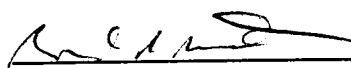


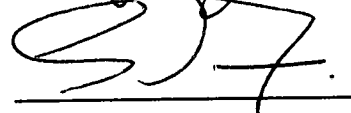
To the Graduate Council:

I am submitting herewith a dissertation written by Ekaterini Bogas entitled "The Coupling of Aryl and Alkyl Groups Utilizing Aldehyde Arenesulfonylhydrazones and Trialkylboranes." I have examined the final copy of this 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.


George W. Kabalka, Major Professor

We have read this dissertation
and recommend its acceptance:





Accepted for the Council:


Associate Vice Chancellor and
Dean of The Graduate School

THE COUPLING OF ARYL AND ALKYL GROUPS UTILIZING ALDEHYDE
ARENESULFONYLHYDRAZONES AND
TRIALKYLBORANES

A Dissertation
Presented for the
Doctor of Philosophy
Degree
The University of Tennessee, Knoxville

Ekaterini Bogas
May 1997

I dedicate this thesis to my parents

Georgios and Evanthia Bogas

ACKNOWLEDGEMENTS

I would like to thank Dr. George W. Kabalka for his help, guidance, and financial support in my research and in completing this dissertation. I would also like to thank Dr.s Ronald Magid, Spiro Alexandratos, and Jayant Joshi for their work as members of my committee. I would like to acknowledge my partner in this project, Dr. John Maddox, as well as Shane Kelley, Emily Ross and David Tejedor for their help with the hydrazone project. Assistance in performing the ^{11}B NMR studies was provided by Dr. Charles Anderson and Michael McGinnis. I am grateful to all my friends in the lab for their time, support and patience. I especially thank my husband Robert Beauvais who provided me with his extensive support during the writing of this dissertation.

ABSTRACT

A series of aryl aldehyde arenesulfonylhydrazones were alkylated by trialkylboranes in the presence of base to produce the corresponding aryl alkanes in excellent yields. The aryl aldehyde tosylhydrazones and trisylhydrazones are readily prepared from the corresponding aryl aldehydes. The trisylhydrazones reacted more readily than the corresponding tosylhydrazones allowing many of the reactions to proceed at room temperature. The reaction tolerates a wide variety of functional groups, thereby allowing functionalized alkyl groups to be transferred. It gives good yields with secondary alkyl groups such as *sec*-butyl and cyclohexyl. The alkylation occurs with rigorously defined regioselectivity at the carbonyl carbon. Various blocked borane derivatives were studied and evaluated. Aryl ketones can also be utilized to give good yields of aryl alkanes.

The mechanism of the reaction was also studied and is postulated to proceed via an organoborate complex at the original carbonyl carbon. This complex would undergo a 1,2-borotropic shift to produce a new trialkylborane. This new borane would then be hydrolyzed to the corresponding alkane by nucleophilic bases.

This reaction is a useful new addition to the known reactions for the alkylation of carbonyl compounds and to the known reactions for the coupling of aryl and alkyl groups.

TABLE OF CONTENTS

	Page
Chapter 1 Organoboranes in Alkylation Reactions	1
1.1 Introduction	1
1.2 Background	1
1.3 Synthesis of Organoboranes	6
1.4 Organoboron Reactions to Yield Unsaturated Compounds	11
1.5 Boron Coupling Reactions to Yield Saturated Compounds	16
1.6 1,2-Addition Reactions	23
1.7 Statement of Purpose	32
Chapter 2 Alkylation of Aldehyde Tosylhydrazones	34
2.1 Introduction	34
2.2 Synthesis of Aryl Aldehyde Tosylhydrazones	37
2.3 Alkylation of Alkyl Aldehyde Tosylhydrazones	58
2.4 Summary	62
Chapter 3 Alkylation of Aryl Aldehyde Trisylhydrazones	64
3.1 Introduction	64
3.2 Synthesis of 2,4,6-Triisopropylbenzenesulfonylhydrazide	64
3.3 Synthesis of Aryl Aldehyde Trisylhydrazones	65
3.4 Results	67
3.5 Ketones	69
3.6 Alkyl Trisylhydrazones	70

3.7	Use of Borane Derivatives	73
3.8	Conclusion	80
Chapter 4	Mechanism of the Alkylation Reaction	82
4.1	Introduction	82
4.2	Generation of Diazo Compounds from Tosylhydrazones	85
4.3	Generation of Diazo Compounds from Trisylhydrazones	87
4.4	NMR Studies	89
4.5	Conclusion	118
4.6	Future Studies	121
Chapter 5	Experimental	123
5.1	General	123
5.2	Synthesis of Tosylhydrazones	123
5.3	Synthesis of Trisylhydrazones	129
5.4	Procedure for Gas Chromatographic Studies	137
5.5	Syntheses Using Tosylhydrazones	139
5.6	Syntheses Using Trisylhydrazones	148
5.7	Syntheses Using Functionalized Organoboranes	153
5.8	Syntheses Utilizing Borane Derivatives	157
5.9	Mechanism Studies	161
	List of References	168
	Appendix	177
	Vita	191

LIST OF TABLES

Table	Page
2-1 Synthesis of Arylaldehyde Tosylhydrazones 3	38
2-2 The Efficiency of Various Bases in the Synthesis of Pentylbenzene ...	40
2-3 Effect of Excess Base on the Yield of Pentylbenzene	42
2-4 Effect of Base Addition on the Yield of Pentylbenzene	43
2-5 Yields of Pentylbenzene with NaOH and Bu ₄ NOH	45
2-6 Hydrolysis of 4 to Yield Pentylbenzene	47
2-7 Reaction of Various Aldehyde Tosylhydrazones with NaOH	49
2-8 Synthesis of Aryl Alkanes 5 from Tosylhydrazones 3 with Bu ₄ NOH ...	52
2-9 Reaction of <i>p</i> -Tolualdehyde Tosylhydrazone with Various Trialkylboranes..	54
2-10 Attempted Alkylation of Heptanal Tosylhydrazone via Tributylborane ..	60
3-1 Synthesis of Aryl Aldehyde Trisylhydrazones 25	66
3-2 Synthesis of Aryl Alkanes 5 from Trisylhydrazones 25	68
3-3 Synthesis of Ketone Trisylhydrazones 27	69
3-4 Synthesis of Aryl Alkanes 28 from Ketone Trisylhydrazones 27	70
3-5 Synthesis of Undecan-5-ol 31 from Heptanal Trisylhydrazone 29	72
4-1 Exp. 1: ¹¹ B NMR of Bu ₃ B in THF and DBU	91
4-2 Exp. 2: ¹¹ B NMR of Benzaldehyde Tosylhydrazone with Bu ₃ B in THF ..	94
4-3 Exp. 3: ¹¹ B NMR of Benzaldehyde Tosylhydrazone with DBU in THF ..	98
4-4 Exp. 4: ¹¹ B NMR of Benzaldehyde Tosylhydrazone with Bu ₃ B and DBU in	

	THF	102
4-5	Exp. 5: ^{11}B NMR of Benzaldehyde Trisylhydrazone with Bu_3B and DBU...	105
4-6	Exp. 6: ^{11}B NMR of Benzaldehyde Trisylhydrazone with Bu_3B and DBU...	112
4-7	Exp. 7: Diazo Cpd. 8 Added to Reaction Mixture of Bu_3B and DBU in THF	116

LIST OF FIGURES

Figure	Page
1 Proposed Transition State for the Hydroboration Reaction	7
2 Dialkylborane Hydroborating Reagents	8
3 Optically Active Hydroborating Reagents	9
4 ^{11}B NMR of Bu_3B in THF	92
5 ^{11}B NMR of Bu_3B and DBU in THF	93
6 ^{11}B NMR of Benzaldehyde Tosylhydrazone with Bu_3B in THF	95
7 ^{11}B NMR of Benzaldehyde Tosylhydrazone with Bu_3B in THF at -3°C . .	96
8 ^{11}B NMR of Benzaldehyde Tosylhydrazone with Bu_3B and DBU in THF at -18°C	99
9 ^{11}B NMR of Benzaldehyde Tosylhydrazone with Bu_3B and DBU in THF at RT	100
10 ^{11}B NMR of Benzaldehyde Tosylhydrazone with Bu_3B and DBU after 5 min at RT	103
11 ^{11}B NMR of Benzaldehyde Trisylhydrazone with Bu_3B in THF	106
12 ^{11}B NMR of Benzaldehyde Trisylhydrazone with Bu_3B and DBU in THF.	107
13 ^{11}B NMR of Benzaldehyde Trisylhydrazone with Bu_3B and DBU after 15 min of reaction	108
14 ^{11}B NMR of Benzaldehyde Trisylhydrazone with Bu_3B and DBU after 65 min of reaction	109
15 ^{11}B NMR of Benzaldehyde Trisylhydrazone with Bu_3B and DBU after 105 min	

	of reaction	110
16	^{11}B NMR of Benzaldehyde Trisylhydrazone with Bu_3B and DBU at $-18\text{ }^\circ\text{C}$.	114
17	^{11}B NMR of Benzaldehyde Trisylhydrazone with Bu_3B and DBU at $25\text{ }^\circ\text{C}$.	115
18	^{11}B NMR of Diazo Compound 8' with Bu_3B and DBU at $-78\text{ }^\circ\text{C}$	117
19	^{11}B NMR of Diazo Compound 8' with Bu_3B and DBU after Completion of the Reaction at $-78\text{ }^\circ\text{C}$	119
20	^{11}B NMR of Diazo Compound 8' with Bu_3B and DBU after Completion of the Reaction at RT	120

LIST OF ABBREVIATIONS AND SYMBOLS

Allyl	Propenyl
9-BBN	9-Borabicyclo[3.3.1]nonane
Bu	Butyl
°C	Degrees Celsius
Chx	Cyclohexyl
CDCl ₃	Chloroform- <i>d</i>
d	Doublet
DBU	1,8-Diazabicyclo[5.4.0]undec-7-ene
dppe	1,3-bis(diphenylphosphino)ethane
dppf	1,1-bis(diphenylphosphino)ferrocene
dppp	1,3-bis(diphenylphosphino)propane
DMSO- <i>d</i> ₆	Deuterated dimethyl sulfoxide
Δ	Heat
ee	Enantiomeric excess
EtOH	Ethanol
EDG	Electron donating group
EWG	Electron withdrawing group
GC	Gas chromatography
h	Hour
HMPA	Hexamethylphosphoramide

lpc	Isopinocampheyl
<i>J</i>	Proton coupling constant in Hetrz
LDA	Lithium diisopropyl amide
m	Multiplet
min	Minute
NMR	Nuclear magnetic resonance spectroscopy
[O]	Oxidation
PTC	Phase transfer conditions
q	Quartet
qt	Quintet
R	Alkyl
RT	Room temperature
s	Singlet
sept	Septet
t	Triplet
THF	Tetrahydrofuran
TLC	Thin layer chromatography
TMANO	Trimethylamine-N-oxide
TPSH	2,4,6-triisopropylbenzenesulfonylhydrazide
Tris	Trisyl (2,4,6-triisopropylbenzenesulfonyl)
Ts	Tosyl (<i>p</i> -toluenesulfonyl)
TMS	Tetramethylsilane

MATERIALS

All materials were purchased from the vendors indicated and used without further purification unless otherwise indicated.

SOLVENTS

Acetone- d_6 , Aldrich Chemical Co..

Chloroform- d , Aldrich Chemical Co..

Chloroform- d , w/1% TMS, Aldrich Chemical Co..

Diethyl ether, anhydrous, Mallinckrodt.

Dimethylsulfoxide- d_6

Ethanol, Warner Graham.

Ethyl Acetate, Mallinckrodt

Hexanes, Mallinckrodt.

Methanol, Mallinckrodt.

Methylene Chloride, Mallinckrodt.

n-Pentane, Aldrich Chemical Co..

Tetrahydrofuran, Mallinckrodt, distilled from sodium-benzophenone ketyl.

Water (distilled), house supply

GASES

Argon, MG Industries.

REAGENTS

9-BBN, Aldrich Chemical Co..

Benzaldehyde, Eastman Kodak.

Borane:THF, Aldrich Chemical Co..

m-Bromobenzaldehyde, Aldrich Chemical Co..

o-Bromobenzaldehyde, Aldrich Chemical Co..

p-Bromobenzaldehyde, Aldrich Chemical Co..

p-Chlorobenzaldehyde, Eastman.

Cyclohexene, Eastman.

1,8-Diazabicyclo[5.4.0]undec-7-ene, Aldrich Chemical Co., distilled from calcium hydride.

Diethylamine, Aldrich Chemical Co..

Hexadecane, Aldrich Chemical Co..

Lutidine, Aldrich Chemical Co..

Magnesium sulphate, anhydrous, Mallinckrodt.

p-Methoxybenzaldehyde, Aldrich Chemical Co..

p-Methylbenzaldehyde, Aldrich Chemical Co..

Methyl-10-undecenoate, Eastman, distilled from potassium carbonate.

m-Nitrobenzaldehyde, Aldrich Chemical Co..

p-Nitrobenzaldehyde, Aldrich Chemical Co..

Silica gel, 320-400 Mesh, Baxter Scientific.

Sodium chloride, Kroger.

Sodium hydroxide, Mallinckrodt.

Tetrabutylammonium hydroxide, Aldrich Chemical Co..

Tributylborane, Aldrich Chemical Co..

Triethylamine, Eastman.

p-Toluenesulphonhydrazide, Aldrich Chemical Co..

CHAPTER 1

ORGANOBORANES IN ALKYLATION REACTIONS

1.1 INTRODUCTION

The formation of new carbon-carbon bonds is an important aspect of organic synthesis. This dissertation is focused on carbon-carbon bond-forming reactions involving trialkylboranes and carbonyl compounds to form alkanes.

1.2 BACKGROUND

There are many classes of reactions in organic chemistry that involve the formation of carbon-carbon bonds. Coupling reactions and carbonyl addition reactions are two important classes. Coupling reactions involve the connection of two alkyl or aryl groups. Both symmetrical and unsymmetrical coupling reactions are possible and unsymmetrical coupling reactions are known as cross-coupling reactions. The unsymmetrical coupling of saturated alkyl groups and the cross-coupling of saturated alkyl and aryl groups constitute the main focus of this dissertation.

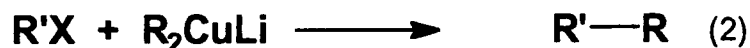
1.2.1 Coupling via Halides

There are numerous reactions involving the coupling of alkyl halides to give alkane products. One of these is the Wurtz reaction, (1), in which alkyl halides



couple upon treatment with sodium to give a symmetrical product. The reaction is, however, not very useful due to competing side reactions such as elimination and rearrangement. The coupling of mixed alkyls is even less efficient because it gives a statistical yield of mixed products. The coupling of an alkyl and an aryl halide is also feasible but again not very useful.¹

There are a variety of reactions which involve the coupling of alkyl halides with organometallic reagents.² The most useful of these involves the cross-coupling of alkyl halides, such as chlorides, bromides and iodides, with lithium dialkylcopper reagents, (2).³ These reactions give very good yields; furthermore, the copper



reagent may contain an aryl group so that the cross coupling of an aryl and alkyl group is feasible. However, this reaction does not work for secondary or tertiary alkyls. This disadvantage has been circumvented by modifying the copper reagent. For example, PhS(R')CuLi will selectively couple a secondary or tertiary R' with a

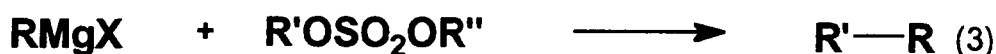
primary iodide, RI, to give R-R'.⁴ Coupling reactions involving secondary alkyl halides utilize $R_2Cu(CN)Li_2$ where R is a primary alkyl.⁵ A disadvantage of all the copper reactions is that 2-5 equivalents of the dialkylcopper reagent are required because of the instability of the copper reagents.

Grignard reagents are also used in coupling reactions but are not as effective as the copper reagents.⁶ Grignards will couple with benzylic halides and tertiary alkyl halides; both alkyl and aryl Grignards can be used but aryl Grignards give better yields.⁷ It is possible to couple Grignards with primary alkyl halides if catalysts, such as Cu(I) salts, are used.⁸ Alkyl or aryl Grignard reagents will also couple in high yields with aryl halides in the presence of nickel(II) catalysts.⁹ The disadvantage of these reactions is that the Grignard reagent will react with carbonyl groups. Therefore, alkyl halides containing these groups cannot be used.

Other organometallic compounds include organosodium and organopotassium reagents. They will couple with alkyl halides but are very unstable. Organoaluminum compounds couple with tertiary and benzylic halides at $-78\text{ }^{\circ}\text{C}$; secondary and primary halides will also react but the reaction requires several days at room temperature.¹⁰ Aryl halides couple with organotin reagents in the presence of palladium complexes as catalysts; if the substrate has a β -hydrogen on an sp^3 carbon, an elimination reaction will occur.¹¹

1.2.2 Other Coupling Reactions Involving Metallic Reagents

Other reagents that couple with organometallic reagents include sulfonates, and alcohols. Sulfonates, such as alkyl tosylates, couple with lithium dialkylcopper reagents. Primary tosylates give high yields while secondary tosylates produce lower yields. Aryl tosylates do not react. Alkyl sulfates and sulfonates also couple with aryl or benzylic Grignard reagents, (3). The sulfonates and sulfates give higher yields than their corresponding alkyl halides discussed in section 1.2.1.¹²



Allylic or benzylic alcohols can be symmetrically coupled via a variety of reagents. Examples of these reagents include methyllithium and titanium chloride at -78 °C,¹³ titanium trichloride and lithium aluminum hydride at reflux,¹⁴ and NbCl₅-NaAlH₄.¹⁵ Primary and secondary alcohols can only be used if they contain an aryl group in the α position.

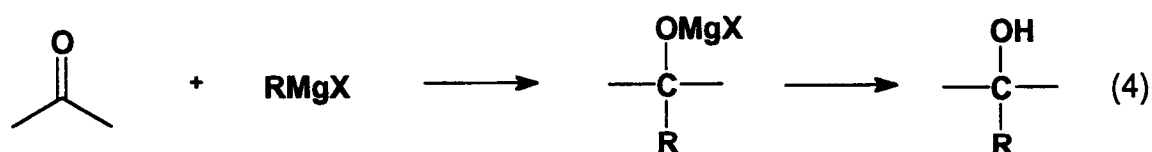
Benzene and other aromatic compounds can be alkylated with alkyllithiums and aryllithiums. The reaction involves an addition by the alkyllithium and then an elimination upon heating to give LiH and the alkylated product.¹⁶

Finally organometallic reagents can dimerize to form the symmetrical products. Lithium dialkylcopper reagents can be oxidized to symmetrical dimers by O₂ at -78 °C in THF.¹⁷ The reaction is successful for primary and secondary alkyl groups as well as for aryls. Lithium organoaluminates are dimerized by treatment

with $\text{Cu}(\text{OAc})_2$.¹⁸ Aryl tin compounds are dimerized with $\text{Cu}(\text{NO}_3)_2$.¹⁹ and alkyl- and aryllithium compounds can be dimerized by transition metal compounds.²⁰

1.2.3 1,2-Addition Reactions

The transfer of an alkyl group to a carbonyl carbon can be achieved by use of traditional active alkylmetals such as the organomagnesium, organolithium, and organozinc reagents (4).² Aldehydes give secondary alcohols while ketones give



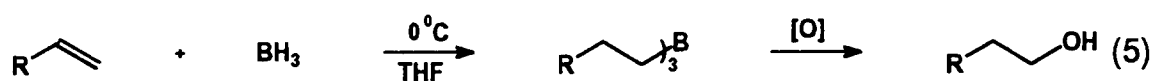
tertiary alcohols. The reaction is very broad in scope and both alkyl and aryl groups can be transferred. The hydrolysis step is usually carried out with dilute HCl; however, tertiary alcohols with at least one alkyl group are easily dehydrated under the acidic conditions. In these cases an aqueous solution of ammonium chloride is used instead of a strong acid. The strongly basic nature of these alkylmetal reagents, however, can cause unwanted side reactions. Enolization, reduction, and condensation reactions often occur and many important functional groups such as alcohols and halides will not tolerate the more reactive alkylmetal reagents.²¹ The utilization of a boron reagent in a Grignard-type reaction, as shown in equation 4, or in the coupling reaction discussed earlier, would have several benefits. First, unwanted side reactions, such as elimination and enolization would be reduced.

Second, organoboranes tolerate a variety of functional groups, so that a wide variety of organic groups could be transferred.²² Third, trialkylboranes are stable under both aqueous and basic conditions as well as at high temperatures.²³

1.3 SYNTHESIS OF ORGANOBORANES

1.3.1 Alkylboranes

Alkylboranes are readily synthesized via the reaction of an alkene with a variety of commercially available borane reagents, (5).²⁴ The borane is usually



added to the unsaturated compound at 0 °C. The organoboranes produced in the hydroboration reaction are readily oxidized to generate the corresponding *anti*-Markovnikoff alcohols. The regioisomer distribution for a simple alkene, such as 1-hexene, is placement of 94% of the boron at the terminal carbon and 6% at the internal carbon of the original double bond. This distribution is not affected by branching of the alkyl group although it is significantly enhanced by increased substitution of the double bond.²⁵

The hydroboration reaction is believed to proceed through a four-membered transition state in which the regiochemistry is controlled by the polarization of the B-H bond (Figure 1).²⁶ Functional groups close to the olefinic position can change

the polarity of the B-H bond and can, therefore, affect the direction of addition. If an oxygen atom, for example, were placed on the olefin, the electron donating ability of the oxygen would place the boron on the internal carbon instead of on the terminal carbon of the alkene.

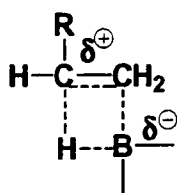
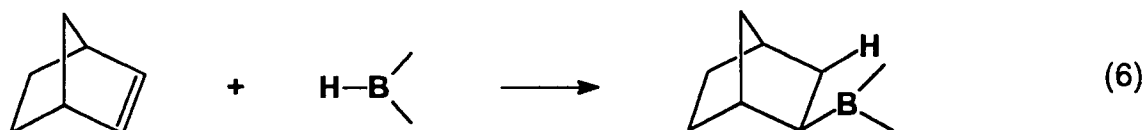


Figure 1. Proposed Transition State for the Hydroboration Reaction.

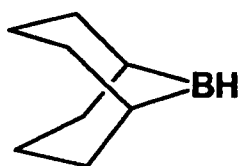
The reaction is also stereoselective and the borane reacts with the double bond via a *syn* addition. The addition also occurs on the less hindered side of the double bond, (6). The *syn* addition of a borane is also true for freely rotating acyclic systems.²⁷



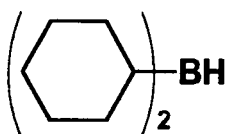
The hydroboration reaction tolerates many functionalities such as ester,

halogen, cyano, and ether groups. The rate of reaction of BH_3 with carbon-carbon double and triple bonds is much faster than the rate of reaction of BH_3 with most functional groups. Thus, functional groups are tolerated during hydroborations with BH_3 and can be present in the alkene substrate.²⁸

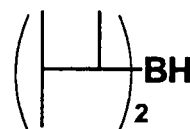
There are a variety of borane complexes that can be used in the hydroboration reaction. Hindered monoalkylboranes, such as thexylborane, are relatively stable species and are useful hydroborating reagents because they enhance the regioselectivity of the overall reaction.²⁹ Dialkylboranes are even more stable and, therefore, more commonly used than monoalkylboranes. Dialkylboranes such as 9-borabicyclo[3.3.1]nonane (9-BBN), disiamylborane, and dicyclohexylborane (Figure 2) are particularly effective, placing >97% of the boron at the less substituted vinyl carbon of the original double bond.⁵



9-BBN



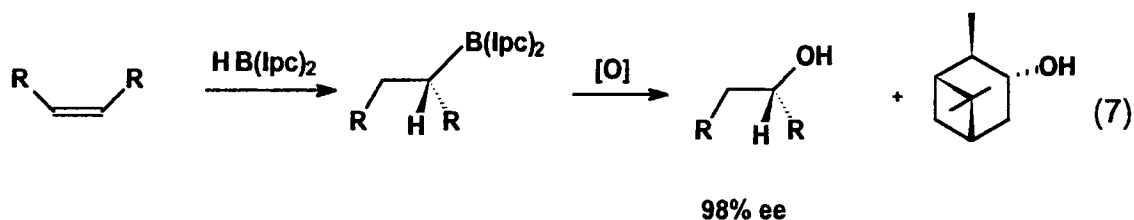
Dicyclohexylborane



Disiamylborane

Figure 2. Dialkylborane Hydroborating Reagents.

Another advantage of the organoboranes is that they can generally transfer an organic group with retention of configuration at the carbon attached to boron. This can be seen in the transfer of an alkyl group from boron to oxygen during a typical oxidation reaction, (7).



It is important, since an organic group can be transferred with retention of configuration, to be able to enantioselectively hydroborate alkenes. Optically active organoboranes such as diisopinocampheylborane, (7), monoisopinocampheylborane, and *trans*-2,5-dimethylborolane can enantioselectively hydroborate alkenes (Figure 3). Optically active diisopinocampheylborane hydroborates (*Z*)-alkenes

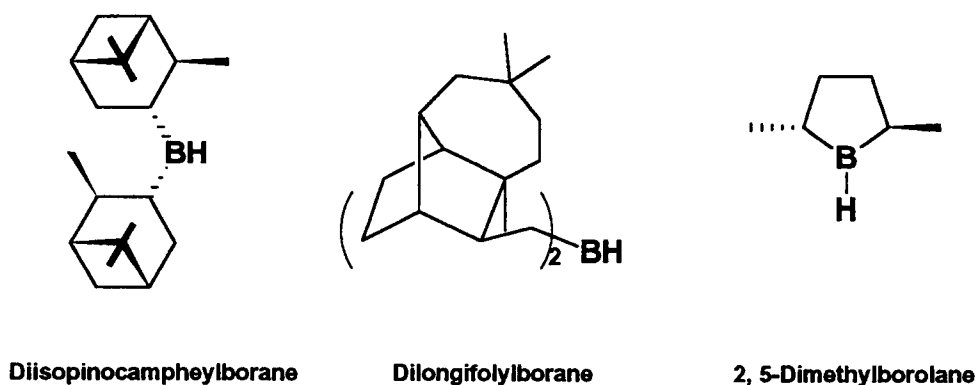
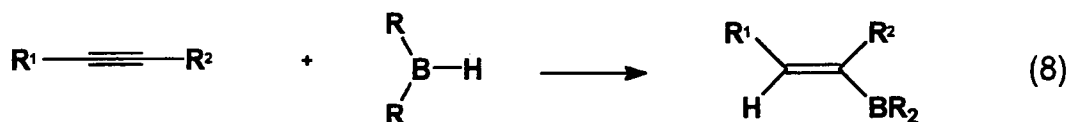


Figure 3. Optically Active Hydroborating Reagents.

to generate products in which enantioselectivities exceed 98% ee.³⁰ Optically active 2,5-dimethylborolane is more versatile and hydroborates both (*E*)- and (*Z*)-alkenes with high enantioselectivities.³¹

1.3.2 Alkenylboranes

Alkenylboranes are readily synthesized via the hydroboration of alkynes with R_2BH . R can be siamyl³², cyclohexyl³³, mesityl³⁴, chloro or bromo³⁵. R_2BH can also be catecholborane.³⁶ All of these reagents allow for the controlled *syn*-hydroboration of terminal and internal alkynes, (8).

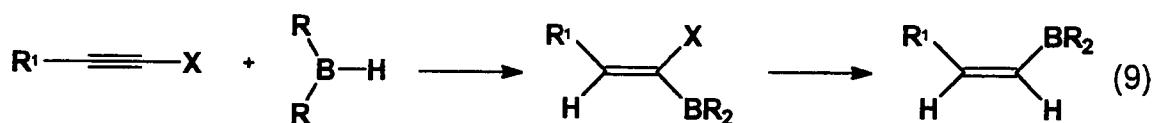


The above reagents all react with terminal alkynes to place the boron on the terminal carbon. For internal alkynes, regioselectivity is less defined. Disiamyl- and dicyclohexylborane hydroborations are mainly directed by steric effects. Dibromoborane and 9-BBN reactions, however, are influenced by electronic factors.^{36a} Dimesitylborane is the most regioselective reagent known for the hydroboration of internal alkynes, and it is influenced only by steric factors.³⁴ Dimesitylborane places, for example, 98% of the boron on C-2 of 1-phenylprop-1-yne (disiamylborane, 81%; 9-BBN, 35%). The reagent reacts very slowly with

alkenes so that alkynes of any type are exclusively hydroborated in the presence of an alkene.

A number of borane reagents may be used to achieve a variety of chemoselective reactions. 9-BBN is a very good hydroborating reagent for enynes. It shows a preference for an alkene over any alkyne and can therefore selectively hydroborate an alkene in the presence of an alkyne.^{36b} Preferential hydroboration of an internal alkyne can be accomplished with dibromoborane-dimethylsulfide which, interestingly, reacts more rapidly with internal alkynes than terminal alkynes.³⁵

It is also possible to obtain the equivalent of an *anti* hydroboration. A 1-haloalkyne can be hydroborated with a dialkylborane. The resulting 1-haloalkenyldialkylborane can then be reduced with potassium triethylhydroborate³⁷ or *t*-butyllithium³⁸ to give the *Z* product, (9).



1.4 ORGANOBORON REACTIONS TO YIELD UNSATURATED COMPOUNDS

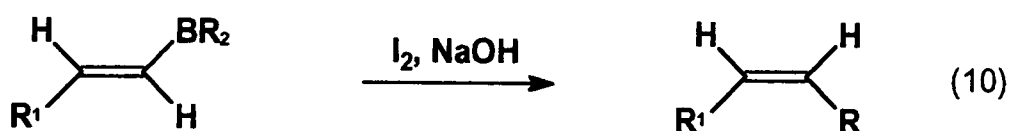
The alkyl- or alkenylboranes formed in the reactions described in the preceding section can be easily utilized to form carbon-carbon bonds. This

remarkable development in boron chemistry has been an area of intense research for the past thirty years. A brief survey of organoborane coupling reactions, to form various saturated and unsaturated organic compounds, follows.

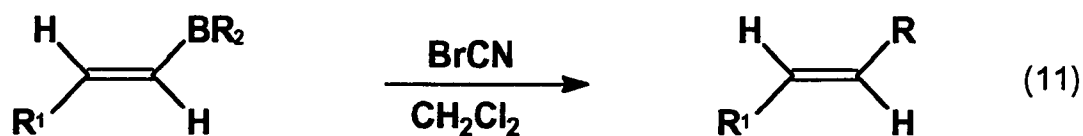
There are numerous reactions involving unsaturated organoboranes in which alkenes, alkynes, dienes, diynes, and enynes can all be synthesized. The reaction conditions can be modified to produce either the *E* or *Z* isomers, and in the case of dienes the *EZ*, *EE*, or *ZZ* isomers. The reactions are high yielding and migrations from boron to carbon proceed with retention of configuration.

1.4.1 Alkenes from Alkenylboranes and Halogen Catalysts

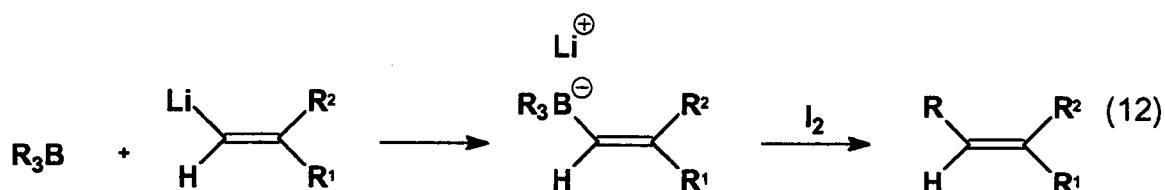
Either *E* or *Z* alkenes can be formed from alkenylboranes via alkenylborates. Alkenyldialkylboranes form borate salts upon reaction with base. These borates then rearrange, on treatment with iodine, to yield *Z*-alkenes, (10).³⁹



It is possible to obtain the *E*-alkenes by using a poorly nucleophilic solvent and cyanogen bromide as the base, (11).⁴⁰



It is also possible to synthesize trisubstituted alkenes using this methodology, (12). Trialkylalkenylborates can be formed by reaction of trialkylboranes with lithiated alkenes. Treatment of these borates with iodine leads to migration followed by *syn*-elimination to yield trisubstituted alkenes in a stereospecific fashion.⁴¹ The reaction proceeds with retention of configuration at the alkenyl terminus.

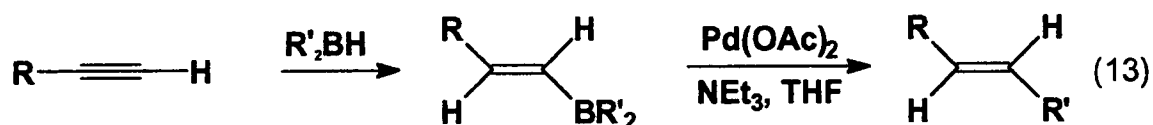


An alternative method is treatment of these trialkylalkenylborates with phenylsulphenyl chloride. This reaction also proceeds with retention of configuration and, if different R groups are utilized, there is migration of the most hindered alkyl group from boron to carbon.

1.4.2 Alkenes from Alkenylboranes and Metal Catalysts

In a similar reaction, unsaturated boranes can be alkylated to produce new alkenes. The alkylating group can be either alkyl, vinyl, alkynyl or aryl. The reaction conditions can be varied so that either the *E* or *Z* alkenes are produced.

Alkenyldialkylboranes, formed from terminal alkynes, as shown on page 10, can be treated with palladium acetate and triethylamine to give good yields of *E*-alkenes, (13). The mechanism involves *syn*-palladoacetoxylation, migration with inversion at the terminus and *syn*- β -elimination.⁴²

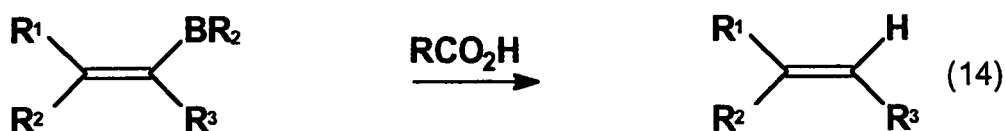


Various halides and boron compounds can cross-couple with the use of palladium catalysts. 1-Alkenyldisiamylboranes can cross-couple with 1-alkenyl or 1-alkynyl halides. The reaction requires only a catalytic amount of $\text{Pd}(\text{PPh}_3)_4$ and a two-fold excess of base. It gives good yields of the dienes or enynes with regio- and stereospecificities of 96-100%. The *E* or *Z* borane reagents can be coupled with either the *E* or *Z* halides to give (*EE*)-, (*ZZ*)-, (*ZE*)-, or (*EZ*)-conjugated dienes stereo- and regiospecifically. Coupling with alkynyl halides will give either the (*E*)- or (*Z*)-alkenynes.^{43, 44}

Alkyl groups can be transferred by using *B*-alkyl-9-BBN in the coupling reaction. Primary alkyl groups can be transferred from *B*-alkyl-9-BBN compounds to alkenyl or aryl halides. This reaction also utilizes palladium(II) as the catalyst for the coupling.⁴⁵ 9-BBN can also be used in the transfer of unsaturated groups. Alkynyl halides can be alkylated with alkenyl 9-BBN compounds using cuprous bromide-dimethyl sulfide as the catalyst. The reaction proceeds via an alkenylcopper intermediate to give high yields of the corresponding *E*-dienes.⁴⁶

1.4.3 Alkenes by Protonation of Alkenylboranes.

Although not a coupling reaction, most alkenylboranes used in the preceding reactions are readily protonolyzed by carboxylic acids at or below room temperature to yield the corresponding alkenes, (14).^{32, 47} Hindered alkenylboranes



may be hydrolyzed with propionic⁴⁸ or isobutyric acids⁴⁹ at elevated temperatures. The reaction proceeds with retention of configuration of the alkenyl group.

Several methods are available for alkenylboranes bearing acid-sensitive groups. The alkenylborane may, for example, be converted into an electron-rich organoborate complex with *n*-butyllithium and then readily hydrolyzed with aqueous

sodium hydroxide.⁵⁰ Use of silver ammonium nitrate provides another gentle hydrolysis method for sensitive groups.⁵¹ Internal alkynes that have been hydroborated with dialkylboranes can be protonolyzed in neutral conditions with catalytic amounts of palladium acetate in THF or acetone.⁵² The proton in this case is provided by the solvent.

1.5 BORON COUPLING REACTIONS TO YIELD SATURATED COMPOUNDS

While there are a variety of coupling reactions utilizing boron that yield unsaturated compounds, reactions that yield saturated compounds and alkylated aryls are not as numerous nor as useful. Only recently has a synthetically useful coupling reaction been discovered for saturated boranes. This reaction is known as the Suzuki reaction and will be summarized in section 1.5.2.

1.5.1 *Coupling of Trialkylboranes*

Treatment of trialkylboranes with base and aqueous silver nitrate results in the precipitation of metallic silver and the formation of the coupled product, (15).⁵³



Primary alkyls result in yields of 60-80% while secondary alkyls give yields of 35-50%. The reaction can be used without difficulties for a wide variety of structures and tolerates many functional groups not compatible with Grignard reagents. The disadvantage of this reaction, as in the Wurtz reaction, is that the ratio of products from mixed alkyls is statistical. Coupling of R and R' would, for example, give 25% RR, 25% R'R', and 50% RR'. This problem can be overcome by utilizing a large excess of one of the trialkylboranes. It is also necessary to choose alkyl groups with sufficient differences in molecular weight so that the cross-coupled product can be readily separated from the symmetrically coupled products. It is also possible to form biaryls in yields of 52-71%.⁵⁴ The triarylboron reagents are formed by treating the corresponding halide with magnesium in the presence of BH_3 .

1.5.2 Coupling Utilizing Palladium catalysts

Palladium catalysts have been utilized in the coupling of boron compounds with halides and triflates. This reaction is known as the Suzuki reaction. The metal-catalyzed reaction was also highlighted in section 1.4.2 where unsaturated compounds could be formed from the reaction of various boranes in the presence of palladium catalysts. The reaction was then extended to produce both alkanes and alkylated aryls.

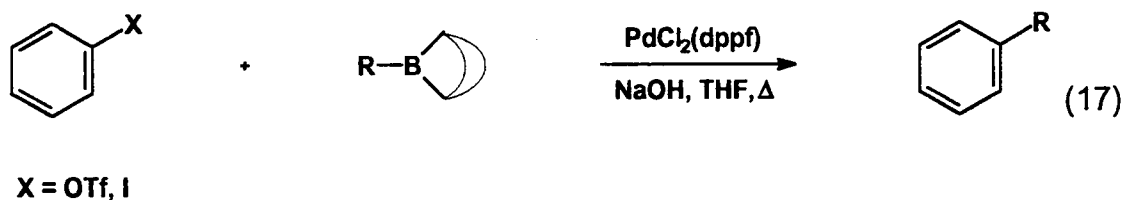
It was initially thought that alkyl halides with an sp^3 carbon having β -hydrogens would not react due to the slow rate of oxidative addition of alkyl halides

to Pd(0) complexes and fast β -hydride elimination. It was found, however, that 9-Alkyl-9-BBN derivatives cross-couple with iodoalkanes in the presence of an organometallic catalyst, to give the coupling products in yields of 45-60%, (16).⁵⁵



The reaction requires 3 equivalents of base, 3 mol % of catalyst, and is run at 60 °C for 24 h. Other palladium catalysts such as $\text{Cl}_2\text{Pd(dppf)}$ do not work well in this reaction. The same is true of other bidentate ligands such as dppp and dppe. As in other borane reactions, compounds with functional groups such as cyano and ester survive the reaction conditions without difficulty. The reaction can be further extended to aryl groups and 9-phenyl-9-BBN reacts with 1-iododecane to give decylbenzene in a 55% yield. The disadvantage of this reaction is that some β -elimination does occur and secondary alkyls do not react at all.

Palladium catalysts are used in a variety of reactions with organoboron reagents and aryl compounds to produce alkylated aryls. Alkyl 9-BBN reagents



react with both haloarenes⁵⁶ and aryl triflates⁵⁷ in the presence of base and a catalytic amount of $\text{PdCl}_2(\text{dppf})$ to give yields of 80-99% for primary alkyl groups, (17). This catalyst works well to suppress the elimination side-reaction. The reaction requires 3 equivalents of base, 1.1 equivalents of the alkyl-9-BBN and 16 h at reflux. The base used for most reactions is sodium hydroxide in THF- H_2O . If functionalities are present that are unstable to this base then powdered potassium carbonate suspended in DMF at 50 °C is utilized. Under these conditions functional groups such as cyano, ester and carbonyl groups could be tolerated on either the borane or the halide.

Other borane reagents which can be utilized in this reaction are disiamylborane, dicyclohexylborane and trialkylboranes. In the case of trioctylborane, only one of the alkyl groups participates in the coupling. Trialkylboranes with secondary groups give yields of 40-65%. Secondary groups attached to 9-BBN were not investigated.

Alkylboronic acid esters, such as octylcatecholborane, also react with arenes in the presence of base and palladium catalyst to give yields ranging from 62-93%, (18).⁵⁸

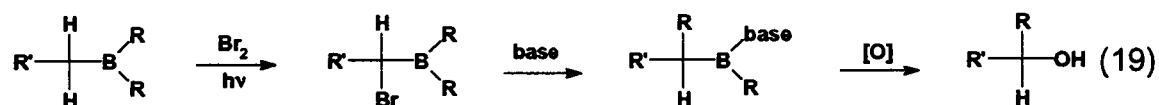


The reaction conditions are very similar to those used in the 9-BBN reaction. It

requires 3 mol% of catalyst, 1 mol of halide, 1.1 mol of the ester, 1.5 eq of base and 16 h at 50 °C. The bases used in the above reactions were not effective for this reaction, hence the use of thallium (II) salts.

1.5.3 α -Bromination Reactions

Light-induced bromination of a trialkylborane in the presence of water results in the coupling of two or three alkyl groups to produce secondary or tertiary alcohols upon oxidation.⁵⁹ Use of one equivalent of Br_2 results in the production of secondary alcohols, (19). A second equivalent of Br_2 would result in tertiary alcohols. Use of a dialkylborinic acid, or hexyldialkylboranes, under the above conditions allows for the combination of two alkyl groups to produce highly substituted tertiary alcohols.⁶⁰

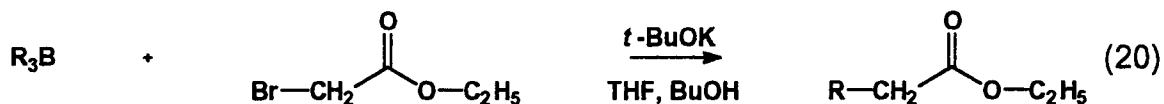


The reaction works well for primary, secondary, and tertiary groups to give yields of 44-97%.

1.5.4 α -Alkylation and Arylation

In a similar reaction, treatment of α -halo esters, ketones, and nitriles with base and trialkylborane results in the replacement of the halogen atom by an alkyl

or aryl group of the organoborane, (20).⁶¹ This reaction works very well to produce

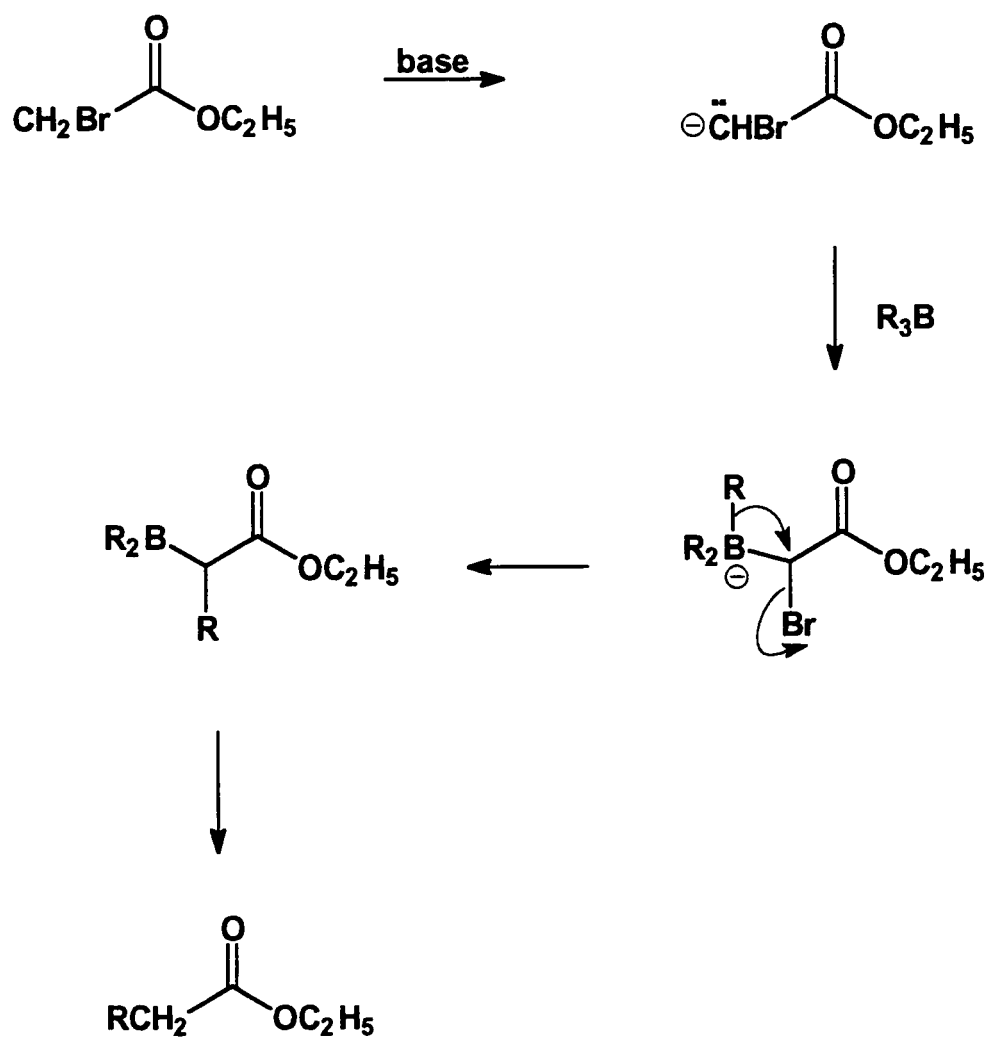


monoalkylation only at the halogenated carbon and side reactions such as elimination and rearrangements do not occur. The reaction is usually carried out between 0 and 20 °C, with 1-2 equivalents of trialkylborane, and gives yields that range from 68-100%. Most yields were in the 80-90% range and the low yields resulted from reactions involving cyclic ketones. The halogens of α,α -dihalo derivatives can be replaced consecutively with different groups. These groups can be primary or secondary. This reaction, therefore, provides a convenient route to α -halo esters and to dialkylacetic acids.

When a trialkylborane is used as the alkylating reagent only one of the groups is transferred. This difficulty can be overcome by use of the B-alkyl-9BBN derivatives. Examples of groups which can be transferred from 9-BBN include methyl, cyclohexyl, *exo*-norbornyl, phenyl, and *p*-tolyl.

The mechanism of this reaction involves the conversion of the halo derivative into the corresponding anion. This anion reacts with the organoborane to generate the boron "ate" complex which is followed by migration of the organic group. The intermediate can then be protonolyzed by the solvent to form the final product, (Scheme 1).

Scheme 1

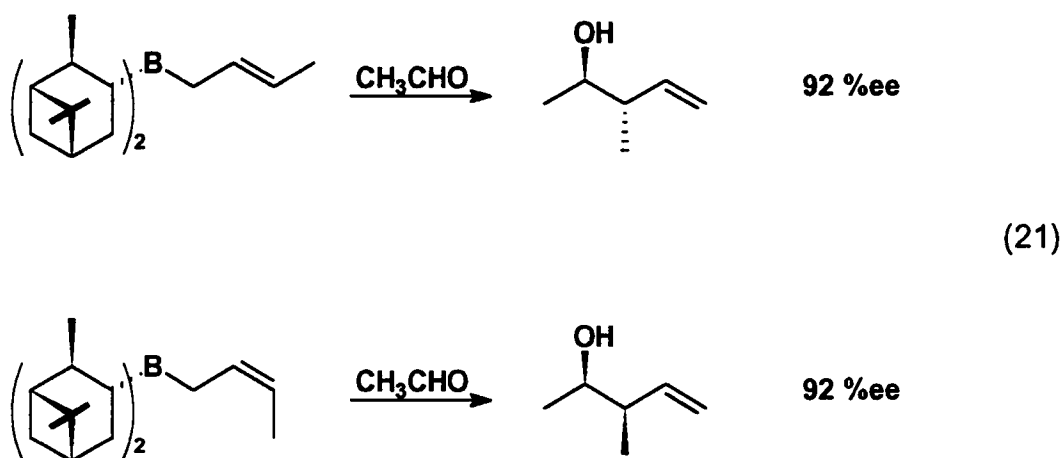


1.6 1,2-ADDITION REACTIONS

1.6.1 Unsaturated Organoboranes

The formation of a new carbon-carbon bond via the 1,2-migration of an organic group from an organoborane, such as an allylborane, to a carbonyl carbon is an important method for assembling a variety of useful carbon skeletons, (21).

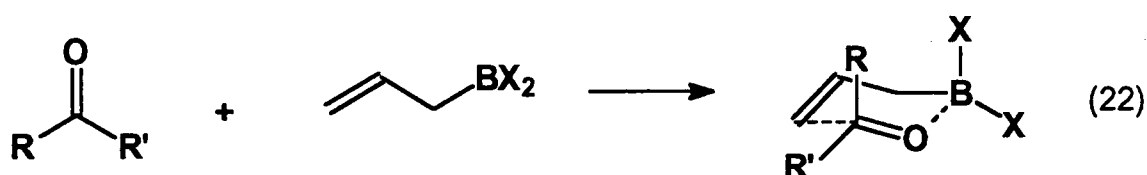
⁶² Two types of organoboranes are known to alkylate carbonyl compounds via a 1,2-migration of an organic group from boron to carbon. These are allylboranes and the unsaturated (vinyl and alkynyl) boranes. These organoboranes add exclusively via a 1,2-migration to the carbonyl group in aldehydes and ketones to



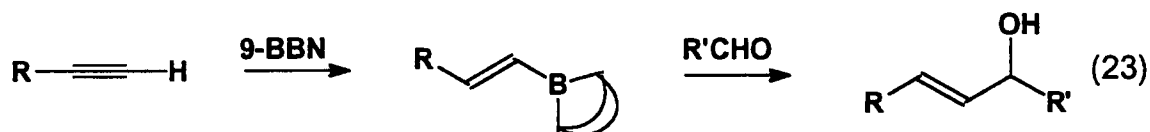
produce the corresponding alcohols after hydrolysis. The homoallylic alcohols generated in the allylboration reaction are obtained in good yield and with high stereoselectivities, (21).⁶³ The chiral blocking group, such as the crotyl group in eqn

21, controls the enantioselectivity while the geometry of the double bond of the borane determines the diastereoselectivity.⁶⁴

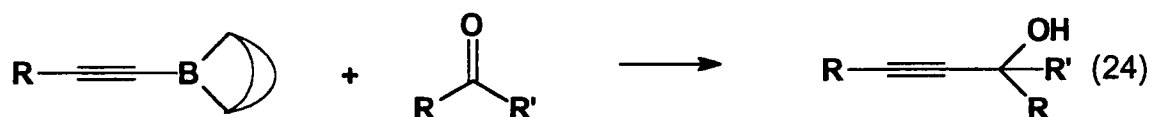
The stereocontrol results from the compact, six-membered transition state, (22), which allows asymmetric induction in the product through the use of chiral modifying groups on the boron. The reaction occurs quickly, cleanly (no mixed products), quantitatively, and with high enantio- or diastereoselectivities.



B-Vinyl-9-borabicyclo[3.3.1]nonanes transfer the vinyl group to the carbonyl carbon of aldehydes with complete retention of configuration at the migrating vinyl group, (23).⁶⁵ The vinyl-9-BBN reagents are readily prepared via hydroboration of the appropriate alkyne with 9-BBN.¹³

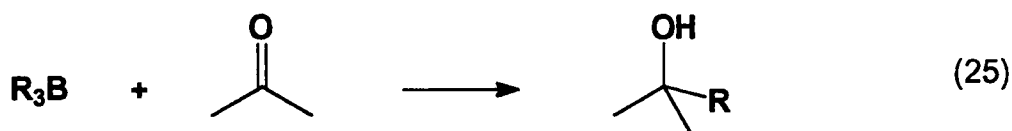


Alkynyl-9-BBN reagents react in a similar fashion with both aldehydes and ketones, (24).⁶⁶

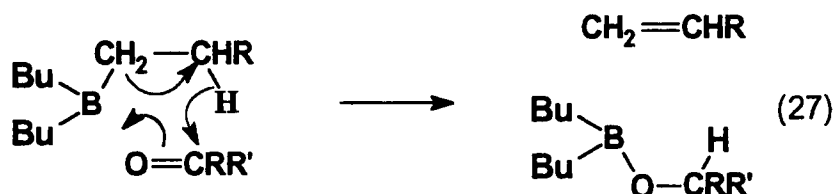
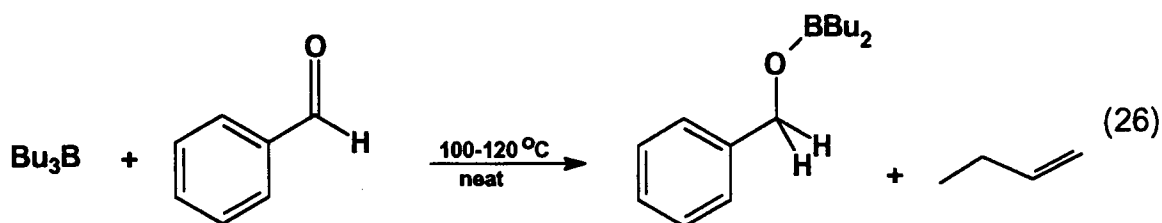


1.6.2 Saturated Organoboranes

Saturated organoboranes are typically unreactive toward carbonyl compounds. The transfer of an alkyl group to a carbonyl compound, via a 1,2-migration, would be a useful addition to the known organoborane reactions, (25).



The earliest attempt at achieving a Grignard-like alkylation reaction using trialkylboranes involved simply heating a mixture of a trialkylborane and an aldehyde. The procedure did not yield the desired alkylated product. Instead a reduction reaction occurred via a β -hydride elimination, (26).⁶⁷ The reaction is believed to occur via a planar, six-membered transition state, (27).



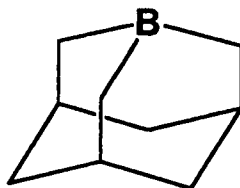
The β -hydride elimination reaction proceeds rapidly with liberation of heat. The first hydride transfer occurs readily. The second alkyl group releases a hydride only after prolonged heating. It was later found that B-alkyl-9-BBN derivatives can be used to efficiently reduce aldehydes such as benzaldehyde. The reaction rate increases significantly with increasing degree of substitution at the β -hydrogen.⁶⁸

A small amount of the desired alkylation reaction was observed when a trialkylborane and a carbonyl compound were heated to 300°C in the presence of hydroquinone.⁶⁹ The reaction does not appear to be synthetically useful.

Although the straightforward addition of a trialkylborane to a carbonyl carbon has not been achieved, certain modifications in either the carbonyl compound or the trialkylborane have resulted in limited success.

1.6.3 1-Boraadamantane and Carbonyl Additions

1-Boraadamantane is an alkylborane that does transfer an alkyl group to a carbonyl carbon. The boron carbon bonds in this unusual organoborane are



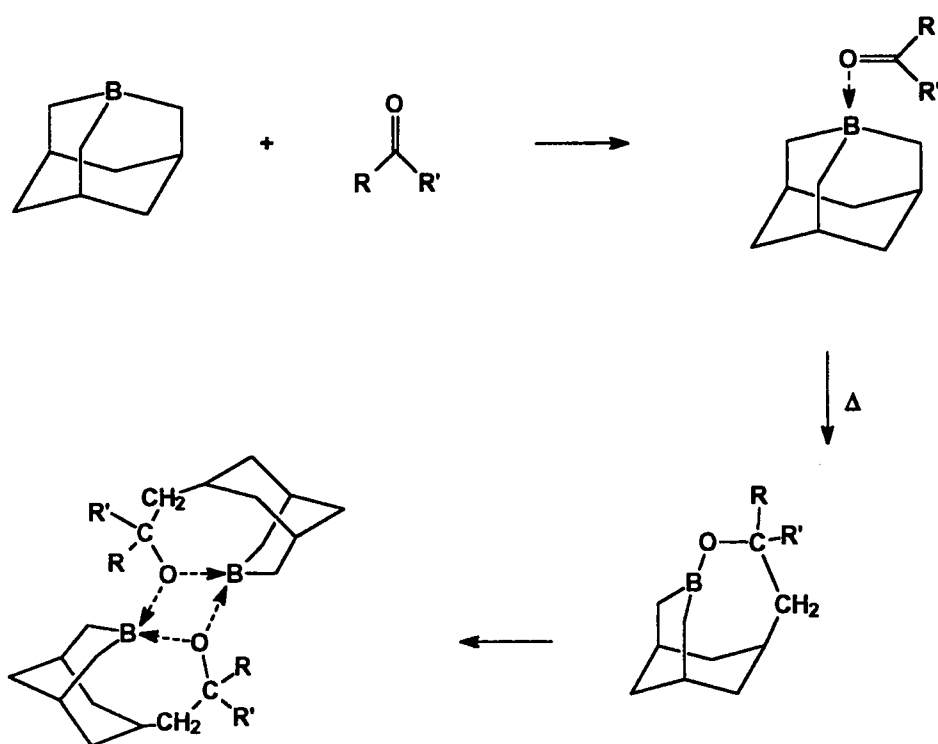
1-Boraadamantane

forced away from their normally trigonal planar geometry into a pyramidal orientation.⁷⁰ 1-Boraadamantane exhibits enhanced reactivity and Lewis acidity, because of this sp^3 -like state when compared to an ordinary trialkylborane such as tributylborane. Its complexing ability is comparable to that of BF_3 , and complexes of 1-boraadamantane with pyridine and triethylamine do not dissociate even at 200 °C.^{71a,b} 1-Boraadamantane undergoes several typical organoborane reactions with ease. It may, for example, be carbonylated to produce 1-adamantyl alcohol⁷¹ or aminated to produce 1-azaadamantane⁷².

1-Boraadamantane's reactions with carbonyl compounds are especially interesting (Scheme 2). The reaction follows the traditional organometallic path of complexation with the carbonyl compound which upon heating undergoes an alkyl transfer to give the alkylated product.⁷³

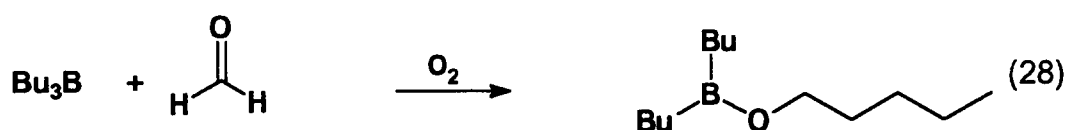
The sp^3 -like state of the boron in 1-boraadamantane is presumably responsible for its reactivity toward carbonyl compounds. The reaction is, however, limited to this single borane and only carbocyclic products are formed. If a way could be found to mimic the nature of the sp^3 hybridization of the boron atom in other trialkylboranes, this reaction would have a much wider scope.

Scheme 2



1.6.4 Alkylation of Formaldehyde using Trialkylboranes

Monomeric formaldehyde reacts with tributylborane in the presence of air to produce the addition reaction, (28).⁷⁴ This is the first reported example of direct 1,2-addition of a simple trialkylborane to a carbonyl compound. The reaction is not general for all aldehydes but several trialkylboranes have been successfully utilized.



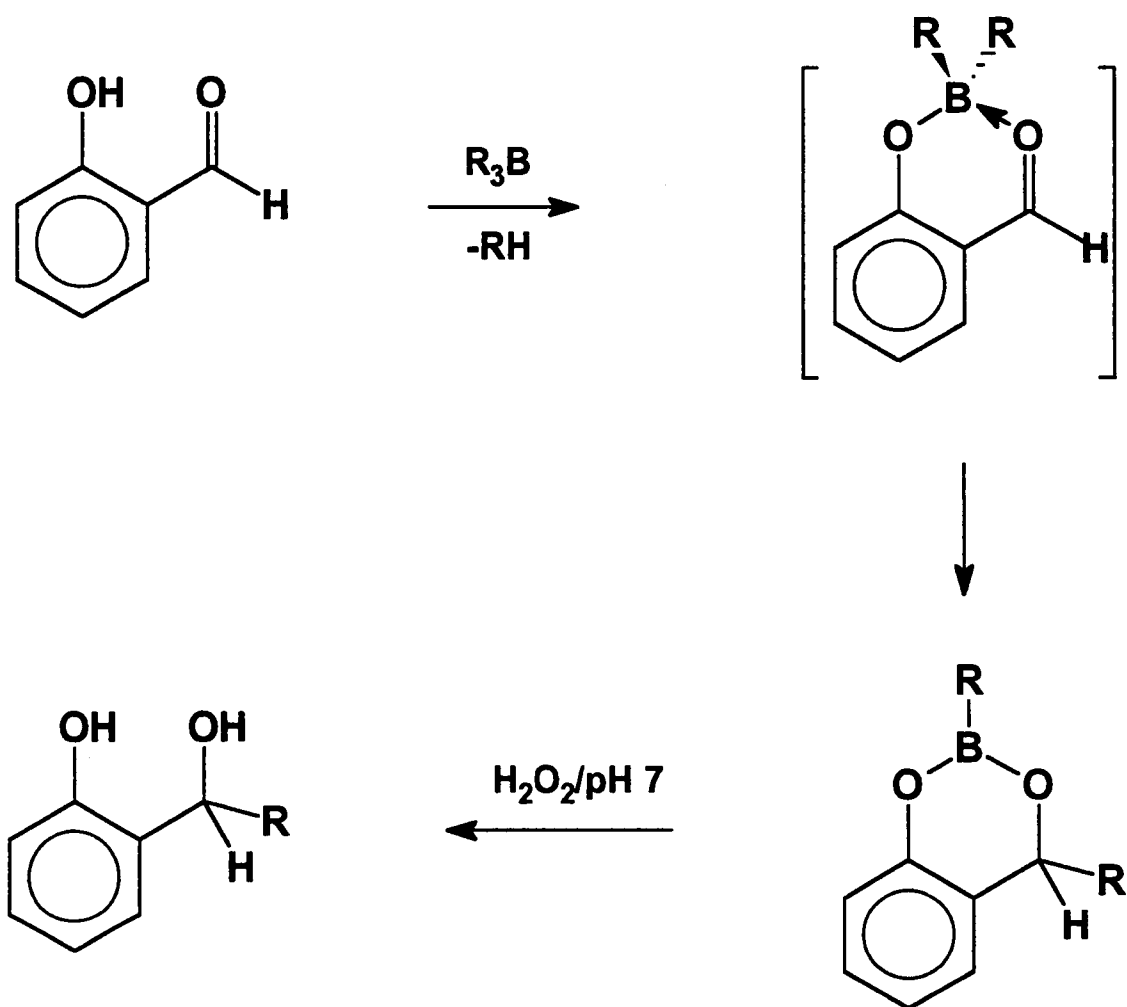
Only one of the alkyl groups migrates to produce acceptable yields of the products.

The reaction is believed to proceed with a free radical mechanism, since there is no alkylation in the absence of oxygen.⁷⁵ Iodine also completely inhibits the alkylation pathway leading to the reductive dealkylation compound as the sole product.

1.6.5 Alkylation of 2-Hydroxyarylaldehydes with Trialkylboranes

Trialkylboranes will alkylate the carbonyl carbon of a 2-hydroxyarylaldehyde (Scheme 3).⁷⁵ The reaction was attempted with several trialkylboranes and using different 1-hydroxyarylaldehydes. The reaction does, however, require both an ortho hydroxy group and a formyl group. The attempted alkylation of 2-methoxybenzaldehyde resulted in complete recovery of the starting material. When

Scheme 3

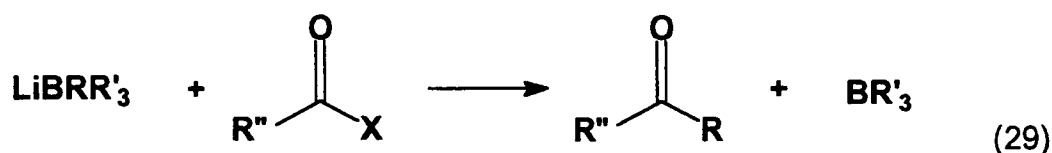


the ketone, 2-hydroxyacetophenone, was used, the reaction produced only the reduced product. In certain reactions, the addition of the radical inhibitor galvinoxyl reduced the yield of product. This suggests a radical pathway, perhaps a 1,4-type addition of an alkyl radical to the enol intermediate.⁷⁶

A wide variety of α -formylketones can also be alkylated with trialkylboranes, giving somewhat lower yields than the reactions with 2-hydroxyarylaldehydes. α -Diketones, however, do not react to give the alkylated product under either photochemical or thermal conditions.

1.6.6 The Reaction of Borate Complexes with Acyl Halides

Lithium tetraorganoborate complexes react with acyl or aroyl halides to produce the corresponding ketones in high yield, (29).⁷⁷ When an organoborane is treated with an organolithium, the corresponding borate anion or "ate" complex is formed. This converts the organoborane into a nucleophilic species.



R, R' = alkyl R'' = alkyl or aryl

The reaction of the "ate" complexes with acyl halides is general for a wide variety of trialkylboranes and acyl halides. Primary groups are transferred preferentially over secondary alkyl groups. The reaction also exhibits a high degree of chemoselectivity. The alkylation takes place exclusively at the acyl halide carbonyl carbon, even in the presence of an alkene and an ester respectively.

It is believed that the "ate" complex is the reacting species. The fact that trialkylboranes do not react with the acyl halides under similar conditions supports this postulation. The reaction of Grignard reagents or organolithiums with acyl halides usually produces the expected tertiary alcohols. The absence of these products further corroborates the above theory. It is, therefore, believed that there is no prior dissociation of the borate anion to the trialkylborane and the alkyllithium. This reaction essentially moderates the reactivity of organolithium reagents to the extent that none of the typical tertiary alcohol products are produced. At the end of the alkylation reaction, the trialkylborane can be recovered quantitatively.

1.7 STATEMENT OF PURPOSE

The selective formation of carbon-carbon bonds is important in organic chemistry. The reactions that are currently available are useful yet the reaction conditions are too vigorous for many functional groups. In addition, the reagents are often unstable and side reactions such as elimination, reduction and enolization can occur. Organoboranes are very useful reagents because they are easily

prepared, stable, and do not react with most functional groups. There are many exciting reactions that organoboranes undergo but they cannot transfer a saturated alkyl group to a carbonyl group. This dissertation summarizes a new reaction that achieves the coupling of an aryl and an alkyl group, utilizing a 1,2-addition reaction of a carbonyl derivative. The reaction conditions are sufficiently mild that functionalities survive and side reactions are minimized.

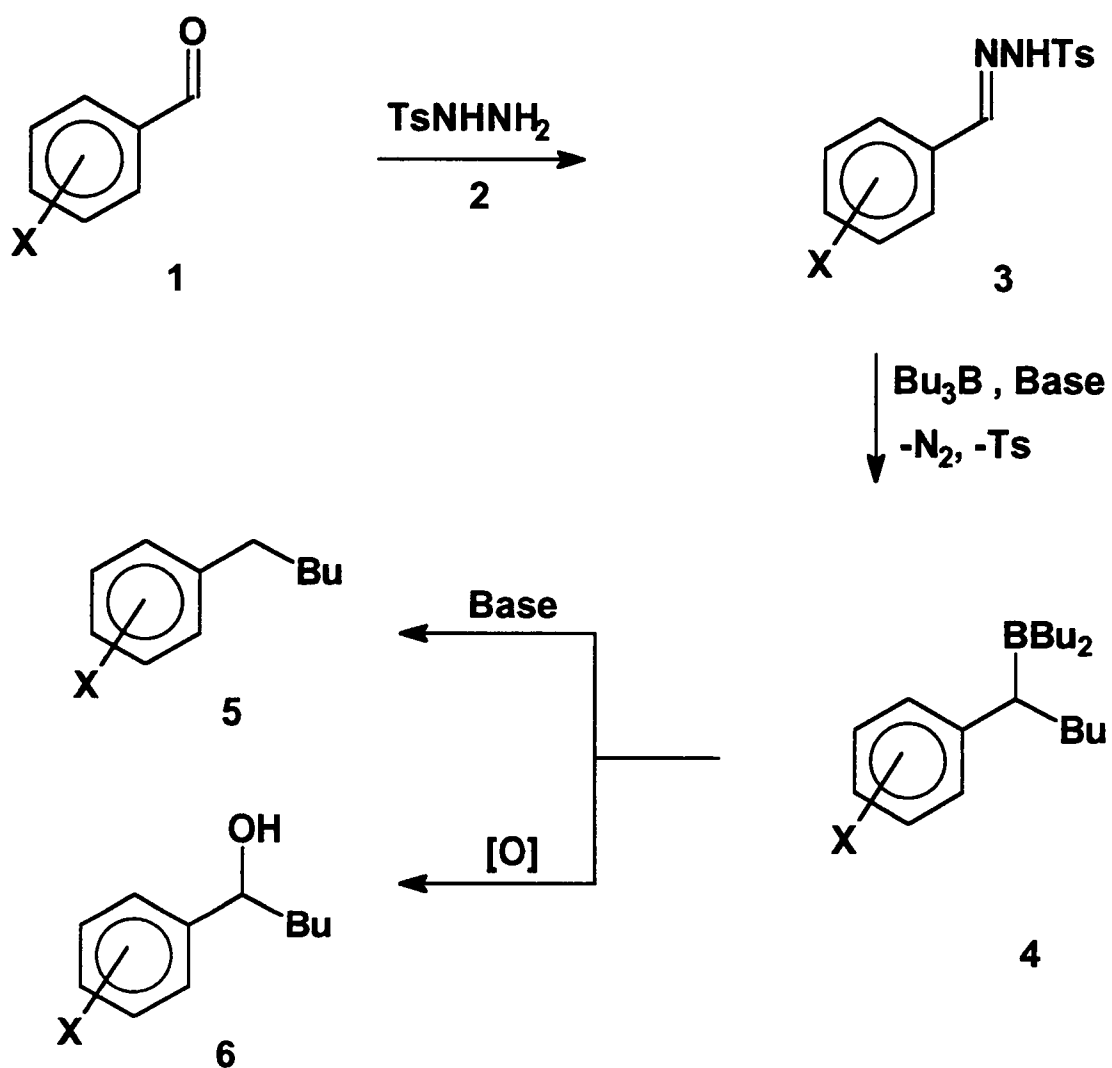
CHAPTER 2

ALKYLATION OF ALDEHYDE TOSYLHYDRAZONES

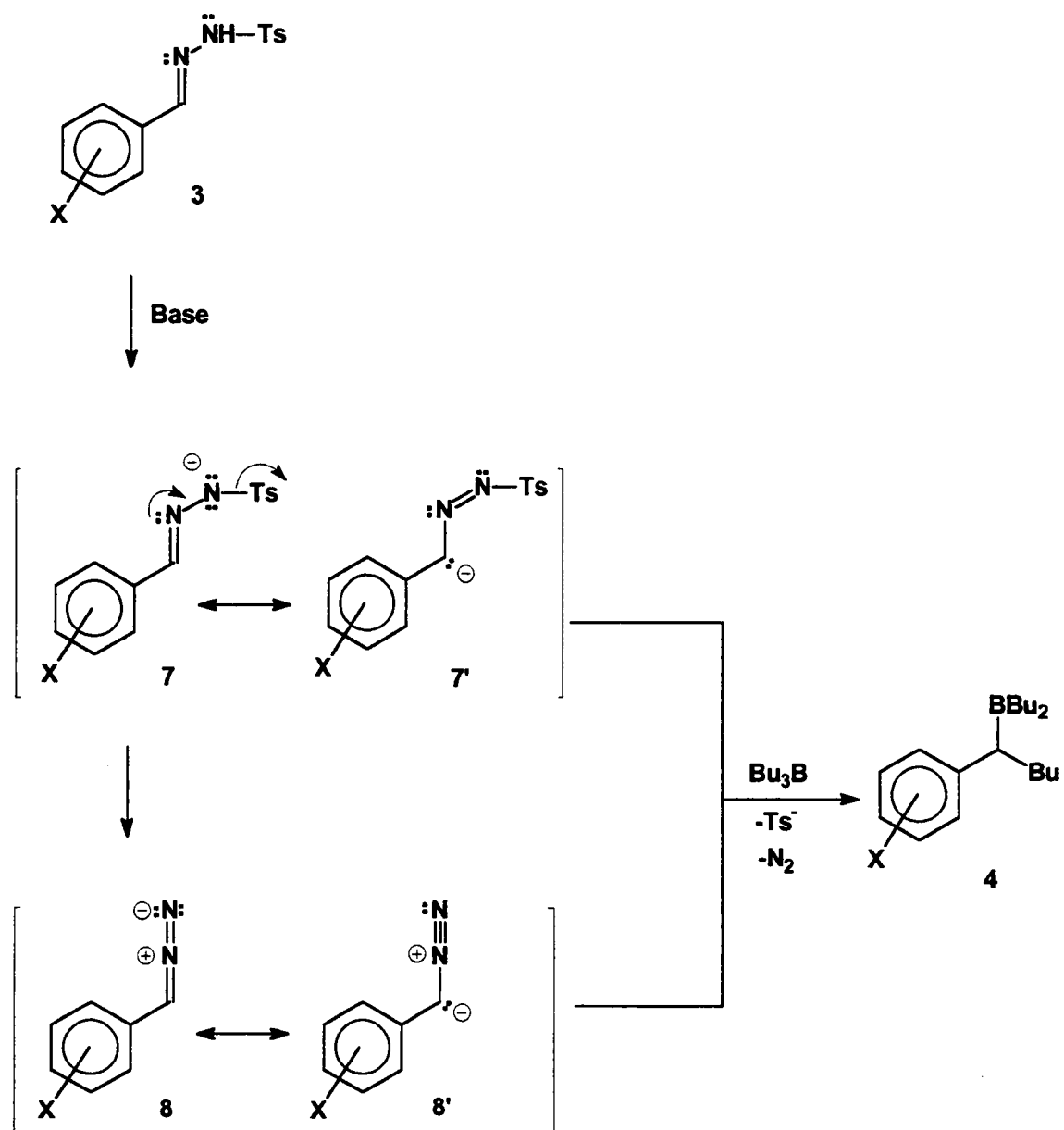
2.1 INTRODUCTION

As noted in Chapter 1, trialkylboranes do not routinely alkylate carbonyl compounds. A new alkylation reaction has been developed which utilizes a trialkylborane to alkylate a carbonyl compound at the carbonyl carbon and thus achieve the overall coupling of an alkyl group and an aryl group. Aryl aldehydes **1** (Scheme 4) are easily converted into their corresponding arenesulfonylhydrazones, such as the *p*-toluenesulfonylhydrazones (tosylhydrazones) **3**. Trialkylboranes, such as tributylborane (Bu_3B), can then react with the aryl aldehyde tosylhydrazones **3** in the presence of base to produce a new trialkylborane **4**.⁷⁸ This benzylborane is readily protonolyzed in the presence of a strong nucleophilic base to alkane **5**.⁷⁹ Alkane **5** is equivalent to the coupling product of an alkylborane and an aryl halide. Alternatively, **4** can be oxidized to produce the alcohol **6**. Alcohol **6** is equivalent to the product of a 1,2-addition of the trialkylborane to the starting aldehyde. In these studies, only the production of alkane **5** was studied. Two possible intermediates in this reaction when proceeding from **3** to **4** are the anion **7** or the diazo compound **8**, (Scheme 5). Both could generate the desired organoborane **4**. The mechanism of this reaction will be discussed in Chapter 4.

Scheme 4

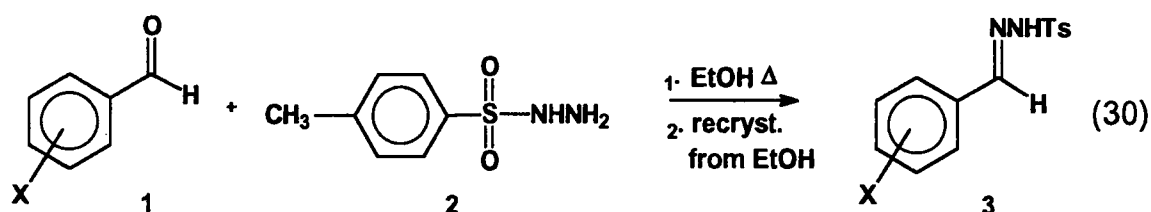


Scheme 5

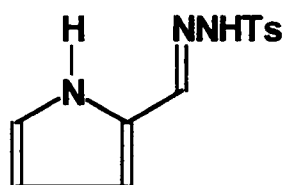


2.2 SYNTHESIS OF ARYL ALDEHYDE TOSYLHYDRAZONES

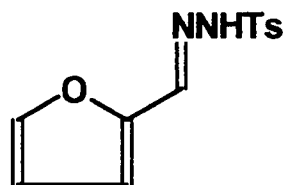
The arenesulfonylhydrazones studied for this dissertation were the tosylhydrazones and 2,4,6-triisopropylbenzenesulfonylhydrazones (trisyldhydrazones). The readily available tosylhydrazones were investigated first. Aryl aldehyde tosylhydrazones are stable, crystalline solids. The derivatizing agent, *p*-toluenesulfonylhydrazide, is commercially available and its hydrazone derivatives have been extensively studied and characterized. They are easily prepared, according to published procedures from *p*-toluenesulfonylhydrazide **2** and the



corresponding aryl aldehyde **1**, (30).⁸⁰ The aldehyde and tosylhydrazine are heated in boiling ethanol for 10 min. The reaction is immediate and a white precipitate is seen. The precipitate is easily purified by recrystallization from a minimum quantity of hot ethanol. Several aryl aldehyde tosylhydrazones were prepared containing various substituents on the ring (Table 2-1). Also prepared were the heterocyclic 2-pyrrolecarboxaldehyde tosylhydrazone **3l** and 2-furaldehyde tosylhydrazone **3m**.



3l



3m

Table 2-1. Synthesis of Arylaldehyde Tosylhydrazones **3**

Entry	X	mp (°C)	% yield ^a
1	2-Methoxy (3a)	151.0-152.0	85
2	3-Methoxy (3b)	107.5-108.5	69
3	4-Methoxy (3c)	123.0-123.5	89
4	4-Methyl (3d)	146.0-147.5	74
5	H (3e)	126.5-128.0	72
6	2-Bromo (3f)	159.0-159.5	84
7	3-Bromo (3g)	115.0-115.5	72
8	4-Bromo (3h)	164.0-164.5	80
9	4-Chloro (3i)	158.0-159.0	67
10	3-Nitro (3j)	159.1-160.2	79
11	4-Nitro (3k)	156.8-158.2	81
12	2-Pyrrolyl (3l)	184.0-185.0 (d)	82
13	2-Furyl (3m)	109.0-110.0 (d)	82

^a All percent yields are isolated yields.

2.2.2 Temperature Study

It is desirable for a reaction to occur readily at a low temperature to ensure a lower probability of undesirable side reactions occurring, such as decomposition of starting material or product, and the reaction is simpler to carry out. The alkylation reaction was, therefore, first attempted at room temperature. Unfortunately none of the desired alkane product was attained after a 24 h period. However, an 83% isolated yield of pentylbenzene was obtained after heating the reaction mixture to gentle reflux at 50-60 °C for 1 h. This higher temperature has been tolerated by all the functional groups investigated to date.

2.2.3 Tributylborane Study

The model compound used in the alkylation reactions was tributylborane. Tributylborane can theoretically transfer three butyl groups. It was found, in a reaction of *p*-chlorobenzaldehyde tosylhydrazone with NaOH and Bu₃B, that only one of the butyl groups transferred. Two reactions in which 0.33 mole equivalents of Bu₃B was utilized gave a 34% and 33% isolated yield of *p*-chloropentylbenzene as compared to a 99% yield of product (based on the carbonyl compound) if 1 equivalent of Bu₃B was used. One equivalent of Bu₃B was thus utilized in all subsequent reactions.

2.2.4 Base Study Using Gas Chromatography

The alkylation reaction requires base. In the absence of base, no reaction occurs within a 24-h period. The choice of base is dependent on two factors. First, the base must be strong enough to remove the sulfonamide proton from the aryl aldehyde tosylhydrazone. Second, The base must be nucleophilic enough to hydrolyze the intermediate borane to the alkane. A gas chromatographic study was performed to determine the efficiency of various bases in the alkylation reaction. Table 2-2 summarizes the effect of these bases on the yield of product.

Table 2-2. The Efficiency of Various Bases in the Synthesis of Pentylbenzene.

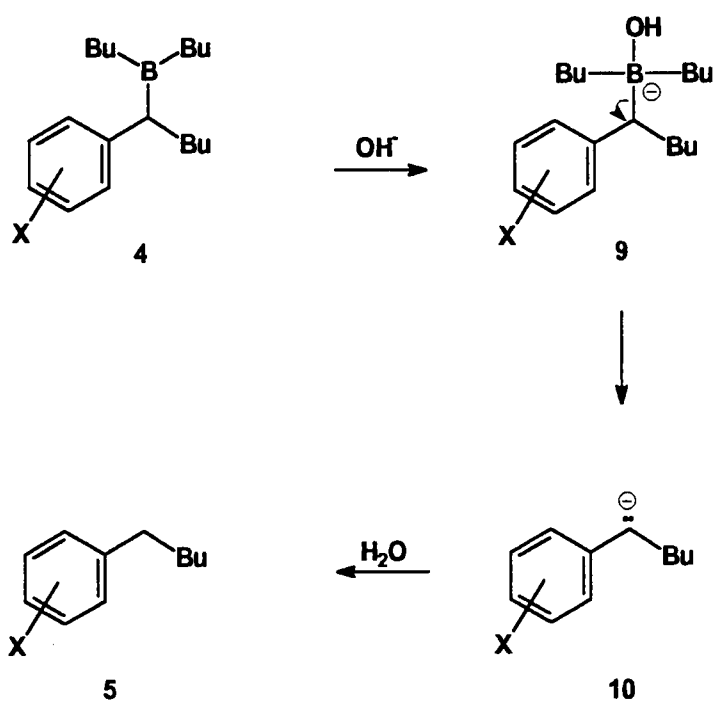
Base	Time (h)	%Yield ^{a,b}
Lutidine	4	0
Triethylamine	4	2
Diethylamine	4	8
DBU	0.5	21
Sodium Hydroxide	1	91
Tetrabutylammonium Hydroxide	1	86

^a All percent yields are GC yields.

^b Yields are determined using a minimum of three GC runs.

Sodium hydroxide and tetrabutylammonium hydroxide produced the highest yields. 1,8-Diazabicyclo[3.3.1]undec-7-ene (DBU) is a strong base and, according to thin layer chromatography (TLC), led to the disappearance of all the starting material in ½ h of reaction. Since it is, however, a non-nucleophilic base it could not deboronate intermediate **4**, Scheme 6, to form the alkane product **5**.

Scheme 6



Intermediate **4** is sufficiently stable, if a non-nucleophilic base is used, to undergo oxidation to form the alcohol product, 1-phenylpentanol (**6**), in 76% isolated yield. The lower yield is due to some hydrolysis of the intermediate borane. Sodium hydroxide and tetrabutylammonium hydroxide are strong nucleophiles and deboronate intermediate **4** to produce good yields of product **5**. The other bases were simply not strong enough to react with the starting benzaldehyde tosylhydrazone. After a 4 h reaction time, a very small amount of product was detected and most of the starting material remained unreacted.

All of the above reactions were carried out using one equivalent of base. In a reaction of benzaldehyde tosylhydrazone with NaOH where only 1/3 equivalent of base was used, the reaction did not go to completion. When 3 equivalents of base were used there was no increase in yield as shown in Table 2-3.

Table 2-3. Effect of Excess Base on the Yield of Pentylbenzene.

Base (equiv.)	Time	% Yield	Time	% Yield
1	1	84	2	82
3	1	82	2	83

Other bases investigated were strong bases such as butyllithium, lithium hexamethyldisilazane, and sodium hydride. These reactions were followed by TLC for the disappearance of starting tosylhydrazone. These bases reacted only partially with the starting tosylhydrazone. The primary drawback to their use is that

they form tosylhydrazone anion salts which precipitate out of solution which impedes further reaction with the trialkylborane.

2.2.5 Method of Base Addition

Two different modes of base addition were examined resulting in slightly different yields of pentylbenzene (Table 2-4). In method A, the base was added

Table 2-4. Effect of Base Addition on the Yield of Pentylbenzene.

Base	Time (h)	% Yield A ^{a,c}	% Yield B ^{b,c}
Lutidine	4	0	0
Diethylamine	4	0	8
DBU	0.5	17	21
NaOH	1	84	91
Bu ₄ NOH	1	81	86

All percent yields are GC yields.

^a %yield using method A. ^b %yield using method B.

^c Yields are determined using a minimum of three GC runs.

to the THF/tosylhydrazone solution and the reaction mixture was then heated. If a strong base was utilized, the solution turned bright orange. The color could be due to anion formation⁸⁰ (7, Scheme 5) or to formation of a diazo intermediate²⁸ (8, Scheme 5). The tributylborane would then be added slowly to the reaction mixture since the reaction would strongly exotherm upon its addition. In method B, the tributylborane was added to the THF/benzaldehyde tosylhydrazone mixture. This was followed by addition of the base and the reaction mixture was then heated.

This second method required less time and produced slightly higher yields of product. Although the difference in yields is not significant, method B was used in all subsequent reactions. It was simpler to use since none of the reactants had to be added slowly, whereas in method A the borane had to be added dropwise.

2.2.6 Time Study

Gas chromatographic (GC) time studies were conducted to determine if the thin layer chromatographic analyses were correctly indicating the endpoint of the reaction. In the reactions of benzaldehyde tosylhydrazone with NaOH and Bu₃B, the starting material would disappear after approximately 1 h of heating. The GC studies supported the TLC observations (Table 2-5). The reactions utilizing Bu₄NOH as the base appeared to be complete within ½ h of heating with only a trace of starting material visible according to TLC. This observation was again supported by the GC studies (Table 2-5) in which the Bu₄NOH reaction, after only ½ h of heating, gave a yield comparable to that of the NaOH reaction. Bu₄NOH is a strong nucleophilic base in methanol. The hydroxide ion in methanol is not as solvated as the hydroxide ion in aqueous solution and can, therefore, deboronate intermediate **4** faster than aqueous NaOH.

Table 2-5. Yields of Pentylbenzene with NaOH and Bu₄NOH.

Time (h)	% Yield with NaOH ^a	% Yield with Bu ₄ NOH ^{a,b}
0.5	70	82
1	81	81
2	82	81

^a All percent yields are GC yields.

^b Yields are determined using a minimum of three GC runs.

2.2.7 Hydrolysis Study

It was of interest to ascertain whether or not the intermediate borane formed in the reaction of DBU with benzaldehyde tosylhydrazone could be hydrolyzed to the alkane product, pentylbenzene. Several reactions were run at reflux with DBU for $\frac{1}{2}$ h and analyzed by GC. This would give the yield of pentylbenzene. NaOH was then added in an attempt to hydrolyze the benzylborane intermediate **4** and allowed to react in a variety of experiments at both RT and at reflux. The GC yields of pentylbenzene were then determined.

The experiments in Table 2-6 demonstrate that the intermediate borane can be hydrolyzed. At room temperature the hydrolysis reaction proceeds to give a yield of only 45% after a reaction time of 2 h. It requires heating the reaction to reflux for $\frac{1}{2}$ h in order to obtain yields of pentylbenzene comparable to those found in the reactions with OH^- . The hydrolysis of **4**, therefore, requires heat to proceed to completion. Since the reaction with DBU requires heat, both the first step of the reaction (to obtain the intermediate benzylborane **4**) and the hydrolysis step (to obtain the final product **5**) require heat.

Table 2-6. Hydrolysis of **4** to Yield Pentylbenzene.

Exp	Method	Temp (°C) ^a	Time (h)	% Yield ^b	% Yield ^c
1	A	RT	0.5	14.6	40
	A	RT	0.5	13.5	35
2		RT	1		41
		RT	2		45
3	A	reflux	0.5	13.8	59
4	B	RT	0.5	9.5	42
5	B	reflux	0.5	21.5	84
		reflux	1		86
6	B	reflux	0.5	20.7	85

^a Temperature of hydrolysis reaction

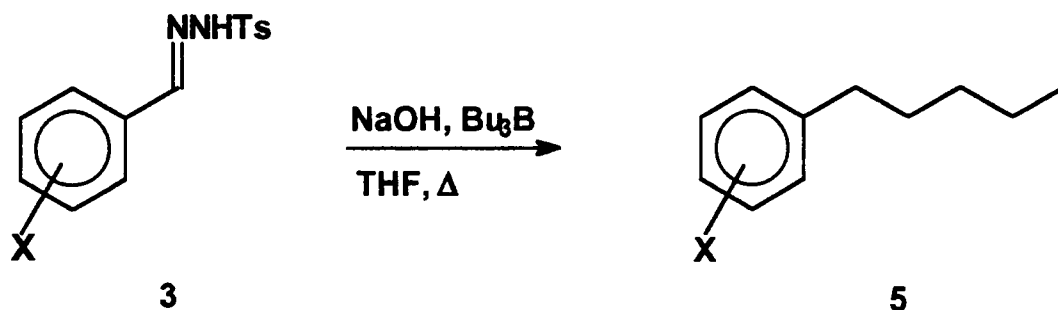
^b GC yield of pentylbenzene after ½ h at reflux with DBU

^c GC yield of pentylbenzene after addition of NaOH to the reaction mixture

2.2.8 Ring Substituent Study Using NaOH

Since NaOH gave good yields of the pentylbenzene and was less expensive than Bu_4NOH it was the first base to be studied. The alkylation reaction was run with various substituted tosylhydrazones. The various substituted aryl tosylhydrazones produced comparable yields of alkane product **5** (Table 2-7). The tosylhydrazones containing electron-withdrawing groups (EWG) on the benzene ring, such as chloro and bromo, gave slightly higher yields of product in shorter reaction times. Longer reaction times were needed for tosylhydrazones containing electron-donating groups (EDG), e.g. methoxy and methyl. Most of the starting material disappeared within 2-4 h when the EDG substituted tosylhydrazones were used. The yields of the isolated products were, however, lower than those generated from the sulfonylhydrazones containing electron withdrawing groups. Even after a reaction time of 5-6 h, the isolated yields from the tosylhydrazones containing EDG were still lower relative to those obtained when the EWG substituted materials were utilized. In these cases, extended reaction times were required before acceptable yields of the desired products could be obtained. Analysis of the reaction mixture by TLC seemed to indicate that the reaction proceeds well initially and most of the starting tosylhydrazone was consumed within the first few hours. However, a spot is seen by TLC which corresponds to the intermediate benzylborane **4** and it disappeared very slowly. This suggests that benzylboranes with EDG on the ring do not deboronate very easily, leading to the longer reaction times for the methoxy and methyl derivatives.

Table 2-7. Reaction of Various Aldehyde Tosylhydrazones with NaOH.



Entry	X	Time (h)	%Yield 5 ^a
1	4-methoxy	4	50 ^b
2	4-methoxy	5	50
3	4-methoxy	9	57 ^c
4	4-methoxy	17	83
5	4-methyl	2	59 ^{b, d}
6	4-methyl	17	89
7	H	1	83
8	2-bromo	1	93
9	3-bromo	1	88
10	4-bromo	1	90
11	4-bromo	5	92
12	4-chloro	1	92
13	4-chloro	1.5	99 ^b
14	3-nitro	1	89 ^e
15	4-nitro	0.5	81
16	4-nitro	1	90
17	4-nitro	23	89

^a Isolated yields based on starting tosylhydrazone. ^b Average of two reactions.

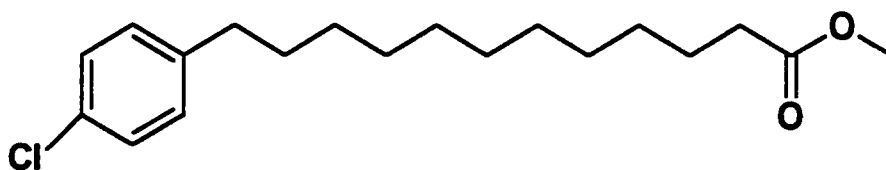
^c Reaction also gave a 35% yield of alcohol. ^d Reaction also gave a 10% yield of alcohol. ^e Average of three reactions.

One of the reactions performed with the methoxy derivative, (Table 2-7, entry 3), was oxidized to test this theory. It produced a 35% yield of alcohol **6** and a 57% yield of alkane **5** to give an overall yield of 92%. The high yield of alcohol supports the theory that the hydrolysis step is the slow step for these derivatives.

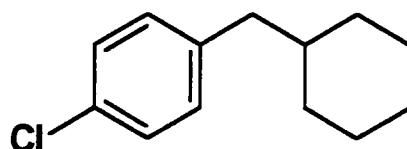
The *p*-nitro group is a very powerful EWG because it can further stabilize the anion formed in the reaction (**7**, **8**, Scheme 5) by delocalization of the charge onto the nitro group. The *p*-nitro substituted tosylhydrazone should, therefore, produce a higher yield of product than the chloro or bromo containing tosylhydrazones. However, the reactions of the *p*-nitro substituted tosylhydrazone did not give yields above 90%. The reactions of *p*-chlorobenzaldehyde tosylhydrazone, in contrast, gave yields of 98 and 99%.

2.2.9 Functionalized Alkyl Groups Using NaOH

One of the advantages of organoboranes is their ability to tolerate many functional groups.²² A reaction was performed in which *p*-chlorobenzaldehyde tosylhydrazone was treated with an organoborane containing an ester functionality. The reaction went well, yielding 92% of the desired alkane product **11** in 1 h. Secondary alkyl groups are also important in organic synthesis. Tricyclohexylborane was used to test the ability of this alkylation reaction to transfer a secondary group. The reaction yielded 24% of the desired alkylation product **12** after a reaction time of 3 h.



11



12

2.2.10 *Use of Bu₄NOH as Base*

Although use of NaOH provides a simple route to the alkanes the use of Bu₄NOH was investigated. Bu₄NOH is commercially available in methanol solution. This solution was kept dry by keeping it under argon, and it remained sufficiently oxygen free for our purposes. The reactions of the various aryl aldehyde tosylhydrazones with this new base produced similar yields to the reactions with NaOH, (Table 2-8). One improvement it led to was the reduction in reaction time.

Table 2-8. Synthesis of Aryl Alkanes **5** from Tosylhydrazones **3** with Bu₄NOH

Entry	X	Time (h)	%Yield 5 ^a
1	2-Methoxy (3a)	2	93
2	3-Methoxy (3b)	2.5	89
3	4-Methoxy (3c)	1.5	83
4	4-Methyl (3d)	1	90
5	H (3e)	1	80
6	H (3e)	1	78 ^b
7	2-Bromo (3f)	1	92
8	3-Bromo (3g)	1	89
9	4-Bromo (3h)	1	94
10	4-Chloro (3i)	1	94
11	3-Nitro (3j)	1	91
12	4-Nitro (3k)	1	98
13	2-Pyrryl (3l)	24	61
14	2-Furyl (3m)	3	66

^a Isolated yields^b Tosylhydrazone generated *in situ* in THF at RT

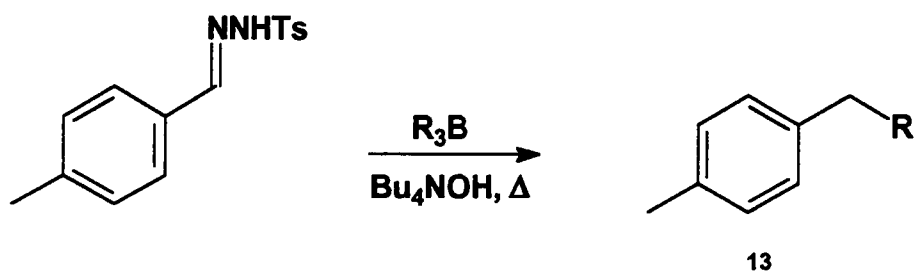
This was important for the hydrazones with EDG as substituents. Even for those groups which retarded the reaction when NaOH was used, the reaction times with Bu₄NOH were only 1-2.5 h. The hydrazones with EWG were complete in under 1 h. They were, however, all allowed to go for 1 h to ensure completion of the reaction and especially of the hydrolysis step. Substitution in the ortho, meta or para positions again seems to have little effect as seen from the methoxy and bromo substituted derivatives.

It was also found that the reaction could be extended to aromatic heterocycles. Both 2-pentylpyrrole and 2-pentylfuran were produced in good yields. The slightly lower yields are presumably due to the increased electron density in the heterocyclic rings as compared to the substituted benzene derivatives. This makes formation of the anion less favorable which results in incomplete hydrolysis under the reaction conditions.

2.2.11 Functionalized Alkyl Groups Using Bu₄NOH

As with NaOH, it was desirable to determine whether or not functional groups would survive the reaction conditions. Several functional groups can be present in the alkyl group transferred in this new alkylation reaction. Table 2-9 lists the yields of the respective alkanes after reaction with *p*-tolualdehyde tosylhydrazone. Entries 1-3 demonstrate that a halo, cyano, and ester group are readily transferred using this methodology. Entries 4 and 5 demonstrate that secondary groups may be transferred as well. In the Suzuki reaction which was discussed in Chapter 1,

Table 2-9. Reaction of *p*-Tolualdehyde Tosylhydrazone with Various Trialkylboranes.



Entry	Product	R	(%) 13 ^a
1	a	-CH ₂ (CH ₂) ₃ CH ₂ Cl	91 ^b
2	b	-CH ₂ (CH ₂) ₃ CH ₂ CN	98
3	c	-CH ₂ (CH ₂) ₉ COOCH ₃	90
4	d	-Chx ^c	71
5	e	-CH(CH ₃)CH ₂ CH ₃	62
6	f	-Ph ^d	80

^a Isolated yields.

^b Two equivalents of Bu₄NOH used.

^c Chx = Cyclohexyl.

^d From triphenylboron.

secondary groups did not transfer at all under some conditions and trialkylboranes transferred secondary groups with low yields.

2.2.12 Blocking Groups

As was noted earlier, only one of the groups on the boron migrates. This is not uncommon in organoborane chemistry and, in fact, it occurs in many reactions involving trialkylboranes. This includes the Suzuki reaction outlined in Chapter 1. When this occurs, borane derivatives with two "blocked" positions are utilized to conserve the alkene substrate. The borane derivatives tried in the reaction of benzaldehyde tosylhydrazone and Bu₄NOH were dibromohexylborane and hexyl-9-BBN.

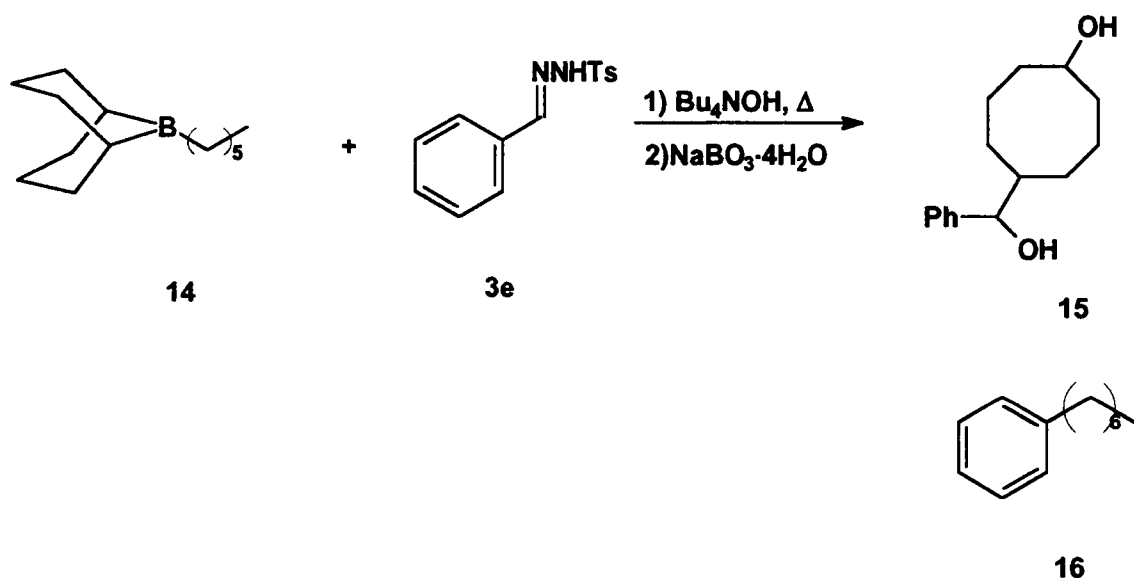
Hexyl-9-BBN

9-Borabicyclo[3.3.1]nonane (9-BBN) can be prepared via the hydroboration of 1,5-octadiene followed by thermal equilibration of the isomers in refluxing THF.⁸¹ The dimer of 9-BBN may be recrystallized from 1,2-dimethoxyethane to give crystals which are stable to air for short periods of time.⁸² 9-BBN is one of the most unhindered dialkylboranes so that it can hydroborate fairly hindered alkenes such as 2,3-dimethyl-2-butene.⁸³ It shows greater selectivity than most dialkylboranes, placing 99.5% of the boron on the terminal carbon of a 1-alkene. In contrast to other dialkylboranes it will preferentially hydroborate alkenes in the presence of the more electron rich alkynes.⁸⁴

Hexyl-9-BBN **14** was prepared from commercially available 9-BBN according

to literature procedure.⁸⁵ It was added to a solution of benzaldehyde tosylhydrazone followed by Bu_4NOH , (Scheme 7). After a reaction period of 1 h the reaction mixture was oxidized with sodium perborate tetrahydrate. Upon purification 49% of the ring-opened product 5-(hydroxyphenylmethyl)cyclooctanol (**15**) was isolated. This product was formed from the transfer of the cyclooctyl-boron bond and oxidation of the intermediate borane. 1-Phenylheptane (**16**) was not isolated. A similar result had been previously noted in the reaction of alkyl-9-BBN compounds with α -diazocarbonyl compounds, where the ring migrated preferentially to the straight chain alkyl group.⁸⁶

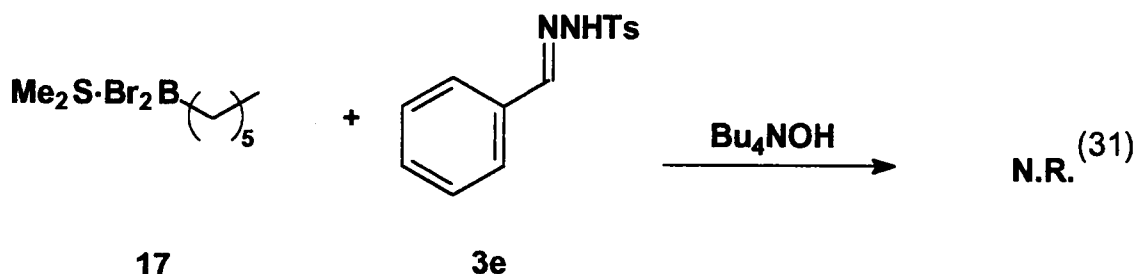
Scheme 7



Dibromohexylborane

Dibromoalkylboranes are typically more reactive than trialkylboranes due to their increased Lewis acidity. They display a regioselectivity similar to that of 9-BBN. It was hoped that by replacing the alkyl groups with the bromine group only the alkyl would migrate.

The dimethylsulfide complex of dibromohexylborane **17** was prepared according to literature procedure⁸⁷ and added to a solution of benzaldehyde tosylhydrazone in THF followed by the addition of Bu_4NOH , (31). The reaction was exothermic and a small amount of gas evolution was seen. After a reaction period of 1 h very little of the starting material appeared to have reacted. Only a few faint spots were observed when the reaction mixture was analyzed by TLC. After 8 h there was no change in the reaction mixture and most of the starting material was still present according to TLC.



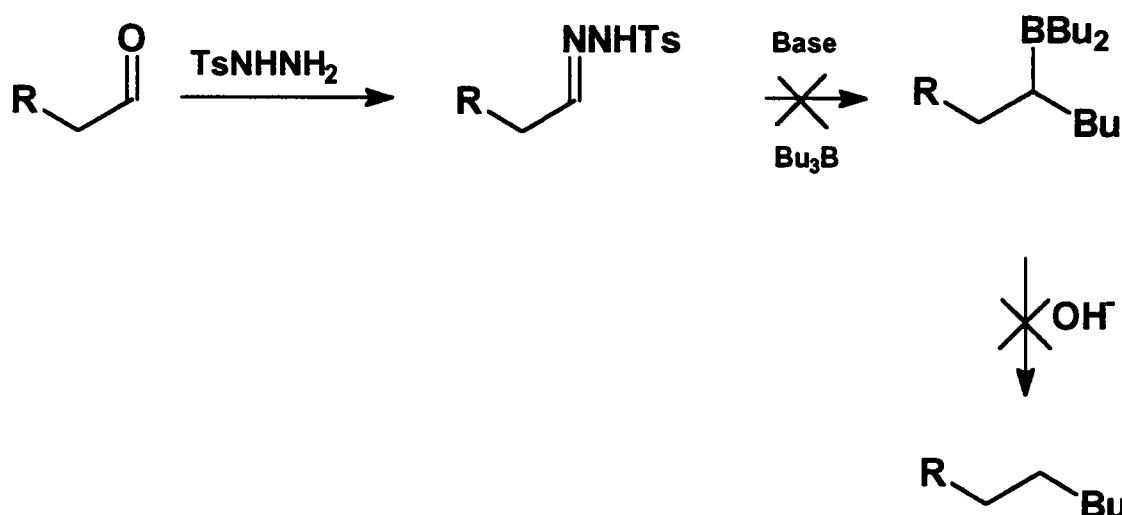
There are two possible explanations for this. Due to its enhanced Lewis acidity, the dibromoborane could form a complex with the nitrogens of the

tritylhydrazone or the base. It is also possible that it is unstable in base and is therefore destroyed before it can react with the tosylhydrazone.

2.3 ALKYLATION OF ALKYL ALDEHYDE TOSYLHYDRAZONES

It was of interest to determine whether the preceding successful methodology could be extended to alkyl aldehydes, (Scheme 8). Based on the mechanisms proposed for the reaction in Section 2.1, it was anticipated that the reactions of the alkyl hydrazone substrate would be more sluggish. The alkyl groups offer little or no stabilization for the developing negative charge on the original carbonyl carbon in the initial alkylation step. They also offer no stabilization for the anion that forms in the deboronation step (Scheme 6). The aryl groups, on the other hand, stabilize these negative charges through benzylic resonance and

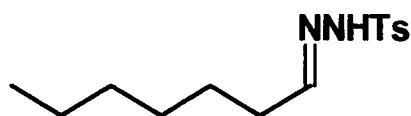
Scheme 8



the inductive electron withdrawing effect of the benzene ring. Despite this drawback, it was desirable to determine if alkyl aldehyde substrates could be included in this new alkylation technology.

2.3.1 *Synthesis of Alkyl Aldehyde Tosylhydrazones*

Heptanal tosylhydrazone, **18**, was chosen as the model substrate for the

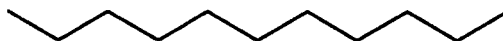


18

study. It is readily prepared from heptanal and *p*-toluenesulfonylhydrazide and it was easily purified by recrystallization from ether.⁸⁸

2.3.2 *Results of the Alkylation of Heptanal Tosylhydrazone*

Several base and solvent combinations were tested to determine if **18** could be alkylated with the standard trialkylborane, tributylborane, to give the coupled product undecane, **19**, (Table 2-10). The first attempt involved the use of NaOH in



19

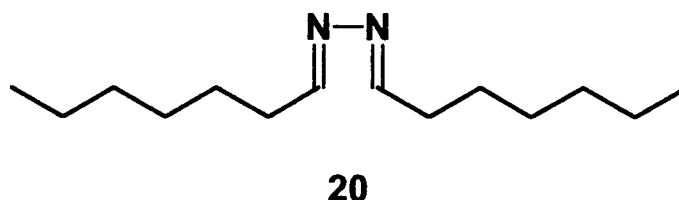
Table 2-10. Attempted Alkylation of Heptanal Tosylhydrazone via Tributylborane.⁸⁹

Entry	Base	Solvent ^(a)	% Yield undecane (19)
1	NaOH	THF	--
2	Bu ₄ NOH	THF	--
3	BuLi	THF	--
4	<i>t</i> -BuLi	THF	--
5	LDA	THF	--
6	NaOH	CH ₂ Cl ₂ /H ₂ O (PTC)	--
7	Bu ₄ NOH	MeOH	--
8	Bu ₄ NOH	MeOH/Hexanes	--
9	BuLi	HMPA	--
10	<i>t</i> -BuLi	HMPA	--

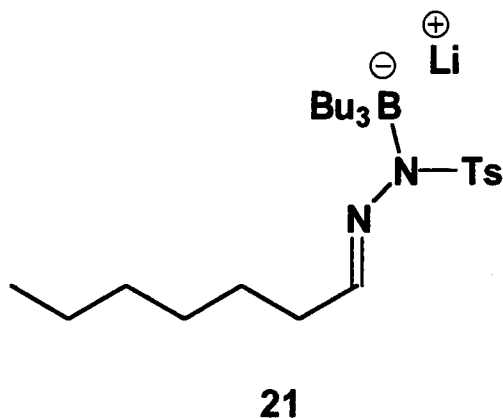
^(a)Reflux.

refluxing THF, the protocol which succeeded with the aryl aldehyde tosylhydrazones. It, however, failed to produce any product with the alkyl substrate. Bu₄NOH, which was more effective in the tosylhydrazone reactions than NaOH, also failed to produce any product. After refluxing overnight with Bu₄NOH there were a multitude of spots but none of the desired product was isolated. A threefold excess of Bu₄NOH also failed to produce product. Since a negative charge is presumed to be forming during the course of the reaction it was thought that a more polar solvent would aid in its formation by stabilizing it. However, when the reaction conditions were changed to include more polar solvents such as methanol or methanol/hexanes there was still no reaction. The reactions were run both at room temperature and at reflux. There was no reaction at room temperature and at reflux

there were once again a multitude of by-products. By-products observed via GC/MS were 5-undecene, and various methyl substituted heptadecenes. One of the isolated by-products was the azine **20**. Azines are a common by-product of diazo compounds which suggests that a diazo intermediate is being formed during the reaction of the alkyl aldehyde tosylhydrazones with base.



Several other bases were tested first at room temperature and then in refluxing THF including BuLi, *t*-BuLi, and lithium diisopropyl amide (LDA). There was no reaction with any of the bases at room temperature; at reflux a multitude of by-products was again observed. These included condensation products of heptanal and the azine by-product. Several of the strong kinetic bases, such as the alkyllithiums, produced a white solid when added to a solution of the tosylhydrazone and tributylborane in THF. This solid is presumably the lithium salt **21** of the borate complex formed by reaction of the nitrogen of the tosylhydrazone anion with the boron of the tributylborane. A ^{11}B NMR of the supernatant, from a reaction in which the solid was present, showed no boron present, which suggests that the tributylborane was trapped in the precipitated complex. Hexamethylphosphoramide (HMPA), a polar aprotic solvent, was utilized in an attempt to solubilize this complex



to allow the boron to react at the carbon of the original carbonyl instead of at the nitrogen. Reactions were performed using strong bases in neat HMPA but no product was produced.

Tosylhydrazones have been reported to be N-alkylated with NaOH and alkyl halides under phase transfer catalysis (PTC) conditions. Adaptation of this technology to utilization of tributylborane also failed to produce any product. The azine was once again observed as a by-product after 24 h at reflux.

2.4 SUMMARY

A new alkylation reaction was developed which is the synthetic equivalent of the cross-coupling of an aryl and an alkyl group. Aryl aldehyde tosylhydrazones are readily alkylated with trialkylboranes in the presence of a nucleophilic base to produce the corresponding substituted aryl alkanes. Several functional groups may be present in either the hydrazone or the trialkylborane. Alkyl aldehyde

tosylhydrazones do not react with trialkylboranes to produce the corresponding alkanes. Alkylborane derivatives, such as B-alkyl-9-BBN and B-alkylcatecholborane, do not react to produce the desired aryl alkanes.

CHAPTER 3

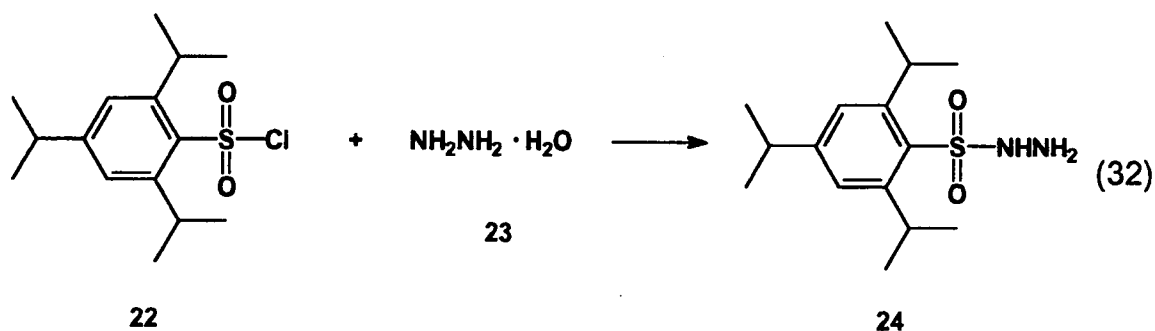
ALKYLATION OF ARYL ALDEHYDE TRISYLHYDRAZONES

3.1 INTRODUCTION

After establishing that aryl aldehyde tosylhydrazones were suitable substrates for the new alkylation reaction it was of interest to explore whether other arenesulfonylhydrazones would function as well. The 2,4,6-triisopropylbenzenesulfonylhydrazones (trisylhydrazones) have proven to be superior to the tosyl hydrazones in production of diazoalkanes.⁹⁰ The trisyl moiety has also proven superior to the tosyl group in the production of diimide from arenesulfonylhydrazides.⁹¹ It was felt that the trisyl's increased reactivity would manifest itself in the new alkylation reaction.

3.2 SYNTHESIS OF 2,4,6-TRIIISOPROPYLBENZENESULFONYLHYDRAZIDE

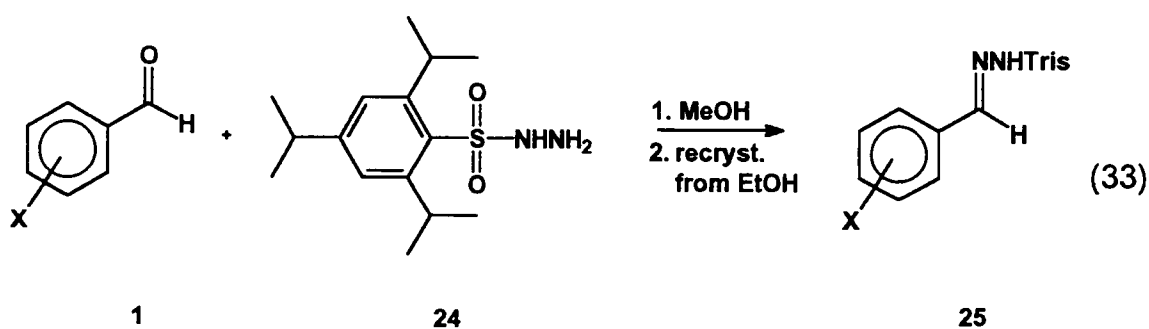
The derivatizing agent, 2,4,6-triisopropylbenzenesulfonylhydrazide (TPSH), is commercially available. It may, however, be simply and inexpensively prepared from the readily available sulfonyl chloride **22** and hydrazine hydrate **23** (32).⁹¹ TPSH, **24**, was prepared and isolated as a snow-white solid in 80-85% yield. It is



a reasonably stable and easily handled material. If stored under refrigeration and in an amber bottle, there is only 5% decomposition in nine months.

3.3 SYNTHESIS OF ARYL ALDEHYDE TRISYLHYDRAZONES

Aryl aldehyde trisylhydrazones are stable crystalline or powdery solids which can be readily prepared by adding the corresponding aryl aldehyde to TPSH in methanol (33).⁹⁰ The reaction is run at room temperature for 1 h. An immediate



reaction is seen in the formation of a precipitate. The resulting precipitate may be recrystallized from a minimum quantity of hot ethanol. Some of the derivatives

which could not be recrystallized were the more polar ones such as the nitro and the bromo substituted benzenes. This was due to their low solubility in hot ethanol. It was, however, not a problem as the unrecrystallized solids were actually analytically pure. Table 3-1 lists several aryl aldehyde trisylhydrazones which were prepared for this study.

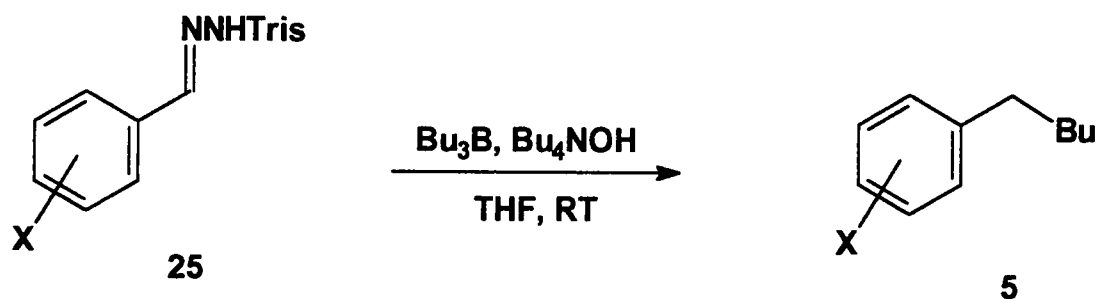
Table 3-1. Synthesis of Aryl Aldehyde Trisylhydrazones **25**

Entry	X	mp (°C)	% yield 25
1	2-Methoxy (25a)	164.5-165.5	54
2	3-Methoxy (25b)	187.0-188.5	62
3	4-Methoxy (25c)	161.5-162.5	62
4	4-Methyl (25d)	165.0-166.0	61
5	H (25e)	186.5-187.5	87
6	2-Bromo (25f)	153.0-154.0	71
7	3-Bromo (25g)	207.5-209.0	54
8	4-Bromo (25h)	197.0-197.8	68
9	4-Chloro (25i)	194.5-195.5	70
10	3-Nitro (25j)	191.0-192.5	80
11	4-Nitro (25k)	196.0-197.0	74
12	2-Furan (25l)	149-150 (d)	87

3.4 RESULTS

The aryl aldehyde trisylhydrazone derivatives were tested as possible substrates in the alkylation reaction, Table 3-2. The derivatives produced the alkanes in excellent yields and, in fact, some proceeded under very mild conditions. Whereas the tosyl derivatives required heating to reflux in THF, the trisyl derivatives all reacted at room temperature. Some of the derivatives required heating so that the deboronation step could proceed at a reasonable rate; these were the substrates with no EWG on the ring. The deboronation step leaves a benzylic anion which needs to be stabilized through resonance into the aromatic ring. The EWG provides this stabilizing force at room temperature so that the *p*-chloro and *p*-bromo substrates, for example, proceed at room temperature to give good yields of product. The unsubstituted benzyl substrate and the substrates with the EDG, such as *p*-methoxy and *p*-methyl, had to be heated in order for this second step to occur readily.

Table 3-2. Synthesis of Aryl Alkanes **5** from Trisylhydrazones **25**.

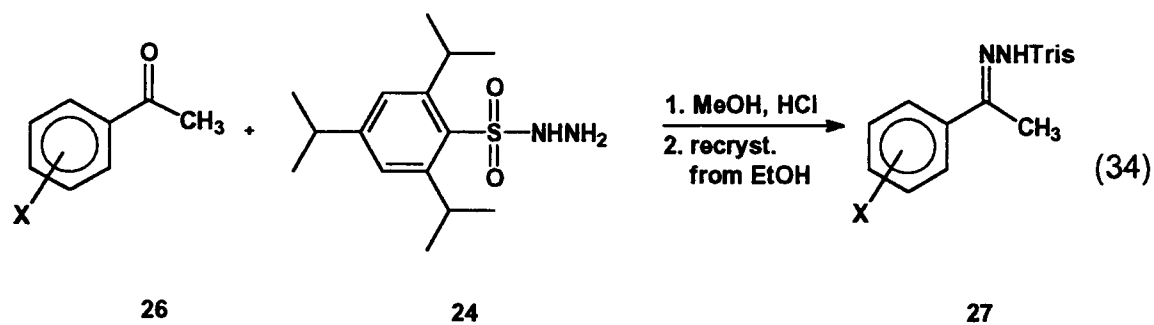


Entry	X	Time (h)	Temperature	%yield 5 ^a
1	4-Methoxy (25c)	1.5	Reflux	68
2	4-Methyl (25d)	1	Reflux	88
3	H (25e)	1	Reflux	93
4	2-Bromo (25f)	0.5	RT	92
5	3-Bromo (25g)	0.5	RT	96
6	4-Bromo (25h)	1	RT	93
7	4-Chloro (25i)	0.5	RT	93
8	3-Nitro (25j)	0.5	RT	96
9	4-Nitro (25k)	0.5	RT	95
10	2-Furan (25l)	1	Reflux	93

^a Isolated yields based on starting trisylhydrazones.

3.5 Ketones

Thus far only aldehydes had been studied. To extend the reaction, the trisylhydrazones of ketones were prepared and used in the coupling reaction, (Table 3-3). Aryl ketone trisylhydrazones were as simple to prepare as aryl aldehyde trisylhydrazones (34).⁹⁰ Once again the ketone and TPSH are combined



with methanol as the solvent. The reaction proceeds at room temperature in 1 h. The only difference is that a catalytic amount of acid is used in the reaction.

Table 3-3. Synthesis of Ketone Trisylhydrazones **27**.

Entry	X	mp	% Yield 27
1	H	166.5-167.5	85
2	4-NO ₂	163.3-164.7	65

The reaction of the ketone trisylhydrazones with tributylborane, (35), produced good yields of the alkylation reaction to give **28** in good yields, (Table 3-4).

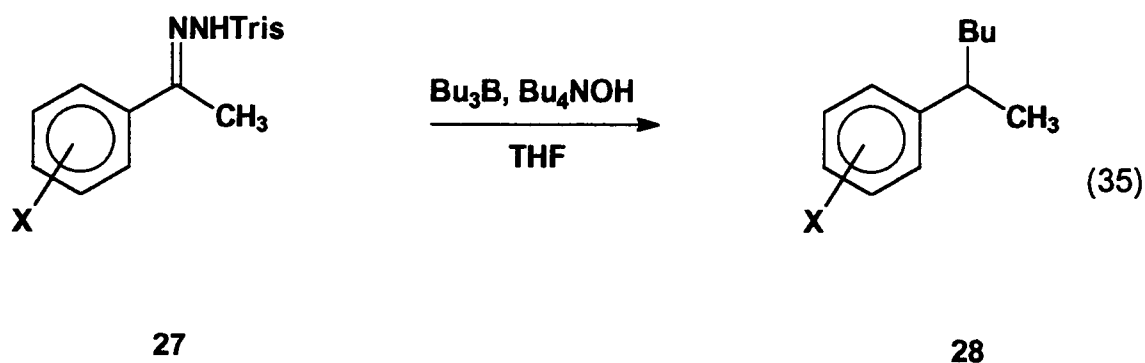


Table 3-4. Synthesis of Aryl Alkanes **28** from Ketone Trisylhydrazones **27**.

Entry	X	Time (h)	Temperature	% Yield 28
1	H	1	reflux	74
2	4-NO ₂	1.5	RT	85

3.6 Alkyl Trisylhydrazones

When the alkylation of heptanal tosylhydrazone **18** was investigated earlier, there were no positive results and none of the coupled product was isolated. It was thought that perhaps the increased reactivity of the trisyl group would enable the reaction to proceed if an alkyl aldehyde trisylhydrazone was used. Heptanal

trisylhydrazone **29** was used for this study. Unlike its tosylhydrazone counterpart, heptanal trisylhydrazone is not very stable or isolable and must be prepared and used *in situ*.⁸⁸ Heptanal and TPSH were dissolved in THF and stirred at room temperature until TLC indicated that the reaction was complete. The THF solution was then dried with anhydrous MgSO_4 and filtered through a short column of celite/anhydrous Na_2SO_4 to remove the water generated during trisylhydrazone formation.

The reaction was carried out with a variety of bases (Scheme 9). A reaction occurred but did not give the coupled product, undecane (**19**). Instead, undecan-5-ol **31** was produced upon oxidation. The intermediate borane, **30**, is too stable to base and can not be deboronated. The negative charge that would form upon deboronation, **32**, has no way of being stabilized.

In the reactions to form the alkylation product, undecan-5-ol, the base that gave the highest yield was DBU (Entry 5, Table 3-5). Propionic acid was used in an attempt to protonolyze the intermediate borane **30**, formed upon reaction of heptanal trisylhydrazone with Bu_3B and DBU. If all of the intermediate reacted, a theoretical yield of 74 % undecane could be obtained. Undecane was, however, formed only in a 14% yield. This was the only reaction utilizing heptanal trisylhydrazone that gave the coupled product **19**.

Scheme 9

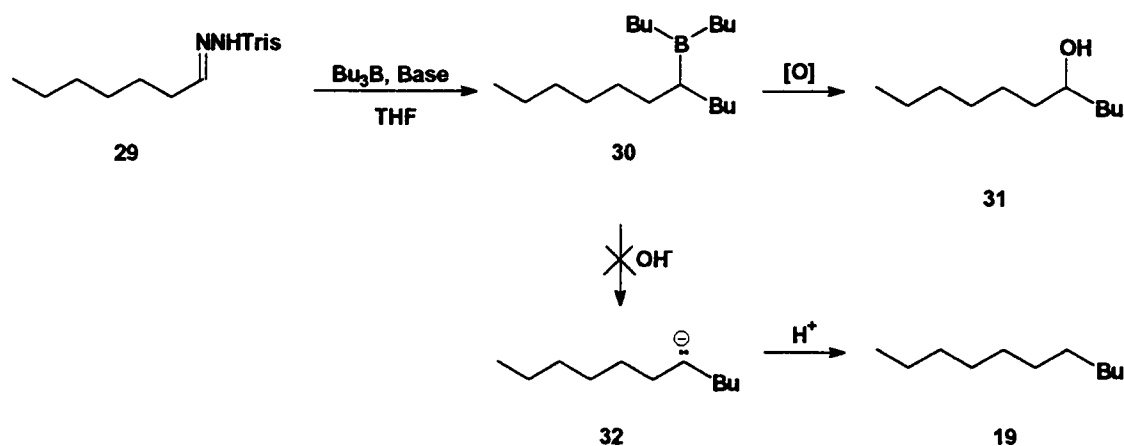


Table 3-5. Synthesis of Undecan-5-ol **31** from Heptanal Trisylhydrazone **29**.⁹²

Entry	Base	Time (h)	Temperature	% Yield
1	Bu_4NOH	0.5	RT	-
2	Bu_4NOH	1	reflux	50
3	<i>t</i> -BuLi	2	RT	-
4	<i>t</i> -BuLi	19	reflux	64
5	DBU	3	reflux	74 ^a

^a 1.5 equivalents of base used

3.7 USE OF BORANE DERIVATIVES

As in the tosylhydrazone case, the stoichiometry of the alkylation reaction between aryl aldehyde trisylhydrazones and tributylborane was equimolar. Only a single group transferred from the three available on the trialkylborane. As in the tosylhydrazone case it was desirable to attempt to conserve the alkyl groups by using borane derivatives with two "blocked" positions. A variety of blocking groups were used in the alkylation of benzaldehyde trisylhydrazone and Bu_4NOH . An investigation into the applicability of these blocked derivatives to this new alkylation reaction follows.

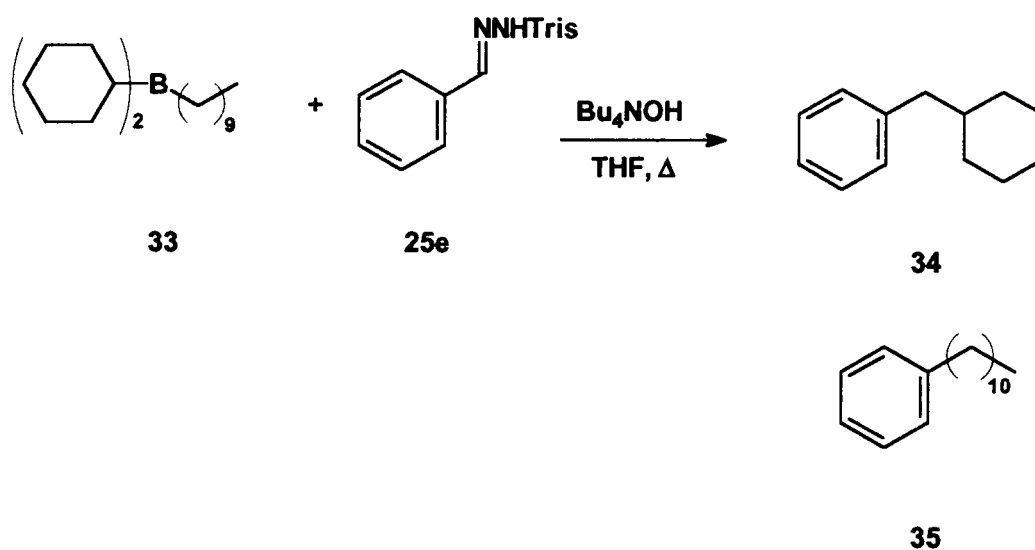
3.7.1 *Dicyclohexyldecylborane*

Dicyclohexylborane is a very stable white solid which exists as a dimer. It has an enhanced regioselectivity relative to BH_3 and places 99% of the boron at the terminal position of a 1-alkene. It will also selectively hydroborate an acyclic double bond in the presence of a cyclic double bond.⁹³

Dicyclohexylborane was prepared from the hydroboration of cyclohexene with BH_3 .⁹⁴ It was then used in the hydroboration of 1-decene to produce decyldicyclohexylborane **33**.⁹⁵ When it was treated with Bu_4NOH and benzaldehyde trisylhydrazone a mixture of cyclohexylphenylmethane, **34**, and 1-phenylundecane, **35**, was produced. **34** and **35** were produced in yields of 61% and 31% respectively giving a ratio of 67:33 or 2:1, (Scheme 10). This ratio shows that the groups

migrated competitively. This blocking group is therefore not useful for the alkylation reaction.

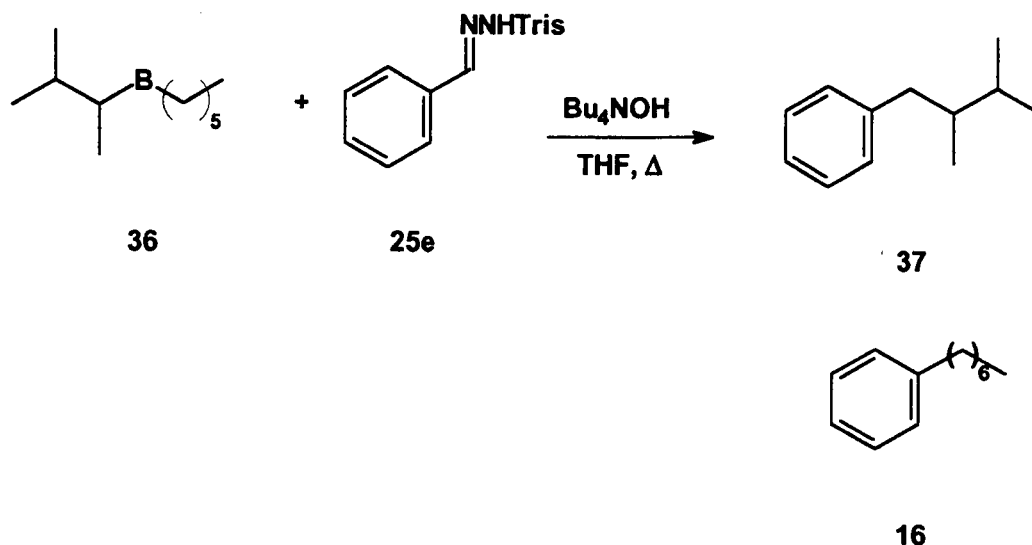
Scheme 10



3.7.2 Hexyldisiamylborane

Disiamylborane is similar to dicyclohexylborane in that it too shows an enhanced regioselectivity relative to BH_3 placing 99% of the boron on the terminal carbon of a 1-alkene.⁹⁶ It was prepared from the reaction of two equivalents of 2-methyl-2-butene with BH_3 .⁹⁷ The resulting borane was used to hydroborate 1-hexene to give hexyldisiamylborane 36,⁹⁸ which was then used in the reaction of benzaldehyde trisylhydrazone with Bu_4NOH to give a mixture of products, (Scheme 11). 2,3-Dimethylbutylbenzene, 37, and 1-phenylheptane, 16, were produced in

Scheme 11



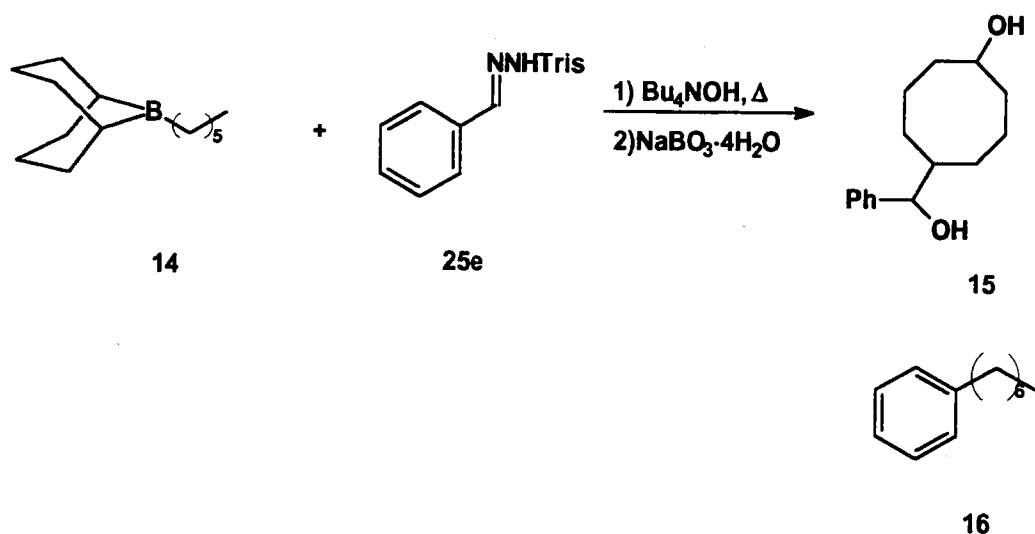
yields of 8% and 41% respectively. This ratio of 16:84 siamyl:hexyl reveals that the hexyl migrated preferentially. This is opposite to the cyclohexyl case and therefore puzzling. One problem might be an incomplete reaction of the 2-methyl-2-butene with BH_3 . ^{11}B NMR, however, showed that the reaction was complete and that all of the BH_3 had reacted to form the dialkylborane.

3.7.3 Hexyl-9-BBN

Hexyl-9-BBN **14** was prepared from the commercially available 9-BBN according to literature procedure.⁸⁵ When it was treated with benzaldehyde trisylhydrazone 25% of **16** was isolated while 48% of the ring opened product **15** was isolated, (Scheme 12). This corresponds to a molar ratio of 34:66. As in the preceding alkyl blocking groups the 9-BBN blocking group competitively transfers

to give a molar ratio close to the theoretical ratio of 33:67.

Scheme 12

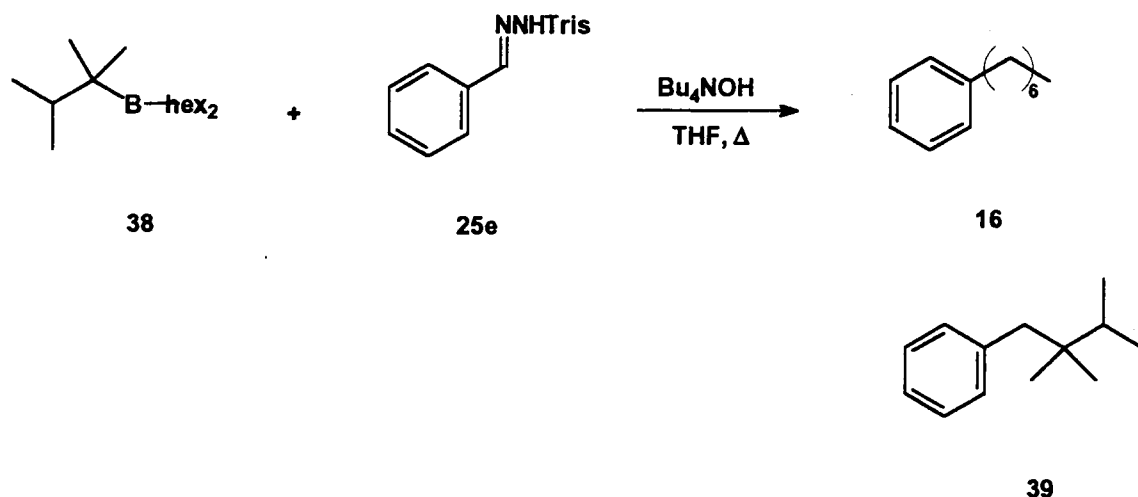


3.7.4 Dihexylthexylborane

Thexylborane is a very hindered monoalkylborane which was prepared by the reaction of 2,3-dimethylbutene with BH_3 .⁹⁹ Two equivalents of 1-hexene were then added to the prepared monoalkylborane to produce dihexylthexylborane **38**, (Scheme 13).¹⁰⁰ The thexyl group is so hindered that it generally does not migrate. When it was used in a reaction with benzaldehyde trisylhydrazone however, it competed effectively with the hexyl group and migrated at the same rate. 1-Phenylheptane, **16**, and 2,3,3-trimethyl-4-phenylbutane, **39**, were produced in yields of 61% and 25% respectively. This corresponds to a molar ratio of 71:29 which is very close to the 67:33 ratio expected if both groups had the same migratory

aptitude. Once again the hindered group migrated at a rate equal to that of the non-hindered group.

Scheme 13



3.7.5 Dibromohexylborane

When dibromohexylborane **17** was used in the reaction of benzaldehyde tosylhydrazone (Section 2.2.13), there was no reaction. It was postulated that either the dibromoborane was too acidic and complexed with the hydrazone without reacting, or that the base was destroying the borane. It was hoped once again that the increased reactivity of the trisyl group would enhance this reaction.

The dimethylsulfide complex of dibromohexylborane was prepared according to a literature procedure⁸⁷ and added to a solution of benzaldehyde trisylhydrazone in THF followed by the addition of Bu_4NOH . After a reaction period of 1 h, most of the starting material had reacted. Several spots were, however, seen when the

reaction mixture was analyzed by TLC and none of them corresponded to **16**. The largest spot observed seemed to correspond to the intermediate benzylborane so perhaps the deboronation step does not work in this reaction.

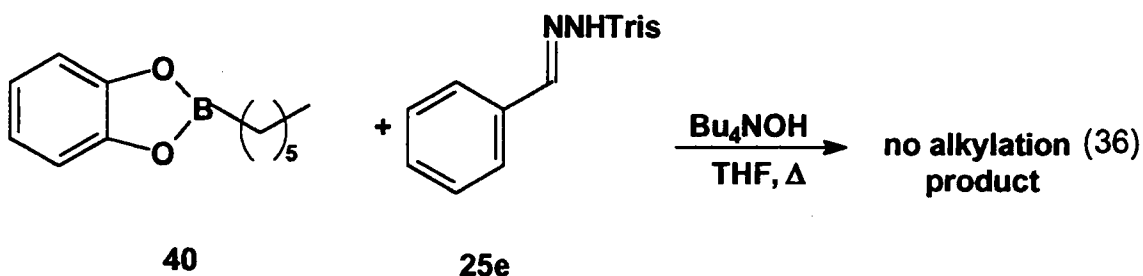
This reaction was in direct contrast to the tosyl case where none of the starting material reacted and only a few faint spots were noted when the reaction mixture was analyzed by TLC. In this case, the trisylhydrazone appears to be reactive enough to reach the benzylborane stage but does not go beyond that to the protonolyzed product. The multiple spots seen on the TLC suggest that the starting material is also decomposing and that side reactions are occurring.

3.7.6 *Hexylcatecholborane*

Catecholborane or 1,3,2-benzodioxaborole is produced from the reaction of BH_3 with catechol.¹⁰¹ It is a solid at 0°C and is quite stable if stored at that temperature. The two oxygens that serve as the blocking groups decrease the Lewis acidity of the boron atom making catecholborane less reactive than the dialkylboranes. It will hydroborate alkynes and alkenes at 70°C and 100 °C, respectively, giving regioselectivities comparable to disiamylborane.¹⁰²

B-Hexylcatecholborane **40** was prepared according to the literature procedure from catecholborane.¹⁰² It was expected that, if a reaction occurred, the oxygens would not migrate making this an ideal blocking group. Use of **40** in a reaction with benzaldehyde trisylhydrazone and base gave similar results to the dibromoborane reaction. The starting benzaldehyde trisylhydrazone reacted within

½ h at reflux but no alkylation product was observed (36). Analysis of the reaction mixture by TLC revealed a spot that corresponded to the intermediate borane. After heating at reflux for an additional 2 h there was still none of the desired product **16** and the intermediate borane was still present. After allowing the reaction to reflux overnight, multiple spots were seen. None of these corresponded to the desired product. This result is similar to that of the dibromoborane reaction.

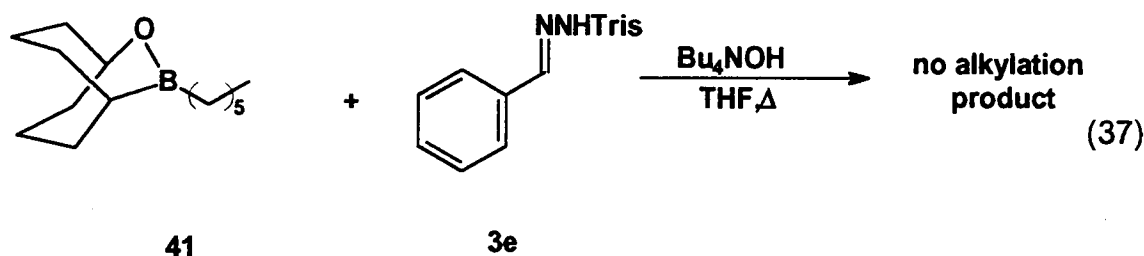


3.7.7 Oxidized 9-BBN

Partially oxidized alkyl 9-BBN has only one oxygen attached to the boron and has been used before in cases where the cyclooctyl ring migrated preferentially to a primary alkyl group as in the hexyl-9-BBN case. Hexyl-9-BBN was prepared as previously described (Section 2.2.13). One of the cyclooctyl ring bonds was then selectively oxidized at the boron with trimethylamine-N-oxide (TMANO) to give **41** which was then purified by distillation.

When **41** was used in a reaction of benzaldehyde trisylhydrazone with base the starting material was still present after 5 h at reflux and no alkylation product

was seen, (37). It is possible that the one oxygen decreased the Lewis acidity to the point that **41** will not react to give the alkylated product **16**.



3.7.8 Summary of Blocking Groups

None of the blocked derivatives were useful for the alkylation of aryl aldehyde trisylhydrazones. Hindered alkyl blocking groups, such as cyclohexyl, 9-BBN, and thexyl, migrated competitively with the primary alkyl group to give mixtures of products. Blocking groups containing boron-oxygen bonds or boron bromine bonds react with the trisylhydrazone but do not give any alkylation product.

3.8 CONCLUSION

Aryl aldehyde trisylhydrazones and tosylhydrazones are readily alkylated using a new alkylation reaction which is the synthetic equivalent of the coupling between an aryl and an alkyl group. The trisylhydrazones react more readily than the corresponding tosylhydrazones, producing alkylated aryls in excellent yields.

Trisylhydrazones containing EWG react at room temperature while trisylhydrazones with EDG require heat for the reaction to go to completion. Alkyl trisylhydrazones do not produce the corresponding alkanes in very good yields and alkylborane derivatives are not useful in this reaction.

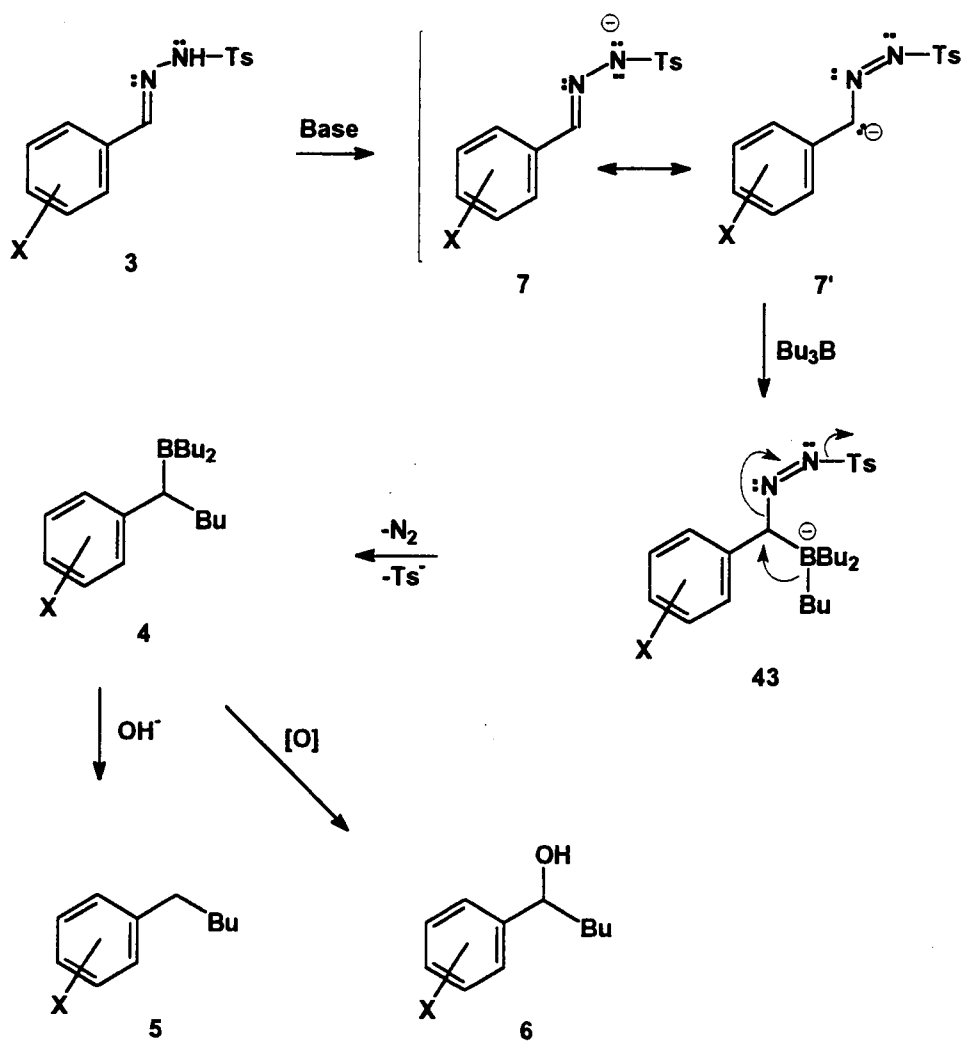
CHAPTER 4

MECHANISM OF THE ALKYLATION REACTION

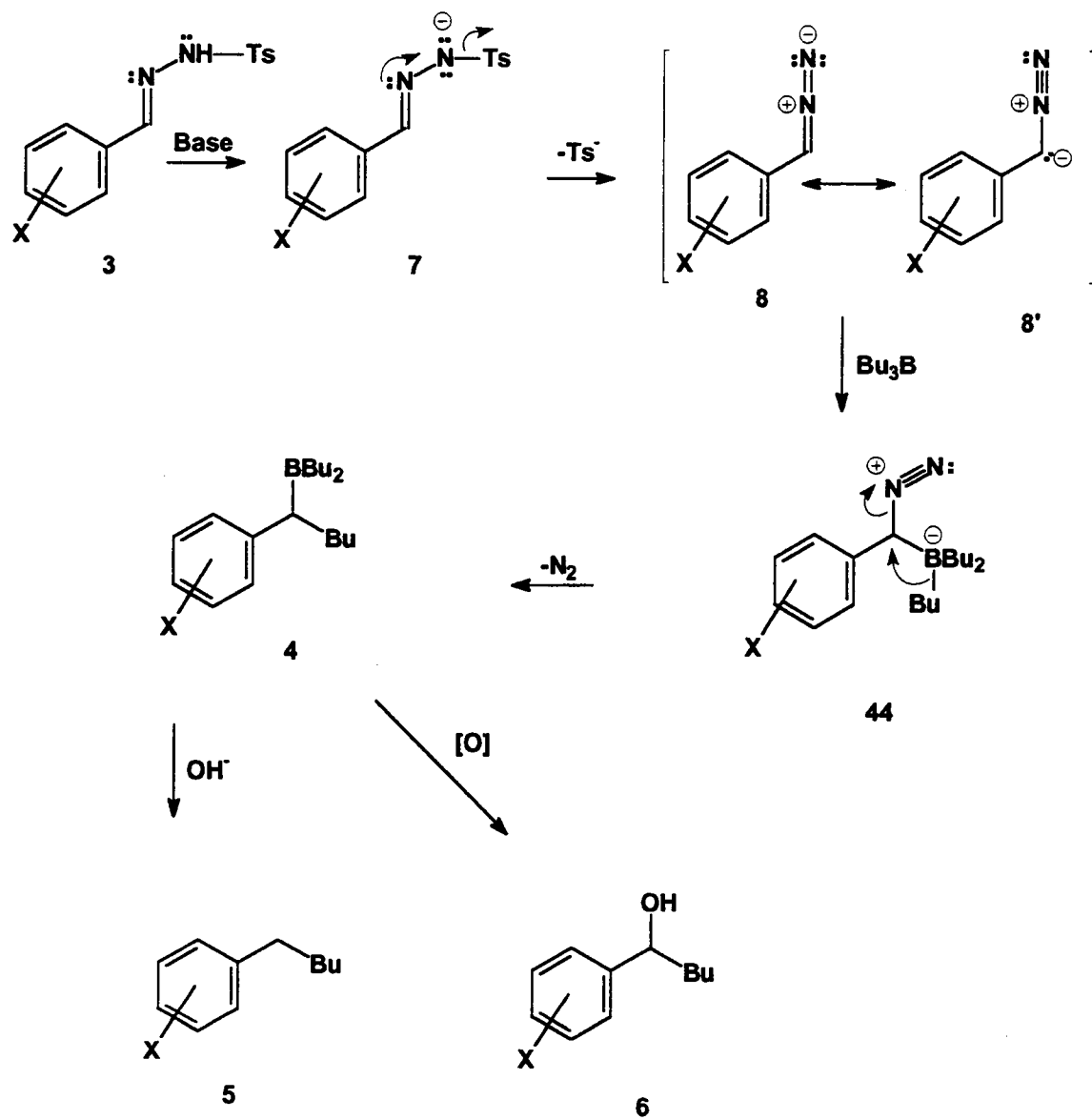
4.1 INTRODUCTION

There are two possible mechanistic courses for the new reaction. In the first, the anion mechanism, removal of a proton from the starting tosylhydrazone **3** would generate an anion **7**, (Scheme 14). The trialkylborane would then react with this anion to form an electron-rich organoborate complex **43** which spontaneously undergoes a 1,2-borotropic shift,¹⁰³ expelling nitrogen and the *p*-toluenesulfinate anion, to produce the new organoborane **4**. The new benzylic borane **4** would then be oxidized to the desired alcohol product **6** or hydrolyzed to the corresponding alkane **5** by nucleophilic bases. Alternatively, the reaction may proceed via a diazo mechanism, (Scheme 15). Removal of a proton from the aryl aldehyde tosylhydrazone would generate the anion **44**, which could then decompose to the intermediate diazo compound, **8'**, prior to reacting with the trialkylborane. The borate complex **44**, once formed, would undergo a spontaneous 1,2-borotropic shift, expelling nitrogen, to generate trialkylborane **4**. Reactions of alpha-diazocarbonyl compounds with trialkylboranes are known.¹⁰⁴ The difficulty in elucidating which mechanism is operative lies in the fact that they differ only in the timing of the tosyl group loss.

Scheme 14



Scheme 15



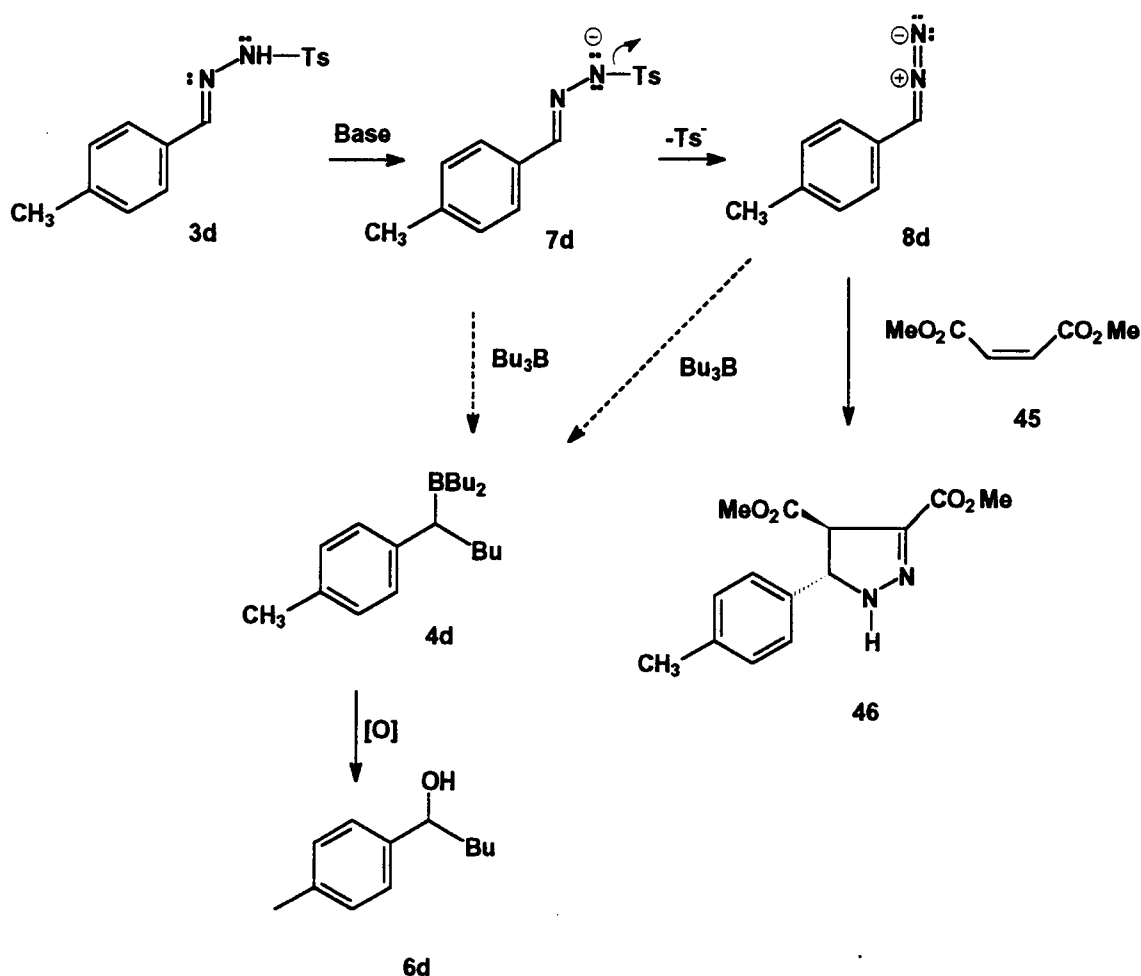
4.2 GENERATION OF DIAZO COMPOUNDS FROM TOSYLHYDRAZONES

Tosylhydrazones have been used to generate diazo compounds¹⁰⁵ and generation of an aryl diazo compound, such as that shown in Scheme 15, is possible under the conditions employed in this new reaction. DBU was used as the base in all of the following mechanistic studies in order to trap and observe the organoboron intermediate that is postulated to form. When *p*-tolualdehyde tosylhydrazone **3d** was treated with DBU in the absence of organoborane under the standard reaction conditions, a deep red color formed which can be attributed to the formation of a diazo compound. In fact, when pentane extracts of this reaction mixture were examined by IR, a sharp band at 2050 cm⁻¹ was noted. The characteristic IR band of aryl diazo compounds has been reported to be in the range 2020-2060 cm⁻¹.¹⁰⁶ The reaction, however, does not go to completion and, as evidenced by TLC, starting tosylhydrazone was still present after the typical reaction period of 1 h. Recovery of the starting material via flash chromatography gave a 29% yield of *p*-tolualdehyde tosylhydrazone. *p*-Toluenesulfonylhydrazide was also detected which indicates that decomposition of the starting hydrazone also took place.

Dimethyl maleate was then used as probe of the reaction mechanism. Dimethyl maleate reacts with aryl diazo compounds via a 1,3-dipolar cycloaddition to generate *trans*-5-aryl-4,5-dihydro-1H-pyrazole-3,4-dicarboxylic acid dimethyl esters, (**46**, Scheme 16).¹⁰⁷ Reaction of *p*-tolualdehyde tosylhydrazone, **3d** with

tributylborane and DBU in refluxing THF produced an 83% yield of alcohol **6d** after oxidation in 1 h. Reaction of *p*-tolualdehyde tosylhydrazone, **3d**, with **45** and DBU in the absence of trialkylborane in refluxing THF produced a 76% isolated yield of **46** in 1.5 h. When the reaction with **45** was run in the presence of trialkylborane, (Scheme 16), an 80% isolated yield of **6d** (trialkylborane reaction) was produced

Scheme 16



after oxidation and none of pyrazoline, **46**, was detected. In an attempt to enhance the rate of the maleate reaction, it was repeated but modified such that the solution

of **3d**, the borane and dimethyl maleate was heated to reflux prior to the addition of DBU. Once again, a 77% yield of alcohol was produced. These results suggest one of two things: either the reaction proceeds via the anion mechanism or the reaction of the trialkylborane with the diazo intermediate is faster than the cycloaddition with dimethyl maleate.

4.3 GENERATION OF DIAZO COMPOUNDS FROM TRISYLHYDRAZONE

The reaction of tributylborane with diazo compound **8'** was then investigated. Diazo compound **8'** (where X=H) was prepared in 90% yield from benzaldehyde trisylhydrazone.⁹¹ Benzaldehyde trisylhydrazone **25e** was heated to reflux in methanol with two equivalents of KOH. The diazo compound formed readily in 10 min. The isolated diazo compound was then treated with tributylborane under a variety of conditions. In the first series of experiments, a solution of tributylborane in THF was added directly to **8'** also in THF at RT. Vigorous gas evolution was observed and several products were formed but none of the desired alcohol or the alkane was obtained after oxidation. Then, a solution of **8'** in THF was added dropwise to a solution of tributylborane in THF. The reaction was immediate and 37% of the alcohol product **6** was isolated after oxidation. If the reaction was repeated with the base, DBU, included in the reaction mixture, 55% of **6** was isolated. This is much lower than the 90% yield typically produced under the normal benzaldehyde trisylhydrazone reaction conditions (2 h at RT). A two-fold excess

of **8'** was necessary to produce 93% of the desired product **6**. It is, therefore, possible to obtain the desired alcohol product from a reaction of the diazo intermediate and tributylborane but a two-fold excess is necessary to obtain a yield comparable to that observed in the *in-situ* reaction.

Benzaldehyde trisylhydrazone was then treated with DBU in THF to determine if the diazo compound is produced under the normal reaction conditions. After 2 h at room temperature very little starting material was utilized and the reaction turned a faint orange indicating that very little diazo compound formed. To eliminate the possibility that tributylborane, a Lewis acid, catalyzes the formation of the diazo intermediate, tribromoborane was added to a mixture of benzaldehyde trisylhydrazone and DBU. Tribromoborane had no effect on the formation of the diazo compound and disappearance of the starting material was not observed.

Earlier in this section it was noted that **8'** readily formed in refluxing methanol with two equivalents of KOH. If the alkylation reaction proceeds via the diazo intermediate **8'** then the reaction rate should increase in the presence of methanol. When benzaldehyde trisylhydrazone was treated with Bu_3B and DBU in MeOH, the reaction yielded 22% of **6** and 62% of **5** in 29 h. This was much slower than the typical alkylation reaction time (2 h) and hydrolysis occurred due to the polar protic solvent. When *p*-chlorobenzaldehyde trisylhydrazone was used in a reaction with Bu_3B and Bu_4NOH , there was an 87% yield of **5** (where $\text{X}=\text{Cl}$) in 3.5 h. Once again, this reaction time is slower than the typical reaction time of 1 h for this trisylhydrazone. KOH was then used to form **8'** in THF from benzaldehyde

trisylhydrazone. The reaction mixture turned orange at room temperature, but there was very little starting material utilized according to TLC. After heating to reflux for 1 h in the presence of 2 equivalents of KOH the reaction remained orange in color, but there was very little change in the amount of the starting trisylhydrazone. This study indicates that the diazo compound does not form easily in THF even with 2 equivalents of base added and with heating and suggests that the diazo compound does not form during the normal alkylation reaction.

These studies verify that Bu_3B will react with the diazo compound **8'** to form the alkylation product **6**. The data do, however, suggest that this is not the preferred pathway for the reaction. First, the diazo compound does not appear to form efficiently under the normal reaction conditions since, in the absence of Bu_3B , the reaction did not develop the deep orange color associated with **8'**. Second, the alkylation reaction proceeded much slower in methanol, whereas the rate should have been enhanced if the reaction was proceeding via **8'**. Finally, although Bu_3B did react with the isolated diazo compound, a two-fold excess of **8'** was necessary to achieve a comparable yield of **6**.

4.4 NMR STUDIES

Both the tosyl and trisyl reactions were monitored by ^{11}B NMR. The ^{11}B isotope has a natural abundance of 81.17% and a nuclear spin I of $3/2$.¹⁰⁸ As in other nuclei, the shielding of the ^{11}B nucleus depends on the chemical nature of the

adjacent atoms. Reaction mechanisms and reaction times involving boron compounds can be determined by monitoring the disappearance of the initial ^{11}B signal and/or the appearance of a new signal. The signals can be integrated in order to determine how much of each compound is present. Intermediates can also be detected if they are present in high enough concentrations. Tri- and tetra-coordinate boron compounds can be observed simultaneously and quantified accurately if the RF power is adjusted appropriately. Tetra-coordinate boron compounds can be readily saturated by too high an RF, leading to loss of signal. It was postulated that, if a difference could be detected in the NMR spectra of the hydrazone reactions and the reaction of the diazo compound **8'**, then conclusions could be drawn concerning the mechanism.

4.4.1 Experiment 1

Bu_3B in THF gives a ^{11}B resonance at 85 ppm, (Table 4-1 and Figure 4) and, upon addition of DBU to a 1 M solution of Bu_3B , this resonance shifts upfield to generate two resonances at 19 ppm and 2 ppm (Table 4-1 entry 2 and Figure 5). The shift is evidence of complex formation between the nitrogens of the DBU and the Bu_3B .¹⁰⁹ In all spectra, the peak at approximately 50 ppm is due to the boronic acid of tributylborane (Bu_2BOH) which is present as a contaminant.

Table 4-1. Exp. 1: ^{11}B NMR of Bu_3B in THF and DBU

Entry	Time	^{11}B signal (ppm) ^c	^{11}B signal (ppm) ^d
1 ^a	0	82.5	85
2 ^b	0	16.5, -0.5	19, 2
3 ^b	60	16.5, -0.5	19, 2

^a Reaction mixture consists of Bu_3B in THF

^b Reaction mixture consists of Bu_3B , THF and DBU

^c Original signals showing borinic acid at 51.5 ppm

^d Corrected signals placing borinic acid at 54 ppm

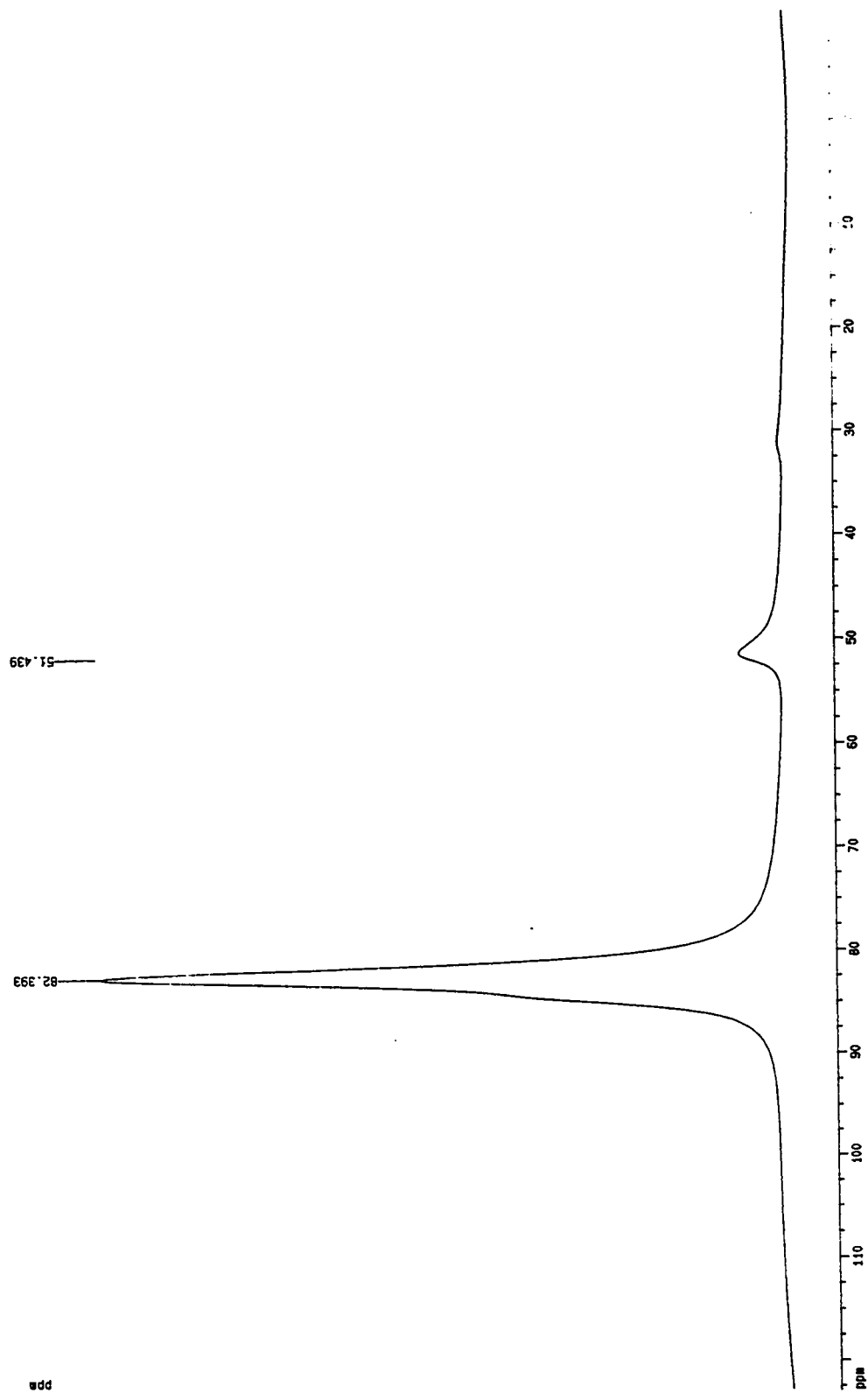


Figure 4. ^{11}B NMR of Bu_3B in THF

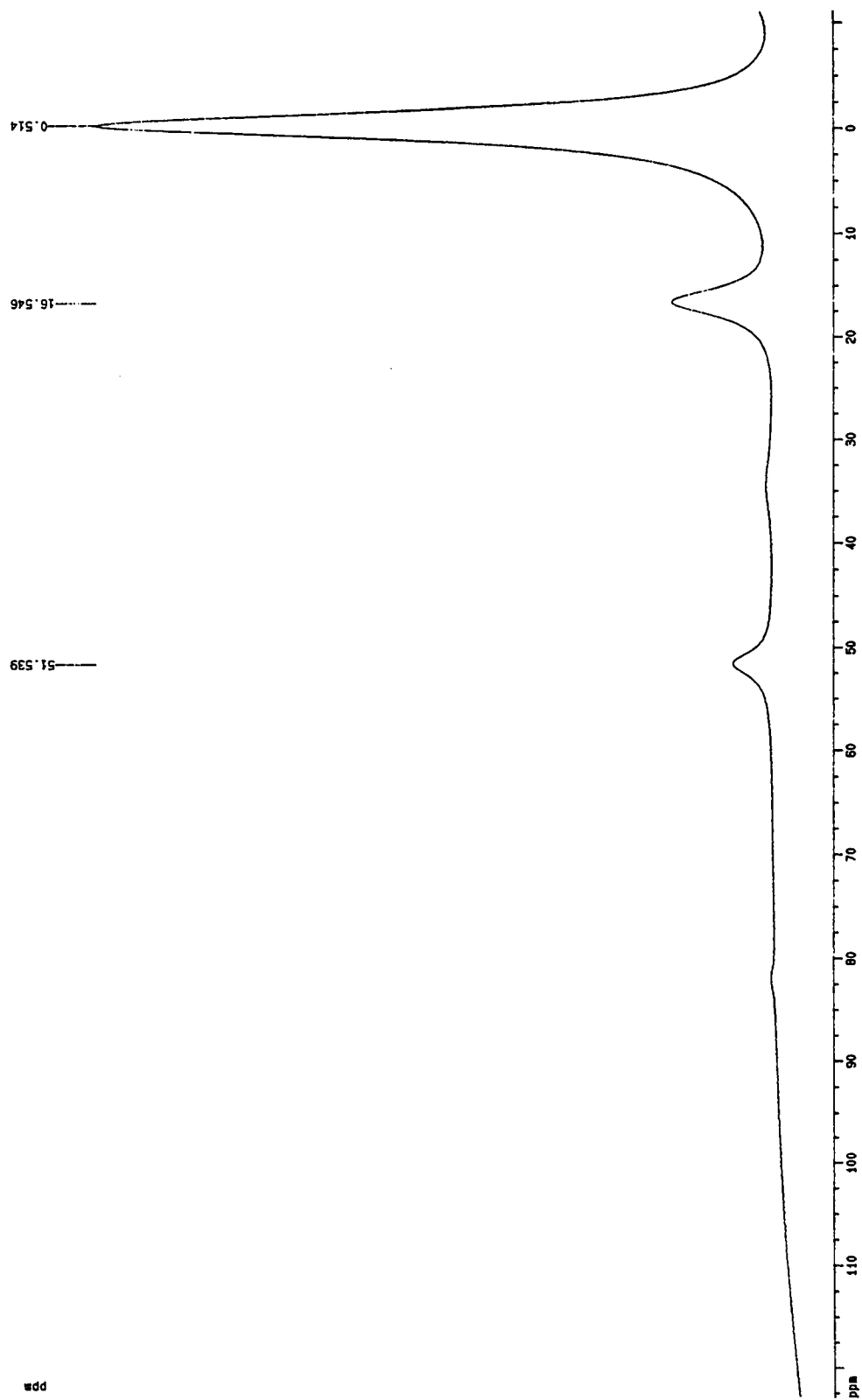


Figure 5. ^{11}B NMR of Bu_3B and DBU in THF

4.4.2 Experiment 2

In a second experiment, a 0.3 M solution of benzaldehyde tosylhydrazone and Bu_3B in THF was prepared in an NMR tube and monitored at various temperatures, (Table 4-2). The Bu_3B signal, originally at 85 ppm, is split into two signals; one at 88 ppm and a larger one at 83 ppm (Figure 6). As the temperature decreases both signals move upfield (eg. Table 4-2 entry 3 and Figure 7). The smaller one moves a few ppm but the larger one moves upfield to 34 ppm. Signals broaden and disappear into the baseline at -53°C so only one of the borane resonances can be observed at the lower temperatures. The temperature was lowered to -78°C but, at that temperature, there were only two very broad low humps visible.

Table 4-2. Exp. 2: ^{11}B NMR of Benzaldehyde Tosylhydrazone with Bu_3B in THF

Entry	Time (min)	Temp ($^\circ\text{C}$)	^{11}B signal (ppm) ^a	^{11}B signal (ppm) ^b
1	0	25	87, 82	88, 83
2	12	12	85, 79	86, 80
3	25	-3	84, 73	86, 74
4	31	-18	83, 58	84, 59
5	43	-23	81, 53	82, 54
6	50	-38	79, 47	80, 48
7	56	-53	34	35
8	70	-68	33	34

^a Original signals showing borinic acid at 53 ppm and boronic acid at 32 ppm

^b Corrected signals placing borinic acid at 54 ppm

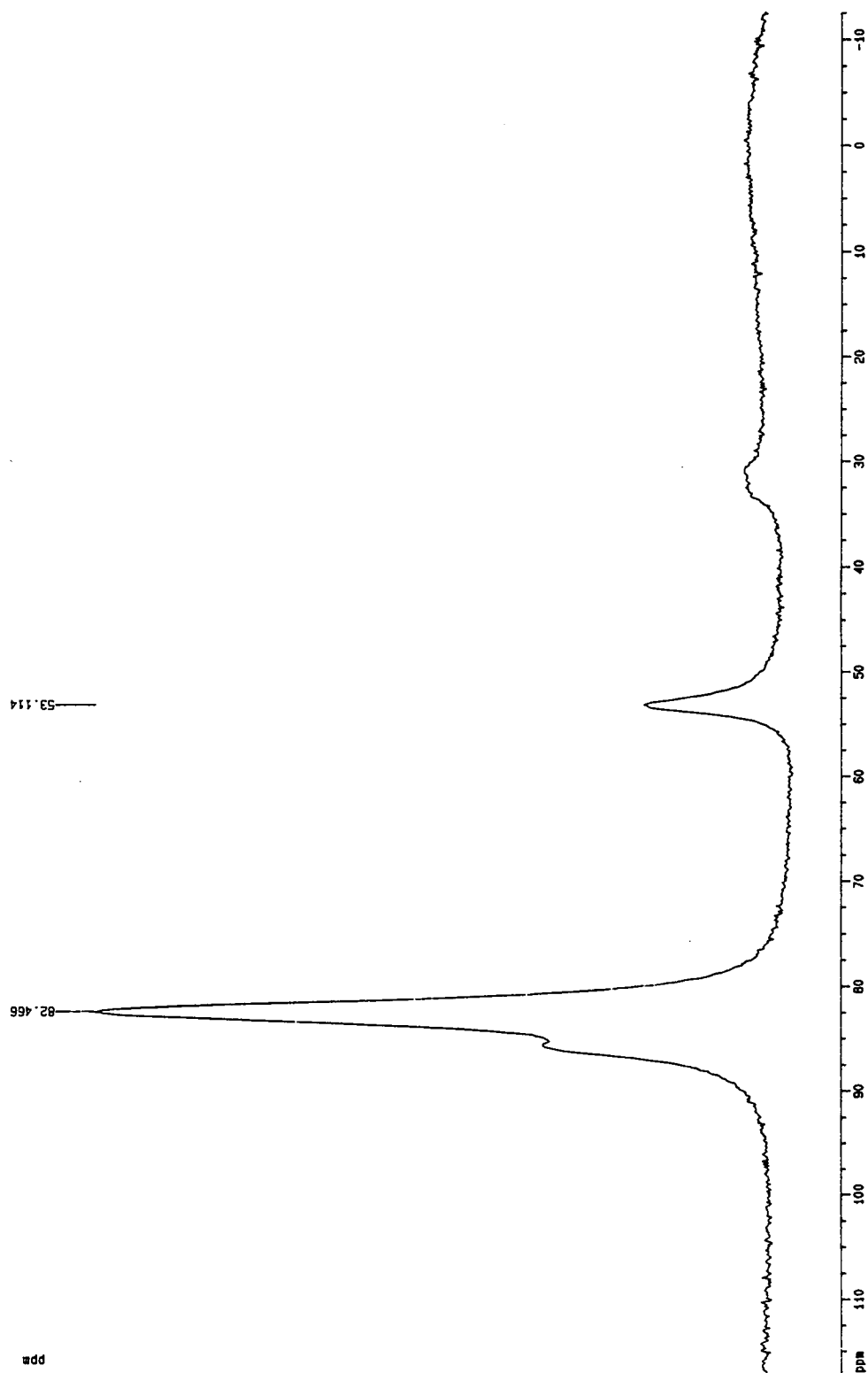


Figure 6. ^{11}B NMR of Benzaldehyde Tosylhydrazone with Bu_3B in THF

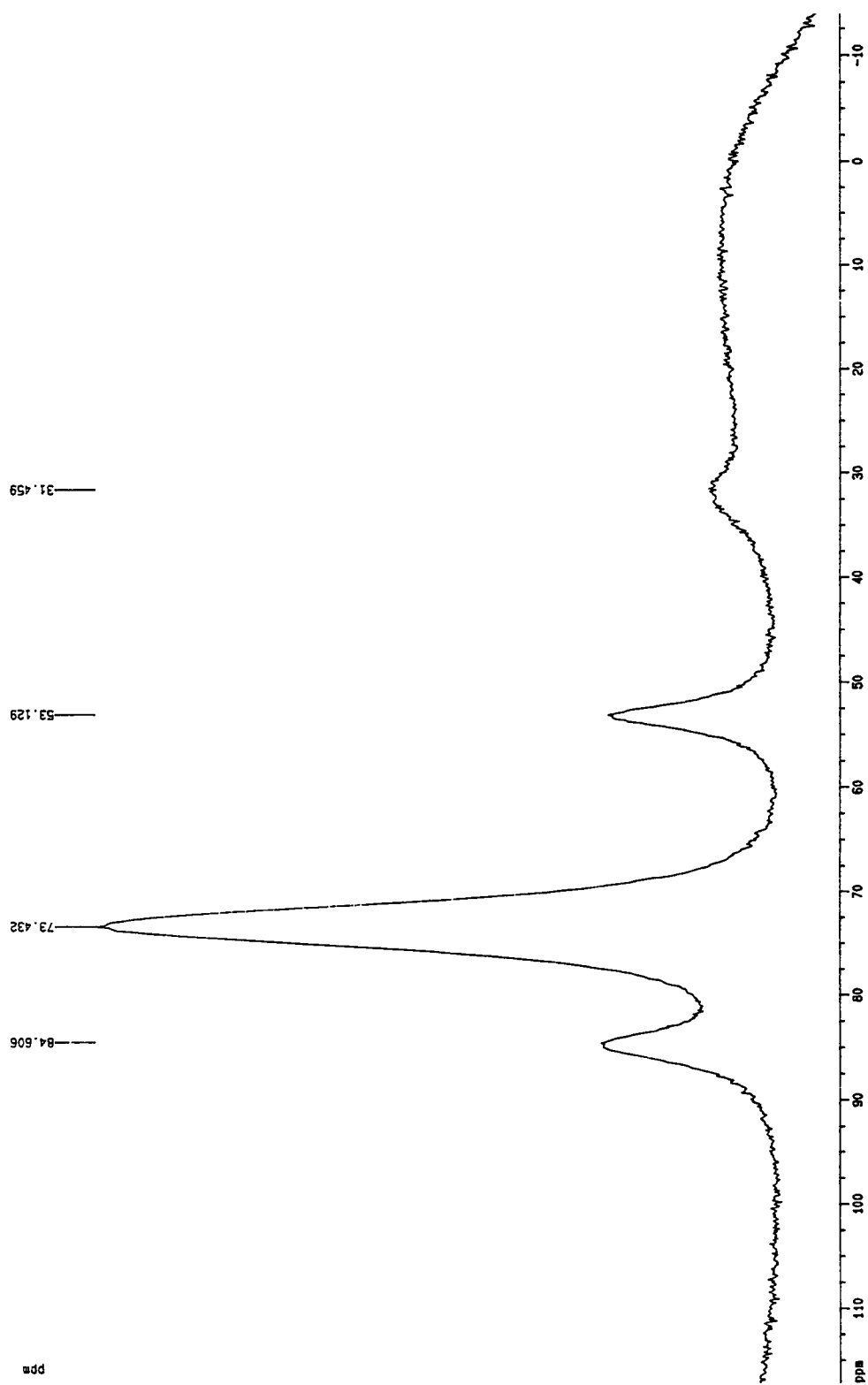


Figure 7. ^{11}B NMR of Benzaldehyde Tosylhydrazone with Bu_3B in THF at -3°C

The splitting of the signals could be from the complexation of the borane with the hydrazone. The shifting of the resonances upfield indicates an increasing strength of the complex.

4.4.3 Experiment 3

While the above reaction mixture described in 4.4.2 was maintained at -78 °C, 1 equivalent of DBU was added. The reaction mixture was then slowly warmed and the NMR spectrum monitored (Table 4-3). The NMR resonances detected between -78 °C and -53 °C were around 4 ppm, broad and not well defined. A new complex was formed upon the addition of DBU as evidenced by the upfield shift of the ^{11}B NMR signals. The complex could be Bu_3B either complexed with the anion **7** or the diazo compound **8**. However, since the diazo compound does not form easily at low temperatures, it is postulated that the complex formed involves the anion.

The resonances noted in entries 1-3 in Table 4-3 are sharper than those observed at the lower temperatures (Figure 8). When the temperature was increased to -3 °C, (Table 4-3, entry 4) the signals broaden and diminish. The observed signal at 12 °C extends from -10 ppm to 35 ppm with a small maximum centered near 25 ppm. The signal at 38 ppm at room temperature (Figure 9) is presumed to be the complex between the hydrazone anion and the tributylborane.

Table 4-3. Exp. 3: ^{11}B NMR of Benzaldehyde Tosylhydrazone with DBU in THF

Entry	Time (min)	Temp ($^{\circ}\text{C}$)	^{11}B signal (ppm) ^a	^{11}B signal (ppm) ^b
1	39	-38	0	1
2	45	-23	0	1
3	60	-18	0	1
4	67	-3	2	3
5	75	12	24	25
6	117	25	37	38

^a Original signals showing borinic acid at 53 ppm

^b Corrected signals placing borinic acid at 54 ppm

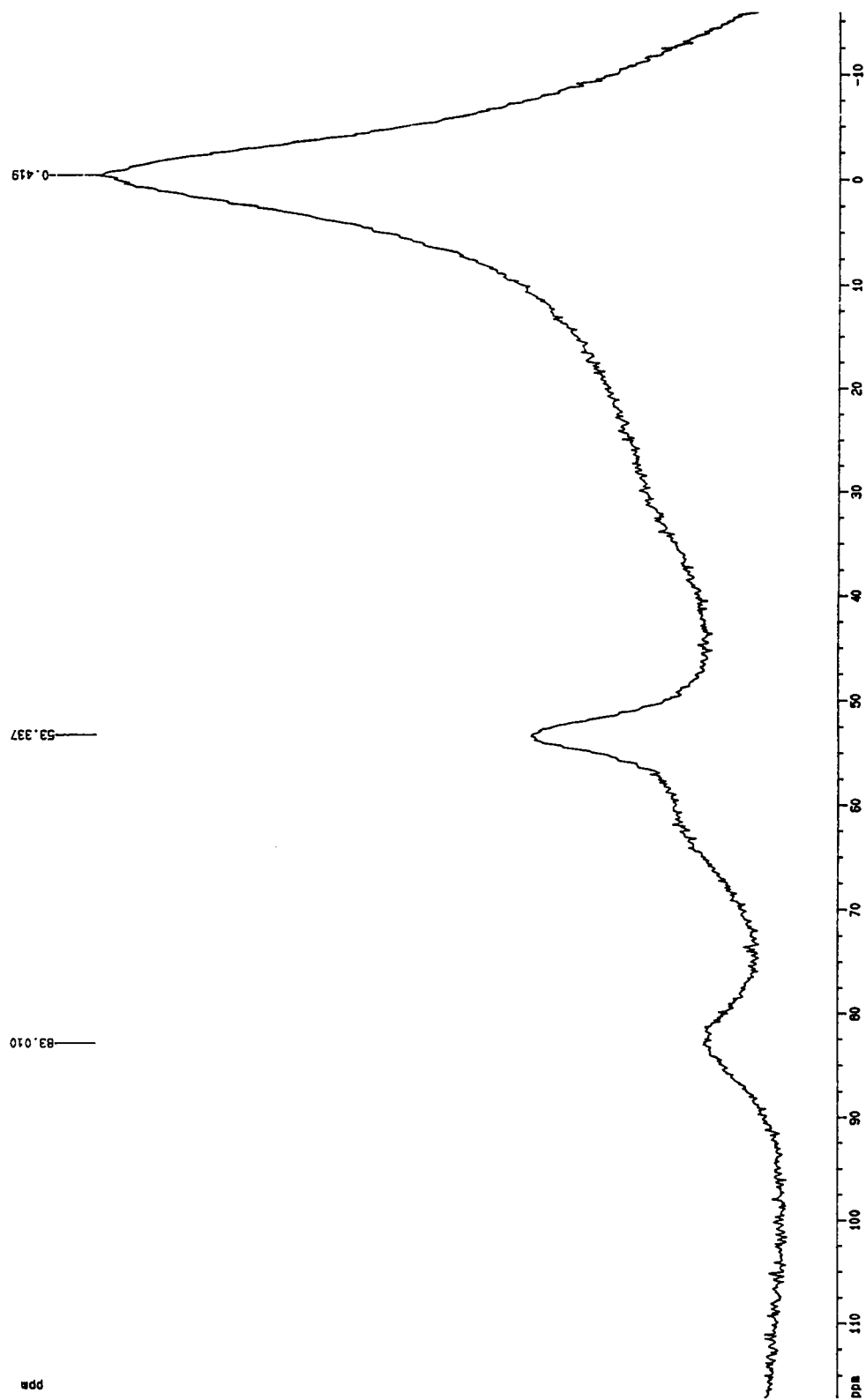


Figure 8. ^{11}B NMR of Benzaldehyde Tosylhydrazone with Bu_3B and DBU in THF at -18°C

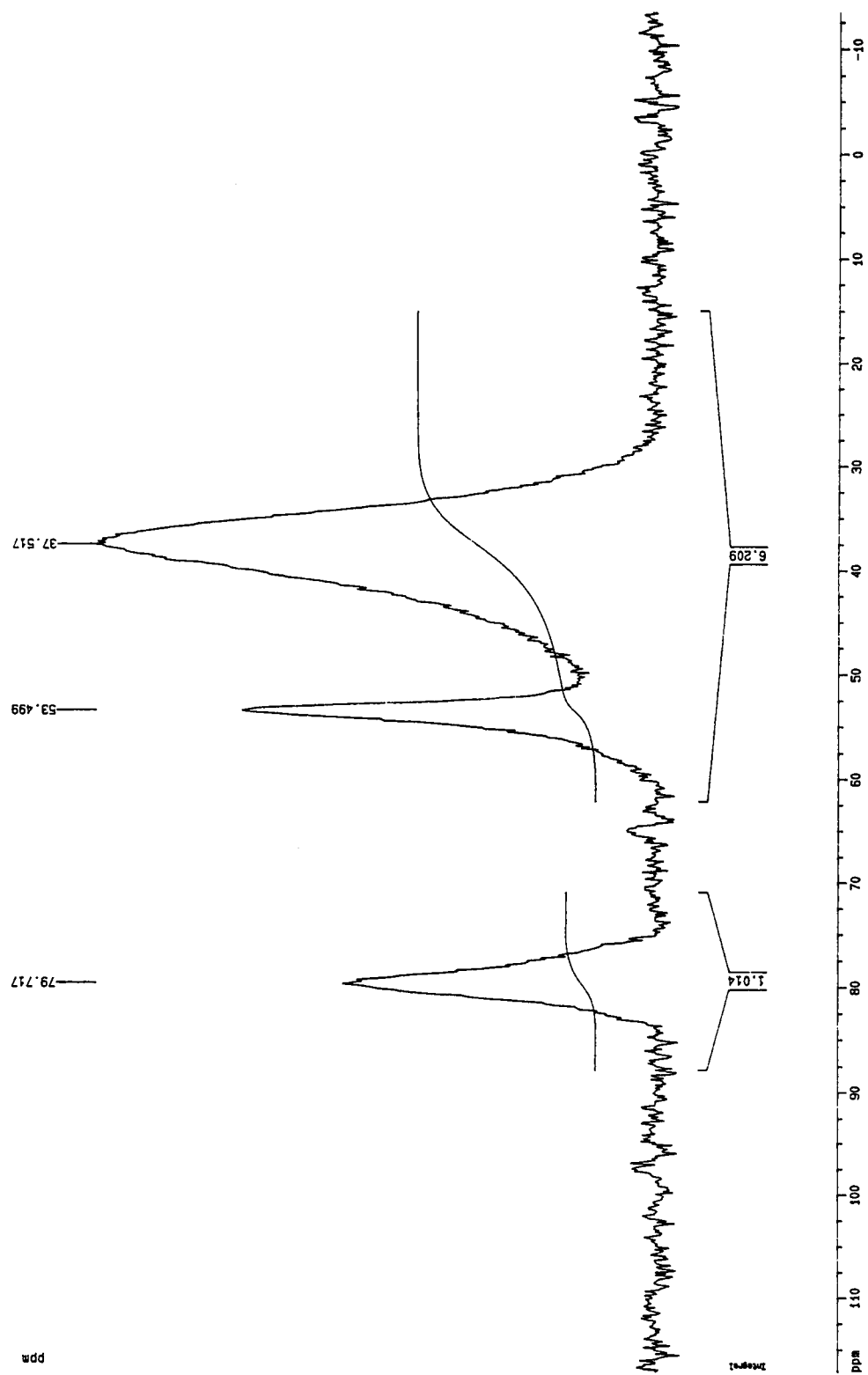


Figure 9. ^{11}B NMR of Benzaldehyde Tosylhydrazone with Bu_3B and DBU in THF at RT

4.4.4 Experiment 4

A new reaction mixture was prepared at room temperature consisting of the same reactants as those described in experiment 3, (Table 4-4). The mixture was cooled to 0 °C in the NMR but no change was observed. At room temperature, signals were observed at 29 and 20 ppm. After allowing the reaction mixture to sit at room temperature for an additional 5 min, the resonance at 29 had disappeared and two new resonances were observed at 36 and 10 ppm (Table 4-4, entry 3 and Figure 10). The signal at 20 ppm had decreased in size considerably. The resonance at 36 ppm could be due to the complexation of the intermediate anion and tributylborane as was postulated in experiment 3 (section 4.4.3). The signal at 20 ppm could have arisen from the complex of excess DBU and Bu₃B. In Table 4-1, one of the signals for the complex between DBU and Bu₃B was observed at 19 ppm. This is close to 20 ppm and could be due to the same intermediate. The 20 ppm resonance disappeared once the reaction mixture had a chance to equilibrate.

The reaction mixture was then heated to reflux in a hot water bath and placed in the NMR spectrometer at room temperature for observation. The resonance at 36 ppm disappeared after the first 5 min of heating and a small peak was seen at 32 ppm. This signal could be due to a small amount of boronic acid, present as an impurity. The signal did not change in size throughout the rest of the experiment. The signal that formed around 8 ppm was approximately 5 ppm wide. The resonance for borate complexes such as **43** or **44** should be seen upfield of 0 ppm and the signal should be sharp. This resonance might, therefore, correspond

Table 4-4. Exp 4:¹¹B NMR of Benzaldehyde Tosylhydrazone with Bu₃B and DBU
in THF

Entry	Time (min)	Temp (°C)	¹¹ B signal (ppm) ^a	¹¹ B signal (ppm) ^b
1	0	0	78	81
2	30	25	26, 17	29, 20
3	34	25	33, 17, 7	36, 20, 10
4	5	reflux	5	8
5	20	reflux	4, -2	7, 1
6	30	reflux	5, -2	8, 1
7	60	reflux	3, -2	6, 1

^a Original signals showing borinic acid at 51 ppm and boronic acid at 29 ppm

^b Corrected signals placing borinic acid at 54 ppm

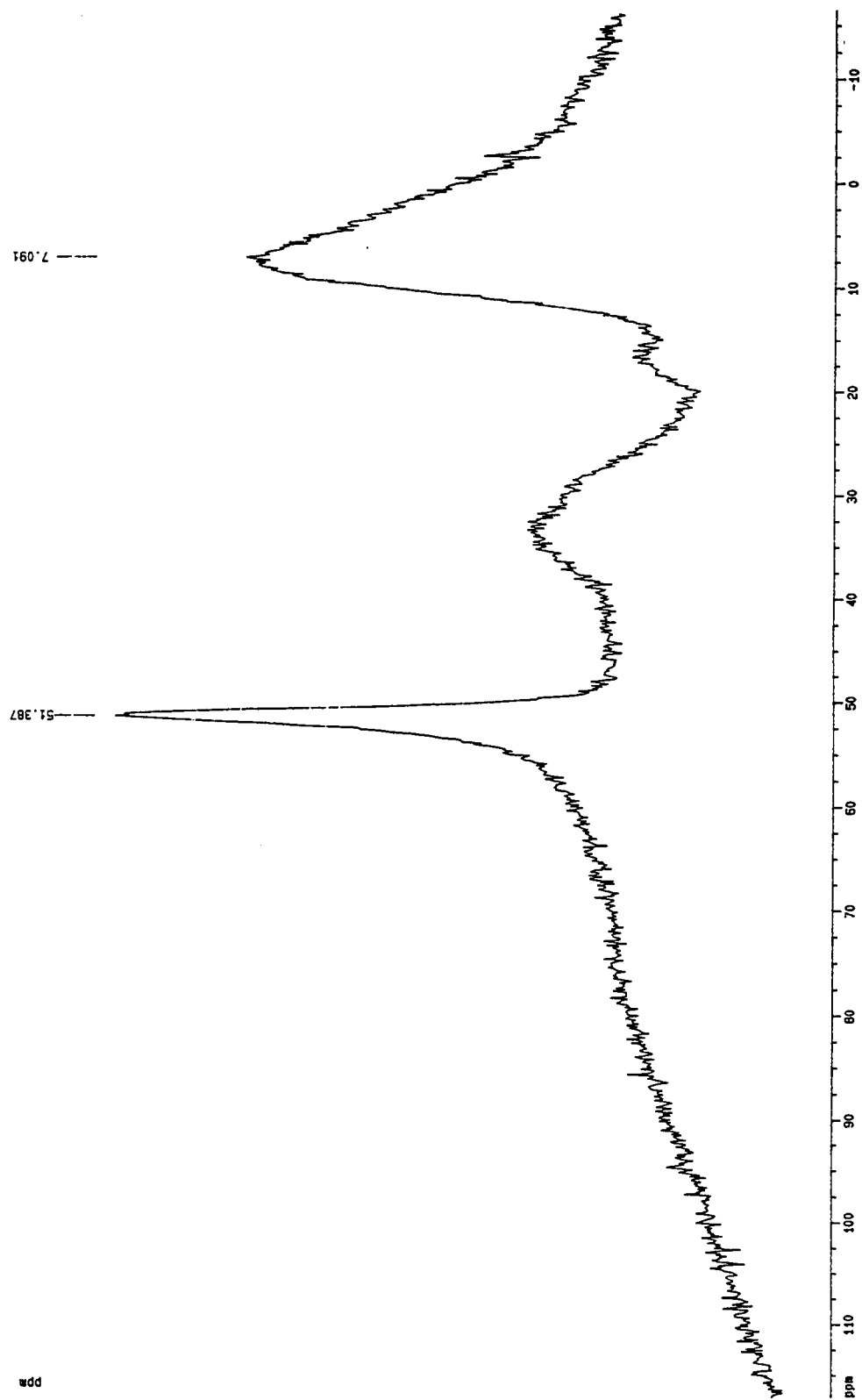


Figure 10. ^{11}B NMR of Benzaldehyde Tosylhydrazone with Bu_3B and DBU after 5 min at RT

to a weak complex of the intermediate boranes. As the reaction continued, the resonance near 8 ppm diminished in intensity and a new peak started forming at 1 ppm. This resonance could correspond to the benzylborane **4** complexed with DBU.

4.4.5 Experiment 5

The NMR experiments were repeated using benzaldehyde trisylhydrazone. The signal for tributylborane was again split into two signals at 86 and 82 ppm, similar to the tosylhydrazone reaction (Table 4-5 and Figure 11). Once DBU was added, the boron resonance shifted and a broad resonance at 20 ppm was observed (Figure 12). The resonance at 20 ppm can be attributed to the complex formed between excess DBU and Bu_3B , (Table 4-1). This signal was almost completely masked by a resonance at 9 ppm which was observed after 15 minutes of reaction (Figure 13). The resonance at 9 ppm corresponded to the resonance around 8 ppm observed in the tosylhydrazone reaction which was then attributed to a weak complex of intermediate **43** or **44**.

At the fourth and sixth time points (65 min and 105 min), a second signal appeared under the impurity at 54 ppm (Figures 14 and 15). This signal was not present in any of the other spectra and the final spectrum at 2 h, looked the same as that at 15 min with no appreciable change in the intensities of the NMR signals. No peak formed at 1 ppm, i.e. in the tosylhydrazone reaction (Table 4-4). The resonance at 9 ppm in this experiment would appear to correspond to the final

Table 4-5. Exp 5: ^{11}B NMR of Benzaldehyde Trisylhydrazone with Bu_3B and DBU

Entry	Time (min)	^{11}B signal (ppm) ^c	^{11}B signal (ppm) ^d
1 ^a	0	80, 84	86, 82
2 ^a	20	80, 84	86, 82
3 ^a	60	80, 84	86, 82
4 ^b	0	18.6	20
5 ^b	15	18, 7	20, 9
6 ^b	25	18, 7	20, 9
7 ^b	40	18, 7	20, 9

^a Reaction mixture consists of benzaldehyde trisylhydrazone, Bu_3B , THF

^b Reaction mixture consists of benzaldehyde trisylhydrazone, Bu_3B , THF, DBU

^c Original signals showing borinic acid at 51.5 - 52 ppm.

^d Corrected signals placing borinic acid at 54 ppm.

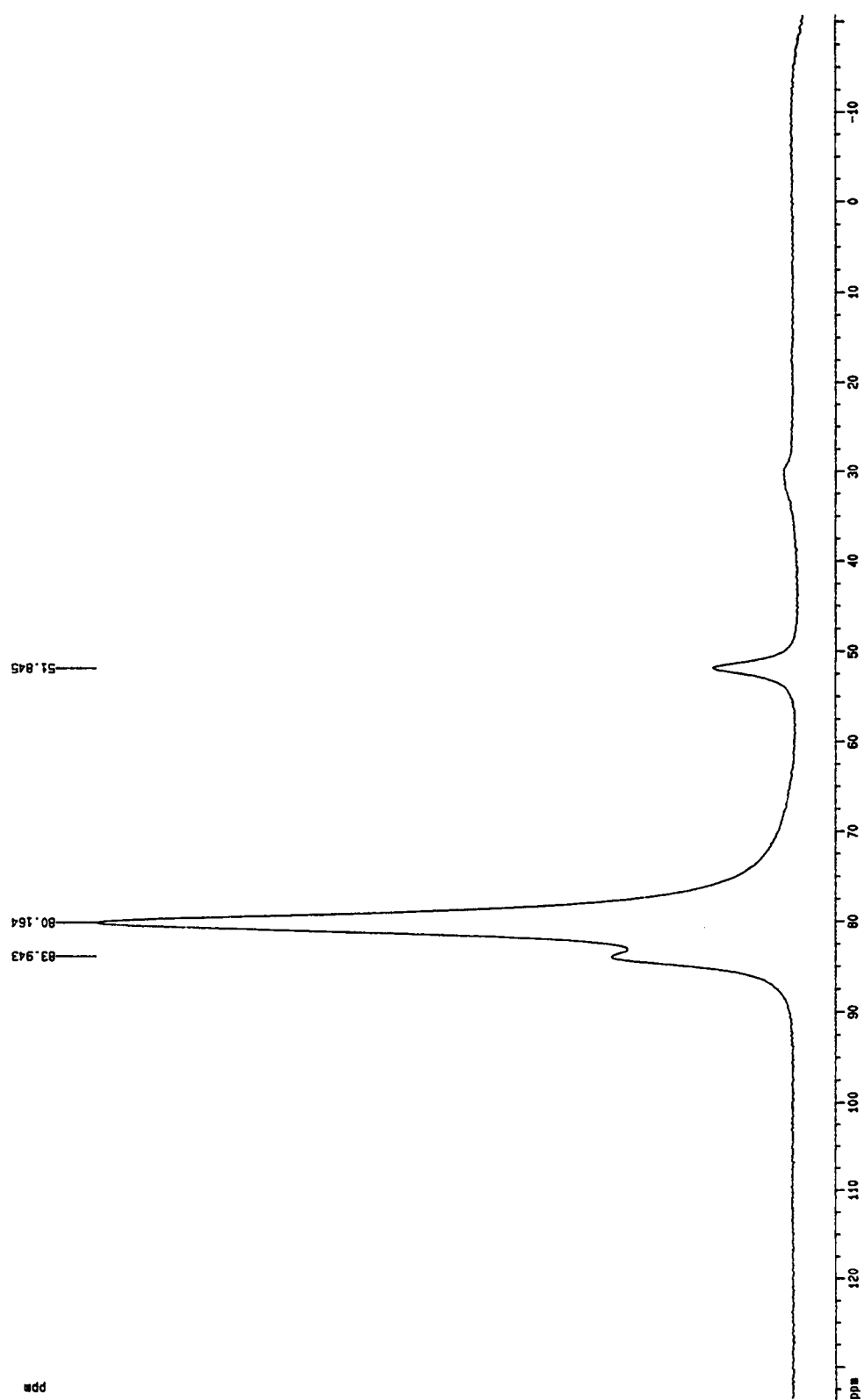


Figure 11. ^{11}B NMR of Benzaldehyde Trisylhydrazone with Bu_3B in THF

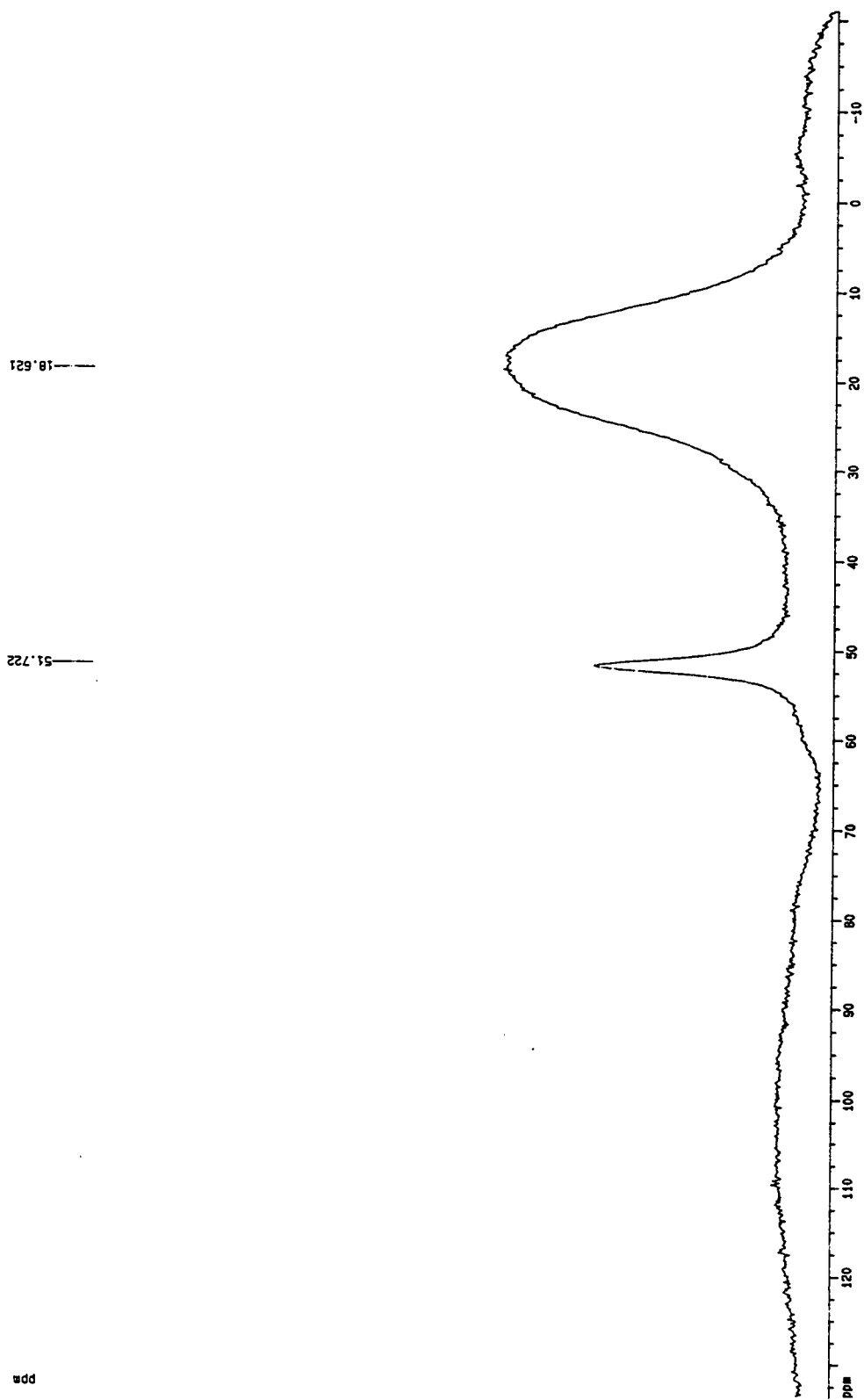


Figure 12. ^{11}B NMR of Benzaldehyde Trisylhydrazone with Bu_3B and DBU in THF

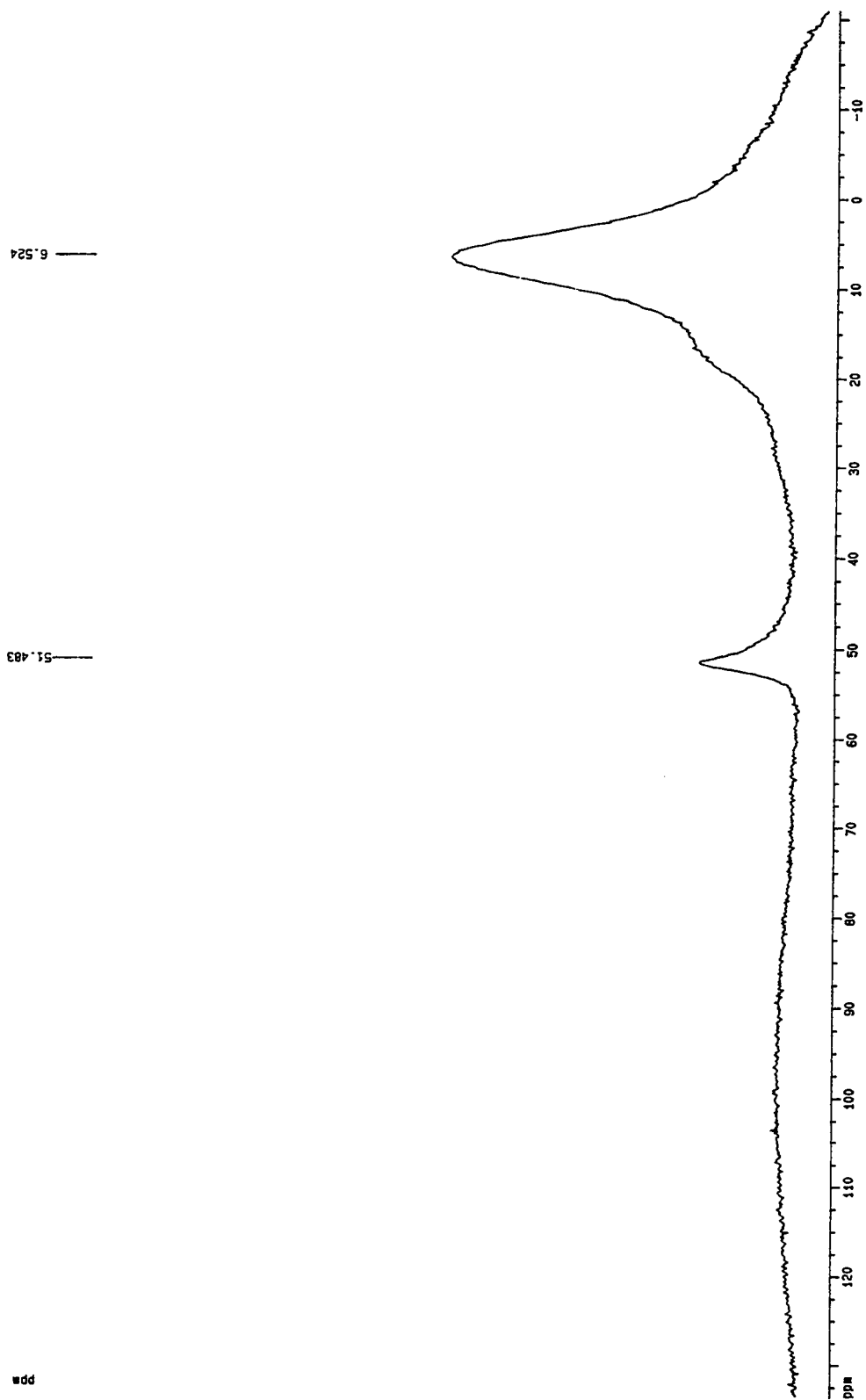


Figure 13. ^{11}B NMR of Benzaldehyde Trisylhydrazone with Bu_3B and DBU after 15 min of Reaction

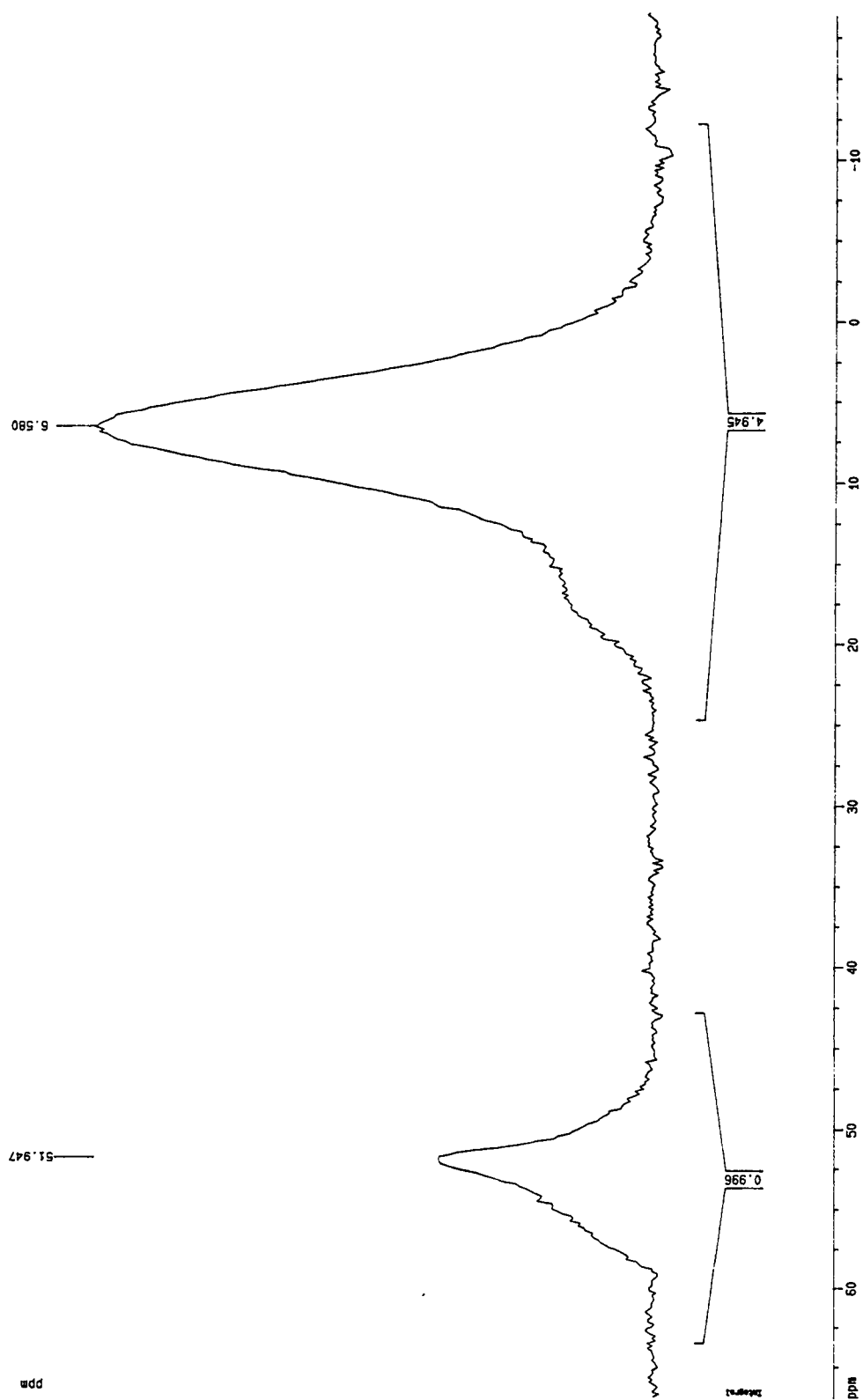


Figure 14. ^{11}B NMR of Benzaldehyde Trisylhydrazone with Bu_3B and DBU after 65 min of Reaction

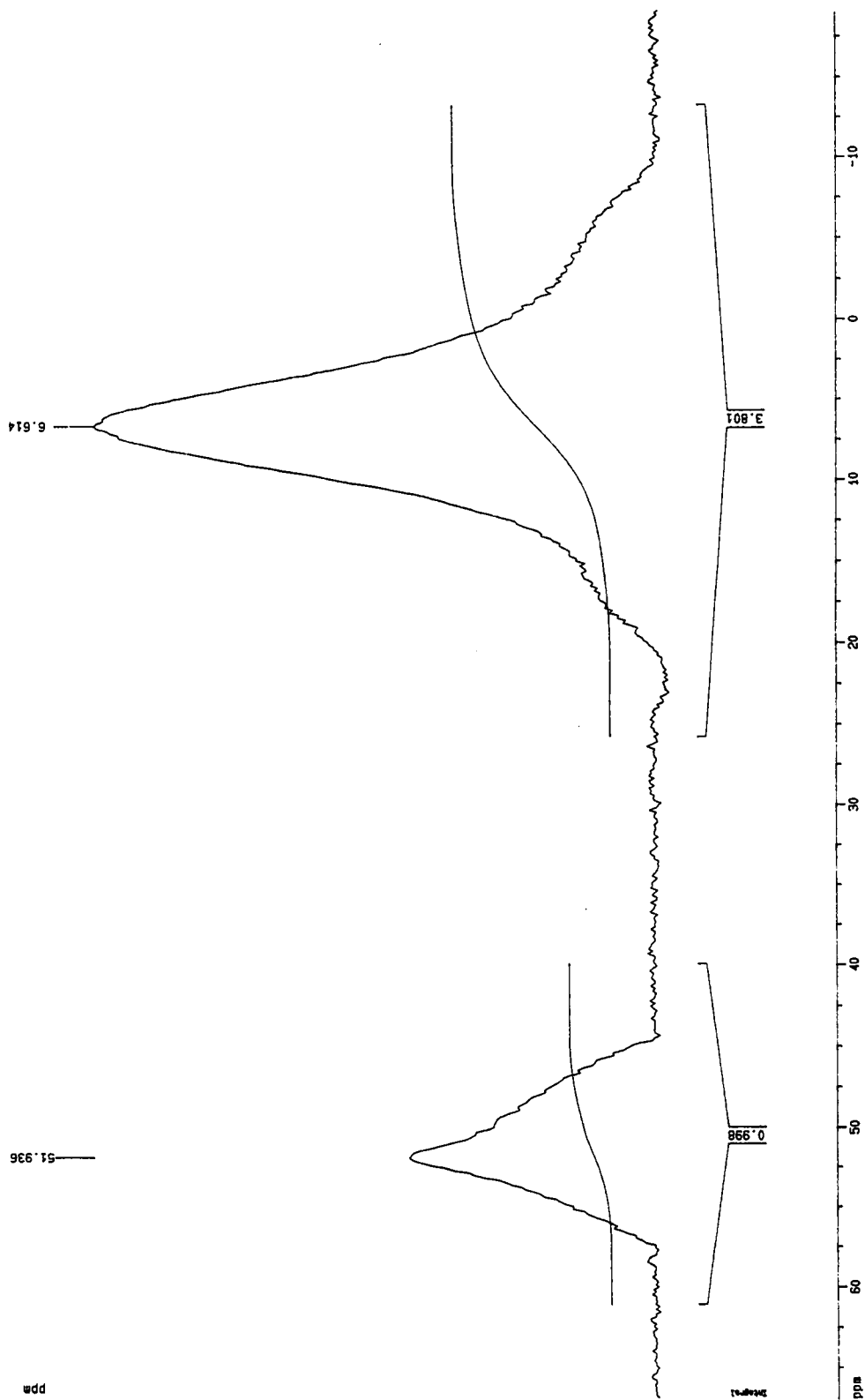


Figure 15. ^{11}B NMR of Benzaldehyde Trisylhydrazone with Bu_3B and DBU after 105 min of Reaction

benzylborane **4** complexed with DBU. It is possible that in experiment 4 the resonance at 1 ppm is not the final benzylborane as initially postulated. According to the results of experiment 5 the reaction is either complete within the first 15 min of reaction or intermediate **4** and the initial complex formed between the borane and the hydrazone nitrogens (after base addition) have nearly identical chemical shifts. Since it is known the reaction takes 2 h to reach completion, it is postulated that the latter situation is occurring.

It also appears that the intermediates **43** or **44** are not observable since no sharp signals were seen upfield of 0 ppm in any of the experiments. This suggests that these intermediates are never present in appreciable amounts and that the boratropic shift to generate the new benzylborane **4** from the borate complex is fast.

4.4.6 Experiment 6

In an attempt to separate the signals for the two intermediates, **4** and the initial Bu_3B :anionic hydrazone complex, the reaction described in section 4.4.5 was repeated. Before the addition of DBU, a spectrum of the solution was taken at 0 °C and then at -78 °C. The resonances were lost in the baseline and the spectrum was a flat line. Base was then added at -78 °C. Again the spectrum of the reaction mixture was not observable. As the temperature was increased to -18 °C, a signal was observed at 0 ppm, (Table 4-6, entries 1 and 2). At 0 °C, the signal disappeared into the baseline. To ensure that the signal was still present, the NMR was brought back down to the lower temperatures. The signal reappeared at 0

Table 4-6. Exp. 6: ^{11}B NMR of Benzaldehyde Trisylhydrazone with Bu_3B and DBU

Entry	Time (min)	Temp ($^{\circ}\text{C}$)	^{11}B signal (ppm) ^a	^{11}B signal (ppm) ^b
1	0	-38	-3	0
2	8	-18	-3	0
3	24	0	—	—
4	33	-18	-3	0
5	43	-38	-3	0
6	64	25	11	14
7	72	12	11	14
8	77	0	11	14
9	83	-18	2	5

^a Original signals showing borinic acid at 51 ppm

^b Corrected signals placing borinic acid at 54 ppm

ppm, (Table 4-6, entries 4, 5 and Figure 16). The NMR was then brought up to room temperature. The resonance at 0 ppm was replaced by one at 14 ppm (Figure 17). This corresponds to none of the resonances in the previous experiments. The temperature was brought back down to determine if the resonance at 14 ppm was identical to the one noted earlier at 0 ppm. The signal was distinct at 0 °C, whereas the signal at 0 ppm could not be observed at that temperature, and was displaced to 5 ppm at -18 °C instead of shifting to 0 ppm. This suggests that the two signals correspond to two different intermediates.

This experiment did not reveal the extra peak at 20 ppm which was presumed to have arisen from excess DBU and Bu_3B in the previous experiments. The resonance at 20 ppm in experiment 6 was sufficiently wide at the baseline that the resonance at 14 could have been hidden underneath it. The resonance at 9, once formed, was also wide enough for a signal at 14 to be buried beneath it.

It is possible then that the resonance at 0 ppm is an initial complex formed between Bu_3B and the anionic nitrogens in **7** or **8**. The resonance at 14 ppm could be attributed to a weaker complex similar to the intermediates **43** or **44** and the resonance at 7-9 ppm could be the benzylborane **4** complexed with DBU. It is also possible that the peak at 0 ppm is a complex between Bu_3B and the oxygens of the sulfonyl group and the resonance at 14 ppm a complex between Bu_3B and the anionic nitrogens in **7** or **8**.

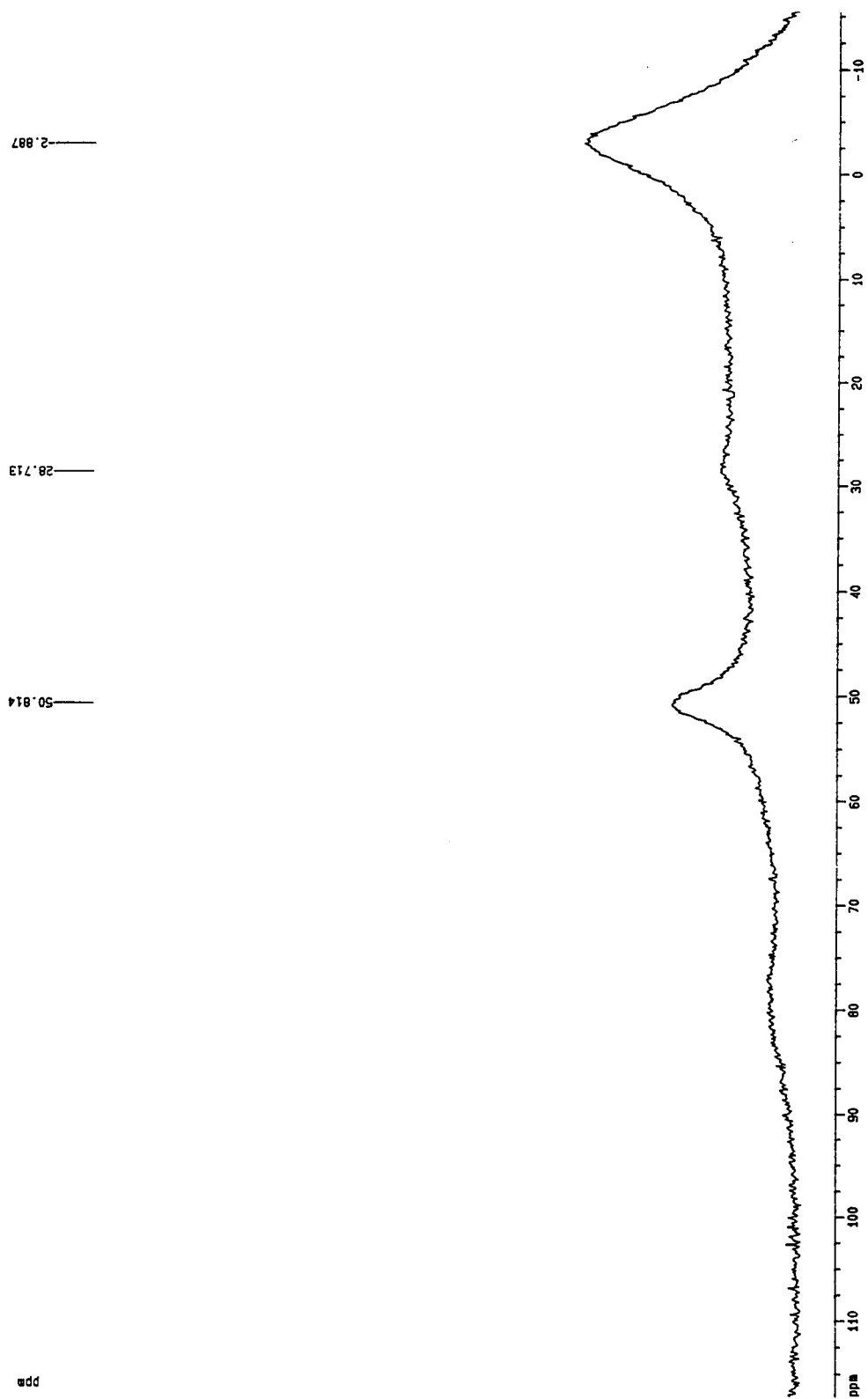


Figure 16. ^{11}B NMR of Benzaldehyde Trisylhydrazone with Bu_3B and DBU at $-18\text{ }^\circ\text{C}$

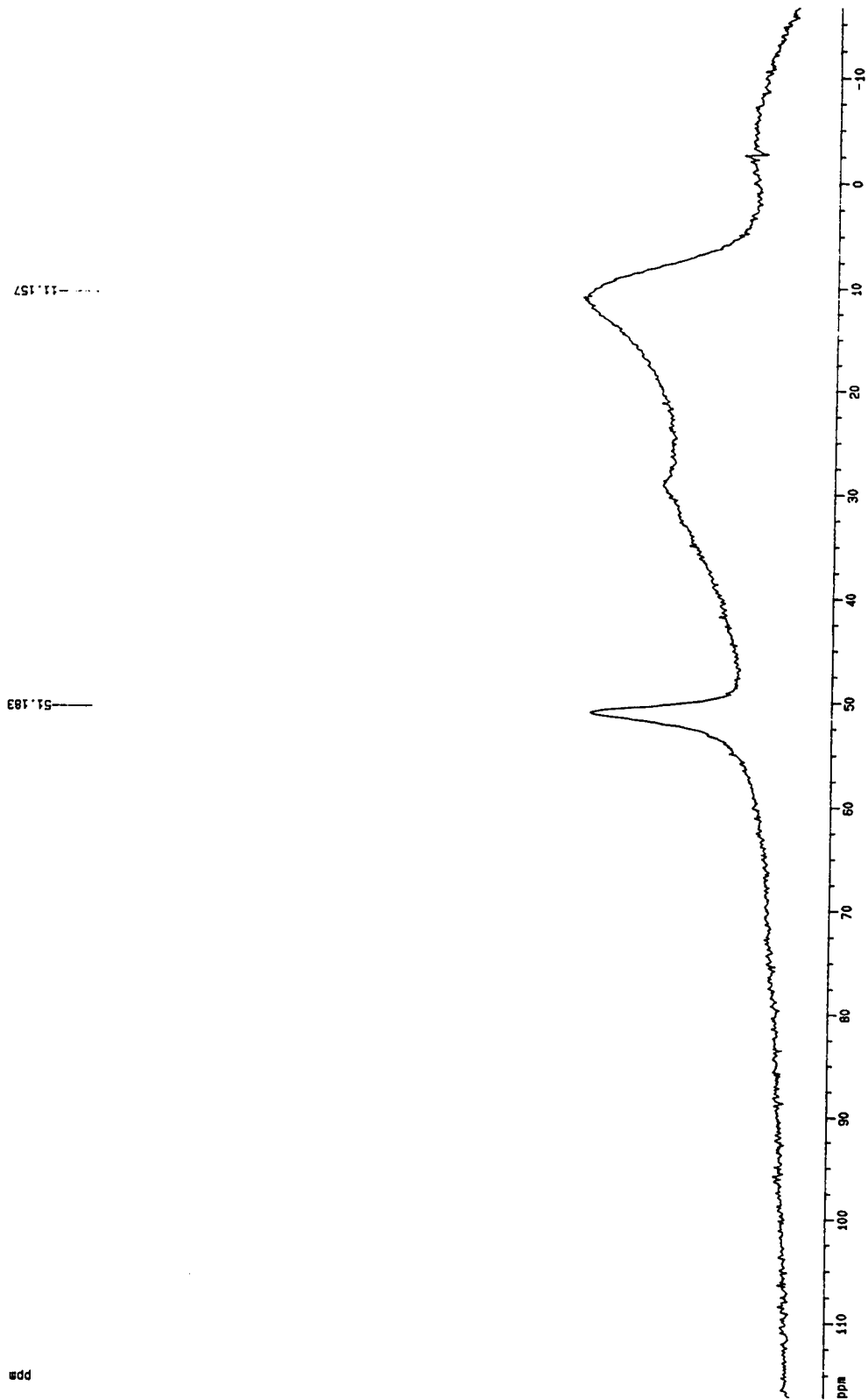


Figure 17. ^{11}B NMR of Benzaldehyde Trisylhydrazone with Bu_3B and DBU at 25 °C

4.4.7 Experiment 7

The diazo compound **8'** was prepared as described previously and added to a solution of DBU and Bu₃B in THF at -100 °C. The low temperature kept the reaction rate very low and it was anticipated that the formation of **44** could be observed. An initial spectrum was taken at -78 °C, (Table 4-7, entry 1). The signal

Table 4-7. Exp 7: Diazo Cpd **8** Added to Reaction Mixture of Bu₃B and DBU in THF

Entry	Time (min)	Temp (°C)	¹¹ B signal (ppm) ^a	¹¹ B signal (ppm) ^b
1	0	-78	0	-4
2	7	-78	-2	-6
3	14	-78	-2	-6
4	38	-38	0	-4
5	72	25	6	2

^a Original signals with entry 5 showing borinic acid at 58 ppm and boronic acid at 30 ppm. ^b Corrected signals placing borinic acid at 54 ppm

at 0 ppm was very distinct, unlike the reactions of the tosylhydrazone and trisylhydrazone with Bu₃B and DBU. It was very broad and extended from -50 ppm to 75 ppm (Figure 18). Any other signals in that region were not observable. After 7 min, the NMR tube was taken out and shaken to ensure thorough mixing. There was an immediate reaction and gas evolution was observed. The spectrum of the shaken reaction gave a slight shift of the initial resonance from -4 ppm to -6 ppm. It was, however, broad at the baseline and no other peaks were observable. After completion of this NMR study the reaction had turned yellow indicating that the

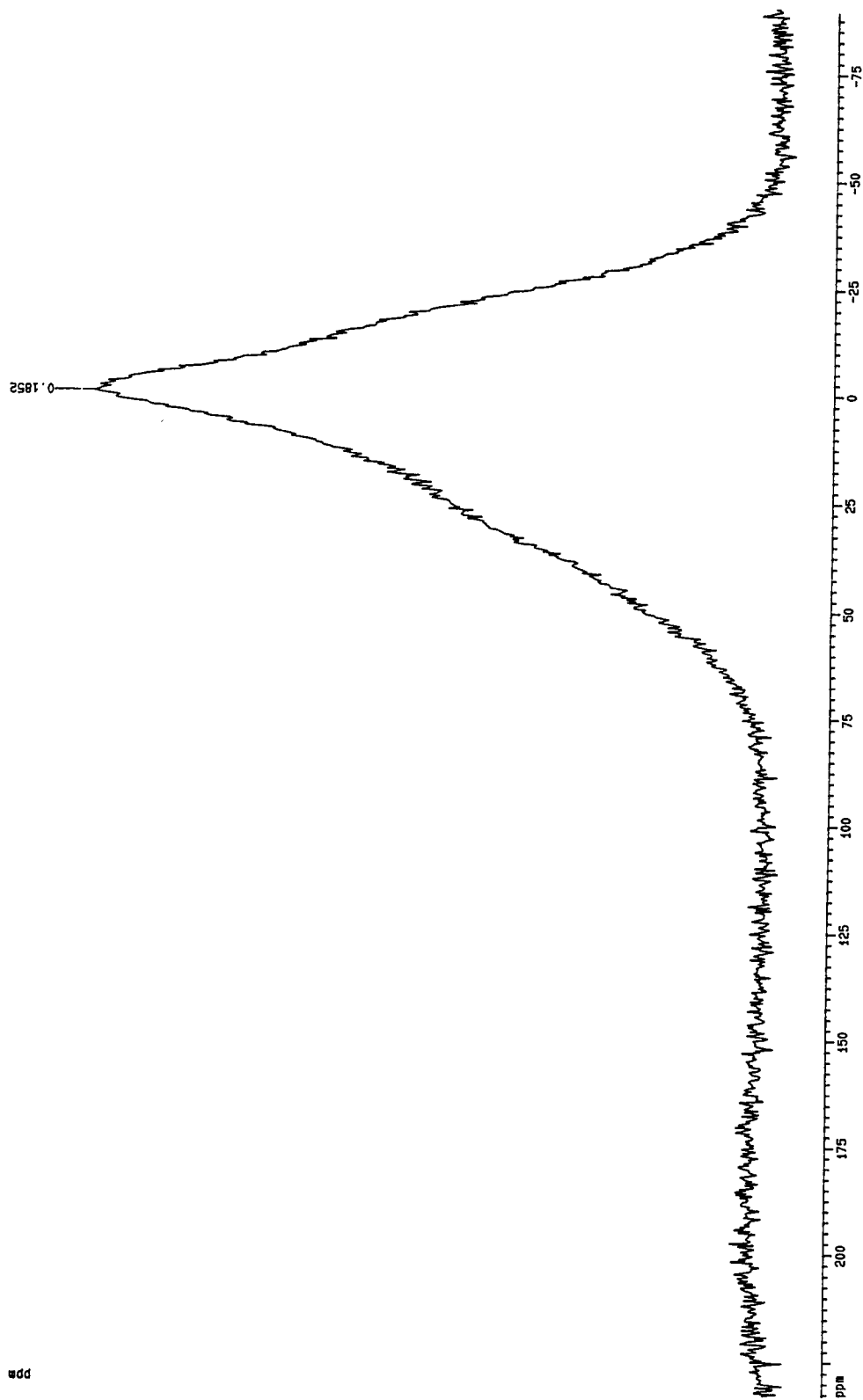


Figure 18. ^{11}B NMR of Diazo Compound 8' with Bu_3B and DBU at -78°C

reaction was over. A spectrum of this yellow reaction mixture revealed the same broad signal at -6 ppm (Figure 19). Upon warming the reaction to room temperature, a sharpening of the signal was observed and the signal shifted to 2 ppm (Figure 20). This signal was sharp and distinct, unlike the signals in the hydrazone reactions which tended to be broad. If this was the final benzylborane **4** it should have been in the region of 7-9 ppm. The difference in appearance and shift from the signals in the hydrazone reactions suggests that the diazo mechanism is not operating in the hydrazone reactions.

4.5 CONCLUSION

The studies involving the formation of diazo compounds from aryl aldehyde arenesulfonylhydrazones suggest that although the diazo compound can form and will react with tributylborane this is not the preferred pathway for the reaction. The diazo compound does not appear to form efficiently under the normal reaction conditions, the alkylation reaction proceeded much slower in methanol, and a two-fold excess of the diazo compound was necessary to achieve a successful alkylation reaction.

The initial NMR studies of the hydrazone reactions revealed that tributylborane does form complexes which could be attributed to either the anionic or diazo mechanisms. The study of the diazo reaction with tributylborane, however,

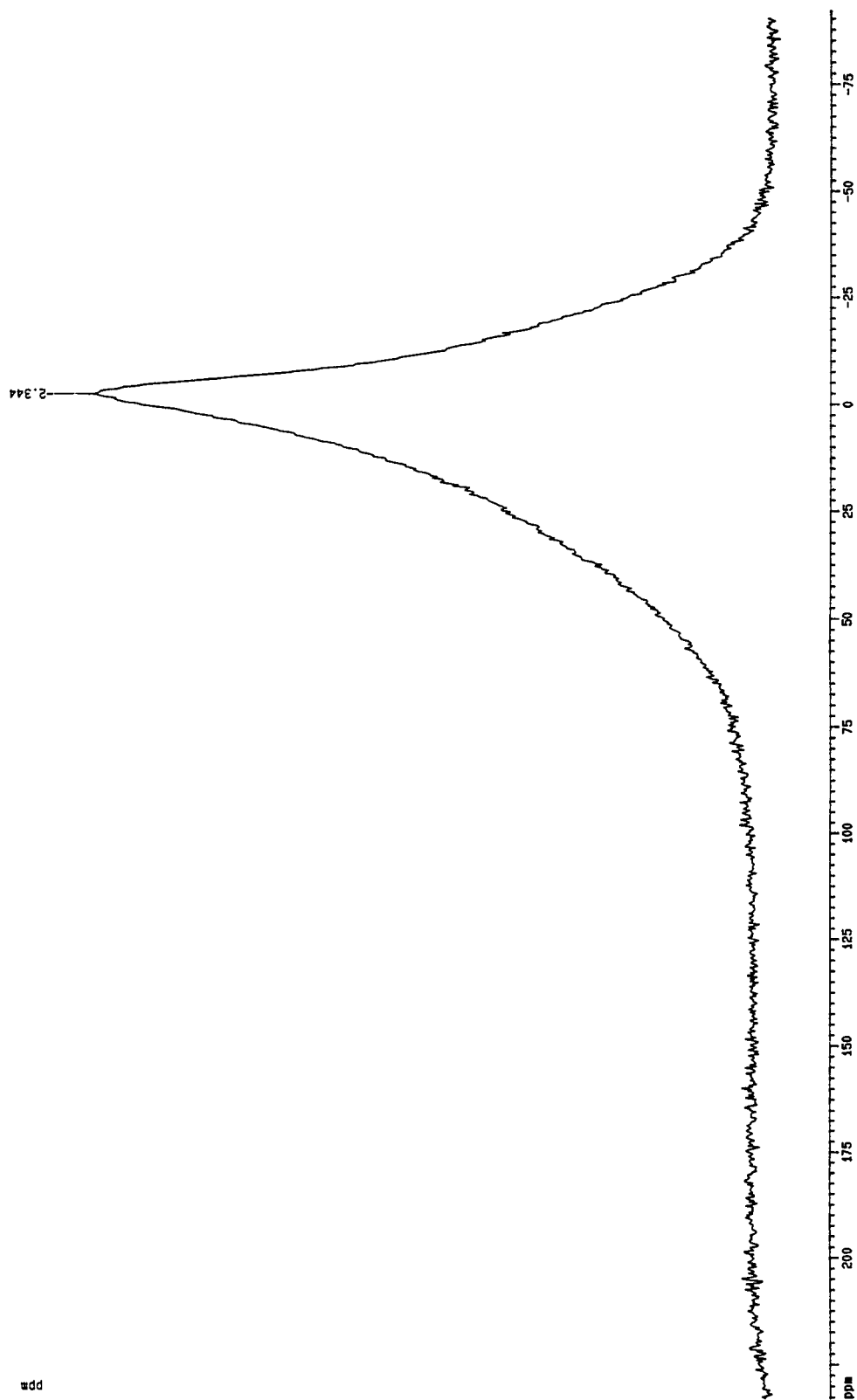


Figure 19. ^{11}B NMR of Diazo Compound 8' with Bu_3B and DBU after Completion of the Reaction at -78°C

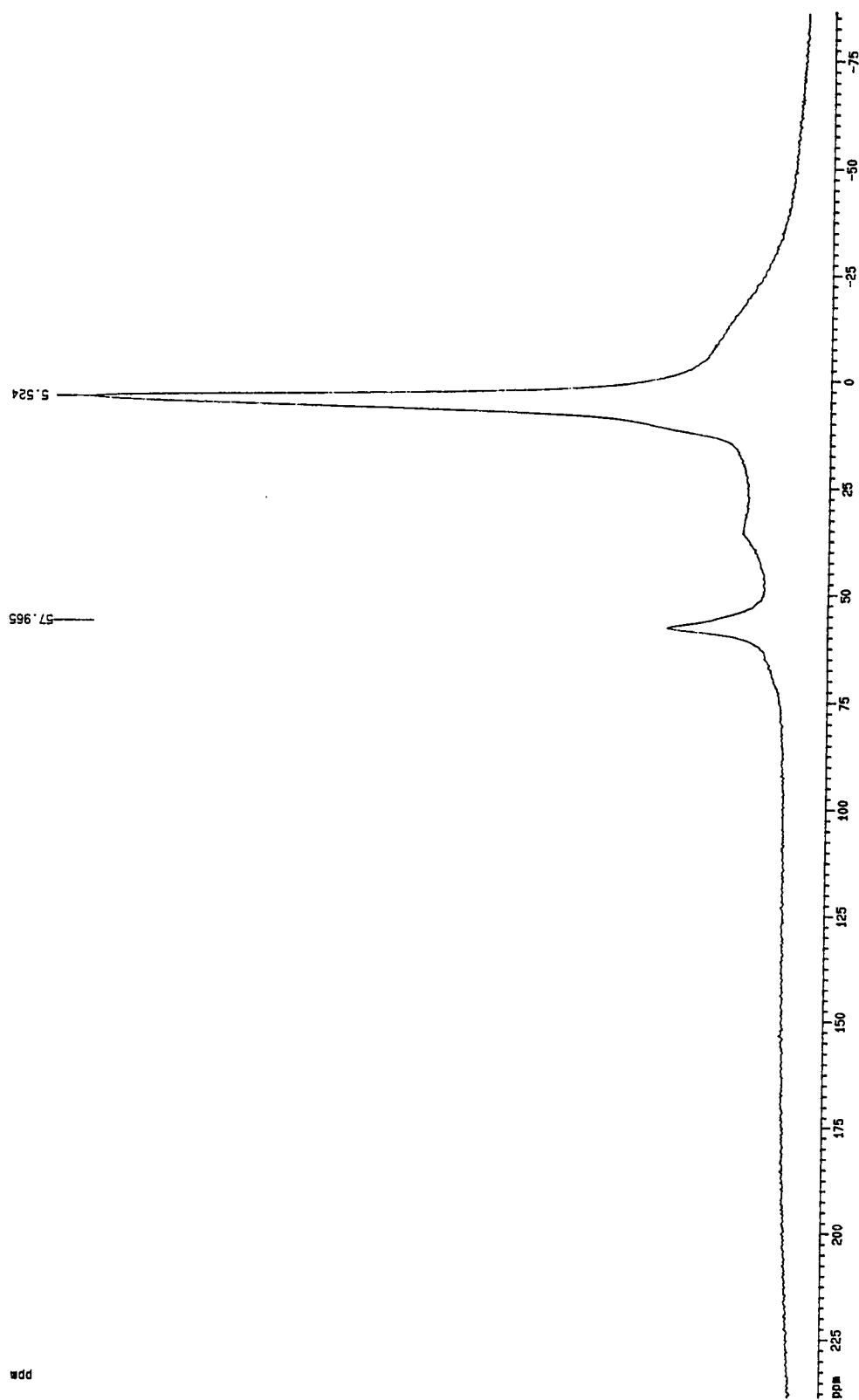


Figure 20. ^{11}B NMR of Diazo Compound 8' with Bu_3B and DBU after Completion of the Reaction at RT

produced results different from those in the hydrazone studies. The NMR studies, therefore, also suggest that the diazo mechanism is not operative in the alkylation reaction.

4.6 FUTURE STUDIES

Future research should be directed at further improving the alkylation reaction. The research would involve the study of alternate leaving groups or solvents and the further study of the alkyl aldehyde hydrazones.

The reaction of the trisylhydrazone derivatives worked well due to relief of steric strain. The alternate leaving groups could focus on the anionic nature of the mechanism. A hydrazone with chloro groups on the aromatic ring, such as 2,4,6-trichlorobenzenesulfonylhydrazone, could stabilize the negative charge upon leaving and therefore make an effective derivative. Non-aromatic derivatives, such as trifluoromethanesulfonylhydrazone, would be another alternative.

A preliminary study of different solvents revealed that polar solvents such as methanol are not appropriate for the reaction. A reaction that was performed in ether, however, was complete within 10 min. Further study of other solvents would reveal the ideal solvent for the reaction.

The combination of a different and more efficient leaving group, as well as a more efficient solvent, could then lead to an improvement of the alkylation of the alkyl derivatives. This could be carried further so that alkyl ketones and cyclic

ketones could be included in this novel alkylation reaction.

Finally, further research is necessary for elucidating the mechanism of the reaction. Although progress has been made and conclusions drawn about the diazo mechanism, the anionic mechanism has still not been proven to be the path of choice.

CHAPTER 5

EXPERIMENTAL

5.1 GENERAL

All ^1H and ^{13}C NMR spectra were obtained using on a 250 MHz Bruker AC250 spectrometer. All ^{11}B spectra were obtained using a 400 MHz Bruker spectrometer. All melting points are uncorrected and were recorded using a MEL-TEMP melting point apparatus equipped with a Glas-Col digital thermometer. Elemental analyses were performed by Atlantic Microlabs, Norcross, Georgia.

All glassware, syringes, and needles were dried in an oven heated to 250 °C for at least 12 h and cooled under argon prior to use. All solvents were dried and distilled prior to use.¹¹⁰ Reactions were magnetically stirred and monitored by TLC.

Products were purified by flash chromatography using 230-400 mesh ASTM 60 Å silica gel.¹¹¹

5.2 SYNTHESIS OF TOSYLHYDRAZONES

All solvents and reagents were used as received from vendors without further purification. Reactions were carried out open to air and the glassware was not oven dried.

5.2.1 General Procedure for the Synthesis of Aryl Aldehyde Tosylhydrazones

To a solution of *p*-toluenesulfonylhydrazide (5.6 g, 30 mmol) in absolute ethanol (20 mL) was added the aldehyde (30 mmol). The reaction mixture was stirred and heated to reflux for 10 min. A white precipitate generally formed at this point which dissolved upon heating. The solution was stirred at gentle reflux for 10 min and then slowly cooled to 0°C. The crystals were collected, washed with cold ethanol and recrystallized from hot ethanol. The recrystallized tosylhydrazone was dried under vacuum for 20 min. Newly prepared derivatives were analyzed by NMR and their purity was determined by elemental analysis.

5.2.2 Benzaldehyde Tosylhydrazone¹¹²

Benzaldehyde (3.2 g, 30 mmol), absolute ethanol (20 mL), and *p*-toluenesulfonylhydrazide (5.6 g, 30 mmol) were added to a 125-mL Erlenmyer flask. An isolated yield of 5.9 g, 72% was produced: mp 126.5-128.0°C; literature mp 127-128°C.

5.2.3 4-Methylbenzaldehyde Tosylhydrazone¹¹³

This material was prepared from 4-methylbenzaldehyde (30 mmol, 3.6 g) and *p*-toluenesulfonylhydrazide to produce an isolated yield of 6.4 g, 74%: mp 146.0-147.5 °C; lit. mp 115 - 116°C.

5.2.4 2-Methoxybenzaldehyde Tosylhydrazone¹¹⁴

This material was prepared from 2-methoxybenzaldehyde (30 mmol, 4.1 g) and p-toluenesulfonylhydrazide to produce an isolated yield of 7.0 g, 85%: mp 151.0-152.0 °C; lit. mp 165-167 °C: Anal. calcd for C₁₅H₁₆N₂O₃S: C, 59.19; H, 5.30; N, 9.20. Found: C, 59.25; H, 5.30; N, 9.28.

5.2.5 3-Methoxybenzaldehyde Tosylhydrazone

This material was prepared from 3-methoxybenzaldehyde (30 mmol, 4.1 g) and p-toluenesulfonylhydrazide to produce an isolated yield of 5.7 g, 69%: mp 107.5-108.5 °C: ¹H-NMR (Acetone-*d*₆) δ 10.14 (s, 1H), 7.95 (s, 1H), 7.85 (d, 2H, *J*=8.28 Hz), 7.37 (d, 2H, *J*=8.11 Hz), 7.28 (t, 1H, *J*=7.83 Hz), 7.20-7.13 (m, 2H), 6.96-6.90 (m, 1H), 3.78 (s, 3H), 2.36 (s, 3H); ¹³C (CDCl₃) δ 159.67, 147.87, 144.22, 135.17, 134.53, 129.64, 129.54, 127.86, 120.43, 116.64, 111.40, 55.26, 21.50. Anal. calcd for C₁₅H₁₆N₂O₃S: C, 59.19; H, 5.30; N, 9.20. Found: C, 59.26; H, 5.34; N, 9.25

5.2.6 4-Methoxybenzaldehyde Tosylhydrazone¹¹⁵

This material was prepared from 4-methoxybenzaldehyde (30 mmol, 4.1 g) and p-toluenesulfonylhydrazide to produce an isolated yield of 8.2 g, 89%: mp 123.0-123.5 °C; lit. mp 112 - 114 °C.

5.2.7 4-Chlorobenzaldehyde Tosylhydrazone¹¹⁶

This material was prepared from 4-chlorobenzaldehyde (30 mmol, 4.2 g) and *p*-toluenesulfonylhydrazide to produce an isolated yield of 6.2 g, 67%: mp 158.0-159.0 °C; lit. mp 148 - 151°C.

5.2.8 2-Bromobenzaldehyde Tosylhydrazone

This material was prepared from 2-bromobenzaldehyde (30 mmol, 5.6 g) and *p*-toluenesulfonylhydrazide to produce an isolated yield of 8.8 g, 84%: mp 159.0-159.5 °C: ¹H-NMR (Acetone-*d*₆) δ 11.76 (s, 1H), 8.32 (s, 1H), 7.92-7.78 (m, 3H), 7.60 (dd, 1H, *J*=7.9 Hz, *J*=1.2 Hz), 7.44-7.25 (m, 4H), 2.38 (s, 3H); ¹³C (Acetone-*d*₆) δ 146.07, 144.83, 137.37, 133.97, 133.69, 132.42, 130.45, 128.78, 128.54, 128.08, 124.26, 21.36. Anal. calcd for C₁₄H₁₃N₂O₂SBr: C, 47.60; H, 3.71; N, 7.93. Found: C, 47.77; H, 3.76; N, 8.00.

5.2.9 3-Bromobenzaldehyde Tosylhydrazone

This material was prepared from 3-bromobenzaldehyde (30 mmol, 5.6 g) and *p*-toluenesulfonylhydrazide to produce an isolated yield of 7.6g, 72%: mp 115.0-115.5 °C: ¹H-NMR (Acetone-*d*₆) δ 7.95 (s, 1H), 7.88-7.25 (m, 7H), 2.38 (s, 3H); ¹³C (Acetone-*d*₆) δ 146.00, 144.73, 137.33, 133.51, 131.48, 130.39, 130.12, 129.02, 128.50, 126.68, 123.14, 21.37. Anal. calcd for C₁₄H₁₃N₂O₂SBr: C, 47.60; H, 3.71; N, 7.93. Found: C, 47.79; H, 3.81; N, 8.01.

5.2.10 4-Bromobenzaldehyde Tosylhydrazone

This material was prepared from 4-bromobenzaldehyde (30 mmol, 5.6g) and *p*-toluenesulfonylhydrazide to produce an isolated yield of 8.5 g, 80%: mp 164.0-164.5 °C; ¹H-NMR (DMSO-*d*₆) δ 11.72 (s, 1H), 8.04 (s, 1H), 7.92 (d, 2H, *J*=8 Hz), 7.70-7.60 (m, 4H), 7.50 (d, 2H, *J*=7.9 Hz), 2.43 (s, 3H); ¹³C (DMSO-*d*₆) δ 145.70, 143.45, 136.12, 132.92, 131.72, 129.63, 128.55, 127.21, 123.30, 20.96. Anal. calcd for C₁₄H₁₃N₂O₂SBr: C, 47.60; H, 3.71; N, 7.93. Found: C, 47.68; H, 3.77; N, 7.98.

5.2.11 3-Nitrobenzaldehyde Tosylhydrazone¹¹⁷

This material was prepared from 3-nitrobenzaldehyde (30 mmol, 4.5 g) and *p*-toluenesulfonylhydrazide to produce an isolated yield of 7.6 g, 79%: mp 159.1 - 160.2°C; lit. mp 160 - 161°C.

5.2.12 4-Nitrobenzaldehyde Tosylhydrazone¹¹⁷

This material was prepared from 4-nitrobenzaldehyde (30 mmol, 4.5 g) and *p*-toluenesulfonylhydrazide to produce an isolated yield of 7.7 g, 81%: mp 156.8 - 158.2°C; lit. mp 158°C.

5.2.13 2-Pyrrolecarboxaldehyde Tosylhydrazone

This material was prepared from and pyrrole carboxaldehyde (2.6 g, 27 mmol) and *p*-toluenesulfonylhydrazide (5.6 g, 30 mmol) to produce an isolated yield of 5.9 g, 82%. This material was not very soluble in ethanol and had to therefore

be recrystallized from a solvent mixture of ethanol/acetone/water. It had to be refrigerated overnight for crystals to form: mp 184.0-185.0 °C (d): ¹H-NMR (DMSO-*d*₆) δ 11.22 (br s, 1H), 7.77 (d, 2H, *J*=8.19 Hz), 7.72 (s, 1H), 7.36 (d, 2H, *J*=8.14 Hz), 6.83 (s, 1H), 6.33 (s, 1H), 6.05 (dd, 1H, *J*=5.28 Hz and 2.38 Hz), 2.34 (s, 3H); ¹³C (DMSO-*d*₆) δ 142.99, 140.26, 136.48, 129.41, 127.23, 126.53, 122.08, 112.76, 108.99, 20.93. Anal. calcd for C₁₂H₁₃N₃O₂S: C, 54.74; H, 4.98; N, 15.96. Found: C, 54.63; H, 5.02; N, 15.93.

5.2.14 2-Furaldehyde Tosylhydrazone

This material was prepared from 2-furaldehyde (2.6 g, 27 mmol) and *p*-toluenesulfonylhydrazide to produce an isolated yield of 5.8 g, 82%: mp 109.0-110.0 °C (d): ¹H-NMR (DMSO-*d*₆) δ 11.42, (s, 1H), 7.80-7.70 (m, 4H), 7.38 (d, 2H, *J*=8.10 Hz), 6.79 (d, 1H, *J*=3.37 Hz), 6.54 (dd, 1H, *J*=3.11 Hz and 1.69 Hz), 2.34 (s, 3H); ¹³C (DMSO-*d*₆) δ 148.55, 145.00, 143.43, 136.88, 136.09, 129.65, 127.12, 113.80, 111.95, 20.94. Anal. calcd for C₁₂H₁₂N₂O₃S: C, 54.53; H, 4.58; N, 10.60. Found: C, 54.66; H, 4.64; N, 10.68.

5.2.15 Heptanal Tosylhydrazone⁸⁸

To a 250-mL, round-bottomed flask equipped with a septum and stir bar was added 9.32 g (50.0 mmol) *p*-toluenesulfonylhydrazide and THF (100 mL). Heptanal (5.42 g, 47.5 mmol) was added and the solution stirred at room temperature for 30 min. After this, the THF was removed under reduced pressure below room

temperature. The resulting cream-colored solid was recrystallized from hot ether to give 5.85 g (44% yield) of heptanal tosylhydrazone: mp 70.0 - 73.0°C; lit. mp 72 - 73°C.

5.3 SYNTHESIS OF TRISYLHYDRAZONES

5.3.1 *General Procedure for Synthesis of Aryl Aldehyde Trisylhydrazones*

To a stirred solution of 2,4,6-triisopropylbenzenesulfonylhydrazide (3.3 g, 11 mmol) in anhydrous methanol (45 mL) was added the aldehyde (10 mmol). A solid immediately precipitated and the mixture was stirred at room temperature for 1 h. The mixture was placed in a refrigerator overnight and the resulting solid was collected by vacuum filtration and washed with 3 x 5 mL of cold methanol. The products were recrystallized from hot ethanol.

Newly prepared derivatives were analyzed by NMR and purity was determined by elemental analyses.

5.3.2 *2,4,6-Triisopropylbenzenesulfonylhydrazide*⁹⁰

To a round-bottom flask equipped with a magnetic stirrer, thermometer, and addition funnel was added 2,4,6-triisopropylbenzenesulfonyl chloride (26.3 g, 86.9 mmol) and THF (50 mL). The solution was cooled to -10 °C in an ice-salt bath and hydrazine monohydrate (9.60 g, 192 mmol) was added over the course of 25 min. The temperature rose to 0 °C during the addition. After the addition, the reaction

mixture was stirred at 0 °C (ice bath) for 3 h and then distilled water (5 mL) was added to dissolve the solids. The mixture was then transferred to separatory funnel, the aqueous layer discarded, and the organic layer washed with ice-cold brine (3 x 20 mL). The organic layer was then dried over anhydrous Na₂SO₄ for 3 h, filtered, and the solvent removed using a rotary evaporator below room temperature. Pentane (100 mL) was added to the resulting solid and the mixture filtered. The solid was washed several times with pentane and then triturated with ice-cold water (4 x 100 mL). The solid was then dried *in vacuo* over P₂O₅ for 24 h to give a yield of 21.4 g 82%: mp 115.0-116.0 °C; lit. mp 118-120°C.

5.3.3 Benzaldehyde Trisylhydrazone⁹¹

This material was prepared from benzaldehyde (1.1 g, 10 mmol) and 2,4,6-triisopropylbenzenesulfonylhydrazide to produce an isolated yield of 3.4 g, 87%: mp 186.5 - 187.5°C; lit. mp 188 - 189°C.

5.3.4 4-Methylbenzaldehyde Trisylhydrazone

This material was prepared from 4-methylbenzaldehyde (1.2 g, 10 mmol) and 2,4,6-triisopropylbenzenesulfonylhydrazide to produce an isolated yield of 2.5 g, 61%: mp 165.0-166.0 °C: ¹H-NMR (DMSO-*d*₆) δ 11.61 (s, 1H), 7.89 (s, 1H), 7.41 (d, 2H, *J*=8.0 Hz), 7.17 (d, 2H, *J*=8.0 Hz), 4.23 (sept, 2H, *J*=6.7 Hz), 2.88 (sept, 1H, *J*=6.9 Hz), 2.27 (s, 3H), 1.21 (d, 12H, *J*=6.8 Hz), 1.17 (d, 6H, *J*=7.1 Hz); ¹³C (DMSO-*d*₆) δ 152.58, 150.37, 144.94, 139.60, 132.56, 131.15, 129.26, 126.47,

123.53, 33.29, 29.14, 24.67, 23.33, 20.86. Anal. calcd for $C_{23}H_{32}N_2O_2S$: C, 68.96; H, 8.05; N, 6.99. Found: C, 68.93; H, 8.06; N, 7.04.

5.3.5 4-Methoxybenzaldehyde Trisylhydrazone

This material was prepared from 4-methoxybenzaldehyde (1.4 g, 10.0 mmol) and 2,4,6-triisopropylbenzenesulfonylhydrazide to produce an isolated yield of 2.6 g, 62%: mp 161.5-162.5 °C: 1H -NMR (DMSO- d_6) δ 11.49 (s, 1H), 7.88 (s, 1H), 7.47 (d, 2H, $J=8.6$ Hz), 7.22 (s, 2H), 6.92 (d, 2H, $J=8.6$ Hz), 4.24 (sept, 2H, $J=6.6$ Hz), 3.74 (s, 3H), 2.88 (sept, 1H, $J=6.8$ Hz), 1.21 (d, 12H, $J=6.7$ Hz), 1.16 (d, 6H, $J=6.9$ Hz); ^{13}C (DMSO- d_6) δ 160.58, 152.53, 150.38, 144.88, 132.61, 128.06, 126.45, 123.49, 114.17, 55.22, 33.30, 29.14, 24.68, 23.32. Anal. calcd. for $C_{23}H_{32}N_2O_3S$: C, 66.31; H, 7.74; N, 6.72. Found: C, 66.49; H, 7.67; N, 6.95.

5.3.6 3-Methoxybenzaldehyde Trisylhydrazone

This material was prepared from 3-methoxybenzaldehyde (1.4 g) and 2,4,6-triisopropylbenzenesulfonylhydrazide to produce an isolated yield of 2.6 g, 62 %: mp 187.0-188.5 °C: 1H -NMR (DMSO- d_6) δ 11.75 (s, 1H), 7.91 (s, 1H), 7.31-7.23 (m overlapping s, 3H), 7.10-7.08 (m, 2H), 6.94-6.90 (m, 1H), 4.26 (sept, 2H, $J=6.7$ Hz), 3.73 (s, 3H), 2.90 (sept, 1H, $J=6.9$ Hz), 1.24 (d, 12H, $J=6.7$ Hz), 1.20 (d, 6H, $J=6.9$ Hz); ^{13}C (CDCl $_3$) δ 159.73, 153.44, 151.29, 146.12, 134.70, 131.20, 129.49, 123.82, 120.58, 116.96, 110.71, 55.20, 34.13, 29.96, 24.79, 23.47. Anal. calcd. for $C_{23}H_{32}N_2O_3S$: C, 66.31; H, 7.74; N, 6.72. Found: C, 66.24; H, 7.78; N, 6.72.

5.3.7 2-Methoxybenzaldehyde Trisylhydrazone

This material was prepared from 2-methoxybenzaldehyde (1.4 g, 10 mmol) and 2,4,6-triisopropylbenzenesulfonylhydrazide to produce an isolated yield of 2.28 g, 54%: mp=164.5-165.5 °C: $^1\text{H-NMR}$ ($\text{DMSO-}d_6$) δ 11.61 (s, 1H), 8.26 (s, 1H), 7.58-7.55 (m, 1H), 7.35-7.29 (m, 1H), 7.22 (s, 2H), 7.03-6.86 (m, 1H), 4.23 (sept, 2H, $J=6.7$ Hz), 3.78 (s, 3H), 2.88 (sept, 1H, $J=6.9$ Hz), 1.20 (d, 12H, $J=6.8$ Hz), 1.17 (d, 6H, $J=6.2$ Hz); ^{13}C (CDCl_3) δ 157.76, 153.27, 151.36, 142.38, 131.41, 126.43, 123.79, 121.88, 120.58, 110.93, 55.15, 30.03, 24.90, 24.82, 23.55. Anal. calcd. for $\text{C}_{23}\text{H}_{32}\text{N}_2\text{O}_3\text{S}$: C, 66.31; H, 7.74; N, 6.72. Found: C, 66.17; H, 7.69; N, 6.79.

5.3.8 4-Bromobenzaldehyde Trisylhydrazone

This material was prepared from 4-bromobenzaldehyde (1.9 g, 10 mmol) and 2,4,6-triisopropylbenzenesulfonylhydrazide to produce an isolated yield of 3.17 g, 68%. This hydrazone was not recrystallized. mp 197.0-197.8 °C: $^1\text{H-NMR}$ ($\text{DMSO-}d_6$) δ 11.80 (s, 1H), 7.92 (s, 1H), 7.52 (m, 4H), 7.22 (s, 2H), 4.25 (sept, 2H, $J=6.6$ Hz), 2.90 (sept, 1H, $J=6.8$ Hz), 1.23 (d, 12H, $J=6.6$ Hz), 1.20 (d, 6H, $J=6.7$ Hz); ^{13}C ($\text{DMSO-}d_6$) δ 152.52, 150.30, 143.40, 133.07, 132.40, 131.53, 128.20, 123.40, 122.87, 33.29, 29.09, 24.60, 23.26. Anal. calcd. for $\text{C}_{22}\text{H}_{29}\text{N}_2\text{O}_2\text{SBr}$: C, 56.77; H, 6.28; N, 6.02. Found: C, 56.58; H, 6.19; N, 6.11.

5.3.9 3-Bromobenzaldehyde Trisylhydrazone

This material was prepared from 3-bromobenzaldehyde (1.9 g, 10 mmol) and 2,4,6-triisopropylbenzenesulfonylhydrazide to produce an isolated yield of 2.5 g, 54%: mp 207.5-209.0 °C: $^1\text{H-NMR}$ ($\text{DMSO-}d_6$) δ 11.93 (s, 1H), 7.89 (s, 1H), 7.74 (s, 1H), 7.52 (t, 2H, $J=8.2$ Hz), 7.32 (t, 1H, $J=7.9$ Hz), 7.24 (s, 2H), 4.22 (sept, 2H, $J=6.7$ Hz), 2.89 (sept, 1H, $J=6.9$ Hz), 1.21 (d, 12H, $J=6.8$ Hz), 1.18 (d, 6H, $J=6.9$ Hz); ^{13}C ($\text{DMSO-}d_6$) δ 152.79, 150.40, 142.88, 136.24, 132.26, 130.88, 128.14, 126.05, 123.59, 122.07, 33.29, 29.19, 24.65, 23.31. Anal. calcd for $\text{C}_{22}\text{H}_{29}\text{N}_2\text{O}_2\text{SBr}$: C, 56.77; H, 6.28; N, 6.02. Found: C, 56.84; H, 6.23; N, 6.06.

5.3.10 2-Bromobenzaldehyde Trisylhydrazone

This material was prepared from 2-bromobenzaldehyde (1.9 g, 10 mmol) and 2,4,6-triisopropylbenzenesulfonylhydrazide to produce an isolated yield of 3.3 g, 71%: mp 153.0-154.0 °C: $^1\text{H-NMR}$ ($\text{Acetone-}d_6$) δ 10.71 (s, 1H), 8.41 (s, 1H), 7.86-7.82 (m, 1H), 7.60-7.56 (m, 1H), 7.39-7.24 (m overlapping s, 4H), 4.36 (sept, 2H, $J=6.8$ Hz), 2.93 (sept, 1H, $J=6.9$ Hz), 1.27 (d, 12H, $J=6.8$ Hz), 1.21 (d, 6H, $J=6.9$ Hz); ^{13}C ($\text{Acetone-}d_6$) δ 154.01, 151.88, 144.50, 133.90, 133.83, 133.46, 132.16, 128.53, 127.86, 124.58, 124.10, 34.70, 30.51, 25.09, 23.70. Anal. calcd for $\text{C}_{22}\text{H}_{29}\text{N}_2\text{O}_2\text{SBr}$: C, 56.77; H, 6.28; N, 6.02. Found: C, 56.88; H, 6.33; N, 6.10.

5.3.11 4-Chlorobenzaldehyde Trisylhydrazone

This material was prepared from 4-chlorobenzaldehyde (1.4 g, 10 mmol) and 2,4,6-triisopropylbenzenesulfonylhydrazide to produce an isolated yield of 2.9 g, 70%: mp 194.5-195.5 °C: $^1\text{H-NMR}$ ($\text{DMSO-}d_6$) δ 11.83 (s, 1H), 7.91 (s, 1H), 7.50-7.40 (m, 4H), 7.23 (s, 2H), 4.22 (sept, 2H, $J=6.7$ Hz), 2.89 (sept, 1H, $J=6.9$ Hz), 1.89 (overlapping d's, $J=7.0$ Hz and 7.1 Hz); ^{13}C ($\text{DMSO-}d_6$) δ 152.70, 150.37, 143.48, 134.23, 132.77, 132.44, 128.79, 128.08, 123.58, 33.29, 29.16, 24.65, 23.32. Anal. calcd for $\text{C}_{22}\text{H}_{29}\text{N}_2\text{SO}_2\text{Cl}$: C, 62.77; H, 6.94; N, 6.65. Found: C, 62.92; H, 6.93; N, 6.73.

5.3.12 4-Nitrobenzaldehyde Trisylhydrazone

This material was prepared from 4-nitrobenzaldehyde (1.5 g, 10 mmol) and 2,4,6-triisopropylbenzenesulfonylhydrazide to produce an isolated yield of 3.2 g, 74%. This hydrazone was not recrystallized as it would not dissolve in hot ethanol. mp 196.0-197.0 °C: $^1\text{H-NMR}$ ($\text{Acetone-}d_6$) δ 8.24 (d, 2H, $J=8.7$ Hz), 8.17 (s, 1H), 7.86 (d, 2H, $J=8.9$ Hz), 7.32 (s, 2H), 4.36 (sept, 2H, $J=6.7$ Hz), 2.94 (sept, 1H, $J=6.9$ Hz), 1.28, 1.23 (overlapping d's, 18H, $J=6.8$ Hz and 6.9 Hz); ^{13}C ($\text{Acetone-}d_6$) δ 154.26, 152.02, 149.21, 143.58, 143.49, 141.27, 133.51, 128.43, 124.73, 34.81, 30.63, 25.16, 23.77.

5.3.13 3-Nitrobenzaldehyde Trisylhydrazone

This material was prepared from 3-nitrobenzaldehyde (1.5 g, 10 mmol) and 2,4,6-triisopropylbenzenesulfonylhydrazide to produce an isolated yield of 3.5 g, 80%. This hydrazone was not recrystallized as it would not dissolve in hot ethanol. $^1\text{H-NMR}$ ($\text{DMSO-}d_6$) δ 12.10 (s, 1H), 8.37 (s, 1H), 8.17 (d, 1H, $J=7.9$ Hz), 8.05 (s, 1H), 7.94 (d, 1H, $J=7.7$ Hz), 7.66 (t, 1H, $J=7.9$ Hz), 7.24 (s, 2H), 4.24 (sept, 2H, $J=6.7$ Hz), 2.89 (sept, 1H, $J=6.9$ Hz), 1.23 (d, 12H, $J=6.7$ Hz), 1.17 (d, 6H, $J=6.8$ Hz); ^{13}C ($\text{DMSO-}d_6$) δ 152.83, 150.43, 148.12, 142.33, 135.64, 133.09, 132.29, 130.35, 123.92, 123.62, 120.04, 33.29, 29.19, 24.64, 23.31. Anal. calcd for $\text{C}_{22}\text{H}_{29}\text{N}_3\text{SO}_4$: C, 61.23; H, 6.77; N, 9.74. Found: C, 61.24; H, 6.72; N, 10.00.

5.3.14 2-Furaldehyde Trisylhydrazone

This material was prepared from 2-furaldehyde (0.96 g, 10 mmol) and 2,4,6-triisopropylbenzenesulfonylhydrazide to produce an isolated yield of 3.3 g, 87%; mp 149-150 d °C: $^1\text{H-NMR}$ ($\text{DMSO-}d_6$) δ 11.65 (s, 1H), 7.81 (s, 1H), 7.70 (s, 1H), 7.22 (s, 2H), 6.73 (d, 1H, $J=3.3$ Hz), 6.53 (d, 1H, $J=1.6$ Hz), 4.22 (sept, 2H, $J=6.7$ Hz), 2.88 (sept, 1H, $J=6.9$ Hz), 1.88 (overlapping d's, 18H, $J=7.2$ Hz); ^{13}C ($\text{DMSO-}d_6$) δ 153.86, 152.04, 150.49, 145.22, 136.33, 133.54, 124.57, 112.76, 112.58, 34.75, 30.49, 25.12, 23.76. Anal. calcd for $\text{C}_{20}\text{H}_{28}\text{N}_2\text{O}_3\text{S}$: C, 63.80; H, 7.50; N, 7.44. Found: C, 63.81; H, 7.48; N, 7.41.

5.3.15 **Acetophenone Trisylhydrazone**⁹¹

This material was prepared from acetophenone (1.2 g, 10 mmol) and 2,4,6-triisopropylbenzenesulfonylhydrazide to produce an isolated yield of 3.4 g, 85%: mp 166.5-167.5, lit mp 172-173 °C: ¹H-NMR (Acetone-*d*₆) δ 7.70-7.67 (m, 2H), 7.33-7.28 (m, 5H), 4.41 (sept, 2H, *J*=6.8 Hz), 2.93 (sept, 1H, *J*=6.9 Hz), 1.26, 1.22 (overlapping d's, 18H, *J*=6.8 Hz and 6.9 Hz); ¹³C (Acetone-*d*₆) δ 153.50, 152.07, 138.21, 133.87, 133.70, 129.38, 128.94, 124.41, 34.77, 30.41, 30.30, 25.6, 23.82.

5.3.16 **4-Nitroacetophenone Trisylhydrazone**

This material was prepared from 4-nitroacetophenone (1.7 g, 10 mmol) and 2,4,6-triisopropylbenzenesulfonylhydrazide to produce an isolated yield of 2.9 g, 65%: mp 163.3-164.7 °C: ¹H-NMR (DMSO-*d*₆) δ 11.19 (s, 1H), 8.17 (d, 2H, *J*=8.9 Hz), 7.82 (d, 2H, *J*=8.9 Hz), 7.22 (s, 2H), 4.30 (sept, 2H, *J*=6.7 Hz), 2.24 (s, 3H), 2.88 (sept, 1H, *J*=6.9 Hz), 1.18 (overlapping d's, 18 H, *J*=6.6 Hz and 6.7 Hz); ¹³C (DMSO-*d*₆) δ 152.79, 150.49, 147.65, 147.39, 143.64, 132.30, 126.87, 123.53, 123.38, 33.29, 28.96, 24.55, 23.31, 14.04. Anal. calcd for C₂₂H₂₉N₃O₄S; C, 61.23; H, 6.78; N, 9.74. Found: C, 61.13; H, 6.83; N, 9.82.

5.3.17 **Heptanal Trisylhydrazone**⁸⁸

As stated in the discussion, heptanal trisylhydrazone is not isolable and must be prepared and used *in situ*. The following is a general procedure for the preparation. To a 25 mL, round-bottom flask equipped with a stir bar and septum

was added TPSH (0.895 g, 3.00 mmol). THF (5 mL) was added to create a clear, colorless solution. Heptanal (0.340 g, 2.98 mmol) was diluted in THF (5 mL) and added to the TPSH solution at room temperature. The reaction mixture was then stirred at room temperature for 30 min. Anhydrous MgSO_4 was then added and the mixture filtered through a short column of celite/anhydrous Na_2SO_4 . THF (7 mL) was used to rinse the flask and column. The trisylhydrazone solution was typically filtered directly into a reaction flask and used immediately.

5.4 PROCEDURE FOR GAS CHROMATOGRAPHIC STUDIES

The following procedure is representative for all G.C. studies. Hexadecane (0.1845g) was placed in an argon-flushed, 15-mL, round-bottomed flask equipped with a side arm, reflux condenser, and stirring bar. THF (17 mL) was added via syringe followed by benzaldehyde tosylhydrazone (1.000 mmol, 0.2776 g). Tributylborane (1.0 mmol, 0.33 mL of a 1.0 M solution in THF) and the base (1.0 mmol) were added via syringe. The reaction was heated to gentle reflux under argon, and monitored by TLC.

A correction factor was obtained for the GC using hexadecane and pentylbenzene. Three runs were performed and the results averaged to give a value (e.g. 1.038) for the first correction factor.

To prepare a sample for the G.C. analysis a small sample was taken from the reaction mixture via syringe and placed over MgSO_4 to dry. An aliquot of the dry

sample was then injected into the G.C.. Three analyses were obtained for each sample and an average yield was calculated.

A second correction factor was obtained in the same manner as above and averaged with the first one.

G.C. temperature conditions: 110°C for 1 min, then ramped to 180°C at 9 °C/min.

Retention times: Pentylbenzene 2.30 min.; Hexadecane 3.55 min.

Mathematic formulas used¹¹⁸

$$\text{Correction Factor} = \frac{\text{Area of standard}}{\text{Area of sample}} \times \frac{\text{Weight of sample}}{\text{Weight of standard}}$$

The correction factor (C.F.) was always approximately equal to 1.

$$\% \text{ Yield} = \frac{\text{Area of product}}{\text{Area of standard}} \times \frac{\text{Weight of standard}}{\text{Weight of product}} \times \text{C.F.} \times 100$$

(Weight of product = theoretical yield.)

5.5 SYNTHESSES USING TOSYLHYDRAZONES

5.5.1 General Procedure for Synthesis of Pentylbenzenes utilizing NaOH

The aldehyde tosylhydrazone (3.00 mmol) was dissolved in 17 mL of THF contained in an argon-flushed, 50 mL, round-bottomed flask equipped with a side-arm, reflux condenser, and stirring bar. Tributylborane (3.0 mmol, 3.0 mL of a 1.0 M solution in THF) was added via syringe, followed by NaOH (3.0 mmol, 1.0 mL of a 3.0 M solution in H₂O). The reaction was heated to gentle reflux under argon and monitored by TLC for the disappearance of starting material. At the end of the reaction, as indicated by TLC, water (10 mL) was added to the reaction mixture and the mixture was allowed to cool to room temperature. The product was extracted into ether (3 × 10 mL). The combined organic layers were dried over anhydrous MgSO₄, filtered, and the solvent removed in vacuo. The product was purified by flash chromatography using a 50-mm diameter column, packed with seven inches of silica gel, and eluted with a solvent system of 5% ethyl acetate in hexanes.

5.5.2 *Pentylbenzene*¹¹⁹

This material was prepared from benzaldehyde tosylhydrazone (3.00 mmol, 0.823 g) to produce an isolated yield of 0.37 g, 83%, according to the above procedure: ¹H NMR (CDCl₃ w/TMS) δ 7.30-7.14 (m, 4H), 2.60 (t, 2H, *J* = 7.0 Hz), 1.62 (q, 2H, *J* = 8.0 Hz), 1.37-1.26 (m, 4H), 0.89 (t, 3H, *J* = 6.7 Hz); ¹³C NMR δ 142.93, 128.37, 128.19, 35.97, 31.54, 31.18, 22.54, 13.99.

5.5.3 1-Methoxy-4-pentylbenzene¹²⁰

This material was prepared from *p*-anisaldehyde tosylhydrazone (3.00 mmol, 0.913 g) to produce an isolated yield of 0.44 g, 83%, according to the above procedure: ¹H NMR (CDCl₃ w/TMS) δ 7.11-7.07 (m, 2 H), 6.84-6.80 (m, 2H), 3.78 (s, 3H), 2.54 (t, 2H, *J* = 7.6 Hz), 1.58 (q, 2H, *J* = 7.4 Hz), 1.37-1.25 (m, 4H), 0.88 (t, 3H, *J* = 6.8 Hz); ¹³C NMR δ 157.63, 135.07, 129.23, 113.66, 55.25, 35.01, 31.47, 31.43, 22.55, 14.02.

5.5.4 1-Methyl-4-pentylbenzene¹²¹

This material was prepared from *p*-tolualdehyde tosylhydrazone (3.00 mmol, 0.865 g) to produce an isolated yield of 0.49 g, 89%, according to the above procedure: ¹H NMR (CDCl₃w/TMS) δ 7.07 (s, 4H), 2.55 (t, 2H, *J* = 7.7 Hz), 2.31 (s, 3H), 1.59 (qt, 2H, *J* = 7.4 Hz), 1.37-1.26 (m, 4H), 0.88 (t, 3H, *J* = 6.7 Hz); ¹³C NMR δ 139.87, 134.92, 128.27, 35.50, 31.54, 31.31, 22.56, 20.96, 14.01.

5.5.5 1-Bromo-2-pentylbenzene¹²²

This material was prepared from *o*-bromobenzaldehyde tosylhydrazone (3.000 mmol, 1.060 g) to produce an isolated yield of 0.63 g, 93%, according to the above procedure: ¹H NMR (CDCl₃ w/TMS) δ 7.50 (d, 1H, *J* = 7.8 Hz), 7.24-7.16(m, 2H), 7.07-6.99 (m, 1H), 2.71 (t, 2H, *J* = 7.8 Hz), 1.61 (q, 2H, *J* = 7.3 Hz), 1.38-1.32 (m, 4H), 0.90 (t, 3H, *J* = 6.7 Hz); ¹³C NMR (CDCl₃) δ 142.14, 132.71, 130.25, 127.28, 124.46, 36.15, 31.57, 29.62, 22.50, 14.02.

5.5.6. 1-Bromo-3-pentylbenzene¹²³

This material was prepared from *m*-bromobenzaldehyde tosylhydrazone (3.000mmol, 1.060g) to produce an isolated yield of 0.60g, 88%, according to the above procedure: ¹H NMR (CDCl₃ w/TMS) δ 7.32-7.27 (m, 2H), 7.16-7.07 (m, 2H), 2.56 (t, 2H, *J* = 7.7 Hz), 1.59 (q, 2H, *J* = 7.4 Hz), 1.24-1.37 (m, 4H), 0.89 (t, 3H, *J* = 6.8 Hz); ¹³C NMR (CDCl₃) δ 145.27, 131.43, 129.74, 128.67, 127.04, 122.31, 35.58, 31.38, 30.91, 22.47, 13.97.

5.5.7 1-Bromo-4-pentylbenzene¹²⁴

This material was prepared from *p*-bromobenzaldehyde tosylhydrazone (3.000 mmol, 1.060 g) to produce an isolated yield of 0.61 g, 90%, according to the above procedure: ¹H NMR (CDCl₃ w/TMS) δ 7.37 (d, 2H, *J* = 8.2 Hz), 7.03 (d, 2H, *J* = 8.2 Hz), 2.54 (t, 2H, *J* = 7.7 Hz), 1.57 (q, 2H, *J* = 7.4 Hz), 1.36-1.26 (m, 4H), 0.88 (t, 3H, *J* = 6.7 Hz); ¹³C NMR (CDCl₃) δ 141.81, 131.24, 130.16, 119.24, 35.31, 31.36, 30.99, 22.50, 13.99.

5.5.8 1-Chloro-4-pentylbenzene¹²⁵

This material was prepared from *p*-chlorobenzaldehyde tosylhydrazone (3.00 mmol, 0.926 g) to produce an isolated yield of 0.54 g, 99%, according to the above procedure: ¹H NMR (CDCl₃ w/TMS) 7.24-7.19 (m, 2H) 7.10-7.07 (m, 2H), 2.56 (t, 2H, *J* = 7.7 Hz), 1.58 (qt, 2H, *J* = 7.4 Hz), 1.37-1.26 (m, 4H), 0.88 (t, 3H, *J* = 6.8

Hz); ^{13}C NMR (CDCl_3) δ 141.32, 131.25, 129.73, 128.30, 128.17, 35.27, 31.38, 31.05, 22.50, 13.98.

5.5.9 1-Nitro-3-pentylbenzene¹²⁶

This material was prepared from *m*-nitrobenzaldehyde tosylhydrazone (3.00 mmol, 0.958 g) to produce an isolated yield of 0.49 g, 85%, according to the above procedure: ^1H NMR (CDCl_3 w/TMS) δ 8.04-8.01 (m, 2H), 7.52-7.40 (m, 2H), 2.71 (t, 2H, $J = 7.7$ Hz), 1.66 (q, 2H, $J = 7.4$ Hz), 1.39-1.26 (m, 4H), 0.90 (t, 3H, $J = 6.6$ Hz); ^{13}C NMR (CDCl_3) δ 148.32, 144.81, 134.65, 129.01, 123.12, 120.79, 35.49, 31.24, 30.72, 22.39, 13.89.

5.5.10 1-Nitro-4-pentylbenzene¹²⁷

This material was prepared from *p*-nitrobenzaldehyde tosylhydrazone (3.00 mmol, 0.958 g) to produce an isolated yield of 0.52 g, 90%, according to the above procedure: ^1H NMR (CDCl_3 w/TMS) δ 8.15-8.10 (m, 2H), 7.34-7.30 (m, 2H), 2.70 (t, 2H, $J = 7.7$ Hz), 1.65 (q, 2H, $J = 7.5$ Hz), 1.39-1.26 (m, 4H), 0.89 (t, 3H, $J = 6.7$ Hz); ^{13}C NMR (CDCl_3) δ 150.75, 146.15, 129.04, 123.41, 135.71, 31.24, 30.54, 22.32, 13.80.

5.5.11 12-(4-Chloro)dodecanoic acid methyl ester

This material was prepared from *p*-chlorobenzaldehyde tosylhydrazone (3.00 mmol, 0.926 g) and tris-(10-methoxycarbonyldecyl)borane (3.0 mmol, 3.0 mL

of a 1.0 M solution in THF) to produce an isolated yield of 0.90 g, 92%, according to the above procedure. ^1H NMR (CDCl_3 w/TMS) δ 7.32-7.19 (m, 2H), 7.17-7.06 (m, 2H), 3.69-3.61 (s, 3H), 2.38-2.24 (t, 2H, $J = 7.5$ Hz), 1.75-1.50 (m, 4H), 1.42-1.24 (m, 16H). ^{13}C NMR (CDCl_3) δ 174.30, 141.90, 139.11, 129.68, 128.25, 51.34, 35.24, 34.06, 33.73, 31.31, 29.48, 29.38, 29.12, 29.00, 28.85, 24.91.

5.5.12 1-Chloro-4-cyclohexylmethylbenzene¹²⁸

This material was prepared from *p*-chlorobenzaldehyde tosylhydrazone (3.00 mmol, 0.926 g) and tricyclohexylborane (3.0 mmol, 1.5 mL of a 2.0 M solution in THF) to produce an isolate yield of 0.15 g, 24%, according to the above procedure. ^1H NMR (CDCl_3 w/TMS) δ 7.00-7.27 (m, 4H), 2.44-2.41 (d, 2H, $J = 7.1$ Hz), 1.69-1.64 (m, 4H), 1.57-1.40 (m, 1H), 1.25-1.13 (m, 4H), 0.98-0.83 (m, 2H). ^{13}C NMR (CDCl_3) δ 139.01, 131.23, 130.46, 128.131, 43.41, 39.73, 33.06, 26.27.

5.5.13 General Procedure for Synthesis of Pentylbenzenes utilizing Bu_4NOH

The aldehyde tosylhydrazone (3.00 mmol) was dissolved in 17 mL THF contained in an argon-flushed, 50 mL, round-bottomed flask equipped with a side-arm, reflux condenser, and stirring bar. Tributylborane (3.0 mmol, 3.0 mL of a 1.0 M solution in THF) was added via syringe, followed by Bu_4OH (3.0 mmol, 1.0 mL of a 3.0 M solution in MeOH). Reactions were allowed to run for at least 1 h. At the end of the reaction, water (10 mL) was added to the reaction mixture and the

mixture was allowed to cool to room temperature. The product was extracted into ether (3 × 10 mL). The combined organic layers were dried over anhydrous MgSO₄, filtered, and the solvent removed in vacuo. The product was purified by flash chromatography using a 50-mm diameter column, packed with seven inches of silica gel, and eluted with a solvent system of 5% ethyl acetate in hexanes.

5.5.14 *Pentylbenzene*

This material was prepared from benzaldehyde tosylhydrazone (3.00 mmol, 0.823 g) to produce an isolated yield of 0.35 g, 80%. Spectral data was consistent with sample prepared previously.

5.5.15 *1-Methoxy-2-pentylbenzene*¹²⁰

This material was prepared from *o*-anisaldehyde tosylhydrazone (3.00 mmol, 0.913 g) to produce an isolated yield of 0.50 g, 93%. ¹H NMR (CDCl₃ w/TMS) δ 7.19-7.09 (m, 2H), 6.90-6.80 (m, 2H), 3.80 (s, 3H), 5.60 (t, 2H, *J* = 7.70 Hz), 1.58 (qt, 2H, *J* = 7.30 Hz), 1.38-1.27 (m, 4H), 0.89 (t, 3H, *J* = 6.68 Hz). ¹³C NMR (CDCl₃) δ 157.43, 131.35, 129.70, 126.69, 120.27, 110.21, 55.20, 31.80, 30.08, 29.53, 22.55, 14.01.

5.5.16 *1-Methoxy-3-pentylbenzene*¹²⁰

This material was prepared from *m*-anisaldehyde tosylhydrazone (3.00 mmol, 0.913 g) to produce an isolated yield of 0.48 g, 89%. ¹H NMR (CDCl₃

w/TMS) δ 7.27-7.16 (m, 1H), 6.84-6.70 (m, 3H), 3.82 (s, 3H), 2.61 (t, 2H, $J = 7.71$ Hz), 1.65 (qt, 2H, $J = 7.40$ Hz), 1.42-1.30 (m, 4H), 0.92 (t, 3H, $J = 6.67$ Hz). ^{13}C NMR (CDCl_3) δ 159.60, 144.58, 129.10, 120.82, 114.18, 110.78, 55.03, 35.98, 31.50, 31.05, 22.52, 13.98.

5.5.17 1-Methoxy-4-pentylbenzene

This material was prepared from *p*-anisaldehyde tosylhydrazone (3.00 mmol, 0.913 g) to produce a yield of 0.44 g, 83%. Spectral data was consistent with sample prepared previously.

5.5.18 1-Methyl-4-pentylbenzene

This material was prepared from *p*-tolualdehyde tosylhydrazone (3.00 mmol, 0.865 g) to produce an isolated yield of 0.44 g, 90%. Spectral data was consistent with sample prepared previously.

5.5.19 1-Bromo-2-pentylbenzene

This material was prepared from *o*-bromobenzaldehyde tosylhydrazone (3.000 mmol, 1.060 g) to produce an isolated yield of 0.63 g, 92%. Spectral data was consistent with sample prepared previously.

5.5.20 1-Bromo-3-pentylbenzene

This material was prepared from *m*-bromobenzaldehyde tosylhydrazone

(3.000mmol, 1.060g) to produce an isolated yield of 0.61 g, 89%. Spectral data was consistent with sample prepared previously.

5.5.21 1-Bromo-4-pentylbenzene

This material was prepared from *p*-bromobenzaldehyde tosylhydrazone (3.000 mmol, 1.060 g) to produce an isolated yield of 0.64 g, 94%. Spectral data was consistent with sample prepared previously.

5.5.22 1-Chloro-4-pentylbenzene

This material was prepared from *p*-chlorobenzaldehyde tosylhydrazone (3.00 mmol, 0.926 g) to produce an isolated yield of 0.52 g, 94%. Spectral data was consistent with sample prepared previously.

5.5.23 1-Nitro-3-pentylbenzene

This material was prepared from *m*-nitrobenzaldehyde tosylhydrazone (3.00 mmol, 0.958 g) to produce an isolated yield of 0.53 g, 91%. Spectral data was consistent with sample prepared previously.

5.5.24 1-Nitro-4-pentylbenzene

This material was prepared from *p*-nitrobenzaldehyde tosylhydrazone (3.00 mmol, 0.958 g) to produce an isolated yield of 0.57 g, 98%. Spectral data was consistent with sample prepared previously.

5.5.25 **2-Pentylpyrrole**¹²⁹

This material was prepared from 2-pyrrolecarboxaldehyde tosylhydrazone (3.00 mmol, g) to produce an isolated yield of 0.26 g, 61%. ¹H NMR (CDCl₃ w/TMS) δ 6.63 (dd, 1H, *J* = 4.1 Hz and 2.6 Hz), 6.12 (dd, 1H, *J* = 5.8 Hz and 2.80 Hz), 5.90 (d, 1H, *J* = 0.9 Hz), 2.57 (t, 2H, *J* = 7.7 Hz), 1.61 (qt, 2H, *J* = 7.4 Hz), 1.70-1.51 (m, 4H), 0.89 (t, 3H, *J* = 6.8 Hz). ¹³C NMR (CDCl₃) δ 132.82, 115.91, 108.14, 104.78, 31.54, 29.32, 27.66, 22.43, 13.95.

5.5.26 **2-Pentylfuran**¹³⁰

This material was prepared from 2-furaldehyde tosylhydrazone (3.00 mmol, 0.g) to produce an isolated yield of 0.27 g, 66%. ¹H NMR (CDCl₃ w/TMS) δ 7.28 (s, 1H), 6.26 (dd, 1H, *J* = 3.1 Hz and 1.9 Hz), 5.95 (dd, 1H, *J* = 3.1 Hz and 1.2 Hz), 2.60 (t, 2H, *J* = 7.6 Hz), 1.63 (qt, 2H, *J* = 7.3 Hz), 1.42-1.29 (m, 4H), 0.89 (t, 3H, *J* = 6.7 Hz). ¹³C NMR (CDCl₃) δ 156.57, 140.56, 109.96, 104.48, 31.36, 27.93, 27.72, 22.39, 13.93

5.5.27 **Alkylation of Heptanal Tosylhydrazone with Tributylborane**

The following procedure for the alkylation reaction with LiHMDS is representative for the study involving various base and solvent combinations summarized in Table 2-10 To a flame-dried, argon-flushed, 50-mL, round-bottomed flask equipped with a side-arm, reflux condenser, stir bar, argon inlet and mercury bubbler was added heptanal tosylhydrazone (0.844 g, 2.99 mmol). This was

dissolved in a 50:50 mixture of THF:HMPA (20 mL). Tributylborane (3.0 mmol, 3.0 mL of a 1.0 M solution in THF) was added via syringe. LiHMDS (3.0 mmol, 3.0 mL of a 1.0 M solution in THF) was added and the reaction mixture heated to reflux. The reaction mixture was heated until reaction stopped progressing as evidenced by TLC (21 h). The reaction was then cooled and placed in a room temperature water bath. Distilled water (10 mL) and sodium perborate (1.41 g, 9.14 mmol) were added and the reaction stirred vigorously for 2 h. The reaction mixture was then transferred to a separatory funnel, extracted with ether (3 x 10 mL), washed with water (2 x 20 mL) to remove HMPA, and washed with brine (1 x 20 mL). The ether extracts were dried over anhydrous MgSO_4 . The solvent was removed and the crude product was flash chromatographed using silica gel and 9% EtOAc/Hexanes to give 0.18 g (34% yield) of undecan-5-ol¹⁵⁴: $^1\text{H-NMR}$ (CDCl_3/TMS) δ 3.74-3.44 (br m, 1H), 1.56-1.04 (m, 17H), 1.04-0.72 (m, 6H); $^{13}\text{C-NMR}$ (CDCl_3) δ 72.02, 37.51, 37.18, 31.84, 29.36, 27.84, 25.60, 22.75, 22.60, 14.04; GCMS m/z 171 (M-1), 154 (m- H_2O).

5.6 SYNTHESSES USING TRISYLHYDRAZONES

5.6.1 General Procedure for the Synthesis of Pentybenzenes Utilizing Bu_4NOH

The aldehyde trisylhydrazone (3.00 mmol) was dissolved in 17 mL of THF contained in an argon-flushed, 50-mL, round-bottomed flask equipped with a side-

arm, reflux condenser, and stirring bar. Tributylborane (3.0 mmol, 3.0 mL of a 1.0 M solution in THF) was added via syringe, followed by Bu₄OH (3.0 mmol, 1.0 mL of a 3.0 M solution in MeOH). Reactions were run at room temperature, unless otherwise noted. At the end of the reaction as indicated by TLC, water (10 mL) was added to the reaction mixture and the mixture was allowed to cool to room temperature. The product was extracted into ether (3 × 10 mL). The combined organic layers were dried over anhydrous MgSO₄, filtered, and the solvent removed in vacuo. The product was purified by flash chromatography using a 50-mm diameter column, packed with seven inches of silica gel, and eluted with a solvent system of 5% ethyl acetate in hexanes.

5.6.2 *Pentylbenzene*

This material was prepared from benzaldehyde trisylhydrazone (3.00 mmol, 1.16 g) to produce an isolated yield of 0.41 g, 93%. Spectral data was consistent with sample prepared previously.

5.6.3 *1-Methoxy-4-pentylbenzene*

This material was prepared from *p*-anisaldehyde trisylhydrazone (3.00 mmol, 1.25 g) to produce an isolated yield of 0.36 g, 68%. This reaction was run at reflux. Spectral data was consistent with sample prepared previously.

5.6.4 1-Methyl-4-pentylbenzene

This material was prepared from *p*-tolualdehyde trisylhydrazone (3.00 mmol, 1.21 g) to produce an isolated yield of 0.43 g, 88%. This reaction was run at reflux. Spectral data was consistent with sample prepared previously.

5.6.5 1-Bromo-2-pentylbenzene

This material was prepared from *o*-bromobenzaldehyde trisylhydrazone (3.00 mmol, 1.40 g) to produce an isolated yield of 0.63 g, 92%. Spectral data was consistent with sample prepared previously.

5.6.6 1-Bromo-3-pentylbenzene

This material was prepared from *m*-bromobenzaldehyde trisylhydrazone (3.00 mmol, 1.40 g) to produce an isolated yield of 0.65 g, 96%. Spectral data was consistent with sample prepared previously.

5.6.7 1-Bromo-4-pentylbenzene

This material was prepared from *p*-bromobenzaldehyde trisylhydrazone (3.00 mmol, 1.40 g) to produce an isolated yield of 0.64 g, 93%. Spectral data was consistent with sample prepared previously.

5.6.8 1-Chloro-4-pentylbenzene

This material was prepared from *p*-chlorobenzaldehyde trisylhydrazone (3.00

mmol, 1.26 g) to produce an isolated yield of 0.51 g, 93%. Spectral data was consistent with sample prepared previously.

5.6.9 1-Nitro-3-pentylbenzene

This material was prepared from *m*-nitrobenzaldehyde trisylhydrazone (3.00 mmol, g) to produce an isolated yield of 0.55 g, 96%. Spectral data was consistent with sample prepared previously.

5.6.10 1-Nitro-4-pentylbenzene

This material was prepared from *p*-nitrobenzaldehyde trisylhydrazone (3.00 mmol, g) to produce an isolated yield of 0.55 g, 95%. Spectral data was consistent with sample prepared previously.

5.6.11 2-Pentylfuran

This material was prepared from 2-furaldehyde trisylhydrazone (3.00 mmol, g) to produce an isolated yield of 0.39 g, 93%. Spectral data was consistent with sample prepared previously.

5.6.12 (1-Methylpentyl)benzene

This material was prepared from acetophenone trisylhydrazone (3.00 mmol, 0.916g) to give a yield of 0.27 g, 74%. ¹H-NMR (CDCl₃/TMS) δ 7.2-7.1 (m, 5H), 2.66 (sextet, 1H, *J*=7.0 Hz), 1.50 (dq, 2H, *J*=8.0 Hz and 2.4 Hz), 1.36-1.04 (d

overlapping m, 7H, d is at 1.16 ppm, $J=6.8$ Hz), 0.84 (t, 3H, $J=7.0$ Hz); ^{13}C -NMR (CDCl_3) δ 147.92, 128.16, 126.91, 125.64, 39.87, 38.09, 29.87, 22.69, 22.23, 13.93.

5.6.13 1-Nitro-4-(1-methylpentyl)benzene

This material was prepared from 4-nitroacetophenone trisylhydrazone (3.00 mmol, 1.34 g) to give a yield of 0.56 g, 85%. ^1H -NMR (CDCl_3/TMS) δ ^{13}C -NMR (CDCl_3) δ 8.15 (d, 2H, $J=8.7$ Hz), 7.34 (d, 2H, $J=8.7$ Hz), 2.81 (sextet, 1H, $J=7.0$ Hz), 1.60 (q, 2H, $J=7.5$ Hz), 1.30-1.10 (d overlapping m, 7H, d is at 1.26 ppm, $J=6.9$ Hz), 0.85 (t, 3H, $J=7.0$ Hz); ^{13}C -NMR (CDCl_3) δ 155.75, 146.18, 127.70, 123.52, 39.96, 37.67, 29.65, 22.55, 21.80, 13.83.

5.6.14 Alkylation of Heptanal Trisylhydrazone via Tributylborane

The following procedure is representative for reactions involving the base and solvent combinations shown in Table 3-5. To a flame-dried, argon flushed, 50 mL, round-bottom flask equipped with a side-arm, reflux condenser, stir-bar, argon inlet, and mercury bubbler was added heptanal trisylhydrazone (3.00 mmol). Tributylborane (3.0 mmol, 3.0 mL of a 1.0 M solution in THF) was added followed by DBU (0.67 mL, 4.5 mmol). The reaction mixture was heated to reflux until TLC indicated the reaction was over (3 h). The mixture was then cooled and oxidized with water (10 mL) and sodium perborate (1.44 g, 9.36 mmol) as described earlier. After the standard work-up and removal of solvent, the crude product was flash chromatographed using 8 inches of silica gel in a 50 mm column with 8%

EtOAc/Hexanes to give 0.38 g (74% yield) of undecan-5-ol¹³¹: ¹H-NMR (CDCl₃/TMS) δ 3.74-3.44 (br m, 1H), 1.56-1.04 (m, 17H), 1.04-0.72 (m, 6H); ¹³C-NMR (CDCl₃) δ 72.02, 37.51, 37.18, 31.84, 29.36, 27.84, 25.60, 22.75, 22.60, 14.04; GCMS *m/z* 171 (M-1), 154 (m-H₂O).

5.7 SYNTHESSES USING FUNCTIONALIZED ORGANOBORANES

A series of alkylated aryls containing functionalized alkyl groups were synthesized by the reaction of 4-methylbenzaldehyde tosylhydrazone with different trialkylboranes and Bu₄NOH. The functionalized trialkylboranes were synthesized from the corresponding alkenes, according to published procedures.

5.7.1 General Synthesis Utilizing Functionalized Organoboranes

The alkene (9.00 mmol) and dry THF (6 mL) were added to an argon-flushed, 20 mL, round-bottomed flask equipped with a side-arm, reflux condenser, and stirring bar. The reaction mixture was cooled to 0 °C and BH₃ (3.0 mmol, 3.0 mL of a 1.0 M solution in THF) was slowly added. The reaction was stirred at 0 °C for 15 min and then at RT for 2 h. *p*-Tolualdehyde tosylhydrazone (3.00 mmol, 0.865 g) was dissolved in 8 mL THF contained in a separate argon-flushed, 50 mL, round-bottomed flask equipped with a side-arm, reflux condenser, and stirring bar.

The borane solution was transferred under argon via a double ended needle to the tosylhydrazone solution and THF (3 x 2 mL) was used to rinse the flask and

needle. Bu₄NOH (3.0mmol, 1.0 mL of a 3.0 M solution in MeOH) was added and the reaction was heated to gentle reflux under argon. At the end of the reaction, as indicated by TLC, water (10 mL) was added to the reaction and the mixture was allowed to cool to room temperature. The product was extracted into ether (3 × 10 mL). The combined organic layers were dried over anhydrous MgSO₄, filtered, and the solvent removed in vacuo. The product was purified by flash chromatography using a 50 mm diameter column, packed with seven inches of silica gel, and eluted with a solvent system of 5% ethyl acetate in hexanes.

5.7.2 1-Chloro-6-*p*-tolylhexane

1-Chloro-6-*p*-tolylhexane was prepared, as described previously, from 5-chloro-1-pentene (9.00 mmol, 0.941 g), *p*-tolualdehyde tosylhydrazone (3.00 mmol, 0.865 g) and Bu₄NOH (6.0 mol, 6.0 mL of a 1M solution in methanol). After 3 h at reflux, 0.57 g, 91% of product was isolated. ¹H-NMR (CDCl₃/TMS) δ 7.07 (s, 4H), 3.51 (t, 2H, *J* = 6.7 Hz), 2.56 (t, 2H, *J* = 7.6 Hz), 2.31 (s, 3H), 1.76 (qt, 2H, *J* = 7.0 Hz), 1.61 (qt, 2H, *J* = 7.5 Hz), 1.56-1.30 (m, 4H); ¹³C-NMR (CDCl₃) δ 139.47, 135.04, 128.94, 128.24, 45.07, 35.33, 32.55, 31.36, 28.48, 26.73, 20.96. Anal. calcd for C₁₃H₁₉Cl: C, 74.09; H, 9.09. Found: C, 74.26; H, 9.24.

5.7.3 7-*p*-Tolylheptanenitrile

7-*p*-Tolylheptanenitrile was prepared, as described previously, from 5-cyano-1-pentene (9.00 mmol, 0.856 g) *p*-tolualdehyde tosylhydrazone (3.00 mmol, 0.865

g). After 2 h at reflux, 0.59 g, 98% of product was isolated. $^1\text{H-NMR}$ (CDCl_3/TMS) δ 7.13-7.01 (m, 4H), 2.57 (t, 2H, $J=7.6$ Hz), 2.31 (overlapping s and t, 5H, $J=7.0$ Hz), 1.68-1.30 (m, 8H); $^{13}\text{C-NMR}$ (CDCl_3) δ 139.24, 135.13, 128.97, 128.22, 35.25, 31.14, 28.51, 28.30, 25.29, 20.96, 17.07. Anal. calcd for $\text{C}_{14}\text{H}_{19}\text{N}$: C, 83.53; H, 9.51; N, 6.96. Found: C, 83.41; H, 9.55; N, 6.82.

5.7.4 12-*p*-Tolyldodecanoic Acid Methyl Ester

12-*p*-tolyldodecanoic acid methyl ester was prepared, as described previously, from methyl-10-undecenoate (9.00 mmol, 0.595 g) *p*-tolualdehyde tosylhydrazone (3.00 mmol, 0.865 g). After 1.5 h at reflux, 0.82 g, 90% of product was isolated. $^1\text{H-NMR}$ (CDCl_3/TMS) δ 7.07 (s, 4H), 3.66 (s, 3H), 2.55 (t, 2H, $J=7.7$ Hz), 2.31 (s overlapping t, 3H and 2H, $J=7.5$ Hz), 1.70-1.50 (m, 4H), 1.26 (br s, 14 H); 174.28, 139.83, 134.88, 128.86, 128.23, 51.37, 35.49, 34.09, 31.60, 29.52, 29.40, 29.360, 29.21, 29.12, 24.93, 20.94. $^{13}\text{C-NMR}$ (CDCl_3) δ 174.28, 139.83, 134.88, 128.86, 128.23, 51.37, 35.49, 34.09, 31.60, 29.52, 29.40, 29.30, 29.21, 29.12, 24.93, 20.94. Anal. calcd for $\text{C}_{20}\text{H}_{32}\text{O}_2$: C, 78.90; H, 10.59. Found: C, 78.67; H, 10.68.

5.7.5 Cyclohexyl-*p*-tolylmethane¹²⁸

Tricyclohexylborane was prepared, as described previously, from cyclohexene (9.00 mmol, 0.739 g) and BH_3 at 50 °C for 3 h. Hexyl-*p*-tolylmethane was prepared, as described previously, from tricyclohexylborane *p*-tolualdehyde

tosylhydrazone (3.00 mmol, 0.865 g). After 1 h at reflux 0.40 g, 71 % of product was isolated. $^1\text{H-NMR}$ (CDCl_3/TMS) δ 7.06 (d, 2H, $J=8.0$ Hz), 7.00 (d, 2H, $J=8.1$ Hz), 2.42 (d, 2H, $J=7.0$ Hz), 2.30 (s, 3H), 1.75-1.58 (m, 5H), 1.54-1.37 (m, 1H), 1.26-1.07 (m, 3H), 0.92 (qt, 2H, $J=10.5$ Hz): $^{13}\text{C-NMR}$ (CDCl_3) δ 138.23, 134.89, 129.04, 128.70, 43.67, 39.82, 33.15, 26.58, 26.33, 20.97. Anal. calcd for $\text{C}_{20}\text{H}_{32}\text{O}_2$: C, 78.90; H, 10.59. Found: C, 78.67; H, 10.68.

5.7.6 2-Methyl-1-*p*-tolylbutane¹³²

2-Methyl-1-*p*-tolylbutane was prepared, as described previously, from tri-*sec*-butylborane (3.0 mmol, 3.0 mL of a 1.0 M solution in THF, Aldrich Chemical Co.) *p*-tolualdehyde tosylhydrazone (3.00 mmol, 0.865 g). After 1.5 h at reflux, 0.30 g, 62% of product was isolated. $^1\text{H-NMR}$ (CDCl_3/TMS) δ 7.11-6.98 (m, 4H), 2.58 (dd, 1H, $J=13.4$ Hz and 6.2 Hz), 2.31 (s overlapping dd, 3H and 1H, $J=13.05$ Hz and 8.0 Hz), 1.60 (octet, 1H, $J=6.6$ Hz), 1.48-1.31 (m, 1H), 1.30-1.08 (m, 1H), 0.89 (t, 3H, $J=7.3$ Hz), 0.83 (d, 3H, $J=6.7$ Hz). $^{13}\text{C-NMR}$ (CDCl_3) δ 138.59, 134.92, 129.07, 128.76, 42.91, 36.70, 29.18, 20.99, 18.95, 11.47.

5.7.7 *p*-Benzyltoluene

p-Benzyltoluene was prepared, as described previously, from triphenylboron (3.00 mmol, 0.726 g, Aldrich Chemical Co.) *p*-tolualdehyde tosylhydrazone (3.00 mmol, 0.865 g). After 1 h at reflux, 0.55 g, 81% of product was isolated. $^1\text{H-NMR}$ (CDCl_3/TMS) δ 7.29-7.00 (m, 9H); 3.90 (s, 2H); 2.28 (s, 3H). $^{13}\text{C-NMR}$ (CDCl_3) δ

141.38, 141.23, 135.45, 129.10, 128.83, 128.39, 127.12, 125.93, 41.50, 20.94.

Anal. calcd for $C_{14}H_{14}$: C, 92.26; H, 7.74. Found: C, 92.06; H, 7.68.

5.8 SYNTHESSES UTILIZING BORANE DERIVATIVES

The general procedure for the synthesis of pentylbenzenes outlined in section 5.6.1 was followed for the reactions presented in this section. One of the following alkylborane derivatives was utilized in the place of Bu_3B , and all reactions were carried out at reflux. This section will present the experimental results for only those reactions which gave alkylated product.

5.8.1 *Reaction of Hexyl-9-BBN with 3e*

Hexyl-9-BBN (3.0 mmol) was prepared according to literature procedure from 1-hexene (3.0 mmol, 0.25 g) and 9-BBN (3.0 mmol, 3.0 mL of a 1 M solution in THF). It was used according to the above procedure in a 1 h reaction with benzaldehyde tosylhydrazone, **3e**, (3.00 mmol, 0.823 g). The reaction mixture was cooled under argon and placed in a room temperature water bath. Distilled water (10 mL) and sodium perborate (1.38 g, 8.97 mmol) were added. The reaction was stirred vigorously for 2 h. The reaction mixture was then transferred to a separatory funnel and the product extracted into ether (3 x 10 mL). The extracts were washed with brine (1 x 20 mL) and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure and the crude product flash chromatographed using silica

gel and 4% MeOH/CH₂Cl₂ to give 0.36 g, 51% yield, 5-(hydroxyphenylmethyl)cyclooctanol.¹³³ ¹H-NMR (CDCl₃/TMS) δ 7.40-7.23 (m, 5H), 4.41 (d, 1H, *J*= 6.8 Hz), 4.01-3.85 (m, 1H), 2.00-1.14 (m, 14H); ¹³C-NMR (CDCl₃) δ 143.69, 128.30, 127.46, 126.61, 79.48, 72.09, 44.28, 36.12, 30.51, 28.57, 23.23, 22.84.

5.8.2 Reaction of Decyldicyclohexylborane with 25e

Decyldicyclohexylborane was prepared according to literature procedure from BH₃ (3.0 mmol, 1.0 mL of a 1M solution in THF), cyclohexene (6.0 mmol, 0.49 g), and 1-decene (3.0 mmol, 0.42 g). It was used according to the above procedure in a 1 h reaction with benzaldehyde trisylhydrazone, **25e**, (3.00 mmol, 1.16 g). The crude product was flash chromatographed using 7 inches of silica gel in a 40 mm column with hexanes to give a yield of 0.53 g of the combined products 1-phenylundecane and cyclohexylphenylmethane. The ¹H NMR of the mixture gave a molar ratio of 33.3:66.7 for the benzyl protons at 2.59 ppm (t, area=2.00) and 2.47 ppm (d, area=3.99) respectively. These ratios were used to calculate a yield of 0.21 g, 31%, for 1-phenylundecane and 0.32 g, 61%, for cyclohexylphenylmethane.

5.8.3 Reaction of Hexyldisiamylborane with 25e

Hexyldisiamylborane was prepared according to literature procedure from BH₃ (3.0 mmol, 1.0 mL of a 1M solution in THF), 2-methyl-2-butene (6.0 mmol, 1.5 ml of a 4 M solution in THF), and 1-hexene (3.0 mmol, 0.25 g). It was used

according to the above procedure in a 1 h reaction with benzaldehyde trisylhydrazone, **25e**, (3.00 mmol, 1.16 g). The crude product was flash chromatographed using 7 inches of silica gel in a 40 mm column with hexanes to give a yield of 0.26 g, 49%, of the combined products 1-phenylheptane and 2,3-dimethylbutylbenzene. The ^1H NMR of the mixture gave a molar ratio of 15.5:84.5 for the benzyl protons at 2.73 ppm (d, area=0.368) and 2.59 ppm (t, area=2.00) respectively. These ratios were used to calculate a yield of 0.22 g, 41%, for 1-phenylheptane and 0.037 g, 7.6%, for 2,3-dimethylbutylbenzene.

5.8.4 Reaction of Hexyl-9-BBN with 25e

Hexyl-9-BBN was prepared according to literature procedure from 1-hexene (3.0 mmol, 0.25 g) and 9-BBN (3.0 mmol, 3.0 mL of a 1 M solution in THF). It was used according to the above procedure in a 1 h reaction with benzaldehyde trisylhydrazone, **25e**, (3.00 mmol, 1.16 g). The reaction mixture was cooled under argon and placed in a room temperature water bath. Distilled water (10 mL) and sodium perborate (1.38 g, 8.97 mmol) were added. The reaction was stirred vigorously for 2 h. The reaction mixture was then transferred to a separatory funnel and the product extracted into ether (3 x 10 mL). The extracts were washed with brine (1 x 20 mL) and dried over anhydrous MgSO_4 . The solvent was removed under reduced pressure and the crude product flash chromatographed using 5 inches of silica gel in a 20 mm column with hexanes to give 0.13 g, 25% yield, of heptylbenzene. ^1H -NMR (CDCl_3/TMS) δ 7.27-7.13 (m, 5H), 2.60 (t, 2H, $J=7.7$),

1.60-1.70 (m, 2H), 1.31-1.23 (m, 8H), 0.88 (t, 3H, $J=6.5$); ^{13}C -NMR (CDCl_3) δ 142.93, 128.38, 128.20, 125.52, 36.00, 31.54, 29.32, 29.21, 23.80, 22.68, 14.10. The column was continued with 2% MeOH/ CH_2Cl_2 to give 0.34 g, 48% yield, of 5-(hydroxyphenyl-methyl)cyclooctanol. ^1H -NMR (CDCl_3/TMS) δ 7.40-7.23 (m, 5H), 4.37 (d, 1H, $J=6.8$ Hz), 3.96-3.82 (m, 1H), 2.00 (s, 2H), 2.00-1.05 (m, 12H); ^{13}C -NMR (CDCl_3) δ 143.65, 128.17, 127.31, 126.56, 79.31, 71.98, 44.18, 35.97, 30.37, 28.50, 23.18, 22.78.

5.8.5 Reaction of Dihexylthexylborane with 25e

Dihexylthexylborane was prepared according to literature procedure from BH_3 (3.0 mmol, 1.0 mL of a 1M solution in THF), 2,3-dimethyl-2-butene (3.0 mmol, 3.0 mL of a 1 M solution in THF), and 1-hexene (6.0 mmol, 0.50 g). It was used according to the above procedure in a 1 h reaction with benzaldehyde trisylhydrazone, **25e**, (3.00 mmol, 1.16 g). The crude product was flash chromatographed using 7 inches of silica gel in a 40 mm column with hexanes to give a yield of 0.45 g of the combined products 1-phenylheptane and 2,2,3-trimethyl-4-phenylbutane. The ^1H NMR of the mixture gave a molar ratio of 71.0:29.0 for the benzyl protons at 2.59 ppm (t, area=2.00), and 2.52 ppm (s, area=0.817) respectively. These ratios were used to calculate a yield of 0.32 g, 61%, for 1-phenylheptane and 0.13 g, 25%, for 2,2,3-trimethyl-4-phenylbutane.

5.9 MECHANISM STUDIES

5.9.1 *trans*-5-*p*-Tolyl-4,5-dihydro-1H-pyrazole-3,4-dicarboxylic Acid Dimethyl Ester¹³⁴

Dimethyl maleate (0.435 g, 3.02 mmol) and *p*-tolualdehyde tosylhydrazone (0.866 g, 3.00 mmol) were added to a flame dried, argon flushed, 50 mL, round-bottom flask equipped with a side-arm, reflux condenser, stir bar, argon inlet, and mercury bubbler. Dry THF (20 mL) was then added followed by DBU (0.45 mL, 3.0 mmol) and the reaction heated to reflux for 1.5 h. The reaction was then cooled to room temperature and distilled water (10 mL) added. The reaction mixture was transferred to a separatory funnel, extracted with ether (3 x 10 mL), washed with brine (1 x 20 mL), and dried over anhydrous MgSO₄. Solvent was removed under reduced pressure and the crude product was flash chromatographed using 7 inches of silica gel in a 40 mm column with 25% EtOAc/Hexanes to give 0.63 g (76% yield) of **46**: ¹H-NMR (CDCl₃/TMS) δ 7.17 (s, 4H), 5.22 (d, 1H, *J*=9.3 Hz), 4.02 (d, 1H, *J*=9.3 Hz), 3.85 (s, 3H), 3.78 (s, 3H), 2.35 (s, 3H), 1.29-1.21 (br s, 1H); ¹³C-NMR (CDCl₃) δ 170.86, 162.24, 138.63, 137.85, 136.24, 129.79, 126.10, 70.43, 57.93, 52.80, 52.25, 21.08.

5.9.2 Competition Experiments

In the first competition experiment, *p*-tolualdehyde tosylhydrazone (3.00 mmol, 0.866 g) was dissolved in 17 mL of THF contained in an argon-flushed, 50

mL, round-bottomed flask equipped with a side-arm, reflux condenser, and stirring bar. Dimethyl maleate (0.433 g, 3.00 mmol) and tributylborane (3.0 mmol, 3.0 mL of a 1.0 M solution in THF) were added via syringe, followed by DBU (3.0 mmol, 0.45 mL). The reaction was heated to a gentle reflux until the tosylhydrazone disappeared as evidenced by TLC, (1.5 h). The reaction mixture was then oxidized with sodium perborate. The reaction vessel was placed in a room temperature water bath. Distilled water (10 mL) and sodium perborate (1.38 g, 8.97 mmol) were then added. The reaction was stirred vigorously for 2 h. The reaction mixture was transferred to a separatory funnel and the product extracted into ether (3 x 10 mL). The extracts were washed with brine (1 x 20 mL) and dried over anhydrous MgSO_4 . The solvent was removed under reduced pressure and the crude product was flash chromatographed using 6.5 inches of silica gel in a 50 mm column with 9% ethyl acetate/hexanes to give 0.43 g (80% yield) of 1-*p*-tolylpentan-1-ol:¹³⁵ ^1H -NMR (CDCl_3/TMS) δ 7.21 (d, 2H, $J=8.1$ Hz), 7.13 (d, 2H, $J=8.1$ Hz), 4.59 (t, 1H, $J=6.7$ Hz), 2.33 (s, 3H), 2.03-1.86 (br s, 1H), 1.84-1.59 (m, 2H), 1.44-1.23 (m, 4H), 0.87 (t, 3H, $J=6.9$ Hz); ^{13}C -NMR (CDCl_3) δ 141.98, 137.02, 129.03, 125.82, 74.46, 38.68, 27.98, 22.57, 21.02, 13.93. Anal. calcd for $\text{C}_{12}\text{H}_{18}\text{O}$: C, 80.85; H, 10.18. Found: C, 80.57; H, 10.29.

The second competition experiment was carried out in the same manner as the first except that the reaction mixture was heated to reflux prior to the addition of DBU. After purification a yield of 0.412 g, 77%, was obtained for 1-*p*-tolylpentan-1-ol.

5.9.3 Synthesis of Diazo Intermediate 8'

Benzaldehyde trisylhydrazone (3.00 mmol, 1.16 g), KOH (3.00 mmol, 0.336 g), and MeOH (9 mL) were placed in an argon-flushed, 50 mL, round-bottomed flask equipped with a side-arm, reflux condenser, and stirring bar. The reaction was heated at reflux for 7 min. It was then cooled with an ice bath and 30 mL of ice-cold water was added to the reaction mixture. The aqueous layer was extracted with methylene chloride (4 × 10 mL) and washed with sodium bicarbonate (3 × 15 mL of a saturated solution in water). The methylene chloride extracts were dried over anhydrous MgSO₄, filtered, and most of the solvent removed in vacuo. If all the solvent is removed 8' becomes very unstable and can explode.

5.9.4 Reaction of 8' with Tributylborane

Experiment 1

Tributylborane (3.0 mmol, 3.0 mL of a 1.0 M solution in THF) was placed in an argon-flushed, 50 mL, round-bottomed flask equipped with a stirring bar and bubbler. 8' prepared in 5.9.2 was diluted with 10 mL THF and was slowly added via syringe over the course of 15 min. Immediate gas evolution was seen and 8' turned from orange to yellow as soon as it came in contact with the reaction mixture. The reaction mixture was oxidized with sodium perborate and worked up as described previously. The crude product was purified via flash chromatography using 6.5 inches of silica gel in a 50 mm column with 8% ethyl acetate/hexanes to give a yield of 0.18 g, 37% of 1-phenylpentan-1-ol.¹³⁶ ¹H-NMR (CDCl₃/TMS) δ 7.37-

7.18 (m, 5H), 4.60 (t, 1H, $J=6.7$ Hz), 2.22-2.05 (br s, 1H), 1.86-1.57 (m, 2H), 1.45-1.14 (m, 4H), 0.87 (t, 3H, $J=7.0$ Hz); ^{13}C -NMR (CDCl_3) δ 144.96, 128.34, 127.37, 125.88, 74.60, 38.76, 27.93, 22.56, 13.95.

Experiment 2

Tributylborane (3.0 mmol, 3.0 mL of a 1.0 M solution in THF) and DBU (3.0 mmol, 0.45 mL) were placed in an argon-flushed, 50 mL, round-bottomed flask equipped with a stirring bar and bubbler. **8'** prepared in 5.9.2 was diluted with 10 mL THF and was slowly added via syringe over the course of 15 min. Immediate gas evolution was seen and **8'** turned from orange to yellow as soon as it came in contact with the reaction mixture. The reaction mixture was oxidized with sodium perborate and worked up as described previously. The crude product was purified via flash chromatography using 6.5 inches of silica gel in a 50 mm column with 8% ethyl acetate/hexanes to give a yield of 0.27 g, 55%, of 1-phenylpentan-1-ol. Spectral data was consistent with sample prepared in experiment 1.

Experiment 3

8' was prepared as described in 5.9.2 using 6 mmol, 2.32 g benzaldehyde trisilylhydrazone. The above reaction was repeated and 0.46 g, 93%, of 1-phenylpentan-1-ol was isolated.

5.9.5 Synthesis of 1-Phenylpentan-1-ol with MeOH as the Solvent

Benzaldehyde trisilylhydrazone (3.00 mmol, 1.16 g) was dissolved in 17 mL MeOH contained in an argon-flushed, 50 mL, round-bottom flask equipped with a

side-arm, reflux condenser, stir bar, argon inlet, and mercury bubbler. Tributylborane (3.0 mmol, 3.0 mL of a 1.0 M solution in THF) and DBU (0.45 mL, 3.0 mmol) were added and the reaction was stirred at room temperature until the trisylhydrazone disappeared as evidenced by TLC (29 h). The reaction mixture was cooled under argon and oxidized as previously described. The crude product flash chromatographed using 8 inches of silica gel in a 50 mm column with 7% EtOAc/hexanes. This produced 0.11 g, 22%, of 1-phenylpentan-1-ol and 0.276 g (62%) of pentylbenzene. Spectral data was consistent with previous samples.

5.9.6 Synthesis of 1-Chloro-4-pentylbenzene with MeOH as the Solvent

p-Chlorobenzaldehyde trisylhydrazone (3.00 mmol, 1.26 g) was used as described in section 5.6.1 with 17 mL of MeOH as the solvent. The reaction was complete in 3.5 h at RT. The crude product was purified with flash chromatography using 5 inches of silica gel in a 40 mm column and 4% ethyl acetate/hexanes to give a yield of 0.55 g, 87%, of 1-Chloro-4-pentylbenzene. Spectral data was consistent with sample prepared previously.

5.9.7 ^{11}B NMR Experiments

All spectra were obtained unlocked and without a standard present in the tube. NMR tubes were quartz and were flame-dried and argon-flushed prior to use. Results of the spectra are presented in tables in Chapter 4.

Experiment # 1

Tributylborane (0.5 mmol, 0.5 mL of 1.0 M solution of in THF) was added to a flame dried, argon-flushed, quartz NMR tube. DBU (0.50mmol, 0.075 mL) was then added to the tube via syringe. Spectra were obtained at 0 and 60 min.

Experiment # 2

Benzaldehyde tosylhydrazone (0.15 mmol, 0.35 mL of a 0.43 M solution in THF) was added to an NMR tube followed by Bu_3B (0.15 mmol, 0.15 mL). The tube was placed in the NMR spectrometer and the temperature was taken down to -78°C . A spectrum was taken and the temperature was then increased to 25°C . The temperature of the NMR was then slowly lowered to -78°C and spectra were taken.

Experiment # 3

To the above NMR tube was added DBU (0.15 mmol, 0.022 mL) at -78°C . The NMR was then slowly brought back up to RT and the NMR spectrum was monitored.

Experiment # 4

Benzaldehyde tosylhydrazone (0.15 mmol, 0.35 mL of a 0.43 M solution in THF) was added to an NMR tube followed by Bu_3B (0.15 mmol, 0.15 mL) and DBU (0.15 mmol, 0.022 mL). An initial spectrum was obtained. A balloon equipped with a syringe needle and containing argon was placed into the septum of the NMR tube. The tube was then placed in a hot water bath and heated to reflux. The heating was stopped at frequent intervals, the balloon was removed, and a spectrum of the reaction was obtained.

Experiment # 5

Benzaldehyde trisylhydrazone (0.15 mmol, 0.058 g) was placed in an NMR tube followed by 0.5 mL of THF and Bu₃B (0.15 mmol, 0.15 mL of a 1.0 M solution in THF). The mixture was monitored by NMR for 60 min. DBU (0.15 mmol, 0.022 mL) was added via syringe and the reaction was monitored by NMR for 2 h.

Experiment # 6

Benzaldehyde trisylhydrazone (0.15 mmol, 0.52 mL of a 0.29 M solution in THF) was placed in an NMR tube followed by Bu₃B (0.15 mmol, 0.15 mL of a 1.0 M solution in THF). The tube was placed in a dry-ice acetone bath and DBU (0.15 mmol, 0.022 mL) was added. The tube was placed in the NMR which was set at -78 °C. The reaction mixture was monitored at various temperatures.

Experiment # 7

Diazo compound **8'** was prepared as previously described and stored at -100 °C. Bu₃B (0.25 mmol, 0.25 mL) and DBU (0.25 mmol, 0.037 mL) were placed in an NMR tube and cooled to -100 °C. **8'** was added and the tube was quickly transferred to the NMR set at -78 °C. After the spectrum was obtained the NMR tube was removed and given one quick shake. The spectrum was repeated at -78 an additional two times. The temperature was then slowly increased to RT and a final spectrum was obtained.

LIST OF REFERENCES

LIST OF REFERENCES

1. Kwa, T. L.; Boelhouwer, C. *Tetrahedron*, **1970**, 25, 5771.
2. For a review of the coupling of halides with organotin, mercury, and copper cpds, see a) Beletskaya, I. P. *J. Organomet. Chem.* **1983**, 250, 551.
b) Larock, R. C. *Organomercury Compounds in Organic Synthesis*; Springer: New York, 1985, pp. 249-262.
3. For a review, see Posner, G. H. *Org. React.* **1975**, 22, 253.
4. a) Posner, G. H.; Whitten, C. E.; Sterling, J. J. *J. Am. Chem. Soc.* **1973**, 95, 7788. B) Posner, G. H.; Whitten, C. E. *Tetrahedron Lett.* **1973**, 1815.
5. Lipshutz, B. H.; Wilhelm, R. S.; Floyd, D. *J. Am. Chem. Soc.* **1981**, 103, 7672.
6. Kharasch, M. S.; Reinmuth, O. *Grignard Reactions of Non-Metallic Substances*; Prentice-Hall: New York, 1954.
7. Ohno, M.; Shimizu, K.; Ishizaki, K.; Sasaki, T.; Eguchi, S. *J. Org. Chem.* **1988**, 53, 729.
8. Tamura, M.; Kochi, J. *Synthesis* **1971**, 303.
9. Corriu, J. P.; Masse, J. P. *J. Chem. Soc., Chem. Commun.* **1972**, 144
10. Miller, D. P. *J. Org. Chem.* **1966**, 31, 908.
11. Stille, J. K. *Angew. Chem., Int. Ed. Engl.* **1986**, 25, 508.
12. Johnson, C. R.; Dutra, G. A. *J. Am. Chem. Soc.* **1973**, 95, 7777, 7783.
13. Sharpless, K. B.; Hanzlik, R. P.; van Tamelen, E. E. *J. Am. Chem. Soc.* **1968**, 90, 209.
14. McMurry, J. E.; Silvestry, M. G.; Fleming, M. P.; Hoz, T.; Grayston, M. W. *J. Org. Chem.* **1978**, 43, 3249.
15. Sato, M.; Oshima, K. *Chem. Lett.* **1982**, 157.
16. Armstrong, D. R.; Mulvey, R. E.; Barr, D.; Snaith, R.; Reed, D. *J. Organomet. Chem.* **1988**, 350, 191.

17. Whitesides, G. M.; Sanfilippo, J.; Casey, C. P.; Panek, E. J. *J. Am. Chem. Soc.* **1967**, *89*, 5302.
18. Sato, F.; Mori, Y.; Sato, M. *Chem. Lett.* **1978**, 1337.
19. Ghosal, S.; Luke, G. P.; Kyler, K. S. *J. Org. Chem.* **1987**, *52*, 4296.
20. Morizur, J. *Bull. Soc. Chim. Fr.* **1964**, 1331.
21. Eicher, T. In *The Chemistry of the Carbonyl Group*, Vol. 1 Patai, S., Ed.; Interscience: New York, 1966; pp 638.
22. Brown, H. C.; Kramer, G. W.; Levy, A. B.; Midland, M. M. *Organic Syntheses via Boranes*; Wiley-Interscience: New York, 1975. p. 11.
23. Pelter, A.; Smith, K.; Brown, H. C. *Borane Reagents*; Academic: New York, 1988. p. 7.
24. *ibid*, p. 165.
25. Brown, H. C.; Zweifel, G. *J. Am. Chem. Soc.* **1960**, *82*, 4708.
26. Miyaura, N.; Itoh, M.; Suzuki, A.; Brown, H. C.; Midland, M. M.; Jacob, III, P. *J. Am. Chem. Soc.* **1972**, *94*, 6549.
27. (a) Kabalka, G. W.; Newton, R. J., Jr.; Jacobus, J. *J. Org. Chem.* **1978**, *43*, 1567. (b) Kabalka, G. W.; Bowman, N. S. *J. Org. Chem.* **1973**, *38*, 1607.
28. Brown, H. C.; Kramer, G. W.; Levy, A. B.; Midland, M. M. *Organic Syntheses via Boranes*; Wiley-Interscience: New York, 1975.
29. Zweifel, G.; Brown, H. C. *J. Am. Chem. Soc.* **1963**, *85*, 2066.
30. a) Brown, H. C.; Ayyangar, N. R.; Zweifel, G. J. *J. Am. Chem. Soc.* **1964**, *86*, 397. b) Brown, H. C.; Desai, M. C.; Jadhav, P. K. *J. Org. Chem.* **1982**, *47*, 5065.
31. Masamune, S.; Kim, B. M.; Petersen, J. S.; Sato, T.; Veenstra, S. J.; Imai, T. *J. Am. Chem. Soc.* **1985**, *107*, 4549.
32. Brown, H. C.; Zweifel, G. *J. Am. Chem. Soc.* **1961**, *83*, 3834.
33. Zweifel, G.; Clark, G. M.; Polston, N. L. *J. Am. Chem. Soc.*, **1971**, *93*, 3395.
34. Pelter, A.; Singaram, S.; Brown, McMurry, Silvestry H. C. *Tetrahedron Lett.* **1983**, *24*, 1433.

35. Brown, H. C.; Campbell Jr., J. B. *J. Org. Chem.* **1980**, *45*, 389.
36. a) Brown, H. C.; Gupta, S. K. *J. Am. Chem. Soc.* **1975**, *97*, 5249. (b) Brown, H. C.; Scouten, C. G.; Liotta, R. *J. Am. Chem. Soc.* **1979**, *101*, 96. c) Hooz, J. *J. Am. Chem. Soc.* **1974**, *96*, 274. d) Brown, C. A.; Coleman, R. A. *J. Org. Chem.* **1979**, *44*, 2328.
37. Negishi, E.; Williams, R. M.; Lew, G.; Yoshida, T. *J. Organomet. Chem.* **1975**, *92*, C4.
38. Campbell Jr., J. B.; Molander, G. A. *J. Organomet. Chem.* **1978**, *156*, 71.
39. Zweifel, G.; Arzoumanian, H.; Whitney, C. C. *J. Am. Chem. Soc.* **1967**, *89*, 3652.
40. Zweifel, G.; Fisher, R. P.; Snow, J. T.; Whitney, C. C. *J. Am. Chem. Soc.* **1972**, *94*, 6560.
41. Lahima Jr., N. J.; Levy, A. B. *J. Org. Chem.* **1978**, *43*, 1279.
42. a) Yatagai, H. *Bull. Chem. Soc. Jpn* **1980**, *53*, 1670. b) Yatagai, H. *J. Chem. Soc., Chem. Commun.* **1977**, 852.
43. Miyaura, N.; Yamada, K.; Suzuki, A. *Tetrahedron Lett.* **1979**, *36*, 3473.
44. Miyaura, N.; Yamada, K.; Suginome, H.; Suzuki, A. *J. Am. Chem. Soc.* **1985**, *107*, 972.
45. Miyaura, N.; Ishiyama, T.; Ishikawa, M.; Suzuki, A. *Tetrahedron Lett.* **1986**, *27*, 6369.
46. Brown, H. C.; Molander, G. A. *J. Org. Chem.* **1981**, *46*, 647.
47. Brown, H. C.; Zweifel, G. *J. Am. Chem. Soc.* **1959**, *81*, 1512.
48. Negishi, E.; Katz, J. J.; Brown, H. C. *Synthesis*, **1972**, 555.
49. Pelter, A.; Bentley, T. W.; Harrison, C. R.; Subrahmanyam, C.; Laub, R. J. *J. Chem. Soc., Perkin Trans. I*, **1976**, 2435.
50. Negishi, E.; Chiu, K. W. *J. Org. Chem.* **1976**, *41*, 3484.
51. Corey, E. J.; Ravindranathan, at. *J. Am. Chem. Soc.* **1972**, *94*, 4013.
52. Yatagai, H.; Yamamoto, Y.; Maruyama, K. *J. Chem. Soc., Chem. Commun.* **1978**, 702.

53. A) Brown, H. C.; Hebert, N. C.; Snyder, C. H. *J. Am. Chem. Soc.* **1961**, 83, 1001. b) Breuer, S. W.; Broster, F. A. *Tetrahedron Lett.* **1972**, 22, 2193.
54. Breuer, S. W.; Broster, F. A. *Tetrahedron Lett.* **1972**, 22, 2193.
55. Ishiyama, T.; Abe, S.; Miyaura, N.; Suzuki, A. *Chem. Lett.* **1992**, 691.
56. Miyaura, N.; Ishiyama, T.; Sasaki, H.; Ishikawa, M.; Satoh, M.; Suzuki, A. *J. Am. Chem. Soc.* **1989**, 111, 314.
57. Oh-e, T.; Mitaura, N.; Suzuki, A. *J. Org. Chem.* **1993**, 58, 2201.
58. Sato, M.; Miyaura, N.; Suzuki, A. *Chem. Lett.* **1989**, 1405.
59. Brown, H. C.; Lane, C. F. *J. Am. Chem. Soc.* **1971**, 93, 1025.
60. a) Brown, H. C.; Lane, C. F. *Synthesis* **1972**, 303. b) Brown, H. C.; Yamamoto Y.; Lane, C. F. *Synthesis* **1972**, 304.
61. a) Brown, H. C.; Rogic, M. M.; Rathke, M. W.; Kabalka, G. W. *J. Am. Chem. Soc.* **1968**, 90, 818. b) Brown, H. C.; Rogic, M. M.; Rathke, M. W. *J. Am. Chem. Soc.* **1968**, 90, 6218.
62. Negishi, E. *Organometallics in Organic Synthesis*; Wiley-Interscience: New York, 1980; Vol 1, p 304.
63. Yamamoto, Y.; Asao, N. *Chem. Rev.* **1993**, 93, 2207.
64. a) Brown, H. C.; Bhat, K. S. *J. Am. Chem. Soc.* **1986**, 108, 293. b) Barrett, A. G. M.; Lebold, S. A. *J. Org. Chem.* **1991**, 56, 4875. c) Brown, H. C.; Bhat, K. S.; Randad, R. S. *J. Org. Chem.* **1989**, 54, 1570.
65. Jacob, III, P.; Brown, H. C. *J. Org. Chem.* **1977**, 42, 579.
66. Brown, H.C.; Knights, E. F.; Scouten, C. G. *J. Am. Chem. Soc.* **1974**, 96, 7765.
67. a) Mikhailov, B. M.; Kiselev, V. G.; Bubnov, Y. N. *Bull. Acad. Sci. USSR, Div. Chem. Sci.* **1965**, 865. b) Mikhailov, B. M.; Bubnov, Y. N.; Kiselev, V. G. *J. Gen. Chem. USSR* **1966**, 36, 65.
68. Midland, M. M.; Tramantano, A.; Zderic, S. A. *J. Organomet.Chem.* **1978**, 156, 203.
69. Kubo, T.; Nose, A. *Yakugaku Zashi* **1975**, 95, 141; *Chem. Abstr.* **1976**, 84, 90200.

70. a) Mikhailov, B. M. *Bull. Acad. Sci. USSR, Div. Chem. Sci.* **1984**, 202. b) Mikhailov, B. M. *Pure Appl. Chem.* **1983**, 55, 1439. c) Mikhailov, B. M. *Pure Appl. Chem.* **1980**, 52, 691.
71. Mikhailov, B. M.; Smirnov, V. N.; Kasparov, V. A. *Bull. Acad. Sci. USSR, Div. Chem. Sci.* **1976**, 25, 2148.
72. Mikhailov, B. M.; Shagova, E. A. *J. Organomet. Chem.* **1983**, 258, 131.
73. Mikhailov, B. M.; Baryshnikova, T. K.; Shashkov, A. S. *J. Organomet. Chem.* **1981**, 219, 301.
74. Miyaura, N.; Itoh, M.; Suzuki, A.; Brown, H. C.; Midland, M. M.; Jacob, III, P. *J. Am. Chem. Soc.* **1972**, 94, 6549.
75. Okada, K.; Hosoda, Y.; Oda, M. *Tetrahedron Lett.* **1986**, 27, 6213.
76. a) Kabalka, G. W. *Intra-Science Chem. Rept.* **1973**, 7, 57. b) Kabalka, G. W.; Brown, H. C.; Suzuki, A.; Honma, S.; Arase, A.; Itoh, M. *J. Am. Chem. Soc.* **1970**, 92, 710. See also (c) Brown, H. C.; Kabalka, G. W. *J. Am. Chem. Soc.* **1970**, 92, 712. d) Brown, H. C.; Kabalka, G. W. *J. Am. Chem. Soc.* **1970**, 92, 714.
77. a) Negishi, E.; Chiu, K.; Yosida, T. *J. Org. Chem.* **1975**, 40, 1676. b) Negishi, E.; Abramovitch, A.; Merrill, R. E. *Chem. Commun.* **1975**, 138.
78. (a) Brown, H. C.; Sharp, R. L. *J. Am. Chem. Soc.* **1966**, 88, 5851. (b) See also: Weinheimer, A. J.; Marsico, W. E. *J. Org. Chem.* **1962**, 27, 1926.
79. Kabalka, G. W.; Hutchins, R. O.; Natale, N. R.; Yang, D. T. C.; Broach, V. *Org. Syn.* **1979**, 59, 42.
80. Kabalka, G. W.; Hutchins, R.; Natale, N. R.; Domonic, T. C.; Yang; Broach, V. *Org. Syn.* **1988**, *Collect. Vol VI*, 293.
81. Brown, H. C.; Knights, E. F.; Scouten, C. G. *J. Am. Chem. Soc.* **1974**, 96, 7765.
82. Soderquist, J. A.; Brown, H. C. *J. Org. Chem.* **1981**, 46, 4599.
83. Brown, H. C.; Liotta, R.; Scouten, C. G. *J. Am. Chem. Soc.* **1976**, 98, 5297.
84. Brown, C. A.; Coleman, R. A. *J. Org. Chem.* **1979**, 44, 2328.
85. Brown, H. C.; Knights, E. F.; Coleman, R. A. *J. Am. Chem. Soc.* **1969**, 91, 2144.

86. (a) Hooz, J.; Gunn, D. M. *Tetrahedron Lett.* **1969**, 3455. (b) Brown, H. C.; Rogic, M. M. *J. Am. Chem. Soc.* **1969**, *91*, 2146.
87. Brown, H. C.; Ravindran, N.; Kulkarni, S. U. *J. Org. Chem.* **1980**, *45*, 384.
88. Bertz, S. H.; Dabbagh, G. *J. Org. Chem.* **1983**, *48*, 116.
89. Maddox, J. T. Ph.D. Dissertation, University of Tennessee, Knoxville, August 1995, p 108.
90. Dudman, C. C.; Reese, C. B. *Synthesis* **1982**, 419.
91. Cusack, N. J.; Reese, C. B.; Risius, A. C.; Roozpeikar, B. *Tetrahedron* **1976**, *32*, 2157.
92. Maddox, J. T. Ph.D. Dissertation, University of Tennessee, Knoxville, August 1995, p 112.
93. Brown, H.C.; Kramer, G. W.; Levy, A. B.; Midland, M. M. *Organic Syntheses via Boranes*; Wiley-Interscience: New York, 1975; p 40
94. *ibid*, p 23.
95. (a) Zweifel, G.; Ayyangar, N. R.; Brown, H. C. *J. Am. Chem. Soc.* **1963**, *85*, 2072. (b) Brown, H. C.; Kabalka, G. W.; Rathke, M. W. *J. Am. Chem. Soc.* **1967**, *89*, 4530.
96. Brown, H.C.; Kramer, G. W.; Levy, A. B.; Midland, M. M. *op. cit.* p 38.
97. Brown, H. C.; Moerikofer, A. W. *J. Am. Chem. Soc.* **1961**, *83*, 3417.
98. Brown, H. C.; Zweifel, G. *J. Am. Chem. Soc.* **1961**, *83*, 1241.
99. Zweifel, G.; Brown, H. C. *J. Am. Chem. Soc.* **1963**, *85*, 2066
100. Brown, H. C.; Pfaffenberger, C. D. *J. Am. Chem. Soc.* **1967**, *89*, 5475.
101. For a review see: Lane, C. F.; Kabalka, G. W. *Tetrahedron* **1976**, *32*, 981.
102. (a) Brown, H. C.; Gupta, S. K. *J. Am. Chem. Soc.* **1975**, *97*, 5249. (b) Brown, H. C.; Chandrasekharan, J. *J. Org. Chem.* **1983**, *48*, 5080.
103. For reviews, see Matteson, in Hartley *The Chemistry of the Metal-Carbon Bond*, vol 4.; Wiley: New York, 1984, pp. 307-409, pp. 346-387; Pelter; Smith; Brown *Borane Reagents*; Academic Press: New York, 1988, pp. 256-301.

104. (a) Hooz, J.; Morrison, G. F. *Can. J. Chem.* **1970**, *48*, 868. (b) Hooz, J.; Linke, S. *J. Am. Chem. Soc.* **1968**, *90*, 5936. (c) Hooz, J.; Linke, S. *J. Am. Chem. Soc.* **1968**, *90*, 6891.
105. (a) Creary, X. *Organic Syntheses*; Wiley: New York, 1990; Collect. Vol. VII, pp 438-443. (b) Woulfman, D. S.; Yousefian, S.; White, J. M. *Synth. Commun.* **1988**, *18*, 2349. (c) Jończyk, A.; Włostowska, J. *Synth. Commun.* **1978**, *8*, 569. (d) Kaufman, G. M.; Smith, J. A.; Vander Stouw, G. G.; Shechter, H. *J. Am. Chem. Soc.* **1965**, *87*, 935. (e) Farnum, D. G. *J. Org. Chem.* **1963**, *28*, 870.
106. Jończyk, A.; Włostowska, J. *Synth. Commun.* **1978**, *8*, 569.
107. Jones, W. M. *J. Am. Chem. Soc.* **1959**, *81*, 5153.
108. Nöth, H.; Wrackmyeyr, B. In *NMR Basic Principles and Progress: Nuclear Magnetic Resonance Spectroscopy of Boron Compounds*; Diehl, P.; Fluck, E.; Kosfeld, R. Ed.; Springer-Verlag: Berlin, 1978; pp 1-5.
109. *ibid*, p 6.
110. Perrin, D. D.; Armarego, W. L. F. *Purification of Laboratory Chemicals*, 3rd ed.; Pergamon, New York: 1988.
111. Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923
112. Kabalka, G. W.; Summers, S. T. *J. Org. Chem.* **1981**, *46*, 1217.
113. Closs, G. L.; Moss, R. A. *J. Am. Chem. Soc.* **1964**, *86*, 4042.
114. Crow, W. D.; McNab, H. *Aust. J. Chem.* **1979**, *32*, 99.
115. Farnum, D. G. *J. Org. Chem.* **1963**, *28*, 870.
116. Sayer, J. M.; Peskin, M.; Jencks, W. P. *J. Am. Chem. Soc.* **1973**, *95*, 4277.
117. Davies, H. W.; Schwarz, M. *J. Org. Chem.* **1965**, *30*, 1242.
118. McNair, H. M.; Boneli, E. J. *Basic Gas Chromatography*; Varian: Palo Alto, CA, 1968; p 139.
119. *Handbook of Chemistry and Physics*, 71st ed.; Lide, D.R., Ed. CRC: Boca Raton, FL, 1990; p 3-86.
120. Nutaitis, C. F.; Bernardo, J. E. *Synth. Commun.* **1990**, *20*, 487.

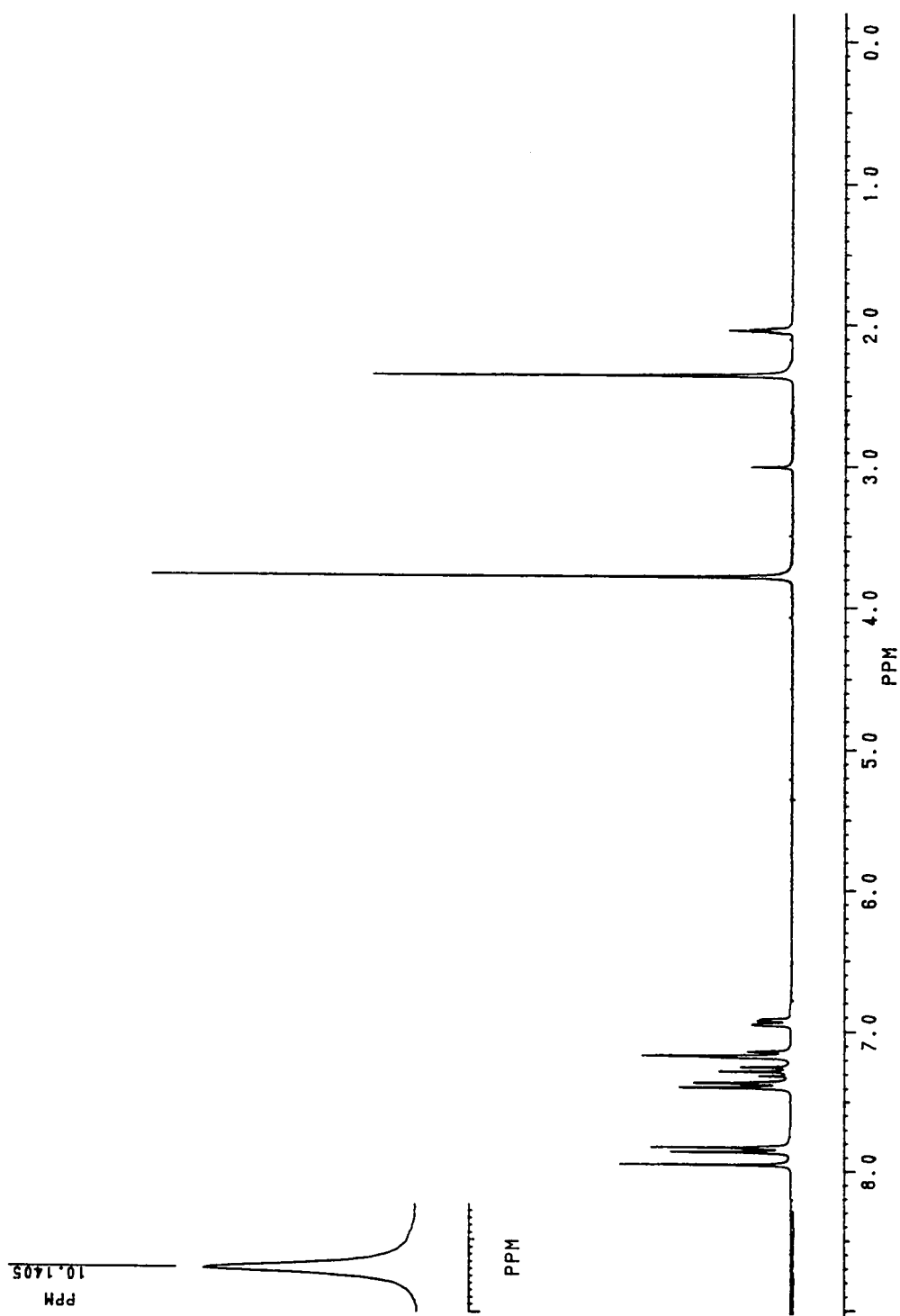
121. Manas, M. M.; Trius, A. *Bull. Chem. Soc. Jpn.* **1983**, 56, 2154
122. deBoer, H. J. R.; Akkerman, O. S.; Bickelhaupt, F. *Organometallics* **1990**, 9, 2898.
123. Marvel, C. S.; Kaplan, J. F.; Himel, C. M. *J. Am. Chem. Soc.* **1941**, 63, 1892.
124. Gray, G. W.; Hird, M.; Lacey, D.; Toyne, K. J. *J. Chem. Soc., Perkin Trans 2*, **1989**, 2041.
125. Manas, M. M.; Trius, A. *Bull. Chem. Soc. Jpn.* **1983**, 56, 2154.
126. Amoretti, L.; Mossini, F. *Farmaco Ed. Sci.* **1967**, 22, 796.
127. Mangold, B. L. K.; Hanna, P. E. *J. Med. Chem.* **1982**, 25, 630.
128. Tomioka, H.; Tabayashi, K.; Ozaki, Y.; Izawa, Y. *Tetrahedron* **1985**, 41, 1435.
129. Muchowski, J. M.; Solas, D. R. *Synth. Commun.* **1984**, 14, 453.
130. Gunn, B. P. *Heterocycles* **1985**, 23, 3061.
131. (a) Cahiez, G.; Figadere, B. *Tetrahedron Lett.* **1986**, 26, 4445. (b) Kauffmann, T.; Pahde, C.; Wingbermühle, D. *Tetrahedron Lett.* **1985**, 26, 4059. (c) Kauffmann, T.; Pahde, C.; Tannert, A.; Wingbermühle, D. *Tetrahedron Lett.* **1985**, 26, 4063. (d) Jung, M. E.; Lewis, P. K. *Synth. Commun.* **1983**, 13, 213.
132. Owen, J. R.; Saunders, W. H., Jr. *J. Am. Chem. Soc.* **1966**, 88, 5809.
133. For a similar compound see: Singleton, D. A.; Martinez, J. P.; Watson, J. V.; Ndip, G. M. *Tetrahedron* **1992**, 48, 5831.
134. For similar compounds see: (a) Hassner, A.; Michelson, M. J. *J. Org. Chem.* **1962**, 27, 3974. (b) Jones, W. M. *J. Am. Chem. Soc.* **1959**, 81, 3776, 5153.
135. (a) Chibale, K.; Greeves, N.; Lyford, L.; Pease, J. E. *Tetrahedron Asymm.* **1993**, 4, 2407. (b) Shi, L-L.; Zhou, Z-L.; Huang, Y-Z. *J. Chem. Soc., Perkin Trans. 1*, **1990**, 2847.
136. Janssen, A. J. M.; Klunder, A. J. H.; Zwanenburg, B. *Tetrahedron* **1991**, 47, 7645.

APPENDIX

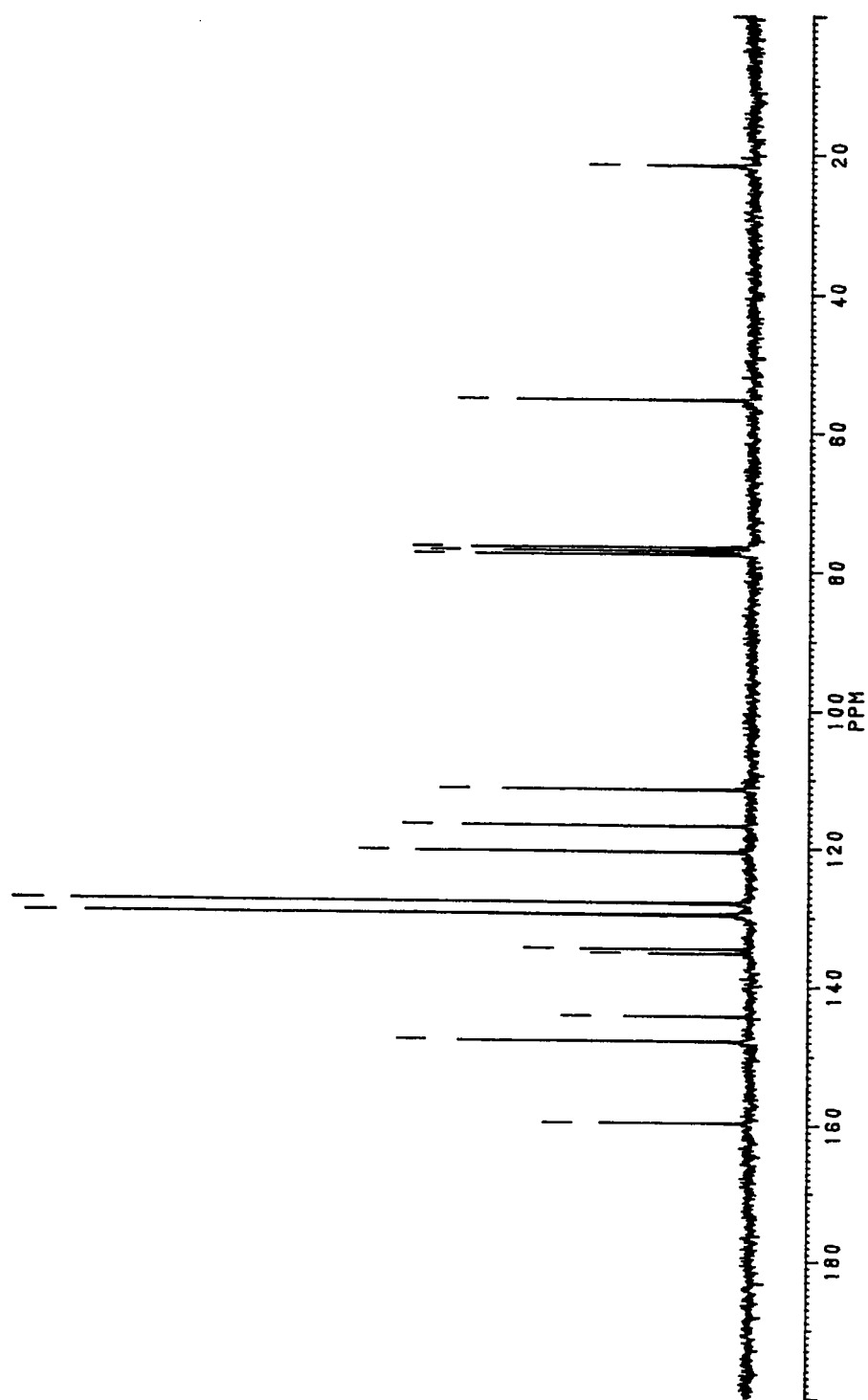
APPENDIX CONTENTS

NMR SPECTRA OF REPRESENTATIVE STARTING MATERIALS AND ALKYLATED BENZENE PRODUCTS

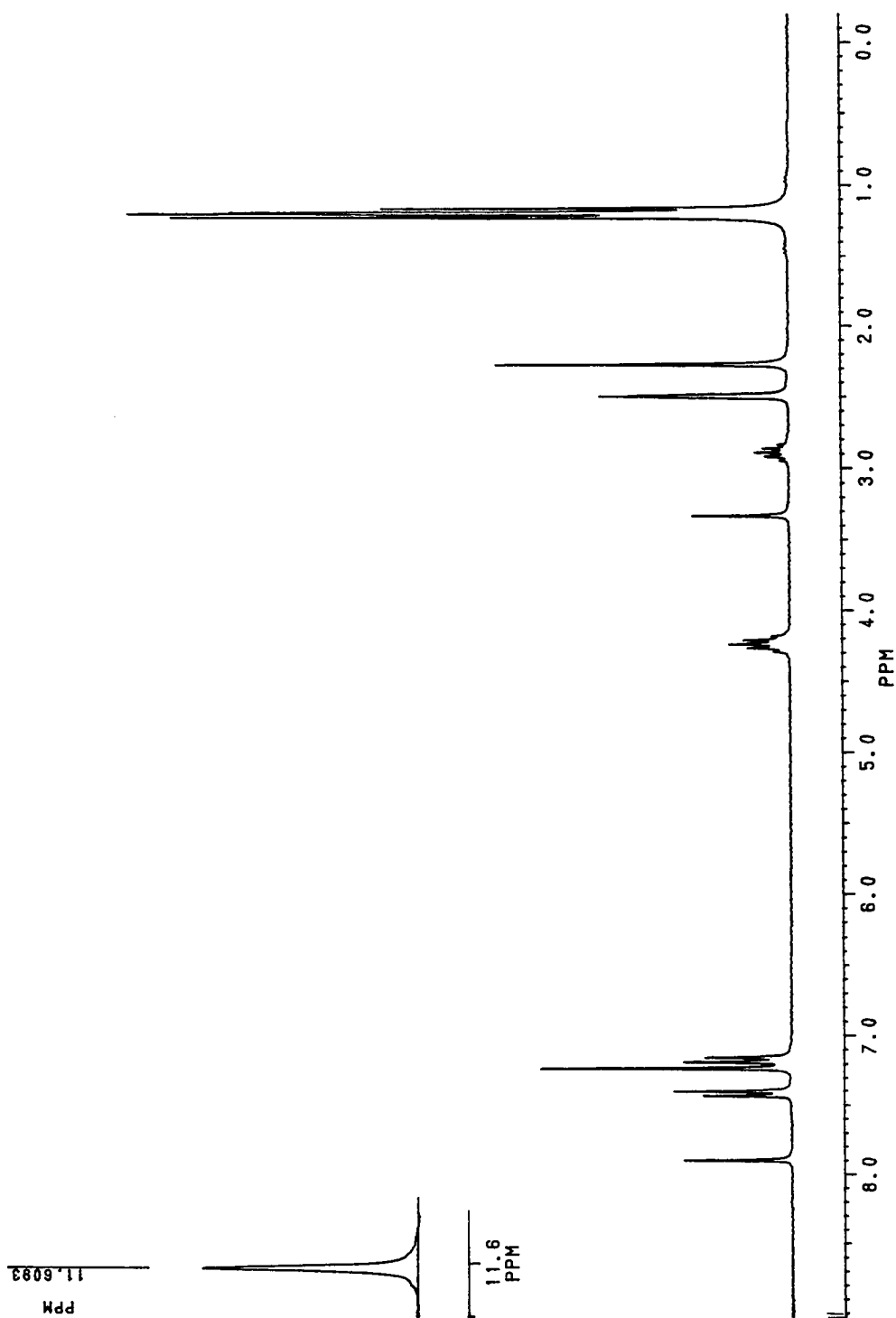
A1.	¹ H NMR of 3-methoxybenzaldehyde tosylhydrazone	179
A2.	¹³ C NMR of 3-methoxybenzaldehyde tosylhydrazone	180
A3.	¹ H NMR of 4-methylbenzaldehyde trisylhydrazone	181
A4.	¹³ C NMR of 4-methylbenzaldehyde trisylhydrazone	182
A5.	¹ H NMR of pentylbenzene	183
A6.	¹³ C NMR of pentylbenzene	184
A7.	¹ H NMR of 1-methoxy-4-pentylbenzene	185
A8.	¹³ C NMR of 1-methoxy-4-pentylbenzene	186
A9.	¹ H NMR of 1-methyl-4-pentylbenzene	187
A10.	¹³ C NMR of 1-methyl-4-pentylbenzene	188
A11.	¹ H NMR of 1-nitro-4-pentylbenzene	189
A12.	¹³ C NMR of 1-nitro-4-pentylbenzene	190



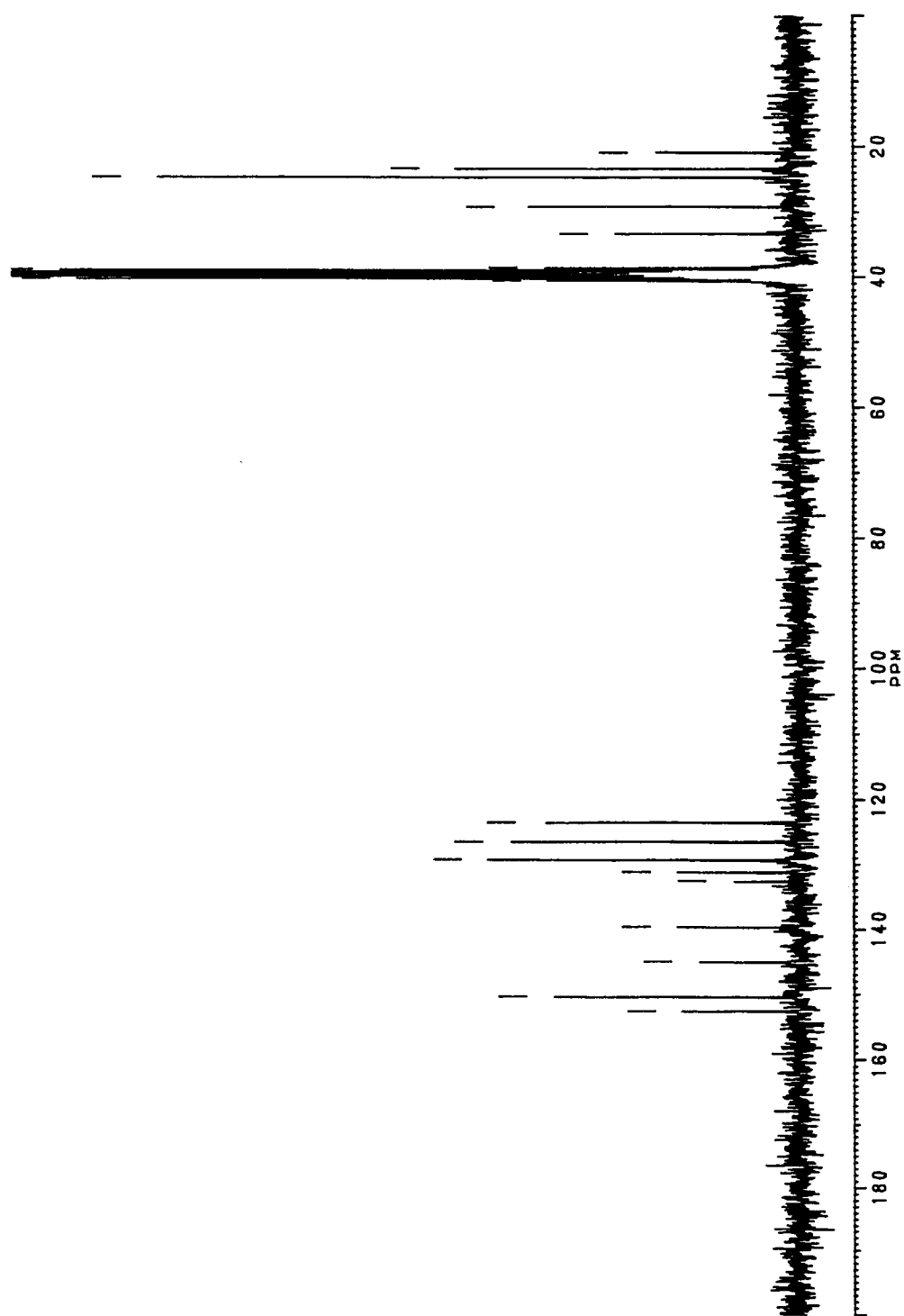
A1. ^1H NMR of 3-Methoxybenzaldehyde Tosylhydrazone



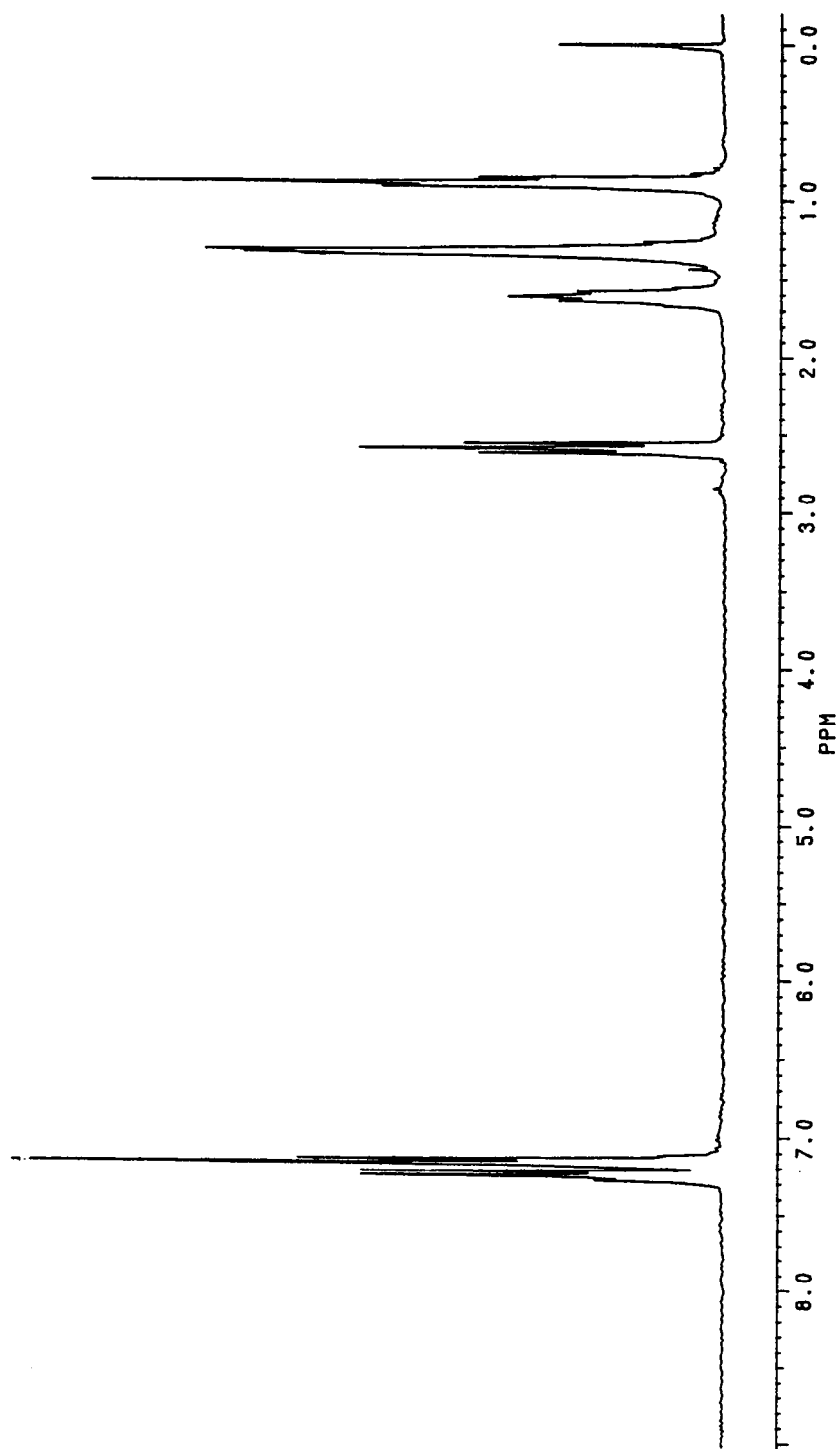
A2. ^{13}C NMR of 3-Methoxybenzaldehyde Tosylhydrazone



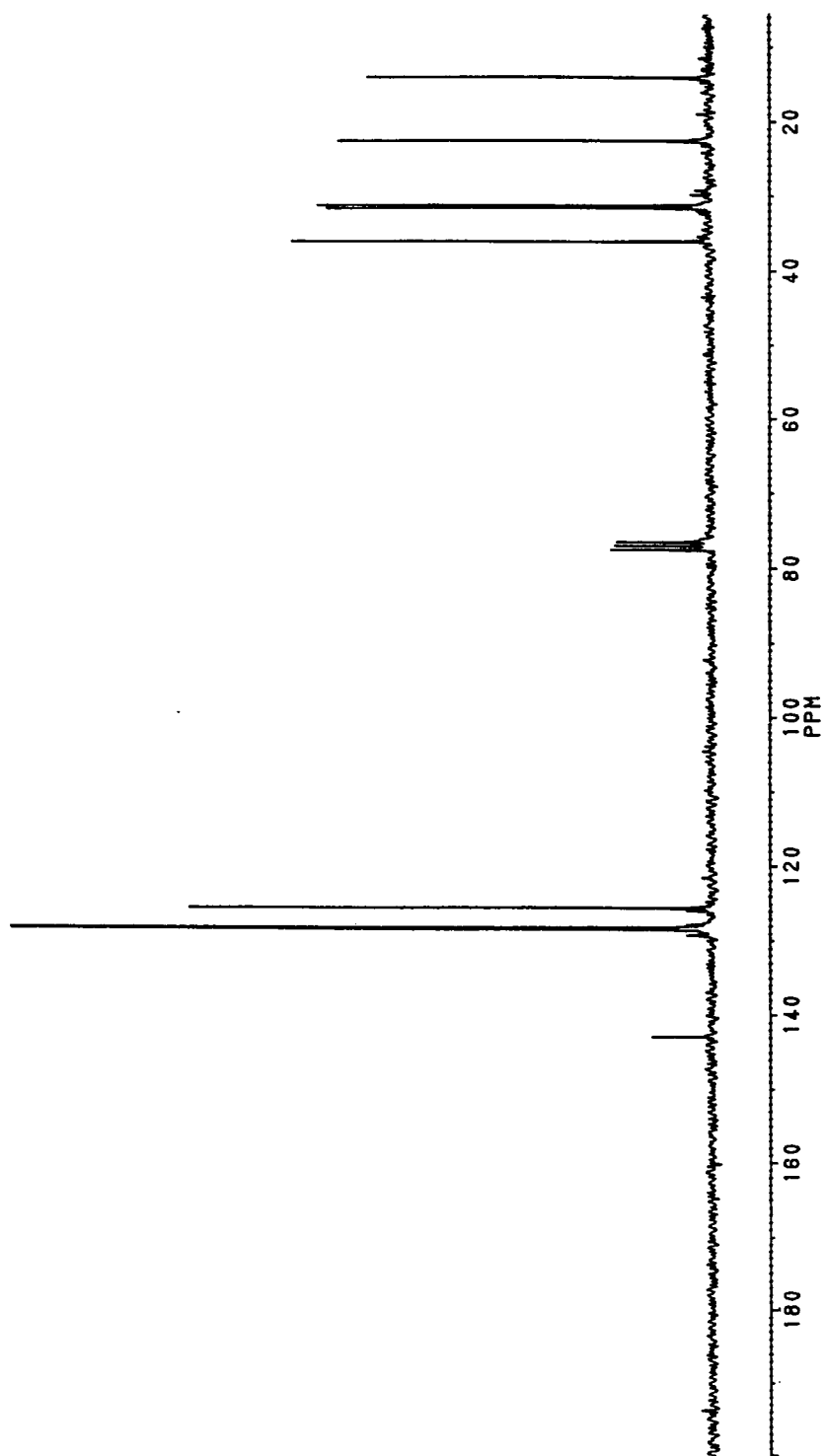
A3. ^1H NMR of 4-Methylbenzaldehyde Trisylhydrazone



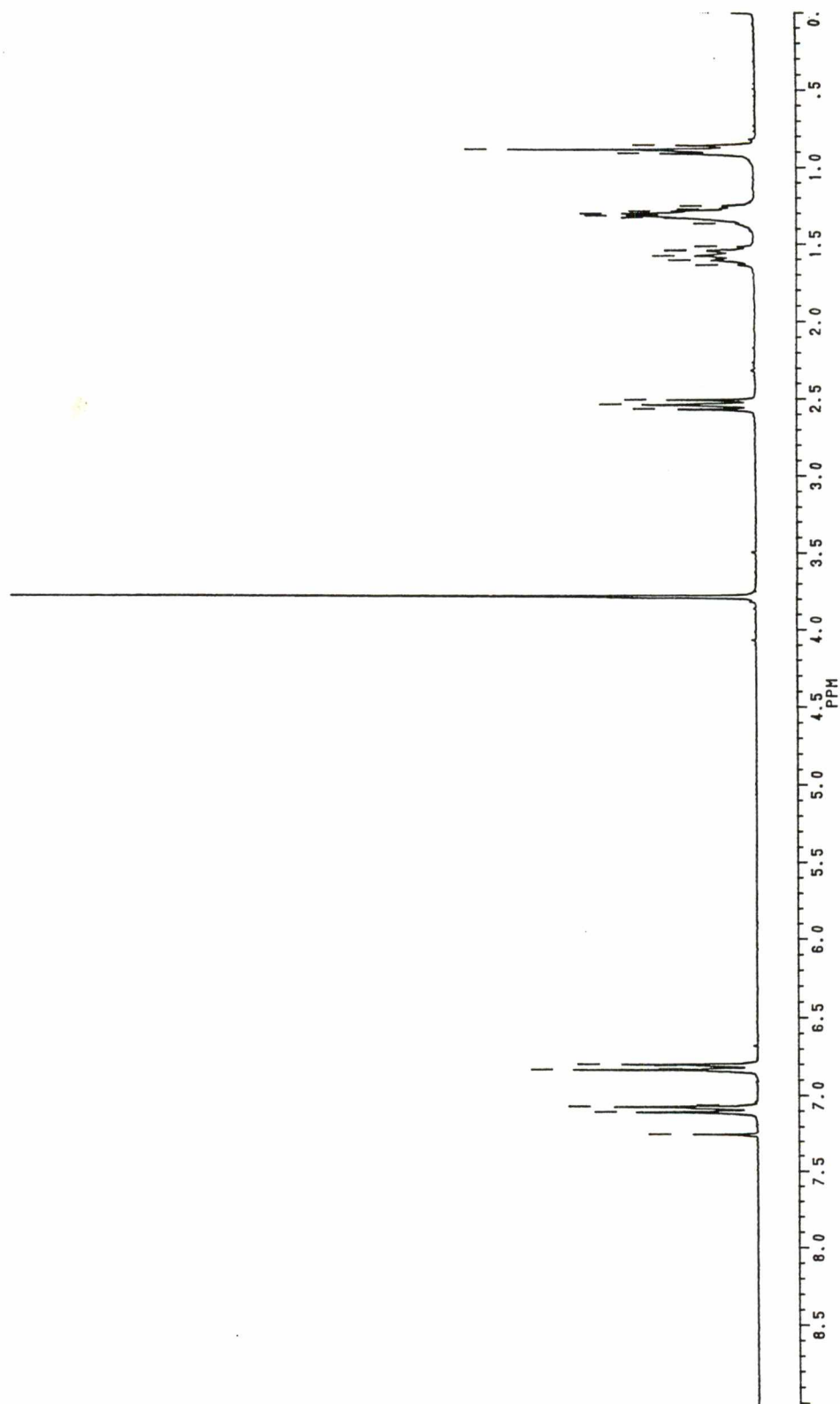
A4. ^{13}C NMR of 4-Methylbenzaldehyde Triethylhydrazone



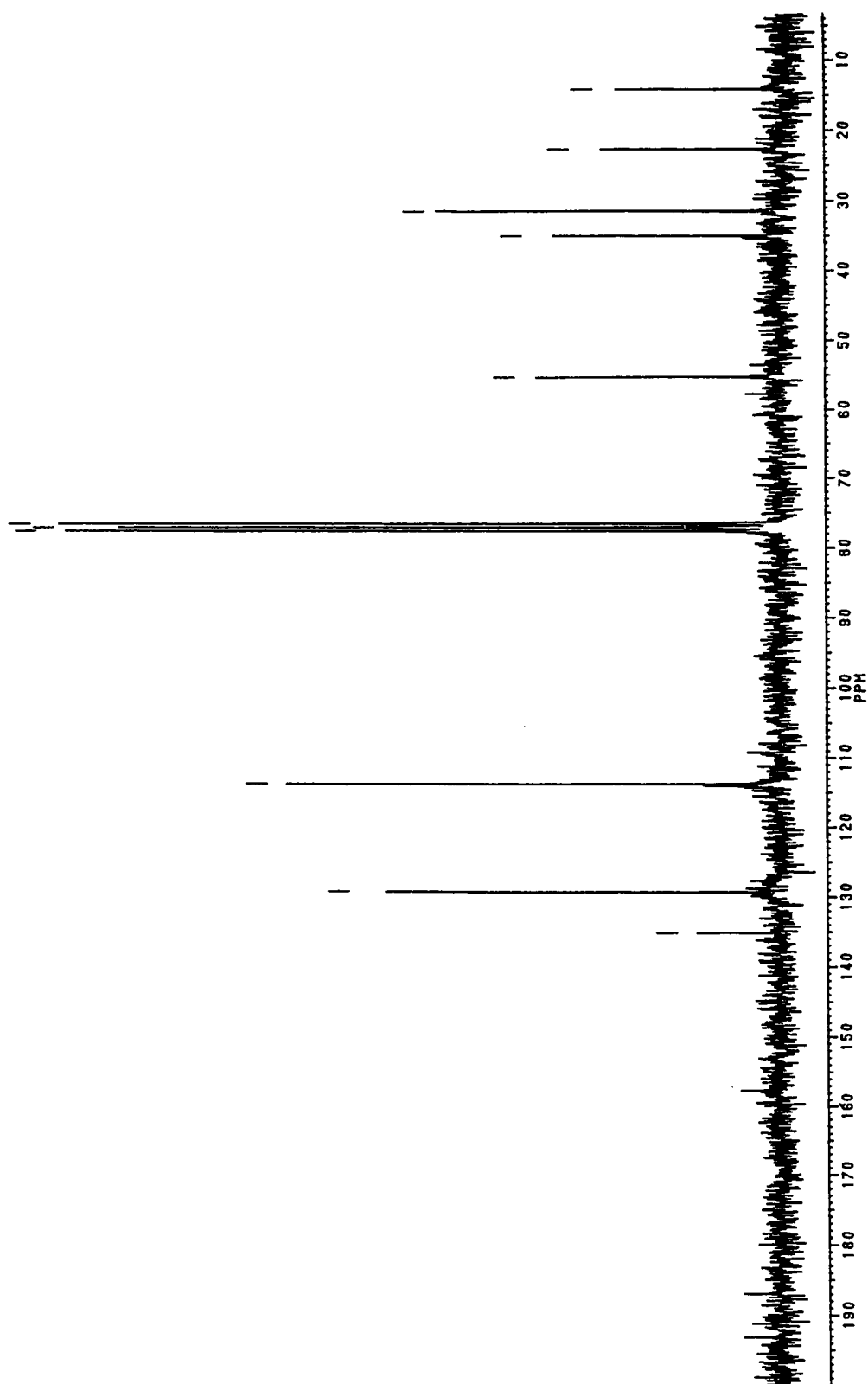
A5. ^1H NMR of Pentybenzene



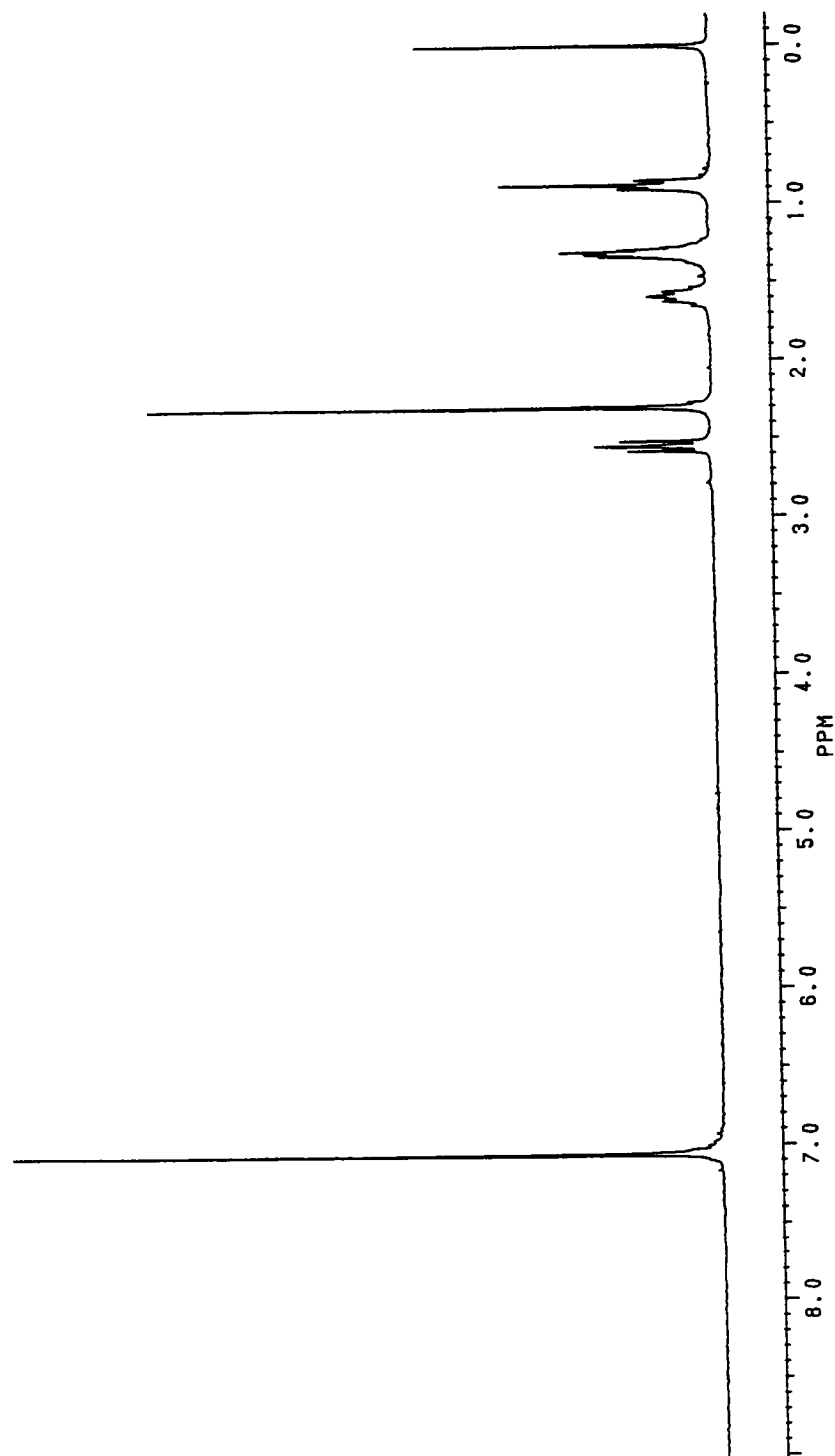
A6. ^{13}C NMR of Pentylbenzene



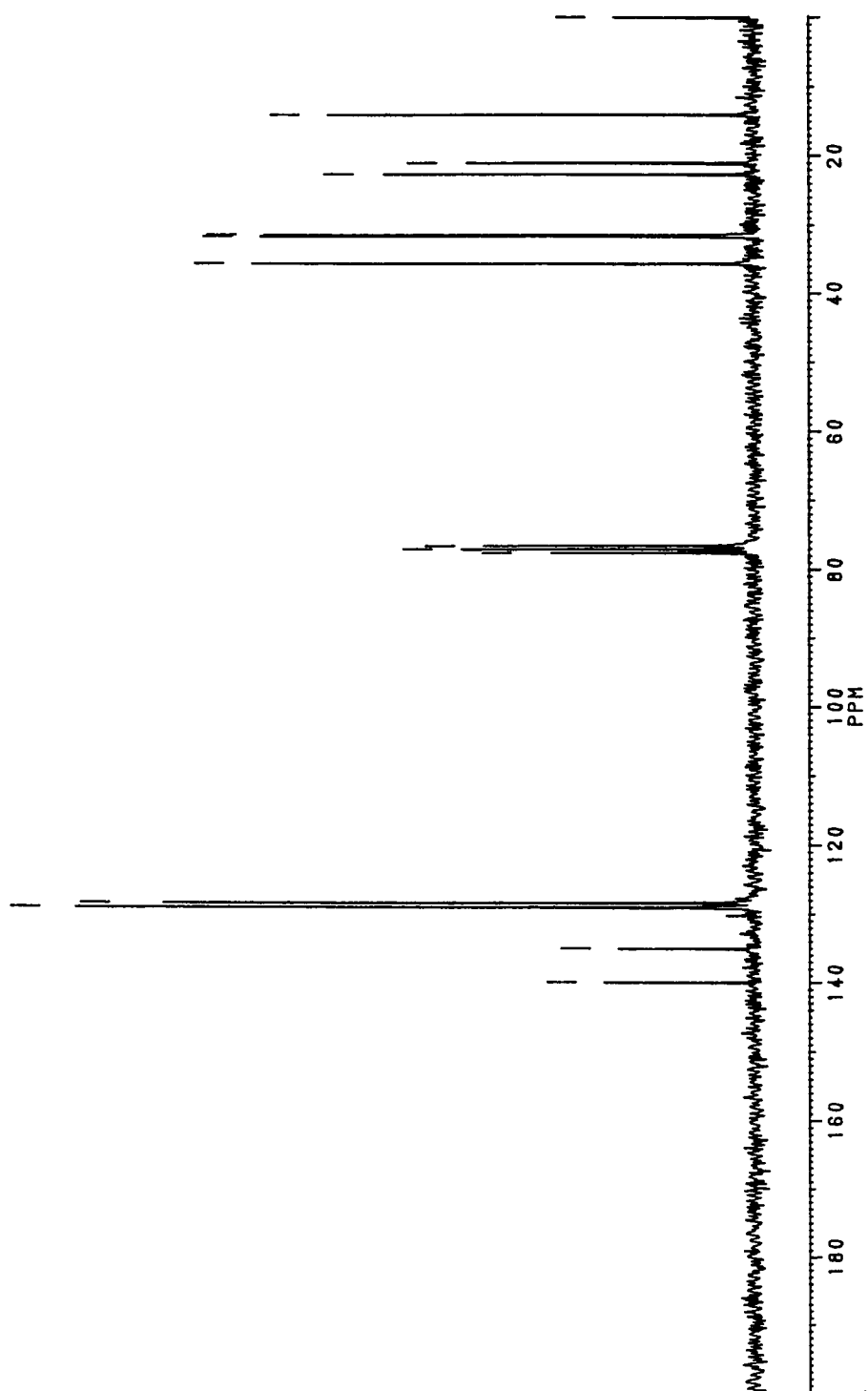
A7. ^1H NMR of 1-methoxy-4-pentylbenzene



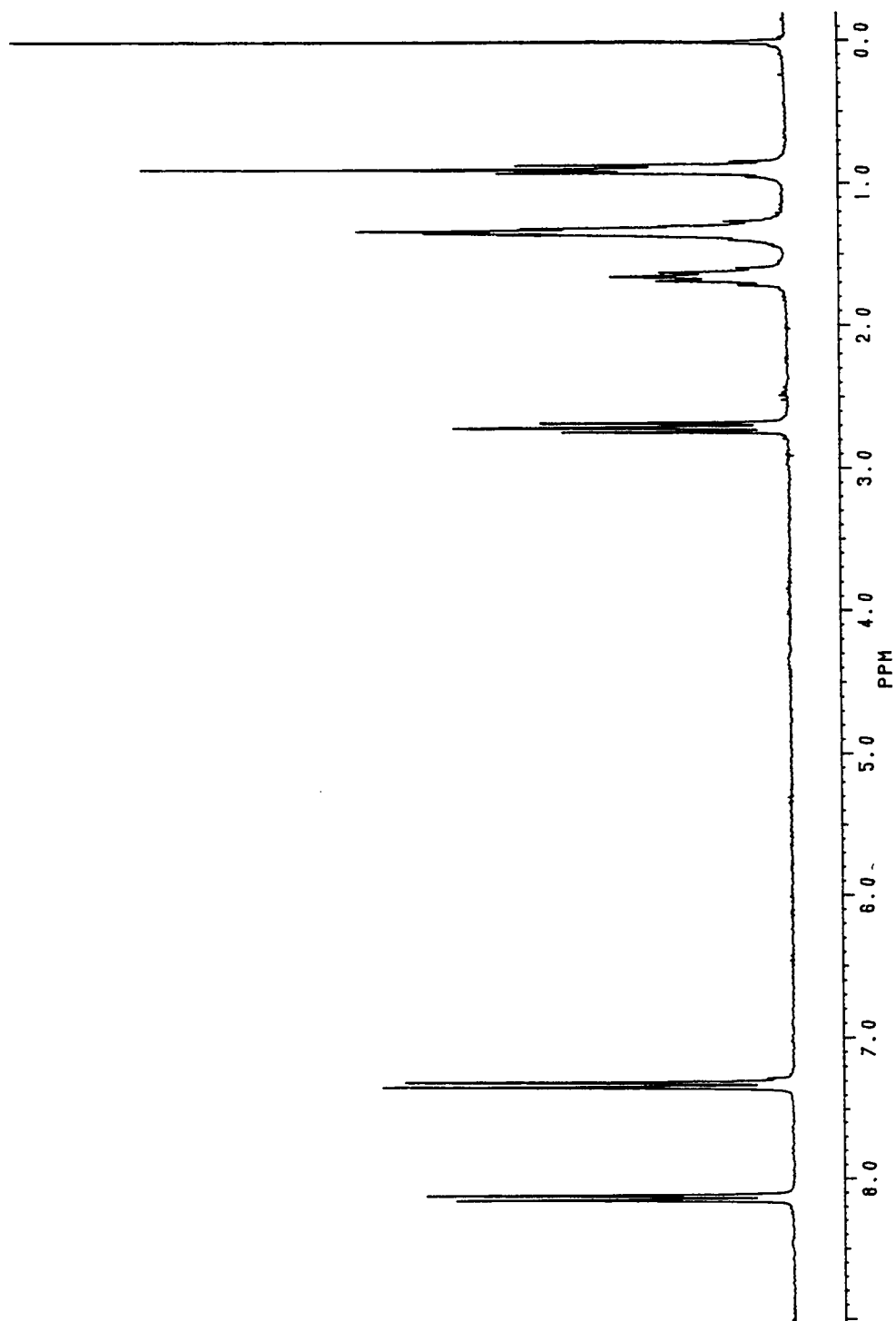
A8. ^{13}C NMR of 1-Methoxy-4-Pentylbenzene



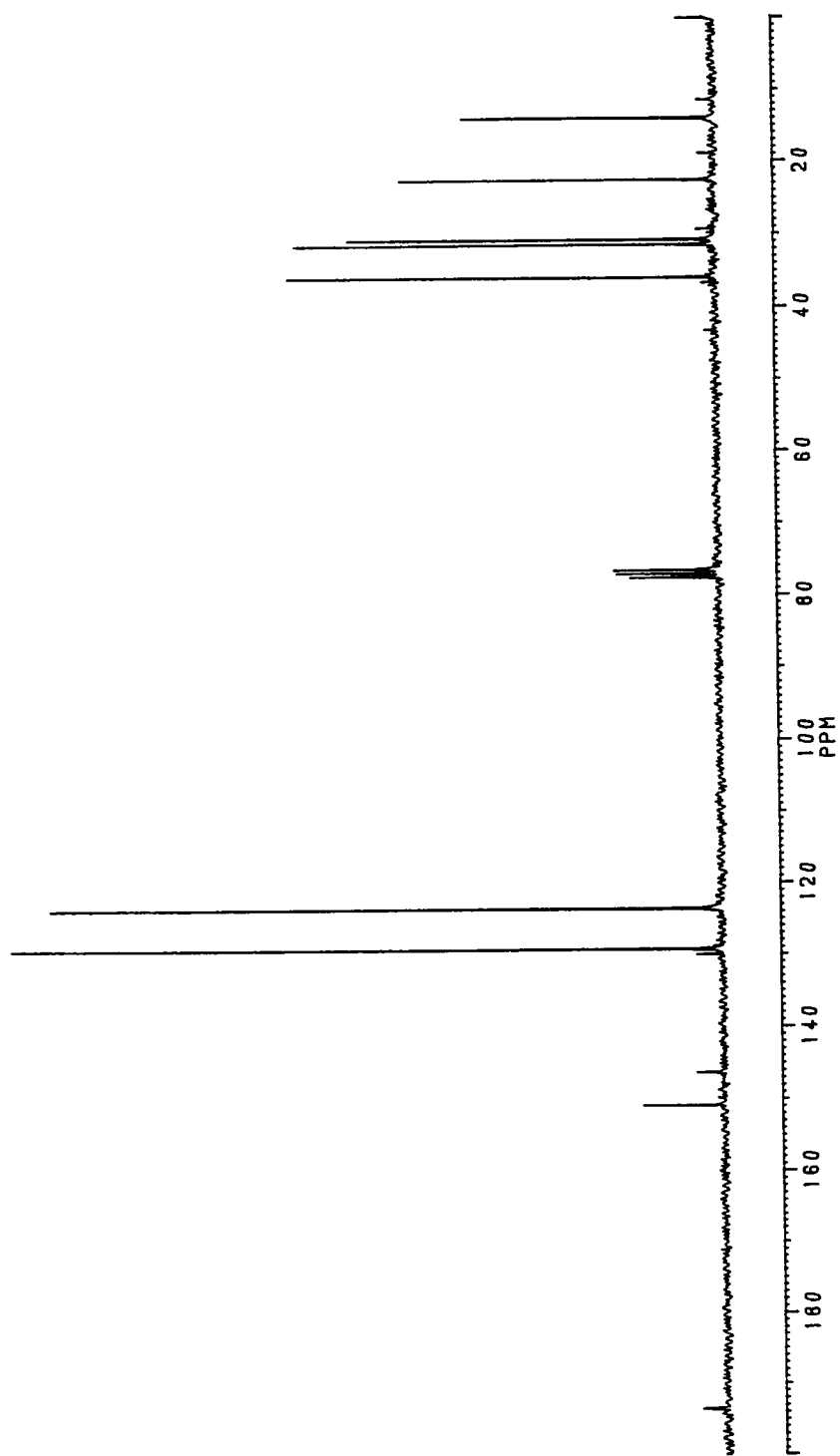
A9. ^1H NMR of 1-Methyl-4-Pentylbenzene



A10. ^{13}C NMR of 1-Methyl-4-Pentylbenzene



A11. ^1H NMR of 1-Nitro-4-Pentylbenzene



A12. ^{13}C NMR of 1-Nitro-4-Pentylbenzene

VITA

Ekaterini Bogas Beauvais was born in Thessaloniki, Greece on March 7, 1971. She graduated from Pinewood, International Schools of Thessaloniki in June 1988. She graduated from St. Andrews College, Laurinburg N.C. with a Bachelor of Science in Chemistry in May 1992. She obtained a Master of Science degree under the direction of Dr. George W. Kabalka at the University of Tennessee, Knoxville, TN in May 1995 and a Ph.D in Chemistry in May 1997.