NEW METHODS AND STRATEGIES TOWARDS TOTAL SYNTHESIS OF (9*S*)-DIHYDROERYTHRONOLIDE A

by

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ABSTRACT OF THE DISSERTATION

NEW METHODS AND STRATEGIES TOWARDS TOTAL SYNTHESIS OF (9*S*)-DIHYDROERYTHRONOLIDE A

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Dissertation Director:

Professor Lawrence J. Williams

Disclosed are studies directed towards the total synthesis of (9*S*)-dihydroerythronolide A. Towards this goal an advanced intermediate, 14 member bis[allene] macrolactone was synthesized. A general method of cuprate-mediated carbon nucleophile delivery to spirodiepoxides was developed. An unprecedented macrolactonization to form bis[allene] macrolactone and macrocyclic stereocontroled epoxidation of this system was achieved. In a separate study, the highly stereocontroled formation of spirodiepoxides and excellent regiocontroled spirodiepoxide opening was developed. This method relies upon the presence of a silyl substituent on the allene. This finding was applied to the total synthesis of epicitreodiol.

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DEDICATION

This dissertation is dedicated to my parents

Table of Contents

List of Tables

List of Figures

List of Schemes

List of Abbreviations

^{o}C	degrees Celsius
Ac	acetate
Bn	benzyl
Bu	Butyl
iBu	isobutyl
Cp	cyclopentadienyl
Ppm	chemical shift (parts per million)
d	doublet
DCM	dichloromethane
DFT	density functional theory
DMAP	4-(*N*,*N*-dimethylamino)pyridine
DMDO	dimethyldioxirane
DMSO	dimethylsulfoxide
ee	enantiomeric excess
FCC	flash column chromatography
h	hour(s)
HOAc	Acetic acid
HMPA	hexamethylphosphorus triamide
Hz	hertz
i	iso
m	multiplet
M	molar (moles/liter)
m/z	mass to charge ratio

m-CBA	meta-chlorobenzoic acid
m-CPBA	meta-chloroperoxybenzoic acid
Me	methyl
min	minutes
MFB	3-fluorobenzyl
ml	milliliters
mol	moles
MOM	methoxymethyl
Ms	methanesulfonyl
n-BuLi	n-butyllithium
NMR	nuclear magnetic resonance
Nu	nucleophile
[O]	oxidant
P	protecting group (generic)
pr	propyl
Ph	phenyl
PMB	(4-methoxy)benzyl
PMP	4-methoxyphenyl
ppm	parts per million
PPTS	pyridinium *p*-toluenesulfonate
PPTS	p-toluene sulfonic acid
q	quartet
R	rectus (Cahn-Inglod-Prelog system)
R	alkyl group (generic)
rt	room temperature

s	singlet
S	sinister (Cahn-Inglod-Prelog system)
SDE	spirodiepoxide
SEM	2-trimethylsilylethoxymethoxy
t	tertiary
t	triplet
TBAF	terta(*n*-butyl)ammonium fluoride
TBDPS	*tert*-butyldiphenylsilyl
TBS	*tert*-butyldimethylsilyl
TEA	Triethyl amine
TES	triethylsilyl
TFA	trifluoroacetic acid
THF	tetrahydrofuran
TLC	thin layer chromatography
TMS	trimethylsilyl
TsDPEN	N-(4-toluenesulfonyl)-1,2-diphenylethylenediamine

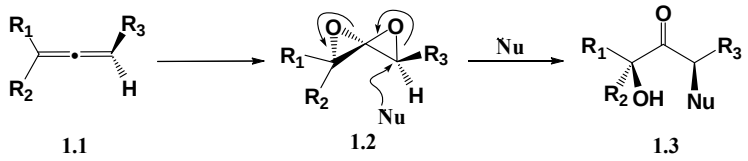
Chapter I

Spirodiepoxide in Synthesis

1.1 Introduction

Cascade reactions are among the most powerful tools available to synthetic chemists in rapidly achieving molecular complexity. As shown in the Scheme 1.1, double epoxidation of allene **1.1** forms spirodiepoxide **1.2**, which can then react with a nucleophile in cascade fashion to generate α-hydroxy, α'-substituted ketone **1.3**.

Scheme 1.1 **Spirodiepoxide**



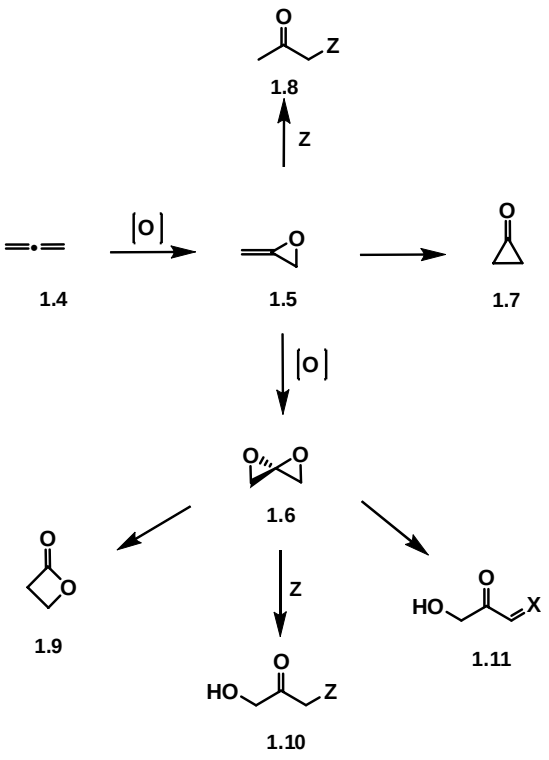
1.1 **1.2** **1.3**

This one flask process (**1.1→1.2→1.3**) allows direct entry to a vicinal triad composed of alcohol, ketone and syn-substituent and thus converts the axial chirality of allene into two centers of chirality. Despite the synthetic potential, the extent of research on spirodiepoxides has been limited. While there are over 10,000 reports describing the use of epoxides in synthesis, less than 25 reports describe spirodiepoxides in any context. The term "spirodiepoxide" (SDE) was coined by the L. J. William's group in 2004.[1] In earlier reports, this functional group has been referred to as dioxaspiro[2a] and bis-epoxide[2b].

1.2 Background

SDEs were first demonstrated to be intermediates in 1968 by Crandall and co-workers as products of peracid promoted allene oxidation.[2a] However, in these preliminary studies, SDE was not isolated, instead several by-products formed (Scheme 1.2).[2a,3a-b] The formation of SDE **1.6** was demonstrated to proceed via allene oxide **1.5**, which was converted to cyclopropanone **1.7** and α-hydroxy ketone **1.8** due to the presence of acid (byproduct of peracid oxidation).

Scheme 1.2 **Products of Allene Oxidation.**

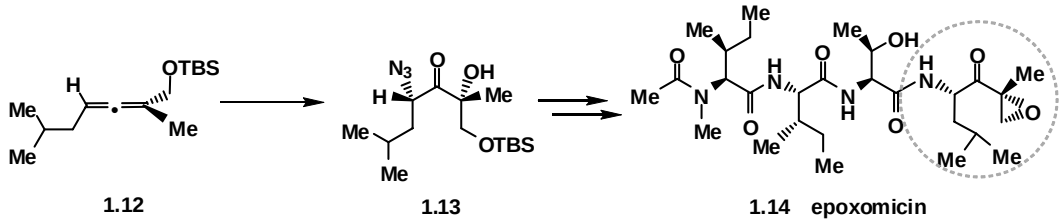


SDEs (**1.6**) were reported as highly unstable in acid and thus uncontrollably converted to oxetanone **1.9**, α-hydroxyketones **1.10** and elimination products (**1.11**). In 1985 Murray and co-workers reported a general method for preparing the highly reactive and selective

oxidizing agent dimethyl dioxirane (DMDO).[4] Subsequently the Crandall group reported the use of DMDO as an oxidant in the formation of SDEs from allenes.[5] Unlike the peracid, DMDO cleanly permitted the double epoxidation of allenes to give isolable SDEs, as the reaction is typically run under neutral, non-nucleophilic conditions. This opened the door for the practical synthetic use of SDEs. Yet in the decade that followed, only a handful number of reports involving SDEs appeared.[2b, 6a-c] In these studies, the allenes used were unfunctionalized, achiral, or symmetric. A limited number of hetereonucleophiles (water, aliphatic alcohols, amines, thiophenol, fluoride and chloride) were tested in nucleophilic opening of SDEs.

In 2004, the Williams' group reported the first application of SDEs in total synthesis, in which the potent proteosome inhibitor epoxomicin **1.14** was prepared (Scheme 1.3).[1] The main focus of the synthesis was construction of the non peptidyl motif (highlighted in circle). Allene **1.12** was treated with DMDO to give SDE intermediate, followed by nucleophilic opening by azide furnished α-azido, α'-hydroxy ketone **1.13**. The latter was then converted to epoxomicin **1.14** in five additional steps.

Scheme 1.3 **Synthesis of Epoxomycin**

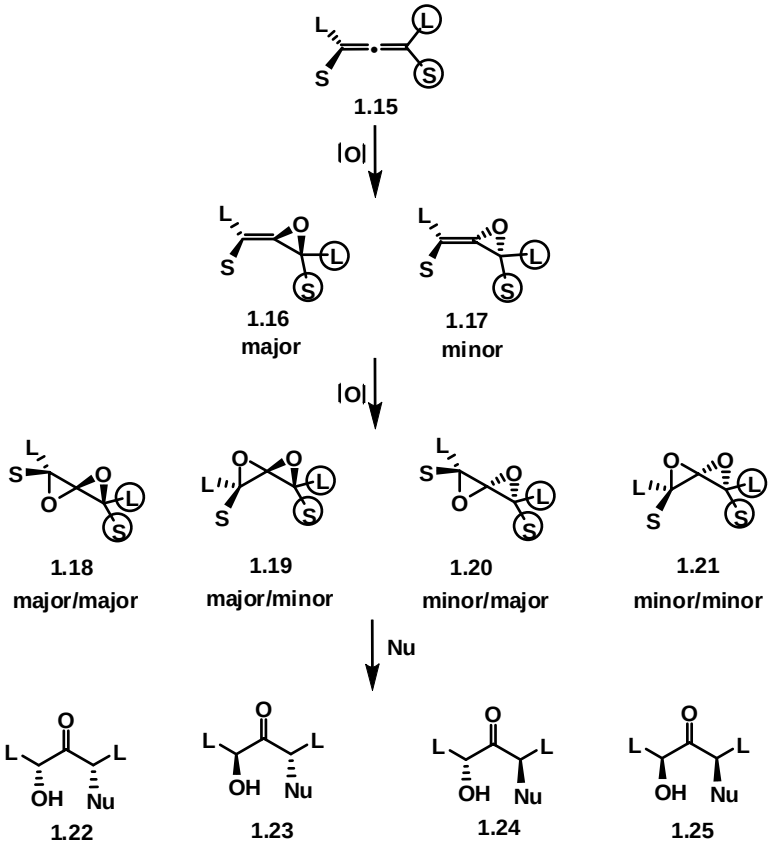


1.12 **1.13** **1.14 epoxomicin**

1.3 Allene Oxidation Model

Chiral allene oxidation is intrinsically diastereoselective. For a non-symmetrically substituted allene **1.15**, the first oxidation takes place at the most electrophilic double bond to form allene oxides **1.16** and **1.17** (Scheme 1.4), (L = large group, S= small group, circled L and S groups are used to emphasize lack of symmetry).

Scheme 1.4 **Allene Oxidation Model**



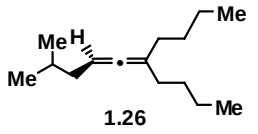
The facial selectivity of the oxidation is dictated by the relative size of the substituents on the non-reacting carbon of the allene. Thus the first oxidation preferentially takes place anti to the large substituent L giving **1.16** as the major allene oxide product. Similarly the

second oxidation preferentially takes place anti to the large L (circled) group. A total four isomers **1.18**, **1.19**, **1.20**, **1.21** may form. Regioselective nucleophilic opening as shown may thereby lead to four addition products (**1.22**, **1.23**, **1.24**, **and 1.25)** with **1.22** being the major product. Two of the isomers, **1.24** and **1.25** reflect the degree of selectivity in the first oxidation. In general these are formed in traced quantities since high selectivity is observed in the first oxidation (>20:1). The anti product **1.23** reflects the degree of selectivity in the second oxidation and may be formed in significant quantities, as the second oxidation is generally less selective than the first.

1.4 Stereoselective Formation of Spirodiepoxide

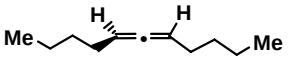
The stereoselectivity of allene oxidation depends on the substituents on the allene as well as on the solvent. The rate of DMDO oxidation of alkenes is higher in chloroform than in acetone.[7] When allene **1.26** was subjected to DMDO in chloroform, it gave a >20:1 ratio of SDE diastereomers, compared to only 10:1 ratio observed in acetone (Scheme 1.5). The diastereomeric ratio of SDEs obtained from allene **1.26** is reflective of the first oxidation at the more substituted side of allene (the two faces of the other double bond are the same). This excellent selectivity suggests that the first oxidation is quite sensitive to the steric difference between an isobutyl group and hydrogen. The second oxidation turns out to be much less stereoselective. When allene **1.27** was treated with DMDO in chloroform it primarily gave two SDE diastereomers in a 2:1 ratio, which is somewhat better compare to the 1:1 ratio observed in acetone.

Scheme 1.5 **Stereoselectivity in Allene Oxidation**



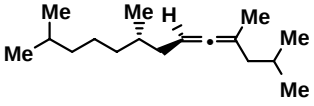
1.26

10 : 1 DMDO/acetone
>20 : 1 DMDO/$CHCl_3$
14 : 1 MEDO
16 : 1 DEDO



1.27

1 : 1 DMDO/acetone
2 : 1 DMDO/$CHCl_3$
1.3 : 1 MEDO
1.5 : 1 DEDO



1.28

1.3 : 1 DMDO/acetone
1.5 : 1 DMDO/$CHCl_3$

The ratio observed for **1.27** is reflective of the selectivity in the second oxidation. Only trace quantities of minor SDE diastereomers are expected to form from the first oxidation (recall that the first oxidation occurs with >20:1 selectivity). Thus, it is not surprising that when allene **1.27** was treated with DMDO, only 1.3:1 and 1.5:1 ratios of SDE diasteomers observed in acetone and chloroform, respectively. One explanation for the improved stereoselectivity were observed with DMDO in chloroform could be that DMDO in chloroform is a more bulky (and more reactive) oxidant because of hydrogen bonding between chloroform and DMDO.

The role of sterics in oxidation stereoselectivity suggests that, in principal, a sterically demanding oxidant would give more selective oxidation. However, when methylethyldioxirane (MEDO)[4] and diethyldioxirane(DEDO)[4] were tested in the oxidation of allenes **1.26** and **1.27**, only slight improvement in selectivity was observed (Scheme 1.5).

1.5 Conclusion

The chemistry of the spirodiepoxide (SDE) functional group remained largely unexplored until recently, despite its enormous synthetic potential. SDEs offer a direct approach to transform axially chiral allenes into stereochemically dense, complex molecular motifs. However, the efficacy of this chirality transfer directly depends on the extent of stereoselectivity in the formation of SDEs from allene. This is one of the central challenges in developing SDE-based synthetic methods. Indeed, the stereoselective formation of SDEs is vital for a successful application of this functional group in target oriented synthesis.

This dissertation describes three successful solutions to this challenge.

1. Acyclic stereocontrol, discussed in Chapter IV.

2. Macrocyclic stereocontrol, discussed in Chapter V and VI.

3. Use of silyl allenes, discussed in Chapter VII.

Additionally, since the context of much of these studies is the advancement of new strategies toward the synthesis of (9*S*)-dihydrothronolide A, important chapters include:

Chapter III: Synthetic Strategy.

Chapter IV: Reaction of Spirodiepoxide with Cuprates.

Chapter V: Erythronolide Model Study.

Chapter VI: Progress Towards the Total Synthesis of (9*S*)-dihydrothronolide A.

1.6 References

1. Katukojvala, S.; Barlett, K. N.; Lotesta, S. D.; Williams, L. J. *J. Am. Chem. Soc*., **2004**, *126*, 15348.
2. a) Crandall, J. K.; Machleder, W. H.; Thomas, M. J. *J. Am. Chem. Soc*., **1968**, *90*, 7346. b) Marshall, J. A.; Tang, Y. *J. Org. Chem*., **1994**, *59*, 1457.
3. a) Crandall, J. K.; Machleder, W. H. *J. Am. Chem. Soc*., **1968**, *90*, 7347.
   b) Crandall, J. K.; Conover, W. W.; Komin, J. B.; Machleder, W. H. *J. Org. Chem.*, **1974**, *39*, 1723.
4. Murray, R. W.; Jeyaraman, R. *J. Org. Chem*. **1985**, *50*, 2847.
5. Crandall, J. K.; Batal, D. J.; Sebesta, D. P.; Lin, F. *J. Org. Chem*. **1991**, *56*, 1153.
6. a) Crandall, J. K.; Batal, D. J.; Lin, F.; Riex, T.; Nadol, G. S.; Ng, R. A. *Tetrahedron*, **1992**, *48*, 1427. b) Crandall, J. K.; Rambo, E. *Tetrahedron Lett*. **1994**, *35*, 1489. c) Crandall, J. K.; Rambo, E. *Tetrahedron*, **2002**, *58*, 7027.
7. Gibert, M.; Ferrer, M.; Sanchez, F.; Messeguer, A. *Tetrahedron*, **1997**, *53*, 8643.

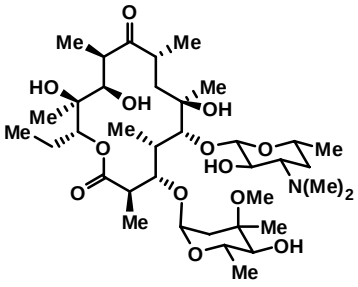
Chapter II

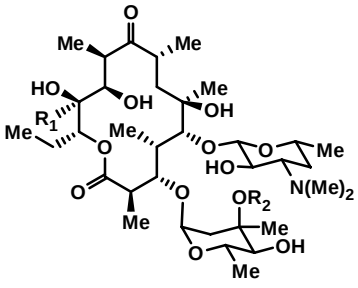
Erythromycins

2.1 Introduction

Erythromycin **2.1** is a widely used broad spectrum antibiotic. It is a secondary metabolite produced by soil inhabating actinomycete family of bacteria *Saccharopolyspora erythraea* (formerly known as *Streptomyces erythraea*). First isolated in 1952 by J. M. McGuire and coworkers at Eli Lilly from soil collected in Philippines,[1] this substance was launched, also in 1952 as commercial antibiotic by Eli Lilly under the brand name llosone®. *Streptomyces*, the largest antibiotic producing genus of bacteria,[2] is also the source of some other well known antibiotics such as streptomycin, vancomycin, and tetracycline among others.

Figure 2.1 Erythromycins





Erythromycin B (2.2) R_1= H, R_2= Me

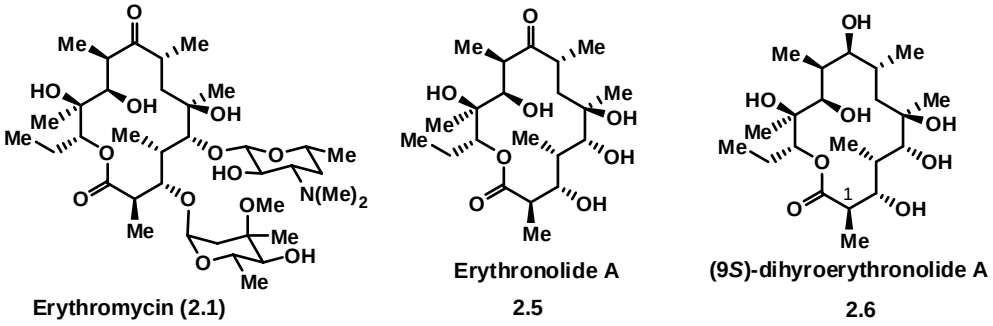
Erythromycin C (2.3) R_1= OH, R_2= H

Erythromycin D (2.4) R_1= H, R_2= H

The erythromicin family includes erythromycin (**2.1**) (also known as erythromycin A) and its congeners erythromycin B (**2.2**), erythromycin C (**2.3**), and erythromycin D (**2.4**) (Figure 2.1). These congeners are biosynthetic precursors of erythromycin .[3]

Erythromycin belongs to the macrolide class of antibiotics. The term "macrolide" was coined by R. B. Woodward in 1957 to abbreviate a class of natural product composed of macrocyclic lactone with one or more deoxysugar attached.[2] Erythromycin is composed of a 14 member macrolactone, designated as erythronolide A (**2.5**) to which is attached the sugars cladinose at C-3 and desosamine at C-5 (Figure 2.2).

Figure 2.2 Erythronolides

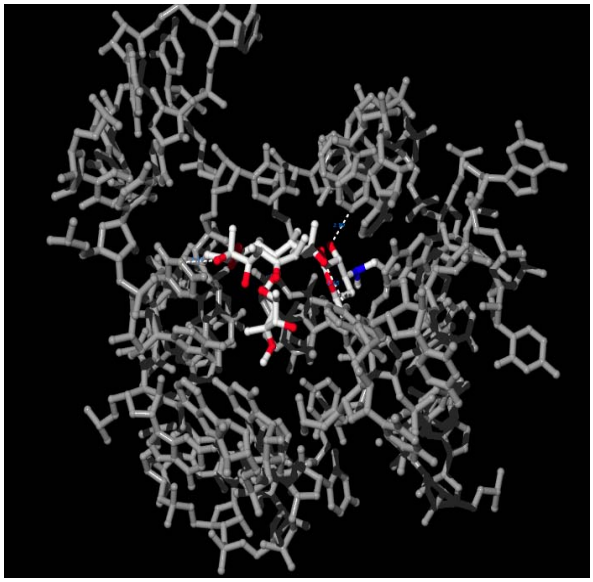


The first complete structural elucidation of **2.1** was done by Wiley et al. in 1957 by using degradation methods.[3] The structural assignment was confirmed by Harris et al. in 1965, when they reported the X-ray structure of **2.1**.[4] The aglycon, erythronolide A (**2.5**), contains 10 stereocenters (5 contiguous). (9*S*)-dihydroerythronolide A (**2.6**) is an advanced synthetic precursor of erythronilide A (**2.5**),[5] where the ketone at C9 is in reduced form. The synthesis of **2.1** from **2.5** is known.[6] Hence a total synthesis of (9*S*)-dihydroerythronolide A (**2.6**), also constitutes a formal synthesis of erythronolide A (**2.5**) and erythromycin (**2.1**).

2.2 Biological Activity

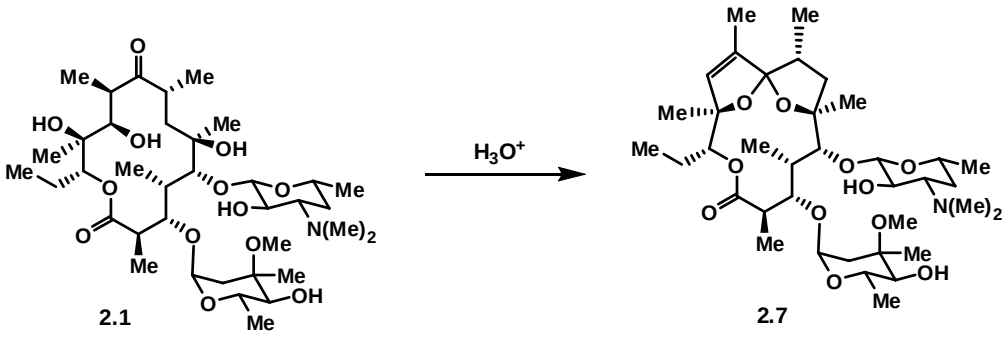
Since its discovery, erythromycin was known to exert antibiotic activity by blocking bacterial protein synthesis. But only recently the molecular details have been uncovered. An X-ray crystal structure of a ribosome-erythromycin complex revealed that erythromycin binds to the 50S ribosomonal subunit and consequently blocks protein translation (Figure 2.3).[7] The presence of the two deoxysugar units appears to be key to the antibacterial activity.[8] Other congeners of erythromycin (**2.2**, **2.3**, **2.4**) show weaker antibiotic activity. The biological study of erythromycin is still under investigation, especially the aspect of bacterial resistance towards erythromycin and in general macrolide antibiotics.[8]

Figure 2.3 Schematic Diagram Showing Erythromycin Bound to the Ribosome



Erythromycin acts as broad spectrum antibiotics due to the highly conserved structure of the ribosome in most bacteria.[8] Mostly used in respiratory infections, erythromycin has been widely used to treat infections in humans and animals before the arrival of the next generation of macrolide antibiotics in the 1990s, and is still widely used in developing countries because of the low cost.[8]

Scheme 2.1 **Acid Induced Transformation of Erythromycin**

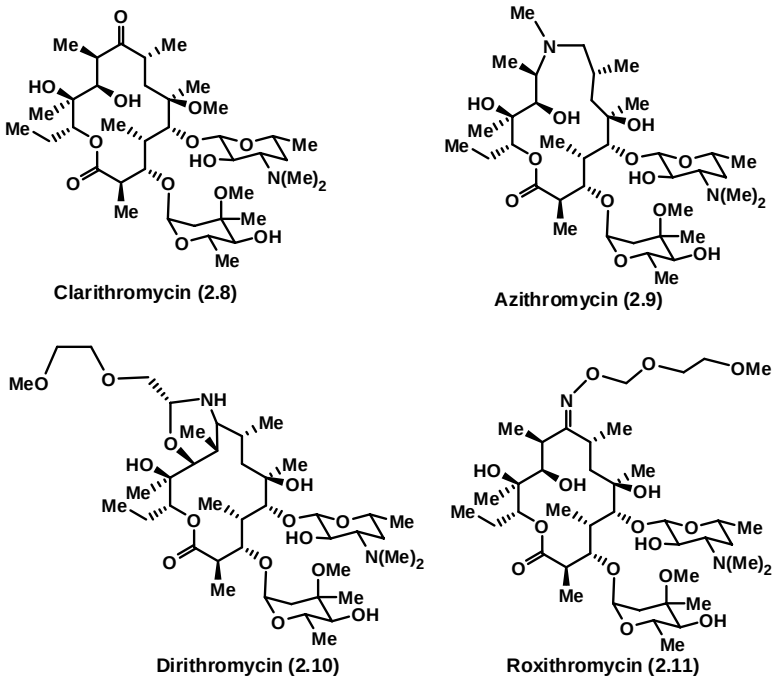


Erythromicin is unstable in the stomach due to acid induced formation of 8, 9-anhydro-6, 9-hemiketal (Scheme 2.1), which is found to be the cause of stomach cramps.[9] Also, erythromycin has a short half life and poor oral bioavailability requiring multiple doses per day.[9] These factors, coupled with growing antibacterial resistance prompted the search for a new and better generation of antibiotics.

2.3 Second and Third Generation Macrolides

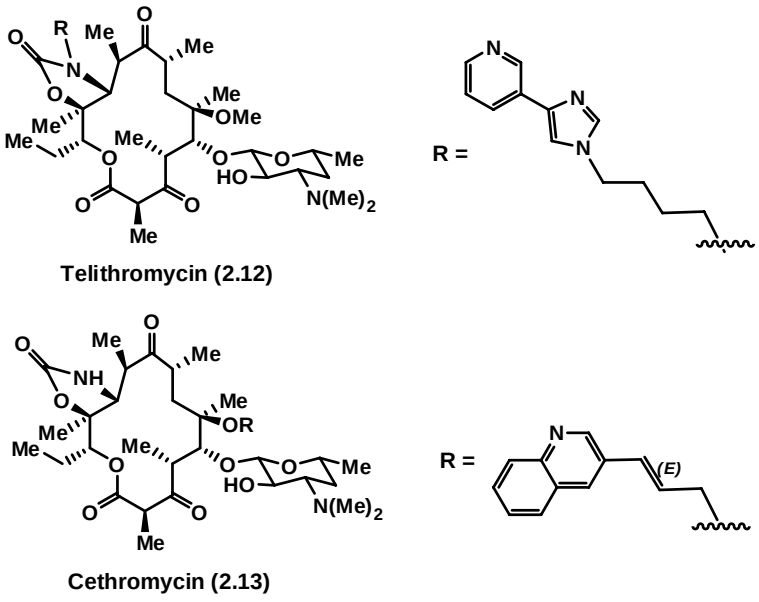
Second generation macrolides were developed in the 1980s, mainly driven by the need for macrolides with improved acid stability.[8] Some of the second generation macrolides which were commercialized are clarithromycin (**2.8**), azithromycin (**2.9**), dirithromycin (**2.10**) and roxithromycin (**2.11**) among others (Figure 2.4). These macrolides are derivatives of erythromycin with modifications at either C6-OH or C9-carbonyl to prevent acid induced hemiketal formation. The two most prominent second generation macrolides, in terms of worldwide commercialization are clarithromycin (marketed by Abbott under the brand name Biaxin®) and azithromycin (marketed by Pfizer under the brand name Zithromax®). Clarithromycin and azithromycin are prepared from erythromycin in 6 and 10 steps respectively.

Figure 2.4 Second Generation Macrolide Antibiotics



Third generation macrolides, telithromycin (**2.12**) and cethromycin (**2.13**) were developed in the 1990s primarily to combat the growing antibacterial resistance towards macrolides (Figure 2.5).[8] They are also referred as "ketolides" to indicate the presence of a 3-Keto group in place of cladinose sugar present in previous generation of macrolides. The only third generation macrolide in clinical use is telithromycin (marketed by Sanofi-Aventis uder the brand name Ketek®).

Figure 2.5 Third Generation Macrolide Antibiotics



2.4 Previous Synthesis

Erythromicin **2.1** has emerged as the focal point of erythromycin target-synthesis and, consequently, has led to the development of new reaction methodologies, including acyclic stereocontrol.[10] Faced with the challenge of the total synthesis of erythromycin, R.B. Woodward wrote in 1956 "Erythromycin, with all our advantages, looks at present quite hopelessly complex, particularly in view of its plethora of asymmetric centers".[11] It took three decades before the first total synthesis of Erythromycin A was reported by Woodward in 1981.[12] To date, numerous syntheses of erythromycins have been achieved. Each of these elegant total syntheses stand as a testament of the power and breadth of synthetic methodology advanced over the last three decades. Following is a list of all the total synthesis of erythromycin (**2.1**), erythronolide A (**2.5**), and (9*S*)-dihydroerythronolide A (**2.6**) reported to date (Table 2.1).

Table 2.1 Previous Syntheses

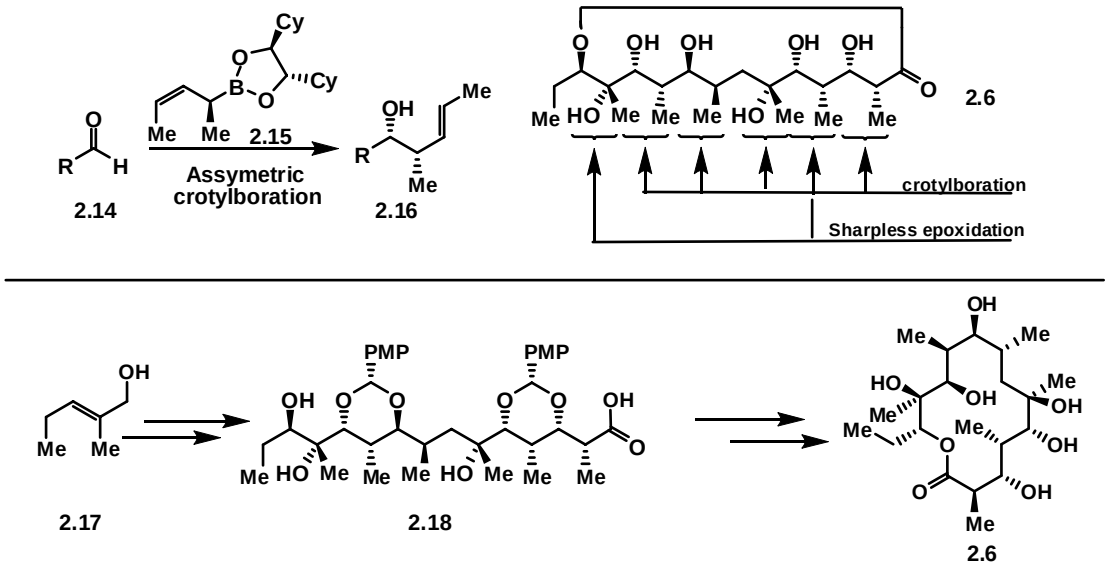
Total syntheses of erythromycin	Comments
1. Woodward et al. *J. Am. Chem. Soc*. **1981**,*103*, 51236.	First and only total synthesis of erythromycin to date. Corey-Nicolaou macrolactonisation was employed to form the macrolactone.
2. Toshima et al. *J. Am. Chem. Soc*. **1995**,*117*, 3717.	Erythromycin was synthesized from (9*S*)-dihydroerythronolide A.
Total synthesis of erythronolide A	**Comments**
1. Corey et al. *J. Am. Chem. Soc.***1979**, *101*, 7131.	First total synthesis of erythronolide A was reported.
2. Nakata et al. *Tetrahedron Lett.* **1986**, *27*, 1815.	Erythronolide A was synthesized through (9*S*)-dihydroerythronolide A.
3. Yonemitsu et al. *Tetrahedron*, **1990**, *47*, 4613	Erythronolide A was synthesized starting from D-glucose.
4. Carriera et al. *Angew. Chem. Int. Ed. Engl*. **2005**, *44*, 4036.	Most recent synthesis of erythronolide A employing 28 liniar steps.

Total Synthesis of (9*S*)-dihydroerythronolide A	Comments
1. Yonemitsu et al. *Tetrahedron Lett.* **1987**, *28*, 4569.	(9S)-dihydroerythronolide A was synthesized from D-glucose.
2. Stork et al. *J. Am. Chem. Soc.***1987**, *101*, 1565.	(9S)-dihydroerythronolide A was synthesized in 26 linear steps.
3. Paterson et al. *Tetrahedron Lett.* **1989**, *30*, 7463.	Macrocyclic stereocontrol was demonstrated.
4 Sviridov et al. *Izvestiya Akademii Nauk SSSR,* **1990**, 1, 195.	(9S)-dihydroerythronolide A was synthesized in 61 steps from L-glucosan.
5 Hoffmann et al. *Angew. Chem. Int. Ed. Engl*. **1993**, *32*, 101.	Shortest total synthesis of (9*S*)-dihydroerythronolide A to date that required 23 linear steps.
6 Woerpel et al. *J. Am. Chem. Soc.* **2003**, *125*, 6018.	Most recent synthesis of (9*S*)-dihydroerythronolide A that required 31 linear steps.

We will focus on three total syntheses of (9*S*)-dihydroerythrolnolide A. viz. Hoffmann, Paterson, and Woerpel.

In 1993 R. W. Hoffmann et al. reported a total synthesis of (9*S*)-dihydroerythronolide A that required 23 linear steps.[13] This is the shortest total synthesis of this molecule to date. Apart from its brevity, this synthesis is also unique in that all the eleven stereocenters were built by external asymmetric induction and in the complete absence of aldol addition chemistry, unlike most syntheses of erythronolide before it.

Scheme 2.2 Hoffmanns' Synthesis of (9*S*)-Dihydroerythronolide A

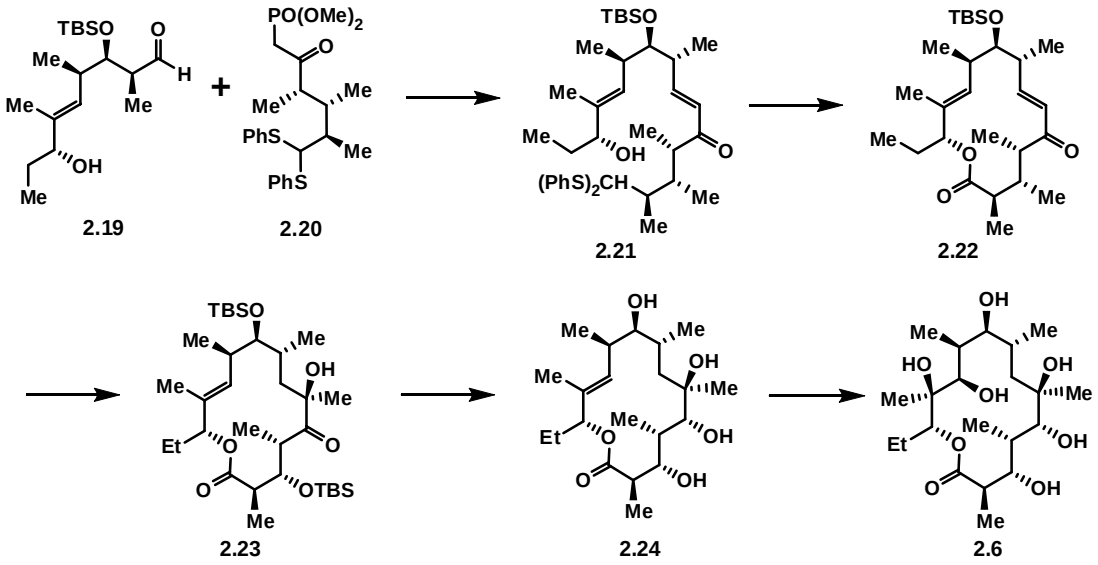


The synthesis was orchestrated in an array of asymmetric crotylborations and asymmetric Sharpless epoxidations (Scheme 2.2). Asymmetric crotylboration to an aldehyde (**2.14**) generated a cis propionate (**2.16**). This synthesis is a beautiful example of the synthetic potential of this transformation by which eight out of eleven stereocenters in the target molecule **2.6** were installed. The synthesis began with a Sharpless epoxidation of allylic

alcohol **2.17** followed by a 20 step synthetic sequence involving four asymmetric crotylborations and a second Sharpless epoxidation to generate the seco acid **2.18**. Yamaguchi macrolactonisation followed by acid hydrolysis of the acetals generated (9*S*)-dihydroerythronolide A.

Paterson et al. in 1989 reported the total synthesis of (9*S*)-dihydroerythronolide A.[14] Unlike other total synthesis of (9*S*)-dihydroerythronolide A, this synthesis was carried out in a combination of acyclic and macrocyclic stereocontrol. Four out of eleven stereocenters were built in eight post macrolactonisation steps.

Scheme 2.3 Patersons' Synthesis of (9*S*)-Dihydroerythronolide A

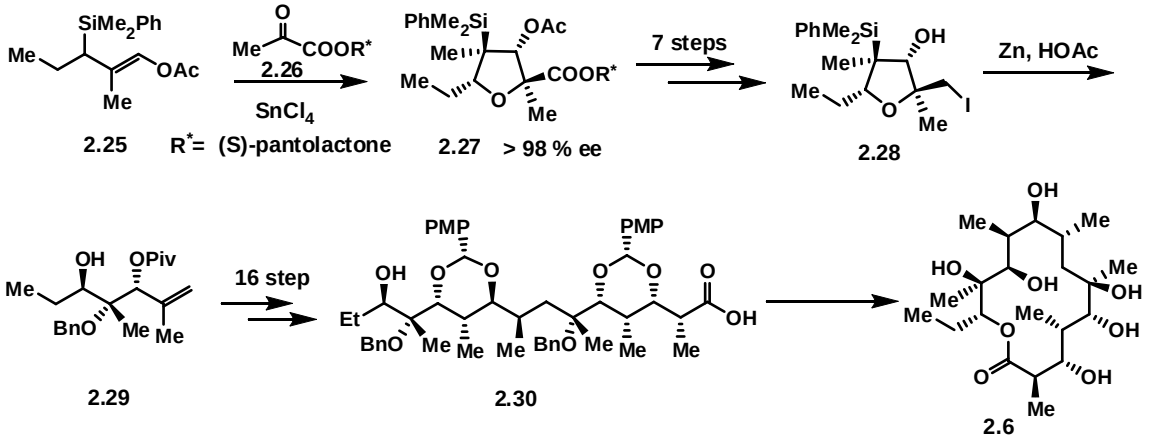


The synthesis converged via a Horner-Wadsworth-Emmons olefination of the intermediates **2.19** and **2.20** to generate *trans* olefin **2.21**. Intermediates **2.19** and **2.20** were prepared from commercially available starting material in seven and eight steps

respectively. The two step conversion of the dithioacetal group of **2.21** to the carboxylic acid followed by Yamaguchi macrolactonisation generated **2.22**. The enone in the macrolactone **2.22** was converted to the α-hydroxyketone **2.23** in four steps. A highly selective chelation controlled hydride reduction of the ketone in **2.23** using zinc borohydride gave the diol **2.24** as a single diastereomer. Removal of the TBS followed by osmylation of the C11-C12 double bond furnished the final target (9*S*)-dihydroerythronolide A.

Recently, 2003 Woerpel et al. reported a total synthesis of (9*S*)-dihydroerythronolide A.[15] This synthesis demonstrates the highly stereoselective [3+2] annulation of allylic silanes as an alternative to acyclic stereocontrol based methods.

Scheme 2.4 Woerpels' Synthesis of (9*S*)-dihydroerythronolide A



The synthesis used a Lewis acid catalysed [3 + 2] annulation of allylic silane **2.25** with (S)-panntolactone pyruvate **2.26** to generate the highly functionalized tetrahudrofuran

2.27 (> 98 % ee) which was converted to the primary iodide **2.28** in a seven step sequence. A zinc-mediated radical ring opening of **2.28** gave **2.29**. This key reaction allowed the conversion of the cyclic intermediate into an acyclic erythromycin stereotriad. Compound **2.29** was then converted to the seco acid **2.30** in 16 linear step sequence. Yamaguchi macrolactonisation followed by global deprotection afforded (9*S*)-dihydroerythronolide A.

2.5 Conclusion

(9*S*)-Dihydroerythronolide A and other members of erythromycin family have inspired generations of synthetic organic chemists. Their syntheses have been used to demonstrate the superiority of new synthetic methods and strategies. Yet, to date syntheses of erythronolides requires 23 or more steps (usually more than 30). With growing antibacterial resistant towards erythromycin[16] and in general towards antibiotics, there is still a need for a practical chemical synthesis of erythronolides which would access new antibiotic erythromycin analogues. This opinion of the author is in harmony with the following comment made by Professor Andrew G. Myers. "The limitations of chemical synthesis frequently present a substantial obstacle to the development and discovery of new antibiotics and of pharmaceutical agents in general. The problem is nowhere more evident than among the structurally complex natural products tetracycline (1) and erythromycin."[17]

2.6 References

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Chapter III

Synthetic Strategy

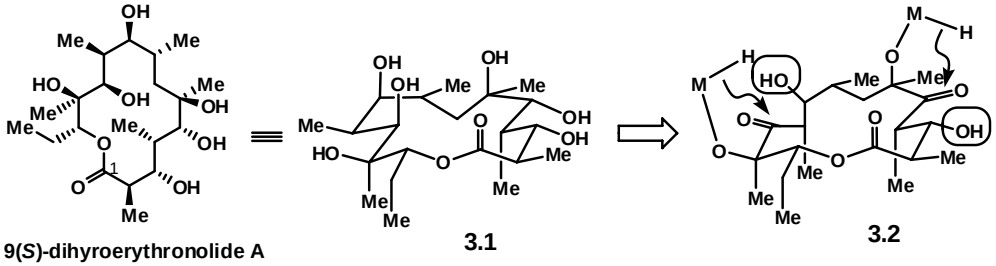
3.1 Introduction

More than half a century after its isolation and following numerous elegant synthetic endeavors from the past three decades, it is the opinion of this author that the erythronolides deserve a fresh and more direct approach. Upon reporting the shortest synthesis to date of (9*S*)-dihydroerythronolide A in 1993, R. W. Hoffmann concluded with this humble note "This does not bring the story of erythronolide synthesis to an end. Inasmuch as our synthesis reflects the present state of the art in the methodology of stereoselective synthesis, more efficient syntheses of erythronolides should become possible with improved methods in the future."[1] As discussed in the introductory chapter (Chapter I), SDEs give us the opportunity to gain direct entry to the stereochemically dense, complex molecular motifs. On the other hand erythronolide provides an ideal stage to demonstrate the power of spirodiepoxide based methodology in total synthesis. To a large degree, the success of this methodology is contingent upon the stereoselective oxidation of the spirodiepoxide. This is an important challenge to meet successfully, as acyclic stereocontrol has remained the central theme in the previous erythronolide syntheses. We envisioned that addressing this challenge and delivering a short synthesis, although difficult, are not mutually exclusive. The two goals combined to lead us to a bold approach towards the synthesis of (9*S*)-dihydroerythronolide A.

3.2 Synthetic Plan

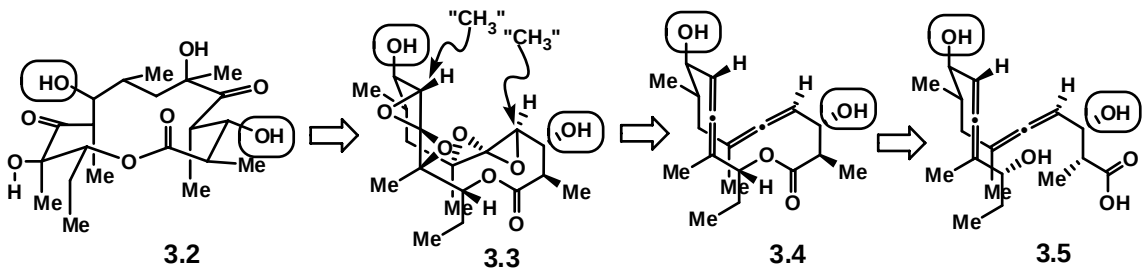
As shown in retrosynthetic format below (Scheme 3.1), (9*S*)-dihyroerythronolide A could be accessed from its immediate precursor **3.2** upon chelation controlled double hydride reduction of each ketone. Patterson et al. has reported the chelation controlled reduction of a substrate analogous to **3.2** (chapter II).[2] In that study, C11 was at the alcohol oxidation state and C6 hydroxyl was used for chelation in the zinc borohydride reduction of the C5 ketone to give a single product with the desired stereochemistry.

Scheme 3.1 **Synthetic Plan (Part I)**



The bis [α-hydroxyketone] **3.2** may be accessible from bis[allene] macrolactone **3.4** via corresponding bis[SDE] **3.3** provided the availability of a suitable method to deliver methyl as a nucleophile (Scheme 3.2). The bis-allene macrolactone **3.4** could be obtained from the precursor bis[allene] seco acid **3.5** via macrolactonisation.

Scheme 3.2 **Synthetic Plan (Part II)**



The strategically conservative strategy in total synthesis is to perform new and not well understood chemistry at the beginning of the synthesis, leaving the easier and more tested reactions for the late stages. Given our limited knowledge of the formation, stability and reactivity profile of SDEs, the proposed synthetic plan, by virtue of its speculative nature, is antithesis to the conventional wisdom. However, these late stage synthetic maneuvers have the following key strategic advantages.

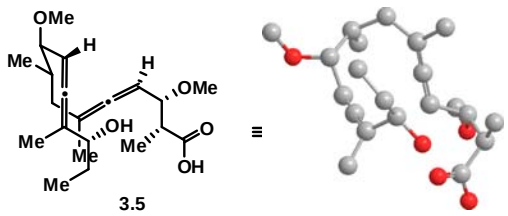
1. Formation of both SDEs should be stereoselective due to macrocyclic stereocontrol.

2. Six out of eleven stereocenters of the final product **3.1** would be built in just 2 steps, from a relatively simple bis[allene] macrolactone **3.4**, thus significantly reducing the total number of steps

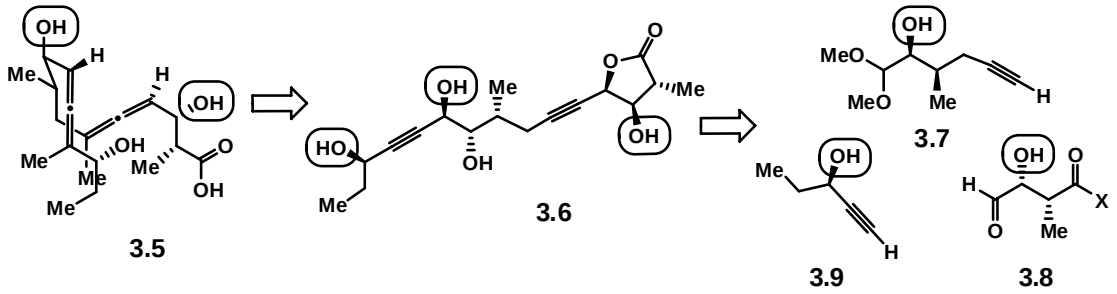
3. Late-stage introduction of several functional groups minimizes inefficiencies associated with protecting group manipulation. Indeed the advanced intermediate **3.4** requires only two protecting group, which in principle could be same.

Computational analysis performed at the MM2 level suggests that the ground state of the bis-allene seco acid **3.5** (the other two hydroxyl groups protected as OMe) populates a favorable conformation in which the free OH and COOH groups are in proximity. This further suggests that lactonisation may be facile (Figure 3.1).

Figure 3.1 **Ground State Minimum Energy Conformation of Seco Acid.**



Scheme 3.3 **Synthetic Plan (Part III)**



The bis-allene **3.5** could easily be prepared from the precursor bis-propargylate **3.6** (Scheme 3.3). The bis-propargylate **3.6** could be assembled in a convergent process, by sequential coupling of terminal alkynes with aldehydes. Thus, first the alkyne **3.7** would be coupled with the aldehyde **3.8**. The acetal in the coupling product could be hydrolyzed to aldehyde, which could be further coupled with alkyne **3.9**. We anticipate the formation of γ-lactone in the course of coupling between **3.7** and **3.8**. The lactone would act as mutual protecting group for both propargyl and carboxyl group, thus further reducing the number of steps required for the total synthesis. The intermediates **3.7**, **3.8** and **3.9** could easily be prepared in five or less steps each from commercial reagents.

3.3 Challenges

The synthetic plan discussed above would enable the synthesis of (9*S*)-dihydroerythronolyde A in about 15 steps, a rout shorter by far than any total synthesis of this molecule reported to date. However the plan also presents the following unique challenges.

- Macrolactonisation of bis[allene] seco acid (unprecedented).
- Stability of bis allene macrolactone **3.4** is a concern, given the strain involved in such macrolactone and the possibility of transannular reactions.
- The formation and stability of bis[SDE] **3.3**, considering SDE itself is strained.
- Addition of methyl nucleophile to SDE (unprecedented).

To address these challenges, we decided to pursue two satellite projects before embarking on the total synthesis.

1. Develop a general method of carbon nucleophile addition to SDE (Chapter IV).
2. Synthesis of a model bis[allene] macrolactone (Chapter V).

3.4 Conclusion

The synthetic plan delineated here is unique compared to the previous erythronolide syntheses. Successful implementation of this plan is contingent upon addressing the implicit challenges. Addressing these challenges would also lead to the development of new chemistry. This strategy would enable the shortest synthesis of (9*S*)-dihydroerythronolide A to date. Realization of these goals would demonstrate in a dramatic way the power of SDE based methods. Moreover, in a broader context, a shorter synthesis of (9*S*)-dihydroerythronolide A could well enable practical chemical syntheses of erythromycin analogues.

3.5 References

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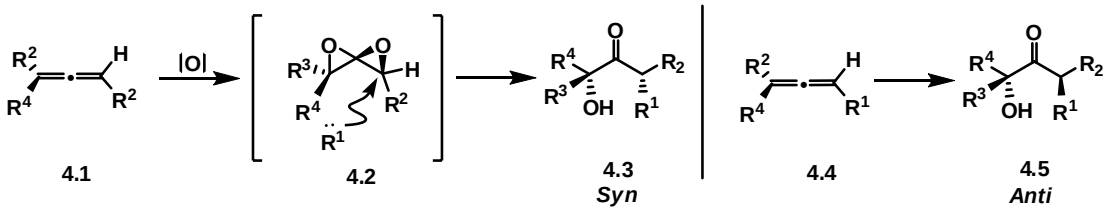
Chapter IV

Reaction of spirodiepoxide with cuprates

4.1 Introduction

Nucleophilic opening of an epoxide by carbon nucleophiles represents an important class of C-C bond forming reaction in organic synthesis.[1] Similar types of reactions involving SDEs hold the potential to be a one-step method for direct entry into densely functionalized α-hydroxy ketones. As shown in the following scheme (Scheme 4.1), such a transformation (**4.1**→ **4.2**→ **4.3**) would set two stereocenters and one C-C bond, and thus result in the formation of a vicinal triad composed of alcohol, ketone, and syn-substituted carbon substituent. Moreover the anti product would be accessible by using R^2 as the nucleophile and R^1 as the allene substituent (**4.4**→ **4.5**).

Scheme 4.1 **General Concept**



This motif, and the closely related motif wherein an alcohol is present instead of a ketone is widely distributed in nature and present in the erythromycins as well as other substances of biomedical relevance such as cytochalasin D,[2a] galbonolide,[2b] oligomycins,[2c] streptovaricins,[2d] ossamycin.[2e]

4.2 The Scope of Adding Carbon Nucleophile to Spirodiepoxide

Although carbon nucleophile mediated opening of a SDE holds significant potential, the scope of such a reaction is contingent upon several constrains.

1. Given the instability of SDEs in acid, the reagent delivering the carbon nucleophile has to be mild, especially if it contains a transition metal. Also the reagent should not be basic enough to scramble the α-stereocenter of the product ketone.
2. The desired carbon nucleophile should not react further with the ketone of the product, after the initial nucleoplic opening of the SDE.

After considering several carbon nucleophile delivering reagents, we focused our study on organocuprates, due to the myriad advantages of these mild reagents.[3] They are readily prepared and well known for their ability to open epoxides. Their addition reactions are compatible with a wide range of substrate functionality, and importantly the ketones are generally stable to these reagents. Cuprates are not basic enough to effect enolization of ketones. Thus, organocuprates satisfy all the above constrains.

4.3 Cuprates as a carbon nucleophile:

Organocuprates, generally formulated as R_2CuM where R and M represents organic ligand and metal respectively, are effective synthetic reagents for delivery of hard anionic nucleophiles such as alkyl, vinyl and aryl anions. Since their first discovery in 1941 by Kharash et al,[4] organocuprates have remained the most useful synthetic reagents among transition metal organometallics.[5] The two archetypical reaction of organocuprates are conjugate addition to α, β-unsaturated carbonyl compounds and substitution of organic halides (including pseudohalides) and epoxides in SN2 and SN2' process.[6] Out of several cuprate reagents known, the two most commonly used are Gilmann reagents and cyanocuprates.[6]

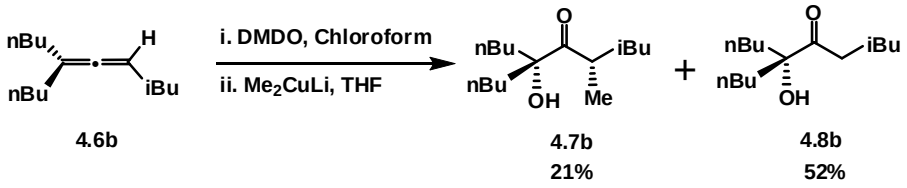
In 1952, Gilmann et. al reported the formation of a colorless solution when two equivalent of MeLi were added to a Cu(I) salt.[7] Later in 1966, House et. al showed that the reactive species in conjugate additions of alkyl lithium in the presence of a Cu(I) salt is actually lithium diorganocuprate(I) and called it a "Gilmann reagent".[8] It is commonly described as R_2CuLi and it is generally the cuprate of choice for halide displacement, tosylate displacement, and epoxide opening.[9] Then in 1981, Lipshutz et al. reported the cyanocuprate, formed by reacting copper cyanide(I) with one or two equivalents of RLi.[10] When one equivalent of RLi was used, the resulting cuprate was proposed to be RCu(CN)Li and designated as a lower order cyanocuprate. When CuCN was allowed to react with two equivalents of RLi, a different species was formed and was proposed to be $R_2CuCNLi_2$ and designated as a higher order cyanocuprate. Lower order cyanocuprates

differ considerably in terms of stability and reactivity from the Gilmann reagent and are typically used to displace activated halides and related leaving groups.[9]

4.4 Results and Discussion

Our entry into reaction of SDEs with organocuprates commenced with the Gilmann reagent, as it is the cuprate of choice for opening epoxides.[9] We were pleased to find that the reaction of SDEs, derived from allene **4.6b**, with the Gilman reagent Me_2CuLi (derived from CuBr and MeLi) gave the desired α-hydroxy, α'-methyl ketone **4.7b**. However, the major product of the reaction was the reduction product α-hydroxy ketone **4.8b** (Scheme 4.2).

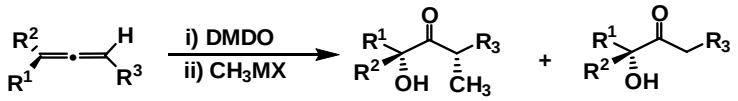
Scheme 4.2 **Addition of Cuprate to SDE**



4.6b **4.7b** **21%** **4.8b** **52%**

Nevertheless this result was encouraging and led us to venture into the optimization of this promising reaction. During the course of optimization, it turned out that the reaction pathway significantly depended on the source of organic ligand, stoichiometry of cuprate reagent, solvent and temperature. A survey methylcuprate reactions with SDEs is tabulated below (Table 4.1).

Table 4.1 Cuprate Optimization



4.6a: R^1, R^3 = n-Bu, R^2 = H
4.6b: R^1, R^2 = n-Bu, R^3 = iBu

entry	Allene	Cuprate Conditions	Solvent	Temperature	Yield (%) 4.7 : 4.8
1	4.6b	Me_2CuLi, LiI	THF	-78^{0}C to 0^{o}C	23 : 53
2	4.6b	Me_2CuLi, LiBr	THF	-78^{0}C to 0^{o}C	21 : 52
3	4.6b	Me_2CuLi, Me_2S, LiBr	THF	-78^{0}C to 0^{o}C	33 : 42
4	4.6b	MeMgBr, CuBr, LiBr	THF	-78^{0}C to 0^{o}C	44 : 15
5	4.6b	$Me_2Cu(CN)Li_2$	Ether	-78^{0}C to 0^{o}C	17 : 52
6	4.6a	MeCu(CN)MgBr	Ether	-10^{o}C to rt	< 3 : 72
7	4.6b	MeCu(CN)MgBr	Ether	-10^{o}C to rt	< 3 : 78
8	4.6b	MeCu(CN)Li	THF	-10^{o}C to rt	51 : 20
9	4.6a	MeCu(CN)Li	Ether	-10^{o}C to rt	74 : < 3
10	4.6b	MeCu(CN)Li	Ether	-10^{o}C to rt	81 : < 3

Reactions employed 3.0 equiv of DMDO in $CHCl_3$, -40^{o}C to rt, 2h.

As shown, exposure of a SDE to an organo cuprate results two predominant transformations: regioselective nucleophilic opening to give the α-hydroxy, α'-methyl ketone **4.7,** and regioselective reductive opening to give the α-hydroxy ketone **4.8**. As with simple epoxide opening diethyl ether turns out to be superior to THF (entry 8 vs 10).[15] The Gilmann reagent gave the reduction product as the major product albeit with low selectivity (entries 1-3). The Cuprate prepared from a 1:1 mixture of methyl Grignard and LiBr-CuBr mixture, which is generally used to displace propargylic acetates, halides and sulfonates in an SN' fashion, gave the desired addition product as the major product with modest selectivity (entry 4).[11] Higher order cyanocuprates gave

the reduction product as the major product (entry 5). On the other hand, lower order cyanocuprates effect SDE transformations with excellent selectivity (entries 6, 7 and 9, 10). For this class of cuprates the more Lewis acidic Grignard derived reagent gave the reduced products with excellent selectivity (entries 6, 7), whereas organolithium derived reagents gave the addition products with excellent selectivity (entries 9, 10).

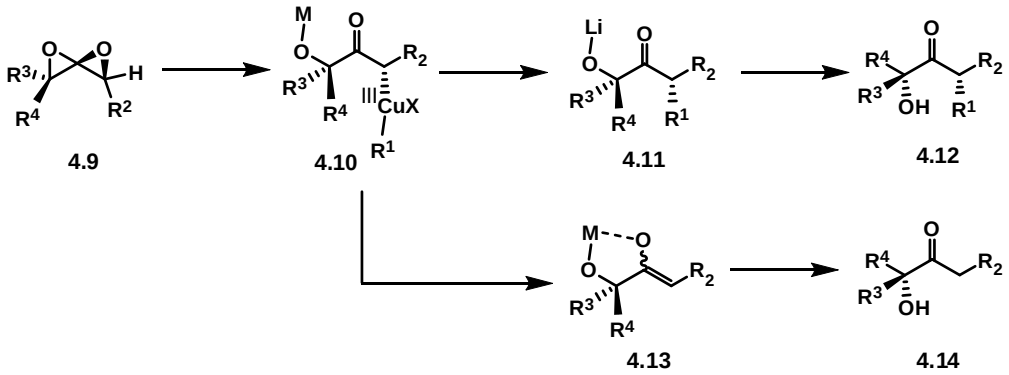
Reduction of alkyl halides and epoxides by Cu(I), in lieu of substitution, is known.[9] When the reaction of entry 7 was quenched with D_2O α-hydroxy, α'-deutero ketone was obtained indicating reduction of SDE to the α-hydroxy α'-ketone enolate or closely related intermediate. Formation of this type of enolate from electrophilic SDE is umplong type reactivity. It may be possible to generate the α-hydroxy, α'-substituted ketones by coupling of the presumed enolate intermediate with suitable electrophiles. Although exploring this mode of SDE reactivity was not the focus of the study described here, a methyl iodide quench of the presumed enolate did not gave the desired α-hydroxy, α'-methyl ketone **4.7**, even after several hours of stirring at room temperature. This is probably due to the strong chelation of the enolate species with the metal. We chose not to investigate this potentially useful reaction further as we turned our focus onto optimizing the addition pathway (→**4.7**), which provides the motif present in erythronolide.

4.5 A mechanistic proposal:

In spite of the long history of organocuprates as a highly useful reagents in organic synthesis, a firm mechanistic understanding of these reagents has not been delineated.[12] There have been several reported crystal structures of cuprate species, but they do not reflect the actual reactive complex in solution. Thus there has been little consensus on the structure of the relevant reactive species.[12]

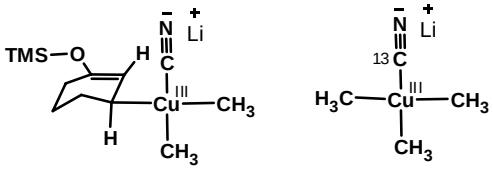
Organocopper mediated C-C bond forming reactions have long been hypothesized to proceed via a copper (III) intermediate.[13] According to this hypothesis, Cu(I) is the nucleophilic atom that reacts with the electrophile and thus leads to the formation of the Cu(III) intermediate. Reductive elimination forms the C-C bond and gives Cu(I). A similar explanation is consistent with our data (Table 4.1). Thus the Cu(I) reagent adds to the SDE to form an α-keto-Cu(III) species **4.10** (Scheme 4.3). Once formed, the Cu(III) intermediate can either reductively eliminate to give **4.12** or isomerize to the corresponding enolate **4.13** and ultimately give **4.14**.

Scheme 4.3 **Mechanistic Proposal**



According to this model, the reductive elimination (→**4.12**) could be faster than the rearrangement in the presence of the lithium counterion, whereas the more acidic magnesium counter ion (gegenion) may induce rearrangement (→**4.14**). The alternative process of Lewis acid promoted carbocation formation followed by single electron transfer from inner sphere Cu(I), though not strictly excluded, is unlikely, given that the regioselectivity of the reduction product is opposite to what would be expected.

Figure 4.1 Cu(III) Intermediates



4.15 **4.16**

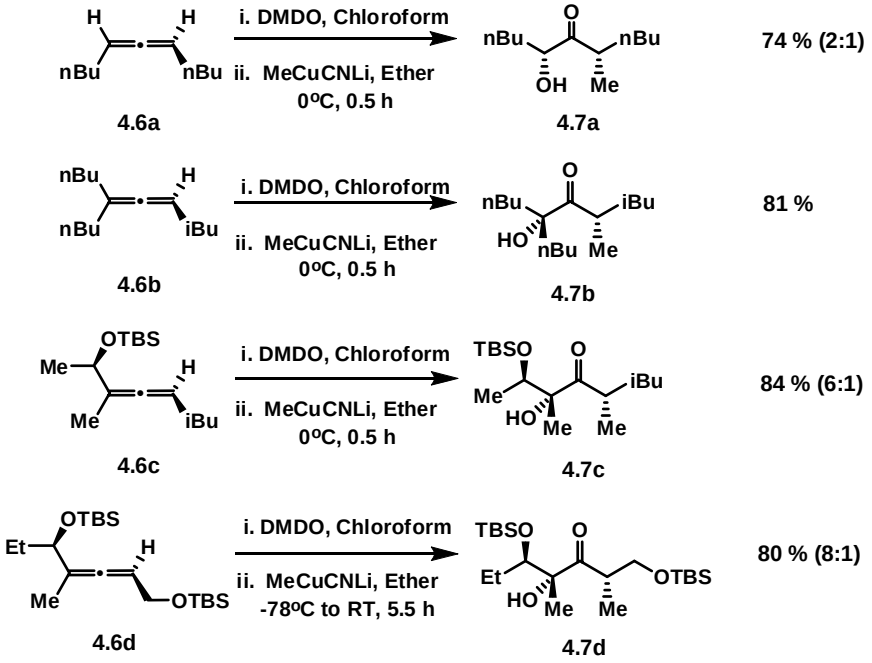
Although the proposition of a Cu(III) intermediate fits well in explaining the several organocuprate mediated reactions, including those with SDEs, until recently, there has not been any direct experimental evidence of its existence. It is noteworthy, however that the theoretical prediction of this species was registered some time ago.[13]

In 2007 Bertz and Ogle reported the first experimentally observed Cu(III) intermediate (**4.15**) for conjugate addition of a Gillman cuprate to 2-cyclohexanone in THF using rapid injection NMR technique (Figure 4.1).[14] Shortly after in 2007, Gschwind et al. reported the experimental observation of a stabilized Cu(III) intermediate (**4.16**) in a substitution reaction of Gilman cuprate with alkyl halides in diethyl ether using proton NMR and HMBC spectroscopy.[15] Both groups confirmed the square planar structure of the observed intermediate, previously predicted by theoretical calculation.[13]

4.6 Development of a General Method

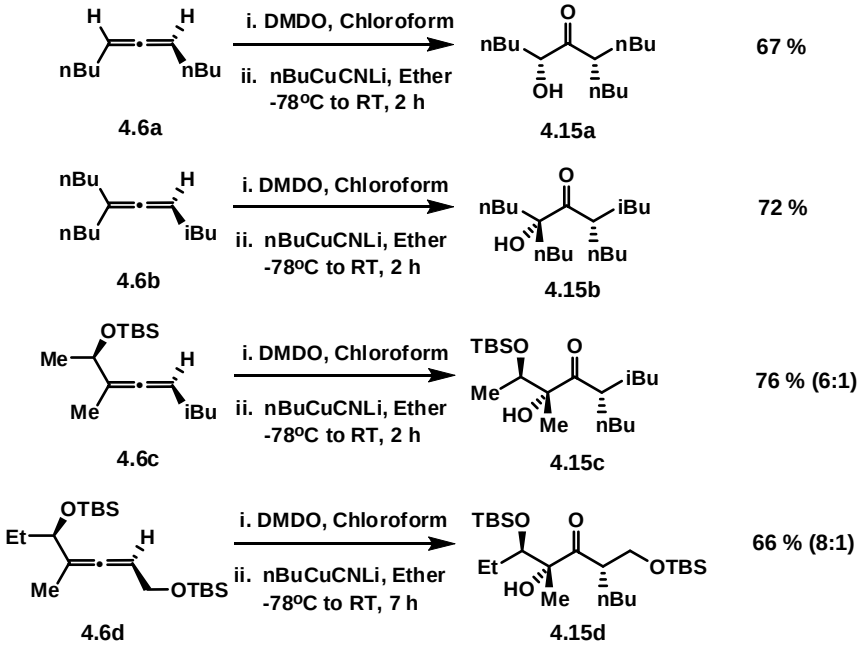
We set to expand the scope of our reaction by testing cuprates with a broad set of allene derived SDEs. The purpose of this was to develop a general method for direct entry into the α-substituted α'-hydroxy ketones from allene. We were pleased to find that several cuprate ligands (Me, nBu, CH_2TMS, Ph) could be delivered to the SDEs derived from a range of allenes, in good to excellent overall yields (Scheme **4.4**, **4.5**, **4.6**, **4.7**). Allenes **4.6a-d** were oxidized with DMDO and then exposed to organocuprates. As expected, the selectivity of the first oxidation (at the more substituted double bond) is excellent (>20:1). The selectivity of the second oxidation is modest to good (8-2:1).

Scheme 4.4 **Methyl Cyanocuprate**



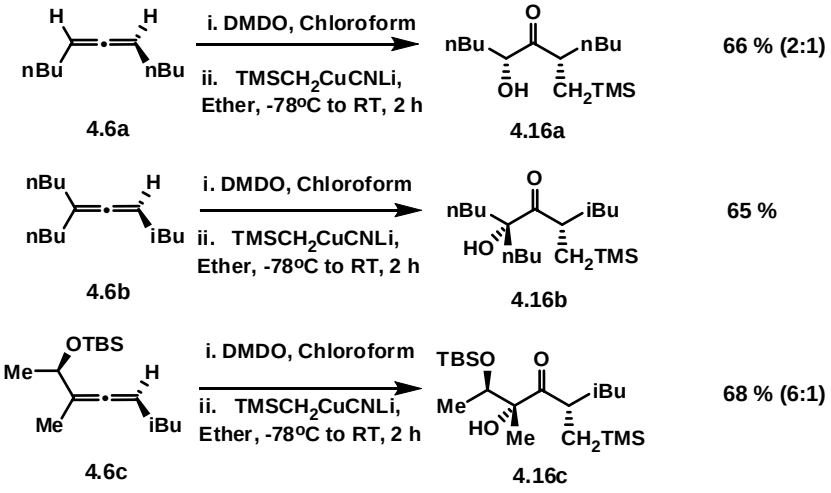
Delivery of the methyl from the cuprate is slow below -10°C but takes place rapidly at 0°C. Consistent with known trends in cuprate addition,

Scheme 4.5 **nButyl Cyanocuprate**

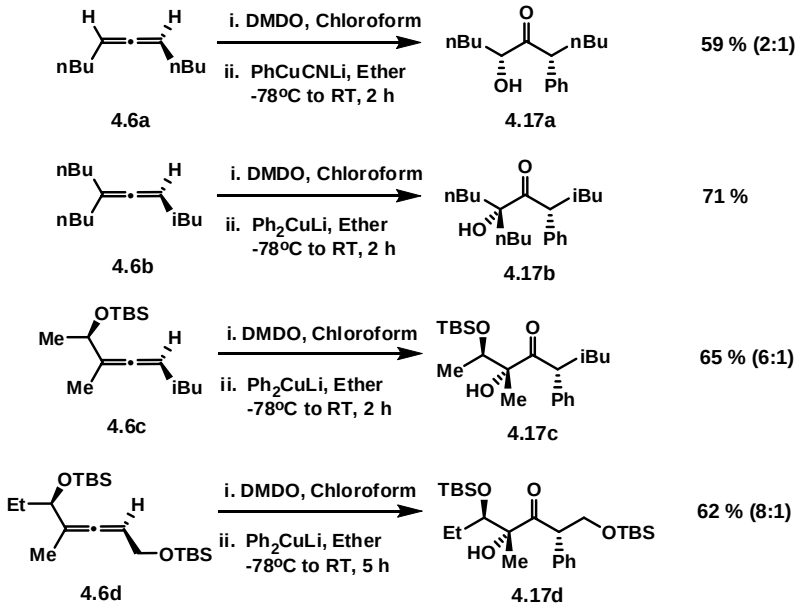


other alkyl ligands (nBu, $TMSCH_2$,Ph) transfer from copper more rapidly than methyl and could be carried out at -78°C or -40°C (data not shown) with no variation in yield. However, a monotonic decrease in yield is discernible with increased β-branching of the ligand (methyl-butyl-$TMSCH_2$) due to increase in the formation of reduction products.

Scheme 4.6 **TMS-methyl Cyanocuprate**



Scheme 4.7 **Phenyl Cuprate**



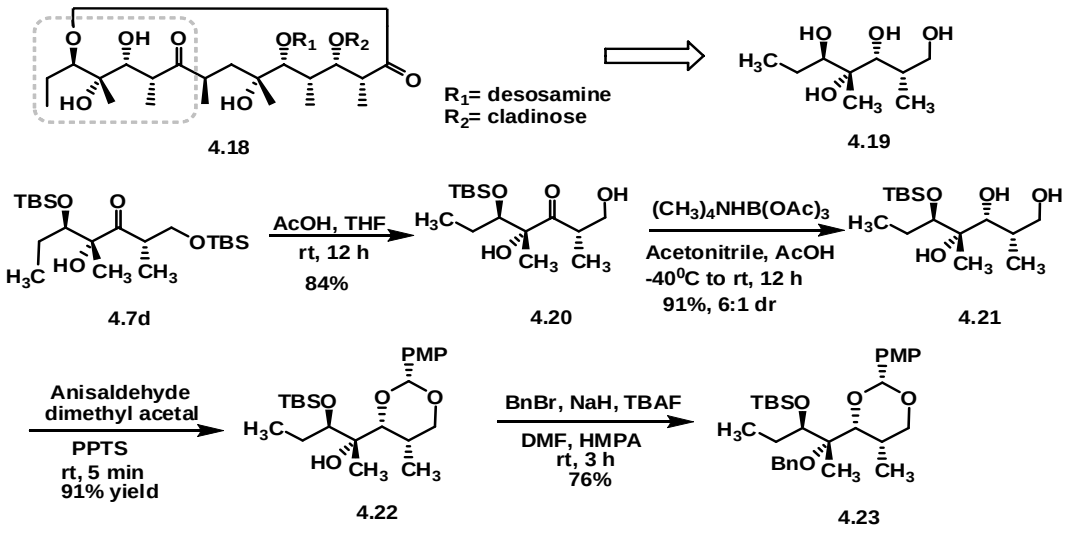
When phenyl was used, the yield with cyanocuprate was low (10-20%) except for SDE derived from di-substituted allene **4.6a**. However we were pleased to find that the more reactive Gilmann reagent efficiently delivered a phenyl group. Indeed, we expect other cuprates to prove useful when fast transferring ligands are of interest, since in such cases ligand transfer may effectively compete with reduction.

In each instance the diastereomeric ratio of products matched with the ratio of SDEs obtained from allene oxidation. Spectra of the known compound **4.7a** (major) matched with that reported in literature.[16] Also X-ray of a derivative of compound **4.7c** (major) confirmed the syn stereochemistry of the addition product. Thus, copper-mediated nucleophilic addition takes place with inversion. In each instance, the nucleophile was delivered regioselectively to the most accessible site of the SDE. No special precautions were performed beyond those normaly employed for cuprate additions. The overall yields, from allene to α-hydroxy ketone are excellent (77-92%) average per step.

4.7 Synthesis of Erythromycin Stereotetrad

To demonstrate the applicability of this new method in the context of erythronolide synthesis, my colleague Steve (Dr. Stephen D. Lotesta) in our group synthesized the stereotetrad **4.19** of erythromycin **4.18** from compound **4.7d** in just two steps (Scheme 4.8).[17] Thus compound **4.7d** was treated with 80 % acetic acid for selective removal of the primary TBS group to give **4.20**. The ketone in the resulting product **4.20** was reduced by sodium triacetoxy borohydride, directed by the primary alcohol to form **4.21** in a 6:1 ratio, which was separated by chromatography.[18] Proof of stereochemical assignment of **4.21** was confirmed by its conversion into known compound **4.23**.[27] Thus selective diol protectection of compound **4.21** as p-methoxy benzylidine followed by formation of the benzyl ether gave the known protected tetrol **4.23**. ^{1}H-NMR and ^{13}C - NMR and optical rotation of the protected tetrol **4.23** matched to the reported compound prepared previously by Woerpel et al.[19]

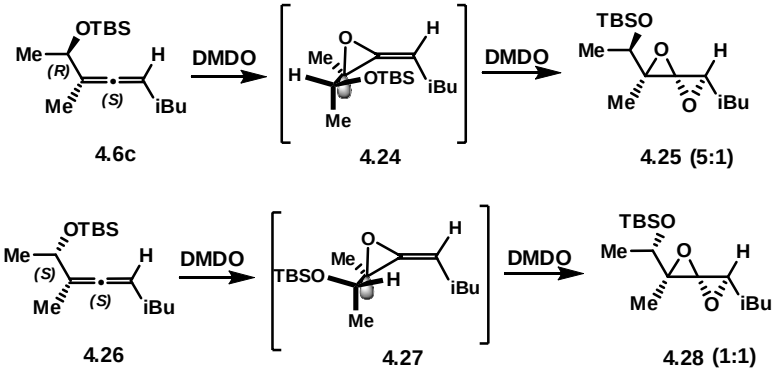
Scheme 4.8 **Synthesis of Erythromycin Stereotetrad**



4.8 Acyclic Stereocontrol in Stereoselective Spirodiepoxidation

The high selectivity in second oxidation observed for allene 4.**6c** and **4.6d** (Scheme 4.6, 4.7) can be traced in part to the conformational preference of the allene oxide formed after first epoxidation. Thus when allene **4.6c** is treated with DMDO, the first oxidation takes place with high selectivity (>20:1) to give the allene oxide **4.24** (Figure 4.2). The chiral (R) center next to the allene oxide may adopt the preferred conformation as shown, in which the electron donating methyl group is anti to the allene oxide C-O bond to maximize the stabilizing σ-σ* interaction. This places the sterically demanding TBS ether in proximity to one face of the allene oxide double bond and thus hinders approach of oxidant to that face (in this case the front face). Therefore the second oxidation takes place with high selectivity (5:1). This same analysis is also applicable to allene **4.6d**.

Figure 4.2 **Acyclic Stereocontrol**



This explanation predicts poor selectivity for the second oxidation of the diatereomeric allene **4.26**, as in this case the preferred allene oxide **4.27** conformation places the hydrogen in the proximity of allene oxide double bond. Indeed, Yue Zhang, a graduate student in our group found that upon subjecting allene **4.26** with DMDO, SDEs formed in 1:1 ratio.

4.9 Conclusion

The first general method of carbon nucleophile addition to the SDE functional group has been developed. This is also the first example of a transition metal-mediated SDE transformation. This C-C bond forming method expands the applicability of SDEs in synthesis. This method will serve as a stepping stone for the future development of methods for delivering a broader range of carbon nucleophiles to SDE. The data obtained in this study also provides mechanistic insight into the reactivity of both SDE and cuprate. This study also demonstrates the use of acyclic stereocontrol in achieving higher selectivity in allene oxidation.

4.10 References

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Chapter V

Erythronolide Model Study

5.1 Introduction

The necessity and relevance of a model study in facilitating an actual synthesis is debatable. There is a balance between how much resource and efforts it takes to perform such a study versus probable valuable insight it will generate in enabling execution of the actual synthesis. Of course, model studies are frequently used in the study of total syntheses.[1] Given the brevity of our proposed synthesis (≤ 15 steps) of (9*S*)-dihydroerythronolide A, pursuit of a model study might seem unnecessary. Yet, given the challenges certain to arise in the course of the proposed synthesis, a model study is quite appropriate. Even though one purpose of this model study was to facilitate the total synthesis of (9*S*)-dihydroerythronolide A, our objectives extend well beyond this single target.

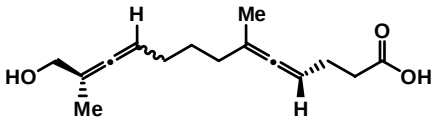
5.2 Objectives

- Test feasibility of bis[allene] macrolactonisation.
- Determine macrolactone stability.
- Investigate viability of bis[SDE] formation.
- Establish the single flask nucleophilic opening of two SDEs in the same molecule.
- Gain insight into the feasibility of synthesizing erythronolide analogues.

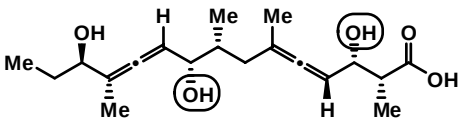
5.3 Synthesis of Bis[allene] macrolactone

We wanted to construct the bis[allene] seco acid **5.1** (Figure 5.1), which is simple, yet closely related to the bis[allene] seco acid **3.5**, to address each of the objectives mentioned above. We planned to synthesize **5.1** following a plan similar to that proposed for the total synthesis. Thus, sequential coupling of terminal alkynes with aldehydes would produce a bis[propargylate], which will be converted to the bis[allene] by way of standard procedures of mesylation, and then methyl cupration. However, in an effort to save time, we opted to non asymmetric propargylation to form bis[propargylate]. Moreover, it will enable us to gain access to both diastereomers of the bis[allene] seco acid **5.1**, both of which could be tested for macrolactonisation to give corresponding diastereomeric bis[allene] macrolactones. This would also lend insight into the effects of allene stereochemistry in the macrolactonisation of the bis[allene], if any.

Figure 5.1 **Bis[Allene] Seco Acid**



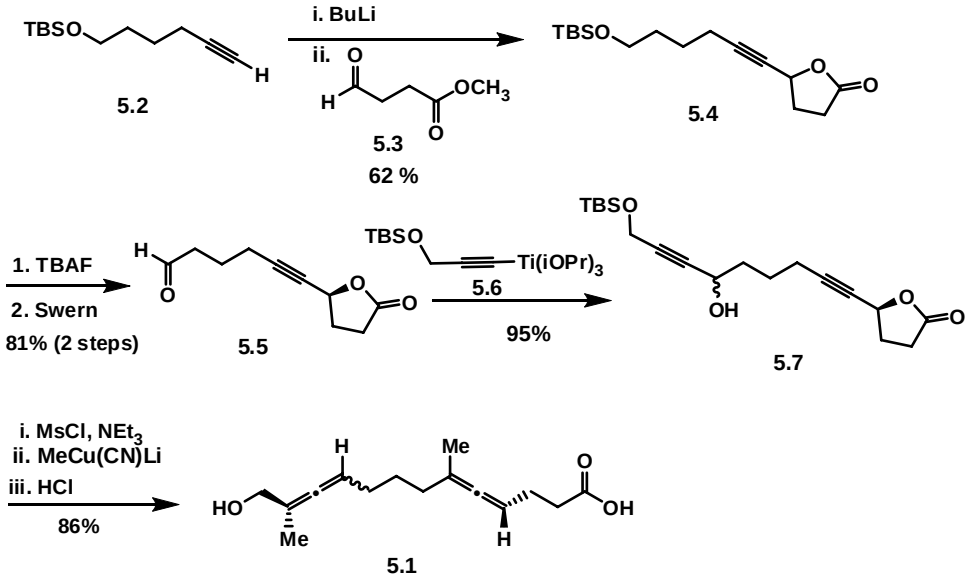
5.1 (1:1 diastereomer mixture)



3.5

Our synthesis began with the known TBS protected 5-hexyne-1-ol **5.2** (Scheme 1).[2] Formation of the alkynylide followed by its addition to the commercially available aldehyde **5.3** gave the γ-lactone **5.4** in 62% yield. Deprotection of TBS with TBAF gave the primary alcohol which upon Swern oxidation produced aldehyde **5.5** in 72% (2 steps) yield.

Scheme 5.1 **Synthesis of Seco Acid**

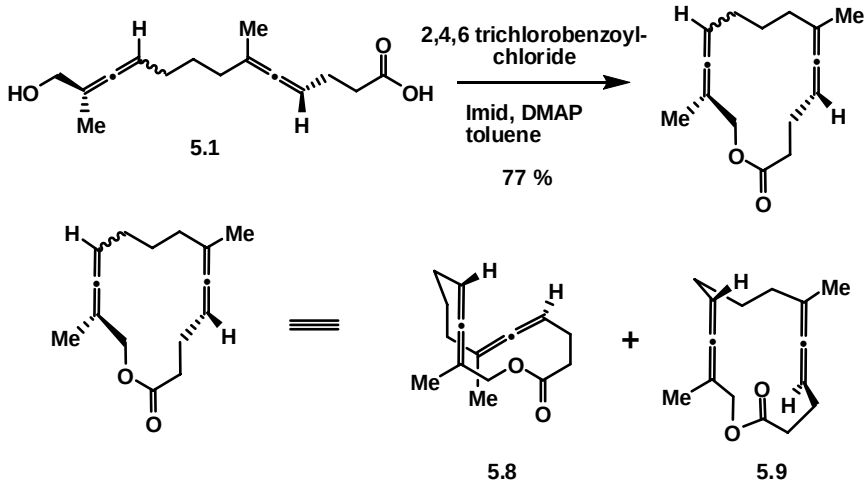


The TBS protected propargyl alcohol was converted to the titanium triisopropoxy alkynylide **5.6** and subsequently added to the aldehyde **5.5** in THF to furnish the bis-propargylate **5.7** as an equal mixture of inseparable diastereomers in 95% yield, which were carried forward in the following steps. A one pot procedure for mesylation of the propargyl alcohol **5.7** in diethyl ether, double addition of methyl cuprate in SN_2' fashion, and then treatment of the reaction mixture with a 10% HCl in THF furnished the bis[allene] seco acid **5.1** as an inseparable (1:1) mixture of diastereomers in 86% yield.

5.4 Results and discussion

After this short synthesis of bis[allene] seco acid, the stage was set to carry out our objectives. The diastereomeric allene mixture **5.1** was subjected to Yamaguchi macrolactonisation conditions. To our delight, the initial trial was successful in macrolactonizing both diastereomers albeit in low yield. Significant amounts of dimer formation were observed. However an optimized process of higher temperature coupled with controlled addition of activated carboxylic ester using syringe pump increased the yield to 77% (Scheme 5.2). This constitutes the first example of macrolactonisation of a bis[allene].

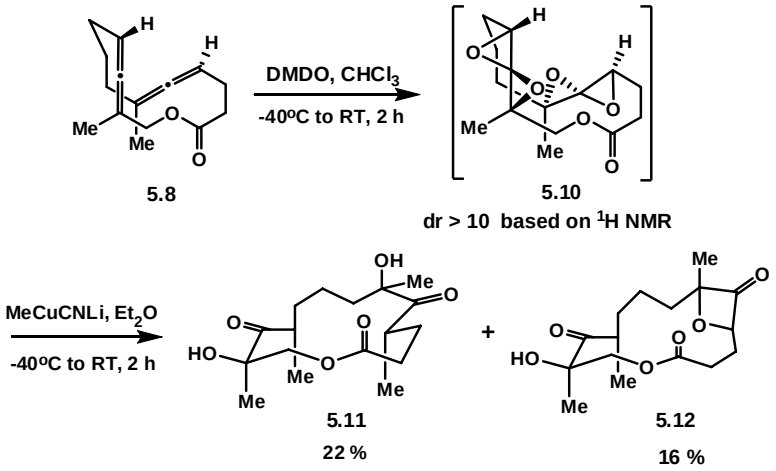
Scheme 5.2 **Macrolactonisation**



At this stage the two diastereomeric macrolactones **5.8** and **5.9** were separated. The allenes in macrolactone **5.8** have the same configuration as the bis[allene] macrolactone **3.5** in the proposed synthetic plan. It is important to note that the exact structures of **5.8** and **5.9** were unknown at this stage. Only upon solving X-ray structures of their subsequent reaction products was this ambiguity resolved.

Bis[allene] macrolactone **5.8** was then treated with DMDO in chloroform (Scheme 5.3). To our delight, an isolable bis[SDE] **5.10** was formed, which turned out to be quite stable at room temperature. ^{1}H NMR of **5.10** showed one major diastereomer with dr > 10:1. Thus macrocyclic stereocontrol proved effective in the stereoselective oxidation of both allenes.

Scheme 5.3 **Cuprate Addition to Bis[SDE]**

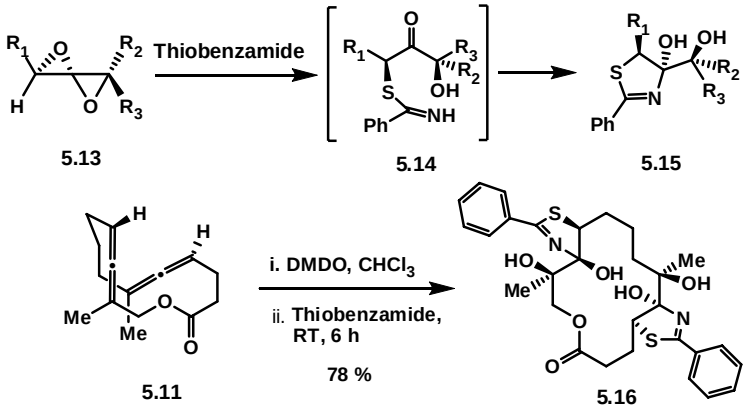


Upon bis[SDE] **5.10** addition to lower-order methyl cyanocuprate, a complex mixture of products was formed, with ample indication of the desired product **5.11** present. After rigorous chromatography, compound **5.11** was separated with 22% yield. The main side product **5.12** was also separated in 16% yield. The structure of both compound **5.11** and **5.12** were confirmed by X-ray crystallography (Appendix). Other side product characterization suggests that one methyl adds to one of the SDE but these products diverge in the other SDE transformation, which seems to include trans-annular reaction, reduction, and other rearrangements. The probable reason for formation of these products is that the intermediate formed from methyl cyanocuprate addition to one of the SDEs

precipitates out, thus making the cuprate addition to the second SDE slower and allowing side reactions to take place. Use of more polar solvent might solve this solubility problem. However, when THF was used instead of diethyl ether, the reaction gave inferior results. This is not surprising as diethyl ether was found to be superior than THF in methyl cuprate opening of SDEs (chapter IV). Nonetheless the 22% yield of the desired product is acceptable considering that in one step four oxygen atoms were introduced, two ketones formed and four stereocenters are set. Further optimization of this reaction may be possible, however the results as such were sufficiently convincing that we turned our attention to the total synthesis of (9*S*)-dierythronolide A.

As part of our objectives we also wanted to use other nucleophiles to open the bis-[SDE]. As discussed above, part of the problem associated with cuprate derived intermediates in the bis[SDE] system was solubility. This may not be an issue with other nucleophiles. One such nucleophile is thiobenzamide. Recently our group published a method to synthesize azolines and azoles from SDEs.[3] As shown in Scheme 5.4, when thioamide reacts with a SDE (**5.13),** thiazoline (**5.15)** is formed via acyclic imine intermediate **5.14**.

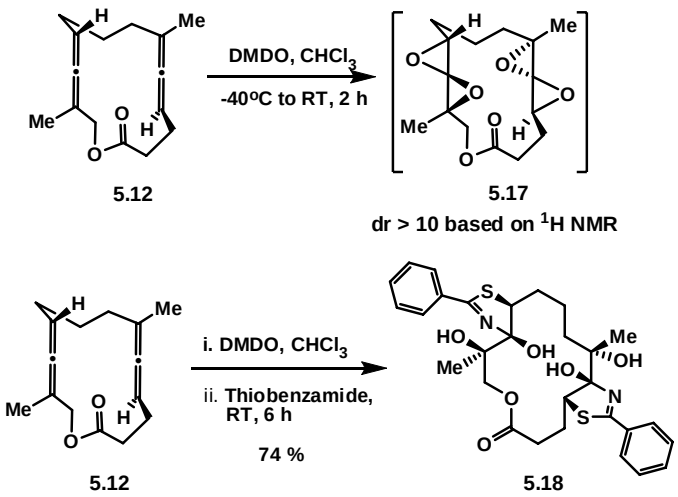
Scheme 5.4 **Thiobenzamide Addition to SDE.**



This reaction is mild, homogeneous and takes place at ambient temperature with excellent yields. Indeed, when the bis[SDE] derived from macrolactone **5.11** was treated with thiobenzamide it furnished the desired bis[thiazoline] **5.16** was isolated as single isolated isomer in excellent (78%) yield. Thus 6 stereocenters, two additional rings and several additional functionalities were introduced in a single step. The structure of **5.16** was confirmed by X-ray crystallography (Appendix).

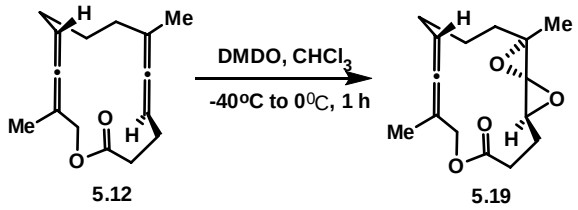
When diastereomeric bis[allene] macrolactone **5.12** was exposed to DMDO in chloroform, it also converted to a stable bis[SDE] **5.17** (Scheme 5.5). Once again ^{1}H NMR spectra of the crude reaction mixture showed dr > 10:1. Thus in the case of bis[allene] **5.1**, macrocyclic stereocontrol was also effective in the stereoselective oxidation of both allenes. Moreover when bis[SDE] **5.17** was treated with thiobenzamide the bis[thiazole] **5.18** was formed in excellent (74%) yield. The successful transformation of both bis[allene] macrolactones **5.11** and **5.12** to bis[thiazoline] **5.16** and **5.18** suggests the possible generality of these convergent reactions.

Scheme 5.5 **Diastereomeric Bis[Allene]**



The relative rate of oxidation of the two allenes in both bis[allenes] **5.11** and **5.12** turns out to be quite different. It was observed that one of the allene was oxidize below -20^{o}C whereas other oxidized only above 0^{o}C. Thus it was possible to stop oxidation at the mono-SDE stage. Indeed when bis-allene **5.12** was treated with only 2 equiv of DMDO (one equiv per double bond) and the temperature was kept below 0^{o}C, the mono[SDE] **5.19** formed (Scheme 5.6). This was also the case with bis[allene] **5.11** (data not shown). At this stage the regioselectivity of mono[SDE] formation was not certain. Based on our knowledge of allene oxidation, we were confident that the allene next to the lactone would be less nucleophilic due to the inductive effect of the acyl oxygen.

Scheme 5.6 **Regioselective Allene oxidation**



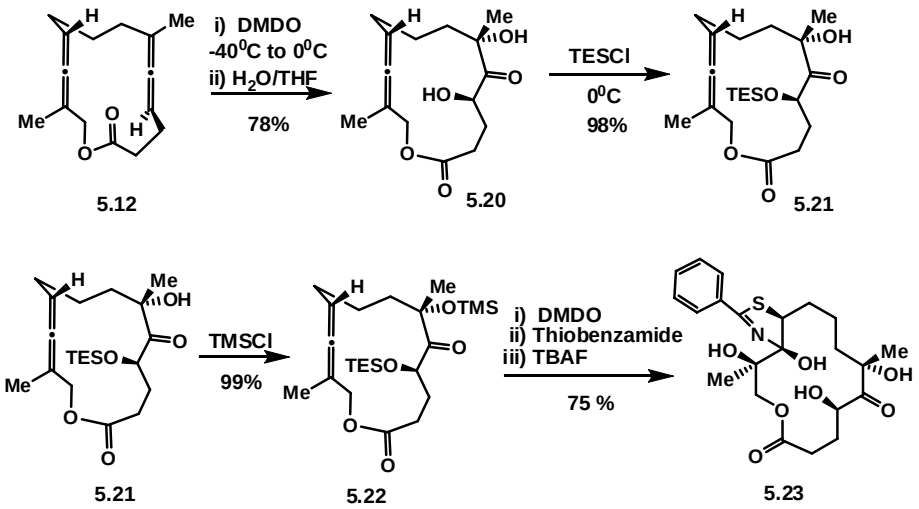
5.12 **5.19**

This differential rate of formation of two spirodiepoxide gives the opportunity to sequentially transform each allene in the macrolactone. Therefore it seemed likely that each SDE could be opened with a different nucleophile in a controlled manner. This prospect expands the scope for diversifying the synthesis of erythronolide analogues.

We tested the viability of this idea, albeit in a limited scope, as shown in Scheme 5.7. Controlled oxidation of bis[allene] with DMDO gave the mono[SDE], which upon reaction with water furnished diol **5.20** in 78% yield. Selective protection of the secondary alcohol with TES gave **5.21** in 98% yield. X-ray of compound **5.21** proved its

structure, thus also confirming our speculation regarding the regioselectivity of mono[SDE] formation.

Scheme 5.7 **Synthesis of hybrid analogues**



The tertiary alcohol of **5.21** was protected with TMS to give **5.22** in 99% yield. This double silyl protection was also performed in one step from diol **5.21** in 98% yield (not shown). Compound **5.22** was exposed to DMDO and the resulting SDE was treated with thiobenzamide to give bis[thiazoline], which upon subjecting to TBAF in the same flask underwent silyl groups deprotection to form the diol-thiazoline hybrid **5.23** in 75% yield.

5.5 Conclusion

The model study described in this chapter satisfactorily addresses the challenges that arise out of our proposed synthetic plan of (9*S*)-dihydroerythronolide A. This study constitutes the first example of bis[allene] macrolactonisation and the first example of bis[SDE] macrolactone formation. The one-step opening of both SDE by methyl cuprate proved acceptable given the degree of complexity introduced in this one step. In fact, in the actual synthesis, the presumed origin of the low yield (i.e insolubility of the intermediate in diethylether), could be overcome by choosing low polarity protecting groups in the bis[allene] macrolactone. Moreover, this study demonstrates that various erythronolide analogues could be synthesize in a few steps from the bis[allene] macrolactone using different nucleophiles to open the SDEs and by taking advantage of the intrinsic differential reactivity of the two allenes.

5.6 References

3 For some recent model studies, directed towards total syntheses see, a) Moreau R. J.; Sorensen E. J. Tetrahedron, **2007**, *63*, 6446. b) Baran, P. S.; Hafensteiner, B. D.; Ambhaikar, N. B.; Guerrero, C. A.; Gallagher, J. D. *J. Am. Chem. Soc*. **2006**, *128*. 8678. c) Furstner, A.; Aissa, C.; Chevrier, C.; Teply, F.; Nevado, C.; Tremblay, M. *Angew. Chem., Int. Ed. Engl.* **2006**, *45*, 5832. d) Taber, D. F.; Liang, J. L.; Chen, B.; Cai, L. *J. Org. Chem*. **2005**, *70*, 8739.

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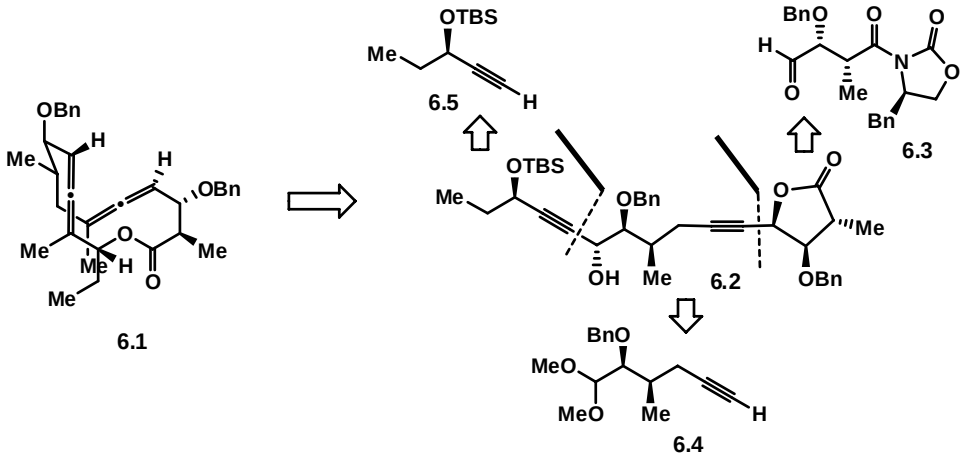
Chapter VI
Progress Towards the Total Synthesis of (9*S*)-Dihydroerythronolide A

6. 1 Synthesis of Bis[Allene] Macrolactone

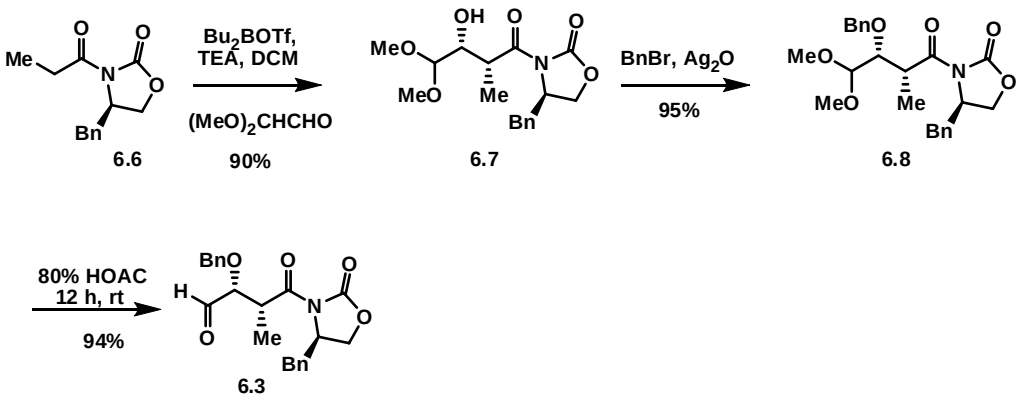
Encouraged by the outcome of the model study, we embarked on the synthesis of (9*S*)-dihydroerythronolide A. Progress towards this is described here. Our initial goal was to synthesize the bis[allene] macrolactone **6.1**. We chose the benzyl ether as the protecting group as deprotection of benzyl group in the final stage of erythronolide synthesis is precedented.[1] In accordance to our original strategy (Chapter III), the bis[allene] macrolactone **6.1** would be accessed from the bis[alkyne] **6.2**, which would be assembled in a sequential coupling of the aldehyde **6.3**, alkyne **6.4** and alkyne **6.5** (Scheme 6.1).

Scheme 6.1 **Synthetic plan**



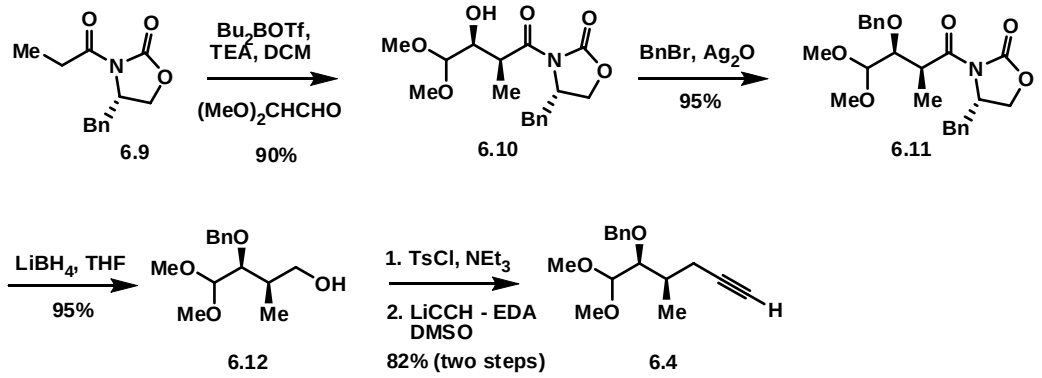
Synthesis of aldehyde **6.3** began with the Evans asymmetric aldol reaction.[2] Thus, addition of 1,1-dimethoxyacetaldehyde to the boron enolate of commercially available 4(R)-benzyl propionyl oxazolidinone **6.6** gave aldol product **6.7** (Scheme 6.2). 1, 1-dimethoxyacetaldehyde is also commercially available, albeit as a hydrated form in water. The anhydrous form of the aldehyde was obtained by first extraction into dichloromethane followed by dehydration with 4 Å molecular sieves. Depending on the efficacy of this dehydration, the yield of the aldol reaction varies, which is generally between 80-90 %. Benzyl protection of the resultant aldol product **6.7** by employing the common method of NaH and BnBr gave several by- products. However, when benzyl bromide was added to a mixture of **6.7**, Ag_2O and 4 Å molecular sieves, the benzyl protected aldol **6.8** formed in excellent 95% yield.[3] The presence of molecular sieves were critical for the success of this reaction. To the best of our knowledge, this is the first example of the Ag_2O mediated benzylation of an Evans aldol product. Hydrolysis of acetal **6.8** with 80% acetic acid in water provided aldehyde **6.3** in 94% yield.

Scheme 6.2 **Synthesis of Aldehyde 6.3**



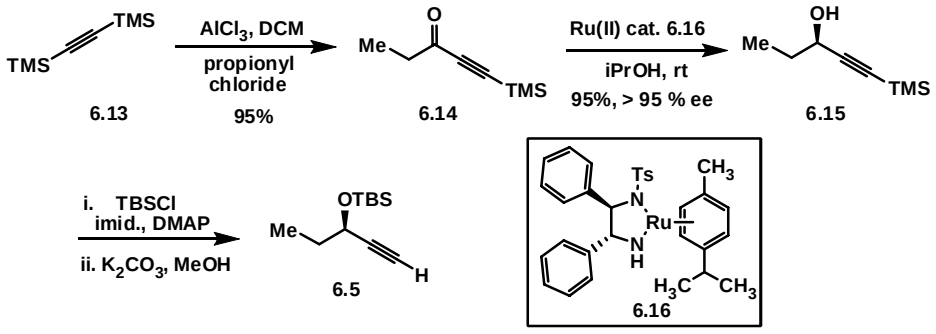
Synthesis of alkyne **6.4** began with the synthesis of benzyl protected aldol **6.11** (Scheme 6.3). Compound **6.11** is the antipode of **6.8** (Scheme 6.2). Therefore, **6.11** was synthesized using identical procedure as above except that 4(S)-benzyl propionyl oxazolidinone **6.9** was used as starting material.

Scheme 6.3 **Synthesis of Alkyne 6.4**



Reductive cleavage of the oxazolidinone auxiliary by lithium borohydride provided the primary alcohol **6.12**.[4] Conversion of the alcohol to the tosylate followed by displacement with acetylide in DMSO provided the terminal alkyne **6.4**.[5]

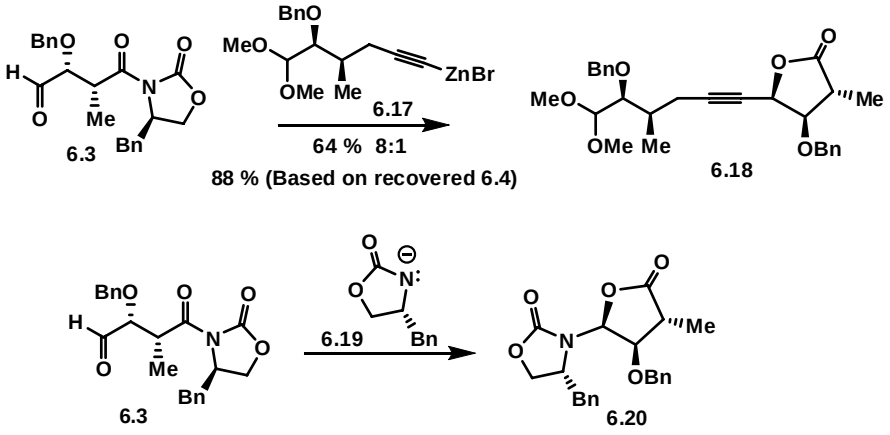
Scheme 6.4 **Synthesis of Alkyne 6.5**



Known propargyl alcohol[6] **6.5** was prepared from commercially available bis-TMS acetylene **6.13** following a procedure developed by my colleague Dr. Stephen D. Lotesta (Scheme 6.4).[7] $AlCl_3$-promoted Friedel-Crafts type acylation gave the alkynone **6.14** in 95% yield. Reduction of **6.14** by Noyori asymmetric transfer hydrogenation resulted in the alkynol **6.15** in 90% yield with > 95 % ee (determined by Mosher ester analysis).[8] A one pot protection of the alcohol with TBS followed by base cleavage of the TMS provided the alkyne **6.5** in 50% yield. The lower yield observed in the final step is largely due to the volatility of the alkyne product **6.5**.

With aldehyde **6.3** and alkyne **6.4** in hand, the stage was ready for their coupling to form the propargyl lactone **6.18**. Chelation controlled addition of the zinc alkynylide **6.17** of alkyne **6.4** to aldehyde **6.3**, followed by spontaneous lactonization in situ gave **6.18** in a modest 64 % yield as 8:1 mixture of diastereomers, which were separated by chromatography (Scheme 6.5).

Scheme 6.5 **Synthesis of Propargyl Lactone 6.18**

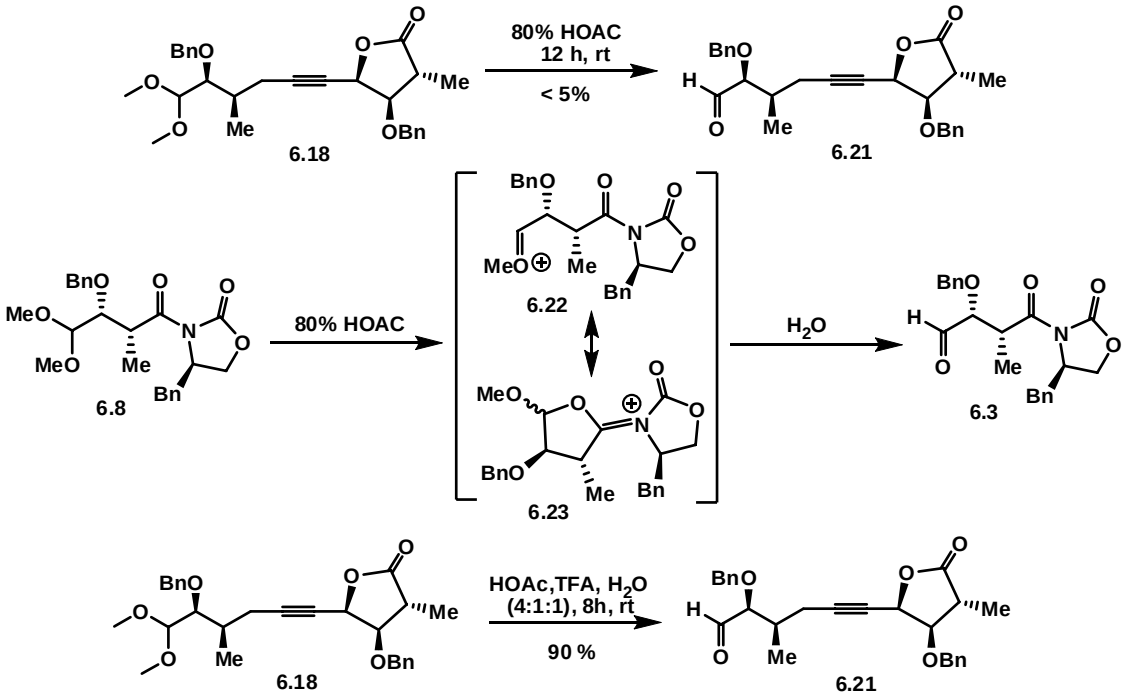


This propargylation competes with a side reaction in which the starting aldehyde **6.3** gets rearranged to **6.20**, promoted by the auxiliary anion **6.19**. As the propargylation proceeds, the amount of auxiliary anion **6.19** increases, which in turn increases the relative rate of the side reaction. Recently Wu et al reported a similar type of rearrangement.[9] Minimizing this side reaction by controlling temperature proved difficult as the above propargylation takes place in a narrow temperature range. The reaction is sluggish below -10^{o}C but takes place rapidly at 0^{o}C. After some optimization (not complete), the highest yield of **6.18** obtained so far was 64 %. However, the yield is an excellent 88%, when calculated based on the recovered alkyne **6.4**.

Chelation controlled addition of zinc alkynalide to the α-alkoxy aldehyde is known to proceed with high syn selectivity.[10] The syn selectivity in the major diastereomer of **6.18** was confirmed by measuring the coupling constant of the propargylic proton in ^{1}H NMR. In the major isomer, the coupling constant is (1H, td, 2.0 Hz, 6.5 Hz) compared to (1H, td, 2.0 Hz, 5.0 Hz) in minor isomer. Although this difference is small, the trend is the same as that for similar substrates reported in the literature.[11]

When propargyl lactone **6.18** was subjected to 80% acetic acid, only trace amount (<5%) of the desired aldehyde **6.21** was obtained after 8 hours at room temperature (Scheme 6.6). This was in sharp contrast to the conversion of **6.8→6.3** in 94% yield under the same condition (Scheme 6.2).

Scheme 6.6 **Hydrolysis of Acetal**

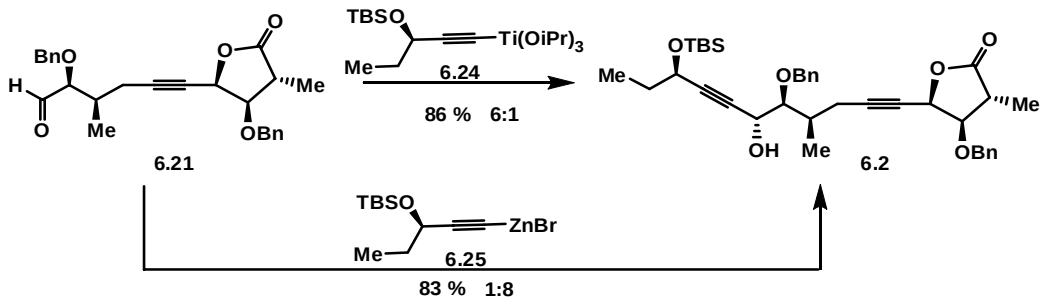


The sluggish hydrolysis of acetal **6.18** under 80% acetic acid condition is not surprising as acetal hydrolysis generally requires stronger acidic condition.[12] Rather, the hydrolysis of the acetal **6.8** appears to be unusually fast. One reason for this could be that in this case the intermediate oxonium ion **6.22** is stabilized by the oxazolidinone **6.23** (Scheme 6.6). Nonetheless, after some optimization, we were pleased to find that subjecting the acetal **6.18** in a 4:1:1 mixture of acetic acid, TFA and water afforded the aldehyde **6.21** in 90%

yield. The aldehyde **6.21** turned out to be somewhat unstable and was quickly advanced to the next reaction.

Non-chelation controlled addition of titanium triisopropoxy alkynalides to α-alkoxy aldehydes are known to proceed with high anti selectivity.[13] Thus, addition of titanium triisopropoxy alkynalide **6.24** of alkyne **6.5** to the aldehyde **6.21** gave the propargyl alcohol product **6.2** in 86 % yield as a 6:1 (anti: syn) mixture of diastereomers, which were separated by chromatography (Scheme 6.7).

Scheme 6.7 **Formation of Bis[Alkyne] 6.2**

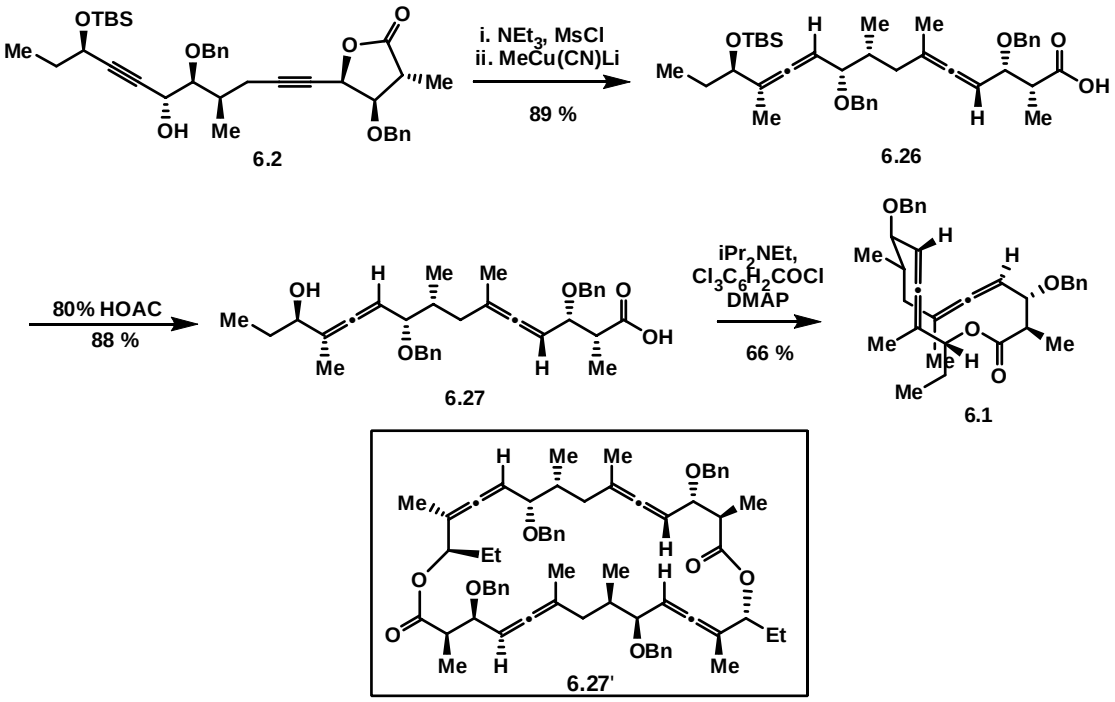


To confirm that the major isomer is indeed the non-chelation controlled anti product, zinc alkynalide **6.25** of alkyne **6.5** was added to the aldehyde **6.21** (zinc alkynalides add to α-alkoxy aldehydes in chelation control way). The product **6.2** was obtained in 83% yield but with a reverse 1:8 ratio (anti: syn). The reversal in relative ratios (1:8 vs 6:1) strongly supports the structural assignment.

A one pot conversion of the hydroxyl unit of **6.2,** first to the mesylate and then by addition of excess lower order methyl cyanocuprate generated bis[allene] **6.26** in 88% yield (Scheme 6.8). Deprotection of the TBS under acidic conditions resulted the

bis[allene] seco acid **6.27** in 92 % yield. Yamaguchi macrolactonisation of the seco acid **6.27** provided bis[allene] macrolactone **6.1** in 66 % yield.[14] The major by-product of this macrolactonisation process is the macrolactone dimer of seco acid **6.27'** (see inset) which could be minimized by further optimization.

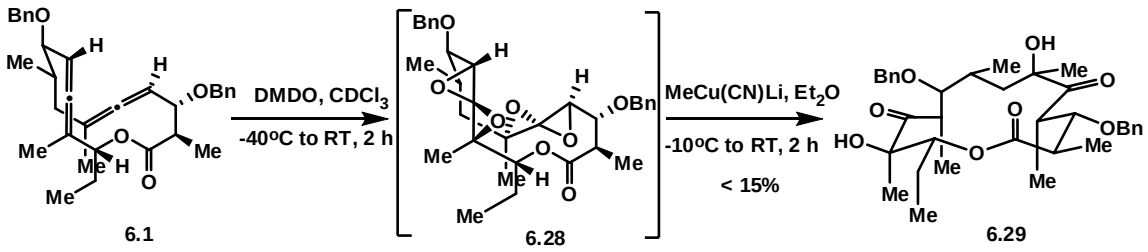
Scheme 6.8 **Synthesis of Bis[Allene] Macrolactone 6.1**



6.2 Formation of Bis[SDE] and Addition of Cuprate

The bis[allene] macrolactone **6.1** was treated with DMDO in $CDCl_3$ to form bis[SDE] **6.28**. Similar to the model study (Chapter V), one allene underwent oxidation to SDE below 0°C while the other allene remained unreacted under these conditions. Only after 15 minutes at room temperature the other allene was completely oxidized to the SDE. However, at room temperature, significant cleavage of the benzyl group was observed (~ 25 % by ^{1}H NMR), which was even more prominent when $CHCl_3$ was used as solvent instead of $CDCl_3$. Due to this benzyl cleavage, the stereoselectivity of the bis[SDE] **6.28** formation could not be determined.

Scheme 6.9 **Formation of Bis[SDE] 6.28 Followed by Addition of Cuprate**



Despite this ambiguity, the product mixture (containing bis[SDE] **6.28** and benzyl cleavage products) obtained upon DMDO oxidation was added to the lower order methyl cyanocuprate at -10°C (Scheme 6.9). The reaction produced a complex mixture of products. Addition of cuprate at lower temperature (-78°C and -40°C) did not improve the outcome. ESI-MS of the reaction mixture showed the peak 619.4, corresponding to the desired product **6.29** (M+23). We were able to locate the source of the ESI-MS peak of 619.4 to a portion of the reaction mixture (30 % by weight of the reaction mixture). The

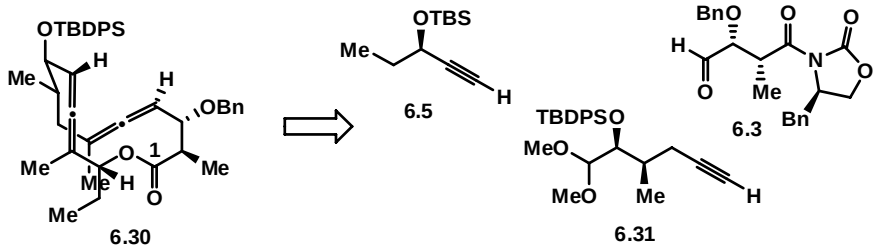
^{1}H NMR of which also hinted at the presence of the product **6.29** (peaks observed between 3.10- 3.60 ppm is typical for the α-methyne proton of α-methyl substituted ketone). Unfortunately, we were not successful in isolating **6.29** in pure form. We did anticipate the formation of several side products in the cuprate addition to the bis-SDE **6.28** as was the case in the model study. However, the additional dimension of benzyl cleavage made the analysis much more complicated. Therefore, we decided to attack the protecting group problem before embarking on the optimization of the cuprate addition reaction.

6.3 Exploring Other Protecting Groups

6.31 Silyl Protecting Group

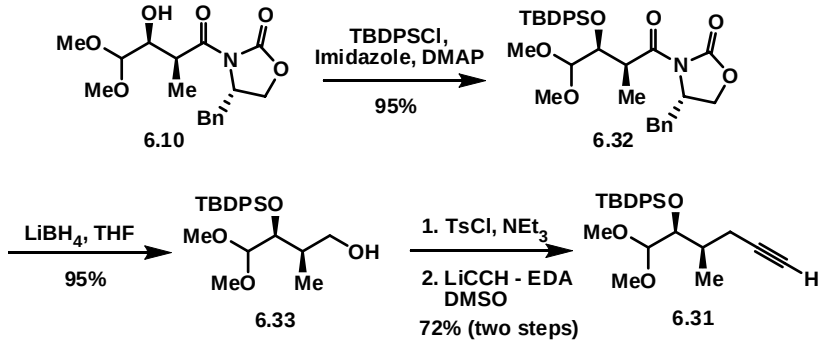
Silyl ethers are stable under DMDO oxidation condition even at room temperature.[15] In addition, they are very non polar and may improve the solubility problem in the cuprate addition to the bis[SDE] (as discussed in chapter V). Therefore, we decided to synthesize the bis[allene] macrolactone **6.30** with TBDPS protecting group at C9 hydroxyl (Scheme 6.10). We planned to construct bis[allene] macrolactone **6.30** by a route similar to that used to synthesize **6.1**, i.e. from aldehyde **6.3**, alkyne **6.31**, and alkyne **6.5**. Use of a TBDPS ether was chosen over other silyl ethers as this group is stable under the acidic hydrolysis conditions used to remove the acetal.[16] In order to switch the benzyl protecting group at the C3 hydroxyl of **6.30** to a silyl ether would require a silyl protected aldehyde (c.f. **6.3)**. However, this would prevent α-chelation in the alkyne **6.31** addition, as silyl ethers generally do not chelate in this type of reaction.[17] Therefore, the C3 hydroxyl in the target bis[allene] **6.30** was left unchanged to the benzyl protecting group.

Scheme 6.10 **Synthetic plan for Bis[Allene] 6.30**



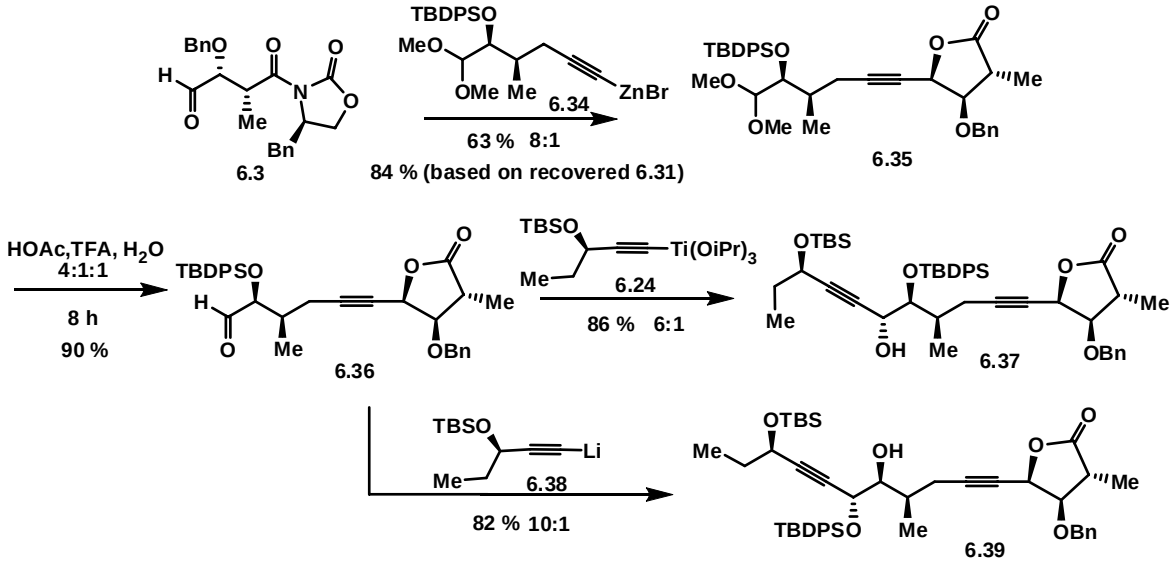
Synthesis of alkyne **6.31** is similar to that of alkyne **6.4** (Scheme 6.11). Thus, protection of **6.10** with TBDPS followed by reductive cleavage of the auxiliary gave primary alcohol **6.33**. Conversion of **6.33** to the tosylate followed by substitution with acetylide provided alkyne **6.31** in 72 % yield (two steps).

Scheme 6.11 **Synthesis of Alkyne 6.31**



Addition of the zinc alkynalide **6.3**, derived from alkyne **6.31,** to aldehyde **6.3** followed by spontaneous in situ lactonization gave propargyl lactone **6.35** in 63% yield as an 8:1

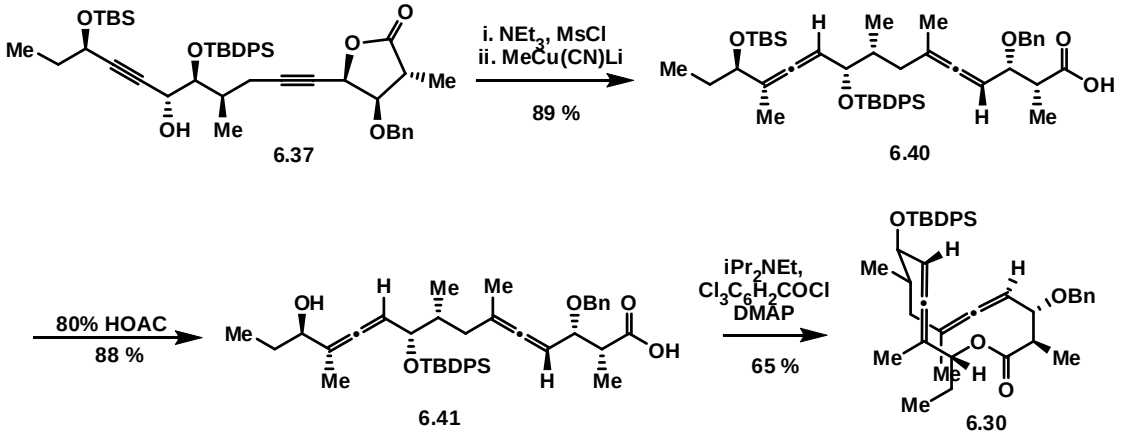
Scheme 6.12 **Synthesis of Bis[Alkyne] 6.37**



mixture of diastereomers, which were separated by chromatography (Scheme 6.12). It is noteworthy that the yield is 84% when calculated based on the recovered alkyne **6.31**. Acidic hydrolysis of the acetal gave aldehyde **6.36** in 90% yield, which was reacted with titanium alkynalide **6.24**, itself derived from alkyne **6.5**, to generate the bis[alkyne] **6.37** in 83% yield as 6:1 mixture of inseparable diastereomer, which were carried to the next reaction. When lithium alkynalide **6.38** was added to the aldehyde **6.3** the product **6.39** formed in high 10:1 diastereoselectivity, albeit with complete migration of TBDPS group to the propargyl alcohol.

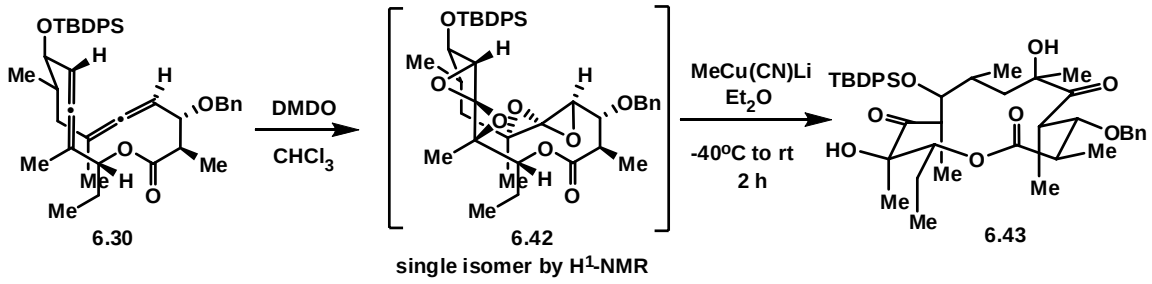
One pot conversion of alcohol **6.37** to mesylate followed by addition of excess lower order methyl cyanocuprate generated bis[allene] **6.40** in 89 % yield (Scheme 6.13). At this stage, the major diastereomer was separated by chromatography. Acidic deprotection of the TBS gave seco acid **6.41**, which upon Yamaguchi macrolactonisation provided bis-allene macrolactone **6.30** in 65% yield.

Scheme 6.13 **Synthesis of Bis[Allene] Macrolactone 6.30**



The bis[allene] **6.30** was then subjected to DMDO oxidation (Scheme 6.14). We were pleased to find that the bis[SDE] **6.42** formed as a single observed diastereomer with little (< 5 %) benzyl cleavage (as indicated by ^{1}H NMR). However, when **6.42** was added to the excess lower order methyl cyanocuprate, a complex reaction mixture was obtained.

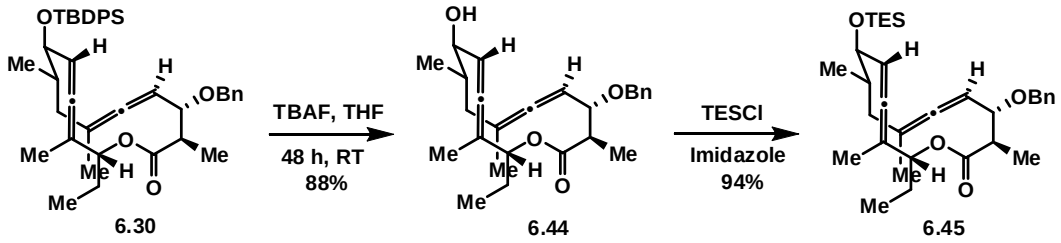
Scheme6.14 **Formation of Bis[SDE] 6.42 Followed by Addition of Cuprate**



Although the product mixture did show ESI-MS peak 767.4 corresponding to the desired product **6.43** (M+23), it was very weak. Also, the crude ^{1}H NMR of the reaction mixture did not appear to show any significant amounts of peaks related to the desired product **6.43**. Thus, the transformation **6.30→6.43** turned out to be less promising than the original **6.1→6.29**. Importantly, these data suggest that oxidation of a fully functionalized macrocycle bis[allene] will proceed with high selectivity.

We anticipated the apparent failure of the above reaction to the bulky TBDPS group which probably hinders the cuprate attack to the SDE. Therefore, we decided to replace TBDPS with less sterically demanding TES.

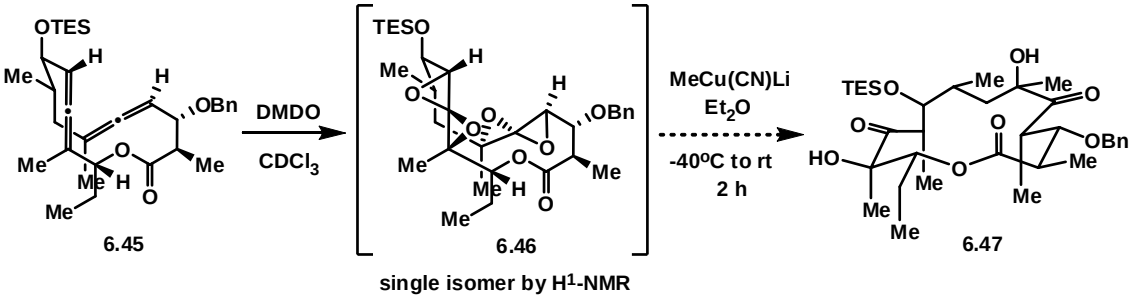
Scheme 6.14 **Synthesis of Bis[Allene] 6.45**



Removal of the TBDPS with TBAF gave the alcohol, **6.44**, in 88% yield, which was then protected with TES (→ **6.45**) in 94% yield (Scheme 6.14).

Treatment of bis[SDE] **6.46** (single diastereomer by ^{1}H NMR) derived from bis[allene] **6.45** with methyl cyanocuprate also appeared to fail to produce significant (<5%) amounts of the desired product **6.47** (Scheme 6.15).

Scheme 6.15 **Formation of Bis[SDE] 6.46 Followed by Addition of cuprate**



Thus, replacement of the TBDPS group with TES did not improve the outcome of the cuprate addition reaction. Following these unsuccessful results with silyl protecting groups, we returned to the benzyl protecting group. However, to deal with the instability of benzyl ether under DMDO oxidation condition, we decided to explore the use of a fluorine substituted benzyl protecting group.

6.32 Fluorine Substituted Benzyl Protecting Group

The benzyl ether of **6.48** cleaves in DMDO, presumably via the formation of hemiacetal **6.49** which then converts to the free alcohol **6.50** and benzaldehyde **6.51** (Scheme 6.16).[18] Since the oxidative cleavage is more prominent with electron rich benzyl ethers such as PMB,[19] we reasoned that an electron withdrawing substituent like fluorine would minimize the benzyl cleavage.

Scheme 6.16 **Mechanism of Benzyl Deprotection in DMDO**

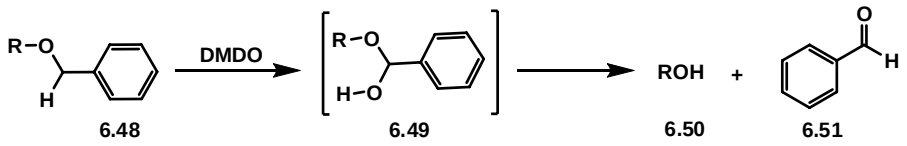


Table 6.1 **Effect of Fluorine Substitution on Benzyl Deprotection**

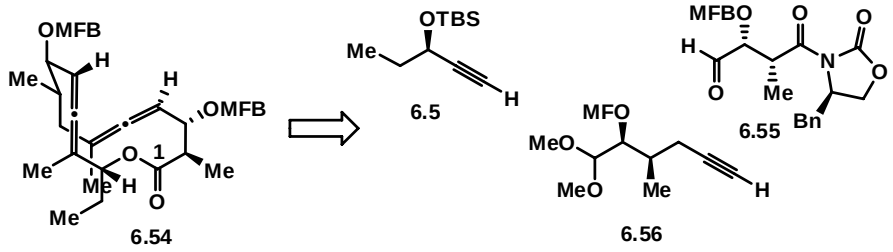
entry	X	6.53 (%)*
1	H	80 - 85%
2	4-fluoro	75 - 80%
3	2,6-difluoro	75 - 80%
4	3-fluoro	> 98 %

* Calculated by ^{1}H NMR

A model study of DMDO oxidation of allene **6.52** to SDE **6.53** showed that the extent of benzyl cleavage depends on the relative position of the fluorine substituent in the benzyl aromatic ring (Table 6.1). Under room temperature DMDO oxidation conditions, 4-fluoro and 2, 6-difluoro benzyl ethers cleaved to approximately same extent (entry 2 and 3) but

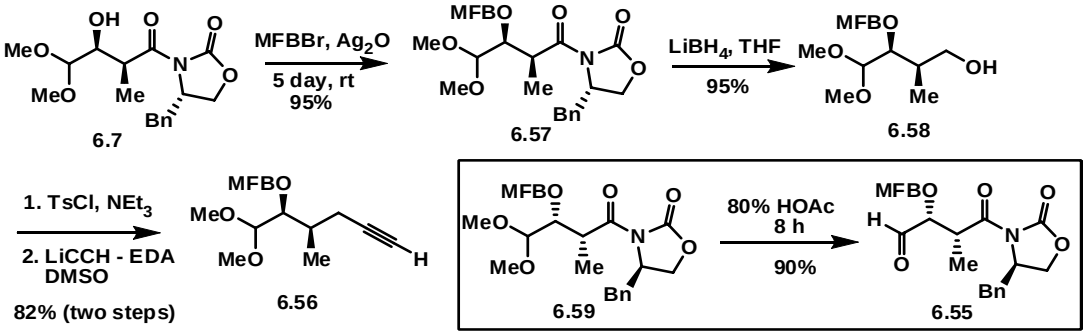
apparently slightly more than the unsubstituted benzyl ether (entry 1) However, under the same conditions, no significant cleavage of the 3-fluoro benzyl ether was observed (entry 4). Encouraged by this result, we embarked on the synthesis of 3-fluorobenzyl protected bis[allene] macrolactone **6.54**, using the original synthetic strategy used for the synthesis of bis[allene] macrolactone **6.1**. Thus, **6.54** would be assembled from the aldehyde **6.55**, alkyne **6.56**, and alkyne **6.5** (Scheme 6.17).

Scheme 6.17 **Synthetic Plan for Bis[Allene] 6.54**



The alcohol of **6.7** was protected with 3-fluorobenzyl group (MFB) using Ag_2O to give **6.57** (Scheme 6.18). The reaction was slow compared to the unsubstituted benzyl protection but the yield was excellent 95%. Lithium borohydride reduction of **6.57** gave primary alcohol **6.58**.

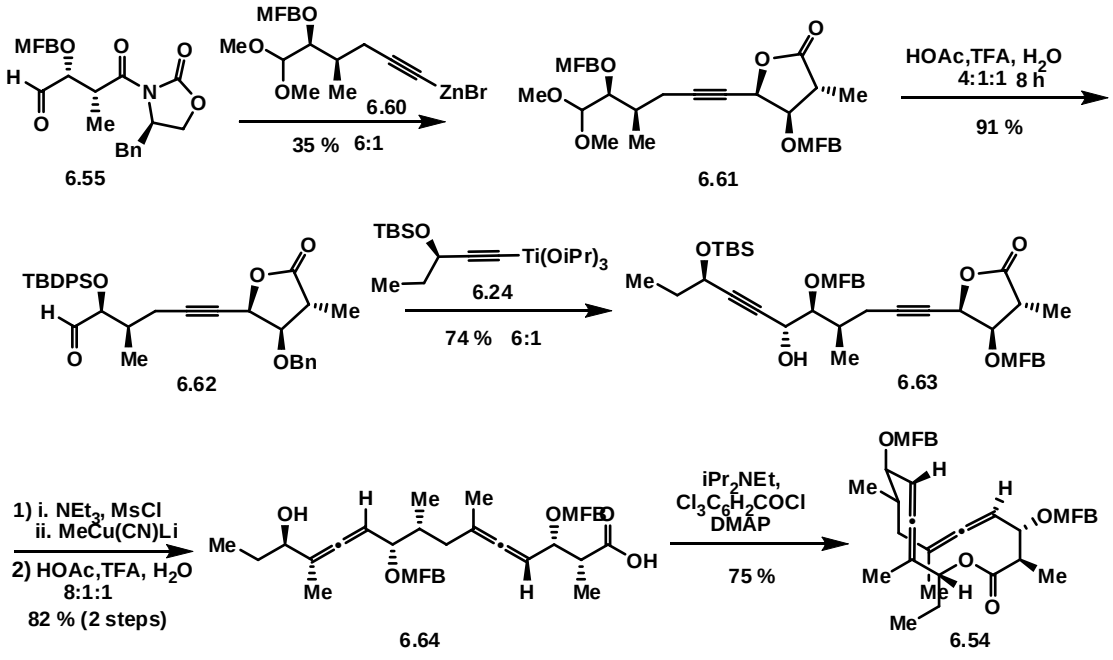
Scheme 6.18 **Synthesis of Aldehyde 6.55 and Alkyne 6.56**



Conversion of the primary alcohol to the tosylate followed by substitution with lithium acetylide in DMSO provided alkyne **6.56**. The 4-fluorobenzyl protected aldol **6.59** was synthesized by employing identical conditions used for the synthesis of its antipode **6.57**. Acid hydrolysis of acetal in **6.59** provided aldehyde **6.55**.

Chelation control addition of zinc alkynalide **6.60** to aldehyde **6.55** gave **6.61** in 35% yield as 6:1 mixture of diastereomers, which were separated by chromatography. The yield and diastereomeric ratio obtained is lower than expected and needs to be optimized. Acidic hydrolysis of acetal **6.61** provided aldehyde **6.62**, to which titanium alkynalide **6.24** was added to produce the bis[alkyne] **6.63** in 74% yield as a 6:1 mixture of diastereomers, which were separated by chromatography.

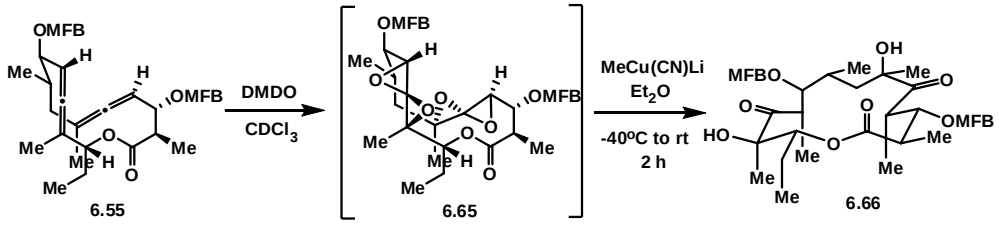
***Scheme* 6.19 Synthesis of Bis[Allene] Macrolactone 6.54**



Single flask mesylation of the propargyl alcohol followed by addition of excess methyl cyanocuprate gave the bis[allene], which upon TBS removal led to formation of bis[allene] seco acid **6.64** in 82% yield (2 steps). Yamaguchi macrolactonization of seco acid **6.64** provided bis[allene] macrolactone **6.54** in 75% yield. The macrolactonization yield obtained here is higher than that of bis[allene] **6.27** and of **6.41**.

DMDO oxidation of bis[allene] **6.55** was performed only once, 30 mg scale, Scheme 6.20. Formation of bis[SDE] **6.65** was accompanied with minor benzyl cleavage (~10 %). Although minor benzyl cleavage was unexpected, given the insignificant amount of 3-fluorobenzyl cleavage observed with allene **6.52** (entry 4, Table 6.1).

Scheme 6.20 **Formation of Bis[SDE] 6.65 Followed by Addition of Cuprate**



We strongly believe that this benzyl cleavage could be minimized with further optimization, which would include controlling reaction temperature and may depend upon the quality and freshness of DMDO. When bis[SDE] **6.65** was subjected to lower order cyanocuprate, a complex product mixture was obtained. However, both ^{1}H NMR and ESI-MS of the crude reaction mixture indicated the presence of the desired product **6.66**. At this point, we decided that the best approach to this problem would be to synthesize bis[allene] **6.55** in multi gram quantities for optimization studies of the methyl cuprate addition to bis-SDE **6.65.** Although this line of research was not pursued further, alternative routes were examined and are discussed below.

6.4 Potential Alternative Routes

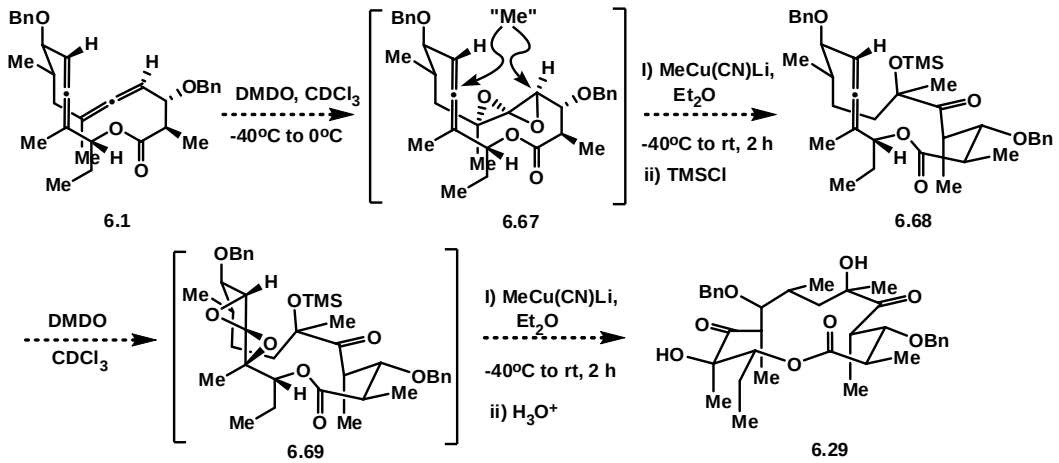
6.41 Introduction

To avoid the problem associated with cuprate addition to both SDEs, we sought possible ways to transform each allene to the α-hydroxyketone (via SDE) in separate steps by taking advantage of the differential formation and reactivity of the two allenes. This approach would increase the total number of steps required for the synthesis of (9*S*)-dihydroerythronolide A somewhat, but the synthesis would still be much shorter than previous erythronolide syntheses. Moreover, as addition of methyl cuprate to SDE can be high yielding (Chapter IV), this increased number of steps would not necessarily decrease the overall yield.

6.42 Alternative Approach I

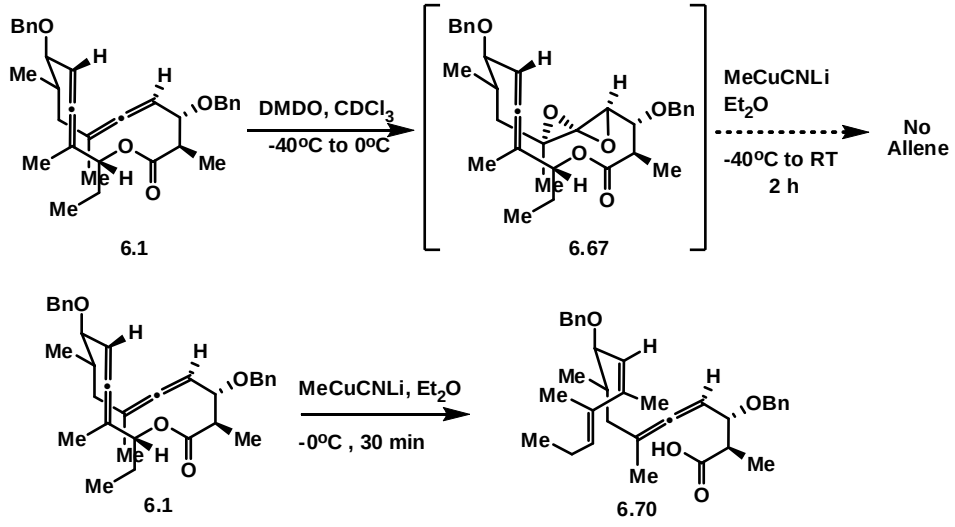
Our first alternative approach sought to take advantage of the intrinsic differential reactivity of the two allenes present in bis[allene] macrolactone **6.1** (Scheme 6.21).

Scheme 6.21 **Alternative Synthetic Plan I**



In the course of the model study (Chapter V), we successfully applied this concept in the synthesis of erythronolide analogues. Thus, we reasoned that controlled DMDO oxidation of bis[allene] macrolactone **6.1** would result in SDE **6.67**. Addition of methyl cyanocuprate followed by quenching the reaction with TMSCl could give **6.68**. It was unclear at this stage, as to the relative reactivity of the SDE in conjunction to the potentially labile allene SN_2' ring opening (Scheme 6.21). DMDO oxidation of the remaining allene in a second step to SDE **6.69** should be stereoselective due to macrocyclic stereocontrol. Addition of methyl cuprate followed by mild acidic workup to remove the tertiary TMS would provide **6.29**. Therefore, by adding just one more step to the original route (Scheme 6.9), we may be able to access key intermediate **6.29**, an advanced precursor to the final target (9*S*)-dihydroerythronolide A.

Scheme 6.22 **Addition of Cuprate to Allene**



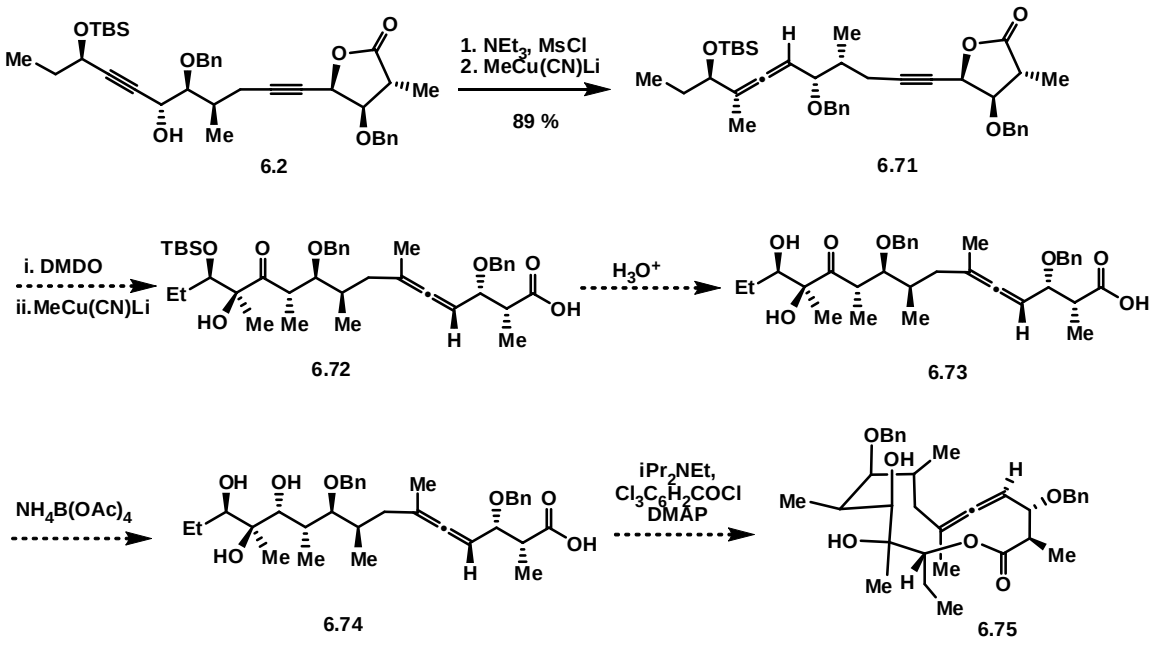
However, when SDE **6.67** was subjected to the lower order methyl cyanocuprate conditions, a mixture of products formed. Examination of the ^{1}H and ^{13}C NMR of the

mixture indicated the absence of the allene. This suggests that the cuprate may have added to the allene and opened the lactone in an SN_2' fashion. This notion has support in finding that subjection of allene **6.1** to the methyl cyanocuprate condition at 0°C resulted in formation of the carboxylic acid **6.70**. Thus, this alternative approach turned out to be unsuccessful.

6.43 Alternative Approach II

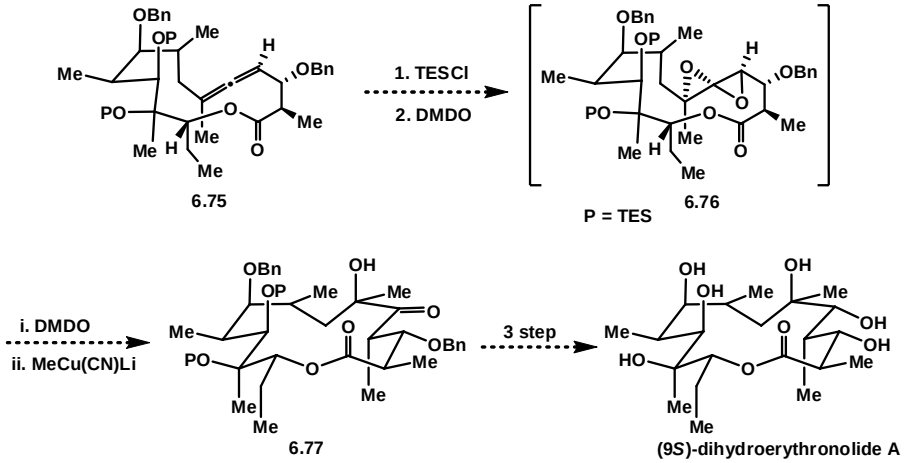
Although not evaluated experimentally, one alternative is to take advantage of the differential rate of formation of the two allenes (Scheme 6.23). When the mesylate derived from bis[alkyne] **6.2** was subjected to methyl cuprate, we observed that SN_2' displacement of the mesylate took place rapidly below -40°C and resulted in formation of the mono allene **6.71**. Subsequent formation of the bis[allene] took place only above 0°C.

Scheme 6.23 **Alternative Synthetic Plan II**



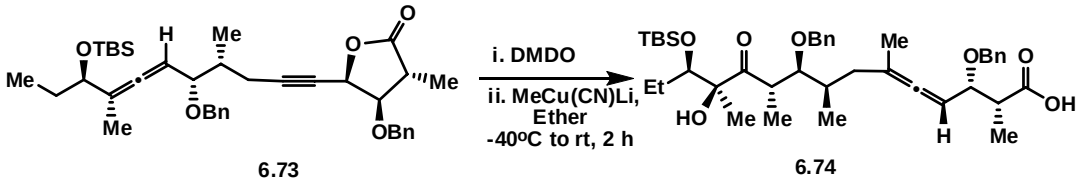
Therefore it should be possible by keeping the temperature below 0°C, in the cuprate reaction, to access allene **6.71**. Chemoselective DMDO oxidation of the allene in the presence of the alkyne could give the corresponding SDE with high selectivity due to acyclic stereocontrol (chapter IV). Upon exposure to excess methyl cuprate, the SDE should open and the allene should form (→ **6.72**). Removal of the TBS group would give the seco acid **6.73**. Ammonium triacetoxyborohydride reduction of the ketone, directed by secondary alcohol would give the diol **6.74**, which upon Yamaguchi macrolactonisation would then provide the allene macrolactone **6.75**. Stereoselective oxidation of the allene to the SDE followed by addition of methyl cuprate should give **6.77**. Hydride addition to the ketones, followed by benzyl deprotection, would complete the total synthesis of (9*S*)-dihydroerythronolide A.

Scheme 6.23 **(Continued)**



When allene **6.73** was treated with DMDO, the SDE formed with apparent high selectivity (the exact ratio could not be obtained due to some benzyl cleavage). Subjection of the SDE to excess methyl cuprate resulted in a mixture of products, almost all of which apparently contain the carboxylic acid functionality (as judged by TLC). These data suggests that formation of the allene is probably faster than addition of the cuprate to the SDE. ESI-MS and ^{1}H NMR analysis indicate the presence of the desired product (**6.74**). However, we were unable to isolate **6.74** from the product mixture.

Scheme 6.24 **Synthesis of Allene 6.74**



6.5 Future Direction

Future efforts in this area should focus on optimization of the methyl cuprate addition to the bis-SDE **6.65**, including cuprates other than lower order cyanocuprates. The problem of benzyl cleavage has been largely solved with 3-fluorobenzyl protecting group and we are confident that it could be further minimized. Yields as low as 15% (62% average per step) of the cuprate addition step may be acceptable to us and we are confident in achieving that goal. Separately, further optimization of cuprate addition to the SDE derived from allene **6.73** (Scheme 23) is warranted. Moreover, as part of our broader goal, efforts directed towards the synthesis of erythronolide analogues, e.g. by adding different nucleophiles to the bis[SDE] macrolactone, is worth study.

6.5 References

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Chapter VII

Silyl Substituted Spirodiepoxides

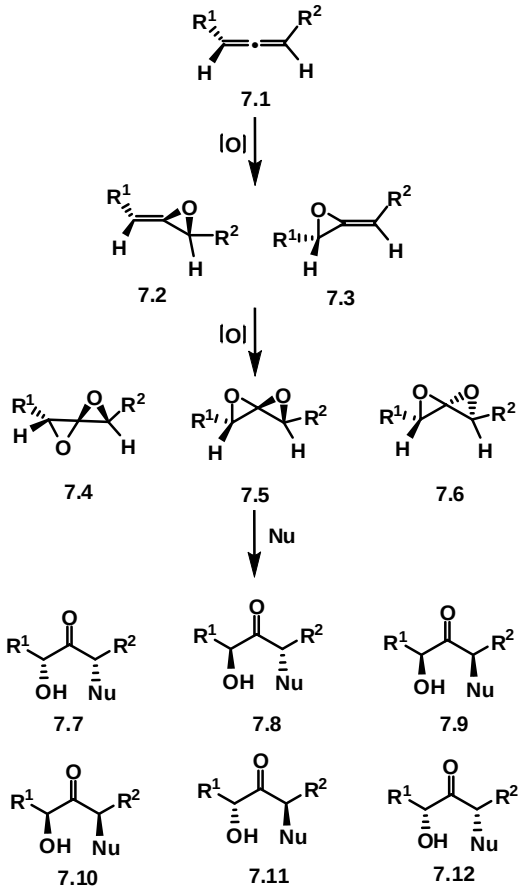
7.1 Introduction

The central challenge to most SDE-based methods is the stereoselective oxidation of the allene oxide (i.e. the second oxidation of the allene). In the previous chapters, we overcame this challenge through specific structural features in certain acyclic systems (chapter IV) and by macrocyclic stereocontrol (Chapter V). However, a general approach to address this challenge would be preferable. Additionally, there remains the challenge of controlling the regioselectivity in the nucleophilic opening of 1,3-disubstituted SDEs. We wondered whether a silyl group could be used as a proton surrogate to address these challenges. During the past few decades, there has been widespread use of silyl containing compounds (including silyl substituted epoxides) in numerous synthetic transformations, where silicon played a pivotal role in controlling stereoselectivity and/or regioselectivity.[1] Silyl allenes are easy to prepare and have been used extensively in numerous synthesis.[1] However, there is only one report of epoxidation of a silyl substituted allene.[2] In this chapter, we will discuss the stereoselective formation and regioselective nucleophilic opening of silyl substituted SDEs and their various synthetic applications, including the first total synthesis of a novel penicillium metabolite, epicitreodiol.[3]

7.2 Challenges Associated with 1, 3-disubstituted SDE

The challenges associated with the SDE based methodology culminates in 1,3-disubstituted SDEs. As shown in Scheme 7.1, the first oxidation of a generalized 1,3-disubstituted allene, **7.1**, would result in two regioisomers **7.2** and **7.3**. This assumes each oxidation is completely stereoselective (generally > 20:1).

Scheme 7.1 **Challenges Associated with 1, 3-Disubstituted SDE**

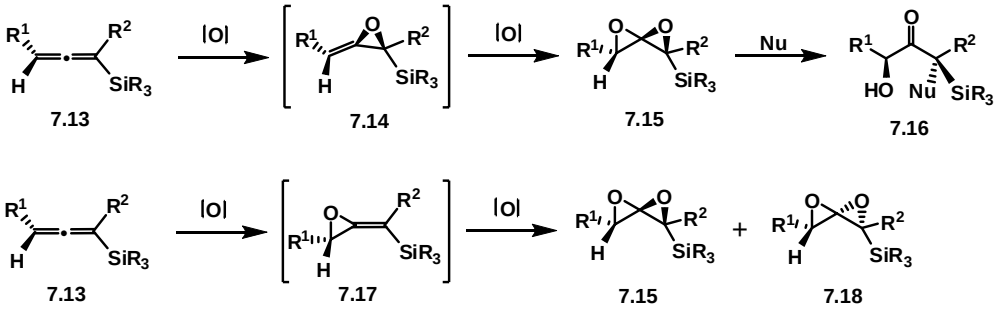


The second oxidation being less stereoselective would result in the formation of three SDEs **7.4**, **7.5**, **7.6**. Worse, the nucleophilic opening of each diastereomer of SDEs would generate two regioisomers, thus, result in the formation of a total of six different isomers.

7.3 The Concept of Silyl-substituted SDE

We wondered whether we could address the above challenges by simply substituting a proton in the 1,3-disubstituted allene with a surrogate silyl group, thus, converting the allene to a trisubstituted allene. As shown in Scheme 7.2, upon subjecting the silyl allene **7.13** to DMDO oxidation conditions, the first oxidation should take place regio and stereoselectively at the more substituted double bond to form the allene oxide (**7.14**). The second oxidation should also take place with high stereoselectively opposite to the bulky silyl group, and would hence generate diastereomer **7.15** as the major product. Importantly, the silyl group may direct nucleophilic addition to the silyl-attached carbon and result in formation of the regioisomer **7.16**.

Scheme 7.2 **Regio and Stereo Control by Silyl-Substituent**



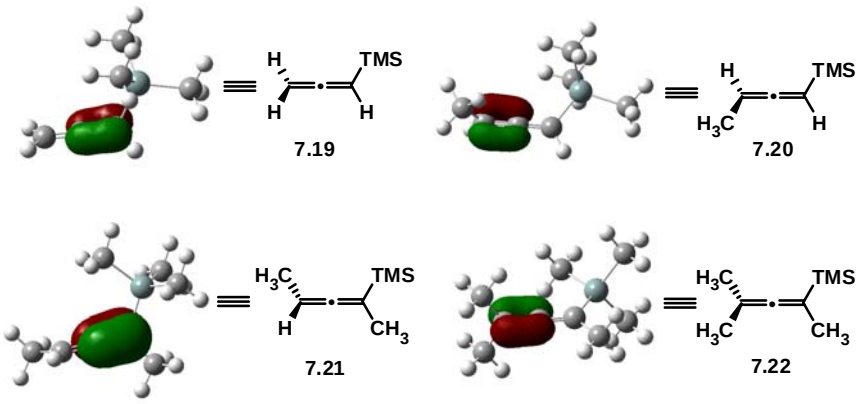
Thus, substituting the 1,3-disubstituted allene with a silyl group may enable access to predominantly one major α-substituted, α'-hydroxy ketone instead of six different isomers. It is noteworthy that in **7.16** the nucleophile and the hydroxyl group are anti, which is also the case with the minor diastereomer obtained from non-silyl SDE (chapter I). Thus, in principle, silyl-SDEs could be used to compliment the non silyl-SDEs in

accessing the anti diastereomer. The prospect of getting **7.16** as a single isomer is dependent on the assumption that the first oxidation would take place at the silyl attached double bond. If the first oxidation takes place at the double bond remote to the silyl group, the subsequent second oxidation of the allene oxide **7.17** would expected to be much less selective, resulting in the formation of SDE **7.18** in addition to **7.15**. Therefore, to gain insight into the nucleophilicity difference between the two double bonds of a silyl substituted allene, we computed the electronic structure of silyl-substituted allenes.

7.4 DFT calculation of sillyl substituted Allenes

My colleague, Jennifer Inghrim, a former graduate student in our group ran Density Functional Calculations (DFT/B3LYP/6-31G) of silyl allenes with varying degree of substitutions to locate the HOMO (highest occupied molecular orbital) in silyl-substituted allenes **7.19**-**7.22** (Figure 7.1).

Figure 7.1 Calculated HOMOs for Silyl Allenes using DFT



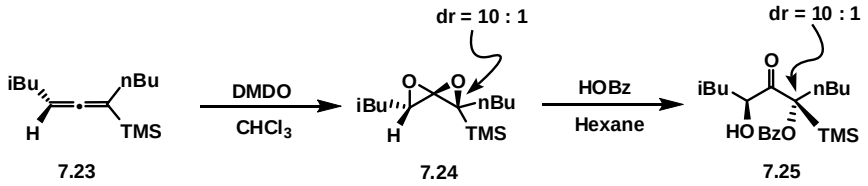
The calculation showed that the location of the HOMO depends on the substitution pattern of the silyl allene. For tri-substituted silyl allene **7.21**, the HOMO lies in the double bond attached to the silyl group. This suggests that upon subjecting a trisubstituted silyl allene of type **7.21** to DMDO oxidation conditions, the first oxidation would take place on the more substituted double bond. Based on steric considerations (the silyl group), therefore, the second oxidation of **7.21**-type allenes should also be selective.

7.5 Results and Discussions

7.51 Preliminary results

Our foray into the study of silyl-SDEs began with the DMDO oxidation of silyl allene **7.23** (Scheme 7.3). We were pleased to find that the resulting silyl-SDE (**7.24**) formed with high diastereoselectivity (dr = 10:1). Presumably, **7.24** turned out to be quite stable even in water and neat alcohols which generally add to non-silyl SDEs.[4] Surprisingly to us SDE **7.24** also remained unreacted with tetrabutyl ammonium azide and acetate. In contrast, benzoic acid reacted smoothly in hexane to give **7.25** retaining the 10:1 diastereomeric ratio.

Scheme 7.3 **Preliminary Results**



These preliminary data suggest that trisubstituted silyl-SDE of type **7.23** react such that the position of the silyl group dictates the regioselectivity of the first oxidation , stereoselectivity of the second oxidation, and regioselectivity of the SDE opening. We then turned to explore three different classes of silyl-SDE transformations that would enable access to synthetically useful motifs.

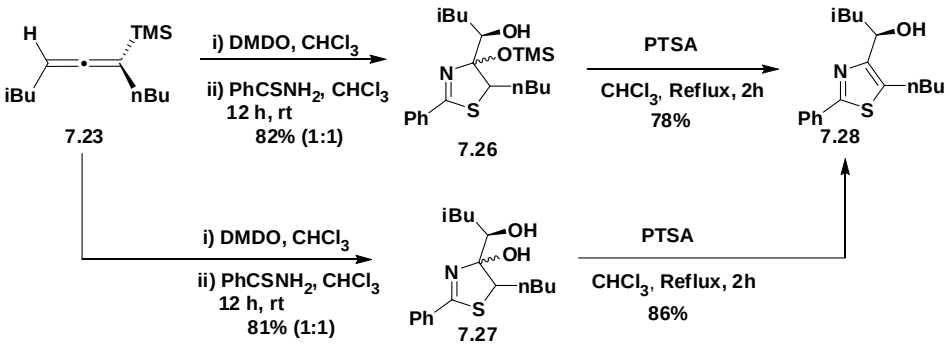
- Addition of amides to form carbinol functionalized azoles.
- Lewis acid promoted hydride addition to form masked polyols.
- Lewis acid promoted eliminative opening to form α-hydroxy enone and ene-diols.

7.52 Synthesis of Carbinol Functionalized Azoles

Recently, our group reported a novel one pot method for synthesizing carbinol functionalized azoles from allenes via SDE's reaction with amides and amide analogues.[5] As the stereochemistry of the carbinol center is directly related to the stereochemistry of the corresponding SDE, the scope of the reported method in asymmetric azole synthesis appears to be limited to trisubstituted allenes. The method could in principle be extended to 1,3-disubstituted allenes using pseudo trisubstituted silyl allenes. In this part of the discussion, the regio and stereoselective synthesis of carbinol functionalized azoles from tri-substituted silyl allenes is described.

When the SDE derived from silyl allene **7.23** was treated with thiobenzamide in chloroform, the thiazoline **7.26** formed in 82% yield as a 1:1 mixture of diastereomers (Scheme 7.4).

Scheme 7.4 **Reaction of Thioamides with silyl-SDE**

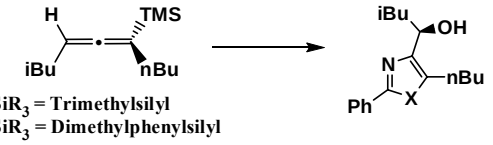


The formation of the thiazoline was accompanied with migration of the silyl group to the adjacent tertiary alcohol. However, when the addition of thiobenzamide to SDE was done in the protic solvent methanol (also in 1:1 THF/water, not shown), thiazoline **7.27** which

lacks the silyl group formed in 81% yield as 1:1 mixture of diastereomers,. Upon treatment with catalytic PTSA in refluxing chloroform, both **7.26** and **7.27** underwent condensation to form thiazole **7.28** in 78% and 86% yield respectively as single isomer. X-ray crystal structure analysis of one of the diastereomer of **7.26** confirmed the regiochemical outcome of thiazoline (**7.29**) and thiazole (**7.28**). With these encouraging results, we set to explore the scope of the reaction.

Enantiomericaly pure silyl allenes **7.23** and **7.29** were oxidized with DMDO and the resulting SDEs were treated with benzamide, thiobenzamide and benzamidine in methanol (Table 7.1). Oxazole **7.30** (X=O) and thiazole **7.28** (X=S) formed upon catalytic PTSA-promoted condensation of the intermediate azolines in a single pot procedure, while the formation of imidazole **7.31** (X=NH) was spontaneous from

Table 7.1 **Synthesis of Carbinol Functionalized Azoles**



7.23 : SiR_3 = Trimethylsilyl
7.29 : SiR_3 = Dimethylphenylsilyl

7.30 : X= O
7.28 : X= S
7.31 : X= NH

entry	Allene	amide	Product	Time (h)	condition	yeild(%)	ee [a]
1	7.23	$C_6H_6CONH_2$	7.30	48 h	A	52	90%
2	7.23	$C_6H_6CSNH_2$	7.28	12 h	A	80	93%
3	7.23	$C_6H_6CNHNH_2$	7.31	48 h	B	72	*
4	7.29	$C_6H_6CONH_2$	7.30	48 h	A	trace	*
5	7.29	$C_6H_6CSNH_2$	7.28	24 h	A	76	95%
6	7.29	$C_6H_6CNHNH_2$	7.31	48 h	B	78	

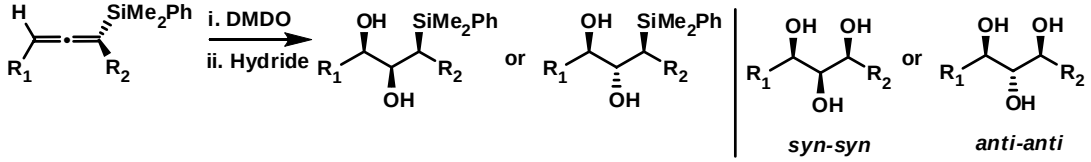
[a]ee determined by chiral HPLC. *yet to be determined. A : DMDO/$CHCl_3$, -40^{0}C to rt, 2h ; 5 eqv amide, MeOH, rt, then 10 mol% p-TsOH, reflux. B : DMDO / $CHCl_3$, -40^{0}C to rt, 2h; 5 eqv amide, MeOH, rt.

imidazoline and did not require acid to aromatize. In general, formation of azolines were slow compared to that with non-silyl SDE. Oxazole formed with modest (entry 1) to trace (entry 4) yields. However, the more nucleophilic thiobenzamide and benzamidine provided excellent yields of thiazole (entry 2, 5) and imidazole (entry 3, 6) respectively. Chiral HPLC analysis[7] revealed that the carbinol functionalized azoles (**7.30**, **7.28**) formed in excellent overall enantiomeric excess, which is indicative of the high selectivity obtained in the second oxidation of silyl-SDEs.

7.53 Synthesis of masked polyol

The dimethylphenylsilyl group has frequently been used as masked hydroxyl group in synthesis.[6] We wondered about the possibility of Lewis acid mediated hydride addition to dimethylphenylsilyl substituted SDE **7.29**, which would first form α-hydroxy, α'-silyl ketone, subsequent reduction of the ketone in situ would provide the diol **7.32** and **7.33** (Scheme 7.5). The dimethylphenyl sillyl group in diols **7.32** and **7.33** could be coverted to the hydroxyl group by employing Tamao-Flemming conditions[6] to form the vicinal triol **7.34** (*syn-syn*) and **7.35** (*anti-anti*).

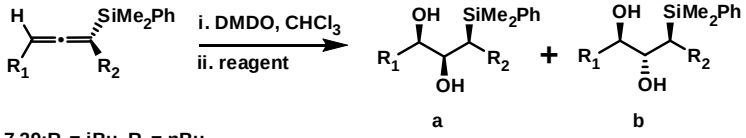
Scheme 7.5 **Vicinal Triol from Silyl Allene**



7.29 **7.32** **7.33** **7.34** **7.35**

Some preliminary studies by Jennifer Inghrim on hydride addition to silyl-SDE are tabulated in Table 7.2. Allene **7.29** and **7.36** was treated with DMDO and the resulting SDEs were treated with metal hydrides. Both lithium borohydride (entry 1,2) and aluminium hydrides (entry 3-6) were found to deliver hydrides to the SDE. However, subsequent reduction of the ketones appears to be less selective. Compound **7.38a** and **7.38b** are known[7] and they were used to determine the relative stereochemistry of compound **7.37a** and **7.37b**. Our initial experiments in accessing vicinal triol using Tamao-Flemming conditions[6] were unsuccessful.

Table 7.2 **Synthesis of Masked Polyol**



7.29:R_1= iBu, R_2= nBu
7.36:R_1=iPr, R_2=Me

7.37:R_1= iBu, R_2= nBu
7.38:R_1=iPr, R_2=Me

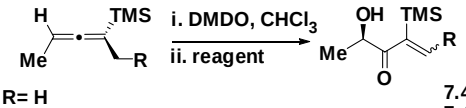
entry	allene	Hydride	Conditions	product (a:b)	Yeild (%)
1	7.29	$LiBH_4$	-78^{0}C, 3 h	7.37 (3:1)	67
2	7.36	$LiBH_4$	-78^{0}C, 12 h	7.38*	38
3	7.29	$LiAlH_4$	-78^{0}C, 3 h	7.37 (2.5:1)	69
4	7.36	$LiAlH_4$	-78^{0}C, 12 h	7.38*	43
5	7.29	Red-Al	-78^{0}C to rt, 16 h	7.37 (3:1)	63
6	7.36	Red-Al	-78^{0}C to rt, 18 h	7.38 (3:1)	27

*Only diastereomer detected

7.54 Regioselective Formation of α-Hydroxy Enone and Ene-diol

During our studies with SDEs, we frequently observed α-hydroxy enones as by-products. We wondered whether silyl-substituted SDE would enable us to access α-hydroxy enone, in a regioselctive way. Indeed, we found that various types of reagents induce the regioselective rearrangement of silyl-SDEs to α-hydroxy enones. Summary of a brief survey is presented in Table 7.3. Treatment of the SDE derived from **7.39** with Bronsted acid PTSA (entry 1), Lewis acid $MgCl_2$ (in combination with TEA, entry 2) and mildly acidic silica gel (entry 3) provided rearranged enone **7.41** in modest yields.

Table 7.3 **Regioselective Rearrangement to α-Hydroxy Enone**



7.39 : R= H
7.23 : R= nPr
7.40 : R= iPr

7.41 : R= H
7.42 : R= nPr
7.43 : R= iPr

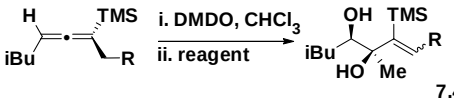
entry	allene	reagent	condition	product (E:Z)	yield (%)
1	7.39	PTSA	Chloroform, -78°C, 1 h	7.41	58
2	7.39	$MgCl_2$, NEt_3	DCM, -40°C, 2 h	7.41	54
3	7.39	SiO_2	Chloroform, rt, 6h	7.41	60
4	7.39	Cp_2TiCl_2, Zn	THF, -60°C,10 min	7.41	66
5	7.23	Cp_2TiCl_2, Zn	THF, -60°C,10 min	7.42 (1:1.1)	72
6	7.40	Cp_2TiCl_2, Zn	THF, -60°C,10 min	7.43 (1:5)	74

Jennifer Inghrim also demonstrated that treatment of a silyl-SDE with cyclopropyl titanium chloride in combination with zinc dust results in the formation of α-hydroxy enone in good yield.[8] Thus upon subjection of the SDE derived from allene **7.39** to a mixture of cyclopropyl titanium chloride and zinc dust in THF gave the enone **7.41** in

good yield (entry 4). Under the same condition enone **7.42** (entry 5) and **7.43** (entry 6) formed in good yields in 1:1.1 and 1:5 E/Z ratios respectively. The titanium method gives access to SDE-opened products with the ketone intact.

In contrast subjection of a silyl-SDE to organometallic reagents MeLi or MeMgBr resulted in the regioselective formation of ene-diol, presumably via the enone (Table 7.4). When MeLi was used, the ene-diols formed in good yield (83-86 %), with good *trans*:*cis* double bond ratio. On the other hand, cis double bond in the product ene-diol were obtained in good selectivity when MeMgBr was used, albeit in lower yield (38-48%). *Cis* selectivity was also obtained in modest yields (69-71%) when MeLi was added to the SDE in addition to MeMgBr. This differential outcome of product double bond geometry in case of MeLi compare to more Lewis acidic MeMgBr and titanium reagent is probably due to two different SDE opening pathways, currently under investigation.

Table 7.4 **Regioselective Rearrangement to Ene-Diol**



7.39 : R= H
7.23 : R= nPr
7.40 : R= iPr

7.44 : R= H
7.45 : R= nPr
7.46 : R= iPr

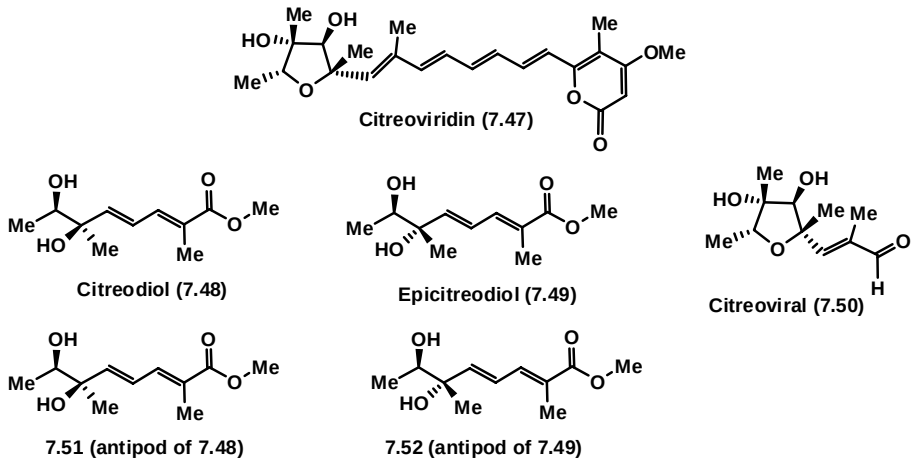
entry	allene	reagent	condition	product (E:Z)	yeild (%)
1	7.39	MeLi	Ether, -40°C to rt, 2h	7.44	85
2	7.23	MeLi	Ether, -40°C to rt, 2h	7.45 (2.2:1)	83
3	7.40	MeLi	Ether, -40°C to rt, 2h	7.46 (16:1)	86
4	7.39	MeMgBr	Ether, -78°C to 0°C, 2h	7.44	48
5	7.23	MeMgBr	Ether, -78°C to 0°C, 2h	7.45 (1:3.4)	40
6	7.40	MeMgBr	Ether, -78°C to 0°C, 2h	7.46 (1:12)	38
7	7.23	MeLi, MeMgBr	Ether, -78°C to 0°C, 2h	7.45 (1:3)	69
8	7.40	MeLi, MeMgBr	Ether, -78°C to 0°C, 2h	7.46 (1:4)	71

7.6 Total Synthesis of Epicitreodiol

7.61 Introduction

The fungus *penicillium citreovitride* is the source of many biologically active and novel metabolites including (-)-citreoviridin **7.47** (Figure 7.1),[9] a potent inhibitor of the mitochondrial ATPase and oxidative phosphorylation,[10] and was recently reported to exhibit anti-HIV activity.[11] In 1984, Yamamura and co workers reported three structurally related novel metabolites, citreodiol (**7.48**), epicitreodiol (**7.49**) and citreoviral (**7.50**), isolated from the mycelium of *Penicillium citreo-viride B.* (IFO 6050).[3] Citreodiol (**7.48**) and epicitreodiol (**7.49**) were isolated as inseparable mixture, and were subsequently separated as the corresponding carbonates. To determine the absolute stereochemistry of **7.48** and **7.49**, the author's also reported syntheses of their antipods **7.51** and **7.52** in 13 steps sequence each starting from L-rhamnose. Our interest in synthesizing epicitreodiol and citreodiol was generated in the context of accessing ene-diol from silyl allenes. Here we present the first total synthesis of epicitreodiol **7.49**.

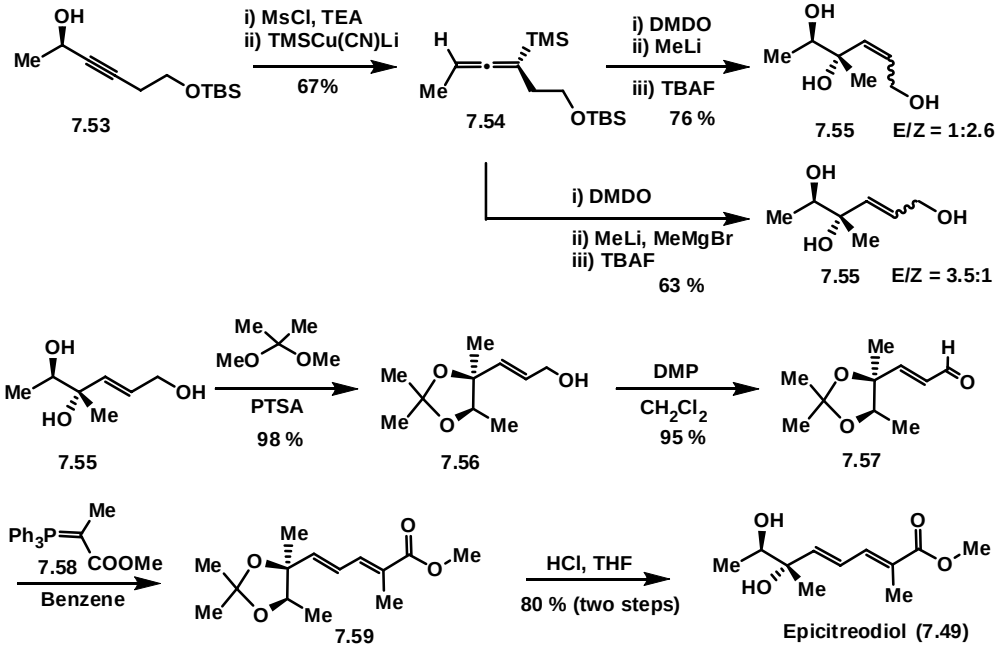
Figure 7.1 **Novel Metabolites from Penicillium Citreo-viride**



7.62 First Total Synthesis of Epicitreodiol

Our synthesis began with the propargyl alcohol **7.53** available in 2 steps (Scheme 7.6).[12] Mesylation of the alcohol followed by addition of trimethylsilyl cuprate provided silyl allene **7.54**. A single flask procedure of DMDO oxidation of **7.54** to SDE followed by treatment of the resulting mixture with MeLi and then removal of the silyl group gave triol **7.55** in 76% yield as a 1: 2.6 (E:Z) mixture of diastereomers. Interestingly, when MeMgBr was added in addition to MeLi, the reaction generated the triol **7.55** in 63% yield as a 3.5:1 (E:Z) mixture of diastereomers. The anti isomer was separated by chromatography and protected as cyclic ketal to form **7.56**. Des-Martin oxidation of the primary alcohol gave aldehyde **7.57** in 90% yield.[13] Wittig olefination of **7.56** followed by hydrolysis of the ketal provided epicitreodiol **7.49** in 80% yield (two steps), ^{1}H NMR of which proved identical with the reported spectra.

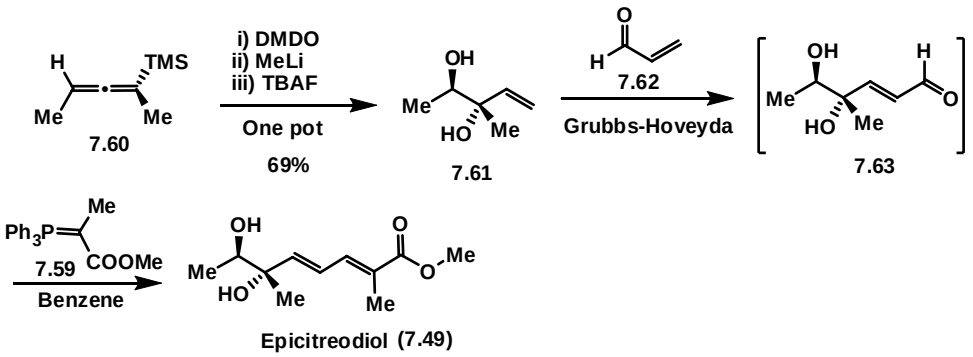
Scheme 7.6 **First Total Synthesis of Epicitreodiol**



7.63 A Concise Synthesis of Epicitreodiol

In the previous section we reported the first total synthesis of epicitreodiol **7.49** in 6 steps from known known propargyl alcohol.[14] We wondered whether the synthesis could be performed more concisely. Joseph R. Cusick a graduate student in our group has completed the total synthesis of epicitreodiol in a two flask procedure starting from allene **7.60** (Scheme 7.7).

Scheme 7.7 **A Concise Synthesis of Epicitreodiol**



The SDE derived from DMDO oxidation of known allene **7.60** was treated with MeLi. Protodesilation of the resulting vinyl silane, in the same flask generated ene-diol **7.61** in 69% yield as a single observed diastereomer. A second single flask procedure, where first Grubbs-Hoveyda[15] cross coupling of **7.61** with acrylldehyde (**7.62**) and then a Wittig olefination provided epicitreodiol **7.49** as a single isomer in excellent overall yield.

7.7 Conclusion

A general approach to the stereoselective formation of silyl substituted SDEs and their subsequent regioselective opening was demonstrated. The silyl group appears to dictate the regioselectivity of the first oxidation, stereoselectivity of the second oxidation, and regioselectivity of the SDE opening. This also constitutes the first study on silyl-substituted SDEs. In the process of which we developed several methods in accessing synthetically useful motifs, and demonstrated the potential and flexibility of silyl-SDEs in two short syntheses of the novel penicillium metabolite epicitreodiol. Moreover, successful methods of converting masked-polyol to polyol in the future will expand the scope of SDE based methodology in accessing important classes of natural products.

7.8 References

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Experimental

General: Starting materials, reagents and solvents were purchased from commercial suppliers (Aldrich, Acros, Lancaster, and Fischer) and used without further purification. Anhydrous THF, Et_2O, $CHCl_3$, and DCM were obtained from a solvent purification system consisting of alumina based columns. All reactions were conducted in oven-dried (135 ^oC) glassware under an inert atmosphere of dry nitrogen. The progress of reactions were monitored by silica gel thin layer chromatography (tlc) plates (mesh size 60Å with fluorescent indicator, Sigma-Aldrich), visualized under UV and charred using cerium or anisaldehyde stain. Products were purified by flash column chromatography (FCC) on 120-400 mesh silica gel (Fisher). Infrared (FTIR) spectra were recorded on an ATI Mattson Genesis Series FT-Infrared spectrophotometer. Proton nuclear magnetic resonance spectra (^1H NMR) were recorded on either a Varian-300 instrument (300 MHz), Varian-400 instrument (400 MHz), or a Varian-500 instrument (500 MHz). Chemical shifts are reported in ppm relative to tetramethylsilane (TMS) as the internal standard. Data is reported as follows: chemical shift, integration, multiplicity (s=singlet, d=doublet, t=triplet, q=quartet, br=broad, m=multiplet), and coupling constants (Hz). Carbon nuclear magnetic resonance spectra (^{13}C NMR) were recorded on either a Varian-300 instrument (75 MHz), Varian-400 instrument (100 MHz) or a Varian-500 instrument (125 MHz). Chemical shifts are reported in ppm relative to tetramethylsilane (TMS) as the internal standard. Optical rotations were recorded at 25^oC using the sodium D line (589 nm), on a Perkin-Elmer 241 polarimeter. Mass spectra were recorded on a Finnigan LCQ-DUO mass spectrometer.

Experimental (Chapter IV)

General procedure for preparation of spirodiepoxides (SDE) from allenes

To a solution of freshly prepared dimethyldioxirane (DMDO) in $CHCl_3$ (~0.20 M, 3 equiv.) was added the allene in $CHCl_3$ dropwise at -40^oC. The reaction was stirred under nitrogen and let to warm to rt over 2 h. Solvent was evaporated and the resulting SDE was dried under vacuum and used for the next step without further purification.

General procedures for cuprate additions

Procedure A:

A suspension of CuCN (activated by a gentle flame under high vacuum) in anhydrous Et_2O was degassed for 2 min with argon. The suspension was cooled to -10^oC and a solution of 1.6 M MeLi in Et_2O was added dropwise. The reaction mixture was warmed to 0^oC at which point it became a colorless homogeneous solution. The solution was cooled back to –10^oC and the SDE in anhydrous Et_2O was added dropwise. The reaction was allowed to warm to rt over 30 min and monitored by tlc. Upon completion by tlc the reaction was quenched with saturated aq. NH_4Cl (2 ml), extracted with Et_2O (3 x 5 ml), dried over anhydrous $MgSO_4$ and evaporated to give crude product, which upon further purification by FCC gave the α-hydroxy ketone.

Procedure B:

A suspension of CuCN (activated by a gentle flame under high vacuum) in anhydrous Et_2O was degassed for 2 min with argon. The suspension was cooled to -78^oC and a

solution of 1.6 M n-BuLi in hexane was added dropwise. The reaction mixture was warmed to -20^{o}C at which point it became a homogeneous solution. The solution was cooled back to –78^{o}C and the SDE in anhydrous Et_2O was added dropwise. The reaction was allowed to warm to rt over 2 h and monitored by tlc. Upon completion by tlc the reaction was quenched with saturated aq. NH_4Cl (2 ml), extracted with Et_2O (3 x 5 ml), dried over anhydrous $MgSO_4$ and evaporated to give crude product, which upon further purification by FCC gave the α-hydroxy ketone.

Procedure C:

A suspension of CuCN (activated by a gentle flame under high vacuum) in anhydrous Et_2O was degassed for 2 min with argon. The suspension was cooled to -78^{o}C and a solution of 1.0 M $TMSCH_2Li$ in pentane was added dropwise. The reaction mixture was warmed to rt at which point it became a homogeneous solution. The solution was cooled back to –78^{o}C and the SDE in anhydrous Et_2O was added dropwise. The reaction was allowed to warm to rt over 2 h and monitored by tlc. Upon completion by tlc the reaction was quenched with saturated aq. NH_4Cl (2 ml), extracted with Et_2O (3 x 5 ml), dried over anhydrous $MgSO_4$ and evaporated to give crude product, which upon further purification by FCC gave the α-hydroxy ketone.

Procedure D:

A suspension of CuCN (activated by a gentle flame under high vacuum) in anhydrous Et_2O was degassed for 2 min with argon. The suspension was cooled to -78^{o}C and a solution of 2.0 M PhLi in dibutylether was added dropwise. The reaction mixture was

warmed to 0°C at which point it became a homogeneous solution. The solution was cooled back to –78°C and the SDE in anhydrous Et_2O was added dropwise. The reaction was allowed to warm to rt over 2 h and monitored by tlc. Upon completion by tlc the reaction was quenched with saturated aq. NH_4Cl (2 ml), extracted with Et_2O (3 x 5 ml), dried over anhydrous $MgSO_4$ and evaporated to give crude product, which upon further purification by FCC gave the α-hydroxy ketone.

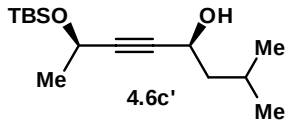
Procedure E:

A suspension of CuI in anhydrous Et_2O was degassed with argon for 2 min and cooled to –78°C. A solution of 2.0 M PhLi in dibutylether was added dropwise to the suspension at -78°C. The reaction mixture was warmed to 0°C at which point a dark black solution was formed. The solution was cooled back to -78°C and the SDE in anhydrous Et_2O was added dropwise. The reaction mixture was allowed to warm to rt over 2 h and monitored by tlc. Upon completion by tlc the reaction was quenched with saturated aq. NH_4Cl (2 ml), extracted with Et_2O (3 x 5 ml), dried over anhydrous $MgSO_4$ and evaporated to give crude product, which upon further purification by FCC gave the α-hydroxy ketone.

Procedure F:

A suspension of CuCN (activated by a gentle flame under high vacuum) in anhydrous Et_2O was degassed for 2 min with argon. The suspension was cooled to -10°C and a solution of 1.0 M MeMgBr in dibutylether was added dropwise. The reaction mixture was warmed to 0°C at which point it became a pale yellow homogeneous solution. The solution was cooled back to –10°C and the SDE in anhydrous Et_2O was added dropwise.

The reaction was allowed to warm to rt over 30 min and monitored by tlc. Upon completion by tlc the reaction was quenched with saturated aq. NH_4Cl (2 ml), extracted with Et_2O (3 x 5 ml), dried over anhydrous $MgSO_4$ and evaporated to give crude product, which upon further purification by FCC gave the α-hydroxy ketone.

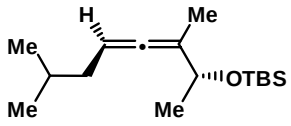


4.6c'

A suspension of $Zn(OTf)_2$ (1.74g, 4.8mmol), (-)-N-Methylephedrine (860 mg, 4.8 mmol) and Et_3N (6.69 ml, 4.80 mmol) in 20 ml of toluene was stirred at room temperature for 30 min. TBS-protected (*R*)-3-butyn-2-ol[1] (800 mg, 4.34 mmol) was added in one portion and the reaction stirred for 30 min. Isovaleraldehyde (380 mg, 4.41 mmol) was added in one portion and the reaction was stirred for an additional 12 h at rt and monitored by tlc. Upon completion by tlc the reaction was quenched with saturated aq. NH_4Cl (10 ml) and extracted with Et_2O (3 x 15 ml). The organic layer was dried over anhydrous MgSO4 and evaporated to give the crude product. FCC using 10% ethyl acetate-hexane gave 856 mg of propargylic alcohol (73%, >95:5 dr) as a clear colorless oil. $[\alpha]^{25}_D$= +33 (*c* = 0.01, $CHCl_3$); IR ν_{max} (neat) /cm^{-1} 3350, 1463, 1255, 1102, 836, δ_H (400 MHz, $CDCl_3$) 4.55 (1H, qd, J= 6.4, 1.2 Hz), 4.43 (1H, q, J= 6.4 Hz), 1.85-1.80 (1H, m), 1.71 (1H, d, J=5.2 Hz), 1.66-1.50 (2H, m), 1.40 (3H, d, J=6.4 Hz), 0.94 (3H, d, J= 6.8 Hz), 0.92 (3H, d, J=7.2 Hz), 0.90 (9H, s), 0.12 (3H, s), 0.11

[1] Obtained in >95% yield by silylation of commercial (*R*)-3-butyn-2-ol (Aldrich, 99% ee) with TBS-Cl / Imidazole

(3H, s); δ_c (100 MHz, $CDCl_3$) 87.4, 84.3, 61.0, 58.9, 46.7, 25.8, 25.4, 24.7, 22.5 (2), 18.2, -4.6, -4.9; m/z (ESIMS) 293.3 $(M+23)^+$.

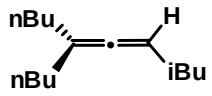


4.6c

To a solution of propargylic alcohol (315 mg, 1.16 mmol) in dry CH_2Cl_2 (5 ml) was added Et_3N (0.2 ml, 1.43 mmol) dropwise. The solution was cooled to 0^oC and MsCl (0.11 ml, 1.42 mmol) was added dropwise and the reaction stirred for 1 h at 0^oC. The reaction was quenched by the addition of water (1 ml). The organic layer was separated, washed with water (2 x 5 ml) and dried over anhydrous $MgSO_4$. The solvent was evaporated and the crude mesylate was dried under vacuum and used for the next step without further purification.

To a suspension of CuCN (160 mg, 1.79 mmol) in anhydrous Et_2O (10 ml) at -40^oC was added 1.6 M MeLi in Et_2O (1.10 ml, 1.76 mmol). The solution was warmed to 0^0C and stirred for 10 min at which point a colorless homogeneous solution had formed. The reaction mixture was then cooled back to -40^oC and the above mesylate in 5 ml of anhydrous Et_2O was added dropwise. The reaction mixture was allowed to warm to rt over 1 h and monitored by tlc. The reaction was quenched with saturated aq. NH_4Cl (5 ml) and extracted with Et_2O (3 x 10 ml). The Et_2O layer was washed with saturated aq. NH_4Cl (10 ml), water (10 ml), brine (10 ml) and dried over anhydrous $MgSO_4$. Evaporation of solvent and FCC purification using hexane gave 290 mg of allene (93%)

as clear colorless oil. $[\alpha]^{25}_{D}$= +36 (*c* = 0.01, $CHCl_3$); IR ν_{max} (neat) /cm^{-1} 1966, 1255, 1463, 1084, 834; δ_H (400 MHz, $CDCl_3$) 5.06-4.94 (1H, m), 4.28 (1H, q, J=6.4 Hz), 1.87 (2H,dd, J_1= 7.2 Hz, J_2= 7.2 Hz), 1.66 (3H, d, J= 2.8 Hz), 1.62-1.68 (1H, m), 1.23 (3H, d, J= 6.4 Hz), 0.91 (6H, d, J= 6.4 Hz), 0.89 (9H, s), 0.06 (6H, s); δ_c (100 MHz, $CDCl_3$) 200.8, 102.6, 89.6, 70.3, 38.5, 28.6, 25.9 (3), 22.9, 22.3, 22.2, 18.2, 13.9, -4.7, -4.9; m/z (ESIMS) 269.1 $(M + 1)^+$.



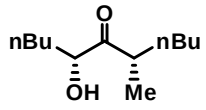
4.6b

To a solution of known propargylic alcohol[2] (1.30 gm, 7.73 mmol) in 20 ml dry CH_2Cl_2 was added Et_3N (1.30 ml, 9.3 mmol) dropwise. The solution was cooled to 0°C and MsCl (0.70 ml, 9.0 mmol) was added dropwise and the reaction stirred for 1 h at 0°C. The reaction was quenched by the addition of water (1 ml). The organic layer was separated, washed with water (2 x 5 ml) and dried over anhydrous $MgSO_4$. The solvent was evaporated and the crude mesylate was dried under vacuum and used for the next step without further purification.

To a suspension of CuCN (860 mg, 9.6 mmol) in anhydrous Et_2O (50 ml) at –40°C was added 1.6 M n-BuLi in hexane (6.0 ml, 9.6 mmol). The solution was warmed to –20°C and stirred for 5 min. at which point a homogeneous solution had formed. The reaction mixture was then cooled back to –40°C and the above mesylate in anhydrous Et_2O (5 ml)

[2]Ma, S.; Wu, B.; Jiang, X.; Zhao, S. *J. Org. Chem.* **2005**, *70*, 2568-2575.

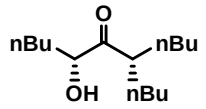
was added dropwise. The reaction mixture was warmed to rt over 1 h and monitored by tlc. The reaction was quenched with saturated aq. NH_4Cl (10 ml) and extracted with Et_2O (3 x 15 ml). The Et_2O layer was washed with saturated aq. NH_4Cl (20 ml), water (20 ml), brine (20 ml) and dried over anhydrous $MgSO_4$. Evaporation of solvent and FCC purification using hexane gave 1.47 g of allene (92%) as a clear colorless oil. IR ν_{max} (neat) /cm^{-1} 1961, 1466, 1379; δ_H (400 MHz, $CDCl_3$) 5.06-4.96 (1H, m), 1.91 (4H, td, J= 7.2, 2.4 Hz), 1.87 (1H, d, J= 7.2 Hz), 1.85 (1H, d, J= 6.8 Hz), 1.68- 1.58 (1H, m), 1.44-1.28 (8H, m), 0.92 (6H, d, J= 6.4 Hz), 0.89 (6H, t, J= 7.2 Hz); δ_c (100 MHz, $CDCl_3$) 201.4, 103.3, 90.2, 39.3, 32.5(2), 30.0 (2), 28.7, 22.5 (2), 22.3(2), 14.0 (2); m/z (ESIMS) 231.2 $(M + 23)^+$.



4.7a

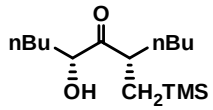
Allene **6a** (60 mg, 0.670 mmol) was converted to the SDE using the general procedure. Procedure A was employed using CuCN (60 mg, 0.670 mmol), 1.6 M MeLi in Et_2O (0.41 ml, 0.656 mmol) and 10 ml Et_2O. FCC using 2% ethyl acetate–hexane gave 39 mg (74 %, 2:1 dr) of known α-hydroxy ketone[3] as a clear colorless oil.

[3] Gosmini, C.; Dubuffet, T.; Sauvêtre, R.; Normant, J.F. *Tetrahedron: Asymmetry*. **1991**, *2*, 223.



4.15a

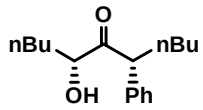
Allene **6a** (40 mg, 0.263 mmol) was converted to the SDE using the general procedure. Procedure B was employed using CuCN (60 mg, 0.670 mmol), 1.6 M n-BuLi in hexanes (0.41 ml, 0.656 mmol) and 10 ml Et_2O. FCC using 2% ethyl acetate–hexane gave 43 mg (67 %) of α-hydroxy ketone as a clear colorless oil. IR ν_{max} (neat) /cm^{-1} 3480, 1706, 1467, 1050; δ_H (400 MHz, $CDCl_3$) 4.24-4.14 (1H, m), 3.48 (1H, d, J= 5.6), 2.70-2.60 (1H, m), 1.88-1.77 (1H, m), 1.73-1.63 (1H, m), 1.60-1.14 (16H, m), 0.92 (3H, t, J= 7.2 Hz), 0.88 (3H, t, J= 7.2 Hz), 0.87 (3H, t, J= 7.2 Hz); δ_c (100 MHz, $CDCl_3$) 216.3, 76.4, 47.1, 33.0, 32.8, 30.2, 29.8, 29.3, 27.5, 22.8, 22.4, 13.9 (2),13.8; m/z (ESIMS) 265.3 $(M+23)^+$.



4.16a

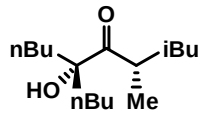
Allene **6a** (60 mg, 0.394 mmol) was converted to the SDE using the general procedure. Procedure C was employed using CuCN (90 mg, 1.00 mmol), 1.0 M $TMSCH_2Li$ in pentane (1 ml, 1.00 mmol) and 15 ml Et_2O. FCC using 2% ethyl acetate–hexane gave 71 mg (66 % 2:1 dr) of α-hydroxy ketone as a clear colorless oil. Spectral data for major isomer: IR ν_{max} (neat) /cm^{-1} 3480, 1708, 1249, 859; δ_H (400 MHz, $CDCl_3$) 4.26-4.17 (0.66H, m), 4.17-4.12 (0.33H, m), 3.47 (0.33H, d, J= 5.2 Hz), 3.41 (0.66H, d, J= 5.6 Hz), 2.76-2.68 (0.33H, m), 2.68-2.59 (0.66H, m), 1.82-1.04 (12H, m), 0.87 (3H, t, J= 6.8 Hz), 0.84 (2H, t, J= 6.8 Hz), 0.84 (1H, t, J= 6.8 Hz), 0.79-0.58 (2H, m), -0.01 (6H,s), -0.02

(3H, s); δ_c (100 MHz, $CDCl_3$) 216.2, 215.9, 76.3, 74.9, 42.9, 42.7, 34.7, 33.6,33.2, 32.4, 29.9, 29.1, 27.7, 27.4, 22.7, 22.4, 22.4, 20.7, 17.8, 13.9, 13.8, -0.9, -1.0; m/z (ESIMS) 295.2 $(M + 23)^+$.



4.17a

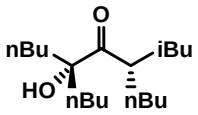
Allene **6a** (60 mg, 0.394 mmol) was converted to the SDE using the general procedure. Procedure D was employed using CuCN (108 mg, 1.20 mmol), 2.0 M in dibutylether PhLi (0.6 ml, 1.2 mmol) and 10 ml Et_2O. FCC using 2% ethyl acetate–hexane gave 49.5 mg (59 %, 2:1 dr) of α-hydroxy ketone as clear colorless oil. Spectral data for major isomer: IR ν_{max} (neat) /cm^{-1} 3482, 1708, 1455, 700; δ_H (400 MHz, $CDCl_3$) 7.34-7.23 (3H, m), 7.20-7.15 (2H, m), 4.15-4.07 (1H, m), 3.80 (1H, t, J= 7.2 Hz), 3.29 (1H, d, J= 5.2 Hz), 2.12-2.05 (1H, m), 1.88-1.68 (2H, m), 1.58-1.05 (9H, m), 0.91 (3H, t, J= 7.2 Hz), 0.86 (3H, t, J= 7.2 Hz); δ_c (100 MHz, $CDCl_3$) 212.2, 138.3, 129.0, 128.2, 128.1, 127.5, 74.7, 54.1, 33.4, 31.8, 29.6, 27.0, 22.5, 22.4, 13.9, 13.8; m/z (ESIMS) 285.2 $(M + 23)^+$.



4.7b

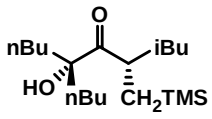
Allene **6b** (40 mg, 0.192 mmol) was converted to the SDE using the general procedure. Procedure A was employed using CuCN (41 mg, 0.480 mmol), 1.6 M MeLi in Et_2O (0.3 ml, 0.480 mmol) and 10 ml Et_2O. FCC using 2% ethyl acetate–hexane gave 42 mg (85%) of an inseparable mixture of methyl addition and reduced product in a 20:1 ratio as

a clear colorless oil. Spectral data for methyl addition product: IR ν_{max} (neat) /cm^{-1} 3479, 1699, 1467, 1054; δ_H (400 MHz, $CDCl_3$) 3.75 (1H, s), 3.03-2.94 (1H, m), 1.77-1.62 (4H, m), 1.55-1.20 (8H, m), 1.06 (3H, d, J= 6.4 Hz), 1.03-0.94 (2H, m), 0.92 (3H, d, J= 6.4 Hz), 0.88 (3H, d, J= 6.0 Hz), 0.88 (6H, t, J= 6.8 Hz); δ_c (100 MHz, $CDCl_3$) 218.9, 82.2, 42.5, 37.8 (2), 36.8, 25.7, 25.2, 23.7, 23.0, 21.5, 16.9, 13.9 (2); m/z (ESIMS) 279.3 $(M + 23)^+$



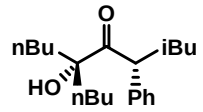
4.15b

Allene **6b** (40 mg, 0.192 mmol) was converted to the SDE using the general procedure. Procedure B was employed using CuCN (41 mg, 0.480 mmol), 1.6 M n-BuLi in hexane (0.3 ml, 0.480 mmol) and 10 ml Et_2O. FCC using 2% ethyl acetate–hexane gave 41 mg (72 %) of α-hydroxy ketone as a clear colorless oil. IR ν_{max} (neat) /cm^{-1} 3477, 1694, 1467; δ_H (400 MHz, $CDCl_3$) 3.52 (1H, s), 2.02-2.92 (1H, m), 1.78-1.52 (6H, m), 1.45-1.20 (11H, m), 1.12-1.00 (2H, m), 0.89 (6H, d, J= 6.8 Hz), 0.89 (9H, t, J= 7.6 Hz); δ_c (100 MHz, $CDCl_3$) 218.0, 81.8, 42.4, 40.8, 37.4, 37.3, 31.3, 29.3, 25.7, 25.6, 25.5, 23.2, 23.0 (2), 22.9, 22.2, 14.0, 13.9 (2); m/z (ESIMS) 321.4 $(M + 23)^+$.



4.16b

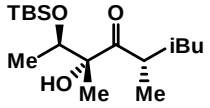
Allene **6b** (40 mg, 0.192 mmol) was converted to the SDE using the general procedure. Procedure C was employed using CuCN (41 mg, 0.480 mmol), 1.0 M $TMSCH_2Li$ in pentane (0.48 ml, 0.480 mmol) and 10 ml Et_2O. FCC using 2% ethyl acetate–hexane gave 41 mg (65 %) of α-hydroxy ketone as a clear colorless oil. IR ν_{max} (neat) /cm^{-1} 3485, 1694, 1467, 1249; δ_H (400 MHz, $CDCl_3$) 3.339 (1H, s), 3.12-3.04 (1H, m), 1.77-1.54 (5H, m), 1.44-1.22 (7H, m), 1.19-1.04 (3H, m), 0.89 (6H, d, J= 6.0 Hz), 0.89 (6H, t, J= 7.2 Hz), 0.63-0.55 (2H, m), 0.06 (9H, s); δ_c (100 MHz, $CDCl_3$) 218.1, 81.7, 42.9, 38.5, 37.6, 37.3, 26.1, 25.7, 25.4, 23.4, 23.0, 22.3, 20.4, 14.0, -0.4; m/z (ESIMS) 351.3 $(M + 23)^+$.



4.17b

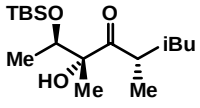
Allene **6b** (40 mg, 0.192 mmol) was converted to the SDE using the general procedure. Procedure E was employed using CuI (110 mg, 0.578 mmol), 2.0 M PhLi in dibutylether (0.58 ml, 1.16 mmol) and 15 ml Et_2O. FCC using 2% ethyl acetate–hexane gave 43 mg (71 %) of α-hydroxy ketone as a clear colorless oil. IR ν_{max} (neat) /cm^{-1} 3485, 1699, 1467; δ_H (400 MHz, $CDCl_3$) 7.32-7.28 (4H, m), 7.25-7.21 (1H, m), 4.116 (1H, dd J_1= 5.2, 4.4 Hz), 3.62 (1H, s), 1.99-1.90 (1H, m), 1.84- 1.66 (2H, m), 1.60-1.48 (3H, m), 1.44-1.22 (5H, m), 1.16-1.04 (1H, m), 1.02-0.92 (1H, m), 0.892 (3H, d, J= 6.4 Hz), 0.890 (3H, t, J= 7.2 Hz), 0.835 (3H, J= 6.4 Hz), 0.78-0.68 (1H, m), 0.542 (3H, t, J= 7.2 Hz), 0.18-0.07 (1H, m); δ_c (100 MHz, $CDCl_3$) 214.8, 138.0, 128.6 (2), 128.5 (2), 127.2, 82.8, 49.7,

43.5, 38.7, 38.1, 25.7, 25.1, 24.9, 23.4, 23.0, 22.6, 21.4, 13.9, 13.7; m/z (ESIMS) 341.3 $(M + 23)^+$.



4.7c

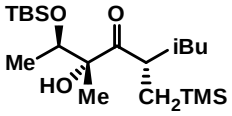
Allene **6c** (40 mg, 0.134 mmol) was converted to the SDE using the general procedure. Procedure A was employed using CuCN (30 mg, 0.335 mmol), 1.6 M MeLi in Et_2O (0.21 ml, 0.336 mmol) and 10 ml Et_2O. FCC using 2% ethyl acetate–hexane gave 36 mg (84 %, 6:1 dr) of α-hydroxy ketone as a clear colorless oil. Spectral data for major isomer: IR ν_{max} (neat) /cm^{-1} 3555, 1709, 1464, 838; δ_H (400 MHz, $CDCl_3$) 3.92 (1H, q, J= 6.0 Hz), 3.31-3.18 (1H, m), 2.92 (1H, s), 1.62-1.46 (2H, m), 1.28 (1H, s), 1.06-1.02 (1H, m), 1.04 (3H, d, J= 6.4 Hz), 1.06 (2.4 H, d, J= 6.4 Hz), 0.91 (6H, d, J=10 Hz), 0.91 (9H, s), 0.10 (3H, s), 0.09 (3H, s); δ_c (100 MHz, $CDCl_3$) 218.5, 82.3, 73.4, 42.1, 38.8, 25.8, 25.6, 24.3, 23.2, 21.9, 18.5, 18.0, 15.7, -4.3, -4.9; m/z (ESIMS) 339.4 $(M + 23)^+$.



4.15c

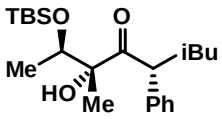
Allene **6c** (32 mg, 0.119 mmol) was converted to the SDE using the general procedure. Procedure B was employed using CuCN (27 mg, 0.301 mmol), 1.6 M n-BuLi in hexane (0.18 ml, 0.288 mmol) and 8 ml Et_2O. FCC using 2% ethyl acetate–hexane gave 32.5 mg

(76 %, 6:1 dr) of α-hydroxy ketone as a clear colorless oil. Spectral data for major isomer: IR ν_{max} (neat) /cm^{-1} 3556, 1706, 1464, 838; δ_H (400 MHz, $CDCl_3$) 3.94 (1H, q, J= 6 Hz), 3.19-3.10 (1H, m), 2.87 (1H, s), 1.68-1.48 (3H, m), 1.31-1.04 (6 H, m), 1.25 (3H, s), 1.05 (3H, d, J= 6.4 Hz), 0.89(9H, d, J= 6.0 Hz), 0.92-0.82 (9H, m), 0.08 (6H, s); δ_c (100 MHz, $CDCl_3$) 217.5, 82.2, 73.3, 44.4, 40.1, 29.9, 29.7, 25.9, 25.8, 24.8, 22.9(2), 22.5, 18.5, 18.0, 13.9, -4.2, -4.9; m/z (ESIMS) 381.5 $(M + 23)^+$.



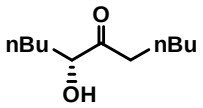
4.16c

Allene **6c** (27 mg, 0.301 mmol) was converted to the SDE using the general procedure. Procedure C was employed using CuCN (27 mg, 0.301 mmol), 1.0 M $TMSCH_2Li$ in pentane (0.3 ml, 0.30 mmol) and 8 ml Et_2O. FCC using 2% ethyl acetate–hexane gave 31.5 mg (68 %, 6:1 dr) of α-hydroxy ketone as a clear colorless oil. Spectral data for major isomer: IR ν_{max} (neat) /cm^{-1} 3557, 1707, 1464, 1250; δ_H (400 MHz, $CDCl_3$) 4.03 (1H, q, J= 6.4 Hz), 3.31- 3.21 (1H, m), 2.66 (1H, s), 1.82-1.72 (1H, m), 1.41-1.28 (1H, m), 1.23 (3H, s), 1.07 (3H, d, J= 6.4 Hz), 1.05-0.90 (2H, m), 0.91 (9H, s), 0.90 (3H, d, J= 6.4 Hz), 0.88 (3H, d, J= 5.6 Hz), 0.38-0.30 (1H, m), 0.1 (6H, s), 0.05 (9H, s); δ_c (100 MHz, $CDCl_3$) 217.0, 82.1, 72.7, 41.6, 39.6, 26.4, 25.8, 24.9, 23.7, 21.9, 18.7, 18.6, 18.0, -0.5, -4.2, -4.9; m/z (ESIMS) 411.4 $(M + 23)^+$.



4.17c

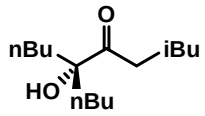
Allene **6c** (50 mg, 0.186 mmol) was converted to the SDE using the general procedure. Procedure E was employed using CuI (107 mg, 0.562 mmol), 2.0 M PhLi in dibutylether (0.55 ml, 1.10 mmol) and 15 ml Et_2O. FCC using 2% ethyl acetate–hexane gave 46mg (65 %, 6:1 dr) of α-hydroxy ketone as a clear colorless oil. Spectral data for major isomer: IR ν_{max} (neat) /cm^{-1} 3583, 1709, 1257, 1108, 838; δ_H (400 MHz, $CDCl_3$) 7.31-7.24 (4H, m), 7.22-7.17 (1H, m), 4.50 (1H, t, J= 7.6 Hz), 2.90 (1H, s), 1.86-1.68 (1H, m), 1.63-1.72 (1H, m), 1.36-1.28 (1H, m), 1.25 (3H, s), 0.90 (3H, d, J=6.4 Hz), 0.87 (3H, d, J=6.4 Hz), 0.88 (9H, s), 0.73 (3H, d, J= 6.0 Hz), 0.05 (3H, s), 0.03 (3H, s); δ_c (100 MHz, $CDCl_3$) 214.2, 138.2, 129.1, 128.3, 126.8, 82.7, 72.9, 50.6, 42.6, 25.8, 25.5, 24.6, 23.0, 22.0, 18.4, 18.0, -4.3, -4.9; m/z (ESIMS) 379.1 $(M + 23)^+$.



4.8a

Allene **6a** (25 mg, 0.140 mmol) was converted to the SDE using the general procedure. Procedure F was employed using CuCN (27 mg, 0.30 mmol), 1.0 M MeMgBr in dibutylether (0.30 ml, 0.30 mmol) and 3 ml Et_2O. FCC using 2% ethyl acetate–hexane gave 18 mg (72 %) of known α-hydroxy ketone[4] as a clear colorless oil.

[4] Hashiyama, T.; Morikawa, K.; Sharpless, K.B. *J. Org. Chem.***1992**, *57*, 5067-5068.



4.8b

Allene **6a** (50 mg, 0.210 mmol) was converted to the SDE using the general procedure. Procedure F was employed using CuCN (39 mg, 0.44 mmol), 1.0 M MeMgBr in dibutylether (0.44 ml, 0.44 mmol) and 5 ml Et_2O. FCC using 2% ethyl acetate–hexane gave 39 mg (78 %) of α-hydroxy ketone as a clear colorless oil. IR ν_{max} (neat) /cm^{-1} 3481.7, 1703.9, 1467.5; δ_H (400 MHz, $CDCl_3$) 3.903 (1H, s), 2.442 (2H, t, J= 7.6 Hz), 1.76-1.65 (4H, m), 1.60-1.46 (4H, m), 1.44-1.23 (7H, m), 0.912 (6H, d, J= 6.4 Hz), 0.873 (6H, t, J= 7.2 Hz); δ_c (100 MHz, $CDCl_3$) 214.8, 81.6, 38.7, 33.8, 32.3, 27.6, 25.4, 22.9, 22.3, 13.9; m/z (ESIMS) 243.0 $(M + 1)^+$.

Crystal structure: Camphor derivative of **4.7c**

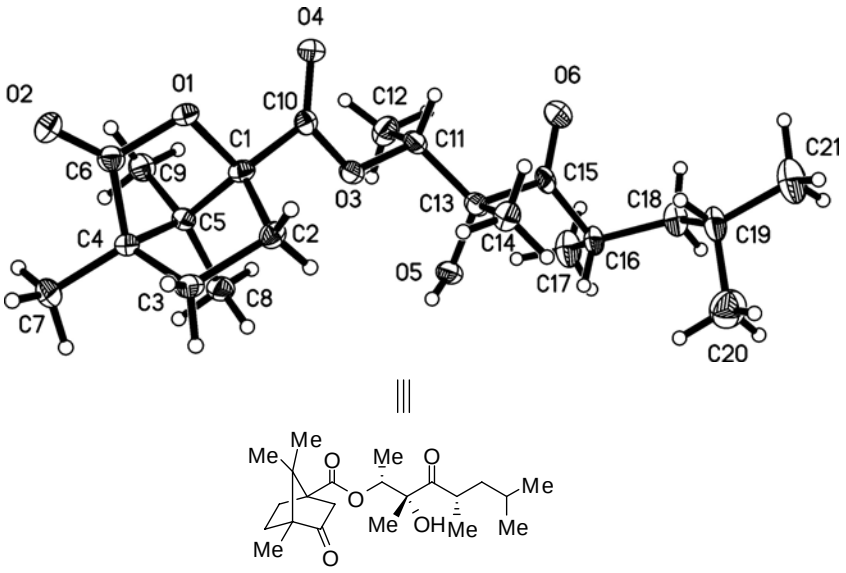


Table 1. Crystal data and structure refinement for C21H34O6.

Empirical formula	C21 H34 O6	
Formula weight	382.48	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2(1)	
Unit cell dimensions	a = 13.4736(8) Å	α= 90°.
	b = 5.9407(3) Å	β= 99.044(1)°.
	c = 13.7189(8) Å	γ= 90°.
Volume	1084.44(11) $Å^3$	

Z	2
Density (calculated)	1.171 Mg/m^3
Absorption coefficient	0.084 mm^{-1}
F(000)	416
Crystal size	0.35 x 0.13 x 0.05 mm^3
Theta range for data collection	1.97 to 30.60°.
Index ranges	-19<=h<=19, -8<=k<=8, -19<=l<=19
Reflections collected	13386
Independent reflections	6527 [R(int) = 0.0303]
Completeness to theta = 30.60°	99.7 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9958 and 0.9711
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	6527 / 1 / 380
Goodness-of-fit on F^2	1.007
Final R indices [I>2sigma(I)]	R1 = 0.0505, wR2 = 0.1135
R indices (all data)	R1 = 0.0579, wR2 = 0.1175

Absolute structure parameter	-0.54(73)
Largest diff. peak and hole	0.396 and -0.206 e.Å^{-3}

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3). For C21H34O6. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	1920(1)	-7241(2)	-375(1)	15(1)
O(2)	3446(1)	-7663(2)	548(1)	22(1)
O(3)	170(1)	-4679(2)	-2273(1)	19(1)
O(4)	310(1)	-8294(2)	-1753(1)	22(1)
O(5)	-770(1)	-1076(2)	-3323(1)	20(1)
O(6)	-2684(1)	-4960(2)	-3944(1)	29(1)
C(1)	1458(1)	-5421(2)	-997(1)	14(1)
C(2)	1215(1)	-3572(3)	-288(1)	16(1)
C(3)	2284(1)	-2760(3)	157(1)	18(1)
C(4)	2993(1)	-4175(3)	-397(1)	16(1)
C(5)	2362(1)	-4452(3)	-1445(1)	16(1)
C(6)	2879(1)	-6523(3)	-3(1)	16(1)
C(7)	4064(1)	-3346(3)	-314(2)	24(1)
C(8)	2158(1)	-2253(3)	-2015(1)	20(1)
C(9)	2814(1)	-6169(3)	-2084(1)	21(1)
C(10)	583(1)	-6353(3)	-1710(1)	14(1)

C(11)	-713(1)	-5113(3)	-3022(1)	17(1)
C(12)	-359(1)	-5633(3)	-3989(1)	25(1)
C(13)	-1323(1)	-2923(3)	-3022(1)	16(1)
C(14)	-1626(1)	-2507(3)	-2008(1)	22(1)
C(15)	-2312(1)	-3126(3)	-3749(1)	17(1)
C(16)	-2795(1)	-959(3)	-4181(1)	20(1)
C(17)	-2506(2)	-698(4)	-5219(1)	31(1)
C(18)	-3938(1)	-1042(4)	-4228(1)	25(1)
C(19)	-4288(1)	-821(4)	-3223(1)	26(1)
C(20)	-4158(2)	1569(4)	-2822(2)	39(1)
C(21)	-5384(2)	-1563(5)	-3302(2)	43(1)

Table 3. Bond lengths [Å] and angles [°] for C21H34O6.

O(1)-C(6)	1.3796(19)	C(2)-C(3)	1.551(2)
O(1)-C(1)	1.4554(18)	C(2)-H(2A)	0.93(2)
O(2)-C(6)	1.1971(19)	C(2)-H(2B)	0.96(2)
O(3)-C(10)	1.3263(19)	C(3)-C(4)	1.557(2)
O(3)-C(11)	1.4678(19)	C(3)-H(3A)	0.96(2)
O(4)-C(10)	1.2091(19)	C(3)-H(3B)	0.950(19)
O(5)-C(13)	1.4231(19)	C(4)-C(7)	1.512(2)
O(5)-H(5O)	0.77(3)	C(4)-C(6)	1.513(2)
O(6)-C(15)	1.212(2)	C(4)-C(5)	1.559(2)
C(1)-C(10)	1.513(2)	C(5)-C(8)	1.525(2)
C(1)-C(2)	1.536(2)	C(5)-C(9)	1.532(2)
C(1)-C(5)	1.559(2)	C(7)-H(7A)	0.97(2)

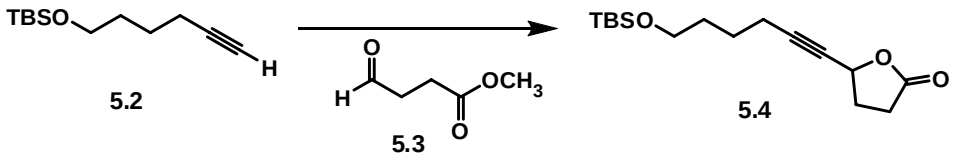
C(7)-H(7B)	0.93(2)	C(15)-C(16)	1.520(2)
C(7)-H(7C)	0.96(3)	C(16)-C(18)	1.533(2)
C(8)-H(8A)	0.93(2)	C(16)-C(17)	1.541(3)
C(8)-H(8B)	0.93(3)	C(16)-H(16)	0.95(2)
C(8)-H(8C)	0.97(2)	C(17)-H(17A)	0.99(3)
C(9)-H(9A)	0.94(2)	C(17)-H(17B)	0.98(3)
C(9)-H(9B)	0.94(2)	C(17)-H(17C)	0.97(3)
C(9)-H(9C)	0.91(2)	C(18)-C(19)	1.531(3)
C(11)-C(12)	1.510(2)	C(18)-H(18A)	0.99(3)
C(11)-C(13)	1.539(2)	C(18)-H(18B)	1.00(2)
C(11)-H(11)	0.940(19)	C(19)-C(20)	1.522(3)
C(12)-H(12A)	0.95(3)	C(19)-C(21)	1.529(3)
C(12)-H(12B)	0.91(3)	C(19)-H(19)	0.98(2)
C(12)-H(12C)	0.95(2)	C(20)-H(20A)	0.95(3)
C(13)-C(14)	1.530(2)	C(20)-H(20B)	1.00(3)
C(13)-C(15)	1.538(2)	C(20)-H(20C)	0.97(3)
C(14)-H(14A)	0.98(2)	C(21)-H(21A)	1.01(4)
C(14)-H(14B)	0.92(2)	C(21)-H(21B)	0.94(4)
C(14)-H(14C)	0.98(2)	C(21)-H(21C)	0.94(3)

C(6)-O(1)-C(1)	106.05(11)	C(10)-C(1)-C(5)	117.23(12)
C(10)-O(3)-C(11)	119.70(12)	C(2)-C(1)-C(5)	104.04(12)
C(13)-O(5)-H(5O)	104.1(19)	C(1)-C(2)-C(3)	101.23(12)
O(1)-C(1)-C(10)	109.00(12)	C(1)-C(2)-H(2A)	110.0(13)
O(1)-C(1)-C(2)	105.89(12)	C(3)-C(2)-H(2A)	112.5(12)
C(10)-C(1)-C(2)	116.72(12)	C(1)-C(2)-H(2B)	108.2(13)
O(1)-C(1)-C(5)	102.52(11)	C(3)-C(2)-H(2B)	113.6(14)

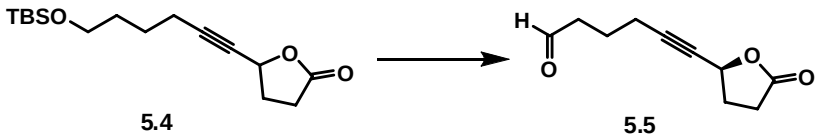
H(2A)-C(2)-H(2B)	110.7(18)	H(7B)-C(7)-H(7C)	111(2)
C(2)-C(3)-C(4)	104.06(12)	C(5)-C(8)-H(8A)	111.5(14)
C(2)-C(3)-H(3A)	111.7(13)	C(5)-C(8)-H(8B)	110.5(15)
C(4)-C(3)-H(3A)	107.2(13)	H(8A)-C(8)-H(8B)	104.9(19)
C(2)-C(3)-H(3B)	114.4(12)	C(5)-C(8)-H(8C)	115.2(14)
C(4)-C(3)-H(3B)	111.7(12)	H(8A)-C(8)-H(8C)	110.6(18)
H(3A)-C(3)-H(3B)	107.6(19)	H(8B)-C(8)-H(8C)	103(2)
C(7)-C(4)-C(6)	115.01(14)	C(5)-C(9)-H(9A)	110.2(15)
C(7)-C(4)-C(3)	116.01(14)	C(5)-C(9)-H(9B)	110.1(13)
C(6)-C(4)-C(3)	102.63(13)	H(9A)-C(9)-H(9B)	104.2(18)
C(7)-C(4)-C(5)	118.68(14)	C(5)-C(9)-H(9C)	109.9(14)
C(6)-C(4)-C(5)	99.23(12)	H(9A)-C(9)-H(9C)	106(2)
C(3)-C(4)-C(5)	102.69(12)	H(9B)-C(9)-H(9C)	116(2)
C(8)-C(5)-C(9)	109.45(13)	O(4)-C(10)-O(3)	126.18(14)
C(8)-C(5)-C(1)	115.42(13)	O(4)-C(10)-C(1)	125.49(14)
C(9)-C(5)-C(1)	112.65(13)	O(3)-C(10)-C(1)	108.33(12)
C(8)-C(5)-C(4)	114.23(13)	O(3)-C(11)-C(12)	108.55(13)
C(9)-C(5)-C(4)	112.91(13)	O(3)-C(11)-C(13)	103.03(12)
C(1)-C(5)-C(4)	91.29(11)	C(12)-C(11)-C(13)	114.58(14)
O(2)-C(6)-O(1)	121.74(14)	O(3)-C(11)-H(11)	108.3(11)
O(2)-C(6)-C(4)	131.05(15)	C(12)-C(11)-H(11)	111.6(11)
O(1)-C(6)-C(4)	107.17(12)	C(13)-C(11)-H(11)	110.3(11)
C(4)-C(7)-H(7A)	111.0(12)	C(11)-C(12)-H(12A)	108.6(17)
C(4)-C(7)-H(7B)	109.0(14)	C(11)-C(12)-H(12B)	109.3(15)
H(7A)-C(7)-H(7B)	109.7(18)	H(12A)-C(12)-H(12B)	109(2)
C(4)-C(7)-H(7C)	107.7(18)	C(11)-C(12)-H(12C)	110.8(14)
H(7A)-C(7)-H(7C)	109(2)	H(12A)-C(12)-H(12C)	110(2)

H(12B)-C(12)-H(12C)	109(2)	H(17B)-C(17)-H(17C)	105(2)
O(5)-C(13)-C(14)	111.45(14)	C(19)-C(18)-C(16)	114.19(14)
O(5)-C(13)-C(15)	108.15(12)	C(19)-C(18)-H(18A)	109.0(13)
C(14)-C(13)-C(15)	105.88(12)	C(16)-C(18)-H(18A)	108.6(14)
O(5)-C(13)-C(11)	110.36(12)	C(19)-C(18)-H(18B)	110.9(13)
C(14)-C(13)-C(11)	110.85(13)	C(16)-C(18)-H(18B)	106.4(13)
C(15)-C(13)-C(11)	110.01(13)	H(18A)-C(18)-H(18B)	107.4(18)
C(13)-C(14)-H(14A)	109.3(13)	C(20)-C(19)-C(21)	110.45(19)
C(13)-C(14)-H(14B)	109.6(15)	C(20)-C(19)-C(18)	111.78(17)
H(14A)-C(14)-H(14B)	112(2)	C(21)-C(19)-C(18)	110.02(17)
C(13)-C(14)-H(14C)	111.5(13)	C(20)-C(19)-H(19)	104.1(13)
H(14A)-C(14)-H(14C)	110.9(18)	C(21)-C(19)-H(19)	109.3(14)
H(14B)-C(14)-H(14C)	103(2)	C(18)-C(19)-H(19)	111.1(13)
O(6)-C(15)-C(16)	122.57(14)	C(19)-C(20)-H(20A)	109(2)
O(6)-C(15)-C(13)	119.97(15)	C(19)-C(20)-H(20B)	108.4(19)
C(16)-C(15)-C(13)	117.45(14)	H(20A)-C(20)-H(20B)	107(3)
C(15)-C(16)-C(18)	110.79(15)	C(19)-C(20)-H(20C)	111.6(17)
C(15)-C(16)-C(17)	106.94(15)	H(20A)-C(20)-H(20C)	109(2)
C(18)-C(16)-C(17)	111.29(14)	H(20B)-C(20)-H(20C)	112(2)
C(15)-C(16)-H(16)	107.2(14)	C(19)-C(21)-H(21A)	112(2)
C(18)-C(16)-H(16)	113.3(14)	C(19)-C(21)-H(21B)	113(2)
C(17)-C(16)-H(16)	107.0(14)	H(21A)-C(21)-H(21B)	106(3)
C(16)-C(17)-H(17A)	108.9(14)	C(19)-C(21)-H(21C)	111.0(19)
C(16)-C(17)-H(17B)	114.0(15)	H(21A)-C(21)-H(21C)	100(3)
H(17A)-C(17)-H(17B)	111(2)	H(21B)-C(21)-H(21C)	115(3
C(16)-C(17)-H(17C)	112.9(16)		
H(17A)-C(17)-H(17C)	105(2)		

Experimental (Chapter V)



To a solution of TBS protected 5-hexyne-1-ol **5.2** (9g, 42.45 mmol) in dry THF (150mL), cooled at -78^{o}C, was added n-BuLi (1.6 M, 28mL, 44.8 mmol) slowly. The reaction was allowed to warm to room temperature slowly over 30 minutes and then cooled back to -78^{o}C. A solution of methyl 4-oxobutanoate **5.3** (5g, 43.1 mmol) in THF (150mL) was then added to the reaction mixture dropwise. Upon completion of addition, the reaction mixture was slowly warmed to 0^{o}C over 2h. The reaction was then quenched with saturated NH_4Cl (50 mL) and extracted with Et_2O (3 x 100 mL). The combined organic phase was washed with water (100 mL), brine (50 mL) and dried over anhydrous $MgSO_4$. Evaporation of solvent and FCC purification using 15% EtOAc in hexanes gave the lactone **5.4** (7.78g, 62% yield) as a colorless oil. IR ν_{max}(neat)/cm^{-1} 2245, 1786; δ_H (400 MHz, $CDCl_3$) 5.16-5.09 (1H, m), 3.65-3.60 (2H, t, J=), 2.72-2.60 (1H, m), 2.56-2.44 (2H, m), 2.30-2.22 (3H, m), 1.66-1.50 (4H, m), 0.893 (9H,s), 0.049 (6H, s); δ_C (100 MHz, $CDCl_3$) 176.2, 88.6, 76.6, 69.7, 62.5, 31.8, 30.1, 27.9, 25.9, 24.7, 18.5, 18.3, -5.3; *m/z* (ESIMS) found: 319 $(M+Na)^+$; calc'd: 319.

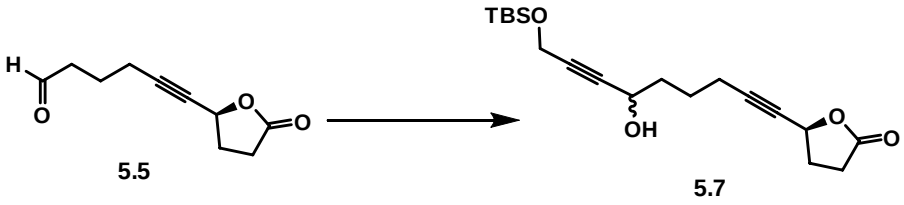


5.4 5.5

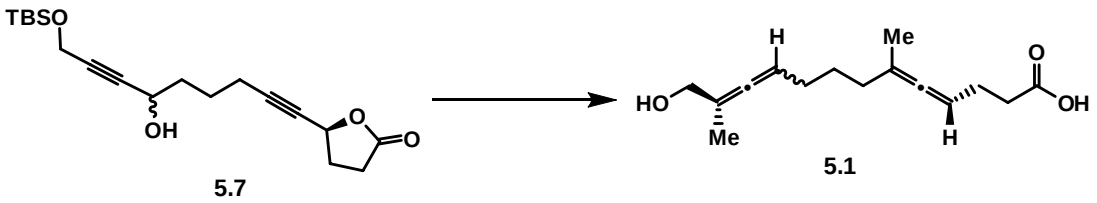
To a solution of lactone **5.4** (7g, 23.6 mmol) in THF (50 mL) was added (25 mL, 25 mmol) TBAF (1.0M solution in THF) at 0°C. The reaction mixture was warmed to room temperature and stirred for 2 hour at room temperature. The reaction was then quenched with saturated NH_4Cl (20 mL) and extracted with EtOAc (3 x 50 mL). The combined organic phase was washed with water (50 mL), brine (50 mL) and dried over anhydrous $MgSO_4$. Evaporation of solvent and FCC purification using 75% EtOAc in hexanes gave hydroxyl lactone **5.4'** (3.76g, 88%yield) as a colorless oil. IR ν_{max}(neat)/cm^{-1} 3424, 2244, 1782; δ_H (400 MHz, $CDCl_3$) 5.18-5.08 (1H, m), 3.66 (2H, t, J=3.0 Hz), 2.72-2.60 (1H, m), 2.56-2.44 (2H, m), 2.30-2.22 (3H, m), 1.80(1H, s), 1.71-1.56 (4H, m); δ_C (100 MHz, $CDCl_3$) 176.4, 88.3, 76.7, 69.6, 62.1, 31.6, 30.0, 27.9, 24.5, 18.4; *m/z* (ESIMS) found: 205 $(M+Na)^+$; calc'd: 205.

A solution of oxalyl chloride (1.1 mL, 12.6 mmol) in DCM (25mL) was cooled to -78°C. To that DMSO (1.75 mL, 24.7 mmol) was added slowly and stirred for 15 min at -78°C. Then the alcohol **5.4'** (1.5g, 8.23 mmol) in DCM (5 mL) was added slowly and stirred for 15 min when Et_3N (5.7 mL, 41.2 mmol) was added. The reaction mixture was then warmed to 0°C and allowed to stir for additional 30 min. The reaction was then quenched with water (15 mL) and extracted with DCM (2 x 50 mL). The combined organic phase was washed with water (15 mL) and dried over anhydrous Na_2SO_4. Evaporation of solvent and FCC purification using 40% EtOAc in

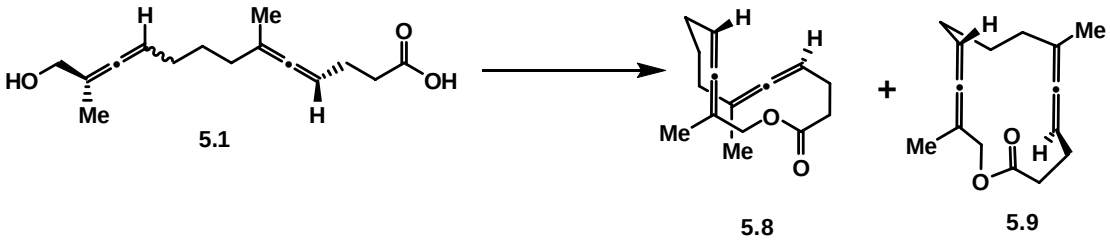
hexanes gave **5.5** (1.35g, 91% yield) as a colorless oil. IR ν_{max}(neat)/cm^{-1} 2243, 1779, 1720; δ_H (400 MHz, $CDCl_3$) 9.81 (1H, t, *J*=0.49), 5.18-5.08 (1H, m), 2.72-2.44 (5H, m), 2.36-2.20 (3H, m), 1.90-1.82 (2H, m); δ_C (100 MHz, $CDCl_3$) 201.5, 176.1, 87.3, 77.6, 69.4, 42.6, 30.0, 27.9, 20.6, 18.1; *m/z* (ESIMS) found: 181 $(M+H)^+$; calc'd: 181.



To a solution of TBS protected propargyl alcohol (1.78g, 10.5 mmol) in THF (45 mL) was added n-BuLi (2.5 M, 3.9 mL, 9.75 M) slowly at -40°C. The reaction was slowly warmed up to room temperature and then cooled back to -40°C. Aldehyde **5.5** (1.35g, 7.5 mmol) in 10 mL THF was then added slowly to the reaction. The reaction mixture was then slowly warmed to room temperature over 1 hour. The reaction was then quenched with saturated NH_4Cl (20 mL) and extracted with Et_2O (3 x 100 mL). The combined organic phase was washed with water (50 mL), brine (50 mL) and dried over anhydrous $NaSO_4$.. Evaporation of solvent and FCC purification using 30% EtOAc in hexanes gave bis[alkyne] **5.7** (2.46g, 2 diastereomers 95% yield) as a colorless oil. IR ν_{max}(neat)/cm^{-1} 3415, 2243, 1778; δ_H (400 MHz, $CDCl_3$) 5.18-5.08 (1H, m), 4.48-4.40 (1H, m), 4.37-4.33 (2H,m), 2.72-2.60 (1H, m), 2.56-2.44 (2H, m), 2.36-2.20 (3H, m), 1.88-1.64 (5H, m), 0.91(9H, s), 0.12(6H, s); δ_C (100 MHz, $CDCl_3$) 176.2, 88.0, 85.3, 83.9, 77.98, 69.6, 61.9, 51.7, 36.5, 30.1, 27.9, 25.8, 23.8, 18.4, 18.3, -5.1; *m/z* (ESIMS) found: 373 $(M+Na)^+$; calc'd: 373.

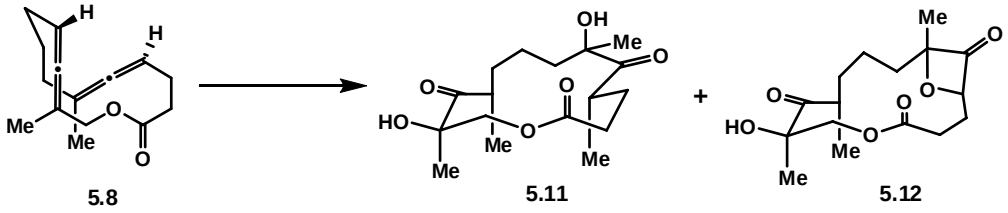


To a solution of **5.7** (2.7g, 7.5mmol) in 50mL ether was added Et_3N (1.56mL, 11.2mmol) and MsCl (0.87mL, 11.2mmol) respectively at 0^oC. The reaction mixture was warmed to room temperature and stirred for 1 hour at room temperature. The reaction was then cooled back to 0^oC and to that was added a solution of methyl cyanocuprate, prepared from CuCN(4g, 44.7mmol) and MeLi (28mL, 44.8mmol) in 75 ml Et_2O. The reaction mixture was then warmed to room temperature and stirred for 2h. The reaction was then diluted with 75 ml THF and to that 10% HCl solution (12ml) was added and stirred for additional 5 hours at room temperature. The reaction mixture was then diluted with Et_2O (200 ml), washed with water (3 x 50 ml) and dried over anhydrous $NaSO_4$. Evaporation of solvent and FCC purification using 80% EtOAc in hexanes gave seco acid **5.1** (1.54g, 86% yield) as a colorless oil. IR ν_{max}(neat)/cm^{-1} 3342, 1966, 1710; δ_H (400 MHz, $CDCl_3$) 5.34-5.24 (1H, m), 5.14-5.06 (1H, m), 4.01 (2H, d, J=3.1Hz), 2.50-2.36 (2H, m), 2.36-2.20 (2H, m), 2.10-1.86 (4H, m), 1.70 (3H, d, *J*=2.8Hz), 1.66 (3H, d, J=2.8Hz), 1.57-1.44 (2H, m); δ_C (100 MHz, $CDCl_3$) 200.9(200.9), 199.3(199.3), 177.9(177.8), 101.4(101.3), 100.6(100.5), 94.3(94.1), 89.0(89.0), 63.7(63.7), 33.3(33.3), 32.9(32.8), 28.7(28.6), 26.9(26.7), 24.0(23.9), 19.4(19.3), 15.7; *m/z* (ESIMS) found: 251 $(M+H)^+$; calc'd: 251.



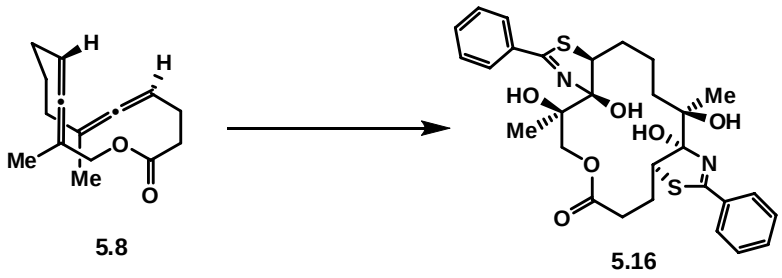
To a solution of seco acid **5.1** (500 mg, 2mmol) in 20mL toluene was added N,N-diisopropylethylamine (1.83mL, 10mmol) and 2,4,6 trichlorobenzoyl chloride (2.44g, 10 mmol) were added respectively to above solution. The solution was stirred for 6h at room temperature. 4-Dimethylaminopyridine (DMAP, 2.45g, 20 mmol) in 180 mL toluene was prepared in another flask. The actived ester was added dropwise to the DMAP solution using syringe pump over 2h and stirred for 2 more hours at room temperature. The reaction was quenched with NH_4Cl (20 mL). The organic layer was decanted and the aqueous layer was extracted with Et_2OAc twice (100 mL). All the organic layers were combined and dried over Na_2SO_4. The crude product was purified by flash chromatography (4% EtOAc/Hexanes) to yield bis[allene] macro lactone **5.8** and **5.9** (354 mg, 1:1, 77% yield) as a colorless oil. **5.8** and **5.9** were separated by another column. **5.8**: IR ν_{max}(neat)/cm^{-1} 1969, 1742; δ_H (400 MHz, $CDCl_3$) 5.30-5.18 (1H, m), 5.08-4.96 (1H, m), 4.84 (1H, d, J=11.6), 4.23 (1H, dd, J=11.6, 2.4Hz), 2.56-2.22 (4H, m), 2.10-1.74 (4H, m), 1.75 (3H, d, J=2.8Hz), 1.66 (3H, d, J=2.8), 1.64-1.42 (2H, m); δ_C (100 MHz, $CDCl_3$) 202.8, 200.8, 172.8, 101.3, 97.6, 91.9, 89.9, 66.2, 33.4, 32.5, 26.3, 24.8, 24.1, 19.8, 16.8; *m/z* (ESIMS) found: 255.2 $(M+Na)^+$; calc'd: 255.2. **5.9**: IR ν_{max}(neat)/cm^{-1} 1968, 1740; δ_H (400 MHz, $CDCl_3$) 5.26-5.18 (1H, m), 5.06 (1H, d, *J*=11.2), 5.04-4.94 (1H, m), 4.10 (1H, dd, *J*=11.2, 2.4Hz), 2.52-

2.26 (4H, m), 2.66-1.80 (4H, m), 1.76 (3H, d, *J*=3.2Hz), 1.67 (3H, d, *J*=2.8), 1.64-1.36 (2H, m); δ_C (100 MHz, $CDCl_3$) 203.9, 201.8, 172.7, 100.9, 97.3, 91.6, 89.3, 66.2, 34.2, 32.9, 27.1, 26.0, 25.6, 19.8, 17.1; *m/z* (ESIMS) found: 233.2 $(M+H)^+$; calc'd: 233.2.



To a solution of freshly prepared dimethyldioxirane (DMDO) in $CHCl_3$ (12.9 mL, 2.586 mmol) was added Bis[allene] macro lactone **5.8** (120 mg, 0.517 mmol) in $CHCl_3$ dropwise at -40^{o}C. The reaction was stirred under nitrogen and let to warm to rt over 2 h. Solvent was evaporated and the resulting bis[SDE] was used as such for the next step. Lower order methyl cyanocuprate was prepared by adding MeLi (3.2 mL, 5.12 mmol) to a slurry of CuCN (460 mg, 5.86 mmol) in diethyl ether (50 mL) at -40^{o}C and then warming to 0^{o}C. The cuprate was cooled back to -40^{o}C and to that a ether solution (2 ml) of bis[SDE] was added slowly. The reaction was warmed to room temperature over 2 hour. The reaction was then quenched with saturated NH_4Cl (10 mL) and extracted with Et_2O (3 x 20 mL). The combined organic phase was washed with water (10 mL), brine (10 mL) and dried over anhydrous $MgSO_4$. Evaporation of solvent and FCC purification using 15% EtOAc in hexanes gave a mixture of **5.11** and **5.12** (63 mg) as colorless oil. Based on 1.4:1 ratio of the product mixture by ^{1}H NMR, the yield calculated for **5.11** and **5.12** are 22% and 16% respectively. **5.11** (white solid) and **5.12** (white solid) were then separated by 4 more

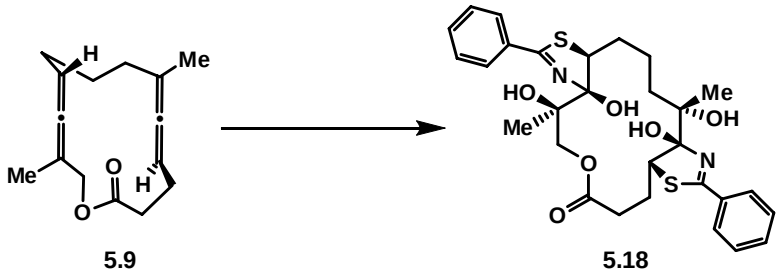
FCC purification. **5.11:** MP 118°C; IR ν_{max}(neat)/cm^{-1} 3473, 2938, 1737, 1706, 1457, 1374; δ_H (500 MHz, $CDCl_3$) 4.37 (1H, d, J= 12 Hz), 4.28 (1H, s), 4.22 (1H, d, J= 12.0 Hz), 4.04 (1H, s), 2.98-2.92 (1H, m), 2.78-2.72 (1H, m), 2.38 (2H, J= 6.5 Hz), 2.10-2.02 (1H, m), 1.90-1.82 (1H, m), 1.76-1.66 (2H, m), 1.44 (3H, s), 1.41 (3H, s), 1.38-1.24 (3H, m), 1.15 (3H, d, J= 7.0 Hz), 1.12 (3H, d, J= 7.0 Hz), 0.88-0.80 (1H, m); δ_C (125 MHz, $CDCl_3$) 217.8, 214.4, 172.1, 78.9, 77.9, 68.9, 41.1, 39.0, 38.3, 35.7, 31.6, 28.0, 25.6, 22.0, 20.8, 20.5, 18.6. ; *m/z* (ESIMS) found: 351.3 $(M+Na)^+$; calc'd: 351.2. **5.12**: MP 151°C; IR ν_{max}(neat)/cm^{-1} 3477, 2928, 1811, 1740, 1709, 1462; 5.42 (1H, dd, J= 4.5 Hz, 3.0 Hz), 4.35 (1H, d, J= 12.0 Hz), 4.25 (1H, s), 4.14 (1H, d, J= 12.0 Hz), 3.04-2.96 (1H, m), 2.51 (1H, ddd, J= 18.0 Hz, 8 Hz, 3 Hz), 2.36 (1H, ddd, J= 16.0 Hz, 10.0 Hz, 3.5 Hz), 2.20- 2.08 (2H, m), 2.06-1.98 (1H, m), 1.76- 1.68 (1H, m), 1.56- 1.50 (1H, m), 1.45 (6H, s), 1.36- 1.28 (2H, m), 1.15 (3H, J= 6.5 Hz), 0.90-0.86 (1H, m); δ_C (125 MHz, $CDCl_3$) 215.7, 206.8, 172.3, 105.6, 96.0, 77.8, 68.9, 40.1, 36.2, 33.9, 30.6, 24.4, 23.2, 22.2, 21.6, 20.3.; *m/z* (ESIMS) found: 335.2 $(M+Na)^+$; calc'd: 335.2.



5.8 **5.16**

To a solution of freshly prepared dimethyldioxirane (DMDO) in $CHCl_3$ (3.22 mL, 0.645 mmol) was added Bis[allene] macro lactone **5.8** (30 mg, 0.129 mmol) in $CHCl_3$ dropwise at -40°C. The reaction was stirred under nitrogen and let to warm to rt over

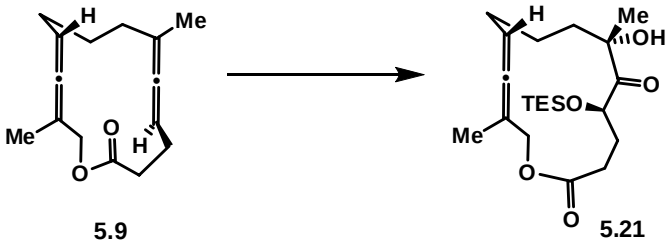
2 h. Solvent was evaporated and the resulting bis[SDE] was dissolved in chloroform. thiobenzamide (70mg, 0.517mmol) was added at 0^{o}C and the reaction mixture was warmed to room temperature and stirred for 6h. Evaporation of the solvent followed by FCC using 15 % EtOAc in Hexanes gave the bis[thiazoline] **5.16** (58 mg, 78% yield) as a white solid. MP 78^{o}C; IR ν_{max}(neat)/cm^{-1} 3442, 1735, 1604, 1576; δ_H (500 MHz, $CDCl_3$) 7.86-7.78 (4H, m), 7.52-7.38 (6H, m), 4.34 (1H, d, *J*=11.6Hz), 4.20 (1H, d, *J*=11.6Hz), 4.11 (1H, dd, *J*=9.6, 3.8Hz), 4.02-3.96 (1H, m), 3.73 (1H, s), 3.61 (1H, s), 3.18 (1H, s), 2.93 (1H, s), 2.70-2.58 (1H, m), 2.40-2.20 (3H, m), 2.10-1.96 (1H, m), 1.94-1.78 (1H, m), 1.76-1.54 (3H, m), 1.29 (3H, s), 1.30-1.20 (1H, m), 1.26 (3H, s); δ_C (125 MHz, $CDCl_3$) 171.3, 169.5, 168.8, 132.5, 132.4, 132.04, 131.97, 128.6, 128.5, 128.4, 128.3, 110.4, 110.0, 77.8, 76.2, 66.4, 53.7, 53.3, 36.2, 34.3, 33.0, 27.6, 27.0, 22.0, 21.5; *m/z* (ESIMS) found: 371 $(M+H)^+$; calc'd: 371.



5.9 **5.18**

Bis[thiazoline] **5.18** (55 mg, 74% yield) was prepared, using same procedure from bis[allene] macrolactone **5.9** (30 mg, 0.129 mmol). MP 158^{o}C; IR ν_{max}(neat)/cm^{-1} 3416, 1734, 1605, 1577; δ_H (400 MHz, $CDCl_3$) 7.84 (2H, d, *J*=7.6Hz), 7.80 (2H, d, *J*=7.6Hz), 7.54-7.34 (6H, m), 4.75 (1H, d, *J*=11.6Hz), 4.61 (1H, s), 4.50 (1H, s), 4.34 (1H, dd, *J*=10.4, 2.8Hz), 3.94 (1H, dd, *J*=10.4, 4Hz), 3.75 (1H, d, J=4Hz), 3.59 (1H, s), 3.05 (1H, s), 3.06-2.94 (1H, m) 2.58-2.40 (1H, m), 2.38-2.22 (1H, m), 2.22-1.88

(4H, m), 1.80-1.66 (1H, m), 1.60-1.40 (1H, m) 1.33 (3H, s), 1.22-1.06 (1H, m), 1.10 (3H, s); δ_C (100 MHz, $CDCl_3$) 172.6, 170.1, 168.1, 132.5, 132.3, 132.0, 131.9, 128.6, 128.5, 128.4, 128.3, 112.3, 110.3, 78.1, 76.7, 66.8, 50.0, 49.1, 34.6, 33.9, 33.6, 28.1, 21.5, 20.7, 20.6; *m/z* (ESIMS) found: 371 $(M+H)^+$; calc'd: 371.

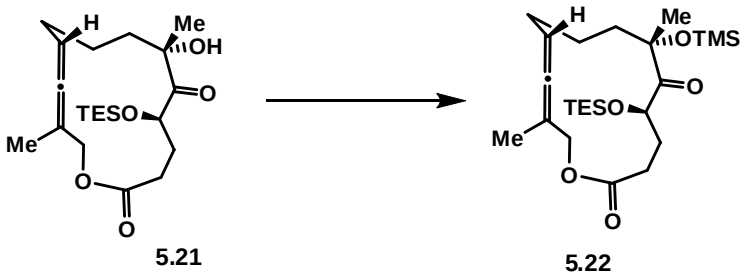


5.9 **5.21**

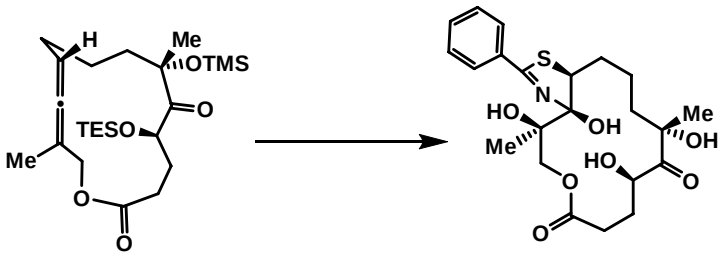
To a solution of freshly prepared dimethyldioxirane (DMDO) in $CHCl_3$ (2.7 mL, 0.593 mmol) was added Bis[allene] macro lactone **5.9** (50mg, 0.216 mmol) in $CHCl_3$ dropwise at -40°C. The reaction was stirred under nitrogen and let to warm to 0°C over 1 h. Solvent was evaporated and the resulting bis[SDE] was dissolved in 5 mL THF/water (1:1) solution at 0°C and stirred for 30 minutes at 0°C. The reaction mixture was then extracted in diethyl ether (3 x 20 mL). Evaporation of the solvent followed by FCC using 25% EtOAc in Hexanes gave the diol **5.20** (47mg, 78% yield) as a colorless oil.

To a solution of diol **5.20** (38 mg, 0.135 mmol) in DCM (5 mL), cooled to 0°C, was added imidazole (14 mg, 0.20 mmol), DMAP (2 mg, 0.016 mmol), and TESCl (24.4 mg, 0.16 mmol) at 0°C. The reaction was stirred 5 minutes at 0°C. Diluted with DCM (20 mL), washed with water (2 x 5 mL). Evaporation of the solvent followed by FCC using 10% EtOAc/Hexanes gave the **5.21** (55mg, 99% yield) as a white solid. MP 54°C; IR ν_{max}(neat)/cm^{-1} 3493, 2954, 1971, 1737, 1750; δ_H (500 MHz, $CDCl_3$) 5.28-

5.20 (1H, m), 4.69 (1H, dd, J= 12.5, 3.5 Hz), 4.44 (1H, dd, J= 8.0, 4.0 Hz), 4.21 (1H, s), 4.20 (1H, dd, J= 12, 2.0 Hz), 2.40- 2.28 (2H, m), 2.10-2.02 (2H, m), 1.98-1.90 (1H, m), 1.84-1.76 (1H, m), 1.71 (3H, d, J= 2.5 Hz), 1.70-1.60 (2H, m), 1.40 (3H, s), 1.26-1.16 (2H, m), 0.97 (9H, t, J= 8 Hz), 0.65 (6H, q, J= 8 Hz); δ_C (125 MHz, $CDCl_3$) 213.0, 202.5, 172.4, 96.6, 93.0, 80.1, 77.1, 64.9, 38.2, 30.0, 29.5, 28.3, 27.3, 23.5, 17.2, 6.9, 5.1. *m/z* (ESIMS) found: 397.1 $(M+H)^+$; calc'd: 397.



To a solution of **5.21** (40 mg, 0.10 mmol) in DCM (5 mL), cooled to 0°C, was added TEA (20 mg, 0.20 mmol), DMAP (2 mg, 0.016 mmol), and TMSCl (16 mg, 0.144 mmol) at 0°C. The reaction was warmed to room temperature and stirred for 1 hour. Diluted with DCM (20 mL), washed with water (2 x 5 mL). Evaporation of the solvent followed by FCC using 5% EtOAc/Hexanes gave the **5.22** (46mg, 97% yield) as a colorless oil. IR ν_{max}(neat)/cm^{-1} 2954, 1970, 1739, 1248, 842; δ_H (400 MHz, $CDCl_3$) 5.20-5.12 (1H, m), 4.76 (1H, dd, J= 13.2, 3.2 Hz), 4.50 (1H, t, J= 6.0 Hz), 4.15 (1H, dd, J= 12.8, 2.4 Hz), 2.54-2.24 (4H, m), 2.14-2.10 (1H, m), 1.98-1.60 (5H, m), 1.70 (3H, d, J= 2.4 Hz), 1.39 (3H, s), 0.94 (9H, t, J= 8.0 Hz), 0.61 (6H, q, J= 8.0 Hz), 0.10 (9H, s); δ_C (100 MHz, $CDCl_3$) 209.9, 202.2, 172.6, 95.9, 92.8, 81.9, 72.8, 64.8, 38.7, 30.4, 29.7, 28.7, 25.7, 23.3, 17.0, 7.0, 5.3, 2.6; *m/z* (ESIMS) found: 491.3 $(M+Na)^+$; calc'd: 491.2.



5.22 **5.23**

To a solution of freshly prepared dimethyldioxirane (DMDO) in $CHCl_3$ (1.3 mL, 0.26 mmol) was added allene **5.22** (50mg, 0.102 mmol) in $CHCl_3$ dropwise at -40^oC. The reaction was stirred under nitrogen and let to warm to rt over 2 h. Solvent was evaporated and the resulting SDE was dissolved in chloroform (3 mL). thiobenzamide (41 mg, 0.3 mmol) was added at 0^oC and the reaction mixture was warmed to room temperature and stirred for 3 hours. Solvent was evaporated and the reaction products was re-dissolved in THF (2 mL) and cooled to 0^oC. Thee drops of 80% glacial acetic acid and TBAF (0.3 mL, 0.3 m) was added to the reaction. The reaction was then warmed to room temperature and stirred for 1 hour. Diluted with ether (50 mL), washed with water (10 mL). Evaporation of the solvent followed by FCC using 15 % EtOAc in Hexanes gave the diol-thiazoline **5.23** (36mg, 75% yield) as a white solid. MP 151^oC; IR ν_{max}(neat)/cm^{-1} 3438, 2932, 1735, 1716, 1239; δ_H (500 MHz, $CDCl_3$) 7.80 (2H, d, J= 8.0 Hz), 7.50 (1H, t, J= 7.0 Hz), 7.41 (2H, t, J= 7.5 Hz), 4.75 (1H, bs), 4.55 (1H, d, J= 11.0 Hz), 3.96 (1H, dd, J= 5.5, 5.5 Hz), 3.90 (1H, d, J= 11.5 Hz), 3.84 (1H, s), 3.51 (1H, s), 3.11 (1H, s), 2.92 (1H, d, J= 4.5 Hz), 2.66-2.58 (1H, m), 2.44-2.32 (1H, m), 2.16- 2.02 (4H, m), 1.90-1.82 (2H, m), 1.70-1.78 (2H, m), 1.46 (3H, s), 1.29 (3H, s); δ_C (125 MHz, $CDCl_3$) 215.3, 172.0, 170.6, 132.7, 132.3, 128.8 (2),

128.6 (2), 109.6, 79.7, 76.1, 70.4, 66.7, 54.2, 39.7, 32.1, 29.2, 29.1, 27.1, 26.9, 21.7; *m/z* (ESIMS) found: 452.2.1 $(M+H)^+$; calc'd: 452.

X-ray structure of **5.11**:

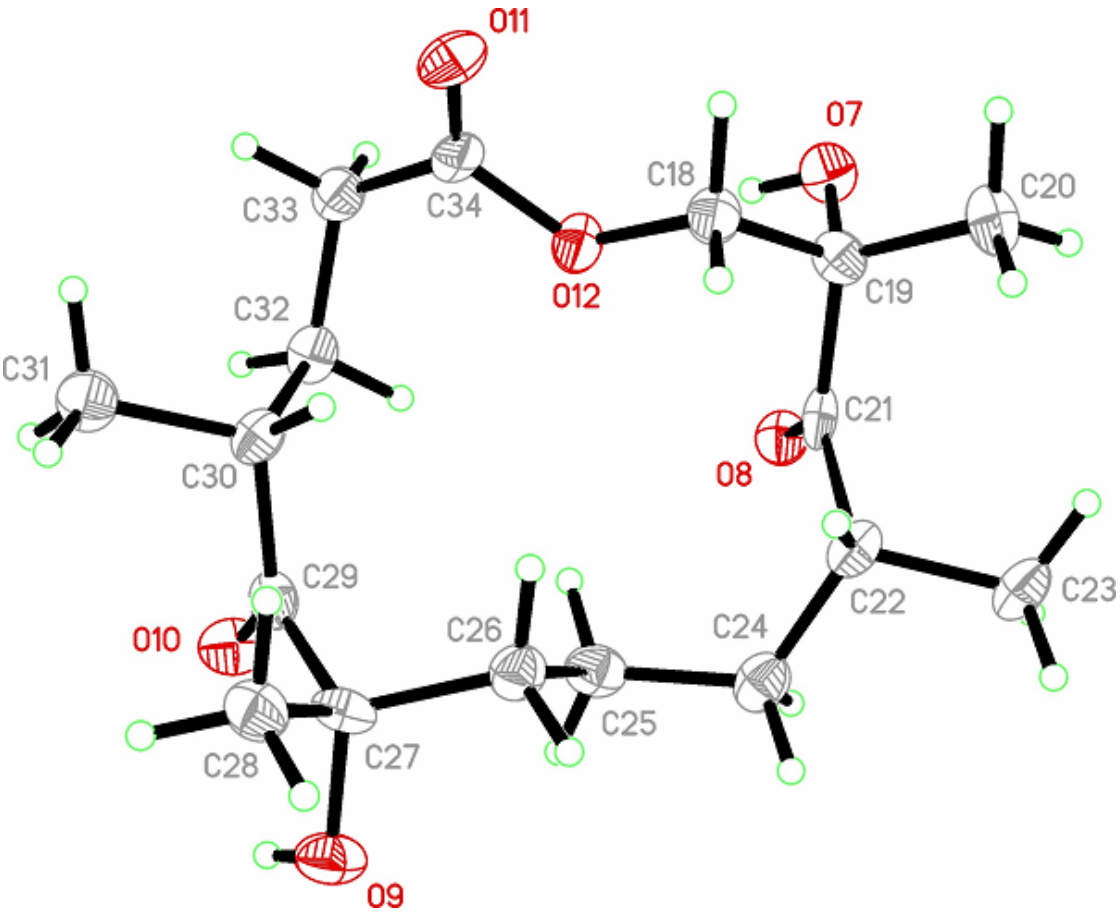


Table 1. Crystal data and structure refinement

Empirical formula	C17 H28 O6
Formula weight	328.39
Temperature	100(2) K
Wavelength	0.71073 Å

Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 10.1289(16) Å	α= 94.122(3)°.
	b = 11.2387(17) Å	β= 108.355(3)°.
	c = 15.895(3) Å	γ = 90.646(3)°.
Volume	1711.8(5) $Å^3$	
Z	4	
Density (calculated)	1.274 Mg/m^3	
Absorption coefficient	0.095 mm^{-1}	
F(000)	712	
Crystal size	0.20 x 0.05 x 0.02 mm^3	
Theta range for data collection	2.18 to 24.71°.	
Index ranges	-11<=h<=11, -13<=k<=13, 0<=l<=18	
Reflections collected	5343	
Independent reflections	5343 [R(int) = 0.0000]	
Completeness to theta = 24.71°	91.6 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9999 and 0.3739	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	5343 / 0 / 428	
Goodness-of-fit on F^2	1.015	
Final R indices [I>2sigma(I)]	R1 = 0.0866, wR2 = 0.1966	
R indices (all data)	R1 = 0.1471, wR2 = 0.2135	

Largest diff. peak and hole 0.402 and -0.351 e.Å^{-3}

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

	x	y	z	U(eq)
O(1)	8415(4)	9549(3)	8724(2)	28(1)
O(2)	8853(4)	8269(3)	7409(2)	27(1)
O(3)	6736(4)	2999(3)	6153(2)	38(1)
O(4)	8312(4)	3202(3)	7794(2)	32(1)
O(5)	5625(4)	6946(3)	9481(2)	32(1)
O(6)	7160(3)	7368(3)	8787(2)	23(1)
C(1)	6329(5)	8342(4)	8415(3)	25(1)
C(2)	7201(5)	9118(4)	8032(3)	25(1)
C(3)	6381(6)	10222(4)	7698(3)	32(1)
C(4)	7623(6)	8406(4)	7295(3)	25(1)
C(5)	6526(6)	7885(4)	6438(3)	27(1)
C(6)	6175(6)	8825(5)	5746(3)	36(2)
C(7)	7090(6)	6795(5)	6050(3)	33(1)
C(8)	7329(6)	5675(5)	6559(3)	30(1)
C(9)	6014(6)	4967(5)	6440(3)	28(1)
C(10)	6192(5)	3674(5)	6741(3)	23(1)
C(11)	4782(6)	3136(5)	6686(3)	31(1)
C(12)	7207(5)	3684(4)	7677(3)	22(1)
C(13)	6839(5)	4301(4)	8453(3)	21(1)

C(14)	6301(6)	3355(5)	8921(3)	29(1)
C(15)	8116(5)	5002(5)	9089(3)	26(1)
C(16)	7741(6)	5852(4)	9767(3)	27(1)
C(17)	6728(6)	6748(4)	9342(3)	24(1)
O(7)	3232(4)	5183(3)	8501(2)	30(1)
O(8)	3906(4)	6385(3)	7342(2)	27(1)
O(9)	1533(4)	11090(3)	5920(2)	33(1)
O(10)	3125(4)	11349(3)	7555(2)	32(1)
O(11)	668(4)	7759(3)	9353(2)	30(1)
O(12)	2025(4)	7394(3)	8495(2)	26(1)
C(18)	1198(5)	6340(4)	8080(3)	26(1)
C(19)	2112(5)	5479(4)	7765(3)	24(1)
C(20)	1284(5)	4322(4)	7377(4)	29(1)
C(21)	2668(6)	6095(4)	7105(3)	22(1)
C(22)	1745(6)	6310(5)	6171(3)	24(1)
C(23)	1792(6)	5198(5)	5547(3)	30(1)
C(24)	2257(6)	7397(4)	5815(3)	28(1)
C(25)	2371(5)	8610(5)	6326(3)	28(1)
C(26)	966(5)	9135(4)	6272(3)	26(1)
C(27)	1053(6)	10494(5)	6533(3)	26(1)
C(28)	-392(5)	10939(5)	6467(3)	28(1)
C(29)	2050(6)	10773(5)	7461(3)	24(1)
C(30)	1735(6)	10350(5)	8257(3)	24(1)
C(31)	1297(6)	11433(5)	8755(3)	30(1)
C(32)	3034(5)	9785(5)	8871(3)	25(1)
C(33)	2681(5)	9049(4)	9549(3)	26(1)

C(34)	1658(6)	8020(4)	9142(3)	22(1)

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

O(1)-C(2)	1.419(6)	C(6)-H(6B)	0.9800
O(1)-H(1)	0.8400	C(6)-H(6C)	0.9800
O(2)-C(4)	1.215(6)	C(7)-C(8)	1.526(7)
O(3)-C(10)	1.409(5)	C(7)-H(7A)	0.9900
O(3)-H(3)	0.8400	C(7)-H(7B)	0.9900
O(4)-C(12)	1.216(6)	C(8)-C(9)	1.497(7)
O(5)-C(17)	1.224(6)	C(8)-H(8A)	0.9900
O(6)-C(17)	1.334(6)	C(8)-H(8B)	0.9900
O(6)-C(1)	1.434(6)	C(9)-C(10)	1.556(7)
C(1)-C(2)	1.519(7)	C(9)-H(9A)	0.9900
C(1)-H(1A)	0.9900	C(9)-H(9B)	0.9900
C(1)-H(1B)	0.9900	C(10)-C(12)	1.518(7)
C(2)-C(3)	1.534(7)	C(10)-C(11)	1.519(7)
C(2)-C(4)	1.543(7)	C(11)-H(11A)	0.9800
C(3)-H(3A)	0.9800	C(11)-H(11B)	0.9800
C(3)-H(3B)	0.9800	C(11)-H(11C)	0.9800
C(3)-H(3C)	0.9800	C(12)-C(13)	1.521(6)
C(4)-C(5)	1.533(7)	C(13)-C(15)	1.534(7)
C(5)-C(7)	1.529(7)	C(13)-C(14)	1.528(6)
C(5)-C(6)	1.544(7)	C(13)-H(13)	1.0000
C(5)-H(5)	1.0000	C(14)-H(14A)	0.9800
C(6)-H(6A)	0.9800	C(14)-H(14B)	0.9800

C(14)-H(14C)	0.9800	C(22)-H(22)	1.0000
C(15)-C(16)	1.529(7)	C(23)-H(23A)	0.9800
C(15)-H(15A)	0.9900	C(23)-H(23B)	0.9800
C(15)-H(15B)	0.9900	C(23)-H(23C)	0.9800
C(16)-C(17)	1.486(7)	C(24)-C(25)	1.520(7)
C(16)-H(16A)	0.9900	C(24)-H(24A)	0.9900
C(16)-H(16B)	0.9900	C(24)-H(24B)	0.9900
O(7)-C(19)	1.411(6)	C(25)-C(26)	1.526(7)
O(7)-H(7)	0.8400	C(25)-H(25A)	0.9900
O(8)-C(21)	1.223(6)	C(25)-H(25B)	0.9900
O(9)-C(27)	1.421(6)	C(26)-C(27)	1.547(7)
O(9)-H(9)	0.8400	C(26)-H(26A)	0.9900
O(10)-C(29)	1.223(6)	C(26)-H(26B)	0.9900
O(11)-C(34)	1.193(6)	C(27)-C(29)	1.511(7)
O(12)-C(34)	1.354(5)	C(27)-C(28)	1.527(7)
O(12)-C(18)	1.435(6)	C(28)-H(28A)	0.9800
C(18)-C(19)	1.513(7)	C(28)-H(28B)	0.9800
C(18)-H(18A)	0.9900	C(28)-H(28C)	0.9800
C(18)-H(18B)	0.9900	C(29)-C(30)	1.506(7)
C(19)-C(20)	1.519(7)	C(30)-C(32)	1.544(7)
C(19)-C(21)	1.538(7)	C(30)-C(31)	1.549(7)
C(20)-H(20A)	0.9800	C(30)-H(30)	1.0000
C(20)-H(20B)	0.9800	C(31)-H(31A)	0.9800
C(20)-H(20C)	0.9800	C(31)-H(31B)	0.9800
C(21)-C(22)	1.523(7)	C(31)-H(31C)	0.9800
C(22)-C(24)	1.534(7)	C(32)-C(33)	1.529(7)
C(22)-C(23)	1.549(7)	C(32)-H(32A)	0.9900

C(32)-H(32B)	0.9900	C(33)-H(33A)	0.9900
C(33)-C(34)	1.508(7)	C(33)-H(33B)	0.9900

C(2)-O(1)-H(1)	109.5	C(7)-C(5)-C(4)	109.8(4)
C(10)-O(3)-H(3)	109.5	C(7)-C(5)-C(6)	108.5(4)
C(17)-O(6)-C(1)	116.9(4)	C(4)-C(5)-C(6)	109.9(4)
O(6)-C(1)-C(2)	107.6(4)	C(7)-C(5)-H(5)	109.5
O(6)-C(1)-H(1A)	110.2	C(4)-C(5)-H(5)	109.5
C(2)-C(1)-H(1A)	110.2	C(6)-C(5)-H(5)	109.5
O(6)-C(1)-H(1B)	110.2	C(5)-C(6)-H(6A)	109.5
C(2)-C(1)-H(1B)	110.2	C(5)-C(6)-H(6B)	109.5
H(1A)-C(1)-H(1B)	108.5	H(6A)-C(6)-H(6B)	109.5
O(1)-C(2)-C(1)	109.1(4)	C(5)-C(6)-H(6C)	109.5
O(1)-C(2)-C(3)	106.1(4)	H(6A)-C(6)-H(6C)	109.5
C(1)-C(2)-C(3)	108.6(4)	H(6B)-C(6)-H(6C)	109.5
O(1)-C(2)-C(4)	109.5(4)	C(8)-C(7)-C(5)	118.3(4)
C(1)-C(2)-C(4)	111.1(4)	C(8)-C(7)-H(7A)	107.7
C(3)-C(2)-C(4)	112.3(4)	C(5)-C(7)-H(7A)	107.7
C(2)-C(3)-H(3A)	109.5	C(8)-C(7)-H(7B)	107.7
C(2)-C(3)-H(3B)	109.5	C(5)-C(7)-H(7B)	107.7
H(3A)-C(3)-H(3B)	109.5	H(7A)-C(7)-H(7B)	107.1
C(2)-C(3)-H(3C)	109.5	C(9)-C(8)-C(7)	113.0(5)
H(3A)-C(3)-H(3C)	109.5	C(9)-C(8)-H(8A)	109.0
H(3B)-C(3)-H(3C)	109.5	C(7)-C(8)-H(8A)	109.0
O(2)-C(4)-C(5)	120.4(5)	C(9)-C(8)-H(8B)	109.0
O(2)-C(4)-C(2)	118.3(5)	C(7)-C(8)-H(8B)	109.0
C(5)-C(4)-C(2)	121.3(5)	H(8A)-C(8)-H(8B)	107.8

C(8)-C(9)-C(10)	116.1(4)	C(13)-C(14)-H(14A)	109.5
C(8)-C(9)-H(9A)	108.3	C(13)-C(14)-H(14B)	109.5
C(10)-C(9)-H(9A)	108.3	H(14A)-C(14)-H(14B)	109.5
C(8)-C(9)-H(9B)	108.3	C(13)-C(14)-H(14C)	109.5
C(10)-C(9)-H(9B)	108.3	H(14A)-C(14)-H(14C)	109.5
H(9A)-C(9)-H(9B)	107.4	H(14B)-C(14)-H(14C)	109.5
O(3)-C(10)-C(12)	109.1(4)	C(16)-C(15)-C(13)	112.3(4)
O(3)-C(10)-C(11)	109.2(4)	C(16)-C(15)-H(15A)	109.1
C(12)-C(10)-C(11)	111.2(4)	C(13)-C(15)-H(15A)	109.1
O(3)-C(10)-C(9)	107.6(4)	C(16)-C(15)-H(15B)	109.1
C(12)-C(10)-C(9)	110.1(4)	C(13)-C(15)-H(15B)	109.1
C(11)-C(10)-C(9)	109.5(4)	H(15A)-C(15)-H(15B)	107.9
C(10)-C(11)-H(11A)	109.5	C(17)-C(16)-C(15)	112.7(4)
C(10)-C(11)-H(11B)	109.5	C(17)-C(16)-H(16A)	109.1
H(11A)-C(11)-H(11B)	109.5	C(15)-C(16)-H(16A)	109.1
C(10)-C(11)-H(11C)	109.5	C(17)-C(16)-H(16B)	109.1
H(11A)-C(11)-H(11C)	109.5	C(15)-C(16)-H(16B)	109.1
H(11B)-C(11)-H(11C)	109.5	H(16A)-C(16)-H(16B)	107.8
O(4)-C(12)-C(10)	119.2(5)	O(5)-C(17)-O(6)	121.7(5)
O(4)-C(12)-C(13)	120.8(5)	O(5)-C(17)-C(16)	125.8(5)
C(10)-C(12)-C(13)	119.9(4)	O(6)-C(17)-C(16)	112.5(4)
C(12)-C(13)-C(15)	110.0(4)	C(19)-O(7)-H(7)	109.5
C(12)-C(13)-C(14)	108.6(4)	C(27)-O(9)-H(9)	109.5
C(15)-C(13)-C(14)	111.6(4)	C(34)-O(12)-C(18)	117.0(4)
C(12)-C(13)-H(13)	108.8	O(12)-C(18)-C(19)	108.1(4)
C(15)-C(13)-H(13)	108.8	O(12)-C(18)-H(18A)	110.1
C(14)-C(13)-H(13)	108.8	C(19)-C(18)-H(18A)	110.1

O(12)-C(18)-H(18B)	110.1	C(22)-C(23)-H(23C)	109.5
C(19)-C(18)-H(18B)	110.1	H(23A)-C(23)-H(23C)	109.5
H(18A)-C(18)-H(18B)	108.4	H(23B)-C(23)-H(23C)	109.5
O(7)-C(19)-C(18)	109.4(4)	C(25)-C(24)-C(22)	118.9(4)
O(7)-C(19)-C(20)	106.3(4)	C(25)-C(24)-H(24A)	107.6
C(18)-C(19)-C(20)	109.1(4)	C(22)-C(24)-H(24A)	107.6
O(7)-C(19)-C(21)	110.0(4)	C(25)-C(24)-H(24B)	107.6
C(18)-C(19)-C(21)	108.1(4)	C(22)-C(24)-H(24B)	107.6
C(20)-C(19)-C(21)	113.9(4)	H(24A)-C(24)-H(24B)	107.0
C(19)-C(20)-H(20A)	109.5	C(24)-C(25)-C(26)	113.7(4)
C(19)-C(20)-H(20B)	109.5	C(24)-C(25)-H(25A)	108.8
H(20A)-C(20)-H(20B)	109.5	C(26)-C(25)-H(25A)	108.8
C(19)-C(20)-H(20C)	109.5	C(24)-C(25)-H(25B)	108.8
H(20A)-C(20)-H(20C)	109.5	C(26)-C(25)-H(25B)	108.8
H(20B)-C(20)-H(20C)	109.5	H(25A)-C(25)-H(25B)	107.7
O(8)-C(21)-C(22)	119.9(4)	C(25)-C(26)-C(27)	113.5(4)
O(8)-C(21)-C(19)	117.8(5)	C(25)-C(26)-H(26A)	108.9
C(22)-C(21)-C(19)	122.3(4)	C(27)-C(26)-H(26A)	108.9
C(21)-C(22)-C(24)	112.1(4)	C(25)-C(26)-H(26B)	108.9
C(21)-C(22)-C(23)	107.9(4)	C(27)-C(26)-H(26B)	108.9
C(24)-C(22)-C(23)	107.8(4)	H(26A)-C(26)-H(26B)	107.7
C(21)-C(22)-H(22)	109.7	O(9)-C(27)-C(29)	109.3(5)
C(24)-C(22)-H(22)	109.7	O(9)-C(27)-C(28)	107.7(4)
C(23)-C(22)-H(22)	109.7	C(29)-C(27)-C(28)	110.6(4)
C(22)-C(23)-H(23A)	109.5	O(9)-C(27)-C(26)	108.7(4)
C(22)-C(23)-H(23B)	109.5	C(29)-C(27)-C(26)	110.5(4)
H(23A)-C(23)-H(23B)	109.5	C(28)-C(27)-C(26)	110.0(4)

C(27)-C(28)-H(28A)	109.5	C(30)-C(31)-H(31C)	109.5
C(27)-C(28)-H(28B)	109.5	H(31A)-C(31)-H(31C)	109.5
H(28A)-C(28)-H(28B)	109.5	H(31B)-C(31)-H(31C)	109.5
C(27)-C(28)-H(28C)	109.5	C(33)-C(32)-C(30)	112.1(4)
H(28A)-C(28)-H(28C)	109.5	C(33)-C(32)-H(32A)	109.2
H(28B)-C(28)-H(28C)	109.5	C(30)-C(32)-H(32A)	109.2
O(10)-C(29)-C(30)	120.4(5)	C(33)-C(32)-H(32B)	109.2
O(10)-C(29)-C(27)	118.7(5)	C(30)-C(32)-H(32B)	109.2
C(30)-C(29)-C(27)	121.0(5)	H(32A)-C(32)-H(32B)	107.9
C(29)-C(30)-C(32)	109.8(4)	C(34)-C(33)-C(32)	114.2(4)
C(29)-C(30)-C(31)	108.5(4)	C(34)-C(33)-H(33A)	108.7
C(32)-C(30)-C(31)	110.8(4)	C(32)-C(33)-H(33A)	108.7
C(29)-C(30)-H(30)	109.3	C(34)-C(33)-H(33B)	108.7
C(32)-C(30)-H(30)	109.3	C(32)-C(33)-H(33B)	108.7
C(31)-C(30)-H(30)	109.3	H(33A)-C(33)-H(33B)	107.6
C(30)-C(31)-H(31A)	109.5	O(11)-C(34)-O(12)	123.3(5)
C(30)-C(31)-H(31B)	109.5	O(11)-C(34)-C(33)	126.3(4)
H(31A)-C(31)-H(31B)	109.5	O(12)-C(34)-C(33)	110.4(4)

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$). 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)	22(2)	25(2)	33(2)	-7(2)	7(2)	-1(2)
O(2)	24(2)	32(2)	30(2)	2(2)	13(2)	5(2)
O(3)	47(3)	35(2)	34(2)	-9(2)	17(2)	2(2)
O(4)	25(2)	34(2)	38(2)	4(2)	11(2)	11(2)
O(5)	28(2)	41(2)	32(2)	5(2)	15(2)	2(2)
O(6)	21(2)	22(2)	30(2)	3(2)	11(2)	3(2)
C(1)	27(3)	20(3)	28(3)	-2(2)	11(3)	3(2)
C(2)	25(3)	19(3)	28(3)	-5(2)	8(3)	3(2)
C(3)	36(4)	23(3)	38(3)	2(2)	15(3)	5(3)
C(4)	31(4)	17(3)	28(3)	7(2)	11(3)	3(3)
C(5)	27(3)	24(3)	28(3)	2(2)	7(3)	1(3)
C(6)	42(4)	33(3)	27(3)	1(3)	0(3)	15(3)
C(7)	46(4)	28(3)	19(3)	0(2)	3(3)	1(3)
C(8)	41(4)	25(3)	21(3)	0(2)	5(3)	-2(3)
C(9)	25(3)	35(3)	20(3)	6(2)	0(2)	-2(3)
C(10)	24(3)	28(3)	20(3)	-5(2)	11(2)	-1(3)
C(11)	30(3)	32(3)	30(3)	8(3)	8(3)	5(3)
C(12)	21(3)	19(3)	30(3)	2(2)	13(2)	1(3)
C(13)	21(3)	23(3)	19(3)	-1(2)	6(2)	2(2)
C(14)	36(4)	30(3)	20(3)	2(2)	8(3)	-1(3)
C(15)	23(3)	27(3)	27(3)	4(2)	8(3)	1(3)
C(16)	29(3)	26(3)	22(3)	2(2)	4(2)	0(3)
C(17)	25(3)	23(3)	19(3)	-7(2)	4(2)	-3(3)

O(7)	25(2)	30(2)	31(2)	3(2)	4(2)	2(2)
O(8)	25(2)	27(2)	29(2)	1(2)	10(2)	1(2)
O(9)	37(3)	36(2)	28(2)	10(2)	10(2)	-6(2)
O(10)	24(2)	41(2)	30(2)	5(2)	6(2)	-6(2)
O(11)	26(2)	42(2)	29(2)	1(2)	17(2)	2(2)
O(12)	25(2)	25(2)	28(2)	-4(2)	11(2)	-1(2)
C(18)	24(3)	25(3)	29(3)	-1(2)	12(3)	-2(3)
C(19)	20(3)	23(3)	28(3)	5(2)	6(2)	5(2)
C(20)	22(3)	23(3)	42(3)	-2(3)	10(3)	0(3)
C(21)	17(3)	18(3)	29(3)	-11(2)	8(3)	-2(2)
C(22)	17(3)	32(3)	21(3)	-4(2)	7(2)	-2(3)
C(23)	29(3)	37(3)	20(3)	-5(2)	4(2)	5(3)
C(24)	25(3)	32(3)	26(3)	-1(2)	8(2)	5(3)
C(25)	24(3)	31(3)	24(3)	6(2)	2(2)	-1(3)
C(26)	26(3)	28(3)	22(3)	0(2)	4(2)	-2(3)
C(27)	27(3)	26(3)	25(3)	11(2)	9(3)	0(3)
C(28)	27(3)	28(3)	30(3)	7(2)	8(3)	4(3)
C(29)	20(3)	21(3)	34(3)	1(2)	15(3)	2(3)
C(30)	23(3)	28(3)	21(3)	-2(2)	6(2)	0(3)
C(31)	29(3)	32(3)	28(3)	3(2)	6(3)	3(3)
C(32)	18(3)	28(3)	25(3)	-1(2)	3(2)	3(2)
C(33)	27(3)	27(3)	23(3)	2(2)	6(2)	6(3)
C(34)	25(3)	27(3)	10(2)	3(2)	-2(2)	8(3)

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

	x	y	z	U(eq)

H(1)	8990	9004	8841	42
H(3)	6934	2321	6337	57
H(1A)	6057	8812	8882	30
H(1B)	5474	8038	7942	30
H(3A)	6224	10692	8199	47
H(3B)	5482	9969	7259	47
H(3C)	6911	10710	7420	47
H(5)	5664	7644	6572	32
H(6A)	6975	8959	5540	55
H(6B)	5957	9576	6019	55
H(6C)	5369	8538	5240	55
H(7A)	6438	6573	5447	39
H(7B)	7987	7042	5977	39
H(8A)	7977	5164	6355	36
H(8B)	7776	5910	7200	36
H(9A)	5455	4921	5803	34
H(9B)	5474	5407	6775	34
H(11A)	4162	3110	6071	47
H(11B)	4380	3627	7071	47
H(11C)	4896	2325	6880	47
H(13)	6084	4870	8218	26
H(14A)	5436	2980	8514	44
H(14B)	6124	3733	9449	44
H(14C)	7000	2748	9101	44
H(15A)	8799	4433	9408	31

H(15B)	8562	5467	8739	31
H(16A)	7341	5381	10137	32
H(16B)	8599	6272	10164	32
H(7)	3722	5800	8735	44
H(9)	2134	11621	6197	50
H(18A)	402	6546	7570	31
H(18B)	827	5970	8511	31
H(20A)	1885	3746	7199	44
H(20B)	497	4480	6857	44
H(20C)	936	3994	7825	44
H(22)	767	6424	6171	28
H(23A)	2746	5104	5534	45
H(23B)	1174	5301	4946	45
H(23C)	1487	4487	5768	45
H(24A)	3188	7222	5767	34
H(24B)	1626	7469	5203	34
H(25A)	2902	9172	6091	33
H(25B)	2903	8534	6958	33
H(26A)	565	8722	6670	31
H(26B)	326	8978	5657	31
H(28A)	-328	11799	6636	42
H(28B)	-764	10520	6868	42
H(28C)	-1012	10783	5855	42
H(30)	951	9740	8053	29
H(31A)	2034	12059	8916	45
H(31B)	1143	11182	9296	45
H(31C)	435	11744	8369	45

H(32A)	3457	9265	8504	30
H(32B)	3727	10425	9190	30
H(33A)	3552	8732	9937	31
H(33B)	2294	9581	9929	31

Table 6. Torsion angles [°].

C(17)-O(6)-C(1)-C(2)	164.1(4)	C(8)-C(9)-C(10)-O(3)	-68.5(5)
O(6)-C(1)-C(2)-O(1)	-60.3(5)	C(8)-C(9)-C(10)-C(12)	50.3(6)
O(6)-C(1)-C(2)-C(3)	-175.5(4)	C(8)-C(9)-C(10)-C(11)	172.9(4)
O(6)-C(1)-C(2)-C(4)	60.6(5)	O(3)-C(10)-C(12)-O(4)	3.6(6)
O(1)-C(2)-C(4)-O(2)	3.0(6)	C(11)-C(10)-C(12)-O(4)	124.1(5)
C(1)-C(2)-C(4)-O(2)	-117.6(5)	C(9)-C(10)-C(12)-O(4)	-114.3(5)
C(3)-C(2)-C(4)-O(2)	120.6(5)	O(3)-C(10)-C(12)-C(13)	-176.8(4)
O(1)-C(2)-C(4)-C(5)	-176.8(4)	C(11)-C(10)-C(12)-C(13)	-56.3(6)
C(1)-C(2)-C(4)-C(5)	62.6(6)	C(9)-C(10)-C(12)-C(13)	65.3(6)
C(3)-C(2)-C(4)-C(5)	-59.2(6)	O(4)-C(12)-C(13)-C(15)	41.3(6)
O(2)-C(4)-C(5)-C(7)	26.7(7)	C(10)-C(12)-C(13)-C(15)	-138.3(4)
C(2)-C(4)-C(5)-C(7)	-153.5(4)	O(4)-C(12)-C(13)-C(14)	-81.2(6)
O(2)-C(4)-C(5)-C(6)	-92.7(6)	C(10)-C(12)-C(13)-C(14)	99.2(5)
C(2)-C(4)-C(5)-C(6)	87.1(6)	C(12)-C(13)-C(15)-C(16)	167.6(4)
C(4)-C(5)-C(7)-C(8)	67.9(6)	C(14)-C(13)-C(15)-C(16)	-71.8(5)
C(6)-C(5)-C(7)-C(8)	-171.9(5)	C(13)-C(15)-C(16)-C(17)	-59.5(6)
C(5)-C(7)-C(8)-C(9)	78.0(6)	C(1)-O(6)-C(17)-O(5)	5.0(7)
C(7)-C(8)-C(9)-C(10)	165.7(4)	C(1)-O(6)-C(17)-C(16)	-173.5(4)

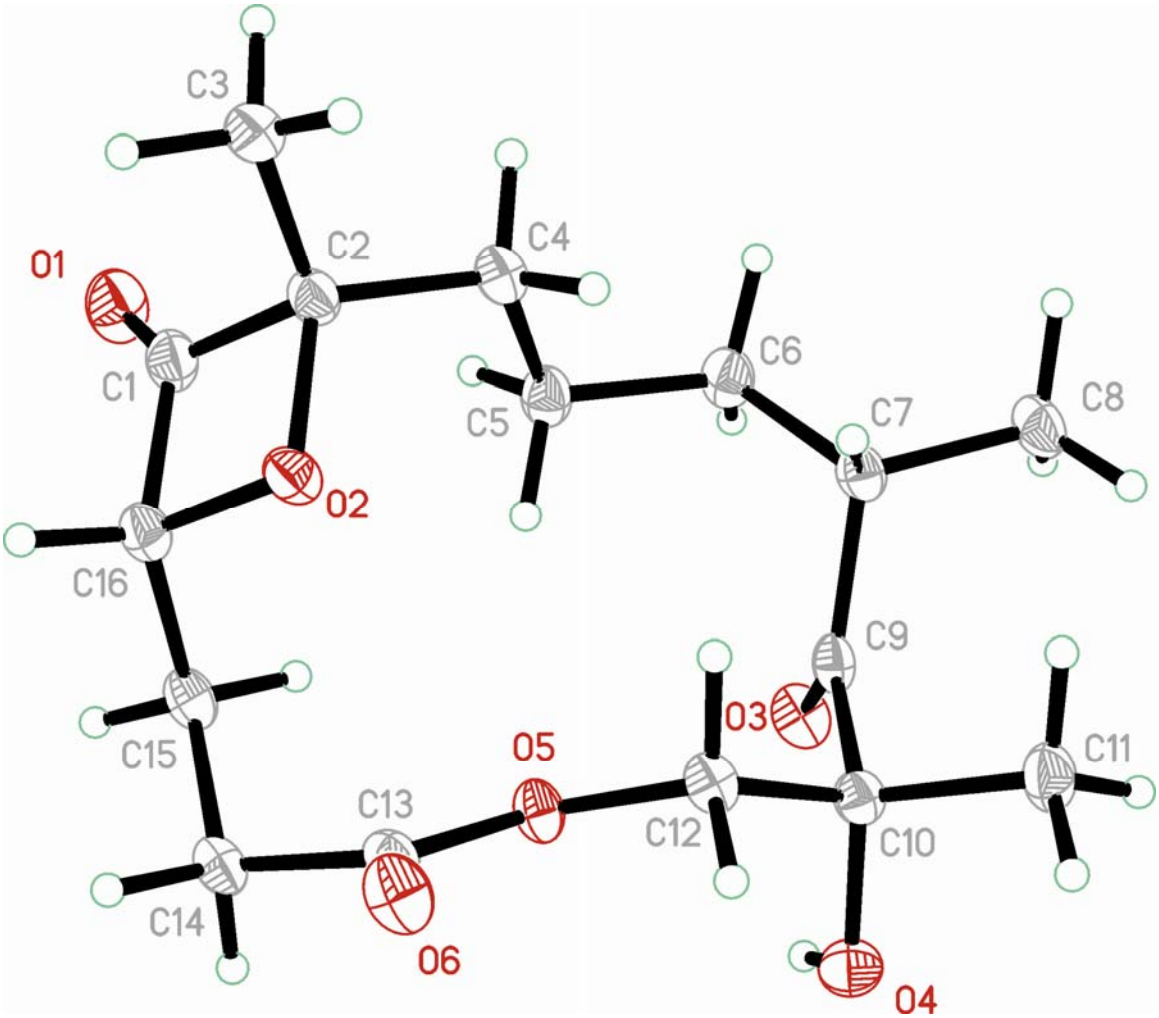
C(15)-C(16)-C(17)-O(5)	126.7(5)	C(28)-C(27)-C(29)-C(30)	56.0(6)
C(15)-C(16)-C(17)-O(6)	-54.8(6)	C(26)-C(27)-C(29)-C(30)	-66.0(6)
C(34)-O(12)-C(18)-C(19)	-151.5(4)	O(10)-C(29)-C(30)-C(32)	-46.6(6)
O(12)-C(18)-C(19)-O(7)	60.4(5)	C(27)-C(29)-C(30)-C(32)	133.1(5)
O(12)-C(18)-C(19)-C(20)	176.3(4)	O(10)-C(29)-C(30)-C(31)	74.5(6)
O(12)-C(18)-C(19)-C(21)	-59.3(5)	C(27)-C(29)-C(30)-C(31)	-105.7(5)
O(7)-C(19)-C(21)-O(8)	-9.7(6)	C(29)-C(30)-C(32)-C(33)	-164.7(4)
C(18)-C(19)-C(21)-O(8)	109.7(5)	C(31)-C(30)-C(32)-C(33)	75.5(5)
C(20)-C(19)-C(21)-O(8)	-128.9(5)	C(30)-C(32)-C(33)-C(34)	60.4(6)
O(7)-C(19)-C(21)-C(22)	168.2(4)	C(18)-O(12)-C(34)-O(11)	-2.8(7)
C(18)-C(19)-C(21)-C(22)	-72.3(6)	C(18)-O(12)-C(34)-C(33)	176.3(4)
C(20)-C(19)-C(21)-C(22)	49.1(6)	C(32)-C(33)-C(34)-O(11)	-133.8(5)
O(8)-C(21)-C(22)-C(24)	-29.6(6)	C(32)-C(33)-C(34)-O(12)	47.2(5)
C(19)-C(21)-C(22)-C(24)	152.5(4)		
O(8)-C(21)-C(22)-C(23)	88.9(5)		
C(19)-C(21)-C(22)-C(23)	-89.0(6)		
C(21)-C(22)-C(24)-C(25)	-59.0(6)		
C(23)-C(22)-C(24)-C(25)	-177.6(4)		
C(22)-C(24)-C(25)-C(26)	-70.8(6)		
C(24)-C(25)-C(26)-C(27)	-162.2(4)		
C(25)-C(26)-C(27)-O(9)	62.8(5)		
C(25)-C(26)-C(27)-C(29)	-57.2(6)		
C(25)-C(26)-C(27)-C(28)	-179.6(4)		
O(9)-C(27)-C(29)-O(10)	-5.8(6)		
C(28)-C(27)-C(29)-O(10)	-124.2(5)		
C(26)-C(27)-C(29)-O(10)	113.8(5)		
O(9)-C(27)-C(29)-C(30)	174.4(4)		

Table 7. Hydrogen bonds [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
O(1)-H(1)...O(11)#1	0.84	2.20	3.035(5)	170.6
O(7)-H(7)...O(5)	0.84	2.25	3.050(5)	159.1
O(9)-H(9)...O(10)	0.84	2.12	2.585(5)	114.6

Symmetry transformations used to generate equivalent atoms: #1 x+1,y,z

X-ray structure of **5.12**:



Crystal data

$C_{16}H_{24}O_6$	F_{000} = 672
IUPAC formula: ?	D_x = 1.306 Mg m^{-3}
M_r = 312.35	Melting point: ? K
Monoclinic, P2(1)/n	Mo Kα radiation

	λ = 0.71073 Å
Hall symbol: -P 2yn	Cell parameters from 9490 reflections
a = 10.0132 (4) Å	θ = 2.4–30.5°
b = 6.5882 (3) Å	μ = 0.10 mm^{-1}
c = 24.5750 (11) Å	T = 100 (2) K
β = 101.457 (1)°	Cell measurement pressure: ? kPa
V = 1588.88 (12) $Å^3$	Lathe, colourless
Z = 4	0.36 × 0.26 × 0.13 mm

Data collection

CCD area detector diffractometer	18133 measured reflections
Radiation source: fine-focus sealed tube	4855 independent reflections
Monochromator: graphite	4233 reflections with I > 2σ(I)
Detector resolution: ? pixels mm^{-1}	R_{int} = 0.022
T = 100(2) K	θ_{max} = 30.5°
P = ? kPa	θ_{min} = 2.1°
phi and ω scans	h = −14→14
Absorption correction: numerical Bruker SAINT	k = −9→9
T_{min} = 0.945, T_{max} = 0.967	l = −35→34

Refinement

Refinement on F^2	Hydrogen site location: inferred from neighbouring sites
Least-squares matrix: full	H-atom parameters constrained
$R[F^2 > 2\sigma(F^2)] = 0.053$	$w = 1/[\sigma^2(F_o^2) + (0.0784P)^2 + 0.3318P]$ where $P = (F_o^2 + 2F_c^2)/3$
$wR(F^2) = 0.135$	$(\Delta/\sigma)_{max} < 0.001$
$S = 1.10$	$\Delta\rho_{max} = 0.60$ e Å^{-3}
4855 reflections	$\Delta\rho_{min} = -0.20$ e Å^{-3}
203 parameters	Extinction correction: none
0 restraints	Absolute structure: ?
? constraints	Flack parameter: ?
Primary atom site location: structure-invariant direct methods	Rogers parameter: ?
Secondary atom site location: difference Fourier map	

Refinement of F^2 against ALL reflections. The weighted R-factor wR and goodness of fit S are based on F^2, conventional R-factors R are based on F, with F set to zero for negative F^2. The threshold expression of $F^2 > 2$sigma(F^2) is used only for calculating R-factors(gt) etc. and is not relevant to the choice of reflections for refinement. R-factors based on F^2 are statistically about twice as large as those based on F, and R- factors based on ALL data will be even larger.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters ($Å^2$)

	x	y	z	U_{iso}*/U_{eq}
O1	0.48950 (10)	-0.42172 (14)	0.25303 (4)	0.0295 (2)
O2	0.57859 (8)	0.03475 (12)	0.22106 (3)	0.01881 (17)
O3	0.24700 (9)	-0.01437 (13)	0.01551 (4)	0.02270 (19)
O4	0.42037 (9)	0.23928 (13)	-0.01146 (3)	0.02146 (18)
H4	0.4030	0.1166	-0.0191	0.032*
O5	0.55556 (8)	0.11560 (12)	0.09427 (3)	0.01706 (17)
O6	0.74221 (8)	0.27764 (13)	0.14007 (4)	0.02362 (19)
C1	0.52484 (11)	-0.25418 (18)	0.24359 (5)	0.0210 (2)
C2	0.46688 (11)	-0.03937 (17)	0.24665 (5)	0.0185 (2)
C3	0.47857 (12)	0.04312 (19)	0.30489 (5)	0.0228 (2)
H3A	0.5694	0.0130	0.3267	0.034*
H3B	0.4094	-0.0206	0.3224	0.034*
H3C	0.4645	0.1904	0.3033	0.034*
C4	0.32836 (11)	0.00651 (19)	0.21056 (5)	0.0217 (2)
H4A	0.3233	0.1541	0.2028	0.026*
H4B	0.2575	-0.0257	0.2322	0.026*

C5	0.29377 (11)	-0.10571 (18)	0.15543 (5)	0.0205 (2)
H5A	0.2858	-0.2526	0.1626	0.025*
H5B	0.3689	-0.0872	0.1351	0.025*
C6	0.16030 (11)	-0.03058 (18)	0.11905 (5)	0.0214 (2)
H6A	0.1253	-0.1361	0.0912	0.026*
H6B	0.0919	-0.0112	0.1427	0.026*
C7	0.17630 (10)	0.16904 (17)	0.08883 (5)	0.0181 (2)
H7	0.2217	0.2718	0.1164	0.022*
C8	0.03545 (12)	0.24956 (19)	0.05997 (5)	0.0236 (2)
H8A	0.0465	0.3797	0.0420	0.035*
H8B	-0.0218	0.2686	0.0876	0.035*
H8C	-0.0078	0.1516	0.0319	0.035*
C9	0.26320 (11)	0.13472 (16)	0.04530 (5)	0.0168 (2)
C10	0.36844 (11)	0.29376 (16)	0.03621 (5)	0.0165 (2)
C11	0.30220 (12)	0.50361 (17)	0.02607 (5)	0.0228 (2)
H11A	0.3706	0.6027	0.0198	0.034*
H11B	0.2655	0.5441	0.0586	0.034*
H11C	0.2282	0.4982	-0.0066	0.034*
C12	0.48762 (11)	0.30944 (16)	0.08574 (5)	0.0168 (2)

H12A	0.5524	0.4148	0.0785	0.020*
H12B	0.4536	0.3486	0.1194	0.020*
C13	0.68377 (10)	0.12171 (17)	0.12513 (4)	0.0169 (2)
C14	0.74444 (11)	-0.08721 (17)	0.13695 (5)	0.0184 (2)
H14A	0.8342	-0.0739	0.1623	0.022*
H14B	0.7600	-0.1468	0.1018	0.022*
C15	0.65601 (11)	-0.23335 (17)	0.16302 (5)	0.0190 (2)
H15A	0.5644	-0.2419	0.1389	0.023*
H15B	0.6971	-0.3705	0.1654	0.023*
C16	0.64228 (11)	-0.16532 (17)	0.22051 (5)	0.0186 (2)
H16	0.7307	-0.1742	0.2478	0.022*

Atomic displacement parameters ($Å^2$)

	U^{11}	U^{12}	U^{13}	U^{22}	U^{23}	U^{33}
O1	0.0257 (4)	-0.0004 (3)	0.0065 (4)	0.0220 (4)	0.0083 (4)	0.0408 (5)
O2	0.0169 (4)	0.0017 (3)	0.0066 (3)	0.0168 (4)	0.0004 (3)	0.0239 (4)
O3	0.0201 (4)	-0.0020 (3)	0.0018 (3)	0.0187 (4)	-0.0056 (3)	0.0280 (4)
O4	0.0233 (4)	-0.0015 (3)	0.0051 (3)	0.0228 (4)	-0.0028 (3)	0.0187 (4)
O5	0.0135 (3)	-0.0004 (3)	-0.0006 (3)	0.0144 (4)	-0.0015 (3)	0.0216 (4)
O6	0.0174 (4)	-0.0038 (3)	-0.0001 (3)	0.0205 (4)	-0.0043 (3)	0.0309 (5)

C1	0.0166 (5)	0.0014 (4)	0.0020 (4)	0.0221 (5)	0.0030 (4)	0.0234 (5)
C2	0.0143 (5)	0.0010 (4)	0.0045 (4)	0.0195 (5)	0.0028 (4)	0.0220 (5)
C3	0.0178 (5)	0.0036 (4)	0.0047 (4)	0.0296 (6)	0.0017 (4)	0.0213 (5)
C4	0.0158 (5)	0.0038 (4)	0.0026 (4)	0.0257 (6)	0.0018 (4)	0.0231 (5)
C5	0.0159 (5)	-0.0007 (4)	0.0013 (4)	0.0203 (5)	0.0030 (4)	0.0241 (5)
C6	0.0140 (5)	-0.0030 (4)	0.0004 (4)	0.0234 (6)	0.0037 (4)	0.0255 (6)
C7	0.0126 (4)	-0.0005 (4)	0.0006 (4)	0.0193 (5)	-0.0002 (4)	0.0213 (5)
C8	0.0144 (5)	0.0042 (4)	0.0005 (4)	0.0282 (6)	-0.0002 (5)	0.0267 (6)
C9	0.0133 (4)	0.0014 (4)	-0.0016 (4)	0.0156 (5)	0.0015 (4)	0.0193 (5)
C10	0.0158 (4)	0.0000 (4)	0.0026 (4)	0.0147 (5)	-0.0004 (4)	0.0185 (5)
C11	0.0209 (5)	0.0026 (4)	0.0038 (4)	0.0167 (5)	0.0042 (4)	0.0301 (6)
C12	0.0155 (4)	-0.0006 (4)	0.0018 (4)	0.0137 (4)	-0.0026 (4)	0.0205 (5)
C13	0.0132 (4)	-0.0009 (4)	0.0024 (4)	0.0204 (5)	-0.0020 (4)	0.0168 (5)
C14	0.0137 (4)	0.0017 (4)	0.0016 (4)	0.0201 (5)	-0.0031 (4)	0.0205 (5)
C15	0.0159 (5)	0.0013 (4)	0.0023 (4)	0.0160 (5)	-0.0029 (4)	0.0245 (5)
C16	0.0162 (5)	0.0021 (4)	0.0033 (4)	0.0161 (5)	0.0014 (4)	0.0231 (5)

Geometric parameters (Å, °)

O1—C1	1.1958 (15)	C6—H6B	0.9900
O2—C16	1.4654 (13)	C7—C9	1.5240 (16)
O2—C2	1.4713 (13)	C7—C8	1.5415 (15)
O3—C9	1.2165 (14)	C7—H7	1.0000
O4—C10	1.4190 (13)	C8—H8A	0.9800
O4—H4	0.8400	C8—H8B	0.9800
O5—C13	1.3558 (13)	C8—H8C	0.9800
O5—C12	1.4426 (13)	C9—C10	1.5336 (15)
O6—C13	1.2030 (14)	C10—C12	1.5295 (15)
C1—C16	1.5205 (16)	C10—C11	1.5323 (15)
C1—C2	1.5371 (16)	C11—H11A	0.9800
C2—C3	1.5136 (16)	C11—H11B	0.9800
C2—C4	1.5209 (15)	C11—H11C	0.9800
C3—H3A	0.9800	C12—H12A	0.9900
C3—H3B	0.9800	C12—H12B	0.9900
C3—H3C	0.9800	C13—C14	1.5092 (15)
C4—C5	1.5218 (17)	C14—C15	1.5319 (16)
C4—H4A	0.9900	C14—H14A	0.9900
C4—H4B	0.9900	C14—H14B	0.9900

C5—C6	1.5348 (15)	C15—C16	1.5145 (16)
C5—H5A	0.9900	C15—H15A	0.9900
C5—H5B	0.9900	C15—H15B	0.9900
C6—C7	1.5343 (16)	C16—H16	1.0000
C6—H6A	0.9900		

C16—O2—C2	94.27 (8)	C7—C8—H8C	109.5
C10—O4—H4	109.5	H8A—C8—H8C	109.5
C13—O5—C12	114.95 (8)	H8B—C8—H8C	109.5
O1—C1—C16	135.10 (11)	O3—C9—C7	121.05 (10)
O1—C1—C2	135.33 (11)	O3—C9—C10	118.52 (10)
C16—C1—C2	89.50 (8)	C7—C9—C10	120.37 (9)
O2—C2—C3	111.25 (9)	O4—C10—C12	108.55 (9)
O2—C2—C4	111.56 (9)	O4—C10—C11	108.16 (9)
C3—C2—C4	111.73 (9)	C12—C10—C11	108.22 (9)
O2—C2—C1	87.60 (8)	O4—C10—C9	108.82 (9)
C3—C2—C1	114.70 (10)	C12—C10—C9	112.35 (9)
C4—C2—C1	117.64 (10)	C11—C10—C9	110.63 (9)
C2—C3—H3A	109.5	C10—C11—H11A	109.5

C2—C3—H3B	109.5	C10—C11—H11B	109.5
H3A—C3—H3B	109.5	H11A—C11—H11B	109.5
C2—C3—H3C	109.5	C10—C11—H11C	109.5
H3A—C3—H3C	109.5	H11A—C11—H11C	109.5
H3B—C3—H3C	109.5	H11B—C11—H11C	109.5
C2—C4—C5	116.27 (10)	O5—C12—C10	109.07 (8)
C2—C4—H4A	108.2	O5—C12—H12A	109.9
C5—C4—H4A	108.2	C10—C12—H12A	109.9
C2—C4—H4B	108.2	O5—C12—H12B	109.9
C5—C4—H4B	108.2	C10—C12—H12B	109.9
H4A—C4—H4B	107.4	H12A—C12—H12B	108.3
C4—C5—C6	112.32 (10)	O6—C13—O5	123.04 (10)
C4—C5—H5A	109.1	O6—C13—C14	124.56 (10)
C6—C5—H5A	109.1	O5—C13—C14	112.38 (9)
C4—C5—H5B	109.1	C13—C14—C15	114.18 (9)
C6—C5—H5B	109.1	C13—C14—H14A	108.7
H5A—C5—H5B	107.9	C15—C14—H14A	108.7

C7—C6—C5	113.31 (9)	C13—C14—H14B	108.7
C7—C6—H6A	108.9	C15—C14—H14B	108.7
C5—C6—H6A	108.9	H14A—C14—H14B	107.6
C7—C6—H6B	108.9	C16—C15—C14	111.80 (9)
C5—C6—H6B	108.9	C16—C15—H15A	109.3
H6A—C6—H6B	107.7	C14—C15—H15A	109.3
C9—C7—C6	109.98 (9)	C16—C15—H15B	109.3
C9—C7—C8	109.02 (9)	C14—C15—H15B	109.3
C6—C7—C8	110.10 (9)	H15A—C15—H15B	107.9
C9—C7—H7	109.2	O2—C16—C15	113.27 (9)
C6—C7—H7	109.2	O2—C16—C1	88.44 (8)
C8—C7—H7	109.2	C15—C16—C1	117.02 (10)
C7—C8—H8A	109.5	O2—C16—H16	112.0
C7—C8—H8B	109.5	C15—C16—H16	112.0
H8A—C8—H8B	109.5	C1—C16—H16	112.0
C16—O2—C2—C3	112.29 (10)	O3—C9—C10—C12	−114.86 (11)

C16—O2—C2—C4	−122.20 (10)	C7—C9—C10—C12	68.15 (12)
C16—O2—C2—C1	−3.34 (8)	O3—C9—C10—C11	124.08 (11)
O1—C1—C2—O2	−173.94 (15)	C7—C9—C10—C11	−52.92 (13)
C16—C1—C2—O2	3.21 (8)	C13—O5—C12—C10	161.32 (9)
O1—C1—C2—C3	73.72 (18)	O4—C10—C12—O5	−60.04 (11)
C16—C1—C2—C3	−109.13 (10)	C11—C10—C12—O5	−177.20 (9)
O1—C1—C2—C4	−60.78 (19)	C9—C10—C12—O5	60.35 (11)
C16—C1—C2—C4	116.36 (10)	C12—O5—C13—O6	−6.71 (15)
O2—C2—C4—C5	67.13 (13)	C12—O5—C13—C14	174.76 (8)
C3—C2—C4—C5	−167.62 (10)	O6—C13—C14—C15	128.06 (12)
C1—C2—C4—C5	−31.85 (14)	O5—C13—C14—C15	−53.44 (12)
C2—C4—C5—C6	−173.03 (9)	C13—C14—C15—C16	−65.58 (12)
C4—C5—C6—C7	78.94 (12)	C2—O2—C16—C15	122.25 (10)

C5—C6—C7—C9	67.76 (12)	C2—O2—C16—C1	3.37 (9)
C5—C6—C7—C8	−172.10 (10)	C14—C15—C16—O2	60.55 (12)
C6—C7—C9—O3	42.74 (14)	C14—C15—C16—C1	161.26 (9)
C8—C7—C9—O3	−78.06 (13)	O1—C1—C16—O2	173.94 (15)
C6—C7—C9—C10	−140.34 (9)	C2—C1—C16—O2	−3.22 (8)
C8—C7—C9—C10	98.85 (11)	O1—C1—C16—C15	58.49 (19)
O3—C9—C10—O4	5.38 (13)	C2—C1—C16—C15	−118.66 (10)
C7—C9—C10—O4	−171.61 (9)		

Hydrogen-bond geometry (Å, °)

D—H···A	D—H	H···A	D···A	D—H···A
C11—H11A···O4^{i}	0.98	2.38	3.3334 (15)	163
C3—H3A···O6^{ii}	0.98	2.45	3.3472 (14)	152
O4—H4···O5^{iii}	0.84	2.50	3.1402 (12)	134

C15—H15B···O6^{iv}	0.99	2.46	3.4111 (14)	160
O4—H4···O3	0.84	2.11	2.5890 (12)	116
C12—H12A···O6	0.99	2.36	2.6407 (14)	95

Symmetry codes: (i) -x+1, -y+1, -z; (ii) -x+3/2, y-1/2, -z+1/2; (iii) -x+1, -y, -z; (iv) x, y-1, z.

All esds (except the esd in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell esds are taken into account individually in the estimation of esds in distances, angles and torsion angles; correlations between esds in cell parameters are only used

X-ray structure of **5.16**:

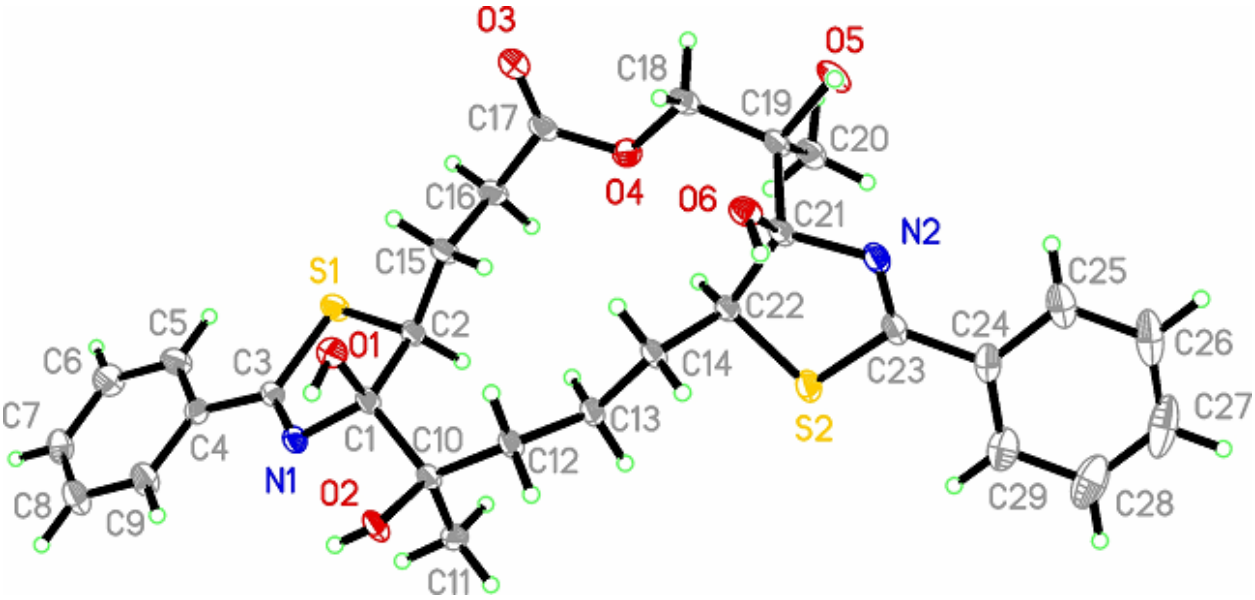


Table 1. Crystal data and structure refinement

Empirical formula	C29 H34 N2 O6 S2	
Formula weight	570.70	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	C2/c	
Unit cell dimensions	a = 22.0931(18) Å	α= 90°.
	b = 12.2588(10) Å	β= 95.794(2)°.
	c = 20.4161(16) Å	γ= 90°.
Volume	5501.1(8) $Å^3$	
Z	8	
Density (calculated)	1.378 Mg/m^3	
Absorption coefficient	0.240 mm^{-1}	
F(000)	2416	
Crystal size	0.21 x 0.09 x 0.04 mm^3	
Theta range for data collection	1.85 to 30.53°.	
Index ranges	-31<=h<=31, -17<=k<=17, -29<=l<=29	
Reflections collected	33027	
Independent reflections	8418 [R(int) = 0.0519]	
Completeness to theta = 30.53°	100.0 %	
Absorption correction	Semi-empirical from equivalents	

Max. and min. transmission	0.9904 and 0.9513
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	8418 / 0 / 366
Goodness-of-fit on F^2	1.013
Final R indices [I>2sigma(I)]	R1 = 0.0550, wR2 = 0.1257
R indices (all data)	R1 = 0.0805, wR2 = 0.1379
Largest diff. peak and hole	0.528 and -0.275 e.$Å^{-3}$

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

	x	y	z	U(eq)
S(1)	10277(1)	6389(1)	1627(1)	20(1)
S(2)	8613(1)	10078(1)	-1117(1)	22(1)
N(1)	9494(1)	4900(1)	1156(1)	17(1)
N(2)	7974(1)	11611(1)	-611(1)	20(1)
O(1)	8752(1)	6023(1)	1522(1)	20(1)
O(2)	8335(1)	5005(1)	409(1)	19(1)
O(3)	9233(1)	10098(1)	2149(1)	27(1)
O(4)	9241(1)	10421(1)	1066(1)	22(1)
O(5)	8301(1)	12751(1)	548(1)	23(1)
O(6)	7728(1)	10737(1)	348(1)	20(1)
C(1)	9160(1)	5927(1)	1031(1)	16(1)
C(2)	9610(1)	6904(1)	1128(1)	17(1)

C(3)	10013(1)	5040(1)	1487(1)	16(1)
C(4)	10399(1)	4135(1)	1759(1)	17(1)
C(5)	10955(1)	4323(2)	2127(1)	25(1)
C(6)	11305(1)	3452(2)	2372(1)	27(1)
C(7)	11110(1)	2394(2)	2250(1)	24(1)
C(8)	10552(1)	2203(2)	1894(1)	27(1)
C(9)	10200(1)	3068(2)	1655(1)	25(1)
C(10)	8784(1)	5850(1)	339(1)	16(1)
C(11)	9175(1)	5540(2)	-201(1)	20(1)
C(12)	8389(1)	6864(1)	162(1)	17(1)
C(13)	8680(1)	7869(1)	-131(1)	18(1)
C(14)	8279(1)	8873(1)	-56(1)	18(1)
C(15)	9350(1)	7896(1)	1452(1)	18(1)
C(16)	9781(1)	8887(1)	1491(1)	20(1)
C(17)	9405(1)	9865(1)	1628(1)	19(1)
C(18)	8807(1)	11298(1)	1108(1)	20(1)
C(19)	8631(1)	11784(1)	423(1)	19(1)
C(20)	9184(1)	12162(2)	92(1)	23(1)
C(21)	8212(1)	11001(1)	-26(1)	18(1)
C(22)	8565(1)	9951(1)	-236(1)	16(1)
C(23)	8154(1)	11259(1)	-1143(1)	19(1)
C(24)	8001(1)	11807(2)	-1787(1)	24(1)
C(25)	7798(1)	12893(2)	-1794(1)	31(1)
C(26)	7639(1)	13402(2)	-2397(1)	41(1)
C(27)	7664(1)	12837(2)	-2977(1)	46(1)
C(28)	7875(1)	11772(2)	-2974(1)	43(1)
C(29)	8056(1)	11266(2)	-2374(1)	30(1)

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

S(1)-C(3)	1.7678(17)	C(3)-C(4)	1.473(2)
S(1)-C(2)	1.8193(17)	C(4)-C(9)	1.389(2)
S(2)-C(23)	1.7652(18)	C(4)-C(5)	1.393(2)
S(2)-C(22)	1.8187(18)	C(5)-C(6)	1.382(3)
N(1)-C(3)	1.282(2)	C(5)-H(5A)	0.9500
N(1)-C(1)	1.468(2)	C(6)-C(7)	1.381(3)
N(2)-C(23)	1.269(2)	C(6)-H(6A)	0.9500
N(2)-C(21)	1.462(2)	C(7)-C(8)	1.387(3)
O(1)-C(1)	1.420(2)	C(7)-H(7)	0.9500
O(1)-H(1)	0.81(2)	C(8)-C(9)	1.375(3)
O(2)-C(10)	1.450(2)	C(8)-H(8)	0.9500
O(2)-H(2)	0.74(2)	C(9)-H(9)	0.9500
O(3)-C(17)	1.199(2)	C(10)-C(11)	1.516(2)
O(4)-C(17)	1.352(2)	C(10)-C(12)	1.540(2)
O(4)-C(18)	1.448(2)	C(11)-H(11A)	0.9800
O(5)-C(19)	1.428(2)	C(11)-H(11B)	0.9800
O(5)-H(5)	0.75(3)	C(11)-H(11C)	0.9800
O(6)-C(21)	1.411(2)	C(12)-C(13)	1.539(2)
O(6)-H(6)	0.82(2)	C(12)-H(12A)	0.9900
C(1)-C(2)	1.556(2)	C(12)-H(12B)	0.9900
C(1)-C(10)	1.568(2)	C(13)-C(14)	1.534(2)
C(2)-C(15)	1.523(2)	C(13)-H(13A)	0.9900
C(2)-H(2A)	1.0000	C(13)-H(13B)	0.9900

C(14)-C(22)	1.526(2)	C(20)-H(20C)	0.9800
C(14)-H(14A)	0.9900	C(21)-C(22)	1.587(2)
C(14)-H(14B)	0.9900	C(22)-H(22)	1.0000
C(15)-C(16)	1.541(2)	C(23)-C(24)	1.486(3)
C(15)-H(15A)	0.9900	C(24)-C(29)	1.385(3)
C(15)-H(15B)	0.9900	C(24)-C(25)	1.404(3)
C(16)-C(17)	1.501(2)	C(25)-C(26)	1.394(3)
C(16)-H(16A)	0.9900	C(25)-H(25)	0.9500
C(16)-H(16B)	0.9900	C(26)-C(27)	1.377(4)
C(18)-C(19)	1.535(3)	C(26)-H(26)	0.9500
C(18)-H(18A)	0.9900	C(27)-C(28)	1.387(4)
C(18)-H(18B)	0.9900	C(27)-H(27)	0.9500
C(19)-C(20)	1.526(3)	C(28)-C(29)	1.395(3)
C(19)-C(21)	1.563(2)	C(28)-H(28)	0.9500
C(20)-H(20A)	0.9800	C(29)-H(29)	0.9500
C(20)-H(20B)	0.9800		

C(3)-S(1)-C(2)	89.89(8)	O(1)-C(1)-C(2)	106.82(13)
C(23)-S(2)-C(22)	90.56(8)	N(1)-C(1)-C(2)	109.54(13)
C(3)-N(1)-C(1)	112.60(14)	O(1)-C(1)-C(10)	108.94(13)
C(23)-N(2)-C(21)	114.09(15)	N(1)-C(1)-C(10)	108.46(13)
C(1)-O(1)-H(1)	102.7(17)	C(2)-C(1)-C(10)	115.75(13)
C(10)-O(2)-H(2)	111.1(19)	C(15)-C(2)-C(1)	113.93(14)
C(17)-O(4)-C(18)	116.44(14)	C(15)-C(2)-S(1)	110.70(12)
C(19)-O(5)-H(5)	112(2)	C(1)-C(2)-S(1)	105.97(11)
C(21)-O(6)-H(6)	109.5(17)	C(15)-C(2)-H(2A)	108.7
O(1)-C(1)-N(1)	106.99(13)	C(1)-C(2)-H(2A)	108.7

S(1)-C(2)-H(2A)	108.7	C(12)-C(10)-C(1)	113.53(13)
N(1)-C(3)-C(4)	123.45(15)	C(10)-C(11)-H(11A)	109.5
N(1)-C(3)-S(1)	118.26(13)	C(10)-C(11)-H(11B)	109.5
C(4)-C(3)-S(1)	118.28(13)	H(11A)-C(11)-H(11B)	109.5
C(9)-C(4)-C(5)	119.03(16)	C(10)-C(11)-H(11C)	109.5
C(9)-C(4)-C(3)	119.34(15)	H(11A)-C(11)-H(11C)	109.5
C(5)-C(4)-C(3)	121.63(16)	H(11B)-C(11)-H(11C)	109.5
C(6)-C(5)-C(4)	119.85(17)	C(13)-C(12)-C(10)	119.19(14)
C(6)-C(5)-H(5A)	120.1	C(13)-C(12)-H(12A)	107.5
C(4)-C(5)-H(5A)	120.1	C(10)-C(12)-H(12A)	107.5
C(7)-C(6)-C(5)	120.54(17)	C(13)-C(12)-H(12B)	107.5
C(7)-C(6)-H(6A)	119.7	C(10)-C(12)-H(12B)	107.5
C(5)-C(6)-H(6A)	119.7	H(12A)-C(12)-H(12B)	107.0
C(6)-C(7)-C(8)	119.83(17)	C(14)-C(13)-C(12)	109.58(14)
C(6)-C(7)-H(7)	120.1	C(14)-C(13)-H(13A)	109.8
C(8)-C(7)-H(7)	120.1	C(12)-C(13)-H(13A)	109.8
C(9)-C(8)-C(7)	119.72(18)	C(14)-C(13)-H(13B)	109.8
C(9)-C(8)-H(8)	120.1	C(12)-C(13)-H(13B)	109.8
C(7)-C(8)-H(8)	120.1	H(13A)-C(13)-H(13B)	108.2
C(8)-C(9)-C(4)	120.99(17)	C(22)-C(14)-C(13)	114.40(14)
C(8)-C(9)-H(9)	119.5	C(22)-C(14)-H(14A)	108.7
C(4)-C(9)-H(9)	119.5	C(13)-C(14)-H(14A)	108.7
O(2)-C(10)-C(11)	109.70(14)	C(22)-C(14)-H(14B)	108.7
O(2)-C(10)-C(12)	102.93(13)	C(13)-C(14)-H(14B)	108.7
C(11)-C(10)-C(12)	112.49(14)	H(14A)-C(14)-H(14B)	107.6
O(2)-C(10)-C(1)	105.01(13)	C(2)-C(15)-C(16)	113.18(15)
C(11)-C(10)-C(1)	112.39(14)	C(2)-C(15)-H(15A)	108.9

C(16)-C(15)-H(15A)	108.9	H(20A)-C(20)-H(20B)	109.5
C(2)-C(15)-H(15B)	108.9	C(19)-C(20)-H(20C)	109.5
C(16)-C(15)-H(15B)	108.9	H(20A)-C(20)-H(20C)	109.5
H(15A)-C(15)-H(15B)	107.8	H(20B)-C(20)-H(20C)	109.5
C(17)-C(16)-C(15)	106.74(14)	O(6)-C(21)-N(2)	109.26(14)
C(17)-C(16)-H(16A)	110.4	O(6)-C(21)-C(19)	105.09(14)
C(15)-C(16)-H(16A)	110.4	N(2)-C(21)-C(19)	107.94(13)
C(17)-C(16)-H(16B)	110.4	O(6)-C(21)-C(22)	112.36(13)
C(15)-C(16)-H(16B)	110.4	N(2)-C(21)-C(22)	109.83(14)
H(16A)-C(16)-H(16B)	108.6	C(19)-C(21)-C(22)	112.16(13)
O(3)-C(17)-O(4)	123.43(16)	C(14)-C(22)-C(21)	114.19(14)
O(3)-C(17)-C(16)	125.92(17)	C(14)-C(22)-S(2)	112.23(12)
O(4)-C(17)-C(16)	110.48(15)	C(21)-C(22)-S(2)	106.11(11)
O(4)-C(18)-C(19)	110.02(14)	C(14)-C(22)-H(22)	108.0
O(4)-C(18)-H(18A)	109.7	C(21)-C(22)-H(22)	108.0
C(19)-C(18)-H(18A)	109.7	S(2)-C(22)-H(22)	108.0
O(4)-C(18)-H(18B)	109.7	N(2)-C(23)-C(24)	122.73(16)
C(19)-C(18)-H(18B)	109.7	N(2)-C(23)-S(2)	118.80(14)
H(18A)-C(18)-H(18B)	108.2	C(24)-C(23)-S(2)	118.47(14)
O(5)-C(19)-C(20)	105.83(14)	C(29)-C(24)-C(25)	120.14(18)
O(5)-C(19)-C(18)	104.28(14)	C(29)-C(24)-C(23)	121.12(18)
C(20)-C(19)-C(18)	112.35(15)	C(25)-C(24)-C(23)	118.74(19)
O(5)-C(19)-C(21)	109.31(14)	C(26)-C(25)-C(24)	119.0(2)
C(20)-C(19)-C(21)	112.40(15)	C(26)-C(25)-H(25)	120.5
C(18)-C(19)-C(21)	112.11(14)	C(24)-C(25)-H(25)	120.5
C(19)-C(20)-H(20A)	109.5	C(27)-C(26)-C(25)	120.4(2)
C(19)-C(20)-H(20B)	109.5	C(27)-C(26)-H(26)	119.8

C(25)-C(26)-H(26)	119.8	C(27)-C(28)-H(28)	120.4
C(26)-C(27)-C(28)	120.8(2)	C(29)-C(28)-H(28)	120.4
C(26)-C(27)-H(27)	119.6	C(24)-C(29)-C(28)	120.2(2)
C(28)-C(27)-H(27)	119.6	C(24)-C(29)-H(29)	119.9
C(27)-C(28)-C(29)	119.3(2)	C(28)-C(29)-H(29)	119.9

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$). 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)	19(1)	15(1)	25(1)	-2(1)	-5(1)	1(1)
S(2)	27(1)	17(1)	22(1)	3(1)	3(1)	5(1)
N(1)	19(1)	13(1)	19(1)	1(1)	-1(1)	3(1)
N(2)	21(1)	14(1)	25(1)	1(1)	-4(1)	2(1)
O(1)	20(1)	20(1)	21(1)	0(1)	3(1)	-1(1)
O(2)	18(1)	10(1)	29(1)	2(1)	-4(1)	0(1)
O(3)	38(1)	18(1)	25(1)	-1(1)	3(1)	4(1)
O(4)	22(1)	21(1)	21(1)	-2(1)	-3(1)	7(1)
O(5)	21(1)	12(1)	36(1)	-4(1)	-1(1)	1(1)
O(6)	16(1)	17(1)	25(1)	-4(1)	-1(1)	-1(1)
C(1)	16(1)	12(1)	19(1)	0(1)	1(1)	2(1)
C(2)	18(1)	12(1)	19(1)	-1(1)	-2(1)	1(1)
C(3)	19(1)	14(1)	17(1)	0(1)	1(1)	2(1)

C(4)	18(1)	16(1)	16(1)	1(1)	1(1)	3(1)
C(5)	25(1)	19(1)	29(1)	-3(1)	-5(1)	2(1)
C(6)	21(1)	27(1)	31(1)	1(1)	-8(1)	3(1)
C(7)	21(1)	22(1)	29(1)	7(1)	1(1)	6(1)
C(8)	25(1)	18(1)	38(1)	7(1)	-3(1)	-1(1)
C(9)	20(1)	20(1)	32(1)	5(1)	-6(1)	-1(1)
C(10)	16(1)	11(1)	20(1)	1(1)	-1(1)	-1(1)
C(11)	23(1)	18(1)	17(1)	-2(1)	-1(1)	4(1)
C(12)	15(1)	12(1)	22(1)	1(1)	-1(1)	1(1)
C(13)	20(1)	13(1)	21(1)	2(1)	1(1)	2(1)
C(14)	19(1)	11(1)	23(1)	1(1)	1(1)	2(1)
C(15)	19(1)	13(1)	22(1)	-3(1)	0(1)	1(1)
C(16)	19(1)	15(1)	24(1)	-4(1)	-4(1)	0(1)
C(17)	18(1)	12(1)	24(1)	-4(1)	-4(1)	-4(1)
C(18)	18(1)	16(1)	25(1)	-5(1)	-2(1)	3(1)
C(19)	19(1)	11(1)	25(1)	-2(1)	-2(1)	1(1)
C(20)	23(1)	16(1)	29(1)	0(1)	1(1)	-3(1)
C(21)	18(1)	11(1)	23(1)	-1(1)	-2(1)	1(1)
C(22)	16(1)	12(1)	19(1)	-1(1)	-2(1)	1(1)
C(23)	17(1)	14(1)	27(1)	3(1)	-2(1)	0(1)
C(24)	18(1)	24(1)	29(1)	11(1)	-1(1)	-1(1)
C(25)	24(1)	25(1)	44(1)	12(1)	-1(1)	0(1)
C(26)	26(1)	37(1)	59(2)	29(1)	0(1)	1(1)
C(27)	25(1)	69(2)	44(1)	37(1)	3(1)	2(1)
C(28)	29(1)	69(2)	31(1)	19(1)	6(1)	1(1)
C(29)	23(1)	38(1)	29(1)	10(1)	3(1)	2(1)

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

	x	y	z	U(eq)
H(1)	8512(11)	5530(20)	1430(12)	30
H(2)	8484(11)	4470(20)	492(12)	29
H(5)	7969(12)	12630(20)	578(12)	35
H(6)	7445(11)	10488(19)	106(12)	29
H(2A)	9732	7125	688	20
H(5A)	11094	5049	2209	29
H(6A)	11682	3581	2626	33
H(7)	11358	1799	2411	29
H(8)	10413	1476	1814	33
H(9)	9816	2934	1416	29
H(11A)	9372	4837	-95	30
H(11B)	9485	6101	-237	30
H(11C)	8919	5480	-621	30
H(12A)	8044	6631	-155	20
H(12B)	8214	7102	567	20
H(13A)	9090	7994	100	22
H(13B)	8725	7742	-603	22
H(14A)	7891	8776	-338	22
H(14B)	8181	8915	406	22
H(15A)	9262	7697	1903	22
H(15B)	8961	8103	1200	22
H(16A)	10114	8785	1847	24

H(16B)	9962	8981	1070	24
H(18A)	8988	11872	1408	24
H(18B)	8439	11015	1291	24
H(20A)	9051	12433	-351	34
H(20B)	9464	11549	62	34
H(20C)	9391	12748	354	34
H(22)	8988	9979	-10	19
H(25)	7769	13274	-1393	38
H(26)	7512	14143	-2408	49
H(27)	7534	13181	-3384	55
H(28)	7897	11391	-3376	51
H(29)	8218	10547	-2367	36

Table 6. Torsion angles [°].

C(3)-N(1)-C(1)-O(1)	-96.68(17)	C(1)-N(1)-C(3)-S(1)	-8.7(2)
C(3)-N(1)-C(1)-C(2)	18.8(2)	C(2)-S(1)-C(3)-N(1)	-3.38(15)
C(3)-N(1)-C(1)-C(10)	145.94(15)	C(2)-S(1)-C(3)-C(4)	177.02(14)
O(1)-C(1)-C(2)-C(15)	-26.33(18)	N(1)-C(3)-C(4)-C(9)	0.4(3)
N(1)-C(1)-C(2)-C(15)	-141.87(15)	S(1)-C(3)-C(4)-C(9)	179.99(14)
C(10)-C(1)-C(2)-C(15)	95.16(18)	N(1)-C(3)-C(4)-C(5)	-178.76(18)
O(1)-C(1)-C(2)-S(1)	95.63(13)	S(1)-C(3)-C(4)-C(5)	0.8(2)
N(1)-C(1)-C(2)-S(1)	-19.92(16)	C(9)-C(4)-C(5)-C(6)	1.1(3)
C(10)-C(1)-C(2)-S(1)	-142.88(12)	C(3)-C(4)-C(5)-C(6)	-179.74(18)
C(3)-S(1)-C(2)-C(15)	137.06(13)	C(4)-C(5)-C(6)-C(7)	0.6(3)
C(3)-S(1)-C(2)-C(1)	13.06(12)	C(5)-C(6)-C(7)-C(8)	-1.6(3)
C(1)-N(1)-C(3)-C(4)	170.87(15)	C(6)-C(7)-C(8)-C(9)	0.9(3)

C(7)-C(8)-C(9)-C(4)	0.8(3)	O(4)-C(18)-C(19)-C(21)	72.42(18)
C(5)-C(4)-C(9)-C(8)	-1.8(3)	C(23)-N(2)-C(21)-O(6)	-131.36(16)
C(3)-C(4)-C(9)-C(8)	178.98(18)	C(23)-N(2)-C(21)-C(19)	114.87(17)
O(1)-C(1)-C(10)-O(2)	-50.34(16)	C(23)-N(2)-C(21)-C(22)	-7.7(2)
N(1)-C(1)-C(10)-O(2)	65.78(16)	O(5)-C(19)-C(21)-O(6)	-62.51(17)
C(2)-C(1)-C(10)-O(2)	-170.69(13)	C(20)-C(19)-C(21)-O(6)	-179.70(13)
O(1)-C(1)-C(10)-C(11)	-169.55(13)	C(18)-C(19)-C(21)-O(6)	52.61(17)
N(1)-C(1)-C(10)-C(11)	-53.43(18)	O(5)-C(19)-C(21)-N(2)	54.01(19)
C(2)-C(1)-C(10)-C(11)	70.10(18)	C(20)-C(19)-C(21)-N(2)	-63.19(18)
O(1)-C(1)-C(10)-C(12)	61.34(17)	C(18)-C(19)-C(21)-N(2)	169.13(14)
N(1)-C(1)-C(10)-C(12)	177.46(14)	O(5)-C(19)-C(21)-C(22)	175.13(14)
C(2)-C(1)-C(10)-C(12)	-59.00(19)	C(20)-C(19)-C(21)-C(22)	57.93(19)
O(2)-C(10)-C(12)-C(13)	-164.06(15)	C(18)-C(19)-C(21)-C(22)	-69.75(19)
C(11)-C(10)-C(12)-C(13)	-46.1(2)	C(13)-C(14)-C(22)-C(21)	-168.44(14)
C(1)-C(10)-C(12)-C(13)	83.00(19)	C(13)-C(14)-C(22)-S(2)	70.75(17)
C(10)-C(12)-C(13)-C(14)	-161.55(15)	O(6)-C(21)-C(22)-C(14)	5.8(2)
C(12)-C(13)-C(14)-C(22)	171.42(14)	N(2)-C(21)-C(22)-C(14)	-116.04(16)
C(1)-C(2)-C(15)-C(16)	-175.15(14)	C(19)-C(21)-C(22)-C(14)	123.94(16)
S(1)-C(2)-C(15)-C(16)	65.54(17)	O(6)-C(21)-C(22)-S(2)	129.95(12)
C(2)-C(15)-C(16)-C(17)	163.65(15)	N(2)-C(21)-C(22)-S(2)	8.12(16)
C(18)-O(4)-C(17)-O(3)	-3.7(2)	C(19)-C(21)-C(22)-S(2)	-111.91(14)
C(18)-O(4)-C(17)-C(16)	171.79(14)	C(23)-S(2)-C(22)-C(14)	120.02(13)
C(15)-C(16)-C(17)-O(3)	76.2(2)	C(23)-S(2)-C(22)-C(21)	-5.35(12)
C(15)-C(16)-C(17)-O(4)	-99.10(17)	C(21)-N(2)-C(23)-C(24)	-175.65(15)
C(17)-O(4)-C(18)-C(19)	-175.51(14)	C(21)-N(2)-C(23)-S(2)	3.6(2)
O(4)-C(18)-C(19)-O(5)	-169.44(13)	C(22)-S(2)-C(23)-N(2)	1.46(15)
O(4)-C(18)-C(19)-C(20)	-55.30(18)	C(22)-S(2)-C(23)-C(24)	-179.24(14)

N(2)-C(23)-C(24)-C(29)	-162.19(18)
S(2)-C(23)-C(24)-C(29)	18.5(2)
N(2)-C(23)-C(24)-C(25)	17.9(3)
S(2)-C(23)-C(24)-C(25)	-161.39(15)
C(29)-C(24)-C(25)-C(26)	1.7(3)
C(23)-C(24)-C(25)-C(26)	-178.38(18)
C(24)-C(25)-C(26)-C(27)	1.9(3)
C(25)-C(26)-C(27)-C(28)	-3.2(3)
C(26)-C(27)-C(28)-C(29)	0.9(3)
C(25)-C(24)-C(29)-C(28)	-3.9(3)
C(23)-C(24)-C(29)-C(28)	176.14(18)
C(27)-C(28)-C(29)-C(24)	2.6(3)

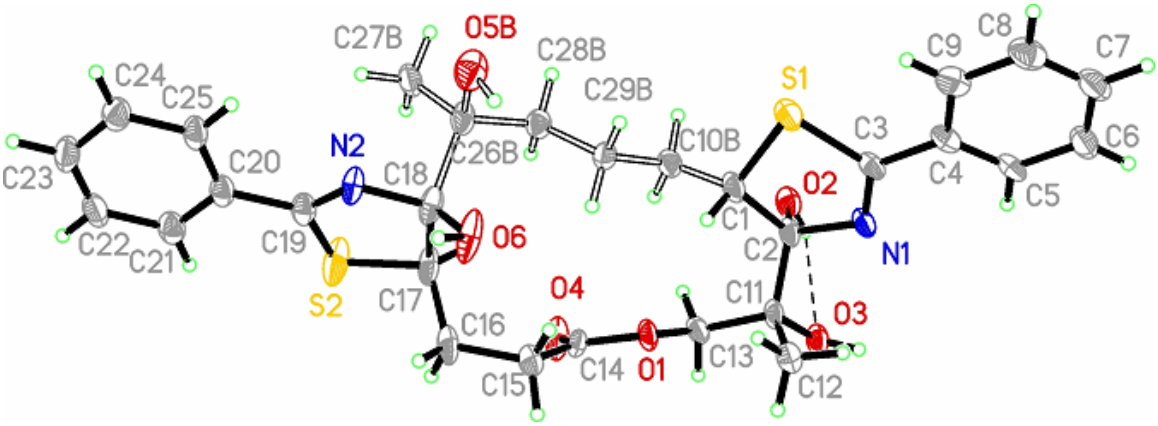
Table 7. Hydrogen bonds [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
O(1)-H(1)...O(2)	0.81(2)	2.18(2)	2.6735(18)	119(2)
O(2)-H(2)...O(5)#1	0.74(2)	2.16(2)	2.7792(17)	142(2)
O(5)-H(5)...N(2)#2	0.75(3)	2.29(3)	2.938(2)	145(3)
O(5)-H(5)...O(6)	0.75(3)	2.42(3)	2.7845(18)	111(2)
O(6)-H(6)...O(2)#3	0.82(2)	2.02(3)	2.8292(18)	171(2)

Symmetry transformations used to generate equivalent atoms:

#1 x,y-1,z #2 -x+3/2,-y+5/2,-z #3 -x+3/2,-y+3/2,-z

X-ray structure of **5.18**:



Empirical formula	C29 H34 N2 O6 S2	
Formula weight	570.70	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2(1)/c	
Unit cell dimensions	a = 15.2379(8) Å	α= 90°.
	b = 7.0663(4) Å	β= 92.623(2)°.
	c = 25.1205(13) Å	γ= 90°.
Volume	2702.0(3) $Å^3$	
Z	4	
Density (calculated)	1.403 Mg/m^3	

Absorption coefficient	0.245 mm^{-1}
F(000)	1208
Crystal size	0.09 x 0.085 x 0.015 mm^3
Theta range for data collection	1.34 to 21.49°.
Index ranges	-15<=h<=15, -7<=k<=7, -25<=l<=25
Reflections collected	15474
Independent reflections	3100 [R(int) = 0.0841]
Completeness to theta = 21.49°	100.0 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.999 and 0.888
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3100 / 731 / 375
Goodness-of-fit on F^2	1.053
Final R indices [I>2sigma(I)]	R1 = 0.0540, wR2 = 0.1077
R indices (all data)	R1 = 0.0851, wR2 = 0.1202
Largest diff. peak and hole	0.290 and -0.220 $e.Å^{-3}$

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

	x	y	z	U(eq)
S(1)	4275(1)	9529(2)	952(1)	32(1)
S(2)	-1304(1)	7774(2)	1457(1)	50(1)
N(1)	4878(2)	10907(5)	1860(1)	25(1)
N(2)	-818(2)	8708(5)	517(1)	27(1)
O(1)	2048(2)	11254(4)	2185(1)	27(1)
O(2)	4269(2)	8216(4)	2236(1)	29(1)
O(3)	4120(2)	11102(4)	2897(1)	30(1)
O(4)	1027(2)	9356(5)	2525(1)	43(1)
O(6)	299(2)	10867(4)	730(1)	44(1)
C(1)	3497(3)	9566(7)	1479(2)	31(1)
C(2)	4056(2)	9992(6)	1997(2)	25(1)
C(3)	5063(2)	10690(6)	1375(2)	23(1)
C(4)	5894(3)	11319(6)	1155(2)	26(1)
C(5)	6592(3)	11813(6)	1502(2)	28(1)
C(6)	7378(3)	12378(6)	1305(2)	34(1)
C(7)	7490(3)	12418(6)	762(2)	38(1)
C(8)	6800(3)	11913(6)	418(2)	37(1)
C(9)	6006(3)	11368(6)	611(2)	32(1)
C(11)	3608(2)	11253(6)	2405(2)	25(1)
C(12)	3532(3)	13295(6)	2230(2)	33(1)
C(13)	2708(2)	10503(6)	2558(2)	27(1)

C(14)	1216(3)	10625(6)	2234(2)	26(1)
C(15)	600(3)	11775(6)	1879(2)	35(1)
C(16)	-285(3)	10824(7)	1746(2)	38(1)
C(17)	-241(3)	8959(6)	1448(2)	34(1)
C(18)	-18(3)	9041(6)	849(2)	30(1)
C(19)	-1459(3)	8046(6)	770(2)	27(1)
C(20)	-2302(3)	7474(6)	507(2)	26(1)
C(21)	-3033(3)	7096(6)	801(2)	31(1)
C(22)	-3819(3)	6552(6)	550(2)	35(1)
C(23)	-3876(3)	6372(6)	5(2)	37(1)
C(24)	-3153(3)	6726(6)	-292(2)	33(1)
C(25)	-2365(3)	7272(6)	-43(2)	29(1)
C(10A)	3033(4)	7430(11)	1504(3)	26(1)
C(26A)	707(4)	7806(10)	746(3)	28(1)
O(5A)	899(7)	8021(15)	195(2)	42(2)
C(27A)	448(5)	5783(10)	841(3)	32(2)
C(28A)	1538(4)	8307(9)	1098(3)	27(1)
C(29A)	2335(4)	7063(9)	1056(2)	24(1)
C(10B)	2882(7)	8246(16)	1422(5)	26(1)
C(26B)	629(5)	7222(14)	623(4)	28(1)
O(5B)	848(11)	7690(20)	88(4)	42(2)
C(27B)	167(7)	5334(15)	604(5)	32(2)
C(28B)	1490(5)	7000(13)	970(4)	27(1)
C(29B)	2110(6)	8654(12)	1023(4)	24(1)

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

S(1)-C(3)	1.768(4)	C(8)-C(9)	1.377(6)
S(1)-C(1)	1.816(4)	C(11)-C(12)	1.511(6)
S(2)-C(19)	1.742(4)	C(11)-C(13)	1.536(5)
S(2)-C(17)	1.824(4)	C(14)-C(15)	1.503(6)
N(1)-C(3)	1.271(5)	C(15)-C(16)	1.530(5)
N(1)-C(2)	1.465(5)	C(16)-C(17)	1.517(6)
N(2)-C(19)	1.277(5)	C(17)-C(18)	1.561(6)
N(2)-C(18)	1.464(5)	C(18)-C(26A)	1.440(8)
O(1)-C(14)	1.354(5)	C(18)-C(26B)	1.731(11)
O(1)-C(13)	1.444(4)	C(19)-C(20)	1.475(5)
O(2)-C(2)	1.422(5)	C(20)-C(25)	1.387(5)
O(3)-C(11)	1.436(4)	C(20)-C(21)	1.389(5)
O(4)-C(14)	1.200(5)	C(21)-C(22)	1.383(6)
O(6)-C(18)	1.414(5)	C(22)-C(23)	1.373(6)
C(1)-C(10B)	1.326(10)	C(23)-C(24)	1.381(6)
C(1)-C(2)	1.552(5)	C(24)-C(25)	1.383(5)
C(1)-C(10A)	1.669(9)	C(10A)-C(29A)	1.533(7)
C(2)-C(11)	1.540(5)	C(26A)-O(5A)	1.436(6)
C(3)-C(4)	1.473(5)	C(26A)-C(27A)	1.505(7)
C(4)-C(9)	1.387(5)	C(26A)-C(28A)	1.552(7)
C(4)-C(5)	1.388(5)	C(28A)-C(29A)	1.507(7)
C(5)-C(6)	1.374(5)	C(10B)-C(29B)	1.537(8)
C(6)-C(7)	1.383(6)	C(26B)-O(5B)	1.439(6)
C(7)-C(8)	1.378(6)	C(26B)-C(27B)	1.508(8)

C(26B)-C(28B)	1.550(8)	C(28B)-C(29B)	1.505(7)
C(3)-S(1)-C(1)	90.22(19)	C(8)-C(7)-C(6)	119.2(4)
C(19)-S(2)-C(17)	91.0(2)	C(9)-C(8)-C(7)	120.6(4)
C(3)-N(1)-C(2)	113.7(3)	C(8)-C(9)-C(4)	120.3(4)
C(19)-N(2)-C(18)	114.3(3)	O(3)-C(11)-C(12)	110.7(3)
C(14)-O(1)-C(13)	116.6(3)	O(3)-C(11)-C(13)	102.4(3)
C(10B)-C(1)-C(2)	125.9(6)	C(12)-C(11)-C(13)	110.2(3)
C(10B)-C(1)-C(10A)	21.4(4)	O(3)-C(11)-C(2)	106.8(3)
C(2)-C(1)-C(10A)	111.2(4)	C(12)-C(11)-C(2)	112.9(3)
C(10B)-C(1)-S(1)	113.1(7)	C(13)-C(11)-C(2)	113.3(3)
C(2)-C(1)-S(1)	105.2(3)	O(1)-C(13)-C(11)	108.2(3)
C(10A)-C(1)-S(1)	107.8(4)	O(4)-C(14)-O(1)	123.5(4)
O(2)-C(2)-N(1)	107.9(3)	O(4)-C(14)-C(15)	127.2(4)
O(2)-C(2)-C(11)	109.3(3)	O(1)-C(14)-C(15)	109.3(4)
N(1)-C(2)-C(11)	108.1(3)	C(14)-C(15)-C(16)	114.4(4)
O(2)-C(2)-C(1)	106.8(3)	C(17)-C(16)-C(15)	115.5(4)
N(1)-C(2)-C(1)	109.3(3)	C(16)-C(17)-C(18)	117.3(4)
C(11)-C(2)-C(1)	115.3(3)	C(16)-C(17)-S(2)	109.5(3)
N(1)-C(3)-C(4)	123.7(4)	C(18)-C(17)-S(2)	105.1(3)
N(1)-C(3)-S(1)	117.2(3)	O(6)-C(18)-C(26A)	104.0(4)
C(4)-C(3)-S(1)	119.2(3)	O(6)-C(18)-N(2)	108.1(3)
C(9)-C(4)-C(5)	119.1(4)	C(26A)-C(18)-N(2)	115.2(4)
C(9)-C(4)-C(3)	121.6(4)	O(6)-C(18)-C(17)	109.2(3)
C(5)-C(4)-C(3)	119.3(4)	C(26A)-C(18)-C(17)	110.7(4)
C(6)-C(5)-C(4)	120.2(4)	N(2)-C(18)-C(17)	109.3(3)
C(5)-C(6)-C(7)	120.6(4)	O(6)-C(18)-C(26B)	113.8(4)

C(26A)-C(18)-C(26B)	15.9(3)	C(18)-C(26A)-C(27A)	109.8(5)
N(2)-C(18)-C(26B)	99.6(4)	O(5A)-C(26A)-C(27A)	108.7(5)
C(17)-C(18)-C(26B)	116.2(4)	C(18)-C(26A)-C(28A)	111.8(5)
N(2)-C(19)-C(20)	123.2(4)	O(5A)-C(26A)-C(28A)	109.2(5)
N(2)-C(19)-S(2)	117.5(3)	C(27A)-C(26A)-C(28A)	109.8(5)
C(20)-C(19)-S(2)	119.3(3)	C(29A)-C(28A)-C(26A)	117.8(5)
C(25)-C(20)-C(21)	119.3(4)	C(28A)-C(29A)-C(10A)	112.6(5)
C(25)-C(20)-C(19)	119.5(4)	C(1)-C(10B)-C(29B)	117.1(8)
C(21)-C(20)-C(19)	121.2(4)	O(5B)-C(26B)-C(27B)	107.6(6)
C(22)-C(21)-C(20)	120.6(4)	O(5B)-C(26B)-C(28B)	108.8(6)
C(23)-C(22)-C(21)	119.6(4)	C(27B)-C(26B)-C(28B)	108.1(6)
C(22)-C(23)-C(24)	120.4(4)	O(5B)-C(26B)-C(18)	107.1(10)
C(23)-C(24)-C(25)	120.2(4)	C(27B)-C(26B)-C(18)	113.3(7)
C(24)-C(25)-C(20)	119.9(4)	C(28B)-C(26B)-C(18)	111.8(7)
C(29A)-C(10A)-C(1)	114.0(6)	C(29B)-C(28B)-C(26B)	118.9(6)
C(18)-C(26A)-O(5A)	107.5(7)	C(28B)-C(29B)-C(10B)	111.7(6)

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$). 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)	22(1)	51(1)	23(1)	-2(1)	1(1)	3(1)
S(2)	34(1)	85(1)	31(1)	10(1)	-6(1)	-31(1)
N(1)	14(2)	40(2)	20(2)	1(2)	2(2)	2(2)

N(2)	21(2)	32(2)	28(2)	8(2)	-8(2)	-9(2)
O(1)	12(2)	40(2)	30(2)	-2(1)	-4(1)	1(1)
O(2)	21(2)	42(2)	24(2)	4(1)	0(1)	-1(1)
O(3)	18(2)	49(2)	24(2)	-4(1)	-1(1)	-5(1)
O(4)	25(2)	63(2)	40(2)	12(2)	-7(2)	-14(2)
O(6)	35(2)	51(2)	44(2)	24(2)	-24(2)	-23(2)
C(1)	14(2)	55(3)	24(2)	-6(2)	-3(2)	3(2)
C(2)	13(2)	43(2)	18(2)	1(2)	-2(2)	-3(2)
C(3)	17(2)	33(2)	19(2)	3(2)	2(2)	7(2)
C(4)	26(2)	28(2)	24(2)	4(2)	9(2)	5(2)
C(5)	21(2)	35(3)	29(2)	-1(2)	10(2)	6(2)
C(6)	25(2)	32(2)	45(3)	0(2)	11(2)	0(2)
C(7)	35(2)	31(3)	50(3)	-2(2)	23(2)	-1(2)
C(8)	46(3)	33(3)	34(2)	3(2)	17(2)	1(2)
C(9)	36(2)	28(2)	32(2)	1(2)	8(2)	4(2)
C(11)	13(2)	40(2)	23(2)	-3(2)	-4(2)	-2(2)
C(12)	21(2)	42(3)	38(3)	-5(2)	3(2)	-1(2)
C(13)	15(2)	45(3)	22(2)	-5(2)	0(2)	3(2)
C(14)	16(2)	35(3)	26(2)	-8(2)	-4(2)	-5(2)
C(15)	20(2)	38(3)	46(3)	-7(2)	-4(2)	4(2)
C(16)	17(2)	54(3)	42(3)	3(2)	-10(2)	-1(2)
C(17)	20(2)	50(3)	31(2)	7(2)	-10(2)	-8(2)
C(18)	26(2)	35(2)	26(2)	12(2)	-12(2)	-11(2)
C(19)	21(2)	29(2)	31(2)	4(2)	-6(2)	2(2)
C(20)	21(2)	24(2)	33(2)	3(2)	-4(2)	2(2)
C(21)	25(2)	25(2)	43(3)	3(2)	-4(2)	4(2)
C(22)	20(2)	30(3)	54(3)	-2(2)	-1(2)	3(2)

C(23)	24(2)	28(2)	57(3)	-6(2)	-10(2)	-2(2)
C(24)	29(2)	27(2)	41(3)	-2(2)	-8(2)	5(2)
C(25)	19(2)	26(2)	39(2)	2(2)	-7(2)	3(2)
C(10A)	20(2)	37(3)	22(2)	0(3)	3(2)	-2(3)
C(26A)	22(2)	37(3)	25(3)	5(2)	2(2)	-12(2)
O(5A)	38(2)	57(4)	31(3)	5(3)	2(2)	-15(2)
C(27A)	17(4)	30(3)	48(4)	-1(3)	2(3)	-1(3)
C(28A)	23(2)	30(3)	28(2)	1(2)	3(2)	-6(2)
C(29A)	20(2)	27(3)	26(2)	-2(2)	1(2)	-4(2)
C(10B)	20(2)	37(3)	22(2)	0(3)	3(2)	-2(3)
C(26B)	22(2)	37(3)	25(3)	5(2)	2(2)	-12(2)
O(5B)	38(2)	57(4)	31(3)	5(3)	2(2)	-15(2)
C(27B)	17(4)	30(3)	48(4)	-1(3)	2(3)	-1(3)
C(28B)	23(2)	30(3)	28(2)	1(2)	3(2)	-6(2)
C(29B)	20(2)	27(3)	26(2)	-2(2)	1(2)	-4(2)

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

	x	y	z	U(eq)
H(2O)	4417	8378	2559	44
H(3O)	4542	11869	2895	45
H(6O)	-43	11385	502	67
H(1)	3043	10568	1411	38
H(5)	6528	11760	1876	33
H(6)	7847	12745	1545	40

H(7)	8037	12789	628	45
H(8)	6871	11940	44	45
H(9)	5535	11025	370	38
H(12A)	3236	14026	2500	50
H(12B)	3190	13367	1890	50
H(12C)	4120	13815	2185	50
H(13A)	2703	9103	2546	33
H(13B)	2585	10906	2925	33
H(15A)	890	12045	1543	41
H(15B)	492	13001	2055	41
H(16A)	-583	10603	2082	46
H(16B)	-654	11712	1528	46
H(17)	205	8138	1640	40
H(21)	-2992	7211	1178	37
H(22)	-4317	6304	753	42
H(23)	-4415	6002	-169	44
H(24)	-3197	6594	-669	39
H(25)	-1868	7509	-248	34
H(10A)	3498	6456	1485	31
H(10B)	2758	7288	1851	31
H(5OA)	988	9035	72	63
H(27A)	923	4941	738	48
H(27B)	-88	5487	627	48
H(27C)	342	5603	1219	48
H(28A)	1711	9617	1011	32
H(28B)	1372	8302	1475	32
H(29A)	2597	7286	708	29

H(29B)	2152	5720	1069	29
H(10C)	2640	8015	1775	31
H(10D)	3167	7059	1312	31
H(5OA)	988	9035	72	63
H(27D)	-371	5432	377	48
H(27E)	17	4966	965	48
H(27F)	555	4378	458	48
H(28C)	1327	6639	1333	32
H(28D)	1820	5923	826	32
H(29C)	1785	9778	1143	29
H(29D)	2340	8947	670	29

Table 6. Torsion angles [°].

C(3)-S(1)-C(1)-C(10B)	-157.2(6)	C(10B)-C(1)-C(2)-C(11)	-81.9(9)
C(3)-S(1)-C(1)-C(2)	-16.3(3)	C(10A)-C(1)-C(2)-C(11)	-99.7(5)
C(3)-S(1)-C(1)-C(10A)	-135.0(3)	S(1)-C(1)-C(2)-C(11)	143.8(3)
C(3)-N(1)-C(2)-O(2)	97.8(4)	C(2)-N(1)-C(3)-C(4)	-173.9(4)
C(3)-N(1)-C(2)-C(11)	-144.1(3)	C(2)-N(1)-C(3)-S(1)	5.0(5)
C(3)-N(1)-C(2)-C(1)	-17.9(5)	C(1)-S(1)-C(3)-N(1)	7.7(3)
C(10B)-C(1)-C(2)-O(2)	39.7(9)	C(1)-S(1)-C(3)-C(4)	-173.4(3)
C(10A)-C(1)-C(2)-O(2)	21.8(5)	N(1)-C(3)-C(4)-C(9)	-168.2(4)
S(1)-C(1)-C(2)-O(2)	-94.7(3)	S(1)-C(3)-C(4)-C(9)	12.9(5)
C(10B)-C(1)-C(2)-N(1)	156.2(8)	N(1)-C(3)-C(4)-C(5)	14.1(6)
C(10A)-C(1)-C(2)-N(1)	138.3(4)	S(1)-C(3)-C(4)-C(5)	-164.8(3)
S(1)-C(1)-C(2)-N(1)	21.8(4)	C(9)-C(4)-C(5)-C(6)	1.3(6)

C(3)-C(4)-C(5)-C(6)	179.1(4)	C(19)-S(2)-C(17)-C(16)	113.7(3)
C(4)-C(5)-C(6)-C(7)	-1.6(6)	C(19)-S(2)-C(17)-C(18)	-13.2(3)
C(5)-C(6)-C(7)-C(8)	1.1(7)	C(19)-N(2)-C(18)-O(6)	-132.7(4)
C(6)-C(7)-C(8)-C(9)	-0.2(7)	C(19)-N(2)-C(18)-C(26A)	111.5(5)
C(7)-C(8)-C(9)-C(4)	-0.1(7)	C(19)-N(2)-C(18)-C(17)	-13.9(5)
C(5)-C(4)-C(9)-C(8)	-0.4(6)	C(19)-N(2)-C(18)-C(26B)	108.3(5)
C(3)-C(4)-C(9)-C(8)	-178.2(4)	C(16)-C(17)-C(18)-O(6)	13.3(5)
O(2)-C(2)-C(11)-O(3)	45.9(4)	S(2)-C(17)-C(18)-O(6)	135.3(3)
N(1)-C(2)-C(11)-O(3)	-71.3(4)	C(16)-C(17)-C(18)-C(26A)	127.3(5)
C(1)-C(2)-C(11)-O(3)	166.1(3)	S(2)-C(17)-C(18)-C(26A)	-110.8(4)
O(2)-C(2)-C(11)-C(12)	167.8(3)	C(16)-C(17)-C(18)-N(2)	-104.8(4)
N(1)-C(2)-C(11)-C(12)	50.6(4)	S(2)-C(17)-C(18)-N(2)	17.2(4)
C(1)-C(2)-C(11)-C(12)	-72.0(4)	C(16)-C(17)-C(18)-C(26B)	143.6(4)
O(2)-C(2)-C(11)-C(13)	-66.1(4)	S(2)-C(17)-C(18)-C(26B)	-94.4(4)
N(1)-C(2)-C(11)-C(13)	176.7(3)	C(18)-N(2)-C(19)-C(20)	-175.3(4)
C(1)-C(2)-C(11)-C(13)	54.1(5)	C(18)-N(2)-C(19)-S(2)	3.4(5)
C(14)-O(1)-C(13)-C(11)	175.1(3)	C(17)-S(2)-C(19)-N(2)	6.7(4)
O(3)-C(11)-C(13)-O(1)	157.1(3)	C(17)-S(2)-C(19)-C(20)	-174.6(3)
C(12)-C(11)-C(13)-O(1)	39.3(4)	N(2)-C(19)-C(20)-C(25)	13.3(6)
C(2)-C(11)-C(13)-O(1)	-88.3(4)	S(2)-C(19)-C(20)-C(25)	-165.3(3)
C(13)-O(1)-C(14)-O(4)	-8.3(6)	N(2)-C(19)-C(20)-C(21)	-168.0(4)
C(13)-O(1)-C(14)-C(15)	170.8(3)	S(2)-C(19)-C(20)-C(21)	13.4(5)
O(4)-C(14)-C(15)-C(16)	-21.0(6)	C(25)-C(20)-C(21)-C(22)	-1.0(6)
O(1)-C(14)-C(15)-C(16)	159.9(3)	C(19)-C(20)-C(21)-C(22)	-179.7(4)
C(14)-C(15)-C(16)-C(17)	-61.2(5)	C(20)-C(21)-C(22)-C(23)	0.5(6)
C(15)-C(16)-C(17)-C(18)	-73.2(5)	C(21)-C(22)-C(23)-C(24)	0.2(7)
C(15)-C(16)-C(17)-S(2)	167.1(3)	C(22)-C(23)-C(24)-C(25)	-0.2(7)

C(23)-C(24)-C(25)-C(20)	-0.3(6)
C(21)-C(20)-C(25)-C(24)	0.9(6)
C(19)-C(20)-C(25)-C(24)	179.7(4)
C(10B)-C(1)-C(10A)-C(29A)	31.8(19)
C(2)-C(1)-C(10A)-C(29A)	168.9(5)
S(1)-C(1)-C(10A)-C(29A)	-76.2(6)
O(6)-C(18)-C(26A)-O(5A)	-60.2(5)
N(2)-C(18)-C(26A)-O(5A)	57.9(6)
C(17)-C(18)-C(26A)-O(5A)	-177.4(4)
C(26B)-C(18)-C(26A)-O(5A)	69.4(17)
O(6)-C(18)-C(26A)-C(27A)	-178.3(4)
N(2)-C(18)-C(26A)-C(27A)	-60.1(6)
C(17)-C(18)-C(26A)-C(27A)	64.5(6)
C(26B)-C(18)-C(26A)-C(27A)	-48.7(17)
O(6)-C(18)-C(26A)-C(28A)	59.6(6)
N(2)-C(18)-C(26A)-C(28A)	177.7(4)
C(17)-C(18)-C(26A)-C(28A)	-57.6(6)
C(26B)-C(18)-C(26A)-C(28A)	-171(2)
C(18)-C(26A)-C(28A)-C(29A)	176.6(6)
O(5A)-C(26A)-C(28A)-C(29A)	-64.5(9)
C(27A)-C(26A)-C(28A)-C(29A)	54.5(8)
C(26A)-C(28A)-C(29A)-C(10A)	-167.5(6)
C(1)-C(10A)-C(29A)-C(28A)	-66.5(8)
C(2)-C(1)-C(10B)-C(29B)	148.8(8)
C(10A)-C(1)-C(10B)-C(29B)	-160(3)
S(1)-C(1)-C(10B)-C(29B)	-79.8(11)
O(6)-C(18)-C(26B)-O(5B)	-44.6(7)
C(26A)-C(18)-C(26B)-O(5B)	-99.4(17)
N(2)-C(18)-C(26B)-O(5B)	70.1(6)
C(17)-C(18)-C(26B)-O(5B)	-172.7(6)
O(6)-C(18)-C(26B)-C(27B)	-163.1(6)
C(26A)-C(18)-C(26B)-C(27B)	142(2)
N(2)-C(18)-C(26B)-C(27B)	-48.4(7)
C(17)-C(18)-C(26B)-C(27B)	68.8(7)
O(6)-C(18)-C(26B)-C(28B)	74.5(7)
C(26A)-C(18)-C(26B)-C(28B)	19.7(15)
N(2)-C(18)-C(26B)-C(28B)	-170.8(5)
C(17)-C(18)-C(26B)-C(28B)	-53.6(7)
O(5B)-C(26B)-C(28B)-C(29B)	59.2(12)
C(27B)-C(26B)-C(28B)-C(29B)	175.8(9)
C(18)-C(26B)-C(28B)-C(29B)	-58.9(11)
C(26B)-C(28B)-C(29B)-C(10B)	174.6(10)
C(1)-C(10B)-C(29B)-C(28B)	176.4(10)

Table 7. Hydrogen bonds [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
O(2)-H(2O)...O(3)	0.84	2.16	2.647(4)	116.7
O(2)-H(2O)...N(1)#1	0.84	2.49	3.040(4)	124.1
O(3)-H(3O)...O(2)#2	0.84	2.09	2.905(4)	164.6
O(5A)-H(5OA)...N(2)#3	0.794(8)	2.183(3)	2.921(9)	154.9(5)
O(5B)-H(5OA)...N(2)#3	0.974(15)	2.183(3)	2.962(13)	136.1(5)
O(6)-H(6O)...O(5B)#3	0.84	1.99	2.826(13)	172.8
O(6)-H(6O)...O(5A)#3	0.84	2.18	2.993(8)	164.3

Symmetry transformations used to generate equivalent atoms:

#1 -x+1,y-1/2,-z+1/2 #2 -x+1,y+1/2,-z+1/2 #3 -x,-y+2,-z

X-ray structure of **5.21**:

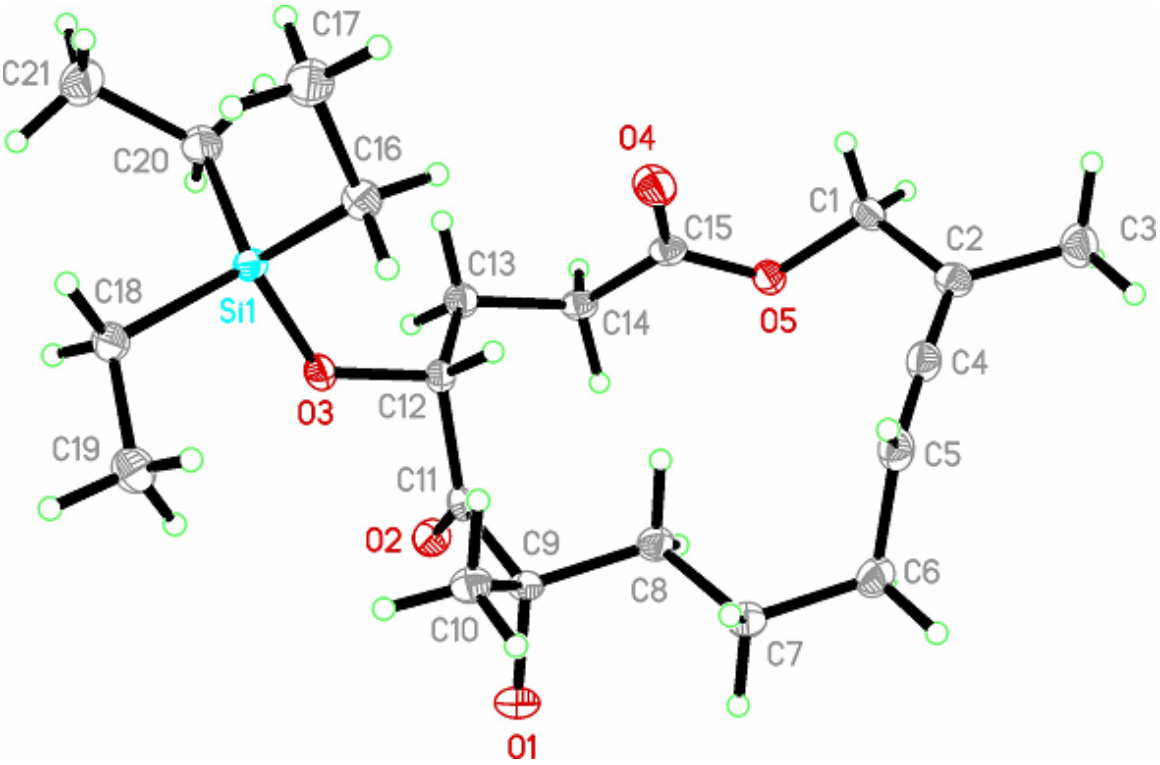


Table 1. Crystal data and structure refinement.

Empirical formula	C21 H36 O5 Si	
Formula weight	396.59	
Temperature	100(2) K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	P2(1)/n	
Unit cell dimensions	a = 15.3280(2) Å	α= 90°.

	b = 8.3368(1) Å β= 106.080(1)°.
	c = 17.8070(3) Å γ = 90°.
Volume	2186.47(5) $Å^3$
Z	4
Density (calculated)	1.205 Mg/m^3
Absorption coefficient	1.171 mm^{-1}
F(000)	864
Crystal size	0.40 x 0.08 x 0.04 mm^3
Theta range for data collection	3.37 to 61.16°.
Index ranges	-17<=h<=17, -9<=k<=8, -19<=l<=19
Reflections collected	9982
Independent reflections	3271 [R(int) = 0.0185]
Completeness to theta = 61.16°	96.9 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9602 and 0.6516
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3271 / 0 / 250
Goodness-of-fit on F^2	1.000
Final R indices [I>2sigma(I)]	R1 = 0.0385, wR2 = 0.0853
R indices (all data)	R1 = 0.0414, wR2 = 0.0869
Largest diff. peak and hole	0.378 and -0.301 $e.Å^{-3}$

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

	x	y	z	U(eq)
Si(1)	6469(1)	6610(1)	10772(1)	14(1)
O(1)	6886(1)	2789(2)	8125(1)	19(1)
O(2)	6049(1)	5576(2)	8138(1)	20(1)
O(3)	6341(1)	6150(2)	9838(1)	16(1)
O(4)	8735(1)	8906(2)	9705(1)	26(1)
O(5)	8897(1)	9021(2)	8486(1)	17(1)
C(1)	9836(1)	9526(2)	8758(1)	18(1)
C(2)	10498(1)	8195(2)	8750(1)	18(1)
C(3)	11378(1)	8757(2)	8612(1)	24(1)
C(4)	10342(1)	6696(2)	8873(1)	20(1)
C(5)	10207(1)	5172(2)	8982(1)	21(1)
C(6)	9721(1)	4015(2)	8359(1)	24(1)
C(7)	8899(1)	3272(2)	8563(1)	21(1)
C(8)	8193(1)	4546(2)	8590(1)	18(1)
C(9)	7309(1)	3883(2)	8728(1)	15(1)
C(10)	7468(1)	2986(2)	9500(1)	19(1)
C(11)	6697(1)	5347(2)	8698(1)	14(1)
C(12)	6941(1)	6551(2)	9382(1)	14(1)
C(13)	6807(1)	8276(2)	9097(1)	18(1)
C(14)	7416(1)	8761(2)	8586(1)	17(1)
C(15)	8408(1)	8880(2)	9008(1)	16(1)

C(16)	7710(1)	6574(2)	11293(1)	20(1)
C(17)	7937(1)	7055(3)	12157(1)	26(1)
C(18)	5808(1)	5043(2)	11122(1)	18(1)
C(19)	5980(1)	3319(2)	10907(1)	23(1)
C(20)	5977(1)	8644(2)	10865(1)	22(1)
C(21)	5546(2)	8808(3)	11544(1)	30(1)

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

Si(1)-O(3)	1.6633(13)	C(3)-H(3A)	0.9800
Si(1)-C(18)	1.8622(19)	C(3)-H(3B)	0.9800
Si(1)-C(16)	1.8728(19)	C(3)-H(3C)	0.9800
Si(1)-C(20)	1.882(2)	C(4)-C(5)	1.310(3)
O(1)-C(9)	1.422(2)	C(5)-C(6)	1.502(3)
O(1)-H(1)	0.8400	C(5)-H(5)	0.9500
O(2)-C(11)	1.211(2)	C(6)-C(7)	1.536(3)
O(3)-C(12)	1.426(2)	C(6)-H(6A)	0.9900
O(4)-C(15)	1.204(2)	C(6)-H(6B)	0.9900
O(5)-C(15)	1.351(2)	C(7)-C(8)	1.526(3)
O(5)-C(1)	1.449(2)	C(7)-H(7A)	0.9900
C(1)-C(2)	1.506(3)	C(7)-H(7B)	0.9900
C(1)-H(1A)	0.9900	C(8)-C(9)	1.545(3)
C(1)-H(1B)	0.9900	C(8)-H(8A)	0.9900
C(2)-C(4)	1.302(3)	C(8)-H(8B)	0.9900
C(2)-C(3)	1.511(3)	C(9)-C(10)	1.523(3)

C(9)-C(11)	1.531(3)	C(17)-H(17A)	0.9800
C(10)-H(10A)	0.9800	C(17)-H(17B)	0.9800
C(10)-H(10B)	0.9800	C(17)-H(17C)	0.9800
C(10)-H(10C)	0.9800	C(18)-C(19)	1.529(3)
C(11)-C(12)	1.542(3)	C(18)-H(18A)	0.9900
C(12)-C(13)	1.520(3)	C(18)-H(18B)	0.9900
C(12)-H(12)	1.0000	C(19)-H(19A)	0.9800
C(13)-C(14)	1.526(2)	C(19)-H(19B)	0.9800
C(13)-H(13A)	0.9900	C(19)-H(19C)	0.9800
C(13)-H(13B)	0.9900	C(20)-C(21)	1.536(3)
C(14)-C(15)	1.501(3)	C(20)-H(20A)	0.9900
C(14)-H(14A)	0.9900	C(20)-H(20B)	0.9900
C(14)-H(14B)	0.9900	C(21)-H(21A)	0.9800
C(16)-C(17)	1.534(3)	C(21)-H(21B)	0.9800
C(16)-H(16A)	0.9900	C(21)-H(21C)	0.9800
C(16)-H(16B)	0.9900		

O(3)-Si(1)-C(18)	104.36(8)	O(5)-C(1)-H(1A)	109.0
O(3)-Si(1)-C(16)	108.29(8)	C(2)-C(1)-H(1A)	109.0
C(18)-Si(1)-C(16)	113.27(9)	O(5)-C(1)-H(1B)	109.0
O(3)-Si(1)-C(20)	110.87(8)	C(2)-C(1)-H(1B)	109.0
C(18)-Si(1)-C(20)	109.56(9)	H(1A)-C(1)-H(1B)	107.8
C(16)-Si(1)-C(20)	110.33(9)	C(4)-C(2)-C(1)	123.43(18)
C(9)-O(1)-H(1)	109.5	C(4)-C(2)-C(3)	122.57(18)
C(12)-O(3)-Si(1)	126.81(11)	C(1)-C(2)-C(3)	113.98(16)
C(15)-O(5)-C(1)	119.03(14)	C(2)-C(3)-H(3A)	109.5
O(5)-C(1)-C(2)	113.09(15)	C(2)-C(3)-H(3B)	109.5

H(3A)-C(3)-H(3B)	109.5	O(1)-C(9)-C(11)	109.79(14)
C(2)-C(3)-H(3C)	109.5	C(10)-C(9)-C(11)	111.52(15)
H(3A)-C(3)-H(3C)	109.5	O(1)-C(9)-C(8)	110.16(14)
H(3B)-C(3)-H(3C)	109.5	C(10)-C(9)-C(8)	113.00(15)
C(2)-C(4)-C(5)	177.9(2)	C(11)-C(9)-C(8)	105.39(14)
C(4)-C(5)-C(6)	125.43(19)	C(9)-C(10)-H(10A)	109.5
C(4)-C(5)-H(5)	117.3	C(9)-C(10)-H(10B)	109.5
C(6)-C(5)-H(5)	117.3	H(10A)-C(10)-H(10B)	109.5
C(5)-C(6)-C(7)	110.88(16)	C(9)-C(10)-H(10C)	109.5
C(5)-C(6)-H(6A)	109.5	H(10A)-C(10)-H(10C)	109.5
C(7)-C(6)-H(6A)	109.5	H(10B)-C(10)-H(10C)	109.5
C(5)-C(6)-H(6B)	109.5	O(2)-C(11)-C(9)	120.61(16)
C(7)-C(6)-H(6B)	109.5	O(2)-C(11)-C(12)	120.76(16)
H(6A)-C(6)-H(6B)	108.1	C(9)-C(11)-C(12)	118.60(15)
C(8)-C(7)-C(6)	111.25(16)	O(3)-C(12)-C(13)	111.36(15)
C(8)-C(7)-H(7A)	109.4	O(3)-C(12)-C(11)	104.10(14)
C(6)-C(7)-H(7A)	109.4	C(13)-C(12)-C(11)	111.75(15)
C(8)-C(7)-H(7B)	109.4	O(3)-C(12)-H(12)	109.8
C(6)-C(7)-H(7B)	109.4	C(13)-C(12)-H(12)	109.8
H(7A)-C(7)-H(7B)	108.0	C(11)-C(12)-H(12)	109.8
C(7)-C(8)-C(9)	114.66(16)	C(12)-C(13)-C(14)	113.70(15)
C(7)-C(8)-H(8A)	108.6	C(12)-C(13)-H(13A)	108.8
C(9)-C(8)-H(8A)	108.6	C(14)-C(13)-H(13A)	108.8
C(7)-C(8)-H(8B)	108.6	C(12)-C(13)-H(13B)	108.8
C(9)-C(8)-H(8B)	108.6	C(14)-C(13)-H(13B)	108.8
H(8A)-C(8)-H(8B)	107.6	H(13A)-C(13)-H(13B)	107.7
O(1)-C(9)-C(10)	107.00(15)	C(15)-C(14)-C(13)	114.90(15)

C(15)-C(14)-H(14A)	108.5	Si(1)-C(18)-H(18A)	108.4
C(13)-C(14)-H(14A)	108.5	C(19)-C(18)-H(18B)	108.4
C(15)-C(14)-H(14B)	108.5	Si(1)-C(18)-H(18B)	108.4
C(13)-C(14)-H(14B)	108.5	H(18A)-C(18)-H(18B)	107.5
H(14A)-C(14)-H(14B)	107.5	C(18)-C(19)-H(19A)	109.5
O(4)-C(15)-O(5)	123.74(17)	C(18)-C(19)-H(19B)	109.5
O(4)-C(15)-C(14)	126.35(17)	H(19A)-C(19)-H(19B)	109.5
O(5)-C(15)-C(14)	109.86(15)	C(18)-C(19)-H(19C)	109.5
C(17)-C(16)-Si(1)	114.19(13)	H(19A)-C(19)-H(19C)	109.5
C(17)-C(16)-H(16A)	108.7	H(19B)-C(19)-H(19C)	109.5
Si(1)-C(16)-H(16A)	108.7	C(21)-C(20)-Si(1)	114.80(14)
C(17)-C(16)-H(16B)	108.7	C(21)-C(20)-H(20A)	108.6
Si(1)-C(16)-H(16B)	108.7	Si(1)-C(20)-H(20A)	108.6
H(16A)-C(16)-H(16B)	107.6	C(21)-C(20)-H(20B)	108.6
C(16)-C(17)-H(17A)	109.5	Si(1)-C(20)-H(20B)	108.6
C(16)-C(17)-H(17B)	109.5	H(20A)-C(20)-H(20B)	107.5
H(17A)-C(17)-H(17B)	109.5	C(20)-C(21)-H(21A)	109.5
C(16)-C(17)-H(17C)	109.5	C(20)-C(21)-H(21B)	109.5
H(17A)-C(17)-H(17C)	109.5	H(21A)-C(21)-H(21B)	109.5
H(17B)-C(17)-H(17C)	109.5	C(20)-C(21)-H(21C)	109.5
C(19)-C(18)-Si(1)	115.35(13)	H(21A)-C(21)-H(21C)	109.5
C(19)-C(18)-H(18A)	108.4	H(21B)-C(21)-H(21C)	109.5

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$). 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}
Si(1)	16(1)	14(1)	14(1)	-1(1)	5(1)	-1(1)
O(1)	24(1)	14(1)	17(1)	-2(1)	1(1)	0(1)
O(2)	18(1)	23(1)	18(1)	-1(1)	3(1)	2(1)
O(3)	16(1)	17(1)	17(1)	0(1)	7(1)	-3(1)
O(4)	26(1)	35(1)	16(1)	-2(1)	4(1)	-8(1)
O(5)	16(1)	18(1)	17(1)	-1(1)	5(1)	-2(1)
C(1)	17(1)	16(1)	21(1)	-1(1)	5(1)	-4(1)
C(2)	19(1)	18(1)	15(1)	-1(1)	3(1)	-2(1)
C(3)	23(1)	23(1)	28(1)	2(1)	11(1)	-1(1)
C(4)	15(1)	24(1)	22(1)	-2(1)	5(1)	2(1)
C(5)	17(1)	22(1)	27(1)	2(1)	8(1)	3(1)
C(6)	24(1)	17(1)	34(1)	-2(1)	14(1)	3(1)
C(7)	23(1)	14(1)	27(1)	-2(1)	10(1)	0(1)
C(8)	20(1)	14(1)	20(1)	0(1)	7(1)	1(1)
C(9)	18(1)	13(1)	15(1)	-2(1)	4(1)	-1(1)
C(10)	22(1)	15(1)	19(1)	0(1)	5(1)	1(1)
C(11)	15(1)	14(1)	15(1)	3(1)	7(1)	-3(1)
C(12)	13(1)	16(1)	15(1)	0(1)	6(1)	-1(1)
C(13)	18(1)	16(1)	19(1)	0(1)	6(1)	1(1)
C(14)	21(1)	11(1)	17(1)	1(1)	5(1)	1(1)
C(15)	24(1)	10(1)	16(1)	0(1)	7(1)	-1(1)

C(16)	19(1)	20(1)	20(1)	-1(1)	5(1)	0(1)
C(17)	23(1)	33(1)	20(1)	-2(1)	4(1)	-2(1)
C(18)	20(1)	19(1)	16(1)	1(1)	6(1)	-2(1)
C(19)	23(1)	21(1)	24(1)	4(1)	6(1)	-1(1)
C(20)	23(1)	18(1)	25(1)	-1(1)	8(1)	1(1)
C(21)	34(1)	21(1)	41(1)	-3(1)	20(1)	3(1)

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

	x	y	z	U(eq)
H(1)	6547	3295	7748	29
H(1A)	9955	9944	9297	22
H(1B)	9939	10413	8423	22
H(3A)	11771	7830	8610	35
H(3B)	11684	9496	9030	35
H(3C)	11250	9309	8108	35
H(5)	10435	4766	9497	26
H(6A)	10145	3154	8305	28
H(6B)	9516	4582	7853	28
H(7A)	8620	2452	8167	25
H(7B)	9103	2733	9078	25
H(8A)	8037	5143	8090	21
H(8B)	8468	5317	9012	21
H(10A)	6884	2651	9571	28

H(10B)	7779	3692	9931	28
H(10C)	7844	2038	9493	28
H(12)	7584	6386	9697	17
H(13A)	6929	8999	9555	21
H(13B)	6165	8425	8794	21
H(14A)	7338	7968	8159	20
H(14B)	7208	9813	8344	20
H(16A)	7945	5478	11257	23
H(16B)	8030	7310	11022	23
H(17A)	7706	8138	12200	39
H(17B)	8597	7040	12385	39
H(17C)	7653	6296	12438	39
H(18A)	5951	5120	11698	22
H(18B)	5153	5280	10905	22
H(19A)	5838	3221	10337	34
H(19B)	5592	2587	11102	34
H(19C)	6619	3044	11143	34
H(20A)	6465	9454	10932	26
H(20B)	5511	8892	10370	26
H(21A)	5044	8044	11472	45
H(21B)	5315	9902	11554	45
H(21C)	6003	8584	12038	45

Table 6. Torsion angles [°]

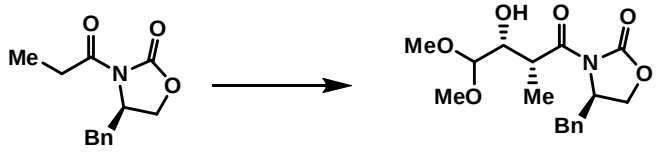
C(18)-Si(1)-O(3)-C(12)	-155.02(14)	O(2)-C(11)-C(12)-C(13)	-39.3(2)
C(16)-Si(1)-O(3)-C(12)	-34.08(16)	C(9)-C(11)-C(12)-C(13)	138.73(16)
C(20)-Si(1)-O(3)-C(12)	87.10(15)	O(3)-C(12)-C(13)-C(14)	-178.49(14)
C(15)-O(5)-C(1)-C(2)	108.49(18)	C(11)-C(12)-C(13)-C(14)	-62.5(2)
O(5)-C(1)-C(2)-C(4)	-32.1(3)	C(12)-C(13)-C(14)-C(15)	-69.0(2)
O(5)-C(1)-C(2)-C(3)	149.76(15)	C(1)-O(5)-C(15)-O(4)	-12.0(3)
C(1)-C(2)-C(4)-C(5)	157(6)	C(1)-O(5)-C(15)-C(14)	165.69(15)
C(3)-C(2)-C(4)-C(5)	-25(6)	C(13)-C(14)-C(15)-O(4)	-13.6(3)
C(2)-C(4)-C(5)-C(6)	-71(6)	C(13)-C(14)-C(15)-O(5)	168.77(15)
C(4)-C(5)-C(6)-C(7)	-121.1(2)	O(3)-Si(1)-C(16)-C(17)	177.25(14)
C(5)-C(6)-C(7)-C(8)	63.5(2)	C(18)-Si(1)-C(16)-C(17)	-67.50(17)
C(6)-C(7)-C(8)-C(9)	175.50(16)	C(20)-Si(1)-C(16)-C(17)	55.73(17)
C(7)-C(8)-C(9)-O(1)	-59.3(2)	O(3)-Si(1)-C(18)-C(19)	47.43(15)
C(7)-C(8)-C(9)-C(10)	60.3(2)	C(16)-Si(1)-C(18)-C(19)	-70.14(16)
C(7)-C(8)-C(9)-C(11)	-177.69(15)	C(20)-Si(1)-C(18)-C(19)	166.21(14)
O(1)-C(9)-C(11)-O(2)	-12.4(2)	O(3)-Si(1)-C(20)-C(21)	145.62(14)
C(10)-C(9)-C(11)-O(2)	-130.77(18)	C(18)-Si(1)-C(20)-C(21)	30.96(18)
C(8)-C(9)-C(11)-O(2)	106.26(18)	C(16)-Si(1)-C(20)-C(21)	-94.41(16)
O(1)-C(9)-C(11)-C(12)	169.65(14)		
C(10)-C(9)-C(11)-C(12)	51.2(2)		
C(8)-C(9)-C(11)-C(12)	-71.73(19)		
Si(1)-O(3)-C(12)-C(13)	-79.63(18)		
Si(1)-O(3)-C(12)-C(11)	159.81(12)		
O(2)-C(11)-C(12)-O(3)	81.03(19)		
C(9)-C(11)-C(12)-O(3)	-100.97(17)		

Table 7. Hydrogen bonds [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
O(1)-H(1)...O(5)#1	0.84	2.20	2.9695(17)	152.7
O(1)-H(1)...O(2)	0.84	2.23	2.6579(18)	111.6

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

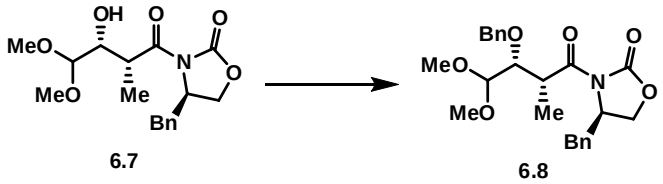
Experimental (Chapter VI)



6.6 6.7

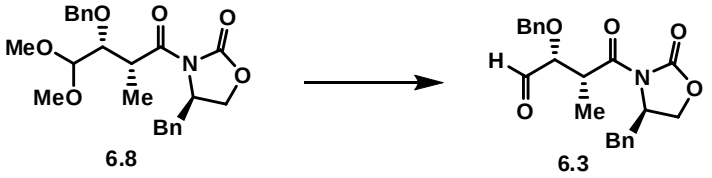
To a solution of 4(R)-benzyl propionyl oxazolidinone **6.6** (9.9g, 42.44 mmol) in DCM (300 mL), cooled at -30^{o}C, were added di-nbutylboron triflate (46.7 mL, 46.7 mmol) and TEA (560 mg, 55.33 mmol) respectively. The reaction mixture was then warmed to 0^{o}C and stirred at that temperature for one hour before cooling back to -78^{o}C. A chloroform solution (0.68 M) of 1,1-dimethoxy acetaldehyde (67 mL, 42.84 mmol) was added to the reaction mixture slowly at -78^{o}C. The reaction was slowly warmed to 0^{o}C over one hour and stirred additional one hour at that temperature. The reaction was then quenched with 100 mL solution of methanol and phosphate buffer (1:3 ratio) at 0^{o}C, followed by addition of 100 mL solution of 30% H_2O_2 and methanol (1:2 ratio). The reaction was then stirred for 10 minutes at 0^{o}C. Diluted with 200 mL DCM, washed with water (2 x 100 mL), dried over anhydrous $MgSO_4$. Evaporation of solvent gave crude product, which upon further purification by FCC using 30% EtOAc in hexane gave aldol product **6.7** as white solid (12.9g, 90% yield). $[\alpha]^{25}_{D}$= -50.0 (*c* = 0.01, $CHCl_3$); MP 67^{o}C; IR ν_{max}(neat)/cm^{-1} 3485, 2937, 1778, 1696, 1386; δ_H (500 MHz, $CDCl_3$) 7.35-7.25 (3H, m), 7.21 (2H, d, J= 7.0 Hz), 4.72-4.65 (1H, m), 4.33 (1H, d, J= 6.0 Hz), 4.23- 4.15 (2H, m), 4.05-3.96 (1H, m), 3.42 (3H, s), 3.38 (3H, s), 3.26 (1H, dd, J= 13.5, 3.5 Hz), 2.78 (1H, dd, J= 13.5, 10 Hz), 2.68-2.60 (1H, bs), 1.32 (3H, d, J= 7.0 Hz); δ_C (125 MHz, $CDCl_3$) 176.1, 153.2,

135.4, 129.6 (2), 129.1 (2), 127.5, 104.9, 71.4, 66.3, 55.4, 54.9, 54.4, 39.2, 38.1, 12.8; *m/z* (ESIMS) found: 360.2 $(M+Na)^+$; calc'd: 360.2.

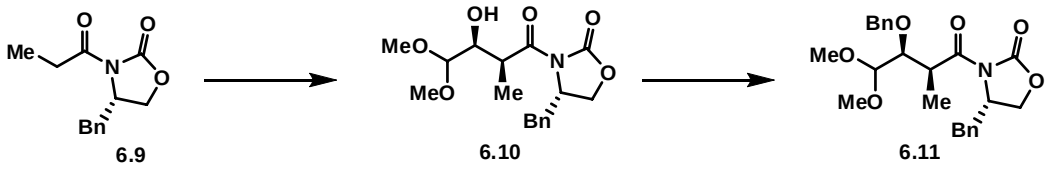


6.7 **6.8**

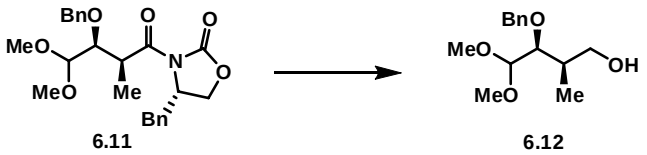
Aldol product **6.7** (10g, 29.67 mmol), Ag_2O (21g, 90.62 mmol) and 4Å powdered molecular sieve (10g) were mixed together and to that dry DCM (200 mL) was added. After stirring for 10 minutes at room temperature BnBr (15.3g, 89.45 mmol) was added to the reaction. The reaction was then stirred thoroughly for 2 days under nitrogen at room temperature. The reaction was then filtered and the solid residue was rinsed with DCM (3 x 100 mL). . Evaporation of the organic filtrate gave crude product, which upon further purification by FCC using 20% EtOAc in hexane gave **6.8** as colorless oil (12.0g, 95% yield). $[\alpha]^{25}_D$= -21.0 (*c* = 0.01, $CHCl_3$); IR ν_{max}(neat)/cm^{-1} 2934, 1778, 1698, 1383, 1107; δ_H (500 MHz, $CDCl_3$) 7.39-7.23 (8H, m), 7.19 (2H, d, J= 7.0 Hz), 4.81 (1H, d, J= 11.5 Hz), 4.64 (1H, J= 11.5 Hz), 4.59-4.53 (1H, m), 4.34 (1H, d, J= 6.0 Hz), 4.14-4.03 (3H, m), 3.84 (1H, dd, J= 7.5, 6.5 Hz), 3.43 (3H, s), 3.34 (3H, s), 3.24 (1H, dd, J= 13.5, 3.5 Hz), 2.75 (1H, dd, J= 13.5, 9.5 Hz), 1.31 (3H, d, J= 7.0 Hz); δ_C (125 MHz, $CDCl_3$) 175.2, 153.3, 138.6, 135.5, 129.6 (2), 129.0 (2), 128.4 (2), 128.2 (2), 127.8, 127.4, 107.0, 79.8, 74.4, 66.1, 55.5, 55.4, 55.2, 39.5, 38.1, 13.8; *m/z* (ESIMS) found: 450.2 $(M+Na)^+$; calc'd: 450.2.



Benzyl protected aldol product **6.8** (1g, 2.34 mmol) was dissolved in 80% acetic acid (20 mL) and stirred for 12 hours at room temperature. The solvent 80% acetic acid was azeotroped with toluene (3 x 20 mL) and resulting crude product upon further purification by FCC using 15% EtOAc in hexane gave **6.3** as colorless viscous oil (841 mg, 94% yield). $[\alpha]^{25}_{D}$= -30.0 (*c* = 0.01, $CHCl_3$); IR ν_{max}(neat)/cm^{-1} 1778, 1730, 1693, 1390, 1212; δ_H (500 MHz, $CDCl_3$) 9.81 (1H, s), 7.38-7.22 (8H, m), 7.17 (2H, d, J= 7.0 Hz), 4.75 (1H, d, J= 12.5 Hz), 4.64-4.54 (1H, m), 4.59 (1H, d, J= 12.5 Hz), 4.32-4.24 (1H, m), 4.16-4.06 (2H, m), 3.92 (1H, d, J= 6.0 Hz), 3.20 (1H, dd, J= 13.5, 3.5 Hz), 2.76 (1H, dd, J= 13.5, 10 Hz), 1.33 (3H, d, J= 7.0 Hz); δ_C (125 MHz, $CDCl_3$) 202.0, 173.8, 153.1, 137.2, 135.1, 129.6 (2), 129.1 (2), 128.7 (2), 128.4, 128.3 (2), 127.5, 83.3, 73.1, 66.4, 55.4, 41.5, 37.8, 13.4; *m/z* (ESIMS) found: 404.2 $(M+Na)^+$; calc'd: 404.2.

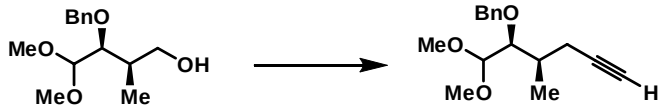


Compound **6.10** and **6.11** were prepared following the same procedure used for the synthesis of their antipods **6.7** and **6.8** respectively. The observed optical rotation ($[\alpha]^{25}_{D}$) for the compound **6.10** and **6.11** are +50.0 (*c* = 0.01, $CHCl_3$), and +21.0 (*c* = 0.01, $CHCl_3$) respectively.



6.11 **6.12**

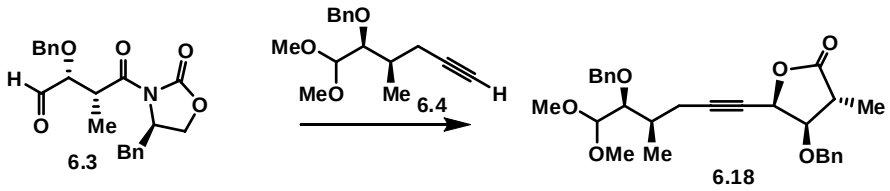
To a solution of **6.11** (6.8g, 15.9 mmol) in diethyl ether (200 mL), 0.2 mL methanol was added. The reaction mixture was cooled to 0^oC and to that 2 M THF solution of $LiBH_4$ (17.5 mL, 35 mmol) was added slowly under nitrogen. After all $LiBH_4$ added, the reaction was warmed slowly to room temperature over 2 hour. The reaction was then quenched with aqueous NH_4Cl (50 mL), extracted with ethyl acetate (3 x 200 mL), dried over anhydrous $MgSO_4$. . Evaporation of the organic filtrate gave crude product, which upon further purification by FCC using 15% EtOAc in hexane gave **6.12** as colorless oil (3.85g, 95% yield). $[\alpha]^{25}_D$= -33.0 (*c* = 0.01, $CHCl_3$); IR ν_{max}(neat)/cm^{-1} 3431, 2934, 1454, 1071; δ_H (500 MHz, $CDCl_3$) 7.38-7.32 (4H, m), 7.30-7.25 (2H, m), 4.82(1H, d, J= 11.5 Hz), 4.58 (1H, d, J= 11.5 Hz), 4.39 (1H, d, J= 6.5 Hz), 3.59 (1H, dd, J= 6.0, 3.5 Hz), 3.59-3.46 (2H, m), 3.49 (3H, s), 3.41 (3H, s), 2.02-1.96 (1H, m), 1.90 (1H, bs), 0.94 (3H, d, J= 7.0 Hz); δ_C (125 MHz, $CDCl_3$) 138.9, 128.5 (2), 128.2 (2), 127.8, 106.5, 79.6, 74.1, 65.8, 56.2, 54.6, 36.9, 11.4; *m/z* (ESIMS) found: 277.2 $(M+Na)^+$; calc'd: 277.2.



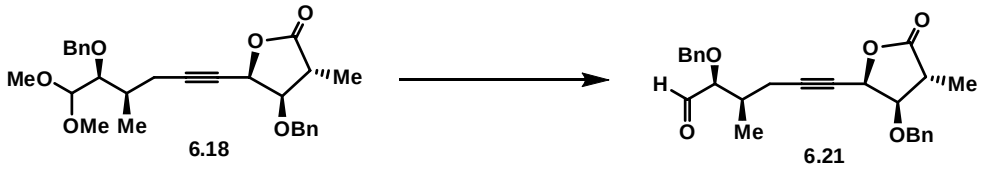
6.12 **6.4**

To a solution of **6.12** (3.84g, 14.94 mmol) in DCM (150 mL) was added pyridine (20 mL) and DMAP (366 mg, 3 mmol). The reaction mixture was cooled to 0^oC and to that tosyl chloride (3.7g, 19.4 mmol) was added. The reaction was then warmed to room temperature and stirred for 12 hours. The reaction was then diluted with 150 mL of DCM, washed with saturated $CuSO_4$ solution (3 x 50 mL), water (50 mL) and dried over anhydrous $MgSO_4$. . Evaporation of the organic filtrate gave crude tosylate, which was used as such for the next reaction.

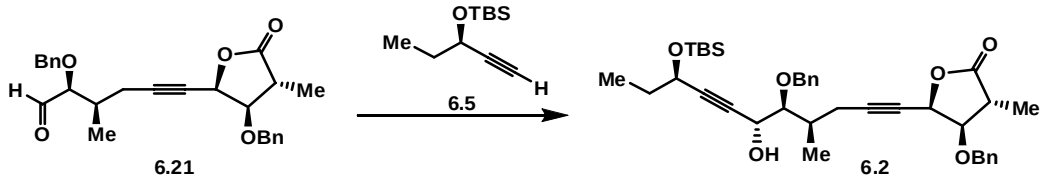
The tosylate was dissolved in dry DMSO (100 mL), and to that lithium acetylide-ethylenediamine (4gm, 4.45 mmol) was added at once. The reaction was vigorously stirred for 3 hours at room temperature. The reaction was then quenched with aqueous NH_4Cl (50 mL), diluted with ethyl acetate (300 ml), washed with water (3 x 100 mL) and dried over anhydrous $MgSO_4$. . Evaporation of the organic filtrate gave crude product, which upon further purification by FCC using 5% EtOAc in hexane gave **6.4** as colorless oil (3.42g, 82% yield). $[\alpha]^{25}_D$= -39.0 (*c* = 0.01, $CHCl_3$); IR ν_{max}(neat)/cm^{-1} 3295, 2935, 2116, 1096; δ_H (500 MHz, $CDCl_3$) 7.38-7.30 (4H, m), 7.28-7.22 (1H, m), 4.68 (1H, d, J= 11.5 Hz), 4.56 (1H, d, J= 11.5 H), 4.36 (1H, d, J= 7.0 Hz), 3.65 (1H, dd, J= 7.0, 3.0 Hz), 3.47 (3H, s), 3.38 (3H, s), 2.23- 2.12 (2H, m), 2.10- 2.00 (1H, m), 1.96 (1H, t, J= 7.5 Hz), 0.98 (3H, d, J= 7.0 Hz); δ_C (125 MHz, $CDCl_3$) 139.3, 128.4 (2), 127.9 (2), 127.6, 106.4, 83.7, 80.3, 74.8, 69.6, 56.0, 53.8, 34.4, 23.5, 14.0; *m/z* (ESIMS) found: 285.1 $(M+Na)^+$; calc'd: 285.2.



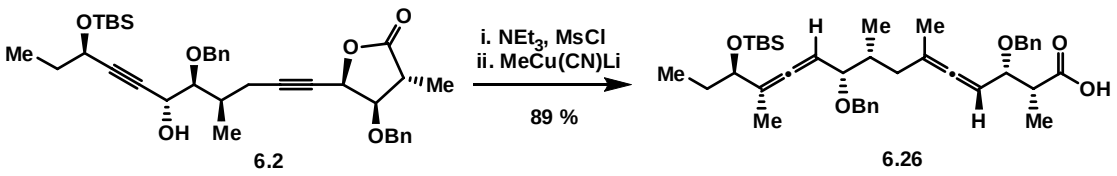
A solution of alkyne **6.4** (2.62g, 10 mmol) in diethyl ether (100 mL) was cooled to -40^{o}C and to that BuLi (4 mL, 10 mmol) was added slowly. The reaction mixture was warmed to 0^{o}C and cooled back to -40^{o}C and to that a solution of $ZnBr_2$ (2.3g, 10.2 mmol) in diethyl ether (20 mL) was added. The reaction was warmed to -10^{o}C and to that a solution of aldehyde 6.3 (3.81g, 10 mmol) in diethyl ether (15 mL) was added drop wise using a syringe pump for 1 hour. The reaction was then quenched with aqueous NH_4Cl (50 mL) at 0^{o}C, diluted with ethyl acetate (200 ml), washed with water (2 x 50 mL) and dried over anhydrous $MgSO_4$. . Evaporation of the organic filtrate gave crude product (8:1 ratio by ^{1}H NMR), which upon further purification by FCC using 10% EtOAc in hexane gave major isomer of **6.18** as colorless oil (2.65g, 57% yield). $[\alpha]^{25}_{D}$= +18.0 (*c* = 0.01, $CHCl_3$); IR ν_{max}(neat)/cm^{-1} 2935, 2238, 1786, 1454 ; δ_H (500 MHz, $CDCl_3$) 7.38-7.24 (10 H, m), 5.12 (1H, td, J= 2.0 Hz, 6.5 Hz), 4.82 (1H, d, J=11.5 Hz), 4.72 (1H, d, J= 12.0 Hz), 5.53 (1H, d, J= 11.5 Hz), 4.51 (1H, d, J= 11.5 Hz), 3.88 (1H, dd, J= 9.5, 6.5 Hz), 3.57 (1H, dd, J= 10.0, 7.0 Hz), 3.47 (3H, s), 3.37 (3H, s), 2.86-2.76 (1H, m), 2.38-2.20 (2H, m), 2.10-2.00 (1H, m), 1.25 (3H, d, J= 7.0 Hz), 0.99 (3H, d, J= 7.0 Hz); δ_C (125 MHz, $CDCl_3$) 176.0, 139.1, 137.1, 128.8 (2), 128.5 (2), 128.4, 128.1 (2), 127.9 (2), 127.7, 106.4, 90.5, 81.0, 80.5, 74.7, 73.9, 72.4, 70.5, 56.1, 54.1, 39.4, 34.4, 24.0, 14.0, 12.7; *m/z* (ESIMS) found: 489.3 $(M+Na)^{+}$; calc'd: 489.2.



Alkyne **6.18** (2.26g, 4.85 mmol) was dissolved in 100 mL solution of acetic acid, TFA and water (4:1:1) at room temperature and stirred for 8. The solvent was azeotroped with toluene (3 x 100 mL) and resulting crude product upon further purification by FCC using 10% EtOAc in hexane gave **6.21** as colorless viscous oil (1.83g, 90% yield). $[\alpha]^{25}_{D}$= +22.0 (*c* = 0.01, $CHCl_3$); IR ν_{max}(neat)/cm^{-1} 2935, 2240, 1786, 1730, 1455 ; δ_H (500 MHz, $CDCl_3$) 9.65 (1H, s), 7.4-7.25 (10H, m), 5.11 (1H, d, J= 6 Hz), 4.67 (2H, d, J= 13 Hz), 4.54 (1H, d, J= 11.5 Hz), 4.46 (1H, d, J= 12 Hz), 3.95-3.85 (2H, m), 2.85-2.75 (1H, m), 2.48-2.26 (2H, m), 2.26- 2.16 (1H, m), 1.27 (3H, d, J= 7.0 Hz), 1.01 (3H, d, J= 6.5 Hz); δ_C (125 MHz, $CDCl_3$) 204.3, 175.9, 137.6, 137.1, 128.8 (2), 128.7 (2), 128.5, 128.3, 128.2 (2), 128.0 (2), 89.2, 85.1, 81.0, 74.9, 73.4, 72.4, 70.4, 39.4, 35.2, 23.1, 14.5, 12.7; *m/z* (ESIMS) found: 443.2 $(M+Na)^+$; calc'd: 443.2.

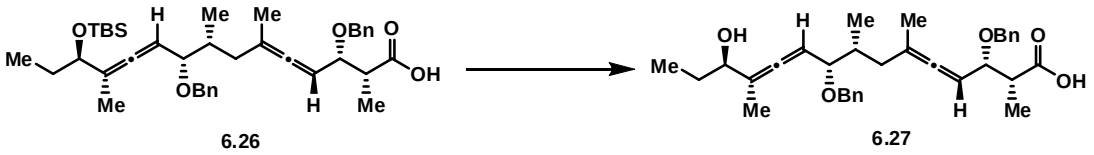


A solution of alkyne **6.5** (1.3g, 6.56 mmol) in THF (100 mL) was cooled to -40^{o}C and to that MeLi (4.1 mL, 6.56 mmol) was added slowly. The reaction mixture was warmed to 0^{o}C and cooled back to -40^{o}C and to that a 1 M hexane solution of titaniumtriisoprpoxy chloride (6.5 mL, 6.5 mmol) was added. The reaction was warmed to -0^{o}C, cooled back to -40^{o}C and to that a solution of aldehyde **6.21** (1.83g, 4.36 mmol) in THF (10 mL) was added slowly. The reaction was then warmed slowly to room temperature over 2 hour. The reaction was then diluted with ethyl acetate (200 ml), washed with water (50 mL) and dried over anhydrous $MgSO_4$. . Evaporation of the organic filtrate gave crude product (6:1 ratio by ^{1}H NMR) which upon further purification by FCC using 10% EtOAc in hexane gave major isomer of **6.2** as colorless oil (1.93g, 72% yield). δ_H (300 MHz, $CDCl_3$) 7.16-7.44 (10H, m), 5.11 (1H, td, J= 2.1 Hz, 6.0 Hz), 4.76 (1H, d, J= 12.0 Hz), 4.72 (1H, d, J= 12.0 Hz), 4.58 (1H, d, J= 12.0 Hz), 4.53 (1H, J= 12.0 Hz), 4.43-4.54 (1H, m), 4.32 (1H, t, J= 6.6 Hz), 3.87 (1H, dd, J= 9.6, 6.6 Hz), 3.58 (1H, dd, J= 5.4, 5.4 Hz), 2.88-2.76 (1H, m), 2.46-2.13 (1H, m), 1.75- 1.60 (1H, m), 1.24 (3H, d, J= 7.2 Hz), 1.06 (3H, d, J= 6.9 Hz), 0.87 (9H, s), 0.08 (3H, s), 0.10 (3H, s).

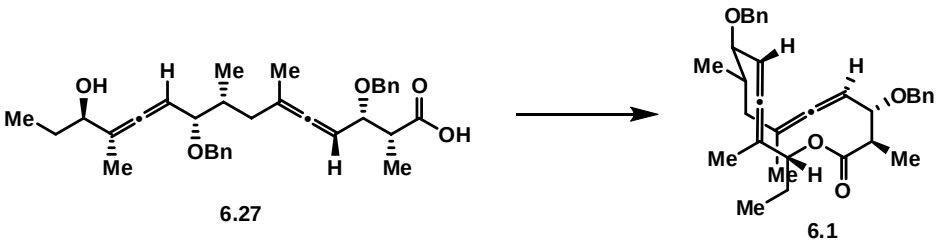


To a solution of **6.2** (1.53g, 2.47 mmol) in 50mL ether was added Et_3N (377 mg, 3.71 mmol) and MsCl (424 mg, 3.71mmol) respectively at 0^oC. The reaction mixture was warmed to room temperature and stirred for 1 hour at room temperature. The reaction was then cooled back to 0^oC and to that was added a solution of methyl cyanocuprate, prepared from CuCN (1.32g, 14.8 mmol) and MeLi (9.2mL, 14.7 mmol) in 75 ml Et_2O. The reaction mixture was then warmed to room temperature and stirred for 2h. The reaction was then quenched with aqueous NH_4Cl (50 mL), extracted in diethyl ether (3 x 100 mL), washed with water (100 mL), dried over anhydrous $MgSO_4$. Evaporation of solvent gave crude product which upon FCC purification using 30% EtOAc in hexanes gave bis[allene] **6.26** (1.39g, 89% yield) as a colorless oil. $[\alpha]^{25}_D$= +47 (*c* = 0.01, $CHCl_3$); IR ν_{max}(neat)/cm^{-1} 2929, 1965, 1710, 1456, 1066; δ_H (500 MHz, $CDCl_3$) 7.36-7.26 (10H, m), 5.05-4.90 (2H, m), 4.70 (1H, d, J= 11.5 Hz), 4.69 (1H, d, J=11.5 Hz), 4.43 (1H, d, J= 11.5 Hz), 4.39 (1H, d, J= 12.0 Hz), 4.03 (1H, dd, J= 8.0 Hz, 6.0 Hz), 4.00 (1H, t, J= 6.0 Hz), 3.66 (1H, dd, J= 9.5, 5.5 Hz), 2.84-2.72 (1H, m), 2.42- 2.32 (1H, m), 1.95-1.85 (1H, m), 1.72 (3H, d, J= 3.0 Hz), 1.65 (3H, d, J= 3.0 Hz), 1.60-1.50 (2H, m), 1.24 (3H, d, J= 7.0 Hz), 0.98 (3H, d, J= 6.5 Hz), 0.88 (9H, s), 0.85 (3H, t, J= 7.5 hz), 0.02 (3H, s), 0.00 (3H, s) ; δ_C (125 MHz, $CDCl_3$) 203.9, 202.9, 177.0, 138.9, 137.8, 128.6 (2), 128.5 (2), 128.0 (4),

127.8, 127.6, 102.5, 100.0, 89.7, 87.7, 82.2, 79.8, 75.8, 70.7, 70.2, 37.7, 36.7, 29.5, 26.1 (3), 19.0, 18.4, 15.7, 13.8, 12.9, 10.3, -4.3, -4.8; *m/z* (ESIMS) found: 655.4 $(M+Na)^+$; calc'd: 655.4.

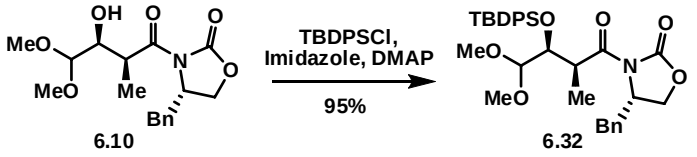


Bis[allene] **6.26** (1.39g, 2.2 mmol) was dissolved in 80% acetic acid (50 mL) and stirred for 8 hours at room temperature. The solvent 80% acetic acid was azeotroped with toluene (3 x 50 mL) and resulting crude product upon further purification by FCC using 50% EtOAc in hexane gave **6.27** as colorless oil (1.14g, 88% yield). $[\alpha]^{25}_D$= +45.0 (*c* = 0.01, $CHCl_3$); IR ν_{max}(neat)/cm^{-1} 3388, 2933, 1965, 1710, 1454; δ_H (500 MHz, $CDCl_3$) 7.36-7.27 (10H, m), 5.18-5.10 (1H, m), 5.08-5.02 (1H, m), 4.70 (1H, d, J= 11.5 Hz), 4.68 (1H, d, J= 12.0 Hz), 4.45 (1h, d, J= 11.5 Hz), 4.41 (1H, d, J= 12.0 Hz), 4.04 (1H, dd, J= 7.0, 7.0 Hz), 3.99 (1H, t, J= 6.5 Hz), 3.69 (1H, dd, J= 8.5, 5 Hz), 2.84-2.76 (1H, m), 2.38-2.32 (1H, m), 1.94-1.84 (1H, m), 1.75 (3H, d, J= 3 Hz), 1.67 (3H, d, J= 2.5 Hz), 1.66-1.50 (2H, m), 1.23 (3H, d, J= 7 Hz), 0.98 (3H, d, J= 6.5 Hz), 0.90 (3H, t, J= 7 Hz); δ_C (125 MHz, $CDCl_3$) 203.6, 201.7, 175.7, 138.9, 137.7, 128.7 (2), 128.5 (2), 128.1, 128.1 (2), 127.8 (2), 127.7, 103.4, 100.6, 92.5, 88.0, 82.1, 79.3, 74.2, 70.7, 70.4, 44.4, 37.6, 37.0, 27.9, 19.4, 15.4, 15.1, 13.3, 9.8; *m/z* (ESIMS) found: 541.3 $(M+Na)^+$; calc'd: 541.3.

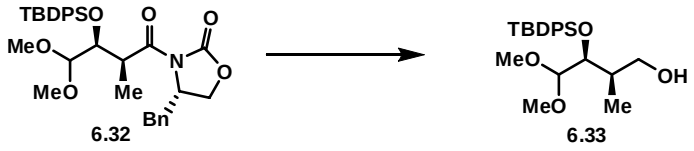


Seco acid **6.27** (960 mg, 1.853 mmol) was azeotroped with benzene (2 x 10 mL) and then dissolved in 20 mL toluene. To that TEA (0.94g, 9.26 mmol) and 2,4,6-trichlorobenzoyl chloride (2.26g, 9.26 mmol) was added at room temperature. The reaction mixture was then stirred for 6 hours at room temperature. The resulting active ester was added dropwise by syringe pump for 2 hours to a solution of DMAP (2.26g, 18.5 mmol) in toluene (800 mL) at 60^{o}C. The reaction was then cooled to room temperature and quenched with aqueous NH_4Cl (100 mL). The organic layer was separated, washed with water (2 x 100 mL) and dried over anhydrous $MgSO_4$. Evaporation of solvent gave the crude product which upon FCC purification using 5% EtOAc in hexanes gave bis[allene] macrolactone **6.1** (612mg, 66% yield) as a colorless oil. $[\alpha]^{25}_{D}$= -50.0 (*c* = 0.01, $CHCl_3$); IR ν_{max}(neat)/cm^{-1} 2970, 1961, 1731, 1454, 1248; δ_H (500 MHz, $CDCl_3$) 7.35-7.26 (10H, m), 5.36 (1H, t, J= 7.0 Hz), 5.16-5.10 (1H, m), 5.10-5.03 (1H, m), 4.65 (1H, d, J= 12.0 Hz), 4.58 (1H, d, J= 12.0 Hz), 4.43 (1H, d, J= 11.5 Hz), 4.37 (1H, d, J= 12.0 Hz), 3.89 (1H, dd, J= 8.0, 4.0 Hz), 3.83 (1H, dd, J= 9.5, 4.5 Hz), 2.82-2.74 (1H, m), 2.00-1.90 (3H, m), 1.72 (3H, d, J= 3.0 Hz), 1.72-1.60 (2H, m), 1.65 (3H, d, J= 3.0 Hz), 1.28 (3H, d, J= 7.0 Hz), 1.02 (3H, d, J= 6.5 Hz), 0.89 (3H, t, J= 7.5 Hz); δ_C (125 MHz, $CDCl_3$) 204.6, 202.6, 172.8, 139.1, 138.8, 128.6 (2), 128.4 (2), 128.1 (2), 128.0 (2), 127.7, 127.6, 102.0, 98.4, 92.3, 91.1,

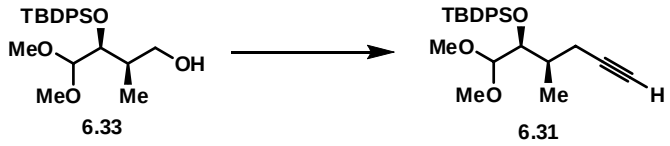
78.0, 76.9, 76.4, 70.4, 69.7, 46.0, 37.5, 36.4, 24.7, 21.5, 15.7, 14.7, 13.6, 9.9; *m/z* (ESIMS) found: 523.3 $(M+Na)^+$; calc'd: 523.3.



To a solution of 6.10 (674 mg, 2.0 mmol) in DCM (20 mL) were added imidazole (400mg, 5.8 mmol), TBDPSCl (1.65g, 6.0 mmol) and DMAP (100 mg, 0.82 mmol) at room temperature. The reaction was then then warmed to 40^{o}C and stirred for 12 hour at that temperature. The reaction was then diluted with DCM (200 mL), washed with water (2 x 50 mL) and dried over anhydrous $MgSO_4$. Evaporation of solvent gave the crude product which upon FCC purification using 10% EtOAc in hexanes gave **6.32** (1.10g, 95% yield) as a viscous colorless oil. IR ν_{max}(neat)/cm^{-1} 2932, 1781, 1700, 1111; δ_H (500 MHz, $CDCl_3$) 7.75 (2H, dd, J= 8.0 Hz, 2.0 Hz), 7.69 (2H, dd, J= 8.0 Hz, 2.0 Hz), 7.50- 7.10 (11H, m), 4.50-4.38 (1H, m), 4.20-4.00 (4H, m), 4.00 (1H, dd, J= 8.0, 8.0 Hz), 3.25 (1H, dd, J= 13.0, 3.0 Hz), 3.15 (3H, s), 2.73 (1H, dd, J= 13.5 Hz, 10 Hz), 2.70 (3H, s), 1.36 (3H, d, J= 6.5 Hz), 1.05 (9H, s); δ_C (125 MHz, $CDCl_3$) 175.2, 153.3, 136.3 (2), 136.0 (2), 135.8, 134.7, 133.6, 129.8, 129.7 (2), 129.5, 129.1 (2), 127.7 (2), 127.5 (2), 127.4, 106.2, 74.0, 66.2, 56.0, 54.5, 54.3, 39.7, 38.1, 27.2 (3), 20.0, 13.9; *m/z* (ESIMS) found: 598.3 $(M+Na)^+$; calc'd: 598.3.



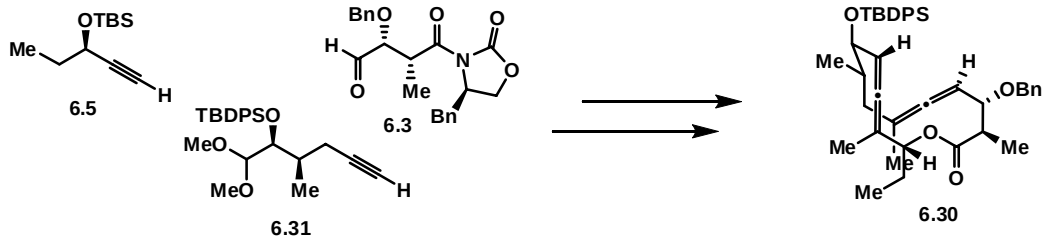
To a solution of **6.32** (16g, 27.8 mmol) in diethyl ether (200 mL), 5 mL methanol was added. The reaction mixture was cooled to 0^{o}C and to that 2 M THF solution of $LiBH_4$ (15 mL, 30 mmol) was added slowly under nitrogen. After all $LiBH_4$ added, the reaction was warmed slowly to room temperature over 2 hour. The reaction was then quenched with aqueous NH_4Cl (50 mL), extracted with ethyl acetate (3 x 200 mL), dried over anhydrous $MgSO_4$. . Evaporation of the organic filtrate gave crude product, which upon further purification by FCC using 15% EtOAc in hexane gave **6.33** as colorless oil (10.5g, 95% yield). IR ν_{max}(neat)/cm^{-1} 3426, 2932, 1473, 1112, 1062; δ_H (500 MHz, $CDCl_3$) 7.78-7.69 (4H, m), 7.45-7.36 (6H, m), 4.21 (1H, d, J= 5.0 Hz), 3.87 (1H, dd, J= 5.0, 3.0 Hz), 3.60-3.48 (2H, m), 3.21 (3H, m), 2.89 (3H, s), 2.05 (1H, d, J= 3.0 Hz), 2.04-1.95 (1H, m), 1.06 (9H, s), 1.01 (3H, d, J= 7.0 Hz); δ_C (125 MHz, $CDCl_3$) 136.3 (2), 136.1 (2), 134.8, 133.9, 129.9, 129.6, 127.8 (2), 127.5 (2), 106.1, 73.6, 65.4, 54.9, 54.2, 38.1, 27.3 (3), 20.0, 12.0; *m/z* (ESIMS) found: 425.2 $(M+Na)^+$; calc'd: 425.2.



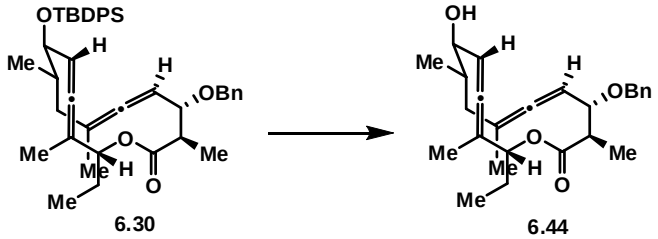
To a solution of **6.33** (1.6g, 3.98 mmol) in DCM (25 mL) was added pyridine (4 mL) and DMAP (100 mg, 0.82 mmol). The reaction mixture was cooled to 0^oC and to that tosyl chloride (915mg, 4.8 mmol) was added. The reaction was then warmed to room temperature and stirred for 12 hours. The reaction was then diluted with 50 mL of DCM, washed with saturated $CuSO_4$ solution (3 x 25 mL), water (25 mL) and dried over anhydrous $MgSO_4$. . Evaporation of the organic filtrate gave crude tosylate, which was used as such for the next reaction.

The tosylate was dissolved in dry DMSO (30 mL), and to that lithium acetylide-ethylenediamine (0.51g, 5.54 mmol) was added at once. The reaction was vigorously stirred for 3 hours at room temperature. The reaction was then quenched with aqueous NH_4Cl (20 mL), diluted with ethyl acetate (100 ml), washed with water (3 x 30 mL) and dried over anhydrous $MgSO_4$. . Evaporation of the organic filtrate gave crude product, which upon further purification by FCC using 3% EtOAc in hexane gave **6.31** as colorless oil (1.17g, 72% yield). $[\alpha]^{25}_D$= -2.0 (*c* = 0.01, $CHCl_3$); IR ν_{max}(neat)/cm^{-1} 3309, 2932, 2117, 1111; δ_H (500 MHz, $CDCl_3$) 7.79-7.74 (2H, m), 7.69-7.65 (2H, m), 7.42-7.33 (6H, m), 4.17 (1H, d, J= 7.0 Hz), 3.91 (1H, dd, J= 6.0, 2.0 Hz), 3.12 (3H, s), 2.70 (3H, s), 2.34-2.16 (2H, m), 2.08-2.00 (1H, m), 1.87 (1H, t, J= 2.5 Hz), 1.10 (3H, d, J= 6.5 Hz), 1.02 (9H, s); δ_C (125 MHz, $CDCl_3$) 136.3 (2), 135.9 (2), 135.4, 133.9, 129.6, 129.2, 127.6 (2), 127.3 (2), 105.1, 83.9, 74.1, 69.3,

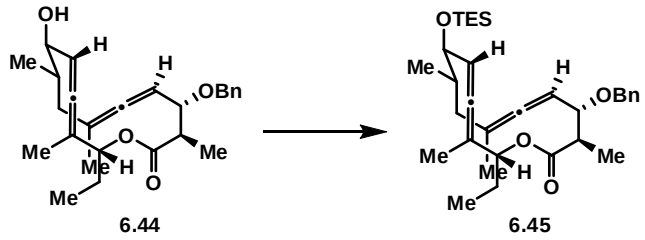
54.2, 52.8, 35.0, 27.4 (3), 23.8, 20.1, 14.0; *m/z* (ESIMS) found: 433.2 $(M+Na)^+$; calc'd: 433.2.



Bis[allene] macrolactone **6.30** was prepared from aldehyde **6.3**, alkyne **6.31** and alkyne **6.5** following similar procedure used to synthesise bis[allene] macrolactone **6.1**. $[\alpha]^{25}_D$= -41.0 (*c* = 0.01, $CHCl_3$); IR ν_{max}(neat)/cm^{-1} 2963, 1969, 1732, 1428, 1110; δ_H (500 MHz, $CDCl_3$) 7.71 (4H, d, J= 7.0 Hz), 7.44- 7.26 (11H, m), 5.40-5.32 (1H, m), 5.13 (1h, t, J= 6.5 Hz), 5.08- 5.02 (1H, m), 4.61 (1H, d, J= 12.0 Hz), 4.46 (1H, d, J= 11.5 Hz), 4.03 (1H, dd, J= 7.0, 7.0 Hz), 3.93 (1H, dd, J= 9.0, 4.0 Hz), 2.78-2.66 (1H, m), 2.08-2.00 (1H, m), 1.90- 1.82 (1H, m), 1.66 (3H, d, J= 3.0 Hz), 1.58-1.48 (3H, m), 1.32 (3H, d, J= 3.0 Hz), 1.25 (3H, d, J= 7.5 Hz), 1.07 (3H, d, J= 6.5 Hz), 1.04 (9H, s), 0.77 (3H, t, J= 7.5 Hz); δ_C (125 MHz, $CDCl_3$) 201.5 (2), 174.2, 138.9, 136.5 (2), 136.2 (2), 135.0, 134.9, 134.2, 129.8, 129.5, 128.5 (2), 127.9 (2), 127.7 (3), 127.5 (2), 102.8, 99.6, 95.4, 91.0, 77.0 (2), 75.8, 70.5, 45.2, 39.2, 38.0, 27.2 (3), 26.8, 25.0, 20.3, 19.8, 17.7, 15.6, 13.3, 9.7; *m/z* (ESIMS) found: 671.4 $(M+Na)^+$; calc'd: .

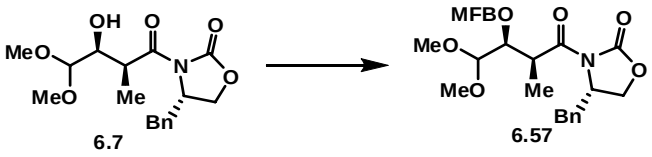


To a solution of **6.30** (350 mg, 0.54 mmol) in THF (5 mL), cooled at 0^{o}C, was added TBAF (3 mL, 3.0 mmol). The reaction was warmed to room temperature and stirred for 3 days. The reaction was then diluted with ethyl acetate (20 mL), washed with water (5 mL) and dried over anhydrous $MgSO_4$. . Evaporation of the organic filtrate gave crude product, which upon further purification by FCC using 10% EtOAc in hexane gave **6.44** as colorless oil (192 mg, 88% yield). δ_H (400 MHz, $CDCl_3$) 7.40-7.26 (5H, m), 5.48-5.38 (1H, m), 5.34-5.24 (1H, m), 5.29 (1H, t, J= 7.2 Hz), 4.63 (1H, d, J= 11.6 Hz), 4.54 (1H, d, J= 11.6 Hz), 4.07 (1H, dd, J= 8.4, 3.6 Hz), 3.79 (1H, dd, J= 8.8, 5.2 Hz), 2.84-2.72 (1H, m), 2.22-2.12 (1H, m), 1.90-1.40 (4H, m), 1.71 (3H, d, J= 2.8 Hz), 1.63 (3H, d, J= 2.8 Hz), 1.27 (3H, d, J= 6.8 Hz), 1.03 (3H, d, J= 6.8 Hz), 0.89 (3H, t, J= 7.2 Hz).



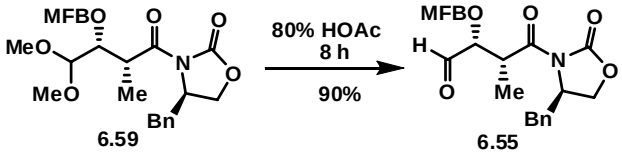
To a solution of **6.44** (192 mg, 0.476 mmol) in DCM (10 mL) were added TESCl (144mg, 0.95 mmol), Imidazole (98 mg, 1.43 mmol) and DMAP (10 mg, 0.08 mmol)

at room temperature. and stirred for 5 minutes. The reaction was then diluted with DCM (30 mL), washed with water (10 mL) and dried over anhydrous $MgSO_4$. . Evaporation of the organic filtrate gave crude product, which upon further purification by FCC using 5% EtOAc in hexane gave **6.45** as colorless oil (241 mg, 94% yield). $[\alpha]^{25}_D$= +37.0 (*c* = 0.01, $CHCl_3$); IR ν_{max}(neat)/cm^{-1} 2959, 1969, 1735, 1456, 1172; δ_H (500 MHz, $CDCl_3$) 7.36-7.25 (5H, m), 5.38-5.32 (1H, m), 5.21 (1H, t, J= 6.0 Hz), 5.16-5.10 (1H, m), 4.66 (1H, d, J=12.0 Hz), 4.49 (1H, d, J= 12.0 Hz), 3.94 (1H, t, J= 7.0 Hz), 3.92 (1H, dd, J= 8.5, 4.5 Hz), 2.82-2.74 (1H, m), 2.22-2.13 (1H, m), 1.76-1.64 (3H, m), 1.72 (3H, d, J= 3.0 Hz), 1.68 (3H, d, J= 3.0 Hz), 1.25 (3H, d, J= 6.5 Hz), 0.99 (3H, d, J= 7.0 Hz), 0.95 (9H, t, J= 8.0 Hz), 0.90 (3H, t, J= 7.5 Hz); δ_C (125 MHz, $CDCl_3$) 201.8, 201.5, 174.2, 138.9, 128.5 (2), 127.9 (2), 127.7, 102.8, 99.5, 96.1, 90.8, 75.9 (2), 70.4, 45.2, 39.4, 37.8, 25.2, 20.3, 17.5, 15.6, 14.0, 9.8, 7.1 (3), 5.3 (3); *m/z* (ESIMS) found: 547.3 $(M+Na)^+$; calc'd: 547.2.

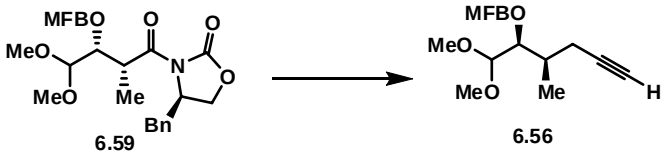


Aldol product **6.7** (7.8g, 23.11 mmol), Ag_2O (19g, 69.43 mmol) and 4Å powdered molecular sieve (12g) were mixed together and to that dry DCM (150 mL) was added. After stirring for 10 minutes at room temperature 3-flurobenzyl bromide (5.68 mL, 46.28 mmol) was added to the reaction. The reaction was then stirred thoroughly for 5 days under nitrogen at room temperature. The reaction was then filtered and the

solid residue was rinsed with DCM (3 x 100 mL). Evaporation of the organic filtrate gave crude product, which upon further purification by FCC using 20% EtOAc in hexane gave **6.57** as colorless oil (9.80g, 95% yield).

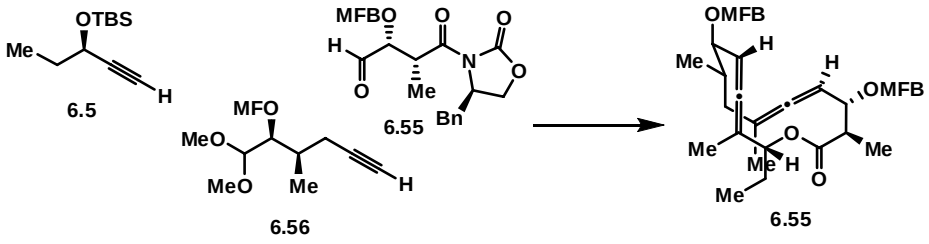


3-flurobenzyl protected aldol product **6.59** (5g, 11.23 mmol) was dissolved in 80% acetic acid (50 mL) and stirred for 12 hours at room temperature. The solvent 80% acetic acid was azeotroped with toluene (3 x 50 mL) and resulting crude product upon further purification by FCC using 15% EtOAc in hexane gave **6.3** as colorless viscous oil (4.25g, 95% yield).

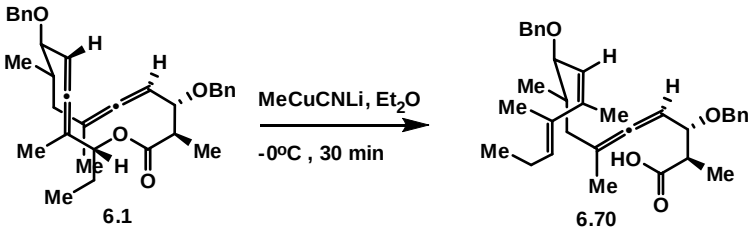


The alkyne **6.56** was prepared from **6.59** in 3 steps using same procedure used for the synthesis of alkyne **6.4**. IR ν_{max}(neat)/cm^{-1} 3306, 2936, 2117, 1789, 1592; δ_H (500 MHz, $CDCl_3$) 7.34-7.23 (1H, m), 7.14-7.03 (2H, m), 6.97-6.91 (1H, m), 4.86 (1H, d, J= 12.0 Hz), 4.56 (1H, d, J= 12.0 Hz), 4.37 (1H, d, J= 7.0 Hz), 3.66 (1H, dd, J= 7.0, 2.5 Hz), 3.47 (3H, s), 3.39 (3H, s), 2.32-2.12 (2H, m), 2.10-2.00 (1H, m), 1.97 (1H, t, J= 2.5 Hz), 0.99 (3H, d, J= 7.0 Hz); δ_C (125 MHz, $CDCl_3$) 164.0, 162.1, 142.0 (d, J= 69 Hz), 129.9 (d, J= 66 Hz), 123.1 (d, J= 29 Hz), 114.6, 114.4, 114.4, 114.2, 106.3,

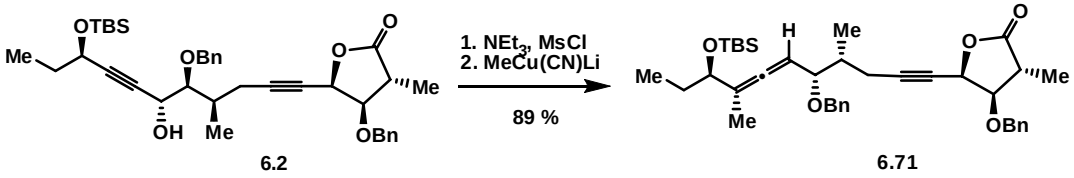
83.5, 80.4, 73.9 (d, J= 7.5 Hz), 69.7, 56.0, 53.8, 34.4, 23.4, 14.0; *m/z* (ESIMS) found: 303.2 $(M+Na)^+$; calc'd: 303.2.



Bis[allene] macrolactone **6.55** was prepared from aldehyde **6.55**, alkyne **6.56** and alkyne **6.5** following similar procedure used to synthesise bis[allene] macrolactone **6.1**. $[\alpha]^{25}_D$= -3.0 (*c* = 0.01, $CHCl_3$); IR ν_{max}(neat)/cm^{-1} 2917, 1969, 1732, 1592, 1174; δ_H (500 MHz, $CDCl_3$) 7.29-7.22 (2H, m), 7.11-7.01 (4H, m), 6.97-6.89 (2H, m), 5.38-5.30 (1H, m), 5.28 (1H, t, J= 6.5 Hz), 5.16-5.08 (1H, m), 4.64 (1H, d, J= 12.5 Hz), 4.52 (1H, d, J= 12.5 Hz), 4.48 (1H, d, J= 12.5 Hz), 4.31 (1H, d, J= 12.0 Hz), 3.96 (1H, dd, J= 8.0, 4.0 Hz), 3.77 (1H, dd, J= 7.0, 7.0 Hz), 2.86-2.76 (1H, m), 2.20-2.14 (1H, m), 2.04-1.94 (1H, m), 1.71 (3H, d, J= 3.0 Hz), 1.70 (3H, d, J= 3.0 Hz), 1.72-1.62 (2H, m), 1.26 (3H, d, J= 7.0 Hz), 1.05 (3H, d, J= 7.0 Hz), 0.90 (3H, t, J= 7.5 Hz); δ_C (125 MHz, $CDCl_3$) 203.8, 201.3, 173.8, 164.1 (d, J= 84 Hz), 162.1 (d, J= 89 Hz), 142.1(d, J= 75 Hz), 141.6 (d, J= 69 Hz), 129.9 (d, J= 46 Hz), 129.8 (d, J= 79 Hz), 123.1 (d, J= 27 Hz), 122.9 (d, J= 27 Hz), 114.6-114.3 (4C, m), 102.6, 99.3, 91.6, 90.5, 81.7, 77.9, 75.8, 70.0 (d, J= 17 Hz), 68.1 (d, J= 19 Hz), 44.9, 37.7, 35.9, 25.1, 20.5, 17.5, 15.3, 14.0, 9.9; *m/z* (ESIMS) found: 559.3 $(M+Na)^+$; calc'd: 559.3.



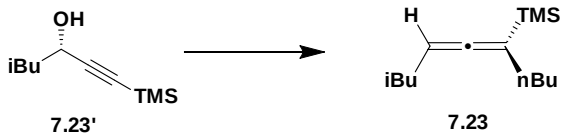
A solution of **6.1** (20 mg, 0.04 mmol) in diethyl ether (1 mL) was added to the lower order methyl cyanocuprate, prepared from CuCN (20 mg, 0.225 mmol) and MeLi (0.14 mL, 0.224 mmol) in 5 mL diethyl ether, at 0°C. The reaction was stirred for 30 minutes at 0°C and then was quenched with aqueous NH_4Cl (2 mL) at 0°C. The reaction was then diluted with ethyl acetate (10 ml), washed with water (5 mL) and dried over anhydrous $MgSO_4$. . Evaporation of the organic filtrate gave crude product which upon further purification by FCC using 20% EtOAc in hexane gave **6.70** as colorless oil (18 mg, 90% yield). IR ν_{max}(neat)/cm^{-1} 3088, 1965, 1709, 1454, 1066; δ_H (500 MHz, $CDCl_3$) 7.41-7.20 (10H, m), 5.14 (1H, d, J= 9.0 Hz), 5.12 (1H, t, J= 7.0 Hz), 5.00-4.90 (1H, m), 4.73 (1H, d, J= 12.0 Hz), 4.54 (1H, d, J= 12.0 Hz), 4.44 (1H, d, J= 11.5 Hz), 4.24 (1H, d, J= 12.0 Hz), 4.10-4.00 (1H, m), 3.93 (1H, dd, J= 9.5 Hz, 4.5 Hz), 2.88-2.72 (1H, m), 2.27-2.17 (1H, m), 2.08-1.74 (3H, m), 1.84 (3H, s), 1.68 (3H, s), 1.64 (3H, s), 1.25 (3H, d, J= 7.0 Hz), 0.96 (3H, d, J= 6.0 Hz), 0.91 (3H, t, J= 7.0 Hz); δ_C (125 MHz, $CDCl_3$) 204.1, 145.7, 139.7, 137.8, 134.2, 129.8, 128.7 (2), 128.4 (2), 128.1 (2), 128.0, 127.6 (2), 127.4, 124.5, 100.3, 87.4, 79.8, 70.8, 70.0, 38.2, 37.0, 23.8, 21.3, 19.0, 15.9, 15.5, 14.4; *m/z* (ESIMS) found: 539.3 $(M+Na)^+$; calc'd: 539.3.



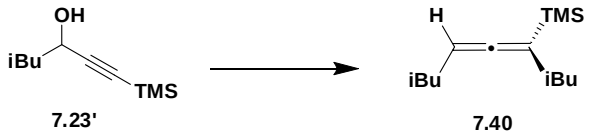
6.2 6.71

To a solution of **6.2** (600 mg, 0.987 mmol) in 20 mL DCM was added Et_3N (203 mg, 2.0 mmol) and MsCl (229 mg, 2 mmol) respectively at 0^{o}C. The reaction mixture was warmed to room temperature and stirred for 20 minutes at room temperature. The reaction was then diluted with DCM (50 ml), washed with water (2 x 20 mL), dried over anhydrous $MgSO_4$.. Evaporation of solvent gave crude mesylate which was added at -40^{o}C to the methyl cyanocuprate, prepared from CuCN (265 mg, 3.2 mmol) and MeLi (2.0 mL, 3.2 mmol) in 30 ml Et_2O. The reaction mixture was warmed to -10^{o}C over 30 minutes and then quenched with aqueous NH_4Cl (10 mL). The reaction mixture was then extracted in diethyl ether (3 x 50 mL), washed with water (50 mL), dried over anhydrous $MgSO_4$.. Evaporation of solvent gave crude product which upon FCC purification using 10% EtOAc in hexanes gave allene **6.71** (542 mg, 89% yield) as a colorless oil. δ_H (500 MHz, $CDCl_3$) 5.12 (1H, d, J= 6.0 Hz), 4.89-4.98 (1H, m), 4.71 (1H, d, J= 12.0 Hz), 4.67 (1H, d, J= 12.0 Hz), 4.53 (1H, d, J=12.0 Hz), 4.36 (1H, d, J= 12.0 Hz), 3.98 (1H, t, J= 6.0 Hz), 3.87 (1H, dd, J= 10.0, 7.0 Hz), 3.67 (1H, dd, J= 10.0, 6.5 Hz), 2.88-2.76 (1H, m), 2.68-2.78 (1H, m), 2.10-2.20 (1H, m), 1.87-1.99 (1H, m), 1.70 (3H, d, J= 3.0 Hz), 1.47-1.64 (3H, m), 1.25 (3H, d, J=7.0 Hz), 1.08 (3H, d, J= 7.0 Hz), 0.87 (9H, s), 0.85 (3H, t, J= 7.5 hz), 0.02 (3H, s), 0.00 (3H, s).

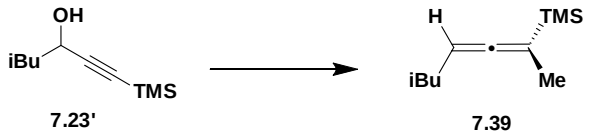
Experimental (Chapter VII)



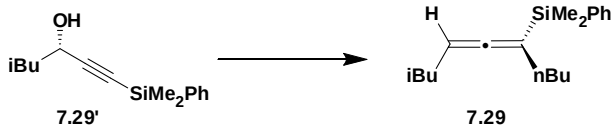
To a solution of propargylic alcohol **7.23'** (2g, 10.86 mmol) in diethyl ether (20 mL) were added Et_3N (1.65 gm, 16.30 mmol) and MsCl (1.85g, 16.30 mmol) respectively at 0^oC. The reaction was warmed to room temperature and stirred for 30 minutes and cooled back to 0^oC. To this resulting mesylate was added methyl cyanocuprate prepared from CuCN (2.9 gm, 32.6 mmol) and nBuLi (20 mL, 32.0 mmol) in 150 mL ether. The reaction was stirred at 0^oC for 30 minutes and then was quenched with aquous NH_4Cl (50 mL). The reaction was then extracted with Et_2O (3 x 100 ml), washed with water (100 ml), brine (100 ml) and dried over anhydrous $MgSO_4$. Evaporation of solvent and FCC purification using hexane gave allene **7.23** (2.21g, 91% yield) as a clear colorless oil. $[\alpha]^{25}_D$= -61.0 (*c* = 0.01, $CHCl_3$); IR ν_{max}(neat)/cm^{-1} 2956, 1933, 1465, 1247, 839; δ_H (400 MHz, $CDCl_3$) 4.80-4.69 (1H, m), 1.98-1.80 (4H, m), 1.66-1.54 (1H, m), 1.48-1.20 (4H, m), 0.91 (6H, d, J= 6.8 Hz), 0.89 (3H, t, J= 7.2 Hz), 0.06 (9H, s); δ_C (100 MHz, $CDCl_3$) 206.1, 95.7, 84.3, 38.6, 31.7, 29.4, 29.2, 22.7, 22.6, 22.5, 14.2, -1.2 (3); *m/z* (ESIMS) found: 225.1 $(M+H)^+$; calc'd: 225.2.



To a solution of propargylic alcohol **7.23'** (5g, 27.1 mmol) in diethyl ether (50 mL) were added Et_3N (3.05g, 30 mmol) and MsCl (3.43g, 30 mmol) respectively at 0^oC. The reaction was warmed to room temperature and stirred for 30 minutes and cooled back to 0^oC. To this resulting mesylate was added methyl cyanocuprate prepared from CuCN (5.3g, 60 mmol) and iBuMgBr (30 mL, 60 mmol) in 200 mL ether. The reaction was stirred at 0^oC for 30 minutes and then was quenched with aqueous NH_4Cl (50 mL). The reaction was then extracted with Et_2O (3 x 200 ml), washed with water (100 ml), brine (100 ml) and dried over anhydrous $MgSO_4$. Evaporation of solvent and FCC purification using hexane gave allene **7.40** (5.63g, 93% yield) as a clear colorless oil. IR ν_{max}(neat)/cm^{-1} 2955, 1934, 1466, 1248, 839; δ_H (500 MHz, $CDCl_3$) 4.77-4.71 (1H, m), 1.93-1.81 (4H, m), 1.79-1.70 (1H, m), 1.67-1.58 (1H, m), 0.93 (3H, d, J= 7.0 Hz), 0.93 (3H, d, J= 7.0 Hz), 0.92 (6H, J= 6.5 Hz), 0.09 (9H, s); δ_C (125 MHz, $CDCl_3$) 206.6, 94.5, 83.8, 39.5, 38.5, 29.3, 28.2, 22.9, 22.8, 22.7, 22.5, -1.1 (3); *m/z* (ESIMS) found: 225.1 $(M+H)^+$; calc'd: 225.2.



To a solution of propargylic alcohol **7.23'** (5g, 27.1 mmol) in diethyl ether (50 mL) were added Et_3N (3.05g, 30 mmol) and MsCl (3.43g, 30 mmol) respectively at 0^oC. The reaction was warmed to room temperature and stirred for 30 minutes and cooled back to 0^oC. To this resulting mesylate was added methyl cyanocuprate prepared from CuCN (5.3g, 60 mmol) and MeLi (37.5 mL, 60 mmol) in 200 mL ether. The reaction was stirred at 0^oC for 30 minutes and then was quenched with aqueous NH_4Cl (50 mL). The reaction was then extracted with Et_2O (3 x 200 mL), washed with water (100 mL), brine (100 mL) and dried over anhydrous $MgSO_4$. Evaporation of solvent and FCC purification using hexane gave allene **7.39** (5.76g, 95% yield) as a clear colorless oil. IR ν_{max}(neat)/cm^{-1} 2956, 1939, 1248, 839; δ_H (500 MHz, $CDCl_3$) 4.72-4.66 (1H, m), 1.84 (1H, t, J= 7.0 Hz), 1.67 (3H, d, J= 3.0 Hz), 1.64-1.56 (1H, m), 0.91(6H, d, J= 7.0 Hz), 0.07 (9H, s); δ_C (125 MHz, $CDCl_3$) 206.5, 90.4, 82.8, 38.3, 29.1, 22.6, 22.4, 16.1, -1.6 (3); *m/z* (ESIMS) found: 183.4 $(M+H)^+$; calc'd: 183.2.

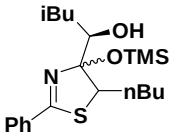


To a solution of propargylic alcohol **7.29'** (1g, 4.06 mmol) in diethyl ether (15 mL) were added Et_3N (610 mg, 6.0 mmol) and MsCl (687 mg, 6 mmol) respectively at 0^oC. The reaction was warmed to room temperature and stirred for 30 minutes and

cooled back to 0°C. To this resulting mesylate was added methyl cyanocuprate prepared from CuCN (2.1g, 24 mmol) and nBuLi (15 mL, 24.0 mmol) in 100 mL ether. The reaction was stirred at 0°C for 30 minutes and then was quenched with aqueous NH_4Cl (50 mL). The reaction was then extracted with Et_2O (3 x 100 ml), washed with water (100 ml), brine (100 ml) and dried over anhydrous $MgSO_4$. Evaporation of solvent and FCC purification using hexane gave allene **7.29** (1.06g, 92% yield) as a clear colorless oil. $[\alpha]^{25}_D$= -21.0 (*c* = 0.01, $CHCl_3$); IR ν_{max}(neat)/cm^{-1} 2956, 1933, 1428, 1111, 812; δ_H (500 MHz, $CDCl_3$) 7.55-7.49 (2H, m), 7.38-7.30 (3H, m), 4.84-4.78 (1H, m), 1.95-1.84 (4H, m), 1.66-1.55 (1H, m), 1.43- 1.21 (4H, m), 0.91 (6H, d, J= 6.5 Hz), 0.82 (3H, t, J= 7.0 Hz), 0.34 (6H, s); δ_C (125 MHz, $CDCl_3$) 207.3, 138.9, 134.1 (2), 129.1, 127.9 (2), 94.4, 85.0, 38.6, 31.5, 29.5, 29.3, 22.7, 22.6, 22.5, 14.2, -2.5, -2.6; *m/z* (ESIMS) found: 287.2 $(M+H)^+$; calc'd: 287.2.

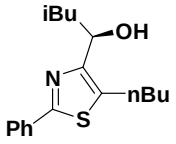
General procedure of forming silyl substituted SDE

To a solution of freshly prepared dimethyldioxirane (DMDO) in $CHCl_3$ (~0.20 M, 2.5 equiv.) was added the silyl allene in $CHCl_3$ dropwise at -40^oC. The reaction was stirred under nitrogen and let to warm to room temperature over 2 h. Solvent was evaporated and the resulting SDE was dried under vacuum and then used for the next step.



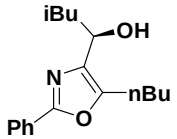
7.26

Allene **7.23** (50 mg, 0.223 mmol) was oxidized to SDE using general procedure. SDE was dissolved in chloroform (5 mL) and to that thiobenzamide (90 mg, 0.657 mmol) was added at room temperature, and stirred for 12 hours. Evaporation of solvent gave the crude product which upon FCC using 5% EtOAc in hexane gave **7.26** (72 mg, 82% yield) MP 86.0; IR ν_{max}(neat)/cm^{-1} 3305, 1570, 1465, 1247, 1140; δ_H (400 MHz, $CDCl_3$) 7.86 (2H, dd, J= 8.0, 1.6 Hz), 7.52-7.38 (3H, m), 4.14 (1H, dd, J= 11.2, 3.2 Hz), 3.91-3.83 (1H, m), 1.96-1.84 (3H, m), 1.64-1.32 (7H, m), 0.97 (3H, d, J= 6.8 Hz), 0.93 (3H, t, J= 6.8 Hz), 0.92 (3H, d, J= 6.4 Hz), 0.13 (9H, s); δ_C (100 MHz, $CDCl_3$) 170.3, 133.2, 131.9, 128.7 (2), 128.6 (2), 111.0, 75.2, 55.4, 39.5, 32.8, 32.0, 25.1, 24.2, 22.9, 21.9, 14.2, 2.0 (3); *m/z* (ESIMS) found: 394.2 $(M+H)^+$; calc'd: 394.2.



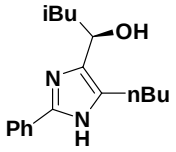
7.28

Allene **7.23** (100 mg, 0.446 mmol) was oxidized to SDE using general procedure. SDE was dissolved in methanol (10 mL) and to that thiobenzamide (183mg, 1.33 mmol) was added at room temperature, and stirred for 12 hours. Methanol was evaporated and crude product was dissolved in chloroform (10 mL) and to that PTSA (5 mg, 0.029 mmol) was added. The reaction was refluxed for two hours then cooled to room temperature. The reaction was then diluted with chloroform (40 mL), washed with water (10 mL), and dried over anhydrous $MgSO_4$. Evaporation of solvent gave the crude product which upon FCC using 5% EtOAc in hexane gave **7.28** (108 mg, 80% yield) $[\alpha]^{25}_D$= -18.0 (*c* = 0.01, $CHCl_3$, 95% ee); IR ν_{max}(neat)/cm^{-1} 3418, 2955, 1464, 761; δ_H (400 MHz, $CDCl_3$) 7.89 (2H, d, J= 7.6 Hz), 7.45-7.34 (3H, m), 4.80 (1H, dd, J= 8.0, 7.5 Hz), 2.79 (2H, t, J= 7.6 Hz), 2.76-2.58 (1H, bs), 1.92-1.76 (2H, m), 1.70-1.52 (3H, m), 1.48-1.37 (2H, m), 0.97 (3H, d, J= 6.4 Hz), 0.97 (3H, d, J= 6.8 Hz), 0.95 (3H, t, J= 7.2 Hz); δ_C (100 MHz, $CDCl_3$) 165.0, 155.0, 134.0, 133.8 (2), 129.8, 129.0 (2), 126.4 (2), 66.8, 47.9, 34.4, 26.0, 24.9, 23.6, 22.5, 22.4, 14.0; *m/z* (ESIMS) found: 304.4 $(M+H)^+$; calc'd: 304.2.



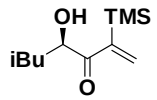
7.30

Allene **7.23** (100 mg, 0.446 mmol) was oxidized to SDE using general procedure. SDE was dissolved in methanol (5 mL) and to that benzamide (270 mg, 2.23 mmol) was added at room temperature, and stirred for 48 hours. Methanol was evaporated and crude product was dissolved in chloroform (10 mL) and to that PTSA (5 mg, 0.029 mmol) was added. The reaction was refluxed for two hours then cooled to room temperature. The reaction was then diluted with chloroform (40 mL), washed with water (10 mL), and dried over anhydrous $MgSO_4$. Evaporation of solvent gave the crude product which upon FCC using 10% EtOAc in hexane gave **7.28** (66 mg, 52% yield) $[\alpha]^{25}_D$= -19.0 (*c* = 0.01, $CHCl_3$, 90% ee) IR ν_{max}(neat)/cm^{-1} 3389, 2956, 1630, 1556, 1450; δ_H (500 MHz, $CDCl_3$) 8.00 (2H, d, J= 7.5 Hz), 7.47-7.38 (3H, m), 4.70 (1H, td, J= 7.0, 7.0 Hz), 2.72 (2H, t, J= 7.5 Hz), 2.22 (1H, d, J= 7.0 Hz), 1.92-1.58 (5H, m), 1.46-1.36 (2H, m), 0.96 (6H, d, J= 6.5 Hz), 0.96 (3H, t, J= 6.5 Hz); δ_C (125 MHz, $CDCl_3$) 160.0, 148.0, 138.4, 130.1, 128.9 (2), 128.0, 126.4 (2), 65.1, 46.6, 30.8, 24.9, 24.8, 23.2, 22.5 (2), 14.0; *m/z* (ESIMS) found: 288.1 $(M+H)^+$; calc'd: 288.2.



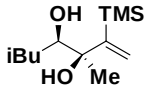
7.31

Allene **7.23** (50 mg, 0.223 mmol) was oxidized to SDE using general procedure. SDE was dissolved in methanol (10 mL) and to that a DCM solution of benzamidine (2ml, 0.10 mmol) was added at room temperature, and stirred for 12 hours. Evaporation of solvent gave the crude product which upon FCC using 50% EtOAc in hexane gave **7.31** (91 mg, 71% yield) $[\alpha]^{25}_{D}$= -20.0 (*c* = 0.01, $CHCl_3$)MP: 156°C; IR ν_{max}(neat)/cm^{-1} 3176, 2956, 1464, 989; δ_H (500 MHz, D_2O) 7.85 (2H, d, J= 8.0 Hz), 7.42 (1H, d, J= 7.5 Hz), 7.40 (1H, d, J= 7.5 Hz), 7.33 (1H, dd, J= 7.5, 7.5 Hz), 4.81 (1H, t, J= 7.0 Hz), 3.36- 3.26 (1H, m), 2.65 (2H, t, J= 7.5 Hz), 1.89-1.81 (1H, m), 1.74-1.58 (4H, m), 1.48-1.38 (2H, m), 0.97 (3H, t, J= 7.5 Hz), 0.96 (3H, d, J= 7.0 Hz), 0.93 (3H, d, J= 6.0 Hz); δ_C (125 MHz, CD_3CN) 146.8, 131.9, 129.9 (2), 129.5, 126.7 (2), 65.7, 47.4, 34.0, 26.2, 23.8, 23.5, 23.0, 14.4; *m/z* (ESIMS) found: 287.2 $(M+H)^+$; calc'd: 287.2.



7.41

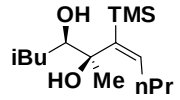
Allene **7.39** (50 mg, 0.274) was oxidized to SDE using general procedure. In a separate flask, Cp_2TiCl (136 mg, 0.548 mmol) and Zn (89 mg, 1.36 mmol) was dissolved in dry THF (3 mL) and stirred for 15 minutes at room themperature, then cooled to -60^{o}C. The resulting reagent was transferred via canula to the THF (2 mL) solution of SDE at -60^{o}C and stirred at that temperature for 10 minutes. The reaction was then quenched with 10% HCl (5 mL), extracted with ethyl acetate (30 mL), washed with water (2 x 5 mL), dried over anhydrous $MgSO_4$. Evaporation of solvent gave crude product which upon FCC using 10% EtOAc in hexane gave **7.41** as colorless oil (39 mg, 66% yield). IR ν_{max}(neat)/cm^{-1} 3474, 2957, 1668, 1249, 842; δ_H (500 MHz, $CDCl_3$) 6.36 (1H, d, J= 1.5 Hz), 6.19 (1H, d, J= 1.5 Hz), 4.78-4.70 (1H, m), 3.45 (1H, d, J= 6.5 Hz), 2.02-1.90 (1H, m), 1.46-1.28 (2H, m), 1.00 (3H, d, J= 6.5 Hz), 0.94 (3H, d, J= 7.0 Hz), 0.18 (9H, s); δ_C (125 MHz, $CDCl_3$) 208.2, 151.3, 136.3, 71.8, 44.9, 25.2, 23.9, 21.4, -1.3 (3); *m/z* (ESIMS) found: 215.8 $(M+H)^+$; calc'd: 215.2.



7.44

Allene **7.39** (50 mg, 0.274) was oxidized to SDE using general procedure. SDE was dissolve in diethyl ether (5 mL) and cooled to -40^{o}C. To that MeLi (0.5 mL, 8 mmol) was added dropwise. The reaction was then slowly warmed to room temperature over

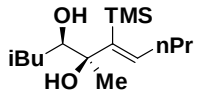
2 hour. The reaction was then quenched with aqueous NH_4Cl (1 mL) at 0^oC, diluted with ethyl acetate (20 ml), washed with water (5 mL) and dried over anhydrous $MgSO_4$. . Evaporation of the organic filtrate gave crude product which upon FCC using 10% EtOAc in hexane gave **7.44** as colorless oil (54 mg, 85% yield). IR ν_{max}(neat)/cm^{-1} 3444, 2955, 1468, 1245, 838; δ_H (500 MHz, $CDCl_3$) 5.55 (1H, d, J= 1.5 Hz), 5.43 (1H, d, J= 2.0 Hz), 3.56 (1H, d, J= 8.5 Hz), 2.07 (1H, s), 2.05-2.00 (1H, bs), 1.80-1.70 (1H, m), 1.33 (3H, s), 1.36-1.16 (2H, m), 0.90 (3H, d, J= 7.0 Hz), 0.84 (3H, d, J= 6.5 Hz), 0.13 (9H, s); δ_C (125 MHz, $CDCl_3$) 158.5, 124.1, 80.2, 75.3, 40.2, 28.1, 24.9, 24.3, 21.5, 0.6 (3); *m/z* (ESIMS) found: 253.2 $(M+Na)^+$; calc'd: 253.2.



7.45 (E)

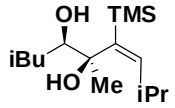
Allene **7.23** (50 mg, 0.223) was oxidized to SDE using general procedure. SDE was dissolve in diethyl ether (5 mL) and cooled to -40^oC. To that MeLi (0.35 mL, 5.6 mmol) was added dropwise. The reaction was then slowly warmed to room temperature over 2 hour. The reaction was then quenched with aqueous NH_4Cl (1 mL) at 0^oC, diluted with ethyl acetate (20 ml), washed with water (5 mL) and dried over anhydrous $MgSO_4$. . Evaporation of the organic filtrate gave crude product which upon FCC using 10% EtOAc in hexane gave **7.45** as 2.2:1 (E:Z) mixture of isomers (50 mg, 83% yield). Majore isomer: IR ν_{max}(neat)/cm^{-1} 3430, 2956, 1466, 1251, 838; δ_H (500 MHz, $CDCl_3$) 5.58 (1H, t, J= 7.0 Hz), 3.92 (1H, d, J= 10.5 Hz), 2.16-1.92 (2H, m), 1.82-1.78 (2H, m), 1.48-1.20 (4H, m), 1.42 (3H, s), 0.93 (3H, d, J= 6.5 Hz),

0.91 (3H, t, J= 7.0 Hz), 0.88 (3H, d, J= 6.5 Hz), 0.12 (9H, s); δ_C (125 MHz, $CDCl_3$) 148.0, 139.1, 80.2, 74.2, 40.8, 33.8, 27.3, 24.7, 24.4, 23.1, 21.4, 14.1, 1.4 (3); *m/z* (ESIMS) found: 295.2 $(M+Na)^+$; calc'd: 295.2.



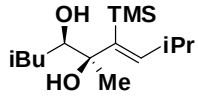
7.45 (Z)

Allene **7.23** (50 mg, 0.223) was oxidized to SDE using general procedure. SDE was dissolve in diethyl ether (5 mL) and cooled to -78^{o}C. To that MeMgBr (0.15 mL, 0.45 mmol) and MeLi (0.28 mL, 0.448 mmol) was added dropwise, respectively. The reaction was then slowly warmed to 0^{o}C over 2 hour. The reaction was then quenched with aqueous NH_4Cl (1 mL) at 0^{o}C, diluted with ethyl acetate (20 ml), washed with water (5 mL) and dried over anhydrous $MgSO_4$. . Evaporation of the organic filtrate gave crude product which upon FCC using 10% EtOAc in hexane gave **7.45** as 1:3 mixture of (E:Z) isomer (43 mg, 71% yield). Major isomer:IR ν_{max}(neat)/cm^{-1} 3395, 2957, 1606, 1243; δ_H (500 MHz, $CDCl_3$) 6.20 (1H, t, J= 7.5 Hz), 3.64 (1H, dd, J= 11.0 Hz, 2.0 Hz), 2.18 (1H, t, J= 7.5 Hz), 2.17 (1H, t, J= 7.5 Hz), 1.84-1.75 (1H, m), 1.78-1.68 (1H, bs), 1.46-1.38 (2H, m), 1.36 (3H, s), 1.33-1.16 (2H, m), 0.93 (3H, d, J= 6.5 Hz), 0.93 (3H, t, J= 7.0 Hz), 0.89 (3H, d, J= 6.5 Hz), 0.23 (9H, s); δ_C (125 MHz, $CDCl_3$) 143.9, 141.7, 79.9, 74.2, 40.5, 33.7, 27.0, 25.0, 24.4, 23.5, 21.8, 14.0, 2.9 (3); *m/z* (ESIMS) found: 295.2 $(M+Na)^+$; calc'd: 295.2.



7.46 (E)

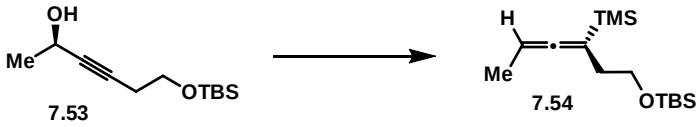
Allene **7.40** (50 mg, 0.223) was oxidized to SDE using general procedure. SDE was dissolve in diethyl ether (5 mL) and cooled to -40^{o}C. To that MeLi (0.35 mL, 5.6 mmol) was added dropwise. The reaction was then slowly warmed to room temperature over 2 hour. The reaction was then quenched with aqueous NH_4Cl (1 mL) at 0^{o}C, diluted with ethyl acetate (20 ml), washed with water (5 mL) and dried over anhydrous $MgSO_4$. . Evaporation of the organic filtrate gave crude product which upon FCC using 10% EtOAc in hexane gave **7.46** as 16:1 (E:Z) mixture of isomers (52 mg, 86% yield). Major isomer: IR ν_{max}(neat)/cm^{-1} 3500, 3333, 1606, 1242, 836; δ_H (500 MHz, $CDCl_3$) 5.33 (1H, d, J= 10.5 Hz), 3.88 (1H, d, J= 10.0 hz), 2.62- 2.50 (1H, m), 1.98 (1H, s), 1.82-1.72 (1H, m), 1.72-1.64 (1H, bs), 1.52-1.42 (1H, m), 1.43 (3H, s), 1.32- 1.22 (1H, m), 0.94 (3H, d, J= 6.5 Hz), 0.92 (3H, d, J= 6.0 Hz), 0.90 (3H, d, J= 6.5 Hz), 0.11 (9H, s); δ_C (125 MHz, $CDCl_3$) 146.4, 144.0, 80.2, 74.6, 40.7, 30.6, 28.4, 24.9, 24.4, 23.2, 22.4, 21.5, 1.5 (3); *m/z* (ESIMS) found: 295.2 $(M+Na)^+$; calc'd: 295.2.



7.46 (Z)

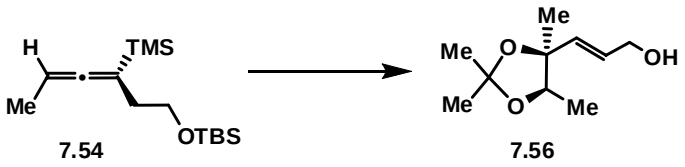
Allene **7.40** (50 mg, 0.223) was oxidized to SDE using general procedure. SDE was dissolve in diethyl ether (5 mL) and cooled to -78^{o}C. To that MeMgBr (0.15 mL, 0.45 mmol) and MeLi (0.28 mL, 0.448 mmol) was added dropwise, respectively. The

reaction was then slowly warmed to 0°C over 2 hour. The reaction was then quenched with aqueous NH_4Cl (1 mL) at 0°C, diluted with ethyl acetate (20 ml), washed with water (5 mL) and dried over anhydrous $MgSO_4$. . Evaporation of the organic filtrate gave crude product which upon FCC using 10% EtOAc in hexane gave **7.46** as 1:4 mixture of (E:Z) isomer (42 mg, 69% yield). Major isomer: IR ν_{max}(neat)/cm^{-1} 3439, 2958, 1601, 1467, 1250; δ_H (400 MHz, $CDCl_3$) 5.95 (1H, d, J= 10.8 Hz), 3.63 (1H, dd, J= 10.0, 7.2 Hz), 2.76-2.60 (1H, m), 1.86- 1.74 (1H, m), 1.73 (1H, s), 1.62 (1H, s), 1.35 (3H, s), 1.32-1.14 (2H, m), 0.96 (6H, d, J= 6.4 Hz), 0.93 (3H, d, J= 6.8 Hz), 0.89 (3H, d, J= 6.4 Hz); δ_C (100 MHz, $CDCl_3$) 148.8, 140.7, 79.6, 74.3, 40.5, 30.3, 26.9, 25.1, 24.4, 23.3, 23.0, 21.8, 3.1 (3); *m/z* (ESIMS) found: 295.4 $(M+Na)^+$; calc'd: 295.2.



To a solution of known propargylic alcohol **7.53** (500mg, 2.19 mmol) in THF (5 mL) were added Et_3N (244 mg, 2.40 mmol) and MsCl (275 mg, 2.40 mmol) respectively at 0°C. The reaction was warmed to room temperature and stirred for 30 minutes to form the mesylate. In a separate flask, hexamethyldisilane (1.02g, 7.0 mmol) was dissolved in HMPA (5 mL) and cooled to -40°C. To that MeLi (3.8 mL, 6.08 mmol) was added and the reaction was warmed to 0°C and stirred for 30 minutes at that temperature. The reaction was then cooled back to -78°C and to that CuCN (585 mg,

6.57 mmol) slurry in THF (15 mL) was added. The reaction was then warmed to -40°C and stirred for 1 hour at that temperature before cooled back to -78°C. To this resulting cuprate was added mesylate at -78°C and the reaction was warmed to 0°C over 1 hour. The reaction was then quenched with aqueous NH_4Cl (2 mL) at 0°C, diluted with ether (50 ml), washed with water (10 mL) and dried over anhydrous $MgSO_4$. . Evaporation of the organic filtrate gave crude product which upon FCC using 2% EtOAc in hexane gave allene **7.54** as colorless oil (417 mg, 67% yield). IR ν_{max}(neat)/cm^{-1} 2956, 1937, 1472, 1249, 838; δ_H (500 MHz, $CDCl_3$) 4.77-4.70 (1H, m), 3.66 (2H, t, J=7.5 Hz), 2.19-2.12 (2H, m), 1.59 (3H, d, J=7.0 Hz), 0.90 (9H, s), 0.07 (3H, s), 0.06 (3H, s); δ_C (125 MHz, $CDCl_3$) 207.1, 92.3, 80.0, 63.6, 32.7, 26.2 (3), 18.6, 14.0, -1.3, -5.0; *m/z* (ESIMS) found: 285.2 $(M+H)^+$; calc'd: 285.2.

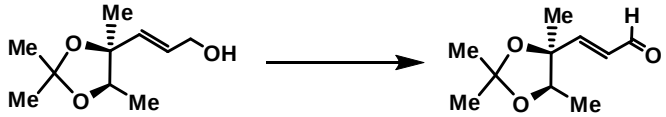


7.54 7.56

Allene 7.53 (100 mg, 0.35 mmol) was oxidized to SDE using general procedure. SDE was dissolved in diethyl ether and cooled to -78°C. To that were added MeMgBr (0.23 mL, 0.69 mmol) and MeLi (0.44 ml, 0.70 mmol) respectively. The reaction was then slowly warmed to 0°C over 2 hours when it was quenched with aqueous NH_4Cl (0.2 mL). Solvent ether was evaporated and acetonitrile was added (8 mL). Then THF solution of TBAF (1.75 mL, 1.75 mmol) was added and the reaction was refluxed for

1 hour. Evaporation of the solvent gave crude product which upon FCC using ethyl acetate gave the anti isomer of triol **7.55** as colorless oil (22 mg, 49% yield).

To a solution of triol **7.55** (15 mg, 0.103 mmol) in acetone (2 mL) was added dimethoxy acetone (0.1 mL) and PTSA (2 mg, 0.012 mmol) at room temperature. The reaction was stirred for 5 minutes at room temperature. Evaporation of solvent gave crude product which upon FCC using 10% EtOAc in hexane gave **7.56** as colorless oil (18 mg, 95% yield). δ_H (400 MHz, $CDCl_3$) 5.89 (1H, td, J= 15.6, 5.6 Hz), 5.70 (1H, td, J= 15.6, 1.6 Hz), 4.18 (2H, d, J= 5.2 Hz), 4.01(1H, q, J= 6.4 Hz), 1.49 (3H, s), 1.40 (3H, s), 1.35 (3H, s), 1.18 (3H, d, J= 6.4 Hz).



7.56 **7.57**

To a solution of **7.56** (18 mg, 0.096 mmol) in DCM (2 mL) were added Dess Martin periodinane (64 mg, 0.15 mmol) and $NaHCO_3$ (10 mg) at room temperature. The reaction was stirred for 1 hour at room temperature. The reaction was then diluted with DCM (10 mL), washed with water (2 mL), and dried over anhydrous $MgSO_4$. Evaporation of solvent gave the crude product which upon FCC using 5% EtOAc in hexane gave the aldehyde **7.57** as colorless oil (16 mg, 90% yield). δ_H (400 MHz, $CDCl_3$) 9.61 (1H, d, J= 8.0 Hz), 6.74 (1H, d, J= 15.6 Hz), 6.34 (1H, dd, J= 15.6 , 7.6 Hz), 4.12 (1H, q, J= 6.4 Hz), 1.51 (3H, s), 1.44 (3H, s), 1.42 (3H, s), 1.25 (3H, d, J= 6.4 Hz).

X-ray structure of **7.26**

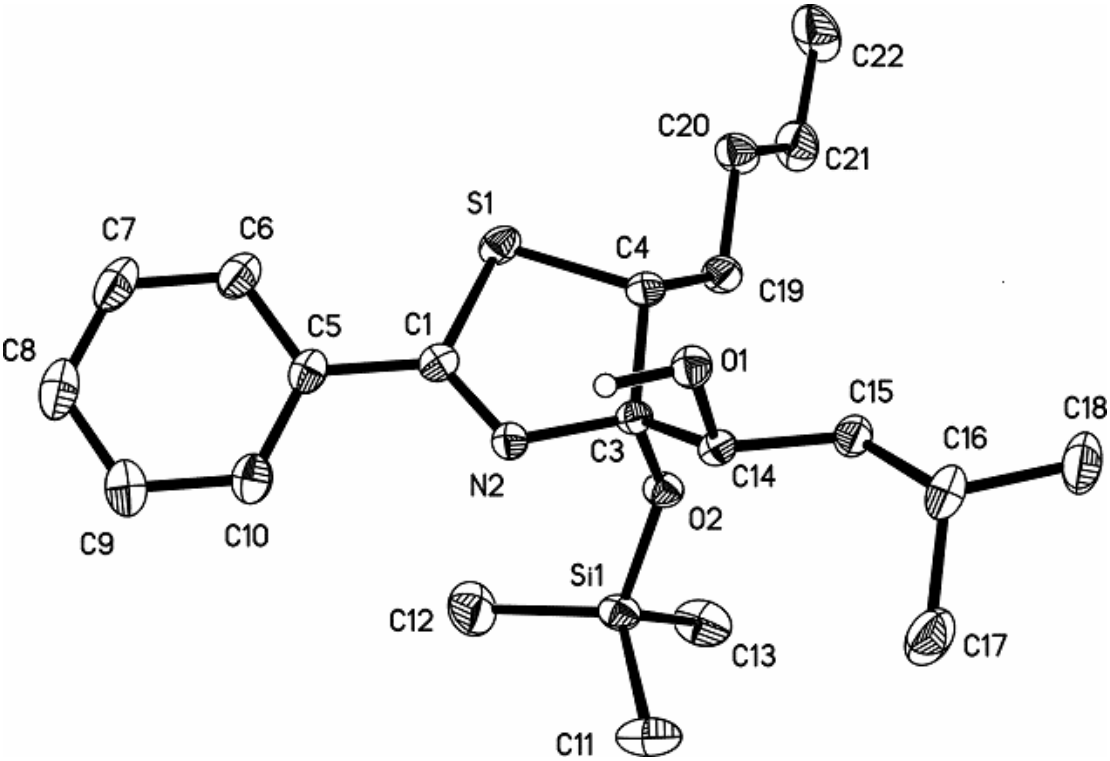


Table 1. Crystal data and structure refinement.

Empirical formula	C21 H35 N O2 S Si
Formula weight	393.65
Temperature	100(2) K
Wavelength	0.71073 Å
Crystal system	Triclinic
Space group	P-1

Unit cell dimensions	a = 8.7862(4) Å α= 86.6340(10)°.
	b = 11.7474(6) Å β= 87.6190(10)°.
	c = 22.7035(11) Å γ = 80.4740(10)°.
Volume	2305.84(19) $Å^3$
Z	4
Density (calculated)	1.134 Mg/m^3
Absorption coefficient	0.206 mm^{-1}
F(000)	856
Crystal size	0.41 x 0.31 x 0.21 mm^3
Theta range for data collection	1.76 to 30.52°.
Index ranges	-12<=h<=12, -16<=k<=16, -32<=l<=32
Reflections collected	27564
Independent reflections	13873 [R(int) = 0.0175]
Completeness to theta = 30.52°	98.3 %
Absorption correction	None
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	13873 / 2 / 749
Goodness-of-fit on F^2	1.007
Final R indices [I>2sigma(I)]	R1 = 0.0416, wR2 = 0.1017
R indices (all data)	R1 = 0.0513, wR2 = 0.1078
Largest diff. peak and hole	0.547 and -0.241 $e.Å^{-3}$

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

orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
S(1)	4569(1)	11318(1)	2639(1)	22(1)
Si(1)	8292(1)	8988(1)	3740(1)	22(1)
O(1)	3382(1)	8130(1)	3084(1)	19(1)
O(2)	6411(1)	9439(1)	3707(1)	20(1)
C(1)	5770(1)	10097(1)	2369(1)	18(1)
N(2)	5993(1)	9178(1)	2709(1)	17(1)
C(3)	5271(1)	9339(1)	3303(1)	17(1)
C(4)	4058(1)	10465(1)	3292(1)	19(1)
C(5)	6495(1)	10191(1)	1773(1)	21(1)
C(6)	5994(2)	11135(1)	1385(1)	28(1)
C(7)	6686(2)	11217(1)	825(1)	34(1)
C(8)	7883(2)	10375(1)	652(1)	33(1)
C(9)	8391(2)	9432(1)	1032(1)	30(1)
C(10)	7696(2)	9335(1)	1591(1)	25(1)
C(11)	8759(2)	7382(1)	3785(1)	37(1)
C(12)	9383(2)	9598(2)	3119(1)	42(1)
C(13)	8750(2)	9594(2)	4435(1)	38(1)
C(14)	4559(1)	8247(1)	3479(1)	17(1)
C(15)	3852(2)	8226(1)	4102(1)	21(1)
C(16)	3436(2)	7046(1)	4310(1)	26(1)
C(17)	4864(2)	6118(1)	4360(1)	38(1)
C(18)	2568(2)	7130(2)	4907(1)	38(1)

C(19)	3966(2)	11174(1)	3840(1)	23(1)
C(20)	2643(2)	12198(1)	3828(1)	27(1)
C(21)	2662(2)	12967(1)	4343(1)	36(1)
C(22)	1309(2)	13957(2)	4358(1)	46(1)
S(2)	5118(1)	7643(1)	756(1)	21(1)
Si(2)	2336(1)	5556(1)	1934(1)	19(1)
O(3)	7214(1)	6796(1)	2397(1)	21(1)
O(4)	4166(1)	5573(1)	1731(1)	19(1)
C(23)	4107(1)	8175(1)	1396(1)	17(1)
N(24)	4266(1)	7531(1)	1873(1)	16(1)
C(25)	5177(1)	6378(1)	1781(1)	16(1)
C(26)	6159(1)	6441(1)	1200(1)	17(1)
C(27)	3095(1)	9315(1)	1350(1)	19(1)
C(28)	3100(2)	10018(1)	832(1)	26(1)
C(29)	2134(2)	11084(1)	792(1)	31(1)
C(30)	1176(2)	11452(1)	1264(1)	29(1)
C(31)	1165(2)	10759(1)	1781(1)	28(1)
C(32)	2116(2)	9689(1)	1824(1)	23(1)
C(33)	2012(2)	5570(2)	2746(1)	34(1)
C(34)	993(2)	6765(1)	1575(1)	30(1)
C(35)	2029(2)	4152(1)	1661(1)	27(1)
C(36)	6158(1)	6018(1)	2332(1)	18(1)
C(37)	7098(1)	4804(1)	2320(1)	21(1)
C(38)	7624(2)	4284(1)	2931(1)	25(1)
C(39)	6285(2)	3915(1)	3298(1)	32(1)
C(40)	8895(2)	3243(2)	2861(1)	43(1)
C(41)	6474(1)	5349(1)	853(1)	21(1)

C(42)	7488(2)	5504(1)	300(1)	26(1)
C(43)	7902(2)	4414(1)	-47(1)	28(1)
C(44)	8910(2)	3433(1)	288(1)	31(1)

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

S(1)-C(1)	1.7581(12)	C(6)-H(6)	0.914(19)
S(1)-C(4)	1.8236(12)	C(7)-C(8)	1.380(2)
Si(1)-O(2)	1.6537(9)	C(7)-H(7)	0.94(2)
Si(1)-C(12)	1.8478(17)	C(8)-C(9)	1.389(2)
Si(1)-C(13)	1.8541(15)	C(8)-H(8)	0.936(18)
Si(1)-C(11)	1.8599(16)	C(9)-C(10)	1.3918(18)
O(1)-C(14)	1.4250(13)	C(9)-H(9)	0.948(18)
O(1)-H(1O)	0.960(3)	C(10)-H(10)	0.970(17)
O(2)-C(3)	1.4098(13)	C(11)-H(11A)	1.00(2)
C(1)-N(2)	1.2830(15)	C(11)-H(11B)	0.94(2)
C(1)-C(5)	1.4789(16)	C(11)-H(11C)	0.94(2)
N(2)-C(3)	1.4740(14)	C(12)-H(12A)	0.98(2)
C(3)-C(14)	1.5440(16)	C(12)-H(12B)	0.93(2)
C(3)-C(4)	1.5551(15)	C(12)-H(12C)	0.96(2)
C(4)-C(19)	1.5287(16)	C(13)-H(13A)	0.92(3)
C(4)-H(4)	0.963(16)	C(13)-H(13B)	0.97(2)
C(5)-C(6)	1.3976(17)	C(13)-H(13C)	0.94(3)
C(5)-C(10)	1.3984(18)	C(14)-C(15)	1.5214(16)
C(6)-C(7)	1.3924(19)	C(14)-H(14)	0.979(14)

C(15)-C(16)	1.5346(17)	Si(2)-C(33)	1.8533(15)
C(15)-H(15A)	0.962(16)	Si(2)-C(35)	1.8602(13)
C(15)-H(15B)	0.960(16)	Si(2)-C(34)	1.8605(14)
C(16)-C(17)	1.523(2)	O(3)-C(36)	1.4230(14)
C(16)-C(18)	1.5258(19)	O(3)-H(3O)	0.962(3)
C(16)-H(16)	0.937(18)	O(4)-C(25)	1.4119(13)
C(17)-H(17A)	1.00(2)	C(23)-N(24)	1.2841(14)
C(17)-H(17B)	0.97(2)	C(23)-C(27)	1.4803(15)
C(17)-H(17C)	0.98(2)	N(24)-C(25)	1.4771(14)
C(18)-H(18A)	0.95(2)	C(25)-C(36)	1.5461(15)
C(18)-H(18B)	0.96(2)	C(25)-C(26)	1.5515(15)
C(18)-H(18C)	0.96(2)	C(26)-C(41)	1.5248(16)
C(19)-C(20)	1.5283(17)	C(26)-H(26)	0.991(15)
C(19)-H(19A)	0.953(17)	C(27)-C(32)	1.3938(17)
C(19)-H(19B)	0.990(17)	C(27)-C(28)	1.3968(17)
C(20)-C(21)	1.521(2)	C(28)-C(29)	1.3918(18)
C(20)-H(20A)	0.931(18)	C(28)-H(28)	0.939(18)
C(20)-H(20B)	0.961(18)	C(29)-C(30)	1.380(2)
C(21)-C(22)	1.521(2)	C(29)-H(29)	0.941(19)
C(21)-H(21A)	1.02(2)	C(30)-C(31)	1.389(2)
C(21)-H(21B)	0.93(2)	C(30)-H(30)	0.963(18)
C(22)-H(22A)	0.96(2)	C(31)-C(32)	1.3892(17)
C(22)-H(22B)	0.96(2)	C(31)-H(31)	0.958(18)
C(22)-H(22C)	0.94(2)	C(32)-H(32)	0.979(17)
S(2)-C(23)	1.7611(12)	C(33)-H(33A)	0.96(2)
S(2)-C(26)	1.8243(11)	C(33)-H(33B)	0.93(2)
Si(2)-O(4)	1.6576(9)	C(33)-H(33C)	0.96(2)

C(34)-H(34A)	0.96(2)	C(39)-H(39C)	1.00(2)
C(34)-H(34B)	0.93(2)	C(40)-H(40A)	0.96(2)
C(34)-H(34C)	0.97(2)	C(40)-H(40B)	0.98(2)
C(35)-H(35A)	0.987(18)	C(40)-H(40C)	1.022(19)
C(35)-H(35B)	0.92(2)	C(41)-C(42)	1.5304(17)
C(35)-H(35C)	0.939(19)	C(41)-H(41A)	0.964(17)
C(36)-C(37)	1.5258(16)	C(41)-H(41B)	1.009(17)
C(36)-H(36)	0.982(14)	C(42)-C(43)	1.5270(18)
C(37)-C(38)	1.5383(16)	C(42)-H(42A)	0.983(18)
C(37)-H(37A)	1.005(16)	C(42)-H(42B)	0.991(16)
C(37)-H(37B)	0.950(16)	C(43)-C(44)	1.5173(19)
C(38)-C(39)	1.522(2)	C(43)-H(43A)	0.993(17)
C(38)-C(40)	1.525(2)	C(43)-H(43B)	1.005(18)
C(38)-H(38)	0.986(16)	C(44)-H(44A)	0.986(19)
C(39)-H(39A)	0.952(19)	C(44)-H(44B)	0.96(2)
C(39)-H(39B)	0.981(19)	C(44)-H(44C)	0.984(18)

C(1)-S(1)-C(4)	90.49(5)	N(2)-C(1)-S(1)	117.76(9)
O(2)-Si(1)-C(12)	112.43(7)	C(5)-C(1)-S(1)	118.63(8)
O(2)-Si(1)-C(13)	101.78(6)	C(1)-N(2)-C(3)	113.16(9)
C(12)-Si(1)-C(13)	109.06(9)	O(2)-C(3)-N(2)	109.57(9)
O(2)-Si(1)-C(11)	111.59(6)	O(2)-C(3)-C(14)	108.96(9)
C(12)-Si(1)-C(11)	110.68(9)	N(2)-C(3)-C(14)	107.00(9)
C(13)-Si(1)-C(11)	110.98(8)	O(2)-C(3)-C(4)	108.79(9)
C(14)-O(1)-H(1O)	107.7(10)	N(2)-C(3)-C(4)	109.59(9)
C(3)-O(2)-Si(1)	134.77(7)	C(14)-C(3)-C(4)	112.89(9)
N(2)-C(1)-C(5)	123.59(11)	C(19)-C(4)-C(3)	115.77(9)

C(19)-C(4)-S(1)	110.36(8)	H(11A)-C(11)-H(11C)	109.4(18)
C(3)-C(4)-S(1)	105.34(8)	H(11B)-C(11)-H(11C)	103.5(17)
C(19)-C(4)-H(4)	109.6(9)	Si(1)-C(12)-H(12A)	109.2(12)
C(3)-C(4)-H(4)	107.9(9)	Si(1)-C(12)-H(12B)	108.3(14)
S(1)-C(4)-H(4)	107.6(9)	H(12A)-C(12)-H(12B)	105.1(18)
C(6)-C(5)-C(10)	119.28(12)	Si(1)-C(12)-H(12C)	110.6(14)
C(6)-C(5)-C(1)	120.54(12)	H(12A)-C(12)-H(12C)	110.0(18)
C(10)-C(5)-C(1)	120.18(11)	H(12B)-C(12)-H(12C)	114(2)
C(7)-C(6)-C(5)	120.14(14)	Si(1)-C(13)-H(13A)	109.9(14)
C(7)-C(6)-H(6)	120.2(11)	Si(1)-C(13)-H(13B)	110.1(13)
C(5)-C(6)-H(6)	119.6(11)	H(13A)-C(13)-H(13B)	106.7(19)
C(8)-C(7)-C(6)	120.16(13)	Si(1)-C(13)-H(13C)	111.8(16)
C(8)-C(7)-H(7)	122.3(12)	H(13A)-C(13)-H(13C)	109(2)
C(6)-C(7)-H(7)	117.5(12)	H(13B)-C(13)-H(13C)	109(2)
C(7)-C(8)-C(9)	120.31(13)	O(1)-C(14)-C(15)	107.49(9)
C(7)-C(8)-H(8)	119.7(11)	O(1)-C(14)-C(3)	110.43(9)
C(9)-C(8)-H(8)	120.0(12)	C(15)-C(14)-C(3)	114.32(9)
C(8)-C(9)-C(10)	119.96(14)	O(1)-C(14)-H(14)	109.8(8)
C(8)-C(9)-H(9)	120.8(11)	C(15)-C(14)-H(14)	109.7(8)
C(10)-C(9)-H(9)	119.2(11)	C(3)-C(14)-H(14)	105.1(8)
C(9)-C(10)-C(5)	120.13(13)	C(14)-C(15)-C(16)	113.34(10)
C(9)-C(10)-H(10)	119.6(10)	C(14)-C(15)-H(15A)	108.2(9)
C(5)-C(10)-H(10)	120.1(10)	C(16)-C(15)-H(15A)	109.6(9)
Si(1)-C(11)-H(11A)	112.4(14)	C(14)-C(15)-H(15B)	109.2(9)
Si(1)-C(11)-H(11B)	110.5(14)	C(16)-C(15)-H(15B)	107.3(9)
H(11A)-C(11)-H(11B)	110.3(18)	H(15A)-C(15)-H(15B)	109.1(13)
Si(1)-C(11)-H(11C)	110.4(13)	C(17)-C(16)-C(18)	109.40(12)

C(17)-C(16)-C(15)	111.78(12)	C(19)-C(20)-H(20B)	109.8(10)
C(18)-C(16)-C(15)	110.19(12)	H(20A)-C(20)-H(20B)	104.4(15)
C(17)-C(16)-H(16)	107.9(11)	C(22)-C(21)-C(20)	113.48(15)
C(18)-C(16)-H(16)	108.8(11)	C(22)-C(21)-H(21A)	109.8(11)
C(15)-C(16)-H(16)	108.7(11)	C(20)-C(21)-H(21A)	108.5(11)
C(16)-C(17)-H(17A)	109.7(12)	C(22)-C(21)-H(21B)	109.4(13)
C(16)-C(17)-H(17B)	114.5(12)	C(20)-C(21)-H(21B)	108.5(13)
H(17A)-C(17)-H(17B)	104.4(17)	H(21A)-C(21)-H(21B)	106.8(17)
C(16)-C(17)-H(17C)	109.7(11)	C(21)-C(22)-H(22A)	110.5(14)
H(17A)-C(17)-H(17C)	112.4(16)	C(21)-C(22)-H(22B)	114.7(13)
H(17B)-C(17)-H(17C)	106.1(16)	H(22A)-C(22)-H(22B)	109.1(19)
C(16)-C(18)-H(18A)	110.7(12)	C(21)-C(22)-H(22C)	112.5(14)
C(16)-C(18)-H(18B)	112.2(11)	H(22A)-C(22)-H(22C)	107.0(19)
H(18A)-C(18)-H(18B)	108.2(16)	H(22B)-C(22)-H(22C)	102.3(18)
C(16)-C(18)-H(18C)	110.5(12)	C(23)-S(2)-C(26)	89.94(5)
H(18A)-C(18)-H(18C)	108.9(16)	O(4)-Si(2)-C(33)	112.41(6)
H(18B)-C(18)-H(18C)	106.2(16)	O(4)-Si(2)-C(35)	101.46(5)
C(20)-C(19)-C(4)	112.95(10)	C(33)-Si(2)-C(35)	110.50(7)
C(20)-C(19)-H(19A)	108.6(10)	O(4)-Si(2)-C(34)	112.71(6)
C(4)-C(19)-H(19A)	109.9(10)	C(33)-Si(2)-C(34)	109.35(8)
C(20)-C(19)-H(19B)	110.6(10)	C(35)-Si(2)-C(34)	110.20(7)
C(4)-C(19)-H(19B)	108.4(10)	C(36)-O(3)-H(3O)	108.4(12)
H(19A)-C(19)-H(19B)	106.3(14)	C(25)-O(4)-Si(2)	133.63(7)
C(21)-C(20)-C(19)	112.47(12)	N(24)-C(23)-C(27)	123.78(10)
C(21)-C(20)-H(20A)	109.3(11)	N(24)-C(23)-S(2)	117.56(8)
C(19)-C(20)-H(20A)	110.0(11)	C(27)-C(23)-S(2)	118.64(8)
C(21)-C(20)-H(20B)	110.5(10)	C(23)-N(24)-C(25)	112.87(9)

O(4)-C(25)-N(24)	109.35(9)	C(31)-C(32)-C(27)	120.05(12)
O(4)-C(25)-C(36)	108.65(9)	C(31)-C(32)-H(32)	119.6(10)
N(24)-C(25)-C(36)	107.67(9)	C(27)-C(32)-H(32)	120.3(10)
O(4)-C(25)-C(26)	109.05(9)	Si(2)-C(33)-H(33A)	112.0(12)
N(24)-C(25)-C(26)	108.69(9)	Si(2)-C(33)-H(33B)	108.3(13)
C(36)-C(25)-C(26)	113.36(9)	H(33A)-C(33)-H(33B)	105.8(17)
C(41)-C(26)-C(25)	116.48(9)	Si(2)-C(33)-H(33C)	111.4(13)
C(41)-C(26)-S(2)	110.74(8)	H(33A)-C(33)-H(33C)	107.7(17)
C(25)-C(26)-S(2)	105.07(7)	H(33B)-C(33)-H(33C)	111.5(18)
C(41)-C(26)-H(26)	109.3(9)	Si(2)-C(34)-H(34A)	112.5(11)
C(25)-C(26)-H(26)	107.4(9)	Si(2)-C(34)-H(34B)	109.0(13)
S(2)-C(26)-H(26)	107.5(9)	H(34A)-C(34)-H(34B)	105.9(17)
C(32)-C(27)-C(28)	119.46(11)	Si(2)-C(34)-H(34C)	112.6(12)
C(32)-C(27)-C(23)	120.08(10)	H(34A)-C(34)-H(34C)	107.9(16)
C(28)-C(27)-C(23)	120.45(11)	H(34B)-C(34)-H(34C)	108.7(17)
C(29)-C(28)-C(27)	120.08(13)	Si(2)-C(35)-H(35A)	110.6(10)
C(29)-C(28)-H(28)	120.8(11)	Si(2)-C(35)-H(35B)	111.4(12)
C(27)-C(28)-H(28)	119.0(11)	H(35A)-C(35)-H(35B)	107.8(15)
C(30)-C(29)-C(28)	120.09(13)	Si(2)-C(35)-H(35C)	110.2(11)
C(30)-C(29)-H(29)	124.0(11)	H(35A)-C(35)-H(35C)	108.9(15)
C(28)-C(29)-H(29)	115.9(11)	H(35B)-C(35)-H(35C)	107.8(16)
C(29)-C(30)-C(31)	120.20(12)	O(3)-C(36)-C(37)	107.30(9)
C(29)-C(30)-H(30)	120.8(10)	O(3)-C(36)-C(25)	110.80(9)
C(31)-C(30)-H(30)	119.0(10)	C(37)-C(36)-C(25)	113.98(9)
C(30)-C(31)-C(32)	120.11(13)	O(3)-C(36)-H(36)	110.1(8)
C(30)-C(31)-H(31)	121.1(11)	C(37)-C(36)-H(36)	110.1(8)
C(32)-C(31)-H(31)	118.8(11)	C(25)-C(36)-H(36)	104.6(8)

C(36)-C(37)-C(38)	114.02(10)	C(26)-C(41)-C(42)	111.72(10)
C(36)-C(37)-H(37A)	106.9(9)	C(26)-C(41)-H(41A)	109.5(10)
C(38)-C(37)-H(37A)	110.3(9)	C(42)-C(41)-H(41A)	110.8(10)
C(36)-C(37)-H(37B)	108.7(9)	C(26)-C(41)-H(41B)	108.6(9)
C(38)-C(37)-H(37B)	108.0(9)	C(42)-C(41)-H(41B)	109.3(9)
H(37A)-C(37)-H(37B)	108.8(13)	H(41A)-C(41)-H(41B)	106.9(13)
C(39)-C(38)-C(40)	109.29(12)	C(43)-C(42)-C(41)	113.66(11)
C(39)-C(38)-C(37)	111.19(11)	C(43)-C(42)-H(42A)	108.7(10)
C(40)-C(38)-C(37)	110.05(12)	C(41)-C(42)-H(42A)	111.4(10)
C(39)-C(38)-H(38)	108.6(9)	C(43)-C(42)-H(42B)	109.6(9)
C(40)-C(38)-H(38)	109.6(9)	C(41)-C(42)-H(42B)	107.5(9)
C(37)-C(38)-H(38)	108.1(9)	H(42A)-C(42)-H(42B)	105.7(14)
C(38)-C(39)-H(39A)	110.8(11)	C(44)-C(43)-C(42)	113.46(11)
C(38)-C(39)-H(39B)	113.9(11)	C(44)-C(43)-H(43A)	109.3(10)
H(39A)-C(39)-H(39B)	103.8(15)	C(42)-C(43)-H(43A)	109.0(10)
C(38)-C(39)-H(39C)	111.4(12)	C(44)-C(43)-H(43B)	109.5(10)
H(39A)-C(39)-H(39C)	106.7(16)	C(42)-C(43)-H(43B)	108.5(10)
H(39B)-C(39)-H(39C)	109.7(16)	H(43A)-C(43)-H(43B)	106.8(13)
C(38)-C(40)-H(40A)	111.6(13)	C(43)-C(44)-H(44A)	111.8(11)
C(38)-C(40)-H(40B)	110.9(13)	C(43)-C(44)-H(44B)	109.2(12)
H(40A)-C(40)-H(40B)	106.0(18)	H(44A)-C(44)-H(44B)	107.6(16)
C(38)-C(40)-H(40C)	107.0(11)	C(43)-C(44)-H(44C)	110.1(10)
H(40A)-C(40)-H(40C)	110.6(17)	H(44A)-C(44)-H(44C)	108.3(14)
H(40B)-C(40)-H(40C)	110.8(17)	H(44B)-C(44)-H(44C)	109.8(15)

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) . 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)	29(1)	15(1)	22(1)	1(1)	-3(1)	-1(1)
Si(1)	17(1)	25(1)	23(1)	-5(1)	-5(1)	-1(1)
O(1)	19(1)	22(1)	18(1)	-1(1)	-2(1)	-5(1)
O(2)	17(1)	24(1)	20(1)	-4(1)	-4(1)	-1(1)
C(1)	19(1)	18(1)	19(1)	-1(1)	-4(1)	-5(1)
N(2)	18(1)	18(1)	17(1)	-1(1)	-1(1)	-4(1)
C(3)	17(1)	16(1)	17(1)	-1(1)	-2(1)	-1(1)
C(4)	19(1)	16(1)	21(1)	-1(1)	-2(1)	-1(1)
C(5)	23(1)	23(1)	18(1)	0(1)	-4(1)	-10(1)
C(6)	30(1)	30(1)	24(1)	6(1)	-5(1)	-7(1)
C(7)	40(1)	41(1)	24(1)	12(1)	-7(1)	-14(1)
C(8)	37(1)	47(1)	19(1)	2(1)	-1(1)	-20(1)
C(9)	34(1)	35(1)	24(1)	-5(1)	4(1)	-12(1)
C(10)	30(1)	26(1)	22(1)	-1(1)	0(1)	-10(1)
C(11)	34(1)	28(1)	45(1)	-9(1)	-16(1)	7(1)
C(12)	25(1)	62(1)	40(1)	2(1)	-1(1)	-13(1)
C(13)	31(1)	46(1)	39(1)	-17(1)	-13(1)	-3(1)
C(14)	19(1)	16(1)	17(1)	0(1)	-2(1)	-2(1)
C(15)	25(1)	21(1)	18(1)	1(1)	0(1)	-3(1)
C(16)	35(1)	27(1)	18(1)	4(1)	-2(1)	-11(1)

C(17)	57(1)	22(1)	32(1)	5(1)	6(1)	-2(1)
C(18)	46(1)	37(1)	30(1)	9(1)	11(1)	-9(1)
C(19)	25(1)	19(1)	22(1)	-4(1)	0(1)	1(1)
C(20)	28(1)	21(1)	31(1)	-5(1)	3(1)	1(1)
C(21)	48(1)	26(1)	31(1)	-7(1)	9(1)	1(1)
C(22)	54(1)	28(1)	52(1)	-11(1)	22(1)	3(1)
S(2)	25(1)	20(1)	16(1)	2(1)	-1(1)	-1(1)
Si(2)	18(1)	19(1)	23(1)	-3(1)	1(1)	-5(1)
O(3)	19(1)	18(1)	25(1)	-1(1)	-3(1)	-2(1)
O(4)	18(1)	17(1)	23(1)	-2(1)	1(1)	-4(1)
C(23)	17(1)	16(1)	19(1)	-1(1)	-3(1)	-4(1)
N(24)	16(1)	15(1)	18(1)	-1(1)	-2(1)	-1(1)
C(25)	16(1)	15(1)	17(1)	0(1)	0(1)	-2(1)
C(26)	18(1)	17(1)	17(1)	1(1)	0(1)	-2(1)
C(27)	21(1)	15(1)	22(1)	0(1)	-7(1)	-4(1)
C(28)	31(1)	21(1)	24(1)	4(1)	-6(1)	-3(1)
C(29)	40(1)	20(1)	33(1)	7(1)	-12(1)	-3(1)
C(30)	35(1)	14(1)	39(1)	-1(1)	-16(1)	1(1)
C(31)	30(1)	20(1)	32(1)	-5(1)	-7(1)	3(1)
C(32)	26(1)	17(1)	25(1)	-1(1)	-6(1)	0(1)
C(33)	38(1)	41(1)	27(1)	-7(1)	9(1)	-20(1)
C(34)	21(1)	22(1)	46(1)	-6(1)	-4(1)	-1(1)
C(35)	28(1)	21(1)	34(1)	-4(1)	-2(1)	-7(1)
C(36)	19(1)	16(1)	18(1)	1(1)	-2(1)	-2(1)
C(37)	23(1)	17(1)	21(1)	1(1)	-2(1)	1(1)
C(38)	31(1)	19(1)	25(1)	4(1)	-9(1)	-2(1)
C(39)	45(1)	26(1)	26(1)	5(1)	-2(1)	-9(1)

C(40)	40(1)	32(1)	49(1)	14(1)	-7(1)	9(1)
C(41)	22(1)	21(1)	19(1)	-2(1)	1(1)	-1(1)
C(42)	32(1)	25(1)	19(1)	-1(1)	4(1)	1(1)
C(43)	33(1)	28(1)	21(1)	-3(1)	0(1)	4(1)
C(44)	30(1)	27(1)	31(1)	2(1)	4(1)	3(1)

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

	x	y	z	U(eq)
H(1O)	3864(18)	8000(15)	2701(4)	35(4)
H(4)	3063(18)	10257(13)	3231(7)	25(4)
H(6)	5210(20)	11695(16)	1501(8)	38(5)
H(7)	6330(20)	11872(17)	579(8)	45(5)
H(8)	8350(20)	10443(16)	277(8)	40(5)
H(9)	9210(20)	8850(16)	917(8)	38(5)
H(10)	8083(19)	8691(15)	1861(7)	31(4)
H(11A)	8200(30)	7030(20)	4120(10)	66(7)
H(11B)	9830(30)	7141(19)	3813(10)	62(6)
H(11C)	8530(20)	7083(18)	3430(9)	52(6)
H(12A)	9230(20)	9217(17)	2757(9)	47(5)
H(12B)	10430(30)	9400(20)	3189(10)	66(7)
H(12C)	9050(30)	10410(20)	3066(10)	66(7)
H(13A)	8470(30)	10380(20)	4412(10)	67(7)
H(13B)	9860(30)	9440(20)	4491(10)	65(7)

H(13C)	8240(30)	9290(20)	4763(12)	80(8)
H(14)	5413(16)	7602(12)	3444(6)	16(3)
H(15A)	2940(18)	8804(13)	4112(7)	22(4)
H(15B)	4577(18)	8407(13)	4372(7)	23(4)
H(16)	2800(20)	6821(16)	4033(8)	38(5)
H(17A)	5580(20)	6344(18)	4645(9)	56(6)
H(17B)	5480(20)	6008(17)	3995(9)	49(5)
H(17C)	4550(20)	5366(18)	4474(8)	45(5)
H(18A)	2300(20)	6399(18)	5039(8)	46(5)
H(18B)	1640(20)	7683(17)	4892(8)	46(5)
H(18C)	3190(20)	7379(17)	5196(9)	46(5)
H(19A)	3837(19)	10693(14)	4185(7)	30(4)
H(19B)	4970(20)	11441(15)	3874(7)	33(4)
H(20A)	2690(20)	12637(16)	3475(8)	38(5)
H(20B)	1670(20)	11924(15)	3823(7)	35(4)
H(21A)	3680(20)	13285(17)	4320(9)	49(5)
H(21B)	2660(20)	12510(19)	4694(10)	58(6)
H(22A)	1320(30)	14450(20)	4007(11)	64(7)
H(22B)	1260(20)	14417(19)	4697(10)	59(6)
H(22C)	350(30)	13698(19)	4383(10)	61(6)
H(3O)	6630(20)	7554(8)	2449(9)	52(6)
H(26)	7154(18)	6660(13)	1301(7)	23(4)
H(28)	3800(20)	9779(15)	523(8)	35(4)
H(29)	2160(20)	11500(16)	425(8)	41(5)
H(30)	500(20)	12185(16)	1240(8)	37(5)
H(31)	520(20)	11008(15)	2114(8)	37(5)
H(32)	2065(19)	9190(15)	2182(7)	32(4)

H(33A)	2630(20)	4920(19)	2947(9)	51(6)
H(33B)	990(20)	5493(18)	2833(9)	52(6)
H(33C)	2260(20)	6260(19)	2897(9)	57(6)
H(34A)	970(20)	7481(17)	1759(8)	45(5)
H(34B)	-10(30)	6601(19)	1615(9)	58(6)
H(34C)	1240(20)	6889(17)	1160(9)	49(5)
H(35A)	2430(20)	4070(15)	1250(8)	36(4)
H(35B)	1000(20)	4092(17)	1669(8)	47(5)
H(35C)	2540(20)	3537(16)	1899(8)	38(5)
H(36)	5404(16)	6063(12)	2665(6)	17(3)
H(37A)	8018(18)	4854(13)	2048(7)	24(4)
H(37B)	6486(17)	4307(13)	2163(7)	23(4)
H(38)	8024(18)	4884(14)	3137(7)	24(4)
H(39A)	5900(20)	3308(16)	3121(8)	39(5)
H(39B)	5380(20)	4523(17)	3329(8)	41(5)
H(39C)	6610(20)	3610(18)	3703(9)	54(6)
H(40A)	9210(30)	2881(19)	3235(10)	61(6)
H(40B)	9820(30)	3474(19)	2669(10)	58(6)
H(40C)	8460(20)	2678(17)	2613(8)	42(5)
H(41A)	5509(19)	5136(14)	752(7)	30(4)
H(41B)	7012(19)	4696(14)	1117(7)	29(4)
H(42A)	7000(20)	6137(15)	33(8)	35(4)
H(42B)	8445(19)	5748(14)	427(7)	27(4)
H(43A)	6940(20)	4153(15)	-153(7)	31(4)
H(43B)	8450(20)	4615(15)	-427(8)	36(4)
H(44A)	9880(20)	3663(16)	408(8)	40(5)
H(44B)	9180(20)	2797(18)	37(9)	50(5)

H(44C)	8350(20)	3186(15)	644(8)	34(4)

Table 6. Torsion angles [°].

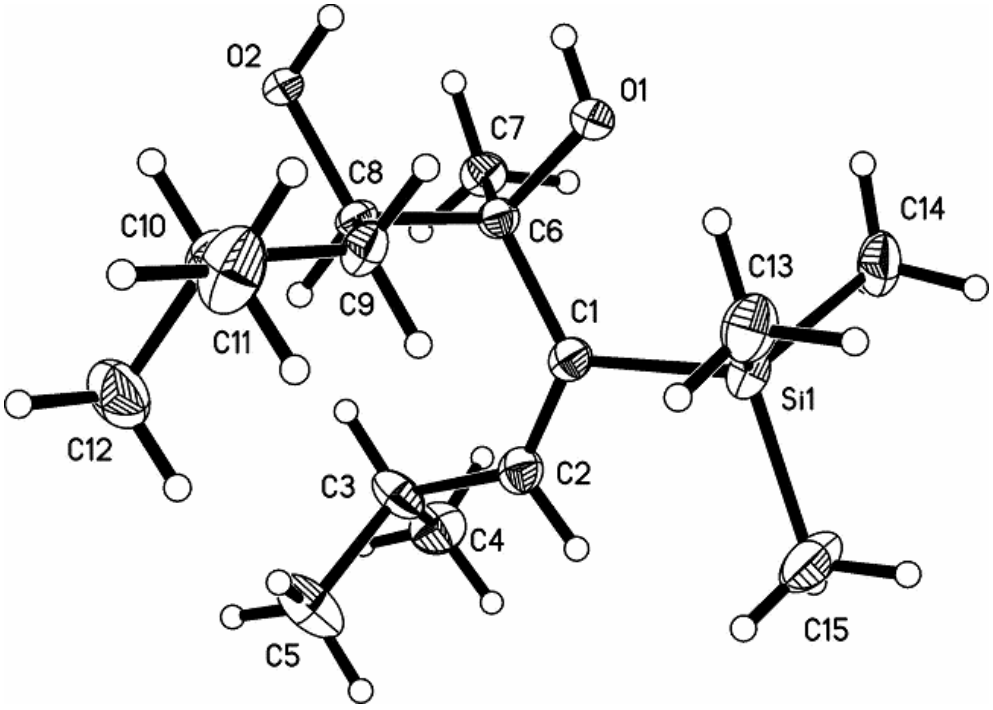
C(12)-Si(1)-O(2)-C(3)	61.85(13)	N(2)-C(1)-C(5)-C(10)	-11.96(17)
C(13)-Si(1)-O(2)-C(3)	178.40(12)	S(1)-C(1)-C(5)-C(10)	166.57(9)
C(11)-Si(1)-O(2)-C(3)	-63.19(13)	C(10)-C(5)-C(6)-C(7)	0.03(19)
C(4)-S(1)-C(1)-N(2)	-7.07(10)	C(1)-C(5)-C(6)-C(7)	179.79(12)
C(4)-S(1)-C(1)-C(5)	174.31(9)	C(5)-C(6)-C(7)-C(8)	-0.8(2)
C(5)-C(1)-N(2)-C(3)	174.08(10)	C(6)-C(7)-C(8)-C(9)	0.9(2)
S(1)-C(1)-N(2)-C(3)	-4.47(13)	C(7)-C(8)-C(9)-C(10)	-0.3(2)
Si(1)-O(2)-C(3)-N(2)	-25.78(14)	C(8)-C(9)-C(10)-C(5)	-0.5(2)
Si(1)-O(2)-C(3)-C(14)	90.97(12)	C(6)-C(5)-C(10)-C(9)	0.62(18)
Si(1)-O(2)-C(3)-C(4)	-145.57(9)	C(1)-C(5)-C(10)-C(9)	-179.15(11)
C(1)-N(2)-C(3)-O(2)	-102.98(11)	O(2)-C(3)-C(14)-O(1)	179.01(8)
C(1)-N(2)-C(3)-C(14)	139.04(10)	N(2)-C(3)-C(14)-O(1)	-62.62(11)
C(1)-N(2)-C(3)-C(4)	16.32(13)	C(4)-C(3)-C(14)-O(1)	58.03(12)
O(2)-C(3)-C(4)-C(19)	-22.32(13)	O(2)-C(3)-C(14)-C(15)	57.65(12)
N(2)-C(3)-C(4)-C(19)	-142.10(10)	N(2)-C(3)-C(14)-C(15)	176.03(9)
C(14)-C(3)-C(4)-C(19)	98.75(12)	C(4)-C(3)-C(14)-C(15)	-63.32(12)
O(2)-C(3)-C(4)-S(1)	99.89(9)	O(1)-C(14)-C(15)-C(16)	68.18(12)
N(2)-C(3)-C(4)-S(1)	-19.88(10)	C(3)-C(14)-C(15)-C(16)	-168.86(10)
C(14)-C(3)-C(4)-S(1)	-139.03(8)	C(14)-C(15)-C(16)-C(17)	64.62(14)
C(1)-S(1)-C(4)-C(19)	140.51(9)	C(14)-C(15)-C(16)-C(18)	-173.50(12)
C(1)-S(1)-C(4)-C(3)	14.88(8)	C(3)-C(4)-C(19)-C(20)	-174.07(10)
N(2)-C(1)-C(5)-C(6)	168.28(11)	S(1)-C(4)-C(19)-C(20)	66.42(12)
S(1)-C(1)-C(5)-C(6)	-13.19(15)	C(4)-C(19)-C(20)-C(21)	-174.10(12)

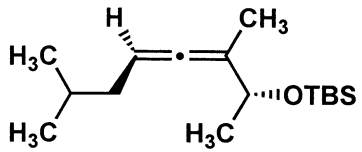
C(19)-C(20)-C(21)-C(22)	-177.05(13)
C(33)-Si(2)-O(4)-C(25)	-63.27(12)
C(35)-Si(2)-O(4)-C(25)	178.69(10)
C(34)-Si(2)-O(4)-C(25)	60.86(11)
C(26)-S(2)-C(23)-N(24)	-8.79(9)
C(26)-S(2)-C(23)-C(27)	172.92(9)
C(27)-C(23)-N(24)-C(25)	172.42(10)
S(2)-C(23)-N(24)-C(25)	-5.77(12)
Si(2)-O(4)-C(25)-N(24)	-20.48(14)
Si(2)-O(4)-C(25)-C(36)	96.79(11)
Si(2)-O(4)-C(25)-C(26)	-139.21(9)
C(23)-N(24)-C(25)-O(4)	-98.31(11)
C(23)-N(24)-C(25)-C(36)	143.82(9)
C(23)-N(24)-C(25)-C(26)	20.64(12)
O(4)-C(25)-C(26)-C(41)	-28.92(13)
N(24)-C(25)-C(26)-C(41)	-148.06(9)
C(36)-C(25)-C(26)-C(41)	92.25(12)
O(4)-C(25)-C(26)-S(2)	94.02(9)
N(24)-C(25)-C(26)-S(2)	-25.12(10)
C(36)-C(25)-C(26)-S(2)	-144.81(8)
C(23)-S(2)-C(26)-C(41)	145.36(8)
C(23)-S(2)-C(26)-C(25)	18.80(8)
N(24)-C(23)-C(27)-C(32)	-7.15(17)
S(2)-C(23)-C(27)-C(32)	171.02(9)
N(24)-C(23)-C(27)-C(28)	173.51(11)
S(2)-C(23)-C(27)-C(28)	-8.32(15)
C(32)-C(27)-C(28)-C(29)	0.07(19)
C(23)-C(27)-C(28)-C(29)	179.42(11)
C(27)-C(28)-C(29)-C(30)	0.4(2)
C(28)-C(29)-C(30)-C(31)	-0.3(2)
C(29)-C(30)-C(31)-C(32)	-0.2(2)
C(30)-C(31)-C(32)-C(27)	0.65(19)
C(28)-C(27)-C(32)-C(31)	-0.59(18)
C(23)-C(27)-C(32)-C(31)	-179.94(11)
O(4)-C(25)-C(36)-O(3)	179.24(8)
N(24)-C(25)-C(36)-O(3)	-62.42(11)
C(26)-C(25)-C(36)-O(3)	57.84(12)
O(4)-C(25)-C(36)-C(37)	58.11(12)
N(24)-C(25)-C(36)-C(37)	176.44(9)
C(26)-C(25)-C(36)-C(37)	-63.29(12)
O(3)-C(36)-C(37)-C(38)	76.57(12)
C(25)-C(36)-C(37)-C(38)	-160.37(10)
C(36)-C(37)-C(38)-C(39)	74.27(14)
C(36)-C(37)-C(38)-C(40)	-164.49(12)
C(25)-C(26)-C(41)-C(42)	-178.39(10)
S(2)-C(26)-C(41)-C(42)	61.66(12)
C(26)-C(41)-C(42)-C(43)	177.17(11)
C(41)-C(42)-C(43)-C(44)	-65.31(16)

Table 7. Hydrogen bonds [Å and °].

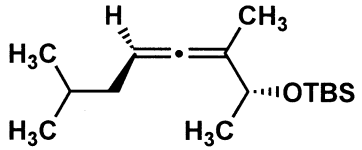
D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
O(1)-H(1O)...N(24)	0.960(3)	1.991(6)	2.9197(12)	162.1(15)
O(3)-H(3O)...N(2)	0.962(3)	2.013(7)	2.9423(13)	161.8(17)

X-ray structure of **7.46** (E)





6c



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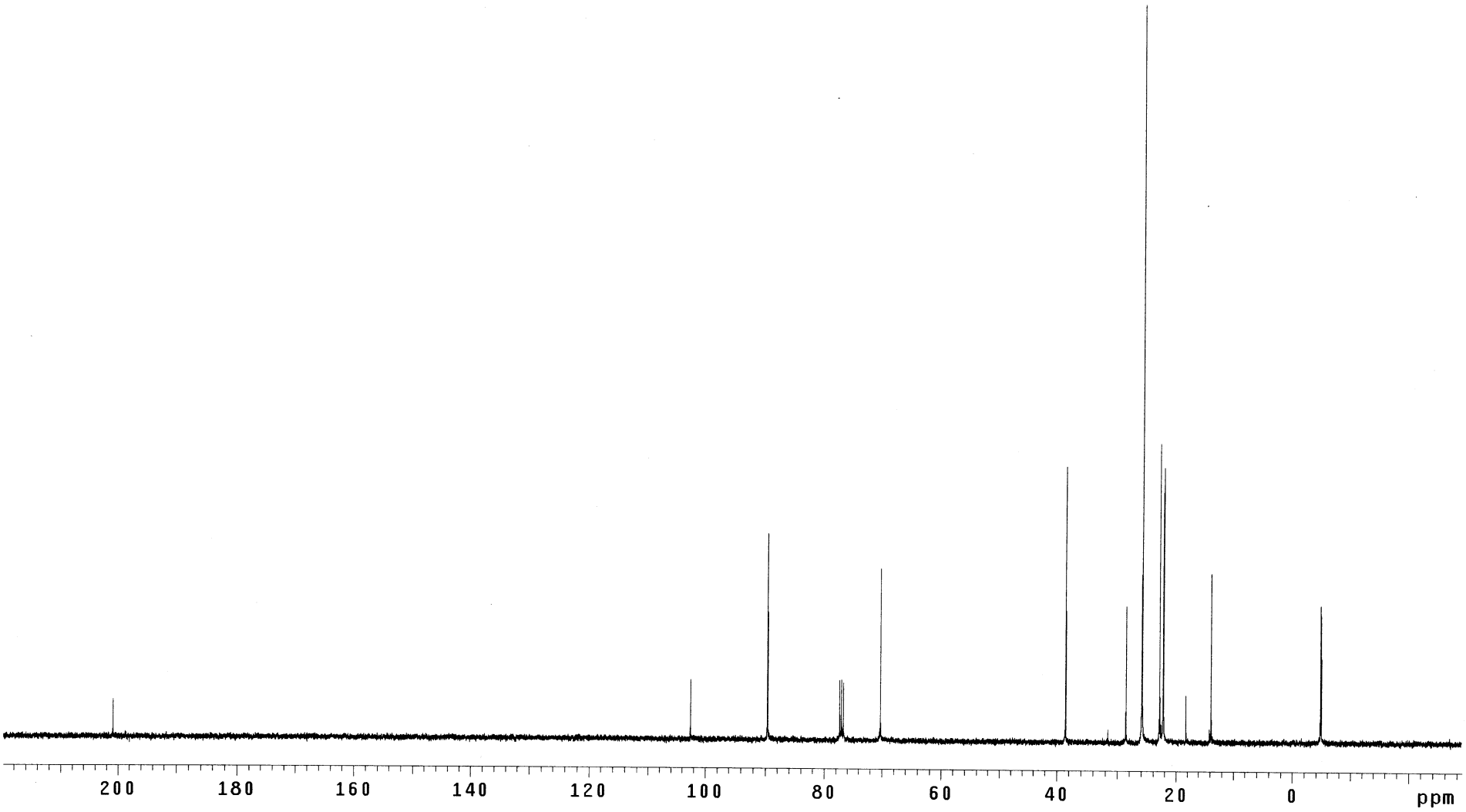

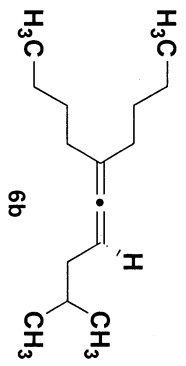
H3C
H3C
6b
H
CH3
CH3

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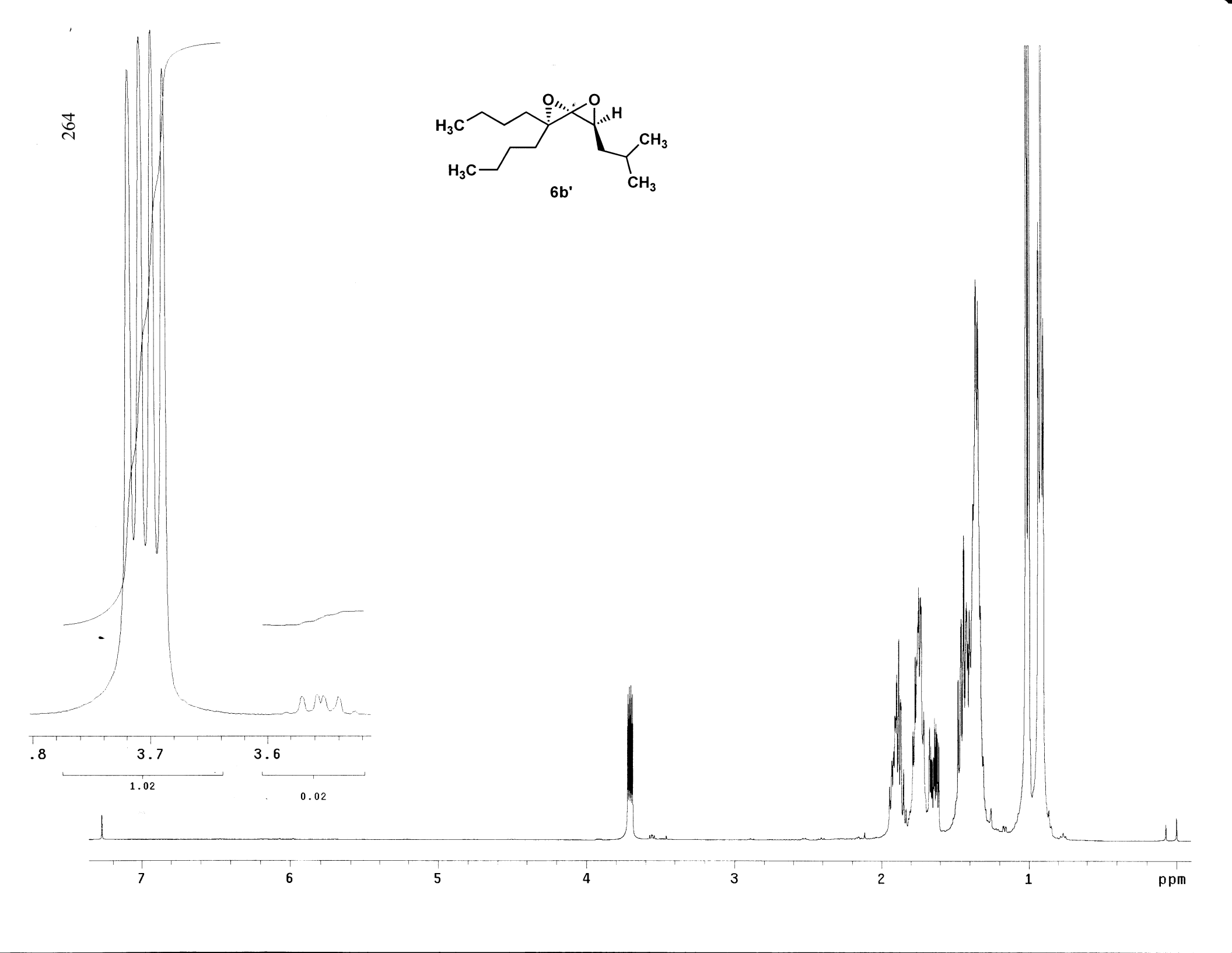
6
5
4
3
2
1
ppm
0.96
1.99
4.12
1.06
8.55
12.00


264
H3C
O
O
H
CH3
H3C
CH3
6b'
.8
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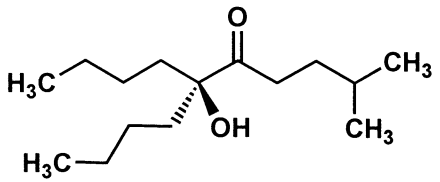
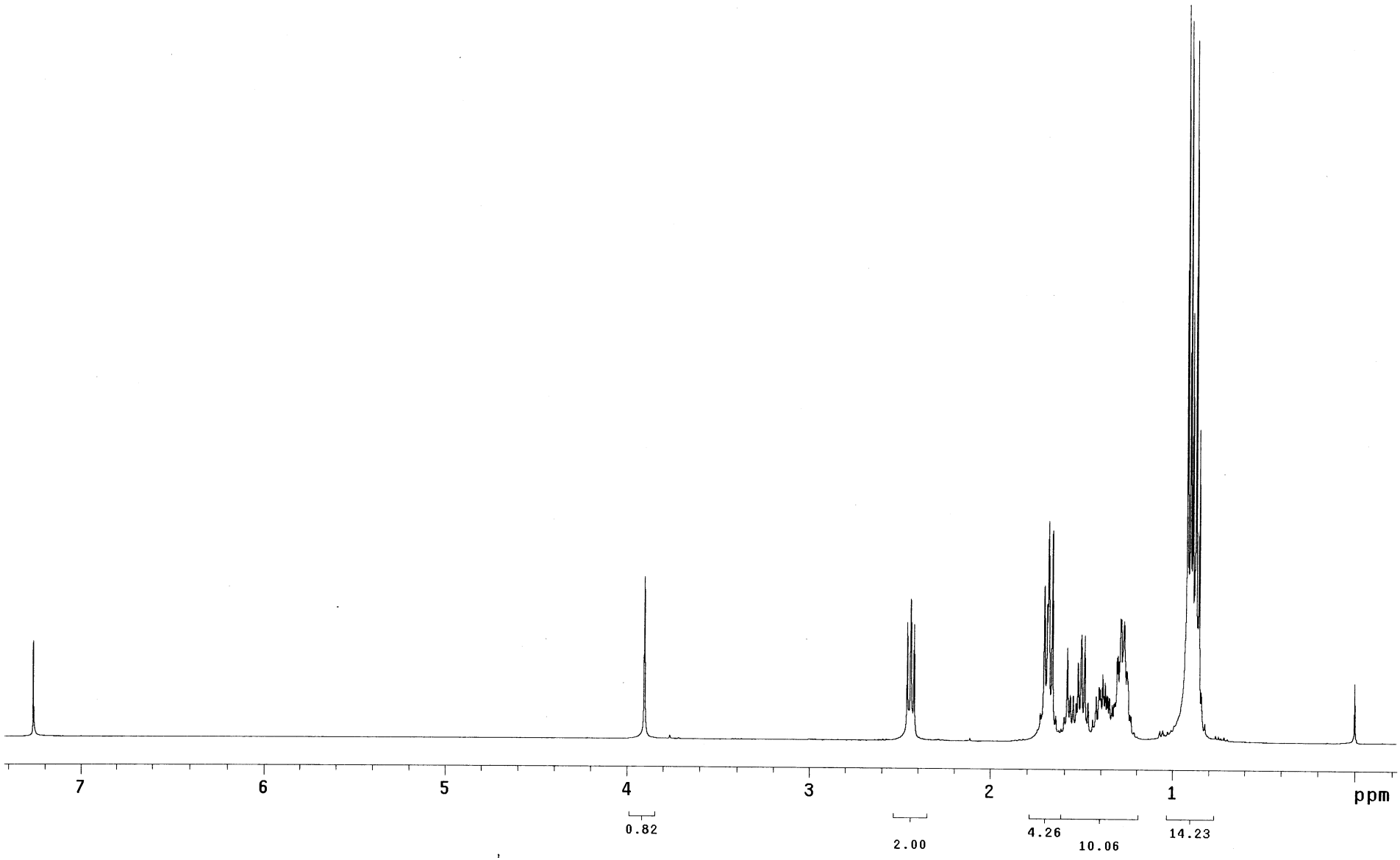
3.6
1.02
0.02
7
6
5
4
3
2
1
ppm

265





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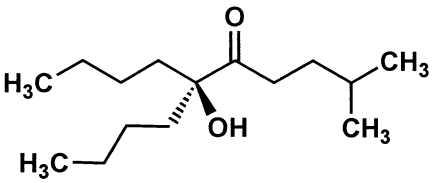

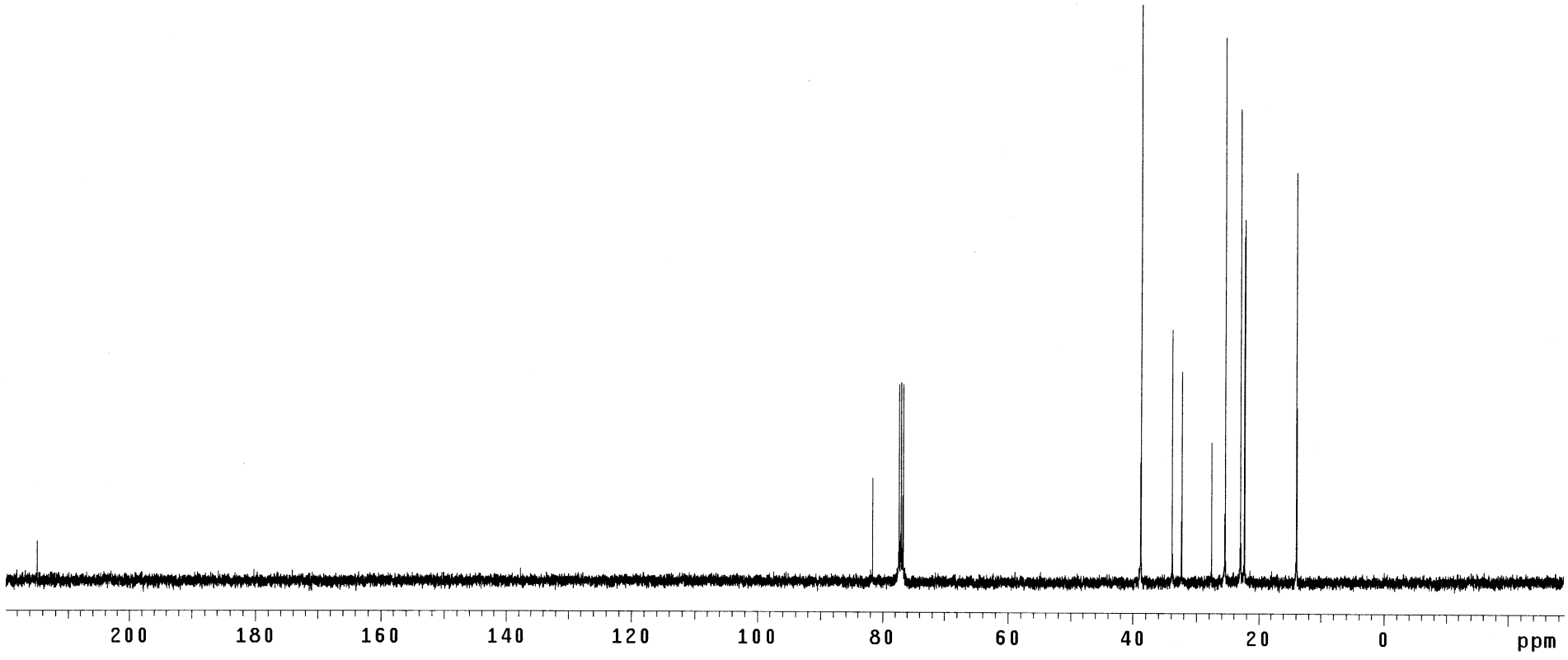

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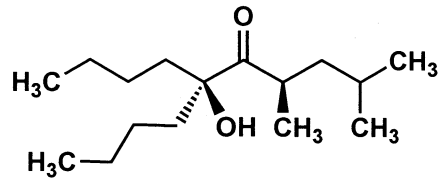
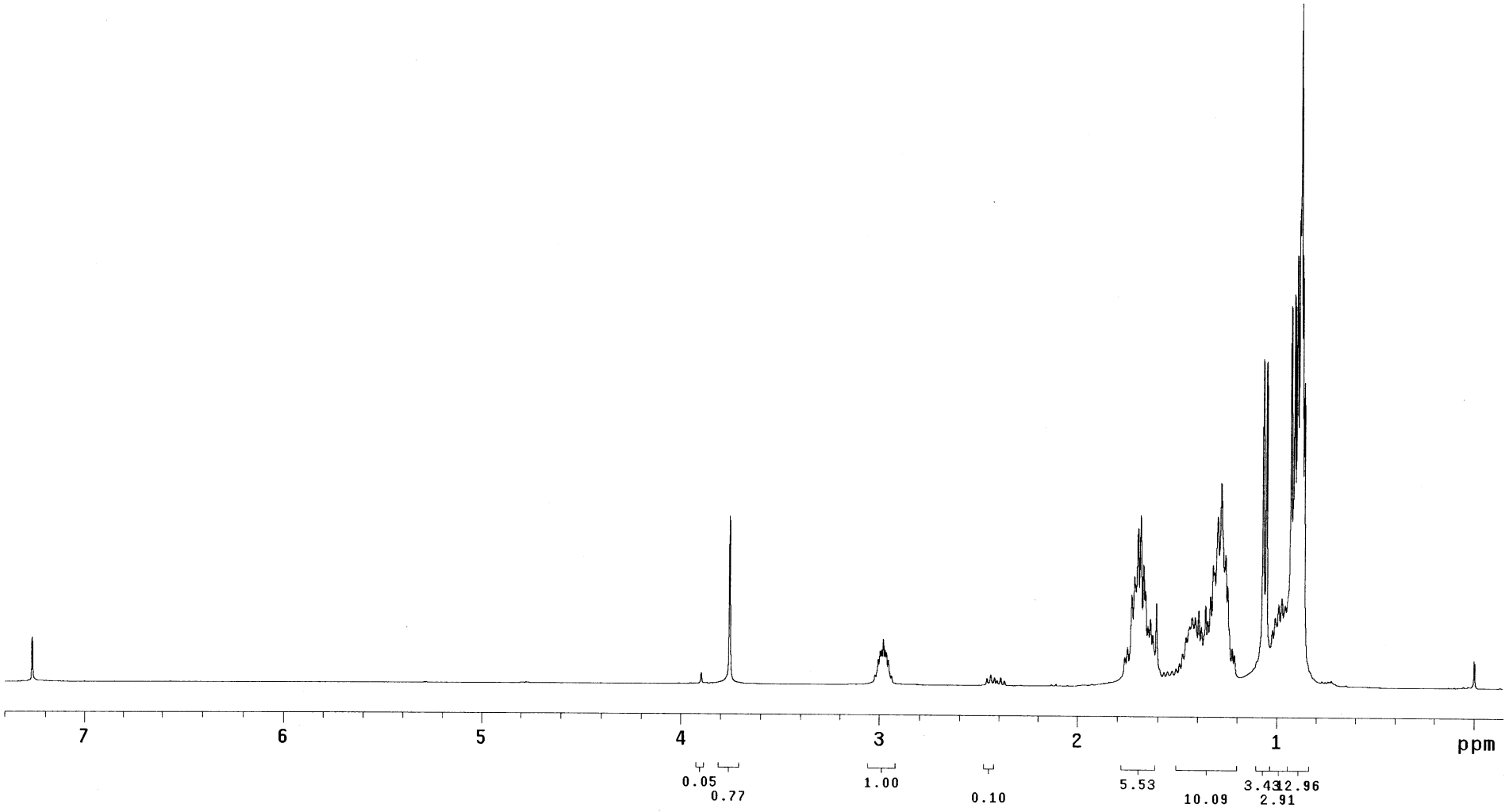

O
H3C
CH3
OH
CH3
CH3
H3C


7
6
5
4
3
2
1
ppm
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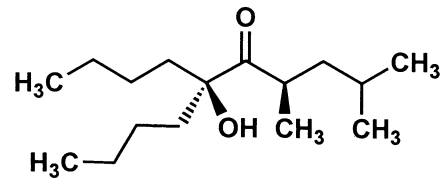
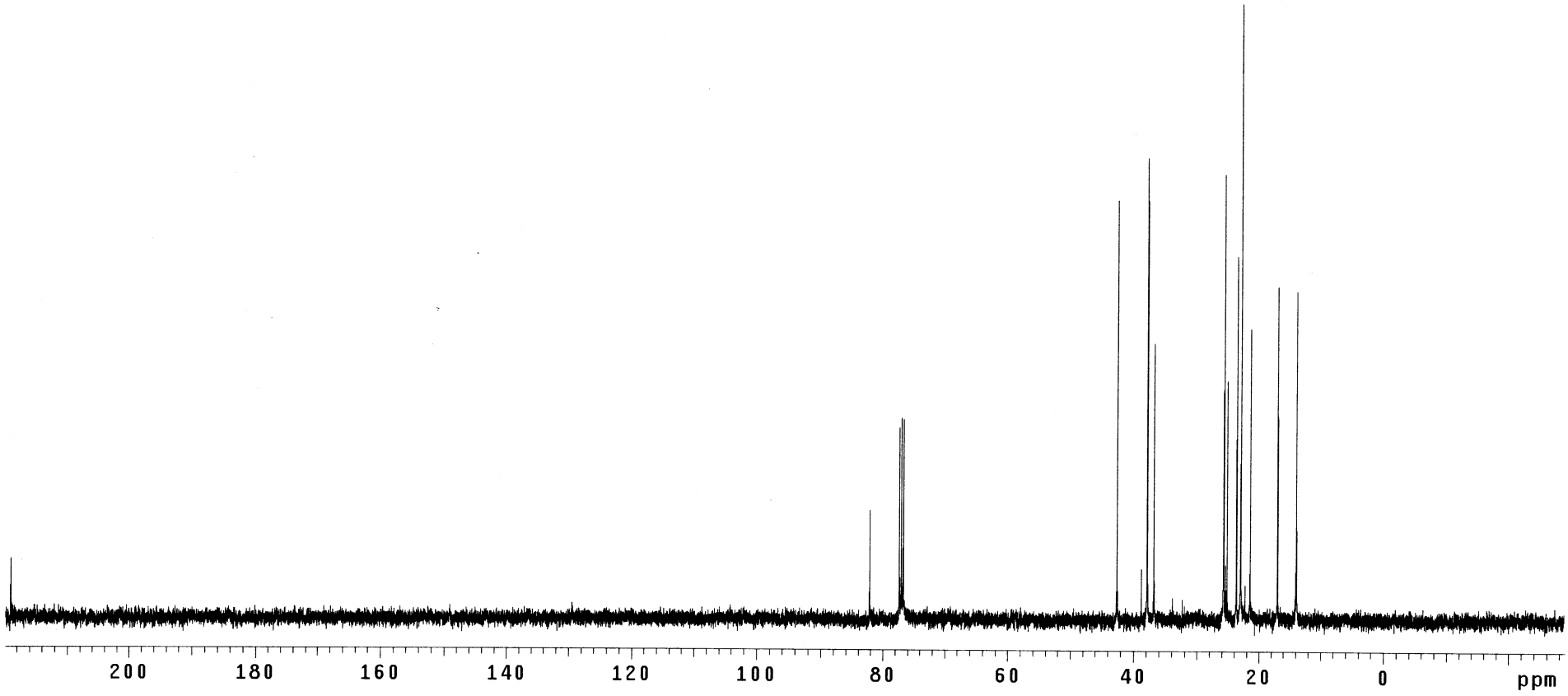
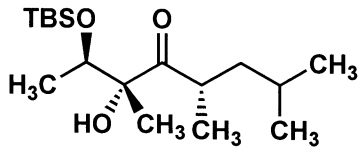
0.77
1.00
0.10
5.53
10.09
3.43
2.91
12.96

268



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H3C
CH3
HO
CH3
CH3
CH3

7
6
5
4
3
2
1
ppm
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0.11
0.83
2.07
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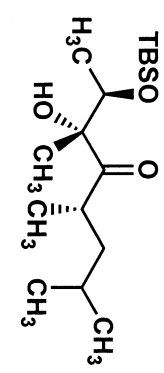
3.21
1.81
6.14
85
6.25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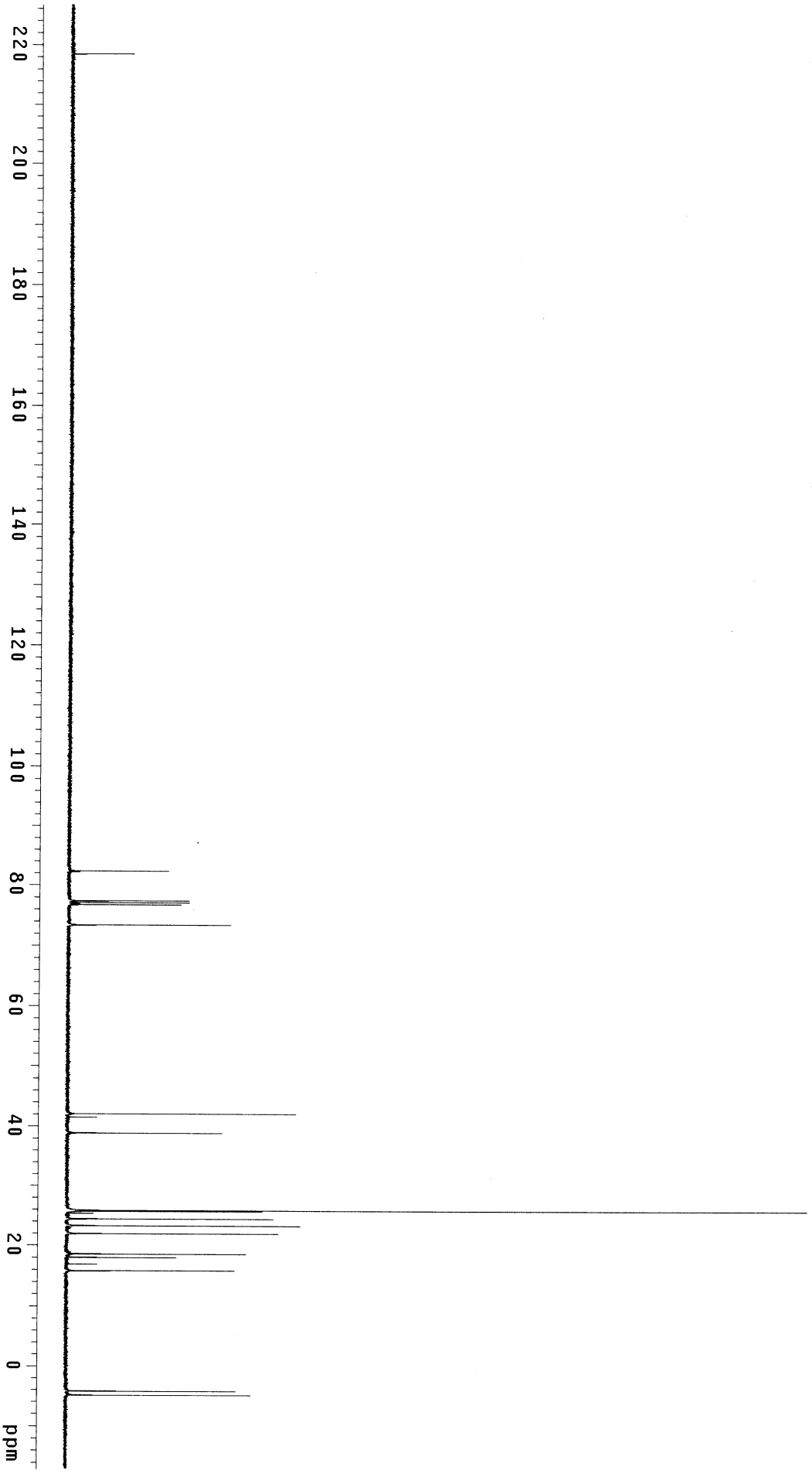
H3C
HO
CH3
CH3
CH3
CH3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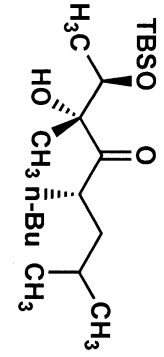
60
40
20
0
ppm


TBSO
O
H3C
HO
CH3
n-Bu
CH3
CH3

7
6
5
4
3
2
1
ppm
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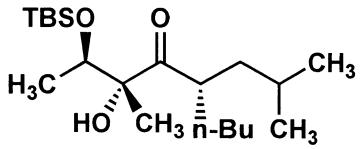
0.13
3.60
1.72
20.23
7.42
3.36
5.94

272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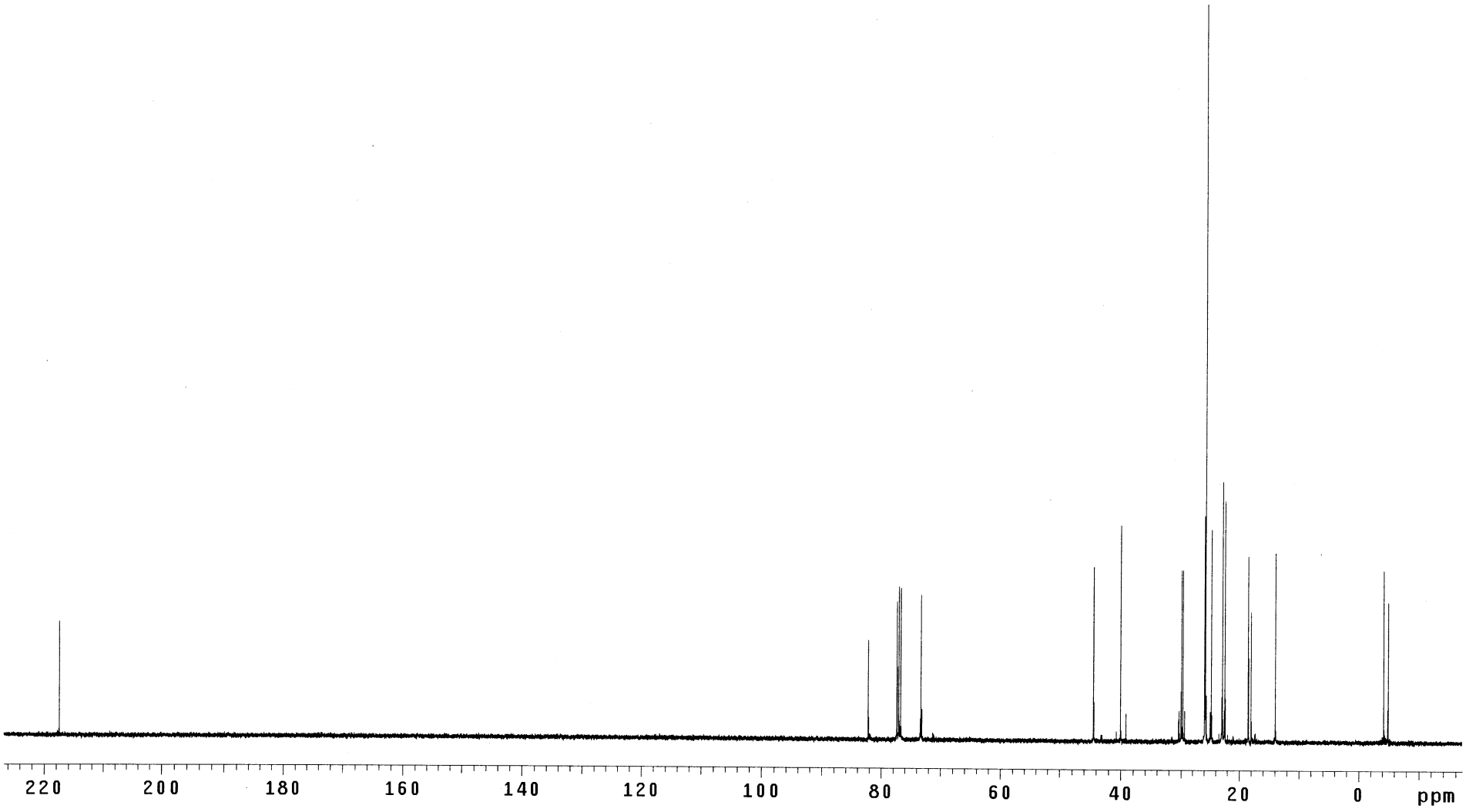
H3C
CH3
HO
CH3
n-Bu
CH3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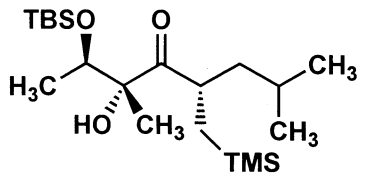
TBSO
O
H3C
CH3
HO
CH3
CH3
TMS

7
6
5
4
3
2
1
ppm
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0.15
1.11
0.15
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0.53
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5.02
19.93
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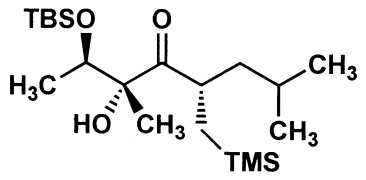
0.96
6.35
9.10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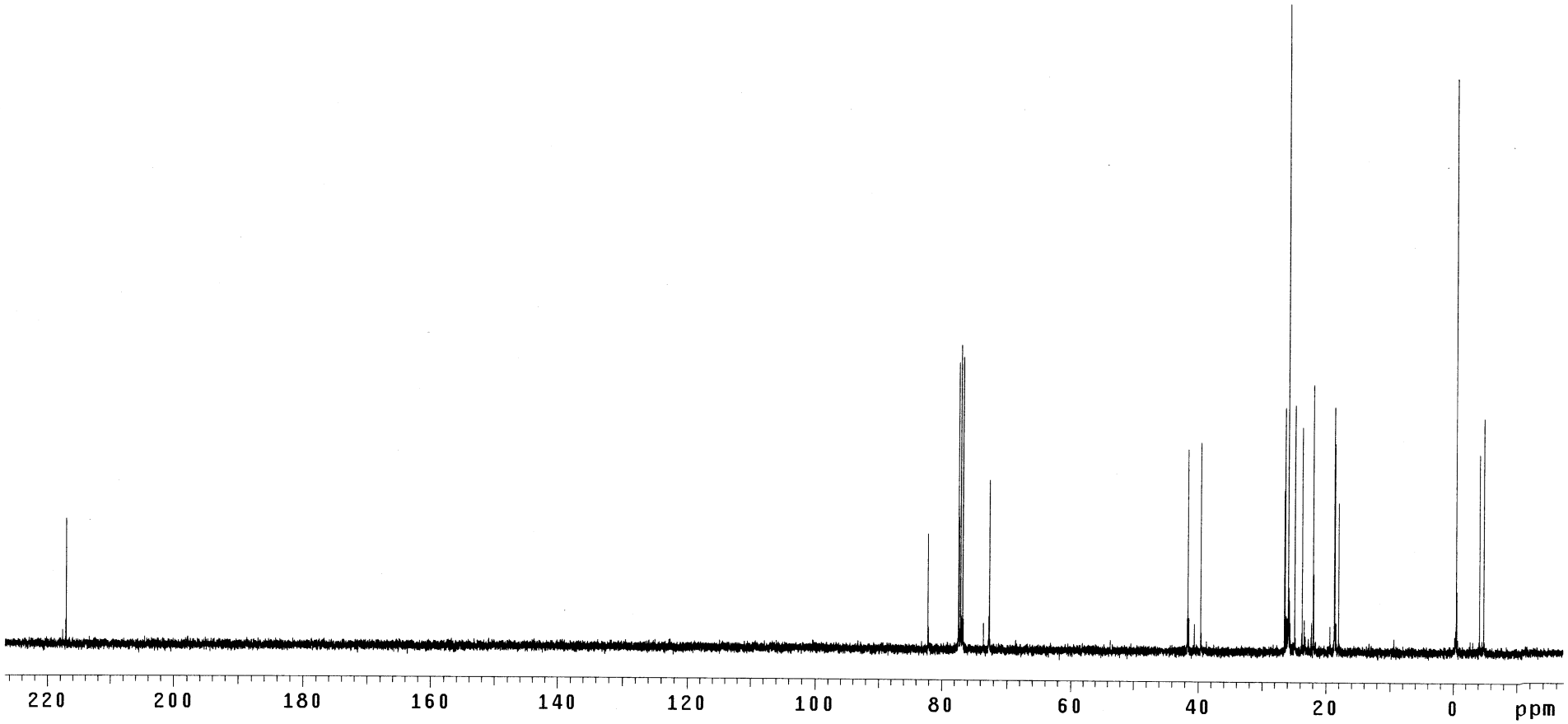
H3C
CH3
HO
CH3
CH3
TMS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100
80
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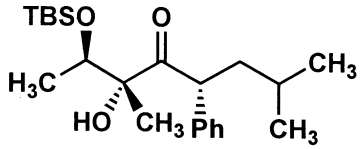
40
20
0
ppm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O
H3C
CH3
HO
CH3
Ph
CH3

7
6
5
4
3
2
1
ppm
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1.00
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1.26
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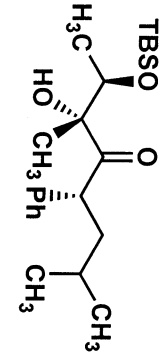
17.45
3.20
6.26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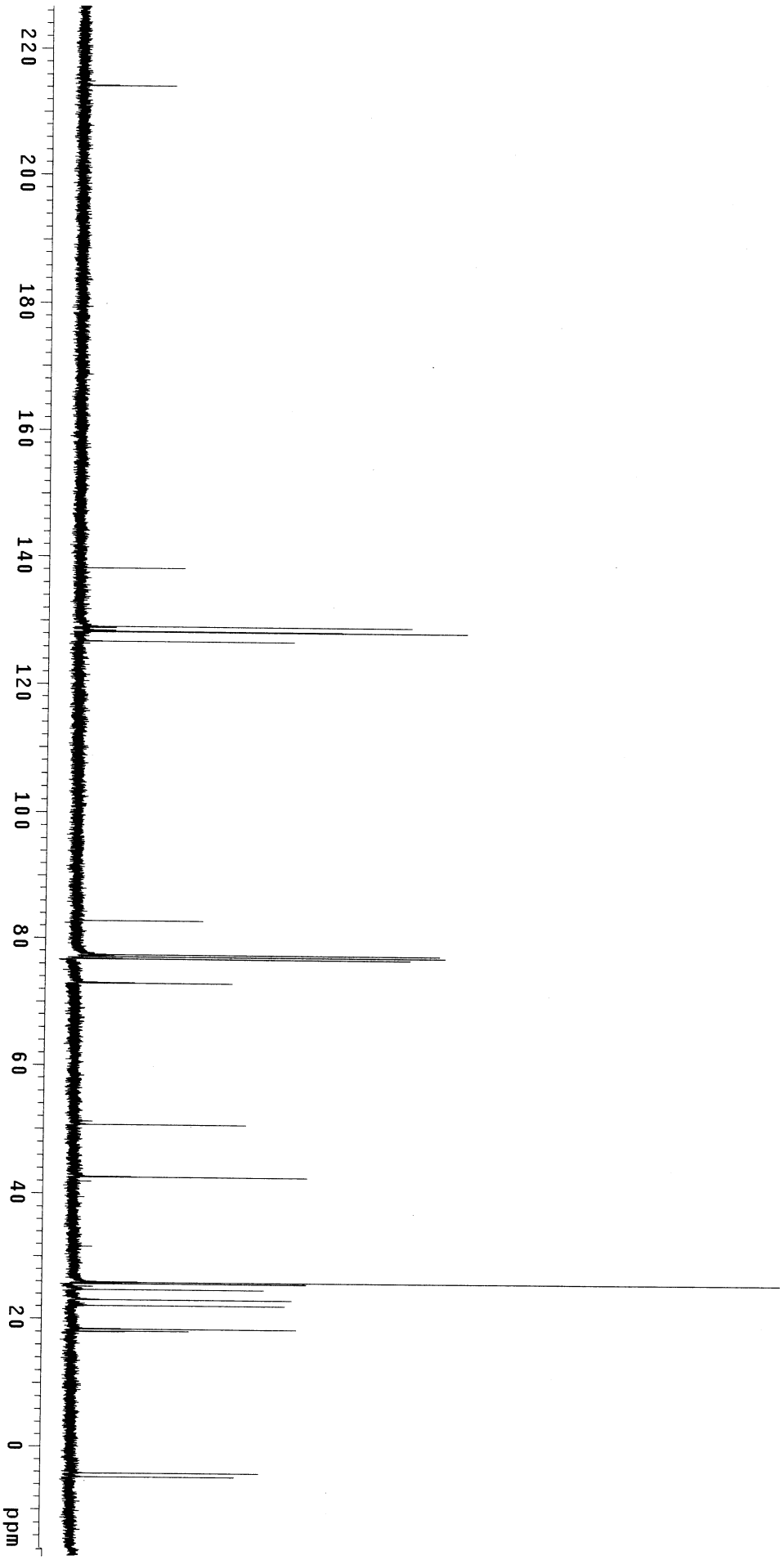
H3C
HO
CH3
Ph
CH3
CH3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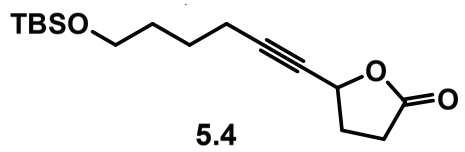
40
20
0
ppm



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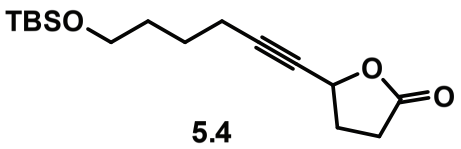

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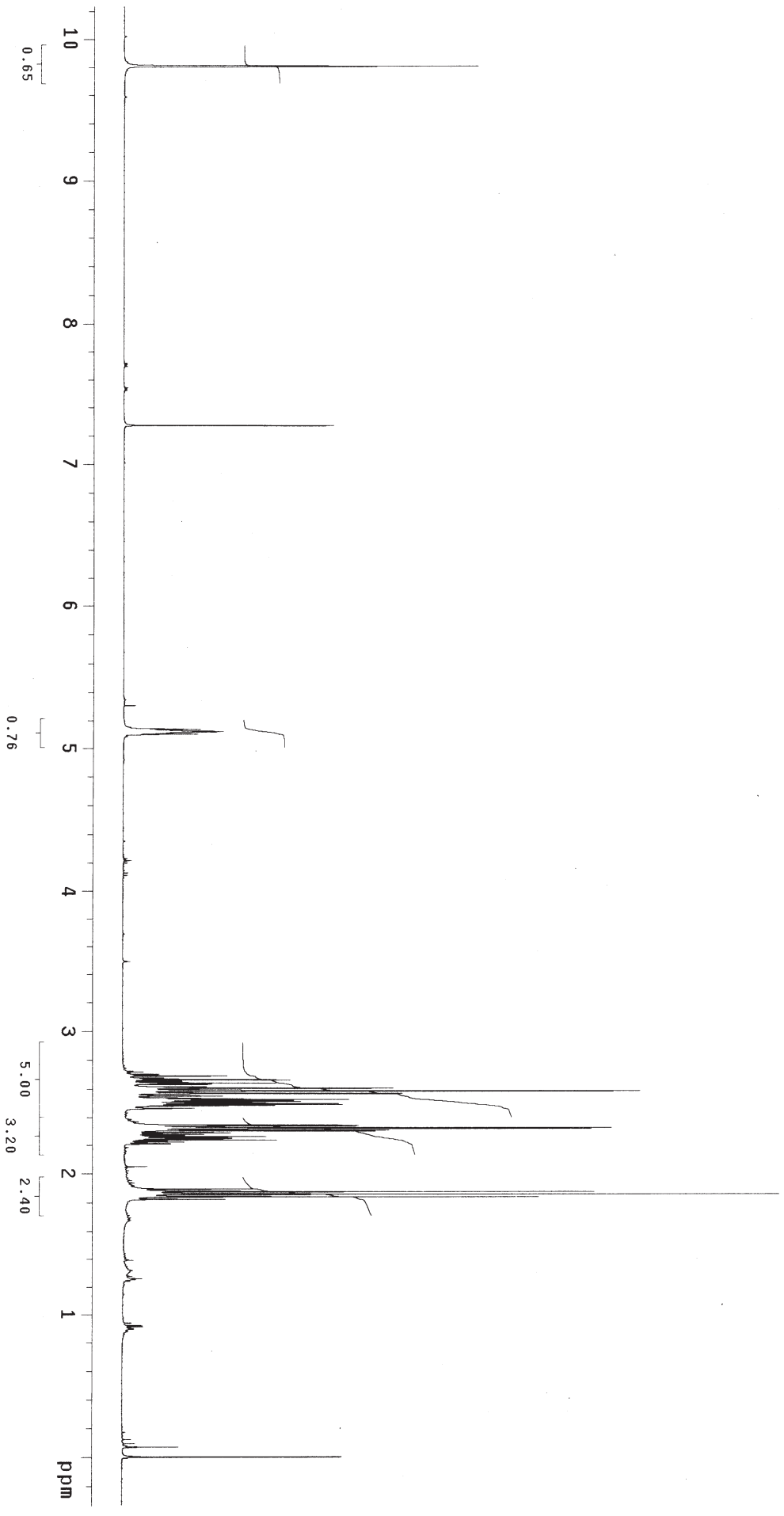

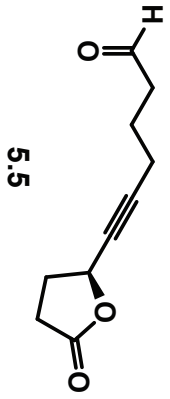

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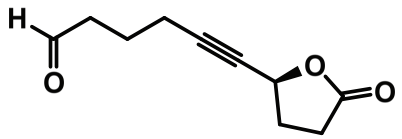

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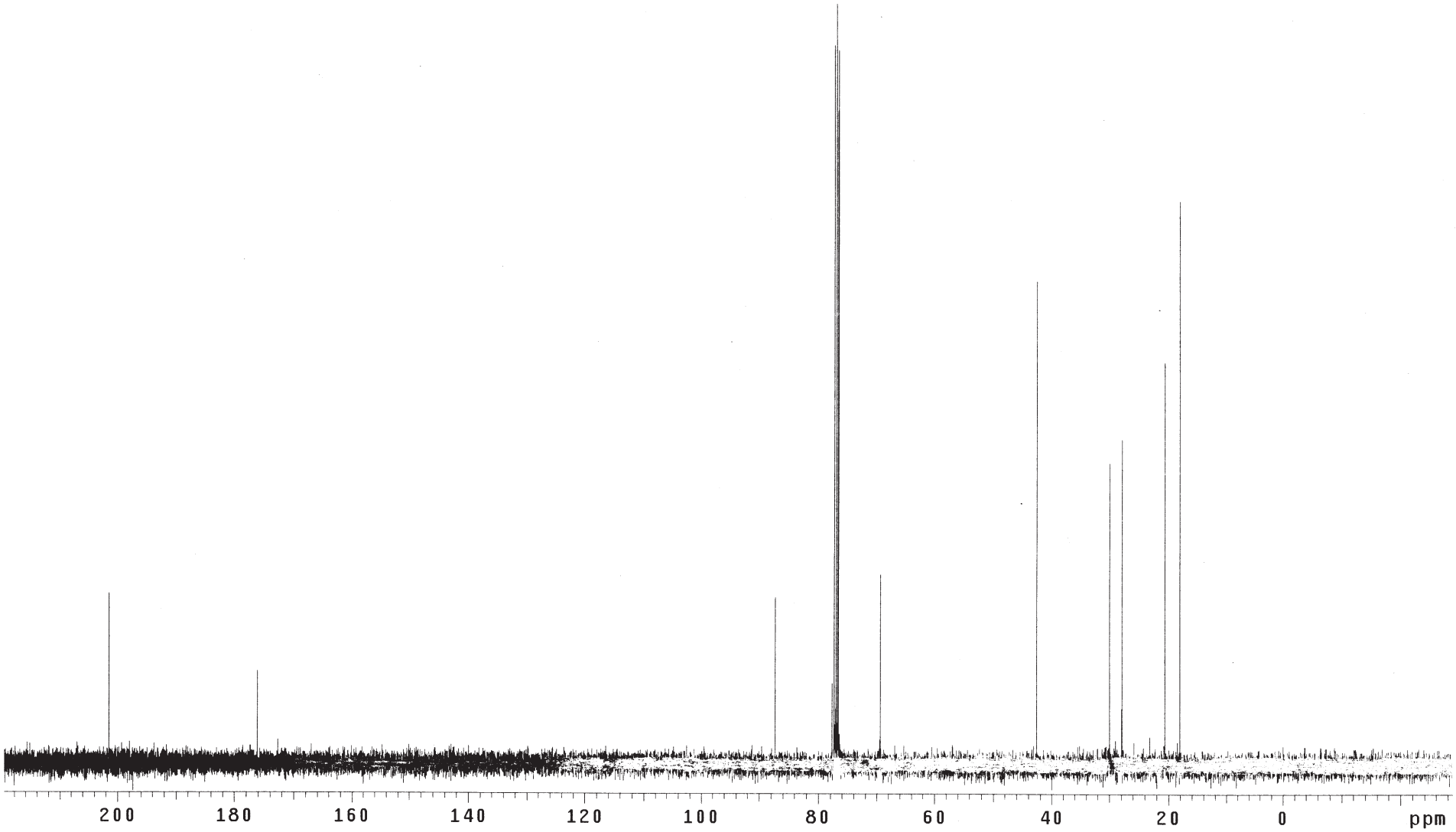

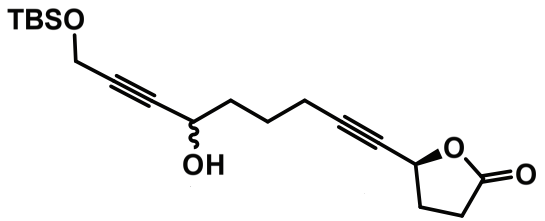

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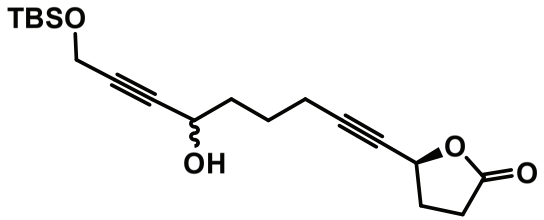

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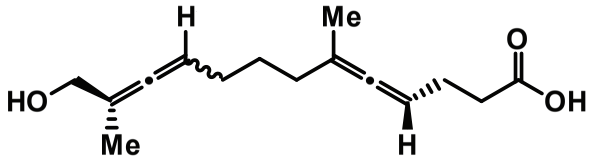

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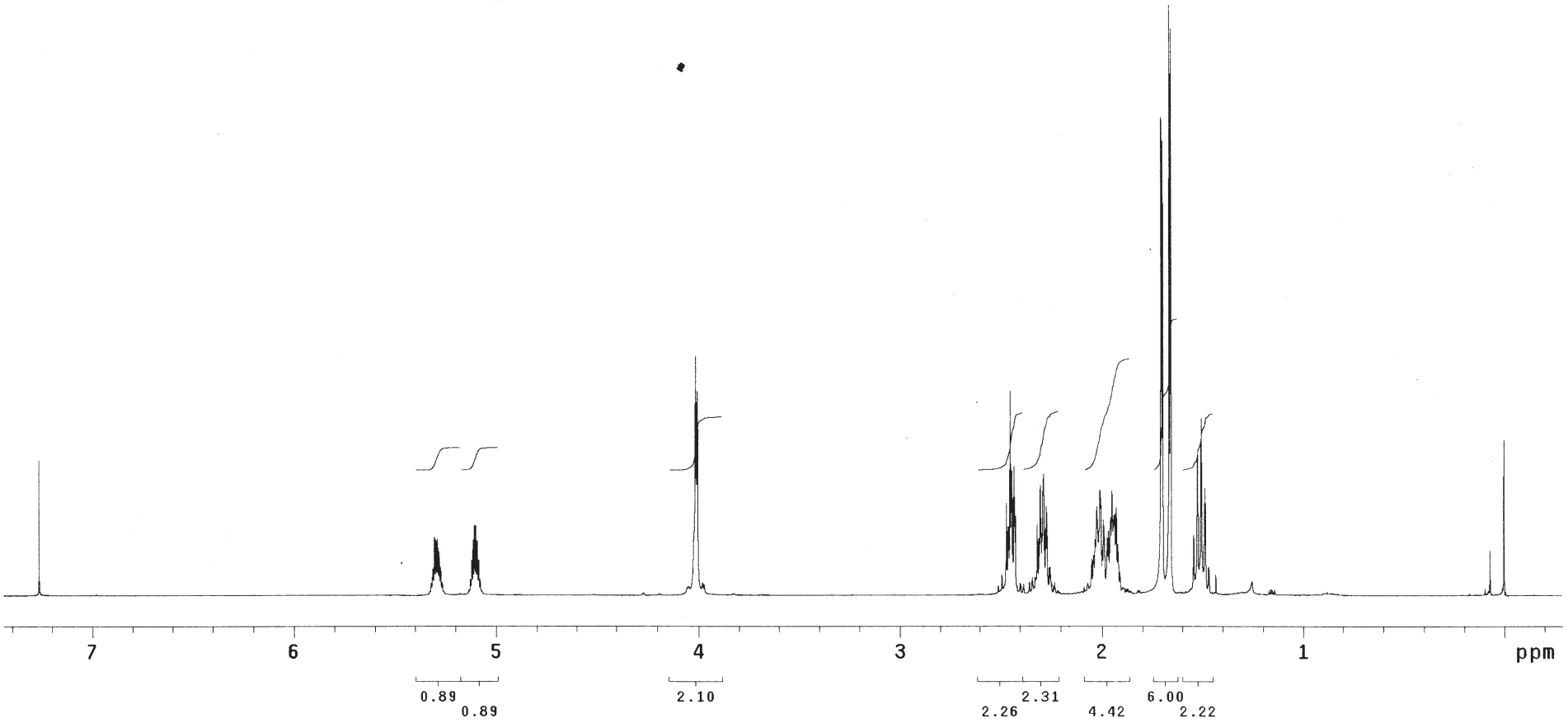

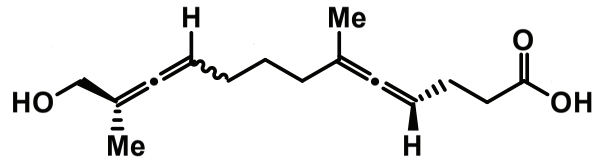

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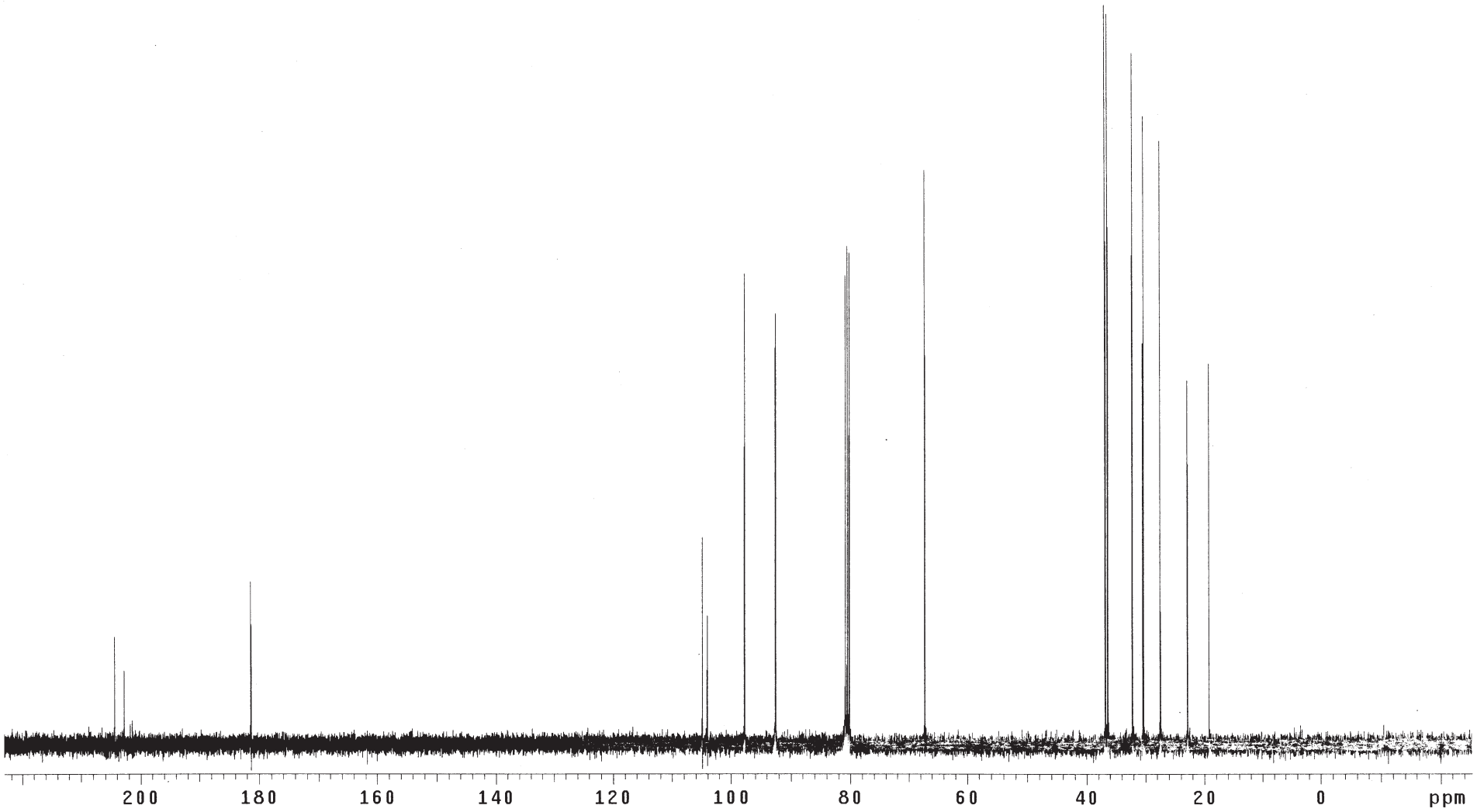

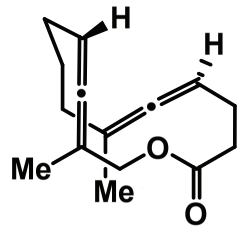

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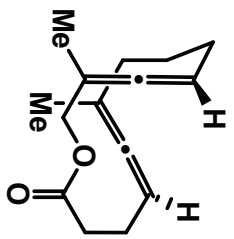

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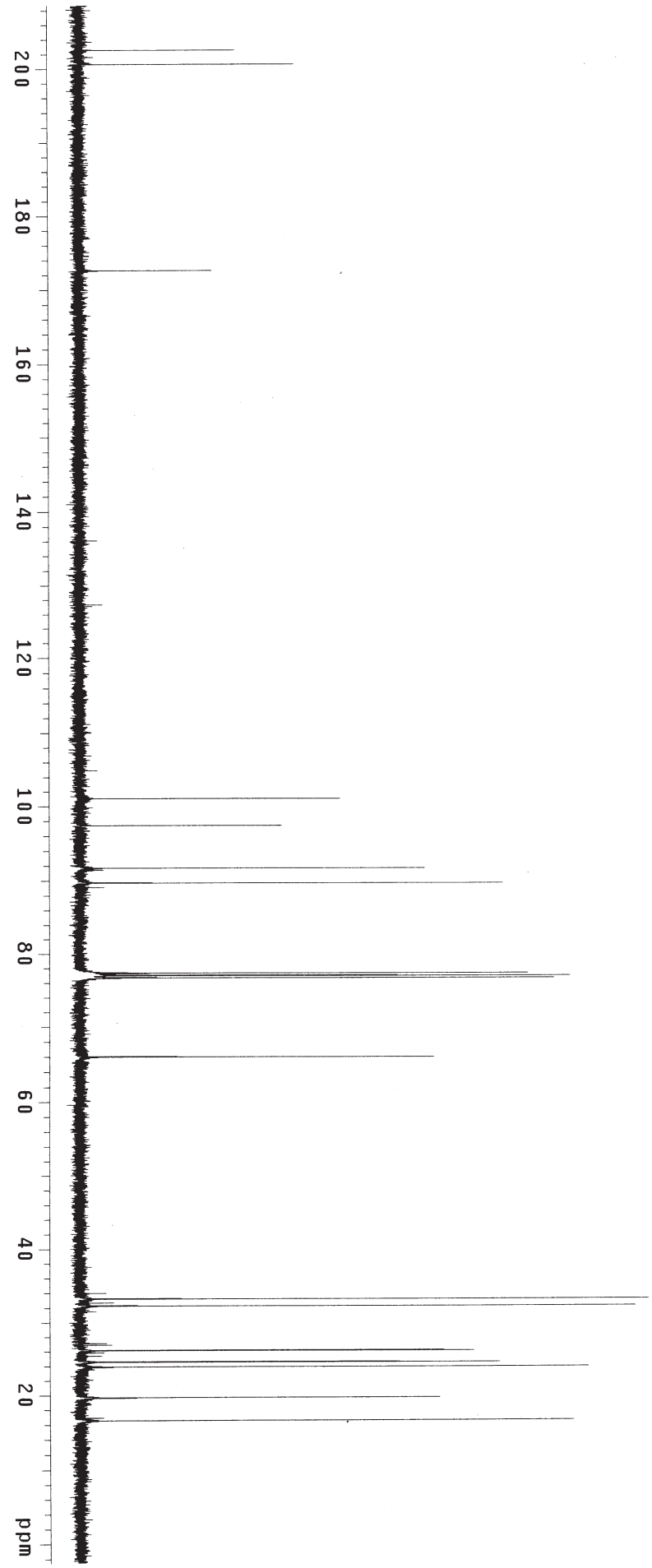
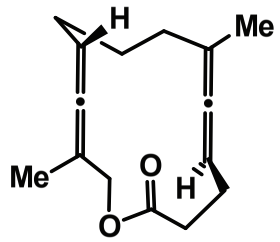
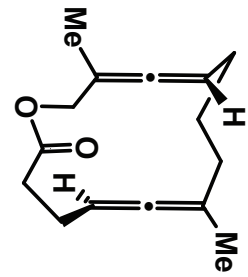


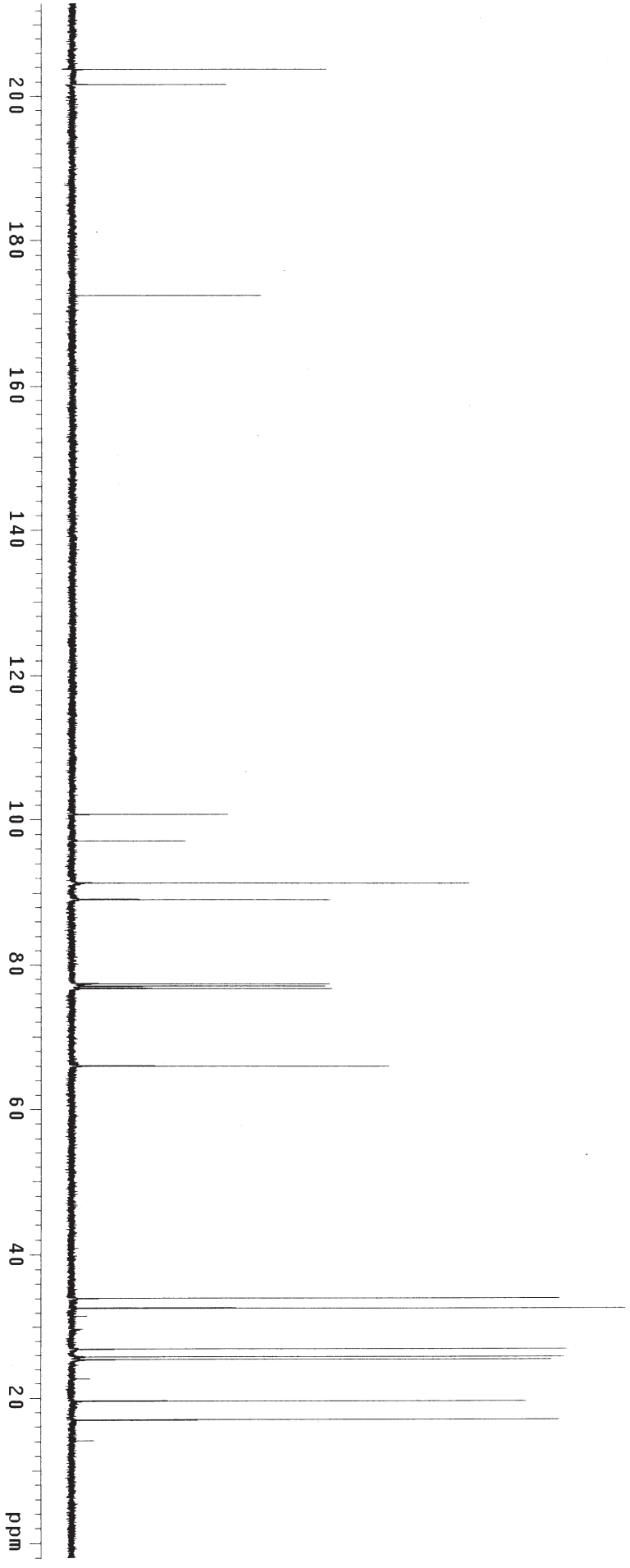

H
Me
Me
O
H
O

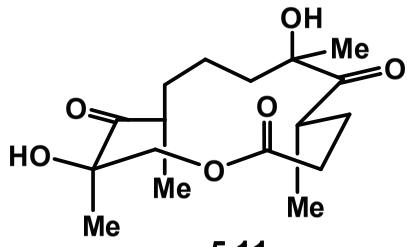
5.9

7
6
5
4
3
2
1
ppm
0.90
0.91
1.00
1.01
1.07
3.12
2.02
3.03
1.13
2.17
3.23
1.10

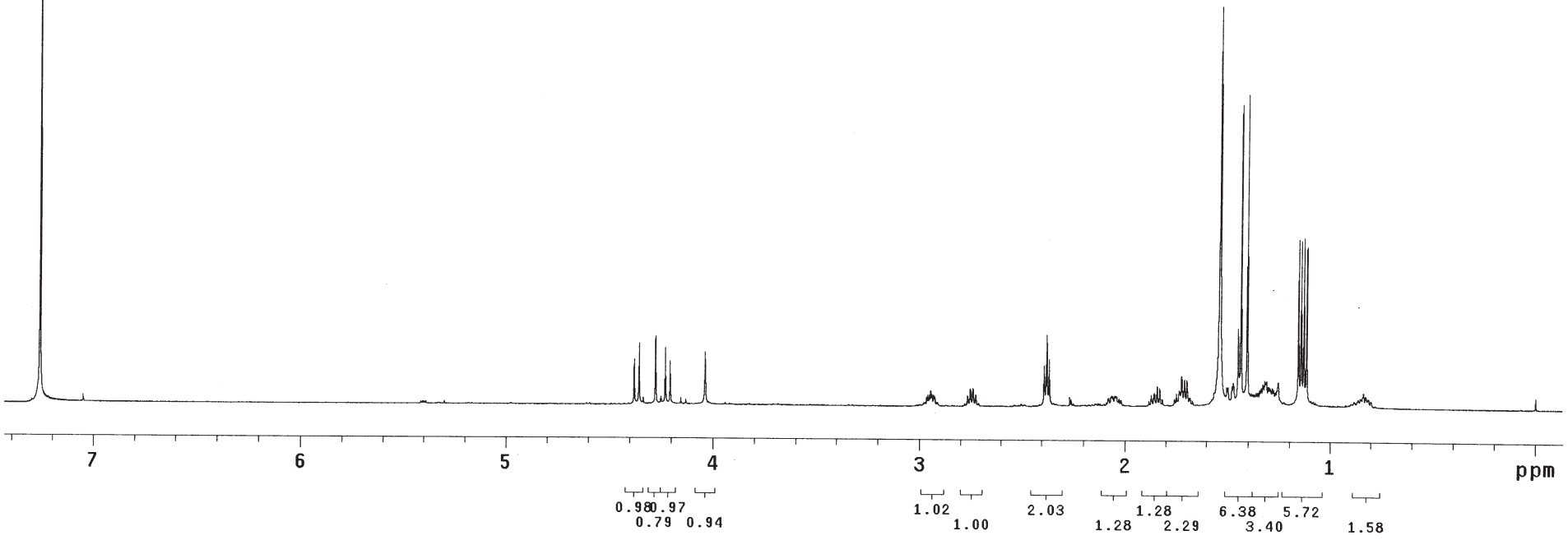


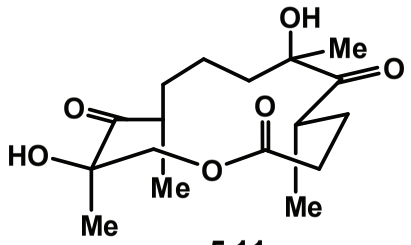
5.9



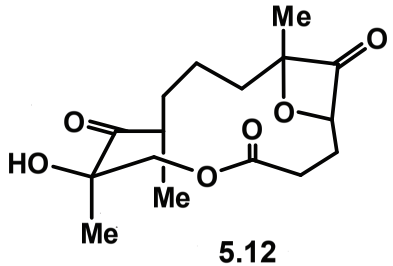

OH
Me
O
O
O
HO
Me
O
Me
Me

5.11


7
6
5
4
3
2
1
ppm
0.98
0.97
0.79
0.94
1.02
1.00
2.03
1.28
1.28
2.29
6.38
3.40
5.72
1.58

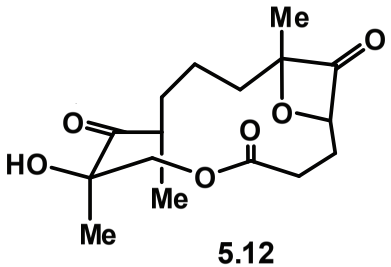


5.11

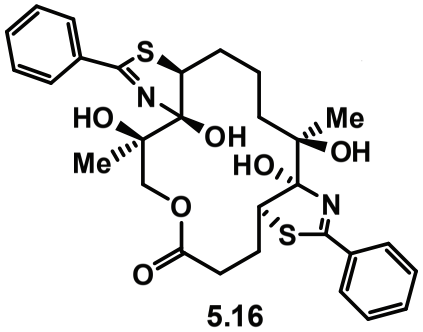

Me
O
O
O
HO
O
Me
Me

5.12

7
6
5
4
3
2
1
ppm
0.83
1.13
1.10 1.07
1.00
1.33
1.05
1.35
2.01
2.97
1.50
5.76
6.53
4.08
1.30

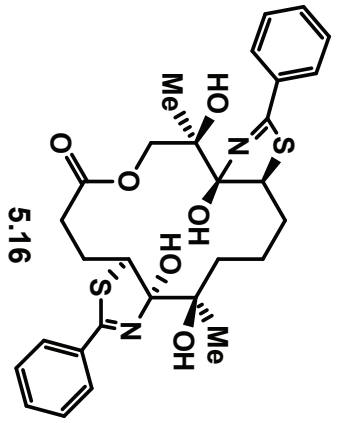


5.12

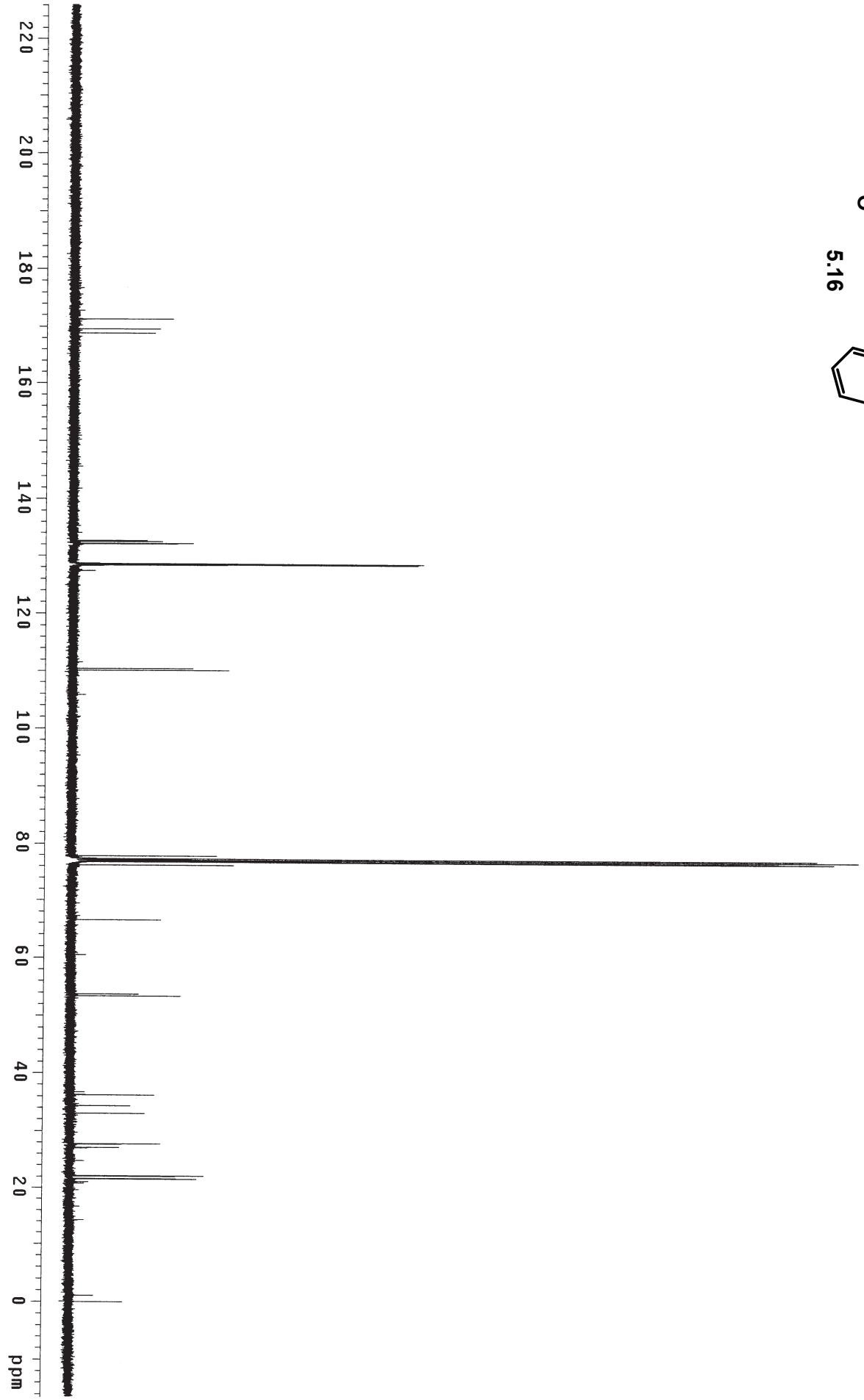

S
N
HO
OH
Me
Me
OH
HO
O
N
S
O

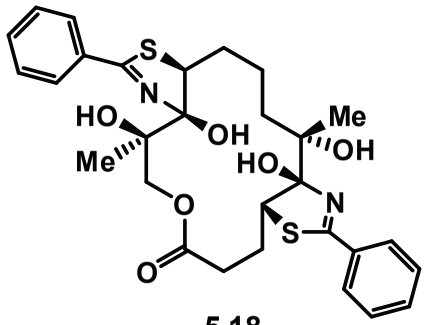
5.16

8
7
6
5
4
3
2
1
0
ppm
4.35
4.52
2.33
1.08
1.27
0.91
1.00
1.28
0.90
1.03
1.04
1.00
2.81
1.79
2.47
1.19
1.66
7.85


HO
Me
N
S
O
O
OH
HO
S
N
Me
OH

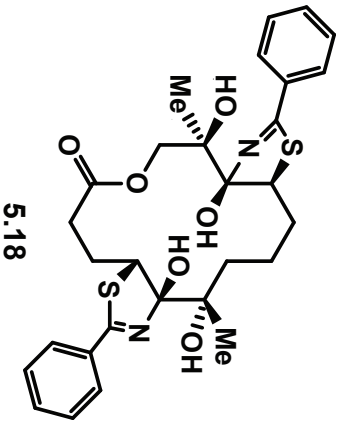
5.16


220
200
180
160
140
120
100
80
60
40
20
0
ppm


S
N
HO
OH
Me
Me
OH
HO
N
O
S
O

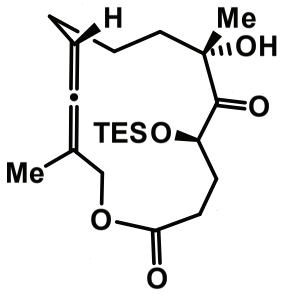
5.18

8
7
6
5
4
3
2
1
ppm
4.34
6.54
1.04
1.01
1.12
1.00
1.05
1.00
1.05
1.11
0.96
1.06
1.08
4.67
3.68
1.23
3.49
3.12

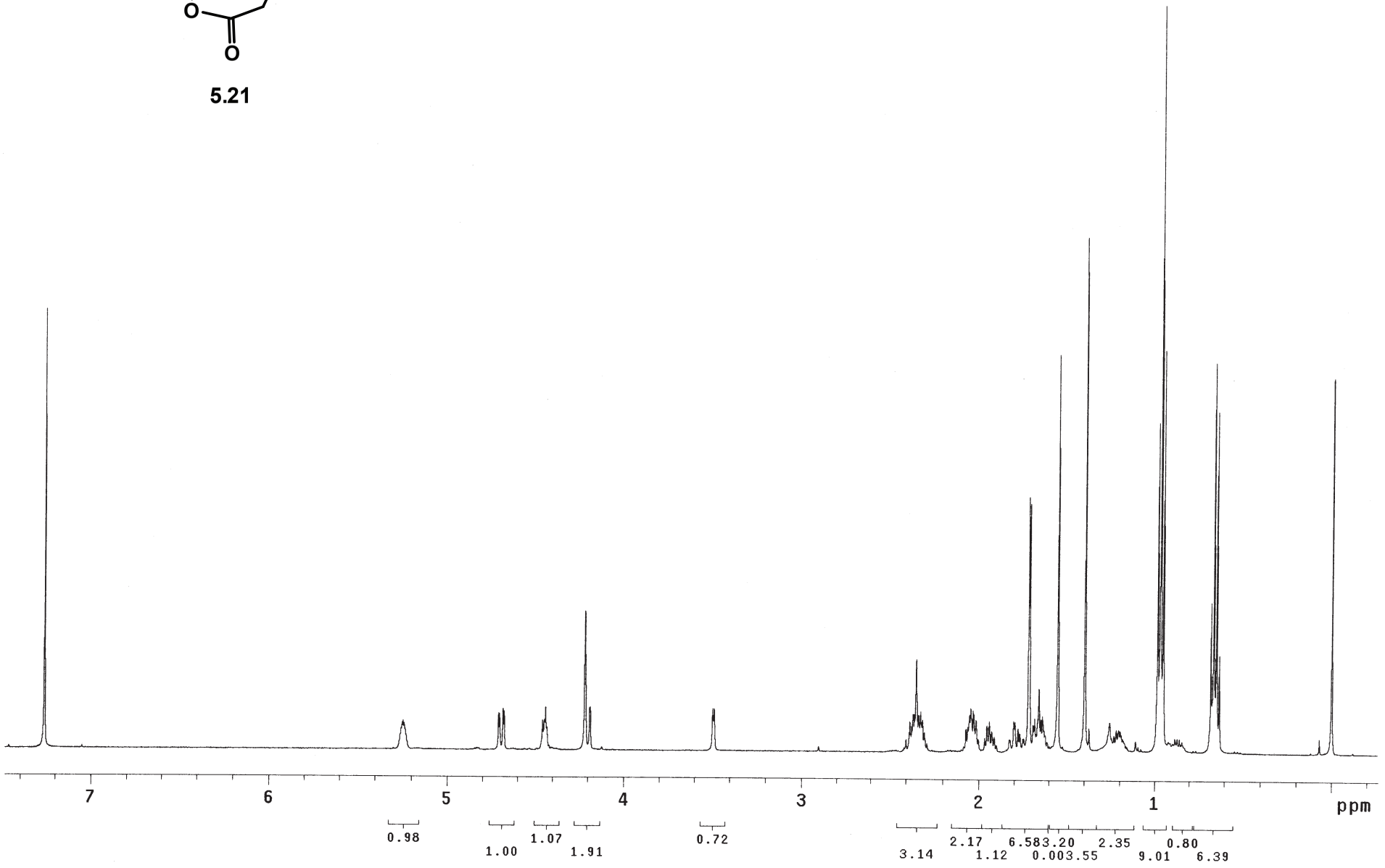

HO
Me
N
S
O
O
OH
HO
S
N
Me
OH

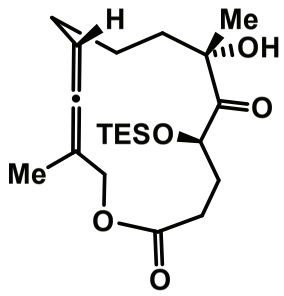
5.18

220
200
180
160
140
120
100
80
60
40
20
0
ppm

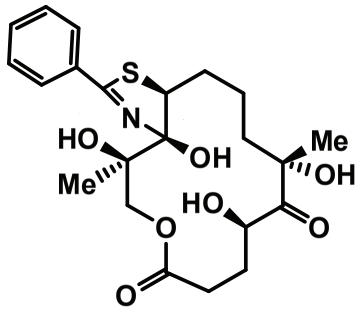

H
Me
OH
O
TESO
Me
O
O

5.21

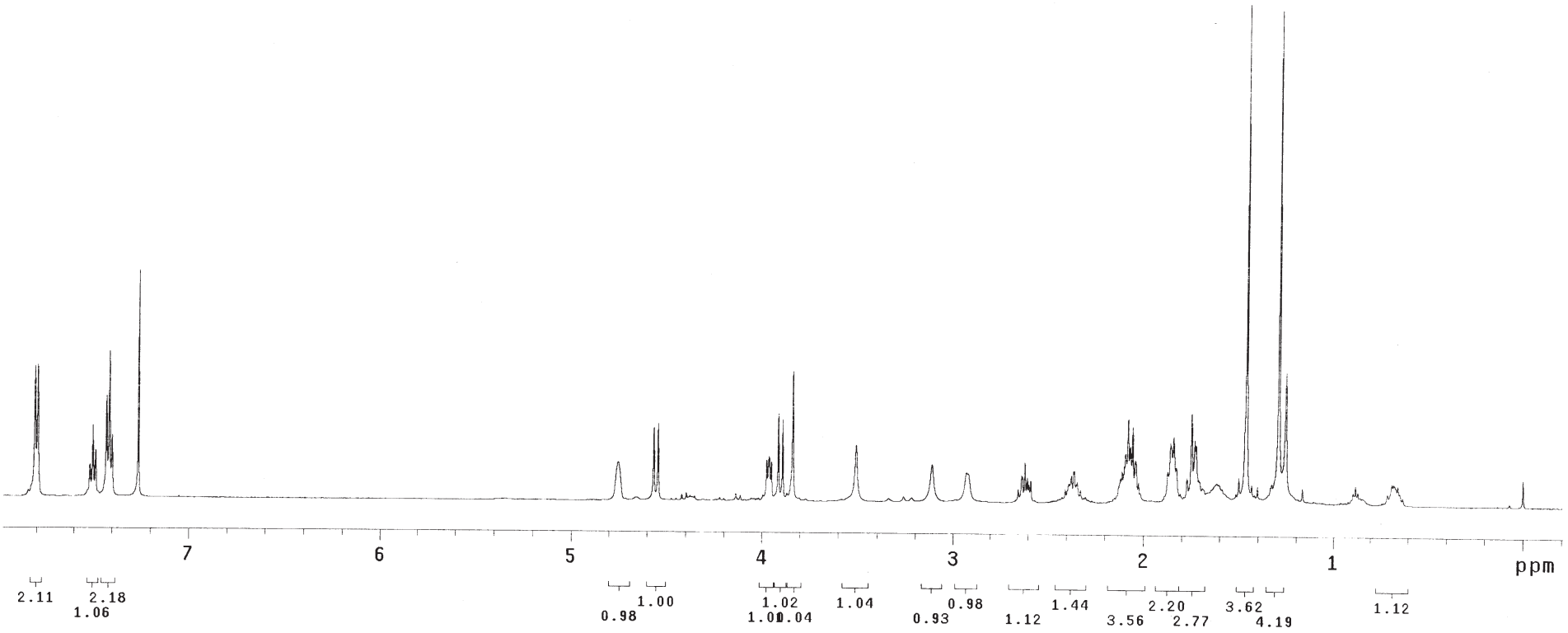

7
6
5
4
3
2
1
ppm
0.98
1.00
1.07
1.91
0.72
3.14
2.17
1.12
6.58
3.20
0.00
3.55
2.35
9.01
0.80
6.39

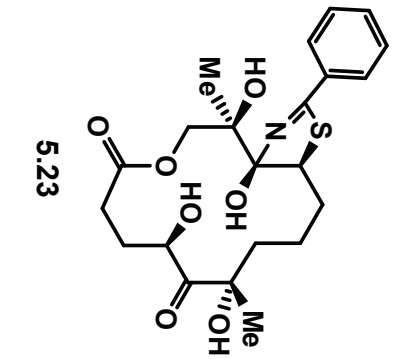


5.21


S
N
HO
OH
Me
Me
OH
HO
O
O
O

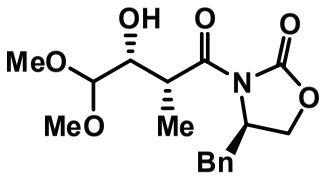
5.23


7
6
5
4
3
2
1
ppm
2.11
2.18
1.06
0.98
1.00
1.02
1.00
1.04
1.04
0.93
0.98
1.12
1.44
3.56
2.20
2.77
3.62
4.19
1.12

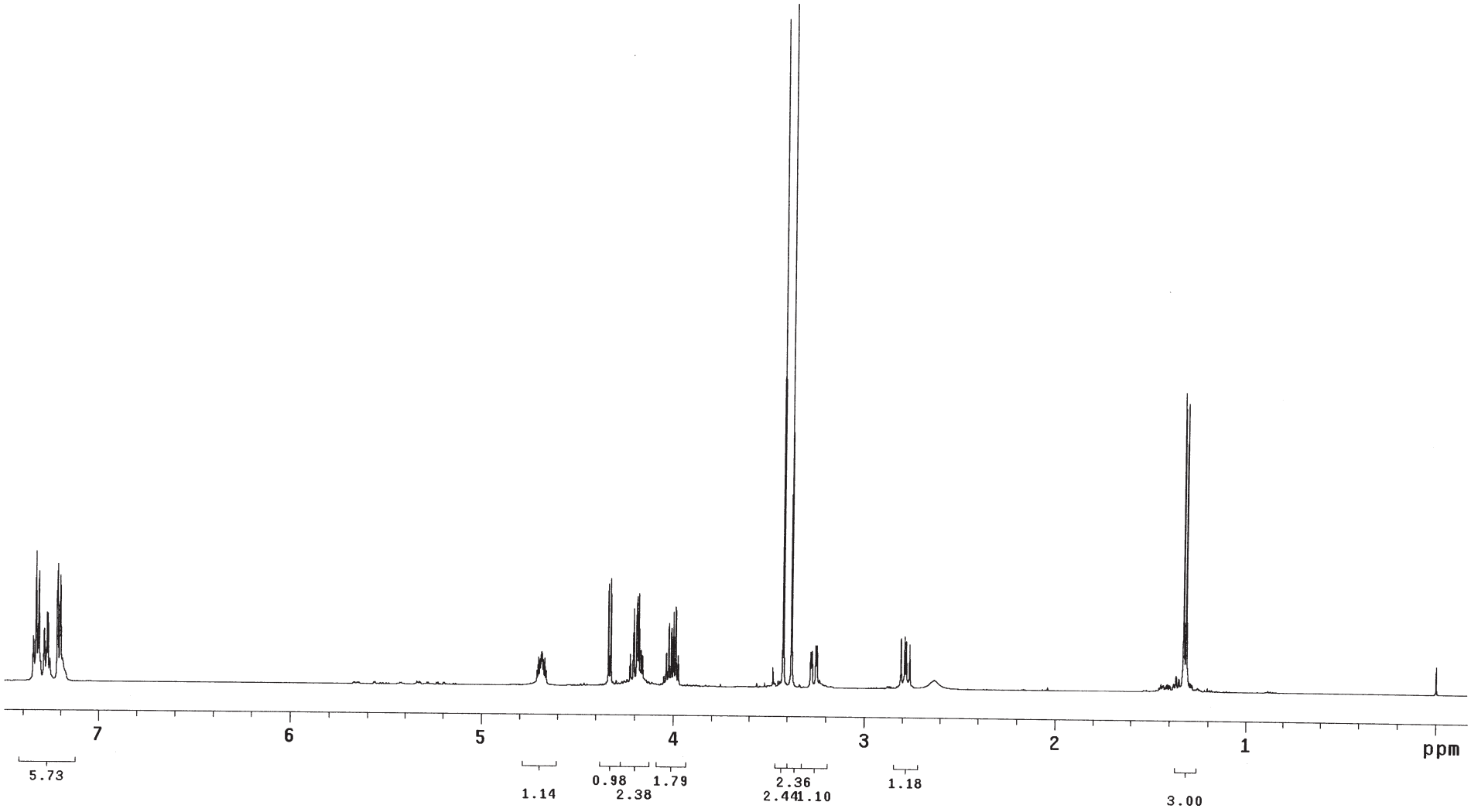

HO
Me
N
S
O
O
HO
OH
O
Me
OH

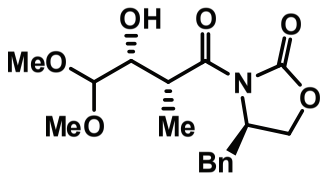
5.23

220
200
180
160
140
120
100
80
60
40
20
0
ppm

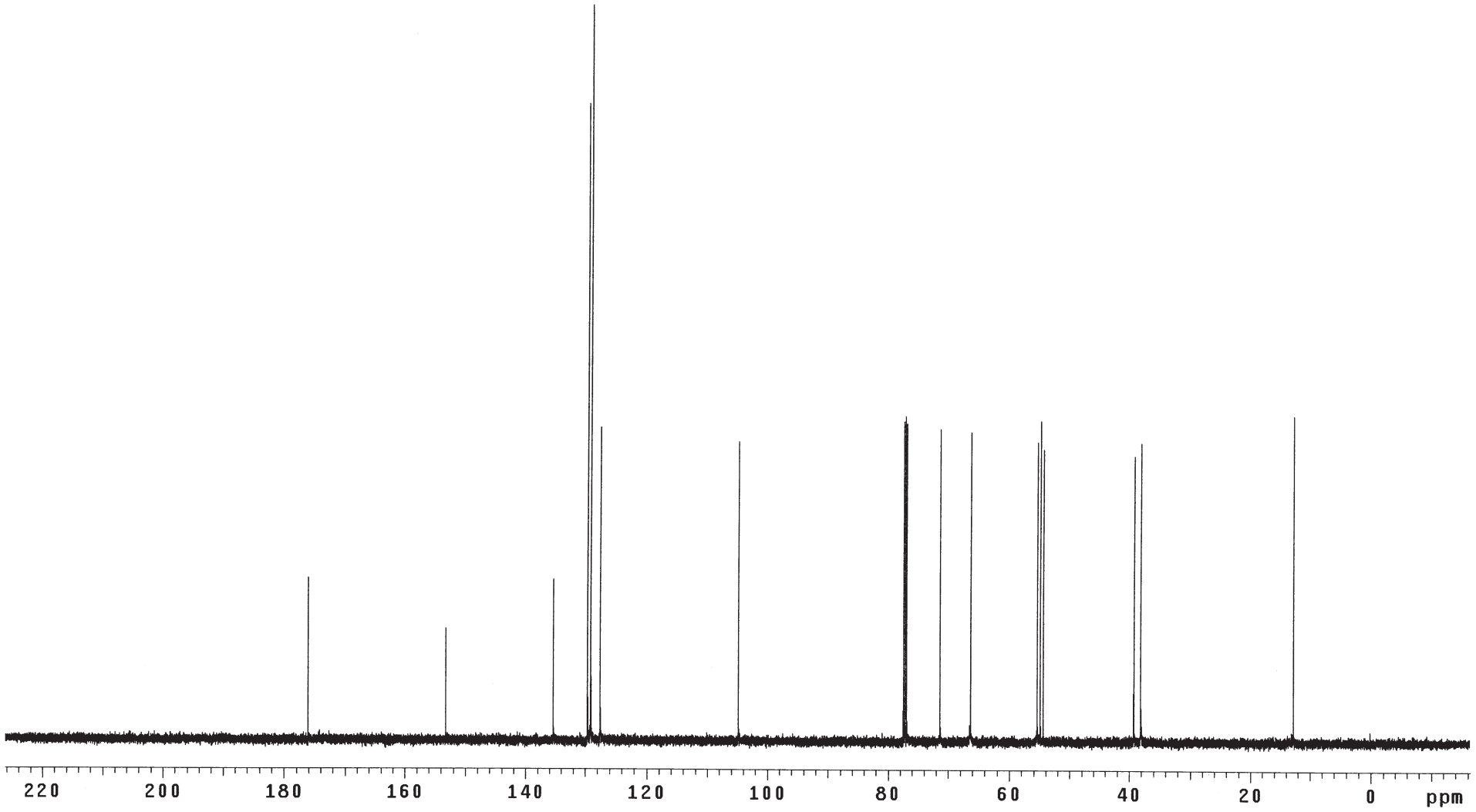

OH
O
O
MeO
N
O
MeO
Me
Bn

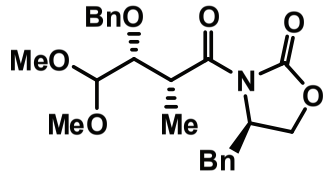
6.7


7
6
5
4
3
2
1
ppm
5.73
1.14
0.98
2.38
1.79
2.36
2.44
1.10
1.18
3.00

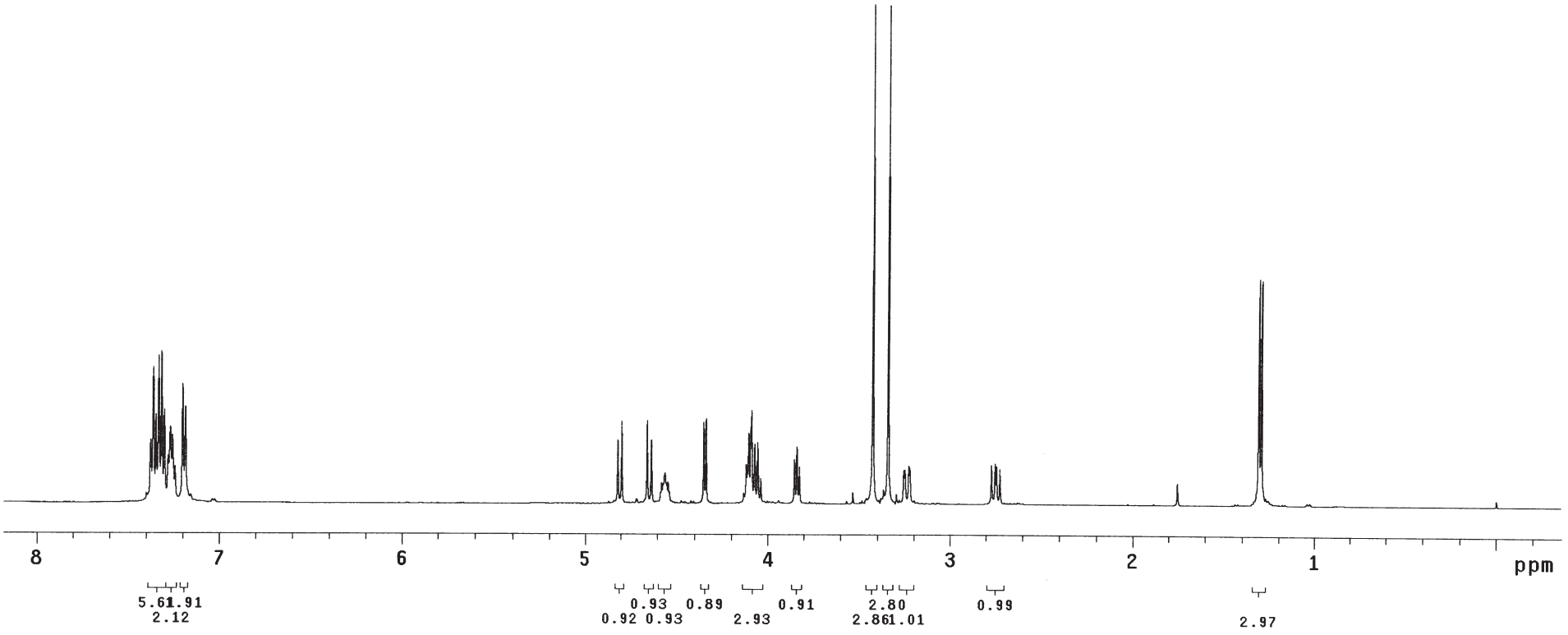


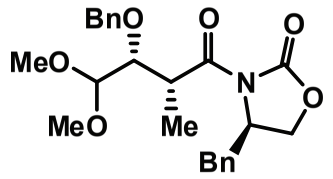
6.7



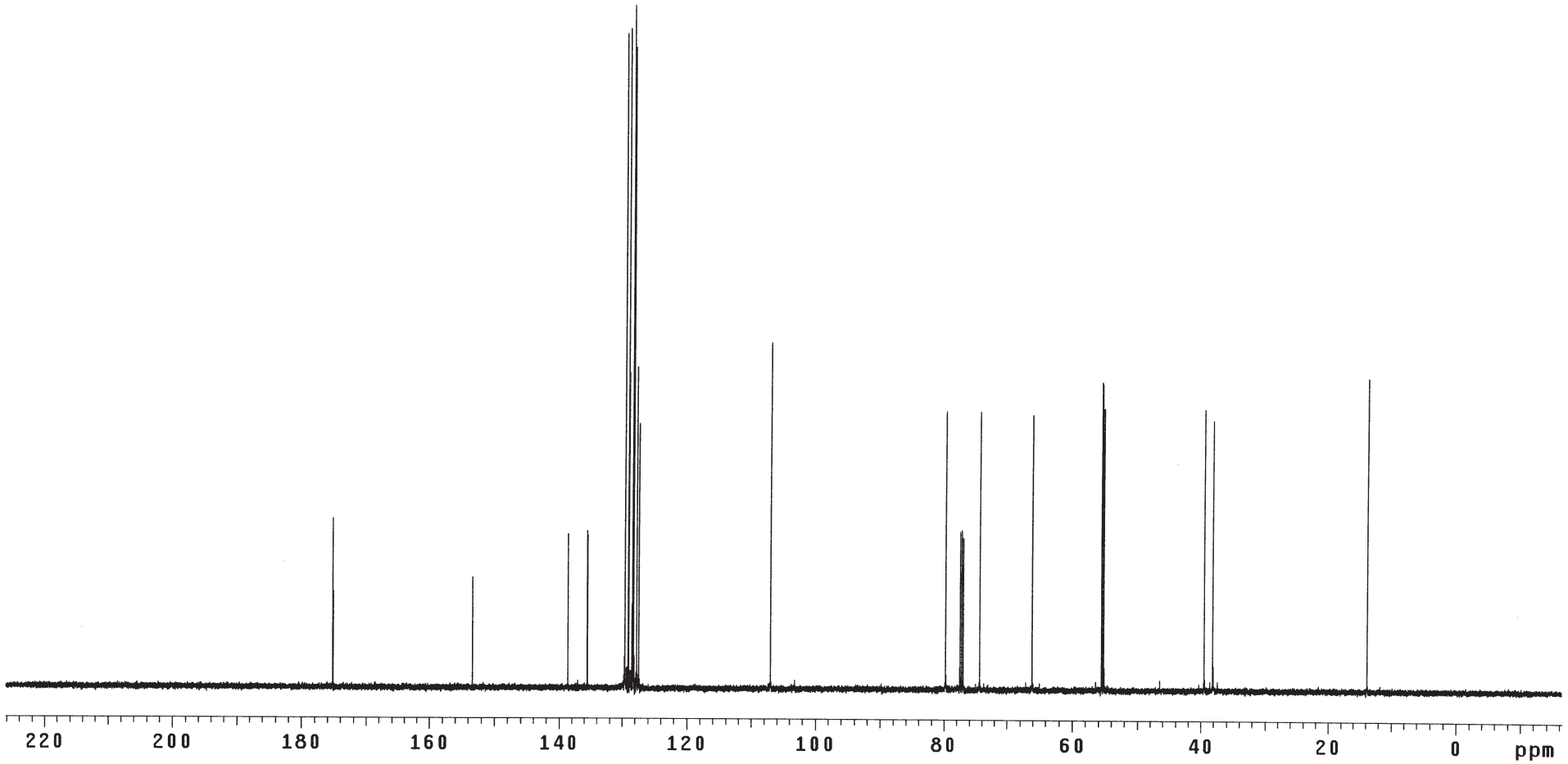

BnO
O
O
MeO
N
O
MeO
Me
Bn

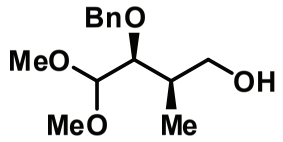
6.8


8
7
6
5
4
3
2
1
ppm
5.61
1.91
2.12
0.92
0.93
0.93
0.89
2.93
0.91
2.80
2.86
1.01
0.99
2.97

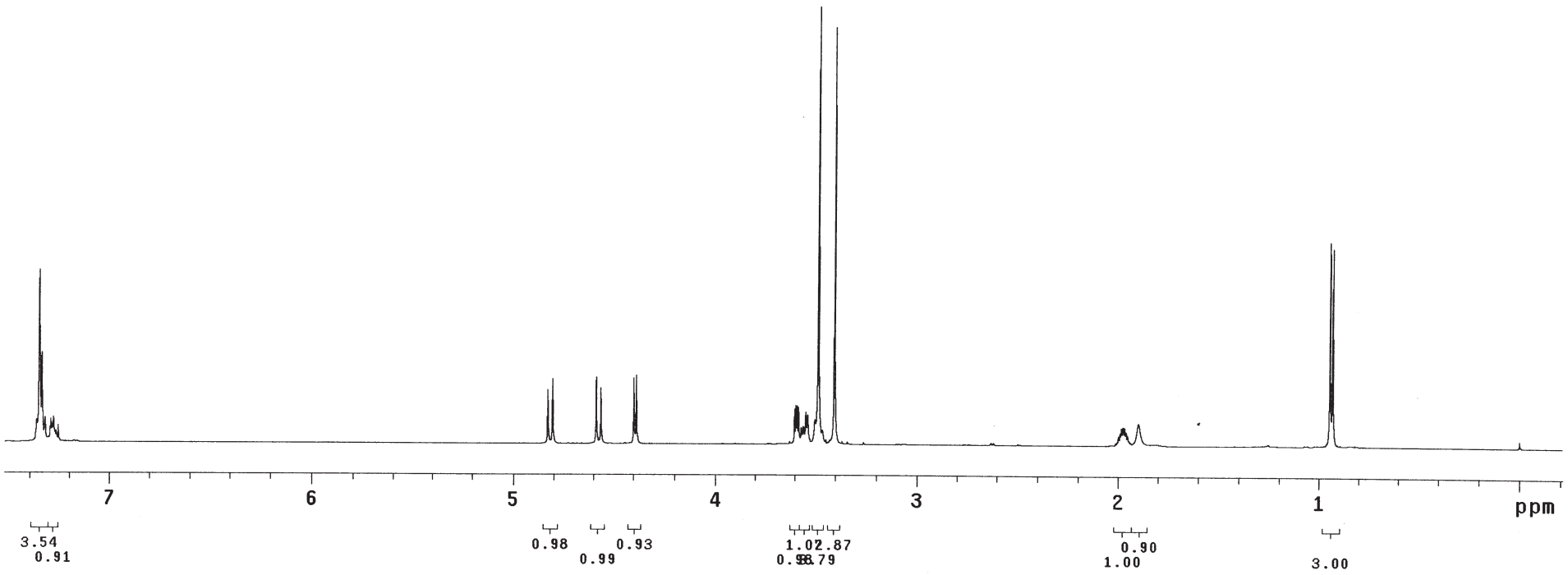

BnO
O
O
MeO
N
O
MeO
Me
Bn

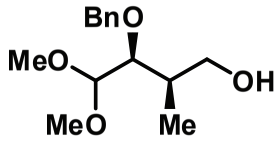
6.8


220
200
180
160
140
120
100
80
60
40
20
0
ppm

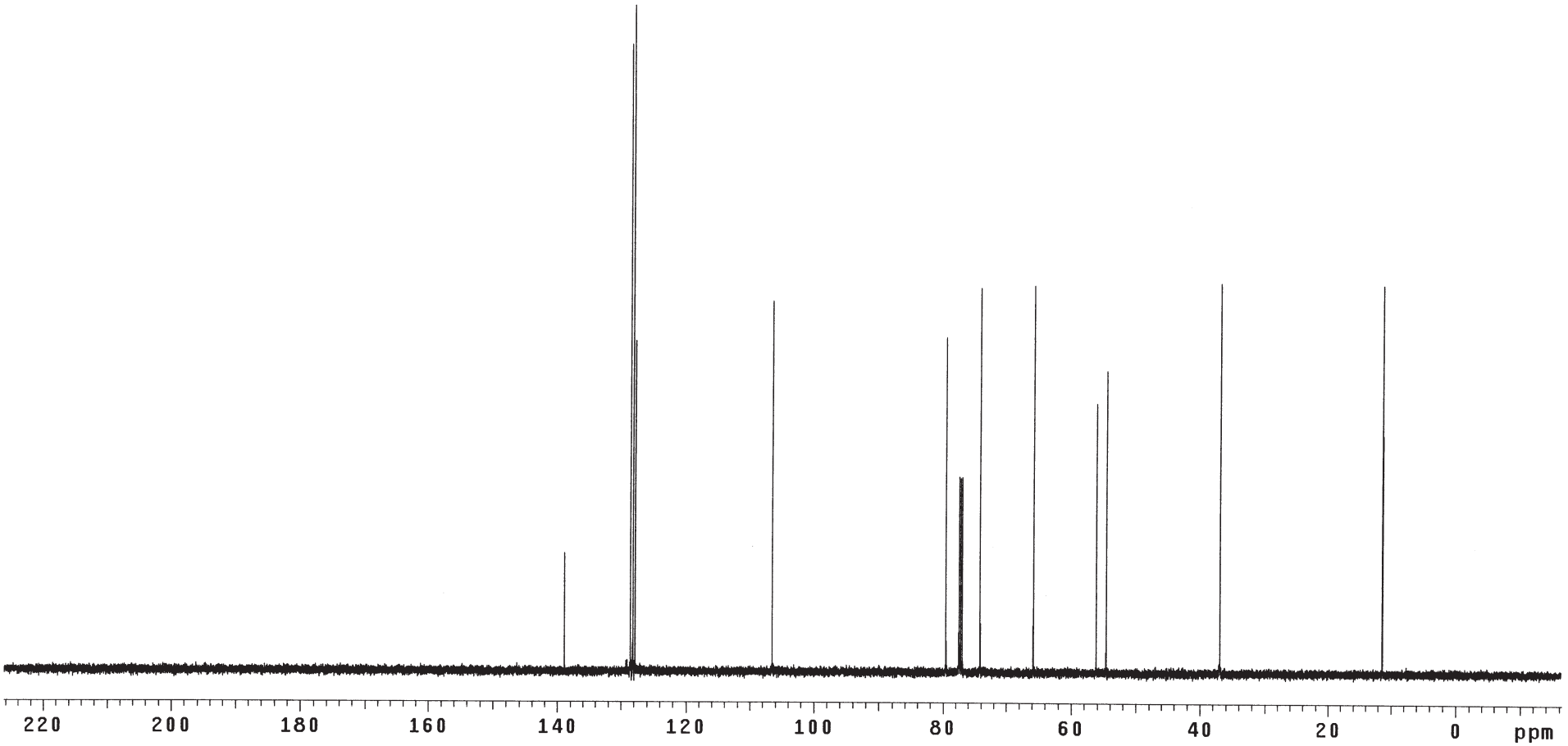

BnO
MeO
OH
MeO
Me

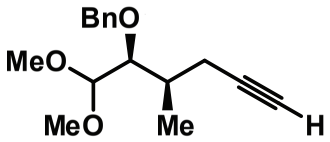
6.12


7
6
5
4
3
2
1
ppm
3.54
0.91
0.98
0.99
0.93
1.02
2.87
0.90
1.00
3.00

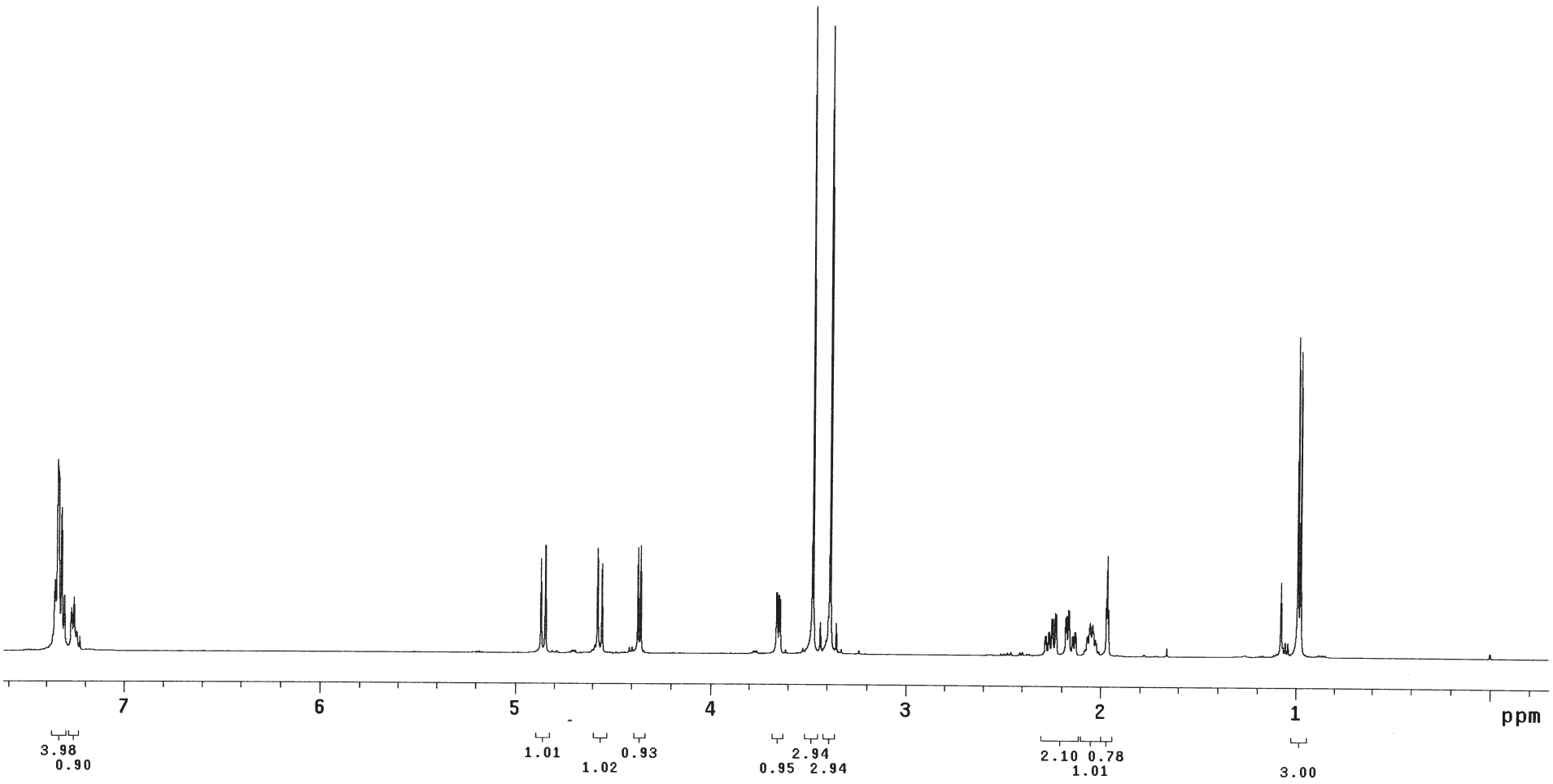


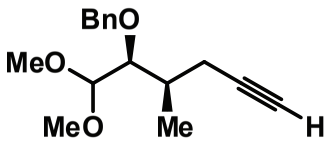
6.12



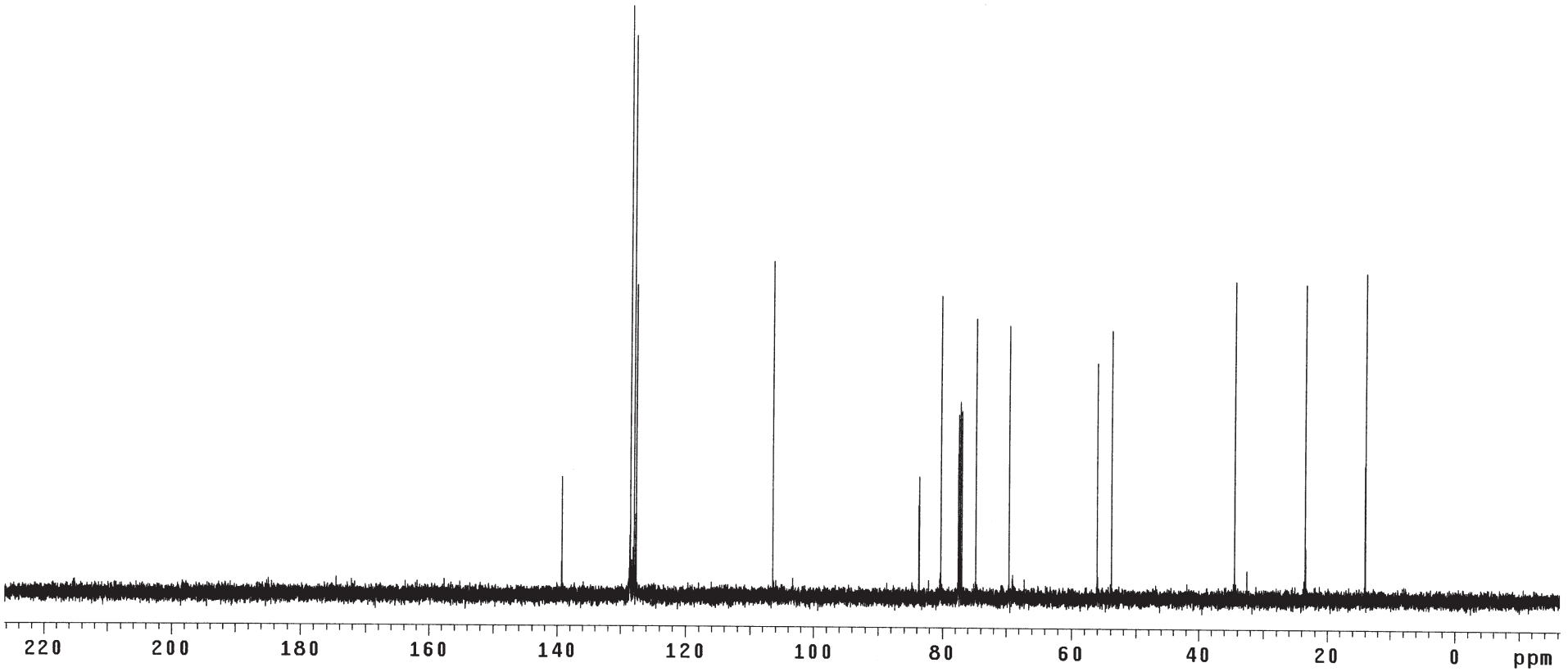

BnO
MeO
MeO
Me
H

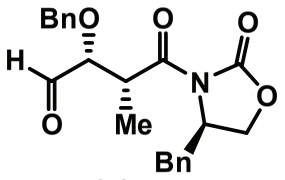
6.4


7
6
5
4
3
2
1
ppm
3.98
0.90
1.01
1.02
0.93
0.95
2.94
2.94
2.10
0.78
1.01
3.00

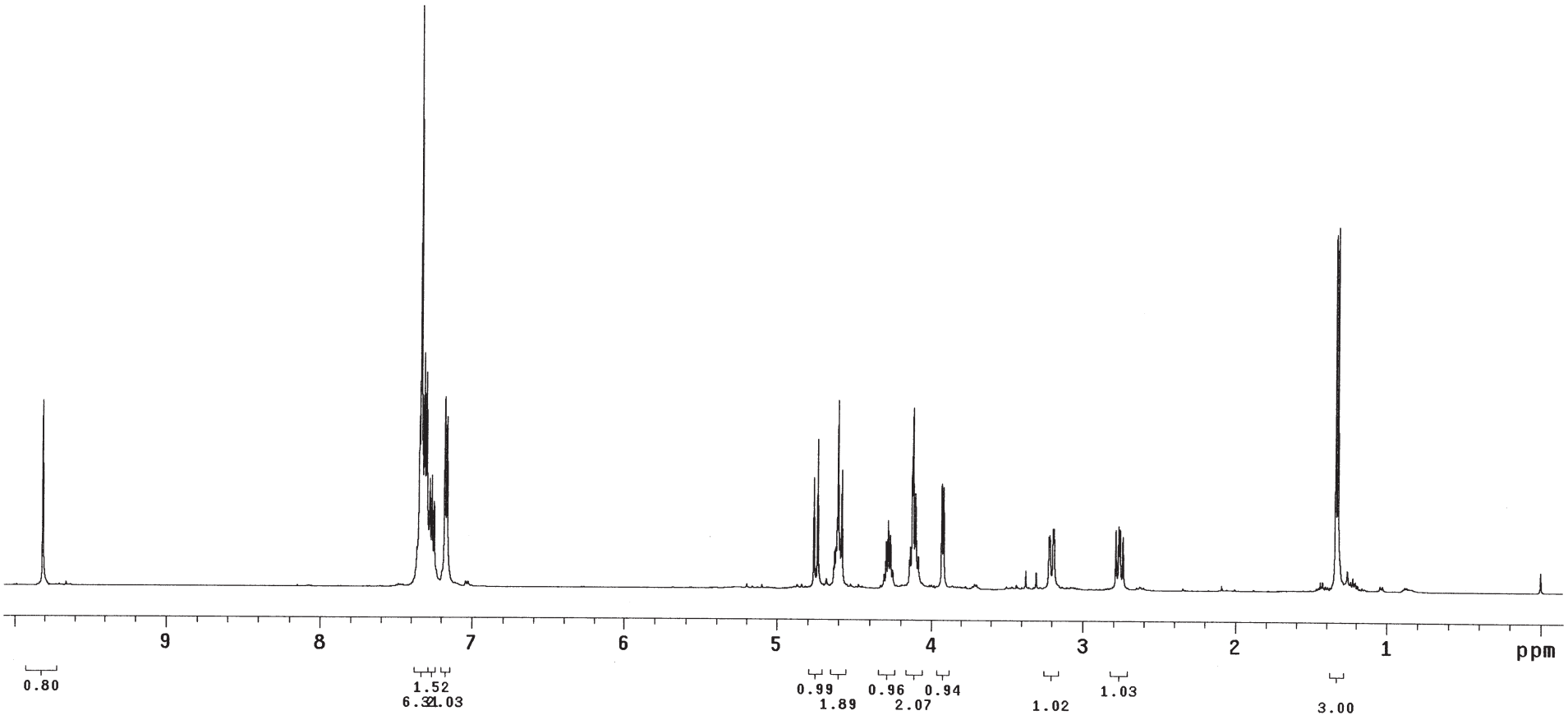


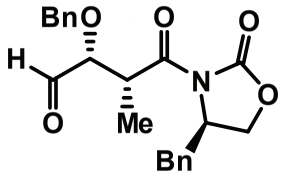
6.4



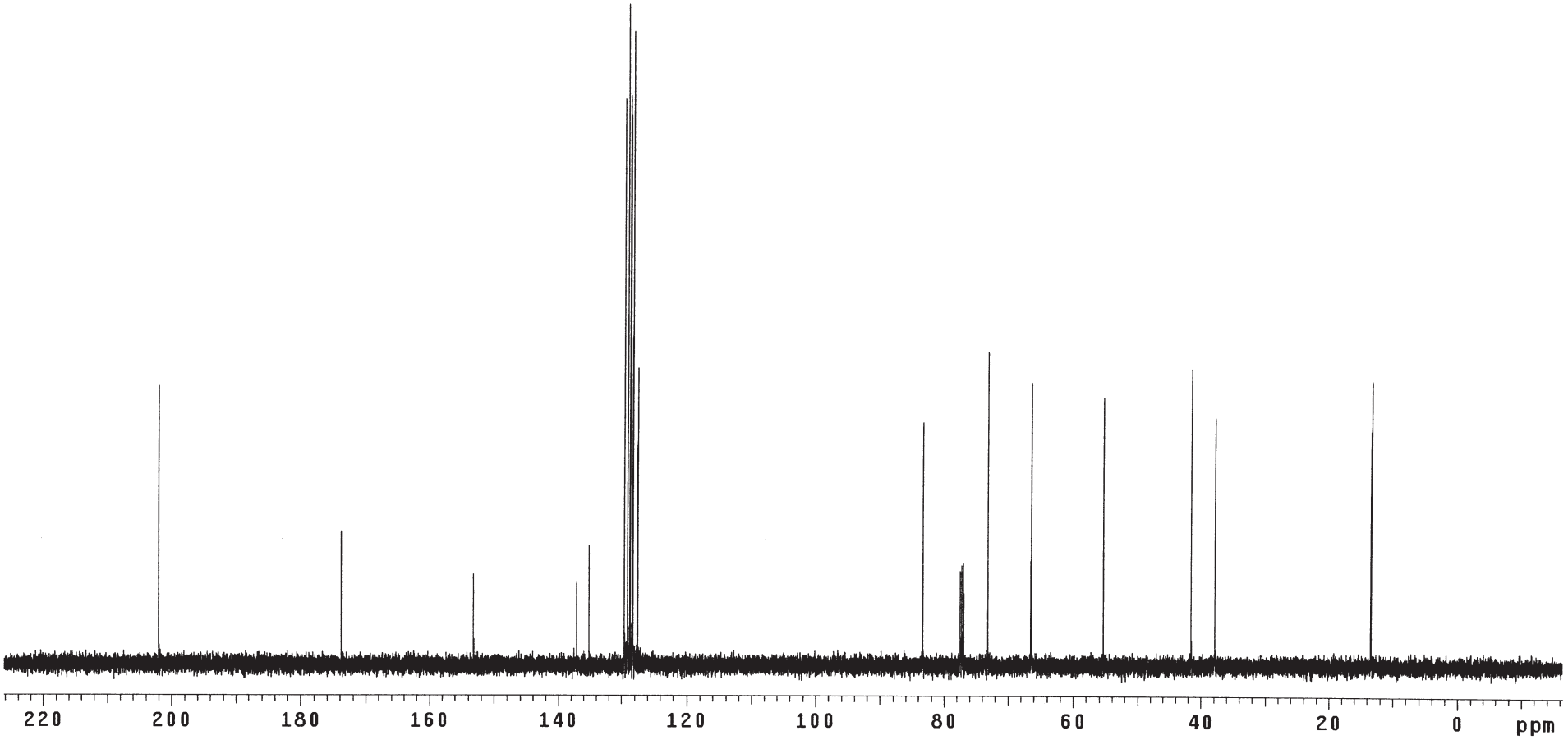

BnO
O
O
H
N
O
O
Me
Bn

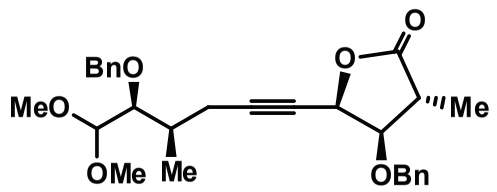
6.3


9
8
7
6
5
4
3
2
1
ppm
0.80
1.52
6.32
1.03
0.99
1.89
0.96
2.07
0.94
1.02
1.03
3.00

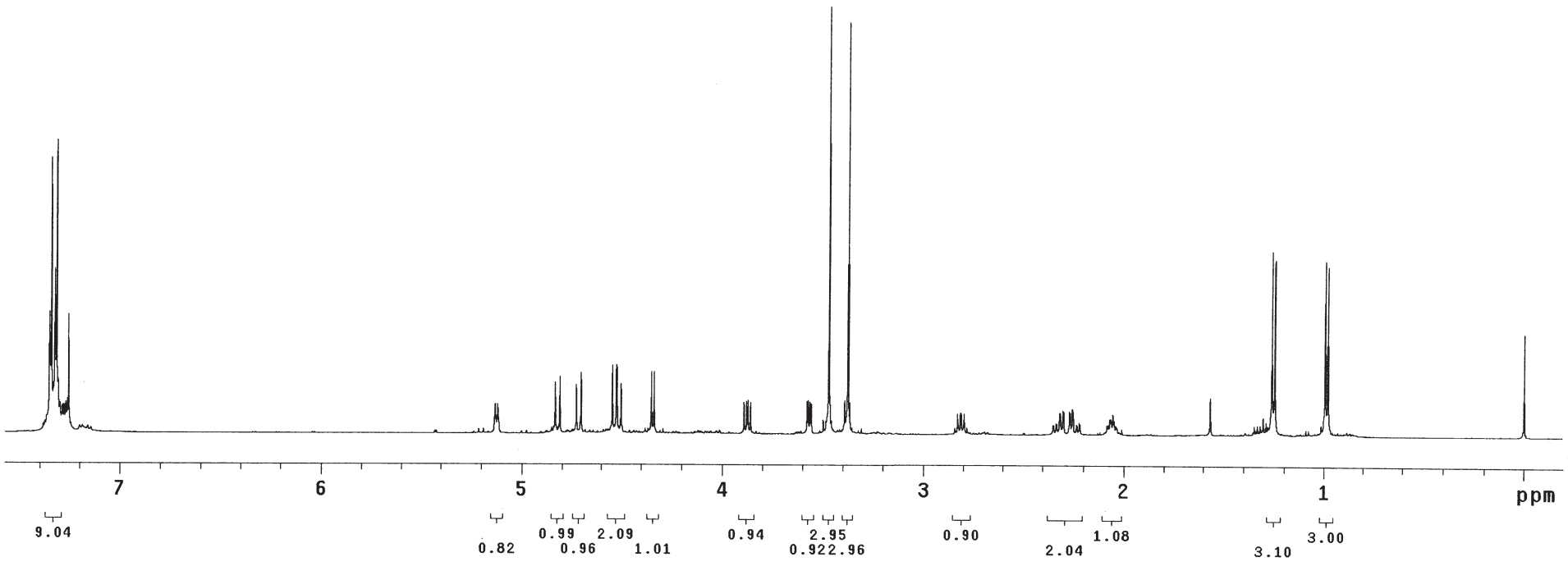


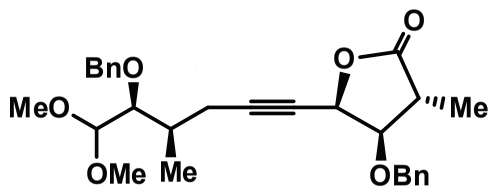
6.3




BnO
MeO
OMe
Me
O
O
Me
OBn

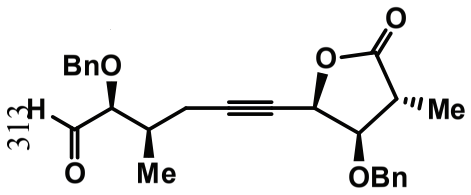
6.18


7
6
5
4
3
2
1
ppm
9.04
0.82
0.99
0.96
2.09
1.01
0.94
2.95
0.92
2.96
0.90
2.04
1.08
3.10
3.00


BnO
MeO
OMe
Me
O
O
Me
OBn

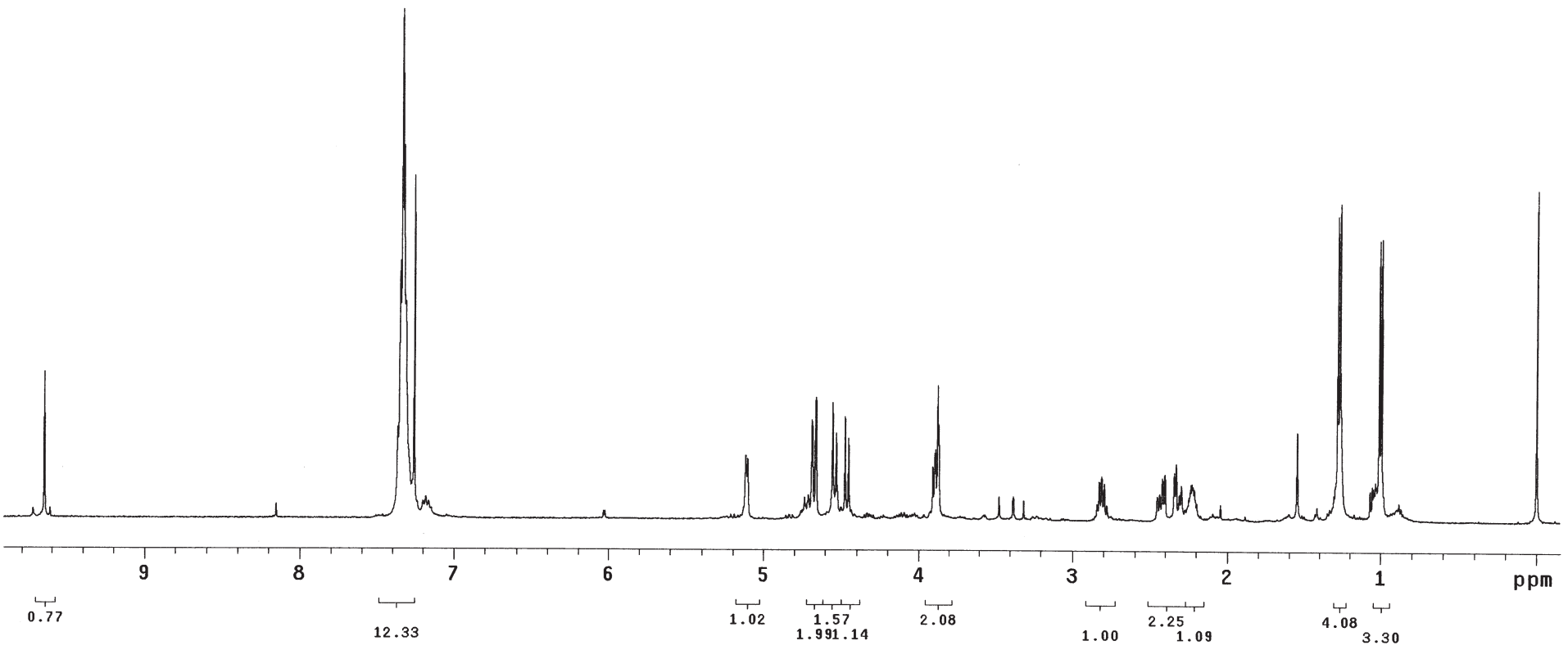
6.18

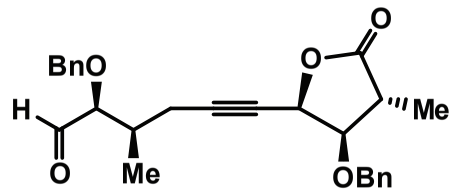
220
200
180
160
140
120
100
80
60
40
20
0
ppm


BnO
O
O
Me
H
O
Me
OBn

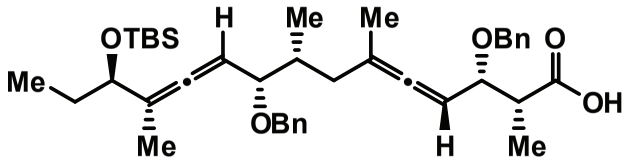
313

6.21


9
8
7
6
5
4
3
2
1
ppm
0.77
12.33
1.02
1.57
1.99
1.14
2.08
1.00
2.25
1.09
4.08
3.30

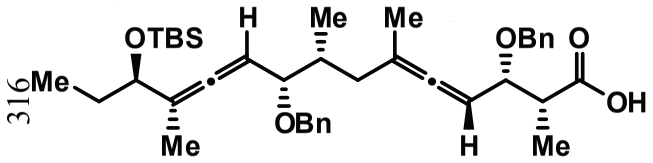


6.21


OTBS
H
Me
Me
OBn
O
Me
OH
OBn
Me
H
Me

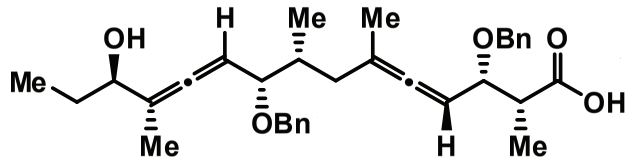
6.26

7
6
5
4
3
2
1
ppm
9.07
1.81
1.94
1.98
1.05
0.90
0.85
1.10
1.06
1.00
3.59
3.83
3.54
15.79
6.00


OTBS
H
Me
Me
OBn
O
Me
OBn
OH
Me
H
Me

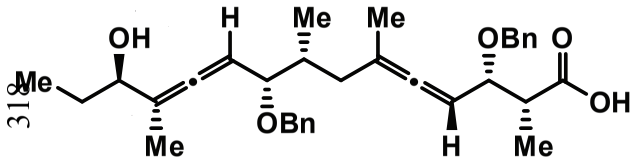
6.26

220
200
180
160
140
120
100
80
60
40
20
0
ppm


OH
H
Me
Me
OBn
O
Me
OBn
OH
Me
H
Me

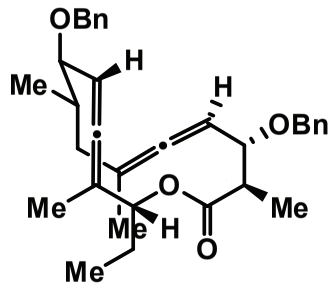
6.27

7
6
5
4
3
2
1
ppm
9.35
0.90
0.95
2.08
2.22
1.09
1.05
1.00
1.12
1.00
0.86
3.25
5.43
1.86
5.39
3.29
4.75

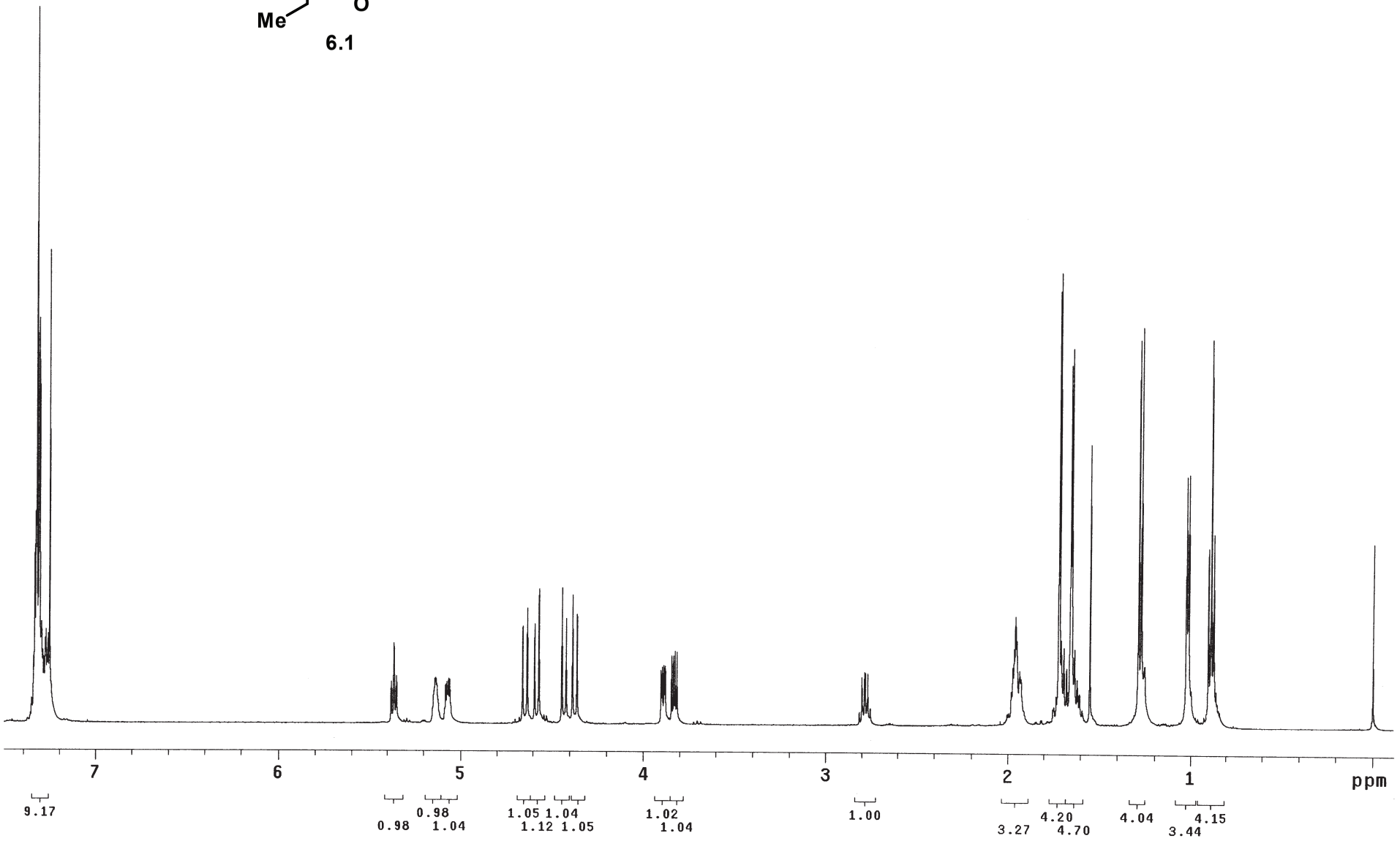

OH
H
Me
Me
OBn
O
Me
OH
OBn
Me
H
Me

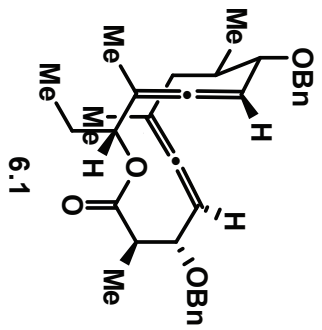
6.27

220
200
180
160
140
120
100
80
60
40
20
0
ppm


OBn
H
Me
H
OBn
Me
O
Me
Me
H
O
Me

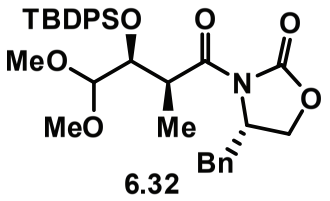
6.1


7
6
5
4
3
2
1
ppm
9.17
0.98
0.98
1.04
1.05
1.12
1.04
1.05
1.02
1.04
1.00
3.27
4.20
4.70
4.04
3.44
4.15


Me
OBn
Me
H
Me
Me
H
O
O
H
Me
OBn

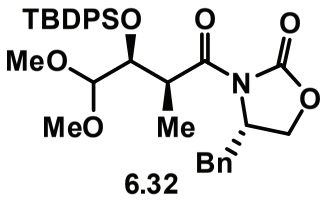
6.1

220
200
180
160
140
120
100
80
60
40
20
0
ppm

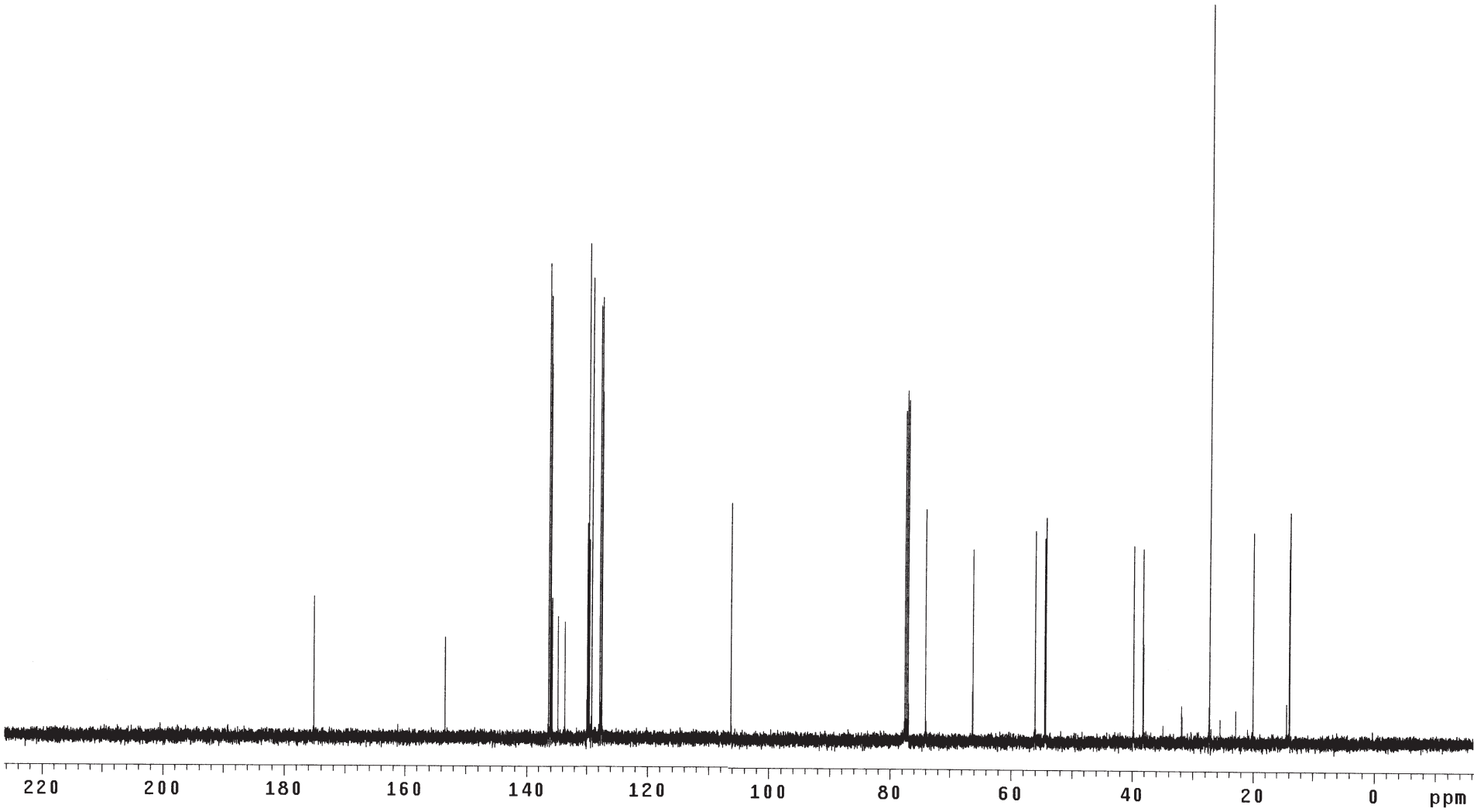

TBDPSO
O
O
MeO
N
O
MeO
Me
Bn

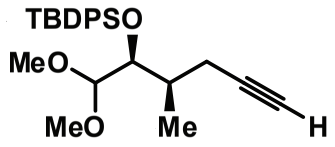
6.32

7
6
5
4
3
2
1
ppm
2.02
1.95
11.11
1.01
4.09
1.01
1.06
3.00
4.02
3.09
9.71


TBDPSO
O
O
MeO
N
O
MeO
Me
Bn

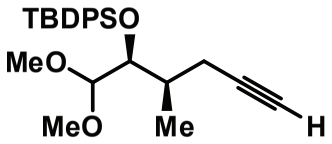
6.32


220
200
180
160
140
120
100
80
60
40
20
0
ppm

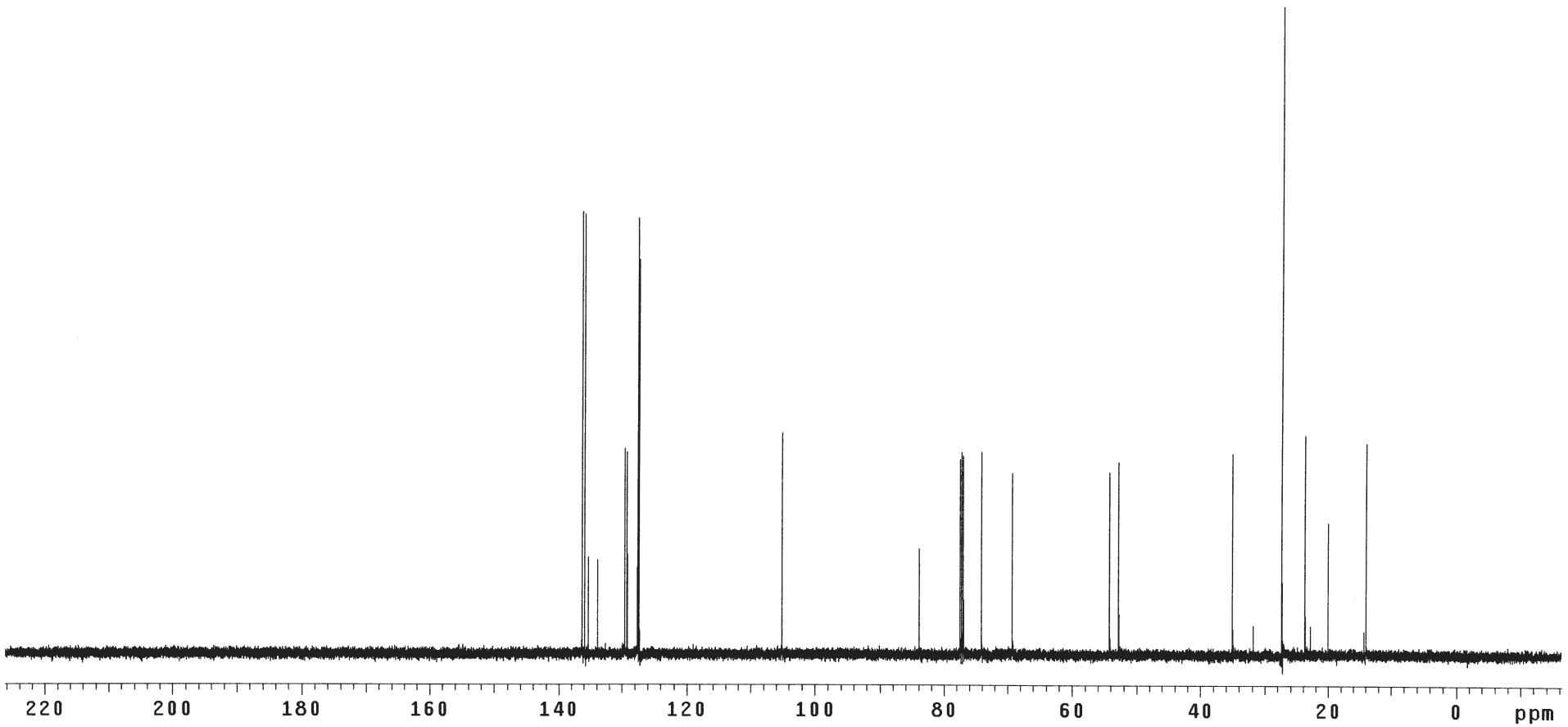

TBDPSO
MeO
MeO
Me
H

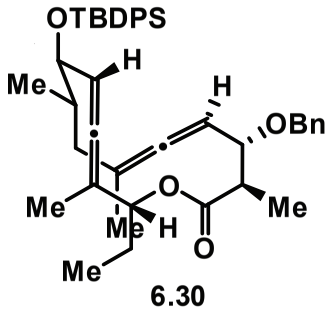
6.31

8
7
6
5
4
3
2
1
ppm
4.29
6.26
1.00
0.97
3.04
3.03
1.98
0.82
0.98
10.41
3.09



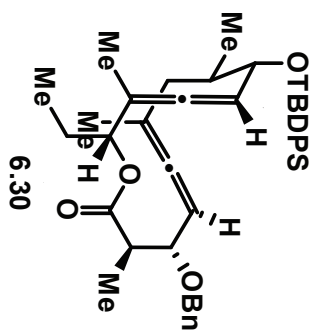
6.31



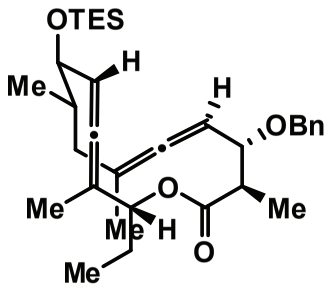

OTBDPS
H
Me
H
OBn
O
Me
Me
Me
H
O
Me

6.30

8
7
6
5
4
3
2
1
ppm
4.47
11.11
1.10
1.03
1.05
1.08
1.08
1.11
1.07
1.00
1.10
0.98
3.17
5.57
4.06
5.20
15.34
3.45

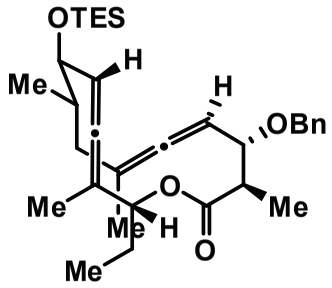

OTBDPS
Me
Me
Me
Me
H
O
O
H
Me
OBn
6.30

220
200
180
160
140
120
100
80
60
40
20
0
ppm


OTES
H
Me
H
OBn
O
Me
Me
Me H
O
Me

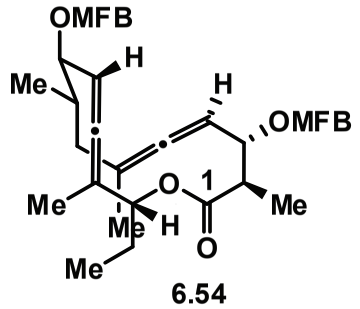
6.45

7
6
5
4
3
2
1
ppm
3.43
1.73
1.03
1.00
0.99
1.04
1.04
2.05
1.00
1.03
9.41
4.63
15.81
6.22

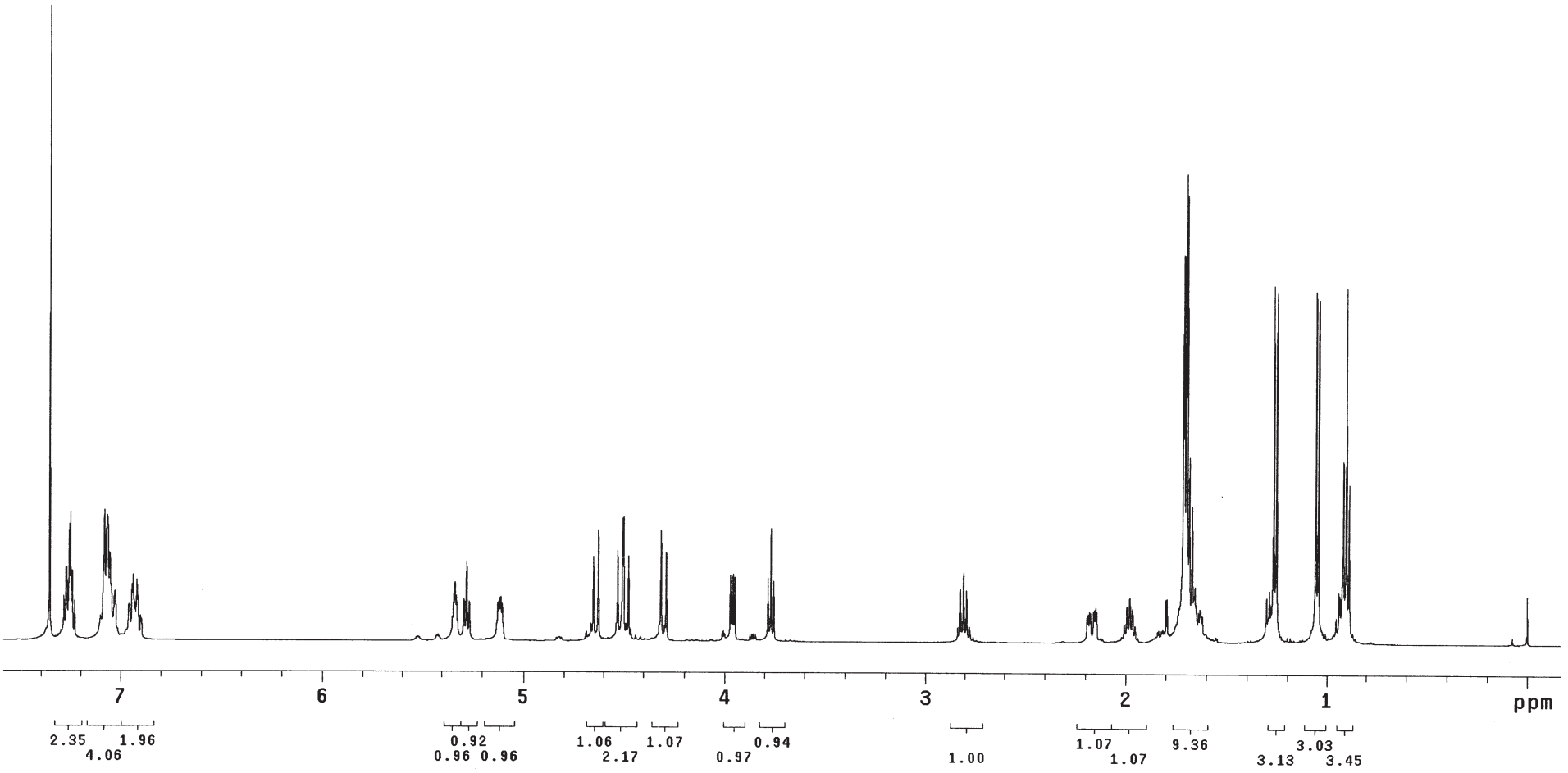

OTES
H
Me
H
OBn
O
Me
Me
Me
H
O
Me

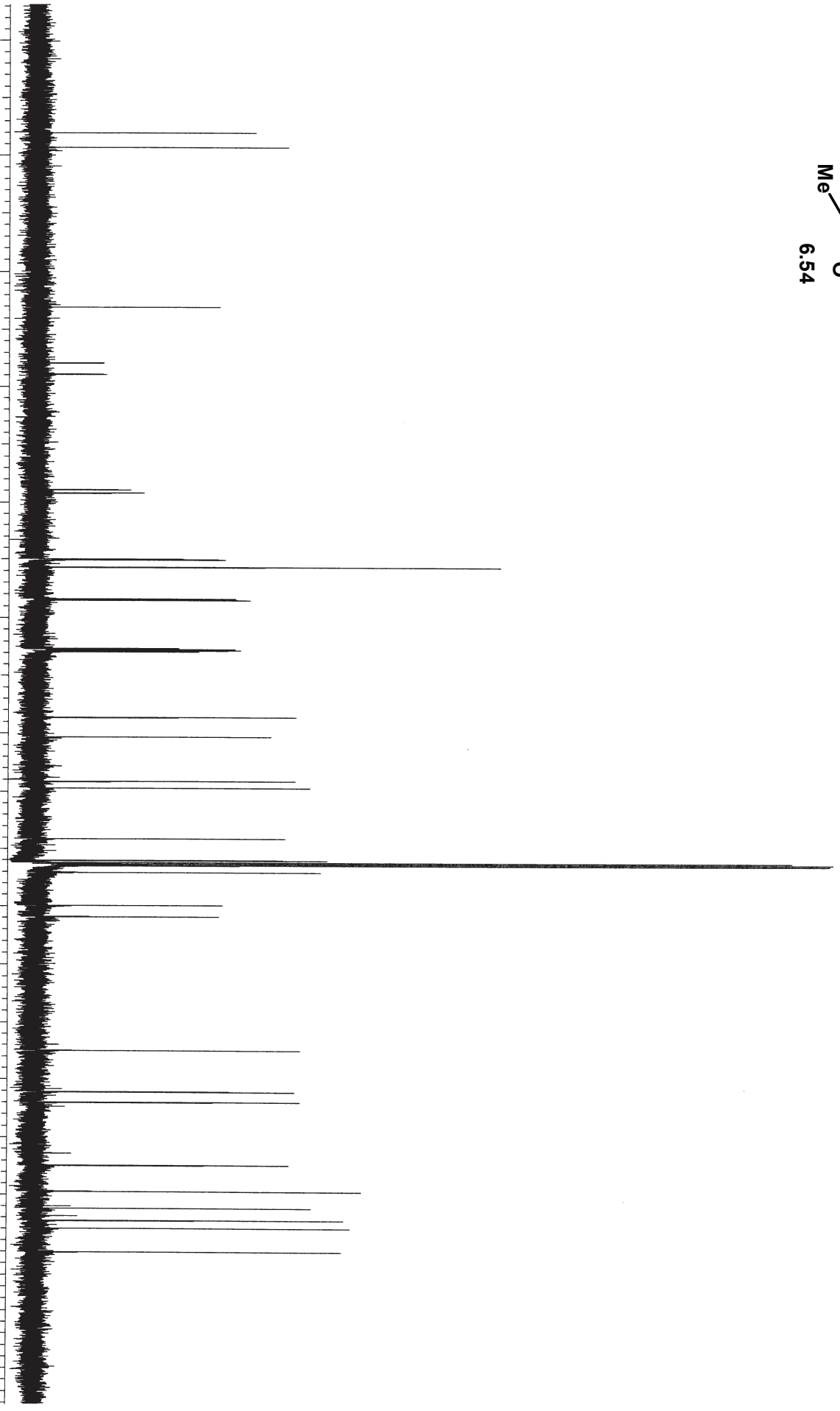
6.45

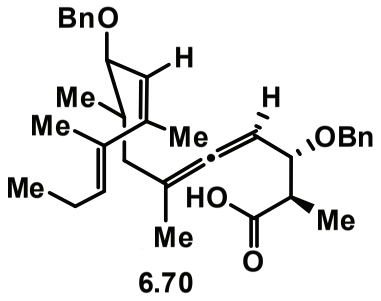
220
200
180
160
140
120
100
80
60
40
20
0
ppm


OMFB
H
Me
H
OMFB
O
1
Me
Me
Me
H
O
Me

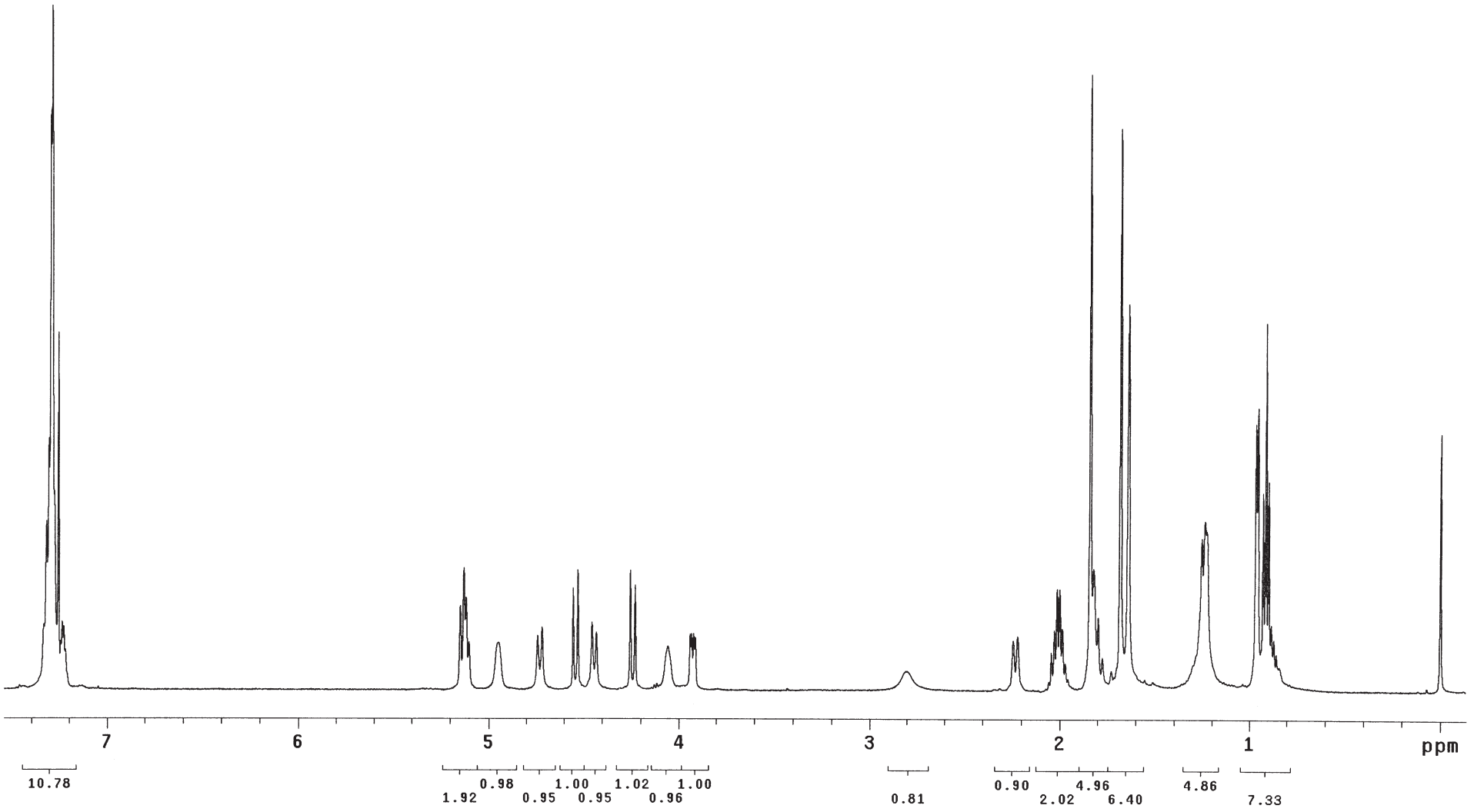
6.54

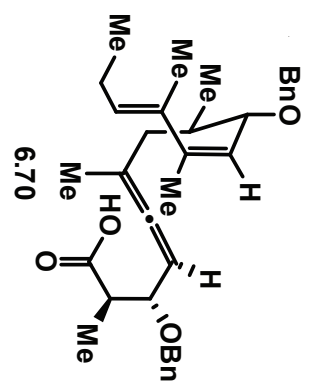

7
6
5
4
3
2
1
ppm
2.35
1.96
4.06
0.92
0.96
0.96
1.06
2.17
1.07
0.97
0.94
1.00
1.07
1.07
9.36
3.13
3.03
3.45


OMFB
Me
H
Me
Me
Me
H
O
1
O
H
OMFB
Me
6.54
220
200
180
160
140
120
100
80
60
40
20
0
ppm


BnO
H
Me
Me
Me
H
OBn
Me
HO
Me
Me
O

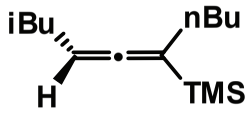
6.70


7
6
5
4
3
2
1
ppm
10.78
1.92
0.98
0.95
1.00
0.95
1.02
0.96
1.00
0.81
0.90
2.02
4.96
6.40
4.86
7.33

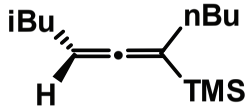

BnO
Me
Me
Me
Me
H
Me
HO
O
H
OBn
Me

6.70

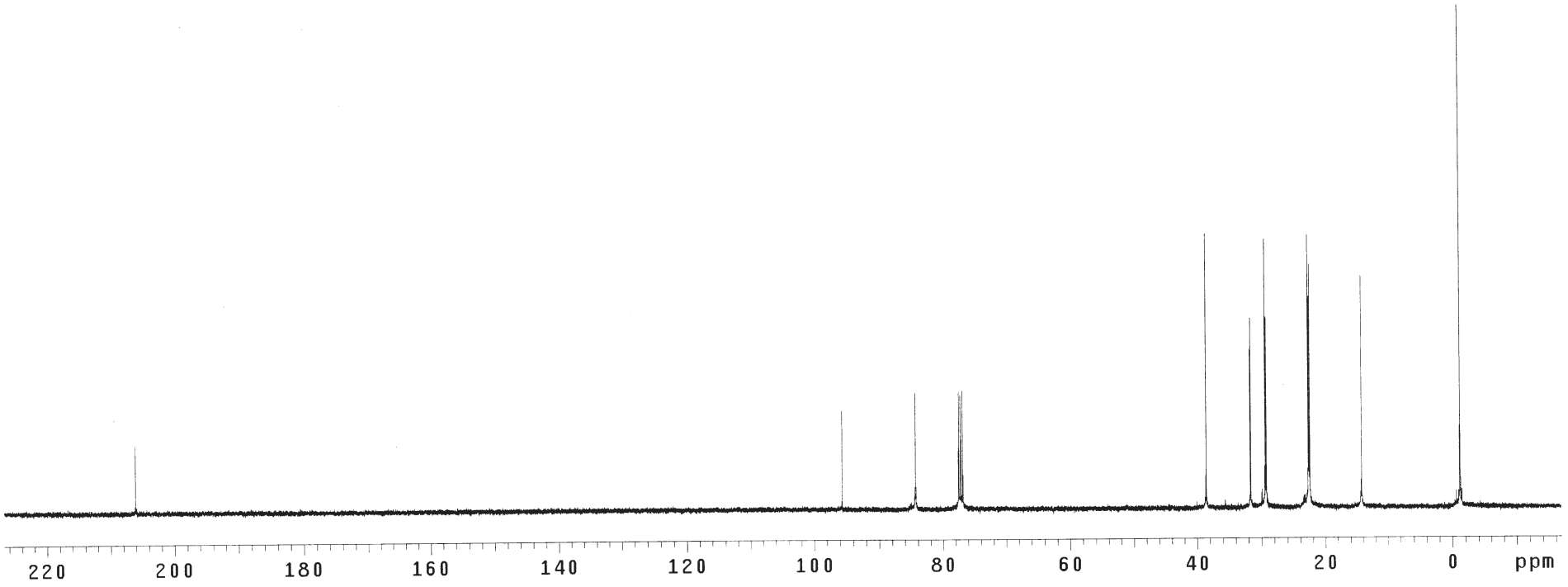
220
200
180
160
140
120
100
80
60
40
20
0
ppm

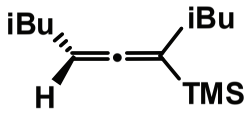


7.23

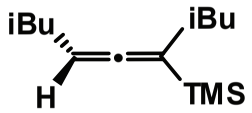


7.23

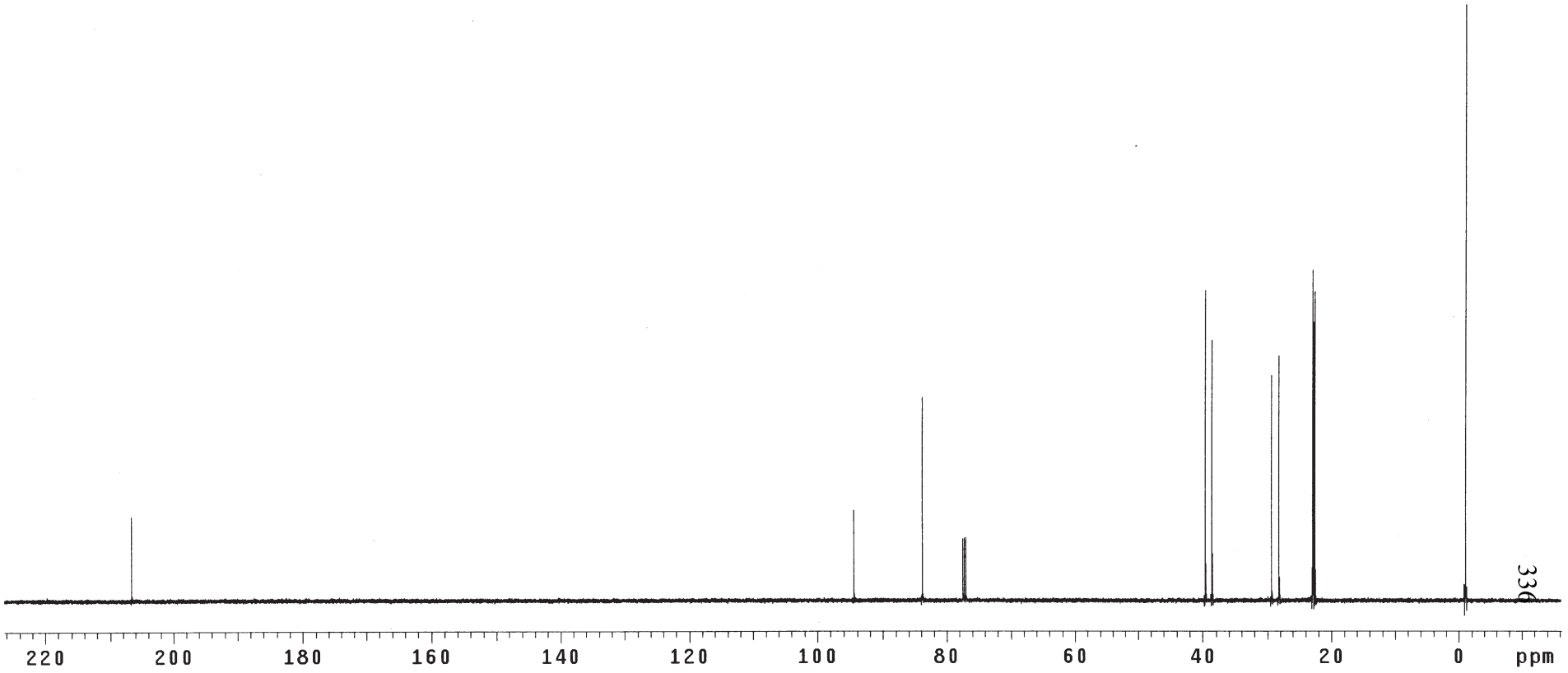


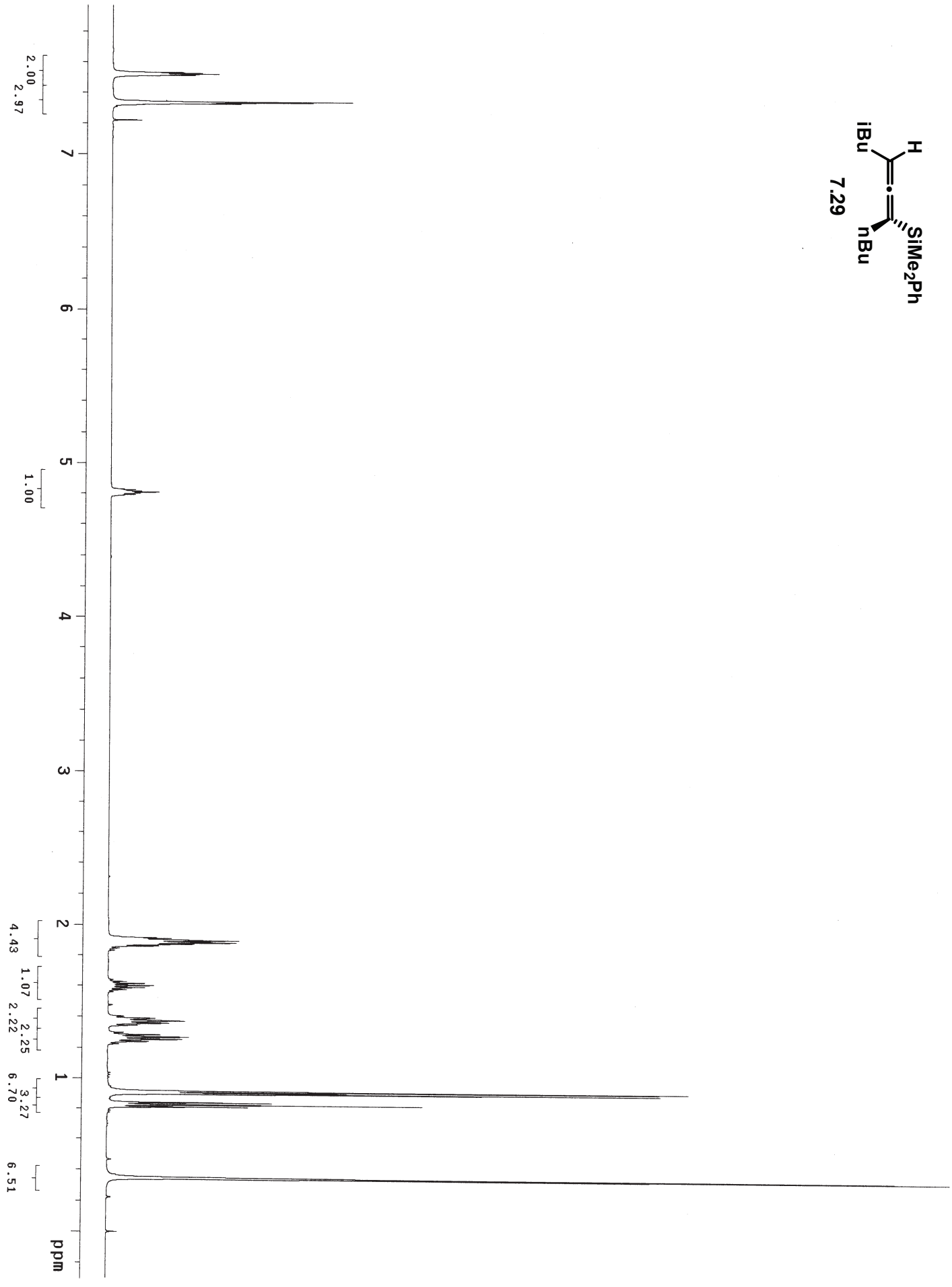


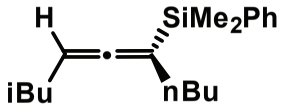
7.40



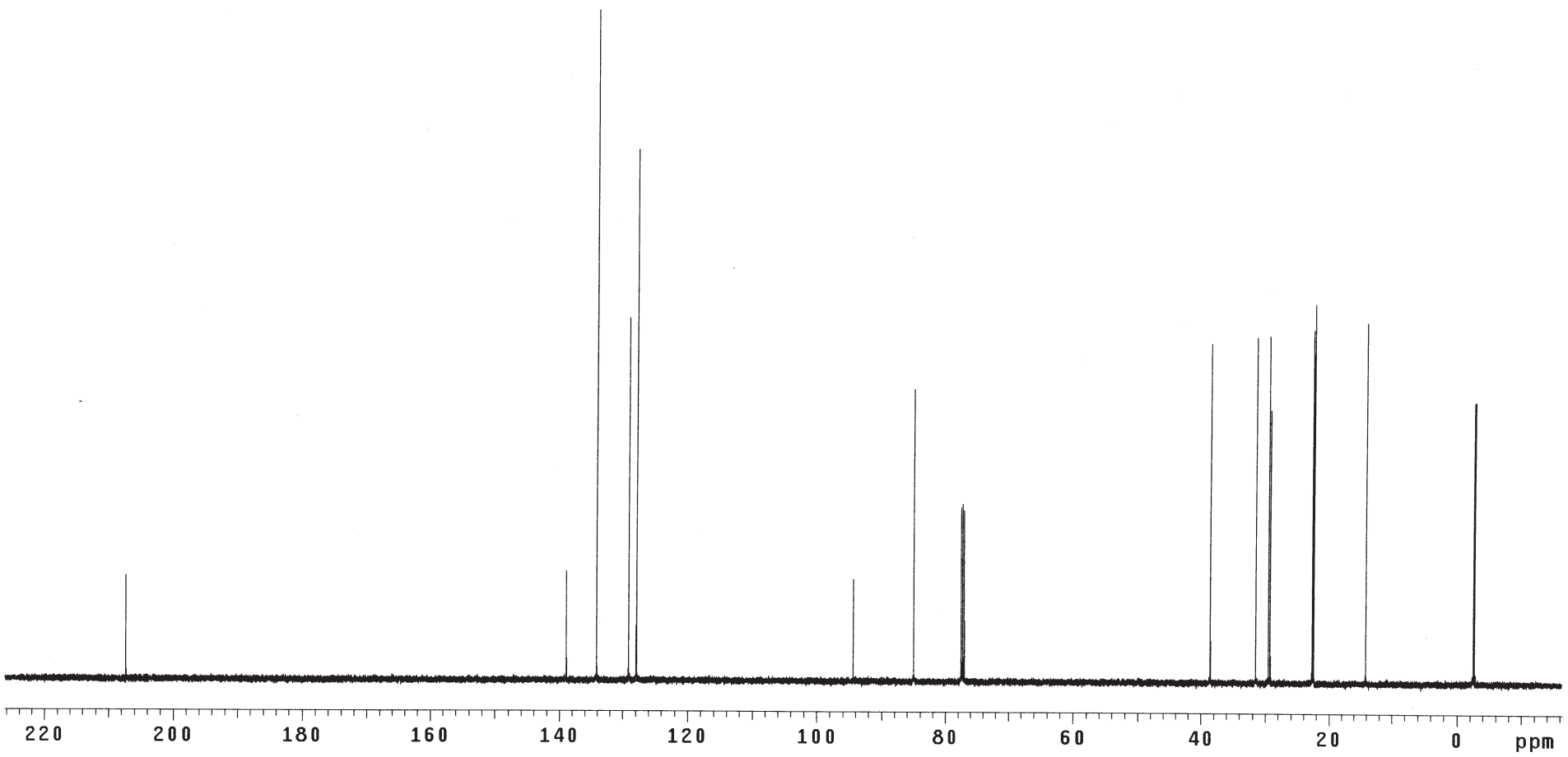
7.40



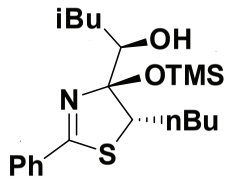

H
iBu
SiMe2Ph
nBu
7.29
2.00
2.97
1.00
4.43
1.07
2.22
2.25
6.70
3.27
6.51
ppm



7.29

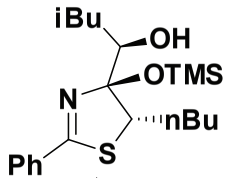


339

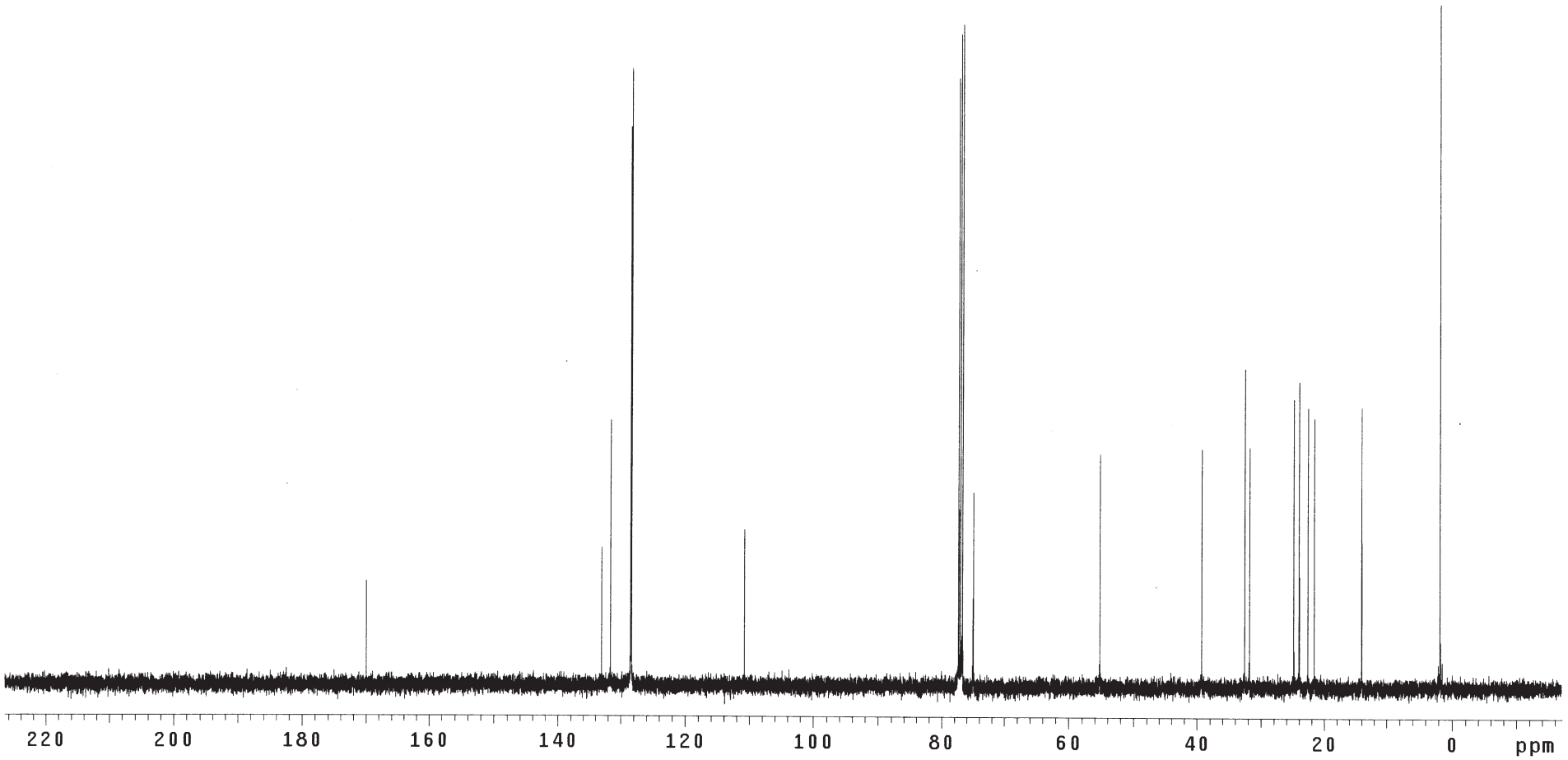

iBu
OH
OTMS
N
nBu
Ph
S

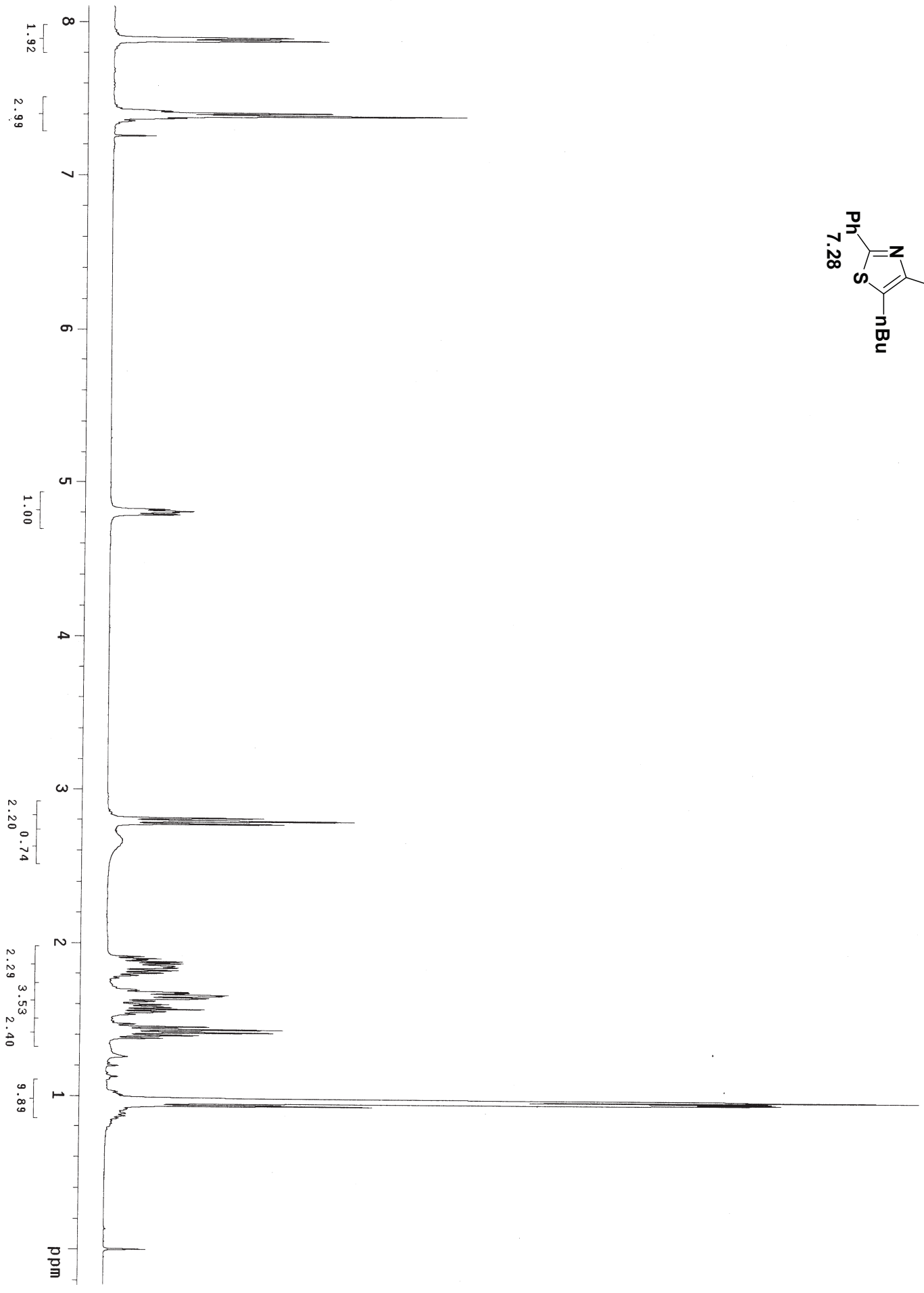
7.26

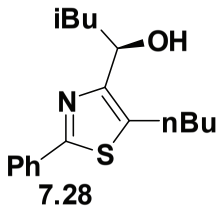
7
6
5
4
3
2
1
ppm
1.90
2.01
0.99
1.00
1.01
3.05
2.84
5.38
3.29
6.22
8.86

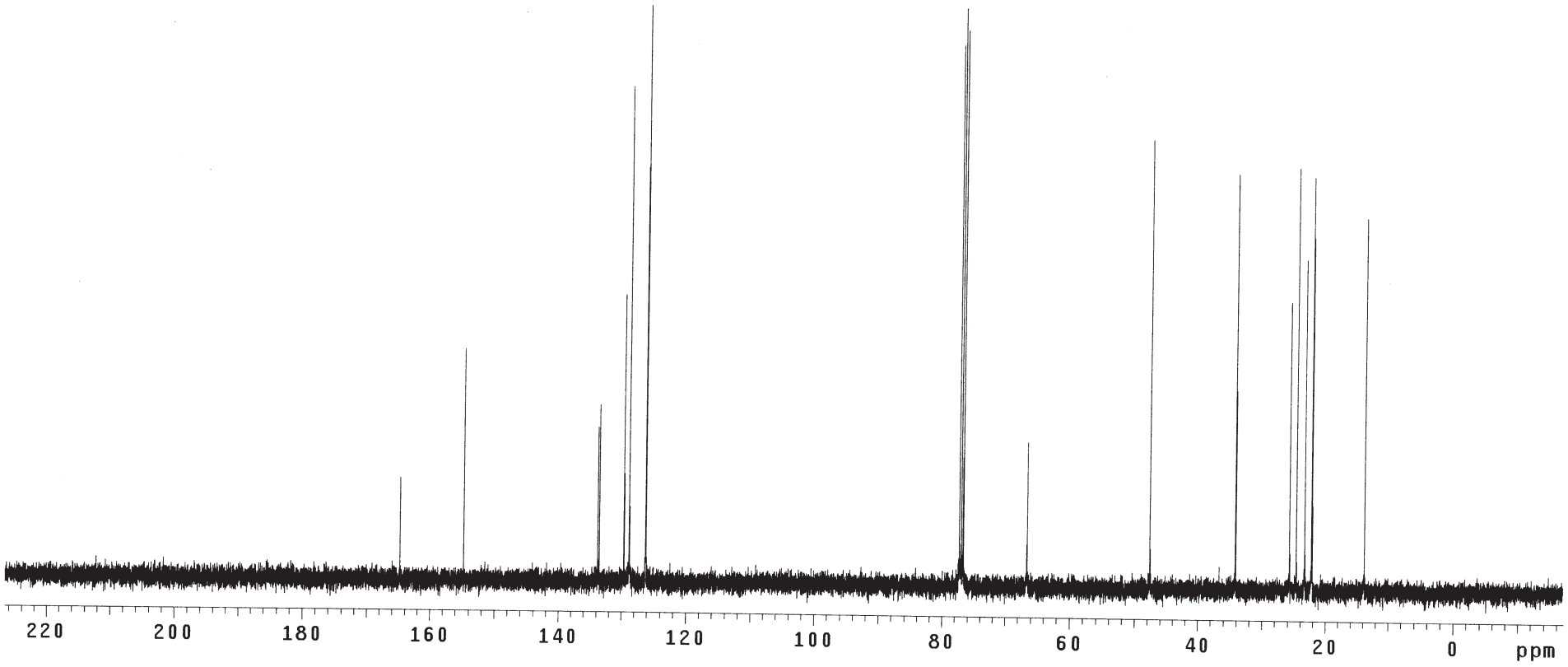


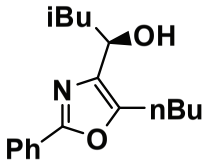
7.26



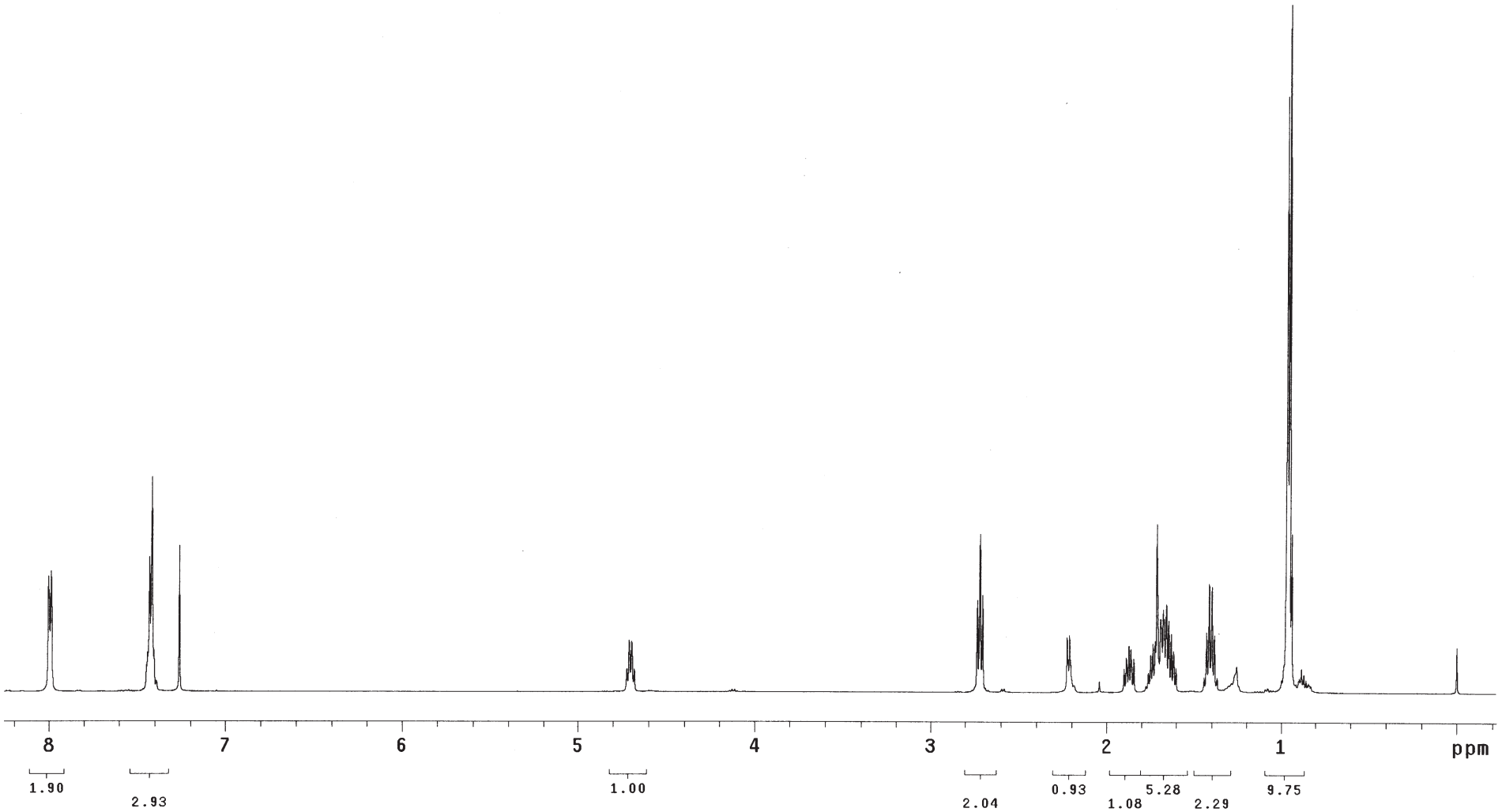

iBu
OH
nBu
N
S
Ph
7.28
8
7
6
5
4
3
2
1
ppm
1.92
2.99
1.00
2.20
0.74
2.29
3.53
2.40
9.89

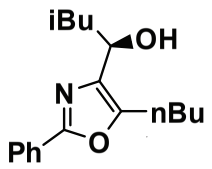

iBu
OH
N
nBu
Ph
S
7.28


220
200
180
160
140
120
100
80
60
40
20
0
ppm

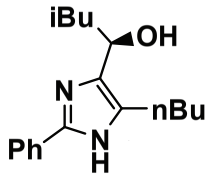

iBu
OH
N
nBu
Ph
O

7.30

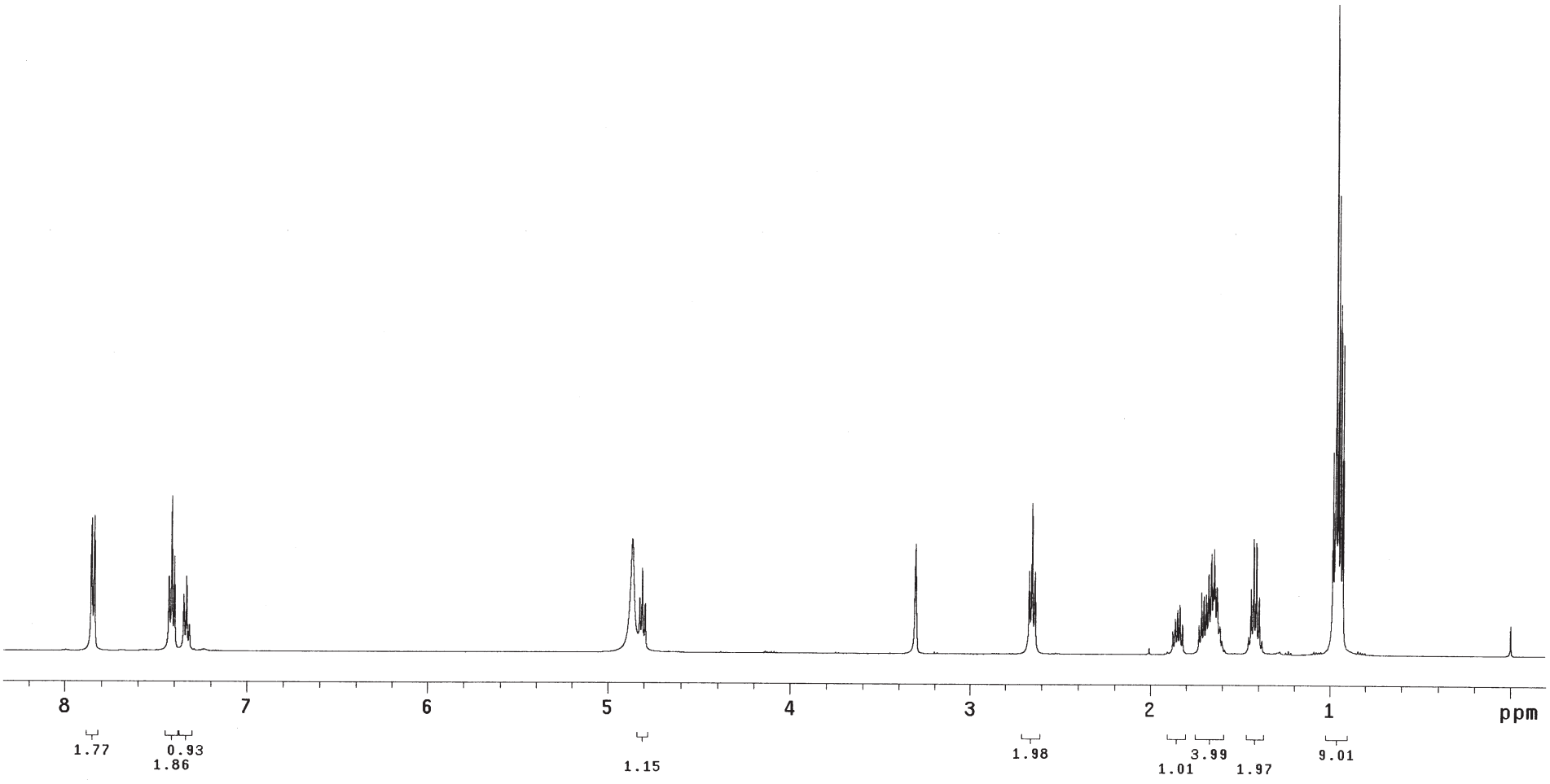

8
7
6
5
4
3
2
1
ppm
1.90
2.93
1.00
2.04
0.93
1.08
5.28
2.29
9.75

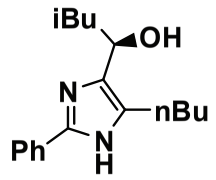


7.30

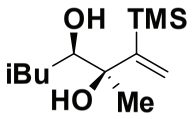

iBu
OH
N
nBu
Ph
N
H

7.31


8
7
6
5
4
3
2
1
ppm
1.77
0.93
1.86
1.15
1.98
1.01
3.99
1.97
9.01



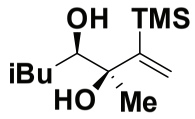
7.31


OH
TMS
iBu
HO
Me

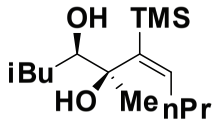
7.44

7
6
5
4
3
2
1
ppm
1.03
0.97
0.98
1.01
1.03
0.99
4.31
1.58
3.56
3.26
9.28

348

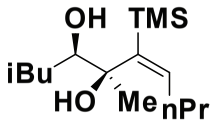


7.44

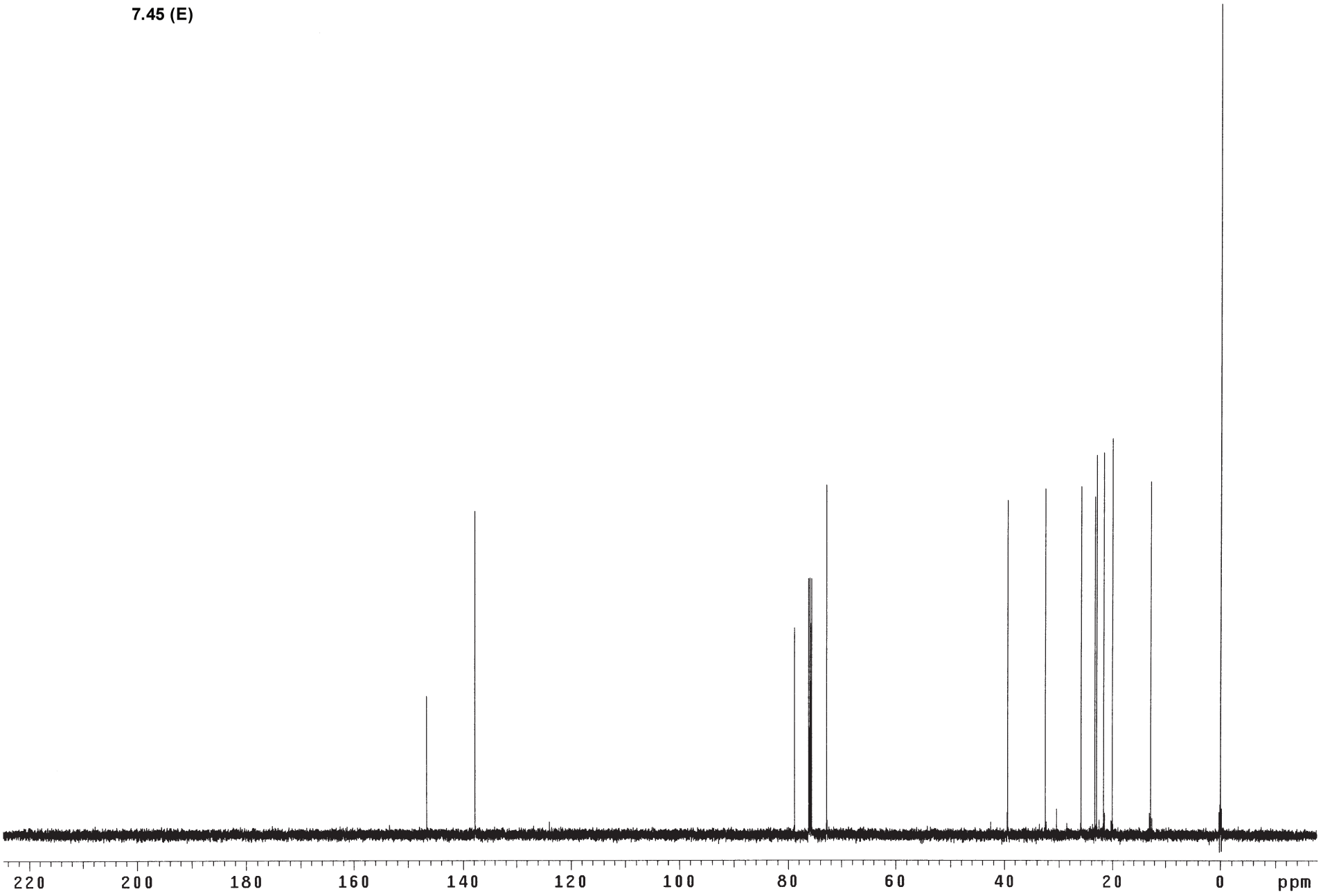

OH
TMS
iBu
HO
Me
nPr

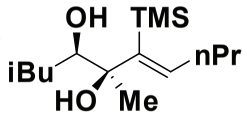
7.45 (E)

7
6
5
4
3
2
1
ppm
1.00
1.02
1.94
1.18
2.29
6.99
2.31
11.55
10.32

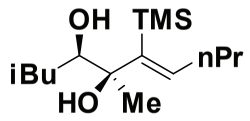


7.45 (E)

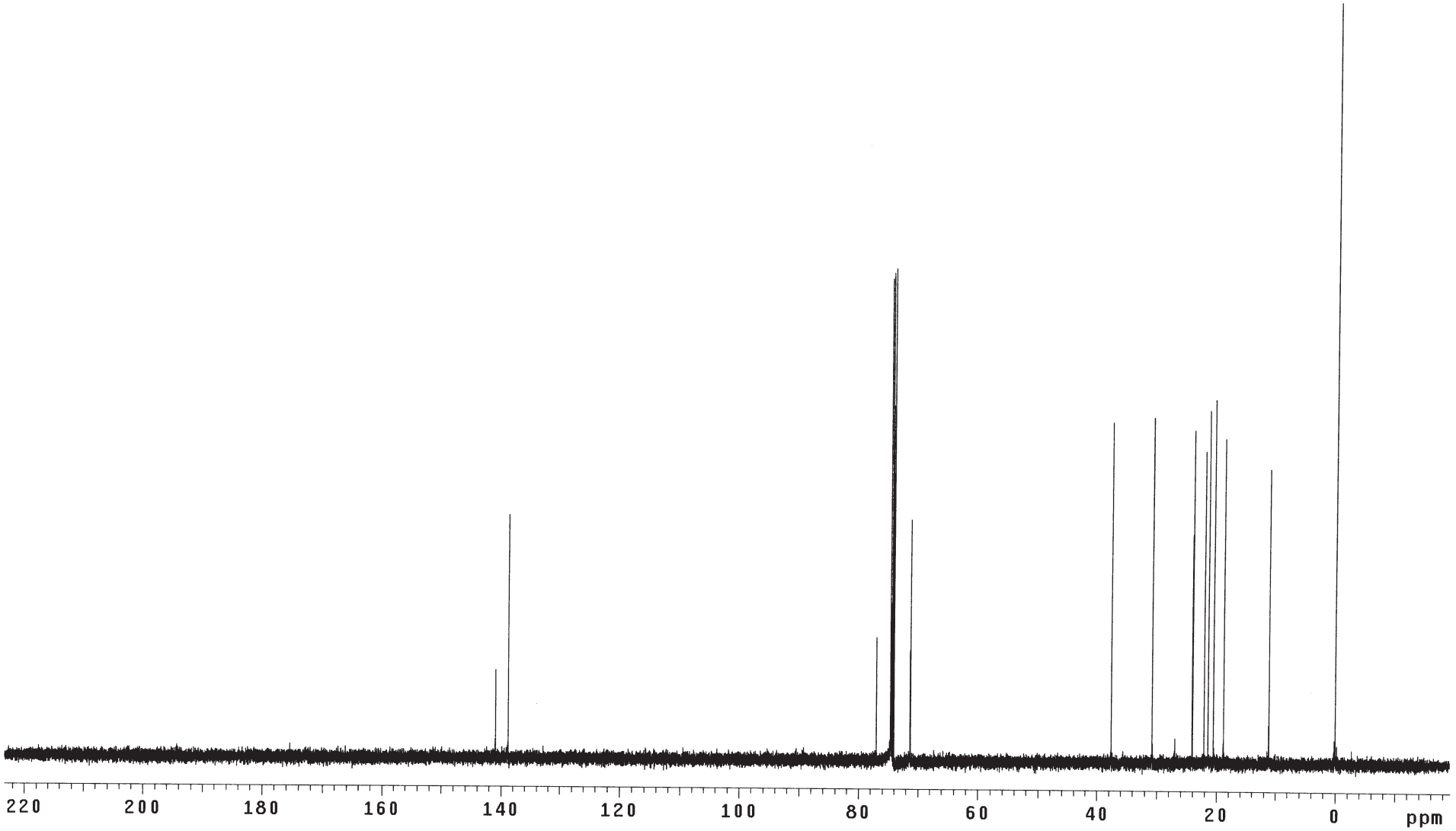




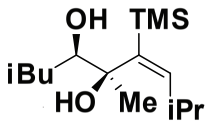
7.45 (Z)



7.45 (Z)

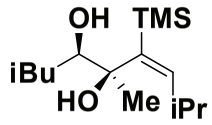


353

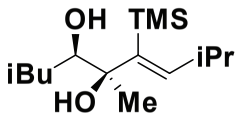

OH
TMS
iBu
HO
Me
iPr

7.46 (E)

7
6
5
4
3
2
1
ppm
1.00
1.02
1.04
1.07
1.07
1.00
4.31
1.94
13.16
9.18



7.46 (E)


OH
TMS
iBu
iPr
HO
Me

7.46 (Z)

7
6
5
4
3
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1
ppm
1.00
1.00
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0.70
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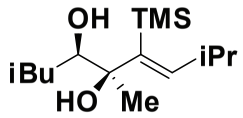
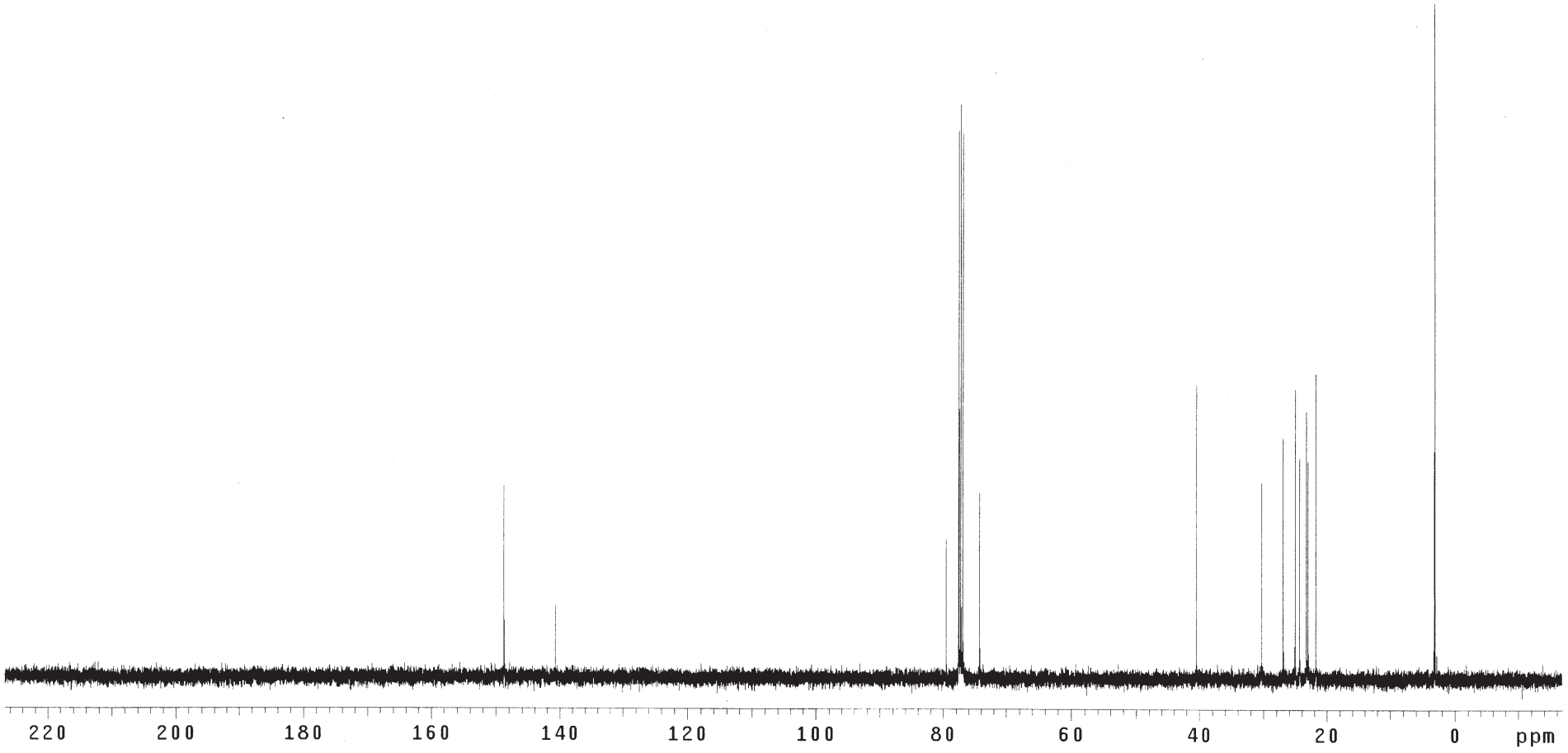
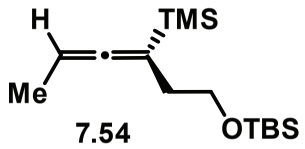
2.79
3.05
12.99
9.14



7.46 (Z)




H
TMS
Me
7.54
OTBS

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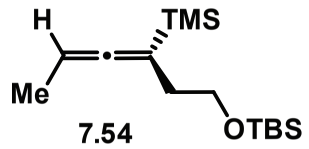
6
5
4
3
2
1
ppm
0.80
2.00
1.89
3.07
10.57
15.16


H
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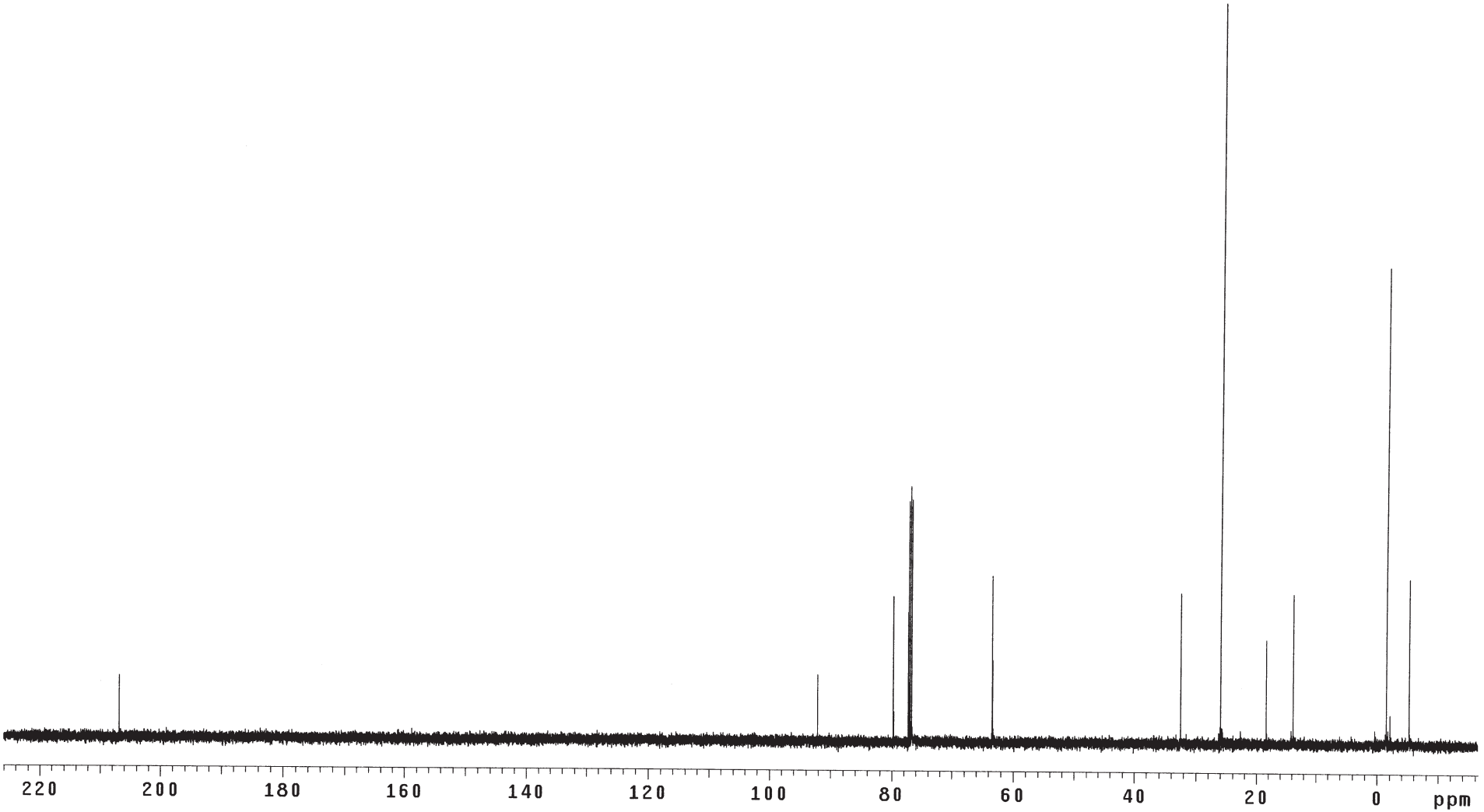
Me
7.54
OTBS


220
200
180
160
140
120
100
80
60
40
20
0
ppm

Curriculum Vitae

Partha Ghosh

September 1996 - July 1999	Calcutta University, India Subject: Chemistry Degree Earned: B.Sc.
August 1996 - July 2002	Indian Institute of Science, India Subject: Organic Chemistry Degree Earned: M.S.
September 2002 - May 2008	Rutgers, The State University of New Jersey New Brunswick, NJ Subject: Organic Chemistry Degree Earned: Ph.D.

Honors and Awards:

S. Krishnamurthy award for independent research in Organic chemistry (2006).

Riemann award for excellence in Teaching Assistantship (2006).

Council for Scientific Research in India (CSIR) Junior Research Fellow (2002).

Indian Institute of Science Scholarship (1999-2002).

Publications:

Ghosh, P.; Lotesta, S.D.; Williams, L.J. *J. Am. Chem. soc*. **2007**, *129*, 2438. "Spirodiepoxides Reaction with Cuprates."

Mehta, G.; Ghosh, P.; Sreenivas, K. *ARKIVOC* **2003**, *3*, 92. "Synthetic studies towards pteridanone, a novel protoilludane-type tricyclic sesquiterpenoid."