Lewis Base Complexes of Borane as Hydride Sources and C–B Bond Forming Reactions of the Resulting Electrophilic Boron

by

Timothy S. DeVries

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Doctoral Committee:

Professor Edwin Vedejs, Chair
Professor John Montgomery
Professor David H. Sherman
Assistant Professor John P. Wolfe

Acknowledgements

Starting at the beginning, and with the most important acknowledgement, I would like to thank God above all else. Without an ordered universe, there could be no systematic study of it. Without natural laws in place that govern the interactions between molecules, there would be no chemical science. As frustrating as research can already be, imagine if every time one observed a reaction one could reasonably expect wildly different, random results! I cannot believe that this order arose spontaneously, but that the Creator of the universe also imparted it with a system of laws to govern it, from the smallest subatomic particle to entire galaxies. This, then, has motivated me to become a scientist: learning about the laws that govern the universe gives us greater insight into the One who created it. As John Calvin wrote in his Institutes of the Christian Religion (translation by Henry Beveridge):

> In attestation of his wondrous wisdom, both the heavans and the earth present us with innumerable proofs, not only those more recondite proofs which astronomy, medicine, and all the natural sciences, are designed to illustrate, but proofs which force themselves on the notice of the most illiterate peasant, who cannot open his eyes without beholding them. It is true, indeed, that those who are more or less intimately acquainted with those liberal studies are thereby assisted and enabled to obtain a deeper insight into the secret workings of divine wisdom.

The surprises, the unexpected results, are what make chemical research exciting to me. "Failed reactions" do not demonstrate a failure on the part of chemistry but rather a failure in our understanding and interpretation of the laws of chemistry. To me they

represent opportunities to learn more about how God has put the universe together on a molecular level.

Next I need to express my profound gratitude to my graduate advisor, Prof. Ed Vedejs. I owe you for teaching me about boron chemistry, and about designing experiments, but more importantly I owe you for showing me what it means to be a scientist. The primary concern is always about the science, about the discovery and application of new concepts. You have taught us by example to question everything, regardless of the source, and this close scrutiny will serve me well throughout my career. But close behind this is your concern for your students' development as chemists. I have always appreciated that you take your role as an advisor, a mentor, very seriously. You seem instinctively to know when you need to step in and help us take a step back to look more clearly at the research but also when we need to be left to make our own mistakes and learn for ourselves.

Thank you also to all my labmates here in the Vedejs group for making the last five years enjoyable and not just productive. Thanks to Matt Zajac and James MacKay for taking the time to teach me lab techniques, including the proper technique for glove shots and dry ice shuffleboard. Thanks also to "cubemates" Cathy Thompson and Trisha Duffey for not only putting up with me, which can be difficult at times, but even developing friendships which will last beyond our time together in Ann Arbor. Thanks to Drew Bobeck, Susan Deeter and Bob Rarig for all the conversations about chemistry (and everything else). Thanks to Matt Scheideman and Julia Clay for opening some of the leads I followed in the reasearch reported in this thesis, and thanks to Angela Sandelin and Aleks Prokofjevs for continuing this work. And special thanks to Trisha and Susan for proofreading parts of this thesis.

Without friends and family this would have been a lonely five years, so thank you to those here in Ann Arbor, back in Grand Rapids, and everywhere else. Thanks especially to my brother Chris De Vries and his wife Hil, and to my sister-in-law Brenda Bierenga and her husband Keith; we have been blessed by having family close by. Thanks to my parents, Eugene and Thea De Vries, and to my wife's parents, Mike and Barb Vander Heide, for supporting me even though you have no idea what I'm doing here (for the record, a PhD in chemistry). Thanks to friends from Ann Arbor Christian Reformed Church, in particular Rosaline Stoehr and Tim and Char Larsen, for making Ann Arbor feel more like home.

Finally, I couldn't have done this without my wife and the love of my life, Beth De Vries. You might have been crazy to marry someone about to start graduate school, especially when you were about to start yourself, but I couldn't imagine doing this without you. You have been supportive even though at times this was hard on you, and you have understood how important this was to me and even made it important to you. I appreciate your listening to my incoherent ramblings about the chemistry on our walks with Chewy, and you can't even imagine how wonderful it's been for me that you've even understood some of it. But I thank you for accompanying me on this part of my journey, and I look forward to moving on with you by my side.

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Abstract

Lewis Base Complexes of Borane as Hydride Sources and
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Chair: Edwin Vedejs

The last 50 years have seen great advances in the field of boron cations, but most reports have focused on their preparation. Trivalent borenium and even divalent borinium ions have been isolated and characterized, although typically stabilized by bulky, electron-donating ligands. Perhaps these limitations explain the lag in applications of boron cations, the most notable exception being the activated oxazaborolidines developed by Corey as catalysts for ketone reduction and Diels-Alder cycloaddition.

The research described in this thesis was directed toward the preparation of relatively unstabilized borenium ions by hydride abstraction from Lewis base-borane complexes ($L{\cdot}BH_3$). Borenium ions do not accumulate under these conditions due to subsequent rapid reaction with $L{\cdot}BH_3$ to form B–H–B bonds. However, reversible cleavage of the 3c2e bond releases borenium ion equivalents, as evidenced by the interaction with weak nucleophiles. This reactivity was applied to expand the scope of hydroboration reagents. The reported solvent-assisted decomposition of

triphenylmethane indicates that the use of trityl tetrakis(pentafluorophenyl)borate for generation of other reactive electrophiles may warrant closer scrutiny.

Trityl activation has also allowed a highly regioselective arene borylation under mild conditions using a number of different heteroatomic directing groups. The observed kinetic isotope effect indicates that the presence of a Brønsted base could accelerate these reactions, but this would require more stabilized borenium cations than $L{\cdot}BH_2^+$. Future development of this methodology could apply the trends that emerge in boron cation literature to find the right balance between stability and reactivity of the cationic boron intermediates.

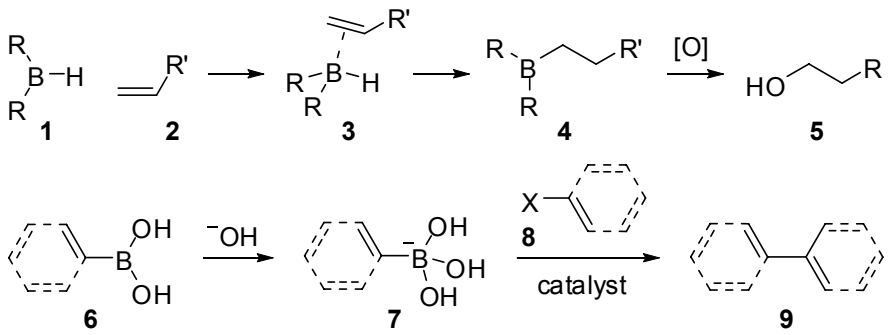
Borane complexes of unsaturated amines and phosphines were used to study hydride transfer to a carbocation formed by protonation of the tethered alkene, achieving directed ionic hydrogenation. Cyclic borane complexes with one face of the intermediate carbocation accessible to the tethered hydride participate in a highly diastereoselective reduction. Amine boranes react by an initial hydride abstraction by the acid, generating an attenuated hydride donor that still reacts with the tethered carbocation. This initial reaction of the strong acid provides an opportunity to introduce a chiral substituent on boron, allowing enantioselective reduction of an unsaturated amine borane.

Chapter 1

Recent Advances in the Formation and Application of Boron Cations

Introduction – Boron Compounds as Lewis Acidic Reaction Promoters

Boron chemistry is dominated by the concept of Lewis acidity. That common reagents such as BF_3 function as Lewis acids to promote reactions hardly needs to be mentioned, but it is worth noting that this reagent is typically purchased, purified and stored as a complex with the weakly Lewis basic diethyl ether. Even two of the better known applications of boron reagents in synthetic organic chemistry depend on the Lewis acidity of neutral, trivalent boron. First, the hydroboration/oxidation sequence developed by Brown (eq 1) is thought to involve coordination of the alkene π electrons to form a borane complex (**3**) from which hydroboration occurs.[1] Second, Suzuki and Miyaura's discovery that coordination of a base into **6** results in a borate complex (**7**) that undergoes facile transmetallation with transition metals has made possible the application of these mild, stable boronic acid reagents in transition metal-catalyzed cross-coupling (eq 2).[2]



Increasing the Lewis acidity at boron has proven important for developing further applications of boron-based reagents and catalysts in organic transformations, for example in the development of the potent electrophile $B(C_6F_5)_3$.[3] One way to increase the electron deficiency is to generate a cationic species.[4] While progress has been made in preparing boron cations, the application of these species to synthetic chemistry has only started to see real progress in the last 10 years. The difficulty, as is often the case in developing new methodology, is a question of balance. Increasing the electron demand at boron encourages unwanted reaction pathways in addition to the desired transformations. For example the preparation of a free, low-valent boron cation has been hampered by coordination of even weakly Lewis basic solvents, mirroring challenges that were also problematic in the search for a free silicon cation.[5] Coordination stabilizes the boron cation, but it in turn reduces the electrophilicity at boron, negating the advantages of preparing cationic boron reagents. This problem will be discussed as it applies to the individual classes of boron cations in the next section.

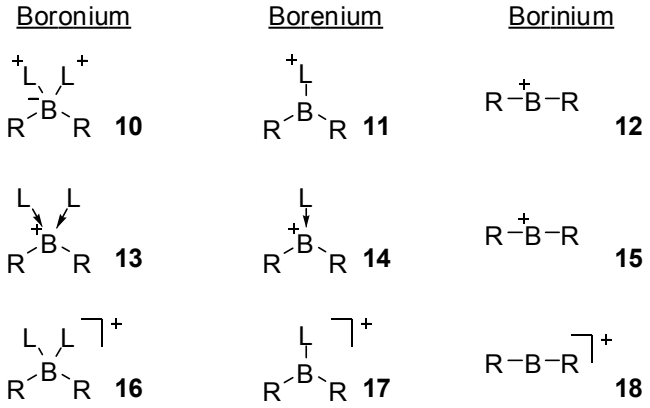
The research for this thesis has focused on the formation of boron cations from stable, neutral borane complexes by in situ electrophilic activation and on selected applications of these cations as reagents in C–B bond-forming reactions. Notwithstanding our best efforts, we have been unable to isolate and fully characterize the cationic boron intermediates, only observing them spectroscopically in solutions. It will nevertheless be useful to begin with a review of recent advances in the formation of boron cations, focusing on evidence for their formation and on their applications to synthetic chemistry.

Observation and Characterization of Boron Cations

Cationic Boron Nomenclature

To assist in this review of cationic boron chemistry, it will be useful to first address issues of nomenclature that are not often encountered by the organic chemist. The IUPAC recommendations for boron nomenclature treat charged species as coordination compounds, e.g. $(C_5H_5N)_2BH_2^+$ would be referred to as dihydrobis-(pyridine)boron(1+).[6] However useful this may be for consistent and systematic nomenclature, it is somewhat awkward and does not make the coordination state at boron immediately obvious. The older literature reports were not consistent in their nomenclature, often using the terms boronium and borenium interchangeably to denote cationic boron with various valencies. In his 1985 review of the cationic boron literature Nöth suggested clearer definitions of these terms, boronium for tetravalent and borenium for trivalent boron cations (**10** and **11** respectively), and he introduced the term borinium to refer to a divalent boron cation (**12**).[4a] Under this sytem $(C_5H_5N)_2BH_2^+$, a cation of the type represented by **10**, would be named bis(pyridine)boronium with no need to specify hydrogen substitution.

Figure 1-1. Nomenclature and Graphical Representations of Boron Cations



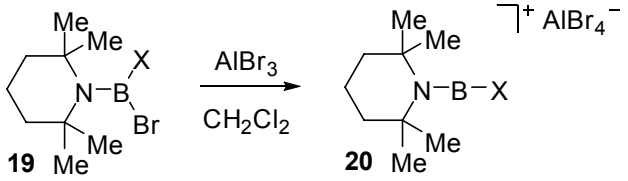
It should be noted at this point that there are a number of different ways to represent these cations on paper. Formal charges (top row of Figure 1-1, **10**-**12**) are quite familiar but not necessarily representative of the actual charge distribution. The central boron atom of **10**, for example, is drawn with a formal negative charge, but the chemistry of boronium ions is typical of electrophilic boron. Formal charge representation also depicts the boron atom of borenium **11** as neutral, but computational work described below shows significant positive charge character at boron.[7] Drawing the bonds between boron and the neutral ligands (L) as dative bonds (middle row of Figure 1-1, **13**-**15**) returns the positive charge to the boron atom for boronium and borenium ions. This is somewhat artificial. While it is useful for allowing us to draw the charge where we want it there is no fundamental physical difference between what we refer to as a covalent bond and what we refer to as a dative bond. Note that the divalent boron cation is represented identically in both systems where R is left unspecified, but the ligands that have allowed observation of borinium ions are almost all capable of stabilizing the empty shell on boron by resonance donation of electrons. In these cases the formal charge could also be placed on the atom directly bonded to boron. The bottom row of Figure 1-1 (**16**-**18**) recognizes that the real charge distribution is likely somewhere inbetween and can vary depending on the nature of both the anionic ligands (R) and the neutral ligands (L). We prefer to draw boron cations in this way, as net cationic species.

Borinium and Boronium Ions

The simplest boron cation conceptually is the borinium ion, formed by removal of an anionic substituent from the neutral trivalent species. The resulting divalent cationic boron is far more difficult to prepare in reality than in concept. The few that have been reported in the condensed phase rely on substituents that can donate electron density to

boron by π-backbonding and that hinder the approach of Lewis bases by steric bulk. For example, an early report of a number of well-characterized borinium ions (**20**), mostly diamidoboron cations (e.g. **20a** and **20b**), relies heavily on the tetramethylpiperidino (tmp) group for the additional lone pair on nitrogen and the steric shielding of the boron

Table 1-1. ^{11}B NMR Data[a] for TMP-Substituted Borinium Ions **20**



entry	X	δ^{11}B for **19**	δ^{11}B for **20**
1	**a**: X = NMe_2	NA[b]	36.7
2	**b**: X = Net_2	30.6	37.6
3	**c**: X = Ph	40.4	56.0
4	**d**: X = Me	41.7	59.6

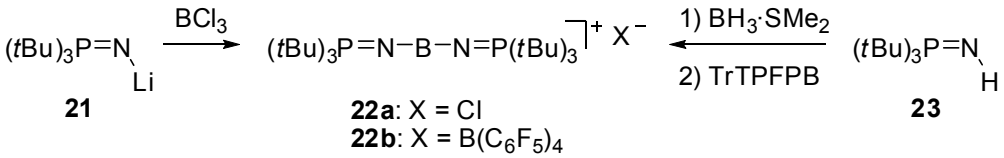
[a] Chemical shifts in ppm relative to $BF_3{\cdot}OEt_2$, measured in CD_2Cl_2. [b] Not available.

center by the α-methyl groups.[8] The ^{11}B NMR signal shifts downfield on abstraction of a bromide from **19** (Table 1-1) as expected from other ^{11}B NMR studies.[9] The typical deshielding arguments apply to boron nuclei as well, such that reduced electron density at boron shifts the signals to lower field. The magnitude of the shift, however, is surprising. The divalent boron cation was expected to be far more electron deficient than the ^{11}B NMR chemical shift reveals, but this again is explained by donation of the nitrogen lone pair into boron. While this is likely an important contribution to the neutral structures **19** as well, the increased electron demand of **20** makes the B=N double bond character more significant. This double bond character is also illustrated by the very short B–N distances in the crystal structure solved for **20a** (1.30 and 1.42 Å). The two amido groups were also found to be normal to each other, recalling an allene structure where orbital overlap at the central atom is maximized. The difference in ^{11}B NMR chemical

shifts between **19d** and **20d**, the only borinium ion described in this report with only one π-donating ligand, is much greater than for the other pairs (precursors and borinium ions in Table 1-1).

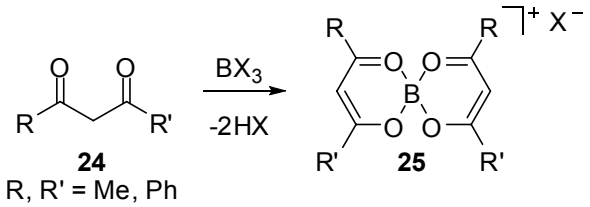
A more recent report takes advantage of bulky, donating phosphinimide ligands to prepare **22** (eq 3), a borinium ion with an extended π-system.[10] Previous studies have indicated that smaller substituents at phosphorus allow dimerization of the borinium cation or coordination of a third phosphinimide to form the neutral trivalent borane. While the X-ray crystal structures of both **22a** and **22b** show a dissociated anion and the free divalent boron, NMR studies in solution are harder to interpret. The ^{31}P NMR signal for **22a** shifts from δ 55.7 ppm in CD_2Cl_2 to δ 28.5 ppm in the less polar C_6D_6, taken to indicate tight ion pairing in the less polar solvent. The ^{31}P NMR chemical shift for **22b** is not solvent-dependent, rationalized by the weakly coorinating $B(C_6F_5)_4^-$ counterion (TrTPFPB = trityl tetrakis(pentafluorophenyl)borate, Ph_3C^+ $^-B(C_6F_5)_4$). The ^{11}B NMR chemical shifts, perhaps more indicative of the coordination environment at the boron atom, also changes for **22a** based on solvent, from δ -6.1 ppm in C_6D_6 to δ 11.9 in CD_2Cl_2. The chemical shift for **22b** is only reported in C_6D_6 ($\delta^{11}B$ = 11.1 ppm) but is similar to the shift for **22a** in the more polar solvent. Note that the intermediate trivalent species prepared as an intermediate from **23** (((*t*Bu)$_3$P=N)$_2$B–H) before hydride abstraction displays an ^{11}B NMR signal at δ 24.6 ppm. This could be taken as evidence for a decreased electron demand on formation of the cationic species, probably due to increased B=N double bond character in **22b**. These surprisingly low ^{11}B NMR chemical shifts indicate a fairly rich electronic environment at boron, which coupled with the steric

bulk of the tri-*tert*-butylphosphinyl groups does not look encouraging for applications of structures related to **22** as Lewis acids.



(3)

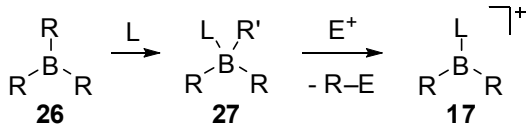
Moving to the other end of the spectrum, boronium ions (**10**) were the first boron cations prepared and characterized, almost certainly due to the stability imparted by coordinative saturation. The earliest reported boron cations, **25**, were prepared in 1905 by the reaction of BCl_3 with β-diketones (eq 4),[11] but these were only characterized by elemental analysis until later groups studied different salts of this cation by spectroscopic means (R = R' = Ph: $\delta^{11}B$ = 9.4 ppm).[12] While numerous methods have been explored to arrive at these cations since the original report, the complete coordination sphere makes them less interesting for applications as Lewis acids. They could activate a substrate by substitution of a ligand at boron in an S_N1 or an S_N2 manner, with both pathways creating the same activated species. For the analogous carbon-based electrophiles, the S_N2 pathway is only accessible to 1° or 2° electrophiles due to steric hindrance at the backside of the bond being broken. Applying this analogy to boronium ions which are commonly substituted by more than one or two ligands other than hydride, the S_N1 pathway would be favored. This more likely dissociative mechanism involves intermediacy of either a neutral or cationic trivalent boron depending on the substituent lost.



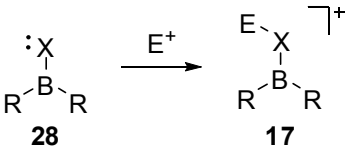
(4)

Borenium Ions

This potential trivalent cationic boron intermediate, a borenium ion, will be considered next. The methods used in the formation of borenium ions from more stable species can be grouped into two common classes: abstraction of an anionic group from neutral tetravalent boron (eq 5) or electrophilic attack at one of the ligands of neutral trivalent boron (eq 6). The first pathway is the first step in the S_N1 mechanism just mentioned for reaction of a boronium ion, and in this I include any displacement of an anionic group from trivalent boron (**26**) with a neutral one. This likely occurs by complex formation to **27** followed by loss of a substituent (eq 5) rather than direct displacement.



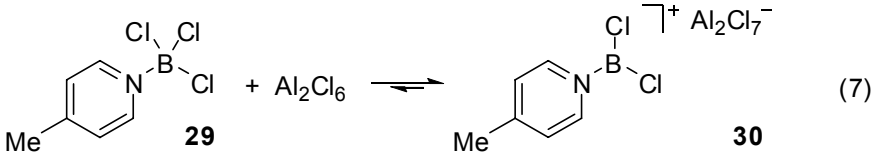
26 **27** **17** (5)



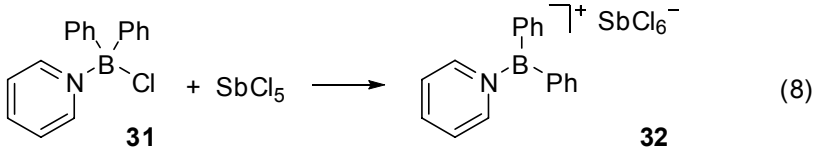
28 **17** (6)

Although trivalent boron cations had been proposed a few years earlier, the first report of a borenium ion with ^{11}B NMR evidence to confirm the coordination around boron was from the Ryschkewitsch laboratory in 1970.[13] Chloride abstraction from 4-picoline·BCl_3 with 2 equiv aluminum chloride produces salt **30** (eq 7). The ^{11}B NMR signal at δ 47 ppm (corrected for the currently used $BF_3{\cdot}OEt_2$ reference) is shifted downfield by 29 ppm relative to tetravalent boron in **29** ($\delta^{11}B$ = 8 ppm). The ^{1}H NMR chemical shifts were observed to depend on the stoichiometry, and the equilibrium constant for eq 7 (K = 20) was approximated by conductance experiments. Recent work from the Fujio laboratory has shown a similar abstraction of chloride from an adduct of

pyridine with chlorodiphenylborane (**31**), generating **32** cleanly. The downfield shift of the ^{13}C NMR signals for phenyl carbons, particularly *ortho* and *para* carbons, served as evidence for formation of **32**, as did the ^{11}B NMR signal at δ 58.2 ppm.[14] This represents a downfield shift of 50 ppm relative to **31** ($\delta^{11}B$ = 8.2 ppm)!



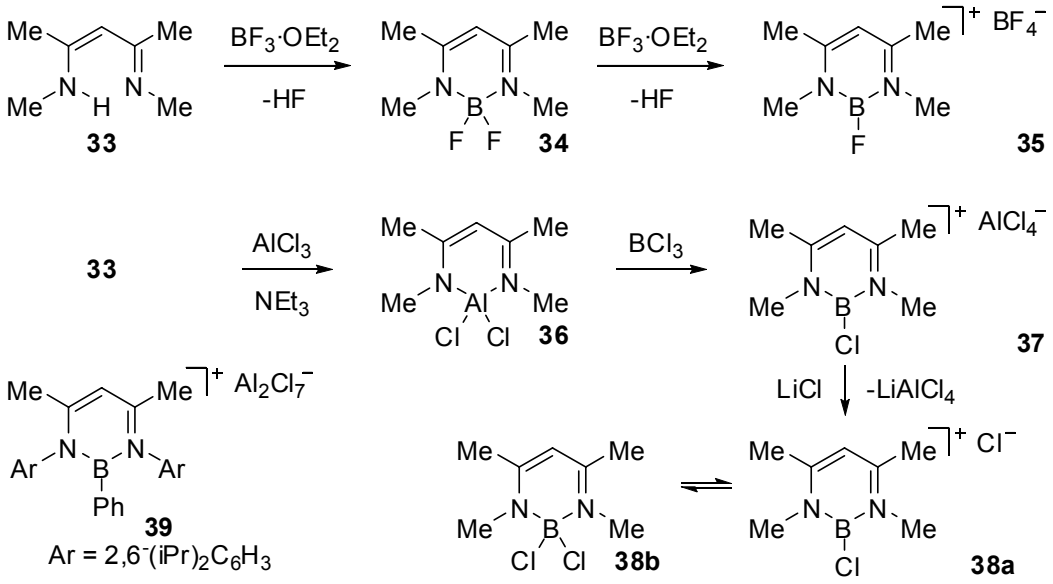
(7)



(8)

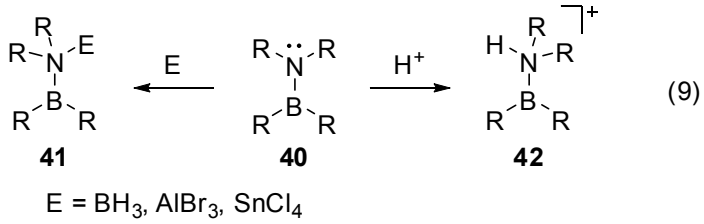
A borenium ion has been prepared by this pathway and shown to exist in the presence of the more strongly coordinating BF_4 and even, to an extent, Cl anions by taking advantage of aromaticity.[15] Reaction of β-diketimine **33** with $BF_3{\cdot}OEt_2$ followed by reaction with a second equivalent of $BF_3{\cdot}OEt_2$ gave aromatic borinium ion **35** (Scheme 1-1). The stability imparted to **35** by aromaticity is great enough that even the tetravalent $BF_3{\cdot}OEt_2$ is sufficiently Lewis acidic to remove a fluoride ion from **34**. This stabilization of the trivalent boron cation is also observed by the ^{11}B NMR shift at δ 23.1 ppm, upfield relative to other borenium ions previously described. Likewise, metathesis of aluminum complex **36** with BCl_3 gives *B*-chloro analogue **37**. Anion metathesis with LiCl generates a species with a concentration-dependent ^{11}B NMR shift, between δ 15 and δ 30 ppm. The concentration dependence was explained by the authors in terms of an equilibrium between **38a** and **38b**, the high end of the range of ^{11}B NMR shifts close to that reported

Scheme 1-1. Preparation of Aromatic 1,3,2-Diazaborinium Ions



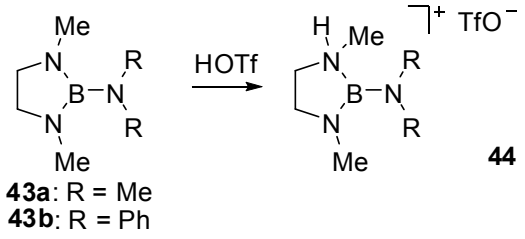
for **37** (δ^{11}B = 32.2 ppm). A crystalline *B*-phenyl analogue (39) was later reported by Cowley, and the planarity of the trivalent boron atom was confirmed by solving its X-ray crystal structure.[15b]

This first pathway for borenium ion formation (eq 5) is also relevant as the mode of boron cation generation that was pursued in this thesis research, discussed more fully in Chapters 2 and 3, with R′ = H and E^+ = trityl cation. Our work focused on attempts to generate boronium ions with a lower substitution pattern than has yet been achieved (**17**, R = H), so the counterion was carefully chosen as the weakly coordinating $B(C_6F_5)_4$ anion already seen in connection with borinium ion **22**. The evidence for intermediacy of a borenium ion generated in this way will be presented in later chapters.



(9)

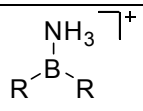
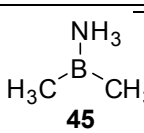
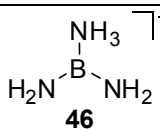
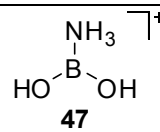
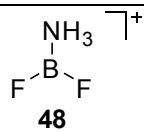
The other pathway for borenium ion generation (eq 6 and 9), activation by coordination to a boron substituent, will be discussed briefly now and again in the next section. Many of the applications described in the next section take advantage of neutral Lewis acids to convert a trivalent nitrogen bonded to the boron atom to tetravalent nitrogen. Thus structure **41** has a borenium subunit with increased electron demand at boron relative to **40**, even though this complex is net neutral. Only the reaction of **40** with a cationic Lewis acid, for example a proton, generates a true borenium cation as in **42**. For example, Nöth found that while reaction of **43** with HCl generated tetravalent boron products, HOTf gave the isolable salt **44**.[16] The X-ray crystal structure of **44b** was solved, confirming the coordination state of boron in the solid state. However, the reported ^{11}B NMR signal, δ 24.9 ppm for **44a** compared to δ 26.5 ppm for **43a**,[17] leaves some question about whether this is truly a trivalent boron cation in solution. Coordination of the anion or even of solvent into boron must be considered as a possibility, but the similarity in ^{11}B NMR chemical shifts could mean that the remaining two amido groups at boron provide sufficient stabilization of the empty shell at boron to negate any effects of loss of stabilization from a third amido group.



(10)

A computational study[7] of a simplified model of **44** (**46**, $(H_2N)_2B{\cdot}NH_3^+$) predicts B–N bond lengths similar to those found in the crystal structure of **44b**, approximately 1.4 Å for bonds to the trivalent nitrogen atoms but 1.6 Å for the bond to the protonated nitrogen (Table 1-2). The B–NH_3 bond length is similar for the series of NH_3-substituted borenium ions in Table 1-2. These calculations also predict a significant charge character at boron, a Mulliken gross charge of +0.83 at boron in **46**. This charge increases as the R substituent is changed to more electronegative substituents (F > O ≈ N > C), with the exception of oxygen-substituted 47 according to the calculations at the 6-31G* level. The charge variation also follows the trend of π-backbonding for the heteroatom-substituted **46-48**, with the highest p electron density at the central boron atom predicted for the more highly stabilized **46**. Although no lone pair is present on the methyl groups of **45**, hyperconjugation places some p electron density at boron.

Table 1-2. 6-31G*//6-31G* (STO-3G//STO-3G) Calculations on Borenium Ions **45-48**[a]

				
45	**46**	**47**	**48**
B–R (Å)	1.56 (1.56)	1.39 (1.38)	1.32 (1.33)	1.28 (1.28)
B–N (Å)	1.60 (1.59)	1.59 (1.59)	1.56 (1.58)	1.55 (1.59)
q_B[b]	0.70 (0.55)	0.83 (0.64)	0.81 (0.67)	0.97 (0.76)
p_π[c]	0.10 (0.12)	0.41 (0.52)	0.33 (0.51)	0.26 (0.46)

[a] All molecules optimized under C_S symmetry with NH_3 and CH_3 groups restricted to local C_{3v} symmetry. [b] Mulliken gross charge on the central boron atom. [c] Mulliken population of the boron p orbital normal to the molecular plane.

The preceding examples demonstrate a few methods of forming boron cations and some evidence for the electron-deficient nature of these species. This is not meant to be an exhaustive review on the topic, simply an introduction to the concept of highly Lewis acidic boron cations, and the challenges that must be overcome particularly in preparing borinium and borenium ions. Many of the means used to obtain these low-valent boron

compounds, however, attenuate the Lewis acidity to an extent. Nevertheless the next section will demonstrate some powerful applications of such borenium ions as catalysts for common organic transformations such as ketone reduction, the Diels-Alder cyclization and the aldol reaction.

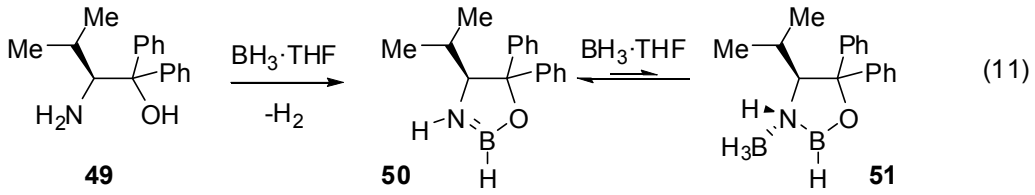
Applications of Activated Oxazaborolidine Catalysts

The Dual Function of Oxazaborolidines in the CBS Reduction

Perhaps the first reported application of a reagent with a borenium subunit was not even recognized at the time as such. In the course of studies directed toward enantioselective ketone reduction, Itsuno reported that a chiral amine borane complex derived from diphenylvalinol (**49**) gave highly enantioselective reduction of a number of different aryl ketones (94-100% ee).[18] The stoichiometry of BH_3·THF to **49** used (2:1) was noted as an important variable, but the role of a second equivalent of borane was not known at the time of the initial report. During optimization of the reaction conditions, Itsuno later found that pretreatment of **49** or other chiral amino alcohols with 1 equiv BH_3·THF at 0 °C allowed isolation of a chiral complex that was not well characterized.[18b] This complex could be used catalytically with stoichiometric reducing agents, including BH_3·THF, for the enantioselective reduction of *O*-methyloximes. The unidentified complex was proposed to coordinate to the oxime ether and accelerate the reduction, but the authors did not indicate activation of borane as a reductant, despite noting that "the reduction with sodium borohydride did not proceed due to its low reactivity."

At the time of this later report on catalytic activity of the pretreated amino alcohol borane complex, Corey had observed a similar catalytic activity from a preformed catalyst.[19] Corey's closer investigation of the structure of this unidentified boron catalyst led to a proposal for the mode of activation of ketones toward reduction. He identified

this complex as **50**, assisted in part by the ^{11}B NMR shift at δ 28.1 ppm, in the range expected for a trivalent boron complex stabilized by a nitrogen and an oxygen substituent. Oxazaborolidine **53a**, formed by the reaction of borane with diphenylprolinol, was a superior catalyst for the ketone reduction. This complex could be used at even lower catalyst loadings (as low as 5 mol% with no change in enantioselectivity), still giving ketone reduction within 1 min at rt using only 0.6 equiv BH_3·THF.



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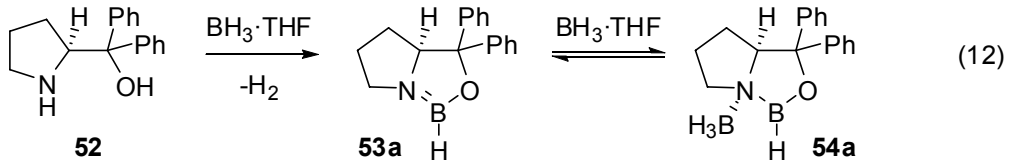

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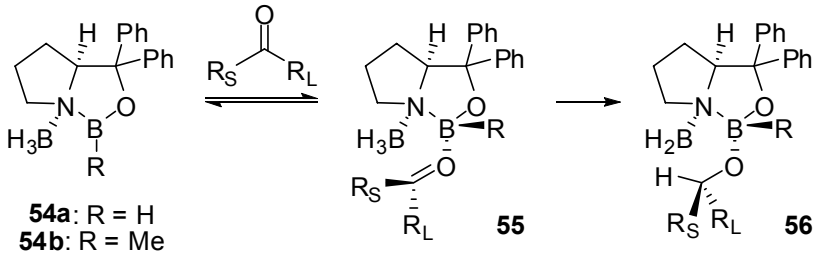
The structure of **53a** was proposed based on IR data and high resolution mass spectrometry as well as NMR data, including the ^{11}B NMR signal at δ 28.3 ppm, with a small amount of dimer ($\delta^{11}B$ = 7.6 ppm). The complex **54a** was proposed based on ^{11}B NMR observation of a solution of **53a** in THF treated with excess BH_3·THF. Two new signals were observed, for the ring boron and the exocyclic N–BH_3, but these signals had chemical shifts at 3.2 and -19.4 ppm, respectively. The endocyclic boron in **54a** would be expected to shift downfield from **53a** if any change is observed. This upfield chemical shift may imply reversible coordination of the reasonably Lewis basic THF into the borenium moiety to form a boronium moiety. The ^{11}B NMR spectrum of **50** with BH_3·THF added showed only minor peaks corresponding to formation of the analogous **51**. A subsequent communication from Corey described the B-methyl analogue of **53a**

(**53b**).[20] This oxazaborolidine has a ^{11}B NMR shift at δ 33.5 ppm similar to **53a**, but borane complexation to form **54b** results in the expected downfield shift for the endocyclic boron nucleus ($\delta^{11}B$ = 36.5 ppm) and a comparable upfield-shifted exocyclic N–*B*H_3 resonance ($\delta^{11}B$ = -15.4 ppm). Apparently solvent does not coordinate to the slightly bulkier, more stabilized *B*-methyl derivative. Note that **54** is described here as possessing a borenium subunit once the nitrogen lone pair is used to form a bond to the Lewis acidic BH_3. Thus **54** is net neutral and not technically a borenium ion, but the endocyclic boron atom is expected to be more electrophilic as a result of the decreased electron donation into the p orbital at boron.

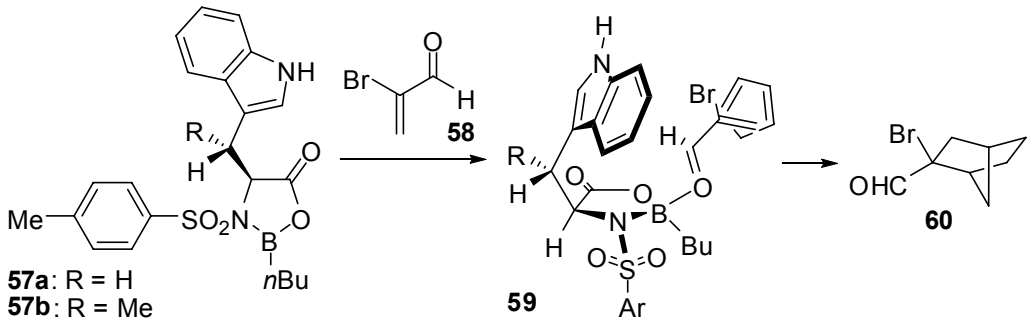
Corey proposed that catalyst **53** functions with dual purpose according to eq 13, activating both substrate (ketone) and reagent (borane) via complex **54**. So Itsuno's original purpose of preparing a chiral amine borane was in fact realized, with reaction likely occuring by hydride transfer from the N–BH_3 of **55**. Itsuno's later report proposing activation of the ketone by coordination to an electrophilic boron promoter (as in **55**) also seems reasonable. Both of these effects combine to allow very fast reactions under mild conditions, and the intramolecular hydride transfer from **55** to **56** can be used to rationalize the high stereoselectivity of the reaction. Intramolecular reaction from **55** would only be viable if the ketone coordinates *cis* to the complexed BH_3, and the favored configuration of the ketone puts the smaller substituent (R_S) *cis* to boron to minize steric interactions with the rest of the oxazaborolidine. Subsequent work has extended this methodology to allow facial discrimination even for ketones with sterically similar substituents and to a number of applications in total synthesis.[21] The CBS reduction (Corey, Bakshi and Shibata[19]) has become one of the most powerful methods for enantioselective ketone reduction available to the organic chemist.



(13)

Development of Efficient Diels-Alder Catalysts

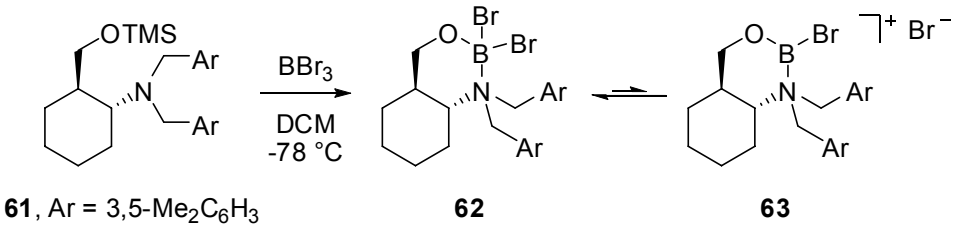
In further attempts to apply boron-based Lewis acids to other reactions, Corey focused on a different mode of decreasing electron density at boron.[22-24] No specific mention is made of any attempts to apply the borane-activated oxazaborolidines **54** to the Diels-Alder reaction, but the use of BH_3·THF as an additive would not be likely to succeed for the desired reaction where one of the substrates is a diene; hydroboration could compete with the cycloaddition. Instead the initial work toward developing an enantioselective Diels-Alder reaction with borane catalysts applied an *N*-sulfonyl oxazaborolidine (**57**) from the parent amino acid. The electron-withdrawing groups at nitrogen and oxygen likely play a similar role as did BH_3 in the CBS reduction by enhancing the Lewis acidity of this catalyst (**57b**: $\delta^{11}B$ = 34 ppm, close to the chemical shift of borane-complexed catalyst **54b** but also to the parent oxazaborolidines **53**). These oxazaborolidines are highly active catalysts, allowing reaction of 2-substituted acroleins with cyclopentadiene within 2 h at -78 °C.



(14)

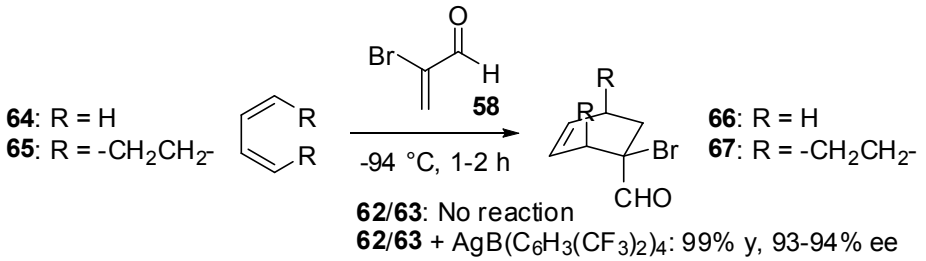
The tethered indolyl group was considered important for organizing the complex, with charge-transfer complexation thought to occur between the dienophile and this electron-rich arene. The strongest evidence for this interaction was a red-orange color that develops on addition of 2-bromoacrolein (**58**) to catalyst **57b** (eq 14) and fades upon warming but returns on cooling the solution.[23b] In the proposed conformation of dienophile-catalyst complex (**59**) the indolyl group blocks one face of the dienophile, directing the diene to the other face and resulting in high facial selectivity (200:1) for the cycloaddition with cyclopentadiene. Additional evidence for this π -π interaction came from a systematic variation of the tethered arene by the Scheeren group; this study found the expected decrease in enantioselectivity using catalysts with less electron rich aryl groups.[25]

A limitation of the catalyst class related to **57** was the substrate scope; most applications involve only cycloaddition of a dienophile with the highly reactive cyclopentadiene. Surmounting this challenge required the development of a "super-reactive" chiral Lewis acid catalyst, a borenium ion.[26] To that end, Corey reported that reaction of the protected chiral amino alcohol **61** with BBr_3 in DCM resulted in cleavage of the silyl ether and formation of a boracycle (**62**). This tetravalent boracycle was in equilibrium with the cationic **63**, an equilibrium that was observed to shift toward the borenium salt in the presence of excess BBr_3 or silver tetrakis(3,5-bis-trifluoromethyl-phenyl)borate. The additives react with the bromide ion forming BBr_4 or the tetraarylborate salt of **63**, respectively. Characterization of these salts was hindered by decomposition of the catalyst mixture at temperatures above -60 °C, even without the added BBr_3 or silver borate. Fortunately, either method for catalyst preparation was effective for promoting the Diels-Alder reaction at temperatures as low as -94 °C within



61, Ar = 3,5-$Me_2C_6H_3$ **62** **63** (15)

1 h. The substrate scope was successfully expanded to the less reactive 1,3-butadiene (**64**) and 1,3-cyclohexadiene (**65**) by using the tetraarylborate salt of **63** prepared by the addition of the silver salt to **62**. In all cases, cycloadducts were obtained in high yields and optical activity (eq 16).



62/**63**: No reaction
62/**63** + $AgB(C_6H_3(CF_3)_2)_4$: 99% y, 93-94% ee (16)

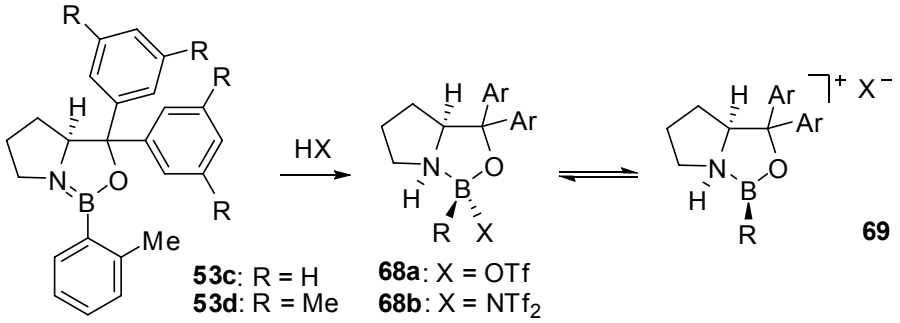
Limited use was made of ^{11}B NMR spectroscopy in this report. It was noted that the addition of excess BBr_3 (up to 1.6 equiv) to **61** generated BBr_4^- as observed by ^{11}B NMR and that the formation of this anion increased as expected with the greater amounts of BBr_3 added. No mention was made, however, of the ^{11}B NMR signal for either **62** or **63**. The chemical shift should be indicative of the coordination environment at boron and would have been an important piece of evidence for formation of this highly Lewis acidic species. The lack of reported data for the electrophilic boron atom is not commented upon, but may be explained by a phenomenon that has been studied for ^{11}B as well as ^{14}N and other quadrupolar nuclei.[27,28]

Nuclei with spin numbers $I > 1/2$ are quadrupolar, having an electric field that is not spherically symmetrical. The fluctuations in the orientation of the resulting electric field gradient due to molecular motion in the liquid state allows a mechanism for nuclear

spin relaxation. This quadrupolar relaxation can be so fast that some nuclei, such as ^{37}Cl, cannot be observed by NMR spectroscopy under typical conditions because peak width is inversely related to relaxation time. The relaxation time for quadrupolar nuclei has been demonstrated to increase with increased temperature in this way, insofar as the quadrupolar relaxation is the dominant relaxation mechanism. The rate of quadrupolar relaxation is proportional not only to a term describing the magnitude and direction of the electric field gradient but also to the correlation time characterizing the reorientation of this gradient (related to molecular motion). The rate of reorientation has been measured in certain cases[27b,28] and was found to increase with temperature. The time the molecule spends in any given orientation, the correlation time, thus decreases with increased temperature, and the rate of quadrupolar relaxation decreases with it. This results in sharper ^{11}B NMR signals at higher temperatures, or the inability to detect the often broad signals particularly at lower temperatures such as Corey used in his studies of **63**. The more symmetrical BBr_4 anion is less sensitive to this quadrupolar relaxation since molecular symmetry results in an electric field closer to spherical symmetry. This is the reason why Corey was able to observe formation of BBr_4^- even at -60 °C.

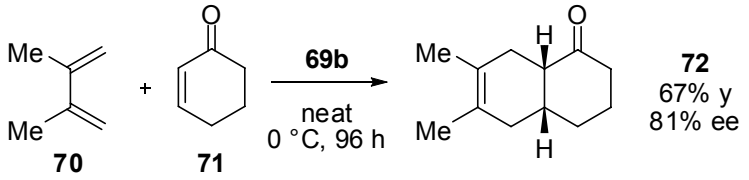
Developing the concept of borenium ion catalysis further, Corey reported that activation of **53c** or **53d** with the strong Brønsted acid CF_3SO_3H (triflic acid, TfOH) gave a powerful catalyst for the Diels-Alder reaction.[29] Even cycloaddition of acroleins to the less reactive 1,3-butadiene (**64**) and 1,3-cyclohexadiene (**65**) were possible at -78 °C (eq 16), although full conversion required 24 h. This puts the catalytic activity using TfOH activation between that of **62**/**63** (no reaction with either **64** or **65**) and that of the tetraarylborate salt of **63** (reactions of **64** and **65** complete within 2 h at -94 °C). Observation of the activated catalyst by ^1H NMR at low temperature (-80 °C) provided

evidence to rationalize this intermediate catalytic efficiency. Peaks progressively downfield from the precatalyst **53** that were assigned to **68a** and **69a**, respectively, were observed in a ratio of 1.5:1 at this temperature. Furthermore, the sharp peaks indicated slow interconversion that became fast on the NMR time scale at 0 °C. No comment was made regarding the ^{11}B NMR spectrum of **69a** even though this catalyst did not decompose even at 0 °C. The equilibrium between **68a** and **69a** may have hindered such efforts.



(17)

Further exploration with the TfOH-activated catalyst system showed that this more reactive borenium ion allowed a greater reaction scope.[30] Oxazaborolidinium ion **69a** was effective for cycloadditions even with somewhat less reactive dienophiles like α,β-unsaturated esters and ketones. The scope was still somewhat limited to fairly reactive substrates. Attempts to catalyze slower reactions with **69a** at higher temperatures were hindered by the instability of **69a** because its decomposition was problematic even



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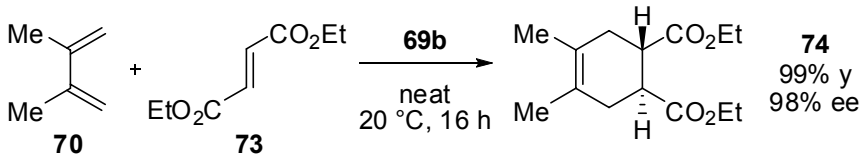

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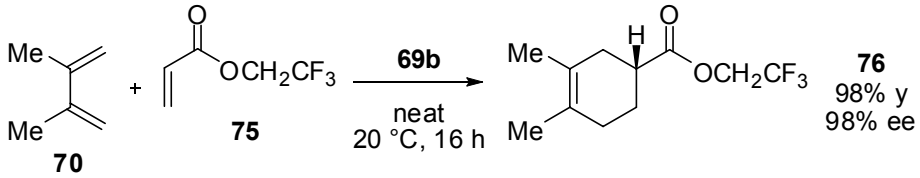
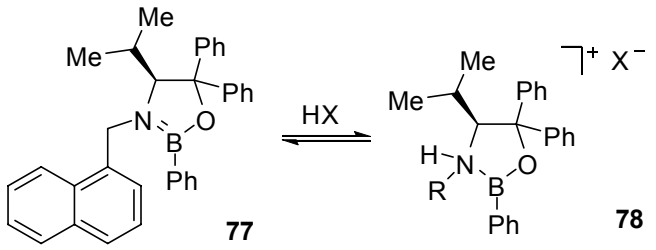


(20)

at 0 °C. Activation with bis(trifluoromethyl)sulfonimide ($HNTf_2$) gave a slightly higher ratio of **69b** and **68b** (1:1.2 compared to 1:1.5 for **69a**/**68a**) by ^{1}H NMR assay at -80 °C.[31] More importantly, this catalyst was stable even at rt, allowing the reaction of cyclic lactones and ketones with less reactive dienes like 2,3-dimethyl-1,3-butadiene (**70**, eq 18). The reaction of **70** with diethyl fumarate (**73**, eq 19) or trifluoroethyl acrylate (**75**, eq 20) was also effective with catalyst **69b**.

A carbon-based strong acid with a bulky conjugate base was also tested for activation of oxazaborolidine-based Lewis acids.[32] Yamamoto did a direct comparison of four different Brønsted acids for activation of **77**, proposed to form borenium ions **78** (eq 21). The cycloaddition of cyclopentadiene with ethyl acrylate (**79**) was used as a test reaction for this purpose (Table 1-3). It was found that to the extent that reaction occurred with any of these activated catalysts, it occurred with high enantioselectivity. Significantly higher yields of product **80** were obtained by activation with Yamamoto's acid ($HC(C_6F_5)Tf_2$), consistent with previous work demonstrating that the counterion of **78d** is more weakly coordinating than TfO^- or even Tf_2N^-.[32b] No attempt to verify this by NMR assay was discussed however. In fact, none of the catalysts **78** nor Corey's

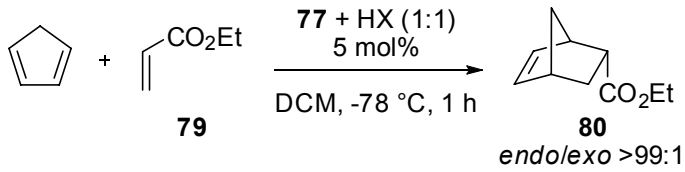
borenium ions **69** have been characterized by ^{11}B NMR spectroscopy. Perhaps the lack of ^{11}B NMR data for these proposed borenium ions reflects attempts to observe cations such as **78** (or Corey's **69** or **63**) at low temperature, conditions that favor quadrupolar relaxation, while instability prevents observation at higher temperatures which might



77 **78** (21)

produce a sharper peak. Also, there is no discussion of the stability of **78** at ambient temperature, although its use at -78 °C might imply instability at higher temperatures. In contrast, **69a** is observed by ^{1}H NMR at 0 °C, and **69b** is still catalytically active at 20 °C.

Table 1-3. Comparison of Brønsted Acids for Activation of **77** as a Diels-Alder Catalyst



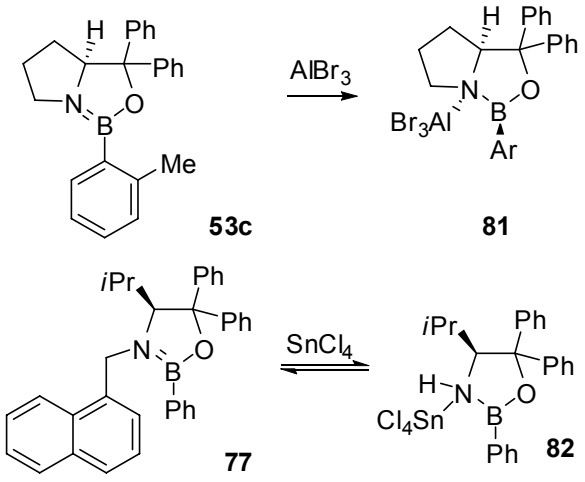
79 **80**
endo/*exo* >99:1

entry	HX	yield[a]	ee[b]
1	MsOH	NR[c]	-
2	TfOH	30%	97%
3	Tf_2NH	43%	97%
4	$Tf_2(C_6F_5)CH$	73%	>99%

[a] By ^{1}H NMR assay using $MeNO_2$ as an internal standard. [b] Enantiomeric excess determined by GC. [c] No reaction.

Finally, two recent reports have returned to the concept applied in the CBS reduction, activation of the oxazaborolidine with a neutral Lewis acid. Again, in these cases the active catalyst is a neutral structure, but it includes what could be referred to as a borenium moiety. Since both substrates in the Diels-Alder reaction are neutral, the lack

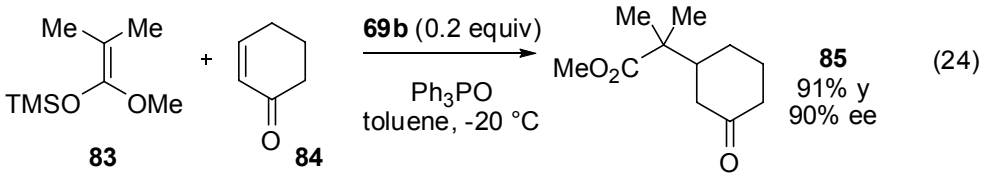
of charge in the promoter should not affect the reaction rates in any way. Activation of Corey's **53c** with $AlBr_3$ in a 1:1 stoichiometry gave a highly reactive catalyst.[33] Complex **81** was effective for promoting the Diels-Alder cycloaddition even with less reactive substrates, and using catalyst loadings as low as 4 mol%. This contrasts with the 10-20 mol% loading needed for similar substrates using **53c** activated with HOTf. The increased turnover of **81** was rationalized by the bulk of the $AlBr_3$ Lewis acid preventing product inhibition of the catalyst. Another interesting recent example of this concept is the activation of Yamamoto's **77** with $SnCl_4$.[34] This Lewis acid was an effective activator even at stoichiometries as low as 1:4 ($SnCl_4$ relative to **77**). This finding prompted a study of the effect of Lewis basic impurities on the catalytic efficiency of **82**. Little change in yield or ee was observed on addition of water, iPrOH, EtOAc or even DMF to the reaction mixture. Demonstrating this advantage, a number of Diels-Alder products were obtained in high yield and ee performing the reaction with catalyst **82** in unpurified DCM at -78 °C open to atmosphere. In these cases, the active species (**81** and **82**) were characterized by ^1H NMR spectroscopy, but ^{11}B NMR data corroborating the electron deficiency at boron were not provided.



(22)

(23)

The activated oxazaborolidine-based catalysts presented here are highly electrophilic, promoting facile reactions with carbonyl substrates at low temperatures with high enantioselectivity. The Tf_2NH activated catalyst (**69b**) has also been applied to the Mukaiyama-Michael reaction (eq 24),[35] but related catalysts have not yet been reported for other reactions. Considering the vast number of reactions of carbonyl substrates, and considering the well-defined manner in which carbonyls coordinate to borenium ion equivalents, this catalyst system is ripe for further exploitation.

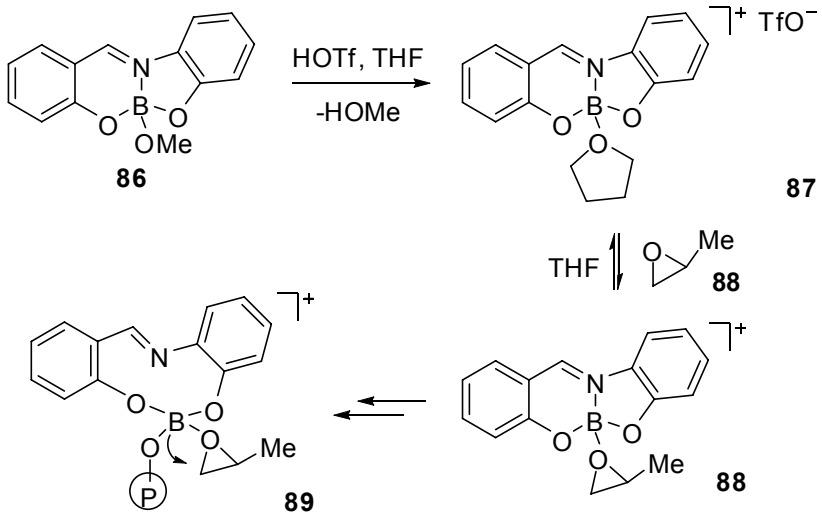


(24)

Other Applications of Boron Cations

Applications of boron cations are sparse apart from the powerful oxazaborolidine-derived catalysts presented in the previous section, but a few will be highlighted here. Only one other example was found of a boron cation being used catalytically. Protonation of neutral, tetravalent precursor complex **86** with TfOH in the presence of THF generates cation **87**.[36] The presence of bound THF was suggested by ^1H NMR data and confirmed by elemental analysis of the salt. The ^{11}B NMR signal at δ 3.9 ppm is also consistent with a tetracoordinate boron center. This species is novel as the first reported boron cation possessing a tridentate ligand, and it is also interesting as a solvent-coordinated boronium ion that could easily lose either the weakly bound imine nitrogen ligand or solvent to generate a borenium intermediate. Cation **87** is active for the polymerization of propylene oxide (**88**, Scheme 1-2), although the oligomers generated were of lower molecular weight than those formed by catalysis with commercially available Bu_2BOTf or with cationic $[salenAl(MeOH)_2]^+BPh_4^-$. The authors propose

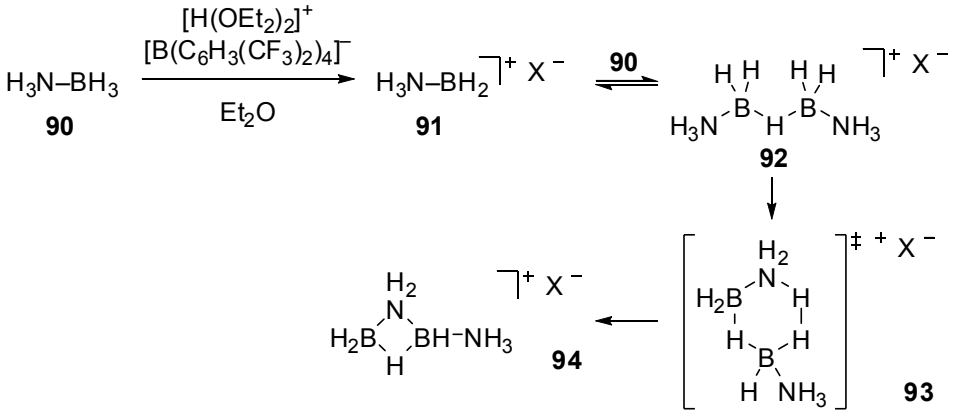
Scheme 1-2. Formation of Boronium Ion **87** and Pathway for Polymerization Catalysis



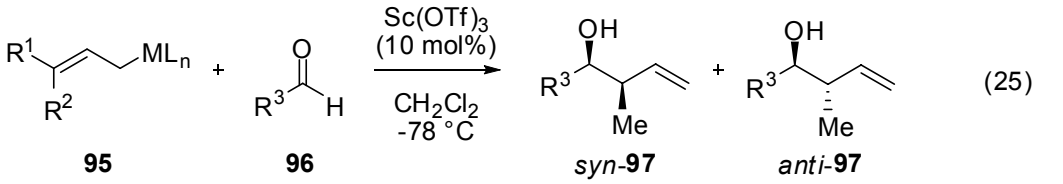
chain propagation via **89**, the product of borenium ion capture and activation of a propylene oxide monomer.

Borenium ions were also implicated as intermediates in the dehydrogenative polymerization of ammonia borane (**90**).[37] A solvent-coordinated cation, boronium ion **91** ($\delta^{11}B$ = 0.2 ppm), was isolated but its potential to lose solvent and coordinate to another molecule of **90** to activate it for intramolecular loss of H_2 was proposed. The intermediacy of hydride-bridged cation **92** was proposed by the authors, and a computational study of the proposed intermediates validated the proposal. Calculations using DFT give a gas-phase stabilization of 47 kcal/mol on forming the hydride bridge in **92** from **91**. This is of note in light of our discovery of similar hydride-bridge stabilization of boron cations to be presented in Chapter 2. The pathway for hydrogen loss from ammonia borane with the more common activators TfOH and $B(C_6F_5)_3$ could be similar to that shown in Scheme 1-3 according to the authors. A better understanding of hydrogen generation could assist in the quest for alternative fuel source using **90** for hydrogen storage.

Scheme 1-3. Proposed Pathway for Initiation of Dehydrogenative Polymerization of **90**

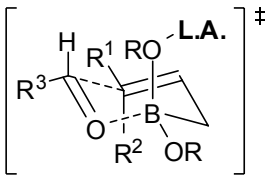


One other example has been reported where a borenium subunit is proposed in the reaction pathway but without its direct observation.[38] In a recent study on the $Sc(OTf)_3$-catalyzed addition of allylboronates to aldehydes it was shown that catalysis does not occur via carbonyl activation by Lewis acid coordination. The reaction of (*E*)- or (*Z*)-crotylboronates (**95a** or **b**) proceeds with high diastereospecificity even under $Sc(OTf)_3$ catalysis (eq 25), implying a closed transition state like that invoked for the uncatalyzed reaction of allylboron reagents. The analogous addition of crotylstannanes (**95c** and **d**) proceeds with high diastereoselectivity but no stereospecificity, as expected for reaction via an open transition state with the Lewis acid coordinated to aldehyde **96**. This led the authors to propose closed transition state **98**, in which the Lewis acid increases the electrophilicity of boron by coordination to one of its alkoxy substituents. This is reminiscent of the activation of oxazaborolidines as Lewis acids by coordination of a Lewis acid to the nitrogen substituent at boron. Additional evidence for this mode of activation is the failure of $Sc(OTf)_3$ to catalyze the addition of an allylic dialkylborane (**95e**, ML_n = –BBN, $R^1 = R^2$ = Me).



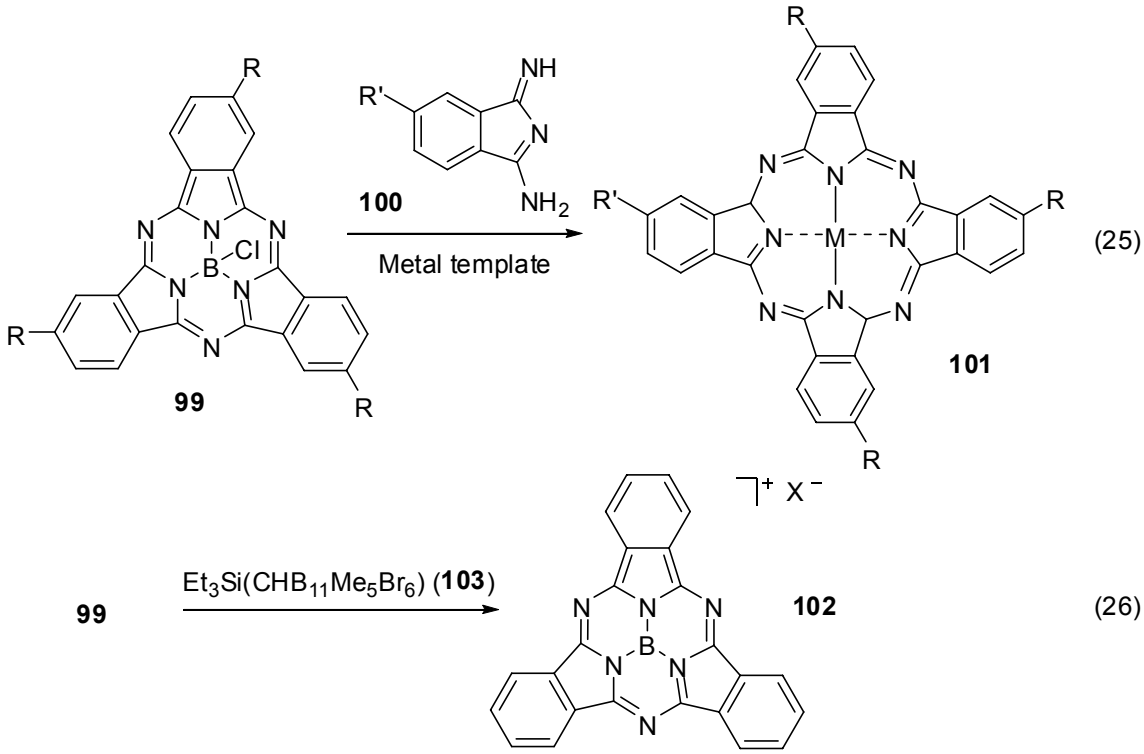
95 **96** *syn*-**97** *anti*-**97** (25)

95a, $ML_n = B(OR)_2$, R^1 = H, R^2 = Me: 98:2
95b, $ML_n = B(OR)_2$, R^1 = Me, R^2 = H: 2:98
95c, $ML_n = SnBu_3$, R^1 = H, R^2 = Me: 98:2
95d, $ML_n = SnBu_3$, R^1 = Me, R^2 = H: 98:2



98

Finally, boron complex **99** is commonly used as a substrate for ring expansion to prepare phthalocyanines **101** with control over formation of mixed tetramers.[39] Condensation of two different diiminoisoindoles (**100**) typically results in the statistical mixture of products. However subphthalocyanine **99** can be prepared from three identical isoindole units and the reaction with a different isoindole results in controlled ring expansion to the phthalocyanine, potentially useful for its optical and electronic properties. This process has been proposed to occur via loss of chloride and coordination of an isoindole, but no boronium or borenium intermediates have been observed in the course of the reaction. Recently Reed prepared a borenium ion (**102**) related to **99** with the weakly coordinating carborane anion.[40] The solubility of **102** was too low for ^{11}B and ^{13}C NMR spectroscopy, but the formation of **102** was confirmed by solving the X-ray structure of this crystalline compound. The potential reaction of **102** with an isoindole **100** was not probed, so this does not constitute an application of a borenium ion in synthesis. It does support the proposed conversion from **99** to **101**, however, and this discovery could lead to higher yields and better regiocontrol for phthalocyanine formation under mild conditions.



Summary

The last 50 years have seen great advances in the field of boron cations. Most reports have focused on the preparation of tetravalent boronium cations, species that are stable due to a complete coordination sphere at boron. Advances have been made that allow the isolation and characterization of trivalent borenium and even the divalent borinium ions. These compounds have been stabilized by ligands which can both donate electron density into boron and sterically shield the boron atom. This comes at a cost to reactivity, and the result is that such species will be difficult to apply as promoters of organic transformations. Indeed, many of the borenium and borinium ions that have been characterized are of interest purely for studies of their fundamental properties, although these studies can provide information useful to the optimization of boron cations used as Lewis acids. The applications of borenium ions which have been developed in the last 20

years demonstrate that these can be powerful catalysts, providing tremendous rate enhancements.

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Chapter 2

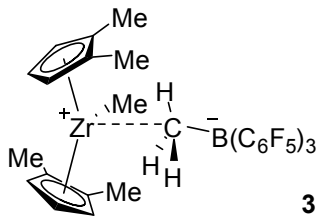
Electrophilic Activation of Lewis Base Complexes of Borane with Trityl Tetrakis(pentafluorophenyl)borate and Application to Hydroboration

Introduction – Trityl Activation to Generate Reactive Cationic Species

Lewis acid cocatalysts have long been employed with transition metal polymerization catalysts, particulary with alkyl metallocene-based systems.[1] These cocatalysts, typically aluminum-based, were thought to enhance the metallocene's activity by promoting the formation of cation-like metal centers. The activation of zirconocene dimethyl complexes with $B(C_6F_5)_3$ (**1**), a more potent Lewis acid,[2] eventually allowed the isolation and more thorough characterization of one of these activated, cation-like catalysts.[3] The catalytic activity of complexes **2**-**4** for ethylene and propylene polymerization was demonstrated to confirm zirconocene activation by **1**. Spectroscopic data suggested transfer of a methyl to boron with formation of cationic zirconium (eq 1), and crystallographic characterization confirmed this for **3**, showing a weak interaction of the cationic zirconium center with the $MeBAr_3$ anion via a bridging methyl.

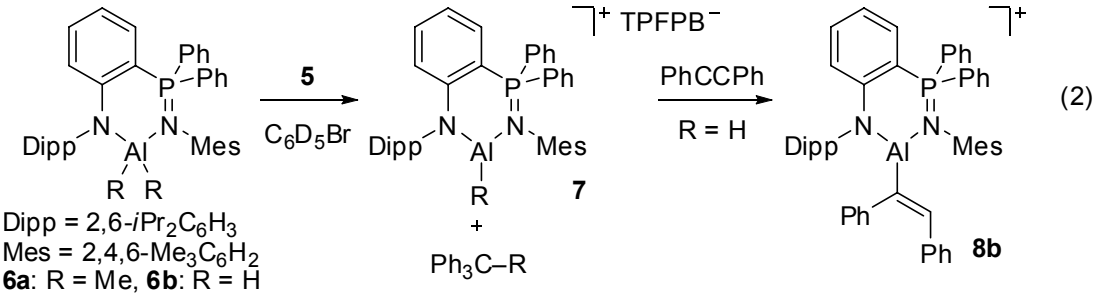
$$L_2ZrMe_2 + \mathbf{1} \xrightarrow[\text{pentane}]{C_6H_6 \text{ or}} L_2ZrMe^+ MeB(C_6F_5)_3^- \quad (1)$$

2: L = η^5-C_5H_5
3: L = η^5-1,2-$(Me)_2C_5H_3$
4: L = η^5-C_5Me_5



3

In a study of analogous organoactinides, Marks found that a marked increase in catalytic activity for polymerization as well as hydrogenation resulted from using the very weakly coordinating $B(C_6F_5)_4$ anion.[4] Around the same time that Marks had demonstrated activation by ammonium salts of this anion, Chien reported a successful activation of *rac*-ethylenebis(indenyl)dimethylzirconium with a triphenylcarbenium salt of this anion ($Ph_3C^+ {}^-B(C_6F_5)_4$, TrTPFPB, **5**).[5] The zirconium precatalyst reacts with the trityl cation by methyl transfer in a manner analogous to activation by **1**, but in this case forms an unreactive triphenylethane byproduct with a stable C–C bond. The resulting cationic zirconium catalyst was shown to be very active for olefin polymerization.



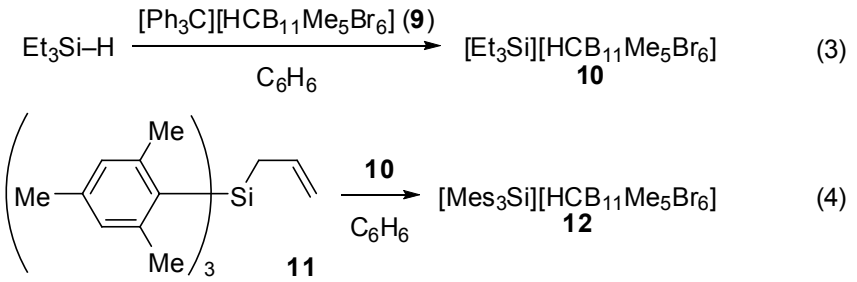
Dipp = 2,6-*i*Pr$_2$C$_6$H$_3$
Mes = 2,4,6-Me$_3$C$_6$H$_2$
6a: R = Me, **6b**: R = H

(2)

Trityl cation has also been used as a potent hydride acceptor to generate reactive cationic species from neutral hydride donors. For example, cationic aluminum species **7a** and **7b** were prepared by the action of TrTPFPB on methyl- or hydrido-aluminum complexes **6a** and **6b** (eq 2).[6] The potential of these cationic aluminum species as catalysts for polymerization and other reactions was implied by the insertion of an alkyne into the AlH bond of **7b**; the methylaluminum cation **7a** was unreactive toward diphenylacetylene even after prolonged heating. Hydride abstraction from M–H bonds of molybdenum and tungsten complexes has also been shown to generate cationic species that cleave H_2 to generate metal dihydrides.[7] These metal dihydrides are active as

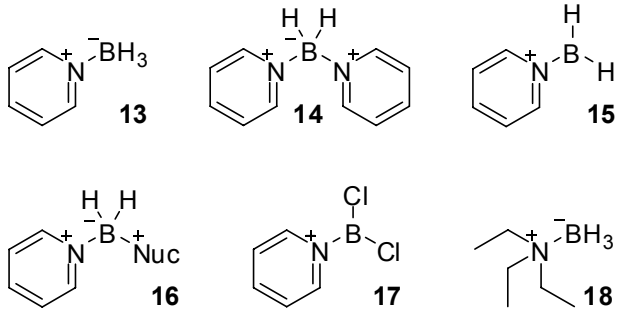
catalysts for ketone hydrogenation by an ionic mechanism, enabling a chemoselective ketone reduction at low pressures (<4 atm H_2).

Hydride abstraction by trityl cation has found numerous applications in the search for a free tricoordinate silyl cation.[8] In an early attempt by Corey to generate such a cation, silyl hydrides were found to react with trityl halides, but the result was formation of a silicon–halogen bond.[9] Recent work has shown that TrTPFPB is effective for generating a more active silicon electrophile,[10] but the $B(C_6F_5)_4$ anion is still too coordinating to allow formation of a trialkylsilyl cation. Ultimately it would require a sterically hindered silicon environment to allow the formation of a free silicon cation, but the trityl cation is itself too bulky to react with silicon donors like trimesitylsilane.[9] While the first crystallographically characterized free trialkylsilyl cation (**12**) was formed by allyl transfer from the neutral silane to a carborane-coordinated triethylsilyl cation (**10**, eq 4), a hydride abstraction by trityl cation was utilized in the preparation of this intermediate activator (eq 3).[11]



In an early example of B–H bond activation with the trityl cation, Benjamin et al. reported the reaction of $Ph_3C^+ {}^-BF_4$ with pyridine borane (**13**) in the presence of pyridine to give $Py_2BH_2^+$ (**14**, a four-coordinate boron cation, bis(pyridine)boronium according to the conventional nomenclature discussed in Chapter 1),[12] as well as Ph_3CH.[13] A three-coordinate boron cation, the (pyridine)borenium ion **15**, was later proposed as an

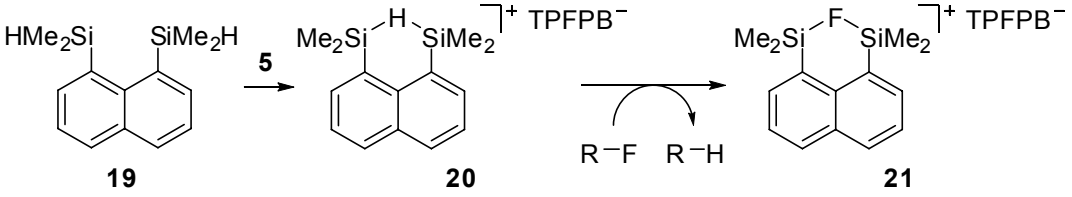
intermediate,[14] but no attempts to detect **15** or other primary borenium ions of the type $L{\cdot}BH_2^+$ have been reported. Despite formal charge assignment in **15** to nitrogen, computational studies of this cation show significant positive charge character at the boron atom,[15] belying a shortcoming of formal charge convention. For the remainder of this chapter formal charges will not be drawn unless necessary for discussion.



The trivalent boron cation was expected to be highly electrophilic at boron allowing chemistry triggered by interaction with weakly nucleophilic n or π electrons, as in **16**. Hydroboration by both intra- and intermolecular pathways has been explored previously in our research group,[16] involving the interaction of π electrons with an activated, albeit still tetravalent, boron electrophile. Applications of TrTPFPB activation to olefin hydroboration will be discussed later in this chapter. Arene borylation,[17] requiring interaction with less nucleophilic aromatic π electrons, requires the more potent electrophile created by the TrTPFPB activation discussed herein.[18] The successful application to a directed electrophilic borylation will be the focus of Chapter 3.

Hydrodefluorination[19] is another interesting potential use for the highly electrophilic boron cations generated here. Activation of triethylsilane by catalytic TrTPFPB has been shown to initiate hydrodefluorination of a number of different trifluoromethylarenes, generating the fully proton substituted toluene derivatives in all cases with fluorotriethylsilane as the byproduct.[19b] A hydride-bridged disilyl cation (**20**),

formed by hydride abstraction from **19** with TrTPFPB, was also found to be effective for hydrodefluorination (eq 5).[10] Triethylsilane regenerates **20** from the fluoride-bridged product **21**, allowing a catalytic cycle in which triethylsilane is the terminal hydride source for reduction of a C–F bond. The marked fluorophilicity of boron makes a cationic boron electrophile an exciting new candidate for this chemistry that has not yet been explored.



19 **20** **21** (5)

Observation of *H*-Bridged Cation

Optimization of TrTPFPB Activation

Borenium ion **15** is isoelectronic with benzyl cation, and should benefit from significant π delocalization. We therefore attempted to observe **15** using NMR methods, although we recognized that this highly electrophilic species may exist as the solvent-coordinated cation (**16**, Nuc = solvent), technically a boronium ion. To avoid confusion, this distinction in nomenclature and structure will be generally left unspecified, and **16** will be considered equivalent to the free borenium ion **15**. While the ^{11}B NMR spectrum of **13** activated by TrTPFPB[5,20] in CD_2Cl_2 (rt) has a major peak (among several) at δ 44 ppm, well within the range where trisubstituted borenium ions have been reported,[12] the signal is not coupled to protons and cannot be due to **15** nor to the solvent adduct (**16**, Nuc = CD_2Cl_2). We have assigned this signal as $PyBCl_2^+$ (**17**) based on ^{11}B chemical shift comparisons and a pyridine quench to form the known $Py_2BCl_2^+$.[21] The formation of this *B*-chlorinated byproduct will be discussed later.

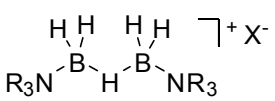
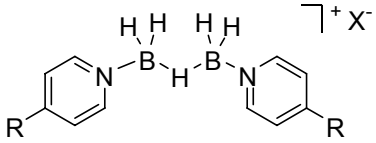
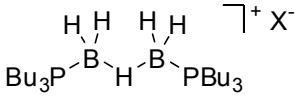
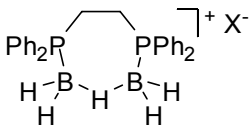
Earlier work by Julia Clay had suggested that activation of **13** by TrTPFPB occurred by pyridine transfer to the electrophile rather than hydride transfer.[22] The evidence for this was that after quenching a reaction of **13** activated by TrTPFPB with methanol after 1 h at rt, none of the expected Ph_3CH was found in the crude product mixture. However, reaction of $Et_3N{\cdot}BH_3$ (**18**) under the same conditions did generate Ph_3CH, although it was isolated in only 70% yield. This led us to suspect that the Ph_3CH that formed, assumed to be inert, was in fact decomposing in the presence of these potent electrophiles. A proposed decomposition pathway will be discussed in detail later, but the immediate concern was to minimize it. Quenching either of these reactions within 1 min after TrTPFPB addition resulted in quantitative recovery of Ph_3CH, confirming that the absence of this product in the original experiment was due to its decomposition, not to activation by a pathway other than hydride transfer. Alternatively, addition of TrTPFPB to either **13** or **18** cooled to -78 °C, quenching after 1 h at this temperature, also allowed isolation of Ph_3CH in >95% yield.

Taking advantage of the slower decomposition at lower temperatures, the reaction of TrTPFPB with **13** or **18** (1:1 mol ratio) was performed at -78 °C in CD_2Cl_2, monitoring by NMR spectroscopy. This procedure gave little decomposition, and better spectra were acquired from activation of $Et_3N{\cdot}BH_3$ (**18**). Samples were allowed to warm to -20 °C for ^1H and ^{11}B NMR analysis, conditions that reduce the line broadening observed especially for the ^{11}B signals at -78 °C.[23] The relaxation of the ^{11}B nucleus (spin number $I = 3/2$) is dominated by quadrupolar relaxation, a faster process at lower temperatures[23b] as explained in Chapter 1. This fast relaxation at low temperatures results in broader peaks since peak width is inversely proportional to the spin relaxation time, making their detection difficult. The temperature chosen (-20 °C) was therefore a compromise

between minimizing line broadening (requiring higher temperatures) and minimizing decomposition (requiring lower temperatures) of the species we were trying to observe.

Surprisingly, ^{1}H NMR assay indicated complete conversion of **18** but only ca. 50% conversion of trityl cation, as evidenced by a 1:1 ratio of Ph_3CH to unreacted Ph_3C^+. A highly shielded peak appeared at δ ^{1}H = -2.6 ppm that integrated for 1H relative to Ph_3CH. By ^{11}B NMR, signals were observed for $^{-}B(C_6F_5)_4$ (sharp singlet at -17 ppm) and for a new broad peak at -3 ppm. Warming the sample to rt resolved coupling to two protons for this peak, but did not result in greater conversion of trityl cation prior to quenching with methanol, and did not produce signals in the trivalent boron region. Qualitatively similar results were obtained when **13**, **18** or other Lewis base borane complexes were treated with 50 mol% TrTPFPB (Table 2-1), although **13** still produced **14** and other contaminants along with **24**. In each example, conversion to a dominant product having a high field ^{1}H NMR signal (δ 0.5 to -3.7 ppm) was observed.

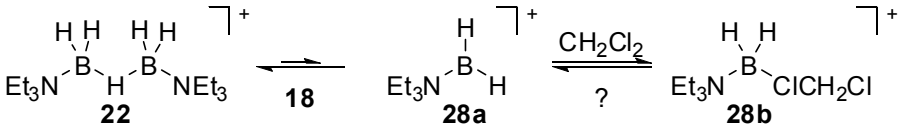
Table 2-1. ^{1}H and ^{11}B NMR Data for Activated Borane Complexes[a]

		$\delta^{1}H^{b}$	$\delta^{11}B$
	**22**: R = Et	-2.6	-3
	23: R = Me	-1.9	0
	**24**: R = H[c]	0.5	-2
	25: R = NMe_2	0.1	-1
	**26**	-3.7	-27
	**27**	-2.2	-27

[a] In CD_2Cl_2 at -20 °C. In all cases X^- = TPFPB. [b] Bridging hydride signal, ppm. [c] Contaminated with **10** and unidentified pyridinium impurities.

Structural Analogies to Other H-Bridged Species

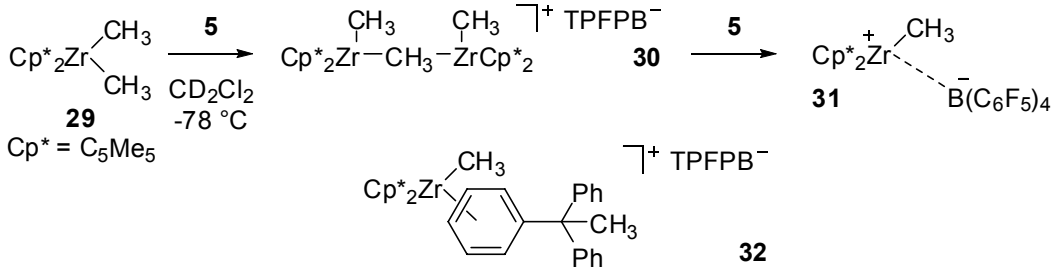
The above data are consistent with the initial formation of transient borenium ion intermediates that undergo rapid capture by the B–H bond of unreacted substrate to form symmetrical cations **22**-**27**. The key event leading to **22** corresponds to overlap between a nucleophilic B–H σ orbital of $Et_3N{\cdot}BH_3$ (**18)** with the empty *p*-orbital of $[Et_3N{\cdot}BH_2]^+$ (**28a**), or the equivalent displacement of dichloromethane (DCM) from the solvent adduct $[Et_3N{\cdot}BH_2{\cdot}Cl_2CD_2]^+$ (**28b**, eq 6). Coordination of B–H bonds into electrophilic centers to form 3-center, 2-electron (3c2e) bonds is well established,[24] but cationic species with the B–H–B structural motif have not been reported previously. The upfield ^{1}H NMR signals for **22**-**27** are in the range of B–H–B bonds of the closest analogies, neutral structures including diborane[25] as well as the $B_2H_7^-$anion[26a] and Katz's hydride sponge, the anionic bis(dimethylboryl) analogue of **20**.[26b] The hydride-bridged structure **22** is also consistent with the -3 ppm ^{11}B NMR chemical shift.[26,27] The "dimeric" structure of **22** explains the stoichiometry, with 50 mol% of the TrTPFPB required for reaction with **18**. Attempts to confirm this structure by X-Ray crystallography were unsuccessful, possibly due to the highly fluorinated anion. This anion was also suspected for difficulties encountered in attempts to crystallize silylium ions, apparently one of the reasons for the use of a carborane-based anion in the study of trimesitylsilylium.[8a,11]



(6)

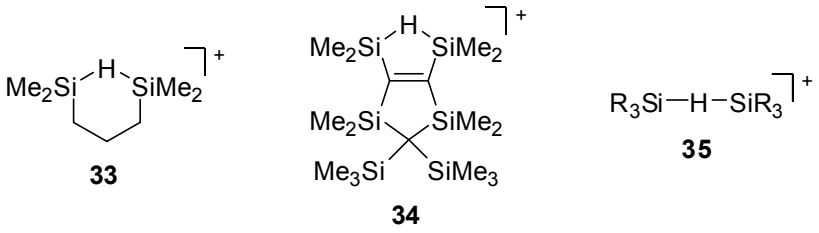
In the absence of nucleophiles, excess TrTPFPB (beyond 50 mol%) did not react with the hydride-bridged products **22**-**27** and did not produce signals that could be assigned to borenium ions.[28] This is in contrast to the reaction of other singly hydride-bridged cationic M–H–M species[4d,29] with trityl cation, a process that typically results in

full conversion to the M^+ cation (M = transition metal).[30] An interesting analogy can be drawn to methyl-bridged cation **30**, part of the ongoing cationic polymerization catalyst studies described above.[31] Initially signals in the ^1H NMR spectrum were taken to suggest coordination of the triphenylethane byproduct to the cationic zirconium center as in **32**.[31a] In a reexamination of this work, the Bochmann group demonstrated that these signals were in fact unreacted trityl cation, due to incomplete conversion of methyl-bridged **30** to free zirconium cation **31** at the low temperatures employed.[31b] Warming the reaction to -40 °C, however, allowed complete methyl abstraction by trityl cation, generating **31** cleanly.



(7)

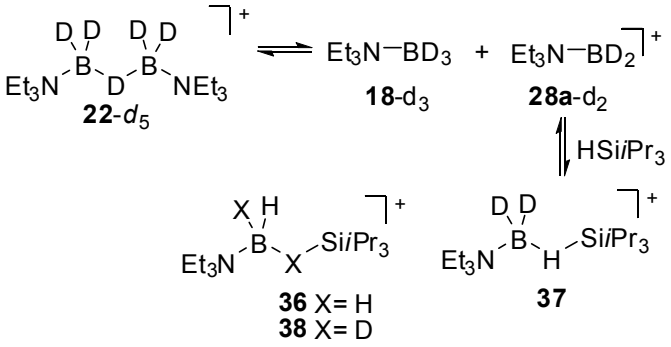
Hydridosilane activation by trityl cation also typically proceeds beyond formation of a hydride-bridged cation. For example, even the internal Si–H–Si 3c2e bond of **20** undergoes further activation, possibly to a highly reactive disilyl cation, upon treatment with TrTPFPB.[10] The only observable products of the activation of **19** with stroichiometric trityl cation are $B(C_6F_5)_3$ and the fluoride-bridged disilyl cation **21**, although the only fluoride source present was the $B(C_6F_5)_4$ anion. Apart from other cyclic hydride-bridged disilyl cations such as **33** and **34**,[32] the only reported case of intermolecular stabilization of a silylium cation with an external Si–H bond (**35**) requires a large excess of silane, suggesting an equilibrium between **35** and solvent- and anion-



coordinated species.[33] In contrast, **22**-**27** were formed in the absence of excess borane complex L·BH_3, and the chemical shifts were not affected by the presence of unreacted L·BH_3. However, the highly electrophilic cations **22**-**27** could not be isolated, and were only observed in solution.

H/D Exchange of Hydrides with Trialkylsilanes

Scheme 2-1. H/D Exchange between **22** and Triisopropylsilane



Given the structural and electronic analogies to silylium cation chemistry,[8] we were interested to learn whether **22** might interact with *i*Pr_3SiH as a potential 3c2e hydride donor. No NMR evidence for an unsymmetrical structure **36** was obtained. However, when **22**-d_5 was generated from **18**-d_3 followed by exposure to *i*Pr_3SiH at rt in CD_2Cl_2 (1 h), H/D exchange was observed in **22** as well as *i*Pr_3SiH by ^1H NMR, ^2H NMR, and MS assay. According to these results, **22**-d_5 dissociates reversibly to release a small amount of the borenium ion **28**-d_2. Reversible formation of a 3c2e bond with *i*Pr_3SiH leads to **37**, and equilibration with **38** provides the pathway for H/D exchange. This experiment was repeated in CH_2Cl_2, and deuteration of the silane was observed by

^{2}H NMR as well as GC/MS. This confirms that **18**-d_3, not solvent, was the deuterium source in these experiments. The symmetrical cation **22** is therefore proposed to function as a source of the highly electrophilic borenium species **28**. We regard these data as strong evidence that monosubstituted borenium ions such as **28a** (or the equivalent DCM adduct **28b**) are viable intermediates.

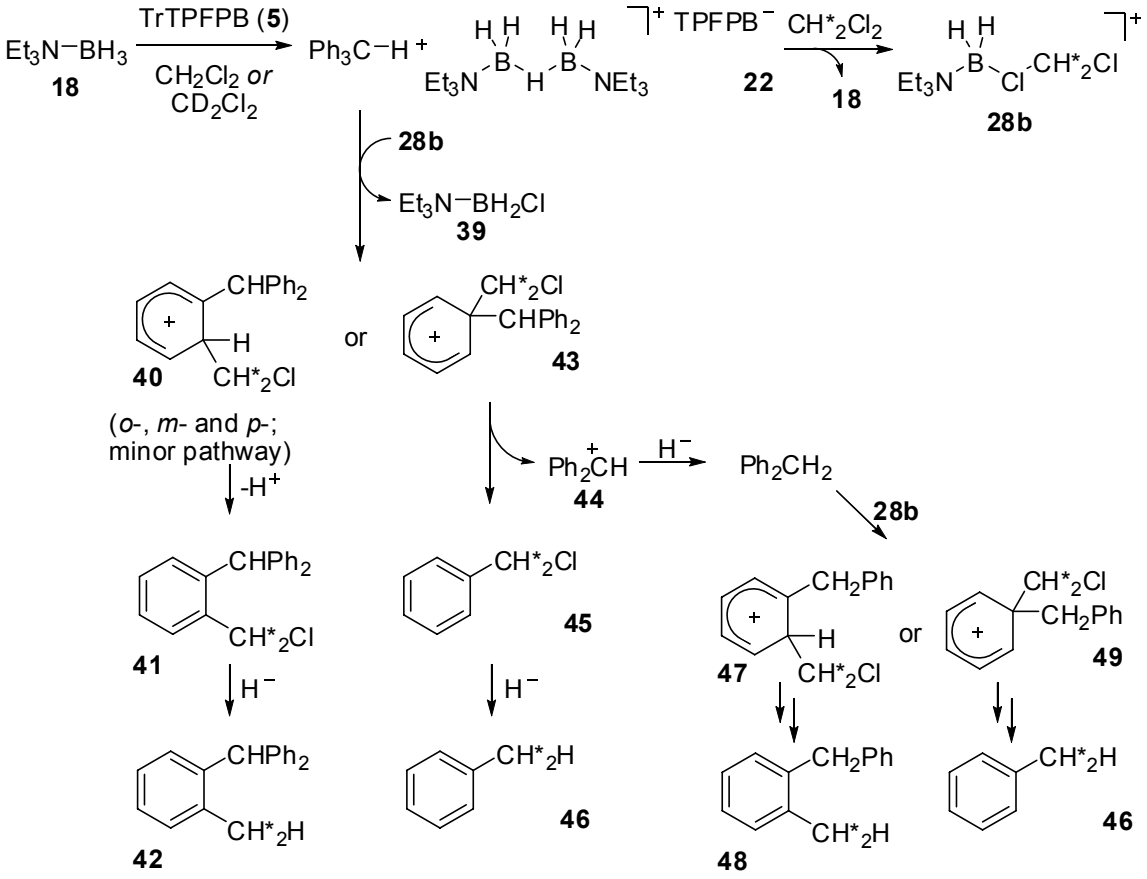
Deuterium incorporation into other trialkylsilanes using **22**-d_5 was also successful, but the resulting deuterated silanes could not be verified by all the means described above for iPr$_3$SiH. Triphenylsilane was examined as a candidate for H/D exchange with **22**-d_5, and after 20 min in the presence of **22**-d_5 the ^{1}H NMR peak for Si-H had decreased in intensity while a peak for the briding hydride of **22** appeared, although equilibrium had not yet been attained. Due to the proximity of the chemical shifts of Ph$_3$Si*H* (5.5 ppm) and dichloromethane (5.32 ppm), ^{2}H NMR could not be used to confirm the deuteration of the silane using CD_2Cl_2 as solvent. The Ph$_3$SiH peak was observed by GC/MS, and its M+1 peak was substantially increased relative to an untreated sample. Triethylsilane also underwent H/D exchange at the silyl hydride on addition to a solution of **22**-d_5, which was confirmed by ^{1}H and ^{2}H NMR spectroscopy. In this case GC/MS could not be used to confirm the ^{2}H enrichhment because of the high volatility of Et$_3$SiH; conditions could not be found where this species comes off the gas chromatograph column sufficiently after the solvent front to allow its analysis by the mass spectrometer.

Solvent-Assisted Decomposition of Triphenylmethane

With a clear picture of the structures formed on addition of **5** to amine boranes, the unexpected decomposition of Ph$_3$CH was studied more closely. Prior literature implicitly assumes that Ph$_3$CH is inert to the potent electrophiles produced by hydride

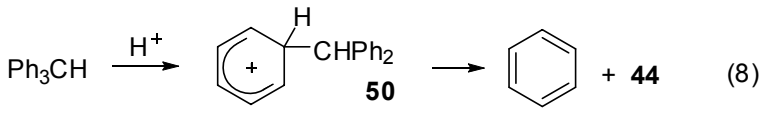
abstraction using TrTPFPB, contrary to our findings at rt. Of the few literature reports that mention the possibility of decomposition, most occur in the presence of a chlorinated solvent, usually DCM.[31b,34] In one interesting example from Bochmann's research group,[34a] a cationic yttrium complex was noted to decompose in chlorinated solvent if the activation was performed with TrTPFPB, but the product of $B(C_6F_5)_3$ activation was stable. This may be due to stabilization of the cationic yttrium product by coordination of the $MeB(C_6F_5)_3$ anion through a bridging methyl, but it is possible that the chloride abstraction from solvent would occur reversibly if not for the presence of Ph_3CH. No mention is made of the fate of this byproduct.

Scheme 2-2. Decomposition of Triphenylmethane in Dichloromethane



Suspecting that Ph_3CH does initially form in all cases of activation of an amine borane complex with TrTPFPB, we began to search for the hydrocarbon byproducts of its decomposition. A reductive quench (Bu_4NBH_4) of the solution obtained from activation of **18** with TrTPFPB (CH_2Cl_2, 1 h, rt) gave Ph_2CH_2 as the major byproduct, along with a complex mixture of hydrocarbons. Analysis by GC/MS revealed benzene, toluene, $MeC_6H_4CH_2Ph$ (**48**), and $MeC_6H_4CHPh_2$ (**42**). The use of CD_2Cl_2 as solvent increased the masses of toluene, **42**, and **48** by 2 amu, indicating solvent incorporation.

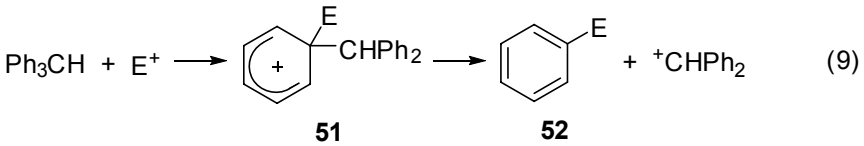
The formation of these hydrocarbons likely occurs from **28b**-d_2 by Cl–C heterolysis, Friedel-Crafts alkylation of Ph_3CH at an *ipso*-carbon via Wheland intermediate **43**,[35a] fragmentation to Ph_2CH^+ (**44**), and trapping by hydride to give Ph_2CH_2 (Scheme 2-2). The heterolytic C–C bond cleavage from **43** would also generate an equivalent of benzyl chloride, which could be reduced by Bu_4NBH_4 to produce the toluene impurity observed. Alternatively, Friedel-Crafts alkylation of Ph_3CH at an unsubstituted carbon leads to the methylated triphenylmethanes (**42**) by a similar pathway, releasing a proton instead of the diphenylmethyl cation **44**. The unusual selectivity of the reaction for substitution at an *ipso*-carbon leading to the major byproduct, Ph_2CH_2, can be explained by the relative stability of diphenylmethyl cation compared to a free proton in the absence of a good base. This proton could also be responsible for the formation of benzene and the more stable **44** by the pathway shown in eq 8. Attack of a chloromethyl cation equivalent on Ph_2CH_2 could lead to another equivalent of toluene by the *ipso*- substitution pathway or to the methylated diphenylmethanes **48** by attack at an unsubstituted carbon.



(8)

The chloroborane adduct **39** was not observed after the hydride quench used here. This would likely be more reactive as a hydride donor toward any of the electrophilic species present (including the unreacted trityl cation) due to the stabilization of a developing empty orbital at boron by resonance donation of lone pairs on chlorine. In the analogous halomethyl cation series, this stabilizing effect is more important than an inductive electron-withdrawing effect of the halide substituent (stability order: $CCl_3^+ > HCCl_2^+ > H_2CCl^+ > CH_3^+$).[35b] This could also explain the earlier observation of $PyBCl_2^+$ (**17**) from activation of **13**. Initial formation of a chloroborane adduct of pyridine via **24** and the solvent adduct **16** (Nuc = CH_2Cl_2) could be followed by another halogen/hydrogen exchange at boron. The $Py{\cdot}BHCl_2$ thus formed gives the relatively stable $PyBCl_2^+$ after hydride abstraction.

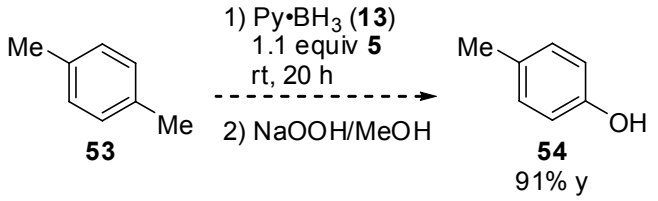
Intermolecular Arene Borylation with Activated Borane Complexes



(9)

Aromatic substitution with electrophiles other than the chloromethyl cation is possible under the reaction conditions (eq 9). Demonstrating this, when the reaction solvent was switched to benzene or toluene, slow formation of Ph_2CH_2 was still observed, indicating the involvement of other sources of E^+ in these solvents. To test the possibility that **22** or **28** can act as E^+, **18** was treated with TrTPFPB in the electron-rich arene, *p*-xylene, as solvent. Oxidative workup after 20 h at rt gave the expected 2,5-dimethylphenol, albeit in <5% yield. This experiment raises the possibility that formation of **51** with E = $BH_2{\cdot}NEt_3$ may also contribute to C–C bond cleavage. Intramolecular reactions from benzylic and homobenzylic amine boranes will be

discussed in the next chapter, but the initial leads for intermolecular aromatic substitution of electrophilic boron are discussed below.

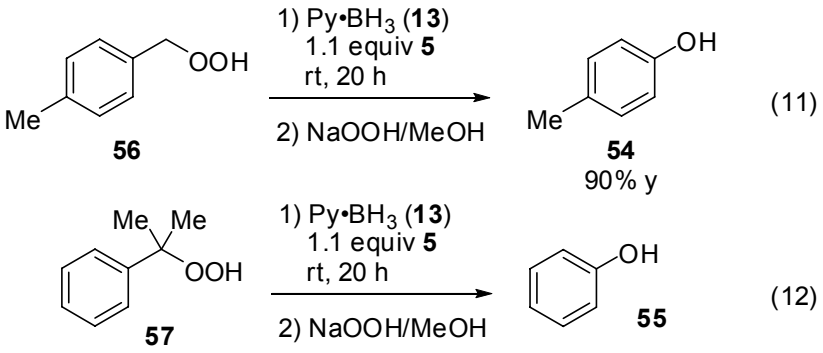


(10)

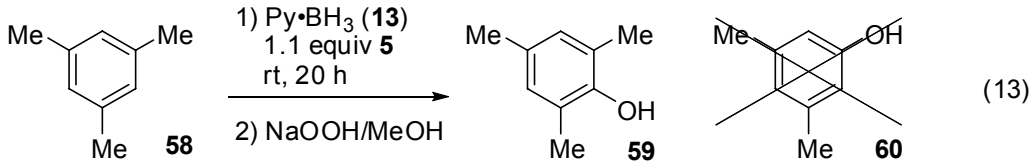
Our initial attempts at electrophilic arene borylation had seemed more promising, but were later shown to indicate the reaction of an impurity in the solvent. The activation of pyridine borane (**13**) in *p*-xylene, chosen because all unsubstituted carbons are equivalent, gave just one product after oxidative workup. Unexpectedly *p*-cresol (**54**), the product of demethylation, was isolated in 91% of the theoretical yield based on **13** (eq 10). Triethylamine and tributylphosphine boranes also produced *p*-cresol after TrTPFPB activation in *p*-xylene but with phenol (**55**) as a byproduct. Initially, this was explained by substitution of triphenylmethane as in eq 9, but later investigations (vida infra) gave a simpler explanation. Activation of amine boranes in mesitylene also gave mixtures of substitution at C–H and C–Me after oxidative workup, but in lower yields.

During the continuing investigation into the intermolecular aromatic substitution reaction, the initial high yields of **54** were not reproducible. The ratio of **55** to **54** decreased as well as the yield of combined phenolic products. Recrystallizing Py•BH_3 and distilling *p*-xylene gave little improvement to the yield and had no effect on the regioselectivity of the substitution, still producing **55** along with **54** in contradiction to the original experiments. It was then noted that the change in regioselectivity, favoring formation of **55**, occurred on switching to a new bottle of *p*-xylene. Using the original sample resulted in a high yield of **54** as before even with purified Py•BH_3. A base

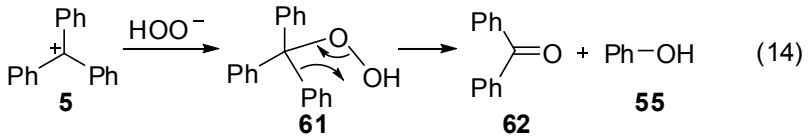
extraction of this *p*-xylene revealed a *p*-methyl-benzyl hydroperoxide (**56**) contaminant that was present in a concentration similar to that of **13** under the conditions of the



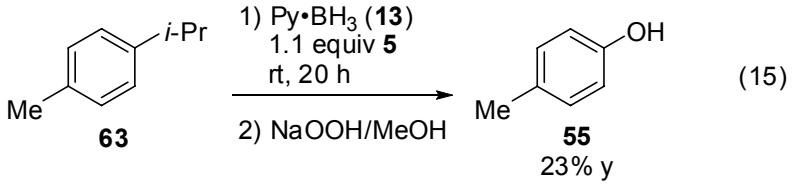
aromatic substitution reactions. To confirm that a benzylic peroxide impurity could actually be converted under the reaction conditions to a phenol as in eq 11, commercially available cumene hydroperoxide (**57**) was subjected to the reaction conditions in distilled *p*-xylene (eq 12). This reaction resulted in isolation of phenol (**55**) in high yield. The initially reported demethylative substitution of mesitylene (**58**), also performed using a sample of this arene from an old bottle, was probably the result of similar contamination. Repeating the reaction with purified reagents led to the isolation of 2,4,6-trimethylphenol (**59**) in low yields without any trace of demethylative substitution product **60** (eq 13).



The phenol (**55**) impurity describe above was originally thought to come from borylation of Ph_3CH at the *ipso*- carbon with electrophilic boron, but this was now called into question as well. Closer inspection of the ^1H NMR spectra showed that when phenol was produced it was in a 1:1 ratio with benzophenone (**62**). This led to the conclusion that **55** was produced by oxidation of excess trityl cation via the intermediate benzylic peroxide **61** (eq 14), verified by exposing **5** to the oxidative workup.



One example of dealkylative substitution with electrophilic boron has been confirmed. After distilling *p*-cymene (**63**) and using it as a solvent for the activation of recrystallized **13**, *p*-cresol (**54**) was the only product observed after oxidation (eq 15). The most likely explanation is borylation at an *ipso*-carbon followed by loss of the 2-propyl cation, but it is questionable whether this cation would be stable enough to be released in preference to a solvated proton. Another mechanistic possibility is that the formation of **54** occurs by hydride removal from the α-carbon of **63** (the isopropyl methine proton) by electrophilic boron followed by oxidation of this cation in a manner analogous to the oxidation of trityl cation shown in eq 14.

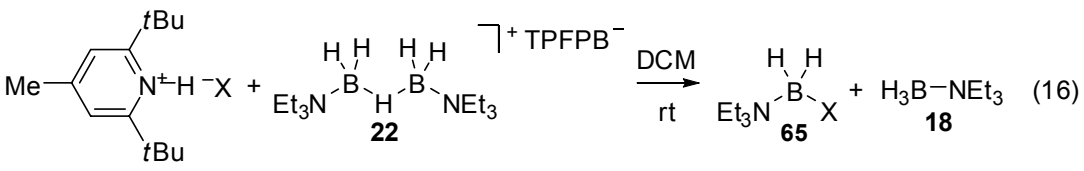


Strong Acid Activation of Triethylamine Borane

We attribute the reactivity of the hydrogen-bridged cation **22** with the weak nucleophiles Ph_3CH and DCM as well as iPr_3SiH to the presence of a small amount of borenium ion $Et_3N{\cdot}BH_2^+$ (**28**) in equilibrium with **22**. To gain further insight, the compatibility of **22** with various weakly nucleophilic counterions was explored. No B–H–B bonded structures were detected when $Et_3N{\cdot}BH_3$ (**18**) was reacted with excess $TrBF_4$, although Ph_3CH (>95%) was formed along with $Et_3N{\cdot}BF_3$;[36] the formation of $Et_3N{\cdot}BF_3$ is evidence that **22** or **28**, as the free borenium **28a** or the solvent adduct $Et_3N{\cdot}BH_2{\cdot}Cl_2CH_2^+$ (**28b**), can extract fluoride from BF_4^-. Activation of **18** with $TrBF_4$

using approximately 3:1 stoichiometry also gave full conversion of **18** to $Et_3N{\cdot}BF_3$, presumably via fluoroborane and difluoroborane complexes. As described above in the context of chloride/hydride exchange at boron, these fluoroboranes could be more potent hydride donors than the parent borane **18** due to fluoride lone pair donation into a developing empty orbital at boron. This would complicate the kinetic studies of hydride transfer from amine boranes to benzhydryl cations performed by the Mayr group, since many of the electrophiles used were BF_4^- or PF_6^- salts.[37]

The compatibility of **22** with less reactive counterions was also investigated. Treatment of **18** with the strong acids HOTf (**64a**) or $HNTf_2$ (**64b**) as hydride acceptors formed tetravalent adducts **65a**,**b** as dominant products. Preformed **22** with X = TPFPB also gave **65a**,**b** (as well as **18**) when the corresponding $^-$OTf or $^-NTf_2$ salts **66a**,**b** were added (eq 16), thereby confirming cleavage of the B–H–B bond by these anions rather than a simple kinetic preference to form **65** over **22**. On the other hand, **22** was only partly converted to **65c** (ca. 1:1.1 **22**:**65c**) upon addition of **66c**, or when **18** was treated with 0.5 equiv of the strong, bulky carbon acid $HC(C_6F_5)Tf_2$ (**64c**)[38] at rt. In this reaction, Et_3NH^+ was a major product observed that was thought to result from water impurity in the commercial sample of **64c**. Confirming this supposition, Et_3NH^+ was still formed but was only a minor product from the reaction of **22** with **66c** if the salt was dried prior to use. In this case, unreacted **18** competes with the weakly nucleophilic anion $^-C(C_6F_5)Tf_2$ for coordination into the unoccupied orbital of borenium ion **28a**.



66a: X = OTf, **66b**: X = NTf_2,
66c: X = $C(C_6F_5)Tf_2$

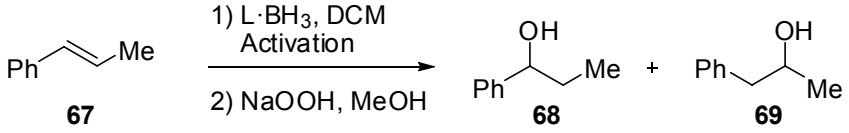
Since **22** was shown to survive in the presence of the weakly nucleophilic $^{-}C(Tf)_2C_6F_5$, activation of **18**-d_3 by Yamamoto's acid was explored for H/D exchange with a silane. Unfortunately, activation by direct reaction with this acid gave an Et_3NH^+ impurity, and the ^{1}H NMR signal for its methylene protons was too close to the hydride of iPr$_3$SiH for accurate integration in the presence of more than a trace of this contaminant. Exchange of the triethylsilane hydride with **18**-d_3 activated by $HC(Tf)_2C_6F_5$ was therefore tested. These conditions gave evidence of H/D exchange by ^{1}H NMR (decreased integral for Et$_3$Si–*H* at δ 3.61 ppm) and by ^{2}H NMR (appearence of a silyl deuteride peak at δ 3.67 ppm).

Hydroboration by TrTPFPB Activation

Trityl Activation of 3° Amine and Phosphine Boranes for Hydroboration

Hydroboration, mentioned earlier in this chapter, is a potential application for the boron cations generated in this study. Intermolecular hydroboration by iodine activation of pyridine borane was explored previously in our research group (Table 2-2).[16c] The activation produces an iodoborane complex of pyridine (**72**, X = I) that undergoes an S_N2-

Table 2-2. Intermolecular Hydroboration with I_2-Activated Pyridine Boranes



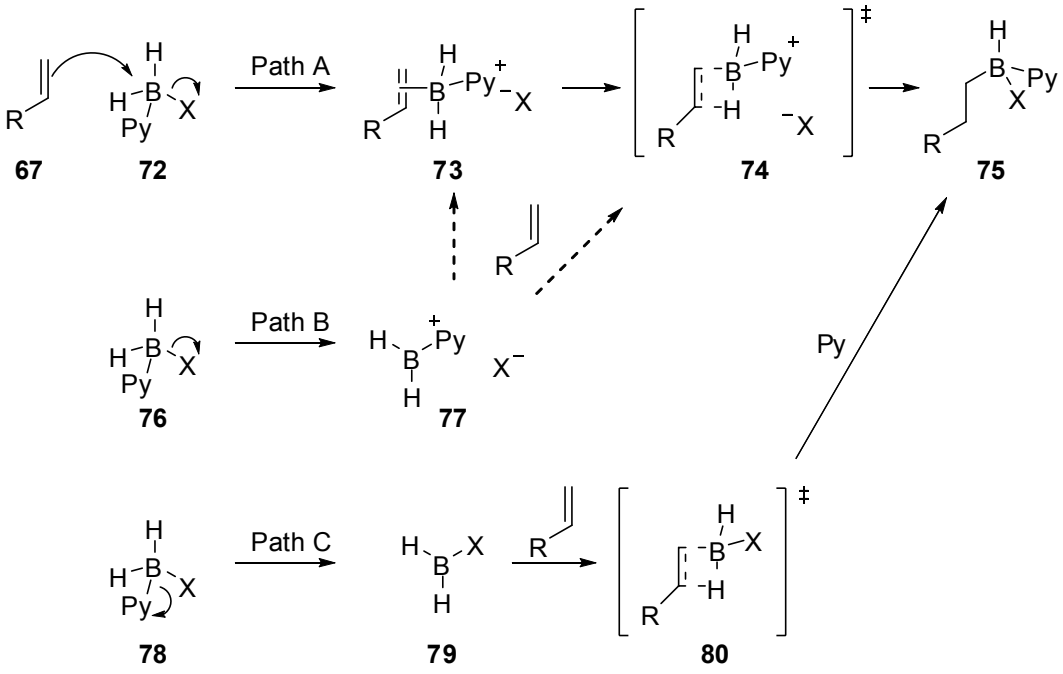
entry	L·BH$_3$[a]	activation	time	**68**:**69**	yield (%)
1	Py·BH$_3$ (**13**)	I_2[b]	2 h	15:1	92
2	Py·BH$_3$ (**13**)	Br_2[b]	12 h	>20:1	10[c]
3	Py·BH$_3$ (**13**)	TfOH[d]	2 h	10:1	72
4	Lut·BH$_3$ (**70**)[e]	I_2[b]	2 h	2.4:1	13[c]
5	Me$_2$S·BH$_2$I (**71**)[f]	--	2 h	3.5:1	62

[a] 1:1 ratio of L·BH$_3$ to alkene, rt. [b] 50 mol%. [c] Reaction quenched prior to

completion. [d] 100 mol%. [e] 2,6-Lutidine borane. [f] Preformed.[39]

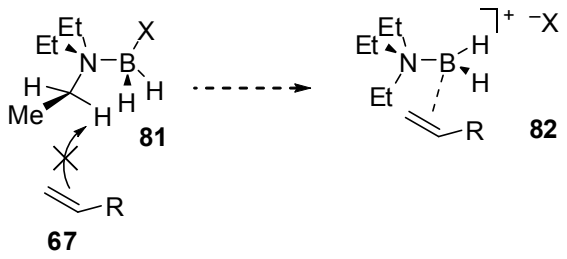
like displacement of iodine by the alkene for hydroboration (Scheme 2-3, Path A). The drastic reduction in the rate of reaction using Br_2 activation (Table 2-2, entry 2) is evidence that displacement of this anion is important, and different regioselectivity relative to using **71**, a source of iodoborane (entry 5), is evidence that the pyridine ligand is still coordinated to boron in the actual hydroboration event, again implying halide displacement. However, the dependence of regioselectivity on the halide (entries 1-3) implies its involvement in the regioselectivity-determining step, formation of intermediate π-complex **73**. This is evidence against an S_N1-like mechanism (Scheme 2-3, Path B or Path C), but a mechanism involving a tight ion pair cannot be ruled out.

Scheme 2-3. Pathways for Hydroboration from Activated Pyridine Borane



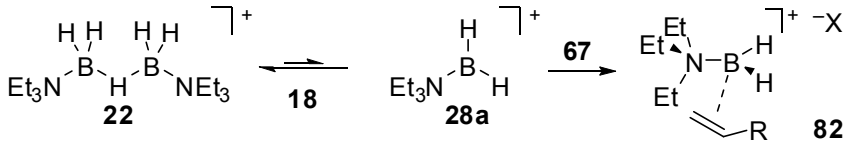
A goal of the hydroboration study for this thesis was to eventually apply the activation methodology to chiral amine and phosphine boranes to effect enantioselective hydroboration. An initial attempt by J. Clay to extend the iodine activation to reagents

other than pyridine yielded only 10% alcohol products from **67** using $NH_3{\cdot}BH_3$.[22] Applying this activation to triethylamine borane or tributylphosphine borane was unsuccessful, producing <5% yield of alcohol products from **67**, even using the more potent $HNTf_2$ to activate the borane complex. The more reactive hydroboration substrate α-methylstyrene (**83**) did not react under the same conditions. This lack of reactivity for $Et_3N{\cdot}BH_2I$ (**81**, X = I) was rationalized by the S_N2-like mechanism of iodide displacement by alkene. The activated haloborane complex of a 3° amine or phosphine is sterically similar to a neopentyl halide, which is unreactive toward S_N2 displacement. The neighboring alkyl groups on nitrogen **81** block the backside of the B–X bond as shown (eq 17). In contrast, $Py{\cdot}BH_2I$ (**72**) is structurally and electronically similar to a benzylic halide, an excellent substrate for nucleophilic substitution.



(17)

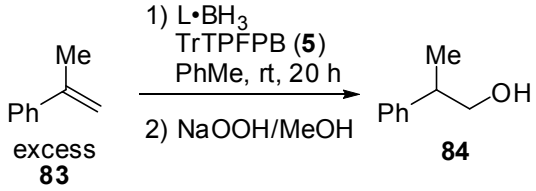
The demonstrated electrophilicity of the hydride-bridged cations (**22**-**27**) was a hindrance in the study of the actual activated species, but it bodes well for interaction with the weakly nucleophilic π electrons of an olefin. Hydroboration by TrTPFPB activation of borane complexes like $Et_3N{\cdot}BH_3$ (**18**) may conceivably proceed through an S_N1-like pathway (Scheme 2-3, Path B or eq 18) via cation **28** that would be viable even for such a sterically demanding environment. However, activation of the bulky tricyclohexyl-phosphine borane (**85**) in DCM gave no product alcohol from α-methyl-



(18)

styrene (Table 2-3, entry 1). This is probably due to the decomposition of DCM described in Scheme 2-2. Thus, switching to toluene, a less reactive solvent, gave high conversion based on TrTPFPB. For reasons that remain unclear, tributyl- and triphenylphosphine boranes (**86** and **87**) gave lower conversion to **84** under the same conditions of activation in toluene. The borane complex of a 3° amine, **18**, was also successful for the hydroboration of **83** with TrTPFPB activation (entry 5). Thus the highest conversions to hydroboration product **84** came from reaction of the most sterically demanding environments (entries 2 and 5).

Table 2-3. Hydroboration by TrTPFPB Activation of 3° Amine and Phosphine Boranes



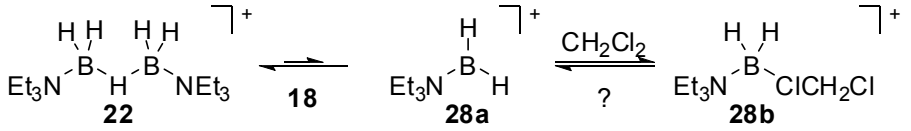
entry	L·BH_3 (amount)	conversion[a]
1	Cy_3P·BH_3 (**85**, 3 equiv)[b]	< 5%
2	Cy_3P·BH_3 (**85**, 3 equiv)	90%
3	Bu_3P·BH_3 (**86**, 3 equiv)	40%
4	Ph_3P·BH_3 (**87**, 3 equiv)	40%
5	Et_3N·BH_3 (**18**, 2 equiv)	75%

[a] By ^{1}H NMR assay, **84** relative to Ph_3CH. [b] DCM solvent.

Bisborane Complexes of Chelating Ligands

The observation that bulkier Lewis bases led to better hydroboration conversions is inconsistent with an S_N2-like mechanism, but could be understood in terms of a dissociative, S_N1-like mechanism. If reactions from the hydride-bridged cations (such as **22**) occur by prior rupture of the 3c2e bond to form borenium ion equivalents (**28**), then a

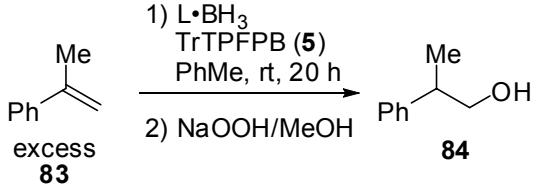
sterically bulky amine ligand could accelerate this process. This would most likely be described by **22** equilibrating with **28** and **18** (eq 19), which would be pushed toward **22**



(19)

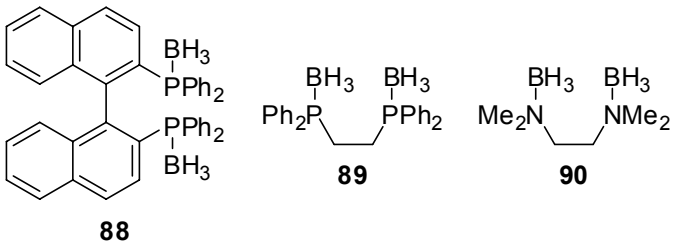
in the presence of a greater excess of reagent **18**. Confirming this proposal, the attempted hydroboration with 10 equiv of **18** (relative to TrTPFPB) gave only 40% conversion to **84** (Table 2-4, entry 2), as opposed to the 75% conversion attained with 2 equiv of this reagent. Likewise, the reaction employing a large excess of **86** gave a significant decrease in the conversion (entries 3 and 4).

Table 2-4. Dependence of Hydroboration on Stoichiometry

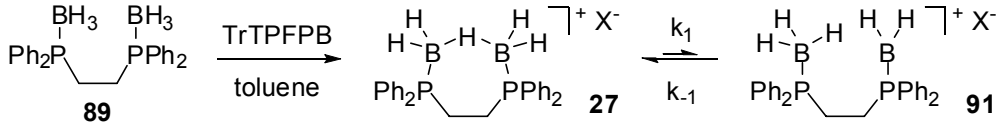


entry	L·BH_3 (amount)	conversion[a]
1	$Et_3N·BH_3$ (**18**, 2 equiv)	75%
2	$Et_3N·BH_3$ (**18**, 10 equiv)	40%
3	$Bu_3P·BH_3$ (**86**, 2 equiv)	45%
4	$Bu_3P·BH_3$ (**86**, 10 equiv)	10%
5	BINAP·$2BH_3$ (**88**, 1 equiv)	ND[b]
6	DIPHOS·$2BH_3$ (**89** (1 equiv)	ND[b]
7	TMEDA·$2BH_3$ (**90** (1 equiv)	ND[b]

[a] By ^1H NMR assay, **84** relative to Ph_3CH. [b] **84** Not detected.



For further evidence of a dissociative mechanism for the hydroboration, we chose to study bisborane complexes of chelating ligands. Trityl activation of complex **89**, for example, forms the internally hydride-bridged **27** shown in Table 2-1 (eq 20). On rupture of the B–H–B bond in this cationic species, the L·BH_3 subunit remains tethered to the borenium ion (**91**, eq 20). The reverse reaction to reform a 3c2e bond is accelerated by the decreased entropy cost of an intramolecular reaction (k_{-1} is higher than for the corresponding intermolecular event), decreasing the equilibrium concentration of a free borenium ion (**91**). In the event, **88-90** were not effective for hydroboration after activation with 1 equiv TrTPFPB (2:1 stoichiometry of complexed borane to trityl cation, as in entries 1 and 3). This confirms our proposal that despite observation of a B–H–B bonded intermediate from activation of Lewis base complexes of borane, there may be a small equilibrium concentration of a free (or at most a solvent-coordinated) borenium cation responsible for the reactions observed in this chapter.

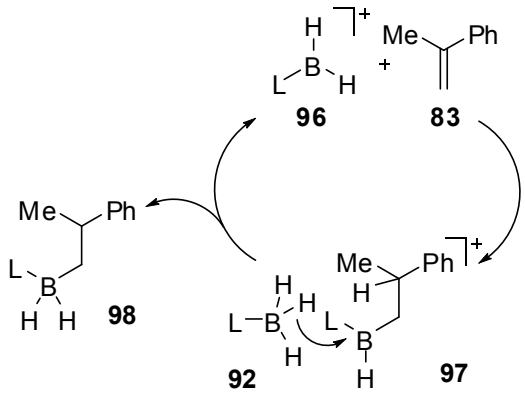


(20)

Borane Complexes of Chiral Lewis Bases for Enantioselective Hydroboration

The development of conditions for trityl activation of borane complexes of alkylamines and -phosphines opened up new possibilities for enantioselective hydroboration. Chiral phosphine borane **92** was selected as the first reagent to be tested,

Scheme 2-4. Possible Pathway for Hydroboration with Substoichiometric TrTPFPB.



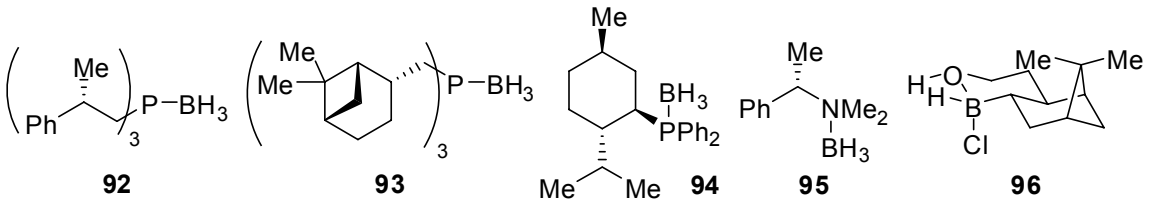
and it gave promising results (entry 1). The high conversion, beyond the amount of TrTPFPB used in the reaction, may be evidence of the catalytic cycle depicted by Scheme 2-4. The immediate hydroboration product, **97**, is drawn as a borenium ion although it could be stabilized by interaction with a B–H bond from the excess **92**. Cleavage of this 3c2e bond could generate either borenium ion, **96** or **97**. Although **97** is expected to be stabilized relative to **96** by the presence of an electron-donating alkyl group, cleavage to form **96** is possible. Another explanation for the apparent turnover is that a second hydroboration could occur from **97**, being an electrophilic species with a vacant coordination site at boron and a remaining B–H bond. Regardless, lowering the reaction temperature lowered the conversion from **92** to <100% but did not affect enantioselectivity. Another borane complex (**93**) of a C_3-symmetric phosphine gave no hydroboration products at all. The borane complex **94** of the known menthyldiphenyl-

Table 2-5. Enantioselective Hydroboration of α-Methylstyrene (**83**)

Entry	L·BH_3	conversion[a]	ee[b]
1	**92**	190%	25%
2	**92**	85%[c]	25%
3	**93**	trace	ND[d]

4	**94**	90%	6%
5	**95**	100%	4%
6	**96**[e]	ND[d]	26%

[a] By ^{1}H NMR assay, **84** relative to Ph_3CH. [b] By HPLC assay. [c] 0 °C, 72 h. [d] Not determined. [e]No activation, 30 °C, in benzene.[41]



92 **93** **94** **95** **96**

phosphine[40] gave product in high yield based on TrTPFPB, but with only 6% ee. Likewise amine borane **95**, from the commercially available *N*,*N*,α-trimethylbenzylamine, was effective for hydroboration but with poor enantioselectivity. Hydroboration of β-methylstyrene generally gave lower conversion to the product alcohols, and only the reaction from **92** was enantioselective (35% ee for the major regioisomeric product, 1-phenyl-1-propanol).

The substrate chosen for these studies was α-methylstyrene (**83**), due not only to its high reactivity toward hydroboration but also to the challenge it poses for enantioselectivity. Highly enantioselective hydroborations of 1,1-disubstituted alkenes remain elusive in general, but specifically the success with **83** has been limited. The highest level of optical purity for **84** obtained to date with traditional hydroboration reagents is only 26% ee using **29**.[41] Even transition metal catalysis has not been solved this problem; rhodium-catalyzed hydroboration with a BINAP ligand gave product with only 38% ee, the best result yet reported for this substrate.[42]

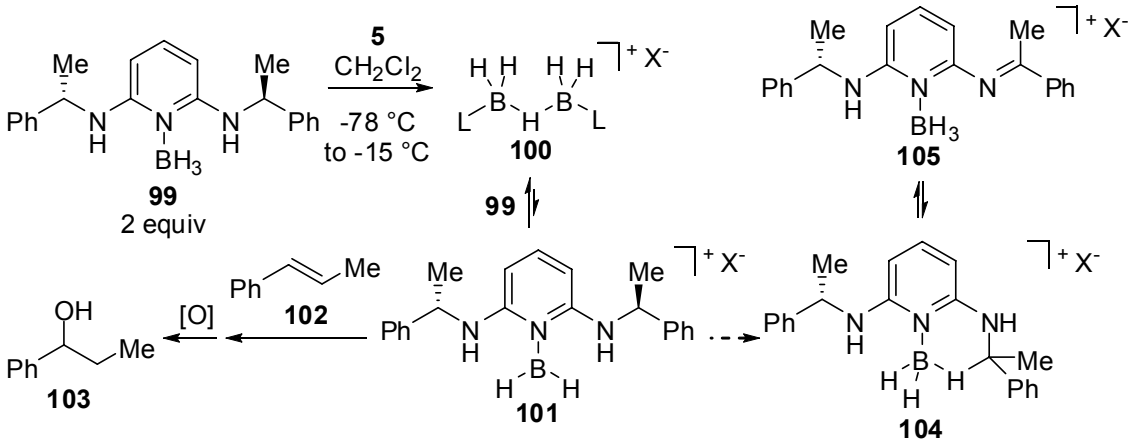
The results in Table 2-4 implicating a free borenium ion as the active hydroborating species guided our selection of chiral Lewis bases to examine next. The idea of a C_2-symmetric Lewis base was attractive due to the planarity expected for an

LBH_2 cation, reducing the number of potential transition states for interaction of the alkene with the activated reagent by a factor of two. For example, the top and bottom faces of trivalent boron cation **101** are equivalent. However, borane complexes of the numerous C_2-symmetric chelating ligands in the literature, e.g. BINAP·$2BH_3$ (**88**) were ruled out based on the results in Table 2-4. We therefore returned to chiral pyridine borane derivative **99**, prepared by J. Clay and used in an early experiment with TrTPFPB activation.[22] This experiment gave racemic product at rt, leading to the suspicion that reaction with trityl cation had occurred by pyridine transfer rather than hydride transfer, releasing free B_2H_6 and BH_3·DCM as the active hydroborating reagents. However, under the more carefully controlled conditions for trityl activation of pyridine borane described above, formation of B_2H_6 was only a minor pathway according to ^{11}B NMR evidence, and was seen only at rt. Under these low temperature activation conditions, pyridine borane **13** generated fairly clean ^1H and ^{11}B NMR spectra for the hydride-bridged cation **24** as described in Table 2-1.

The optimal conditions of low-temperature activation (-78 °C followed by warming the solution to -15 °C) were applied to chiral reagent **99** in a 2:1 stoichiometry with TrTPFPB (**5**). The activated species was effective for hydroboration of β-methylstyrene, the substrate used in J. Clay's studies, but only 20% conversion to product **103** was observed. Furthermore, the hydroboration proceeds with only modest enantioselectivity, giving **103** with 14% ee. The possibility of catalyst racemization was then examined under the suspicion that borenium **101** could be stabilized by formation of an internal 3c2e bond with an activated C–H (**104**). This C–H–B bond could cleave to generate the relative stable iminium ion **105**, while the reverse reaction would occur without stereospecificity. Epimerization of either stereocenter gives an achiral meso

stereoisomer of **101**. To rule out this possibility, the activation of **99** was performed in the absence of alkene, followed by quenching with Bu_4NBH_4 after 2 h, but **99** was recovered without epimerization. The *meso* borane complex was prepared by the palladium-catalyzed reaction of 2,6-dibromopyridine with racemic α-methylbenzylamine followed by borane complexation to confirm its absence in the previous experiment. It may be that this configurationally stable reagent simply has stereocenters too far removed from the reactive site to promote enantioselective hydroboration. On the other hand, the relatively low conversion to hydroboration products is not consistent with the simple activation mechanism that was proposed (Scheme 2-5).

Scheme 2-5. Hydroboration and Potential Epimerization Pathways from Activated **99**.



Summary

To summarize, borenium ions do not accumulate under the conditions of hydride abstraction from Lewis base-borane complexes ($L{\cdot}BH_3$) due to subsequent rapid reaction with $L{\cdot}BH_3$ to form B–H–B bonds. Hydride bridged cations such as **22** are sufficiently stabilized to resist abstraction of the remaining hydride by excess trityl cation. However, reversible cleavage of the 3c2e bond releases borenium ion equivalents, as evidenced by the interaction with weak nucleophiles. This reactivity was applied to effect

hydroboration from reagents that are hindered at boron, including the complexes of chiral amines and phosphines albeit with modest enantioselectivity. The isotopic exchange between **22**-d_5 and $HSiEt_3$ suggests that borenium ions such as **28a** may resemble silylium cations in terms of electrophilicity. Considering the solvent-assisted decomposition of Ph_3CH reported here, the use of TrTPFPB for generation of other reactive electrophiles may warrant closer scrutiny, especially in cases where decomposition of cationic products has been noted.[31b, 34]

Experimental

General Methods. The following chemicals were commercially available and used as received: trityl tetrakis(pentafluorophenyl)borate (TrTPFPB, **5**), trimethylamine borane, tributylphosphine borane, triphenylphosphine borane, trityl tetrafluoroborate ($TrBF_4$), trifluoromethanesulfonic acid (TfOH, **64a**), bis(trifluoromethane)sulfonimide (Tf_2NH, **64b**), 2,3,4,5,6-pentafluorophenylbis(trifluoromethane-sulfonyl)methane ($C_6F_5CHTf_2$, **64c**), (*S*)-2-phenyl-1-propanol, phosphorus trichloride, (–)-*cis*-myrtanol, menthol and chlorodiphenylphosphine. The known complexes 4-dimethylaminopyridine borane ($DMAP{\cdot}BH_3$),[43] 1,2-bis(diphenylphosphino)ethane bis(borane) (**89**),[44] tricyclohexyl-phosphine borane (**85**),[45] 2,2'-bis(diphenylphosphino)-1,1'binaphthyl bis(borane) (**88**), tetramethylethylenediamine bis(borane) (**90**)[46] and *N*,*N*,α-trimethylbenzylamine borane (**95**) were prepared by treatment of the commercially available Lewis base with $BH_3{\cdot}THF$ as reported.[43] Pyridine borane (**13**) and triethylamine borane (**18**) were recrystallized from dichloromethane/hexane, isolated and dried under vacuum at 0 °C and -20 °C respectively. Dichloromethane (DCM), *n*-hexane and tetrahydrofuran (THF) were dried by passing through a column of activated alumina; toluene and *p*-xylene were distilled from CaH_2 under an N_2 atmosphere; CD_2Cl_2 was dried by storing over activated 4Å molecular sieves. All reactions were performed at room temperature under an N_2 atmosphere unless otherwise stated. Nuclear magnetic resonance experiments were performed on Varian Inova 500, Inova 400 and Mercury 300 spectrometers at the following frequencies: ^1H 500 MHz; $\{^1H\}^{11}B$ 160 MHz; $\{^1H\}^{19}F$ 376 MHz, unless otherwise stated. All spectra were recorded in CD_2Cl_2 and referenced to solvent unless otherwise stated.

Room Temperature Activation of Pyridine Borane (13) with TrTPFPB (5).

Pyridine borane (5.0 μL, 49 μmol) was added by syringe to a stirred solution of TrTPFPB (50 mg, 54 μmol) in 0.6 mL anhydrous CD_2Cl_2 under an N_2 atmosphere. After 1 h, the solution was transferred to an N_2-flushed NMR tube capped with a rubber septum and the ^1H and ^{11}B NMR spectra were recorded. The ^1H NMR spectrum had no peak for Ph_3CH, but $Ph_2C\mathit{H}_2$ (3.99 ppm) was observed along with a number of other peaks around 4 ppm and 2.3 ppm. The ^{11}B NMR spectrum had one major peak at 43.7 ppm ($PyBCl_2^+$, cf. 4-Me-$C_6H_4NBCl_2^+$ $^-Al_2Cl_7$ at $\delta^{11}B$ = 47 ppm[21]) with other smaller, unidentified peaks at 47.8, 17.5 and 7.3 ppm, all broad singlets, and a sharp singlet at -16.7 ppm (TPFPB anion).

Quenching the reaction by addition of pyridine (5.0 μL, 62 μmol) by syringe followed by stirring for 1 h before transferring to an N_2-flushed NMR tube gave an ^{11}B NMR peak at 8.3 ppm corresponding to the known $Py_2BCl_2^+$,[47] a peak at -16.7 ppm (TPFPB anion), and unidentified broad singlets at 5.8, 3.8 and -3.6 ppm.

Representative Procedure for Activation of Borane Complexes (Table 1): Detection of H-Bridged Species

22: Triethylamine borane (8.0 μL, 54 μmol) was added by syringe to a stirred solution of TrTPFPB (50 mg, 54 μmol) in 0.6 mL anhydrous CD_2Cl_2 at -78 °C under an N_2 atmosphere. After a few minutes, this solution was transferred via syringe to an N_2-flushed NMR tube cooled to -78 °C, and the sample was kept in a -78 °C bath (ca. 60 min) until allowing it to warm to -20 °C in the NMR spectrometer for data acquisition at that temperature. Residual TrTPFPB: ^1H NMR: δ 8.24 (3H, t, J = 7.6 Hz), 7.85 (6H, t, J

= 7.6 Hz), 7.65 (6H, d, J = 7.3 Hz); ^{11}B NMR: δ -16.7 (s). Ph_3CH: ^{1}H NMR: δ 7.28 (6H, t, J = 7.3 Hz), 7.21 (3H, t, J = 7.3 Hz), 7.10 (6H, d, J = 7.3 Hz), 5.55 (1H, s). Compound **22**: ^{1}H NMR: δ 2.88 (12H, q, J = 7.2 Hz), 2.6 (4H, br s), 1.19 (18H, t, J = 7.3 Hz), -2.6 (1H, br s); ^{11}B NMR: δ -3.4 (br s), -16.7 (s).

Addition of triethylamine borane (7.2 μL, 49 μmol) to 50 mol% TrTPFPB (22 mg, 24 μmol) in 0.6 mL anhydrous CD_2Cl_2 at -78 °C under an N_2 atmosphere gave identical chemical shifts to those reported for **18** and Ph_3CH but showed no remaining TrTPFPB. A small amount of residual triethylamine borane was observed, as well as a small amount of Et_3NH^+ due to hydrolysis of **22** by adventitious water.

23: ^{1}H NMR: δ 2.76 (18H, s), 2.7 (4H, br s), -1.9 (1H, br s); ^{11}B NMR: δ -0.2 (br s), -16.7 (s).

24: ^{1}H NMR: δ 8.52 (4H, d, 5.5 Hz), 8.34 (2H, t, J = 7.8 Hz), 7.86 (4H, m), 3.3 (4H, br s), 0.5 (1H, br s); ^{11}B NMR: δ -1.5 (br s), -16.7 (s).

25: ^{1}H NMR: δ 7.84 (4H, d, J = 7.5 Hz), 6.59 (4H, d, J = 7.5 Hz), 3.13 (12H, s), 3.1 (4H, br s), 0.1 (1H, br s); ^{11}B NMR: δ -1.3 (br s), -16.7 (s).

26: ^{1}H NMR: δ 1.74 (12H, m), 1.5 (4H, br s), 1.40 (24H, br s), 0.91 (18H, t, J = 7.0 Hz), -3.7 (1H, br s); ^{11}B NMR: δ -16.7 (s), -27.5 (br s).

27: ^{1}H NMR: δ 7.69 (4H, m), 7.60 (16H, m), 2.85 (4H, m), 2.7 (4H, br s), -2.2 (1H, br s); ^{11}B NMR: δ -16.7 (s), -27.2 (br s).

H/D Exchange between 22-d$_5$ and *i*Pr$_3$SiH

18-d$_3$ (5.8 mg, 49 μmol) was added by syringe as a solution in 0.2 mL anhydrous CD_2Cl_2 to a stirred solution of TrTPFPB (20 mg, 22 μmol) in 0.6 mL anhydrous CD_2Cl_2 under an N_2 atmosphere. After 10 min, *i*Pr$_3$SiH (7.0 μL, 34 μmol, distilled from activated 4Å molecular sieves) was added by syringe, then the solution was transferred to an N_2-flushed NMR tube capped with a rubber septum. The ^{1}H NMR spectrum acquired 20 min after silane addition had a decreased peak for the hydride of *i*Pr$_3$SiH (δ 3.31 ppm, s, 0.40H relative to isopropyl protons) but showed peaks for terminal and bridging hydrides of **7** (bridging hydride: δ -2.6 ppm, br s, 0.15H relative to N-C*H*$_2$-CH$_3$), showing some H/D exchange. After 60 min the exchange was essentially complete; the hydride of *i*Pr$_3$SiH integrated for 0.35H and the bridging hydride of **22** for 0.30H. ^{2}H NMR (77 MHz) confirms deuteration to *i*Pr$_3$SiD with a peak at δ 3.37 ppm. After quenching by addition of $NaBH_4$ (6.0 mg, 160 μmol) and stirring 1 h before filtering through a plug of silica gel and flushing with an additional 3 mL CH_2Cl_2, GC/MS (8 μL injection volume; Restek 5% PhMe siloxane column, 30 m length, 0.25 mm ID, 0.25 mm film thickness; 1 mL/min He; hold at 30 °C for 1 min, increase by 5 °C/min to 90 °C then by 20 °C/min to 250 °C, hold at 250 °C for 5 min; EI ionization) also confirms the deuteration to *i*Pr$_3$SiD (14.0 min; m/z = 159 (5), 158 (4) (*i*Pr$_3$SiH$^{\bullet+}$), 116 (13), 115 (15), 88 (16), 87 (24), 74 (23), 73 (53), 60 (26), 59 (100), 46 (16), 45 (47), 44 (14), 43 (22)), giving a 1 : 1.09 ratio

of $M^{\bullet+}$ at m/z = 158.1 to $(M+1)^{\bullet+}$ at m/z = 159.1, compared to a 1 : 0.16 ratio in untreated *i*Pr_3SiH.

The above reaction was also performed in anhydrous CH_2Cl_2, and the $\{^1H\}^2H$ NMR spectrum was recorded at 77 MHz.

GC/MS Analysis of Ph_3CH Decomposition Products

Triethylamine borane (7.2 μL, 49 μmol) was added by syringe to a stirred solution of TrTPFPB (50 mg, 54 μmol) in 0.6 mL anhydrous CH_2Cl_2 under an N_2 atmosphere. After 1 h, the reaction was quenched by addition of Bu_4NBH_4 (6.0 mg, 160 μmol) and stirred 1 h before filtering through a plug of silica gel and flushing with an additional 3 mL CH_2Cl_2, GC/MS (8 μL injection volume; Restek 5% PhMe siloxane column, 30 m length, 0.25 mm ID, 0.25 mm film thickness; 1 mL/min He; hold at 30 °C for 1 min, increase by 5 °C/min to 90 °C then by 20 °C/min to 250 °C, hold at 250 °C for 5 min; EI ionization) gave peaks corresponding to toluene (5.1 min; m/z = 93 (2), 92 (22) ($M^{\bullet+}$), 91 (30), 66 (1), 65 (7), 63 (5), 52 (2), 51 (6), 50 (5), 46 (2), 45 (3), 44 (10), 40 (100)), diphenylmethane (18.8 min; m/z = 169 (14), 168 (100) ($M^{\bullet+}$), 167 (100), 166 (13), 165 (40), 153 (28), 152 (25), 139 (5), 115 (10), 91 (31), 90 (7), 89 (13), 83 (39), 77 (9), 76 (6), 65 (32), 64 (5), 63 (21), 62 (6), 52 (5), 51 (36), 50 (16)), 4-methyldiphenylmethane (**48**; 19.6 min; m/z = 183 (2), 182 (67) ($M^{\bullet+}$), 169 (7), 167 (100), 165 (29), 104 (10), 91 (19), 89 (15), 77 (22), 65 (31), 63 (18), 51 (41), 50 (9), 44 (21), 41 (9)) and triphenylmethane (22.8 min; m/z = 245 (17), 244 (86) ($M^{\bullet+}$), 243 (26), 229 (8), 228 (5), 215 (5), 168 (11), 167 (80), 166 (48), 165 (100), 164 (9), 163 (5), 153 (6), 152 (27), 139 (6), 119 (6), 115 (10), 107 (9), 63 (8), 51 (14)), all confirmed by spiking a sample with the authentic compounds. In addition, peaks at 19.5 min and 19.6 min were

observed, assigned as isomers of $MeC_6H_4CH_2Ph$ based on the molecular ion and fragmentation pattern, and a set of 3 peaks at 23.3 min was assigned as isomers of $MeC_6H_4CHPh_2$ (**42**; m/z = 258 (27) ($M^{\bullet+}$), 244 (15), 243 (40), 207 (20), 181 (10), 179 (7), 167 (41), 166 (37), 165 (100), 152 (11), 115 (6), 91 (6), 78 (13), 77 (17), 65 (8), 63 (8), 51 (39), 44 (25), 41 (11)).

Repeating the above experiment using CD_2Cl_2 as the reaction solvent gave the same GC peaks, but with masses increased by 2 amu for toluene (5.1 min; m/z = 94 (6) ($M^{\bullet+}$), 93(8), 92 (3), 91 (2), 67 (1), 66 (1), 65 (1), 44 (10), 40 (100)), $MeC_6H_4CH_2Ph$ (3 peaks near 19.6 min; m/z = 185 (16), 184 (32) ($M^{\bullet+}$), 168 (15), 167 (100), 91 (6), 65 (7), 51 (35), 44 (54), 40 (10)) and $MeC_6H_4CHPh_2$ (3 peaks near 23.3 min; m/z = 260 (7) ($M^{\bullet+}$), 243 (21), 167 (23), 166 (22), 165 (100), 78 (7), 77 (11), 63 (7), 51 (39), 44 (21)).

Representative Procedure for Aromatic Substitution/Oxidation of *p*-Xylene and Isolation of 2,5-Dimethylphenol.

Triethylamine borane (7.2 μL, 49 μmol) was added by syringe to a stirred suspension of TrTPFPB (50 mg, 54 μmol) in distilled *p*-xylene (0.60 mL, 4.9 mmol). After 1 h, H_2O_2 (35% aq., 0.1 mL), NaOH (20% aq., 0.2 mL) and MeOH (1 mL) were added as an oxidative quench. The resulting biphasic mixture was stirred vigorously 20 h, diluted with 5% aq. NaOH (5 mL) and washed with hexanes (2 x 5 mL). The aqueous layer was acidified with 6M HCl and extracted with DCM (2 x 5 mL), the combined organic layers dried over Na_2SO_4 and reduced by rotary evaporation. Two phenolic products were identified by ^1H NMR in $CDCl_3$: PhOH (peaks at δ 7.23, 6.92 and 6.81) and 2,5-dimethylphenol (peaks at δ 6.98, 6.65 and 6.58), confirmed by addition of an authentic sample. Phenol is present as the product of oxidation of unreacted trityl cation,

which was verified by subjecting TrTPFPB to the oxidative workup and isolation conditions. In another experiment, addition of diphenylmethane as an internal standard allowed quantification, showing 3.3 μmol phenol and 0.4 μmol 2,5-dimethylphenol (1.6% y based on **18**).

Reaction of Hydroperoxide 57 with Activated Pyridine Borane (13)

Cumene hydroperoxide (80% in cumene, 10.0 μL, 54 μmol) was added by syringe to a stirred suspension of TrTPFPB (52 mg, 56 μmol) in distilled *p*-xylene (0.50 mL, 4.1 mmol) with vigorous gas evolution on each drop, followed after a few minutes by the addition of recrystallized pyridine borane (5.0 μL, 49 μmol) by syringe. After 20 h, H_2O_2 (35% aq., 0.1 mL), NaOH (20% aq., 0.2 mL) and MeOH (1 mL) were added as an oxidative quench, the phenolic products extracted as in the previous experiment. Only a trace of 2,5-dimethylphenol was identified by ^{1}H NMR in $CDCl_3$; the major product was PhOH (peaks at δ 7.23, 6.92 and 6.81).

Reaction of $TrBF_4$ with $Et_3N{\cdot}BH_3$ (18)

Triethylamine borane (7.2 μL, 49 μmol) was added by syringe to a stirred solution of $TrBF_4$ (18 mg, 54 μmol) in 0.6 mL CD_2Cl_2 with immediate loss of the yellow color of the trityl cation. After 1h, this solution was transferred via syringe to an N_2-flushed NMR tube, and ^{1}H and ^{11}B NMR spectra were acquired. By ^{1}H NMR assay, Ph_3CH, $Et_3N{\cdot}BF_3$,[36] $Et_3N{\cdot}BH_3$ (**18**) and B_2H_6 were identified in a ratio of 26:18:5:1 based on signals at δ 5.55, 2.93, 2.76 and 4.0 ppm, with no trace of unreacted trityl cation. The ^{11}B NMR spectrum confirmed the presence of $Et_3N{\cdot}BF_3$, **18** and B_2H_6.

In another experiment, triethylamine borane (8.0 μL, 54 μmol) was added by syringe to a stirred solution of 3 equiv $TrBF_4$ (51.5 mg, 156 μmol) in 0.6 mL CD_2Cl_2 with a significant decrease in the intensity of the yellow color. After 1h, this solution was transferred via syringe to an N_2-flushed NMR tube, and ^1H NMR assay confirmed almost complete conversion of trityl cation, finding Ph_3C^+ in a ratio of <1:100 with Ph_3CH, which was found in a ratio of 2.9:1 with $Et_3N{\cdot}BF_3$.

General Procedure for Reaction of 22 with 66.

A solution of **66c** was made by addition of 2,6-di-*tert*-butyl-4-methylpyridine (**106**, 5.3 mg, 26 μmol) to a solution of $C_6F_5CHTf_2$ (**64c**, 11 mg, 25 μmol) in 0.4 mL CD_2Cl_2. For optimal results, the solution was dried over activated 4Å molecular sieves for 1 d before use. Triethylamine borane (7.6 μL, 51 μmol) was added by syringe to a stirred solution of TrTPFPB (24 mg, 26 μmol) in 0.6 mL CD_2Cl_2, and after about 10 minutes the solution of **66c** was added via syringe. The resulting solution was transferred via syringe to an N_2-flushed NMR tube, and ^1H and ^{11}B NMR spectra were acquired. By ^1H NMR assay, $Et_3N{\cdot}BH_2$-H-$H_2B{\cdot}NEt_3^+$ (**22**), $Et_3N{\cdot}BH_2(CTf_2C_6F_5)$ (**65c)**, $Et_3N{\cdot}BH_3$ (**18**) and Et_3NH^+ were identified in a ratio of 1.8:2:3:1. The ^{11}B NMR spectrum confirmed the presence of **22**, **65c**, **18** and the TPFPB anion. Failure to dry the solution of **66c** led to a greater amount of **7** and Et_3NH^+ but a similar ratio of **22** to **65c**.

65c: ^1H NMR: δ 2.96 (6H, q, J = 7.3 Hz), 1.26 (9H, t, J = 7.1 Hz); ^{11}B NMR: δ 0.2 (br s).

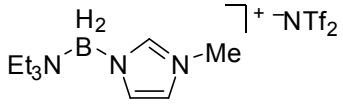
The reactions of **22** with **66a** and **6b** were carried out in the same way, but **65a** and **65b** were detected in a 1:1 ratio with **18** with only a trace of Et_3NH^+.

65a: ^{1}H NMR: δ 2.87 (6H, q, J = 7.3 Hz), 1.19 (9H, t, J = 7.3 Hz); ^{11}B NMR: δ -0.8 (t, J = 116 Hz).

65b: ^{1}H NMR: δ 2.90 (6H, q, J = 7.3 Hz), 1.21 (9H, t, J = 7.3 Hz); ^{11}B NMR: δ 0.6 (br s).

Due to the sensitivity of products **65**, they were characterized as boronium ion derivatives. Addition of triethylamine borane (**18**, 35 μL, 0.24 mmol) to a solution of Tf_2NH (**64b**, 61 mg, 0.22 mmol) in 2.0 mL CH_2Cl_2 was followed by addition of *N*-methylimidazole (20 μL, 0.25 mmol) and removal of solvent after 1 h. The residue was washed with water and extracted with $CHCl_3$, giving 58 mg (51% y) of the known boronium salt (**107**).[48]

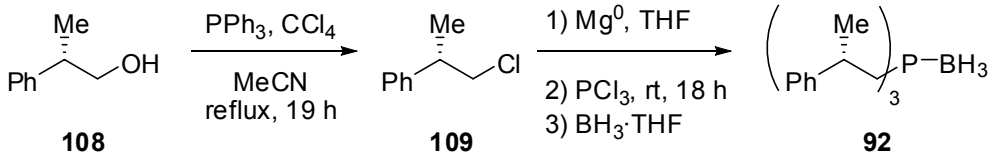
The above procedure was repeated with TfOH (**64a**, 20 μL, 0.23 mmol), giving 41.6 mg (53% y) of the boronium triflate. To 7.9 mg (23 μmol) of this compound was added $LiNTf_2$ (77.6 mg, 270 μmol) in 1.0 mL deionized water to effect anion metathesis. This also gave the known boronium salt **107** (9.0 mg, 83% y).



107

Preparation of Phosphine Borane 92

Distilled carbon tetrachloride (1.35 mL, 14.0 mmol) was added under an N_2 atmosphere to a solution of triphenylphosphine (3.72 g, 14.2 mmol) in distilled acetonitrile (15 mL) which had been cooled to 0 °C in a 50 mL round bottom flask fused to a reflux condenser.[49] To this yellow mixture was added (*S*)-2-phenyl-1-propanol (**108**, 1.00 mL, 7.1 mmol) by syringe, the color fading after the addition of a few drops of alcohol. The resulting mixture was stirred at 0 °C for 1 h, then heated slowly to reflux, the triphenylphosphine dissolving and the yellow color returning on heating. After 19 h, the solution was cooled to rt and extracted with hexanes (4 x 15 mL), and the combined hexanes layers were washed with water (50 mL) and brine (50 mL) then dried over Na_2SO_4. The product was purified by flash chromatography (FC) on silica gel (15 cm x 50 mm diameter, hexanes eluent), isolating 780 mg product **109** (71% y).



108 **109** **92**

Chloride **109** (770 mg, 5.0 mmol) was added as a solution in anhydrous THF (2.0 + 1.0 mL) to a suspension of magnesium (activated by grinding with a mechanical stirrer under N_2 atmosphere,[50] stored in the glovebox, 170 mg, 7.0 mmol) in THF (2 mL) at 0 °C. After 1 h, the mixture was warmed to rt, but still showed no signs of reaction at the magnesium surface, so the mixture was heated to reflux for 3 h, showing consumption of chloride by TLC. The mixture was then cooled to 0 °C, and PCl_3 (0.11 mL, 1.3 mmol) was added by syringe, allowing the mixture to warm slowly to rt after the addition. After 17 h, the mixture was again cooled to 0 °C and BH_3·THF (1.0 M solution in THF, 2.0 mL, 2.0 mmol) was added by syringe. After stirring 2 h at 0 °C, the mixture was warmed

to rt and diluted with Et_2O (10 mL) and washed with water (10 mL). The aqueous layer was extracted with DCM (3 x 10 mL), and the combined organic layers were washed with saturated aq. $NaHCO_3$ (20 mL) and dried over $MgSO_4$. The solvent was removed under reduced pressure and the product purified by FC on silica gel (15 cm x 30 mm diameter, 19:1 hexanes/acetone), isolating 458 mg tri-((*S*)-2-phenyl-propyl)-phosphine borane (**92**): Molecular ion calculated for $C_{27}H_{36}BNaP$: 425.2545; [M+Na], ESMS found *m*/*z* = 425.2550; IR (neat, cm^{-1}) 2360, B–H; ^1H NMR: δ 7.24 (6H, t, J = 7.3 Hz), 7.20-7.14 (3H, m), 7.08 (6H, d, J = 7.3 Hz), 3.04-2.94 (3H, m), 1.48 (3H, td, J = 14.2, 8.3 Hz), 1.28-1.20 (3H, m), 1.13 (9H, d, J = 6.8 Hz), 1.0-0.3 (3H, br m); ^{13}C NMR: δ 146.7, 128.6, 127.0, 126.5, 35.0, 33.3 (d, J = 32 Hz), 25.2 (d, J = 9 Hz); ^{11}B NMR: δ -38.5 to -41.7 (br m); ^{31}P NMR: δ 18.3-16.6 (br m).

Trialkylphosphine borane **93**[51] and alkyldiphenylphosphine borane **94**[52] were made in a similar manner from the commercially available (–)-*cis*-myrtanol and menthol via the alkyl chlorides by the action of the respective Grignard reagents on PCl_3 or $ClPPh_2$.

Representative Hydroboration of 83 by TrTPFPB Activation of 92

A suspension of **5** (12 mg, 13 μmol) in distilled toluene (3 x 0.1 mL) was added to a solution of **92** (18 mg, 44 μmol) in toluene (0.4 mL) under an N_2 atmosphere, adding alkene **83** (5.5 μL, 42 μmol) quickly after. After 20 h, the solvent was removed by a stream of N2 and the residue oxidized by addition of MeOH (2 mL), 20% aq. NaOH (0.5 mL) and 35% aq. H_2O_2 (0.5 mL), stirring 15 min before acidifying with 10% aq. HCl (2 mL). The resulting mixture was diluted with H_2O (5 mL) and extracted with Et_2O (2 x

10 mL), and the combined organic layers were reduced by rotary evaporation. Assay by ^{1}H NMR shows product alcohol **84** in a ratio of 1.9:1 with the Ph_3CH byproduct with no trace of the Ph_2CH_2 byproduct that typically indicates decomposition. The product was isolated by preparative thin layer chromatography (PLC) on silica gel (20 x 20 cm x 250 μm, 4:1 hexanes/EtOAc), isolating only 1.8 mg (98% y based on TrTPFPB, 25% ee) of the product alcohol (Rf = 0.23). Conditions for enantiomeric excess assay by HPLC (Chiralcel OB column, 2% EtOH/hexane, 0.5 mL/min) were optimized using achiral **84** from hydroboration with $Cy_3P{\cdot}BH_3$ (**85**) activated by TrTPFPB in a similar manner, with peaks at 29 and 32 minutes.

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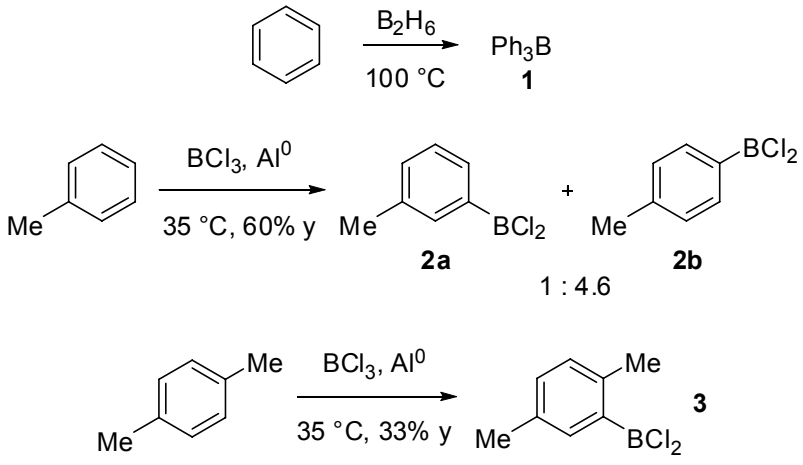
Chapter 3

Directed Borylation by Electrophilic Activation of Borane Complexes of Lewis Bases with Tethered Arenes

Introduction – Other Methods for Arene Borylation

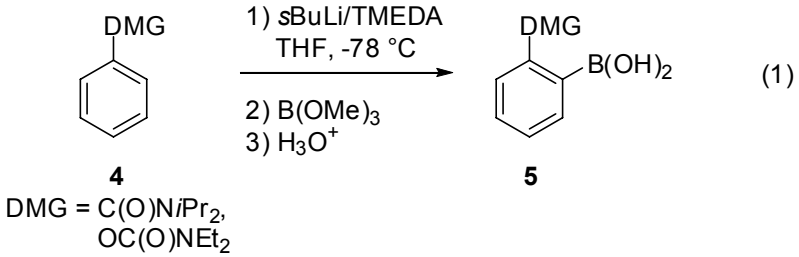
Arylboron derivatives are valuable intermediates in organic synthesis due to their reactivity to further functionalization including C–C bond formation.[1] The C–B bond is commonly formed by trapping an arylmagnesium or -lithium with a boron electrophile,[2] but the reaction of electrophilic boranes with unactivated arenes has also been demonstrated at elevated temperatures (Scheme 3-1).[3] In an early example, diborane reacts with benzene with loss of H_2 at 100 °C to form triphenylboron (**1**).[3a] The more electrophilic BCl_3 was found to react with unactivated arenes under milder conditions with aluminum metal catalysis, presumably making $AlCl_3$ in situ.[3b] The reaction of

Scheme 3-1. Intermolecular Borylation of Unactivated Arenes



toluene under these conditions gives a mixture of *m*- and *p*-substituted products **2a** and **2b** in a ratio of 1:4.6; raising the reaction temperature from 35 °C to 140 °C gives a less selective reaction but still no *ortho*-substitution. Boron substitution *ortho*- to an alkyl group was only observed for substrates such as *p*-xylene where there is no other possibility, and these reactions require higher temperatures (150 °C) for comparable yields. At higher temperatures, however, the reaction was complicated by isomerization of *p*-xylene to *m*-xylene catalyzed by the HCl byproduct, resulting in primarily 1-(dichloroboryl)-3,5-dimethylbenzene.[3c]

Transition metal catalysis can effect arene borylation at room temperature.[1a,4] The research groups of Hartwig and Miyaura have thoroughly studied the iridium-catalyzed reactions of diboron reagents with arenes.[4a] These reactions give high yields of the arylboronic acid esters but suffer from poor regioselectivity and difficult *ortho*-functionalization as in the case of aluminum-catalyzed reactions. The Smith group has found a way around this problem in the reactions of 4-substituted benzonitriles.[4b] Again using iridium catalysis, substitution occurs *ortho*- to the less sterically bulky cyano group with excellent regioselectivities in some cases.

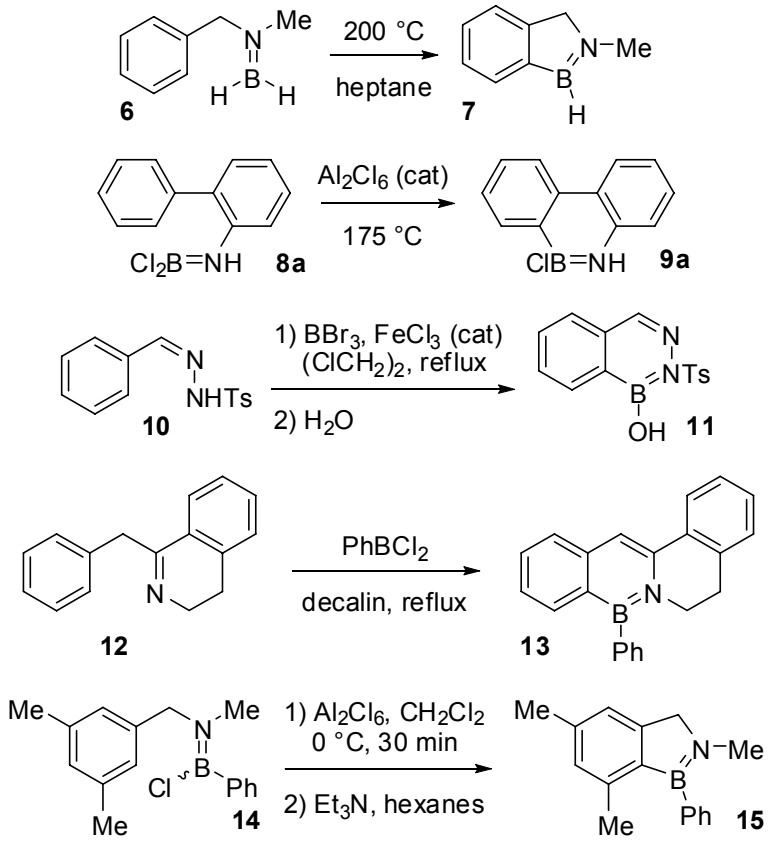


(1)

Directed reactions have been reported which solve these problems, giving access to *ortho*-substituted products with high regioselectivity. Directed ortho metalation[2c] by deprotonation of an arene substituted with a Lewis basic functional group (eq 1, **4**) has been successfully applied to the synthesis of arylboronic acids.[2b] Heteroatom direction

has also allowed highly regioselective electrophilic borylations (Scheme 3-2). For example aminoborane **6** cyclizes to **7**, but only at 200 °C,[5a] and 2-aminobiphenyl complex **8a** requires aluminum chloride catalysis along with high temperatures for formation of aromatic product **9a** with a C–B bond.[5b] Tosylhydrazone **10** (minor (*Z*)-isomer illustrated for convenience) also undergoes selective *ortho*-borylation after exposure to BBr_3 with $FeCl_3$ catalysis, requiring slightly lower temperatures.[5c]

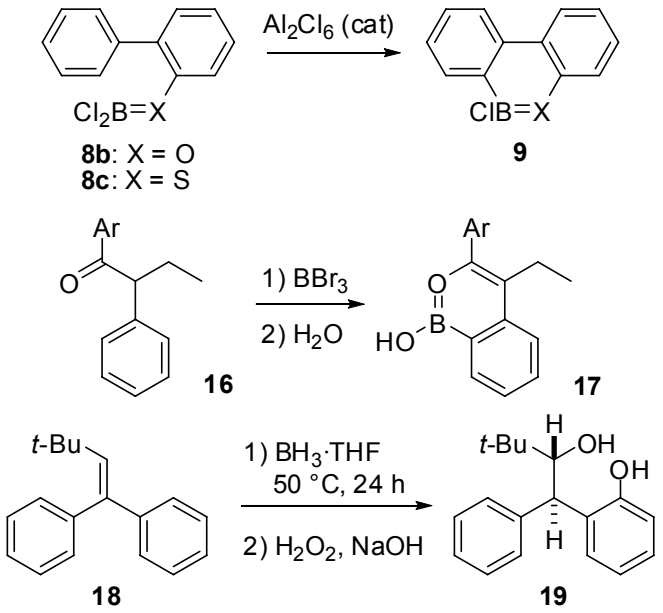
Scheme 3-2. Nitrogen-Directed Electrophilic Boryation



Direction by other heteroatoms has been successful, typically under milder conditions (Scheme 3-3).[6] 2-Hydroxy- and 2-mercaptobiphenyl both react with BCl_3 to form compounds analogous to **8a** which cyclize after exposure to catalytic aluminum chloride but at much lower temperatures. The oxygen complex **8b** forms product **9b** in refluxing petroleum ether;[6a] sulfur complex **8c** cyclizes at rt.[6b] Perhaps the less donating

oxygen and sulfur substituents on boron result in a still more electron-deficient active intermediate, allowing more facile reactions with the tethered arene. Likewise, the oxygen-directed reaction of benzylic ketone **16**, the enol form of which is structurally similar to 2-hydroxybiphenyl, proceeds at rt with excess BBr_3, giving product **17** after aqueous workup.[6c]

Scheme 3-3. Other Directed Boryations

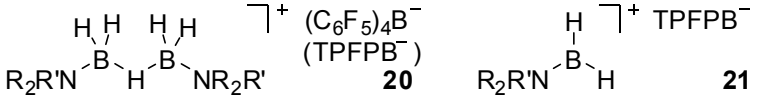


Nitrogen-directed arene borylation can occur under similarly mild conditions if $PhBCl_2$ is used instead of BCl_3 as the electrophilic boron reagent. For example, the reaction of benzylic imine **12** is thought to proceed via an *N*-boryl-enamine intermediate similar to a *B*-phenyl derivative of **8a**. The further reaction to form cyclized product **13** occurs without aluminum chloride catalysis, albeit at high temperatures.[7a] Recently **14**, a *B*-chloro-*B*-phenyl benzylic amine derivative, was reported to cyclize to the *B*-phenyl product **15** at 0 °C in the presence of stoichiometric aluminum chloride.[7b] This activation was proposed to occur via protonation of **14** at nitrogen due to protic impurities activated by the Lewis acid, giving an intermediate trivalent boron cation.

The Lewis acid-catalyzed versions of these reactions likely proceed via cationic boron intermediates that may be stabilized by formation of B–H–B and B–Cl–B bonds as described for activation of amine boranes in the previous chapter or by interaction with a counterion. The *B*-phenyl substituent in **14**, however, may provide enough stabilization to allow the formation of a free trivalent boron cation as a major species, which is expected to be highly reactive toward interaction with nucleophiles like the arene π electrons. The discussion is complicated by the stabilization that *B*-phenyl substitution should provide this borenium ion, raising the activation energy required for its further reaction. However, the reaction from a B–H–B or B–Cl–B bonded intermediate may also occur via release of a free borenium ion, and the formation of trivalent boron could be the slow step in the reactions of these less substituted boron electrophiles. Although the resulting borenium ions would be more reactive toward the arene, their formation in appreciable concentrations would be disfavored by this high reactivity. Arene borylation under mild conditions apparently requires a careful balance between boron cation stability and reactivity.

Styrene derivative **18** demonstrates *C*-directed arene borylation via the hydroboration product, giving a cyclic product with two C–B bonds.[8] This reaction proceeds at 50 °C apparently without any activation of the intermediate organoborane. The authors note that only sterically bulky substrates cyclize after initial hydroboration. This is explained by a conformational requirement for the reaction, that the intermediate organoborane must exist with the boron atom in close physical proximity to an aryl C–H bond for C–B bond formation to occur. These bulky organoborane intermediates would also be more likely to exist in monomeric form, allowing reaction at electrophilic boron without any need for further activation.

It was shown in Chapter 2 that removal of a hydride from a borane complex of a tertiary amine forms a cationic species **20**, considered formally equivalent to the trivalent boron cation **21** and expected to be more reactive toward electrophilic aromatic substitution than the neutral species. As shown in the next sections, activation of an amine or phosphine borane by a hydride acceptor does indeed promote the directed intramolecular electrophilic substitution of a tethered arene at room temperature.[9]



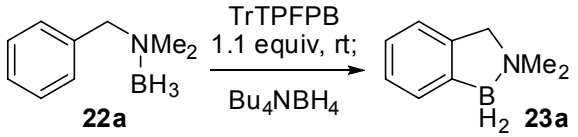
Directed Borylation of Benzylamine Boranes

Optimization of Conditions for Dimethylbenzylamine Borane Cyclization

Optimization of directed arene borylation conditions began with activation of borane complex **22a** using excess trityl tetrakis(pentafluorophenyl)borate (TrTPFPB) as the hydride acceptor (in CH_2Cl_2, Table 3-1, entry 1). Considering the CH_2Cl_2-assisted decomposition of **20** with Ph_3CH described in the previous chapter, this solvent was replaced with toluene, increasing conversion to **23a**. Bromobenzene gave still higher conversion and better isolated yield of the desired product (entry 3). This more polar solvent helps dissolve both TrTPFPB and the activated species **20a**. Due to the low volatility of PhBr, PhCl and PhF were also evaluated, giving similar yields of **23a** but with slightly more decomposition to form Ph_2CH_2. On the labororatory scale the low volatility of PhBr is only a minor inconvenience, so it was used in further studies.

The Bu_4NBH_4 workup described here has also been optimized from initial attempts. An oxidative workup gave at most a 34% yield of the phenolic product corresponding to oxidation of the C–B bond in **23a**. These yields may have been low due

Table 3-1. Optimization of Conditions for Cyclization of **22a**



entry	solvent	time	conversion[a]
1	CH_2Cl_2	4 h	27%
2	Toluene	4 h	48%
3	PhBr	4 h	63%[b]
4	PhBr	1 h	58%
5	PhBr	1 h[c]	1%
6	PhBr	4 h[d]	72%[b]
7	PhBr	20 h[d]	52%

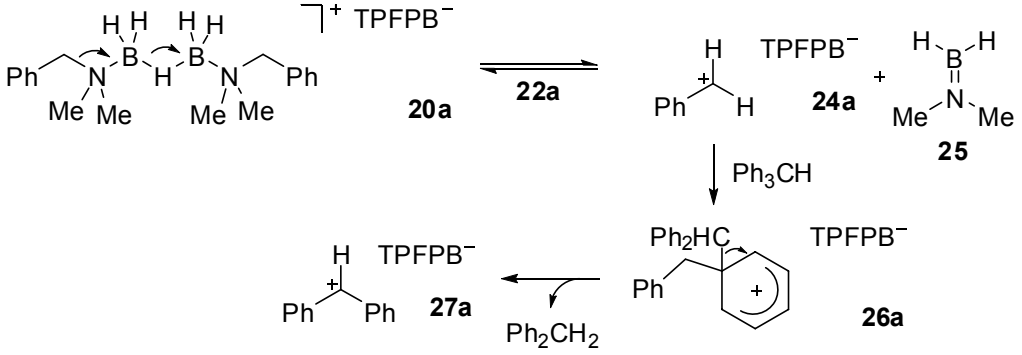
[a] By ^{1}H NMR spectroscopy, **23a** relative to Ph_3CH.
[b] Isolated yield. [c] 0 °C. [d] 0.9 equiv TrTPFPB.

to inefficient oxidation or to difficulty isolating the phenolic amine product. Reductive workup was then examined to give the known benzazaborolidine **23a**.[10] The borane complex of 4-dimethylaminopyridine gave moderate but variable yields of **23a** along with a number of byproducts, likely due to further reactions of borenium-like species generated from the reducing agent as byproducts. Sodium borohydride was examined, an advantage being that the byproduct of the activation should be the volatile diborane. Unfortunately this required the addition of ethereal solvents to solubilize the borohydride salt, and these solvents seem to interact with the product of the reaction at a rate competitive with the hydride quench, resulting in a complex mixture. Only a slurry of $NaBH_4$ in diethylene glycol dimethyl ether (diglyme) gave acceptable yields of **23a** (63% isolated yield under the optimized conditions in entry 6). Finally the organic-soluble Bu_4NBH_4 was selected, combining the advantages of the other hydride sources and resulting in isolation of fairly clean **23a**.[10]

While the reaction had progressed to a significant extent after just 1 h at rt, cooling to 0 °C prevented C–B bond formation. Extended reaction times (entry 7)

resulted in slightly lower isolated yields with a more complex product mixture. One of the byproducts identified was diphenylmethane, possibly formed by interaction of an electrophilic species with Ph_3CH as described in Chapter 2. A benzyl cation formed by C–N bond cleavage from the reactive intermediate **20a** was considered as a possible electrophile, which would yield one equivalent of diphenylmethane directly along with the diphenylmethyl cation **27** (Scheme 3-4). The shorter reaction times and also use of TrTPFPB as the limiting reagent (entry 6) gave a cleaner crude product and higher yield of the aromatic substitution product. Although using the reagent in excess would be desirable in more complex systems, with these relatively simple substrates the expensive TrTPFPB makes sense as a limiting reagent.

Scheme 3-4. Potential Decomposition Pathway for Formation of Ph_2CH_2 from **20a**



Finally, the purification of product **23a** along with recovery of unreacted **22a** was optimized. The crude residue after removal of PhBr was dissolved in CH_2Cl_2 which was then diluted with hexanes to load onto a silica gel column for flash chromatography (FC). The $Bu_4NB(C_6F_5)_4$ salt generated as a byproduct forms a sticky solid under these conditions, and material recovery from FC was variable. Purification by preparative thin layer chromatography (PLC) gave yields comparable to FC, but the salt byproduct stayed at the baseline of the plate, causing uneven development in some cases and again giving variable recovery. Finally, the quenched reaction mixture still in PhBr was loaded

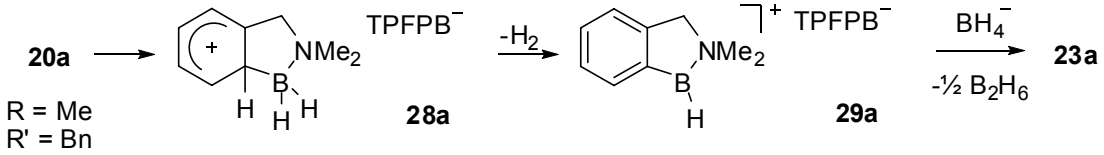
directly onto a column of silica gel for FC, causing the column to crack severely but eliminating the inconvenience of removing this nonvolatile solvent. The cracking led to poor separation of **22** and **23**, particularly with some of the substrates listed in Table 3-2 with small differences in Rf. However this gave >95% material recovery from the reaction of **22a** and >90% for a number of other substrates, demonstrating that over the 4 h reaction time very little decomposition by side reactions occurred.

Investigation into the Reaction Pathway

Having demonstrated a directed aromatic substitution, we sought to elucidate the pathway from **22** to **23**. As mentioned earlier, activation of amine boranes with TrTPFPB generates cations **20** as reactive intermediates. This was verified for borane complex **22a** using the same conditions, activation at -78 °C in CD_2Cl_2. Assay by ^1H NMR at -20 °C showed conversion of **22a** to **20a**, which has an upfield peak at $\delta\ ^1H$ = -1.9 ppm. This chemical shift is in the range of the reported 3-center, 2-electron B–H–B bonds discussed in the previous chapter.[11] The hydride-bridged structure **20a** is also consistent with the δ 0 ppm ^{11}B NMR chemical shift. The solution was then observed by ^1H and ^{11}B NMR 1 h after activation of **22a** at rt in C_6D_5Br. A highly deshielded peak with proton coupling appeared at $\delta\ ^{11}B$ = 59 ppm, consistent with corrected data (vide infra) for the stabilized trivalent boron cation **29a** (Scheme 3-5). A peak was also observed at $\delta\ ^1H$ = 5.4 ppm which is coupled to boron and integrates to 1H. By analogy to the typical Friedel-Crafts reaction pathway,[12] the highly electrophilic boron cation **20a** would form a σ-bonded intermediate (**28a**) which could lose H_2 to form **29a**. Quenching

this cation with Bu_4NBH_4 would then result in hydride transfer to boron, providing the isolable **23a**.

Scheme 3-5. Proposed Pathway for Cyclization to **23a**

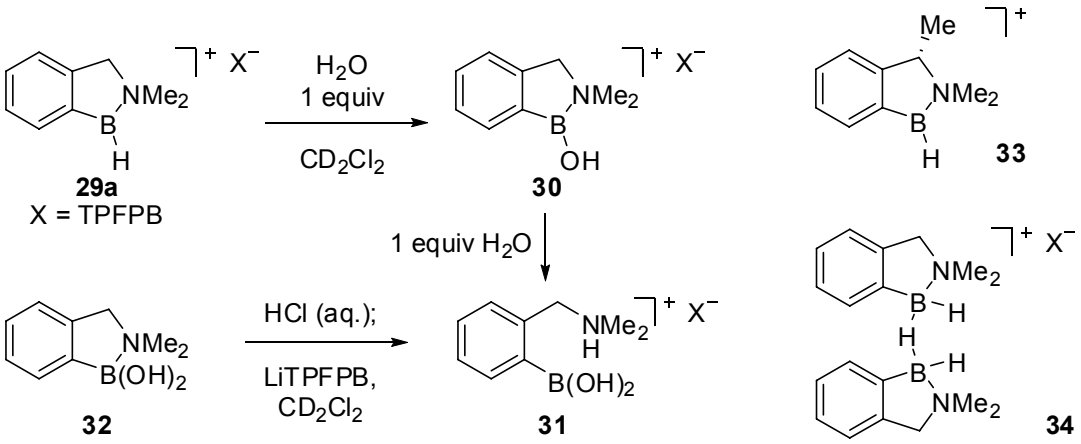


The spectral data observed for **29a** in this study do not match those previously reported for this cation in earlier work from our group.[10,13] Chiral borenium ion **33** was initially sought by Schrimpf for potential applications to enantioselective hydroboration of alkenes and to Lewis acid-promoted additions into imines.[13a] This cation was surprisingly reactive toward weak nucleophiles, abstracting fluoride from the tetrafluoroborate counterion and even from the more weakly coordinating tetrakis(3,5-bistrifluoromethylphenyl)borate anion. In order to study the behavior of the free cation hydride abstraction from **23a** was carried out with trityl cation using the still less reactive tetrakis(pentafluorophenyl)borate (TPFPB) as a counterion.[13b] Nguyen chose to explore activation of the achiral **23a** to facilitate interpretation of the resulting spectra.

With only slight modifications to Nguyen's procedure, hydride abstraction from **23a** with TrTPFPB in CD_2Cl_2 at rt was performed with careful exclusion of moisture. This experiment gave the same chemical shifts described above, confirming the current assignment of **29a**. Addition of 1 equiv of water produced the species previously observed[10] as the major product (^{1}H NMR shifts in accord with those reported; δ ^{11}B = 39 ppm with no proton coupling), which we now assign to structure **30** (Scheme 3-6). Addition of another equivalent of H_2O to **30** gave the protonated boronic acid **31** (δ ^{11}B = 29 ppm; δ ^{1}H = 5.29 (2H, br s, OH), 4.28 (2H, d, benzylic CH_2), 2.89 (6H, d, NMe_2)

ppm), identical to the species formed by protonation of known boronic acid **32** followed by anion metathesis and extraction with CD_2Cl_2.

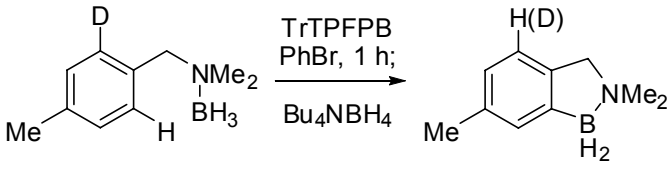
Scheme 3-6. Assignment of Structure **30**



Nguyen also reports isolation of the *B*-pyridine adduct of **29a** as confirmation of the structural assignment;[10] the formation of this adduct had to be rationalized in the context of our reassignment to structure **30**. Taking a fresh look at the spectra recorded by Nguyen revealed a number of different species present from activation of **23a**. One of the major species present was tentatively identified as a hydride-bridged cation **34** by the δ 11 ppm ^{11}B NMR chemical shift and the ^{1}H NMR chemical shifts at δ 4.11 and 2.84 ppm (bridging hydride signal outside the printed region of Nguyen's spectra), downfield from neutral **23a** but upfield from *B*-hydroxyborenium cation **30**. This has now been prepared by the reaction of TrTPFPB with 2 equiv **23a**, confirming its presence in Nguyen's experiment. Quenching this cation with pyridine would generate the adduct previously isolated and characterized as well as an equivalent of **23a**, which was also isolated from Nguyen's pyridine quench.

To gain further insight into the formation of **29** under aromatic subsitution conditions, the rate-determining step was probed by a deuterium labelling study (eq 2).

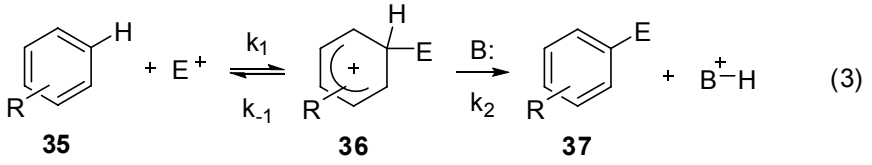
The monodeuterated substrate **22b**-d_1 was prepared by *ortho*-lithiation of *p*-methyl-*N*,*N*-dimethylbenzylamine followed by D_2O quench[14] and borane complexation, giving 95% deuterium incorporation. The directed borylation of this substrate can occur at the protonated carbon with retention of deuterium in the product, while reaction at the deuterated site results in loss of the deuterium label. The ratio of **23b**-d_1 to **23b** therefore corresponds to the relative rate of reaction for substitution of a proton compared to deuterium (k_H/k_D). Substrate **22b** was chosen for this study rather than the simpler **22a** because the ^{1}H NMR signal for the *ortho*-C–H of **23a** overlaps with another aromatic proton signal. All aromatic proton signals for **22b** are fully resolved in the 500 MHz ^{1}H NMR spectrum. The magnitude of the kinetic isotope effect (KIE) observed, in this case k_H/k_D = 2.8 (eq 2), indicates a primary KIE; this means that the C–H(D) bond at which boron substitution occurs is broken during or before the slow step. According to the pathway shown in Scheme 3-5, this precludes all steps but the deprotonation of **28** from being rate-limiting. Direct interaction of electrophilic boron with the C–H(D) σ electrons with concomitant deprotonation cannot be ruled out, but the lack of a strong Brønsted base in these reaction conditions is more consistent with the pathway shown. It is also impossible to determine from this data whether loss of H_2 occurs intramolecularly via a 4-membered transition state or by the action of an external hydride source or other base.



(2)

This result was surprising since most electrophilic aromatic substitution reactions proceed with no KIE.[12,15] In his seminal work Melander reported a negligible KIE in the nitration of a number of simple monotritiated substrates including benzene, toluene and

naphthalene.[15a] These results were subsequently confirmed for nitration of benzene-d_1,[15b] and similar results were obtained in a number of electrophilic aromatic substitution reactions.[12] This was taken as evidence not only that a σ-bonded intermediate (**36**) was involved in the reaction but also that its formation was rate-limiting (eq 3). Observation of a small, inverse secondary KIE in the nitration[15c] and bromination[15d] of perdeuterated arenes was reported as further evidence that formation of a Wheland intermediate (**36**) occurs in the slow step; this inverse KIE is consistent with the change in hybridization of the C–H(D) bonding orbital from sp^2 to sp^3 at the site of subsititution. Recent advances have also allowed measurements of k_H/k_D equal to about 1 for $AlCl_3$-catalyzed acetylation of benzene using natural abundance ^2H NMR spectroscopy.[15e]



(3)

Several cases have, however, been reported in which loss of a proton from **36** is the slow step.[12c,16] For example, the mercuration of benzene with $Hg(OAc)_2$ and $HClO_4$ is six times faster than the reaction of benzene-d_6 under the same conditions; this KIE was attributed to a weak C–Hg bond, increasing the rate of its cleavage from **36** back to **35** relative to deprotonation to form **37** (an increase in k_{-1} relative to $k_2[B]$).[16a] Similarly, iodinations of phenol[16b] and anisole[16c] are subject to a significant KIE ($k_H/k_D \sim 4$ in both cases), possibly due to a weaker C–I bond as described for mercuration but also due to decreased acidity of **36** afforded by oxygen stabilization of the cationic intermediate. The magnitude of the KIE in the reaction of an arene with *p*-chlorobenzenediazonium was found to be dependent on the concentration of added pyridine base.[16d] At a pyridine concentration of 0.905M, k_H/k_D decreases to 3.62 from 6.55 in its absence, showing that

deprotonation to **37** is slowed relative to initial interaction of the electrophile with the arene. The addition of base increases $k_2[B]$, but k_{-1} remains unchanged. Similar conditions exist in the present study, where even the hydride acceptor's counterion was chosen to be as weakly basic as possible. Finally, this phenomenon has recently been observed in an acylation of toluene, for which k_H/k_D decreases from 1.85 in the presence of TfOH to 1.14 in the presence of a hindered 2,4,6-tri-*t*-butylpyridine base.[16e] It was also noted that the *para*/*ortho* ratio in the product increases from 2.4 in the base-promoted conditions to 10.4 with added TfOH. Under the conditions of added base $k_2[B]$ is much greater than k_{-1}, meaning that k_1 is the rate- and also regioselectivity-deteremining step. Under the acidic conditions, $k_2[B]$ decreases relative to k_{-1}; this reverse reaction becomes more important, allowing the intermediates **36** to equilibrate such that the increased steric repulsions for *o*-substituted **36** have a greater effect in determining regioselectivity.

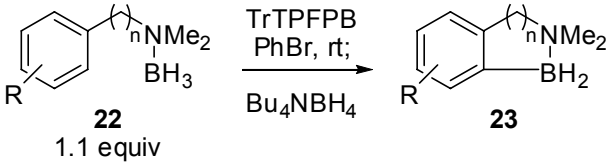
Substrate Scope and Limitations

In addition to facilitating the measurement of a KIE, the reaction of **22b**-d_1 demonstrates tolerance of the directed borylation to aryl substitution, warranting further investigation into the scope of the reaction. Although the isolated yield of **23b** from **22b** was modest (Table 3-2, entry 2), *m*- and *o*-methyl substitution gave higher yields of cyclized products. Halogen substituents were also compatible, although longer reaction times were required for good conversion to **23e-k** (entries 5-10). It is noteworthy that substrates with *ortho*-halogen substitution (entries 8-10) required still longer reaction times and gave lower yields than the corresponding *para*-substituted substrates (entries 5-7), possibly indicating non-productive formation of a B–X bond between electrophilic

boron and the *ortho*-halogen. Testing the tether length showed that even formation of the 7-membered ring was viable (entry 12), but this required 16 h and gave only 42% of **23n**.

Table 3-2. Scope of the Directed Borylation

entry	substrate	R	n	time	Yield
1	**22a**	H	1	4 h	72%
2	**22b**	*p*-Me	1	4 h	41%
3	**22c**	*m*-Me	1	4 h	79%[a]
4	**22d**	*o*-Me	1	4 h	76%
5	**22e**	*p*-Br	1	8 h	53%
6	**22f**	*p*-Cl	1	8 h	73%
7	**22g**	*p*-F	1	16 h	59%
8	**22h**	*o*-Br	1	16 h	55%
9	**22j**	*o*-Cl	1	16 h	55%
10	**22k**	*o*-F	1	16 h	39%
11	**22m**	H	2	4 h	74%
12	**22n**	H	3	16 h	42%

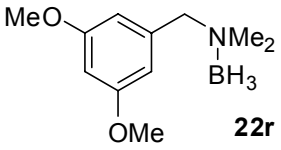


[a] 3:1 mixture of regioisomers.

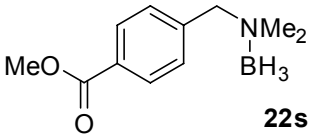
Although the yields from substrates **22k** and **22n** were low, 30-40% of the starting material was recovered from these reactions. The decomposition described in Scheme 3-4 should be disfavored from **22k** due to the destabilizing effect of the strongly electron-withdrawing *ortho*-fluorine on **24k**. For **22n**, the C–N bond cleavage previously described would result in a primary carbocation; while the desired reaction is slowed in both of these cases, the side reactions are slowed as well. Thus these sluggish substrates result in higher recovery of starting material despite the longer reaction times. In the other entries 10-20% of the starting material was recovered.

The longer reaction times required for halogen-substituted **22e-k** provide additional evidence for a mechanism similar to the typical electrophilic aromatic

substitution.[12] Electron-withdrawing groups on the arene would disfavor formation of **28**, which occurs before the rate-limiting step. Electron-donating groups should therefore

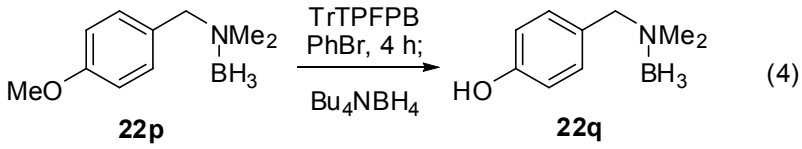


22r



22s

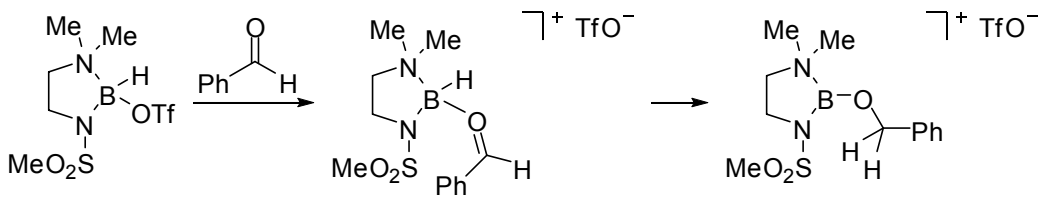
accelerate the reaction, so a 3,5-dimethoxy substituted substrate (**22r**) was tested, but the crude product was a complex mixture with no evidence of a cyclized product. The simpler monosubstituted substrate **22p** was then tested to determine the compatibility of a methyl ether with the reaction conditions (eq 4). After 4 h at rt no product **23p** was detected after the typical borohydride quench. In addition to recovered starting material (57%), **22q** was isolated (25%). Evidently, the methyl aryl ether is partly cleaved under



22p **22q** (4)

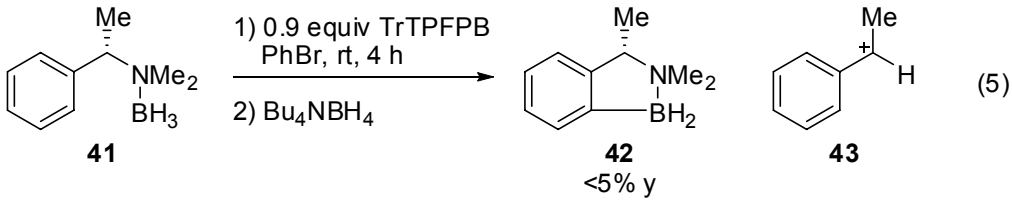
the reaction conditions, and the resulting phenol derivative interferes with subsequent cyclization. An ester functionality was examined by testing 4-carbomethoxy substituted benzylic amine borane **22s**, but this also gave a complex product mixture in which no cyclized product was observed. A similar O-Me cleavage could be responsible, but coordination of the Lewis basic carbonyl oxygen followed by hydride transfer to the activated carbonyl carbon is also precedented (Scheme 3-7).[13b]

Scheme 3-7. Reduction of a Carbonyl by Hydride Bound to Electrophilic Boron



38 **39** **40**

Reactions of Diastereomeric 2-Phenylpyrrolidine Boranes



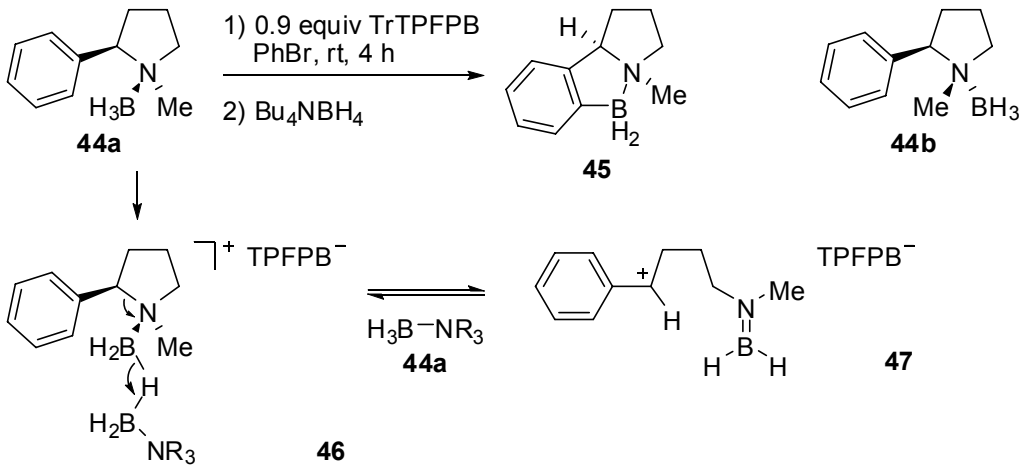
41 **42** <5% y **43** (5)

As part of our research group's hydroboration efforts, it has been proposed that borenium ion **29** would be reactive toward an alkene. It was hoped that cyclization of **41**, the borane complex of commercially available (*S*)-*N*,*N*-dimethyl-α-methylbenzylamine, would finally provide access to **33** for enantioselective hydroboration, quenching the cyclization with an alkene instead of with borohydride. The cyclization of **41** was tested by A. Prokofjevs, but unfortunately this substrate failed to cyclize, giving byproducts indicating C–N bond cleavage from the active intermediate (**20**).[17] This will be a greater problem for the cyclization of any α-substituted substrate due to the greater stability of the resulting 2° benzylic carbocation (**43**).

It was then proposed that a cyclic substrate, **44**, prepared by methylation of (*R*)-2-phenylpyrrolidine[18] followed by exposure to BH_3·THF, could prevent this decomposition. Reducing the conformational flexibility of the substrate, holding the electrophilic boron formed on activation in proximity to the phenyl ring as in diastereomer **44a**, should accelerate the desired arene borylation but should not affect the rate of C–N bond cleavage. Furthermore, tethering the amine to the benzylic position means that even if C–N bond cleavage to **47** does occur as a side reaction, the reverse reaction (Scheme 3-8) would be faster than in an acyclic case, perhaps faster than the subsequent interaction of

the benzylic cation with an external nucleophile. Unfortunately this may also result in epimerization of both stereocenters.

Scheme 3-8. Cyclization of **44a** and Possible Epimerization via **47**



In the event, activation of **44a** (impure with the diastereomeric borane complex **44b** in a ratio of 17:1) followed by the standard hydride quench resulted in ca. 74% conversion to product **45** by ^{1}H NMR assay. Purification gave only a 24% yield of **45**; 2D TLC confirmed decomposition of this product on silica gel. Also recovered was a mixture of **44a** and its diastereomer **44b**. The amount of **44b** calculated in this mixture corresponds to 195% recovery of the **44b** impurity taken in to the activation, implying its formation from **44a** as well under the reaction conditions. The simplest explanation is that formation of **47** indeed occurs as a reversible side reaction, and the reverse reaction occurs without stereospecificity. However this is not a major reaction pathway, as the amount of **44b** formed in the reaction accounts for the fate of only about 5% of **44a**.

Diastereomerically pure **44b** was also subjected to the activation, but the crude ^{1}H NMR spectrum showed no evidence of a C–B bonded product. This is consistent with a rate enhancement for cyclization from **44a** due to the *cis*-relationship between the phenyl group and borane; likewise the *trans*-relationship of these substituents in **44b** prevents

interaction of the arene with electrophilic boron. The crude product mixture contained an unknown byproduct but also a mixture of **44a** and **4b** in a ratio of ca. 1:1. Since the substrate used in this experiment was diastereomerically pure, the formation of **44a** is again taken as evidence of reversible C–N bond cleavage of the reactive intermediate to **47**. The presence of **44b** in the reaction mixture apparently interferes with formation of **45** from **44a** although the basis of this inhibition is not understood.

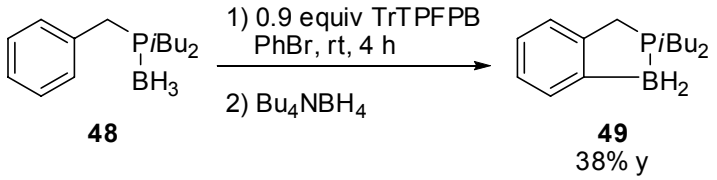
In conclusion, the evidence presented above demonstrates that electrophilic arene borylation proceeds at room temperature following activation of benzylamine boranes with a hydride acceptor. This nitrogen-directed reaction results in highly *ortho*-selective C–B bond formation, giving arylborane products without further boron substitution. This regioselectivity is complementary to transition metal-catalyzed arene borylation, which typically gives mixtures of meta- and para-substituted products[1a,4a] although borylation *ortho*- to the nitrile group in 4-substituted benzonitriles has been reported.[4b] The pathway was shown to involve a hydride-bridged cation **20**, and the kinetic isotope effect supports rate-limiting deprotonation of the Wheland intermediate **28**. The reaction is tolerant of the presence of substituents at any position on the arene but is slowed by electron-withdrawing groups, consistent with an electrophilic aromatic substitution pathway.

Directed Borylation of Phosphine Boranes

Activation of a Benzylic Phosphine Borane

After succesfully developing a nitrogen-directed arene borylation under conditions of trityl activation of a borane complex, out attention turned to other potential directing groups. Phosphine boranes were a logical choice, having been shown to behave

in a manner similar to amine boranes under the activation conditions in Chapter 2. Therefore the borane complex of a known benzylic phosphine[19] was examined (eq 6). Under the optimized conditions for nitrogen-directed arene borylation product **49** was isolated in only 38% yield, significantly lower than from the analogous benzylic amine borane.

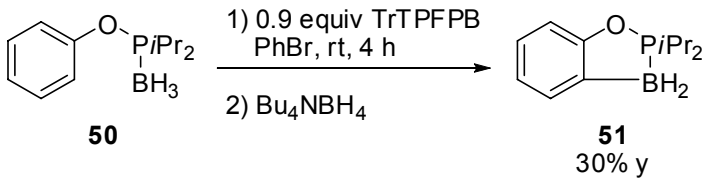


48 **49** 38% y (6)

A significant amount of the typical decomposition byproduct Ph_2CH_2 was also isolated from the reaction mixture in a ratio of ca. 1:3 with Ph_3CH, more than was observed from the reaction of **22a** after 4 h. This may have resulted from formation of a benzyl cation by the same pathway described earlier (Scheme 3-4). In this case a simple benzyl cation is invoked as would be the case from **22a**. More facile formation of the benzyl cation is a result of cleavage of the weaker C–P bond, explaining the lower yields and increased formation of decomposition byproducts.

Phenol-Derived Substrate

Since benzylic phosphine boranes suffered from problems thought to stem from a weakness of the bond between phosphorus and the benzylic carbon, the next generation replaced this carbon with a heteroatom. This should prevent heterolytic cleavage by the pathway described above, forming a cationic sextet oxygen atom from **50** if decomposition were to occur by the same mechanism. This borane complex of phenyl diispropylphosphinite[20] should also benefit from an electron-donating effect of the oxygen substituent in the electrophilic aromatic substitution, and the phosphine might be a removable directing group, making this borylation effectively hydroxyl-directed.



50 **51** 30% y (7)

Activation of **50** under standard conditions followed by a borohydride quench (eq 7) resulted in 83% conversion to product **51** by ^{1}H NMR assay, but this product was only obtained in about 30% yield due to instability to silica gel. Other workup methods that would result in a product with an intact C–B bond were therefore examined. The pinacol ester of the boronic acid in particular was sought due to demonstrated applications of the free phenol derivative (**52**) in Suzuki-Miyaura cross-couplings.

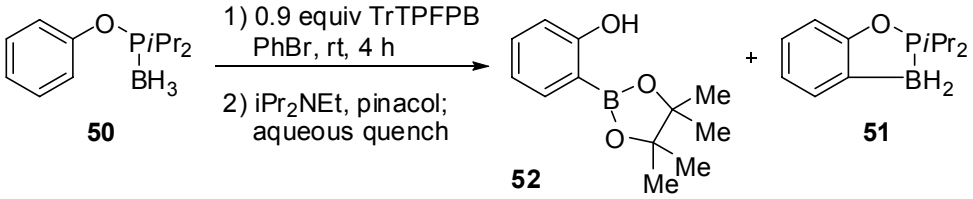
Promising results came from an initial quench with Hünig's base and a solution of pinacol followed by an aqueous quench (Table 3-3, entry 1), a procedure that had been optimized for formation of vinylboronates via alkyne hydroboration.[21] Surprisingly, this gave a product mixture composed of both **52** and the reduced product **51** in a 1.5:1 ratio. Replacement of the water added after pinacol with 5% aq. NaOH gave traces of **52** in addition to isolation of a small amount of catechol, indicating oxidation of the C–B bond. No reduced product **51** was present to account for the remainder of the material, but under these conditions a deeply colored insoluble material formed during the 16 h exposure to NaOH, similar to the "dark polymeric material" reported from decomposition of *o*-hydroxyphenyl trifluoroborate under basic aqueous conditions.[22] Using a less basic solution of 10% aq. Na_2CO_3 (entry 3) gave higher apparent conversion to **52** but with formation of the same insoluble material. This 72% conversion is based on integration of the ^{1}H NMR peaks relative to Ph_3CH and Ph_2CH_2 in the crude product; since the composition of the insoluble material is unknown this may not be an accurate estimate of the actual amount of **52** recovered, but purification attempts have not been successful.

Therefore the lower apparent conversion using saturated $NaHCO_3$ (entry 6) should be viewed in context of the absence of this insoluble material; it is a more reliable estimate. After the observation of catechol in entry 2, an inert atmosphere was maintained during

Table 3-3. Optimization of the Pinacol Workup

Entry	aqueous quench[a]	conv. to **52**[b]	conv. to **51**[b]
1	H_2O	53	34
2	5% NaOH	trace	ND[c]
3	10% Na_2CO_3	72	ND[c]
4	10% Na_2CO_3[d]	26	38
5	10% Na_2CO_3[e]	40	38
6	saturated $NaHCO_3$	32	ND[c]
7	saturated $NaHCO_3$[d]	47	37
8	1M HCl	29	56

[a] Standard conditions for 100 μmol scale reaction: 4 equiv iPr_2NEt added to quench followed by 4 equiv pinacol, then after 1 h 0.4 mL H_2O added, stirring open to atmosphere 16 h. [b] By ^1H NMR assay, integrated relative to sum of Ph_3CH and Ph_2CH_2. [c] Not detected. [d] Kept under N_2. [e] Exposed to aqueous Na_2CO_3 1 h.



the aqueous quench to prevent oxidation due to atmospheric oxygen (entries 4 and 7), again resulting in recovery of a significant amount of reduced product **51**. Some hydride exchange must occur between cationic intermediates of the cyclization related to **29** after nucleophilic attack on boron, but after exposure to air under basic conditions this product **51** is oxidized to derivatives of **52**. These oxidation pathways may also be responsible for some of the insoluble material since it was minimized in entries 4 and 7 as well, with exclusion of air. Likewise, 1M HCl (entry 8) resulted in a clean crude product but with a low ratio of **52** to **51**. Despite the success of cyclization from **50**, the challenge of cleaving the O–P bond and isolating an *o*-hydroxyphenyl boronic acid derivative, effecting a net hydroxy-directed borylation, remains.

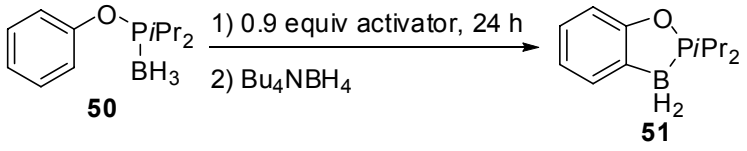
Strong Acid Activation

Cyclization of phenyl phosphinite borane **50** under TrTPFPB activation led to a desire to test the added arene reactivity toward electrophilic aromatic substitution afforded by an oxygen substituent. Specifically, previous attempts at strong acid activation for the cyclization of benzylic amine borane **22a** had proven ineffective. In all cases the product was simply a BH_2X complex of the amine, showing that even slightly more coordinating anions than $(C_6F_5)_4B^-$, such as I^-, TfO^-, and even Tf_2N^-, were not good enough leaving groups for attack of the arene at boron.

Table 3-4. Strong Acid Activation for Cyclization of **51**

entry	activator	solvent	temperature	conv.[a]
1	Tf_2NH	PhBr	rt	<1%
2	Tf_2NH	CH_2Cl_2	rt	<1%
3	Tf_2NH	PhBr	100 °C	69%
4	Tf_2NH	toluene	100 °C	34%
5	Tf_2NH	*o*-$C_6H_4Cl_2$	100 °C	67%
6	Tf_2NH	CH_2Br_2	100 °C	49%[b]
7	Tf_2NH[c]	PhBr	100 °C	58%
8	TfOH[c]	PhBr	100 °C	<1%[b]
9	I_2[d]	PhBr	100 °C	5%

[a] By ^{1}H NMR assay, integration of **51** relative to **50**. [b] *i*Pr methine region of ^{1}H NMR spectrum complex. [c] 1.1 equiv acid used. [d] 0.6 equiv.



50 **51**

Initially, treatment of **50** with Tf_2NH at rt showed only traces of cyclization product **51** on quenching with Bu_4NBH_4 even after 24 h (Table 3-4, entry 1). Heating the reaction to 100 °C gave 69% conversion to **51**, but attempts to improve this were

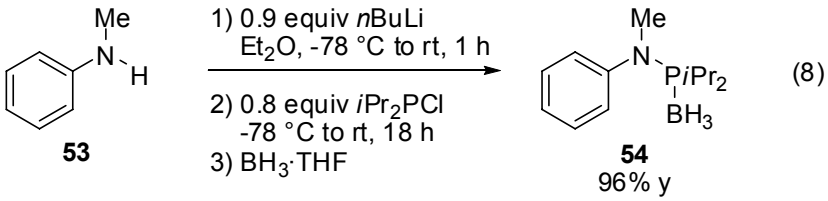
unsuccessful. Unlike activation with TrTPFPB, this reaction is proposed to proceed via a neutral intermediate, the less electrophilic BH_2NTf_2 complex, with rate-limiting formation of a charged Wheland intermediate analgous to **28**. If this is true, a more polar solvent should accelerate the reaction by stabilizing charge development in the transition state. Using the less polar toluene as reaction solvent (entry 4) did in fact result in lower conversion over the same time, but the more polar *o*-dichlorobenzene did not improve conversion relative to bromobenzene. The polar aliphatic solvent dibromomethane gave slightly lower apparent conversion, but this may be due to side reactions involving relatively labile C–Br bonds.

Activation with other strong acid sources gave only slight conversion to product after 24 h. Trifluoromethanesulfonic acid (entry 8), gave only trace **51**, but this slightly stronger Brønsted acid[23] might lead to side reactions other than simple hydride abstraction. Iodine activation, using a little more than half an equivalent to allow initial B–H bond reaction with I_2 and subsequent activation with the hydroiodic acid thus formed as described in Chapter 2, surprisingly gave a quantifiable amount of product **51**. However the boundaries of electrophilicity required for reaction of an oxygen-substituted arene are clear.

Aniline-Derived Substrate

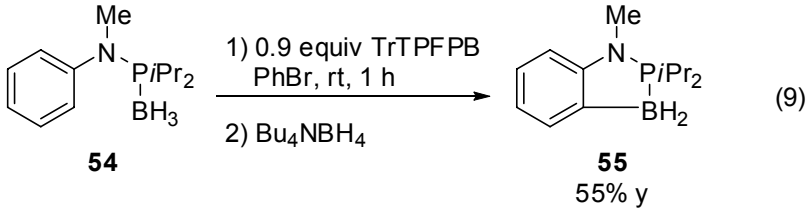
With clear evidence of the reactivity enhancement due to an oxygen substituent and directing group, analogous direction by aniline nitrogen was sought. Replacement of oxygen in **50** with the more cation-stabilizing nitrogen was hoped to give cyclization under still milder conditions. This substrate, however, proved more difficult to prepare. Unlike phenol, the reaction of the less acidic *N*-methylaniline (**53**) with $i Pr_2PCl$ in the presence of Et_3N did not go to conversion even in refluxing toluene. Deprotonation of **53**

with *n*BuLi led to efficient formation of **54**,[24] but the reaction stoichiometry had to be adjusted to minimize formation of an inseparable $n\text{Bu}(i\text{Pr})_2\text{P}\cdot\text{BH}_3$ side product (eq 8).



(8)

This substrate was tested under the typical directed borylation conditions, but quenching after 4 h resulted in a complex crude product mixture without any trace of the desired product **55** but also with very little unreacted **54**. Quenching after just 1 h led to 56% conversion to **55** by ^{1}H NMR assay and allowed isolation of this silica gel-stable cyclized product in 55% yield (eq 9). Similar conversion to **55** was observed within just 10 min, demonstrating the pronounced reactivity of this *N*-substituted arene.



(9)

Considering the additional activation provided by nitrogen in **54**, its Tf_2NH-promoted reaction was explored. After 24 h at 100 °C, or even at rt, no product **55** was obtained after reductive workup but very little **54** remained. The major species present in the complex crude mixture was $i\text{Pr}_2\text{P(O)H}$, the product of hydrolysis of **54**. Using a shorter reaction time (1 h) allowed recovery of **54** and a smaller amount of $i\text{Pr}_2\text{P(O)H}$, but in no case was the desired intramolecular borylation product **55** isolated.

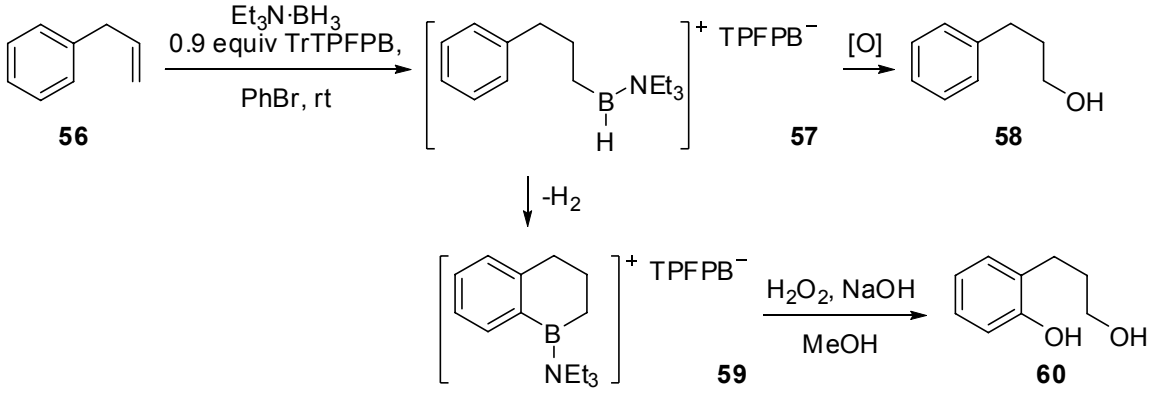
Phosphorus direction has therefore been demonstrated with carbon, nitrogen and oxygen tethers, providing access to *ortho*-heteroatom borylation products. The C–P bond was a liability in the benzylphosphine borane substrate **48**, while phenyl phosphinite

borane **50** gave a product that is unstable to silica gel. So far other workup methods have proven difficult to evaluate. However, this substrate allowed us to realize the exciting possibility of strong acid activation albeit at high temperatures, circumventing the need for the expensive TrTPFPB.

Attempts at *C*-Directed Borylation via Hydroboration of Allylic Arenes

Inspired by the example from Knochel's research group,[8] an example of carbon-directed arene borylation seemed a fitting conclusion to these studies. An important contribution would be to address a limitation of that work in the stated need for bulky substituents. In the discussion of substrate **18** in the introduction to this chapter, this requirement was proposed to stem from a need for dimeric hydroboration products to dissociate prior to aromatic substitution. The previously developed intermolecular hydroboration with TrTPFPB activation (Chapter 2) is believed to yield a cationic trivalent boron intermediate (**57**). This species is more likely to exist as a monomer due to charge repulsion that should discourage formation of the dimer. Structure **57** may also be more reactive for subsequent electrophilic aromatic substitution due to its positive charge (Scheme 3-9).

Scheme 3-9. Proposed Pathway for Hydroboration/*C*-Directed Arene Borylation



Application of the optimized hydroboration conditions to allylbenzene gave 3-phenyl-1-propanol (**58**) in 74% yield as the only product after 4 h. If the reaction time was extended to 24 h before oxidative quench, a small amount of **60** was isolated (<1%); similar results were obtained on replacing the solvent with DCM. This shows that the hydroboration is successful under these conditions, but the *C*-directed arene borylation does not proceed at an appreciable rate at rt. Heating the reaction mixture to 100 °C after adding **56** to activated $Et_3N{\cdot}BH_3$ at rt gave only slightly better results, a 3% yield of **60** along with ca. 90% conversion to **58**. A 3,5-dimethyl derivative of **56** was prepared by reaction of the aryl Grignard reagent with allyl bromide[25] in hopes that the addition of two electron-donating methyl substituents would sufficiently enhance the reactivity of the arnene, but hydroboration of this substrate still occurred without *C*-directed borylation. The reasons for this apparently slow cyclization from **57** were not investigated in depth, but a possible explanation is steric interaction with the triethylamine ligand on boron preventing interaction with the arene. The rest of the substrates explored in this chapter were substituted only by hydrides at the terminal boron. Any sterically bulky substituents were in the tether, which may even enhance reactivity by a Thorpe-Ingold effect.

Summary

We have shown herein that a highly regioselective arene borylation can in fact be achieved under mild conditions with trityl activation. This reaction occurs from borane complexes of a number of different heteroatomic directing groups. While we have discovered much about how these reactions proceed and about the behavior of the reactive intermediates, examples such as the surprisingly sluggish tandem

hydroboration/arene borylation reveal the gaps in our understanding of these highly electrophilic species. A clearer picture of the desired reaction pathway as well as the side reactions will aid the development of activation conditions with greater functional group tolerance and perhaps the development of a broader scope with respect to the directing group, providing ample opportunities for further development of this methodology. From the observed KIE for the reaction of **22b** it can be concluded that the presence of a Brønsted base will accelerate these reactions. This base could take the form of something as simple as a more reactive counterion than $B(C_6F_5)_4^-$, but a more stabilized borenium cation than $R_3N{\cdot}BH_2^+$ will have to be found to prevent a more basic anion from quenching the reactive intermediate. It would be interesting to explore the effects of boron substitution that emerge from analysis of the examples of electrophilic arene borylation in the literature. Future development of this methodology could apply these trends to find the right balance between stability of the cationic boron intermediates while maintaining high reactivity toward the arene nucleophile, but the room temperature activation of stable, isolable BH_3 complexes of Lewis bases described here already represents an improvement over similar methodologies described in the literature.

Experimental

General Methods. The following chemicals were commercially available and used as received: dimethylbenzylamine; borane tetrahydrofuran, 1.0 M solution in tetrahydrofuran; trityl tetrakis(pentafluorophenyl)borate (TrTPFPB); lithium tetrakis-(pentafluorophenyl)borate, ethyl ether complex; tetrabutylammonium borohydride; 4-methylbenzyl bromide; dimethylamine, 5.6 M solution in ethanol; 3-methylbenzyl bromide; 2-methylbenzyl bromide; 4-bromobenzyl bromide; 4-chlorobenzyl bromide; 4-fluorobenzyl bromide; 2-bromobenzyl bromide; 2-chlorobenzyl bromide; 2-fluorobenzyl bromide; (2-bromoethyl)benzene; (3-bromopropyl)benzene. Bromobenzene, C_6D_5Br and CD_2Cl_2 were dried by storing over activated 4Å molecular sieves; dichloromethane (DCM), ethyl ether (Et_2O) and tetrahydrofuran (THF) were dried by passing through a column of activated alumina; toluene was distilled from CaH_2 under an N_2 atmosphere. All reactions were performed at room temperature under an N_2 atmosphere unless otherwise stated. Nuclear magnetic resonance experiments were performed on Varian Inova 500 and Inova 400 spectrometers at the following frequencies: ^1H 500 MHz; $\{^1H\}^{13}C$ 101 MHz; ^{11}B 160 MHz; ^{19}F 376 MHz, unless otherwise stated. All spectra were recorded in $CDCl_3$ and referenced to the ^1H signal of internal Me_4Si (unless otherwise stated) according to recommendations,[26] using a Ξ of 25.145020 for Me_4Si (^{13}C), a Ξ of 32.083974 for $BF_3{\cdot}OEt_2$ (^{11}B), and a Ξ of 94.094011 for CCl_3F (^{19}F).

Preparation of Dimethylbenzylamine Borane (22a).

$BH_3{\cdot}THF$ (9.0 mL, 9.0 mmol) was added by syringe under an N_2 atmosphere to neat dimethylbenzylamine (1.2 mL, 8.0 mmol). After 1 h, the solution was filtered

through a plug of silica gel, flushing with DCM and removing solvent by rotary evaporation. The solid product was further dried under high vacuum, yielding 1.12 g **22a** (94%). ^{1}H, ^{13}C and ^{11}B NMR spectral data matched those reported for **22a**.[27]

General Procedure for Preparation of Borane Complexes for Directed Borylation (22b-n)

A solution of 3-methylbenzyl bromide (1.02 g, 5.5 mmol) in DCM (used without drying, 2 x 2 mL) was added to dimethylamine (5.6 M solution in ethanol, 2.0 mL, 11 mmol) diluted with DCM (used without drying, 25 mL) with stirring. After 3 h the reaction was quenched by addition of 5% aq. NaOH (20 mL), separating the layers and extracting the aqueous layer with 2 x 10 mL DCM. The combined organic layers were washed with brine (25 mL), dried over Na_2SO_4 and reduced by rotary evaporation. The crude product was dissolved in anhydrous DCM (10 mL) and reacted with BH_3·THF (1.0 M in THF, 6.0 mL, 6.0 mmol), stirring 1 h before filtering the solution through a plug of silica gel, flushing with 20 mL DCM. The filtrate was reduced under a stream of N_2, giving 395 mg 5c as a slightly yellowish oil (44% y). 3-Methylbenzyldimethylamine borane (**22c**): analytical thin layer chromatography (TLC) on K6F silica gel 60Å, 4:1 hexanes/EtOAc, Rf = 0.49. Molecular ion calculated for $C_{10}H_{18}BNNa$: 186.1430; [M+Na], ESMS found *m*/*z* = 186.1423; IR (neat, cm^{-1}) 2366, B–H; 2319, B–H; 2273, B–H; 1466, B–N; 1167, C–N; ^{1}H NMR: δ 7.29 (1H, t, J = 7.5 Hz), 7.22 (1 H, d, J = 7.7 Hz), 7.13-7.10 (2H, m), 3.95 (2H, s), 2.50 (6H, s), 2.38 (3H, s), 2.2-1.4 (3H, br m); ^{13}C NMR: δ 138.1, 132.9, 131.1, 129.8, 129.2, 128.3, 67.4, 49.6, 21.3; ^{11}B NMR: δ -8.2 (q, J = 94 Hz).

4-Methylbenzyldimethylamine borane (**22b**, 54% y): TLC on K6F silica gel 60Å, 4:1 hexanes/EtOAc, Rf = 0.44. Molecular ion calculated for $C_{10}H_{18}BNNa$: 186.1430; [M+Na], ESMS found *m*/*z* = 186.1436; IR (neat, cm^{-1}) 2362, B–H; 2312, B–H; 2271, B–H; 1465, B–N; 1167, C–N; ^{1}H NMR: δ 7.20 (4H, s), 3.95 (2H, s), 2.49 (6H, s), 2.38 (3H, s), 2.2-1.4 (3H, br m); ^{13}C NMR: δ 139.1, 132.1, 129.1, 128.2, 67.2, 49.5, 21.2; ^{11}B NMR: δ -8.3 (q, J = 91 Hz).

2-Methylbenzyldimethylamine borane (**22d**, 79% y): TLC on K6F silica gel 60Å, 4:1 hexanes/EtOAc, Rf = 0.39. Molecular ion calculated for $C_{10}H_{18}BNNa$: 186.1430; [M+Na], ESMS found *m*/*z* = 186.1431; IR (neat, cm^{-1}) 2364, B–H; 2315, B–H; 2271, B–H; 1470, B–N; 1165, C–N; ^{1}H NMR: δ 7.33-7.20 (4H, m), 4.09 (2H, s), 2.53 (6H, s), 2.43 (3H, s), 2.2-1.4 (3H, br m); ^{13}C NMR: δ 139.0, 133.3, 131.3, 129.8, 129.2, 125.8, 63.6, 49.7, 20.3; ^{11}B NMR: δ -8.0 (q, J = 95 Hz).

4-Bromobenzyldimethylamine borane (**22e**, 77% y): TLC on K6F silica gel 60Å, 4:1 hexanes/EtOAc, Rf = 0.30. Molecular ion calculated for $C_{9}H_{15}BBrNNa$: 250.0379; [M+Na], ESMS found *m*/*z* = 250.0389; IR (neat, cm^{-1}) 2366, B–H; 2321, B–H; 2269, B–H; 1463, B–N; 1167, C–N; ^{1}H NMR: δ 7.54 (2H, d, J = 8.8 Hz), 7.22 (2H, d, J = 8.8 Hz), 3.93 (2H, s), 2.51 (6H, s), 2.2-1.4 (3H, br m); ^{13}C NMR: δ 133.8, 131.7, 130.2, 123.7, 66.9, 49.9; ^{11}B NMR: δ -8.3 (q, J = 90 Hz).

4-Chlorobenzyldimethylamine borane (**22f**, 91% y): TLC on K6F silica gel 60Å, 4:1 hexanes/EtOAc, Rf = 0.28. Molecular ion calculated for $C_{9}H_{15}BClNNa$: 206.0884;

[M+Na], ESMS found *m/z* = 206.0876; IR (neat, cm^{-1}) 2368, B–H; 2315, B–H; 2279, B–H; 1461, B–N; 1169, C–N; ^{1}H NMR: δ 7.38 (2H, d, J = 8.4 Hz), 7.29 (2H, d, J = 8.4 Hz), 3.94 (2H, s), 2.51 (6H, s), 2.2-1.4 (3H, br m); ^{13}C NMR: δ 135.4, 133.5, 129.6, 128.6, 66.8, 49.9; ^{11}B NMR: δ -8.4 (q, J = 90 Hz).

4-Fluorobenzyldimethylamine borane (**22g**, 91% y): TLC on K6F silica gel 60Å, 2:1 hexanes/EtOAc, Rf = 0.47. Molecular ion calculated for $C_{10}H_{19}BFNNaO$: 222.1441; [M+Na+MeOH], ESMS found *m/z* = 222.1435; IR (neat, cm^{-1}) 2366, B–H; 2319, B–H; 2277, B–H; 1468, B–N; 1162, C–N; ^{1}H NMR: δ 7.35-7.30 (2H, m), 7.12-7.16 (2H, m), 3.95 (2H, s), 2.51 (6H, s), 2.2-1.4 (3H, br m); ^{13}C NMR: δ 163.2 (d, J = 249 Hz), 134.0 (d, J = 9 Hz), 127.2 (d, J = 4 Hz), 115.5 (d, J = 21 Hz), 66.7, 49.8; ^{11}B NMR: δ -8.5 (q, J = 95 Hz); ^{19}F NMR: δ -112.2 (m).

2-Bromobenzyldimethylamine borane (**22h**, 81% y): TLC on K6F silica gel 60Å, 4:1 hexanes/EtOAc, Rf = 0.31. Molecular ion calculated for $C_9H_{15}BBrNNa$: 250.0379; [M+Na], ESMS found *m/z* = 250.0373; IR (neat, cm^{-1}) 2360, B–H; 2315, B–H; 2271, B–H; 1465, B–N; 1167, C–N; ^{1}H NMR: δ 7.66 (1H, dd, J = 8.1, 1.5 Hz), 7.52 (1H, dd, J = 7.9, 1.9 Hz), 7.37 (1H, td, J = 7.8 Hz, 1.5 Hz), 7.27 (1H, td, J = 7.7, 1.9 Hz), 4.24 (2H, s), 2.61 (6H, s), 2.2-1.4 (3H, br m); ^{13}C NMR: δ 134.7, 133.7, 131.1, 130.8, 127.3, 127.2, 65.4, 50.2; ^{11}B NMR: δ -8.1 (q, J = 98 Hz).

2-Chlorobenzyldimethylamine borane (**22j**, 73% y): TLC on K6F silica gel 60Å, 9:1 hexanes/Et_2O, Rf = 0.19. Molecular ion calculated for $C_9H_{15}BClNNa$: 206.0884;

[M+Na], ESMS found *m*/*z* = 206.0876; IR (neat, cm^{-1}) 2364, B–H; 2317, B–H; 2273, B–H; 1466, B–N; 1167, C–N; ^{1}H NMR: δ 7.49 (1H, dd, J = 7.3, 2.0 Hz), 7.46 (1H, dd, J = 7.8, 1.5 Hz), 7.36 (1H, td, J = 7.8 Hz, 1.9 Hz), 7.32 (1H, td, J = 7.3, 1.5 Hz), 4.21 (2H, s), 2.59 (6H, s), 2.2-1.4 (3H, br m); ^{13}C NMR: δ 136.4, 134.8, 130.7, 130.3, 129.4, 126.7, 63.1, 50.1; ^{11}B NMR: δ -8.1 (q, J = 95 Hz).

2-Fluorobenzyldimethylamine borane (**22k**, 32% y): TLC on K6F silica gel 60Å, 9:1 hexanes/Et_2O, Rf = 0.17. Molecular ion calculated for $C_9H_{15}BFNNa$: 190.1179; [M+Na], ESMS found *m*/*z* = 190.1186; IR (neat, cm^{-1}) 2364, B–H; 2317, B–H; 2271, B–H; 1470, B–N; 1169, C–N; ^{1}H NMR: δ 7.44-7.39 (1H, m), 7.37 (1H, td, J = 7.5, 1.9 Hz), 7.20 (1H, td, J = 7.3 Hz, 1.0 Hz), 7.14 (1H, ddd, J = 9.8, 8.3, 1.0 Hz), 4.07 (2H, s), 2.54 (6H, s), 2.2-1.4 (3H, br m); ^{13}C NMR: δ 161.9 (d, J = 248 Hz), 134.6 (d, J = 4 Hz), 131.4 (d, J = 8 Hz), 124.1 (d, J = 4 Hz), 118.6 (d, J = 15 Hz), 115.9 (d, J = 23 Hz), 60.2 (d, J = 2 Hz), 49.9 (d, J = 2 Hz); ^{11}B NMR: δ -8.1 (q, J = 95 Hz); ^{19}F NMR: δ -113.7 (m).

***N*,*N*-Dimethylphenethylamine borane** (**22m**, 93% y): TLC on K6F silica gel 60Å, 4:1 hexanes/EtOAc, Rf = 0.31. Molecular ion calculated for $C_{10}H_{18}BNNa$: 186.1430; [M+Na], ESMS found *m*/*z* = 186.1424; IR (neat, cm^{-1}) 2362, B–H; 2314, B–H; 2277, B–H; 1453, B–N; 1167, C–N; ^{1}H NMR: δ 7.31 (2H, t, J = 7.3 Hz), 7.26-7.19 (3H, m), 3.09-2.94 (4H, m), 2.66 (6H, s), 2.1-1.3 (3H, br m); ^{13}C NMR: δ 138.0, 128.8, 126.7, 66.1, 51.8, 30.9; ^{11}B NMR: δ -10.0 (q, J = 98 Hz).

1-(Dimethylamino)-3-phenylpropane borane (**22n**, 91% y): TLC on K6F silica gel 60Å, 2:1 hexanes/EtOAc, Rf = 0.49. Molecular ion calculated for $C_{11}H_{20}BNNa$: 200.1586; [M+Na], ESMS found *m*/*z* = 200.1588; IR (neat, cm^{-1}) 2366, B–H; 2319, B–H; 2271, B–H; 1463, B–N; 1167, C–N; ^{1}H NMR: δ 7.31 (2H, t, J = 7.8 Hz), 7.24-7.18 (3H, m), 2.81-2.76 (2H, m), 2.63 (t, J = 7.8 Hz), 2.56 (6H, s), 2.11-2.03 (2H, m), 2.1-1.3 (3H, br m); ^{13}C NMR: δ 140.7, 128.6, 128.3, 126.3, 64.2, 51.4, 33.3, 25.5; ^{11}B NMR: δ -9.9 (q, J = 95 Hz).

4-Methoxybenzyldimethylamine borane (**22p**, 89% y): TLC on K6F silica gel 60Å, 4:1 hexanes/EtOAc, Rf = 0.31. Molecular ion calculated for $C_{10}H_{18}BNNaO$: 202.1379; [M+Na], ESMS found *m*/*z* = 202.1378; IR (neat, cm^{-1}) 2366, B–H; 2319, B–H; 2271, B–H; 1466, B–N; 1165, C–N; ^{1}H NMR: δ 7.24 (2H, d, J = 8.4 Hz), 6.91 (2H, d, J = 8.4 Hz), 3.93 (2H, s), 3.83 (3H, s), 2.48 (6H, s), 2.2-1.4 (3H, br m); ^{13}C NMR: δ 160.2, 133.4, 123.3, 113.8, 66.9, 55.3, 49.5; ^{11}B NMR: δ -8.5 (q, J = 90 Hz).

Representative Procedure for Directed Borylation (Table 3-2)

Dimethylbenzylamine borane (**22a**, 179 mg, 1.20 mmol) was dissolved in anhydrous bromobenzene (12 mL) and activated by addition of a solution of TrTPFPB (1000 mg, 1.08 mmol) in bromobenzene (4 + 1 mL) under an N_2 atmosphere. After 4 h the reaction was quenched with a solution of Bu_4NBH_4 (297 mg, 1.15 mmol) in bromobenzene (2 + 1 mL), added by syringe. The solvent was removed by a stream of N_2, and the residue was purified either by flash chromatography (FC) on silica gel (15 cm x 20 mm diameter) as in the case of **23a** (4:1 hexanes EtOAc) or by preparative thin layer

chromatography (PLC) (K6F silica gel 60Å, 1000 μm thickness), isolating 115 mg product (Rf = 0.28, 72% y based on TrTPFPB) and recovering 30 mg **22a** (Rf = 0.41, 17%). ^{1}H and ^{11}B NMR spectral data matched those reported for **23a**.[10]

2,2,5-Trimethyl-2,3-benzazaborolidine (23b): Purified by FC (4:1 hexanes/EtOAc, Rf = 0.32, 41% y of **23b**, recovered 21% of **22b**). Molecular ion calculated for $C_{10}H_{16}BNNa$: 184.1273; [M+Na], ESMS found *m*/*z* = 184.1276; IR (neat, cm^{-1}) 2339, B–H; 2306, B–H; 1463, B–N; 1071, C–N; ^{1}H NMR: δ 7.25 (1H, s), 6.97 (1H, d, J = 7.4 Hz), 6.90 (1H, d, J = 7.4 Hz), 4.01 (2H, s), 3.2-2.4 (2H, br m), 2.76 (6H, s), 2.32 (3H, s); ^{13}C NMR: δ 136.5, 135.8, 130.4, 125.6, 121.4, 69.5, 50.9, 21.5; ^{11}B NMR: δ -1.4 (t, J = 99 Hz).

2,2,4-Trimethyl-2,3-benzazaborolidine and 2,2,6-trimethyl-2,3-benzazaborolidine (23c): Purified by PLC (4:1 hexanes/EtOAc, Rf = 0.34, 79% y of **23c** as inseparable mixture of regioisomers in a 3:1 ratio, recovered 13% of **22c**). Molecular ion calculated for $C_{10}H_{15}BN$: 160.1298; [M-H], EIMS found *m*/*z* = 160.1305; IR (neat, cm^{-1}) 2341, B–H; 2294, B–H; 1459, B–N; 1055, C–N; ^{1}H NMR: δ 7.31 (1H-minor isomer, d, J = 7.3 Hz), 7.04-6.97 (2H-major isomer + 1H-minor isomer, m), 6.91-6.88 (1H-major isomer + 1H-minor isomer, m), 4.05 (2H-major isomer, s), 4.01 (2H-minor isomer, s), 3.2-2.4 (2H-major isomer + 2H-minor isomer, br m), 2.77 (6H-major isomer, s), 2.76 (6H-minor isomer, s), 2.30 (3H-minor isomer, s), 2.29 (3H-major isomer, s); ^{13}C NMR: δ 139.5, 139.0, 138.2, 134.3, 129.5, 128.0, 127.5, 125.3, 122.4, 118.7, 69.9, 69.6, 51.1, 50.9, 21.7, 21.3; ^{11}B NMR: δ -1.9 (major isomer, t, J = 97 Hz).

2,2,7-Trimethyl-2,3-benzazaborolidine (23d): Purified by FC (4:1 hexanes/EtOAc, Rf = 0.29, 76% y of **23d**, recovered 10% of **22d**). Molecular ion calculated for $C_{10}H_{16}BNNa$: 184.1273; [M+Na], ESMS found *m*/*z* = 184.1268; IR (neat, cm^{-1}) 2342, B–H; 2298, B–H; 1461, B–N; 1061, C–N; ^{1}H NMR: δ 7.24 (1H, d, J = 7.2 Hz), 7.11 (1H, t, J = 7.3 Hz), 6.89 (1H, d, J = 7.2 Hz), 4.03 (2H, s), 3.2-2.4 (2H, br m), 2.77 (6H, s), 2.19 (3H, s); ^{13}C NMR: δ 137.4, 130.9, 127.3, 126.9, 126.1, 68.4, 51.3, 18.9; ^{11}B NMR: δ -1.4 (t, J = 99 Hz).

5-Bromo-2,2-dimethyl-2,3-benzazaborolidine (23e): Purified by PLC (4:1 hexanes/EtOAc, Rf = 0.15, 53% y of **23e**, recovered 15% of **22e**). Molecular ion calculated for $C_9H_{12}BBrN$: 224.0246; [M-H], EIMS found *m*/*z* = 224.0254; IR (neat, cm^{-1}) 2344, B–H; 2298, B–H; 1455, B–N; 1069, C–N; ^{1}H NMR: δ 7.52 (1H, br s), 7.20 (1H, dd, J = 7.9, 1.9 Hz), 6.94 (1H, d, J = 7.9 Hz), 3.98 (2H, s), 3.1-2.3 (2H, br m), 2.75 (6H, s); ^{13}C NMR: δ 137.4, 132.5, 127.7, 123.4, 122.1, 69.1, 50.9; ^{11}B NMR: δ -1.7 (t, J = 99 Hz).

5-Chloro-2,2-dimethyl-2,3-benzazaborolidine (23f): Purified by PLC (4:1 hexanes/EtOAc, Rf = 0.14, 73% y of **23f**, recovered 17% of **22f**). Molecular ion calculated for $C_9H_{12}BClN$: 180.0751; [M-H], EIMS found *m*/*z* = 180.0753; IR (neat, cm^{-1}) 2352, B–H; 2302, B–H; 1455, B–N; 1077, C–N; ^{1}H NMR: δ 7.36 (1H, br s), 7.20 (1H, dd, J = 8.0, 1.9 Hz), 6.94 (1H, d, J = 8.0 Hz), 4.00 (2H, s), 3.1-2.3 (2H, br m), 2.75 (6H, s); ^{13}C NMR: δ 136.9, 133.3, 129.6, 124.8, 122.9, 69.0, 50.9; ^{11}B NMR: δ -1.7 (t, J = 100 Hz).

5-Fluoro-2,2-dimethyl-2,3-benzazaborolidine (23g): Purified by PLC (2:1 hexanes/EtOAc, Rf = 0.31, 59% y of **23g**, recovered 22% of **22g**). Molecular ion calculated for $C_9H_{12}BFN$: 164.1047; [M-H], EIMS found *m*/*z* = 164.1045; IR (neat, cm^{-1}) 2356, B–H; 2317, B–H; 1461, B–N; 1063, C–N; ^1H NMR: δ 7.08 (1H, d, J = 8.9 Hz), 7.00 (1H, dd, J = 8.2, 4.9 Hz), 6.74 (1H, td, J = 8.8, 2.5 Hz), 4.01 (2H, s), 3.1-2.3 (2H, br m), 2.76 (6H, s); ^{13}C NMR: δ 162.9 (d, J = 244 Hz), 133.9 (d, J = 2 Hz), 122.8 (d, J = 7 Hz), 116.0 (d, J = 19 Hz), 111.5 (d, J = 23 Hz), 69.0, 50.9; ^{11}B NMR: δ -1.6 (t, J = 102 Hz) ; ^{19}F NMR: δ -117.0 (m).

7-Bromo-2,2-dimethyl-2,3-benzazaborolidine (23h): Purified by FC (9:1 hexanes/Et_2O, Rf = 0.24, 55% y of **23h**, recovered 16% of **22h**). Molecular ion calculated for $C_9H_{12}BBrN$: 224.0246; [M-H], EIMS found *m*/*z* = 224.0255; IR (neat, cm^{-1}) 2356, B–H; 2296, B–H; 1443, B–N; 1071, C–N; ^1H NMR: δ 7.31 (1H, d, J = 7.4 Hz), 7.21 (1H, d, J = 7.9 Hz), 7.06 (1H, t, J = 7.5 Hz), 4.12 (2H, s), 3.2-2.4 (2H, br m), 2.79 (6H, s); ^{13}C NMR: δ 138.2, 129.2, 128.2, 127.9, 117.4, 70.2, 51.2; ^{11}B NMR: δ -1.0 (t, J = 103 Hz).

7-Chloro-2,2-dimethyl-2,3-benzazaborolidine (23j): Purified by FC (9:1 hexanes/Et_2O, Rf = 0.24, 55% y of **23j**, recovered 20% of **22j**). Molecular ion calculated for $C_9H_{12}BClN$: 180.0751; [M-H], EIMS found *m*/*z* = 180.0749; IR (neat, cm^{-1}) 2354, B–H; 2298, B–H; 1447, B–N; 1073, C–N; ^1H NMR: δ 7.28 (1H, d, J = 7.3 Hz), 7.13 (1H, t, J = 7.6 Hz), 7.05 (1H, d, J = 8.1 Hz), 4.14 (2H, s), 3.2-2.4 (2H, br m), 2.78 (6H, s); ^{13}C NMR: δ 136.2, 128.9, 128.3, 127.7, 125.0, 68.3, 51.3; ^{11}B NMR: δ -1.1 (t, J = 100 Hz).

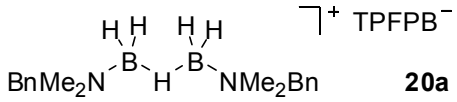
7-Fluoro-2,2-dimethyl-2,3-benzazaborolidine (23k): Purified by PLC (9:1 hexanes/Et_2O, Rf = 0.19, 33% y of **23k**, recovered 36% of **22k**). Molecular ion calculated for $C_9H_{13}BFN$: 164.1047; [M-H], EIMS found *m*/*z* = 164.1044; IR (neat, cm^{-1}) 2352, B–H; 2314, B–H; 1465, B–N; 1075, C–N; ^1H NMR: δ 7.18-7.15 (2H, m), 6.79-6.73 (1H, m), 4.13 (2H, s), 3.2-2.4 (2H, br m), 2.79 (6H, s); ^{13}C NMR: δ 158.2 (d, J = 248 Hz), 129.2 (d, J = 5 Hz), 125.0 (d, J = 3 Hz), 114.6 (d, J = 22 Hz), 111.3 (d, J = 19 Hz), 65.4, 51.1; ^{11}B NMR: δ -1.4 (t, J = 100 Hz); ^{19}F NMR: δ -121.1 (m).

2,2-Dimethyl-2,1-benzazaborinane (23m): Purified by FC (4:1 hexanes/EtOAc, Rf = 0.18, 74% y of **23m**, recovered 17% of **22m**). Molecular ion calculated for $C_{10}H_{16}BNNa$: 184.1273; [M+Na], ESMS found *m*/*z* = 184.1279; IR (neat, cm^{-1}) 2314, B–H; 1436, B–N; 1084, C–N; ^1H NMR: δ 7.26 (1H, d, J = 6.9 Hz), 7.12 (1H, td, J = 6.9, 1.9 Hz), 7.08-7.01 (2H, m), 3.07 (4H, s), 3.0-2.2 (2H, br m), 2.66 (6H, s); ^{13}C NMR: δ 134.1, 132.9, 126.9, 125.6, 124.5, 59.2, 50.5, 28.4; ^{11}B NMR: δ -5.2 (t, J = 96 Hz).

2,2-Dimethyl-2,1-benzazaborepane (23n): Purified by PLC (2:1 hexanes/EtOAc, Rf = 0.43, 42% y of **23n**, recovered 31% of **22n**). Molecular ion calculated for $C_{11}H_{18}BNNa$: 198.1430; [M+Na], ESMS found *m*/*z* = 198.1425; IR (neat, cm^{-1}) 2329, B–H; 1455, B–N; 1102, C–N; ^1H NMR: δ 7.44 (1H, t, J = 4.1 Hz), 7.11-7.06 (2H, m), 7.02-6.97 (1H, m), 3.1-2.3 (2H, br m), 3.08 (2H, br s), 2.97 (2H, br s), 2.52 (6H, s), 1.87 (2H, pentet, J = 5.6 Hz); ^{13}C NMR: δ 146.9, 137.0, 126.8, 126.0, 125.3, 67.5, 51.4, 36.5, 26.0; ^{11}B NMR: δ -1.8 (t, J = 93 Hz).

4-Hydroxybenzyldimethylamine borane (22q): Purified by PLC (4:1 hexanes/EtOAc, Rf = 0.12, 25% y of **22q**, recovered 57% of **22p**). Molecular ion calculated for $C_9H_{16}BNNaO$: 188.1223; [M+Na], ESMS found *m*/*z* = 188.1219; IR (neat, cm^{-1}) 3396, O–H; 2371, B–H; 2323, B–H; 1466, B–N; 1165, C–N; ^{1}H NMR: δ 7.20 (2H, d, J = 8.8 Hz), 6.85 (2H, d, J = 8.8 Hz), 4.86 (1H, br s), 3.91 (2H, s), 2.48 (6H, s), 2.2-1.4 (3H, br m); ^{13}C NMR: δ 156.3, 133.7, 123.5, 115.3, 66.9, 49.5; ^{11}B NMR: δ -8.5 (t, J = 97 Hz).

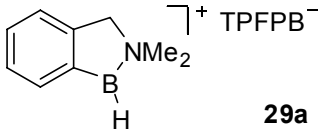
Low Temperature Activation of Dimethylbenzylamine Borane (22a) with TrTPFPB: Detection of *H*-Bridged Species 20a



20a

A solution of **22a** (9.5 mg, 64 μmol) in anhydrous CD_2Cl_2 (0.2 mL + 0.1 mL) was added by syringe to a stirred solution of TrTPFPB (23 mg, 25 μmol) in 0.6 mL anhydrous CD_2Cl_2 at -78 °C under an N_2 atmosphere. After a few minutes, this solution was transferred via syringe to an N_2-flushed NMR tube cooled to -78 °C, and the sample was kept in a -78 °C bath (ca. 60 min) and was then allowed to warm to -20 °C in the NMR spectrometer for data acquisition at that temperature (^{1}H spectrum referenced to residual $CHDCl_2$). Ph_3CH: ^{1}H NMR: δ 7.29 (6H, t, J = 7.3 Hz), 7.21 (3H, t, J = 7.3 Hz), 7.11 (6H, d, J = 7.3 Hz), 5.56 (1H, s). *H*-bridged cation **20a**: ^{1}H NMR: δ 7.53-7.43 (6H, m), 7.34 (4H, d, J = 6.8 Hz), 4.00 (4H, s), 2.62 (12H, s), 3.0-2.1 (4H, br m), -1.9 (1H, br s); ^{11}B NMR: δ 0 (br s), -16.7 (s).

Room Temperature Activation of Dimethylbenzylamine Borane (22a): Detection of Cationic Trivalent Boron Intermediate 29a



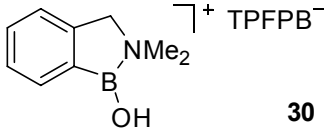
29a

A solution of **22a** (7.3 mg, 49 μmol) in anhydrous C_6D_5Br (2 x 0.2 mL) was added by syringe to a stirred solution of TrTPFPB (51 mg, 56 μmol) in 0.6 mL anhydrous C_6D_5Br under an N_2 atmosphere. After 1 h the solution was transferred to an N_2-flushed NMR tube capped with a rubber septum. Assay by ^1H NMR (referenced to *para*-C–H peak of solvent) shows Ph_3CH, **29a** and unreacted trityl cation in a ratio of 4.3:2.8:1. Ph_3CH: ^1H NMR: δ 7.47-7.41 (6H, m), 7.41-7.33 (9H, m), 5.74 (1H, s). Trivalent boron cation **29a**: ^1H NMR: δ 7.92 (1H, d, J = 7.9 Hz), 7.72 (1H, t, 7.9 Hz), 7.47-7.41 (1H, m; overlaps with Ph_3CH), 7.22 (1H, d, J = 7.9 Hz), 5.4 (1H, br s; shaper in a ^{11}B decoupling experiment), 4.16 (2H, s), 2.64 (6H, s); ^{11}B NMR: δ 59 (br s), -15.9 (s). TrTPFPB: ^1H NMR: δ 7.99 (3H, t, J = 7.7 Hz), 7.62 (6H, t, 8.1 Hz), 7.41-7.38 (6H, m); ^{11}B NMR: δ -15.9.

Structure Assignment for 30 (*B*-Hydroxy Analogue of 29a)

A solution of TrTPFPB (52 mg, 56 μmol) in anhydrous CD_2Cl_2 (0.4 mL + 0.2 mL) was added to a solution of **23a** (7.4 mg, 50 μmol) in CD_2Cl_2 (0.6 mL) under an N_2 atmosphere. After 30 min the solution was transferred to an N_2-flushed NMR tube capped with a rubber septum. Assay by ^1H NMR (referenced to solvent) shows Ph_3CH and **29a** in a ratio of 1.3:1, with **30** as a minor impurity. **29a**: ^1H NMR: δ 8.26 (1H, d, J = 8.3 Hz), 8.01 (1H, t, J = 8.0 Hz), 7.71 (1H, t, J = 7.6 Hz), 7.56 (1H, d, J = 7.8 Hz), 6.5-5.2

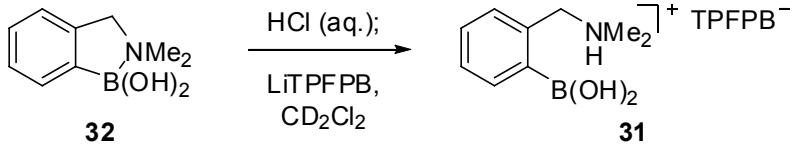
(1H, br m; sharper in a ^{11}B decoupling experiment), 4.83 (2H, s), 3.27 (6H, s); ^{11}B NMR: δ 61 (d), -16.7 (s). Repeating this experiment using C_6D_5Br as solvent gave ^{1}H and ^{11}B NMR shifts as reported above for compound **295a** in C_6D_5Br.



30

Activation of **23a** (32 mg, 220 μmol) with TrTPFPB (224 mg, 243 μmol) in CD_2Cl_2 (3.0 mL total) as above, but followed by addition of water (4.0 μL, 220 μmol) before transferring an aliquot to an NMR tube gave **30** (^{11}B NMR: δ 39 ppm), consistent with what was reported previously as **29a**.[10] Cation **30**: ^{1}H NMR: δ 7.93-7.83 (1H, m, overlaps with unreacted Tr^+), 7.69-7.60 (1H, m, overlaps with unreacted Tr^+), 7.49 (1H, d, J = 7.9 Hz), 5.4 (1H, br s), 4.67 (2H, s), 3.16 (6H, s); ^{11}B NMR: δ 39 (br s), -16.7 (s).

To an aliquot of **30** from the experiment above (1.2 mL, ca. 90 μmol) was added an additional equivalent of water (2.0 μL, 110 μmol) before transferring to an NMR tube, giving major ^{11}B NMR signals at δ 29 ppm as well as major signals by ^{1}H NMR identical with chemical shifts assigned to **31** as reported below.

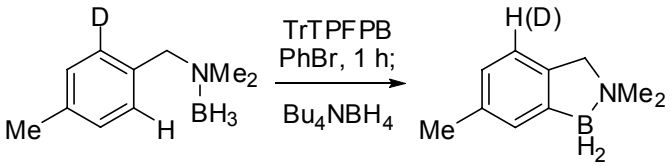


32 **31**

The known 2-dimethylaminobenzeneboronic acid (**32**, 9.9 mg, 55 μmol)[28] was protonated by addition of 0.5 M HCl (1.0 mL, 1.0 mmol) with stirring for 1 h at rt. Next, solid $Li(OEt_2)_nB(C_6F_5)_4$ (50 mg, ca. 60 μmol) was added with vigorous stirring for 10 min followed by extraction with 0.7 mL CD_2Cl_2. Assay by ^{1}H NMR showed compound **31** and Et_2O in a ratio of ca. 1.5:1. Ammonium salt **31**: ^{1}H NMR: δ 8.3-7.9 (1H, br m),

7.90-7.86 (1H, m), 7.65-7.59 (2H, m), 7.37-7.32 (1H, m), 5.9 (2H, br s), 4.28 (2H, d, J = 5.9 Hz), 2.89 (6H, d, J = 5.4 Hz); ^{11}B NMR: δ 29 (br s), -16.7 (s).

Kinetic Isotope Effect Study: Preparation and Reaction of 22b-*d*$_1$



22b-*d*$_1$ **23b**-*d*$_1$: **23b** = 2.8 : 1

4-Methylbenzyldimethylamine (170 mg, 1.14 mmol), prepared from dimethylamine and 4-methylbenzyl bromide,[29] was dissolved in Et_2O (0.3 mL) in a 5 ML round bottom flask fused to a reflux condenser and reacted with n-BuLi in hexane (2.14 M, 0.80 mL, 1.7 mmol) under an N_2 atmosphere, heating to reflux (bath temperature: 75 °C) for 2 h with stirring.[30] The orange solution was then cooled to rt and diluted with anhydrous THF (1 mL), and the resulting reddish solution was transferred by cannula (rinsing the flask with 1 mL THF) to a flask containing a mixture of D_2O (0.30 mL, 17 mmol) and THF (1 mL) with vigorous stirring. After 1 h the layers were separated, the supernatant was filtered, the flask rinsed with 2 x 5 mL Et_2O, and the combined filtrate was dried over $MgSO_4$ and reduced by a stream of N_2.

The crude product from the deuteration was taken up in 2 mL anhydrous DCM and treated with BH_3·THF (1.0 M, 1.5 mL, 1.5 mmol) under an N_2 atmosphere. After 2 h the solution was filtered through a plug of silica gel, flushing with 20 mL DCM, and the sample was reduced under a stream of N_2, collecting 129 mg **22b-*d*$_1$** (69% y over two steps). The ^{1}H NMR spectrum of a sample shows peaks consistent with the desired product (see spectroscopic data for **22b** below), the aromatic region integrating for 3.05H, indicating 95% deuteration.

Borane complex **22b-d_1** (17.8 mg, 108 μmol) was dissolved in anhydrous PhBr (1.2 mL) and activated with a solution of TrTPFPB (91 mg, 99 μmol) in PhBr (2 x 0.4 mL) under an N_2 atmosphere. After stirring 1 h the reaction was quenched by addition of a solution of Bu_4NBH_4 (33 mg, 130 μmol) in PhBr (2 x 0.4 mL), and the solvent was then removed under a stream of N_2. The residue was purified by PLC on silica gel (20 cm x 20 cm x 1000 μm, 4:1 hexanes/EtOAc) recovering 2.1 mg product **23b** with ^{1}H NMR data matching that reported earlier for **13b**. The ^{1}H NMR peak corresponding to the *ortho*-C–H integrates for 0.27H, indicating 73% deuteration.

Preparation and Reaction of *trans*-1-Methyl-2-phenylpyrrolidine Borane (44a)

According to the published procedure,[31] (*R*)-2-phenylpyrrolidine (1.008 g, 6.85 mmol) was dissolved in formic acid (1.5 mL, 40 mmol) and cooled to 0 °C before addition of formaldehyde (37% solution in water, 0.20 mL, 2.7 mmol) with vigorous stirring. The resulting solution was heated to reflux, with gas evolution observed during heating. After this gas evolution had seemed to subside after a few minutes at reflux, additional formaldehyde was added in four portions (additional 0.35 mL, 4.7 mmol), waiting for the now vigorous gas evolution to subside between additions. The solution was heated at reflux for 17 h then cooled to rt and quenched by addition of 1.7 mL 6M HCl, removing the water and excess formic acid under reduced pressure. The residue was neutralized with 10% aq. NaOH (2.4 mL) and extracted with Et_2O (3 x 5 mL), the aqueous layer then made basic by the addition of 10% aq. NaOH and again extracted with Et_2O (2 x 5 mL). The combined organic extracts were washed with brine and dried over $MgSO_4$ then reduced by a stream of N_2.

The residue was taken up in DCM and reacted with BH_3·THF (8.0 mL, 8.0 mmol) as described for **22c**, giving a mixture of **44a** and **44b** in a ratio of 1:1.8 by ^{1}H NMR assay of the crude product. These products were purified by FC (4:1 hexanes/EtOAc), giving 450 mg (38% yield over two steps) of diasteromerically pure *cis*-1-methyl-2-phenylpyrrolidine borane **44b**: TLC on K6F silica gel 60Å, 4:1 hexanes/EtOAc, Rf = 0.31. Molecular ion calculated for $C_{11}H_{17}BN$: 174.1454; [M-H], EIMS found *m*/*z* = 174.1457; IR (neat, cm^{-1}) 2362, B–H; 2314, B–H; 2265, B–H; 1455, B–N; 1164, C–N; ^{1}H NMR: δ 7.45-7.35 (5H, m), 4.40 (1H, t, J = 8.3 Hz), 3.40 (1H, ddd, J = 11.7, 8.8, 6.3 Hz), 3.04 (1H, ddd, J = 11.7, 8.3, 6.8 Hz), 2.54-2.45 (1H, m), 2.38-2.29 (1H, m), 2.28-2.18 (1H, m), 2.22 (3H, s), 2.13-2.04 (1H, m), 2.1-1.3 (3H, br m); ^{13}C NMR: δ 135.0, 130.2, 129.0, 128.3, 73.9, 63.0, 45.4, 28.9, 21.3; ^{11}B NMR: δ -9.9 (q, J = 96 Hz). FC also allowed isolation of 223 mg of *trans*-1-methyl-2-phenylpyrrolidine borane **44a** (dr of 17:1, 19% yield over two steps): TLC on K6F silica gel 60Å, 4:1 hexanes/EtOAc, Rf = 0.26. Molecular ion calculated for $C_{11}H_{17}BN$: 174.1454; [M-H], EIMS found *m*/*z* = 174.1460; IR (neat, cm^{-1}) 2362, B–H; 2323, B–H; 2279, B–H; 1455, B–N; 1171, C–N; ^{1}H NMR: δ 7.56-7.50 (2H, m), 7.40-7.32 (3H, m), 3.69 (1H, dd, J = 12.2, 7.3 Hz), 3.56 (1H, ddd, J = 10.5, 8.6, 1.9 Hz), 2.84 (1H, q, J = 10.0 Hz), 2.72 (1H, qd, J = 12.0, 6.0 Hz), 2.56 (3H, s), 2.39-2.28 (1H, m), 2.21-2.14 (1H, m), 1.97-1.88 (1H, m), 1.7-1.0 (3H, br m); ^{13}C NMR: δ 133.1, 131.1, 129.2, 127.7, 75.9, 65.2, 50.7, 28.6, 20.1; ^{11}B NMR: δ -14.9 (q, J = 96 Hz). The reported stereochemistry was confirmed for **44a** by a nuclear Overhauser effect (NOE) experiment, irradiation of the benzylic C–H peak at δ 3.69 ppm resulting in a 2.4% NOE enhancement of the methyl peak at δ 2.56 ppm showing the *cis*-relationship between these groups; no NOE enhancement of the methyl signal in **44b** (δ

2.22 ppm) was observed on irradiation of the corresponding benzylic proton (δ 4.40 ppm). A mixture of **44a** and **44b** in a ratio of ca. 1:1 was also isolated from mixed fractions from FC, yielding an additional 221 mg (18% combined yield over two steps), for a total recovery of 894 mg (75% yield over two steps).

A solution of **44a** (17:1 dr, 19.8 mg, 113 μmol) in anhydrous PhBr (1.2 mL) was activated with a solution of TrTPFPB (95 mg, 103 μmol) in PhBr (2 x 0.4 mL), quenching after 4 h with a solution of Bu_4NBH_4 (32 mg, 120 μmol) in PhBr (2 x 0.4 mL) as described above for **23a**. The residue was purified by PLC on silica gel (20 cm x 20 cm x 1000 μm, 9:1 hexanes/acetone) recovering 7.3 mg of a mixture of product **45**, isomerized **44b** and unreacted **44a** in a ratio of 4.6:2.3:1 by ^{1}H NMR assay. This corresponds to 4.2 mg **45** (24% yield): TLC on K6F silica gel 60Å, 9:1 hexanes/acetone, Rf = 0.23. Molecular ion calculated for $C_{11}H_{16}BN$: 172.1298; [$M^{\bullet+}$], EIMS found *m*/*z* = 172.1301; IR (neat, cm^{-1}) 2341, B–H; 2310, B–H; 1447, B–N; 1187, C–N; ^{1}H NMR: δ 7.38 (1H, d, J = 7.3 Hz), 7.18 (1H, t, J = 7.3 Hz), 7.11 (1H, t, J = 7.3 Hz), 6.99 (1H, d, J = 7.3 Hz), 4.42 (1H, dd, J = 8.8, 3.8 Hz), 3.34 (1H, dt, J = 11.7, 7.6 Hz), 3.3-2.5 (2H, br m), 2.93 (1H, ddd, J = 11.7, 7.3, 6.3 Hz), 2.80 (3H, s), 2.48-2.40 (1H, m), 2.22-2.14 (1H, m), 2.13-1.97 (1H, m): ^{13}C NMR: δ 143.3, 129.5, 127.2, 125.2, 121.4, 79.3, 61.3, 49.5, 30.8, 24.0; ^{11}B NMR: δ -2.2 (t, J = 99 Hz).

Preparation and Reaction of Benzyldiisobutylphosphine Borane (48)

According to the literature procedure,[19] diisobutylphosphine (0.38 mL, 2.0 mmol) was added via syringe to a suspension of 4Å molecular sieves (1.0 g) and $CsOH·H_2O$ in anhydrous DMF (used as received, 15 mL) under N_2 atmosphere. After stirring vigorously 2 h benzyl bromide (0.29 mL, 2.4 mmol) was added by syringe, and the mixture was stirred an additional 26 h then diluted with 2% aq. NaOH (deoxygenated by bubbling N_2 into the solution using a diffuser for 2 h, 60 mL), extracted with DCM (N_2-purged and dried by passing through a column of activated alumina, 3 x 60 mL) keeping it under N_2 atmosphere, stirring vigorously to mix layers at all stages and transferring between flasks via cannula. The combined organic extracts were washed with 2% NaOH (deoxygenated, 2 x 60 mL), dried over Na_2SO_4, decanted off the drying agent and reduced by a stream of N_2.

The residue was taken up in DCM and reacted with $BH_3·THF$ (2.5 mL, 2.5 mmol) as described for **22c**, and 118 mg of the title compound (23% yield) was isolated by FC. Benzyldiisobutylphosphine borane **48**: TLC on K6F silica gel 60Å, 19:1 hexanes/Et_2O, Rf = 0.30. Molecular ion calculated for $C_{15}H_{28}BNaP$: 273.1919; [M+Na], ESMS found *m*/*z* = 273.1916; IR (neat, cm^{-1}) 2362, B–H; 2339, B–H; ^1H NMR: δ 7.33 (2H, t, J = 7.6 Hz), 7.29-7.24 (1H, overlaps $CHCl_3$), 7.18-7.14 (2H, m), 3.05 (2H, d, J = 10.3 Hz), 2.09-1.92 (2H, m), 1.47 (2H, ABq dd, J = 14.6, 11.7, 5.9 Hz), 1.38 (2H, ABq dd, J = 14.6, 10.3, 6.8), 1.1-0.1 (3H, br m), 1.03 (6H, d, J = 6.3 Hz), 1.02 (6H, d, J = 6.3 Hz); ^{13}C NMR: δ 132.9 (d, J = 8 Hz), 129.9 (d, J = 4 Hz), 128.6 (d, J = 2 Hz), 126.9 (d, J = 2 Hz), 33.5 (d, J = 31 Hz), 32.7 (d, J = 32 Hz), 25.0 (d, J = 9 Hz), 24.8 (d, J = 6 Hz), 24.3; ^{11}B NMR: δ -39.1 (qd, J = 94, 58 Hz); ^{31}P NMR: δ 14 (br m).

A solution of **48** (13.3 mg, 53 μmol) in anhydrous PhBr (0.6 mL) was activated with a solution of TrTPFPB (47 mg, 51 μmol) in PhBr (0.3 mL), quenching after 4 h with

a solution of Bu_4NBH_4 (17 mg, 70 μmol) in PhBr (0.3 mL) as described above for **23a**. The residue was purified by PLC on silica gel (20 cm x 20 cm x 1000 μm, 4:1 hexanes/Et_2O) recovering 5.6 mg of a mixture of product **49**, unreacted **48** and Ph_3CH in a ratio of 1.9:1:2.0 by ^1H NMR assay as well as 3.7 mg of a mixture of product **49** and unreacted **48** in a ratio of 2.3:1 by ^1H NMR assay, giving a combined recovery of 4.8 mg or 38% yield of **49**. Further purification by PLC increased the ratio of **49** to **48** to 7:1. 2,2-Diisobutyl-2,3-benzophosphaborolidine (**49**): TLC on K6F silica gel 60Å, 4:1 hexanes/Et_2O, Rf = 0.47. Molecular ion calculated for $C_{15}H_{26}BP$: 247.1787; [$M^{\bullet+}$], EIMS found *m/z* = 247.1794; IR (neat, cm^{-1}) 2377, B–H; ^1H NMR: δ 7.45 (1H, d, J = 6.3 Hz), 7.12-7.05 (2H, m), 7.04-6.99 (1H, m), 3.17 (1H, d, J = 9.3 Hz), 2.5-1.7 (2H, br m), 2.05-1.93 (2H, m), 1.76 (4H, dd, J = 10.3, 7.4 Hz), 1.04-1.00 (12H, m); ^{13}C NMR: δ 133.2 (d, J = 20 Hz), 127.3 (d, J = 24 Hz), 126.4, 125.5 (d, J = 13 Hz), 124.9, 33.9 (d, J = 40 Hz), 31.9 (d, J = 32 Hz), 25.1 (d, J = 2 Hz), 24.5 (d, J = 8 Hz), 24.4 (d, J = 7 Hz); ^{11}B NMR: δ -23.3 to -25.9 (br m); ^{31}P NMR: δ 23 (br m).

Preparation and Reaction of Phenyl Diisopropylphosphinite Borane (50)

According to the literature procedure,[20] phenol (383 mg, 4.1 mmol) was azeotropically dried by refluxing with toluene (10 mL, distilled under an N_2 atmosphere) for 3 h using a Dean-Stark trap; the 5 mL of solution remaining was added, rinsing with 2 mL toluene, to chlorodiisopropylphosphine (0.60 mL, 3.8 mmol) dissolved in 3 mL distilled toluene in a 10 mL round-bottom flask fused to a reflux condensor. To the resulting solution was added Et_3N (0.64 mL, 4.6 mmol, distilled under an N_2 atmosphere) and the resulting slurry was heated to reflux for 13 h. After cooling the mixture it was

filtered under N_2 pressure through a pad of Celite which had been flushed with N_2, washing with hexanes (N_2-purged, 3 x 5 mL) and reducing under a stream of N_2.

The residue was taken up in DCM and reacted with BH_3·THF (5.0 mL, 5.0 mmol) as described for **22c**, isolating 646 mg (76% yield over two steps) of title compound by FC. Phenyl diisopropylphosphinite borane **50**: TLC on K6F silica gel 60Å, 19:1 hexanes/Et_2O, Rf = 0.38. Molecular ion calculated for $C_{12}H_{21}BOP$: 223.1423; [M-H], EIMS found *m*/*z* = 223.1429; IR (neat, cm^{-1}) 2383, B–H; 2337, B–H; 1206, O–P; ^1H NMR: δ 7.31-7.26 (2H, m), 7.15-7.08 (3H, m), 2.23 (2H, octet, J = 7.3 Hz), 1.31 (6H, dd, J = 14.1, 7.1 Hz), 1.25 (6H, dd, J = 15.9, 7.2 Hz), 0.9-0.1 (3H, br m); ^{13}C NMR: δ 153.6 (d, J = 6 Hz), 129.3, 124.1 (d, J = 1 Hz), 120.8 (d, J = 3 Hz), 26.3 (d, J = 37 Hz), 16.4 (d, J = 2 Hz), 15.8 (d, J = 2 Hz); ^{11}B NMR: δ -43.4 (qd, J = 97, 59 Hz); ^{31}P NMR: δ 143.6 (q, J = 59 Hz).

A solution of **50** (11.7 mg, 52 μmol) in anhydrous PhBr (0.6 mL) was activated with a solution of TrTPFPB (47 mg, 51 μmol) in PhBr (0.3 mL), quenching after 4 h with a solution of Bu_4NBH_4 (17 mg, 70 μmol) in PhBr (0.3 mL) as described above for **23a**. The residue was purified by PLC on silica gel (20 cm x 20 cm x 1000 μm, 4:1 hexanes/Et_2O) recovering 1.2 mg of pure product **51** as well as 2.7 mg of a mixture of product **51** and unreacted **50** in a ratio of 4:1 by ^1H NMR assay, giving a combined recovery of 3.3 mg or 30% yield of **51**. 2,2-Diisopropyl-1,2,3-benzoxaphospha-borolidine (**51**): TLC on K6F silica gel 60Å, 4:1 hexanes/Et_2O, Rf = 0.47. Molecular ion calculated for $C_{12}H_{20}BOP$: 221.1266; [$M^{\bullet+}$], EIMS found *m*/*z* = 221.1271; IR (neat, cm^{-1}) 2364, B–H; 1175, O–P; ^1H NMR: δ 7.43 (1H, d, J = 7.0 Hz), 7.03 (1H, t, J = 7.8 Hz), 6.94 (1H, t, J = 7.2 Hz), 6.85 (1H, d, J = 7.9 Hz), 2.4-1.6 (2H, br m), 2.34 (2H, octet, J =

7.3 Hz), 1.24 (6H, dd, J = 14.2, 7.3 Hz), 1.22 (6H, dd, J = 17.6, 7.3 Hz); ^{13}C NMR: δ 160.9 (d, J = 10 Hz), 133.5 (d, J = 15 Hz), 126.1, 122.5, 111.8 (d, J = 8 Hz), 24.2 (d, J = 24 Hz), 15.3 (d, J = 3 Hz); ^{11}B NMR: δ -29.8 to -32.4 (br m); ^{31}P NMR: δ 139 (br m).

Representative Procedure for Pinacol Quench for the Cyclization of 50 (Table 3-3)

Borane complex **50** (25 mg, 112 μmol) was dissolved in anhydrous PhBr (1.2 mL) and activated with a solution of TrTPFPB (93 mg, 100 μmol) in PhBr (2 x 0.4 mL) as described above for **23a**, quenching after 4 h by addition of *i*Pr$_2$NEt (distilled, 0.07 mL, 400 μmol) via syringe, resulting in a deep orange color, followed by a solution of pinacol (50 mg, 430 μmol) in anhydrous DCM with loss of the deep color. After 1 h, 10% aq. Na_2CO_3 (0.3 mL) was added and the mixture was stirred open to atmosphere for 16 h, with a black semisolid developing. The mixture was diluted with H_2O (1 mL), separated (most of the dark semisolid remained insoluble), and the aqueous layer was extracted with DCM (2 x 1 mL). The combined organic extracts were reduced by a stream of N_2, the residue assayed by ^{1}H NMR.

Representative Procedure for Strong Acid Activation in the Cyclization of 50 (Table 3-4)

A solution of **50** (29 mg, 131 μmol) in anhydrous PhBr (2 x 0.4 mL) was added to a suspension of Tf_2NH (33 mg, 116 μmol) in PhBr (1.4 mL) in a 3 mL flask fused to a reflux condenser, with slow gas evolution observed along with slow dissolution of Tf_2NH. The mixture was heated to 100 °C, cooling to rt after 24 h before quenching with

a solution of Bu_4NBH_4 (34 mg, 130 μmol) in DCM (2 x 0.3 mL), removing solvent with a stream of N_2 after 1 h. The residue was assayed by ^1H NMR.

Preparation and Reaction of *N*-Methyl-*N*-phenyl-*P*,*P*-diisopropylphosphinous Amide Borane (54)

According to the following modifications of the literature procedure,[24] a solution of *N*-methylaniline (distilled from KOH, 0.56 mL, 5.2 mmol) in anhydrous Et_2O (6 mL) was cooled to -78 °C then reacted with *n*BuLi (1.32 M in hexane, 3.1 mL, 4.1 mmol), warming the solution slowly to rt over the course of 1 h. This was then cooled back to -78 °C and neat chlorodiisopropylphosphine (0.68 mL, 4.3 mmol) was added by syringe, allowing the solution to warm to rt in the cold bath. After 18 h, BH_3·THF (6.5 mL, 6.5 mmol) was added by syringe, filtering the solution through a plug of silica gel after 1 h as described for **22c**. The borane complex was purified by FC (9:1 hexanes/Et_2O, Rf = 0.33), yielding 969 mg (96% yield) of *N*-Methyl-*N*-phenyl-*P*,*P*-diisopropylphosphinous amide borane (**54**): Molecular ion calculated for $C_{13}H_{25}BNP$: 237.1818; [$M^{\bullet+}$Na], EIMS found *m*/*z* = 237.1815; IR (neat, cm^{-1}) 2362, B–H; 2314, B–H; 2265, B–H; 1455, B–N; 1164, C–N; ^1H NMR: δ 7.33-7.28 (2H, m), 7.17-7.09 (3H, m), 3.18 (3H, d, J = 7.2 Hz), 2.33 (2H, dqq, J = 11.0, 7.3, 6.9 Hz), 1.23 (6H, dd, J = 15.7, 6.9 Hz), 1.16 (6H, dd, J = 14.2, 7.3 Hz), 0.8-0 (3H, br m); ^{13}C NMR: δ 147.3, 128.9, 124.8, 124.3, 40.8 (d, J = 5 Hz), 26.3 (d, J = 36 Hz), 17.4 (d, J = 3 Hz), 17.0 (d, J = 1 Hz); ^{11}B NMR: δ -43.4 (qd, J = 96, 25 Hz); ^{31}P NMR: δ 86 (br m).

Borane complex **54** (27.5 mg, 116 μmol) was dissolved in anhydrous PhBr (1.2 mL) and activated with a solution of TrTPFPB (98 mg, 106 μmol) in PhBr (2 x 0.4 mL),

quenching after 1 h with a solution of Bu_4NBH_4 (32 mg, 120 μmol) in PhBr (2 x 0.4 mL) as described above for **23a**. The residue was purified by FC (4:1 hexanes/EtOAc, Rf = 0.31) isolating 20.7 mg of a mixture of **55** and Ph_3CH in a ratio of 2.0:1 by ^1H NMR assay, giving 13.6 mg or 55% yield of **55**. 1-Methyl-2,2-diisopropyl-1,2,3-benzazaphosphaborolidine (**55**): Molecular ion calculated for $C_{13}H_{23}BNP$: 235.1661; [$M^{\bullet+}$], EIMS found *m*/*z* = 235.1661; IR (neat, cm^{-1}) 2346, B–H; 1459, B–N; ^1H NMR: δ 7.38 (1H, d, J = 6.9 Hz), 7.04 (1H, t, J = 7.8 Hz), 6.79 (1H, t, J = 7.3 Hz), 6.49 (1H, d, J = 7.8 Hz), 2.99 (3H, d, J = 5.5 Hz), 2.36 (2H, dqq, J = 9.3, 6.9, 6.8 Hz), 1.20 (6H, t, J = 6.9 Hz), 1.17 (6H, dd, J = 6.8, 3.9 Hz); ^{13}C NMR: δ 153.1 (d, J = 26 Hz), 132.7 (d, J = 18 Hz), 125.2, 119.5 (d, J = 2 Hz), 107.0 (d, J = 8 Hz), 31.2 (d, J = 4 Hz), 23.5 (d, J = 32 Hz), 16.5 (d, J = 3 Hz), 16.0 (d, J = 4 Hz); ^{11}B NMR: δ -30.2 to -30.8 (br m); ^{31}P NMR: δ 88 (br m).

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Chapter 4

Directed Ionic Hydrogenation of Unsaturated Phosphine and Amine Boranes

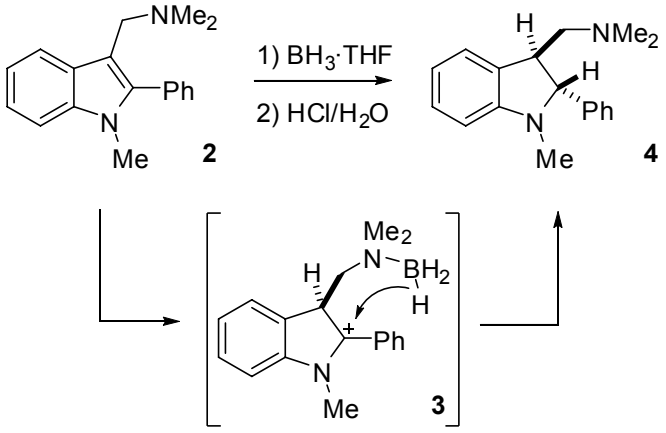
Introduction – Ionic Hydrogenation Using Amine Boranes as Hydride Sources

Since the discovery that hydroxyl groups can direct the catalytic *syn*-hydrogenation of alkenes,[1] this concept has been extended to the diastereoselective reduction of double bonds directed by a number of different Lewis basic functionalities.[2] Directed hydrogenation has only been applied to unprotected amines in a few cases, under heterogeneous conditions.[3] While amine coordination at the metal surface does provide excellent stereocontrol in the alkene reduction, the amine can bind too tightly and poison the catalyst,[4] limiting the applications of this methodology in principle. The use of a separate proton source and hydride donor, referred to as ionic hydrogenation, circumvents the need for such catalysts. A directed delivery of a tethered hydride was therefore explored to develop a highly diastereoselective alkene reduction for unsaturated phosphine and amine boranes.

Kursanov's pioneering ionic hydrogenation studies focused on CF_3CO_2H and Et_3SiH,[5] but numerous hydride sources have been paired with compatible acids. Borane complexes of Lewis bases are orders of magnitude more reactive toward preformed carbocations than are trialkylsilanes,[6] but not so reactive that they are sensitive to hydrolysis.[7] For example, trimethylamine borane (**1**) reduces indole substrates in the

presence of HCl, although excess borane complex is required.[8a] A similar acid-catalyzed reduction of an indole (**2**) by a tethered amine borane has been reported (Scheme 4-1).[8b] Only the *trans*-substituted product **4** was observed in this reaction, while ionic hydrogenation of **2** with $Me_3N{\cdot}BH_3$ (**1**) also gave the *cis* diastereomer. The stereocontrol provided by intramolecular hydride delivery from **3** to **4** is an interesting example of a directed reduction, but the scope was limited to relatively basic indole substrates.

Scheme 4-1. Directed Ionic Hydrogenation of Indole **2**

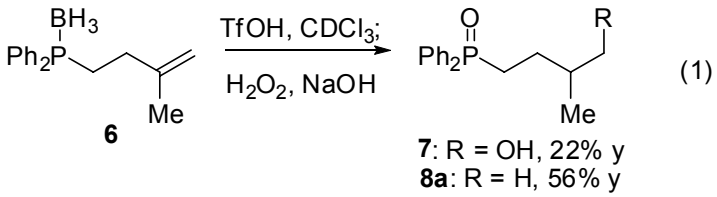


Ionic Hydrogenation of Unsaturated Phosphine Boranes

Tuning the Acid Strength for Alkene Reduction

Extension to the reduction of simpler alkenes is complicated by the need for a more acidic environment, which will require the use of a weaker hydride donor.[9] For example, the reaction of **1** with CF_3CO_2H, the typical proton source in ionic hydrogenation using silanes, proceeds to >50% conversion within 45 min at rt with evolution of H_2. This side reaction destroys both acid and hydride source and could interfere with reduction of the alkene. A logical starting point for the optimization of the directed ionic hydrogenation is therefore an unsaturated phosphine borane. The lower

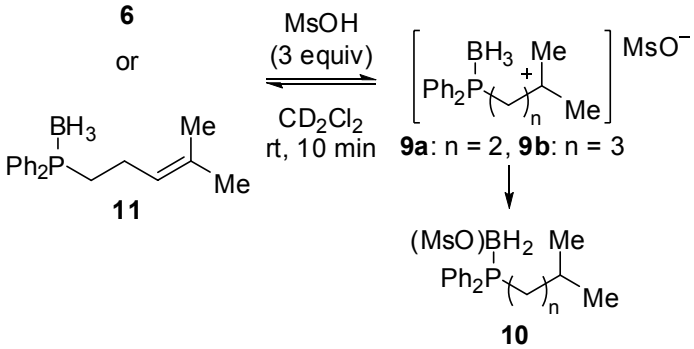
hydridicity of borane complexed to a phosphine is exemplified by the reaction of CF_3CO_2H with $Bu_3P{\cdot}BH_3$ (**5**) under the same conditions as above, with less than 2% consumption of **5** by ^1H NMR assay after 45 min.



(1)

Another relevant observation came from previous work in our laboratory on the directed hydroboration of unsaturated phosphine boranes.[10] Activation of **6** with trifluoromethanesulfonic acid (TfOH) gives product **8a** with a reduced side chain in 56% yield after oxidative workup (eq 1). The lower reactivity of phosphine boranes as hydride donors allows protonation of the alkene to occur competitively even with this strong acid. However some hydride abstraction from **6** by TfOH does occur, resulting in the expected hydroboration and the isolation of **7** in 22% yield.

Scheme 4-2. Reaction Pathway for Ionic Hydrogenation

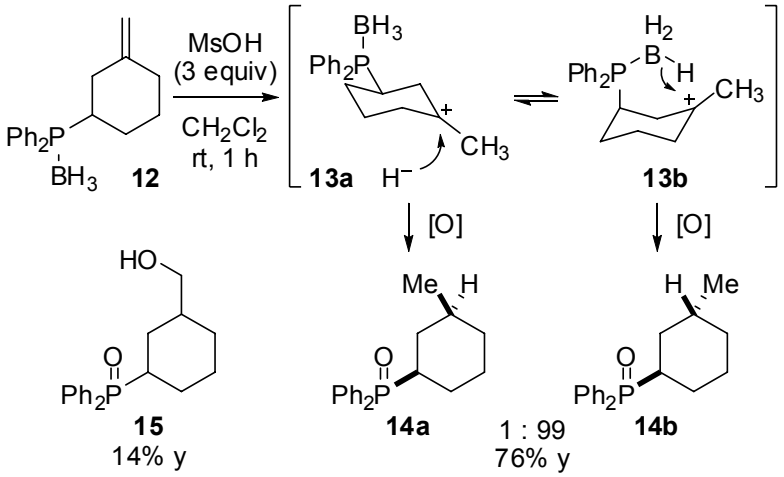


Weaker acids were examined in an attempt to minimize hydroboration, but **6** was unreactive at rt (1 h) toward CF_3CO_2H. The more acidic methanesulfonic acid (MsOH) did protonate the alkene (Scheme 4-2), although the reduction was slow with stoichiometric MsOH. Using 3 equiv of acid, the alkene was consumed within 10 min

according to ^{1}H NMR spectroscopy. The major product observed is tentatively assigned structure **10a**, based on the downfield shift of the B–*H* signal (centered at δ 3.3 ppm, compared to δ 1.0 ppm for the B–*H* signal of **6**) that integrates for 2H and the observation of a singlet integrating for 3H at δ 2.84 ppm (H_3CSO_3–B). A minor phosphonium salt byproduct resulting from P–B bond protonolysis was also indicated by a small doublet of triplets at δ 7.8 ppm ($^{1}J_{PH}$ = 508 Hz, $^{3}J_{HH}$ = 6.2 Hz) in the ^{1}H NMR spectrum. Oxidative workup of the reaction mixture gave **8a** in 78% yield along with 12% of **7**. Substrate **11** also reacted with MsOH via carbocation **9b**, the homologue of intermediate **9a**, giving reduction of the appended olefin within 10 min at rt.

Directed Ionic Hydrogenation of a Cyclic Substrate

Scheme 4-3. Diastereoselective Ionic Hydrogenation of **12**



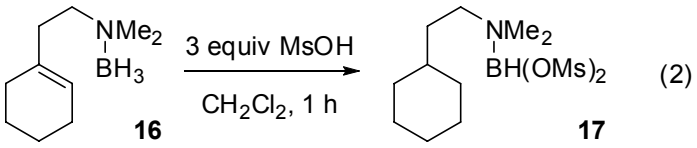
Phosphine borane **12** was prepared by Wittig methylenation of the known cyclohexanone[11] to explore diastereoselective reduction of the exocylic alkene. Subjecting **12** to the reaction conditions optimized for **6**, followed by oxidative workup, resulted in isolation of **14b** as the sole reduction product; no trace of **14a** was observed by ^{1}H NMR assay (>99:1 dr). This remarkable stereoselectivity did not erode until the

concentration of **12** was increased from ca. 0.1 M to 1.0 M, still giving a reasonably good 7:1 ratio favoring intramolecular reaction product **14b**. The addition of 10 equiv $Bu_3 \cdot PBH_3$ (**5**) had no observable effect on the diastereoselectivity of the reduction of **12** (**14b** was obtained with >99:1 dr).

Protonation of the double bond of **12** gives tertiary carbocation **13**; hydride addition to this cation could occur from either face of the ring. Considering a possible intermolecular pathway, holding the bulky phosphorus substituent in a pseudoequatorial position (Scheme 4-3, **13a**) followed by the favored axial attack[12] of an external hydride results in *cis*-substituted product **14a**. A ring flip requires putting the phosphinyl group in a pseudoaxial position, but allows intramolecular delivery of hydride for *syn*-hydrogenation of the olefin to give the *trans*-substituted product **14b**. The high diastereoselectivity is evidence that the intramolecular pathway is much faster than hydride abstraction from an external source by **13**.

Ionic Hydrogenation of Unsaturated Amine Boranes

Intermediacy of a Mesylatoborane Complex

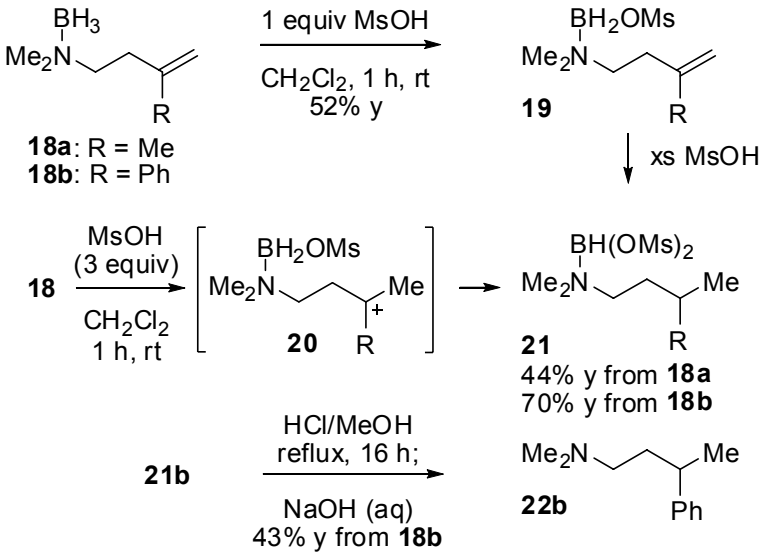


16 **17** (2)

After demonstrating a preference for the intramolecular pathway in the ionic hydrogenation of unsaturated phosphine boranes, we sought to apply this methodology to the reduction of unsaturated amine boranes. Tertiary amine boranes such as **16** had been found to be poor substrates for directed hydroboration at rt with I_2 activation.[13] A closer look at the spectra from those attempted hydroborations revealed a minor byproduct that

appeared to have a saturated cyclohexyl group. Treatment of **16** with MsOH, under the conditions developed for **6**, resulted in complete consumption of alkene within 1 h by ^{1}H NMR assay. Identification of the major product as a $BH(OMs)_2$ adduct of the saturated amine by ^{1}H NMR integration of the methyl signals was confirmed by mass spectrometry. Separation of the product mixture on silica gel resulted in product with an inseparable impurity. A corrected yield of 42% of theoretical was calculated based on the tentative assignment of this impurity as an isomeric product. The assignment of the major product as structure **17** was confirmed by its independent synthesis via MsOH treatment of the borane complex of the known (2-cyclohexylethyl)-dimethylamine.[14]

Scheme 4-4. Directed Ionic Hydrogenation of Amine Boranes



The order of events in the directed reduction of an amine borane with MsOH to form a saturated amine coordinated to $BH(OMs)_2$ remained unknown. Stoichiometric MsOH reacted with the simpler acyclic analogue **18a**, by hydride abstraction as expected by its reaction with CF_3CO_2H, generating complex **19a** along with H_2 (Scheme 4-4). However, further reaction of **19a** with excess MsOH was effective for reduction of the appended olefin, giving product **21a** presumably via cationic intermediate **20a**. Although

the generation of H_2 does remove one equivalent each of proton and hydride from the system, borane complex **18** has three equivalents of hydride available. Thus ionic hydrogenation is still possible in the presence of excess acid. Furthermore, **19** differs from **18** by the presence of an electron-withdrawing group on the boron atom that attenuates borane hydridicity. While hydride abstraction from **18** by MsOH occurs faster than alkene protonation, this is apparently not the case for the less hydridic **19**.

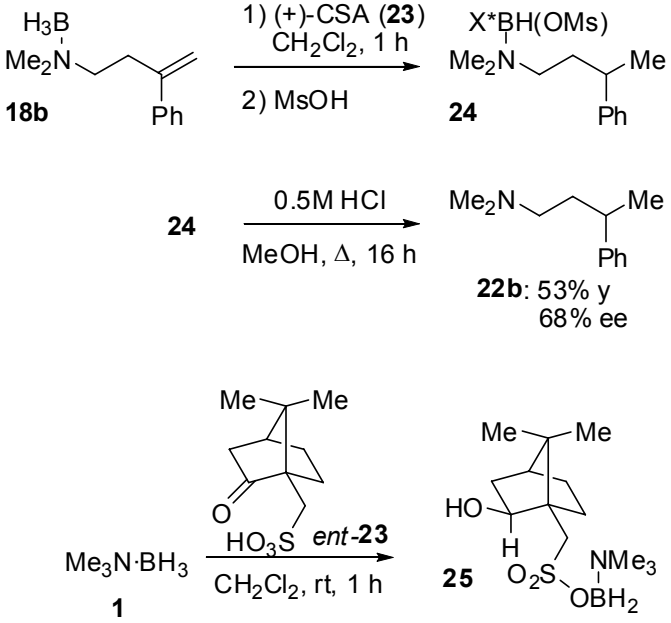
Reaction of phenyl-substituted alkene **18b** with MsOH occurred in a similar fashion. This alkene should be more basic due to stabilization of the resulting benzylic carbocation, but reaction of MsOH with the first hydride was still faster. However, further treatment of **19b** with excess MsOH, or treatment of **18b** directly with 3 equiv MsOH, also resulted in reduction of the double bond. The cleavage of complex **21b** to give the known amine **22** was also explored. This complex was surprisingly robust, unreactive toward $LiAlH_4$, Bu_4NF and methanolic KHF_2 at rt (16 h). It was eventually found that **21b** could be cleaved by refluxing in acidic MeOH for 16 h, giving the free amine **22** after basic workup. Reaction with 8 equiv 4-dimethylamino-pyridine in refluxing MeOH or with neat pyrrolidine at reflux gave comparable yields of **22b**, but purification was complicated by the large excess of amines in these reactions.

Pretreatment with Chiral Acid for Diastereoselective Reduction

Pretreatment of **18b** with (+)-camphorsulfonic acid (CSA, **23**), a chiral derivative of MsOH, allowed enantioselective reduction of the appended alkene by subsequent reaction with 2 equiv MsOH. Cleavage of the product **24** with HCl in refluxing MeOH gave **22b** with 68% ee, effecting a net enantioselective reduction of the unsaturated amine. Using CSA creates a chiral derivative of **19b**, imparting diastereoselectivity in the hydride transfer from **20b**. However CSA alone is not acidic enough for reduction of

the alkene; the addition of MsOH is necessary. This is preferred in any case, avoiding the use of a superstoichiometric chiral additive.

Scheme 4-5. Enantioselective Reduction of **18b** with CSA

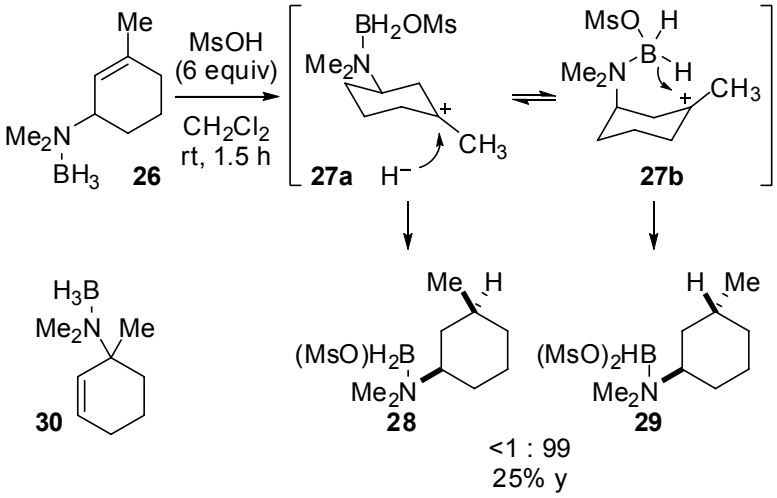


The reaction of CSA with **18b** appeared to be more complicated than implied by a simple hydride abstraction from the borane complex. The vigorous gas evolution typical of reactions of strong acids with amine boranes was not observed in this case, and the ^{1}H NMR spectrum of the intermediate complex had an unexpected signal at δ 4.1 ppm. A ^{13}C NMR peak at δ 76.4 ppm also indicated reduction of the ketone moiety in **23** by **18b**, and infrared spectroscopy confirmed this by the absence of a carbonyl stretch along with the appearance of an O–H stretch at 3496 cm^{-1}. The analogous reaction with **1** gave similar spectroscopic data, and crystalline product **25** was isolated, structure confirmed by X-ray crystallography. This means that CSA is altered in the course of the reaction and could not be recovered, but a reduced CSA could potentially be recovered from **24** and reused to pretreat amine borane **18b**. Ideally, a catalytic amount of some chiral

additive could be used along with stoichiometric MsOH or some other activator, with reversible substitution of $^{-}$OMs from **19**. A more electron rich chiral additive would have to be used, creating a more hydridic species from **19** and facilitating stereoselective hydride transfer from a small concentration of this chiral species.

Directed Ionic Hydrogenation of a Cyclic Substrate

Scheme 4-6. Diastereoselective Ionic Hydrogenation of **26**



Cyclohexenylamine borane **26** was prepared to compare the diastereoselective reduction via cation **27** with the reduction of phosphine borane **12** via intermediate **13**. The free amine was made by amination of the mesylate of 3-methyl-2-cyclohexen-1-ol, and substrate **26** was contaminated by ca. 15% of the inseparable isomeric allylic amine borane **30**. An initial attempt at the directed ionic hydrogenation showed very slow alkene consumption even with the 3 equiv MsOH used in other cases, but the reaction with a larger excess of MsOH was successful. By ^{1}H NMR assay, the isolated product **29** was nearly diastereomerically pure; only a trace of the upfield methyl doublet was observed (δ 0.97 ppm, compared to δ 1.05 ppm for **29**) that indicates **28** by analogy to the corresponding phosphine diastereomers (NMR signal for methyl doublets of **14a**: δ^{1}H =

0.86, **14b**: δ^1H = 0.96 ppm). The harsher conditions required for reaction of **26** are rationalized in the context of the requirement that the bulky amino substituent be put in a pseudoaxial position (conformer **27b**) for directed reduction. The free energy cost of an amino group in the axial versus equatorial position is expected to be higher than for a phosphino group due to the longer C–P bonds. For comparison, the free energy of preference for the equatorial position for a diphenylphospinoyl ($Ph_2P(O)$-) group is 2.46 kcal/mol,[15] but the borane-complexed dimethylamino group has steric bulk similar to a *tert*-butyl group, the *A*-value of which has been estimated to be at least 5.4 kcal/mol.[16]

Summary

In conclusion, ionic hydrogenation has been shown to be effective for reducing alkenes tethered to amine or phosphine groups via the borane complexes. In the case of the less hydridic phosphine boranes this occurs by simple protonation of the double bond followed by hydride transfer. For amine boranes an initial hydride abstraction by MsOH generates an attenuated hydride donor that is still reactive toward a tethered carbocation formed by protonation of the olefin with excess acid. For cyclic borane complexes **12** or **26** where only one face of the intermediate carbocation (**13** or **27**) is accessible to the tethered hydride a highly diastereoselective reduction follows. The initial reaction of the strong acid with amine boranes provides an opportunity to introduce a chiral substituent on boron that can later be removed, allowing net enantioselective reduction of an unsaturated amine borane.

Experimental

General Methods. The following chemicals were commercially available and used as received: trimethylamine borane; tributylphosphine borane; trifluoroacetic acid; methanesulfonic acid; borane tetrahydrofuran, 1.0 M solution in tetrahydrofuran; methyltriphenylphosphonium bromide; sodium bis(trimethylsilyl)amide; 3-methylcyclohexanol, mixture of *cis* and *trans*; *p*-toluenesulfonyl chloride; diphenylphosphine; (+)-camphorsulfonic acid; 3-methyl-2-cyclohexen-1-ol; methanesulfonyl chloride; dimethylamine, 33% in absolute ethanol. Chloroform-*d* and methylene chloride-d_2 were dried by storing over activated 4Å molecular sieves; dichloromethane (DCM) and tetrahydrofuran (THF) were dried by passing through a column of activated alumina; triethylamine was distilled from CaH_2 and pyridine from KOH under an N_2 atmosphere. All reactions were performed at room temperature under an N_2 atmosphere unless otherwise stated. Nuclear magnetic resonance experiments were performed on Varian Inova 500 and Inova 400 spectrometers at the following frequencies: ^{1}H 500 MHz; $\{^{1}H\}^{13}C$ 101 MHz; ^{11}B 160 MHz; ^{19}F 376 MHz, unless otherwise stated. All spectra were recorded in $CDCl_3$ and referenced to the ^{1}H signal of internal Me_4Si (unless otherwise stated) according to recommendations,[17] using a Ξ of 25.145020 for Me_4Si (^{13}C), a Ξ of 32.083974 for $BF_3{\cdot}OEt_2$ (^{11}B), and a Ξ of 94.094011 for CCl_3F (^{19}F).

Representative Procedure for Reaction of $Me_3N{\cdot}BH_3$ (1) with CF_3CO_2H.

Neat CF_3CO_2H (6 μL, 78 μmol) was added by syringe to a stirred solution of **1** (4.8 mg, 66 μmol) in anhydrous CD_2Cl_2 (1.0 mL) under an N_2 atmosphere. After 45 min, this solution was transferred via syringe to an N_2-flushed NMR tube. Assay by ^1H NMR showed ca. 45% of **1** remaining by integration of its B–*H* signal at δ 2.0-1.3 ppm relative to the methyl singlet at δ 2.61 ppm (overlapping $Me_3N{\cdot}BH_3$ and $Me_3N{\cdot}BH_2(O_2CCF_3)$ signals). The product trifluoroacetoxyborane complex was confirmed by reaction of **1** with 10 equiv CF_3CO_2H (50 μL, 650 μmol) under the same conditions, giving $Me_3N{\cdot}BH_2(O_2CCF_3)$ as the major product after 1 h: ^1H NMR: δ 3.1-2.0 (2H br s), 2.63 (9H, s).

The reaction of $Bu_3P{\cdot}BH_3$ (**5**, 20 μL, 75 μmol) with CF_3CO_2H (6 μL, 78 μmol) in 1.0 mL CD2Cl2 was performed under the same conditions, assay by 1H NMR after 45 min showing less than 2% conversion to $Bu_3P{\cdot}BH_2(O_2CCF_3)$ by integration of its α-C*H*$_2$ at δ 1.76-1.67 ppm relative to the α-C*H*$_2$ peak for unreacted **5** at δ 1.60-1.50 ppm. This product trifluoroacetoxyborane complex was also confirmed by reaction of **5** with 10 equiv CF_3CO_2H (50 μL, 650 μmol) under the same conditions, giving $Bu_3P{\cdot}BH_2(O_2CCF_3)$ as the major product after 1 h: ^1H NMR: δ 3.4-2.3 (2H br s), 1.76-1.67 (6H, m), 1.53-1.37 (6H, m), 0.94 (9H, t, J = 7.1 Hz); ^{31}P NMR: δ 3.1-0.4 (br m).

Representative Procedure for Ionic Hydrogenation of Phosphine Borane 6

Neat MsOH (100 μL, 1.54 mmol) was added by syringe to a stirred solution of **6** (138 mg, 0.51 mmol) in anhydrous DCM (5 mL) under an N_2 atmosphere. After 10 min, this solution was quenched by addition of 10 mL MeOH, 1 mL 20% aq. NaOH and 1 mL

35% aq. H_2O_2. After an additional 1 h, this mixture was diluted with 10 mL H_2O, separated and the aqueous layer extracted with 2 x 10 mL DCM. The combined organic layers were dried over Na_2SO_4 and reduced by rotatory evaporation. The product was purified by flash chromatography (FC) on silica gel (15 cm x 20 mm diameter, 19:1 DCM/EtOH), isolating 110 mg product **8a** (Rf = 0.3, 78% y) and recovering 18 mg **7** (Rf = 0.07, 12% y). ^{1}H and ^{13}C NMR spectral data matched those reported for **7** and **8a**.[10]

Preparation and Ionic Hydrogenation of Phosphine Borane 12

Methyltriphenylphosphonium bromide (520 mg, 1.46 mmol) and sodium bis(trimethylsilyl)-amide (242 mg, 1.32 mmol) were transferred under an N_2 atmosphere to an oven-dried 50 mL round-bottom flask fused to a reflux condenser and dissolved in anhydrous THF (20 mL). After 30 min the now yellow solution was heated to reflux, cooling after 1 h and filtering through an N_2-flushed fritted filter into a flask containing a stirred solution of 3-diphenylphosphinylcyclohexanone borane[11] (355 mg, 1.20 mmol) in anhydrous THF (10 mL), rinsing the flask in which the phosphonium ylide was formed with 10 mL THF. After 1 d the reaction mixture was washed with H_2O (50 mL) and brine (50 mL), dried over $MgSO_4$, and reduced by rotatory evaporation. The product was purified by FC on silica gel (15 cm x 30 mm diameter, 2:1 hexanes/Et_2O), isolating 337 mg (3-Methylenecyclohexyl)-diphenylphosphine Borane (**12**): analytical thin layer chromatography (TLC) on K6F silica gel 60Å, 2:1 hexanes/Et_2O, Rf = 0.53. Molecular ion calculated for $C_{19}H_{24}BNaP$: 317.1606; [M+Na], ESMS found *m/z* = 317.1591; IR (neat, cm^{-1}) 2381, B–H; 2348, B–H; 1650, C=C; ^{1}H NMR: δ 7.78-7.70 (4H, m), 7.52-7.41 (6H, m), 4.66 (1H, s), 4.57 (1H, s), 2.55-2.45 (1H, m), 2.31 (1H, br d, J = 13.1 Hz), 2.28-2.17 (2H, m), 2.00 (1H, td, J = 13.4, 4.4 Hz), 1.95-1.87 (1H, m), 1.73-1.66 (1H, m),

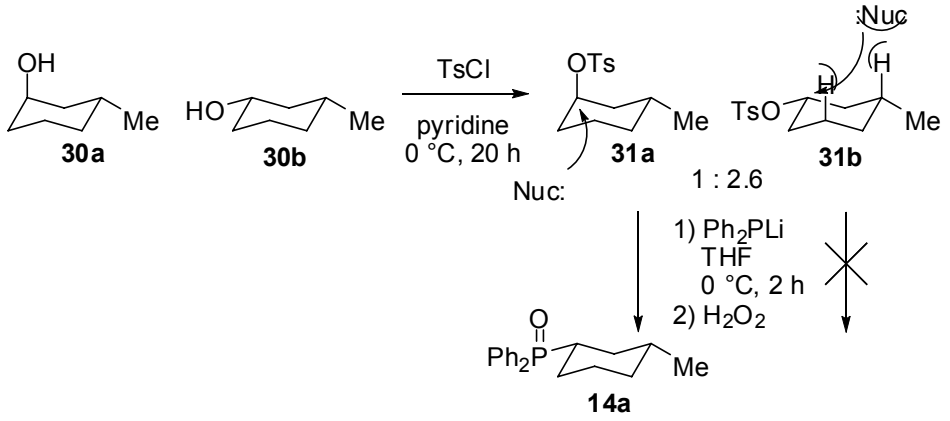
1.61 (1H, qt, J = 12.7, 4.4 Hz), 1.35 (1H, qt, J = 13.0, 3.9 Hz), 1.3-0.5 (3H, br m); ^{13}C NMR: δ 147.4 (d, J = 12 Hz), 132.6 (d, J = 9 Hz), 132.6 (d, J = 8 Hz), 131.2 (d, J = 2 Hz), 131.1 (d, J = 2 Hz), 128.8 (d, J = 10 Hz), 128.8 (d, J = 10 Hz), 128.3 (d, J = 54 Hz), 128.0 (d, J = 53 Hz), 108.6, 35.0 (d, J = 10 Hz), 34.8 (d, J = 27 Hz), 34.4 (d, J = 2 Hz), 27.9 (d, J = 12 Hz), 26.1; ^{11}B NMR: δ -42.1 (qd, J = 93, 30 Hz); ^{31}P NMR: δ 19.7-18.0 (br m).

Reaction of **12** under the same conditions as for **6** above gave ionic hydrogenation product **14b** (76% y) and hydroboration product **15** (14% y). *trans*-(3-Methylcyclohexyl)-diphenylphosphine oxide (**14b**): TLC on K6F silica gel 60Å, 19:1 DCM/EtOH, Rf = 0.18. Molecular ion calculated for $C_{19}H_{23}NaOP$: 298.1486; [$M^{\bullet+}$], EIMS found *m*/*z* = 298.1478; IR (neat, cm^{-1}) 1181, P=O; ^{1}H NMR: δ 7.82-7.74 (4H, m), 7.52-7.41 (6H, m), 2.55-2.45 (1H, m), 2.15-2.06 (1H, m), 1.87-1.77 (1H, m), 1.71-1.40 (6H, m), 1.38-1.30 (1H, m), 0.96 (3H, d, J = 7.1 Hz); ^{13}C NMR: δ 132.6 (d, J = 94 Hz), 132.4 (d, J = 94 Hz), 131.4 (d, J = 3 Hz), 131.4 (d, J = 3 Hz), 131.0 (d, J = 8 Hz), 131.0 (d, J = 8 Hz), 128.6 (d, J = 11 Hz), 128.5 (d, J = 11 Hz), 31.7, 31.5 (d, J = 73 Hz), 31.0 (d, J = 3 Hz), 27.1 (d, J = 10 Hz), 25.0 (d, J = 3 Hz), 20.8 (d, J = 11 Hz), 18.5; ^{31}P NMR: δ 36.4.

Independent Synthesis of Minor Diastereomer 14a

Pyridine (5 mL, 62 mmol) was added to *p*-toluenesulfonyl chloride (1.63 g, 8.5 mmol) at 0 °C under an N_2 atmosphere to dissolve; the solution developed a yellow color. To this was added the commercially available mixture of *cis*- and *trans*-3-methylcyclohexanol (**30b** and **30a**), the yellow color fading on alcohol addition. After 20 h at 0 °C, the reaction was quenched by pouring onto 150 mL iced 1 M aq. HCl,

extracting with ethyl ether (3 x 20 mL), drying the combined organic layers over $MgSO_4$ before reducing by rotatory evaporation, leaving 1.74 g (88% y) of residue. ^{1}H NMR assay shows a mixture of *cis*- and *trans*-3-methylcyclohexyl-*p*-toluenesulfonates (**31b** and **31a**) in a ratio of 2.6:1 by integration of the methyl doublets at 0.89 and 0.82 ppm, respectively. This crude tosylate mixture was taken on without purification.



Diphenylphosphine (0.62 g, 3.3 mmol) was charged to a 50 mL round-bottom flask under an N_2 atmosphere and dissolved in anhydrous THF (17 mL). After cooling the solution to -40 °C, a solution of *n*BuLi (1.98 M in hexane, 1.7 mL, 3.4 mmol) was added slowly, the resulting solution developing a deep red color. After stirring 4 h, the solution was warmed to 0 °C and a mixture of *cis*- and *trans*-3-methylcyclohexyl-*p*-toluenesulfonate (**31**, 0.96 g, 3.6 mmol) was added by syringe. After 2 h the deep red color had mostly faded to a light orange, and the mixture was oxidized by the addition of 5 mL 35% aq. H_2O_2. After warming to rt, the layers were separated and the aqueous layer washed with ethyl ether (2 x 20 mL), the combined organic layers dried over $MgSO_4$ and reduced by rotatory evaporation. Assay of the crude product mixture (1.14 g) by ^{1}H NMR shows unreacted tosylate further enriched in the *cis*-isomer (**31b**) and only the *cis*-diastereomer of the product (**14a**); no trace of *trans*-(3-methylcyclohexyl)-diphenylphosphine oxide (**14b**) was observed. Reaction of the *cis*-tosylate **31b** by an S_N2

mechanism requires displacement of an equitorial tosylate, disfavored in cyclohexyl systems by steric repulsion of the incoming nucleophile by C–H bonds at the 3- and 5-positions. Purification of a portion of the crude product (176 mg) by preparative thin layer chromatography (PLC) on silica gel (20 x 20 cm x 1000 μm, EtOAc) gave pure *cis*-(3-methylcyclohexyl)-diphenylphosphine oxide (**14a**, 23 mg, 50% y based on *trans*-3-methylcyclohexyl-*p*-toluenesulfonate): TLC on K6F silica gel 60Å, EtOAc, Rf = 0.42. Molecular ion calculated for $C_{19}H_{23}NaOP$: 298.1486; [$M^{\bullet+}$], EIMS found *m*/*z* = 298.1490; IR (neat, cm^{-1}) 1181, P=O; ^1H NMR: δ 7.82-7.74 (4H, m), 7.54-7.43 (6H, m), 2.33-2.24 (1H, m), 1.86-1.79 (1H, m), 1.74-1.65 (3H, m), 1.54-1.17 (4H, m), 0.92 (1H, qd, J = 12.6, 3.7 Hz), 0.86 (3H, d, J = 6.6 Hz); ^{13}C NMR: δ 132.2 (d, J = 94 Hz), 132.1 (d, J = 94 Hz), 131.4 (d, J = 3 Hz), 131.4 (d, J = 3 Hz), 131.1 (d, J = 9 Hz), 128.6 (d, J = 11 Hz), 128.5 (d, J = 12 Hz), 37.1 (d, J = 73 Hz), 36.6, 32.9 (d, J = 13 Hz), 32.7 (d, J = 3 Hz), 26.3 (d, J = 14 Hz), 24.3 (d, J = 3 Hz), 22.7; ^{31}P NMR: δ 34.1.

Preparation of Borane Complexes of Amines

BH_3·THF (6.3 mL, 6.3 mmol) was added by syringe under an N_2 atmosphere to the known (3-methyl-3-butenyl)-dimethylamine[18] (1.0 mL, 6.8 mmol) in anhydrous DCM (20 mL). After 1 h, the solution was filtered through a plug of silica gel, flushing with DCM and removing solvent by rotary evaporation, yielding 0.78 g (3-methyl-3-butenyl)-dimethylamine borane **18a** (97% y): TLC on K6F silica gel 60Å, 9:1 hexanes/Et_2O, Rf = 0.26. Molecular ion calculated for $C_7H_{17}BN$: 126.1454; [M-H], EIMS found *m*/*z* = 126.1452; IR (neat, cm^{-1}) 2366, B–H; 2319, B–H; 2273, B–H; 1650, C=C; 1459, B–N; 1167, C–N; ^1H NMR: δ 4.81 (1H, s), 4.73 (1H, s), 2.90-2.85 (2H, m), 2.61 (6H, s), 2.46-

2.41 (2H, m), 2.1-1.3 (3H, br m), 1.77 (3H, s); ^{13}C NMR: δ 141.9, 112.1, 63.0, 51.4, 32.1, 22.7; ^{11}B NMR: δ -9.9 (q, J = 98 Hz).

Borane complexation from (3-phenyl-3-butenyl)-dimethylamine[19] under the same conditions gave **18b** (67% y): TLC on K6F silica gel 60Å, 2:1 hexanes/EtOAc, Rf = 0.27. Molecular ion calculated for $C_{12}H_{20}BNNa$: 212.1586; [M+Na], ESMS found *m*/*z* = 212.1582; IR (neat, cm^{-1}) 2366, B–H; 2319, B–H; 2273, B–H; 1627, C=C; 1461, B–N; 1167, C–N; ^{1}H NMR: δ 7.44-7.41 (2H, m), 7.37-7.33 (2H, m), 7.32-7.28 (1H, m), 5.38 (1H, d, J = 1.0 Hz), 5.15 (1H, q, J = 1.0 Hz), 3.02-2.97 (2H, m), 2.85-2.80 (2H, m), 2.61 (6H, s), 2.1-1.3 (3H, br m); ^{13}C NMR: δ 144.8, 139.8, 128.6, 128.0, 126.0, 114.6, 63.6, 51.8, 30.4; ^{11}B NMR: δ -10.2 (q, J = 97 Hz).

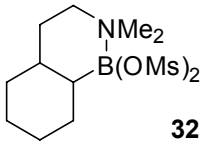
Borane complexation from crude (2-(1-cyclohexenyl)-ethyl)-dimethylamine, prepared by the reaction of the primary amine with formalin and $NaBH_3CN$,[20] under the same conditions gave **16** (purified by FC, 15% y over 2 steps from 2-(1-cyclohexenyl)-ethylamine): TLC on K6F silica gel 60Å, 9:1 hexanes/acetone, Rf = 0.38. Molecular ion calculated for $C_{10}H_{22}BNNa$: 190.1743; [M+Na], ESMS found *m*/*z* = 190.1739; IR (neat, cm^{-1}) 2366, B–H; 2317, B–H; 2271, B–H; 1459, B–N; 1167, C–N; ^{1}H NMR: δ 5.47 (1H, br s), 2.86-2.80 (2H, m), 2.59 (6H, s), 2.35-2.30 (2H, m), 2.02-1.90 (4H, m), 1.65-1.51 (4H, m), 2.0-1.2 (3H, br m); ^{13}C NMR: δ 133.9, 123.5, 63.3, 51.2, 32.3, 28.5, 25.2, 22.8, 22.2; ^{11}B NMR: δ -9.8 (q, J = 96 Hz).

Representative Procedure for Ionic Hydrogenation of Amine Borane 18a

Neat MsOH (100 μL, 1.54 mmol) was added by syringe to a stirred solution of **18a** (64 mg, 0.50 mmol) in anhydrous DCM (5 mL) under an N_2 atmosphere. After 1 h, the reaction was quenched by addition of 5 mL 5% aq. NaOH, separated and the aqueous layer extracted with 2 x 5 mL DCM. The combined organic layers were dried over Na_2SO_4 and reduced by rotatory evaporation. The product was purified by flash chromatography (FC) on silica gel (15 cm x 20 mm diameter, 1:2 hexanes/EtOAc), isolating 71 mg (3-methylbutyl)-dimethylamine bis(methylsulfonyloxy)borane (**21a**, 44% y): TLC on K6F silica gel 60Å, 1:2 hexanes/EtOAc, Rf = 0.20. Molecular ion calculated for $C_9H_{24}BNNaO_6S_2$: 340.1036; [M+Na], ESMS found *m*/*z* = 340.1027; IR (neat, cm^{-1}) 2508, B–H; 1484, B–N; 1318, B–O; 1173, C–N; ^1H NMR: δ 3.8-2.8 (1H, br m), 3.07 (6H, s), 2.95-2.90 (2H, m), 2.61 (6H, s), 1.65-1.52 (3H, m), 0.96 (6H, d, J = 6.4 Hz); ^{13}C NMR: δ 57.8, 44.5, 38.9, 30.4, 26.6, 22.4; ^{11}B NMR: δ 1.0 (d, J = 134 Hz).

(3-Phenylbutyl)-dimethylamine bis(methylsulfonyloxy)borane was purified by reverse-phase PLC on K18F silica gel (**21b**, 70% y): TLC on K18F silica gel 60Å, 4:1 MeOH/H_2O buffered with 0.5% Et_3N and 0.5% CF_3CO_2H, Rf = 0.62. Molecular ion calculated for $C_{14}H_{25}BNO_6S_2$: 378.1216; [M-H], EIMS found *m*/*z* = 378.1215; IR (neat, cm^{-1}) 2512, B–H; 1484, B–N; 1322, B–O; 1177, C–N; ^1H NMR: δ 7.33 (2H, t, J = 7.5 Hz), 7.23 (1H, t, J = 7.3 Hz), 7.18 (2H, d, J = 7.3 Hz), 3.02 (3H, s), 3.01 (3H, s), 2.95 (1H, td, J = 12.7, 4.9 Hz), 2.74-2.66 (1H m), 2.60 (1H, td, J = 12.7, 4.4 Hz), 2.56 (3H, s), 2.52 (3H, s), 2.07-1.90 (2H, m), 1.32 (3H, d, J = 7.1 Hz); ^{13}C NMR: δ 145.0, 128.9, 126.8, 126.7, 58.3, 45.0, 44.7, 38.9, 38.9, 38.2, 30.3, 22.5; ^{11}B NMR: δ 0.8 (d, J = 111 Hz).

Purification of the product from reaction of **16** with 3 equiv MsOH gave a 55% yield of **17** impure with what is proposed to be hydroboration byproduct **32** (ratio of **32** to **17** about 1:3 ratio). This corresponds to a 42% yield of **17** after correcting for this or an isomeric byproduct. This impurity could not be isolated from **17**, and was not reactive toward oxidative quench. Analytically pure **17** was prepared by reaction of the borane complex of (2-cyclohexylethyl)-dimethylamine[14] with 6 equiv MsOH for 5 h. (2-Cyclohexylethyl)-dimethylamine bis(methylsulfonyloxy)borane (**17**): TLC on K6F silica gel 60Å, 1:2 hexanes/EtOAc, Rf = 0.24. Molecular ion calculated for $C_{12}H_{27}BNO_6S_2$: 356.1373; [M-H], EIMS found *m*/*z* = 356.1373; IR (neat, cm^{-1}) 2516, B–H; 2368, B–H; 1482, B–N; 1324, B–O; 1177, C–N; ^{1}H NMR: δ 3.8-2.8 (1H, br m), 3.07 (6H, s), 2.97-2.91 (2H, m), 2.60 (6H, s), 1.75-1.52 (6H, m), 1.30-1.10 (5H, m), 0.96 (2H, q, J = 12.0 Hz); ^{13}C NMR: δ 57.4, 44.4, 38.9, 35.9, 33.2, 29.1, 26.2, 26.0; ^{11}B NMR: δ 1.0 (d, J = 123 Hz).



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Reaction of 18a with Stoichiometric MsOH

Neat MsOH (40 μL, 0.62 mmol) was added by syringe to a stirred solution of **18a** (64 mg, 0.50 mmol) in anhydrous DCM (5 mL) under an N_2 atmosphere. After 1 h, the reaction was quenched by addition of 2 mL 5% aq. NaOH, diluted with 3 mL H_2O, separated and the aqueous layer extracted with 2 x 5 mL DCM. The combined organic layers were dried over Na_2SO_4 and reduced by rotatory evaporation. The product was

purified by flash chromatography (FC) on silica gel (15 cm x 20 mm diameter, 1:2 hexanes/EtOAc), isolating 57 mg (3-methyl-3-butenyl)-dimethylamine methylsulfonyl-oxyborane (**19a**, 52% y): TLC on K6F silica gel 60Å, 1:2 hexanes/EtOAc, Rf = 0.37. Molecular ion calculated for $C_8H_{20}BNNaO_3S$: 244.1155; [M+Na], ESMS found *m*/*z* = 244.1156; IR (neat, cm^{-1}) 2347, B–H; 2325, B–H; 1466, B–N; 1314, B–O; 1146, C–N; ^{1}H NMR: δ 4.85 (1H, s), 4.76 (1H, s), 3.0-2.1 (2H, br m), 2.97-2.92 (2H, m), 2.91 (3H, s), 2.61 (6H, s), 2.42-2.36 (2H, m), 1.77 (3H, s); ^{13}C NMR: δ 141.1, 112.9, 59.0, 46.9, 37.7, 30.9, 22.6; ^{11}B NMR: δ 3.2 to -1.2 (br m).

Cleavage of $BH(OMs)_2$ Complex 21b

Neat MsOH (25 μL, 0.39 mmol) was added by syringe to a stirred solution of **18b** (24 mg, 0.13 mmol) in anhydrous DCM (3 mL) in a 10 mL round-bottom flask fused to a reflux condenser under an N_2 atmosphere. After 1 h, the solvent was removed by a stream of N_2, and the residue was dissolved in MeOH (3.0 mL) which was then acidified by addition of 0.25 mL 6M aq. HCl before heating to reflux 16 h. The mixture was cooled to rt, made alkaline with 5% aq. NaOH and extracted with Et_2O (2 x 5 mL), the organic layers dried over $MgSO_4$ and reduced by rotatory evaporation. The product was purified by PLC on silica gel (20 x 20 cm x 250 μm, 65:33:2 hexanes/acetone/Et_3N), isolating 10 mg (3-phenylbutyl)-dimethylamine (**22b**, 43% y). ^{1}H NMR spectral data matched those reported for **22b**.[21]

Stereoselective Reduction of 18b with CSA

Solid (+)-camphorsulfonic acid (CSA, **23**, 35 mg, 0.15 mmol) was added to a stirred solution of **21b** (25 mg, 0.13 mmol) in anhydrous DCM (5 mL) which was then quickly capped with a septum and an N_2 inlet. After stirring 2 h, neat MsOH (15 μL, 0.23 mmol) was added by syringe, monitoring the reaction by MS. After 1 h, the major peak corresponded to **22b** with a smaller peak for **24**, both indicating alkene reduction. The solvent was then removed by a stream of N_2, and the residue was dissolved in MeOH (1.0 mL) which was then acidified by addition of 0.10 mL 6M aq. HCl before heating to reflux 16 h. The mixture was cooled to rt, made alkaline with 5% aq. NaOH and extracted with Et_2O (2 x 5 mL), the organic layers dried over $MgSO_4$ and reduced by rotatory evaporation. The product was purified by PLC on silica gel (20 x 20 cm x 250 μm, 65:33:2 hexanes/acetone/Et_3N), isolating 12 mg (3-phenylbutyl)-dimethylamine (**22b**, 53% y, 68% ee). Conditions for enantiomeric excess assay by HPLC (Chiralcel OD column, 0.1% *i*PrOH/hexane, 1 mL/min) were optimized using achiral **22b** from the previous experiment, with peaks at 13 and 23 minutes (peak at 40 minutes for (3-phenyl-3-butenyl)-dimethylamine impurity).

Reaction of 1 with (–)-Camphorsulfonic Acid

Solid (–)-camphorsulfonic acid (*ent*-CSA, *ent*-**23**, 152 mg, 0.65 mmol) was added to a stirred solution of $Me_3N{\cdot}BH_3$ (**1**, 43 mg, 0.59 mmol) in anhydrous DCM (2.2 mL) which was then quickly capped with a septum and an N_2 inlet. After stirring 4 h the solution was washed with H_2O (5 mL), the layers separated and the aqueous layer extracted with 5 mL DCM. The combined organic layers were dried over Na_2SO_4 and reduced by rotatory evaporation. The residue was taken up in minimal DCM (ca. 1 mL) and hexanes was added until the solution started to turn cloudy (ca. 15 mL). The flask

was left open to allow solvent evaporation, collecting the long needles that formed after 1 d, rinsing with hexanes and collecting 41 mg trimethylamine ((1*S*,2*R*,4*R*)-2-hydroxy-7,7-dimethyl-bicyclo[2.2.1]hept-1-yl)-methylsulfonyloxyborane (**25**, 27% y): Molecular ion calculated for $C_{13}H_{25}BNO_4S$: 302.1597; [M-H_2-H^-], EIMS found *m*/*z* = 302.1595; IR (neat, cm^{-1}) 3512, O–H, 2427, B–H; 2342, B–H; 1468, B–N; 1316, B–O; 1138, C–N; ^{1}H NMR: δ 4.15-4.08 (1H, m), 3.44 (1H, d, J = 14.0 Hz), 3.37 (1H, d, J = 3.3 Hz), 2.93 (1H, d, J = 14.0 Hz), 2.90 (1H, d, J = 4.0 Hz), 2.8-2.0 (2H, br m), 2.64 (9H, s), 1.88-1.47 (6H, m), 1.08 (3H, s), 0.83 (3H, s); ^{13}C NMR: δ 76.4, 50.0, 49.9, 49.7, 48.5, 44.5, 38.8, 30.5, 27.4, 20.6, 19.9; ^{11}B NMR: δ 3.4 to -0.2 (br m).

Preparation and Ionic Hydrogenation of 26

Methanesulfonyl chloride (2.0 mL, 26 mmol) was added slowly to a solution of 3-methyl-2-cyclohexen-1-ol (2.6 mL, 22 mmol) and distilled Et_3N (4.1 mL, 29 mmol) in anhydrous DCM (100 mL) which had been cooled to -78 °C under an N_2 atmosphere. After the addition was complete, the solution was allowed to warm slowly to -15 °C, and dimethylamine (ca. 5.6 M in EtOH, 40 mL, 220 mmol) was added directly to the crude mesylate. The solution was allowed to warm to rt and stirred 16 h. The reaction mixture was neutralized by the addition of saturated aq. $NaHCO_3$ (100 mL) and the layers separated, reducing the organic layer by rotary evaporation, and the residue was taken up in pentane (100 mL) and washed with water (100 mL) to remove ethanol, removing pentane under reduced pressure (520 mg crude product).

Half of this crude product was filtered through a plug of silica gel, eluting with DCM to remove nonpolar impurities followed by 99:1 DCM/Et_3N to obtain the product amine. Assay by ^{1}H NMR showed the desired amine in a 3:1 ratio with a regioisomeric

allylic amine, 1-methyl-1-dimethylamino-2-cyclohexene, along with remaining EtOH and Et_3N impurities, which were removed by dissolving in pentane and washing with water as before then coevaporating with $CHCl_3$ under reduced pressure. This residue (196 mg, ca. 1.4 mmol) was dissolved in anhydrous DCM (5 mL) and treated with BH_3·THF (0.9 mL, 0.9 mmol), added by syringe under an N_2 atmosphere. After stirring 1 h the solvent was removed under reduced pressure and the residue was purified by FC on silica gel (15 cm x 20 mm diameter, 4:1 hexanes/Et_2O), isolating 118 mg of a mixture of ca. 5:1 **26** and isomeric amine borane **30** (7% combined yield from 3-methyl-2-cyclohexen-1-ol). (3-Methyl-cyclohex-2-enyl)-dimethylamine borane (**26**) and (1-methyl-cyclohex-2-enyl)-dimethylamine borane (**30**): TLC on K6F silica gel 60Å, 4:1 hexanes/Et_2O, Rf = 0.40. Molecular ion calculated for $C_9H_{20}BNNa$: 176.1586; [M+Na], ESMS found *m*/*z* = 176.1851; IR (neat, cm^{-1}) 2371, B–H; 2321, B–H; 2277, B–H; 1466, B–N; 1167, C–N. Major peaks in NMR spectra assigned to **26**: ^{1}H NMR: δ 5.80 (1H, s), 3.52-3.46 (1H, m), 2.52 (3H, s), 2.51 (3H, s), 2.18 (1H, q, J = 5.9 Hz), 2.08-1.80 (m, overlaps with **30**), 1.74 (3H, s), 1.67-1.10 (m, overlaps with **30**); ^{13}C NMR: δ 140.9, 118.2, 67.1, 48.1, 47.2, 46.8, 29.5, 24.1, 23.6, 21.7; ^{11}B NMR: δ -10.1 (q, J = 96 Hz). Minor peaks in NMR spectra assigned to **30**: ^{1}H NMR: δ 6.00-5.93 (1H, m), 5.90-5.85 (1H, m), 2.55 (3H, s), 2.54 (3H, s), 2.08-1.80 (m, overlaps with **26**), 1.67-1.10 (m, overlaps with **26**), 1.46 (3H, s); ^{13}C NMR: δ 130.6, 128.3, 65.1, 29.8, 24.3, 22.7, 20.9; ^{11}B NMR: δ -12.5 (q, J = 97 Hz).

To a solution of **26** (15 mg, impure with **30**, 95 μmol combined) in anhydrous CD_2Cl_2 (1.0 mL) was added MsOH (38 μL, 590 μmol) dropwise by syringe, waiting for the gas evolution to subside between each drop. A portion of the solution was transferred

to an NMR tube and monitored by ^{1}H NMR spectroscopy, showing no change after 105 min. The NMR sample was returned to the flask and the reaction quenched by addition of 5% aq. NaOH (2 mL), separating the layers and extracting the aqueous layer with DCM (2 x 3 mL). The combined organic layers were reduced by rotary evaporation, the residue purified by reverse-phase PLC on K18F silica gel, giving 6.9 mg of *trans*-(3-methylcyclohexyl)-dimethylamine bis(methylsulfonyloxy)borane (**29**, 25% y based on calculated amount of **26**): TLC on K18F silica gel 60Å, 2:1 MeOH/H_2O buffered with 0.5% Et_3N and 0.5% CF_3CO_2H, Rf = 0.55. ^{1}H NMR: δ 3.07 (3H, s), 3.06 (3H, s), 2.55 (3H, s), 2.53 (3H, s), 1.05 (3H, d, J = 7.3 Hz).

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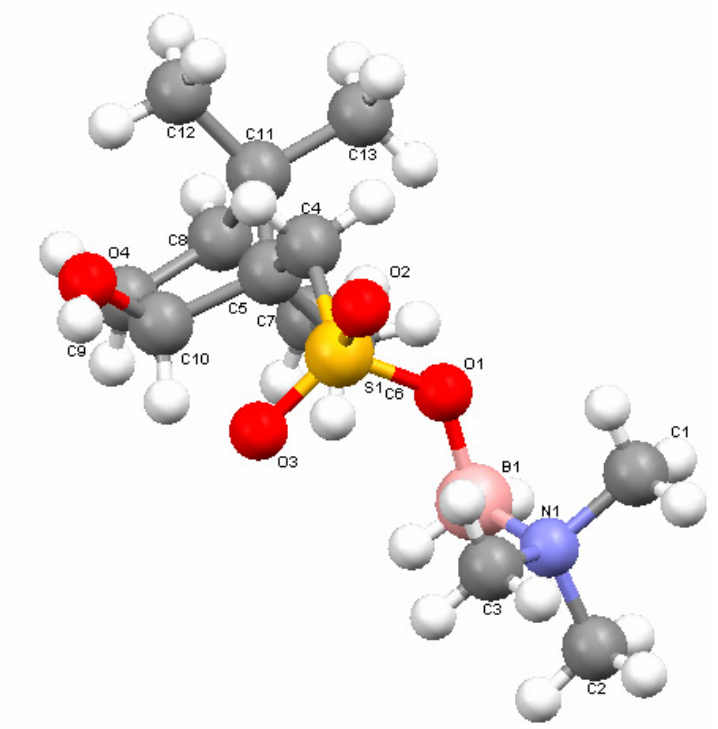
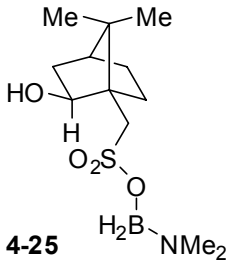
Appendices

Appendix A

X-ray Crystal Structure of **4-25**





4-25

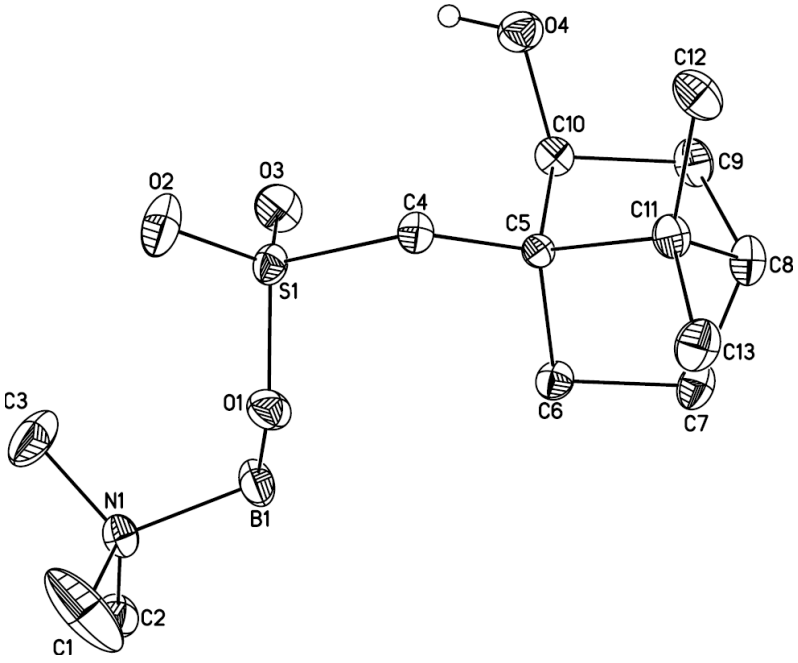


Table 1. Crystal data and structure refinement for **4-25**.

Identification code	**4-25**
Empirical formula	C13 H28 B N O4 S
Formula weight	305.23
Temperature	85(2) K
Wavelength	0.71073 A
Crystal system, space group	Orthorhombic, P2(1)2(1)2(1)
Unit cell dimensions	a = 6.8265(5) A alpha = 90 deg. b = 9.4699(8) A beta = 90 deg. c = 24.772(2) A gamma = 90 deg.
Volume	1601.4(2) A^3
Z, Calculated density	4, 1.266 Mg/m^3
Absorption coefficient	0.214 mm^-1
F(000)	664
Crystal size	0.50 x 0.34 x 0.22 mm
Theta range for data collection	1.64 to 28.34 deg.
Limiting indices	-9<=h<=9, -12<=k<=12, -33<=l<=33
Reflections collected / unique	57330 / 3997 [R(int) = 0.0376]
Completeness to theta = 28.34	100.0 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9545 and 0.9007
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3997 / 0 / 190
Goodness-of-fit on F^2	1.171
Final R indices [I>2sigma(I)]	R1 = 0.0330, wR2 = 0.0892

R indices (all data)	R1 = 0.0332, wR2 = 0.0893
Absolute structure parameter	0.04(6)
Largest diff. peak and hole	0.356 and -0.189 e.A^-3

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for **4-25**. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)
B(1)	3664(3)	6617(2)	8546(1)	26(1)
N(1)	4294(2)	5263(1)	8193(1)	18(1)
S(1)	502(1)	7984(1)	8102(1)	17(1)
O(1)	1510(2)	6860(1)	8448(1)	22(1)
O(2)	-633(2)	7258(2)	7697(1)	30(1)
O(3)	1845(2)	9044(1)	7918(1)	26(1)
O(4)	-708(2)	11747(1)	8363(1)	23(1)
C(1)	2985(3)	4063(2)	8310(1)	59(1)
C(2)	6321(3)	4857(2)	8345(1)	26(1)
C(3)	4276(3)	5583(3)	7609(1)	45(1)
C(4)	-1217(2)	8733(2)	8555(1)	15(1)
C(5)	-429(2)	9704(1)	8990(1)	12(1)
C(6)	1174(2)	9081(2)	9361(1)	17(1)
C(7)	1072(2)	10025(2)	9875(1)	22(1)
C(8)	-559(2)	11080(2)	9733(1)	20(1)
C(9)	260(2)	12077(2)	9299(1)	22(1)
C(10)	396(2)	11134(2)	8787(1)	16(1)
C(11)	-2028(2)	10165(2)	9410(1)	16(1)
C(12)	-3744(2)	11000(2)	9172(1)	23(1)
C(13)	-2899(2)	8950(2)	9737(1)	21(1)

Table 3. Bond lengths [A] and angles [deg] for **4-25**.

B(1)-O(1)	1.507(2)
B(1)-N(1)	1.610(2)
N(1)-C(1)	1.474(2)
N(1)-C(3)	1.478(2)
N(1)-C(2)	1.485(2)
S(1)-O(3)	1.4340(12)
S(1)-O(2)	1.4428(12)
S(1)-O(1)	1.5306(11)
S(1)-C(4)	1.7716(14)
O(4)-C(10)	1.4174(18)
C(4)-C(5)	1.5162(18)
C(5)-C(6)	1.5458(19)
C(5)-C(10)	1.5510(19)
C(5)-C(11)	1.5692(19)
C(6)-C(7)	1.556(2)
C(7)-C(8)	1.536(2)
C(8)-C(9)	1.536(2)
C(8)-C(11)	1.548(2)
C(9)-C(10)	1.554(2)
C(11)-C(13)	1.527(2)
C(11)-C(12)	1.532(2)
O(1)-B(1)-N(1)	107.18(13)
C(1)-N(1)-C(3)	110.3(2)
C(1)-N(1)-C(2)	108.39(15)
C(3)-N(1)-C(2)	108.03(14)
C(1)-N(1)-B(1)	110.15(15)
C(3)-N(1)-B(1)	111.43(14)
C(2)-N(1)-B(1)	108.48(12)
O(3)-S(1)-O(2)	117.10(8)
O(3)-S(1)-O(1)	112.21(7)
O(2)-S(1)-O(1)	107.45(7)
O(3)-S(1)-C(4)	110.20(7)
O(2)-S(1)-C(4)	105.97(7)
O(1)-S(1)-C(4)	102.78(6)
B(1)-O(1)-S(1)	129.38(12)
C(5)-C(4)-S(1)	117.27(10)
C(4)-C(5)-C(6)	116.26(11)
C(4)-C(5)-C(10)	115.32(11)
C(6)-C(5)-C(10)	105.60(11)
C(4)-C(5)-C(11)	113.19(12)
C(6)-C(5)-C(11)	101.81(11)
C(10)-C(5)-C(11)	102.98(10)

C(5)-C(6)-C(7)	103.59(12)
C(8)-C(7)-C(6)	102.69(12)
C(7)-C(8)-C(9)	107.17(13)
C(7)-C(8)-C(11)	102.92(12)
C(9)-C(8)-C(11)	102.57(12)
C(8)-C(9)-C(10)	103.89(12)
O(4)-C(10)-C(5)	113.89(12)
O(4)-C(10)-C(9)	109.76(12)
C(5)-C(10)-C(9)	102.41(11)
C(13)-C(11)-C(12)	107.18(12)
C(13)-C(11)-C(8)	113.56(12)
C(12)-C(11)-C(8)	113.95(13)
C(13)-C(11)-C(5)	114.34(12)
C(12)-C(11)-C(5)	114.82(12)
C(8)-C(11)-C(5)	92.76(11)

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters (A^2 x 10^3) for **4-25**. The anisotropic displacement factor exponent takes the form: -2 pi^2 [h^2 a*^2 U11 + ... + 2 h k a* b* U12]

	U11	U22	U33	U23	U13	U12
B(1)	26(1)	25(1)	27(1)	-11(1)	-8(1)	9(1)
N(1)	16(1)	17(1)	22(1)	-3(1)	3(1)	-3(1)
S(1)	16(1)	20(1)	14(1)	-2(1)	2(1)	1(1)
O(1)	21(1)	20(1)	23(1)	2(1)	4(1)	5(1)
O(2)	27(1)	43(1)	20(1)	-12(1)	-1(1)	-1(1)
O(3)	25(1)	26(1)	28(1)	4(1)	11(1)	-1(1)
O(4)	25(1)	24(1)	21(1)	5(1)	2(1)	1(1)
C(1)	35(1)	19(1)	122(2)	-10(1)	35(1)	-9(1)
C(2)	25(1)	26(1)	28(1)	-4(1)	-3(1)	9(1)
C(3)	41(1)	76(2)	18(1)	-6(1)	-2(1)	33(1)
C(4)	12(1)	18(1)	15(1)	-2(1)	0(1)	-1(1)
C(5)	11(1)	13(1)	13(1)	0(1)	1(1)	0(1)
C(6)	13(1)	21(1)	16(1)	-1(1)	-2(1)	0(1)
C(7)	21(1)	28(1)	16(1)	-4(1)	-1(1)	-2(1)
C(8)	19(1)	23(1)	19(1)	-6(1)	3(1)	-3(1)
C(9)	22(1)	18(1)	26(1)	-5(1)	2(1)	-5(1)

C(10)	14(1)	16(1)	20(1)	1(1)	2(1)	-3(1)
C(11)	13(1)	19(1)	18(1)	-1(1)	3(1)	0(1)
C(12)	14(1)	23(1)	32(1)	-1(1)	4(1)	3(1)
C(13)	19(1)	25(1)	20(1)	1(1)	6(1)	-4(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (A^2 x 10^3) for **4-25**.

	x	y	z	U(eq)
H(1A)	3910	6440	8934	31
H(1B)	4428	7456	8434	31
H(4A)	-190(40)	11600(30)	8054(11)	41(7)
H(1D)	1648	4297	8197	88
H(1E)	2998	3869	8699	88
H(1F)	3437	3227	8114	88
H(2B)	6381	4679	8735	40
H(2C)	7223	5625	8252	40
H(2D)	6698	3999	8150	40
H(3B)	4731	4756	7407	67
H(3C)	5145	6385	7537	67
H(3D)	2940	5821	7497	67
H(4B)	-2189	9269	8340	18
H(4C)	-1927	7950	8734	18
H(6A)	2479	9142	9189	20
H(6B)	892	8082	9450	20
H(7A)	728	9462	10198	26
H(7B)	2332	10514	9939	26
H(8A)	-1142	11572	10052	25
H(9A)	1567	12439	9404	26
H(9B)	-631	12886	9239	26
H(10A)	1795	11022	8675	20
H(12A)	-4491	10392	8927	34
H(12B)	-3240	11816	8972	34
H(12C)	-4599	11327	9464	34
H(13A)	-3650	9332	10041	32
H(13B)	-1840	8350	9874	32
H(13C)	-3765	8390	9505	32

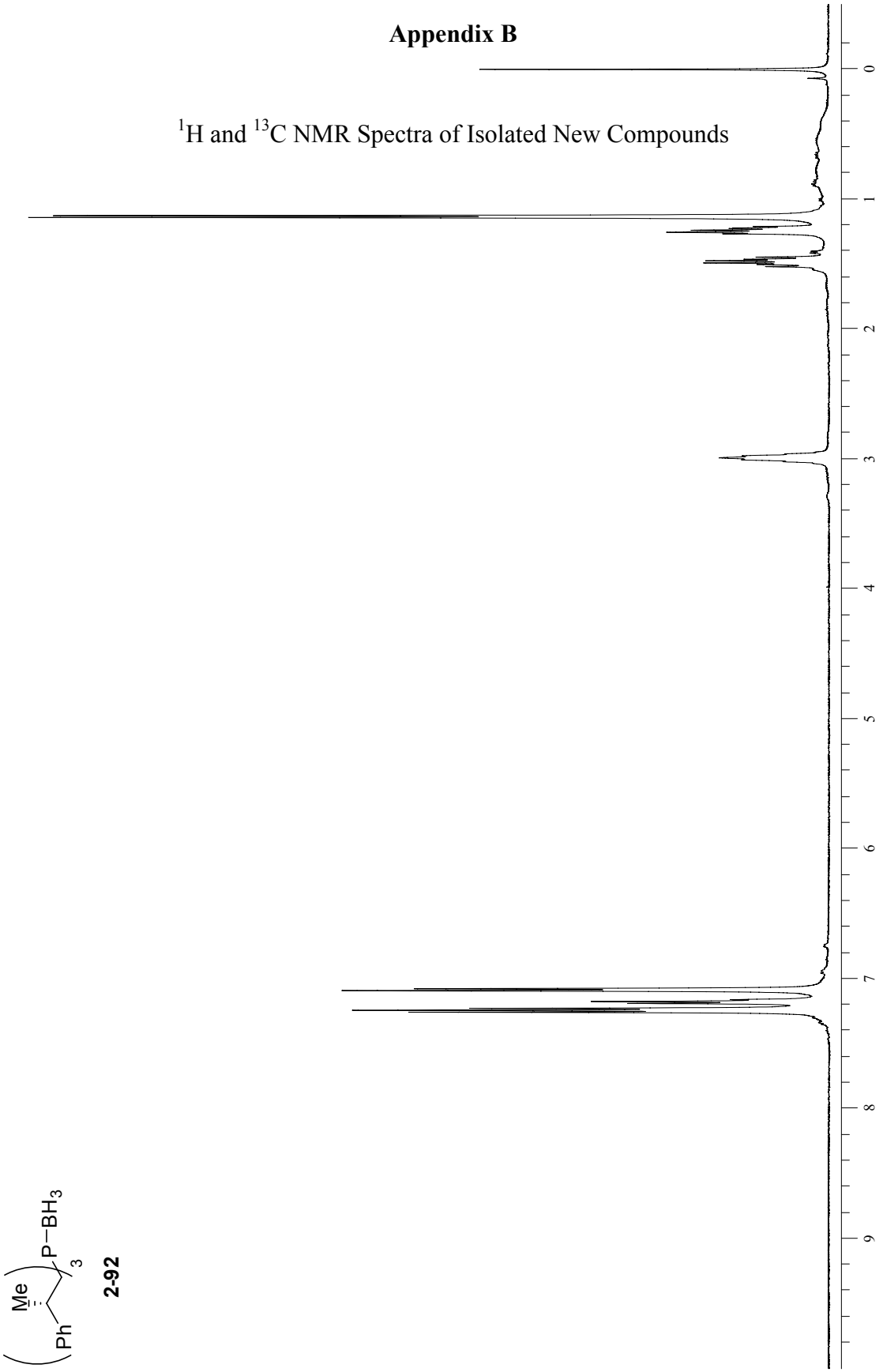
Table 6. Hydrogen bonds for **4-25** [A and deg.].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
O(4)-H(4A)...O(2)#1	0.85(3)	2.04(3)	2.8228(16)	152(2)

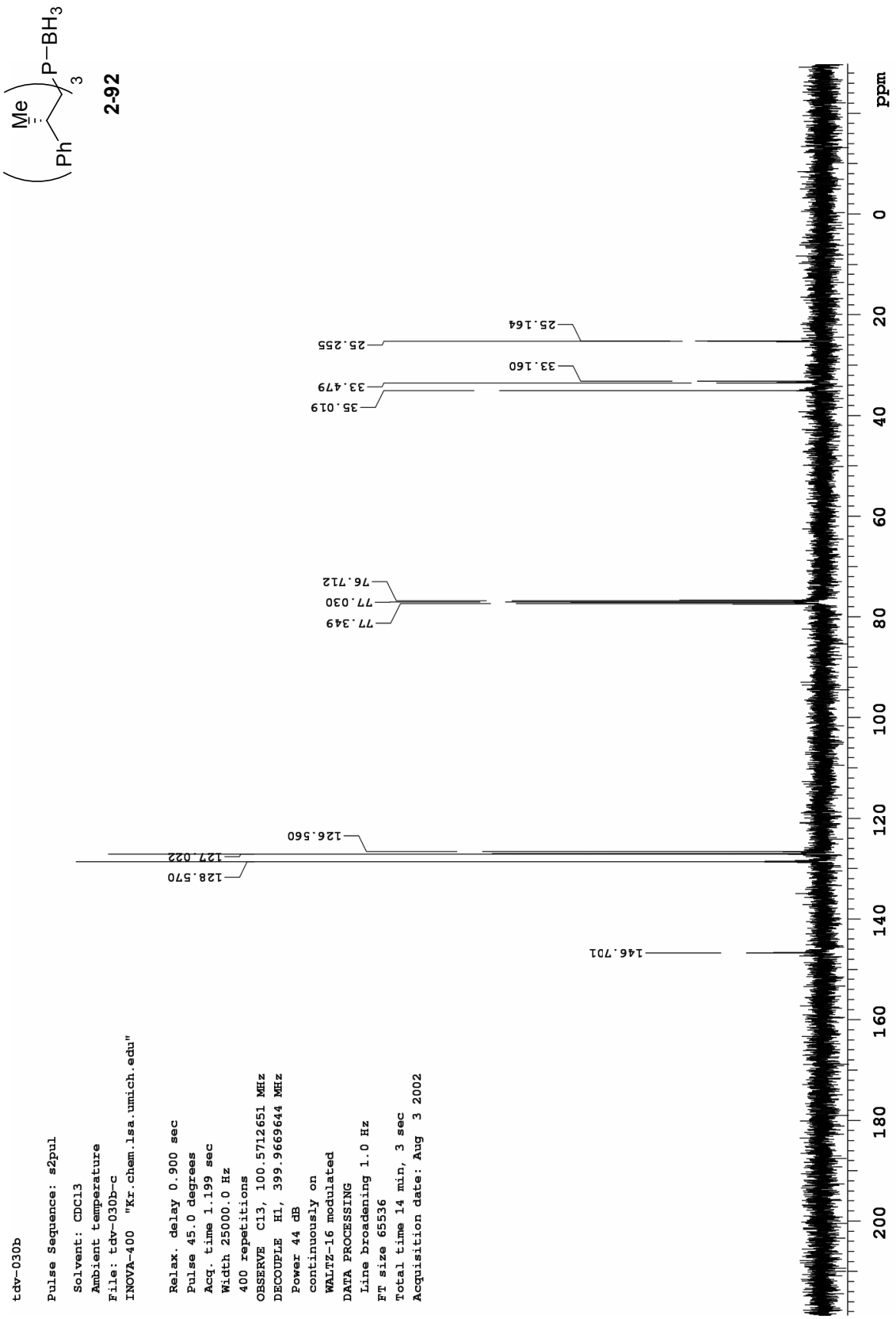
Symmetry transformations used to generate equivalent atoms: #1 -x,y+1/2,-z+3/2

Appendix B

^{1}H and ^{13}C NMR Spectra of Isolated New Compounds



2-92


Me
Ph
P–BH3
3
2-92
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Solvent: CDCl3
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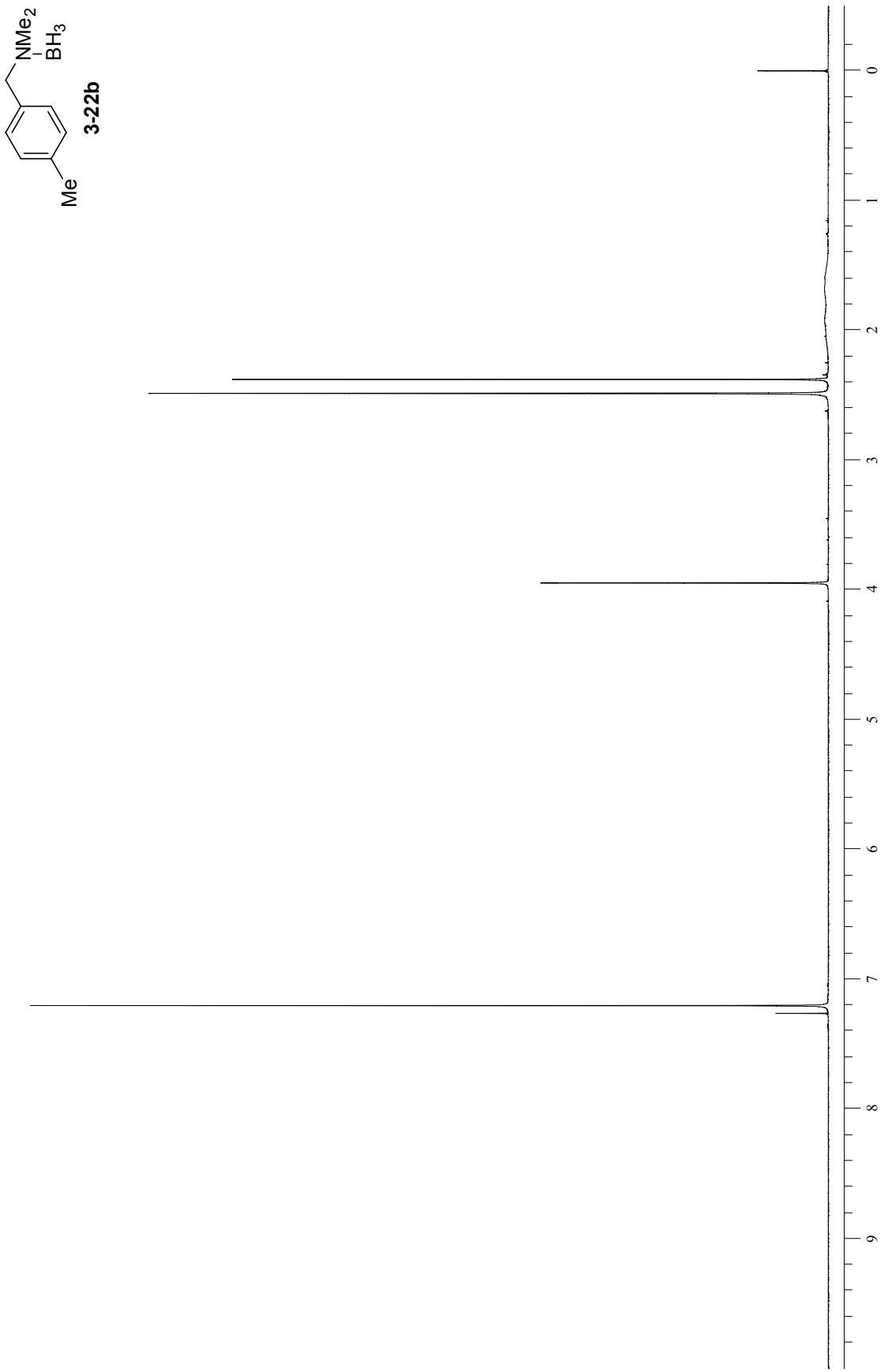
Pulse 45.0 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
400 repetitions
OBSERVE C13, 100.5712651 MHz
DECOUPLE H1, 399.9669644 MHz
Power 44 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 14 min, 3 sec
Acquisition date: Aug 3 2002
146.701
128.570
127.022
126.560
77.349
77.030
76.712
35.019
33.479
33.160
25.255
25.164
ppm
200
180
160
140
120
100
80
60
40
20
0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BH3
Me
3-22b
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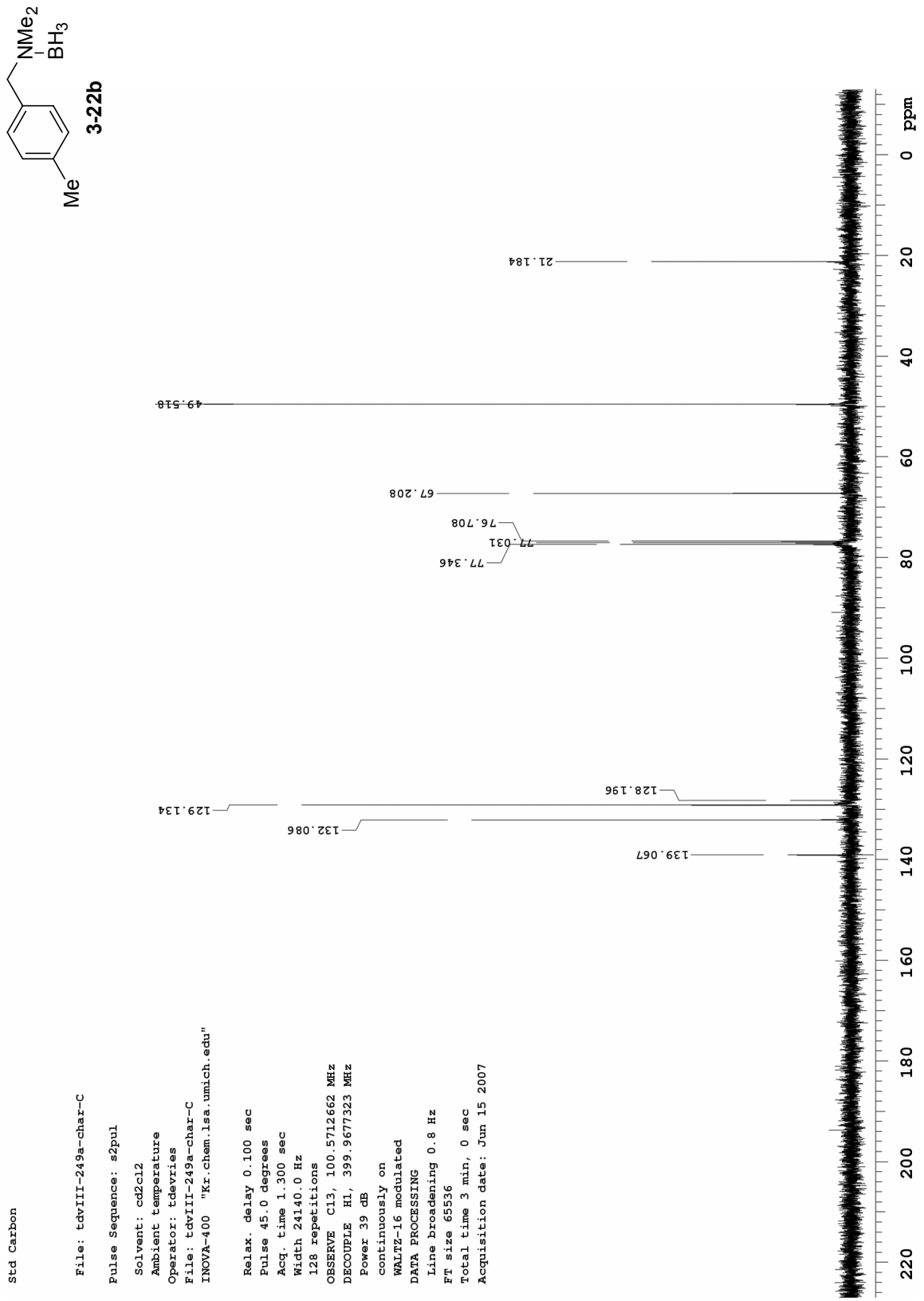
1
2
3
4
5
6
7
8
9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BH3
Me
3-22b
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Solvent: cd2cl2
Ambient temperature
Operator: tdevries
File: tdvIII-249a-char-C
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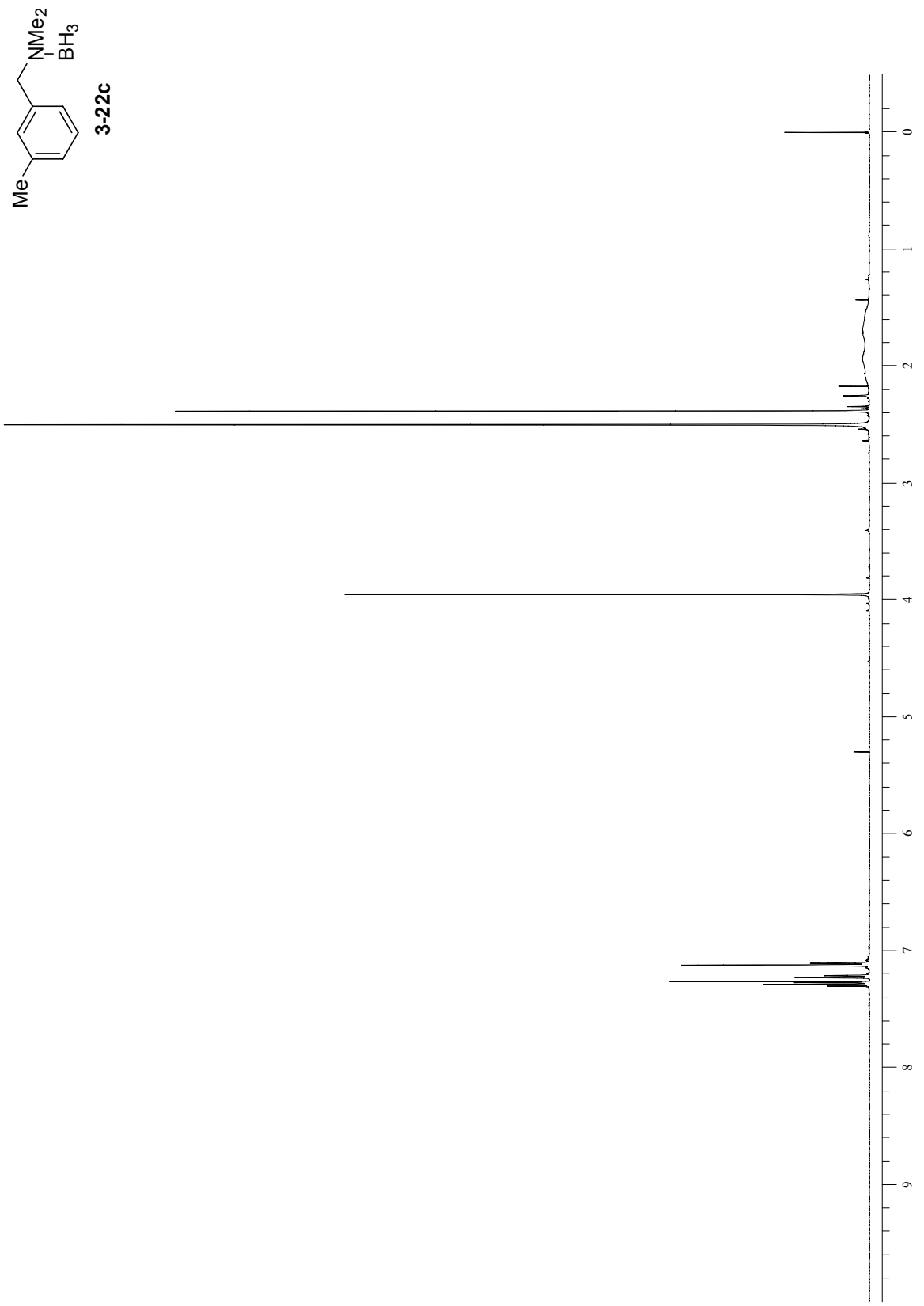
Relax. delay 0.100 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 24140.0 Hz
128 repetitions
OBSERVE C13, 100.5712662 MHz
DECOUPLE H1, 399.9677323 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.8 Hz
FT size 65536
Total time 3 min, 0 sec
Acquisition date: Jun 15 2007
21.184
49.518
67.208
76.708
77.031
77.346
128.196
129.134
132.086
139.067
0 ppm
20
40
60
80
100
120
140
160
180
200
220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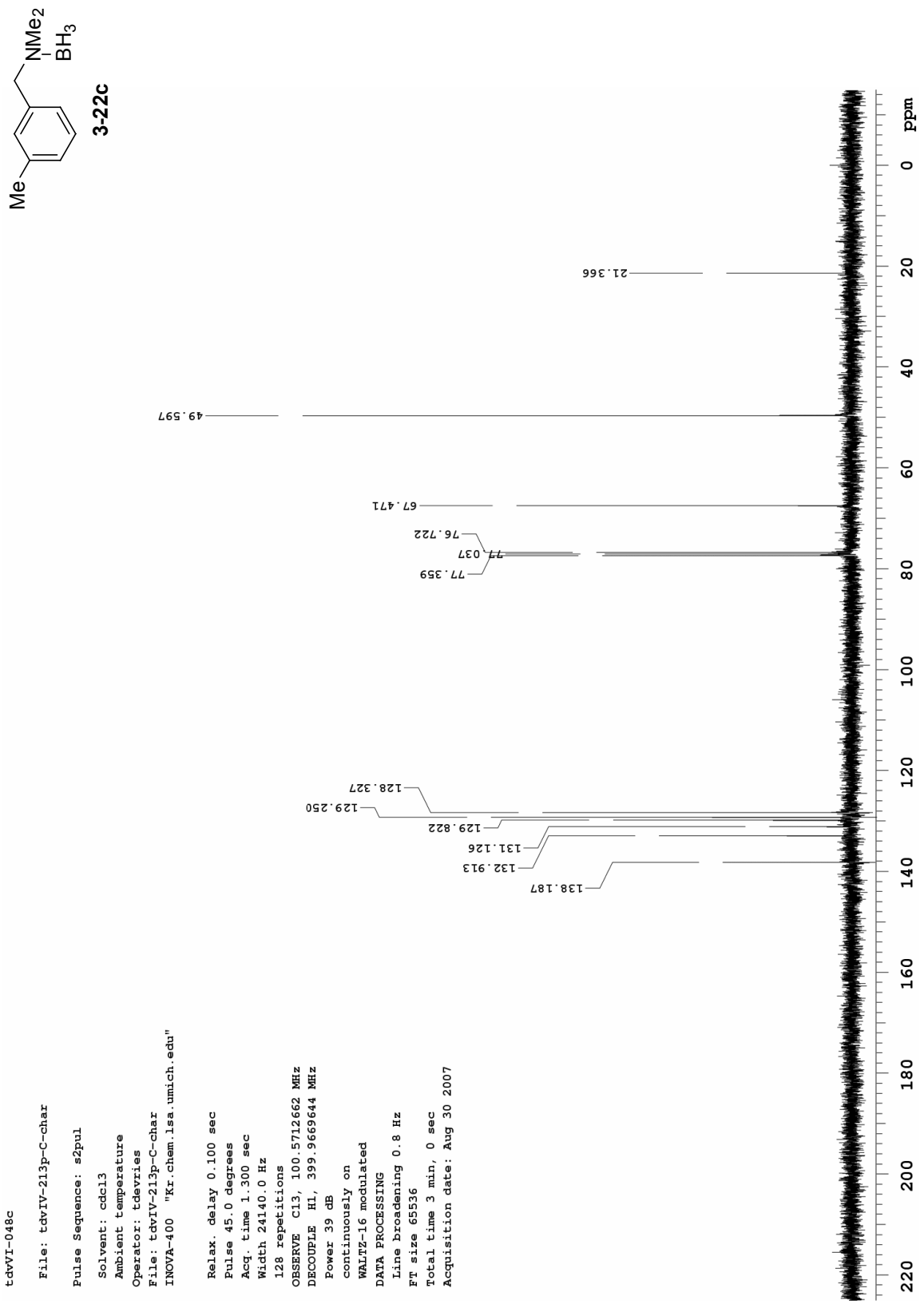
BH3
Me
3-22c
0
1
2
3
4
5
6
7
8
9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BH3
Me
3-22c
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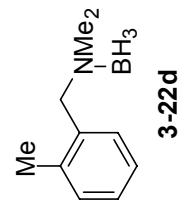
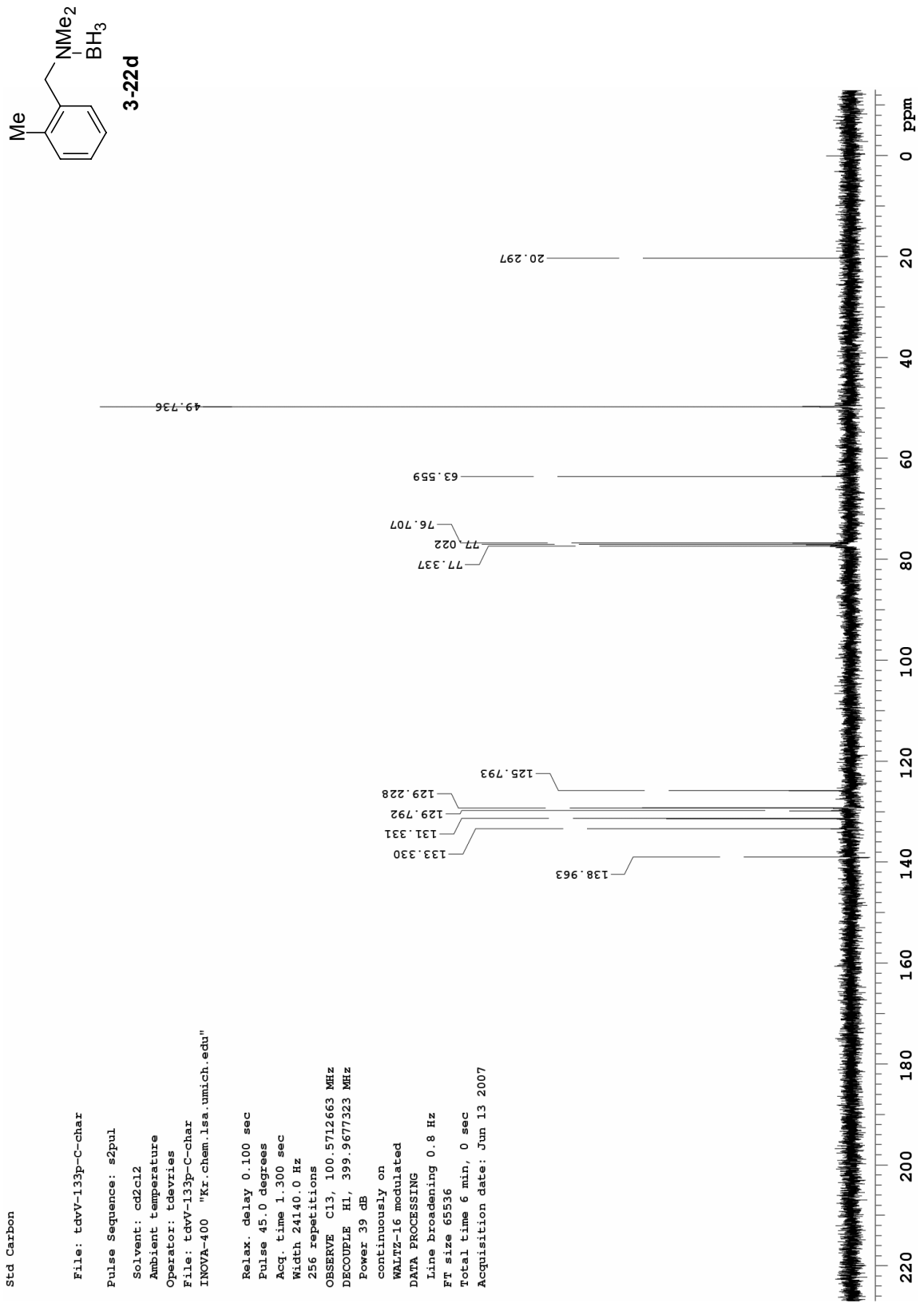
Pulse Sequence: s2pul
Solvent: cdcl3
Ambient temperature
Operator: tdevries
File: tdvIV-213p-C-char
INOVA-400 "Kr.chem.lsa.umich.edu"
Relax. delay 0.100 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 24140.0 Hz
128 repetitions
OBSERVE C13, 100.5712662 MHz
DECOUPLE H1, 399.9669644 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.8 Hz
FT size 65536
Total time 3 min, 0 sec
Acquisition date: Aug 30 2007
21.366
49.597
67.471
76.722
77.037
77.359
128.327
129.250
129.822
131.126
132.913
138.187
ppm



3-22d


Me
NMe2
BH3
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Ambient temperature
Operator: tdevries
File: tdvV-133p-C-char
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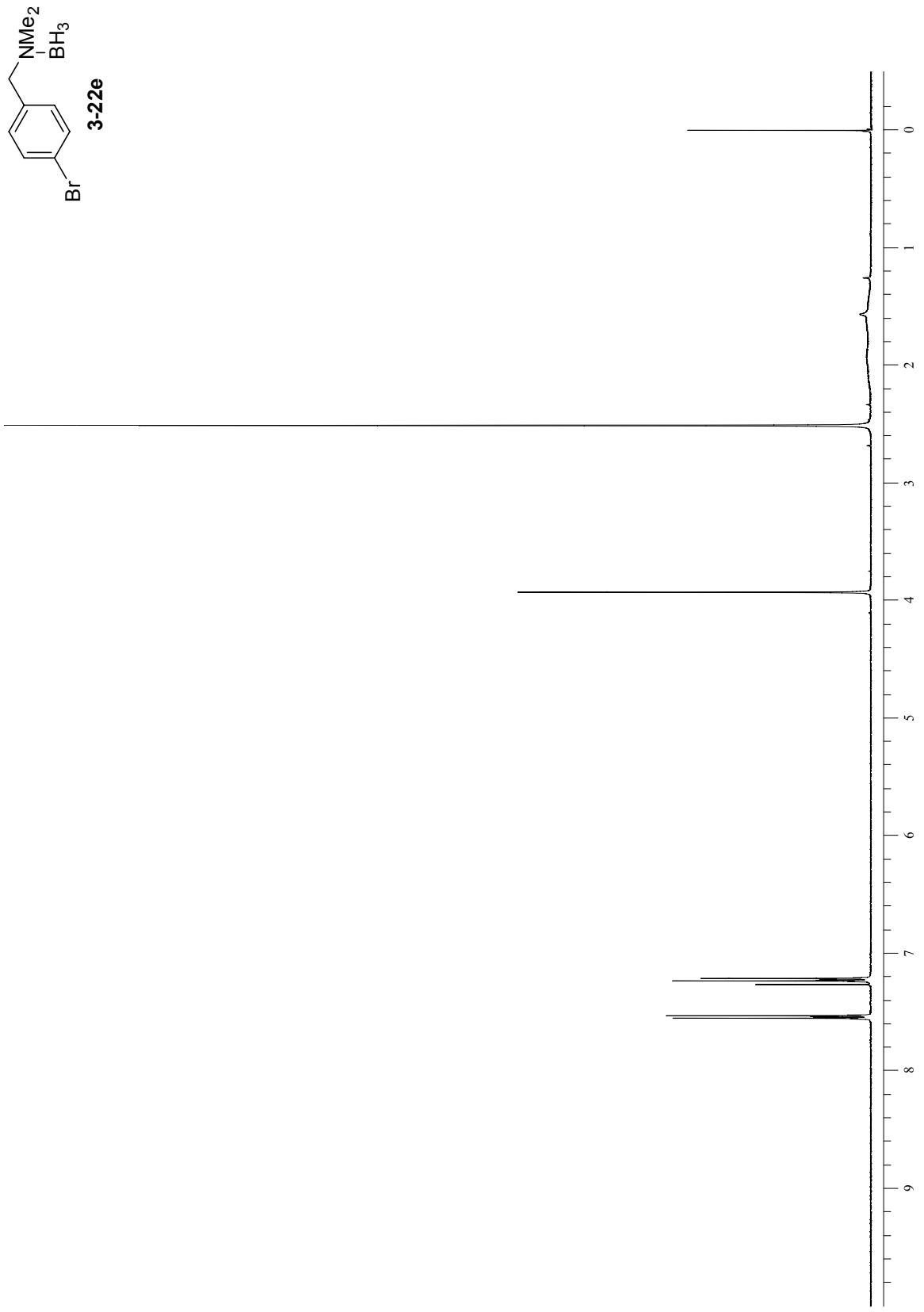
Relax. delay 0.100 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 24140.0 Hz
256 repetitions
OBSERVE C13, 100.5712663 MHz
DECOUPLE H1, 399.9677323 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.8 Hz
FT size 65536
Total time 6 min, 0 sec
Acquisition date: Jun 13 2007
20.297
49.736
63.559
76.707
77.022
77.337
125.793
129.228
129.792
131.331
133.330
138.963
220
200
180
160
140
120
100
80
60
40
20
0
ppm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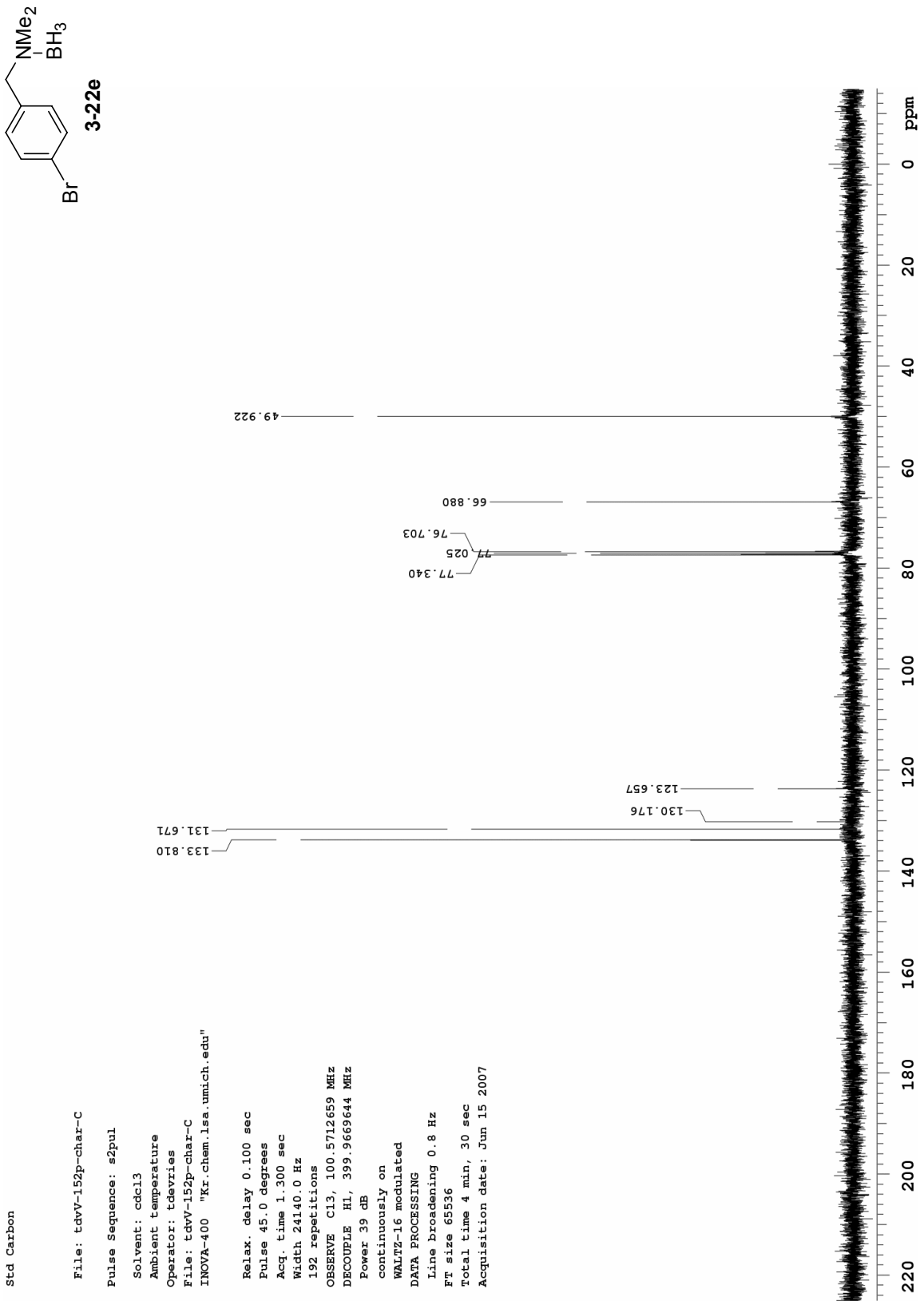
BH3
Br
3-22e
0
1
2
3
4
5
6
7
8
9



Std Carbon

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192 repetitions
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DECOUPLE H1, 399.9669644 MHz
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WALTZ-16 modulated
DATA PROCESSING
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FT size 65536
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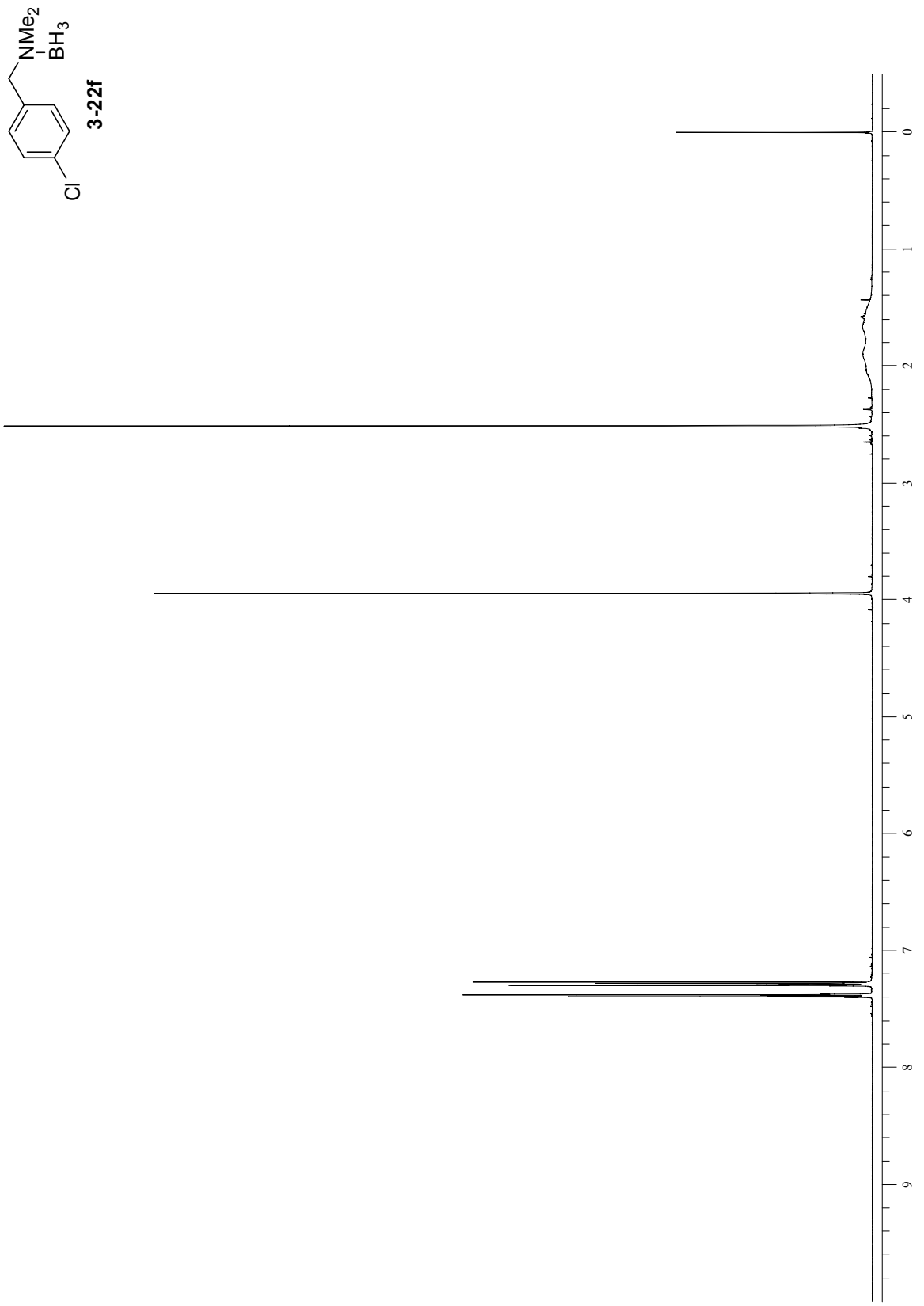
Acquisition date: Jun 15 2007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BH3
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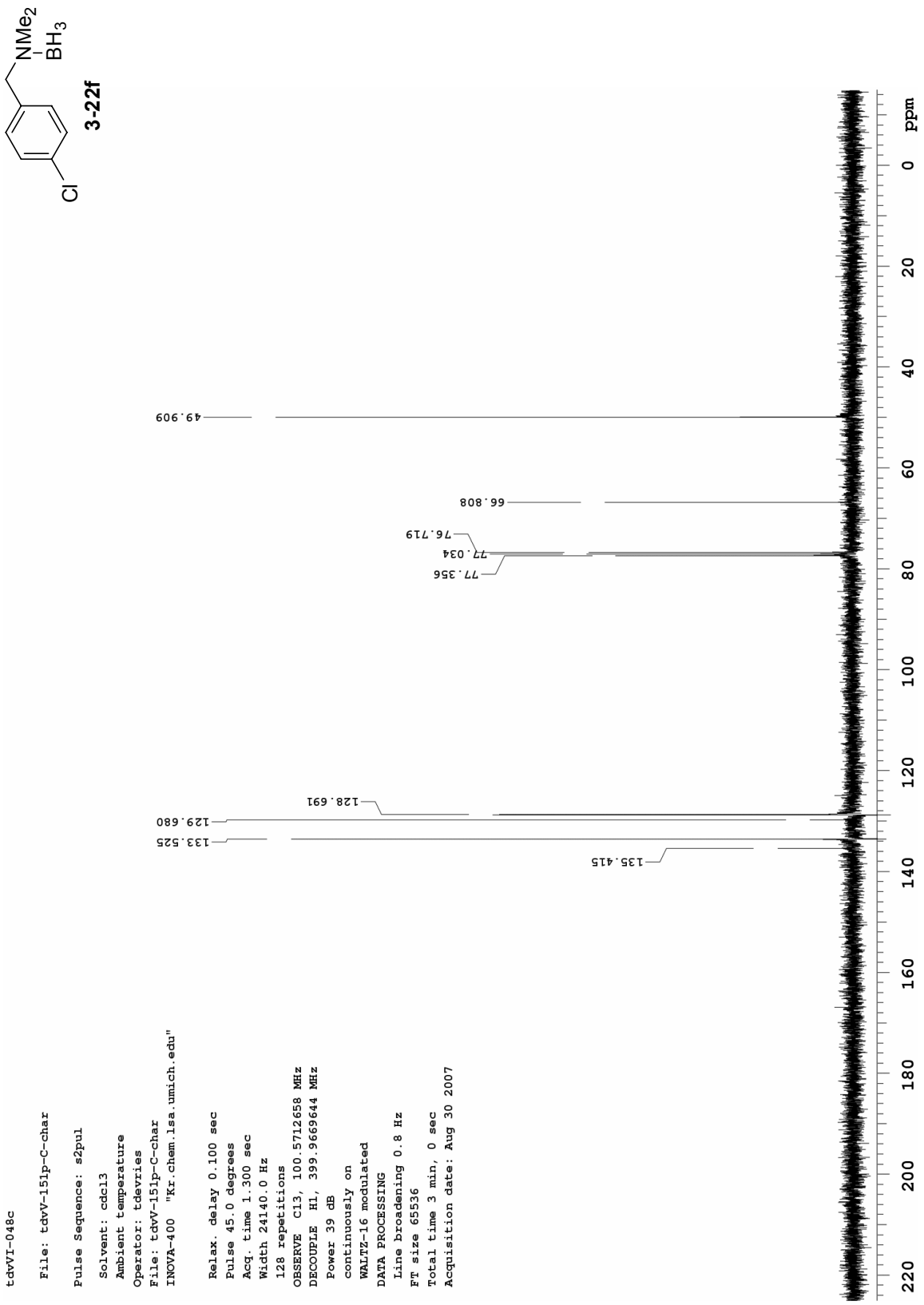
6
7
8
9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BH3
Cl
3-22f
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Solvent: cdcl3
Ambient temperature
Operator: tdevries
File: tdvV-151p-C-char
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Width 24140.0 Hz
128 repetitions
OBSERVE C13, 100.5712658 MHz
DECOUPLE H1, 399.9669644 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.8 Hz
FT size 65536
Total time 3 min, 0 sec
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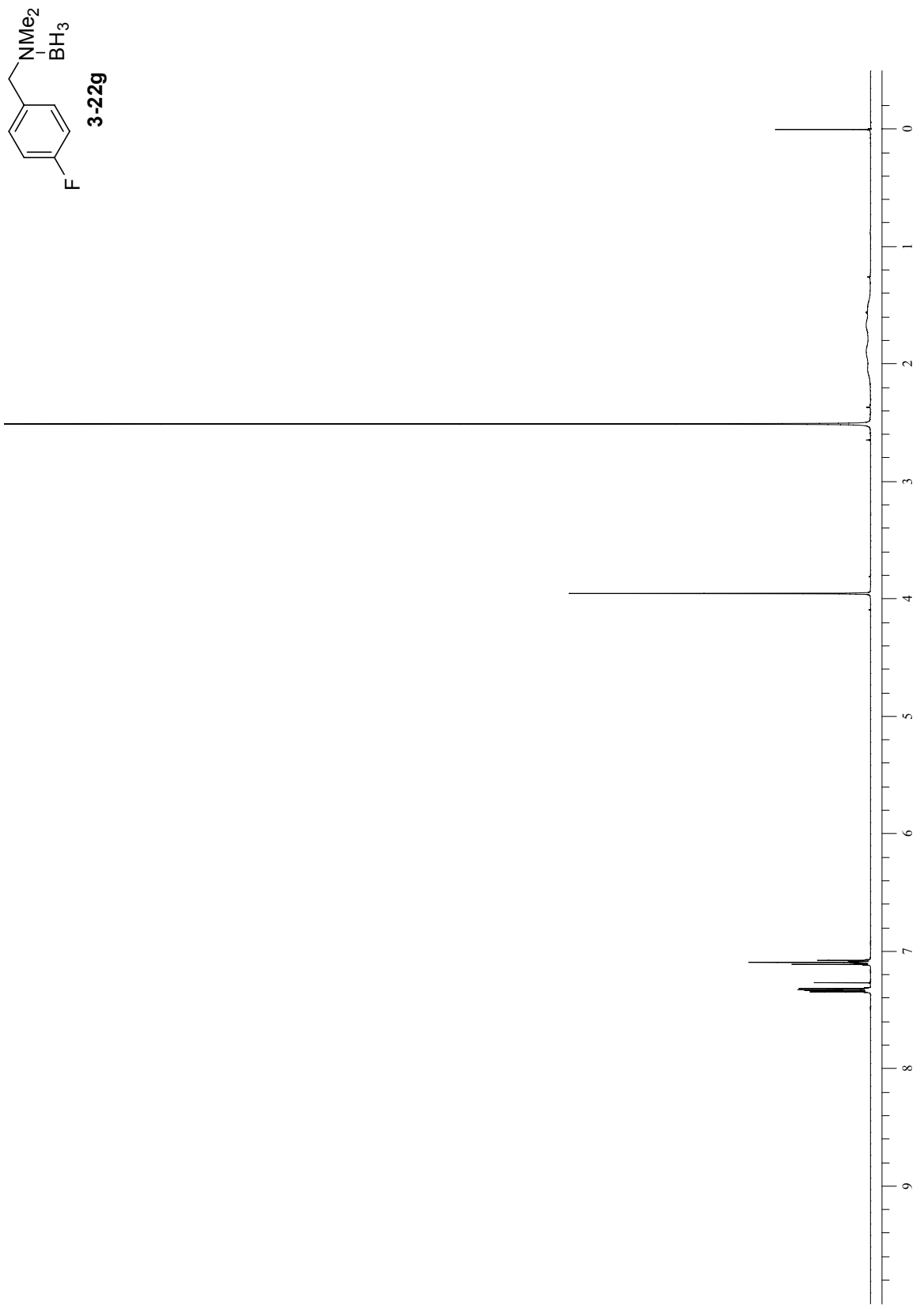
77.356
128.691
129.680
133.525
135.415
ppm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BH3
F
3-22g
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2
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6
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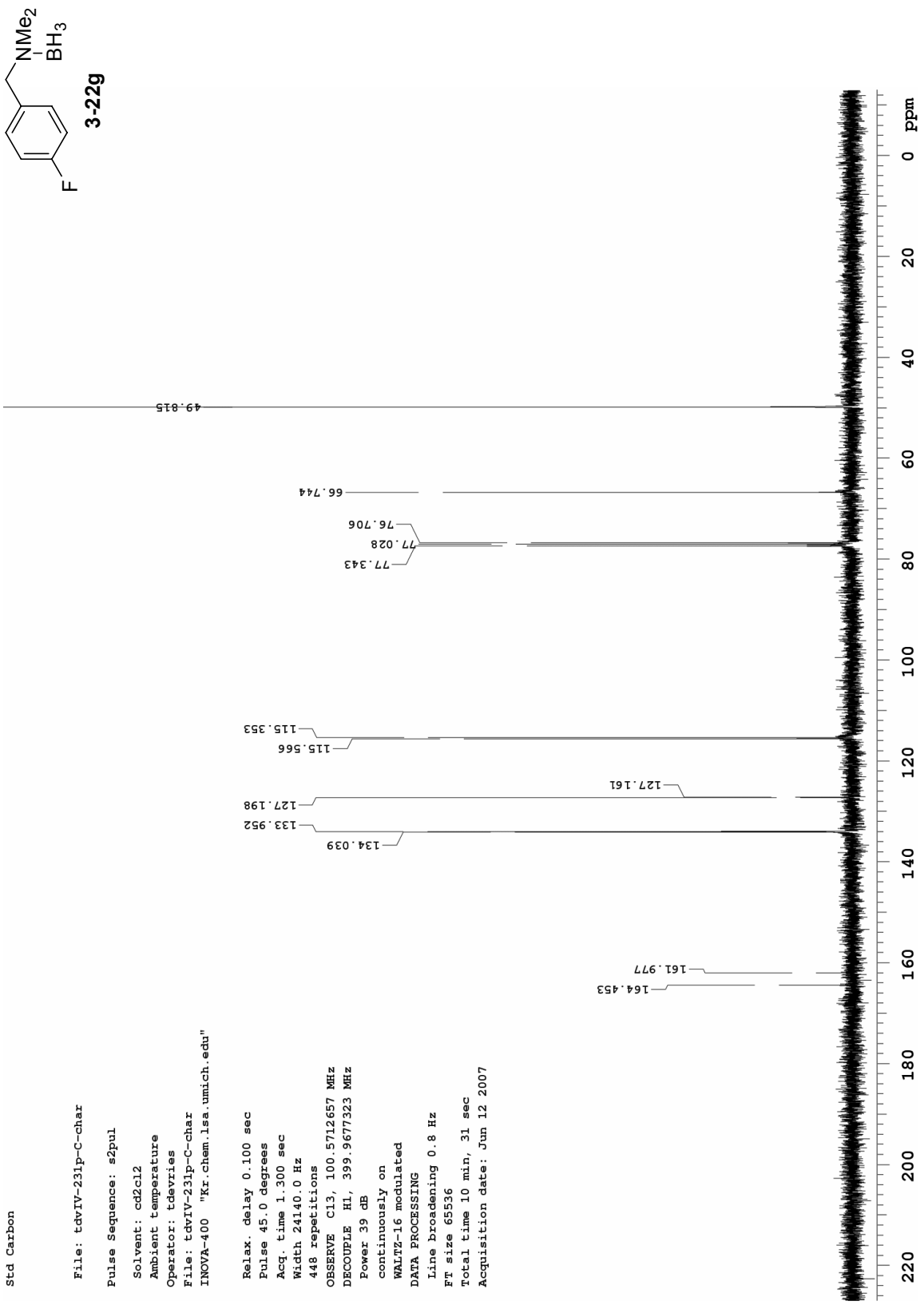
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77.343
115.353
115.566
127.161
127.198
133.952
134.039
161.977
164.453
0 ppm
20
40
60
80
100
120
140
160
180
200
220
Std Carbon
File: tdvIV-231p-C-char
Pulse Sequence: s2pul
Solvent: cd2cl2
Ambient temperature
Operator: tdevries
File: tdvIV-231p-C-char
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OBSERVE C13, 100.5712657 MHz
DECOUPLE H1, 399.9677323 MHz
Power 39 dB
continuously on
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Line broadening 0.8 Hz
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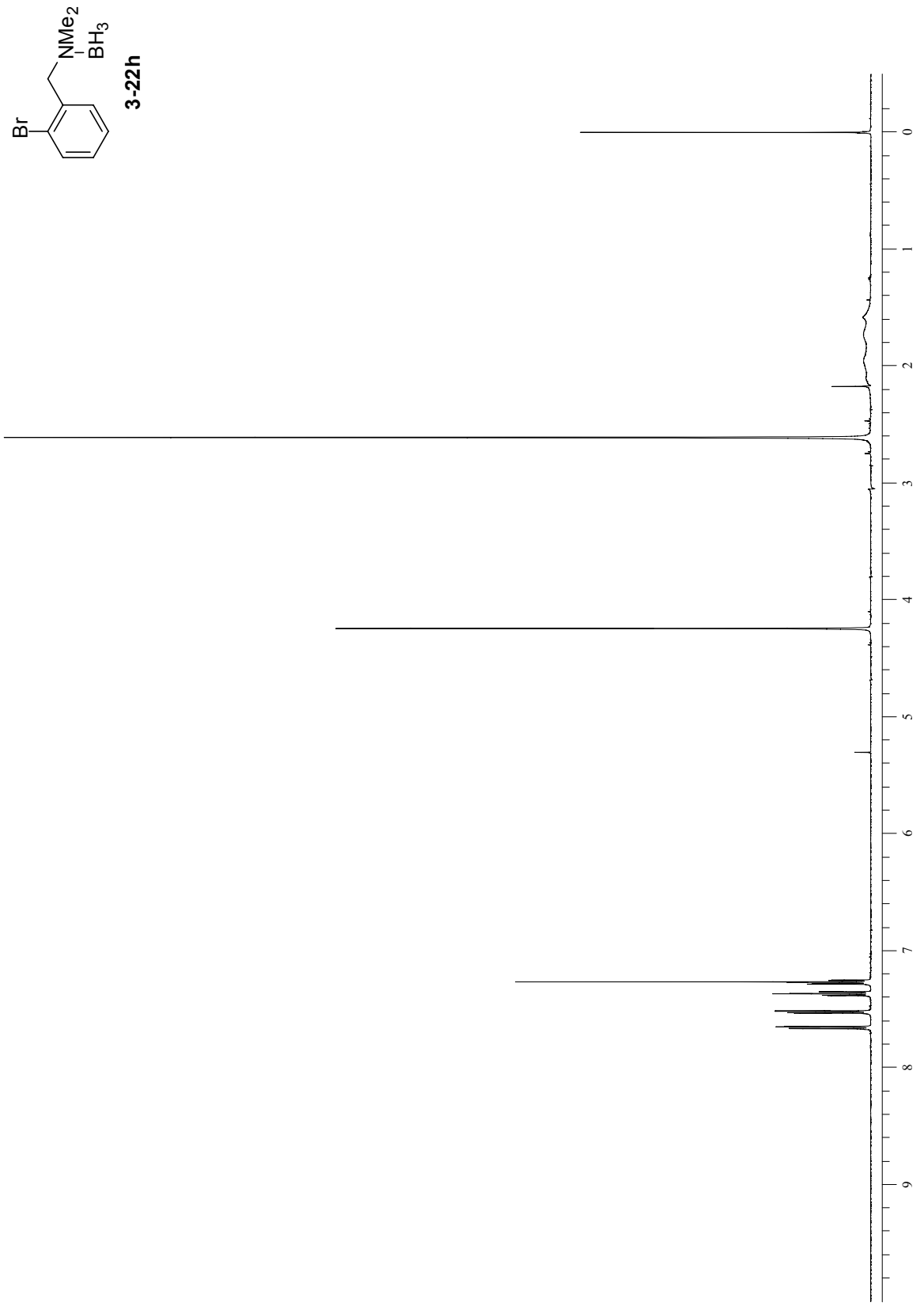
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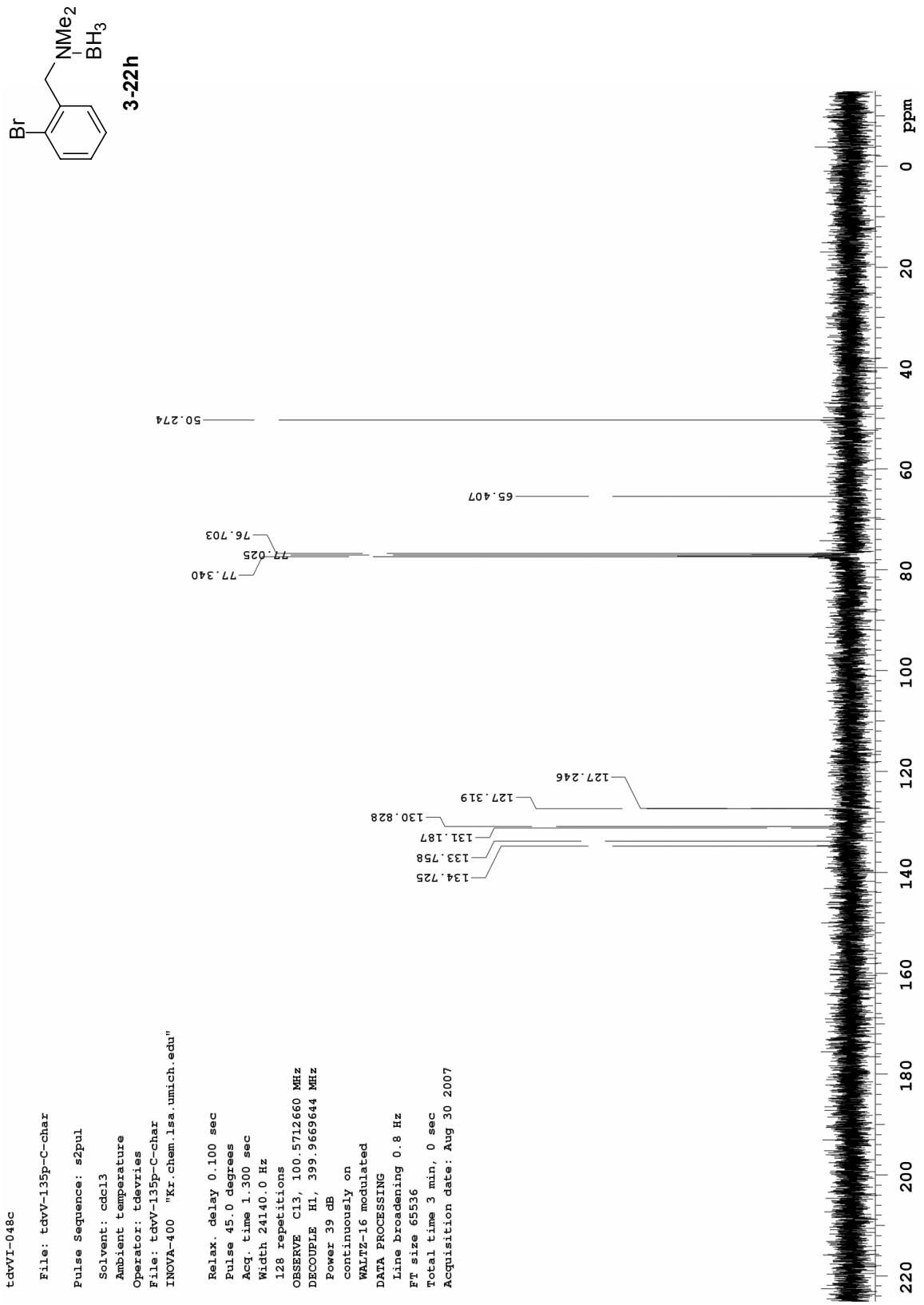
BH3
Br
3-22h
0
1
2
3
4
5
6
7
8
9



tdvVI-048c

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Solvent: cdcl3
Ambient temperature
Operator: tdevries
File: tdvV-135p-C-char
INOVA-400 "Kr.chem.lsa.umich.edu"

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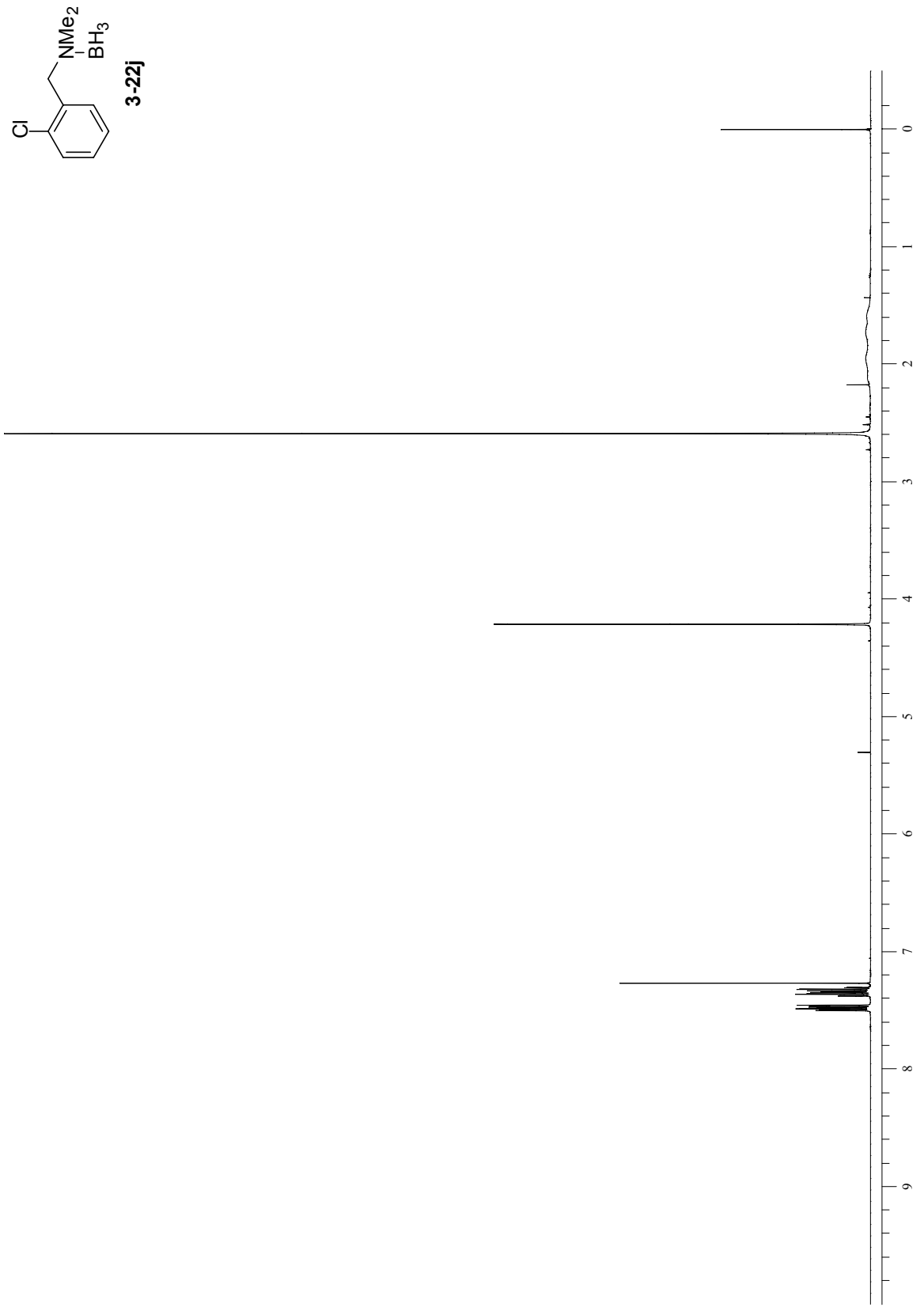
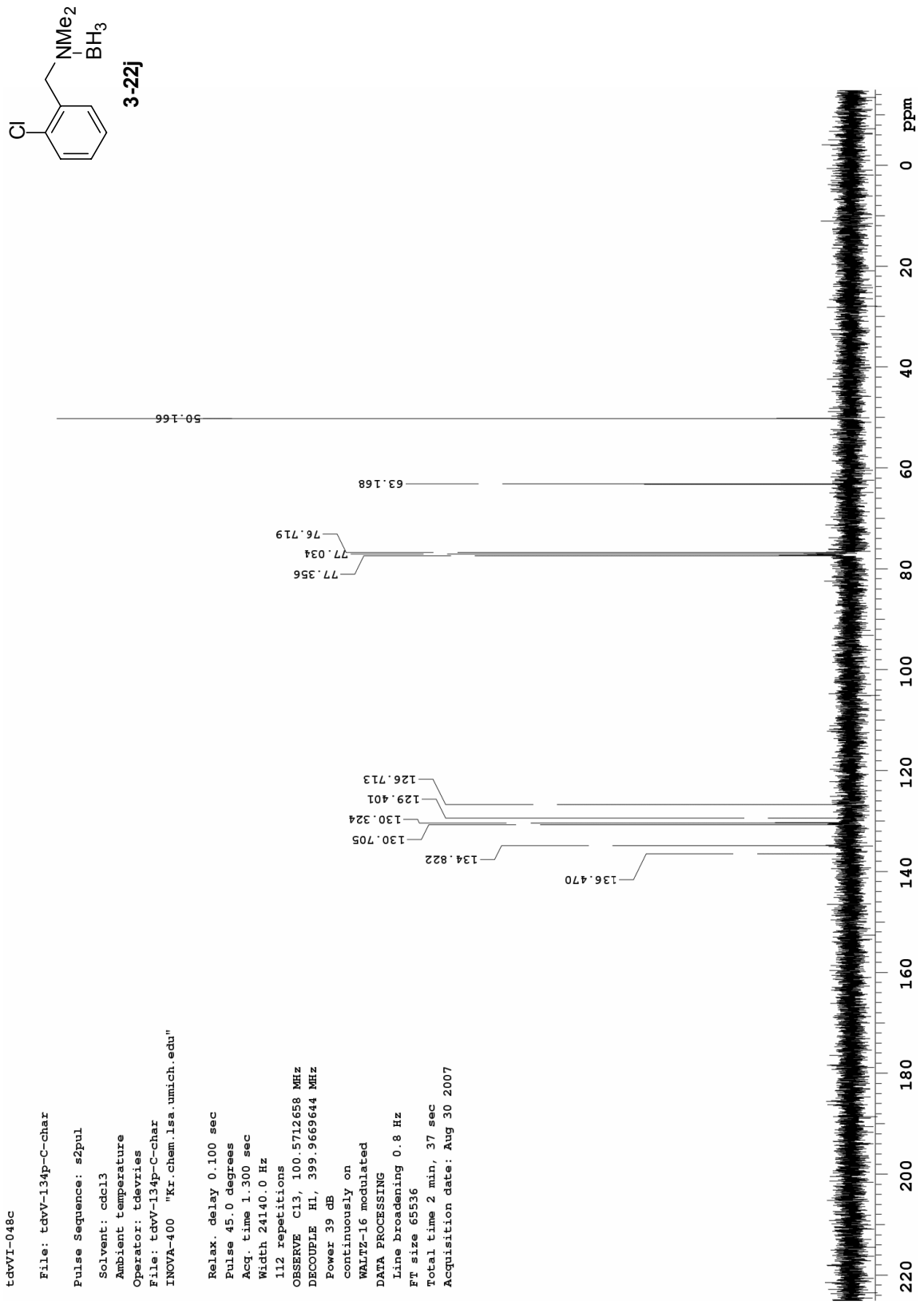
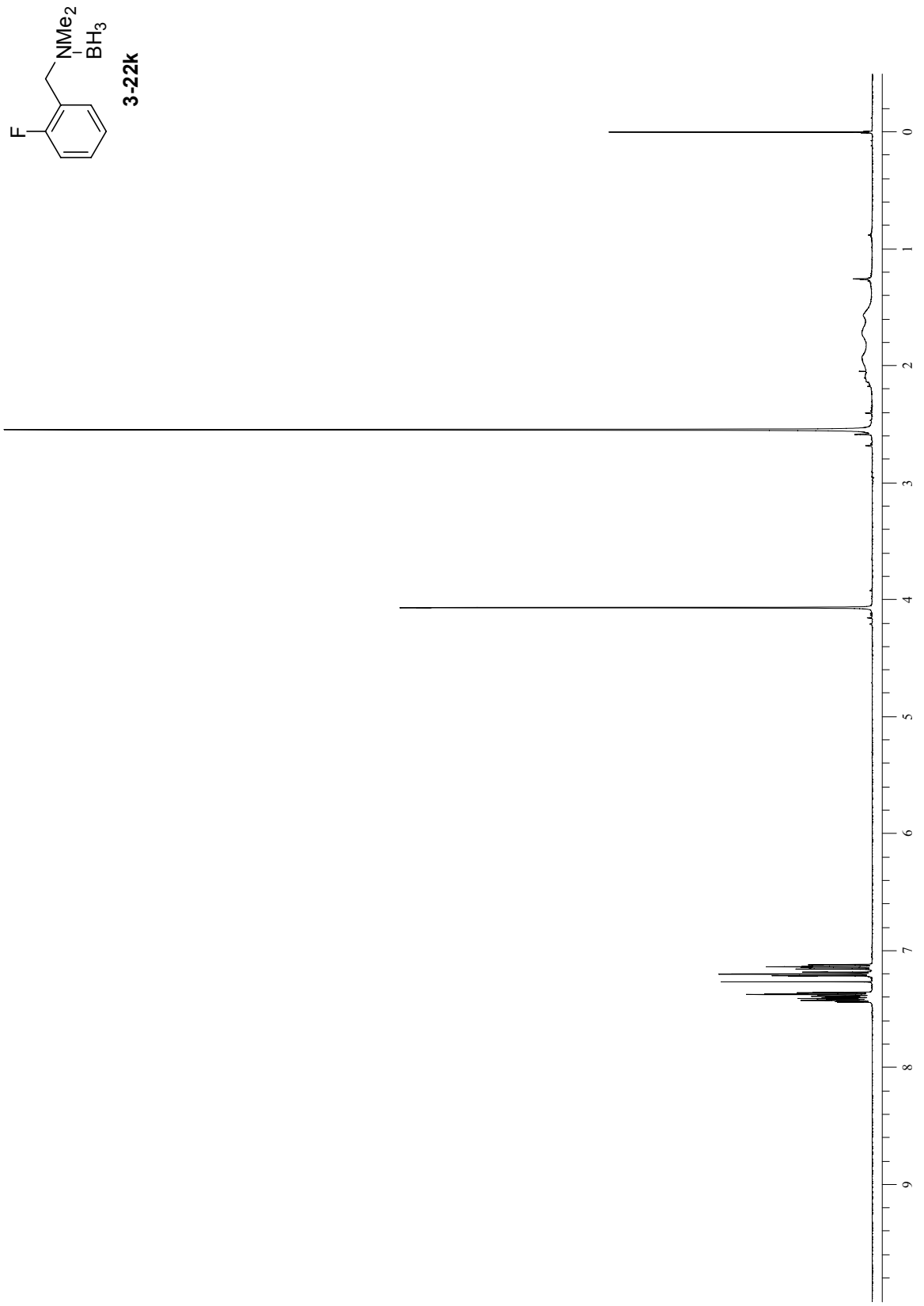
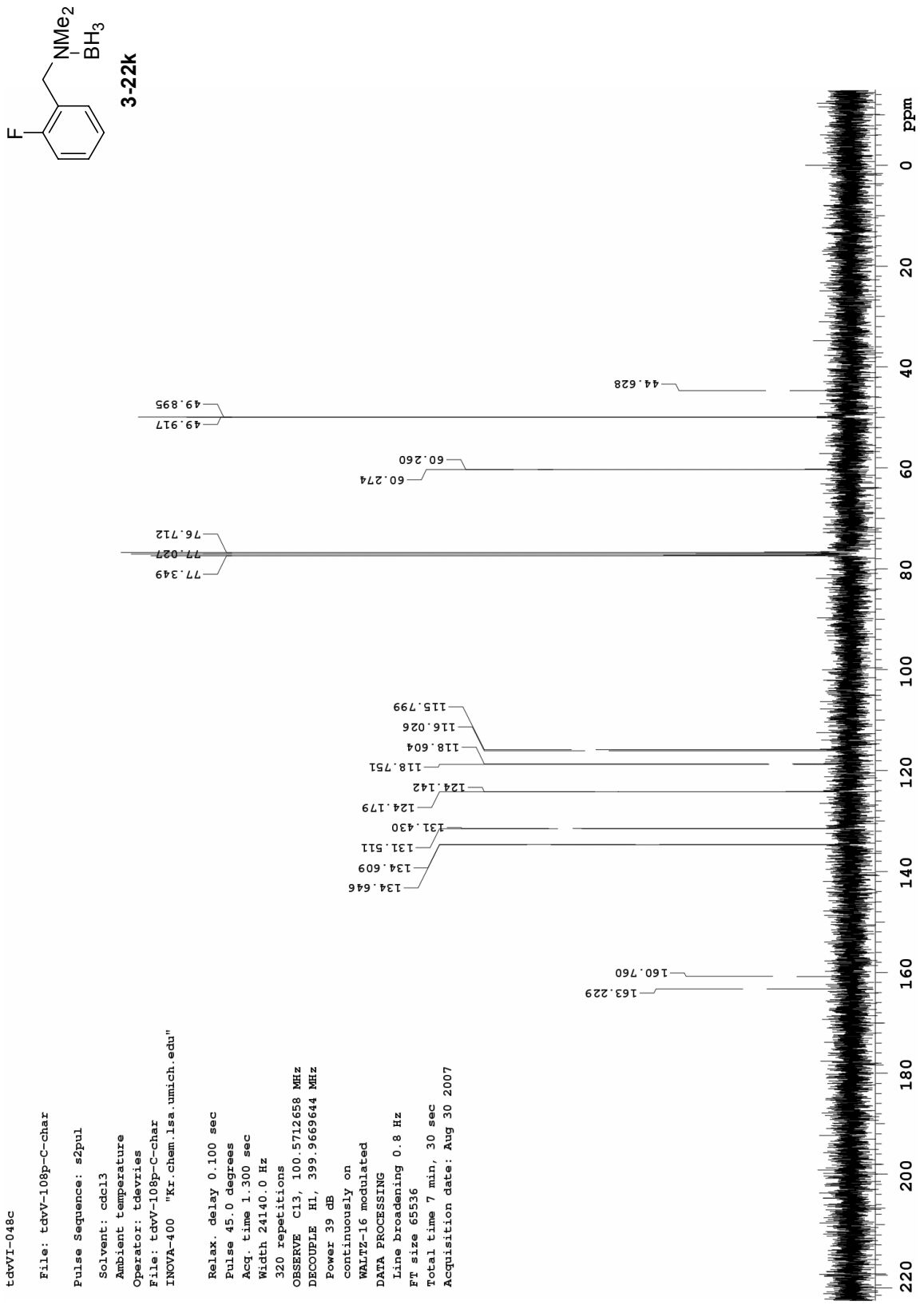
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 24140.0 Hz
128 repetitions
OBSERVE C13, 100.5712660 MHz
DECOUPLE H1, 399.9669644 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.8 Hz
FT size 65536
Total time 3 min, 0 sec
Acquisition date: Aug 30 2007

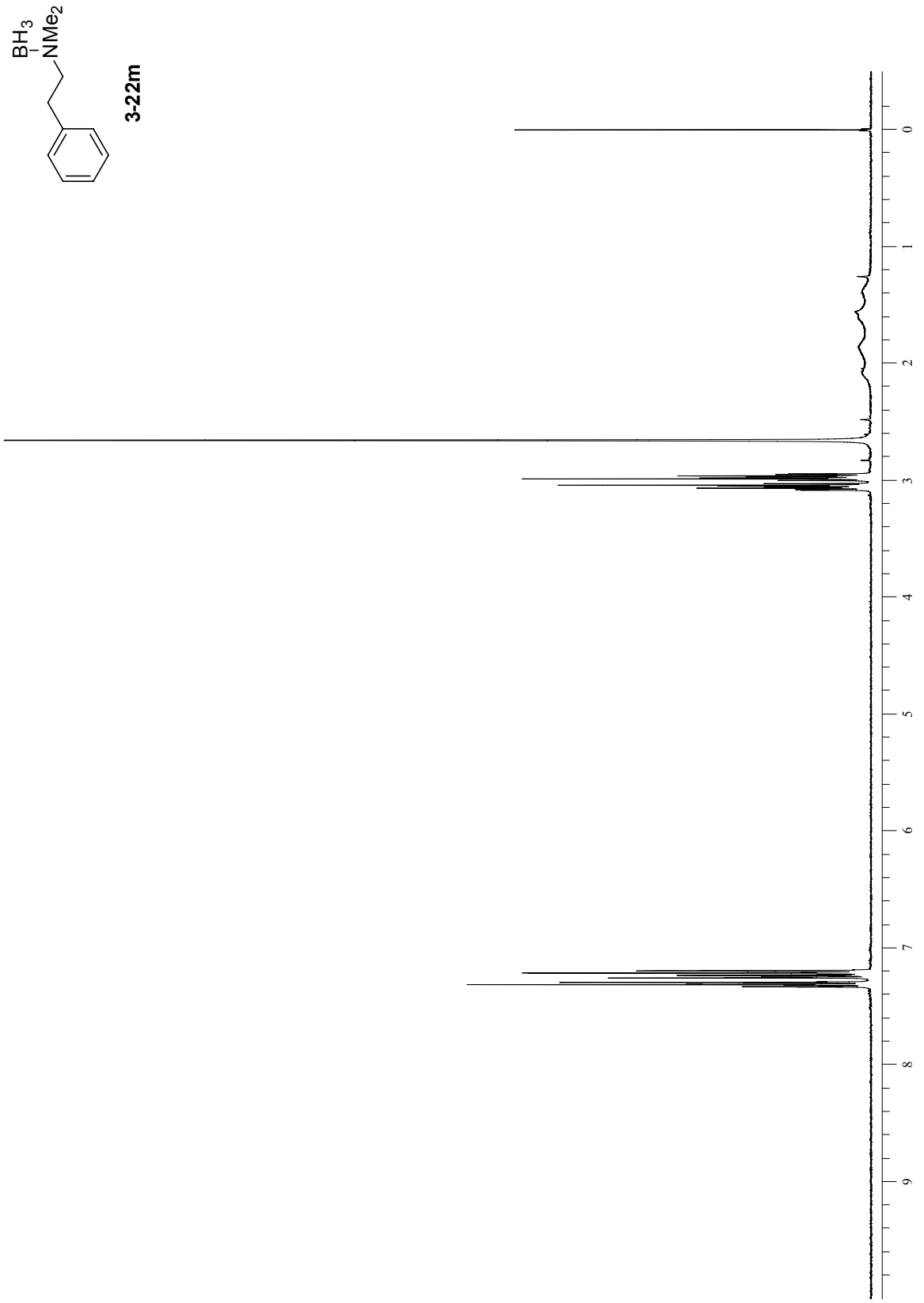

NMe2
BH3
Cl
3-22j
0
1
2
3
4
5
6
7
8
9

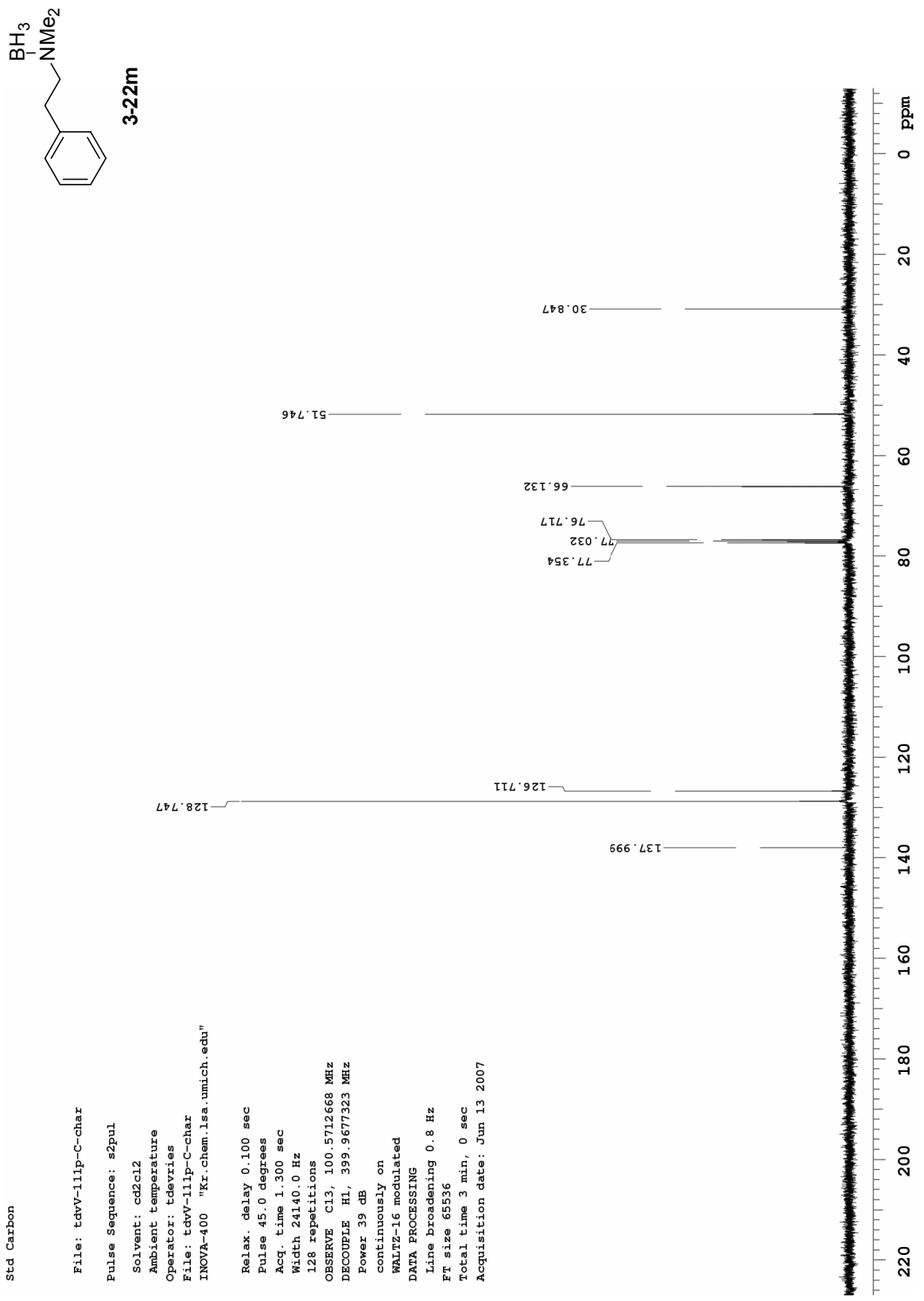


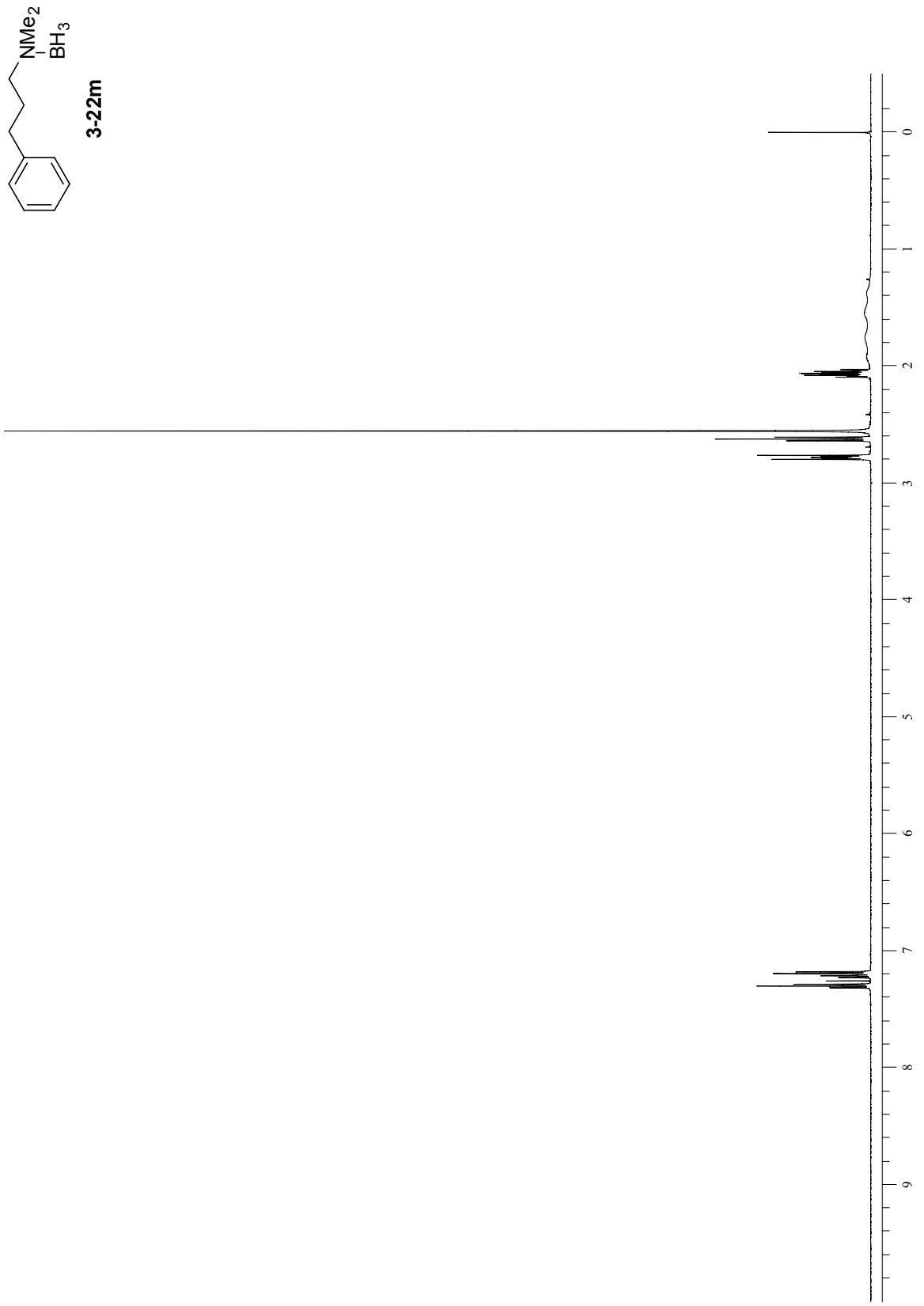

```
tdvVI-048c

  File: tdvV-134p-C-char

Pulse Sequence: s2pul

  Solvent: cdcl3
  Ambient temperature
Operator: tdevries
File: tdvV-134p-C-char
INOVA-400  "Kr.chem.lsa.umich.edu"

  Relax. delay 0.100 sec
  Pulse 45.0 degrees
  Acq. time 1.300 sec
  Width 24140.0 Hz
  112 repetitions
OBSERVE  C13, 100.5712658 MHz
DECOUPLE  H1, 399.9669644 MHz
  Power 39 dB
  continuously on
  WALTZ-16 modulated
DATA PROCESSING
  Line broadening 0.8 Hz
FT size 65536
Total time 2 min, 37 sec
Acquisition date: Aug 30 2007
```

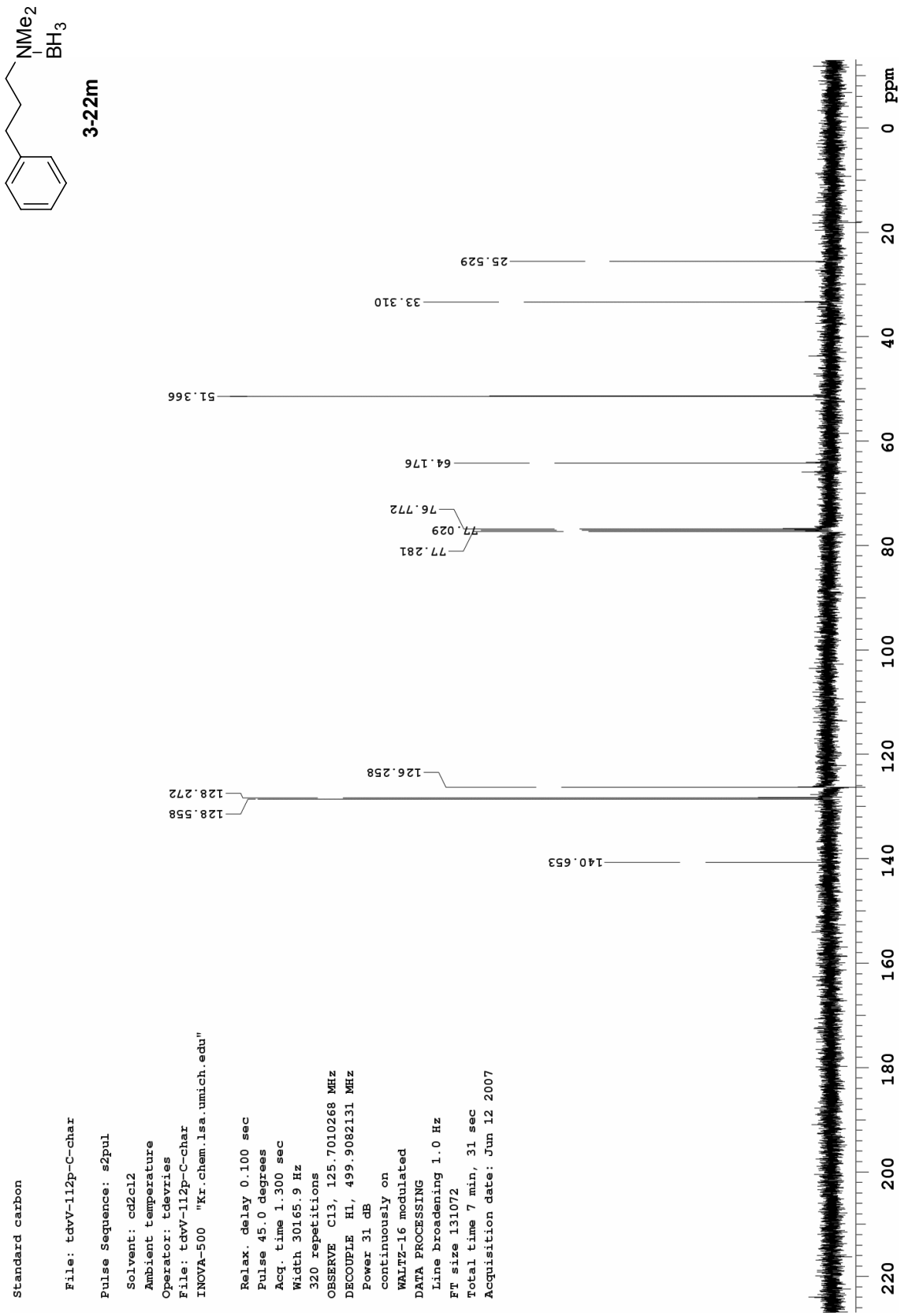

NMe2
BH3
F
3-22k
0
1
2
3
4
5
6
7
8
9

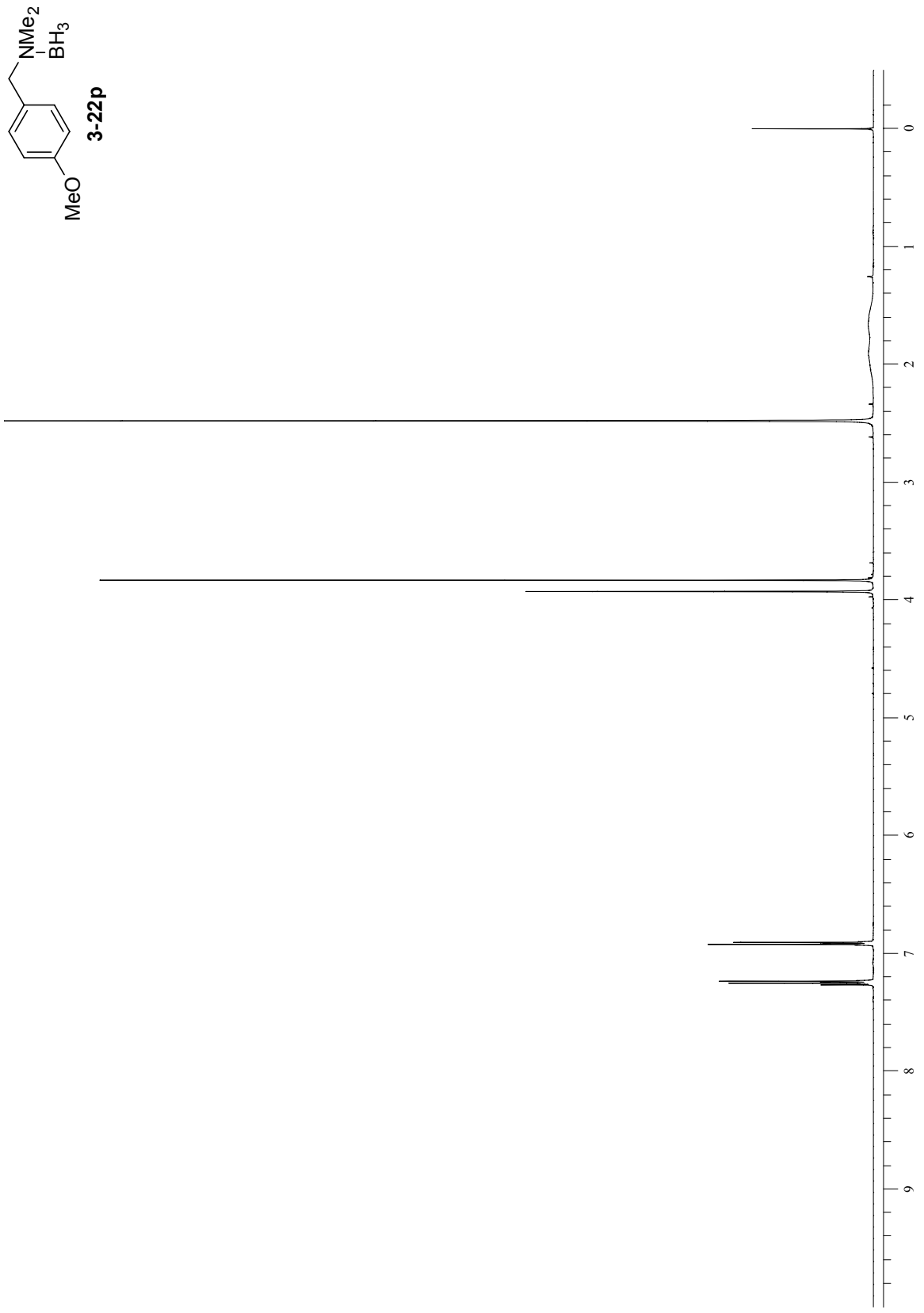

3-22k
F
NMe2
BH3
ppm
0
20
40
60
80
100
120
140
160
180
200
220
44.628
49.895
49.917
60.260
60.274
76.712
77.027
77.349
115.799
116.026
118.604
118.751
124.142
124.179
131.430
131.511
134.609
134.646
160.760
163.229
tdvVI-048c
File: tdvV-108p-C-char
Pulse Sequence: s2pul
Solvent: cdcl3
Ambient temperature
Operator: tdevries
File: tdvV-108p-C-char
INOVA-400 "Kr.chem.lsa.umich.edu"
Relax. delay 0.100 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 24140.0 Hz
320 repetitions
OBSERVE C13, 100.5712658 MHz
DECOUPLE H1, 399.9669644 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.8 Hz
FT size 65536
Total time 7 min, 30 sec
Acquisition date: Aug 30 2007

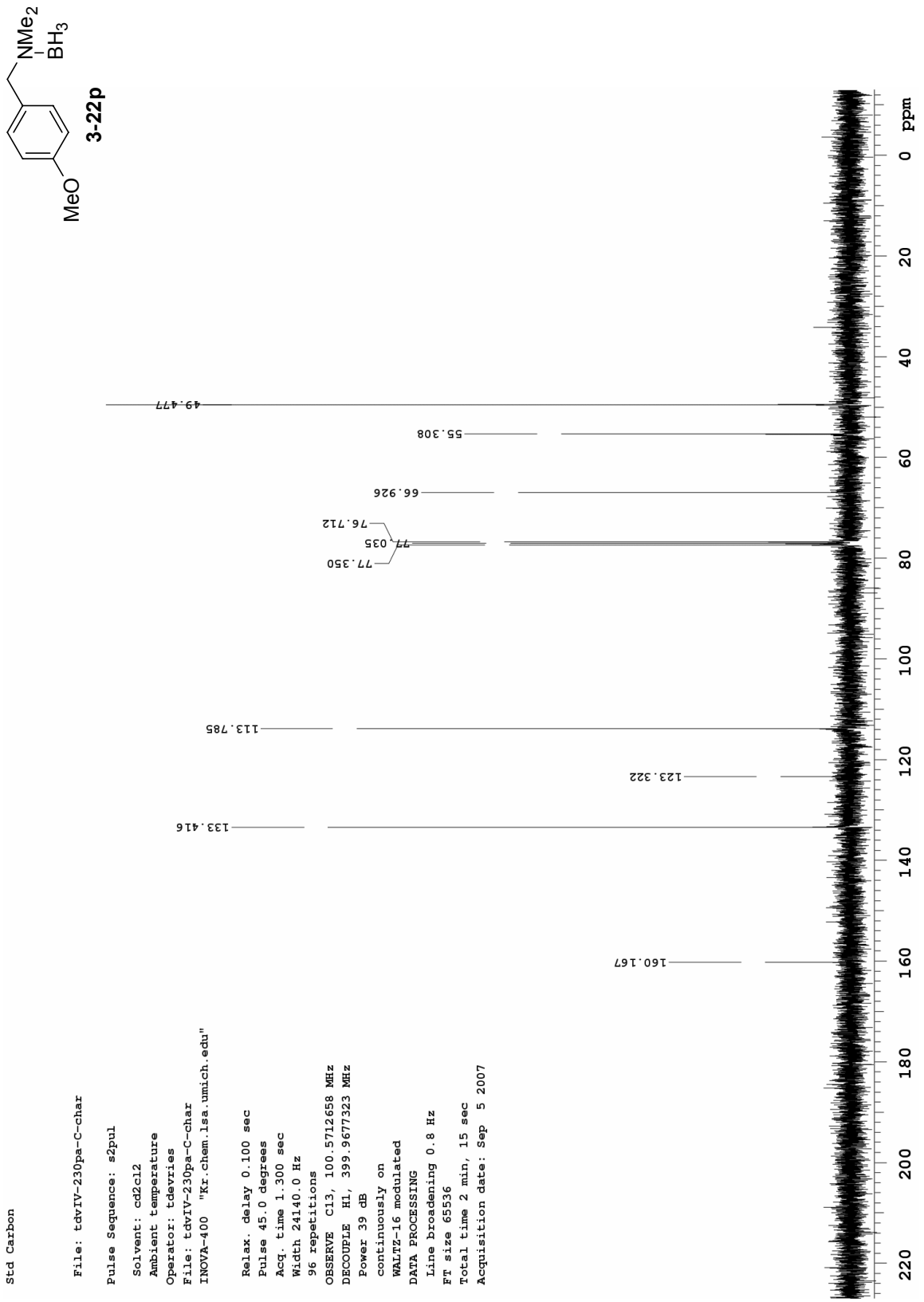

BH3
NMe2
3-22m
0
1
2
3
4
5
6
7
8
9

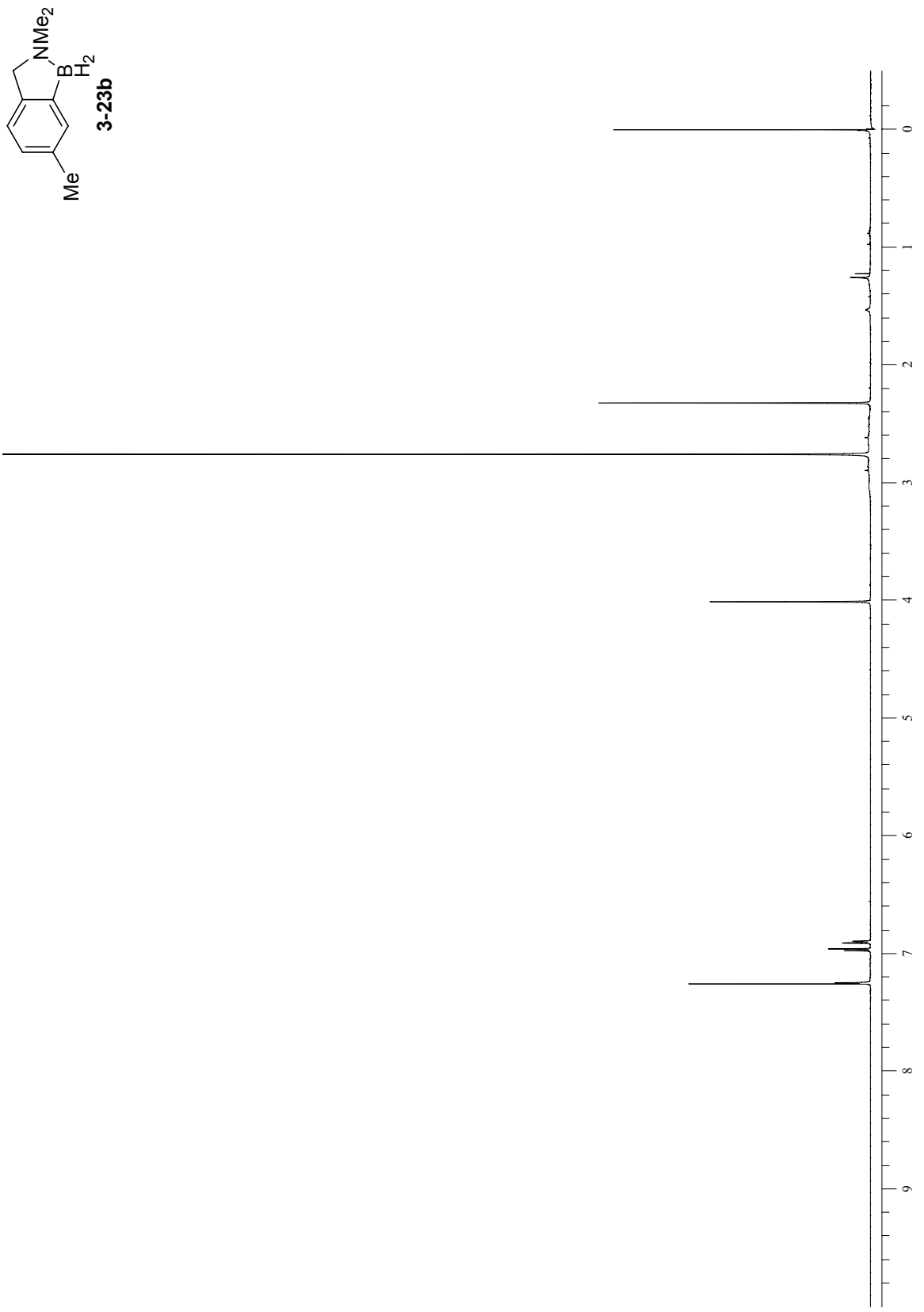

BH3
NMe2
3-22m
Std Carbon
File: tdvV-111p-C-char
Pulse Sequence: s2pul
Solvent: cd2cl2
Ambient temperature
Operator: tdevries
File: tdvV-111p-C-char
INOVA-400 "Kr.chem.lsa.umich.edu"
Relax. delay 0.100 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 24140.0 Hz
128 repetitions
OBSERVE C13, 100.5712668 MHz
DECOUPLE H1, 399.9677323 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.8 Hz
FT size 65536
Total time 3 min, 0 sec
Acquisition date: Jun 13 2007
128.747
126.711
137.999
77.354
77.032
76.717
66.132
51.746
30.847
220
200
180
160
140
120
100
80
60
40
20
0
ppm

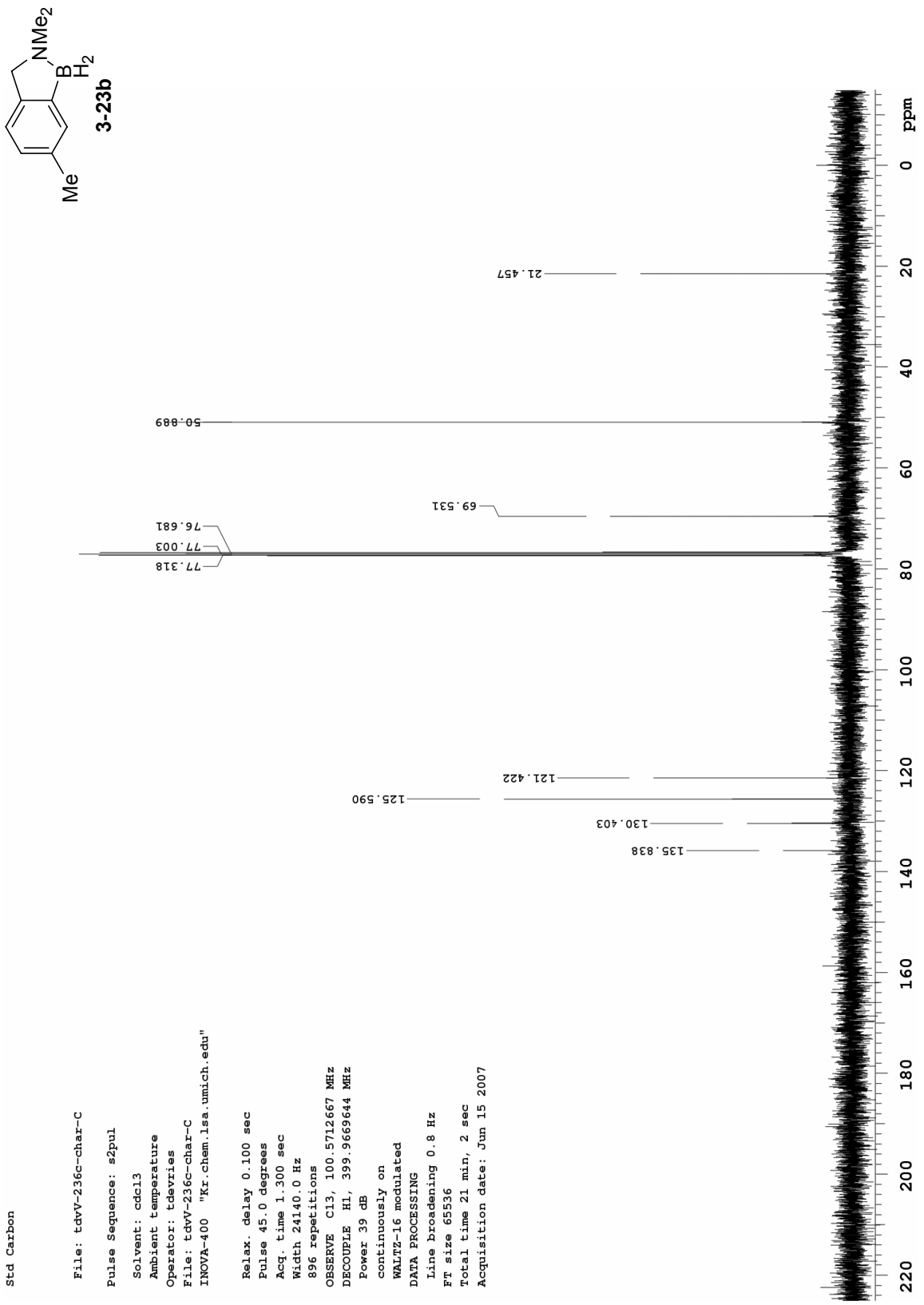

NMe2
BH3
3-22m
0
1
2
3
4
5
6
7
8
9

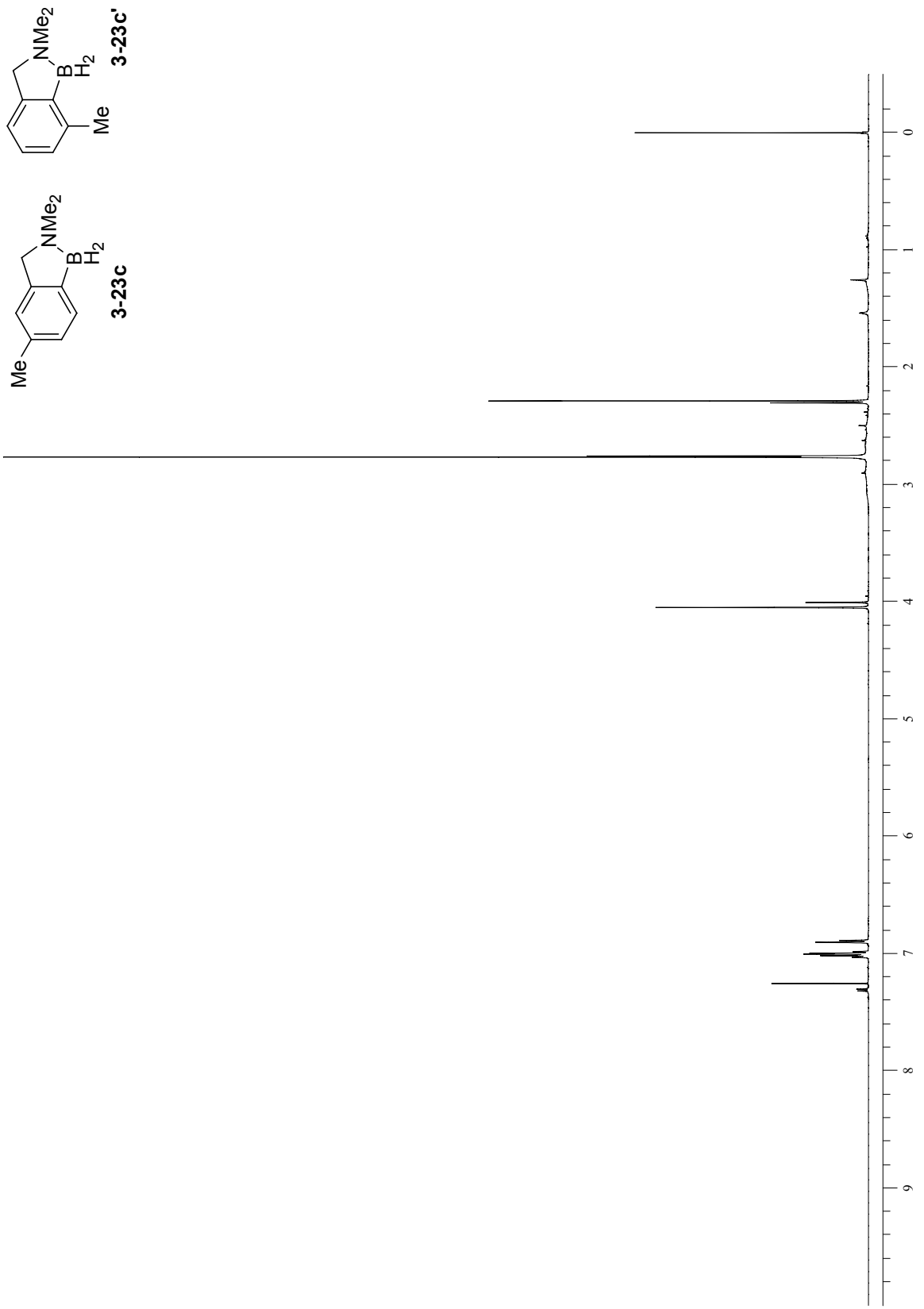

NMe2
BH3
3-22m
Standard carbon
File: tdvV-112p-C-char
Pulse Sequence: s2pul
Solvent: cd2cl2
Ambient temperature
Operator: tdevries
File: tdvV-112p-C-char
INOVA-500 "Kr.chem.lsa.umich.edu"
Relax. delay 0.100 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 30165.9 Hz
320 repetitions
OBSERVE C13, 125.7010268 MHz
DECOUPLE H1, 499.9082131 MHz
Power 31 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 131072
Total time 7 min, 31 sec
Acquisition date: Jun 12 2007
140.653
128.558
128.272
126.258
77.281
77.029
76.772
64.176
51.366
33.310
25.529
220
200
180
160
140
120
100
80
60
40
20
0 ppm

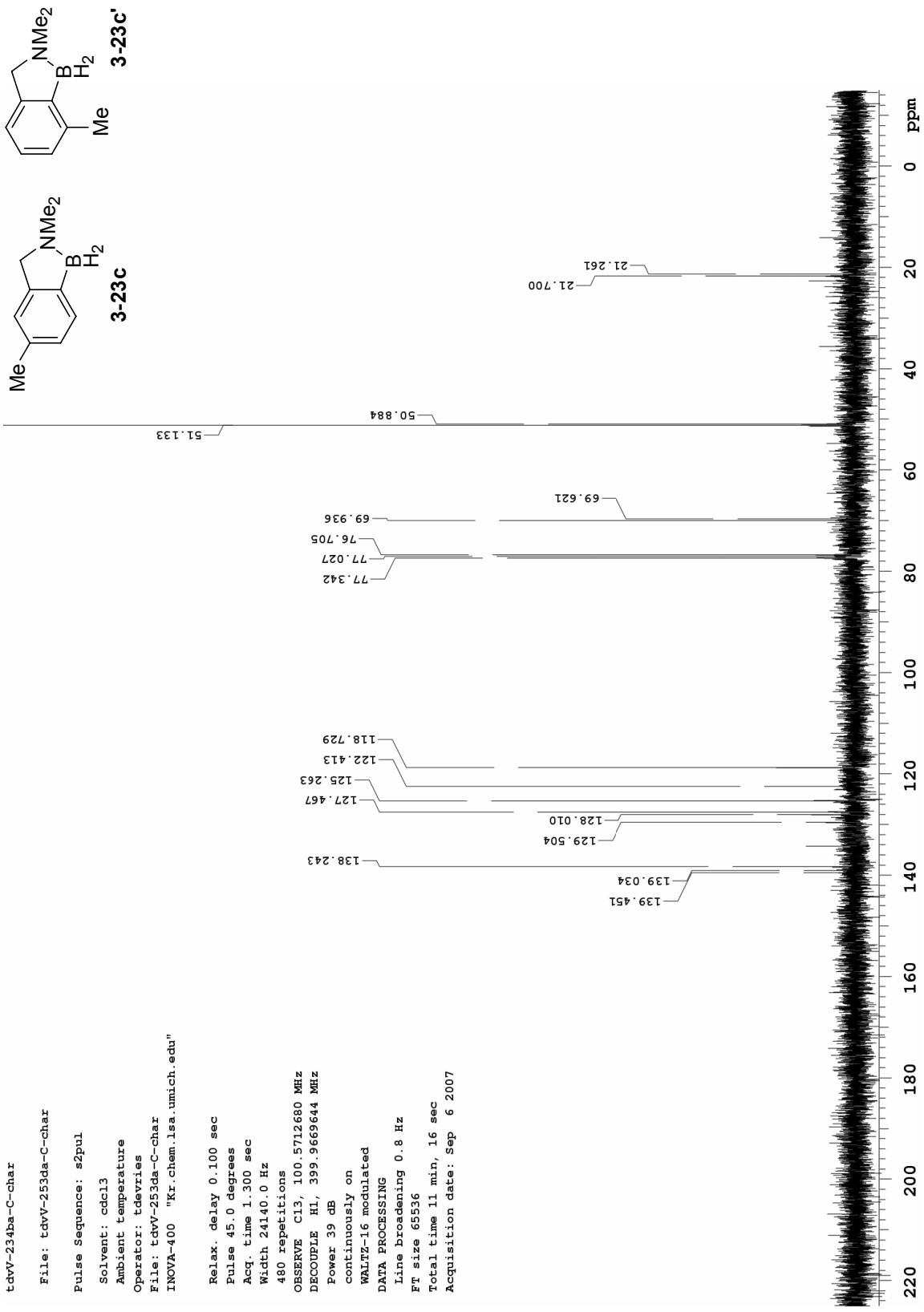

NMe2
BH3
MeO
3-22p
0
1
2
3
4
5
6
7
8
9

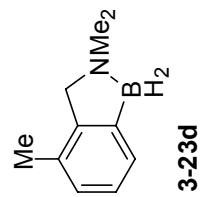

NMe2
BH3
MeO
3-22p
Std Carbon
File: tdvIV-230pa-C-char
Pulse Sequence: s2pul
Solvent: cd2cl2
Ambient temperature
Operator: tdavries
File: tdvIV-230pa-C-char
INOVA-400 "Kr.chem.lsa.umich.edu"
Relax. delay 0.100 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 24140.0 Hz
96 repetitions
OBSERVE C13, 100.5712658 MHz
DECOUPLE H1, 399.9677323 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.8 Hz
FT size 65536
Total time 2 min, 15 sec
Acquisition date: Sep 5 2007
49.477
55.308
66.926
76.712
77.035
77.350
113.785
123.322
133.416
160.167
0 ppm
20
40
60
80
100
120
140
160
180
200
220


NMe2
B
H2
Me
3-23b
0
1
2
3
4
5
6
7
8
9

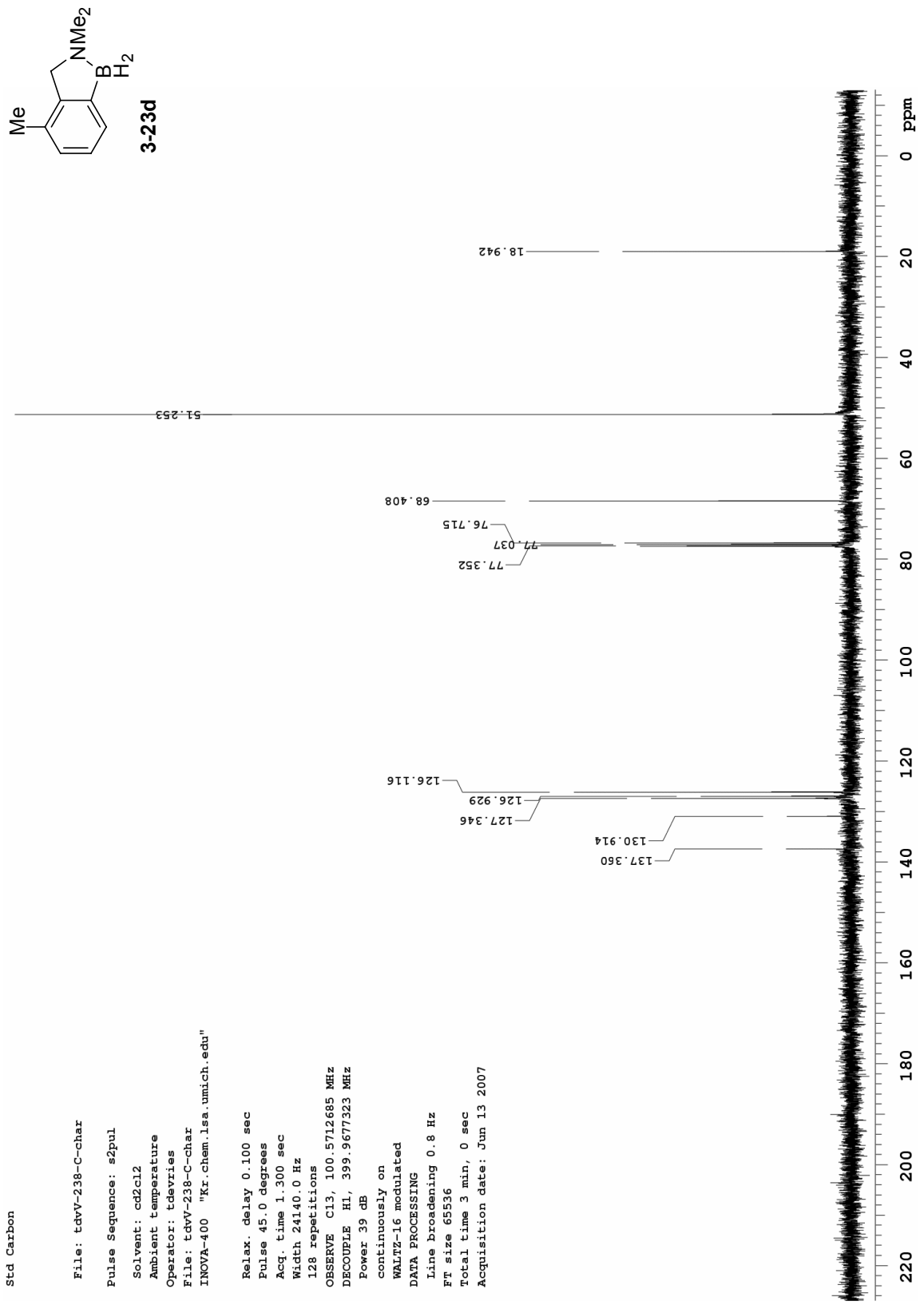

NMe2
B
H2
Me
3-23b
Std Carbon
File: tdvV-236c-char-C
Pulse Sequence: s2pul
Solvent: cdcl3
Ambient temperature
Operator: tdevries
File: tdvV-236C-char-C
INOVA-400 "Kr.chem.lsa.umich.edu"
Relax. delay 0.100 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 24140.0 Hz
896 repetitions
OBSERVE C13, 100.5712667 MHz
DECOUPLE H1, 399.9669644 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.8 Hz
FT size 65536
Total time 21 min, 2 sec
Acquisition date: Jun 15 2007
21.457
50.889
69.531
76.681
77.003
77.318
121.422
125.590
130.403
135.838
ppm
0
20
40
60
80
100
120
140
160
180
200
220

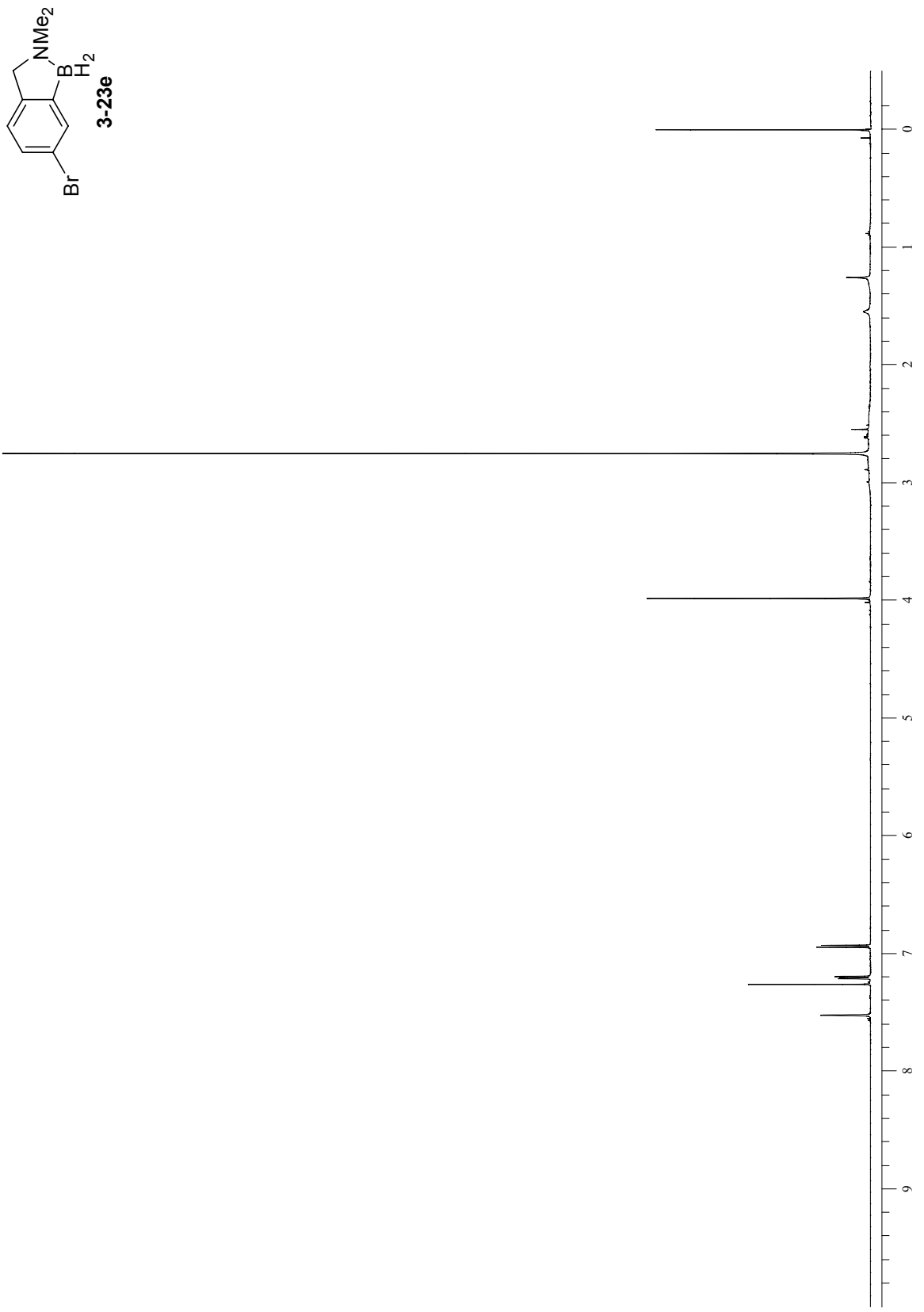

NMe2
B
H2
Me
3-23c'
NMe2
B
H2
Me
3-23c
0
1
2
3
4
5
6
7
8
9

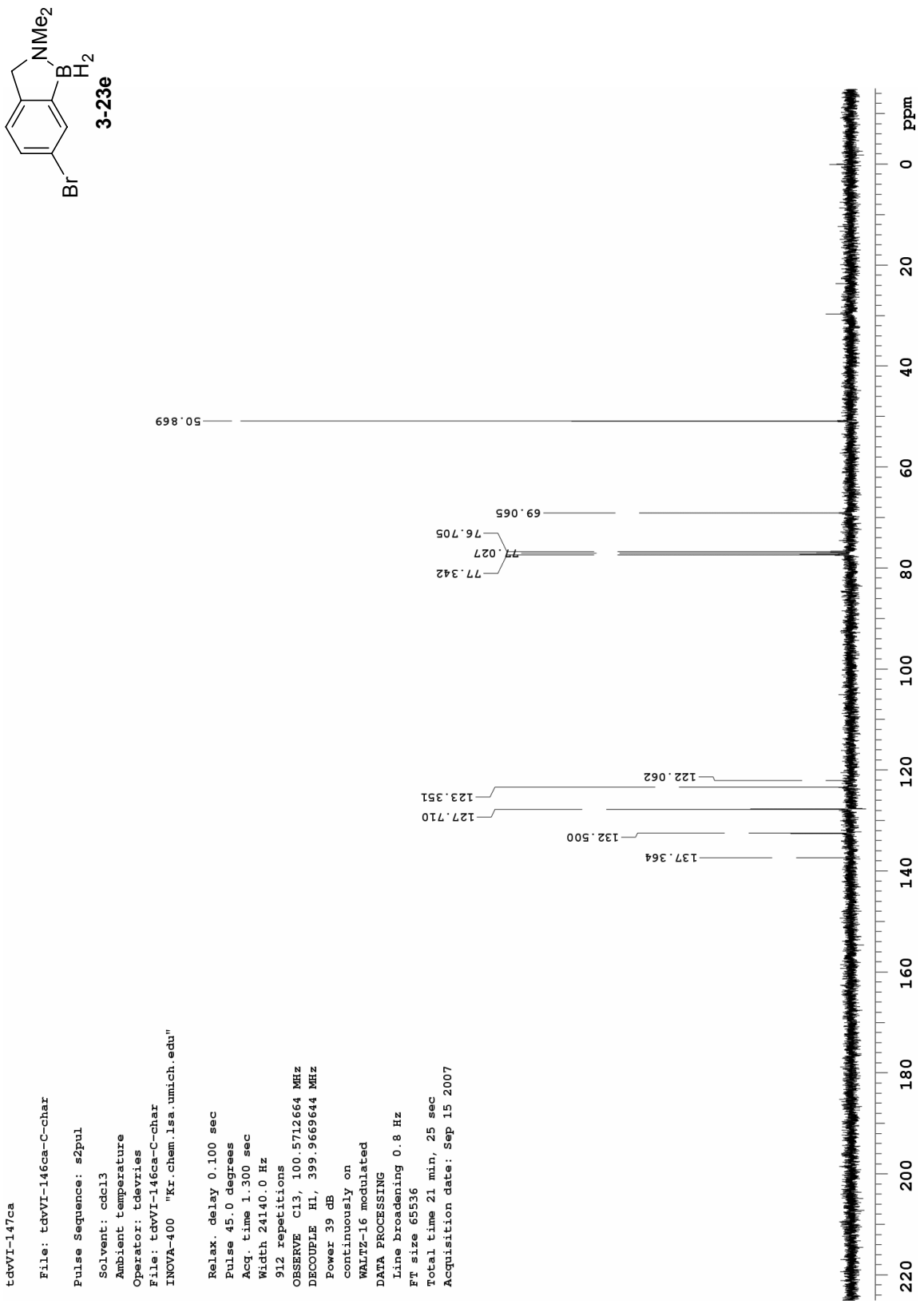

tdvV-234ba-C-char
File: tdvV-253da-C-char
Pulse Sequence: s2pul
Solvent: cdcl3
Ambient temperature
Operator: tdevries
File: tdvV-253da-C-char
INOVA-400 "Kr.chem.lsa.umich.edu"
Relax. delay 0.100 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 24140.0 Hz
480 repetitions
OBSERVE C13, 100.5712680 MHz
DECOUPLE H1, 399.9669644 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.8 Hz
FT size 65536
Total time 11 min, 16 sec
Acquisition date: Sep 6 2007
NMe2
B
H2
Me
3-23c
NMe2
B
H2
Me
3-23c'
21.261
21.700
50.884
51.133
69.621
69.936
76.705
77.027
77.342
118.729
122.413
125.263
127.467
128.010
129.504
138.243
139.034
139.451
ppm
0
20
40
60
80
100
120
140
160
180
200
220



3-23d


Me
NMe2
B
H2
3-23d
18.942
51.253
68.408
76.715
77.037
77.352
126.116
126.929
127.346
130.914
137.360
0 ppm
20
40
60
80
100
120
140
160
180
200
220
Std Carbon
File: tdvV-238-C-char
Pulse Sequence: s2pul
Solvent: cd2cl2
Ambient temperature
Operator: tdevries
File: tdvV-238-C-char
INOVA-400 "Kr.chem.lsa.umich.edu"
Relax. delay 0.100 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 24140.0 Hz
128 repetitions
OBSERVE C13, 100.5712685 MHz
DECOUPLE H1, 399.9677323 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.8 Hz
FT size 65536
Total time 3 min, 0 sec
Acquisition date: Jun 13 2007


NMe2
B
H2
Br
3-23e
0
1
2
3
4
5
6
7
8
9



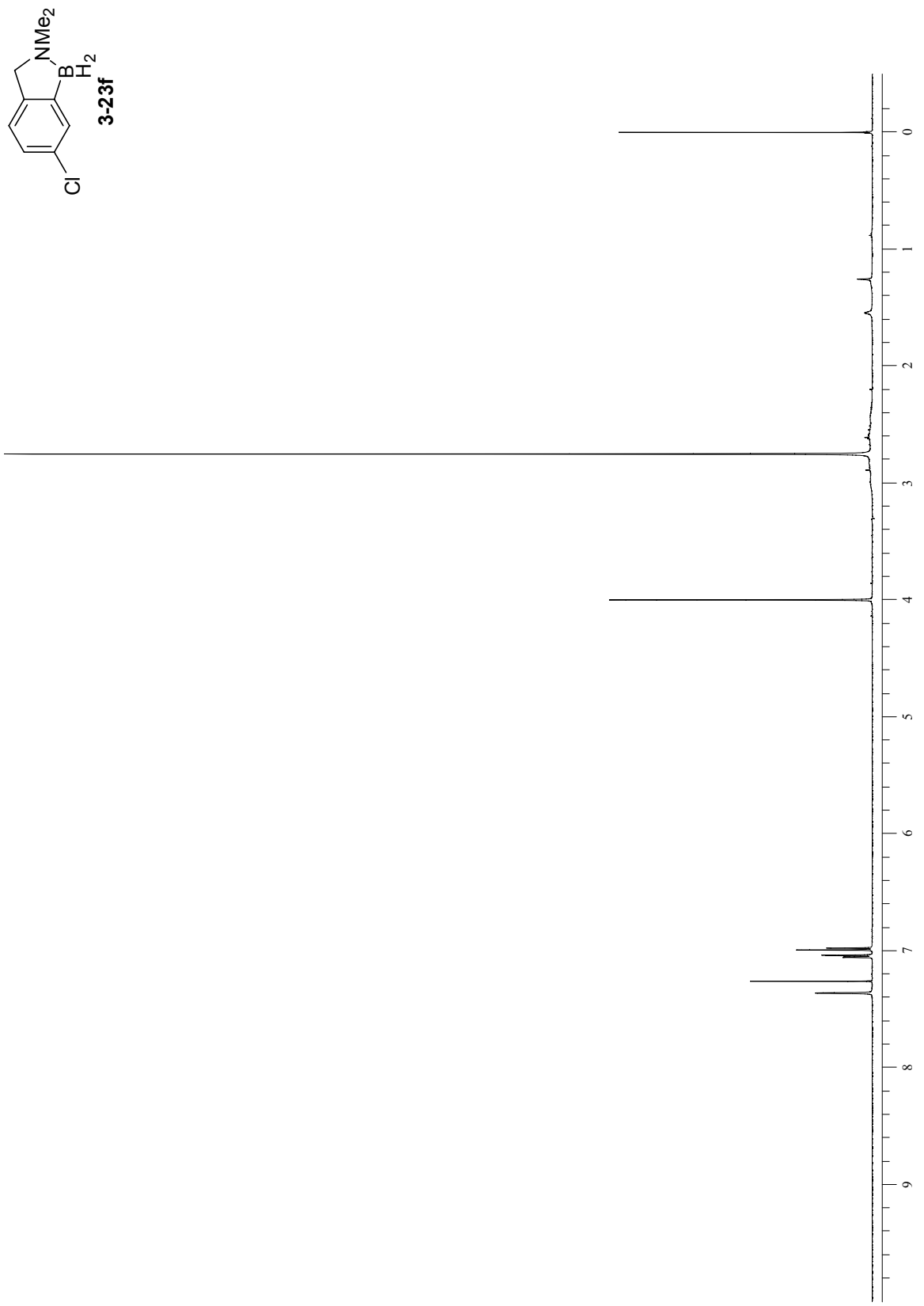
tdvVI-147ca

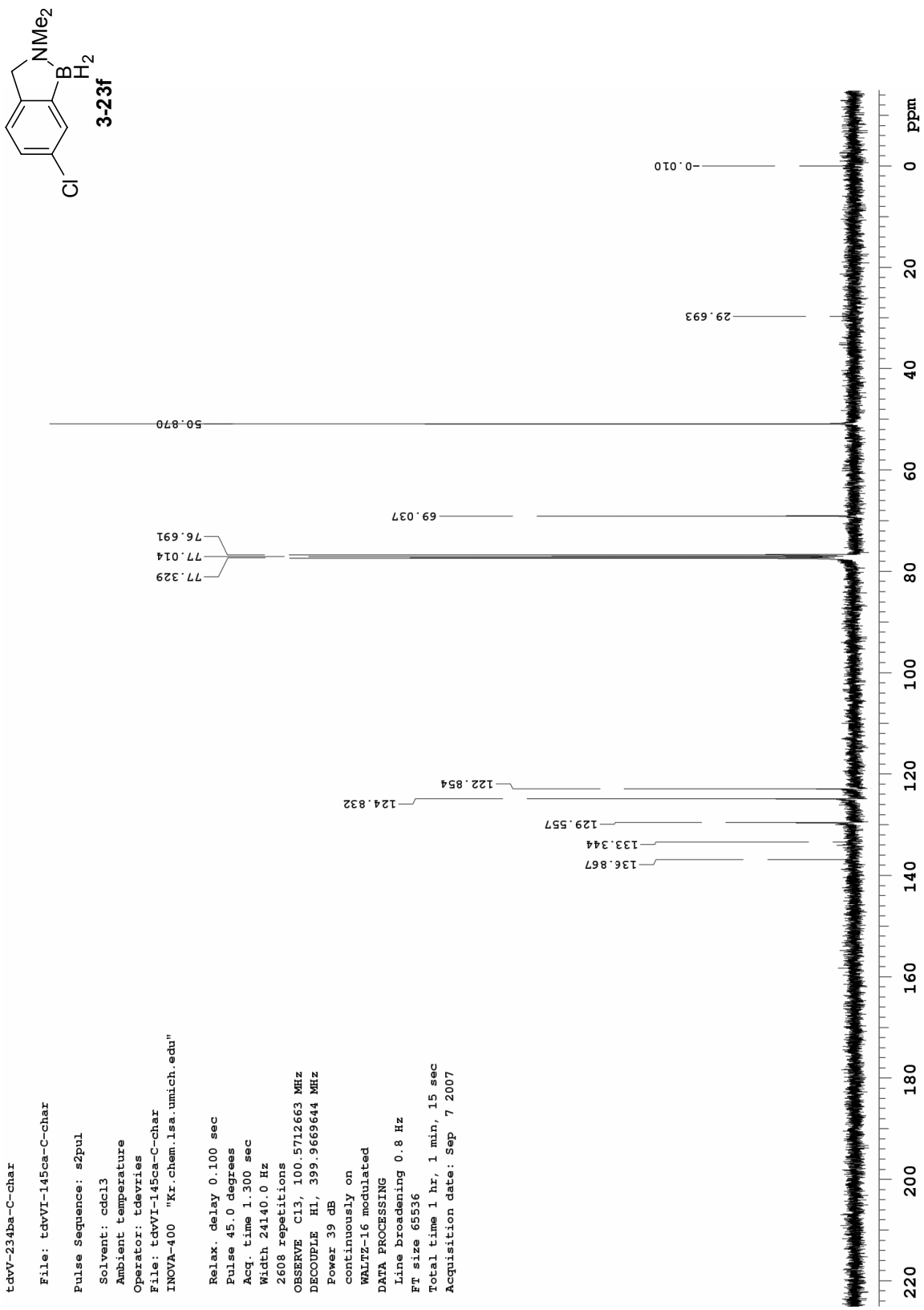
File: tdvVI-146ca-C-char

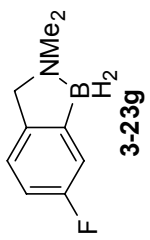
Pulse Sequence: s2pul

Solvent: cdcl3
Ambient temperature
Operator: tdevries
File: tdvVI-146ca-C-char
INOVA-400 "Kr.chem.lsa.umich.edu"

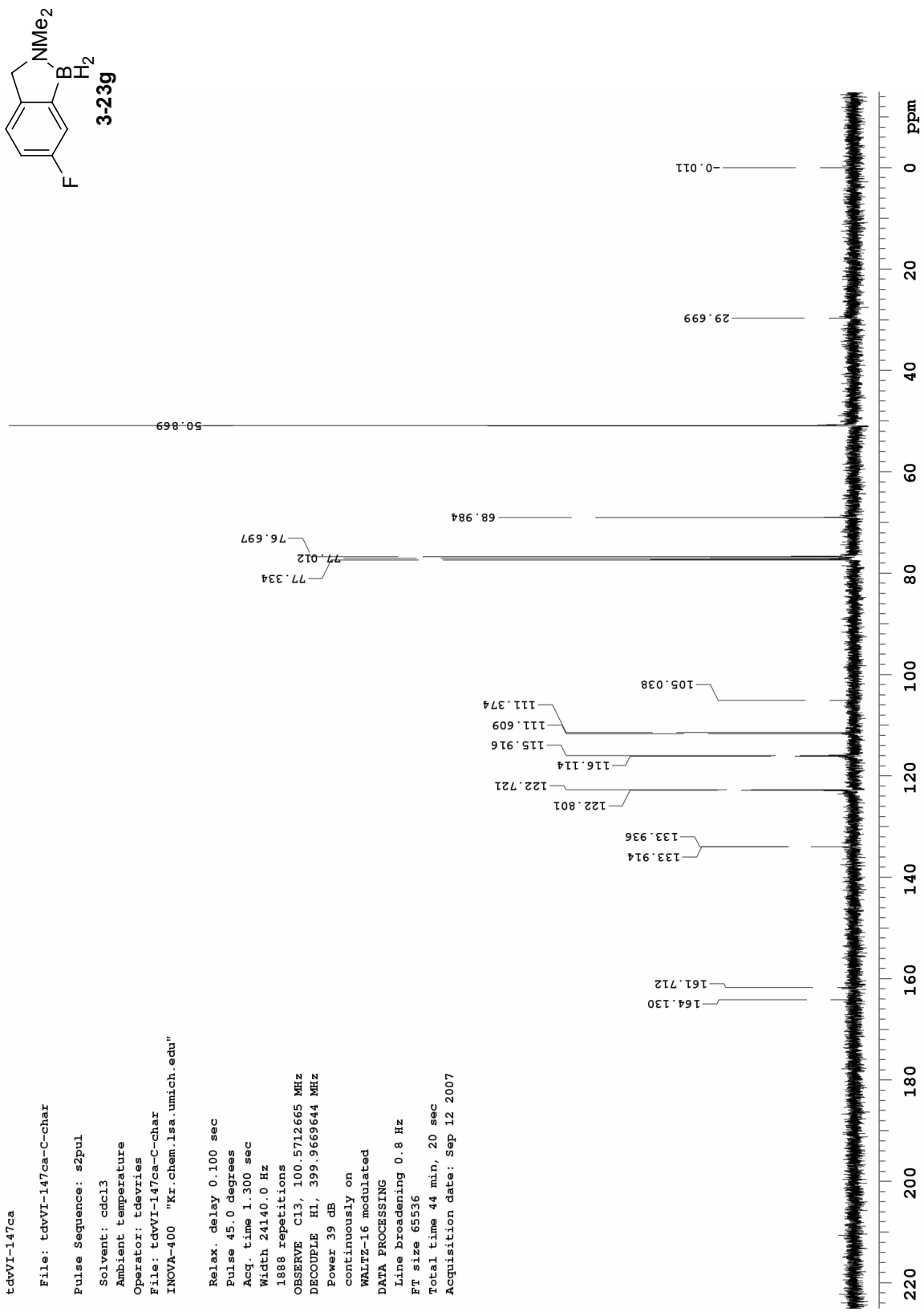
Relax. delay 0.100 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 24140.0 Hz
912 repetitions
OBSERVE C13, 100.5712664 MHz
DECOUPLE H1, 399.9669644 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.8 Hz
FT size 65536
Total time 21 min, 25 sec
Acquisition date: Sep 15 2007

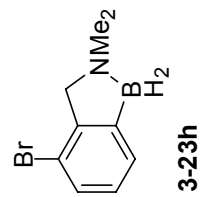

NMe2
B
H2
Cl
3-23f
0
1
2
3
4
5
6
7
8
9


NMe2
B
H2
Cl
3-23f
-0.010
29.693
50.870
69.037
76.691
77.014
77.329
122.854
124.832
129.557
133.344
136.867
ppm
0
20
40
60
80
100
120
140
160
180
200
220
tdvV-234ba-C-char
File: tdvVI-145ca-C-char
Pulse Sequence: s2pul
Solvent: cdcl3
Ambient temperature
Operator: tdevries
File: tdvVI-145ca-C-char
INOVA-400 "Kr.chem.lsa.umich.edu"
Relax. delay 0.100 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 24140.0 Hz
2608 repetitions
OBSERVE C13, 100.5712663 MHz
DECOUPLE H1, 399.9669644 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.8 Hz
FT size 65536
Total time 1 hr, 1 min, 15 sec
Acquisition date: Sep 7 2007

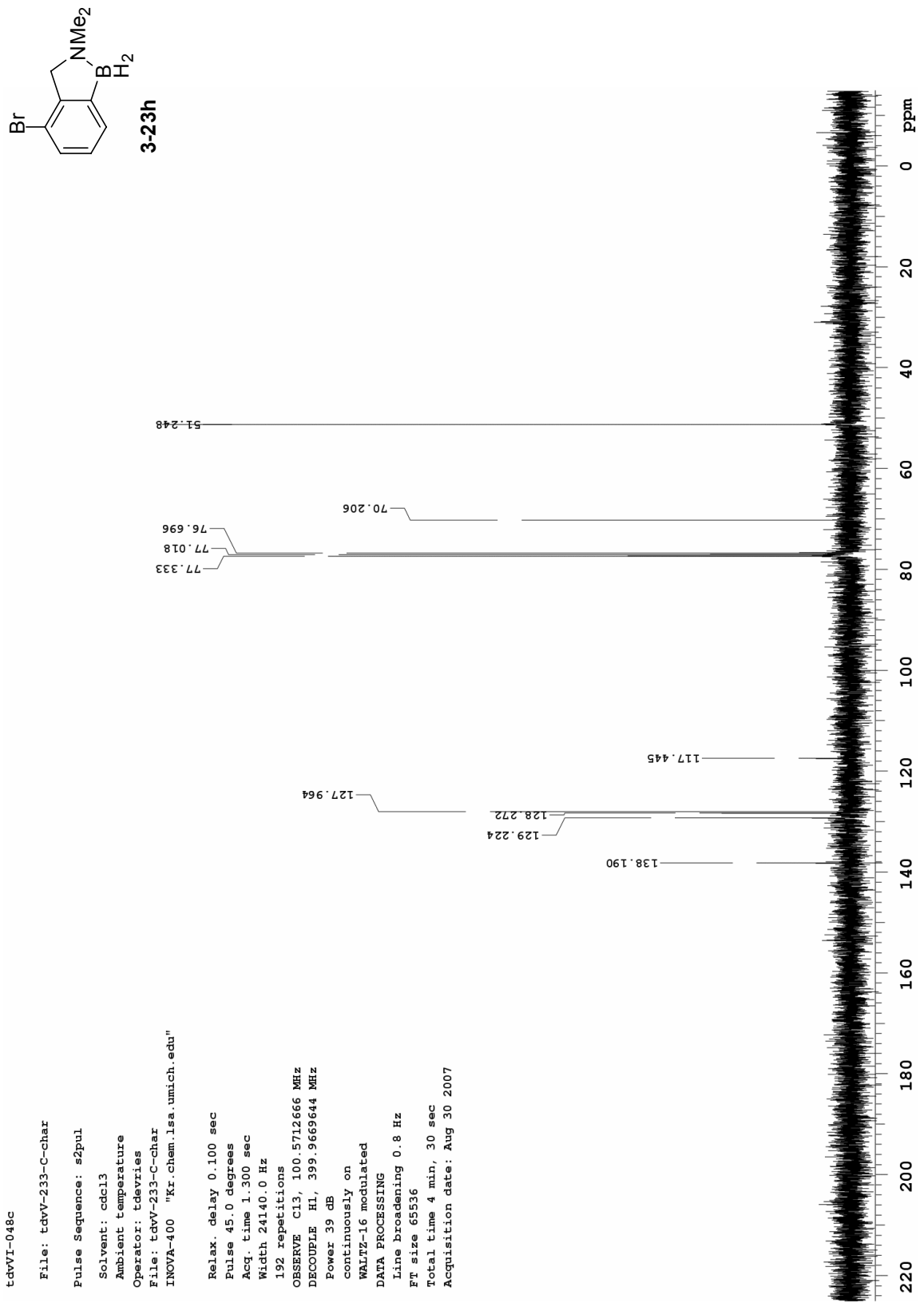


3-23g


NMe2
B
H2
F
3-23g
tdvVI-147ca
File: tdvVI-147ca-C-char
Pulse Sequence: s2pul
Solvent: cdcl3
Ambient temperature
Operator: tdevries
File: tdvVI-147ca-C-char
INOVA-400 "Kr.chem.lsa.umich.edu"
Relax. delay 0.100 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 24140.0 Hz
1888 repetitions
OBSERVE C13, 100.5712665 MHz
DECOUPLE H1, 399.9669644 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.8 Hz
FT size 65536
Total time 44 min, 20 sec
Acquisition date: Sep 12 2007
-0.011
29.699
50.869
68.984
76.697
77.012
77.334
105.038
111.374
111.609
115.916
116.114
122.721
122.801
133.914
133.936
161.712
164.130
ppm
0
20
40
60
80
100
120
140
160
180
200
220



3-23h



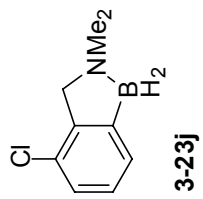
tdvVI-048c

File: tdvV-233-C-char

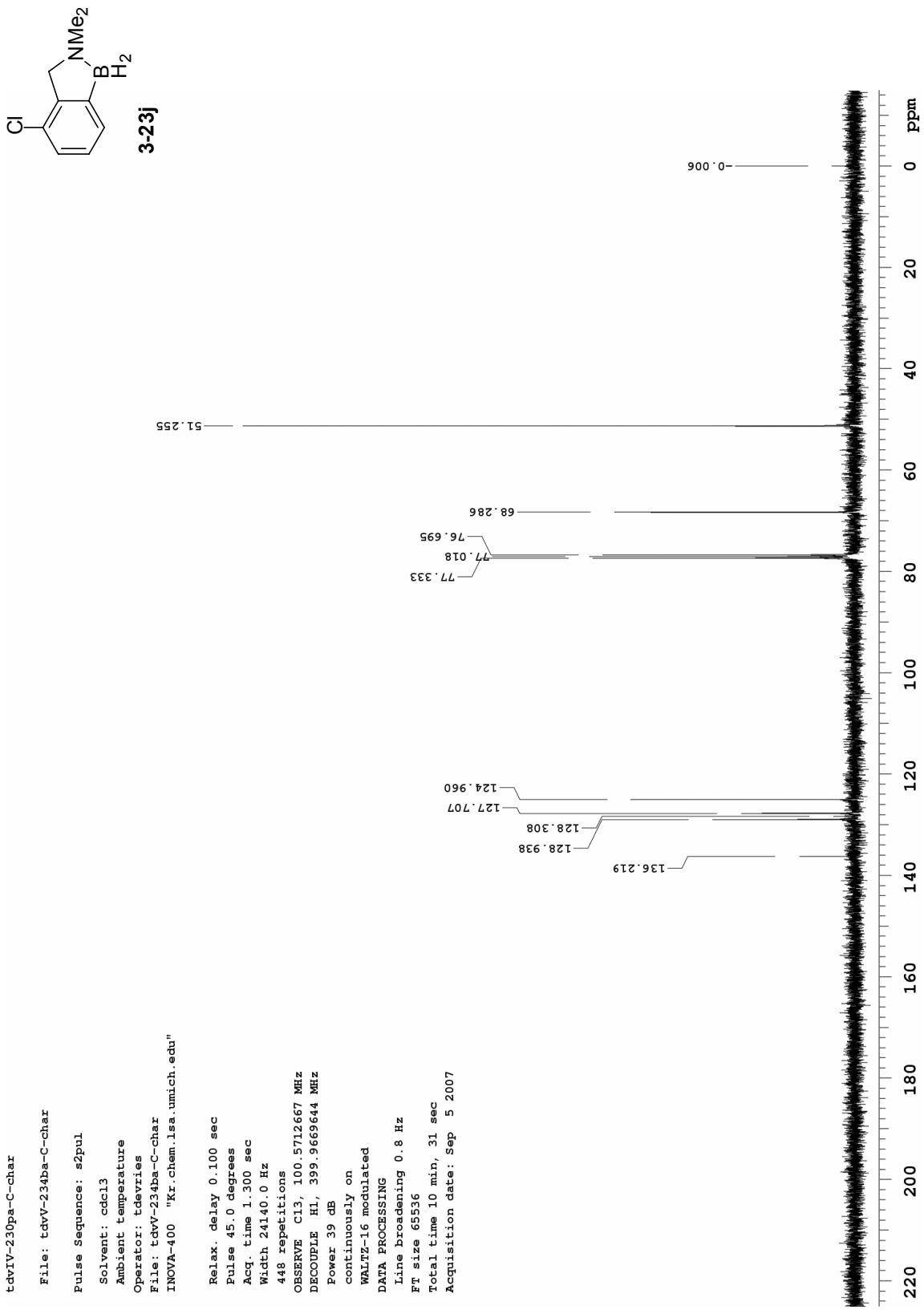
Pulse Sequence: s2pul

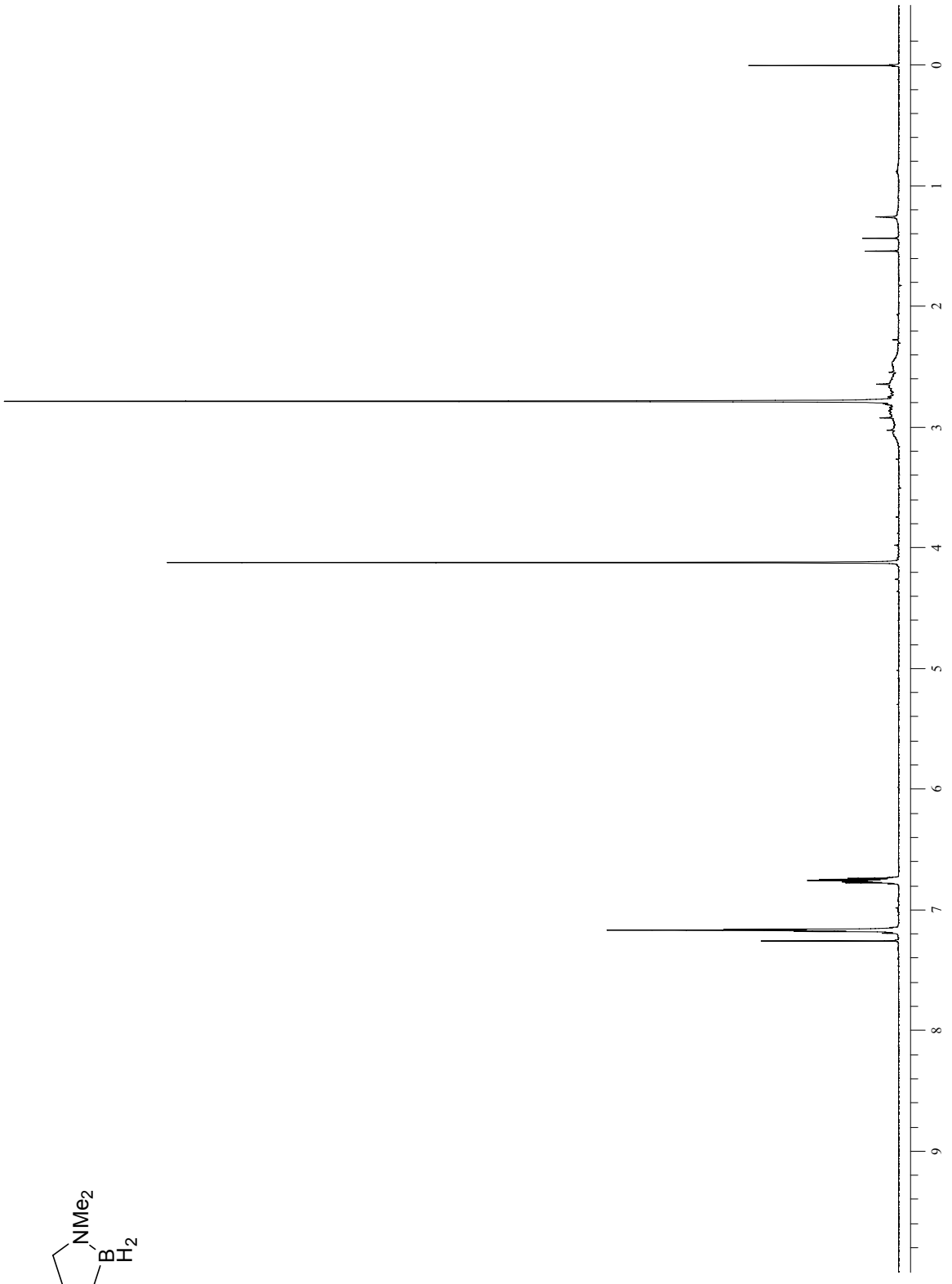
Solvent: cdcl3
Ambient temperature
Operator: tdevries
File: tdvV-233-C-char
INOVA-400 "Kr.chem.lsa.umich.edu"

Relax. delay 0.100 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 24140.0 Hz
192 repetitions
OBSERVE C13, 100.5712666 MHz
DECOUPLE H1, 399.9669644 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.8 Hz
FT size 65536
Total time 4 min, 30 sec
Acquisition date: Aug 30 2007

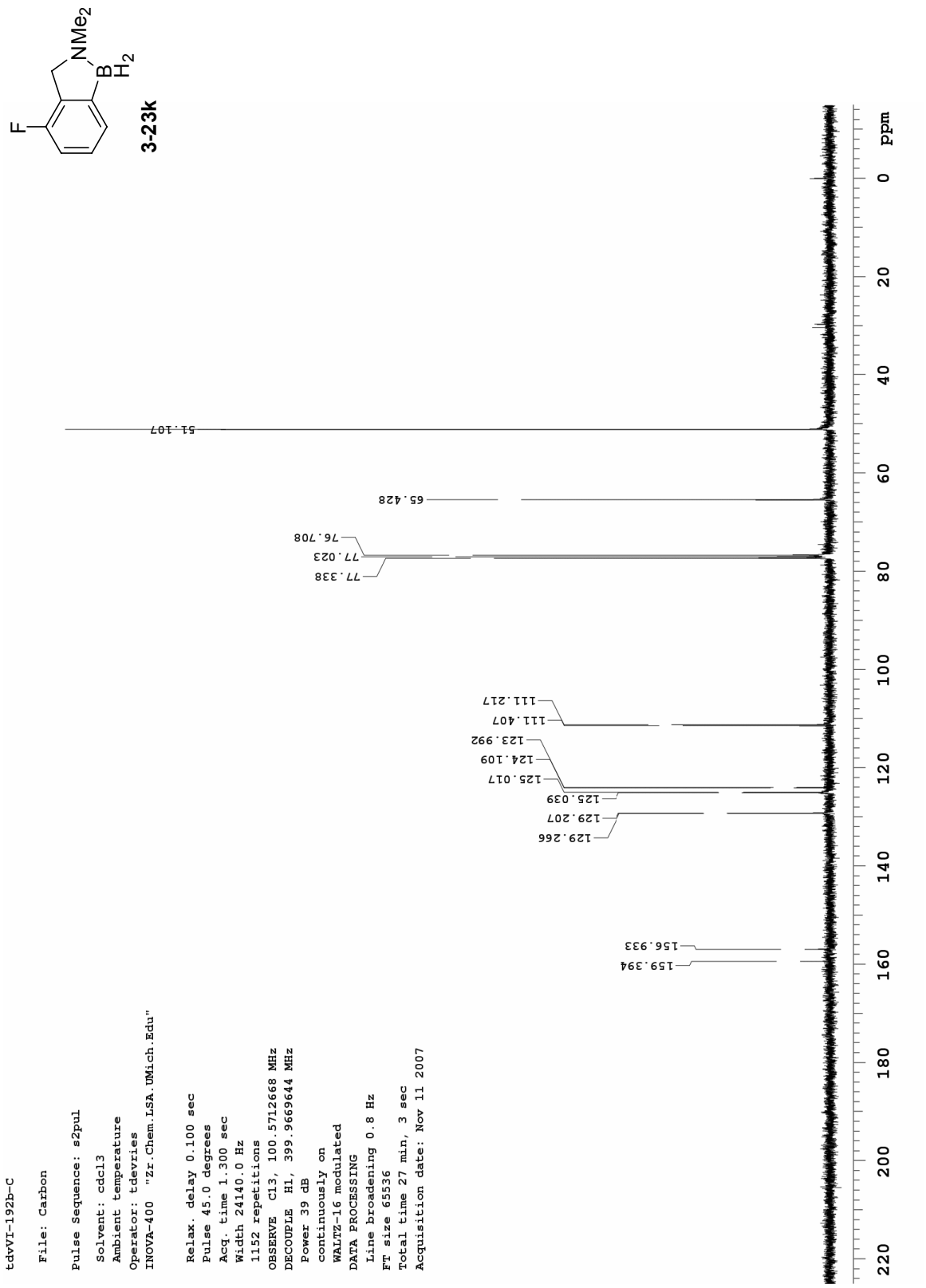


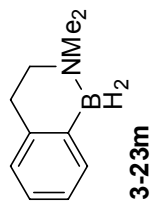
3-23j


tdvIV-230pa-C-char
File: tdvV-234ba-C-char
Pulse Sequence: s2pul
Solvent: cdcl3
Ambient temperature
Operator: tdevries
File: tdvV-234ba-C-char
INOVA-400 "Kr.chem.lsa.umich.edu"
Relax. delay 0.100 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 24140.0 Hz
448 repetitions
OBSERVE C13, 100.5712667 MHz
DECOUPLE H1, 399.9669644 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.8 Hz
FT size 65536
Total time 10 min, 31 sec
Acquisition date: Sep 5 2007
Cl
NMe2
B
H2
3-23j
-0.006
51.255
68.286
76.695
77.018
77.333
124.960
127.707
128.308
128.938
136.219
ppm
0
20
40
60
80
100
120
140
160
180
200
220

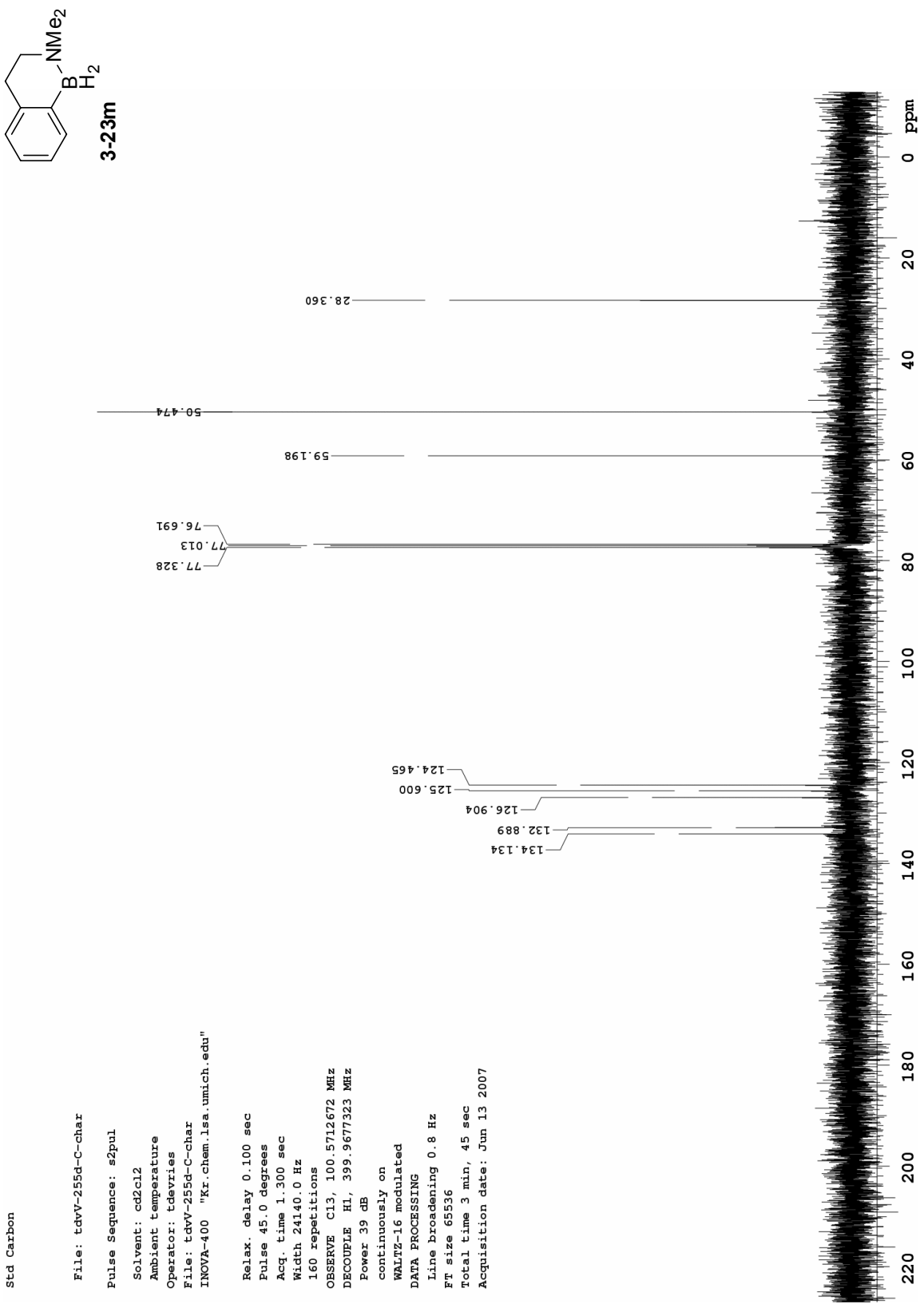


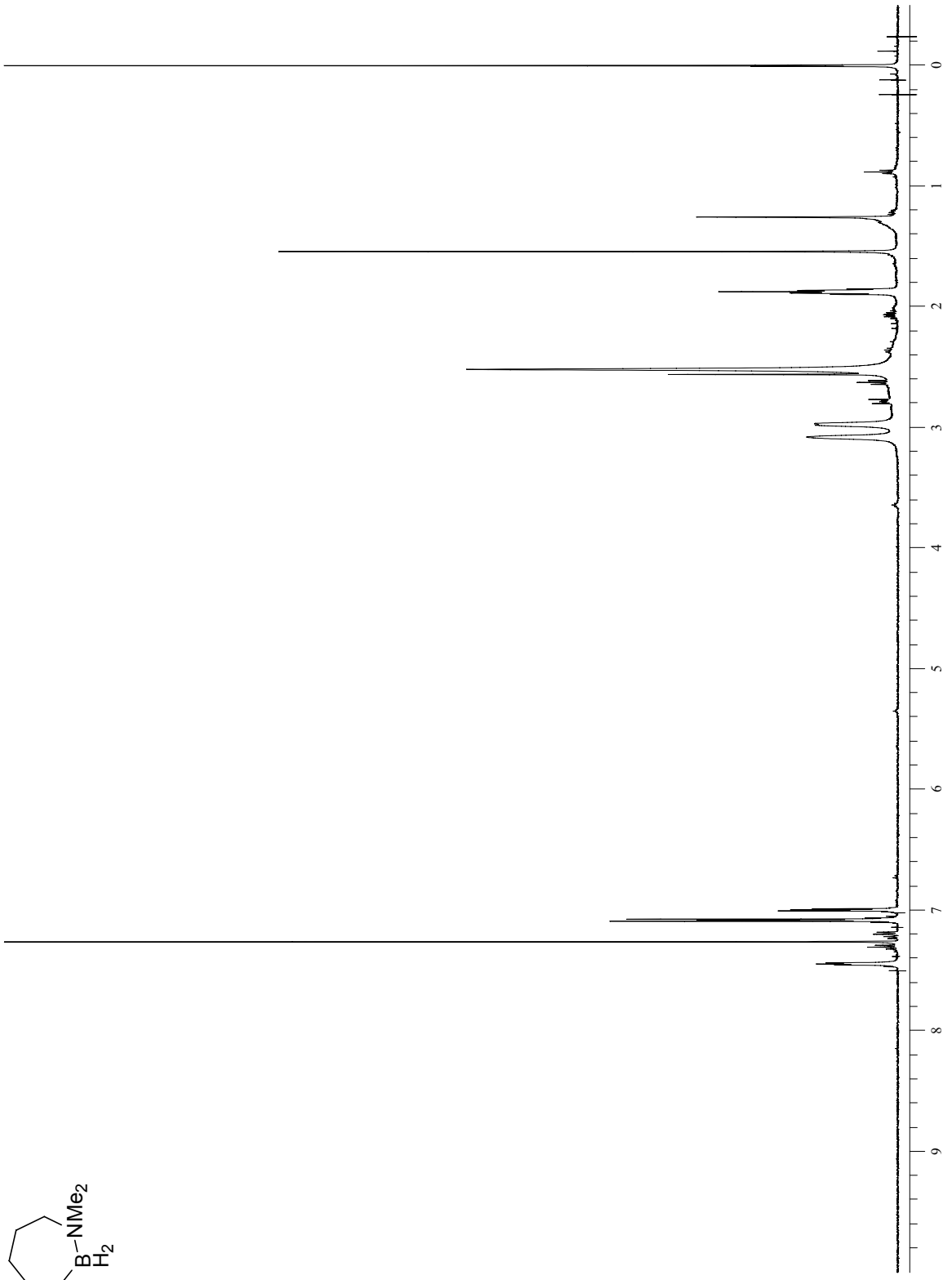
3-23k

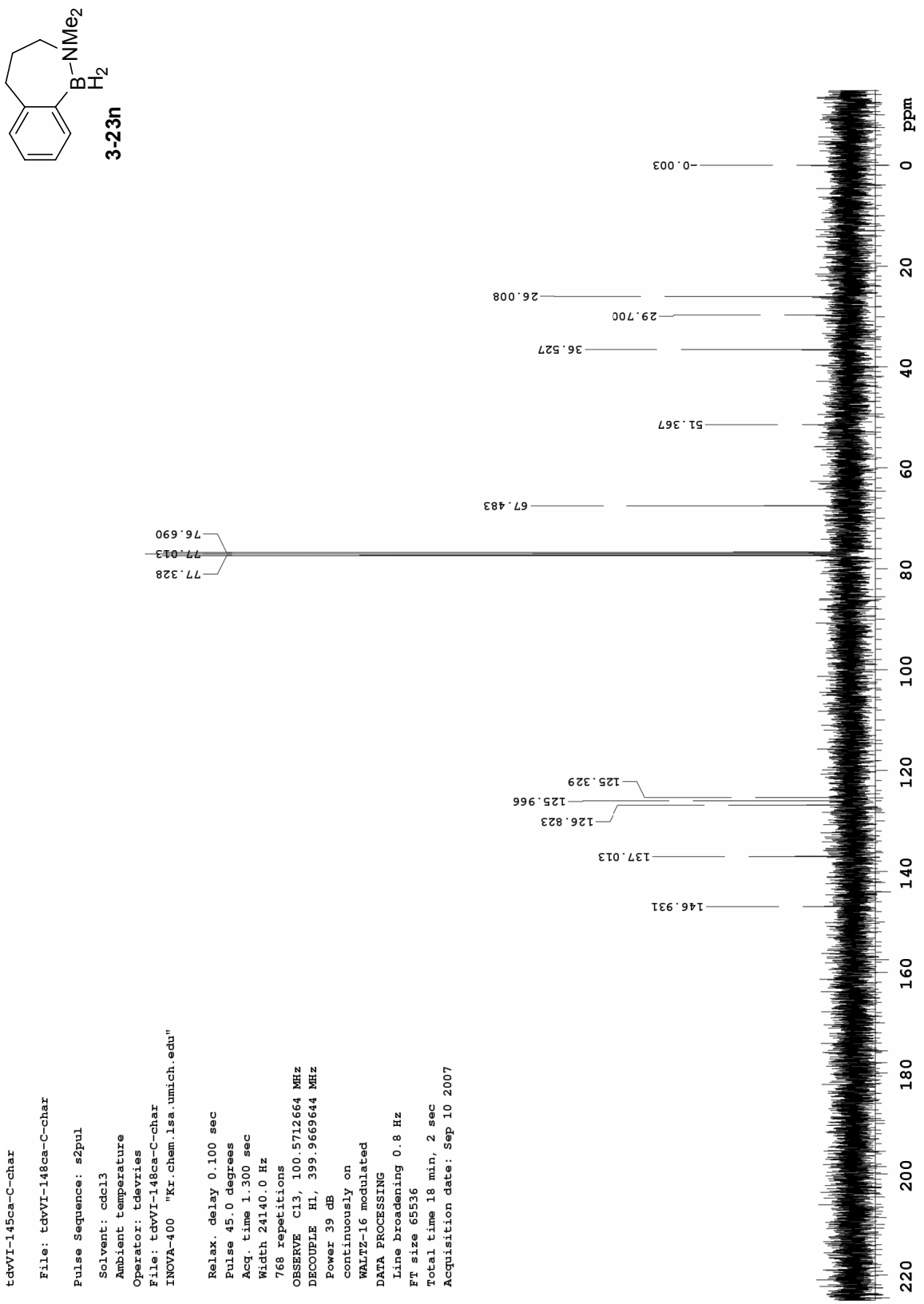

NMe2
B
H2
F
3-23k
51.107
65.428
76.708
77.023
77.338
111.217
111.407
123.992
124.109
125.017
125.039
129.207
129.266
156.933
159.394
ppm
0
20
40
60
80
100
120
140
160
180
200
220
tdvVI-192b-C
File: Carbon
Pulse Sequence: s2pul
Solvent: cdcl3
Ambient temperature
Operator: tdevries
INOVA-400 "Zr.Chem.LsA.UMich.Edu"
Relax. delay 0.100 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 24140.0 Hz
1152 repetitions
OBSERVE C13, 100.5712668 MHz
DECOUPLE H1, 399.9669644 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.8 Hz
FT size 65536
Total time 27 min, 3 sec
Acquisition date: Nov 11 2007



3-23m


Std Carbon
File: tdvV-255d-C-char
Pulse Sequence: s2pul
Solvent: cd2cl2
Ambient temperature
Operator: tdevries
File: tdvV-255d-C-char
INOVA-400 "Kr.chem.lsa.umich.edu"
Relax. delay 0.100 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 24140.0 Hz
160 repetitions
OBSERVE C13, 100.5712672 MHz
DECOUPLE H1, 399.9677323 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.8 Hz
FT size 65536
Total time 3 min, 45 sec
Acquisition date: Jun 13 2007
NMe2
B
H2
3-23m
28.360
50.474
59.198
76.691
77.013
77.328
124.465
125.600
126.904
132.889
134.134
0 ppm
20
40
60
80
100
120
140
160
180
200
220


B–NMe2
H2
3-23n



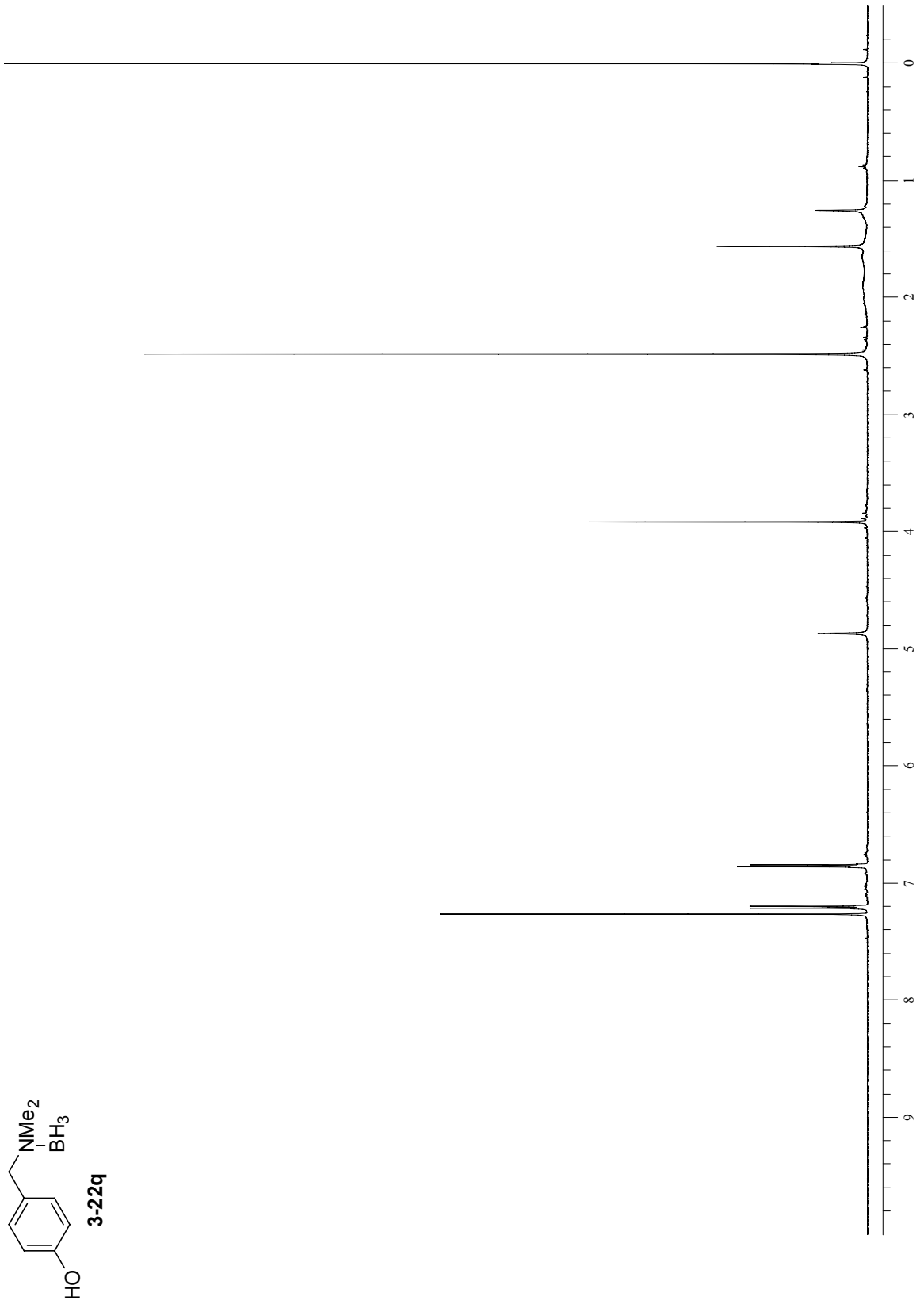
tdvVI-145ca-C-char

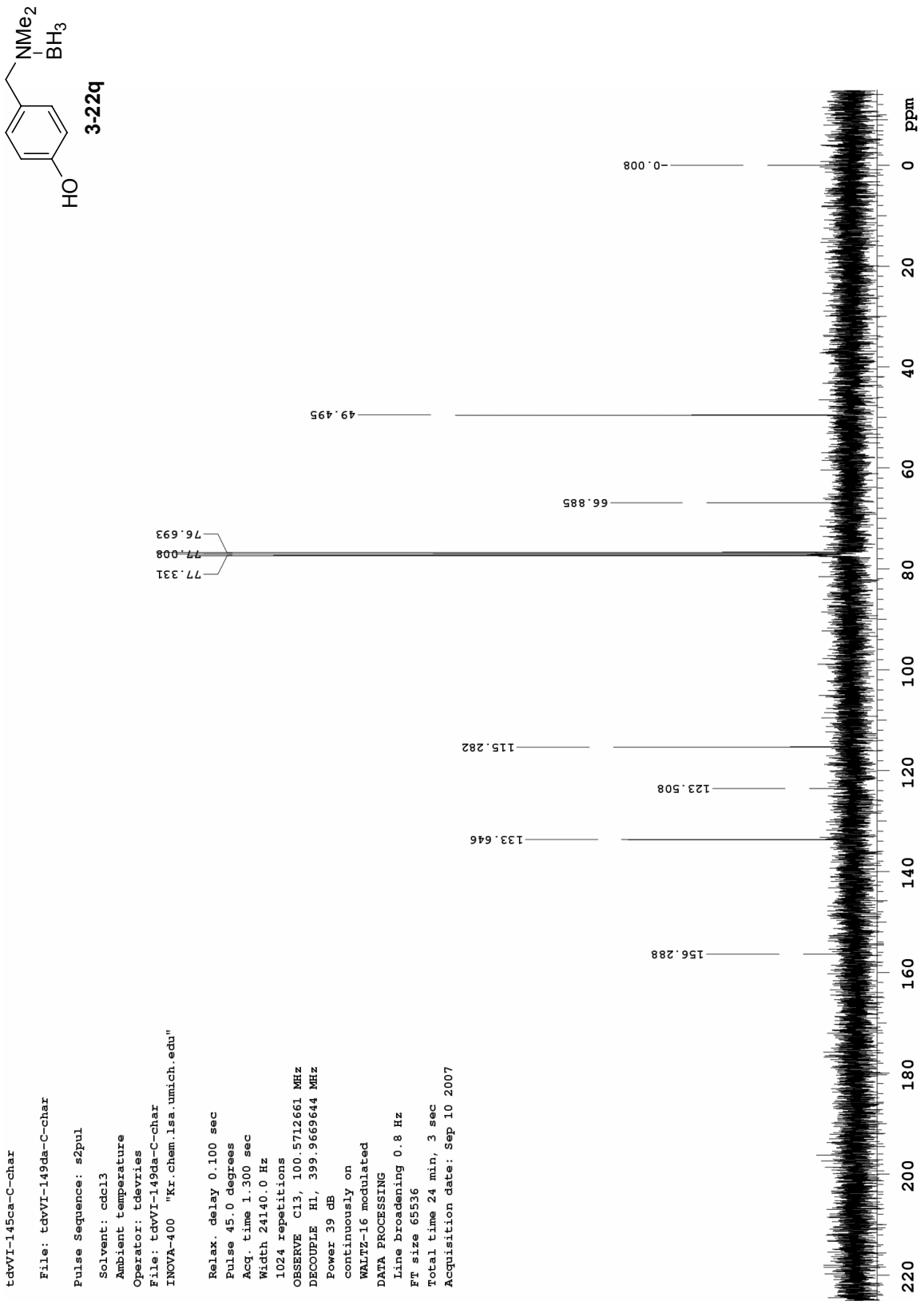
File: tdvVI-148ca-C-char

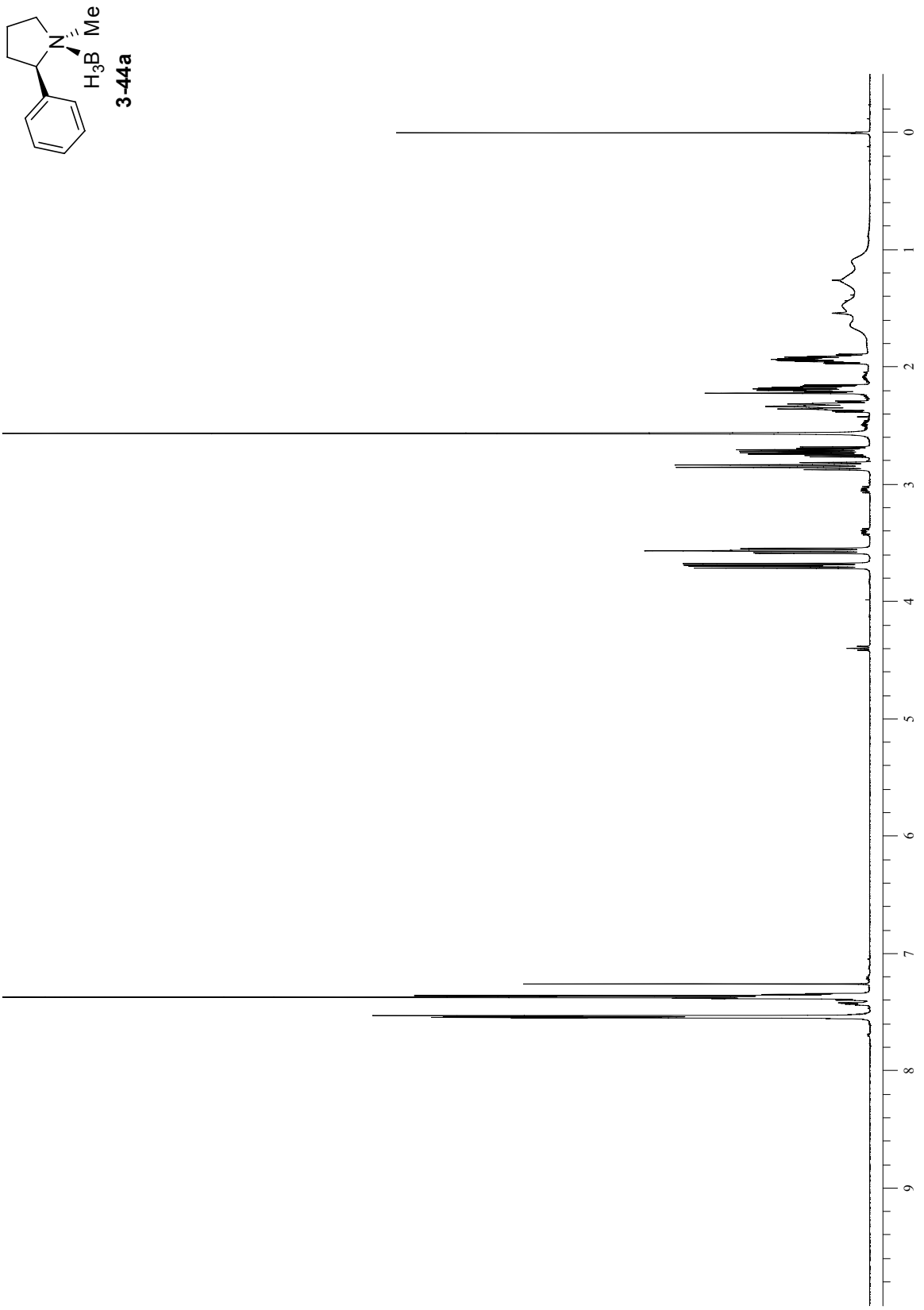
Pulse Sequence: s2pul

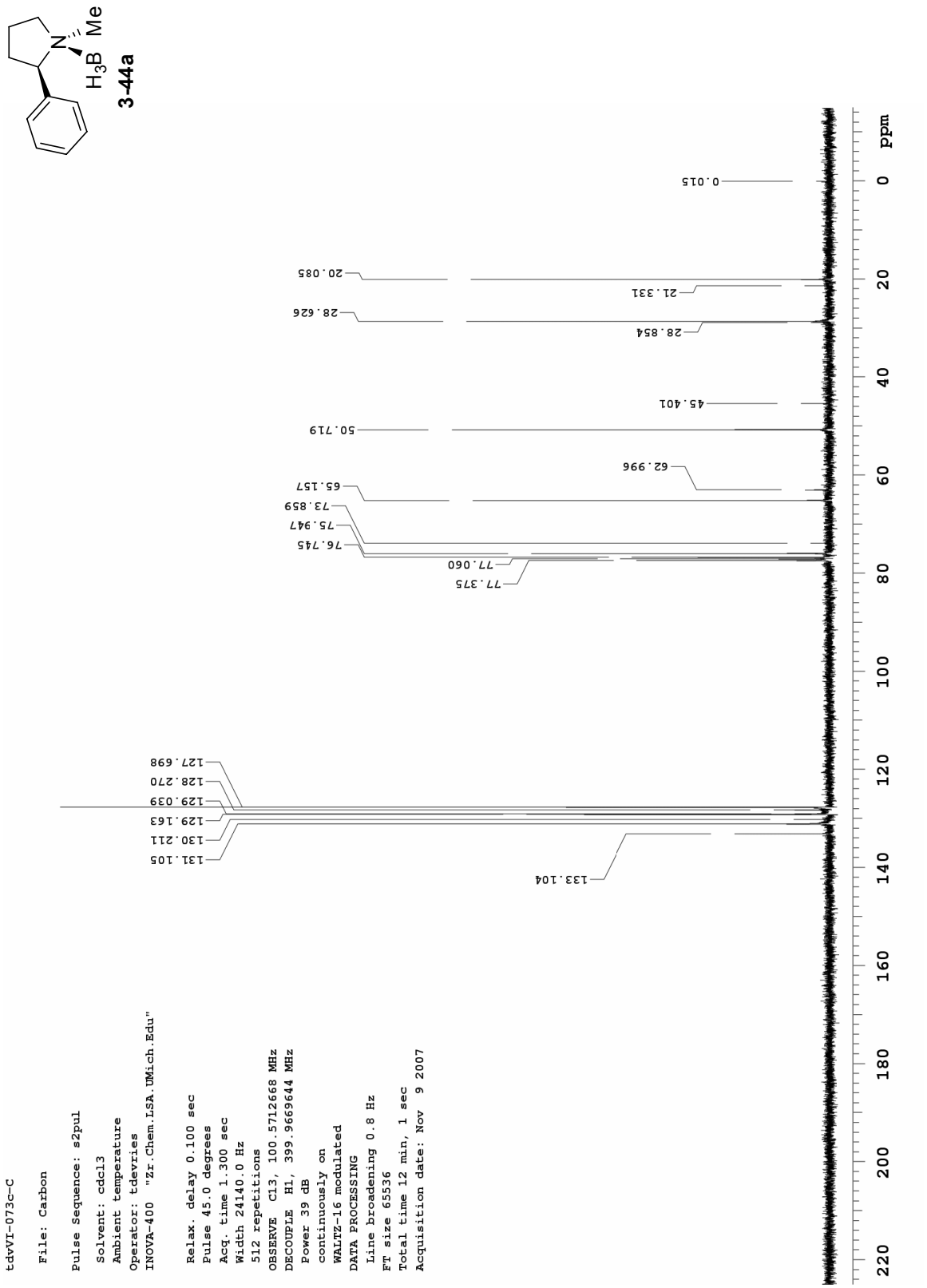
Solvent: cdcl3
Ambient temperature
Operator: tdevries
File: tdvVI-148ca-C-char
INOVA-400 "Kr.chem.lsa.umich.edu"

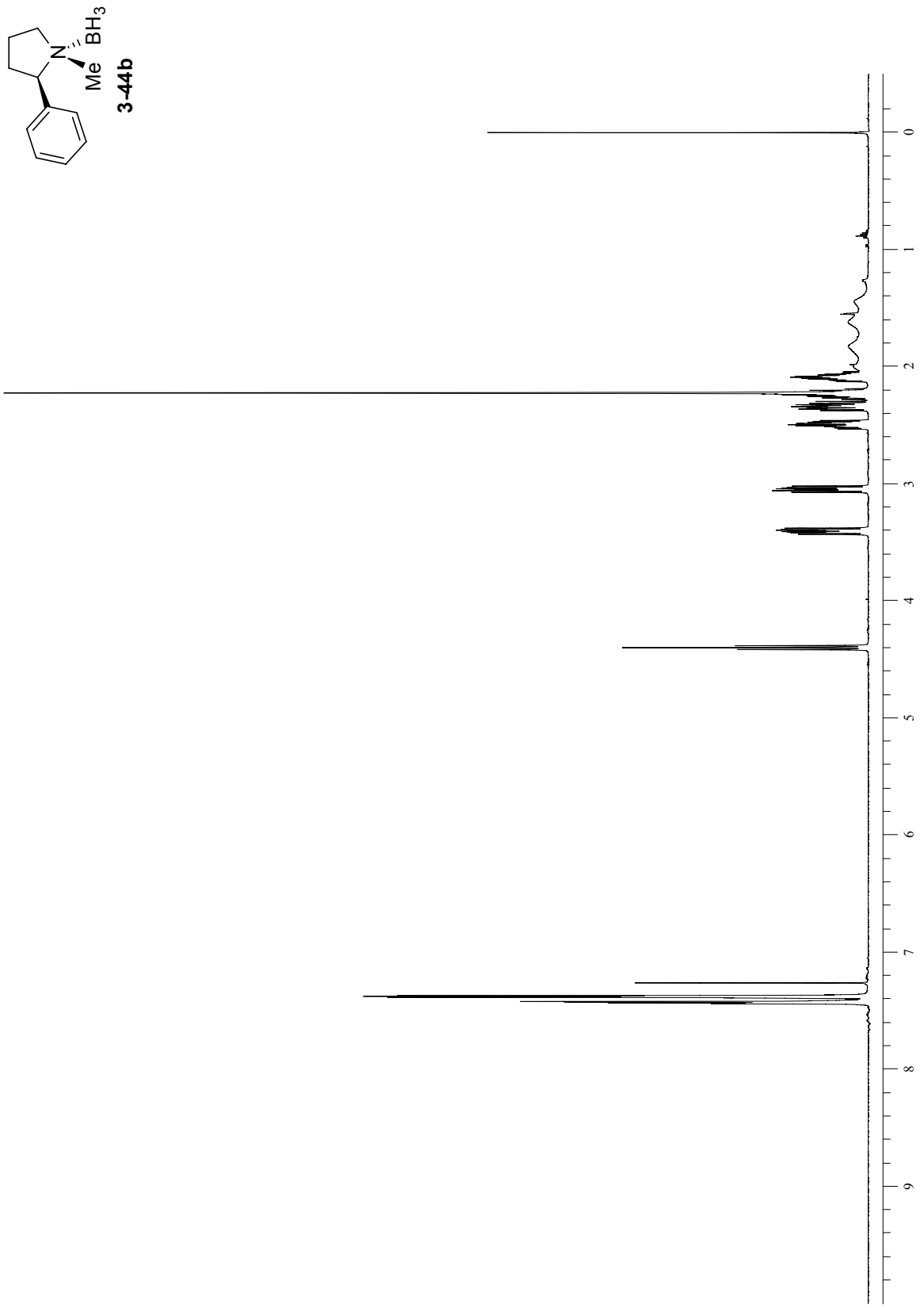
Relax. delay 0.100 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 24140.0 Hz
768 repetitions
OBSERVE C13, 100.5712664 MHz
DECOUPLE H1, 399.9669644 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.8 Hz
FT size 65536
Total time 18 min, 2 sec
Acquisition date: Sep 10 2007

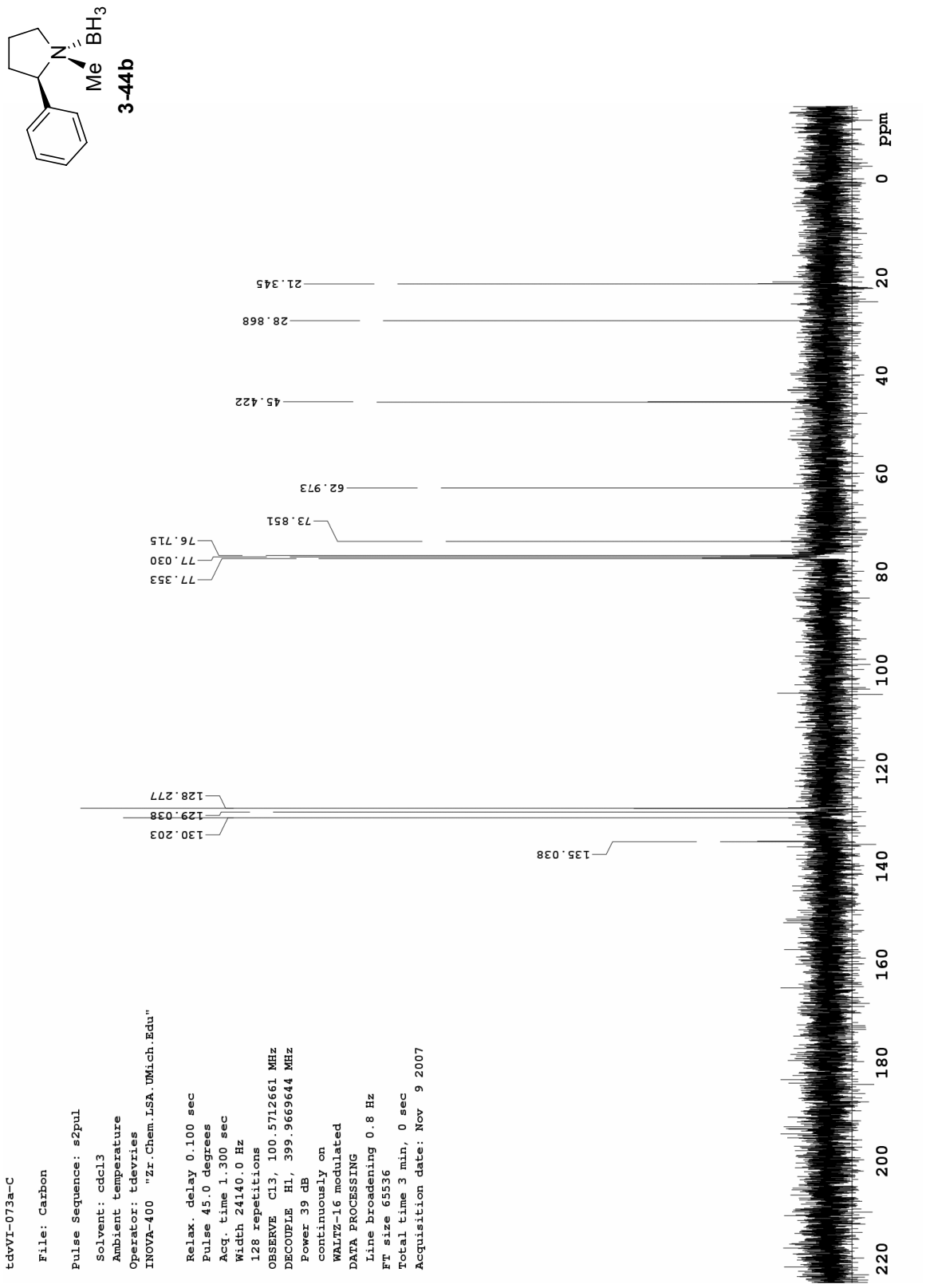

NMe2
BH3
HO
3-22q
0
1
2
3
4
5
6
7
8
9

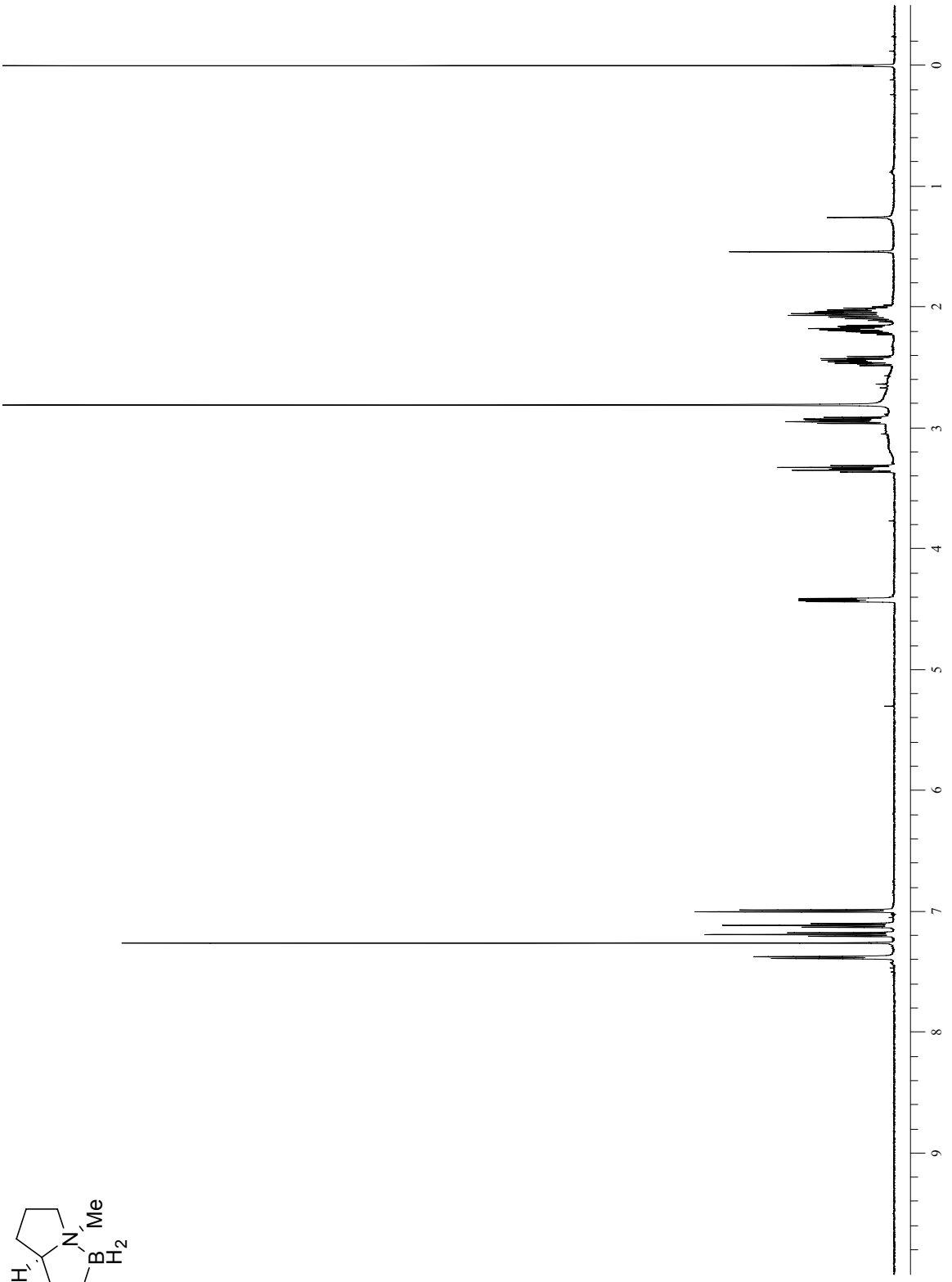

NMe2
BH3
HO
3-22q
tdvVI-145ca-C-char
File: tdvVI-149da-C-char
Pulse Sequence: s2pul
Solvent: cdcl3
Ambient temperature
Operator: tdevries
File: tdvVI-149da-C-char
INOVA-400 "Kr.chem.lsa.umich.edu"
Relax. delay 0.100 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 24140.0 Hz
1024 repetitions
OBSERVE C13, 100.5712661 MHz
DECOUPLE H1, 399.9669644 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.8 Hz
FT size 65536
Total time 24 min, 3 sec
Acquisition date: Sep 10 2007
156.288
133.646
123.508
115.282
77.331
77.008
76.693
66.885
49.495
-0.008
220
200
180
160
140
120
100
80
60
40
20
0
ppm


N
H3B Me
3-44a
0
1
2
3
4
5
6
7
8
9

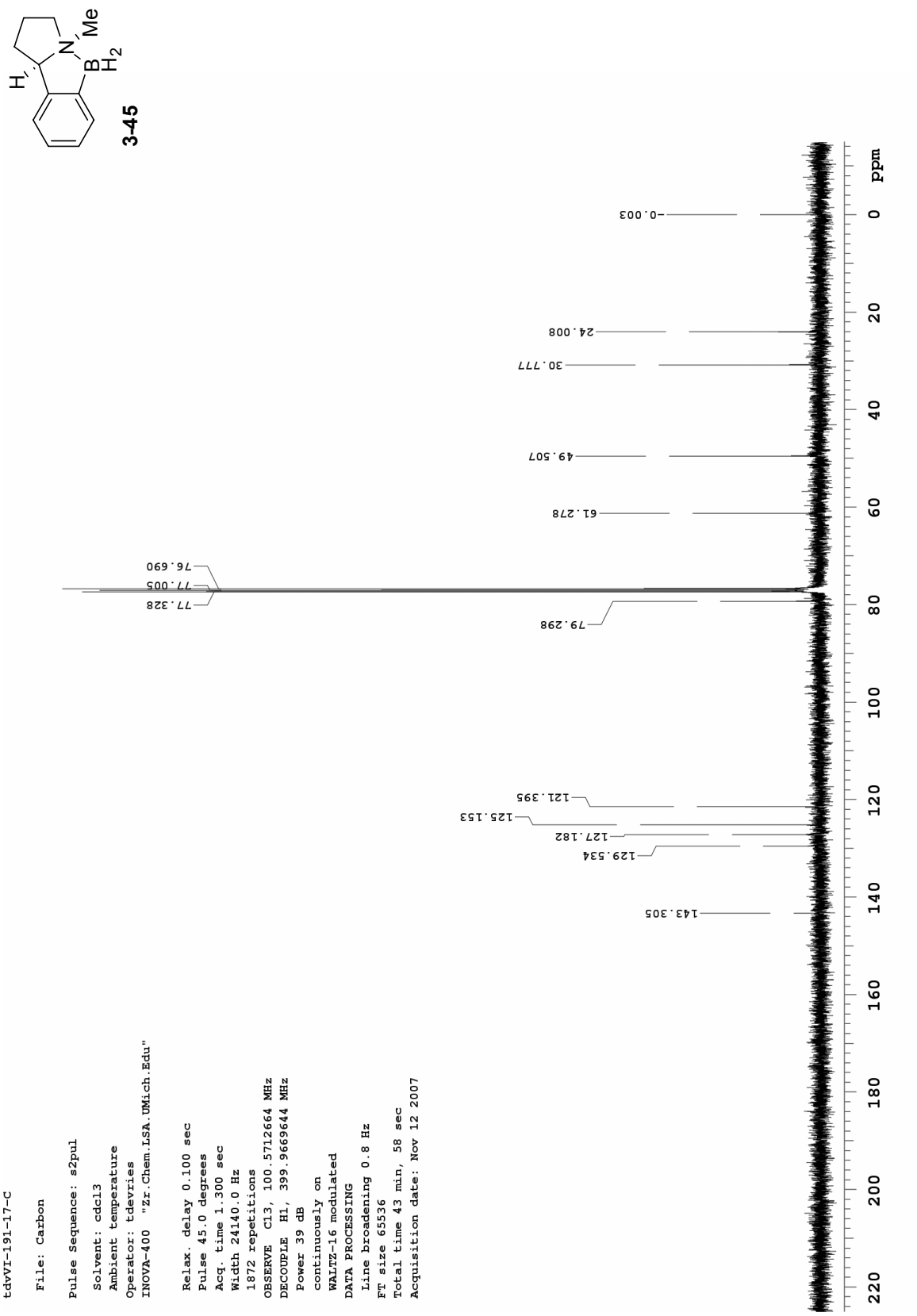

H3B Me
3-44a
tdvVI-073c-C
File: Carbon
Pulse Sequence: s2pul
Solvent: cdcl3
Ambient temperature
Operator: tdevries
INOVA-400 "Zr.Chem.LsA.UMich.Edu"
Relax. delay 0.100 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 24140.0 Hz
512 repetitions
OBSERVE C13, 100.5712668 MHz
DECOUPLE H1, 399.9669644 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.8 Hz
FT size 65536
Total time 12 min, 1 sec
Acquisition date: Nov 9 2007
0.015
20.085
21.331
28.626
28.854
45.401
50.719
62.996
65.157
73.859
75.947
76.745
77.060
77.375
127.698
128.270
129.039
129.163
130.211
131.105
133.104
ppm
0
20
40
60
80
100
120
140
160
180
200
220

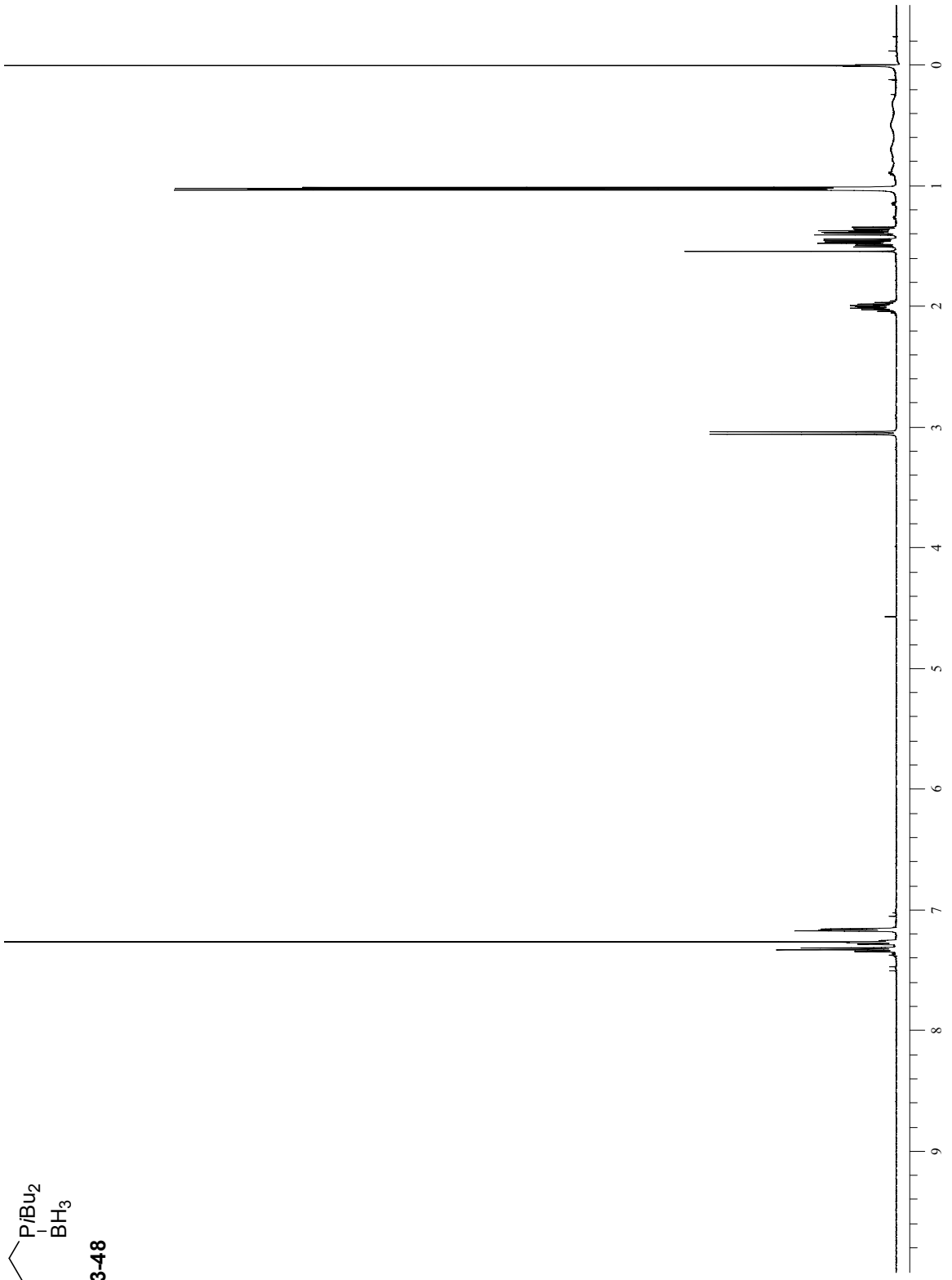

Me
BH3
3-44b


Me
BH3
N
3-44b
21.345
28.868
45.422
62.973
73.851
76.715
77.030
77.353
128.277
129.038
130.203
135.038
ppm
0
20
40
60
80
100
120
140
160
180
200
220
tdvVI-073a-C
File: Carbon
Pulse Sequence: s2pul
Solvent: cdcl3
Ambient temperature
Operator: tdevries
INOVA-400 "Zr.Chem.LsA.UMich.Edu"
Relax. delay 0.100 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 24140.0 Hz
128 repetitions
OBSERVE C13, 100.5712661 MHz
DECOUPLE H1, 399.9669644 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.8 Hz
FT size 65536
Total time 3 min, 0 sec
Acquisition date: Nov 9 2007

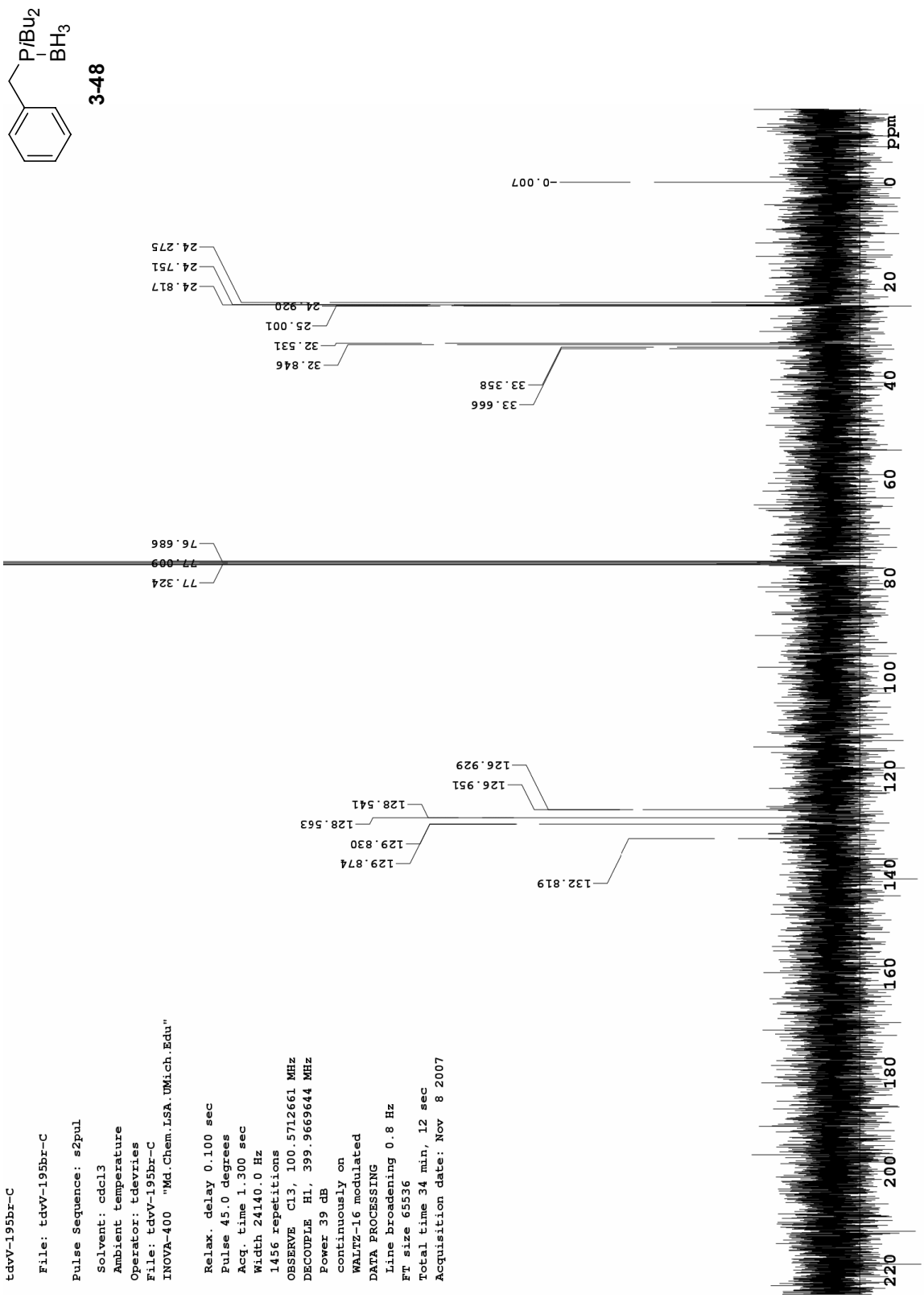


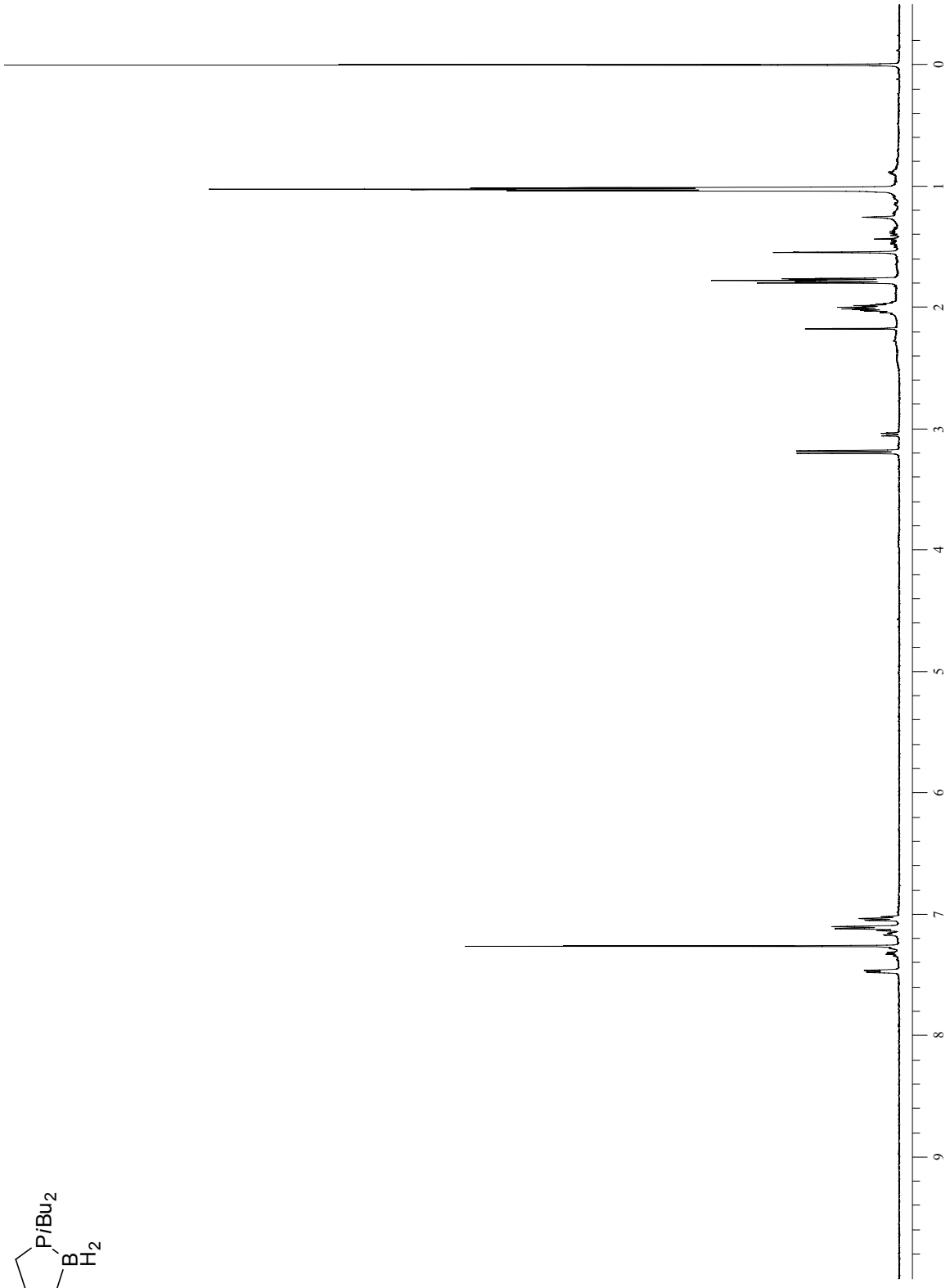
3-45


tdvVI-191-17-C
File: Carbon
Pulse Sequence: s2pul
Solvent: cdcl3
Ambient temperature
Operator: tdevries
INOVA-400 "Zr.Chem.LSA.UMich.Edu"
Relax. delay 0.100 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 24140.0 Hz
1872 repetitions
OBSERVE C13, 100.5712664 MHz
DECOUPLE H1, 399.9669644 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.8 Hz
FT size 65536
Total time 43 min, 58 sec
Acquisition date: Nov 12 2007
3-45
-0.003
24.008
30.777
49.507
61.278
76.690
77.005
77.328
79.298
121.395
125.153
127.182
129.534
143.305
ppm

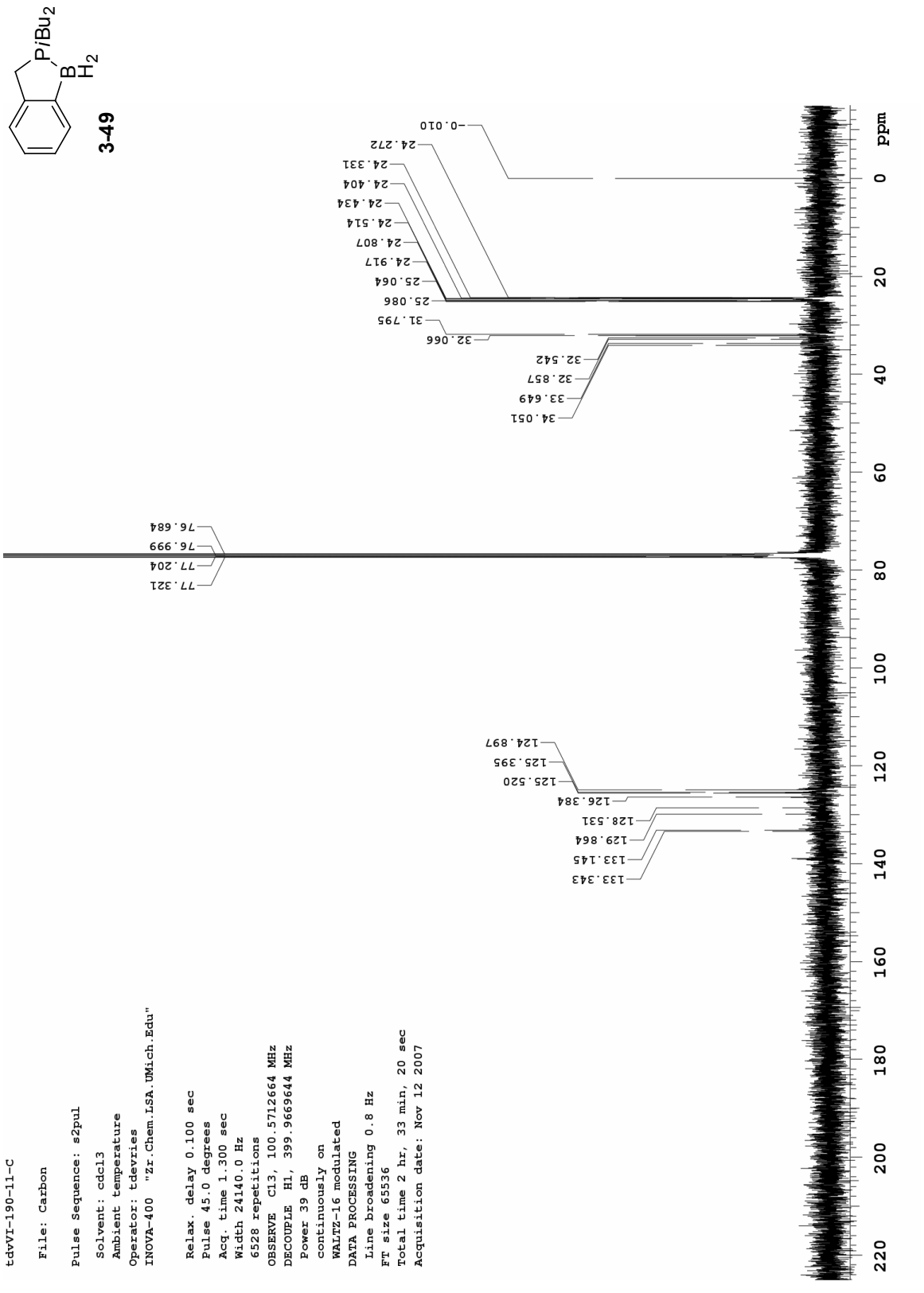


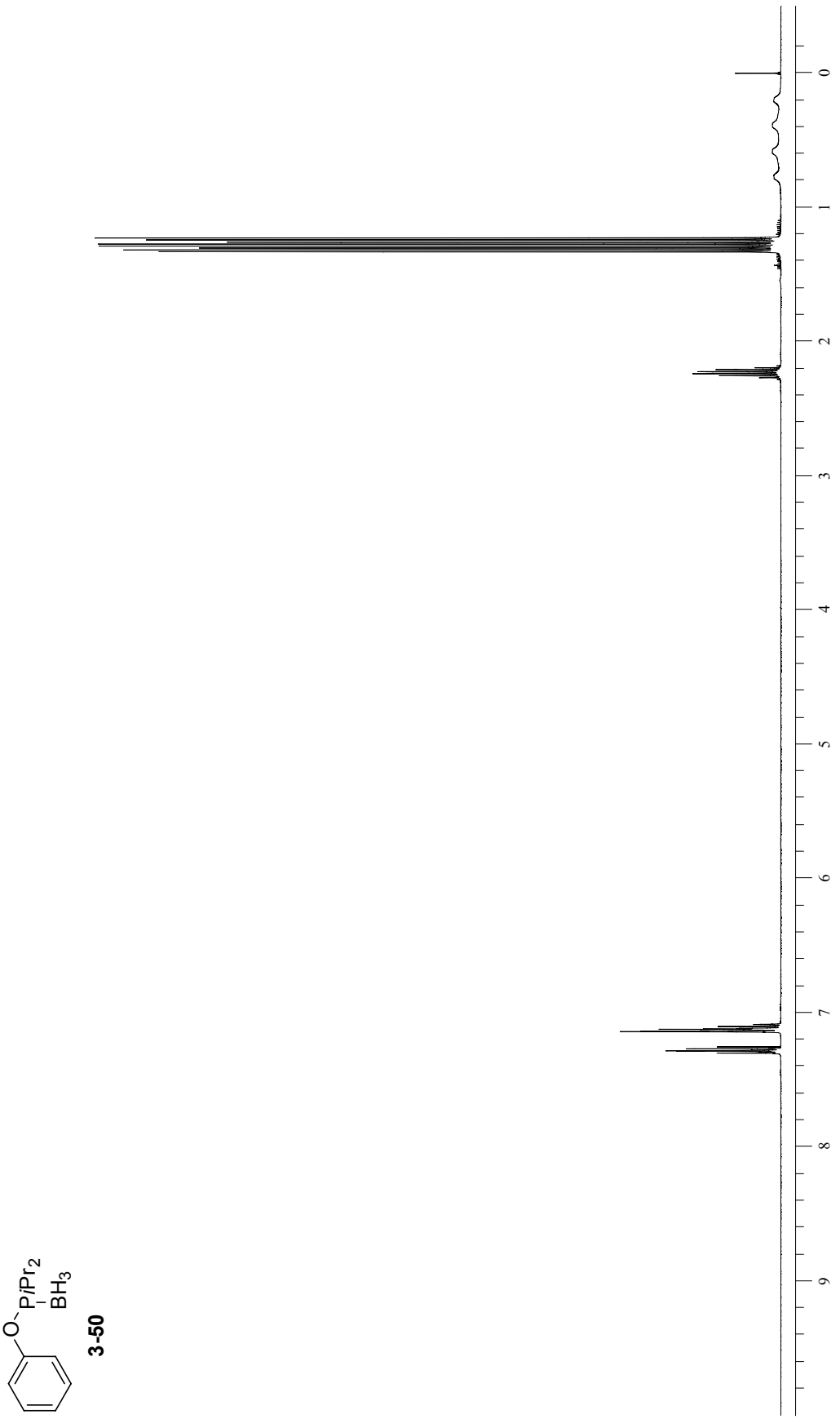
3-48


P/Bu2
BH3
3-48
tdvV-195br-C
File: tdvV-195br-C
Pulse Sequence: s2pul
Solvent: cdcl3
Ambient temperature
Operator: tdevries
File: tdvV-195br-C
INOVA-400 "Md.Chem.LSA.UMich.Edu"
Relax. delay 0.100 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 24140.0 Hz
1456 repetitions
OBSERVE C13, 100.5712661 MHz
DECOUPLE H1, 399.9669644 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.8 Hz
FT size 65536
Total time 34 min, 12 sec
Acquisition date: Nov 8 2007
-0.007
24.275
24.751
24.817
24.920
25.001
32.531
32.846
33.358
33.666
76.686
77.009
77.324
126.929
126.951
128.541
128.563
129.830
129.874
132.819
ppm
0
20
40
60
80
100
120
140
160
180
200
220

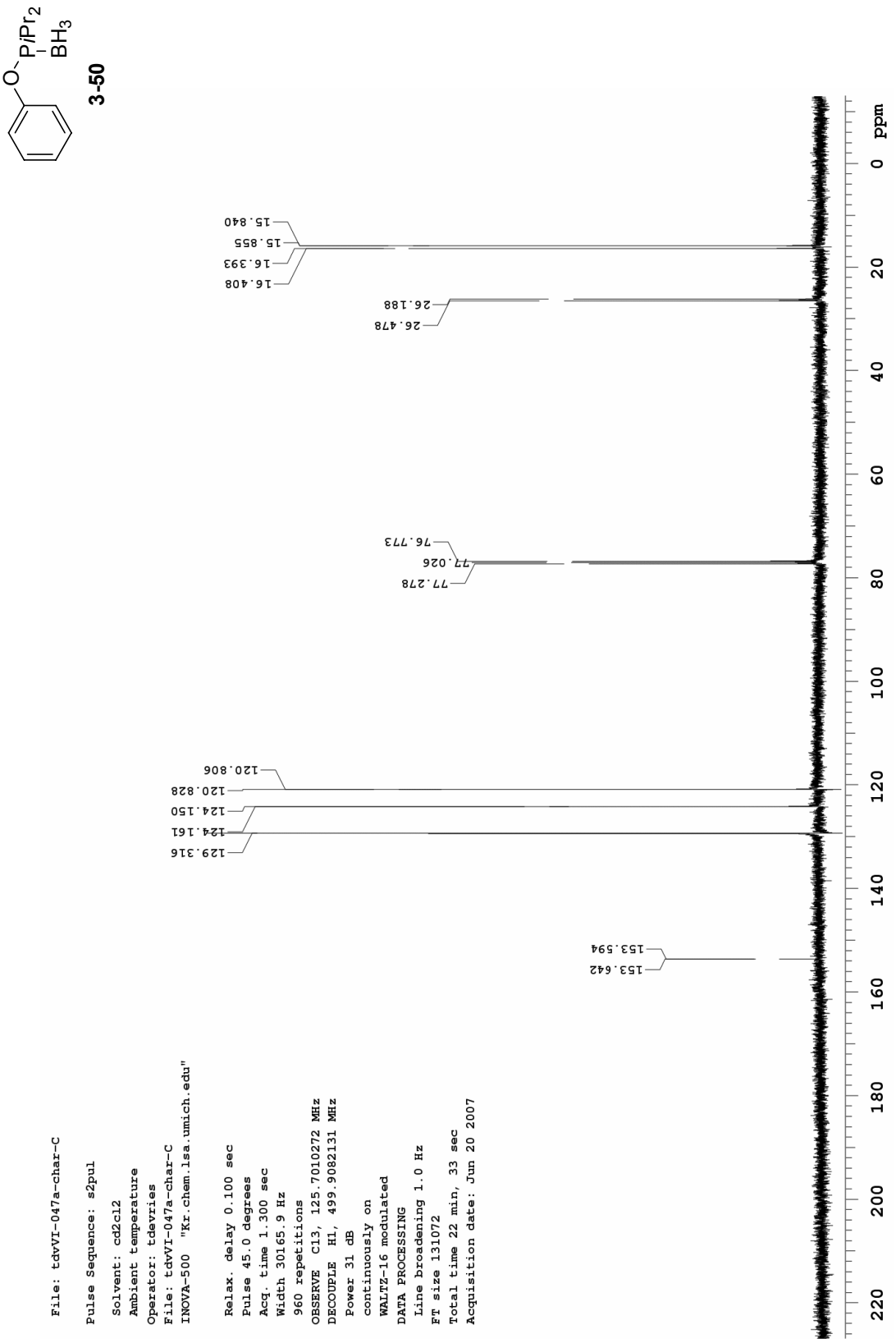


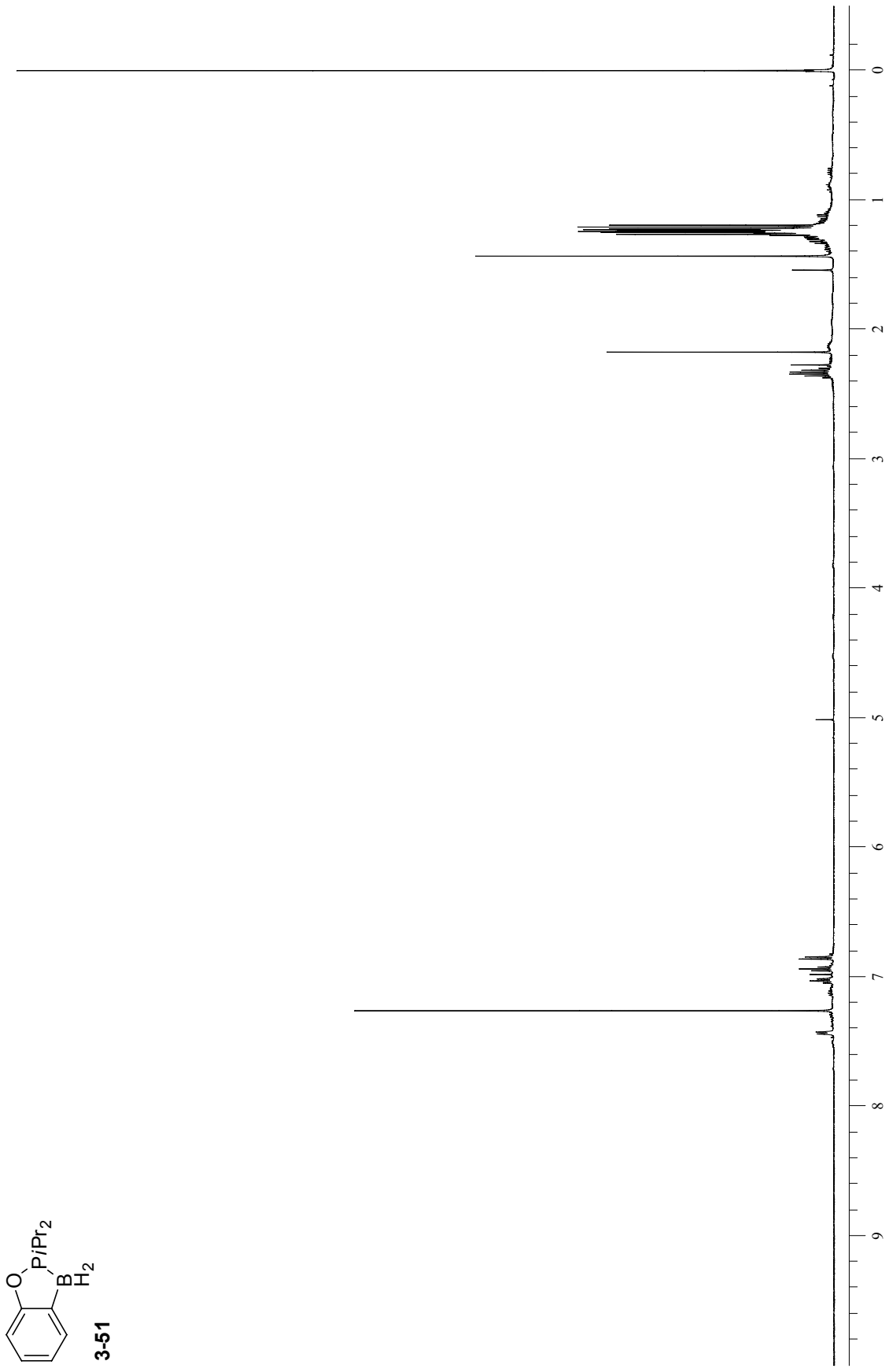
3-49


P*i*Bu2
B
H2
3-49
tdvVI-190-11-C
File: Carbon
Pulse Sequence: s2pul
Solvent: cdcl3
Ambient temperature
Operator: tdevries
INOVA-400 "Zr.Chem.LsA.UMich.Edu"
Relax. delay 0.100 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 24140.0 Hz
6528 repetitions
OBSERVE C13, 100.5712664 MHz
DECOUPLE H1, 399.9669644 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.8 Hz
FT size 65536
Total time 2 hr, 33 min, 20 sec
Acquisition date: Nov 12 2007
77.321
77.204
76.999
76.684
34.051
33.649
32.857
32.542
32.066
31.795
25.086
25.064
24.917
24.807
24.514
24.434
24.404
24.331
24.272
-0.010
133.343
133.145
129.864
128.531
126.384
125.520
125.395
124.897
ppm
0
20
40
60
80
100
120
140
160
180
200
220

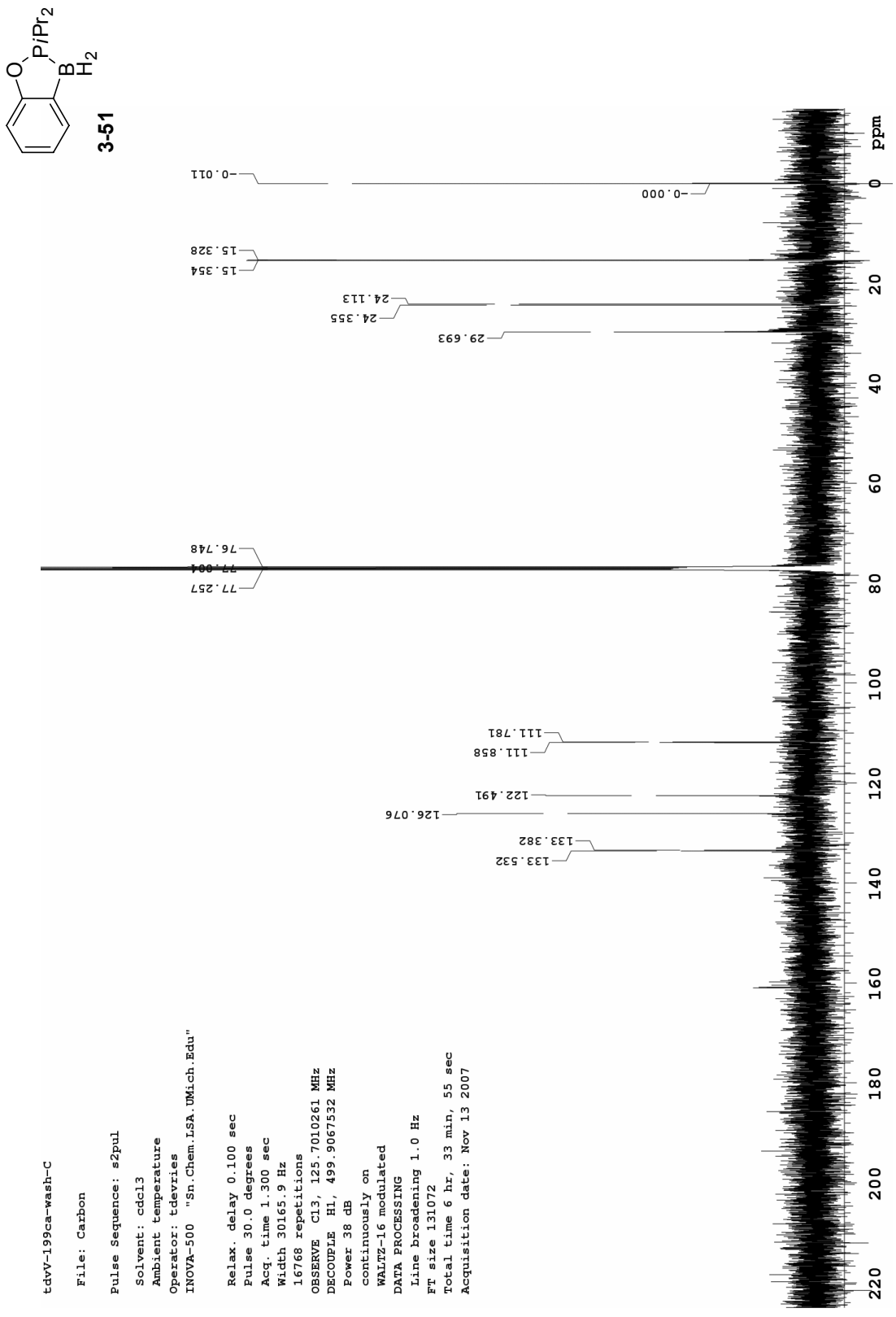


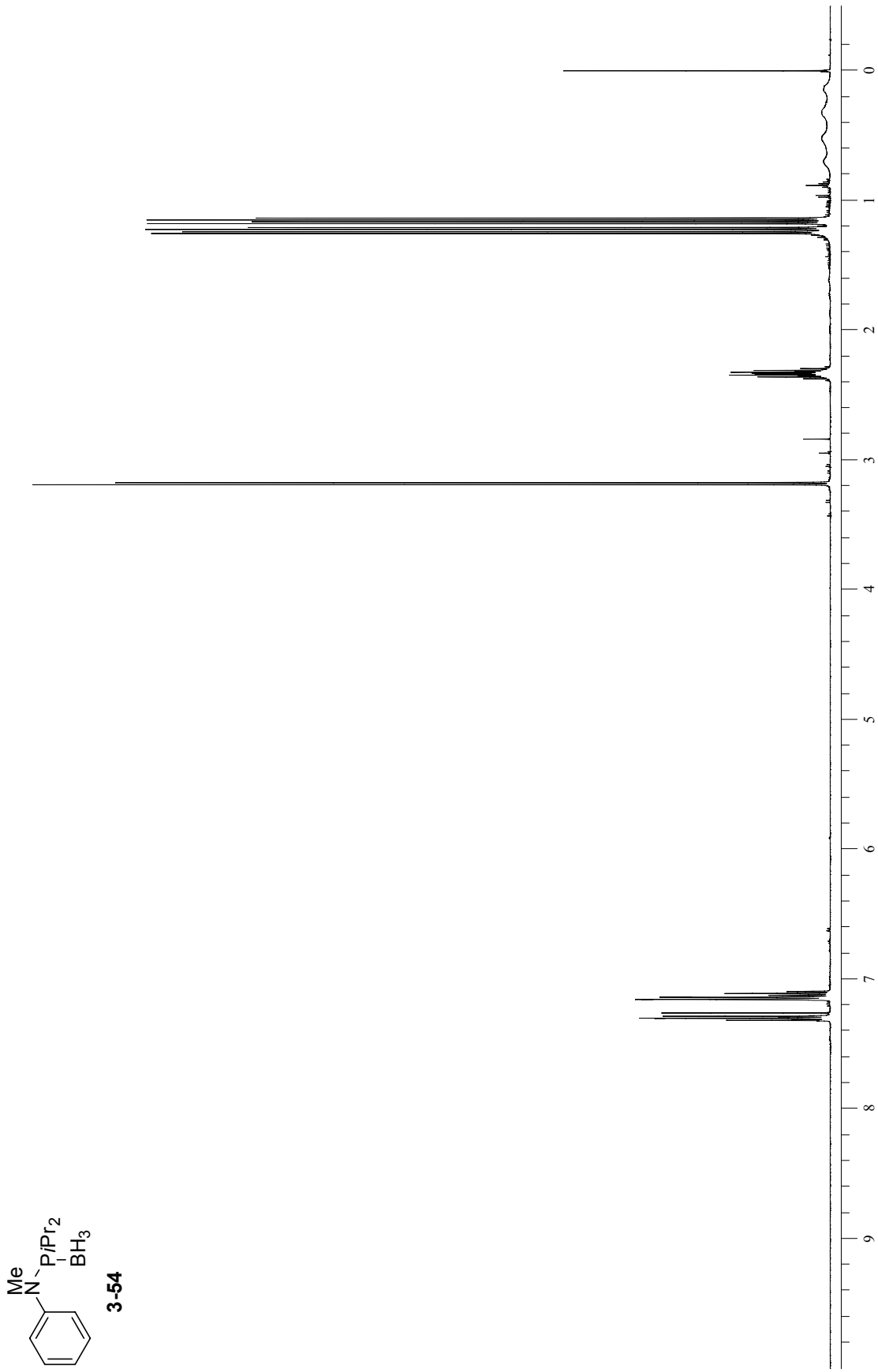
3-50

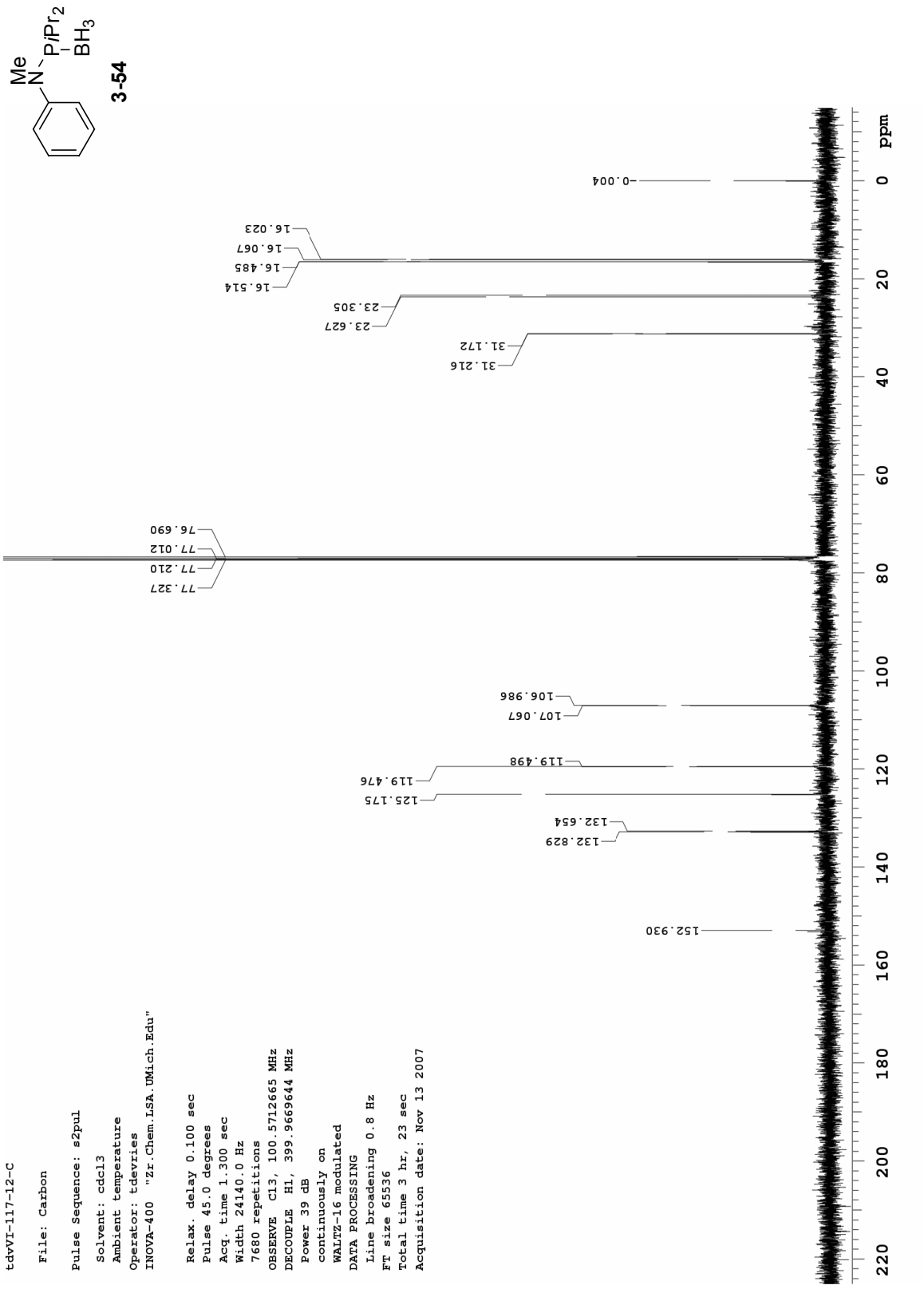

O
P/Pr2
BH3
3-50
153.642
153.594
129.316
124.161
124.150
120.828
120.806
77.278
77.026
76.773
26.478
26.188
16.408
16.393
15.855
15.840
0 ppm
20
40
60
80
100
120
140
160
180
200
220
File: tdvVI-047a-char-C
Pulse Sequence: s2pul
Solvent: cd2cl2
Ambient temperature
Operator: tdevries
File: tdvVI-047a-char-C
INOVA-500 "Kr.chem.lsa.umich.edu"
Relax. delay 0.100 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 30165.9 Hz
960 repetitions
OBSERVE C13, 125.7010272 MHz
DECOUPLE H1, 499.9082131 MHz
Power 31 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 131072
Total time 22 min, 33 sec
Acquisition data: Jun 20 2007

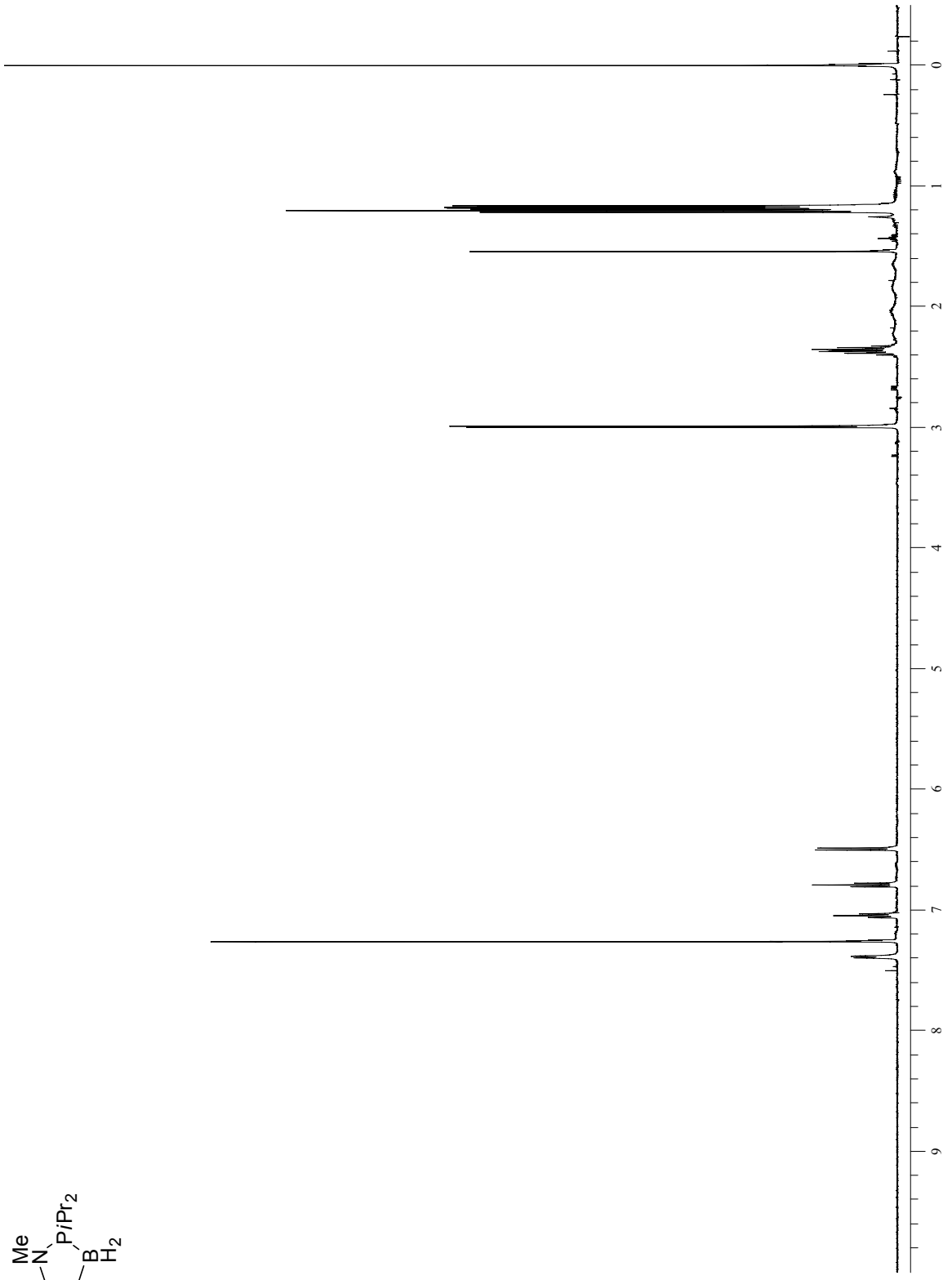


3-51

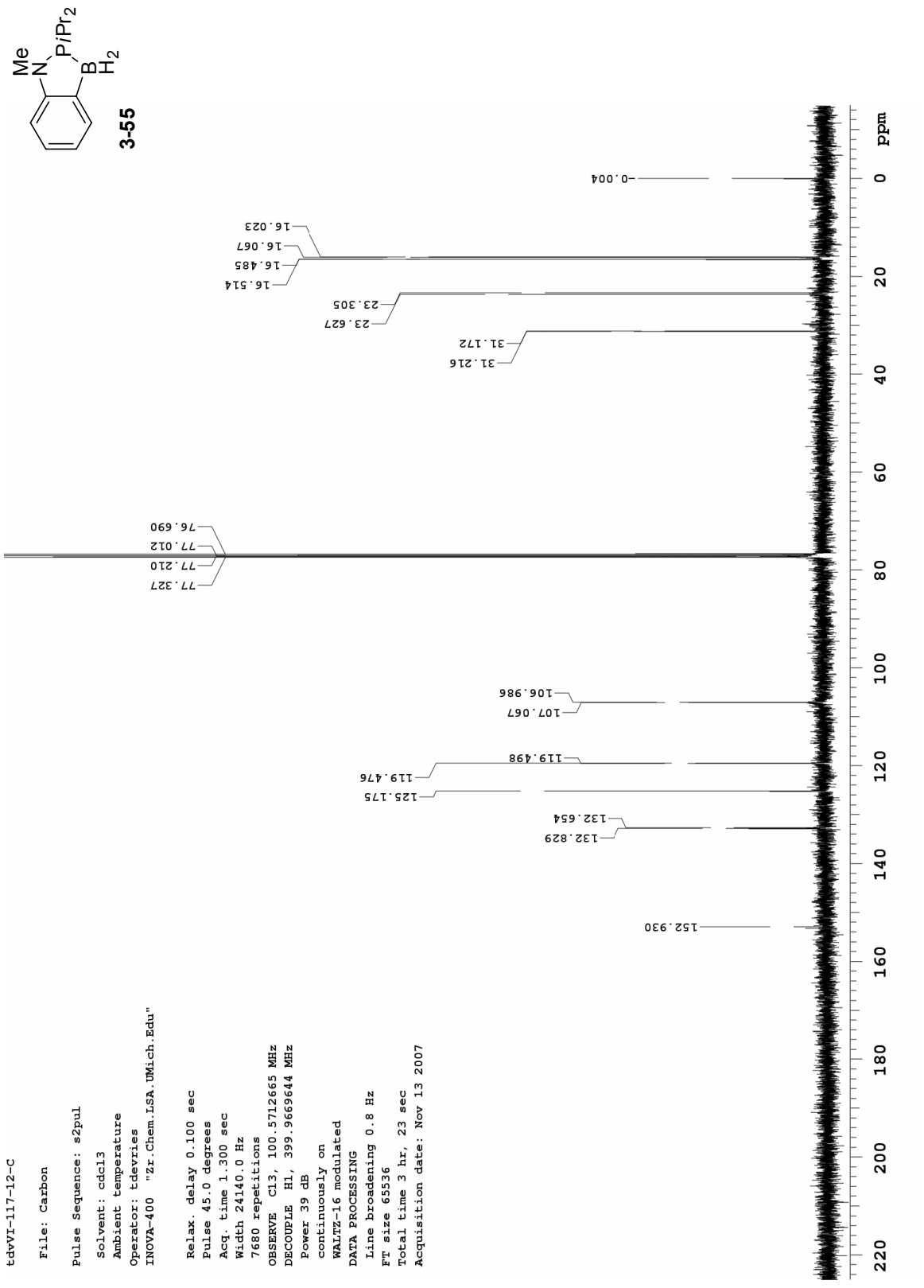

3-51
tdvV-199ca-wash-C
File: Carbon
Pulse Sequence: s2pul
Solvent: cdcl3
Ambient temperature
Operator: tdevries
INOVA-500 "Sn.Chem.LSA.UMich.Edu"
Relax. delay 0.100 sec
Pulse 30.0 degrees
Acq. time 1.300 sec
Width 30165.9 Hz
16768 repetitions
OBSERVE C13, 125.7010261 MHz
DECOUPLE H1, 499.9067532 MHz
Power 38 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 131072
Total time 6 hr, 33 min, 55 sec
Acquisition date: Nov 13 2007
-0.011
-0.000
15.354
15.328
24.113
24.355
29.693
76.748
77.257
111.858
111.781
122.491
126.076
133.382
133.532
ppm

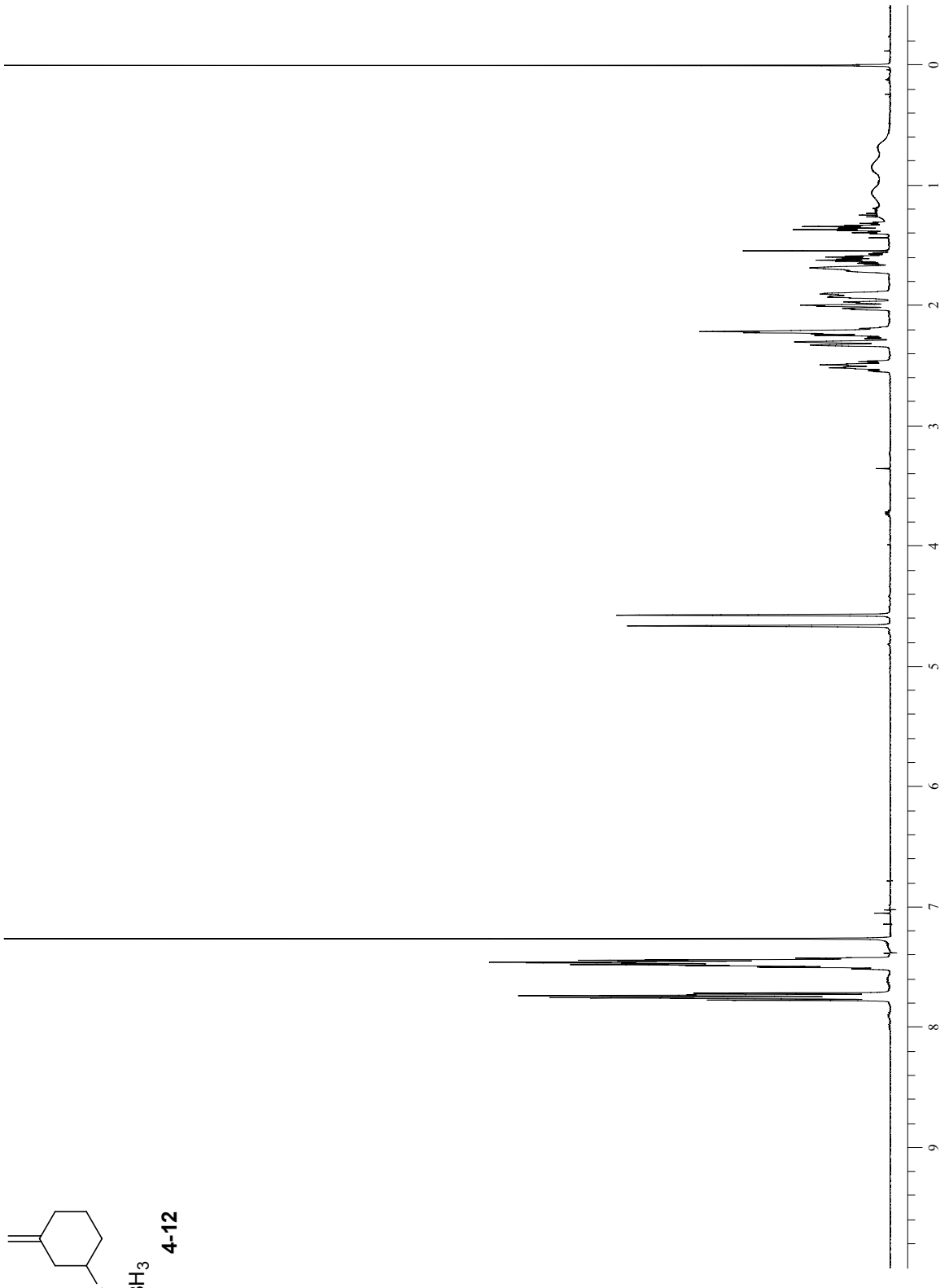

Me
N
P*i*Pr$_2$
BH$_3$
3-54
0
1
2
3
4
5
6
7
8
9

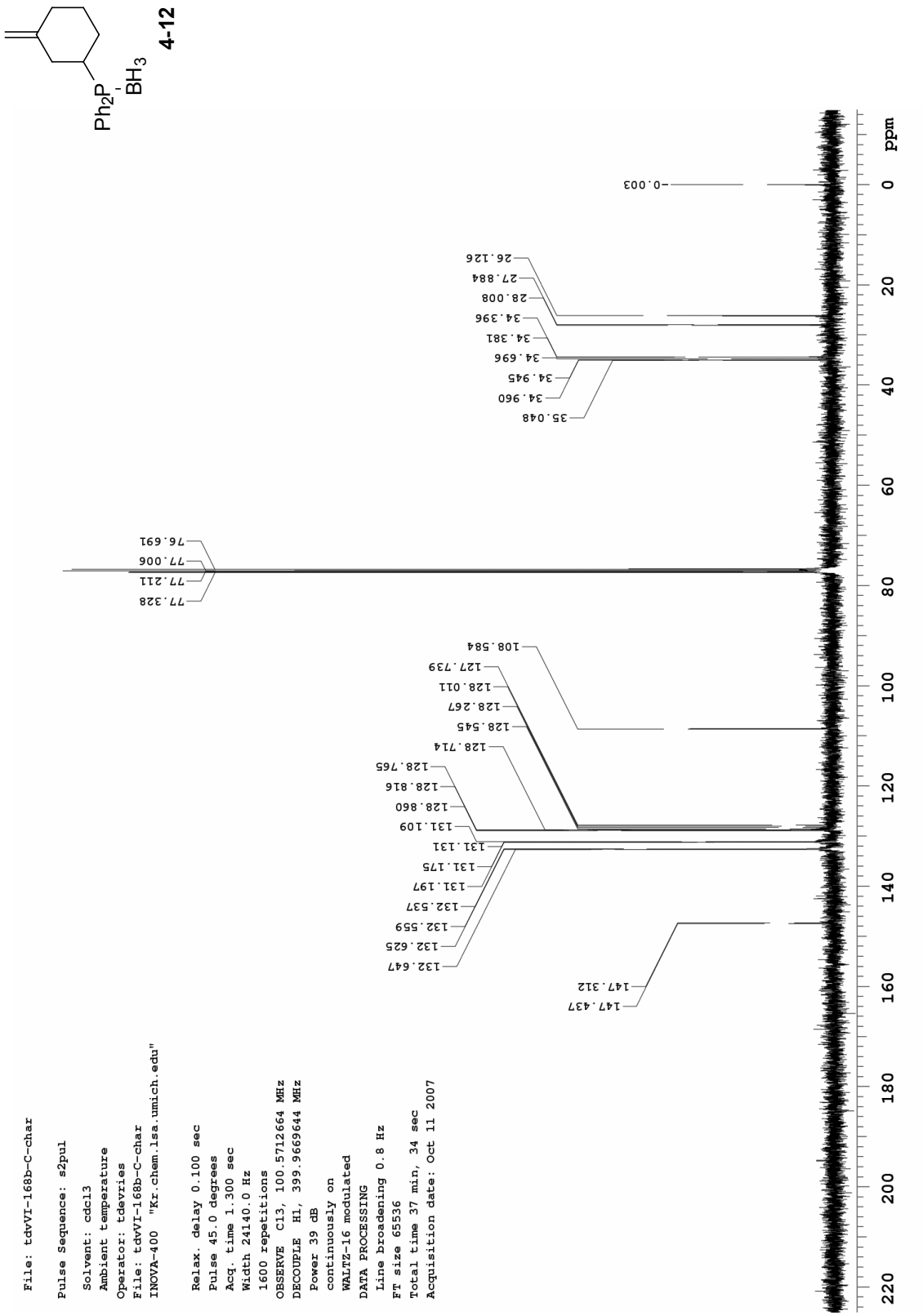

Me
N
P*i*Pr2
BH3
3-54
tdvVI-117-12-C
File: Carbon
Pulse Sequence: s2pul
Solvent: cdcl3
Ambient temperature
Operator: tdevries
INOVA-400 "Zr.Chem.LSA.UMich.Edu"
Relax. delay 0.100 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 24140.0 Hz
7680 repetitions
OBSERVE C13, 100.5712665 MHz
DECOUPLE H1, 399.9669644 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.8 Hz
FT size 65536
Total time 3 hr, 23 sec
Acquisition date: Nov 13 2007
-0.004
16.023
16.067
16.485
16.514
23.305
23.627
31.172
31.216
76.690
77.012
77.210
77.327
106.986
107.067
119.498
119.476
125.175
132.654
132.829
152.930
ppm
0
20
40
60
80
100
120
140
160
180
200
220

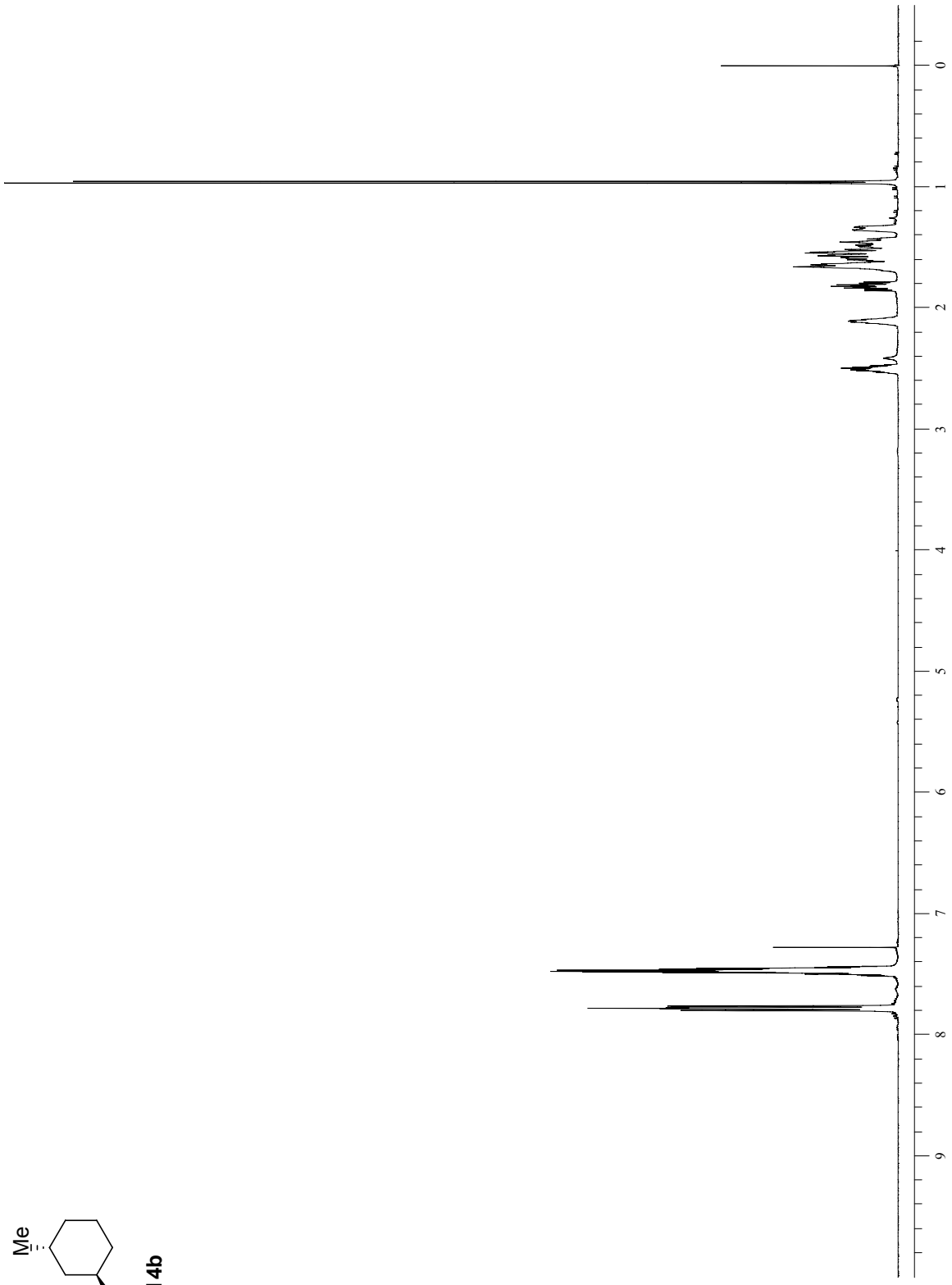


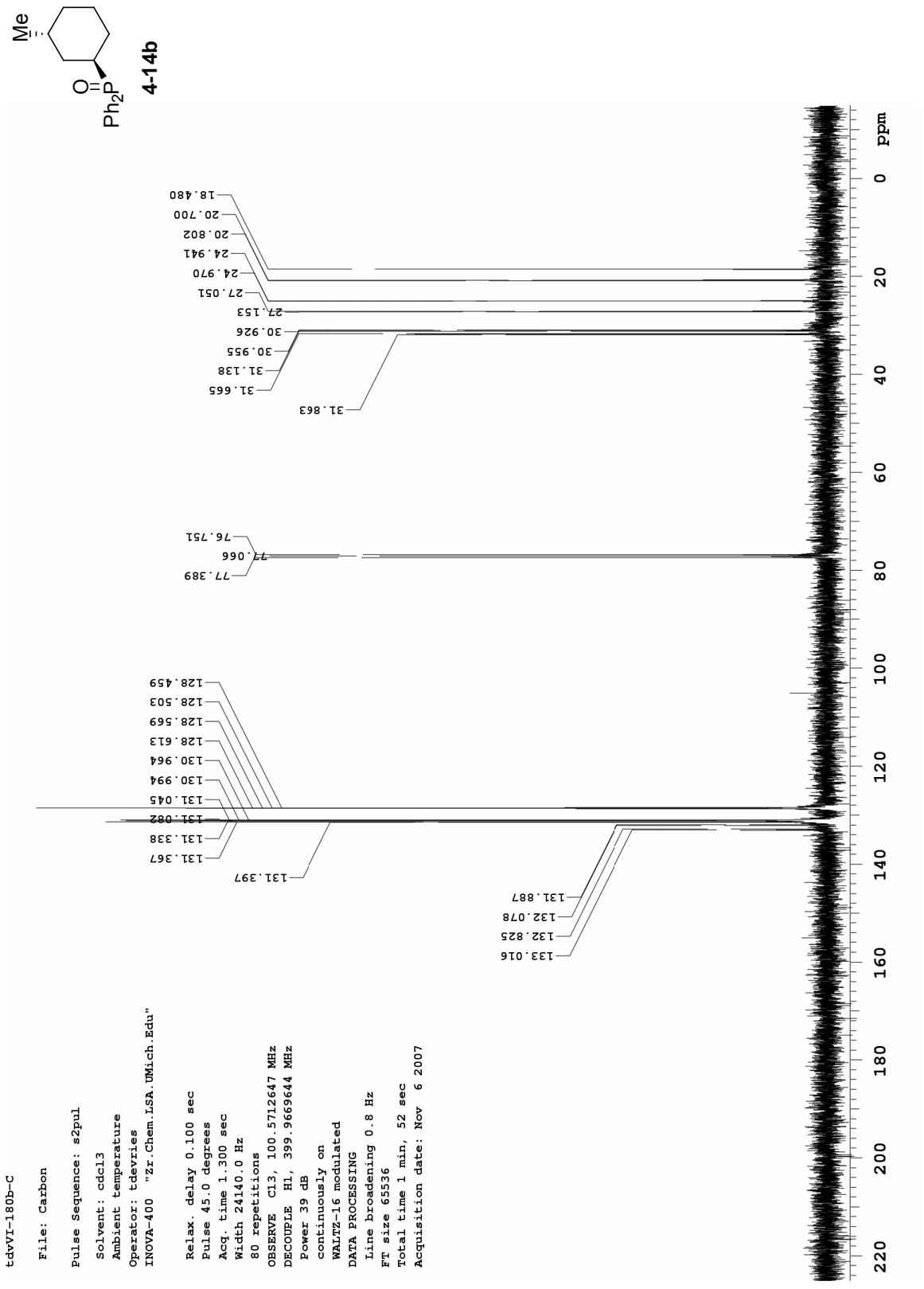
3-55

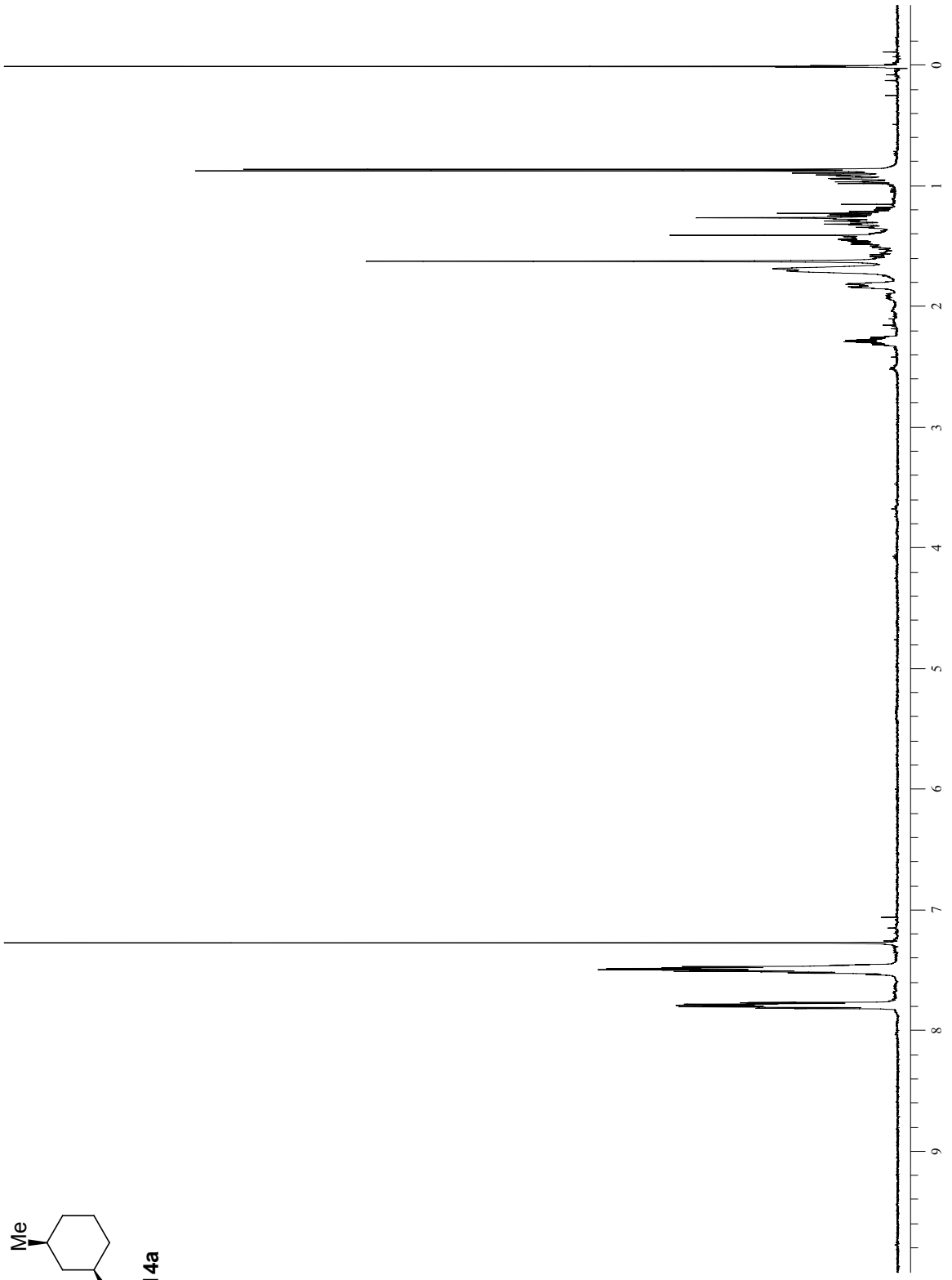

Me
N
PiPr2
B
H2
3-55
-0.004
16.023
16.067
16.485
16.514
23.305
23.627
31.172
31.216
76.690
77.012
77.210
77.327
106.986
107.067
119.476
119.498
125.175
132.654
132.829
152.930
ppm
0
20
40
60
80
100
120
140
160
180
200
220
tdVVI-117-12-C
File: Carbon
Pulse Sequence: s2pul
Solvent: cdcl3
Ambient temperature
Operator: tdevries
INOVA-400 "Zr.Chem.LsA.UMich.Edu"
Relax. delay 0.100 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 24140.0 Hz
7680 repetitions
OBSERVE C13, 100.5712665 MHz
DECOUPLE H1, 399.9669644 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.8 Hz
FT size 65536
Total time 3 hr, 23 sec
Acquisition date: Nov 13 2007

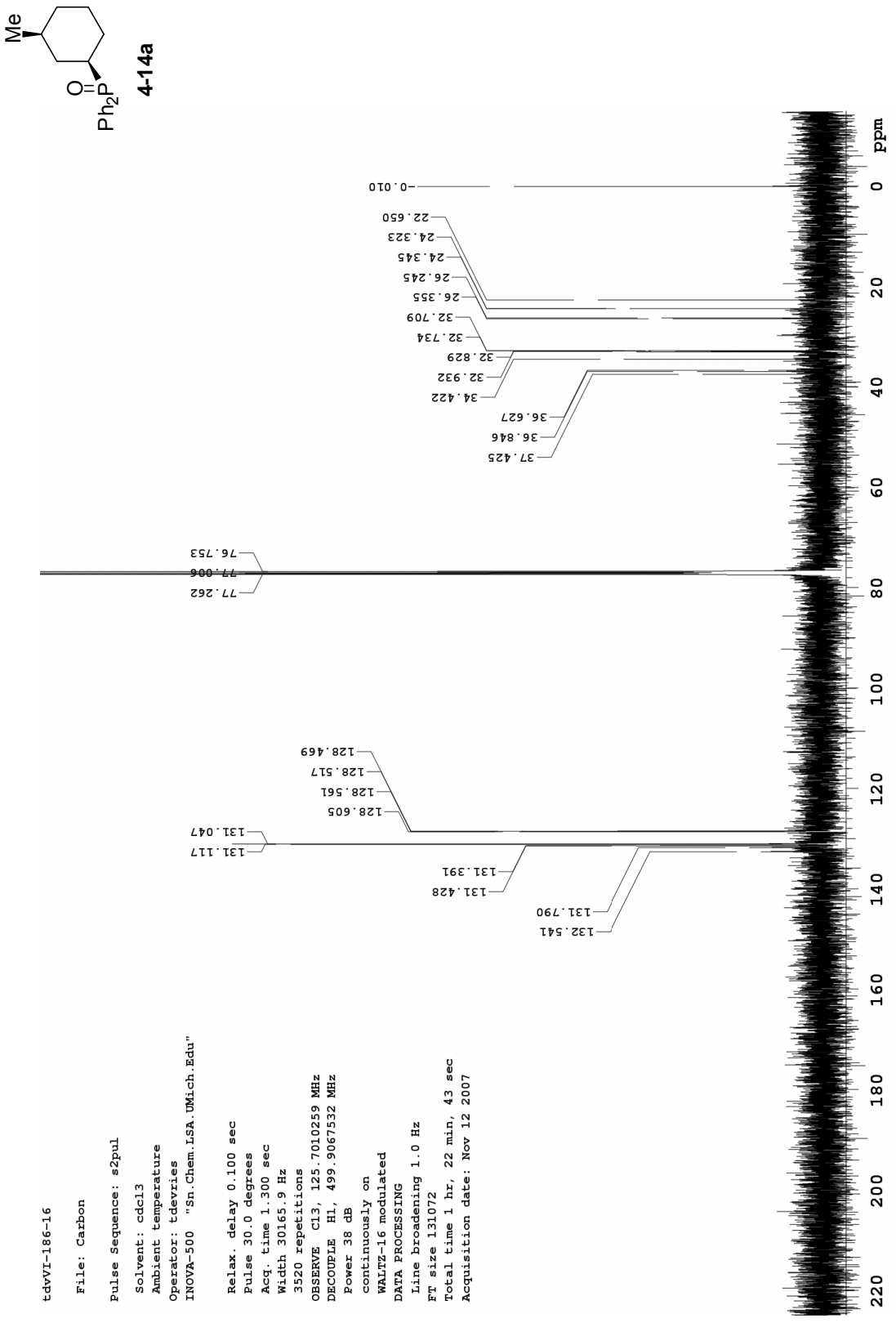

Ph2P
BH3
4-12
0
1
2
3
4
5
6
7
8
9

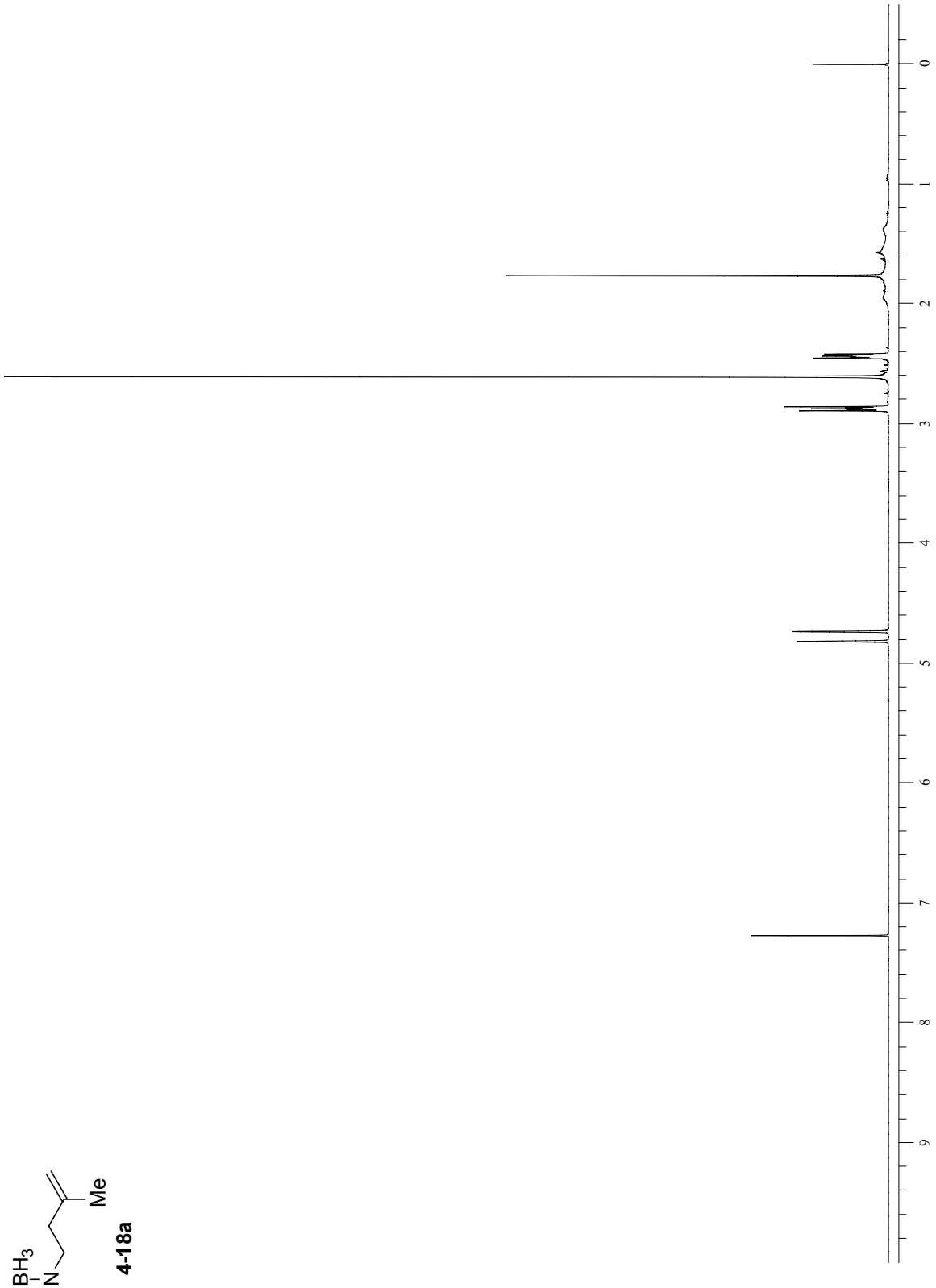

Ph2P
BH3
4-12
File: tdvVI-168b-C-char
Pulse Sequence: s2pul
Solvent: cdcl3
Ambient temperature
Operator: tdevries
File: tdvVI-168b-C-char
INOVA-400 "Kr.chem.lsa.umich.edu"
Relax. delay 0.100 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 24140.0 Hz
1600 repetitions
OBSERVE C13, 100.5712664 MHz
DECOUPLE H1, 399.9669644 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.8 Hz
FT size 65536
Total time 37 min, 34 sec
Acquisition date: Oct 11 2007
147.437
147.312
132.647
132.625
132.559
132.537
131.197
131.175
131.131
131.109
128.860
128.816
128.765
128.714
128.545
128.267
128.011
127.739
108.584
77.328
77.211
77.006
76.691
35.048
34.960
34.945
34.696
34.381
34.396
28.008
27.884
26.126
-0.003
ppm
0
20
40
60
80
100
120
140
160
180
200
220

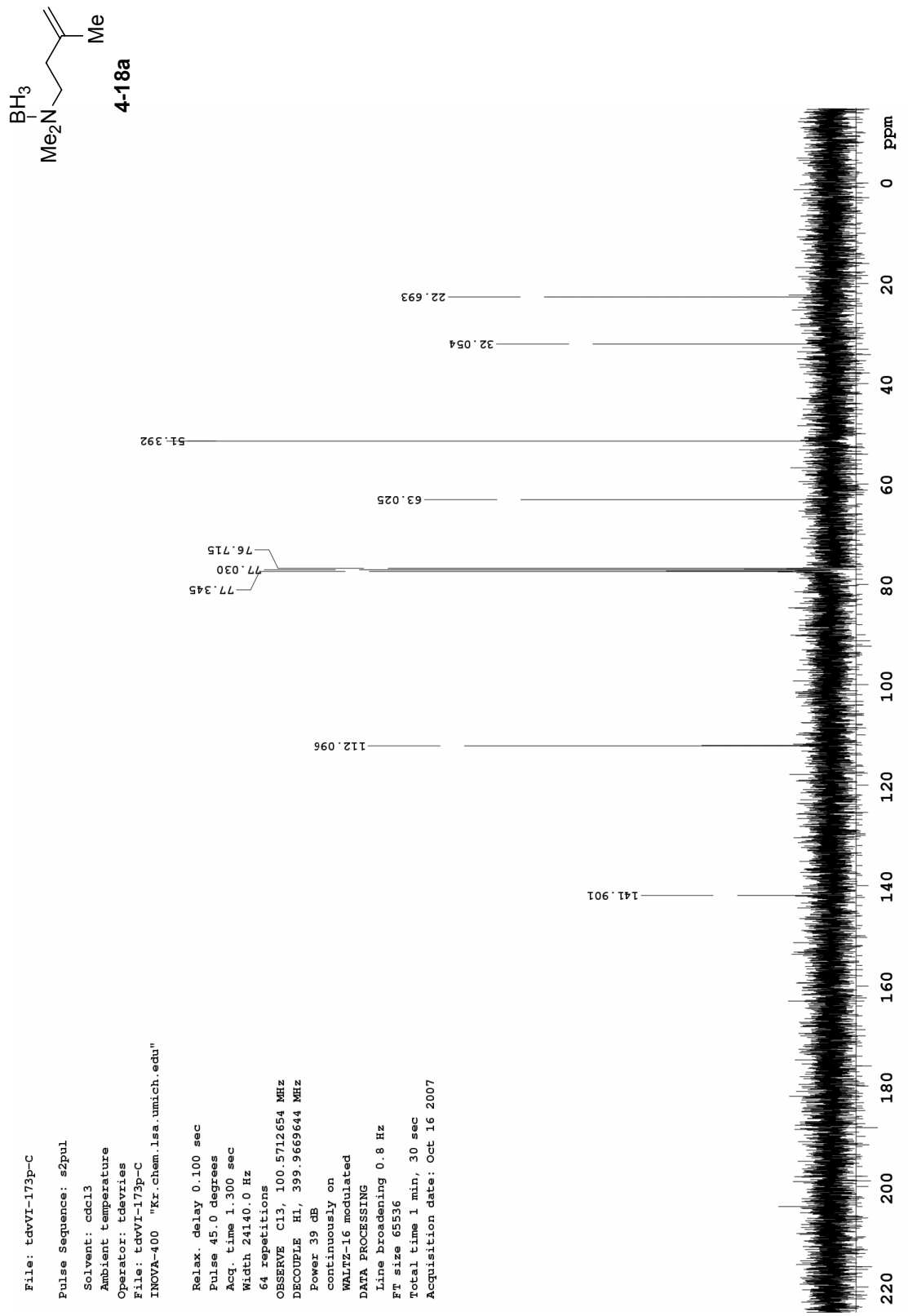

Me
O
Ph2P
4-14b
0
1
2
3
4
5
6
7
8
9

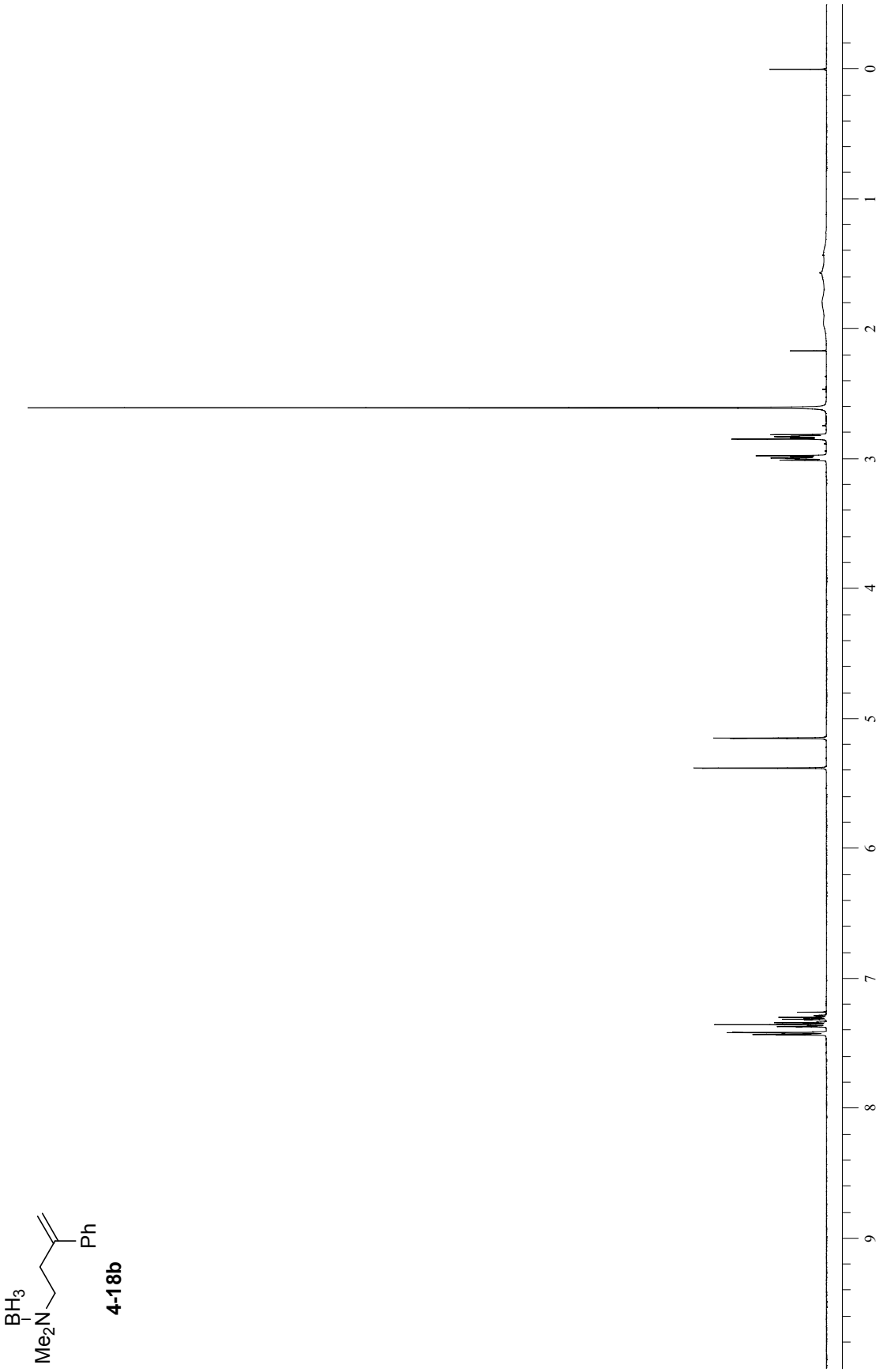

Me
O
Ph2P
4-14b
tdvVI-180b-C
File: Carbon
Pulse Sequence: s2pul
Solvent: cdcl3
Ambient temperature
Operator: tdevries
INOVA-400 "Zr.Chem.LsA.UMich.Edu"
Relax. delay 0.100 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 24140.0 Hz
80 repetitions
OBSERVE C13, 100.5712647 MHz
DECOUPLE H1, 399.9669644 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.8 Hz
FT size 65536
Total time 1 min, 52 sec
Acquisition date: Nov 6 2007
18.480
20.700
20.802
24.941
24.970
27.051
27.153
30.926
30.955
31.138
31.665
31.863
76.751
77.066
77.389
128.459
128.503
128.569
128.613
130.964
130.994
131.045
131.082
131.338
131.367
131.397
131.887
132.078
132.825
133.016
ppm
0
20
40
60
80
100
120
140
160
180
200
220


Me
O
Ph2P
4-14a
0
1
2
3
4
5
6
7
8
9

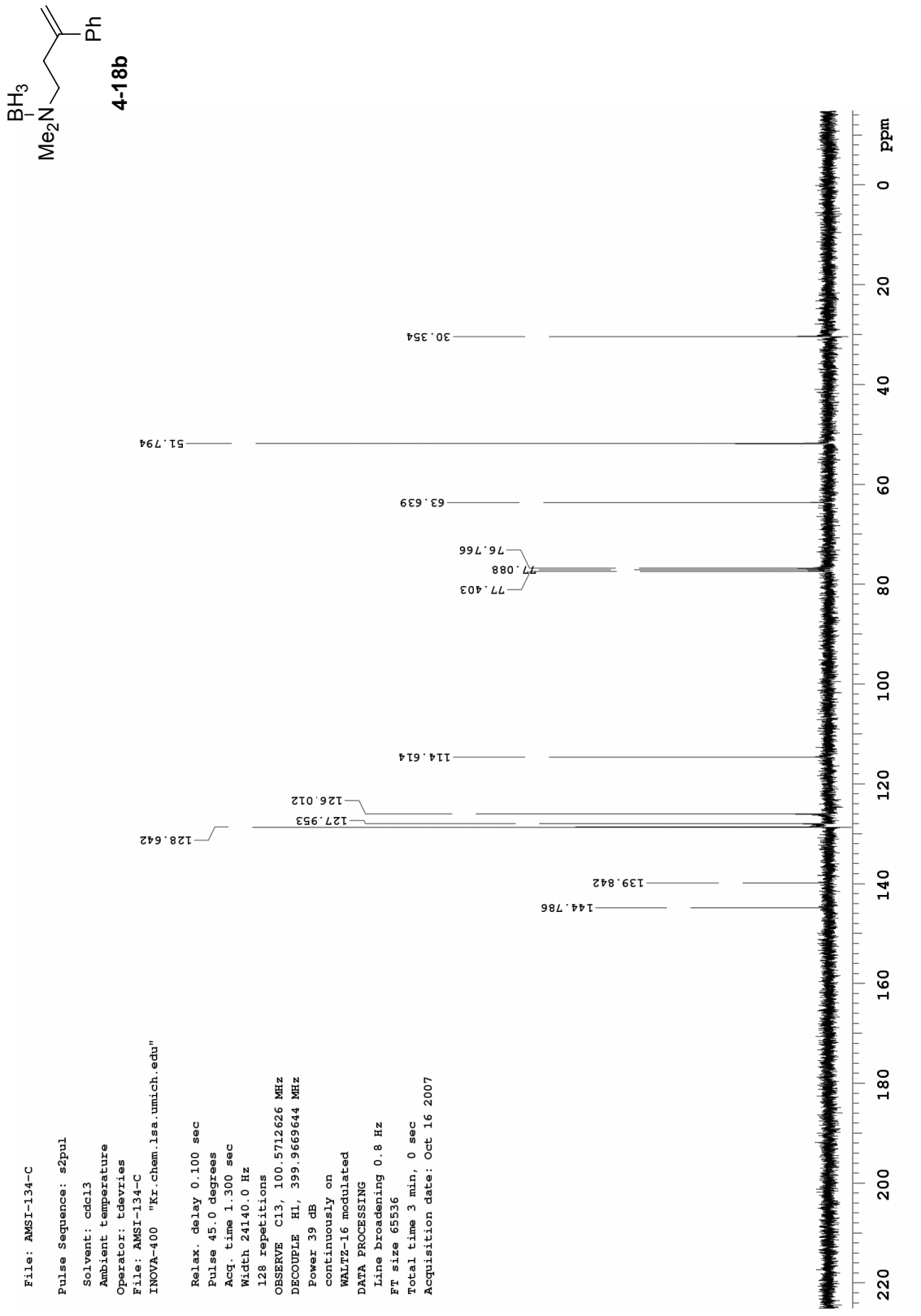

Me
O
Ph2P
4-14a
tdvVI-186-16
File: Carbon
Pulse Sequence: s2pul
Solvent: cdcl3
Ambient temperature
Operator: tdevries
INOVA-500 "Sn.Chem.LSA.UMich.Edu"
Relax. delay 0.100 sec
Pulse 30.0 degrees
Acq. time 1.300 sec
Width 30165.9 Hz
3520 repetitions
OBSERVE C13, 125.7010259 MHz
DECOUPLE H1, 499.9067532 MHz
Power 38 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 131072
Total time 1 hr, 22 min, 43 sec
Acquisition date: Nov 12 2007
-0.010
22.650
24.323
24.345
26.245
26.355
32.709
32.734
32.829
32.932
34.422
36.627
36.846
37.425
76.753
77.006
77.262
128.469
128.517
128.561
128.605
131.047
131.117
131.391
131.428
131.790
132.541
ppm
0
20
40
60
80
100
120
140
160
180
200
220

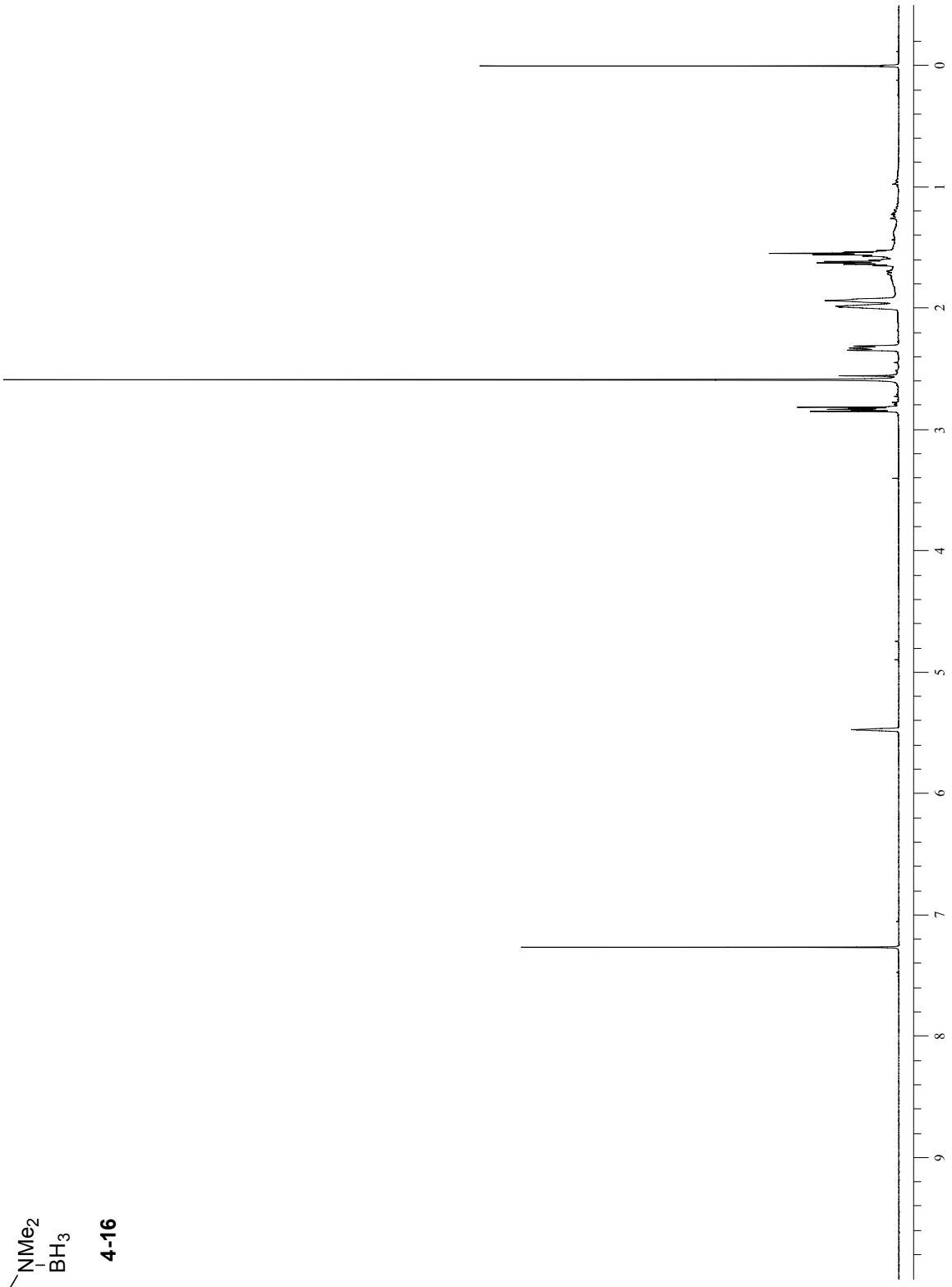

BH3
Me2N
Me
4-18a
0
1
2
3
4
5
6
7
8
9

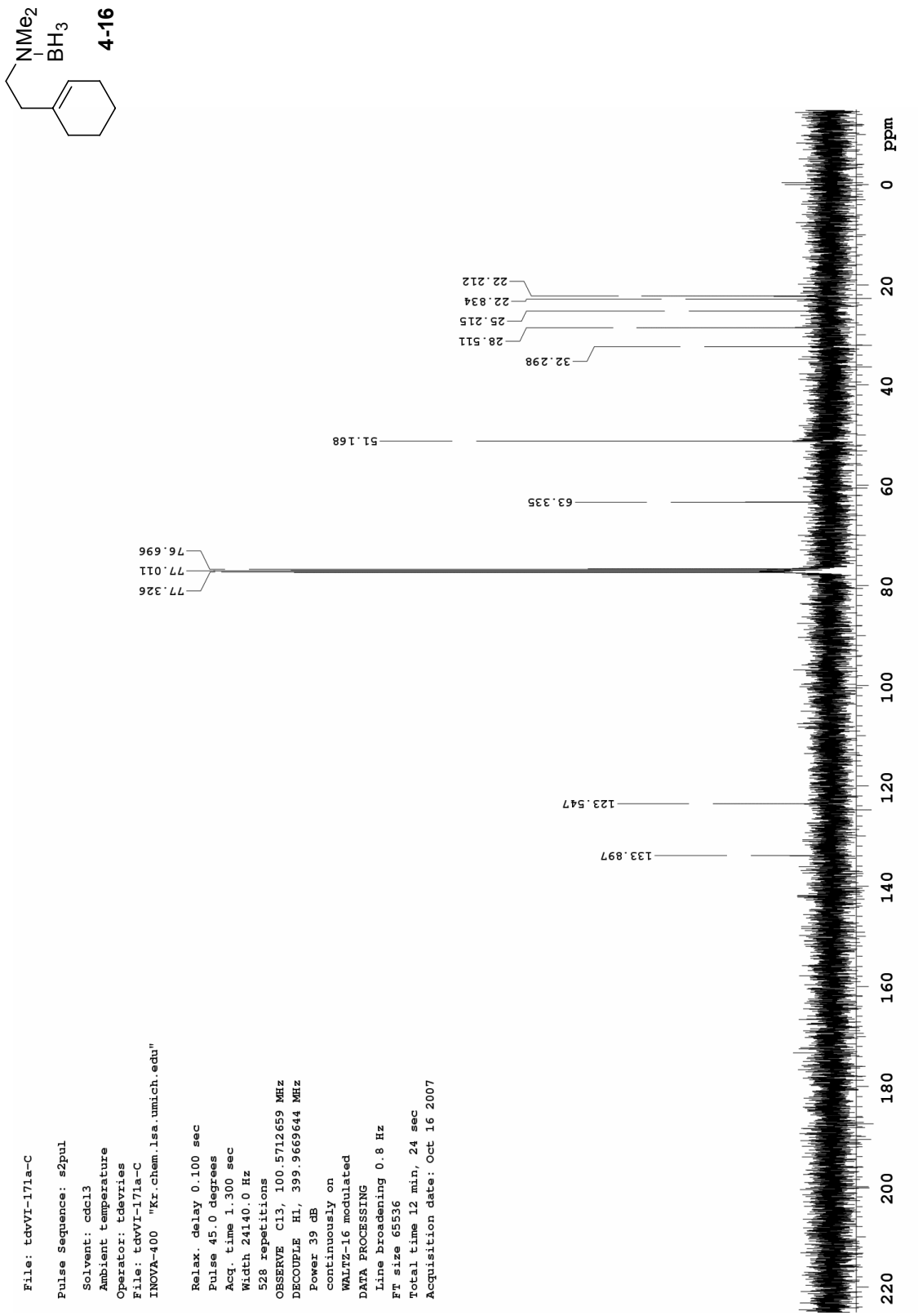

BH3
Me2N
Me
4-18a
22.693
32.054
51.392
63.025
76.715
77.030
77.345
112.096
141.901
ppm
0
20
40
60
80
100
120
140
160
180
200
220
File: tdvVI-173p-C
Pulse Sequence: s2pul
Solvent: cdcl3
Ambient temperature
Operator: tdevries
File: tdvVI-173p-C
INOVA-400 "Kr.chem.lsa.umich.edu"
Relax. delay 0.100 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 24140.0 Hz
64 repetitions
OBSERVE C13, 100.5712654 MHz
DECOUPLE H1, 399.9669644 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.8 Hz
FT size 65536
Total time 1 min, 30 sec
Acquisition date: Oct 16 2007

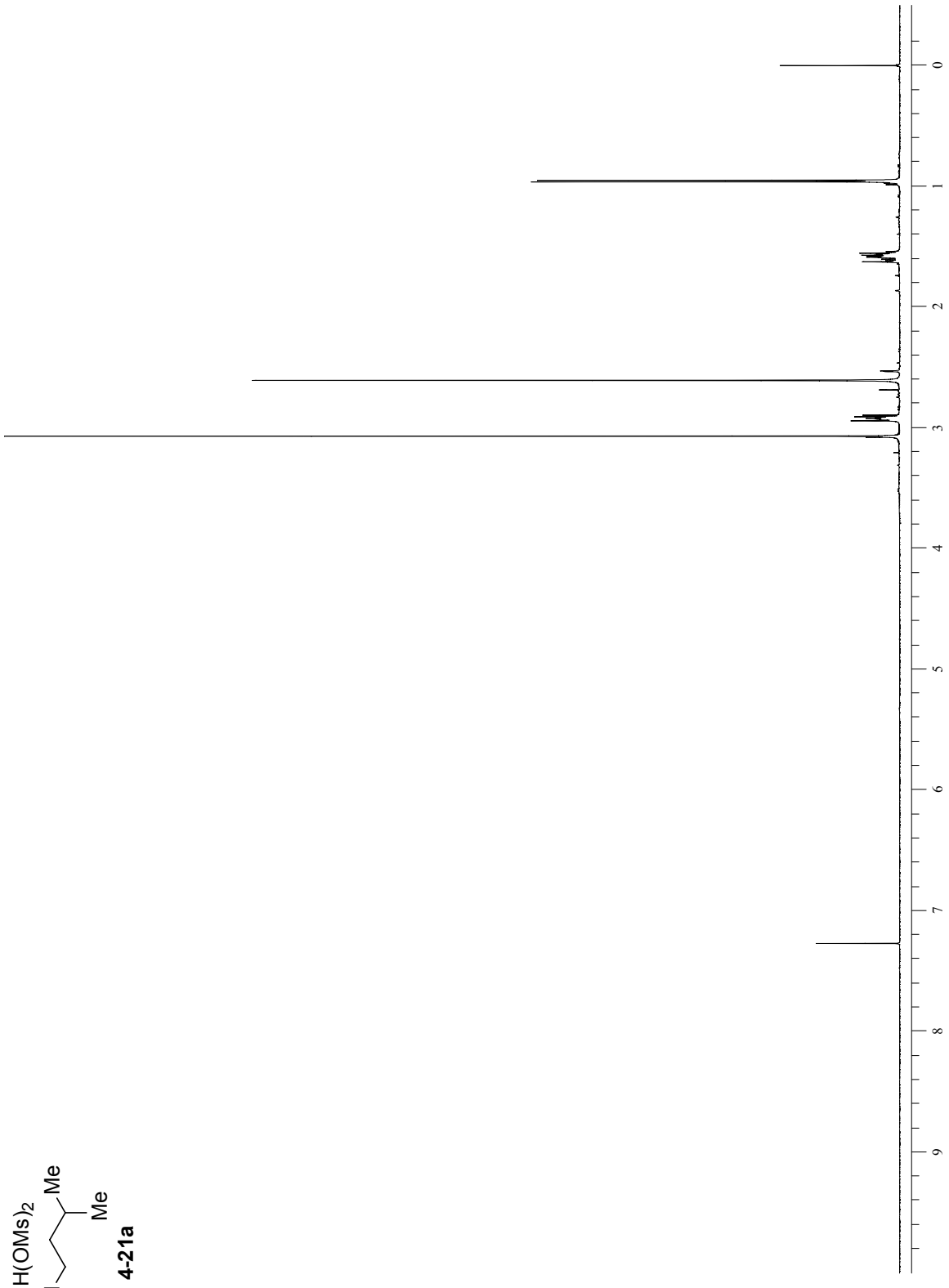


4-18b

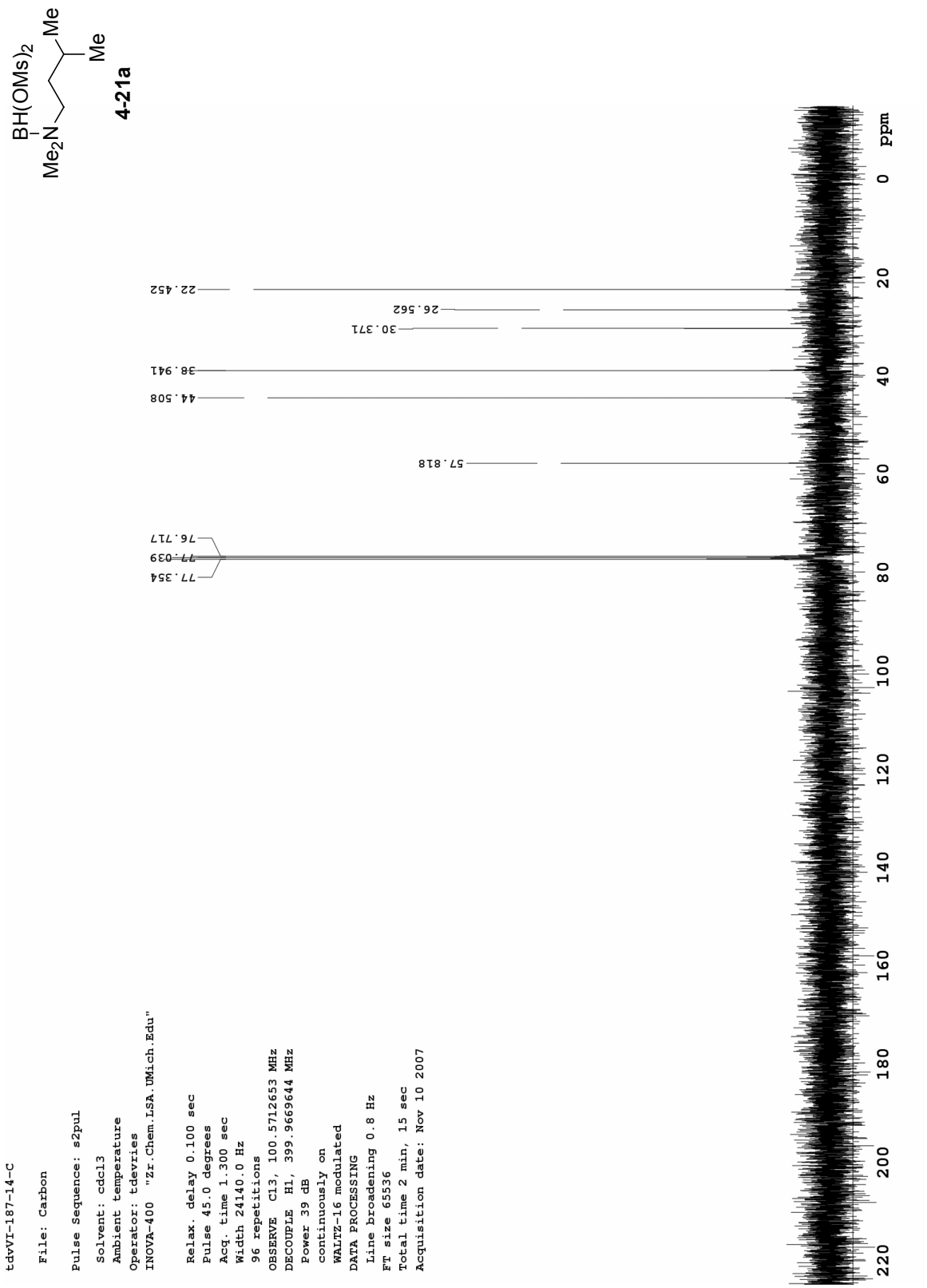

BH3
Me2N
Ph
4-18b
30.354
51.794
63.639
76.766
77.088
77.403
114.614
126.012
127.953
128.642
139.842
144.786
ppm
0
20
40
60
80
100
120
140
160
180
200
220
File: AMSI-134-C
Pulse Sequence: s2pul
Solvent: cdcl3
Ambient temperature
Operator: tdevries
File: AMSI-134-C
INOVA-400 "Kr.chem.lsa.umich.edu"
Relax. delay 0.100 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 24140.0 Hz
128 repetitions
OBSERVE C13, 100.5712626 MHz
DECOUPLE H1, 399.9669644 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.8 Hz
FT size 65536
Total time 3 min, 0 sec
Acquisition date: Oct 16 2007

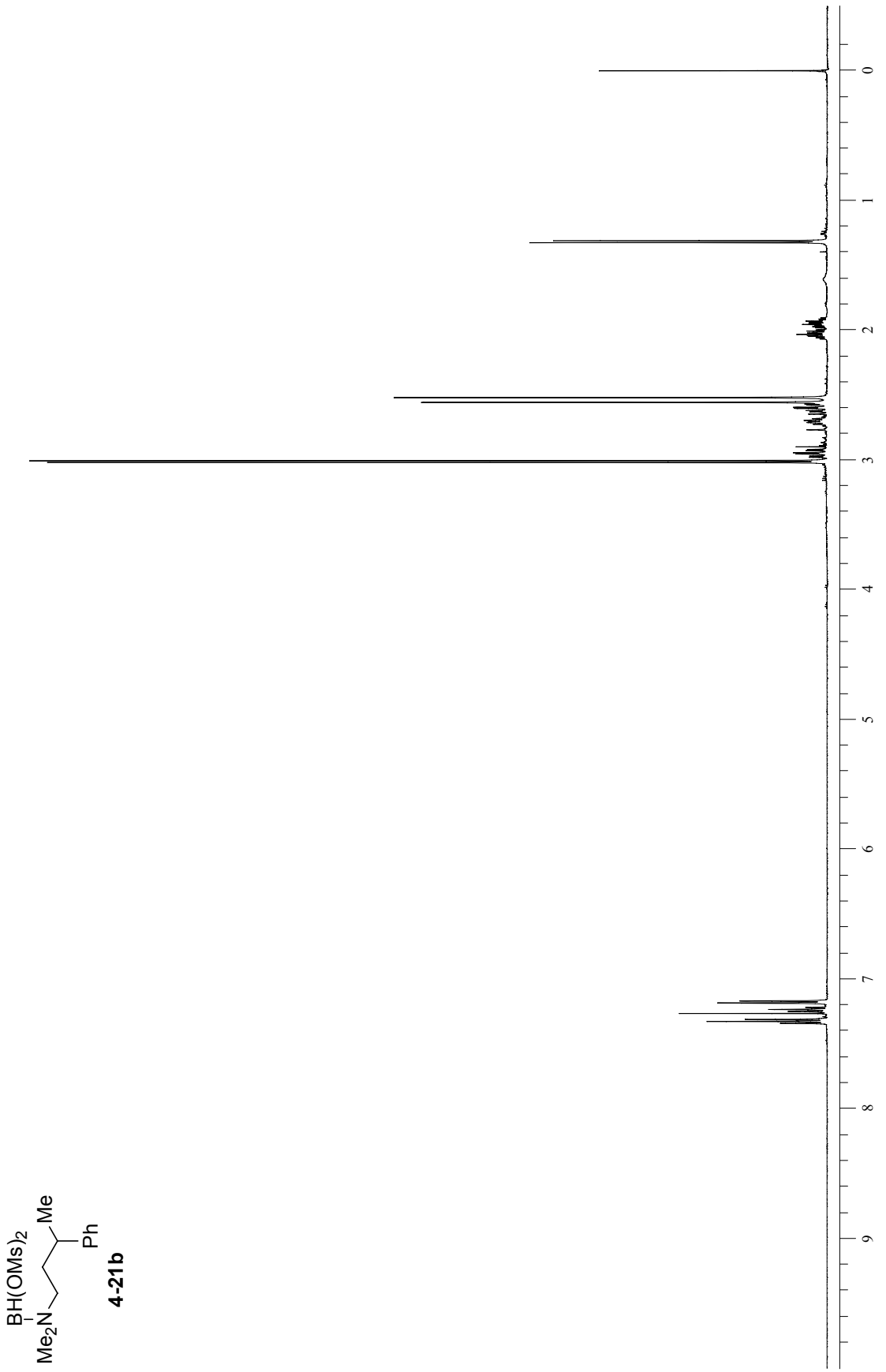

NMe2
BH3
4-16
0
1
2
3
4
5
6
7
8
9

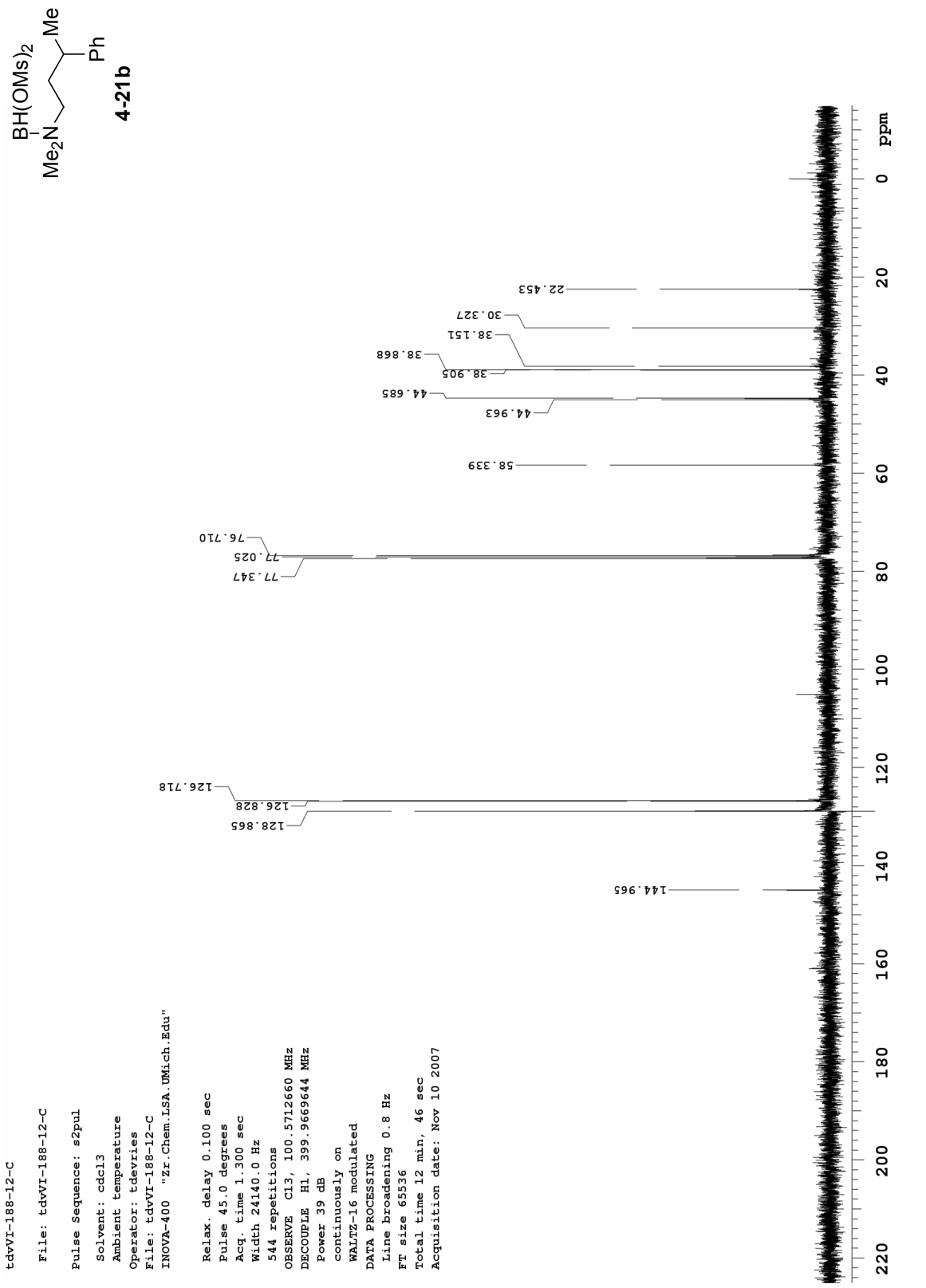

NMe2
BH3
4-16
22.212
22.834
25.215
28.511
32.298
51.168
63.335
76.696
77.011
77.326
123.547
133.897
ppm
0
20
40
60
80
100
120
140
160
180
200
220
File: tdvVI-171a-C
Pulse Sequence: s2pul
Solvent: cdcl3
Ambient temperature
Operator: tdevries
File: tdvVI-171a-C
INOVA-400 "Kr.chem.lsa.umich.edu"
Relax. delay 0.100 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 24140.0 Hz
528 repetitions
OBSERVE C13, 100.5712659 MHz
DECOUPLE H1, 399.9669644 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.8 Hz
FT size 65536
Total time 12 min, 24 sec
Acquisition date: Oct 16 2007

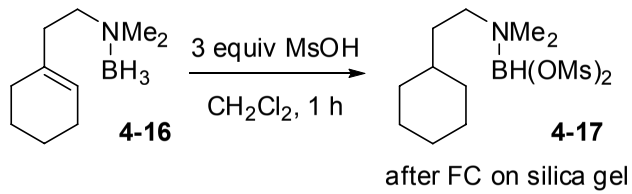


4-21a


BH(OMs)2
Me2N
Me
Me
4-21a
22.452
26.562
30.371
38.941
44.508
57.818
76.717
77.039
77.354
ppm
0
20
40
60
80
100
120
140
160
180
200
220
tdVVI-187-14-C
File: Carbon
Pulse Sequence: s2pul
Solvent: cdcl3
Ambient temperature
Operator: tdevries
INOVA-400 "Zr.Chem.LsA.UMich.Edu"
Relax. delay 0.100 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 24140.0 Hz
96 repetitions
OBSERVE C13, 100.5712653 MHz
DECOUPLE H1, 399.9669644 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.8 Hz
FT size 65536
Total time 2 min, 15 sec
Acquisition date: Nov 10 2007

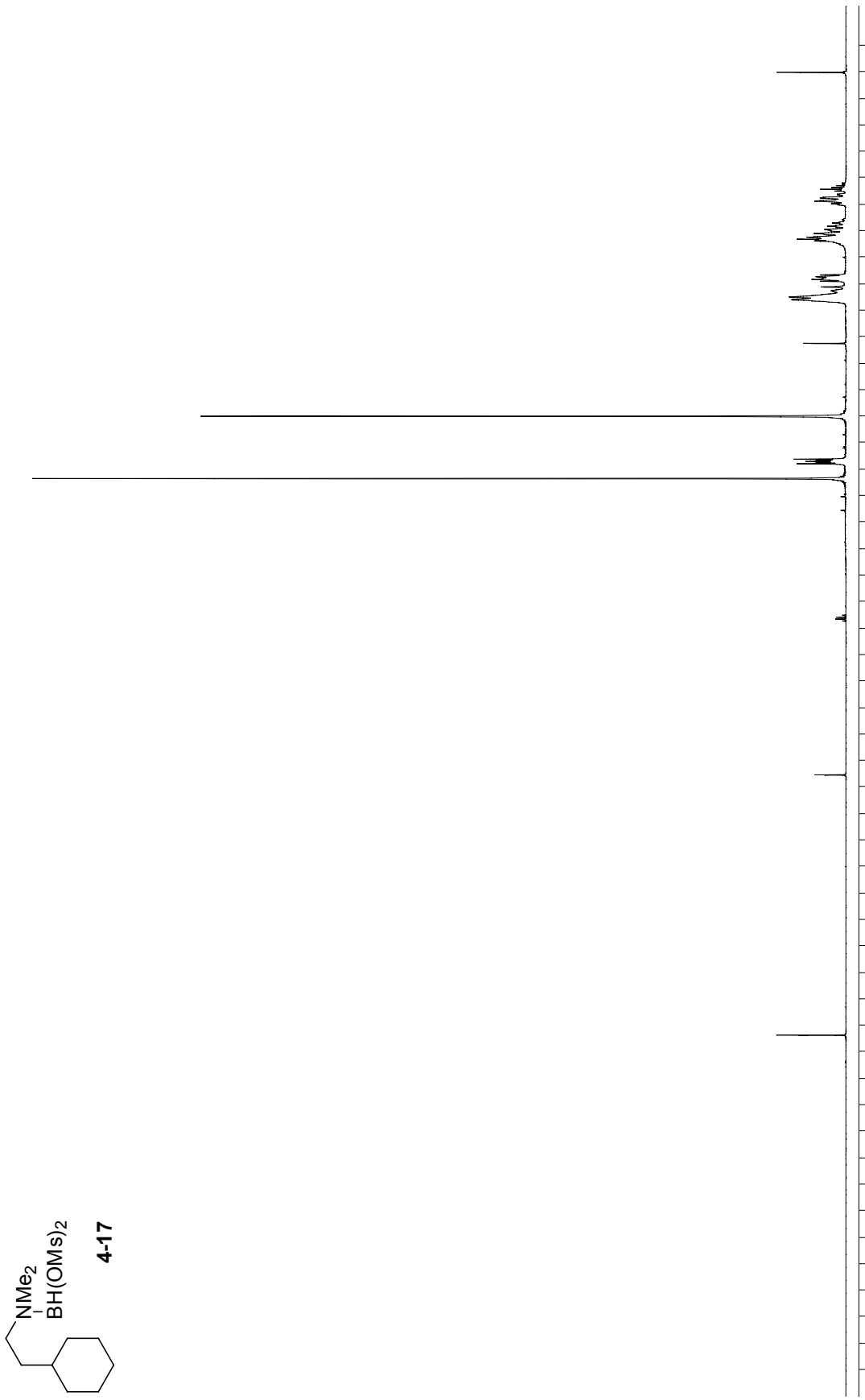

BH(OMs)2
Me2N
Me
Ph
4-21b
0
1
2
3
4
5
6
7
8
9

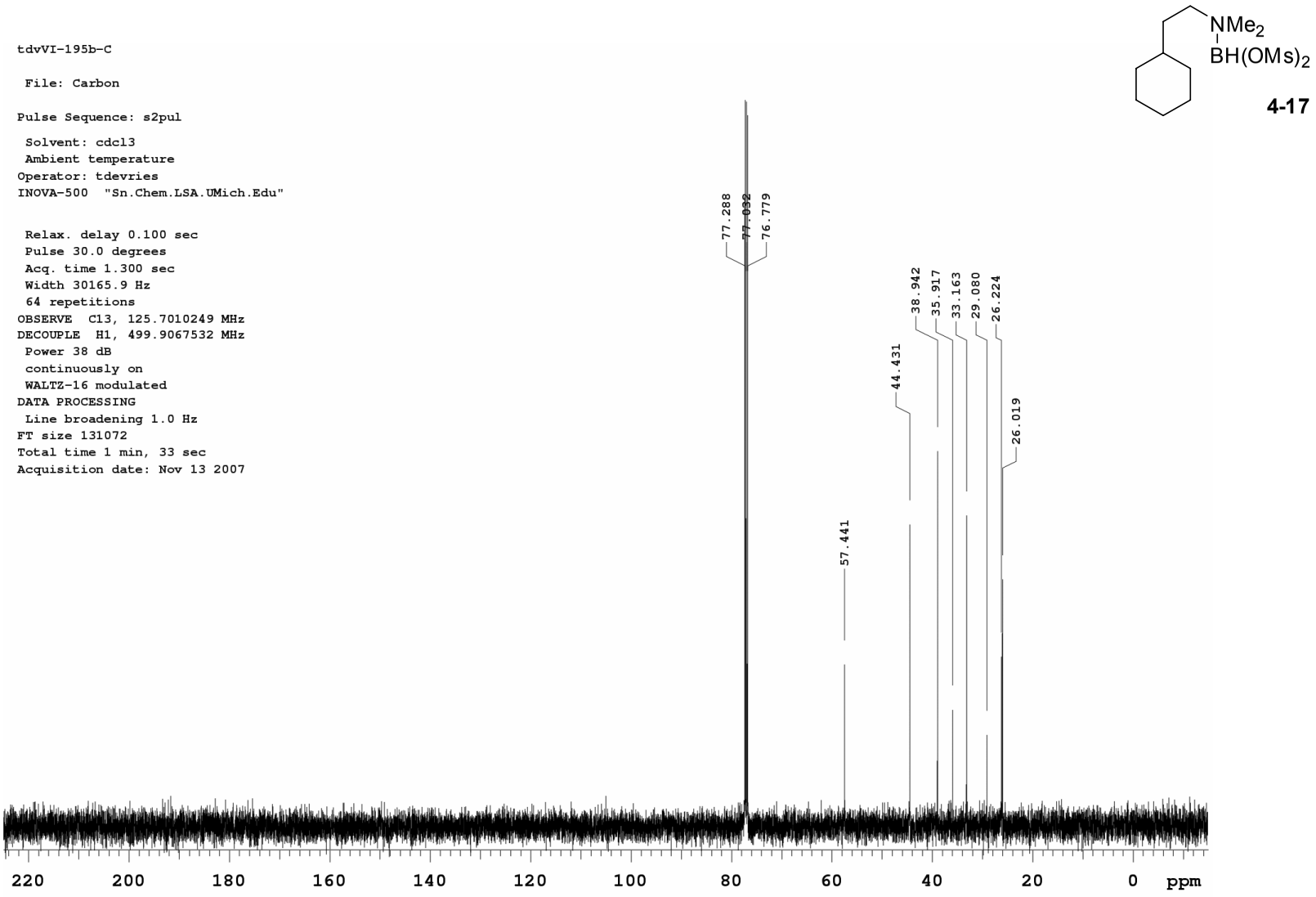

BH(OMs)2
Me2N
Me
Ph
4-21b
tdvVI-188-12-C
File: tdvVI-188-12-C
Pulse Sequence: s2pul
Solvent: cdcl3
Ambient temperature
Operator: tdevries
File: tdvVI-188-12-C
INOVA-400 "Zr.Chem.LSA.UMich.Edu"
Relax. delay 0.100 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 24140.0 Hz
544 repetitions
OBSERVE C13, 100.5712660 MHz
DECOUPLE H1, 399.9669644 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.8 Hz
FT size 65536
Total time 12 min, 46 sec
Acquisition date: Nov 10 2007
144.965
128.865
126.828
126.718
77.347
77.025
76.710
58.339
44.963
44.685
38.905
38.868
38.151
30.327
22.453
ppm



4-16 **4-17**

after FC on silica gel

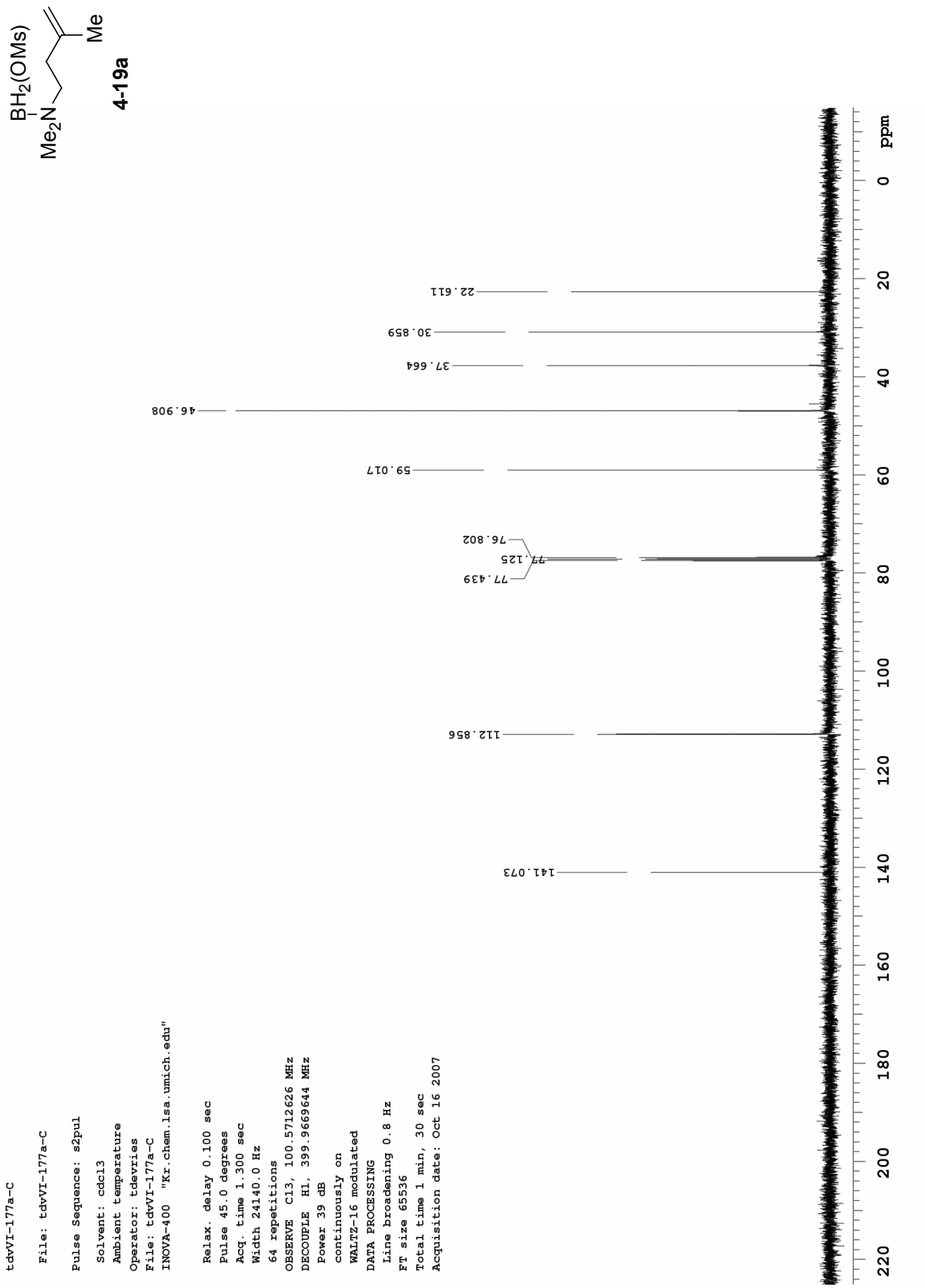

NMe2
BH(OMs)2
4-17
0
1
2
3
4
5
6
7
8
9

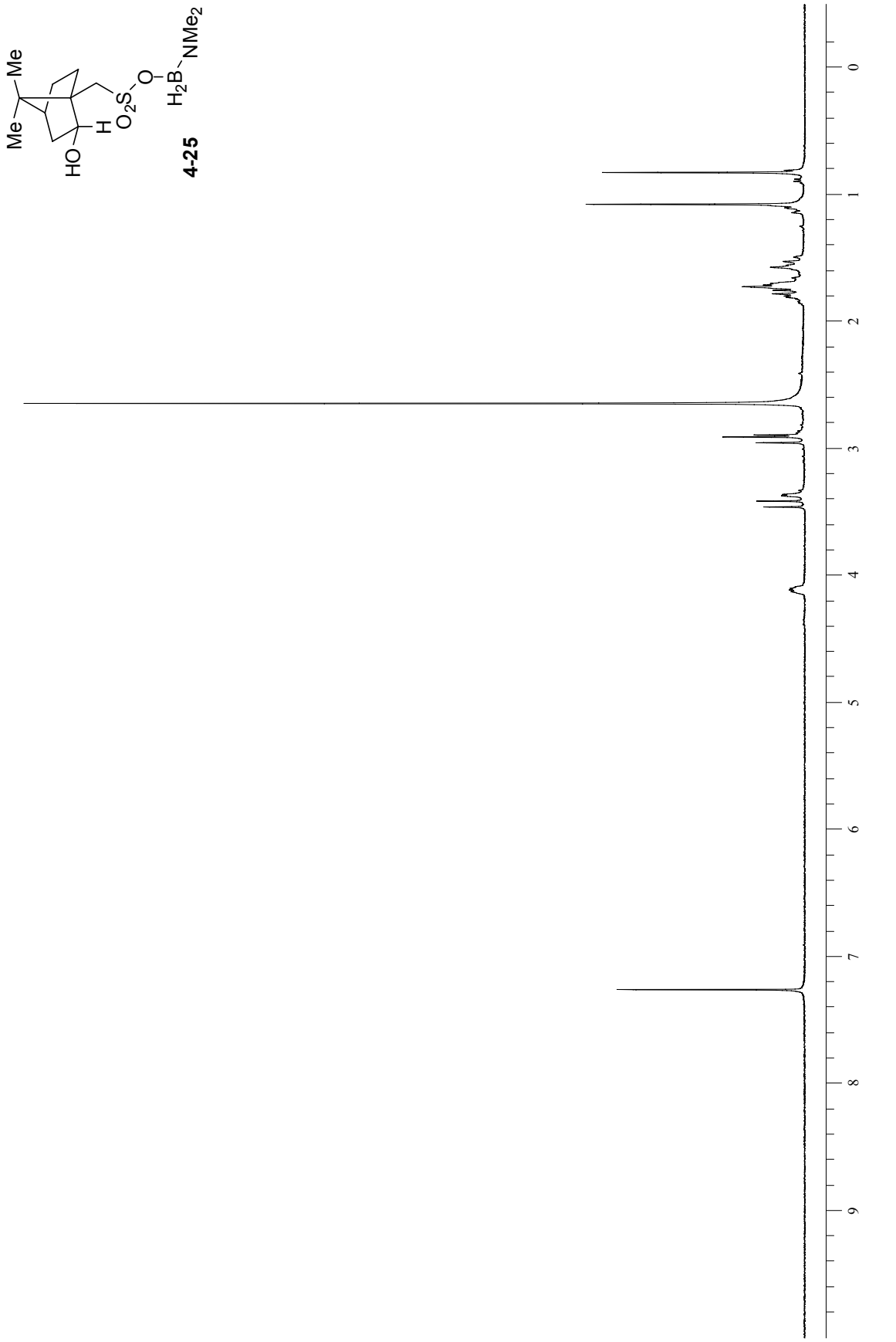

tdvVI-195b-C
File: Carbon
Pulse Sequence: s2pul
Solvent: cdcl3
Ambient temperature
Operator: tdevries
INOVA-500 "Sn.Chem.LSA.UMich.Edu"
Relax. delay 0.100 sec
Pulse 30.0 degrees
Acq. time 1.300 sec
Width 30165.9 Hz
64 repetitions
OBSERVE C13, 125.7010249 MHz
DECOUPLE H1, 499.9067532 MHz
Power 38 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 131072
Total time 1 min, 33 sec
Acquisition date: Nov 13 2007
77.288
77.032
76.779
57.441
44.431
38.942
35.917
33.163
29.080
26.224
26.019
220
200
180
160
140
120
100
80
60
40
20
0
ppm

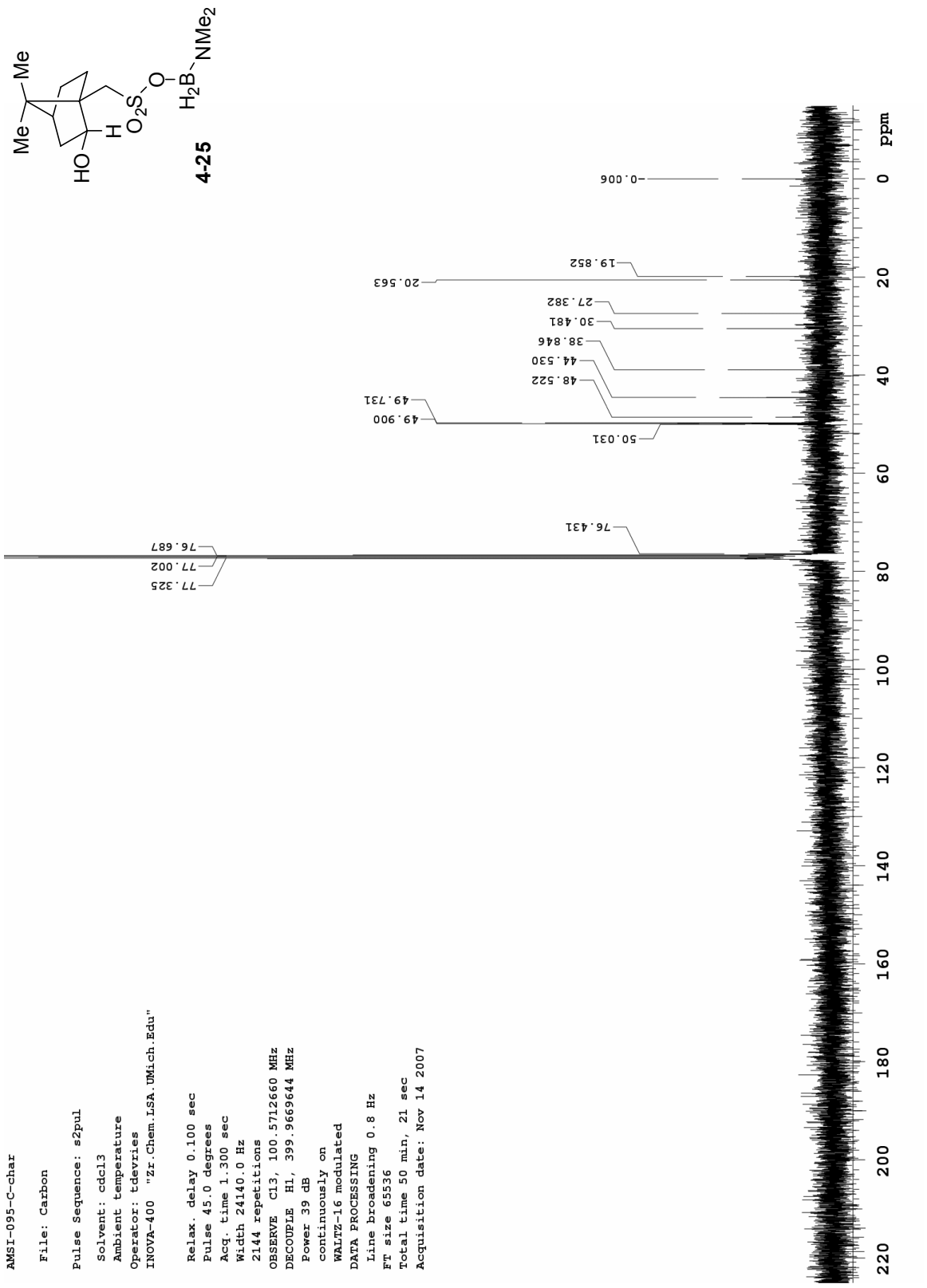
NMe2
BH(OMs)2

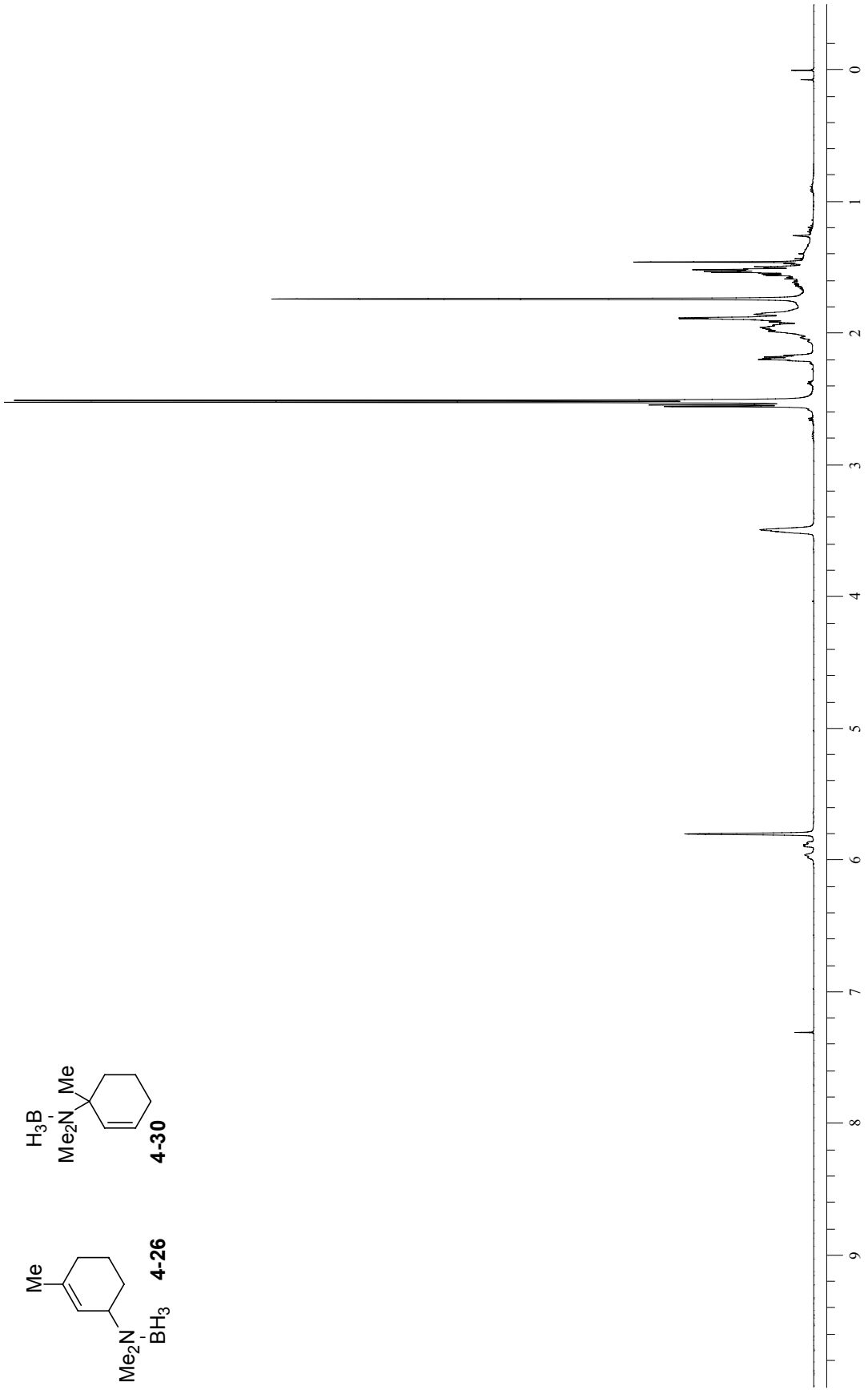
4-17

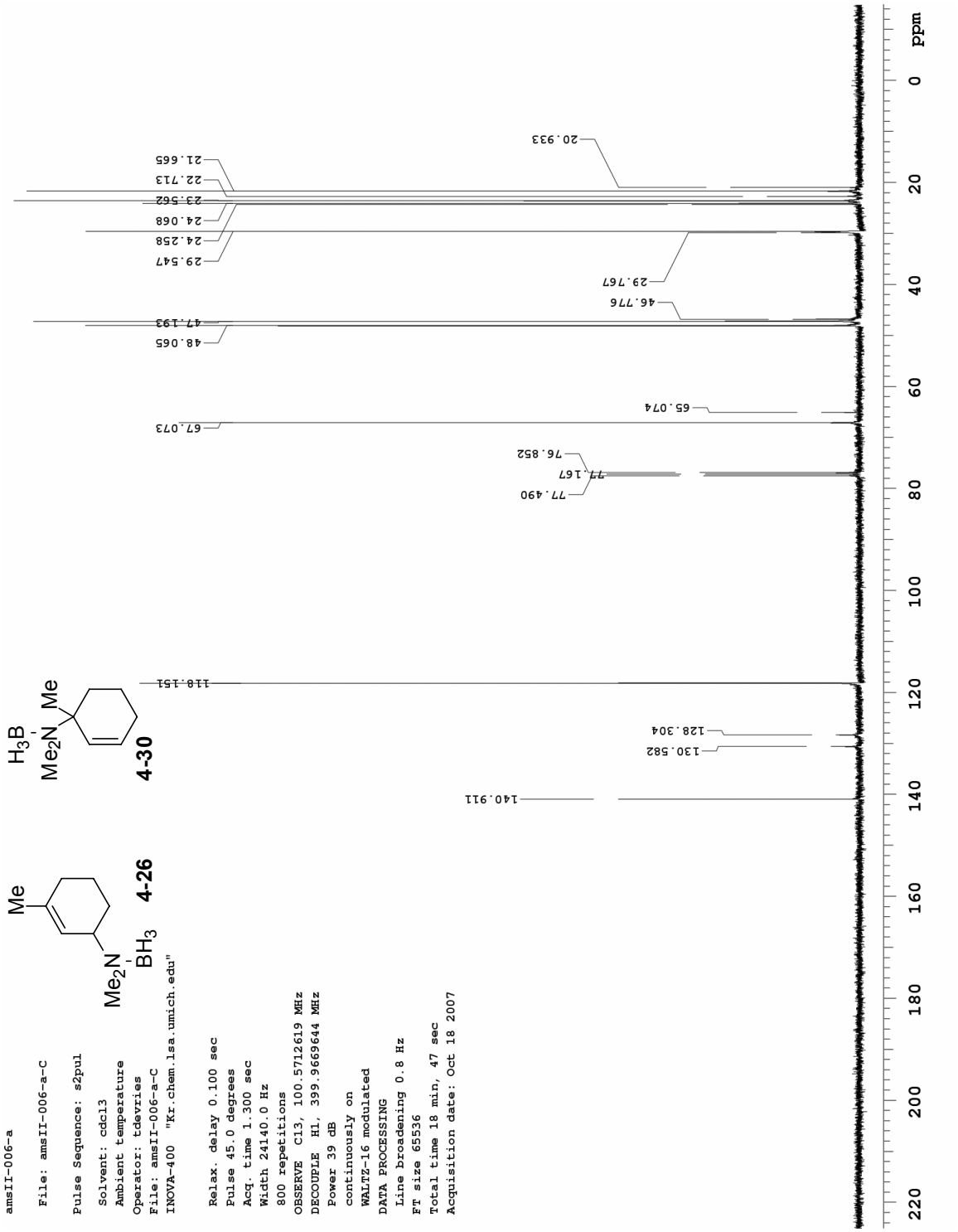

BH2(OMs)
Me2N
Me
4-19a
0
1
2
3
4
5
6
7
8
9


BH2(OMs)
Me2N
Me
4-19a
tdvVI-177a-C
File: tdvVI-177a-C
Pulse Sequence: s2pul
Solvent: cdcl3
Ambient temperature
Operator: tdevries
File: tdVI-177a-C
INOVA-400 "Kr.chem.lsa.umich.edu"
Relax. delay 0.100 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 24140.0 Hz
64 repetitions
OBSERVE C13, 100.5712626 MHz
DECOUPLE H1, 399.9669644 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.8 Hz
FT size 65536
Total time 1 min, 30 sec
Acquisition date: Oct 16 2007
141.073
112.856
77.439
77.125
76.802
59.017
46.908
37.664
30.859
22.611
ppm


Me
Me
HO
H
O2S
O
H2B
NMe2
4-25
0
1
2
3
4
5
6
7
8
9


Me
Me
HO
H
O2S
O
H2B
NMe2
4-25
-0.006
19.852
20.563
27.382
30.481
38.846
44.530
48.522
49.731
49.900
50.031
76.431
76.687
77.002
77.325
ppm
0
20
40
60
80
100
120
140
160
180
200
220
AMSI-095-C-char
File: Carbon
Pulse Sequence: s2pul
Solvent: cdcl3
Ambient temperature
Operator: tdevries
INOVA-400 "Zr.Chem.LsA.UMich.Edu"
Relax. delay 0.100 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 24140.0 Hz
2144 repetitions
OBSERVE C13, 100.5712660 MHz
DECOUPLE H1, 399.9669644 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.8 Hz
FT size 65536
Total time 50 min, 21 sec
Acquisition date: Nov 14 2007


Me
Me2N
BH3
4-26
H3B
Me2N
Me
4-30


amsII-006-a
File: amsII-006-a-C
Pulse Sequence: s2pul
Solvent: cdcl3
Ambient temperature
Operator: tdevries
File: amsII-006-a-C
INOVA-400 "Kr.chem.lsa.umich.edu"
Relax. delay 0.100 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 24140.0 Hz
800 repetitions
OBSERVE C13, 100.5712619 MHz
DECOUPLE H1, 399.9669644 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.8 Hz
FT size 65536
Total time 18 min, 47 sec
Acquisition date: Oct 18 2007
Me
Me2N
BH3
4-26
H3B
Me2N
Me
Me
4-30
118.151
140.911
130.582
128.304
67.073
65.074
48.065
47.193
46.776
29.767
29.547
24.258
24.068
23.562
22.713
21.665
20.933
77.490
77.167
76.852
ppm
0
20
40
60
80
100
120
140
160
180
200
220