Applications of Iridium-Catalyzed Isomerization Claisen Rearrangements (ICR) to Complex Molecule Synthesis

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Applications of Iridium-Catalyzed Isomerization Claisen Rearrangements (ICR) to Complex Molecule Synthesis

Benjamin D. Stevens, Ph.D.

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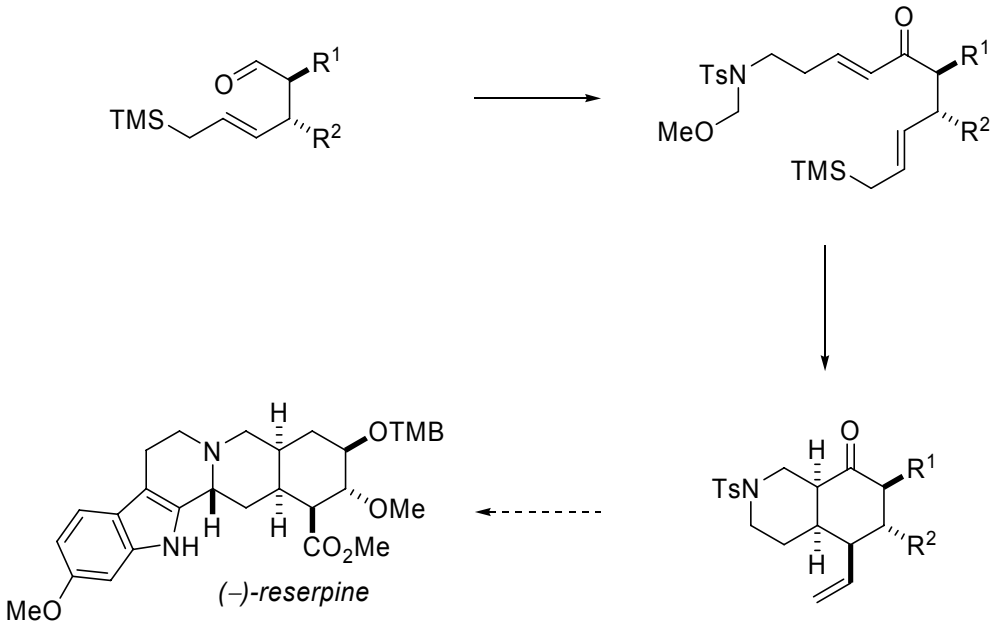
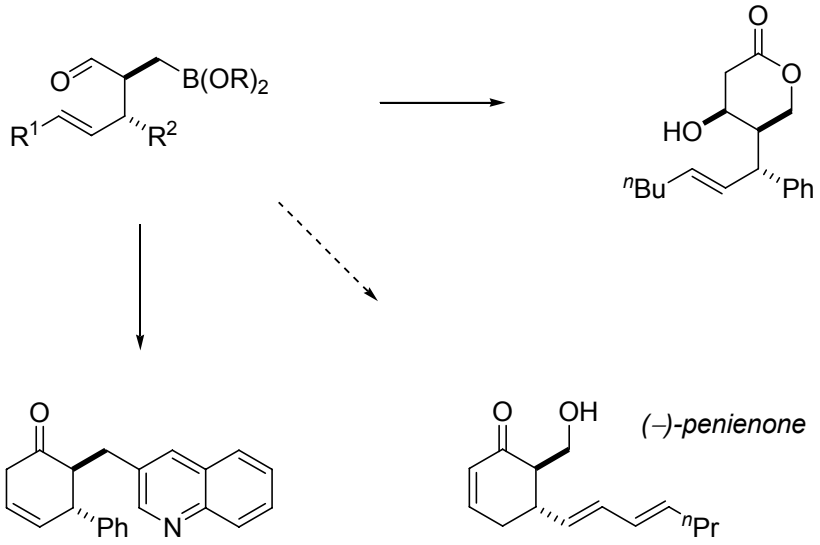
The iridium-catalyzed isomerization Claisen rearrangement (ICR) methodology developed in the Nelson group has provided access to a broad range of diastereomerically enriched α,β-disubstituted, δ,γ-unsaturated aldehydes. Allylsilyl aldehydes produced by the ICR reaction have been further elaborated into substrates for highly diastereoselective intramolecular Hosomi-Sakurai annulation reactions. The Sakurai annulation has proven to be particularly powerful when carried out in tandem with intramolecular aldol or Mannich reactions to form complex fused ring systems. An attempted strategic application of this methodology toward the synthesis of the *Rauwolfia* alkaloids (–)-reserpine and α-yohimbine is detailed.



Vinyl boronic esters have been demonstrated to be effective precursors for the ICR reaction providing diastereomerically enriched β-boronic aldehydes. The potential for intramolecular chelation between the newly formed aldehyde and proximal boronic ester has been investigated. The boron functionality has proven to be useful for accessing alkoxy- and aryl-substituted compounds that are typically unavailable from the ICR reaction. A synthesis of the plant growth inhibitor (–)-penienone was explored in order to demonstrate the practical application of this methodology to complex molecule construction.



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PREFACE

I'd like to start off with the words of Andy Kassick and just say that I am eternally grateful to almighty god for letting me persevere through the last five years here at Pittsburgh. I'm not an exceptionally religious man, but if there is one thing I am sure of it is that there is no way that I could made it through without some help from above. I've learned a lot of things here in Pittsburgh, and most of them were completely unrelated to chemistry. In particular, I have learned a lot about myself. I found weakness where I thought I was strong and strengths where I felt vulnerable. I think the most important thing I have learned, or maybe I am just starting to learn, is the true meaning of responsibility. I hope that what I have learned will make me a proficient leader to those who will later look to me for direction, but I pray that I will also be able to relax and enjoy life and infuse those around me with the same spirit.

Of course, nothing in life would be possible without my parents whose love and support I value beyond anything I could possibly hope to achieve here or in the future. In addition, the friends who I have had the great fortune of meeting and keeping throughout my life have done more to preserve my sanity than I can express. From home, Jay Amentas, Mike McLean, Jordan Luchini, Amy Hill and Joe Corti – I've known you all for most of my life, it's time I actually spent some of it near you! From college, Neel Choudhury (also HS!), Andy Blom, Steve Palumbo, Chris Lamb – great friends, all doing great things with their lives – who would have thought that we could watch Tombstone so much and manage to get anything productive done?

From the MS, Gabe Kapur – I can't wait to get back to NYC and show you the proper way to use a turntable – you just gotta takit easie! And of course from Pittsburgh, Mike Green, Brian Albert, Brianne Raccor, Gustavo Moura-Letts, Jim Mignone, Chris Meta, Matt Clements, Mark Ams, Aparna Agarwal, Jolie DeForrest, Erika Englund, Nilu Jayasuriya and Adam Hoye - can't wait to see you all on the other side - it's all downhill from here! Some special thanks must go to some of the wonderful coworkers I have had throughout the last few years in the Nelson group. In particular, Cheng Zhu, Chris Bungard and Andy Kassick who basically taught me everything I know about doing chemistry and endured my endless bone-headed inquisitions in the early days – I am truly grateful. I was fortunate to have an exceptionally tolerant lab-mate, Xiaoqiang Shen – thanks for dealing with my 'fa-ching everyday' without demanding a lab transfer! Thanks also to Jeremy Raelin and Nessan Kerrigan for lending a patient ear when I became frustrated, and enduring the various drunken beatings you were subject to on my behalf. A special thanks goes to Apsara Gopalarathnam for being a wonderful friend the past few years – I'm so happy that everything worked out for you and I am honored to have had the chance to spend five years as your labmate. And of course, I'd like to thank Kelly who I have only come to know over the last year, but whose companionship has meant all the difference through these times.

Many people are responsible for making me what I am at the professional level. Probably the earliest of these individuals would be my highschool chemistry teacher, Mark Tretter, who was instrumental in driving me towards the pursit of a higher degree in the sciences. In Rochester, Prof. Andrew Kende and then-postdoc Catherine Mineur provided me with a truly inspiring opportunity to learn bench top organic chemistry, which was a far cry from the exercises of drawing curved arrows and memorizing named reactions that most people normally associate our science with. Finally, and perhaps most importantly, Prof. Michael Calter took me

under his wing for a MS stint during a time in my life when I was completely in limbo and without direction. I have no doubt that I would never have earned a doctorate without his early guidance and his confidence. Of course I have to thank my advisor, Scott Nelson, for all of the support during graduate school. To say it has been a learning experience is a vast understatement; I will remember everything I have seen here and use it to guide me through the rest of my days both inside an outside of the lab. I would also like to thank my committee members, Prof. Dennis Curran, Prof. Peter Wipf and Prof. Billy Day for their incredible patience with my incessant demand for recommendations! Thanks also to Prof. Floreancig for mentoring my proposal. Thanks especially to Fran Nagy for laboring endlessly in the front office to keep me on track in regards to the hectic administrative material; I am sure I would still be schlepping around Cheveron if it wasn't for you! It has been a pleasure to have you all involved with my work here at Pittsburgh. Please forgive me if there is anybody who I have forgotten to mention here, and know that I have valued all of the interactions I have had with so many people I have met throughout my life; you are not forgotten!

Screw Ithaca, I’m headed home…

1.0 DEVELOPMENT OF DIASTEREOSELECTIVE INTRAMOLECULAR SAKURAI-ALDOL AND MANNICH REACTIONS

1.1 BACKGROUND

1.1.1 Intramolecular Hosomi-Sakurai Annulation

Terpenes are a broad class of functionalized small molecule natural products. In addition to serving as building blocks for complex synthetic targets, these compounds represent important members of the "chiral pool" and are particularly useful as auxiliaries or ligands for asymmetric catalysis.[1] Though readily available in enantiomerically enriched form at minimal cost from natural sources, many of the common six-membered ring terpenes possess limited functionality and are not amenable to direct modification at particular ring positions. This factor considerably restricts the utility of these compounds in synthetic endeavors. A general methodology that grants access to a wide variety of differentially substituted six-membered carbocycles in a highly diastereo- and enantioselective manner would be of great synthetic value.

Significant efforts have been directed towards the use of vinylic, allylic, and propargylic silanes in ring forming reactions.[2-6] In 1977, Sakurai and Hosomi reported the first example of a Lewis acid-mediated conjugate addition of allyl silanes to α,β-unsaturated ketones.[7] Since that time, the intramolecular variant of the Hosomi-Sakurai reaction has become a powerful method

for the synthesis of various ring systems. The four basic cyclization classes that have been explored are monoannulation, extended annulation, spirocyclization, and ring fusion (Figure 1).

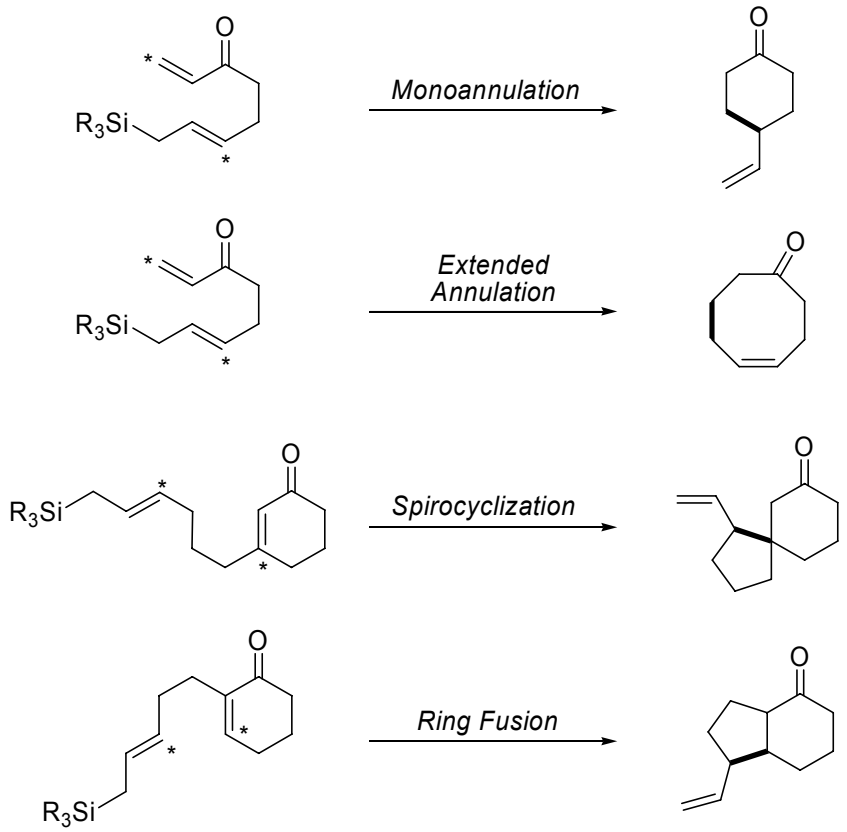


Figure 1. Major classes of intramolecular Hosomi-Sakurai annulations

Spirocyclization reactions have been studied extensively in the context of natural product synthesis. In 1990, Yamamoto and Furuta described an intramolecular Hosomi-Sakurai spirocyclization utilizing unsaturated ketone **1**.[8] Unfortunately, this reaction provided a nearly equimolar mixture of diastereomers from which the desired spirocycle **2** resulting from cyclization *via* a synclinal transition state was separated (Figure 2). The advanced intermediate **2** was then elaborated into the natural product (±)-α-acoradiene in 3 steps.

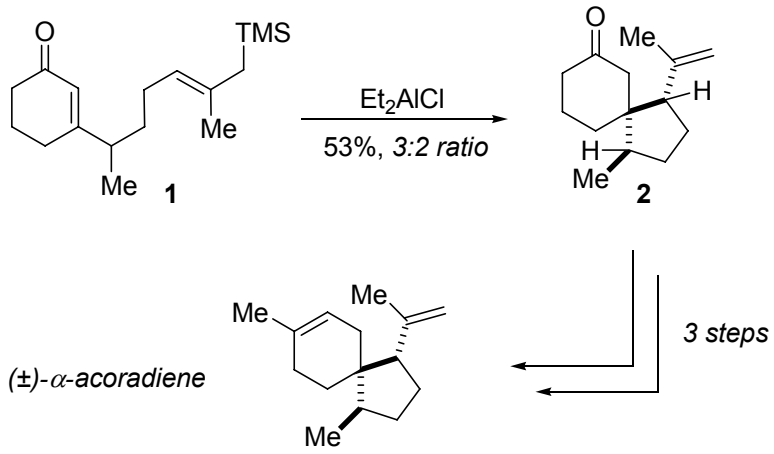


Figure 2. Yamamoto's synthesis of (±)-α-acoradiene

A wide variety of ring fusion reactions have been performed utilizing the intramolecular Hosomi-Sakurai reaction, many of which proceed with significant degrees of diastereoselectivity. Both Majetich and Schinzer have explored the moderately diastereoselective intramolecular conjugate addition of allyl silanes to α,β-unsaturated cyclohexanones leading to substituted hydrindanones.[9, 10] The observed relative stereochemistry of the cyclization products is strongly dependent on the nature of the reaction mediator (Figure 3). Interestingly, fluoride and Lewis acid-induced cyclizations give epimeric products at the R^2 bearing stereocenter. Majetich rationalized that the synclinal attack mode may be favored for the Lewis acid-mediated cyclization due to minimization of charge separation in the transition state. Alternatively, fluoride-mediated cyclizations, which generally proceed under kinetic control, favor the sterically less encumbered *anti*-transition state. For this reason, the diastereoselectivity of fluoride-mediated bicyclizations falls off markedly with decreasing size of the R^1 and R^2 substituents.

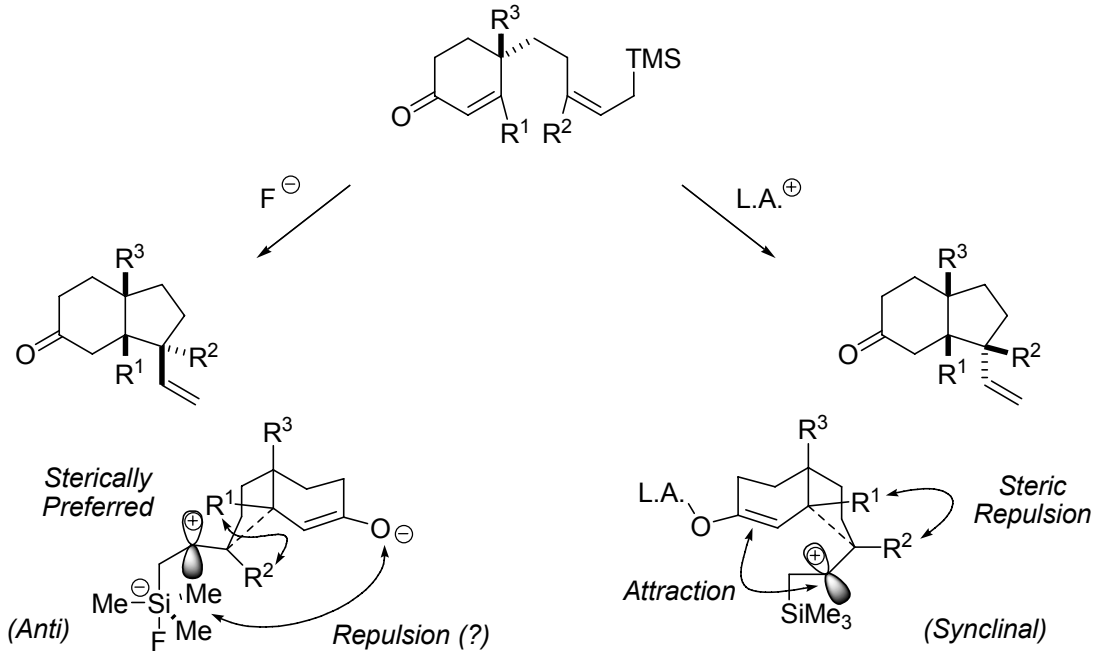


Figure 3. Majetich's hydrindanone syntheses

Tokoroyama *et al.* achieved an elegant synthesis of the natural product (±)-linaridial utilizing a novel, highly diastereoselective Hosomi-Sakurai ring fusion reaction (Figure 4).[11, 12] Cyclization of α,β-unsaturated cyclohexanone **3** gave the intermediate titanium enolate **4** which reacted with chloromethyl methyl sulfide leading to the alkylated product **7** in 77% yield as a single stereoisomer. *cis*-Decalinone **7** served as an advanced intermediate that was readily transformed into the target natural product over several steps.

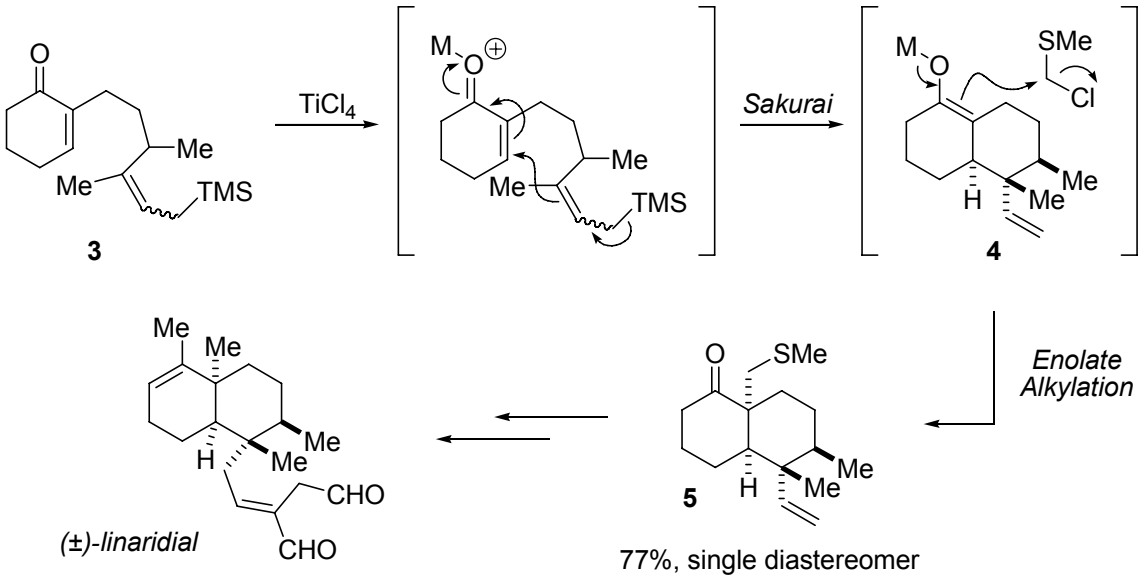
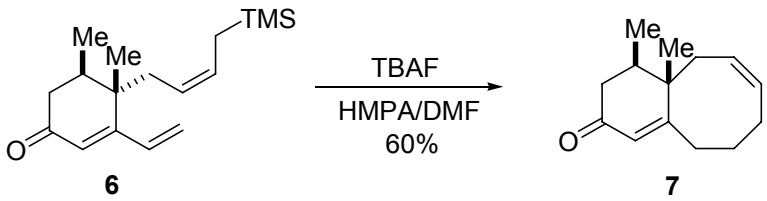
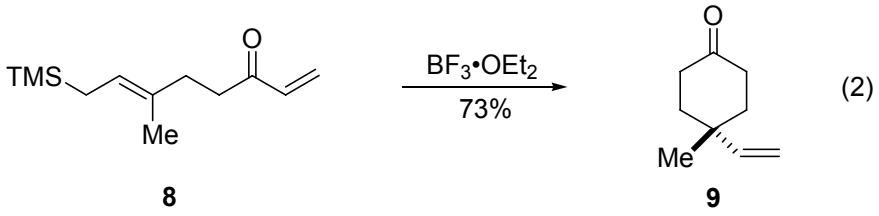


Figure 4. Tokoroyama's synthesis of (±)-linaridial

Extended annulations with allyl silanes can effectively provide access to complex carbocycles containing internal olefins. For example, Majetich *et al.* demonstrated the synthesis of fused [6.4.0] ring systems utilizing fluoride-mediated intramolecular addition of allyl silane **6** to yield bicyclic unsaturated ketone **7** (Eq. 1).[13] As expected, this sequence is strongly dependent on the reaction mediator and use of Lewis acids leads primarily to the analogous [4.4.0] ring system.



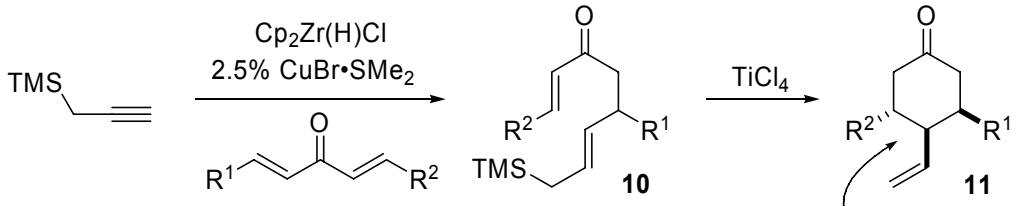
There is little precedent for the intramolecular Hosomi-Sakurai cyclization of linear chain allyl silyl α,β-unsaturated ketones. Wilson and Price reported the earliest example of this annulation in 1982 whereby δ,γ-allylsilyl enone **8** was converted into the corresponding



8 **9** (2)

cyclohexanone **9** in 73% yield with boron trifluoride etherate (Eq. 2).[14] More recently, Huang and Pi demonstrated a diastereoselective variant of this annulation reaction. Hydrozirconation of propargyl trimethylsilane and conjugate addition of the vinyl zirconocene to dibenzylideneacetone derivatives *via* copper catalysis afforded the δ,γ-allylsilyl unsaturated ketone substrates **10** (Scheme 1).[15] Intramolecular Hosomi-Sakurai annulation of the unsaturated ketones **10** mediated by titanium tetrachloride leads to the desired trisubstituted cyclohexanones

Scheme 1. A diastereoselective Hosomi-Sakurai monoannulation reaction



R^1	R^2	Yield **10** (%)	Yield **11** (%)
$-C_6H_5$	$-C_6H_5$	86	86
$-C_6H_5$	-Me	78	82
$-C_6H_5$	-H	73	78
$-^n$Bu	$-^n$Bu	68	81

11 in excellent yields. The authors note that the diastereoselectivity of this transformation is 'remarkable' but do not provide analytical data to support their claim. The relative stereochemistry was established by examining the nOe data for one of the symmetrically substituted cyclohexanone products. Unfortunately, the symmetrical nature of the molecule

leaves some ambiguity in determining whether the *cis*- or *trans*-relative stereochemistry is formed across the new carbon-carbon bond.

1.1.2 Introduction to ICR Methodology; Application to Hosomi-Sakurai Annulation

Reactions that selectively activate stable atomic bonds are among the most powerful methods available in modern synthetic chemistry. These transformations proceed without dependence on reactive functional groups which serves to streamline synthetic routes to complex molecules. Unfortunately, functional groups also target reactivity, hence it is often a difficult task to identify reactions that activate inert bonds in a selective fashion. Transition metals have proven to be useful in this regard as demonstrated by their employment for selective C-H bond activation.[16-18]

In 2003, the Nelson group identified a highly reactive cationic iridium(I)-tricyclohexylphosphine catalyst that selectively activates the allylic C-H bond of diallyl ethers (Figure 5). The thermodynamic bias offered by both increasing olefin substitution (when R_1 =

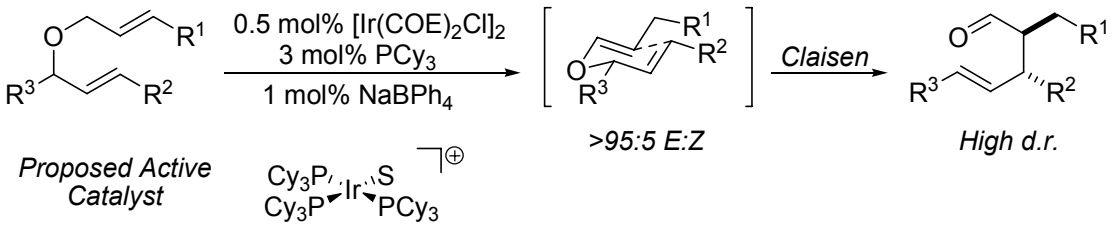


Figure 5. Selective C-H activation leading to Claisen precursors

H) and conjugation with oxygen lone pairs facilitates alkene isomerization providing intermediate vinyl ethers with high geometrical purity (>95:5 *E:Z*).[19] Allyl vinyl ethers are precursors for the thermal Claisen rearrangement, which leads to diastereomerically enriched

α,β-disubstituted, δ,γ-unsaturated aldehydes.[20-24] It is notable that the vinyl ether isomeric ratio is directly related to the diastereomeric ratio of the aldehyde produced by the Claisen rearrangement. The ICR route provides access to a wide assortment of vinyl ethers that are difficult to prepare using previously established methods.[25-29] Earlier C-H activation catalysts utilized for such isomerizations exhibited poor geometrical selectivity or employed basic additives that lead to aldehyde epimerization.[30] The ICR catalyst does not suffer from these drawbacks, giving aldehydes with a wide range of functionality all in excellent yields and diastereomeric ratios (Figure 6). Aldehydes may be prepared from enantioenriched precursors arrived at *via* asymmetric additions to α,β-unsaturated aldehydes.

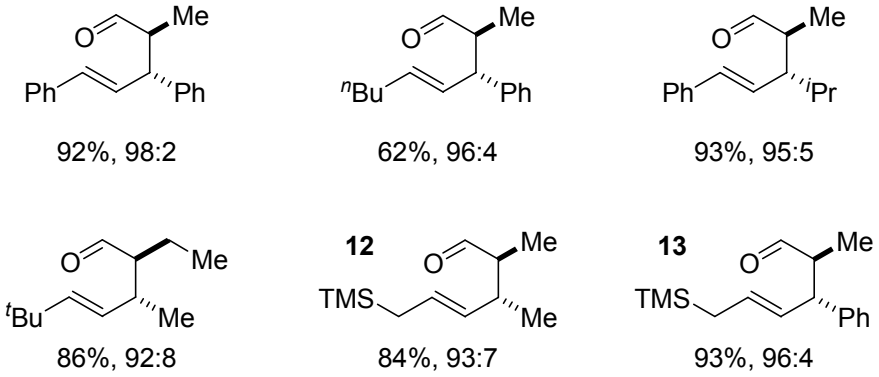


Figure 6. Represenative products of the ICR reaction

We envisioned that δ,γ-allyl silyl aldehydes such as **12** and **13** could serve as synthetic precursors for a wide array of Hosomi-Sakurai annulation substrates. Retrosynthetically, simple allyl or vinyl metal additions to the ICR-derived aldehydes followed by oxidation would lead to α,β-unsaturated ketone starting materials required for the annulation reaction (Figure 7). This convergent sequence would provide access to a diverse family of carbocycles limited only by the spectrum of viable vinyl nucleophiles or ICR-derived allylsilyl aldehydes. Based on the existing

precedent, we predicted that the cyclization reactions would proceed with a significant degree of

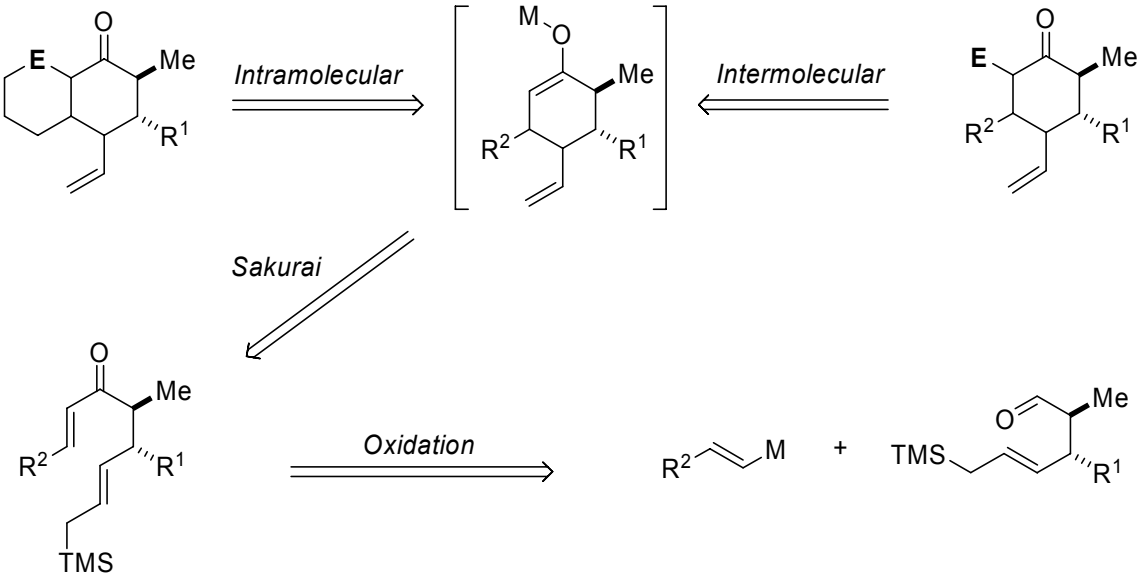


Figure 7. Retrosynthetic analysis of Sakurai products

diastereoselectivity. Higher levels of complexity could be achieved by direct trapping of the intermediate titanium enolate with a variety of electrophiles. Formulation of this reaction sequence in a fully intramolecular manifold would potentially lead to complex bicyclic ring construction. The following pages describe the development of this sequence and observations regarding the mechanism and stereoselectivity of the cyclization.

1.2 RESULTS AND DISCUSSION

1.2.1 ICR Precursor Synthesis and Optimization

The first objective of this project was to develop a convenient and scalable synthesis of the allylsilyl aldehyde substrates. The preparation of diallyl ether precursors was problematic in this

case given the propensity of β-silyl alcohols to undergo Peterson olefination under Williamson etherification conditions (Figure 8).[31, 32] A mild etherification method employing an *in situ*-prepared zinc alkoxide had been employed in the original ICR study to synthesize the requisite β-silyl diallyl ethers.[33] The enhanced covalency of the zinc-oxygen bond compared to that of the sodium or lithium-oxygen bond effectively minimizes competing Peterson olefination while enabling effective attack on π-allyl palladium complexes to yield the desired ether products.

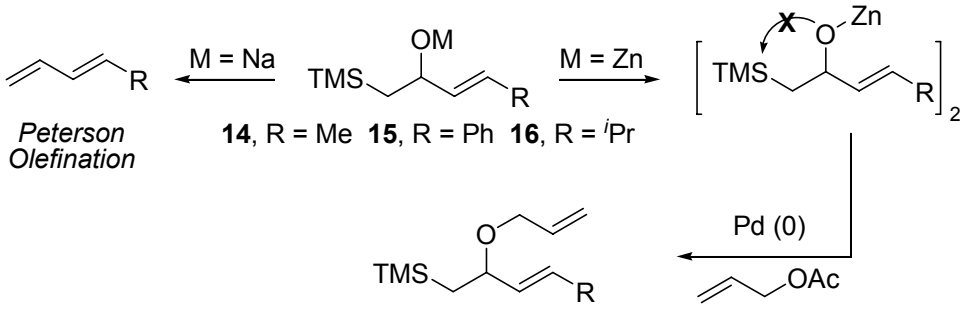
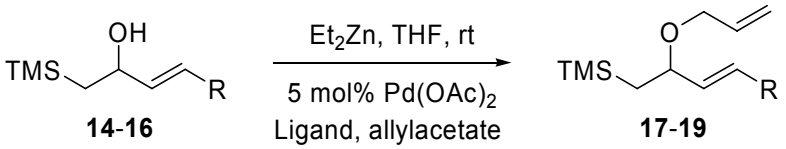


Figure 8. Synthesis of silyl diallyl ethers

The π-allyl etherification reactions had been performed on small scale with tetrakis(triphenylphosphine)palladium (0) resulting in variable yields. In order to establish an effective general approach, the synthesis of diallyl ethers **17**-**19** was optimized using *in situ* generated catalysts. Several phosphine ligands were screened and ligand-to-metal stoichiometry was varied in order to determine the effect on reaction conversion (Table 1). The highest conversions from alcohols **14** and **16** to diallyl ether products were observed for reactions employing a 5:1 ratio of phosphine to palladium acetate. Following a 12 hr reaction time, conversions with either strongly σ-basic phosphines or π-acidic phosphines were approximately 60%. The independence of the reaction rate and conversion on ligand electronics indicated that the formation of the palladium allyl complex or generation of Pd(0) is not rate limiting, implying

that zinc alkoxide attack is the slowest step. After an initial 12 hour period, 5 days or longer was required for reactions to reach conversions of 90% by ^{1}H-NMR, which demonstrates that a rate

Table 1. Optimization of *in situ* generated Pd(0)-catalyzed allyl etherification

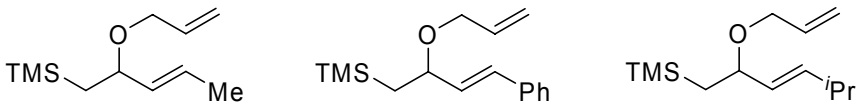


14-16 **17-19**

Alcohol	Conditions[a]	Conversion to Ether (%)[b]
14	7.5% PPh_3	16
"	7.5% PCy_3	10
"	25% PPh_3	63
"	25% PCy_3	61
"	25% PPh_3	88[c]
16	25% $AsPh_3$	30
"	25% $P(furyl)_3$	61
"	25% PPh_3	92[c]

[a]5% $Pd(OAc)_2$ was used in all cases. [b]Conversion was determined by comparrison of the alcohol methine and ether allylic methylene integration by crude ^{1}H-NMR. [c]Reaction was performed over 5 d.

reduction occurs during the course of the reaction. One possible explanation for this behavior is interference of the reaction due to product inhibition (e.g., $Zn(OAc)_2$). Although long reaction times (5-7 days) are a considerable drawback, the etherification of β-silyl alcohols **14-16** with 5% palladium(0) prepared *in situ* from triphenylphosphine and palladium(II) acetate proved to be a reliable protocol. The method is also scaleable, enabling the routine production of 3-8 g batches of diallyl ethers **17-19** (Figure 9). Homostyryl alcohol **15** was prone to competing Peterson olefination during the reaction due to labilization of the C-O bond.

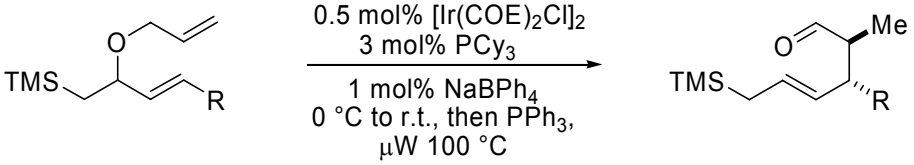


17, 8.0 g, 79% (7d) **18**, 3.1 g, 52% (2d) **19**, 5.7 g, 93% (7d)

Figure 9. Diallyl ethers prepared by *in situ* palladium(0) conditions

Having optimized the synthesis of diallyl ethers **17-19**, the next priority was to demonstrate the performance of the ICR reaction on preparatory scale (Table 2). The standard allyl ether isomerization was performed over 15-30 minutes at ambient temperature, followed by

Table 2. Optimized synthesis of aldehydes **20-22**



Aldehyde	R	Time (min)	Yield (%)	d.r.[a]
20	-Me	45	98	93:7
21	-Ph	60	100	92:8
22	-^{i}Pr	75	100	81:7[a] (*syn & anti E*), 12 (*Z*)

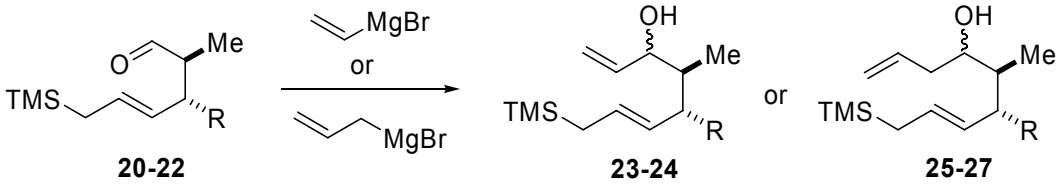
[a]*syn:anti:Z* Ratios determined by integration of aldehyde resonances by ^{1}H-NMR or combination 500 MHz ^{1}H-NMR and GC for aldehyde **22**.

addition of triphenylphosphine to quench the Lewis acidic catalyst. Unfortunately, large-scale isomerizations were observed to be mildly exothermic, yielding aldehydes of diminished diastereomeric ratios. Cooling the reaction vessel to 0 °C during catalyst addition effectively prevented this erosion of diastereoselectivity. By the original protocol, vinyl ethers derived from substrates **17** and **18** required 12 hours in refluxing CH_2Cl_2 to affect the Claisen rearrangement.

For less active substrates such as **19**, however, only 60-70% conversion to the desired aldehyde was observed following 3 days in refluxing CH_2Cl_2. Fortunately, microwave irradiation was found to be an effective alternative to conventional heating for the thermal Claisen rearrangement. Irradiation of the intermediate vinyl ethers derived from **17**-**19** at 100 °C facilitated rapid conversion (45-75 min) to the desired aldehydes **20**-**22** in excellent diastereomeric ratios. This optimized procedure was used routinely to prepare multi gram batches of the desired aldehyde substrates.

1.2.2 Sakurai Substrate Preparation

Table 3. Synthesis of allylic and homoallylic alcohols **23**-**27**



20-22 **23-24** **25-27**

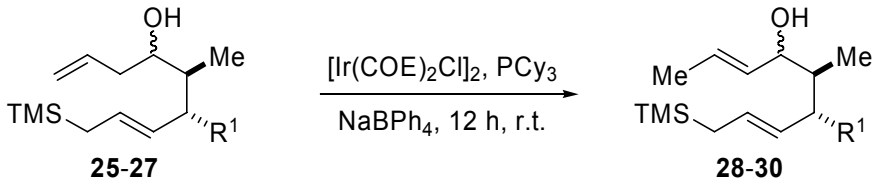
R	Yield (%) Allylic OH[a]	Yield (%) Homoallylic OH[a]
-Me	50 (**23**)	66 (**25**)
-Ph	72 (**24**)	62 (**26**)
-^{i}Pr	—	68 (**27**)

[a]All alcohols were isolated as an approximately 1:1 - 3:1 mixture of diastereomers.

With substantial quantities of the allylsilyl aldehydes now available, efforts were made to elaborate these compounds into the unsaturated ketone Sakurai substrates. Commercially available vinyl and allyl Grignard reagents were added to crude aldehydes **20**-**22** to yield the desired allylic and homoallylic alcohols **23**-**27** in moderate yields (avg. 65%) as a

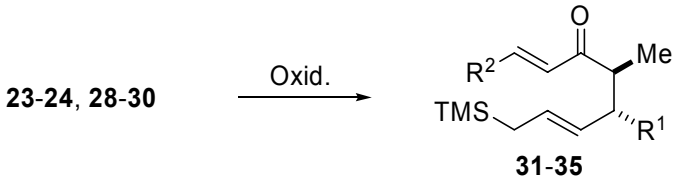
inconsequential mixture of diastereomers (Table 3). It was impossible to observe the allylic alcohols produced from the *anti*-aldehyde diastereomer by routine inspection of the crude ^{1}H-NMR. At this stage, allylic alcohols **23** and **24** could be directly oxidized to the desired unsaturated ketones, while homoallylic alcohols **25-27** required an olefin transposition step prior

Table 4. Synthesis of Sakurai substrates



25-27 **28-30**

	R^1	Catalyst (mol%)	Yield (%)
28	-Me	1	90
29	-Ph	1	81
30	-^{i}Pr	2	81



31-35

	R^1	R^2	Oxidant	Yield (%)	Isolated Product Ratio[a]
31	-Me	-Me	SO_3•Pyr.	86	82.5:7.9:9.7
32	-Ph	-Me	"	62	86:6:8[b]
33	-^{i}Pr	-Me	"	83	81.4:6.0:10.6:2.0[c]
34	-Me	-H	"	85	77.4:10.2:12.3
35	-Ph	-H	DMP	63	83.8:8.1:8.1

[a]Product ratios determined by GC-MS following flash chromatography. Listed in order: *syn*-ketone, *anti*-ketone, *Z*-allyl silane. [b]Product ratio determined by 500MHz ^{1}H-NMR by integration of Me_3Si- resonances. [c]Due to the lower d.r. of the ^{i}Pr Claisen, the *anti-Z*-ketone accounts for the fourth impurity.

to oxidation. Gratifyingly, exposure of **25-27** to the ICR catalyst for 12 hours at ambient

temperature gave the allylic alcohols **28**-**30** in 80-90% yield as the *E*-olefin isomer exclusively (Table 4). Unexpectedly, 2% catalyst loading was necessary to efficiently isomerize substrate **28**. It is unlikely that the isopropyl moiety could impede catalyst activity sterically given its distal relationship to the reactive site, hence the molecular conformation must play a considerable role in determining isomerization rate. Oxidation of alcohols **23** and **28**-**30** was accomplished using Parikh-Doering conditions to afford the desired unsaturated ketones **31**-**34** in good yields.[34] Interestingly, SO_3•Pyr oxidation of **24** failed to afford ketone **35**, while Dess-Martin periodinane provided 63% yield of desired enone.[35-38]

Following purification by flash chromatography, isolated unsaturated ketones **31**-**35** contained two contaminants (excluding ketone **33**, which contained a third minor impurity) of equal molecular mass to the parent compound as indicated by GC-MS (Figure 10). The minor

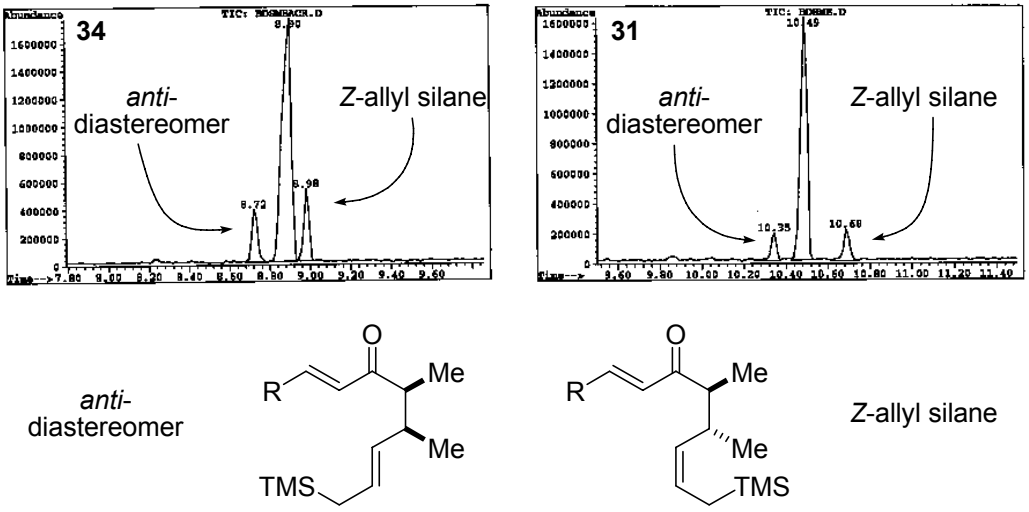


Figure 10. GC-EIMS total ion chromatogram of isolated **34** and **31**

components cannot be *Z*-enone isomers by virtue of the fact that unsubstituted enones **34** and **35** possess an equal number of impurities to methyl enones **31** and **32**. Subjecting enone **32** to

repeated cycles of flash chromatography gave a small aliquot of one impurity for which the ^{1}H-NMR spectra closely resembled *syn*-**32** (unsaturated ketone, allylsilyl olefin and methylene, aromatic ring, methyl doublets), with slightly altered chemical shifts (Figure 11). The coupling

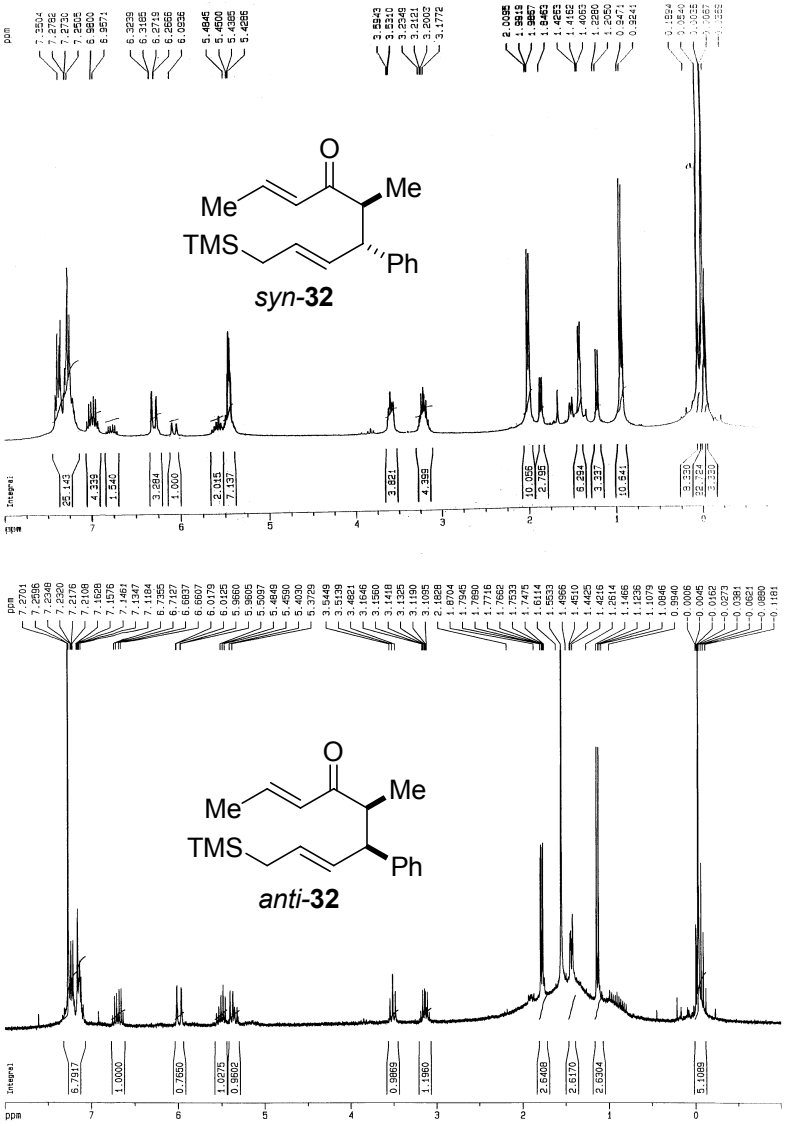


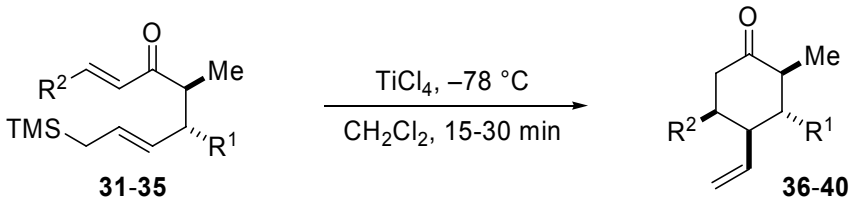
Figure 11. ^{1}H-NMR spectra of **32** enriched in impurities (*top*) and isolated impurity (*bottom*)

constant calculated for the allylsilyl olefin C-H resonance at 5.5 ppm is 15.2 Hz, implying a *trans* geometry. These observations suggest that the impurity is *anti*-**32** derived from the minor

anti-diastereomer of aldehyde **20**. The only remaining possibility for the identity of the second impurity is the *Z*-allylsilane isomer, which has yet to be isolated. It is unclear at which point during the synthetic sequence that this isomerization occurs.

1.2.3 Intramolecular Sakurai Annulation

Table 5. Sakurai annulation reactions



31-35 **36-40**

R^1	R^2	Claisen d.r.[f]	Ketone Ratio[a]	Yield (%)	Iso. Pdt. Ratio[e]
-Me	-Me	93:7 (**20**)	82.5:7.9:9.7 (**31**)	67 (**36**)[b]	91.7:8.3
-Ph	-Me	92:8 (**21**)	86:6:8 (**32**)	82 (**37**)	94.6:3.8:1.7
-^{i}Pr	-Me	81:7:12 (**22**)	81.4:6.0:10.6:2.0 (**33**)	87 (**38**)	89.0:8.2:2.7
-Me	-H	93:7 (**20**)	77.4:10.2:12.3 (**34**)	59 (**39**)[b,c]	89.8:10.2
-Ph	-H	92:8 (**21**)	83.8:8.1:8.1 (**35**)	82 (**40**)[d]	92.6:5.3:2.1

[a]Compound ratios determined by GC-MS following flash chromatography. Listed in order: *syn*-ketone, *anti*-ketone, *Z*-allyl silane. [b]Compounds are volatile. [c]~10% Polymeric material isolated with product by ^{1}H-NMR. [d] ~1% Unidentified impurity indicated in GC-MS. [e]Compound ratios determined by GC-MS following flash chromatography. [f]*syn:anti:Z* Ratios determined by integration of aldehyde resonances by ^{1}H-NMR or combined 500MHz ^{1}H-NMR and GC for aldehyde **22**

Having determined the composition unsaturated ketones **31-35**, the performance of the substrates in the Hosomi-Sakurai annulation process was assessed. Gratifyingly, exposure of **31-35** to $BF_3{\cdot}OEt_2$ or $TiCl_4$ resulted in a highly stereoselective cyclization that yielded cyclohexanones **36-40** following an ammonium chloride quench (Table 5). Yields for the cyclization coincide

with values observed by Huang and Pi, excluding those for the volatile compounds **36** and **39**.[15] The cyclization of unsubstituted enones **34** and **35** produced polymeric byproducts that were easily distinguished by laddering on TLC and broad peaks in the alkyl region of the crude ^{1}H-NMR. Polymerization occurs by intermolecular Michael addition of the formed titanium enolate to enone starting material followed by propagation of the newly formed enolate. Weak Lewis acids ($TiCl_4(THF)_2$, $BiBr_3$) promoted this polymerization by producing low concentrations of the reactive enolate in the presence of the electrophilic starting material (Figure 12). Running the

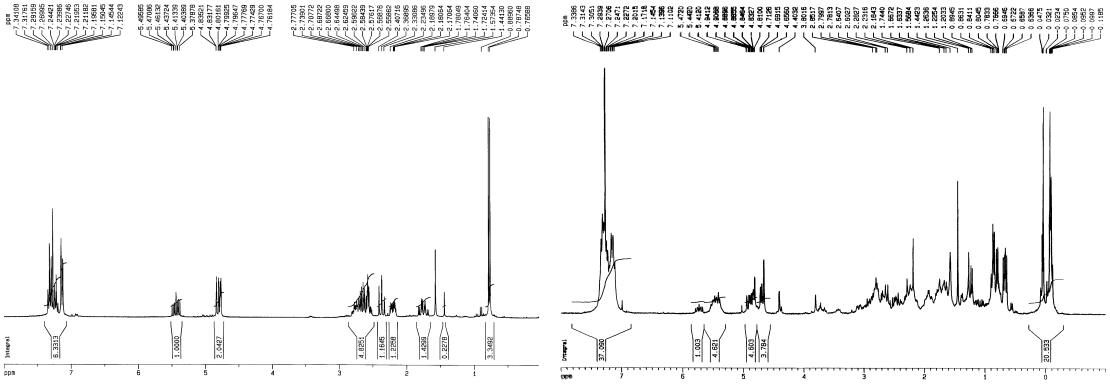


Figure 12. $TiCl_4$ (*left*) and $TiCl_4(THF)_2$ (*right*) mediated cyclizations of **35**

cyclization reaction in dilute conditions (0.05M enone) with reverse addition of substrate to Lewis acid effectively minimizes the formation of these polymeric impurities.

Although the isolated diastereomeric ratios of cyclohexanones **36**-**40** were excellent, the multiple components of the Sakurai products were yet to be identified. This analysis was particularly problematic owing to the isomeric contaminants present in unsaturated ketone starting materials. Upon cyclization of crude unsaturated ketone **31** (*syn*-ketone 82.5 : *anti*-ketone 7.9 : *Z*-allylsilane 9.7), GC-MS analysis indicated the conversion of the three starting

materials **31a-c** into two diastereomeric cyclization products **36a**/**b** & **36c** (91.7:8.3) (Figure 13). The integration of the major diastereomeric product peak **36a**/**b** was equal to the sum of the *syn*-ketone peak **31a** and the *Z*-allylsilane peak **31b**. The cyclization product ratio was nearly identical to the observed Claisen diastereomeric ratio (92:8 vs. 93:7). Though it is possible that **36a/b** may be due to an overlap of two compounds that possess identical retention times, enone **34** and cyclohexanone **39** behaved similarly (three starting materials, two products), suggesting that coincidental elution rates are unlikely to be responsible. This data implies that the *E*- and *Z*-allylsilane isomers form the same diastereomeric cyclohexanone and that the minor product stems from cyclization of the *anti*-ketone diastereomer. This analysis is consistent with observations made during Tokoroyama's synthesis of (±)-linaridial.

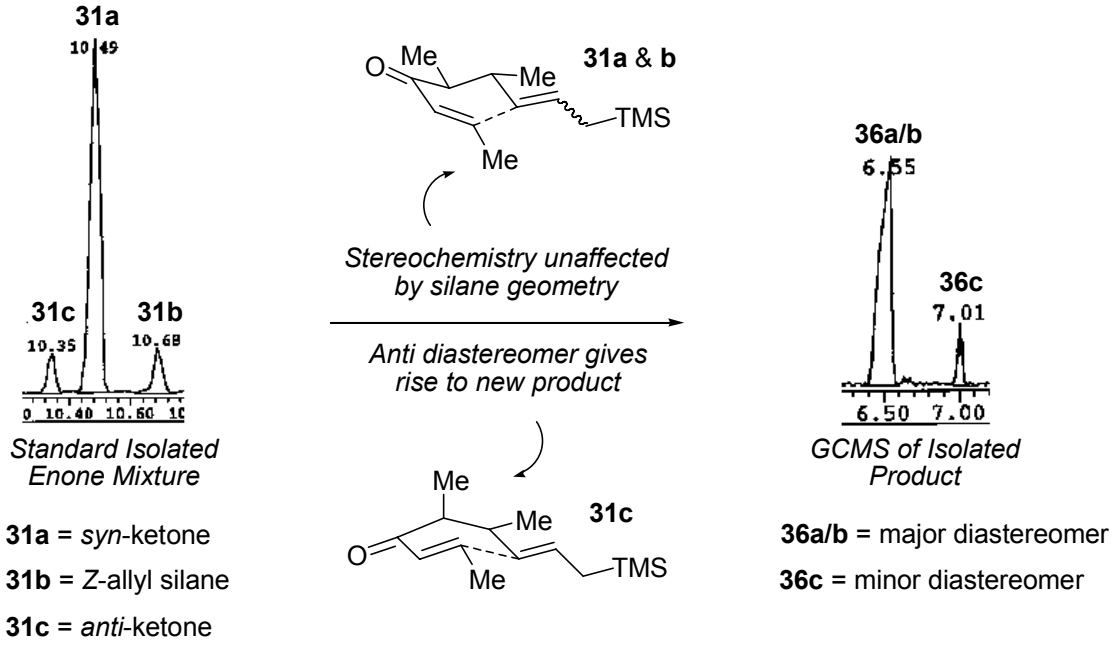


Figure 13. Effect of allylsilane geometry on diastereomeric ratios for **36**

For the phenyl substrates **37** and **40**, three products were detected by GC-MS, which initially suggested that the *Z*-allylsilane isomers produced new diastereomeric cyclohexanones, in contrast to **31** (Figure 14). Closer inspection of the integration values for the major product peaks in **37** and **40** revealed that they equal the sum of the *syn*-ketone and *Z*-allyl silane peaks in **32** and **35** [8 + 86 (**32**) = 94 (**37** = 94.6) and 8.1 + 83.8 (**35**) = 91.9 (**40** = 92.6)]. The sum of the two minor cyclization diastereomer peaks matched the integration value of the *anti*-ketone peak in the starting material [1.7 + 3.8 (**37**) = 5.5 (**32** = 6) and 5.3 + 2.1 (**40**) = 7.4 (**35** = 8.1)].

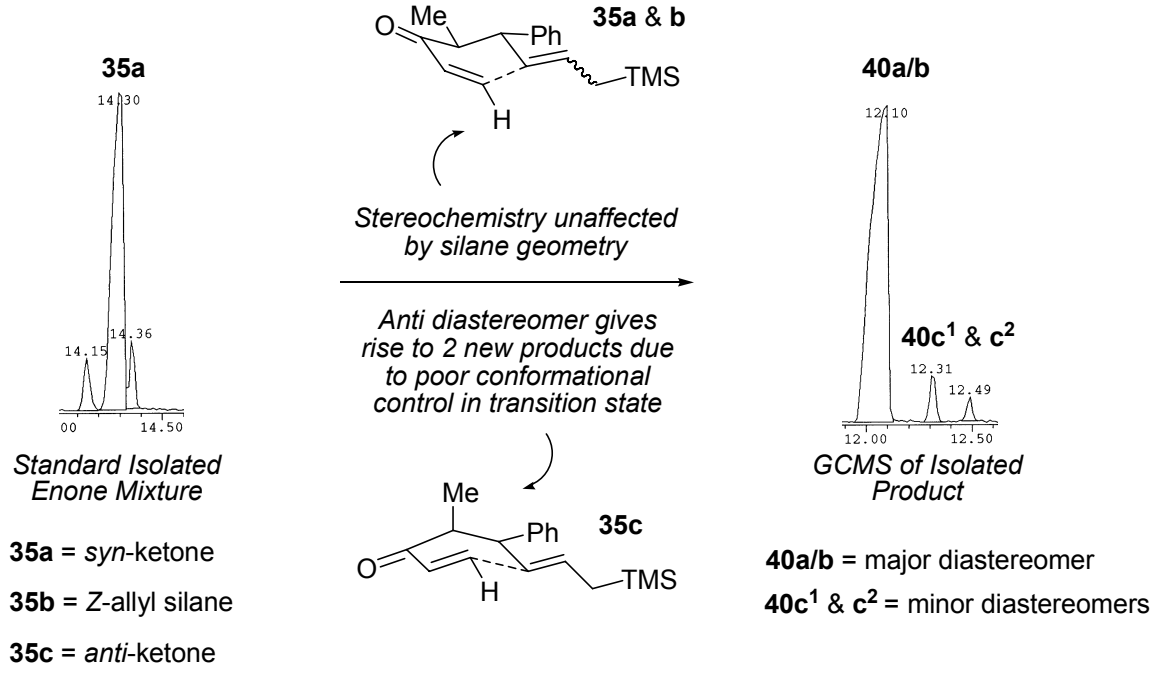


Figure 14. Rationalization of diastereomeric ratios for **37** & **40**

Comparison of the integration of the major diastereomer of **37** and **40** to the sum of the two minor diastereomers gave ratios almost identical to the *syn*-*anti* ratio of the Claisen rearrangement (**37** = 95:5, **40** = 93:7 vs. 92:8). Taken together, these calculations suggest that the *anti*-ketones derived from **32** and **35** cyclize with poor diastereoselectivity while the *anti*-

ketones from **31** and **34** cyclize with high diastereoselectivity. Therefore, *anti*-ketones must proceed through a transition state in which diastereoselectivity is highly dependent on the functionality at the enone α and β stereocenters. Conversely, the stereoselectivity of the *syn*-enone cyclization appears to be independent of the identity of proximal functional groups.

Support for this hypothesis would be strengthened by demonstrating that the cyclization of *syn*- and *anti*-ketones proceeds through different transition states. Following workup, concentration of crude **36** unintentionally led to a significant degree of α-epimerization by residual Lewis acidic titanium salts. Analysis of this product mixture by GC-MS indicated the presence of two compounds in addition to the two that were normally observed (Figure 15).

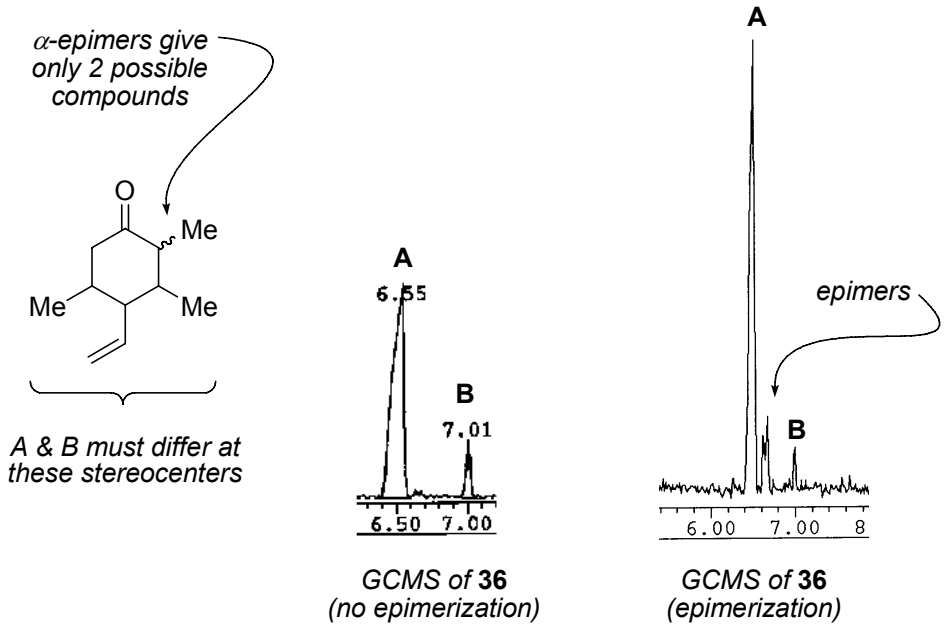


Figure 15. GC-EIMS total ion chromatagram of epimerized cyclohexanone **36**

Epimerization of cyclohexanones differing only at the α-stereocenter would simply cause a shift in the product ratios. Therefore, *syn*- and *anti*-ketones must lead to cyclohexanones differing at

multiple stereocenters, which implies that the two cyclizations occur through different transition states.

The most important remaining question at this point regarded the *intrinsic* diastereoselectivity of the *syn*-ketone cyclization reaction. In order to determine this value, approximately 1 mg of pure unsaturated ketone **31** was isolated by analytical HPLC (chiral OD-H column). Cyclization of **31** was induced with excess titanium tetrachloride and the product ratio determined by GC-MS of the crude reaction mixture (Figure 16). The GC-MS data clearly indicated that cyclization of **31** produced a single diastereomer of cyclohexanone **34**, demonstrating that the *syn*-enone Hosomi-Sakurai annulation is exclusively diastereoselective.

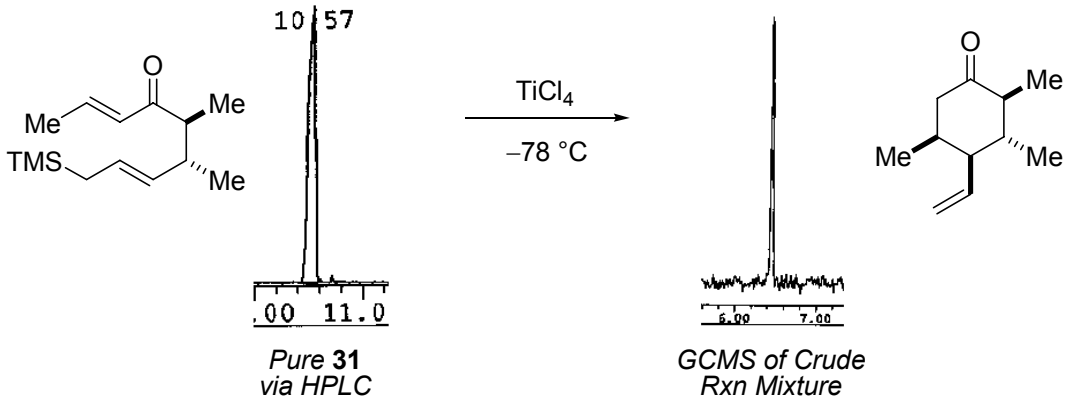


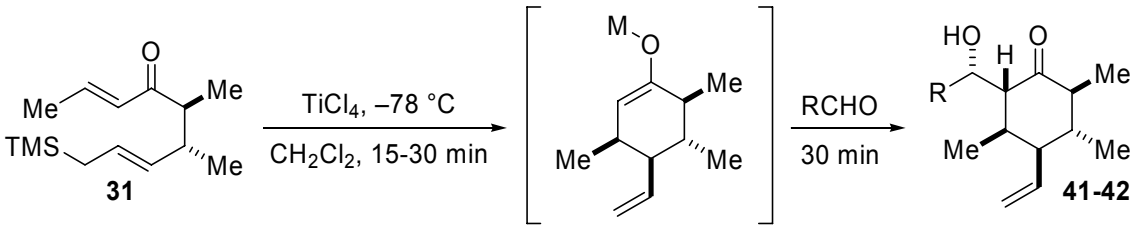
Figure 16. GC-EIMS total ion chromatogram following cyclization of pure **31**

1.2.4 Tandem Intermolecular Sakurai-Aldol Reactions

Given the encouraging results from the Sakurai cyclizations, we set out to explore the feasibility of a tandem aldol reaction. Gratifyingly, addition of isobutyraldehyde or benzaldehyde to the cyclized enolate of **31** at –78 °C afforded the desired aldol products **41** and **42** in good

diastereomeric ratios and moderate yields (Table 6). Note that the reported diastereomeric ratios were determined following purification by flash chromatography. The isolated product ratios are reflective of the crude product ratios since the diastereomeric products were inseparable on silica gel. The approximate intrinsic diastereoselectivity of the aldol reaction can be determined by analyzing the data for β-hydroxy cyclohexanone **41**. In this case, 7% of the product mixture for **41** should be from the minor *anti*-ketone. The remaining product ratio (84.7:8.1) is produced by the aldol reaction of the major *syn*-ketone **31**, hence the intrinsic aldol diastereoselectivity with isobutyraldehyde is 91:9.

Table 6. Sakurai-aldol reactions



Claisen d.r.[a]	Ketone Pdt. Ratio[b]	R	Yield (%)	Iso. Pdt. Ratio[c]
93:7 (**20**)	82.5:7.9:9.7 (**31**)	-^{i}Pr	52 (**41**)	84.7:8.1:7.2
"	"	-Ph	52 (**42**)	84.9:10.4:3.2:1.6

[a]*syn:anti:Z* Ratios determined by integration of aldehyde resonances by ^{1}H-NMR. [b]Listed in order: *syn*-ketone, *anti*-ketone, Z-allyl silane. [c]Isolated product ratios determined by GC-MS following flash chromatography.

1.2.5 Intermolecular Sakurai-Aldol Relative Stereochemistry

In order to establish the relative stereochemistry of β-hydroxy cyclohexanone **42**, esterification was carried out using *p*-bromobenzoyl chloride to give 80% yield of benzoate **43** that provided crystals suitable for X-ray analysis (Figure 17). From the X-ray structure of **43**, it is clear that the initial Sakurai annulation gives the *trans* relative stereochemistry across the pre-existing carbon-carbon bond and the *cis* stereochemistry across the newly formed carbon-carbon bond. The ensuing *syn*-aldol reaction occurs from the bottom face of the cyclohexanone, *trans* to the axial C–3 methyl group.

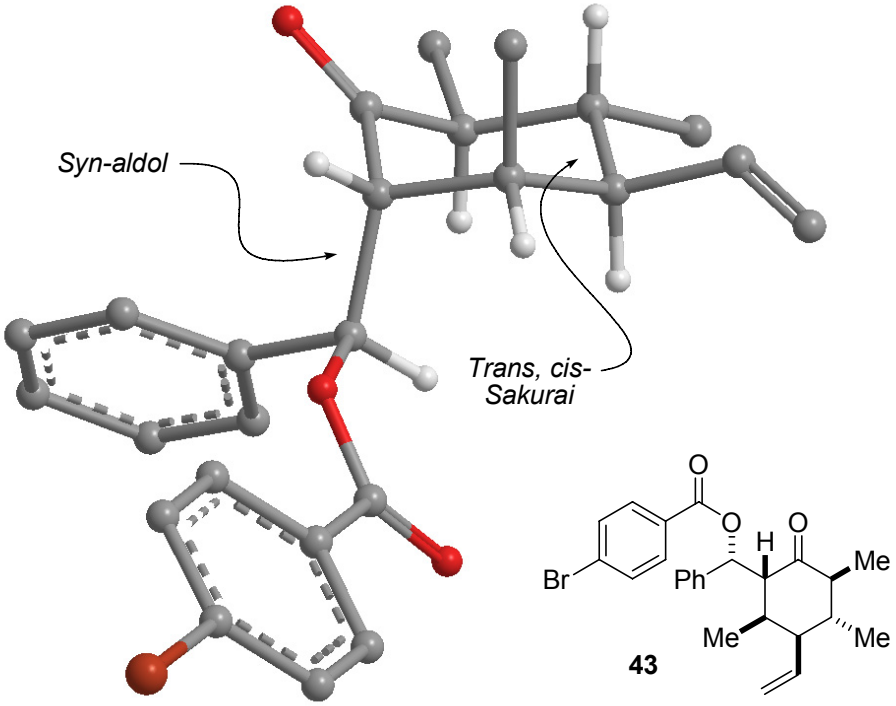


Figure 17. X-Ray structure of compound **43**

There are two possible explanations for the observed relative stereochemistry produced by the Sakurai annulation (Figure 18A). Majetich proposed that the considerable build-up of charge manifested at the α-center of the ketone and the β-position of the allylsilane would be mutually stabilized if brought into proximity through a four-centered transition state.[9] This type

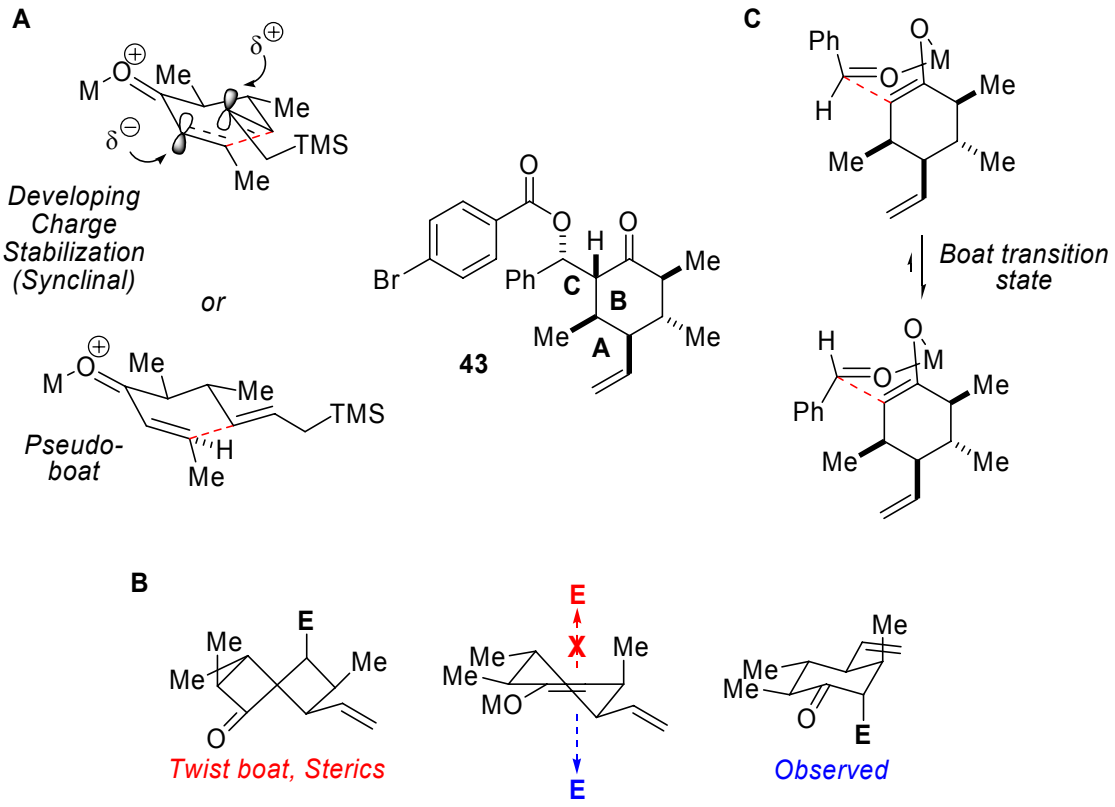


Figure 18. Rationalization of Sakurai-aldol stereochemistry

of secondary orbital overlap is not unlike the Alder-endo effect, and also explains the common formation of cyclobutanes during Sakurai reactions with less reactive allylsilanes.[39] Alternatively, the relative stereochemistry of polyene cyclizations is well rationalized by the Stork-Eschenmoser postulate; however, in this case, the electrophile is not a simple alkene, but an unsaturated ketone that must remain in conjugation for effective LUMO activation by the

Lewis acid.[40, 41] This conformational distinction could lead to a pseudo-boat transition state that produces the observed *cis* stereochemistry.

The *trans* stereochemistry between C_2−C_3 is determined strictly by facial approach of the electrophile on the half-chair enolate (Figure 18B). Steric shielding of the enolate top face by the axial methyl group effectively screens this point of approach. Top-face attack also leads to a twist-boat product conformation, while bottom face attack produces a chair conformation, further favoring the latter trajectory. Therefore, the observed stereochemistry is favored in either an early or late transition state, which is an important consideration since the thermodynamics of aldol reactions is often strongly substrate dependant.

It is perplexing that the *syn*-aldol reaction occured predominantly, since ring constraints preclude *Z*-enolate formation (Figure 18C). Given that typical closed transition states with *E*-enolates give *anti*-aldol products, this situation must be considerably more complex. It is certain that closed transition states with titanium would be significantly distorted from the standard Zimmerman-Traxler model by unique bond angles of the metal (e.g., 90^o if O_h), possibly leading unexpected selectivity. Evans has observed this behavior for aliphatic *anti*-aldol reactions with zirconium enolates.[42] Alternatively, the aldol reaction could proceed through a boat transition state in order to avoid steric interactions with the six-membered ring. In this arrangement, equatorial placement of the R-group is clearly preferable to the axial conformation. Reetz has observed similar results for a closely related *syn*-aldol reaction using alkoxytitanium enolates of cyclohexanone (Figure 19).[43] In this case, the basicity of the alkoxide ligands on titanium would favor reaction *via* an open transition state, hence the direct relevance to the chlorotitanium enolate system is questionable.

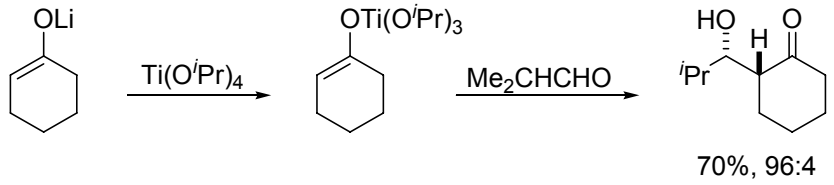
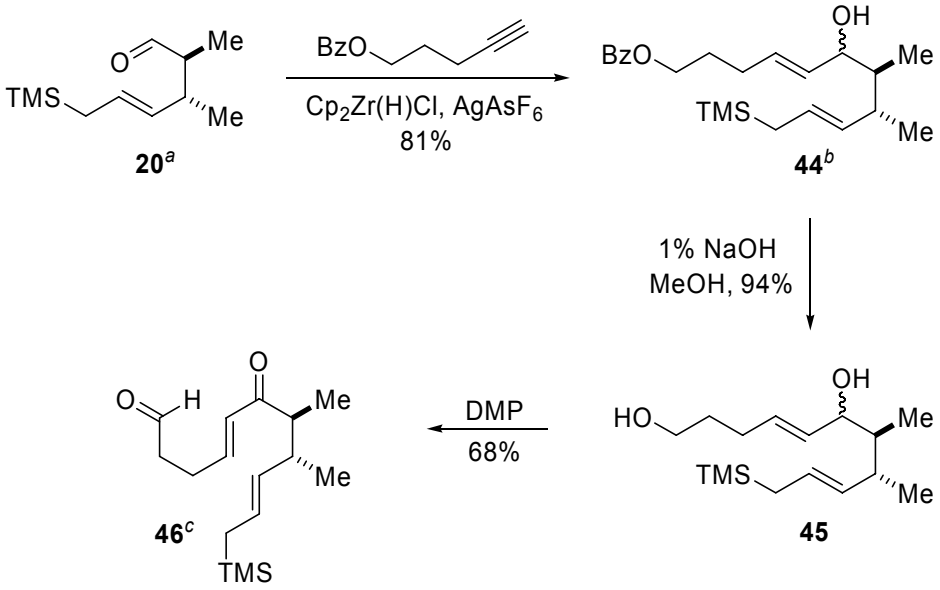


Figure 19. Reetz's *syn*-selective titanium aldol reaction

1.2.6 Tandem Intramolecular Sakurai-Aldol Bicyclization

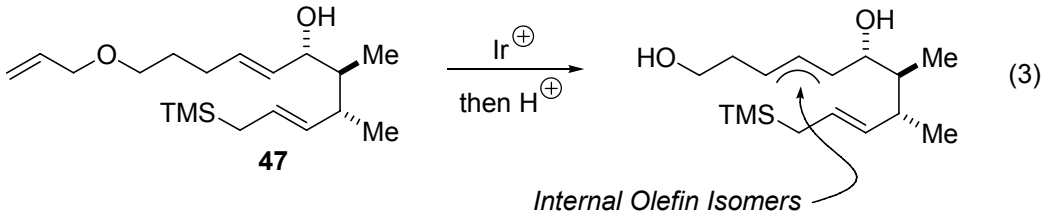
Scheme 2. Preparation of bicyclization precursor **46**



[a]93:7 *syn*:*anti* Determined by integration of aldehyde resonances in ^{1}H-NMR. [b]1:1 Mixture of alcohol stereoisomers. [c]Compound ratio determined by GC-MS following flash chromatography. Isolated ratio 87.8:6.1:6.1.

Having demonstrated a one-pot intermolecular diastereoselective Sakurai-aldol reaction, we envisioned that both transformations could be carried out in an intramolecular fashion to produce highly functionalized bicycles. An efficient sequence was designed and implemented for the preparation of ketoaldehyde substrate **46** (Scheme 2). Hydrozirconation of benzoyl pentynol and silver-catalyzed addition to ICR-derived aldehyde **20** gave allylic alcohol **44** in 81%.[44] Removal

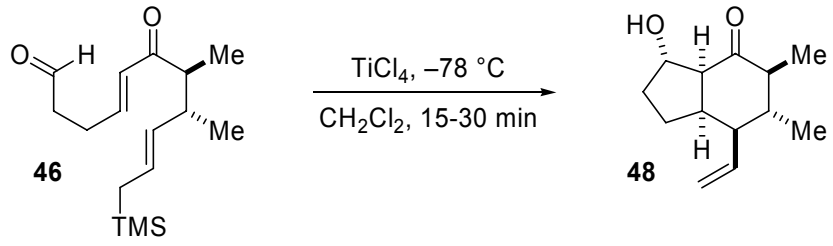
of the benzoate under alkaline conditions gave 94% of diol **45**, which could be subsequently oxidized with Dess-Martin periodinane to afford **46** in 68% yield. Initial attempts at employing allyl protecting groups failed due to scrambling of the internal olefin position of **47** by the ICR catalyst and poor yields with alternative isomerization catalysts (Eq. 3). Exposure of **46** to



(3)

titanium tetrachloride produced the characteristic red enolate color, but the solution quickly paled following intramolecular attack of the aldehyde. Hydrindanone **46** was obtained in 52% yield following aqueous workup and purification by flash chromatography (Table 7).[45] Assuming that 6% of the hydrindanone product mixture is produced by the *anti*-ketoaldehyde impurity in **46**, the remaining product ratio, 88:12 (83:6+5), is reflective of the intrinsic intramolecular aldol diastereoselection.

Table 7. Intramolecular Sakurai-aldol reaction



Claisen d.r.[a]	Ketone Pdt. Ratio	Yield (%)	Iso. Pdt. Ratio[b]
93:7 (**20**)	87.8:6.1:6.1 (**46**)	52 (**48**)	82.8:6.1:5.8:5.3

[a]*syn:anti:Z* Ratios determined by integration of aldehyde resonances by ^{1}H-NMR.
[b]Isolated product ratios determined by GC-MS following flash chromatography.

1.2.7 Intramolecular Sakurai-Aldol Relative Stereochemistry

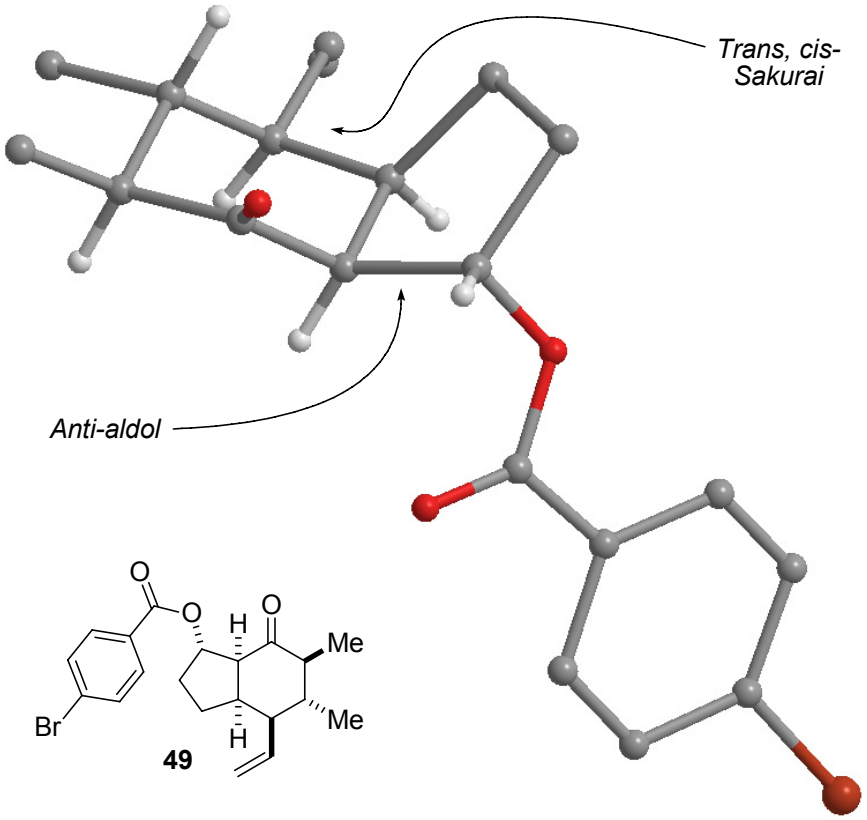


Figure 20. X-ray structure of compound **49**

Hydrindanone **46** was acylated to give bromobenzoate **49** in 55% yield as a crystalline solid that was suitable for X-ray analysis (Figure 20). The Sakurai reaction gave the expected *trans*, *cis* relative stereochemistry, however, facial approach on the enolate was reversed, as was the relative stereochemistry of the aldol reaction. Facial approach of the aldehyde on the half-chair enolate determines the stereochemical relationship across C_2–C_3. In the most stable half-chair conformer, the aldehyde occupies the axial position and must be attacked from the top-face of the enolate (Figure 21B). Note that in the intramolecular case, the aldehyde has replaced the

sterically shielding axial methyl group, effectively eliminating this factor. It is possible to rationalize the *anti*-aldol reaction *via* a Zimmerman-Traxler transition state; however, this invokes the formation of a nine-membered chelate, which is much larger than the more common six- or seven-membered titanium chelates (Figure 21C).[46]

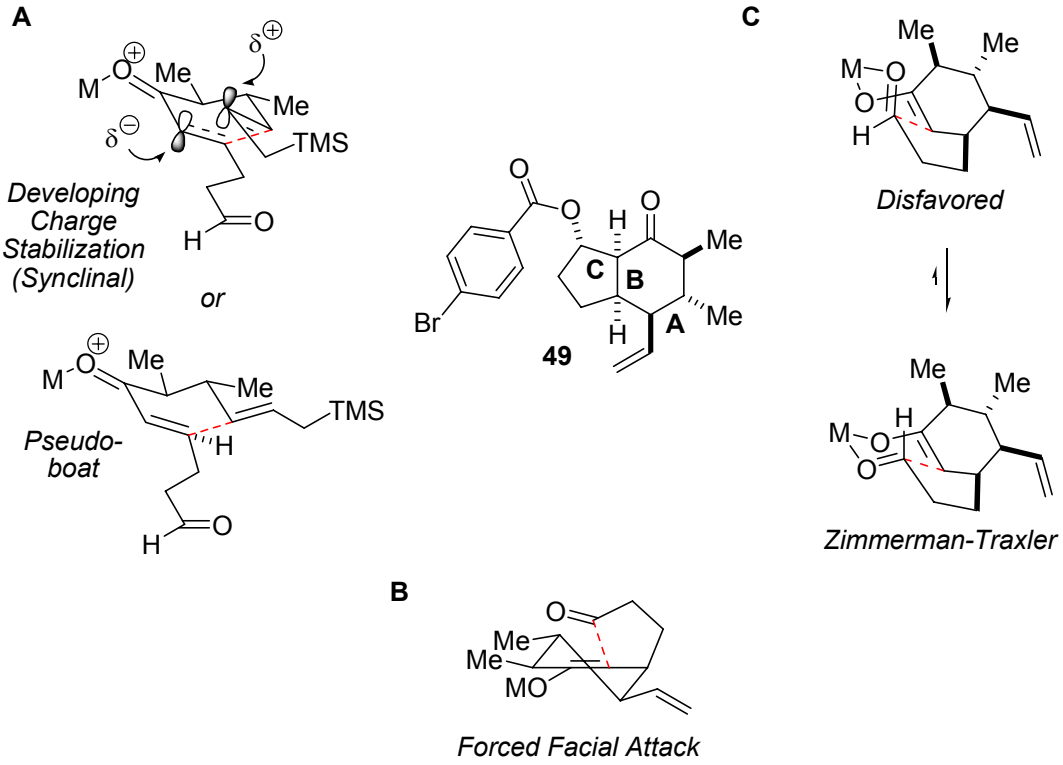


Figure 21. Rationalization of the intramolecular bicyclization relative stereochemistry

1.2.8 Tandem Intramolecular Sakurai-Mannich Bicyclization

The formation of hydrindanone **48** was an important observation since it implied that the intramolecular bicyclization reaction may be general for a variety of electrophiles. Iminium ions were particularly interesting in this context since cyclization of these substrates in an intramolecular Mannich reaction would provide a general route to highly functionalized N-

heterocycles.[47-51] The Lewis acidic conditions of the Sakurai reaction could potentially be used for the *in situ* formation of iminium ions from stable aminal precursors (Figure 22). Allylsilyl

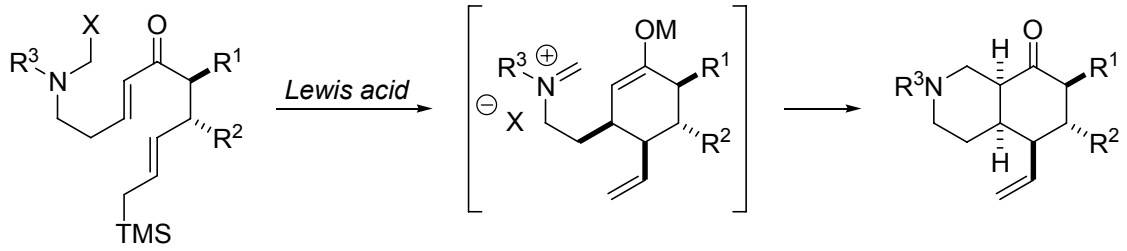


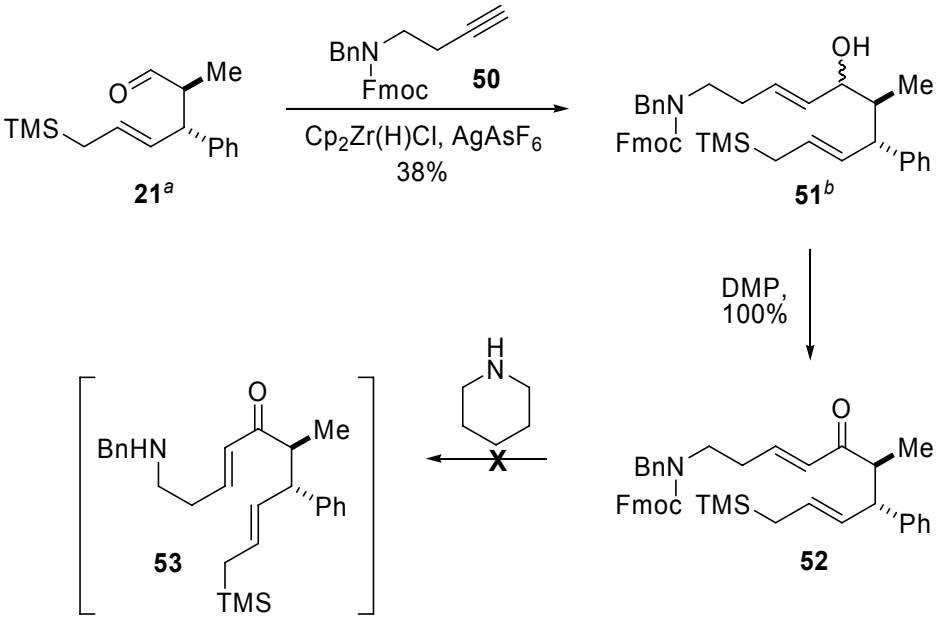
Figure 22. A tandem intramolecular Sakurai-Mannich reaction

aldehydes derived from the ICR reaction would again serve as substrate precursors for this transformation. Identification of a suitable iminium ion precursor would be integral to both the substrate preparation and the success of the Mannich reaction.

At the outset, we planned to use geminal alkoxy dialkylamines due to their high reactivity and exploitation in related systems.[52-54] Acyclic alkyl aminals are only moderately stable to ambient conditions, hence a synthetic sequence was designed to employ a protected nitrogen which could be unveiled and functionalized at a late stage (Scheme 3).[55] Hydrozirconation of Fmoc-protected benzylamino alkyne **50** and addition to allylsilyl aldehyde **21** gave the desired allylic alcohol **51** in poor yield as a mixture of epimers.[56-58] Dess-Martin oxidation of **51** produced ketone **52** quantitatively; however, repeated attempts at deprotection of the fluorenyl carbamate with piperidine lead only transiently to the highly unstable free amine **53**.

Discouraged by both the poor yielding vinyl metal addition and the instability of **53**, a new approach using a robust nitrogen protecting group that would liberate the free amine under Lewis acidic conditions was considered (Figure 23).[59] It was envisioned that an appropriate electrophile could then be added to the reaction leading to *in situ* generation of the iminium ion

Scheme 3. Attempted preparation of Sakurai-Mannich precursor **53**



[a]92:8 *syn*:*anti* Determined by integration of aldehyde resonances in ^{1}H-NMR. [b]1:1 Mixture of alcohol stereoisomers.

and subsequent Mannich cyclization. Alternatively, in the event of enolate alkylation, β-alkoxy elimination would produce an unsaturated ketone, which could manufacture the formal Mannich

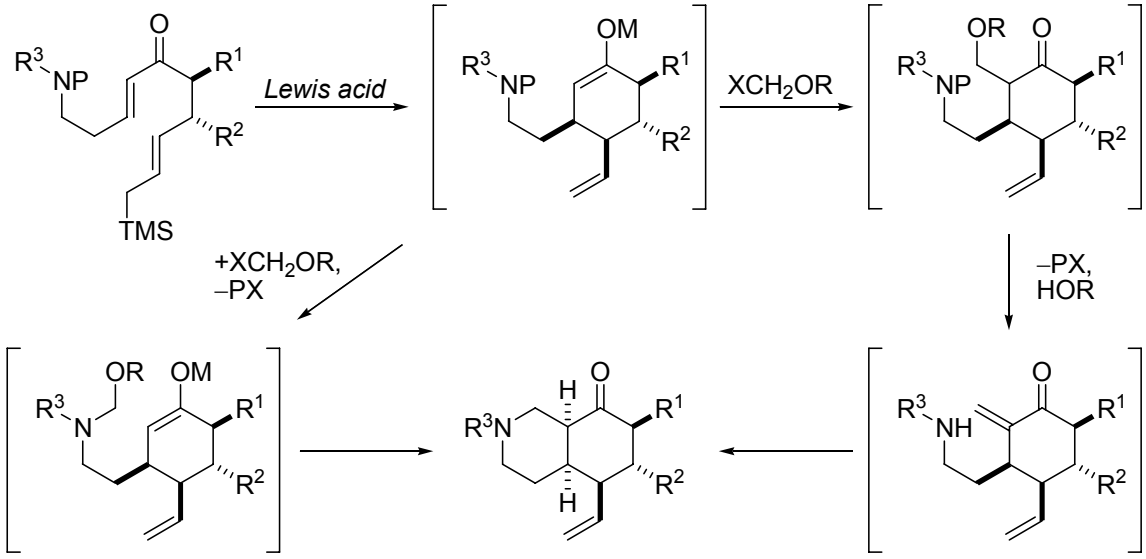
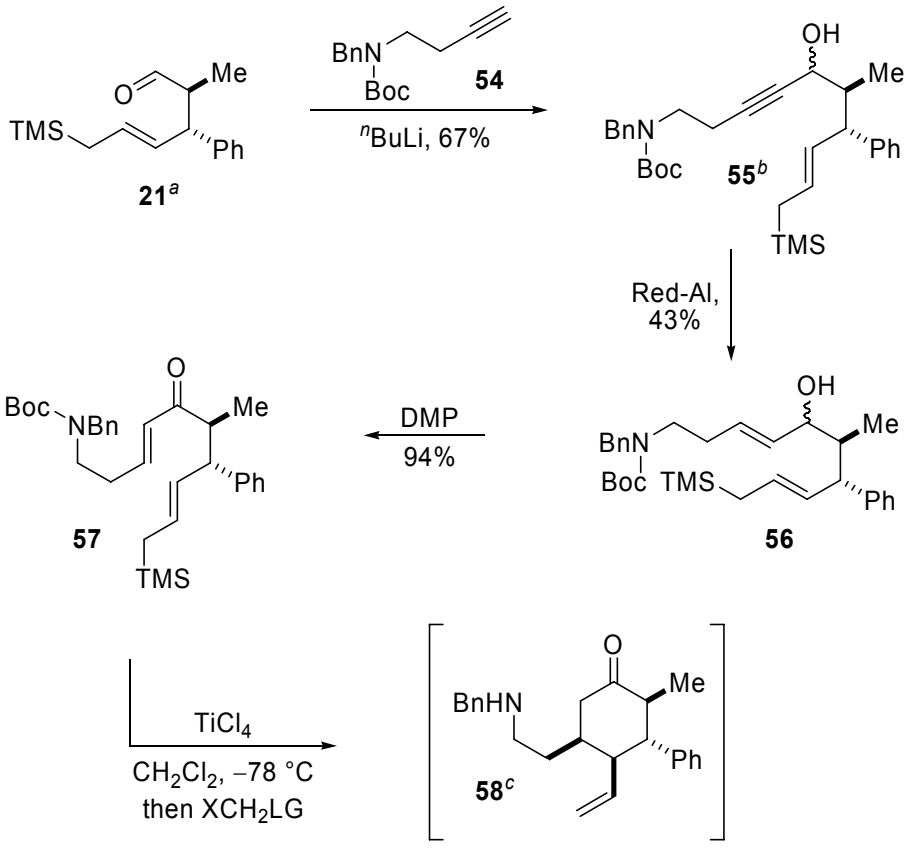


Figure 23. Alternative approach to tandem intramolecular Sakurai-Mannich reaction

product through an intramolecular amino-Michael addition.[60] In order to avoid the inefficient vinyl zirconocene addition reaction, we opted to proceed through propargylic alcohol **55**, which was prepared by addition of the alkynyl lithium species generated from carbamate **54** to aldehyde **21** (Scheme 4). Reduction of **55** to the corresponding allylic alcohol **56** with Red-Al yielded the

Scheme 4. Attempted *in situ* deprotection approach to Sakurai-Mannich reaction



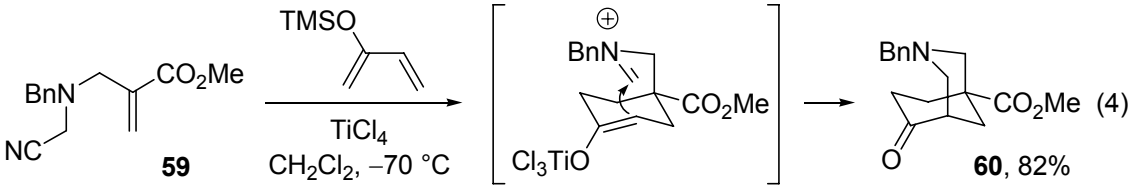
[a]92:8 *syn*:*anti* Determined by integration of aldehyde resonances in ^{1}H-NMR. [b]1:1 Mixture of alcohol stereoisomers. [c]Compound decomposes upon concentration *in vacuo*. Crude ^{1}H-NMR indicates high d.r. for Sakurai reaction.

product in a mediocre 43% yield due to substantial carbamate deprotection.[61] Oxidation with Dess-Martin periodinane produced the desired cyclization substrate **57** in excellent yield. Subjection of substrate **57** to the standard Sakurai reaction followed by addition of various

electrophiles including paraformaldehyde, chloromethyl methyl ether and sulfide, and iodoacetonitrile yielded only the intermediate amino cyclohexanone **58** as determined by ^{1}H-NMR analysis of the crude products. Attempts to isolate **58** were fruitless due to decomposition upon concentration *in vacuo*. Deprotection of the Boc group failed under a variety of mild conditions that were consistently incompatible with the allylsilane moiety.[62]

1.2.9 Preparation and Evaluation of Cyanoaminals for Sakurai-Mannich Bicyclization

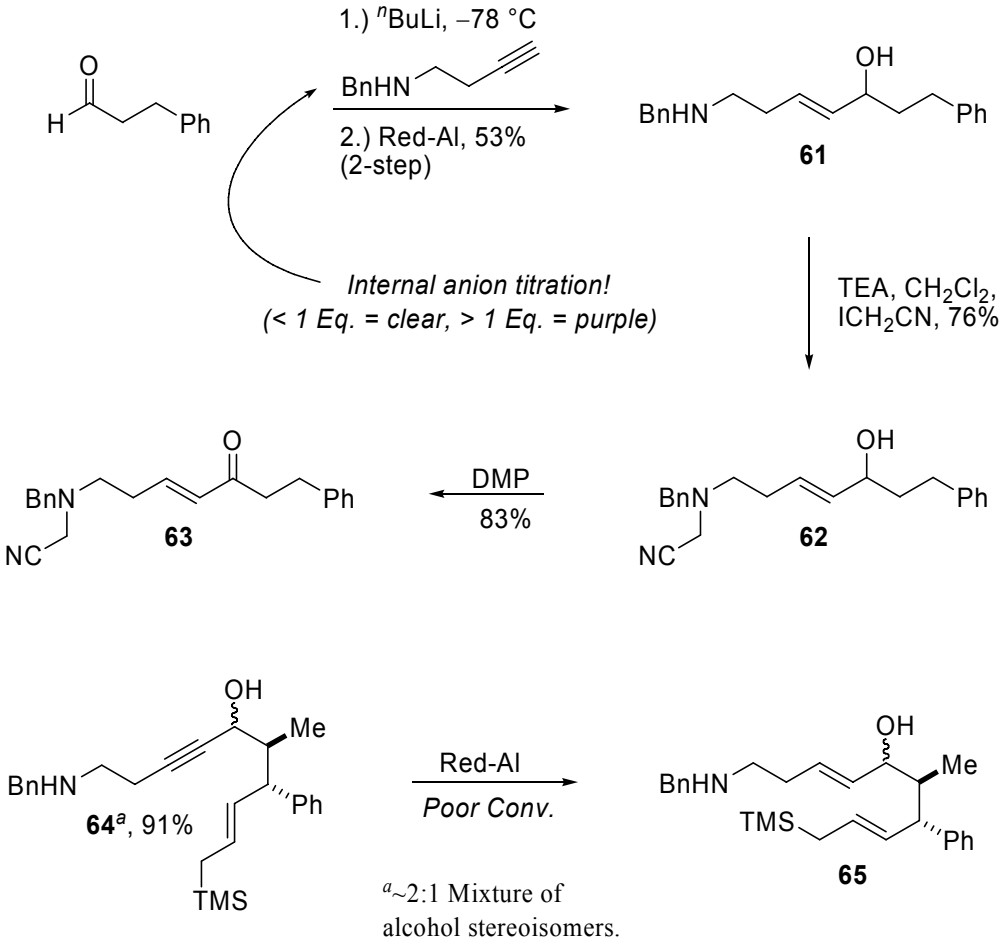
With the variety of challenges involved in preparing acyclic alkyl aminals, we sought a more stable leaving group that could be selectively activated under Lewis acidic conditions. Cyanoaminals appeared to be appealing targets in this regard due to their high stability and use as iminium ion precursors in the presence of various acids.[63-66] Furthermore, Yang has demonstrated that cyanoaminal substrate **59** is able to engage in a tandem Diels-Alder Mannich cyclization which proceeds *via* a titanium enolate iminium ion addition to form the bicyclic alkaloid **60** (Eq. 4).[67, 68] This route is reminiscent of our strategy, hence it seemed reasonable to investigate these iminium ion precursors more closely.



A test synthetic sequence based on hydrocinnamaldehyde was designed to evaluate the preparation of cyanoaminals and their stability to oxidative conditions (Scheme 5). Addition of the alkynyl lithium species generated from the known benzyl aminoalkyne to

hydrocinnamaldehyde followed by Red-Al reduction of the crude propargylic alcohol gave allylic alcohol **61** in 53% yield over two steps. Interestingly, addition of greater than one equivalent of butyllithium to the starting alkyne resulted in a purple colored solution that could be back-titrated by addition of excess alkyne. This phenomenon enables the convenient determination of anion stoichiometery. Selective *N*-alkylation of the benzylamine in the presence of the free hydroxyl using iodoacetonitrile and triethylamine produced cyanoaminal **62**

Scheme 5. Evaluation of cyanoaminal substrate synthesis on test aldehyde

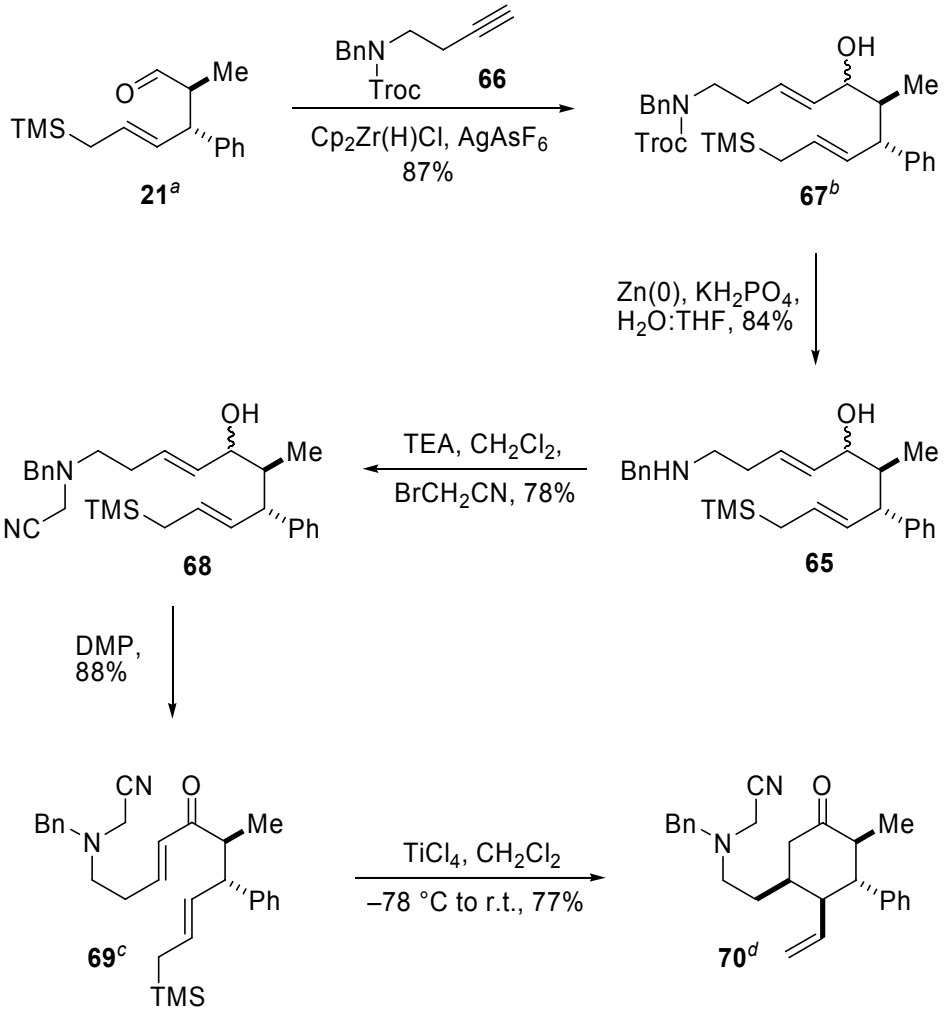


in 76% yield. Cyanoaminal **62** was completely stable to mild oxidative conditions, which afforded unsaturated ketone **63** in 83% yield. Having demonstrated the viability of this sequence in the context of a test substrate, the alkynyl lithium addition was performed on aldehyde **21** to give the desired propargylic alcohol **64** in 91%. Unfortunately, Red-Al reduction of this intermediate was problematic and only gave poor conversion to allylic alcohol **65**.

Given the poor performance of the Red-Al reduction with multiple substrates, the vinyl zirconium addition chemistry was reevaluated in the context of more robust bis-*N*-protected alkynes. Since the deprotection of Boc analogues was problematic in the presence of the allyl silane, the trichloroethyl carbamate protecting group (Troc), which is highly stabile but can be cleaved under mild reductive conditions, was used.[69-71] Following preparation of Troc-protected alkyne **66**, treatment with Schwartz's reagent and addition of the vinyl zirconocene to aldehyde **21** under Suzuki's conditions provided allylic alcohol **67** in a gratifying 87% yield (Scheme 6). This result clearly demonstrates that the poor yields observed previously were due to the acidic fluorenyl hydrogen. Addition of aqueous potassium dihydrogen phosphate to a mixture of alcohol **67** and zinc dust cleanly produced the free amine **65** in 84% yield. Standard oxidation conditions afforded the cyclization substrate **69** in good yield. Exposing cyanoaminal **69** to the optimized Sakurai conditions led to rapid monocyclization; however, the desired perhydroisoquinilone was not observed even upon warming of the reaction mixture.

From these observations, it can be concluded that the cyanoaminal is reluctant to ionize under the reaction conditions, which is puzzling in light of Yang's precedent. In order to form the iminium ion more effectively, silver salts were examined given their propensity to strongly coordinate with cyano groups. Addition of silver triflate or hexafluoroantimonate to a solution

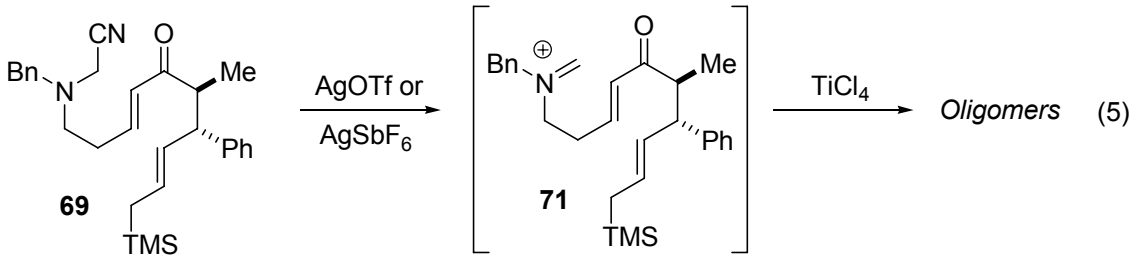
Scheme 6. Evaluation of cyanoaminal substrate **69** for Sakurai-Mannich bicyclization



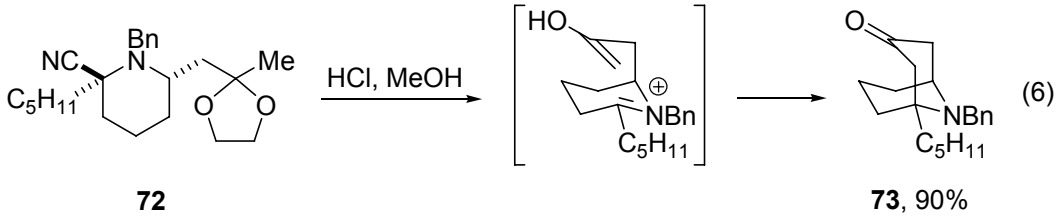
[a]92:8 *syn*:*anti* Determined by integration of aldehyde resonances in ^{1}H-NMR. [b]1:1 Mixture of alcohol stereoisomers. [c]Compound ratio determined by HPLC following flash chromatography. Isolated ratio 87.9:5.7:6.3. [d]Crude ^{1}H-NMR indicates high d.r. for Sakurai reaction, however isolated ratio not rigorously determined.

of **69** immediately formed a precipitate and produced an intermediate which is consistent with iminium ion **71** as determined by ^{1}H-NMR analysis of the reaction mixture (Eq. 5). Subsequent introduction of titanium tetrachloride to the reaction medium unfortunately yielded only complex oligomeric mixtures.

Substrate **70** is a potential intermediate for the synthesis of perhydroisoquinilones by a less elegant 2-step approach. Husson has demonstrated the protic acid-mediated Mannich



cyclization of neopentyl cyanoaminal **72** to give bicycle **73** in 90% yield (Eq. 6).[72] Cyanoaminal substrate **70** was reluctant to ionize in refluxing 10% hydrochloric acid in methanol or Amberlyst sulfonic acid resin, however, resulting only in minor amounts of α-epimerization.

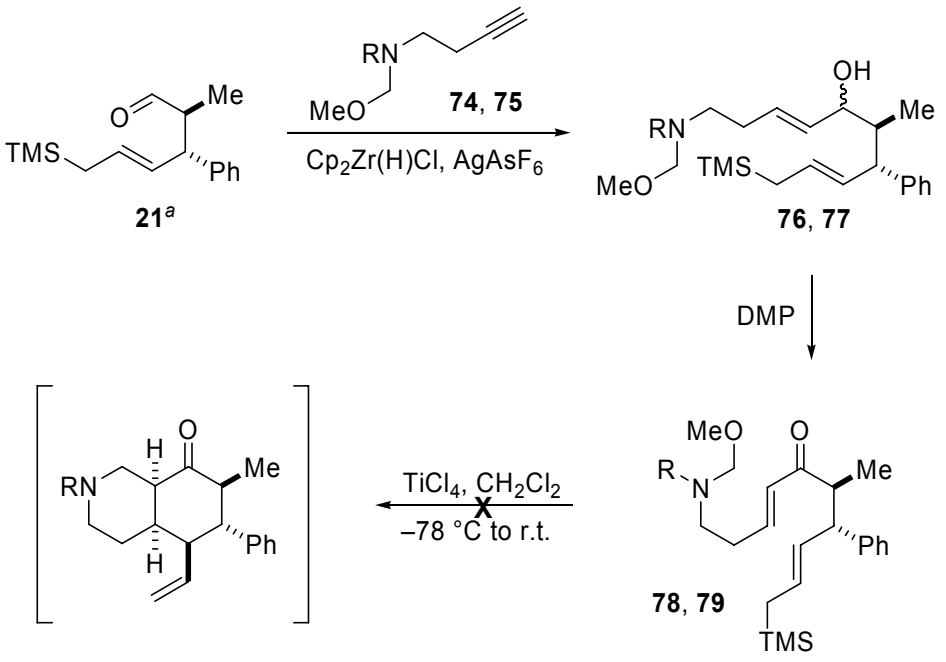


1.2.10 Preparation and Evaluation of Acyl Aminals for Sakurai-Mannich Bicyclization

The completed studies indicated that a more effective ionizable group would be necessary to facilitate the formation of iminium ions under the Sakurai reaction conditions. Acyl aminals seemed a prudent choice given their balance between reactivity and ease of preparation.[73, 74] Methyl (Moc) and trimethylsilylethyl (Teoc) carbamate-protected alkynes **74** and **75** were obtained by a Curtius rearrangement of pentynoic acid followed by addition of methanol or trimethylsilyl ethanol, respectively, and subsequent *N*-alkylation with chloromethyl methyl ether

(Table 8).[75-77] Trimethylsilylethyl carbamate substrate **75** was chosen primarily since it should deprotect at low temperature affording a neutral imine, which could potentially function more effectively than the corresponding iminium ion. Hydrozirconation of **74** and **75** followed by

Table 8. Synthesis and attempted cyclization of acyl aminals **78** & **79**



R	Zr Addition Yield (%)[b]	w/Impure Aldehyde (%)[c]	Oxidation (%)[d]
-Moc	80 (**76**)	49	64 (**78**)
-Teoc	72 (**77**)	53	83 (**79**)

[a]92:8 *syn*:*anti* Determined by integration of aldehyde resonances in ^{1}H-NMR. [b]1:1 Mixture of alcohol stereoisomers. **21** Purified by flash chromatography prior to use. [c]Crude ICR aldehyde used following several months stored at –20 °C following purity check by ^{1}H-NMR. [d]Isomeric ratio not determined.

silver-catalyzed addition to aldehyde **21** gave good yields of the allylic alcohols **76** and **77**. Interestingly, yields of the vinyl zirconium addition reaction were highly sensitive to the purity

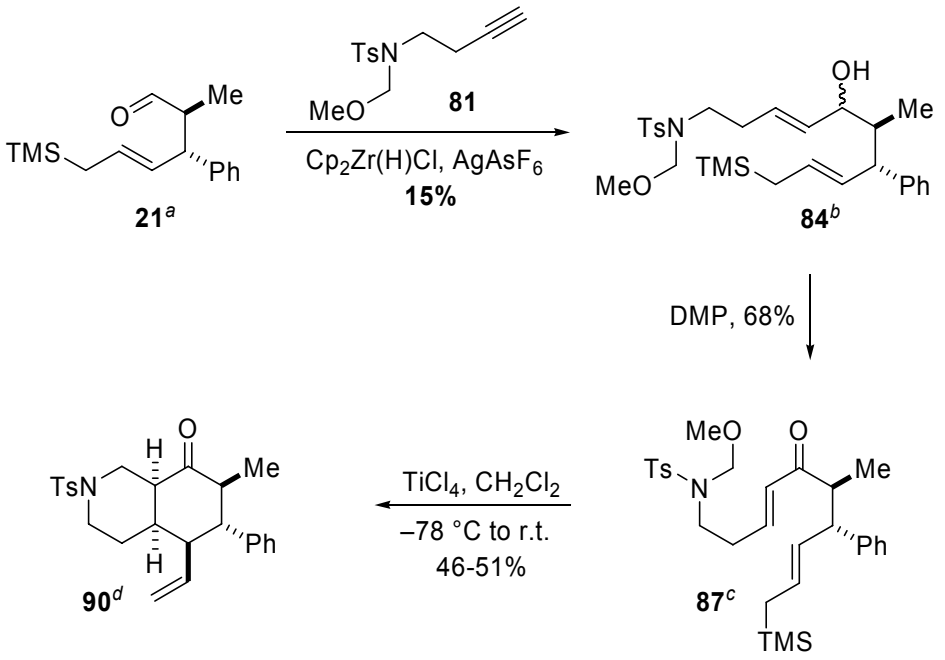
of the starting aldehyde. Crude ICR-derived **21** that had been stored at –20 °C for several months gave inferior yields in the addition reaction even though the aldehyde had only minor additional impurities as determined by ^{1}H-NMR analysis. Oxidation of **76** and **77** proceeded uneventfully to give the desired enones **78** and **79**. Regrettably, upon exposure to titanium tetrachloride, both **78** and **79** failed to form the desired perhydroisoquinilones, giving complex mixtures by crude ^{1}H-NMR analysis.

1.2.11 Preparation and Evaluation of Tosyl Aminals for Sakurai-Mannich Bicyclization

We hypothesized that the primary reason for the decomposition of **78** and **79** under the Sakurai reaction conditions was related to carbamate deprotection and subsequent formation of various undesired reactive intermediates. Tosyl aminals are electronically related to acyl aminals with the distinction that sulfonamides are exceptionally robust protecting groups and have no propensity to deprotect under Lewis acidic conditions.[78] Motivated by this insight, the standard synthetic route was applied to the preparation of enone substrate **87** (Scheme 7). The alkynyl sulfonamide was produced according to Weinreb's protocol followed by alkylation with chloromethyl methyl ether to give aminal **81**.[79, 80] Surprisingly, addition of the vinyl zirconocene prepared *in situ* from **81** to aldehyde **21** was highly inefficient, giving only 15% isolated yield of alcohol **84** following extended reaction times. Oxidation was not problematic, however, providing 68% yield of enone **87** in a comparable ratio of diastereomers to those observed for the related Sakurai substrates **31**-**35**. Gratifyingly, exposure of enone **87** to the optimized Sakurai conditions afforded the desired *cis*-perhydroisoquinilone **90** in 46-51% yield as a single isolated stereoisomer as determined by HPLC analysis. This diastereomeric ratio cannot be rationalized in light of the product mixtures obtained for the analogous Sakurai cyclizations (**31**-**35**, **46**).[81] It

is tempting to reason that the minor products are separated chromatographically, yet crude ^{1}H-NMR analysis of **90** does not indicate the presence of minor diastereomeric components.

Scheme 7. Evaluation of tosylaminal substrate **85** for Sakurai-Mannich bicyclization

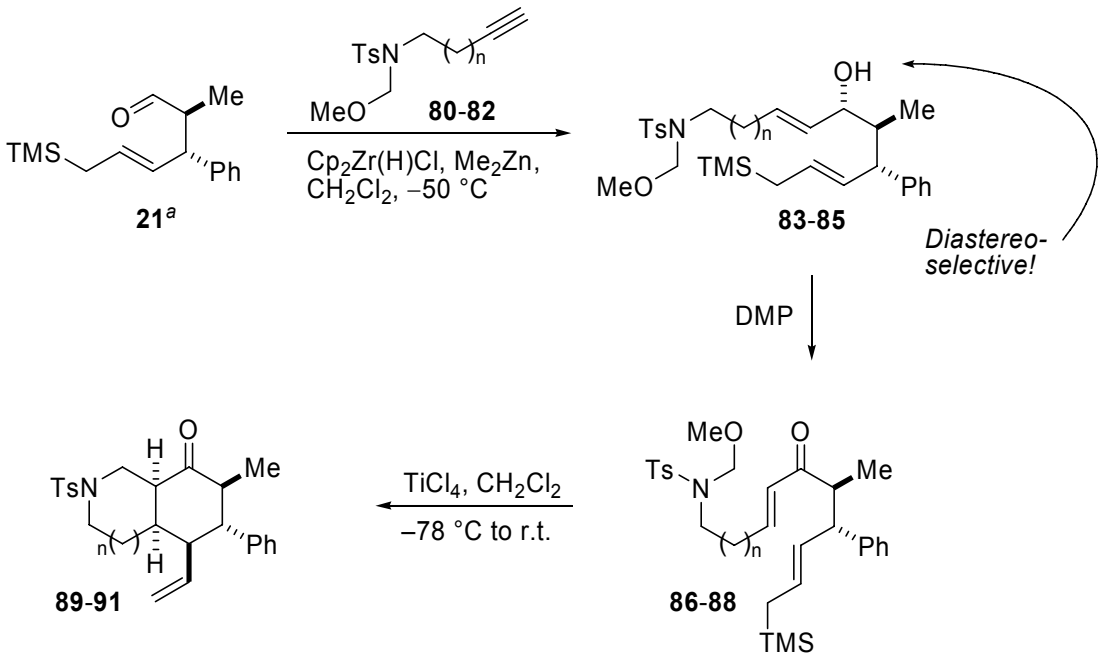


[a]92:8 *syn*:*anti* Determined by integration of aldehyde resonances in ^{1}H-NMR. [b]1:1 Mixture of alcohol stereoisomers. [c]Compound ratio determined by HPLC following flash chromatography. Isolated ratio 87.1:6.6:6.3. [d]Compound ratio determined by HPLC following flash chromatography. Single stereoisomer.

Although the desired Sakurai-Mannich cascade reaction was successfully affected, the yield of the vinyl metal addition to form requisite alcohol **84** was unacceptable. It is likely that the cationic zirconium species generated following halide abstraction is incompatible with the sulfonamide protecting group. Transmetallation of vinyl zirconocenes to the corresponding zinc species has been pioneered by Wipf and demonstrated to be a broadly applicable approach to the preparation of highly sensitive allylic alcohols.[82, 83] Hydrozirconation of **81** followed by

treatment with dimethylzinc and addition of **21** produced to the desired allylic alcohol **84** in a greatly improved 53% yield with moderate degrees of Felkin induction (Table 9).

Table 9. Application of tandem intramolecular Sakurai-Mannich reaction



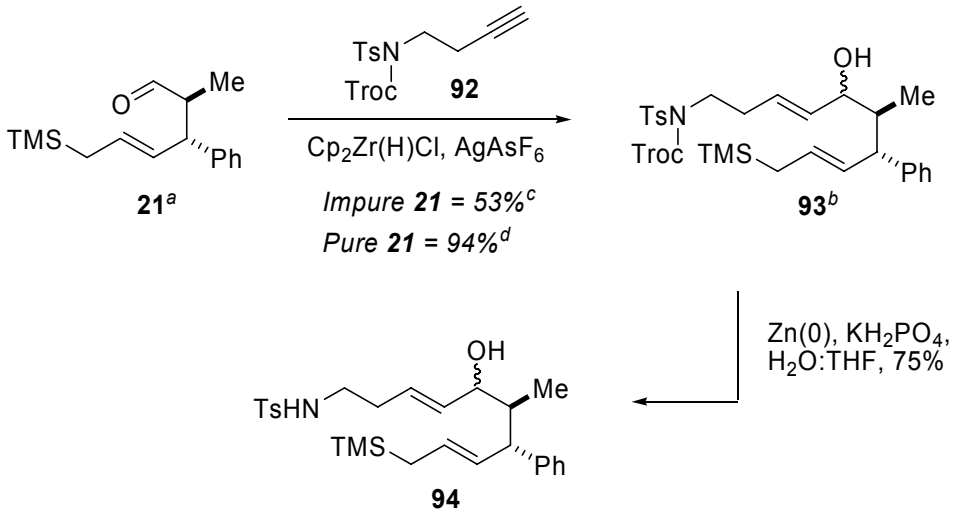
n	Addition (%)[b]	Oxidation (%)	Ketone Ratio[c]	Cyclization (%)	Iso. Pdt. Ratio[c]
0 (**80**)	33 (**83**)	83 (**86**)	84.6:7.5:7.9	41 (**89**)	Single
1 (**81**)	53 (**84**)	68 (**87**)	87.1:6.6:6.3	46-51 (**90**)	Single
2 (**82**)	67 (**85**)	59 (**88**)	7.7:83.4:4.2:4.6	44 (**91**)	87.9:12.1

[a]92:8 *syn*:*anti* Determined by integration of aldehyde resonances in ^{1}H-NMR. [b]d.r. Obtained by crude ^{1}H-NMR. Ratios are included in experimental section. [c]Compound ratio determined by HPLC following flash chromatography.

We recognized that modification of the tether length for alkyne **81** would potentially access various heterocyclic ring sizes through the ensuing bicyclization reaction. To determine the viability of this approach, the n-1 (**80**) and n+1 (**82**) analogues of **81** were prepared and used for

the subsequent vinyl metal addition reaction. Addition of substrate **82** to **21** performed respectably, giving **85** in good yield, while reaction with **80** was far less effective, yielding only 33% of **83**. Interestingly, the fidelity of the oxidation reaction followed the opposite trend; alcohol **85** gave the poorest conversion to enone **88**, which contained multiple impurities, while oxidation of **83** was clean and high yielding. Subjecting **86** and **88** to the standard Sakurai conditions lead to the expected fused pyrrolidine (**89**) and azapane (**91**) ring systems with excellent diastereoselectivity; however, isolated yields were attenuated. It is worth mentioning that although these reactions were low yielding, the crude mixture was remarkably clean and generally exhibited only a single spot by thin layer chromatography. Although the origin of these diminished yields has yet to be determined, it is likely that optimization of reaction conditions should address the issue.

Scheme 8. Alternative pathway to sulfonamide-substituted allylic alcohols



[a]92:8 *syn*:*anti* Determined by integration of aldehyde resonances in ^{1}H-NMR. [b]1:1 Mixture of alcohol stereoisomers. [c]Crude ICR aldehyde used following several months stored at –20 °C following purity check by ^{1}H-NMR. [d]**21** Purified by flash chromatography prior to use.

Given the labile nature of the aminal functionality, it was expected that a protected variant of the tosyl alkyne substrate would provide higher yields for the problematic vinyl metal addition reaction. Indeed, addition of Troc-protected alkyne **92** to crude aldehyde **21** was equally effective as the reaction of **81**, whereas prior purification of **21** lead to a dramatically enhanced 94% yield of **93** (Scheme 8). Deprotection of **93** gave free sulfonamide **94**, which should be a suitable intermediate for derivatization into various useful iminium ion precursors.

1.2.12 Intramolecular Sakurai-Mannich Relative Stereochemistry

Reduction of perhydroisoquinilone **90** with diisobutylaluminium hydride gave the corresponding alcohol **95** in 83% as a 90:10 ratio of stereoisomers. X-ray analysis of crystals prepared from **95**

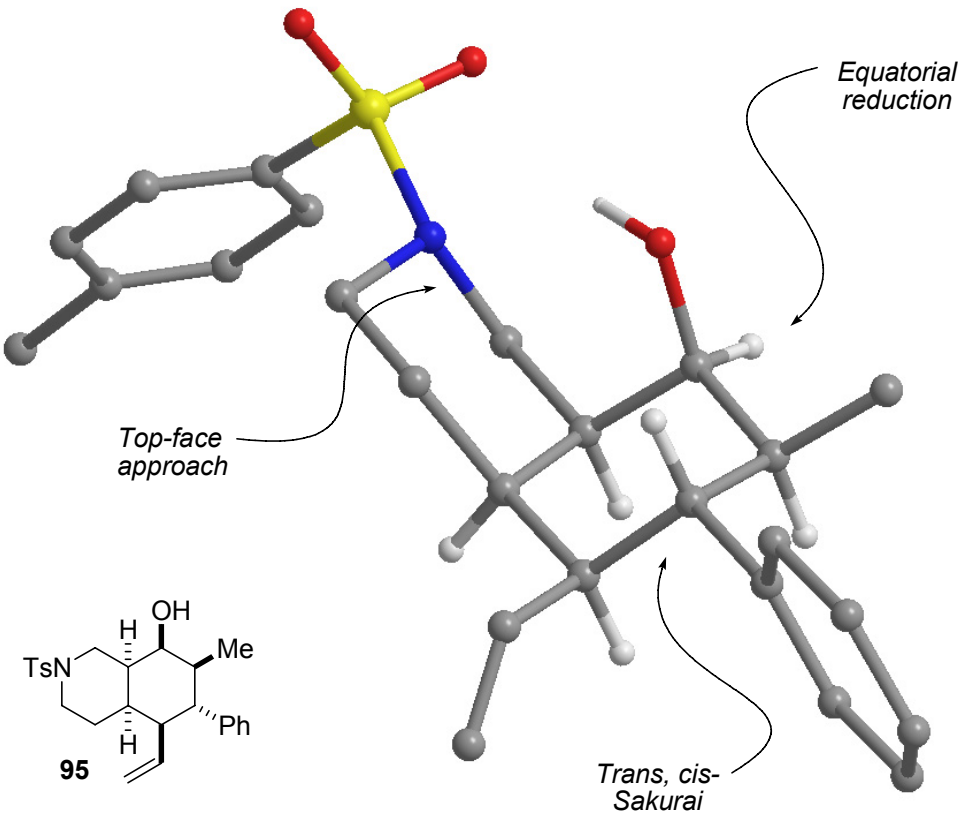


Figure 24. X-Ray structure of alcohol **95**

demonstrated that the Sakurai reaction produces the same *trans*, *cis* relative stereochemistry, while the Mannich reaction occurs from the top face of the enolate (Figure 24). The diastereoselectivity of the reduction is clearly driven by steric effects with the bulky aluminium hydride preferring approach to the convex face of the cup-shaped quinilone. It is worth emphasizing that this sequence enables the formation of products possessing six contiguous stereocenters arrayed around a cyclohexane with nearly perfect stereocontrol in seven steps from commercially available reagents.

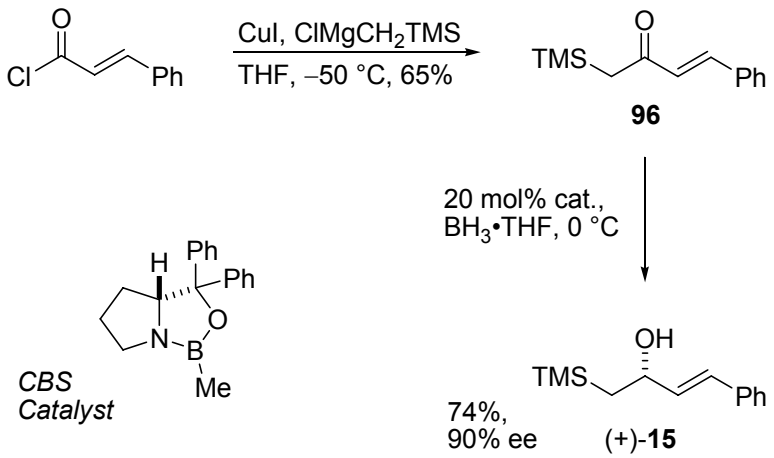
1.2.13 A General Route to Optically Active Substrates

The methodology presented thus far is limited to the preparation of the racemic product series. This fact considerably restricts the potential implementation of the Sakurai annulation for industrial or academic applications. Fortunately, these reactions benefit from the fact that all of the cyclization substrates stem from a common silyl alcohol precursor. An enantioselective synthesis of these alcohols would immediately render all of the subsequent Sakurai products available in optically enriched forms. Enantioselective reduction of the corresponding α-silyl ketone precursors would provide the most direct route to the requisite alcohols.

The CBS (Corey-Bakshi-Shibata) is among the most convenient methods for catalytic, asymmetric alcohol synthesis.[84, 85] Either antipode of the CBS catalyst is available from commercial sources for a nominal price, common borane reducing agents are employed in the reaction, and catalyst loadings are typically low. For these reasons, we felt a precursor synthesis relying on this technique would be particularly valuable to the scientific community. Synthesis of α-silyl ketone **96** was accomplished by addition of the trimethylsilyl methylene cuprate to commercially available cinnamoyl chloride (Scheme 9).[86] Use of alternative iron-catalyzed

coupling reactions resulted in significant α-desilylation.[87, 88] Silyl ketones are highly unstable to acid, hence **96** could be utilized crude for the ensuing reduction or isolated on Iatrobeads pH 7 silica gel in 65% yield. Reduction of **96** with 20 mol% of the CBS catalyst with BH_3·THF gave the desired optically active alcohol (+)-**15** in 74% yield with 90% enantiomeric excess. Any alteration of reaction temperature resulted in attenuated enantioselectivity. Reduction with catecholborane occurred at much lower catalyst loadings (<5%) giving nearly an enantiopure product (>98% ee). Unfortunately, significant decomposition presumably due to Peterson-type elimination led to low isolated yields.

Scheme 9. Formation of optically enriched Sakurai precursors



1.3 CONCLUSIONS

The power of the intramolecular Sakurai reaction for the preparation of a wide array of diastereomerically enriched cyclohexanones has been demonstrated. Reaction precursors were

prepared from ICR-derived allylsilyl aldehydes using a concise synthetic sequence. Various analytical techniques were exploited to observe the intrinsic diastereoselectivity of these reactions. Coupling the Sakurai reaction with inter- and intramolecular electrophile addition reactions revealed a highly effective method for the synthesis of various carbo- and heterocycles.[81] Although the Sakurai-Mannich reaction is low yielding, there are few precedented methods that promote such a significant augmentation of molecular complexity in the course of a single reaction. The entire family of Sakurai reaction products was rendered asymmetric by virtue of a convenient synthesis of optically enriched alcohol precursors using the reliable CBS reduction.

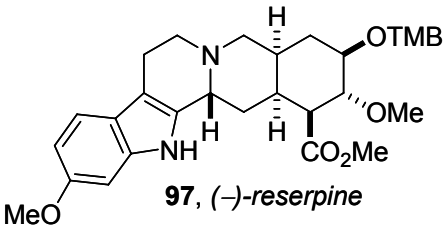
2.0 EFFORTS TOWARD A TOTAL SYNTHESIS OF (–)-RESERPINE AND RELATED INDOLE ALKALOIDS

2.1 BACKGROUND

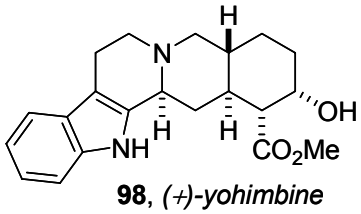
2.1.1 A General Introduction to (–)-Reserpine and Related Alkaloids

The indole alkaloids are a broad class of complex natural products that have been the focus of intense research efforts for nearly a century. Among the most complicated members of this family is (–)-reserpine (**97**), which was first isolated in 1952 by Schlittler from *Rauwolfia serpentina* Benth (Figure 25).[89, 90] The yohimbine alkaloids, which are primarily isolated from the bark of the *Pausinystalia yohimbe* tree, possess a perhydroisoquinoline core structure that is closely related to reserpine but lack the additional trimethoxybenzoyl group.[91-94] In particular, the core of α-yohimbine (**99**), a diastereomer of yohimbine (**98**), exhibits identical relative stereochemistry to the reserpine core. Both reserpine and the yohimbine alkaloids have been widely employed as folk medicines, the former serving as a cure for snake bites and a sedative, the later finding applications as a fertility drug and an aphrodisiac. Reserpine was one of the first widely utilized hypertensive agents in modern medicine, although it has been almost completely replaced by contemporary theraputics.[95] The lack of therapeutic application is largely due to the significant side effects of reserpine treatment, which include fatigue and depression. There are

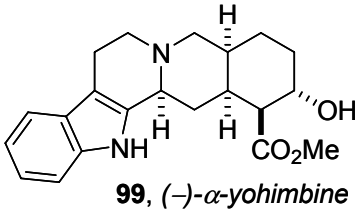
also reports that implicate reserpine in neoplastic disorders, although these findings continue to be the subject of debate.[96, 97] Yohimbine continues to be sold commercially as an herbal aphrodisiac and male potency enhancement. Although the biological activity of this natural product has been validated, limited clinical investigations have suggested that it is perhaps more suited for a group treatment regimen with drugs that activate the nitric oxide pathway in the corpus cavernosum.[98]



97, *(–)-reserpine*



98, *(+)-yohimbine*



99, *(–)-α-yohimbine*

Figure 25. Structures of (–)-reserpine, (+)-yohimbine and (–)-α-yohimbine

2.1.2 Biological Activity

Interestingly, (–)-reserpine and the yohimbine alkaloids exhibit opposing bioactivities, which are manifested in the peripheral sympathetic nervous system (Figure 26). Reserpine is able to

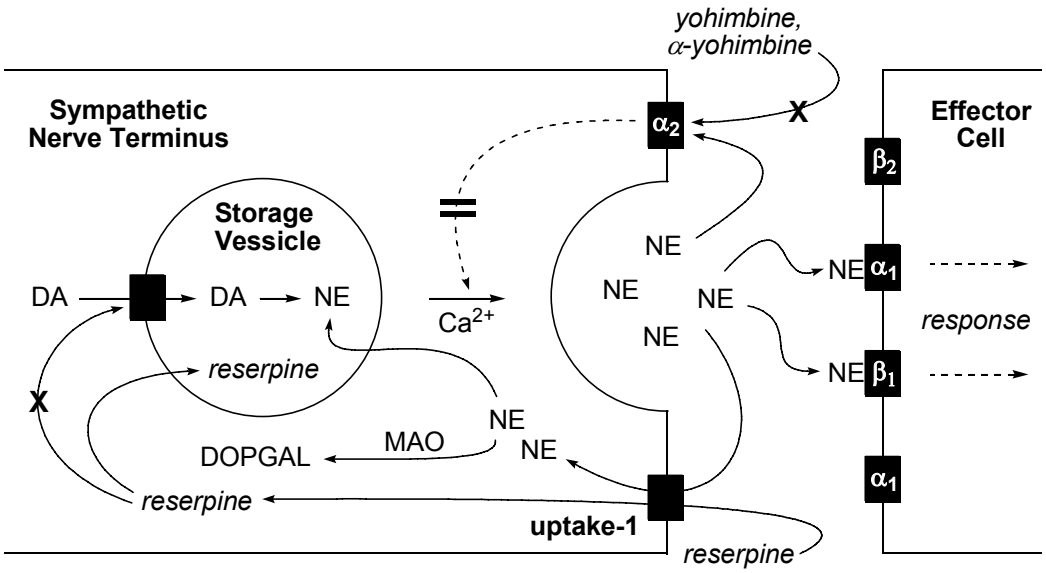


Figure 26. Bioactivity of (–)-reserpine, (+)-yohimbine and (–)-α-yohimbine

enter nerve cells *via* uptake-1, the primary route by which norepinephrine reenters cells following its release into the nerve synapse. Once in the cell, reserpine inhibits dopamine active transports that are membrane-bound to catecholamine storage vesicles while simultaneously replacing norepinephrine contained in these vesicles. This significantly reduces the basal cell level of norepinephrine, resulting in an attenuated adrenergic response following depolarization of the nerve. This effect is characterized by reduced heart rate and blood pressure, hence the role of reserpine as an anti-hypertensive. Yohimbine and α-yohimbine are particularly interesting among related alkaloids since they selectively inhibit the α_2 adrenergic receptor class.[99] The α_2

receptors are predominantly pre-ganglionic and regulate the adrenergic response through feedback inhibition triggered by excess norepinephrine in the synapse. Inhibition of peripheral α_2 receptors results in an increased adrenergic response characterized by increased heart rate, hypertension and anxiety.[100-103] The overall action of these alkaloids is far more complex, however, due to various poorly understood interactions with 5HT receptors and activity in the central nervous system.

2.1.3 Previous Total Syntheses of (–)-Reserpine

Reserpine has served as a benchmark in the scientific community for the evaluation of novel methodology in the context of target-oriented synthesis. Over the years since its isolation, the

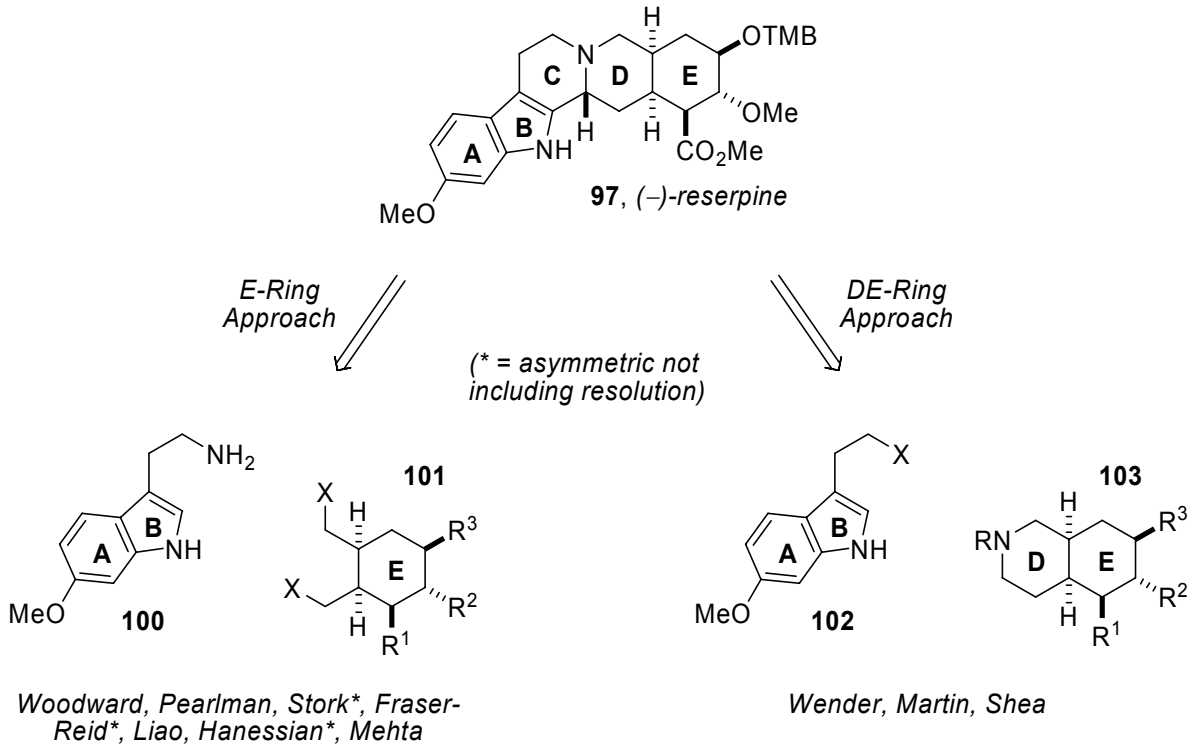


Figure 27. Strategic approaches to (–)-reserpine

groups of Woodward, Pearlman, Stork, Fraser-Reid, Liao, Hanessian, Mehta, Wender, Martin and Shea have successfully surmounted the synthetic challenges posed by this complex alkaloid.[104-118] Two major retrosynthetic disconnections have emerged from the cumulative discoveries made by these individual groups. By far the most commonly used strategy involves a linchpin appendage of methoxytryptamine **100** across a fully functionalized E ring **101** followed by a Bischler-Napieralski indole alkylation (Figure 27). This route was pioneered by Woodward and continues to be a highly effective strategy for the synthesis of reserpine.[105] The syntheses of Fraser-Reid and Hanessian were carried out in an asymmetric manner using D-glucose and (–)-quinic acid, respectively, while optically enriched 3-cyclohexene carboxylic acid was employed for Stork's enantioselective synthesis.[108, 109, 112]

The second retrosynthetic strategy engages the fully formed DE ring system **103** in an oxidative cyclization with bromo or tosyl methoxytryptophan **102** following its attachment to the perhydroisoquinoline core *via N*-alkylation. This disconnection has only been applied to racemic syntheses of reserpine since the enantioenriched series would require unknown asymmetric variants of the Diels-Alder reactions, which are employed in all three routes to form intermediates **104-106** (Figure 28). Though elegant, this route suffers from low yields and regioselectivity during the oxidative cyclization reaction to form the C ring.

Intermediates that are prepared using the known E ring or DE ring routes are relatively limited in terms of their capacity to be differentiated at selected positions. This is especially the case for the asymmetric routes of Hanessian and Frasier-Reid, which rely on starting materials derived from the chiral pool.[109, 112] This fact has severely limited the availability of comprehensive studies regarding the biological activity of synthetic derivatives, which is reflected by a dearth of literature precedence. These same considerations are also true for the

yohimbine alkaloids, as pointed out by Aube; "Finally, note that practically the entire structure-activity relationship described in the literature has been obtained with naturally occurring compounds instead of incrementally modified synthetic derivatives."[91] Furthermore, industrial interest in these compounds is limited due to the fact that their maturity in the chemical field presents issues regarding patentability. This unique combination of factors has made reserpine and yohimbine 'orphan' drugs with a huge potential for producing unique biological activity given a synthetic strategy that would enable rapid derivative synthesis.[119]

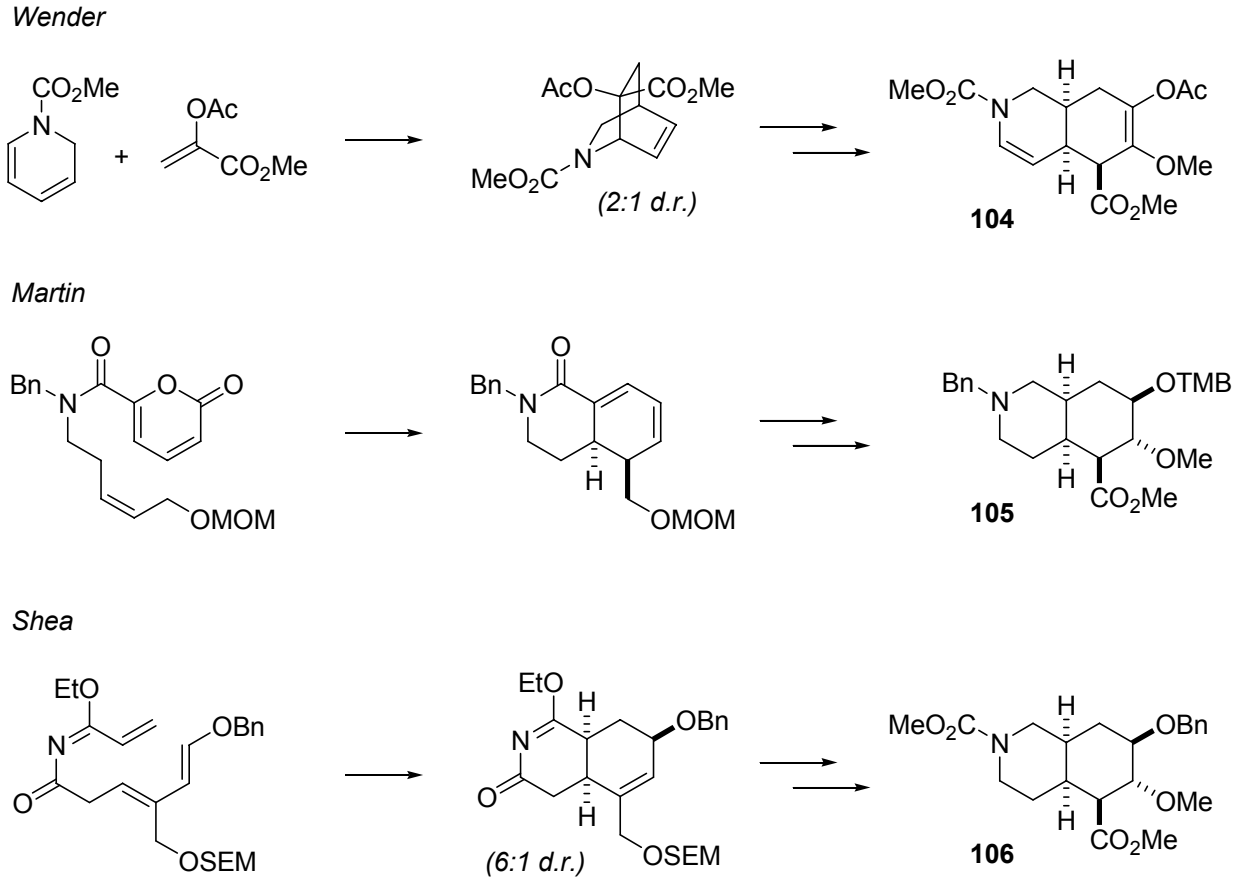


Figure 28. Application of Diels-Alder reactions to the synthesis of the (–)-reserpine core (all products are racemates)

2.1.4 Retrosynthesis of (–)-Reserpine

Here, initial interest in reserpine was driven by its obvious structural and stereochemical relationship to perhydroisoquinilones derived from the intramolecular Sakurai-Mannich chemistry described previously (ch. 1). Martin's intermediate **105**, which is six steps from (–)-reserpine, would emerge from the Sakurai-Mannich reaction of oxygenated unsaturated ketone **107** followed by several subsequent functional group manipulations (Figure 29). Disconnection

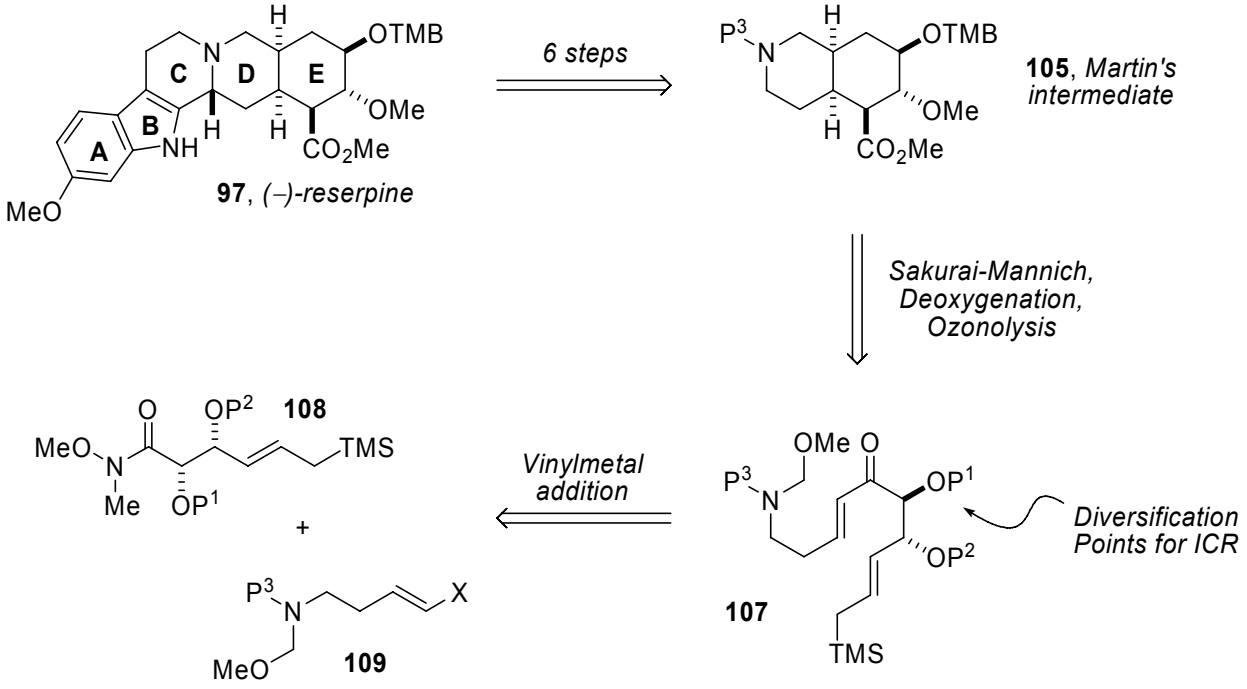


Figure 29. Retrosynthetic analysis of (–)-reserpine

of **107** across the unsaturated ketone reveals fragments **108** and **109**, which are of comparable complexity. We felt that this approach was particularly well suited for derivative synthesis because it is convergent and enables the *direct modification of every position of the reserpine*

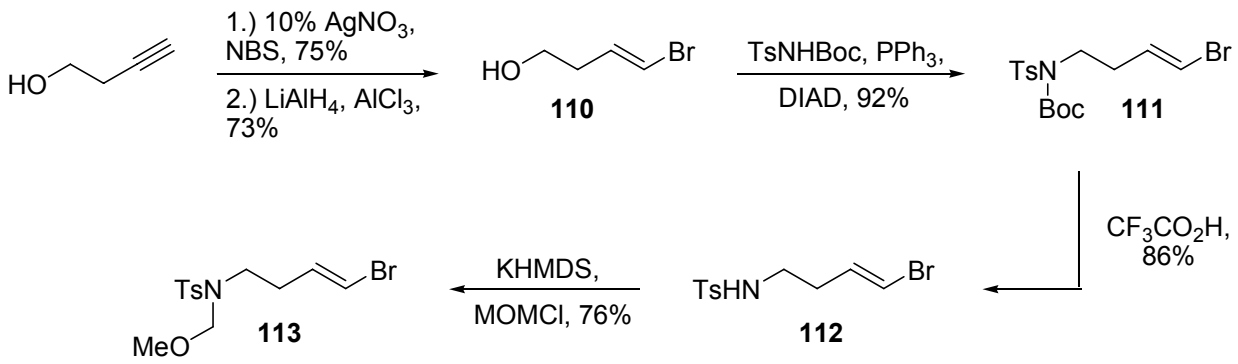
core. The availability of enantioenriched starting materials using the CBS reduction would provide clear advantages to derivative synthesis *via* ICR methodology over chiral pool or resolution-based approaches. In order to prepare the parent natural product however, it is clear that amide **108** is unavailable from Claisen-based approaches. It was envisioned that an Evans glycolate aldol reaction would facilitate the enantioselective preparation of **108** and various other derivatives given the high substrate generality of this methodology. Vinyl metal fragment **109** would be prepared along similar lines as described previously.

2.2 RESULTS AND DISCUSSION

2.2.1 Synthesis of Vinyl Bromide Fragment 113

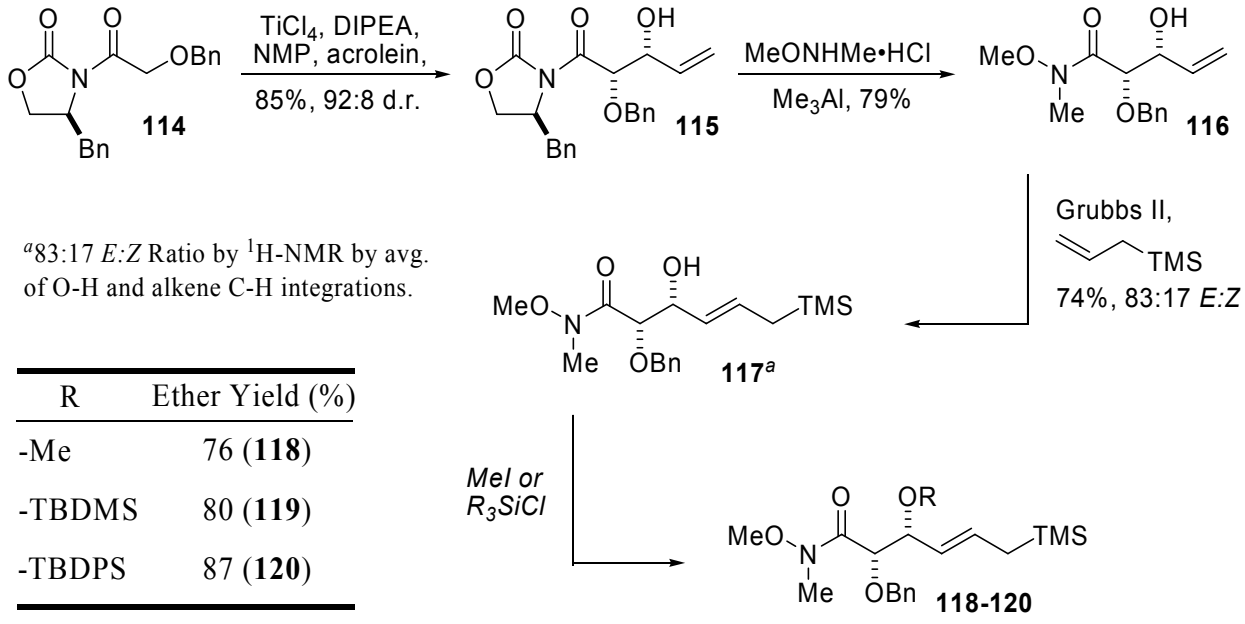
The most direct route to vinyl metal species **109** is through lithium halogen exchange of a suitable vinyl halide. Given the previous success of tosyl protecting groups for the intramolecular Sakurai-Mannich process, we speculated that aminal **113** would be an appropriate vinyl metal precursor (Scheme 10). Bromoalcohol **110** was prepared by a two-step literature procedure in high yields from 1-butynol.[120] Using Weinreb's precedent, **110** was converted into the Boc-protected sulfonamide **111** in 92% yield.[79] Deprotection of **111** using trifluoroacetic acid produced the free sulfonamide **112**, which was then subject to alkylation using chloromethyl methyl ether to give 76% yield of the desired tosylaminal **113**. This sequence would readily tolerate a significant degree of substrate diversity.

Scheme 10. Synthesis of vinyl bromide **113**



2.2.2 Synthesis of Weinreb Amide Fragments 118-120

Scheme 11. Synthesis of Weinreb amides **118-120**



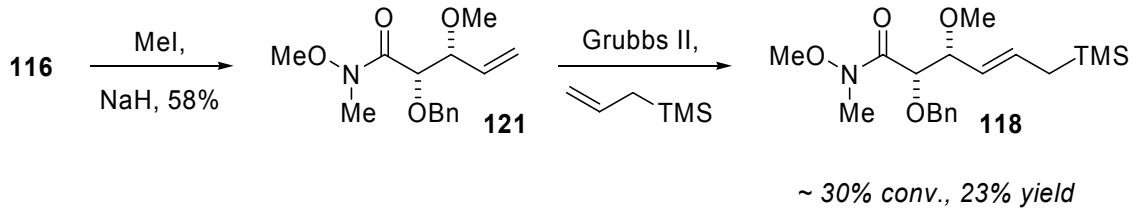
[a]83:17 *E:Z* Ratio by ^{1}H-NMR by avg. of O-H and alkene C-H integrations.

R	Ether Yield (%)
-Me	76 (**118**)
-TBDMS	80 (**119**)
-TBDPS	87 (**120**)

Synthesis of methoxy enone **118** began with the known Evans glycolate aldol reaction of benzyl oxazolidinone **114** with acrolein to give **115** in 85% yield as a 92:8 ratio of diastereomers

(Scheme 11).[121-125] Transformation of **115** into known Weinreb amide **116** was accomplished in good yield using standard conditions.[126] The free benzyl oxazolidinone and amide **116** were inseparable by flash chromatography under various solvent systems without a 5% triethylamine additive in the eluent. Gratifyingly, subjecting **116** to Grubbs' second generation catalyst and allyltrimethylsilane gave the desired cross-metathesis product **117** in 74% yield as a 83:17 ratio of geometrical isomers.[127-130] Alkylation of **117** with sodium hydride and methyl iodide produced ether **118** in 76% yield.[131] As noted in the literature, the free hydroxy group of **116** dramatically enhances its reactivity as a cross metathesis partner with allyltrimethylsilane (Scheme 11). Exposure of **121**, which was prepared by methylation of **116**, to the

Scheme 12. Effects of the free hydroxy group of **116** on cross-metathesis



metathesis reaction resulted in only ~30% conversion and 23% isolated yield of **118** (Scheme 12). This difference in reactivity is obviously not related to sterics, hence it is likely that the hydroxyl acts as a directing group for the catalyst.

During the design of the reserpine synthesis, it became apparent that Lewis acid coordination to the β-alkoxy group of enone **107** could cause undesired side reactions. Substrates **119** and **120** prepared in order to provide a selection of sterically hindered β-alkoxy groups that would reduce Lewis acid coordination in the case that parent methoxy enone **118** suffered from this issue.

2.2.3 Fragment Joining

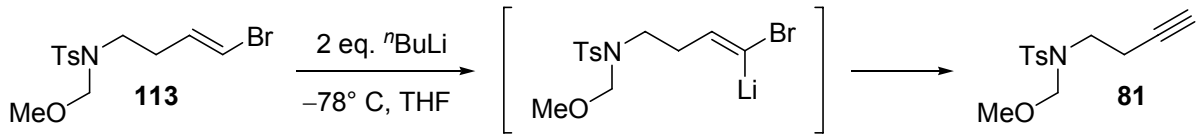
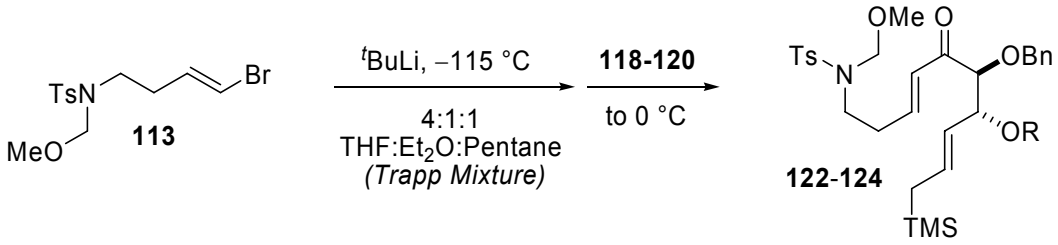


Figure 30. Rearrangement of vinyl bromide **113**

Initial attempts at affecting the desired metal-halogen exchange with substrate **113** using butyllithium in THF at –78 °C met with considerable difficulty. The vinyl bromide was prone to competing geminal deprotonation and carbene formation under the reaction conditions, leading to a rapid 1,2-hydride shift that yielded alkyne **81** following workup (Figure 30). Fortunately, the intermediate vinyllithium species was successfully prepared by employing conditions

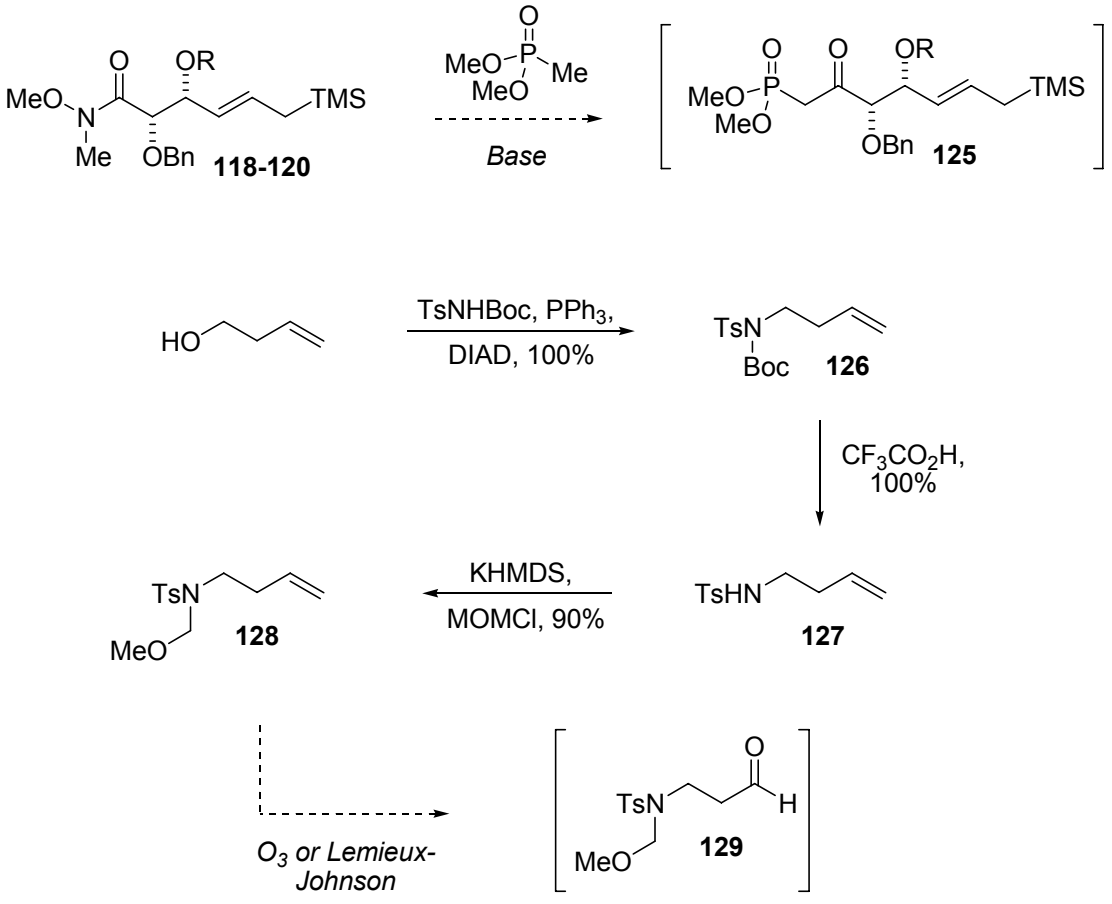
Table 10. Preparation of enones **122-124** *via* vinyl lithium addition



R	Addn. Yield (%)
-Me (**118**)	55 (**122**)
-TBDMS (**119**)	23 (**123**)
-TBDPS (**120**)	60 (**124**)

developed by Seebach (2.1 equiv. *t*-butyllithium, –115 °C, Trapp solvent mixture).[132] Addition of Weinreb amide substrates **118-120** to the reaction mixture followed by warming to 0 °C led to formation of the expected unsaturated ketones **122-124** in moderate yield (Table 10). Substrate **119** suffered considerable desilylation under the reaction conditions, accounting for the attenuated yield of enone **123**. Given the disappointing yields of the vinyllithium coupling reaction, studies into alternative enone preparations were initiated (Scheme 13). Specifically,

Scheme 13. Alternative sequence to unsaturated ketone substrates



preparation of the corresponding phosphonate esters from amides **118-120** would enable Horner-Emmons homologation with aldehyde **129** to give **122-124**. Application of the standard aminal

synthetic sequence to 1-butenol led to intermediates **126-128** in the highest yields of any substrates yet prepared. Aldehyde **129** has yet to be prepared *via* oxidative olefin cleavage, although precedent for such transformations exists.[133-138]

2.2.4 Evaluation of 122-124 for Sakurai-Mannich Bicyclization

At this point, the propensity of ketones **122-124** to engage in a diastereoselective Sakurai-Mannich annulation that would afford the (–)-reserpine core was investigated. Unfortunately, this cyclization reaction has yet to be realized under a variety of reaction conditions.

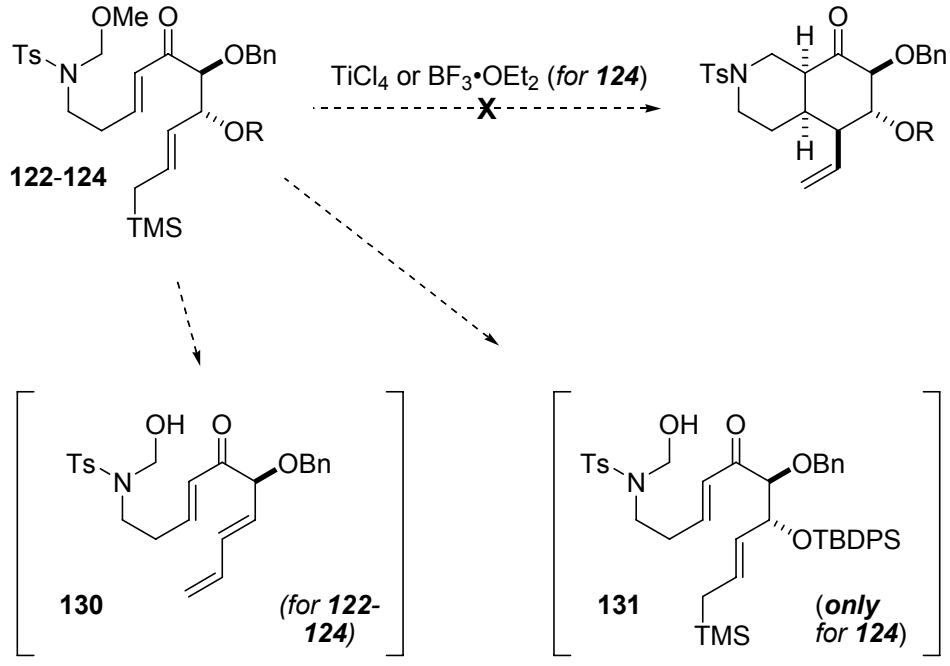


Figure 31. Attempted Sakurai-Mannich reaction of bisalkoxy enone substrates **122-124**

Exposure of **122** to the standard Sakurai conditions led to a complex reaction mixture from which a compound that appeared consistent with diene **130** by ^{1}H-NMR was isolated (Figure

31). Structure **130** is the expected product of coordination of the Lewis acid to the β-methoxy group and subsequent allylsilane elimination in addition to iminium ion hydrolysis. Compound **123** performed comparably, and analysis of the crude product by ^{1}H-NMR indicated nearly complete elimination of the silyl peaks at ~0 ppm and new alkene peaks suggestive of diene formation. Since this setback was anticipated, it was envisioned that the exceptionally bulky and Lewis acid stabile tert-butyldiphenylsilyl (TBDPS) protected substrate **124** would resist the β-alkoxy elimination. Subjecting **124** to the Sakurai reaction conditions again lead to a complex reaction mixture. Analysis of the ^{1}H-NMR spectra of the major isolated compound from the reaction was consistent with enone **131**. Note that the structures of **130** and **131** have not been confirmed by full characterization.

Formation of **131** implies that the TBDPS group effectively protects the alkoxy group from Lewis acid coordination; however, the substrate is unable to undergo the intramolecular Sakurai annulation. One possible explanation for this behavior is that the steric bulk of the TBDPS group prevents alignment of the allylsilane moiety with the electrophilic enone, which effectively prevents the cyclization reaction. Another possibility is that the α-chelating benzyloxy group causes the Lewis acid to coordinate to the opposite side of the carbonyl oxygen, thereby permitting the enone to occupy the more stable extended conformation (Figure 32). The extended conformation is normally disfavored by allylic interactions with the Lewis acid, leading to population of the reactive conformation for the Sakurai reaction.

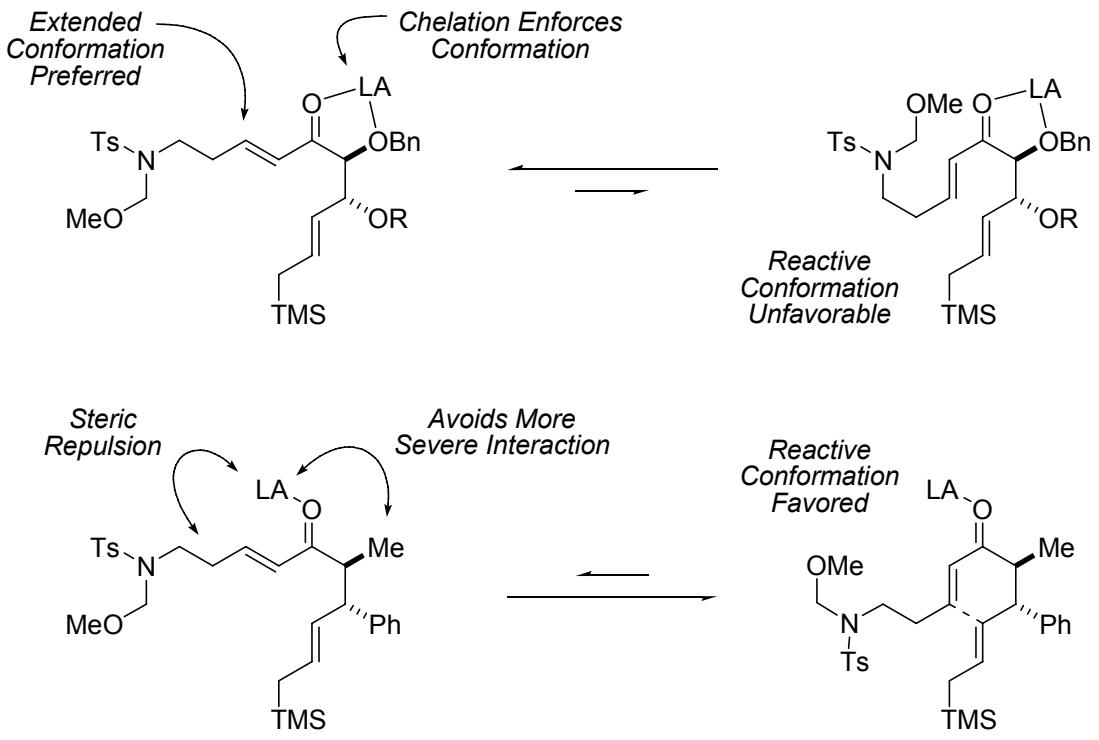


Figure 32. Possible involvement of α-chelation with failed cyclization of substrates **122**-**124**

2.2.5 Effects of α-Chelation and Retrosynthesis of α-Yohimbine

In order to explore the effect of α-chelation on the subsequent cyclization event, plans were made to prepare enone substrate **132**. Although the interest in this reaction was primarily mechanistic in origin, the Sakurai-Mannich reaction product of **132** would be a direct progenitor to the indole alkaloid (–)-α-yohimbine (Figure 33). Enone **132** would be prepared using the previously established synthetic route from alkyne **81** and the allyl silane fragment derived from enantioenriched β-lactone **133** or β-hydroxy ester **134**.[139-141] A direct asymmetric and diastereoselective synthesis of (–)-α-yohimbine has yet to be reported.[142]

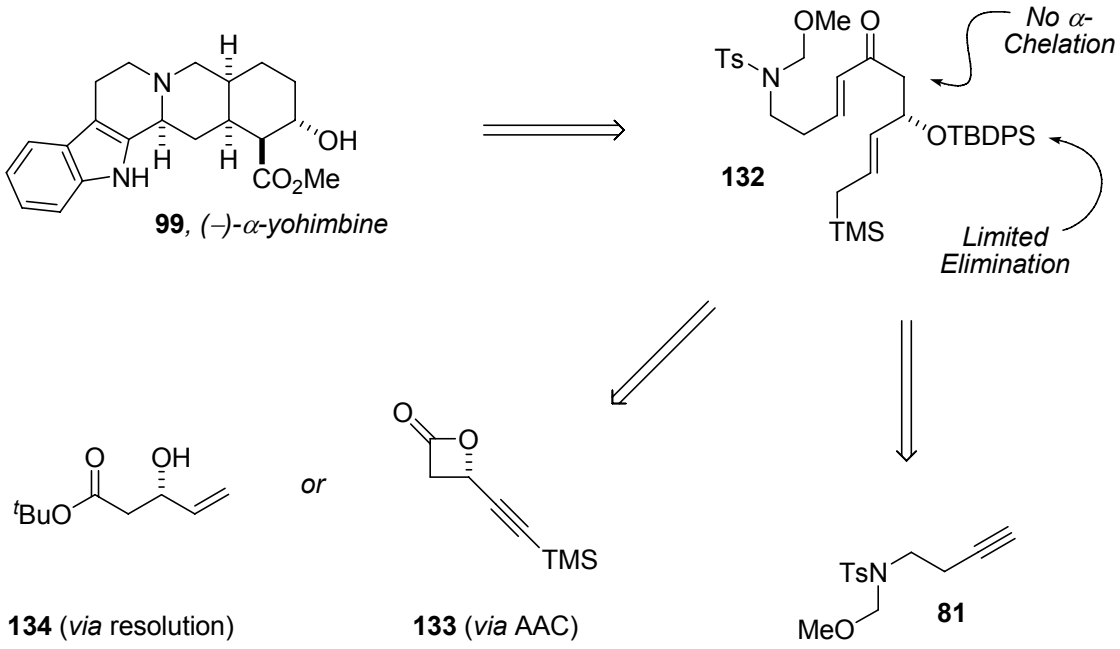
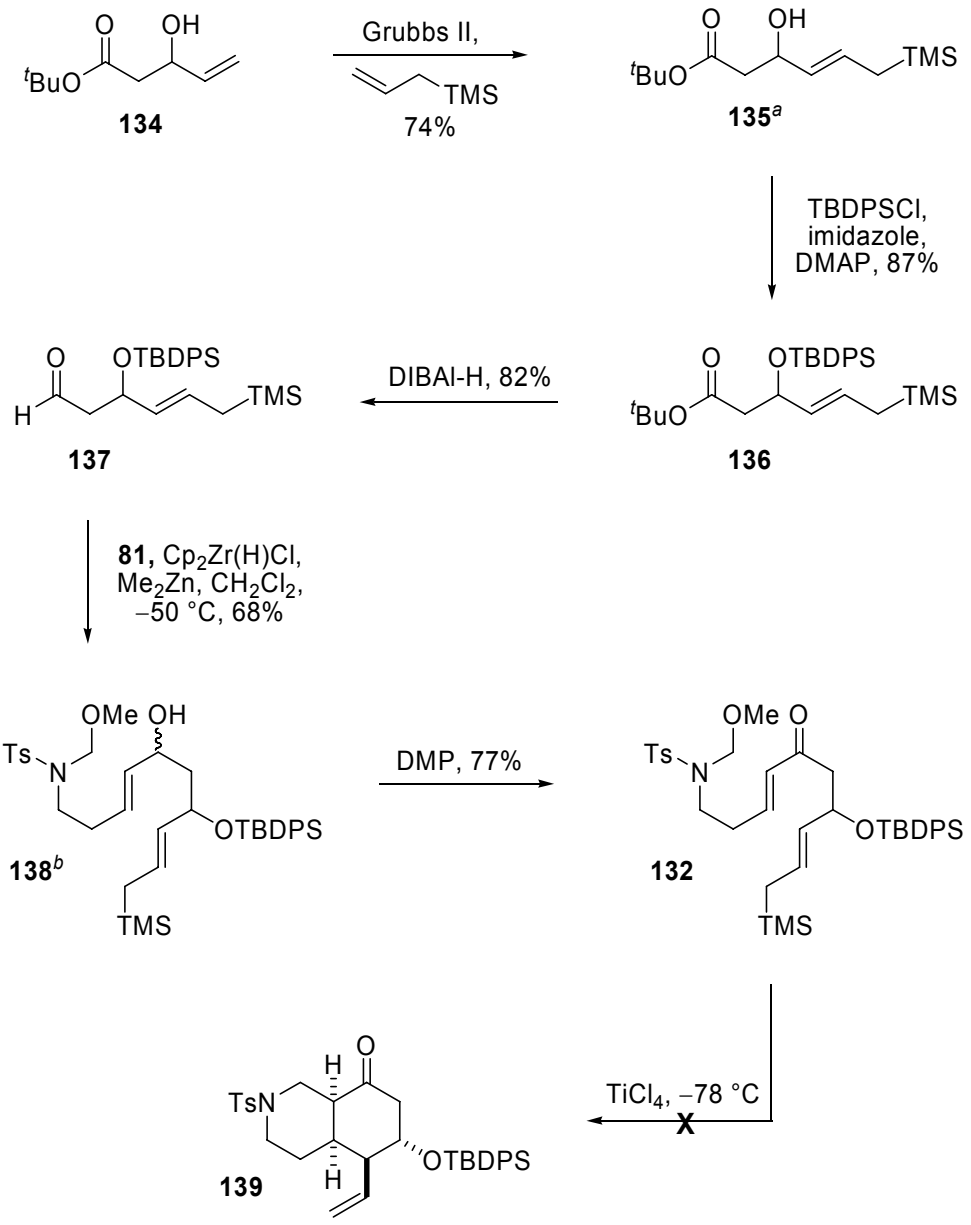


Figure 33. Retrosynthesis of (–)-α-yohimbine

Synthesis of **132** began with the known acetate aldol reaction of tert-butyl acetate with acrolein to give **134** in 72% yield (Scheme 14).[139] Cross metathesis of the terminal alkene with allyltrimethylsilane effectively produced the corresponding product **135** in 72% yield with good selectivity for the *E*-isomer. Protection of the free hydroxyl group as the TBDPS ether proceeded to give **136** in excellent yield. Subsequent reduction of ester **136** yielded 82% of the desired aldehyde **137**. The vinyl zinc species was again prepared from **81** using the Wipf protocol and was added to **137** to give allylic alcohol **138** in 68% yield as approximately a 1:1 mixture of diastereomers. Oxidation with the Dess-Martin reagent afforded the expected cyclization substrate **132** in 77% yield. Unfortunately, attempts to promote the cyclization of **132** under the standard Sakurai conditions produced exceptionally complex reaction mixtures that were devoid of diagnostic peaks by analysis of the ^{1}H-NMR spectra. This result indicates

that the α-chelating group does indeed reduce the activity of the Lewis acid (hence, the isolation **131**); however, it is not responsible for the inability of alkoxy functionalized enones to undergo the annulation reaction.

Scheme 14. Synthesis and attempted cyclization of α-unsubstituted enone **132**



[a]89:11 *E:Z* Ratio by ^{1}H-NMR by avg. of O-H and O-H methine integrations. [b]1:1 Mixture of alcohol stereoisomers.

2.3 CONCLUSIONS

A convergent, asymmetric route to two indole alkaloid natural products, (–)-reserpine and (–)-α-yohimbine was investigated. The synthetic approach to these compounds depended on a diastereoselective intramolecular Sakurai-Mannich reaction of alkoxy-substituted allylsilyl enones based on previous results with the related ICR-derived systems. Expeditious routes to the cyclization substrates **122**-**124**, and **132** were developed, although the synthetic yields for several transformations require optimization. Regretfully, the cyclization reaction of these substrates has yet to be affected under the narrow range of reaction conditions explored.

3.0 BROADENING THE SCOPE OF ICR METHODOLOGY THROUGH THE SYNTHESIS OF β-BORONIC ALDEHYDES

3.1 BACKGROUND

3.1.1 Limitations of the ICR Reaction

Although the ICR reaction has proven to be a remarkably general method for the synthesis of various diastereomerically enriched α,β-disubstituted aldehydes, there are several noteworthy limitations. The iridium-catalyzed isomerization reaction is driven forward by the increasing thermodynamic stability gained by engaging the transposed olefin in conjugation with oxygen lone pairs. Due to this fact, most groups at R^1 that are conjugated to the apical olefin completely shut down isomerization (Figure 33). Therefore, aldehydes possessing aryl, alkoxy or amino functionality are inaccessible from the original ICR reaction. Aldehydes prepared from the ICR reaction also exhibit poor diastereoselectivity with several common nucleophilic reagents. As demonstrated previously (ch. 1), this fact complicates analysis of synthetic intermediates and can reduce the throughput and efficiency of a sequence that requires a single diastereomeric product.

One solution that would circumvent both of these issues was the implementation of a replaceable directing group. This group would guide a broad range of nucleophiles in the transition state to give diastereoenriched alcohol products. Following its role as a directing

group, this functionality would be readily manipulated to produce a diverse range of compounds that are inaccessible from the parent ICR reaction.

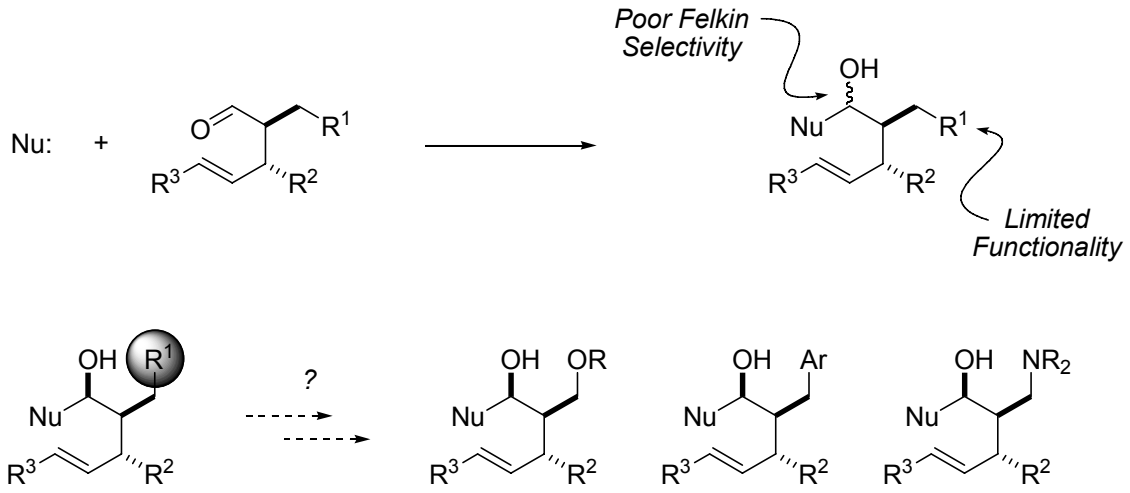
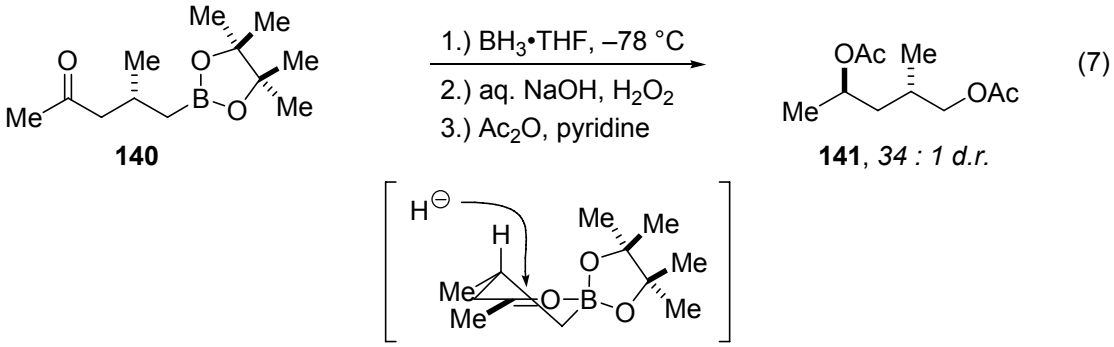


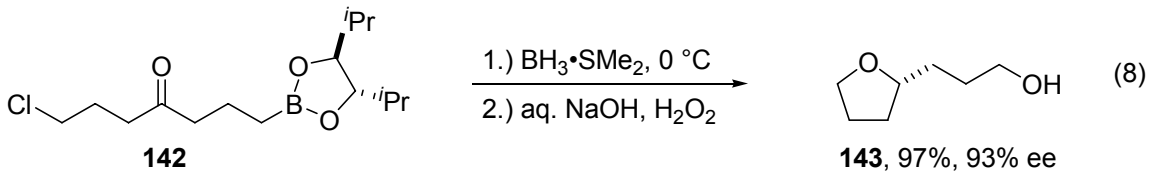
Figure 34. Limitations of the ICR reaction and product aldehydes

3.1.2 Intramolecular Coodination Can Mimic Cram Chelation

Manipulating chelation is often a crucial consideration in stereoselective organic synthesis. This is exemplified by the extensive impact of Cram-type chelation on acyclic stereoinduction.[143] In most cases, chelation occurs in an intermolecular fashion between a substrate and an external Lewis acid. There is limited precedent for intramolecular chelation between Lewis acidic and basic functional groups on the same molecule. For example, Molander *et al.* have demonstrated the highly diastereoselective reduction of γ-boronic ketones with excellent diastereoselectivity (Eq. 7).[144] It is presumed that the enhanced diastereoselectivity is due to an internal six-membered chelate between the boronic ester and carbonyl of **140**, leading to a half-chair conformation in which hydride delivery occurs from the top face to give *anti*-acetate **141**. No

spectroscopic evidence was used to support internal chelation (^{11}B-NMR, X-ray), hence the authors suggest that small concentrations of this intermediate react preferentially with the hydride nucleophile. An enantioselective variant of this reaction relying on 1,7-stereoinduction from chiral ligands at boron (**142** to **143**) has also been reported (Eq. 8).[145]





Whiting *et al.* have demonstrated the deprotonation of β-boronate carbonyl derivatives to form the corresponding internally chelated enolates (Figure 35).[146] Treatment of a variety of boronate-substituted carbonyls **144** with LDA lead to the expected *E*- and *Z*-enolates **145** and **146**. The proximal boronic ester moiety formed an internal chelate **148** in the case of the *Z*-enolates **146**; however, geometrical constraints precluded this mode of coordination for the corresponding *E*-enolates **145**, leading to intermolecular chelates **147**. Interestingly, the *E*-enolates **147** gave attenuated *anti*-selectivity in the aldol reaction with benzaldehyde (~1:1) while the *Z*-enolates produced *syn*-aldolates with enhanced diastereoselection.

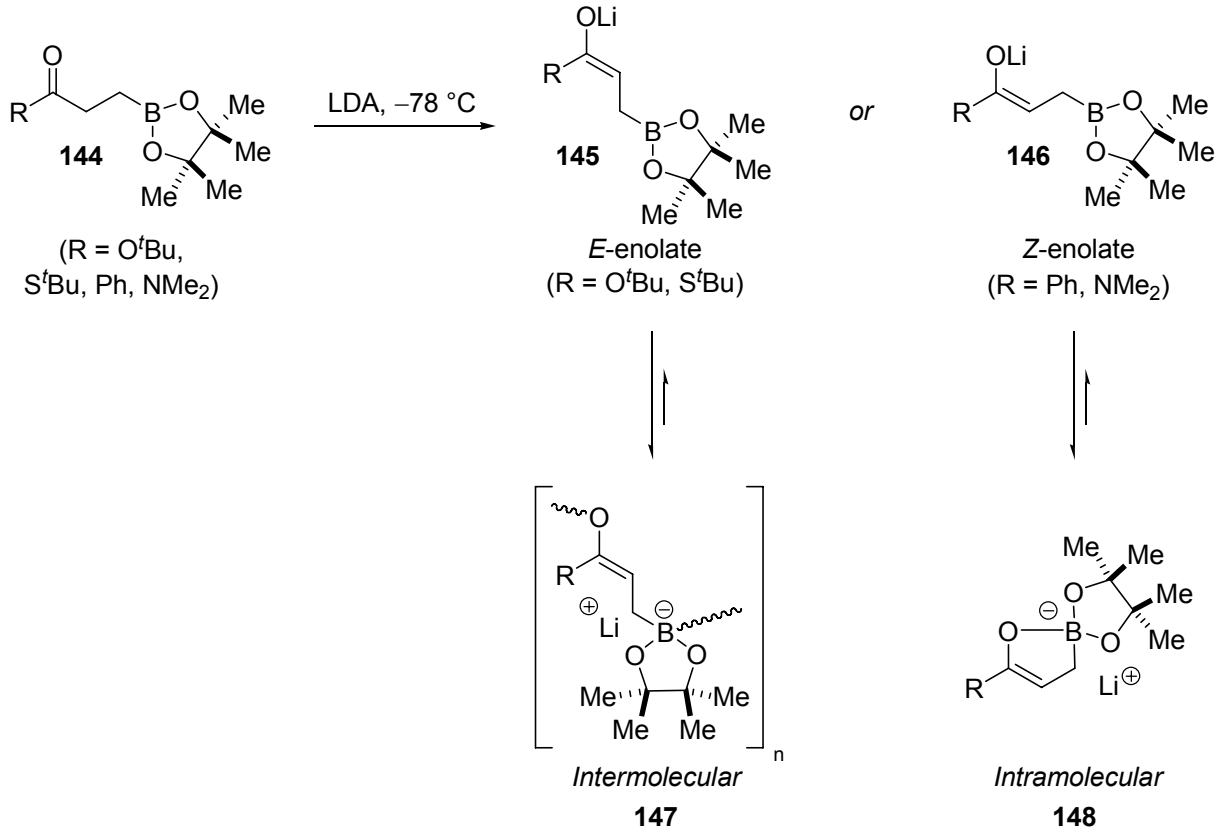


Figure 35. Internally chelated borate enolates

Whiting also investigated enantioselective reductions of ketones and oximes that presumably proceed through a five-membered internal boron chelate.[147-149] Although the enantioselectivity for reductions using achiral reagents were poor, the authors demonstrated that the effects of double diastereoselectivity are pronounced when employing chiral boranes (Figure 36). Treatment of **149** and its enantiomer with the same oxazoborolidine reagent followed by several further synthetic transformations gave the acetamide products (*S*)- and (*R*)-**150**, demonstrating the inability of the chiral reducing agent to override the stereoinduction of the boronate ester. This observation implies that internal chelation is operative in these systems;

however, it is not clear whether this coordination occurs between the boron and nitrogen atom (five-membered) or the boron and oxygen atom (six-membered) of the oxime. As in the case of Molander's studies, spectroscopic evidence was not provided to support the hypothetical internal coordination complex.

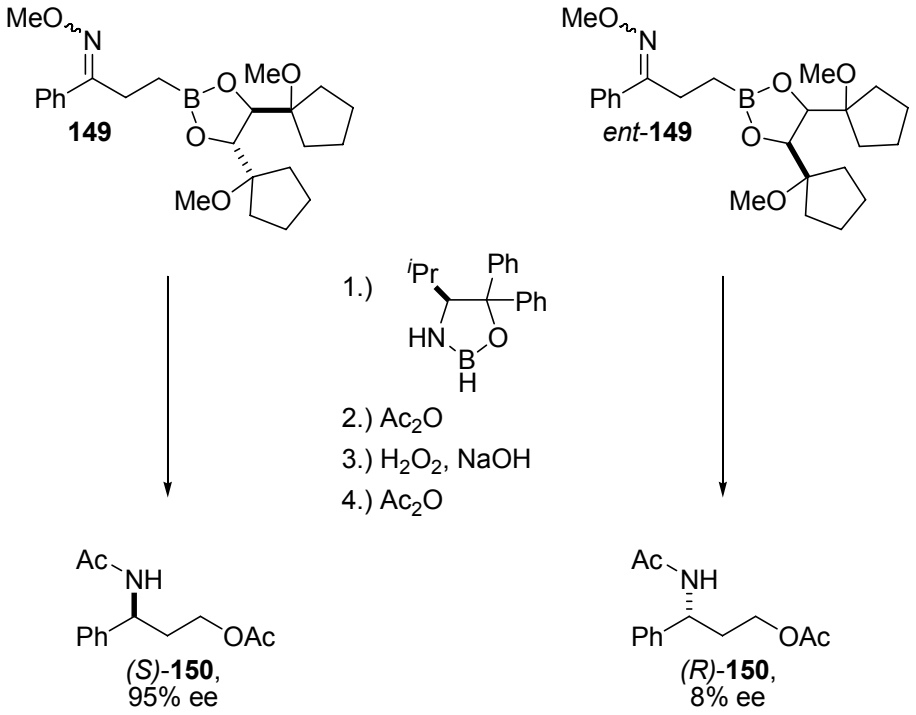


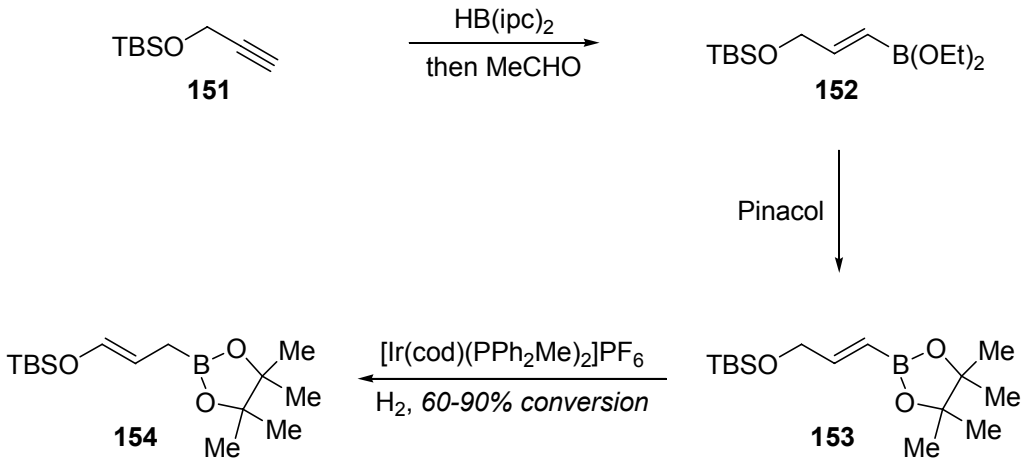
Figure 36. Double diastereoselection guided by internal boron chelation

3.1.3 Isomerization of Vinyl Boronic Esters

The prospect of using internal boron chelation to drive diastereoselective carbonyl addition reactions was intriguing. Further manipulation of the versatile boronate into alkoxy, aryl and amino functionality would enhance the scope and utility of the ICR reaction. It was not initially

clear how we would arrive at suitable Claisen substrates that would afford the desired boron-containing aldehydes. Fortunately, Miyaura *et al.* investigated the isomerization of vinyl boronic esters and silyl ethers using cationic iridium catalysts (Scheme 15).[150-153] Hydroboration of readily available propargyl silyl ether **151** followed by treatment with acetaldehyde gave the desired ethoxyvinyl boronic ester **152**, which could be transesterified with pinacol to provide **153**. Treatment of boronate **153** and several other boronic esters with a cationic iridium species generated *in situ* by precatalyst hydrogenation yielded the corresponding silyl enol ether **154** in 60-90% conversion with excellent selectivity for the *E*-olefin isomer.

Scheme 15. Isomerization of vinyl boronic esters with cationic iridium catalysts



Miyaura's work suggested that replacement of the silyl ether from **154** with a homoallyl group would provide effective substrates for the ICR reaction (Figure 37). The most direct route to the requisite vinyl boronic ester precursors would be through hydroboration of propargylic ethers **155**. Subsequent isomerization would lead to vinyl ethers **156**, which would afford the desired β-boronic aldehydes **157** following thermolysis. Internal boron chelation to the aldehyde

would be expected to enhance the diastereoselectivity of nucleophile additions while providing an adaptable handle for derivatization (**158**).

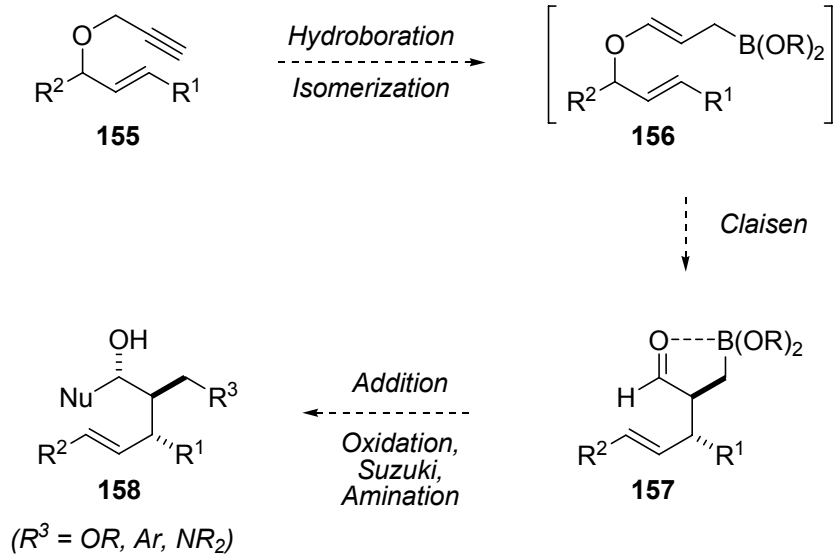


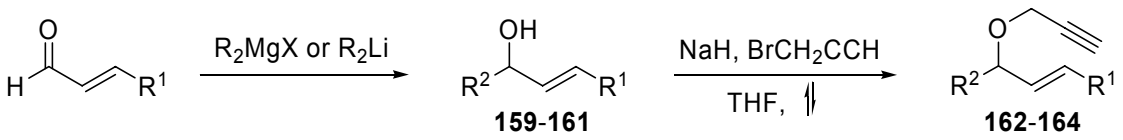
Figure 37. Strategy for the preparation of β-boronic aldehydes through ICR methodology

3.2 RESULTS AND DISCUSSION

3.2.1 Synthesis of β-Boronic Aldehydes

At the outset, the requisite propargylic ethers **162-164** were prepared (Table 11). Addition of Grignard or organolithium reagents to α,β-unsaturated aldehydes gave good yields of the intermediate allylic alcohols **155-157**. Alkylation was accomplished using sodium hydride and propargyl bromide affording the desired ethers **158-161**. Although **158-161** were pure as determined by ^{1}H-NMR analysis, distillation was necessary to remove minor contaminants.

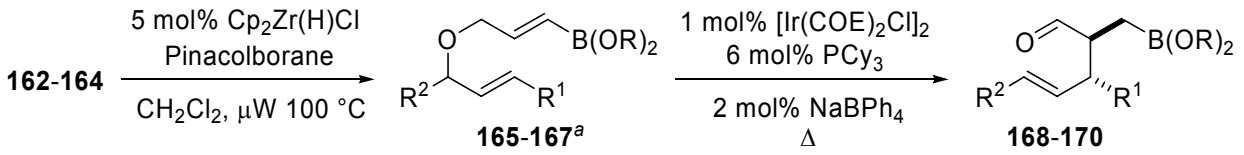
Table 11. Preparation of propargylic ethers **162-164**



R^1	R^2	Addn. Yield (%)	Ether Yield (%)
-Ph	-^{n}Bu	89 (**159**)	75 (**162**)
-Me	-Ph	93 (**160**)	84 (**163**)
-Me	-Np	66 (**161**)	73 (**164**)

Hydroboration of **162-164** proved to be a difficult task, and a wide variety of reagents including 9-BBN, dimesityl-, pinacol-, catechol-, and Ipc borane gave complex mixtures from which the desired boranes could not be isolated. Fortunately, a modified procedure by Srebnik *et al.* utilizing Schwartz's reagent as a catalyst efficiently facilitated the selective hydroboration of alkynes **162-164** to give vinyl boronic esters **165-167** (Table 12).[154, 155] The isolated vinyl boronic esters were subject to 2 mol% of the active ICR catalyst for 90 min. then heated in refluxing dichloroethane to promote the thermal Claisen rearrangement which provided β-boronic aldehydes **168-170** in good yields and diastereomeric ratios.[156] Aldehydes **168-170** are prone to hydrolysis and epimerization on silica gel, hence isolation on Iatrobeads neutral silica gel was necessary to ensure reproducible results. As mentioned previously, minor impurities contained in propargylic ethers **162-164** that were carried into the ICR reaction significantly retarded the isomerization in a batch dependant fashion. This negative effect is presumably due to strong coordination of the cationic catalyst to alkyne moieties contained in these contaminants.

Table 12. Hydroboration and boron-ICR reactions



R^1	R^2	Hydroboration Yield (%)	Claisen Yield (%)	d.r.[b]
-Ph	-^{n}Bu	75 (**165**)	67 (**168**)	92:8
-Me	-Ph	83 (**166**)	84 (**169**)	92:8
-Me	-Np	77 (**167**)	76 (**170**)	91:9

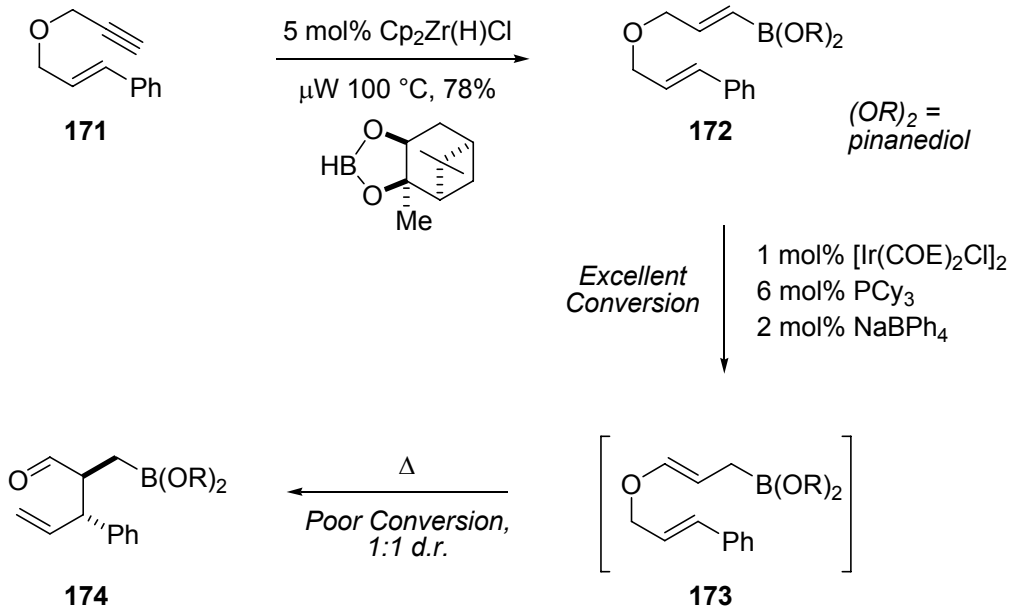
[a]$B(OR)_2$ Refers to pinacolboronic ester. [b]Compound ratios determined by ^{1}H-NMR following flash chromatography on Iatrobeads pH 7 silica. Listed in order *syn*:*anti*.

3.2.2 Asymmetric Induction by Chiral Boronic Ester Ligands

Following the successful preparation of boronic aldehydes **168-170**, we subsequently recognized that chiral boronic esters could potentially serve as cleavable auxiliaries for the preparation of enantioenriched aldehydes. To evaluate this strategy, achiral propargylic ether **171** was prepared using the standard protocol and subjected to hydroboration using Matteson's chiral pinanediol-derived reagent (Scheme 16).[157] Vinyl boronic ester **172** was exceptionally stable compared to the corresponding pinacolate esters and underwent facile isomerization to vinyl ether **173** upon exposure to 2 mol% of the active ICR catalyst. Unfortunately, thermolysis of **173** led to

considerable decomposition and no appreciable stereoinduction in the limited amount of aldehyde **174** produced (1:1 d.r. by ^{1}H-NMR analysis of the crude product).

Scheme 16. Attempted asymmetric boron ICR reaction



3.2.3 Solid State Structure of Aldehyde 170

A solid state structure of a carbonyl compound possessing a proximal 'chelatable' boronic ester has yet to be reported. Fortunately, under very select conditions (pentane, –20 °C), aldehyde **170** formed crystals that were suitable for X-ray analysis. The boron atom is approximately 2.9 Å from the oxygen of the carbonyl and there is no angle deviation from an sp^2 hybridization (120°) (Figure 38). From this data, it is clear that intra- or intermolecular boron chelation is not an important factor in determining the solid state conformation of β-boronic aldehydes; however, this observation does not dismiss its potential importance in the solution phase. The X-ray

structure of aldehyde **170** indicates that it occupies the most stable ground state conformation as described by Karabatsos with the boronic ester group eclipsing the carbonyl.[158] By Karabatsos' model, the boron methylene substituent would therefore act as the 'medium' sized group in a Felkin transition state. Nucleophiles would then be expected to approach from the same trajectory regardless of whether the reaction proceeded through the chelated or unchelated aldehyde.[159, 160]

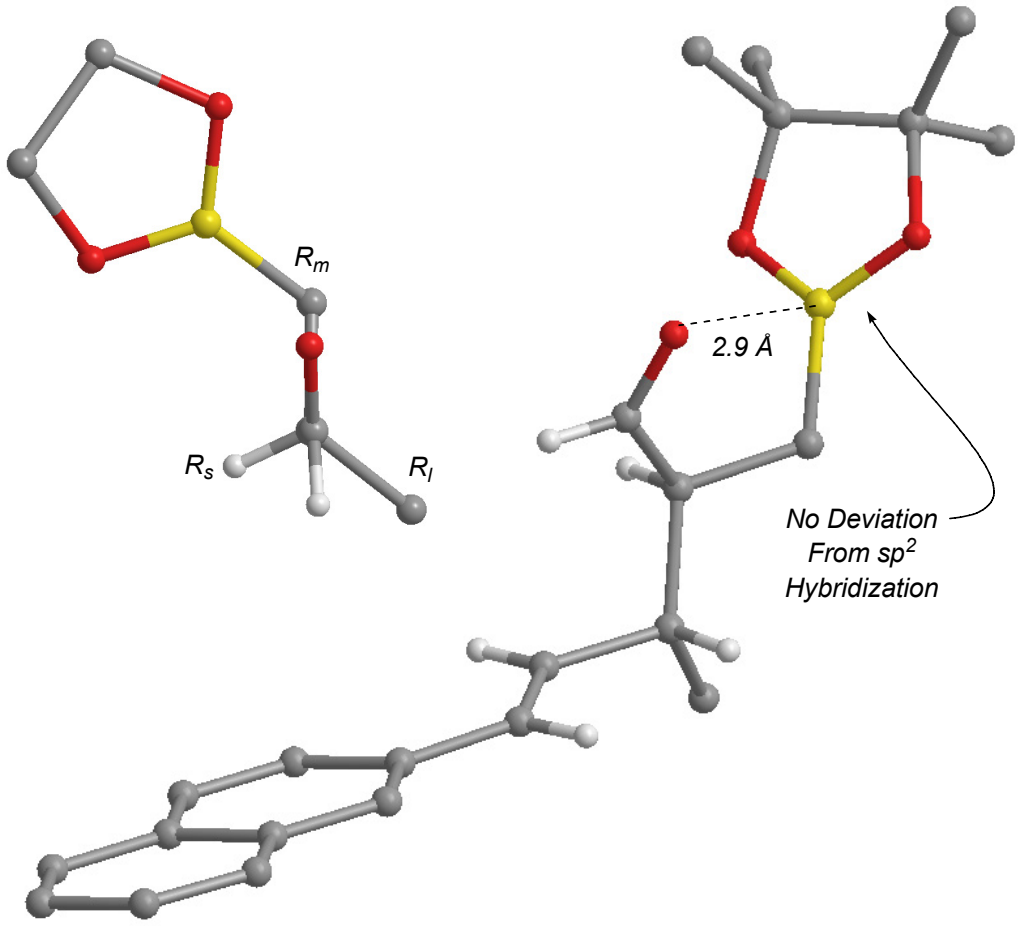
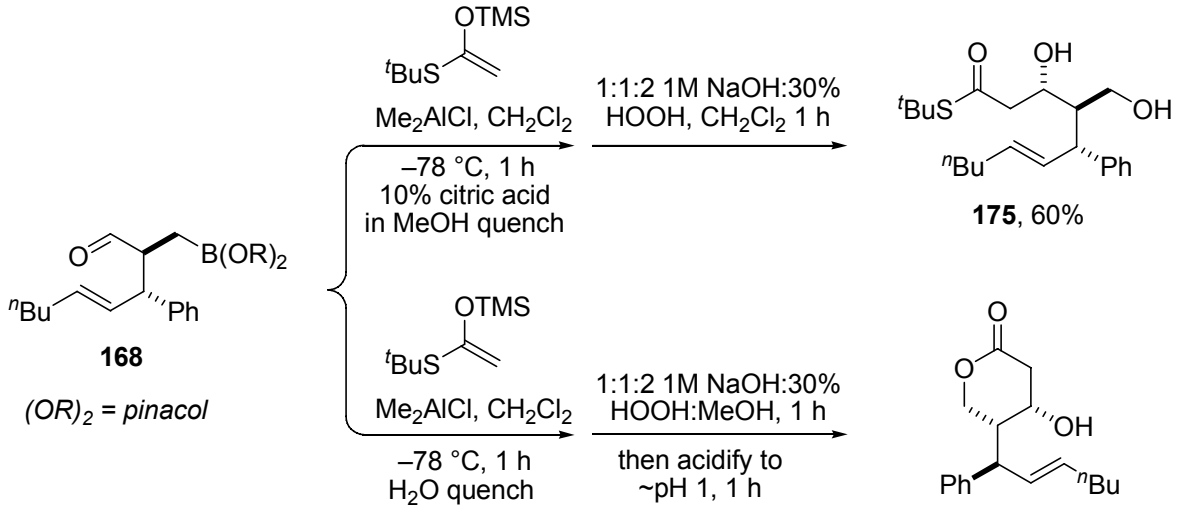


Figure 38. X-ray structure of aldehyde **170**

3.2.4 Mukaiyama Aldol Reactions and Access to Oxygenated Products

To probe the inherent electrophilicity of the β-boronic aldehydes, acetate-derived thioester trimethylsilyl ketene acetal was added to several substrates in dichloromethane. Following an extended time period (>24 h), only recovered starting material was observed. This result further implies the lack of internal chelate activation in solution. Addition of external Lewis acids, such as dimethylaluminum chloride, however, promoted a highly diastereoselective Mukaiyama aldol reaction at –78 °C.[161-163] In order to arrive at alkoxy compounds that are unavailable through the parent ICR reaction, intermediates from the aldol reaction were treated under optimized oxidative conditions to afford thioester **175** or δ-lactone **176** (Scheme 17).

Scheme 17. Mukaiyama aldol reaction of β-boronic aldehyde **168**



[a]Determined by GC-MS following isolation by flash chromatography

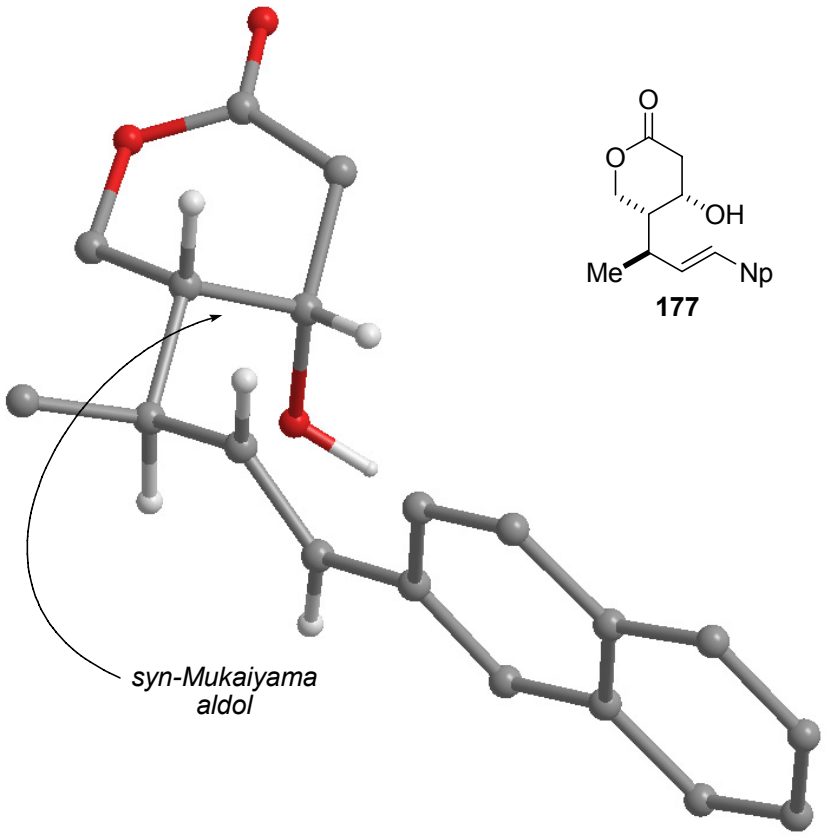
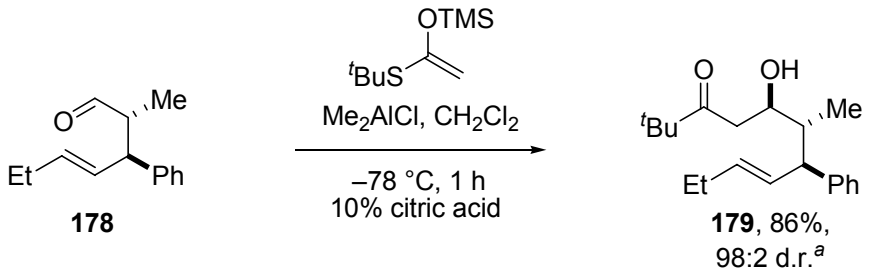


Figure 39. X-ray structure of δ-lactone **177**

The relative stereochemistry of the related naphthyl δ-lactone **177** derived from aldehyde **170** was determined by X-ray analysis and is identical to that observed by Heathcock for products of highly diastereoselective Mukaiyama aldol reactions on simple α-chiral aldehydes (Figure 39).[164, 165] Aldehyde **178**, which possesses a similar structure to **168-170** but lacks a β-borane moiety, performed comparably in the aldol reaction giving **179** in 98:2 d.r.[166] The observation that both aldehydes react similarly leads to the conclusion that the high stereoselectivity of Mukaiyama aldol reactions with β-boronic aldehydes is a product of Felkin control through an open transition state, not a function of internal boron chelation (Figure 40).



[a]Determined by GC-MS following isolation by flash chromatography

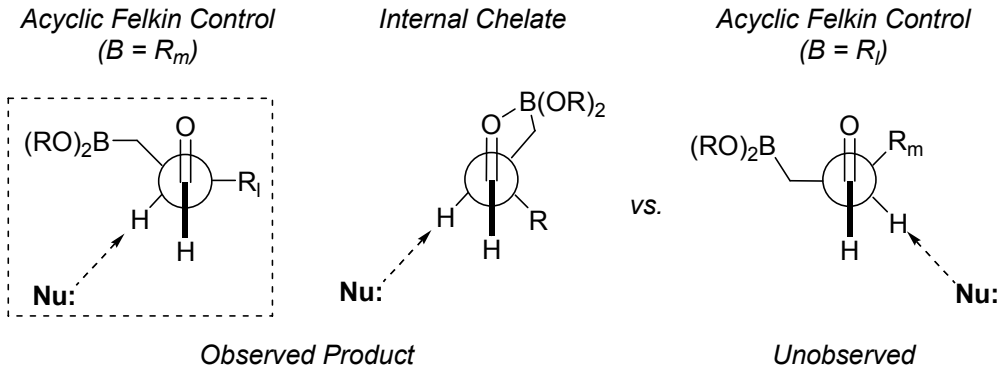


Figure 40. Control experiment and rationale for relative stereochemistry

3.2.5 Stoichiometric Formation of a Boron 'ate' Acetal

We suspected that the reason for the apparent lack of internal chelation observed with aldehydes **168-170** was due to the fact that the carbonyl carbon and oxygen and the boron atom are sp^2 hybridized. Organizing these atoms in the context of a five-membered ring intramolecular coordination complex would impose a significant degree of angle strain. This conclusion was supported by observations made during the attempted formation of boron 'ate' complexes. Based on recent literature precedent, it was hypothesized that conversion of the boronic ester to the 'ate' complex would affect the selectivity of subsequent nucleophilic additions.[167] To form

the 'ate' complex, aldehyde **168** was added to an *in situ* generated solution of lithium n-propoxide and the reaction mixture was then subjected to a four-fold excess of *tert*-butyllithium. Surprisingly, following 1 h of stirring and an aqueous workup, the starting aldehyde was re-isolated with no detectable change in diastereomeric ratio. This result suggests that the lithium alkoxide attacks the aldehyde instead of the boronic ester, leading to a rehybridization of the carbonyl carbon and oxygen from sp^2 to sp^3. This rehybridization consequently enables internal coordination of the newly formed alkoxide to boron, leading to a stabilized boron 'ate' acetal.

A ^{1}H-NMR study provided ample support to this postulate (Figure 41).[168] Upon addition of the lithium alkoxide solution to the aldehyde, a ^{1}H-NMR taken within 5 min indicates a slight reduction in the aldehyde integration, along with new resonances appearing at ~ 3.0 ppm. It is believed that this peak at 3.0 ppm represents the methane protons at the newly formed acetal center. Following 15 min at ambient temperature, subsequent ^{1}H-NMR analysis indicates complete disappearence of the aldehyde resonance; the methane resonance now becomes increasingly intense. Even more revealing is the fact that the characteristic resonance for the methylene protons α to the boronate at ~ -1.0 ppm disappears, and is replaced by a high-field resonance at ~ -2.0 ppm. This is strong evidence for the formation of the 'ate' complex, which would increase local electron density, effectively serving to shield the methylene protons.

This selective acetal formation could be of significant use for differential protection of aldehydes that are otherwise similar in reactivity. The resilience of this temporary protecting group in presence of alkyl carbanions has already been demonstrated, while cleavage appears to be rapid and complete with a simple aqueous workup.

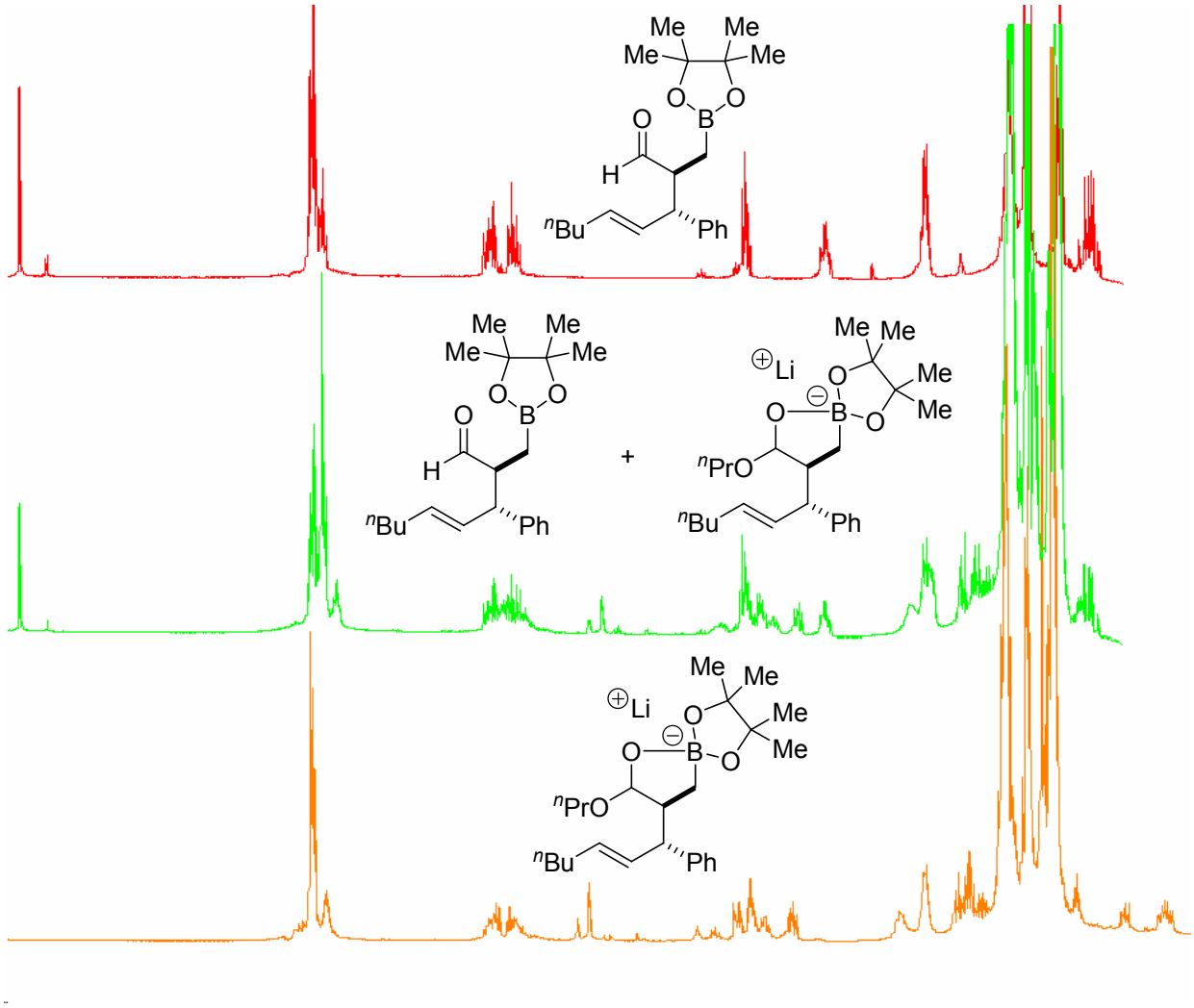


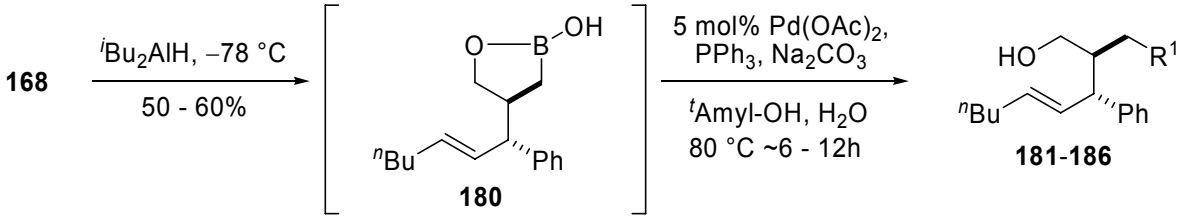
Figure 41. ^{1}H-NMR experiment for boron 'ate' acetal formation

3.2.6 Access to β-Aryl Substituted ICR products through Suzuki Crosscoupling

As demonstrated in the previous section, β-boronic aldehydes increase the scope of the ICR reaction by providing access to oxygenated products. Ideally, Suzuki crosscoupling reactions could be implemented to append a variety of aryl and vinyl substituents, greatly complementing the original ICR methodology. Attempts to affect direct Suzuki crosscoupling

on aldehyde **168** or the corresponding potassium trifluoroborate salt with bromobenzene were unfruitful due primarily to competing β-hydride elimination or epimerization.[169-175] Reduction of the aldehyde using diisobutylaluminum hydride lead in moderate yield to intermediate **180**, which was assigned the putative cyclic borinic acid structure**.** This assignment was based primarily on chemical behavior (non-polar, low tendency for ligand exchange), although the free boronic acid or a polymeric form cannot be excluded based on the spectroscopic data. Borane **180** readily participates in Suzuki reactions with a variety of aryl and heteroaryl bromides, leading to substrates unavailable from the original ICR methodology (Table 13).[176, 177]

Table 13. Suzuki crosscoupling of intermediate **180**

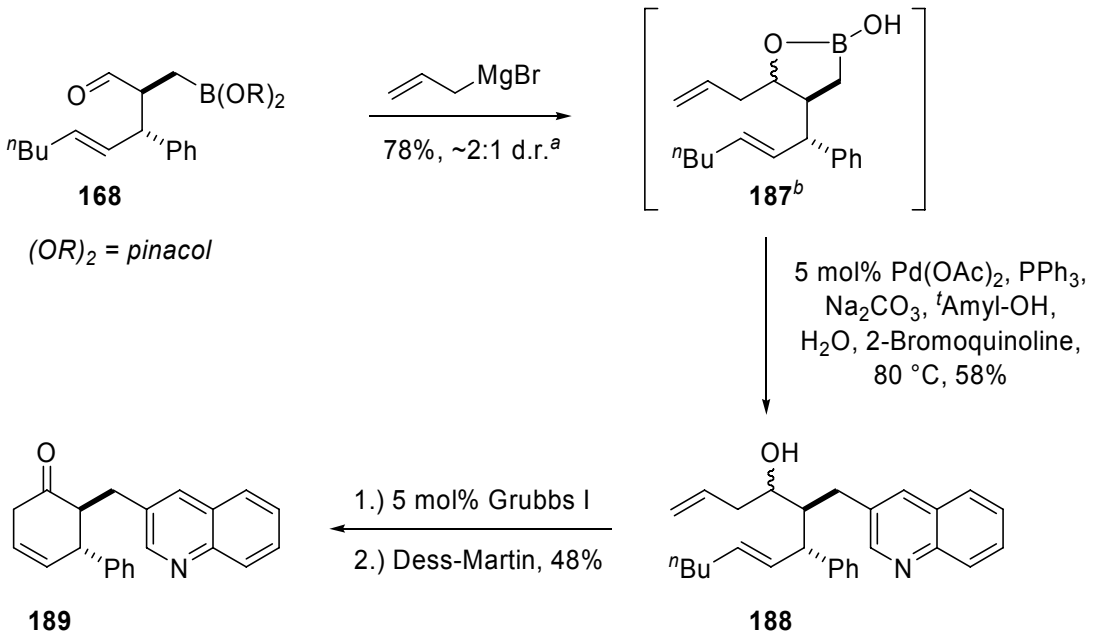


R^1	Suzuki Yield (%)[a]
-Ph	67 (**181**)
-4-NO_2Ph	81 (**182**)
-Np	67 (**183**)
-2-Pyr	36 (**184**)
-3-Pyr	78 (**185**)
-3-Quinoline	89 (**186**)

[a]Yields and catalyst loadings are calculated based on free boronic acid molecular mass. Values based on structure **180** are ~5% lower than reported.

As a final example of the utility of ICR-derived β-boronic aldehydes for synthetic purposes, the combined use of nucleophile addition and Suzuki reaction was demonstrated (Table 14). Addition of allylmagnesium bromide to aldehyde **168** yielded an inconsequential mixture of diastereomeric homoallylic borinic acids **187**. Note that the poor diastereomeric ratio observed for this transformation reflects those obtained for allyl additions to the standard ICR-

Scheme 18. Nucleophile addition to **168** followed by Suzuki crosscoupling



[a]Determined by ^{1}H-NMR of **188** following isolation. [b]Structure tentatively assigned, not confirmed by full characterization.

derived aldehydes (~1:1 – 2:1). This casts further doubt on the role of internal chelation in determining the stereoselectivity of these transformations. Exposing **187** to optimized Suzuki conditions with 2-bromoquinoline gave the coupling product **188** in 58% yield as an equimolar mixture of diastereomers. Subjection of **188** to Grubbs' first generation catalyst followed by oxidation of the epimeric alcohols using the Dess-Martin reagent afforded the desired β,γ-

unsaturated ketone **189** in 48% yield.[178-182] This route demonstrates the versatility of boron ICR products for rapid diversification into a variety of potentially useful compounds.

3.3 CONCLUSIONS

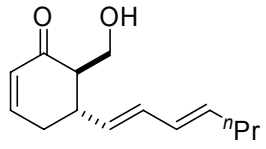
Vinyl boronic esters have been demonstrated to be effective precursors for the ICR reaction, leading to β-boronic aldehydes in high diastereoselectivities and yields.[183] Mukaiyama aldol reactions carried out on these aldehydes are highly diastereoselective and the boron moiety can be oxidized under mild conditions. The potential for intramolecular aldehyde chelation to the proximal boronic ester has been shown to be relatively unimportant in determining the stereoselectivity of various nucleophilic addition reactions. Suzuki reaction conditions have been derived which enable the synthesis of aryl-substituted products that are typically unavailable from the ICR reaction.

4.0 ATTEMPTED SYNTHESIS OF (–)-PENIENONE VIA BORON ICR METHODOLOGY

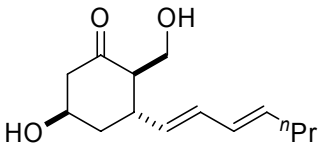
4.1 BACKGROUND

4.1.1 Structure and Bioactivity

Penienone (**190**) and penihydrone (**191**) were isolated from the fermentation broth of the fungus *Penicillium* sp. No. 13 by Kimura, Mizuno and Shimada in 1997.[184] Both molecules are promising potential herbicides. While penienone completely inhibited hypocotyl elongation and root growth of lettuce seedlings at 300 mg/L, penihydrone only inhibited elongation by 41% while *accelerating* root growth by 280%. The hydroxymethylene group has been shown to be critical for maintaining the biological activity of these natural products.[185]



(–)-penienone (**190**)



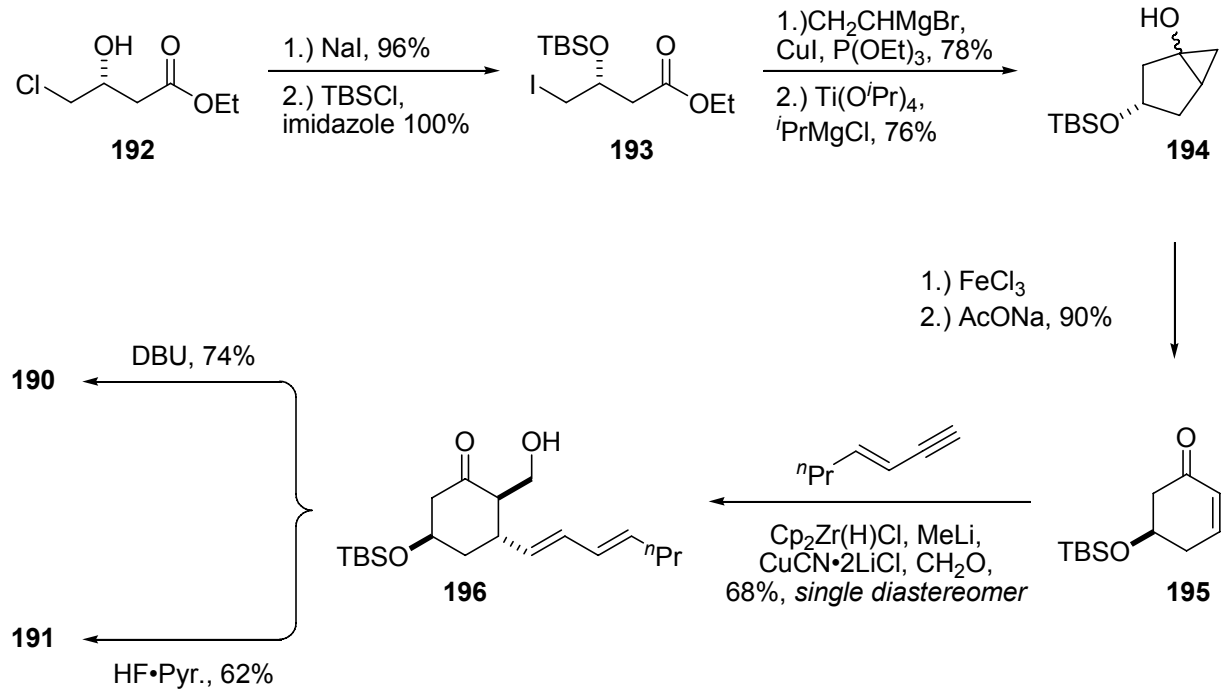
(+)-penihydrone (**191**)

Figure 42. Structures of the plant growth regulators penienone and penihydrone

4.1.2 Prior Syntheses of Penienone and Penihydrone

Both **190** and **191** were prepared by Sato and coworkers two years following their isolation (Scheme 19).[186] Enantioenriched 3-chloro-2-oxybutyrate **192** was obtained by an enantioselective Ru-BINAP hydrogenation (98% ee) and readily underwent a Finkelstein reaction and hydroxyl protection to produce silyl ether **193** in excellent yields.[187] Displacement of the primary iodide with *in situ* generated vinyl cuprate followed by an intramolecular Kulinkovich reaction yielded the desired cyclopentane **194** as a mixture of alcohol epimers.[188]

Scheme 19. Sato's synthesis of (–)-penienone and (+)-penihydrone

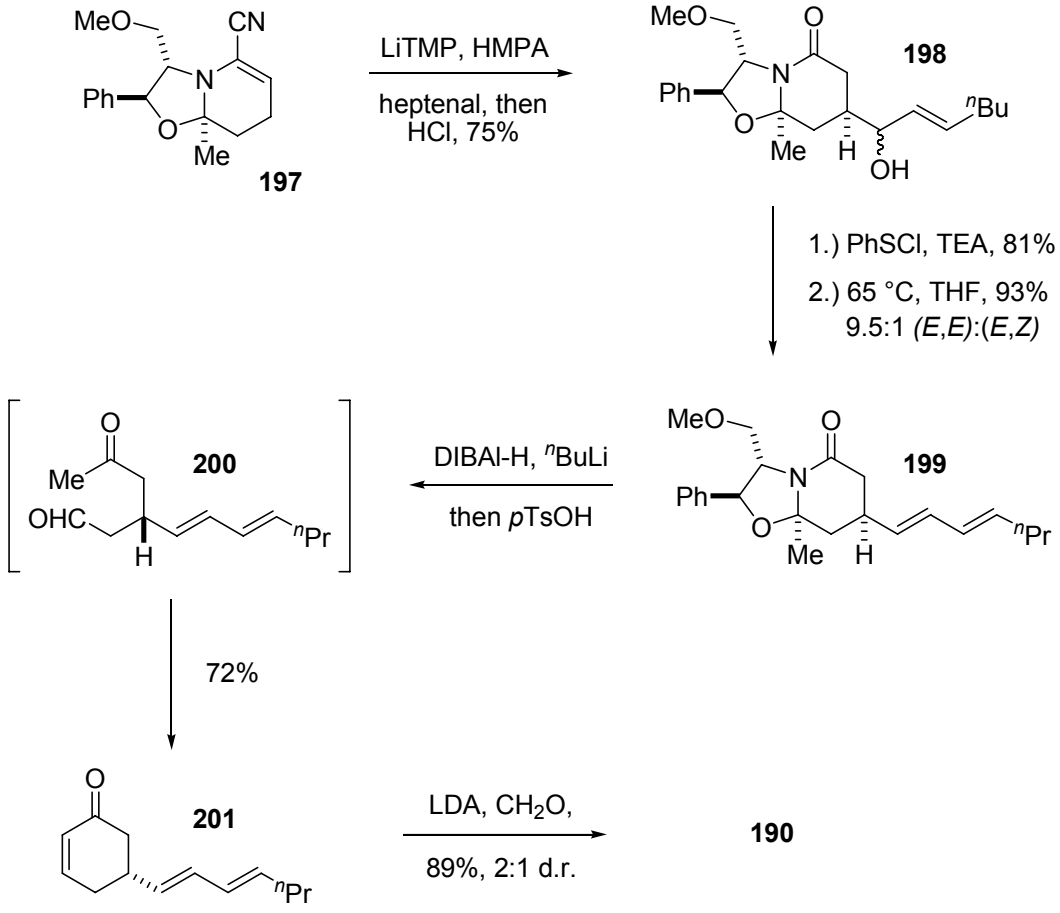


Fragmentation of the cyclopropane of **194** using iron trichloride followed by halide elimination with sodium acetate produced the versatile intermediate cyclohexenone **195**, which was used as a

template for several stereoselective conjugate addition reactions. Copper-mediated conjugate addition of the *in situ* prepared dienyl zirconocene followed by trapping of the transient copper enolate with formaldehyde afforded advanced intermediate **196** in 68% yield as a single diastereomer. Hydroxycyclohexanone **196** was converted into **190** *via* β-elimination or into **191** through hydroxyl group deprotection.

Meyers *et al.* reported a second synthesis of **190** in 2000 based on enantioselective bicyclic lactam auxiliary methodology (Scheme 20).[189] Starting with cyano-substituted bicycle **197**, alkylation with heptenal followed by hydrolysis of the enamine produced the corresponding

Scheme 20. Meyers' synthesis of (–)-penienone



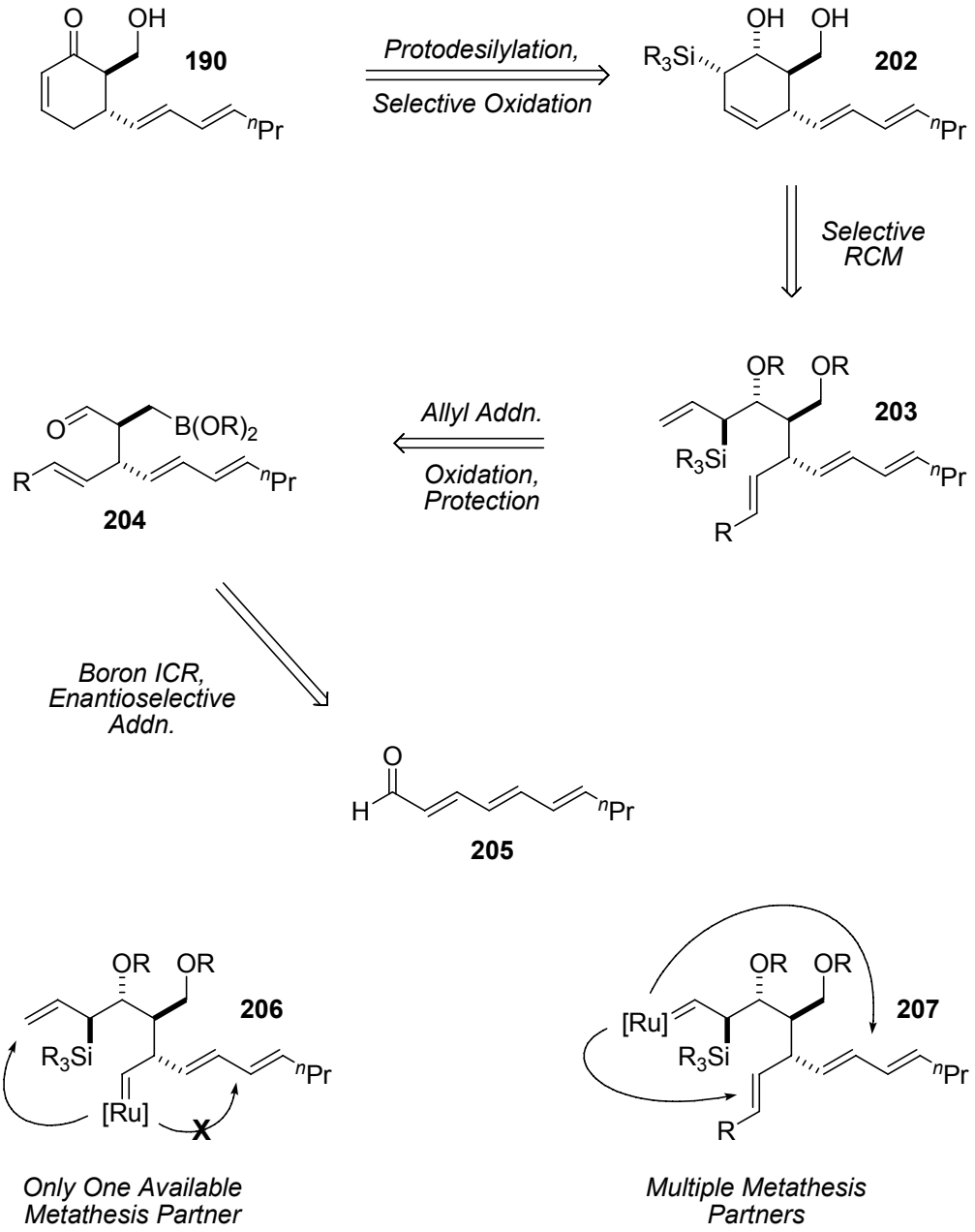
lactam **198** as 7:5 ratio of alcohol stereoisomers. Conversion of **198** to the sulfenate ester and subsequent Mislow-Evans rearrangement gave the intermediate sulfoxide in 81% yield. Thermal elimination of the sulfenic acid afforded 93% of the desired diene **199** in a 9.5:1 ratio of alkene isomers which were carried through the synthesis. Reduction of **199** to the bis-aminal and acid-mediated hydrolysis unveiled the transient keto-aldehyde **200**, which promptly underwent an intramolecular aldol condensation which yielded cyclohexanone **201**. The enolate of **201** was treated with formaldehyde to produce **190** with only modest diastereoselectivity.

4.1.3 Retrosynthesis of (–)-Penienone

We were initially drawn to **190** as a synthetic target due to the *trans*-relationship between the dienyl and hydroxymethylene cyclohexenone ring substituents. Retrosynthetically, **190** could be envisioned to proceed from olefin transposition and oxidation of cyclic secondary alcohol **202** (Scheme 21).[190-193] Cyclohexene **202** would arrive from a selective ring closing metathesis of homoallylic alcohol **203**, following the strategy described in the previous chapter. Though clearly a challenging step, this disconnection seemed rational since dienes are known to tolerate metathesis conditions in the presence of more reactive olefins.[194,195] Also, if metal carbene formation could be forced to occur on the internal olefin (**206**), there would be only one ring closing metathesis partner available due to geometrical and spatial constraints. Alternatively, carbene formation on the terminal olefin would allow for RCM at multiple sites (**207**). It was envisioned that **203** could be derived from allylation of aldehyde **204**, which in turn would be accessed *via* boron ICR methodology. The requisite diallyl ether Claisen substrate would be prepared from aldehyde **205** following an enantioselective addition reaction. This approach is

beneficial since nearly any enantioselective carbon-carbon bond forming reaction could be used to obtain **204** in enantioenriched form.

Scheme 21. Retrosynthesis of (–)-penienone

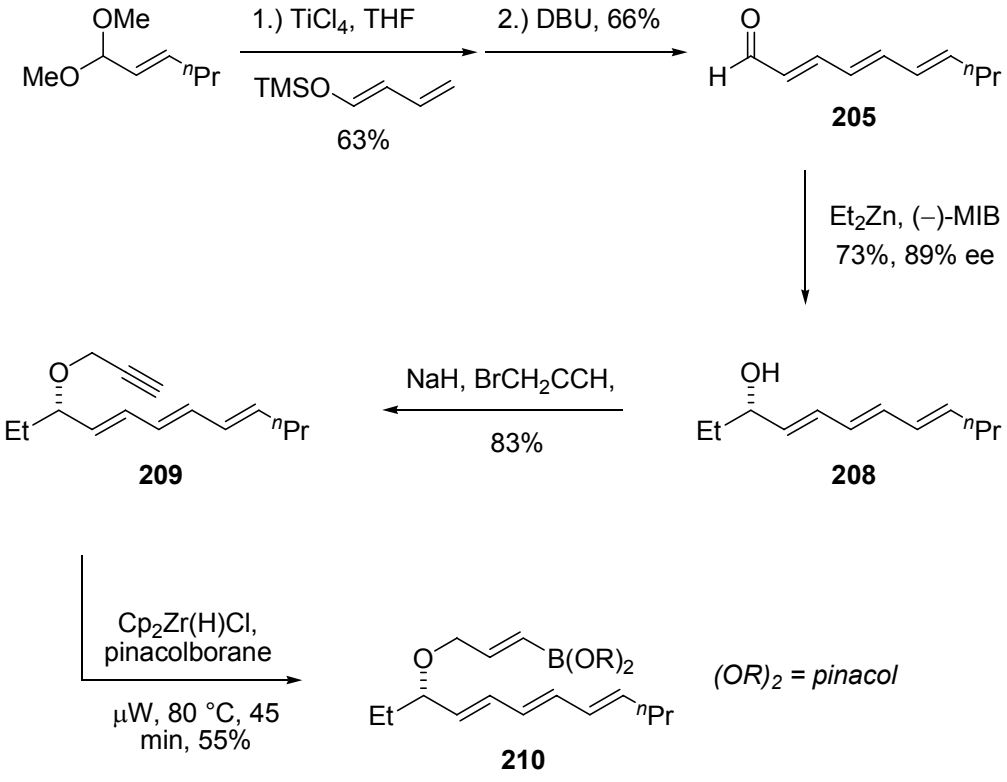


4.2 RESULTS AND DISCUSSION

4.2.1 Synthesis of Vinyl Boronic Ester Precursor 210

Synthesis of aldehyde **205** was carried out in two steps according to the literature procedure.[196] The trienal aldehyde was then subjected to an asymmetric diethyl zinc addition reaction catalyzed by the MIB ligand to give alcohol **208** in 73% yield and 89-90% ee.[197-201] Alcohol **208** was highly sensitive and could only be stored for several days when frozen in a benzene matrix at –80 °C. Etherification of **208** proceeded uneventfully with sodium hydride and propargyl

Scheme 22. Synthesis of vinyl boronic ester **210**

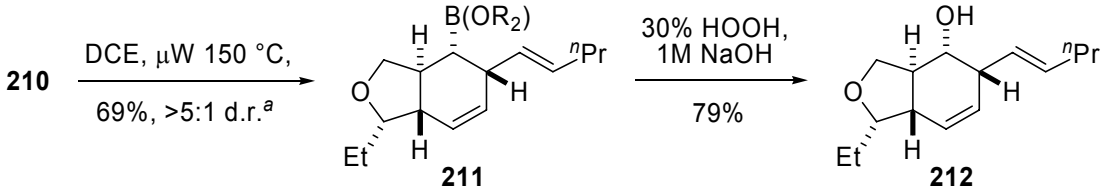


bromide affording propargylic ether **209** in 83% yield. Hydroboration of **209** was found to be highly sensitive to the reaction temperature, and optimal yields of vinyl boronic ester **210** (55%) were obtained with microwave heating to 80 °C for 45 min.

4.2.2 An Unexpected Side Reaction

The low yield for the hydroboration reaction of **209** was initially perplexing. During optimization studies, the formation of a single major byproduct along with boronic ester **209** was observed. The byproduct was determined to be bicyclic furan **211**, which is formed by the intramolecular Diels-Alder reaction of **210** (Scheme 23). Analogous reactions are well known in the literature; however, these generally rely on the more highly reactive alkyl borane

Scheme 23. Boron Diels-Alder reaction



[a]Diastereomeric ratio was determined by the mass of the isolated products. [b]The relative stereochemistry has not been rigorously established and is based on literature precedent.

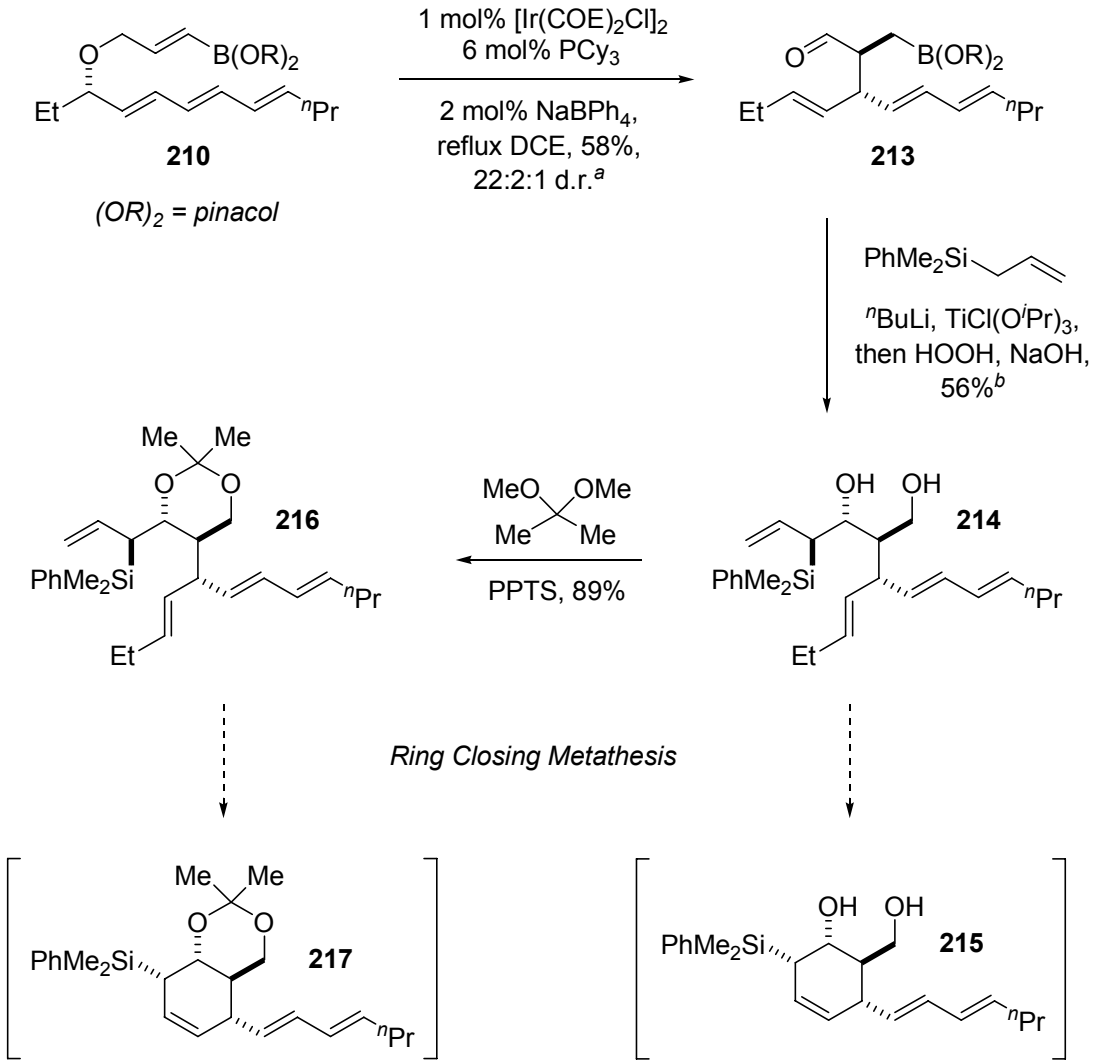
reducing agents and must be derivatized prior to isolation.[202-204] Furan **211**, however, is quite stable and can be isolated by standard silica gel chromatography and stored for extensive periods of time. The optimized reaction conditions for the synthesis of **211** is depicted above (Scheme 23). The boronic ester moiety of **211** can be readily modified by standard transformations. For

example, exposing **211** to basic hydrogen peroxide gave the desired furanol **212** in 79% yield. Furanol **212** is a highly crystalline material; however, an X-ray structure of this intermediate was not obtained, and therefore its relative stereochemistry was not rigorously established. The depicted relative stereochemistry of **212** is derived from a very closely related literature reaction emerging from the expected 'endo' transition state.[205] A one-pot hydroboration, Diels-Alder reaction has also been accomplished, however yields stand at approximately 30-40%.

4.2.3 Preparation of RCM Precursors 214 and 216

With reasonable quantities of **210** available from the optimized hydroboration reaction, the ensuing key Claisen rearrangement was explored. Treatment of **210** with 2 mol% of the active cationic iridium complex followed by heating in refluxing dichloroethane provided the 58% yield of aldehyde **211** with 22:2:1 d.r.. Aldehyde **211** was treated with an *in situ* prepared allyl titanium species and the intermediate borane oxidized with basic hydrogen peroxide, providing homoallylic diol **214** in 56% yield.[206] Unfortunately, **214** was inert in the subsequent RCM reaction with either generation of the Grubbs catalyst presumably due to catalyst deactivation by the diol moiety. To circumvent this complication, the free diol of **214** was protected as the corresponding acetonide **216**. Acetonide **216** was also a poor metathesis substrate for formation of cyclohexene **217** with Grubbs' first generation catalyst. The second generation catalyst and Schrock's molybdenum catalyst appeared to react primarily with the internal diene of **217**, suggesting that the isolated olefins are particularly hindered.[207] Various attempts at protecting the free diene of **213**, **214** or **216** as the corresponding iron complex with UV activation or using Knolker's iron transfer reagent were unsuccessful.[208-215]

Scheme 24. Preparation and evaluation of ring closing metathesis substrates **214** and **216**



[a]Diastereomeric ratio determined by ^{1}H-NMR following flash chromatography *via* integration of the aldehyde resonances. [b]Diastereomeric ratio not determined for this reaction.

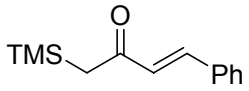
4.3 CONCLUSIONS

An approach to the total synthesis of the plant growth inhibitor (–)-penienone was explored in order to demonstrate the practical application of boron ICR methodology to complex molecule construction. During the course of these studies, a remarkable variant of the intramolecular boron Diels-Alder reaction was discovered. It is likely that further studies into this transformation would provide the basis for a novel methodology project. The key boron Claisen rearrangement was effective for the preparation of advanced intermediates **214** and **216** which were unfortunately ineffective substrates for RCM under various conditions. This failure is likely due to sterics, a conjecture which is supported by results with related systems lacking the bulky silane moiety.[216]

5.0 EXPERIMENTAL SECTION FOR CHAPTER 1

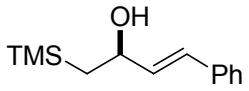
General Information for Chapters 5-8: Unless otherwise stated all reactions were performed in dry glassware under an atmosphere of oxygen free nitrogen using standard inert atmosphere techniques for the manipulation of solvents and reagents. Anhydrous solvents were obtained by passing through successive alumina columns on a solvent purification system. $[IrCl(C_8H_{14})_2]_2$ and PCy_3 were stored and weighed out in a glove box.[217] Pinacolborane was purchased from Aldrich, distilled under partial vacuum, and stored under nitrogen in a freezer. Temperatures for the thermal Claisen rearrangements were controlled using an Ika® Werke hotplate/stirrer. Infrared spectra were recorded on a Nicolet Avatar 360 FT-IR spectrometer**.** ^{1}H-NMR spectra were recorded on a Bruker Advance-300 (300 MHz) or Advance-500 (500 MHz) spectrometer. Chemical shifts are reported relative to following reference peaks for ^{1}H-NMR (multiplicity, shift); $CDCl_3$ (1, 7.27 ppm), C_6D_6 (1, 7.16 ppm), D_3CCN (5, 1.94 ppm), d_6-DMSO (5, 2.50 ppm) and for ^{13}C-NMR (multiplicity, shift); $CDCl_3$ (1, 77.0 ppm), C_6D_6 (3, 128.39 ppm), D_3CCN (1, 118.69 ppm or 7, 1.39 ppm), d_6-DMSO (7, 39.51 ppm). Mass spectra were obtained on a VG-7070 or Fisons Autospec high-resolution magnetic sector mass spectrometer. Analytical thin layer chromatography was performed on EM Reagent 0.25 mm silica gel 60-F plates. Flash chromatography was performed as previously described on EM silica gel 60 (230-240 mesh) or Iatrobeads 6RS-8060 (pH 7 silica gel), purchased from Shell-USA, or EM silica gel 60 (230-240 mesh).[218] Medium pressure liquid chromatography was performed on a Biotage Flash-25^{TM}

MPLC system. Analytical high performance liquid chromatography (HPLC) was performed on a Hewlett Packard 1100 liquid chromatograph equipped with a variable wavelength UV detector (deuterium lamp, 190-600 nm), using a Chiracel^{TM} OD-H or AS-H column (250 x 4.6 mm) (Daicel Inc.) or a Zorbax^{TM} Sil column (240 x 4.6 mm) (Rockland Technologies, Inc.). HPLC grade ethyl acetate, isopropanol and hexanes were used as the eluting solvents. Analytical gas liquid chromatography (GLC) was performed on a Varian 3900 gas chromatograph with a flame ionization detector and split mode capillary injection system using a Chrompack^{TM} CP-Sil 5 CB (30 m x 0.25 mm) (Varian Inc.) or a Varian CP-Wax 52 CB (30 m x 0.25 mm) (Varian Inc.). GC-MS was performed on a Hewlett Packard 5890 Series II gas chromatograph with a Hewlett Packard Series 5970 mass selective detector in electron ionization (EI) mode and split mode capillary injection system using a HP-1 (12 m x 0.20 mm) (Hewlett Packard Inc.). LC-MS was performed on a Hewlett Packard 1100 Series liquid chromatograph system with using a X-terra C-18 column. Microwave reactions were performed using a CEM Discover microwave. Melting points were determined using a Laboratory Devices Mel-temp II.



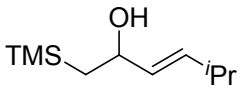
(*E*)-1-Trimethylsilyl-4-phenylbut-3-en-2-one (96):[86] To 0.84g (4.4 mmol) of CuI in 2.0 mL of THF at –40 °C was added 7.3 mL (4.4 mmol) of $TMSCH_2MgCl$ in Et_2O (0.6 M). Following 10 min, a solution of 0.66 g (4.0 mmol) of cinnamoyl chloride in 2.2 mL of THF was added *via* cannula. The reaction was stirred for 2h and quenched with H_2O. The mixture was passed through a plug of celite with Et_2O and the biphasic mixture was transferred to a separatory funnel. The aqueous layer was extracted with Et_2O (3x) and the combined organic extracts were

dried over Na_2SO_4 and filtered. The crude product was concentrated *in vacuo*. Purification by flash chromatography (10:1 hexanes/EtOAc) on Iatrobeads afforded 0.56 g (65%) of the ketone as a clear oil: IR (thin film) 3027, 2956, 1674, 1640, 1607, 1576, 1495, 1251, 979, 852, 707 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.57–7.53 (m, 2H), 7.48 (d, J = 16.0 Hz, 1H), 7.42–7.38 (m, 3H), 6.69 (d, J = 16.0 Hz, 1H), 2.46 (s, 2H), 0.15 (s, 9H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 198.8, 141.7, 134.6, 130.1, 128.8, 128.1, 127.3, 36.8, –1.1; MS (EI) *m/z* 218 ($M^{+\bullet}$), 203, 161, 131, 128, 103, 75; HRMS (EI) *m/z* calculated for $C_{13}H_{18}OSi$: 218.1127, found 218.1117.



(+)-(*E*)-1-Trimethylsilyl-4-phenylbut-3-en-2-ol (15):[84] In a dry round bottom flask, 0.10 g (0.46 mmol) of ketone **96** was diluted to 0.28 mL with THF. A 92 μL (0.092 mmol) aliquot of commercial (*R*)-methyloxazaborolidine in toluene (1M) was added to a separate dry round bottom flask, the toluene was removed *in vacuo*, and 2.3 mL of THF was added. The oxazaborolidine solution was cooled to 0 °C and both the ketone solution and 0.28 mL (0.28 mmol) of BH_3 in THF (1M) were added simultaneously by syringe pump over 1 h. Following the addition, the reaction was slowly quenched with 0.11 mL of MeOH, stirred 10-20 min at 0 °C (H_2 evolution), then raised to rt for 30 min. The reaction mixture was transferred to a separatory funnel with H_2O and Et_2O, the aqueous layer was extracted with Et_2O (3x) and the combined organic layers were dried over Na_2SO_4. The organic extracts were filtered and the crude product was concentrated *in vacuo*. Purification by flash chromatography on SiO_2 (10:1 hexanes/EtOAc) yielded 76 mg (74%) of the alcohol as a wax (low melting point). Separation of the enantiomers by chiral HPLC (Daicel Chiracel™ AS-H column, flow rate 1.0 mL/min, 3.0%

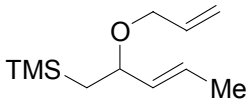
i-PrOH, 97.0% hexanes) provided the enantiomeric ratio: 5.2% (*S*, Tr = 8.1): 94.8% (*R*, Tr = 9.6) (90% ee): $[\alpha]_D^{26}$ = +41.2 (c 1.13, $CHCl_3$)[219]; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.40–7.26 (m, 5H), 6.54 (d, *J* = 15.8 Hz, 1H), 6.22 (dd, *J* = 15.8, 7.2 Hz, 1H), 4.52–4.44 (m, 1H), 1.51 (d, *J* = 3.9 Hz, 1H), 1.14 (dd, *J* = 14.2, 6.9 Hz, 1H), 1.02 (dd, *J* = 14.3, 7.8 Hz, 1H), 0.07 (s, 9H).



(*E*)-5-Methyl-1-trimethylsilylhex-3-en-2-ol (16): To a 250 mL single-neck flask containing 3.7 g (0.15 mol) of mechanically activated Mg(0) equipped with stirbar and condenser with dry ice sleeve was added 75 mL of Et_2O. A solution of I_2 in $BrCH_2CH_2Br$ (cat.) was added to the stirring suspension. Upon reaction initiation (brown → clear/white color shift), 11 mL (9.4 g, 76 mmol) of chloromethyltrimethyl silane in 10 mL of Et_2O was carefully added at a rate to maintain a gentle reflux. Following stirring at ambient temperature for 1 h, the resulting Grignard reagent was added slowly *via* syringe to a solution of 5.0 g (5.9 mL, 51 mmol) of 4-methyl-2-pentenal in 150 mL of Et_2O at –78 °C. After 30 min, the reaction was quenched at –78 °C with sat. aq. NH_4Cl and the resulting biphasic mixture was warmed to ambient temperature. The aqueous layer was extracted with Et_2O (3x), the combined organics were dried over $MgSO_4$, and concentrated to give the crude product. Purification *via* Kughelrohr distillation (43 °C, 200 mtorr) yielded 7.7 g (81%) of the title compound as a colorless oil: IR (thin film) 3358, 2957, 1670, 1248, 971, 839 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 5.59 (dd, *J* = 15.4, 6.3 Hz, 1H), 5.42 (dd, *J* = 15.4, 7.4 Hz, 1H), 4.28–4.20 (m, 1H), 2.36–2.23 (m, 1H), 1.35 (d, *J* = 3.7 Hz, 1H), 1.03 (dd, *J* = 14.1, 6.2 Hz, 1H), 1.00 (d, *J* = 6.8 Hz, 6H), 0.92 (dd, *J* = 14.1, 8.5 Hz, 1H), 0.03 (s, 9H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 137.6, 132.2, 71.3, 30.3, 26.7, 22.1, 22.0, –1.0; MS (EI) *m/z* 185

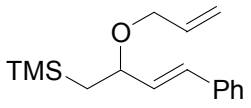
($M^{+\bullet}$-H), 169, 143, 73; HRMS (EI) *m/z* calculated for $C_{10}H_{21}OSi$ ($M^{+\bullet}$-H): 185.1362, found 185.1363.

General Procedure A for Preparation of Diallylethers 17–19:[33] Optimal reaction times were found to be approximately 5-7 d. To a solution of the allylic alcohol (20 mmol) in 13 mL THF was added 13 mL (13 mmol) of Et_2Zn in hexanes (1.0 M) dropwise. The solution was stirred at ambient temperature for 1 h. Into a separate flask, 0.22 g (1.0 mmol) of $Pd(OAc)_2$ and 1.3 g (5.0 mmol) of PPh_3 were weighed, purged with N_2 and were dissolved in 26 mL THF. Following 10 min of vigorous stirring, 3.2 mL (3.0 g, 30 mmol) of allyl acetate was added to the active catalyst in a single portion and the mixture was stirred an additional 10 min. The zinc alkoxide solution was then cannulated into the active catalyst, and the reaction mixture was stirred for the indicated time. The reaction underwent a color change from yellow → orange, returning to the original color upon complete conversion. The solvent was removed *in vacuo* and salts were precipitated by addition of Et_2O followed by filtration through florisil. The crude product mixture was purified as indicated.

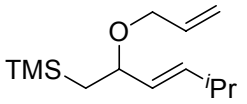


(*E*)-2-Allyloxypent-3-enyltrimethylsilane (17):[19] The general procedure **A** was followed employing 8.0 g (51 mmol) of (*E*)-1-trimethylsilanylpent-3-en-2-ol for 7 d.[220] Purification *via* Kughelrohr distillation (35 °C, 150 mtorr) followed by Biotage MPLC (39:1 hexanes/Et_2O) yielded 8.0 g (79%) of the title compound as a colorless oil: ^{1}H-NMR (300 MHz, $CDCl_3$): δ 5.96–5.84 (m, 1H), 5.55 (dq, *J* = 15, 6.4 Hz, 1H), 5.28 (ddq, *J* = 15, 8.5, 1.6 Hz, 1H), 5.23 (dq,

J = 17, 1.7 Hz, 1H), 5.12 (dq, *J* = 10, 1.3 Hz, 1H), 3.97 (ddt, *J* = 13, 5.3, 1.5 Hz, 1H), 3.80–3.70 (m, 2H), 1.70 (dd, *J* = 6.5, 1.5 Hz, 1H), 1.06 (dd, *J* = 14, 6.7 Hz, 1H), 0.85 (dd, *J* = 14, 8.0 Hz, 1H), 0.01 (s, 9H).



(*E*)-2-Allyloxy-4-phenylbut-3-enyltrimethylsilane (18):[19] The general procedure **A** was followed employing 5.0 g (23 mmol) of (*E*)-4-phenyl-1-trimethylsilanylbut-3-en-2-ol for 2 d.[221] Purification by Biotage MPLC (39:1 hexanes/Et_2O) yielded 3.1 g (52%) of the title compound as a colorless oil: ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.61–7.24 (m, 5H), 6.04 (dd, *J* = 16, 8.3 Hz, 1H), 5.92 (m, 1H), 5.26 (ddd, *J* = 17, 3.5, 1.6 Hz, 1H), 5.15 (ddd, *J* = 10, 3.2, 1.3 Hz, 1H), 4.10–3.95 (m, 2H), 3.83 (ddt, *J* = 13, 5.9, 1.4 Hz, 1H), 1.17 (dd, *J* = 14, 7.2 Hz, 1H), 0.96 (dd, *J* = 14, 7.5 Hz, 1H), 0.28 (s, 9H).

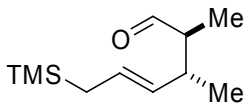


(*E*)-2-Allyloxy-5-methylhex-3-enyltrimethylsilane (19): The general procedure **A** was followed employing 5.1 g (27 mmol) of α-silyl alcohol **16** for 7 d. Purification *via* Kughelrohr distillation (35 °C, 150 mtorr) followed with Biotage MPLC (39:1 hexanes/Et_2O) yielded 5.7 g (93%) of the title compound as a colorless oil: IR (thin film) 2957, 1670, 1650, 1247, 1071, 972, 838 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 5.91, (dddd, *J* = 17.2, 10.4, 5.8, 5.3 Hz, 1H), 5.51 (dd, *J* = 15.5, 6.5 Hz, 1H), 5.28–5.17 (m, 2H), 5.14 (ddt, *J* = 9.1, 1.9, 1.3 Hz, 1H), 3.98 (ddt, *J* = 14.2, 5.3, 1.5 Hz, 1H), 3.80–3.72 (m, 2H), 2.39–2.23 (m, 1H), 1.08 (dd, *J* = 14.3, 6.5 Hz, 1H), 0.88

(dd, J = 14.3, 8.3 Hz, 1H), 1.01 (d, J = 6.8 Hz, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 140.0, 135.5, 129.5, 116.2, 78.5, 68.4, 30.6, 25.1, 22.4, 22.1, –0.6; MS (EI) *m/z* 183 ($M^{+\bullet}$-^{i}Pr), 169, 139, 73; HRMS (EI) *m/z* calculated for $C_{10}H_{19}OSi$ ($M^{+\bullet}$-^{i}Pr): 183.1205, found 183.1200.

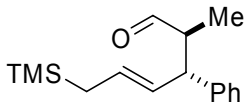
General Procedure B for ICR Reactions 20–22:[19] Large scale isomerizations (~ 2.0 g) were shown to be moderately exothermic; cooling to 0 °C prior to allyl ether addition generally facilitated a higher *E*:*Z* ratio of the vinyl ether. Microwave irradiation was found to be a practical alternative to conventional heating.

A solution of 6.8 mg (0.020 mmol) of $NaBPh_4$ in CH_2Cl_2/acetone (25:1) (1.5 mL) was added to 9.0 mg (0.010 mmol) of $[IrCl(C_8H_{14})_2]_2$ and 17 mg of (0.060 mmol) PCy_3 in 1.5 mL of anhydrous CH_2Cl_2 and the resulting yellow solution stirred for 30 min at ambient temperature. The allyl ether substrate (2.0 mmol) was added dropwise at 0 °C and following addition the reaction was stirred for 15-30 min while warming to ambient temperature. Triphenylphosphine (16 mg, 0.060 mmol) was added and the resulting solution was transferred to a microwave tube. The mixture was irradiated at 100 °C, 150 W for the indicated period of time, and the solvent was removed *in vacuo*. Residual salts were removed by adding hexanes and filtering through celite to yield the crude aldehyde, which was used as isolated. An aliquot of each compound was further purified *via* flash chromatography on SiO_2 to provide the included spectral data.

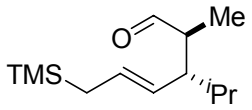


***R**-(*E*,2*S*,3*R*)-2,3-Dimethyl-6-trimethylsilylhex-4-enal (20):** The general procedure **B** was followed employing 2.00 g (10.1 mmol) of diallylether **17** and μW time of 45 min. 1.96 g

(98%) of the crude compound was isolated as a yellow oil. Alternatively, the aldehyde can be purified on Iatrobeads (pH 7 silica, 23:1 hexanes/EtOAc) to yield 1.8 g (90%) of the product as a clear oil (d.r. 93:7 *via* 300 MHz ^{1}H-NMR, aldehyde C**H**O): IR (thin film) 3018, 2958, 2700, 1727, 1673, 1248, 967, 854 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 9.67 (d, *J* = 2.2 Hz, 1H), 5.46 (dtd, *J* = 15.3, 8.0, 1.0 Hz, 1H) 5.21 (ddt, *J* = 15.2, 7.7, 1.1 Hz, 1H), 2.54 (m, 1H), 2.31 (pd, *J* = 7.0, 2.2 Hz, 1H), 1.44 (dd, *J* = 8.0, 0.9 Hz, 2H), 1.05 (d, *J* = 7.0 Hz, 3H), 1.02 (d, *J* = 6.9 Hz, 3H), 0.01 (s, 9H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 205.6, 131.0, 127.0, 51.4, 37.9, 22.7, 17.4, 10.3, –2.0; MS (EI) *m/z* 198 ($M^{+\bullet}$), 183, 130, 115, 73; HRMS (EI) *m/z* calculated for $C_{11}H_{22}OSi$: 198.1440, found 198.1431.



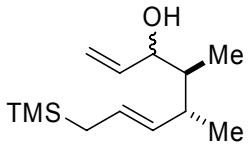
***R**-(*E*,2*S*,3*R*)-2-Methyl-6-trimethylsilyl-3-phenylhex-4-enal (21):** The general procedure **B** was followed employing 2.0 g (7.7 mmol) of diallylether **18** and μW time of 60 min. 2.0 g (100%) of the crude compound was isolated as a yellow oil (d.r. 92:8 *via* 300 MHz ^{1}H-NMR, aldehyde C**H**O): IR (thin film) 3062, 3027, 2955, 2706, 1727, 1653, 1601, 1248, 966, 851 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 9.68 (d, *J* = 3.3 Hz, 1H), 7.39–7.16 (m, 5H), 5.54 (dt, *J* = 15.1, 6.9 Hz, 1H), 5.50 (dd, *J* = 15.2, 7.3 Hz, 1H), 3.46 (dd, *J* = 9.5, 7.5 Hz, 1H), 2.73 (dqd, *J* = 9.6, 6.9, 3.2 Hz, 1H), 1.43 (d, *J* = 6.7 Hz, 2H) 0.91 (d, *J* = 6.9 Hz, 3H), –0.04 (s, 9H); ^{13}C-NMR (75 MHz, D_3CCN): δ 205.8, 143.8, 130.6, 129.6 (2C), 129.0, 127.5, 51.8, 51.7, 23.3, 13.1, –1.7; MS (EI) *m/z* 260 ($M^{+\bullet}$), 203, 130, 73; HRMS (EI) *m/z* calculated for $C_{16}H_{24}OSi$: 260.1596, found 260.1602.



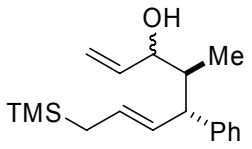
***R**-(*E*,2*S*,3*R*)-3-Isopropyl-2-methyl-6-trimethylsilylhex-4-enal (22):** The general procedure **B** was followed employing 2.0 g (8.8 mmol) of diallylether **19** and μW time of 75 min. 2.0 g (100%) of the crude compound was isolated as a yellow oil (d.r. *E syn:anti* 81:7.1 (A:A*), *Z syn:anti* 9.9:1.5 (B:B*) *via* combined 500 MHz ^{1}H-NMR (A = δ 9.61, A* = δ 9.57, B = δ 9.64, B* = δ 9.59, aldehyde C**H**O) and GC (T_{rA} + T_{rA*} = 27.47, T_{rB} = 29.04, T_{rB*} = 28.83) [CP-Wax 52 CB (30 m x 0.25 mm), method: 60 °C for 5.00 min, ramp @ 3 °C/min to 250 °C, hold for 20 min]): IR (thin film) 2958, 2701, 1727, 1655, 1248, 971, 853 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 9.61 (d, *J* = 3.1 Hz, 1H), 5.42 (dt, *J* = 15.1, 8.0 Hz, 1H), 5.07 (ddt, *J* = 15.1, 9.7, 1.1 Hz, 1H), 2.47 (pd, *J* = 6.9, 3.2 Hz, 1H), 1.97 (ddd, *J* = 9.7, 7.7, 5.8 Hz, 1H), 1.89–1.76 (m, 1H), 1.46 (dd, *J* = 7.9, 1.0 Hz, 2H), 1.05 (d, *J* = 6.9 Hz, 3H), 0.92 (d, *J* = 6.7 Hz, 3H), 0.83 (d, *J* = 6.8 Hz, 3H), 0.00 (s, 9H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 205.8, 130.1, 126.4, 51.9, 48.1, 28.4, 23.0, 21.4, 18.3, 12.5, –1.8; MS (EI) *m/z* 183 ($M^{+\bullet}$-^{i}Pr), 169, 139, 84, 73; HRMS (EI) *m/z* calculated for $C_{10}H_{19}OSi$ ($M^{+\bullet}$-^{i}Pr): 183.1205, found 183.1197.

General Procedure C for Preparation of Allylic and Homoallylic Alcohols 23–30: To a solution of the crude aldehyde (1.0 mmol) in 2.5 mL of CH_2Cl_2 at –78 °C was added a solution of either 1.5 mL (1.5 mmol) of allylmagnesium bromide in Et_2O (1.0 M) or 1.5 mL (1.5 mmol) of vinylmagnesium bromide in THF (1.0 M). Following 15 min-1 h of stirring, the mixture was carefully quenched with sat. aq. NH_4Cl, then slowly warmed to ambient temperature. The aqueous layer was extracted with Et_2O (3-5x), the organics were dried over $MgSO_4$, and the solvent was removed *in vacuo*. The crude oil was purified as specified to yield a ~ 1:1 – 3:1

diastereomeric mixture of the allylic or homoallylic alcohols. The diastereomeric ratios were not established for these reactions. In each case, the high R_f diastereomer was isolated *via* flash chromatography and fully characterized.

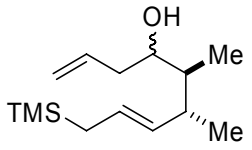


***R**-(*E*,3*R*,4*S*,5*R*)-4,5-Dimethyl-8-trimethylsilylocta-1,6-dien-3-ol + *R**-(*E*,3*S*,4*S*,5*R*)-4,5-Dimethyl-8-trimethylsilylocta-1,6-dien-3-ol (23):** The general procedure **C** was followed using 1.38 g (6.96 mmol) of aldehyde **20** and 10.4 mL (10.4 mmol) of vinylmagnesium bromide. Purification of the crude extract by flash chromatography on SiO_2 (25:1 hexanes/EtOAc) yielded 792 mg (50%) of the product as a yellow oil: IR (thin film) 3373, 3078, 2958, 1650, 1644, 1248, 851 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 5.88 (ddd, *J* = 17.2, 10.5, 5.4 Hz, 1H), 5.43 (dt, *J* = 15.8, 8.0 Hz, 1H), 5.24 (dt, *J* = 17.2, 1.6 Hz, 1H), 5.14 (dt, *J* = 10.5, 1.6 Hz, 1H), 5.27–5.12 (m, 1H), 4.29–4.23 (m, 1H), 2.17 (sextet, *J* = 7.1 Hz, 1H), 1.48 (d, *J* = 5.3 Hz, 1H), 1.43 (dd, *J* = 7.8, 0.9 Hz, 2H), 1.47–1.33 (m, 1H), 0.97 (d, *J* = 6.8 Hz, 3H), 0.88 (d, *J* = 6.9 Hz, 3H), 0.00 (s, 9H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 140.9, 133.9, 125.8, 114.3, 74.4, 43.7, 39.5, 22.7, 18.1, 10.6, –1.9; MS (EI) *m/z* 226 ($M^{+\bullet}$), 211, 141, 73; HRMS (EI) *m/z* calculated for $C_{13}H_{26}OSi$: 226.1753, found 226.1756.



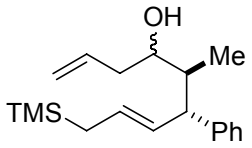
***R**-(*E*,3*R*,4*S*,5*R*)-4-Methyl-8-trimethylsilyl-5-phenylocta-1,6-dien-3-ol + *R**-(*E*,3*S*,4*S*,5*R*)-4-Methyl-8-trimethylsilyl-5-phenylocta-1,6-dien-3-ol (24):** The general procedure **C** was

followed using 1.00 g (3.84 mmol) of aldehyde **21** and 5.76 mL (5.76 mmol) of vinylmagnesium bromide. Purification of the crude extract by flash chromatography on SiO_2 (25:1 → 10:1 hexanes/EtOAc) yielded 802 mg (72%) of the product as a yellow oil: IR (thin film) 3475, 3083, 3062, 3026, 2954, 1645, 1601, 1248, 966, 854 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.34–7.15 (m, 5H), 5.95 (ddd, *J* = 17.2, 10.6, 4.8 Hz, 1H), 5.55 (dt, *J* = 15.0, 7.4 Hz, 1H), 5.46 (dd, *J* = 15.1, 8.2 Hz, 1H), 5.28 (dt, *J* = 17.2, 1.6 Hz, 1H), 5.18 (dt, *J* = 10.6, 1.6 Hz, 1H), 4.55–4.50 (m, 1H), 3.24 (dd, *J* = 10.2, 8.7 Hz, 1H), 1.91 (dqd, *J* = 10.3, 6.9, 2.3 Hz, 1H), 1.46 (d, *J* = 4.1 Hz, 1H), 1.43 (d, *J* = 6.2 Hz, 2H), 0.66 (d, *J* = 6.9 Hz, 3H), –0.05 (s, 9H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 144.7, 140.7, 131.6, 128.4, 127.7 (2C), 125.8, 114.1, 72.9, 53.1, 42.9, 22.9, 10.9, –1.8; MS (EI) *m/z* 288 ($M^{+\bullet}$), 270, 203, 73; HRMS (EI) *m/z* calculated for $C_{18}H_{28}OSi$: 288.1909, found 288.1918.

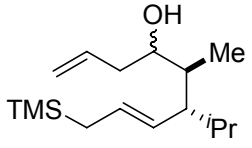


***R**-(*E*,4*R*,5*S*,6*R*)-5,6-Dimethyl-9-trimethylsilylnona-1,7-dien-4-ol + *R**-(*E*,4*S*,5*S*,6*R*)-5,6-Dimethyl-9-trimethylsilylnona-1,7-dien-4-ol (25):** The general procedure **C** was followed using 1.9 g (9.4 mmol) of aldehyde **20** and 11 mL (1.2 equiv., 11 mmol) of allylmagnesium bromide. Purification of the crude extract by flash chromatography on SiO_2 (25:1 hexanes/EtOAc) yielded 1.5 g (66 %) of the product as a yellow oil: IR (thin film) 3423, 3077, 2958, 1650, 1641, 1248, 853 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 5.82 (ddt, *J* = 17.1, 10.2, 7.0 Hz, 1H), 5.42 (dt, *J* = 15.6, 8.0 Hz, 1H), 5.19 (dd, *J* = 15.2, 8.4 Hz, 1H), 5.15–5.08 (m, 2H), 3.79 (ddd, *J* = 8.2, 5.0, 3.2 Hz, 1H), 2.31–2.08 (m, 3H), 1.50 (s, 1H), 1.43 (dd, *J* = 7.9, 0.8 Hz, 2H), 1.33 (pd, *J* = 6.9, 3.1 Hz, 1H), 0.98 (d, *J* = 6.8 Hz, 3H), 0.90 (d, *J* = 6.9 Hz, 3H), 0.00 (s, 9H) ;

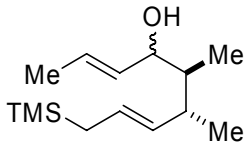
^{13}C-NMR (75 MHz, $CDCl_3$): δ 135.7, 133.8, 125.7, 117.2, 71.8, 42.9, 40.0, 39.9, 22.7, 18.5, 10.6, –1.9; MS (EI) *m/z* 240 ($M^{+\bullet}$), 225, 199, 141, 73; HRMS (EI) *m/z* calculated for $C_{14}H_{28}OSi$: 240.1909, found 240.1912.



***R**-(*E*,4*R*,5*S*,6*R*)-5-Methyl-9-trimethylsilyl-6-phenylnona-1,7-dien-4-ol + *R**-(*E*,4*S*,5*S*,6*R*)-5-Methyl-9-trimethylsilyl-6-phenylnona-1,7-dien-4-ol (26):** The general procedure **C** was followed using 918 mg (3.52 mmol) of aldehyde **21** and 5.29 mL (5.29 mmol) of allylmagnesium bromide. Purification of the crude extract by flash chromatography on SiO_2 (25:1 → 10:1 hexanes/EtOAc) yielded 0.660 g (62%) of the product as a yellow oil: IR (thin film) 3475, 3081, 3026, 2953, 1650, 1641, 1601, 1248, 966, 851 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.31–7.14 (m, 5H), 5.85 (ddt, *J* = 17.1, 10.1, 6.9 Hz, 1H), 5.52 (dt, *J* = 15.1, 7.6 Hz, 1H), 5.42 (dd, *J* = 15.1, 8.8 Hz, 1H), 5.15 (dq, *J* = 17.1, 1.6 Hz, 1H), 5.12 (dm, *J* = 10.0 Hz, 1H), 4.02 (dtd, *J* = 9.2, 4.7, 2.0 Hz, 1H), 3.21 (dd, *J* = 10.3, 9.0 Hz, 1H), 2.38–2.16 (m, 2H), 1.82 (dqd, *J* = 10.4, 6.8, 1.8 Hz, 1H), 1.42 (br. d, *J* = 7.2 Hz, 2H), 1.41 (d, *J* = 4.4 Hz, 1H), 0.69 (d, *J* = 6.9 Hz, 3H), –0.05 (s, 9H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 145.0, 135.6, 131.5, 128.4, 127.7, 127.5, 125.8, 117.5, 70.7, 53.6, 42.0, 40.1, 22.8, 10.5, –1.9; MS (EI) *m/z* 302 ($M^{+\bullet}$), 261, 245, 203, 73; HRMS (EI) *m/z* calculated for $C_{19}H_{30}OSi$: 302.2066, found 302.2081.

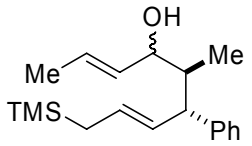


***R**-(*E*,4*R*,5*S*,6*R*)-6-Isopropyl-5-methyl-9-trimethylsilylnona-1,7-dien-4-ol + *R**-(*E*,4*S*,5*S*,6*R*)-6-Isopropyl-5-methyl-9-trimethylsilylnona-1,7-dien-4-ol (27):** The general procedure **C** was followed using 1.07 g (4.70 mmol) of aldehyde **22** and 7.06 mL (7.06 mmol) of allylmagnesium bromide. Purification of the crude extract by flash chromatography on SiO_2 (25:1 hexanes/EtOAc) yielded 853 mg (68%) of the product as a yellow oil: IR (thin film) 3439, 3076, 2957, 1646, 1641, 1248, 974, 854 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 5.81 (ddt, *J* = 17.2, 10.1, 7.1 Hz, 1H), 5.40 (dt, *J* = 15.5, 7.9 Hz, 1H), 5.13–5.01 (m, 3H), 3.83 (dtd, *J* = 9.3, 4.9, 1.7 Hz, 1H), 2.35–2.24 (m, 1H), 2.16–2.07 (m, 1H), 1.95–1.71 (m, 2H), 1.55–1.46 (m, 1H), 1.48 (br. d, *J* = 8.4 Hz, 2H), 1.45 (br. d, *J* = 4.4 Hz, 1H), 0.87 (d, *J* = 5.9 Hz, 3H), 0.85 (d, *J* = 5.7 Hz, 3H), 0.75 (d, *J* = 6.7 Hz, 3H), 0.01 (s, 9H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 136.0, 129.3, 127.8, 116.9, 71.4, 52.2, 40.0, 38.5, 27.7, 23.1, 22.2, 16.5, 10.5, –2.1; MS (EI) *m/z* 268 ($M^{+\bullet}$), 253, 225, 211, 167, 73; HRMS (EI) *m/z* calculated for $C_{16}H_{32}OSi$: 268.2222, found 268.2218.



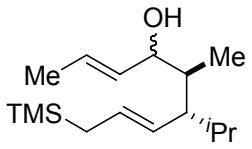
***R**-(2*E*,4*R*,5*S*,6*R*,7*E*)-5,6-Dimethyl-9-trimethylsilylnona-2,7-dien-4-ol + *R**-(2*E*,4*S*,5*S*,6*R*,7*E*)-5,6-Dimethyl-9-trimethylsilylnona-2,7-dien-4-ol (28):** The catalyst was prepared according to general procedure **B** with 25 mg (0.028 mmol) of $[IrCl(C_8H_{14})_2]_2$, 19 mg (0.056 mmol) of $NaBPh_4$ and 47 mg (0.17 mmol) of PCy_3. To the active catalyst mixture was cannulated 1.34 g (5.57 mmol) of allylic alcohol **25** in 1.5 mL of CH_2Cl_2. The flask was rinsed with an additional 1.5 mL of CH_2Cl_2. After 12 h, the reaction was quenched with hexanes and filtered through florsil. The crude product was purified *via* flash chromatography on SiO_2 (25:1 hexanes/EtOAc) to afford 1.21 g (90%) of the title compound mixture as an oil. The high R_f

diastereomer was isolated *via* flash chromatography and fully characterized: IR (thin film) 3385, 2958, 1671, 1652, 1248, 967, 851 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 5.65 (dqd, *J* = 15.3, 7.5, 1.0 Hz, 1H), 5.51 (ddq, *J* = 15.3, 6.4, 1.4 Hz, 1H), 5.41 (dtd, *J* = 15.2, 7.7, 0.7 Hz, 1H), 5.21 (ddt, *J* = 15.2, 8.0, 1.0 Hz, 1H), 4.15–4.10 (m, 1H), 2.16 (sextet, *J* = 7.0 Hz, 1H), 1.72 (dt, *J* = 6.2, 1.1 Hz, 3H), 1.43 (dd, *J* = 7.9, 0.7 Hz, 2H), 1.42–1.34 (m, 2H), 0.94 (d, *J* = 6.8 Hz, 3H), 0.88 (d, *J* = 6.9 Hz, 3H), 0.00 (s, 9H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 134.0, 133.6, 126.3, 125.5, 74.6, 44.1, 39.1, 22.7, 17.7, 17.4, 10.7, –1.9; MS (EI) *m/z* 240 ($M^{+\bullet}$), 225, 197, 141, 73; HRMS (EI) *m/z* calculated for $C_{14}H_{28}OSi$: 240.1909, found 240.1913.



***R**-(2*E*,4*R*,5*S*,6*R*,7*E*)-5-Methyl-9-trimethylsilyl-6-phenylnona-2,7-dien-4-ol + *R**-(2*E*,4*S*,5*S*,6*R*,7*E*)-5-Methyl-9-trimethylsilyl-6-phenylnona-2,7-dien-4-ol (29):** The catalyst was prepared according to general procedure **B** with 14.1 mg (0.0157 mmol) of $[IrCl(C_8H_{14})_2]_2$, 10.8 mg (0.0315 mmol) of $NaBPh_4$ and 26.5 mg (0.0944 mmol) of PCy_3 in 1.6 mL of 50:1 CH_2Cl_2:acetone. The active catalyst mixture was added to a solution of 476 mg (1.57 mmol) of allylic alcohol **26** in 1.6 mL of 50:1 CH_2Cl_2:acetone. After 12 h, the reaction was quenched with hexanes and filtered through florsil. The crude product was purified *via* flash chromatography on SiO_2 (15:1 hexanes/EtOAc) yielding 384 mg (81%) of the product as an oil. The high R_f diastereomer was isolated *via* flash chromatography and fully characterized: IR (thin film) 3469, 3061, 3026, 2954, 1653, 1601, 1248, 964, 854 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.34–7.14 (m, 5H), 5.70 (dqd, *J* = 15.3, 6.2, 1.0 Hz, 1H), 5.63–5.56 (m, 1H), 5.53 (dd, *J* = 12.7, 5.4 Hz, 1H), 5.44 (dd, *J* = 15.1, 8.2 Hz, 1H), 4.44–4.37 (m, 1H), 3.23 (dd, *J* = 10.2, 8.5 Hz, 1H), 1.87

(dqd, J = 10.3, 6.9, 2.5 Hz, 1H), 1.74 (d, J = 6.0 Hz, 3H), 1.43 (br. d, J = 7.5 Hz, 2H), 1.39 (d, J = 5.4 Hz, 1H), 0.68 (d, J = 6.9 Hz, 3H), –0.04 (s, 9H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 144.8, 133.2, 131.6, 128.4, 127.7, 127.6, 126.2, 125.8, 72.9, 53.1, 43.2, 22.8, 17.8, 11.1, –1.9; MS (EI) *m/z* 302 ($M^{+\bullet}$), 287, 203, 73; HRMS (EI) *m/z* calculated for $C_{19}H_{30}OSi$: 302.2066, found 302.2057.

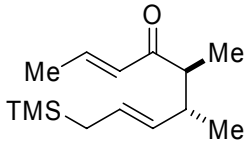


***R**-(2*E*,4*R*,5*S*,6*R*,7*E*)-6-Isopropyl-5-methyl-9-trimethylsilyl-nona-2,7-dien-4-ol + *R**-(2*E*,4*S*,5*S*,6*R*,7*E*)-6-Isopropyl-5-methyl-9-trimethylsilylnona-2,7-dien-4-ol (30):** The catalyst was prepared according to general procedure **B** with 4.1 mg (0.0046 mmol) of $[IrCl(C_8H_{14})_2]_2$, 3.1 mg (0.0091 mmol) of $NaBPh_4$ and 7.6 mg (0.027 mmol) of PCy_3 in 1.5 mL 50:1 of CH_2Cl_2:acetone. The active catalyst mixture was added to 123 mg (0.458 mmol) of neat allylic alcohol **27**. After 12 h, the reaction was quenched with hexanes and filtered through florsil. The crude product was purified *via* flash chromatography on SiO_2 (25:1 hexanes/EtOAc) yielding 0.100 g (81%) of the product as an oil. The high R_f diastereomer was isolated *via* flash chromatography and fully characterized: IR (thin film) 3465, 2958, 1665, 1655, 1248, 969, 851 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 5.64 (dqd, J = 15.4, 6.2, 1.1 Hz, 1H), 5.54 (ddq, J = 15.4, 5.5, 1.2 Hz, 1H), 5.41 (dt, J = 15.2, 7.9 Hz, 1H), 5.09 (ddt, J = 15.2, 9.9, 1.0 Hz, 1H), 4.29–4.26 (m, 1H), 1.93–1.77 (m, 2H), 1.71 (dt, J = 6.0, 1.1 Hz, 3H), 1.59–1.47 (m, 1H), 1.49 (dt, J = 7.9, 1.2 Hz, 2H), 1.43 (d, J = 5.4 Hz, 1H), 0.86 (d, J = 6.9 Hz, 3H), 0.85 (d, J = 6.6 Hz, 3H), 0.76 (d, J = 6.7 Hz, 3H), 0.02 (s, 9H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 133.5, 129.4, 127.9, 125.4, 73.3,

51.7, 40.0, 27.6, 23.1, 22.2, 17.7, 16.3, 11.1, –1.8; MS (EI) *m/z* 225 ($M^{+\bullet}$-^{i}Pr), 169, 149, 73; HRMS (EI) *m/z* calculated for $C_{13}H_{25}OSi$ ($M^{+\bullet}$-^{i}Pr): 225.1675, found 225.1669.

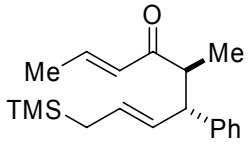
General Procedure D for Preparation of Unsaturated Ketones 31–35:[34] To the allylic or homoallylic alcohol (1.0 mmol) in 3.7 mL of CH_2Cl_2 and 2.9 mL of DMSO was added 0.70 mL (5.0 mmol) of triethylamine. The stirring solution was chilled to 0 °C and 0.48 g (3.0 mmol) of pyridine sulfur trioxide was added in a single portion. The reaction was stirred for ~ 1-4 h until complete by TLC, then quenched with pH 7 buffer. The aqueous layer was extracted with Et_2O (3x), the combined organic layers were dried over $MgSO_4$, and the solvent was removed *in vacuo*. The product was purified as indicated.

The final product mixture is comprised of the desired compound, the Claisen diastereomer, and the *Z*-allyl silane isomer (~ 10%). Aliquots of each sample were further purified for the purpose of characterization; as a consequence, spectra are not indicative of isolated product purity. Isolated purity is established by means of GC-MS [HP-1 (12 m x 0.20 mm), pressure 21 kPa, method: 70 °C for 2.00 min, ramp @ 10 °C/min to 300 °C, hold for 60 min], and/or ^{1}H-NMR, which are included in all cases.

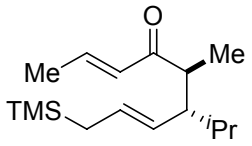


***R**-(2*E*,5*S*,6*R*,7*E*)-5,6-Dimethyl-9-trimethylsilylnona-2,7-dien-4-one (31):** The general procedure **D** was followed employing 1.38 g (5.74 mmol) of allylic alcohol **28**. Flash chromatography on SiO_2 (25:1 hexanes/EtOAc) afforded 1.18 g (86%) of the product as a clear oil. Product ratio by GC-MS: 7.88% (T_r = 10.35), 82.5% (T_r = 10.49), 9.65% (T_r = 11.69).

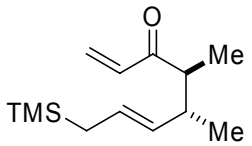
Product ratio by ^{1}H-NMR (300 MHz) (Si–**$(CH_3)_3$**): 7.61% (δ 0.0114), 6.91% (δ –0.0054), 85.5% (δ –0.0286): IR (thin film) 2959, 1696, 1670, 1631, 1248, 969, 853 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 6.90 (dq, *J* = 15.6, 6.9 Hz, 1H), 6.18 (dq, *J* = 15.5, 1.6 Hz, 1H), 5.37 (dtd, *J* = 15.2, 8.0, 6.9 Hz, 1H), 5.16 (ddt, *J* = 15.2, 7.6, 1.0 Hz, 1H), 2.65 (p, *J* = 6.9 Hz, 1H), 2.56–2.36 (m, 1H), 1.89 (dd, *J* = 6.9, 1.6 Hz, 3H), 1.38 (br. dd, *J* = 7.9, 0.8 Hz, 2H), 1.02 (d, *J* = 6.9 Hz, 3H), 0.93 (d, *J* = 6.8 Hz, 3H), –0.03 (s, 9H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 202.9, 141.5, 132.2, 131.1, 125.9, 49.0, 38.9, 22.6, 18.0, 17.2, 12.8, –2.1; MS (EI) *m/z* 239 ($M^{+\bullet}$+H), 170, 155, 141, 73, 69; HRMS (EI) *m/z* calculated for $C_{14}H_{26}OSi$: 238.1753, found 238.1758.



***R**-(2*E*,5*S*,6*R*,7*E*)-5-Methyl-9-trimethylsilyl-6-phenylnona-2,7-dien-4-one (32):** The general procedure **D** was followed employing 272 mg (0.899 mmol) of allylic alcohol **29**. Flash chromatography on SiO_2 (20:1 hexanes/EtOAc) afforded 167 mg (62%) of the product as a clear oil. Product ratio by ^{1}H-NMR (500 MHz) (Si–**$(CH_3)_3$**): 7.73% (δ –0.0260), 86.3% (δ –0.0852), 5.98% (δ –0.1141): IR (thin film) 3027, 2954, 1694, 1668, 1629, 1247, 851 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.33–7.17 (m, 5H), 6.91 (dq, *J* = 15.6, 6.9 Hz, 1H), 6.21 (dq, *J* = 15.5, 1.4 Hz, 1H), 5.38 – 5.34 (m, 2H), 3.50 (dtd, *J* = 10.4, 6.4, 3.2 Hz, 1H), 3.14 (dq, *J* = 10.4, 6.9 Hz, 1H), 1.92 (dd, *J* = 6.8, 1.4 Hz, 3H), 1.35–1.33 (m, 2H), 0.92 (d, *J* = 6.9 Hz, 3H), –0.09 (s, 9H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 203.1, 143.2, 142.5, 131.3, 129.9, 128.4, 128.1, 127.9, 126.2, 52.1, 48.9, 22.8, 18.2, 16.2, –1.9; MS (EI) *m/z* 301 ($M^{+\bullet}$+H), 286, 232, 203, 73; HRMS (EI) *m/z* calculated for $C_{19}H_{28}OSi$: 300.1909, found 300.1921.

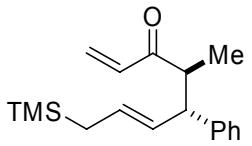


***R**-(2*E*,5*S*,6*R*,7*E*)-6-Isopropyl-5-methyl-9-trimethylsilylnona-2,7-dien-4-one (33):** The general procedure **D** was followed employing 1.08 g (4.02 mmol) of allylic alcohol **30**. Flash chromatography on SiO_2 (40:1 hexanes/EtOAc) afforded 893 mg (83%) of the product as a clear oil. Product ratio by GC-MS: 81.6% (T_r = 12.02), 5.99% (T_r = 12.10), 10.6% (T_r = 12.23), 2.01% (T_r = 12.34). Product ratio by ^{1}H-NMR (500 MHz) (Si–**$(CH_3)_3$**): 1.71% (δ = 0.0199), 8.16% (δ 0.0038), 5.09% (δ –0.0013), 85.0% (δ –0.0350): IR (thin film) 2958, 1696, 1671, 1630, 1247, 969, 853 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 6.82 (dq, *J* = 15.4, 6.9 Hz, 1H), 6.15 (dq, *J* = 15.5, 1.6 Hz, 1H), 5.29 (dt, *J* = 15.3, 7.9 Hz, 1H), 5.00 (ddt, *J* = 15.1, 9.6, 1.2 Hz, 1H), 2.81 (dq, *J* = 9.3, 6.9 Hz, 1H), 2.05 (dt, *J* = 9.4, 4.3 Hz, 1H), 1.88 (dd, *J* = 6.9, 1.6 Hz, 3H), 1.90–1.80 (m, 1H), 1.38 (dd, *J* = 7.9, 1.2 Hz, 2H), 1.05 (d, *J* = 6.9 Hz, 3H), 0.87 (d, *J* = 6.8 Hz, 3H), 0.79 (d, *J* = 6.8 Hz, 3H), –0.04 (s, 9H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 211.1, 145.5, 134.2, 132.9, 129.0, 50.1, 44.3, 24.4, 19.7, 18.5, 14.7, 13.1, 11.6, –6.6; MS (EI) *m/z* 266 ($M^{+\bullet}$), 251, 223, 197, 73, 69; HRMS (EI) *m/z* calculated for $C_{16}H_{30}OSi$: 266.2066, found 266.2065.



***R**-(*E*,4*S*,5*R*)-4,5-Dimethyl-8-trimethylsilylocta-1,6-dien-3-one (34):** The general procedure **D** was followed employing 792 g (3.50 mmol) of allylic alcohol **23**. Flash chromatography on SiO_2 (25:1 hexanes/EtOAc) afforded 665 mg (85%) of the product as a clear oil. Product ratio by GC-MS: 10.2% (T_r = 8.72), 77.4% (T_r = 8.90), 12.3% (T_r = 8.98). Product ratio by ^{1}H-NMR

(300 MHz) (Si–$\mathbf{(CH_3)_3}$): 8.58% (δ 0.0114), 9.85% (δ –0.0054), 81.6% (δ –0.0286): IR (thin film) 2958, 1698, 1678, 1612, 1248, 966, 855 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 6.43 (dd, *J* = 17.4, 10.4 Hz, 1H), 6.23 (dd, *J* = 17.4, 1.6 Hz, 1H), 5.73 (dd, *J* = 10.4, 1.6 Hz, 1H), 5.38 (dtd, *J* = 15.2, 8.0, 1.0 Hz, 1H), 5.16 (ddt, *J* = 15.2, 7.6, 1.1 Hz, 1H), 2.74 (p, *J* = 6.9 Hz, 1H), 2.54–2.43 (m, 1H), 1.38 (br. dd, *J* = 8.0, 0.9 Hz, 2H), 1.05 (d, *J* = 6.9 Hz, 3H), 0.94 (d, *J* = 6.9 Hz, 3H), –0.03 (s, 9H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 203.2, 135.6, 131.9, 127.5, 126.1, 49.1, 38.9, 22.5, 17.2, 12.7, –2.1; MS (EI) *m/z* 224 ($M^{+\bullet}$), 209, 141, 73; HRMS (EI) *m/z* calculated for $C_{13}H_{24}OSi$: 224.1596, found 224.1599.

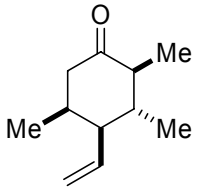


***R**-(*E*,*4*S,5*R*)-4-Methyl-8-trimethylsilyl-5-phenylocta-1,6-dien-3-one (35):**[35-38] To 813 mg (2.82 mmol) of allylic alcohol **24** in 30 mL of CH_2Cl_2 at 0 °C was added 1.80 g (4.23 mmol) of Dess-Martin periodinane. The reaction was stirred at 0 °C for 1 h, then slowly warmed to ambient temperature over an additional 1.5 h. The reaction was quenched with excess hexanes, filtered through florsil (5:1 hexanes/EtOAc) and the crude product mixture was concentrated *in vacuo*. Flash chromatography on SiO_2 (25:1 hexanes/EtOAc) yielded 513 mg (63%) of the title compound as a clear oil. Product ratio by GC-MS: 8.12% (T_r = 14.15), 83.8% (T_r = 14.30), 8.11% (T_r = 14.36). Product ratio by ^{1}H-NMR (300 MHz) (Si–$\mathbf{(CH_3)_3}$): 6.90% (δ –0.0346), 86.7% (δ –0.862), 6.42% (δ –0.1120): IR (thin film) 3061, 3026, 2954, 1698, 1678, 1611, 1248, 964, 854 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.34–7.18 (m, 5H), 6.46 (dd, *J* = 17.5, 10.3 Hz, 1H), 6.29 (dd, *J* = 17.5, 1.4 Hz, 1H), 5.80 (dd, *J* = 10.3, 1.4 Hz, 1H), 5.39–5.36 (m, 2H), 3.52 (ddd, *J* = 10.4, 4.1, 2.7 Hz, 1H), 3.21 (dq, *J* = 10.4, 6.9 Hz, 1H), 1.35–1.33 (m, 2H), 0.88 (d, *J* =

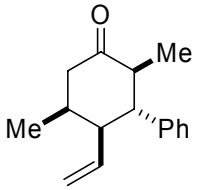
6.9 Hz, 3H), –0.09 (s, 9H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 203.4, 143.0, 135.9, 129.8, 128.5, 128.1 (2C), 127.9, 126.3, 52.0, 48.5, 22.8, 16.1, –1.9; MS (EI) *m/z* 286 ($M^{+\bullet}$), 271, 257, 203, 73; HRMS (EI) *m/z* calculated for $C_{18}H_{26}OSi$: 286.1753, found 286.1755.

General Procedure E for Sakurai Annulations 36–40:[81, 222] Titanium salts were found to epimerize the α-chiral ketone products upon crude product concentration. Filtration through a fine glass frit effectively minimizes these deleterious byproducts. Products **36** and **39** were found to be volatile, therefore improved yields are often observed on larger scale reactions. Due to the enhanced reactivity of acrylates, the cyclized product **39** is isolated with ~10-15% inseparable polymeric material. Reported yield includes these products, however Kughelrohr distillation can be used to eliminate the non-volatile byproduct, and was performed to obtain pure material for full characterization.

To 1.2 mL (1.2 mmol) of a vigorously stirred solution of $TiCl_4$ in CH_2Cl_2 (1.0 M) at –78 °C was slowly added the unsaturated ketone (1.0 mmol) in 10 mL of CH_2Cl_2 (clear → deep red). The syringe and receptacle were washed with 1 mL of additional CH_2Cl_2 and added to the reaction vessel. Following 15 min of stirring at –78 °C, the reaction was carefully quenched with sat. aq. NH_4Cl, then the biphasic mixture was slowly warmed to ambient temperature. The aqueous layer was extracted with CH_2Cl_2 (3x), and the combined organic layers were dried over Na_2SO_4 and filtered with Et_2O through a fine glass frit. Removal of the solvent *in vacuo* yielded the crude product, which was purified as specified. Isolated diastereomeric ratio is quoted from included GC-MS data [HP-1 (12 m x 0.20 mm), pressure 21 kPa, method: 70 °C for 2.00 min, ramp @ 10 °C/min to 300 °C, hold for 60 min].

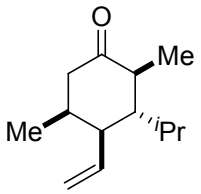


***R**-(2*S*,3*R*,4*S*,5*S*)-2,3,5-Trimethyl-4-vinylcyclohexanone (36):** The general procedure **E** was performed employing 0.10 g (0.42 mmol) of enone **31**. Flash chromatography on SiO_2 (20:1 pentane/Et_2O) afforded 46 mg (67%) of the product as a clear, volatile, oil. Isolated diastereomeric ratio by GC-MS: 91.7% (T_r = 6.49), 8.30% (T_r = 6.99): IR (thin film) 3076, 2969, 1713, 1638, 915 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 5.67 (dt, *J* = 18.0, 9.3 Hz, 1H), 5.11–5.06 (m, 2H), 2.63 (dd, *J* = 13.0, 5.0 Hz, 1H), 2.37–2.18 (m, 3H), 2.02 (dqd, *J* = 12.9, 6.5, 0.7 Hz, 1H), 1.60–1.46 (m, 1H), 1.04 (d, *J* = 6.5 Hz, 3H), 0.98 (d, *J* = 6.5 Hz, 3H), 0.83 (d, *J* = 6.9 Hz. 3H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 212.2, 140.6, 116.2, 52.2, 50.6, 48.6, 38.8, 36.9, 19.2, 13.9, 11.8; MS (EI) *m/z* 166 ($M^{+\bullet}$), 138, 96, 68; HRMS (EI) *m/z* calculated for $C_{11}H_{18}O$: 166.1358, found 166.1357.

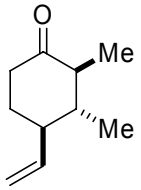


***R**-(2*S*,3*R*,4*S*,5*S*)-2,5-Dimethyl-3-phenyl-4-vinylcyclohexanone (37):** The general procedure **E** was performed employing 0.050 g (0.17 mmol) of enone **32**. Flash chromatography on SiO_2 (20:1 pentane/Et_2O) afforded 31 mg (82%) of the product as a white solid. Isolated diastereomeric ratio by GC-MS: 94.6% (T_r = 12.80), 3.75% (T_r = 12.99), 1.66% (T_r = 13.08): m.p. 86-88 °C; IR (thin film) 3064, 3027, 2969, 1712, 1639, 914 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.34–7.13 (m, 5H), 5.52 (ddd, *J* = 17.8, 9.8, 8.5 Hz, 1H), 4.82 (dm, *J* = 10.0 Hz, 1H), 4.81 (dm, *J* = 17.0 Hz, 1H), 2.97 (td, *J* = 9.8, 3.3 Hz, 1H), 2.86 (dd, *J* = 13.0, 5.4 Hz, 1H), 2.65

(t, J = 11.6 Hz, 1H), 2.65–2.55 (m, 1H), 2.50–2.45 (m, 1H), 2.38 (dd, J = 12.9, 2.9 Hz, 1H), 0.97 (d, J = 7.1 Hz, 3H), 0.79 (d, J = 6.1 Hz, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 211.6, 142.4, 139.3, 128.5, 128.0, 126.6, 116.3, 51.7, 50.8, 50.2, 48.8, 37.0, 13.7, 12.2; MS (EI) *m/z* 228 ($M^{+\bullet}$), 118, 68; HRMS (EI) *m/z* calculated for $C_{16}H_{20}O$: 228.1514, found 228.1512.

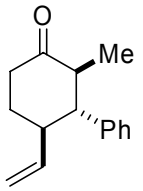


***R**-(2*S*,3*R*,4*S*,5*S*)-3-Isopropyl-2,5-dimethyl-4-vinylcyclohexanone (38):** The general procedure **E** was performed employing 0.10 g (0.38 mmol) of enone **33**. Flash chromatography on SiO_2 (25:1 hexanes/EtOAc) afforded 65 mg (87%) of the product as a clear oil. Isolated diastereomeric ratio by GC-MS: 89.0% (T_r = 8.83), 8.24% (T_r = 8.99), 2.73% (T_r = 9.07): IR (thin film) 3090, 2960, 1713, 1637, 913 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 5.65 (dt, J = 16.8, 10.0, 1H), 5.04 (dd, J = 10.3, 1.8 Hz, 1H), 5.00 (dd, J = 16.8, 1.8 Hz, 1H), 2.42 (dd, J = 16.2, 4.8 Hz, 1H), 2.47–2.36 (m, 2H), 2.34–2.23 (m, 1H), 2.11 (d, J = 16.0, 8.9 Hz, 1H), 2.04–1.94 (m, 1H), 1.39 (ddd, J = 8.3, 5.5, 2.8 Hz), 1.06 (d, J = 6.4 Hz, 3H), 0.96 (d, J = 7.0 Hz, 3H), 0.95 (d, J = 7.0 Hz, 3H), 0.90 (d, J = 6.8 Hz, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 214.4, 140.1, 115.7, 50.4, 45.2, 45.0, 44.5, 32.7, 29.6, 20.3, 17.5, 16.9, 13.2; MS (EI) *m/z* 194 ($M^{+\bullet}$), 179, 166, 151, 68; HRMS (EI) *m/z* calculated for $C_{13}H_{22}O$: 194.1671, found 194.1680.



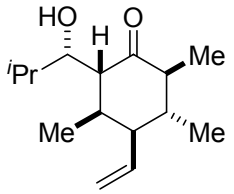
***R**-(2*S*,3*R*,4*R*)-2,3-Dimethyl-4-vinylcyclohexanone (39):** The general procedure **E** was performed employing 0.050 g (0.22 mmol) of acrylate **34**. Flash chromatography on SiO_2 (20:1

pentane/Et_2O) afforded 0.020 g (59%) of the product as a clear, highly volatile oil. Isolated diastereomeric ratio by GC-MS: 89.8% (T_r = 5.43), 10.2% (T_r = 5.92): IR (thin film) 3077, 2971, 1713, 1643, 914 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 5.57 (ddd, *J* = 17.2, 10.1, 8.8 Hz, 1H), 5.06 (dd, *J* = 17.1, 2.0 Hz, 1H), 5.03 (dd, *J* = 10.2, 1.8 Hz, 1H), 2.47–2.33 (m, 2H), 2.17–2.08 (m, 1H), 2.09 (dd, *J* = 11.2, 6.7 Hz, 1H), 2.06–1.95 (m, 1H), 1.67–1.50 (m, 1H), 1.34–1.20 (m, 1H), 1.04 (d, *J* = 6.5 Hz, 3H), 1.01 (d, *J* = 6.5 Hz, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 212.2, 141.6, 115.3, 50.4, 48.8, 44.6, 40.9, 33.2, 18.7, 11.8; MS (EI) *m/z* 152 ($M^{+\bullet}$), 126, 111; HRMS (EI) *m/z* calculated for $C_{10}H_{16}O$: 152.1201, found 152.1196.

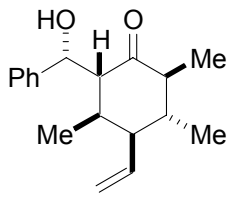


***R**-(2*S*,3*R*,4*R*)-2-Methyl-3-phenyl-4-vinylcyclohexanone (40):** The general procedure **E** was performed employing 0.050 g (0.17 mmol) of acrylate **35**. Flash chromatography on SiO_2 (10:1 pentane/Et_2O) afforded 0.030 g (82%) of the product as a clear, viscous oil. Isolated diastereomeric ratio by GC-MS: 92.6% (T_r = 12.10), 5.31% (T_r = 12.31), 2.14% (T_r = 12.14), + ~1% impurity: IR (thin film) 3081, 3027, 2970, 1712, 913 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.34–7.12 (m, 5H), 5.44 (ddd, *J* = 17.6, 10.4, 7.5 Hz, 1H), 4.81 (dm, *J* = 17.3 Hz, 1H), 4.78 (dm, *J* = 10.4 Hz, 1H), 2.82–2.51 (m, 4H), 2.37 (t, *J* = 11.5 Hz, 1H), 2.20 (ddt, *J* = 13.4, 6.1, 3.1 Hz, 1H), 1.75 (qd, *J* = 13.4, 5.1 Hz, 1H), 0.78 (d, *J* = 6.5 Hz, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 211.8, 142.2, 140.1, 128.5, 127.9, 126.6, 114.9, 57.9, 49.9, 47.2, 41.1, 32.5, 12.3; MS (EI) *m/z* 214 ($M^{+\bullet}$), 147, 118, 68; HRMS (EI) *m/z* calculated for $C_{15}H_{18}O$: 214.1358, found 214.1353.

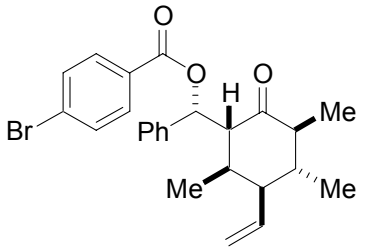
General Procedure F for Tandem Intermolecular Sakurai-Aldol Reactions 41–42:[81] The general procedure for the Sakurai annulation was followed as stated above with the following modifications. The neat aldehyde (1.2 mmol) was added dropwise to the pre-generated titanium enolate. The solution was stirred for ~ 1 h at –78 °C until complete by TLC. Workup was performed in the same fashion as above. Compounds were purified as specified. Isolated diastereomeric ratio is quoted from included LC-MS [X-terra C-18, method: 35%:65% MeCN:H_2O for 24.00 min, ramp to 50:50 MeCN:H_2O] or 500 MHz ^{1}H-NMR data.



***R**-(2*R*,3*R*,4*R*,5*R*,6*S*)-2-(*S*)-1-Hydroxy-2-methylpropyl-3,5,6-trimethyl-4-vinylcyclohexanone (41):** The general procedure **F** was performed employing 0.050 g (0.21 mmol) of enone **31** and 23 μL (18 mg, 0.25 mmol) of isobutyraldehyde. Flash chromatography on SiO_2 (5:1 hexanes/EtOAc) afforded 26 mg (52%) of the product as a clear oil. Isolated diastereomeric ratio by ^{1}H-NMR (500 MHz, $CDCl_3$) (C**H**–OH): 8.05% (δ 3.98), 84.7% (δ 3.88), 7.24% (δ 3.32): IR (thin film) 3454, 3076, 2965, 1704, 1639, 999, 914 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 5.67 (ddd, *J* = 16.8, 10.4, 9.0 Hz, 1H), 5.10 (dm, *J* = 10.3 Hz, 1H), 5.07 (dm, *J* = 16.8 Hz, 1H), 3.92–3.86 (m, 1H), 2.38–2.28 (m, 3H), 2.12 (qdd, *J* = 7.1, 4.3, 3.1 Hz, 1H), 1.90 (pd, *J* = 6.9, 3.5 Hz, 1H), 1.63–1.52 (m, 1H), 1.51 (d, *J* = 7.8 Hz, 1H), 1.08 (d, *J* = 6.5 Hz, 3H), 1.04 (d, *J* = 6.9 Hz, 3H), 1.01 (d, *J* = 6.4 Hz, 3H), 0.89 (d, *J* = 7.2 Hz, 3H), 0.85 (d, *J* = 6.8 Hz, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 214.7, 140.4, 116.4, 75.7, 61.2, 48.4, 48.1, 38.6, 37.9, 30.5, 20.1, 19.2, 15.1, 14.7, 12.4; MS (EI) *m/z* 220 ($M^{+\bullet}$-H_2O), 205, 195, 166, 98, 68; HRMS (EI) *m/z* calculated for $C_{15}H_{24}O$ ($M^{+\bullet}$-H_2O): 220.1827, found 220.1835.

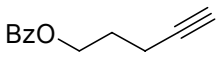


***R**-(2*R*,3*R*,4*R*,5*R*,6*S*)-2-(*R*)-Hydroxyphenylmethyl-3,5,6-trimethyl-4-vinylcyclohexanone (42):** The general procedure **F** was performed employing 0.050 g (0.21 mmol) of enone **31** and 25 μL (27 mg, 0.25 mmol) of benzaldehyde. Flash chromatography on SiO_2 (5:1 hexanes/EtOAc) afforded 31 mg of the product (52%) as a clear oil. Isolated diastereomeric ratio by LC-MS (X-terra C-18 column, flow rate 1.0 mL/min, 35.0% CH_3CN, 65.0% H_2O 24 min, then ramp to 50.0% CH_3CN, 50.0% H_2O): 3.17% (T_r = 34.68), 84.9% (T_r = 37.49), 10.4% (T_r = 39.56), 1.6% (T_r = 42.32): IR (thin film) 3427, 3067, 3030, 2970, 1698, 1639, 915 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.39–7.24 (m, 5H), 5.67 (ddd, *J* = 17.6, 9.6, 8.7 Hz, 1H), 5.15–5.06 (m, 3H), 2.61 (dd, *J* = 7.9, 3.8 Hz, 1H), 2.60 (d, *J* = 3.8 Hz, 1H), 2.55–2.43 (m, 2H), 1.92 (dq, *J* = 10.6, 6.5 Hz, 1H), 1.53 (ddq, *J* = 10.6, 8.9, 6.5 Hz, 1H), 1.00 (d, *J* = 6.5 Hz, 3H), 0.92 (d, *J* = 6.4 Hz, 3H), 0.90 (d, *J* = 6.9 Hz, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 213.9, 141.5, 139.9, 128.6, 128.2, 126.3, 116.4, 73.3, 64.0, 49.8, 48.3, 39.0, 35.6, 19.6, 15.3, 12.2; MS (EI) *m/z* 272 ($M^{+\bullet}$), 254, 166, 106, 69; HRMS (EI) *m/z* calculated for $C_{18}H_{24}O_2$: 272.1776, found 272.1784.



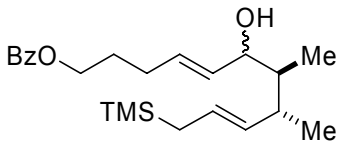
***R**-(*R*)-(1*R*,2*R*,3*R*,4*R*,5*S*)-2,4,5-Trimethyl-6-oxo-3-vinylcyclohexylphenylmethyl-4-bromobenzoate (43):** To 54 mg (0.20 mmol) of cyclohexanone **41** in 2 mL of CH_2Cl_2 at 0 °C was added 2.4 mg (0.020 mmol) of 4-(dimethylamino)pyridine and 52 mg (0.24 mmol) of 4-

bromobenzoyl chloride. 42 μL (31 mg, 0.24 mmol) of N,N-diisopropylethylamine was then added dropwise. The solution was stirred for 5 h while slowly warming to ambient temperature, and quenched with aq. 1M HCl. The aqueous layer was extracted with EtOAc (4x), the combined organic layers were dried over $MgSO_4$, and the crude product mixture was concentrated *in vacuo*. Purification by flash chromatography on SiO_2 (10:1 hexanes/EtOAc) yielded 71 mg (80%) of the title compound as a colorless crystalline solid. Recrystallization from hexanes/EtOAc (slow evaporation) gave crystals suitable for X-ray analysis: m.p. 154-156 °C; IR (thin film) 3069, 2972, 1713, 1591, 1267, 914 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.92 (d, *J* = 8.5 Hz, 2H), 7.60 (d, *J* = 8.5 Hz, 2H), 7.37–7.31 (m, 5H), 6.56 (d, *J* = 10.5 Hz, 1H), 5.64 (dt, *J* = 17.1, 10.0 Hz, 1H), 5.09 (d, *J* = 17.2 Hz, 1H), 5.08 (d, *J* = 10.1 Hz, 1H), 2.99 (dd, *J* = 10.5, 2.3 Hz, 1H), 2.75 (td, *J* = 10.8, 4.1 Hz, 1H), 2.43–2.28 (m, 1H), 2.16 (dq, *J* = 12.7, 6.4 Hz, 1H), 1.63–1.53 (m, 1H), 1.05 (d, *J* = 6.4 Hz, 3H), 0.94 (d, *J* = 7.7 Hz, 3H), 0.92 (d, *J* = 6.6 Hz, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 210.4, 165.0, 139.8, 137.2, 131.8, 131.2, 129.0, 128.8, 128.7, 128.4, 127.1, 116.9, 74.6, 64.0, 49.7, 47.3, 39.5, 38.2, 19.2, 14.5, 11.8; MS (EI) *m/z* 456 ($M^{+\bullet}$), 271, 254, 185, 183; HRMS (EI) *m/z* calculated for $C_{25}H_{27}O_3Br$: 454.1144, found 454.1139.



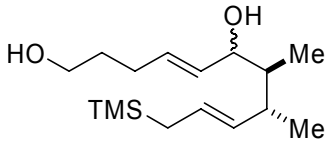
Pent-4-ynyl benzoate:[223] To 1.1 mL (1.0 g, 12 mmol) of 4-pentyn-1-ol in 40 mL of CH_2Cl_2 at 0 °C was added 2.0 g (14 mmol) of benzoyl chloride and 145 mg (1.19 mmol) of 4-(dimethylamino)pyridine, then 2.5 mL (1.8 g, 14 mmol) of N,N-diisopropylethylamine. The solution was slowly warmed to ambient temperature and stirred for ~ 12 h. The reaction was quenched with excess aq. 1M HCl, and the aqueous layer was extracted with EtOAc (4x). The

combined organic layers were washed with brine, dried over $MgSO_4$, and the crude product mixture was concentrated *in vacuo*. Flash chromatography on SiO_2 (20:1 hexanes/EtOAc) afforded 2.0 g (90%) of the product as a clear oil: ^{1}H-NMR (300 MHz, $CDCl_3$): δ 8.08–8.04 (m, 2H), 7.60–7.54 (m, 1H), 7.48–7.42 (m, 2H), 4.44 (t, *J* = 6.2 Hz, 2H), 2.40 (td, *J* = 7.1, 2.6 Hz, 2H), 2.02 (p, *J* = 6.5 Hz, 2H), 2.01–1.99 (m, 1H).



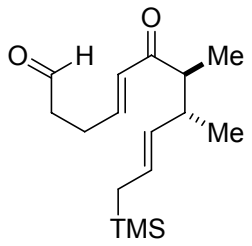
***R**-(4*E*,6*R*,7*S*,8*R*,9*E*)-6-Hydroxy-7,8-dimethyl-11-trimethylsilylundeca-4,9-dienylbenzoate + *R**-(4*E*,6*S*,7*S*,8*R*,9*E*)-6-Hydroxy-7,8-dimethyl-11-trimethylsilylundeca-4,9-dienylbenzoate (44):**[44, 224] To 221 mg (0.861 mmol) of $Cp_2Zr(H)Cl$ in 2.5 mL of CH_2Cl_2 at 0 °C was added 171 mg (0.909 mmol) of pent-4-ynyl benzoate. The mixture was warmed to ambient temperature and stirred until homogenous. To the stirring solution was then added 0.100 g (0.504 mmol) of aldehyde **20**. A separate flask was charged with 15 mg (0.050 mmol) of $AgAsF_6$ and 2.5 mL of CH_2Cl_2 and the original aldehyde mixture was added carefully *via* syringe (clear → brown color shift). The reaction was stirred for 10 min, then quenched with sat. aq. $NaHCO_3$. The aqueous layer was extracted with EtOAc (4x), the combined organics were dried over Na_2SO_4, and the crude product mixture was concentrated *in vacuo*. Flash chromatography on SiO_2 (5:1 hexanes/EtOAc) yielded 159 mg (81%) of the title compound mixture as a clear oil. The high R_f diastereomer was isolated *via* flash chromatography and fully characterized: IR (thin film) 3515, 2957, 1721, 1602, 1274, 1248, 970, 853, 675 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 8.05 (dd, *J* = 7.1, 1.4 Hz, 2H), 7.57 (tt, *J* = 7.3, 1.3 Hz, 1H), 7.45 (t, *J* = 7.3 Hz, 2H), 5.68 (dt, *J* = 15.4, 6.5 Hz, 1H), 5.55 (dd, *J* = 15.4, 6.0 Hz, 1H), 5.41 (dt, *J* = 15.2, 7.9 Hz, 1H), 5.21 (dd, *J* = 15.2, 8.1 Hz,

1H), 4.35 (t, *J* = 6.6 Hz, 2H), 4.21–4.14 (m, 1H), 2.24 (q, *J* = 6.9 Hz, 2H), 2.22–2.09 (m, 1H), 1.88 (p, *J* = 6.6 Hz, 2H), 1.43–1.33 (m, 1H), 1.43 (br. d, *J* = 7.9 Hz, 2H), 0.95 (d, *J* = 6.8 Hz, 3H), 0.88 (d, *J* = 6.9 Hz, 3H), 0.00 (s, 9H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 166.6, 133.9, 133.4, 132.8, 130.5, 129.8, 129.6, 128.3, 125.6, 74.2, 64.3, 44.1, 39.3, 28.8, 28.4, 22.7, 17.7, 10.7, –1.9; MS (ESI) *m/z* 411 $(M+Na)^+$; HRMS (ESI) *m/z* calculated for $NaC_{23}H_{36}O_3Si$ $(M+Na)^+$: 411.2331, found 411.2340.

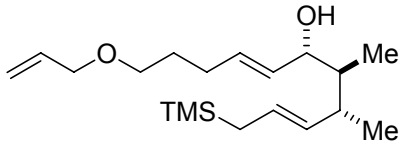


***R**-(4*E*,6*R*,7*S*,8*R*,9*E*)-7,8-Dimethyl-11-trimethylsilylundeca-4,9-diene-1,6-diol + *R**-(4*E*,6*S*,7*S*,8*R*,9*E*)-7,8-Dimethyl-11-trimethylsilylundeca-4,9-diene-1,6-diol (45):**[225] To 524 mg (1.39 mmol) of benzoate **44** was added 13.9 mL of a 1% w/v solution of NaOH in MeOH at ambient temperature. The mixture was stirred for 1 h, then diluted with brine to form a biphasic mixture. The aqueous layer was extracted with Et_2O (3x), the combined organic layers were dried with Na_2SO_4, and the crude product mixture was concentrated *in vacuo*. Purification by flash chromatography on SiO_2 (1:1 hexanes/EtOAc) yielded 373 mg (94%) of the product as a clear oil. The high R_f diastereomer was isolated at the benzoate stage, cleaved under identical conditions, isolated *via* flash chromatography and fully characterized: IR (thin film) 3353, 2957, 1656, 1247, 969, 852 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 5.66 (dt, *J* = 15.6, 6.5 Hz, 1H), 5.53 (dd, *J* = 15.5, 6.1 Hz, 1H), 5.42 (dt, *J* = 15.4, 7.8 Hz, 1H), 5.21 (dd, *J* = 15.2, 8.1 Hz, 1H), 4.17 (t, *J* = 4.9 Hz, 1H), 3.67 (t, *J* = 6.5 Hz, 2H), 2.19–2.12 (m, 1H) 2.16 (q, *J* = 6.8 Hz, 2H), 1.68 (p, *J* = 6.5 Hz, 2H), 1.44–1.34 (m, 1H), 1.43 (br. d, *J* = 7.3 Hz, 2H), 0.94 (d, *J* = 6.8 Hz, 3H), 0.88 (d, *J* = 6.9 Hz, 3H), 0.00 (s, 9H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 134.0, 133.0, 130.6, 125.6, 74.3,

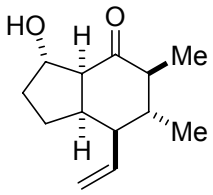
62.4, 44.1, 39.2, 32.2, 28.6, 22.7, 17.8, 10.7, –1.7; MS (EI) *m/z* 284 ($M^{+\bullet}$), 269, 266, 169, 141, 73; HRMS (EI) *m/z* calculated for $C_{16}H_{32}O_2Si$: 284.2172, found 284.2170.



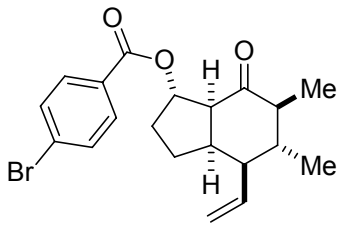
***R**-(4*E*,7*S*,8*R*,9*E*)-7,8-Dimethyl-11-trimethylsilyl-6-oxoundeca-4,9-dienal (46):** To 237 mg (0.833 mmol) of allylic alcohol **45** in 8.3 mL of CH_2Cl_2 at 0 °C was added 883 mg (2.08 mmol) of Dess-Martin periodinane. The reaction was stirred at 0 °C for 1 h, then slowly warmed to ambient temperature over an additional 3 h. The reaction was quenched with excess hexanes, filtered through florsil (5:1 hexanes/EtOAc) and the crude product mixture was concentrated *in vacuo*. Flash chromatography on SiO_2 (5:1 hexanes/EtOAc) yielded 0.160 g (68%) of the title compound as a clear oil. Product ratio by GC-MS: 6.05% (T_r = 14.51), 87.8% (T_r = 14.71), 6.12% (T_r = 14.90). Product ratio by ^{1}H-NMR (300 MHz): 7.78% (δ 0.0127), 6.94% (δ –0.0070), 85.3% (δ –0.0289): IR (thin film) 2958, 1727, 1694, 1668, 1628, 1247, 971, 853 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 9.91 (s, 1H), 6.80 (dt, *J* = 15.7, 6.7 Hz, 1H), 6.18 (dt, *J* = 15.6, 1.4 Hz, 1H), 5.37 (dt, *J* = 15.2, 7.9 Hz, 1H), 5.15 (dd, *J* = 15.2, 7.6 Hz, 1H), 2.69–2.42 (m, 6H), 1.38 (br. d, *J* = 7.8 Hz, 2H), 1.02 (d, *J* = 6.9 Hz, 3H), 0.93 (d, *J* = 6.8 Hz, 3H), –0.02 (s, 9H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 202.9, 200.3, 143.6, 132.1, 130.1, 126.2, 49.9, 42.0, 39.0, 24.7, 22.6, 16.9, 12.8, –2.0; MS (EI) *m/z* 280 ($M^{+\bullet}$), 265, 183, 73; HRMS (EI) *m/z* calculated for $C_{16}H_{28}O_2Si$: 280.1859, found 280.1857.



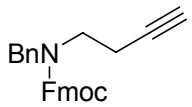
***R**-11-Allyloxy-4,5-dimethyl-1-trimethylsilanylundeca-2,7-dien-6-ol (47):**[226] To 814 mg (6.55 mmol) of 5-allyloxy-pent-1-yne in 13 mL of CH_2Cl_2 at 0 °C was added 1.56 g (6.05 mmol) of $Cp_2Zr(H)Cl$ in portions.[227] The mixture was then slowly warmed to ambient temperature (cloudy → clear yellow color shift) for 20 min, upon which time the flask was immersed in a –60 °C bath ($CHCl_3$/dry ice). To the solution was added 6.1 mL (6.1 mmol) of Et_2Zn in hexanes (1.0 M) *via* syringe pump over 90 min, following which time the mixture was raised to 0 °C. At 0 °C, 1.00 g (5.04 mmol) of aldehyde **20** was added dropwise and the reaction was stirred for 4 h. The reaction was carefully quenched with 5% $NaHCO_3$ in 100 mL ice water and passed through celite. The aqueous layer was extracted with Et_2O (4x), and the combined organics back-extracted with brine. The solvent was filtered and removed *in vacuo*. Purification *via* flash chromatography on SiO_2 (7:1 hexanes/EtOAc) gave 0.750 g (46%) of the product as a clear oil. The diastereomeric ratio for this substrate was not determined: IR (thin film) 3434, 2957, 1648, 1248, 1104, 969, 852 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 5.91 (ddt, *J* = 17.2, 10.5, 5.6 Hz, 1H), 5.63 (dt, *J* = 15.5, 6.5 Hz, 1H), 5.50 (dd, *J* = 15.4, 6.2 Hz, 1H), 5.40 (dt, *J* = 15.4, 7.9 Hz, 1H), 5.26 (dm, *J* = 17.2 Hz, 1H), 5.20 (dd, *J* = 15.2, 7.0 Hz, 1H), 5.17 (dm, *J* = 10.4 Hz, 1H), 4.13 (dt, *J* = 5.3, 4.9 Hz, 1H), 3.96 (dt, *J* = 5.6, 1.1 Hz, 2H), 3.43 (t, *J* = 6.6 Hz, 2H), 2.13 (q, *J* = 7.1 Hz, 2H), 2.21–2.10 (m, 1H), 1.67 (p, *J* = 7.7 Hz, 2H), 1.48 (d, *J* = 4.9 Hz, 1H), 1.43–1.32 (m, 1H), 1.42 (br. d, *J* = 7.7 Hz, 2H), 0.93 (d, *J* = 6.8 Hz, 3H), 0.87 (d, *J* = 6.9 Hz, 3H), –0.01 (s, 9H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 134.9, 133.9, 132.7, 130.7, 125.4, 116.7, 74.4, 71.8, 69.6, 44.0, 39.0, 29.2, 28.8, 22.6, 17.4, 10.7, –2.0; MS (EI) *m/z* 324 ($M^{+\bullet}$), 309, 306, 141, 73; HRMS (EI) *m/z* calculated for $C_{19}H_{36}O_2Si$: 324.2485, found 324.2488.



***R**-(3a*S*,5*S*,6*R*,7*R*,7a*R*)-Octahydro-3-hydroxy-5,6-dimethyl-7-vinylinden-4-one (48):** To 65 mg (23 mmol) of ketoaldehyde **46** in 4.6 mL of CH_2Cl_2 at –78 °C was added 0.28 mL (0.28 mmol) of $TiCl_4$ in CH_2Cl_2 (1.0 M). Following 20 min, the reaction was carefully quenched with an equal volume of sat. aq. NH_4Cl and the biphasic mixture was slowly raised to ambient temperature. The aqueous layer was extracted with CH_2Cl_2 (3x), the combined organic layers were dried over Na_2SO_4, filtered through a fine glass frit with Et_2O, and the crude product mixture was concentrated *in vacuo*. Purification of the crude compound by flash chromatography on SiO_2 (2:1 hexanes/EtOAc) gave 25 mg (52%) of the title compound as a clear, viscous oil. Isolated diastereomeric ratio by GC-MS: 5.78% (T_r = 10.15), 6.10% (T_r = 10.42), 5.33% (T_r = 11.63), 82.8% (T_r = 11.95): IR (thin film) 3400, 3075, 2969, 1706, 1639, 998, 913 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 5.59 (dt, *J* = 17.1, 9.8 Hz, 1H), 5.12 (dd, *J* = 17.0, 1.9 Hz, 1H), 5.09 (dd, *J* = 9.9, 1.9 Hz, 1H), 4.83 (dd, *J* = 6.4, 2.3 Hz, 1H), 2.85–2.73 (m, 2H), 2.48 (td, *J* = 10.3, 4.7 Hz, 1H), 2.20–2.09 (m, 2H), 1.81–1.71 (m, 1H), 1.58–1.40 (m, 3H), 1.26–1.09 (m, 1H), 1.03 (d, *J* = 6.5 Hz, 3H), 0.99 (d, J = 6.4 Hz, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 212.2, 140.5, 116.2, 72.3, 61.2, 50.1, 49.2, 46.6, 39.4, 33.1, 23.7, 18.7, 11.7; MS (EI) *m/z* 208 ($M^{+\bullet}$), 190, 140, 122, 68; HRMS (EI) *m/z* calculated for $C_{13}H_{20}O_2$: 208.1463, found 208.1468.

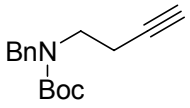


***R**-(3a*S*,5*S*,6*R*,7*R*,7a*R*)-Octahydro-5,6-dimethyl-4-oxo-7-vinyl-1H-inden-3-yl-4-bromobenzoate (49):** To 25 mg (0.12 mmol) of hydrindanone **48** in 1.2 mL of CH_2Cl_2 at 0 °C was added 1.5 mg (0.012 mmol) of 4-(dimethylamino)pyridine and 31.4 mg (0.143 mmol) of 4-bromobenzoyl chloride. 25 μL (19 mg, 0.15 mmol) of N,N-diisopropylethylamine was then added dropwise. The reaction was stirred 24 h while slowly warming to ambient temperature, and then quenched with aq. 1M HCl. The aqueous layer was extracted with EtOAc (4x), and the combined organic layers were dried over Na_2SO_4. The crude product mixture was concentrated *in vacuo*. Purification by flash chromatography on SiO_2 (2x) (2:1 hexanes/EtOAc then 10:1 hexanes/EtOAc) yielded 26 mg (55%) of the title compound as a colorless crystalline solid. Recrystallization from pentane/Et_2O (slow evaporation) gave crystals suitable for X-ray analysis: m.p. 98-100 °C; IR (thin film) 3090, 2971, 1718, 1590, 1270 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.86 (d, *J* = 8.5 Hz, 2H), 7.57 (d, *J* = 8.5 Hz, 2H), 5.90 (dd, *J* = 7.1, 1.9 Hz, 1H), 5.61 (dt, *J* = 17.1, 9.8 Hz, 1H), 5.15 (dd, *J* = 17.1, 1.8 Hz, 1H), 5.12 (dd, *J* = 10.0, 1.9 Hz, 1H), 3.05 (d, *J* = 7.3 Hz, 1H), 2.82–2.72 (m, 1H), 2.52 (td, *J* = 10.6, 5.1 Hz, 1H), 2.41–2.27 (m, 1H), 2.23–2.13 (m, 1H), 1.86–1.66 (m, 2H), 1.62–1.48 (m, 1H), 1.33–1.18 (m, 1H), 1.05 (d, *J* = 6.5 Hz, 3H), 1.00 (d, *J* = 6.4 Hz, 3H); ^{13}C-NMR (75 MHz, D_3CCN): δ 211.6, 166.1, 142.0, 132.8, 132.1, 130.9, 128.4, 116.7, 77.4, 59.5, 50.6, 49.7, 48.5, 40.4, 31.0, 24.3, 19.0, 12.1; MS (ESI) *m/z* 413 $(M+Na)^+$; HRMS (ESI) *m/z* calculated for $NaC_{20}H_{23}O_3Br$ $(M+Na)^+$: 413.0728, found 413.0749.



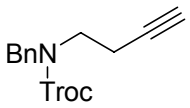
***N*-Fluoren-9-ylmethyl-*N*-benzylbut-3-ynylcarbamate (50):**[56] To a mixture of 1.0 g (6.3 mmol) of *N*-benzylbut-3-yn-1-amine and 1.7 g (16 mmol) of Na_2CO_3 in 8.1 mL of dioxane and

17 mL of H_2O at 0 °C was added a solution of 1.6 g (6.3 mmol) of fluorenyl methyl chloroformate in 16.2 mL of dioxane. Following 30 min at 0 °C, the reaction was raised to ambient temperature over 3 h. The reaction was quenched with H_2O and the mixture transferred to a separatory funnel. The aqueous layer was extracted with Et_2O (3x), and the combined organic layers were dried over Na_2SO_4, filtered and concentrated *in vacuo*. Purification by flash chromatography on SiO_2 (5:1 hexanes/EtOAc) afforded 2.2 g (92%) of the title compound as a clear oil: IR (thin film) 3291, 3064, 2949, 1699, 1476, 1451, 1240, 1213, 740 cm^{-1}; ^{1}H-NMR (300 MHz, D_6-DMSO, 358 K): δ 7.83 (d, *J* = 7.5 Hz, 2H), 7.59 (d, *J* = 7.2 Hz, 2H), 7.39 (t, *J* = 7.4 Hz, 2H), 7.32–7.23 (m, 5H), 7.09–7.06 (m, 2H), 4.53 (d, *J* = 5.7 Hz, 2H), 4.36 (s, 2H), 4.28 (t, *J* = 5.7 Hz, 1H), 3.18 (br. t, *J* = 5.5 Hz, 2H), 2.61 (t, *J* = 2.6 Hz, 1H), 2.17 (br. s, 2H); ^{13}C-NMR (75 MHz, D_6-DMSO, 353 K): δ 155.0, 143.5, 140.5, 137.4, 127.9, 127.0, 126.8, 126.6, 126.5, 124.3, 119.5, 81.2, 71.4, 66.1, 49.7, 46.6, 45.0, 16.9; MS (ESI) *m/z* 404 $(M+Na)^+$; HRMS (ESI) *m/z* calculated for $NaC_{26}H_{23}NO_2$ $(M+Na)^+$: 404.1626, found 404.1628.



***Tert*-butyl-*N*-benzylbut-3-ynylcarbamate (54):**[59] To 1.4 g (8.8 mmol) of *N*-benzylbut-3-yn-1-amine in 16 mL of $CHCl_3$ was added 0.74 g (8.8 mmol) of $NaHCO_3$ in 13 mL of H_2O. A 1.5 g (26 mmol) aliquot of NaCl was then added followed by slow addition of a solution of 2.1 g (9.7 mmol) of Boc anhydride in ~2.8 mL of $CHCl_3$. The reaction vessel was equipped with a condenser and the mixture was brought to reflux for 2 h, then quenched with sat. aq. $NaHCO_3$. The mixture was partitioned between sat. aq. $NaHCO_3$ and CH_2Cl_2 and the aqueous layer was extracted with CH_2Cl_2 (3x). The combined organic layers were dried over Na_2SO_4, filtered, and

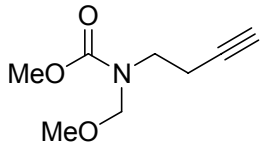
the crude product was concentrated *in vacuo*. Purification by flash chromatography on SiO_2 (25:1 hexanes/EtOAc) afforded 2.2 g (97%) of the title compound as a clear oil: IR (thin film) 3303, 2976, 1694, 1496, 1413, 1366, 1247, 1165 cm^{-1}; ^{1}H-NMR (300 MHz, D_6-DMSO, 343 K): δ 7.37–7.22 (m, 5H), 4.44 (s, 2H), 3.23 (t, J = 7.1 Hz, 2H), 2.66 (t, J = 2.6 Hz, 1H), 2.34 (td, J = 7.0, 2.7 Hz, 2H), 1.41 (s, 9H); ^{13}C-NMR (75 MHz, D_6-DMSO, 343 K): δ 154.4, 138.1, 127.9, 126.8, 126.6, 81.5, 78.7, 71.3, 49.8, 45.1, 27.6, 17.3; MS (EI) *m/z* 259 ($M^{+\bullet}$), 220, 203, 164, 120, 91; HRMS (EI) *m/z* calculated for $C_{16}H_{21}NO_2$: 259.1572, found 259.1545.



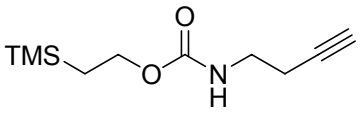
2,2,2-Trichloroethylbenzylbut-3-ynylcarbamate (66):[69] To 2.0 g (13 mmol) of *N*-benzylbut-3-yn-1-amine in 24.5 mL of CH_2Cl_2 was added 1.1 g (13 mmol) of $NaHCO_3$ in 18.8 mL of H_2O. A 2.3 g (39 mmol) aliquot of NaCl was then added followed by slow addition of a solution of 3.0 g (14 mmol) of 2,2,2-trichloroethyl chloroformate in ~4.1 mL of CH_2Cl_2. The reaction vessel was equipped with a condenser and the mixture was brought to reflux for 2 h, then quenched with sat. aq. $NaHCO_3$. The mixture was partitioned between sat. aq. $NaHCO_3$ and CH_2Cl_2 and the aqueous layer was extracted with CH_2Cl_2 (3x). The combined organic layers were dried over Na_2SO_4, filtered, and the crude product was concentrated *in vacuo*. Purification by flash chromatography on SiO_2 (15:1 hexanes/EtOAc) afforded 3.9 g (92%) of the title compound as a clear oil: IR (thin film) 3302, 2952, 1717, 1496, 1471, 1207, 1126, 718, 700 cm^{-1}; ^{1}H-NMR (300 MHz, D_6-DMSO, 353 K): δ 7.38–7.25 (m, 5H), 4.88 (s, 2H), 4.59 (s, 2H), 3.42 (t, J = 7.1 Hz, 2H), 2.67 (t, J = 2.7 Hz, 1H), 2.44 (td, J = 7.1, 2.6 Hz, 2H); ^{13}C-NMR (75 MHz, D_6-DMSO, 353

K): δ 153.4, 136.8, 128.0, 127.0, 126.9, 95.5, 80.9, 74.2, 71.5, 50.2, 45.3, 17.0; MS (EI) *m/z* 334 ($M^{+\bullet}$), 298, 294, 91; HRMS (EI) *m/z* calculated for $C_{14}H_{14}NO_2Cl_3$: 333.0090, found 333.0097.

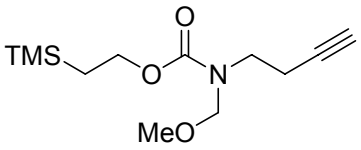
General Procedure G for Preparation of Methoxyaminals 74, 75, 80–82: To a solution of the carbamate or sulfonamide (1.0 mmol) in 10 mL of THF was added 1.1 mL (1.1 mmol) of KHMDS in toluene (0.5M) at 0 °C. After 5 min, 0.23 mL (0.24 g, 3.0 mmol) of chloromethyl methyl ether was added dropwise and the mixture was stirred for 15 min at 0 °C then raised to rt for 15 min. The reaction was quenched with H_2O, partitioned between H_2O and Et_2O and the aqueous layer was extracted with Et_2O (3x). The combined organic extracts were dried over Na_2SO_4, filtered and the crude product was concentrated *in vacuo*. The products were purified by flash chromatography under the specified conditions.



Methyl-but-3-ynylmethoxymethylcarbamate (74): The general procedure **G** was performed employing 0.10 g (0.79 mmol) of methyl-but-3-ynylcarbamate.[76] Flash chromatography on SiO_2 (5:1 hexanes/EtOAc) afforded 89 mg (66%) of the product as an oil: IR (thin film) 3288, 2955, 1710, 1480, 1444, 1213, 668 cm^{-1}; ^{1}H-NMR (300 MHz, D_6-DMSO, 353 K): δ 4.69 (s, 2H), 3.65 (s, 3H), 3.39 (t, *J* = 7.2 Hz, 2H), 3.20 (s, 3H), 2.65 (t, *J* = 2.7 Hz, 1H), 2.42 (td, *J* = 7.3, 2.6 Hz, 2H); ^{13}C-NMR (75 MHz, D_6-DMSO, 353 K): δ 155.5, 81.3, 78.6, 71.1, 54.5, 51.9, 44.6, 17.6; MS (EI) *m/z* 171 ($M^{+\bullet}$), 156, 140, 132, 102, 88; HRMS (EI) *m/z* calculated for $C_8H_{13}NO_3$: 171.0895, found 171.0896.

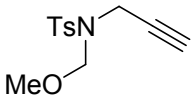


2-Trimethylsilylethyl-but-3-ynylcarbamate:[76] To a mixture of 1.0 g (10 mmol) of 4-pentynoic acid and 1.4 mL (1.0 g, 10 mmol) of triethylamine in 0.7 mL of toluene was slowly added 2.2 mL (2.8 g, 10 mmol) of diphenylphosphoryl azide. The resulting mixture was heated at 80 °C (N_2 evolution) for 2h. The reaction was then cooled to 50 °C whereupon 4.2 mL (3.5 g, 30 mmol) of trimethylsilyl ethanol was added and the mixture was stirred for an additional 12 h. The crude reaction mixture was concentrated *in vacuo*, partitioned between H_2O and Et_2O and the aqueous layer was extracted with Et_2O (10x). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and the crude product was concentrated *in vacuo*. Purification by flash chromatography on SiO_2 (5:1 hexanes/EtOAc) yielded 1.7 g (80%) of the product as a yellow oil: IR (thin film) 3312, 2953, 1698, 1526, 1250, 860, 838, 636 cm^{-1}; ^{1}H-NMR (300 MHz, D_6-DMSO, 353 K): δ 6.8 (br. s, 1H), 4.06 (t, J = 8.1 Hz, 2H), 3.11 (td, J = 7.1, 6.0 Hz, 2H), 2.60 (t, J = 2.7 Hz, 1H), 2.29 (td, J = 7.2, 2.7 Hz, 2H), 0.93 (t, J = 8.2 Hz, 2H), 0.03 (s, 9H); ^{13}C-NMR (75 MHz, D_6-DMSO, 353 K): δ 155.7, 81.5, 70.8, 61.1, 39.2, 18.8, 17.1, –2.0; MS (EI) *m/z* 214 ($M^{+\bullet}$+H), 170, 146, 101, 73; HRMS (EI) *m/z* calculated for $C_{10}H_{20}NO_2Si$ ($M^{+\bullet}$+H): 214.1263, found 214.1279.

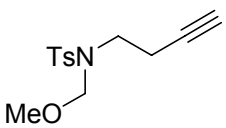


2-Trimethylsilylethylbut-3-ynylmethoxymethylcarbamate (75): The general procedure **G** was performed employing 0.50 g (2.3 mmol) of 2-(trimethylsilyl)ethyl-but-3-ynylcarbamate.

Flash chromatography on SiO_2 (10:1 hexanes/EtOAc) afforded 0.50 g (83%) of the product as an oil: IR (thin film) 3311, 2954, 1706, 1477, 1251, 939, 839, 636 cm^{-1}; ^{1}H-NMR (300 MHz, D_6-DMSO, 333 K): δ 4.68 (s, 2H), 4.16 (t, *J* = 8.1 Hz, 2H), 3.38 (t, *J* = 7.2 Hz, 2H), 3.20 (s, 3H), 2.68 (t, *J* = 2.7 Hz, 1H), 2.41 (td, *J* = 7.3, 2.6 Hz, 2H), 0.98 (t, *J* = 8.2 Hz, 2H), 0.04 (s, 9H); ^{13}C-NMR (75 MHz, D_6-DMSO, 343 K): δ 155.1, 81.3, 78.4, 71.4, 62.8. 54.6, 44.5, 17.7, 16.9, –1.9; MS (EI) *m/z* 242 ($M^{+\bullet}$-Me), 229, 214, 190, 174, 101, 89, 75; HRMS (EI) *m/z* calculated for $C_{11}H_{20}NO_3Si$ ($M^{+\bullet}$-Me): 242.1212, found 242.1215.

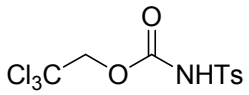


***N*-Methoxymethyl-*N*-tosylprop-2-yn-1-amine (80):** The general procedure **G** was performed employing 0.60 g (2.9 mmol) of *N*-tosylprop-2-yn-1-amine.[228] Flash chromatography on SiO_2 (6:1 hexanes/EtOAc) afforded 0.59 g (79%) of the product as a white solid: m.p. 39-41 °C; IR (thin film) 3279, 2936, 1598, 1495, 1446, 1347, 1170, 1072, 815, 661 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.74 (d, *J* = 8.3 Hz, 2H), 7.30 (d, *J* = 8.4 Hz, 2H), 4.79 (s, 2H), 4.12 (d, *J* = 2.5 Hz, 2H), 3.36 (s, 3H), 2.43 (s, 3H), 2.08 (t, *J* = 2.5 Hz, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 143.6, 136.8, 129.5, 127.2, 78.3, 76.7, 73.3, 55.7, 34.8, 21.4; MS (EI) *m/z* 253 ($M^{+\bullet}$), 222, 155, 98, 91, 65; HRMS (EI) *m/z* calculated for $C_{12}H_{15}NO_3S$: 253.0773, found 253.0766.



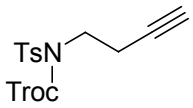
***N*-Methoxymethyl-*N*-tosylbut-3-yn-1-amine (81):** The general procedure **G** was performed employing 1.0 g (4.5 mmol) of *N*-tosylbut-3-yn-1-amine.[79] Flash chromatography on SiO_2 (6:1

hexanes/EtOAc) afforded 1.1 g (91%) of the product as a white solid: m.p. 39-41 °C; IR (thin film) 3287, 2937, 1598, 1452, 1341, 1159, 1077, 815, 658 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.74 (d, *J* = 8.3 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 4.78 (s, 2H), 3.35 (t, *J* = 7.3 Hz, 2H), 3.31 (s, 3H), 2.51 (td, *J* = 7.4, 2.7 Hz, 2H), 2.43 (s, 3H), 1.97 (t, *J* = 2.6 Hz, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 143.5, 137.3, 129.6, 127.2, 80.9, 80.7, 70.1, 55.6, 46.0, 21.5, 19.5; MS (EI) *m/z* 228 ($M^{+\bullet}$-OMe), 198, 155, 129, 91, 65; HRMS (EI) *m/z* calculated for $C_{12}H_{14}NO_2S$ ($M^{+\bullet}$-OMe): 236.0745, found 236.0744.

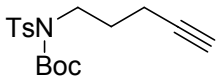


2,2,2-Trichloroethyl-*N*-tosylcarbamate:[79] To 4.8 mL (7.5 g, 50 mmol) of 2,2,2-trichloroethanol was slowly added 1.5 mL (2.0 g, 10 mmol) of tosyl isocyanate while monitoring the reaction temperature by a thermometer. The mixture was stirred for 24 h, upon which time the residual alcohol was removed by Kughelrohr distillation. The crude material was passed through a silica gel plug (20:1 CH_2Cl_2/MeOH) and the product was concentrated *in vacuo*. Residual impurities were removed by washing the solid with pentane (3x) which afforded 3.0 g (87%) of the product as a white solid: m.p. 99-101 °C; IR (thin film) 3236, 1763, 1597, 1448, 1351, 1209, 1159, 813 cm^{-1}; ^{1}H-NMR (300 MHz, D_6-DMSO): δ 7.79 (d, *J* = 7.4 Hz, 2H), 7.43 (d, *J* = 7.9 Hz, 2H), 4.82 (s, 2H), 3.60–3.10 (br. s, 1H), 2.39 (s, 3H); ^{13}C-NMR (75 MHz, D_6-DMSO): δ 150.0, 144.5, 136.0, 129.7, 127.6, 94.9, 74.0, 21.1; MS (EI) *m/z* 347 ($M^{+\bullet}$+H), 310, 281, 197, 155, 108, 91; HRMS (EI) *m/z* calculated for $C_{10}H_{10}NO_4SCl_3$ ($M^{+\bullet}$): 344.9396, found 344.9389.

General Procedure H for Synthesis of Boc-Protected Sulfonamides:[79] To a solution of the sulfonamide (1.5 mmol) in 9.1 mL THF was added 0.79 g (3.0 mmol) of PPh_3. The alcohol (1.0 mmol) was then added followed by 0.30 mL (0.30 g, 1.5 mmol) of DIAD. The mixture was stirred between 3-12 h, concentrated *in vacuo*, and the crude product was purified by flash chromatography under the specified conditions.

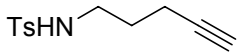


2,2,2-Trichloroethyl-*N*-tosylbut-3-ynylcarbamate (92): The general procedure **H** was performed employing 1.5 g (4.3 mmol) of 2,2,2-trichloroethyl-*N*-tosyl-carbamate and 0.22 mL (0.20 g, 2.9 mmol) of 3-butyn-1-ol. Flash chromatography on SiO_2 (10:1 hexanes/EtOAc) afforded 1.2 g (100%) of the product as a white solid: m.p. 95-97 °C; IR (thin film) 3296, 2961, 1745, 1597, 1449, 1361, 1271, 1172, 813 cm^{-1}; ^{1}H-NMR (300 MHz, D_6-DMSO, 353 K): δ 7.89 (d, *J* = 8.4 Hz, 2H), 7.43 (d, *J* = 8.0 Hz, 2H), 4.87 (s, 2H), 4.02 (t, *J* = 7.1 Hz, 2H), 2.75 (t, *J* = 2.7 Hz, 1H), 2.65 (td, *J* = 7.1, 2.7 Hz, 2H), 2.41 (s, 3H); ^{13}C-NMR (75 MHz, D_6-DMSO, 353 K): δ 149.9, 144.5, 135.3, 129.1, 127.5, 94.1, 79.7, 74.9, 72.4, 45.2, 20.5, 18.8; MS (EI) *m/z* 397 ($M^{+\bullet}$), 360, 155, 91, 65; HRMS (EI) *m/z* calculated for $C_{14}H_{14}NO_4SCl_3$: 396.9709, found 396.9693.

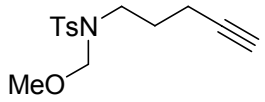


***Tert*-butyl-*N*-tosylpent-4-ynylcarbamate:** The general procedure **H** was performed employing 2.4 g (8.9 mmol) of *t*-butyl-*N*-tosyl-carbamate and 0.55 mL (0.50 g, 5.9 mmol) of 4-pentyn-1-ol. Flash chromatography on SiO_2 (10:1 hexanes/EtOAc) afforded 1.8 g (90%) of the product as a

white solid: m.p. 99-101 °C; IR (thin film) 3287, 2980, 1728, 1598, 1495, 1455, 1355, 1286, 1258, 1157, 1088, 814, 674 cm^{-1}; ^{1}H-NMR (300 MHz, D_6-DMSO): δ 7.76 (d, *J* = 8.3 Hz, 2H), 7.43 (d, *J* = 8.2 Hz, 2H), 3.82 (t, *J* = 7.4 Hz, 2H), 2.82 (t, *J* = 2.6 Hz, 1H), 2.40 (s, 3H), 2.21 (td, *J* = 7.0, 2.6 Hz, 2H), 1.80 (p, *J* = 7.1 Hz, 2H), 1.25 (s, 9H); ^{13}C-NMR (75 MHz, D_6-DMSO): δ 150.3, 144.2, 136.8, 129.5, 127.4, 83.8, 83.2, 71.6, 45.9, 28.6, 27.3, 21.0, 15.2; MS (ESI) *m/z* 360 $(M+Na)^+$; HRMS (ESI) *m/z* calculated for $NaC_{17}H_{23}NO_4S$ $(M+Na)^+$: 360.1245, found 360.1247.



***N*-Tosylpent-4-yn-1-amine:**[79] To 0.90 g (2.7 mmol) of *tert*-butyl-*N*-tosylpent-4-ynylcarbamate in 9.0 mL CH_2Cl_2 was slowly added 0.62 mL (0.92 g, 8.1 mmol) of trifluoroacetic acid at rt. Following 16 h, the reaction mixture was cooled to 0 °C and carefully quenched with sat. aq. $NaHCO_3$. The aqueous layer was extracted with CH_2Cl_2 (3x) and the combined organic layers are dried over Na_2SO_4, filtered, and the crude product was concentrated *in vacuo*. Purification by flash chromatography on SiO_2 (4:1 hexanes/EtOAc) yielded 0.58 g (89%) of the product as a white solid: m.p. 60-62 °C; IR (thin film) 3275, 2950, 1446, 1320, 1157, 816, 672 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.76 (d, *J* = 8.3 Hz, 2H), 7.33 (d, *J* = 8.5 Hz, 2H), 4.54 (br. t, *J* = 5.7 Hz, 1H), 3.09 (q, *J* = 6.7 Hz, 2H), 2.44 (s, 3H), 2.24 (dt, *J* = 6.9, 2.6 Hz, 2H), 1.96 (t, *J* = 2.7 Hz, 1H), 1.70 (p, *J* = 6.8 Hz, 2H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 143.4, 136.8, 129.7, 127.0, 82.8, 69.3, 42.1, 28.1, 21.5, 15.6; MS (EI) *m/z* 237 ($M^{+\bullet}$), 184, 172, 155, 145, 91, 82, 65; HRMS (EI) *m/z* calculated for $C_{12}H_{15}NO_2S$ ($M^{+\bullet}$-allyl): 236.0745, found 236.0742.

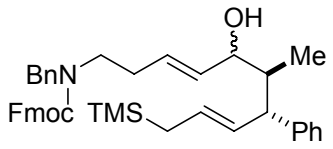


***N*-Methoxymethyl-*N*-tosylpent-4-yn-1-amine (82):** The general procedure **G** was performed employing 0.29 g (1.2 mmol) of *N*-tosylpent-4-yn-1-amine. Flash chromatography on SiO_2 (6:1 hexanes/EtOAc) afforded 0.27 g (80%) of the product as an oil: IR (thin film) 3287, 2936, 1598, 1494, 1461, 1339, 1159, 1083, 815, 658 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.73 (d, *J* = 8.3 Hz, 2H), 7.30 (d, *J* = 8.6 Hz, 2H), 4.73 (s, 2H), 3.32 (s, 3H), 3.26 (t, *J* = 7.3 Hz, 2H), 2.43 (s, 3H), 2.20 (td, *J* = 7.0, 2.7 Hz, 2H), 1.96 (t, *J* = 2.6 Hz, 1H), 1.82 (p, *J* = 7.1 Hz, 2H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 143.3, 137.1, 129.5, 127.1, 83.0, 80.3, 69.0, 55.5, 46.2, 27.5, 21.4, 15.7; MS (EI) *m/z* 281 ($M^{+\bullet}$), 280, 250, 222, 155, 91, 65; HRMS (EI) *m/z* calculated for $C_{14}H_{18}NO_4S$ ($M^{+\bullet}$-H): 280.1007, found 280.1005.

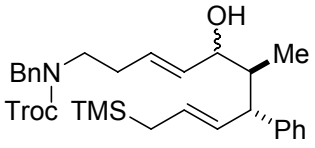
General Procedure I for Silver(I)-Mediated Preparation of Amino-Substituted Allylic Alcohols 51, 67, 76, 77, & 93:[44] Use of ICR-derived aldehydes freshly purified by flash chromatography generally results in yield increases of approximately 20%. In all cases, the diastereoselectivity of the addition reaction is approximately ~1:1 however the ratios were not rigorously determined. Products were either partially characterized by IR and MS for the diastereomeric mixture of alcohols or fully characterized for the high R_f product that was isolated by flash chromatography.

To 0.44 g (1.7 mmol) of $Cp_2Zr(H)Cl$ in 5.0 mL of CH_2Cl_2 at 0 °C was added the amino alkyne (1.8 mmol). The mixture was warmed to ambient temperature and stirred until homogenous. To the stirring solution was then added the aldehyde (1.0 mmol). A separate flask was charged with 0.030 g (0.10 mmol) of $AgAsF_6$ and 5.0 mL of CH_2Cl_2 and the original

aldehyde mixture was added carefully *via* syringe (clear → brown color shift). The reaction was stirred for the specified time, then quenched with sat. aq. $NaHCO_3$. The aqueous layer was extracted with EtOAc (3-4x), the combined organics were dried over Na_2SO_4 and filtered through a plug of 1:1 celite:florsil followed by concentration of the crude product *in vacuo*.

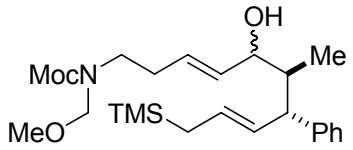


***R**-*N*-Fluoren-9-ylmethyl-*N*-benzyl-(3*E*,5*R*,6*S*,7*R*,8*E*)-5-hydroxy-6-methyl-10-trimethylsilyl-7-phenyldeca-3,8-dienylcarbamate + *R**-*N*-Fluoren-9-ylmethyl-*N*-benzyl-(3*E*,5*S*,6*S*,7*R*,8*E*)-5-hydroxy-6-methyl-10-trimethylsilyl-7-phenyldeca-3,8-dienylcarbamate (51):** The general procedure **I** was performed employing 0.84 g (2.2 mmol) of carbamate **50** and 0.30 g (1.2 mmol) of aldehyde **21** for ~30 min. Flash chromatography on SiO_2 (3:1 hexanes/EtOAc) afforded 0.29 g (38%) of the product as an highly viscous oil. The diastereomeric mixture was characterized by IR and MS: IR (thin film) 3458, 3026, 2953, 1698, 1477, 1451, 1246, 967, 852, 740 cm^{-1}; MS (EI) *m/z* 643 ($M^{+\bullet}$), 625, 513, 495, 423, 342, 179; HRMS (EI) *m/z* calculated for $C_{42}H_{49}NO_3Si$: 643.3482, found 643.3484.

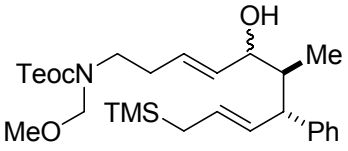


***R**-2,2,2-Trichloroethylbenzyl-(3*E*,5*R*,6*S*,7*R*,8*E*)-5-hydroxy-6-methyl-10-trimethylsilyl-7-phenyldeca-3,8-dienylcarbamate + *R**-2,2,2-Trichloroethylbenzyl-(3*E*,5*S*,6*S*,7*R*,8*E*)-5-hydroxy-6-methyl-10-trimethylsilyl-7-phenyldeca-3,8-dienylcarbamate (67):** The general procedure **I** was performed employing 0.90 g (2.7 mmol) of carbamate **66** and 0.40 g (1.5 mmol)

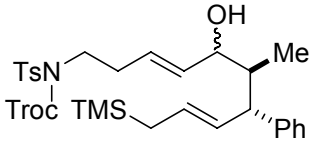
of aldehyde **21** for ~30 min. Flash chromatography on SiO_2 (5:1 hexanes/EtOAc) afforded 0.78 g (87%) of the product as a clear oil. The high R_f diastereomer was fully characterized: IR (thin film) 3479, 3026, 2952, 1717, 1470, 1453, 1247, 1124, 966, 848, 759, 718, 700 cm^{-1}; ^{1}H-NMR (300 MHz, C_6D_6, 333 K): δ 7.20–7.00 (m, 10H), 5.63–5.46 (m, 4H), 4.68 (s, 2H), 4.50–4.44 (m, 1H), 4.40 (s, 2H), 3.37–3.31 (m, 1H), 3.26 (t, *J* = 6.8 Hz, 2H), 2.21 (qd, *J* = 6.2, 1.3 Hz, 2H), 1.85 (dqd, *J* = 9.4, 6.8, 2.4 Hz, 1H), 1.40–1.38 (m, 2H), 1.02 (d, *J* = 5.1 Hz, 1H), 0.79 (d, *J* = 6.8 Hz, 3H), –0.06 (s, 9H); ^{13}C-NMR (75 MHz, D_6-DMSO, 353 K): δ 153.8, 144.7, 137.2, 136.0, 131.7, 128.1 (2C), 127.8, 127.6, 127.2, 127.0, 126.2, 125.2, 95.8, 74.4, 70.3, 51.6, 50.2, 46.6, 42.9, 30.3, 22.0, 10.7, –2.2; MS (EI) *m/z* 597 ($M^{+\bullet}$), 595, 579, 577, 449, 420, 375, 203; HRMS (EI) *m/z* calculated for $C_{30}H_{38}NO_2SiCl_3$ ($M^{+\bullet}$-H_2O): 577.1737, found 577.1718.



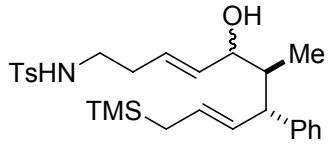
***R**-Methyl-(3*E*,5*R*,6*S*,7*R*,8*E*)-5-hydroxy-6-methyl-10-trimethylsilyl-7-phenyldeca-3,8-dienylmethoxymethylcarbamate + *R**-Methyl-(3*E*,5*S*,6*S*,7*R*,8*E*)-5-hydroxy-6-methyl-10-trimethylsilyl-7-phenyldeca-3,8-dienylmethoxymethylcarbamate (76):** The general procedure **I** was performed employing 0.15 g (0.88 mmol) of carbamate **74** and 0.13 g (0.49 mmol) of purified aldehyde **21** for 12 h. Flash chromatography on SiO_2 (3:1 hexanes/EtOAc) afforded 0.17 g (80%) of the product as an oil. The diastereomeric mixture was characterized by IR and MS: IR (thin film) 3475, 3025, 2954, 1712, 1479, 1451, 1247, 1087, 967, 851, 701 cm^{-1}; MS (EI) *m/z* 433 ($M^{+\bullet}$), 418, 401, 383, 271, 203, 73; HRMS (EI) *m/z* calculated for $C_{24}H_{39}NO_4Si$: 433.2648, found 433.2636.



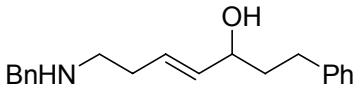
***R**-2-Trimethylsilylethyl-(3*E*,5*R*,6*S*,7*R*,8*E*)-5-hydroxy-6-methyl-10-trimethylsilyl-7-phenyldeca-3,8-dienylmethoxymethylcarbamate + *R**-2-trimethylsilylethyl (3*E*,5*S*,6*S*,7*R*,8*E*)-5-hydroxy-6-methyl-10-trimethylsilyl-7-phenyldeca-3,8-dienylmethoxymethylcarbamate (77):** The general procedure **I** was performed employing 0.15 g (0.58 mmol) of carbamate **75** and 83 mg (0.32 mmol) of purified aldehyde **21** for 12 h. Flash chromatography on SiO_2 (4:1 hexanes/EtOAc) afforded 0.12 g (72%) of the product as an oil. The diastereomeric mixture was characterized by IR and MS: IR (thin film) 3479, 2953, 1705, 1249, 1086, 965, 839, 700 cm^{-1}; MS (EI) *m/z* 519 ($M^{+\bullet}$), 504, 487, 476, 460; HRMS (EI) *m/z* calculated for $C_{28}H_{49}NO_4Si_2$: 519.3200, found 519.3223.



***R**-2,2,2-Trichloroethyl-*N*-tosyl-(3*E*,5*R*,6*S*,7*R*,8*E*)-5-hydroxy-6-methyl-10-trimethylsilyl-7-phenyldeca-3,8-dienylcarbamate + *R**-2,2,2-Trichloroethyl-*N*-tosyl-(3*E*,5*S*,6*S*,7*R*,8*E*)-5-hydroxy-6-methyl-10-trimethylsilyl-7-phenyldeca-3,8-dienylcarbamate (93):** The general procedure **I** was performed employing 0.47 g (1.4 mmol) of carbamate **92** and 0.20 g (0.77 mmol) of purified aldehyde **21** for ~30 min. Flash chromatography on SiO_2 (5:1 hexanes/EtOAc) afforded 0.43 g (94%) of the product as an oil. The diastereomeric mixture was characterized by IR and MS: IR (thin film) 3565, 3026, 2956, 1745, 1598, 1494, 1385, 1248, 1171, 968, 852, 702 cm^{-1}; MS (EI) *m/z* 659 ($M^{+\bullet}$), 643, 420, 342, 203, 155, 91, 73; HRMS (EI) *m/z* calculated for $C_{30}H_{40}NO_5SSi$: 659.1462, found 659.1421.



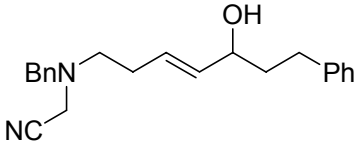
***R**-(3*E*,5*R*,6*S*,7*R*,8*E*)-6-Methyl-10-trimethylsilyl-7-phenyl-1-tosylaminodeca-3,8-dien-5-ol + *R**-(3*E*,5*S*,6*S*,7*R*,8*E*)-6-Methyl-10-trimethylsilyl-7-phenyl-1-tosylaminodeca-3,8-dien-5-ol (94):**[71] To a solution of 0.060 g (0.091 mmol) of alcohol **93** in 0.33 mL of THF was added 65 mg (1.0 mmol) of zinc dust and 65 μL of aq. 1M KH_2PO_4. After 24 h, an identical mixture of THF, zinc dust and 1M KH_2PO_4 is added. Following a further 24 h period, the heterogeneous mixture is filtered through glass wool with Et_2O and the crude product is concentrated *in vacuo*. Purification by flash chromatography on SiO_2 (5:2 → 2:1 hexanes/EtOAc) afforded 33 mg (75%) of the title compound as an oil. The high R_f diastereomer was fully characterized: IR (thin film) 3455, 3284, 3026, 2953, 1599, 1494, 1453, 1325, 1247, 1159, 1094, 967, 853, 701 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.75 (d, *J* = 8.3 Hz, 2H), 7.33–7.13 (m, 7H), 5.61–5.48 (m, 3H), 5.43 (dd, *J* = 15.1, 8.5 Hz, 1H), 4.48–4.38 (m, 2H), 3.19 (dd, *J* = 10.2, 8.8 Hz, 1H), 3.03 (q, *J* = 6.7 Hz, 2H), 2.44 (s, 3H), 2.23 (q, *J* = 6.5 Hz, 2H), 1.84 (dqd, *J* = 10.3, 7.0, 2.6 Hz, 1H), 1.43 (d, *J* = 6.8 Hz, 2H), 0.63 (d, *J* = 6.9 Hz, 3H), –0.07 (s, 9H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 144.6, 143.4, 137.1, 136.0, 131.4, 129.7, 128.4, 127.9, 127.8, 127.1, 125.9 (2C), 72.2, 53.1, 43.0, 42.5, 32.4, 22.9, 21.5, 11.1, –1.9; MS (EI) *m/z* 485 ($M^{+\bullet}$), 467, 370, 355, 338, 256, 203, 91, 73; HRMS (EI) *m/z* calculated for $C_{27}H_{39}NO_3SSi$: 485.2420, found 485.2378.



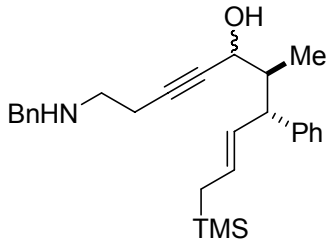
(*E*)-7-Benzylamino-1-phenylhept-4-en-3-ol (61): A solution of 0.53 g (3.3 mmol) of *N*-benzylbut-3-yn-1-amine in 30 mL of Et_2O at –78 °C was treated with 2.1 mL (3.3 mmol) of *n*-

butyllithium in hexanes (1.6 M). Following 15 min, 0.39 mL (0.40 g, 3.0 mmol) of hydrocinnamaldehyde was added and the mixture was slowly raised to rt over 30 min. The reaction was quenched with H_2O, and the aqueous layer was extracted with Et_2O (3x) and filtered. The crude product was concentrated *in vacuo* and utilized directly for the following transformation.

A round bottom flask equipped with a condenser was charged with the crude alkyne and 15 mL of THF and cooled to 0 °C. To this mixture was added 1.9 mL (6.0 mmol) of Red-Al in toluene (65%/wt) (blue solution) and the solution was slowly warmed to rt over 2 h (blue → yellow solution, H_2 evolution). The reaction was brought to reflux for 24 h (yellow → red solution), then carefully quenched with sat. aq. Rochelle's salt. The crude mixture was partitioned between water and Et_2O, extracted with Et_2O (3x), and the combined organic layers were dried over Na_2SO_4. The extracts were filtered and the crude product concentrated *in vacuo*. Purification by flash chromatography on SiO_2 (5:1 EtOAc/hexanes + 5% TEA) afforded 0.48 g (53%) of the product over 2-steps as a yellow oil: IR (thin film) 3304, 3025, 2921, 2854, 1495, 1453, 1100, 1061, 971, 744, 698 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.28–7.14 (m, 10H), 5.69–5.49 (m, 2H), 4.05 (q, J = 5.9 Hz, 1H), 3.76 (s, 2H), 2.74–2.59 (m, 4H), 2.24 (q, J = 6.8 Hz, 2H), 1.89–1.70 (m, 2H), 1.46 (br. s, 2H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 142.0, 140.0, 135.0, 129.0, 128.3, 128.2 (2C), 128.1, 126.9, 125.7, 71.8, 53.7, 48.4, 38.7, 32.5, 31.7; MS (EI) *m/z* 296 ($M^{+\bullet}$+H), 295 ($M^{+\bullet}$), 160, 120, 91; HRMS (EI) *m/z* calculated for $C_{20}H_{25}NO$ ($M^{+\bullet}$): 295.1936, found 295.1950.

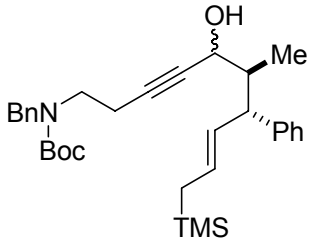


2-*N*-Benzyl-*N*-(*E*)-5-hydroxy-7-phenylhept-3-enylaminoacetonitrile (62): To 0.10 g (0.34 mmol) of amine **61** in 1.7 mL of CH_2Cl_2 was added 39 μL (68 mg, 0.41 mmol) of iodoacetonitrile and 56 μL (41 mg, 0.41 mmol) of triethylamine. Following 1h, an identical quantity of iodoacetonitrile and triethylamine was added. The reaction was stirred for 12 h at ambient temperature, then quenched with H_2O. The mixture was partitioned between H_2O and EtOAc and the aqueous layer was extracted with EtOAc (3x), the combined organic layers were dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude material was filtered through a pad of SiO_2 (2:1 hexanes/EtOAc) and was further purified by flash chromatography on SiO_2 (2:1 hexanes/EtOAc) to give 87 mg (76%) of the product as a yellow oil: IR (thin film) 3424, 3027, 2924, 1495, 1454, 1421, 1127, 969 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.34–7.15 (m, 10H), 5.69 (dt, *J* = 15.5, 6.1 Hz, 1H), 5.60 (dd, *J* = 15.5, 5.9 Hz, 1H), 4.15–4.07 (m, 1H), 3.68 (s, 2H), 3.46 (s, 2H), 2.79–2.63 (m, 4H), 2.31 (q, *J* = 7.3 Hz, 2H), 1.95–1.76 (m, 2H), 1.46 (d, *J* = 3.9 Hz, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 141.8, 137.1, 134.8, 128.9, 128.7, 128.6, 128.4 (2C), 127.8, 125.8, 114.7, 72.1, 58.3, 53.7, 41.2, 38.7, 31.7, 30.2; MS (ESI) *m/z* 357 $(M+Na)^+$; HRMS (ESI) *m/z* calculated for $NaC_{22}H_{26}N_2O$ $(M+Na)^+$: 357.1943, found 357.1976.



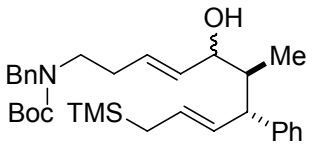
***R**-(*E*,5*R*,6*S*,7*R*)-1-Benzylamino-6-methyl-10-trimethylsilyl-7-phenyldec-8-en-3-yn-5-ol + *R**-(*E*,5*S*,6*S*,7*R*)-1-Benzylamino-6-methyl-10-trimethylsilyl-7-phenyldec-8-en-3-yn-5-ol (64):** A solution of 0.35 g (2.2 mmol) of *N*-benzylbut-3-yn-1-amine in 22 mL of Et_2O at –78 °C was treated with 1.4 mL (2.2 mmol) of *n*-butyllithium in hexanes (1.6 M) (clear → bright

pink).[58] Additional amine was added to the solution until the pink color dissipated. Following 15 min, 0.52 g (2.0 mmol) of aldehyde **21** was added as a solution in 2.0 mL of Et_2O and the mixture was slowly raised to rt over 1 hr. The reaction was quenched with H_2O, and the aqueous layer was extracted with Et_2O (3x) and filtered. Purification by flash chromatography on SiO_2 (2x) (5:1 EtOAc/hexanes then 2:1 EtOAc/hexanes) provided 0.85 g (91%) of the title compound as an oil. The diastereomeric mixture was characterized by IR and MS: IR (thin film) 3300, 3026, 2953, 1601, 1494, 1453, 1247, 965, 851, 736, 699 cm^{-1}; MS (EI) *m/z* 419 ($M^{+\bullet}$), 404, 346, 328, 318, 300, 120; HRMS (EI) *m/z* calculated for $C_{27}H_{37}NOSi$: 419.2644, found 419.2669.

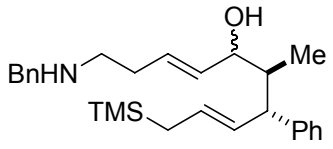


***R*-N-Tert*-butyl-*N*-benzyl-(*E*,5*R*,6*S*,7*R*)-5-hydroxy-6-methyl-10-trimethylsilyl-7-phenyldec-8-en-3-ynylcarbamate + *R*-N-Tert*-butyl-*N*-benzyl(*E*,5*S*,6*S*,7*R*)-5-hydroxy-6-methyl-10-trimethylsilyl-7-phenyldec-8-en-3-ynylcarbamate (55):** A solution of 0.29 g (1.1 mmol) of carbamate **54** in 11 mL of Et_2O at –78 °C was treated with 0.69 mL (1.1 mmol) of *n*-butyllithium in hexanes (1.6 M). Following 15 min, 0.26 g (1.0 mmol) of aldehyde **21** was added as a solution in 1.0 mL of Et_2O and the mixture was slowly raised to rt over 1 hr. The reaction was quenched with sat. aq. NH_4Cl, and the aqueous layer was extracted with Et_2O (3x) and filtered. Purification by flash chromatography on SiO_2 (8:1 hexanes/EtOAc) provided 0.35 g (67%) of the title compound as an oil. The diastereomeric mixture was characterized by IR and MS: IR (thin film) 3443, 3027, 2974, 1659, 1495, 1465, 1415, 1367, 1248, 1164, 852, 700 cm^{-1}; MS (ESI) *m/z*

542 $(M+Na)^+$; HRMS (ESI) *m/z* calculated for $NaC_{32}H_{45}NO_3Si$ $(M+Na)^+$: 542.3066, found 542.3021.

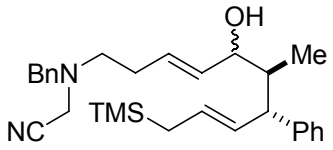


***R*-N-Tert*-butyl-*N*-benzyl-(3*E*,5*R*,6*S*,7*R*,8*E*)-5-hydroxy-6-methyl-10-trimethylsilyl-7-phenyldeca-3,8-dienylcarbamate + *R*-N-Tert*-butyl-*N*-benzyl-(3*E*,5*S*,6*S*,7*R*,8*E*)-5-hydroxy-6-methyl-10-trimethylsilyl-7-phenyldeca-3,8-dienylcarbamate (56):**[61] To a solution of 0.16 g (0.30 mmol) of alkyne **55** in 3.0 mL of THF at 0 °C was added 0.12 mL (0.40 mmol) of Red-Al in toluene (65%/wt) and the solution was stirred for 30 min, then slowly warmed to rt over 1 h. The reaction was then heated to 45 °C for 7 h, then carefully quenched with sat. aq. Rochelle's salt. The crude mixture was partitioned between water and Et_2O, extracted with Et_2O (3x), and the combined organic layers were dried over Na_2SO_4. The extracts were filtered and the crude product concentrated *in vacuo*. Purification by flash chromatography on SiO_2 (8:1 hexanes/EtOAc) afforded 0.070 g (43%) of the product as an oil. The diastereomeric mixture was characterized by IR and MS: IR (thin film) 3466, 3026, 2973, 1694, 1495, 1453, 1416, 1366, 1247, 1165, 965, 854, 699 cm^{-1}; MS (EI) *m/z* 521 ($M^{+\bullet}$), 503, 447, 421, 334, 203, 120, 73; HRMS (EI) *m/z* calculated for $C_{32}H_{47}NO_3Si$: 521.3325, found 521.3308.



***R*-(3E,5R,6S,7R,8E)-1-Benzylamino-6-methyl-10-trimethylsilyl-7-phenyldeca-3,8-dien-5-ol + *R*-(3E,5S,6S,7R,8E)-1-Benzylamino-6-methyl-10-trimethylsilyl-7-phenyldeca-3,8-dien-5-**

ol (65):[71] To a solution of 0.37 g (0.62 mmol) of alcohol **67** in 2.3 mL of THF was added 0.44 g (6.8 mmol) of zinc dust and 0.45 mL of aq. 1M KH_2PO_4. After 24 h, an identical mixture of THF, zinc dust and 1M KH_2PO_4 is added. Following a further 24 h period, the heterogeneous mixture is filtered through glass wool with Et_2O and the crude product is concentrated *in vacuo*. Purification by flash chromatography on SiO_2 (20:1 CH_2Cl_2/MeOH) gave 0.22 g (84%) of the title compound as an oil. The high R_f diastereomer was fully characterized: IR (thin film) 3407, 3026, 2952, 1494, 1453, 1247, 966, 853, 699 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.36–7.13 (m, 10H), 5.72–5.60 (m, 2H), 5.53 (dt, *J* = 15.0, 7.3 Hz, 1H), 5.45 (dd, *J* = 15.1, 8.3 Hz, 1H), 4.47–4.42 (m, 1H), 3.81 (s, 2H), 3.21 (dd, *J* = 10.1, 8.5 Hz, 1H), 2.72 (t, *J* = 6.9 Hz, 2H), 2.31 (q, *J* = 6.4 Hz, 2H), 1.87 (dqd, *J* = 9.4, 6.9, 2.4 Hz, 1H), 1.50–1.38 (m, 4H), 0.66 (d, *J* = 6.9 Hz, 3H), –0.06 (s, 9H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 144.7, 140.3, 134.3, 131.6, 128.3 (3C), 128.1, 127.8, 127.6, 126.9, 125.8, 72.5, 53.8, 53.0, 48.6, 43.2, 32.8, 22.8, 11.1, –1.9; MS (EI) *m/z* 421 ($M^{+\bullet}$), 406, 334, 272, 218, 203, 121; HRMS (EI) *m/z* calculated for $C_{27}H_{39}NOSi$: 421.2801, found 421.2814.

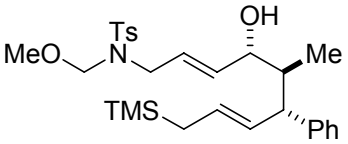


***R**-2-*N*-Benzyl-*N*-(3*E*,5*R*,6*S*,7*R*,8*E*)-5-hydroxy-6-methyl-10-trimethylsilyl-7-phenyldeca-3,8-dienylaminoacetonitrile + *R**-2-*N*-Benzyl-*N*-(3*E*,5*S*,6*S*,7*R*,8*E*)-5-hydroxy-6-methyl-10-trimethylsilyl-7-phenyldeca-3,8-dienylaminoacetonitrile (68):** To 0.27 g (0.64 mmol) of amine **65** in 2.1 mL of CH_2Cl_2 was added 70 μL (0.12 g, 0.96 mmol) of bromoacetonitrile and 0.13 mL (97 mg, 0.96 mmol) of triethylamine. Following 1h, an identical quantity of iodoacetonitrile and triethylamine was added. The reaction was stirred for 24 h at ambient

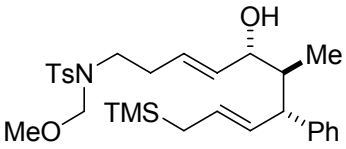
temperature, then quenched with H_2O. The mixture was partitioned between H_2O and EtOAc and the aqueous layer was extracted with EtOAc (3x), the combined organic layers were dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude material was purified by filtration through a plug of SiO_2 (2:1 hexanes/EtOAc) to afford 0.23 g (78%) of the title compound as an oil. The high R_f diastereomer was fully characterized: IR (thin film) 3519, 3027, 2952, 1601, 1494, 1453, 1247, 1152, 966, 852, 740, 700 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.40–7.15 (m, 10H), 5.75–5.62 (m, 2H), 5.55 (dt, *J* = 15.1, 7.6 Hz, 1H), 5.46 (dd, *J* = 15.1, 8.3 Hz, 1H), 4.50–4.45 (m, 1H), 3.68 (s, 2H), 3.46 (s, 2H), 3.22 (dd, *J* = 10.1, 8.8 Hz, 1H), 2.72 (t, *J* = 7.1 Hz, 2H), 2.33 (q, *J* = 7.1 Hz, 2H), 1.88 (dqd, *J* = 10.3, 6.9, 2.4 Hz, 1H), 1.46–1.41 (m, 3H), 0.67 (d, *J* = 6.9 Hz, 3H), –0.05 (s, 9H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 144.7, 137.1, 134.2, 131.5, 128.9, 128.6, 128.4, 127.7 (4C), 125.8, 114.7, 72.5, 58.3, 53.8, 53.1, 43.2, 41.1, 30.4, 22.8, 11.0, –1.9; MS (EI) *m/z* 460 ($M^{+\bullet}$), 445, 434, 220, 369, 361, 203; HRMS (EI) *m/z* calculated for $C_{29}H_{40}N_2OSi$: 460.2910, found 460.2908.

General Procedure J for Zinc(II)-Mediated Preparation of Diastereomerically-Enriched Amino-Substituted Allylic Alcohols 83–85:[82, 83, 226] To the alkyne (1.0 mmol) in 3.3 mL of CH_2Cl_2 at 0 °C was added 0.28 g (1.1 mmol) of $Cp_2Zr(H)Cl$ in portions. The mixture was then slowly warmed to ambient temperature (cloudy → clear yellow color shift) for 20 min, then stirred 20 min longer following dissolution of the solid. The flask was immersed in a –55 °C bath (cryocool) and 0.58 mL (1.15 mmol) of Me_2Zn in toluene (2.0 M) was added. The reaction was stirred for 45 min at –55 °C then warmed to 0 °C for 5 min whereupon 0.31 g (1.2 mmol) of aldehyde **21** was added dropwise and the reaction was stirred for the specified time period. The reaction was carefully quenched with sat. aq. Rochelle's salt, stirred for 30 min, then the aqueous

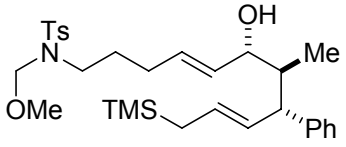
layer was extracted with Et_2O (3x). The combined organic layers were dried over Na_2SO_4, filtered through florsil with Et_2O, and the crude product was concentrated *in vacuo*. The product was purified *via* flash chromatography under the specified conditions. In each case, the high R_f diastereomer was isolated *via* flash chromatography and fully characterized. Diastereomeric ratios were determined by ^{1}H-NMR analysis of the recombined epimeric alcohols following flash chromatography.



***R**-(2*E*,4*S*,5*S*,6*R*,7*E*)-1-*N*-Methoxymethyl-*N*-tosylamino-5-methyl-9-trimethylsilyl-6-phenylnona-2,7-dien-4-ol (83):** General procedure **J** was carried out with 0.10 g (0.40 mmol) of alkyne **80** with 1h for transmetallation at –50 °C, addition of aldehyde **21** at –40 °C and stirring at this temperature for 6 h, followed by warming to –25 °C for 14 h. Flash chromatography on SiO_2 (3:2 hexanes/Et_2O) gave 69 mg (33%) of the product as an oil. Diastereomeric ratio by ^{1}H-NMR (300 MHz, $CDCl_3$) (CH_3O–C**H$_2$**–N): 87% (δ 4.71), 13% (δ 4.68): IR (thin film) 3566, 2956, 1652, 1495, 1340, 1247, 1162, 1060, 851, 701 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.74 (d, *J* = 8.3 Hz, 2H), 7.32–7.10 (m, 7H), 5.69 (dd, *J* = 15.6, 4.9 Hz, 1H), 5.60–5.37 (m, 3H), 4.71 (s, 2H), 4.50–4.42 (m, 1H), 3.84 (d, *J* = 6.3 Hz, 2H), 3.28 (s, 3H), 3.18 (t, *J* = 10.0 Hz, 1H), 2.42 (s, 3H), 1.81 (dqd, *J* = 10.4, 6.6, 2.3 Hz, 1H), 1.41 (d, *J* = 7.3 Hz, 2H), 1.38 (d, *J* = 5.6 Hz, 1H), 0.59 (d, *J* = 6.9 Hz, 3H), –0.08 (s, 9H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 144.5, 143.4, 137.6, 137.4, 131.3, 129.6, 128.5, 127.9, 127.6, 127.3, 125.9, 124.1, 78.4, 71.7, 55.7, 53.1, 47.5, 42.9, 22.8, 21.5, 10.9, –1.9; MS (ESI) *m/z* 538 $(M+Na)^+$; HRMS (ESI) *m/z* calculated for $NaC_{28}H_{41}NO_4SSi$ $(M+Na)^+$: 538.2423, found 538.2413.



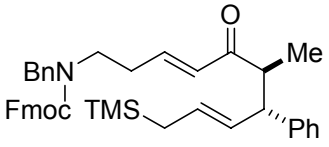
***R**-(3*E*,5*S*,6*S*,7*R*,8*E*)-1-*N*-Methoxymethyl-*N*-tosylamino-6-methyl-10-trimethylsilyl-7-phenyldeca-3,8-dien-5-ol (84):** General procedure **J** was carried out with 86 mg (0.32 mmol) of alkyne **81** for 5.5 h. Flash chromatography on SiO_2 (4:1 hexanes/EtOAc) gave 0.10 g (59%) of the product as an oil. Diastereomeric ratio by ^{1}H-NMR (300 MHz, $CDCl_3$) (CH_3O–C**H$_2$**–N): 82% (δ 4.73), 18% (δ 4.70): IR (thin film) 3539, 3026, 2952, 1599, 1494, 1451, 1342, 1247, 1158, 964, 852, 701 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.72 (d, *J* = 8.3 Hz, 2H), 7.32–7.10 (m, 7H), 5.63–5.55 (m, 2H), 5.51 (dt, *J* = 15.1, 7.4 Hz, 1H), 5.44 (dd, *J* = 15.2, 8.4 Hz, 1H), 4.73 (s, 2H), 4.43–4.39 (m, 1H), 3.31 (s, 3H), 3.24–3.17 (m, 3H), 2.43 (s, 3H), 2.39–2.32 (m, 2H), 1.84 (dqd, *J* = 10.3, 7.1, 2.4 Hz, 1H), 1.44–1.39 (m, 3H), 0.64 (d, *J* = 6.9 Hz, 3H), –0.07 (s, 9H), ; ^{13}C-NMR (75 MHz, D_3CCN): δ 146.4, 144.7, 138.7, 136.7, 132.9, 130.6, 129.3, 128.8 128.2, 128.1, 126.9, 126.6, 81.0, 72.2, 56.0, 53.8, 47.8, 44.0, 32.6, 23.2, 21.5, 11.4, –1.8; MS (ESI) *m/z* 552 $(M+Na)^+$; HRMS (ESI) *m/z* calculated for $NaC_{29}H_{43}NO_4SSi$ $(M+23)^+$: 552.2580, found 552.2589.



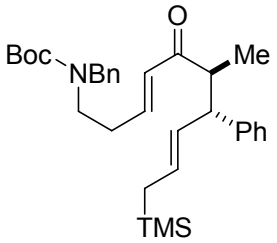
***R**-(2*E*,4*R*,5*S*,6*S*,7*E*)-11-*N*-Methoxymethyl-*N*-tosylamino-5-methyl-1-trimethylsilyl-4-phenylundeca-2,7-dien-6-ol (85):** General procedure **J** was carried out with 0.10 g (0.36 mmol) of alkyne **82** for 5.5 h. Flash chromatography on SiO_2 (4:1 hexanes/EtOAc) gave 0.13 g (67%) of the product as an oil. Diastereomeric ratio by ^{1}H-NMR (300 MHz, $CDCl_3$) (CH_3O–C**H$_2$**–N): 86% (δ 4.72), 14% (δ 4.70): IR (thin film) 3537, 3026, 2951, 1651, 1599, 1341, 1247, 1159,

1079, 964, 851, 701 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.71 (d, *J* = 8.3 Hz, 2H), 7.34–7.14 (m, 7H), 5.66–5.49 (m, 3H), 5.45 (dd, *J* = 15.1, 8.1 Hz, 1H), 4.72 (s, 2H), 4.47–4.40 (m, 1H), 3.31 (s, 3H), 3.21 (dd, *J* = 9.9, 8.3 Hz, 1H), 3.15 (t, *J* = 7.3 Hz, 2H), 2.41 (s, 3H), 2.04 (q, *J* = 6.9 Hz, 2H), 1.85 (dqd, *J* = 10.3, 6.8, 2.3 Hz, 1H), 1.69 (p, *J* = 7.6 Hz, 2H), 1.44 (d, *J* = 3.0 Hz, 1H), 1.43 (d, *J* = 6.4 Hz, 2H), 0.65 (d, *J* = 6.8 Hz, 3H), –0.06 (s, 9H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 144.7, 143.3, 137.4, 133.1, 131.5, 129.5, 128.4, 127.7 (2C), 127.1 (2C), 125.8, 79.9, 72.6, 55.6, 53.0, 46.6, 43.2, 29.3, 28.1, 22.8, 21.5, 11.1, –1.9; MS (EI) *m/z* 543 ($M^{+\bullet}$), 512, 494, 398, 358, 338, 292, 205, 184, 124; HRMS (EI) *m/z* calculated for $C_{30}H_{45}NO_4SSi$: 543.2839, found 543.2864.

General Procedure K for the Preparation of Amino-Substituted Unsaturated Ketones 52, 57, 63, 69, 78, 79, 86-88:[35-38] To a solution of the allylic alcohol (1.0 mmol) in 10 mL of CH_2Cl_2 at 0 °C was added Dess-Martin periodinane (1.5-3.0 mmol) and the mixture was stirred for the specified time period. The mixture was warmed to rt and again stirred for the specified time period with addition of further Dess-Martin reagent for less reactive substrates. The reaction was then quenched by addition of hexanes, filtered through florsil (2:1 hexanes/EtOAc) and concentrated *in vacuo*. Purification by flash chromatography under the specified conditions afforded the desired products. In all cases, the ketones were isolated as product mixtures that were quantified by HPLC analysis in representative cases.

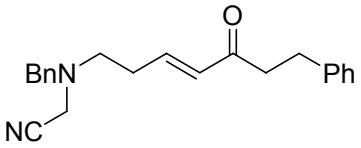


***R**-*N*-Fluoren-9-ylmethyl-*N*-benzyl-(3*E*,6*S*,7*R*,8*E*)-6-methyl-10-trimethylsilyl-5-oxo-7-phenyldeca-3,8-dienylcarbamate (52):** The general procedure **K** was performed employing 33 mg (0.051 mmol) of alcohol **51** and 33 mg (0.077 mmol) of Dess-Martin periodinane for 10 min at 0 °C, 45 min at rt, then an additional 33 mg of oxidant for 15 min at rt. Purification by flash chromatography on SiO_2 (6:1 hexanes/EtOAc) afforded 33 mg (100%) of the title compound as an oil. The compound ratio was not determined for this substrate: IR (thin film) 3027, 2953, 1701, 1668, 1626, 1477, 1451, 1246, 1122, 964, 852, 741 cm^{-1}; ^{1}H-NMR (300 MHz, D_6-DMSO, 353 K): δ 7.83 (d, *J* = 7.5 Hz, 2H), 7.58 (d, *J* = 7.3 Hz, 2H), 7.39 (t, *J* = 7.4 Hz, 2H), 7.31–7.13 (m, 10H), 7.08 (d, *J* = 7.8 Hz, 2H), 6.63 (dt, *J* = 15.7, 6.6 Hz, 1H), 6.05 (d, *J* = 15.8 Hz, 1H), 5.40–5.21 (m, 2H), 4.55 (d, *J* = 5.6 Hz, 2H), 4.31 (s, 2H), 4.30–4.25 (m, 1H), 3.44 (dd, *J* = 9.9, 7.0 Hz, 1H), 3.22–3.12 (m, 3H), 2.23–2.16 (m, 2H), 1.29 (d, *J* = 6.8 Hz, 2H), 0.75 (d, *J* = 6.9 Hz, 3H), –0.14 (s, 9H); ^{13}C-NMR (75 MHz, D_6-DMSO, 353 K): δ 201.3, 155.2, 143.6, 142.7, 142.6, 140.5, 137.4, 130.6, 129.8, 127.9, 127.8, 127.5, 127.1, 126.9, 126.6 (2C), 126.5, 125.6, 124.2, 119.4, 66.0, 51.0, 49.7, 47.2, 46.8, 45.1, 30.3, 21.7, 15.3, –2.5; MS (ESI) *m/z* 664 $(M+Na)^+$; HRMS (ESI) *m/z* calculated for $Na_1C_{42}H_{47}NO_3Si$ $(M+Na)^+$: 664.3223, found 664.3161.



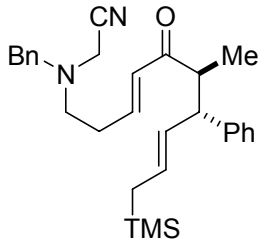
***R**-*N*-*Tert*-butyl-*N*-benzyl-(3*E*,6*S*,7*R*,8*E*)-6-methyl-10-trimethylsilyl-5-oxo-7-phenyldeca-3,8-dienylcarbamate (57):** The general procedure **K** was performed employing 0.16 g (0.31 mmol) of alcohol **56** and 0.33 g (0.78 mmol) of Dess-Martin periodinane for 1 h at rt, then additional oxidant was added until the reaction was complete by TLC. Purification by flash

chromatography on SiO_2 (8:1 hexanes/EtOAc) afforded 0.15 g (94%) of the title compound as an oil. The compound ratio was not determined for this substrate: IR (thin film) 3027, 2955, 1694, 1626, 1495, 1453, 1413, 1366, 1247, 1164, 964, 852, 700 cm^{-1}; ^{1}H-NMR (300 MHz, D_6-DMSO, 353 K): δ 7.36–7.13 (m, 10H), 6.77 (dt, *J* = 15.8, 7.0 Hz, 1H), 6.17 (dt, *J* = 15.8, 1.4 Hz, 1H), 5.36 (dd, *J* = 15.3, 6.9 Hz, 1H), 5.28 (dt, *J* = 15.2, 7.2 Hz, 1H), 4.40 (s, 2H), 3.45 (dd, *J* = 9.9, 7.0 Hz, 1H), 3.32 (t, *J* = 7.0 Hz, 2H), 3.19 (dq, *J* = 10.0, 6.9 Hz, 1H), 2.39 (qd, *J* = 7.0, 1.3 Hz, 2H), 1.39 (s, 9H), 1.31 (d, *J* = 6.8 Hz, 2H), 0.76 (d, *J* = 6.9 Hz, 3H), –0.12 (s, 9H); ^{13}C-NMR (75 MHz, D_6-DMSO, 353 K): δ 201.1, 154.4, 143.1, 142.6, 138.1, 130.4, 129.9, 127.8 (2C), 127.7, 127.5, 126.8, 126.5, 125.5, 78.6, 51.0, 49.6, 47.2, 45.0, 30.6, 27.6, 21.7, 15.2, –2.5; MS (EI) *m/z* 464 ($M^{+\bullet}$-*t*Bu,+H), 419, 333, 236, 203, 120, 91, 73; HRMS (EI) *m/z* calculated for $C_{28}H_{37}NO_3Si$ ($M^{+\bullet}$-*t*Bu,+H): 463.2543, found 463.2524.

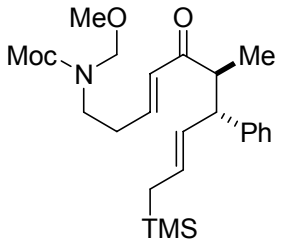


2-*N*-Benzyl-*N*-(*E*)-5-oxo-7-phenylhept-3-enylaminoacetonitrile (63): The general procedure **K** was performed employing 30 mg (0.090 mmol) of alcohol **62** and 59 mg (0.14 mmol) of Dess-Martin periodinane for ~10 min at 0 °C, ~45 min at rt, then additional oxidant was added until the reaction was complete by TLC. The mixture was passed through a plug of silica (2:1 hexanes/EtOAc) and concentrated *in vacuo* to afford 25 mg (83%) of the product as an oil: IR (thin film) 3061, 2922, 1673, 1629, 1495, 1454, 974, 740, 699 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.37–7.18 (m, 10H), 6.80 (dt, *J* = 15.9, 6.8 Hz, 1H), 6.17 (dt, *J* = 15.9, 1.5 Hz, 1H), 3.68 (s, 2H), 3.46 (s, 2H), 2.99–2.94 (m, 2H), 2.91–2.85 (m, 2H), 2.78 (t, *J* = 7.0 Hz, 2H), 2.45 (qd, *J* = 6.8, 1.4 Hz, 2H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 199.2, 143.9, 141.2, 136.8, 131.5,

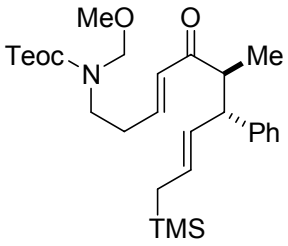
128.9, 128.7, 128.5, 128.3, 127.9, 126.1, 114.5, 58.2, 52.4, 41.8, 41.3, 30.3, 30.0; MS (ESI) *m/z* 355 $(M+Na)^+$; HRMS (ESI) *m/z* calculated for $NaC_{22}H_{24}N_2O$ $(M+Na)^+$: 355.1786, found 355.1786.



***R**-2-*N*-Benzyl-*N*-(3E,6S,7R,8E)-6-methyl-10-trimethylsilyl-5-oxo-7-phenyldeca-3,8-dienylaminoacetonitrile (69):** The general procedure **K** was performed employing 0.23 g (0.50 mmol) of alcohol **68** and 0.32 g (0.75 mmol) of Dess-Martin periodinane for ~10 min at 0 °C and 30-45 min at rt. Purification by flash chromatography on SiO_2 (7:1 hexanes/EtOAc) afforded 0.20 g (88%) of the title compound as an oil. Isolated compound ratio by HPLC (Zorbax™ Sil column, flow rate 1.0 mL/min, 2.0% *i*-PrOH, 98.0% hexanes): 87.9% (Tr = 8.90), 5.7% (Tr = 9.58), 6.3% (Tr = 10.16): IR (thin film) 3027, 2953, 1692, 1667, 1626, 1494, 1453, 1247, 967, 853, 740, 700 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.38–7.19 (m, 10H), 6.86 (dt, *J* = 15.8, 6.8 Hz, 1H), 6.24 (dt, *J* = 15.7, 1.4 Hz, 1H), 5.41–5.33 (m, 2H), 3.71 (s, 2H), 3.55–3.49 (m, 1H), 3.47 (s, 2H), 3.14 (dq, *J* = 10.2, 6.9 Hz, 1H), 2.80 (t, *J* = 7.1 Hz, 2H), 2.48 (qd, *J* = 6.9, 1.2 Hz, 2H), 1.35–1.33 (m, 2H), 0.88 (d, *J* = 6.9 Hz, 3H), –0.09 (s, 9H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 202.7, 143.7, 143.0, 136.7, 130.9, 129.6, 128.9, 128.6, 128.4, 128.0 (2C), 127.9, 114.5, 58.1, 52.4, 52.0, 49.0, 41.1, 30.3, 22.7, 16.2, –2.1; MS (EI) *m/z* 458 ($M^{+\bullet}$), 431, 359, 229, 203, 159, 91, 73; HRMS (EI) *m/z* calculated for $C_{29}H_{38}N_2OSi$: 458.2753, found 458.2765.

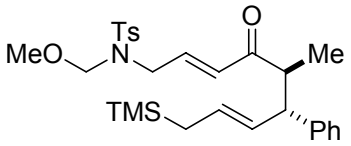


***R**-Methyl-*N*-methoxymethyl-(3*E*,6*S*,7*R*,8*E*)-6-methyl-10-trimethylsilyl-5-oxo-7-phenyldeca-3,8-dienylcarbamate (78):** The general procedure **K** was performed employing 0.17 g (0.39 mmol) of alcohol **76** and 0.33 g (0.78 mmol) of Dess-Martin periodinane for 1.5 h at 0 °C and 45 min at rt. Purification by flash chromatography on SiO_2 (4:1 hexanes/EtOAc) afforded 0.11 g (64%) of the title compound as an oil. The compound ratio was not determined for this substrate: IR (thin film) 3026, 2954, 1713, 1669, 1626, 1476, 1451, 1247, 1086, 851, 701 cm^{-1}; ^{1}H-NMR (300 MHz, D_6-DMSO, 353 K): δ 7.35–7.13 (m, 5H), 6.81 (dt, *J* = 15.8, 7.0 Hz, 1H), 6.21 (dt, *J* = 15.8, 1.4 Hz, 1H), 5.37 (dd, *J* = 15.3, 7.0 Hz, 1H), 5.29 (dt, *J* = 15.2, 5.1 Hz, 1H), 4.66 (s, 2H), 3.65 (s, 3H), 3.46 (dd, *J* = 10.0, 6.9 Hz, 1H), 3.41 (t, *J* = 6.4 Hz, 2H), 3.22 (dq, *J* = 10.0, 6.9 Hz, 1H), 3.22 (s, 1H), 2.47 (qd, *J* = 7.0, 1.4 Hz, 2H), 1.32 (d, *J* = 6.8 Hz, 2H), 0.76 (d, *J* = 6.8 Hz, 3H), –0.10 (s, 9H); ^{13}C-NMR (75 MHz, D_6-DMSO, 353 K): δ 201.3, 155.6, 143.0, 142.6, 130.5, 129.9, 127.7, 127.5, 126.5, 125.5, 78.4, 54.5, 51.8, 51.0, 47.2, 44.6, 30.9, 21.7, 15.2, –2.6; MS (EI) *m/z* 431 ($M^{+\bullet}$), 416, 399, 384, 301, 271, 257; HRMS (EI) *m/z* calculated for $C_{24}H_{37}NO_4Si$: 431.2492, found 431.2488.



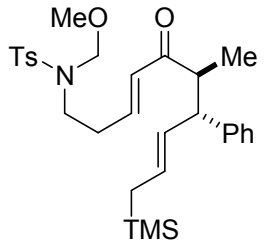
***R**-2-Trimethylsilylethylmethoxymethyl-(3*E*,6*S*,7*R*,8*E*)-6-methyl-10-trimethylsilyl-5-oxo-7-phenyldeca-3,8-dienylcarbamate (79):** The general procedure **K** was performed employing

0.12 g (0.23 mmol) of alcohol **77** and 0.20 g (0.46 mmol) of Dess-Martin periodinane for 1.5 h at 0 °C and 45 min at rt. Purification by flash chromatography on SiO_2 (5:1 hexanes/EtOAc) afforded 0.10 g (83%) of the title compound as an oil. The compound ratio was not determined for this substrate: IR (thin film) 3027, 2953, 1705, 1670, 1626, 1452, 1249, 961, 839, 700 cm^{-1}; ^{1}H-NMR (300 MHz, D_6-DMSO, 353 K): δ 7.30–7.14 (m, 5H), 6.81 (dt, *J* = 15.8, 6.9 Hz, 1H), 6.20 (d, *J* = 15.8 Hz, 1H), 5.36 (dd, *J* = 15.4, 7.1 Hz, 1H), 5.29 (dt, *J* = 15.2, 7.2 Hz, 1H), 4.65 (s, 2H), 4.15 (t, *J* = 8.1 Hz, 2H), 3.45 (dd, *J* = 10.0, 6.9 Hz, 1H), 3.40 (t, *J* = 7.1 Hz, 2H), 3.29–3.15 (m, 1H), 3.21 (s, 3H), 2.46 (qd, *J* = 7.1, 1.2 Hz, 2H), 1.31 (d, *J* = 6.8 Hz, 2H), 0.98 (t, *J* = 8.3 Hz, 2H), 0.75 (d, *J* = 6.8 Hz, 3H), 0.03 (s, 9H), –0.11 (s, 9H); ^{13}C-NMR (75 MHz, D_6-DMSO, 353 K): δ 201.2, 155.2, 143.0, 142.6, 130.5, 129.9, 127.7, 127.5, 126.5, 125.5, 78.3, 62.6, 54.5, 51.0, 47.2, 44.4, 31.0, 21.7, 16.9, 15.2, –2.1, –2.5; MS (ESI) *m/z* 540 $(M+Na)^+$; HRMS (ESI) *m/z* calculated for $NaC_{28}H_{47}NO_4Si_2$ $(M+Na)^+$: 540.2941, found 540.2968.



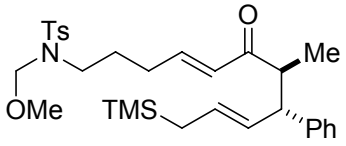
***R**-(2*E*,5*S*,6*R*,7*E*)-1-*N*-Methoxymethyl-*N*-tosylamino-5-methyl-9-trimethylsilyl-6-phenylnona-2,7-dien-4-one (86):** The general procedure **K** was performed employing 63 mg (0.12 mmol) of alcohol **83** and 0.15 g (0.36 mmol) of Dess-Martin periodinane for 15 min at 0 °C, 45 min at rt. Purification by flash chromatography on SiO_2 (3:1 hexanes/EtOAc) afforded 52 mg (83%) of the title compound as an oil. Isolated compound ratio by HPLC (Zorbax™ Sil column, flow rate 1.0 mL/min, 2.0% *i*-PrOH, 98.0% hexanes): 84.6% (Tr = 11.21), 7.5% (Tr = 11.97), 7.9% (Tr = 12.97): IR (thin film) 3026, 2953, 1696, 1673, 1633, 1599, 1494, 1453, 1346, 1248, 1162, 1076, 852, 702 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.75 (d, *J* = 8.3 Hz, 2H), 7.33–

7.09 (m, 7H), 6.59 (dt, *J* = 15.8, 5.9 Hz, 1H), 6.19 (d, *J* = 15.8 Hz, 1H), 5.38–5.30 (m, 2H), 4.71 (d, *J* = 10.5 Hz, 1H), 4.67 (d, *J* = 10.5 Hz, 1H), 3.98 (dd, *J* = 5.8, 1.2 Hz, 2H), 3.54–3.39 (m, 1H), 3.30 (s, 3H), 3.06 (dq, *J* = 9.9, 6.9 Hz, 1H), 2.42 (s, 3H), 1.33 (d, *J* = 6.5 Hz, 2H), 0.82 (d, *J* = 6.9 Hz, 3H), –0.10 (s, 9H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 202.4, 143.8, 142.8, 139.7, 137.3, 131.4, 129.7, 129.6, 128.5, 128.2, 128.0, 127.3, 126.3, 79.3, 55.8, 51.9, 49.1, 47.0, 22.8, 21.5, 16.0, –2.0; MS (ESI) *m/z* 536 $(M+Na)^+$; HRMS (ESI) *m/z* calculated for $NaC_{28}H_{39}NO_4SSi$ $(M+Na)^+$: 536.2267, found 536.2288.



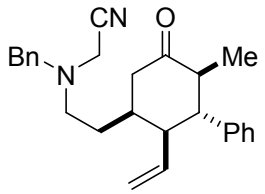
R*-(3E,6S,7R,8E)-1-N-Methoxymethyl-N-tosylamino-6-methyl-10-trimethylsilyl-7-phenyldeca-3,8-dien-5-one (87): The general procedure **K** was performed employing 63 mg (0.12 mmol) of alcohol **84** and 0.15 g (0.36 mmol) of Dess-Martin periodinane for 15 min at 0 °C, 45 min at rt. Purification by flash chromatography on SiO_2 (3:1 hexanes/EtOAc) afforded 52 mg (83%) of the title compound as an oil. Isolated compound ratio by HPLC (Zorbax™ Sil column, flow rate 1.0 mL/min, 3.0% *i*-PrOH, 97.0% hexanes): 87.1% (Tr = 9.25), 6.6% (Tr = 10.08), 6.3% (Tr = 11.00): IR (thin film) 3027, 2953, 1693, 1668, 1627, 1599, 1494, 1453, 1344, 1247, 1160, 1078, 963, 852, 702 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.73 (d, *J* = 8.3 Hz, 2H), 7.33–7.16 (m, 7H), 6.75 (dt, *J* = 15.8, 7.0 Hz, 1H), 6.18 (dt, *J* =15.8, 1.4 Hz, 1H), 5.39–5.31 (m, 2H), 4.72 (s, 2H), 3.52–3.47 (m, 1H), 3.32 (s, 3H), 3.28 (t, *J* = 7.3 Hz, 2H), 3.12 (dq, *J* = 10.3, 6.8 Hz, 1H), 2.55 (qd, *J* = 7.3, 1.3 Hz, 2H), 2.44 (s, 3H), 1.33-1.31 (m, 2H), 0.85 (d, *J* = 6.9 Hz, 3H), –0.10 (s, 9H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 202.7, 143.5, 143.0, 142.4, 137.2, 131.4,

129.8, 129.7, 128.4, 128.0 (2C), 127.2, 126.2, 80.4, 55.7, 52.0, 48.9, 45.9, 32.1, 22.8, 21.5, 16.1, –2.0; MS (EI) *m/z* 527 ($M^{+\bullet}$), 495, 480, 397, 382, 228, 91, 73; HRMS (EI) *m/z* calculated for $C_{29}H_{41}NO_4SSi$: 537.2526, found 527.2519.



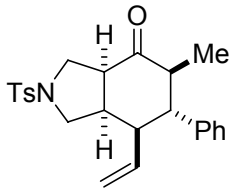
***R*-(2E,4R,5S,7E)*-11-*N*-Methoxymethyl-*N*-tosylamino-5-methyl-1-trimethylsilyl-4-phenylundeca-2,7-dien-6-one (88):** The general procedure **K** was performed employing 0.14 g (0.26 mmol) of alcohol **85** and 0.33 g (0.78 mmol) of Dess-Martin periodinane for 15 min at 0 °C, 45 min at rt. Purification by flash chromatography on SiO_2 (4:1 hexanes/EtOAc) afforded 85 mg (62%) of the title compound as an oil. Isolated compound ratio by HPLC (Zorbax™ Sil column, flow rate 1.0 mL/min, 3.0% *i*-PrOH, 97.0% hexanes): 7.7% (Tr = 8.07), 83.4% (Tr = 9.09), 4.2% (Tr = 9.82), 4.6% (Tr = 10.64): IR (thin film) 3027, 2952, 1693, 1667, 1625, 1599, 1494, 1452, 1343, 1247, 1159, 1079, 962, 852, 702 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.72 (d, *J* = 8.3 Hz, 2H), 7.40–7.12 (m, 7H), 6.82 (dt, *J* = 15.7, 6.8 Hz, 1H), 6.18 (dt, *J* = 15.7, 1.4 Hz, 1H), 5.45–5.29 (m, 2H), 4.72 (s, 2H), 3.56–3.46 (m, 1H), 3.32 (s, 3H), 3.17 (t, *J* = 7.2 Hz, 2H), 3.17–3.05 (m, 1H), 2.43 (s, 3H), 2.23 (q, *J* = 7.2 Hz, 2H), 1.78 (p, *J* = 7.2 Hz, 2H), 1.33–1.31 (m, 2H), 0.86 (d, *J* = 6.9 Hz, 3H), –0.10 (s, 9H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 202.9, 145.5, 143.4, 143.1, 137.3, 130.1, 129.9, 129.6, 128.4, 128.1, 127.9, 127.2, 126.2, 80.2, 55.7, 52.0, 49.1, 46.8, 29.5, 27.3, 22.8, 21.5, 16.2, –2.0; MS (ESI) *m/z* 564 $(M+Na)^+$; HRMS (ESI) *m/z* calculated for $NaC_{30}H_{43}NO_4SSi$ $(M+Na)^+$: 564.2580, found 564.2560.

General Procedure L for Tandem Intermolecular Sakurai-Mannich Reactions 70, 89-91: To 1.5-2.0 mL (1.5-2.0 mmol) of a vigorously stirred solution of $TiCl_4$ in CH_2Cl_2 (1.0 M) at –78 °C was slowly cannulated the unsaturated ketone (1.0 mmol) in 20 mL of CH_2Cl_2 (clear → deep red). The cannula and receptacle were washed with 2x1 mL of CH_2Cl_2 and added to the reaction vessel. Following 15 min of stirring at –78 °C, the reaction was warmed to rt over 15-20 min (red → yellow-brown precipitate). The reaction was quenched with H_2O and the aqueous layer was extracted with CH_2Cl_2 (3x), the combined organic layers were dried over Na_2SO_4 and filtered. Removal of the solvent *in vacuo* yielded the crude product, which was purified as specified. Isolated diastereomeric ratio was established by HPLC analysis.

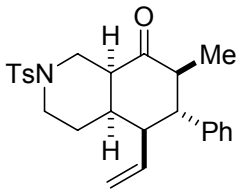


***R**-2-*N*-Benzyl-*N*-2-(1*S*,2*S*,3*R*,4*S*)-4-methyl-5-oxo-3-phenyl-2-vinylcyclohexylethylamino-acetonitrile (70):** The general procedure **L** was performed with 58 mg (0.13 mmol) of ketone **69** and 0.20 mL (0.20 mmol) of $TiCl_4$ in CH_2C1_2 (1M) for 30 min at –78 °C followed by quenching with H_2O at this temperature. Purification *via* flash chromatography on SiO_2 (5:1 hexanes/EtOAc) yielded 39 mg (77%) of the product as an oil. The diastereomeric ratio was not determined for this substrate: IR (thin film) 3062, 2970, 1709, 1639, 1494, 1453, 918, 740, 700 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.35–7.14 (m, 10H), 5.55 (ddd, *J* = 17.8, 9.9, 8.2 Hz, 1H), 4.88 (br. d, *J* = 12.1 Hz, 1H), 4.88 (br. d, *J* = 15.2 Hz, 1H), 3.70 (d, *J* = 13.2 Hz, 1H), 3.60 (d, *J* = 13.2 Hz, 1H), 3.42 (s, 2H), 3.08–2.98 (m, 1H), 2.77–2.60 (m, 5H), 2.51 (dd, *J* = 13.5, 3.5 Hz, 1H), 2.48–2.39 (m, 1H), 1.84–1.73 (m, 1H), 1.36–1.24 (m, 1H), 0.80 (d, *J* = 5.8 Hz, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 211.3, 142.2, 138.6, 137.0, 128.9, 128.6 (2C), 127.9, 127.7, 126.7,

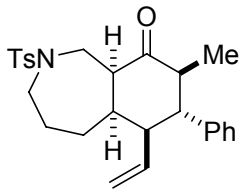
117.0, 114.6, 58.3, 52.6, 51.8, 50.6, 50.1, 45.1, 41.1, 39.4, 24.7, 10.0; MS (EI) *m/z* 386 ($M^{+\bullet}$), 346, 295, 159, 91; HRMS (EI) *m/z* calculated for $C_{26}H_{30}N_2O$: 386.2358, found 386.2348.



***R**-(3a*S*,5*S*,6*R*,7*R*,7a*R*)-Octahydro-5-methyl-6-phenyl-2-tosyl-7-vinylisoindol-4-one (89):** The general procedure **L** was performed with 47 mg (0.091 mmol) of ketone **86** and 0.18 mL (0.18 mmol) of $TiCl_4$ in CH_2C1_2 (1M). Purification *via* flash chromatography on SiO_2 (1:1 hexanes/Et_2O) yielded 15 mg (41%) of the product as an oil. Isolated diastereomeric ratio by HPLC (Zorbax^{TM} Sil column, flow rate 1.0 mL/min, 15.0% EtOAc, 85.0% hexanes): 100% (Tr = 29.16): IR (thin film) 3028, 2974, 1714, 1641, 1598, 1454, 1341, 1160, 921, 703 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.77 (d, *J* = 8.2 Hz, 2H), 7.37–7.17 (m, 5H), 7.06 (d, *J* = 8.4 Hz, 2H), 5.32 (ddd, *J* = 16.5, 10.8, 8.6 Hz, 1H), 4.83 (d, *J* = 10.3 Hz, 1H), 4.82 (d, *J* = 17.4 Hz, 1H), 4.23 (d, *J* = 9.8 Hz, 1H), 3.54 (td, *J* = 6.9, 1.4 Hz, 1H), 3.26 (dd, *J* = 9.8, 6.2 Hz, 1H), 3.15–3.07 (m, 1H), 3.07 (t, *J* = 6.0 Hz, 1H), 2.97–2.87 (m, 1H), 2.84 (dd, *J* = 11.6, 8.5 Hz, 1H), 2.70–2.59 (m, 1H), 2.48 (t, *J* = 11.7 Hz, 1H), 2.46 (s, 3H), 0.67 (d, *J* = 6.4 Hz, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 207.3, 143.4, 140.9, 137.2, 134.6, 129.6, 128.7, 127.8, 127.5, 127.0, 117.6, 51.7, 50.9, 49.2, 46.6 (3C), 46.3, 21.6, 12.2; MS (EI) *m/z* 409 ($M^{+\bullet}$), 254, 227, 222, 155, 136; HRMS (EI) *m/z* calculated for $C_{24}H_{27}NO_3S$: 409.1712, found 409.1712.

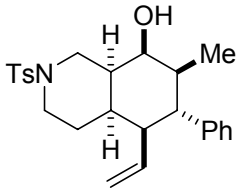


***R**-(4a*R*,5*S*,6*R*,7*S*,8a*S*)-Octahydro-7-methyl-6-phenyl-2-tosyl-5-vinylisoquinolin-8(8aH)-one (90):** The general procedure **L** was performed with 0.15 g (0.28 mmol) of ketone **87** and 0.42 mL (0.42 mmol) of $TiCl_4$ in CH_2C1_2 (1M). Purification *via* flash chromatography on SiO_2 (3:1 hexanes/EtOAc) yielded 57 mg (46%) of the product as a white solid. Isolated diastereomeric ratio by HPLC (Zorbax™ Sil column, flow rate 1.0 mL/min, 15.0% EtOAc, 85.0% hexanes): 100% (Tr = 18.16): m.p. 191-193 °C; IR (thin film) 2926, 1714, 1598, 1494, 1454, 1340, 1165, 914, 817, 720 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.72 (d, *J* = 8.2 Hz, 2H), 7.34–7.15 (m, 5H), 7.10 (d, *J* = 8.2 Hz, 2H), 5.48 (ddd, *J* = 17.6, 9.9, 8.5 Hz, 1H), 4.82 (br. d, *J* = 15.7 Hz, 1H), 4.81 (br. d, *J* = 11.9 Hz, 1H), 4.40 (dt, *J* = 11.5, 1.7 Hz, 1H), 3.82 (d, *J* = 11.4 Hz, 1H), 3.02 (ddd, *J* = 11.6, 8.6, 4.1 Hz, 1H), 2.81 (s, 1H), 2.66 (t, *J* = 11.8 Hz, 1H), 2.53 (p, *J* = 6.3 Hz, 1H), 2.44 (s, 3H), 2.25–2.13 (m, 3H), 1.76 (dd, *J* = 13.0, 2.2 Hz, 1H), 1.46 (qd, *J* = 12.9, 4.0 Hz, 1H), 0.86 (d, *J* = 6.4 Hz, 3H); ^{13}C-NMR (75 MHz, D_6-DMSO, 353 K): δ 207.0, 143.3, 141.9, 138.1, 133.6, 129.5, 128.6, 128.0 (2C), 126.8, 117.0, 51.2, 50.2, 50.1, 48.3, 46.0, 44.4, 43.5, 23.2, 21.5, 12.3; MS (EI) *m/z* 423 ($M^{+\bullet}$), 358, 304, 268, 155, 91; HRMS (EI) *m/z* calculated for $C_{25}H_{29}NO_3S$: 423.1868, found 423.1871.



***R**-(5a*R*,6*S*,7*R*,8*S*,9a*S*)-Octahydro-8-methyl-7-phenyl-2-tosyl-6-vinyl-1H-benzo[c]azepin-9(9aH)-one (91):** The general procedure **L** was performed with 85 mg (0.16 mmol) of ketone **88** and 0.32 mL (0.32 mmol) of $TiCl_4$ in CH_2C1_2 (1M). Purification *via* flash chromatography on SiO_2 (3:1 hexanes/EtOAc) yielded 31 mg (44%) of the product as a white foam. Isolated

diastereomeric ratio by HPLC (Zorbax™ Sil column, flow rate 1.0 mL/min, 15.0% EtOAc, 85.0% hexanes): 87.9% (Tr = 8.46), 12.1% (Tr = 10.72): IR (thin film) 3027, 2976, 1704, 1599, 1494, 1454, 1335, 1157, 924, 701 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.69 (d, *J* = 8.2 Hz, 2H), 7.35–7.10 (m, 7H), 5.50 (ddd, *J* = 17.9, 10.6, 7.5 Hz, 1H), 4.91 (br. d, *J* = 17.8 Hz, 1H), 4.90 (br. d, *J* = 10.5 Hz, 1H), 3.99 (dd, *J* = 13.8, 4.0 Hz, 1H), 3.89 (dd, *J* = 15.5, 7.6 Hz, 1H), 3.48–3.32 (m, 2H), 3.10 (ddd, *J* = 11.3, 7.4, 3.9 Hz, 1H), 2.74 (dt, *J* = 9.4, 4.7 Hz, 1H), 2.65–2.49 (m, 2H), 2.44 (s, 3H), 1.82 (dt, *J* = 14.2, 3.6 Hz, 1H), 1.77–1.52 (m, 3H), 1.08–0.94 (m, 1H), 0.76 (d, *J* = 6.1 Hz, 3H); ^{13}C-NMR (75 MHz, D_3CCN): δ 211.7, 144.5, 143.7, 140.7, 138.3, 130.8, 129.4, 129.1, 127.6, 127.5, 117.0, 53.1, 53.0, 52.8, 51.4, 51.3, 48.0, 47.3, 30.8, 24.2, 21.5, 12.6; MS (EI) *m/z* 437 ($M^{+\bullet}$), 282, 197, 179; HRMS (EI) *m/z* calculated for $C_{26}H_{31}NO_3S$: 437.2025, found 437.2027.

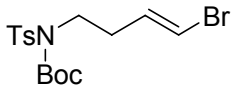


***R**-(4a*R*,5*S*,6*R*,7*S*,8*S*,8a*S*)-Decahydro-7-methyl-6-phenyl-2-tosyl-5-vinylisoquinolin-8-ol (95):** To 0.010 g (0.024 mmol) of perhydroisoquinilone **90** in 0.24 mL of toluene was added 29 μL (0.029 mmol) of DIBAl-H in hexanes (1.0 M). Following 30 min, the reaction was quenched with sat. aq. Rochelle's salt and stirred 30 min while warming to rt. The aqueous layer was extracted with EtOAc (3x) and the combined organic layers were dried over Na_2SO_4 and filtered. Concentration of the extracts *in vacuo* gave 8.5 mg (83%) of the pure product as a white solid. Diastereomeric ratio by ^{1}H-NMR (300 MHz, $CDCl_3$) (C–C**H$_3$**): 10% (δ 0.83), 90% (δ 0.75): m.p. 249-251 °C; IR (thin film) 3496, 3061, 2852, 1597, 1343, 1162, 939, 714, 701 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.68 (d, *J* = 8.3 Hz, 2H), 7.36 (d, *J* = 8.1 Hz, 2H), 7.28–7.08 (m, 5H), 5.51

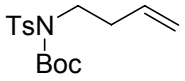
(ddd, J = 16.9, 10.4, 9.0 Hz, 1H), 4.72–4.65 (m, 2H), 4.15 (s, 1H), 3.99–3.88 (m, 2H), 3.40 (s, 1H), 2.79 (t, J = 11.5 Hz, 1H), 2.56–2.48 (m, 1H), 2.48–2.43 (m, 1H), 2.46 (s, 3H), 2.37–2.25 (m, 1H), 2.20–2.10 (m, 1H), 1.85 (s, 1H), 1.78–1.63 (m, 3H), 0.75 (d, J = 6.8 Hz, 3H); MS (ESI) *m/z* 448 $(M+Na)^+$; HRMS (ESI) *m/z* calculated for $NaC_{25}H_{31}NO_3S$ $(M+Na)^+$: 448.1922, found 448.1907.

6.0 EXPERIMENTAL SECTION FOR CHAPTER 2

General Procedure A for Synthesis of Boc-Protected Sulfonamides 111 & 126:[79] To a solution of the sulfonamide (1.5 mmol) in 9.1 mL THF was added 0.79 g (3.0 mmol) of PPh_3. The alcohol (1.0 mmol) was then added followed by 0.30 mL (0.30 g, 1.5 mmol) of DIAD. The mixture was stirred between 3-12 h, concentrated *in vacuo*, and the crude product was purified by flash chromatography under the specified conditions.

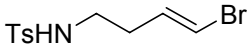


***N*-*Tert*-butylcarbamate-*N*-tosyl-(*E*)-4-bromobut-3-ene (111):** The general procedure **A** was performed employing 0.54 g (2.0 mmol) of *t*-butyl-*N*-tosyl-carbamate and 0.20 g (1.3 mmol) of (*E*)-4-bromobut-3-en-1-ol.[120] Flash chromatography on SiO_2 (10:1 hexanes/EtOAc) afforded 0.47 g (92%) of the product as a white solid: m.p. 70-72 °C; IR (thin film) 2980, 1727, 1622, 1598, 1447, 1356, 1287, 1258, 1156, 814 cm^{-1}; ^{1}H-NMR (300 MHz, D_6-DMSO, 353 K): δ 7.77 (d, *J* = 8.4 Hz, 2H), 7.42 (d, *J* = 8.0 Hz, 2H), 6.34 (dt, *J* = 13.5, 1.2 Hz, 1H), 6.18 (dt, *J* = 13.5, 7.2 Hz, 1H), 3.85 (t, *J* = 7.0 Hz, 2H), 2.44 (qd, *J* = 7.2, 1.2 Hz, 2H), 2.42 (s, 3H), 1.30 (s, 9H); ^{13}C-NMR (75 MHz, D_6-DMSO, 353 K): δ 149.9, 143.6, 136.7, 133.8, 128.9, 126.9, 106.3, 83.4, 44.8, 32.5, 27.0, 20.4; MS (EI) *m/z* 349, 347 ($M^{+\bullet}$-^{t}Bu), 268, 184, 155, 91; HRMS (EI) *m/z* calculated for $C_{12}H_{14}NO_4SBr$ ($M^{+\bullet}$-^{t}Bu): 346.9827, found 346.9830.



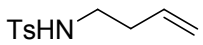
***N*-*Tert*-butylcarbamate-*N*-tosyl-(*E*)-but-3-ene (126):** The general procedure **A** was performed employing 1.0 g (3.7 mmol) of *t*-butyl-*N*-tosyl-carbamate and 0.21 mL (0.18 g, 2.5 mmol) of 3-butene-1-ol. Flash chromatography on SiO_2 (10:1 hexanes/EtOAc) afforded 0.80 g (100%) of the product as a white solid: m.p. 56-57 °C; IR (thin film) 3078, 2980, 1729, 1643, 1598, 1449, 1356, 1258, 1155, 919, 812 cm^{-1}; ^{1}H-NMR (300 MHz, D_6-DMSO, 353 K): δ 7.77 (d, *J* = 8.4 Hz, 2H), 7.42 (d, *J* = 8.1 Hz, 2H), 5.80 (ddt, *J* = 17.1, 10.2, 6.8 Hz, 1H), 5.10 (dq, *J* = 17.3, 1.4 Hz, 1H), 5.06 (dq, *J* = 10.3, 1.2 Hz, 1H), 3.83 (t, *J* = 7.2 Hz, 2H), 2.42 (qt, *J* = 7.2, 1.3 Hz, 2H), 2.41 (s, 3H), 1.29 (s, 9H); ^{13}C-NMR (75 MHz, D_6-DMSO, 353 K): δ 150.0, 143.5, 136.9, 134.1, 128.8, 126.9, 116.4, 83.2, 45.4, 33.4, 27.0, 20.4; MS (EI) *m/z* 284 ($M^{+\bullet}$-allyl), 269, 184, 155; HRMS (EI) *m/z* calculated for $C_{13}H_{18}NO_4S$ ($M^{+\bullet}$-allyl): 284.0957, found 284.0954.

General Procedure B for the Deprotection of Boc-Protected Sulfonamides 112 & 127:[79] To the carbamate (1.0 mmol) in 3.3 mL CH_2Cl_2 was slowly added 0.23 mL (0.34 g, 3.0 mmol) of trifluoroacetic acid at rt. Following 16 h, the reaction mixture was cooled to 0 °C and carefully quenched with sat. aq. $NaHCO_3$. The aqueous layer was extracted with CH_2Cl_2 (3x) and the combined organic layers were dried over Na_2SO_4, filtered, and the crude product was concentrated *in vacuo*. The product was purified by flash chromatography under the specified conditions.



(*E*)-4-Bromo-*N*-tosylbut-3-en-1-amine (112): General procedure **B** was carried out with 0.23 g (0.57 mmol) of carbamate **111**. Flash chromatography on SiO_2 (4:1 hexanes/EtOAc) yielded

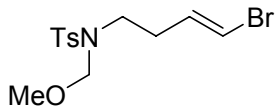
0.15 g (86%) of the product as a white solid: m.p. 55-57 °C; IR (thin film) 3281, 3065, 2924, 1622, 1598, 1422, 1324, 1158, 940, 814, 550 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.75 (d, *J* = 8.3 Hz, 2H), 7.33 (d, *J* = 8.0 Hz, 2H), 6.08 (d, *J* = 13.6 Hz, 1H), 5.99 (dt, *J* = 13.6, 6.6 Hz, 1H), 4.43 (br. t, *J* = 5.8 Hz, 1H), 3.03 (q, *J* = 6.6 Hz, 2H), 2.45 (s, 3H), 2.23 (q, *J* = 6.6 Hz, 2H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 143.4, 136.5, 133.5, 129.6, 126.9, 107.2, 41.7, 32.8, 21.4; MS (EI) *m/z* 304 ($M^{+\bullet}$), 302, 240, 224, 184, 155, 91; HRMS (EI) *m/z* calculated for $C_{11}H_{14}NO_2SBr$: 302.9929, found 302.9922.



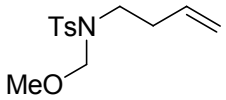
***N*-Tosylbut-3-en-1-amine (127):** General procedure **B** was carried out with 0.40 g (1.2 mmol) of carbamate **126**. Flash chromatography on SiO_2 (5:1 hexanes/EtOAc) yielded 0.27 g (100%) of the product as an oil: IR (thin film) 3281, 3078, 2979, 1642, 1598, 1495, 1325, 1160, 918, 815 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.75 (d, *J* = 8.3 Hz, 2H), 7.32 (d, *J* = 8.5 Hz, 2H), 5.63 (ddt, *J* = 17.1, 10.3, 6.9 Hz, 1H), 5.08 (dq, *J* = 10.3, 1.1 Hz, 1H), 5.04 (dq, *J* = 17.0, 1.5 Hz, 1H), 4.39 (m, 1H), 3.03 (q, *J* = 6.6 Hz, 2H), 2.21 (qt, *J* = 6.7, 1.2 Hz, 2H), 2.44 (s, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 143.3, 136.9, 134.1, 129.6, 127.0, 117.8, 42.1, 33.5, 21.4; MS (EI) *m/z* 225 ($M^{+\bullet}$), 198, 184, 155, 91, 65; HRMS (EI) *m/z* calculated for $C_{11}H_{15}NO_2S$: 225.0824, found 225.0821.

General Procedure C for Preparation of Methoxyaminals 113 & 128: To a solution of the sulfonamide (1.0 mmol) in 10 mL of THF was added 1.1 mL (1.1 mmol) of KHMDS in toluene (0.5M) at 0 °C. After 5 min, 0.23 mL (0.24 g, 3.0 mmol) of chloromethyl methyl ether was added dropwise and the mixture was stirred for 15 min at 0 °C then raised to rt for 15 min. The

reaction was quenched with H_2O, partitioned between H_2O and Et_2O and the aqueous layer was extracted with Et_2O (3x). The combined organic extracts were dried over Na_2SO_4, filtered and the crude product was concentrated *in vacuo*. The products were purified by flash chromatography under the specified conditions.

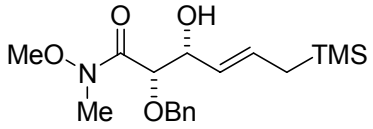


(*E*)-4-Bromo-*N*-methoxymethyl-*N*-tosylbut-3-en-1-amine (113): General procedure **C** was performed using 0.30 g (0.99 mmol) of sulfonamide **112**. Flash chromatography on SiO_2 (7:1 hexanes/EtOAc) gave 0.26 g (76%) of the product as an oil: IR (thin film) 3066, 2931, 1621, 1598, 1495, 1453, 1341, 1159, 1082, 941, 815, 583 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.71 (d, J = 8.3 Hz, 2H), 7.31 (d, J = 8.0 Hz, 2H), 6.09 (d, J = 13.6 Hz, 1H), 6.02 (dt, J = 13.5, 6.9 Hz, 1H), 4.71 (s, 2H), 3.32 (s, 3H), 3.21 (t, J = 7.2 Hz, 2H), 2.44 (s, 3H), 2.35 (q, J = 7.4 Hz, 2H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 143.5, 137.0, 133.9, 129.7, 127.1, 106.8, 80.3, 55.6, 46.0, 32.6, 21.5; MS (EI) *m/z* 318 ($M^{+\bullet}$-OMe), 228, 198, 155, 139, 91, 65; HRMS (EI) *m/z* calculated for $C_{12}H_{15}NO_2SBr$ ($M^{+\bullet}$-OMe): 316.0007, found 315.9992.



***N*-Methoxymethyl-*N*-tosylbut-3-en-1-amine (128):** General procedure **C** was performed using 0.13 g (0.58 mmol) of sulfonamide **127**. Flash chromatography on SiO_2 (5:1 hexanes/EtOAc) gave 0.14 g (90%) of the product as an oil: IR (thin film) 3077, 2935, 1642, 1598, 1495, 1453, 1341, 1159, 1077, 943, 815 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.73 (d, J = 8.3 Hz, 2H), 7.30

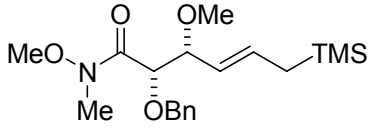
(d, *J* = 8.3 Hz, 2H), 5.69 (ddt, *J* = 17.0, 10.2, 6.8 Hz, 1H), 5.05 (dq, *J* = 17.1, 1.5 Hz, 1H), 5.02 (dm, *J* = 10.2 Hz, 1H), 4.73 (s, 2H), 3.28 (s, 3H), 3.22 (t, *J* = 7.6 Hz, 2H), 2.39 (s, 3H), 2.34 (qd, *J* = 7.6, 1.1 Hz, 2H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 143.3, 137.4, 134.6, 129.5, 127.1, 116.9, 80.0, 55.6, 46.4, 33.1, 21.4; MS (EI) *m/z* 238 ($M^{+\bullet}$-OMe), 228, 198, 155, 139, 91, 65; HRMS (EI) *m/z* calculated for $C_{12}H_{16}NO_2S$ ($M^{+\bullet}$-OMe): 238.0902, found 238.0896.



(*E*,2*S*,3*R*)-2-Benzyloxy-3-hydroxy-*N*-methoxy-*N*-methyl-6-trimethylsilylhex-4-enamide (117):[128] A round bottom flask equipped with a condenser was charged with 43 mg (0.16 mmol) of (2*S*,3*R*)-2-benzyloxy-3-hydroxy-N-methoxy-*N*-methylpent-4-enamide and 0.80 mL of CH_2Cl_2.[125, 229] To this mixture was cannulated a premixed solution of 0.10 mL (74 mg, 0.64 mmol) of trimethylallylsilane and 6.8 mg (0.0080 mmol) of Grubbs II catalyst (stored in glovebox) in 0.80 mL of CH_2Cl_2. The reaction was stirred for 15 min at rt, heated to reflux for 2 h then cooled to rt and quenched with 28 μL of DMSO. After 12 h further stirring at rt, the mixture was concentrated *in vacuo*. Purification by flash chromatography on SiO_2 (2:1 hexanes:EtOAc) afforded 43 mg (75%) of the product as a brown oil. Geometrical isomer ratio by ^{1}H-NMR (300 MHz, $CDCl_3$) (CH_2–C**H**=CH–CH–O**H**): 87% (δ 5.77), 13% (δ 5.64) and 87% (δ 2.72), 13% (δ 2.66): $[\alpha]_D^{26}$ = –44.4 (c 1.20, $CHCl_3$); IR (thin film) 3454, 3030, 2952, 1663, 1497, 1455, 1248, 1094, 989, 854, 739 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.39–7.28 (m, 5H), 5.77 (dtd, *J* = 15.3, 8.2, 0.8 Hz, 1H), 5.34 (ddt, *J* = 15.2, 7.4, 1.3 Hz, 1H), 4.74 (d, *J* = 11.7 Hz, 1H), 4.51 (d, *J* = 11.7 Hz, 1H), 4.37 (td, *J* = 7.0, 3.8 Hz, 1H), 4.30 (br. d, *J* = 5.6 Hz, 1H), 3.58 (s, 3H), 3.19 (s, 3H), 2.72 (d, *J* = 3.7 Hz, 1H), 1.48 (dt, *J* = 8.2, 1.3 Hz, 2H), –0.01 (s, 9H); ^{13}C-

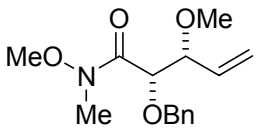
NMR (75 MHz, $CDCl_3$): δ 170.8, 137.3, 131.9, 128.4, 128.1, 127.9, 125.6, 78.8, 73.7, 72.1, 61.3, 32.4, 23.0, –2.0; MS (ESI) *m/z* 374 $(M+Na)^+$; HRMS (ESI) *m/z* calculated for $NaC_{18}H_{29}NO_4Si$ $(M+Na)^+$: 374.1764, found 374.1755.

General Procedure D for O-Methylation 118 & 121:[131] To a mixture of the hydroxyamide (1.0 mmol) and 0.62 mL (1.4 g, 10 mmol) of iodomethane in 10 mL of 2:1 THF:DMF was added 0.10 g (2.5 mmol) of sodium hydride (60% dispersion in mineral oil) in portions. Following the specified time period, the reaction was quenched at 0 °C with aq. pH 7 buffer and the aqueous layer was extracted with Et_2O (3x). The combined organic extracts were dried over Na_2SO_4, filtered and concentrated *in vacuo*. The compounds were purified by flash chromatography under the specified conditions.



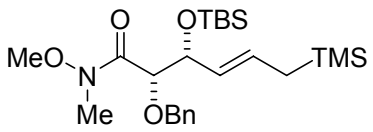
(*E*,2*S*,3*R*)-2-Benzyloxy-*N*-3-dimethoxy-*N*-methyl-6-trimethylsilylhex-4-enamide (118): General procedure **D** was performed using 59 mg (0.17 mmol) of hydroxyamide **117** for 1.5 h. Flash chromatography on SiO_2 (2x) (4:1 hexanes/EtOAc) gave 48 mg (76%) of the product as an oil: $[\alpha]_D^{26}$ = –23.8 (c 1.04, $CHCl_3$); IR (thin film) 3030, 2953, 1673, 1497, 1454, 1248, 1097, 991, 853, 698 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.12–6.96 (m, 5H), 5.45 (dt, J = 15.3, 8.1 Hz, 1H), 4.94 (dd, J = 15.3, 8.8 Hz, 1H), 4.46 (d, J = 12.1 Hz, 1H), 4.33 (d, J = 12.2 Hz, 1H), 4.12 (br. s, 1H), 3.68 (dd, J = 8.5, 7.1 Hz, 1H), 3.22 (s, 3H), 3.04 (s, 3H), 2.87 (s, 3H), 1.26–1.19 (m, 2H), –0.27 (s, 9H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 170.7, 138.0, 133.8, 128.2, 127.9, 127.1, 123.7, 83.7, 78.8, 72.2, 61.1, 56.3, 32.6, 23.1, –1.9; MS (EI) *m/z* 351 ($M^{+\bullet}$+H, -Me), 281, 224,

228, 209, 190, 157; HRMS (ESI) *m/z* calculated for $NaC_{19}H_{31}NO_4Si$ $(M+Na)^+$: 388.1920, found 388.1885.

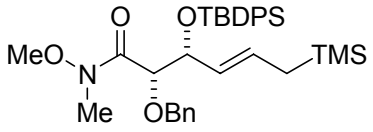


(2*S*,3*R*)-2-Benzyloxy-*N*-3-dimethoxy-*N*-methylpent-4-enamide (121): General procedure **D** was performed using 0.050 g (0.19 mmol) of (2*S*,3*R*)-2-benzyloxy-3-hydroxy-N-methoxy-*N*-methylpent-4-enamide for 16-18 hr. Flash chromatography on SiO_2 (2:1 hexanes/EtOAc) gave 32 mg (58%) of the product as an oil: $[\alpha]_D^{26} = -34.4$ (c 1.04, $CHCl_3$); IR (thin film) 3030, 2936, 1670, 1497, 1454, 1093, 991, 739 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.40–7.25 (m, 5H), 5.77 (ddd, J = 17.7, 10.3, 7.9 Hz, 1H), 5.31 (d, J = 17.3 Hz, 1H), 5.29 (d, J = 10.3 Hz, 1H), 4.75 (d, J = 12.2 Hz, 1H), 4.59 (d, J = 12.2 Hz, 1H), 4.42 (br. d, J = 5.6 Hz, 1H), 4.01 (t, J = 7.3 Hz, 1H), 3.49 (s, 3H), 3.37 (s, 3H), 3.16 (s, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 170.5, 137.8, 134.1, 128.3, 127.9, 127.7, 119.5, 83.9, 78.5, 72.3, 61.1, 57.2, 32.5; MS (EI) *m/z* 280 ($M^{+\bullet}$+H), 264, 248, 219, 180, 173, 141, 111; HRMS (EI) *m/z* calculated for $C_{15}H_{22}NO_4$ ($M^{+\bullet}$+H): 280.1549, found 280.1551.

General Procedure E for O-Silylation 119, 120, 136: To the alcohol (1.0 mmol) in 3.3 mL of DMF was added 12 mg (0.10 mmol) of DMAP and 0.12 g (1.8 mmol) of imidazole followed by the chlorosilane (1.5 mmol). The reaction was quenched after 12 h by the addition of brine and the aqueous layer was extracted with CH_2Cl_2 (3x). The combined organic layers were dried over Na_2SO_4, filtered and concentrated *in vacuo*. The products were purified by flash chromatography under the specified conditions.



(*E*,2*S*,3*R*)-2-Benzyloxy-3-*tert*-butyldimethylsilyloxy-*N*-methoxy-*N*-methyl-6-trimethylsilylhex-4-enamide (119): General procedure **E** was carried out with 37 mg (0.11 mmol) of hydroxyamide **117** and 26 mg (0.17 mmol) of *t*-butyldimethylsilyl chloride. Purification *via* flash chromatography on SiO_2 (8:1 hexanes/EtOAc) provided 41 mg (80%) of the product as a clear oil: $[\alpha]_D^{26} = -11.9$ (c 1.08, $CHCl_3$); IR (thin film) 2954, 2856, 1672, 1463, 1249, 1115, 967, 837, 777 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.38–7.26 (m, 5H), 5.64 (dt, *J* = 15.2, 8.1 Hz, 1H), 5.26 (dd, *J* = 15.3, 7.5 Hz, 1H), 4.68 (d, *J* = 12.1 Hz, 1H), 4.59 (d, *J* = 12.2 Hz, 1H), 4.42 (t, *J* = 7.5 Hz, 1H), 4.29 (br. d, *J* = 6.5 Hz, 1H), 3.45 (s, 3H), 3.12 (s, 3H), 1.44–1.41 (m, 2H), 0.90 (s, 9H), 0.09 (s, 3H), 0.07 (s, 3H), 0.00 (s, 9H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 171.6, 138.1, 130.2, 128.1, 127.9, 127.5, 127.2, 80.5, 75.7, 72.5, 61.1, 32.4, 25.9, 22.9, 18.2, –1.9, –4.4; MS (EI) *m/z* 450 ($M^{+\bullet}$-OMe), 408, 257, 232, 190, 127, 115, 73; HRMS (EI) *m/z* calculated for $C_{20}H_{34}NO_4Si_2$ ($M^{+\bullet}$-^{t}Bu): 408.2026, found 408.2027.

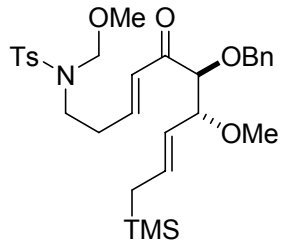


(*E*,2*S*,3*R*)-2-Benzyloxy-3-*tert*-butyldiphenylsilyloxy-*N*-methoxy-*N*-methyl-6-trimethylsilylhex-4-enamide (120): General procedure **E** was carried out with 0.080 g (0.23 mmol) of hydroxyamide **117** and 87 μL (93 mg, 0.34 mmol) of *t*-butyldiphenylsilyl chloride. Purification *via* flash chromatography on SiO_2 (8:1 hexanes/EtOAc) provided 0.12 g (87%) of the product as a clear oil: $[\alpha]_D^{26} = -29.4$ (c 1.14, $CHCl_3$); IR (thin film) 3070, 2955, 1669, 1472,

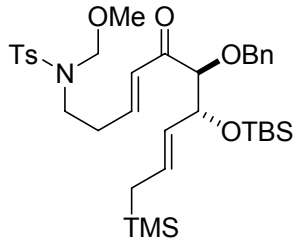
1427, 1248, 1076, 852, 701 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.71 (d, *J* = 6.6 Hz, 2H), 7.66 (d, *J* = 6.7 Hz, 2H), 7.40–7.22 (m, 11H), 5.33–5.19 (m, 2H), 4.64–4.52 (m, 1H), 4.56 (d, *J* = 12.4 Hz, 1H), 4.47 (d, *J* = 11.5 Hz, 1H), 4.36 (br. s, 1H), 3.42 (s, 3H), 3.03 (s, 3H), 1.24 (d, *J* = 6.6 Hz, 2H), 1.05 (s, 9H), –0.13 (s, 9H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 171.0, 137.8, 136.1, 136.0, 134.4 (2C), 131.3, 129.2 (2C), 128.0 (2C), 127.4, 127.2, 127.1, 126.5, 82.0, 76.1, 72.2, 60.9, 32.4, 27.0, 22.7, 19.4, –2.0; MS (EI) *m/z* 574 ($M^{+\bullet}$-Me), 532, 381, 281, 239, 190, 135; HRMS (EI) *m/z* calculated for $C_{33}H_{44}NO_4Si_2$ ($M^{+\bullet}$-Me): 574.2809, found 574.2791.

General Procedure F for Vinyl Lithium Addition to Weinreb Amides 122-124:[132] Addition of *t*-butyllithium to vinyl bromide at –115 °C can occasionally cause the reaction mixture to freeze following several minutes. Addition of the amide solution to this solidified medium remains an effective method for carrying out the reaction.

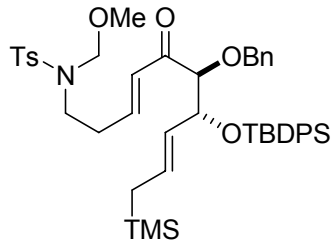
To a solution of 0.52 g (1.5 mmol) of vinyl bromide **113** in 6.5 mL of the Trapp solvent mixture (4:1:1 THF:Et_2O:pentane) was added 2.0 mL (3.0 mmol) of *t*-butyllithium in pentane (titrated to 1.53 M) (clear → yellow) at –115 °C (liquid N_2 in EtOH). Following 10 min, a solution of the Weinreb amide (1.0 mmol) in 6.5 mL of the Trapp solvent mixture was added dropwise *via* a microliter syringe followed by 2 x 2 mL washes with the same solvent system. The reaction was maintained at –115 °C for 10 min and flask was then immersed in an ice water bath (yellow → dark brown) and stirred for 30 min at 0 °C. Quench, workup and purification by flash chromatography were carried out as specified.



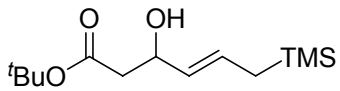
(3*E*,6*S*,7*R*,8*E*)-*N*-Methoxymethyl-*N*-tosylamino-6-benzyloxy-7-methoxy-10-trimethylsilyldeca-3,8-dien-5-one (122): The general procedure **F** was performed employing 0.020 g (0.055 mmol) of Weinreb amide **118**. The reaction was quenched with water and the aqueous layer was extracted with Et_2O (3x). The aqueous layer was then acidified with sat. aq. $NaHSO_4$ and extracted again with Et_2O (3x). The combined organic extracts were dried over Na_2SO_4, filtered and the crude product was concentrated *in vacuo*. Flash chromatography on SiO_2 (4:1 hexanes/EtOAc) afforded 17 mg (55%) of the product as a clear oil: $[\alpha]_D^{26} = -34.2$ (c 1.07, $CHCl_3$); IR (thin film) 3030, 2951, 1694, 1653, 1626, 1598, 1496, 1454, 1343, 1248, 1159, 1079, 970, 853, 816, 698 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.71 (d, J = 8.3, 2H), 7.40–7.25 (m, 7H), 6.78 (dt, J = 15.7, 6.8 Hz, 1H), 6.58 (d, J = 15.8 Hz, 1H), 5.70 (dt, J = 15.3, 8.2 Hz, 1H), 5.29 (dd, J = 15.2, 8.2 Hz, 1H), 4.71 (s, 2H), 4.62 (d, J = 11.8 Hz, 1H), 4.48 (d, J = 11.9 Hz, 1H), 3.85–3.80 (m, 2H), 3.31 (s, 3H), 3.26 (t, J = 7.1 Hz, 2H), 3.20 (s, 3H), 2.52 (q, J = 6.6 Hz, 2H), 2.43 (s, 3H), 1.51 (d, J = 8.1 Hz, 2H), –0.02 (s, 9H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 199.7, 143.5, 143.1, 137.3, 137.2, 133.5, 129.7, 128.4, 128.2, 127.9, 127.8, 127.2, 124.0, 87.3, 83.9, 80.3, 73.5, 56.3, 55.7, 45.8, 32.2, 23.1, 21.5, –1.7; MS (ESI) *m/z* 596 $(M+Na)^+$; HRMS (ESI) *m/z* calculated for $NaC_{30}H_{43}NO_6SSi$ $(M+Na)^+$: 596.2478, found 596.2453.



(3*E*,6*S*,7*R*,8*E*)-*N*-Methoxymethyl-*N*-tosylamino-6-benzyloxy-7-*tert*-butyldimethylsilyloxy-10-trimethylsilyldeca-3,8-dien-5-one (123): The general procedure **F** was performed employing 0.10 g (0.21 mmol) of Weinreb amide **119**. The reaction was quenched with sat. aq. NH_4Cl and the aqueous layer was extracted with Et_2O (3x). The combined organic extracts were dried over Na_2SO_4, filtered and the crude product was concentrated *in vacuo*. Flash chromatography on SiO_2 (3:1 hexanes/Et_2O) afforded 55 mg (39%) of the product as a clear oil: $[\alpha]_D^{26} = -34.2$ (c 0.97 , $CHCl_3$); IR (thin film) 3031, 2929, 1695, 1626, 1496, 1471, 1345, 1160, 1079, 838 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.71 (d, *J* = 8.3 Hz, 2H), 7.38–7.27 (m, 7H), 6.74 (dt, *J* = 15.7, 6.9 Hz, 1H), 6.53 (d, *J* = 15.8 Hz, 1H), 5.58 (dt, *J* = 15.7, 8.4 Hz, 1H), 5.31 (dd, *J* = 15.3, 7.4 Hz, 1H), 4.70 (s, 2H), 4.59 (d, *J* = 12.0 Hz, 1H), 4.44 (d, *J* = 12.0 Hz, 1H), 4.33 (dd, *J* = 7.1, 4.9 Hz, 1H), 3.79 (d, *J* = 4.9 Hz, 1H), 3.31 (s, 3H), 3.23 (t, *J* = 7.2 Hz, 2H), 2.50 (q, *J* = 7.0 Hz, 2H), 2.43 (s, 3H), 1.44 (d, *J* = 7.9 Hz, 2H), 0.84 (s, 9H), 0.06 (s, 3H), 0.01 (s, 3H), 0.02 (s, 9H); ^{13}C-NMR (125 MHz, $CDCl_3$): δ 199.5, 143.5, 142.6, 137.5, 137.1, 129.8, 129.7, 128.5, 128.3, 128.0, 127.7, 127.4, 127.2, 88.5, 80.3, 75.5, 72.9, 55.6, 45.7, 32.2, 25.8, 22.7, 21.5, 18.1, –1.9, –4.4, –4.8; MS (ESI) *m/z* 696 $(M+Na)^+$; HRMS (ESI) *m/z* calculated for $NaC_{35}H_{55}NO_6SSi_2$ $(M+Na)^+$: 696.3186, found 696.3155.

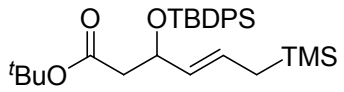


(3*E*,6*S*,7*R*,8*E*)-*N*-Methoxymethyl-*N*-tosylamino-6-benzyloxy-7-*tert*-butyldiphenylsilyloxy-10-trimethylsilyldeca-3,8-dien-5-one (124): The general procedure **F** was performed employing 0.12 g (0.20 mmol) of Weinreb amide **120**. The reaction was quenched with sat. aq. NH_4Cl and the aqueous layer was extracted with Et_2O (3x). The combined organic extracts were dried over Na_2SO_4, filtered and the crude product was concentrated *in vacuo*. Flash chromatography on SiO_2 (3:1 hexanes/Et_2O) afforded 0.10 g (65%) of the product as a clear oil: $[\alpha]_D^{26} = -30.8$ (c 1.18 , $CHCl_3$); IR (thin film) 3031, 2953, 1695, 1626, 1428, 1345, 1160, 1112, 1078, 852, 702 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.75–7.64 (m, 6H), 7.40–7.18 (m, 13H), 6.69 (dt, *J* = 15.8, 6.8 Hz, 1H), 6.46 (d, *J* = 15.8 Hz, 1H), 5.27 (dd, *J* = 15.3, 7.1 Hz, 1H), 5.16 (dt, *J* = 15.3, 7.8 Hz, 1H), 4.69 (s, 2H), 4.43 (d, *J* = 11.8 Hz, 1H), 4.45–4.38 (m, 1H), 4.30 (d, *J* = 11.6 Hz, 1H), 3.80 (d, *J* = 5.2 Hz, 1H), 3.20 (s, 3H), 3.18 (t, *J* = 7.5 Hz, 2H), 2.44 (q, *J* = 7.4 Hz, 2H), 2.42 (s, 3H), 1.27–1.12 (m, 2H), 0.99 (s, 9H), –0.15 (s, 9H); ^{13}C-NMR (125 MHz, $CDCl_3$): δ 198.9, 143.5, 142.6, 137.5, 137.1, 136.0, 135.9, 133.9 (2C), 131.0, 129.6, 129.5, 129.3, 128.3, 128.2, 127.9, 127.6, 127.4, 127.2, 127.1, 126.2, 88.5, 80.3, 76.2, 72.7, 55.6, 45.7, 32.2, 26.9, 22.6, 21.4, 19.3, –2.1; MS (ESI) *m/z* 820 $(M+Na)^+$; HRMS (ESI) *m/z* calculated for $NaC_{45}H_{59}NO_6SSi_2$ $(M+Na)^+$: 820.3499, found 820.3463.



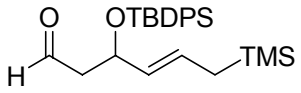
(*E*)-*Tert*-butyl-3-hydroxy-6-trimethylsilylhex-4-enoate (135):[128] A round bottom flask equipped with a condenser was charged with 0.50 g (2.9 mmol) of *tert*-butyl 3-hydroxypent-4-

enoate and 14.5 mL of CH_2Cl_2.[139] To this mixture was cannulated a premixed solution of 1.9 mL (1.4 g, 12 mmol) of trimethylallylsilane and 0.13 g (0.15 mmol) of Grubbs II catalyst (stored in glovebox) in 14.5 mL of CH_2Cl_2. The reaction was stirred for 15 min at rt, heated to reflux for 22 h then cooled to rt and quenched with 0.52 mL of DMSO. After 12 h further stirring at rt, the mixture was concentrated *in vacuo*. Purification by flash chromatography on SiO_2 (3:1 hexanes:Et_2O) afforded 0.54 g (72%) of the product as a brown oil. Geometrical isomer ratio by ^{1}H-NMR (300 MHz, $CDCl_3$) (C**H**–O**H**): 9% (δ 4.75), 91% (δ 4.44) and 87% (δ 2.94), 13% (δ 2.83) (Avg. = 89:11 *E*:*Z*): IR (thin film) 3439, 2978, 1731, 1393, 1249, 1155, 965, 852 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 5.71 (dt, *J* = 15.3, 8.2 Hz, 1H), 5.33 (dd, *J* = 15.2, 6.8 Hz, 1H), 4.44 (p, *J* = 6.5 Hz, 1H), 2.94 (d, *J* = 4.0 Hz, 1H), 2.49-2.41 (m, 2H), 1.59-1.40 (m, 2H), 1.47 (s, 9H), 0.00 (s, 9H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 171.8, 129.4, 129.0, 81.1, 69.3, 43.0, 28.1, 22.7, –2.0; MS (EI) *m/z* 201 ($M^{+\bullet}$-^{t}Bu), 169, 143, 117, 112, 101, 91, 73; HRMS (EI) *m/z* calculated for $C_9H_{17}O_3Si$ ($M^{+\bullet}$-^{t}Bu): 201.0947, found 201.0949.

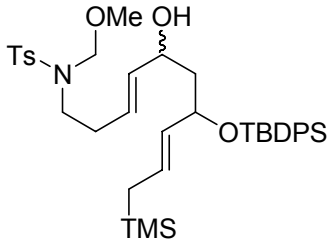


(*E*)-*Tert*-butyl-3-*tert*-butyldiphenylsilyloxy-6-trimethylsilylhex-4-enoate (136): General procedure **E** was carried out with 0.40 g (1.5 mmol) of hydroxyester **135** and 0.59 mL (0.63 g, 2.3 mmol) of *t*-butyldiphenylsilyl chloride. Purification *via* flash chromatography on SiO_2 (50:1 hexanes/Et_2O) provided 0.64 g (87%) of the product as a clear oil: IR (thin film) 3072, 2956, 1732, 1659, 1473, 1428, 1367, 1249, 1136, 1070, 850, 702 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.73–7.66 (m, 4H), 7.44–7.32 (m, 6H), 5.36–5.24 (m, 2H), 4.54 (q, *J* = 6.4 Hz, 1H), 2.48 (dd, *J* = 14.4, 6.0 Hz, 1H), 2.32 (dd, *J* = 14.4, 6.0 Hz, 1H), 1.38 (s, 9H), 1.32–1.24 (m, 2H), 1.04 (s, 9H), –0.09 (s, 9H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 170.1, 135.9 (2C), 134.3 (2C), 130.2, 129.5, 129.

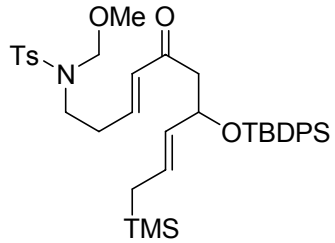
4, 128.3, 127.4, 127.3, 80.1, 72.0, 45.3, 28.1, 27.0, 22.4, 19.3, –2.0; MS (ESI) *m/z* 519 $(M+Na)^+$; HRMS (ESI) *m/z* calculated for $NaC_{29}H_{44}O_3Si_2$ $(M+Na)^+$: 519.2727, found 519.2723.



(*E*)-3-*Tert*-butyldiphenylsilyloxy-6-trimethylsilylhex-4-enal (137):[140] To a solution of 0.30 g (0.60 mmol) of ester **136** in 3.5 mL of toluene at –78 °C was added 0.72 mL (0.72 mmol) of DIBAl-H in hexanes (1.0 M). Following 30 min, the reaction was quenched at –78 °C with sat. aq. NH_4Cl, warmed to rt, and diluted with sat. aq. Rochelle's salt. The mixture was stirred vigorously for 15 min, then partitioned between brine and EtOAc. The aqueous layer was extracted with EtOAc (3x) and the combined organic layers were dried with Na_2SO_4. The organic layers were filtered and crude product concentrated *in vacuo*. Purification by flash chromatography on SiO_2 (30:1 hexanes/EtOAc) afforded 0.21 g (82%) of the product as an oil: IR (thin film) 3072, 2955, 1726, 1659, 1248, 1112, 851, 702 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 9.73 (t, *J* = 2.6 Hz, 1H), 7.71–7.66 (m, 4H), 7.48–7.35 (m, 6H), 5.49 (dt, *J* = 15.1, 7.7 Hz, 1H), 5.36 (dd, *J* = 15.3, 6.4 Hz, 1H), 4.63 (q, *J* = 5.9 Hz, 1H), 2.51–2.41 (m, 2H), 1.37 (d, *J* = 7.5 Hz, 2H), 1.07 (s, 9H), –0.04 (s, 9H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 201.8, 135.9, 135.8, 133.8 (2C), 129.8 (2C), 129.6, 128.8, 127.7, 127.5, 70.5, 51.6, 27.0, 22.6, 19.3, –2.0; MS (ESI) *m/z* 447 $(M+Na)^+$; HRMS (ESI) *m/z* calculated for $NaC_{25}H_{36}O_2Si_2$ $(M+Na)^+$: 447.2152, found 447.2127.



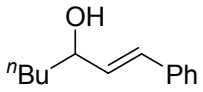
***R**-(3*E*,5*S*,7*R*,8*E*)-1-*N*-Methoxymethyl-*N*-tosylamino-7-*tert*-butyldiphenylsilyloxy-10-trimethylsilyldeca-3,8-dien-5-ol + *R**-(3*E*,5*R*,7*R*,8*E*)-1-*N*-Methoxymethyl-*N*-tosylamino-7-*tert*-butyldiphenylsilyloxy-10-trimethylsilyldeca-3,8-dien-5-ol (138):**[83] To 0.050 g (0.19 mmol) of alkyne **81** in 0.63 mL of CH_2Cl_2 at 0 °C was added 54 mg (0.21 mmol) of $Cp_2Zr(H)Cl$ in portions. The mixture was then slowly warmed to ambient temperature (cloudy → clear yellow color shift) for 20 min, then stirred 20 min longer following dissolution of the solid. The flask was immersed in a –55 °C bath (cryocool) and 0.11 mL (1.15 mmol) of Me_2Zn in toluene (2.0 M) was added. The reaction was stirred for 45 min at –55 °C then warmed to 0 °C for 5 min whereupon 98 mg (0.23 mmol) of aldehyde **137** was added dropwise and the reaction was stirred for 4 h. The reaction was carefully quenched with sat. aq. Rochelle's salt, stirred for 30 min, then the aqueous layer was extracted with Et_2O (3x). The combined organic layers were dried over Na_2SO_4, filtered through florsil with Et_2O, and the crude product was concentrated *in vacuo*. Purification by flash chromatography on SiO_2 (3:2 hexanes/Et_2O) gave 91 mg (68%) of the product as an oil. The diastereomeric ratio for this substrate was not determined (approximately 1:1). The diastereomeric mixture was characterized by IR and MS: IR (thin film) 3521, 2953, 1428, 1343, 1158, 1111, 967, 852, 703 cm^{-1}; MS (ESI) *m/z* 716 $(M+Na)^+$; HRMS (ESI) *m/z* calculated for $NaC_{38}H_{55}NO_5SSi_2$ $(M+Na)^+$: 716.3237, found 716.3252.



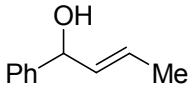
(3*E*,8*E*)-1-*N*-Methoxymethyl-*N*-tosylamino-7-*tert*-butyldiphenylsilyloxy-10-trimethylsilyldeca-3,8-dien-5-one (132):[35, 36] To 0.090 g (0.13 mmol) of alcohol **138** in 1.3 mL

of CH_2Cl_2 was added 0.17 g (0.39 mmol) of Dess-Martin periodinane at 0 °C. The mixture was stirred at 0 °C for 1.5 hr then raised to rt for 1 h. The reaction was quenched with hexanes, filtered through florsil (2:1 hexanes/EtOAc) and the crude product was concentrated *in vacuo*. Purification by flash chromatography on SiO_2 (3:2 hexanes/Et_2O) afforded 72 mg (77%) of the product as an oil: IR (thin film) 2954, 1695, 1668, 1471, 1345, 1248, 1160, 1073, 965, 851, 703 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.72–7.61 (m, 6H), 7.45–7.25 (m, 8H), 6.44 (dt, *J* = 15.9, 6.9 Hz, 1H), 5.92 (d, *J* = 15.9 Hz, 1H), 5.32 (dt, *J* = 15.1, 7.3 Hz, 1H), 5.24 (dd, *J* = 15.3, 6.4 Hz, 1H), 4.69 (s, 2H), 4.60 (q, *J* = 6.4 Hz, 1H), 3.31 (s, 3H), 3.20 (t, *J* = 7.3 Hz, 1H), 2.75 (dd, *J* = 14.4, 6.3 Hz, 1H), 2.54 (dd, *J* = 14.3, 6.9 Hz, 1H), 2.44 (q, *J* = 7.3 Hz, 2H), 2.43 (s, 3H), 1.28 (d, *J* = 7.0 Hz, 2H), 1.02 (s, 9H), –0.12 (s, 9H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 197.8, 143.6, 142.6, 137.2, 135.9 (2C), 134.1 (2C), 132.6, 130.1, 129.7, 129.6, 129.5, 128.4, 127.5, 127.4, 127.2, 80.4, 71.8, 55.7, 49.2, 45.8, 32.1, 27.0, 22.4, 21.5, 19.3, –2.0; MS (ESI) *m/z* 714 $(M+Na)^+$; HRMS (ESI) *m/z* calculated for $NaC_{38}H_{53}NO_5SSi_2$ $(M+Na)^+$: 714.3081, found 714.3053.

7.0 EXPERIMENTAL SECTION FOR CHAPTER 3

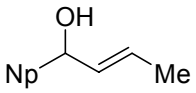


1-Phenylhept-1-en-3-ol (159):[230] To 1.90 mL (2.00 g, 15.1 mmol) of cinnamaldehyde in 15 mL of Et_2O at –78 °C was added 10.4 mL (16.6 mmol) of *n*-butyllithium in hexanes (1.6 M) *via* syringe. The mixture was stirred at –78 °C for 30 min, then quenched carefully with sat. aq. NH_4Cl. The aqueous layer was extracted with Et_2O (3x), the combined organic layers were dried over Na_2SO_4, filtered and the crude product mixture concentrated *in vacuo*. Purification by flash chromatography on SiO_2 (7.5:1 hexanes/EtOAc) yielded 2.57 g (89%) of the title compound as a yellow oil: ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.46–7.22 (m, 5H), 6.58 (d, J = 16.0 Hz, 1H), 6.23 (dd, J = 15.9, 6.8 Hz, 1H), 4.29 (q, J = 6.5 Hz, 1H), 1.69–1.50 (m, 2H), 1.49–1.30 (m, 4H), 0.93 (t, J = 6.7 Hz, 3H).



1-Phenylbut-2-en-1-ol (160):[231] To 4.74 g (3.18 mL, 30.2 mmol) of bromobenzene in 200 mL of Et_2O at –78 °C was added 35.5 mL (60.4 mmol) of *t*-butyllithium in pentane (1.7 M). Following 1 h, 2.51 mL (2.12 g, 30.2 mmol) of crotonaldehyde was added slowly *via* syringe, and the mixture was stirred an additional 20 min. The reaction was quenched carefully with H_2O and slowly raised to ambient temperature. The aqueous layer was extracted with Et_2O (3x), the

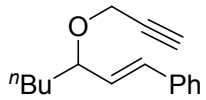
combined organic layers were dried over Na_2SO_4, filtered and the crude product mixture concentrated *in vacuo*. The crude product was used as isolated: ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.40–7.27 (m, 5H), 5.85–5.67 (m, 2H), 5.18 (br. dd, *J* = 6.4, 3.2 Hz, 1H), 1.85 (d, *J* = 3.5 Hz, 1H), 1.73 (d, *J* = 5.5 Hz, 3H).



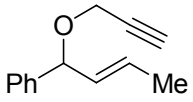
1-Naphthalen-2-ylbut-2-en-1-ol (161):[232] To 1.2 g (49 mol) of mechanically activated Mg(0) was added 15 mL of THF and I_2 (cat., in 0.5 mL of THF). Initiation was afforded by brief warming with a heatgun (brown → clear/white color shift), following which 0.010 kg (48 mmol) of 2-bromonapthalene in 10 mL of THF was carefully added over 30 min to maintain a gentle reflux. The mixture was refluxed 15 min longer with a heatgun, then stirred at ambient temperature for 1 h. In a separate flask, 4.8 mL (4.1 g) of crotonaldehyde was dissolved in 19 mL of THF and the temperature reduced to –78 °C. The active Grignard reagent was added *via* syringe over 15 min and after 1 h, the reaction was quenched carefully with sat. aq. NH_4Cl and raised to ambient temperature. The aqueous layer was extracted with Et_2O (3x), the combined organic layers were dried over Na_2SO_4, filtered and the crude product mixture concentrated *in vacuo*. The product was purified by flash chromatography on SiO_2 (6:1 hexanes/EtOAc) to afford 7.5 g (79%) of the product as a highly viscous, yellow oil: ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.86–7.82 (m, 4H), 7.51–7.45 (m, 3H), 5.90–5.73 (m, 2H), 5.35 (d, *J* = 5.1 Hz, 1H), 2.00 (s, 1H), 1.76 (d, *J* = 5.6 Hz, 3H).

General Procedure A for Preparation of Propargylic Ethers 162-164, 171: To 0.080 g (2.0 mmol) of sodium hydride (60% dispersion in mineral oil, pre-washed 3x with pentane) was

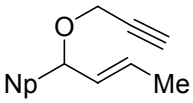
added 1.4 mL of THF. The solution was cooled to 0 °C, and the allylic alcohol (1.0 mmol) was added *via* syringe or Pasteur pipette. The reaction was stirred at 0 °C for ~15 min, then warmed slowly to ambient temperature. At this time, a condenser was attached to the reaction vessel and the reaction mixture was heated to reflux for 30 min, whereupon 0.30 g (2.0 mmol) of propargyl bromide in toluene (80%/wt) was added carefully through the condenser. Following 1 h at reflux, the solution was cooled to ambient temperature and quenched carefully with H_2O. The aqueous layer was extracted with Et_2O (3x), the combined organic layers were dried over $MgSO_4$, and the solvent was filtered and removed *in vacuo*. The product was purified as indicated.



3-Prop-2-ynyloxyhept-1-enylbenzene (162): The general procedure **A** was followed employing 1.14 g (6.00 mmol) of allylic alcohol **159**. Purification by flash chromatography on SiO_2 (40:1 hexanes/EtOAc) afforded 1.03 g (75%) of the product as a red-orange oil. Further purification was accomplished by distillation at low pressure (~100 °C): IR (thin film) 3301, 3027, 2956, 2116, 1494, 1071, 969, 750, 693 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.43–7.24 (m, 5H), 6.58 (d, *J* = 15.9 Hz, 1H), 6.03 (dd, *J* = 15.9, 8.3 Hz, 1H), 4.23 (dd, *J* = 15.6, 2.1 Hz, 1H), 4.08 (dd, *J* = 15.5, 2.1 Hz, 1H), 4.05 (q, *J* = 6.7 Hz, 1H), 2.42 (t, *J* = 2.2 Hz, 1H), 1.78–1.69 (m, 1H), 1.65–1.53 (m, 1H), 1.49–1.32 (m, 4H), 0.91 (t, *J* = 6.7 Hz, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 136.3, 133.0, 129.3, 128.5, 127.7, 126.4, 80.2, 79.6, 73.8, 55.0, 35.2, 27.4, 22.5, 13.9; MS (EI) *m/z* 228 ($M^{+\bullet}$), 198, 189, 171, 131, 85, 57; HRMS (EI) *m/z* calculated for $C_{16}H_{20}O$: 228.1514, found 228.1508.



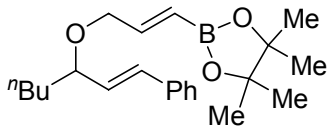
1-Prop-2-ynyloxybut-2-enylbenzene (163): The general procedure **A** was followed employing 889 mg (6.00 mmol) of allylic alcohol **160**. The product was purified by flash chromatography on SiO_2 (40:1 hexanes/EtOAc) to afford 939 mg (84%) of the product as a red-orange oil: IR (thin film) 3295, 3029, 2916, 2116, 1493, 1451, 1062, 968, 755, 700 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.39–7.26 (m, 5H), 5.78 (dq, *J* = 15.3, 6.2 Hz, 1H), 5.60 (ddq, *J* = 15.3, 7.2, 1.3 Hz, 1H), 4.98 (d, *J* = 7.4 Hz, 1H), 4.17 (dd, *J* = 15.7, 2.4 Hz, 1H), 4.09 (dd, *J* = 15.7, 2.4 Hz, 1H), 2.42 (t, *J* = 2.4 Hz, 1H), 1.74 (dd, *J* = 6.4, 1.4 Hz, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 140.7, 131.1, 129.1, 128.3, 127.5, 126.8, 80.8, 79.9, 74.1, 54.7, 17.1; MS (EI) *m/z* 186 ($M^{+\bullet}$), 171, 147, 131, 105, 91, 77, 69; HRMS (EI) *m/z* calculated for $C_{13}H_{14}O$: 186.1045, found 186.1039.



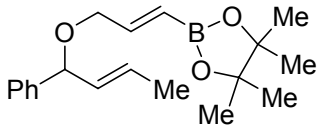
2-1-Prop-2-ynyloxybut-2-enylnaphthalene (164): The general procedure **A** was followed employing 1.42 g (7.16 mmol) of allylic alcohol **161**, 0.480 g (12.0 mmol) of NaH, and 1.79 g (12.0 mmol) of propargyl bromide. Purification by flash chromatography on SiO_2 (50:1 → 25:1 hexanes/EtOAc) afforded 1.23 g (73%) of the product as a viscous, red-orange oil. Further purification was accomplished by distillation at low pressure (~120 °C): IR (thin film) 3293, 3056, 2854, 2116, 1508, 1440, 1062, 967, 750 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.86–7.82 (m, 4H), 7.50–7.45 (m, 3H), 5.83 (dq, *J* = 15.2, 6.2 Hz, 1H), 5.68 (ddq, *J* = 15.4, 7.2, 1.4 Hz, 1H), 5.15 (d, *J* = 7.2 Hz, 1H), 4.22 (dd, *J* = 15.6, 2.3 Hz, 1H), 4.12 (dd, *J* = 15.8, 2.3 Hz, 1H), 2.45 (t, *J* = 2.4 Hz, 1H), 1.75 (d, *J* = 6.4 Hz, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 138.0, 133.2, 133.0, 131.0, 129.5, 128.2, 127.9, 127.6, 126.0, 125.8, 125.7, 124.8, 81.0, 79.9, 74.3, 55.0, 17.7;

MS (EI) *m/z* 236 ($M^{+\bullet}$), 221, 197, 179, 155, 141, 127; HRMS (EI) *m/z* calculated for $C_{17}H_{16}O$: 236.1201, found 236.1201.

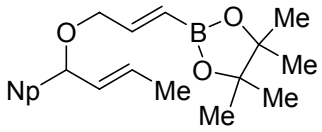
General Procedure B for Preparation of Vinylborolanes 165-167, 170:[154, 155] The alkyne (1.0 equiv) was added to a suspension of $Cp_2Zr(H)Cl$ (0.05 equiv) in CH_2Cl_2 (3.0 M) at 0 °C in a microwave reaction vessel. Pinacolborane (1.1 equiv) was added and the resulting suspension was warmed directly to ambient temperature, then heated at 100 °C in a microwave reactor for 45 min. The solvent was removed *in vacuo* and the residue purified by flash chromatography on Iatrobeads 6RS-8060 silica gel.



2-(1*E*)-3-(*E*)-1-Phenylhept-1-en-3-yloxyprop-1-enyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (165): General Procedure **B** was followed employing 1.00 g (4.38 mmol) of alkyne **162**. Purification by flash chromatography (5% EtOAc/hexanes) gave 1.18 g (75%) of the title compound as a colorless oil: ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.42–7.20 (m, 5H), 6.66 (dt, *J* = 18, 4.6 Hz, 1H), 6.49 (d, *J* = 16 Hz, 1H), 6.05 (dd, *J* = 16, 8.0 Hz, 1H), 5.73 (dt, *J* = 18, 1.8 Hz, 1H), 4.15 (ddd, *J* = 15, 4.4, 1.9 Hz, 1H), 3.96 (ddd, *J* = 15, 4.8, 1.8 Hz, 1H), 3.85 (dt, *J* = 6.5, 7.3 Hz, 1H), 1.78–1.50 (m, 2H), 1.27 (s, 12H), 1.40–1.24 (m, 4H), 0.89 (m, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 149.8, 136.5, 132.0, 130.5, 128.4, 127.5, 126.3, 118.6 (br), 83.0, 80.4, 69.5, 35.5, 27.4, 24.6, 22.6, 14.0; MS (EI) *m/z* 356 ($M^{+\bullet}$), 341, 326, 299, 270, 257, 199, 173, 167, 155, 143, 131, 117, 105, 91, 85, 77, 67, 57; HRMS *m/z* calculated for $C_{22}H_{33}BO_3$: 356.2523, found 356.2523.



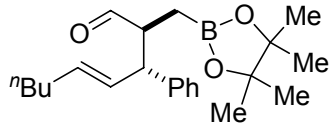
2-(1*E*)-3-(*E*)-1-Phenylbut-2-enyloxyprop-1-enyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (166): General Procedure **B** was followed employing 1.14 g (6.14 mmol) of alkyne **163**. Purification by flash chromatography (5% EtOAc/hexanes) gave 1.60 g (83%) of the title compound as a colorless oil: ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.40–7.20 (m, 5H), 6.67 (dt, *J* = 18, 4.5 Hz, 1H), 5.76 (dt, *J* = 16, 1.8 Hz, 1H), 5.70 (ddq, *J* = 15, 5.9, 0.6 Hz, 1H), 5.57 (ddq, *J* = 15, 7.2. 1.2 Hz, 1H), 4.74 (d, *J* = 7.0 Hz, 1H), 4.07 (ddd, *J* = 15, 4.5, 1.8 Hz, 1H), 4.00 (ddd, *J* = 15, 4.5, 1.8 Hz, 1H), 1.70 (dd, *J* = 6.3, 1.3 Hz, 3H), 1.27 (s, 12H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 149.4, 141.5, 132.0, 128.2, 128.0, 127.2, 126.5, 118.9 (br), 83.0, 81.8, 69.3, 24.6, 17.6; MS (EI) *m/z* 314 ($M^{+\bullet}$), 299, 284, 271, 256, 230, 214, 208, 199, 169, 147, 131, 119, 91, 85, 69, 59; HRMS *m/z* calculated for $C_{19}H_{27}BO_3$: 314.2053, found 314.2060.



2-(1*E*)-3-(*E*)-1-Naphthalen-2-ylbut-2-enyloxyprop-1-enyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (167): General Procedure **B** was followed employing 1.00 g (4.23 mmol) of alkyne **164**. Purification by flash chromatography (8% EtOAc/hexanes) gave 1.19 g (77%) of the title compound as a colorless oil: ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.81 (m, 4H), 7.46 (m, 3H), 6.70 (dt, *J* = 18, 4.5 Hz, 1H), 5.81–5.61 (m, 3H), 4.92 (d, *J* = 6.6 Hz, 1H), 4.11 (ddd, *J* = 15, 4.5, 1.8 Hz, 1H), 4.05 (ddd, *J* = 15, 4.5, 1.9 Hz, 1H), 1.72 (d, *J* = 5.8 Hz, 3H), 1.27 (s, 12H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 149.4, 138.9, 133.1, 132.8, 131.8, 128.2, 128.0, 127.8, 127.5, 125.8, 125.6, 125.2, 124.7, 118.8 (br), 83.0, 81.9, 69.3, 24.6, 17.6; MS (EI) *m/z* 364 ($M^{+\bullet}$), 349, 280,

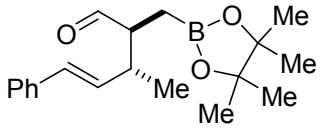
197, 181, 169, 155, 141, 127, 115, 101, 85, 69, 59; HRMS *m/z* calculated for $C_{23}H_{29}BO_3$: 364.2210, found 364.2228.

General Procedure C for Preparation of Boronic Aldehydes 168-170:[19, 183] Note that distillation of propargylic ethers **162-164** benefits the reproducibility of iridium catalyzed isomerizations. A solution of $[IrCl(C_8H_{14})_2]_2$ (1.0 mol%, 0.02 equiv Ir) and PCy_3 (6.0 mol%, 0.06 equiv) in anhydrous CH_2Cl_2 or 1,2-dichloroethane (1,2-DCE) was added to a solution of $NaBPh_4$ (2.0 mol%, 0.02 equiv) in and equal volume of CH_2Cl_2/acetone (25:1) or 1,2-DCE/acetone (25:1) (0.67M final concentration in substrate) and the resulting yellow solution stirred for 5 min at ambient temperature. The vinylborolane (1.0 equiv) was added and the reaction stirred for 90 min at ambient temperature whereupon PPh_3 (6.0 mol%, 0.06 equiv) was added and the resulting solution heated at (40 or 80 °C) for the indicated time. The solvent was removed *in vacuo* and the residue purified by flash chromatography on Iatrobeads 6RS-8060 silica gel. Diastereomeric ratios were determined by integration of the specified resonances from 300 MHz ^{1}H-NMR.

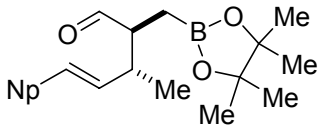


***R**-(*E*,2*R*,3*S*)-2-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-ylmethyl-3-phenylnon-4-enal (168):** General Procedure **C** (1,2-DCE, 80 °C) was followed employing 1.15 g (3.23 mmol) of boronic ester **165** and a reaction time of 2.5 h. Purification by flash chromatography (6% EtOAc/hexanes) gave 0.772 g (67%) of the title compound as a colorless oil (C**H**O, *syn:anti* = 92:8): ^{1}H-NMR (300 MHz, $CDCl_3$): δ 9.77 (d, *J* = 1.8 Hz, 1H), 7.35–7.25 (m, 2H), 7.25–7.15

(m, 3H), 5.67 (ddt, J = 15, 8.7, 1.2 Hz, 1H), 5.53 (dt, J = 15, 6.6 Hz, 1H), 3.53 (t, J = 8.6 Hz, 1H), 2.94 (m, 1H), 2.00 (m, 2H), 1.21 (s, 6H), 1.35–1.19 (m, 4H), 1.18 (s, 6H), 0.87 (m, 3H), 0.80 (dd, J = 16, 9.6 Hz, 1H), 0.68 (dd, J = 16, 5.0 Hz, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 205.1, 142.1, 132.9, 129.9, 128.4, 127.8, 126.4, 83.0, 52.6, 51.1, 32.1, 31.3, 24.7, 24.5, 22.0, 13.8, 9.7 (br).

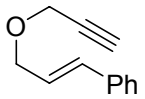


***R**-(*E*,2*R*,3*S*)-3-Methyl-2-4,4,5,5-tetramethyl-1,3,2-dioxaboro-lan-2-ylmethyl-5-phenylpent-4-enal (169):** General Procedure **C** (CH_2Cl_2, 40 °C) was followed employing 0.500 g (1.59 mmol) of boronic ester **166** and a reaction time of 4 h. Purification by flash chromatography (8% EtOAc/hexanes) gave 0.326 g (65%) of the title compound as a colorless oil (vinyl C**H**, *syn:anti* = 92:8): ^{1}H-NMR (300 MHz, $CDCl_3$): δ 9.76 (d, J = 0.8 Hz, 1H), 7.36–7.20 (m, 5H), 6.42 (d, J = 16 Hz, 1H), 6.19 (dd, J = 16, 7.5 Hz, 1H), 2.85 (m, 1H), 2.70 (m, 1H), 1.24 (s, 6H), 1.21 (s, 6H), 1.12 (d, J = 6.9 Hz, 1H), 1.00 (dd, J = 16, 10 Hz, 1H), 0.82 (dd, J = 16, 5.0 Hz, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 204.8, 137.1, 132.7, 130.1, 128.4, 127.1, 126.0, 83.1, 53.2, 37.8, 24.7, 24.5, 16.4, 6.7 (br).

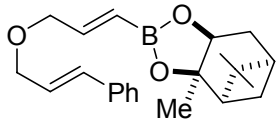


***R**-(*E*,2*R*,3*S*)-3-Methyl-2-4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-ylmethyl-5-naphthalen-2-ylpent-4-enal (170):** General Procedure **C** (CH_2Cl_2, 40 °C) was followed employing 0.264 g (0.723 mmol) of boronic ester **167** and a reaction time of 4 hr. Purification by flash

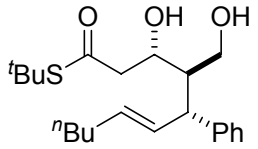
chromatography (10% EtOAc/hexanes) gave 0.159 g (61%) of the title compound as a colorless oil (C**H**O, *syn:anti* = 91:9). Slow evaporation from pentane at –22 °C afforded crystals which were suitable for X-Ray analysis: ^{1}H-NMR (300 MHz, $CDCl_3$): δ 9.79 (d, *J* = 0.9 Hz, 1H), 7.80–7.75 (m, 3H), 7.69 (s, 1H), 7.56 (dd, *J* = 8.6, 1.7 Hz, 1H), 7.48–7.39 (m, 2H), 6.58 (d, *J* = 16 Hz, 1H), 6.32 (dd, *J* = 16, 7.5 Hz, 1H), 2.91 (m, 1H), 2.76 (m, 1H), 1.24 (s, 6H), 1.21 (s, 6H), 1.16 (d, *J* = 6.9 Hz, 3H), 1.04 (dd, *J* = 16, 10 Hz, 1H), 0.86 (dd, *J* = 16, 5.1 Hz, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 204.7, 134.5, 133.5, 133.1, 132.7, 130.2, 128.0, 127.7, 127.5, 126.1, 125.7, 125.5, 123.4, 83.1, 53.2, 37.9, 24.7, 24.5, 16.4, 6.9 (br).



1-(*E*)-3-Prop-2-ynyloxyprop-1-enylbenzene (171): The general procedure **A** was followed employing 1.0 g (7.5 mmol) of cinnamyl alcohol. Purification by flash chromatography on SiO_2 (25:1 hexanes/EtOAc) followed by Kughelrohr distillation (65-68 °C, 150 mtorr) gave 1.0 g (77%) of the product as a clear oil: IR (thin film) 3293, 3082, 2851, 2116, 1655, 1599, 1386, 1117, 1081, 967, 744 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.41 (d, *J* = 7.4, 2H), 7.35 (t, *J* = 7.3 Hz, 2H), 7.28–7.24 (m, 1H), 6.66 (d, *J* = 15.9 Hz, 1H), 6.29 (dt, *J* = 15.9, 6.2 Hz, 1H), 4.26 (dd, *J* = 6.2, 1.0 Hz, 2H), 4.22 (d, *J* = 2.3 Hz, 2H), 2.47 (t, *J* = 2.3 Hz, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 136.5, 133.3, 128.5, 127.7, 126.5, 125.0, 79.7, 74.4, 70.1, 57.0; MS (EI) *m/z* 172 ($M^{+\bullet}$), 142, 129, 117, 91, 79, 65; HRMS (EI) *m/z* calculated for $C_{12}H_{12}O$ ($M^{+\bullet}$-H): 171.0810, found 171.0815.

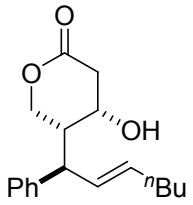


(*R*,*S*)-3,6,6-Trimethylbicyclo[3.1.1]heptane-2,3-oxy-(1*E*)-3-cinnamyloxy-prop-1-enylboronic ester (172): General Procedure **B** was followed employing 0.10 g (0.58 mmol) of alkyne **171** and 0.12 g (0.64 mmol) of (–)-pinaneborane as an alternative to pinacolborane.[157] Purification by flash chromatography on SiO_2 (15:1 hexanes/EtOAc) gave 0.16 g (78%) of the title compound as a colorless oil: $[\alpha]_D^{26} = -10.8$ (c 1.10, $CHCl_3$); IR (thin film) 3026, 2917, 1645, 1599, 1495, 1121, 1031, 776 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.39 (d, *J* = 7.4, 2H), 7.32 (t, *J* = 7.4 Hz, 2H), 7.28–7.23 (m, 1H), 6.69 (dt, *J* = 18.1, 4.7 Hz, 1H), 6.63 (d, *J* = 15.9, 1H), 6.30 (dt, *J* = 15.9, 5.9 Hz, 1H), 5.78 (d, *J* = 18.2 Hz, 1H), 4.33 (dd, *J* = 8.8, 1.8 Hz, 1H), 4.18 (dd, *J* = 5.9, 1.0 Hz, 2H), 4.14 (dd, *J* = 4.7, 1.6 Hz, 2H), 2.36 (ddt, *J* = 13.7, 8.8, 2.4 Hz, 1H), 2.22 (dtd, *J* = 10.9, 6.1, 2.2 Hz, 1H), 2.08 (t, *J* = 5.3 Hz, 1H), 1.94–1.91 (m, 1H), 1.91–1.86 (m, 1H), 1.56 (s, 3H), 1.30 (s, 3H), 1.16 (d, *J* = 10.9 Hz, 1H), 0.86 (s, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 149.0, 136.8, 132.3, 128.5, 127.6, 126.5, 126.0, 119 (br), 85.7, 77.8, 71.7, 70.9, 51.4, 39.5, 38.1, 35.5, 28.6, 27.1, 26.4, 24.0; MS (EI) *m/z* 352 ($M^{+\bullet}$), 283, 248, 200, 133, 117, 105; HRMS (EI) *m/z* calculated for $C_{22}H_{29}BO_3$: 352.2210, found 352.2202.



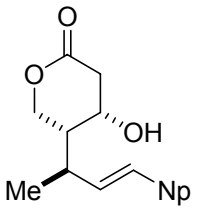
***R**-3-Hydroxy-4-hydroxymethyl-5-phenylundec-6-enethioic acid S-tert-butyl ester (175):** To 0.15 g (0.42 mmol) of β-boronic aldehyde **168** (92:8 *syn:anti*) in 4.2 mL CH_2Cl_2 was added 112 mg (0.547 mmol) of (1-tert-butylsulfanyl-vinyloxy)-trimethyl-silane, and the flask was immersed in a –78 °C bath.[233] To the mixture was added 0.63 mL (0.63 mmol) of dimethylaluminum chloride in hexanes (1.0 M) dropwise and the reaction was stirred for 1 h at –78 °C. The reaction was quenched with 10% w/w citric acid in MeOH and slowly raised to

ambient temperature. Water was added to form a biphasic mixture, and the aqueous layer was extracted with Et_2O (3x). The combined organic layers were dried over Na_2SO_4, filtered, and the solvent removed. The crude borane was passed through a plug of silica (5:1 hexanes/EtOAc) and isolated *in vacuo*. The compound mixture was then subject to 12 mL of a 2:1:1 CH_2Cl_2:1M NaOH:30% HOOH solution for 1.5 h. Following this time, the aqueous layer was extracted with CH_2Cl_2 (3x), and the combined organic layers were dried over Na_2SO_4. The solvent was filtered and removed *in vacuo*. Purification by flash chromatography on SiO_2 (5:1 hexanes/EtOAc) yielded 95 mg (60%) of the product as a clear, viscous oil: IR (thin film) 3364, 3027, 2960, 1679, 1454, 1364, 1054, 969, 758, 700 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.33–7.17 (m, 5H), 5.68–5.52 (m, 2H), 4.55 (dq, *J* = 9.6, 3.3 Hz, 1H), 3.79 (dt, *J* = 11.6, 2.6 Hz, 1H), 3.74 (dd, *J* = 10.9, 8.4 Hz, 1H), 3.33 (ddd, *J* = 11.8, 8.0, 3.8 Hz, 1H), 3.31 (d, *J* = 4.1 Hz, 1H), 2.95 (dd, *J* = 15.6, 9.6 Hz, 1H), 2.67 (dd, *J* = 15.7, 3.3 Hz, 1H), 2.62 (dd, *J* = 8.0, 2.6 Hz, 1H), 2.03 (q, *J* = 6.7 Hz, 2H), 1.64–1.56 (m, 1H), 1.49 (s, 9H), 1.40–1.24 (m, 4H), 0.88 (t, *J* = 7.1 Hz, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 200.2, 143.6, 132.6, 131.6, 128.6, 127.8, 126.2, 69.8, 60.5, 50.3, 48.5, 48.0, 47.6, 32.2, 31.4, 29.7, 22.1, 13.8; MS (EI) *m/z* 360 ($M^{+\bullet}$-H_2O), 304, 173, 117, 91; HRMS (EI) *m/z* calculated for $C_{22}H_{32}O_2S$ ($M^{+\bullet}$-H_2O): 360.2123, found 360.2128.



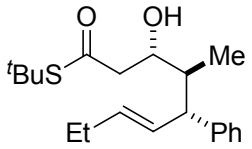
***R**-4-Hydroxy-5-1-phenylhept-2-enyl-tetrahydropyran-2-one (176):** To 0.050 g (0.14 mmol) of β-boronic aldehyde **168** (92:8 *syn:anti*) in 1.4 mL CH_2Cl_2 was added 37 mg (0.18 mmol) of (1-tert-butylsulfanyl-vinyloxy)-trimethyl-silane, and the flask was immersed in a –78 °C bath.[233]

To the mixture was added 0.21 mL (0.21 mmol) of dimethylaluminum chloride in hexanes (1.0 M) dropwise and the reaction was stirred for 1 h at –78 °C. The reaction was quenched at –78 °C by addition of H_2O and slowly raised to ambient temperature. The aqueous layer was extracted with Et_2O (3x) and the combined organic layers were dried over Na_2SO_4. Filtration of the organic extracts followed by removal of the solvent *in vacuo* left a residue that was immediately subject to 4 mL of a 2:1:1 MeOH:1M NaOH:30% HOOH solution for 1 h. Following this time, the solution was acidified with aq. 1M HCl to ~pH 0.5 and stirred for 2 h. The aqueous layer was then extracted with Et_2O (3x) and the combined organic layers were dried over Na_2SO_4, filtered and the crude product mixture was concentrated *in vacuo*. Remaining solvents were removed under high vacuum. Purification of flash chromatography on SiO_2 (7:3 hexanes/EtOAc) afforded 29 mg (71%) of the title compound as a clear, viscous oil. Separation of the diastereomers by GC-MS provided the diastereomer ratio: 2.7% (T_r = 19.26), 97.3% (T_r = 19.38). IR (thin film) 3431, 3028, 2957, 2926, 1720, 1188, 1064, 982, 702 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.36–7.16 (m, 5H), 5.69–5.54 (m, 2H), 4.48–4.35 (m, 1H), 4.32 (t, *J* = 11.5 Hz, 1H), 3.81 (dd, *J* = 11.6, 4.9 Hz, 1H), 3.25 (dd, *J* = 10.9, 8.3 Hz, 1H), 2.79 (dd, *J* = 18.2, 2.9 Hz, 1H), 2.72 (dd, *J* = 18.2, 3.9 Hz, 1H), 2.24 (tdd, *J* = 11.6, 4.9, 1.6 Hz, 1H), 2.02 (q, *J* = 6.8 Hz, 2H), 1.36–1.25 (m, 4H), 0.88 (t, *J* = 7.0 Hz, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 170.3, 141.7, 133.1, 130.3, 128.9, 127.2, 126.9, 68.3, 63.4, 47.5, 41.8, 39.3, 32.1, 31.3, 22.2, 13.8; MS (EI) *m/z* 270 ($M^{+\bullet}$-H_2O), 210, 173, 117, 91; HRMS (EI) *m/z* calculated for $C_{18}H_{22}O_2$ ($M^{+\bullet}$-H_2O): 270.1620, found 270.1623.



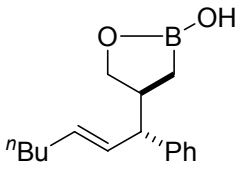
R-4-Hydroxy-5-3-naphthalen-2-yl-1-phenylallyl-tetrahydropyran-2-one (177):* To 0.17 mg (0.48 mmol) of β-boronic aldehyde **170** (91:9 *syn:anti*) (1 mmol) in 4.8 mL CH_2Cl_2 was added 127 mg (0.621 mmol) of (1-tert-butylsulfanyl-vinyloxy)-trimethyl-silane, and the flask was immersed in a –78 °C bath.[233] To the mixture was added 0.72 mL (0.71 mmol) of dimethylaluminum chloride in hexanes (1.0 M) dropwise and the reaction was stirred for 1 h at –78 °C. The reaction was quenched at –78 °C with 10% w/w citric acid in MeOH and slowly raised to ambient temperature. Water was added to form a biphasic mixture and the aqueous layer was extracted with Et_2O (3x). The combined organic layers were dried over Na_2SO_4, filtered and the solvent removed. The crude borane was passed through a plug of silica (5:1 hexanes/EtOAc) and isolated *in vacuo*. The product mixture was then subject to 12 mL of a 2:1:1 CH_2Cl_2:1M NaOH:30% HOOH solution for 1.5 h. Following this time, the aqueous layer was extracted with CH_2Cl_2 (3x), and the organic layers were dried over Na_2SO_4. The layers were filtered and the solvent removed *in vacuo*. The crude product was then treated with 12 mL 1M NaOH in MeOH for 1 h at ambient temperature, then acidified to ~ pH 2 with aq. 1M HCl and stirred for an additional 1 h. The reaction was then diluted with H_2O, and aqueous layer was extracted with Et_2O (3x). The combined organic layers were dried over Na_2SO_4, filtered, and the crude product mixture concentrated *in vacuo*. Remaining solvents were removed under high vacuum. Purification by flash chromatography on SiO_2 (3:2 hexanes/EtOAc) gave 54 mg (38%) of the product as a white foam. Recrystallization from hexanes/EtOAc (slow evaporation) gave crystals suitable for X-ray analysis: m.p. 117-119 °C; IR (KBr) 3362, 3053, 2965, 1709, 1195,

1041, 971 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.81–7.43 (m, 7H), 6.66 (d, *J* = 15.8 Hz, 1H), 6.21 (dd, *J* = 15.8, 9.3 Hz, 1H), 4.54 (t, *J* = 11.1 Hz, 1H), 4.47 (dd, *J* = 10.9, 5.7 Hz, 1H), 4.35–4.30 (m, 1H), 2.73 (dd, *J* = 18.1, 2.8 Hz, 1H), 2.65 (dd, *J* = 18.1, 3.7 Hz, 1H), 2.51 (tq, *J* = 9.2, 6.8 Hz, 1H), 1.87 (td, *J* = 9.7, 5.9 Hz, 1H), 1.18 (d, *J* = 6.7 Hz, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 170.1, 134.2, 133.5, 133.0, 132.8, 130.8, 128.2, 127.8, 127.6, 126.3, 125.9 (2C), 123.3, 68.3, 63.9, 42.5, 39.4, 36.0, 18.6; MS (EI) *m/z* 296 ($M^{+\bullet}$), 278, 181; HRMS (EI) *m/z* calculated for $C_{19}H_{20}O_3$: 296.1412, found 296.1401.



***R**-3-Hydroxy-4-methyl-5-phenylnon-6-enethioic acid S-tert-butyl ester (179):** To 0.100 g (0.494 mmol) of aldehyde **178** in 5 mL CH_2Cl_2 was added 131 mg (0.641 mmol) of (1-tert-butylsulfanyl-vinyloxy)-trimethyl-silane, and the flask was immersed in a –78 °C bath.[19, 233] To the mixture was added 0.74 mL (0.74 mmol) of dimethylaluminum chloride in hexanes (1.0 M) dropwise and the reaction was stirred for 1 h at –78 °C. The reaction was quenched by addition of 10% w/v citric acid in MeOH and slowly raised to ambient temperature; stirring was continued for 1 h. The reaction was diluted with H_2O and the aqueous layer was extracted with Et_2O (3x). The combined organic layers were dried over Na_2SO_4, filtered and the crude product mixture was concentrated *in vacuo*. Remaining solvents were removed under high vacuum. Purification *via* flash chromatography on SiO_2 (10:1 hexanes/EtOAc) afforded 143 mg (86%) of the product as a clear, viscous oil. Separation of the diastereomers by GC-MS provided the diastereomer ratio: 97.8% (T_r = 17.70), 2.2% (T_r = 17.77): IR (thin film) 3485, 3026, 2964, 1678, 1454, 1364, 969, 753, 700 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.32–7.14 (m, 5H), 5.63–5.52

(m, 2H), 4.42 (ddd, J = 9.5, 3.1, 2.2 Hz, 1H), 3.23 (dd, J = 10.4, 8.6 Hz, 1H), 2.77 (dd, J = 15.5, 9.5 Hz, 1H), 2.54 (dd, J = 15.5, 3.2 Hz, 1H), 2.03 (qd, J = 7.4, 4.7 Hz, 2H), 1.73 (ddq, J = 10.5, 6.9, 2.2 Hz, 1H), 1.49 (s, 9H), 0.97 (t, J = 7.4 Hz, 3H), 0.68 (d, J = 6.8 Hz, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 200.3, 144.5, 133.4, 131.5, 128.5, 127.8, 126.0, 68.3, 52.8, 49.9, 48.4, 42.4, 29.8, 25.5, 13.7, 10.9; MS (ESI) *m/z* 357 $(M+Na)^+$; HRMS (ESI) *m/z* calculated for $NaC_{20}H_{30}O_2S$ $(M+Na)^+$: 357.1864, found 357.1847.



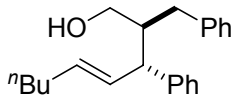
Cyclic borinic acid (180): Note that emulsions can form following large-scale reductions. In order to prevent this complication, aqueous 1M HCl can be added dropwise until the salts dissolve or a florsil plug can be utilized following extraction. Yield is based on the free boronic acid molecular weight.

To a solution of 1.1 g (3.1 mmol) boronic aldehyde **168** in 31 mL pentane at –78 °C is slowly added 3.7 mL (3.7 mmol) DIBAl-H in hexanes (1.0M). The reaction is stirred at –78 °C for 30 min, then quenched slowly with H_2O and warmed to ambient temperature. The cloudy biphasic mixture is extracted with Et_2O (3x) and the combined organic extracts are dried over Na_2SO_4. Following filtration, the solvents are removed *in vacuo* to afford the crude boronic alcohol. Purification of the product *via* flash chromatography on SiO_2 (3:1 hexanes/EtOAc) afforded 0.46 g (55%) of the product as a clear, viscous oil.

General Procedure D for Suzuki Crosscoupling Reactions 181-186, 188:[176, 177] CEM microwave tubes with snap-on septa were utilized for all coupling reactions and were found to be

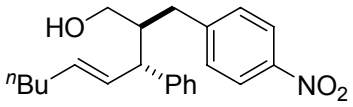
convenient alternatives to Schlenk tubes for low temperature applications. For reproducible results, it is essential to remove all atmospheric oxygen from the borane/pre-catalyst mixture *via* high vacuum prior to introduction of the solvent. Degassed solvents are required to give optimal yields for large-scale applications. Yields and catalyst loadings are based on the free boronic acid molecular weight.

A mixture of 11 mg (0.05 mmol, 5 mol%) of palladium acetate, 39 mg (0.15 mmol) of triphenylphosphine and the boronic alcohol (1.0 mmol) are placed in a CEM microwave tube. The tube is sealed with Teflon tape and the atmosphere is removed under vacuum for 30 min. The reaction vessel is backfilled with nitrogen 3x, following which time 2 mL of ^{t}amyl alcohol is added. To the stirring solution is immediately added the aryl bromide (2.1 mmol) followed by 0.92 mL of aq. 1.3M sodium carbonate. The reaction is stirred for 60 min at ambient temperature followed by heating at 80 °C for the indicated period of time (yellow → white suspension or clear solution). Upon completion, the reaction is diluted with H_2O, the biphasic mixture is transferred to a separatory funnel and the aqueous layer is extracted 3x with EtOAc. The combined organics are dried over Na_2SO_4, filtered, and the solvent is removed *in vacuo*. The crude alcohol is purified as specified. Representative isolated diastereomeric ratios were determined by GC-MS [HP-1 (12 m x 0.20 mm), pressure 21 kPa, method: 70 °C for 2.00 min, ramp @ 10 °C/min to 300 °C, hold for 60 min].



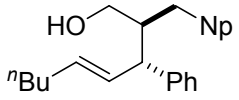
***R**-(*E*,2*S*,3*R*)-2-Benzyl-3-phenylnon-4-en-1-ol (181):** General Procedure **D** was followed employing 75 mg (0.27 mmol) of boronic alcohol **180**, 3.1 mg (0.014 mmol) of palladium

acetate, 11 mg (0.042 mmol) of triphenylphosphine, 0.060 mL (0.090 g, 0.57 mmol) of bromobenzene, 0.25 mL of aq. 1.3M sodium carbonate, and a reaction time of 5.5 h. Purification by flash chromatography (6:1 hexanes/EtOAc) on SiO_2 gave 54 mg (67%) of the title compound as a colorless oil. Separation of the diastereomers by GC-MS provided the diastereomer ratio: 4.5% (T_r = 18.80), 95.5% (T_r =18.97): IR (thin film) 3389, 3026, 2926, 1601, 1494, 1453, 1030, 970, 700 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.37–7.09 (m, 10H), 5.69 (dd, *J* = 15.2, 8.8 Hz, 1H), 5.58 (dt, *J* = 15.1, 6.1 Hz, 1H), 3.70 (dd, *J* = 11.2, 4.0 Hz, 1H), 3.55 (dd, *J* = 11.3, 4.2 Hz, 1H), 3.34 (t, *J* = 9.1 Hz, 1H), 2.55 (dd, *J* = 13.8, 4.8 Hz, 1H), 2.46 (dd, *J* = 13.7. 9.7 Hz, 1H), 2.14 (m, 1H), 2.03 (q, *J* = 6.8 Hz, 2H), 1.33 (m, 4H), 0.88 (t, *J* = 7.0 Hz, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 144.0, 140.9, 132.0, 131.9, 129.0, 128.6, 128.3, 127.9, 126.2, 125.8, 62.1, 51.2, 47.7, 35.2, 32.2, 31.5, 22.2, 13.9; MS (EI) *m/z* 308 ($M^{+\bullet}$), 290, 233, 199, 173, 117, 91; HRMS (EI) *m/z* calculated for $C_{22}H_{28}O$: 308.2140, found 308.2147.



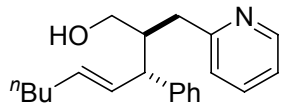
***R**-(*E*,2*S*,3*R*)-2-(4-Nitrobenzyl)-3-phenylnon-4-en-1-ol (182):** General Procedure **D** was followed employing 75 mg (0.27 mmol) of boronic alcohol **180**, 3.1 mg (0.014 mmol) of palladium acetate, 11 mg (0.042 mmol) of triphenylphosphine, 0.12 g (0.57 mmol) of 1-bromo-4-nitrobenzene, 0.25 mL of aq. 1.3M sodium carbonate, and a reaction time of 15 h. Purification by flash chromatography (5:1 hexanes/EtOAc) on SiO_2 gave 79 mg (81%) of the title compound as a colorless oil. Separation of the diastereomers by GC-MS provided the diastereomer ratio: 1.2% (T_r = 22.58), 98.8% (T_r = 22.74): IR (thin film) 3441, 3027, 2927, 1600, 1518, 1345, 700 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 8.10 (d, *J* = 8.8 Hz, 2H), 7.38 – 7.21 (m, 7H), 5.66 (dd, *J* =

15.2, 8.3 Hz, 1H), 5.58 (dt, *J* = 15.1, 6.0 Hz, 1H), 3.71 (dt, *J* = 11.1, 4.3 Hz, 1H), 3.50 (ddd, *J* = 11.0, 5.6, 3.9 Hz, 1H), 3.32 (t, *J* = 9.1 Hz, 1H), 2.68 (dd, *J* = 13.6, 9.5 Hz, 1H), 2.58 (dd, *J* = 13.6, 4.7 Hz, 1H), 2.14 (m, 1H), 2.03 (q, *J* = 6.7 Hz, 2H), 1.31 (m, 4H), 0.88 (t, *J* = 7.3 Hz, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 149.2, 146.4, 143.5, 132.4, 131.5, 129.9, 128.8, 127.8, 126.5, 123.5, 61.5, 51.3, 47.5, 35.1, 32.2, 31.5, 22.2, 13.9; MS (EI) *m/z* 353 ($M^{+\bullet}$), 278, 253, 199, 174, 131, 115; HRMS (EI) *m/z* calculated for $C_{22}H_{27}NO_3$: 353.1991, found 353.2002.

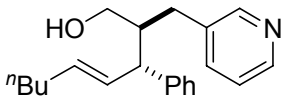


***R**-(*E*,2*S*,3*R*)-2-(Naphthalen-3-ylmethyl)-3-phenylnon-4-en-1-ol (183):** General Procedure **D** was followed employing 75 mg (0.27 mmol) of boronic alcohol **180**, 3.1 mg (0.014 mmol) of palladium acetate, 11 mg (0.042 mmol) of triphenylphosphine, 0.12 g (0.57 mmol) of 2-bromonapthalene, 0.25 mL of aq. 1.3M sodium carbonate, and a reaction time of 1.5 h. Purification by flash chromatography (8:1 hexanes/EtOAc) on SiO_2 gave 63 mg (67%) of the title compound as a colorless oil. Separation of the diastereomers by GC-MS provided the diastereomer ratio: 1.4% (T_r = 23.15), 98.6% (T_r = 23.39): IR (thin film) 3382, 3025, 2926, 1600, 1452, 1028, 969, 815, 747, 700 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.81–7.73 (m, 3H), 7.54 (s, 1H), 7.48–7.21 (m, 8H), 5.71 (dd, *J* = 15.2, 9.1 Hz, 1H), 5.60 (dt, *J* = 15.2, 6.4 Hz, 1H), 3.73 (dt, *J* = 11.1, 5.6 Hz, 1H), 3.57 (dt, *J* = 10.9, 5.9 Hz, 1H), 3.39 (t, *J* = 9.0 Hz, 1H), 2.71 (dd, *J* = 13.7, 5.1 Hz, 1H), 2.64 (dd, *J* = 13.6, 9.2 Hz, 1H), 2.29–2.18 (m, 1H), 2.04 (q, *J* = 6.7 Hz, 2H), 1.41–1.27 (m, 4H), 0.89 (t, *J* = 6.9 Hz, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 144.0, 138.4, 133.5, 132.1, 132.0, 131.8, 128.6, 127.9, 127.8, 127.6, 127.5, 127.4, 127.3, 126.3, 125.9, 125.1, 62.0, 51.3,

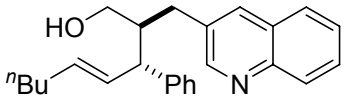
47.6, 35.3, 32.2, 31.5, 22.2, 13.9; MS (EI) *m/z* 358 ($M^{+\bullet}$), 340, 283, 269, 255, 199, 173, 142, 117; HRMS (EI) *m/z* calculated for $C_{26}H_{30}O$: 358.2297, found 358.2300.



***R**-(*E*,2*S*,3*R*)-3-Phenyl-2-pyridin-2-ylmethylnon-4-en-1-ol (184):** General Procedure **D** was followed employing 75 mg (0.27 mmol) of boronic alcohol **180**, 3.1 mg (0.014 mmol) of palladium acetate, 11 mg (0.042 mmol) of triphenylphosphine, 0.090 g (0.57 mmol) of 2-bromopyridine, 0.25 mL of aq. 1.3M sodium carbonate, and a reaction time of 48 h. Purification by flash chromatography (2:1 → 1:1 hexanes/EtOAc) on SiO_2 gave 0.030 g (36%) of the title compound as a light yellow oil: IR (thin film) 3373, 3025, 2925, 1593, 1569, 1472, 969, 756, 701 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 8.48 (d, *J* = 4.8 Hz, 1H), 7.55 (td, *J* = 7.7, 1.7 Hz, 1H), 7.35–7.10 (m, 6H), 6.85 (d, *J* = 7.8 Hz, 1H), 5.56 (dd, *J* = 15.2, 7.6 Hz, 1H), 5.47 (dt, *J* = 15.1, 5.9 Hz, 1H), 5.08 (br. s, 1H), 3.69 (dd, *J* = 11.6, 4.2 Hz, 1H), 3.61 (dd, *J* = 11.6, 6.0 Hz, 1H), 3.21 (dd, *J* = 10.4, 8.2 Hz, 1H), 2.80 (dd, *J* = 14.1, 4.2 Hz, 1H), 2.69 (dd, *J* = 14.1, 7.8 Hz, 1H), 2.35 (dddt, *J* = 10.3, 8.1, 6.0, 4.2 Hz, 1H), 1.97 (q, *J* = 6.5 Hz, 2H), 1.35–1.23 (m, 4H), 0.86 (t, *J* = 6.9 Hz, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 160.3, 148.5, 144.1, 136.7, 132.1, 131.7, 128.6, 128.0, 126.2, 124.0, 121.2, 63.5, 51.3, 45.0, 38.4, 32.2, 31.5, 22.2, 13.9; MS (EI) *m/z* 309 ($M^{+\bullet}$), 278, 174, 169, 136, 118, 106, 91; HRMS (EI) *m/z* calculated for $C_{21}H_{27}NO$: 309.2093, found 309.2106.

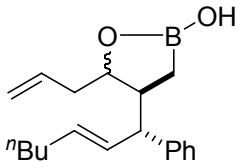


***R**-(*E*,2*S*,3*R*)-3-Phenyl-2-pyridin-3-ylmethylnon-4-en-1-ol (185):** General Procedure **D** was followed employing 75 mg (0.27 mmol) of boronic alcohol **180**, 3.1 mg (0.014 mmol) of palladium acetate, 11 mg (0.042 mmol) of triphenylphosphine, 55 μL (0.090 g, 0.57 mmol) of 3-bromopyridine, 0.25 mL of aq. 1.3M sodium carbonate, and a reaction time of 20 h. Purification by flash chromatography (1:1 hexanes/EtOAc → 2:1 EtOAc/hexanes) on SiO_2 gave 66 mg (78%) of the title compound as a light yellow oil: IR (thin film) 3276, 3027, 2925, 1597, 1577, 1424, 1029, 968, 702 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 8.42 (dd, *J* = 4.8, 1.5 Hz, 1H), 8.34 (d, *J* = 1.9 Hz, 1H), 7.40 (dt, *J* = 7.8, 1.9 Hz, 1H), 7.37–7.21 (m, 5H), 7.17 (dd, *J* = 7.8, 5.0 Hz, 1H), 5.66 (dd, *J* = 15.2, 8.5 Hz, 1H), 5.56 (dt, *J* = 15.1, 6.2 Hz, 1H), 3.70 (dt, *J* = 11.2, 4.9 Hz, 1H), 3.53 (dt, *J* = 10.8, 4.5 Hz, 1H), 3.33 (t, *J* = 9.0 Hz, 1H), 2.59–2.47 (m, 2H), 2.18–2.06 (m, 1H), 2.02 (q, *J* = 6.7 Hz, 2H), 1.49 (t, *J* = 5.0 Hz, 1H), 1.39–1.22 (m, 4H), 0.88 (t, *J* = 6.9 Hz, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 150.4, 147.2, 143.7, 136.6, 136.4, 132.2, 131.6, 128.7, 127.8, 126.3, 123.2, 61.2, 50.9, 47.3, 32.2, 32.0, 31.5, 22.2, 13.9; MS (EI) *m/z* 309 ($M^{+\bullet}$), 173, 117, 91; HRMS (EI) *m/z* calculated for $C_{21}H_{27}NO$: 309.2093, found 309.2099.



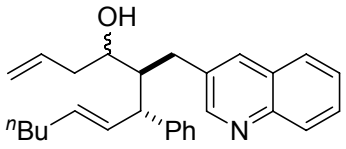
***R**-(*E*,2*S*,3*R*)-3-Phenyl-2-quinolin-3-ylmethylnon-4-en-1-ol (186):** General Procedure **D** was followed employing 75 mg (0.27 mmol) of boronic alcohol **180**, 3.1 mg (0.014 mmol) of palladium acetate, 11 mg (0.042 mmol) of triphenylphosphine, 78 μL (0.12 g, 0.57 mmol) of 3-bromoquinoline, 0.25 mL of aq. 1.3M sodium carbonate, and a reaction time of 12 h. Purification by flash chromatography (3:2 hexanes/EtOAc) on SiO_2 gave 85 mg (89%) of the title compound as a yellow oil: IR (thin film) 3290, 3026, 2925, 1601, 1574, 1495, 1452, 1034,

967, 787, 752, 701 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 8.66 (d, *J* = 2.2 Hz, 1H), 8.07 (d, *J* = 8.5 Hz, 1H), 7.83 (d, *J* = 1.8 Hz, 1H), 7.73 (d, *J* = 8.2 Hz, 1H) , 7.66 (ddd, *J* = 8.4, 6.9, 1.4 Hz, 1H), 7.52 (ddd, *J* = 8.0, 7.0, 1.1 Hz, 1H), 7.34–7.22 (m, 5H), 5.69 (dd, *J* = 15.2, 8.6 Hz, 1H), 5.59 (dt, *J* = 15.2, 5.9 Hz, 1H), 3.74 (dt, *J* = 11.0, 4.8 Hz, 1H), 3.60 (dt, *J* = 11.0, 5.3 Hz, 1H), 3.38 (t, *J* = 9.1 Hz, 1H), 2.76 (dd, *J* = 13.8, 8.7 Hz, 1H), 2.70 (dd, *J* = 14.0, 5.2 Hz, 1H), 2.28–2.18 (m, 1H), 2.03 (q, *J* = 6.7 Hz, 2H), 1.60 (t, *J* = 5.4 Hz, 1H), 1.40–1.23 (m, 4H), 0.88 (t, *J* = 6.9 Hz, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 152.3, 146.7, 143.7, 135.2, 133.7, 132.3, 131.6, 129.1, 128.8, 128.6, 128.0, 127.9, 127.3, 126.5, 126.4, 61.4, 51.1, 47.4, 32.2 (2C), 31.5, 22.2, 13.9; MS (EI) *m/z* 359 ($M^{+\bullet}$), 342, 328, 262, 173, 142, 117, 91; HRMS (EI) *m/z* calculated for $C_{25}H_{29}NO$: 359.2249, found 359.2258.



Cyclic homoallylic borinic acid (187): Note that emulsions can form with large-scale allylations. As in the case of reduction product, aqueous 1M HCl can be added dropwise to dissolve the salts prior to extraction. Yield is based on the free boronic acid molecular weight.

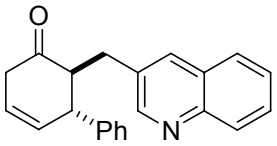
To a solution of 0.96 g (2.7 mmol) boronic aldehyde **168** in 27 mL Et_2O at –78 °C is slowly added 3.2 mL (3.2 mmol) allylmagnesium bromide in Et_2O (1.0M). The reaction is stirred at –78 °C for 1 h, then quenched slowly with H_2O and warmed to ambient temperature. The cloudy biphasic mixture is extracted with Et_2O (3x) and the combined organic extracts are dried over Na_2SO_4. Following filtration, the solvents are removed *in vacuo* to afford the crude boronic alcohol. Purification of the product *via* flash chromatography on SiO_2 (4:1 hexanes/EtOAc) afforded 0.67 g (78%) of the product as a clear, viscous oil.



***R**-(*E*,4*R*,5*S*,6*R*)-6-Phenyl-5-(quinolin-3-ylmethyl)dodeca-1,7-dien-4-ol + *R**-(*E*,4*S*,5*S*,6*R*)-6-phenyl-5-(quinolin-3-ylmethyl)dodeca-1,7-dien-4-ol (188):** General Procedure **D** was followed employing 0.75 g (2.4 mmol) of homoallylic boronic alcohol **187**, 27 mg (0.12 mmol) of palladium acetate, 94 mg (0.36 mmol) of triphenylphosphine, 0.65 mL (1.0 g, 5.0 mmol) of 3-bromoquinoline, 2.2 mL of aq. 1.3M sodium carbonate, and a reaction time of 7 h. Purification by flash chromatography (2:1 hexanes/EtOAc) on SiO_2 gave 0.54 g (58%) of the title compound as a yellow oil (d.r. 2:1 by 300 MHz ^{1}H-NMR, aryl C**H**): *Diastereomer A* - IR (thin film) 3336, 3062, 2955, 1639, 1600, 1573, 1495, 1451, 1049, 750 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 8.52 (d, *J* = 2.1 Hz, 1H), 8.03 (d, *J* = 8.3 Hz, 1H), 7.65–7.58 (m, 3H), 7.48 (t, *J* = 7.7 Hz, 1H), 7.22–7.09 (m, 5H), 5.84–5.76 (m, 1H), 5.70 (dd, *J* = 15.0, 9.3 Hz, 1H), 5.53 (dt, *J* = 14.9, 6.5 Hz, 1H), 5.17 (d, *J* = 11.7 Hz, 1H), 5.16 (d, *J* = 14.5 Hz, 1H), 3.95–3.88 (m, 1H), 3.39 (t, *J* = 9.0 Hz, 1H), 2.98 (dd, *J* = 14.3, 6.0 Hz, 1H), 2.61 (dd, *J* = 14.2, 6.7 Hz, 1H), 2.53–2.42 (m, 2H), 2.30–2.18 (m, 1H), 2.02 (q, *J* = 6.7 Hz, 2H), 1.68 (d, *J* = 4.3 Hz, 1H), 1.39–1.26 (m, 4H), 0.89 (t, *J* = 7.0 Hz, 3H); ^{13}C-NMR (75 MHz, D_3CCN): δ 153.3, 147.4, 145.6, 137.0, 136.6, 135.5, 133.4, 132.9, 129.7, 129.3 (2C), 129.2, 128.9, 128.4, 127.3, 127.0, 117.2, 71.3, 53.2, 49.9, 41.6, 32.9, 32.4, 31.2, 22.9, 14.2; MS (EI) *m/z* 399 ($M^{+\bullet}$), 381, 358, 340, 191, 173, 142, 117; HRMS (EI) *m/z* calculated for $C_{28}H_{33}NO$: 399.2570, found 399.2562.

Diastereomer B - ^{1}H-NMR (300 MHz, $CDCl_3$): δ 8.52 (d, *J* = 2.1 Hz, 1H), 8.03 (d, *J* = 8.3 Hz, 1H), 7.65–7.58 (m, 3H), 7.48 (t, *J* = 7.7 Hz, 1H), 7.22–7.09 (m, 5H), 5.84–5.76 (m, 1H), 5.70 (dd, *J* = 15.0, 9.3 Hz, 1H), 5.53 (dt, *J* = 14.9, 6.5 Hz, 1H), 5.17 (d, *J* = 11.7 Hz, 1H), 5.16 (d, *J* =

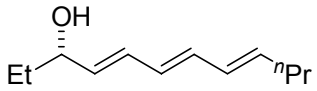
14.5 Hz, 1H), 3.95–3.88 (m, 1H), 3.39 (t, *J* = 9.0 Hz, 1H), 2.98 (dd, *J* = 14.3, 6.0 Hz, 1H), 2.61 (dd, *J* = 14.2, 6.7 Hz, 1H), 2.53–2.42 (m, 2H), 2.30–2.18 (m, 1H), 2.02 (q, *J* = 6.7 Hz, 2H), 1.68 (d, *J* = 4.3 Hz, 1H), 1.39–1.26 (m, 4H), 0.89 (t, *J* = 7.0 Hz, 3H); MS (EI) *m/z* 399 ($M^{+\bullet}$), 381, 358, 340, 191, 173, 142, 117; HRMS (EI) *m/z* calculated for $C_{28}H_{33}NO$: 399.2610, found 399.2562.



***R**-(5*R*,6*S*)-5-phenyl-6-(quinolin-3-ylmethyl)cyclohex-3-enone (189):** To a solution of 32 mg (0.08 mmol) of diastereomeric homoallylic alcohols **188** in 8 mL CH_2Cl_2 is cannulated a solution of 3.4 mg (0.0040 mmol) Grubbs II catalyst (stored in glovebox) in 8 mL CH_2Cl_2. The reaction is stirred at ambient temperature for 3 h, then quenched with 15 μL of DMSO and left for 12 h.[182] The crude reaction mixture is concentrated *in vacuo*, and the residue subject to purification *via* flash chromatography on SiO_2 (2:1 EtOAc/hexanes). The purified RCM product is immediately oxidized using 51 mg (0.12 mmol) of Dess-Martin periodinane in CH_2Cl_2 (1 mL) for 30 min (0 °C → rt). The crude ketone is passed through a plug of florsil (1:1 hexanes/EtOAc) to remove heterogeneous impurities, and concentrated *in vacuo*. Purification by flash chromatography (2:1 hexanes/EtOAc) on SiO_2 gave 12 mg (48%) of the title compound as a viscous, moderately unstable yellow oil (may contain ~ 5% polymeric material): IR (thin film) 3029, 2924, 1716, 1678, 1602, 1571, 1494, 787, 751, 702 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 8.52 (d, *J* = 1.5 Hz, 1H), 8.04 (d, *J* = 8.5 Hz, 1H), 7.84 (d, *J* = 1.3 Hz, 1H), 7.71 (d, *J* = 8.0 Hz, 1H), 7.64 (td, *J* = 7.0, 1.4 Hz, 1H), 7.50 (t, *J* = 7.8 Hz, 1H), 7.41–7.22 (m, 5H), 5.87–5.82 (m, 2H), 3.62 (dt, *J* = 9.5, 2.4 Hz, 1H), 3.27 (dd, *J* = 13.8, 8.7 Hz, 1H), 3.15–3.09 (m, 2H), 2.95 (dm,

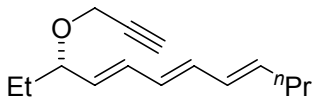
J = ~15.8 Hz, 1H), 2.75 (dd, *J* = 13.8, 3.3 Hz, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 208.4, 152.0, 146.5, 142.3, 135.7, 133.1, 131.2, 129.1, 128.8 (3C), 128.0, 127.4 (2C), 126.6, 124.1, 57.5, 50.5, 40.5, 30.2; MS (EI) *m/z* 313 ($M^{+\bullet}$), 222, 182, 143, 130, 115; HRMS (EI) *m/z* calculated for $C_{22}H_{19}NO$: 313.1467, found 313.1464.

8.0 EXPERIMENTAL SECTION FOR CHAPTER 4



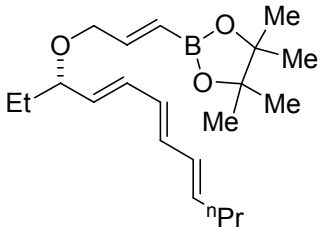
(*S*,4*E*,6*E*,8*E*)-Dodeca-4,6,8-trien-3-ol (208):[198] To a solution of 41 mg (0.17 mmol) of MIB in 3.3 mL toluene was added 6.6 mL (6.6 mmol) of Et_2Zn in hexanes (1.0 M) at ambient temperature. Following 30 min, the flask was immersed in an ice bath and 0.50 g (3.3 mmol) of the aldehyde was added dropwise by syringe.[196] The reaction was stirred at 0 °C for 30 min, then quenched carefully with sat. aq. Rochelle's salt and stirred vigorously for 30 min while warming to ambient temperature. The aqueous layer was extracted with EtOAc (3x), the combined organic layers were dried over Na_2SO_4, filtered, and the crude product mixture was concentrated *in vacuo*. Purification by flash chromatography on SiO_2 (6:1 hexanes/EtOAc) yielded 0.43 g (73%) of the title compound as a clear oil. Separation of the enantiomers by chiral HPLC (Daicel Chiracel^{TM} OD-H column, flow rate 1.0 mL/min, 2.0% *i*-PrOH, 98.0% hexanes) provided the enantiomeric ratio: 94.5 (*S*, Tr = 12.1): 5.5 (*R*, Tr = 13.3) (89% ee): $[\alpha]_D^{26}$ = +24.0 (c 1.24, $CHCl_3$); IR (thin film) 3354, 3015, 2961, 1636, 1436, 995 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$): δ 6.26–6.18 (m, 2H), 6.11 (dd, *J* = 15.0, 10.4 Hz, 1H), 6.07 (dd, *J* = 15.0, 10.6 Hz, 1H), 5.73 (dt, *J* = 14.5, 7.1 Hz, 1H), 5.66 (dd, *J* = 15.2, 6.9 Hz, 1H), 4.11–4.06 (m, 1H), 2.09 (q, *J* = 7.2 Hz, 2H), 1.65–1.51 (m, 2H), 1.46–1.39 (m, 3H), 0.93 (t, *J* = 7.1 Hz, 3H), 0.91 (t, *J* = 7.1 Hz, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 135.6, 135.0, 133.4, 130.9, 130.3, 129.6, 74.0, 34.8,

30.1, 22.4, 13.6, 9.6; MS (EI) *m/z* 180 ($M^{+\bullet}$), 162, 147, 133, 119, 105, 91; HRMS (EI) *m/z* calculated for $C_{12}H_{20}O$: 180.1514, found 180.1506.

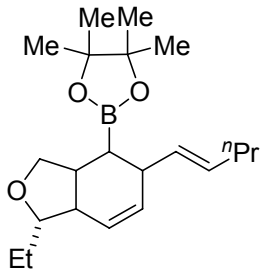


(*S*,4*E*,6*E*,8*E*)-3-(Prop-2-ynyloxy)dodeca-4,6,8-triene (209): To 0.97 g (24 mmol) of sodium hydride (60% dispersion in mineral oil, pre-washed 3x with pentane) was added 17 mL of THF. The solution was cooled to 0 °C, and 2.1 g (12 mmol) of alcohol **208** was added *via* syringe. The reaction was stirred at 0 °C for ~15 min, then warmed slowly to ambient temperature. At this time, a condenser was attached to the reaction vessel and the reaction mixture was heated to reflux. Following 30 min, the reaction was cooled to ambient temperature whereupon 3.6 g (24 mmol) of propargyl bromide in toluene (80%/wt) was added carefully through the condenser. Following 1.5 h at reflux, the solution was cooled to ambient temperature and quenched carefully with H_2O. The aqueous layer was extracted with Et_2O (3x), the combined organic layers were dried over $MgSO_4$ and filtered. The crude product was concentrated *in vacuo*. Purification by flash chromatography on SiO_2 (50:1 hexanes/EtOAc) afforded 2.2 g (83 %) of the product as a yellow oil: $[\alpha]_D^{26}$ = –141 (c 1.32, $CHCl_3$); IR (thin film) 3307, 3016, 2962, 2116, 1636, 1463, 1072, 997, 663 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 6.27–6.04 (m, 4H), 5.75 (dt, *J* = 14.6, 7.0 Hz, 1H), 5.44 (dd, *J* = 15.4, 8.4 Hz, 1H), 4.17 (dd, *J* = 15.6, 2.3 Hz, 1H), 4.01 (dd, *J* = 15.7, 2.3 Hz, 1H), 3.84 (dt, *J* = 8.3, 6.5 Hz, 1H), 2.39 (t, *J* = 2.3 Hz, 1H), 2.09 (q, *J* = 7.2 Hz, 2H), 1.72–1.61 (m, 1H), 1.60–1.48 (m, 1H), 1.48–1.37 (m, 2H), 0.91 (t, *J* = 7.3 Hz, 3H), 0.91 (t, *J* = 7.5 Hz, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 136.0, 133.8 (2C), 131.8, 130.2, 129.4, 80.9. 80.4, 73.6,

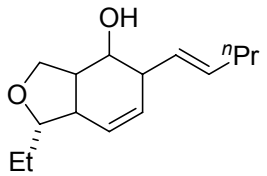
55.1, 34.9, 28.4, 22.4, 13.6, 9.7; MS (EI) *m/z* 218 ($M^{+\bullet}$), 189, 162, 133, 119, 107, 91, 79; HRMS (EI) *m/z* calculated for $C_{15}H_{22}O$: 218.1671, found 218.1665.



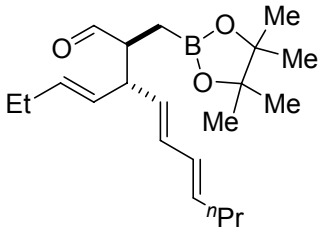
2-(1*E*)-3-(*S*,4*E*,6*E*,8*E*)-Dodeca-4,6,8-trien-3-yloxyprop-1-enyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (210):[154, 155] To a suspension of 52 mg (0.20 mmol) of $Cp_2Zr(H)Cl$ and 2.0 mL CH_2Cl_2 in a microwave reaction vessel was added 0.88 g (4.0 mmol) of alkyne **209** at 0 °C. To this mixture was added 0.56 g (4.4 mmol) of pinacolborane and the resulting suspension was warmed to ambient temperature, then heated at 80 ^oC in a microwave reactor for 45 min. The solvent was removed *in vacuo*. Purification by flash chromatography (22:1 hexanes/EtOAc) on Iatrobeads gave 0.75 g (55 %) of the title compound as a colorless oil: $[\alpha]_D^{26}$ = –14.2 (c 1.22, $CHCl_3$); IR (thin film) 2976, 1644, 1463, 1354, 1146, 996, 850, 628 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$): δ 6.64 (dt, *J* = 18.1, 4.5 Hz, 1H), 6.24–6.04 (m, 4H), 5.72 (dt, *J* = 14.9, 7.1 Hz, 1H), 5.71 (d, *J* = 18.0 Hz, 1H), 5.48 (dd, *J* = 14.4, 8.1 Hz, 1H), 4.10 (ddd, *J* = 14.7, 4.2, 1.7 Hz, 1H), 3.91 (ddd, *J* = 14.7, 4.7, 1.6 Hz, 1H), 3.66 (dt, *J* = 7.8, 6.5 Hz, 1H), 2.08 (q, *J* = 7.1, 2H), 1.70–1.62 (m, 1H), 1.56–1.49 (m, 1H), 1.46–1.38 (m, 2H), 1.27 (s, 12H), 0.91 (t, *J* = 7.5 Hz, 3H), 0.89 (t, *J* = 7.6 Hz, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 149.9, 135.6, 133.3, 133.2, 132.8, 130.3, 129.6, 118.6 (br), 83.1, 81.5, 69.6, 34.9, 28.6, 24.8, 22.4, 13.6, 9.7; MS (EI) *m/z* 346 ($M^{+\bullet}$), 317, 288, 248, 187, 179, 163, 107; HRMS (EI) *m/z* calculated for $C_{21}H_{35}BO_3$: 346.2679, found 346.2679.



2-(1*S*)-1-Ethyl-1,3,3a,4,5,7a-hexahydro-5-(*E*)-pent-1-enylisobenzofuran-4-yl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (211):[202, 203, 205] The relative stereochemistry has not been established for this compound. A solution of 0.13 g (3.8 mmol) of vinylborolane **210** in 3.8 mL of 1,2-DCE was heated in a microwave reactor to 150 °C at 150 W for 45 min. The crude product was concentrated *in vacuo*. Purification by flash chromatography on SiO_2 (15:1 hexanes/EtOAc) yielded 79 mg (61%) of the title compound as a clear oil and 11 mg (8%) of a diastereomeric product (88:12 d.r. by mass): $[\alpha]_D^{26}$ = +177 (c 1.98, $CHCl_3$); IR (thin film) 3015, 2931, 1642, 1464, 1379, 1144, 966, 851 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$): δ 5.83 (d, *J* = 9.9 Hz, 1H), 5.53 (dt, *J* = 9.8, 3.3 Hz, 1H), 5.49–5.41 (m, 2H), 4.13 (t, *J* = 7.2 Hz, 1H), 3.44 (ddd, *J* = 10.9, 7.0, 4.6 Hz, 1H), 3.33 (dd, *J* = 11.2, 7.4 Hz, 1H), 3.14–3.09 (m, 1H), 2.16–2.08 (m, 1H), 2.03–1.90 (m, 2H), 1.83 (tq, *J* = 10.6, 1.9 Hz, 1H), 1.65–1.13 (m, 1H), 1.61–1.52 (m, 1H), 1.44–1.32 (m, 3H), 1.22 (s, 6H), 1.20 (s, 6H), 1.00 (t, *J* = 7.5 Hz, 3H), 0.89 (t, *J* = 7.4 Hz, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 132.6, 131.8, 131.3, 124.9, 83.1, 82.4, 70.6, 49.6, 41.0, 40.6, 34.6, 27.4, 25.2, 24.5, 22.4, 13.7, 10.1; MS (EI) *m/z* 346 ($M^{+\bullet}$), 288, 231, 205, 188, 160, 133, 101, 84; HRMS (EI) *m/z* calculated for $C_{21}H_{35}BO_3$: 346.2679, found 346.2675.

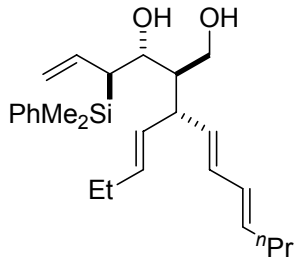


(1*S*)-1-Ethyl-1,3,3a,4,5,7a-hexahydro-5-(*E*)-pent-1-enylisobenzofuran-4-ol (212): To a solution of 67 mg (0.19 mmol) of dioxaborolane **211** in 1.9 mL of MeOH at ambient temperature was slowly added 1.9 mL of 1:1 1M NaOH:30% HOOH. Following 2 h, the reaction mixture was concentrated in vacuo, diluted with H_2O and CH_2Cl_2 and the aqueous layer was extracted with CH_2Cl_2 (3x). The combined organic layers were dried over Na_2SO_4, filtered and the crude product was concentrated *in vacuo*. Purification by flash chromatography on SiO_2 (5:2 hexanes/EtOAc) gave 35 mg (79%) of the product as a white crystalline solid: m.p. 75-77 °C; $[\alpha]_D^{26}$ = +247 (c 1.18, $CHCl_3$); IR (thin film) 3378, 3018, 2930, 1455, 1344, 1252, 1085, 1001, 981, 720 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 5.77 (d, *J* = 9.6 Hz, 1H), 5.68 (dt, *J* = 15.3, 6.8 Hz, 1H), 5.58 (ddd, *J* = 9.6, 4.0, 2.7 Hz, 1H), 5.33 (ddt, *J* = 15.3, 9.2, 1.2 Hz, 1H), 4.09 (t, *J* = 6.9 Hz, 1H), 3.93 (dd, *J* = 10.1, 6.8 Hz, 1H), 3.67 (dd, *J* = 10.2, 7.8 Hz, 1H), 3.56 (ddd, *J* = 10.0, 7.2, 4.5 Hz, 1H), 3.26–3.16 (m, 1H), 2.21–2.02 (m, 4H), 1.79–1.53 (m, 3H), 1.49–1.37 (m, 2H), 1.02 (t, *J* = 7.4 Hz, 3H), 0.92 (t, *J* = 7.3 Hz, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 137.5, 131.7, 126.7, 124.8, 82.7, 71.6, 69.5, 49.5, 47.3 (2C), 34.7, 27.5, 22.4, 13.6, 10.2; MS (EI) *m/z* 236 ($M^{+\bullet}$), 207, 163, 151, 121, 109, 91, 79; HRMS (EI) *m/z* calculated for $C_{15}H_{24}O_2$: 236.1776, found 236.1777.



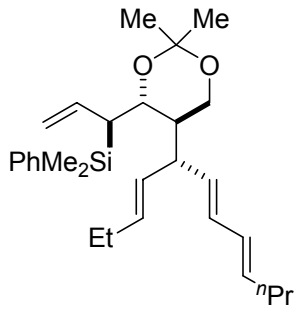
(2*S*,3*S*,4*E*,6*E*)-3-(*E*)-But-1-enyl-2-4,4,5,5-tetramethyl-1,3,2-dioxa-borolan-2-ylmethyldeca-4,6-dienal (213): A solution of 13 mg (0.038 mmol) of $NaBPh_4$ in CH_2Cl_2/acetone (25:1) (1.4 mL) was added to 17 mg (0.019 mmol) of $[IrCl(C_8H_{14})_2]_2$ and 31 mg (0.11 mmol) of PCy_3 in 1.4 mL of anhydrous CH_2Cl_2 and the resulting yellow solution stirred for 30 min at ambient

temperature. To this solution was added 0.67 g (1.9 mmol) of vinylborolane **210** and the reaction was stirred for 90 min. The reaction was quenched with PPh_3 (6.0 mol%, 0.06 equiv) and the crude vinyl ether was concentrated *in vacuo*. The crude oil was then diluted with 6.7 mL 1,2-DCE, and the flask was equipped with a reflux condenser. The solution was heated at 60 °C for 5 h following which time the crude aldehyde was concentrated *in vacuo*. Purification by flash chromatography (18:1 hexanes/EtOAc) on Iatrobeads gave 0.39 g (58 %) of the title compound as an orange oil (C**H**O, = 88:7:5): $[\alpha]_D^{26}$ = +24.7 (c 1.47, $CHCl_3$); IR (thin film) 2963, 2725, 1724, 1461, 1371, 1146, 989, 847 cm^{-1}; ^{1}H-NMR (300 MHz, C_6D_6): δ 9.68 (d, *J* = 0.8 Hz, 1H), 6.03 (dd, *J* = 14.4, 10.4 Hz, 1H), 5.95 (dd, *J* = 14.4, 10.3 Hz, 1H), 5.51 (dd, *J* = 14.3, 7.0 Hz, 1H), 5.46–5.33 (m, 2H), 5.29 (dd, *J* = 15.4, 7.3 Hz, 1H), 3.00 (q, *J* = 7.0 Hz, 1H), 2.70 (br dt, *J* = 9.9, 5.9 Hz, 1H), 1.97–1.80 (m, 2H), 1.36–1.23 (m, 1H), 1.17 (dd, *J* = 16.0, 10.0 Hz, 1H), 1.10 (s, 6H), 1.09 (s, 6H), 0.96 (dd, *J* = 16.0, 4.8 Hz, 1H), 0.83 (t, *J* = 7.4 Hz, 3H), 0.82 (t, *J* = 7.3 Hz, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 204.9, 134.5, 133.9, 131.9, 130.9, 130.0, 128.4, 83.2, 52.5, 47.7, 34.7, 25.6, 24.8, 24.7, 22.4, 13.7 (B-**C** = *unobserved*).



(2*R*,3*R*,4*S*)-2-(*S*,3*E*,6*E*,8*E*)-Dodeca-3,6,8-trien-5-yl-4-dimethylphenyl-silylhex-5-ene-1,3-diol (214):[207] To a solution of 86 mg (0.49 mmol) of dimethylphenyl allylsilane in 1.5 mL of THF was added 0.31 mL (0.49 mmol) of *n*-butyllithium in hexanes (1.6 M) at ambient temperature.[234] Following 15 min, the mixture was cooled to –78 °C and 0.13 mL (0.14 g, 0.54 mmol) of $TiCl(O^iPr)_3$ was added in 0.3 mL THF. The reaction was stirred for 20 min, then a solution of

0.15 g (0.43 mmol) of aldehyde **213** in 0.45 mL of THF was added *via* cannula followed by two 0.15 mL THF washes. After 1.5 h, the reaction was quenched with sat. aq. NH_4Cl, and the aqueous layer was extracted with Et_2O (3x). The combined organic extracts were dried over Na_2SO_4, filtered through 2:1 celite:florsil and the crude borane was concentrated *in vacuo*. The crude product was then subject to 4 mL of a 2:1:1 MeOH:1M NaOH:30% HOOH solution for 15-20 min at 0 °C. The mixture was diluted with H_2O and CH_2Cl_2, and the aqueous layer was extracted with CH_2Cl_2 (3x). The combined organic extracts were dried over Na_2SO_4, filtered, and the crude product was concentrated *in vacuo*. Purification by flash chromatography on SiO_2 (7:1 hexanes/EtOAc) afforded 0.10 g (56%) of the product as an oil: $[\alpha]_D^{26}$ = –9.12 (c 2.17, $CHCl_3$); IR (thin film) 3383, 3070, 2960, 1622, 1427, 1247, 1112, 989, 834, 700 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.56–7.48 (m, 2H), 7.39–7.32 (m, 3H), 6.03–5.86 (m, 3H), 5.61 (dt, *J* = 13.8, 6.8 Hz, 1H), 5.44 (dtd, *J* = 15.3, 6.2, 1.0 Hz, 1H), 5.37–5.29 (m, 1H), 5.22 (ddt, *J* = 15.4, 8.5, 1.4 Hz, 1H), 5.12 (dd, *J* = 10.2, 2.0 Hz, 1H), 4.98 (dd, *J* = 16.6, 1.4 Hz, 1H), 3.94 (t, *J* = 5.4 Hz, 1H), 3.81 (d, *J* = 10.7 Hz, 1H), 3.65–3.53 (m, 1H), 2.98 (q, *J* = 7.1 Hz, 1H), 2.6 (br. s, 1H), 2.5 (br. s, 1H), 2.22 (dd, *J* = 10.5, 5.0 Hz, 1H), 2.06 (q, *J* = 7.0 Hz, 2H), 1.98 (q, *J* = 7.4 Hz, 2H), 1.57 (qd, *J* = 6.3, 2.6 Hz, 1H), 1.49–1.37 (m, 2H), 0.95 (t, *J* = 7.4 Hz, 3H), 0.93 (t, *J* = 7.4 Hz, 3H), 0.35 (s, 3H), 0.33 (s, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 137.7, 135.4, 134.0, 133.4, 133.1, 131.8, 131.2, 130.4, 130.1, 129.2, 127.9, 115.7, 73.7, 62.4, 48.0, 44.6, 40.5, 34.7, 25.6, 22.5, 13.7 (2C), –3.3, –4.1; MS (ESI) *m/z* 435 $(M+Na)^+$; HRMS (ESI) *m/z* calculated for $NaC_{26}H_{40}O_2Si$ $(M+Na)^+$: 435.2695, found 435.2679.



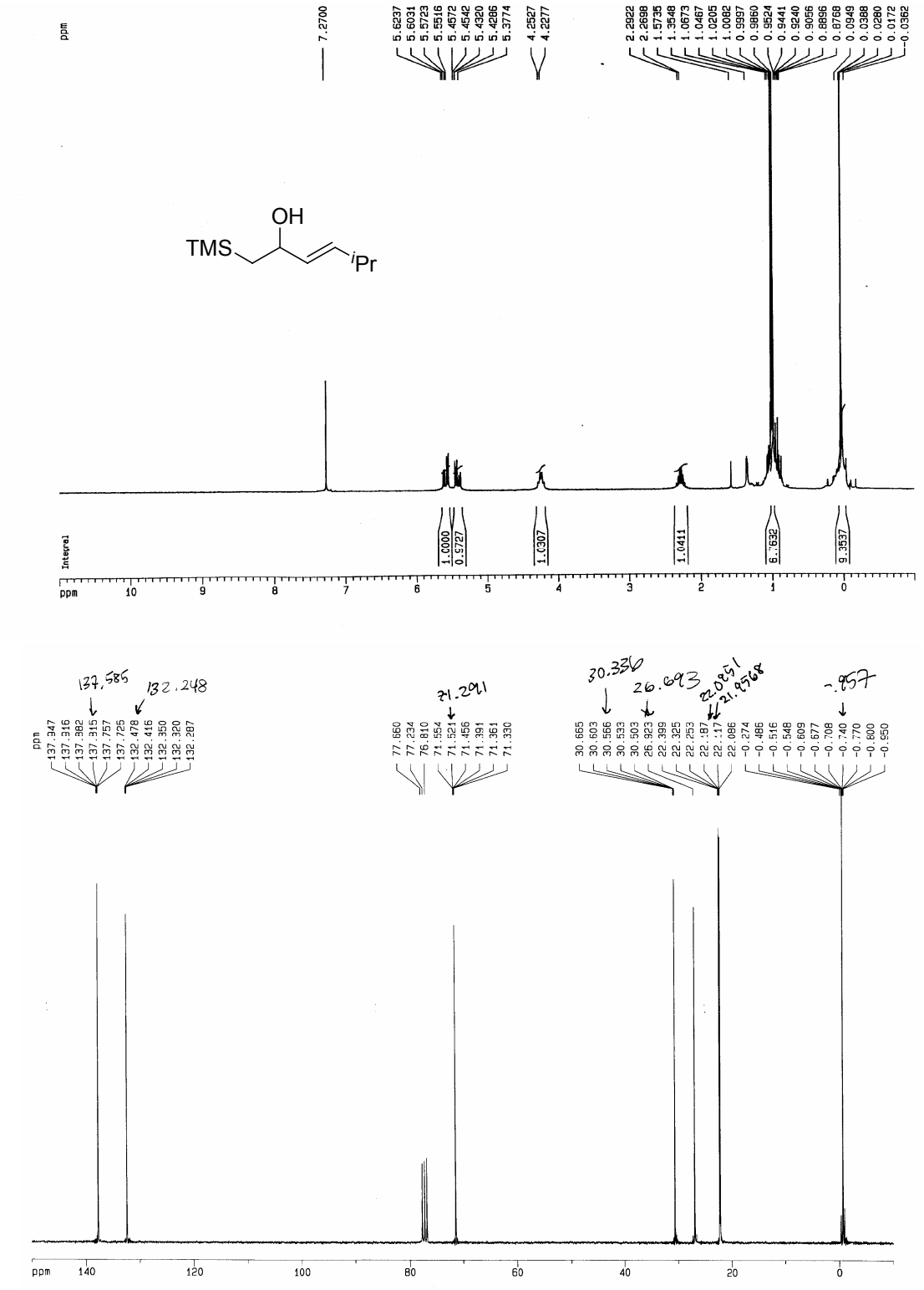
(*S*)-1-(4*R*,5*R*)-5-(S,3*E*,6*E*,8*E*)-dodeca-3,6,8-trien-5-yl-2,2-dimethyl-1,3-dioxan-4-ylallyldimethylphenylsilane (215): To a solution of 0.11 g (0.27 mmol) of diol **214** in 2.8 mL of 1:1 2,2-dimethoxypropane:DMF was added 14 mg (0.054 mmol) of pyridine *p*-toluenesulphonic acid. Following 1 h, the reaction was quenched with H_2O and the aqueous layer was extracted with Et_2O (3x). The combined organic extracts were dried over Na_2SO_4, filtered and concentrated *in vacuo*. Purification by filtration through florsil (5:1 hexanes/EtOAc) gave 0.11 g (89%) of the product as a clear oil: $[\alpha]_D^{26}$ = –8.02 (c 1.47, $CHCl_3$); IR (thin film) 3070, 2961, 1622, 1456, 1379, 1245, 1198, 1114, 988, 837, 814, 700 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.48–7.44 (m, 2H), 7.38–7.29 (m, 3H), 6.08–5.86 (m, 3H), 5.68 (dt, *J* = 14.2, 6.9 Hz, 1H), 5.45–5.34 (m, 2H), 5.27 (ddt, *J* = 15.4, 6.3, 1.3 Hz, 1H), 5.02 (dd, *J* = 10.2, 2.2 Hz, 1H), 4.86 (dd, *J* = 17.3, 1.9 Hz, 1H), 3.77–3.53 (m, 3H), 2.85–2.79 (m, 1H), 2.21–1.84 (m, 6H), 1.53–1.40 (m, 2H), 1. 22 (s, 3H), 1.02 (s, 3H), 0.95 (t, *J* = 7.2 Hz, 3H), 0.94 (t, *J* = 7.3 Hz, 3H), 0.32 (s, 3H), 0.24 (s, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 138.1, 135.1, 134.0, 133.5, 132.9, 132.2, 130.1, 129.8, 129.5, 128.7, 127.4, 114.7, 97.7, 71.1, 60.7, 43.6, 41.3, 37.2, 34.7, 29.2, 25.5, 22.5, 18.8, 13.7 (2C), –3.3, –4.5; MS (EI) *m/z* 452 ($M^{+\bullet}$), 394, 379, 365, 285, 204, 193, 163, 135; HRMS (EI) *m/z* calculated for $C_{29}H_{44}O_2Si$: 452.3111, found 452.3136.

APPENDIX A

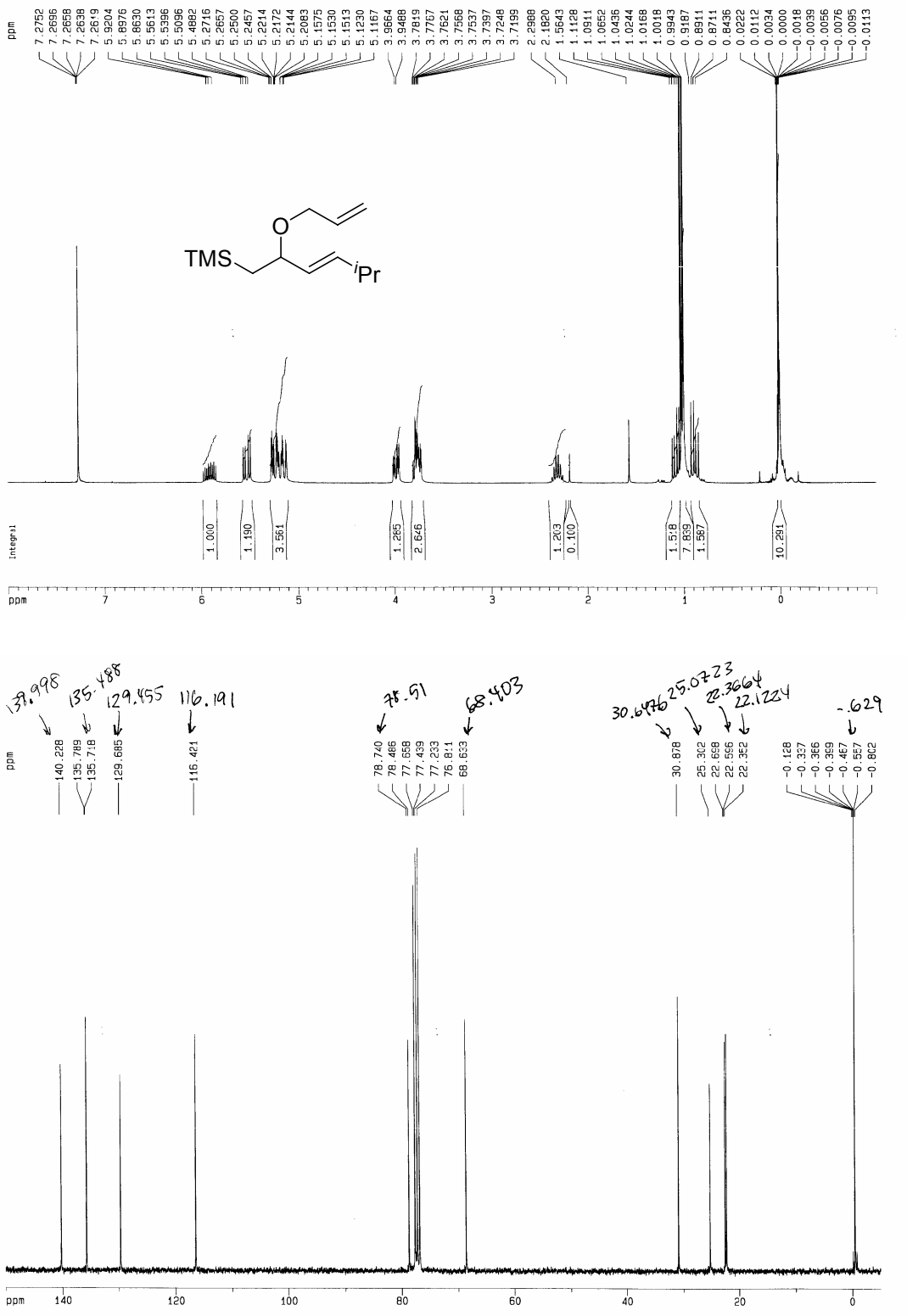
^{1}H AND ^{13}C SPECTRA OF ALL COMPOUNDS

(in numerical order)

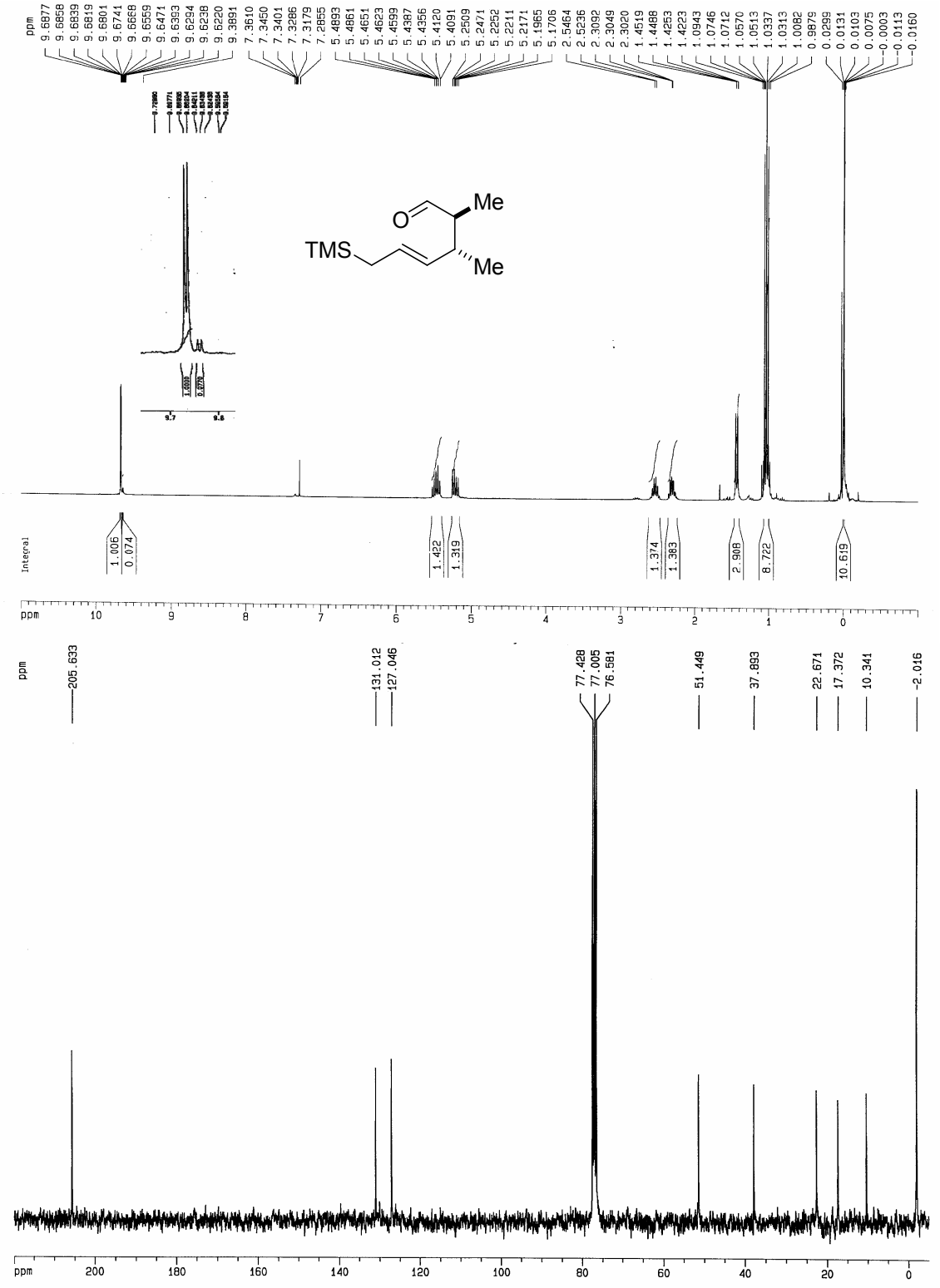
A.1 COMPOUND 16



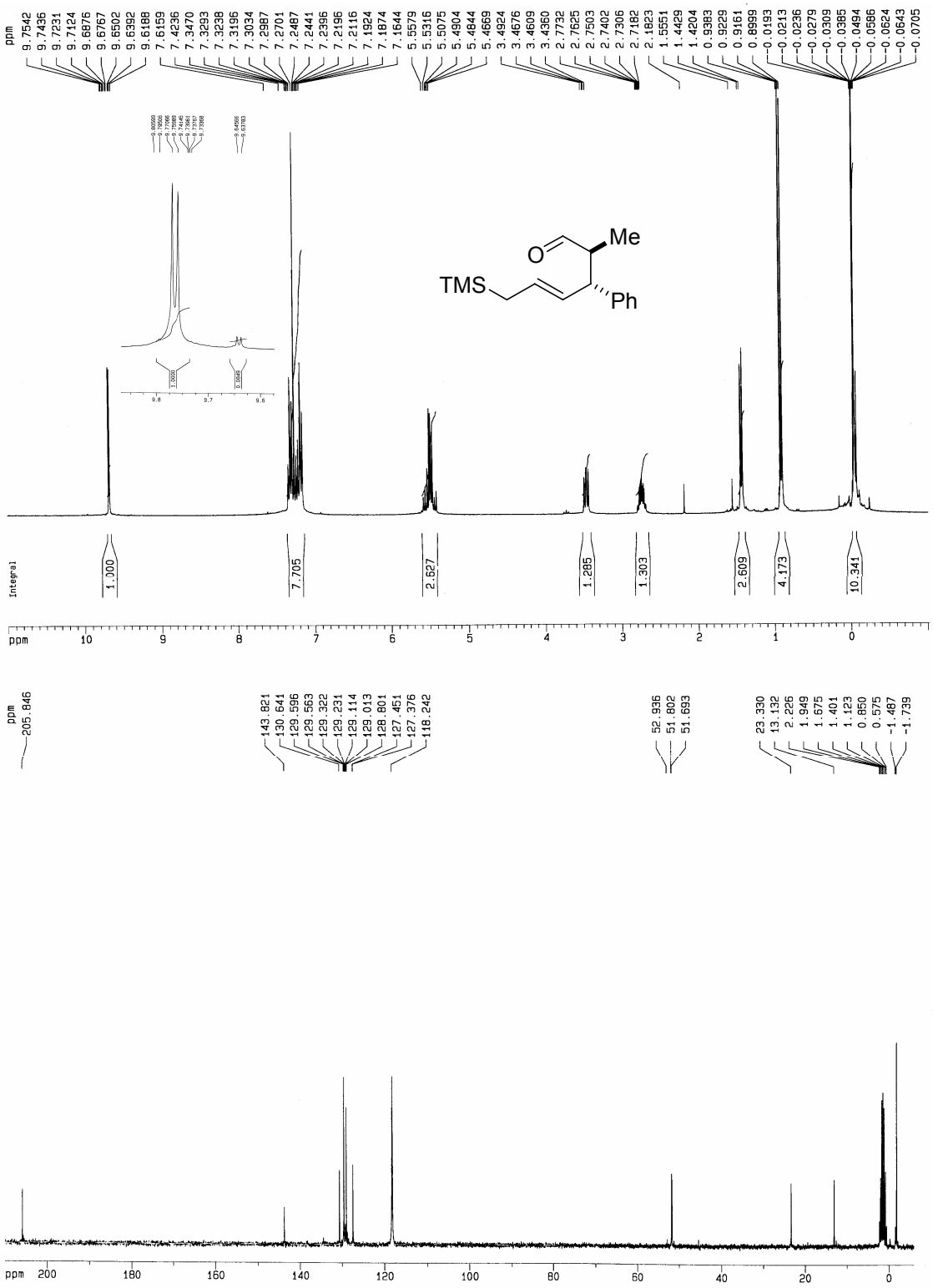
A.2 COMPOUND 19



A.3 COMPOUND 20

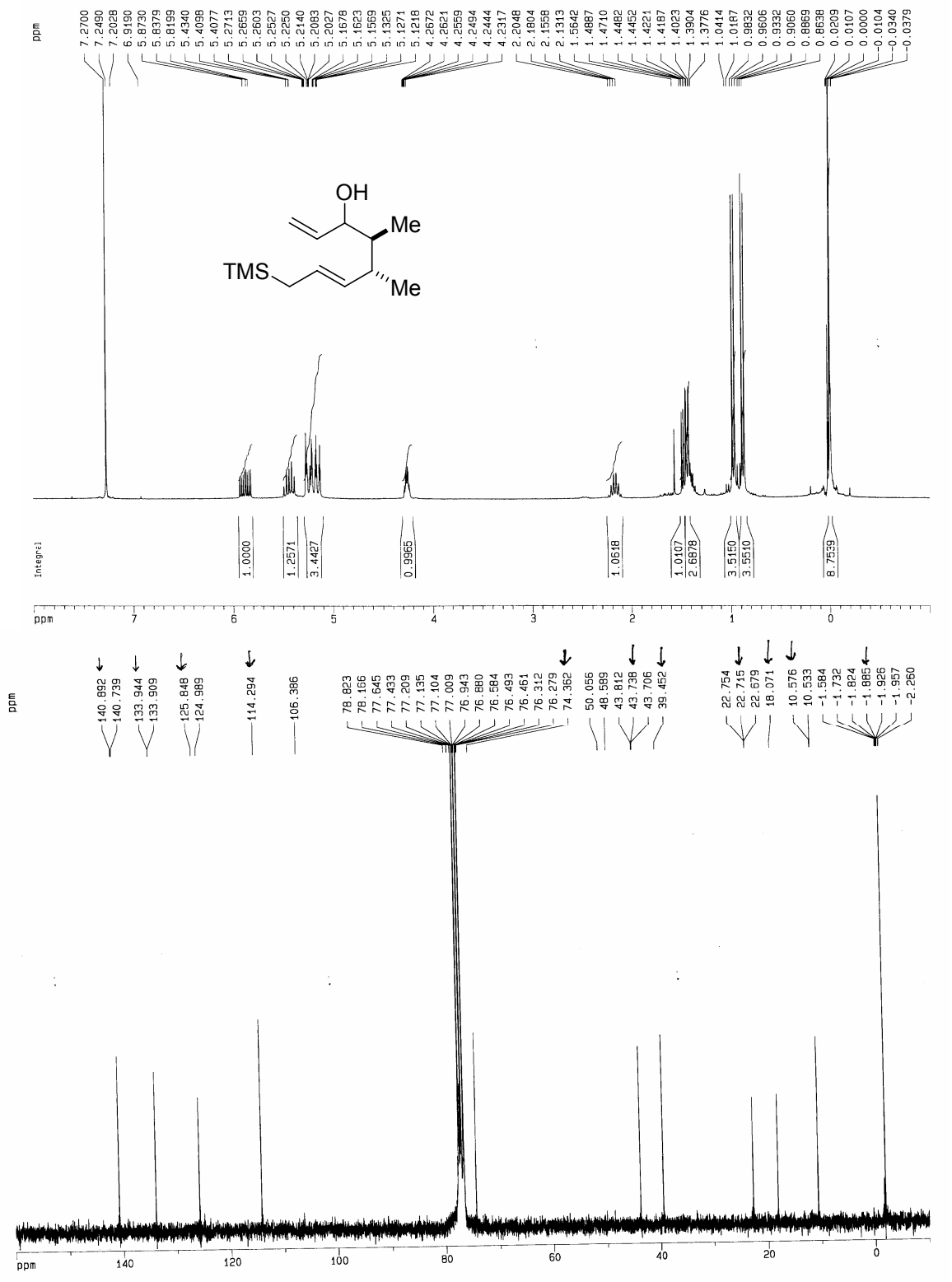


A.4 COMPOUND 21

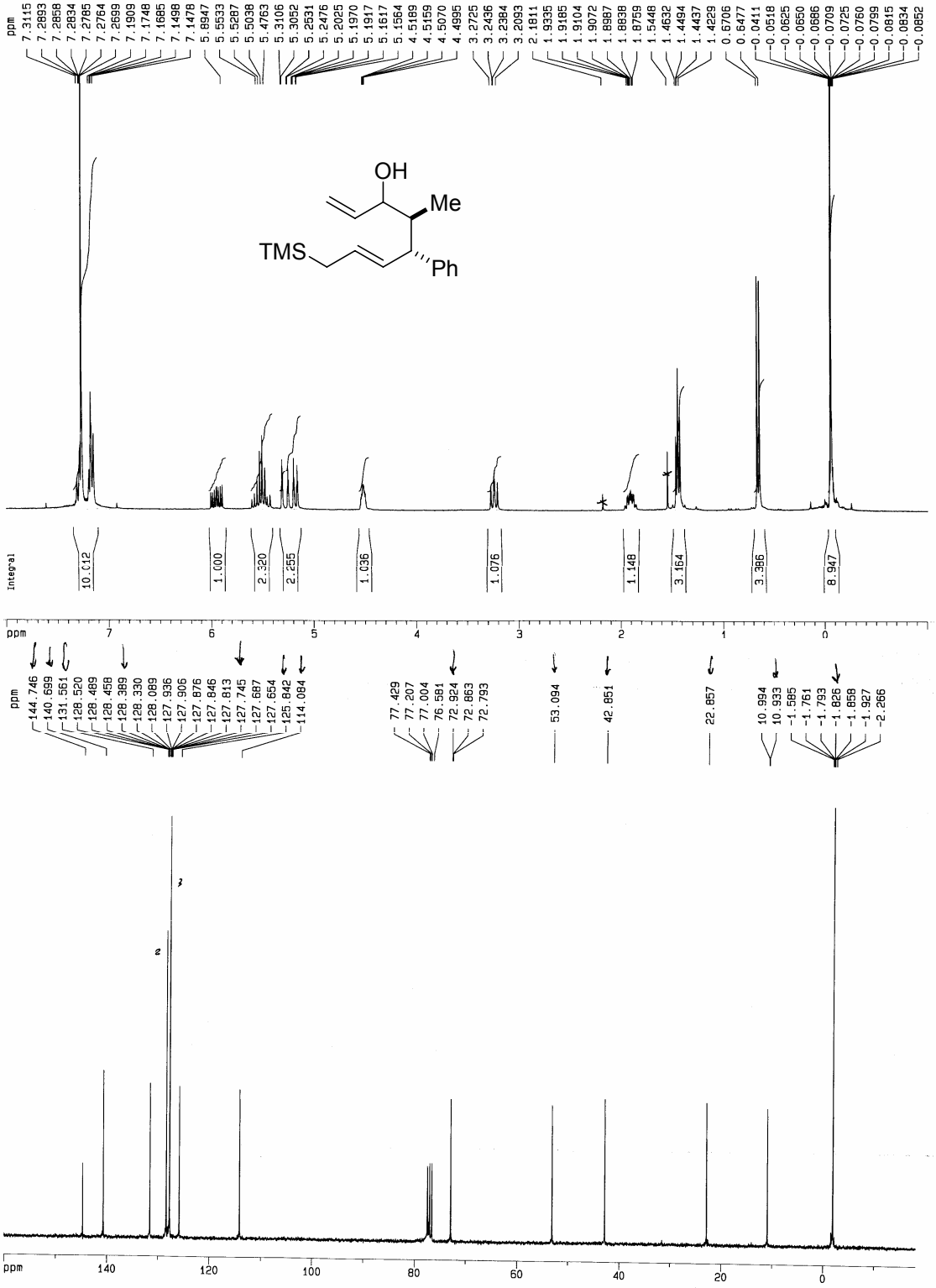


A.5 COMPOUND 22

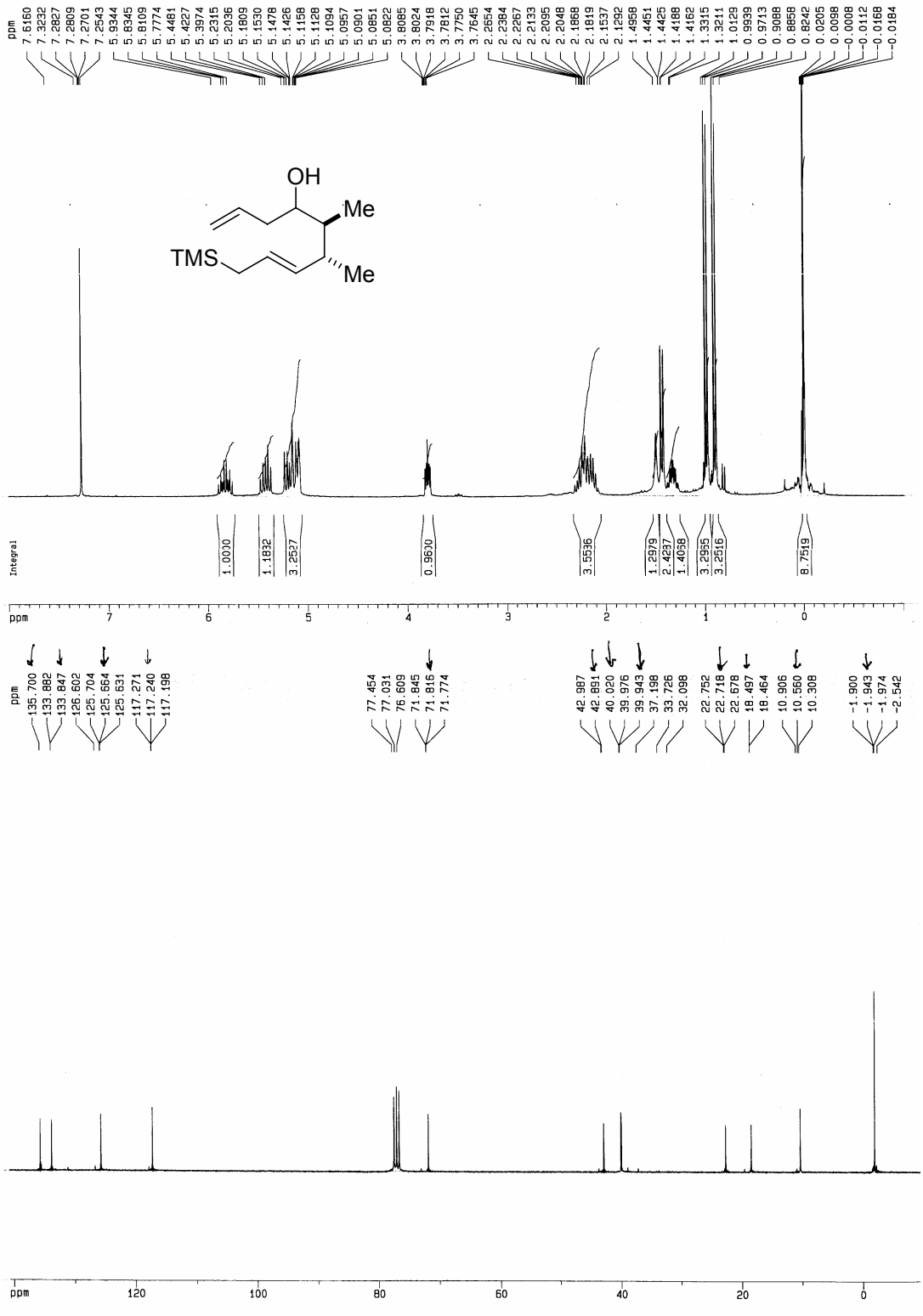
A.6 COMPOUND 23



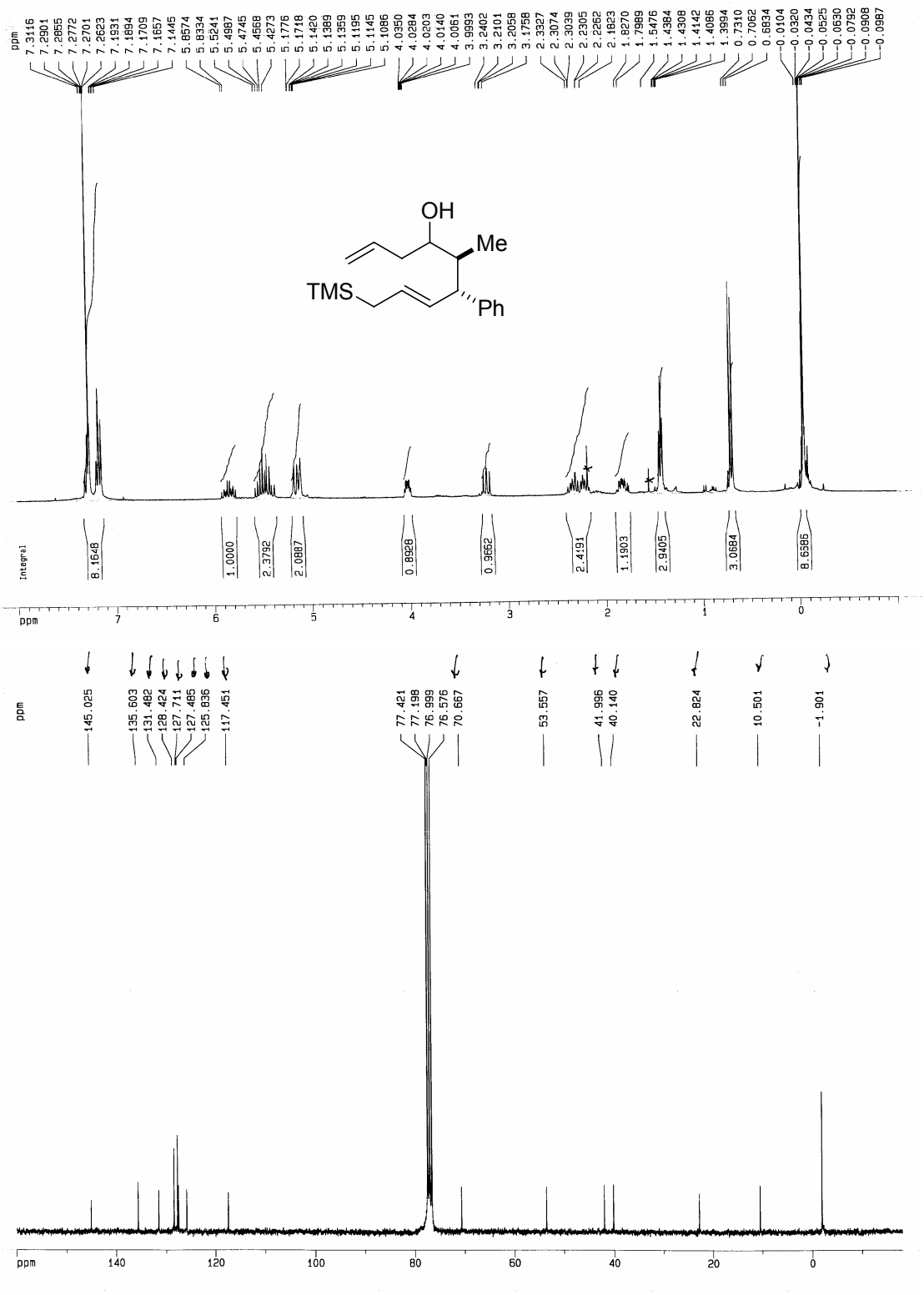
A.7 COMPOUND 24



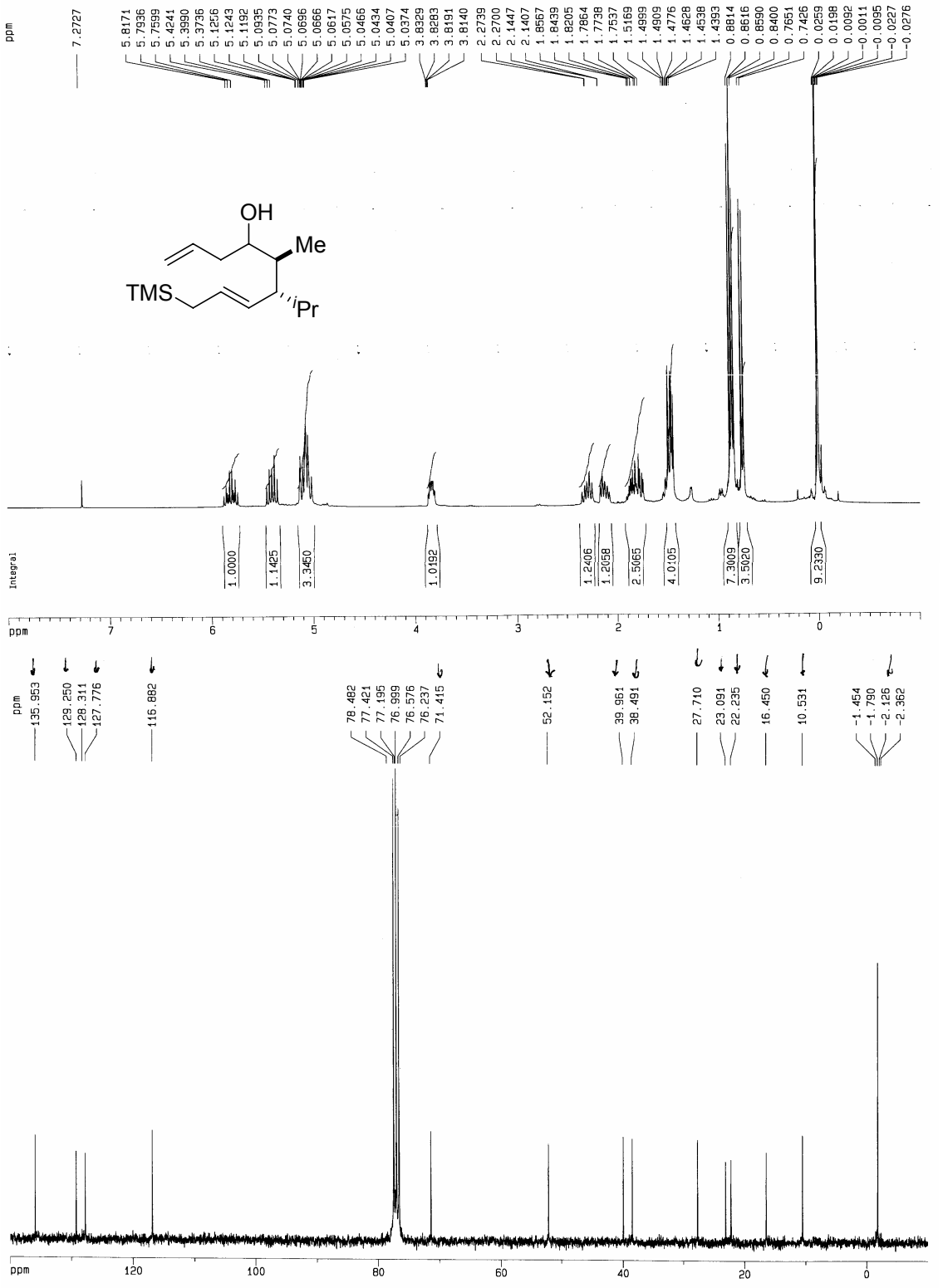
A.8 COMPOUND 25



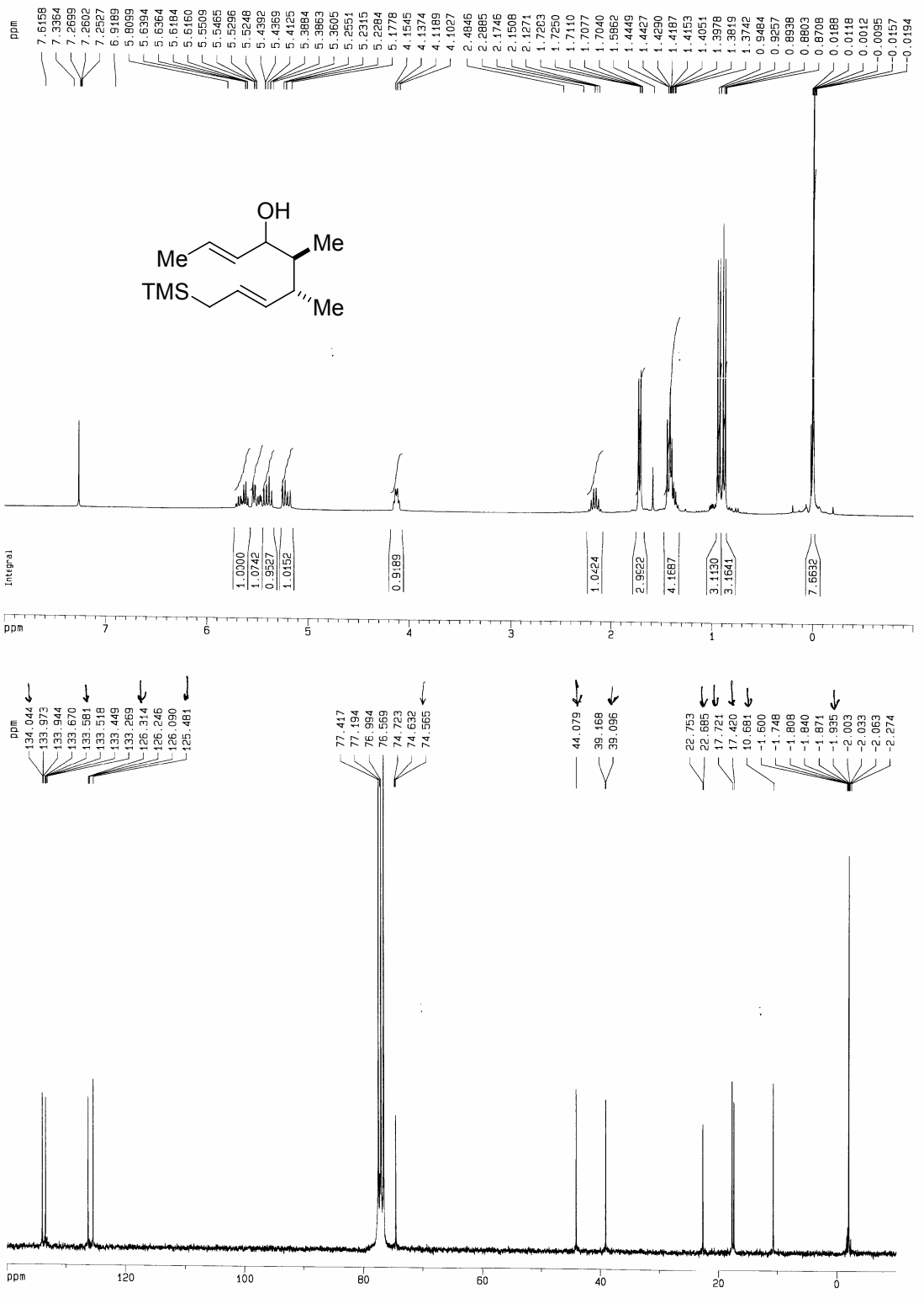
A.9 COMPOUND 26



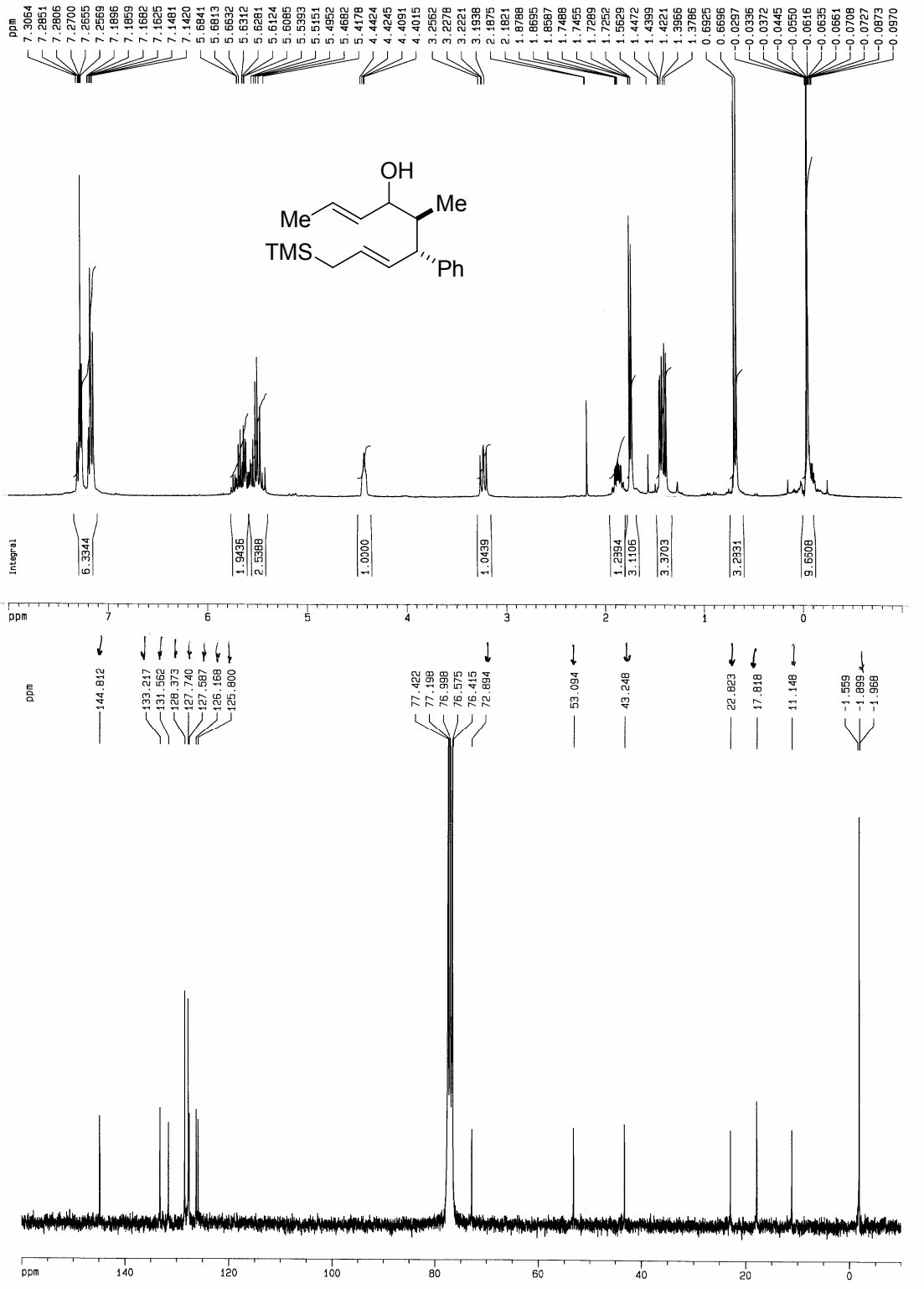
A.10 COMPOUND 27



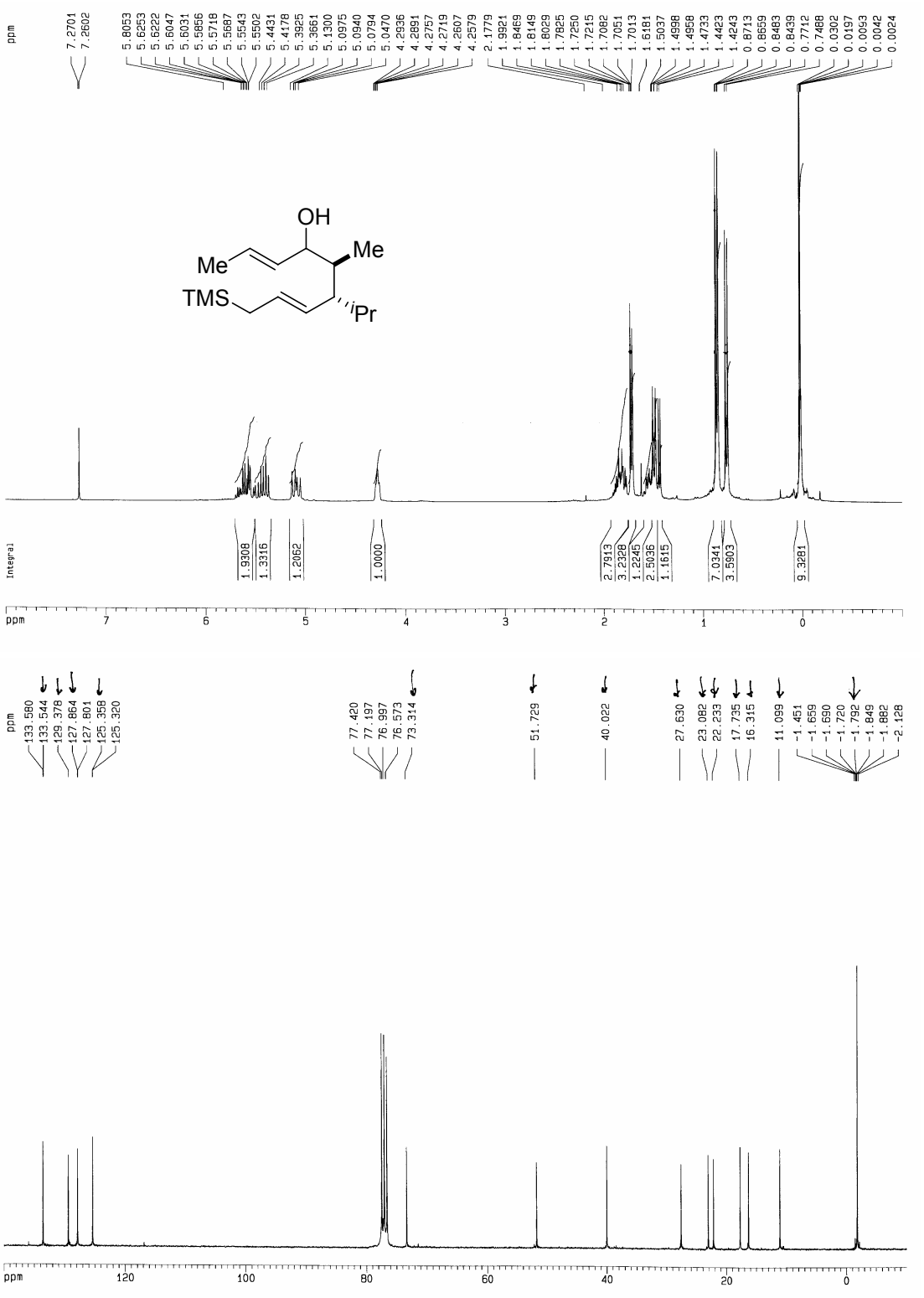
A.11 COMPOUND 28



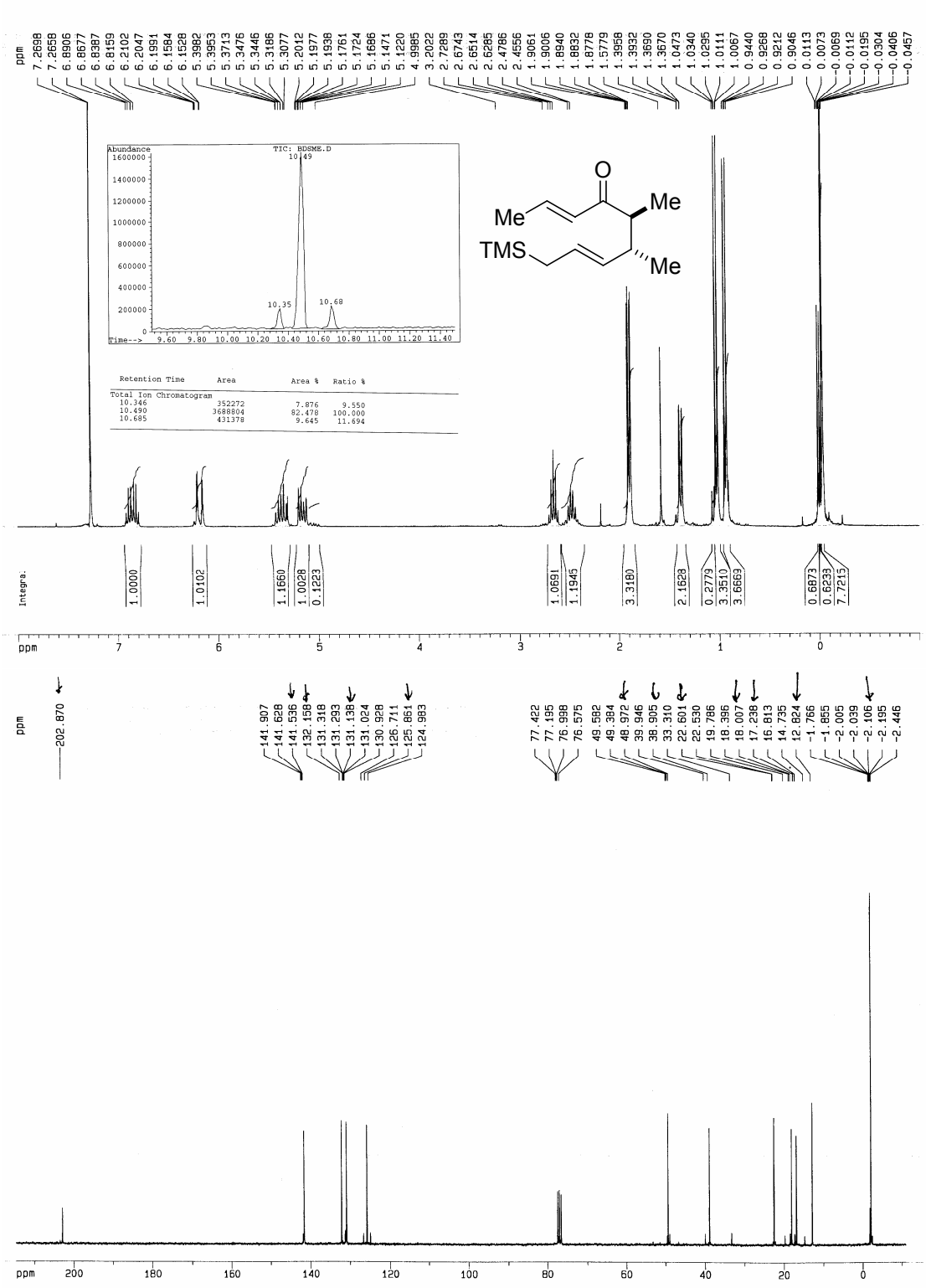
A.12 COMPOUND 29



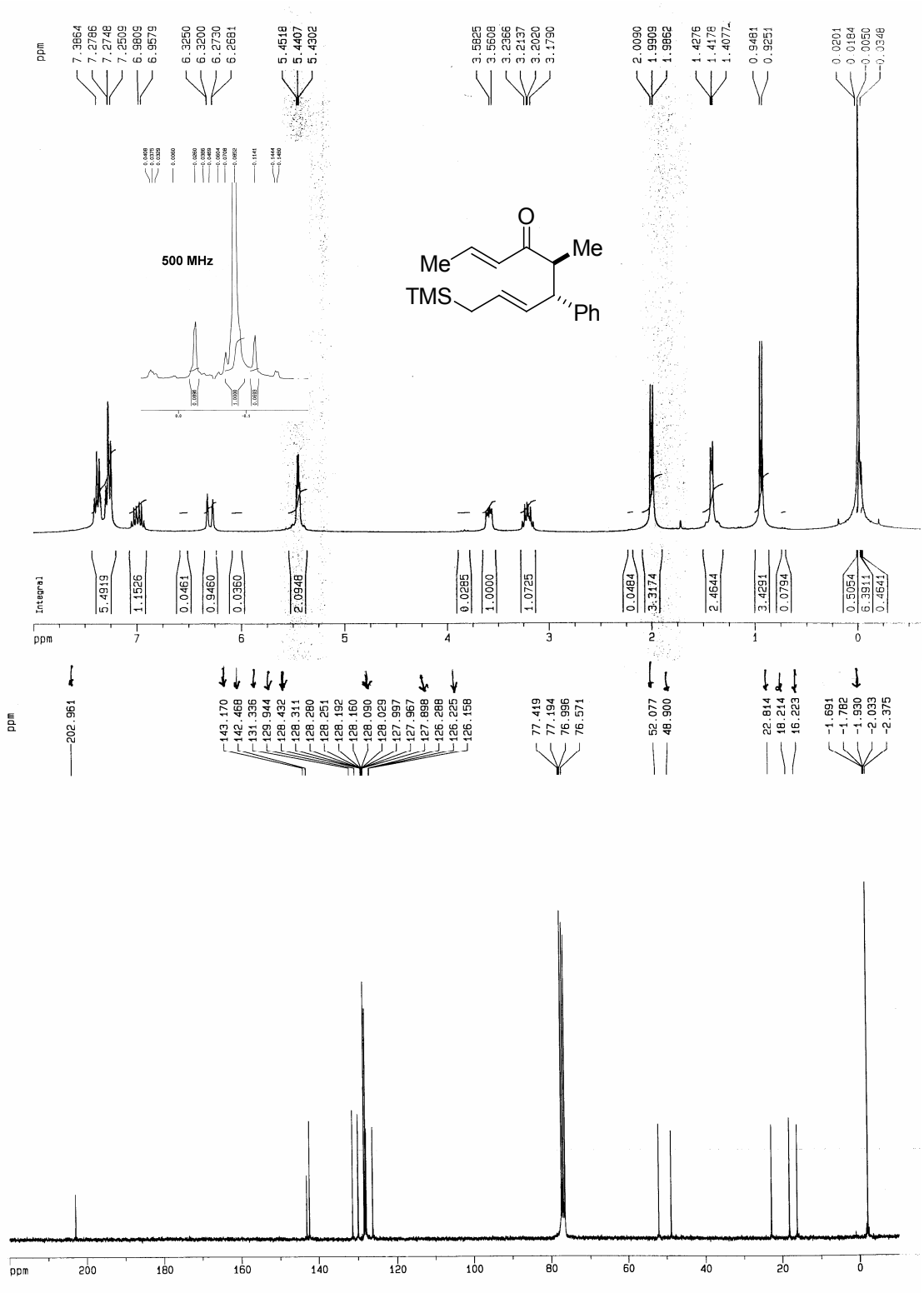
A.13 COMPOUND 30



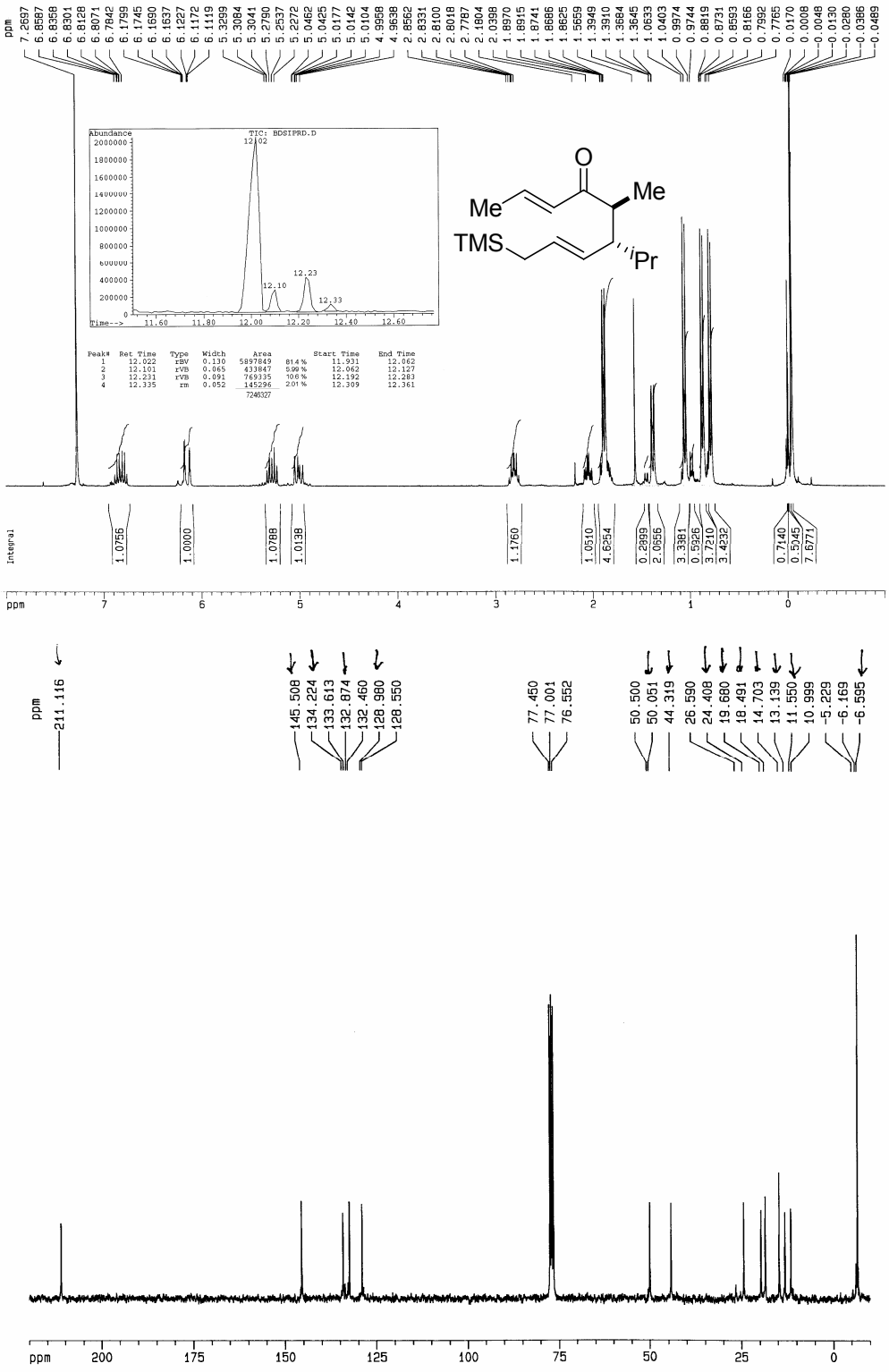
A.14 COMPOUND 31



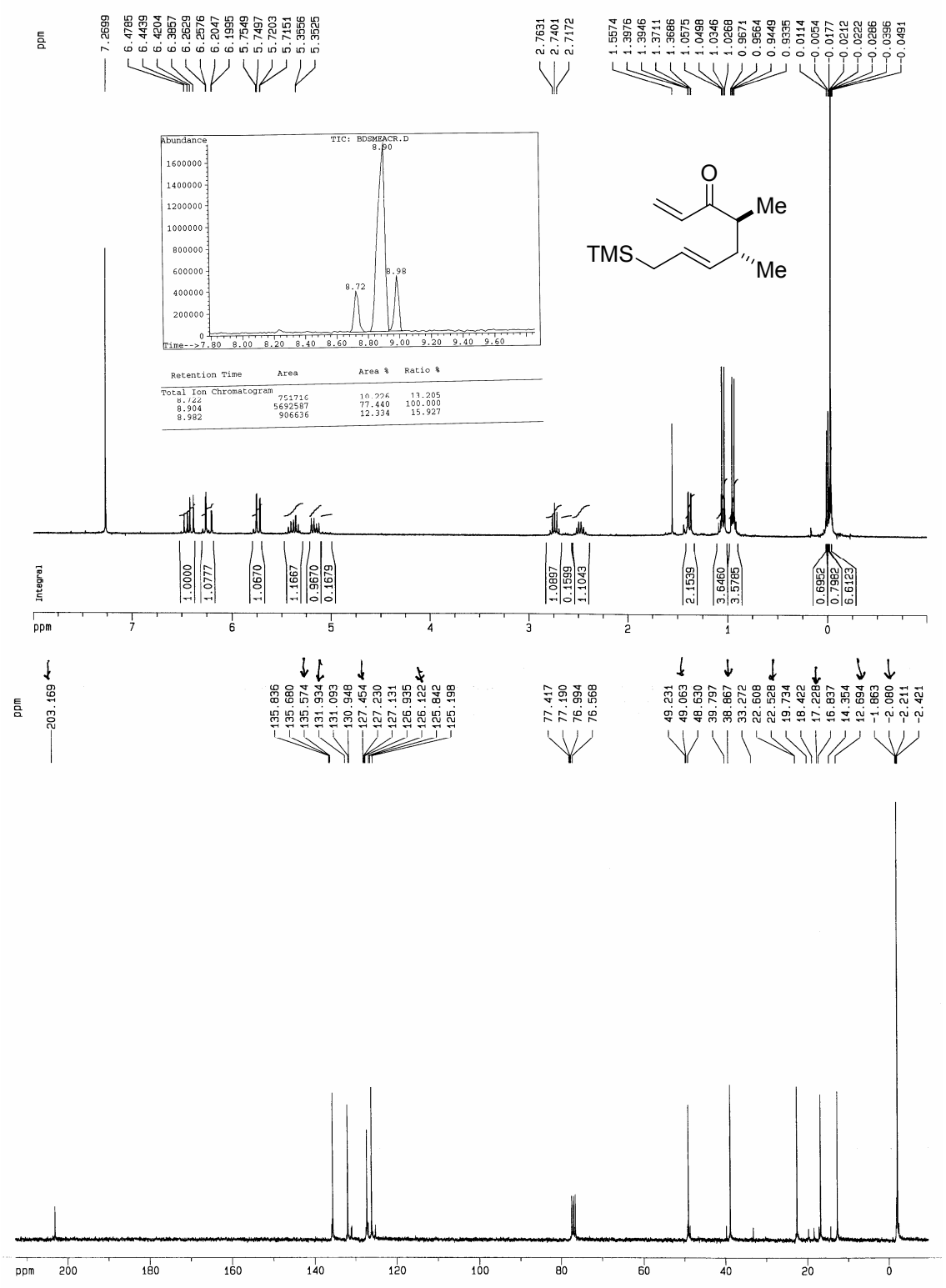
A.15 COMPOUND 32



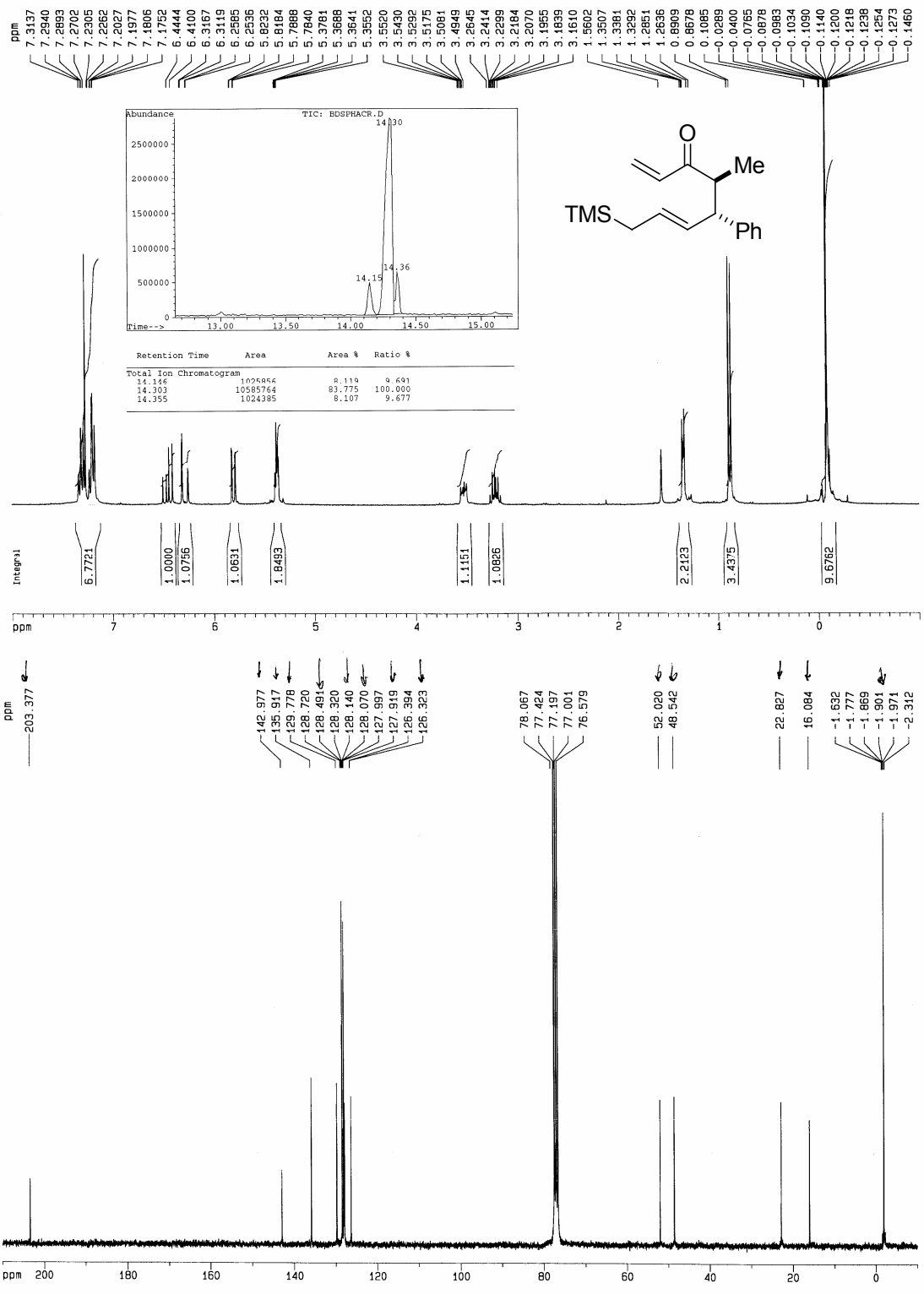
A.16 COMPOUND 33



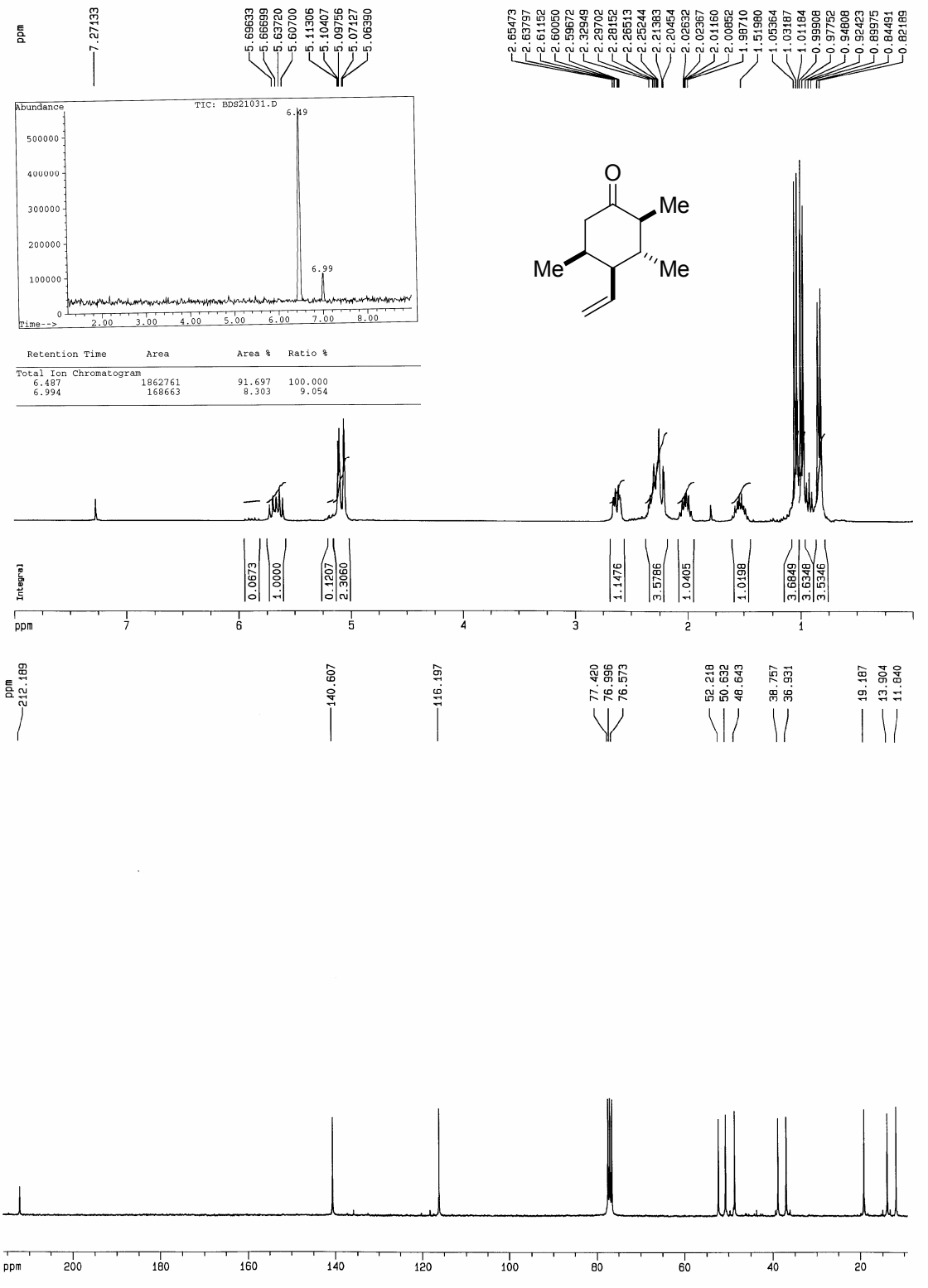
A.17 COMPOUND 34



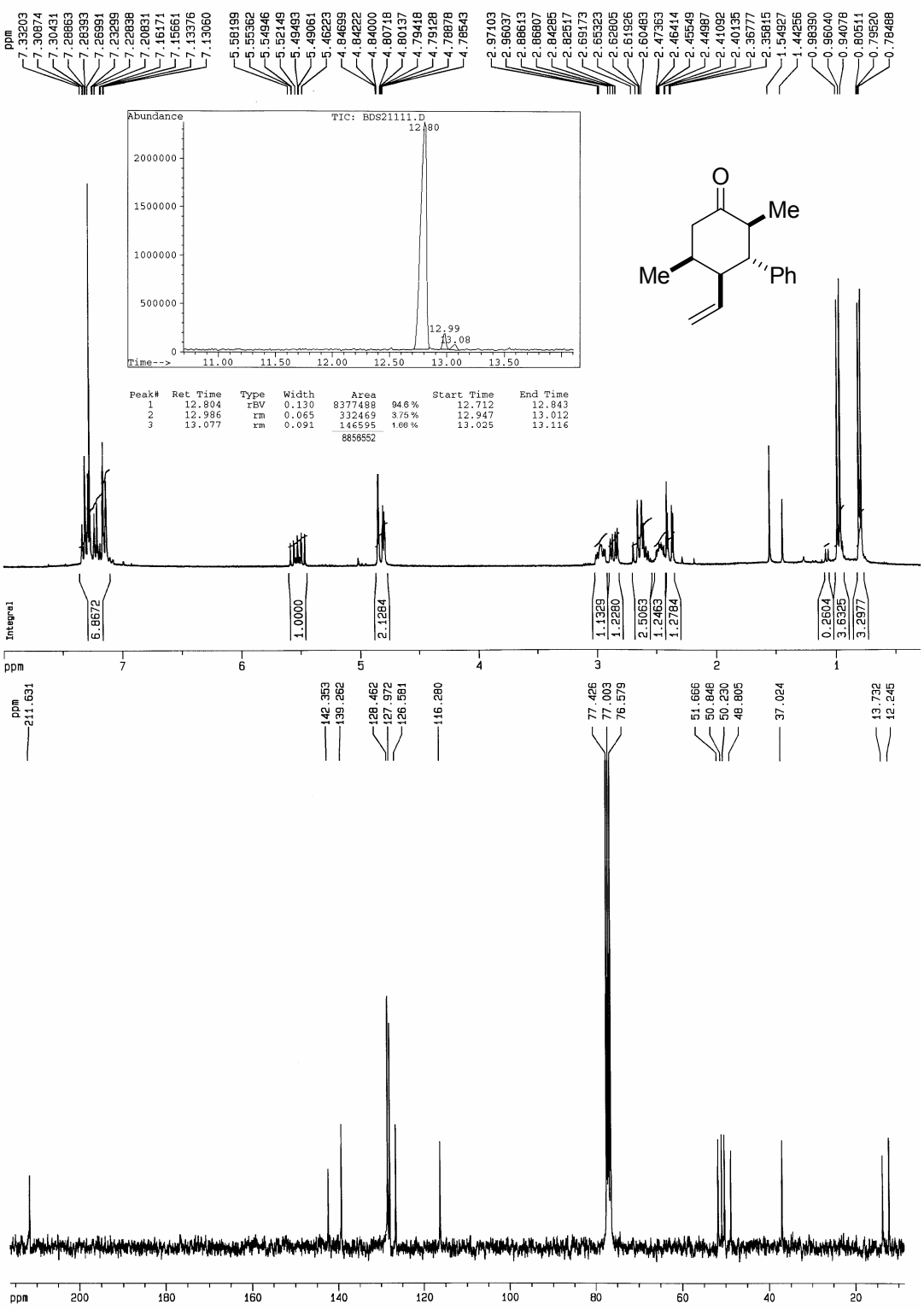
A.18 COMPOUND 35



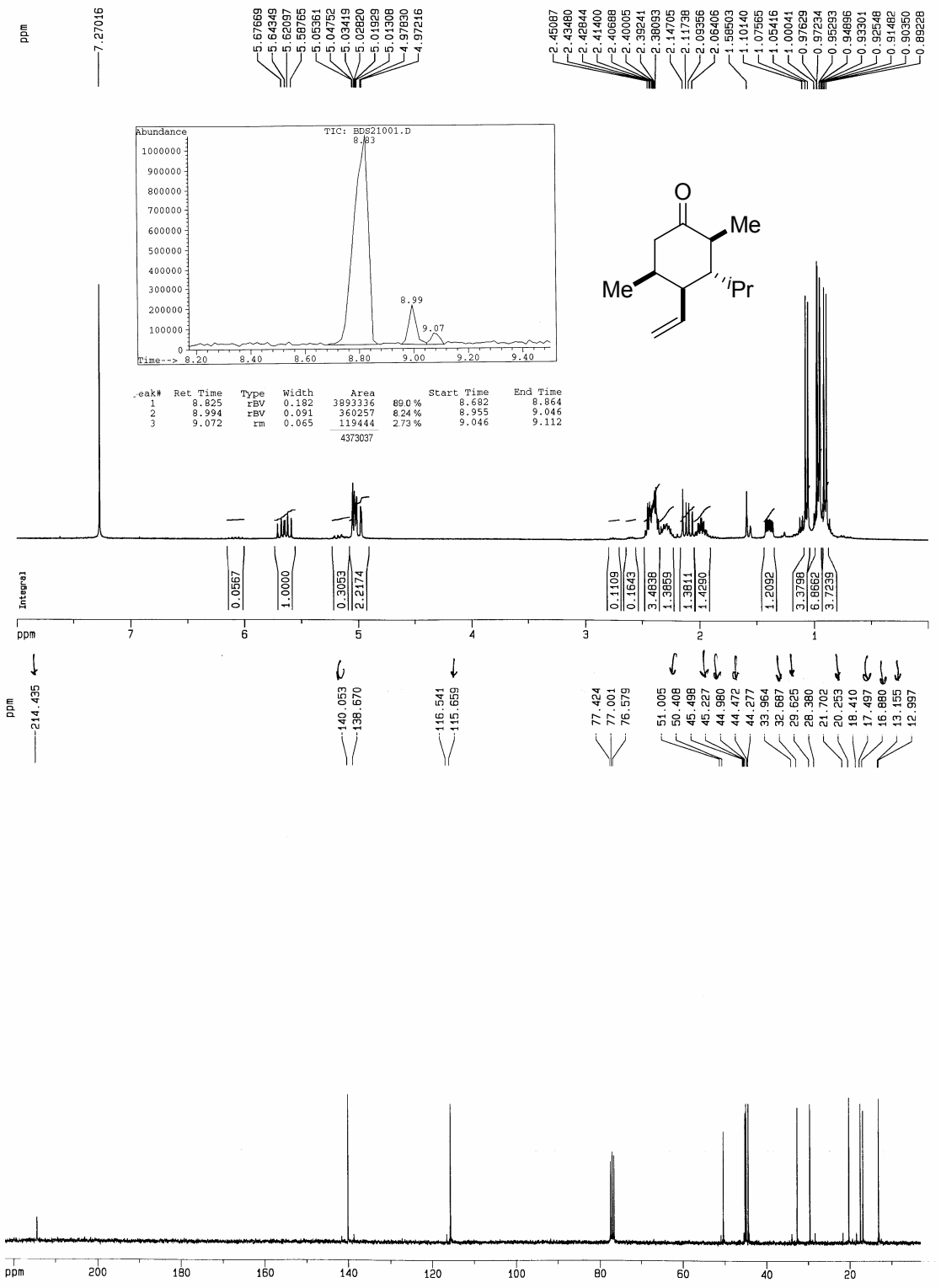
A.19 COMPOUND 36



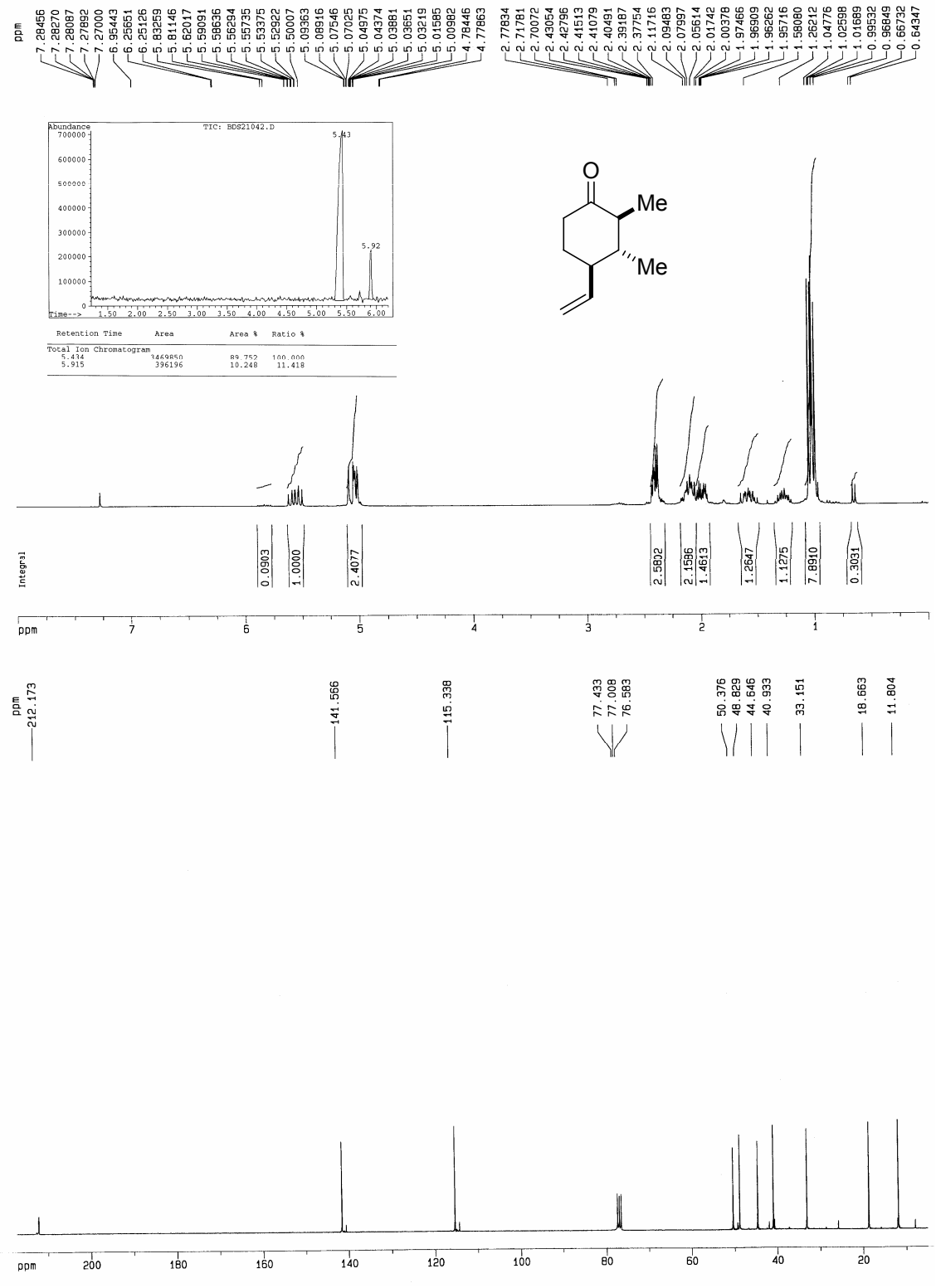
A.20 COMPOUND 37



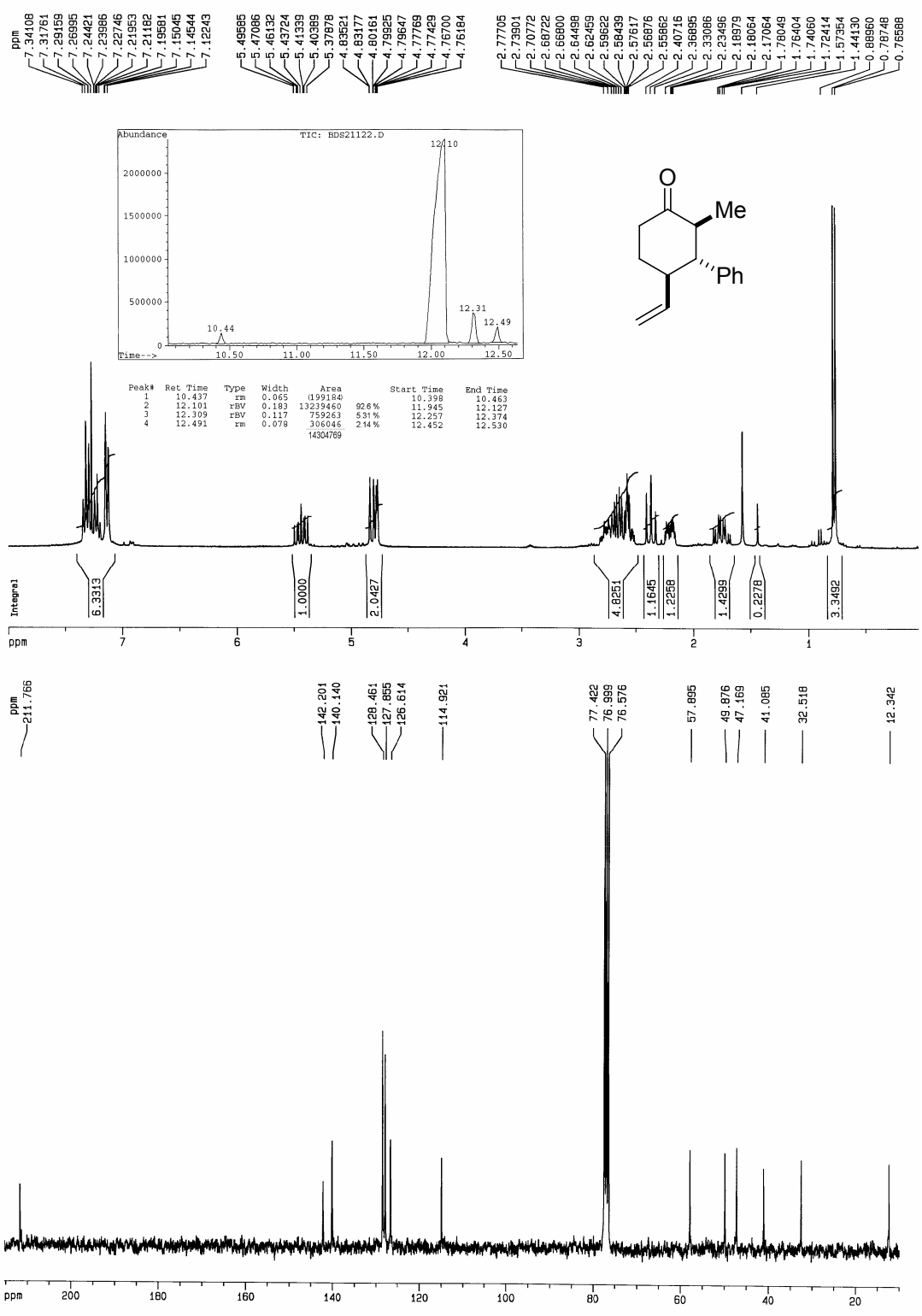
A.21 COMPOUND 38



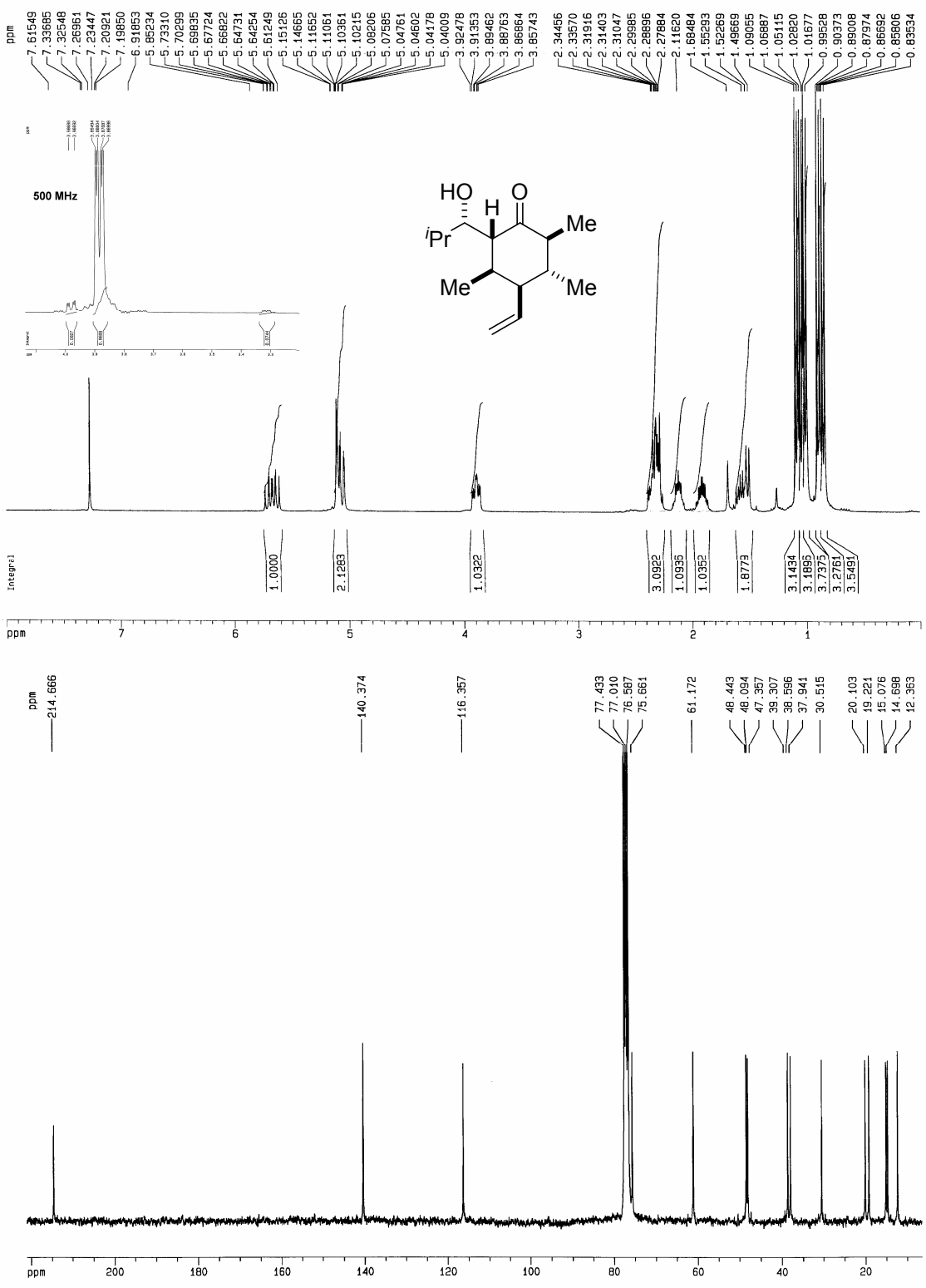
A.22 COMPOUND 39



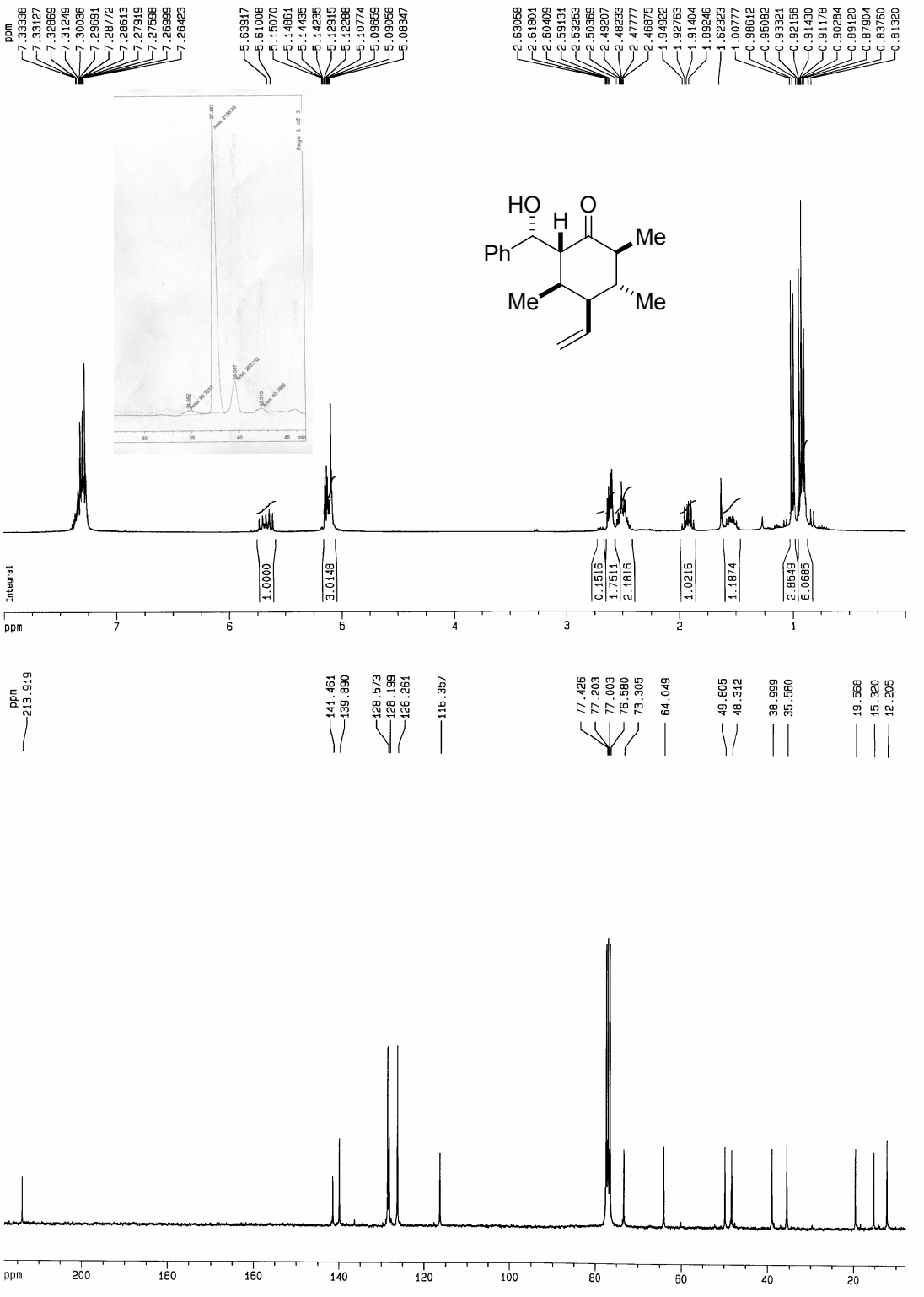
A.23 COMPOUND 40



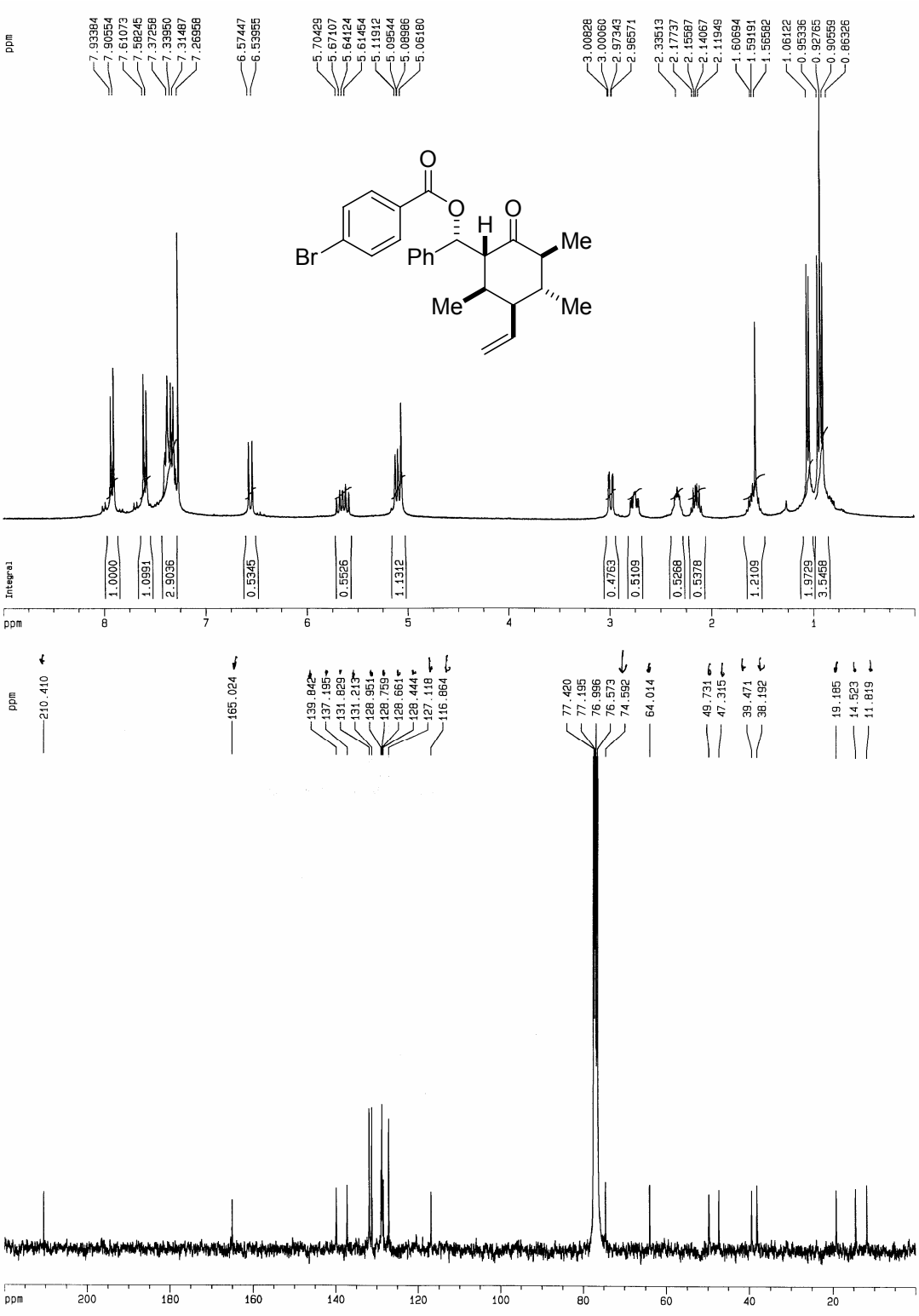
A.24 COMPOUND 41



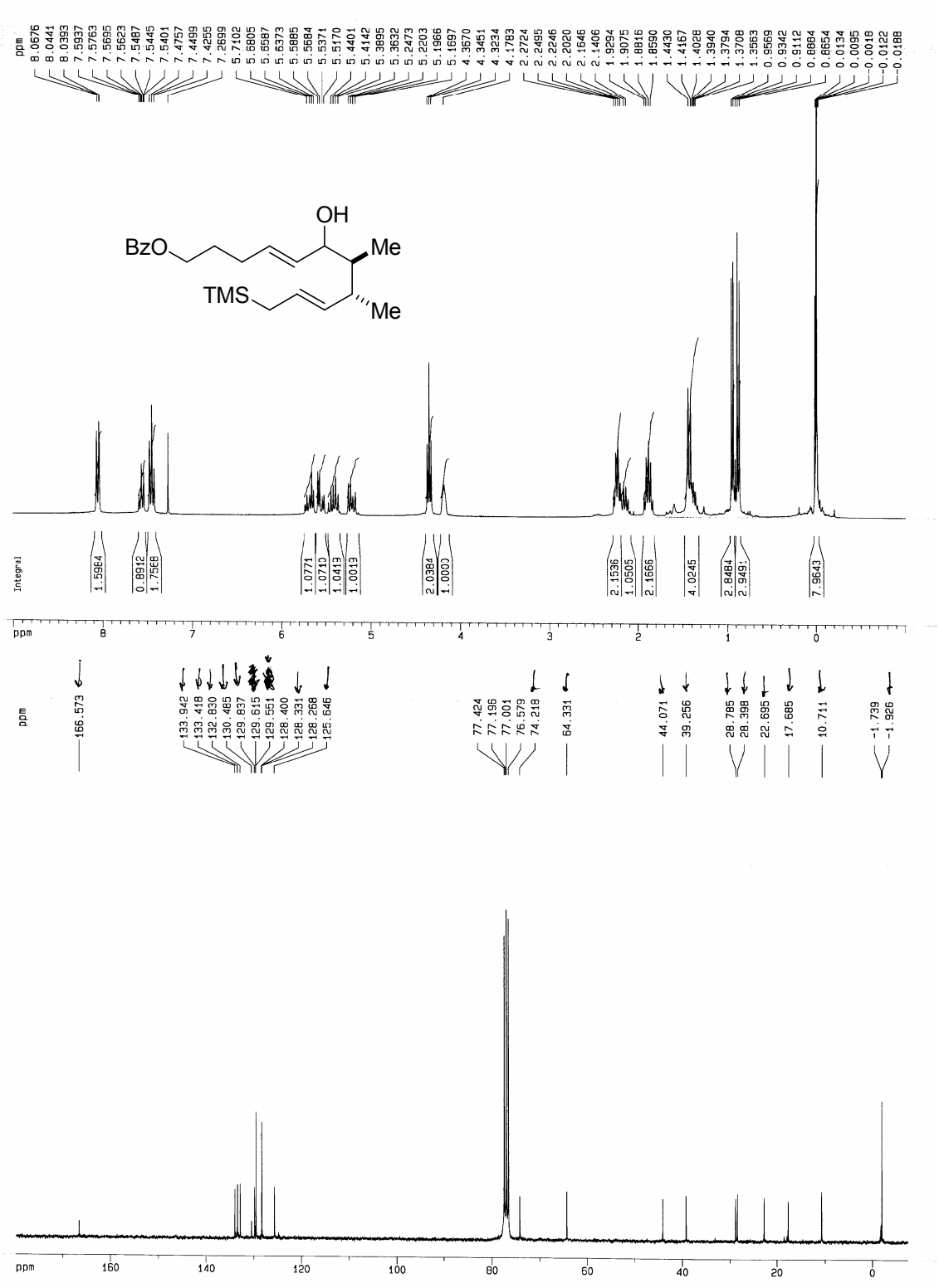
A.25 COMPOUND 42



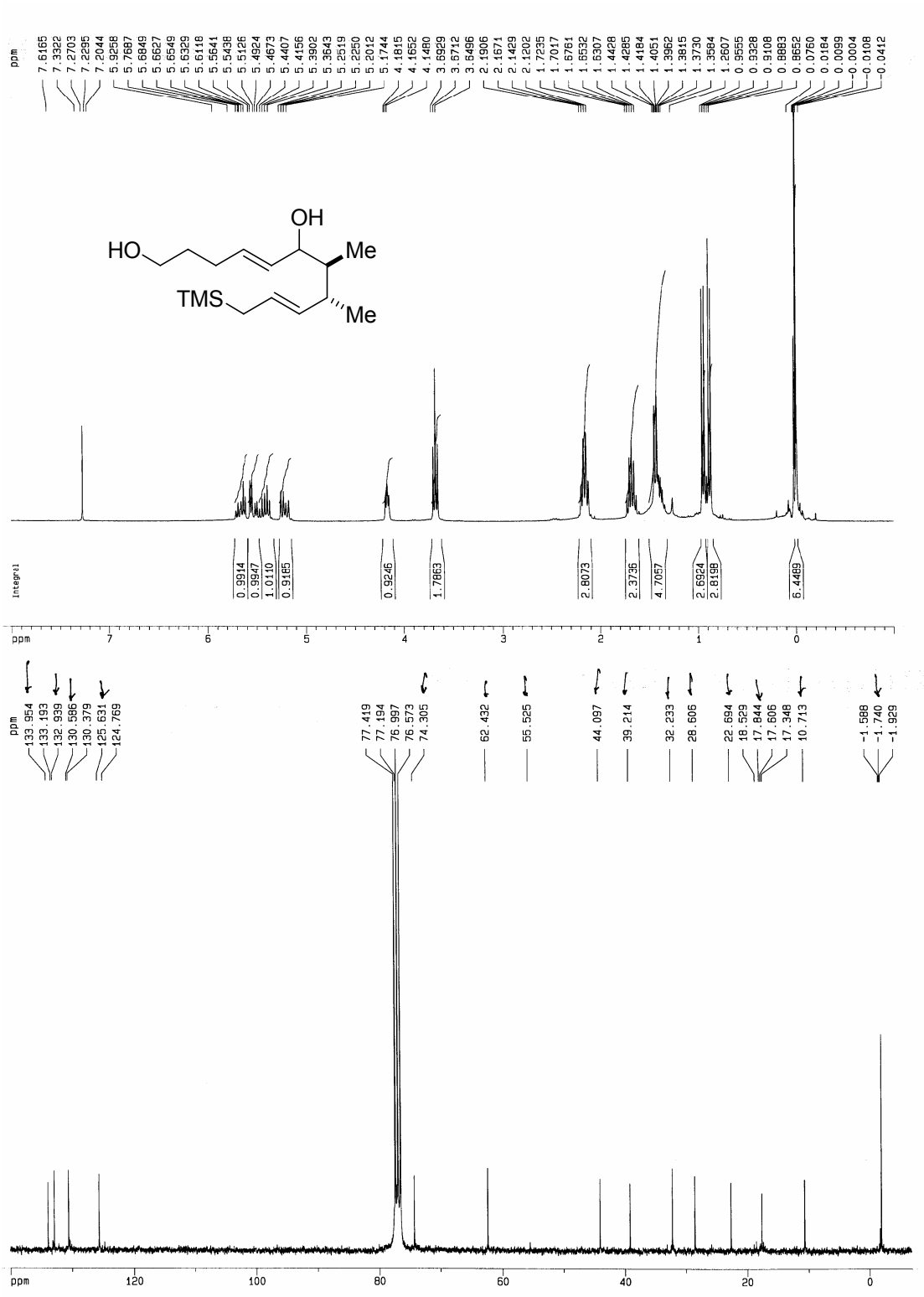
A.26 COMPOUND 43



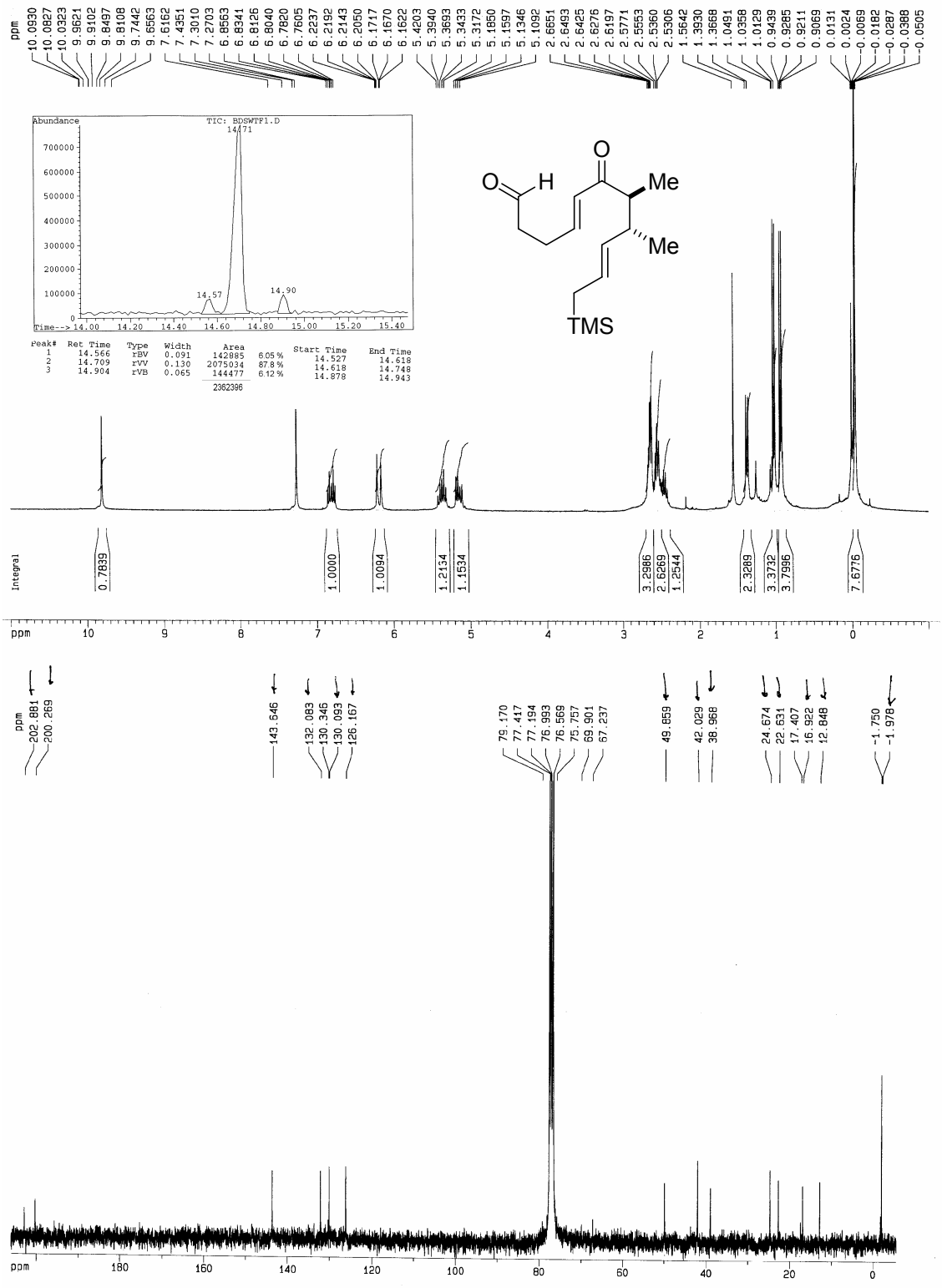
A.27 COMPOUND 44



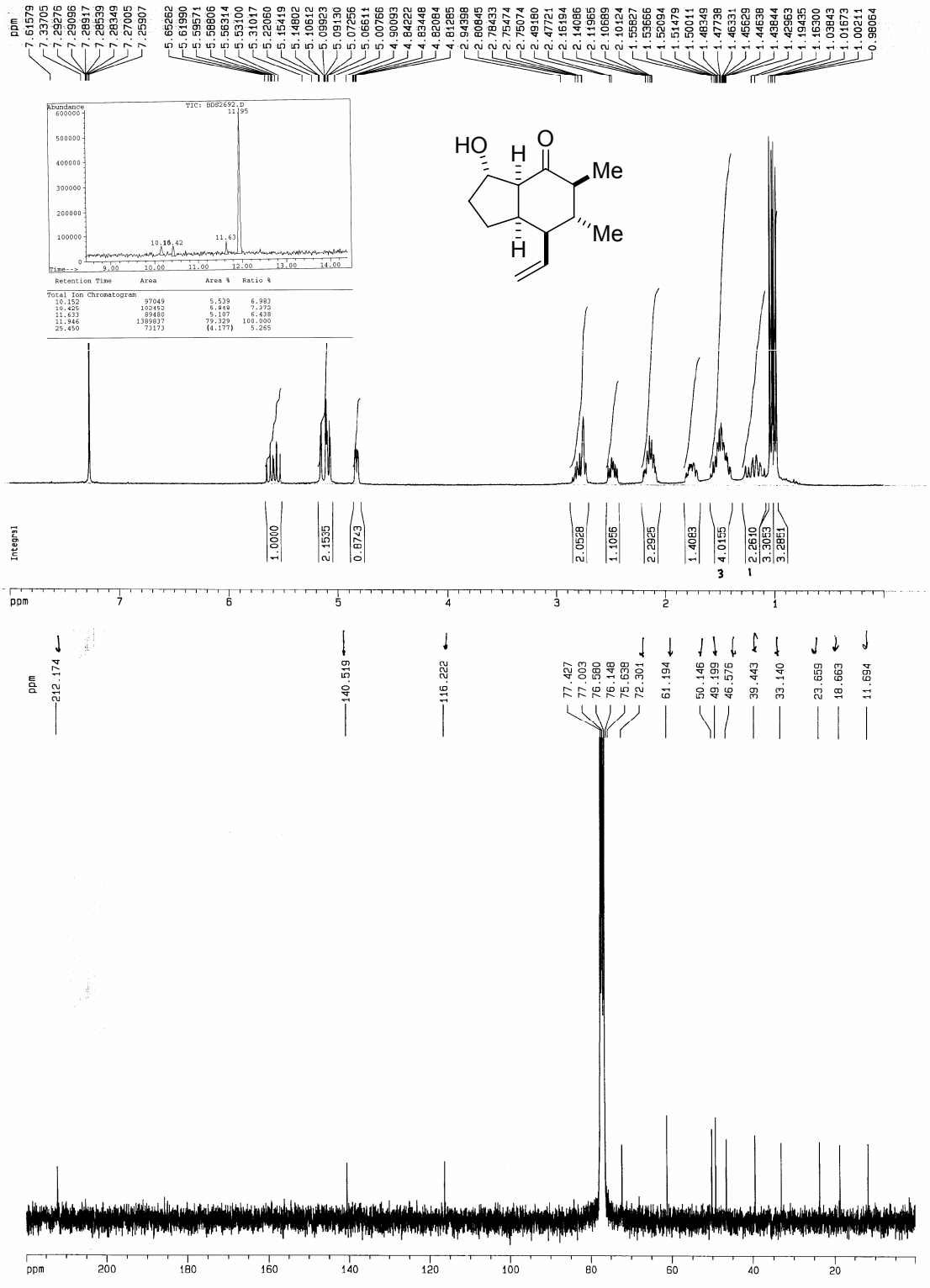
A.28 COMPOUND 45



A.29 COMPOUND 46

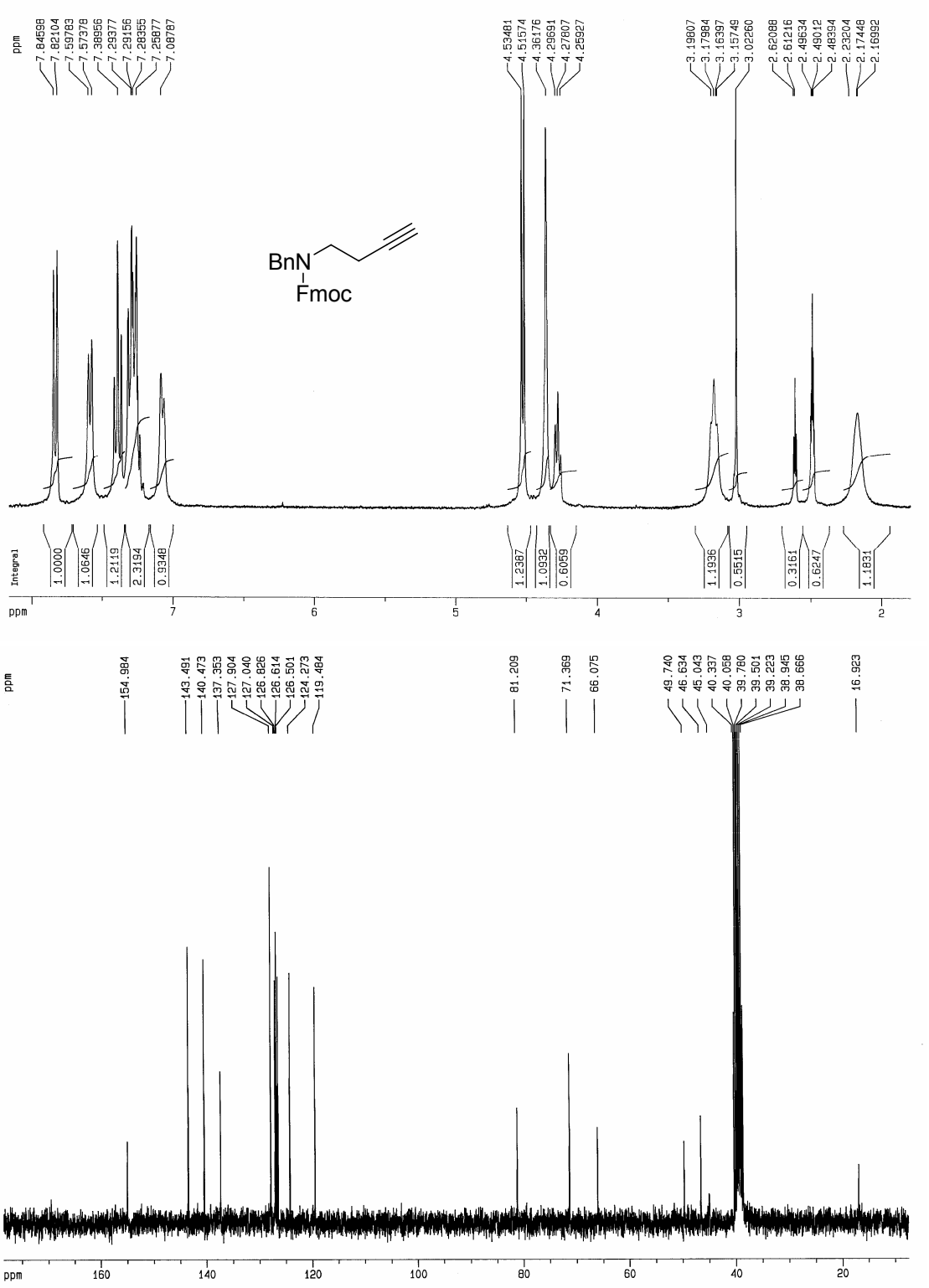


A.30 COMPOUND 48

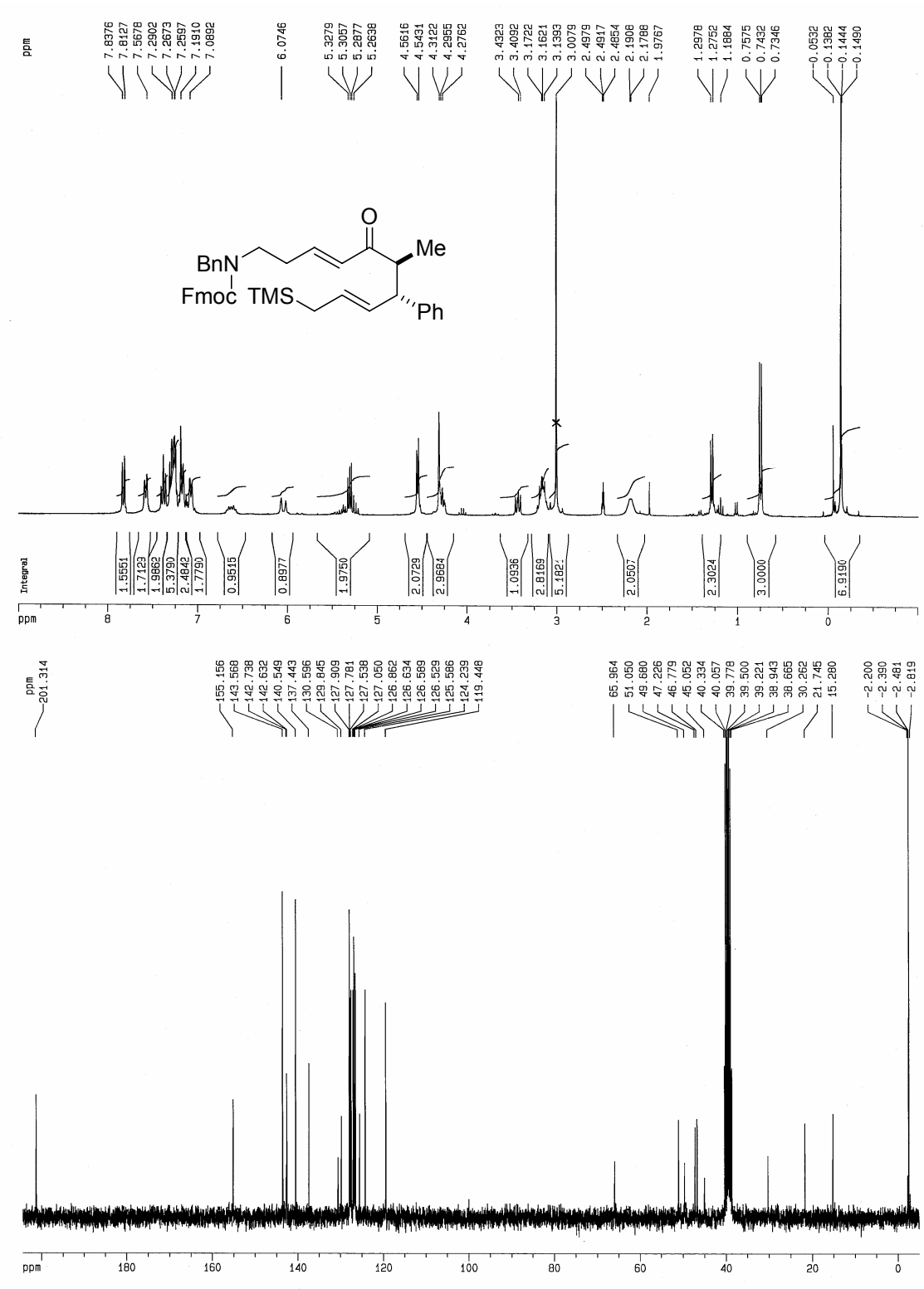


A.31 COMPOUND 49

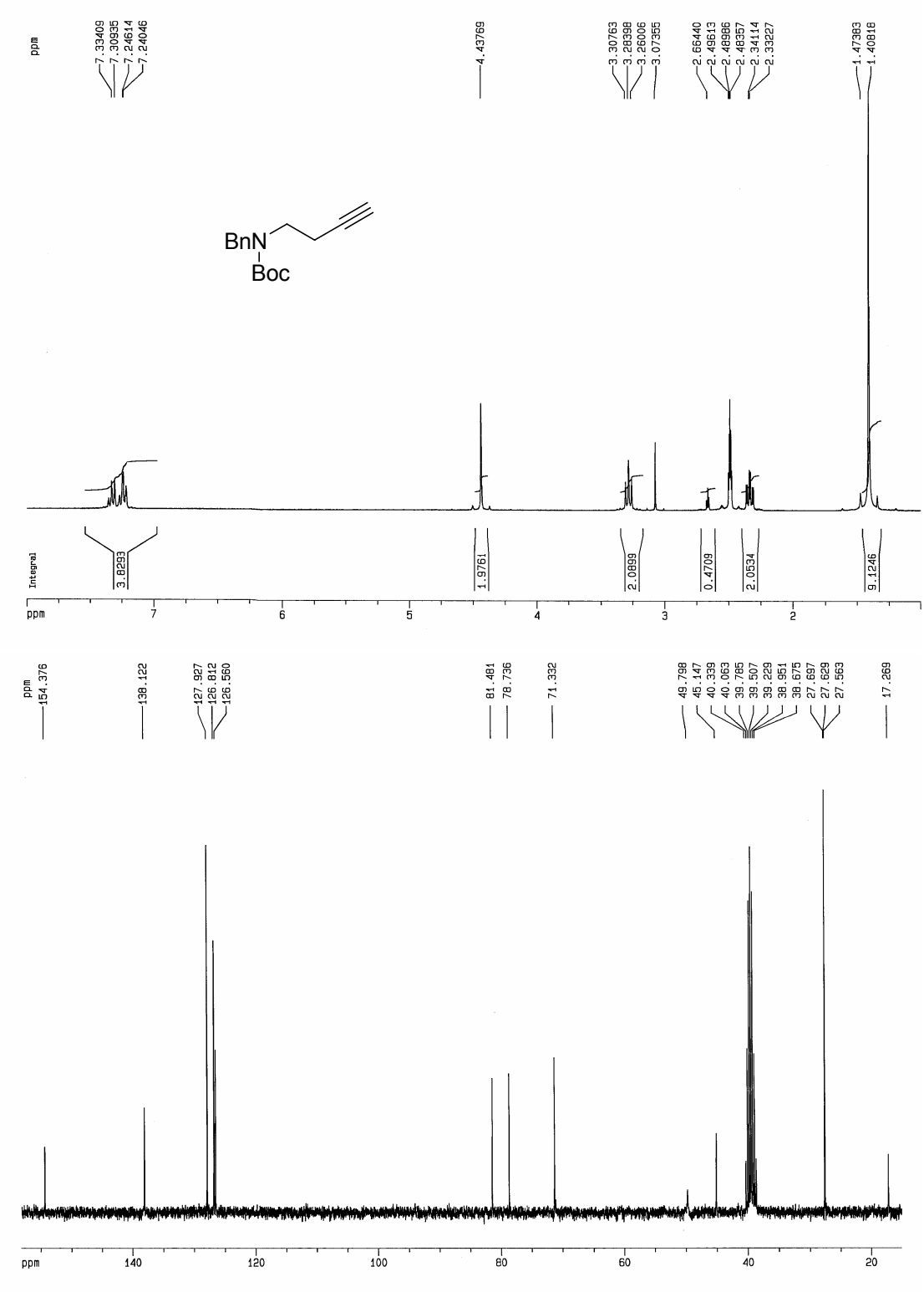
A.32 COMPOUND 50



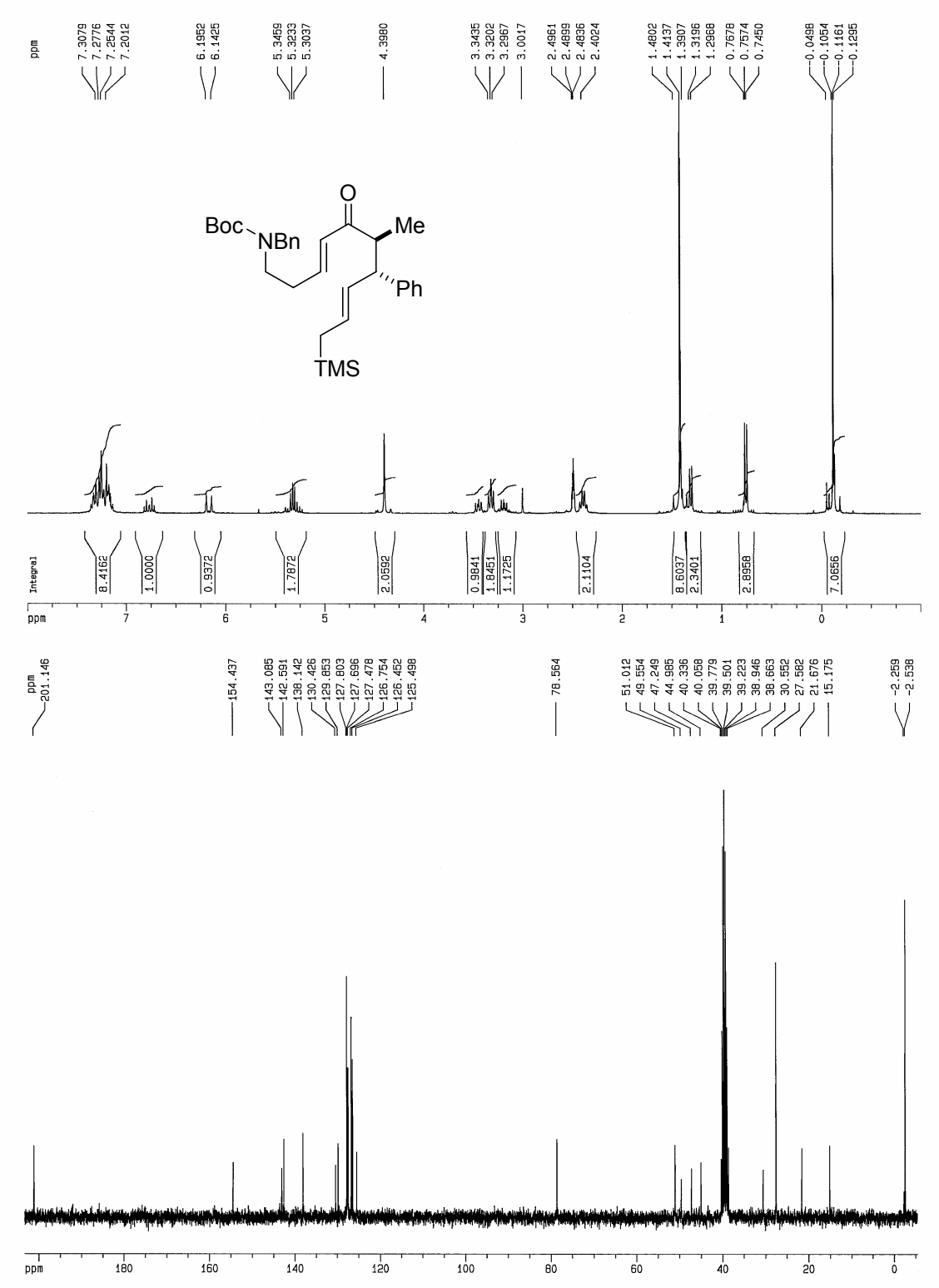
A.33 COMPOUND 52



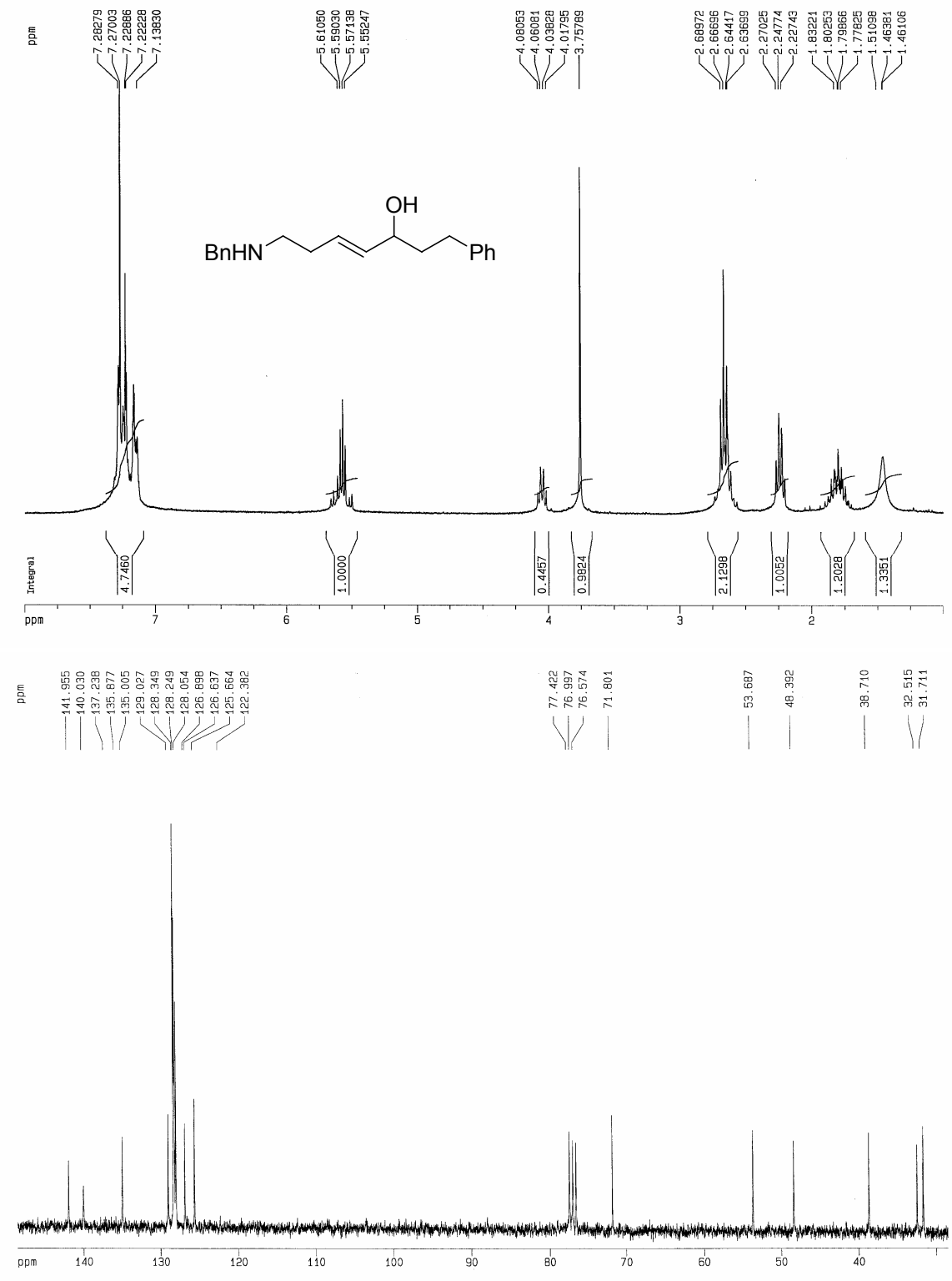
A.34 COMPOUND 54



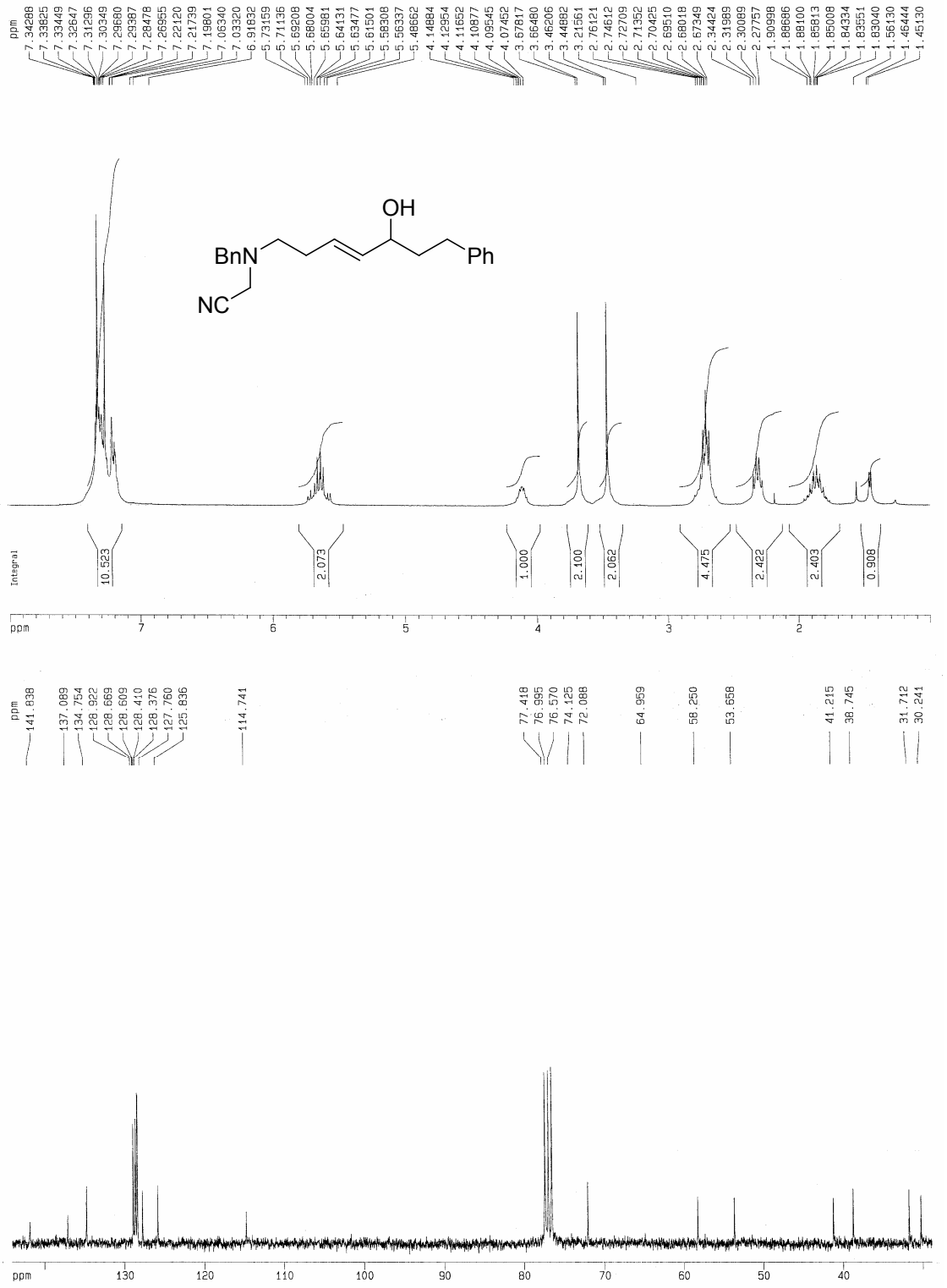
A.35 COMPOUND 57



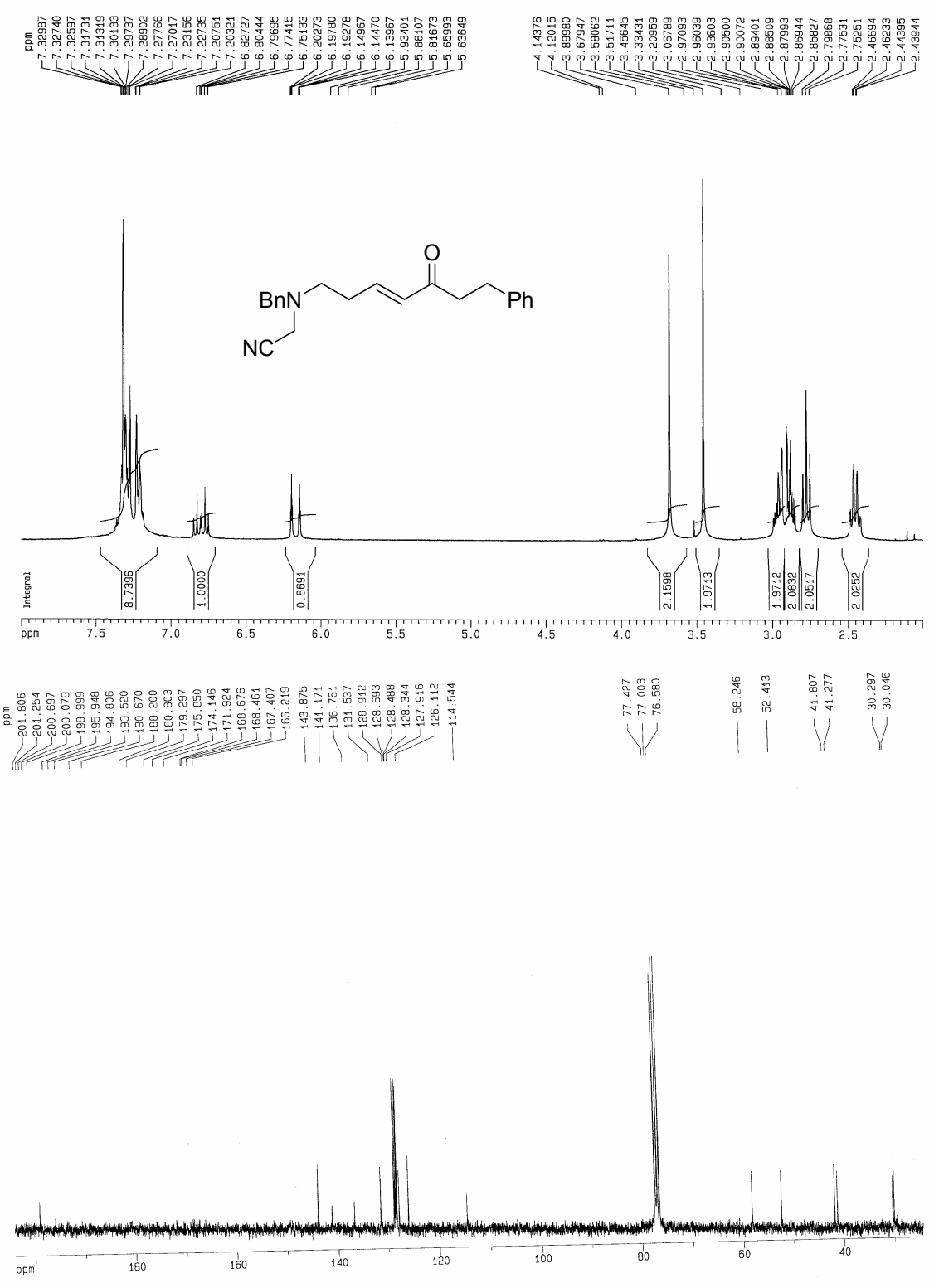
A.36 COMPOUND 61



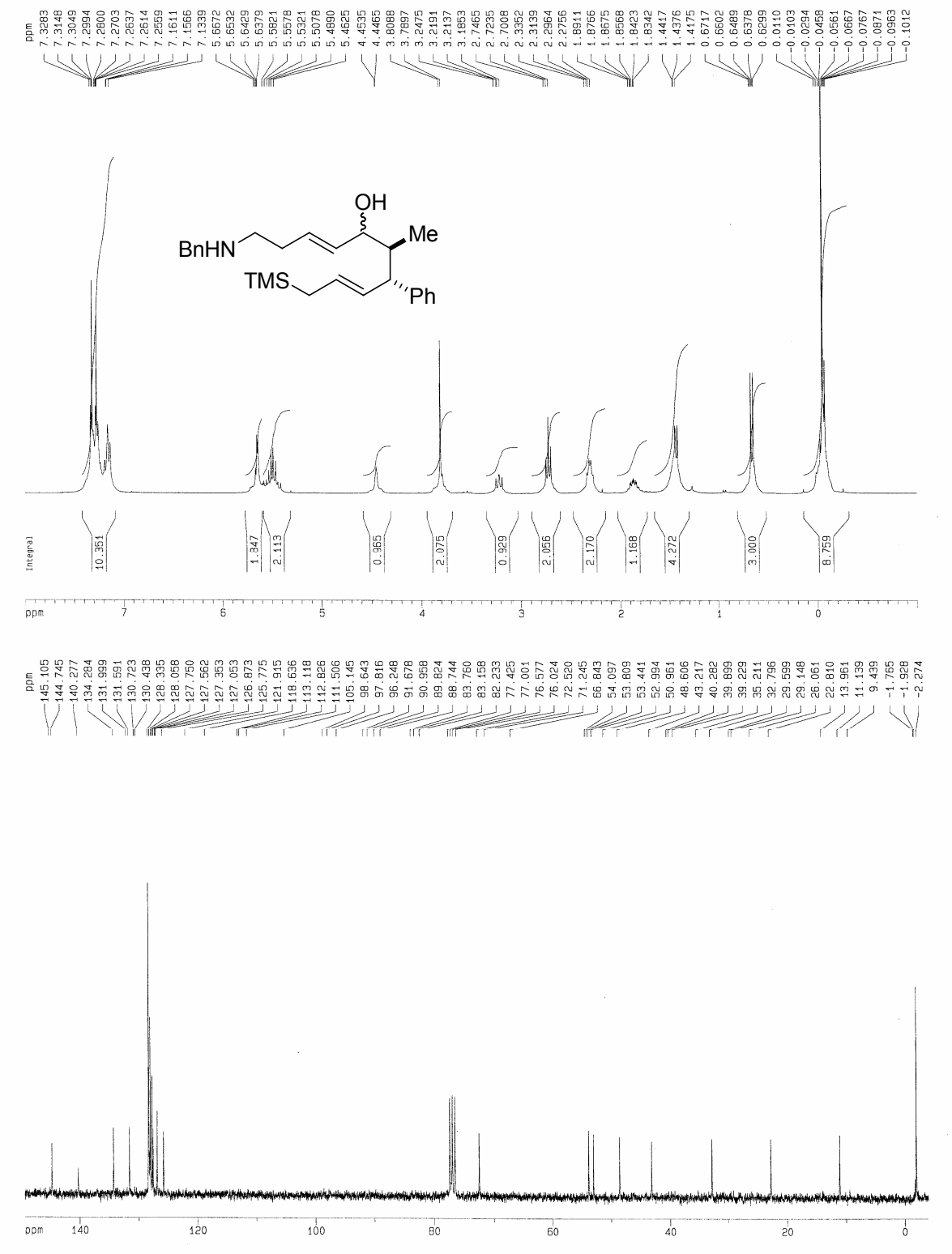
A.37 COMPOUND 62



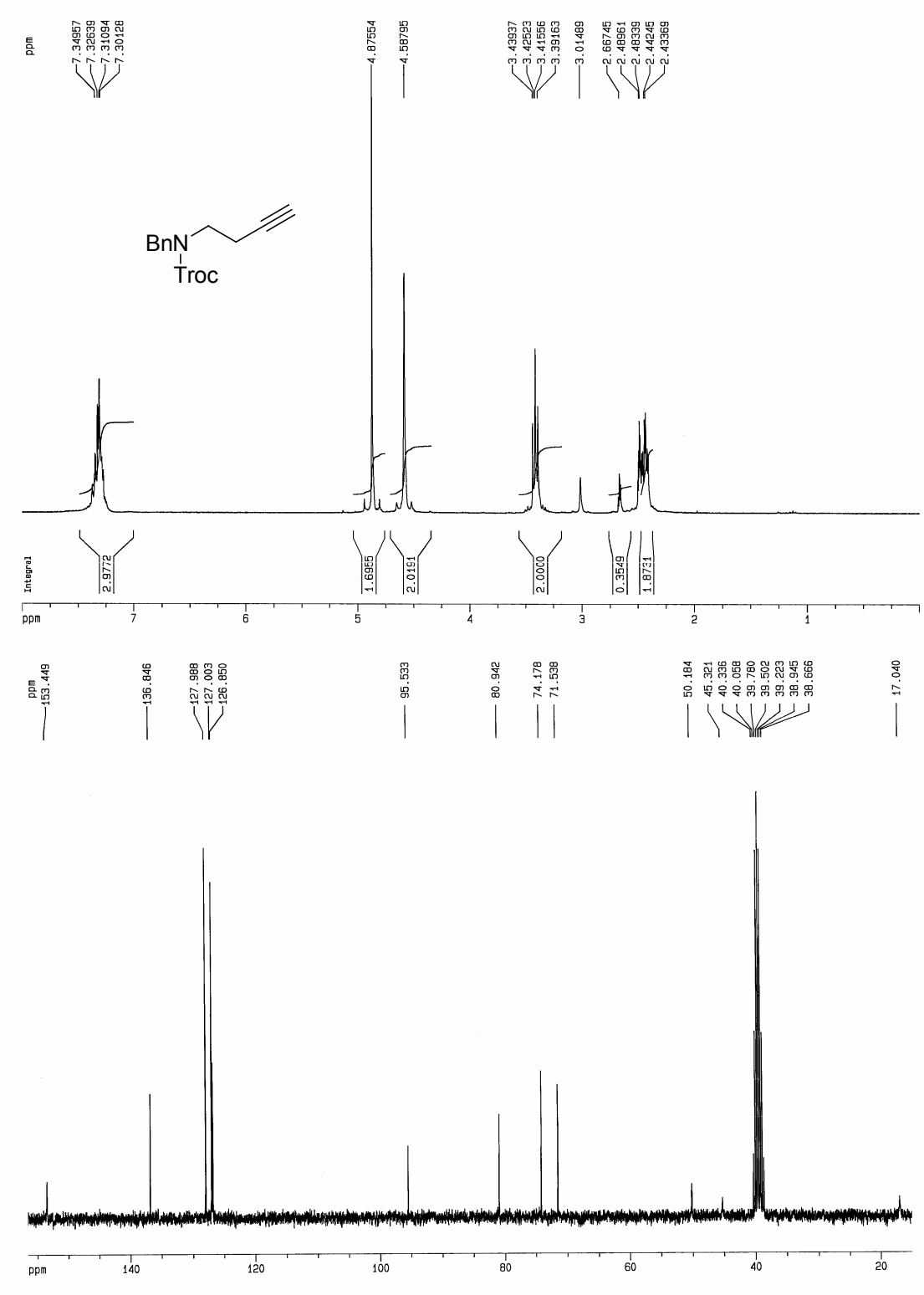
A.38 COMPOUND 63



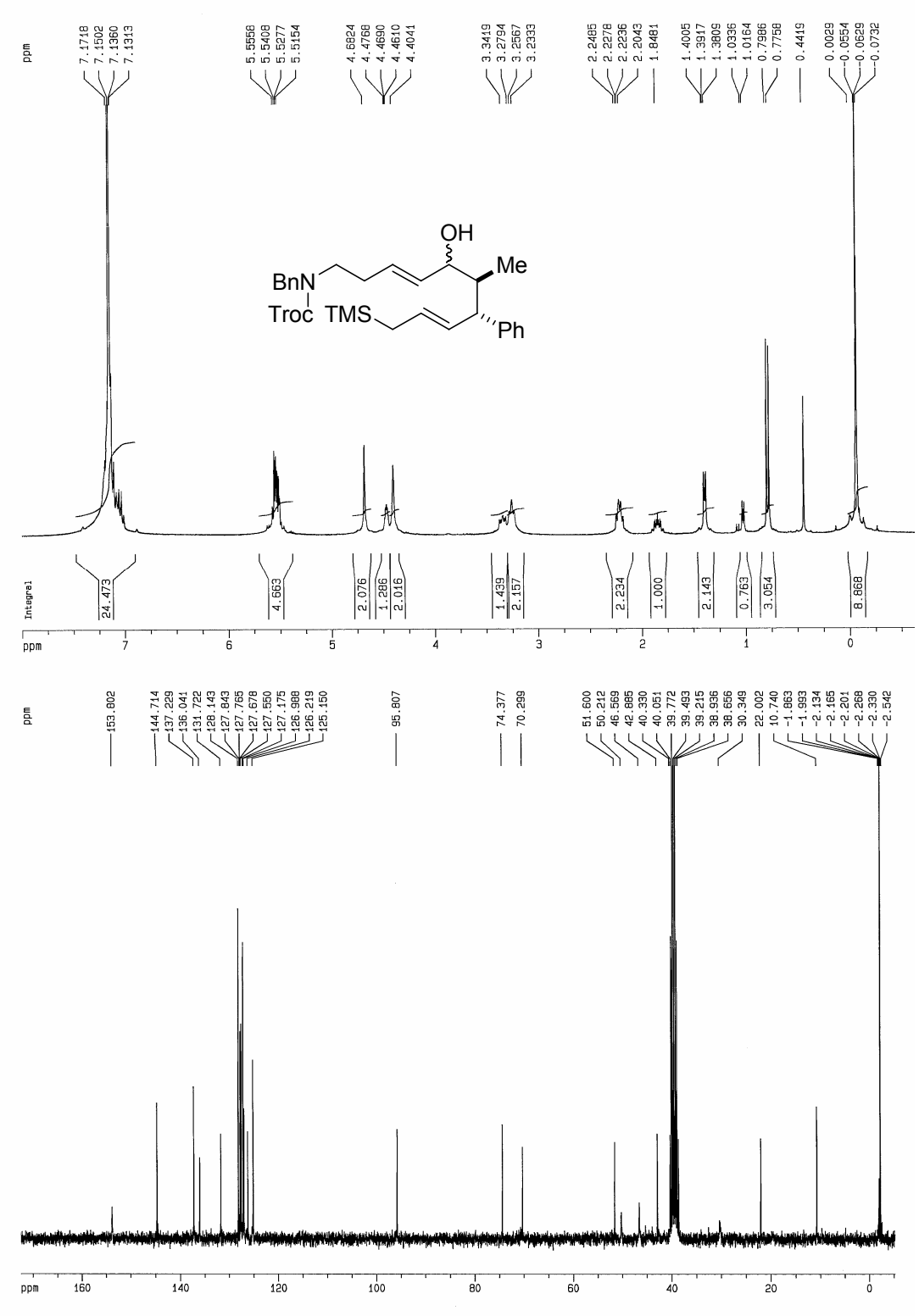
A.39 COMPOUND 65



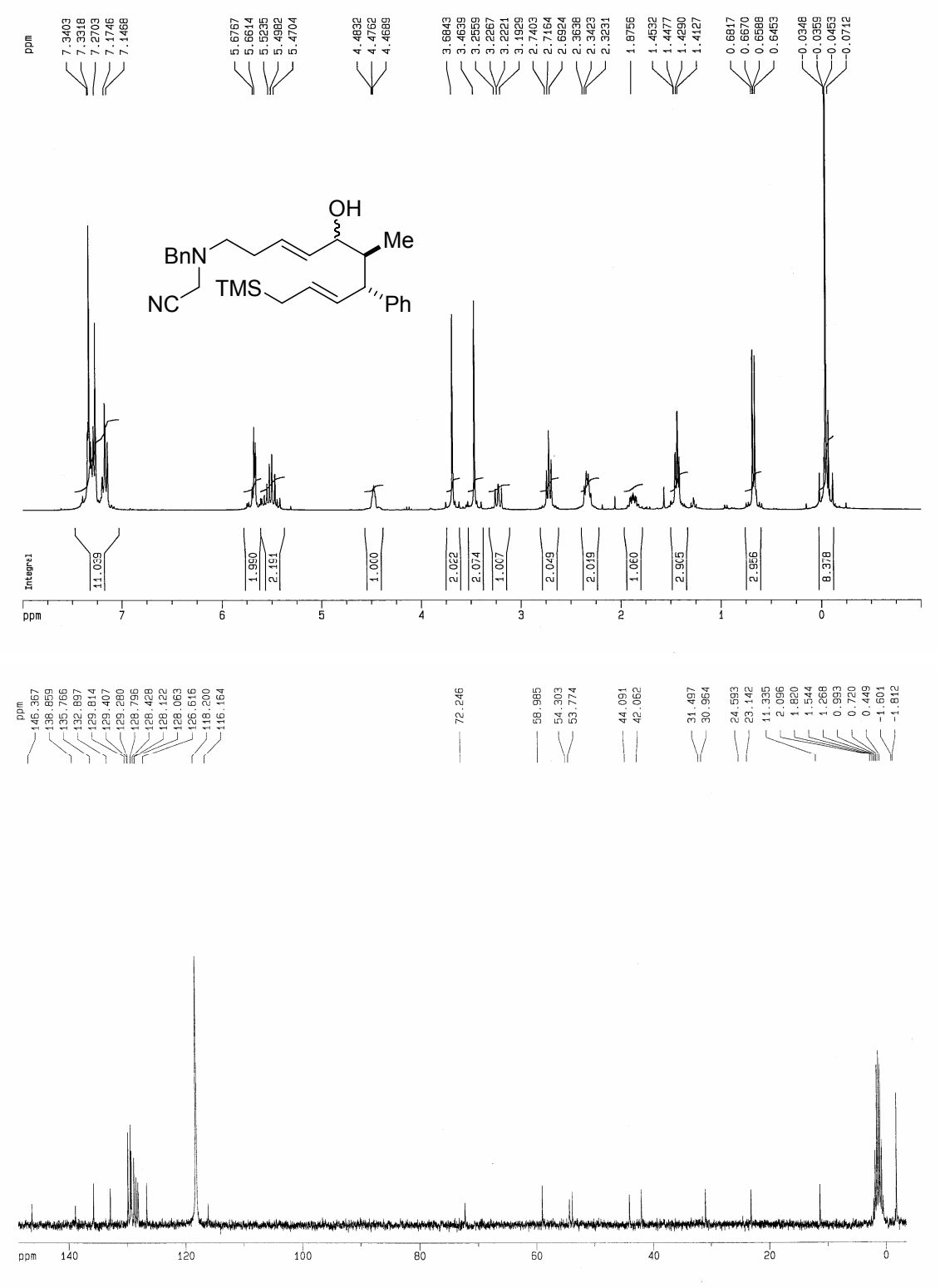
A.40 COMPOUND 66



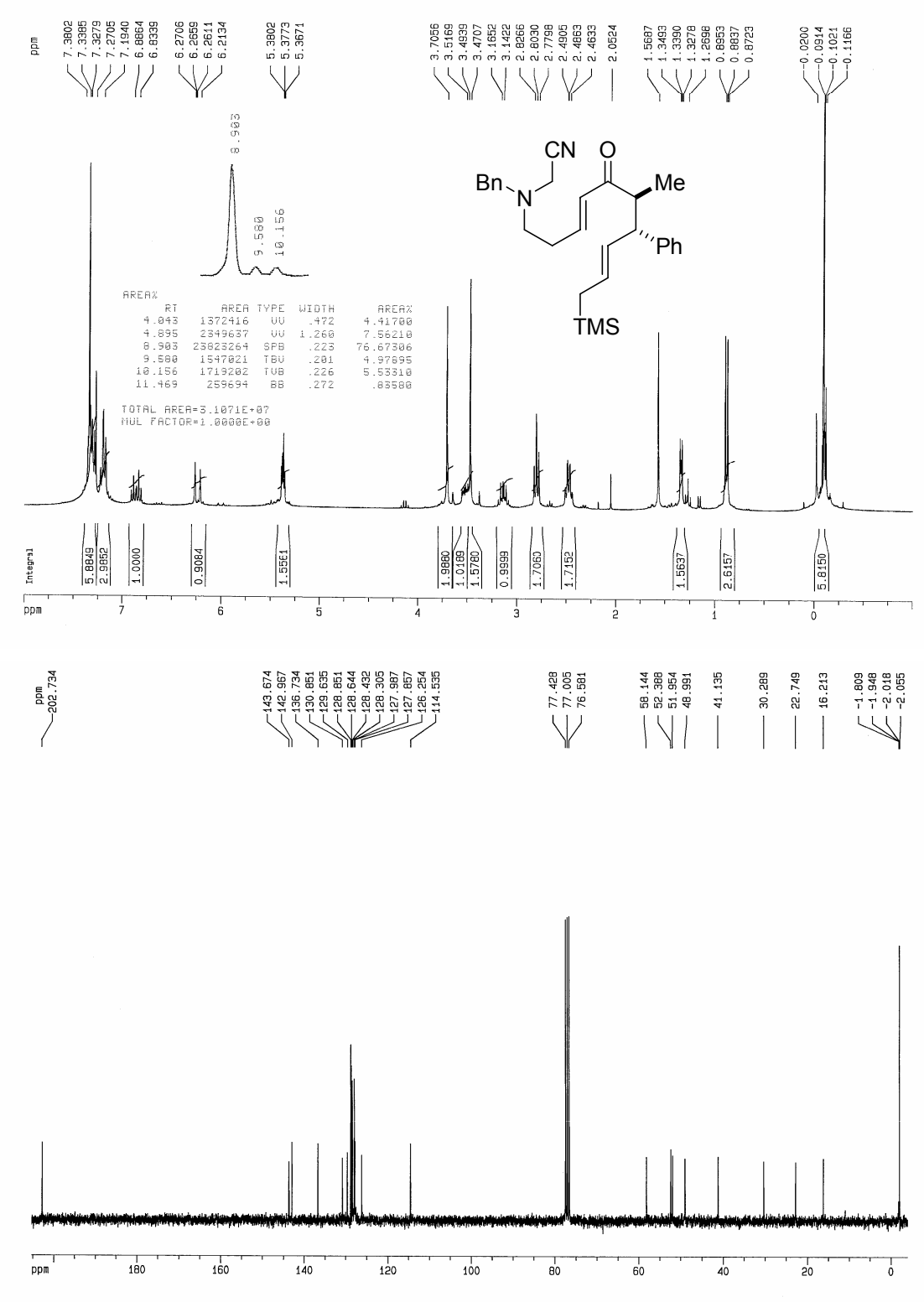
A.41 COMPOUND 67



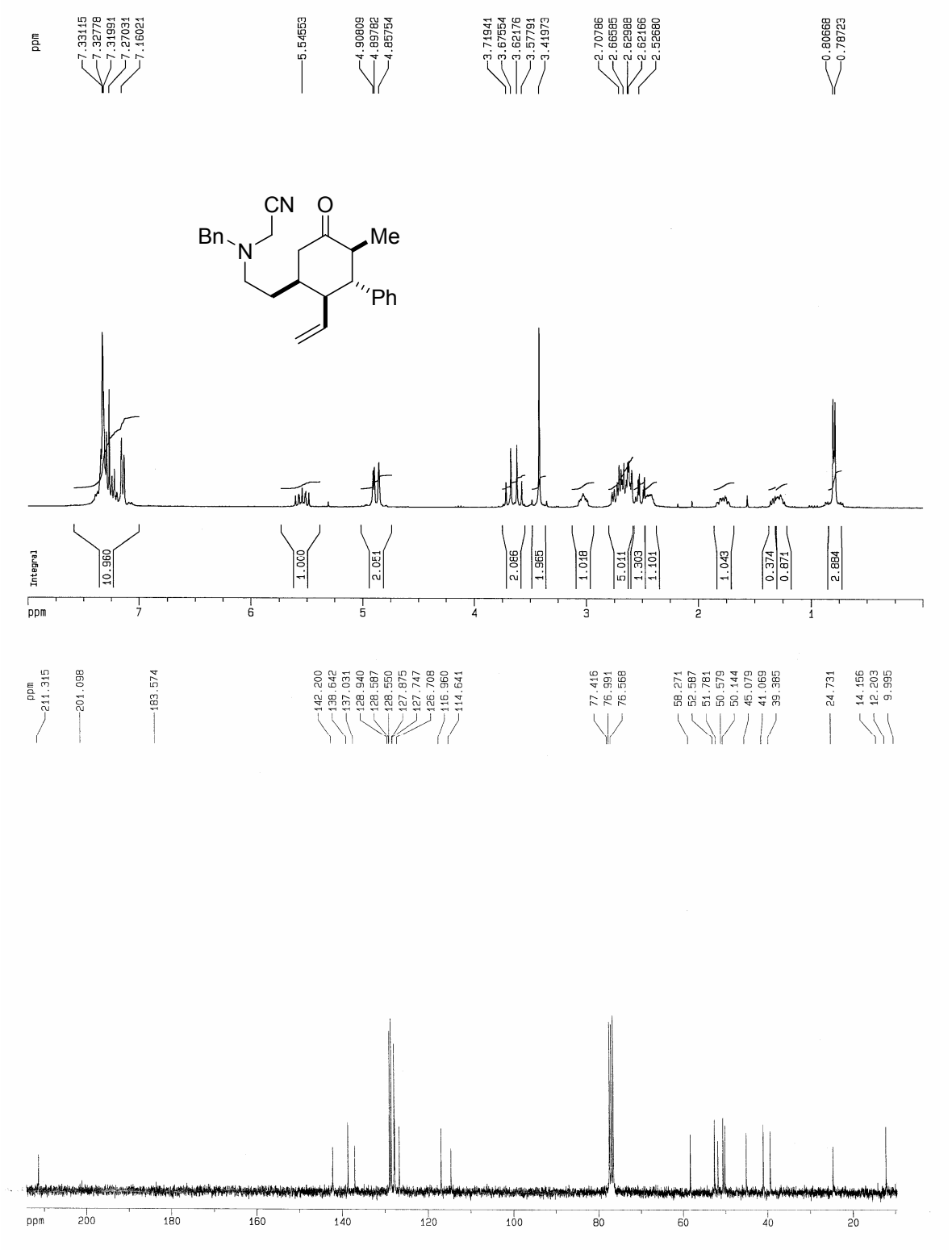
A.42 COMPOUND 68



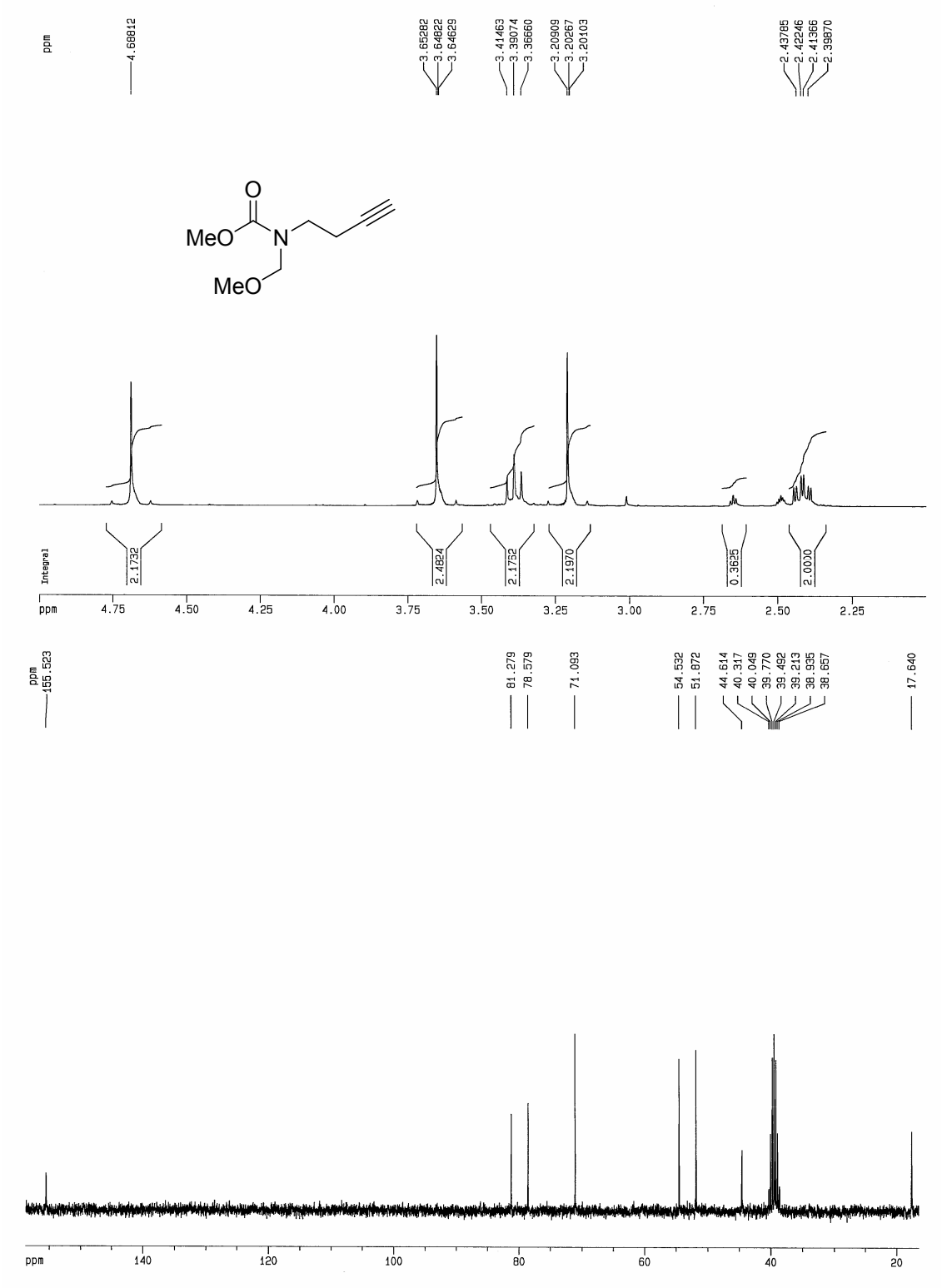
A.43 COMPOUND 69



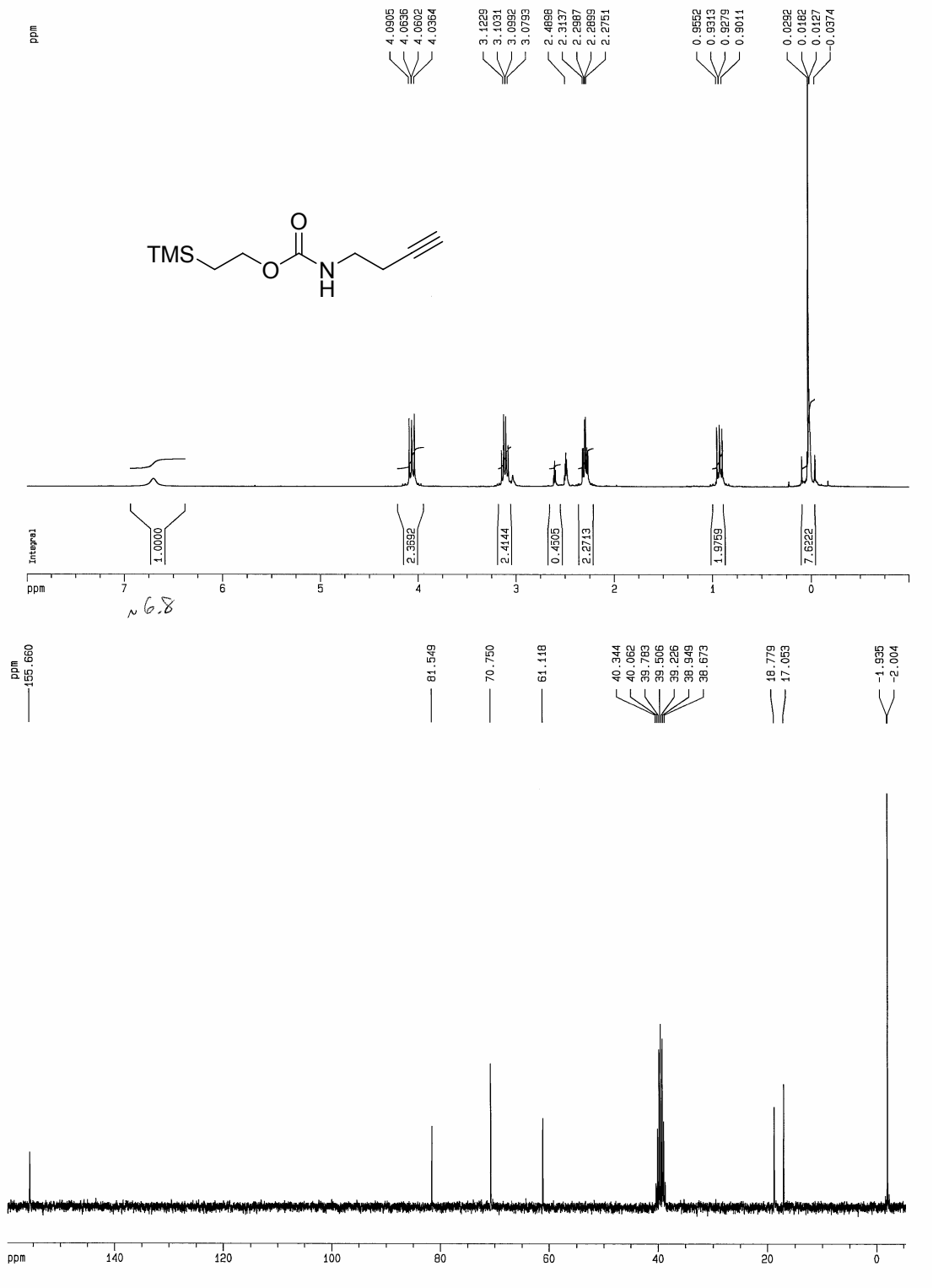
A.44 COMPOUND 70



A.45 COMPOUND 74



A.46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O
N
H
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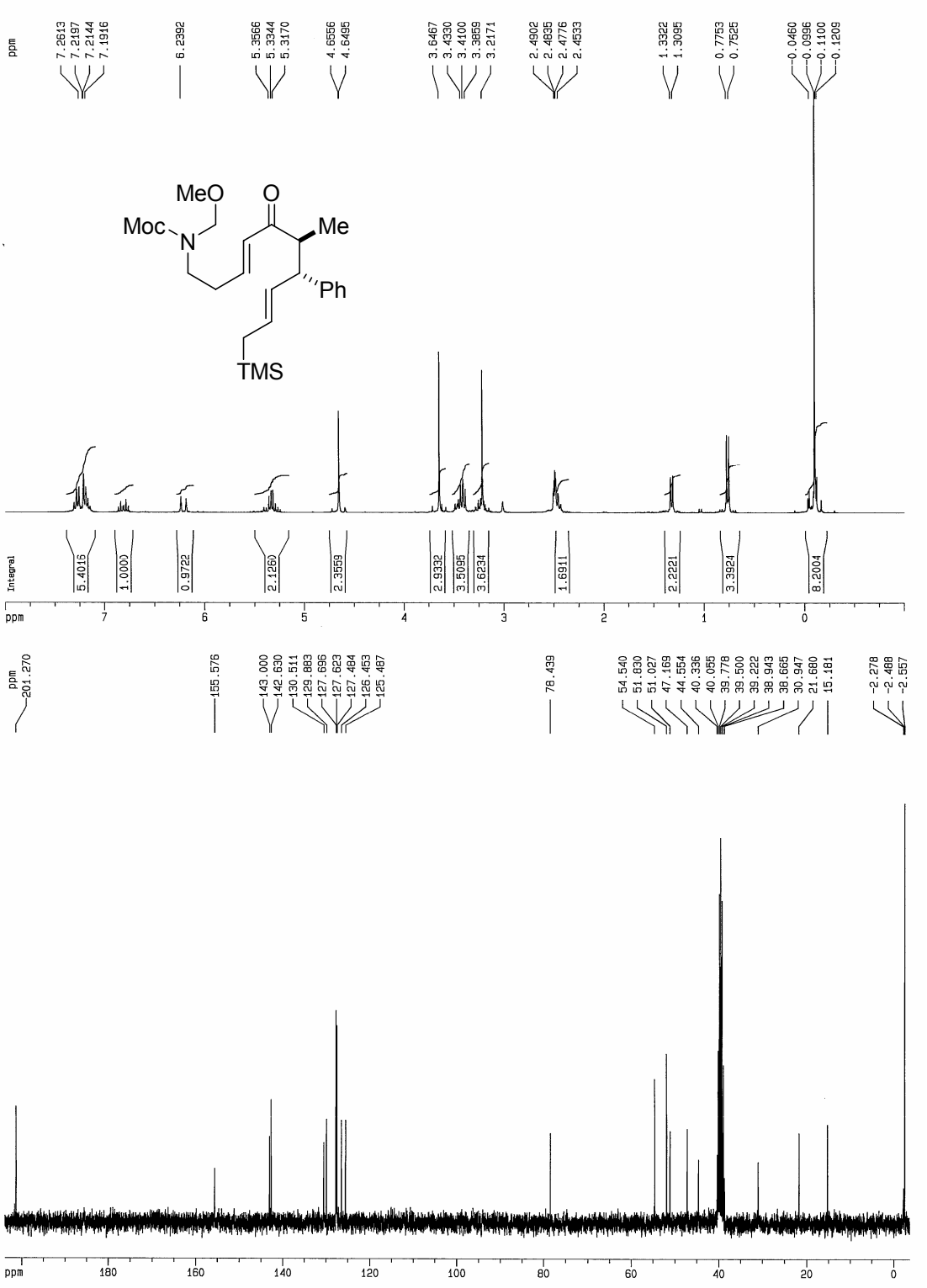
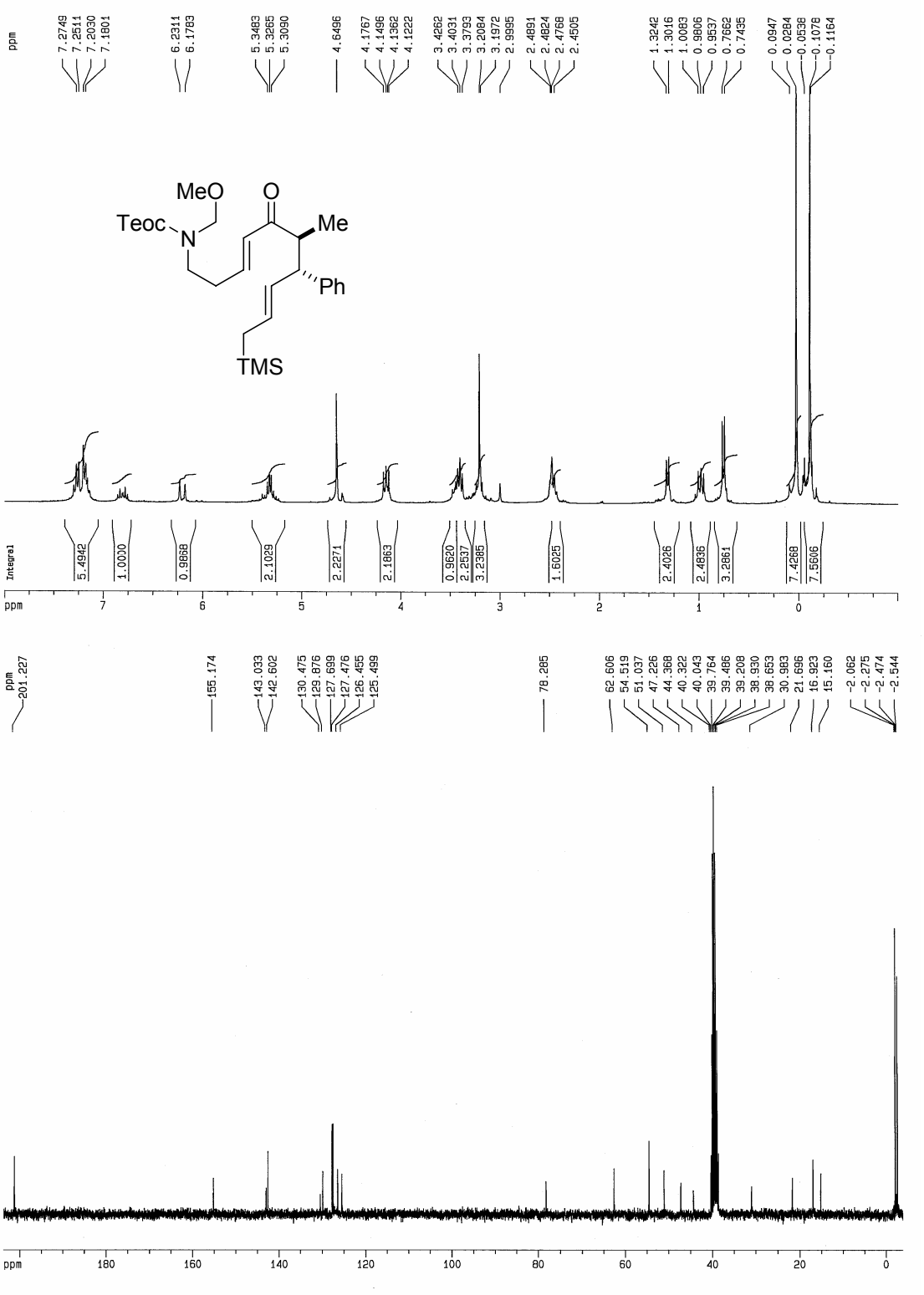
4.0364
3.1229
3.1031
3.0992
3.0793
2.4698
2.3137
2.2987
2.2899
2.2751
0.9552
0.9313
0.9279
0.9011
0.0292
0.0182
0.0127
-0.0374
Integral
1.0000
2.3692
2.4144
0.4505
2.2713
1.9759
7.6822
ppm
7
6
5
4
3
2
1
0
~6.8
ppm
155.660
81.549
70.750
61.118
40.344
40.062
39.783
39.506
39.226
38.949
38.673
18.779
17.053
-1.935
-2.004
ppm
140
120
100
80
60
40
20
0

A.47 COMPOUND 75

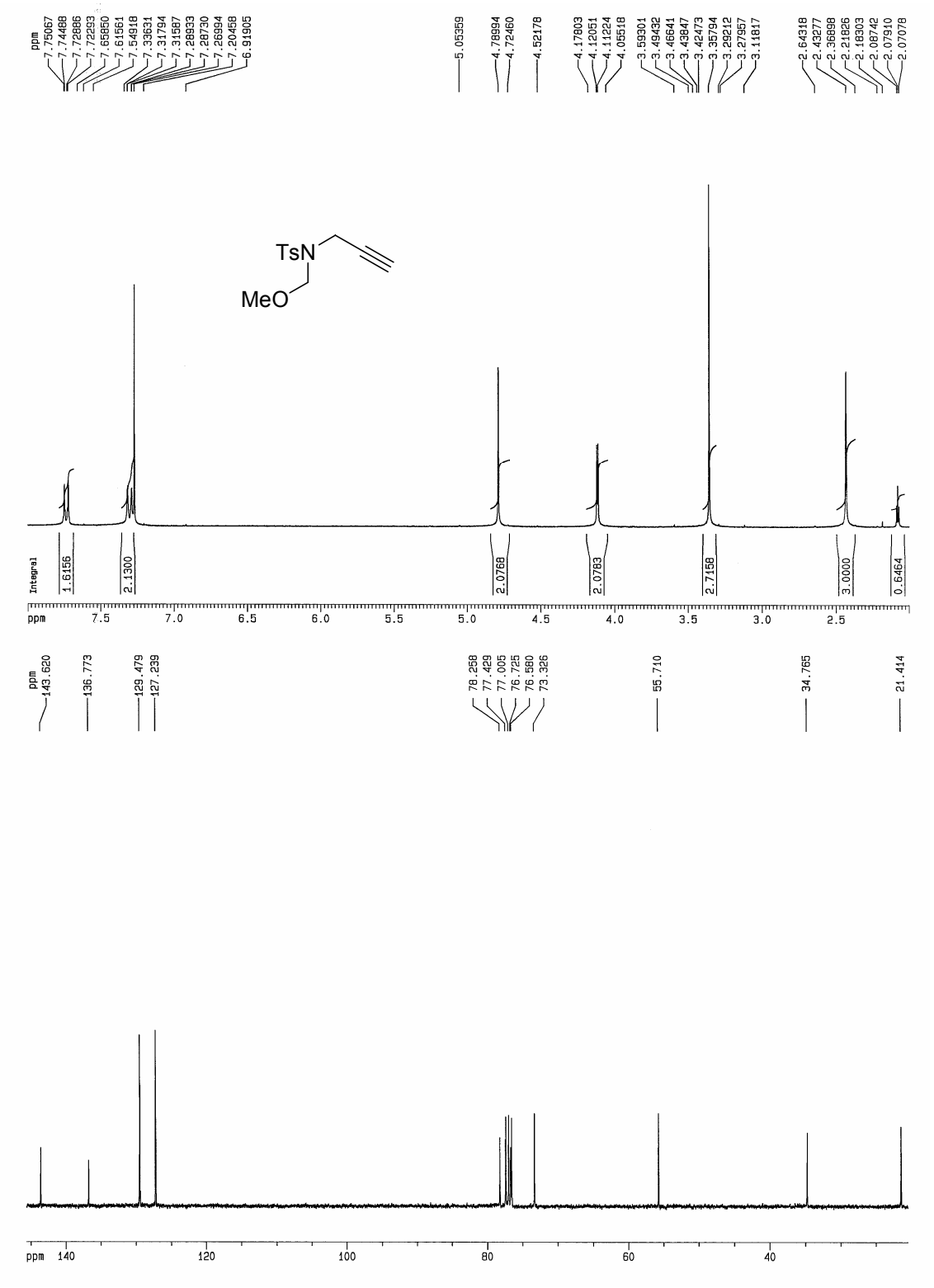
A.48 COMPOUND 78



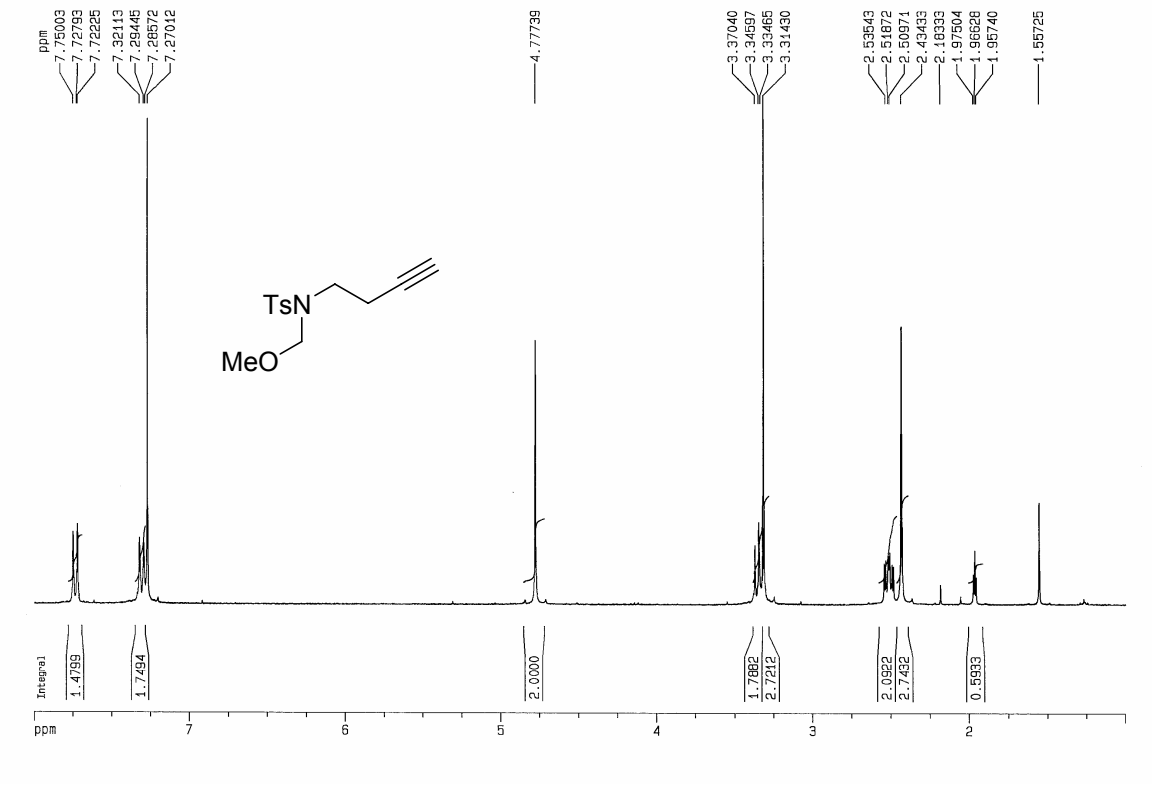
A.49 COMPOUND 79

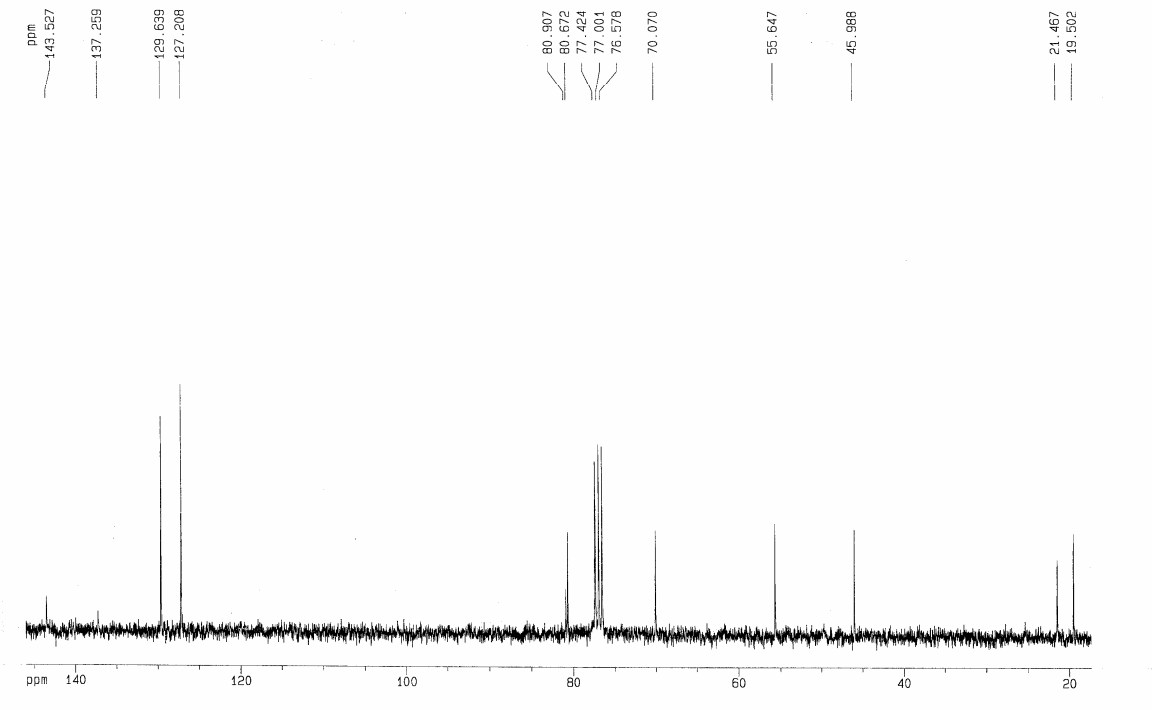


A.50 COMPOUND 80

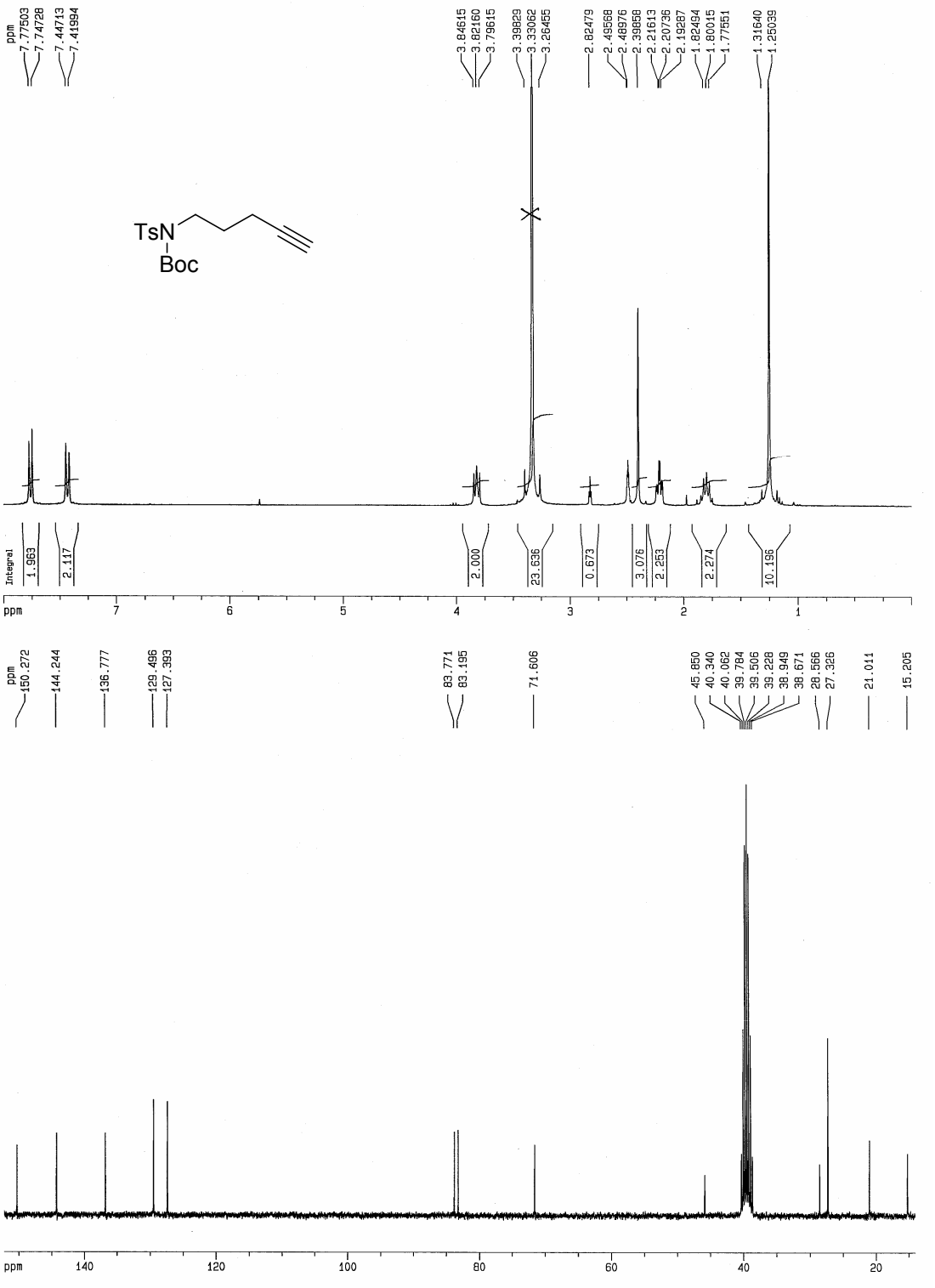


A.51 COMPOUND 81





A.52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3.39829
3.33062
3.26455
2.82479
2.49568
2.48976
2.39856
2.21613
2.20736
2.19287
1.82494
1.80015
1.77551
1.31640
1.25039
Integral
1.963
2.117
2.000
23.636
0.673
3.076
2.253
2.274
10.196
ppm
150.272
144.244
136.777
129.496
127.393
83.771
83.195
71.606
45.850
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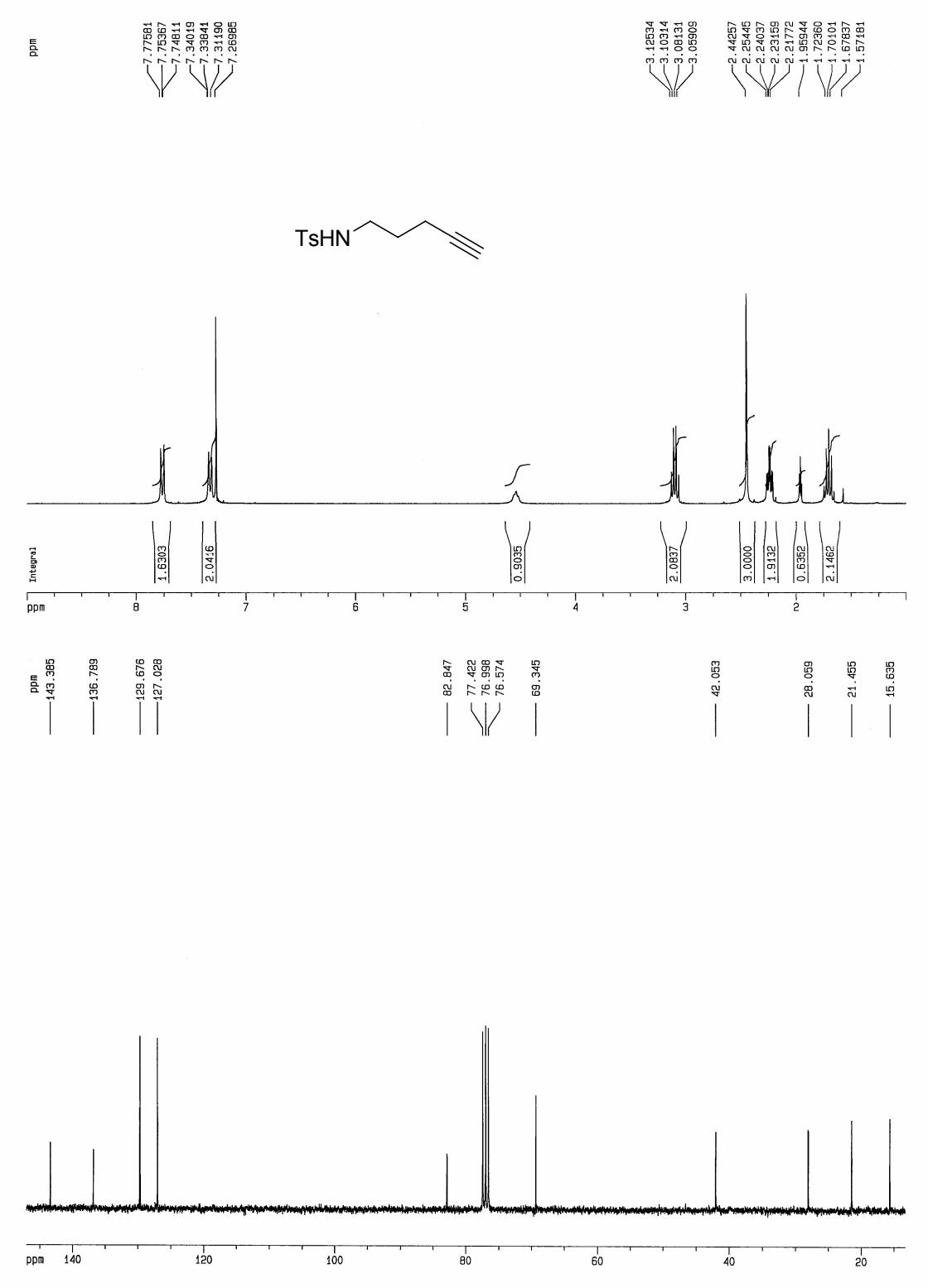
39.506
39.228
38.949
38.671
28.566
27.326
21.011
15.205

A.53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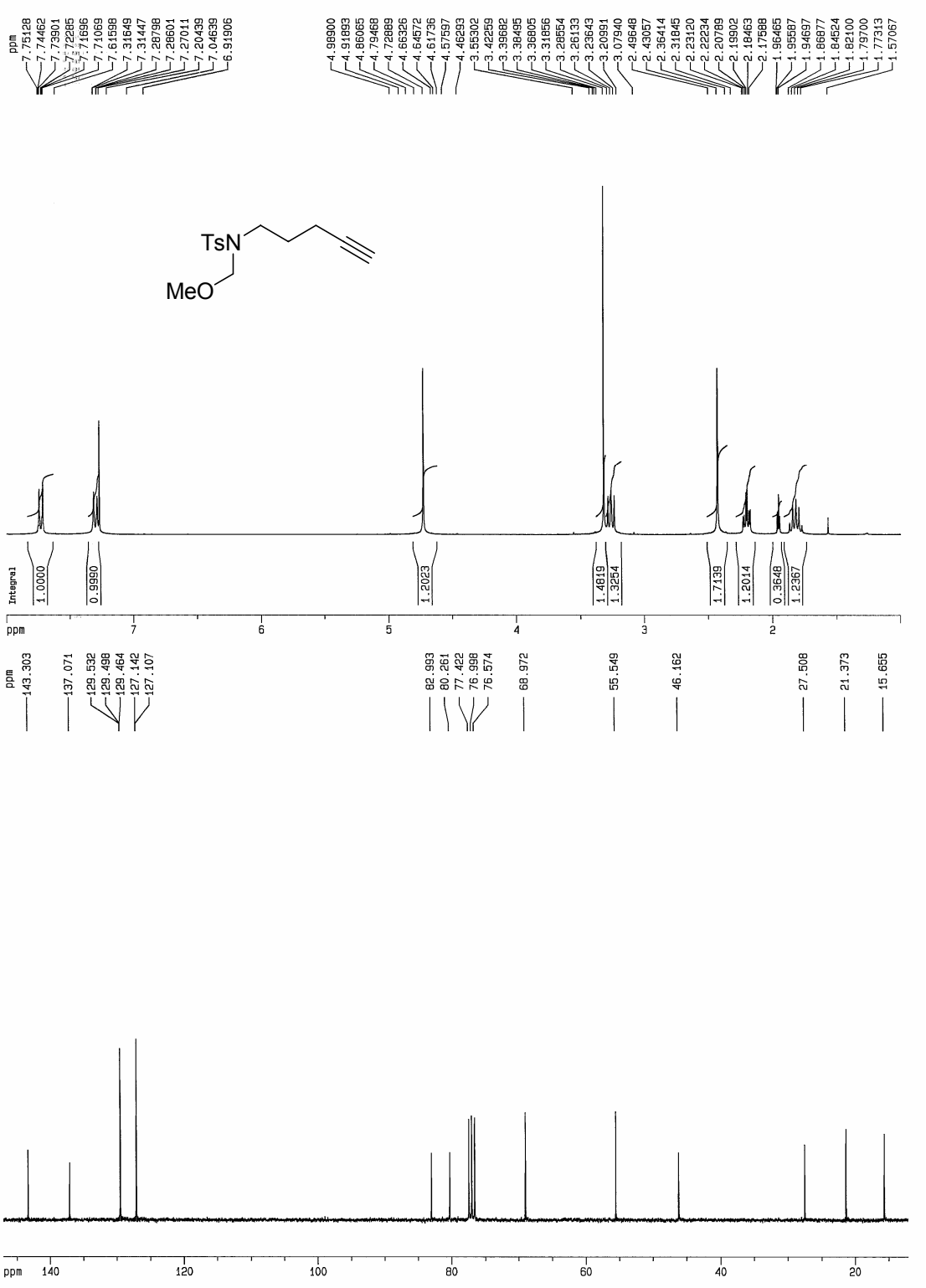
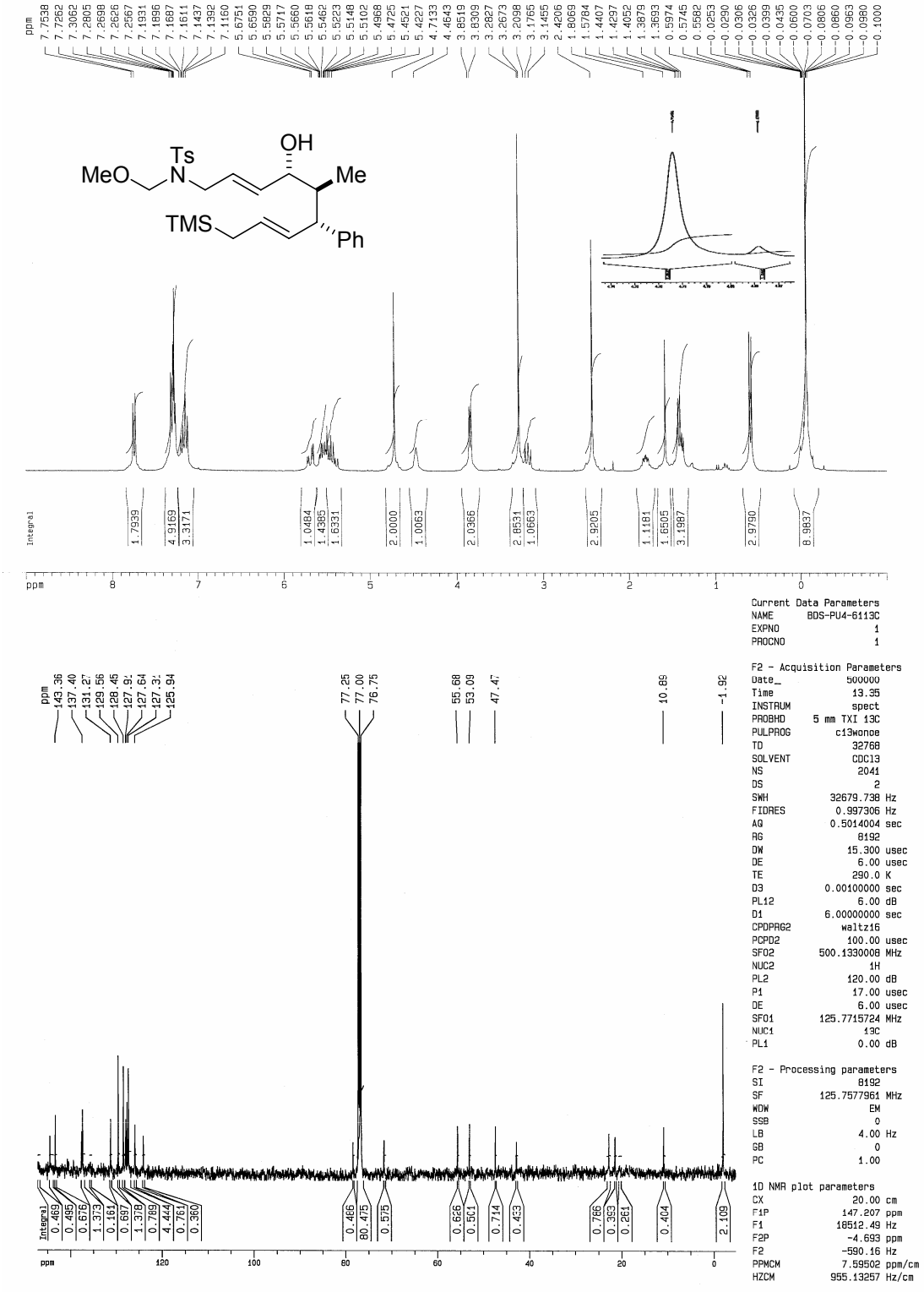
7.26985
3.12534
3.10314
3.08131
3.05909
2.44257
2.25445
2.24037
2.23159
2.21772
1.95944
1.72360
1.70101
1.67837
1.57181
TsHN
Integral
1.6303
2.0416
0.9035
2.0837
3.0000
1.9132
0.6352
2.1462
ppm
8
7
6
5
4
3
2
ppm
143.385
136.789
129.676
127.028
82.847
77.422
76.998
76.574
69.345
42.053
28.059
21.455
15.635
ppm
140
120
100
80
60
40
20

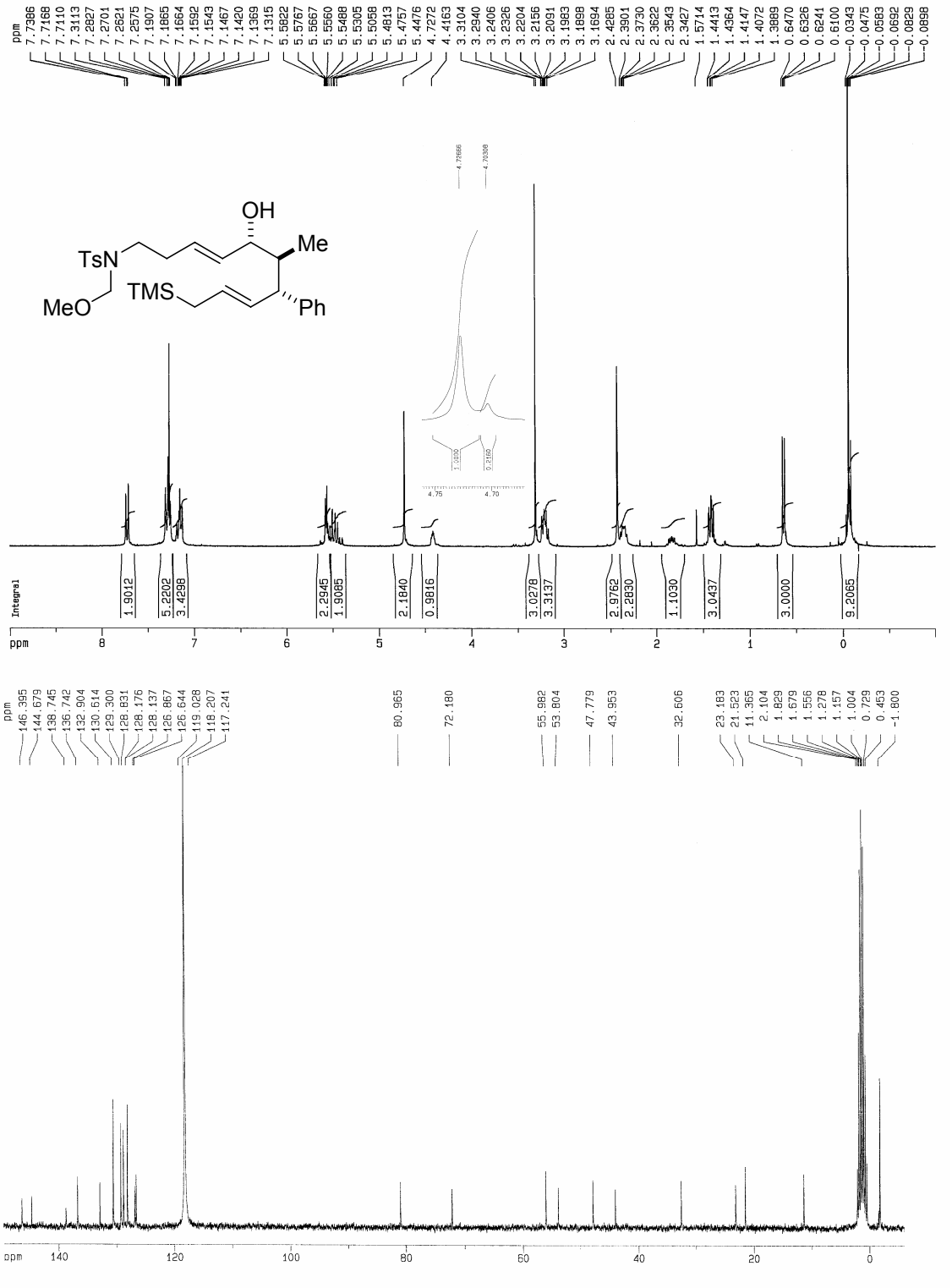
A.54 COMPOUND 82



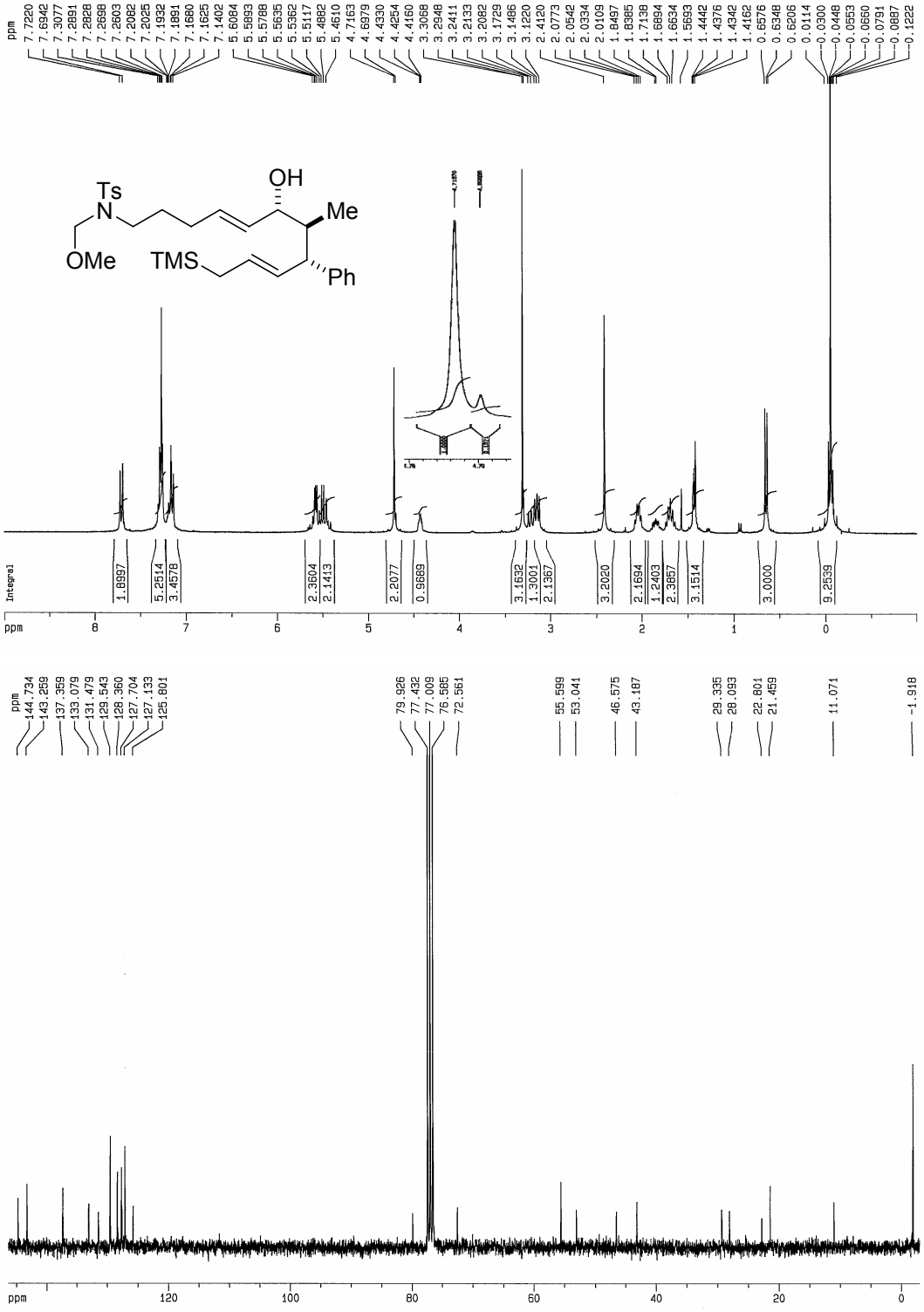
A.55 COMPOUND 83



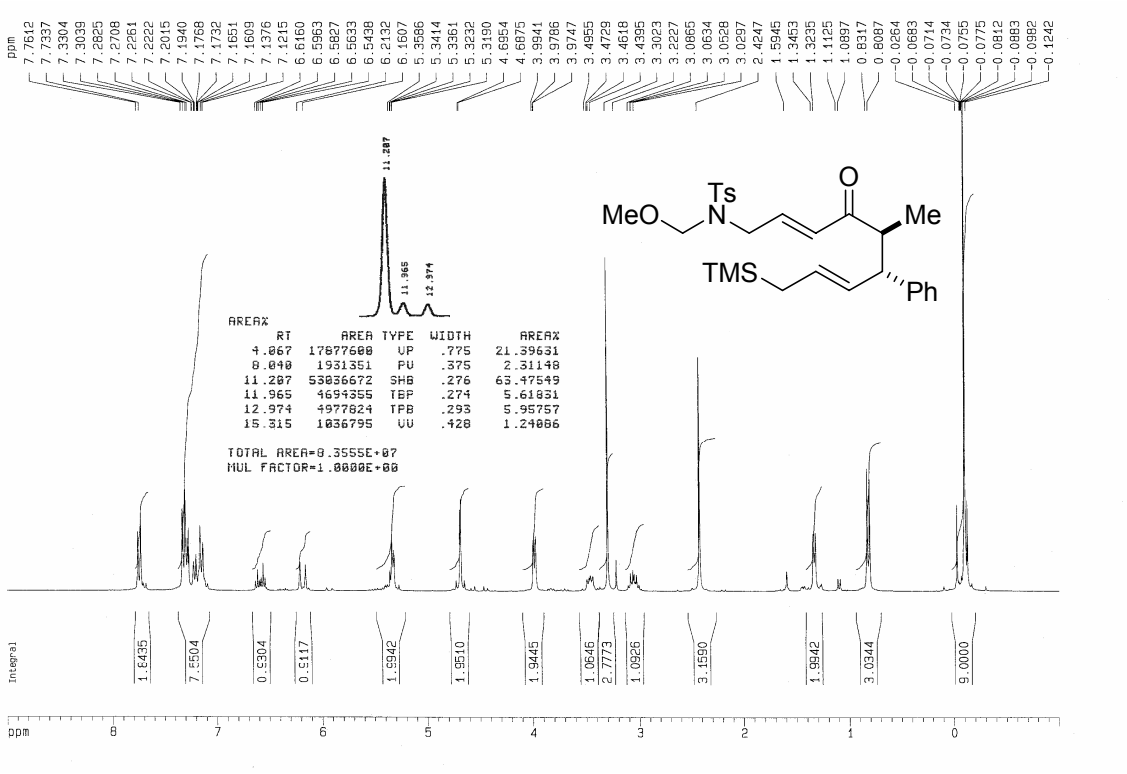
A.56 COMPOUND 84

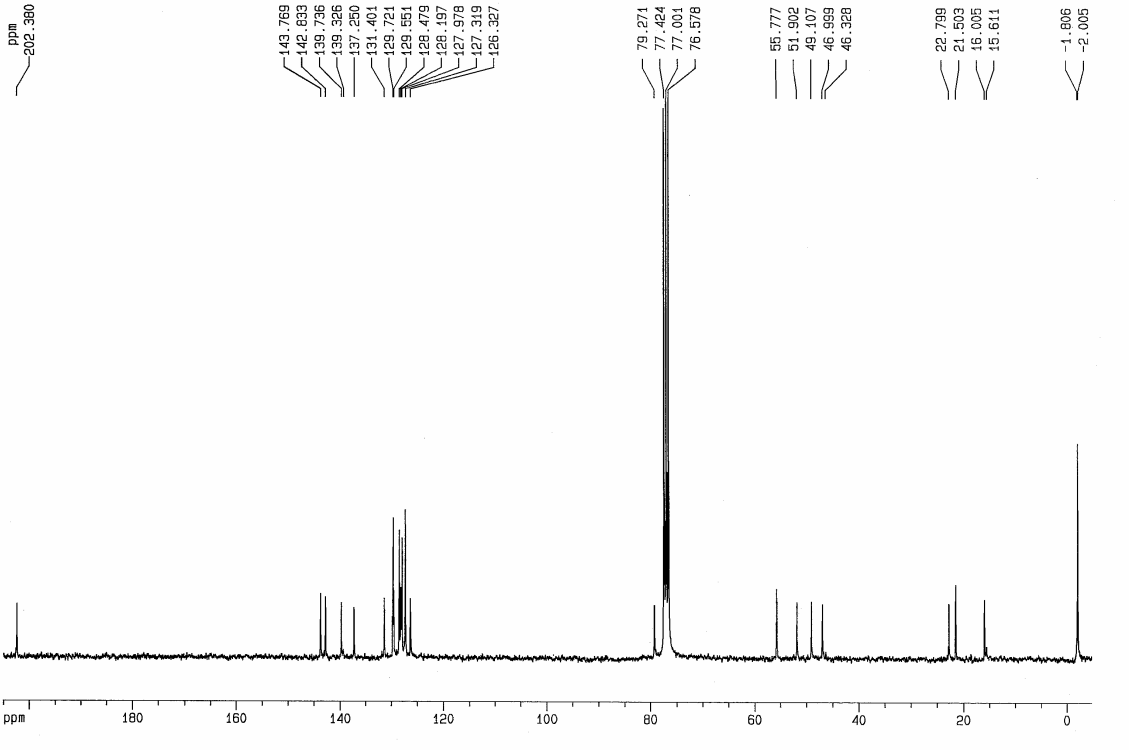


A.57 COMPOUND 85

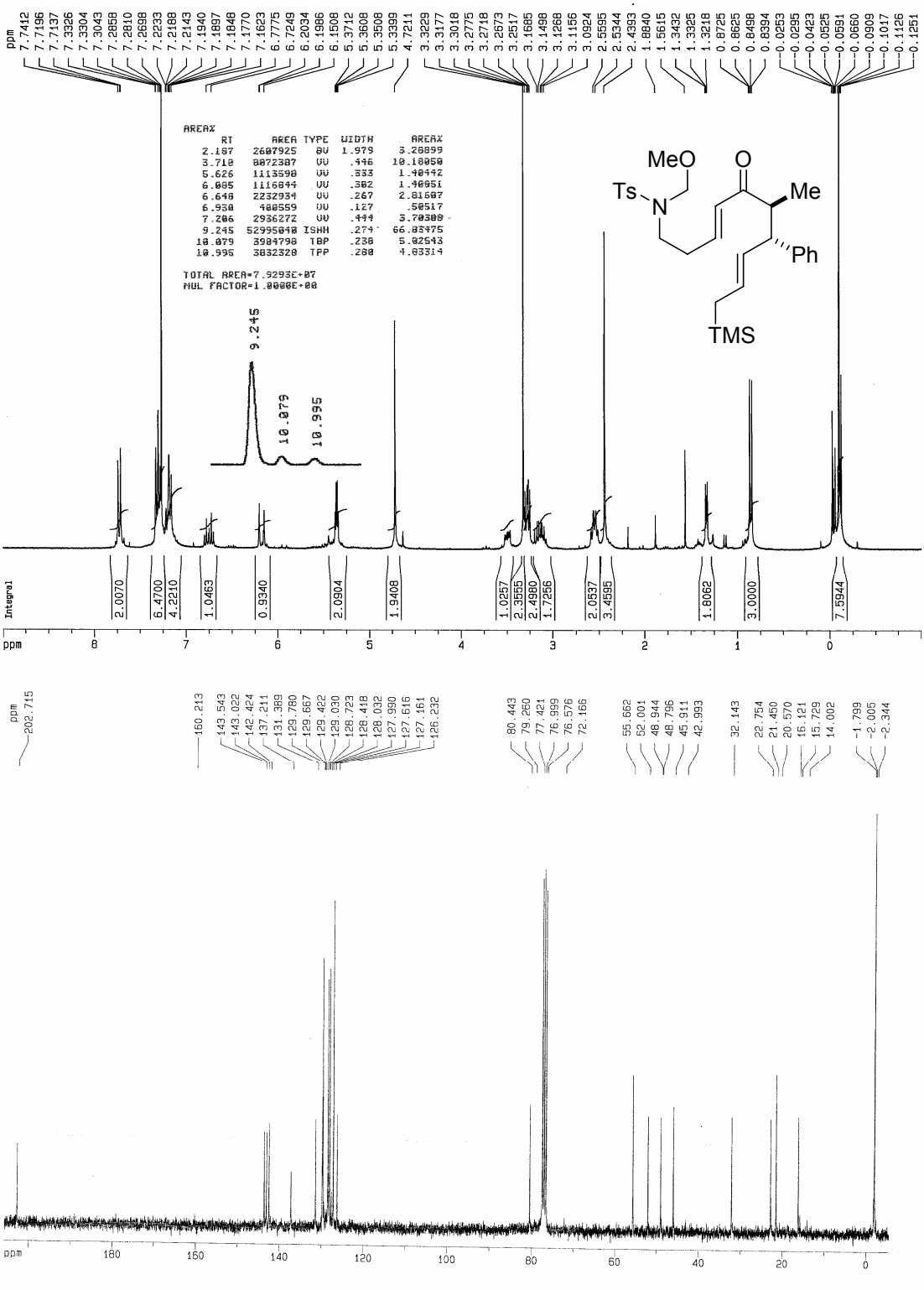


A.58 COMPOUND 86

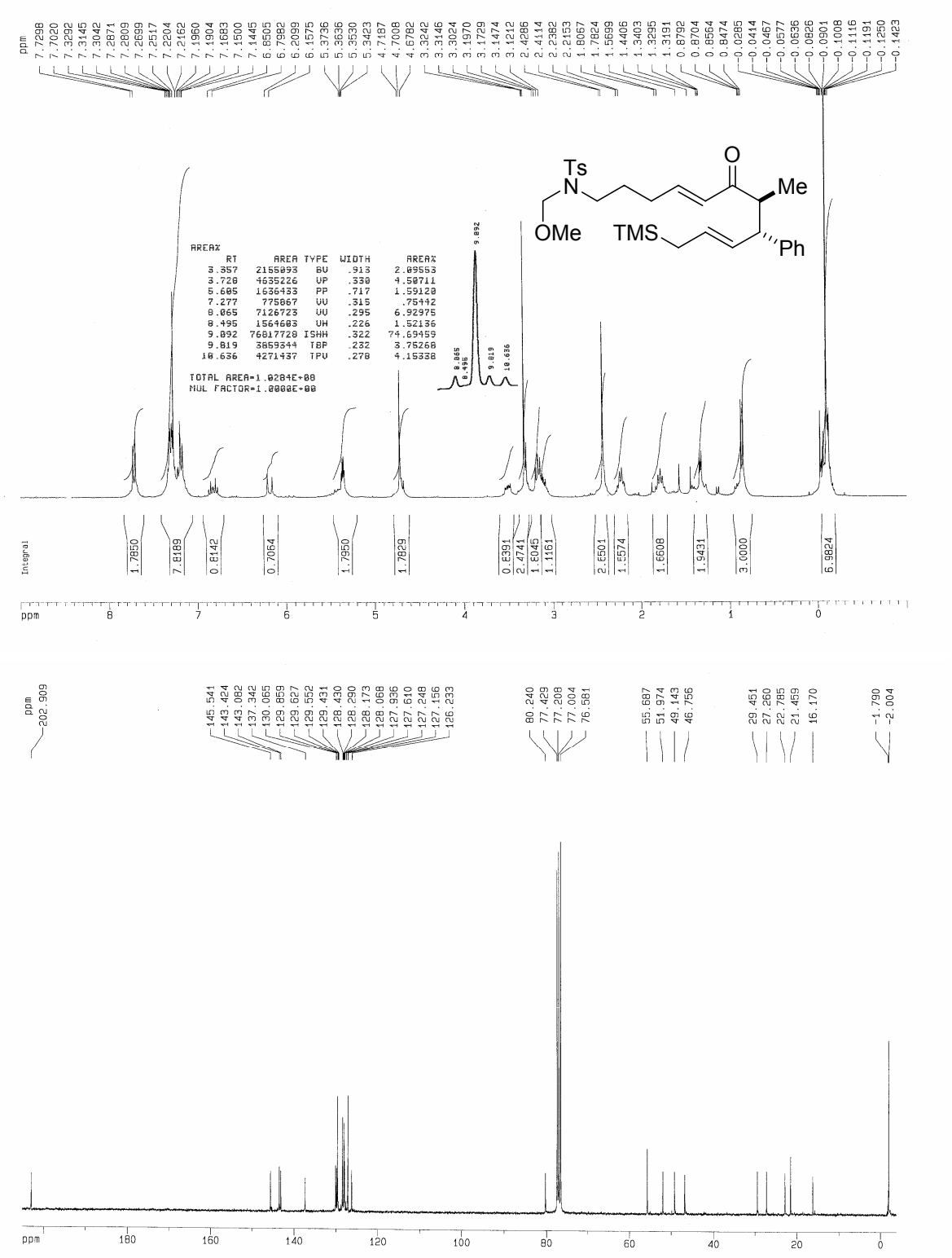




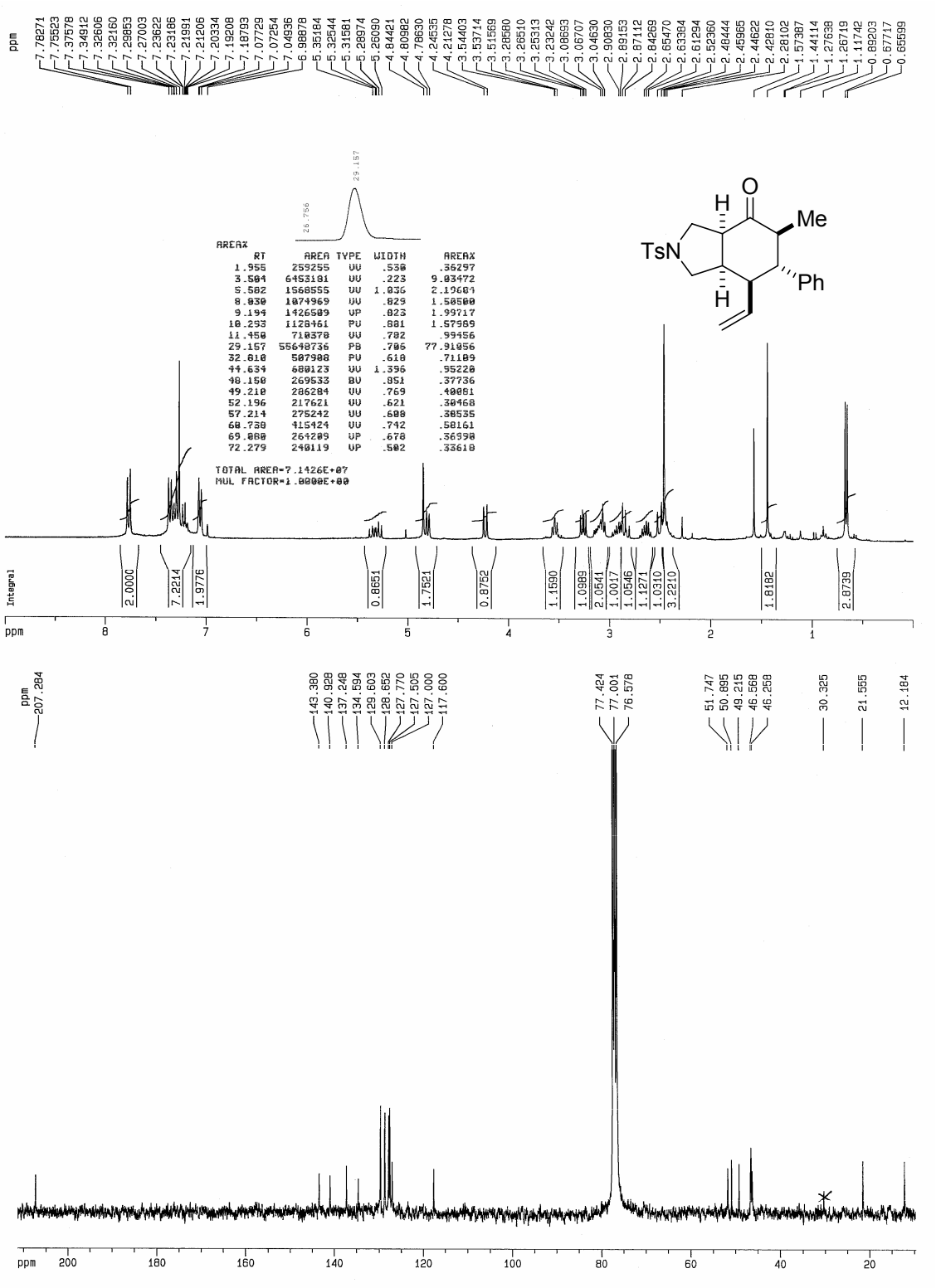
A.59 COMPOUND 87



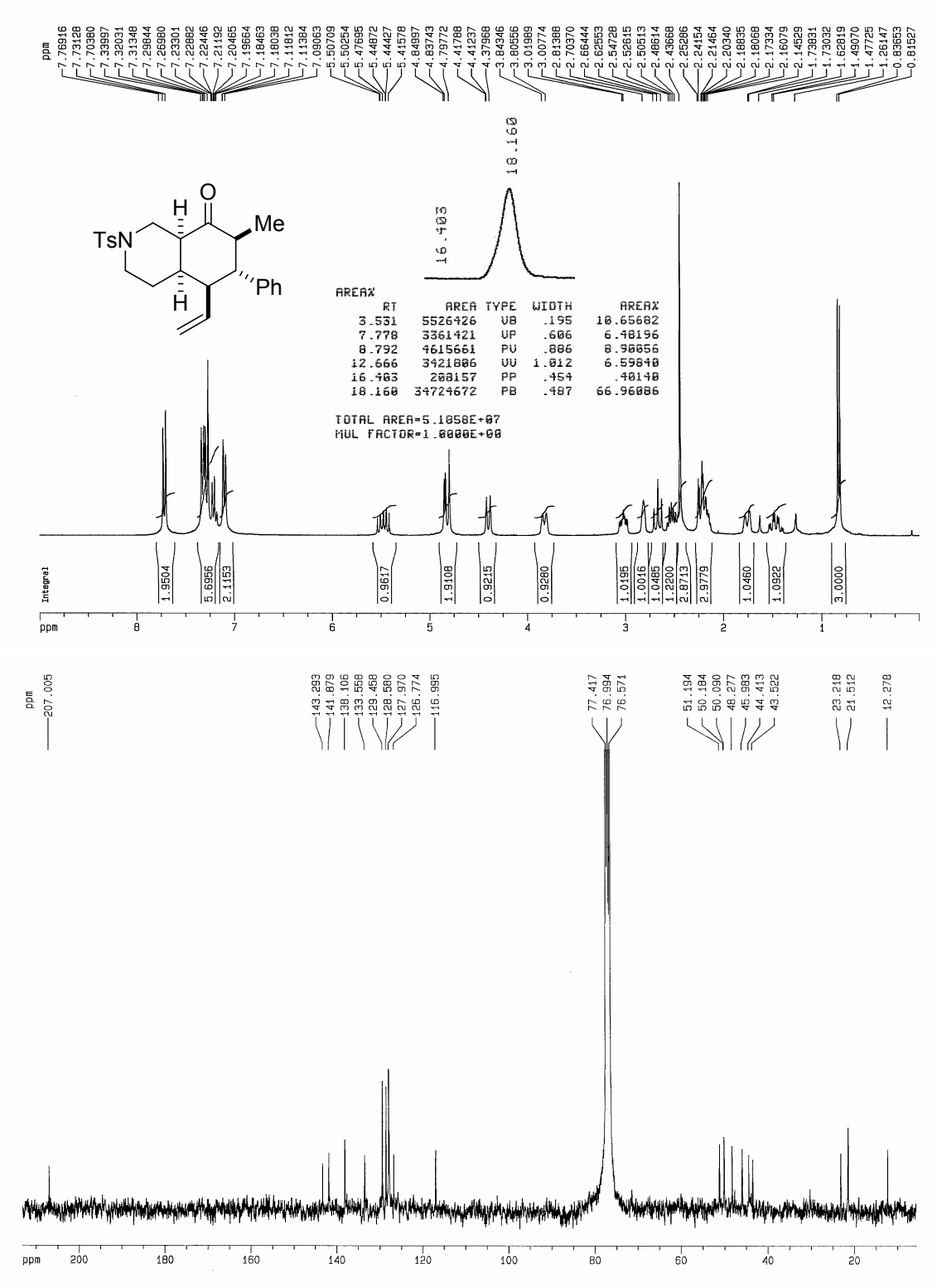
A.60 COMPOUND 88



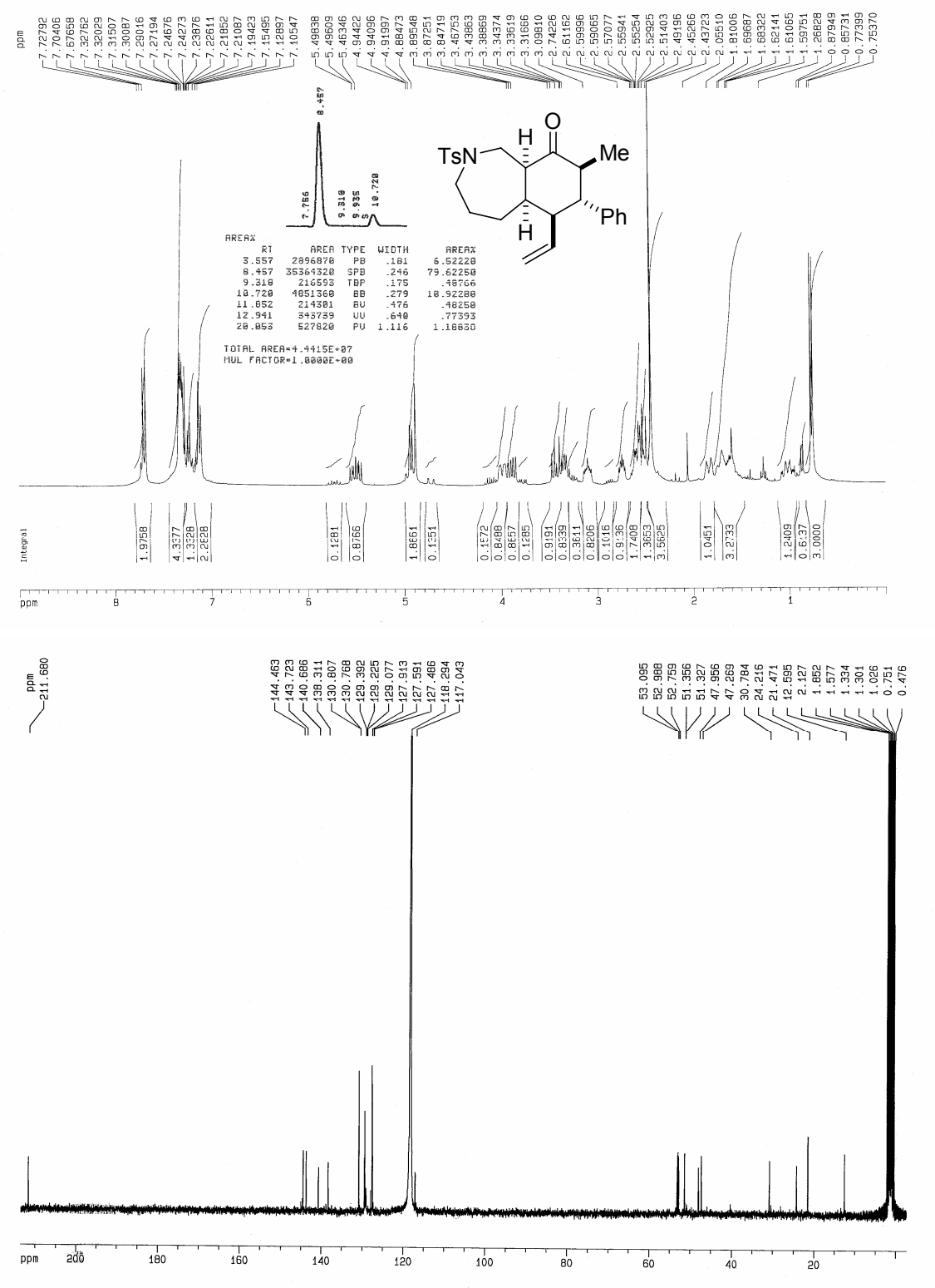
A.61 COMPOUND 89



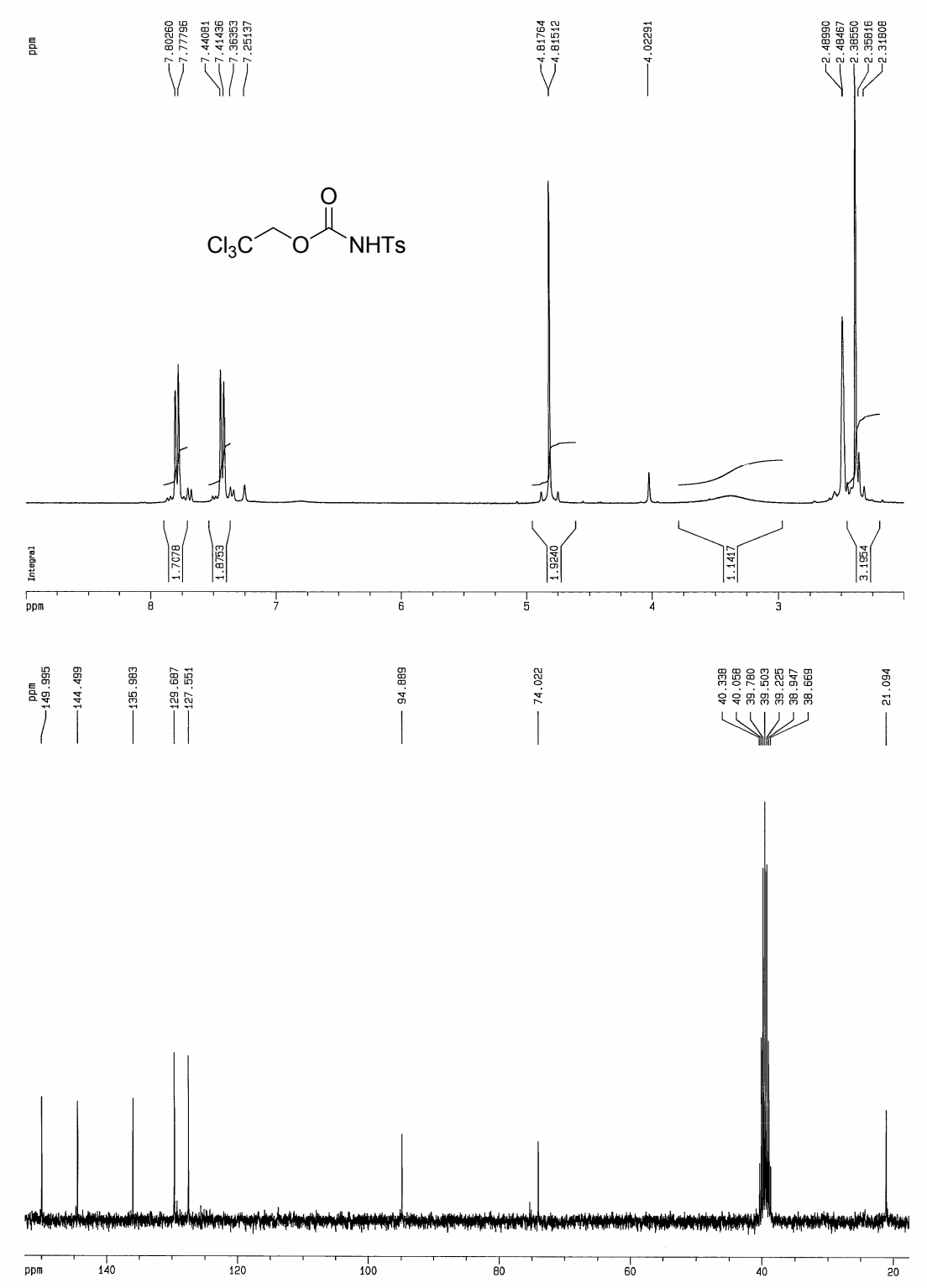
A.62 COMPOUND 90



A.63 COMPOUND 91



A.64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4.81512
4.02291
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2.48467
2.36650
2.35816
2.31808
O
Cl3C
O
NHTs
Integral
1.7078
1.8763
1.9240
1.1417
3.1954
ppm
8
7
6
5
4
3
ppm
149.995
144.499
135.983
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127.551
94.889
74.022
40.338
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39.780
39.503
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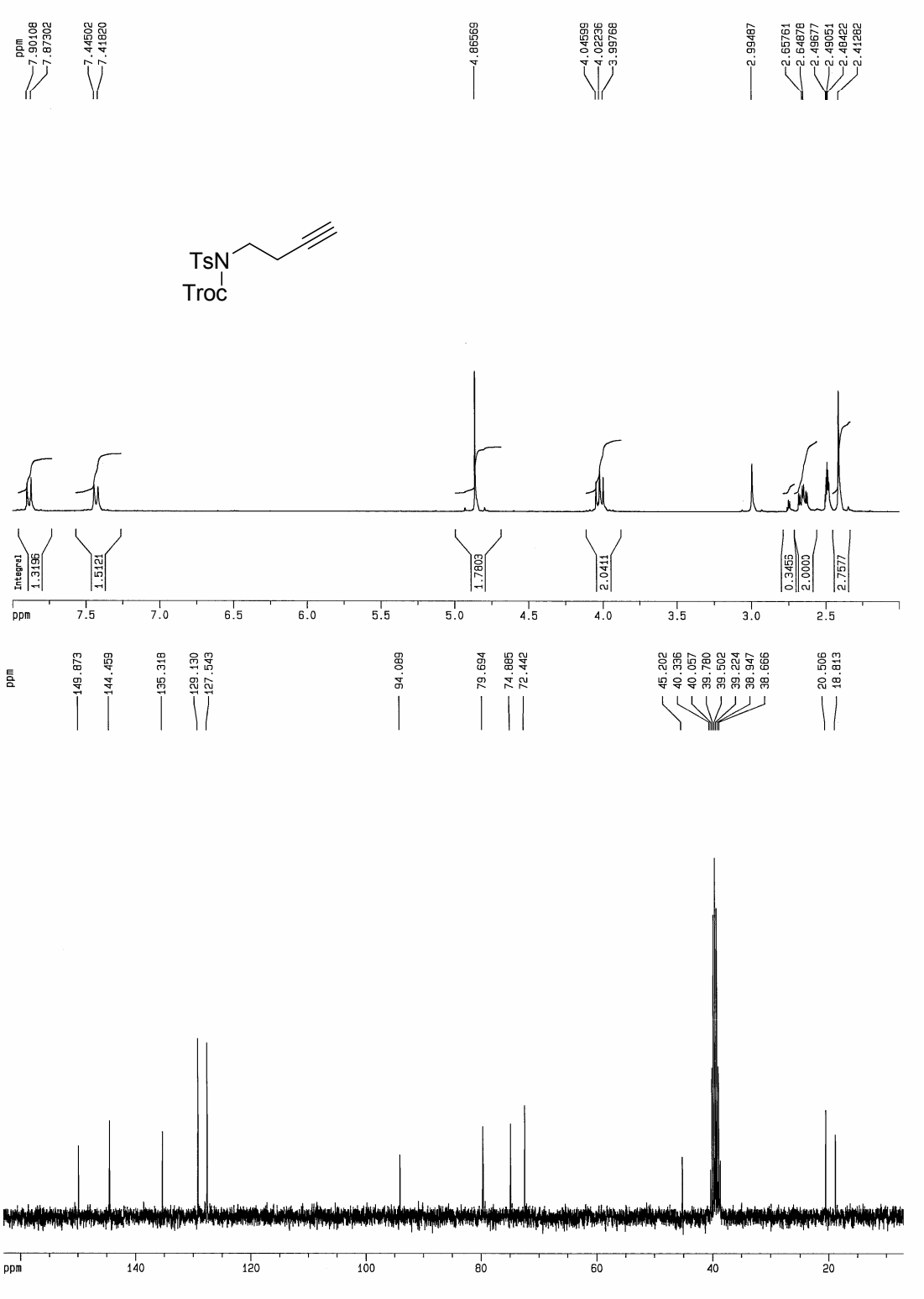
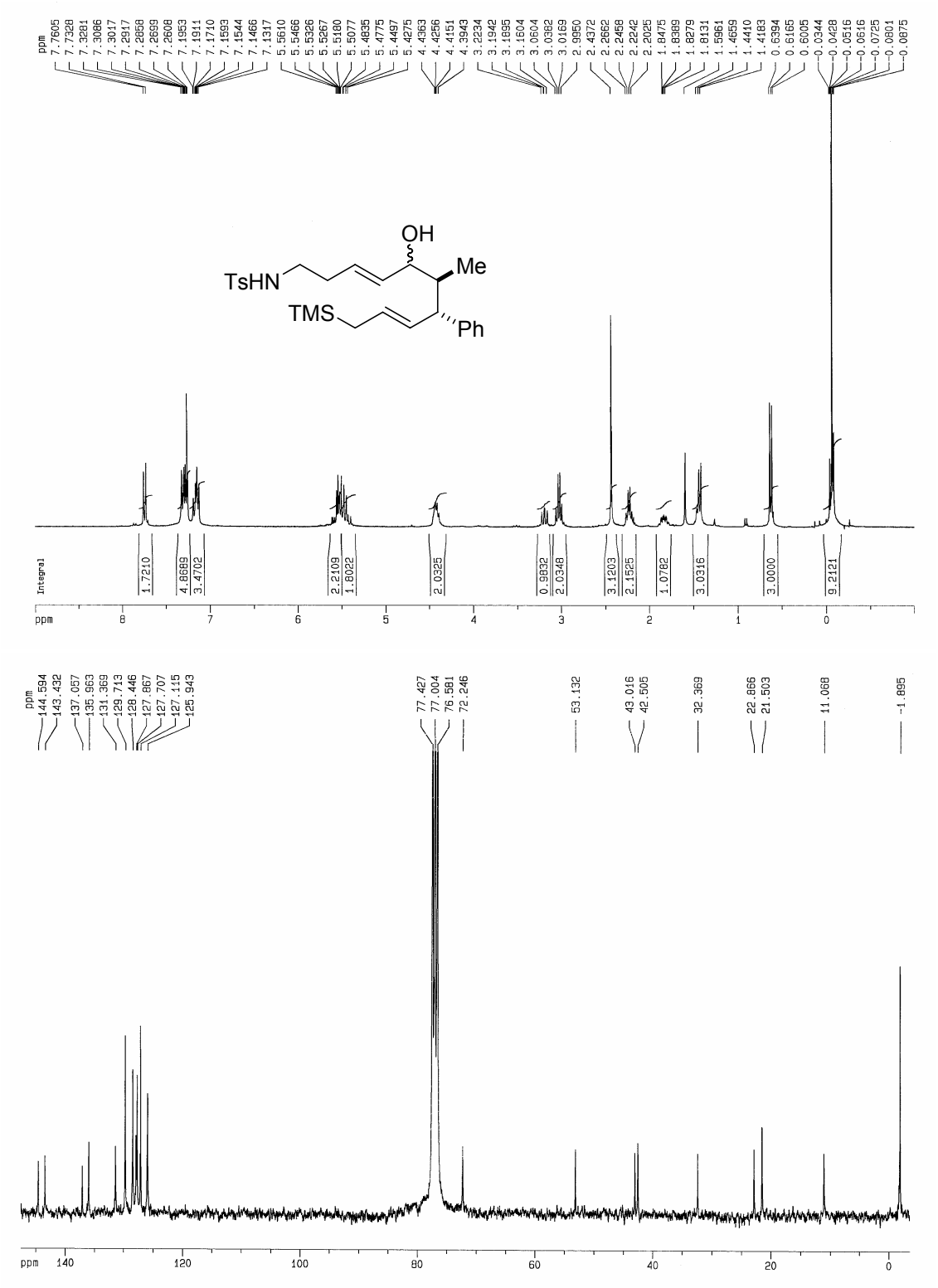
38.669
21.094
ppm
140
120
100
80
60
40
20

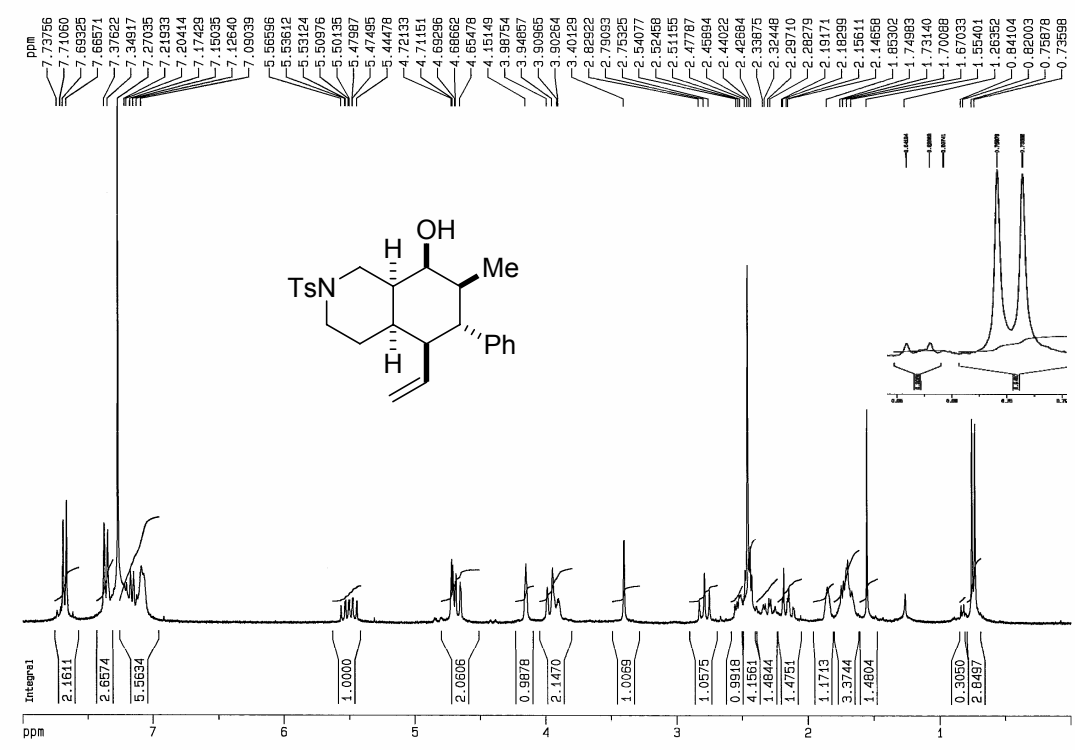
A.65 COMPOUND 92



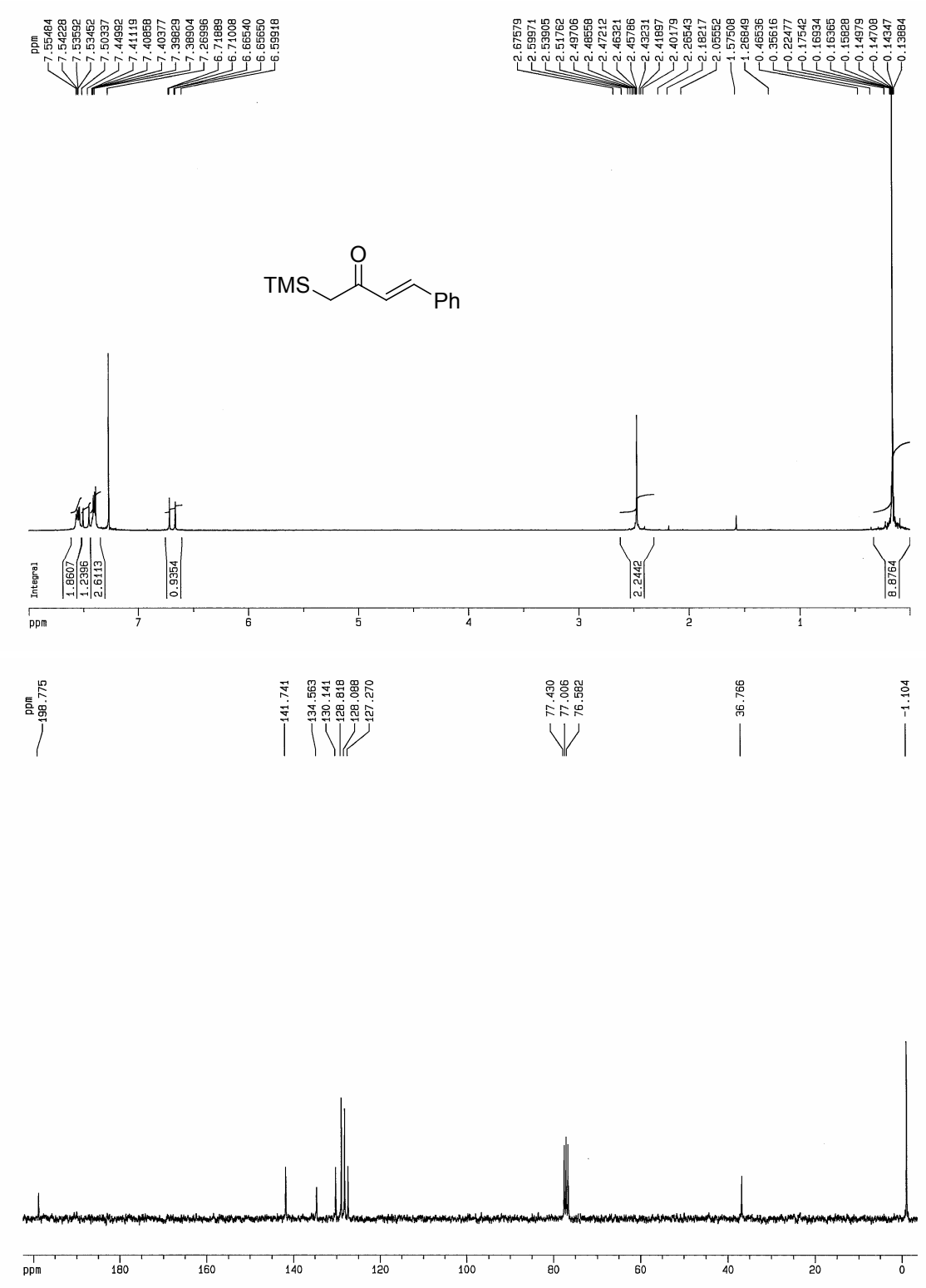
A.66 COMPOUND 94



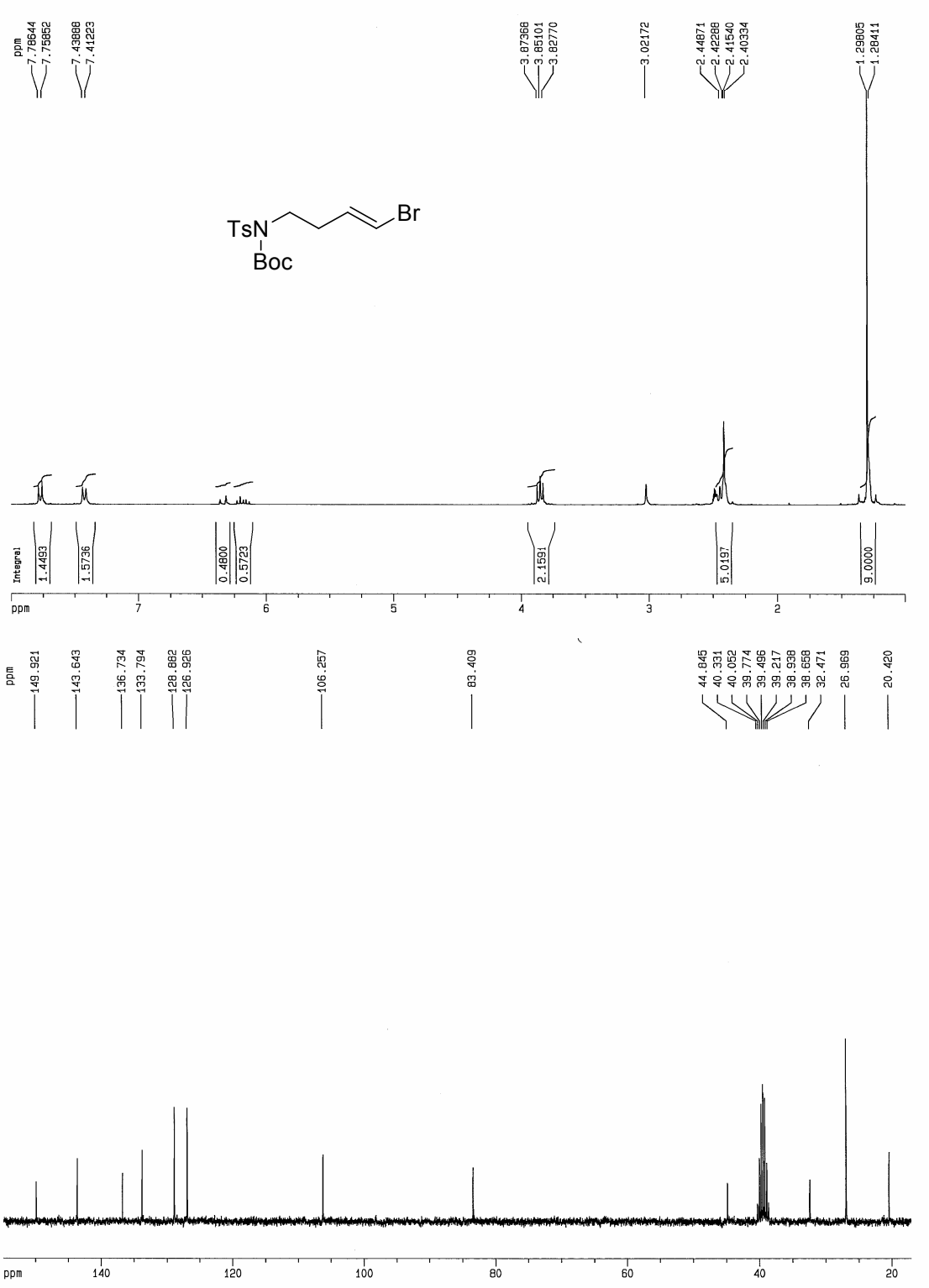
A.67 COMPOUND 95



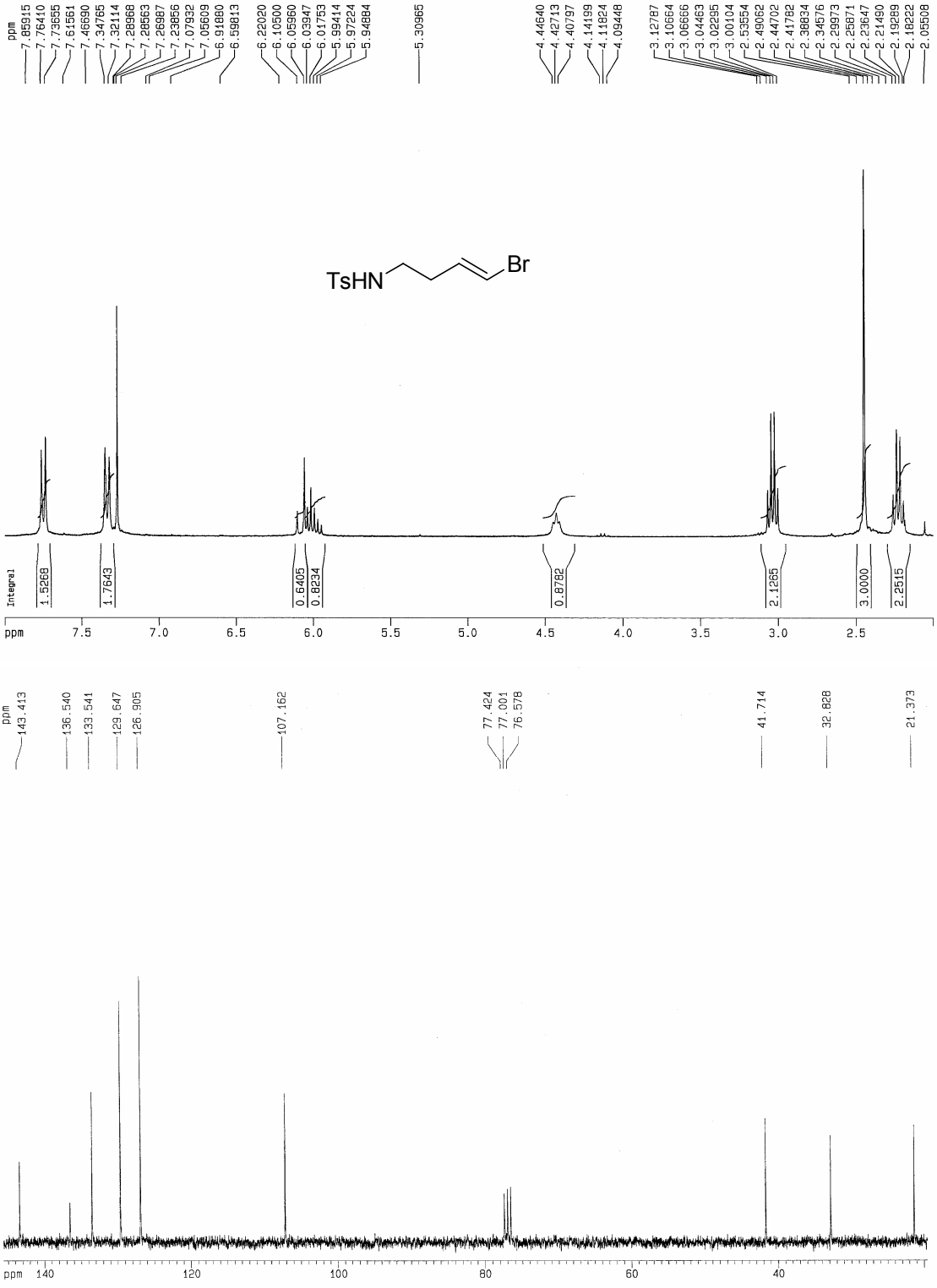
A.68 COMPOUND 96



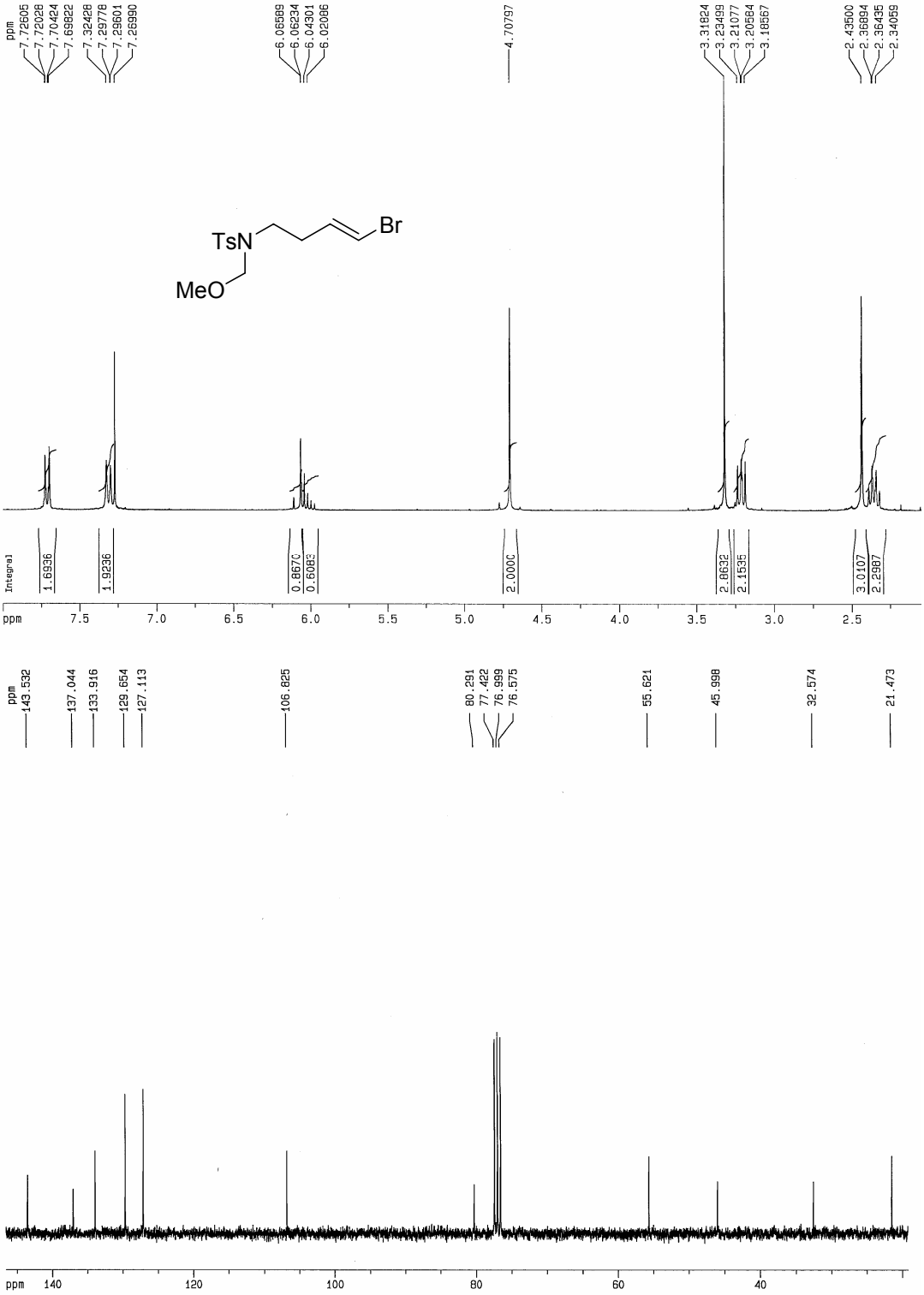
A.69 COMPOUND 111



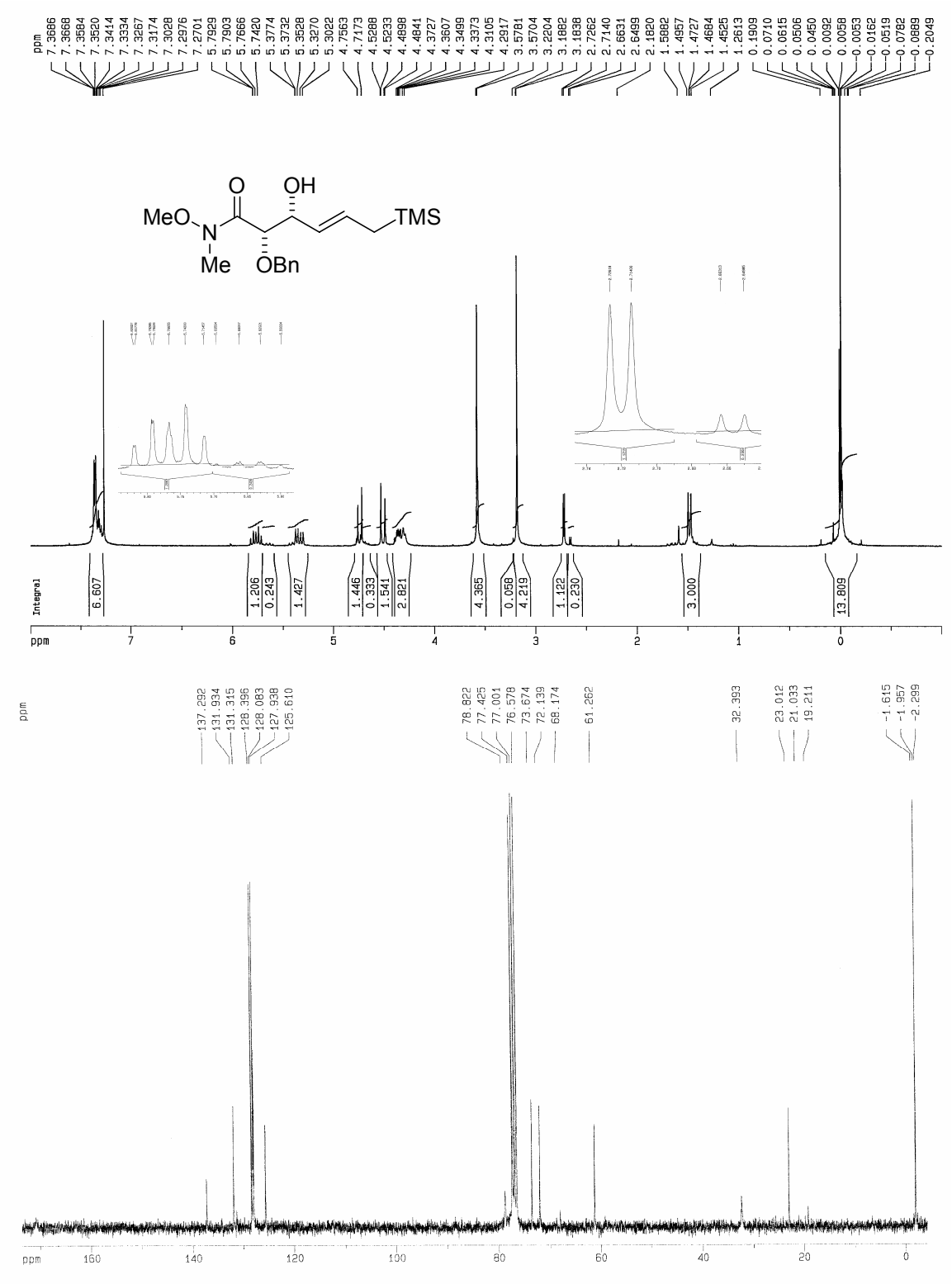
A.70 COMPOUND 112



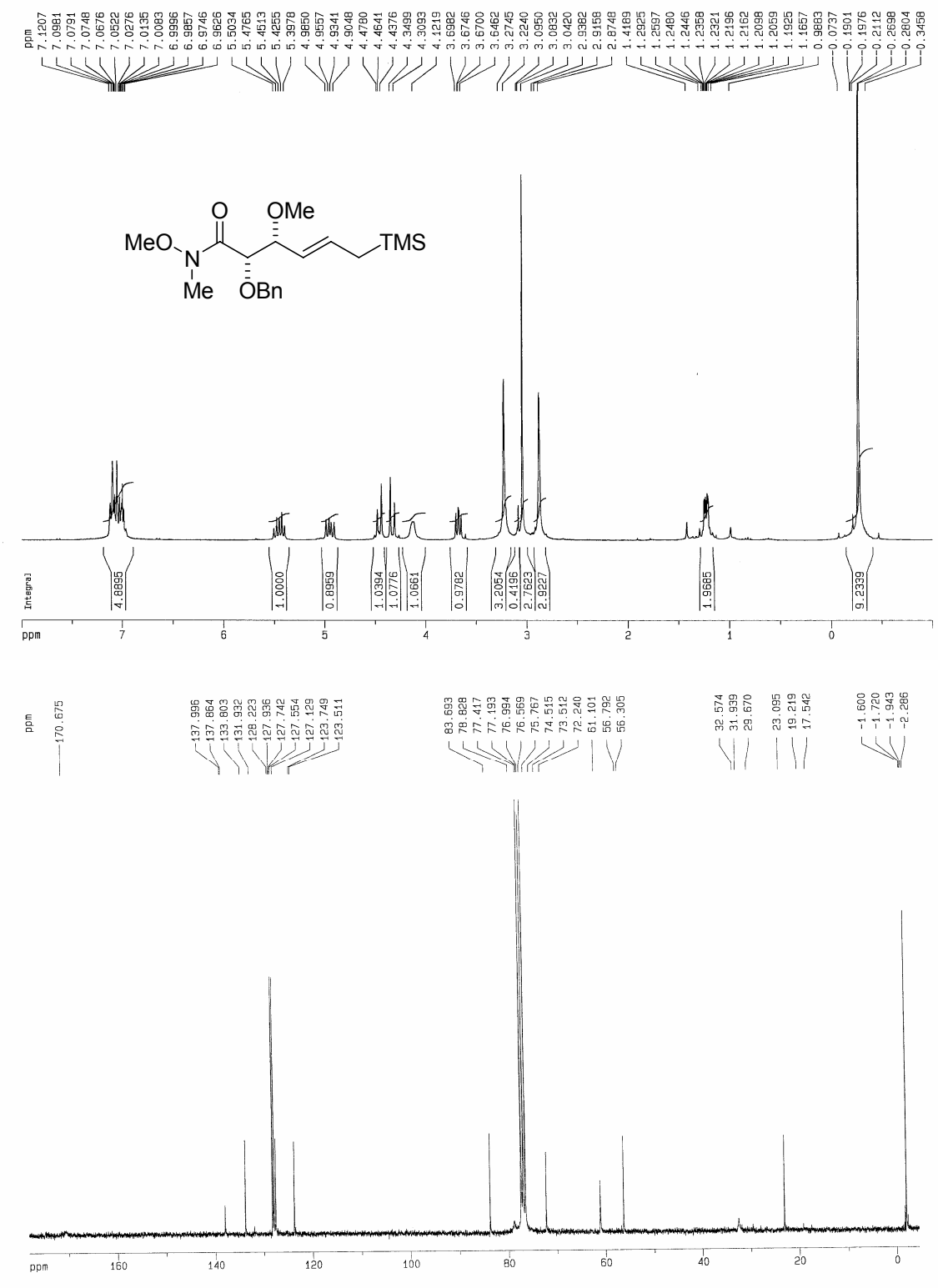
A.71 COMPOUND 113



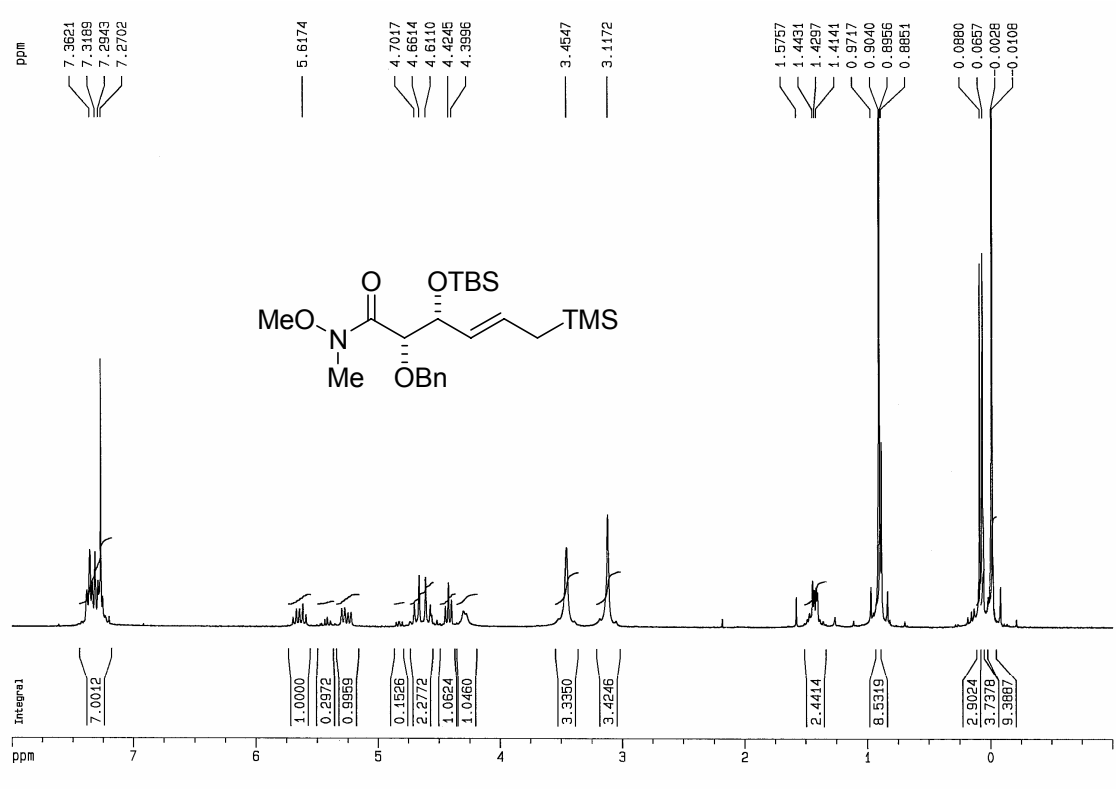
A.72 COMPOUND 117

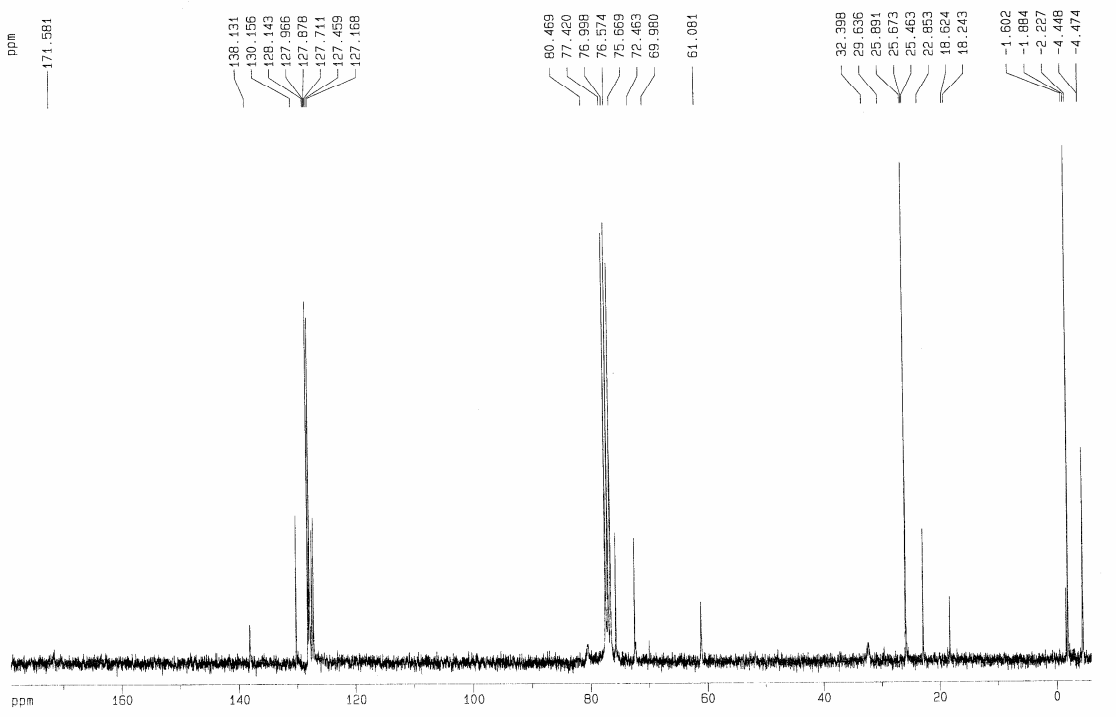


A.73 COMPOUND 118

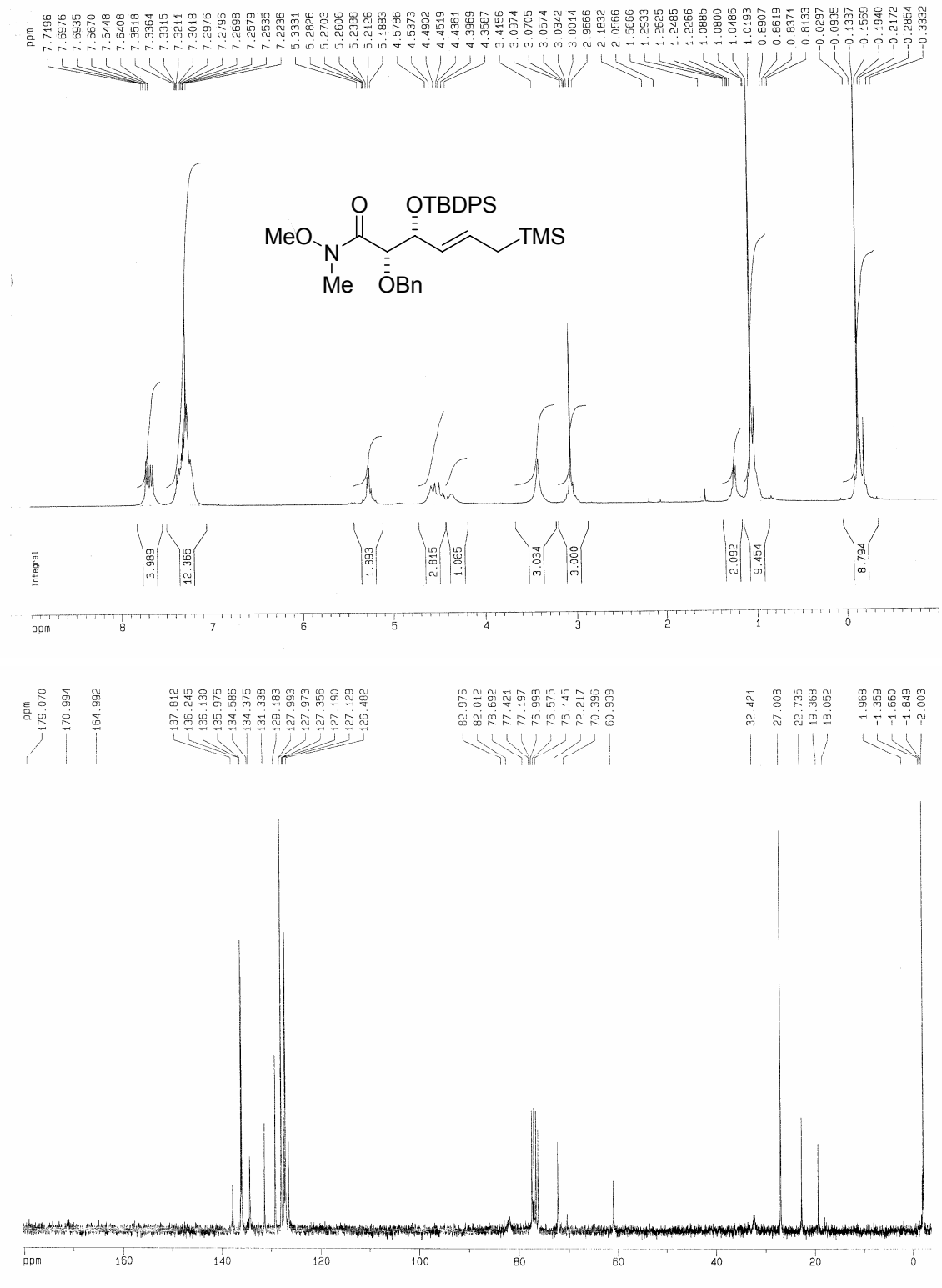


A.74 COMPOUND 119

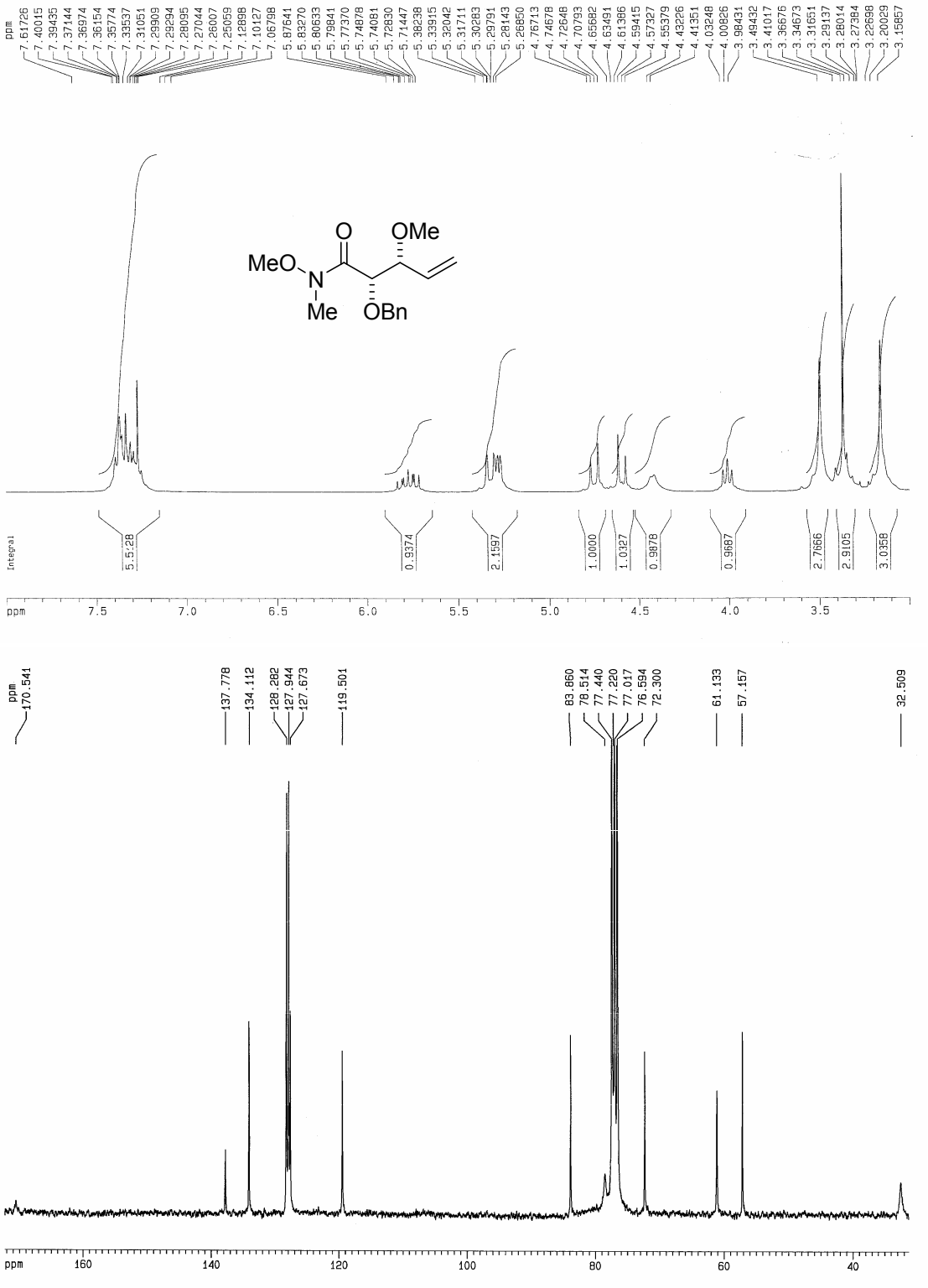




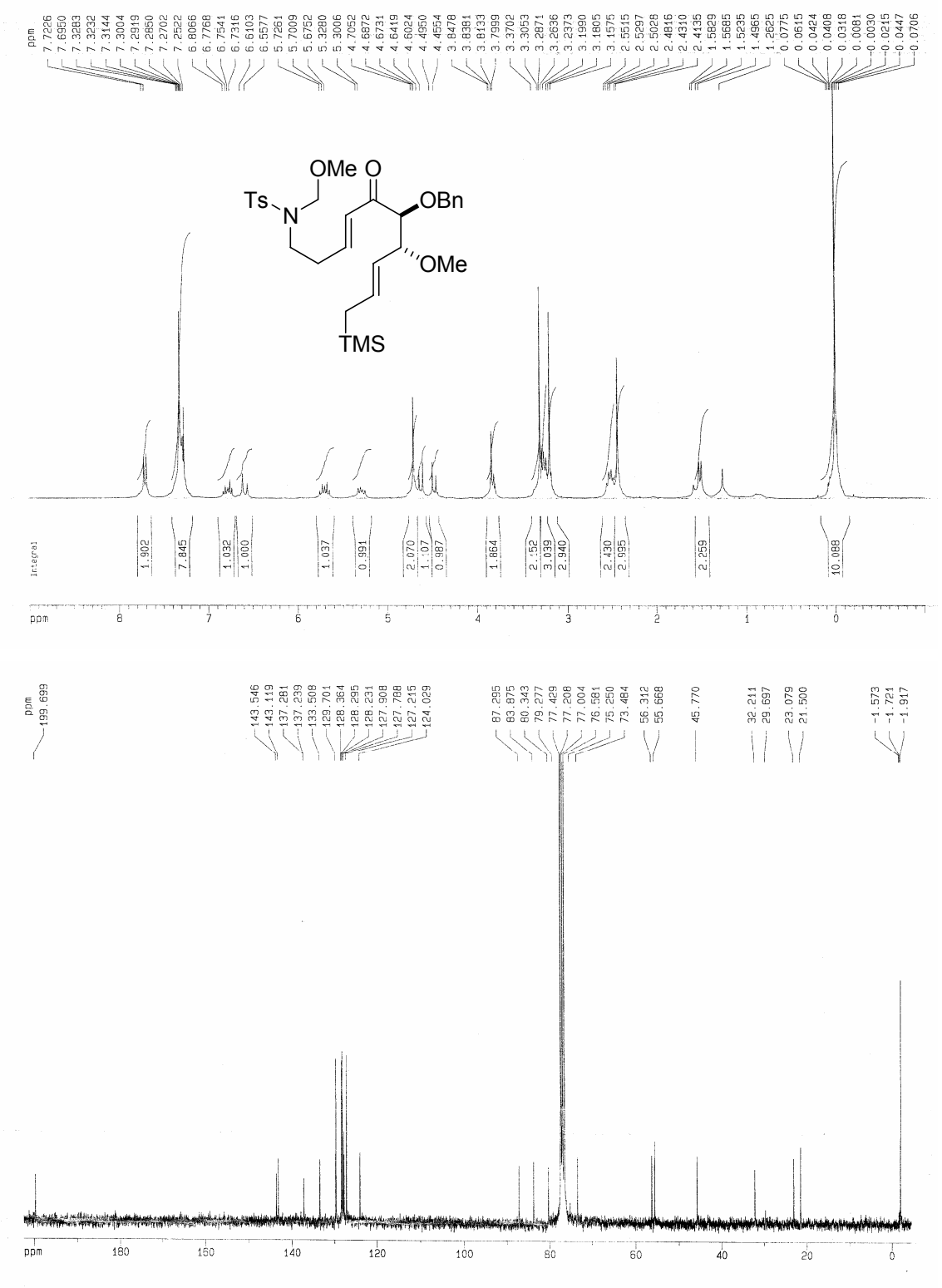
A.75 COMPOUND 120



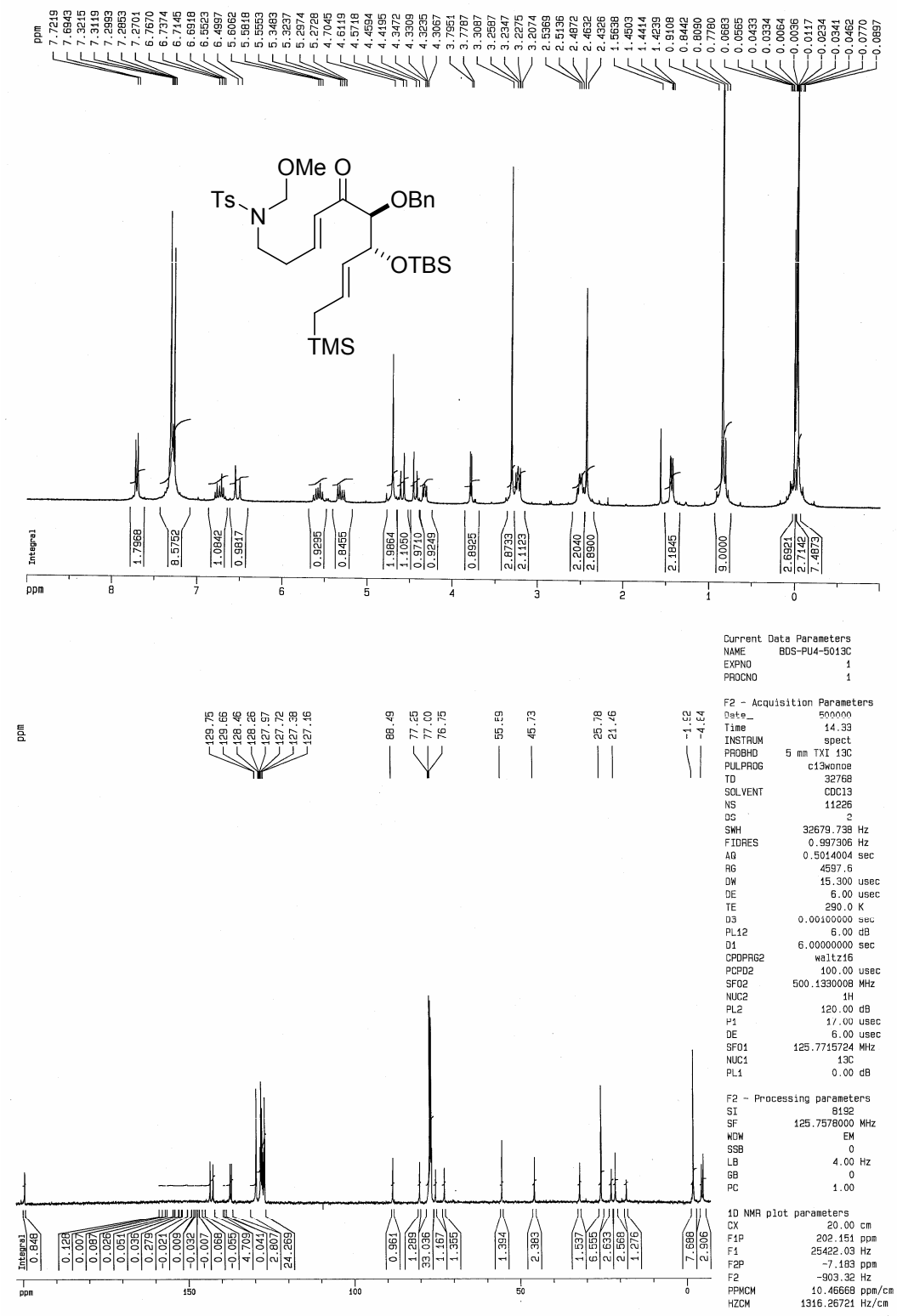
A.76 COMPOUND 121



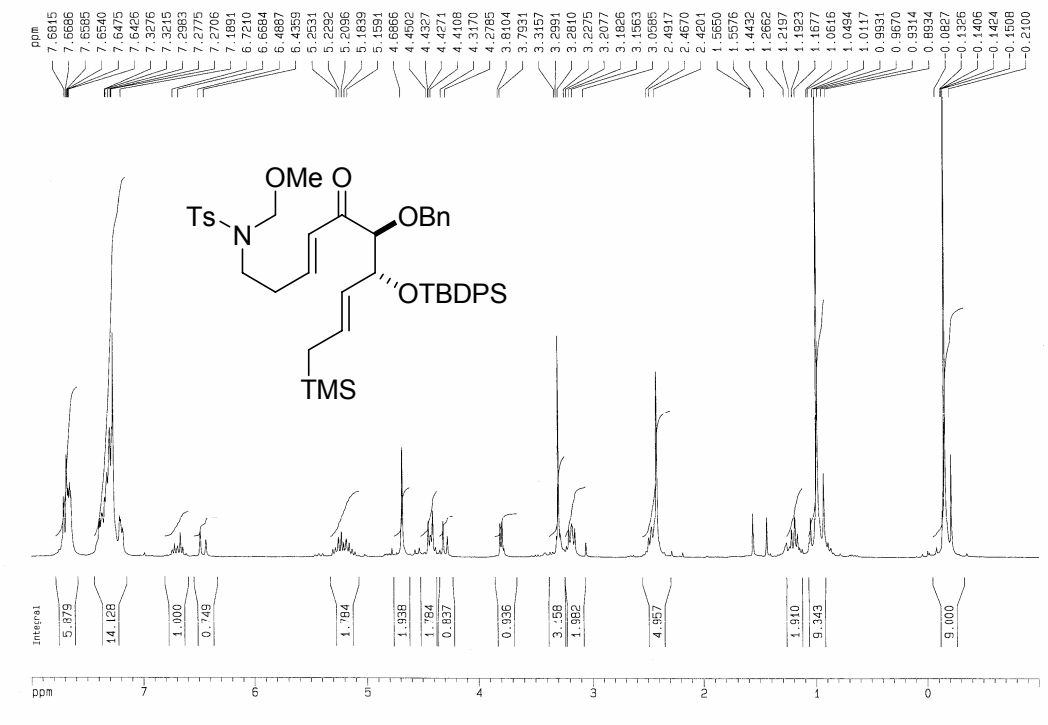
A.77 COMPOUND 122

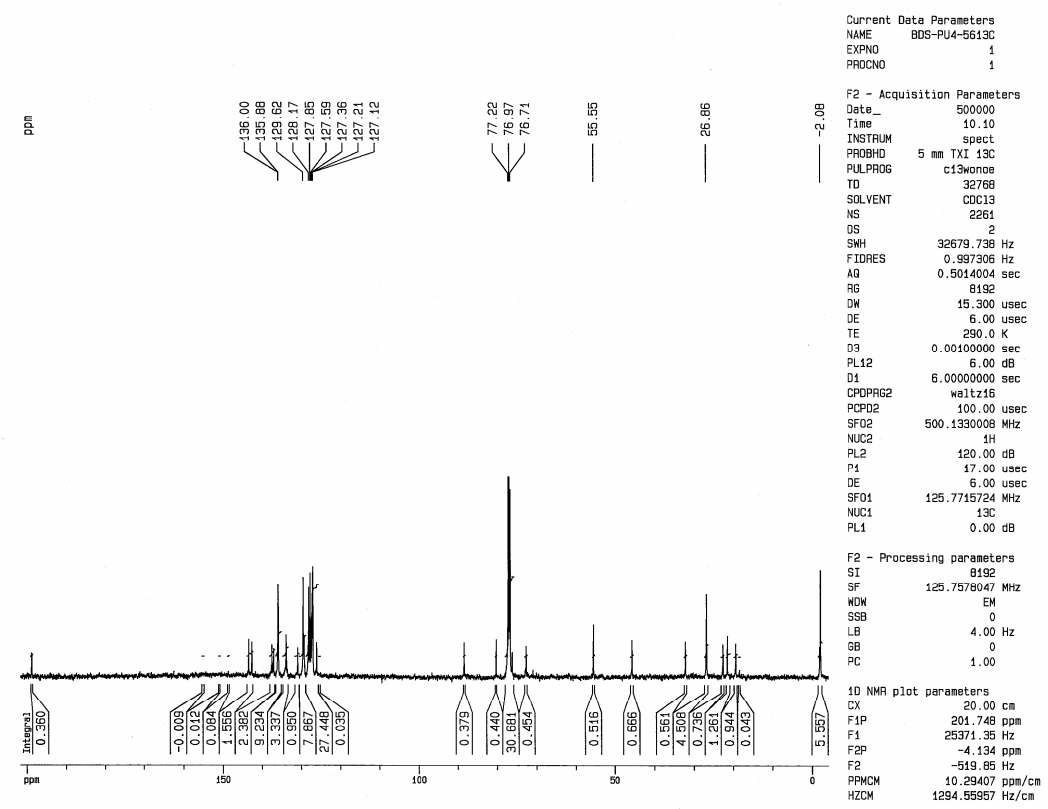


A.78 COMPOUND 123

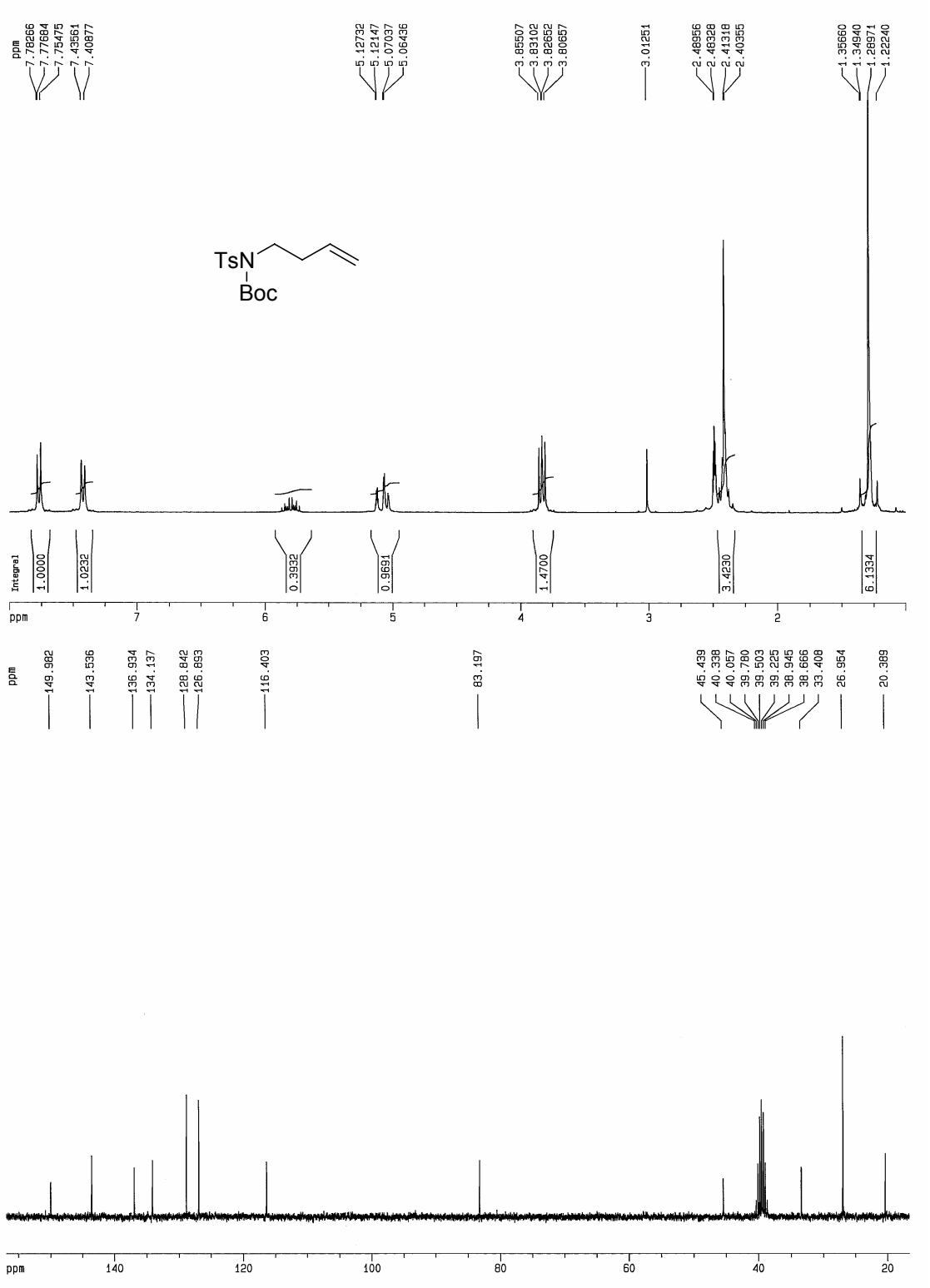


A.79 COMPOUND 124

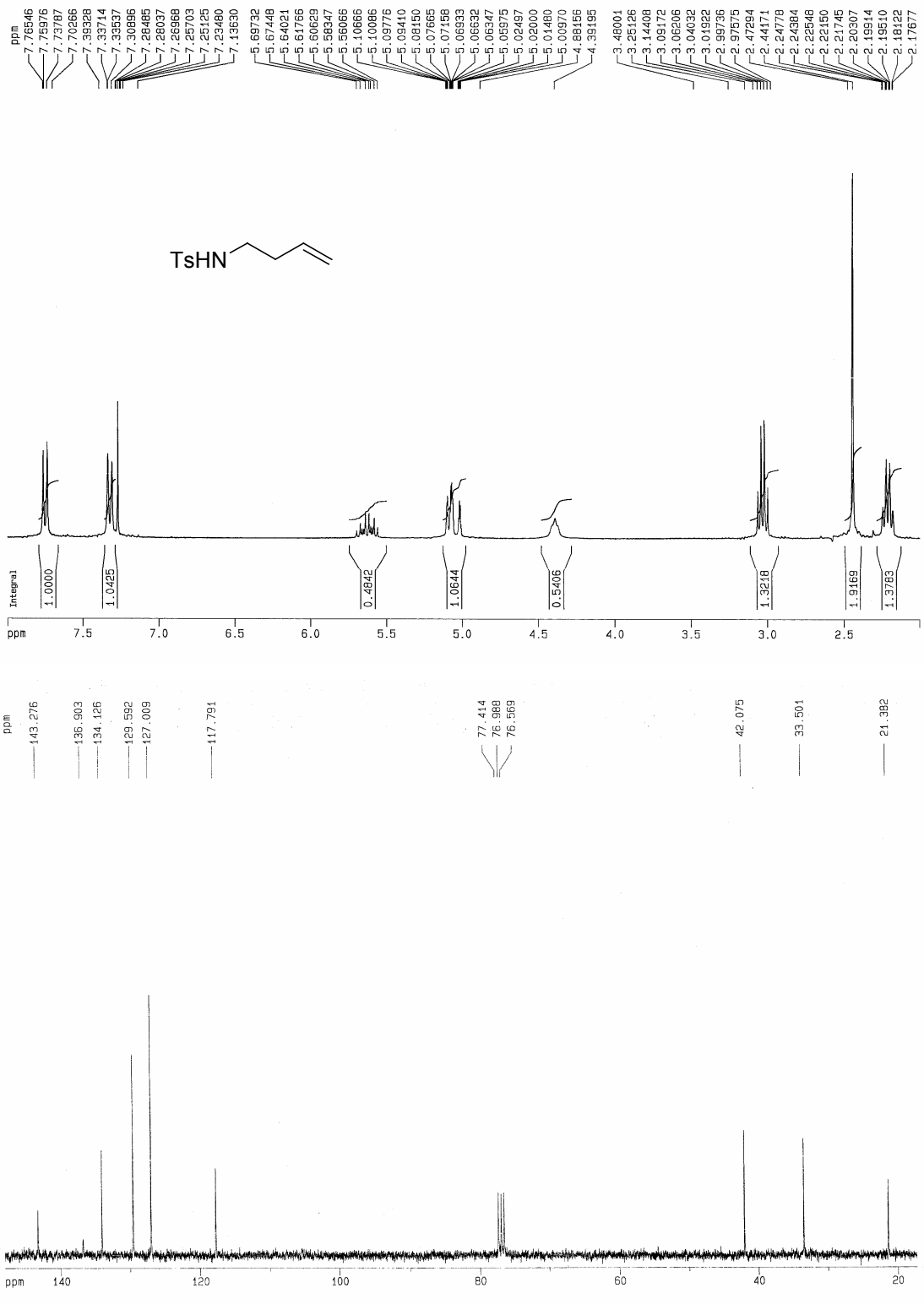




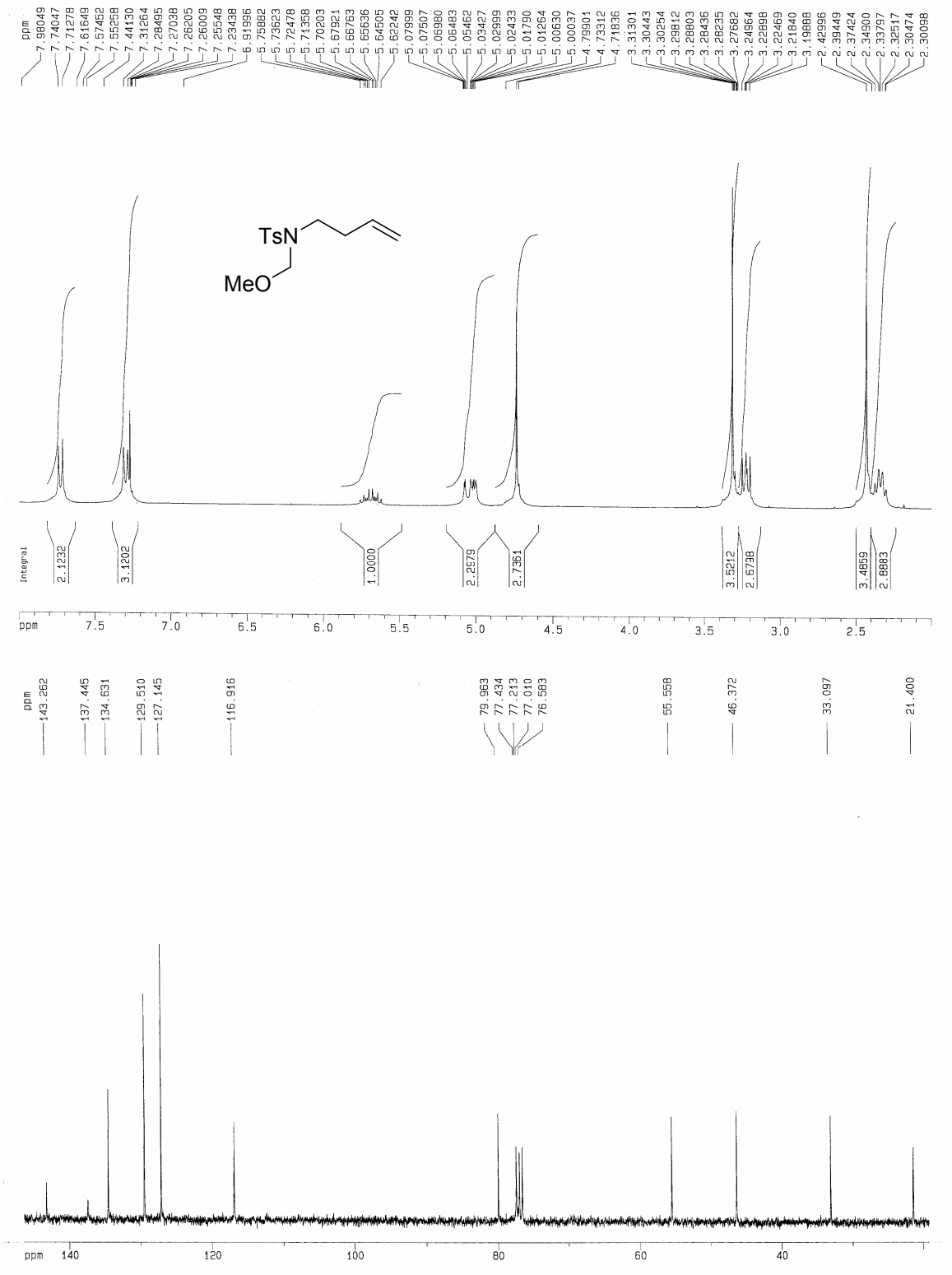
A.80 COMPOUND 126



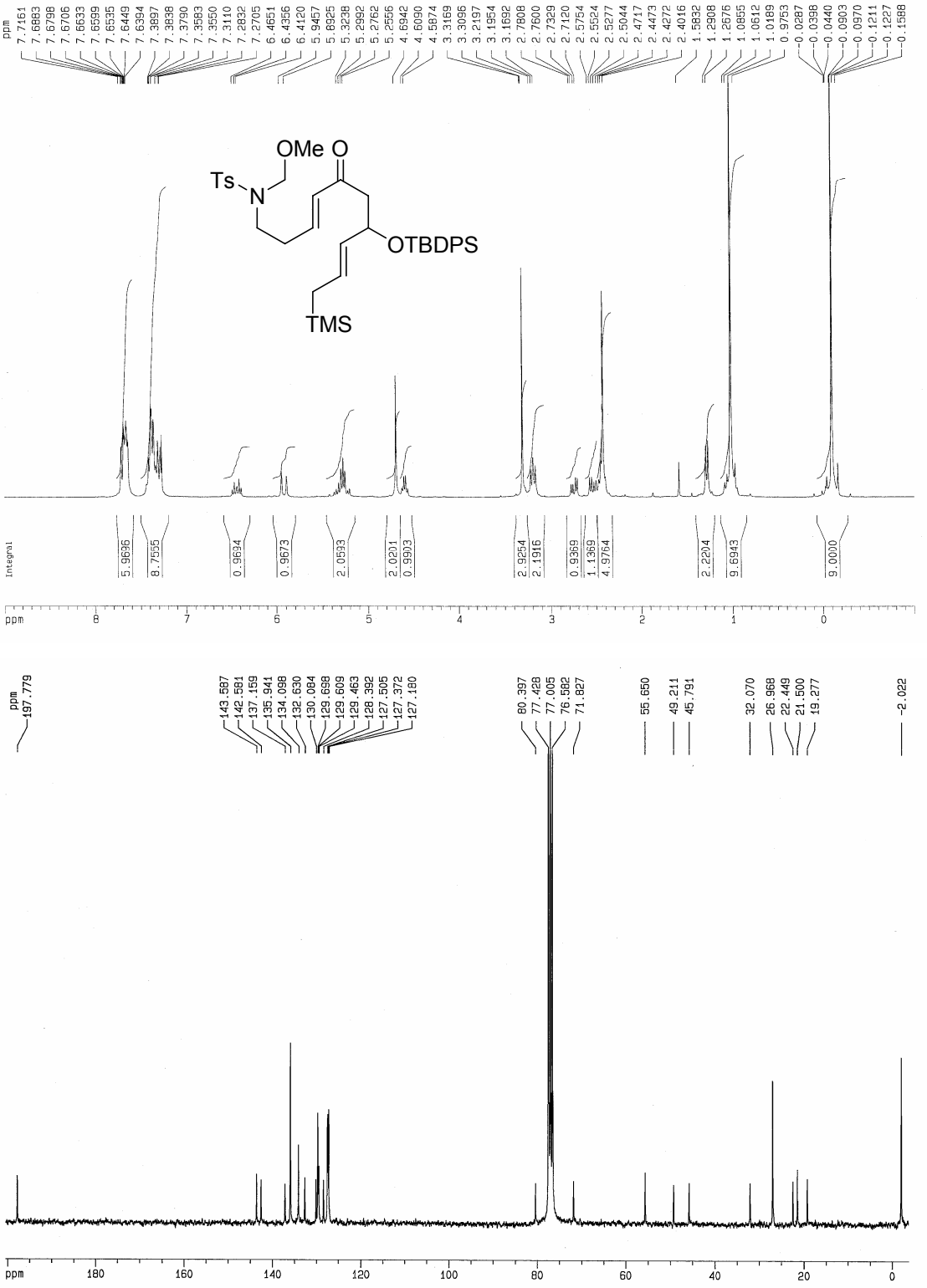
A.81 COMPOUND 127



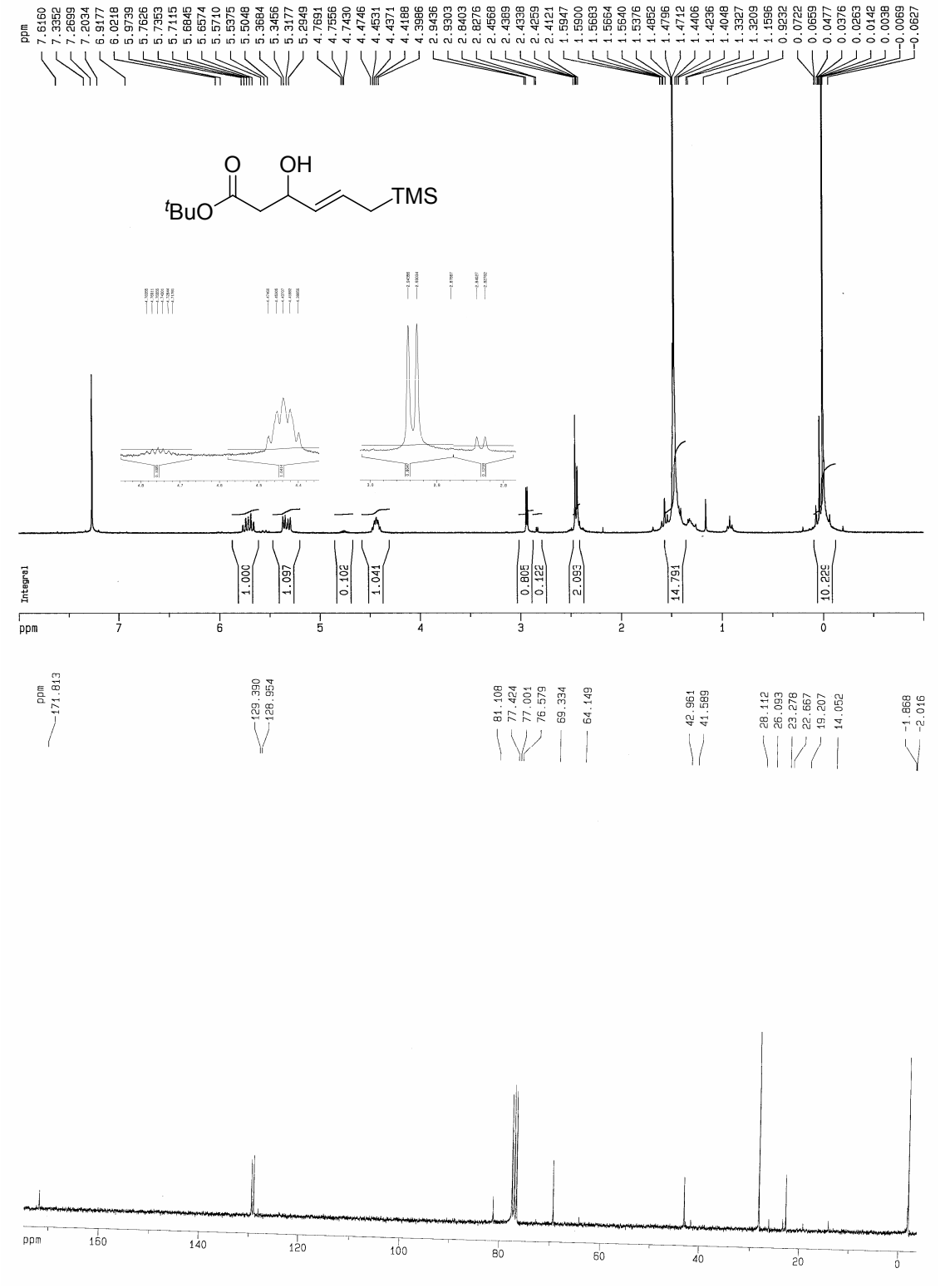
A.82 COMPOUND 128



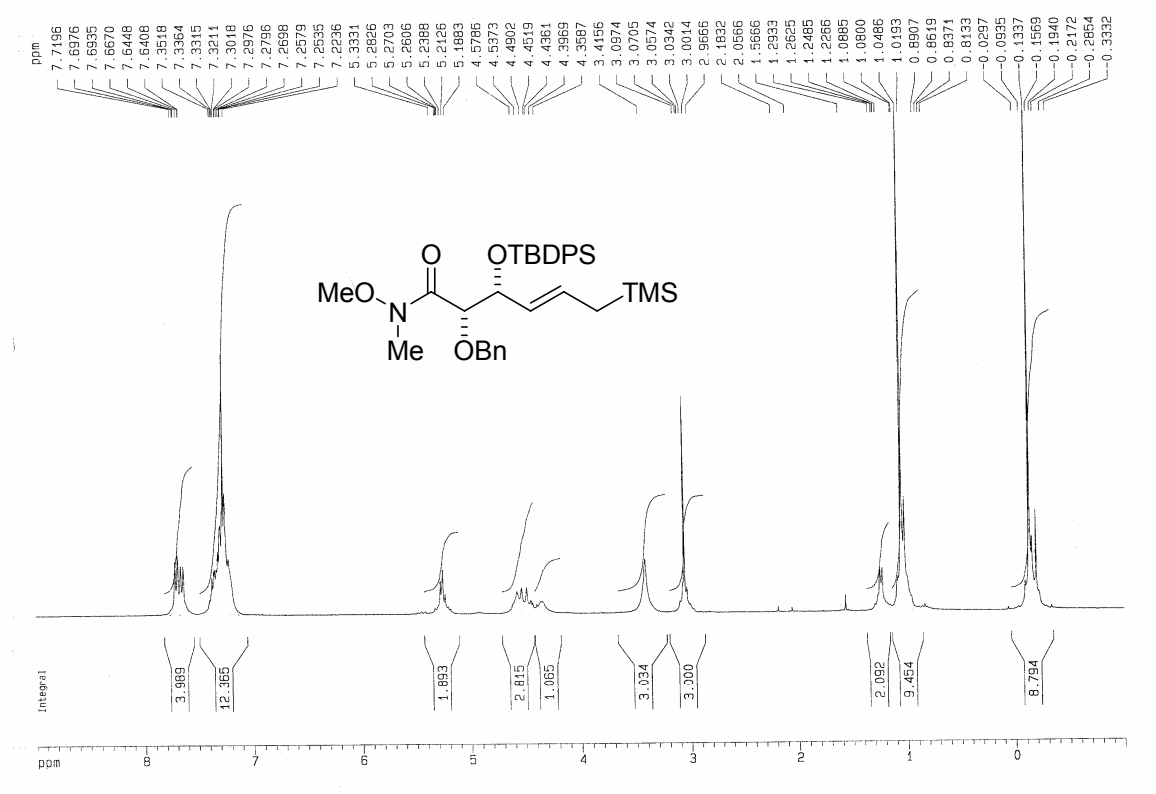
A.83 COMPOUND 132

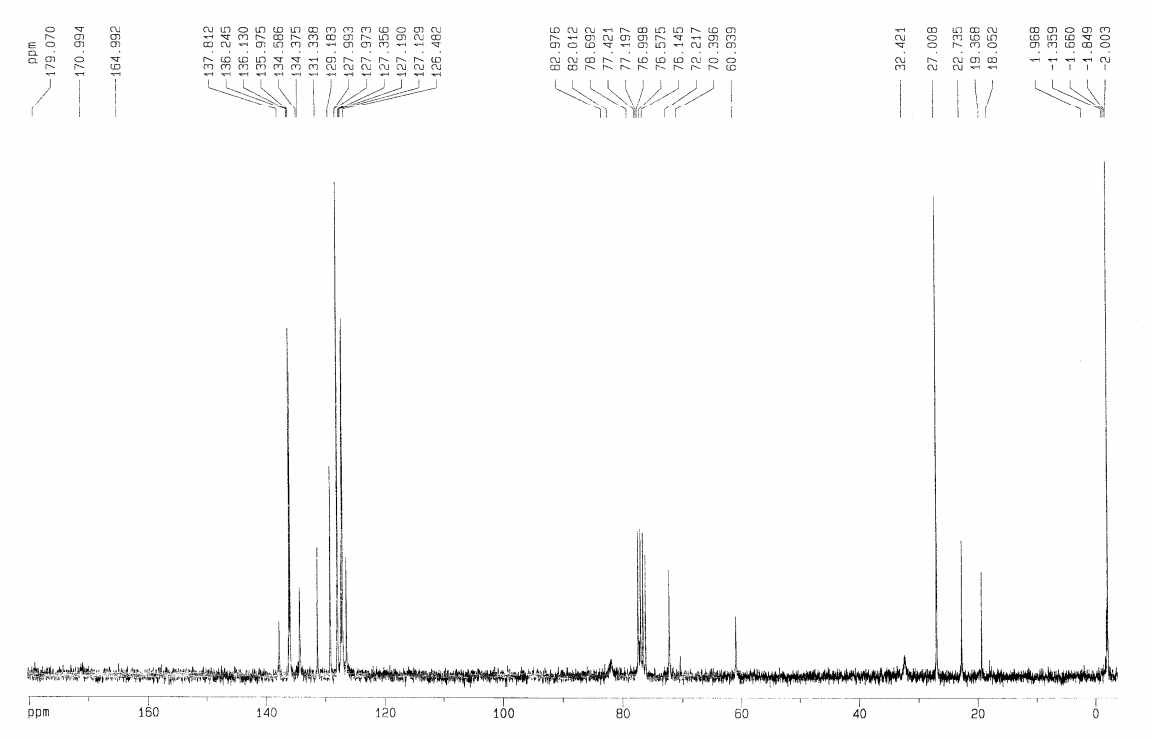


A.84 COMPOUND 135

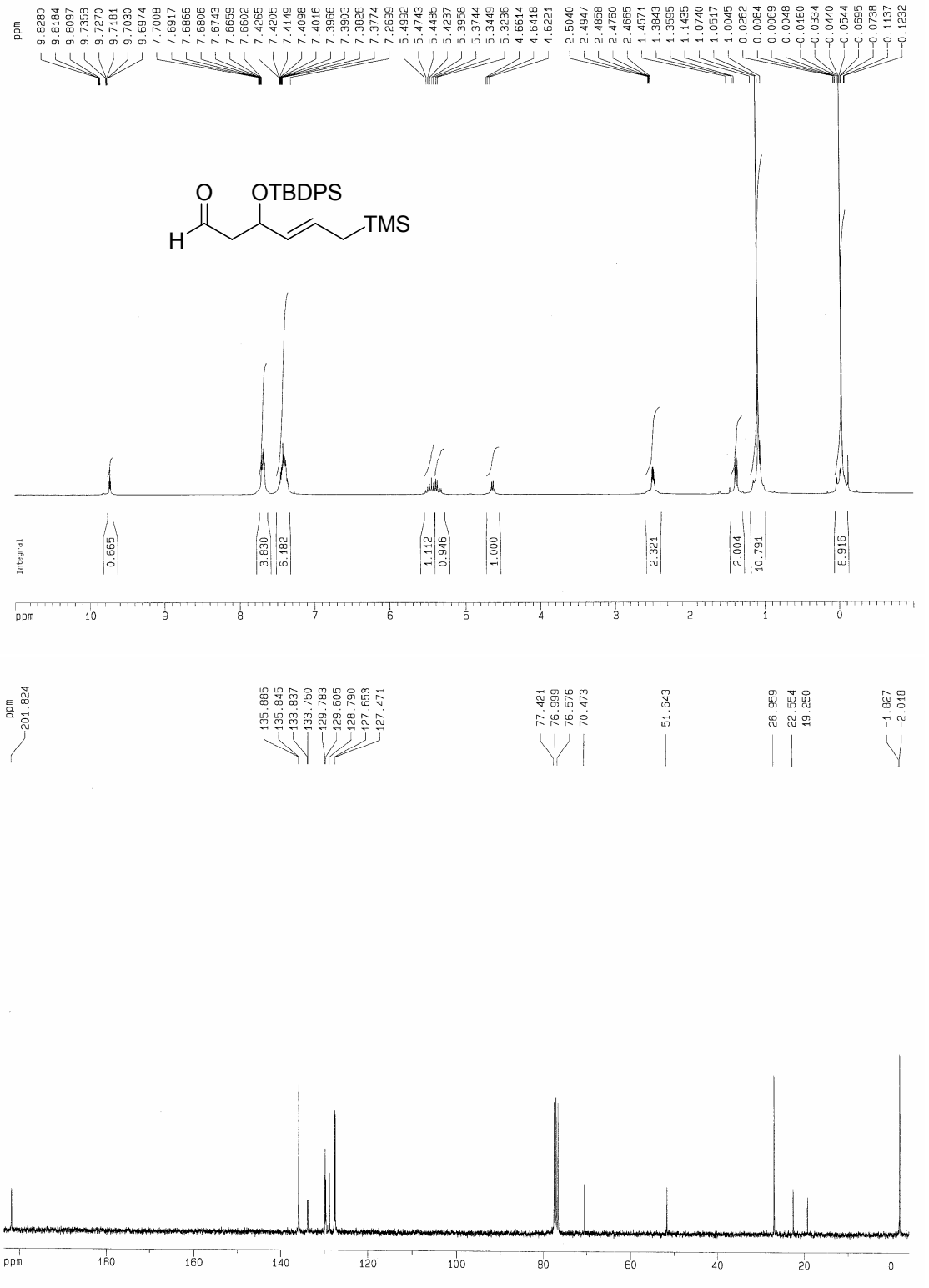


A.85 COMPOUND 136

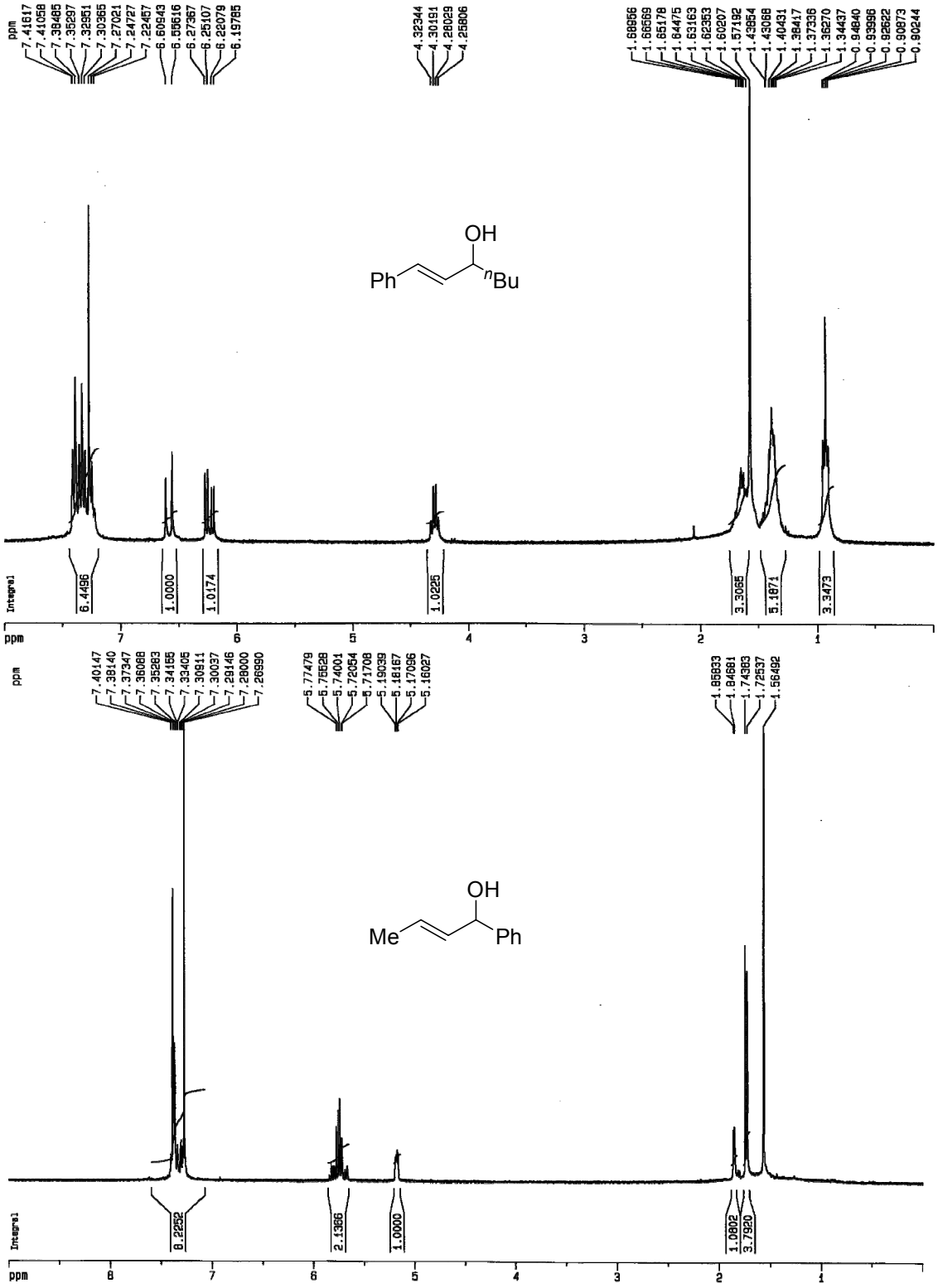




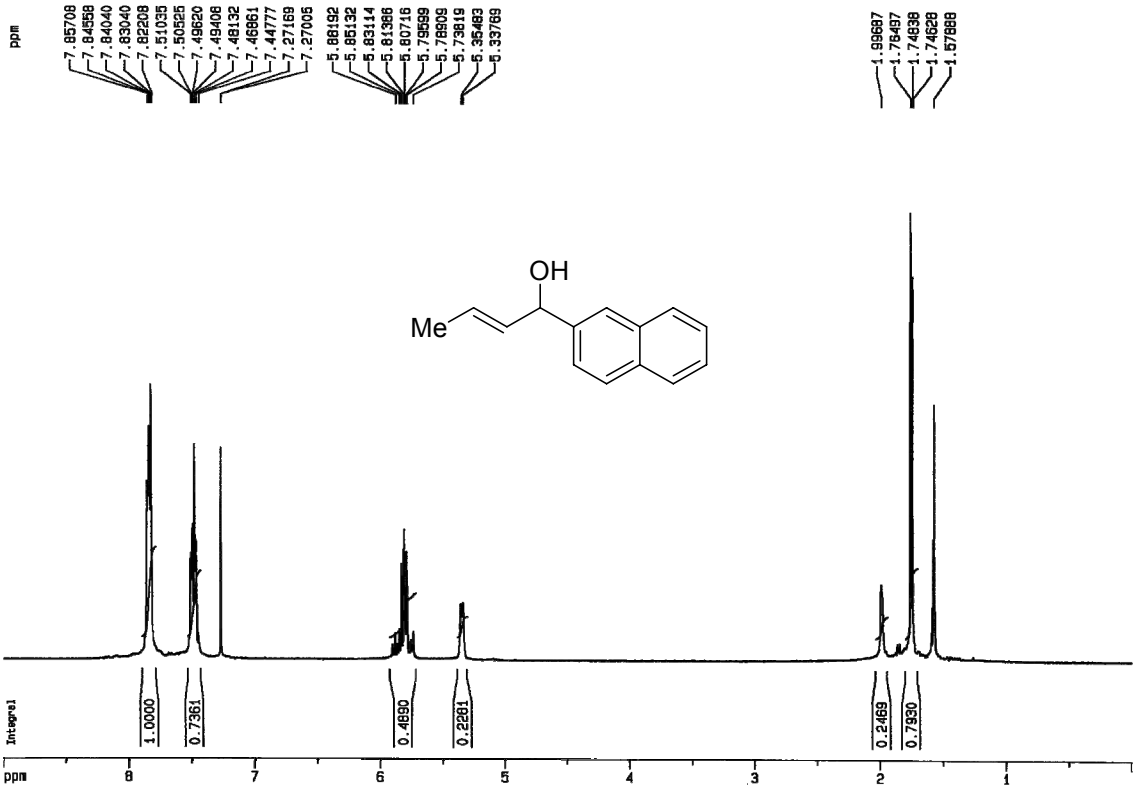
A.86 COMPOUND 137



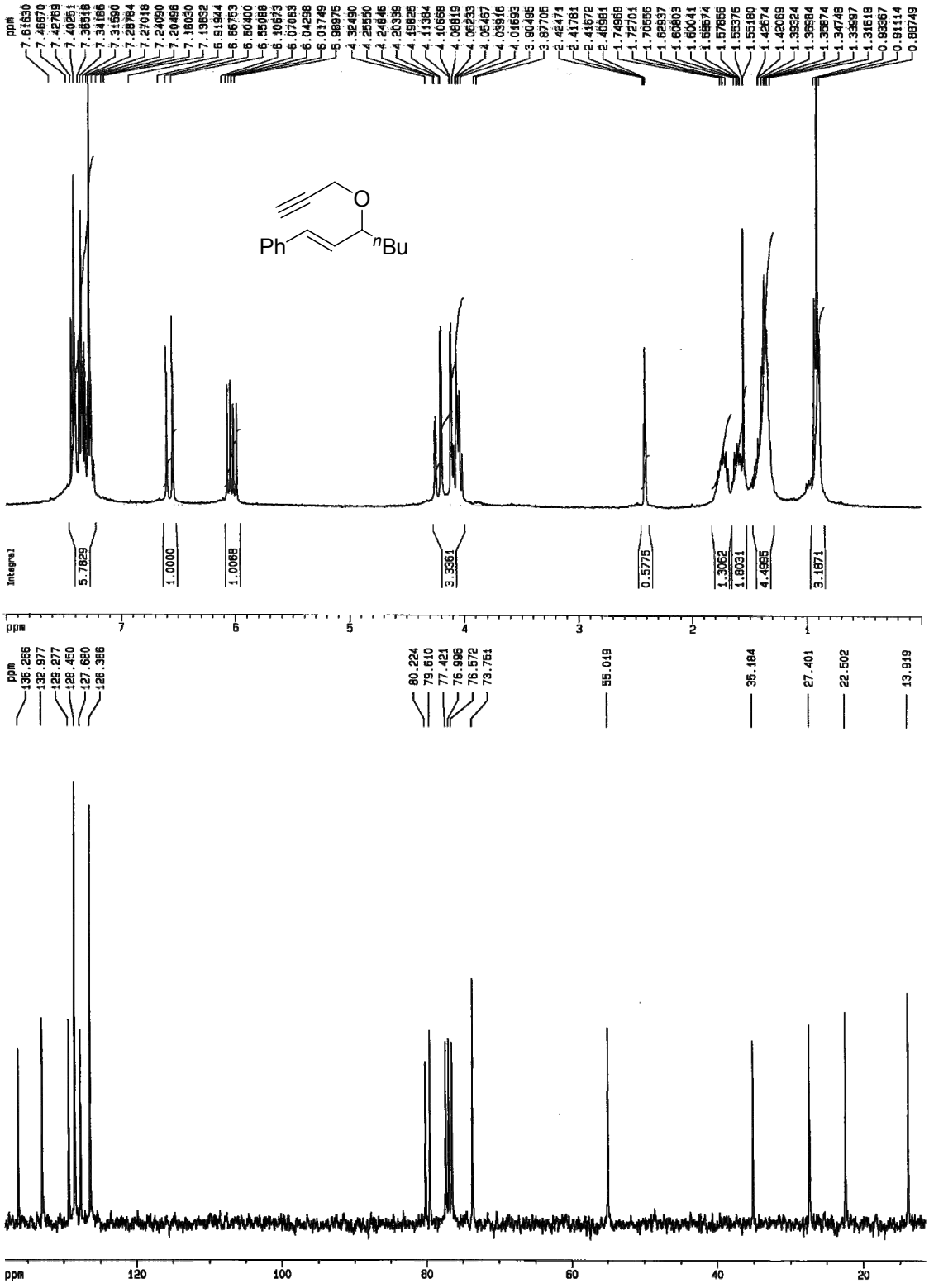
A.87 COMPOUND 159 & 160



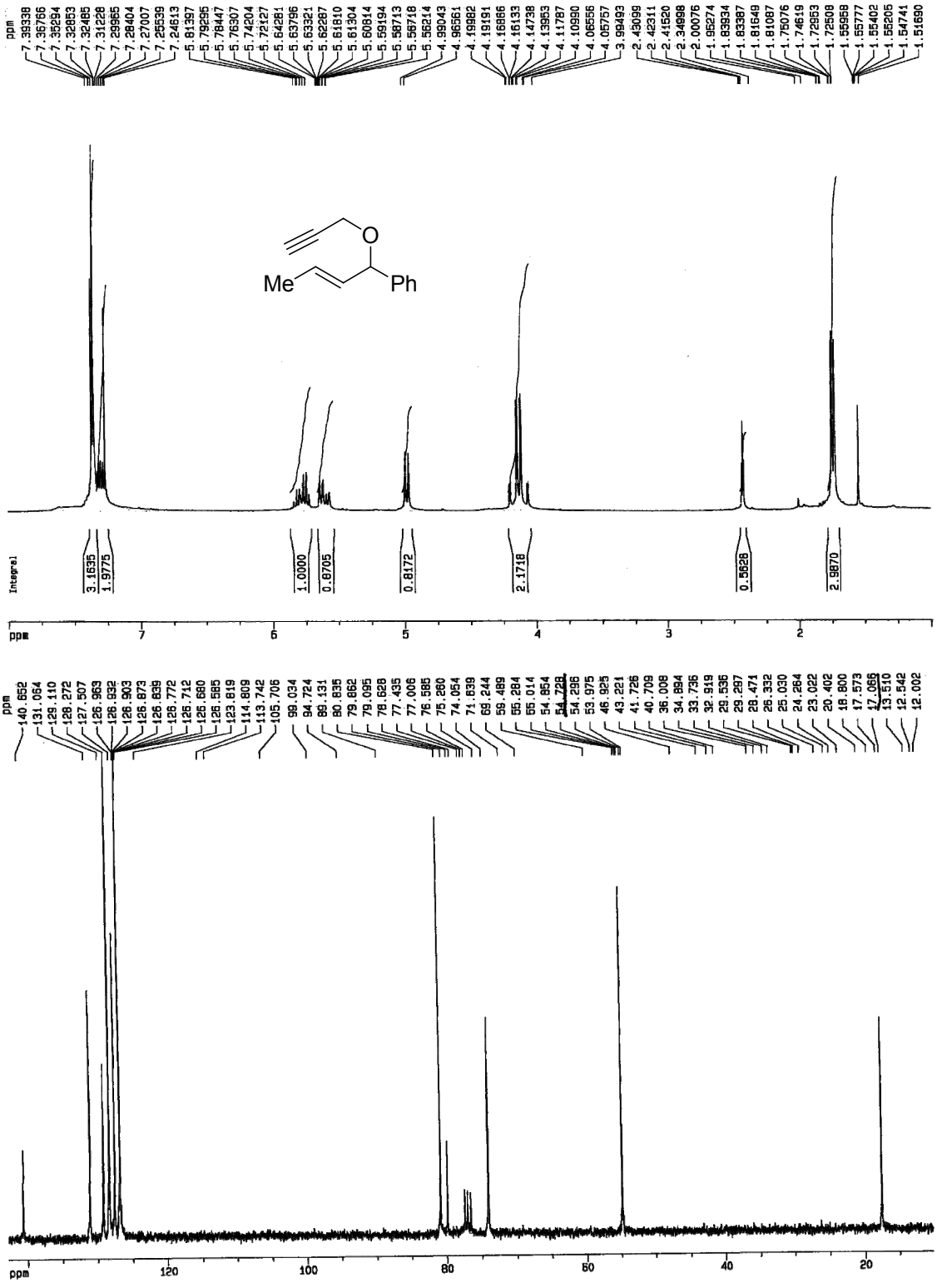
A.88 COMPOUND 161



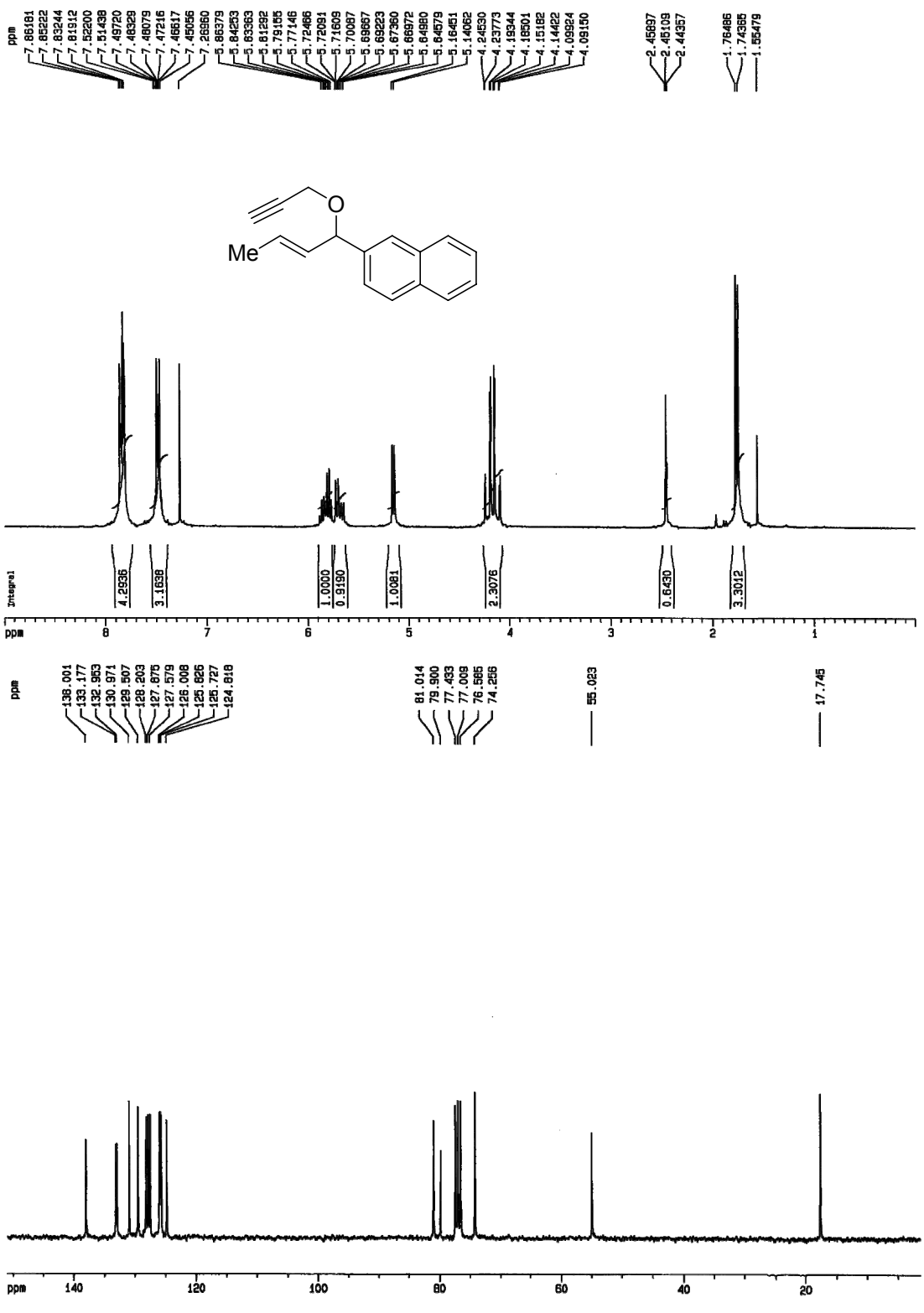
A.89 COMPOUND 162



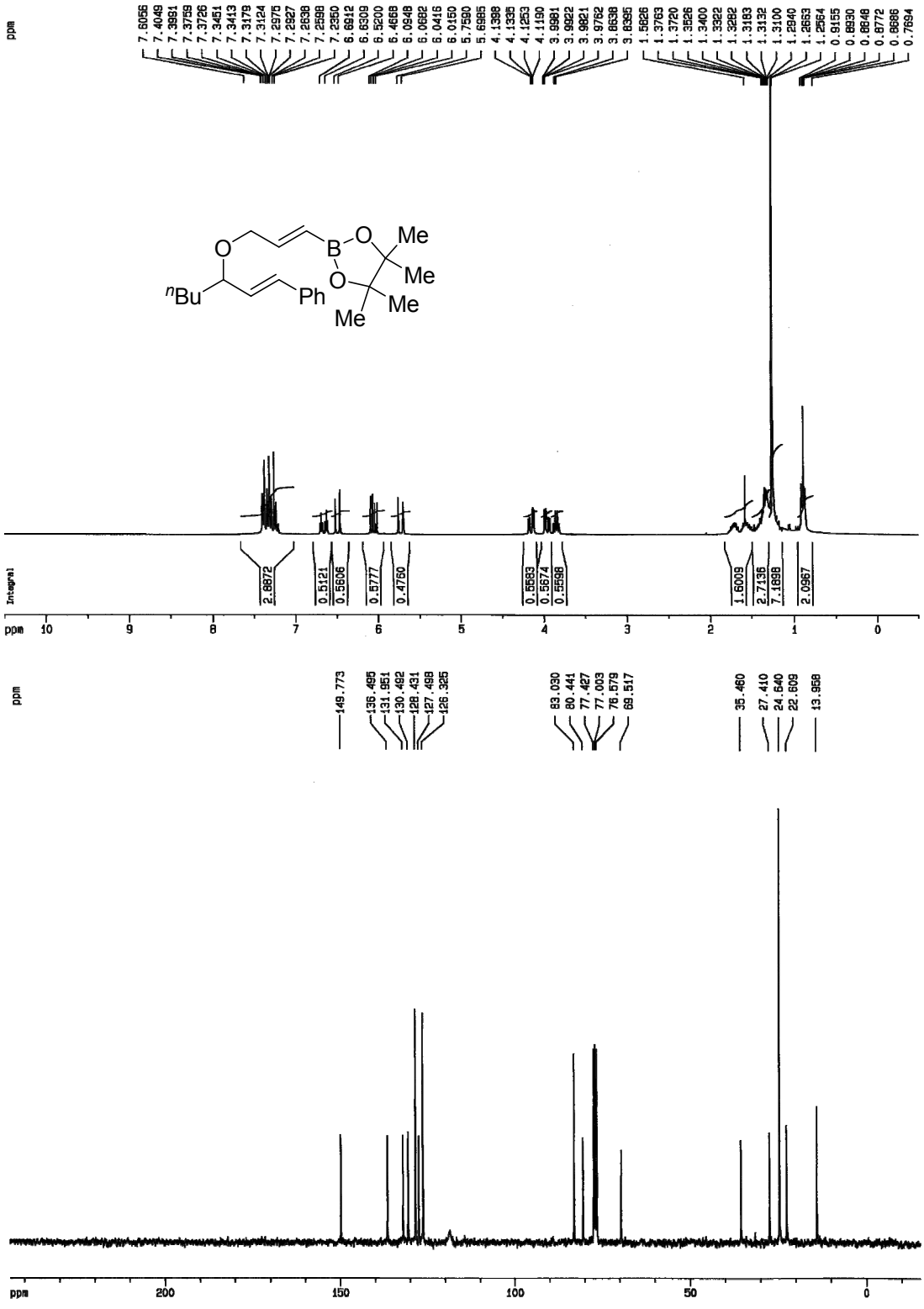
A.90 COMPOUND 163



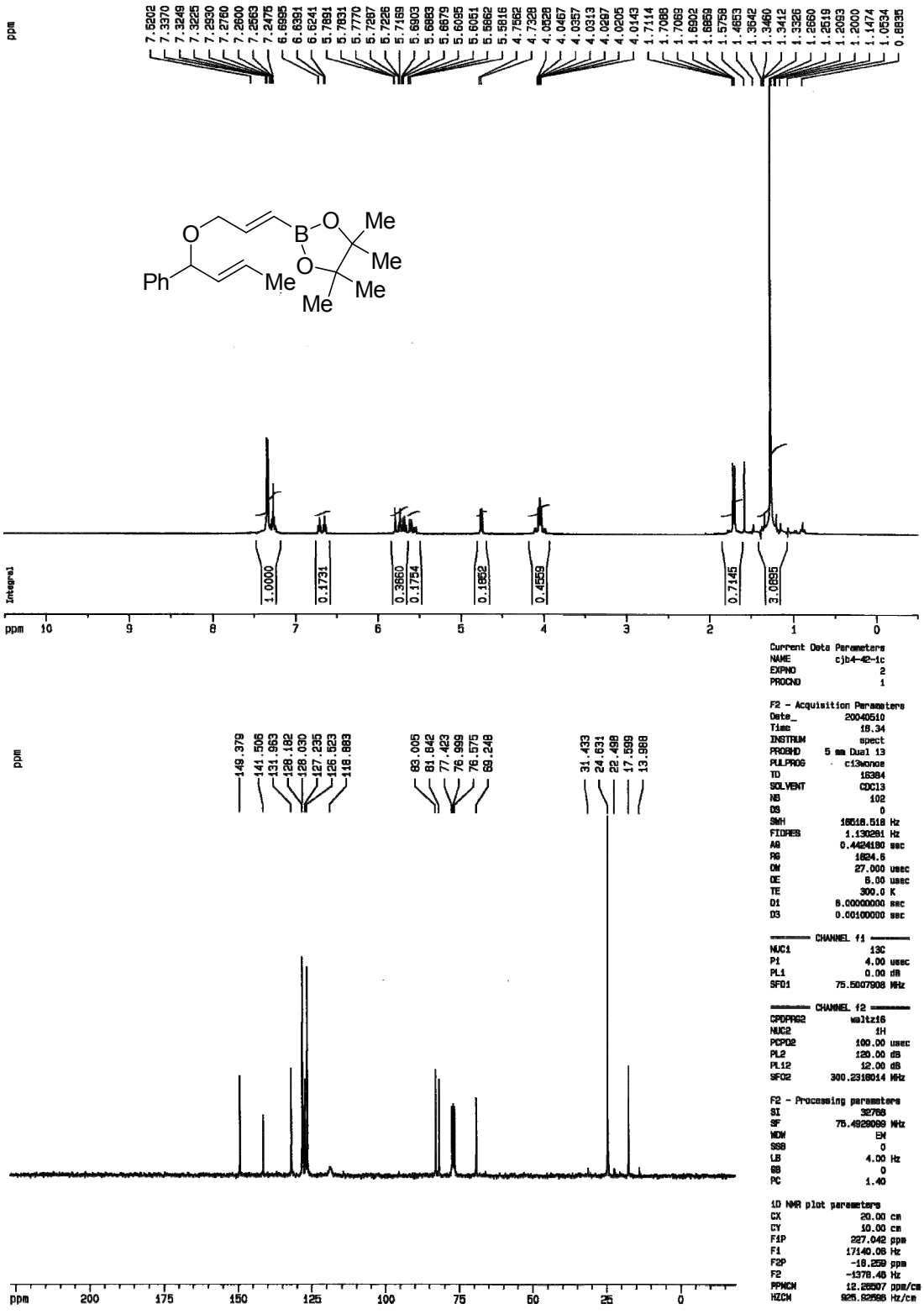
A.91 COMPOUND 164



A.92 COMPOUND 165



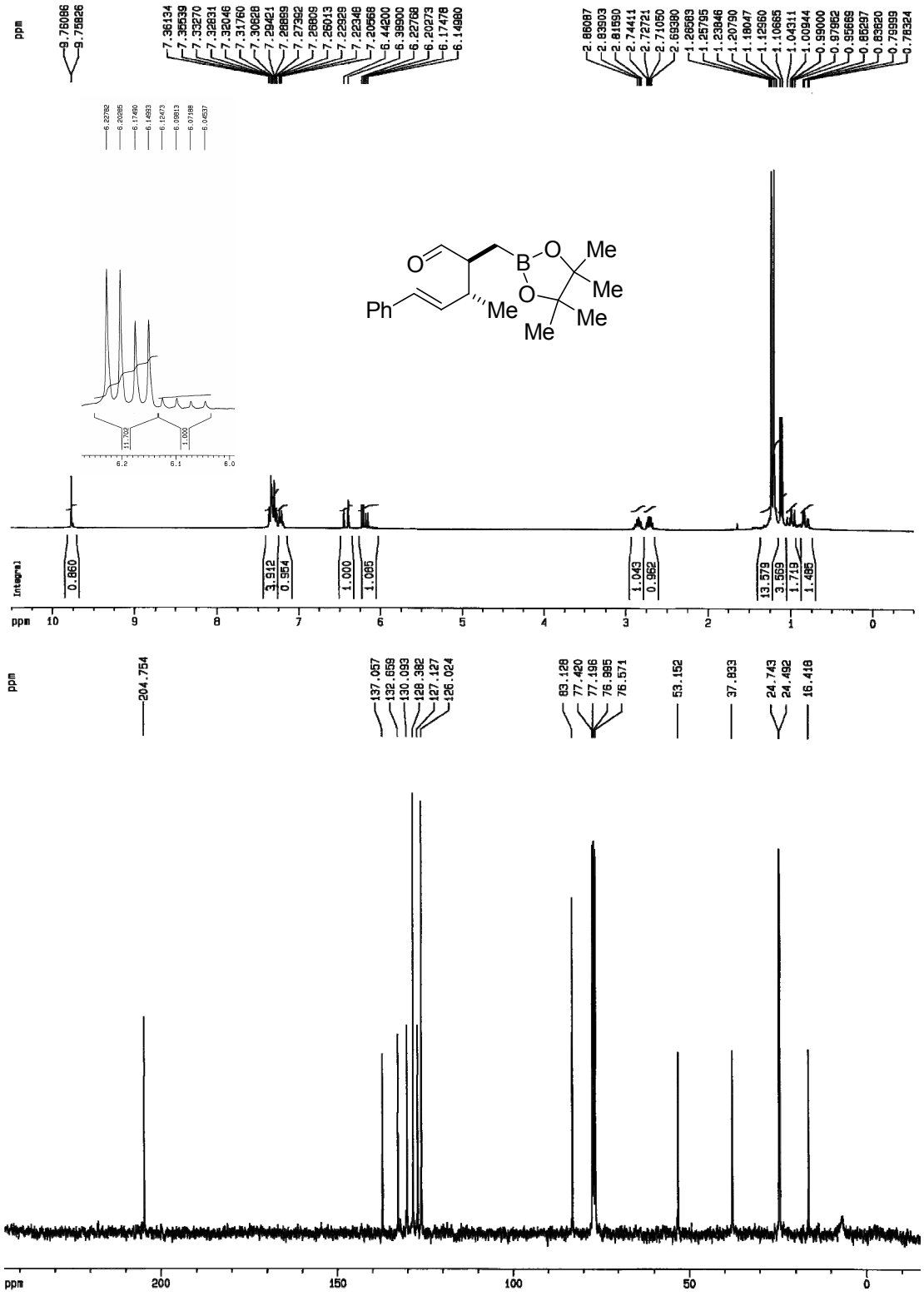
A.93 COMPOUND 166



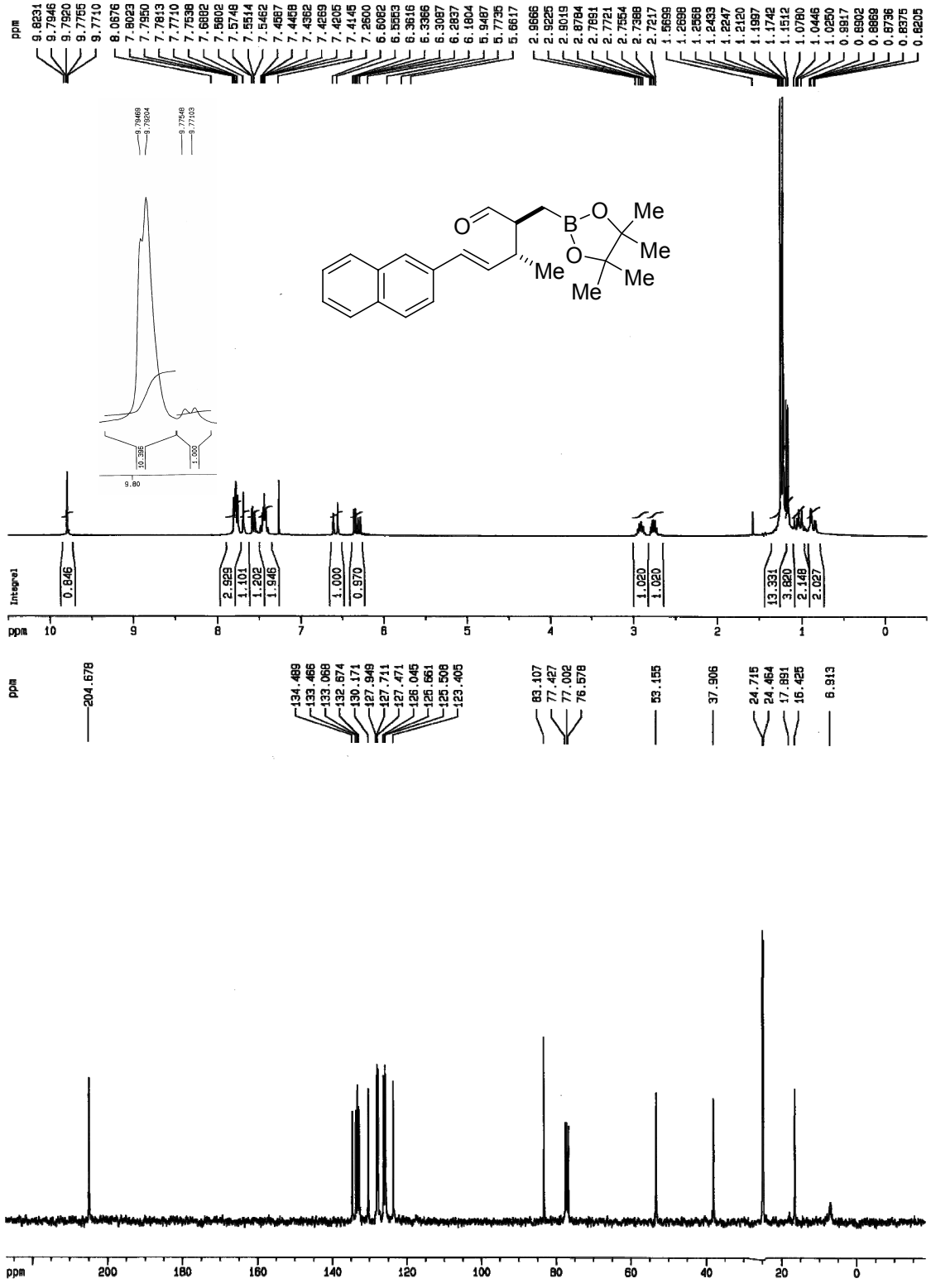
A.94 COMPOUND 167

A.95 COMPOUND 168

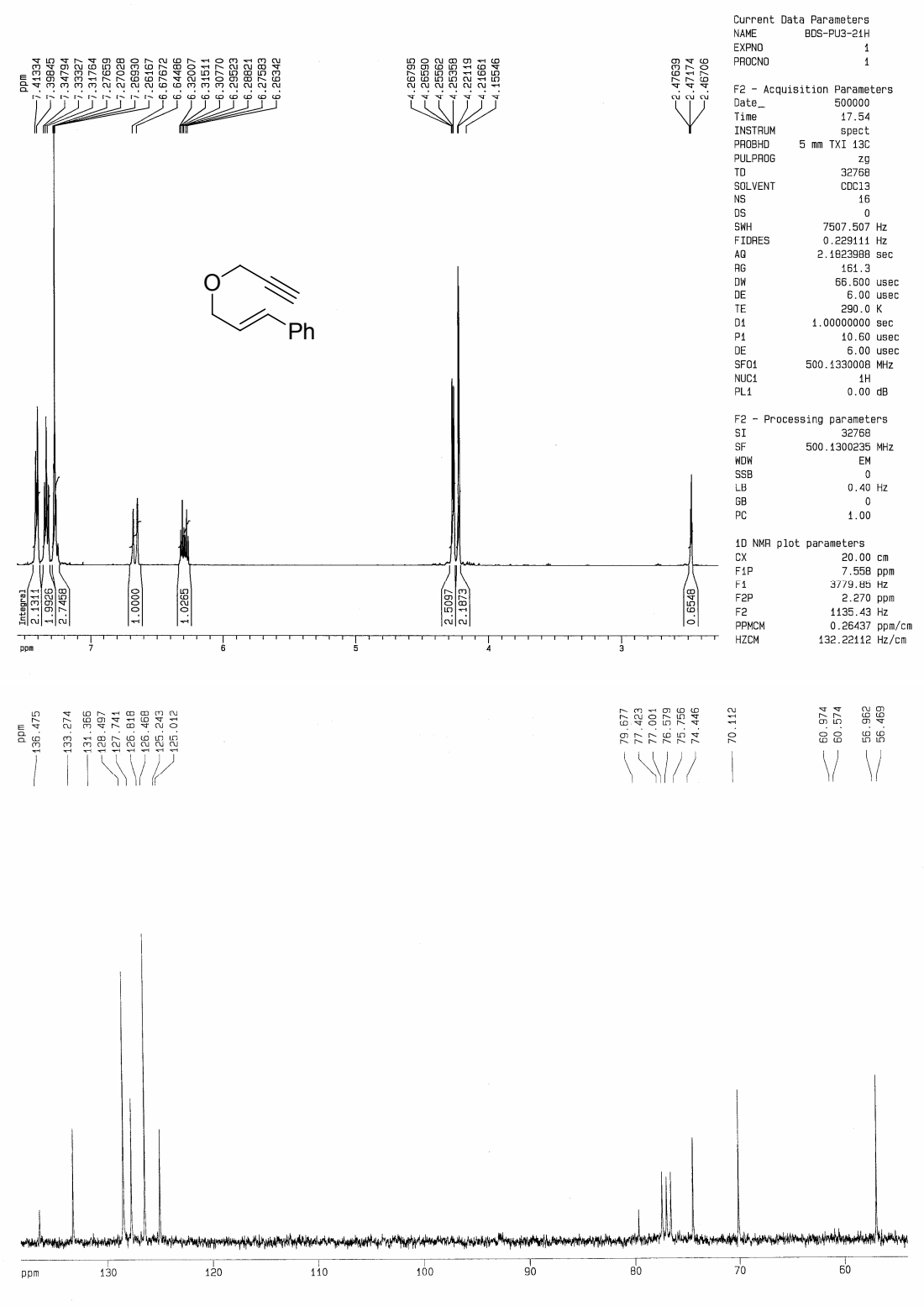
A.96 COMPOUND 169



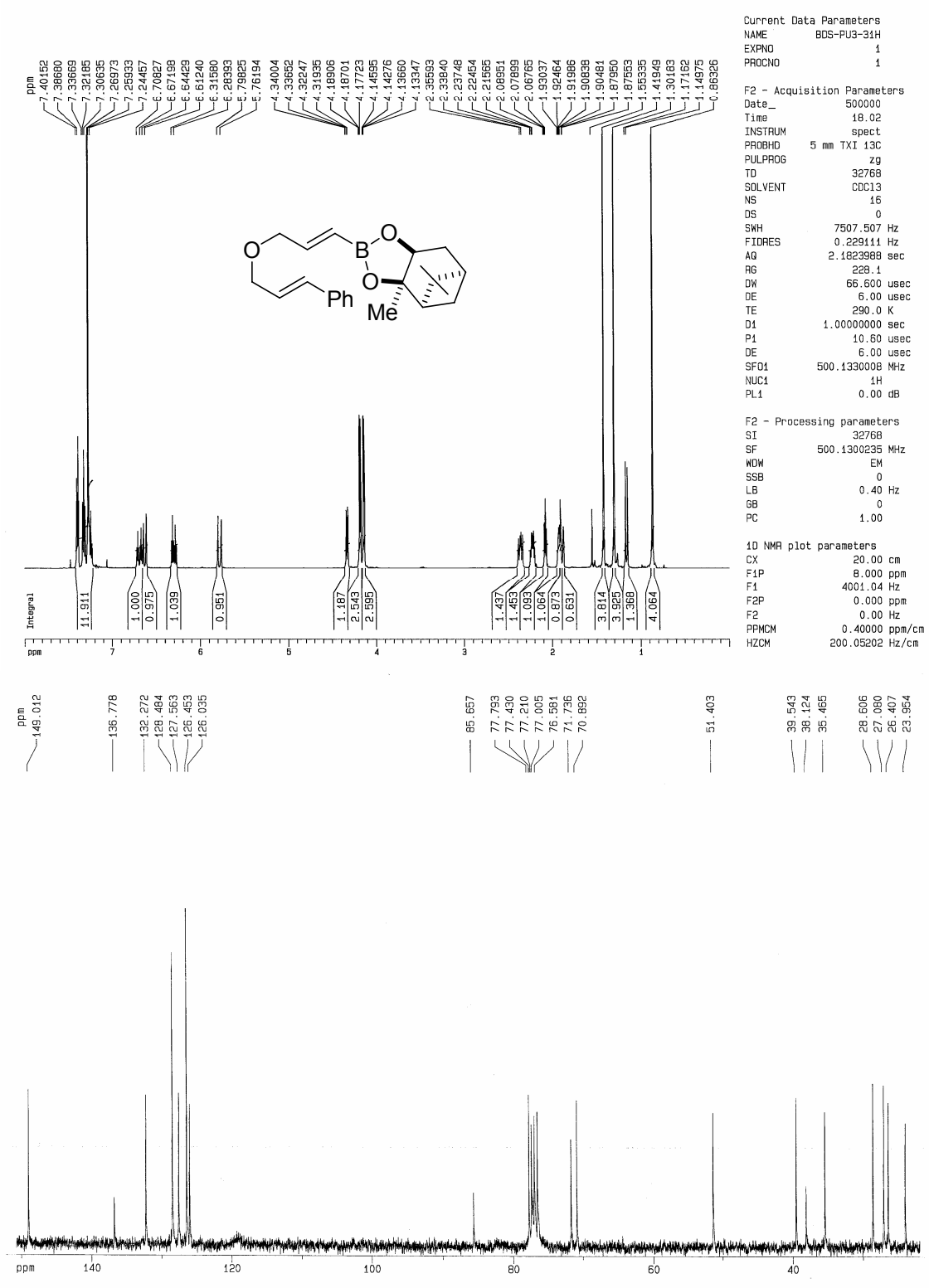
A.97 COMPOUND 170



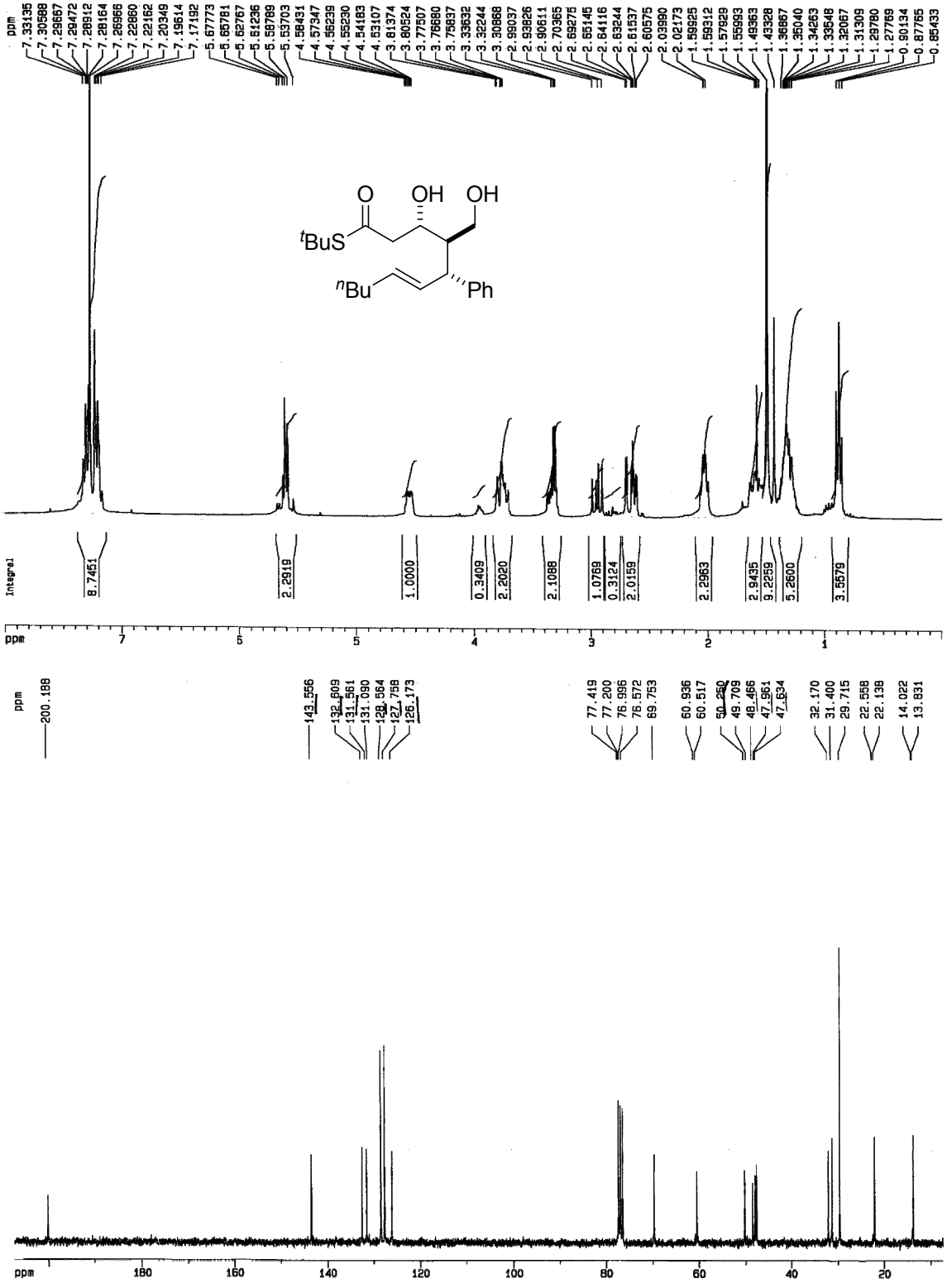
A.98 COMPOUND 171



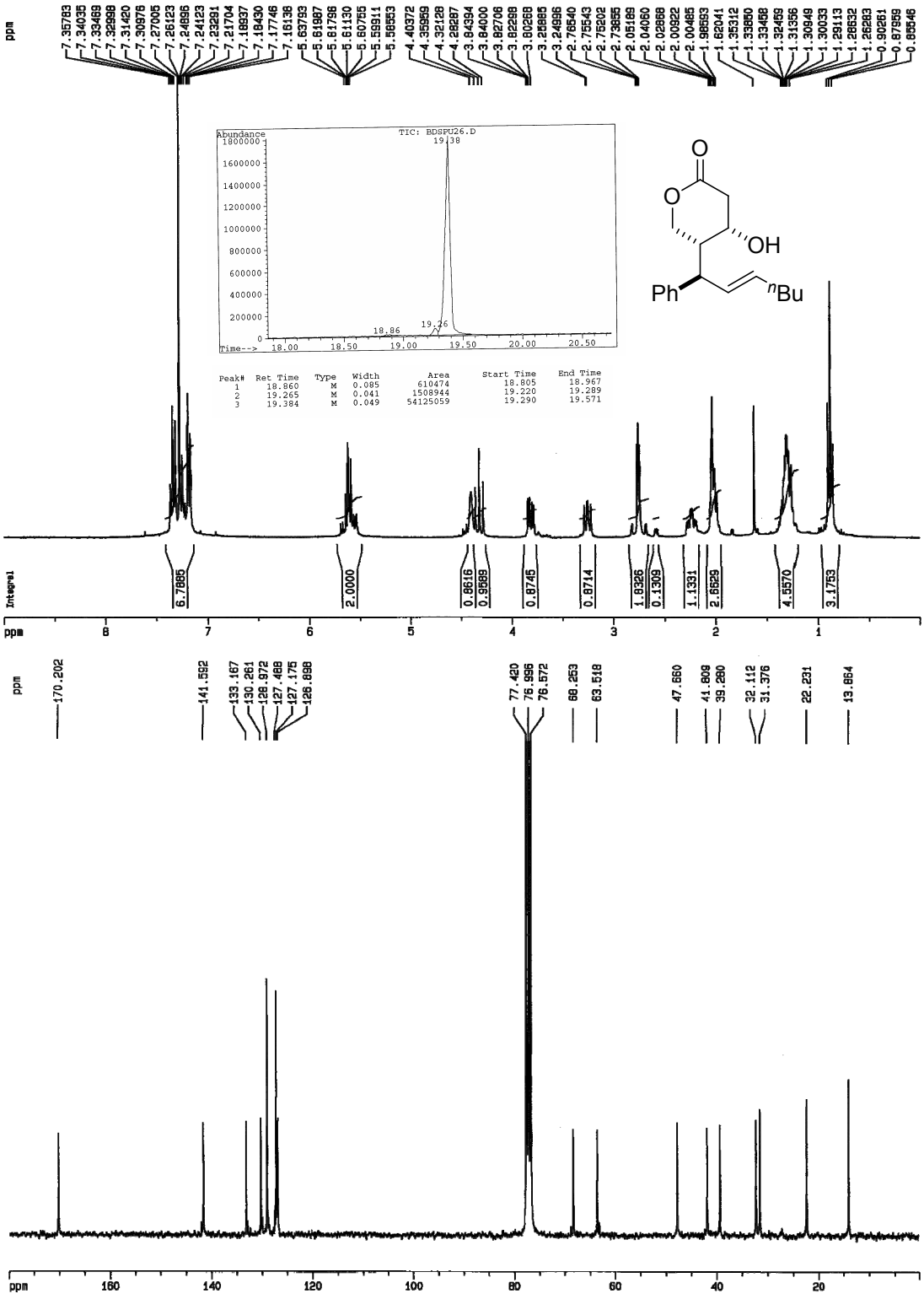
A.99 COMPOUND 172



A.100 COMPOUND 175

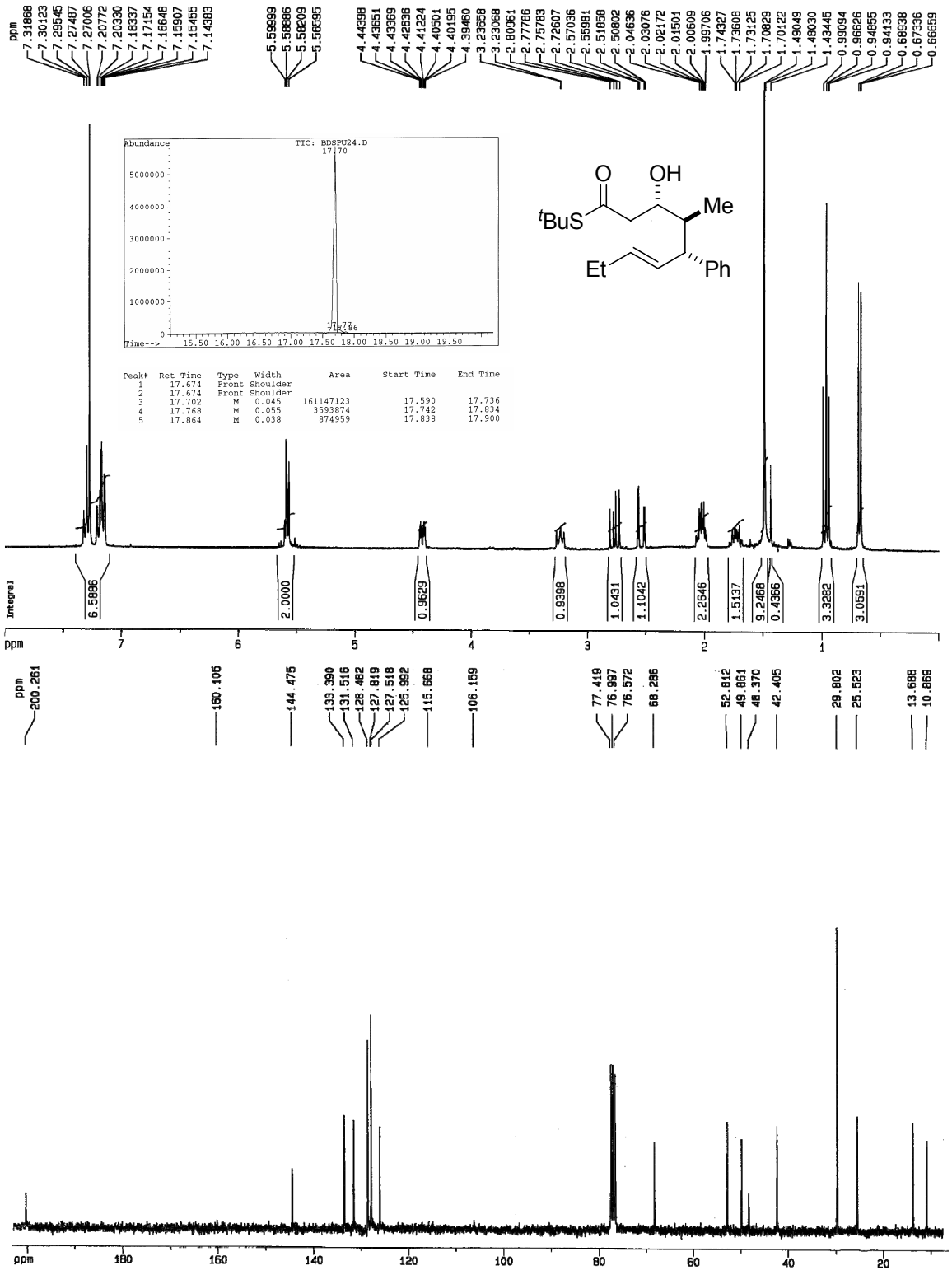


A.101 COMPOUND 176

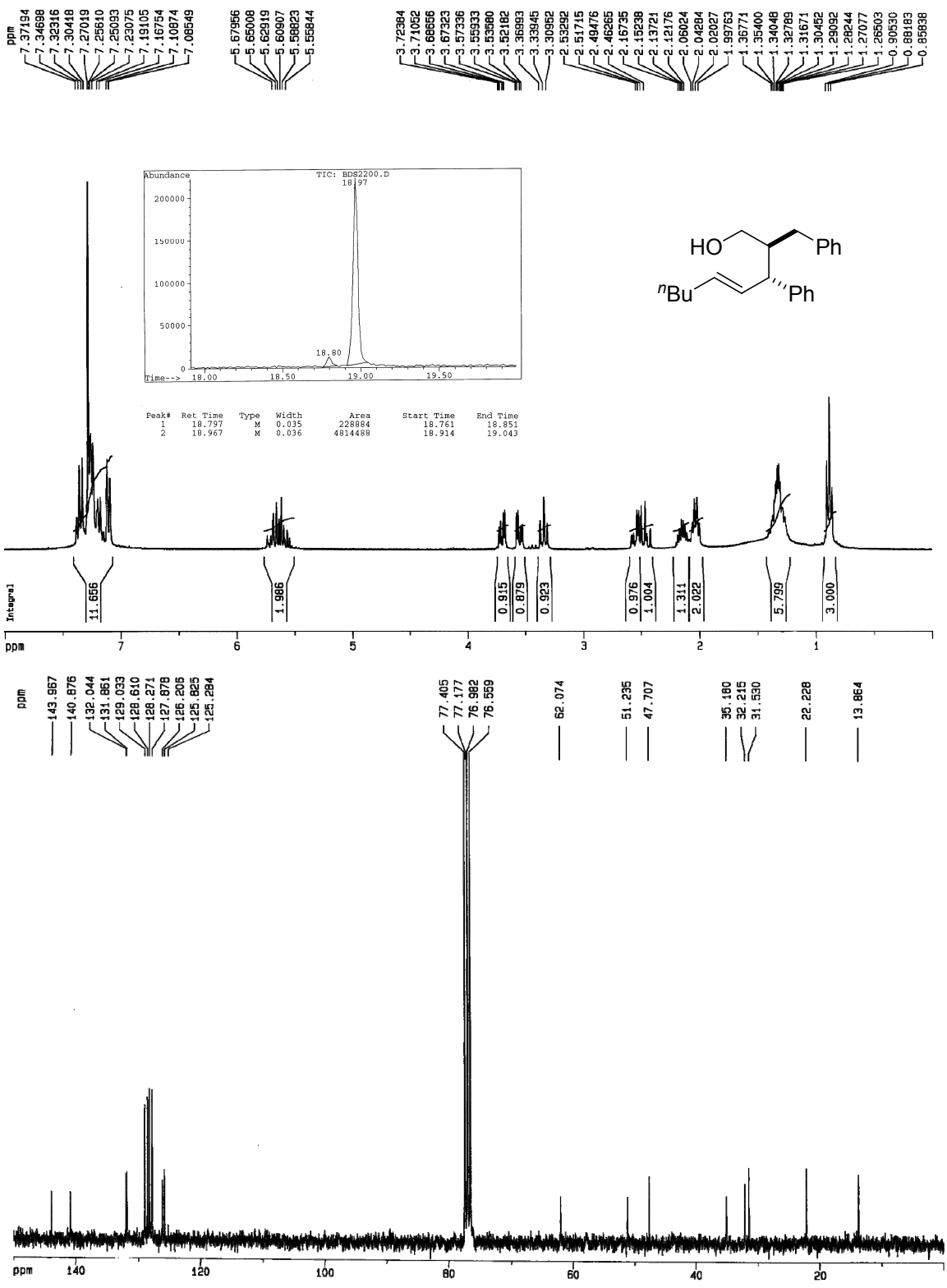


A.102 COMPOUND 177

A.103 COMPOUND 179



A.104 COMPOUND 181



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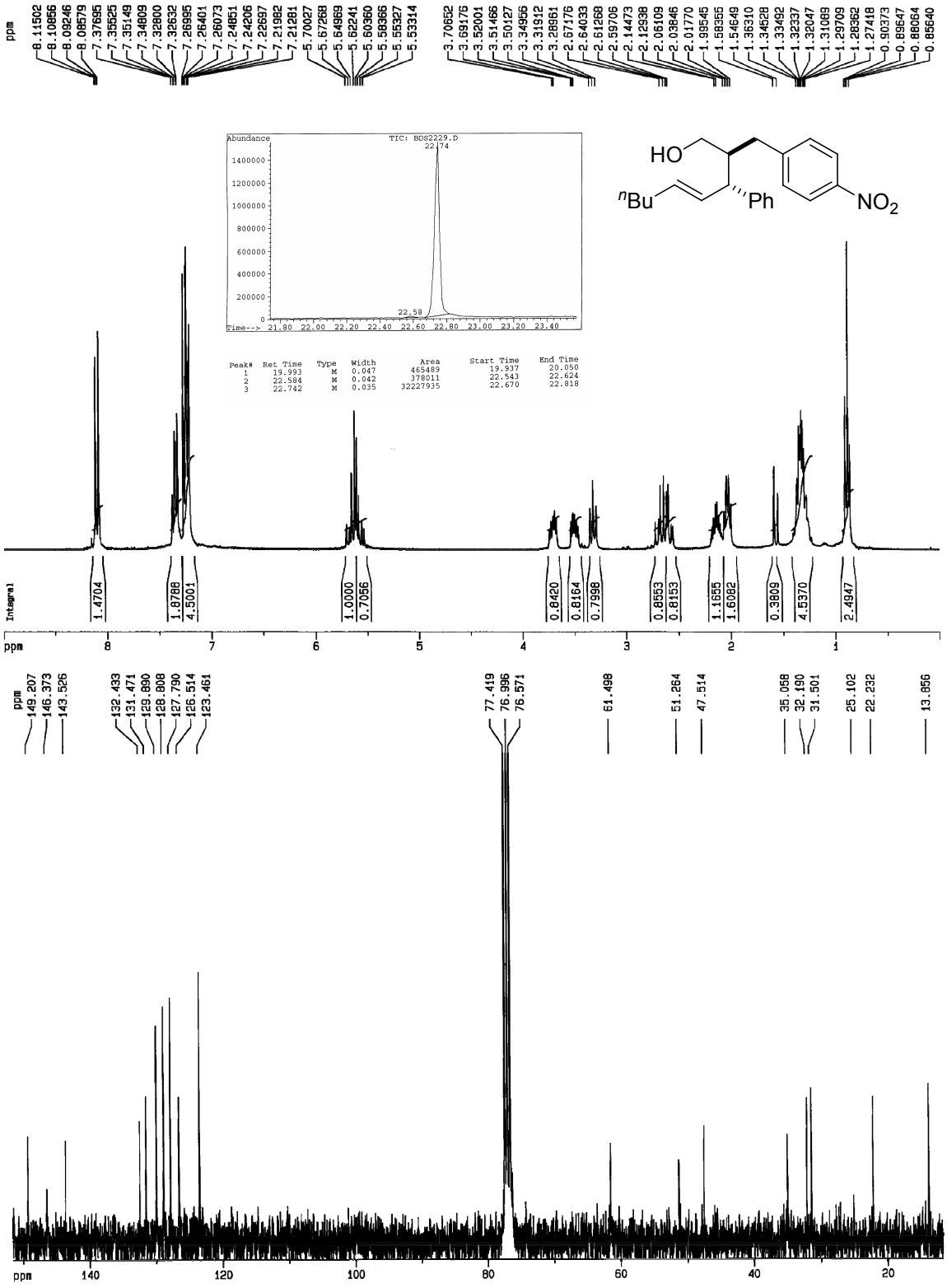
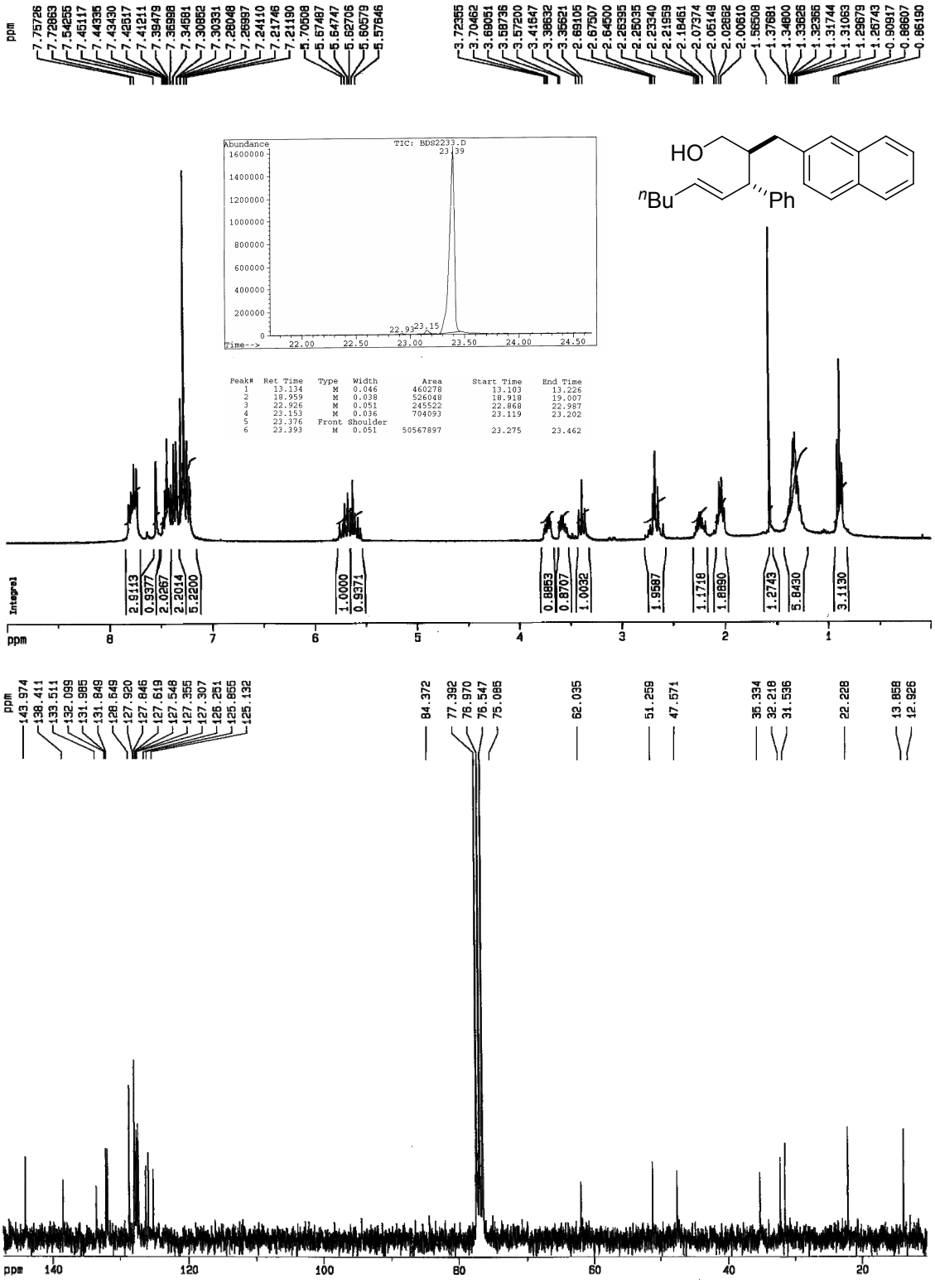
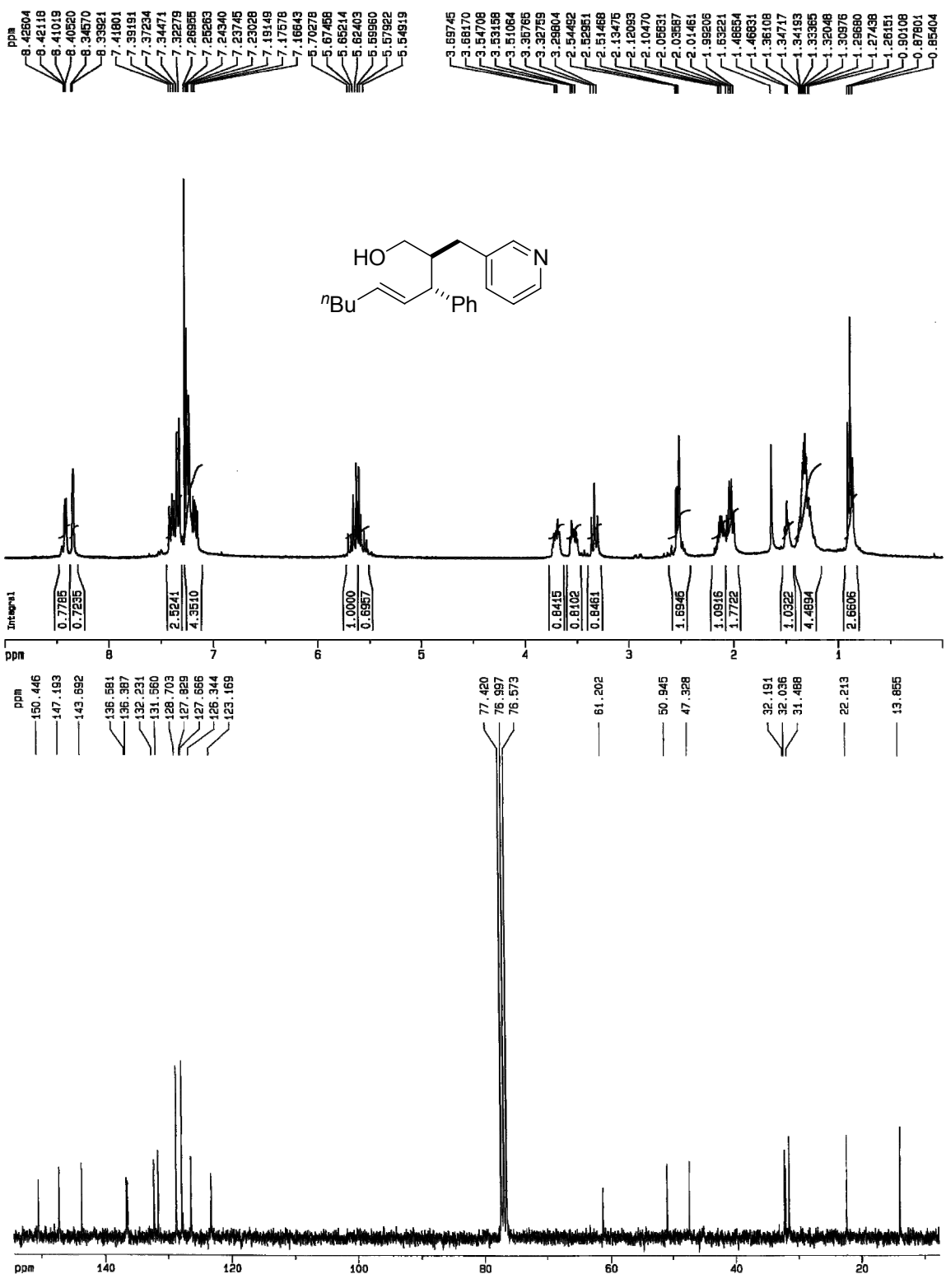


A.106 COMPOUND 183

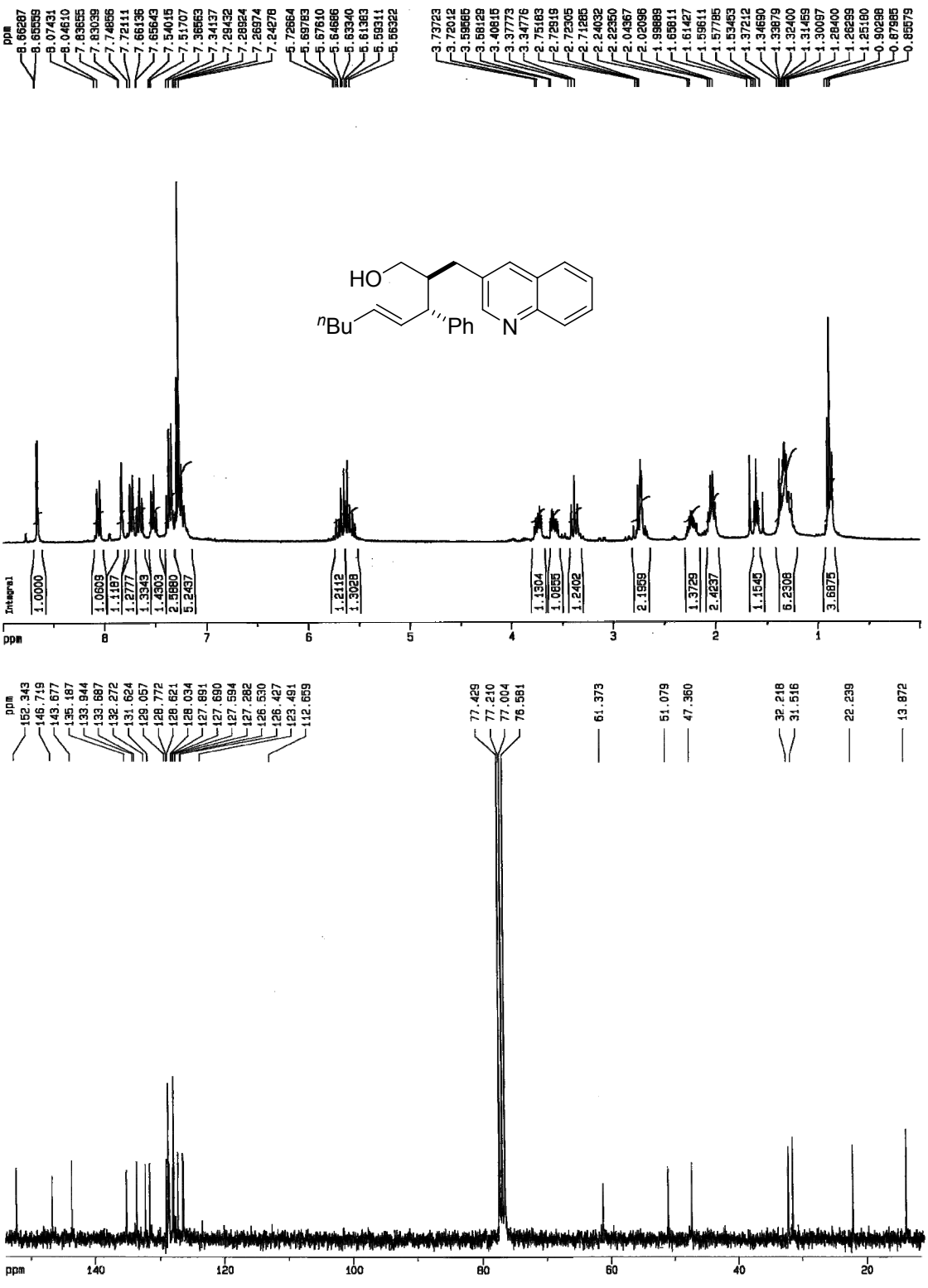


A.107 COMPOUND 184

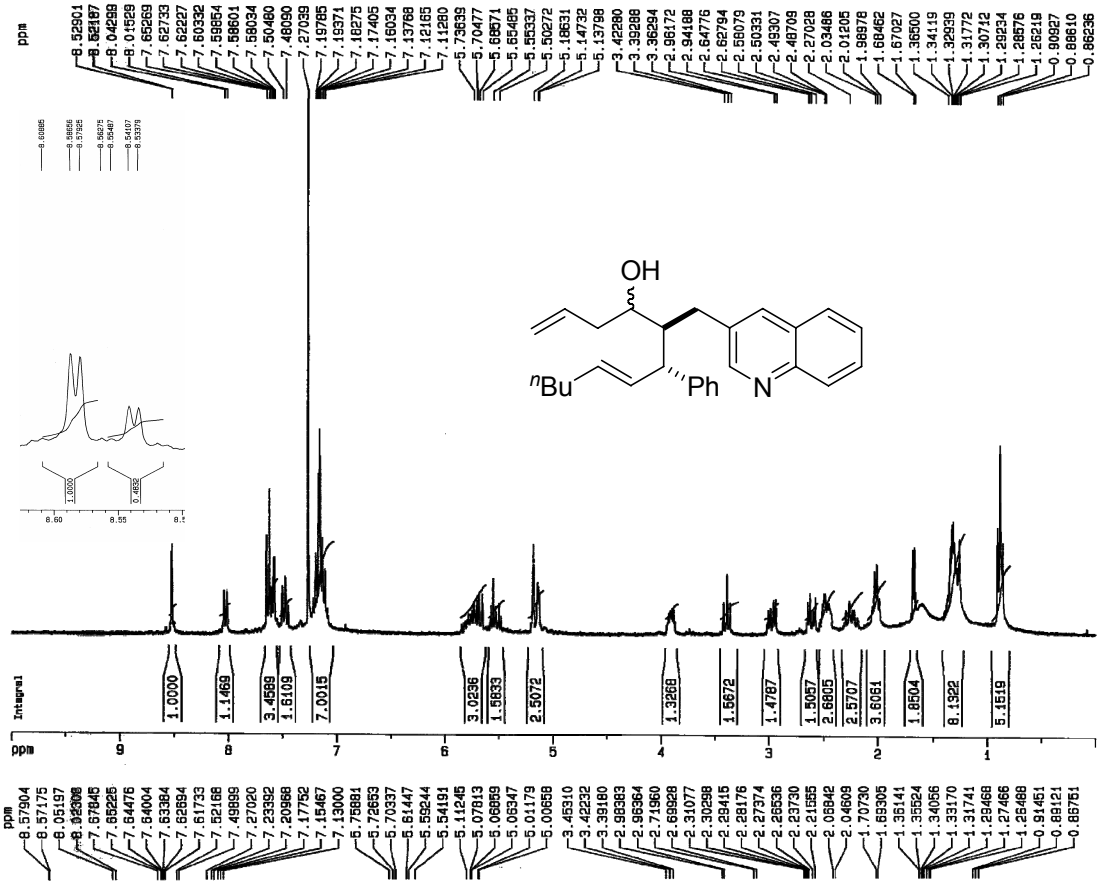
A.108 COMPOUND 185

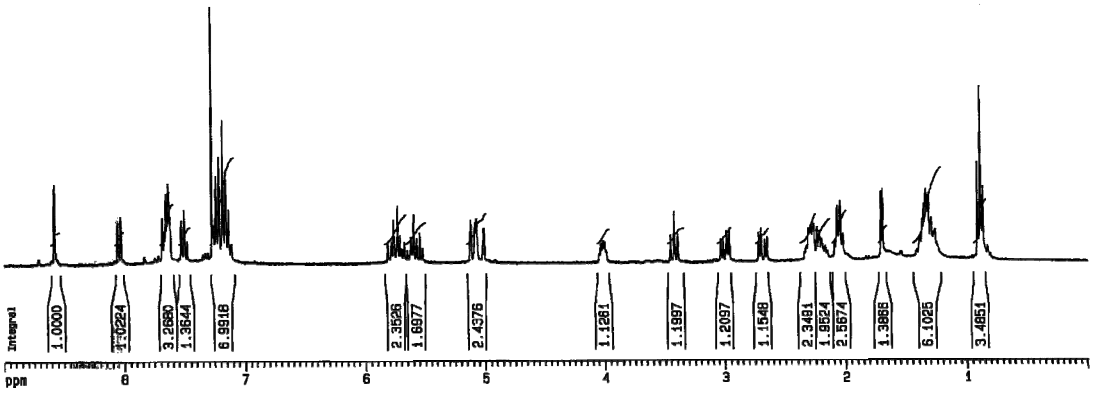


A.109 COMPOUND 186

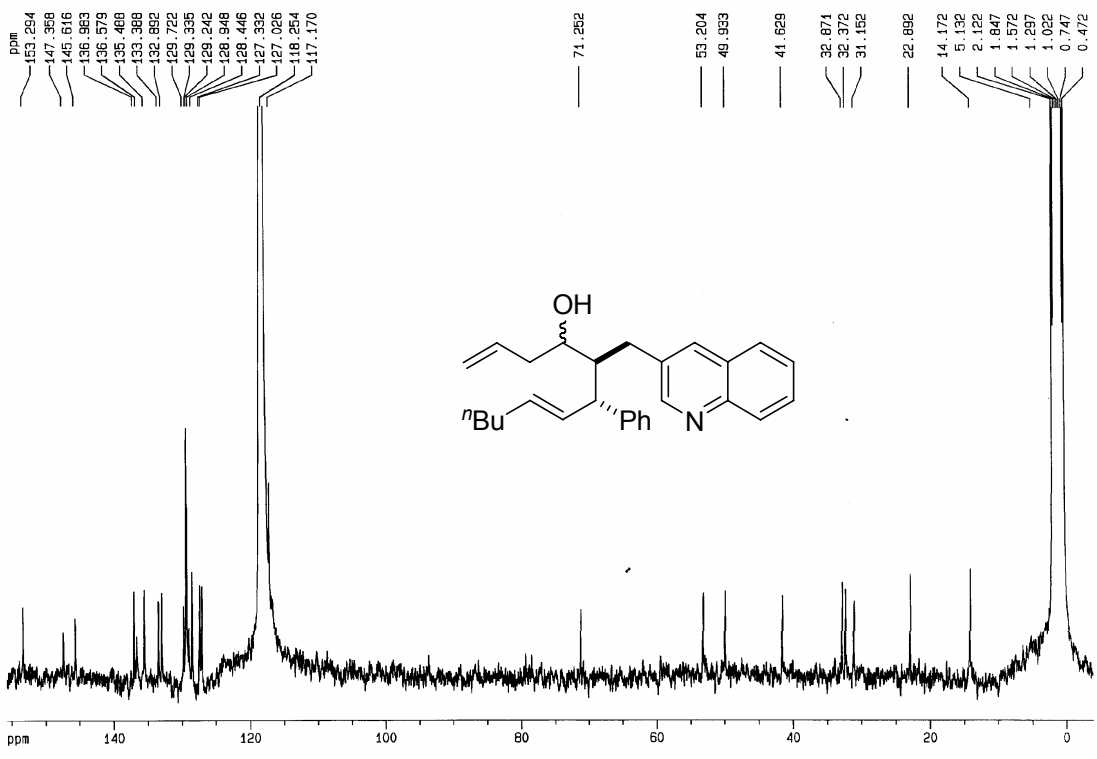


A.110 COMPOUND 188

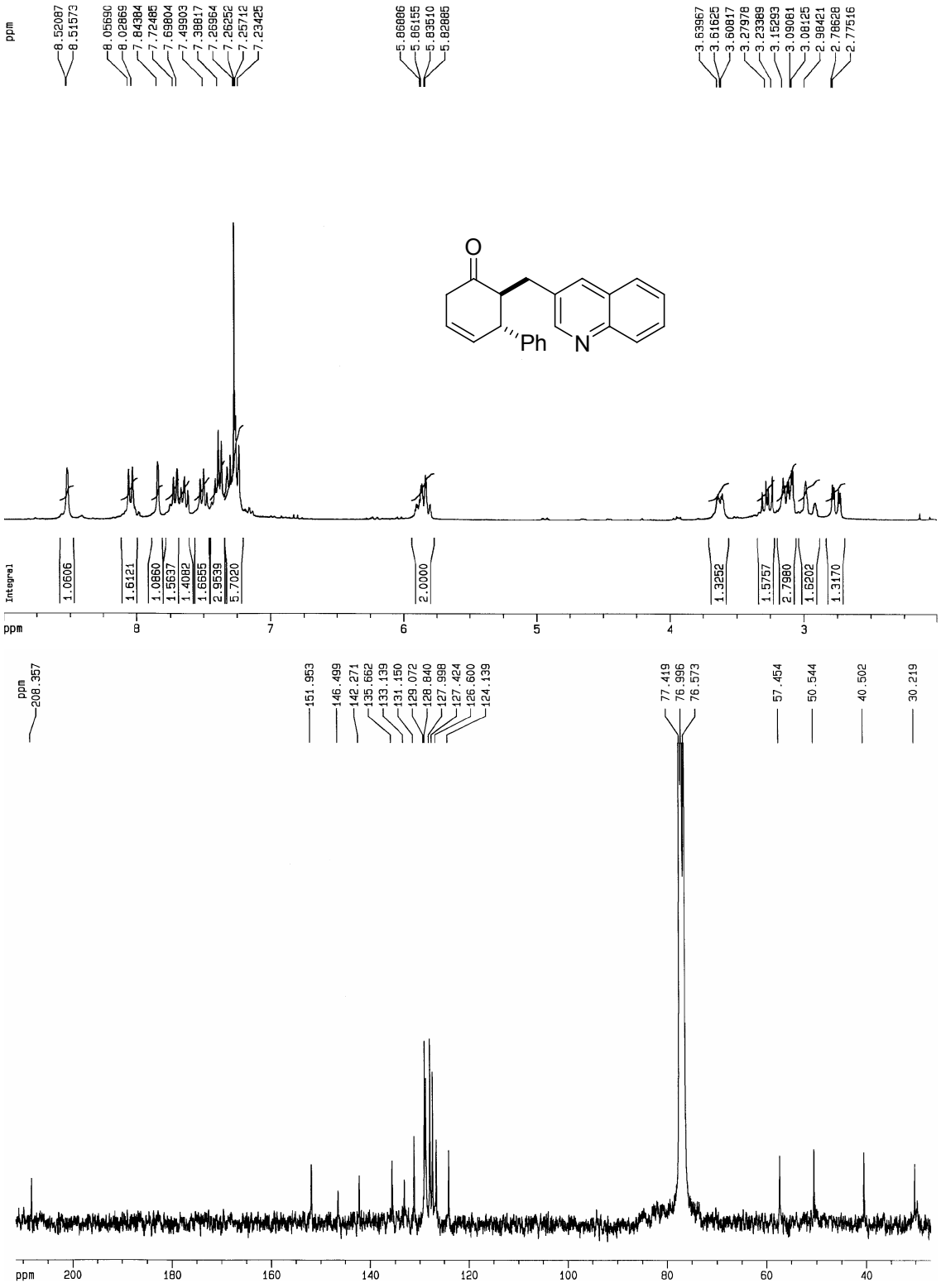




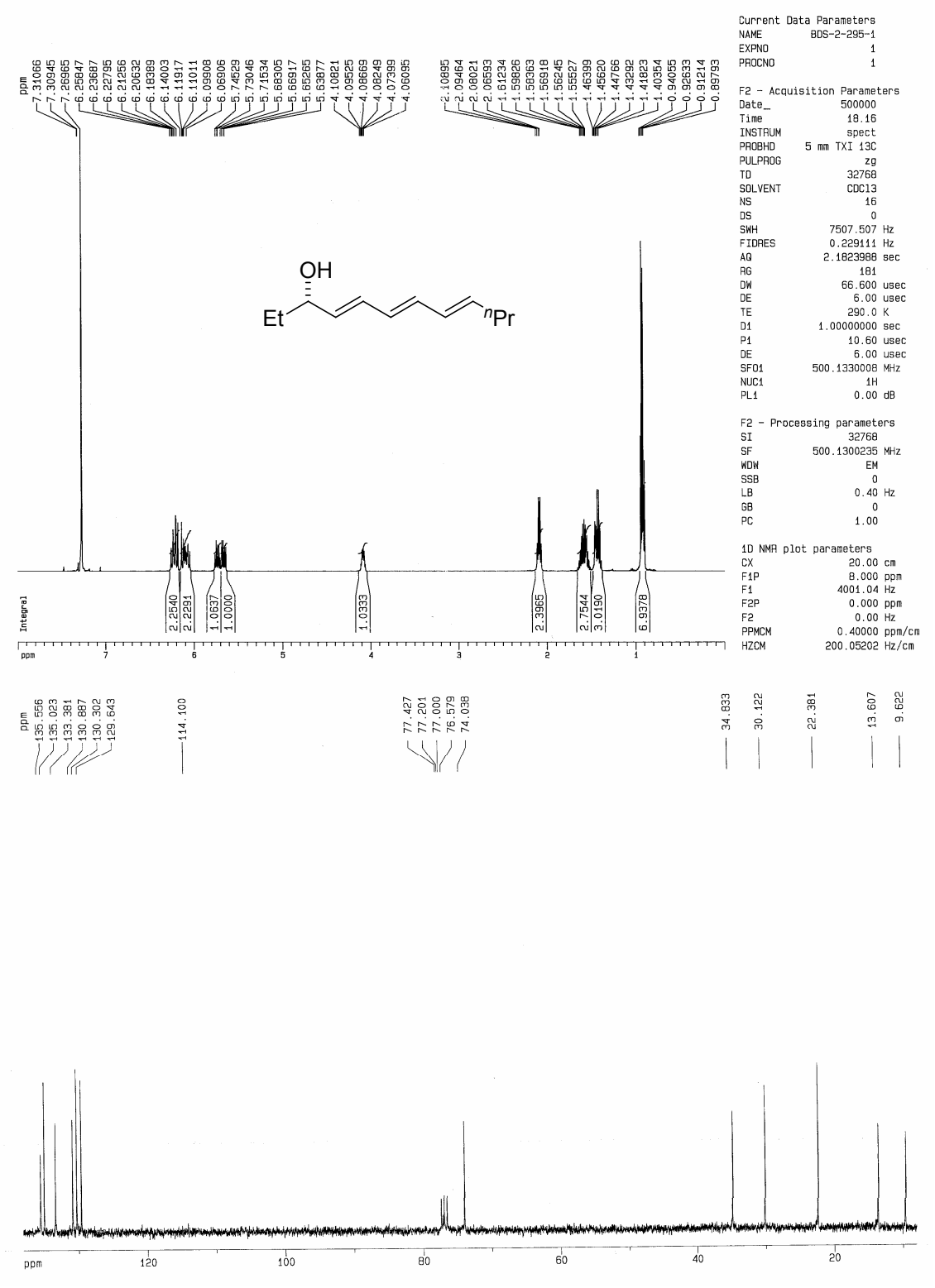
A.111 COMPOUND 188



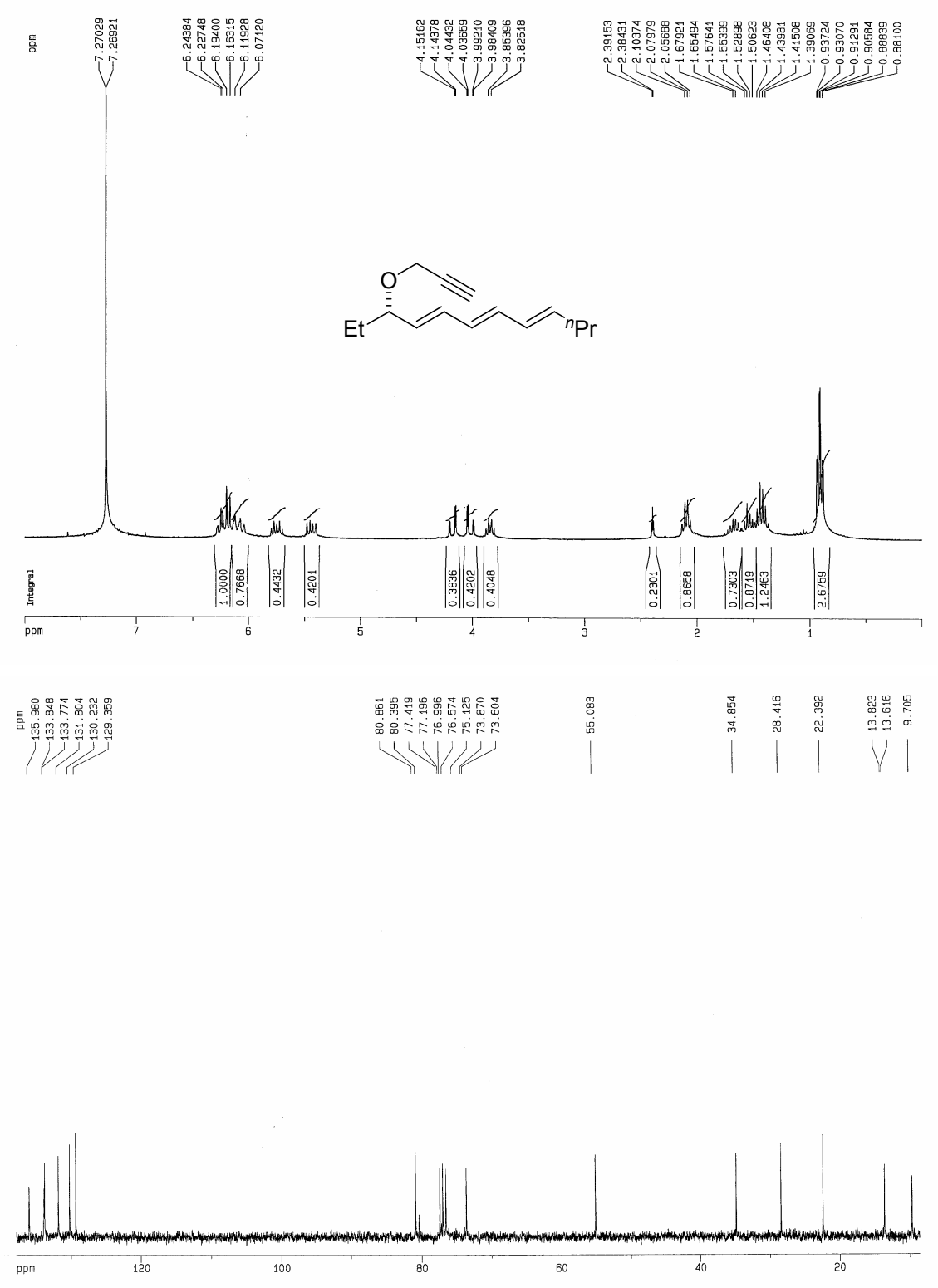
A.112 COMPOUND 189



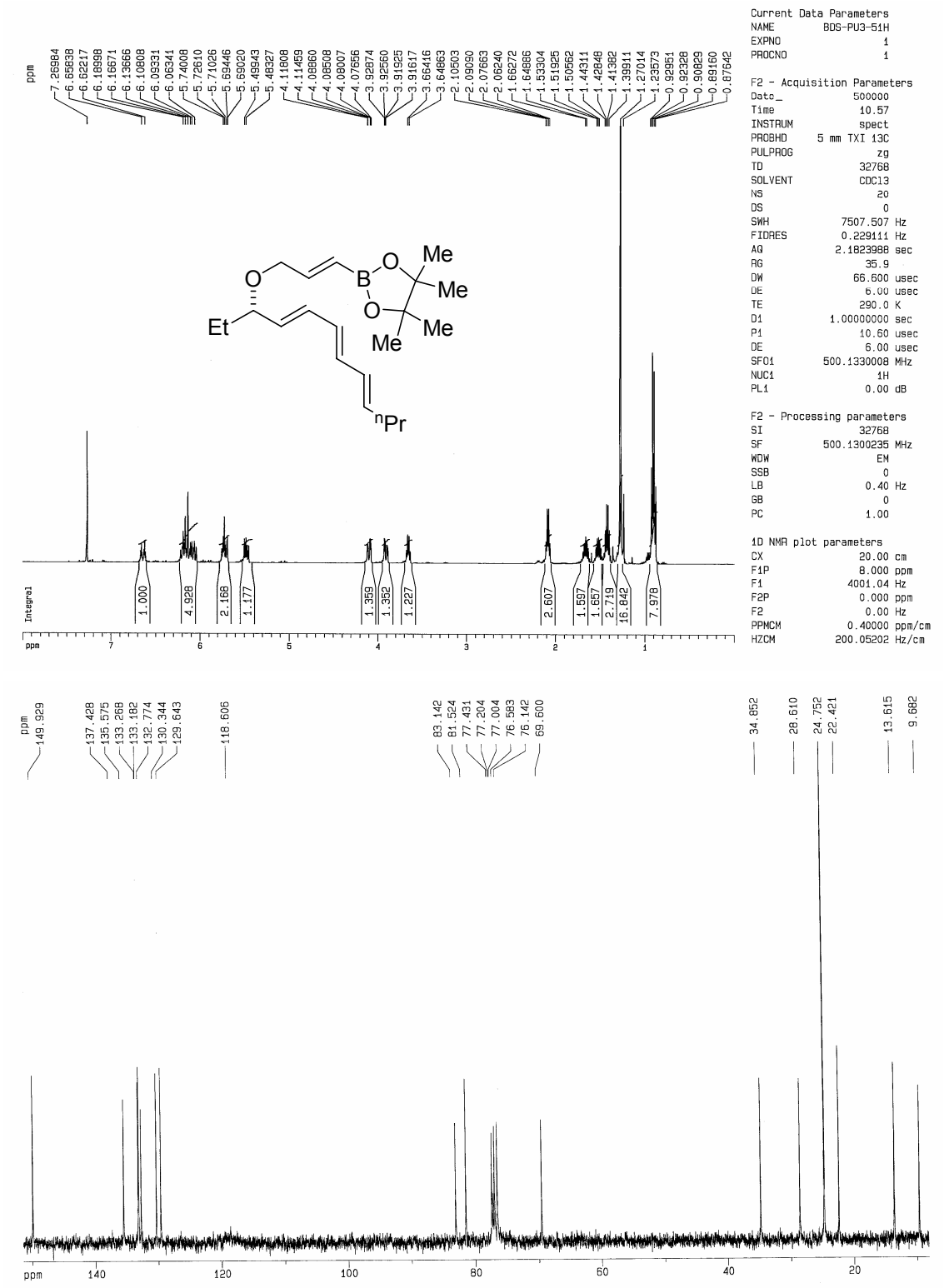
A.113 COMPOUND 208



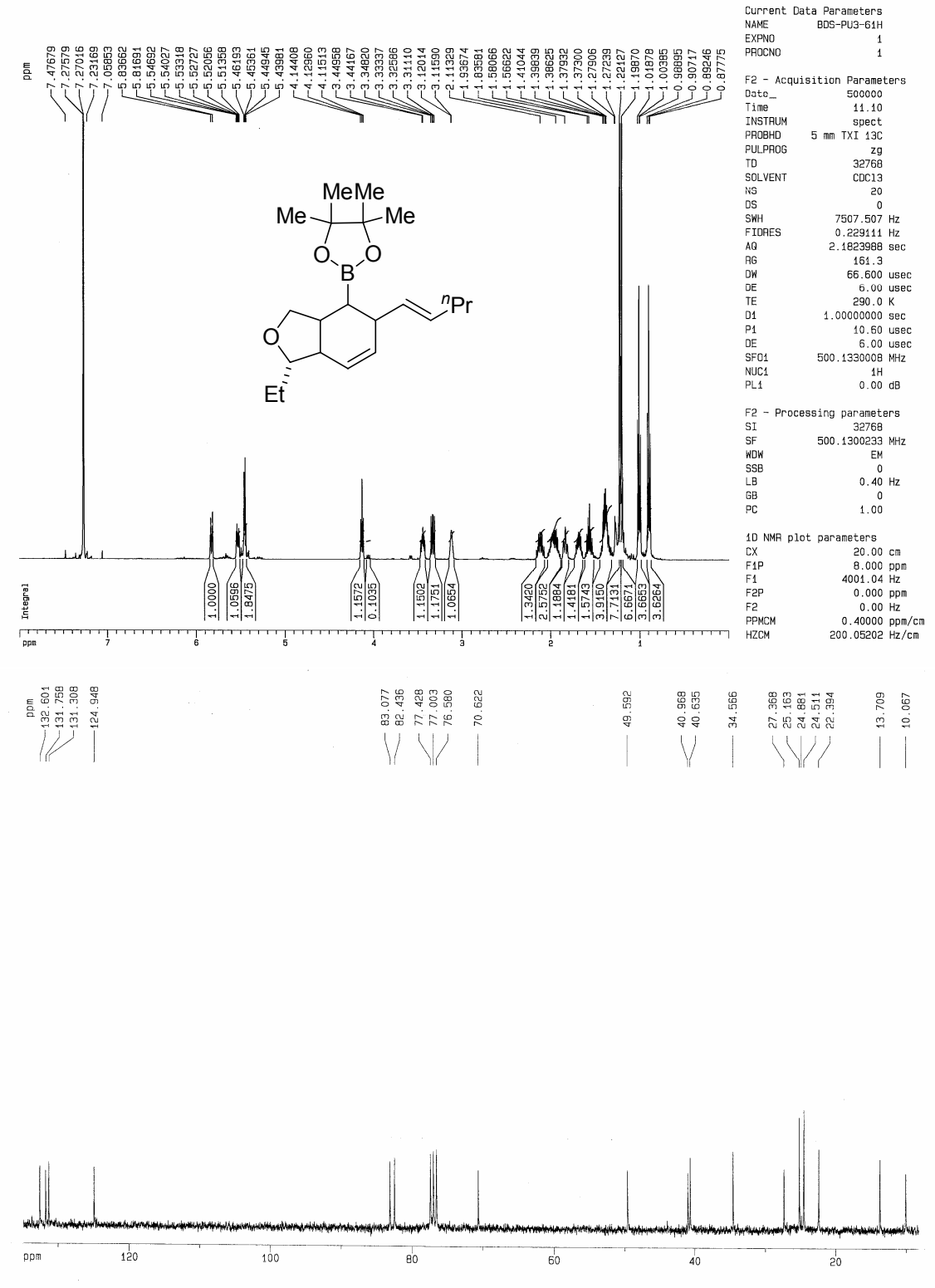
A.114 COMPOUND 209



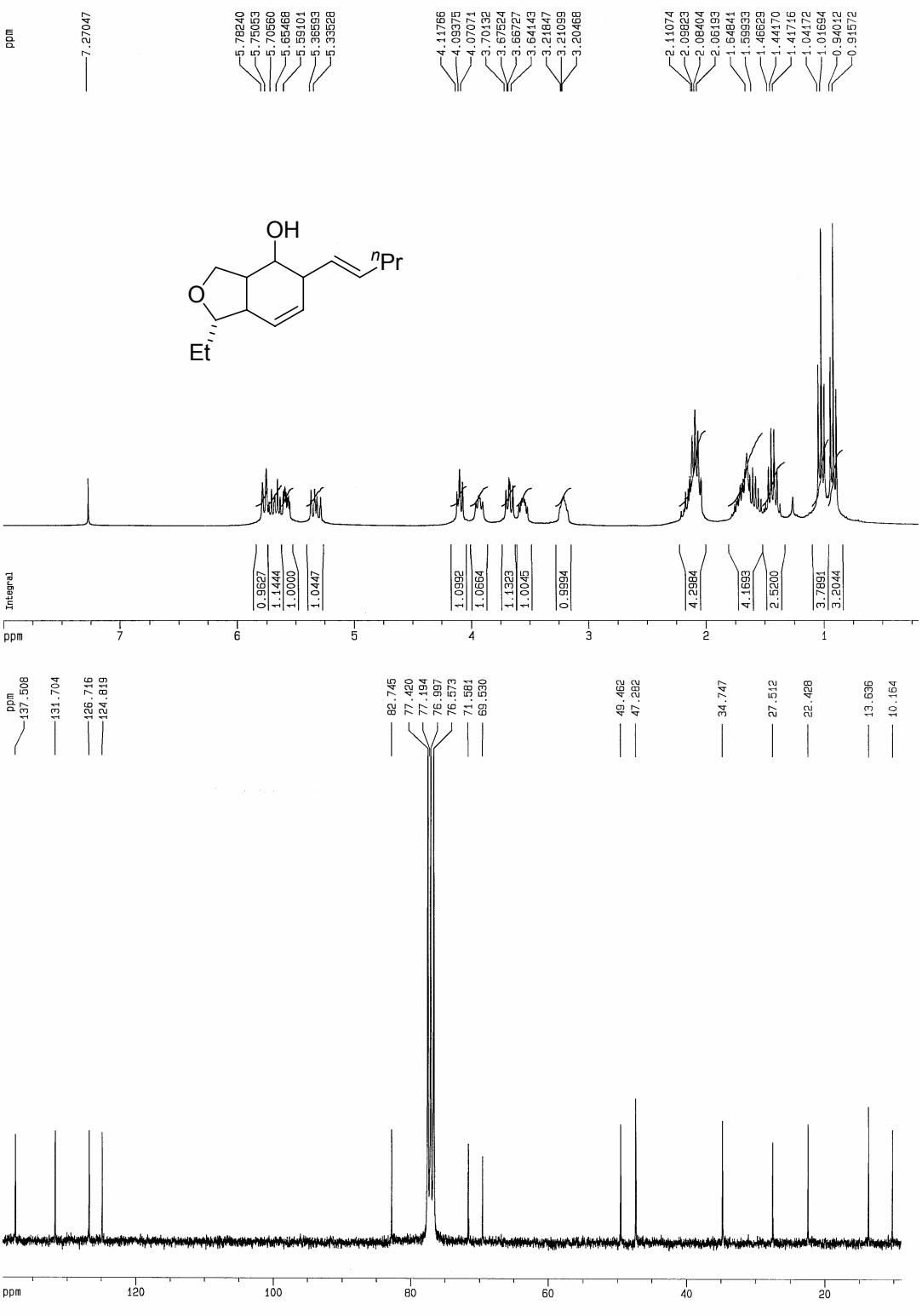
A.115 COMPOUND 210



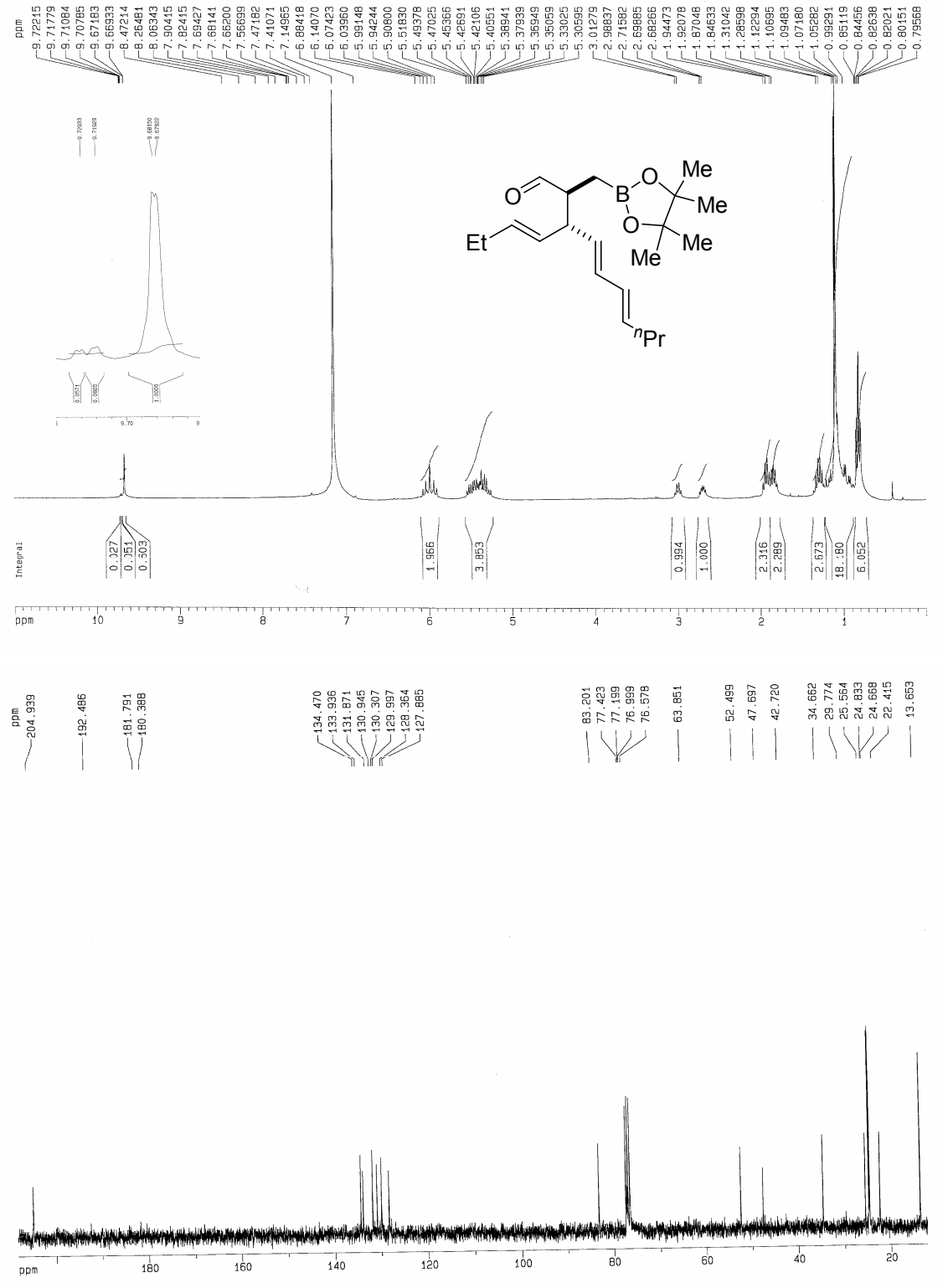
A.116 COMPOUND 211



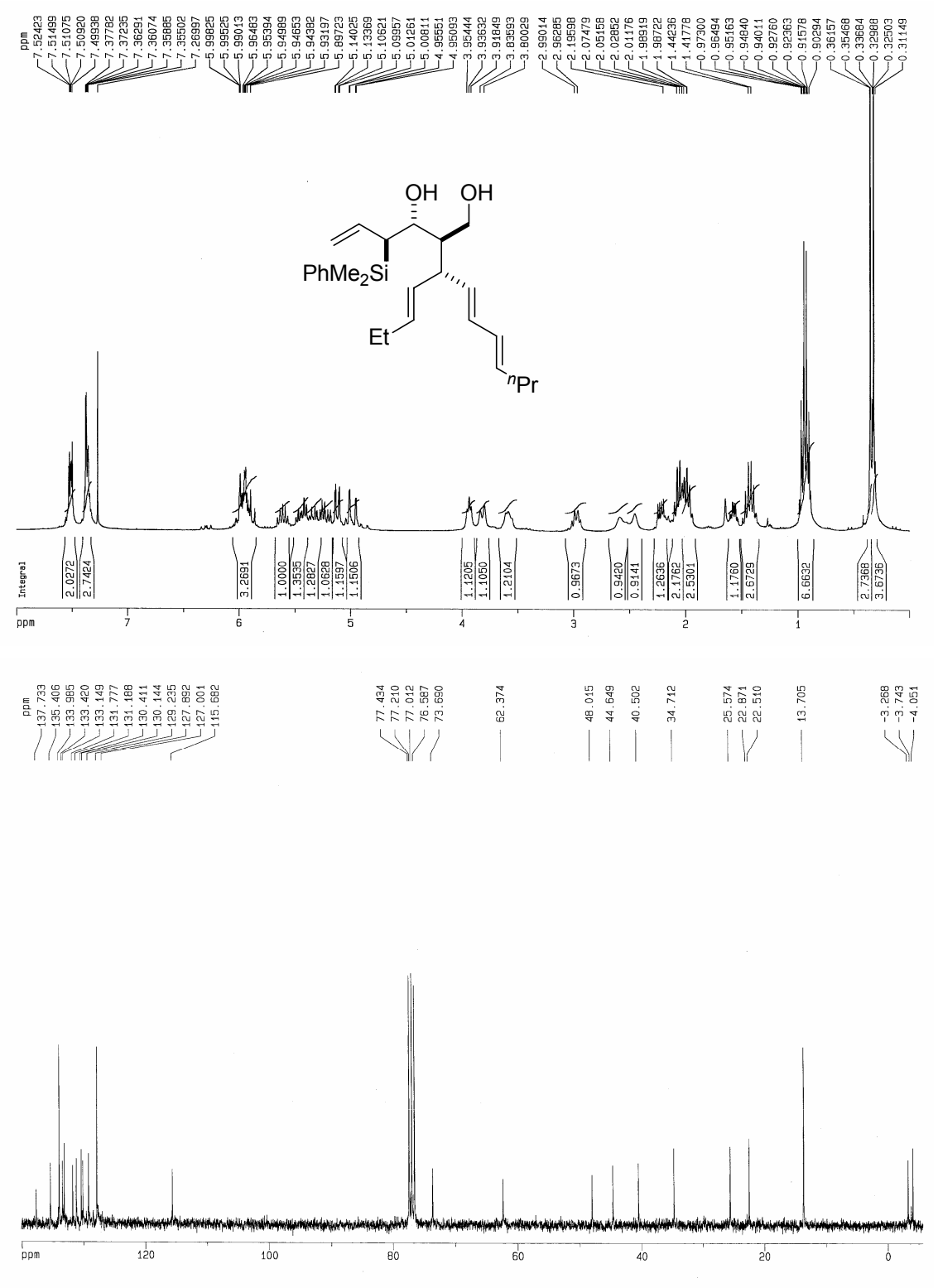
A.117 COMPOUND 212



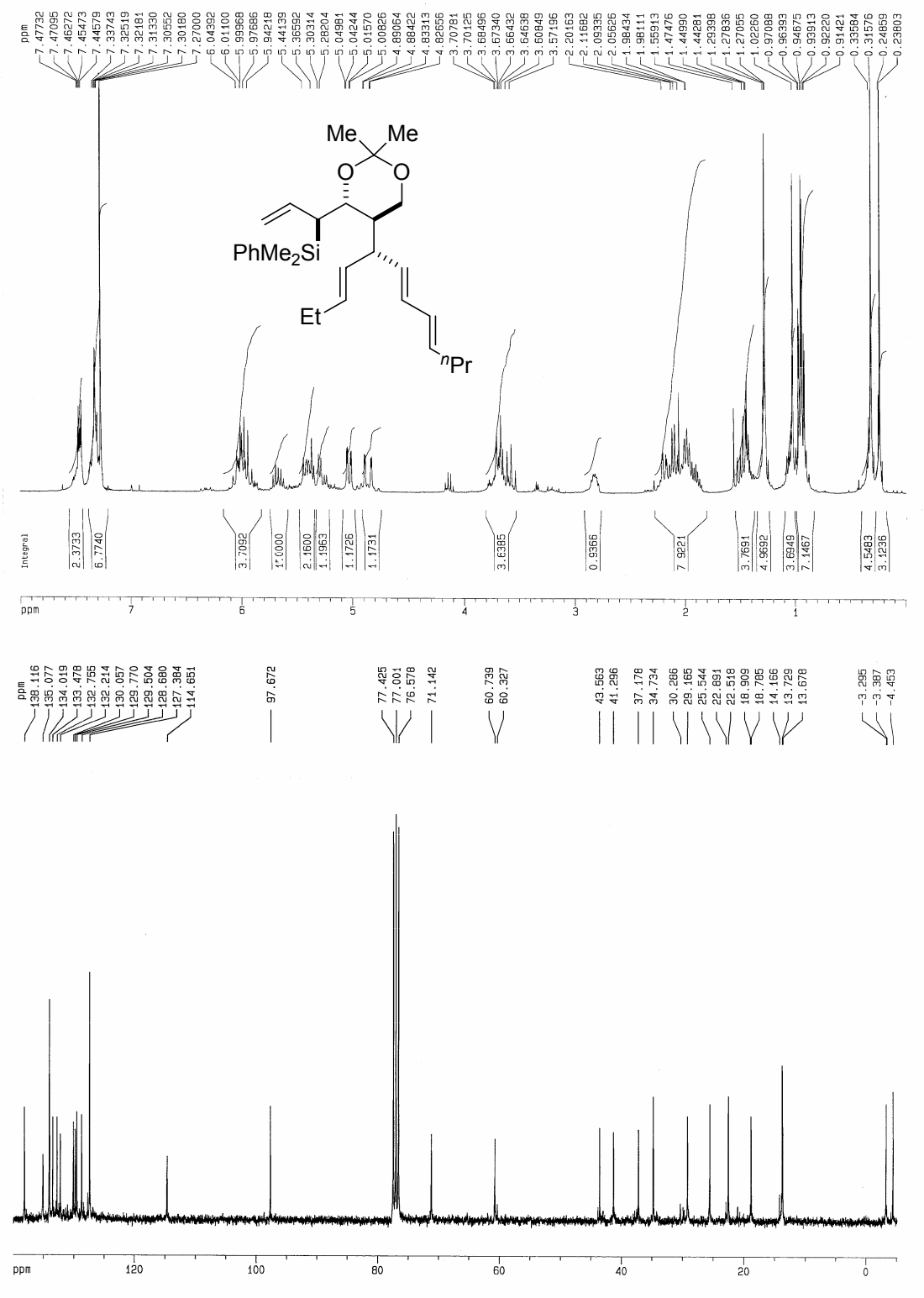
A.118 COMPOUND 213



A.119 COMPOUND 214



A.120 COMPOUND 216



APPENDIX B

X-RAY STRUCTURE DATA

B.1 COMPOUND 43

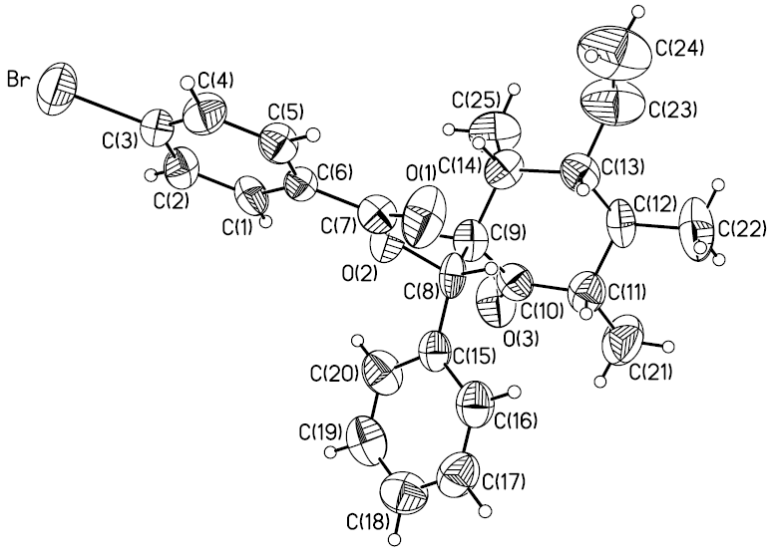


Table 1. Crystal data and structure refinement for bs0405t.

Identification code	bs0405t
Empirical formula	C25 H27 Br O3
Formula weight	455.38
Temperature	295(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic

Space group	P2(1)/c	
Unit cell dimensions	a = 22.148(3) Å	α= 90°.
	b = 6.0518(8) Å	β= 93.333(3)°.
	c = 16.921(2) Å	γ = 90°.
Volume	2264.1(5) $Å^3$	
Z	4	
Density (calculated)	1.336 Mg/m^3	
Absorption coefficient	1.838 mm^{-1}	
F(000)	944	
Crystal size	0.29 x 0.06 x 0.06 mm^3	
Theta range for data collection	1.84 to 25.00°.	
Index ranges	-26<=h<=26, -7<=k<=7, -20<=l<=20	
Reflections collected	17088	
Independent reflections	3982 [R(int) = 0.1137]	
Completeness to theta = 25.00°	100.0 %	
Absorption correction	None	
Max. and min. transmission	0.8977 and 0.6178	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3982 / 0 / 262	
Goodness-of-fit on F^2	1.107	
Final R indices [I>2sigma(I)]	R1 = 0.0841, wR2 = 0.1723	
R indices (all data)	R1 = 0.1744, wR2 = 0.1974	
Largest diff. peak and hole	0.424 and -0.428 $e.Å^{-3}$	

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for bs0405t. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Br	4217(1)	7461(2)	788(1)	87(1)
O(1)	6769(2)	12535(8)	2436(3)	85(2)
O(2)	6869(2)	9060(6)	2839(3)	57(1)
O(3)	8383(2)	5440(9)	4101(3)	82(2)
C(1)	5787(3)	7789(10)	2207(4)	49(2)
C(2)	5253(3)	7072(9)	1825(4)	49(2)
C(3)	4945(3)	8457(11)	1296(4)	46(2)

C(4)	5167(3)	10500(12)	1135(4)	57(2)
C(5)	5695(3)	11228(11)	1511(4)	49(2)
C(6)	6012(3)	9873(9)	2043(3)	38(1)
C(7)	6588(3)	10664(11)	2451(4)	47(2)
C(8)	7410(3)	9480(9)	3357(4)	48(2)
C(9)	7844(3)	7628(10)	3132(4)	50(2)
C(10)	8337(3)	7194(12)	3754(4)	55(2)
C(11)	8793(3)	9038(12)	3881(4)	64(2)
C(12)	9103(3)	9408(12)	3107(4)	66(2)
C(13)	8632(3)	9808(11)	2415(4)	58(2)
C(14)	8133(3)	8071(9)	2339(4)	54(2)
C(15)	7225(3)	9421(10)	4184(4)	47(2)
C(16)	7351(3)	11226(12)	4696(5)	62(2)
C(17)	7180(3)	11150(14)	5461(5)	70(2)
C(18)	6893(3)	9346(15)	5753(5)	75(2)
C(19)	6759(3)	7647(15)	5247(6)	83(2)
C(20)	6934(3)	7655(11)	4485(5)	65(2)
C(21)	9240(4)	8542(16)	4585(5)	99(3)
C(22)	9562(4)	11278(15)	3189(6)	109(3)
C(23)	8936(5)	10046(16)	1651(5)	109(4)
C(24)	8799(6)	11041(17)	1062(7)	141(4)
C(25)	8365(4)	5837(11)	2019(4)	82(2)

Table 3. Bond lengths [Å] and angles [°] for bs0405t.

Br-C(3)	1.883(6)
O(1)-C(7)	1.202(7)
O(2)-C(7)	1.309(7)
O(2)-C(8)	1.464(7)
O(3)-C(10)	1.214(7)
C(1)-C(2)	1.385(8)
C(1)-C(6)	1.390(7)
C(2)-C(3)	1.377(8)
C(3)-C(4)	1.364(8)
C(4)-C(5)	1.371(8)
C(5)-C(6)	1.379(8)
C(6)-C(7)	1.493(8)
C(8)-C(15)	1.482(8)
C(8)-C(9)	1.538(8)
C(9)-C(10)	1.495(9)
C(9)-C(14)	1.545(9)
C(10)-C(11)	1.513(9)
C(11)-C(12)	1.530(9)
C(11)-C(21)	1.533(9)
C(12)-C(22)	1.522(9)
C(12)-C(13)	1.541(9)
C(13)-C(23)	1.498(11)
C(13)-C(14)	1.525(8)
C(14)-C(25)	1.554(8)
C(15)-C(20)	1.362(8)
C(15)-C(16)	1.413(9)
C(16)-C(17)	1.369(10)
C(17)-C(18)	1.371(10)
C(18)-C(19)	1.359(10)
C(19)-C(20)	1.369(10)
C(23)-C(24)	1.189(11)
C(7)-O(2)-C(8)	121.3(5)
C(2)-C(1)-C(6)	119.9(6)

C(3)-C(2)-C(1)	119.3(6)
C(4)-C(3)-C(2)	120.8(6)
C(4)-C(3)-Br	120.6(5)
C(2)-C(3)-Br	118.7(5)
C(3)-C(4)-C(5)	120.4(6)
C(4)-C(5)-C(6)	120.0(6)
C(5)-C(6)-C(1)	119.6(6)
C(5)-C(6)-C(7)	120.0(6)
C(1)-C(6)-C(7)	120.4(6)
O(1)-C(7)-O(2)	124.0(6)
O(1)-C(7)-C(6)	124.8(6)
O(2)-C(7)-C(6)	111.3(6)
O(2)-C(8)-C(15)	107.4(5)
O(2)-C(8)-C(9)	103.1(5)
C(15)-C(8)-C(9)	115.2(5)
C(10)-C(9)-C(8)	113.3(5)
C(10)-C(9)-C(14)	108.6(5)
C(8)-C(9)-C(14)	112.6(5)
O(3)-C(10)-C(9)	122.1(6)
O(3)-C(10)-C(11)	122.6(6)
C(9)-C(10)-C(11)	115.2(6)
C(10)-C(11)-C(12)	108.3(6)
C(10)-C(11)-C(21)	111.2(6)
C(12)-C(11)-C(21)	113.1(6)
C(22)-C(12)-C(11)	111.2(7)
C(22)-C(12)-C(13)	111.8(6)
C(11)-C(12)-C(13)	110.9(5)
C(23)-C(13)-C(14)	110.7(6)
C(23)-C(13)-C(12)	110.7(6)
C(14)-C(13)-C(12)	114.2(5)
C(13)-C(14)-C(9)	112.4(5)
C(13)-C(14)-C(25)	112.1(6)
C(9)-C(14)-C(25)	108.3(5)
C(20)-C(15)-C(16)	117.3(7)
C(20)-C(15)-C(8)	122.3(6)
C(16)-C(15)-C(8)	120.4(6)

C(17)-C(16)-C(15)	119.9(7)
C(16)-C(17)-C(18)	121.9(8)
C(19)-C(18)-C(17)	117.6(8)
C(18)-C(19)-C(20)	121.9(8)
C(15)-C(20)-C(19)	121.4(8)
C(24)-C(23)-C(13)	131.8(11)

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for bs0405t. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Br 64(1)	110(1)	84(1)	10(1)	-17(1)	-26(1)
O(1)89(4)	50(3)	110(4)	35(3)	-34(3)	-22(3)
O(2)52(3)	35(3)	80(3)	10(2)	-19(2)	0(2)
O(3)69(3)	68(4)	107(4)	39(3)	-7(3)	2(3)
C(1)40(4)	51(4)	56(4)	14(4)	10(3)	-1(3)
C(2)50(4)	30(4)	66(4)	-8(3)	6(3)	-8(3)
C(3)40(4)	51(4)	46(4)	-1(3)	0(3)	-5(3)
C(4)57(4)	62(5)	52(4)	12(4)	-8(4)	7(4)
C(5)55(4)	39(4)	53(4)	8(3)	4(3)	-5(3)
C(6)41(4)	33(4)	40(3)	0(3)	4(3)	-1(3)
C(7)52(4)	38(4)	50(4)	8(3)	3(3)	5(4)
C(8)38(4)	30(4)	75(5)	4(3)	-6(4)	-12(3)
C(9)49(4)	31(3)	70(4)	5(4)	0(3)	5(3)
C(10)51(4)	56(5)	59(4)	6(4)	7(3)	5(4)
C(11)50(4)	66(5)	75(5)	-3(4)	-1(4)	6(4)
C(12)44(4)	57(5)	98(6)	1(4)	8(4)	-15(4)
C(13)66(5)	46(4)	62(5)	7(4)	10(4)	0(4)
C(14)67(4)	31(4)	63(4)	-5(3)	-2(4)	4(3)
C(15)35(4)	41(4)	64(5)	1(4)	1(3)	4(3)
C(16)49(4)	57(5)	80(6)	1(4)	0(4)	3(4)
C(17)69(5)	61(5)	80(6)	-13(5)	-4(5)	1(4)
C(18)82(6)	76(6)	66(5)	9(5)	6(5)	9(5)

C(19)70(5)	81(6)	100(7)	10(6)	15(5)	-10(5)
C(20)71(5)	44(4)	83(6)	8(5)	17(4)	-4(4)
C(21)83(6)	119(7)	92(6)	13(6)	-30(5)	-21(5)
C(22)78(6)	95(7)	154(9)	23(7)	0(6)	-38(5)
C(23)165(10)	81(7)	83(7)	27(6)	11(7)	21(6)
C(24)224(14)	84(8)	120(10)	-18(7)	53(10)	20(8)
C(25)105(6)	60(5)	82(5)	-11(4)	11(5)	25(5)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^{-3}) for bs0405t.

	x	y	z	U(eq)
H(1A)	5995	6878	2572	58
H(2A)	5103	5670	1925	59
H(4A)	4960	11404	767	69
H(5A)	5839	12636	1408	58
H(8A)	7582	10928	3238	58
H(9A)	7605	6269	3068	60
H(11A)	8573	10390	4002	76
H(12A)	9323	8053	2991	79
H(13A)	8437	11224	2516	69
H(14A)	7816	8623	1961	65
H(16A)	7550	12464	4515	75
H(17A)	7261	12357	5790	84
H(18A)	6793	9285	6279	90
H(19A)	6543	6446	5425	100
H(20A)	6852	6428	4165	78
H(21A)	9023	8364	5056	149
H(21B)	9521	9744	4657	149
H(21C)	9457	7207	4484	149
H(22A)	9851	10961	3618	164
H(22B)	9357	12636	3294	164
H(22C)	9766	11417	2706	164

H(23A)	9298	9273	1635	131
H(24A)	8443	11861	1026	169
H(24B)	9047	10999	638	169
H(25A)	8541	6076	1522	123
H(25B)	8033	4824	1948	123
H(25C)	8664	5230	2392	123

B.2 COMPOUND 49

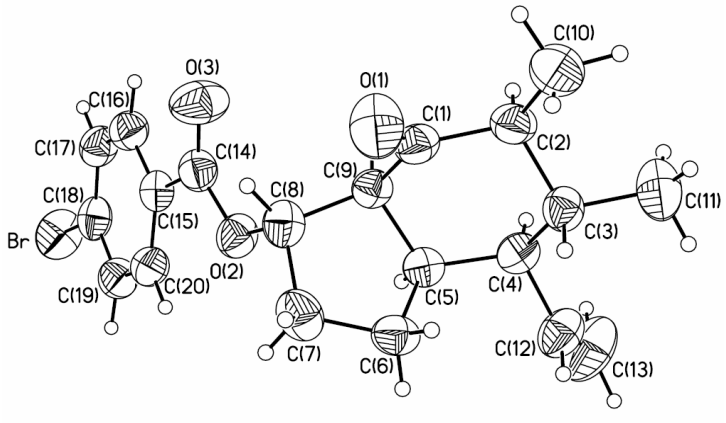


Table 1. Crystal data and structure refinement for bs03171s.

Identification code	bs03171s	
Empirical formula	C20 H23 Br O3	
Formula weight	391.29	
Temperature	295(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2(1)/c	
Unit cell dimensions	a = 8.0654(4) Å	α= 90°.
	b = 22.8205(13) Å	β= 111.4580(10)°.
	c = 10.8106(6) Å	γ = 90°.
Volume	1851.84(17) Å^3	
Z	4	

Density (calculated)	1.403 Mg/m^3
Absorption coefficient	2.234 mm^{-1}
F(000)	808
Crystal size	0.33 x 0.14 x 0.03 mm^3
Theta range for data collection	1.78 to 32.50°.
Index ranges	-11<=h<=12, -34<=k<=34, -16<=l<=16
Reflections collected	24011
Independent reflections	6565 [R(int) = 0.0489]
Completeness to theta = 32.50°	98.0 %
Absorption correction	Sadabs
Max. and min. transmission	0.9401 and 0.5260
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	6565 / 0 / 309
Goodness-of-fit on F^2	0.987
Final R indices [I>2sigma(I)]	R1 = 0.0523, wR2 = 0.1127
R indices (all data)	R1 = 0.1259, wR2 = 0.1394
Largest diff. peak and hole	0.447 and -0.179 $e.Å^{-3}$

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for bs03171s. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Br	6739(1)	286(1)	2929(1)	76(1)
O(1)	-2014(3)	2437(1)	6891(2)	73(1)
O(2)	2290(2)	1895(1)	5979(2)	50(1)
O(3)	382(3)	1145(1)	5368(2)	74(1)
C(1)	-1886(3)	2658(1)	5913(2)	45(1)
C(2)	-3215(3)	3096(1)	5077(3)	50(1)
C(3)	-2277(3)	3681(1)	5030(2)	46(1)
C(4)	-713(3)	3582(1)	4559(2)	44(1)
C(5)	562(3)	3106(1)	5345(2)	39(1)
C(6)	1667(4)	3247(1)	6798(2)	50(1)
C(7)	2260(4)	2661(1)	7486(3)	58(1)
C(8)	1131(3)	2192(1)	6552(2)	48(1)
C(9)	-331(3)	2525(1)	5488(2)	40(1)

C(10)	-4759(4)	3169(2)	5539(5)	77(1)
C(11)	-3593(5)	4127(2)	4162(4)	74(1)
C(12)	276(4)	4139(1)	4573(3)	60(1)
C(13)	568(6)	4373(2)	3569(5)	92(1)
C(14)	1754(3)	1368(1)	5435(2)	47(1)
C(15)	3051(3)	1102(1)	4908(2)	43(1)
C(16)	2520(4)	604(1)	4118(3)	51(1)
C(17)	3620(4)	361(1)	3543(3)	53(1)
C(18)	5259(3)	612(1)	3764(2)	51(1)
C(19)	5835(3)	1094(1)	4569(3)	53(1)
C(20)	4714(3)	1341(1)	5141(2)	49(1)

Table 3. Bond lengths [Å] and angles [°] for bs03171s.

Br-C(18)	1.892(2)
O(1)-C(1)	1.209(3)
O(2)-C(14)	1.339(3)
O(2)-C(8)	1.464(3)
O(3)-C(14)	1.195(3)
C(1)-C(2)	1.501(3)
C(1)-C(9)	1.516(3)
C(2)-C(10)	1.510(4)
C(2)-C(3)	1.545(3)
C(2)-H(2)	0.91(2)
C(3)-C(11)	1.522(4)
C(3)-C(4)	1.540(3)
C(3)-H(3)	0.99(2)
C(4)-C(12)	1.498(3)
C(4)-C(5)	1.524(3)
C(4)-H(4)	0.85(2)
C(5)-C(6)	1.530(3)
C(5)-C(9)	1.542(3)
C(5)-H(5)	0.92(2)
C(6)-C(7)	1.520(4)
C(6)-H(6A)	0.92(2)

C(6)-H(6B)	0.88(3)
C(7)-C(8)	1.525(4)
C(7)-H(7A)	0.90(3)
C(7)-H(7B)	0.96(3)
C(8)-C(9)	1.516(3)
C(8)-H(8)	0.98(3)
C(9)-H(9)	0.88(2)
C(10)-H(10C)	0.98(3)
C(10)-H(10A)	0.96(4)
C(10)-H(10B)	0.99(4)
C(11)-H(11A)	0.99(4)
C(11)-H(11B)	0.85(3)
C(11)-H(11C)	0.95(4)
C(12)-C(13)	1.305(4)
C(12)-H(12)	0.91(3)
C(13)-H(13A)	0.97(3)
C(13)-H(13B)	0.99(3)
C(14)-C(15)	1.491(3)
C(15)-C(20)	1.383(3)
C(15)-C(16)	1.391(3)
C(16)-C(17)	1.373(3)
C(16)-H(16)	0.89(3)
C(17)-C(18)	1.379(4)
C(17)-H(17)	0.88(3)
C(18)-C(19)	1.373(4)
C(19)-C(20)	1.388(3)
C(19)-H(19)	0.95(3)
C(20)-H(20)	0.90(3)

C(14)-O(2)-C(8)	116.59(18)
O(1)-C(1)-C(2)	122.2(2)
O(1)-C(1)-C(9)	121.7(2)
C(2)-C(1)-C(9)	116.04(19)
C(1)-C(2)-C(10)	111.6(3)
C(1)-C(2)-C(3)	110.14(19)
C(10)-C(2)-C(3)	112.8(2)

C(1)-C(2)-H(2)	104.2(15)
C(10)-C(2)-H(2)	109.6(15)
C(3)-C(2)-H(2)	108.0(16)
C(11)-C(3)-C(4)	111.4(2)
C(11)-C(3)-C(2)	111.1(2)
C(4)-C(3)-C(2)	110.74(18)
C(11)-C(3)-H(3)	105.8(12)
C(4)-C(3)-H(3)	108.8(12)
C(2)-C(3)-H(3)	108.9(12)
C(12)-C(4)-C(5)	110.6(2)
C(12)-C(4)-C(3)	111.69(19)
C(5)-C(4)-C(3)	112.81(18)
C(12)-C(4)-H(4)	106.8(15)
C(5)-C(4)-H(4)	110.1(15)
C(3)-C(4)-H(4)	104.5(15)
C(4)-C(5)-C(6)	116.26(19)
C(4)-C(5)-C(9)	115.06(18)
C(6)-C(5)-C(9)	101.33(18)
C(4)-C(5)-H(5)	109.7(12)
C(6)-C(5)-H(5)	108.4(12)
C(9)-C(5)-H(5)	105.2(12)
C(7)-C(6)-C(5)	106.1(2)
C(7)-C(6)-H(6A)	111.2(15)
C(5)-C(6)-H(6A)	107.0(15)
C(7)-C(6)-H(6B)	112.0(17)
C(5)-C(6)-H(6B)	114.9(16)
H(6A)-C(6)-H(6B)	106(2)
C(6)-C(7)-C(8)	106.8(2)
C(6)-C(7)-H(7A)	110.1(18)
C(8)-C(7)-H(7A)	109.0(18)
C(6)-C(7)-H(7B)	111.5(17)
C(8)-C(7)-H(7B)	111.0(17)
H(7A)-C(7)-H(7B)	108(2)
O(2)-C(8)-C(9)	110.57(17)
O(2)-C(8)-C(7)	106.6(2)
C(9)-C(8)-C(7)	105.1(2)

O(2)-C(8)-H(8)	105.8(15)
C(9)-C(8)-H(8)	114.2(14)
C(7)-C(8)-H(8)	114.4(15)
C(1)-C(9)-C(8)	111.78(18)
C(1)-C(9)-C(5)	109.11(17)
C(8)-C(9)-C(5)	104.17(18)
C(1)-C(9)-H(9)	104.1(15)
C(8)-C(9)-H(9)	114.5(15)
C(5)-C(9)-H(9)	113.3(15)
C(2)-C(10)-H(10C)	108.7(18)
C(2)-C(10)-H(10A)	109(2)
H(10C)-C(10)-H(10A)	104(3)
C(2)-C(10)-H(10B)	107(2)
H(10C)-C(10)-H(10B)	110(3)
H(10A)-C(10)-H(10B)	117(3)
C(3)-C(11)-H(11A)	110(2)
C(3)-C(11)-H(11B)	112(2)
H(11A)-C(11)-H(11B)	107(3)
C(3)-C(11)-H(11C)	113(2)
H(11A)-C(11)-H(11C)	106(3)
H(11B)-C(11)-H(11C)	109(3)
C(13)-C(12)-C(4)	126.5(3)
C(13)-C(12)-H(12)	119.7(19)
C(4)-C(12)-H(12)	113.7(19)
C(12)-C(13)-H(13A)	118(2)
C(12)-C(13)-H(13B)	120.6(19)
H(13A)-C(13)-H(13B)	121(3)
O(3)-C(14)-O(2)	123.5(2)
O(3)-C(14)-C(15)	124.5(2)
O(2)-C(14)-C(15)	111.95(19)
C(20)-C(15)-C(16)	119.6(2)
C(20)-C(15)-C(14)	122.6(2)
C(16)-C(15)-C(14)	117.8(2)
C(17)-C(16)-C(15)	120.2(2)
C(17)-C(16)-H(16)	121.7(17)
C(15)-C(16)-H(16)	118.1(17)

C(16)-C(17)-C(18)	119.4(2)
C(16)-C(17)-H(17)	114.5(17)
C(18)-C(17)-H(17)	126.1(16)
C(19)-C(18)-C(17)	121.5(2)
C(19)-C(18)-Br	119.44(19)
C(17)-C(18)-Br	119.07(19)
C(18)-C(19)-C(20)	118.9(2)
C(18)-C(19)-H(19)	122.1(17)
C(20)-C(19)-H(19)	118.9(17)
C(15)-C(20)-C(19)	120.3(2)
C(15)-C(20)-H(20)	118.1(15)
C(19)-C(20)-H(20)	121.5(15)

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for bs03171s. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Br 87(1)	71(1)	89(1)	-8(1)	56(1)	10(1)
O(1)74(1)	81(1)	84(1)	25(1)	52(1)	14(1)
O(2)50(1)	44(1)	62(1)	-1(1)	28(1)	5(1)
O(3)60(1)	70(1)	105(2)	-24(1)	46(1)	-13(1)
C(1)44(1)	42(1)	54(1)	-3(1)	23(1)	-6(1)
C(2)40(1)	50(1)	60(2)	-8(1)	19(1)	-4(1)
C(3)46(1)	44(1)	50(1)	-1(1)	22(1)	5(1)
C(4)51(1)	43(1)	41(1)	-4(1)	20(1)	-3(1)
C(5)40(1)	44(1)	40(1)	-5(1)	22(1)	-1(1)
C(6)43(1)	54(1)	53(1)	-12(1)	17(1)	-5(1)
C(7)58(2)	67(2)	43(1)	-4(1)	13(1)	10(1)
C(8)51(1)	49(1)	49(1)	2(1)	25(1)	7(1)
C(9)42(1)	39(1)	38(1)	-7(1)	16(1)	-1(1)
C(10)51(2)	69(2)	124(3)	3(2)	47(2)	1(2)
C(11)73(2)	71(2)	83(2)	19(2)	34(2)	22(2)
C(12)71(2)	47(1)	73(2)	2(1)	40(2)	-2(1)

C(13)134(3)	61(2)	117(3)	12(2)	88(3)	-2(2)
C(14)45(1)	47(1)	49(1)	4(1)	18(1)	4(1)
C(15)46(1)	40(1)	43(1)	5(1)	17(1)	7(1)
C(16)48(1)	47(1)	59(2)	2(1)	21(1)	0(1)
C(17)62(2)	44(1)	52(1)	-5(1)	20(1)	1(1)
C(18)58(1)	46(1)	54(1)	7(1)	27(1)	12(1)
C(19)46(1)	53(1)	65(2)	2(1)	25(1)	4(1)
C(20)50(1)	43(1)	53(1)	-3(1)	18(1)	2(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for bs03171s.

	x	y	z	U(eq)
H(2)	-3610(30)	2937(11)	4240(20)	52(7)
H(3)	-1810(30)	3853(9)	5940(20)	34(5)
H(4)	-1210(30)	3479(9)	3750(20)	38(6)
H(5)	1330(30)	3007(9)	4922(19)	29(5)
H(6A)	930(30)	3441(10)	7140(20)	47(6)
H(6B)	2570(40)	3485(11)	6920(20)	52(7)
H(7A)	3420(40)	2597(12)	7620(30)	65(8)
H(7B)	2120(40)	2649(13)	8330(30)	69(8)
H(8)	700(30)	1886(11)	6990(20)	57(7)
H(9)	-820(30)	2335(10)	4730(20)	47(6)
H(10C)	-5280(40)	2782(14)	5560(30)	76(9)
H(10A)	-4310(50)	3294(17)	6450(40)	109(14)
H(10B)	-5640(50)	3427(15)	4890(40)	100(12)
H(11A)	-2960(50)	4498(18)	4140(30)	98(11)
H(11B)	-4400(50)	4213(14)	4470(30)	85(11)
H(11C)	-4150(50)	4002(15)	3270(40)	95(12)
H(12)	730(40)	4313(13)	5390(30)	73(9)
H(13A)	1230(50)	4735(16)	3720(40)	104(12)
H(13B)	90(40)	4187(14)	2680(30)	84(10)
H(16)	1430(40)	461(12)	3970(30)	56(7)

H(17)	3190(30)	44(13)	3070(30)	55(7)
H(19)	7000(40)	1249(13)	4790(30)	72(8)
H(20)	5060(30)	1647(11)	5700(20)	52(7)

B.3 COMPOUND 95

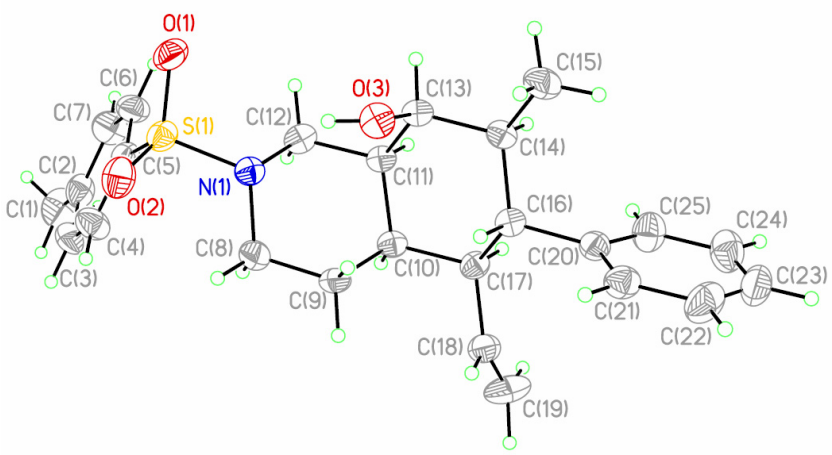


Table 1. Crystal data and structure refinement for bens021s.

Identification code	bens021s	
Empirical formula	C25 H31 N O3 S	
Formula weight	425.57	
Temperature	295(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	Cc	
Unit cell dimensions	a = 15.6571(16) Å	α= 90°.
	b = 5.7841(6) Å	β= 106.896(2)°.
	c = 26.019(3) Å	γ = 90°.
Volume	2254.6(4) $Å^3$	
Z	4	

Density (calculated)	1.254 Mg/m^3
Absorption coefficient	0.170 mm^{-1}
F(000)	912
Crystal size	? x ? x ? mm^3
Theta range for data collection	1.64 to 27.50°.
Index ranges	-20<=h<=20, -7<=k<=7, -33<=l<=33
Reflections collected	10587
Independent reflections	5135 [R(int) = 0.0406]
Completeness to theta = 27.50°	100.0 %
Absorption correction	None
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	5135 / 2 / 284
Goodness-of-fit on F^2	0.949
Final R indices [I>2sigma(I)]	R1 = 0.0570, wR2 = 0.1192
R indices (all data)	R1 = 0.0811, wR2 = 0.1285
Absolute structure parameter	0.40(8)
Largest diff. peak and hole	0.323 and -0.172 $e.Å^{-3}$

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for bens021s. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
S(1)	-828(1)	13147(1)	8807(1)	44(1)
O(1)	-301(2)	13644(4)	8455(1)	58(1)
N(1)	-167(2)	11731(4)	9317(1)	39(1)
C(1)	-3695(3)	6201(7)	7776(2)	79(1)
O(2)	-1204(2)	15002(4)	9032(1)	58(1)
C(2)	-2997(2)	8006(6)	8020(1)	54(1)
O(3)	1655(2)	12959(4)	9838(1)	47(1)
C(3)	-3065(2)	9417(7)	8436(2)	61(1)
C(4)	-2432(2)	11009(7)	8665(1)	55(1)
C(5)	-1686(2)	11219(5)	8479(1)	41(1)
C(6)	-1605(2)	9859(7)	8066(1)	54(1)
C(7)	-2261(3)	8273(7)	7840(2)	63(1)
C(8)	-554(2)	11202(6)	9760(1)	48(1)

C(9)	186(2)	10588(5)	10262(1)	43(1)
C(10)	756(2)	8581(5)	10172(1)	36(1)
C(11)	1064(2)	8971(5)	9666(1)	35(1)
C(12)	293(2)	9684(5)	9184(1)	41(1)
C(13)	1870(2)	10589(5)	9761(1)	36(1)
C(14)	2629(2)	9863(5)	10244(1)	37(1)
C(15)	3433(2)	11443(6)	10316(2)	54(1)
C(16)	2315(2)	9715(5)	10752(1)	36(1)
C(17)	1540(2)	7959(5)	10665(1)	38(1)
C(18)	1236(2)	7667(6)	11152(1)	47(1)
C(19)	1098(3)	5743(9)	11362(2)	74(1)
C(20)	3072(2)	9163(5)	11247(1)	41(1)
C(21)	3323(2)	10673(6)	11672(1)	50(1)
C(22)	4038(3)	10197(8)	12118(2)	68(1)
C(23)	4509(3)	8195(8)	12146(2)	68(1)
C(24)	4271(3)	6655(7)	11738(2)	67(1)
C(25)	3556(2)	7133(7)	11290(2)	58(1)

Table 3. Bond lengths [Å] and angles [°] for bens021s.

S(1)-O(1)	1.428(2)
S(1)-O(2)	1.428(3)
S(1)-N(1)	1.645(3)
S(1)-C(5)	1.764(3)
N(1)-C(12)	1.477(4)
N(1)-C(8)	1.484(4)
C(1)-C(2)	1.511(5)
C(1)-H(1A)	0.9600
C(1)-H(1B)	0.9600
C(1)-H(1C)	0.9600
C(2)-C(7)	1.372(5)
C(2)-C(3)	1.386(5)
O(3)-C(13)	1.439(3)
O(3)-H(3O)	0.86(5)
C(3)-C(4)	1.357(5)

C(3)-H(3A)	0.9300
C(4)-C(5)	1.394(4)
C(4)-H(4A)	0.9300
C(5)-C(6)	1.366(5)
C(6)-C(7)	1.376(5)
C(6)-H(6A)	0.9300
C(7)-H(7A)	0.9300
C(8)-C(9)	1.514(5)
C(8)-H(8A)	0.9700
C(8)-H(8B)	0.9700
C(9)-C(10)	1.523(4)
C(9)-H(9A)	0.9700
C(9)-H(9B)	0.9700
C(10)-C(17)	1.538(4)
C(10)-C(11)	1.546(4)
C(10)-H(10A)	0.9800
C(11)-C(12)	1.524(4)
C(11)-C(13)	1.531(4)
C(11)-H(11A)	0.9800
C(12)-H(12A)	0.9700
C(12)-H(12B)	0.9700
C(13)-C(14)	1.516(4)
C(13)-H(13A)	0.9800
C(14)-C(15)	1.522(4)
C(14)-C(16)	1.541(4)
C(14)-H(14A)	0.9800
C(15)-H(15A)	0.9600
C(15)-H(15B)	0.9600
C(15)-H(15C)	0.9600
C(16)-C(20)	1.509(4)
C(16)-C(17)	1.547(4)
C(16)-H(16A)	0.9800
C(17)-C(18)	1.489(4)
C(17)-H(17A)	0.9800
C(18)-C(19)	1.285(5)
C(18)-H(18A)	0.9300

C(19)-H(19A)	0.97(4)
C(19)-H(19B)	1.03(5)
C(20)-C(21)	1.374(4)
C(20)-C(25)	1.385(5)
C(21)-C(22)	1.385(5)
C(21)-H(21A)	0.9300
C(22)-C(23)	1.364(6)
C(22)-H(22A)	0.9300
C(23)-C(24)	1.353(6)
C(23)-H(23A)	0.9300
C(24)-C(25)	1.389(5)
C(24)-H(24A)	0.9300
C(25)-H(25A)	0.9300

O(1)-S(1)-O(2)	119.66(16)
O(1)-S(1)-N(1)	105.77(13)
O(2)-S(1)-N(1)	106.31(13)
O(1)-S(1)-C(5)	108.55(15)
O(2)-S(1)-C(5)	109.07(15)
N(1)-S(1)-C(5)	106.75(14)
C(12)-N(1)-C(8)	110.7(2)
C(12)-N(1)-S(1)	116.42(19)
C(8)-N(1)-S(1)	115.23(19)
C(2)-C(1)-H(1A)	109.5
C(2)-C(1)-H(1B)	109.5
H(1A)-C(1)-H(1B)	109.5
C(2)-C(1)-H(1C)	109.5
H(1A)-C(1)-H(1C)	109.5
H(1B)-C(1)-H(1C)	109.5
C(7)-C(2)-C(3)	117.6(3)
C(7)-C(2)-C(1)	120.8(4)
C(3)-C(2)-C(1)	121.6(4)
C(13)-O(3)-H(3O)	104(3)
C(4)-C(3)-C(2)	122.0(3)
C(4)-C(3)-H(3A)	119.0
C(2)-C(3)-H(3A)	119.0

C(3)-C(4)-C(5)	119.1(3)
C(3)-C(4)-H(4A)	120.5
C(5)-C(4)-H(4A)	120.5
C(6)-C(5)-C(4)	120.1(3)
C(6)-C(5)-S(1)	120.8(2)
C(4)-C(5)-S(1)	119.0(2)
C(5)-C(6)-C(7)	119.4(3)
C(5)-C(6)-H(6A)	120.3
C(7)-C(6)-H(6A)	120.3
C(2)-C(7)-C(6)	121.7(3)
C(2)-C(7)-H(7A)	119.1
C(6)-C(7)-H(7A)	119.1
N(1)-C(8)-C(9)	109.5(2)
N(1)-C(8)-H(8A)	109.8
C(9)-C(8)-H(8A)	109.8
N(1)-C(8)-H(8B)	109.8
C(9)-C(8)-H(8B)	109.8
H(8A)-C(8)-H(8B)	108.2
C(8)-C(9)-C(10)	112.5(3)
C(8)-C(9)-H(9A)	109.1
C(10)-C(9)-H(9A)	109.1
C(8)-C(9)-H(9B)	109.1
C(10)-C(9)-H(9B)	109.1
H(9A)-C(9)-H(9B)	107.8
C(9)-C(10)-C(17)	114.4(2)
C(9)-C(10)-C(11)	111.2(2)
C(17)-C(10)-C(11)	111.9(2)
C(9)-C(10)-H(10A)	106.3
C(17)-C(10)-H(10A)	106.3
C(11)-C(10)-H(10A)	106.3
C(12)-C(11)-C(13)	112.8(2)
C(12)-C(11)-C(10)	111.8(2)
C(13)-C(11)-C(10)	113.4(2)
C(12)-C(11)-H(11A)	106.1
C(13)-C(11)-H(11A)	106.1
C(10)-C(11)-H(11A)	106.1

N(1)-C(12)-C(11)	110.3(2)
N(1)-C(12)-H(12A)	109.6
C(11)-C(12)-H(12A)	109.6
N(1)-C(12)-H(12B)	109.6
C(11)-C(12)-H(12B)	109.6
H(12A)-C(12)-H(12B)	108.1
O(3)-C(13)-C(14)	107.9(2)
O(3)-C(13)-C(11)	113.0(2)
C(14)-C(13)-C(11)	112.1(2)
O(3)-C(13)-H(13A)	107.9
C(14)-C(13)-H(13A)	107.9
C(11)-C(13)-H(13A)	107.9
C(13)-C(14)-C(15)	110.9(3)
C(13)-C(14)-C(16)	110.9(2)
C(15)-C(14)-C(16)	112.7(3)
C(13)-C(14)-H(14A)	107.3
C(15)-C(14)-H(14A)	107.3
C(16)-C(14)-H(14A)	107.3
C(14)-C(15)-H(15A)	109.5
C(14)-C(15)-H(15B)	109.5
H(15A)-C(15)-H(15B)	109.5
C(14)-C(15)-H(15C)	109.5
H(15A)-C(15)-H(15C)	109.5
H(15B)-C(15)-H(15C)	109.5
C(20)-C(16)-C(14)	112.2(2)
C(20)-C(16)-C(17)	112.0(2)
C(14)-C(16)-C(17)	110.0(2)
C(20)-C(16)-H(16A)	107.5
C(14)-C(16)-H(16A)	107.5
C(17)-C(16)-H(16A)	107.5
C(18)-C(17)-C(10)	111.1(2)
C(18)-C(17)-C(16)	112.3(2)
C(10)-C(17)-C(16)	111.8(2)
C(18)-C(17)-H(17A)	107.1
C(10)-C(17)-H(17A)	107.1
C(16)-C(17)-H(17A)	107.1

C(19)-C(18)-C(17)	126.5(4)
C(19)-C(18)-H(18A)	116.8
C(17)-C(18)-H(18A)	116.8
C(18)-C(19)-H(19A)	123(2)
C(18)-C(19)-H(19B)	122(2)
H(19A)-C(19)-H(19B)	115(3)
C(21)-C(20)-C(25)	116.9(3)
C(21)-C(20)-C(16)	121.5(3)
C(25)-C(20)-C(16)	121.6(3)
C(20)-C(21)-C(22)	121.3(3)
C(20)-C(21)-H(21A)	119.3
C(22)-C(21)-H(21A)	119.3
C(23)-C(22)-C(21)	120.5(4)
C(23)-C(22)-H(22A)	119.7
C(21)-C(22)-H(22A)	119.7
C(24)-C(23)-C(22)	119.7(4)
C(24)-C(23)-H(23A)	120.2
C(22)-C(23)-H(23A)	120.2
C(23)-C(24)-C(25)	119.9(4)
C(23)-C(24)-H(24A)	120.0
C(25)-C(24)-H(24A)	120.0
C(20)-C(25)-C(24)	121.7(3)
C(20)-C(25)-H(25A)	119.1
C(24)-C(25)-H(25A)	119.1

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for bens021s. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
S(1)43(1)	44(1)	43(1)	7(1)	9(1)	-7(1)
O(1)51(1)	70(2)	48(1)	20(1)	9(1)	-12(1)
N(1)40(1)	39(1)	38(1)	-1(1)	11(1)	-4(1)
C(1)65(2)	75(3)	84(3)	-3(2)	2(2)	-26(2)
O(2)63(1)	39(1)	64(2)	4(1)	9(1)	3(1)
C(2)40(2)	59(2)	54(2)	4(2)	-1(2)	-9(2)
O(3)53(2)	31(1)	57(2)	-2(1)	16(1)	-5(1)
C(3)36(2)	82(3)	65(2)	0(2)	16(2)	-5(2)
C(4)43(2)	70(2)	53(2)	-15(2)	15(2)	-6(2)
C(5)40(2)	45(2)	37(2)	3(1)	8(1)	-3(1)
C(6)41(2)	79(3)	44(2)	-3(2)	15(2)	-9(2)
C(7)60(2)	73(3)	54(2)	-15(2)	14(2)	-9(2)
C(8)41(2)	53(2)	53(2)	7(2)	18(2)	0(2)
C(9)45(2)	55(2)	34(2)	1(1)	18(1)	-1(2)
C(10)39(2)	33(2)	38(2)	-2(1)	13(1)	-9(1)
C(11)43(2)	28(1)	37(2)	-2(1)	15(1)	-3(1)
C(12)52(2)	34(2)	36(2)	-7(1)	11(2)	-10(1)
C(13)43(2)	32(2)	36(2)	-3(1)	16(1)	-4(1)
C(14)37(2)	36(2)	41(2)	-6(1)	14(1)	-5(1)
C(15)48(2)	59(2)	60(2)	-2(2)	23(2)	-12(2)
C(16)42(2)	31(2)	36(2)	-3(1)	13(1)	-3(1)
C(17)42(2)	35(2)	36(2)	2(1)	11(1)	-5(1)
C(18)47(2)	56(2)	40(2)	-1(2)	15(2)	-5(2)
C(19)104(4)	75(3)	53(2)	3(2)	41(3)	-24(3)
C(20)38(2)	44(2)	42(2)	2(1)	13(1)	-7(1)
C(21)54(2)	53(2)	45(2)	-8(2)	17(2)	-4(2)
C(22)74(3)	78(3)	43(2)	-8(2)	3(2)	-18(2)
C(23)51(2)	87(3)	56(2)	19(2)	-1(2)	-5(2)
C(24)58(2)	59(2)	80(3)	13(2)	11(2)	10(2)
C(25)58(2)	54(2)	55(2)	-9(2)	5(2)	1(2)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^{-3}) for bens021s.

	x	y	z	U(eq)
H(1A)	-4157	6251	7951	118
H(1B)	-3424	4697	7823	118
H(1C)	-3949	6509	7400	118
H(3O)	1140(30)	13160(70)	9611(17)	72(14)
H(3A)	-3560	9269	8563	73
H(4A)	-2495	11946	8942	66
H(6A)	-1109	10003	7940	65
H(7A)	-2206	7360	7557	75
H(8A)	-968	9918	9659	58
H(8B)	-881	12533	9830	58
H(9A)	-74	10185	10546	52
H(9B)	564	11931	10378	52
H(10A)	364	7224	10097	43
H(11A)	1266	7461	9575	42
H(12A)	517	10039	8883	49
H(12B)	-127	8415	9080	49
H(13A)	2086	10520	9444	44
H(14A)	2812	8306	10172	45
H(15A)	3598	11490	9989	81
H(15B)	3924	10862	10601	81
H(15C)	3284	12972	10405	81
H(16A)	2081	11237	10807	43
H(17A)	1770	6458	10591	45
H(18A)	1136	9011	11322	57
H(19A)	870(20)	5660(60)	11668(15)	56(10)
H(19B)	1210(30)	4170(80)	11209(18)	89(14)
H(21A)	3006	12042	11661	60
H(22A)	4198	11251	12399	81
H(23A)	4992	7890	12445	82
H(24A)	4585	5278	11757	81

H(25A)	3399	6062	11012	70

B.4 COMPOUND 170

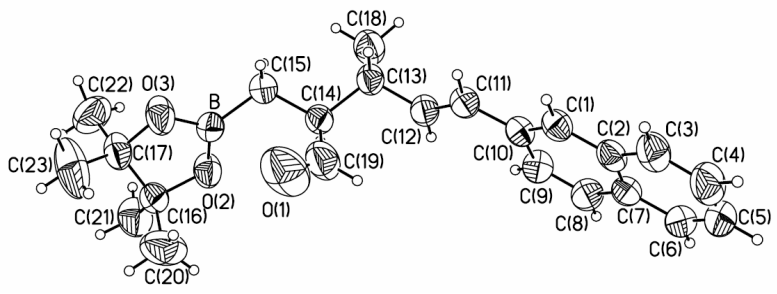


Table 1. Crystal data and structure refinement for bs1022.

Identification code	bs1022	
Empirical formula	C23 H29 B O3	
Formula weight	364.27	
Temperature	295(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	Pca2(1)	
Unit cell dimensions	a = 12.5986(6) Å	α= 90°.
	b = 8.2876(4) Å	β= 90°.
	c = 20.2572(10) Å	γ = 90°.
Volume	2115.10(18) $Å^3$	
Z	4	
Density (calculated)	1.144 Mg/m^3	
Absorption coefficient	0.073 mm^{-1}	
F(000)	784	
Crystal size	0.29 x 0.21 x 0.21 mm^3	
Theta range for data collection	2.01 to 27.50°.	
Index ranges	-16<=h<=16, -10<=k<=10, -26<=l<=26	
Reflections collected	19669	
Independent reflections	4849 [R(int) = 0.0223]	

Completeness to theta = 27.50°	100.0 %
Absorption correction	None
Max. and min. transmission	0.9848 and 0.9791
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4849 / 1 / 250
Goodness-of-fit on F^2	1.139
Final R indices [I>2sigma(I)]	R1 = 0.0492, wR2 = 0.1268
R indices (all data)	R1 = 0.0614, wR2 = 0.1335
Absolute structure parameter	0.4(12)
Extinction coefficient	0.0000(16)
Largest diff. peak and hole	0.213 and -0.139 e.$Å^{-3}$

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for bs1022. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
B	5226(2)	8579(2)	1043(1)	53(1)
C(1)	198(2)	12945(2)	3067(1)	51(1)
O(1)	2963(2)	8806(3)	1121(2)	130(1)
O(2)	5405(1)	7171(2)	1357(1)	64(1)
C(2)	-709(2)	12824(2)	3472(1)	53(1)
O(3)	5453(2)	8509(2)	397(1)	80(1)
C(3)	-1690(2)	13561(3)	3310(1)	69(1)
C(4)	-2546(2)	13400(3)	3713(2)	82(1)
C(5)	-2476(2)	12507(3)	4302(2)	79(1)
C(6)	-1560(2)	11790(3)	4469(1)	69(1)
C(7)	-649(2)	11911(2)	4060(1)	54(1)
C(8)	324(2)	11139(3)	4215(1)	61(1)
C(9)	1174(2)	11274(2)	3812(1)	57(1)
C(10)	1134(1)	12174(2)	3218(1)	49(1)
C(11)	2036(2)	12267(2)	2766(1)	52(1)
C(12)	2925(2)	11430(2)	2791(1)	56(1)
C(13)	3836(2)	11600(2)	2317(1)	54(1)
C(14)	4067(2)	10003(2)	1941(1)	52(1)
C(15)	4899(2)	10187(2)	1399(1)	67(1)

C(16)	5607(2)	5945(2)	857(1)	57(1)
C(17)	5966(2)	6969(3)	266(1)	66(1)
C(18)	4822(2)	12181(3)	2686(1)	74(1)
C(19)	3082(2)	9271(3)	1668(2)	87(1)
C(20)	4563(2)	5082(4)	739(2)	115(1)
C(21)	6430(2)	4780(3)	1113(1)	86(1)
C(22)	7167(2)	7313(4)	276(2)	105(1)
C(23)	5637(4)	6405(5)	-409(2)	122(1)

Table 3. Bond lengths [Å] and angles [°] for bs1022.

B-O(3)	1.343(3)
B-O(2)	1.347(3)
B-C(15)	1.570(3)
C(1)-C(10)	1.375(3)
C(1)-C(2)	1.410(3)
C(1)-H(1)	0.9300
O(1)-C(19)	1.182(4)
O(2)-C(16)	1.458(2)
C(2)-C(7)	1.413(3)
C(2)-C(3)	1.417(3)
O(3)-C(17)	1.455(2)
C(3)-C(4)	1.360(4)
C(3)-H(3)	0.9300
C(4)-C(5)	1.407(4)
C(4)-H(4)	0.9300
C(5)-C(6)	1.341(4)
C(5)-H(5)	0.9300
C(6)-C(7)	1.420(3)
C(6)-H(6)	0.9300
C(7)-C(8)	1.418(3)
C(8)-C(9)	1.351(3)
C(8)-H(8)	0.9300
C(9)-C(10)	1.416(3)
C(9)-H(9)	0.9300

C(10)-C(11)	1.462(3)
C(11)-C(12)	1.318(3)
C(11)-H(11)	0.9300
C(12)-C(13)	1.502(3)
C(12)-H(12)	0.9300
C(13)-C(18)	1.528(3)
C(13)-C(14)	1.554(3)
C(13)-H(13)	0.9800
C(14)-C(19)	1.488(3)
C(14)-C(15)	1.526(3)
C(14)-H(14)	0.9800
C(15)-H(15A)	0.9700
C(15)-H(15B)	0.9700
C(16)-C(21)	1.509(3)
C(16)-C(20)	1.516(4)
C(16)-C(17)	1.536(3)
C(17)-C(23)	1.502(4)
C(17)-C(22)	1.539(4)
C(18)-H(18A)	0.9600
C(18)-H(18B)	0.9600
C(18)-H(18C)	0.9600
C(19)-H(19)	0.9300
C(20)-H(20A)	0.9600
C(20)-H(20B)	0.9600
C(20)-H(20C)	0.9600
C(21)-H(21A)	0.9600
C(21)-H(21B)	0.9600
C(21)-H(21C)	0.9600
C(22)-H(22A)	0.9600
C(22)-H(22B)	0.9600
C(22)-H(22C)	0.9600
C(23)-H(23A)	0.9600
C(23)-H(23B)	0.9600
C(23)-H(23C)	0.9600

O(3)-B-O(2)	112.80(17)

O(3)-B-C(15)	122.69(18)
O(2)-B-C(15)	124.22(18)
C(10)-C(1)-C(2)	122.20(17)
C(10)-C(1)-H(1)	118.9
C(2)-C(1)-H(1)	118.9
B-O(2)-C(16)	107.75(15)
C(7)-C(2)-C(1)	118.97(17)
C(7)-C(2)-C(3)	118.26(18)
C(1)-C(2)-C(3)	122.76(19)
B-O(3)-C(17)	108.06(15)
C(4)-C(3)-C(2)	120.7(2)
C(4)-C(3)-H(3)	119.7
C(2)-C(3)-H(3)	119.7
C(3)-C(4)-C(5)	120.7(2)
C(3)-C(4)-H(4)	119.6
C(5)-C(4)-H(4)	119.6
C(6)-C(5)-C(4)	120.1(2)
C(6)-C(5)-H(5)	119.9
C(4)-C(5)-H(5)	119.9
C(5)-C(6)-C(7)	121.1(2)
C(5)-C(6)-H(6)	119.4
C(7)-C(6)-H(6)	119.4
C(2)-C(7)-C(8)	118.33(17)
C(2)-C(7)-C(6)	119.10(19)
C(8)-C(7)-C(6)	122.6(2)
C(9)-C(8)-C(7)	120.96(19)
C(9)-C(8)-H(8)	119.5
C(7)-C(8)-H(8)	119.5
C(8)-C(9)-C(10)	121.90(18)
C(8)-C(9)-H(9)	119.1
C(10)-C(9)-H(9)	119.1
C(1)-C(10)-C(9)	117.63(17)
C(1)-C(10)-C(11)	120.22(16)
C(9)-C(10)-C(11)	122.14(15)
C(12)-C(11)-C(10)	127.53(16)
C(12)-C(11)-H(11)	116.2

C(10)-C(11)-H(11)	116.2
C(11)-C(12)-C(13)	125.12(17)
C(11)-C(12)-H(12)	117.4
C(13)-C(12)-H(12)	117.4
C(12)-C(13)-C(18)	109.80(18)
C(12)-C(13)-C(14)	112.12(15)
C(18)-C(13)-C(14)	110.82(16)
C(12)-C(13)-H(13)	108.0
C(18)-C(13)-H(13)	108.0
C(14)-C(13)-H(13)	108.0
C(19)-C(14)-C(15)	110.2(2)
C(19)-C(14)-C(13)	111.90(16)
C(15)-C(14)-C(13)	113.39(15)
C(19)-C(14)-H(14)	107.0
C(15)-C(14)-H(14)	107.0
C(13)-C(14)-H(14)	107.0
C(14)-C(15)-B	115.20(16)
C(14)-C(15)-H(15A)	108.5
B-C(15)-H(15A)	108.5
C(14)-C(15)-H(15B)	108.5
B-C(15)-H(15B)	108.5
H(15A)-C(15)-H(15B)	107.5
O(2)-C(16)-C(21)	109.06(18)
O(2)-C(16)-C(20)	106.67(19)
C(21)-C(16)-C(20)	110.4(2)
O(2)-C(16)-C(17)	102.01(14)
C(21)-C(16)-C(17)	114.82(18)
C(20)-C(16)-C(17)	113.2(2)
O(3)-C(17)-C(23)	108.41(19)
O(3)-C(17)-C(16)	102.23(15)
C(23)-C(17)-C(16)	117.1(2)
O(3)-C(17)-C(22)	105.8(2)
C(23)-C(17)-C(22)	109.9(3)
C(16)-C(17)-C(22)	112.4(2)
C(13)-C(18)-H(18A)	109.5
C(13)-C(18)-H(18B)	109.5

H(18A)-C(18)-H(18B) 109.5
C(13)-C(18)-H(18C) 109.5
H(18A)-C(18)-H(18C) 109.5
H(18B)-C(18)-H(18C) 109.5
O(1)-C(19)-C(14) 126.0(3)
O(1)-C(19)-H(19) 117.0
C(14)-C(19)-H(19) 117.0
C(16)-C(20)-H(20A) 109.5
C(16)-C(20)-H(20B) 109.5
H(20A)-C(20)-H(20B) 109.5
C(16)-C(20)-H(20C) 109.5
H(20A)-C(20)-H(20C) 109.5
H(20B)-C(20)-H(20C) 109.5
C(16)-C(21)-H(21A) 109.5
C(16)-C(21)-H(21B) 109.5
H(21A)-C(21)-H(21B) 109.5
C(16)-C(21)-H(21C) 109.5
H(21A)-C(21)-H(21C) 109.5
H(21B)-C(21)-H(21C) 109.5
C(17)-C(22)-H(22A) 109.5
C(17)-C(22)-H(22B) 109.5
H(22A)-C(22)-H(22B) 109.5
C(17)-C(22)-H(22C) 109.5
H(22A)-C(22)-H(22C) 109.5
H(22B)-C(22)-H(22C) 109.5
C(17)-C(23)-H(23A) 109.5
C(17)-C(23)-H(23B) 109.5
H(23A)-C(23)-H(23B) 109.5
C(17)-C(23)-H(23C) 109.5
H(23A)-C(23)-H(23C) 109.5
H(23B)-C(23)-H(23C) 109.5

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for bs1022. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
B 52(1)	53(1)	55(1)	-1(1)	8(1)	2(1)
C(1)59(1)	48(1)	46(1)	-3(1)	-5(1)	5(1)
O(1)118(2)	130(2)	142(2)	-50(2)	-29(2)	-14(1)
O(2)79(1)	64(1)	49(1)	2(1)	8(1)	16(1)
C(2)54(1)	47(1)	56(1)	-14(1)	-5(1)	2(1)
O(3)121(1)	61(1)	58(1)	10(1)	23(1)	35(1)
C(3)61(1)	70(1)	76(1)	-11(1)	-5(1)	11(1)
C(4)52(1)	85(1)	110(2)	-21(2)	-4(1)	10(1)
C(5)62(1)	73(1)	102(2)	-17(1)	22(1)	-6(1)
C(6)72(1)	60(1)	74(1)	-9(1)	18(1)	-10(1)
C(7)59(1)	49(1)	55(1)	-11(1)	3(1)	-6(1)
C(8)68(1)	61(1)	54(1)	7(1)	2(1)	1(1)
C(9)57(1)	62(1)	53(1)	5(1)	-3(1)	7(1)
C(10)53(1)	47(1)	48(1)	-5(1)	-3(1)	3(1)
C(11)60(1)	50(1)	45(1)	1(1)	-1(1)	5(1)
C(12)66(1)	53(1)	50(1)	6(1)	7(1)	10(1)
C(13)58(1)	52(1)	50(1)	3(1)	6(1)	10(1)
C(14)56(1)	45(1)	55(1)	3(1)	5(1)	8(1)
C(15)72(1)	54(1)	76(1)	-7(1)	24(1)	-1(1)
C(16)59(1)	51(1)	60(1)	-2(1)	4(1)	5(1)
C(17)84(1)	62(1)	51(1)	-1(1)	7(1)	24(1)
C(18)74(1)	75(1)	73(1)	-16(1)	3(1)	0(1)
C(19)65(1)	78(2)	116(2)	-31(2)	9(1)	3(1)
C(20)74(2)	79(2)	193(4)	-19(2)	11(2)	-14(1)
C(21)103(2)	73(1)	82(2)	14(1)	2(1)	32(1)
C(22)83(2)	95(2)	138(3)	18(2)	47(2)	5(1)
C(23)168(3)	139(3)	59(1)	-27(2)	-20(2)	73(3)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^{-3}) for bs1022.

	x	y	z	U(eq)
H(1)	162	13567	2686	62
H(3)	-1748	14161	2923	83
H(4)	-3186	13886	3598	99
H(5)	-3065	12414	4576	95
H(6)	-1522	11203	4860	83
H(8)	378	10531	4599	73
H(9)	1804	10761	3928	68
H(11)	1977	13003	2421	62
H(12)	2994	10674	3127	68
H(13)	3645	12424	1991	64
H(14)	4354	9239	2264	62
H(15A)	5530	10667	1590	80
H(15B)	4629	10931	1070	80
H(18A)	4676	13201	2891	111
H(18B)	5399	12301	2380	111
H(18C)	5011	11406	3018	111
H(19)	2508	9170	1953	104
H(20A)	4283	4709	1152	173
H(20B)	4678	4179	451	173
H(20C)	4068	5813	539	173
H(21A)	7071	5356	1215	129
H(21B)	6576	3979	783	129
H(21C)	6168	4264	1505	129
H(22A)	7325	8176	-24	158
H(22B)	7546	6361	144	158
H(22C)	7378	7615	714	158
H(23A)	4892	6167	-409	183
H(23B)	6029	5451	-523	183
H(23C)	5781	7237	-726	183

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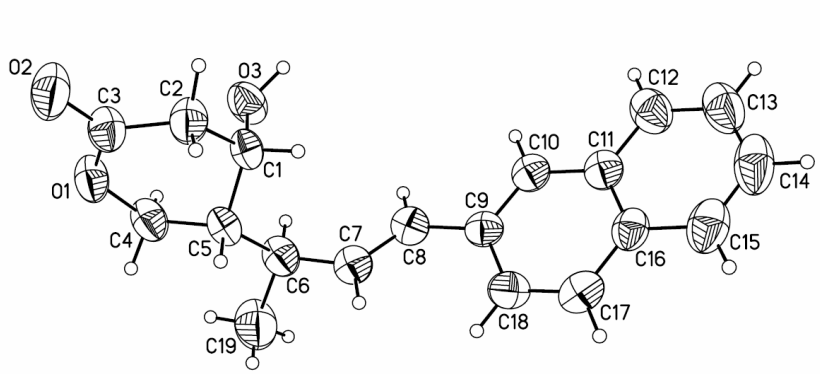

Table 1. Crystal data and structure refinement for bens819s.

Identification code	bens819s	
Empirical formula	C20.50 H20 O3	
Formula weight	314.36	
Temperature	295(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2(1)/n	
Unit cell dimensions	a = 10.3590(5) Å	α= 90°.
	b = 21.7109(10) Å	β= 106.2630(10)°.
	c = 16.1006(7) Å	γ = 90°.
Volume	3476.2(3) $Å^3$	
Z	8	
Density (calculated)	1.201 Mg/m^3	
Absorption coefficient	0.080 mm^{-1}	
F(000)	1336	
Crystal size	0.27 x 0.21 x 0.08 mm^3	
Theta range for data collection	1.62 to 25.00°.	
Index ranges	-12<=h<=12, -25<=k<=25, -19<=l<=19	
Reflections collected	27806	
Independent reflections	6121 [R(int) = 0.0685]	
Completeness to theta = 25.00°	100.0 %	
Absorption correction	None	
Max. and min. transmission	0.9937 and 0.9788	

Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	6121 / 0 / 432
Goodness-of-fit on F^2	1.079
Final R indices [I>2sigma(I)]	R1 = 0.0764, wR2 = 0.1658
R indices (all data)	R1 = 0.1535, wR2 = 0.1899
Largest diff. peak and hole	0.176 and -0.129 e.Å^{-3}

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3) for bens819s. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	5103(3)	1857(1)	8135(2)	84(1)
O(2)	4256(3)	1679(1)	9197(2)	113(1)
O(3)	3413(3)	3084(1)	7506(2)	89(1)
O(4)	4473(3)	-997(1)	8336(2)	85(1)
O(5)	2896(3)	-894(2)	7132(2)	130(1)
O(6)	4358(2)	436(1)	8811(2)	74(1)
C(1)	4619(4)	3132(2)	8180(2)	65(1)
C(2)	4581(4)	2731(2)	8937(2)	82(1)
C(3)	4618(4)	2062(2)	8761(3)	80(1)
C(4)	5503(4)	2264(2)	7534(2)	81(1)
C(5)	5770(3)	2922(2)	7836(2)	65(1)
C(6)	5938(4)	3347(2)	7102(2)	77(1)
C(7)	6253(4)	3980(2)	7441(2)	73(1)
C(8)	5462(4)	4460(2)	7244(2)	69(1)
C(9)	5696(4)	5086(2)	7595(2)	65(1)
C(10)	4646(4)	5485(2)	7491(2)	69(1)
C(11)	4807(4)	6073(2)	7877(2)	71(1)
C(12)	3731(5)	6480(2)	7796(3)	96(1)
C(13)	3923(7)	7034(2)	8199(4)	109(2)
C(14)	5179(8)	7213(2)	8710(4)	118(2)
C(15)	6251(6)	6833(2)	8804(3)	105(2)
C(16)	6091(4)	6252(2)	8377(2)	73(1)
C(17)	7184(4)	5848(2)	8451(3)	88(1)
C(18)	6987(4)	5278(2)	8082(3)	81(1)

C(19)	6993(5)	3105(2)	6692(3)	127(2)
C(20)	5235(3)	258(1)	8311(2)	57(1)
C(21)	4396(4)	-58(2)	7495(2)	72(1)
C(22)	3856(4)	-668(2)	7646(3)	84(1)
C(23)	5528(3)	-746(2)	9042(2)	68(1)
C(24)	6263(3)	-201(1)	8814(2)	53(1)
C(25)	7251(3)	67(2)	9630(2)	59(1)
C(26)	7888(3)	643(2)	9432(2)	63(1)
C(27)	7856(3)	1188(2)	9795(2)	65(1)
C(28)	8477(3)	1763(2)	9629(2)	63(1)
C(29)	8267(3)	2298(2)	10026(2)	68(1)
C(30)	8815(4)	2869(2)	9876(2)	68(1)
C(31)	8568(4)	3425(2)	10254(3)	97(1)
C(32)	9100(6)	3966(2)	10076(4)	112(2)
C(33)	9927(6)	3975(3)	9528(4)	117(2)
C(34)	10197(5)	3451(3)	9155(3)	106(1)
C(35)	9634(4)	2884(2)	9309(3)	82(1)
C(36)	9859(4)	2336(2)	8920(3)	96(1)
C(37)	9289(4)	1795(2)	9059(2)	83(1)
C(38)	8328(4)	-403(2)	10066(2)	82(1)
C(39)	6398(10)	4874(8)	415(6)	207(4)
C(40)	5812(17)	5391(5)	387(6)	190(3)
C(41)	4504(14)	5515(3)	77(6)	157(2)

Table 3. Bond lengths [Å] and angles [°] for bens819s.

O(1)-C(3)	1.322(4)
O(1)-C(4)	1.452(4)
O(2)-C(3)	1.212(4)
O(3)-C(1)	1.410(4)
O(4)-C(22)	1.325(5)
O(4)-C(23)	1.446(4)
O(5)-C(22)	1.206(4)
O(6)-C(20)	1.426(4)
C(1)-C(2)	1.507(4)

C(1)-C(5)	1.518(4)
C(2)-C(3)	1.482(5)
C(4)-C(5)	1.510(5)
C(5)-C(6)	1.548(5)
C(6)-C(7)	1.482(5)
C(6)-C(19)	1.521(5)
C(7)-C(8)	1.309(4)
C(8)-C(9)	1.466(5)
C(9)-C(10)	1.363(5)
C(9)-C(18)	1.411(5)
C(10)-C(11)	1.409(5)
C(11)-C(12)	1.399(5)
C(11)-C(16)	1.403(5)
C(12)-C(13)	1.355(6)
C(13)-C(14)	1.386(7)
C(14)-C(15)	1.357(6)
C(15)-C(16)	1.423(6)
C(16)-C(17)	1.410(5)
C(17)-C(18)	1.362(5)
C(20)-C(24)	1.516(4)
C(20)-C(21)	1.521(4)
C(21)-C(22)	1.483(5)
C(23)-C(24)	1.507(4)
C(24)-C(25)	1.536(4)
C(25)-C(26)	1.488(4)
C(25)-C(38)	1.530(4)
C(26)-C(27)	1.324(4)
C(27)-C(28)	1.464(4)
C(28)-C(29)	1.372(4)
C(28)-C(37)	1.411(5)
C(29)-C(30)	1.411(5)
C(30)-C(31)	1.408(5)
C(30)-C(35)	1.411(5)
C(31)-C(32)	1.361(6)
C(32)-C(33)	1.390(6)
C(33)-C(34)	1.351(6)

C(34)-C(35)	1.413(6)
C(35)-C(36)	1.394(5)
C(36)-C(37)	1.361(5)
C(39)-C(40)	1.271(10)
C(39)-C(41)#1	1.342(10)
C(40)-C(41)	1.334(11)
C(41)-C(39)#1	1.342(10)

C(3)-O(1)-C(4)	123.0(3)
C(22)-O(4)-C(23)	122.5(3)
O(3)-C(1)-C(2)	111.1(3)
O(3)-C(1)-C(5)	108.3(3)
C(2)-C(1)-C(5)	108.8(3)
C(3)-C(2)-C(1)	113.8(3)
O(2)-C(3)-O(1)	117.2(4)
O(2)-C(3)-C(2)	122.1(4)
O(1)-C(3)-C(2)	120.6(4)
O(1)-C(4)-C(5)	114.9(3)
C(4)-C(5)-C(1)	108.0(3)
C(4)-C(5)-C(6)	111.6(3)
C(1)-C(5)-C(6)	111.6(3)
C(7)-C(6)-C(19)	111.7(3)
C(7)-C(6)-C(5)	109.4(3)
C(19)-C(6)-C(5)	112.0(3)
C(8)-C(7)-C(6)	126.3(4)
C(7)-C(8)-C(9)	128.3(4)
C(10)-C(9)-C(18)	118.6(4)
C(10)-C(9)-C(8)	120.1(3)
C(18)-C(9)-C(8)	121.1(3)
C(9)-C(10)-C(11)	122.0(4)
C(12)-C(11)-C(16)	118.7(4)
C(12)-C(11)-C(10)	122.6(4)
C(16)-C(11)-C(10)	118.7(4)
C(13)-C(12)-C(11)	120.7(5)
C(12)-C(13)-C(14)	121.3(5)
C(15)-C(14)-C(13)	119.9(5)

C(14)-C(15)-C(16)	120.3(5)
C(11)-C(16)-C(17)	119.0(4)
C(11)-C(16)-C(15)	119.1(4)
C(17)-C(16)-C(15)	121.9(5)
C(18)-C(17)-C(16)	120.6(4)
C(17)-C(18)-C(9)	120.9(4)
O(6)-C(20)-C(24)	109.9(2)
O(6)-C(20)-C(21)	108.0(3)
C(24)-C(20)-C(21)	108.1(3)
C(22)-C(21)-C(20)	114.3(3)
O(5)-C(22)-O(4)	117.9(4)
O(5)-C(22)-C(21)	121.8(4)
O(4)-C(22)-C(21)	120.2(4)
O(4)-C(23)-C(24)	115.3(3)
C(23)-C(24)-C(20)	108.6(2)
C(23)-C(24)-C(25)	110.5(3)
C(20)-C(24)-C(25)	114.1(3)
C(26)-C(25)-C(38)	110.4(3)
C(26)-C(25)-C(24)	111.3(3)
C(38)-C(25)-C(24)	111.5(3)
C(27)-C(26)-C(25)	126.0(3)
C(26)-C(27)-C(28)	128.0(3)
C(29)-C(28)-C(37)	117.6(3)
C(29)-C(28)-C(27)	120.2(3)
C(37)-C(28)-C(27)	122.2(3)
C(28)-C(29)-C(30)	122.6(3)
C(31)-C(30)-C(29)	123.3(4)
C(31)-C(30)-C(35)	118.3(4)
C(29)-C(30)-C(35)	118.4(4)
C(32)-C(31)-C(30)	121.0(5)
C(31)-C(32)-C(33)	120.2(5)
C(34)-C(33)-C(32)	120.7(5)
C(33)-C(34)-C(35)	120.6(5)
C(36)-C(35)-C(34)	122.4(5)
C(36)-C(35)-C(30)	118.5(4)
C(34)-C(35)-C(30)	119.1(4)

C(37)-C(36)-C(35)	121.9(4)
C(36)-C(37)-C(28)	120.9(4)
C(40)-C(39)-C(41)#1	106.8(10)
C(39)-C(40)-C(41)	128.1(11)
C(40)-C(41)-C(39)#1	124.0(9)

Symmetry transformations used to generate equivalent atoms:

#1 -x+1,-y+1,-z

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for bens819s. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)116(2)	56(2)	86(2)	2(1)	36(2)	13(1)
O(2)168(3)	70(2)	117(2)	16(2)	65(2)	2(2)
O(3)71(2)	80(2)	102(2)	-8(2)	0(2)	14(2)
O(4)83(2)	65(2)	100(2)	-2(2)	15(2)	-22(1)
O(5)102(2)	138(3)	127(3)	-3(2)	-6(2)	-59(2)
O(6)77(2)	67(2)	89(2)	4(1)	42(1)	8(1)
C(1)76(3)	52(2)	64(2)	-6(2)	15(2)	8(2)
C(2)109(3)	64(3)	80(3)	0(2)	39(2)	0(2)
C(3)94(3)	68(3)	78(3)	11(2)	23(2)	8(2)
C(4)99(3)	73(3)	74(3)	4(2)	32(2)	21(2)
C(5)71(2)	59(2)	63(2)	-2(2)	14(2)	14(2)
C(6)91(3)	76(3)	67(2)	8(2)	29(2)	15(2)
C(7)75(2)	77(3)	66(2)	4(2)	18(2)	0(2)
C(8)75(3)	77(3)	52(2)	7(2)	14(2)	3(2)
C(9)68(3)	75(3)	57(2)	5(2)	25(2)	-1(2)
C(10)75(3)	74(3)	59(2)	10(2)	21(2)	-3(2)
C(11)85(3)	74(3)	59(2)	11(2)	28(2)	-1(2)
C(12)112(4)	87(3)	96(3)	18(3)	40(3)	20(3)
C(13)153(5)	78(4)	116(4)	17(3)	71(4)	23(3)
C(14)199(7)	70(3)	106(4)	1(3)	79(5)	-11(4)
C(15)144(5)	83(3)	95(3)	2(3)	46(3)	-22(3)
C(16)91(3)	63(3)	69(2)	7(2)	30(2)	-8(2)

C(17)79(3)	96(3)	87(3)	5(3)	20(2)	-16(3)
C(18)70(3)	87(3)	89(3)	1(2)	27(2)	2(2)
C(19)175(5)	99(3)	144(4)	10(3)	106(4)	18(3)
C(20)59(2)	60(2)	55(2)	3(2)	19(2)	-9(2)
C(21)64(2)	81(3)	68(2)	4(2)	13(2)	-13(2)
C(22)72(3)	91(3)	87(3)	-9(3)	20(3)	-22(2)
C(23)74(2)	59(2)	73(2)	3(2)	25(2)	3(2)
C(24)53(2)	54(2)	55(2)	1(2)	22(2)	3(2)
C(25)59(2)	70(2)	52(2)	-3(2)	22(2)	0(2)
C(26)55(2)	79(3)	56(2)	-11(2)	18(2)	-5(2)
C(27)62(2)	78(3)	56(2)	-2(2)	18(2)	-2(2)
C(28)62(2)	69(2)	56(2)	-2(2)	12(2)	-5(2)
C(29)67(2)	74(3)	59(2)	-4(2)	12(2)	-3(2)
C(30)72(2)	64(3)	58(2)	0(2)	2(2)	-3(2)
C(31)114(3)	82(3)	86(3)	-10(3)	15(3)	-6(3)
C(32)138(4)	74(3)	104(4)	1(3)	1(3)	-12(3)
C(33)134(5)	96(4)	100(4)	29(3)	-3(4)	-25(3)
C(34)114(4)	96(4)	99(3)	18(3)	19(3)	-12(3)
C(35)81(3)	84(3)	76(3)	14(2)	12(2)	-7(2)
C(36)98(3)	105(4)	97(3)	3(3)	48(3)	-10(3)
C(37)91(3)	84(3)	82(3)	-4(2)	35(2)	-8(2)
C(38)75(3)	93(3)	71(2)	7(2)	10(2)	7(2)
C(39)197(9)	243(11)	176(8)	-68(9)	45(7)	17(10)
C(40)226(12)	177(9)	166(7)	16(6)	53(9)	23(8)
C(41)177(8)	162(6)	124(5)	-25(5)	26(5)	-20(7)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^{2}x 10^{3}) for bens819s.

	x	y	z	U(eq)
H(3)	2840(50)	3390(20)	7600(30)	150(20)
H(6)	4420(50)	870(20)	8840(30)	160(20)
H(1A)	4761	3562	8370	78

H(2A)	5341	2834	9425	98
H(2B)	3767	2821	9100	98
H(4A)	4800	2262	6990	97
H(4B)	6310	2099	7425	97
H(5A)	6603	2934	8311	78
H(6A)	5076	3360	6653	92
H(7A)	7093	4043	7832	88
H(8A)	4648	4396	6827	83
H(10A)	3798	5366	7156	83
H(12A)	2876	6369	7463	115
H(13A)	3197	7301	8131	131
H(14A)	5287	7592	8988	141
H(15A)	7092	6952	9149	126
H(17A)	8046	5971	8755	106
H(18A)	7713	5013	8153	97
H(19A)	7017	3362	6211	191
H(19B)	6770	2691	6493	191
H(19C)	7859	3108	7112	191
H(20A)	5687	620	8161	69
H(21A)	3650	208	7215	87
H(21B)	4945	-110	7100	87
H(23A)	6177	-1069	9271	82
H(23B)	5139	-624	9500	82
H(24A)	6787	-346	8432	63
H(25A)	6740	171	10039	71
H(26A)	8352	617	9015	75
H(27A)	7379	1207	10205	78
H(29A)	7743	2284	10410	81
H(31A)	8033	3423	10632	116
H(32A)	8910	4330	10321	134
H(33A)	10298	4345	9418	141
H(34A)	10758	3464	8795	127
H(36A)	10415	2341	8556	115
H(37A)	9438	1441	8773	100
H(38A)	8895	-231	10592	122
H(38B)	8861	-503	9684	122

H(38C)	7904	-769	10197	122

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