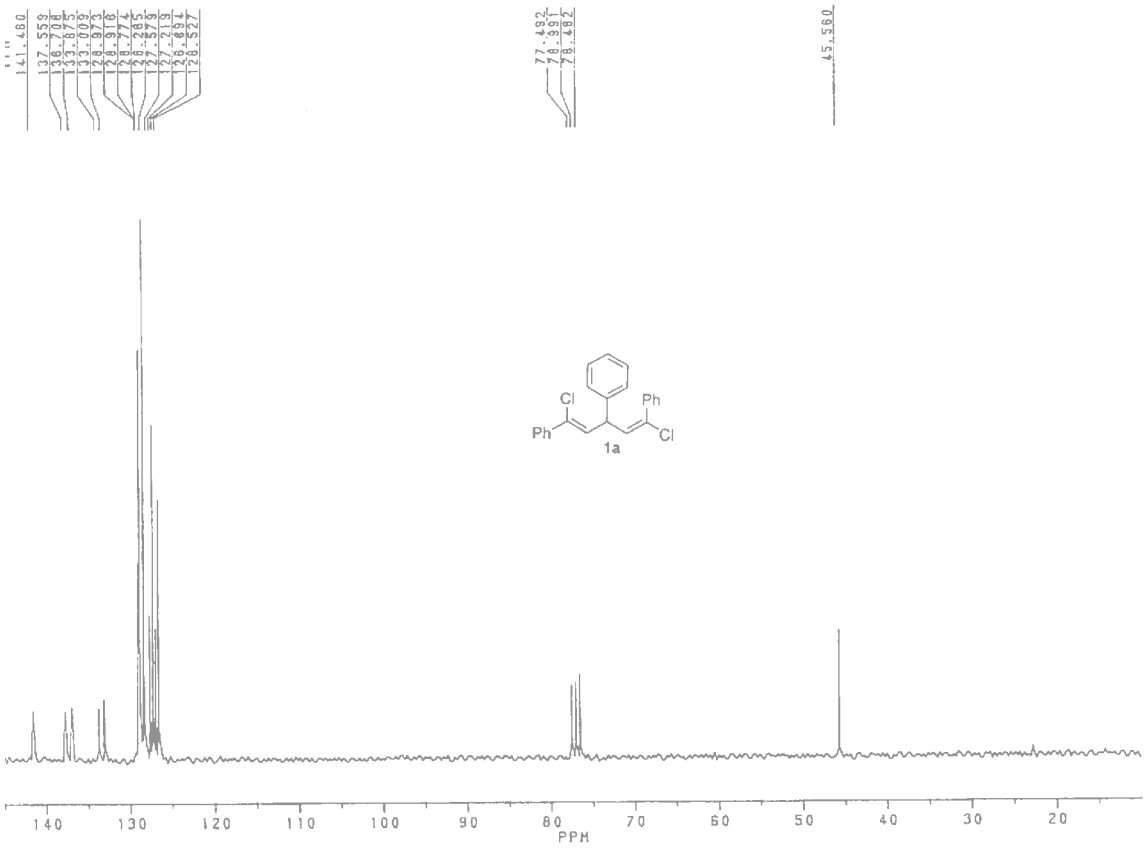
(*E*,*E*)-1-Chloro-1,3,5-triphenyl-1,4-pentadiene (14): ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.44-7.17 (m, 15H), 6.48-6.20 (m, 3H), 4.32 (dd, 1H, J = 10.6 and 10.5 Hz). ^{13}C NMR ($CDCl_3$): δ 142.3, 136.9, 131.6, 131.2, 130.8, 130.4, 128.9, 128.8, 128.6, 128.4, 127.6, 127.5, 126.8, 126.3, 48.4. Anal. Calcd for $C_{23}H_{19}Cl$: C, 83.50; H, 5.79. Found: C, 83.44; H, 5.82.

3.4.8 Representative NMR Spectra

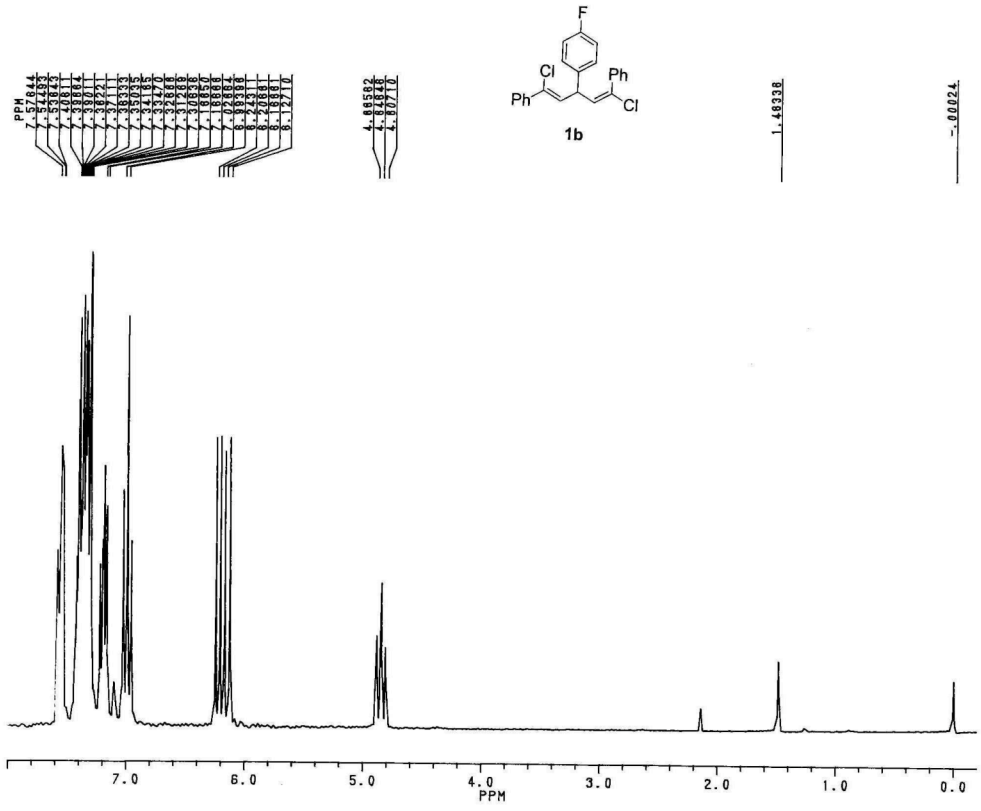
^{1}H spectrum of 1a



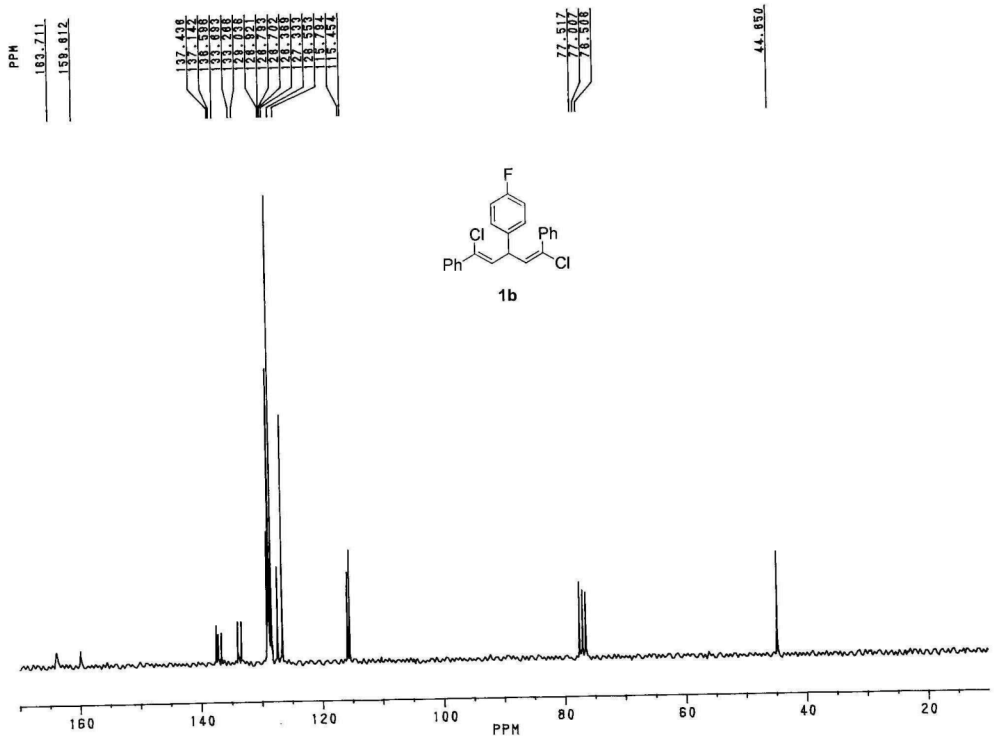
^{13}C spectrum of 1a



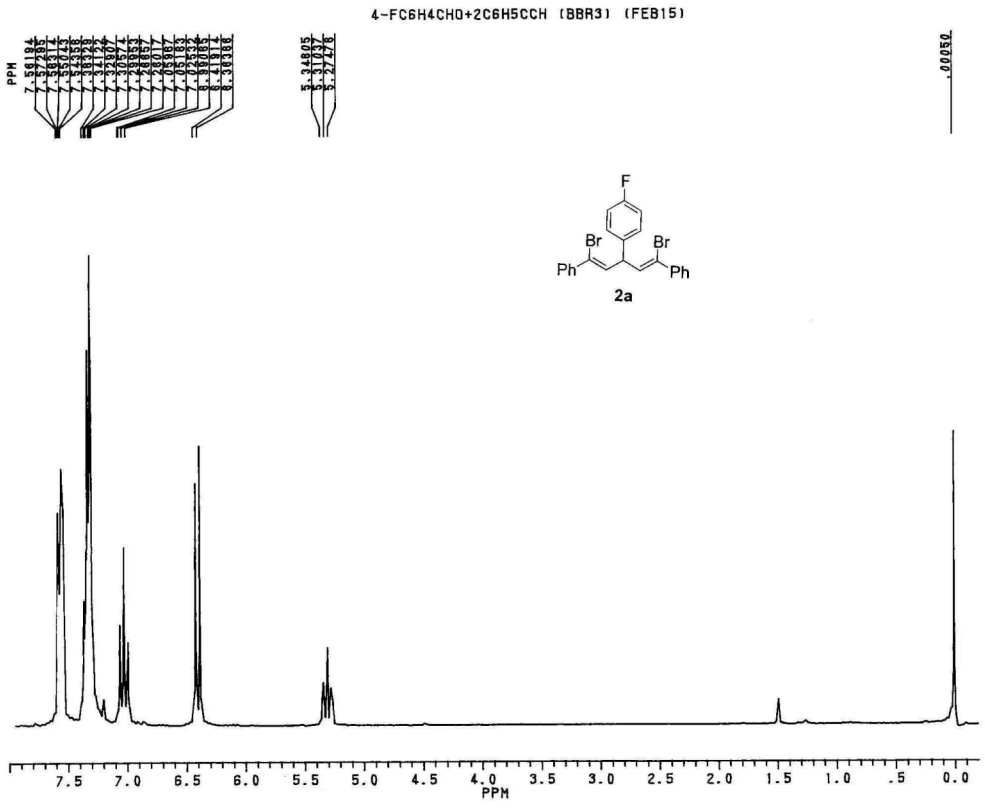
^{1}H spectrum of 1b



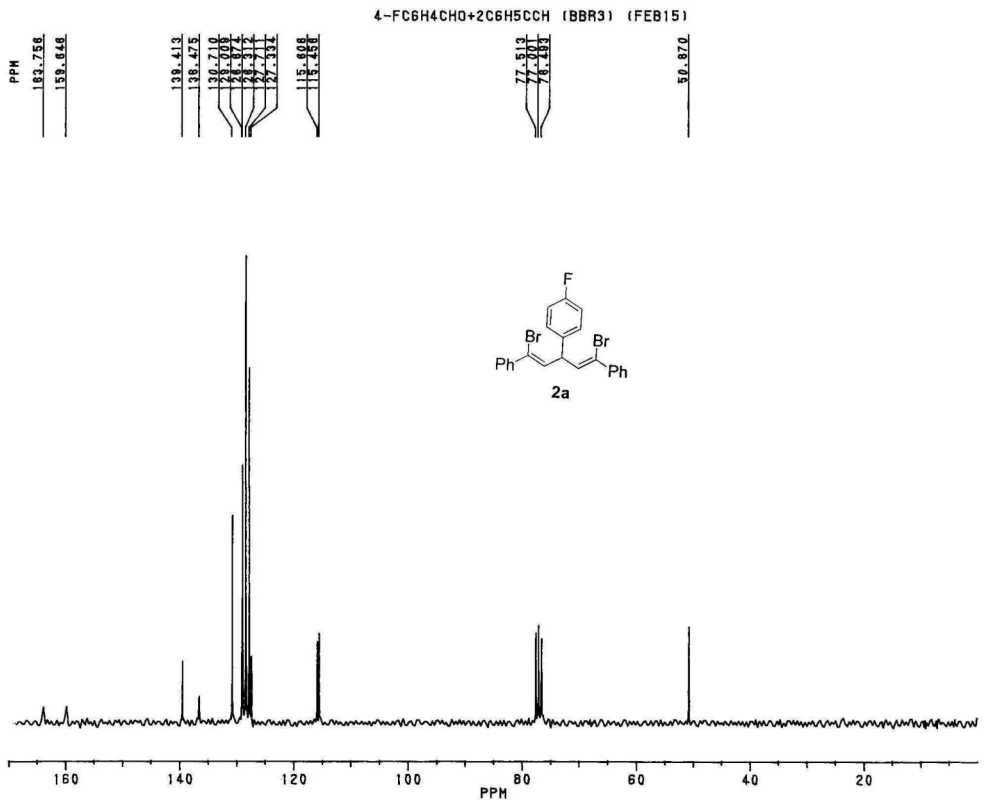
^{13}C spectrum of 1b



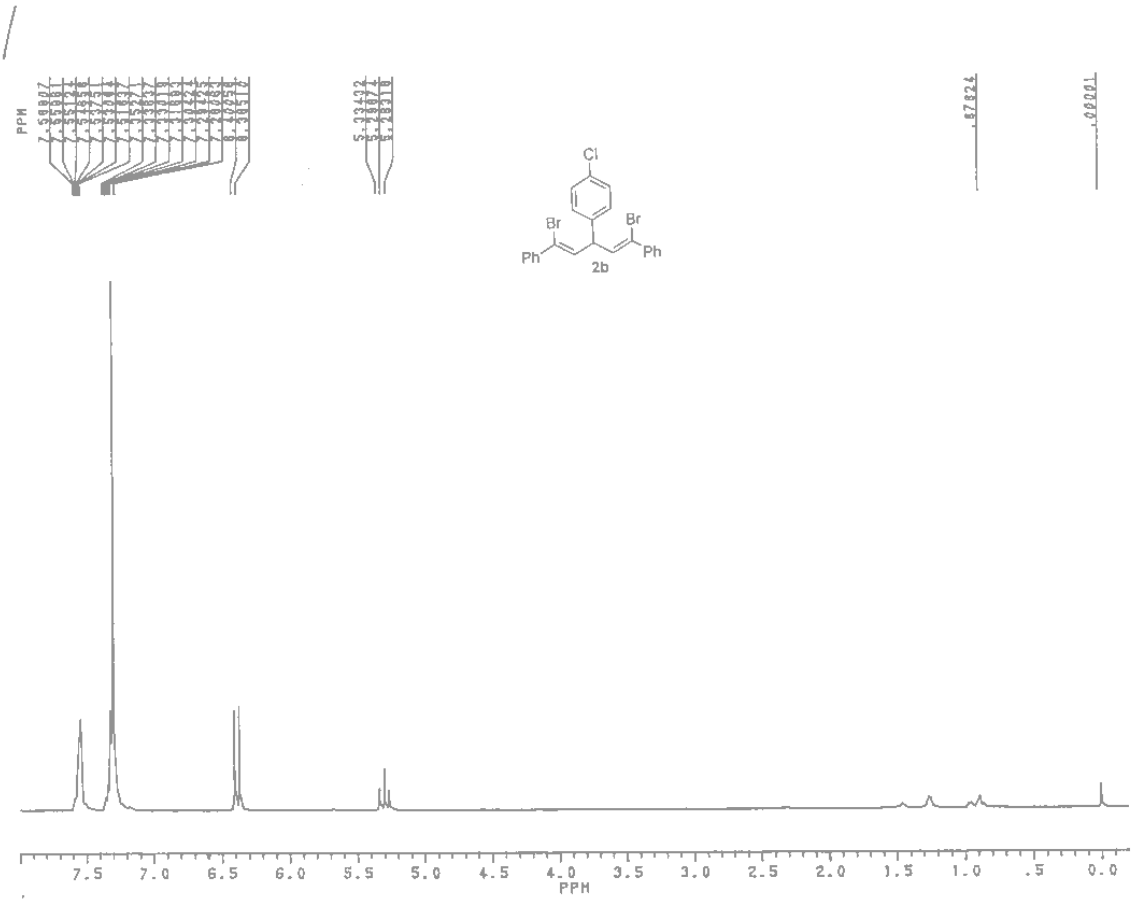
^{1}H spectrum of 2a



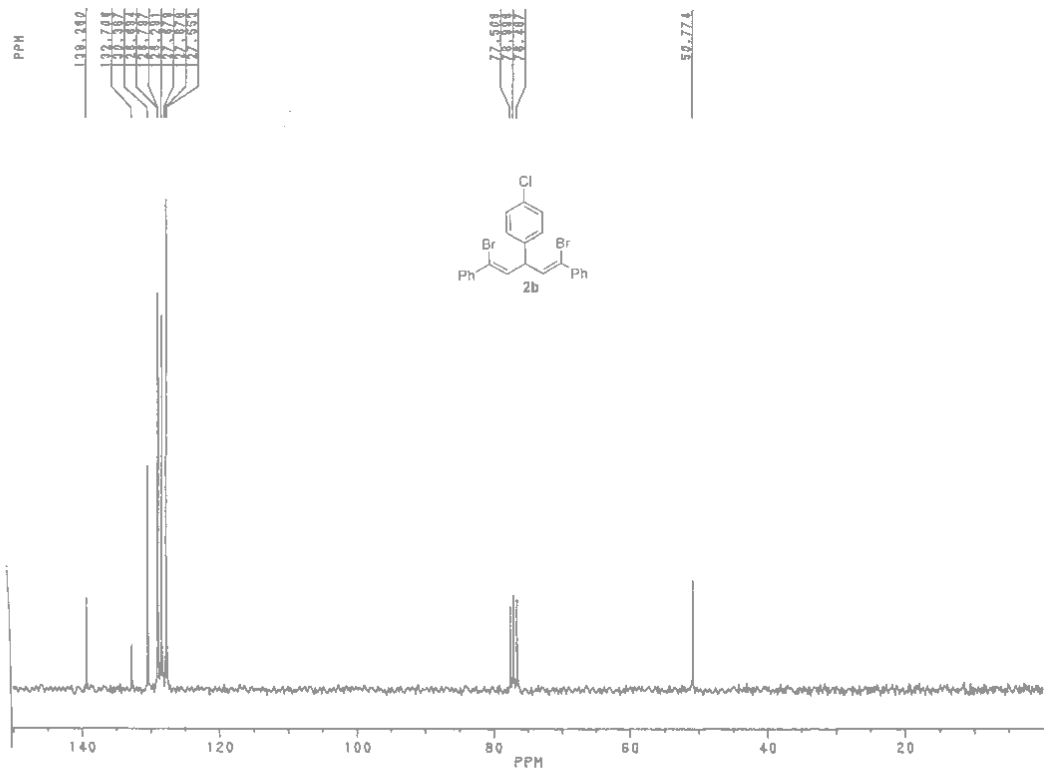
^{13}C spectrum of 2a



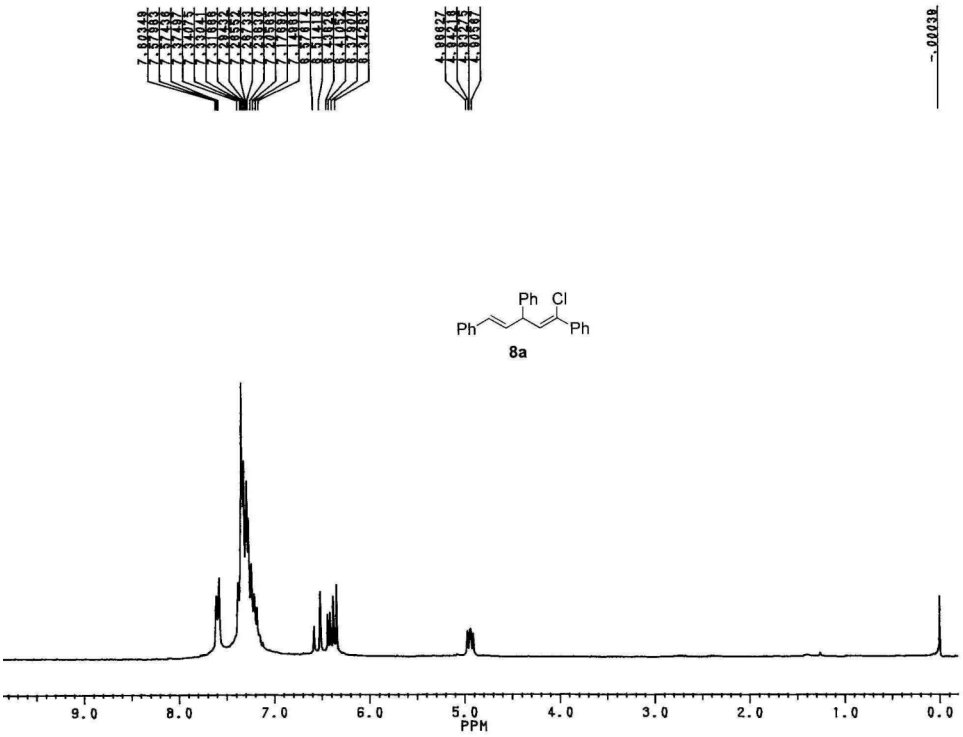
^{1}H spectrum of 2b



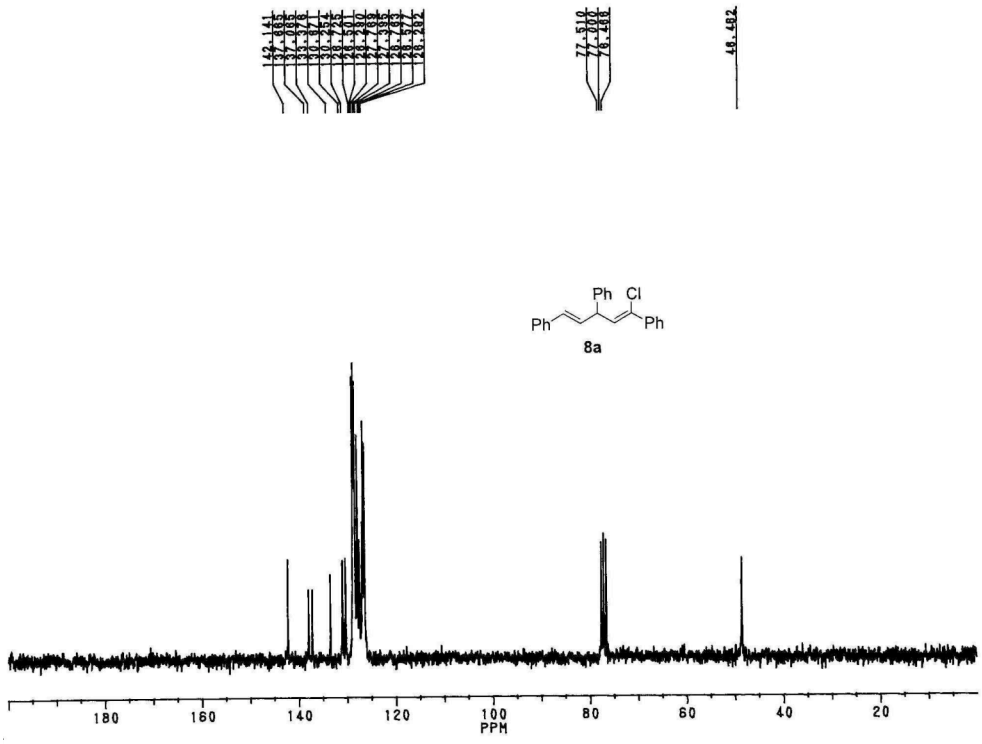
^{13}C spectrum of 2b



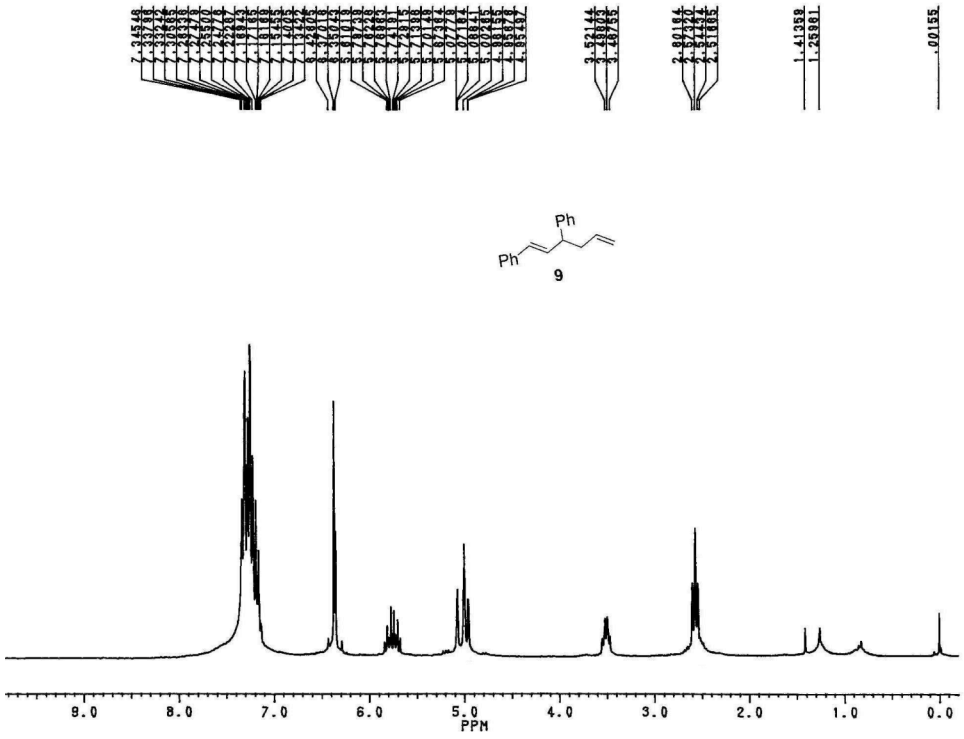
^{1}H spectrum of 8a



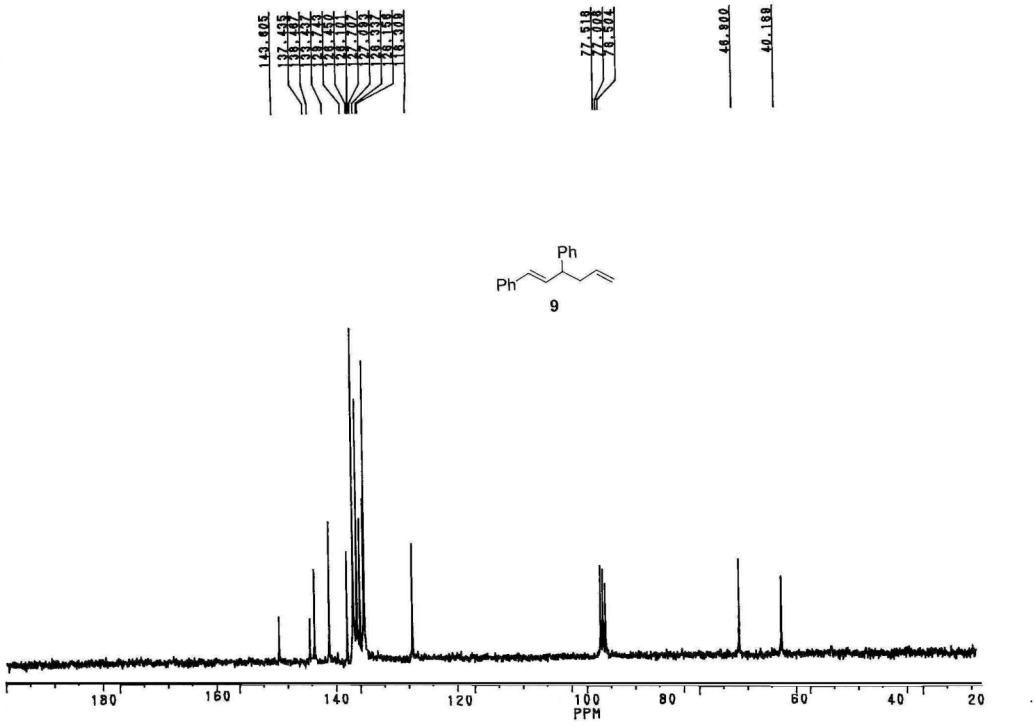
^{13}C spectrum of 8a



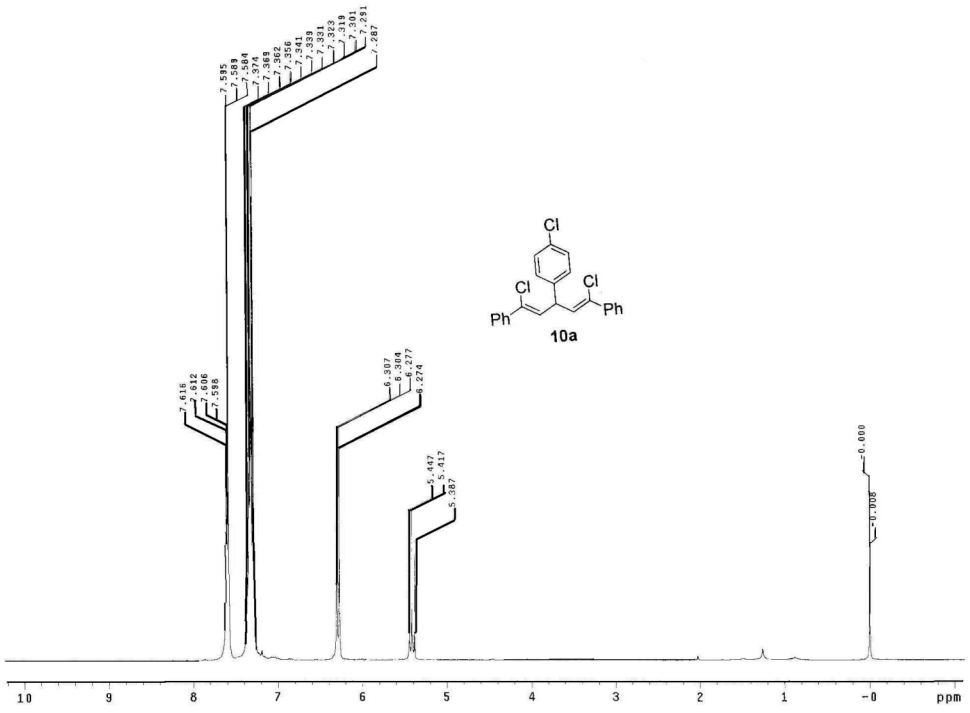
^{1}H spectrum of 9



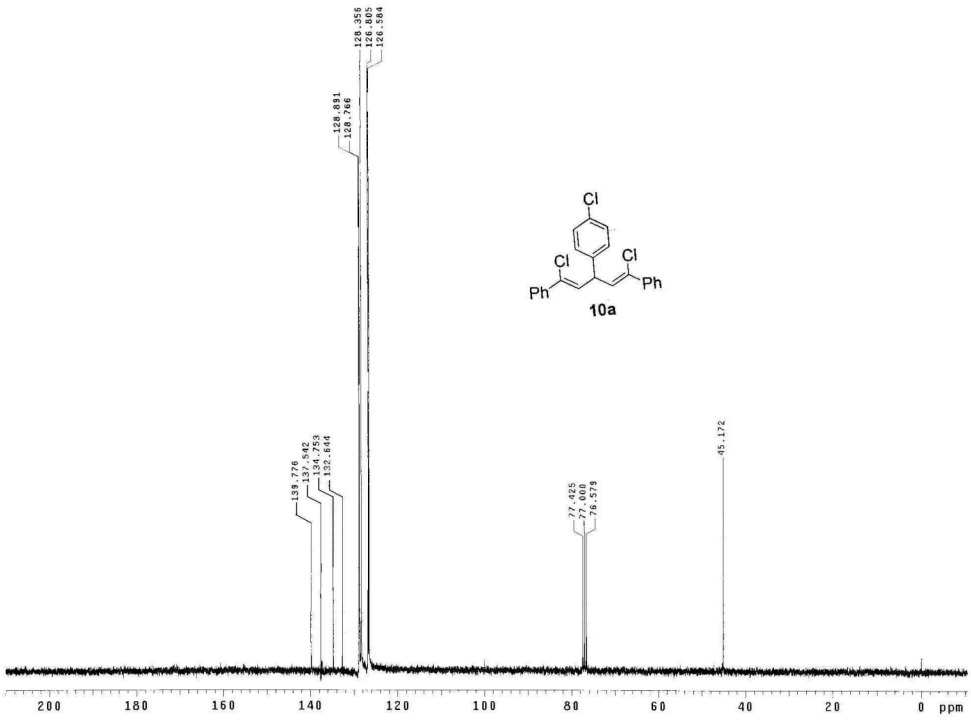
^{13}C spectrum of 9



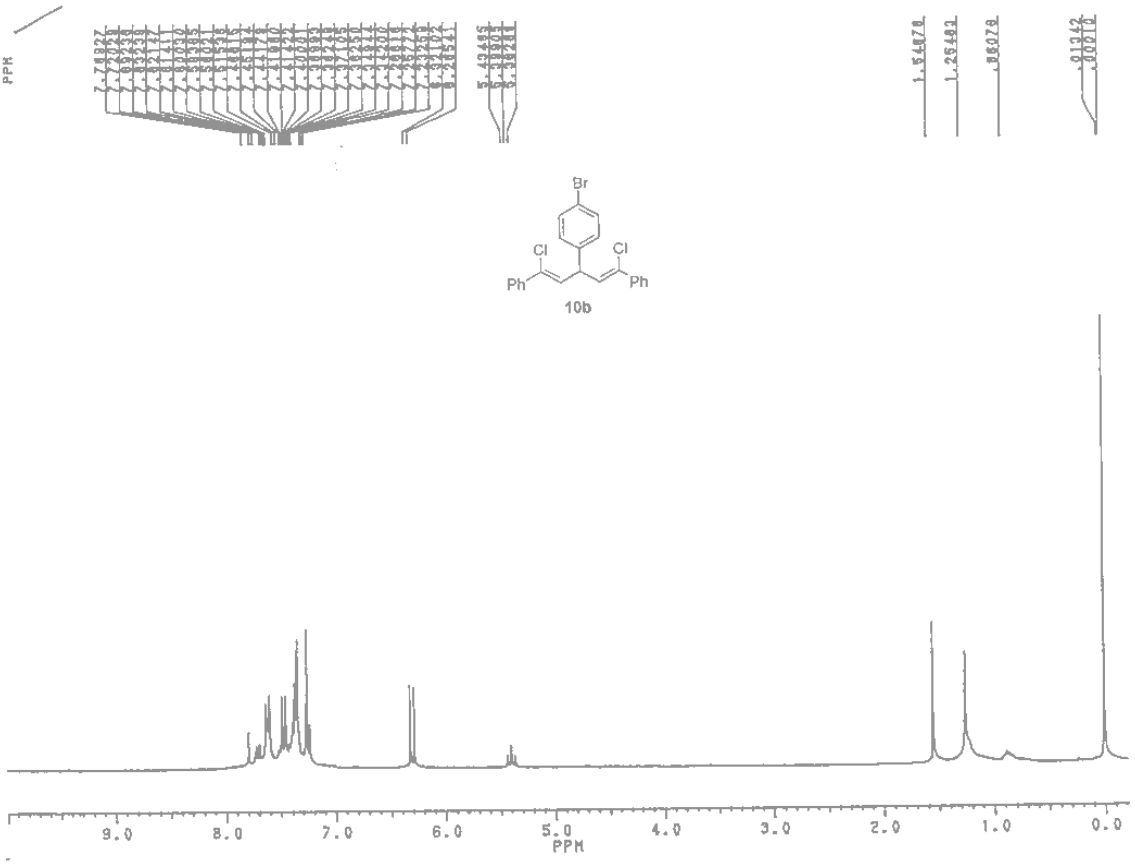
^{1}H spectrum of 10a



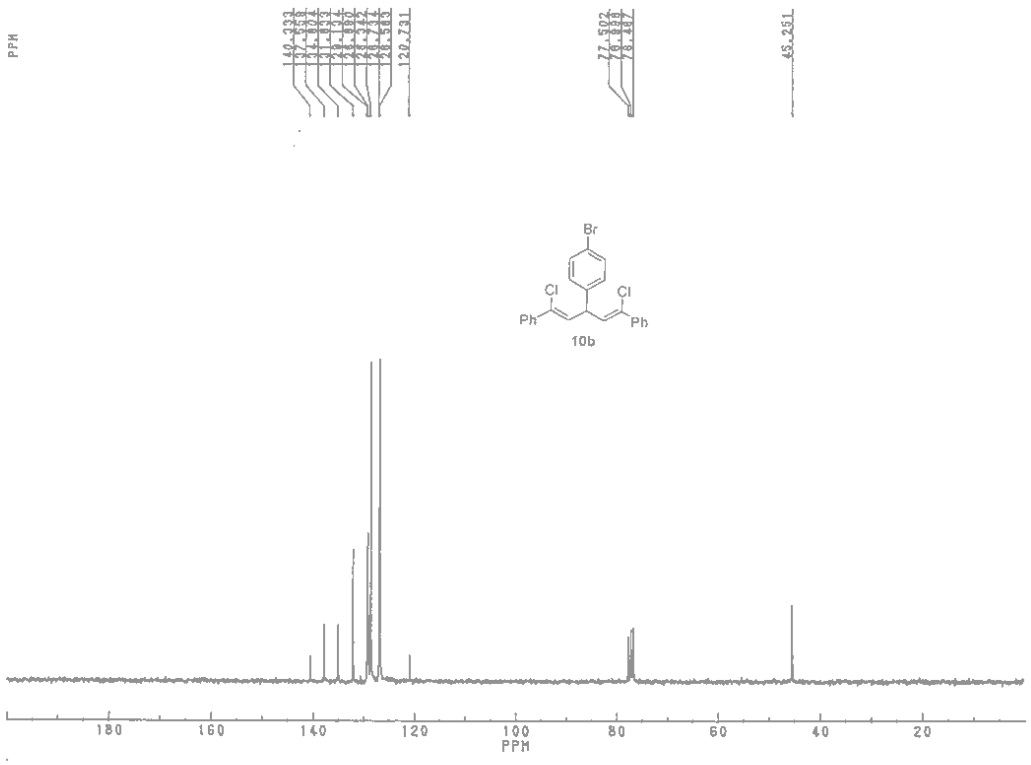
^{13}C spectrum of 10a



^{1}H spectrum of 10b



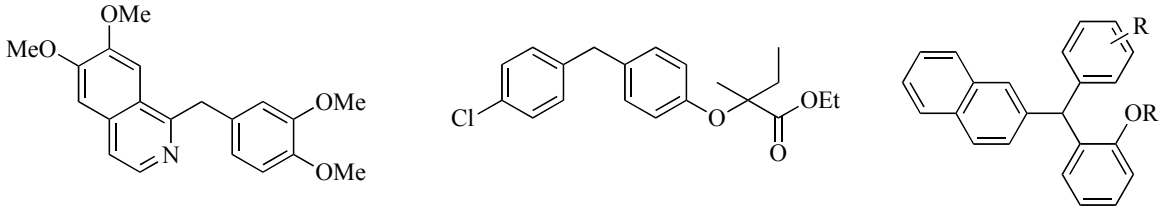
^{13}C spectrum of 10b



Chapter 4. Iron(III) Chloride Mediated Diarylmethane Formation from Benzylic Alcohols and Benzylic Alcohol Salts

4.1 Introduction

The diarylmethane and triarylmethane framework is found in a variety of important molecules, such as papaverine (**1**) and beclobrate (**2**) (**Scheme 4-1**). Diarylnaphthalenes (**3**), for example, are known for their biological activity including their use as anti-inflammatory, anti-tuberculosis, and antichagasic agents.[91] In 2008, it was reported that triarylmethanes containing a thiophenyl group also exhibit antitubercular activity.[92]



Papaverine **1** | Beclobrate **2** | Diaryl naphthalenes **3**

Scheme 4-1 Natural products containing di- and triarylmethane moieties

Although Friedel-Crafts alkylation is a useful method for synthesizing these types of compounds, it sometimes suffers from regioselectivity limitations owing to functional groups on the aryl ring.[25,93] Therefore, the exploration of novel methods to prepare diarylmethanes and triarylmethanes is still desirable.[94]

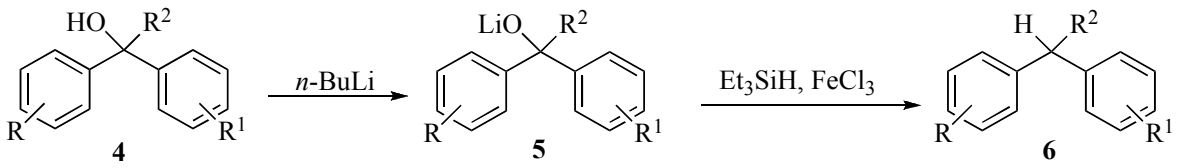
As an alternative strategy, the dehydroxylation of benzylic alcohols has drawn attention in recent decades. Reducing systems developed for dehydroxylation include $Mo(CO)_6$-Lawesson's reagent,[95] hypophosphorus-iodine,[96] indium trichloride-triethylsilane,[97] $B(C_6F_5)_3$-triethylsilane,[98] lithium-ammonia,[99] iodotrimethylsilane,[100] zinc iodide-sodium cyanoborohydride,[101] triphenylsilane in trifluoroacetic acid,[102] sodium borohydride-trifluoroacetic acid[103] and lithium aluminum hydride–aluminum chloride[104]. Unfortunately, most of these methods suffer from undesired side reactions, such as ether cleavage, reduction of unsaturated carbon-carbon bonds and cyano moieties, hydrogenolysis of halogen atoms and ester hydrolysis. These side reactions occur due to either the use of highly acidic conditions or strongly reducing reagents.

Recently we discovered that vinyl,[64] alkynyl[65] and allyl[67] groups could substitute the hydroxyl group in benzylic alcohols under very mild reaction conditions through the corresponding alkoxides. With this knowledge, we investigated the feasibility of hydroxyl group substitution by hydrogen, through the use iron(III) chloride and triethylsilane.

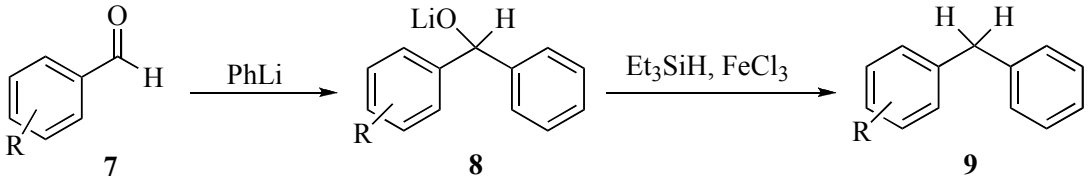
4.2 Results and Discussion

In this study, we investigated the $FeCl_3$-mediated reactions of alkoxides with triethylsilane. The alkoxides were generated from the reaction of diarylmethanols with *n*-butyllithium addition (**Scheme 4-2**) or generated *in situ* by reaction of aryl aldehydes with phenyllithium (**Scheme 4-3**). This investigation offered major advantages: acid-sensitive groups such as –OBn, $–OSiR_3$ and –OMe, etc were readily tolerated; and,

halogens on phenyl rings were retained. (Ether linkage cleavage and dehalogenation are common problems in known dehydroxylation reactions[96-104]).



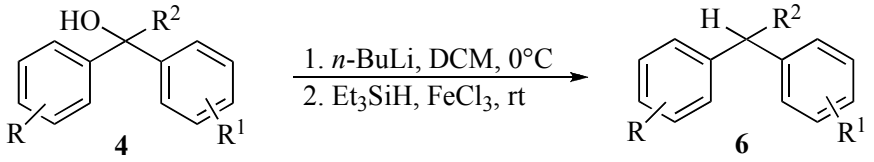
Scheme 4-2 Generation of alkoxide from diarylmethanols using *n*-butyllithium



Scheme 4-3 Generation of alkoxide from aryl aldehydes using phenyllithium

We now demonstrate that diarylmethanols undergo dehydroxylation under reaction conditions (**Table 4-1**) similar to those reported earlier. Benzhydrols, in dichloromethane, are treated with *n*-butyllithium at 0 °C and allowed to warm to room temperature for thirty minutes. Triethylsilane, followed by iron(III) chloride, are added at room temperature and allowed to react overnight. Following work-up and chromatography, the dehydroxylated benzhydrols **6a-6i** are obtained in moderate to excellent yield.

Table 4-1 Dehydroxylation of Benzhydrols *via* Iron(III) Chloride and Triethylsilane[a]

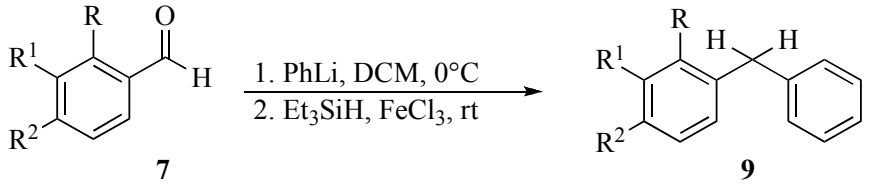


Entry	R	R^1	R^2	Product	Yield (%)
1	H	H	H	**6a**	93
2	2-Me	H	H	**6b**	92
3	4-Me	H	H	**6c**	88
4	H	H	Me	**6d**	66
5	4-OTBDMS	H	H	**6e**	98
6	4-Cl	H	H	**6f**	95
7	4-F	4-F	H	**6g**	88
8	H	H	Ph	**6h**	95
9	4-OMe	4-OMe	H	**6i**	85

[a] Reaction carried out at 0°C for 10 minutes, then maintained at room temperature (see Experimental for details).

Generation of a lithium salt *in situ* provides for even more possibilities for arylmethane formation. **Table 4-2** contains a summary of the conditions used. Aryl aldehydes in dichloromethane were treated with phenyllithium at 0 °C and allowed to react for thirty minutes. Triethylsilane, along with iron(III) chloride, were added at room temperature and allowed to react overnight. Following work-up and chromatography, the substituted benzyl derivatives **9a-9e** were obtained in moderate to excellent yields.

Table 4-2 *In situ* Lithium Alkoxide Generation and Cleavage *via* Iron(III) Chloride and Triethylsilane[a]



7 **9**

Entry	R	R^1	R^2	Product	Yield (%)
1	H	H	BnO	**9a**	77
2	Naphthyl		H	**9b**	79
3	H	H	Cl	**9c**	88
4	Me	H	H	**9d**	91
5	H	H	H	**9e**	89

[a] Reaction carried out at 0 °C for 10 minutes, then maintained at room temperature (see Experimental for details)

4.3 Conclusions

Two methods for synthesizing diarylmethane derivatives *via* the usage of triethylsilane and iron(III) chloride are described. It is now possible to generate diarylmethane derivatives by two different alkoxide-generating reactions (from a diarylmethanol *via n*-butyllithium or adding phenyllithium to an aryl aldehyde), followed by addition of triethylsilane and iron(III) chloride. Several examples illustrate that the reaction conditions do not cleave ether or halogen moieties. Presumably, any diarylmethanol derivative or *in situ* generated diarylmethanoxide will undergo the reaction conditions described in this study.

4.4 Experimental

4.4.1 General Methods

All reagents were used as received. Column chromatography was performed using silica gel (60 Å, 230–400 mesh, ICN Biomedicals GmbH, Eschwege, Germany). Analytical thin-layer chromatography was performed using 250 μm silica (Analtech, Inc., Newark, DE).

^{1}H NMR and ^{13}C NMR spectra were recorded at 250.13 and 62.89 MHz, respectively. Chemical shifts for ^{1}H NMR and ^{13}C NMR spectra were referenced to TMS and measured with respect to the residual protons in the deuterated solvents. Atlantic Microlab, Inc., Norcross, Georgia, performed microanalysis.

4.4.2 Typical Reaction Procedure: Diarylmethanol to Diarylmethane

Benzhydrol (0.28 g, 1.5 mmol) and dichloromethane (20 mL) were placed in a dry, argon-flushed, 100 mL round-bottomed flask equipped with a magnetic stirring bar. The solution was cooled to 0 °C in an ice bath and *n*-butyllithium (1.0 mL, 1.6 mmol of a 1.0 *M* hexanes solution) was added *via* syringe. The solution was allowed to stir for 10 minutes at 0 °C and then for 30 minutes at room temperature. Triethylsilane (0.32 mL, 1.95 mmol) was added *via* syringe, followed by iron(III) chloride (0.268 g, 1.65 mmol) as an anhydrous powder. The reaction solution gradually turned dark purple and was allowed to react overnight. The resulting mixture was hydrolyzed with water (15 mL) and extracted into hexanes (3 x 10 mL). The organic layer was separated and dried over anhydrous $MgSO_4$. Product **6a** (0.23 g, 93% yield) was isolated by flash column chromatography, using hexanes as eluent.

4.4.3 Characterization of Compounds 6a-6i

Diphenylmethane (6a)[105]**:** δ 7.23-7.09 (m, 10H), 3.86 (s, 2H). ^{13}C NMR ($CDCl_3$): δ 141.1, 128.7, 128.4, 126.9, 41.7.

1-Benzyl-2-methylbenzene (6b)[106]**:** ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.23-7.06 (m, 9H), 3.96 (s, 2H), 2.21 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 139.9, 138.4, 136.1, 129.7, 128.2, 127.9, 125.9, 125.5, 125.4, 38.94, 19.11.

1-Benzyl-4-methylbenzene (6c)[107]**:** ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.22-7.13 (m, 5H), 7.05 (s, 4H), 3.89 (s, 2H), 2.27 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 141.4, 136.0, 135.4, 129.1, 128.8, 128.7, 126.4, 125.9, 41.5, 20.9.

1,1-Diphenylethane (6d)[108]**:** ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.31-7.12 (m, 10H), 4.12 (q, 1H, ^{3}J = 7.2 Hz), 1.63 (d, ^{3}J = 7.2 Hz). ^{13}C NMR ($CDCl_3$): δ 146.4, 128.3, 128.1, 127.6, 126.0, 44.8, 21.9.

(4-Benzylphenoxy)(*tert*-butyl)dimethylsilane (6e): δ 7.27-7.13 (m, 5H), 7.01 (d, 1H, ^{3}J = 8.3 Hz), 6.74 (d, 1H, ^{3}J = 8.3 Hz), 3.86 (s, 2H), 0.99 (s, 9H), 0.17 (s, 6H). ^{13}C NMR ($CDCl_3$): δ 153.9, 141.5, 133.7, 129.8, 128.8, 128.4, 125.9, 119.9, 41.1, 25.9, 18.2, -4.4.

1-Benzyl-4-chlorobenzene (6f)[109]**:** ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.26-7.04 (m, 9H), 3.89 (s, 2H). ^{13}C NMR ($CDCl_3$): δ 140.5, 139.5, 131.6, 130.2, 128.8, 128.5 126.2, 41.2.

***Bis*(4-fluorophenyl)methane (6g)**[110]**:** ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.12-7.08 (m, 4H), 6.99-6.93 (m, 4H), 3.91 (s, 2H). ^{13}C NMR ($CDCl_3$): δ 159.8, 138.4, 130.2, 115.4, 40.2.

Triphenylmethane (6h)[111]**:** ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.24-7.09 (m, 15H), 5.51 (s, 1H). ^{13}C NMR ($CDCl_3$): δ 143.9, 129.4, 128.3, 126.2, 56.8.

***Bis*(4-methoxyphenyl)methane (6i)**[112]**:** ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.05 (d, 4H, ^{3}J = 9.9 Hz), 6.80 (d, 4H, ^{3}J = 10.0 Hz), 3.82 (s, 2H), 3.72 (s, 6H). ^{13}C NMR ($CDCl_3$): δ 157.9, 133.7, 129.7, 113.8, 55.1, 40.1.

4.4.4 Typical Reaction Procedure: Aryl Aldehyde to Diarylmethane

p-Chlorobenzaldehyde (0.25 g, 1.8 mmol) and dichloromethane (20 mL) were placed in a dry, argon-flushed, 100 mL round-bottomed flask equipped with a magnetic stirring bar. The solution was cooled to 0 °C in an ice bath and phenyllithium (1.0 mL, 1.8 mmol of a 1.8 *M* di-*n*-butyl ether solution) was added *via* syringe. The solution was allowed to stir for 10 minutes 0 °C and then for 30 minutes at room temperature. Triethylsilane (0.38 mL, 2.3 mmol) was added *via* syringe, followed by iron(III) chloride

(0.32 g, 1.98 mmol) as an anhydrous powder. The reaction solution gradually turned dark purple and was allowed to react overnight. The resulting mixture was hydrolyzed with water (15 mL) and extracted into hexanes (3 x 10 mL). The organic layer was separated and dried over anhydrous $MgSO_4$. Product **9a** (0.32 g, 88% yield) was isolated by flash column chromatography, using hexanes as eluent.

4.4.5 Characterization of Compounds 9a-9e

1-Benzyl-4-(benzyloxy)benzene (9a)[113]**:** ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.41-6.85 (m, 14H), 4.99 (s, 2H), 3.90 (s, 2H). ^{13}C NMR ($CDCl_3$): δ 157.1, 141.5, 137.1, 133.5, 129.8, 128.8, 128.5, 128.4, 127.9, 127.4, 125.9, 114.8, 69.9, 41.0.

1-Benzylnaphthalene (9b)[114]**:** ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.93-7.97 (m, 1H); 7.78-7.82 (m, 1H); 7.71 (d, 1H, ^3J = 7.5 Hz), 7.42-7.13 (m, 9H), 4.37 (s, 2H). ^{13}C NMR ($CDCl_3$): δ 140.6, 136.6, 133.9, 132.1, 128.7, 128.6, 128.4, 127.3, 127.1, 126.0, 125.9, 125.5, 124.3, 38.8.

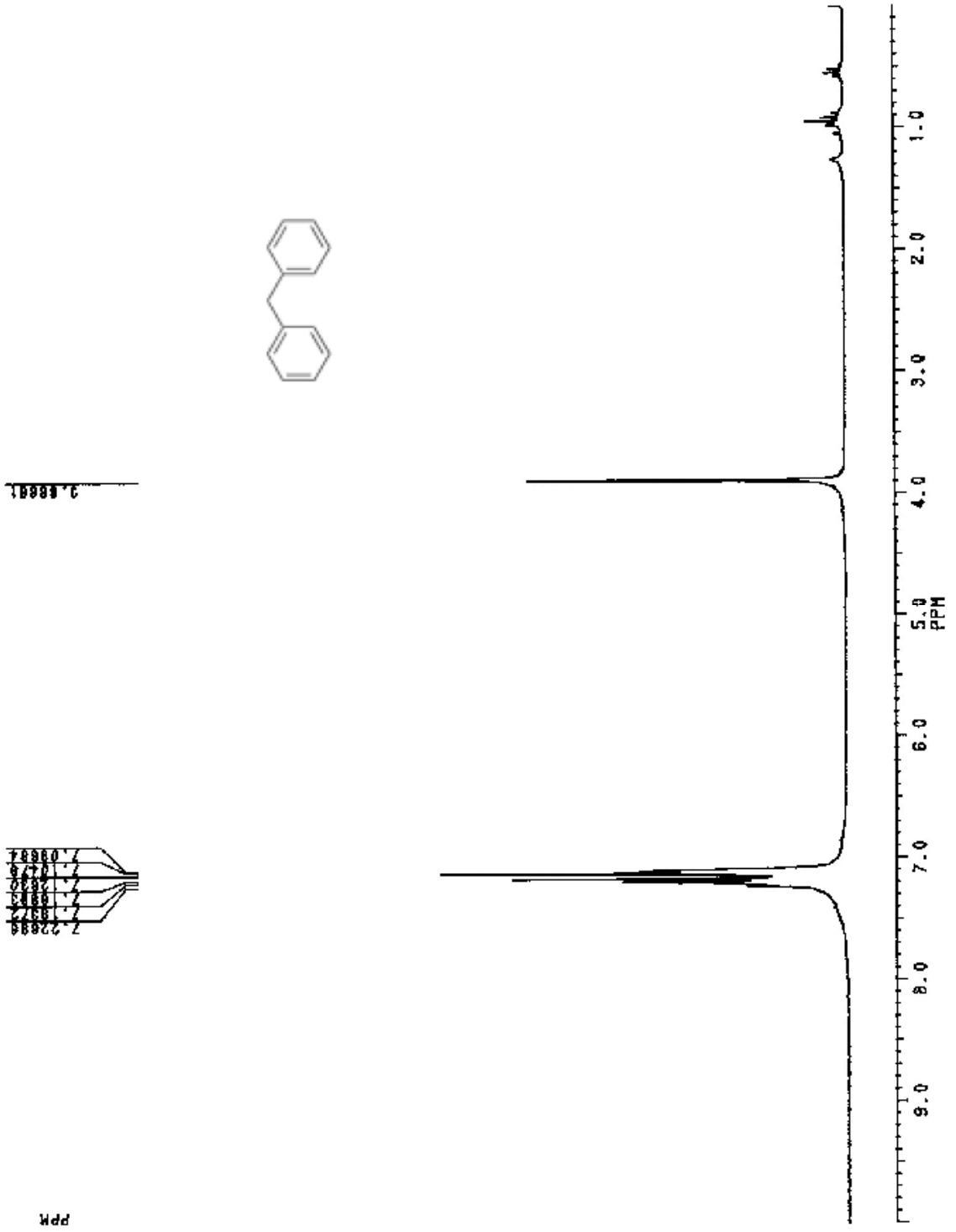
1-Benzyl-4-chlorobenzene (9c)[109]**:** ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.44-7.05 (m, 9H), 3.90 (s, 2H). ^{13}C NMR ($CDCl_3$): δ 141.5, 139.6, 130.2, 128.8, 128.5, 127.2, 127.1, 126.3, 41.2.

1-Benzyl-2-methylbenzene (9d)[106]**:** ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.23-7.08 (m, 9H), 3.96 (s, 2H), 2.21 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 140.4, 138.9, 136.6, 130.3, 129.9, 128.7, 128.4, 126.4, 125.9, 39.5, 19.6.

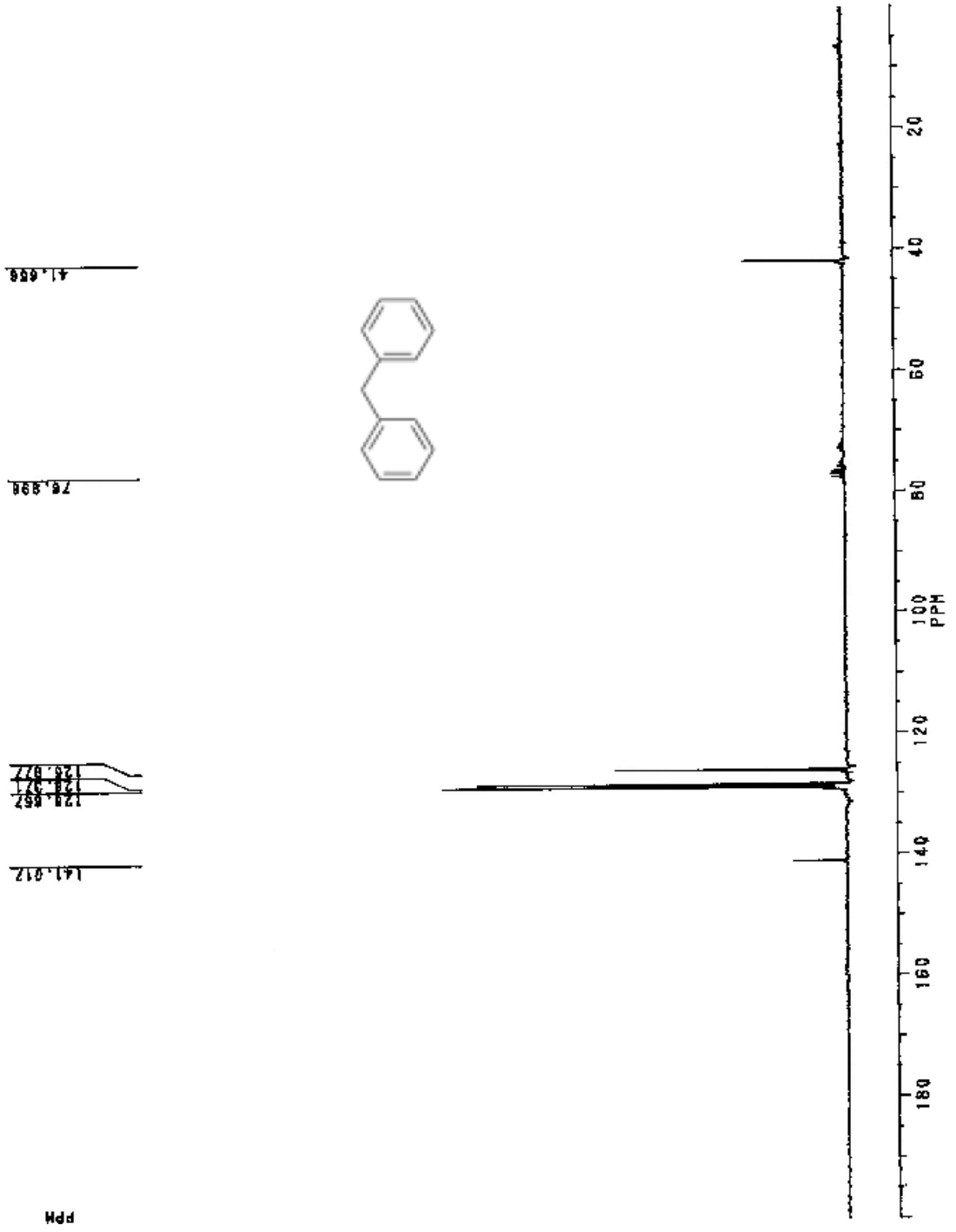
Diphenylmethane (9e)[105]**:** ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.23-7.08 (m, 9H), 3.96 (s, 2H), 2.21 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 140.4, 138.9, 136.6, 130.3, 129.9, 128.7, 128.4, 126.4, 125.9, 39.5, 19.6.

4.4.6 Representative NMR Spectra

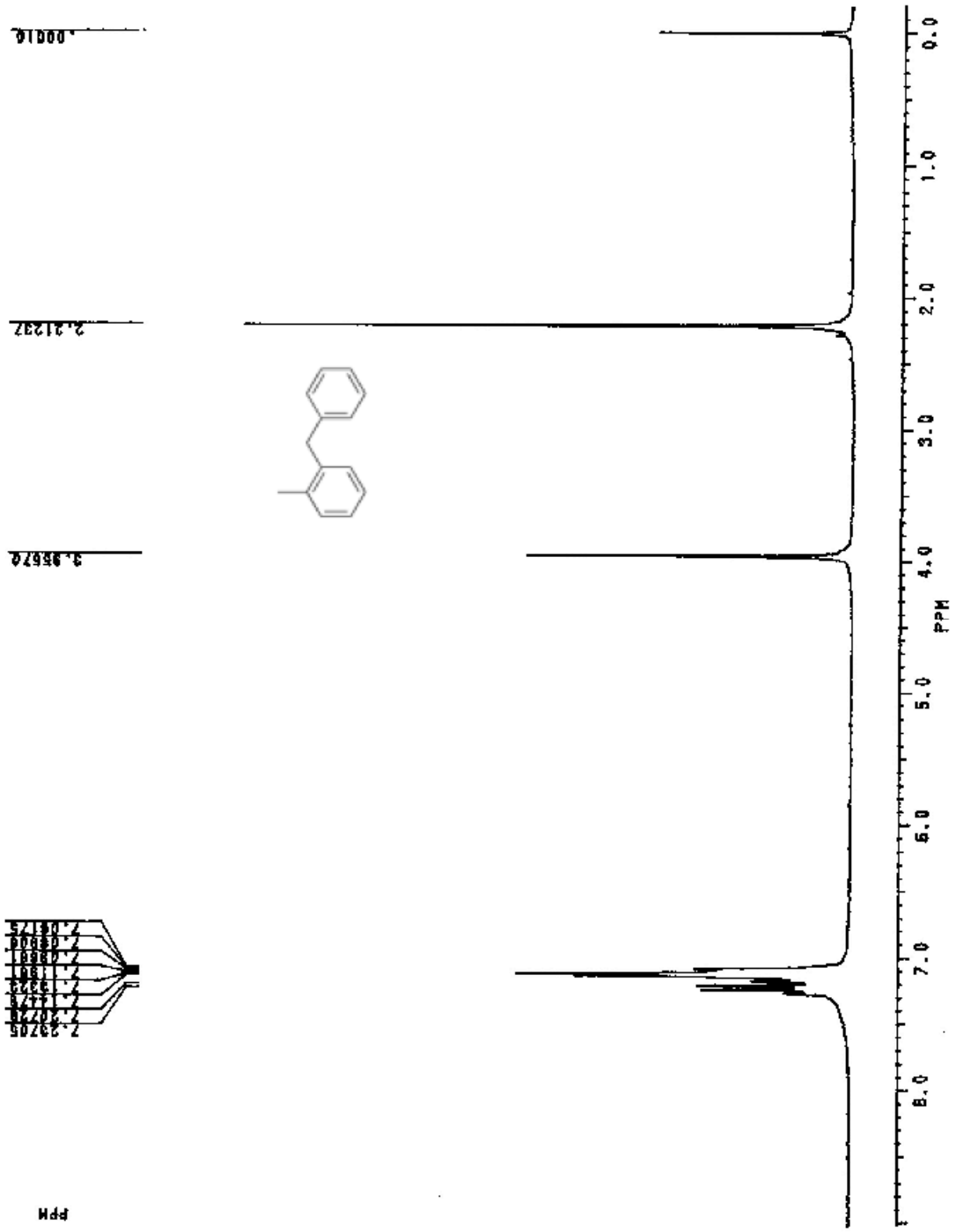
^{1}H spectrum of 6a



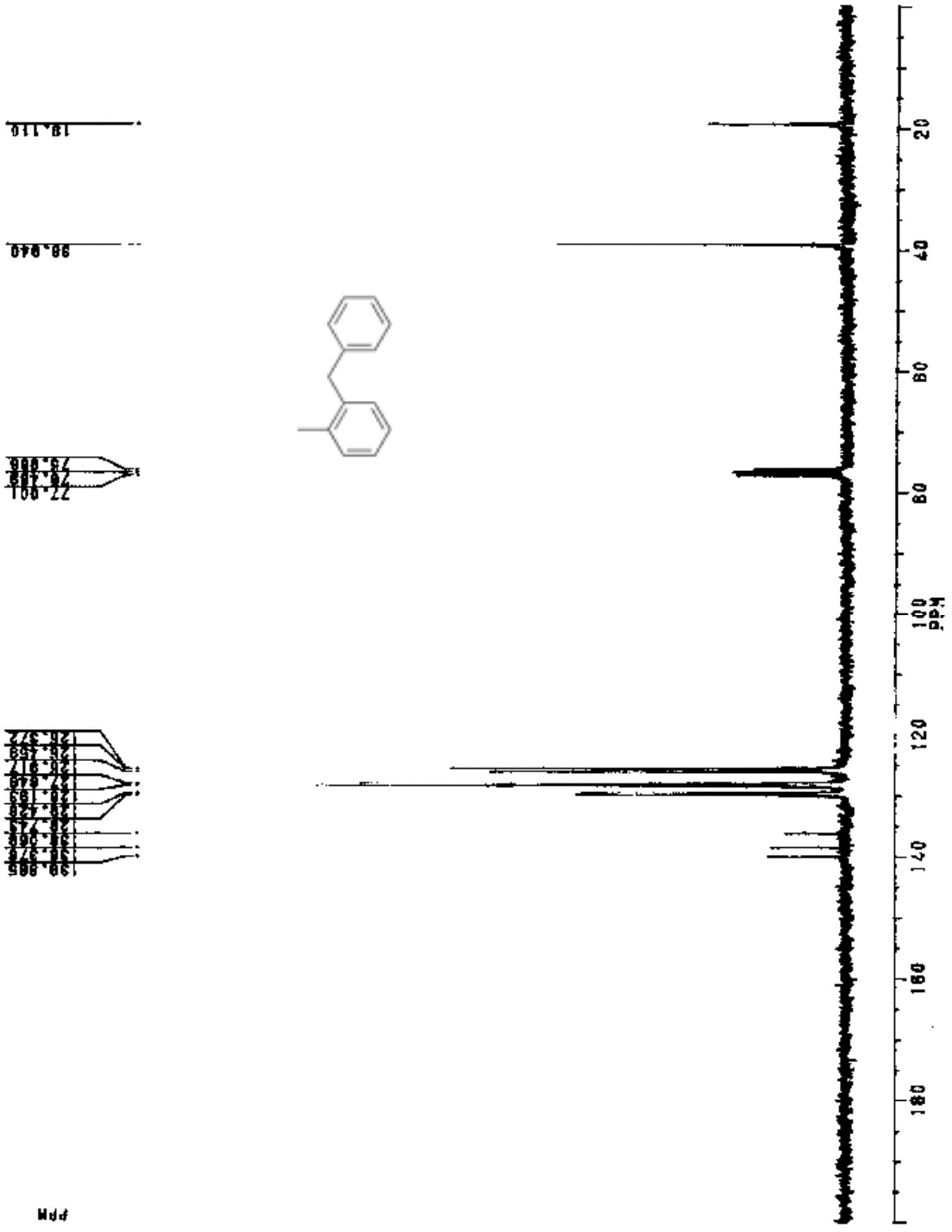
^{13}C spectrum of 6a



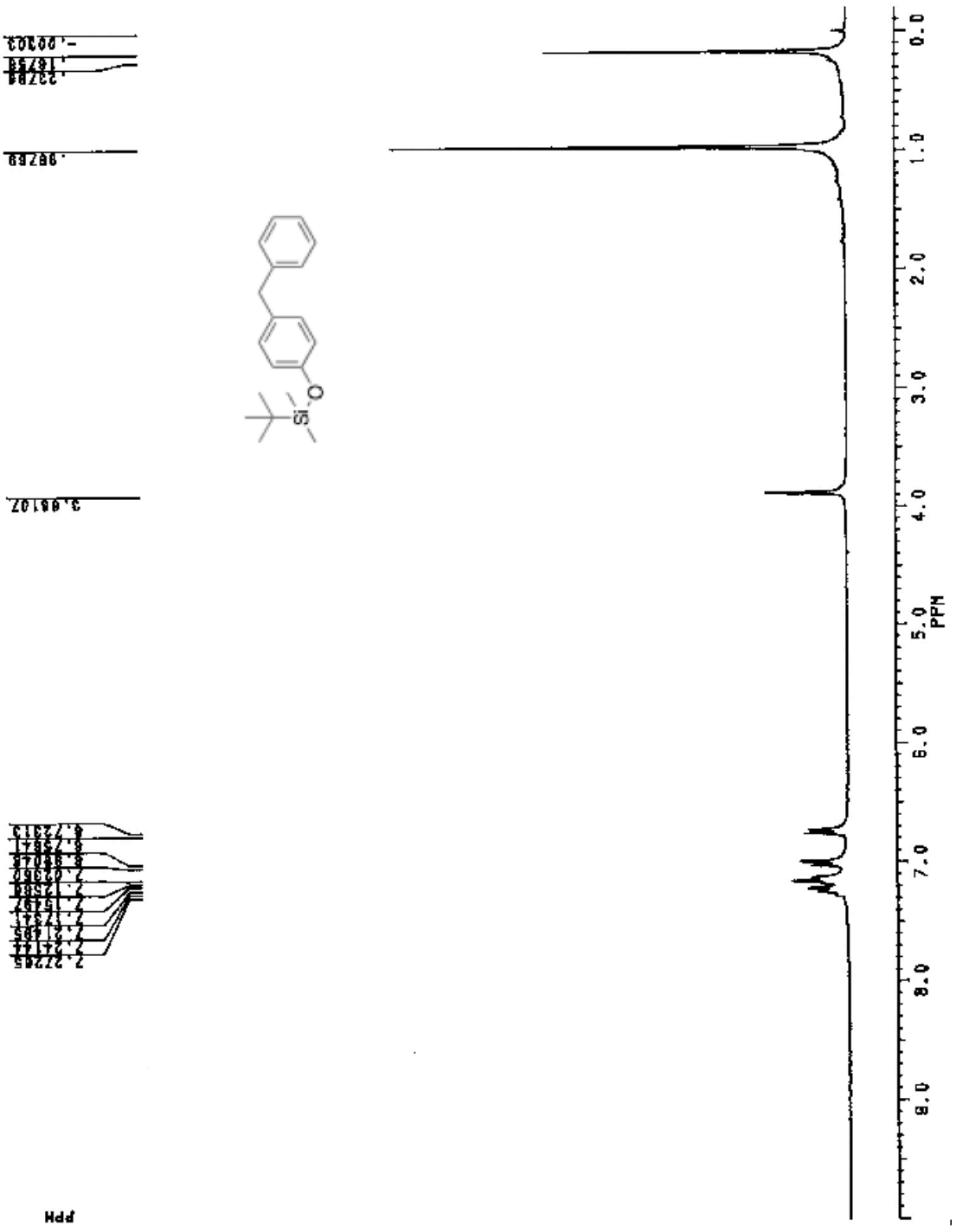
^{1}H spectrum of 6b



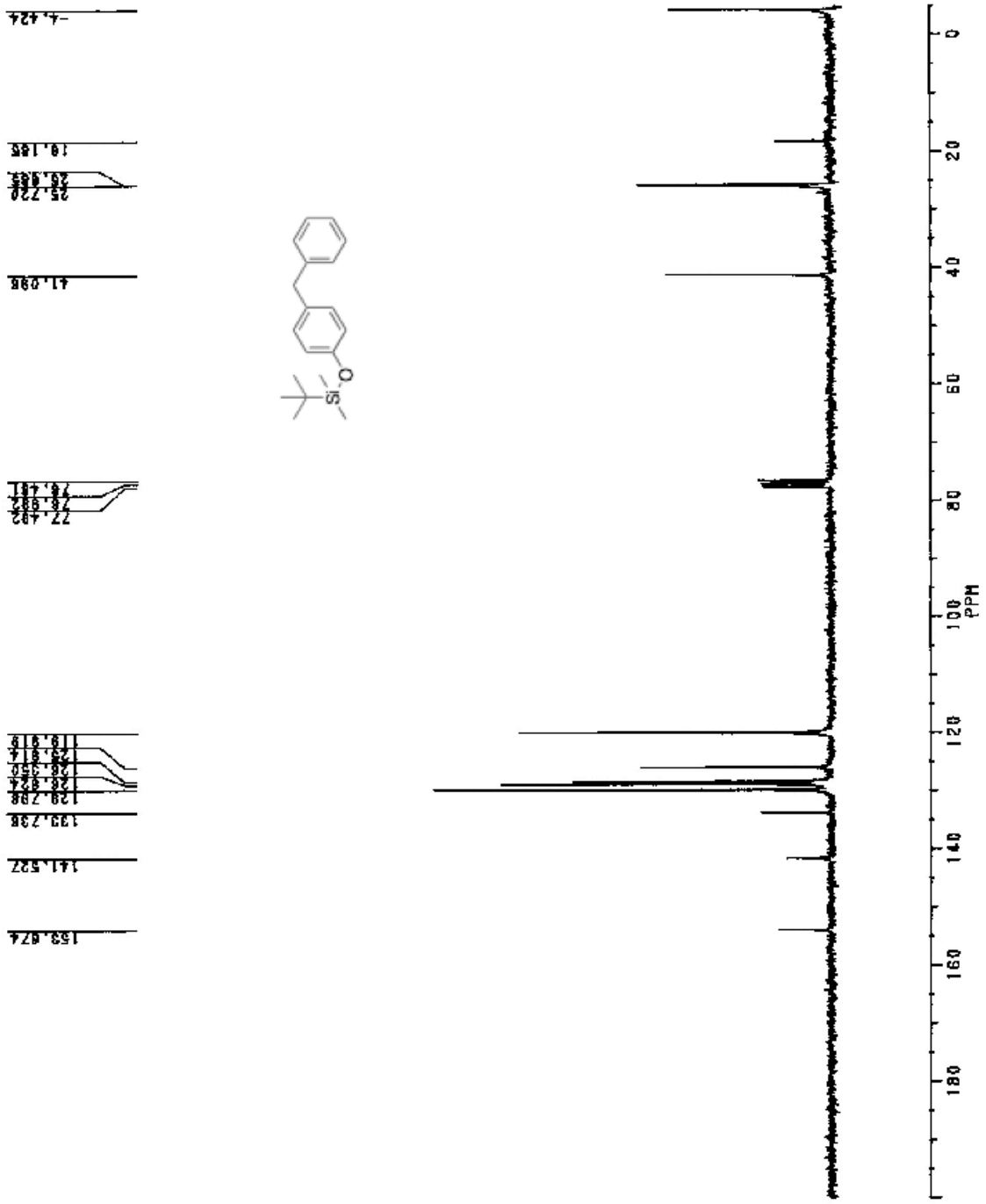
^{13}C spectrum of 6b



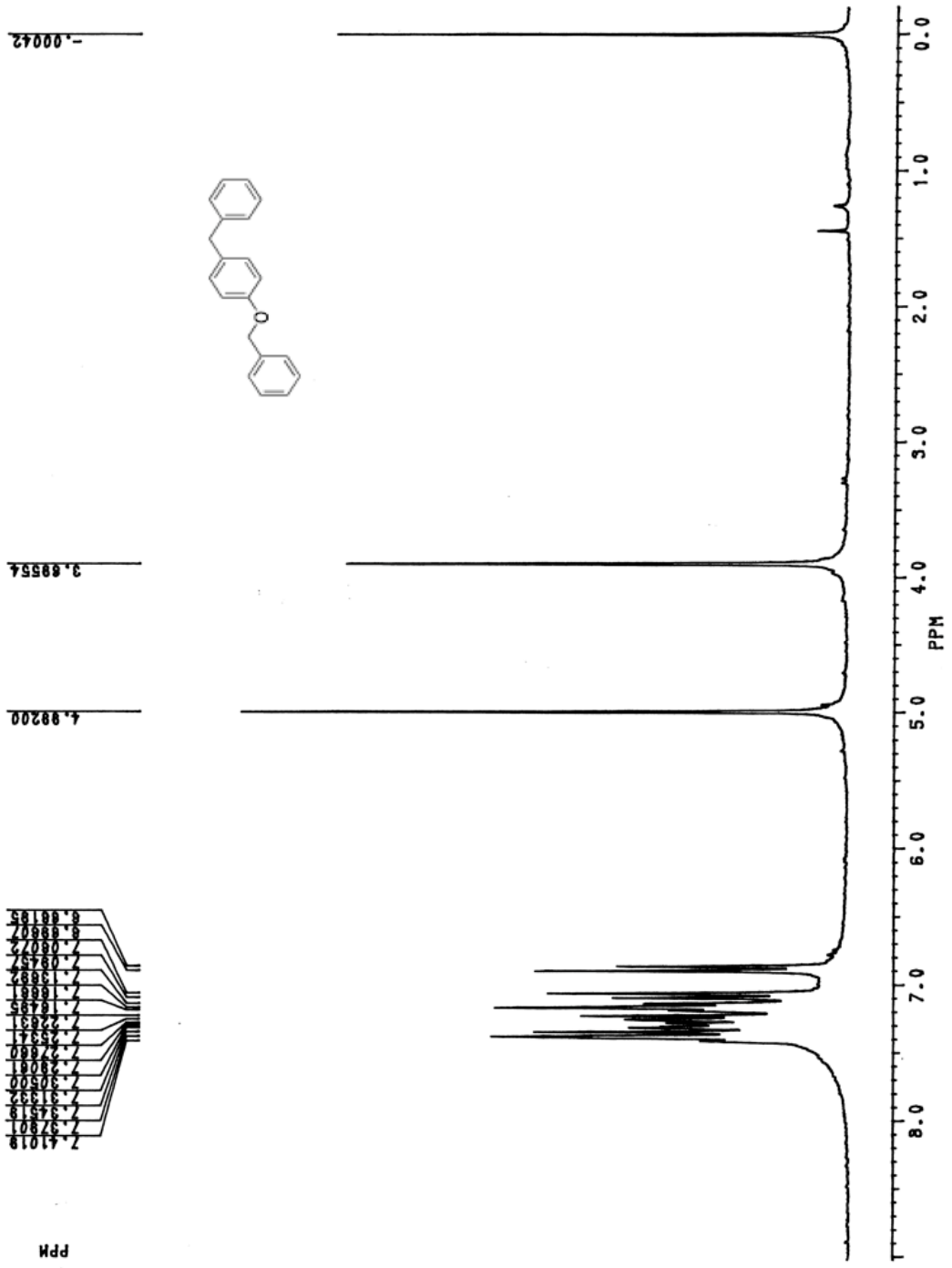
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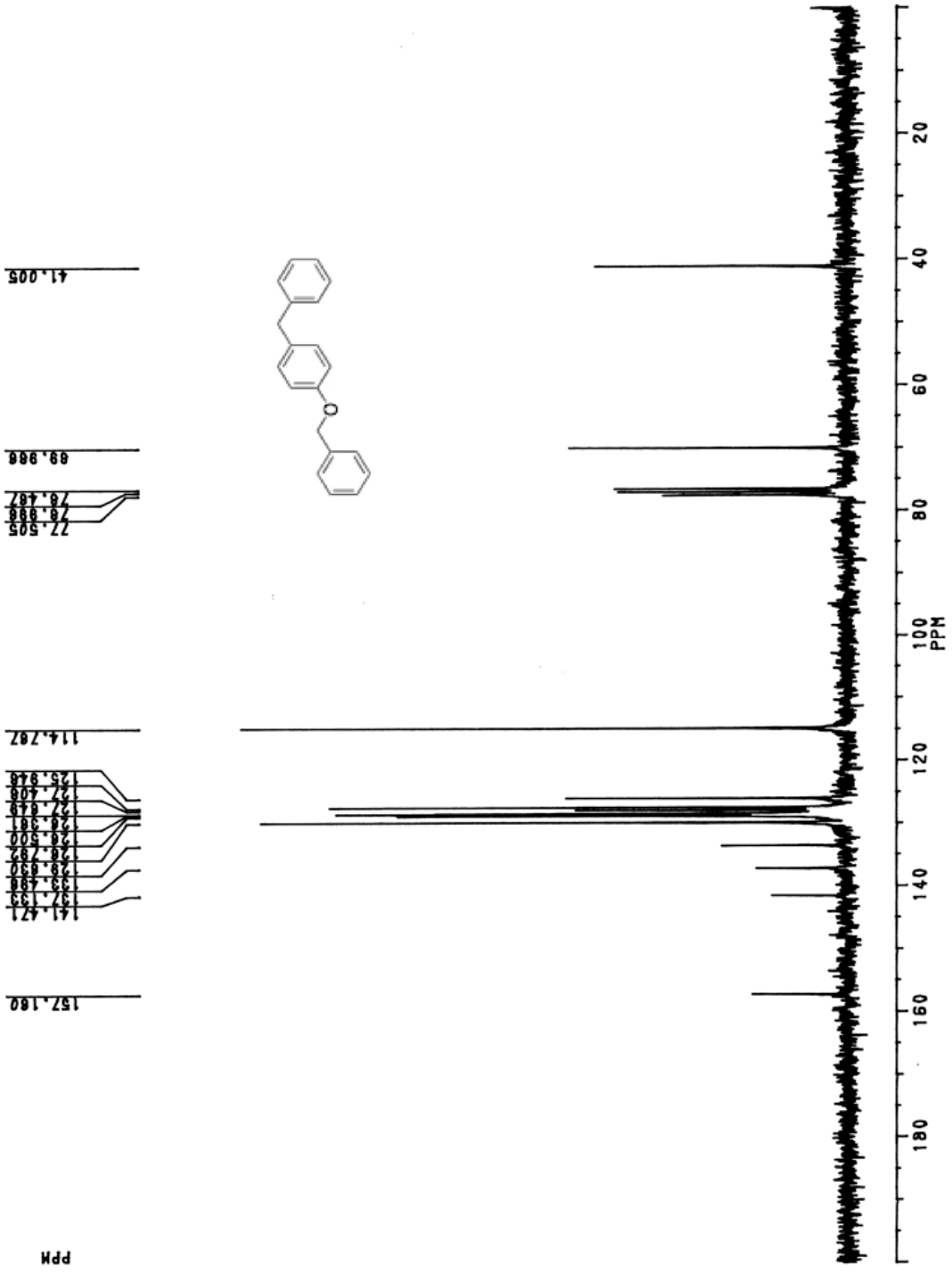
^{13}C spectrum of 6e



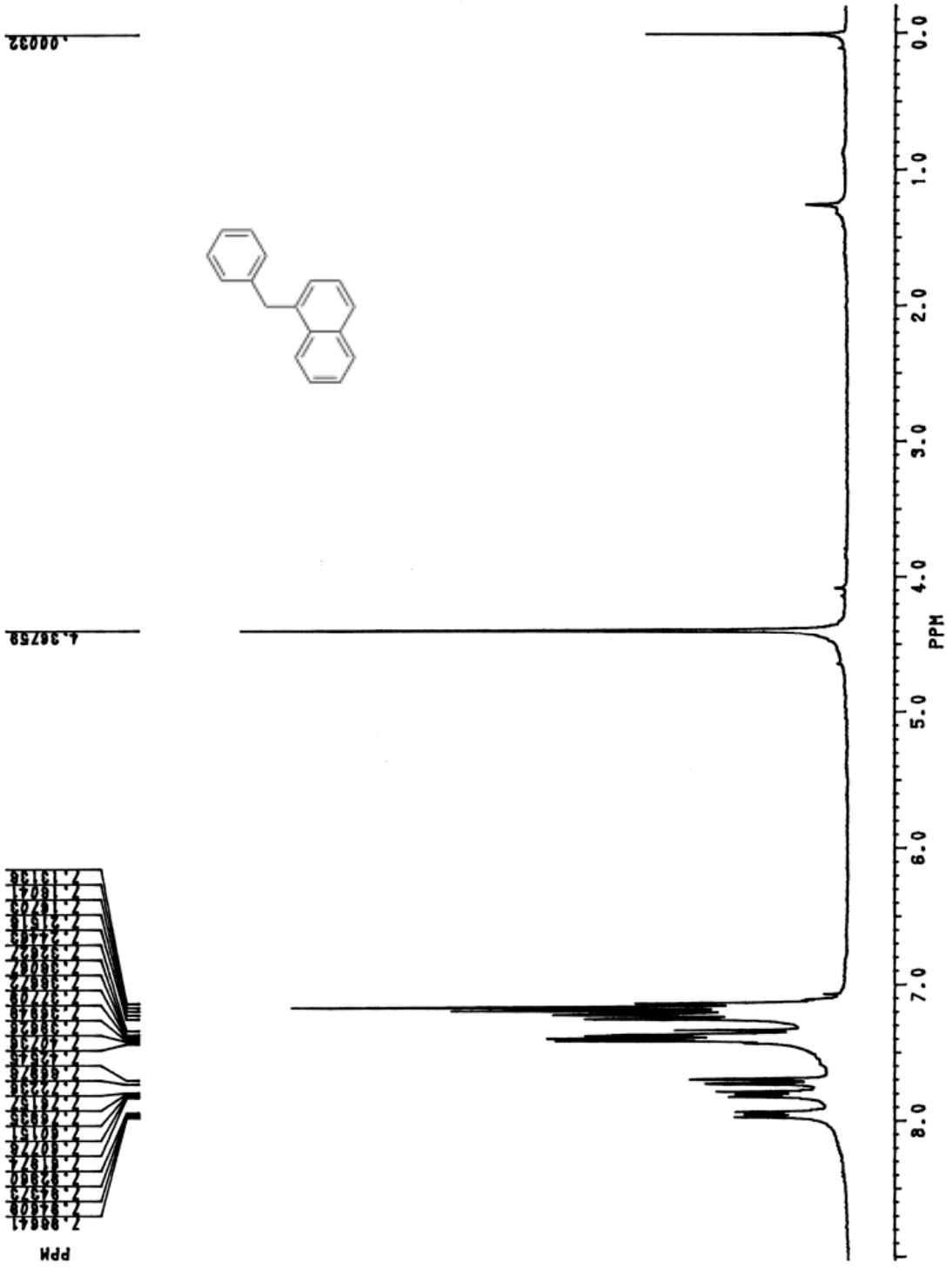
^{1}H spectrum of 9a



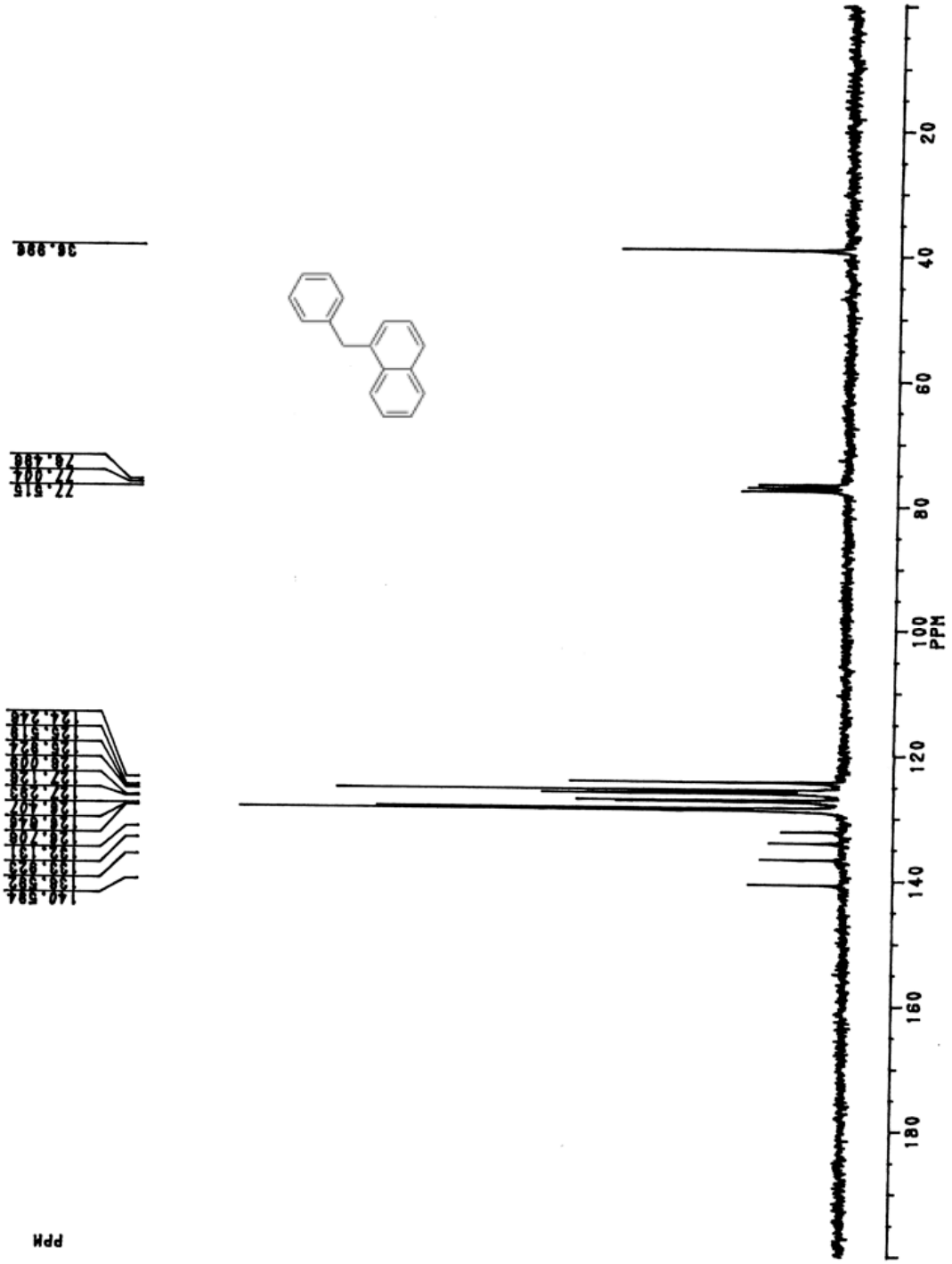
^{13}C spectrum of 9a



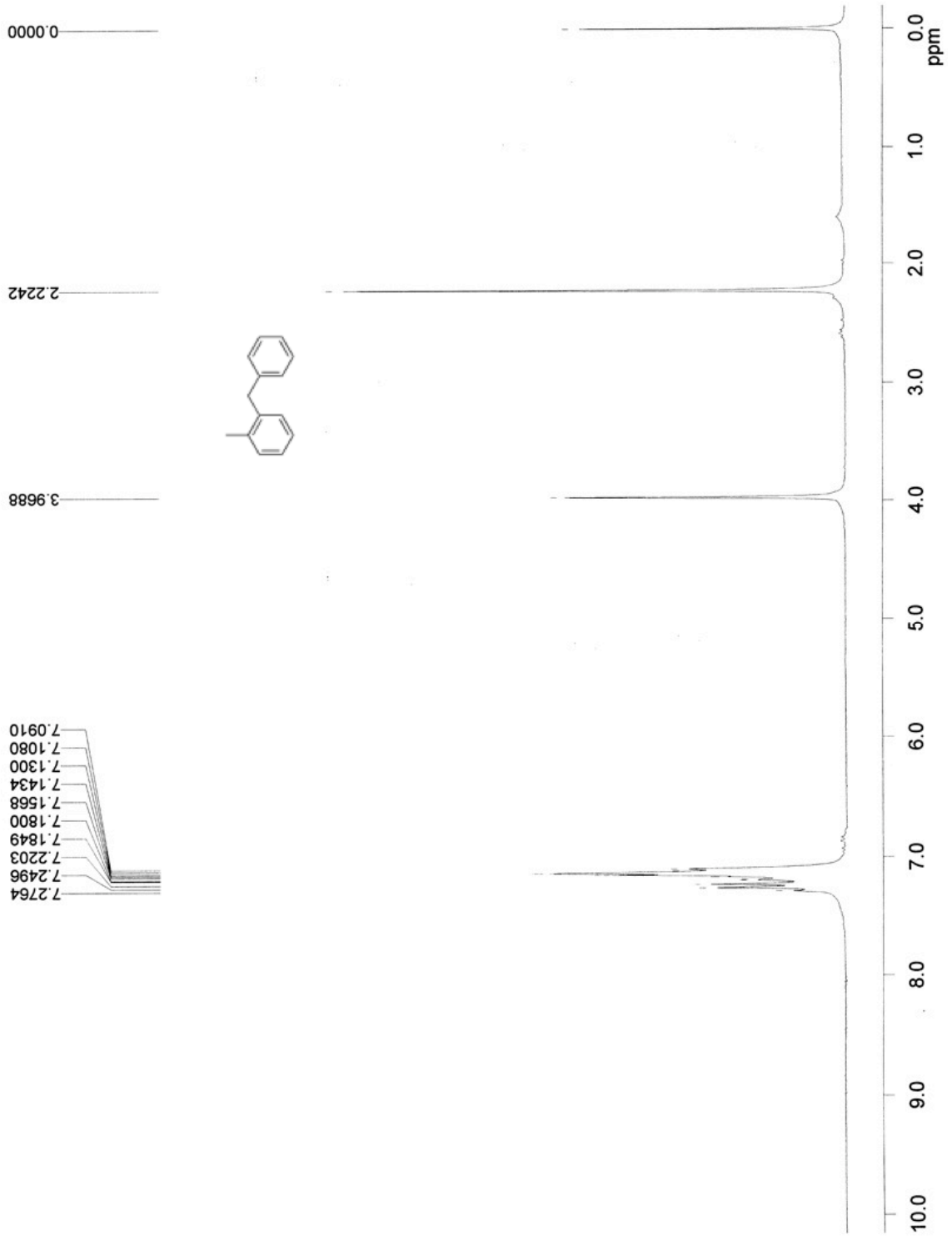
^{1}H spectrum of 9b



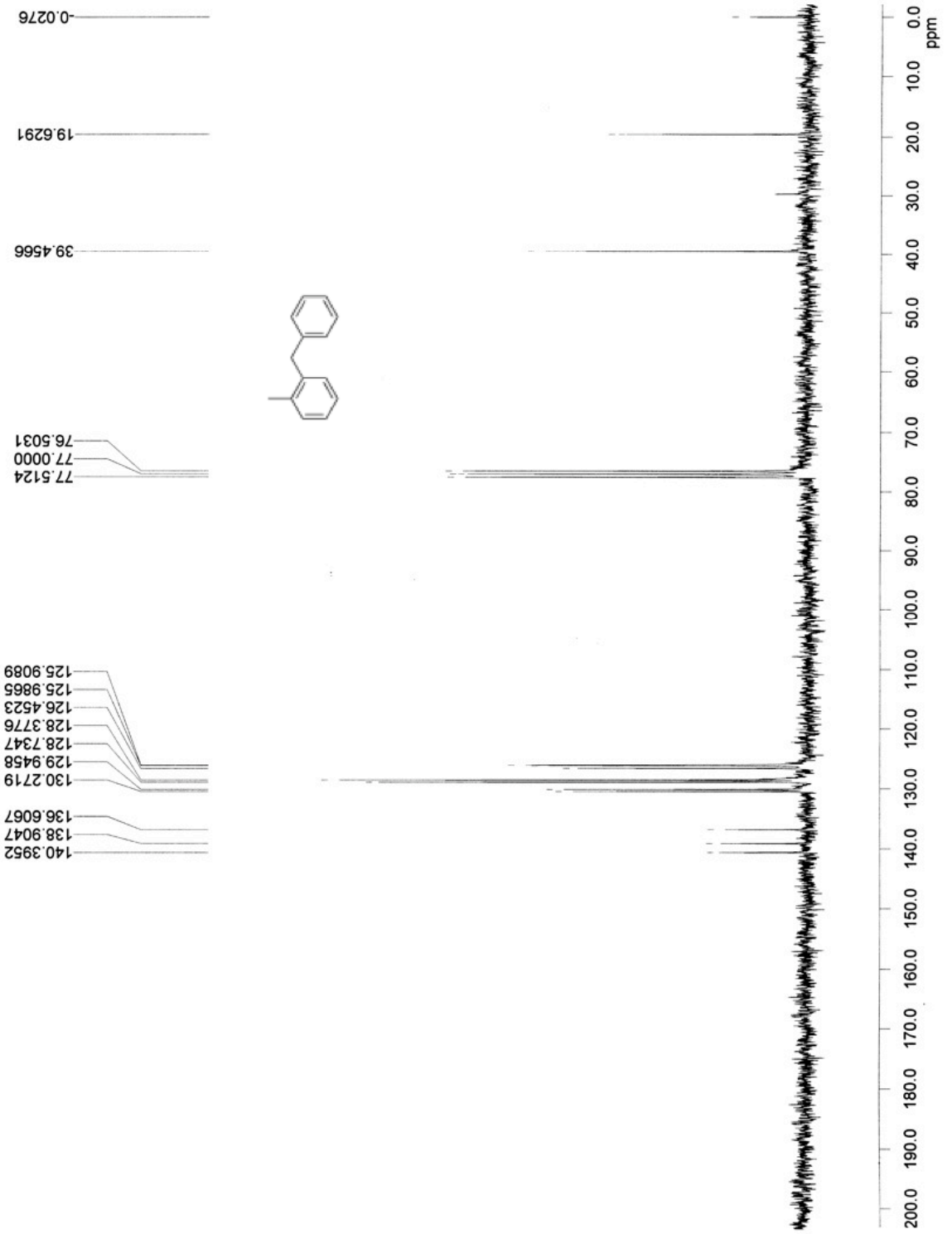
^{13}C spectrum of 9b



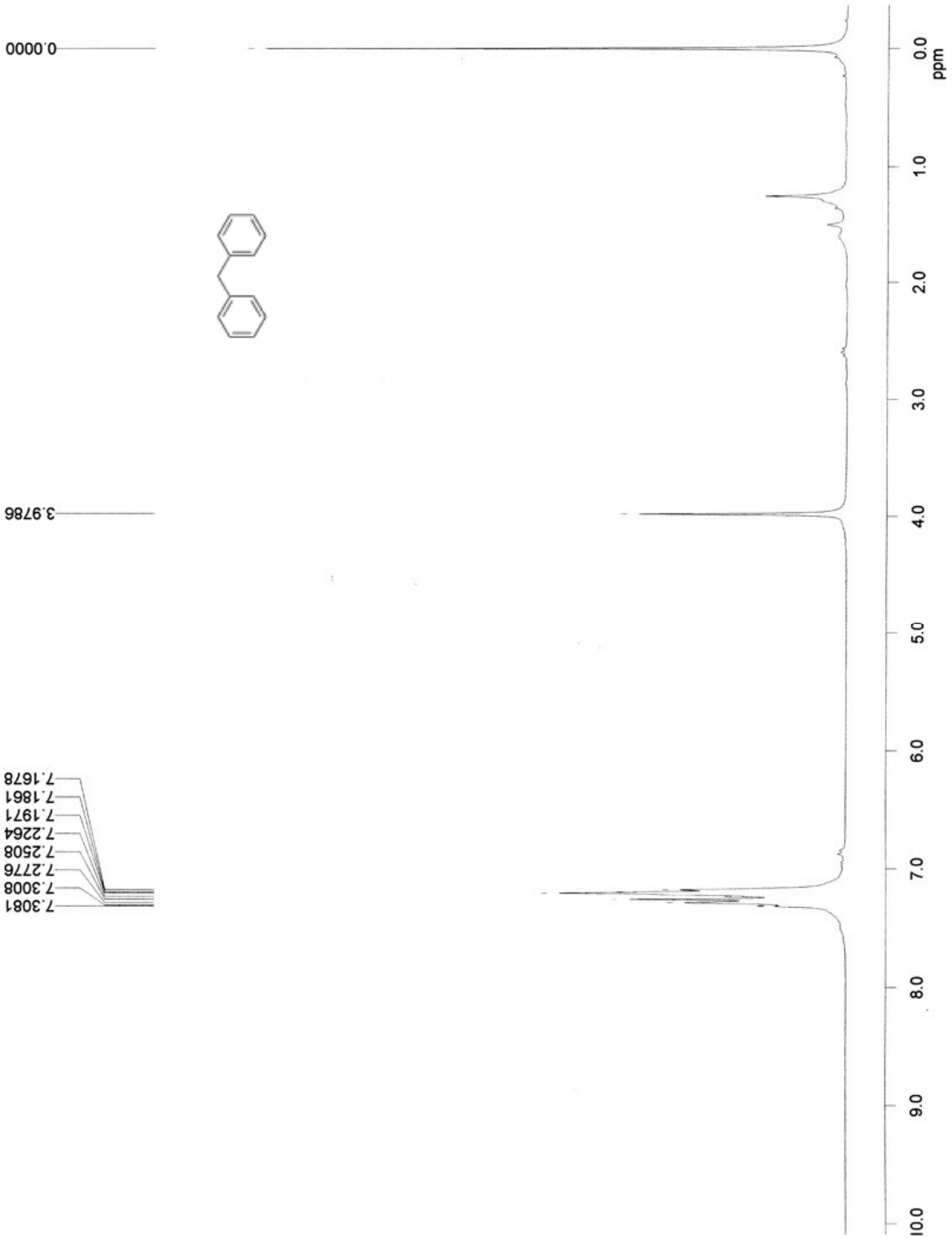
^{1}H spectrum of 9d



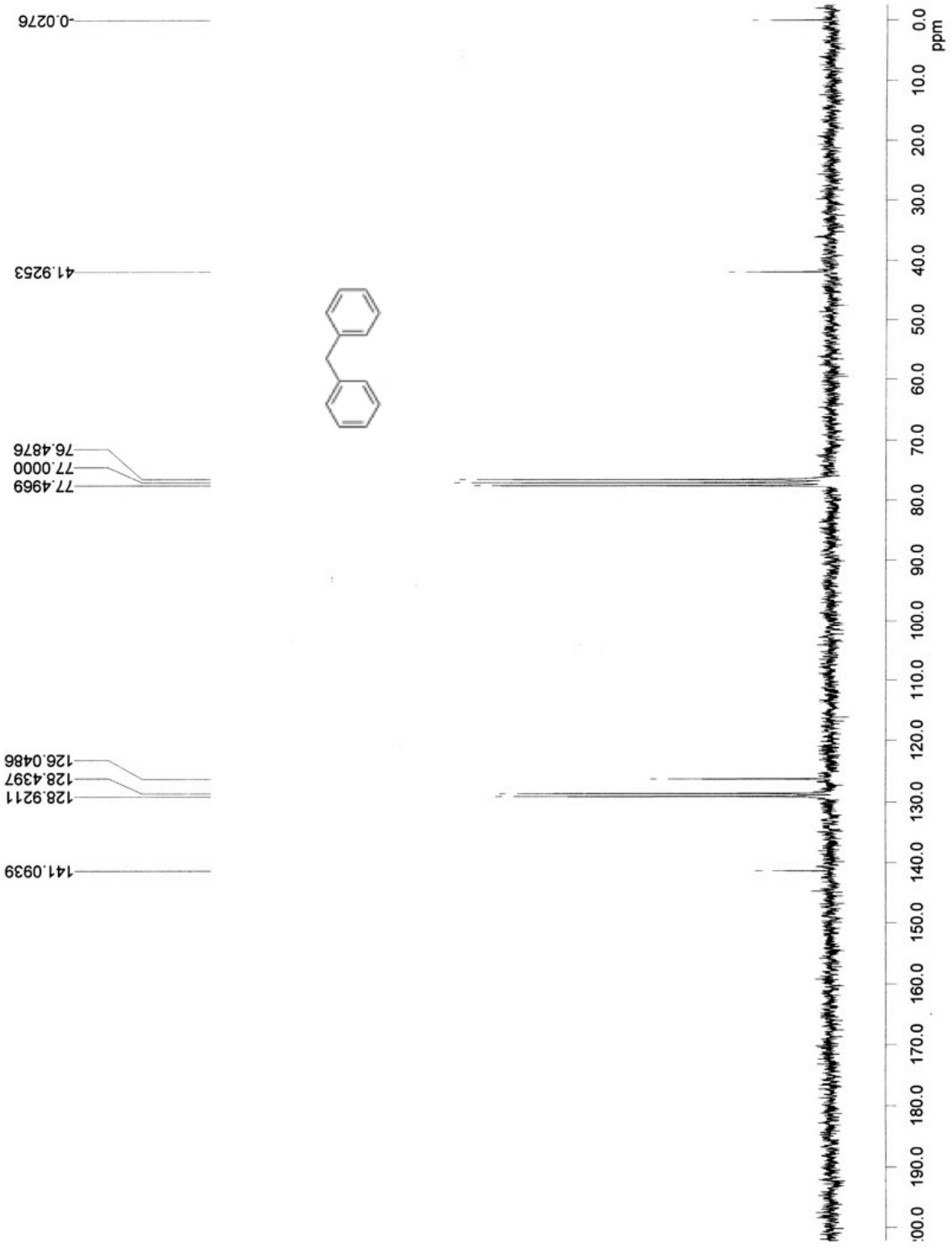
^{13}C spectrum of 9d



^{1}H spectrum of 9e



^{13}C spectrum of 9e



Chapter 5. Titanium(IV) Halide Mediated Alkenylation of Allylic, Benzylic and Propargylic Alcohols

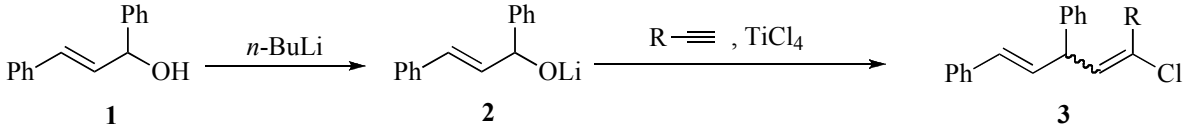
5.1 Introduction

Allylic, benzylic and propargylic alcohols constitute ideal starting materials in synthesis due to their structural diversity, ready availability and low cost. Classic methods for substitution of the hydroxyl group in these types of alcohols are centered on transformation of the hydroxyl moiety into a more reactive leaving group (Br, I, OTF, etc.). Strategies for direct carbon-carbon bond coupling using these alcohols generally require transition–metal catalysts that include palladium,[115] ruthenium,[56] rhenium,[116] copper,[117] gold[49] and rhodium.[50] These reactions typically require stringent reaction conditions (high reaction temperatures and sealed tubes) and prolonged periods of time.

Previously, our research group demonstrated the alkenylation of allylic[63] and benzylic[64] alcohols using boron trihalide. In these studies, a stereodefined alkenylboron dihalide was coupled with an allylic alcohol, or a vinylboron dihalide was coupled with a benzylic alcohol. In both of these studies, the products were all obtained as the *Z* stereoisomer. A preliminary reaction was run with titanium(IV) chloride replacing boron trihalide, resulting in the formation of primarily the *E* stereoisomer. To investigate this outcome further, the selected alcohols were treated with *n*-butyllithium and, sequentially, substituted phenylacetylenes and titanium(IV) halide. These conditions afforded the products in moderate to good yields, with high (*E*,*Z*) ratios.

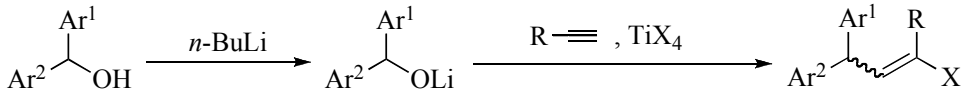
5.2 Results and Discussion

In this study, we investigated the TiX_4-mediated reactions of alkoxides with substituted phenylacetylenes. The alkoxides were generated from the reaction of *n*-butyllithium with, allylic alcohols (**Scheme 5-1**), benzylic alcohols (**Scheme 5-2**) and propargylic alcohols (**Scheme 5-3**). Subsequent addition of a substituted phenylacetylene and titanium(IV) halide generated the products. This investigation offered several advantages: acid-sensitive groups such as –OMe were readily tolerated; halogens on phenyl rings were retained; and free alkenes and alkynes were not transformed.



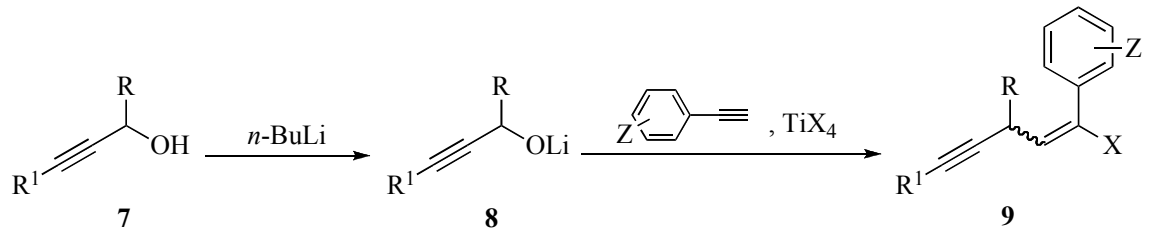
1 **2** **3**

Scheme 5-1 Alkenylation of 1,3-diphenyl-prop-3-en-2-ol using *n*-butyllithium, substituted phenylacetylene and titanium(IV) chloride



4 **5** **6**

Scheme 5-2 Alkenylation of benzylic alcohols using *n*-butyllithium, substituted phenylacetylene and titanium(IV) halide

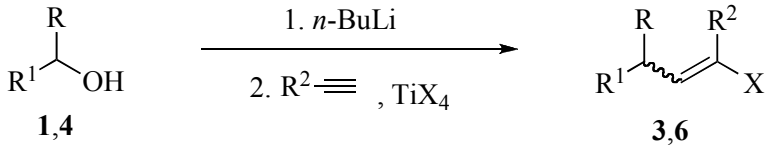


7 **8** **9**

Scheme 5-3 Alkenylation of propargylic alcohols using *n*-butyllithium, substituted phenylacetylene, and titanium(IV) halide

We now demonstrate that allylic, benzylic, and propargylic alcohols undergo alkenylation in these titanium(IV) halide mediated reactions (**Table 5-1** and **Table 5-2**). Alcohols, in dichloromethane, are treated with *n*-butyllithium at 0 °C and allowed to warm to room temperature for thirty minutes. Phenylacetylenes, followed by titanium(IV) halide, are added at room temperature and the reaction allowed to proceed overnight. Following work-up and chromatography, the alkenylated alcohols **3a-3c**, **6a-6l** and **9a-9j** are obtained in moderate to good yield.

Table 5-1 Alkenylation of Allylic and Benzylic Alcohols with Substituted Phenylacetylenes and Titanium(IV) Halide[a]



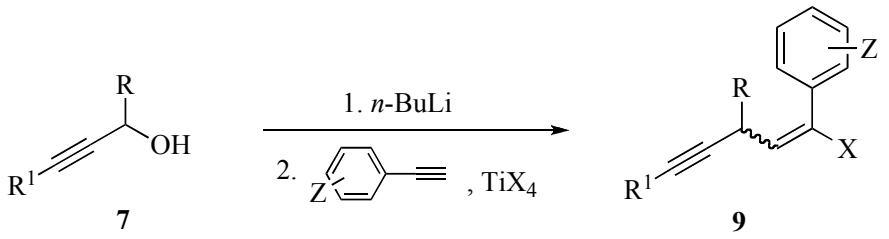
1,**4** **3**,**6**

Entry	R	R^1	R^2	X	Product	*E*/*Z*[b]	Yield
1	Ph	(*E*)-PhCH=CH	Ph	Cl	**3a**	100/0	68
2	Ph	(*E*)-PhCH=CH	3-FC_6H_4	Cl	**3b**	99/1	52
3	Ph	(*E*)-PhCH=CH	3-$MeOC_6H_4$	Cl	**3c**	98/2	46
4	Ph	2-MeC_6H_4	Ph	Cl	**6a**	99/1	58
5	4-FC_6H_4	4-FC_6H_4	Ph	Cl	**6b**	98/2	81
6	Ph	4-MeC_6H_4	Ph	Cl	**6c**	98/2	61
7	Ph	Ph	Ph	Cl	**6d**	96/4	78
8	Ph	4-ClC_6H_4	Ph	Cl	**6e**	96/4	65
9	4-FC_6H_4	4-FC_6H_4	4-MeC_6H_4	Cl	**6f**	98/2	76
10	Ph	Ph	4-MeC_6H_4	Cl	**6g**	98/2	55
11	4-$MeOC_6H_4$	4-$MeOC_6H_4$	Ph	Cl	**6h**	92/8	43
12	Ph	Ph	*n*-Bu	Cl	**6i**	70/30	62
13	Ph	Ph	4-MeC_6H_4	Br	**6j**	98/2	79
14	4-$MeOC_6H_4$	4-$MeOC_6H_4$	4-MeC_6H_4	Br	**6k**	96/4	59
15	4-$MeOC_6H_4$	4-$MeOC_6H_4$	Ph	Br	**6l**	96/4	64

[a] Reaction carried out at 0°C for 10 minutes, then maintained at room temperature (see Experimental for details).

[b] *E*/*Z* ratio determined by NMR.

Table 5-2 Alkenylation of Propargylic Alcohols with Substituted Phenylacetylenes and Titanium(IV) Halide[a]

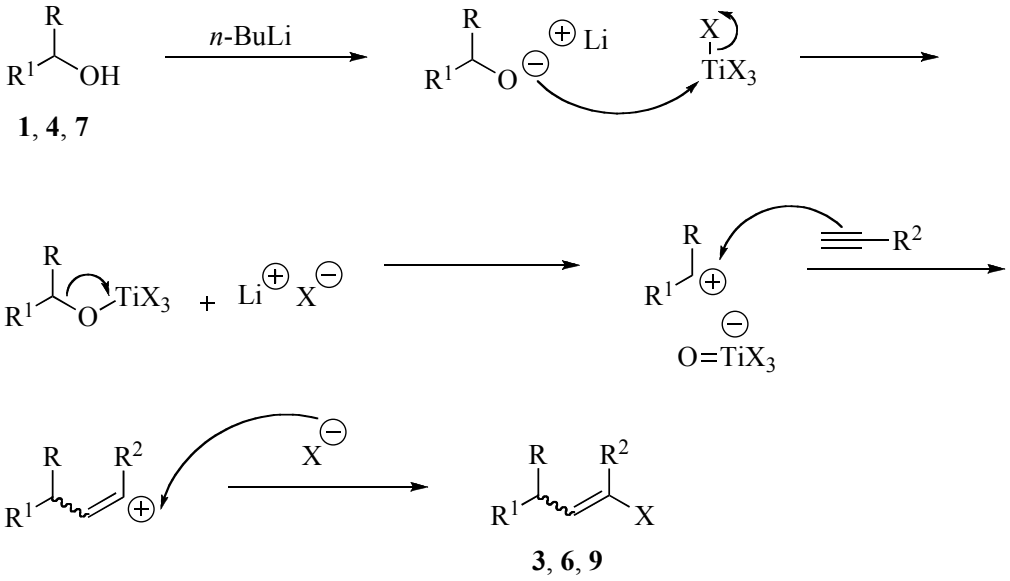


Entry	R	R^1	Z	X	Product	*E*/*Z*[b]	Yield(%)
1	4-ClC_6H_4	*n*-Bu	H	Cl	**9a**	99/1	68
2	4-ClC_6H_4	*n*-Bu	4-Me	Cl	**9b**	99/1	68
3	4-MeC_6H_4	*n*-Bu	H	Cl	**9c**	99/1	67
4	Ph	Ph	H	Cl	**9d**	98/2	75
5	*n*-Hx	Ph	H	Cl	**9e**	97/3	67
6	*n*-Pr	Ph	H	Cl	**9f**	96/4	71
7	Ph	*n*-Bu	H	Br	**9g**	99/1	76
8	Ph	Ph	H	Br	**9h**	99/1	74
9	Ph	*n*-Bu	4-Me	Br	**9i**	99/1	66
10	4-ClC_6H_4	*n*-Bu	H	Br	**9j**	98/2	66

[a] Reaction carried out at 0°C for 10 minutes, then maintained at room temperature (see Experimental for details).

[b] *E*/*Z* ratio determined by NMR.

In general, these reactions produce a high ratio of the *E* product to the *Z* product. The lowest (*E*,*Z*) ratio was obtained during the reaction of benzhydrol with 1-hexyne and titanium(IV) chloride (**6i**, **Table 5-1**). It is possible that the lower (*E*,*Z*) ratio for this entry could be due to the lack of steric bulk when R^2 is the *n*-butyl group (**Scheme 5-4**). The other entries have R^2 as an aryl group, thus hindering attack of the halide ion sufficiently to result in little of the *Z* isomer. Also, when R^2 is an aryl group, the carbocation is stabilized through resonance. **Scheme 5-4** contains a possible mechanism for the reaction of allylic, benzylic, or propargylic alcohols with *n*-butyllithium, followed by addition of alkyne and titanium(IV) halide.



Scheme 5-4 Proposed mechanism for the formation of alkenylated products **3**, **6** and **9**

5.3 Conclusions

A method for synthesizing alkenylated allylic, benzylic, and propargylic derivatives using phenylacetylenes and titanium(IV) halide is described. It is now possible to generate alkenylated products in a 100:0 (*E*,*Z*) ratio using the conditions described. Several examples illustrate that the reaction conditions do not cleave ether moieties, dehalogenate phenyl rings, or destroy double or triple bonds present in the starting materials. Presumably, any allylic, benzylic or propargylic alcohol will be alkenylated by phenylacetylenes in the presence of titanium(IV) halide, using the conditions described in this study.

5.4 Experimental

5.4.1 General Methods

All reagents were used as received. Reagents not commercially available were prepared following known procedures. Column chromatography was performed using silica gel (60 Å, 230–400 mesh, ICN Biomedicals GmbH, Eschwege, Germany). Analytical thin-layer chromatography was performed using 250 μm silica (Analtech, Inc., Newark, DE). Atlantic Microlabs (Norcross, GA) performed microanalysis.

^{1}H NMR and ^{13}C NMR spectra were recorded at 250.13 and 62.89 MHz, respectively. Chemical shifts for ^{1}H NMR and ^{13}C NMR spectra were referenced to TMS and measured with respect to the residual protons in the deuterated solvents.

5.4.2 Typical Reaction Procedure: Alcohol to Alkenylated Allylic, Benzylic and Propargylic Systems

Phenyl(*o*-tolyl)methanol (0.30 g, 1.5 mmol) and dichloromethane (15 mL) were placed in a dry, argon-flushed, 100 mL round-bottomed flask equipped with a magnetic stirring bar. The solution was cooled to 0 °C in an ice bath and *n*-butyllithium (1.0 mL, 1.6 mmol of a 1.0 *M* hexanes solution) was added *via* syringe. The solution was allowed to stir for 10 minutes at 0 °C and then for 30 minutes at room temperature. Phenylacetylene (0.16 mL, 1.5 mmol) was added *via* syringe, followed by titanium(IV) chloride (1.65 mL g, 1.65 mmol of a 1.0 *M* dichloromethane solution). The reaction solution gradually turned dark purple and was allowed to react overnight. The resulting mixture was hydrolyzed with water (15 mL) and extracted into dichloromethane (3 x 15 mL). The organic layer was separated and dried over anhydrous $MgSO_4$. Product **6a** (0.28 g, 99:1 (*E*,*Z*), 58% yield) was isolated by flash column chromatography, using hexanes as eluent.

5.4.3 Characterization of Compounds 3a-3c, 6a-6l and 9a-9j

((4*E*)-1-Chloropenta-1,4-diene-1,3,5-triyl)tribenzene (3a): ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.12-7.45 (m, 15H); 6.20-6.47 (m, 3H); 4.29-4.35 (m, 1H). ^{13}C NMR ($CDCl_3$): δ 142.2, 136.9, 131.6, 131.2, 130.7, 128.8, 128.7, 128.5, 128.3, 127.6, 127.5, 126.8, 126.3, 48.4. Anal. Calcd For $C_{23}H_{19}Cl$: C, 83.50; H, 5.79. Found: C, 83.61; H, 5.97.

((1*E*)-5-Chloro-5-(3-fluorophenyl)penta-1,4-diene-1,3-diyl)dibenzene (3b)[118]: ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.03-7.38 (m, 14H); 6.19-6.42 (m, 3H); 4.31 (t, 1H, ^{3}J = 8.3 Hz). ^{13}C NMR ($CDCl_3$): δ 160.5, 141.9, 136.8, 131.3, 130.9, 130.0, 129.9, 128.9, 128.6, 127.6, 127.2, 126.9, 126.3, 124.3, 116.1, 115.9, 115.8, 48.5.

((1*E*)-5-Chloro-5-(3-methoxyphenyl)penta-1,4-diene-1,3-diyl)dibenzene (3c): ^{1}H NMR (250 MHz, $CDCl_3$): δ 6.76-7.49 (m, 14H); 6.19-6.49 (m, 3H); 4.36 (t, 1H, ^{3}J = 6.0 Hz); 3.74 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 159.4, 142.3, 138.2, 136.9, 131.2, 130.8, 130.4, 129.4, 128.8, 128.5, 127.6, 127.5, 126.8, 126.3, 119.1, 114.9, 113.8, 55.2, 48.5. Anal. Calcd For $C_{24}H_{21}ClO$: C, 79.88; H, 5,87. Found: C, 79.42; H, 6.13.

(1-Chloro-3-*o*-tolylprop-1-ene-1,3-diyl)dibenzene (6a): ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.05-7.30 (m, 14H); 6.41 (d, 1H, ^{3}J = 10.7 Hz); 4.94 (d, 1H, ^{3}J = 10.7 Hz); 1.91 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 143.2, 141.5, 136.9, 135.9, 131.4, 131.2, 130.7, 128.8, 128.6, 128.5, 128.3, 127.9, 126.7, 126.5, 126.4, 47.5, 20.5. Anal. Calcd. for $C_{22}H_{19}Cl$: C, 82.87; H, 6.01. Found: C, 83.17; H, 6.13.

4,4'-(3-Chloro-3-phenylprop-2-ene-1,1-diyl)bis(fluorobenzene) (6b): ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.28-7.32 (m, 5H); 6.96-7.10 (m, 8H); 6.36 (d, 1H, ^{3}J = 9.0 Hz); 4.74 (d, 1H, ^{3}J = 9.0 Hz). ^{13}C NMR ($CDCl_3$): δ 159.9, 138.9, 136.6, 130.9, 129.6, 129.5, 129.1, 128.5, 115.7, 115.4, 49.2. Anal. Calcd. for $C_{21}H_{15}ClF_2$: C, 74.01; H, 4.44. Found: C, 74.47; H, 4.45.

(1-Chloro-3-*p*-tolylprop-1-ene-1,3-diyl)dibenzene (6c): ^{1}H NMR (250 MHz, $CDCl_3$): δ 6.97-7.37 (m, 14H); 6.44 (d, 1H, ^{3}J = 11.0 Hz); 4.74 (d, 1H, ^{3}J = 11.0 Hz); 2.27 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 143.5, 140.3, 136.9, 136.1, 131.6, 131.2, 129.3, 128.8, 128.6, 128.3, 128.0, 127.9, 126.5, 50.3, 20.9. Anal. Calcd. for $C_{22}H_{19}Cl$: C, 82.87; H, 6.01. Found: C, 83.87; H, 6.22.

(3-Chloroprop-2-ene-1,1,3-triyl)tribenzene (6d): ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.08-7.36 (m, 15H); 6.45 (d, 1H, ^{3}J = 11.0 Hz); 4.78 (d, 1H, ^{3}J = 11.0 Hz). ^{13}C NMR ($CDCl_3$): δ 143.3, 136.9, 131.5, 131.4, 128.9, 128.6, 128.3, 128.1, 126.6, 50.7. Anal. Calcd. for $C_{21}H_{17}Cl$: C, 82.75; H, 5.62. Found: C, 82.68; H, 5.63.

(1-Chloro-3-(4-chlorophenyl)prop-1-ene-1,3-diyl)dibenzene (6e): ^{1}H NMR (250 MHz, $CDCl_3$): δ 6.96-7.34 (m, 14H); 6.38 (d, 1H, ^{3}J = 11.0 Hz); 4.74 (d, 1H, ^{3}J = 11.0 Hz). ^{13}C NMR ($CDCl_3$): δ 142.7, 141.8, 136.7, 131.9, 130.8, 129.4, 128.9, 128.7, 128.5, 128.4, 127.9, 126.8, 50.1. Anal. Calcd For $C_{21}H_{16}Cl_2$: C, 74.35; H, 4.75. Found: C, 74.49; H, 4.70.

4,4'-(3-Chloro-3-*p*-tolylprop-2-ene-1,1-diyl)bis(fluorobenzene) (6f)[64]: ^{1}H NMR (250 MHz, $CDCl_3$): δ 6.94-7.24 (m, 12H); 6.31 (d, 1H, ^{3}J = 9.0 Hz); 4.74 (d, 1H, ^{3}J = 9.0 Hz); 2.35 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 159.9, 139.1, 138.9, 133.7, 132.1, 130.5, 129.5, 129.1, 128.4, 115.6, 49.2, 21.3.

(3-Chloro-3-*p*-tolylprop-2-ene-1,1-diyl)dibenzene (6g): ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.10-7.30 (m, 14H); 6.41 (d, 1H, ^{3}J = 11.0 Hz); 4.79 (d, 1H, ^{3}J = 11.0 Hz); 2.33 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 143.4, 138.8, 133.9, 130.9, 129.0, 128.6, 128.5, 128.3, 128.1, 126.6, 50.7, 21.3. Anal. Calcd. For $C_{22}H_{19}Cl$: C, 82.87; H, 6.01. Found: C, 82.66; H, 6.04.

4,4'-(3-Chloro-3-phenylprop-2-ene-1,1-diyl)bis(methoxybenzene) (6h)[64]: ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.28-7.37 (m, 5H); 7.00-7.05 (m, 4H); 6.79-6.85 (m, 4H); 6.39 (d, 1H, ^{3}J = 11.0 Hz); 4.68 (d, 1H, ^{3}J = 11.0 Hz); 3.74 (s, 6H). ^{13}C NMR ($CDCl_3$): δ 158.2, 135.7, 131.9, 129.6, 128.7, 128.6, 128.3, 128.0, 126.6, 113.9, 55.1, 49.0.

(3-Chlorohept-2-ene-1,1-diyl)dibenzene (6i)[119]: ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.02-7.32 (m, 20H); 6.09 (d, 1H, ^{3}J = 10.2 Hz); 5.96 (d, 1H, ^{3}J = 9.4 Hz); 5.22 (d, 1H, ^{3}J = 9.4 Hz); 4.86 (d, 1H, ^{3}J = 10.1 Hz); 2.36-2.47 (m, 4H); 1.47-1.62 (m, 4H); 1.10-1.41 (m, 4H); 0.80-0.98 (m, 6H). ^{13}C NMR ($CDCl_3$): δ 143.5, 135.5, 129.9, 128.5, 128.2, 126.5, 126.3, 49.8, 39.3, 33.7, 29.4, 21.9, 13.9.

(3-Bromo-3-*p*-tolylprop-2-ene-1,1-diyl)dibenzene (6j)[64]: ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.08-7.27 (m, 14H); 6.65 (d, 1H, ^{3}J = 11.0 Hz); 4.73 (d, 1H, ^{3}J = 11.0 Hz); 2.30, (s, 3H). ^{13}C NMR ($CDCl_3$): δ 143.0, 138.7, 135.4, 135.1, 128.9, 128.6, 128.5, 128.3, 128.1, 126.5, 121.5, 51.6, 21.3.

4,4'-(3-Bromo-3-*p*-tolylprop-2-ene-1,1-diyl)bis(methoxybenzene) (6k)[64]: ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.23 (d, 2H, ^{3}J = 8.2 Hz); 7.13 (d, 2H, ^{3}J = 8.0 Hz); 7.02 (d, 4H, ^{3}J = 8.5 Hz); 6.82 (d, 4H, ^{3}J = 8.5 Hz); 6.58 (d, 1H, ^{3}J = 10.7 Hz); 4.62 (d, 1H, ^{3}J = 10.7 Hz); 3.76 (s, 6H); 2.34 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 158.2, 138.6, 135.7, 135.5, 129.1, 128.9, 128.6, 127.6, 120.9, 113.9, 55.2, 50.0, 21.3.

4,4'-(3-Bromo-3-phenylprop-2-ene-1,1-diyl)bis(methoxybenzene) (6l)[64]: ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.32 (s, 5H); 7.02 (d, 4H, ^{3}J = 8.6 Hz); 6.82 (d, 4H, ^{3}J = 8.9 Hz); 6.61 (d, 1H, ^{3}J = 11.0 Hz); 4.62 (d, 1H, ^{3}J = 11.0 Hz); 3.75 (s, 6H). ^{13}C NMR ($CDCl_3$): δ 158.2, 136.0, 135.4, 129.2, 128.7, 128.5, 128.2, 127.7, 120.6, 113.9, 55.2, 49.9.

1-Chloro-4-(1-chloro-1-phenylnon-1-en-4-yn-3-yl)benzene (9a): ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.19-7.52 (m, 9H); 5.97 (d, 1H, ^{3}J = 10.4 Hz); 4.41 (d, 1H, ^{3}J = 10.4 Hz); 2.23-2.30 (m, 2H); 1.39-1.57 (m, 4H); 0.90-0.96 (m, 3H). ^{13}C NMR ($CDCl_3$): δ 138.6, 136.4, 132.6, 131.9, 129.4, 129.1, 128.7, 128.6, 128.5, 85.2, 78.3, 36.9, 30.9, 21.9, 18.6, 13.6. Anal. Calcd. for $C_{21}H_{20}Cl_2$: C, 73.47; H, 5.88. Found: C, 73.88; H, 6.02.

1-Chloro-4-(1-chloro-1-*p*-tolylnon-1-en-4-yn-3-yl)benzene (9b)[12]: ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.38-7.43 (m, 2H); 7.18-7.27 (m, 6H); 5.94 (d, 1H, ^{3}J = 10.4 Hz); 4.41 (d, 1H, ^{3}J = 10.4 Hz); 2.35 (s, 3H); 2.23-2.31 (m, 2H); 1.38-1.56 (m, 4H); 0.90-0.96 (m, 3H). ^{13}C NMR ($CDCl_3$): δ 139.1, 138.7, 133.5, 132.7, 132.1, 129.1, 128.9, 128.6, 85.1, 78.4, 36.9, 30.9, 21.9, 21.3, 18.5, 13.6.

1-(1-Chloro-1-phenylnon-1-en-4-yn-3-yl)-4-methylbenzene (9c)[12]: ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.09-7.54 (m, 9H); 6.01 (d, 1H, ^{3}J = 10.5 Hz); 4.39 (d, 1H, ^{3}J = 10.5 Hz); 2.31 (s, 3H); 2.21-2.35 (m, 2H); 1.32-1.59 (m, 4H); 0.88-0.96 (m, 3H). ^{13}C NMR ($CDCl_3$): δ 137.2, 136.6, 131.3, 130.1, 129.4, 129.2, 128.9, 128.8, 128.4, 128.2, 127.1, 84.5, 79.0, 37.1, 30.9, 21.9, 20.9, 18.6.

(1-Chloropent-1-en-4-yne-1,3,5-triyl)tribenzene (9d): ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.15-7.54 (m, 15H); 6.09 (d, 1H, ^{3}J = 10.4 Hz); 4.65 (d, 1H, ^{3}J = 10.4 Hz). ^{13}C NMR ($CDCl_3$): δ 137.9, 136.3, 133.1, 132.8, 131.7, 129.2, 128.8, 128.6, 128.3, 126.5, 122.9, 87.8, 84.8, 37.4. Anal. Calcd. for $C_{23}H_{17}Cl$: C, 84.01; H, 5.22. Found: C, 84.12; H, 4.87.

(1-Chloro-3-hexylpent-1-en-4-yne-1,5-diyl)dibenzene (9e)[12]**:** ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.24-7.50 (m, 10H); 5.96 (d, 1H, ^{3}J = 10.4 Hz); 3.32 (dt, 1H, ^{3}J = 10.4 Hz); 1.51-1.67 (m, 2H); 1.21-1.37 (m, 8H); 0.82-0.88 (m, 3H). ^{13}C NMR ($CDCl_3$): δ 136.8, 131.7, 131.6, 129.7, 128.8, 128.7, 128.3, 128.2, 127.8, 123.5, 90.3, 82.4, 35.8, 32.6, 31.6, 28.8, 26.8, 22.6, 14.0.

(1-Chloro-3-propylpent-1-en-4-yne-1,5-diyl)dibenzene (9f)[12]**:** ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.27-7.50 (m, 10H); 5.95 (d, 1H, ^{3}J = 10.4 Hz); 3.33 (dt, 1H, ^{3}J = 10.4 Hz); 1.37-1.65 (m, 4H); 0.82-0.88 (m, 3H). ^{13}C NMR ($CDCl_3$): δ 131.9, 131.6, 129.7, 128.8, 128.7, 128.3, 128.2, 127.8, 126.6, 123.5, 90.3, 82.3, 37.9, 32.4, 20.1, 13.7.

(1-Bromonon-1-en-4-yne-1,3-diyl)dibenzene (9g)[12]**:** ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.17-7.50 (m, 10H); 6.26 (d, 1H, ^{3}J = 10.4 Hz); 4.37 (d, 1H, ^{3}J = 10.4 Hz); 2.23-2.28 (m, 2H); 1.36-1.59 (m, 4H); 0.89-0.95 (m, 3H). ^{13}C NMR ($CDCl_3$): δ 139.8, 137.9, 133.8, 128.9, 128.5, 128.4, 127.2, 126.9, 121.2, 84.9, 78.5, 38.4, 30.9, 21.9, 18.6, 13.6.

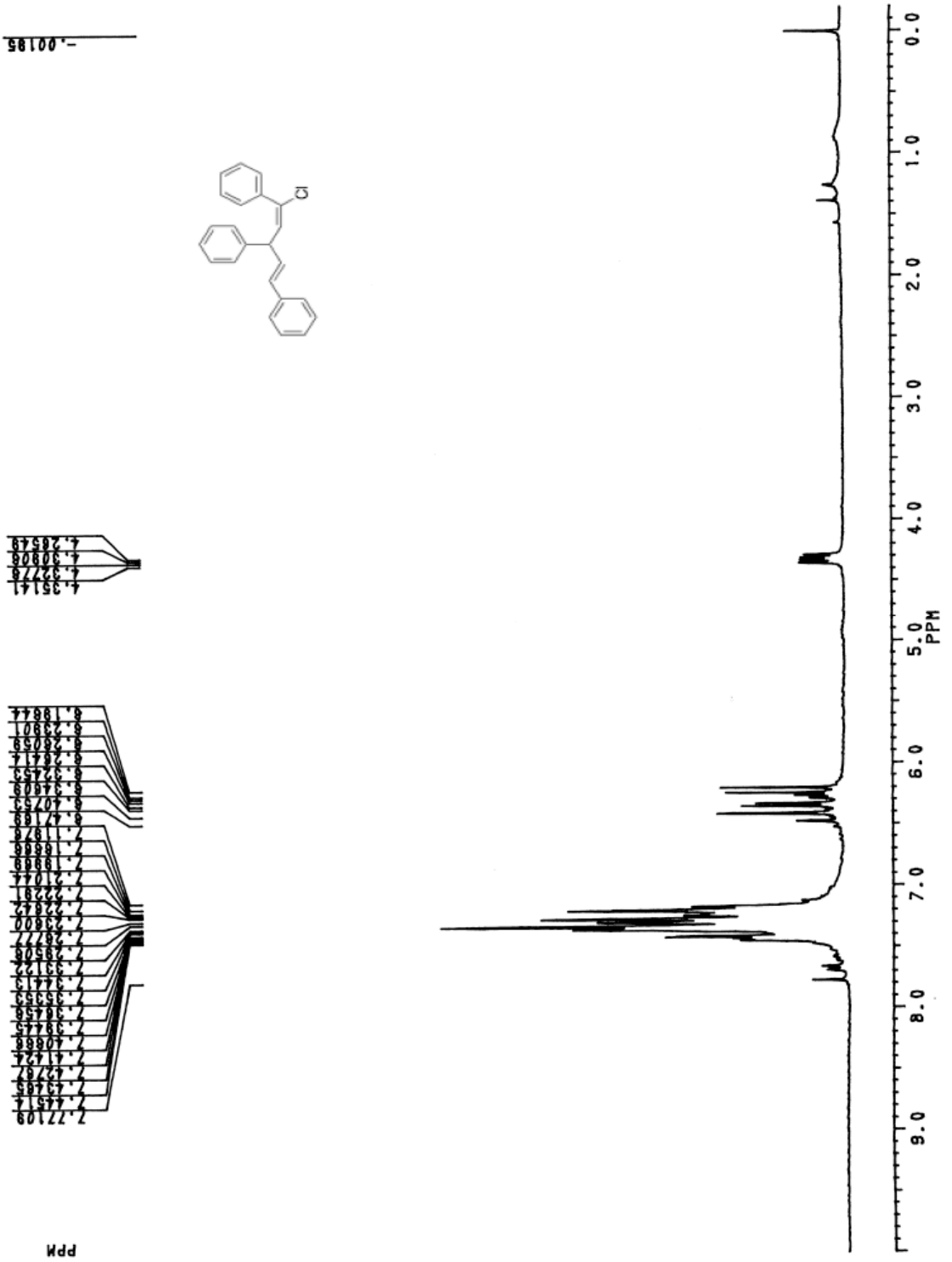
(1-Bromopent-1-en-4-yne-1,3,5-triyl)tribenzene (9h)[12]**:** ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.21-7.53 (m, 15H); 6.37 (d, 1H, ^{3}J = 10.3 Hz); 4.62 (d, 1H, ^{3}J = 10.3 Hz). ^{13}C NMR ($CDCl_3$): δ 139.2, 137.9, 132.9, 131.7, 129.0, 128.9, 128.7, 128.5, 128.3, 128.2, 127.3, 123.1, 122.0, 88.0, 84.5, 38.9.

1-(1-Bromo-3-phenylnon-1-en-4-ynyl)-4-methylbenzene (9i)[12]**:** ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.13-7.40 (m, 9H); 6.22 (d, 1H, ^{3}J = 10.3 Hz); 4.39 (d, 1H, ^{3}J = 10.3 Hz); 2.34 (s, 3H); 2.22-2.30 (m, 2H); 1.38-1.58 (m, 4H); 0.89-0.95 (m, 3H). ^{13}C NMR ($CDCl_3$): δ 139.9, 138.8, 135.1, 133.5, 129.0, 128.8, 128.5, 127.2, 126.9, 121.5, 84.8, 78.6, 38.4, 30.9, 21.9, 21.2, 18.6, 13.6.

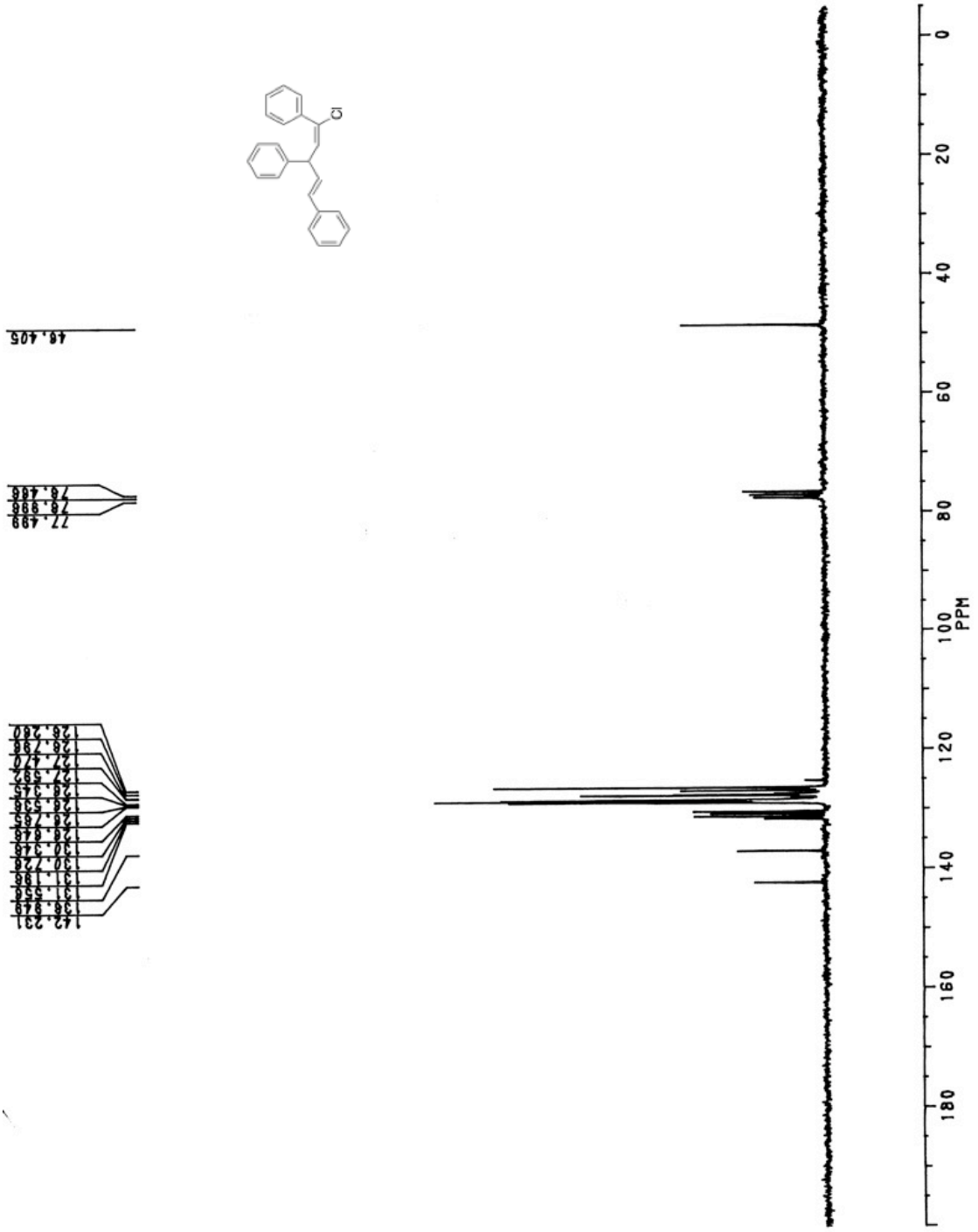
1-(1-Bromo-1-phenylnon-1-en-4-yn-3-yl)-4-chlorobenzene (9j)[12]**:** ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.19-7.49 (m, 9H); 6.20 (d, 1H, ^{3}J = 10.4 Hz); 4.33 (d, 1H, ^{3}J = 10.4 Hz); 2.23-2.29 (m, 2H); 1.36-1.59 (m, 4H); 0.90-0.96 (m, 3H). ^{13}C NMR ($CDCl_3$): δ 138.4, 137.8, 133.3, 132.8, 129.0, 128.8, 128.6, 128.5, 128.4, 121.7, 85.3, 78.1, 37.9, 30.9, 21.9, 18.6, 13.6.

5.4.4 Representative NMR Spectra

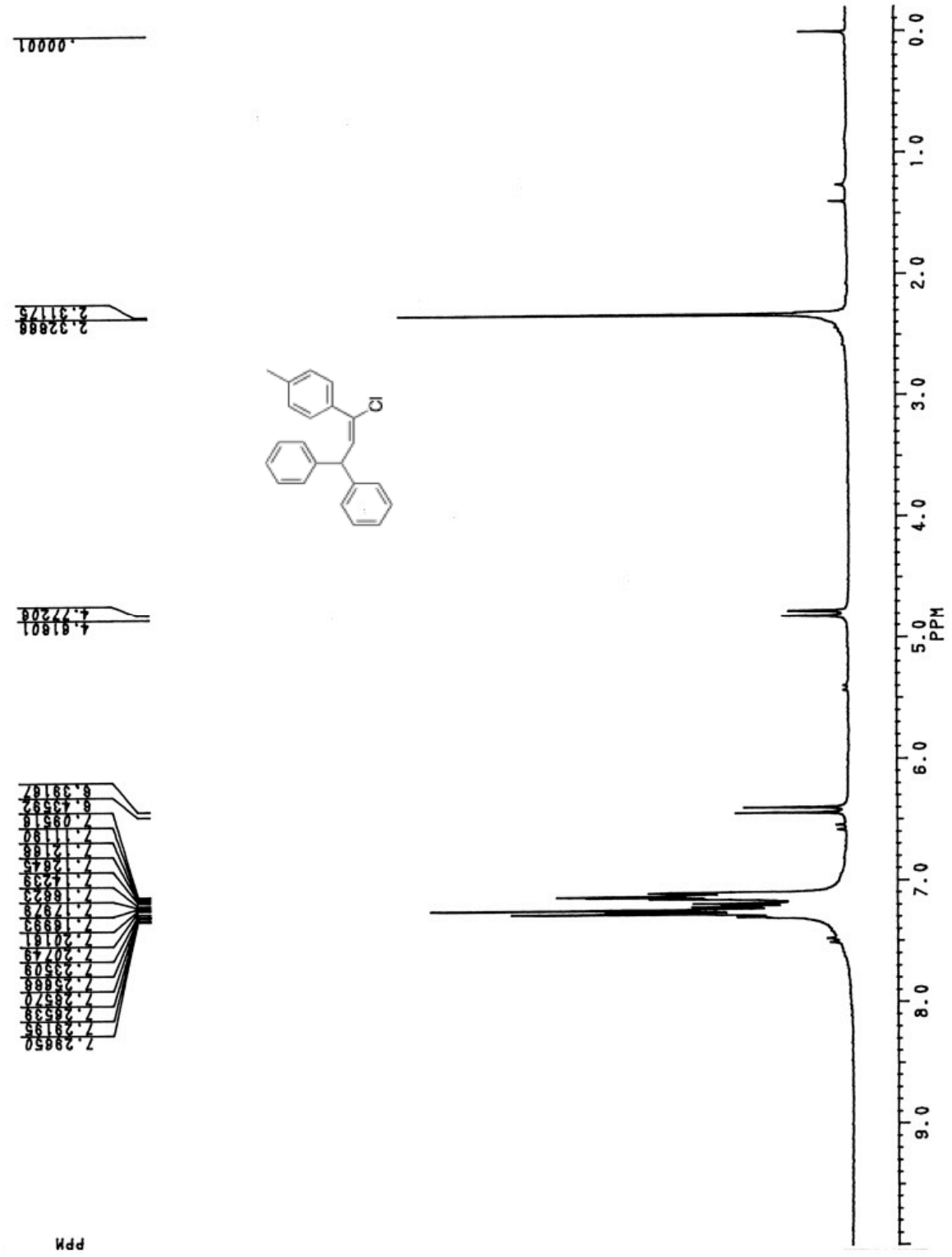
^{1}H spectrum of 3a



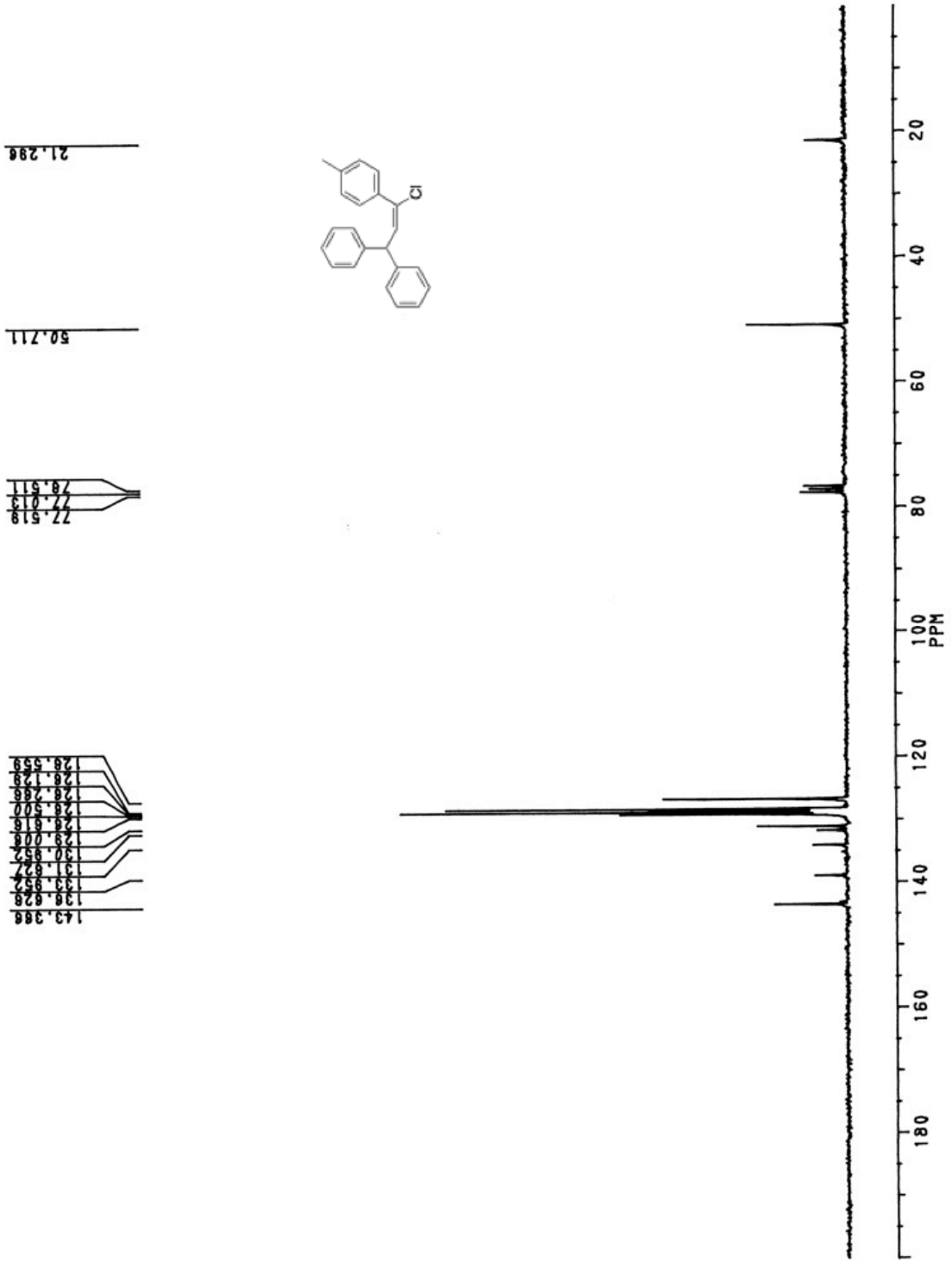
^{13}C spectrum of 3a



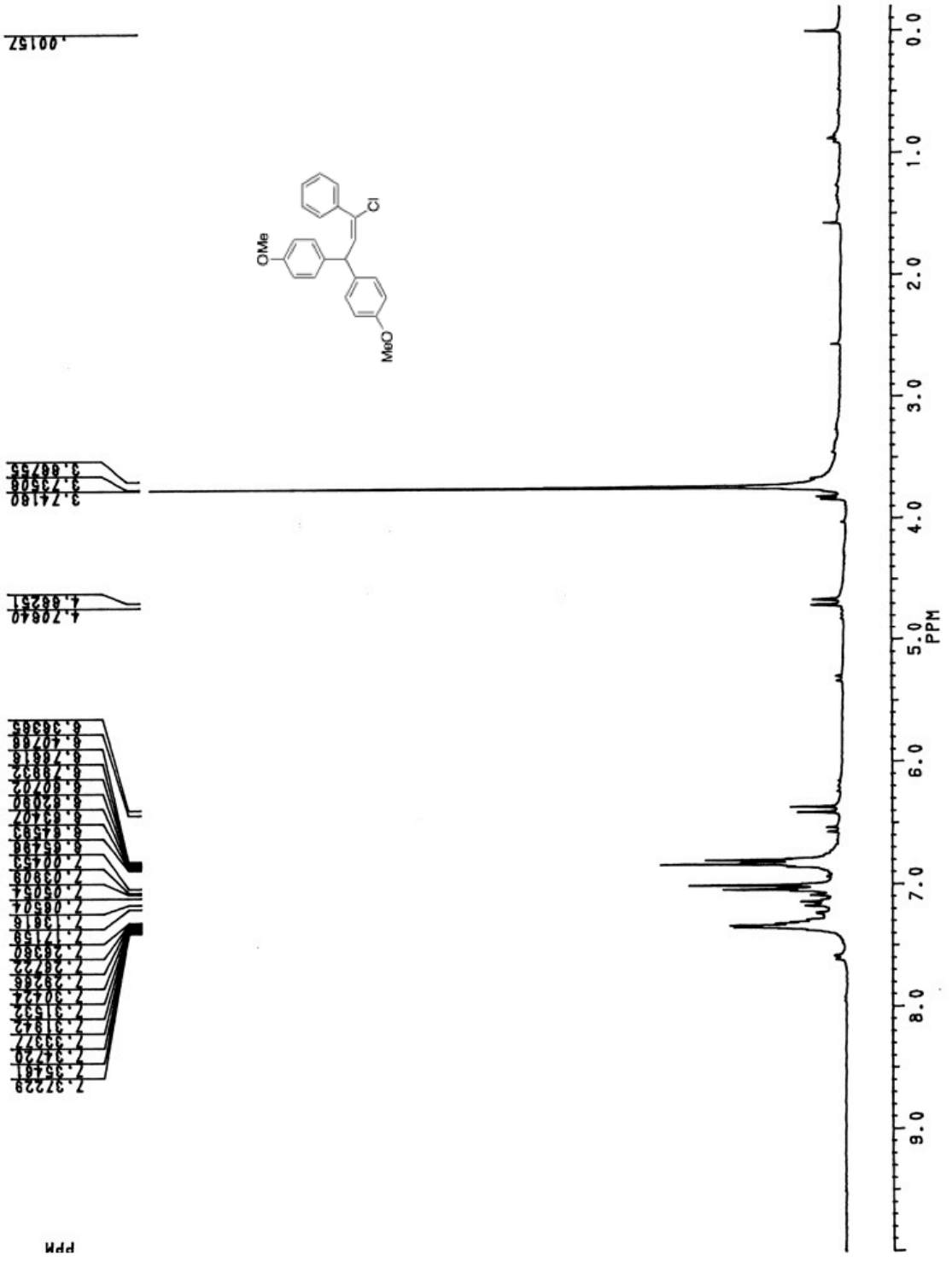
^{1}H spectrum of 6g



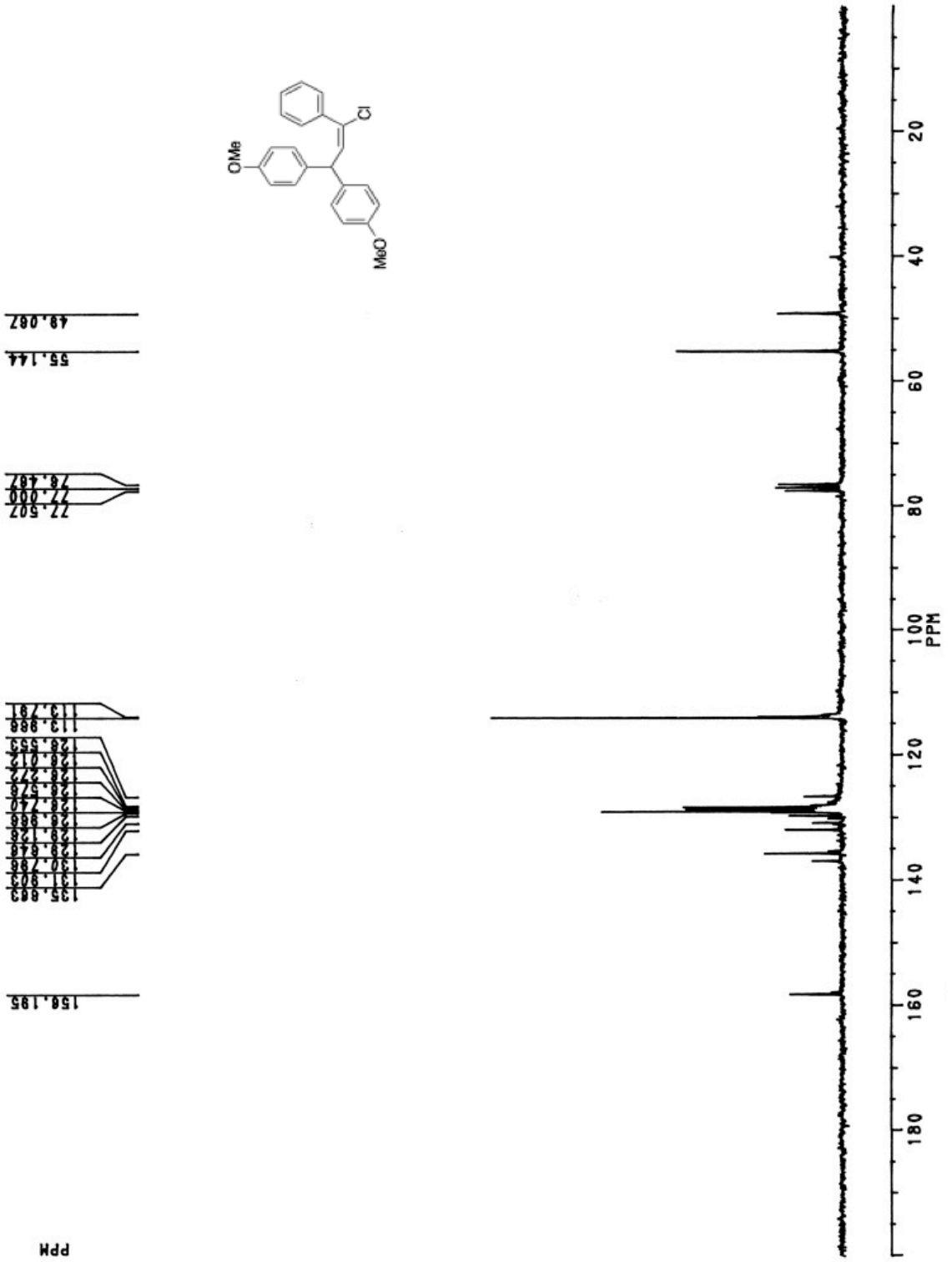
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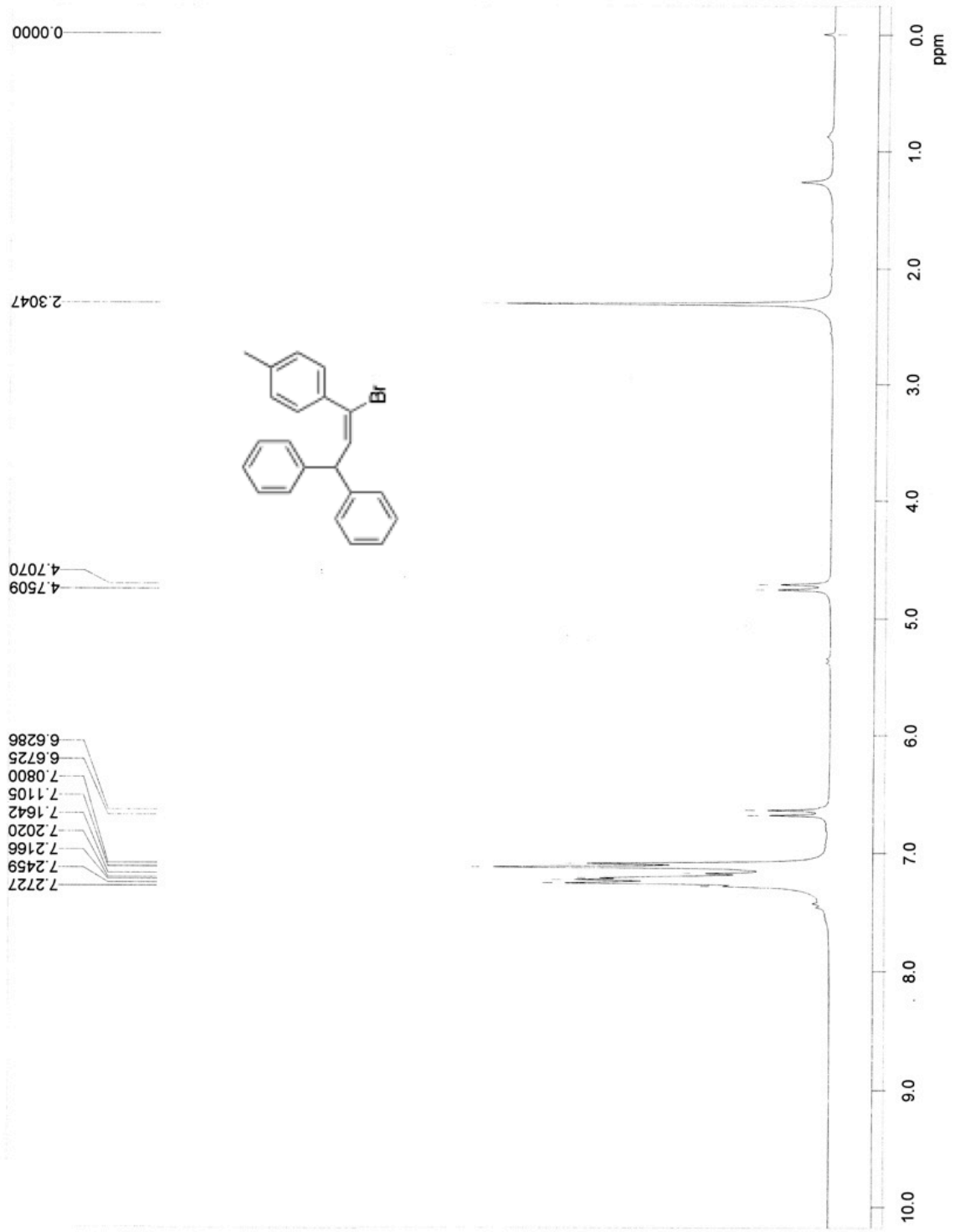
^{1}H spectrum of 6h



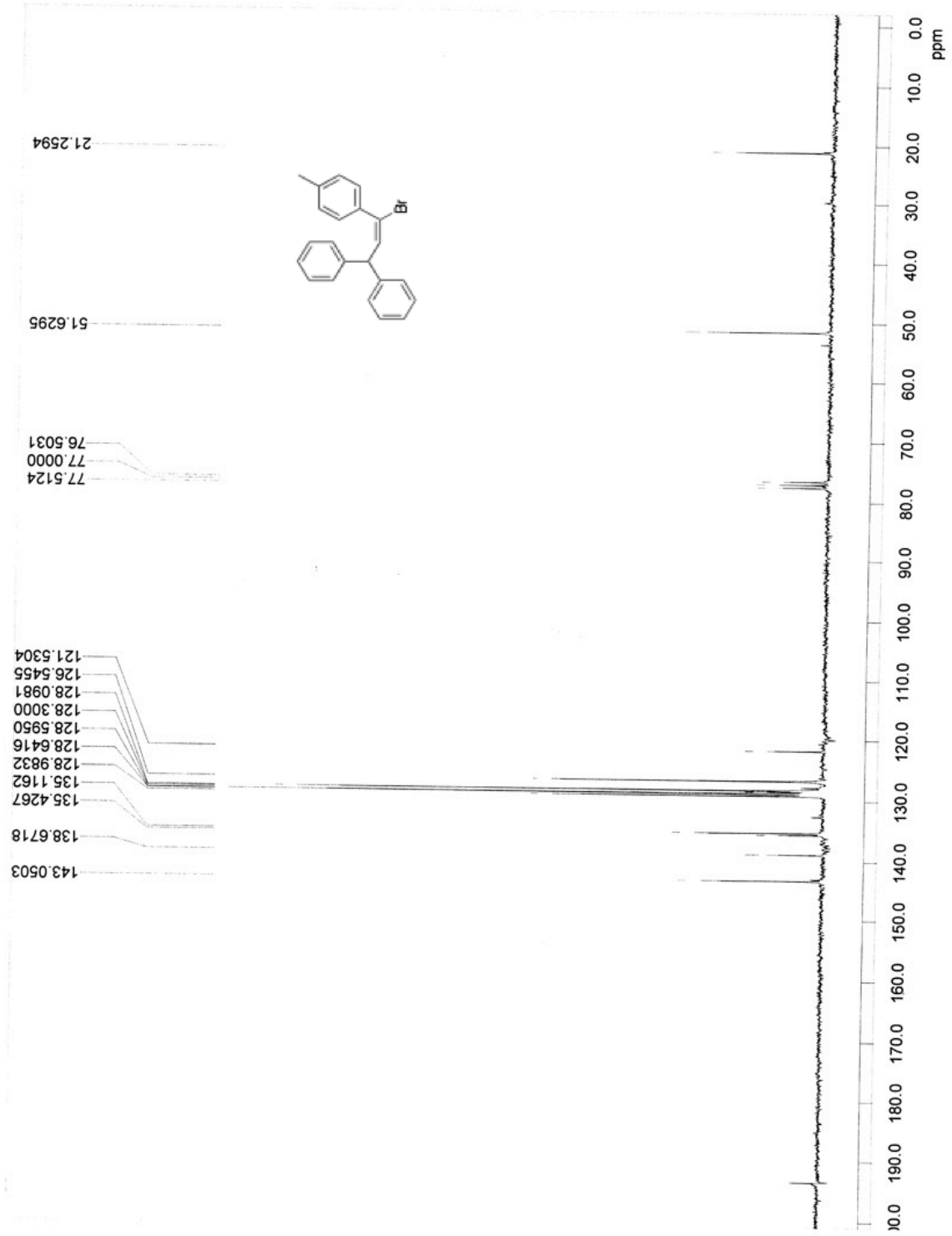
^{13}C spectrum of 6h



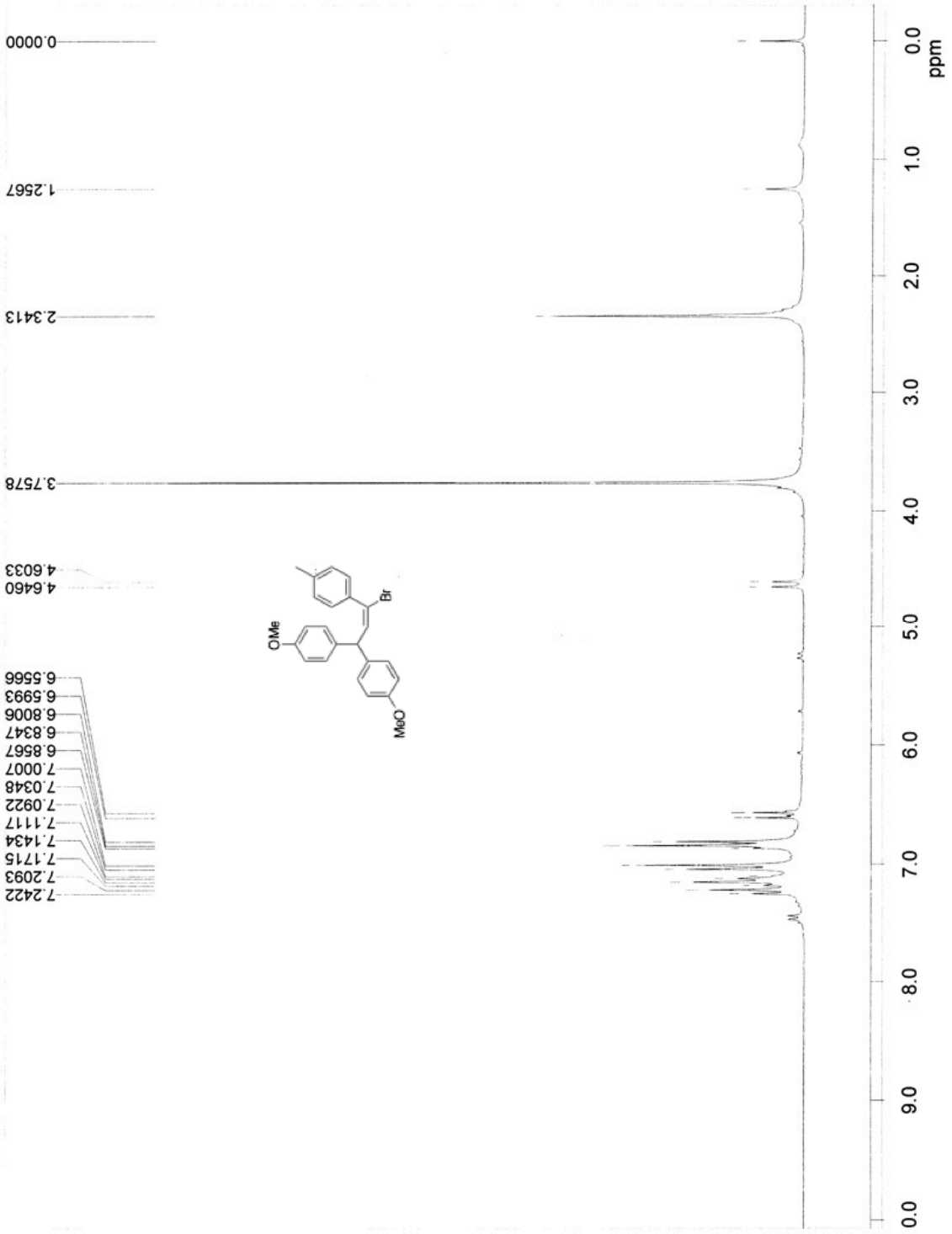
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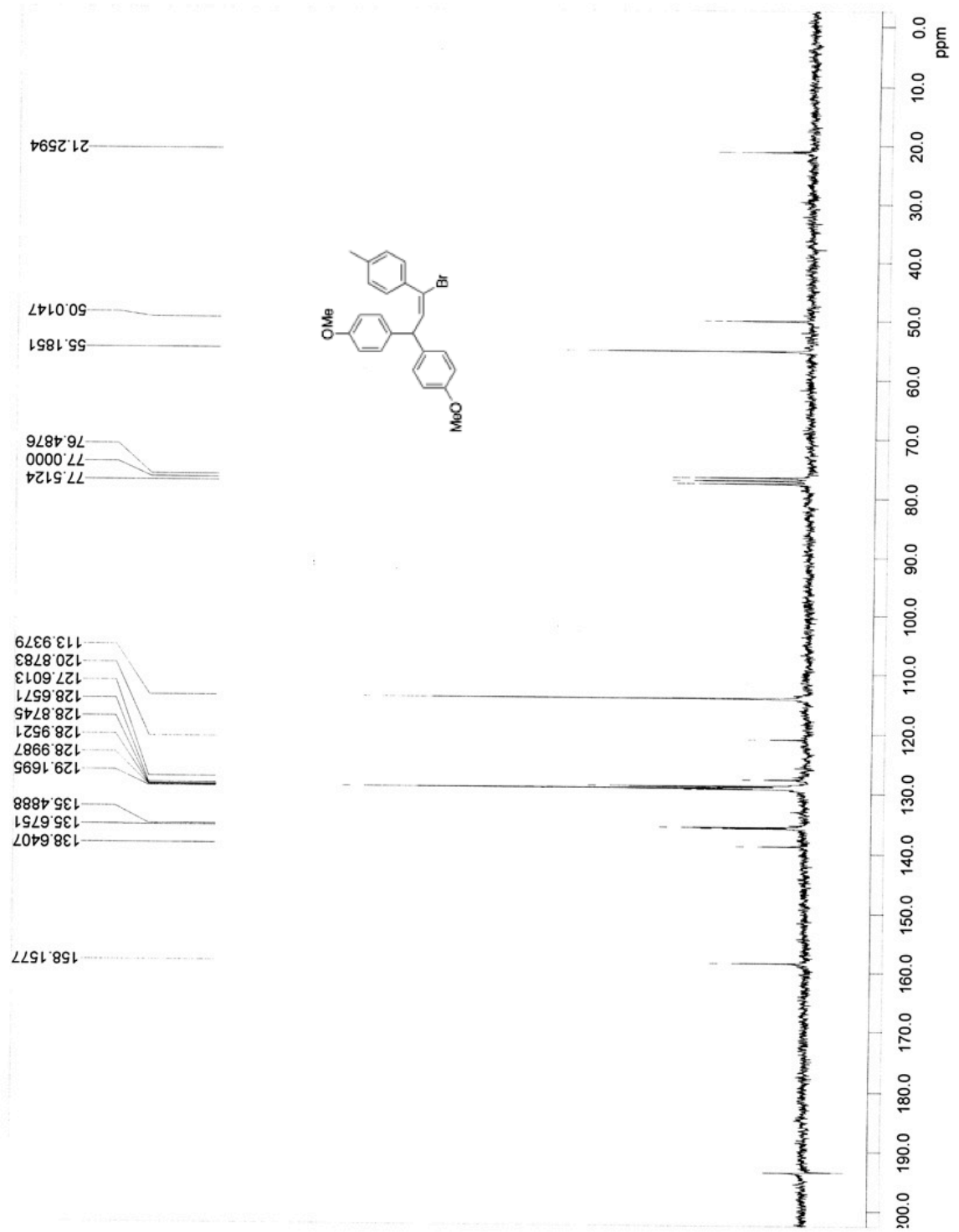
^{13}C spectrum of 6j



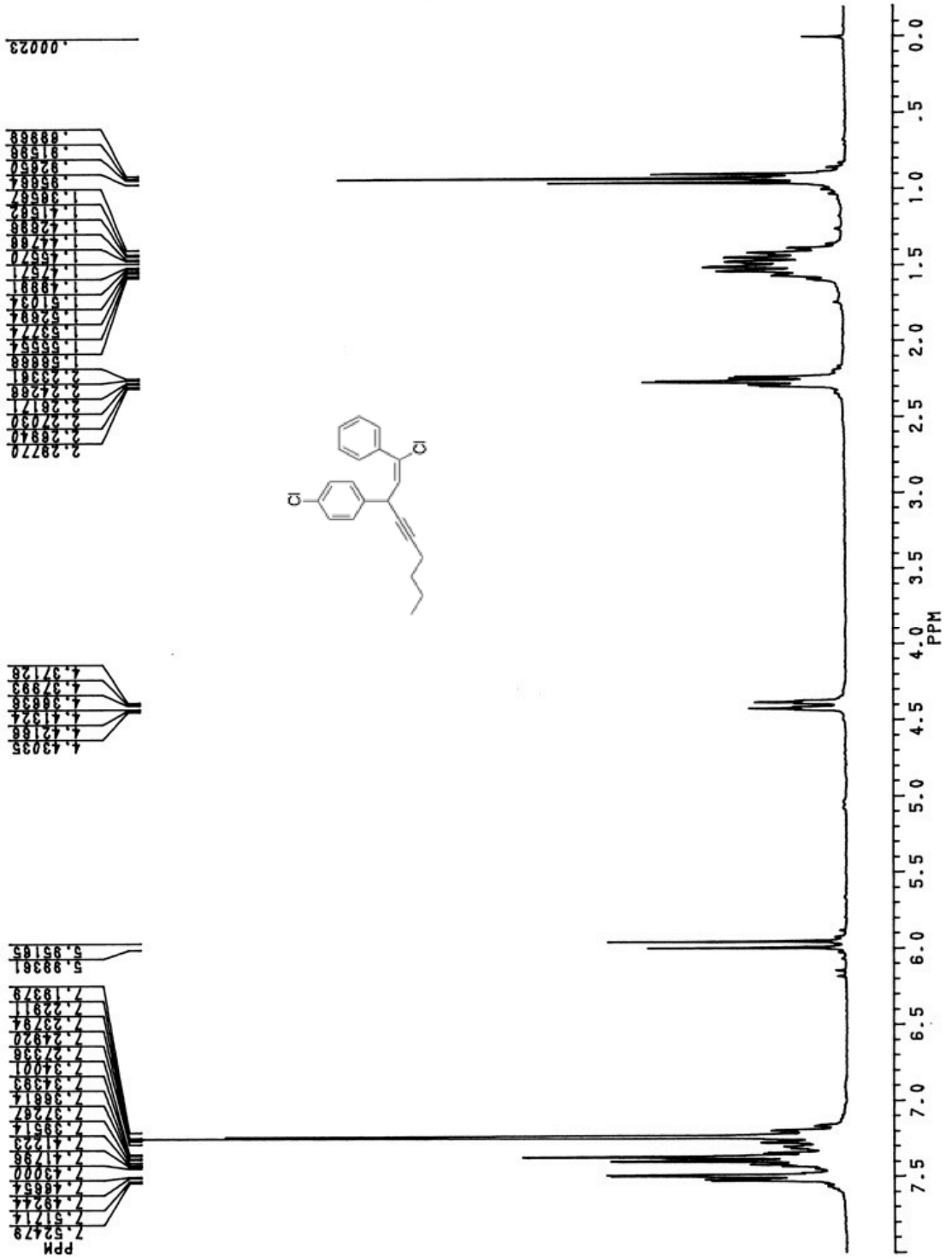
^{1}H spectrum of 6k



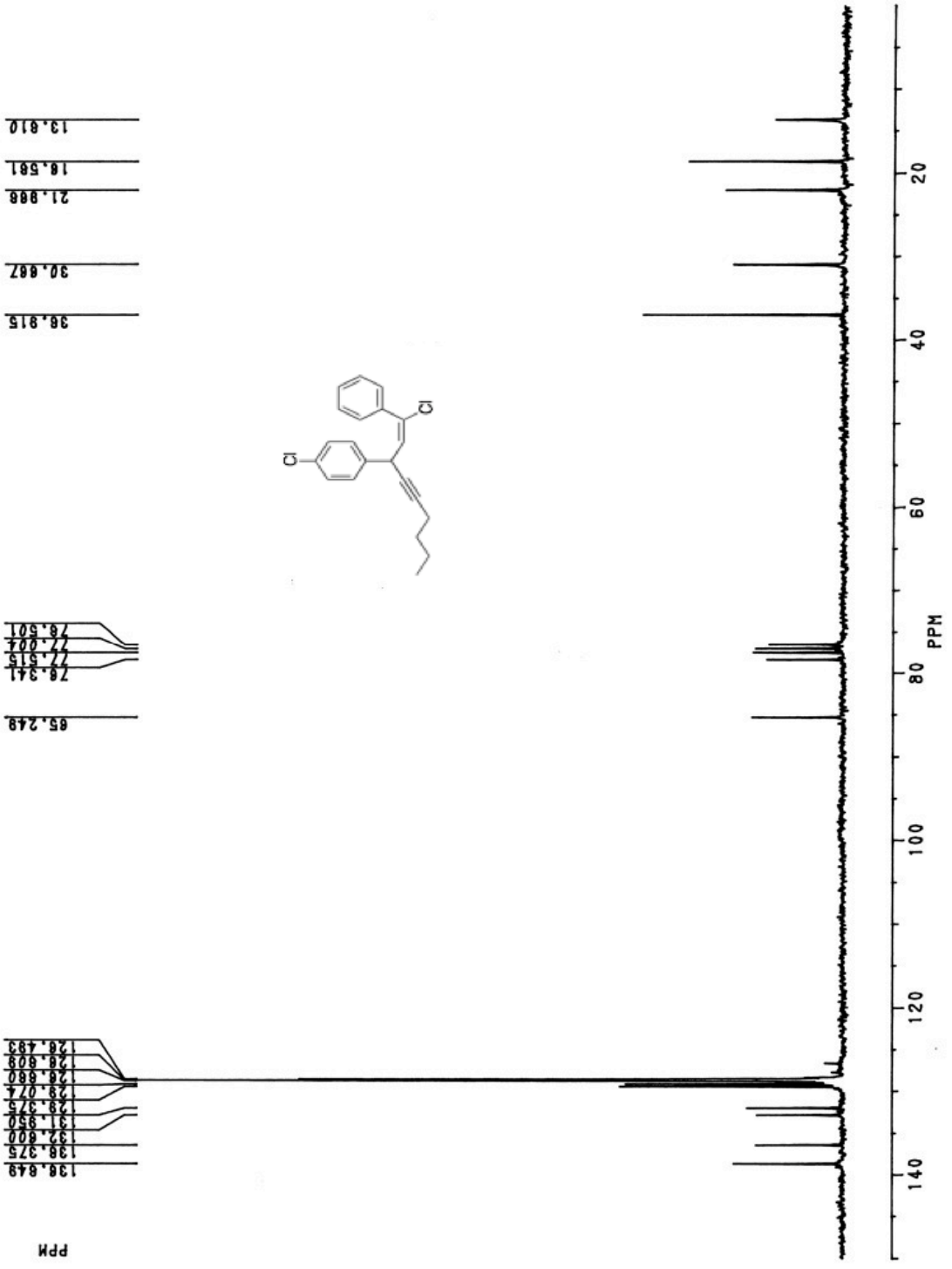
^{13}C spectrum of 6k



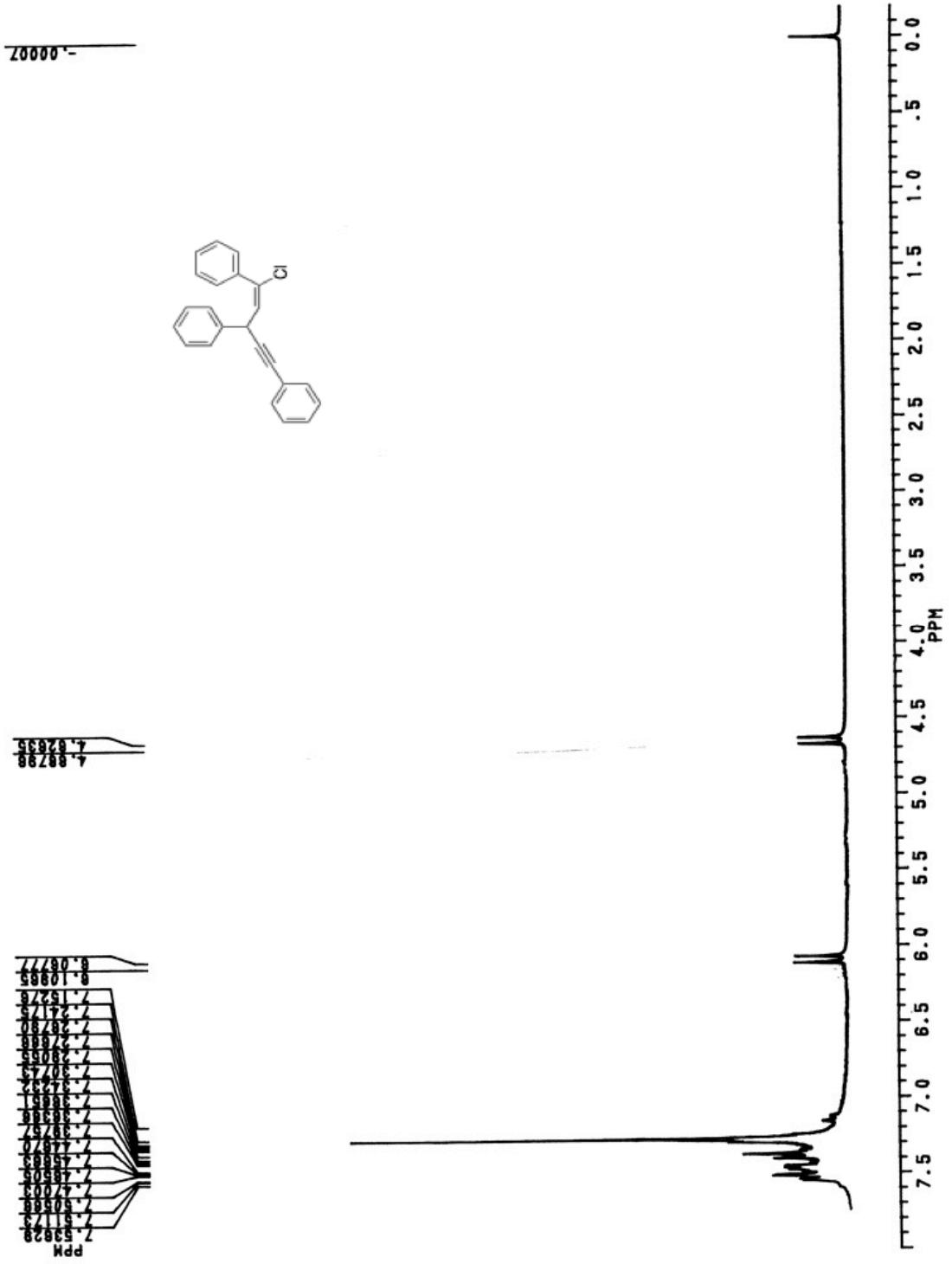
^{1}H spectrum of 9a



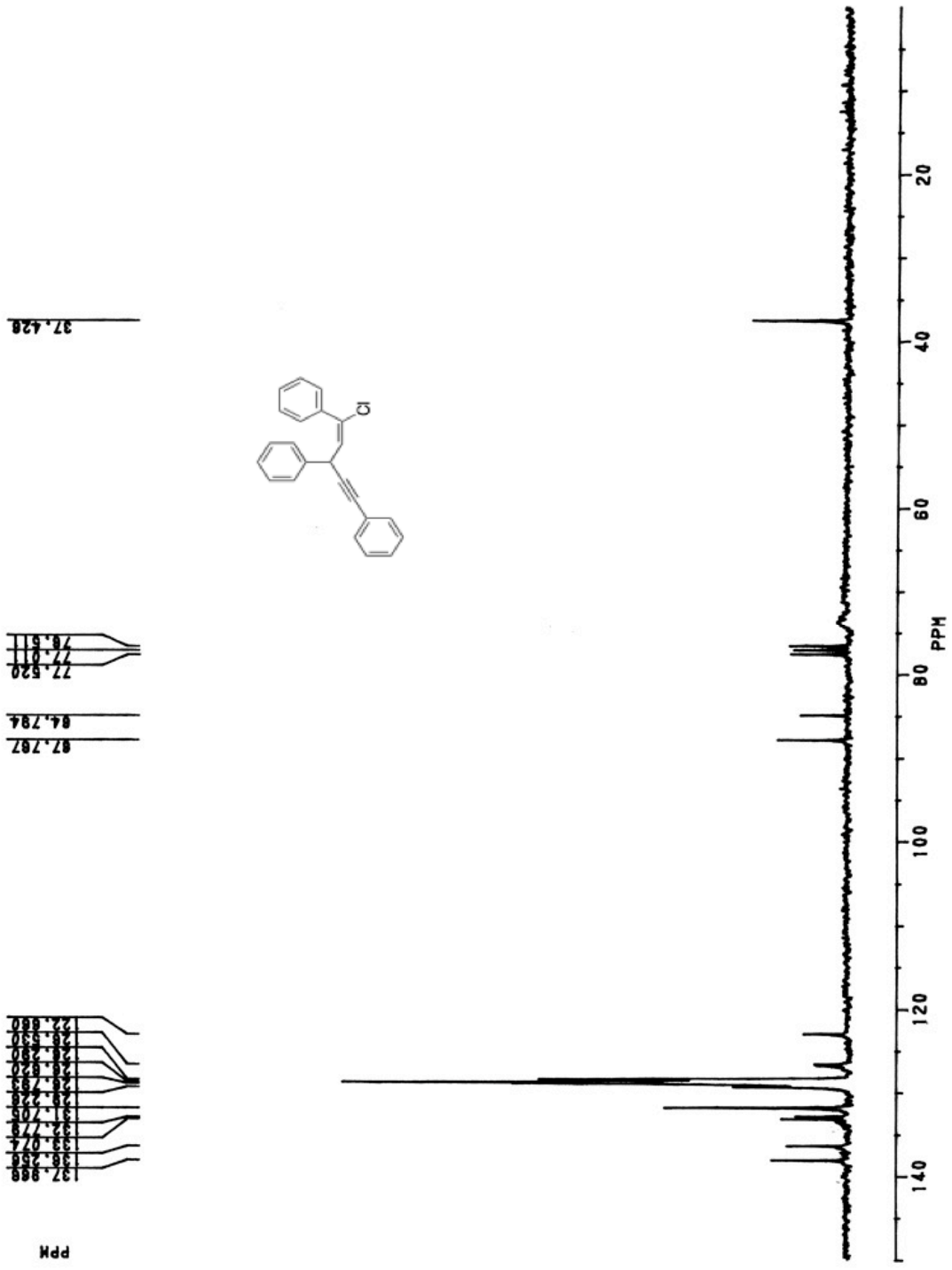
^{13}C spectrum of 9a



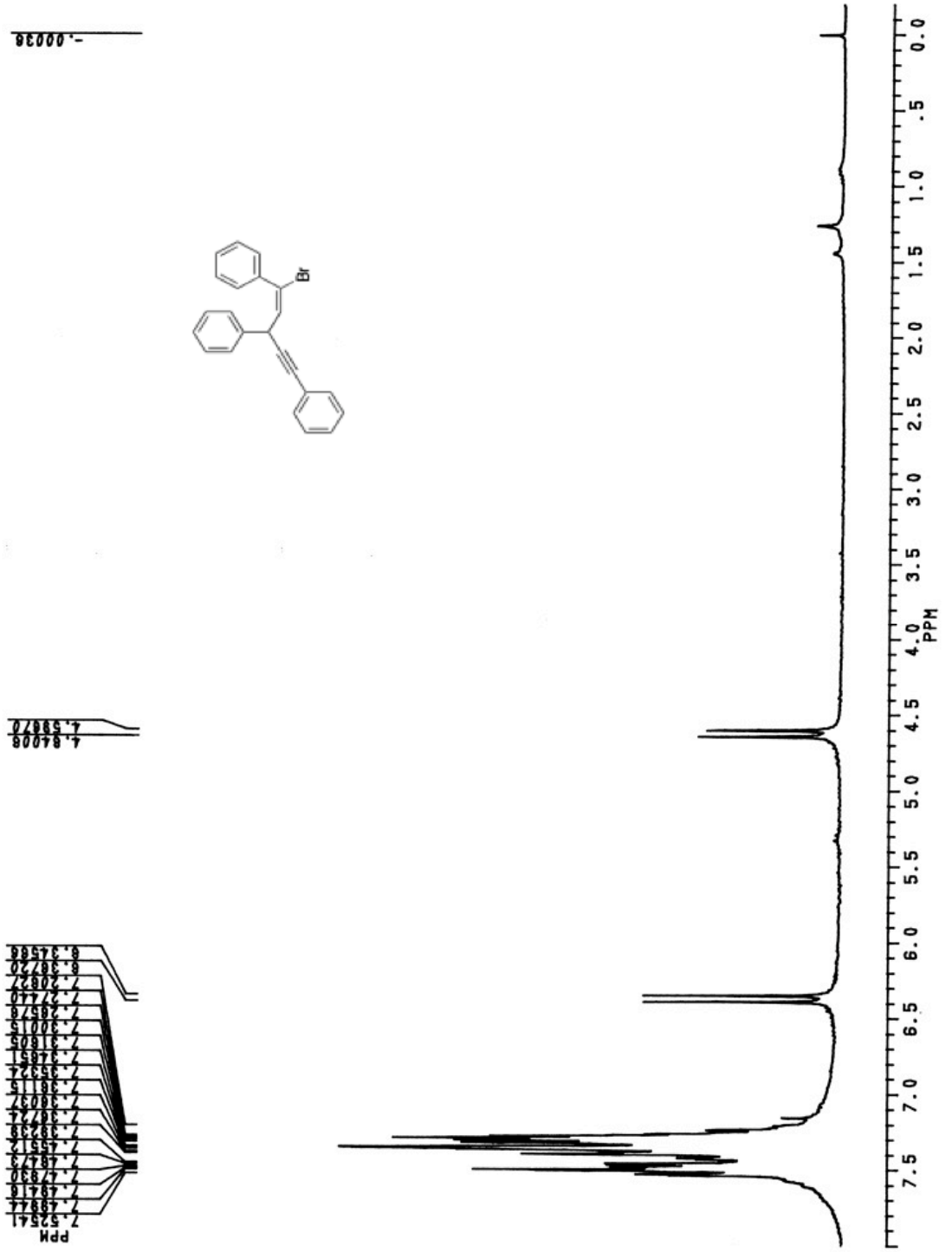
^{1}H spectrum of 9d



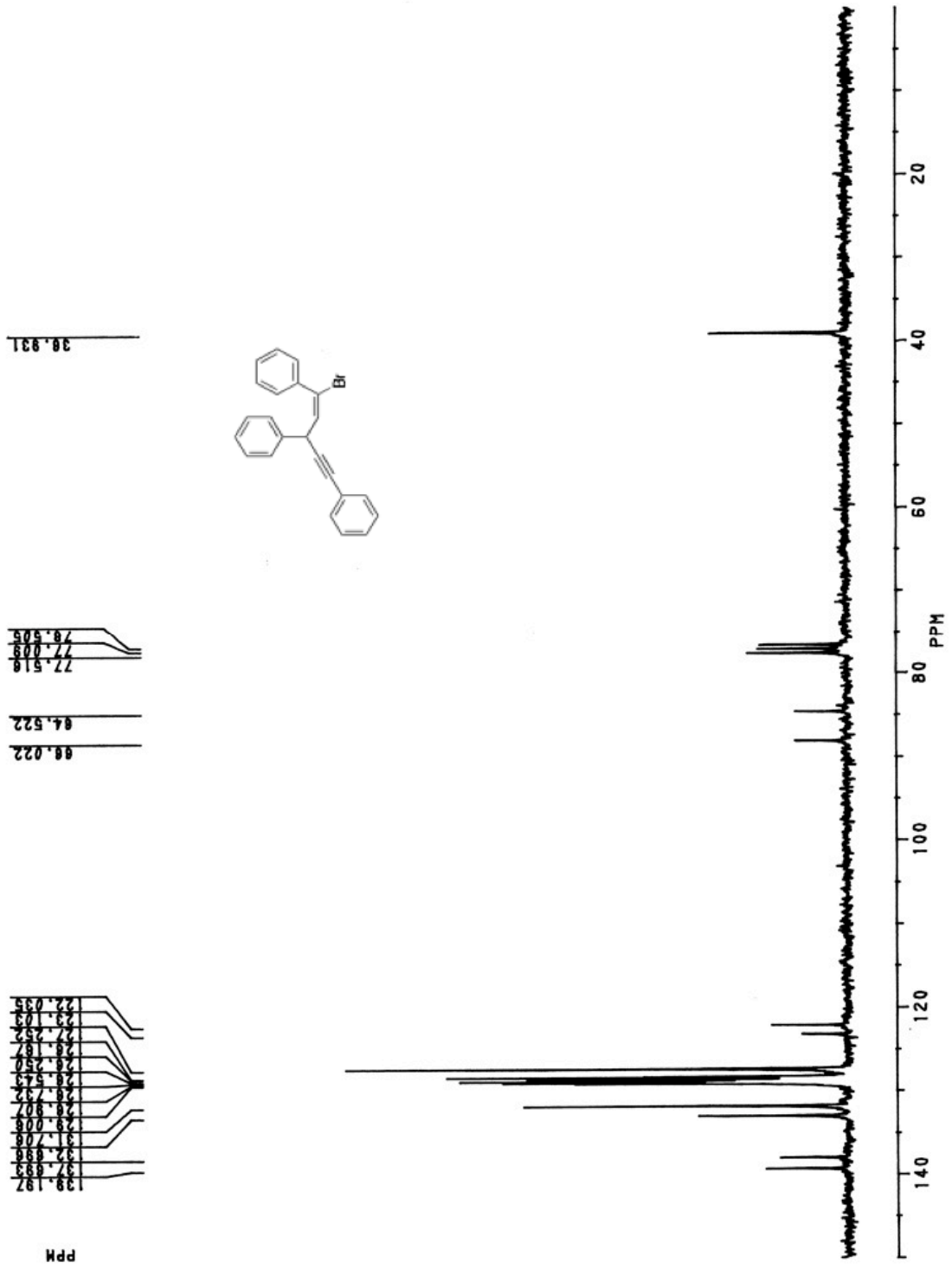
^{13}C spectrum of 9d



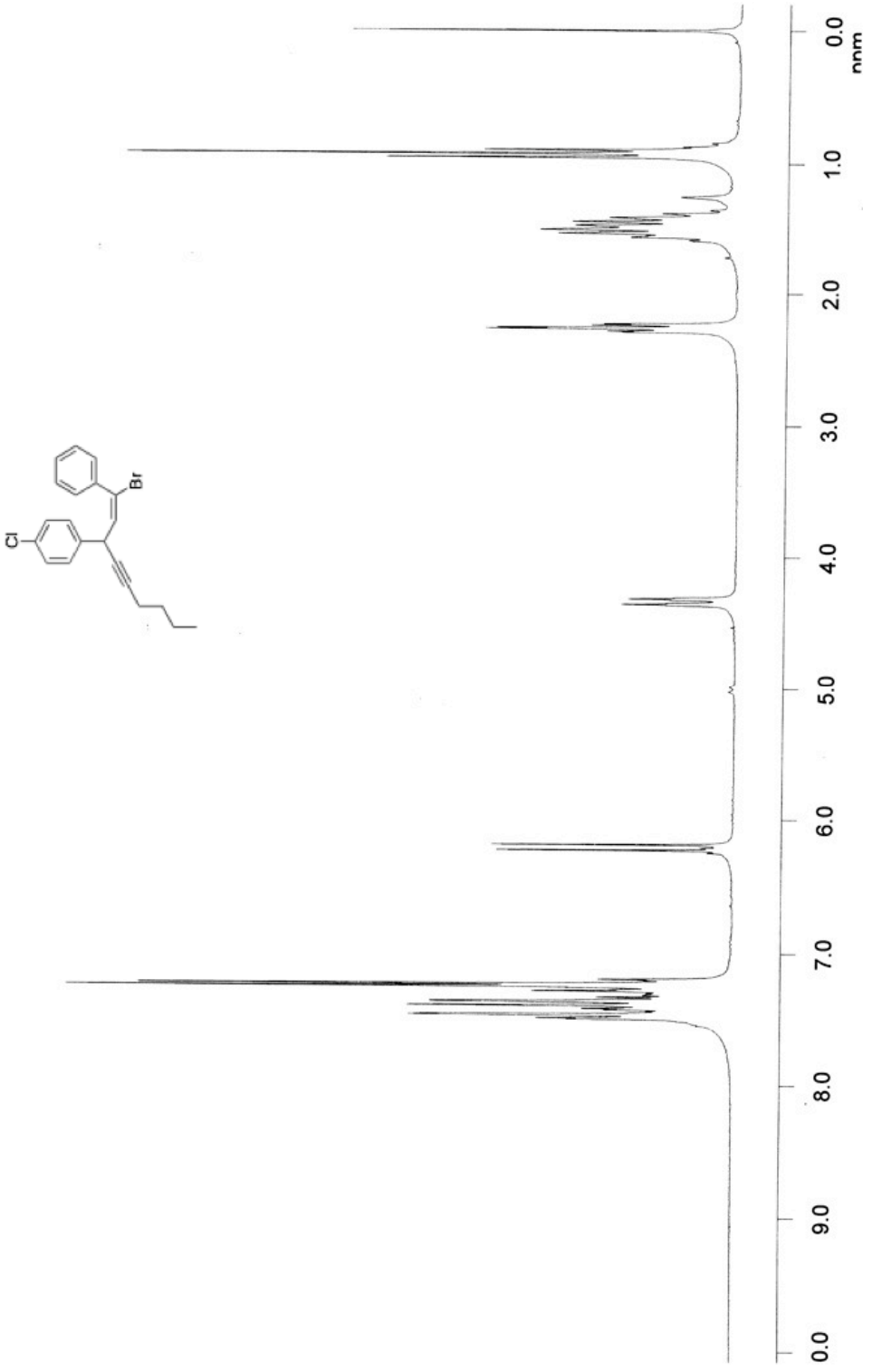
^{1}H spectrum of 9h



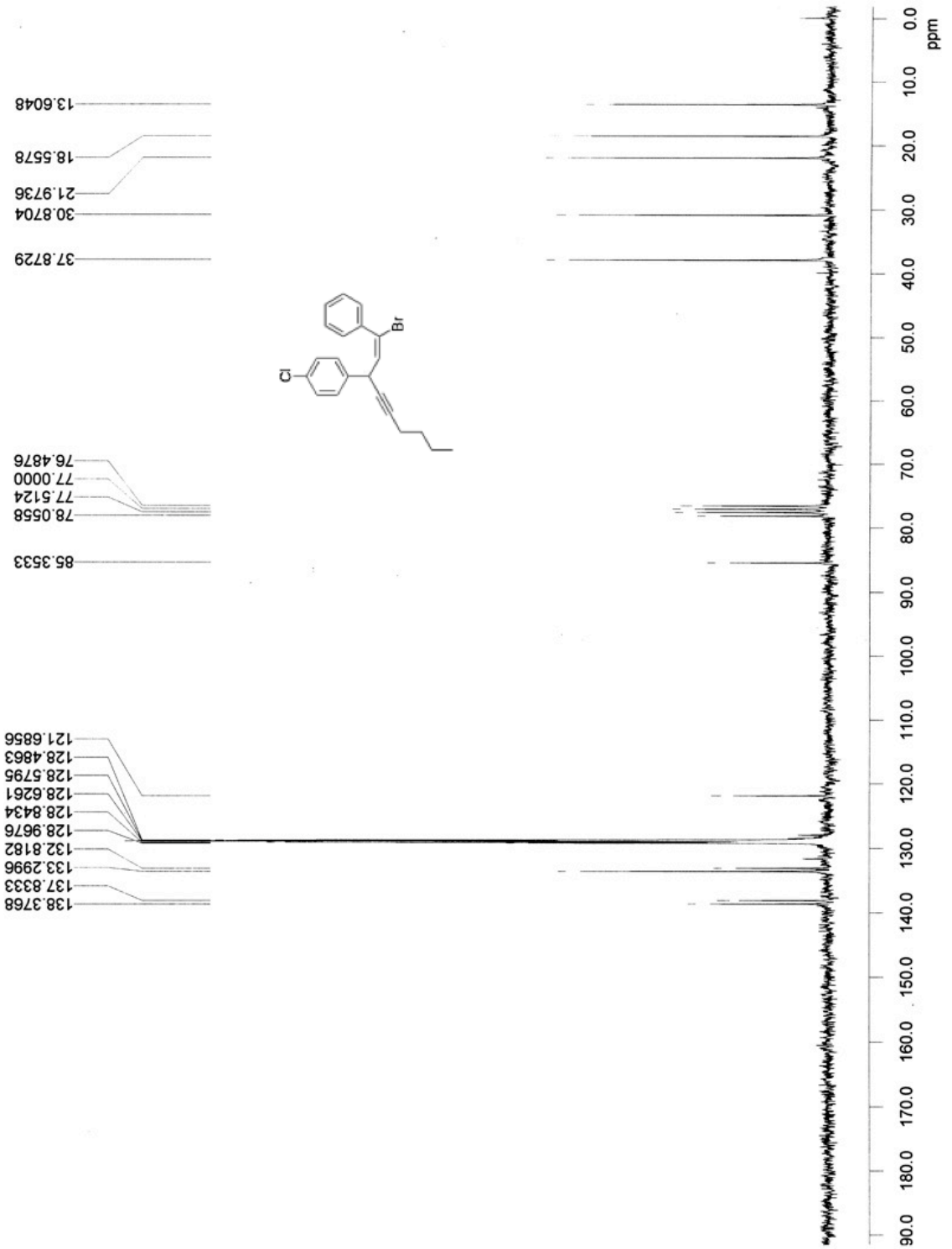
^{13}C spectrum of 9h



^{1}H spectrum of 9j



^{13}C spectrum of 9j



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VITA

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