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Matthew Allen Boone Date

Chapter 1. Part 1: Novel Synthesis and Biological Evaluation of 1,5-Linked D-Mannoseptanosides. Part 2: Synthesis of D-Glucoseptanosides

Chapter 2. Biomimetic Total Synthesis of the Proposed Structure of *ent*-Muzitone

By

Matthew Allen Boone

Doctor of Philosophy

Chemistry

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Date

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B.A. University of Virginia's College at Wise, *summa cum laude*, 2004

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An Abstract of
A dissertation submitted to the Faculty of the
James T. Laney School of Graduate Studies of Emory University
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Doctor of Philosophy
in Chemistry
2009

Abstract

Chapter 1. Part 1: Novel Synthesis and Biological Evaluation of 1,5-Linked D-Mannoseptanosides. Part 2: Synthesis of D-Glucoseptanosides

Chapter 2. Biomimetic Total Synthesis of the Proposed Structure of *ent*-Muzitone

By Matthew Allen Boone

1,5-Linked D-Mannoseptanosides. Part 2: Synthesis of D-Glucoseptanosides

Part 1. Using the tungsten-catalyzed cycloisomerization of an appropriately protected alkynyl alcohol, highly functionalized seven-membered ring (septanose) glycals were synthesized. We used dimethyldioxirane (DMDO) glycal epoxidation/epoxide opening to construct septanose sugars with D-*manno* absolute configuration, which were glycosylated to give the first known 1,5-linked D-mannoseptanoside mono-, di-, and trisaccharides. These unnatural sugars were found to be innocuous to α-mannosidase-catalyzed hydrolysis. Thus, we believe these unique carbohydrate structures have potential application as biomaterials or drug delivery vehicles. Part 2. Using a known strategy of protecting group manipulation of a hexose sugar, we have synthesized a variety of D-glucoseptanose substrates. Our ultimate goal was to construct higher order oligosaccharides composed of D-glucoseptanose monomer units. While that goal remained elusive, we gained much insight into the reactivity patterns of these substrates, which will be of much utility in future studies.

Chapter 2. Biomimetic Total Synthesis of the Proposed Structure of *ent*-Muzitone

Muzitone, a marine sponge-derived polycyclic ether triterpenoid natural product, was synthesized using a bioinspired strategy. Starting from a C30 squalene-like precursor, we successfully implemented tandem biomimetic cyclizations of

epoxy-ene substrates to construct *ent*-muzitone. This synthetic investigation revealed that the structural and/or stereochemical assignment of muzitone was incorrect.

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Claney Pereira stands out amongst the people I've met while at Emory. He has made the last half of graduate school a delightful experience. We have become the closest of friends and will remain so. His culinary skills were truly amazing, and it is to Claney that I owe my fondness of curry. Our trips to Peachtree-Dekalb and Hartsfield will be truly missed, though I do not think our plane spotting days are over.

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This thesis is dedicated to my grandparents who have been a source of constant inspiration. Their love for me is unfailing, as is my respect and adoration for them.

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Chapter 1. Part 1: Novel Synthesis and Biological Evaluation of 1,5-Linked D-Mannoseptanosides. Part 2: Synthesis of D-Glucoseptanosides

Abbreviations

Ac	Acetyl
Aq	Aqueous
Bn	Benzyl
Bz	Benzoyl
Bu_4NI/TBAI	tetrabutylammonium iodide
CSA	camphorsulfonic acid
d	doublet
DABCO	1,4-diazobicyclo[2.2.2]octane
DIBAL-H	diisobutylaluminum hydride
DIPEA	*N*,*N*-diisopropylethyl amine
DIPT	diisopropyl tartrate
DMAP	*N*,*N*-dimethylaminopyridine
DMDO	dimethyldioxirane
DMPU	1,3-dimethyl-3,4,5,6-tetrahydro-2(1*H*)-pyrimidinone
DTBMP	2,6-di-*tert*-butyl-4-methylpyridine
dppp	1,3-bis(diphenylphosphino)propane
DMF	*N*,*N*-dimethylformamide
EtOAc	ethyl acetate
imid	imidazole
HF	hydrogen fluoride
LDA	lithiumdiisopropylamine
m	multiplet

MeCN	acetonitrile
Me_3SiOTf	trimethylsilyl triflate
Me_2S	dimethyl sulfide
mL	milliliter
mmol	millimole
n-BuLi	*n*-butyllithium
NBS	*N*-bromosuccinimide
NIS	*N*-iodosuccinimide
p-NO_2Bz	*para*-nitrobenzoyl
Ph	phenyl
s	singlet
SEM	trimethylsilylethoxymethyl
SO_3-pyr	sulfur trioxide-pyridine
t	triplet
Bu_4F/TBAF	tetrabutylammonium fluoride
t-$BuMe_2Si$/TBS	*tert*-butyldimethylsilyl
t-BuOOH	*tert*-butylhydroperoxide
TBDPS	*tert*-butyldiphenylsilyl
TES	triethylsilyl
THF	tetrahydrofuran
$Ti(O\text{-}i\text{-}Pr)_4$	titanium tetraisopropoxide
TIPS	triisopropylsilyl
Trityl	triphenylmethyl

$W(CO)_6$	tungsten hexacarbonyl

Chapter 1

Chapter 1

Part 1: Novel Synthesis and Biological Evaluation of 1,5-Linked D-Mannoseptanosides. Part 2: Synthesis of D-Glucoseptanosides

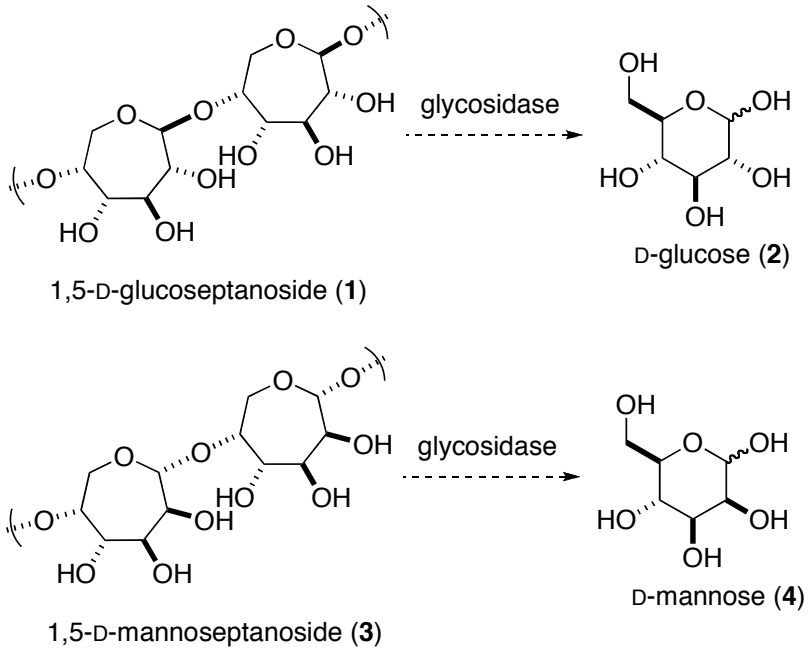
1.1. Introduction and Background

1.1.1. Potential Application of Septanose Carbohydrates

Seven-membered ring (septanose) oligosaccharides are unknown in nature as the thermodynamic preference of five- and six-membered furanose and pyranose rings dominate the structural motifs of natural sugars and their glycoconjugates. Since classical methods of carbohydrate synthesis favor furanose and pyranose isomers over their seven-membered ring counterpart, this area of research has remained largely unexplored.[1] The synthesis of higher order oligosaccharide structures bearing septanose monomers is a novel area of research that seeks to identify unnatural, ring-expanded carbohydrate analogues with interesting biological and/or materials properties. Specifically, the absence of primary hydroxyl groups and conformational differences of these molecules would dramatically impact the ability of a glycosidase enzyme to hydrolyze the linkages of a septanose oligosaccharide. Moreover, a 1,5-linked septanose oligosaccharide bearing monomer units with D-*gluco* or D-*manno* absolute stereochemistry (**1**-**2**, respectively) would yield an innocuous hexose byproduct of D-glucose (**3**) or D-mannose (**4**), respectively, upon enzymatic or non-enzymatic hydrolytic cleavage. Thus, if septanose oligosaccharides could be harnessed as

biomaterials or drug delivery vehicles, any decomposition would yield a biologically ubiquitous hexose sugar (Figure 1).

Figure 1. Proposed hydrolysis of 1,5-septanosides

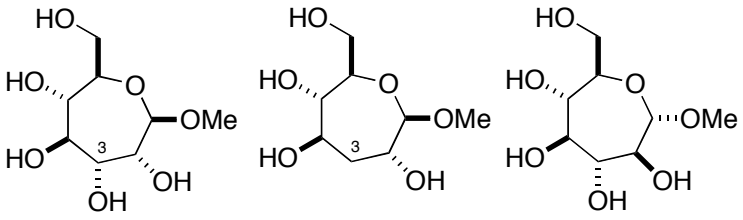


1.1.2. Enzyme recognition of septanose carbohydrates

Any application of septanose sugars in a biomedicinal context would be dependent upon evidence of how proteins would respond to these unnatural structures, albeit through binding and potential hydrolytic degradation of glycosidic linkages or through no recognition at all. In support of this hypothesis, the Peczuh and Kumar laboratories revealed that concanavalin A, a common lectin (carbohydrate-binding protein), preferably binds β-methylseptanosides, albeit with modest affinity, in preference to the corresponding α-methylseptanosides. This was the first example of a ring-expanded septanose sugar being bound by a natural carbohydrate-binding protein. Specifically, β-methylseptanoside **5** and the corresponding 3-deoxy variant **6** have a weak

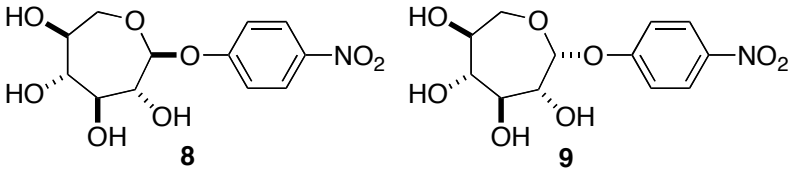
binding affinity for concanavalin A (ConA) (5.2 x 10^2 M^{-1} and 3.9 x 10^2 M^{-1}, respectively, as determined by Isothermal Titration Calorimetry (ITC)). Interestingly, α-methylseptanoside **7** did not bind to ConA (Figure 2).[2]

Figure 2. Recognition of septanose oligosaccharides by concanavilin A



More recently, a collaboration between Stütz and Withers gave further insight into the ability of glycosidase enzymes to recognize unnatural septanose carbohydrates. β-L-*para*-nitro-idoseptanoside **8** was found to be a reactive substrate for the hydrolytic enzyme β-glucosidase from *Agrobacterium*. α-Glucosidase from *Saccharomyces cerevisiae* was found to catalyze a slow hydrolysis of α-L-*para*-nitro-idoseptanoside **9** (Figure 3).[3]

Figure 3. β and α-L-*para*-nitrophenol-idoseptanosides

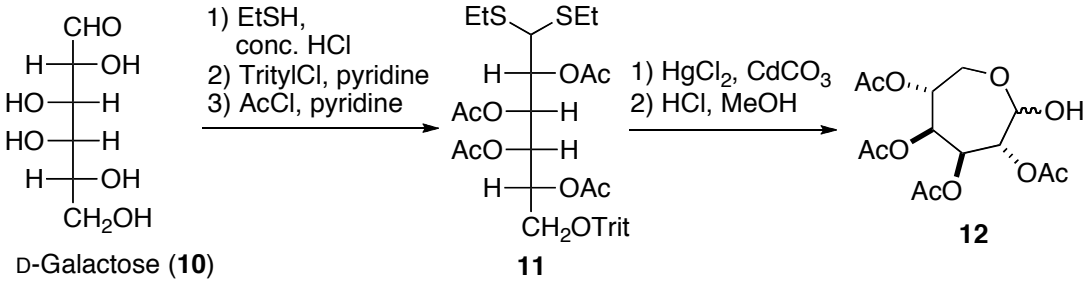


1.1.3. Synthetic Approaches to Septanose Carbohydrates

Despite the energetic barriers that disfavor septanose carbohydrate formation, numerous synthetic methods have been developed to avoid this thermodynamic restriction. The first known method of septanose carbohydrate synthesis was reported in 1933 by the Micheel laboratory. D-Galactose (**10**) was

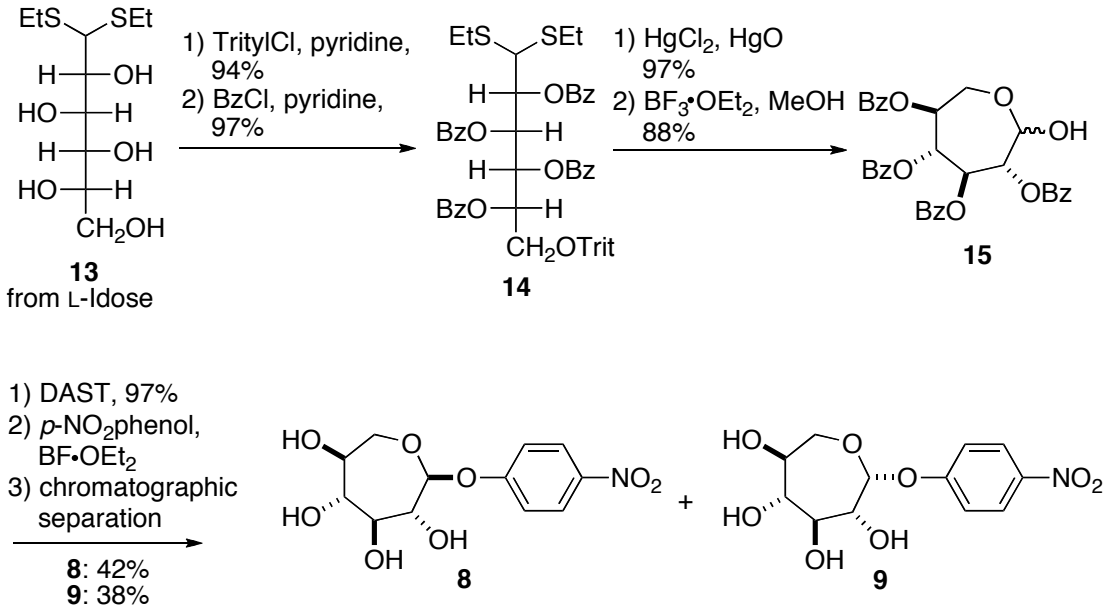
orthogonally protected as the 2,3,4,5-tetra-*O*-acetyl-6-*O*-trityl diothioacetal **11**. Mercurcy-catalyzed dithioacetal cleavage revealed the aldehyde, which then was subjected to acidic removal of the trityl protecting group, resulting in ring closure to tetra-*O*-acetyl-D-galactoseptanose **3** (Scheme 1).[4] Despite the use of toxic reagents, namely mercury(II) chloride ($HgCl_2$) and cadmium carbonate ($CdCO_3$), this method of generating a septanose sugar was a synthetic achievement that has only recently received considerable recognition.

Scheme 1. Micheel synthesis of tetra-*O*-acetyl-D-galactoseptanose



Specifically, Stütz and Withers in the synthesis of β and α-L-*para*-nitrophenol-idoseptanosides **8** and **9** relied upon a slightly modified Micheel procedure. Starting from the dithioacetal of L-idose (**13**), the orthogonally protected 2,3,4,5-tetra-*O*-benzoyl-6-*O*-trityl dithioacetal derivative **14** was prepared, followed by mercury-catalyzed cleavage of the dithioacetal and subsequent trityl ether cleavage using $BF_3 \bullet OEt_2$. Deprotection of the primary alcohol led to a rapid closure to the seven-membered ring isomer **15**, which was ultimately converted to **8** and **9** (Scheme 2).[2]

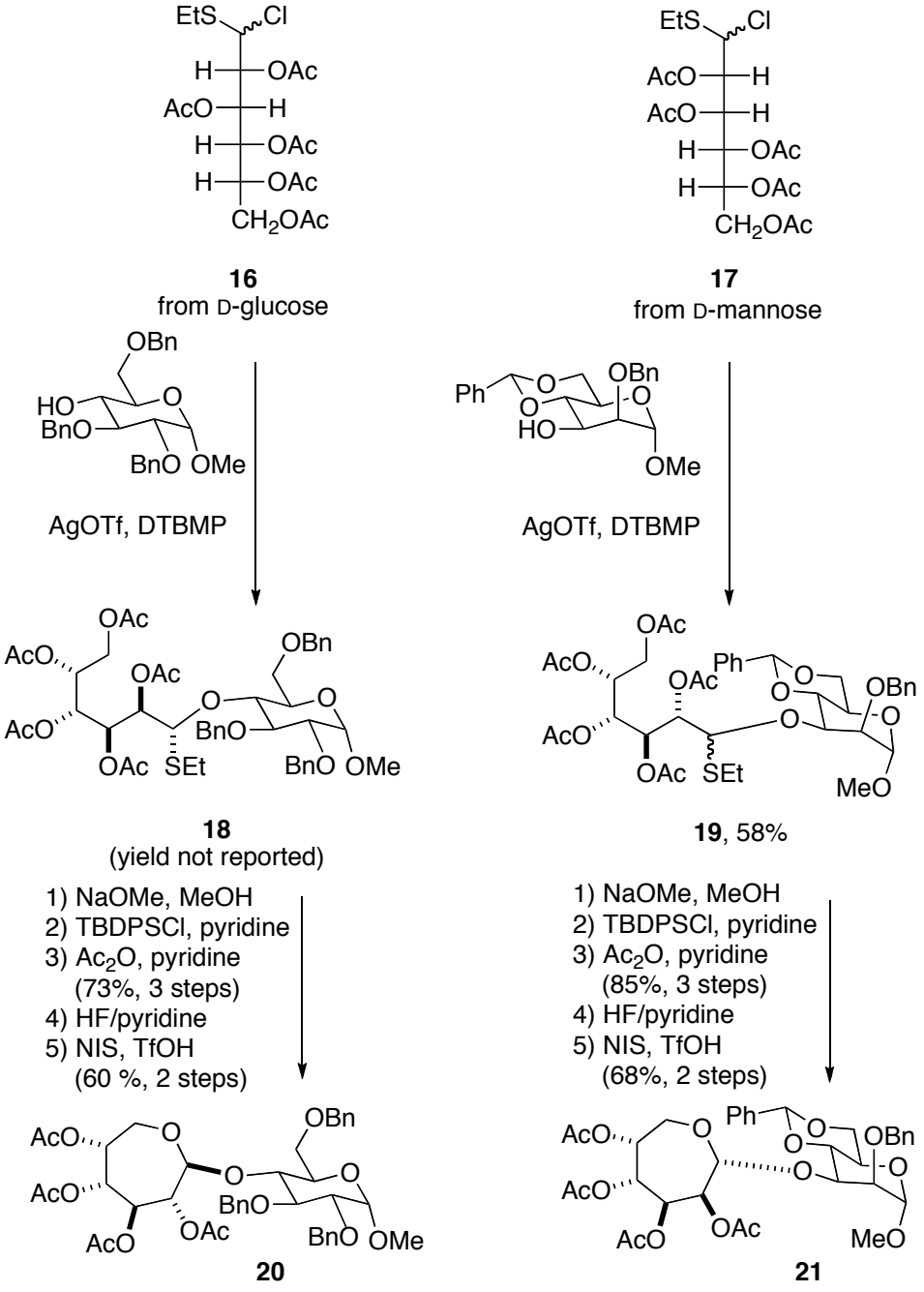
Scheme 2. Stütz and Withers synthesis of β and α-L-*para*-nitrophenol-idoseptanosides



The Hindsgaul laboratory has also reported a novel method for the introduction of septanose monomer units in the synthesis of disaccharides containing D-gluco and D-manno septanosyl residues. Using the 1-chloro-1-(ethylthio) derivatives of D-glucose and D-mannose (**16**-**17**, respectively), a silver triflate (AgOTf)-promoted glycosylation in the presence of 2,6-di-*tert*-butyl-4-methylpyridine (DTBMP) with an alcohol acceptor gave the corresponding D-gluco *O*,*S*-acetal **18** and D-manno *O*,*S*-acetal **19**. Extensive protecting group manipulation was then required to selectively protect the secondary alcohols in the presence of an unprotected primary alcohol. This involved methanolysis of the acetate protecting groups, followed by selective primary alcohol protection as the *tert*-butyldiphenylsilyl (TBDPS) ether. Reprotection of the seconday alcohols as the acetate derivatives was then required, followed by silyl ether cleavage

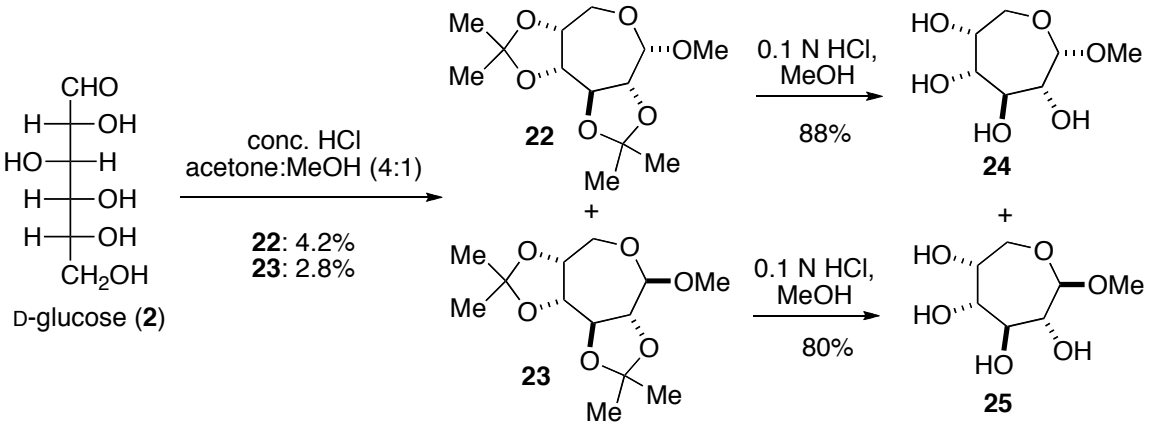
using HF•pyridine. The ring closure was then accomplished using N-iodosuccinimide (NIS) and triflic acid (TfOH)-promoted intramolecular glycosylation to afford disaccharides **20**-**21** (Scheme 3).[5]

Scheme 3. Hindsgaul's synthesis of the first septanose-containing disaccharides



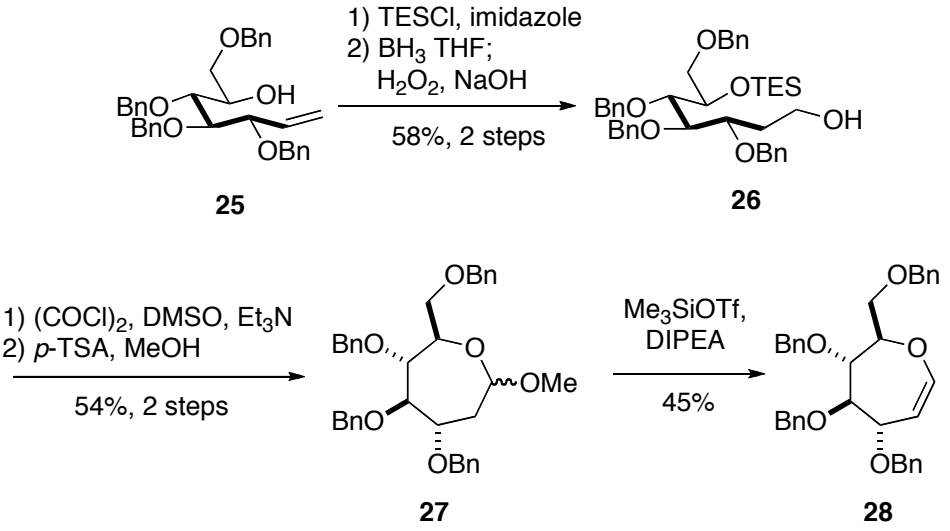
A straightforward approach to the synthesis of septanose carbohydrates has been developed by Stevens. Exposure of D-glucose (**2**) to a mixture of concentrated hydrochloric acid (HCl) in acetone and methanol gave D-glucoseptanosides **22** and **23** in low yield over an extended reaction time of eight days. Treatment of **22** and **23** using milder acidic conditions resulted in acetonide cleavage to yield the fully unprotected α and β methyl glycosides **24** and **25**, respectively (Scheme 4).[6]

Scheme 4. Stevens' synthesis of D-glucoseptanosides



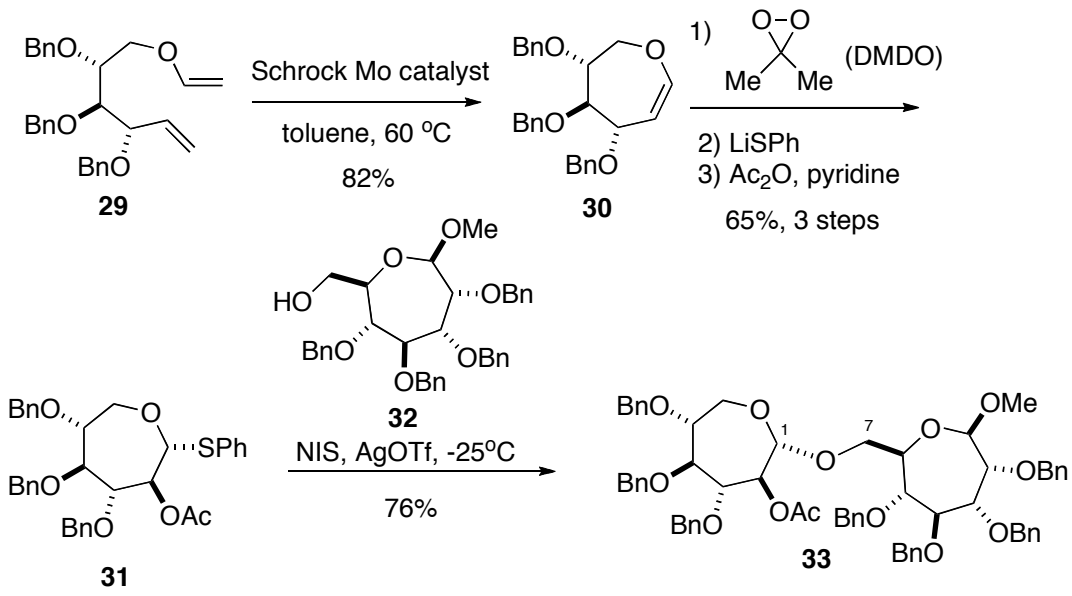
Significant contributions in this area of research were made by the Peczuh laboratory, which has provided considerable insight into the synthesis and biological evaluation of septanose carbohydrates. Using the well-established utility of cyclic enol ethers (glycals) in carbohydrate synthesis[7], Peczuh has developed novel synthetic methods for the synthesis of seven-membered ring glycals (oxepines). One such method involves functionalization of a hexose sugar through a cyclization-elimination sequence for access to highly complex oxepines (Scheme 5).[8]

Scheme 5. Cyclization-elimination route to septanose glycals



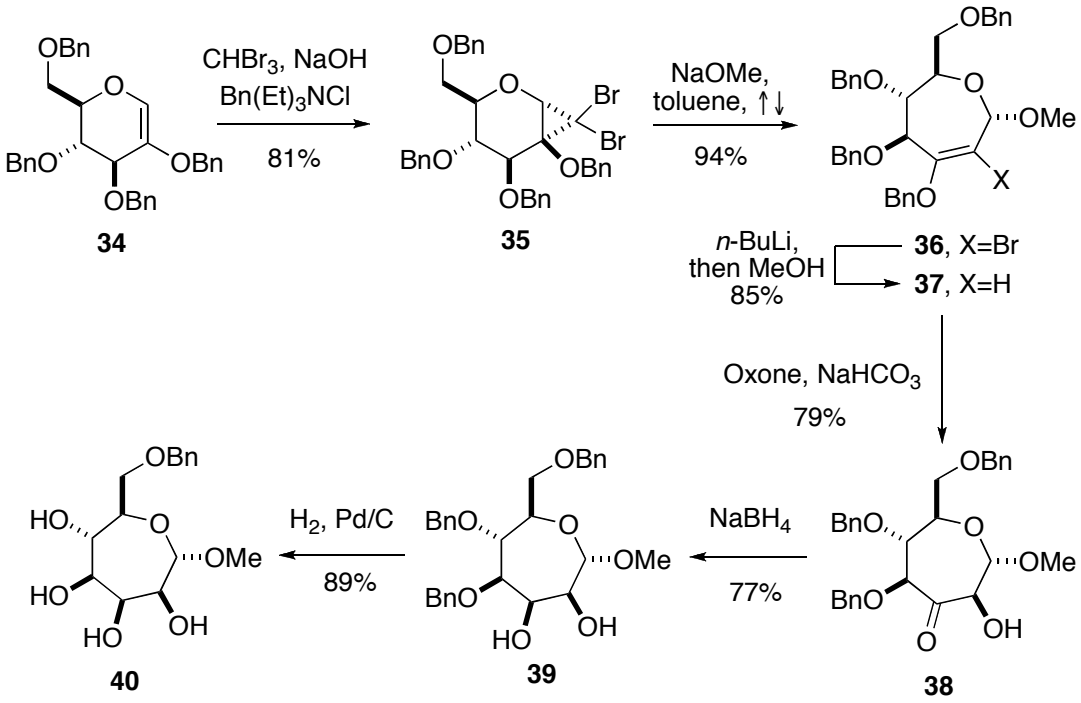
Additionally, Peczuh has exploited ring-closing metathesis using the Schrock molybdenum catalyst by converting the vinyl ether derivative **29** to the seven-membered ring D-xylose-based oxepine **30**. The glycal-like reactivity of oxepine **29** was thoroughly investigated, namely the reaction of the septanose glycal with dimethyldioxirane (DMDO) followed by epoxide opening with a variety of nucleophiles.[9] Given the well precedented use of thioglycosides in glycosylation reactions, Peczuh elected to open the epoxide with the lithium salt of thiophenoxide to synthesize thioglycoside donor **31**. After protection of the C-2 alcohol as the acetate derivative, the thioglycoside was then used as a donor in a NIS/AgOTf promoted glycosylation with heptose **32** to yield α-1,7-linked septanose disaccharide **33**. Disaccharide **33** represented the first known example of an oligosaccharide containing a septanose sugar at both the reducing and non-reducing ends (Scheme 6).[10]

Scheme 6. Peczuh's septanose glycal and septanose disaccharide syntheses



The cyclopropanation of a six-membered ring glycal and subsequent ring expansion to the seven-membered ring oxacycle has been developed as a method of entry into septanose carbohydrate monomers.[11] More recently, Jayaraman reported a novel approach to highly functionalized septanoses starting from an appropriately protected 2-hydroxyglycal. Dibromocyclopropanation of 2-hydroxyglycal 34 gave cyclopropane **35**, which was subjected to basic methanolysis to trigger the ring expansion to seven-membered ring oxacycle **36**. Lithium-halogen exchange and subsequent quenching of the vinyl lithiate with methanol (MeOH) provided **37**, which was further modified via a Rubottom-like oxidaton of the enol ether using oxone under basic conditions to provide the α-hydroxy ketone **38**. A straightforward reduction of **38** with sodium borohydride ($NaBH_4$) led to diol **39** that was globally deprotected to polyol **40** using palladium-catalyzed hydrogenolysis (Scheme 7).[12]

Scheme 7. Cyclopropanation/ring expansion route to septanose carbohydrates

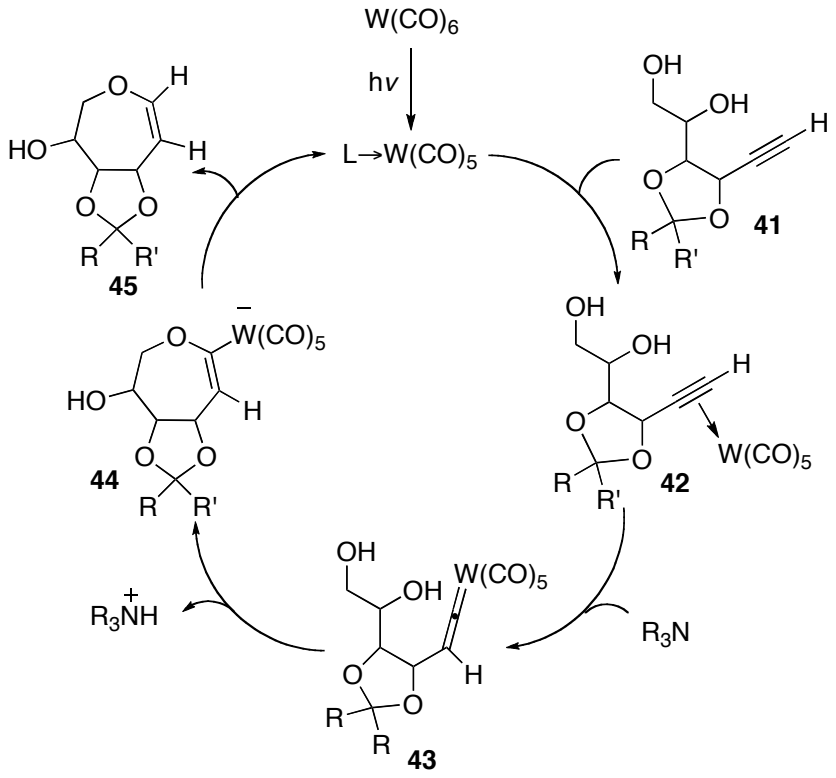


1.1.4. McDonald's tungsten hexacarbonyl ($W(CO)_6$)-catalyzed synthesis of septanose glycals

The McDonald laboratory has made significant contributions in the area of five- and six-membered ring glycal synthesis using group VI metal-catalyzed reactions. The method was elegantly highlighted in the syntheses of digitoxin,[13] desosamine,[14],vancosamine, saccharosamine,[15] and substructures of the antitumor antibiotic altromycin B.[16] In 2004, the McDonald laboratory reported the synthesis of seven-membered ring glycals via the *endo*-selective alkynyl alcohol cycloisomerization using catalytic tungsten hexacarbonyl ($W(CO)_6$), which is thought to proceed by the formation of a tungsten vinylidene carbene. The mechanism probably involved an η^2 coordination of an activated $W(CO)_5$

species to the alkyne **41** to give intermediate **42**, which then rearranged to the tungsten vinylidene carbene **43**. Attack of the distal oxygen to the vinylidene carbene led to tungstate complex **44**, which, after proton transfer, would reductively eliminate to give the product seven-membered ring glycal **45** (Scheme 8).[17]

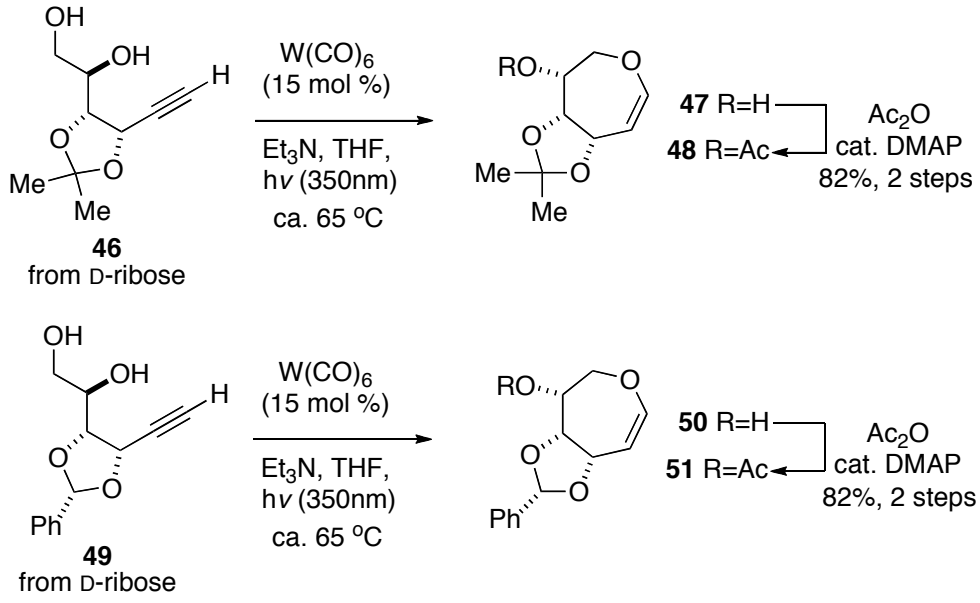
Scheme 8. Seven-membered glycal synthesis and proposed mechanism



The initial discovery of septanose glycal synthesis was made when Dr. Eva Alcázar subjected the acetonide protected alkynyl alcohol **46** (derived from D-ribose) to optimized $W(CO)_6$ cycloisomerization conditions. The major product was the seven-membered ring glycal **47**, which was elaborated to the acetate derivative **48** to facilitate purification. The six-membered ring glycal, though the expected product from the reaction, could only be observed in trace quantities by

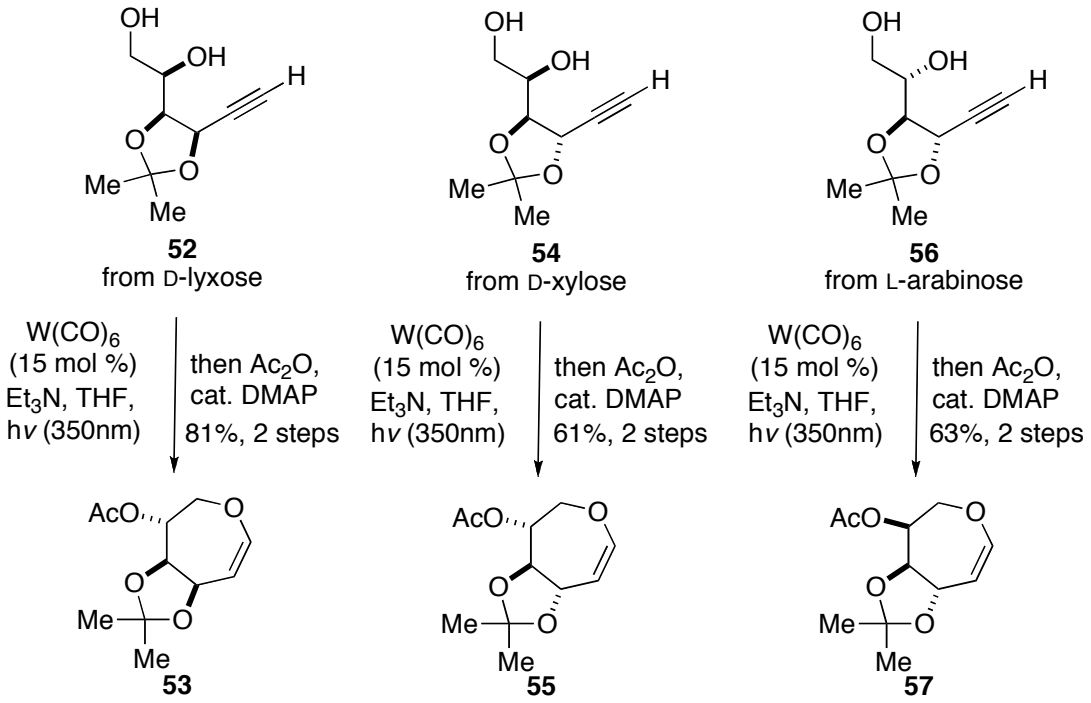
^{1}H NMR analysis of the crude reaction mixture. The nature of the cyclic acetal protecting group did not affect the regioselectivity of the reaction, as the 7-*endo* mode of cyclization was still observed for the benzylidene acetal protected alkynyl alcohol **49** (Scheme 9).

Scheme 9. Synthesis of septanose glycals via alkynyl alcohol isomerization



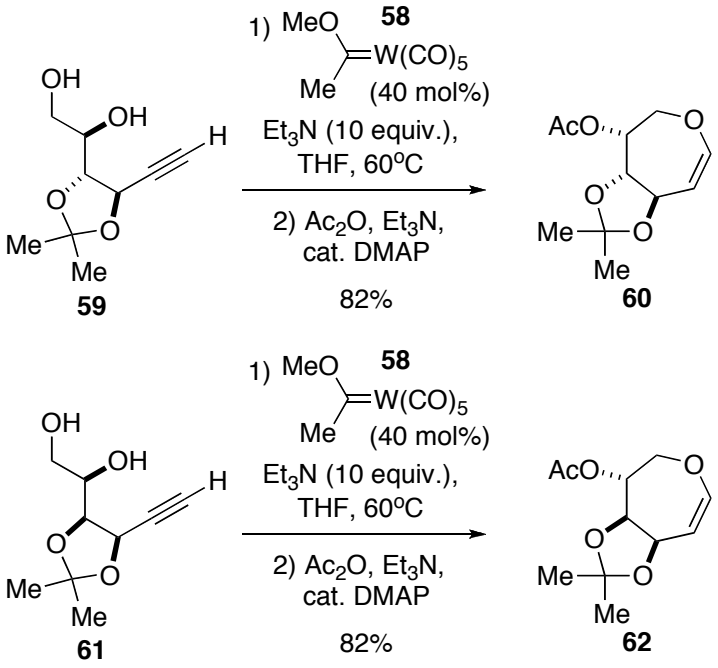
The synthesis of seven-membered ring glycals proved to be general, as the reaction worked well for other diastereomers of acetonide protected alkynyl alcohol **46**. Even for alkynyl diols **54** (from D-xylose) and **56** (from L-arabinose) with a *trans*-acetonide, the 7-*endo* regiochemical course of the reaction was unchanged (Scheme 10).

Scheme 10. Seven-membered ring glycal synthesis of various alkynyl diol diastereomers



An additional method of glycal synthesis that does not require photochemical activation of the tungsten-based catalyst system was reported by McDonald in 2007.[18] Using bench-stable Fischer carbene **58** in the presence of a tertiary amine base and heating, the cycloisomerization of alkynyl diol to glycal was accomplished for a broad scope of substrates, including the formation of seven-membered ring glycals **65** and **67**. The formation of seven-membered ring glycals using this method required slightly higher catalyst loadings of **58** (40 mol % relative to 25 mol % for all other substrates) and a higher reaction temperature of 60 °C (an increase from 40 °C for all other substrates) (Scheme 11).

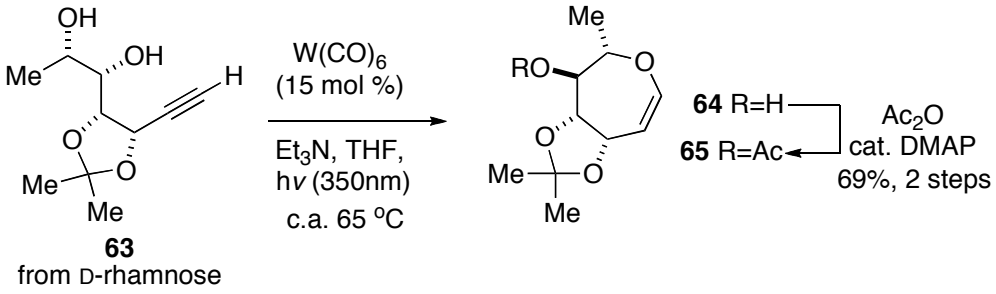
Scheme 11. Fischer carbene catalysis of alknyl alcohol isomerization: non-photochemical synthesis of seven-membered ring glycals



The rationale for the seven-membered ring formation centered around the cyclic acetal protecting group of the C3, C4-diol, which was believed to serve as a conformational lock of the alkynyl alcohol that brings the distal alcohol in close proximity to the intermediate vinylidene carbene. Additionally, the resulting 5,7 fused ring system could be thermodynamically favored, as the corresponding 5,6 fused ring system of a six-membered ring glycal could suffer severe strain. To further probe the origin of the 7-*endo* selectivity, alkynyl diol substrate **63** bearing two secondary alcohols was synthesized from D-rhamnose. Surprisingly, the 7-*endo* mode of cyclization was still observed despite the absence of a primary alcohol. The behavior of this compound in the cycloisomerization proved that a primary alcohol was not required for seven-membered ring formation. This result

reinforces the previous assertion that the cyclic acetal protecting group is responsible for the regioselectivity (Scheme 12).

Scheme 12. Cyclization of alkynyl diol 63



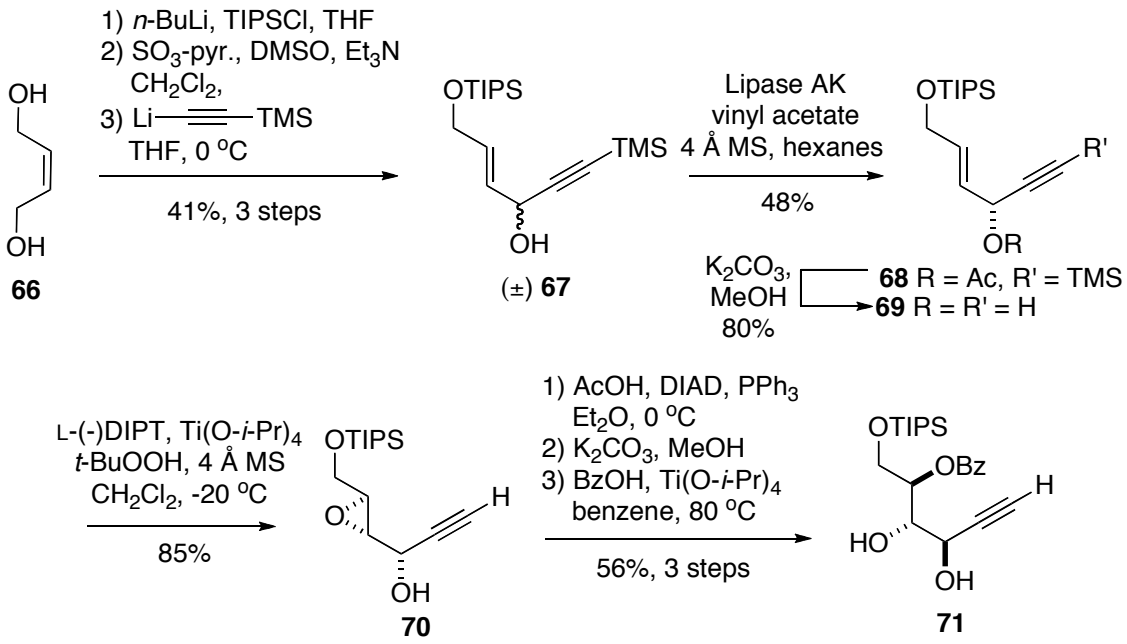
63
from D-rhamnose

1.2. Results and Discussion

1.2.1. Synthesis of 1,5-linked D-mannoseptanose mono-, di-, and trisaccharides[19]

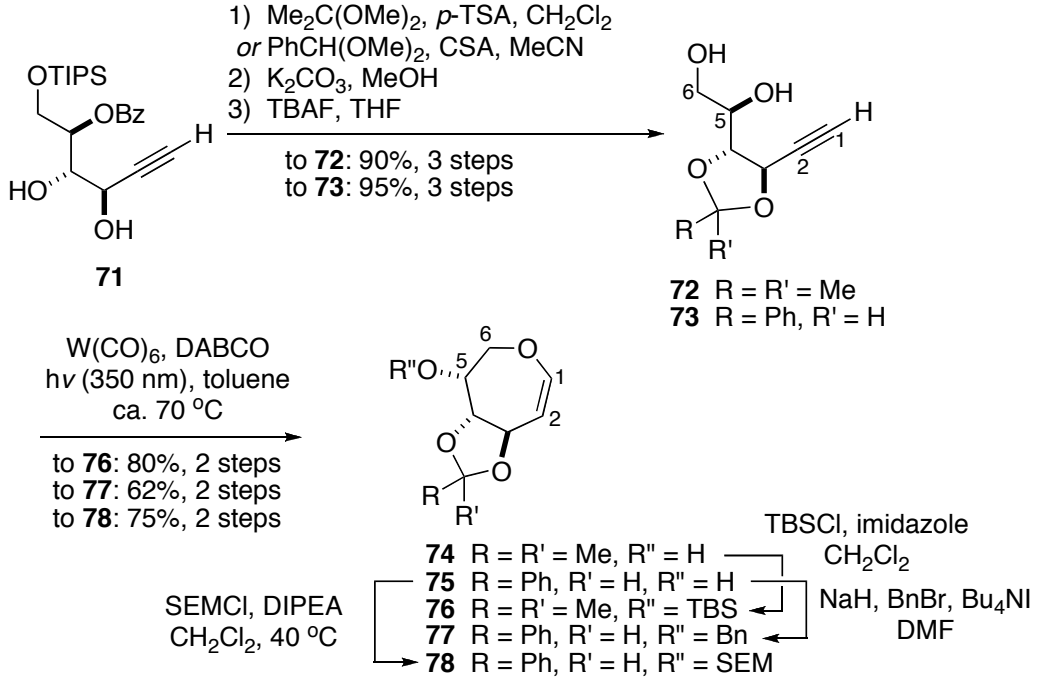
The initial synthesis of the alkynyl diol substrates involved one-carbon homologation of aldehyde to alkyne[20] of an appropriately protected pentose. Unfortunately, preparation of the alkynol substrate for the D-arabino glycal (precursor to D-manno- and D-glucoseptanosides) was much more difficult than for the other three diastereomers. Thus, an asymmetric synthesis of alkynyl diol **71** was designed that provided multi-gram scale quantities of the D-arabinoseptanose glycals, while offering flexibility in protective group patterns. Key features of this synthesis include the lipase-catalyzed enzymatic resolution of (±)-**67**[21] which was more easily conducted on multigram scale than enantioselective alkynylation[22] or Sharpless kinetic resolution of (±)-**67**.[23] From compound **69**, the chiral secondary alcohols were introduced with Sharpless epoxidation[24] to **70**, followed by Mitsunobu inversion[25] and Ti(O-*i*-Pr_4)-promoted regioselective addition of benzoic acid[26] to alkynyl diol **71** (Scheme 13).

Scheme 13. Asymmetric synthesis of D-arabino alkynyl alcohol



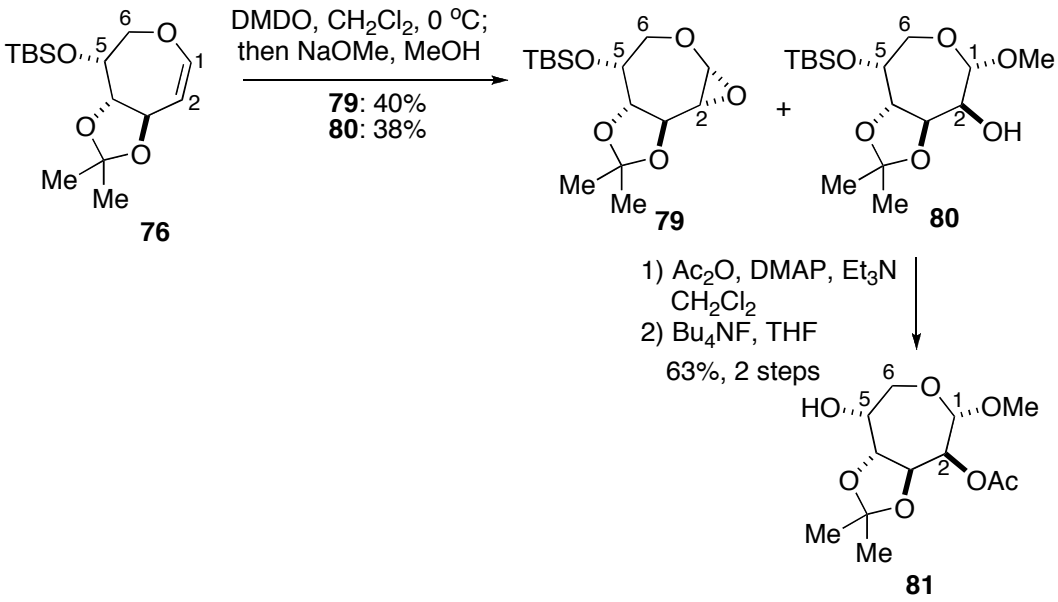
After introduction of the required cyclic protective group as acetonide **72** or as benzylidene acetal **73**, tungsten-catalyzed alkynol cycloisomerization[27] provided the respective septanose glycals **74**-**75**, which were isolated after protection of the 5-hydroxyl as the glycals **76**-**78** (Scheme 14).[28]

Scheme 14. Cyclic acetal protection and cycloisomerization



Our original intention was to functionalize the septanose glycal **76** by dimethyldioxirane (DMDO) epoxidation followed by nucleophilic epoxide-opening. However, the epoxidation of acetonide glycal **76** was not stereoselective. Upon basic methanolysis, a 1:1 mixture of the D-glucoseptanosyl epoxide **79** and the methanol addition product **80** arising from the D-mannoseptanoside epoxide was obtained. The epoxide **79** was remarkably stable to a variety of nucleophilic addition conditions. The protecting group manipulations from **80** to **81** were straightforward (Scheme 15).

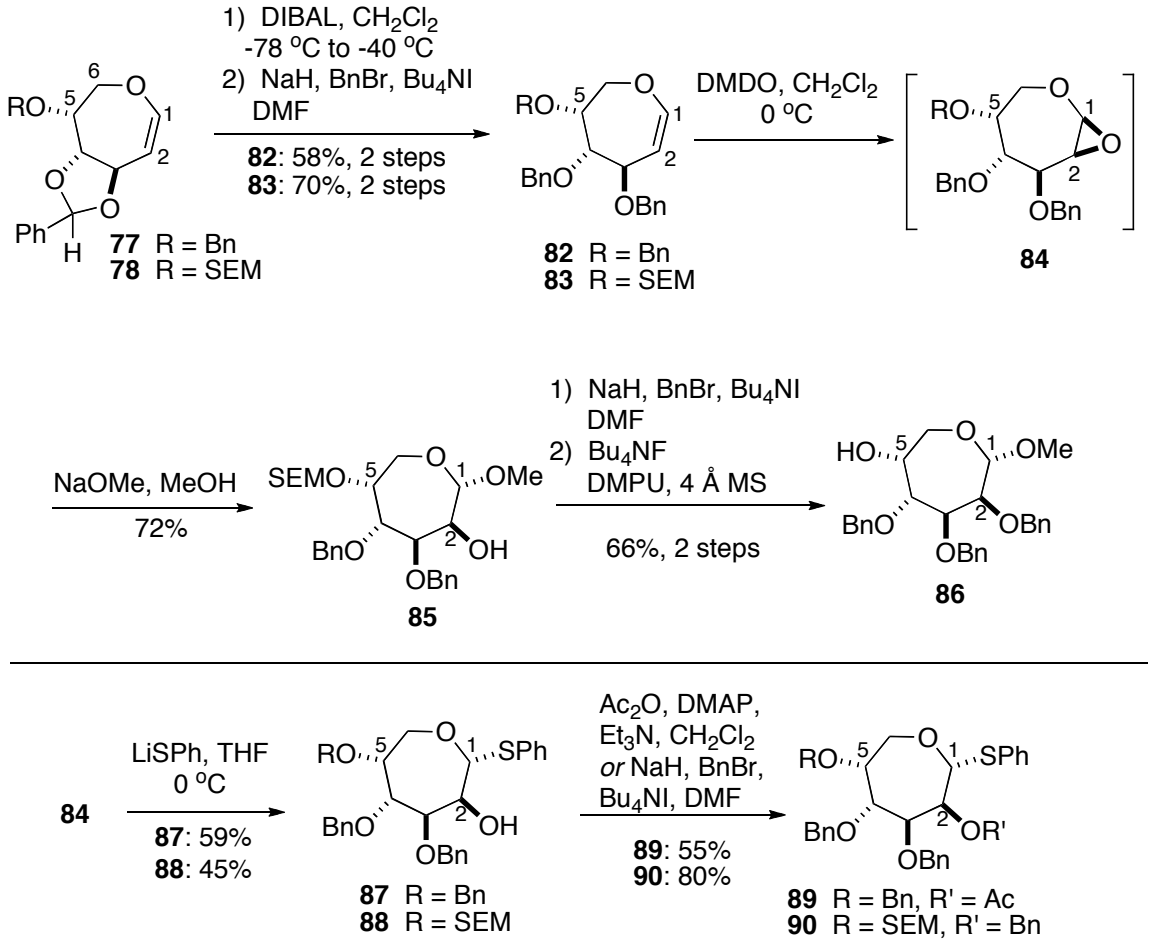
Scheme 15. Non-stereoselective DMDO epoxidation of glycal 81



On the other hand, the reaction of **77** with DMDO resulted in a complex mixture, consistent with competitive oxidation of the benzylidene acetal.[29] Thus reductive cleavage of the benzylidene acetals **77** and **78** was followed by *O*-benzylation to afford the septanose glycals **82** and **83** in excellent yield. DMDO epoxidations of glycals **82** and **83** were stereoselective, so that addition of sodium methoxide to the epoxide intermediate **84** provided the partially protected D-mannoseptanoside **85**, whereas lithium thiophenoxide addition resulted in the formation of thioglycosides **87**-**88**. For **87**-**88**, the epoxidation occurred *cis*- to the allylic C3 benzyloxy substituent but *trans*- to both C4 and C5 substituents, consistent with observations in several six-membered ring glycals.[30] The protective group manipulations of **87**-**88** to **89**-**90** were straightforward, other than observing that deprotection of the trimethylsilylethoxymethyl (SEM)-group to the free C5-alcohol of methyl α-mannoseptanoside acceptor synthon **85** was

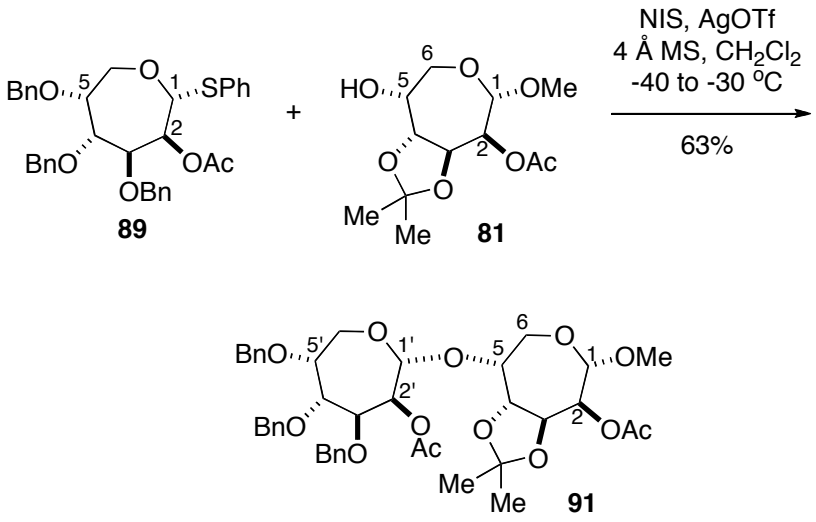
possible only with DMPU solvent in conjunction with molecular sieves (Scheme 16).[31,32]

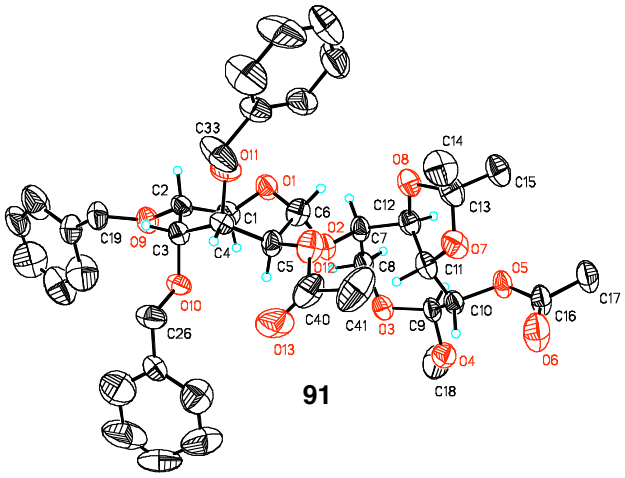
Scheme 16. DMDO epoxidation and functionalization of glycals 77 and 78



Encouraged by Peczuh's report of glycosylations of other septanose thioglycosides,[5e] we first studied the glycosylation of septanoside acceptor synthon **81** with the thioglycoside donor synthon **89**. This transformation provided fully protected disaccharide **91**, for which the crystal structure confirmed the stereochemical assignments for the compounds arising from epoxidation and ring-opening products **81** and **87** (Scheme 17).

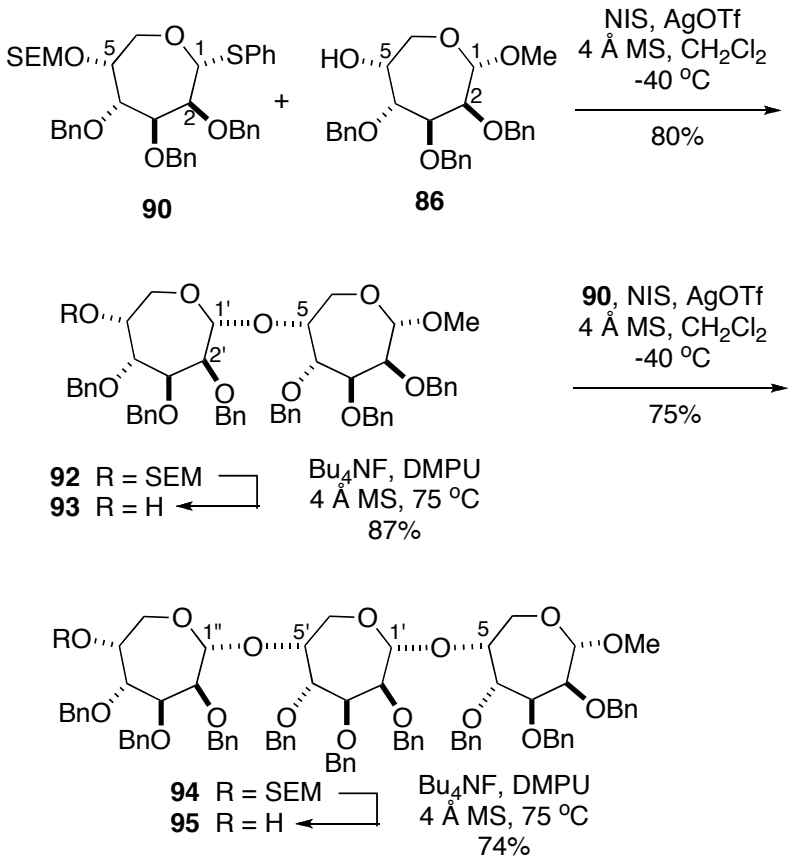
Scheme 17. Synthesis and thermal ellipsoid of disaccharide 91





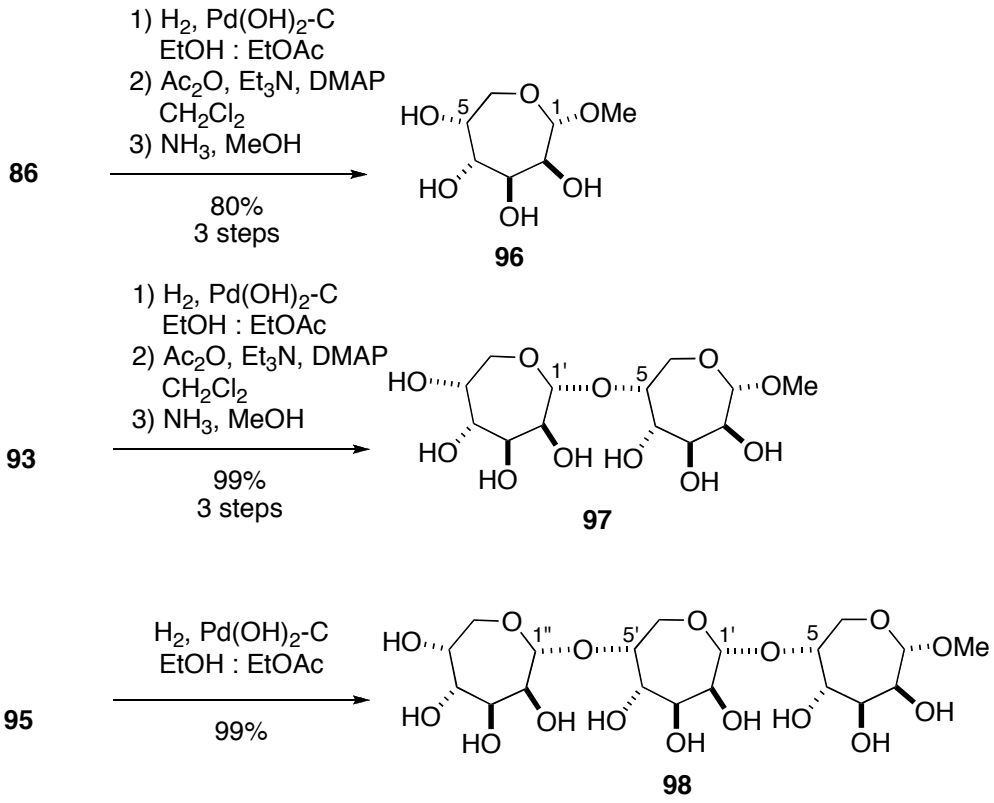
A more practical combination of O5-SEM-protected thioglycoside **90** with C5-alcohol **86** provided the disaccharide **92**, again with α-selectivity despite the absence of a participating group at C2. After removal of the SEM protective group, disaccharide alcohol **93** was glycosylated again with **90** to provide trisaccharide **94**. Gratifyingly, the glycosylation with a more complex acceptor synthon did not substantially affect the yield (Scheme 18).

Scheme 18. Synthesis of disaccharide 92 and trisaccharide 94



Each mannoseptanoside was fully deprotected by global debenzylation via $Pd(OH)_2$-C catalyzed hydrogenolysis. The crude polyols **96-97** were purified by forming the peracetate derivatives and silica gel chromatography, followed by ammoniacal methanolysis, whereas the trisaccharide **98** was obtained analytically pure without further purification (Scheme 19).

Scheme 19. Global deprotection to polyols 96-98



Although the seven-membered ring isomers of the naturally occurring pyranosides exhibit substantially different arrangements of the hydroxyls, including the incorporation of the primary C6 carbon into the ring, we still wondered if the common arrangement of hydroxyls at C2, C3, and C4 would be sufficient for **96-98** to serve as substrates for glycosidase hydrolysis. Thus we evaluated the jack bean α-mannosidase-catalyzed hydrolysis of *para*-nitrophenyl α-D-mannopyranoside (PNP-Man) in the presence of varying concentrations of α-mannoseptanosides **96-98** (Table 1).[33] Remarkably, none of our mannoseptanosides showed significant inhibition of PNP-Man hydrolysis, suggesting that these seven-membered ring-size isomers did not interact with the matched enzyme for α-mannopyranoside hydrolysis. Given the different

conformations of mannoseptanosides and mannopyranosides, future enzyme inhibition studies might benefit from testing additional members of the glycosidase family, in order to cover a broader range of substrate specificity.

In conclusion, tungsten-catalyzed cycloisomerizations of alkynyl alcohols have ultimately permitted access to a unique family of non-natural septanosyl oligosaccharide ring-size isomers of α-mannopyranosides. As the 1,5-linked D-mannoseptanosyl di- and trisaccharides have not previously been reported in the literature, the demonstration of this glycosylation strategy involving more complex glycosyl acceptors and donors is an important achievement towards future applications of this concept to the synthesis of long-chain oligoseptanosides via larger fragment coupling strategies.

Table 1. Kinetic parameters for *para*-nitrophenyl mannopyranoside (PNP-Man) hydrolysis by α-mannosidase in the absence and presence of septanosyl oligosaccharides 96-98[a]

	control[b]	0.75 mM **96**	6.0 mM **96**	0.75 mM **97**	6.0 mM **97**	0.75 mM **98**	6.0 mM **98**
K_m (mM)	3.8 ± 0.5	3.1 ± 0.3	3.6 ± 0.3	2.7 ± 0.2	4.3 ± 0.4	2.1 ± 0.2	2.4 ± 0.3
Kcat (s^{-1})	44 ± 1	38 ± 1	41 ± 1	45 ± 1	41 ± 1	44 ± 1	46 ± 2

[a] Inhibition of jack bean α-mannosidase-catalyzed hydrolysis of PNP-Man (0-30 mM) in the absence of mannoseptanosides (control) or in the presence of 0.75 mM or 6.0 mM of mannoseptanosides **96**, **97**, and **98**. [b] The literature reports K_M values for jack bean α-mannosidase-catalyzed hydrolysis of PNP-Man ranging from 2.5 mM[34] to 4.67 mM[35].

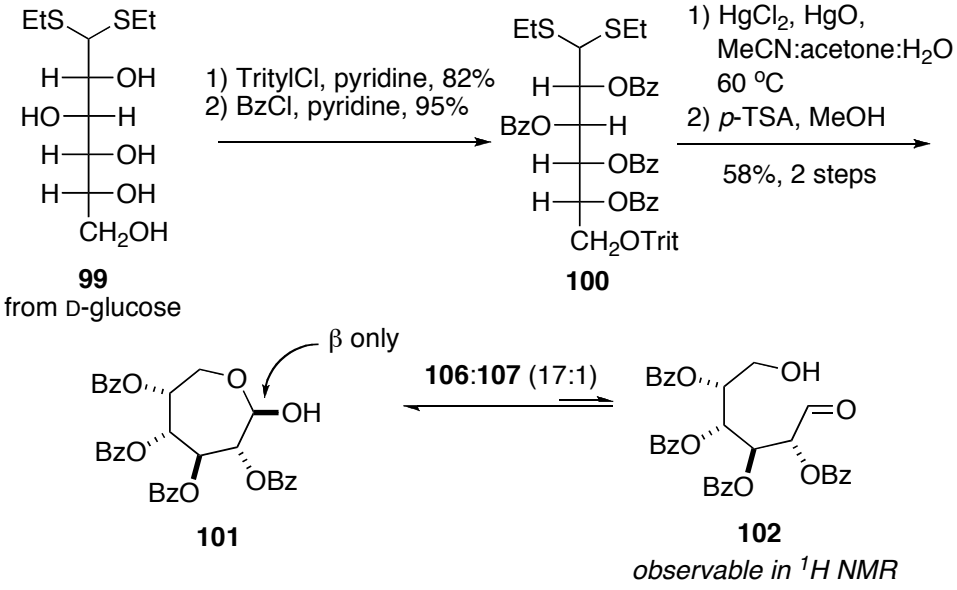
1.2.2. Synthesis of D-glucoseptanoses

We established that the tungsten-catalyzed cycloisomerization of an alkynyl alcohol with D-*arabino* absolute stereochemistry ultimately provided septanose monomers with D-*manno* absolute stereochemistry. The DMDO epoxidation of every substrate in this series of septanose glycals proceeded with unexpected facial selectivity (*cis*- to the allylic C3 benzyloxy substituent but *trans*- to both C4 and C5 substituents). Thus, the ultimate desire of synthesizing unnatural, septanose carbohydrates bearing monomer units with D-*gluco* absolute stereochemistry could not be easily realized using a glycal derived from tungsten-catalyzed cycloisomerization. After considering various methods for the synthesis of D-glucoseptanoses, we focused on the method of D-galactoseptanose synthesis pioneered by Micheel (later modified by Stütz and Withers in the synthesis of L-idoseptanoses) using protecting group manipulation of a hexose precursor as way of gaining rapid access to these unnatural sugars. Notably, there are currently no reports of D-glucoseptanose monomer synthesis using this method.

Gratifyingly, D-glucoseptanose **101** can be easily prepared in gram-scale quantities from dithioacetal **99** (from D-glucose). A trityl ether protection of the C6-hydroxyl and protection of the secondary alcohols as benzoate esters gave 2,3,4,5-tetra-*O*-benzoyl-6-*O*-trityl diothioacetal derivative **100**. After revealing the aldehyde using a mercury-catalyzed dithioacetal cleavage, the C6-hydroxyl was unmasked using *para*-toluenesulfonic acid (*p*-TSA) in methanol to give tetra-*O*-benzoyl-D-glucoseptanose **101** as the β anomer. Interestingly, the ^{1}H NMR

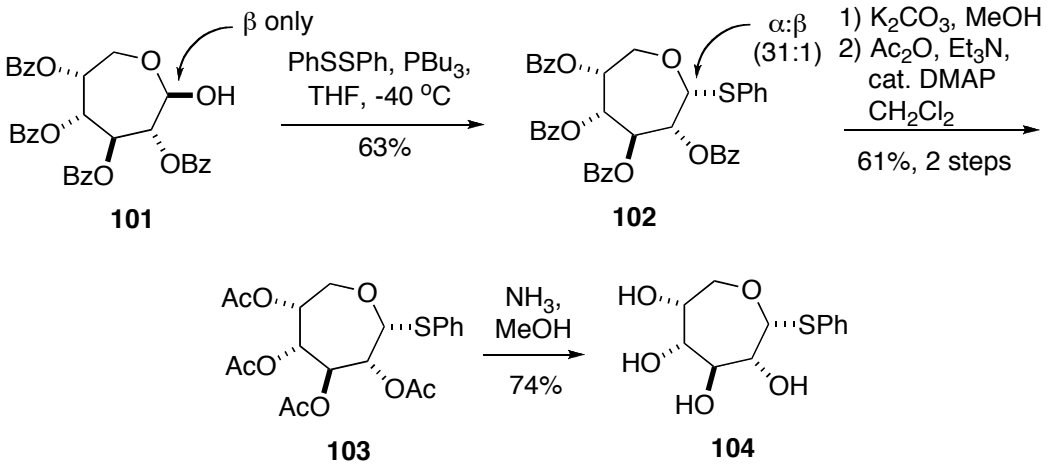
($CDCl_3$) of glucoseptanose **101** clearly shows an equilibrium mixture composed of the the open-chain aldehyde **102** as a 17:1 mixture favoring the closed-chain lactol **101**.

Scheme 20. Synthesis of D-glucoseptanose perbenzoate 101



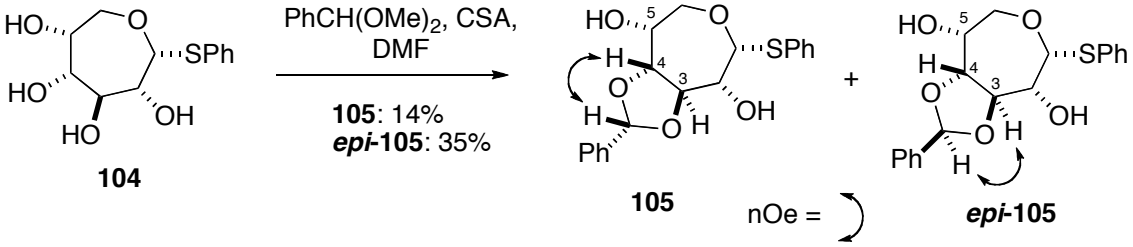
Having demonstrated the success of thioglycosides as glycosyl donors in the synthesis of D-mannoseptanosides, we elected to convert **101** to the corresponding α-thioglycoside **102**.[36] Upon hydrolysis of the benzoate esters, the crude poylol **103** was purified by forming the peracetate derivatives and silica gel chromatography, followed by ammoniacal methanolysis to give the D-glucoseptanose polyol **104** (Scheme 21)**.**

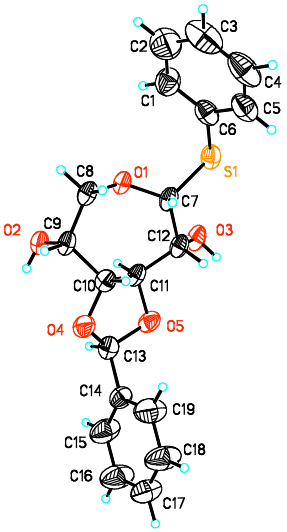
Scheme 21. Synthesis of D-glucoseptanose polyol 104



After establishing a multigram-scale synthesis of D-glucoseptanose **104**, we focused attention on the differentiation of the four secondary alcohols. Orthogonal protection of polyol substrates in carbohydrate chemistry is often challenging and remains the focus of much research.[37] We envisioned that a straightforward method of alcohol differentiation for **104** would involve formation of the 1,2-acetal (acetonide or benzylidene acetal), with the expectation that the C4, C5 *cis*-diol would be selectively protected. However, exposure of **104** to benzaldehyde dimethyl acetal ($PhCH(OMe)_2$) in camphorsulfonic acid (CSA) gave the benzylidene acetals **105**-***epi*-105**, which was the result of *exclusive* protection of the C3, C4 *trans*-diol. The regioselectivity and stereochemistry of the acetals were determined through COSY and 1D CYCLENOE experiments. Absolute structure confirmation was obtained via an X-ray crystal structure of ***epi*-105** (Scheme 22).

Scheme 22. Regioselective benzylidene acetal formation and thermal ellipsoid of *epi*-105

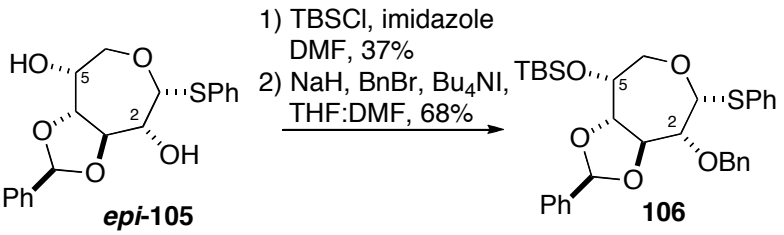




***epi*-105**

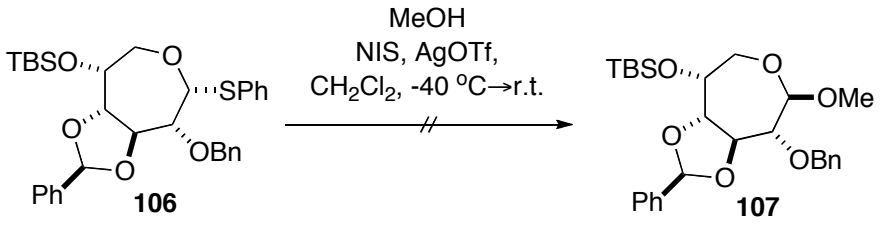
With the synthesis of 1,5-linked D-glucoseptanoses in mind, we felt the C3, C4 regioselectivity of benzylidene acetal formation would be beneficial, leaving only the differentiation of the C5 and C2 hydroxyls. We also realized that a bulky protecting group could be selectively installed at the C5 position considering the difference in the local steric environment relative to the C2 hydroxyl. Thus, the C5 hydroxyl was successfully protected as the *tert*-butyl dimethyl silyl (TBS) ether, albeit in modest yield. The C2 hydroxyl was easily converted to the benzyloxy derivative **106** (Scheme 23).

Scheme 23. Orthogonal protecting group manipulation of 105



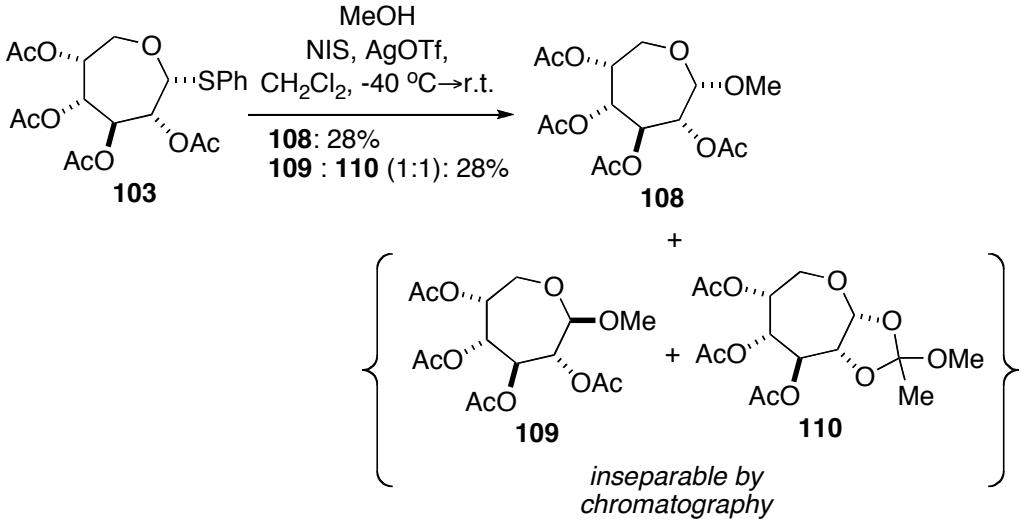
Thioglycoside **106** was originally intended to act as a glycosylation donor and the precursor for methyl glycoside **108**, which after protecting group manipulation, was to serve as the glycosylation acceptor. However, upon exposure of **106** to NIS/AgOTf activation conditions in the presence of an excess of MeOH, no reaction was observed, even at room temperature. This result led us to conclude that the benzylidene acetal is acting as a conformational restraint against donor activation in the glycosylation. Ley has extensively studied the effects of cyclic acetal protecting groups on diminishing the reactivity of glycosyl donors.[38] In accordance with Ley's observations, we believe the cyclic acetal protecting group prevented planarization to the intermediate oxacarbenium ion, thereby leading to the deactivation of the donor (Scheme 24).

Scheme 24. Attempted methyl glycoside formation from thioglycoside 106



To circumvent this problem, an alternative method of methyl glycoside formation was used starting from the non-acetal-protected peracetate thioglycoside **103**. Using standard NIS/AgOTf activation conditions in the presence of MeOH, the α-methyl glycoside **108** was synthesized in low yield, along with an inseparable mixture of the corresponding β anomer **109** and orthoester **110** (Scheme 25).

Scheme 25. Formation of methyl glycoside 108



In conclusion, we have successfully demonstrated the synthesis of D-glucoseptanoses following Micheel's precedent of protective group manipulation of a hexose sugar. The unexpected yet interesting reactivity patterns of our D-glucoseptanose substrates provided valuable insight into the future planning of protecting group and synthetic strategies to achieve a synthesis of 1,5-linked oligosaccharides composed of D-glucoseptanose units.

1.3. Experimental Details

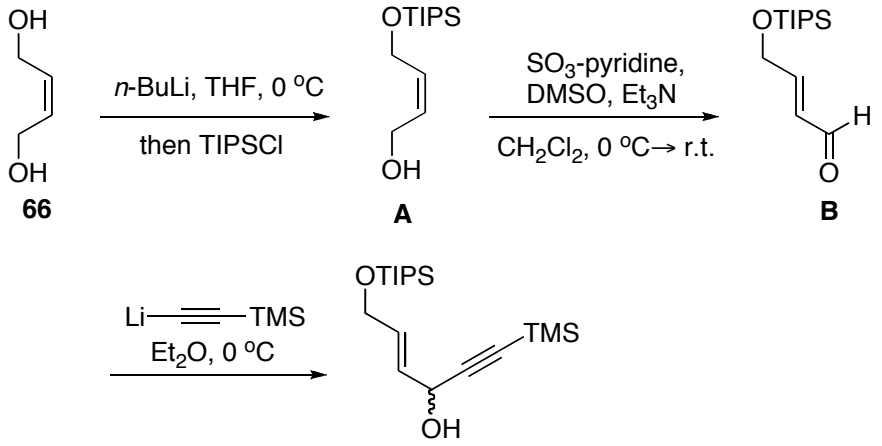
1.3.1. 1,5-D-Mannoseptanosides

General information: ^{1}H and ^{13}C NMR spectra were recorded on a Varian INOVA-400 spectrometer (400 MHz for ^{1}H, 100 MHz for ^{13}C), or an INOVA-600 spectrometer (600 MHz for ^{1}H, 150 MHz for ^{13}C). NMR spectra were recorded as solutions in deuterated chloroform ($CDCl_3$) with residual chloroform (7.27 ppm for ^{1}H NMR and 77.23 ppm for ^{13}C NMR) taken as the internal standard or deuterated methanol (CD_3OD) with residual methanol (4.78 ppm for ^{1}H, 49.15 ppm for ^{13}C) taken as the standard, and were reported in parts per million (ppm). Abbreviations for signal coupling are as follows: s, singlet; d, doublet; t, triplet; dd, doublet of doublets; dt, doublet of triplets; qt, quartet of triplets; dtd, doublet of triplet of doublets; ddt, doublet of doublet of triplets; ddd, doublet of doublet of doublets; m, multiplet. IR spectra were collected on a Mattson Genesis II FT-IR spectrometer with samples as neat films. Mass spectra (high resolution FAB or EI) were recorded on a VG 70-S Nier Johason mass spectrometer or a Thermo Finnigan LTQ FT spectrometer. Optical rotations were recorded at 23 ^{o}C with a Perkin-Elmer Model 341 polarimeter (concentration in g/100mL). Analytical thin layer chromatography (TLC) was performed on precoated glass backed plates purchased from Whatman (silica gel 60 F_{254}; 0.25 mm thickness). Flash column chromatography was carried out with silica gel 60 (230-400 mesh ASTM) from EM Science.

All reactions except as mentioned were conducted with anhydrous solvents in oven- dried or flame-dried and argon-charged glassware. All anhydrous

solvents were dried over 3Å or 4Å molecular sieves (beads). Trace water content was tested with Coulometric KF titrator from Denver Instruments. All solvents used in work-up, extraction and column chromatography were used as received from commercial suppliers without prior purification. During reaction workup, the reaction mixture was usually diluted to three times the original volume, and washed with an equal volume of water and/or aqueous solutions as needed. All reagents were purchased from Sigma-Aldrich and Amano. *para*-Nitrophenyl-α-D-mannopyranoside and Jack Bean Mannosidase were purchased from Sigma Aldrich. Spectrophotometric inhibition studies were carried out using a Cary UV 50 Bio Spectrophotometer (Varian).

Preparation of enynol (±)-67



(±)-67

Commercially available 1,4-*cis*-2-buten-ol (**66**) (20 g, 19 mL, 230 mmol) was added to THF (0.50 M, 500 mL). The solution was cooled to 0 °C, and *n*-BuLi (2.5 M in hexanes, 100 mL, 250 mmol) was slowly added over a 20 minute period. The reaction was stirred for 30 minutes at 0 °C, at which point TIPSCl (43 mL, 225 mmol) was added dropwise over a 5 minute period. The reaction

was allowed to warm to room temperature over a 2 hour period. The reaction was then quenched by the addition of a saturated solution of NH_4Cl (300 mL). The aqueous layer was extracted with EtOAc (2 x 100 mL). The combined organics were dried with $MgSO_4$, filtered, and concentrated under reduced pressure. Chromatography (20:1→1:1 hexanes:EtOAc) afforded TIPS-protected compound **A** as a colorless oil (47 g, 85%).

^1H NMR (400 MHz, $CDCl_3$) δ 5.71 (m, 2H), 4.33 (d, J = 4.2 Hz, 2H), 4.21 (d, J = 4.8 Hz, 2H), 2.20 (s, 1H), 1.08 (m, 21H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 131.6, 130.1, 60.0, 59.2, 18.1, 12.1; IR (KBr) 3351, 2943, 2867, 1463, 1097, 883, 682 cm^{-1}; HRMS (ESI) [M+H^+] Calcd. for $C_{23}H_{29}O_2Si_1$, 245.19314, found 245.19300.

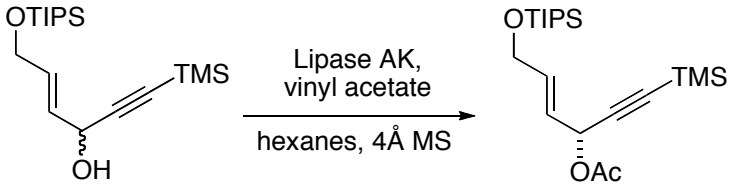
Compound **A** (11.5 g, 47 mmol) was dissolved in CH_2Cl_2 (0.50M, 100 mL). DMSO (6.7 mL, 94 mmol) and Et_3N (13 mL, 94 mmol) were added sequentially to the stirring solution, which was then cooled to 0 ^oC. SO_3-pyridine (15 g, 94 mmol) was then added to the solution all at once. The reaction was allowed to warm to r.t. and was stirred for 3 hours. The reaction was quenched by the addition of H_2O (150 mL). The aqueous layer was extracted with CH_2Cl_2 (2 x 50 mL). The organics were combined and dried over $MgSO_4$. After filtration and concentration under reduced pressure, the crude mixture was purified via chromatography (20:1→9:1 hexanes:EtOAc) to give aldehyde **B** as a pale yellow oil (8.5 g, 75%). This procedure was optimal at the reported scale, thus the oxidation was repeated twice to provide sufficient material for the subsequent step.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.63 (d, *J* = 8.0 Hz, 1H), 6.9 (dt, *J* = 3.2, 15.2 Hz, 1H), 6.48 (ddt, *J* = 2.0, 8.0, 15.2 Hz, 1H), 4.56 (dd, *J* = 2.0, 3.2 Hz), 1.08 (m, 21H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 180**,** 156.9, 130.7, 62.8, 18.1, 12.1; IR (KBr) 2943, 2867, 2722, 1692, 1463, 1149, 1116, 966, 883, 684 cm^{-1}; HRMS (ESI) [M +H] Calcd. for $C_{13}H_{27}O_2Si_1$, 243.17749, found 243.17764.

To a stirring solution of TMS acetylene (16 mL, 114 mmol) in THF (0.50 M, 190 mL) at 0 ^{o}C was slowly added *n*-BuLi (2.5 M in hexanes, 42 mL, 105 mmol) over a period of 30 minutes. Upon completion of the addition, the solution was allowed to stir for an additional 30 minutes at 0 ^{o}C. Then aldehyde **B** (23 g, 95 mmol) was slowly added via syringe over a 10 minute period. The reaction was stirred for 1 hour upon addition of **B**. The reaction was quenched by the addition of a saturated solution of NH_4Cl (100 mL), followed by extraction of the aqueous layer with EtOAc (1 x 100 mL). The organic extracts were combined and dried with $MgSO_4$. After filtration and concentration, **(±)-67** was obtained as a yellow oil (32 g, 95%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.01 (dtd, *J* = 1.2, 4.0, 15.2 Hz, 1H), 5.91 (ddt, *J* = 1.6, 6.0, 15.2 Hz, 1H), 4.91 (ddd, *J* = 1.2, 5.2, 6.6 Hz, 1H), 4.31 (m, 2H), 1.83 (d, *J* = 6.4 Hz, 1H) 1.09 (m, 21H), 0.19 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 132.6, 128.1, 104.6, 91.1, 63.1, 63.0, 18.2, 12.2, 0.011; IR (KBr) 3368, 2944, 2867, 2173, 1463, 1383, 1131, 1100, 963, 845, 761, 683 cm^{-1}; HRMS (APCI) [M+H$^+$] Calcd. for $C_{18}H_{37}O_2Si_2$ 341.23266, found 341.23226.

Synthesis of acetate 68 via lipase-catalyzed resolution

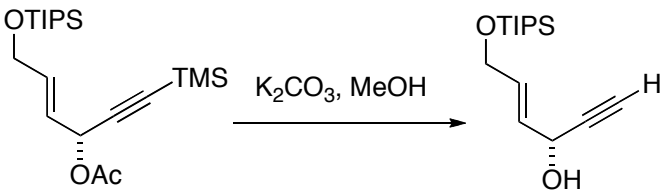


(±)-67 **68**

The racemic alcohol **(±)-67** (42 g,120 mmol) was dissolved in hexanes (0.50 M, 240 mL) and 4Å MS (42 g, powdered) were added. Then Lipase AK Amano (21 g) was added all at once, followed by the addition of vinyl acetate (84 mL). The solution was vigorously stirred at r.t. for 72 hours, after which time the mixture was filtered through celite. The volatiles were evaporated under reduced pressure. Chromatography (25:1→20:1→10:1 hexanes:EtOAc) yielded **68** as a pale yellow oil (20 g, 48 %).

$[\alpha]_D^{23}$ = -1.4 (c 1.00, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 6.08 (dtd, *J* = 0.80, 4.0, 15.2 Hz, 1H), 5.94 (dd, *J* = 0.80, 6.0, 1H), 5.83 (ddt, *J* = 1.6, 6.0, 15.2 Hz, 1H), 4.31 (m, 2H), 2.09 (s, 3H) 1.08 (m, 21H), 0.19 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.9, 135.2, 124.2, 100.9, 92.2, 64.3, 62.8, 21.4, 18.2, 12.2, -0.048; IR (KBr) 2944, 2867, 2181, 1746, 1464, 1370, 1227, 1130, 1014, 847, 761, 683 cm^{-1}; HRMS (ESI) [M+H^+] Calcd. for $C_{20}H_{39}O_3Si_2$ 383.24323, found 383.24339.

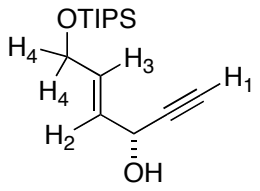
Synthesis of enynol (-)-69



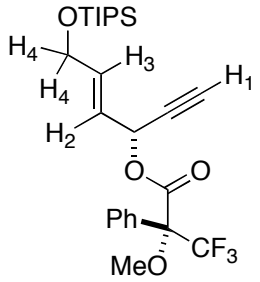
68 **(-)-69**

To a stirring solution of acetate ester **68** (20 g, 52 mmol) in MeOH (0.50 M, 100 mL) was added K_2CO_3 (11 g, 78 mmol) all at once. After stirring for 30 minutes at r.t., the reaction was diluted with Et_2O (100 mL) and quenched with a saturated solution of NH_4Cl (150 mL). The aqueous layer was extracted with Et_2O (2 x 50 mL). The organic were combined, dried with $MgSO_4$, and filtered. The volatiles were evaporated under reduced pressure to provide enynol **(-)-69** (14 g, Quant.). $[\alpha]_D^{23}$ = -10.9 (c 1.00, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 6.05 (dtd, *J* = 1,2, 4.0, 15.2 Hz, 1H), 5.93 (ddt, *J* = 2.0, 5.2, 15.2 Hz, 1H), 4.93 (m, 1H), 4.31 (m, 2H), 2.58 (d, *J* = 2.0 Hz, 1H), 1.85 (d, *J* = 6.4 Hz, 1H), 1.09 (m, 21H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 132.9, 127.7, 83.1, 74.4, 62.9, 62.6, 18.2, 12.2; IR (KBr) 3311, 2943, 2868, 1463, 1383, 1248, 1131, 1014, 965, 883, 682 cm^{-1}; HRMS (ESI) [M+H$^+$] Calcd. for $C_{15}H_{29}O_2Si_1$ 269.19314, found 269.19288.

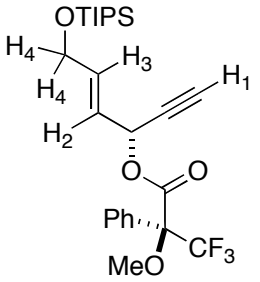
Mosher ester data for enynol (-)-69



(-)-69



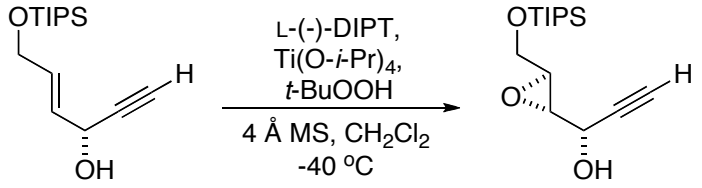
(*R*) Mosher Ester



(*S*) Mosher Ester

H	**69** ($CDCl_3$)	(*R*) Mosher Ester ($CDCl_3$)	(*S*) Mosher Ester ($CDCl_3$)
1	2.58 (d)	2.65 (d)	2.60 (d)
2	5.93 (ddt)	5.82 (ddt)	5.92 (ddt)
3	6.05 (m)	6.09 (m)	6.17 (m)
4	4.31 (m)	4.26 (m)	4.30 (m)

Synthesis of epoxyalcohol 70

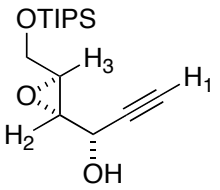


(-)-69 **70**

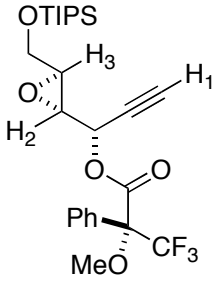
Enynol **(-)-69** (13.5 g, 50 mmol) was dissolved in CH_2Cl_2 and 4 Å MS (14 g, powdered) was added to the solution. L-(-)-DIPT (4.2 mL, 20 mmol) was added to the solution, which was then cooled to -40 °C and stirred for 20 minutes. Then Ti(O-*i*-Pr)$_4$ (4.4 mL, 15 mmol) was added all at once, and the solution was stirred for 20 additional minutes at -40 °C. Then *t*-BuOOH (5.5 M in decane, 18 mL, 100 mmol) was added dropwise via syringe pump over a 3 hour period. After the addition was complete, the reaction was transferred to a -20 °C freezer for 16 hours. The reaction was then warmed to 0 °C. A solution of citric acid (3.2 g, 15 mmol) in Et_2O:acetone (1:1, 200 mL) was then added to the solution all at once and stirred for 30 minutes. After filtration through celite with a thin top layer of silica gel, the volatiles were evaporated. Chromatography (20:1→10:1→4:1 hexanes:EtOAc) afforded epoxyalcohol **70** as a colorless oil (13.3 g, 94%).

$[\alpha]_D^{23}$ = -7.8 (c 1.00, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.68 (m, 1H), 4.03 (dd, *J* = 2.4, 12.0 Hz, 1H), 3.84 (dd, *J* = 4.0, 12.0 Hz, 1H), 3.33 (m, 2H), 2.52 (d, *J* = 2.0 Hz, 1H), 2.16 (d, *J* = 5.6 Hz, 1H), 1.08 (m, 21H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 80.2, 75.0, 62.3, 60.8, 56.6, 56.4, 18.1, 12.1; IR (KBr) 3413, 3311, 2944, 2867, 2121, 1463, 1385, 1248, 1121, 1014, 883, 783, 683 cm^{-1}; HRMS (ESI) [M+H$^+$] Calcd. for $C_{15}H_{29}O_3Si_1$ 285.18805, found 285.18817.

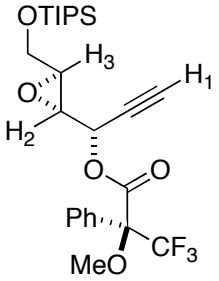
Mosher ester data for epoxyalcohol 70



70



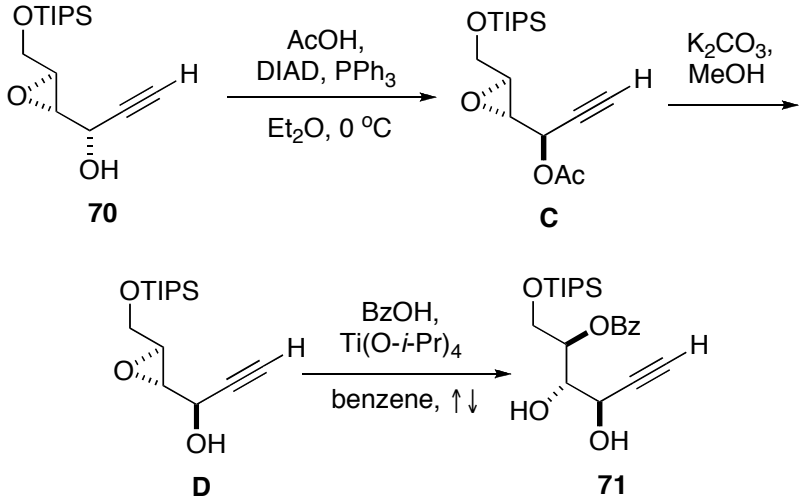
(*R*) Mosher Ester



(*S*) Mosher Ester

H	**70** ($CDCl_3$)	(*R*) Mosher Ester	(*S*) Mosher Ester
1	2.52 (d)	2.62 (d)	2.56 (d)
2	4.03 (dd)	3.90 (dd)	3.94 (dd)
3	3.84 (dd)	3.74 (dd)	3.78 (dd)

Preparation of diol 71



Epoxyalcohol **70** (13.3 g, 47 mmol) was dissolved in Et_2O (0.50 M, 100 mL). PPh_3 (13 g, 51 mmol) was then added all at once, and the solution was cooled to 0 °C. DIAD (9.8 mL, 51 mmol) was then added all at once, which resulted in the immediate formation of a white precipitate. The reaction was stirred for 15

minutes, at which point Et_2O (100 mL) was added, and the mixture was filtered through celite. The volatiles were evaporated. Chromatography (10:1 hexanes:EtOAc) afforded epoxyacetate **C** as a yellow oil (15 g, 98 %).

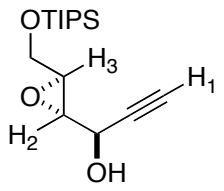
$[\alpha]_D^{23}$ = -29.6 (c 1.00, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 5.25 (dd, *J* = 2.4, 6.4 Hz, 1H), 3.99 (dd, *J* = 2.8, 12.0 Hz, 1H), 3.85 (dd, *J* = 4.0, 12.0 Hz, 1H), 3.32 (dd, *J* = 2.0, 6.4 Hz, 1H), 3.21 (m, 1H), 2.53 (d, *J* = 2.4 Hz, 1H), 2.15 (s, 3H), 1.08 (m, 21H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.7, 77.3, 75.5, 64.5, 62.2, 56.9, 54.9, 21.0, 18.1, 12.1; IR (KBr) 3276, 2943, 2867, 1750, 1464, 1371, 1227, 1139, 1024, 883, 684 cm^{-1}; HRMS (ESI) [M+H^+] Calcd. for $C_{17}H_{31}O_4Si_1$ 327.19861, found 327.19826.

Epoxyacetate **C** (15 g, 46 mmol) was dissolved in MeOH (0.50 M, 100 mL). K_2CO_3 (7.9 g, 57 mmol) was added all at once. The reaction was complete after 30 minutes of stirring at r.t. The reaction was diluted with Et_2O (100 mL) and quenched with a saturated solution of NH_4Cl (150 mL). The aqueous layer was extracted with Et_2O (2 x 50 mL). The organic layers were combined and dried with $MgSO_4$. Following filtration and removal of the volatiles under reduced pressure, epoxyalcohol **D** was isolated as a colorless oil without further purification (11 g, 84 %).

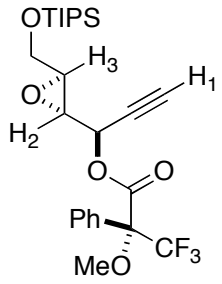
$[\alpha]_D^{23}$ = -8.3 (c 1.27, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 4.40 (m, 1H), 3.99 (dd, *J* = 3.0, 12.0 Hz, 1H), 3.82 (dd, *J* = 2.4, 12.0 Hz, 1H), 3.27 (dd, *J* = 2.4, 4.8 Hz, 1H), 2.53 (d, *J* = 2.4 Hz, 1H), 2.23 (d, *J* = 7.8 Hz, 1H), 1.07 (m, 21H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 81.2, 74.2, 62.5, 61.7, 57.5, 56.7, 18.1, 12.1; IR (KBr) 3431,

3293, 2946, 2870, 1463, 1385, 1247, 1124, 1016, 883, 782, 682 cm^{-1}; HRMS (ESI) [M+H$^+$] Calcd. for $C_{15}H_{29}O_3Si_1$ 285.18805, found 285.18807.

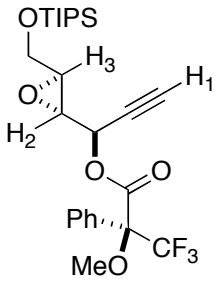
Mosher ester data for epoxyalcohol D



D



(*R*) Mosher Ester



(*S*) Mosher Ester

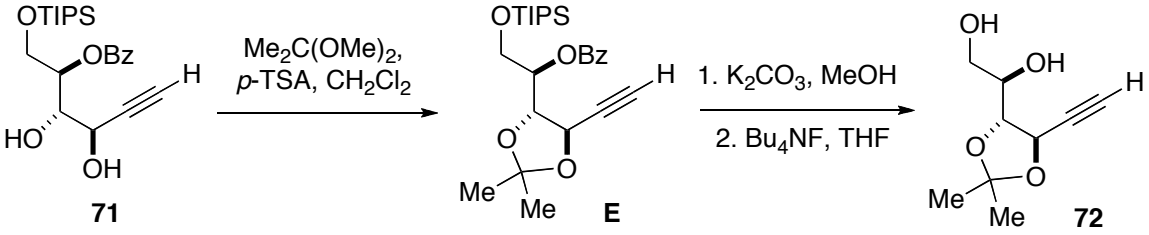
H	**D** ($CDCl_3$)	(*R*) Mosher Ester	(*S*) Mosher Ester
1	2.53 (d)	2.58 (d)	2.63 (d)
2	3.82 (dd)	3.81 (dd)	3.78 (dd)
3	3.99 (dd)	3.94 (dd)	3.91 (dd)

Epoxyalcohol **D** (11 g, 37 mmol) was dissolved in benzene (3.0 M, 12 mL). Benzoic acid (6.8 g, 56 mmol) was added to the solution, and the flask was equipped with a reflux condenser. The reaction was then heated to 75 ^oC, at which point all of the benzoic acid had dissolved. Ti(O-*i*-Pr)$_4$ (13.3 mL, 45 mmol) was then carefully added to the flask all at once. The reaction was heated at reflux for 2 hours, at which point Et_2O (100 mL) was added. Then H_2SO_4 (5 % aqueous solution, 100 mL) was added to the solution, and the biphasic mixture was stirred until each layer was transparent (typically 2 hours). The aqueous layer was extracted with EtOAc (1 x 100 mL). The organic extracts were combined and dried with $MgSO_4$. After filtration and evaporation of the volatiles,

chromatography (9:1→4:1→2:1 hexanes:EtOAc) provided diol **71** as a yellow oil (11.5 g, 77 %).

$[\alpha]_D^{23}$ = -4.7 (c 1.12, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.09 (m, 2H), 7.59 (m, 1H), 7.47 (m, 2H), 5.23 (ddd, *J* = 3.5, 4.0, 6.4 Hz, 1H), 4.52 (dd, *J* = 2.4, 3.6 Hz, 1H), 4.20 (dd, *J* = 4.0, 11.2 Hz, 1H), 4.14 (m, 3H), 2.51 (d, *J* = 2.4 Hz, 1H), 1.07 (m, 21H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.2, 133.9, 133.6, 130.4, 130.1, 129.7, 128.7, 82.0, 75.0, 74.4, 72.7, 63.5, 63.0, 18.1, 11.9; IR (KBr) 3434, 3298, 2956, 2866, 1715, 1603, 1454, 1258, 1119, 1069, 882, 687 cm^{-1}; HRMS (ESI) $[M+H^+]$ Calcd. for $C_{22}H_{35}O_5Si_1$ 407.22483, found 407.22446.

Preparation of acetonide 72



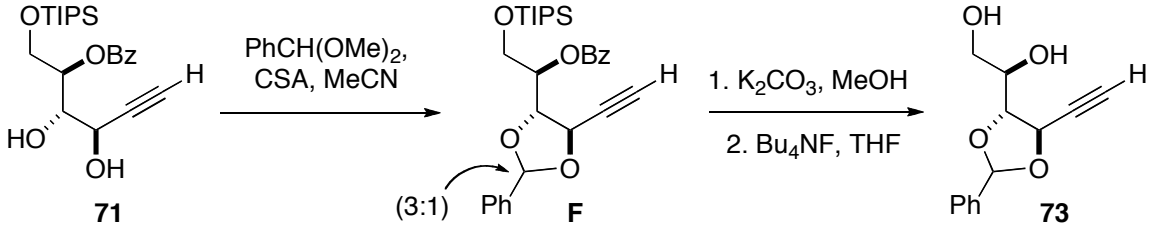
Diol **71** (9.6 g, 24 mmol) was dissolved in 2,2-dimethoxypropane (0.50 M, 48 mL) and then *p*-TSA (450 mg, 2.4 mmol) was added to the solution all at once. The reaction was stirred for one hour at r.t. and then diluted with CH_2Cl_2 (100 mL). The reaction was quenched by the addition of a saturated solution of $NaHCO_3$ (50 mL). The aqueous layer was extracted with CH_2Cl_2 (2 x 50 mL). The organic extracts were combined and dried with $MgSO_4$. After filtration, the volatiles were evaporated under reduced pressure. Chromatography (4:1 hexanes:EtOAc) gave acetonide **E** as a pale yellow oil (8.4 g, 79 %). $[\alpha]_D^{23}$ = +2.7 (c 1.2, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.07 (m, 2H), 7.57 (m, 1H), 7.44 (m, 2H), 5.34 (dd,

J = 4.8, 10.4 Hz, 1H), 4.83 (dd, *J* = 2.0, 6.8 Hz, 1H), 4.52 (dd, *J* = 6.0, 6.8 Hz, 1H), 4.07 (dd, *J* = 4.4, 10.8 Hz, 1H), 4.01 (dd, *J* = 4.4, 10.8 Hz, 1H), 2.48 (d, *J* = 2.0 Hz, 1H), 1.52 (s, 3H), 1.38 (s, 3H), 1.04 (m, 21H); ^{13}C NMR (100 MHz, $CHCl_3$) δ 165.9, 133.3, 130.1, 130.0, 128.5, 111.1, 81.6, 80.2, 74.8, 74.1, 67.5, 62.4; IR (KBr) 3310, 2943, 2868, 1724, 1464, 1383, 1269, 1109, 1068, 881 cm^{-1}; HRMS (ESI) [M+H$^+$] Calcd. for $C_{25}H_{39}O_5Si_1$ 447.25613, found 447.25568.

Acetonide **E** (8.4 g, 19 mmol) was dissolved in MeOH (0.50 M, 40 mL). K_2CO_3 (2.7 g, 19 mmol) was added all at once, and the reaction was stirred for 1 hour at r.t. The reaction was diluted with Et_2O (100 mL) and quenched with a saturated solution of NH_4Cl (150 mL). The aqueous layer was extracted with Et_2O (2 x 50 mL). The organic layers were combined and dried with $MgSO_4$. After filtration, the volatiles were evaporated under reduced pressure, and the crude oil was then re-dissolved in THF (0.50 M, 40 mL). Bu_4NF (1.0 M in THF, 19 mL, 19 mmol) was then added to the solution all at once, and the reaction was stirred at r.t. for 2 hours. The reaction was then diluted with EtOAc (100 mL) and quenched with H_2O (100 mL). The aqueous layer was extracted with EtOAc (2 x 100 mL). The organic extracts were combined, dried with $MgSO_4$, and then filtered. Chromatography (4:1→0:1 hexanes:EtOAc) provided **72** as a pale yellow oil (5.1 g, 80 %). $[\alpha]_D^{23}$ = + 9.6 (c 1.10, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.70 (dd, *J* = 2.0, 7.2 Hz, 1H), 4.15 (dd, *J* = 5.2, 7.2 Hz, 1H), 3.92 (m, 1H), 3.81 (m, 1H), 3.72 (m, 1H), 2.57 (d, *J* = 2.0 Hz, 1H), 1.51 (s, 3H), 1.44 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 110.9, 82.1, 81.6, 74.9, 71.5, 66.6, 63.3, 27.0,

26.1; IR (KBr) 3417, 3292, 2989, 2918, 1383, 1215, 1065 cm^{-1}; HRMS (ESI) [M +H^+] Calcd. for $C_9H_{15}O_4$ 187.09649, found 187.09593.

Preparation of benzylidene acetal 73



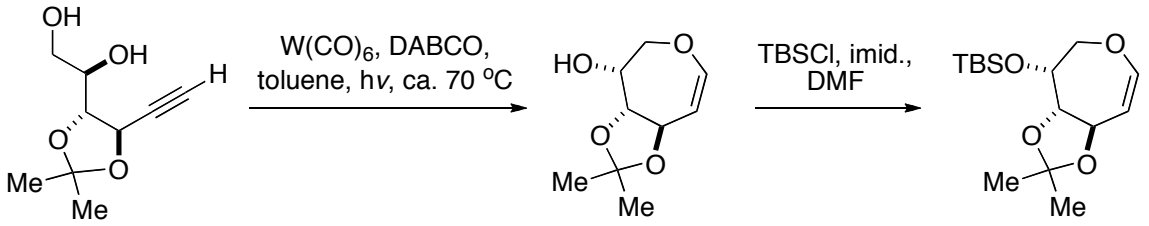
Diol **71** (10.6 g, 26 mmol) was dissolved in MeCN (0.25 M, 100 mL). Benzylidene dimethyl acetal (4.4 mL, 29 mmol) was added all at once, followed by the addition of CSA (300 mg, 1.3 mmol). The reaction was stirred at r.t. for three hours. The reaction was then diluted with CH_2Cl_2 (100 mL) and quenched by the addition of a saturated solution of $NaHCO_3$ (100 mL). The aqueous layer was extracted with EtOAc (100 mL). The organic extracts were combined and dried with $MgSO_4$. After filtration and evaporation of the volatiles, chromatography (20:1 hexanes:EtOAc) afforded benzylidene acetal **F** (3:1 mixture of diastereomers) as a colorless oil (10.0 g, 78 %).

$[\alpha]_D^{23}$ = -32.6 (c 1.00, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.08 (m, 2H), 7.29-7.26 (m, 9H), 6.04 (s, 1H), 5.39 (dd, *J* = 4.0, 8.8 Hz, 1H), 5.14 (dd, *J* = 2.0, 4.8 Hz, 1H), 4.66 (t, *J* = 4.8 Hz, 1H), 4.09 (m, 2H), 2.59 (d, *J* = 2.0 Hz, 1H), 1.05 (m, 21H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.9, 136.0, 133.5, 133.4, 130.0, 129.8, 129.7, 128.6, 128.5, 128.5, 128.4, 127.1, 126.9, 105.2, 103.8, 81.9, 81.4, 80.2, 75.3, 74.2, 74.1, 68.9, 67.7, 62.4, 62.3, 18.1, 12.1; IR (KBr) 3305, 3068, 2926, 2121, 1724, 1603, 1454, 1267, 1066, 883, 636 cm^{-1}; HRMS (ESI) [M+H^+] Calcd. for $C_{29}H_{39}O_5Si_1$ 495.25613, found 495.25551.

Benzylidene acetal **F** (10.0 g, 20 mmol) was dissolved in MeOH (0.50 M, 40 mL). K_2CO_3 (4.2 g, 30 mmol) was added all at once and the reaction was stirred for 1 hour at r.t. The reaction was diluted with Et_2O (100 mL) and quenched with a saturated solution of NH_4Cl (150 mL). The aqueous layer was extracted with Et_2O (2 x 50 mL). The organic layers were combined and dried with $MgSO_4$. After filtration, the volatiles were evaporated under reduced pressure, and the crude oil was then re-dissolved in THF (0.50 M, 40 mL). Bu_4NF (1.0 M in THF, 40 mL, 40 mmol) was then added to the solution all at once, and the reaction was stirred at r.t. for 2 hours. The reaction was then diluted with EtOAc (100 mL) and quenched with H_2O (100 mL). The aqueous layer was extracted with EtOAc (2 x 100 mL). The organic extracts were combined and dried with $MgSO_4$. After filtration and evaporation of the volatiles under reduced pressure, the resulting semi-solid was re-dissolved in a minimal amount of acetone and purified via chromatography on a short plug of silica gel (4:1→0:1 hexanes:EtOAc) to give alkynyl diol **73** as a white solid (3.5 g, 75 %).

$[\alpha]_D^{23}$ = -12.1 (c 1.30, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (m, 5H), 6.03 (s, 1H), 4.98 (dd, *J* = 2.0, 5.2 Hz, 1H), 4.25 (dd, *J* = 5.2, 10.4 Hz, 1H), 3.92 (m, 1H), 3.84 (m, 1H), 3.77 (m, 1H), 2.64 (d, *J* = 2.0 Hz, 1H), 2.48 (d, *J* = 4.8 Hz, 1H), 1.91 (m, 1H); ^{13}C NMR (100 MHz, CD_3OD) δ 137.8, 130.8, 130.6, 129.5, 129.4, 128.3, 128.2, 106.1, 105.1, 84.6, 83.7, 82.7, 76.7, 76.3, 73.8, 72.9, 69.4, 64.4; IR (KBr) 3348, 2927, 2348, 1643, 1090, 1068, 758 cm^{-1}; HRMS (ESI) [M+H$^+$] Calcd. for $C_{13}H_{15}O_4$ 235.09649, found 235.09669.

Cycloisomerization of 72 to glycal 74 and protection as silyl ether 76

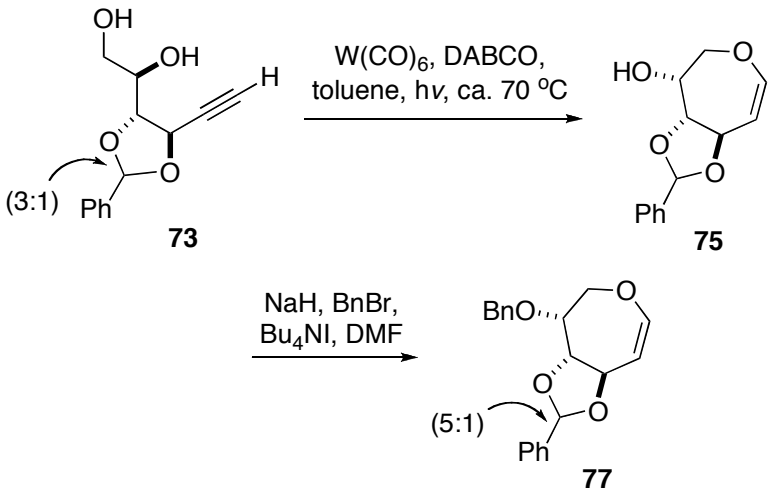


72 **74** **76**

Alkynyl diol **72** (1.7 g, 9.3 mmol) was dissolved in toluene (0.20 M, 47 mL). DABCO (2.1 g, 19 mmol) and $W(CO)_6$ (980 mg, 2.8 mmol) were sequentially added to the solution. The round bottom flask was equipped with a reflux condenser, placed into a Rayonet photoreactor, and irradiated at 350 nm (without cooling) for 12 hours. The volatiles were then evaporated, and the crude mixture containing glycal alcohol **74** was dissolved in DMF (1.0 M, 9.3 mL). TBSCl (2.1 g, 14 mmol) was added to the solution, followed by the addition of imidazole (1.3 g, 19 mmol). The reaction was stirred for 2 hours. The reaction was then diluted with CH_2Cl_2 (100 mL) and quenched with H_2O (100 mL). The aqueous layer was extracted with CH_2Cl_2 (2 x 50 mL). The organic extracts were combined and dried with $MgSO_4$. After filtration, the volatiles were evaporated under reduced pressure. Chromatography (4:1 hexanes:EtOAc) afforded glycal **76** as a colorless oil (2.2 g, 80 %) $[\alpha]_D^{23}$ = - 46.9 (c 1.50, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.36 (ddd, *J* = 1.2, 3.2, 6.4 Hz, 1H), 5.16 (ddd, *J* = 1.6, 2.8, 6.4 Hz, 1H), 4.89 (m, 1H), 4.37 (m, 1H), 4.09 (ddd, *J* = 0.80, 4.8, 12.0 Hz, 1H), 4.82 (ddd, *J* = 0.80, 3.6, 9.6 Hz, 1H), 3.64 (ddd, *J* = 0.80, 7.6, 12.4 Hz, 1H), 1.45 (s, 3H), 1.42 (s, 3H), 0.91 (s, 9H), 0.11 (s, 3H), 0.093 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.5, 109.9, 109.4, 80.4, 74.5, 71.9, 67.3, 27.5, 26.9, 25.9, 18.4, -4.25, -4.89; IR

(KBr) 2933, 2858, 1639, 1464, 1371, 1246, 1171, 1088, 951, 835, 779 cm^{-1}; HRMS (ESI) [M+H-H_2] Calcd. for $C_{15}H_{27}O_4Si_1$ 299.16731, found 299.16706.

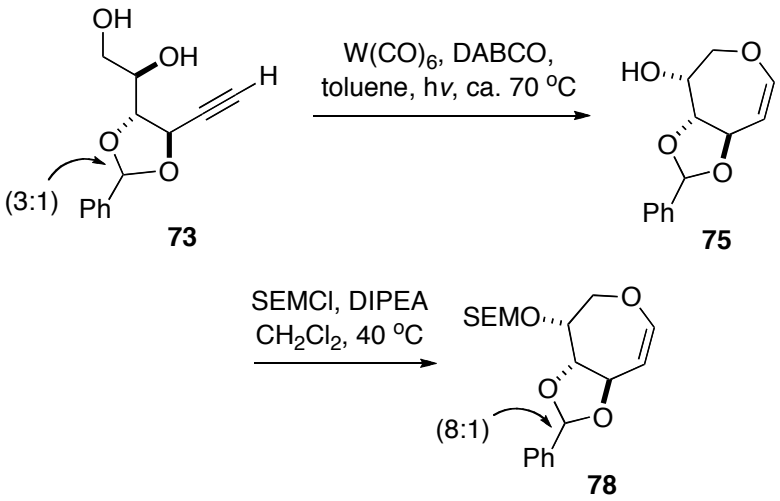
Cycloisomerization of 73 to glycal 75 and protection as benzyl ether 77



Alkynyl diol **73** (1.3 g, 5.5 mmol) was dissolved in toluene (0.20 M, 28 mL). DABCO (1.2 g, 11 mmol) and $W(CO)_6$ (280 mg, 0.83 mmol) were sequentially added to the solution. The round bottom flask was equipped with a reflux condenser, placed into a Rayonet photoreactor, and irradiated at 350 nm (without cooling) for 16 hours. The volatiles were then evaporated, and the crude mixture was dissolved in CH_2Cl_2 (150 mL). The organic layer was then washed with a saturated solution of NH_4Cl (100 mL). The aqueous layer was extracted with CH_2Cl_2 (100 mL). The organic extracts were combined and dried with $MgSO_4$. After filtration, the volatiles were evaporated under reduced pressure. The crude mixture containing glycal alcohol **75** was then dissolved in DMF (0.20 M, 28 mL). The solution was cooled to 0 °C, and NaH (60 % dispersion in mineral oil, 330 mg, 8.3 mmol) was added. The reaction was stirred for 20 minutes. Then BnBr (0.73 mL, 6.1 mmol) was added all at once, followed by the addition of Bu_4NI (10

mg). The reaction was warmed to r.t. and stirred overnight. The reaction was then diluted with Et_2O (50 mL) and quenched by the addition of a saturated solution of NH_4Cl (50 mL). The aqueous layer was then extracted with EtOAc (1 x 50 mL). The organic layers were combined and dried with $MgSO_4$. After filtration, the volatiles were evaporated under reduced pressure, and chromatography (25:1→20:1 hexanes:EtOAc) provided glycal **77** (5:1 mixture of diastereomers) as a yellow oil (1.1 g, 62 %). $[\alpha]_D^{23}$ = + 24.3 (c 1.10, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.57-7.29 (m, 10H), 6.39 (dd, *J* = 2.0, 6.4 Hz, 1H), 6.13 (s, 1H), 5.26 (dd, *J* = 2.0, 6.8 Hz, 1H), 5.09 (m, 1H), 4.95 (d, *J* = 11.6 Hz, 1H), 4.68 (d, *J* = 11.6 Hz, 1H), 4.39 (m, 1H), 4.15 (m, 2H), 3.80 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.1, 148.6, 139.2, 138.7, 138.3, 129.7, 129.4, 128.7, 128.6, 128.6, 128.1, 127.9, 127.8, 126.8, 126.8, 109.6, 108.7, 104.7, 83.2, 81.8, 74.9, 73.9, 73.8, 73.4, 72.9, 72.3, 72.2, 72.0; IR (KBr) 3292, 3153, 2927, 1460, 1406, 1068, 966, 912, 758, 698 cm^{-1}; HRMS (ESI) [M+H$^+$] Calcd. for $C_{20}H_{21}O_4$ 325.14344, found 325.14352.

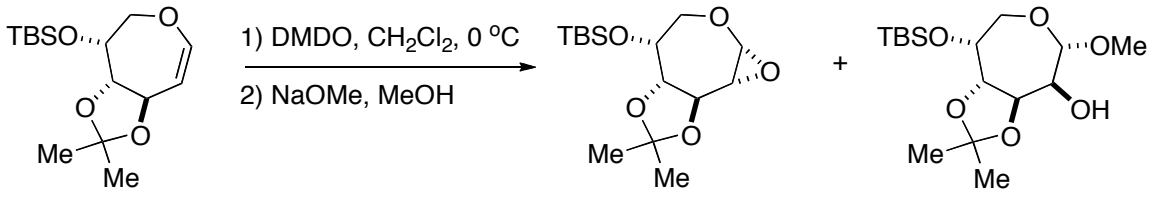
Protection of glycal alcohol 75 as trimethylsilylethoxymethyl ether 78



The glycal alcohol **75** was prepared as described above by the irradiation of alkynyl diol **73** (2.0 g, 8.5 mmol) in toluene (0.20 M, 43 mL) with DABCO (1.9 g, 17 mmol) and $W(CO)_6$ (750 mg, 2.1 mmol) for 20 hours. The crude mixture containing **75** was then dissolved in CH_2Cl_2 (1.0 M, 8.5 mL), and DIPEA (7.4 mL, 43 mmol) was added to the solution all at once. Then SEMCl (3.0 mL, 17 mmol) was carefully added to the reaction. The reaction was stirred at 40 ^oC for 3 hours. The reaction was then diluted with EtOAc (100 mL) and washed with H_2O (3 x 50 mL). The organic layer was dried with $MgSO_4$. After filtration, the volatiles were evaporated under reduced pressure, and chromatography (9:1 hexanes:EtOAc) provided glycal **78** (8:1 mixture of benzylidene acetal diastereomers) as a yellow oil (2.3 g, 75 %).

$[\alpha]_D^{23}$ = + 49.8 (c 1.00, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.53-7.36 (m, 5H), 6.41 (dd, *J* = 2.0, 6.4 Hz, 1H), 6.09 (s, 1H), 5.29 (dd, *J* = 1.6, 6.4 Hz, 1H), 5.00 (m, 1H), 4.92 (d, *J* = 7.2 Hz, 1H), 4.79 (d, *J* = 6.8 Hz, 1H), 4.56 (m, 1H), 4.19 (dd, *J* = 4.8, 12.8 Hz, 1H), 4.05 (dd, *J* = 3.6, 9.6 Hz, 1H), 3.83 (dd, *J* = 7.6, 12.4 Hz, 1H), 3.73 (m, 1H), 3.55 (m, 1H), 0.93 (m, 2H), -0.002 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.6, 139.3, 129.4, 128.6, 126.7, 110.5, 104.7, 95.4, 82.4, 72.6, 72.2, 70.8, 65.7, 18.4, -1.19; IR (KBr) 2953, 2892, 1639, 1247, 1116, 1055, 837, 697 cm^{-1}; HRMS (ESI) $[M+NH_4^+]$ Calcd. for $C_{19}H_{32}O_5N_1Si_1$ 382.20443, found 382.20462.

Epoxidation of glycal 76 and conversion to 79 and 80



76 **79** **80**

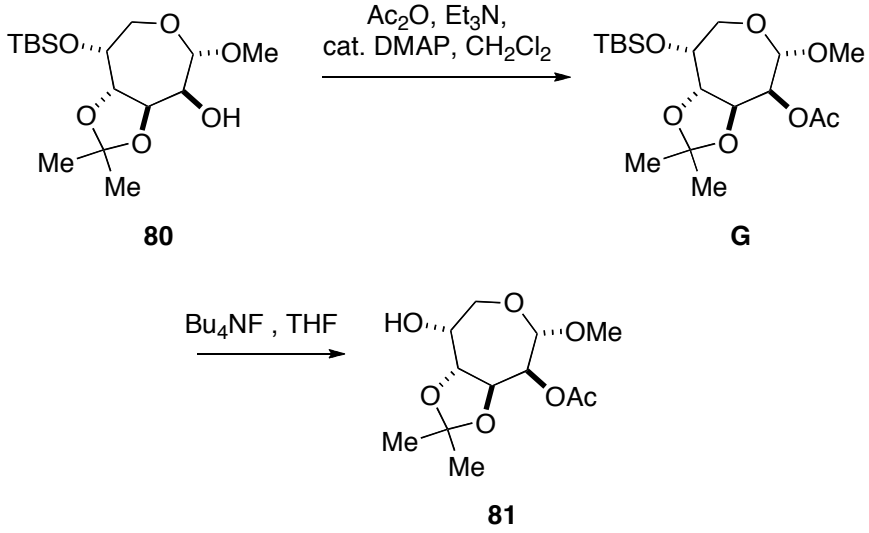
Glycal **76** (500 mg, 1.7 mmol) was dissolved in CH_2Cl_2 (0.10 M, 10 mL) and cooled to 0 °C. Then dimethyldioxirane (DMDO,[39] 34 mL, 3.4 mmol) was added to the solution, and the reaction was stirred at 0 °C for 30 minutes. The volatiles were then evaporated under reduced pressure. The crude epoxide was then dissolved in MeOH (0.10 M, 10 mL). NaOMe (0.50 M solution in MeOH, 6.8 mL, 3.4 mmol) was added all at once. The reaction was allowed to stir for 16 hours at r.t. Then the reaction was diluted with CH_2Cl_2 (100 mL) and quenched with a saturated solution of NH_4Cl (50 mL). The aqueous layer was extracted with CH_2Cl_2 (1 x 50 mL). The organics were combined and dried with $MgSO_4$. After filtration and evaporation of the volatiles under reduced pressure, chromatography (4:1→2:1 hexanes:EtOAc) gave epoxide **79** (220 mg, 40 %) and methyl glycoside **80** (230 mg, 38 %).

79:$[\alpha]_D^{23}$ = - 66.4 (c 0.50, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.75 (d, *J* = 2.0 Hz, 1H), 4.32 (dd, *J* = 4.4, 9.6 Hz, 1H), 4.18 (m, 1H), 3.82 (dd, *J* = 2.4, 10.0 Hz, 1H), 3.77 (dd, *J* = 3.2, 13.2 Hz, 1H), 3.68 (dd, *J* = 1.6, 13.6 Hz, 1H), 3.02 (dd, *J* = 2.4, 4.4 Hz, 1H), 1.46 (s, 3H), 1.41 (s, 3H), 0.91 (s, 9H), 0.088 (s, 3H), 0.080 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 111.2, 79.1, 77.8, 74.8, 68.6, 67.4, 56.3, 27.4, 27.1, 25.9, 18.4, -4.25, -4.89; IR (KBr) 3458, 2931, 1452, 1381, 1252, 1032, 831,

688 cm^{-1}; HRMS (ESI) [M+H^+] Calcd. for $C_{15}H_{29}O_5Si_1$ 317.17788, found 317.17751.

80:$[\alpha]_D^{23}$ = - 38.2 (c 0.50, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 4.49 (dd, *J* = 4.8, 9.2 Hz, 1H), 4.16 (d, *J* = 6.0 Hz, 1H), 4.14 (m, 1H), 4.12 (d, *J* = 1.6 Hz, 1H), 4.09 (m, 1H), 4.02 (dd, *J* = 2.0, 9.6 Hz, 1H), 3.59 (dd, *J* = 2.0, 13.6 Hz, 1H), 3.46 (s, 3H), 1.45 (s, 3H), 1.44 (s, 3H), 0.926 (s, 9H), 0.102 (s, 3H), 0.093 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 111.8, 109.7, 76.3, 74.9, 73.3, 70.2, 70.0, 56.3, 27.4, 27.1, 26.1, 18.4, -4.19, -4.74; IR (KBr) 3456, 2931, 1464, 1369, 1252, 1041 cm^{-1}; HRMS (ESI) [M+H^+] Calcd. for $C_{16}H_{33}O_6Si_1$ 349.20409, found 349.20425.

Preparation of D-mannoseptanoside acceptor synthon 81



80 **G** **81**

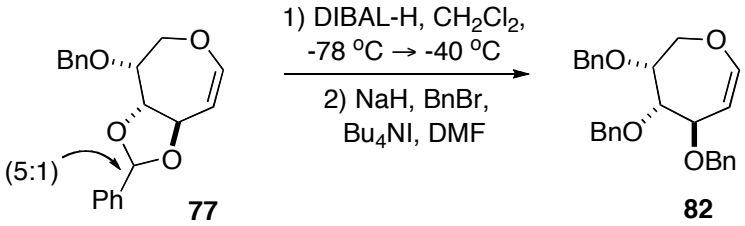
Methyl glycoside **80** (200 mg, 0.57 mmol) was dissolved in CH_2Cl_2 (0.10 M, 5.7 mL). Et_3N (0.20 mL, 1.1 mmol) and Ac_2O (0.10 mL, 1.1 mmol) were sequentially added to the solution, followed by DMAP (10 mg). The reaction was stirred for 1 hour at r.t. The reaction was diluted with CH_2Cl_2 (50 mL) and quenched by the addition of H_2O (50 mL). The aqueous layer was extracted with CH_2Cl_2 (1 x 50

mL). The organic extracts were combined and dried with $MgSO_4$. After filtration and evaporation of the volatiles under reduced pressure, chromatography (9:1→4:1 hexanes:EtOAc) gave acetate **G** (220 mg, quant.). $[\alpha]_D^{23}$ = - 17.9 (c 0.50, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 5.39 (t, *J* = 5.2 Hz, 1H), 4.56 (dd, *J* = 4.4, 9.2 Hz, 1H), 4.29 (d, *J* = 5.2 Hz, 1H), 4.18 (m, 1H), 4.09 (dd, *J* = 2.4, 9.2 Hz, 1H), 4.03 (dd, *J* = 2.8, 13.2 Hz, 1H), 3.64 (dd, *J* = 2.4, 12.8 Hz, 1H), 3.39 (s, 3H), 2.11 (s, 3H), 1.41 (s, 3H), 1.35 (s, 3H), 0.916 (s, 9H), 0.094 (s, 3H), 0.085 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.8, 109.9, 108.5, 76.8, 73.2, 72.3, 71.4, 69.3, 56.3, 27.3, 26.9, 26.1, 21.2, 18.4, -4.19, -4.74; IR (KBr) 2931, 2858, 1753, 1369, 1232, 1086, 1034, 829 cm^{-1}; HRMS (ESI) [M+H^+] Calcd. for $C_{18}H_{35}O_7Si_1$ 391.21466, found 391.21394.

Acetate **G** (220 mg, 0.57 mmol) was dissolved in THF (0.20 M, 3.0 mL). Bu_4NF (1.0 M solution in THF, 0.63 mL, 0.63 mmol) was then added all at once. The reaction was stirred at r.t. for 3 hours. The reaction was diluted with EtOAc (100 mL) and quenched by the addition of H_2O (100 mL). The aqueous layer was extracted with EtOAc (1 x 100 mL). The organic extracts were combined and dried with $MgSO_4$. After filtration and evaporation of the volatiles under reduced pressure, chromatography (2:1→1:1 hexanes:EtOAc) afforded alcohol **81** as a colorless oil (100 mg, 64 %). $[\alpha]_D^{23}$ = - 11.3 (c 1.50, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 5.42 (t, *J* = 4.0 Hz, 1H), 4.46 (dd, *J* = 5.2, 8.8 Hz, 1H), 4.36 (d, *J* = 4.0 Hz, 1H), 4.21 (m, 1H), 4.17 (d, *J* = 3.2 Hz, 1H), 4.14 (dd, *J* = 3.2, 13.2 Hz, 1H), 3.73 (dd, *J* = 3.2, 13.2 Hz, 1H), 3.39 (s, 3H), 2.48 (2, 1H), 2.12 (s, 3H), 1.44 (s, 3H), 1.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.7, 109.9, 107.3, 76.1, 72.2,

71.4, 69.0, 67.5, 56.3, 27.1, 26.9, 21.2; IR (KBr) 3533, 3435, 2966, 2918, 1730, 1443, 1373, 1234, 1171, 1078, 877 cm^{-1}; HRMS (ESI) [M+H$^+$] Calcd. for $C_{12}H_{21}O_7$ 277.12818, found 277.12809.

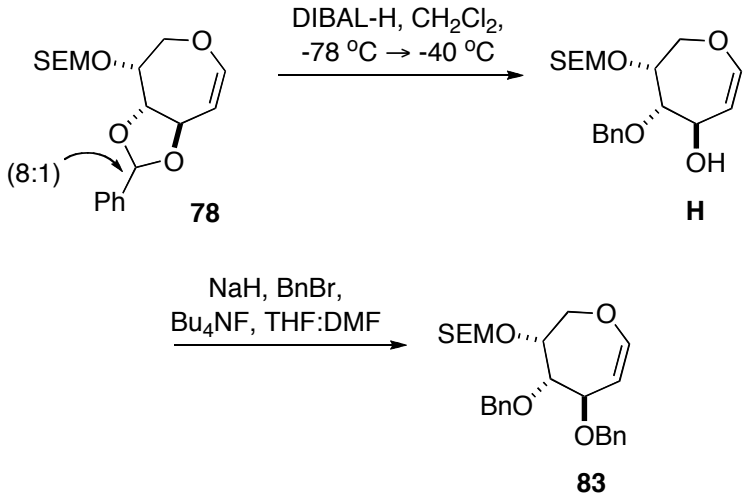
Reductive opening of benzylidene acetal 77 and protection as benzyl ether 82



Glycal **77** (1.2 g, 3.4 mmol) was dissolved in CH_2Cl_2 (0.20 M, 7.0 mL). The solution was cooled to -78 °C and DIBAL-H (1.0 M solution in CH_2Cl_2, 30 mL, 30 mmol) was added over a period of 5 minutes. The reaction was slowly warmed to -40 °C and allowed to stir for 2 hours. Then the reaction was diluted with EtOAc (100 mL) and quenched by the addition of a saturated solution of Rochelle's salt (100 mL). The resulting gelatinous mixture was allowed to stir for 2 hours until each layer was transparent and could be easily separated. The aqueous layer was extracted with EtOAc (2 x 50 mL). The organic extracts were combined and dried with $MgSO_4$. After filtration, the volatiles were evaporated under reduced pressure. The crude mixture was then dissolved in DMF (0.20 M, 20 mL) was added to the solution. The solution was cooled to 0 °C, and NaH (60 % dispersion in mineral oil, 200 mg, 4.8 mmol) was added all at once. The reaction was allowed to stir for 20 minutes. Then BnBr (0.57 mL, 4.8 mmol) was added all at once, followed by the addition of Bu_4NI (10 mg). The reaction was

allowed to warm to r.t. and stirred for 2 hours. After diluting with Et_2O (50 mL), a saturated solution of NH_4Cl (25 mL) was slowly added to quench the reaction. The aqueous layer was then extracted with EtOAc (2 x 20 mL). The organic extracts were combined and dried with $MgSO_4$. After filtration and evaporation of the volatiles under reduced pressure, chromatography (20:1→9:1 hexanes: EtOAc) gave **82** as a colorless oil (810 mg, 58%). $[\alpha]_D^{23}$ = - 59.7 (c 1.00, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (m, 15H), 6.32 (dd, *J* = 0.80, 7.6 Hz, 1H), 4.76 (dd, *J* = 4.8, 7.6 Hz, 1H), 4.72 (s, 2H), 4.69 (d, *J* = 6.4 Hz, 2H), 4.68 (d, *J* = 11.6 Hz, 1H), 4.56 (d, *J* = 12.0 Hz, 1H), 4.21 (m, 2H), 3.99 (m, 1H), 3.86 (m, 2H); ^{1}H NMR (400 MHz, C_6D_6 [for better resolution of chemical shift and coupling constant values]) 7.33-7.07 (m, 15H), 6.29 (dd, *J* = 0.80, 8.0 Hz, 1H), 4.69 (dd, *J* = 4.8, 8.0 Hz, 1H), 4.61-4.38 (m, 6H), 4.29 (ddd, *J* = 0.80, 4.8, 6.4 Hz, 1H), 4.24 (dd, *J* = 8.4, 12.0 Hz, 1H), 3.94 (ddd, *J* = 2.4, 4.4, 7.6 Hz, 1H), 3.85 (dd, *J* = 2.0, 6.4 Hz, 1H), 3.74 (dd, *J* = 1.6, 12.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.2, 138.8, 138.7, 138.4, 128.6, 128.5, 128.5, 127.9, 127.9, 127.9, 127.8, 127.8, 106.3, 80.6, 76.4, 74.5, 73.4, 72.1, 71.9, 68.6; IR (KBr) 3031, 2872, 1650, 1496, 1454, 1295, 1070, 732, 698 cm^{-1}; HRMS (ESI) [M+H$^+$] Calcd. for $C_{27}H_{29}O_4$ 417.20604, found 417.20567.

Reductive opening of benzylidene acetal 78 and protection as benzyl ether 83



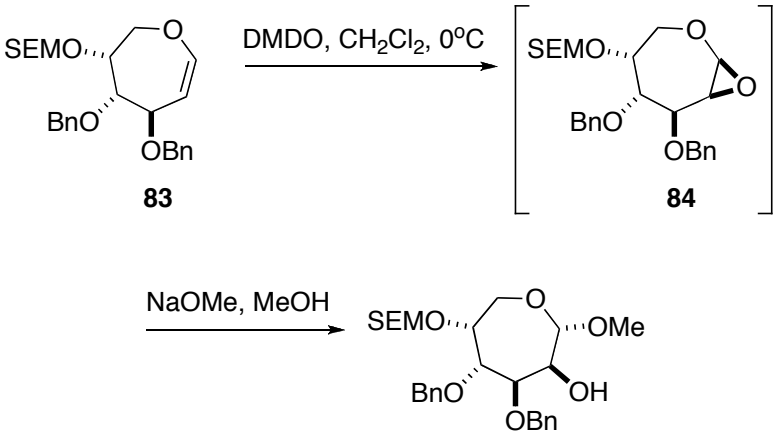
As described above, the reduction of benzylidene acetal **78** (1.3 g, 3.6 mmol) in CH_2Cl_2 (1.0 M, 4.0 mL) with DIBAL-H (1.0 M solution in CH_2Cl_2, 18 mL, 18 mmol) provided a single alcohol **H**, which was purified by chromatography (9:1→4:1 hexanes:EtOAc) to give a colorless oil (1.3 g, quant.).

$[\alpha]_D^{23}$ = - 74.4 (c 1.30, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.36 (m, 5H), 6.38 (dd, *J* = 1.6, 7.2 Hz, 1H), 4.86 (m, 3H), 4.73 (d, *J* = 11.2 Hz, 1H), 4.58 (d, *J* = 11.2 Hz, 1H), 4.34 (ddd, *J* = 1.6, 3.2, 8.4 Hz, 1H), 4.12 (m, 2H), 3.97 (dd, *J* = 2.0, 12.4 Hz, 1H), 3.90 (dd, 3H), 3.69 (m, 2H), 2.99 (d, *J* = 3.6 Hz, 1H), 0.96 (m, 2H), 0.029 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.9, 138.2, 128.7, 128.1, 108.1, 95.4, 76.3, 76.1, 73.7, 71.7, 71.6, 65.8, 18.3, -1.21; IR (KBr) 3468, 2952, 2892, 1651, 1250, 1028, 837 cm^{-1}; HRMS (ESI) [M+NH_4^+] Calcd. for $C_{19}H_{34}O_5N_1Si_1$ 384.22008, found 384.22010.

The glycal alcohol **H** (800 mg, 2.2 mmol) was dissolved in THF (1.0 M, 2.2 mL). Then DMF (0.10 mL) was added as a co-solvent. The solution was cooled to 0 ^{o}C. NaH (60 % in mineral oil, 96 mg, 2.4 mmol) was added to the solution all at once and stirred for 20 minutes. Then BnBr (0.39 mL, 3.3 mmol) was added to the solution all at once, followed by the addition of Bu_4NI (41 mg, 0.11 mmol). The reaction was allowed to warm to r.t. and stirred overnight. After diluting with Et_2O (20 mL), a saturated solution of NH_4Cl (10 mL) was slowly added to quench the reaction. The aqueous layer was then extracted with EtOAc (2 x 10 mL). The organic extracts were combined and dried with $MgSO_4$. After filtration and evaporation of the volatiles under reduced pressure, chromatography (20:1→9:1 hexanes:EtOAc) gave dibenzyl ether **83** as a colorless oil (700 mg, 70 %).

$[\alpha]_D^{23}$ = - 43.4 (c 1.30, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (m, 10H), 6.30 (dd, *J* = 1.2, 7.6 Hz, 1H), 4.82 (m, 2H), 4.74 (m, 3H), 4.65 (s, 2H), 4.27 (m, 1H), 4.18 (m, 2H), 3.84 (m, 1H), 3.72 (m, 2H), 3.62 (m, 1H), 0.939 (m, 2H), 0.013 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.7, 138.8, 138.7, 128.6, 127.9, 127.9, 127.8, 127.7, 106.9, 94.8, 81.7, 75.3, 74.4, 73.4, 72.3, 69.7, 65.6, 18.3, -1.22; IR (KBr) 3033, 2951, 2889, 1651, 1454, 1249, 1029, 836, 738, 697 cm^{-1}; HRMS (ESI) [M+Na$^+$] Calcd. for $C_{26}H_{36}O_5Na_1Si_1$ 479.22242, found 479.22230.

Synthesis of methyl glycoside 85



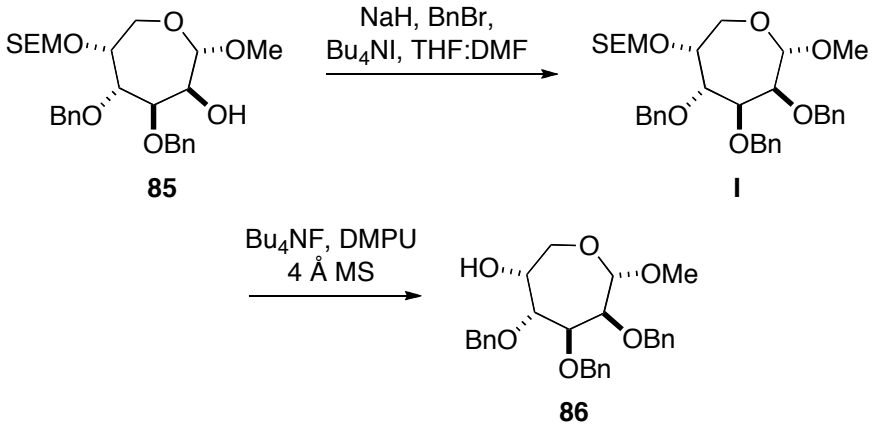
83 **84**

Glycal **83** (200 mg, 0.44 mmol) was dissolved in CH_2Cl_2 (0.10 M, 4.4 mL) and cooled to 0 °C. A freshly prepared solution of DMDO (13 mL, 1.3 mmol) was then added to the solution. After 30 minutes, the volatiles were evaporated under reduced pressure with a rotary evaporator, and placed on a high vacuum for 10 minutes to provide epoxide **84** as an oil. Epoxide intermediate **84** was dissolved in MeOH (0.10 M, 4.4 mL), and then NaOMe (0.50 M solution in MeOH, 4.4 mL, 2.2 mmol) was added all at once. The reaction was stirred at r.t. overnight. The reaction was then diluted with CH_2Cl_2 (20 mL) and quenched by the addition of a saturated solution of NH_4Cl (20 mL). The aqueous layer was extracted with EtOAc (1 x 20 mL). The organic extracts were combined and dried with $MgSO_4$. After filtration and evaporation of the volatiles under reduced pressure, chromatography (4:1→2:1 hexanes:EtOAc) gave methyl glycoside alcohol **85** as a colorless oil (160 mg, 72 %).

$[\alpha]_D^{23}$ = + 18.3 (c 1.10, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.31 (m, 10H), 4.74-4.64 (m, 5H), 4.51 (m, 2H), 4.21 (m, 1H), 4.10 (m, 1H), 4.00 (dd, *J* = 9.2, 12.8 Hz, 1H), 3.88 (dd, *J* = 2.0, 6.0 Hz, 1H), 3.82 (m, 1H), 3.62 (m, 3H), 3.42 (s,

3H), 2.14 (d, J = 5.2 Hz, 1H), 0.934 (m, 2H), 0.018 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.5, 128.7, 128.5, 127.9, 127.9, 127.8, 103.7, 94.3, 79.6, 76.8, 75.5, 74.2, 73.6, 72.8, 65.5, 62.3, 55.6, 18.3, -1.19; IR (KBr) 3460, 2953, 2895, 1454, 1248, 1093, 1028, 835, 698 cm^{-1}; HRMS (ESI) [M+NH_4^+] Calcd. for $C_{27}H_{44}O_7N_1Si_1$ 522.28816, found 522.28806.

Preparation of D-mannoseptanoside acceptor synthon 86



Methyl glycoside alcohol **85** (160 mg, 0.32 mmol) was dissolved in THF (0.32 M, 1.0 mL). Then DMF (0.10 mL) was added as a co-solvent. The solution was cooled to 0 °C, and NaH (60 % dispersion in mineral oil, 19 mg, 0.48 mmol) was added all at once and stirred for 20 minutes. BnBr (0.060 mL, 0.48 mmol) was then added all at once, followed by the addition of Bu_4NI (10 mg). The reaction was allowed to warm to r.t. and stirred overnight. After diluting with Et_2O (20 mL), a saturated solution of NH_4Cl (10 mL) was slowly added to quench the reaction. The aqueous layer was extracted with EtOAc (2 x 10 mL). The organic extracts were combined and dried with $MgSO_4$. After filtration and evaporation of the volatiles under reduced pressure, chromatography (20:1→4:1 hexanes:EtOAc) gave benzyl ether **I** as a colorless oil (160 mg, 84 %).

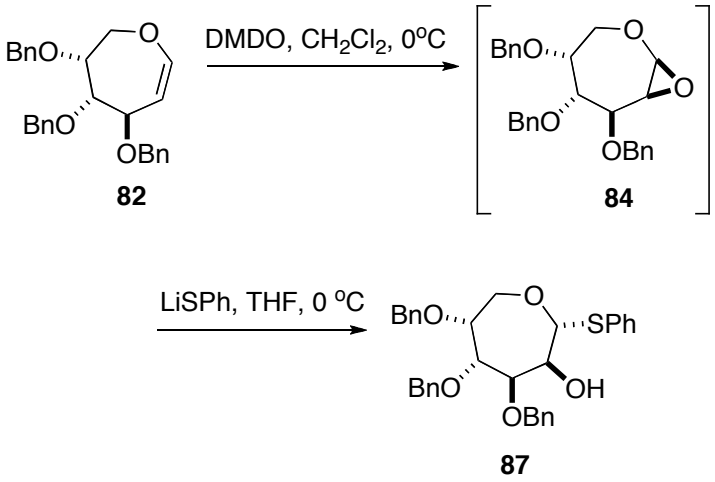
$[\alpha]_D^{23}$ = + 6.8 (c 0.53, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.35-7.15 (m, 15H), 4.77 (d, *J* = 12.8 Hz, 1H), 4.56-4.69 (m, 6H), 4.43 (d, *J* = 12.0 Hz, 1H), 4.36 (d, *J* = 12.0 Hz, 1H), 4.02 (m, 3H), 3.83 (d, *J* = 6.0 Hz, 1H), 3.72 (m, 1H), 3.61 (m, 2H), 3.49 (m, 1H), 3.43 (s, 3H), 0.940 (m, 2H), 0.020 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.9, 138.7, 128.5, 128.5, 128.0, 127.9, 127.9, 127.8, 127.7, 103.7, 94.1, 80.1, 78.3, 76.2, 75.6, 73.7, 73.3, 65.5, 60.4, 55.4, 18.3, -1.16; IR (KBr) 3031, 2936, 1454, 1249, 1059, 837, 697 cm^{-1}; HRMS (ESI) $[M+NH_4^+]$ Calcd. for $C_{34}H_{50}O_7N_1Si_1$ 612.33511, found 612.33490.

SEM-protected **I** (270 mg, 0.52 mmol) was dissolved in DMPU (0.50 M, 1.0 mL) and freshly activated 4 Å MS (750 mg, powdered) were added.[40] Then Bu_4NF (1.0 M in THF, 1.6 mL, 1.6 mmol) was added all at once. The reaction was stirred for 3 hours at r.t. Then the reaction was diluted with EtOAc (100 mL) and quenched by the addition of H_2O (50 mL). The aqueous layer was extracted with EtOAc (2 x 50 mL). The organic layers were combined and dried with $MgSO_4$. After filtration and evaporation of the volatiles under reduced pressure, chromatography (4:1→2:1 hexanes:EtOAc) afforded methyl glycoside alcohol **86** as a colorless oil (190 mg, 79 %).

$[\alpha]_D^{23}$ = - 8.9 (c 0.50, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.25-7.34 (m, 12H), 7.07 (m, 2H), 4.81 (d, *J* = 12.4 Hz, 1H), 4.69 (d, *J* = 6.8 Hz, 1H), 4.64 (d, *J* = 11.6 Hz, 1H), 4.43 (d, *J* = 12.0 Hz, 1H), 4.29 (d, *J* = 11.6 Hz, 1H), 4.20 (d, *J* = 11.6 Hz, 1H), 3.99 (m, 1H), 3.92 (dd, *J* = 6.0, 18.4 Hz, 1H), 3.73 (t, *J* = 12.4 Hz, 1H), 3.67 (t, *J* = 4.4 Hz, 1H), 3.41 (s, 3H), 2.29 (d, *J* = 10.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.8, 138.5, 137.5, 128.8, 128.6, 128.6, 128.4, 128.2, 128.2, 127.9,

127.8, 103.6, 79.5, 77.9, 77.5, 73.7, 73.4, 69.2, 62.2, 55.4; IR (KBr) 3460, 2927, 1454, 1066, 739, 698 cm^{-1}; HRMS (ESI) [$M+NH_4^+$] Calcd. for $C_{28}H_{36}O_6N_1$ 482.25371, found 482.25372.

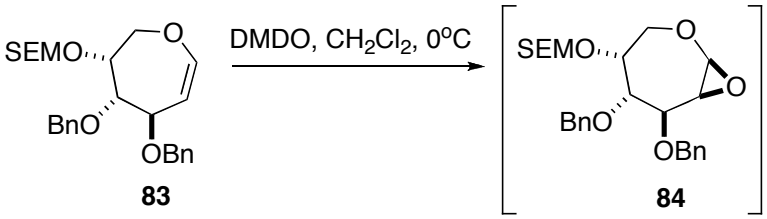
Synthesis of thioglycoside 87



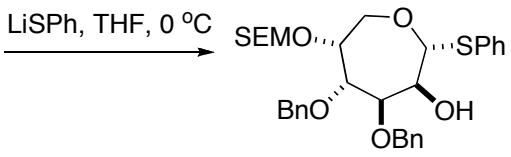
Glycal **82** (310 mg, 0.74 mmol) was dissolved in CH_2Cl_2 (0.10 M, 7.0 mL), and the solution was then cooled to 0 °C. Then DMDO (15 mL, 1.5 mmol) was slowly added, and the reaction was stirred for 30 minutes at 0 °C. Then the volatiles were evaporated under reduced pressure and the crude epoxide **84** was used directly in the next step. In a separate flask, thiophenol (0.70 mL, 7.4 mmol) was dissolved in THF (0.10 M, 7.0 mL), and the solution was cooled to 0 °C. *n*-BuLi (2.5 M solution in hexanes, 2.9 mL, 7.3 mmol) was added dropwise and subsequently stirred for 10 minutes. Then the crude epoxide **84** was dissolved in THF (2.0 mL) and slowly added to the freshly prepared lithium thiophenoxide solution at 0 °C. After 30 minutes, the reaction was quenched by the addition of H_2O (20 mL). The aqueous layer was extracted with EtOAc (1 x 20 mL). The organic extracts were combined and dried with $MgSO_4$. After filtration and

evaporation of the volatiles under reduced pressure, chromatography (9:1→4:1 hexanes:EtOAc) gave thioglycoside **87** as a pale yellow oil (240 mg, 59 %). $[\alpha]_D^{23}$ = + 87.1 (c 0.50, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.54 (m, 2H), 7.30 (m, 16H), 7.21 (m, 2H), 5.18 (d, *J* = 8.8 Hz, 1H), 4.73 (d, *J* = 11.6 Hz, 1H), 4.66 (d, *J* = 12.0 Hz, 1H), 4.58 (m, 3H), 4.49 (d, *J* = 12.0 Hz, 1H), 4.32 (ddd, *J* = 1.6, 5.2, 6.0 Hz, 1H), 4.14 (dd, *J* = 9.2, 12.8 Hz, 1H), 3.96 (dd, *J* = 1.6, 6.0 Hz, 1H), 3.90 (m, 1H), 3.82 (m, 1H), 3.65 (dd, *J* = 3.2, 12.4 Hz, 1H), 2.25 (d, *J* = 5.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.5, 138.4, 138.4, 134.5, 132.1, 129.1, 128.7, 128.6, 128.6, 128.1, 128.1, 127.9, 127.8, 127.6, 91.4, 80.3, 75.8, 74.4, 73.7, 72.1, 71.6, 62.2; IR (KBr) 3465, 3062, 3030, 2873, 1583, 1496, 1439, 1074, 739, 696 cm^{-1}; HRMS (ESI) [M+Na^+] Calcd. for $C_{33}H_{34}O_5Na_1S_1$ 565.20192, found 565.20178.

Synthesis of thioglycoside 88



83 **84**



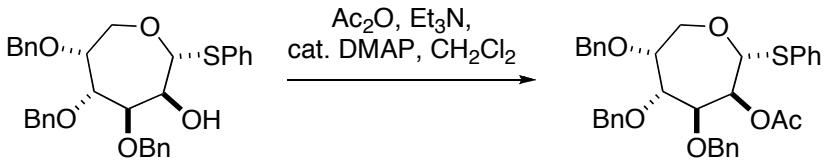
88

As described above, reaction of the glycal **83** (300 mg, 0.66 mmol) in CH_2Cl_2 (0.10 M, 6.6 mL) with DMDO (15 mL, 1.5 mmol) provided an epoxide **84** which was dissolved in THF (2.0 mL) and added to lithium thiophenoxide prepared from

thiophenol (0.68 mL, 6.6 mmol) and *n*-BuLi (2.5 M solution in hexanes, 2.6 mL, 6.5 mmol) in THF (0.10 M, 6.6 mL), to provide thioglycoside **88** as a colorless oil (170 mg, 45 %). This procedure was repeated to give sufficient material for the subsequent glycosylations.

$[\alpha]_D^{23}$ = + 78.9 (c 1.10, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.53 (m, 2H), 7.31 (m, 13H), 5.18 (d, *J* = 9.2 Hz, 1H), 4.67 (m, 5H), 4.55 (d, *J* = 12.0 Hz, 1H), 4.29 (ddd, *J* = 2.0, 5.6, 9.2, 1H), 4.13 (m, 2H), 3.98 (dd, *J* = 2.0, 6.0, 1H), 3.85 (m, 1H), 3.63 (m, 4H), 2.29 (d, *J* = 5.2 Hz, 1H), 0.930 (t, *J* = 8.8 Hz, 2H), 0.018 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.4, 138.3, 134.5, 129.1, 128.7, 128.6, 128.1, 128.0, 127.6, 94.5, 91.2, 80.2, 75.4, 74.4, 73.6, 71.6, 65.6, 63.4, 18.3, -1.17 18.3; IR (KBr) 3458, 3062, 3030, 2951, 2360, 1585, 1454, 1248, 1072, 918, 858, 740, 696 cm^{-1}; HRMS (ESI) $[M+NH_4^+]$ Calcd. for $C_{32}H_{46}O_6N_1S_1Si_1$ 600.28097, found 600.28102.

Preparation of D-mannoseptanoside donor synthon 89

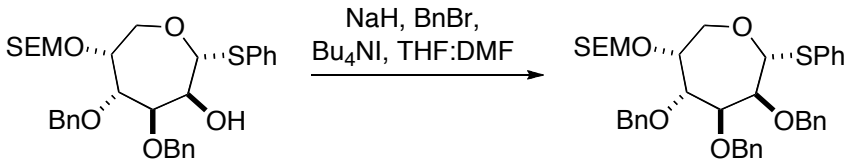


87 **89**

Thioglycoside **87** (240 mg, 0.56 mmol) was dissolved in CH_2Cl_2 (0.10 M, 5.6 mL). Pyridine (0.20 mL, 1.1 mmol) was added, followed by DMAP (10 mg) and acetic anhydride (0.10 mL, 1.1 mmol). The reaction was stirred for 30 minutes at r.t. The reaction was diluted with CH_2Cl_2 (20 mL) and quenched by the addition of H_2O (10 mL). The aqueous layer was extracted with CH_2Cl_2 (1 x 10 mL). The organic extracts were combined and filtered with $MgSO_4$. After filtration and

evaporation of the volatiles under reduced pressure, chromatography (9:1 hexanes:EtOAc) gave acetate **89** as a colorless oil (180 mg, 55 %). $[\alpha]_D^{23}$ = + 54.4 (c 1.00, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.50 (m, 2H), 7.30 (m, 16H), 7.15 (m, 2H), 5.68 (d, *J* = 9.2 Hz, 1H), 5.33 (d, *J* = 9.6 Hz, 1H), 4.72 (d, *J* = 12.0 Hz, 1H), 4.66 (d, *J* = 12.8 Hz, 1H), 4.59 (d, *J* = 12.0, 1H), 4.48 (m, 2H), 4.26 (dd, *J* = 9.6, 12.4 Hz, 1H), 3.90 (m, 1H), 3.78 (m, 2H), 3.65 (dd, *J* = 2.8, 12.4 Hz, 1H), 2.01 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.7, 138.4, 138.3, 137.8, 135.0, 131.7, 129.0, 128.6, 128.5, 128.3, 128.2, 128.1, 127.9, 127.9, 127.8, 127.3, 87.3, 78.5, 74.2, 73.7, 73.4, 72.7, 71.9, 60.9; IR (KBr) 3062, 3030, 2893, 1745, 1454, 1369, 1228, 1076, 739, 698 cm^{-1}; HRMS (ESI) $[M+NH_4^+]$ Calcd. for $C_{35}H_{40}O_6N_1S_1$ 602.25709, found 602.25767.

Preparation of D-mannoseptanoside donor synthon 90



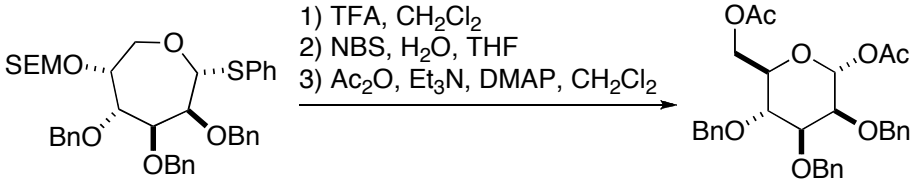
88 **90**

Thioglycoside alcohol **88** (520 mg, 0.89 mmol) was dissolved in THF (0.10 M, 8.9 mL). Then DMF (0.10 mL) was added as a co-solvent. The solution was cooled to 0 °C, and NaH (60 % dispersion in mineral oil, 52 mg, 0.48 mmol) was added all at once and stirred for 20 minutes. BnBr (0.15mL, 1.3 mmol) was then added all at once, followed by the addition of Bu_4NI (10 mg). The reaction was allowed to warm to r.t. and stirred overnight. After diluting with Et_2O (20 mL), a saturated solution of NH_4Cl (10 mL) was slowly added to quench the reaction. The aqueous layer was extracted with EtOAc (2 x 15 mL). The organic extracts were

combined and dried with $MgSO_4$. After filtration and evaporation of the volatiles under reduced pressure, chromatography (20:1→4:1 hexanes:EtOAc) gave **90** as a colorless oil (480 mg, 80 %).

$[\alpha]_D^{23}$ = + 55.4 (c 0.60, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.53 (m, 2H), 7.29 (m, 18H), 5.38 (d, *J* = 8.8 Hz, 1H), 4.75 (d, *J* = 12.4 Hz, 1H), 4.64 (m, 5H), 4.41 (dd, *J* = 8.0, 12.0 Hz, 1H), 4.13 (m, 3H), 3.88 (d, *J* = 6.0, 1H), 3.77 (m, 1H), 3.61 (m, 3H), 0.930 (dd, *J* = 7.2, 10.0 Hz, 2H), 0.031 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.6, 138.5, 138.2, 135.4, 131.8, 128.9, 128.6, 128.5, 128.5, 128.1, 128.0, 127.9, 127.9, 127.8, 127.0, 94.2, 89.0, 80.2, 77.8, 76.4, 75.6, 74.0, 73.8, 73.6, 65.6, 61.6, 18.3, -1.16; IR (KBr) 3030, 2951, 2889, 1583, 1454, 1365, 1248, 1074, 837, 741, 698 cm^{-1}; HRMS (ESI) [$M+NH_4^+$] Calcd. for $C_{39}H_{52}O_6N_1S_1Si_1$ 690.32792, found 690.32855.

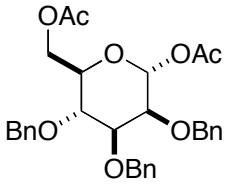
The stereochemistry of mannoseptanoside **90** was confirmed by conversion into the known mannopyranoside **J**:



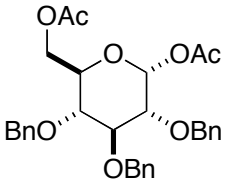
90 **synthetic J**

Thioglycoside **90** (130 mg, 0.19 mmol) was dissolved in CH_2Cl_2 (0.10 M, 2.0 mL). TFA (0.10 mL, 1.3 mmol) was added all at once. The reaction was stirred for 20 min. at r.t, at which point TLC indicated consumption of the starting material. A saturated solution of $NaHCO_3$ (2 mL) was added, and the mixture was stirred until elution of CO_2 stopped. The aqueous layer was then extracted with Et_2O (3

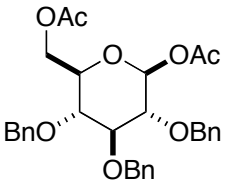
x 2 mL). The combined organic layers were dried with $MgSO_4$ and filtered. After removal of the volatiles under reduced pressure, the crude material was dissolved in a mixture of THF:H_2O (1:1) (0.10 M, 2.0 mL) with vigorous stirring. NBS (21 mg, 0.12 mmol) was added all at once. The solution immediately turned orange-brown in color. After 5 minutes, reaction mixture was colorless, and TLC indicated consumption of the starting material. The reaction was diluted with H_2O (2 mL) and EtOAc (2 mL). After the layers were separated, the aqueous layer was extracted with EtOAc (1 x 2 mL). The organic extracts were combined and dried with $MgSO_4$. After filtration, the volatiles were removed under reduced pressure. The crude material was then dissolved in CH_2Cl_2 (1.0 mL). Et_3N (0.04 mL, 0.29 mmol and Ac_2O (0.03 mL, 0.29 mmol) were sequentially added to the reaction mixture. DMAP (1 mg) was then added. After 10 minutes of stirring, TLC indicated the consumption of the starting material. The reaction was diluted with CH_2Cl_2 (2 mL) and quenched by the addition of a saturated solution of NH_4Cl (2 mL). After separation of the layers, the aqueous layer was extracted with CH_2Cl_2 (2 x 2 mL). The organic extracts were combined and dried with $MgSO_4$. After filtration, the volatiles were removed under reduced pressure. The crude material was loaded onto a prep TLC plate (1,000 microns, Analtech). The plate was developed using 1:1 hexanes:EtOAc. **Synthetic J,** α-1,6-diacetyl-2,3,4-tri-*O*-benzyl-D-mannopyranose, was isolated as a white solid (21 mg, 21%), for spectroscopic comparison with literature spectra for α-1,6-diacetyl-2,3,4-tri-*O*-benzyl-D-mannopyranose (**J**),[41] as well as α- and β-anomers of 1,6-diacetyl-2,3,4-tri-*O*-benzyl-D-glucopyranose (**K** and **L**).[42]



J



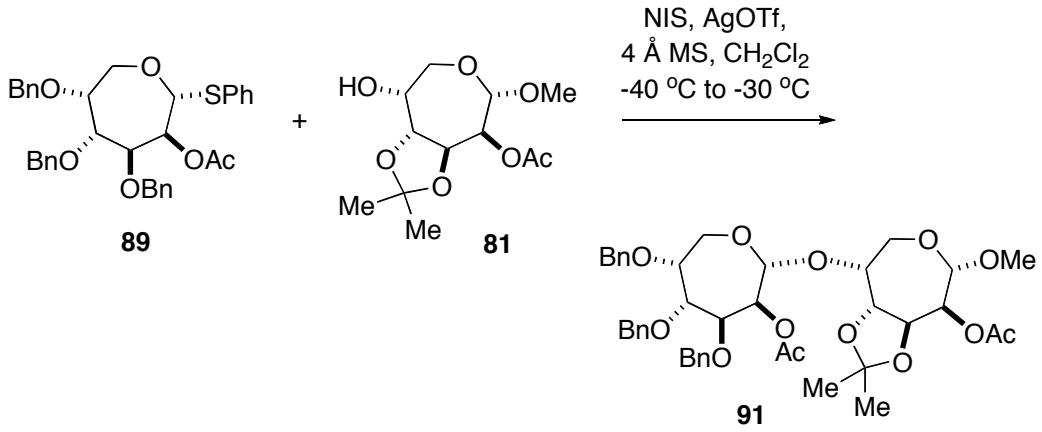
K



L

	Synthetic J	**J** (ref. 2)	**K** (ref. 3)	**L** (ref. 3)
$[\alpha]_D^{23}$	+ 29.5 (c 1.05, $CHCl_3$)	+ 31.3 (c 1.0, $CHCl_3$)	+ 58.2 (c 0.89, $CHCl_3$)	+ 25.3 (c 0.225, $CHCl_3$)
H	(ppm)	(ppm)	(ppm)	(ppm)
1	6.19 (d, *J*=1.6 Hz, 1H)	6.19 (d, *J*=2.0 Hz, 1H)	6.25 (d, J=3.6 Hz, 1H)	5.85 (d, J=8.1 Hz, 1H)
2	3.75 (dd, J=2.4 Hz, 1H)	3.75 (dd, *J*=2.9 Hz, 1H)	3.60 (dd, J=3.6, 9.5 Hz, 1H)	3.50 (dd, J=8.1, 9.0 Hz, 1H)
3	3.88 (m,2H)	3.88 (m,2H)	3.90 (dd, J=9.0, 9.5 Hz, 1H)	3.68 (dd, J=8.8, 9.0 Hz, 1H)
4	3.99 (a-t, J=9.6 Hz, 1H)	3.99 (a-t, *J*=9.5 Hz, 1H)	3.50 (dd, J=9.0, 10.0 Hz, 1H)	3.49 (dd, J=8.8, 9.8 Hz, 1H)
5	3.88 (m, 2H)	3.88 (m, 2H)	3.85 (ddd, J=2.4, 3.9, 10.0 Hz, 1H)	3.58 (ddd, J=2.2, 4.4, 9.8 Hz, 1H)
6	4.33 (m, 2H)	4.33 (m, 2H)	4.17 (dd, J=2.4, 12.2 Hz, 1H)	4.16 (dd, J=4.4, 12.2 Hz, 1H)
6'	4.33 (m, 2H)	4.33 (m, 2H)	4.21 (dd, J=3.9, 12.2 Hz, 1H)	4.21 (dd, J=2.2, 12.2 Hz, 1H)
CH_2Ph	4.61 (m, 3H)	4.60 (m, 3H)	4.50 (d, J=11.0 Hz, 1H)	4.49 (d, J=10.8 Hz, 1H)
CH_2Ph			4.57 (d, *J*=11.3 Hz, 1H)	4.68 (d, *J*=11.2 Hz, 1H)
CH_2Ph			4.64 (d, *J*=11.3 Hz, 1H)	4.71 (d, *J*=11.2 Hz, 1H)
CH_2Ph	4.73 (d, *J*=12.4 Hz, 1H)	4.73 (d, *J*=12.1 Hz, 1H)	4.76 (d, *J*=10.7 Hz, 1H)	4.75 (d, *J*=10.7 Hz, 1H)
CH_2Ph	4.78 (d, J=12.4 Hz, 1H)	4.78 (d, *J*=12.1 Hz, 1H)	4.82 (d, *J*=10.7 Hz, 1H)	4.78 (d, *J*=10.7 Hz, 1H)
CH_2Ph	4.96 (d, J=10.4 Hz, 1H)	4.96 (d, *J*=10.6 Hz, 1H)	4.92 (d, J=11.0 Hz, 1H)	4.85 (d, J=10.8 Hz, 1H)
Aryl	7.31-7.42 (m, 15H)	7.29-7.42 (m, 15H)	7.19-7.29 (m, 15H)	7.17-7.28 (m,15H)
MeC=O	2.04 (s, 3H)	2.04 (s, 3H)	1.96 (s, 3H)	1.96 (s, 3H)
MeC=O	2.07 (s, 3H)	2.07 (s, 3H)	2.08 (s, 3H)	1.98 (s,3H)

Synthesis and thermal ellipsoid of disaccharide 91



Thioglycoside **89** (160 mg, 0.27 mmol) and methyl glycoside **81** (85 mg, 0.30 mmol) were dissolved in CH_2Cl_2 (0.10 M, 2.7 mL). 4 Å MS (400 mg, powdered) were then added to the solution. The solution was cooled to -40 °C. Then NIS (76 mg, 0.34 mmol) and AgOTf (21 mg, 0.08 mmol) were simultaneously added to the solution. The reaction was allowed to warm to -30 °C, at which point the reaction became magenta in color. Upon the color change, TLC indicated the completion of the reaction. The reaction was quenched by the addition of Et_3N (1.0 mL), which caused an immediate color change to yellow. The mixture was filtered through celite, and the volatiles were evaporated under reduced pressure. Chromatography (4:1 hexanes:EtOAc) gave disaccharide **91** as white crystalline needles (130 mg, 63 %). mp 76 - 79 °C; $[\alpha]_D^{23}$ = + 44.6 (c 2.50, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.32 (m, 13H), 7.16 (m, 2H), 5.58 (d, *J* = 7.6 Hz, 1H), 5.42 (t, *J* = 4.8 Hz, 1H), 5.25 (d, *J* = 7.2 Hz, 1H), 4.72 (d, *J* = 11.6 Hz, 1H), 4.66 (d, *J* = 12.4 Hz, 1H), 4.56 (d, *J* = 12.0 Hz, 1H), 4.49 (d, *J* = 12.0 Hz, 1H), 4.46 (m, 1H), 4.31 (m, 2H), 4.22 (dd, *J* = 2.4, 9.2 Hz, 1H), 4.17 (dd, *J* = 2.0, 12.0 Hz, 1H), 4.12 (dd, *J* = 3.2, 13.6 Hz, 1H), 3.82 (m, 3H), 3.69 (dd, *J* = 3.2, 13.6 Hz, 1H), 3.56 (m,

1H), 3.38 (s, 3H), 2.11 (s, 3H), 1.96 (s, 3H) 1.45 (s, 3H), 1.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.9, 169.7, 138.4, 138.4, 137.9, 128.6, 128.5, 128.3, 128.1, 128.1, 127.9, 127.8, 109.8, 107.9, 100.1, 77.1, 76.8, 74.3, 74.2, 73.5, 73.2, 72.9, 71.8, 71.4, 71.4, 70.7, 60.2, 56.3, 26.9, 26.5, 21.4, 21.2; IR (KBr) 2926, 2856, 1747, 1371, 1232, 1086, 1028, 739, 698 cm^{-1}; HRMS (ESI) [M $+NH_4^+$] Calcd. for $C_{41}H_{54}O_{13}N_1$ 768.35897, found 768.35737.

Slow recrystallization of compound **91** from a mixture of hexanes and ether provided crystals suitable for structural characterization by X-ray crystallography, resulting in the thermal ellipsoid diagram below:

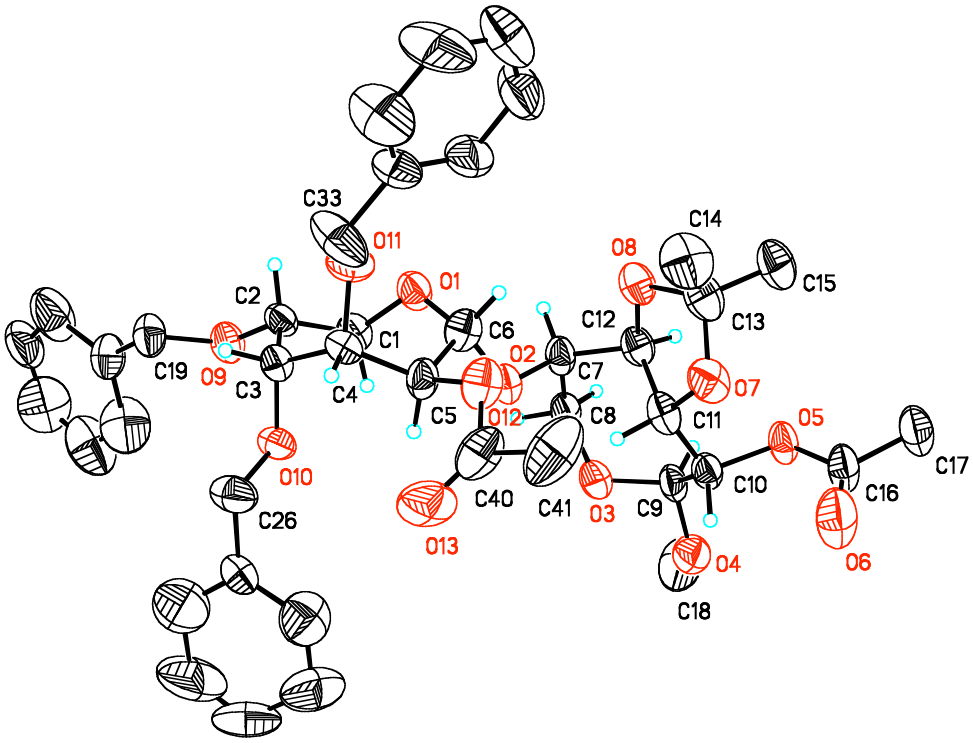


Table 2. Crystal data and structure refinement for compound **91**

Identification code	b103_3_29	
Empirical formula	C41.25 H50 O13.13	
Formula weight	755.81	
Temperature	173(2) K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	C2	
Unit cell dimensions	a = 39.015(3) Å	α= 90°.
	b = 9.2033(9) Å	β= 101.259(6)°.
	c = 23.6697(19) Å	γ = 90°.
Volume	8335.4(13) $Å^3$	
Z	8	
Density (calculated)	1.205 Mg/m^3	
Absorption coefficient	0.742 mm^{-1}	
F(000)	3220	
Crystal size	0.66 x 0.06 x 0.03 mm^3	
Theta range for data collection	2.31 to 66.10°.	
Index ranges	-44<=h<=45, -10<=k<=6, -26<=l<=23	
Reflections collected	13811	
Independent reflections	8386 [R(int) = 0.0794]	
Completeness to theta = 66.10°	82.9 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9781 and 0.6402	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	8386 / 1 / 984	
Goodness-of-fit on F^2	1.114	
Final R indices [I>2sigma(I)]	R1 = 0.0935, wR2 = 0.2368	
R indices (all data)	R1 = 0.1392, wR2 = 0.2752	
Absolute structure parameter	-0.2(4)	
Extinction coefficient	0.00047(8)	
Largest diff. peak and hole	0.667 and -0.364 $e.Å^{-3}$	

Table 3. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for compound **91** (b103_3_29). U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor

	x	y	z	U(eq)
C(1)	7152(2)	6024(10)	9105(4)	43(2)
C(2)	7410(2)	7089(9)	9468(4)	38(2)
C(3)	7255(2)	8582(9)	9531(3)	36(2)
C(4)	6921(2)	8611(11)	9782(3)	43(2)
C(5)	6607(2)	7945(10)	9372(4)	43(2)
C(6)	6577(2)	6302(11)	9360(4)	48(2)
C(7)	6237(2)	4564(10)	8689(4)	43(2)
C(8)	6205(2)	4307(10)	8057(4)	41(2)
C(9)	5595(2)	4784(10)	7631(3)	42(2)
C(10)	5400(2)	5498(10)	8056(4)	41(2)
C(11)	5626(2)	5715(10)	8637(3)	44(2)
C(12)	5873(2)	4443(11)	8847(3)	43(2)
C(13)	5561(3)	4975(12)	9557(4)	57(3)
C(14)	5606(3)	5818(16)	10102(4)	73(3)
C(15)	5323(3)	3669(14)	9547(5)	62(3)
C(16)	4797(2)	5038(11)	8130(5)	54(2)
C(17)	4545(3)	3883(14)	8218(5)	65(3)
C(18)	5527(3)	4380(20)	6626(4)	87(5)
C(19)	7987(2)	7996(12)	9428(4)	50(2)
C(20)	8258(2)	7745(13)	9070(4)	55(2)
C(21)	8603(3)	7404(16)	9307(8)	100(5)
C(22)	8834(3)	7073(17)	8842(7)	87(4)
C(23)	8714(5)	7300(20)	8302(8)	103(5)
C(24)	8394(5)	7750(20)	8093(7)	102(5)
C(25)	8154(4)	7960(20)	8454(5)	93(4)
C(26)	7212(3)	10759(11)	8953(4)	57(3)
C(27)	7135(2)	11228(11)	8328(4)	48(2)
C(28)	7396(4)	11562(18)	8019(7)	101(5)
C(29)	7302(5)	11970(20)	7423(7)	118(6)
C(30)	7003(5)	12121(15)	7161(5)	87(4)
C(31)	6710(4)	11743(19)	7473(6)	98(5)
C(32)	6796(3)	11342(18)	8042(5)	82(4)
C(33)	6925(4)	8838(15)	10813(5)	83(4)
C(34)	6753(3)	8027(12)	11234(4)	52(2)
C(35)	6778(4)	8497(16)	11779(5)	92(4)

C(36)	6614(5)	7802(19)	12172(5)	98(5)
C(37)	6426(4)	6622(18)	12017(6)	88(4)
C(38)	6388(3)	6169(19)	11483(5)	89(5)
C(39)	6542(3)	6861(15)	11084(4)	66(3)
C(40)	6154(3)	9744(15)	9364(5)	64(3)
C(41)	5810(3)	9930(20)	9551(6)	99(5)
C(1B)	3310(3)	826(12)	6626(4)	54(2)
C(2B)	3043(2)	1754(10)	6202(4)	45(2)
C(3B)	3168(2)	3282(10)	6121(3)	40(2)
C(4B)	3521(2)	3369(10)	5937(3)	40(2)
C(5B)	3823(2)	2877(10)	6424(4)	41(2)
C(6B)	3880(2)	1239(11)	6444(4)	47(2)
C(7B)	4238(2)	-414(10)	7122(4)	45(2)
C(8B)	4260(2)	-655(11)	7769(4)	52(2)
C(9B)	4853(2)	-207(11)	8217(4)	48(2)
C(10B)	5068(2)	485(9)	7809(3)	37(2)
C(11B)	4839(2)	729(10)	7209(3)	42(2)
C(12B)	4591(2)	-524(10)	6974(3)	41(2)
C(13B)	4901(3)	55(14)	6283(4)	64(3)
C(14B)	4837(4)	1135(19)	5760(5)	91(4)
C(15B)	5147(4)	-1228(17)	6227(7)	100(5)
C(16B)	4874(3)	-580(20)	9186(5)	109(6)
C(17B)	5664(2)	30(11)	7741(4)	49(2)
C(18B)	5907(3)	-1172(11)	7667(5)	58(3)
C(19B)	2473(3)	787(17)	6272(6)	83(4)
C(20B)	2174(2)	1115(13)	6594(6)	110(6)
C(21B)	1847(3)	560(15)	6351(7)	169(10)
C(22B)	1565(2)	791(18)	6618(9)	222(18)
C(23B)	1609(4)	1580(20)	7129(9)	300(30)
C(24B)	1936(5)	2133(19)	7372(7)	320(30)
C(25B)	2219(3)	1902(17)	7104(6)	169(12)
C(26B)	2908(3)	5028(12)	6683(4)	55(3)
C(27B)	2829(2)	6115(11)	6203(4)	47(2)
C(28B)	2486(3)	6244(13)	5869(4)	60(3)
C(29B)	2408(4)	7238(14)	5408(4)	72(3)
C(30B)	2670(4)	8018(15)	5253(5)	90(5)
C(31B)	3014(4)	7937(14)	5587(5)	80(3)
C(32B)	3084(3)	6952(11)	6049(4)	61(3)
C(33B)	3719(7)	2960(30)	5073(6)	203(15)
C(34B)	3736(4)	1786(18)	4627(6)	91(4)

C(35B)	3495(4)	550(20)	4552(6)	104(5)
C(36B)	3501(5)	-440(20)	4091(8)	118(6)
C(37B)	3723(6)	-270(30)	3702(8)	140(8)
C(38B)	3962(5)	980(30)	3754(8)	140(8)
C(39B)	3979(5)	1920(30)	4210(7)	130(7)
C(40B)	4234(3)	4842(13)	6569(4)	59(3)
C(41B)	4576(3)	5330(17)	6475(6)	84(4)
C(1S)	4189(10)	7000(50)	4987(16)	56(9)
C(2S)	3815(8)	6120(40)	4948(12)	35(7)
O(1)	6901(1)	5539(7)	9440(3)	49(2)
O(2)	6375(1)	6000(7)	8797(2)	44(1)
O(3)	5947(1)	5282(7)	7715(2)	44(1)
O(4)	5431(2)	5226(9)	7067(3)	57(2)
O(5)	5118(1)	4461(7)	8102(3)	47(2)
O(6)	4737(2)	6294(10)	8065(5)	90(3)
O(7)	5428(2)	5921(8)	9076(3)	53(2)
O(8)	5902(2)	4546(8)	9472(2)	50(2)
O(9)	7691(1)	7106(7)	9176(2)	46(1)
O(10)	7182(2)	9218(7)	8965(2)	42(1)
O(11)	6974(2)	7893(8)	10334(2)	52(2)
O(12)	6284(2)	8391(8)	9551(3)	56(2)
O(13)	6307(2)	10568(10)	9104(4)	80(2)
O(1B)	3580(2)	384(7)	6348(3)	53(2)
O(2B)	4085(2)	1015(7)	7007(2)	49(2)
O(3B)	4502(1)	321(7)	8102(2)	44(1)
O(4B)	5013(2)	246(11)	8772(2)	72(2)
O(5B)	5347(1)	-554(7)	7776(2)	45(1)
O(6B)	5724(2)	1263(8)	7773(4)	76(2)
O(7B)	5060(2)	875(8)	6784(2)	56(2)
O(8B)	4573(2)	-426(8)	6369(3)	55(2)
O(9B)	2724(2)	1908(8)	6423(3)	58(2)
O(10B)	3202(1)	4119(7)	6635(2)	44(2)
O(11B)	3506(2)	2580(8)	5416(2)	55(2)
O(12B)	4148(1)	3487(7)	6347(3)	49(2)
O(13B)	4036(2)	5536(10)	6800(4)	80(2)
O(1S)	4402(8)	6080(40)	4937(12)	71(8)

Table 4. Bond lengths [Å] and angles [°] for compound **91** (b103_3_29)

C(1)-O(1)	1.446(11)	C(19)-C(20)	1.494(13)
C(1)-C(2)	1.541(12)	C(20)-C(21)	1.389(15)
C(2)-O(9)	1.406(10)	C(20)-C(25)	1.450(16)
C(2)-C(3)	1.519(12)	C(21)-C(22)	1.58(2)
C(3)-O(10)	1.439(10)	C(22)-C(23)	1.290(18)
C(3)-C(4)	1.533(12)	C(23)-C(24)	1.32(2)
C(4)-O(11)	1.442(10)	C(24)-C(25)	1.40(2)
C(4)-C(5)	1.535(12)	C(26)-O(10)	1.424(12)
C(5)-O(12)	1.462(11)	C(26)-C(27)	1.514(13)
C(5)-C(6)	1.516(14)	C(27)-C(32)	1.366(14)
C(6)-O(1)	1.426(11)	C(27)-C(28)	1.401(19)
C(6)-O(2)	1.436(10)	C(28)-C(29)	1.44(2)
C(7)-O(2)	1.431(11)	C(29)-C(30)	1.22(2)
C(7)-C(8)	1.495(12)	C(30)-C(31)	1.52(2)
C(7)-C(12)	1.541(13)	C(31)-C(32)	1.374(17)
C(8)-O(3)	1.468(10)	C(33)-O(11)	1.471(14)
C(9)-O(3)	1.422(10)	C(33)-C(34)	1.503(15)
C(9)-O(4)	1.422(10)	C(34)-C(35)	1.346(14)
C(9)-C(10)	1.525(12)	C(34)-C(39)	1.357(16)
C(10)-O(5)	1.476(11)	C(35)-C(36)	1.385(19)
C(10)-C(11)	1.495(11)	C(36)-C(37)	1.32(2)
C(11)-O(7)	1.424(10)	C(37)-C(38)	1.313(18)
C(11)-C(12)	1.535(13)	C(38)-C(39)	1.369(16)
C(12)-O(8)	1.465(10)	C(40)-O(13)	1.206(15)
C(13)-O(8)	1.440(12)	C(40)-O(12)	1.385(15)
C(13)-O(7)	1.446(12)	C(40)-C(41)	1.500(18)
C(13)-C(14)	1.487(15)	C(1B)-O(1B)	1.407(12)
C(13)-C(15)	1.514(16)	C(1B)-C(2B)	1.554(13)
C(16)-O(6)	1.183(14)	C(2B)-O(9B)	1.448(11)
C(16)-O(5)	1.375(12)	C(2B)-C(3B)	1.514(13)
C(16)-C(17)	1.489(15)	C(3B)-O(10B)	1.423(10)
C(18)-O(4)	1.409(15)	C(3B)-C(4B)	1.525(12)
C(19)-O(9)	1.447(11)	C(4B)-O(11B)	1.422(11)

C(4B)-C(5B)	1.546(11)	C(27B)-C(28B)	1.421(12)
C(5B)-O(12B)	1.431(11)	C(28B)-C(29B)	1.410(16)
C(5B)-C(6B)	1.523(13)	C(29B)-C(30B)	1.36(2)
C(6B)-O(1B)	1.391(11)	C(30B)-C(31B)	1.422(18)
C(6B)-O(2B)	1.429(10)	C(31B)-C(32B)	1.406(16)
C(7B)-O(2B)	1.447(11)	C(33B)-O(11B)	1.319(17)
C(7B)-C(12B)	1.492(13)	C(33B)-C(34B)	1.52(3)
C(7B)-C(8B)	1.534(13)	C(34B)-C(35B)	1.47(2)
C(8B)-O(3B)	1.425(11)	C(34B)-C(39B)	1.50(2)
C(9B)-O(4B)	1.405(10)	C(35B)-C(36B)	1.43(2)
C(9B)-O(3B)	1.426(10)	C(36B)-C(37B)	1.39(3)
C(9B)-C(10B)	1.536(13)	C(37B)-C(38B)	1.47(3)
C(10B)-O(5B)	1.461(10)	C(38B)-C(39B)	1.37(3)
C(10B)-C(11B)	1.539(11)	C(40B)-O(13B)	1.211(13)
C(11B)-O(7B)	1.455(10)	C(40B)-O(12B)	1.370(13)
C(11B)-C(12B)	1.537(12)	C(40B)-C(41B)	1.467(15)
C(12B)-O(8B)	1.423(10)	C(1S)-O(1S)	1.21(5)
C(13B)-O(8B)	1.409(14)	C(1S)-C(2S)	1.65(5)
C(13B)-O(7B)	1.440(12)		
C(13B)-C(15B)	1.541(19)	O(1)-C(1)-C(2)	109.1(7)
C(13B)-C(14B)	1.569(18)	O(9)-C(2)-C(3)	113.6(7)
C(16B)-O(4B)	1.427(17)	O(9)-C(2)-C(1)	102.7(6)
C(17B)-O(6B)	1.159(13)	C(3)-C(2)-C(1)	113.7(7)
C(17B)-O(5B)	1.369(11)	O(10)-C(3)-C(2)	106.7(6)
C(17B)-C(18B)	1.487(15)	O(10)-C(3)-C(4)	108.9(6)
C(19B)-O(9B)	1.421(15)	C(2)-C(3)-C(4)	115.9(7)
C(19B)-C(20B)	1.542(17)	O(11)-C(4)-C(3)	111.1(6)
C(20B)-C(21B)	1.3900	O(11)-C(4)-C(5)	110.2(7)
C(20B)-C(25B)	1.3900	C(3)-C(4)-C(5)	112.5(7)
C(21B)-C(22B)	1.3900	O(12)-C(5)-C(6)	102.6(7)
C(22B)-C(23B)	1.3900	O(12)-C(5)-C(4)	109.4(7)
C(23B)-C(24B)	1.3900	C(6)-C(5)-C(4)	117.4(7)
C(24B)-C(25B)	1.3900	O(1)-C(6)-O(2)	109.9(7)
C(26B)-O(10B)	1.444(11)	O(1)-C(6)-C(5)	115.2(7)
C(26B)-C(27B)	1.500(14)	O(2)-C(6)-C(5)	103.7(7)
C(27B)-C(32B)	1.364(15)	O(2)-C(7)-C(8)	106.3(7)

O(2)-C(7)-C(12)	110.9(7)	C(30)-C(29)-C(28)	124.5(16)
C(8)-C(7)-C(12)	109.3(6)	C(29)-C(30)-C(31)	117.6(13)
O(3)-C(8)-C(7)	111.6(7)	C(32)-C(31)-C(30)	118.6(12)
O(3)-C(9)-O(4)	106.6(6)	C(27)-C(32)-C(31)	122.1(12)
O(3)-C(9)-C(10)	111.2(7)	O(11)-C(33)-C(34)	111.1(9)
O(4)-C(9)-C(10)	107.7(7)	C(35)-C(34)-C(39)	115.5(10)
O(5)-C(10)-C(11)	109.4(7)	C(35)-C(34)-C(33)	121.2(10)
O(5)-C(10)-C(9)	104.3(7)	C(39)-C(34)-C(33)	123.1(9)
C(11)-C(10)-C(9)	112.6(7)	C(34)-C(35)-C(36)	122.7(13)
O(7)-C(11)-C(10)	112.5(7)	C(37)-C(36)-C(35)	119.8(11)
O(7)-C(11)-C(12)	105.1(7)	C(38)-C(37)-C(36)	118.7(12)
C(10)-C(11)-C(12)	114.5(7)	C(37)-C(38)-C(39)	122.3(13)
O(8)-C(12)-C(11)	101.4(7)	C(34)-C(39)-C(38)	120.8(10)
O(8)-C(12)-C(7)	110.2(6)	O(13)-C(40)-O(12)	122.6(9)
C(11)-C(12)-C(7)	114.5(7)	O(13)-C(40)-C(41)	129.6(13)
O(8)-C(13)-O(7)	104.7(7)	O(12)-C(40)-C(41)	107.8(13)
O(8)-C(13)-C(14)	107.8(8)	O(1B)-C(1B)-C(2B)	109.0(7)
O(7)-C(13)-C(14)	109.4(10)	O(9B)-C(2B)-C(3B)	106.0(7)
O(8)-C(13)-C(15)	111.1(9)	O(9B)-C(2B)-C(1B)	109.6(7)
O(7)-C(13)-C(15)	110.0(8)	C(3B)-C(2B)-C(1B)	113.6(7)
C(14)-C(13)-C(15)	113.4(9)	O(10B)-C(3B)-C(2B)	111.9(7)
O(6)-C(16)-O(5)	122.0(9)	O(10B)-C(3B)-C(4B)	106.1(7)
O(6)-C(16)-C(17)	126.6(10)	C(2B)-C(3B)-C(4B)	114.6(7)
O(5)-C(16)-C(17)	111.3(9)	O(11B)-C(4B)-C(3B)	109.6(7)
O(9)-C(19)-C(20)	106.0(7)	O(11B)-C(4B)-C(5B)	113.2(7)
C(21)-C(20)-C(25)	119.6(11)	C(3B)-C(4B)-C(5B)	111.7(7)
C(21)-C(20)-C(19)	122.9(11)	O(12B)-C(5B)-C(6B)	105.4(7)
C(25)-C(20)-C(19)	117.4(9)	O(12B)-C(5B)-C(4B)	110.9(7)
C(20)-C(21)-C(22)	113.8(13)	C(6B)-C(5B)-C(4B)	113.5(7)
C(23)-C(22)-C(21)	120.7(12)	O(1B)-C(6B)-O(2B)	111.9(8)
C(22)-C(23)-C(24)	123.9(16)	O(1B)-C(6B)-C(5B)	116.3(7)
C(23)-C(24)-C(25)	120.8(16)	O(2B)-C(6B)-C(5B)	103.0(7)
C(24)-C(25)-C(20)	120.5(14)	O(2B)-C(7B)-C(12B)	112.4(7)
O(10)-C(26)-C(27)	107.6(7)	O(2B)-C(7B)-C(8B)	105.1(7)
C(32)-C(27)-C(28)	117.3(10)	C(12B)-C(7B)-C(8B)	110.4(7)
C(32)-C(27)-C(26)	119.6(9)	O(3B)-C(8B)-C(7B)	111.4(8)
C(28)-C(27)-C(26)	123.1(10)	O(4B)-C(9B)-O(3B)	108.2(7)
C(27)-C(28)-C(29)	119.8(14)	O(4B)-C(9B)-C(10B)	105.5(7)

O(3B)-C(9B)-C(10B)	111.1(7)	O(11B)-C(33B)-C(34B)	110.7(14)
O(5B)-C(10B)-C(9B)	105.4(7)	C(35B)-C(34B)-C(39B)	117.1(15)
O(5B)-C(10B)-C(11B)	110.5(6)	C(35B)-C(34B)-C(33B)	121.5(13)
C(9B)-C(10B)-C(11B)	110.5(6)	C(39B)-C(34B)-C(33B)	121.1(15)
O(7B)-C(11B)-C(12B)	103.6(7)	C(36B)-C(35B)-C(34B)	118.9(15)
O(7B)-C(11B)-C(10B)	109.6(7)	C(37B)-C(36B)-C(35B)	122.7(18)
C(12B)-C(11B)-C(10B)	115.7(7)	C(36B)-C(37B)-C(38B)	119.9(18)
O(8B)-C(12B)-C(7B)	111.3(6)	C(39B)-C(38B)-C(37B)	119.3(17)
O(8B)-C(12B)-C(11B)	102.8(7)	C(38B)-C(39B)-C(34B)	121.8(19)
C(7B)-C(12B)-C(11B)	114.2(7)	O(13B)-C(40B)-O(12B)	121.5(9)
O(8B)-C(13B)-O(7B)	107.6(8)	O(13B)-C(40B)-C(41B)	126.0(11)
O(8B)-C(13B)-C(15B)	111.7(11)	O(12B)-C(40B)-C(41B)	112.5(10)
O(7B)-C(13B)-C(15B)	107.3(9)	O(1S)-C(1S)-C(2S)	106(4)
O(8B)-C(13B)-C(14B)	107.7(9)	C(6)-O(1)-C(1)	116.9(7)
O(7B)-C(13B)-C(14B)	107.2(11)	C(7)-O(2)-C(6)	117.7(7)
C(15B)-C(13B)-C(14B)	115.1(11)	C(9)-O(3)-C(8)	114.8(6)
O(6B)-C(17B)-O(5B)	123.6(9)	C(18)-O(4)-C(9)	113.7(9)
O(6B)-C(17B)-C(18B)	127.7(10)	C(16)-O(5)-C(10)	117.0(7)
O(5B)-C(17B)-C(18B)	108.6(9)	C(11)-O(7)-C(13)	109.5(7)
O(9B)-C(19B)-C(20B)	106.5(11)	C(13)-O(8)-C(12)	105.5(6)
C(21B)-C(20B)-C(25B)	120.0	C(2)-O(9)-C(19)	116.2(6)
C(21B)-C(20B)-C(19B)	116.4(9)	C(26)-O(10)-C(3)	115.0(6)
C(25B)-C(20B)-C(19B)	123.6(9)	C(4)-O(11)-C(33)	114.2(8)
C(20B)-C(21B)-C(22B)	120.0	C(40)-O(12)-C(5)	116.4(8)
C(23B)-C(22B)-C(21B)	120.0	C(6B)-O(1B)-C(1B)	116.2(7)
C(22B)-C(23B)-C(24B)	120.0	C(6B)-O(2B)-C(7B)	116.2(7)
C(23B)-C(24B)-C(25B)	120.0	C(8B)-O(3B)-C(9B)	113.4(7)
C(24B)-C(25B)-C(20B)	120.0	C(9B)-O(4B)-C(16B)	108.9(10)
O(10B)-C(26B)-C(27B)	112.0(8)	C(17B)-O(5B)-C(10B)	116.0(7)
C(32B)-C(27B)-C(28B)	117.6(9)	C(13B)-O(7B)-C(11B)	107.6(7)
C(32B)-C(27B)-C(26B)	121.7(8)	C(13B)-O(8B)-C(12B)	107.3(6)
C(28B)-C(27B)-C(26B)	120.6(10)	C(19B)-O(9B)-C(2B)	116.0(9)
C(29B)-C(28B)-C(27B)	121.4(11)	C(3B)-O(10B)-C(26B)	116.0(6)
C(30B)-C(29B)-C(28B)	119.5(11)	C(33B)-O(11B)-C(4B)	118.2(9)
C(29B)-C(30B)-C(31B)	120.1(12)	C(40B)-O(12B)-C(5B)	117.7(7)
C(32B)-C(31B)-C(30B)	119.0(13)		
C(27B)-C(32B)-C(31B)	122.1(10)		

Symmetry transformations used to generate equivalent atoms:

Table 5. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for compound **91** (b103_3_29). 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}
C(1)	43(4)	39(5)	52(5)	-2(4)	17(4)	2(4)
C(2)	39(4)	31(5)	47(4)	8(4)	12(3)	-1(4)
C(3)	35(4)	32(4)	43(4)	-2(4)	13(3)	-1(4)
C(4)	46(5)	40(5)	42(5)	9(4)	10(3)	-4(4)
C(5)	28(4)	38(5)	65(5)	0(5)	9(4)	2(4)
C(6)	43(5)	48(6)	54(5)	-8(5)	9(4)	3(5)
C(7)	34(4)	30(5)	65(5)	-1(4)	10(4)	-5(4)
C(8)	31(4)	30(4)	65(5)	5(4)	16(3)	6(4)
C(9)	30(4)	39(5)	61(5)	5(4)	19(4)	-2(4)
C(10)	35(4)	32(5)	59(5)	5(4)	13(4)	-2(4)
C(11)	45(5)	38(5)	53(5)	-9(4)	23(4)	-8(4)
C(12)	42(5)	42(5)	50(5)	-4(4)	19(4)	-3(4)
C(13)	59(6)	53(6)	67(6)	-9(5)	32(5)	-6(5)
C(14)	86(7)	81(9)	60(6)	-23(6)	34(5)	1(7)
C(15)	54(6)	65(7)	76(6)	-3(6)	35(5)	-4(6)
C(16)	37(5)	36(6)	95(7)	-4(5)	23(4)	-4(5)
C(17)	47(5)	62(7)	94(7)	3(6)	30(5)	-9(5)
C(18)	69(7)	150(14)	45(5)	-23(7)	16(5)	-8(8)
C(19)	42(5)	61(6)	49(5)	-10(5)	14(4)	-13(5)
C(20)	42(5)	61(6)	65(6)	-11(5)	16(4)	-5(5)
C(21)	52(6)	73(9)	180(13)	43(10)	34(8)	9(7)
C(22)	52(6)	90(10)	125(11)	33(9)	29(7)	-13(7)
C(23)	98(11)	90(11)	127(13)	-11(10)	34(9)	17(10)
C(24)	124(13)	95(11)	101(10)	-26(9)	60(9)	-26(10)
C(25)	101(9)	111(12)	73(7)	-26(8)	33(7)	-14(9)
C(26)	88(7)	40(5)	40(5)	0(4)	3(4)	-11(5)
C(27)	54(5)	39(5)	53(5)	1(4)	16(4)	-9(5)
C(28)	111(11)	74(10)	117(11)	2(9)	18(9)	3(9)
C(29)	150(16)	123(15)	97(11)	53(11)	61(10)	20(13)
C(30)	138(13)	60(8)	63(7)	17(6)	21(8)	45(9)
C(31)	101(10)	102(12)	91(9)	25(8)	12(8)	42(9)
C(32)	73(7)	101(11)	77(7)	-4(8)	28(6)	4(8)
C(33)	135(11)	67(8)	60(6)	-13(6)	51(6)	-42(8)

C(34)	72(6)	48(6)	41(5)	2(5)	21(4)	-1(5)
C(35)	151(12)	68(8)	63(7)	-32(7)	37(7)	-35(9)
C(36)	164(14)	102(11)	42(6)	-1(7)	51(7)	-7(11)
C(37)	90(9)	82(10)	106(11)	10(8)	56(7)	-16(8)
C(38)	91(9)	122(12)	58(7)	-10(7)	28(6)	-53(9)
C(39)	77(7)	82(9)	39(5)	5(5)	12(4)	-17(7)
C(40)	46(6)	67(8)	77(7)	-15(7)	6(5)	23(6)
C(41)	59(7)	126(13)	108(9)	-30(9)	6(6)	38(8)
C(1B)	63(6)	49(6)	52(5)	9(5)	14(4)	-1(5)
C(2B)	41(5)	39(5)	53(5)	1(4)	3(4)	1(4)
C(3B)	47(5)	38(5)	37(4)	5(4)	8(3)	11(4)
C(4B)	38(4)	37(5)	48(5)	3(4)	13(3)	12(4)
C(5B)	39(5)	37(5)	46(5)	-5(4)	6(3)	2(4)
C(6B)	54(5)	38(5)	44(5)	-6(4)	1(4)	0(5)
C(7B)	42(5)	26(4)	67(6)	1(4)	8(4)	-2(4)
C(8B)	40(5)	40(5)	74(6)	3(5)	10(4)	0(4)
C(9B)	45(5)	49(6)	51(5)	-3(5)	8(4)	2(5)
C(10B)	35(4)	27(4)	50(5)	-5(4)	11(3)	-1(4)
C(11B)	51(5)	33(5)	46(5)	5(4)	17(4)	-5(4)
C(12B)	45(5)	36(5)	44(5)	-8(4)	9(3)	-5(4)
C(13B)	74(7)	63(7)	57(6)	-5(6)	16(5)	-2(6)
C(14B)	105(9)	108(11)	58(6)	17(7)	11(6)	-3(9)
C(15B)	77(8)	79(9)	152(12)	-44(9)	38(8)	6(8)
C(16B)	81(8)	200(20)	51(6)	35(9)	12(5)	17(10)
C(17B)	42(5)	37(6)	74(6)	8(5)	24(4)	3(5)
C(18B)	54(5)	37(5)	90(7)	10(5)	29(5)	7(5)
C(19B)	58(6)	82(9)	106(9)	27(8)	9(6)	-11(7)
C(20B)	43(6)	91(11)	203(16)	80(12)	37(8)	2(7)
C(21B)	62(9)	115(15)	340(30)	92(19)	65(12)	19(10)
C(22B)	61(9)	150(20)	480(50)	160(30)	108(17)	38(12)
C(23B)	260(40)	220(40)	510(60)	280(40)	310(40)	160(30)
C(24B)	340(40)	280(40)	450(50)	270(40)	360(50)	200(40)
C(25B)	159(19)	210(30)	171(18)	63(19)	110(16)	80(20)
C(26B)	62(6)	55(6)	45(5)	-8(5)	3(4)	18(5)
C(27B)	42(5)	39(5)	58(5)	-2(4)	6(4)	14(5)
C(28B)	63(6)	61(7)	52(5)	-6(5)	1(4)	12(6)
C(29B)	100(9)	51(7)	53(6)	-11(6)	-15(6)	-4(7)
C(30B)	121(11)	54(7)	79(8)	2(7)	-22(8)	24(9)

C(31B)	107(9)	44(6)	88(8)	4(6)	17(7)	-4(7)
C(32B)	78(7)	36(5)	66(6)	-6(5)	3(5)	-1(6)
C(33B)	310(30)	260(30)	65(8)	-87(13)	95(13)	-220(30)
C(34B)	89(9)	94(11)	97(9)	-8(8)	37(7)	3(9)
C(35B)	105(10)	114(13)	103(9)	-31(10)	42(8)	-31(10)
C(36B)	125(13)	92(12)	138(13)	-40(11)	29(11)	-14(10)
C(37B)	146(16)	150(20)	139(15)	-45(14)	53(13)	-16(16)
C(38B)	164(17)	150(19)	133(14)	-51(14)	93(13)	-22(17)
C(39B)	123(13)	152(19)	127(13)	-33(13)	56(10)	-21(13)
C(40B)	48(5)	60(7)	66(6)	-18(6)	7(5)	-1(5)
C(41B)	52(6)	95(10)	114(9)	-37(8)	36(6)	-29(7)
O(1)	41(3)	40(4)	68(4)	9(3)	14(3)	0(3)
O(2)	38(3)	41(4)	54(3)	-4(3)	11(2)	-9(3)
O(3)	45(3)	37(3)	54(3)	-4(3)	16(2)	-7(3)
O(4)	53(4)	67(5)	51(3)	3(4)	9(3)	-7(4)
O(5)	35(3)	30(3)	79(4)	-1(3)	17(3)	-6(3)
O(6)	53(4)	44(5)	178(9)	5(5)	33(5)	6(4)
O(7)	52(3)	55(4)	61(4)	-1(3)	32(3)	11(3)
O(8)	46(3)	56(4)	54(3)	-2(3)	23(3)	-3(3)
O(9)	42(3)	45(4)	54(3)	-6(3)	18(3)	-3(3)
O(10)	57(3)	35(3)	33(3)	2(3)	7(2)	-7(3)
O(11)	64(4)	58(4)	38(3)	4(3)	19(3)	8(3)
O(12)	46(3)	57(4)	67(4)	-16(3)	15(3)	4(3)
O(13)	79(5)	68(6)	95(6)	22(5)	22(4)	35(5)
O(1B)	42(3)	39(4)	72(4)	-6(3)	-1(3)	3(3)
O(2B)	52(3)	37(3)	51(3)	-2(3)	-4(3)	12(3)
O(3B)	37(3)	41(3)	54(3)	-2(3)	7(2)	1(3)
O(4B)	54(4)	120(7)	42(3)	-10(4)	11(3)	-7(5)
O(5B)	37(3)	32(3)	66(4)	1(3)	11(2)	1(3)
O(6B)	51(4)	30(4)	149(7)	-1(4)	23(4)	-9(3)
O(7B)	65(4)	61(4)	45(3)	-5(3)	19(3)	-17(4)
O(8B)	51(4)	54(4)	58(4)	-3(3)	8(3)	-1(3)
O(9B)	43(3)	56(4)	81(4)	5(4)	25(3)	-2(3)
O(10B)	42(3)	48(4)	40(3)	-2(3)	5(2)	6(3)
O(11B)	64(4)	61(4)	41(3)	-3(3)	15(3)	6(4)
O(12B)	38(3)	43(4)	63(4)	-10(3)	8(3)	-5(3)
O(13B)	74(5)	67(5)	102(5)	-39(5)	28(4)	-18(5)

Table 6. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for compound **91** (b103_3_29)

	x	y	z	U(eq)
H(1A)	7029	6512	8749	52
H(1B)	7281	5180	8992	52
H(2)	7491	6663	9860	46
H(3)	7436	9188	9782	43
H(4)	6865	9652	9844	51
H(5)	6604	8306	8973	52
H(6)	6444	5981	9658	58
H(7)	6399	3838	8913	51
H(8A)	6435	4461	7951	49
H(8B)	6135	3286	7967	49
H(9)	5589	3702	7666	50
H(10)	5298	6447	7899	50
H(11)	5771	6604	8621	52
H(12)	5760	3502	8702	52
H(14A)	5658	5152	10431	110
H(14B)	5391	6356	10116	110
H(14C)	5801	6503	10120	110
H(15A)	5292	3196	9170	93
H(15B)	5096	3985	9618	93
H(15C)	5429	2980	9847	93
H(17A)	4370	4293	8418	98
H(17B)	4671	3098	8451	98
H(17C)	4429	3497	7844	98
H(18A)	5780	4465	6644	131
H(18B)	5402	4728	6251	131
H(18C)	5467	3362	6676	131
H(19A)	8077	7708	9833	60
H(19B)	7920	9034	9419	60
H(21)	8691	7372	9710	120
H(22)	9064	6701	8962	105

H(23)	8866	7141	8040	124
H(24)	8325	7926	7691	122
H(25)	7922	8257	8294	111
H(26A)	7451	11062	9139	68
H(26B)	7044	11214	9163	68
H(28)	7635	11517	8203	122
H(29)	7486	12138	7220	142
H(30)	6955	12461	6775	104
H(31)	6473	11784	7280	118
H(32)	6613	11137	8244	98
H(33A)	6778	9680	10659	100
H(33B)	7154	9211	11014	100
H(35)	6914	9338	11899	110
H(36)	6636	8173	12552	118
H(37)	6320	6112	12287	105
H(38)	6250	5331	11368	106
H(39)	6500	6521	10698	79
H(41A)	5779	10959	9640	149
H(41B)	5808	9343	9894	149
H(41C)	5620	9623	9240	149
H(1B1)	3408	1406	6972	65
H(1B2)	3192	-37	6750	65
H(2B)	2989	1255	5820	54
H(3B)	2991	3766	5818	48
H(4B)	3563	4411	5853	48
H(5B)	3773	3209	6802	49
H(6B)	4024	974	6154	56
H(7B)	4079	-1158	6900	54
H(8B1)	4026	-511	7864	62
H(8B2)	4334	-1668	7869	62
H(9B)	4856	-1291	8187	58
H(10B)	5170	1428	7971	45
H(11B)	4700	1640	7215	51
H(12B)	4701	-1470	7118	50
H(14D)	4720	621	5412	136
H(14E)	5062	1518	5699	136

H(14F)	4689	1939	5841	136
H(15D)	5241	-1622	6610	150
H(15E)	5339	-889	6048	150
H(15F)	5015	-1987	5986	150
H(16A)	4619	-602	9076	164
H(16B)	4942	-127	9566	164
H(16C)	4966	-1572	9199	164
H(18D)	6093	-795	7485	87
H(18E)	5777	-1931	7424	87
H(18F)	6009	-1581	8045	87
H(19C)	2578	-173	6389	99
H(19D)	2384	779	5851	99
H(21B)	1817	22	6002	202
H(22B)	1342	411	6452	267
H(23B)	1416	1735	7311	357
H(24B)	1967	2670	7721	383
H(25B)	2442	2282	7271	202
H(26C)	2958	5549	7056	66
H(26D)	2700	4409	6679	66
H(28B)	2304	5648	5958	72
H(29B)	2174	7361	5208	87
H(30B)	2623	8618	4920	108
H(31B)	3195	8541	5500	96
H(32B)	3317	6867	6261	73
H(33C)	3956	3134	5304	243
H(33D)	3636	3884	4875	243
H(35B)	3337	410	4806	125
H(36B)	3347	-1249	4047	141
H(37B)	3721	-961	3403	168
H(38B)	4105	1131	3477	168
H(39B)	4148	2670	4262	156
H(41D)	4621	6321	6623	126
H(41E)	4578	5318	6061	126
H(41F)	4758	4679	6676	126

Table 7. Torsion angles [°] for compound **91** (b103_3_29)

O(1)-C(1)-C(2)-O(9)	162.3(6)
O(1)-C(1)-C(2)-C(3)	-74.5(9)
O(9)-C(2)-C(3)-O(10)	51.6(8)
C(1)-C(2)-C(3)-O(10)	-65.4(8)
O(9)-C(2)-C(3)-C(4)	173.1(6)
C(1)-C(2)-C(3)-C(4)	56.1(9)
O(10)-C(3)-C(4)-O(11)	176.0(7)
C(2)-C(3)-C(4)-O(11)	55.7(9)
O(10)-C(3)-C(4)-C(5)	52.0(9)
C(2)-C(3)-C(4)-C(5)	-68.3(9)
O(11)-C(4)-C(5)-O(12)	72.4(9)
C(3)-C(4)-C(5)-O(12)	-163.0(7)
O(11)-C(4)-C(5)-C(6)	-43.9(11)
C(3)-C(4)-C(5)-C(6)	80.7(10)
O(12)-C(5)-C(6)-O(1)	-154.6(7)
C(4)-C(5)-C(6)-O(1)	-34.7(12)
O(12)-C(5)-C(6)-O(2)	85.3(8)
C(4)-C(5)-C(6)-O(2)	-154.8(7)
O(2)-C(7)-C(8)-O(3)	-65.2(8)
C(12)-C(7)-C(8)-O(3)	54.5(9)
O(3)-C(9)-C(10)-O(5)	-155.2(6)
O(4)-C(9)-C(10)-O(5)	88.4(8)
O(3)-C(9)-C(10)-C(11)	-36.7(10)
O(4)-C(9)-C(10)-C(11)	-153.1(7)
O(5)-C(10)-C(11)-O(7)	-45.2(10)
C(9)-C(10)-C(11)-O(7)	-160.6(7)
O(5)-C(10)-C(11)-C(12)	74.7(9)
C(9)-C(10)-C(11)-C(12)	-40.7(10)
O(7)-C(11)-C(12)-O(8)	-25.9(8)
C(10)-C(11)-C(12)-O(8)	-149.9(7)
O(7)-C(11)-C(12)-C(7)	-144.6(7)
C(10)-C(11)-C(12)-C(7)	91.4(9)
O(2)-C(7)-C(12)-O(8)	-68.8(9)
C(8)-C(7)-C(12)-O(8)	174.3(7)

O(2)-C(7)-C(12)-C(11)	44.7(9)
C(8)-C(7)-C(12)-C(11)	-72.1(9)
O(9)-C(19)-C(20)-C(21)	-130.3(11)
O(9)-C(19)-C(20)-C(25)	53.8(13)
C(25)-C(20)-C(21)-C(22)	-8.4(18)
C(19)-C(20)-C(21)-C(22)	175.7(11)
C(20)-C(21)-C(22)-C(23)	9(2)
C(21)-C(22)-C(23)-C(24)	-3(3)
C(22)-C(23)-C(24)-C(25)	-2(3)
C(23)-C(24)-C(25)-C(20)	2(2)
C(21)-C(20)-C(25)-C(24)	4(2)
C(19)-C(20)-C(25)-C(24)	-180.0(13)
O(10)-C(26)-C(27)-C(32)	80.4(13)
O(10)-C(26)-C(27)-C(28)	-99.8(12)
C(32)-C(27)-C(28)-C(29)	-1(2)
C(26)-C(27)-C(28)-C(29)	178.8(14)
C(27)-C(28)-C(29)-C(30)	3(3)
C(28)-C(29)-C(30)-C(31)	-5(3)
C(29)-C(30)-C(31)-C(32)	4(2)
C(28)-C(27)-C(32)-C(31)	1(2)
C(26)-C(27)-C(32)-C(31)	-179.1(13)
C(30)-C(31)-C(32)-C(27)	-2(2)
O(11)-C(33)-C(34)-C(35)	159.2(12)
O(11)-C(33)-C(34)-C(39)	-26.3(18)
C(39)-C(34)-C(35)-C(36)	3(2)
C(33)-C(34)-C(35)-C(36)	177.9(15)
C(34)-C(35)-C(36)-C(37)	1(3)
C(35)-C(36)-C(37)-C(38)	-3(3)
C(36)-C(37)-C(38)-C(39)	1(2)
C(35)-C(34)-C(39)-C(38)	-4.5(19)
C(33)-C(34)-C(39)-C(38)	-179.3(14)
C(37)-C(38)-C(39)-C(34)	3(2)
O(1B)-C(1B)-C(2B)-O(9B)	165.7(7)
O(1B)-C(1B)-C(2B)-C(3B)	-75.9(10)
O(9B)-C(2B)-C(3B)-O(10B)	54.2(8)
C(1B)-C(2B)-C(3B)-O(10B)	-66.2(10)

O(9B)-C(2B)-C(3B)-C(4B)	175.1(6)
C(1B)-C(2B)-C(3B)-C(4B)	54.6(10)
O(10B)-C(3B)-C(4B)-O(11B)	-178.8(7)
C(2B)-C(3B)-C(4B)-O(11B)	57.2(9)
O(10B)-C(3B)-C(4B)-C(5B)	55.0(9)
C(2B)-C(3B)-C(4B)-C(5B)	-69.0(9)
O(11B)-C(4B)-C(5B)-O(12B)	79.1(9)
C(3B)-C(4B)-C(5B)-O(12B)	-156.7(7)
O(11B)-C(4B)-C(5B)-C(6B)	-39.3(11)
C(3B)-C(4B)-C(5B)-C(6B)	85.0(10)
O(12B)-C(5B)-C(6B)-O(1B)	-161.8(7)
C(4B)-C(5B)-C(6B)-O(1B)	-40.4(11)
O(12B)-C(5B)-C(6B)-O(2B)	75.5(8)
C(4B)-C(5B)-C(6B)-O(2B)	-163.0(7)
O(2B)-C(7B)-C(8B)-O(3B)	-66.4(9)
C(12B)-C(7B)-C(8B)-O(3B)	55.1(10)
O(4B)-C(9B)-C(10B)-O(5B)	88.3(8)
O(3B)-C(9B)-C(10B)-O(5B)	-154.7(6)
O(4B)-C(9B)-C(10B)-C(11B)	-152.3(7)
O(3B)-C(9B)-C(10B)-C(11B)	-35.2(10)
O(5B)-C(10B)-C(11B)-O(7B)	-43.3(9)
C(9B)-C(10B)-C(11B)-O(7B)	-159.6(7)
O(5B)-C(10B)-C(11B)-C(12B)	73.5(9)
C(9B)-C(10B)-C(11B)-C(12B)	-42.9(10)
O(2B)-C(7B)-C(12B)-O(8B)	-67.9(9)
C(8B)-C(7B)-C(12B)-O(8B)	175.0(7)
O(2B)-C(7B)-C(12B)-C(11B)	47.9(9)
C(8B)-C(7B)-C(12B)-C(11B)	-69.1(9)
O(7B)-C(11B)-C(12B)-O(8B)	-28.4(8)
C(10B)-C(11B)-C(12B)-O(8B)	-148.4(7)
O(7B)-C(11B)-C(12B)-C(7B)	-149.1(7)
C(10B)-C(11B)-C(12B)-C(7B)	90.9(9)
O(9B)-C(19B)-C(20B)-C(21B)	154.9(8)
O(9B)-C(19B)-C(20B)-C(25B)	-26.0(13)
C(25B)-C(20B)-C(21B)-C(22B)	0.0
C(19B)-C(20B)-C(21B)-C(22B)	179.2(10)

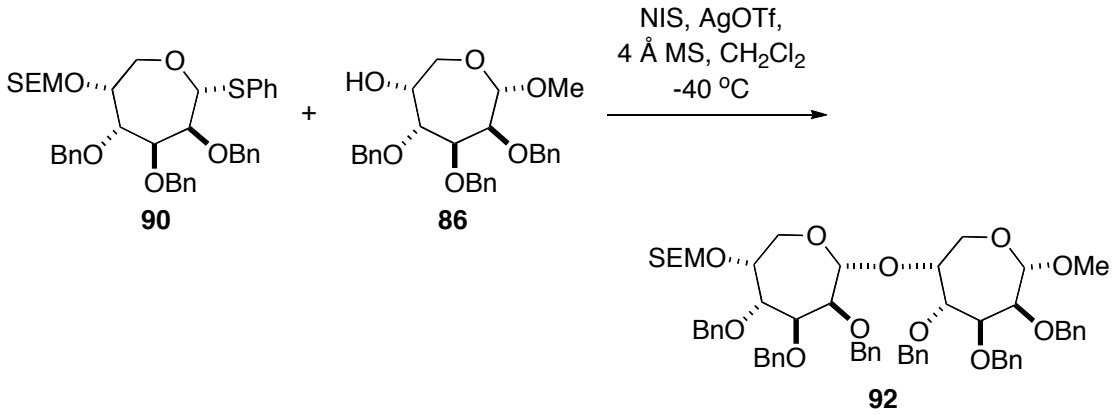
C(20B)-C(21B)-C(22B)-C(23B)	0.0
C(21B)-C(22B)-C(23B)-C(24B)	0.0
C(22B)-C(23B)-C(24B)-C(25B)	0.0
C(23B)-C(24B)-C(25B)-C(20B)	0.0
C(21B)-C(20B)-C(25B)-C(24B)	0.0
C(19B)-C(20B)-C(25B)-C(24B)	-179.1(11)
O(10B)-C(26B)-C(27B)-C(32B)	-48.3(12)
O(10B)-C(26B)-C(27B)-C(28B)	128.0(9)
C(32B)-C(27B)-C(28B)-C(29B)	-2.2(15)
C(26B)-C(27B)-C(28B)-C(29B)	-178.7(9)
C(27B)-C(28B)-C(29B)-C(30B)	4.7(17)
C(28B)-C(29B)-C(30B)-C(31B)	-6.1(19)
C(29B)-C(30B)-C(31B)-C(32B)	5.3(19)
C(28B)-C(27B)-C(32B)-C(31B)	1.4(15)
C(26B)-C(27B)-C(32B)-C(31B)	177.8(10)
C(30B)-C(31B)-C(32B)-C(27B)	-2.9(17)
O(11B)-C(33B)-C(34B)-C(35B)	10(3)
O(11B)-C(33B)-C(34B)-C(39B)	-175.9(18)
C(39B)-C(34B)-C(35B)-C(36B)	-1(2)
C(33B)-C(34B)-C(35B)-C(36B)	174.0(19)
C(34B)-C(35B)-C(36B)-C(37B)	-1(3)
C(35B)-C(36B)-C(37B)-C(38B)	-1(3)
C(36B)-C(37B)-C(38B)-C(39B)	4(4)
C(37B)-C(38B)-C(39B)-C(34B)	-6(3)
C(35B)-C(34B)-C(39B)-C(38B)	4(3)
C(33B)-C(34B)-C(39B)-C(38B)	-171(2)
O(2)-C(6)-O(1)-C(1)	69.5(9)
C(5)-C(6)-O(1)-C(1)	-47.2(10)
C(2)-C(1)-O(1)-C(6)	95.2(8)
C(8)-C(7)-O(2)-C(6)	-152.0(7)
C(12)-C(7)-O(2)-C(6)	89.3(8)
O(1)-C(6)-O(2)-C(7)	69.2(9)
C(5)-C(6)-O(2)-C(7)	-167.1(7)
O(4)-C(9)-O(3)-C(8)	-144.3(7)
C(10)-C(9)-O(3)-C(8)	98.5(8)
C(7)-C(8)-O(3)-C(9)	-85.0(8)

O(3)-C(9)-O(4)-C(18)	75.5(10)
C(10)-C(9)-O(4)-C(18)	-165.2(9)
O(6)-C(16)-O(5)-C(10)	7.0(15)
C(17)-C(16)-O(5)-C(10)	-175.9(8)
C(11)-C(10)-O(5)-C(16)	99.1(9)
C(9)-C(10)-O(5)-C(16)	-140.2(8)
C(10)-C(11)-O(7)-C(13)	131.0(8)
C(12)-C(11)-O(7)-C(13)	5.8(9)
O(8)-C(13)-O(7)-C(11)	17.2(9)
C(14)-C(13)-O(7)-C(11)	132.6(8)
C(15)-C(13)-O(7)-C(11)	-102.2(8)
O(7)-C(13)-O(8)-C(12)	-34.5(9)
C(14)-C(13)-O(8)-C(12)	-150.9(9)
C(15)-C(13)-O(8)-C(12)	84.2(9)
C(11)-C(12)-O(8)-C(13)	37.0(9)
C(7)-C(12)-O(8)-C(13)	158.7(8)
C(3)-C(2)-O(9)-C(19)	58.6(9)
C(1)-C(2)-O(9)-C(19)	-178.2(7)
C(20)-C(19)-O(9)-C(2)	175.7(7)
C(27)-C(26)-O(10)-C(3)	178.7(7)
C(2)-C(3)-O(10)-C(26)	-148.7(8)
C(4)-C(3)-O(10)-C(26)	85.5(9)
C(3)-C(4)-O(11)-C(33)	118.9(9)
C(5)-C(4)-O(11)-C(33)	-115.8(9)
C(34)-C(33)-O(11)-C(4)	142.7(10)
O(13)-C(40)-O(12)-C(5)	-5.2(14)
C(41)-C(40)-O(12)-C(5)	175.4(8)
C(6)-C(5)-O(12)-C(40)	-151.9(8)
C(4)-C(5)-O(12)-C(40)	82.8(9)
O(2B)-C(6B)-O(1B)-C(1B)	74.4(9)
C(5B)-C(6B)-O(1B)-C(1B)	-43.4(10)
C(2B)-C(1B)-O(1B)-C(6B)	95.9(9)
O(1B)-C(6B)-O(2B)-C(7B)	65.3(10)
C(5B)-C(6B)-O(2B)-C(7B)	-169.1(7)
C(12B)-C(7B)-O(2B)-C(6B)	90.0(9)
C(8B)-C(7B)-O(2B)-C(6B)	-149.8(7)

C(7B)-C(8B)-O(3B)-C(9B)	-87.3(9)
O(4B)-C(9B)-O(3B)-C(8B)	-144.2(8)
C(10B)-C(9B)-O(3B)-C(8B)	100.4(9)
O(3B)-C(9B)-O(4B)-C(16B)	72.6(12)
C(10B)-C(9B)-O(4B)-C(16B)	-168.4(10)
O(6B)-C(17B)-O(5B)-C(10B)	5.0(14)
C(18B)-C(17B)-O(5B)-C(10B)	-175.8(7)
C(9B)-C(10B)-O(5B)-C(17B)	-143.5(7)
C(11B)-C(10B)-O(5B)-C(17B)	97.0(8)
O(8B)-C(13B)-O(7B)-C(11B)	7.0(11)
C(15B)-C(13B)-O(7B)-C(11B)	-113.4(10)
C(14B)-C(13B)-O(7B)-C(11B)	122.5(9)
C(12B)-C(11B)-O(7B)-C(13B)	13.3(9)
C(10B)-C(11B)-O(7B)-C(13B)	137.4(8)
O(7B)-C(13B)-O(8B)-C(12B)	-26.4(11)
C(15B)-C(13B)-O(8B)-C(12B)	91.1(10)
C(14B)-C(13B)-O(8B)-C(12B)	-141.6(9)
C(7B)-C(12B)-O(8B)-C(13B)	156.3(8)
C(11B)-C(12B)-O(8B)-C(13B)	33.7(9)
C(20B)-C(19B)-O(9B)-C(2B)	175.4(8)
C(3B)-C(2B)-O(9B)-C(19B)	149.7(8)
C(1B)-C(2B)-O(9B)-C(19B)	-87.3(10)
C(2B)-C(3B)-O(10B)-C(26B)	-95.7(9)
C(4B)-C(3B)-O(10B)-C(26B)	138.6(8)
C(27B)-C(26B)-O(10B)-C(3B)	-59.6(10)
C(34B)-C(33B)-O(11B)-C(4B)	165.2(13)
C(3B)-C(4B)-O(11B)-C(33B)	153.7(17)
C(5B)-C(4B)-O(11B)-C(33B)	-80.9(19)
O(13B)-C(40B)-O(12B)-C(5B)	-3.4(13)
C(41B)-C(40B)-O(12B)-C(5B)	178.7(8)
C(6B)-C(5B)-O(12B)-C(40B)	-150.4(7)
C(4B)-C(5B)-O(12B)-C(40B)	86.4(9)

Symmetry transformations used to generate equivalent atoms:

Synthesis of disaccharide 92

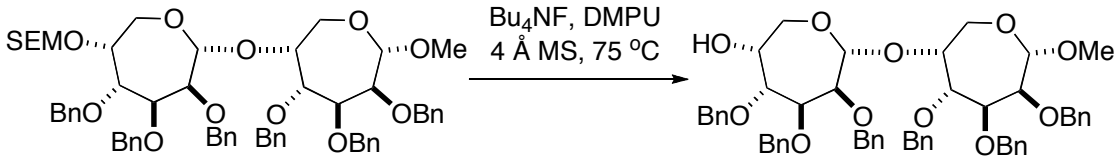


Thioglycoside **90** (190 mg, 0.28 mmol) and methyl glycoside alcohol **86** were dissolved in CH_2Cl_2 (0.10 M, 2.8 mL). 4 Å MS (400 mg, powdered) were then added to the solution. The solution was cooled to -40 °C. Then NIS (79 mg, 0.35 mmol) and AgOTf (21 mg, 0.08 mmol) were simultaneously added to the solution. The reaction was allowed to warm to -38 °C, at which point the reaction became magenta in color. Upon the color change, TLC indicated the completion of the reaction. The reaction was quenched by the addition of Et_3N (1.0 mL), which caused an immediate color change to yellow. The mixture was filtered through celite, and the volatiles were evaporated under reduced pressure. Chromatography (4:1 hexanes:EtOAc) afforded disaccharide **92** as a colorless oil (230 mg, 80 %).

$[\alpha]_D^{23}$ = + 13.2 (c 1.20, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.33-7.18 (m, 28H), 7.05 (m, 2H), 4.89 (d, *J* = 6.8 Hz, 1H), 4.79 (d, *J* = 12.4 Hz, 1H), 4.79 (d, *J* = 12.4 Hz, 1H), 4.75-4.55 (m, 9H), 4.49 (d, *J* = 12.0 Hz, 1H), 4.43 (d, *J* = 11.6 Hz, 1H), 4.39-4.27 (m, 3H), 4.18 (m, 1H), 4.07 (m, 5H), 3.82-3.71 (m, 4H), 3.63 (m, 3H), 3.50 (m, 1H), 3.43 (s, 3H), 0.966 (dd, *J* = 6.4, 9.6 Hz, 2H), 0.041 (s, 9H); ^{13}C

NMR (100 MHz, $CDCl_3$) δ 138.9, 138.9, 138.7, 138.7, 138.6, 128.6, 128.5, 128.5, 128.4, 128.4, 128.3, 128.0, 127.9, 127.9, 127.6, 127.5, 103.5, 101.8, 94.1, 80.2, 78.4, 77.7, 77.4, 76.1, 75.8, 75.4, 73.9, 73.8, 73.7, 73.6, 73.2, 72.8, 65.5, 61.4, 66.4, 55.3, 18.3, -1.16; IR (KBr) 3030, 2951, 1454, 1093, 1066, 735, 698 cm^{-1}; HRMS (ESI) [M+NH_4^+] Calcd. for $C_{61}H_{78}O_{12}N_1Si_1$ 1044.52878, found 1044.53162.

Synthesis of disaccharide alcohol 93



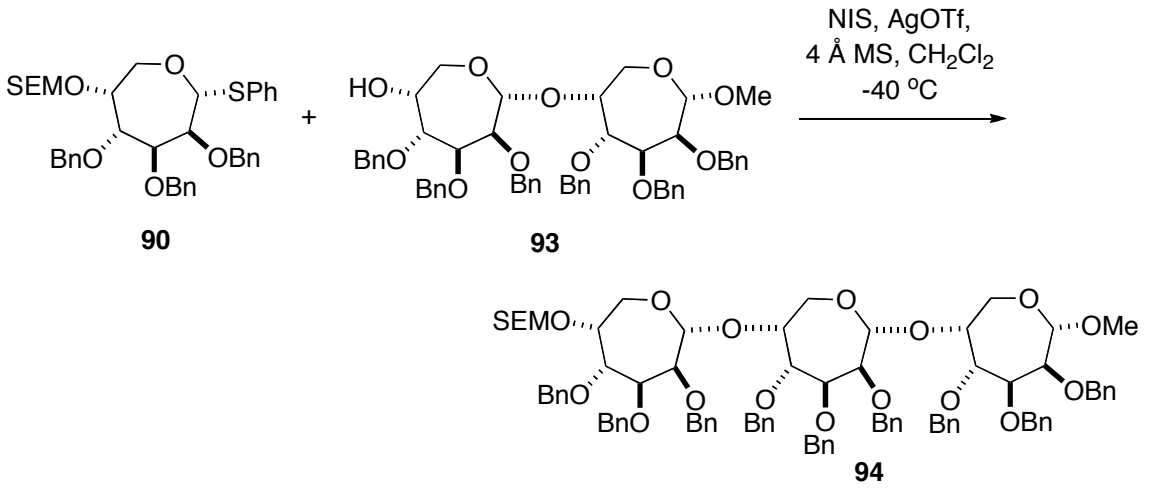
92 **93**

Disaccharide **92** (230 mg, 0.23 mmol) was dissolved in DMPU (0.23 M, 1.0 mL) and freshly activated 4 Å MS (200 mg, powdered) were added. Then Bu_4NF (1.0 M in THF, 1.1 mL, 1.1 mmol) was added all at once. The reaction was stirred for 24 hours at 75 °C. Then the reaction was diluted with EtOAc (100 mL) and quenched by the addition of H_2O (50 mL). The aqueous layer was extracted with EtOAc (2 x 50 mL). The organic layers were combined and dried with $MgSO_4$. After filtration and evaporation of the volatiles under reduced pressure, chromatography (4:1→2:1 hexanes:EtOAc) afforded disaccharide alcohol **93** as a colorless oil (180 mg, 87 %).

$[\alpha]_D^{23}$ = + 3.4 (c 1.00, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.36-7.19 (m, 26H), 7.07 (m, 4H), 4.91 (d, *J* = 6.4 Hz, 1H), 4.83 (d, *J* = 12.4 Hz, 1H), 4.75 (d, *J* = 12.4 Hz, 1H), 4.67 (m, 3H), 4.64-4.42 (m, 3H), 4.41 (d, *J* = 11.6 Hz, 1H), 4.35 (d, *J* = 12.0 Hz, 1H), 4.29 (m, 2H), 4.22 (d, *J* = 11.2 Hz, 1H), 4.18 (dt, *J* = 3.2, 9.6 Hz,

1H), 4.07-3.96 (m, 4H), 3.91 (dd, *J* = 6.0, 14.4 Hz, 1H), 3.82 (d, *J* = 6.4 Hz, 1H), 3.76 (m, 3H), 3.67 (m, 1H), 3.58 (dd, *J* = 3.2, 12.0 Hz, 1H), 3.43 (s, 3H), 2.25 (d, *J* = 10.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.9, 138.7, 138.6, 138.6, 138.3, 137.5, 128.8, 128.6, 128.5, 128.4, 128.4, 128.3, 128.1, 127.9, 127.8, 127.7, 127.6, 127.5, 103.6, 101.7, 80.1, 79.6, 78.3, 77.8, 76.7, 75.9, 75.7, 73.7, 73.7, 73.6, 73.5, 73.2, 72.9, 69.0, 62.3, 61.4, 55.3; IR (KBr) 3467, 3030, 2895, 1496, 1454, 1092, 737, 698 cm^{-1}; HRMS (ESI) [M+H$^+$] Calcd. for $C_{55}H_{61}O_{11}$ 897.42084, found 897.41925.

Synthesis of trisaccharide 94

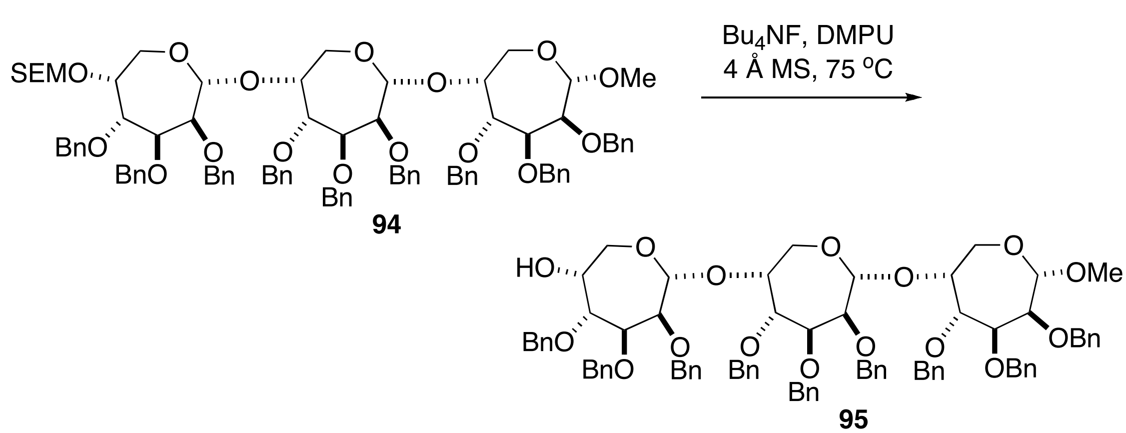


Thioglycoside **90** (71 mg, 0.11 mmol) and disaccharide alcohol **93** (93 mg, 0.10 mol) were dissolved in CH_2Cl_2 (0.10 M, 1.1 mL). 4 Å MS (200 mg, powdered) were then added to the solution. The solution was cooled to -40 °C. Then NIS (31 mg, 0.14 mmol) and AgOTf (8 mg, 0.03 mmol) were simultaneously added to the solution. The reaction was allowed to warm to -38 °C, at which point the reaction became magenta in color. Upon the color change, TLC indicated the completion of the reaction. The reaction was quenched by the addition of Et_3N

(1.0 mL), which caused an immediate color change to yellow. The mixture was filtered through celite, and the volatiles were evaporated under reduced pressure. Chromatography (4:1 hexanes:EtOAc) gave trisaccharide **94** as a colorless oil (110 mg, 75 %).

$[\alpha]_D^{23}$ = + 9.7 (c 0.50, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.32-7.17 (m, 41H), 7.04 (m, 4H), 4.88 (t, J = 7.2 Hz, 2H), 4.78 (d, J = 12.0 Hz, 1H), 4.73-4.54 (m, 13H), 4.51-4.34 (m, 5H), 4.27 (m, 2H), 4.16 (m, 2H), 4.04 (m, 6H), 3.78 (m, 6H), 3.62 (m, 4H), 3.52 (m,1H), 3.43 (s, 3H), 1.27 (m, 2H), 0.958 (m, 2H), 0.036 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.9, 138.9, 138.8, 138.7, 138.6, 138.6, 128.5, 128.4, 128.4, 128.4, 128.3, 128.3, 128.3, 128.1, 127.9, 127.8, 127.8, 127.7, 127.7, 127.5, 127.5, 103.5, 101.7, 93.9, 80.2, 78.5, 77.8, 76.1, 75.8, 75.8, 75.3, 74.0, 73.9, 73.8, 73.7, 73.6, 73.5, 73.1, 72.8, 72.7, 65.5, 61.4, 60.4, 55.3, 29.9, 18.2, 14.4, -1.16; IR (KBr) 3030, 2895, 1496, 1454, 1248, 1092, 837, 733, 698 cm^{-1}; HRMS (ESI) $[M+Na^+]$ Calcd. for $C_{88}H_{102}O_{17}Na_1Si_1$ 1481.67785, found 1481.68252.

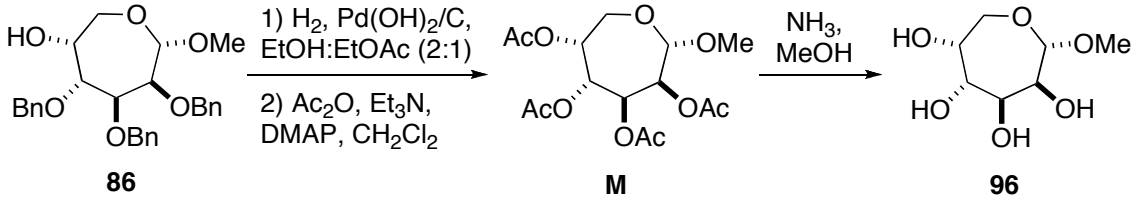
Synthesis of trisaccharide alcohol 95



Trisaccharide **94** (110 mg, 0.08 mmol) was dissolved in DMPU (0.08 M, 1.0 mL) and freshly activated 4 Å MS (200 mg, powdered) were added. Then Bu_4NF (1.0 M in THF, 0.40 mL, 0.40 mmol) was added all at once. The reaction was stirred for 3 hours at 75 °C. Then the reaction was diluted with EtOAc (100 mL) and quenched by the addition of H_2O (50 mL). The aqueous layer was extracted with EtOAc (2 x 50 mL). The organic layers were combined and dried with $MgSO_4$. After filtration and evaporation of the volatiles under reduced pressure, chromatography (4:1→2:1 hexanes:EtOAc) afforded trisaccharide alcohol **95** as a colorless oil (78 mg, 74%).

$[\alpha]_D^{23}$ = + 10.8 (c 2.00, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.37-7.03 (m, 45H), 4.92 (d, *J* = 6.8 Hz, 1H), 4.88 (d, *J* = 6.8 Hz, 1H), 4.82 (d, *J* = 12.4 Hz, 1H), 4.77-4.52 (m, 8H), 4.47-4.24 (m, 7H), 4.17 (m, 2H), 4.04 (m, 5H), 3.94 (m, 2H), 3.78 (m, 5H), 3.69 (m, 1H), 3.60 (m, 2H), 3.44 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.9, 138.9, 138.7, 138.7, 138.6, 138.4, 137.5, 128.8, 128.6, 128.5, 128.5, 128.4, 128.4, 128.3, 128.3, 128.1, 127.9, 127.9, 127.8, 127.7, 127.6, 127.5, 103.5, 101.8, 101.6, 80.2, 79.7, 78.5, 77.8, 75.9, 75.9, 75.6, 73.9, 73.8, 73.8, 73.7, 73.6, 73.2, 73.0, 72.7, 69.1, 62.3, 61.5, 60.6, 55.3; IR (KBr) 3479, 3030, 2893, 1496, 1454, 1336, 1244, 1207, 1092, 735, 698 cm^{-1}; HRMS (ESI) [M +Na^+] Calcd. for $C_{82}H_{88}O_{16}Na_1$ 1351.59646, found 1351.59487.

Synthesis of methyl α-D-mannoseptanoside 96



86 **M** **96**

Methyl glycoside **86** (220 mg, 0.47 mmol) was dissolved in EtOH:EtOAc (2:1) (0.08 M, 4.0 mL). The solution was then purged with argon for approximately 10 minutes. Then 10 % $Pd(OH)_2/C$ (20 mg) was added to the solution, and the reaction was placed under an atmosphere of H_2 (1 atm). The reaction was stirred for 2.5 hours, and then diluted with EtOH (4 mL). The mixture was then filtered though celite, and the volatiles were evaporated under reduced pressure. The crude mixture was then dissolved in CH_2Cl_2 (0.10 M, 3 mL), and Ac_2O (0.15 mL, 1.5 mmol) and Et_3N (0.28 mL, 2.0 mmol) were sequentially added. DMAP (10 mg) was then added. The reaction was stirred for 3 hours. The reaction was diluted with CH_2Cl_2 (25 mL) and quenched by the addition of H_2O (20 mL). The aqueous layer was extracted with CH_2Cl_2 (1 x 50 mL). The organic extracts were combined and dried with $MgSO_4$. After filtration and evaporation of the volatiles under reduced pressure, chromatography (2:1 hexanes:EtOAc) gave tetraacetate **M** as a colorless syrup (136 mg, 80%).

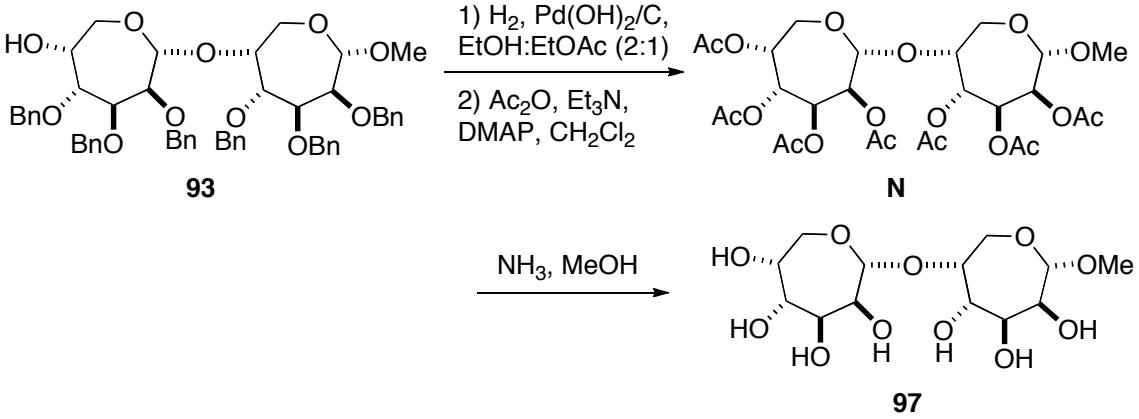
$[\alpha]_D^{23}$ = + 58.6 (c 2.00, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 4.81 (dd, *J* = 1.6, 6.8 Hz, 1H), 5.38 (m, 2H), 5.22 (m, 1H), 4.63 (d, *J* = 6.4 Hz, 1H), 4.05 (dd, *J* = 8.8, 13.2 Hz, 1H), 3.61 (dd, *J* = 4.0, 12.4 Hz, 1H), 3.39 (s, 3H), 2.12 (s, 6H), 2.07 (s, 3H), 2.05 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.9, 169.9, 169.8, 100.9, 72.3, 70.2, 69.8, 68.6, 60.4, 55.8, 21.1, 20.9, 20.9; IR (KBr) 2964, 1749, 1371, 1227, 1051, 756 cm^{-1}; HRMS (ESI) [$M+H^+$] Calcd. for $C_{15}H_{23}O_{10}$ 363.12857, found 363.12888.

Peracetate **M** (136 mg, 0.38 mmol) was dissolved in MeOH (0.10 M, 3.0 mL). NH_3 (g) was then bubbled through the solution for 10 minutes. The flask was

capped, and the reaction was stirred for 16 hours. Then the volatiles were evaporated under reduced pressure. The resulting colorless oil was placed on a high vacuum overnight to yield methyl mannoseptanoside **96** as a colorless syrup (74 mg, quant.).

$[\alpha]_D^{23}$ = + 121.1 (c 1.00, MeOH); ^{1}H NMR (400 MHz, CD_3OD) δ 4.30 (d, *J* = 6.8 Hz, 1H), 3.93 (dd, *J* = 1.2, 6.8 Hz, 1H), 3.87-3.70 (m, 4H), 3.26 (s, 3H), 3.24 (m, 2H); ^{13}C NMR (100 MHz, CD_3OD) δ 105.9, 76.2, 72.6, 72.5, 70.8, 63.5, 55.7; IR (KBr) 3381, 2914, 1051 cm^{-1}; HRMS (APCI) [M+NH_4^+] Calcd. for $C_7H_{18}O_6N_1$ 212.11286, found 212.11261.

Synthesis of mannoseptanosyl disaccharide 97



Disaccharide **93** (74 mg, 0.08 mmol) was dissolved in EtOH:EtOAc (2:1) (0.04 M, 2 mL). Argon was bubbled through the solution for 10 minutes. Then 10 % $Pd(OH)_2/C$ (20 mg) was added to the solution, and the reaction was placed under an atmosphere of H_2 (1 atm). The reaction was stirred for 2.5 hours, and then diluted with EtOH (3 mL). The mixture was then filtered though celite, and the volatiles were evaporated under reduced pressure. The crude mixture was then dissolved in CH_2Cl_2 (0.04 M, 2 mL), and Et_3N (0.12 mL, 0.90 mmol) and Ac_2O

(0.07 mL, 0.8 mmol) were sequentially added. DMAP (10 mg) was then added. The reaction was stirred for 3 hours. The reaction was diluted with CH_2Cl_2 (50 mL) and quenched by the addition of H_2O (50 mL). The aqueous layer was extracted with CH_2Cl_2 (1 x 50 mL). The organic extracts were combined and dried with $MgSO_4$. After filtration and evaporation of the volatiles under reduced pressure, chromatography (2:1→1:1 hexanes:EtOAc) gave peracetate **N** as a colorless oil (52 mg, quant.).

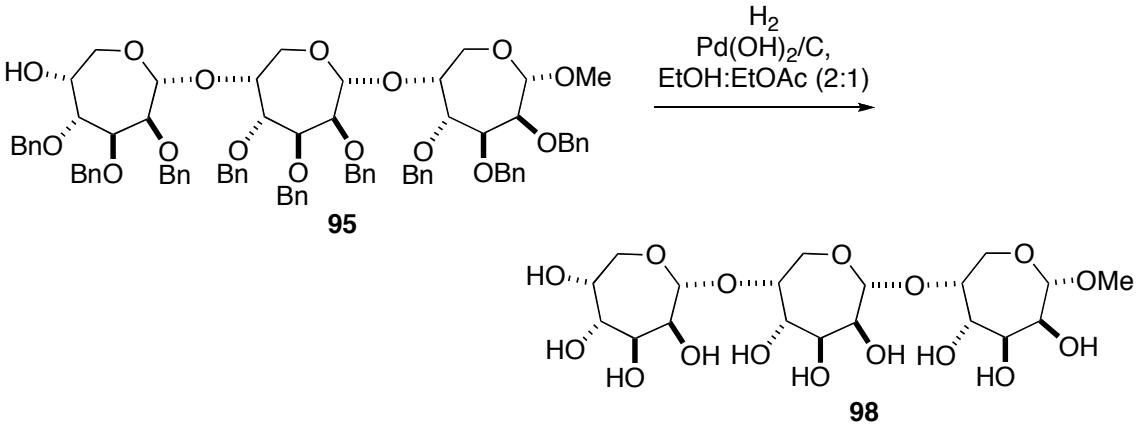
$[\alpha]_D^{23}$ = + 83.3 (c 1.50, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 5.42 (m, 2H), 5.36 (m, 2H), 5.28 (m, 2H), 5.19 (m, 1H), 4.82 (d, *J* = 6.8 Hz, 1H), 4.60 (d, *J* = 6.4 Hz, 1H), 4.06 (m, 3H), 3.62 (dd, *J* = 3.6, 12.4 Hz, 1H), 3.56 (m, 1H), 3.39 (s, 3H), 2.15 (s, 3H), 2.14 (s, 3H), 2.13 (s, 3H), 2.10 (s, 3H), 2.05 (s, 3H), 2.04 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.9, 169.9, 169.8, 169.7, 169.7, 100.7, 99.7, 73.6, 72.3, 71.3, 70.4, 70.2, 69.6, 68.0, 67.8, 61.4, 60.5, 55.6, 21.0, 21.0, 20.9, 20.9, 20.8; IR (KBr) 2937, 1753, 1371, 1223, 1049 cm^{-1}; HRMS (ESI) $[M+NH_4^+]$ Calcd. for $C_{27}H_{42}O_{18}N_1$ 668.23964, found 668.23987

Peracetate **N** (52 mg, 0.08 mmol) was dissolved in MeOH (0.02 M, 4.0 mL). NH_3 (g) was then bubbled through the solution for 10 minutes. The flask was capped, and the reaction was stirred for 16 hours. Then the volatiles were evaporated under reduced pressure. The resulting colorless oil was placed on a high vacuum overnight. Disaccharide **97** was obtained as a colorless syrup (26 mg, quant.).

$[\alpha]_D^{23}$ = + 166.4 (c 0.75, MeOH); ^1H NMR (400 MHz, CD_3OD) δ 4.57 (d, *J* = 6.4 Hz, 1H), 4.32 (d, *J* = 6.8 Hz, 1H), 3.98 (dd, *J* = 1.2, 6.8 Hz, 1H), 3.92 (m, 2H),

3.87 (m, 3H), 3.80 (m, 4H), 3.31 (m, 1H), 3.26 (s, 3H), 3.19 (m, 2H); ^{13}C NMR (100 MHz, CD_3OD) δ 105.6, 103.9, 76.7, 76.2, 75.9, 72.7, 72.5, 72.1, 70.9, 70.6, 63.6, 62.6, 55.8; IR (KBr) 3399, 2926, 1660, 1402, 1248, 1045 cm^{-1}; HRMS (ESI) [M+Na$^+$] Calcd. for $C_{13}H_{24}O_{11}Na_1$ 379.12108, found 379.12106.

Synthesis of mannoseptanosyl trisaccharide 98



Trisaccharide **95** (40 mg, 0.03 mmol) was dissolved in EtOH:EtOAc (2:1, 0.01 M, 3 mL). Argon was bubbled through the solution for 10 minutes. Then 10 % $Pd(OH)_2$/C (20 mg) was added to the solution, and the reaction was placed under an atmosphere of H_2 (1 atm). The reaction was stirred for 2.5 hours, and then diluted with EtOH (3 mL). The mixture was then filtered through celite, and the volatiles were evaporated under reduced pressure to give trisaccharide **98** as a colorless syrup (15 mg, quant.).

$[\alpha]_D^{23}$ = + 112.0 (c 1.00, MeOH); ^{1}H NMR (400 MHz, CD_3OD) δ 4.67 (t, *J* = 6.8 Hz, 2H), 4.42 (d, *J* = 6.4 Hz, 1H), 4.09-3.84 (m, 18H), 3.42 (m, 1H), 3.36 (s, 3H); ^{13}C NMR (100 MHz, CD_3OD) δ 105.6, 103.9, 103.6, 76.8, 76.7, 76.2, 75.9, 75.7, 72.6, 72.5, 72.1, 70.9, 70.6, 63.6, 62.8, 62.6, 55.8; IR (KBr) 3390, 2929, 1641,

1444, 1248, 1043 cm^{-1}; HRMS (ESI) [M+Na^+] Calcd. for $C_{19}H_{34}O_{16}Na_1$ 541.17391, found 541.17548.

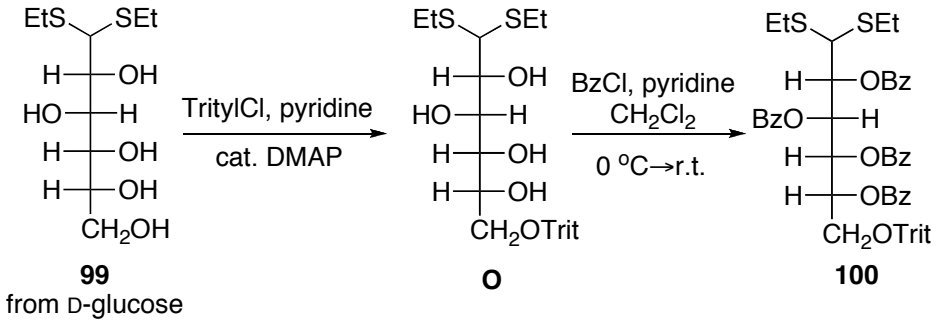
ENZYME INHIBITION STUDIES

PNP-Mannose Assay: The catalytic activity of Jack Bean α-mannosidase was assayed by a discontinuous colorimetric assay, using *para*-nitrophenyl-α-D-mannopyranoside (PNP-Man). In a typical 100-µL reaction mixture, 0.5 to 30 mM PNP-Man in 10 mM sodium citrate buffer (pH 4.5) was preincubated at 25 °C for 10 minutes. The hydrolysis assay was initiated by addition of 2 µL of α-mannosidase (250 ng/µL). Over the 20-minute assay period, multiple aliquots (20 µL) were removed from the reaction mixture (t = 0 min, 10 min, and 20 min) and immediately quenched in 1000 µL of 1 M sodium carbonate buffer (pH 12). The product of the hydrolysis, *para*-nitrophenolate (PNP), was detected spectrophotometrically at 400 nm ($\varepsilon = 1.77 \times 10^4$ $M^{-1}cm^{-1}$) in a microtiterplate reader. All experiments were performed in triplicates and corrected for background. Observed turnover rates (k_{cat}) and apparent binding constants (K_M) were determined by fitting the data to the Michaelis-Menten equation, using non-linear regression analysis in the Origin7 software.

For the α-mannosidase inhibition studies with compounds **96**, **97**, and **98**, the above reaction mixture was supplemented with the analogs at 0.75 mM and 6 mM, respectively. All experiments were done in triplicates and the resulting steady-state kinetics data were fitted to the modified Michaelis-Menten equation for competitive inhibition.

1.3.2. D-Glucoseptanosides

Synthesis of 2,3,4,5-tetra-*O*-benzoyl-6-*O*-trityl diothioacetal 100



99 from D-glucose

O

100

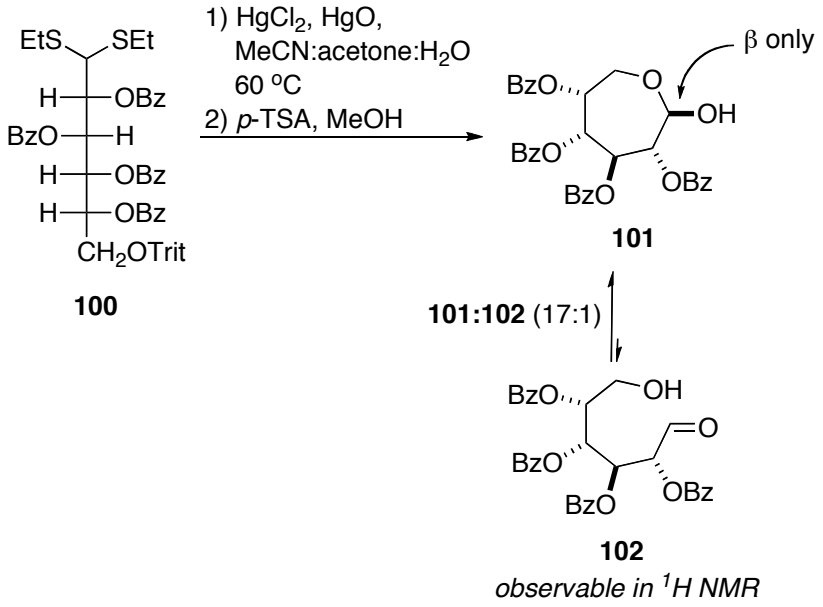
Dithioacetal **99** (15.0 g, 52.0 mmol) was dissolved in pyridine (0.50 M, 100 mL). Trityl chloride (22.0 g, 78.0 mmol) was then added all at once, followed by DMAP (100 mg). The solution was then stirred for 29 hours at room temperature. Pyridine was then removed under reduced pressure. The resulting residue was then dissolved in CH_2Cl_2 (500 mL) and consecutively washed with HCl (1.0 M, 250 mL) and saturated $NaHCO_3$ (250 mL). The organic layer was then dried with $MgSO_4$ and filtered. After removal of the volatiles, the crude mixture contained pyridine. The crude oil was then dissolved in CH_2Cl_2 (500 mL) and washed with saturated $CuSO_4$ (300 mL). After separation of the layers, the organic layer was dried with $MgSO_4$ and filtered. After removal of the volatiles, the crude green oil was chromatographed (4:1→1:1 hexanes:EtOAc). After concentration, the resulting oil was green in color, indicating the presence of a copper impurity. Thus, the oil was dissolved in EtOAc (200 mL) and consecutively washed with HCl (1.0 M, 100 mL) and saturated $NaHCO_3$ (200 mL). The organic layer was dried with $MgSO_4$ and filtered. After concentration, **O** was isolated as a thick gum (22.6 g, 82%). $[\alpha]_D^{23}$ = + 21.7 (c 1.78, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.47

(m, 8H), 7.28 (m, 7H), 4.30 (d, *J* = 7.6 Hz, 1H), 4.08 (d, *J* = 8.8 Hz, 1H), 3.83 (m, 1H), 3.68 (m, 2H), 3.40 (m, 3H), 3.05 (d, *J* = 8.0 Hz, 1H), 2.89 (d, *J* = 5.6 Hz, 1H), 2.78 - 2.61 (m, 4H), 1.27 (t, *J* = 7.6 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.9, 128.8, 128.1, 127.3, 87.1, 75.3, 74.3, 71.2, 68.4, 64.9, 55.4, 26.0, 23.9, 14.8, 14.6; IR (KBr) 3414, 3059, 2927, 1448, 1205, 758, 705 cm^{-1}; HRMS (ESI) [M +NH_4^+] Calcd. for $C_{29}H_{40}O_5N_1S_2$ 546.23424, found 546.23376.

O (22.6 g, 37.0 mmol) was dissolved in pyridine (200 mL) and CH_2Cl_2 (100 mL) then cooled to 0 ^{o}C. Then benzoyl chloride (21.0 mL, 180 mmol) was added quickly, and the ice bath was removed after 5 minutes. The reaction was then stirred for 18 hrs at r.t. The heterogeneous mixture was then filtered using Et_2O to precipitate additional pyridinium hydrochloride. After concentration, the residue was dissolved in CH_2Cl_2 (250 mL) and successively washed with HCl (1.0 M, 200 mL) and $NaHCO_3$ (300 mL). The organic layer was then dried with $MgSO_4$ and filtered. After concentration, hexane was added and the crude gum was scraped until precipitation of a white solid occurred. After decantation of the organics, **100** was obtained as a white solid (33.3 g, 95%). mp 158-160 ^{o}C; $[\alpha]_D^{23}$ = + 44.7 (c 1.00, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25-6.96 (m, 35H), 6.51 (dd, *J* = 1.2, 9.2 Hz, 1H), 6.35 (dd, *J* = 1.2, 9.6 Hz, 1H), 5.87 (dd, *J* = 3.2, 8.8 Hz, 1H), 5.39 (dt, *J* = 3.2, 9.2 Hz, 1H), 4.92 (d, *J* = 3.2 Hz, 1H), 3.56 (dd, *J* = 2.0, 11.2 Hz, 1H), 3.12 (dd, *J* = 3.2, 7.6 Hz, 1H), 3.10 - 2.93 (m, 2H), 2.69 - 2.57 (m, 2H), 1.55 (t, *J* = 7.2 Hz, 3H), 1.26 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.8, 165.6, 165.5, 165.4, 143.5, 133.7, 133.4, 133.2, 133.1, 130.2, 130.1, 130.0, 129.9, 129.4, 129.3, 129.2, 128.7, 128.7, 128.6, 128.3, 127.8,

127.0, 86.7, 73.4, 71.5, 70.7, 68.7, 61.5, 51.0, 26.1, 25.5, 15.1, 14.7; IR (KBr) 3062, 2971, 1727, 1602, 1451, 1258, 1105, 909, 707 cm^{-1}; HRMS (ESI) $[M+NH_4^+]$ Calcd. for $C_{57}H_{56}O_9N_1S_2$ 962.33910, found 962.33962.

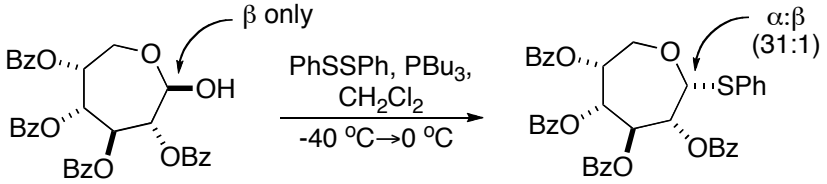
Synthesis of tetrabenzoate glucuseptanose 101



Dithioacetal **100** (15.0 g, 15.9 mmol) was dissolved in acetone:H_2O:MeCN (2:1:2) (0.08 M, 200 mL). Then HgO (5.5 g, 25.4 mmol) and $HgCl_2$ (6.8 g, 25.4 mmol) were then added simultaneously. The reaction was heated at 60 °C for 8 hrs. After cooling the orange, heterogeneous mixture to r.t., the salts were filtered away and washed with acetone. The volatiles were then removed under reduced pressure giving a white solid, which was then dissolved in CH_2Cl_2 (250 mL) and consecutively washed with KI (1.0 M, 200 mL) and saturated $Na_2S_2O_3$ (300 mL). The organic layer was then dried with $MgSO_4$ and filtered. After concentration, the crude aldehyde was dissolved in MeOH:CH_2Cl_2 (2:1) (0.05 M, 300 mL). *p*-TSA (4.1 g, 23.9 mmol) was then added all at once. After stirring for 4 hours at

r.t., saturated $NaHCO_3$ (200 mL) was added. The layers were separated, and the aqueous component was extracted with EtOAc (200 mL). The organics were combined and dried with $MgSO_4$ and filtered. After concentration, the crude material was chromatographed (2:1→1:1 hexanes:EtOAc) giving **101** as a sticky foam. $[\alpha]_D^{23}$ = - 78.0 (c 1.00, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.38-7.20 (m, 20H), 6.33 (dd, *J* = 7.6, 9.6 Hz, 1H), 5.96 (dd, *J* = 2.4, 9.6 Hz, 1H), 5.82 (dd, *J* = 2.4, 6.4 Hz, 1H), 5.61 (at, *J* = 7.6 Hz, 1H), 5.47 (d, *J* = 6.8 Hz, 1H), 4.56 (dd, *J* = 4.4, 14.0 Hz, 1H), 4.19 (dd, *J* = 4.0, 14.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.5, 165.8, 165.5, 133.8, 133.6, 133.5, 133.4, 130.3, 130.1, 130.1, 129.9, 129.8, 129.6, 129.1, 128.9, 128.9, 128.5, 96.3, 76.4, 71.8, 71.7, 69.3, 65.2; IR (KBr) 3450, 2960, 1726, 1452, 1267, 1106, 708 cm^{-1}; HRMS (ESI) $[M+H^+]$ Calcd. for $C_{34}H_{29}O_{10}$ 597.17552, found 597.17550.

Synthesis of tetrabenzoate thioglycoside 102

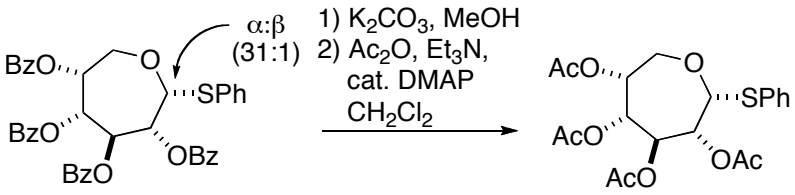


101 **102**

Lactol **101** (5.1 g, 8.58 mmol) was dissolved in CH_2Cl_2 (0.10 M, 86 mL). PhSSPh (2.8 g, 12.9 mmol) was added, and the flask was cooled to -40 °C. Then PBu_3 (3.2 mL, 12.9 mmol) was added all at once. After 10 minutes, the reaction was warmed to 0 °C and stirred for an additional 15 minutes. Then H_2O (100 mL) was added. The layers were separated, and the aqueous layer was extracted with Et_2O (100 mL). The organics were combined and dried with $MgSO_4$ and

filtered. The volatiles were then removed under reduced pressure. After chromatography (4:1→3:1 hexanes:EtOAc), **102** was isolated as a white foam (3.5 g, 59 %). mp 74-77 ^{o}C; $[\alpha]_D^{23}$ = - 42.7 (c 1.23, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.18, (m, 2H), 8.07 (m, 2H), 7.83 (m, 2H), 7.74 (m, 2H), 7.58-7.32 (m, 14H), 7.16 (m, 3H), 6.40 (dd, *J* = 6.0, 9.0 Hz, 1H), 6.08 (dd, *J* = 3.6, 6.6 Hz, 1H), 5.86 (dd, *J* = 1.8, 9.0 Hz, 1H), 5.62 (m, 1H), 5.40 (d, *J* = 3.6 Hz, 1H), 4.54 (dd, *J* = 3.6, 13.8 Hz, 1H), 3.88 (dd, *J* = 3.0, 13.8 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.01, 165.5, 133.7, 133.5, 133.3, 133.2, 132.8, 130.4, 130.4, 129.9, 129.6, 129.4, 129.2, 129.1, 128.9, 128.8, 128.7, 128.6, 128.4, 128.4, 91.1, 75.3, 72.5, 71.5, 71.1, 70.7; IR (KBr) 3064, 1727, 1451, 1262, 1092, 708 cm^{-1}; HRMS (ESI) [M+Na^{+}] Calcd. for $C_{40}H_{32}O_9Na_1S_1$ 711.16843, found 711.16668.

Synthesis of peracetate thioglycoside 103

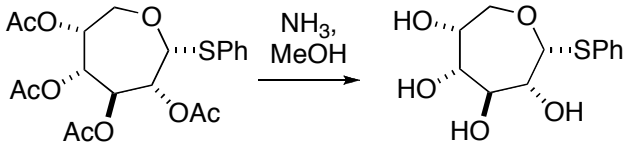


102 **103**

Thioglycoside **102** (3.1 g, 4.4 mmol) was dissolved in MeOH : THF (10 : 1) (0.04 M, 110 mL). Then K_2CO_3 (3.1 g, 22 mmol) was added all at once. The reaction was stirred for 1.5 hours, after which solid NH_4Cl (2.7 g, 5.1 mmol) was added. The solids were filtered away, and the volatiles were evaporated under reduced pressure. CH_2Cl_2 (0.10 M, 44 mL) was added to the crude mixture, followed by sequential addition of Et_3N (6.2 mL, 44 mmol) and Ac_2O (4.1 mL, 44 mmol). DMAP (100 mg) was then added. The reaction was stirred for 1 hour and then

diluted with CH_2Cl_2 (100 mL). Saturated $NaHCO_3$ (200 mL) was then added. The layers were separated. The aqueous layer was extracted with Et_2O (100 mL). The organics were combined and dried with $MgSO_4$. After filtration, the mixture was concentrated. Chromatography (9:1→1:1 hexanes:EtOAc) gave peracetate **103** as a white solid (1.6 g, 84 %). mp 41-44 °C; $[\alpha]_D^{23}$ = - 32.5 (c 1.25, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (m, 2H), 7.33 (m, 3H), 5.65 (dd, *J* = 6.0, 9.2 Hz, 1H), 5.55 (dd, *J* = 2.8, 6.0 Hz, 1H), 5.25 (dd, *J* = 1.6, 10.0 Hz, 1H), 5.19 (m, 1H), 4.99 (d, *J* = 2.8 Hz, 1H), 4.13 (dd, *J* = 2.4, 14.0 Hz, 1H), 3.52 (dd, *J* = 2.8, 14.0 Hz, 1H), 2.16 (2, 6H), 2.03 (s, 3H), 2.00 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.3, 169.8, 169.7, 169.6, 133.4, 132.9, 132.7, 129.4, 129.2, 128.8, 90.9, 75.1, 72.0, 71.2, 71.1, 69.8, 21.1, 20.8, 20.8, 20.7; IR (KBr) 2953, 1748, 1372, 1224, 1045 cm^{-1}; HRMS (ESI) [M+Na$^+$] Calcd. for $C_{20}H_{24}O_9S_1Na_1$ 463.10333, found 463.10374.

Synthesis of polyol 104

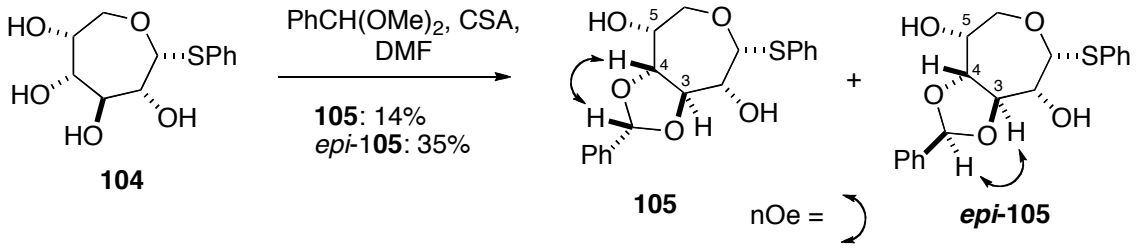


103 **104**

Peracetate thioglycoside **103** (1.5 g, 3.5 mmol) was dissolved in MeOH (0.18 M, 20 mL). NH_3 (g) was then bubbled through the reaction over a 10 minute period. The reaction was fitted with a stopper and tightly sealed. After stirring for 17 hours, the volatiles were removed under reduced pressure. Toluene and Et_2O were added to the crude gum, and the mixture was scraped until a white solid was obtained. The organics were decanted, and the solid was placed under high

vacuum for 24 hours giving analytically pure polyol **104** (710 mg, 74%). mp 120-125 °C; $[\alpha]_D^{23}$ = + 6.6 (c 1.23, MeOH); ^{1}H NMR (400 MHz, CD_3OD) δ 7.38 (m, 2H), 7.17 (m, 3H), 4.99 (d, *J* = 2.0 Hz, 1H), 3.89 (m, 2H), 3.80 (m, 2H), 3.70 (dd, *J* = 1.6, 6.8 Hz, 1H), 3.42 (dd, *J* = 2.8, 12.8 Hz, 1H); ^{13}C NMR (100 MHz, CD_3OD) δ 136.6, 133.0, 130.1, 128.5, 91.7, 78.9, 76.5, 75.3, 73.2, 72.9; IR (KBr) 3350, 2912, 1662, 1439, 1392, 1057, 739 cm^{-1}; HRMS (ESI) [M+Na$^+$] Calcd. for $C_{12}H_{16}O_5Na_1S_1$ 295.06107, found 295.06120.

Synthesis of benzylidene acetals 105 - *epi*-105



Thioglycoside polyol **104** (850 mg, 3.1 mmol) was dissolved in DMF (0.10 M, 31 mL). Benzylidene dimethyl acetal (0.94 mL, 6.3 mmol) was added followed by the addition of CSA (780 mg, 3.1 mmol). After 1.2 hours, additional benzylidene dimethyl acetal (1.0 mL, 6.6 mmol) was added to the reaction mixture. After 1 hour of stirring, the reaction was diluted with EtOAc (75 mL) and quenched by the addition of saturated $NaHCO_3$ (100 mL). After separation, the aqueous layer was then extracted with EtOAc (100 mL). The organics were combined and dried with $MgSO_4$. After filtration, the volatiles were evaporated under reduced pressure. The crude mixture was dissolved in Et_2O and washed with saturated $CuSO_4$ to remove excess DMF. The organic layer was then dried with $MgSO_4$. After filtration, the volatiles were evaporated under reduced pressure.

Chromatography (2:1→1:1 hexanes:EtOAc) gave benzylidene acetal **105** (160 mg, 14%) and benzylidene acetal ***epi*-105** (390 mg, 35%). **105**: mp 172-175 °C; $[\alpha]_D^{23}$ = - 38.8 (c 0.44, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.58-7.47 (m, 4H), 7.42-7.34 (m, 6H), 6.11(s, 1H), 4.87 (d, *J* = 3.6 Hz, 1H), 4.69 (dd, *J* = 7.6, 10.0 Hz, 1H), 4.34 (ddd, *J* = 3.6, 6.4, 10.4 Hz, 1H), 4.30 (dd, *J* = 1.2, 14.0 Hz, 1H), 4.19 (m, 1H), 4.00 (dd, *J* = 2.0, 9.2 Hz, 1H), 3.44 (dd, *J* = 2.4, 14.4 Hz, 1H), 2.57 (d, *J* = 6.4 Hz, 1H), 2.38 (m, 1H); ^{13}C NMR (100 MHz, CD_3OD) δ 139.8, 136.1, 133.8, 130.5, 130.1, 129.4, 128.8, 128.0, 106.5, 97.6, 82.1, 79.6, 78.2, 74.9, 70.7; IR (KBr) 3390, 2916, 1658, 1439, 1313, 1211, 1057, 997, 750 cm^{-1}; HRMS (ESI) [M+H^+] Calcd. for $C_{19}H_{21}O_5S_1$ 361.11042, found 361.11065.

***epi*-105**: mp 165-168 °C; $[\alpha]_D^{23}$ = + 22.5 (c 0.70, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.59-7.49 (m, 4H), 7.43-7.34 (m, 6H), 6.08(s, 1H), 4.91 (d, *J* = 3.6 Hz, 1H), 4.62 (dd, *J* = 7.2, 9.2 Hz, 1H), 4.31-4.23 (m, 3H), 4.07 (dd, *J* = 2.0, 9.2 Hz, 1H), 3.45 (dt, *J* = 2.4, 14.0 Hz, 1H), 2.50 (d, *J* = 6.4 Hz, 1H), 2.27 (m, 1H); ^{13}C NMR (100 MHz, CD_3OD) δ 139.8, 136.3, 133.8, 130.5, 130.1, 129.3, 128.8, 128.3, 105.4, 97.3, 80.9, 80.3, 78.6, 75.7, 69.4; IR (KBr) 3417, 2889, 1458, 1406, 1219, 1066, 1024, 735 cm^{-1}; HRMS (ESI) [M+H] Calcd. for $C_{19}H_{21}O_5S_1$ 361.11042, found 361.11130.

Slow recrystallization of compound ***epi*-105** from a mixture of hexanes and ether provided crystals suitable for structural characterization by X-ray crystallography, resulting in the thermal ellipsoid diagram below:

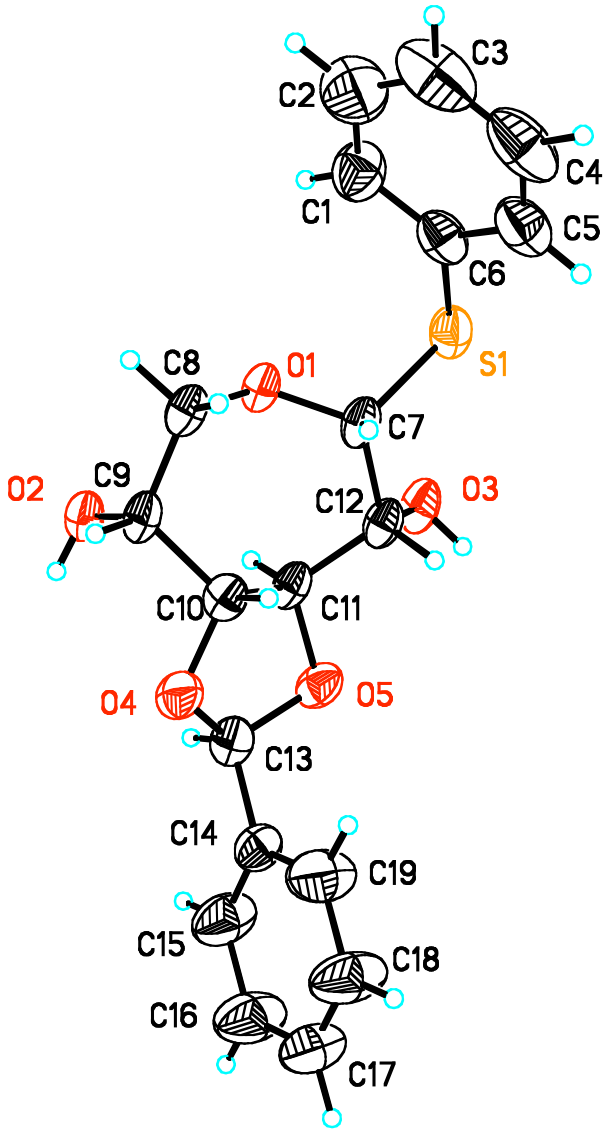

C3
C2
C4
C1
C5
C6
S1
C8
O1
C7
C9
O2
C12
O3
C10
C11
O4
O5
C13
C14
C19
C15
C18
C16
C17

Table 8. Crystal data and structure refinement for ***epi*-105**

Identification code	b103_4_253s	
Empirical formula	C19 H20 O5 S	
Formula weight	360.41	
Temperature	173(2) K	
Wavelength	1.54178 Å	
Crystal system	Orthorhombic	
Space group	P2(1)2(1)2(1)	
Unit cell dimensions	a = 13.6655(13) Å	α= 90°.
	b = 30.786(3) Å	β= 90°.
	c = 8.6246(7) Å	γ = 90°.
Volume	3628.4(5) $Å^3$	
Z	8	
Density (calculated)	1.320 Mg/m^3	
Absorption coefficient	1.810 mm^{-1}	
F(000)	1520	
Crystal size	0.52 x 0.35 x 0.04 mm^3	
Theta range for data collection	2.87 to 64.43°.	
Index ranges	-15<=h<=12, -35<=k<=32, -9<=l<=9	
Reflections collected	22313	
Independent reflections	5677 [R(int) = 0.0542]	
Completeness to theta = 64.43°	95.8 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9311 and 0.4528	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	5677 / 0 / 455	
Goodness-of-fit on F^2	1.051	
Final R indices [I>2sigma(I)]	R1 = 0.0429, wR2 = 0.0967	
R indices (all data)	R1 = 0.0573, wR2 = 0.1033	
Absolute structure parameter	0.039(19)	
Largest diff. peak and hole	0.174 and -0.213 e.$Å^{-3}$	

Table 9. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for ***epi*-105** (b103_4_253s). U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor

	x	y	z	U(eq)
C(1)	6916(3)	11243(1)	10074(4)	56(1)
C(2)	7310(4)	11589(2)	9244(6)	77(1)
C(3)	6797(4)	11767(2)	8015(5)	77(2)
C(4)	5899(4)	11602(1)	7613(5)	74(1)
C(5)	5508(3)	11256(1)	8429(4)	58(1)
C(6)	6006(3)	11078(1)	9675(4)	44(1)
C(7)	6194(2)	10202(1)	10017(3)	35(1)
C(8)	7927(2)	10087(1)	9738(4)	37(1)
C(9)	8075(2)	9600(1)	9590(3)	36(1)
C(10)	7129(2)	9370(1)	9161(3)	35(1)
C(11)	6330(2)	9398(1)	10381(3)	34(1)
C(12)	5634(2)	9775(1)	10265(3)	35(1)
C(13)	6542(2)	8685(1)	9857(4)	42(1)
C(14)	6130(3)	8319(1)	8910(4)	41(1)
C(15)	6154(3)	7903(1)	9468(5)	68(1)
C(16)	5749(4)	7562(1)	8637(5)	79(2)
C(17)	5314(3)	7642(1)	7218(4)	63(1)
C(18)	5297(4)	8053(1)	6663(5)	81(2)
C(19)	5695(4)	8391(1)	7506(5)	73(1)
C(1A)	2106(3)	11295(1)	9736(5)	57(1)
C(2A)	2524(3)	11623(1)	8854(5)	68(1)
C(3A)	2023(4)	11789(1)	7566(5)	68(1)
C(4A)	1107(4)	11627(1)	7197(5)	65(1)
C(5A)	700(3)	11300(1)	8083(4)	53(1)
C(6A)	1191(3)	11135(1)	9365(4)	44(1)
C(7A)	1252(2)	10249(1)	9838(3)	33(1)
C(8A)	2944(2)	10075(1)	9428(4)	38(1)
C(9A)	2974(2)	9589(1)	9239(4)	37(1)
C(10A)	1973(2)	9399(1)	8864(3)	36(1)
C(11A)	1231(2)	9444(1)	10175(3)	35(1)
C(12A)	614(2)	9854(1)	10181(3)	35(1)

C(13A)	1253(3)	8738(1)	9489(4)	43(1)
C(14A)	747(3)	8399(1)	8510(4)	46(1)
C(15A)	1310(3)	8091(1)	7768(4)	59(1)
C(16A)	846(4)	7759(1)	6909(5)	72(1)
C(17A)	-162(4)	7738(1)	6842(5)	66(1)
C(18A)	-722(3)	8048(1)	7572(4)	64(1)
C(19A)	-265(3)	8381(1)	8405(4)	53(1)
O(1)	7138(1)	10203(1)	10763(2)	34(1)
O(2)	8444(2)	9442(1)	11052(2)	40(1)
O(3)	5063(2)	9801(1)	11648(2)	42(1)
O(4)	7307(2)	8909(1)	9040(3)	45(1)
O(5)	5800(2)	9000(1)	10128(2)	40(1)
O(1A)	2206(1)	10223(1)	10508(2)	34(1)
O(2A)	3349(2)	9405(1)	10666(3)	42(1)
O(3A)	163(2)	9902(1)	11677(2)	42(1)
O(4A)	2052(2)	8935(1)	8676(3)	50(1)
O(5A)	602(2)	9075(1)	9903(2)	42(1)
S(1)	5458(1)	10647(1)	10743(1)	44(1)
S(1A)	610(1)	10729(1)	10525(1)	44(1)

Table 10. Bond lengths [Å] and angles [°] for ***epi*-105** (b103_4_253s)

C(1)-C(6)	1.387(5)
C(1)-C(2)	1.391(6)
C(2)-C(3)	1.383(6)
C(3)-C(4)	1.373(7)
C(4)-C(5)	1.384(6)
C(5)-C(6)	1.385(5)
C(6)-S(1)	1.781(4)
C(7)-O(1)	1.442(4)
C(7)-C(12)	1.535(4)
C(7)-S(1)	1.812(3)
C(8)-O(1)	1.440(3)
C(8)-C(9)	1.517(4)
C(9)-O(2)	1.443(4)
C(9)-C(10)	1.520(4)

C(10)-O(4)	1.443(4)
C(10)-C(11)	1.519(4)
C(11)-O(5)	1.440(4)
C(11)-C(12)	1.503(4)
C(12)-O(3)	1.428(3)
C(13)-O(5)	1.423(4)
C(13)-O(4)	1.437(4)
C(13)-C(14)	1.501(5)
C(14)-C(19)	1.367(5)
C(14)-C(15)	1.369(5)
C(15)-C(16)	1.386(5)
C(16)-C(17)	1.382(5)
C(17)-C(18)	1.352(5)
C(18)-C(19)	1.380(5)
C(1A)-C(6A)	1.381(5)
C(1A)-C(2A)	1.388(6)
C(2A)-C(3A)	1.401(6)
C(3A)-C(4A)	1.385(6)
C(4A)-C(5A)	1.381(5)
C(5A)-C(6A)	1.390(5)
C(6A)-S(1A)	1.785(4)
C(7A)-O(1A)	1.429(3)
C(7A)-C(12A)	1.527(4)
C(7A)-S(1A)	1.818(3)
C(8A)-O(1A)	1.445(3)
C(8A)-C(9A)	1.506(4)
C(9A)-O(2A)	1.449(4)
C(9A)-C(10A)	1.522(4)
C(10A)-O(4A)	1.443(4)
C(10A)-C(11A)	1.524(4)
C(11A)-O(5A)	1.445(4)
C(11A)-C(12A)	1.517(4)
C(12A)-O(3A)	1.437(3)
C(13A)-O(5A)	1.411(4)
C(13A)-O(4A)	1.432(4)
C(13A)-C(14A)	1.511(5)

C(14A)-C(15A)	1.379(5)
C(14A)-C(19A)	1.386(5)
C(15A)-C(16A)	1.413(6)
C(16A)-C(17A)	1.381(6)
C(17A)-C(18A)	1.376(6)
C(18A)-C(19A)	1.399(5)

C(6)-C(1)-C(2)	119.9(4)
C(3)-C(2)-C(1)	120.1(5)
C(4)-C(3)-C(2)	119.9(4)
C(3)-C(4)-C(5)	120.1(4)
C(4)-C(5)-C(6)	120.6(4)
C(5)-C(6)-C(1)	119.3(4)
C(5)-C(6)-S(1)	119.3(3)
C(1)-C(6)-S(1)	121.5(3)
O(1)-C(7)-C(12)	112.7(2)
O(1)-C(7)-S(1)	109.9(2)
C(12)-C(7)-S(1)	108.9(2)
O(1)-C(8)-C(9)	113.3(3)
O(2)-C(9)-C(8)	107.8(2)
O(2)-C(9)-C(10)	110.6(3)
C(8)-C(9)-C(10)	111.6(3)
O(4)-C(10)-C(11)	103.2(2)
O(4)-C(10)-C(9)	109.5(2)
C(11)-C(10)-C(9)	114.6(2)
O(5)-C(11)-C(12)	109.2(2)
O(5)-C(11)-C(10)	102.0(2)
C(12)-C(11)-C(10)	116.9(3)
O(3)-C(12)-C(11)	109.6(2)
O(3)-C(12)-C(7)	109.8(2)
C(11)-C(12)-C(7)	110.8(3)
O(5)-C(13)-O(4)	105.8(3)
O(5)-C(13)-C(14)	109.5(3)
O(4)-C(13)-C(14)	111.5(3)
C(19)-C(14)-C(15)	118.3(3)
C(19)-C(14)-C(13)	121.6(3)

C(15)-C(14)-C(13)	120.1(3)
C(14)-C(15)-C(16)	121.1(4)
C(17)-C(16)-C(15)	119.6(4)
C(18)-C(17)-C(16)	119.2(4)
C(17)-C(18)-C(19)	120.7(4)
C(14)-C(19)-C(18)	121.1(4)
C(6A)-C(1A)-C(2A)	120.4(4)
C(1A)-C(2A)-C(3A)	119.9(4)
C(4A)-C(3A)-C(2A)	119.6(4)
C(5A)-C(4A)-C(3A)	119.9(4)
C(4A)-C(5A)-C(6A)	120.8(4)
C(1A)-C(6A)-C(5A)	119.4(4)
C(1A)-C(6A)-S(1A)	121.5(3)
C(5A)-C(6A)-S(1A)	119.2(3)
O(1A)-C(7A)-C(12A)	113.4(2)
O(1A)-C(7A)-S(1A)	110.8(2)
C(12A)-C(7A)-S(1A)	108.0(2)
O(1A)-C(8A)-C(9A)	113.7(3)
O(2A)-C(9A)-C(8A)	107.9(3)
O(2A)-C(9A)-C(10A)	110.4(3)
C(8A)-C(9A)-C(10A)	112.2(3)
O(4A)-C(10A)-C(9A)	109.6(3)
O(4A)-C(10A)-C(11A)	102.9(2)
C(9A)-C(10A)-C(11A)	113.9(2)
O(5A)-C(11A)-C(12A)	108.9(2)
O(5A)-C(11A)-C(10A)	101.8(2)
C(12A)-C(11A)-C(10A)	116.6(3)
O(3A)-C(12A)-C(11A)	109.1(2)
O(3A)-C(12A)-C(7A)	109.6(2)
C(11A)-C(12A)-C(7A)	110.2(3)
O(5A)-C(13A)-O(4A)	107.1(3)
O(5A)-C(13A)-C(14A)	111.1(3)
O(4A)-C(13A)-C(14A)	111.6(3)
C(15A)-C(14A)-C(19A)	119.9(4)
C(15A)-C(14A)-C(13A)	118.6(4)
C(19A)-C(14A)-C(13A)	121.4(3)

C(14A)-C(15A)-C(16A)	119.4(4)
C(17A)-C(16A)-C(15A)	120.2(4)
C(18A)-C(17A)-C(16A)	120.2(4)
C(17A)-C(18A)-C(19A)	119.7(4)
C(14A)-C(19A)-C(18A)	120.6(4)
C(8)-O(1)-C(7)	113.3(2)
C(13)-O(4)-C(10)	108.3(2)
C(13)-O(5)-C(11)	104.3(2)
C(7A)-O(1A)-C(8A)	113.2(2)
C(13A)-O(4A)-C(10A)	107.9(2)
C(13A)-O(5A)-C(11A)	104.1(2)
C(6)-S(1)-C(7)	98.77(15)
C(6A)-S(1A)-C(7A)	99.85(15)

Table 11. Anisotropic displacement parameters ($Å^2$x 10^3)for ***epi*-105** (b103_4_253s). The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U^{11} + ... + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(1)	53(3)	64(3)	52(2)	9(2)	-8(2)	-1(2)
C(2)	73(3)	71(3)	88(3)	17(3)	13(3)	-2(2)
C(3)	110(4)	62(3)	58(3)	16(2)	32(3)	21(3)
C(4)	110(4)	66(3)	45(2)	5(2)	0(3)	39(3)
C(5)	75(3)	53(2)	45(2)	-7(2)	-13(2)	22(2)
C(6)	53(2)	46(2)	34(2)	-2(2)	4(2)	14(2)
C(7)	28(2)	53(2)	24(2)	-1(1)	-3(1)	-1(1)
C(8)	27(2)	52(2)	32(2)	1(2)	1(2)	-6(1)
C(9)	24(2)	53(2)	31(2)	-2(2)	1(2)	-2(1)
C(10)	32(2)	45(2)	28(2)	-4(2)	5(1)	-2(1)
C(11)	25(2)	50(2)	26(2)	-3(2)	1(1)	-5(1)
C(12)	26(2)	52(2)	28(2)	-1(1)	2(1)	-4(1)
C(13)	36(2)	50(2)	40(2)	-1(2)	-1(2)	0(2)
C(14)	42(2)	45(2)	37(2)	1(2)	-5(2)	-4(2)
C(15)	87(3)	55(2)	61(2)	11(2)	-32(2)	-15(2)
C(16)	113(4)	45(2)	78(3)	11(2)	-35(3)	-15(2)

C(17)	81(3)	52(2)	57(2)	0(2)	-14(2)	-18(2)
C(18)	129(4)	52(2)	62(2)	5(2)	-48(3)	-13(3)
C(19)	108(4)	47(2)	66(3)	6(2)	-37(3)	-2(2)
C(1A)	49(3)	61(2)	60(2)	5(2)	-12(2)	-2(2)
C(2A)	65(3)	67(3)	74(3)	-2(2)	-11(2)	-9(2)
C(3A)	86(4)	58(3)	60(3)	8(2)	6(3)	7(3)
C(4A)	81(3)	59(3)	54(2)	4(2)	-11(2)	17(2)
C(5A)	55(3)	51(2)	52(2)	-11(2)	-13(2)	12(2)
C(6A)	41(2)	48(2)	44(2)	-10(2)	-7(2)	9(2)
C(7A)	26(2)	50(2)	22(2)	-4(1)	-4(1)	0(1)
C(8A)	26(2)	55(2)	33(2)	2(2)	4(2)	-3(1)
C(9A)	28(2)	51(2)	33(2)	0(2)	7(2)	1(1)
C(10A)	30(2)	47(2)	30(2)	-3(1)	4(1)	-2(2)
C(11A)	26(2)	50(2)	29(2)	-4(2)	-1(1)	-9(1)
C(12A)	21(2)	57(2)	26(2)	-3(1)	0(1)	-2(1)
C(13A)	45(2)	48(2)	37(2)	1(2)	8(2)	-2(2)
C(14A)	57(3)	46(2)	34(2)	3(2)	-1(2)	-9(2)
C(15A)	66(3)	58(3)	54(2)	-4(2)	13(2)	-4(2)
C(16A)	101(4)	48(2)	66(3)	-11(2)	12(3)	-7(2)
C(17A)	89(4)	59(3)	51(2)	-9(2)	-4(2)	-23(2)
C(18A)	72(3)	64(3)	57(2)	-5(2)	-9(2)	-22(2)
C(19A)	58(3)	52(2)	48(2)	-4(2)	-3(2)	-9(2)
O(1)	24(1)	49(1)	29(1)	-3(1)	-2(1)	-1(1)
O(2)	29(1)	49(1)	40(1)	0(1)	-6(1)	2(1)
O(3)	24(1)	69(2)	31(1)	-7(1)	9(1)	-2(1)
O(4)	33(1)	49(1)	52(1)	-11(1)	9(1)	-5(1)
O(5)	32(1)	48(1)	41(1)	-5(1)	7(1)	-11(1)
O(1A)	23(1)	49(1)	28(1)	-2(1)	0(1)	-1(1)
O(2A)	30(1)	50(1)	47(1)	3(1)	-3(1)	1(1)
O(3A)	25(1)	70(2)	30(1)	-8(1)	7(1)	-4(1)
O(4A)	39(2)	50(2)	60(2)	-13(1)	15(1)	-8(1)
O(5A)	34(1)	50(1)	40(1)	-6(1)	5(1)	-11(1)
S(1)	34(1)	55(1)	43(1)	-6(1)	-1(1)	5(1)
S(1A)	35(1)	54(1)	44(1)	-7(1)	-2(1)	7(1)

Table 12. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for ***epi*-105** (b103_4_253s)

	x	y	z	U(eq)
H(1)	7271	11120	10913	68
H(2)	7931	11704	9521	93
H(3)	7067	12004	7449	92
H(4)	5545	11725	6773	88
H(5)	4892	11139	8132	69
H(7)	6293	10244	8879	42
H(8A)	8540	10220	10126	44
H(8B)	7794	10209	8698	44
H(9)	8573	9543	8765	43
H(10)	6880	9483	8150	42
H(11)	6632	9393	11437	40
H(12)	5187	9726	9364	42
H(13)	6796	8571	10867	50
H(15)	6454	7846	10442	82
H(16)	5771	7275	9039	95
H(17)	5031	7412	6640	76
H(18)	5008	8110	5682	97
H(19)	5667	8677	7103	88
H(1A)	2450	11180	10600	68
H(2A)	3150	11735	9122	82
H(3A)	2310	12011	6951	82
H(4A)	759	11741	6335	78
H(5A)	76	11187	7812	63
H(7A)	1327	10274	8688	39
H(8A1)	3592	10176	9789	45
H(8A2)	2818	10209	8404	45
H(9A)	3435	9516	8377	45
H(10A)	1709	9534	7895	43
H(11A)	1569	9411	11197	42
H(12A)	93	9829	9370	42

H(13A)	1507	8598	10454	52
H(15A)	2003	8102	7834	71
H(16A)	1229	7549	6375	86
H(17A)	-471	7509	6290	79
H(18A)	-1416	8036	7511	77
H(19A)	-650	8597	8903	64
H(2B)	8572	9176	10977	59
H(3B)	4527	9674	11512	62
H(2A1)	3385	9133	10579	63
H(3A1)	-378	9772	11683	62

Table 13. Torsion angles [°] for ***epi*-105** (b103_4_253s)

C(6)-C(1)-C(2)-C(3)	-0.4(7)
C(1)-C(2)-C(3)-C(4)	0.0(7)
C(2)-C(3)-C(4)-C(5)	-0.4(7)
C(3)-C(4)-C(5)-C(6)	1.3(6)
C(4)-C(5)-C(6)-C(1)	-1.7(5)
C(4)-C(5)-C(6)-S(1)	177.6(3)
C(2)-C(1)-C(6)-C(5)	1.3(6)
C(2)-C(1)-C(6)-S(1)	-178.0(3)
O(1)-C(8)-C(9)-O(2)	-69.1(3)
O(1)-C(8)-C(9)-C(10)	52.6(3)
O(2)-C(9)-C(10)-O(4)	-59.8(3)
C(8)-C(9)-C(10)-O(4)	-179.8(2)
O(2)-C(9)-C(10)-C(11)	55.5(3)
C(8)-C(9)-C(10)-C(11)	-64.5(4)
O(4)-C(10)-C(11)-O(5)	-31.7(3)
C(9)-C(10)-C(11)-O(5)	-150.7(3)
O(4)-C(10)-C(11)-C(12)	-150.7(3)
C(9)-C(10)-C(11)-C(12)	90.4(3)
O(5)-C(11)-C(12)-O(3)	76.4(3)
C(10)-C(11)-C(12)-O(3)	-168.5(2)
O(5)-C(11)-C(12)-C(7)	-162.3(2)
C(10)-C(11)-C(12)-C(7)	-47.2(3)
O(1)-C(7)-C(12)-O(3)	89.0(3)

S(1)-C(7)-C(12)-O(3)	-33.2(3)
O(1)-C(7)-C(12)-C(11)	-32.1(3)
S(1)-C(7)-C(12)-C(11)	-154.3(2)
O(5)-C(13)-C(14)-C(19)	56.0(5)
O(4)-C(13)-C(14)-C(19)	-60.7(5)
O(5)-C(13)-C(14)-C(15)	-121.9(4)
O(4)-C(13)-C(14)-C(15)	121.5(4)
C(19)-C(14)-C(15)-C(16)	-0.1(7)
C(13)-C(14)-C(15)-C(16)	177.9(4)
C(14)-C(15)-C(16)-C(17)	0.1(8)
C(15)-C(16)-C(17)-C(18)	0.4(8)
C(16)-C(17)-C(18)-C(19)	-0.9(8)
C(15)-C(14)-C(19)-C(18)	-0.5(7)
C(13)-C(14)-C(19)-C(18)	-178.4(4)
C(17)-C(18)-C(19)-C(14)	1.0(8)
C(6A)-C(1A)-C(2A)-C(3A)	-0.9(6)
C(1A)-C(2A)-C(3A)-C(4A)	0.8(7)
C(2A)-C(3A)-C(4A)-C(5A)	-0.9(6)
C(3A)-C(4A)-C(5A)-C(6A)	1.2(6)
C(2A)-C(1A)-C(6A)-C(5A)	1.1(6)
C(2A)-C(1A)-C(6A)-S(1A)	-177.3(3)
C(4A)-C(5A)-C(6A)-C(1A)	-1.2(5)
C(4A)-C(5A)-C(6A)-S(1A)	177.2(3)
O(1A)-C(8A)-C(9A)-O(2A)	-69.8(3)
O(1A)-C(8A)-C(9A)-C(10A)	52.0(3)
O(2A)-C(9A)-C(10A)-O(4A)	-60.4(3)
C(8A)-C(9A)-C(10A)-O(4A)	179.2(2)
O(2A)-C(9A)-C(10A)-C(11A)	54.2(3)
C(8A)-C(9A)-C(10A)-C(11A)	-66.2(4)
O(4A)-C(10A)-C(11A)-O(5A)	-33.1(3)
C(9A)-C(10A)-C(11A)-O(5A)	-151.7(3)
O(4A)-C(10A)-C(11A)-C(12A)	-151.4(3)
C(9A)-C(10A)-C(11A)-C(12A)	90.0(3)
O(5A)-C(11A)-C(12A)-O(3A)	81.4(3)
C(10A)-C(11A)-C(12A)-O(3A)	-164.2(2)
O(5A)-C(11A)-C(12A)-C(7A)	-158.2(2)

C(10A)-C(11A)-C(12A)-C(7A)	-43.9(3)
O(1A)-C(7A)-C(12A)-O(3A)	83.4(3)
S(1A)-C(7A)-C(12A)-O(3A)	-39.8(3)
O(1A)-C(7A)-C(12A)-C(11A)	-36.7(3)
S(1A)-C(7A)-C(12A)-C(11A)	-159.9(2)
O(5A)-C(13A)-C(14A)-C(15A)	168.2(3)
O(4A)-C(13A)-C(14A)-C(15A)	48.7(4)
O(5A)-C(13A)-C(14A)-C(19A)	-14.7(4)
O(4A)-C(13A)-C(14A)-C(19A)	-134.2(3)
C(19A)-C(14A)-C(15A)-C(16A)	-0.1(5)
C(13A)-C(14A)-C(15A)-C(16A)	177.0(3)
C(14A)-C(15A)-C(16A)-C(17A)	-1.4(6)
C(15A)-C(16A)-C(17A)-C(18A)	2.0(7)
C(16A)-C(17A)-C(18A)-C(19A)	-1.1(6)
C(15A)-C(14A)-C(19A)-C(18A)	1.1(6)
C(13A)-C(14A)-C(19A)-C(18A)	-176.0(3)
C(17A)-C(18A)-C(19A)-C(14A)	-0.5(6)
C(9)-C(8)-O(1)-C(7)	-84.7(3)
C(12)-C(7)-O(1)-C(8)	96.4(3)
S(1)-C(7)-O(1)-C(8)	-142.0(2)
O(5)-C(13)-O(4)-C(10)	13.8(3)
C(14)-C(13)-O(4)-C(10)	132.7(3)
C(11)-C(10)-O(4)-C(13)	11.3(3)
C(9)-C(10)-O(4)-C(13)	133.7(3)
O(4)-C(13)-O(5)-C(11)	-34.7(3)
C(14)-C(13)-O(5)-C(11)	-154.9(2)
C(12)-C(11)-O(5)-C(13)	165.2(2)
C(10)-C(11)-O(5)-C(13)	40.9(3)
C(12A)-C(7A)-O(1A)-C(8A)	97.9(3)
S(1A)-C(7A)-O(1A)-C(8A)	-140.4(2)
C(9A)-C(8A)-O(1A)-C(7A)	-81.9(3)
O(5A)-C(13A)-O(4A)-C(10A)	10.9(3)
C(14A)-C(13A)-O(4A)-C(10A)	132.8(3)
C(9A)-C(10A)-O(4A)-C(13A)	135.6(3)
C(11A)-C(10A)-O(4A)-C(13A)	14.0(3)
O(4A)-C(13A)-O(5A)-C(11A)	-32.8(3)

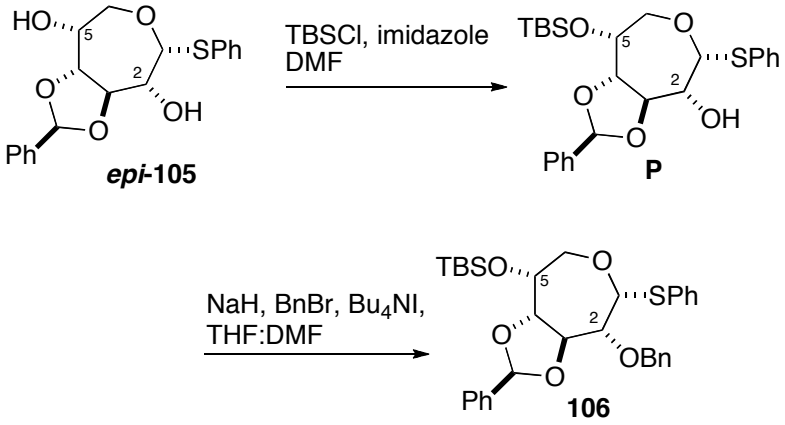
C(14A)-C(13A)-O(5A)-C(11A)	-154.9(2)
C(12A)-C(11A)-O(5A)-C(13A)	164.1(2)
C(10A)-C(11A)-O(5A)-C(13A)	40.4(3)
C(5)-C(6)-S(1)-C(7)	105.4(3)
C(1)-C(6)-S(1)-C(7)	-75.3(3)
O(1)-C(7)-S(1)-C(6)	77.6(2)
C(12)-C(7)-S(1)-C(6)	-158.5(2)
C(1A)-C(6A)-S(1A)-C(7A)	-79.0(3)
C(5A)-C(6A)-S(1A)-C(7A)	102.6(3)
O(1A)-C(7A)-S(1A)-C(6A)	77.5(2)
C(12A)-C(7A)-S(1A)-C(6A)	-157.7(2)

Table 14. Hydrogen bonds for ***epi*-105** (b103_4_253s) [Å and °]

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
O(3A)-H(3A1)...O(2)#1	0.84	1.98	2.795(3)	163.2
O(3)-H(3B)...O(2A)	0.84	1.95	2.774(3)	166.1

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

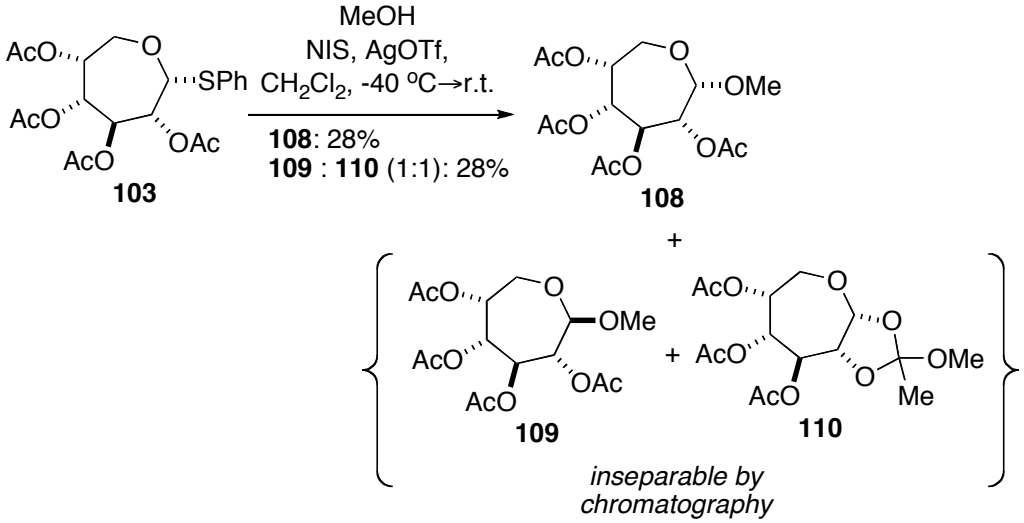
Synthesis of thioglycoside 106



***Epi*-105** (140 mg, 0.39 mmol) was dissolved in DMF (0.39 M, 1.0 mL). Then imidazole (82 mg, 1.2 mmol) was added all at once followed by TBSCl (71 mg, 0.47 mmol). The reaction was allowed to stir for 15 hours. The reaction was diluted with EtOAc (3 mL) followed by H_2O (3 mL). After separation, the aqueous layer was extracted with EtOAc (2 x 2 mL). The organic extracts were combined and dried with $MgSO_4$. After filtration, the volatiles were evaporated under reduced pressure. Chromatography (4:1→2:1 hexanes:EtOAc) gave **P** as an oil (67 mg, 36%). $[\alpha]_D^{23}$ = - 41.9 (c 1.07, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.59-7.47 (m, 4H), 7.41-7.31 (m, 6H), 6.06 (s, 1H), 4.80 (d, *J* = 3.6 Hz, 1H), 4.58 (dd, *J* = 6.4, 9.2 Hz, 1H), 4.27 (dd, *J* = 3.6, 6.8 Hz, 1H), 4.24 (dd, *J* = 1.2, 14.0 Hz, 1H), 4.16 (m, 1H), 4.02 (dd, *J* = 1.6, 9.6 Hz, 1H), 3.33 (dd, *J* = 2.0, 13.6 Hz, 1H), 0.99 (s, 9H), 0.23 (s, 3H), 0.20 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.4, 134.9, 133.6, 129.5, 129.1, 128.7, 128.2, 126.4, 104.1, 92.3, 79.7, 79.5, 76.0, 75.9, 68.5, 26.3, 18.8, -3.83, -4.85; IR (KBr) 3431, 2927, 2856, 1462, 1254, 1068, 837, 781 cm^{-1}; HRMS (ESI) [M+Na^+] Calcd. for $C_{25}H_{34}O_5Na_1S_1Si_1$ 497.17885, found 497.17950.

P (67 mg, 0.14 mmol) was then dissolved in THF (0.18 M, 0.80 mL) and DMF (0.01M, 0.05 mL). The solution was cooled to 0 ^{o}C. NaH (60% dispersion, 110 mg, 0.28 mmol) was then added, followed by BnBr (0.033 mL, 0.28 mmol) and Bu_4NI (10 mg). The reaction was allowed to warm to r.t. After 15 minutes, TLC indicated consumption of the starting material. The reaction was diluted with Et_2O (2 mL) and quenched with saturated NH_4Cl (2 mL). After separation, the aqueous layer was extracted with EtOAc (2 x 5 mL). The organic extracts were combined and dried with $MgSO_4$. After filtration, the volatiles were removed under reduced pressure. Chromatography (9:1→4:1 hexanes:EtOAc) gave **106** as an oil (52 mg, 66 %). $[\alpha]_D^{23}$ = + 13.1 (c 2.62, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57-7.50 (m, 5H), 7.37 - 7.26 (m, 6H), 5.99 (s, 1H), 4.81 (d, *J* = 3.2 Hz, 1H), 4.71 (dd, *J* = 6.4, 9.2 Hz, 1H), 4.69 (d, *J* = 12.0 Hz, 1H), 4.63 (d, *J* = 12.0 Hz, 1H) 4.26 (m, 2H), 4.04 (dd, *J* = 1.6, 9.2 Hz, 1H), 3.93 (m, 1H), 3.23 (m,1H), 3.23 (dd, *J* = 1.6, 13.6 Hz, 1H), 0.97 (s, 9H), 0.21 (s, 3H), 0.15 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.7, 138.4, 135.2, 133.5, 129.3, 128.9, 128.4, 128.4, 128.0, 127.9, 127.6, 126.8, 104.3, 97.4, 79.9, 76.4, 75.3, 74.9, 72.9, 26.3, 18.8, -3.84, -4.94; IR (KBr) 2927, 2856, 1462, 1254, 1065, 839, 696 cm^{-1}; HRMS (APCI) [M+H$^+$] Calcd. for $C_{32}H_{41}O_5S_1Si_1$ 565.24385 , found 565.24416.

Synthesis of methyl glycoside glucoseptanose 108



Thioglycoside **103** (1.5 g, 3.4 mmol) was dissolved in CH_2Cl_2 (0.10 M, 34 mL). Freshly dried, powdered 4 Å MS (1.0 g) were added, and the solution was cooled to -40 °C. MeOH (0.28 mL, 6.8 mmol) was added. Then NIS (960 mg, 4.3 mmol) and AgOTf (260 mg, 1.0 mmol) were added simultaneously. The reaction was then warmed to r.t., at which point the reaction became magenta in color. The reaction was quenched with Et_3N (1 mL) and filtered through a pad of celite. After concentration, chromatography gave **108** (350 mg, 28%). $[\alpha]_D^{23}$ = + 35.9 (c 1.00, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 5.52 (at, *J* = 7.6 Hz, 1H), 5.24 (m, 3H), 4.60 (d, *J* = 2.4 Hz, 1H), 4.10 (dd, *J* = 5.2, 13.6 Hz, 1H), 3.73 (dd, *J* = 3.2, 13.6 Hz, 1H), 3.44 (s, 3H), 2.13 (s, 3H), 2.10 (s, 3H), 2.06 (s, 3H), 2.04 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.2, 170.1, 169.9, 169.6, 101.6, 73.5, 71.3, 71.0, 70.7, 65.2, 56.5, 21.1, 20.9, 20.8; IR (KBr) 2958, 1747, 1371, 1227, 1036 cm^{-1}; HRMS (ESI) [M+H$^+$] Calcd. for $C_{15}H_{23}O_{10}$ 363.12857, found 363.12881.

Chapter 2

Chapter 2

Biomimetic Total Synthesis of the Proposed Structure of *ent*-Muzitone

2.1. Introduction and Background

2.1.1. Biogenetic origin of squalene-derived natural products

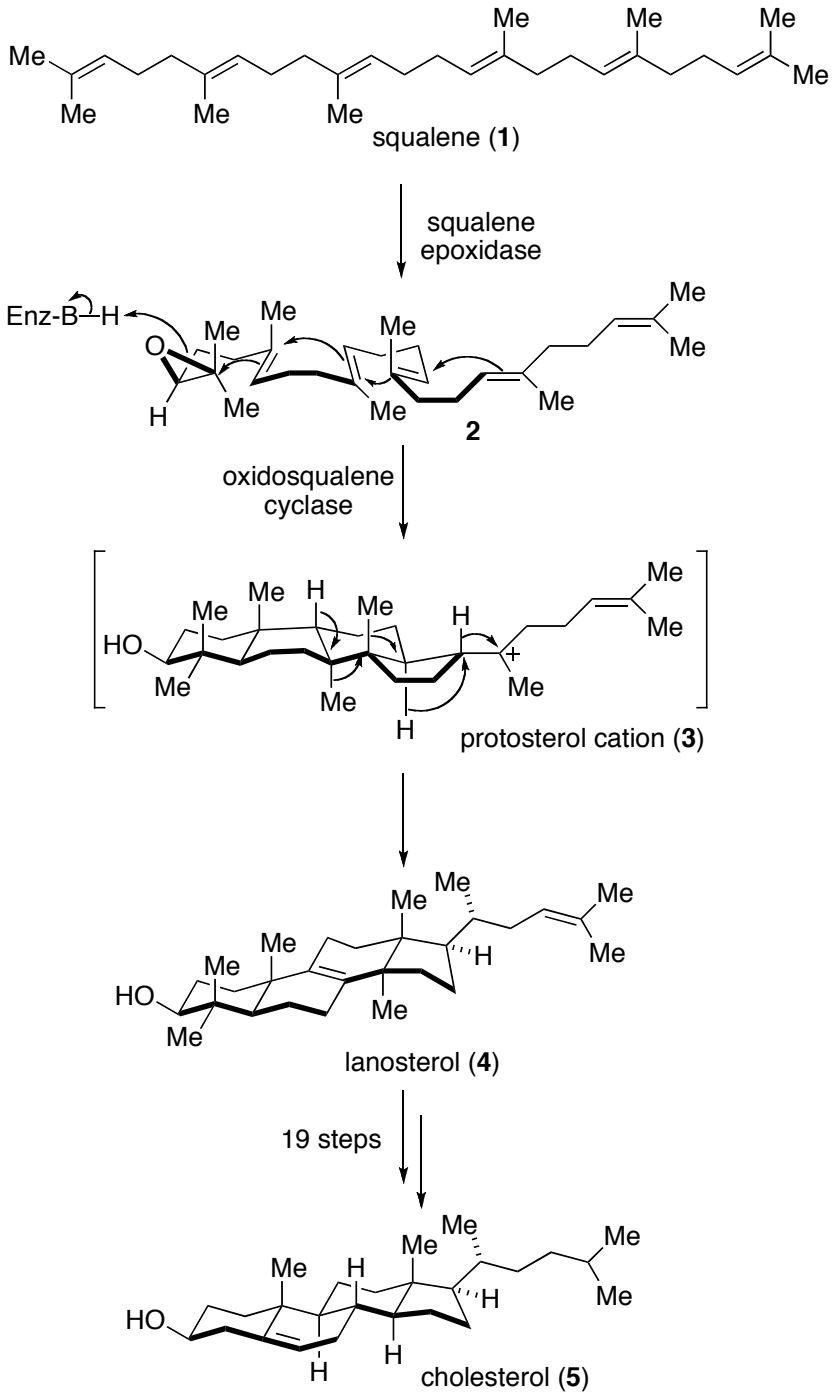
2.1.1.1. Importance of the biomimetic synthesis of polycyclic isoprenoid natural products; Stereospecificity of polycyclization cascades

Curiosity has been a long standing impetus for scientific discovery. It is with no exception that the vast array of complex chemical architectures in the realm of natural products raises a question born out of a simple curiosity of how nature goes about "putting together" such molecules. As the science of natural product total synthesis has developed in parallel with a continually expanding understanding of the biochemical pathways involved in natural product biosynthesis, synthetic chemists have been able to harness great inspiration from the elegance and efficiency of natural product biogenesis by developing total syntheses of natural products based on the proposed biogenetic postulates for such structures. Thus, when Robinson[43] demonstrated the concept of biomimetic synthesis in his disclosure of the biomimetic total synthesis of tropinone almost a century ago, he pioneered a vast area of scientific discovery that retains intense interest in the modern day.

The success of biomimetic synthesis as a viable area of science has been directly linked to the discovery of biosynthetic pathways involved in natural

product biosynthesis. This synergism has ultimately led to the discovery of novel synthetic methodologies and has served as a means of drug discovery. For example, much effort has focused on the elucidation of the biogenesis of polycyclic isoprenoid natural products, such as hopene, lanosterol, cholesterol, sophoradiol, and progesterone, each ubiquitous biologically important molecules in the natural world.[44] The great insight into the biogenesis of cholesterol (**1**) has led to the discovery of novel therapeutic agents for the treatment of hypercholesterolemia.[45] The stereocontrolled construction of cholesterol (**1**) is considered to be a paragon of biosynthetic chemistry (Scheme 1). Decades of research have given considerable experimental support to the biogenetic origins of cholesterol and related polycyclic isoprenoid natural products.[46] Notable among these contributions were early investigations from Stork[47] and Eschenmoser[48], whom independently demonstrated the stereospecificity of carbacyclizations (*Z*-alkenes lead to *cis*-fused ring junctions; *E*-alkenes lead to *trans*-fused ring junctions).

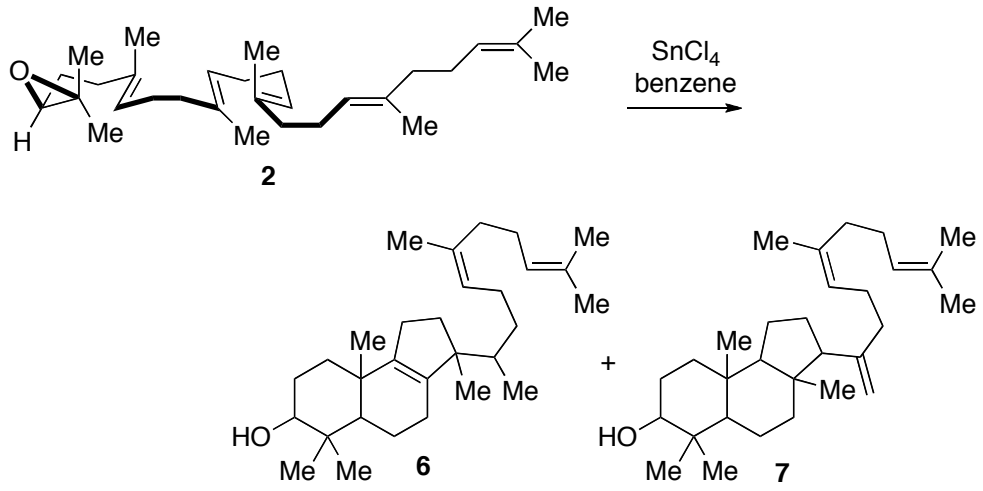
Scheme 1. Polycyclization of squalene 2,3-oxidosqualene: Biosynthesis of cholesterol



2.1.1.2. Biomimetic total synthesis of squalene-derived natural products featuring polycyclization cascades: experimental evidence for the biogenesis of squalene-derived natural products

van Tamelen provided an early yet notable contribution in the biomimetic cyclization of 2,3-oxidosqualene in an effort to provide the first chemical evidence for the biogenetic origin of squalene-derived natural products.[49] The cyclization of 2,3-oxidosqualene was initiated by treatment with $SnCl_4$. Interestingly, under these abiological conditions, the expected 5-*exo* Markovnikov closure of the C ring was observed in the isolated products **6** and **7**, thus implicating what would later become understood as the significant role of the cyclase enzyme in the observed 6-*endo* anti-Markovnikov C ring closure (Scheme 2).

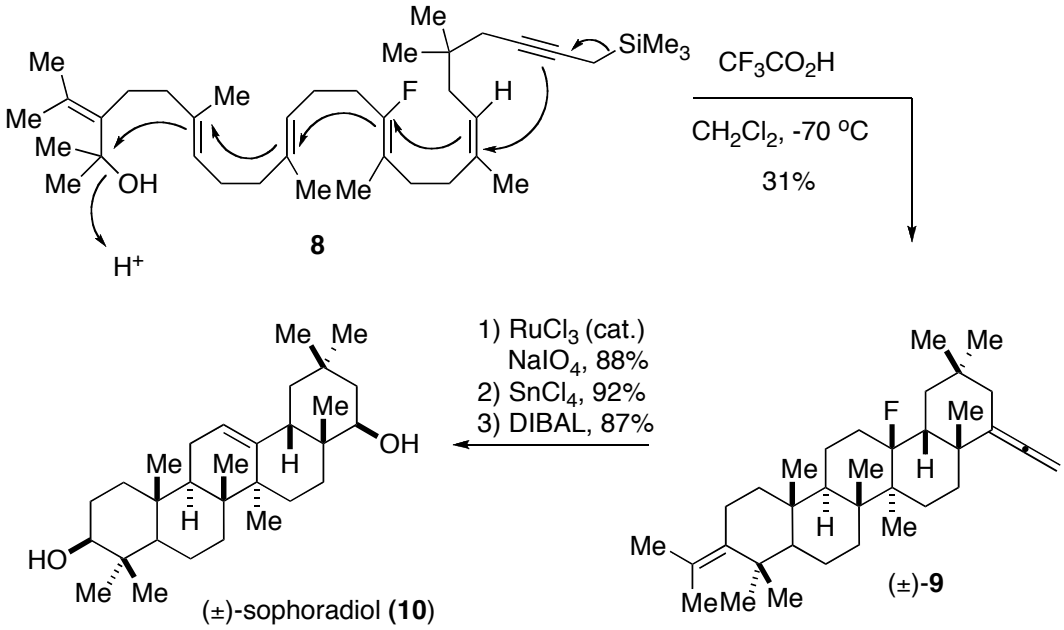
Scheme 2. van Tamelen's polycyclization of 2,3-oxidosqualene



The first experimental confirmations of the "Stork-Eschenmoser" hypothesis and the postulate for isoprenoid polycyclication came in a landmark biomimetic total synthesis of the natural product (±)-sophoradiol (**10**) by Johnson.[50] Johnson's impact on the area of biomimetic polycyclization of squalene-derived

natural products was extraordinary.[51] Among his contributions, Johnson demonstrated that fluoride could be used as a cation-stabilizing group, which served to induce "proper" C ring closure involving a 6-*endo* anti-Markovnikov cyclization. This circumvented the earlier problem of Markovnikov C ring closure observed by van Tamelen. Johnson also demonstrated that an alkyne was an effective nucleophilic terminator in a *pentacyclization* cascade, a remarkable feat that was highlighted in the total synthesis of (±)-sophoradiol (**10**)(Scheme 3).

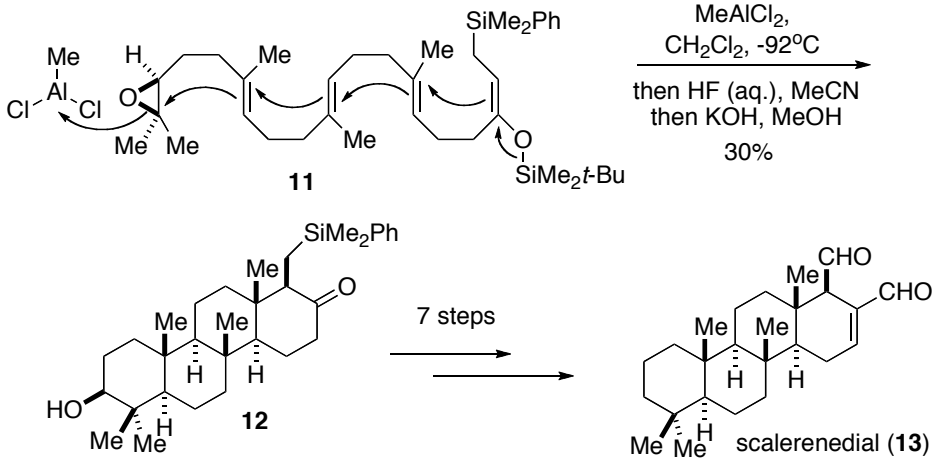
Scheme 3. Johnson's biomimetic total synthesis of (±)-sophoradiol

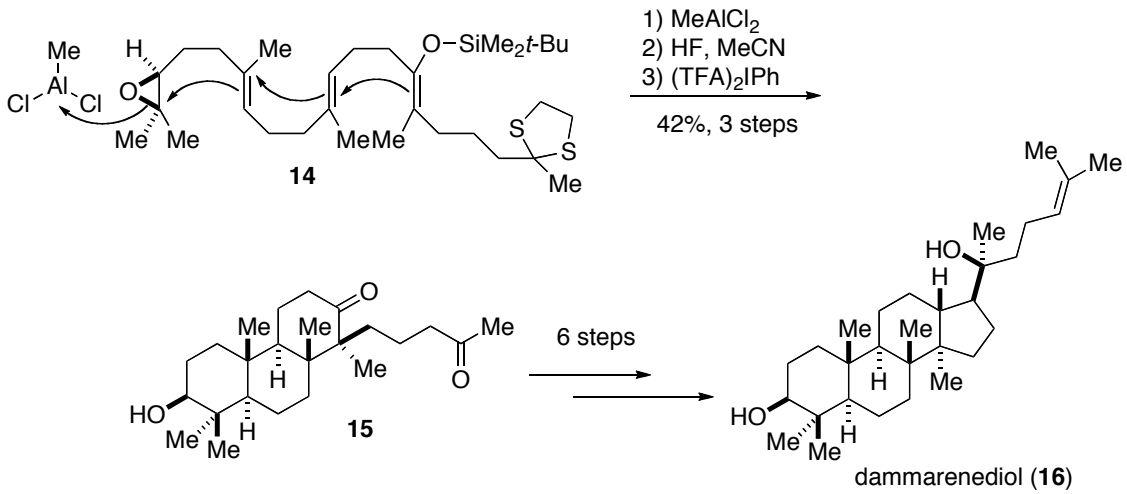


More recent synthetic achievements in the area of biomimetic polycyclization cascades of squalene-like epoxy-ene substrates have come from Corey, whom has harnessed modern methods of asymmetric synthesis to construct polycyclic frameworks with control of stereochemistry. Corey's notable achievement in this area was in the application of an enolsilane as a nucleophilic terminator for the cascade cyclization and as the source for anti-Markovnikov regiocontrol in C ring

formation. Corey made effective use of the enolsilane in cascade polycyclizations as featured in the elegant total syntheses of scalarenedial (**13**)[52] and dammarenediol II (**16**)[53] (Scheme 4).

Scheme 4. Corey's biomimetic syntheses of scalarenedial (13) and dammarenediol (16)



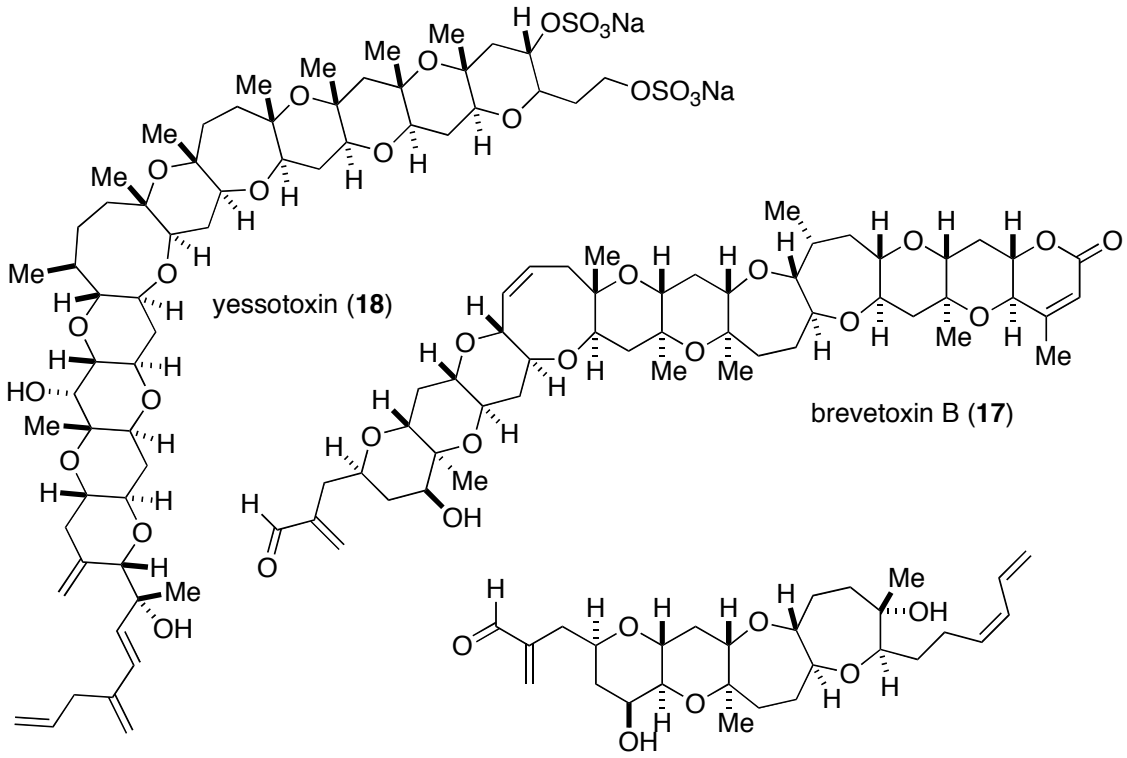


2.1.2. Biomimetic synthesis of polycyclic ether natural products

2.1.2.1. Biogenetic origin of polycyclic ether natural products

Nakanishi and Clardy reported the isolation and structure of brevetoxin B (**17**) in 1981, the first known member of the marine polycyclic ether natural product family (Figure 1).[54] Since the disclosure of brevetoxin B (**17**), numerous members of the polycyclic ether family have been isolated and characterized (Figure 1). These polycyclic ether natural products are potent toxins produced by harmful algal blooms, which are responsible for the "red-tide" phenomenon that reeks havoc on marine environments by causing massive fish and marine mammal kills.[55] Thus, the interesting molecular frameworks and biological activities of these molecules have provided a hotbed of research opportunities in the realms of synthetic and medicinal chemistry.

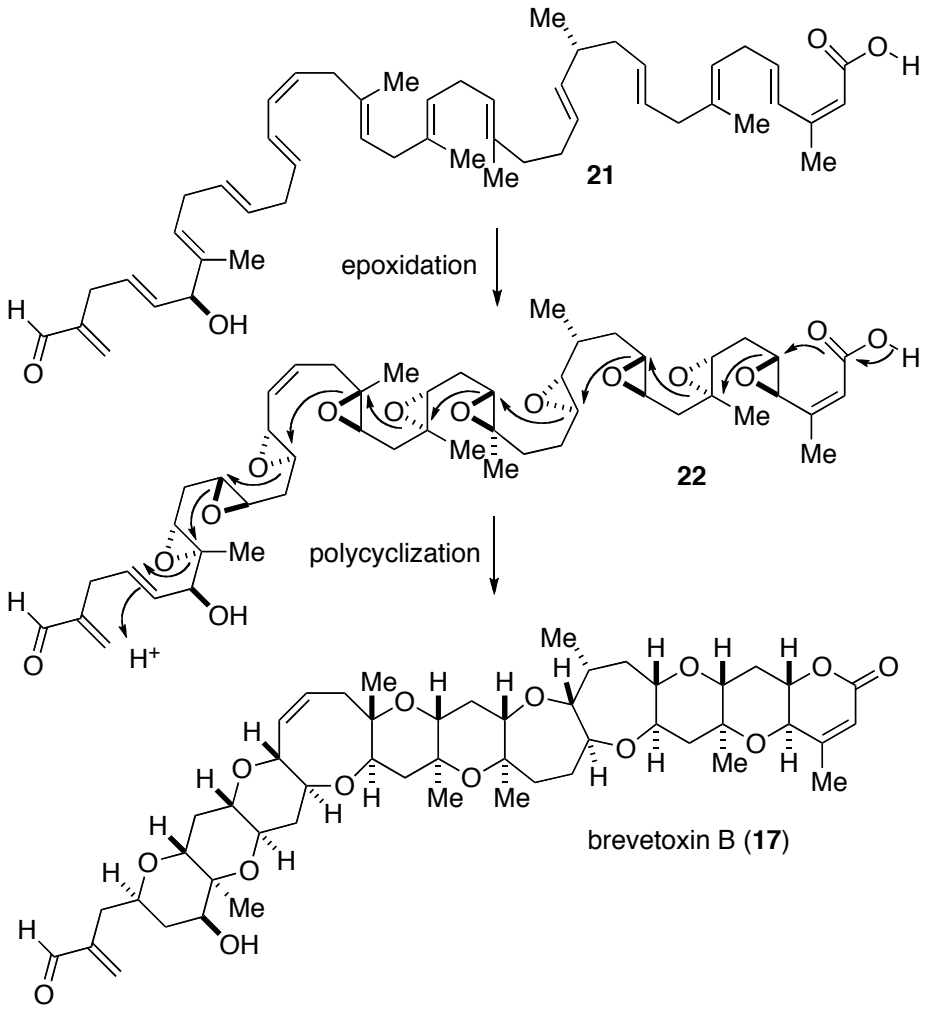
Figure 1. Representative marine polycyclic ether natural products



The current understanding of how these complex architectures are assembled was embodied in the proposed biogenetic hypothesis for brevetoxin B (**17**) by Nakanishi[56] (first postulated by Cane, Celmer, and Westley[57]), which was later supported by Shimizu[58] (Scheme 5). The common thread among these proposals was that the structural and stereochemical similarity among the

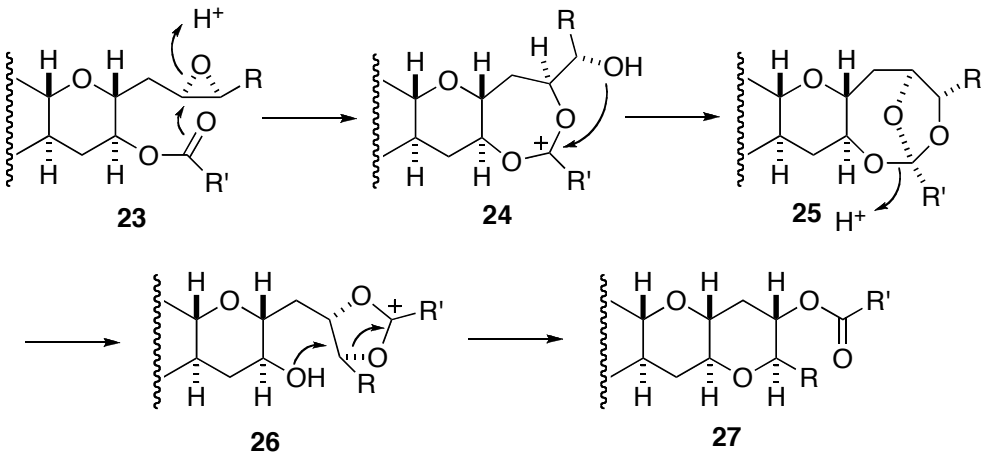
polycyclic ether family of natural products could be best explained by the commonality of the biosynthetic origin. The biogenetic hypothesis of brevetoxin B (**17**) requires a *uniformly stereoselective* epoxidation of a polyene precursor **21** to generate a polyepoxide precursor **22** that then undergoes a polyepoxide cascade cyclization to brevetoxin B (**17**). Despite the aesthetic appeal of such a proposal, Baldwin's rules[59] dictate that epoxide opening reactions of this type would tend to give the favored 5-*exo* pathway over the corresponding 6-*endo* pathway.

Scheme 5. Nakanishi's biosynthetic hypothesis for brevetoxin B (17)



While the Nakanishi hypothesis has provided a general basis for understanding the construction of such complex polyether scaffolds, there remains an ongoing effort to probe the validity of the claim and, in the case of Giner and Mullins[60], to propose a completely novel biogenetic postulate of the polyether motifs found in many natural products. This *untested* proposal involves a series of discrete cyclization steps involving an ester **23** that acts as a nucleophile to open an epoxide. The resulting stabilized carbenium ion **24** would then react with a proximal hydroxyl group to form the orthoester intermediate **25**. The orthoester could then rearrange, presumably via intermediate **26** in an acid - catalyzed process, thus forming the cyclic ether and regenerating ester **27** for another iteration to elaborate the polyether backbone (Scheme 6).

Scheme 6. The Giner-Mullins biogenetic postulate for marine polycyclic ether natural products

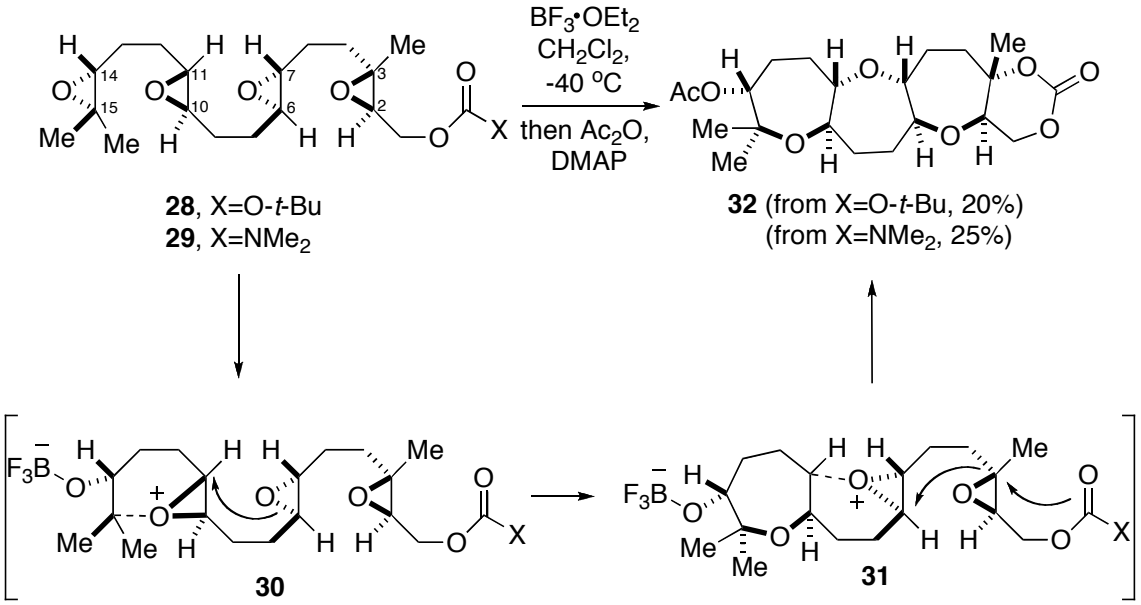


2.1.2.2. Methodologies for the construction of polycyclic ether motifs

While the Nakanishi hypothesis provides a provocative insight into the possible origins of such complex natural products, experimental insight must be

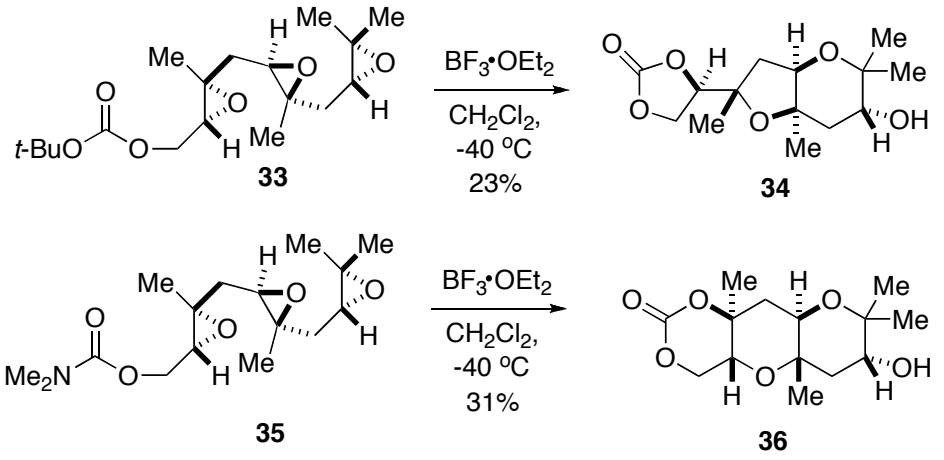
provided to substantiate the biogenetic postulate. Fortunately, there have been recent and considerable contributions in the area of biomimetic synthesis of polycyclic ether motifs from the laboratories of McDonald and Jamison. McDonald pioneered the development of modern methods for the construction of polycyclic ether scaffolds via the Lewis acid-catalyzed cascade cyclization of polyepoxides.[61] Notable among these contributions, McDonald and Valentine reported the cascade oxacyclization of tetraepoxide **28**-**29** using $BF_3 \bullet OEt_2$ as the cyclization promoter.[62] This cascade reaction was thought to proceed via the activation of the terminal 14,15-epoxide with $BF_3 \bullet OEt_2$. The internal 10,11-epoxide then acted as a pendant nucleophile to open the activated epoxide, which resulted in the formation of the theoretical epoxonium ion **30**.[63] The resultant epoxonium ion was then opened by the proximal 6,7-epoxide forming yet another epoxonium ion **31**. Iteration of the process led to the termination of the epoxide cascade with the carbonate to provide the *trans*-*syn*-*trans* tetracyclic ether **32**. The observed uniform *endo*-selectivity was only achieved through methyl or trimethylsilyl substitution at C3 and C15 (Scheme 7). In the context of natural product total synthesis, the need for a directing group was a limitation to this methodology because any synthetic application must allow for flexibility in the substitution (i.e. hydrogen) at the ring junctions.

Scheme 7. McDonald and Valentine's BF_3•OEt_2-catalyzed biomimetic polyepoxide oxacyclization cascade



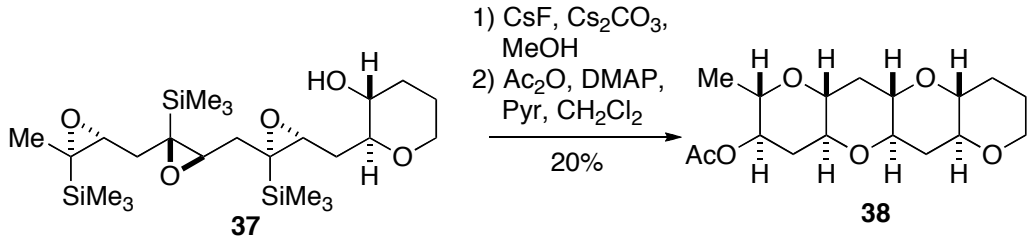
McDonald and Bravo also investigated the effects of terminating nucleophile on the regiochemical course of a methyl-directed cascade for the synthesis of tetrahydropyran motifs.[64] The ladder polypyran **36** was obtained through the BF_3•OEt_2 activation of the *carbamate* poylepoxide **35**. Surprisingly, the BF_3•OEt_2 activation of *carbonate* polyepoxide **33** yielded only the fused tetrahydrofuran/tetrahydropyran product **34** from the oxacyclization cascade.

Scheme 8. McDonald and Bravo's biomimetic synthesis of fused polypyrans



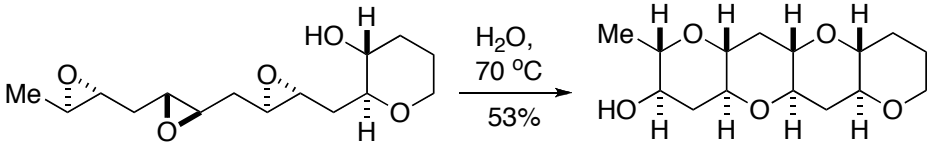
Jamison also made significant contributions in the area of polycyclic ether synthesis. The epoxide-opening cascade of polyepoxide **37** was a noteworthy example that highlights "disappearing" silyl groups.[65] Using CsF in the presence of Cs_2CO_3, polyepoxide **37** underwent a cascade cyclization affording ladder polyether **38** (Scheme 9). The authors proposed that the sequence of the cascade cyclization probably involved a silyl-directed epoxide-opening followed by proteodesilylation (homo-Brook rearrangement pathway), which revealed a free alcohol nucleophile to continue the cascade. Again, the major drawback to this methodology was the need for a directing group. The authors concede that an "ideal" cascade cyclization would not require a directing group and should have the flexibility of incorporating various substitutions at the ring-junctions (Scheme 9).

Scheme 9. Jamison's epoxide-opening cascade with "disappearing" silyl group



To this end, Jamison reported an impressive epoxide-opening cascade that does not require directing groups. Moreover, this cascade was simply promoted by heating (70 °C) a polyepoxide substrate, such as **39**, in H_2O to give the tetracyclization product **40**.[66] The authors rationalized the remarkable *endo* selectivity by proposing a synergistic effect of the epoxide template and catalysis by water. The current model for the cascade involves activation of the terminal epoxide by a molecule of H_2O that is H-bonded to another molecule of H_2O that is activating the alcohol nucleophile for attack onto the activated epoxide (Scheme 10).

Scheme 10. Jamison's H_2O-promoted epoxide-opening cascade

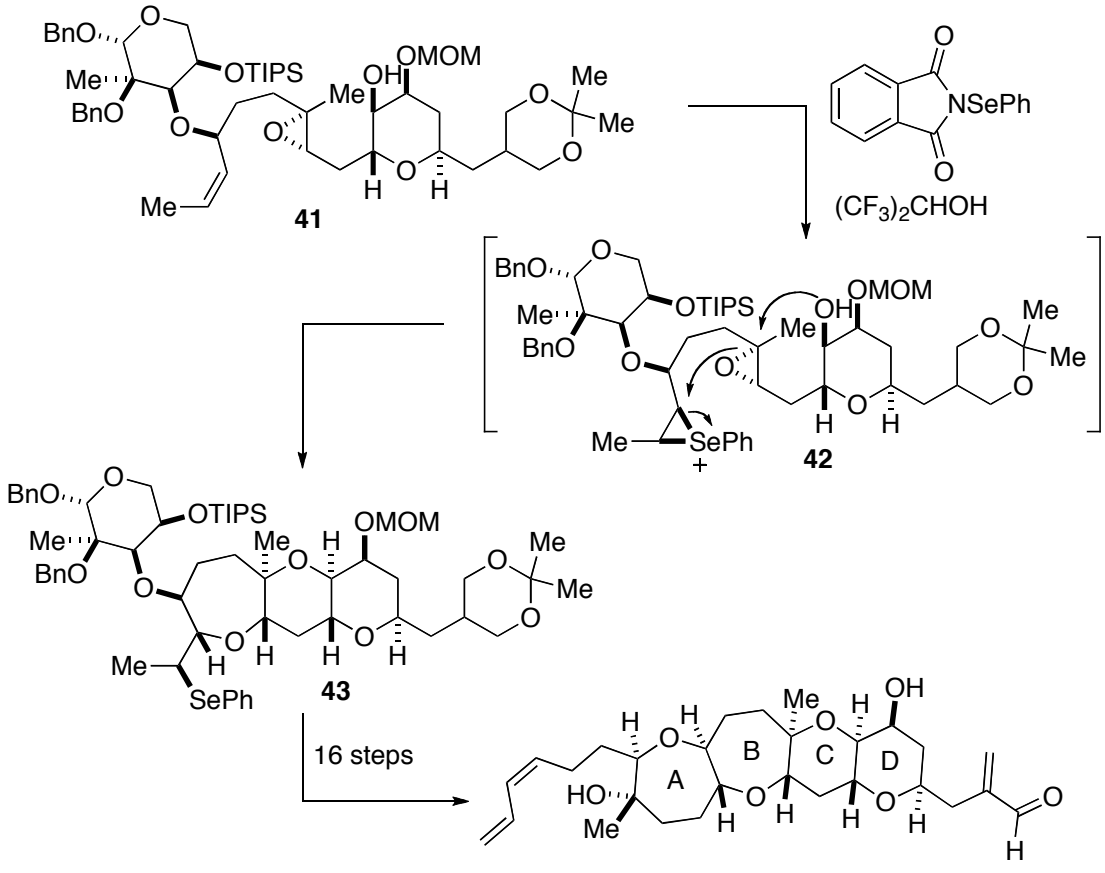


2.1.2.3. Biomimetic total syntheses involving epoxide-opening cascades *en route* to polycyclic ether natural products

Holton was the first to apply an epoxide-opening cascade in the total synthesis of hemibrevetoxin B (**19**).[67] The desired formation of the B and C rings

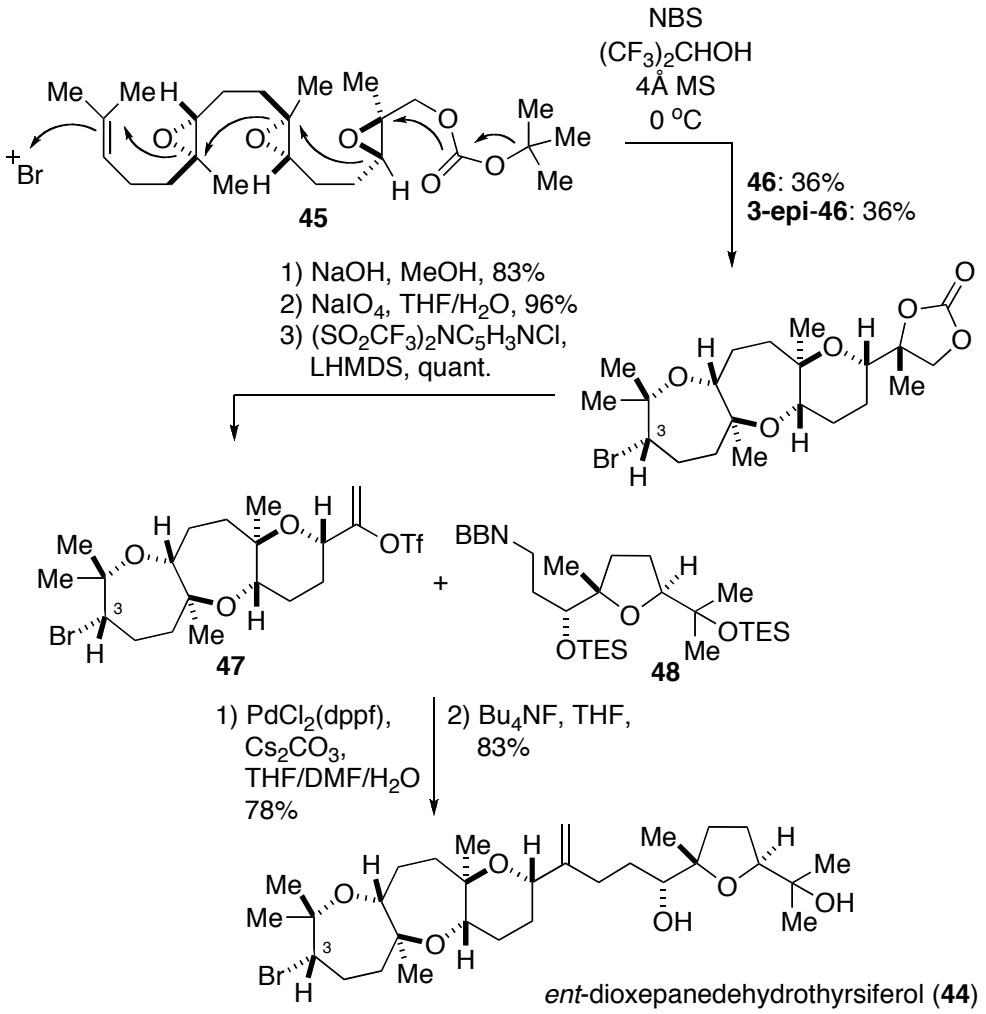
of the natural product occurred in a single operation by activating the alkene of **41** with *N*-(phenylseleno)phthalimide in highly polar 1,1,1,3,3,3-hexafluoro-*iso*-propanol ($(CF_3)_2CHOH$) to generate episelenonium ion **42**. This electrophilic species was then attacked by the proximal epoxide that was simultaneously opened by the alcohol nucleophile to complete the closure of the BC ring system of compound **43**. While the use of stoichiometric selenium was certainly undesirable, the involvement of an epoxide in such a cascade represented a remarkable synthetic achievement (Scheme 11).

Scheme 11. Holton and Zakarian's synthesis of hemibrevetoxin B involving an epoxide-opening cascade



Biomimetic epoxide-opening cascades have also found great utility outside of the ladder-type polycyclic ether natural products. Jamison reported the first total synthesis of the marine natural product *ent*-dioxepanedehydrothyrsiferol (**44**) using an elegant biomimetic approach featuring a bromonium-initiated epoxide opening cascade.[68] Relying on the foundational work of *tert*-butylcarbonate terminated epoxide cascades by McDonald and co-workers[22,23], Jamison demonstrated that exposure of triepoxide carbonate **45** to *N*-bromosuccinimide (NBS) in highly polar $(CF_3)_2CHOH$ gave a facile tetracyclization to the *trans-anti-trans* product **46** in an impressive 72% combined yield of a 1:1 mixture of C3 epimers. After forming the enol triflate **47**, the key fragment coupling occurred via cross-coupling with the alkyl borane furan derivative **48**. After deprotection, *ent*-dioxepanedehydrothyrsiferol (**44**) was obtained, thus completing a remarkably efficient biomimetic total synthesis (Scheme 12).

Scheme 12. Jamison's biomimetic total synthesis of *ent*-dioxepanedehydrothyrsiferol

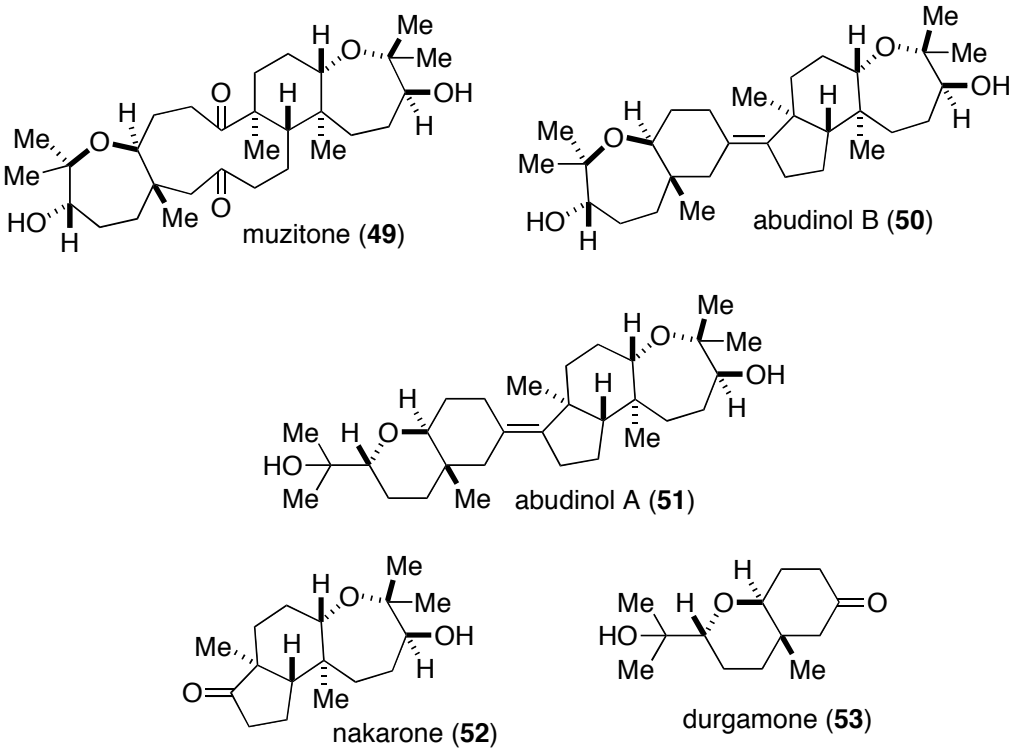


2.1.3. McDonald's synthetic efforts towards squalene-derived polycyclic ether natural products

In 1999, Kashman reported the isolation and characterization of a family of polycyclic ether terpenoid natural products that are thought to arise biogenetically from the polycyclization of squalene tetraepoxide. Muzitone (**49**), abudinol B (**50**), abudinol A (**51**), nakarone (**52**), and durgamone (**53**) are representative

members of this family of marine natural products that were isolated from a sea sponge (*Ptilocaulis spiculifer* of the Axinellidae family) located in the Red Sea waters of the Dahlak archipelago off the coast of Eritrea (Figure 2).[69] Given McDonald's longstanding interest in exploring higher order polycyclization cascades in the context of biomimetic total synthesis, this family of polycyclic ether terpenoid natural products seemed predisposed for synthetic investigation.

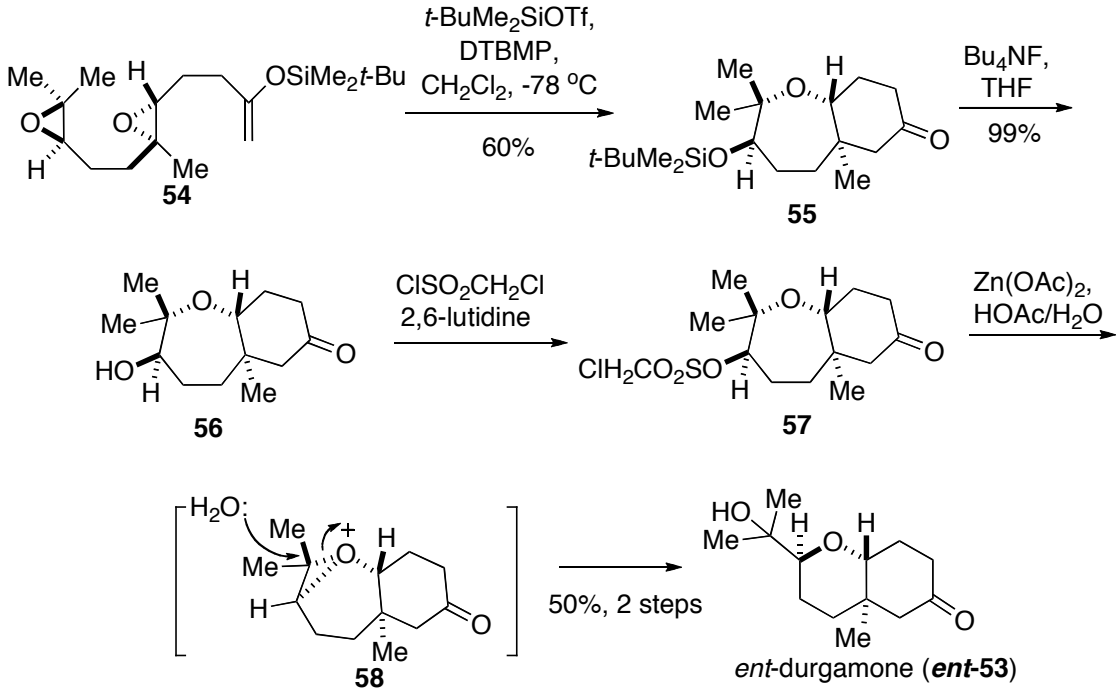
Figure 2. Marine sponge derived polycyclic ether terpenoid natural products



Thus, McDonald and Tong recently reported first-generation biomimetic total syntheses of the polycyclic ether terpenoid natural products *ent*-durgamone (***ent*-53**), *ent*-nakarone (***ent*-52**), and *ent*-abudinol B (***ent*-50**) that featured novel oxa/ carbacyclization cascades.[70] The total synthesis of *ent*-durgamone (***ent*-53**) started from diepoxy enolsilane **54**, which upon treatment with *tert*-

butyldimethylsilyl triflate (*t*-BuMe$_2$SiOTf) in the presence of 2.6-di-*tert*-butyl-4-methylpyridine (DTBMP) triggered the cascade leading to tricyclic ketone **55**. This tandem cyclization demonstrated the efficacy of the enolsilane as a terminating nucleophile in this type of polycyclization cascade. After removal of the silyl ether to **56**, the alcohol was transformed to the chloromesylate derivative **57**, which upon exposure to Zn(OAc)$_2$ and AcOH caused a ring contraction giving *ent*-durgamone (***ent*-53**) (Scheme 13).

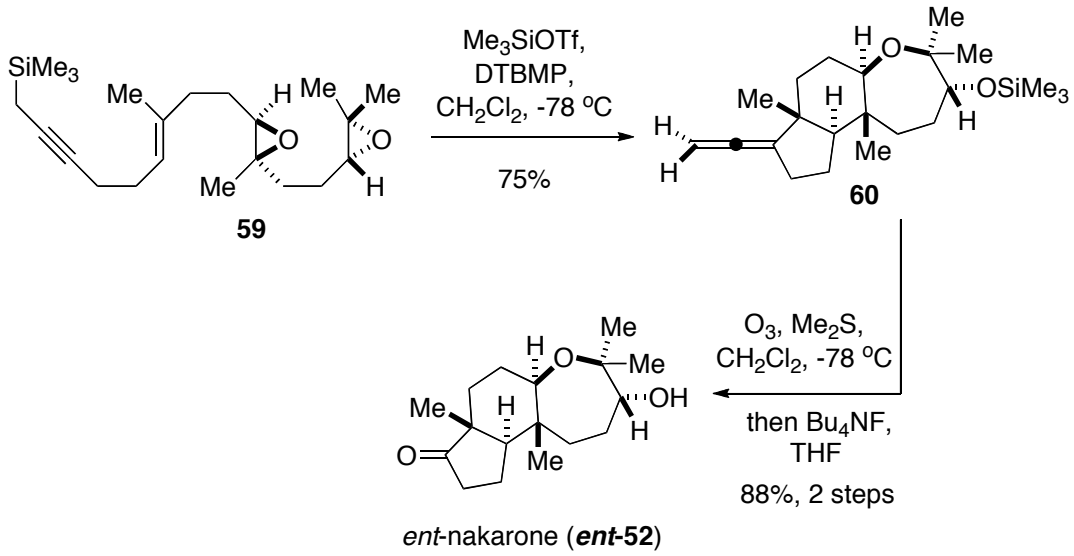
Scheme 13. McDonald, Tong, and Valentine's biomimetic total synthesis of *ent*-durgamone (*ent*-53)



McDonald and Tong also reported the use of a hybrid oxa/carbacyclization cascade in the total synthesis of *ent*-nakarone (***ent*-52**). Exposure of the propargylic silane bisepoxide **59** to Me$_3$SiOTf in the presence of DTBMP triggered a highly efficient tricyclization cascade to allene **60**. An ozonolysis of

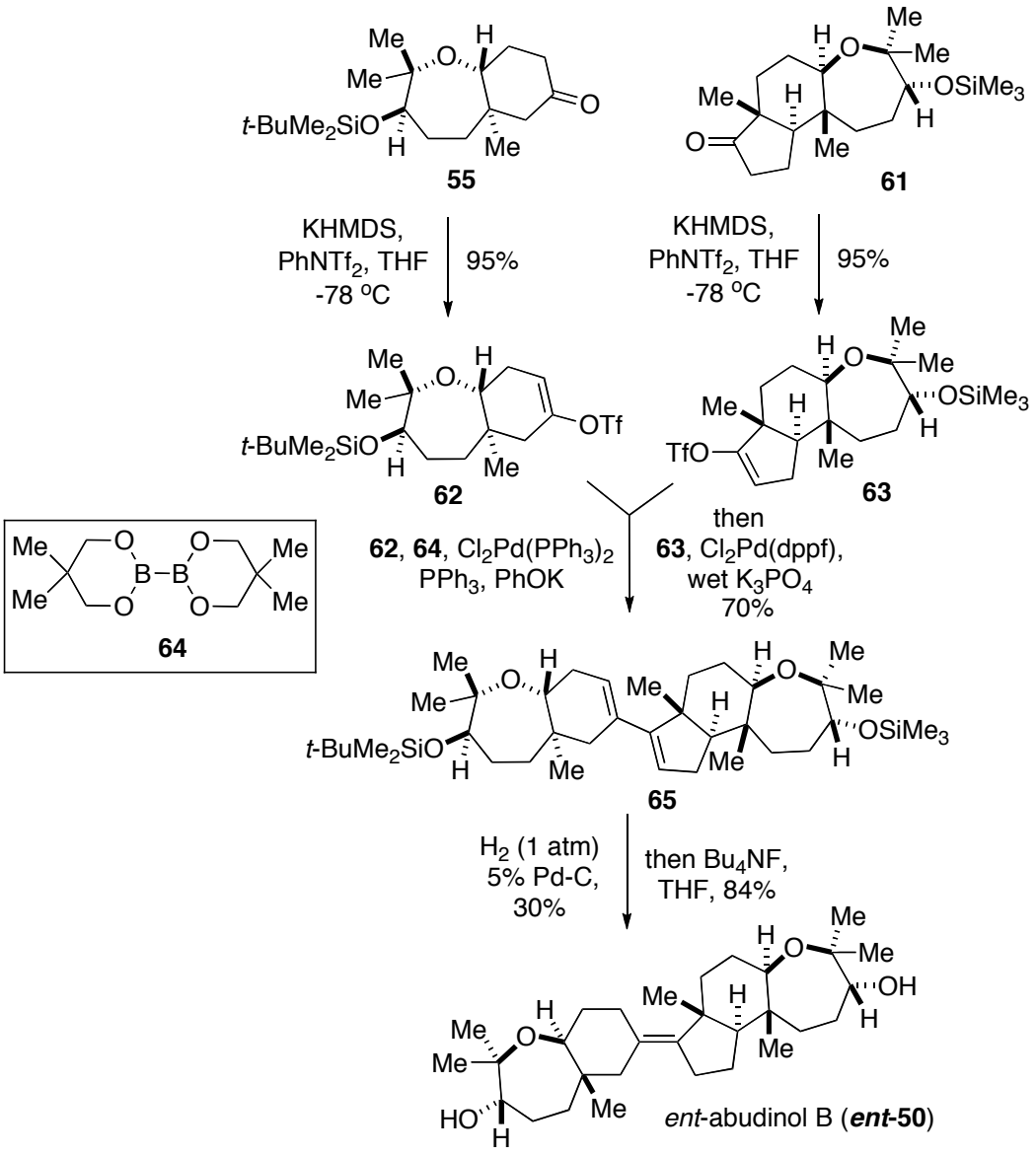
the allene revealed the ketone, which upon silyl ether cleavage, gave *ent*-nakarone (***ent*-52**) in excellent overall yield (Scheme 14).

Scheme 14. McDonald and Tong's Biomimetic total synthesis of *ent*-nakarone (*ent*-52)



ent-Abudinol B (***ent*-50**), a highly complex member of this family featuring a pentacyclic core, was also assembled in a clever "retro-ozonolysis" of the bicyclic ketone **55** and tricyclic ketone **61**. Each ketone was converted to the corresponding enol triflate derviatives **62** and **63**, respectively, which were joined using a Suzuki coupling protocol to give diene **65**. In order to install the central tetrasubstituted alkene, the use of standard hydrogenation conditions resulted in the formation of the tetrasubstituted alkene, albeit in modest yield. A straightforward global deprotection gave *ent*-abudinol B (***ent*-50**), completing a significant achievement in the realm of biomimetic total synthesis (Scheme 15).

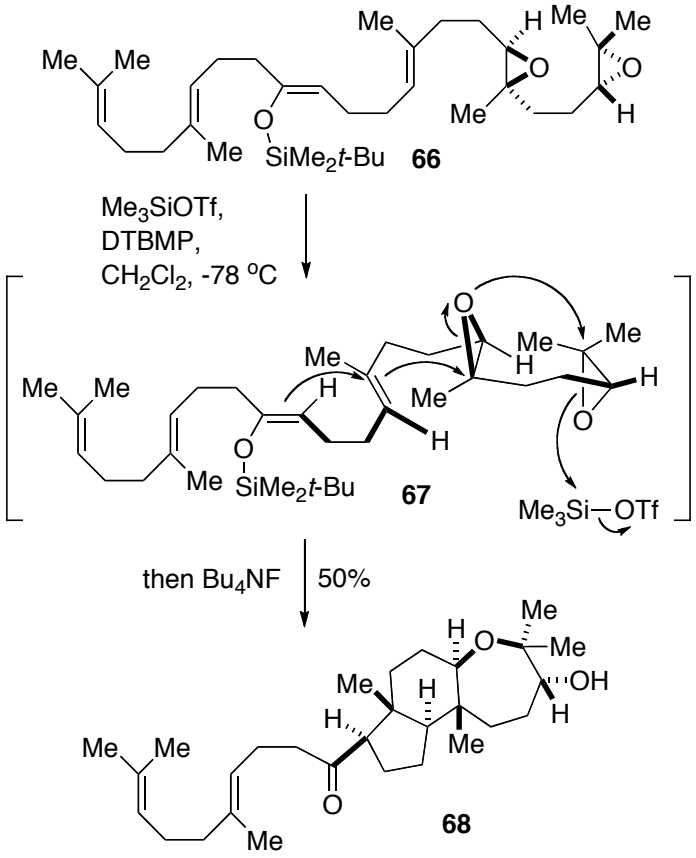
Scheme 15. "Retro-ozonolysis": Total synthesis of *ent*-abudinol B (*ent*- 50)



After further consideration of the postulated biogenesis for abudinol B (**50**) (*vide infra*), McDonald and Tong also reported a second generation biomimetic total synthesis of *ent*-abudinol B (***ent*-50**) that more closely mimicked the likely biosynthetic pathway involving polycyclization of squalene tetraepoxide.[71] While the second-generation synthesis was linear in sequence, this approach was remarkable for the rapid generation of complexity in a relatively concise total

synthesis. The synthesis featured a tandem oxa/carbacyclization of the C29 framework **66** with a strategically placed enolsilane as the nucleophilic terminator of a first-stage biomimetic cascade. The first-stage tricyclization formed the ABC ring system of ketone **68**, presumably through the extended chair-like transition state **67** (Scheme 16).

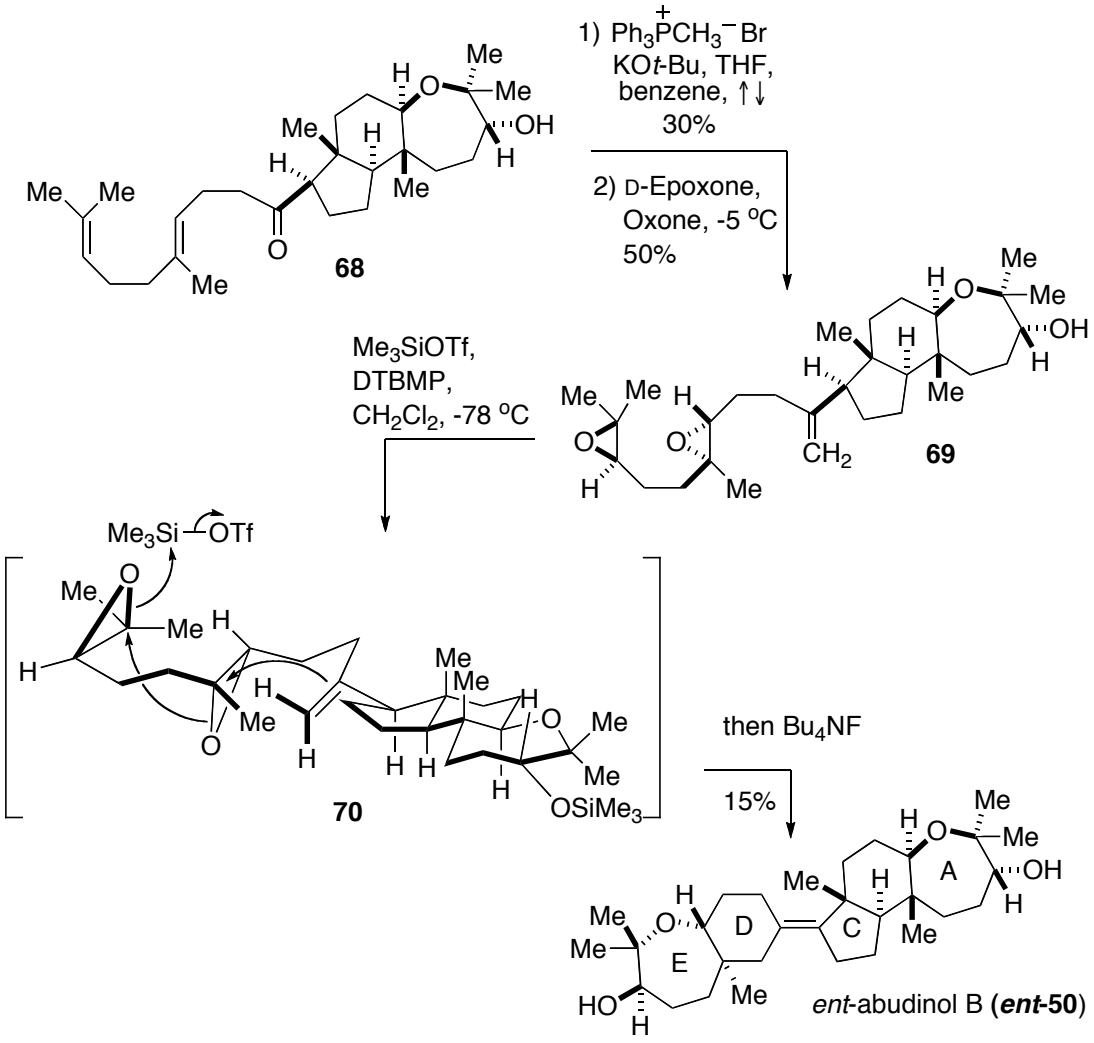
Scheme 16. McDonald and Tong's second-generation biomimetic total synthesis of abudinol B: First-stage tricyclization



After the ketone was transformed to the 1,1-disubstituted alkene, a regioselective Shi epoxidation to diepoxide **69** was performed on the triene intermediate. The authors noted that this unique transformation was the first known example of a regio- and enantioselective epoxidation of two trisubstituted

alkenes in the presence of a 1,1-disubstituted alkene. The diepoxide **69** was then subjected to Me_3SiOTf activation in the presence of DTBMP, which resulted in the formation of the DE ring system via chair-like transition state **70**. After desilylation, *ent*-abudinol B (***ent*-50**) was obtained in 15% yield. The low yield in this final cyclization cascade was explained by the poor nucleophilicity of the 1,1-disubstituted alkene (Scheme 17).

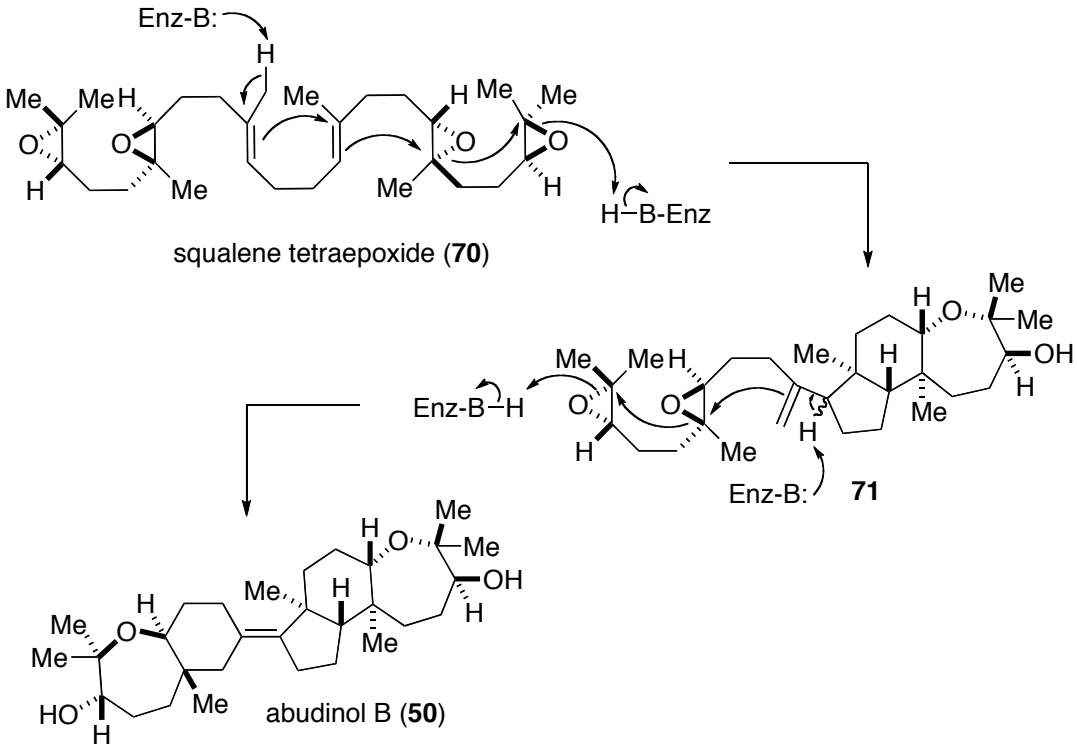
Scheme 17. McDonald and Tong's second-generation biomimetic total synthesis of *ent*-abudinol B (*ent*-50): Second-stage tricyclization



2.1.3.1. Postulated biogenesis of muzitone (49)

Among the family of squalene-derived polycyclic ether natural products reported by Kashman[27b], muzitone (**49**) was perhaps the most structurally distinct featuring a central 11-membered macrocycle—bearing two ketones—that appended two hydroxy oxepane moieties. Kashman[27b] and Norte[72] proposed biogenetic hypotheses for muzitone (**49**) that implicated abudinol B **(50**) as an intermediate in the biosynthesis. According to Norte, the biosynthesis of abudinol B (**50**) most likely involved a two-stage cascade cyclization of squalene tetraepoxide (**70**) (Scheme 18).

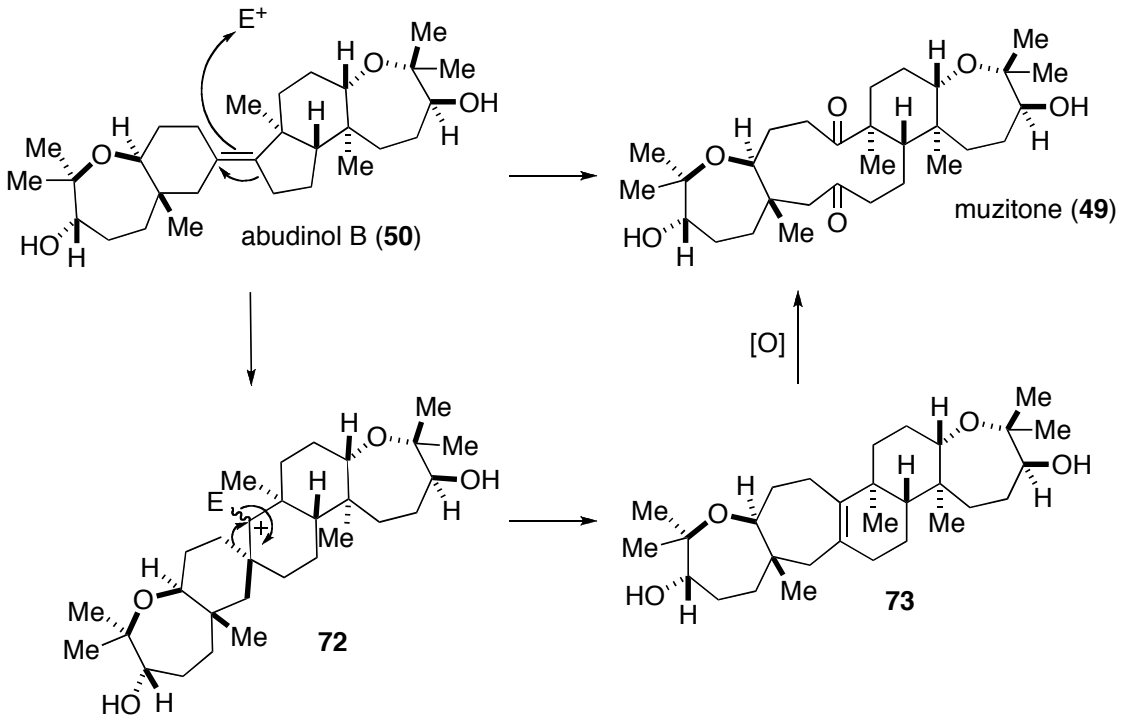
Scheme 18. Norte's biosynthetic postulate for abudinol B (50)



Kashman's proposal for the biosynthesis of muzitone (**49**) involved an activation of the central tetrasubstituted alkene by an electrophilic species within the enzyme. Upon activation of the alkene, a 1,2 shift would lead to a spirocylic

carbenium ion **72**, that would then trigger a second 1,2 shift and subsequent elimination to the ring-expanded tetrasubstituted alkene **73**, an isomer of abudinol B (**50**). This tetrasubstituted alkene **73** would then be oxidized to the diketone macrocycle of muzitone (**49**) (Scheme 19). Interestingly, the tetrasubstituted alkene **73** was not isolated by Kashman.

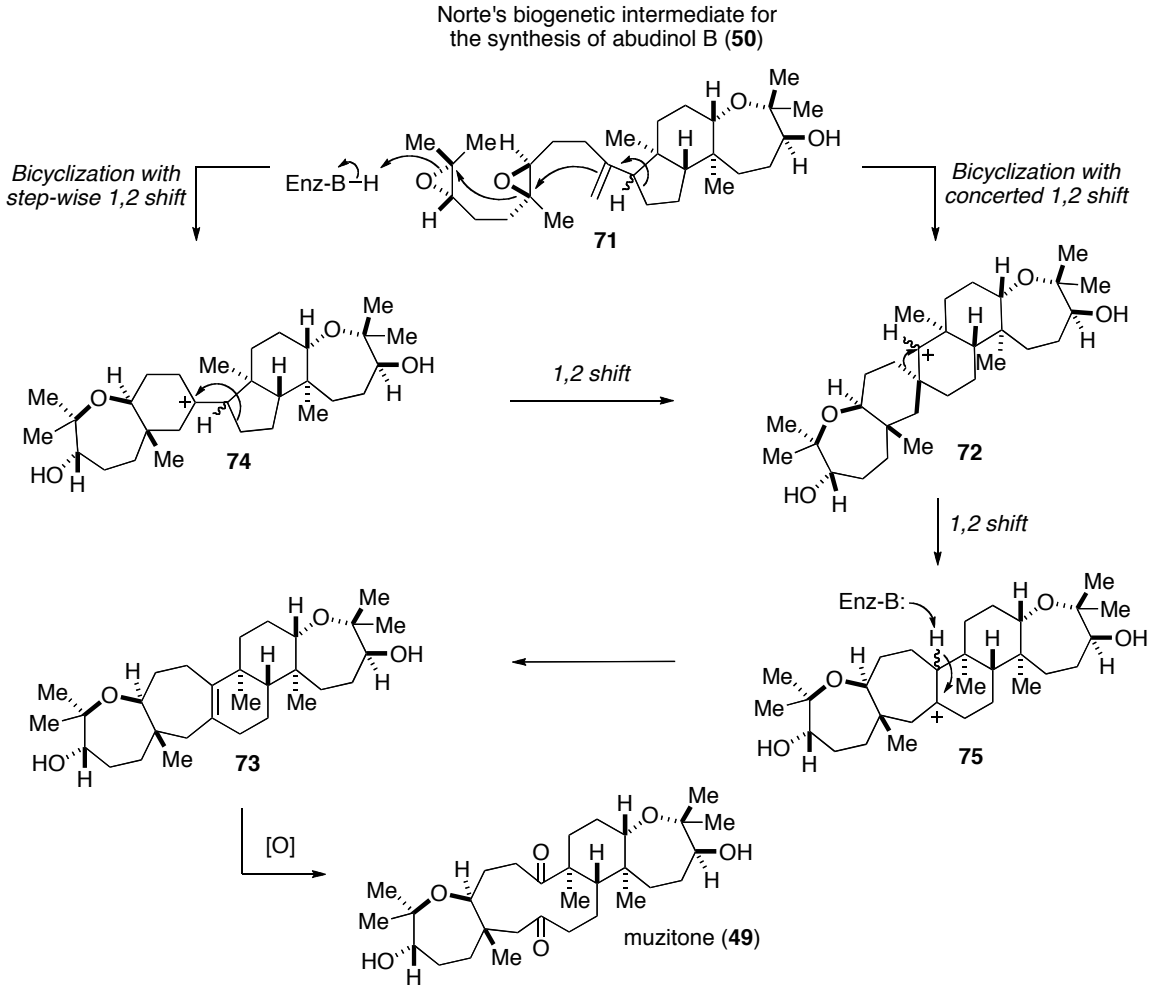
Scheme 19. Kashman's proposal for the biosynthesis of muzitone (49)



Norte's proposal for the biogenetic origin of muzitone (**49**) differed from Kashman only in how the spirocyclic carbenium ion **72** would be generated within the enzyme. Instead of invoking the presence of an electrophilic species to trigger the cascade of 1,2 shifts, Norte envisioned the *direct* synthesis of the spirocyclic carbenium ion **72** from the second-stage cyclization of **71**, the theoretical intermediate found in Norte's biosynthetic hypothesis for abudinol B (**50**). Instead of concomitant elimination in the second-stage cyclization leading

to abudinol B (**50**), Norte proposed a bicyclization with a concerted 1,2 shift to provide the spirocyclic carbenium ion **72**, which, as proposed by Kashman, would undergo a 1,2 shift and subsequent elimination to the ring-expanded tetrasubstituted alkene **73**. An alternative formation of **72** involved a step-wise mechanism involving bicyclization to tertiary carbenium ion **74** followed by a 1,2 shift. Oxidation of the tetrasubstituted alkene would provide muzitone (**49**) (Scheme 20).

Scheme 20. Norte's proposal for the biosynthesis of muzitone (49)

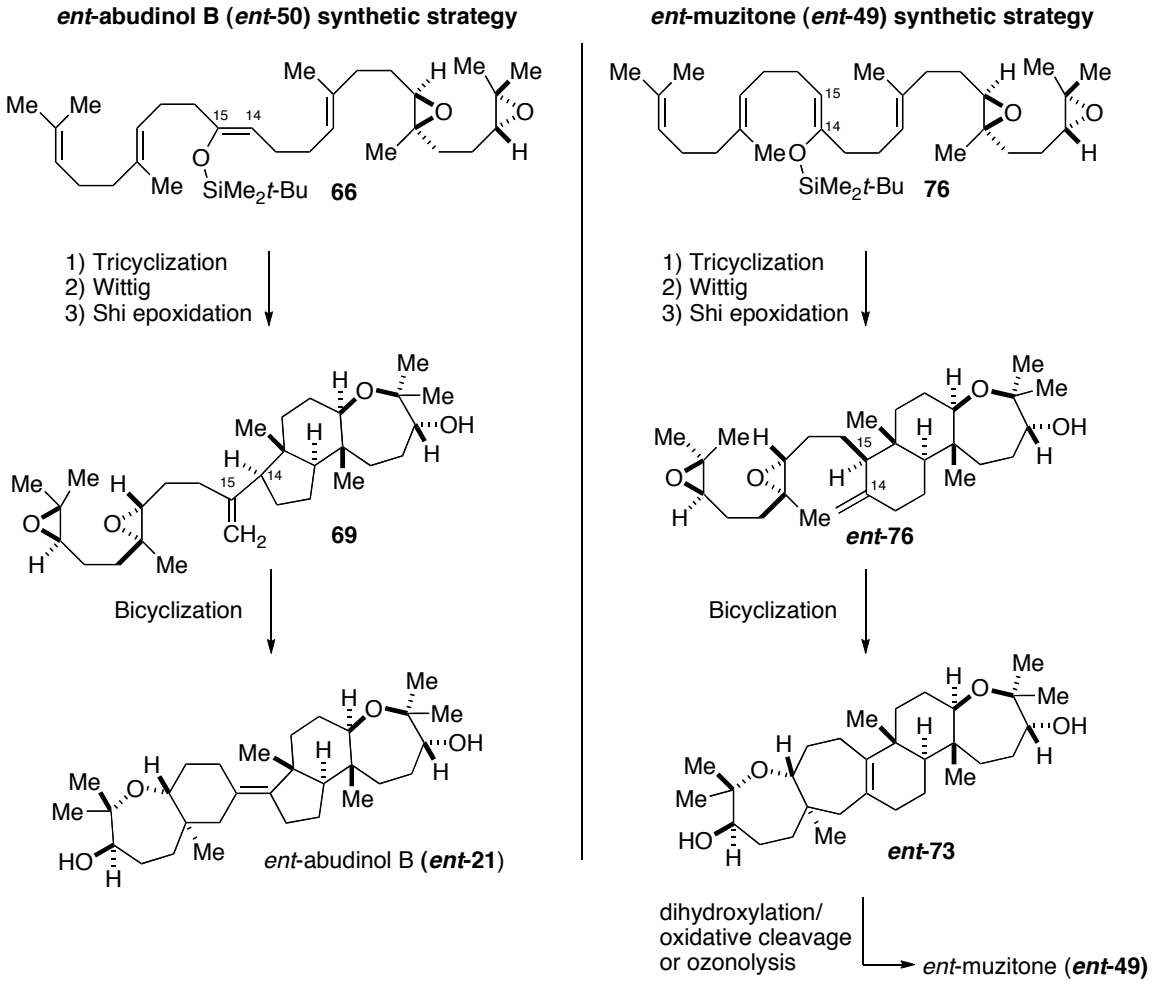


2.2. Biomimetic synthesis of *ent*-muzitone (*ent*-49) from a squalene-like precursor

2.2.1. Retrosynthesis

With McDonald's successful completion of the second-generation biomimetic total synthesis of *ent*-abudinol B (***ent*-50**) from a squalene-like precursor, we realized that a slight modification to the key C29 fragment bearing the enolsilane would give access to the 6,6,7 tricyclic ketone that could serve as an intermediate for the total synthesis of *ent*-muzitone (***ent*-49**). Thus, a similar synthetic approach seemed logical considering the potential biogenetic link between these natural products. Specifically, if the placement of the enol silane oxygen was at C14 and not C15 (compound **76**) a similar synthetic strategy would mimic the biosynthetic postulates. Thus, a Wittig homologation and regioselective Shi epoxidation would give the diepoxy alkene ***ent*-76** for bicyclization. Upon successful bicyclization to the pentacyclic dioxepane ***ent*-73**, an oxidation of the tetrasubstituted alkene using standard dihydroxylation/ oxidative cleavage or ozonolysis would give *ent*-muzitone (***ent*-49**) (Scheme 22).

Scheme 22. Biomimetic strategy for the total synthesis of *ent*-muzitone (*ent*-49)



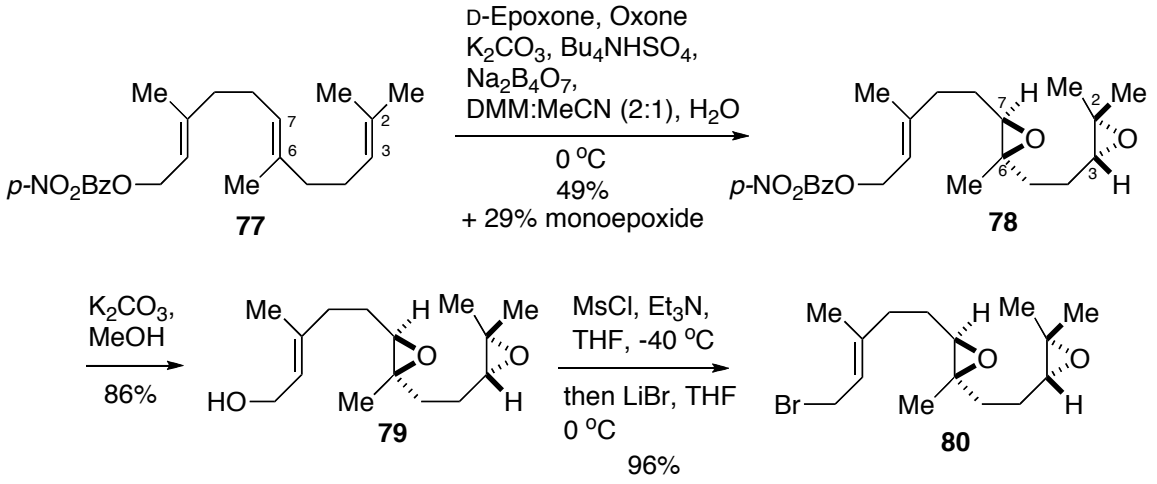
2.2.2. Results and Discussion

The synthesis of the squalene-like enolsilane **76** began with the preparation of allylic bromide **80**. Previously, Dr. Rongbiao Tong of the McDonald laboratory demonstrated the regio- and enantioselective Shi epoxidation[73] of farnesyl acetate to give the (3*R*,6*R*,7*R*) diepoxidation product. However, undesired epoxidation of the allylic C10-C11 alkene was problematic, especially when we conducted the reaction on a larger scale (i.e. 10 grams). Likewise, reproducing

this epoxidation with larger scale transformations proved difficult because the acetate protecting group did not provide adequate electronic deactivation of the allylic alkene to prevent over-epoxidation.

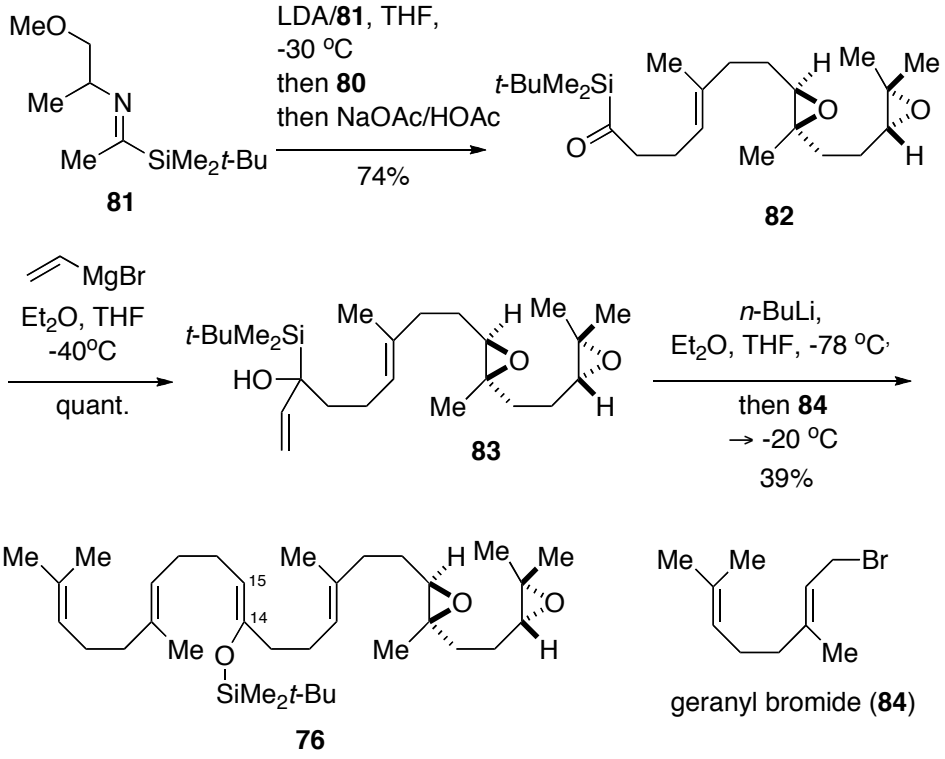
In an effort to solve this problem, we screened different allylic alcohol protecting groups and found that *para*-nitrobenzoyl ester deactivated the allylic alkene thereby suppressing epoxidation. Thus, *trans*-*trans*-farnesol was protected as the *para*-nitrobenzoyl ester derivative **77**, and Shi epoxidation afforded the (3*R*,6*R*,7*R*) diepoxidation product **78** with only trace triepoxide formation on multi-gram scale (i.e. 20-30 grams). While this method proved scalable, the diastereoselectivity was modest (4:1) but was consistent with a literature report for a similar farnesol-derived substrate.[74] Because D-epoxone was easily prepared—requiring only two steps from D-fructose—the enantioselective epoxidations of compound **78** provided the antipode of the diepoxide ultimately required for muzitone. The diepoxy allylic alcohol **79** was synthesized via methanolysis of the *para*-nitrobenzoyl ester using K_2CO_3 in MeOH. We produced diepoxy allylic bromide **80** through a two-step sequence of mesylation and subsequent bromination (Scheme 23).

Scheme 23. Preparation of diepoxy allylic bromide 80



The diepoxy allylic bromide **80** was converted to the corresponding acyl silane **82** by alkylation using the metalloenamine generated from lithiumdiisopropylamine (LDA) deprotonation of **81**.[75] Adding vinylmagnesium bromide to **82** in the presence of the diepoxide proved to be a sensitive transformation. However, upon screening reaction conditions, α-silyl allylic alcohol **83** could be obtained in quantitative yield by performing the reaction at -40 °C and controlling the rate of addition of the Grignard reagent via syringe pump. The α-silyl allylic alcohol **83** was then treated with *n*-BuLi to trigger a Brook rearrangement to the corresponding homoenolate. The intermediate homoenolate was alkylated with geranyl bromide (**84**), giving enolsilane **76** with complete *Z* selectivity (Scheme 3). Our placement of the C14-C15 enolsilane was intentional, as we sought to take advantage of the presence of a more reactive terminating nucleophile at C14 relative to the likely placement of a methyl substituent in the putative biosynthetic substrate.

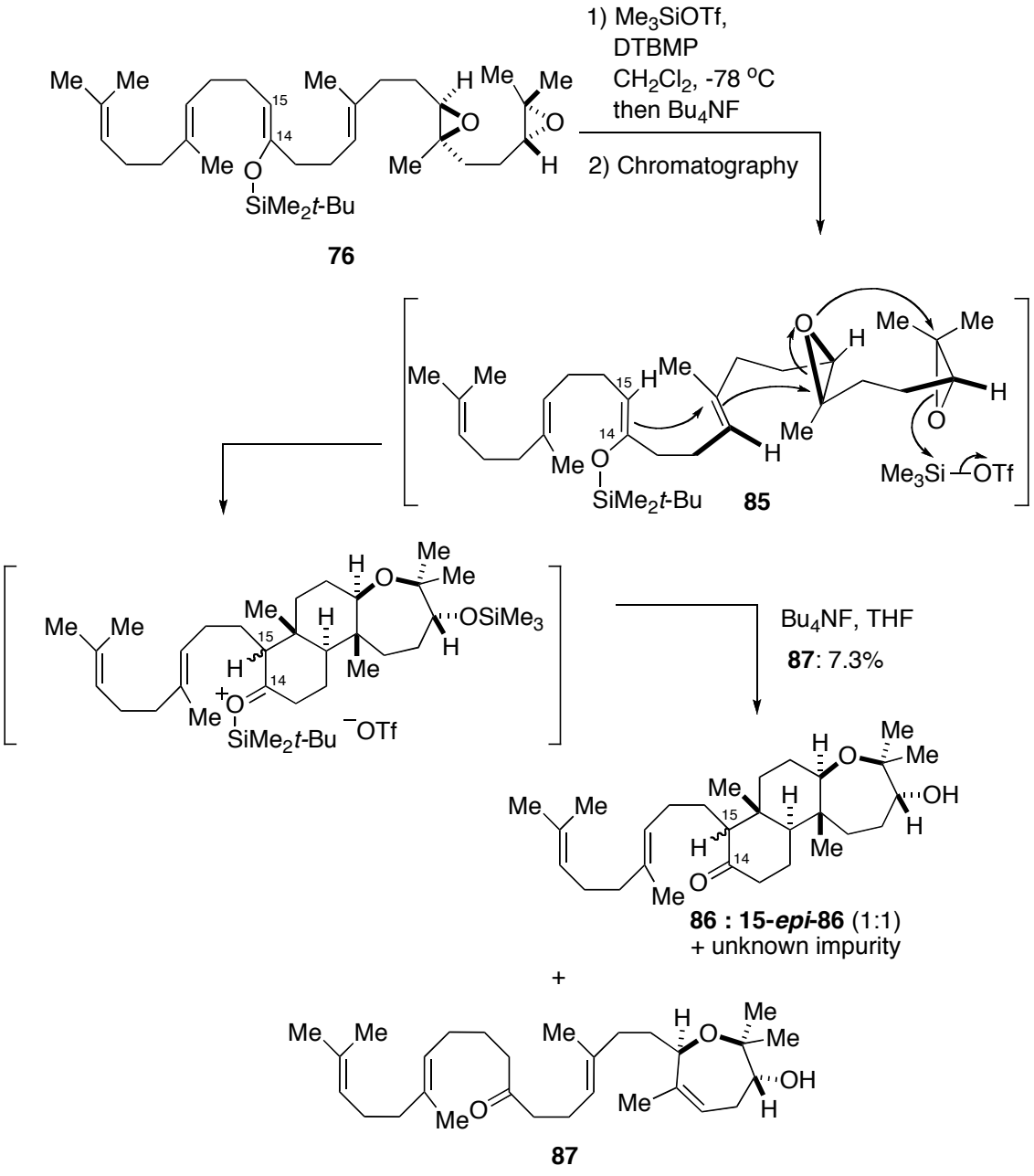
Scheme 24. Construction of the C29 skeleton: synthesis of enolsilane 76



The first-stage biomimetic tricyclization cascade was initiated through treatment of enolsilane **76** with Me_3SiOTf in the presence of DTBMP at -78 °C. This gave *trans-anti-trans* 6,6,7 tricyclic ketone **86** (1:1 mixture of inseparable C15 epimers), which presumably reacted through chair-like transition state **85**. The presence of the monocyclization byproduct **87** in the reaction was intellectually provocative because the early termination of the cascade pathway had more significant thermodynamic implications on the behavior of this transformation. The formation of the tricyclic substrate was theoretically dependent upon pre-organization of the C29 framework for a successful outcome. The entropic barrier for even this *intramolecular* transformation must

play a significant role, which could explain why early termination is kinetically allowed to give the monocyclization product (Scheme 25).

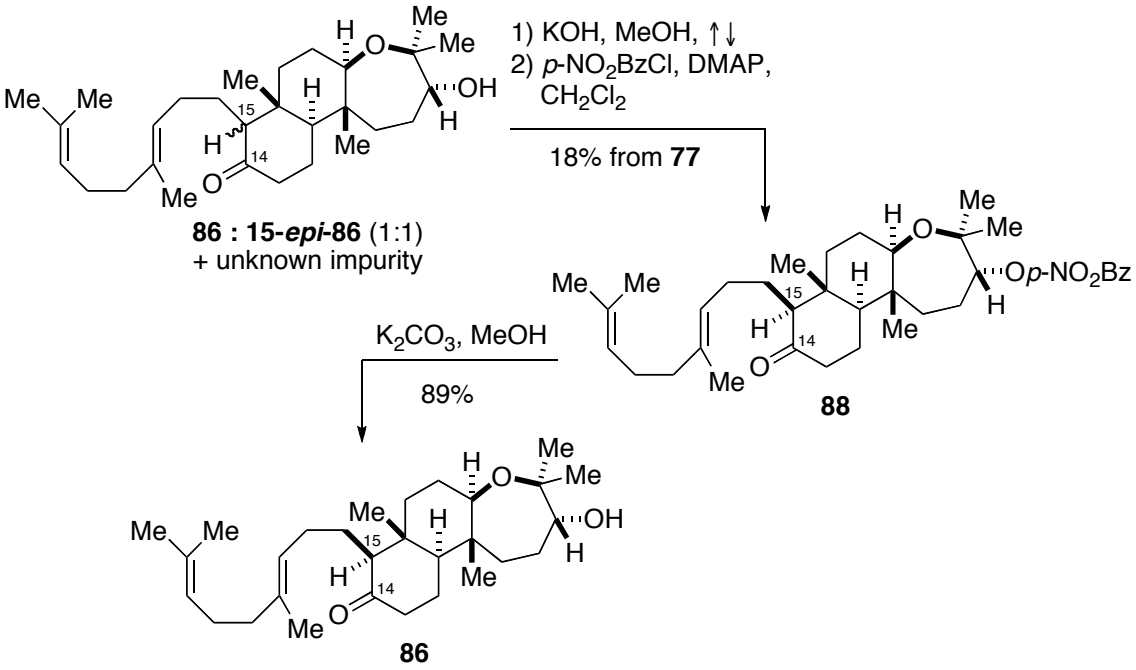
Scheme 25. First-stage biomimetic tricyclization



Despite the success of this complex transformation, two problems arose that required further consideration: the C15 selectivity was not optimal and after a

single chromatography, the tricyclic ketone **86** was contaminated with an inseparable and unidentifiable byproduct. Therefore, we subjected the 1:1 mixture of C15 epimers to KOH in refluxing MeOH to induce epimerization of the C15 position.[76] Gratifyingly, this resulted in *exclusive* formation of the pseudoequatorial side chain epimer **86**. We then addressed the purification issue by protecting the free alcohol of **86** as the *para*-nitrobenzoyl ester **88**. Upon ester formation, *para*-nitrobenzoyl ester tricyclic ketone **88** was successfully purified resulting in an 18% yield over the 4 synthetic operations. After a basic methanolysis, the desired tricyclic ketoalcohol **86** was obtained (Scheme 26).

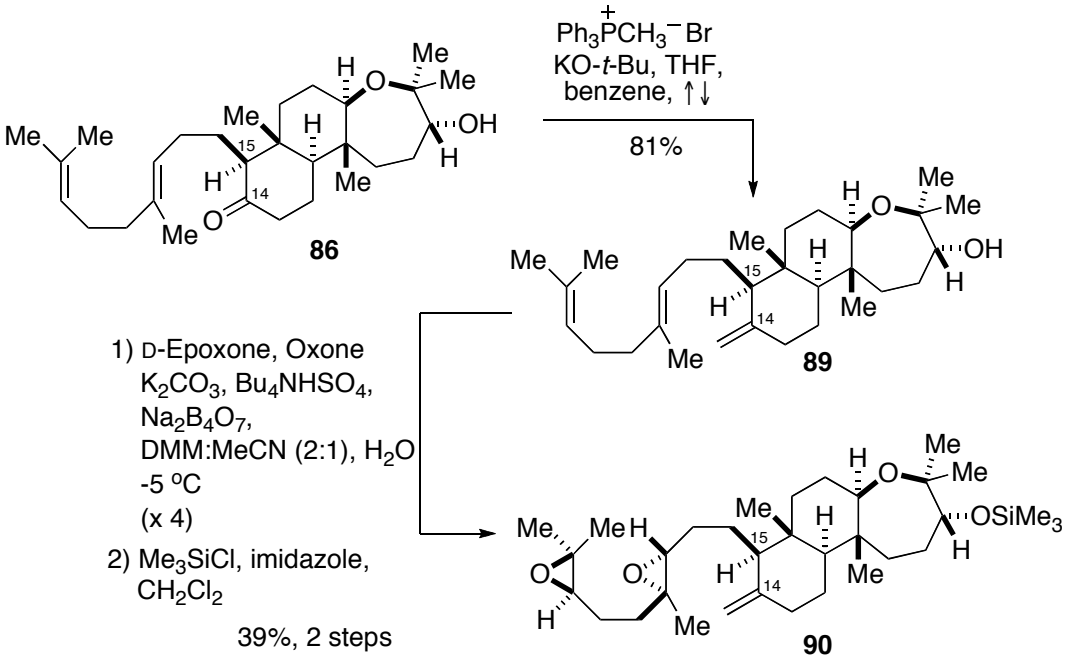
Scheme 26. Epimerization and purification of ketoalcohol 86



Having constructed the C29 framework bearing the tricyclic ketone, we addressed the olefination of the ketone in order to install the final carbon of the C30 squalene-like skeleton. We ultimately relied on Wittig homologation (using

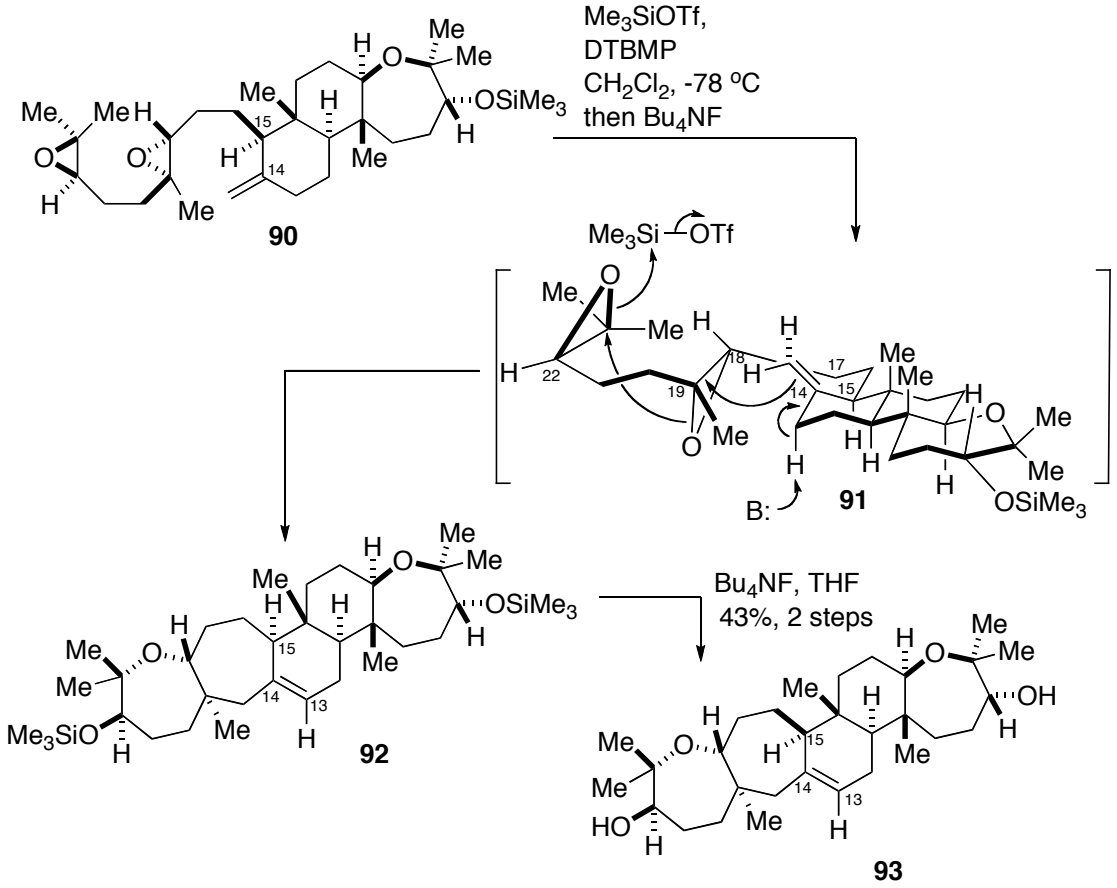
Ph_3PCH_3Br and KO-*t*-Bu in refluxing benzene[32]) to yield the desired methylenation product **89**, which proceeded smoothly in 80% yield without C15 epimerization. Regio- and enantioselective Shi epoxidation of the triene alcohol proceeded in modest yield. This transformation proved to be a considerable challenge. For a successful outcome, the progress of the reaction was monitored extensively by TLC to prevent over-epoxidation of the 1,1-disubstituted alkene. While cumbersome, the reaction was stopped upon TLC visualization of significant triepoxide formation. After isolation of the triene, monoepoxide, and desired diepoxide via column chromatography, the triene and monoepoxide were re-subjected to the Shi epoxidation conditions following the same procedure but modifying the stoichiometry of K_2CO_3 and oxone. Ultimately, this required four different Shi epoxidations. The desired diepoxide was cleanly obtained upon protection of the alcohol as the trimethylsilyl ether derivative **90** in 38% total yield (derivatization of the alcohol was necessary for purification, as D-epoxone was an inseparable contaminant) (Scheme 27).

Scheme 27. Wittig homologation; regioselective Shi epoxidation to diepoxy trimethylsilyl ether 90



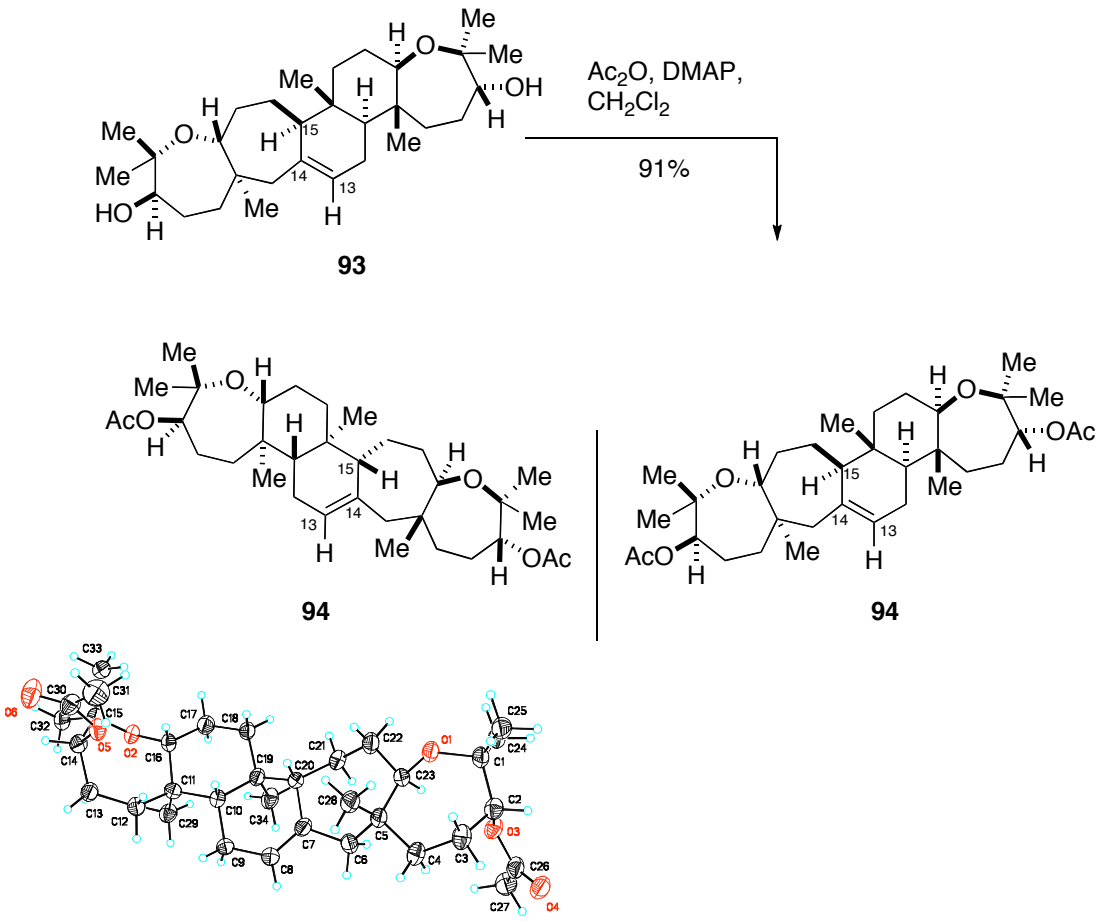
Having intermediate **90** in hand, we explored the second-stage biomimetic bicyclization. Using Me_3SiOTf and DTBMP at -78 °C, the desired bicyclization (presumably via chair-like transition state **91**) occurred with kinetic deprotonation at C13 leading to the C13-C14 trisubstituted alkene diol **93** in excellent yield (43%). Moreover, this reaction was performed on an impressive 615 mg scale, giving 250 mg of **93**. The bicyclization and concomitant deprotonation are presumably proceeding in a concerted manner, as no tetrasubstituted alkene or other alkene regioisomers were isolated (Scheme 27).

Scheme 27. Second-stage biomimetic bicyclization



Given the need for the tetrasubstituted alkene regioisomer, our efforts to modify the conditions for bicyclization to achieve a different regiochemical course of tetrasubstituted alkene formation were not fruitful, as changes in temperature (i.e. -40 °C) or reactant stoichiometry (i.e. equivalents of DTBMP) had no effect. Thus, we focused on the isomerization of the trisubstituted alkene as a means of entry into the desired alkene regiochemistry. Alcohol protection of **93** was necessary to explore the alkene isomerization (*vide infra*), so the diacetate derivative **94** was synthesized. Serendipitously, an X-ray structure of **94** was obtained, giving confirmation to the absolute stereochemistry and regioselectivity of trisubstituted alkene formation in the previous cyclization (Scheme 28).

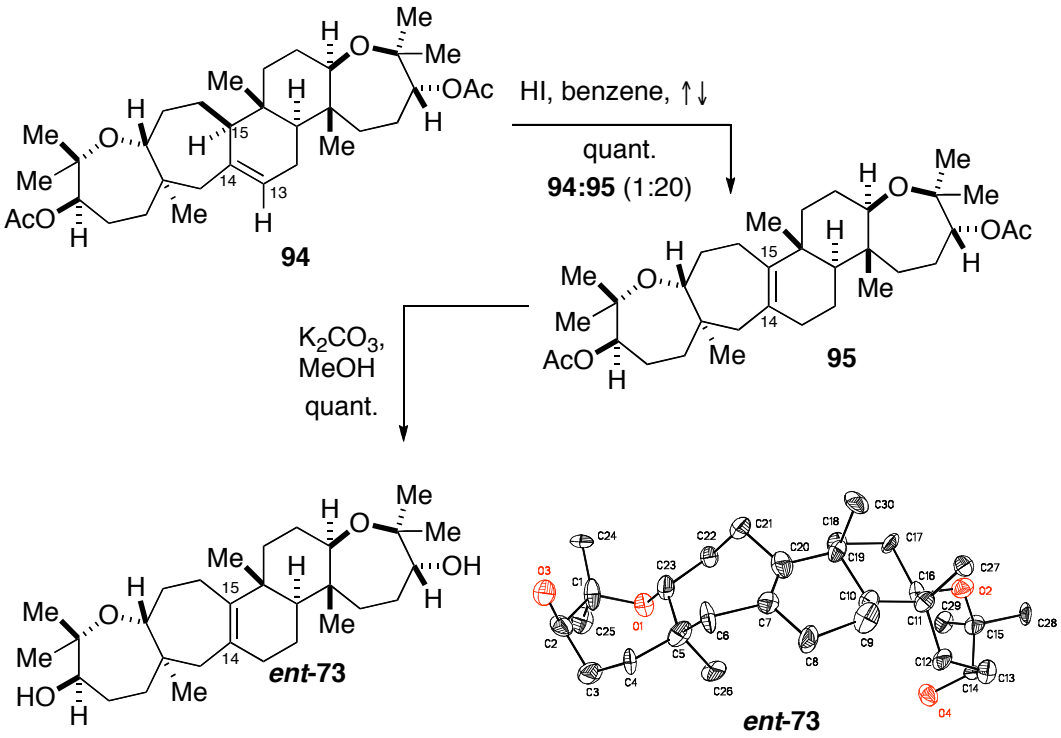
Scheme 28. Acetylation of 93 and thermal ellipsoid of diacetate 94



For a related system, I_2 in refluxing benzene was successfully utilized in the migration of a trisubstituted alkene into a tetrasubstituted alkene at a ring fusion.[77] However, our trisubstituted alkene **94** behaved poorly under these conditions resulting in decomposition with only a trace amount of the tetrasubstituted alkene regioisomer.[78] We were somewhat surprised, albeit pleasantly so, that exposure of the diacetate trisubstituted alkene **94** to catalytic HI in benzene at 70 °C resulted in a clean conversion to the tetrasubstituted alkene isomer **95** (20:1 tetrasubstituted:trisubstituted) . We had in mind that the cleavage of "simple" ethers using HI in benzene was a well-precedented

transformation[79], so the robustness of our dioxepane under these conditions was unexpected. However, we believed the acetate protecting groups inductively deactivated the cyclic ether oxygens from protonation under such strongly acidic conditions. The acetate protection of the alcohols proved critical in serving the dual purpose of improving the crystallinity of the compound for X-ray analysis and by effectively "protecting" the cyclic ethers from decomposition during the isomerization (Scheme 29).

Scheme 29. HI-catalyzed isomerization of trisubstituted alkene 94 to tetrasubstituted alkene 95; deacetylation to diol *ent*-73 and thermal ellipsoid of *ent*-73

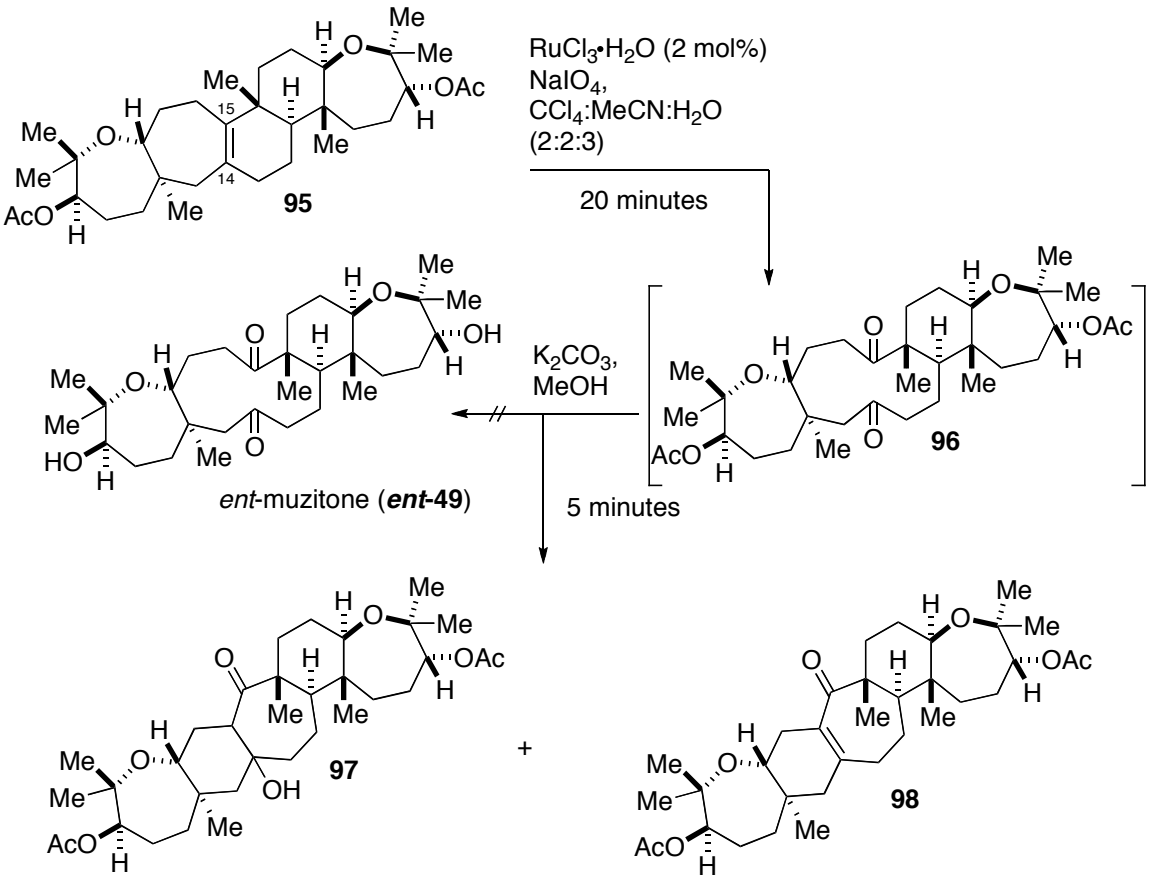


After completing the syntheses of the key pentacyclic tetrasubstituted alkene diacetate **95** and corresponding diol ***ent*-73**, we turned our attention to the

biomimetic oxidation of the alkene to complete the synthesis of *ent*-muzitone (***ent*-49**). Subjection of the diacetate **95** to a RuO_4-catalyzed alkene cleavage resulted in a rapid conversion to the intermediate diacetoxy diketone **96**, which, after work-up, was immediately exposed to K_2CO_3 in MeOH to cleave the acetate esters. This resulted in a quick conversion (5 minutes) to what was presumed to be the natural product *ent*-muzitone (***ent*-49**). However, upon analysis of the crude ^1H NMR, the acetate esters were intact and multiple products were present in what was indicated by TLC to be a clean transformation. Apparently, upon exposure to basic conditions, the diketone underwent a transannular aldol reaction giving possible aldol products **97** and **98** (while the crude ^1H NMR seemed to indicate the presence of these compounds, we speculated as to the exact structures of these byproducts, as isolation of the individual components of the reaction mixture was not possible). With these results in hand, we realized that the biomimetic alkene oxidation must occur as the last step of the synthetic sequence. Protecting group manipulation of the two hydroxyl groups in the presence of the diketone was deemed too risky, as we could not find a suitable alcohol protecting group that could be easily removed under relatively neutral conditions as required by the sensitive nature of the molecule. Thus, we opted for a strategy of alkene dihydroxylation of diacetoxy **95** followed by deacetylation to a tetraol intermediate. Upon tetraol formation, a $NaIO_4$- or $Pb(OAc)_4$-catalyzed cleavage of the *syn*-diol would give the natural product. Alternatively, a direct cleavage of ***ent*-73** was considered, though we had in mind that the oxidative alkene cleavage in the presence of *unprotected* hydroxyl groups could be

problematic. Nonetheless, we also explored the alkene cleavage on ***ent*-73** (Scheme 30).

Scheme 30: Attempted RuO_4-catalyzed alkene cleavage and deacetylation to *ent*-muzitone (*ent*-49)

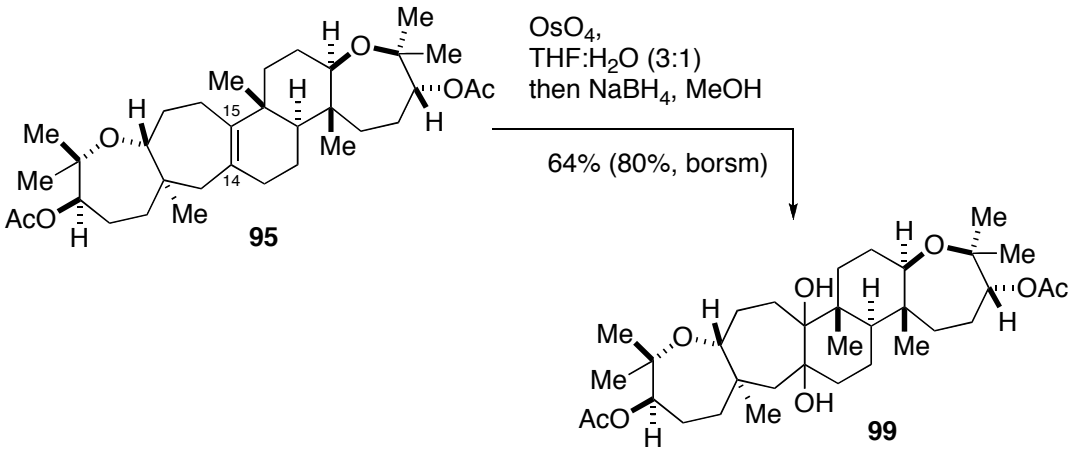


Possible transannular aldol products

Therefore, a dihydroxylation of diacetate **95** was first explored. We ultimately found that a standard dihydroxylation of this material could be accomplished using *stoichiometric* OsO_4. Regardless of the use of additives, such as methanesulfonamide or *N*-methylmorpholine-*N*-oxide (NMO), an excess of OsO_4 was required. Furthermore, the cyclic osmate ester was found to be incredibly stable to "standard" reduction conditions using $NaHSO_3$ or NaS_2O_3 and was

subjected to silica gel chromatography without degradation. Encouraged by a report from Sharpless[80] where $NaBH_4$ was found to be an effective reducing agent for hindered 1,1-disubstituted or trisubstituted osmate esters, we subjected the crude osmate ester derived from **95** to $NaBH_4$ reduction in MeOH. This led to a rapid reduction of the osmate ester, which liberated the diacetate diol **99**. Interestingly, the dihydroxylation proceeded with complete facial selectivity, though we could not elucidate the obtained diastereomer (we suspect the substrate controlled dihydroxylation is occurring *anti* to the allylic angular methyl group) (Scheme 31).

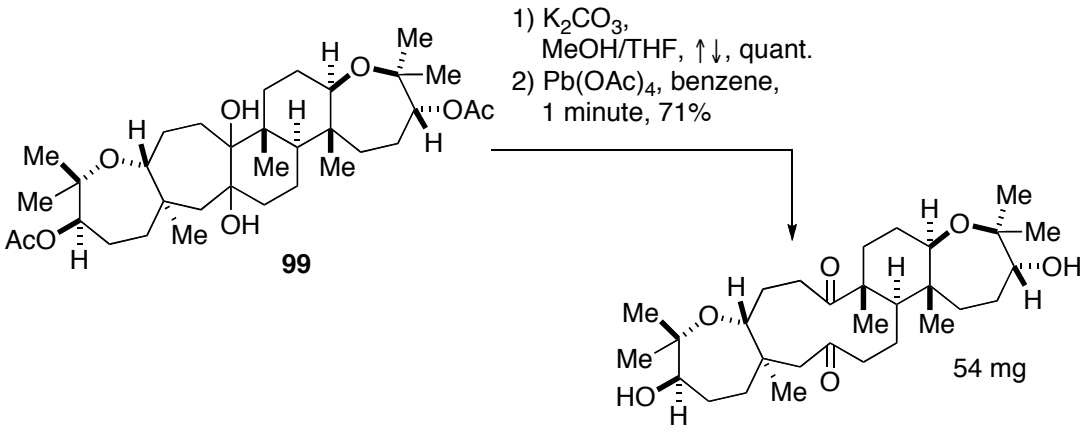
Scheme 31. Dihydroxylation of tetrasubstituted alkene diacetate 95



With the base-sensitive nature of the diketone in mind, we elected to cleave the acetate esters at this stage to avoid undesired transannular aldol reactions. Thus, deacetylation of **100** to the corresponding tetraol proceeded smoothly using K_2CO_3 in refluxing MeOH/THF. Exposure of the intermediate tetraol to $Pb(OAc)_4$ in benzene at room temperature resulted in a rapid and clean oxidative cleavage (ca. 1 minute) to the final diketone of *ent*-muzitone (***ent*-49**) in excellent yield. $NaIO_4$ was also found to promote the oxidative cleavage to ***ent*-49** but this

transformation was sluggish (ca. 48 hours) providing only a trace amount of recoverable diketone (Scheme 32).

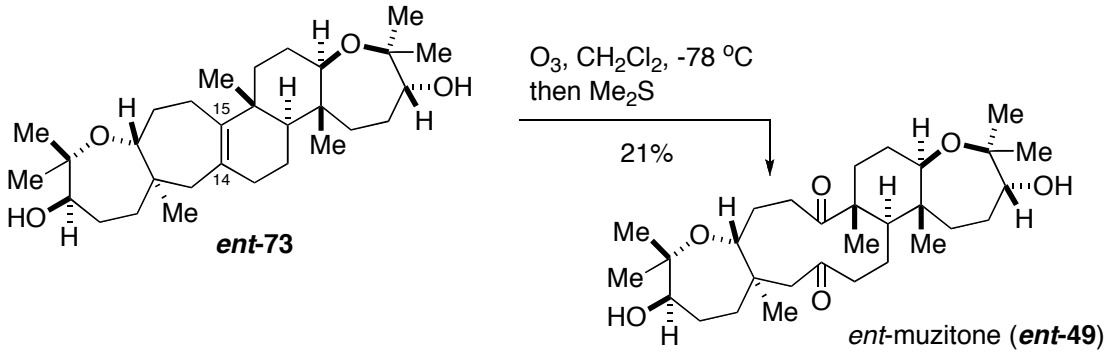
Scheme 32. $Pb(OAc)_4$-promoted oxidative cleavage: completion of the proposed structure of *ent*-muzitone (*ent*-49)



ent-muzitone (***ent*-49**)

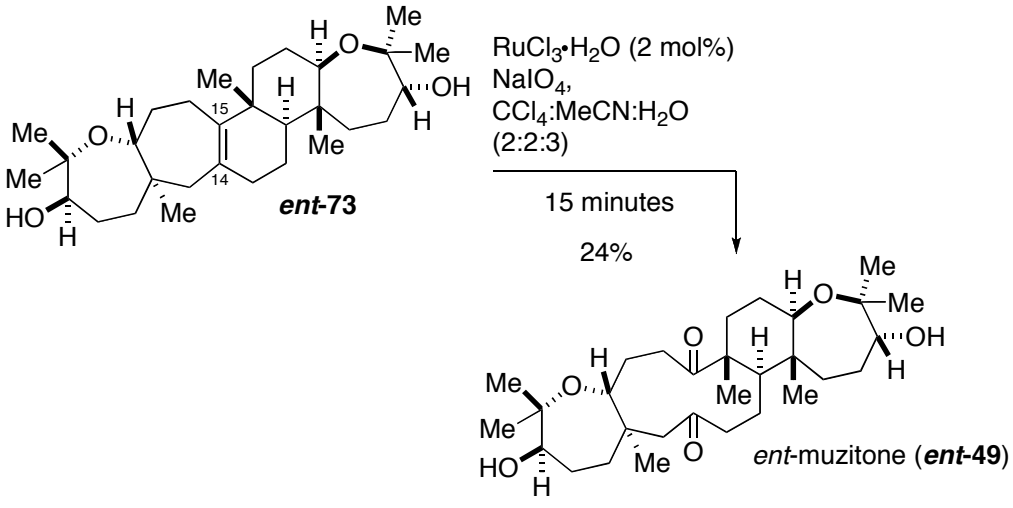
Having completed the synthesis of the proposed structure of *ent*-muzitone (***ent*-49**), we were somewhat surprised to find major discrepancies in our characterization data when compared to those reported by Kashman. Most obvious among these differences, Kashman reported that muzitone (**49**) was an oil, whereas our synthetic material was a white, crystalline solid with a melting point of 210-213 ^{o}C. Concerned that the final oxidative cleavage was giving an unfathomable outcome other than diketone formation, we elected to subject tetrasubstituted alkene diol ***ent*-73** to an ozonolysis with Me_2S reductive work-up. After much experimentation, we were able to successfully perform an ozonolysis on ***ent*-73** giving the *identical* compound obtained from the dihydroxylation/ oxidative cleavage, albeit in lower yield (Scheme 33).

Scheme 33. Ozonolysis of *ent*-73: completion of the proposed structure of *ent*-muzitone (*ent*-49)



To further substantiate our structural assignment, we elected to subject ***ent*-73** to the $RuCl_3/NaIO_4$ conditions that was previously shown to effectively cleave diacetoxy **95**. Gratifyingly, this method also gave a clean and rapid conversion (15 minutes) to the proposed structure of *ent*-muzitone (***ent*-73**). Apparently, our concern over ruthenium-catalyzed over-oxidation of the unprotected alcohols was unmerited, though the low yield of the reaction may indicate some incompatibility with the conditions (Scheme 34).

Scheme 34: RuO_4-catalyzed cleavage of *ent*-73: completion of the proposed structure of *ent*-muzitone (*ent*-49)

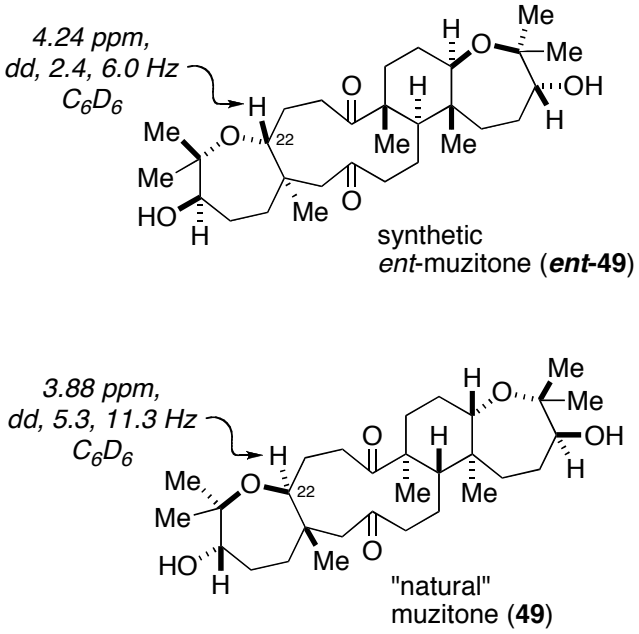


Thus, we demonstrated that $Pb(OAc)_4$- or $NaIO_4$-promoted oxidative cleavage of a diol, ozonolysis, as well as RuO_4-promoted alkene cleavage all led to the same diketone compound, consistent with the proposed structure of *ent*-muzitone (***ent*-49**). We believed that three mechanistically distinct transformations leading to the same compound gave incredible weight to our structural assignment. Moreover, the crystal structure of the "pre-muzitone" tetrasubstituted alkene diol ***ent*-73** had alleviated any consternation over unexpected skeletal rearrangement during the critical HI-catalyzed alkene isomerization.

Upon further consideration of key characterization details, we focused on the ^{1}H NMR data. The four most deshielded protons were the obvious choice for comparison. While the general signal pattern of the synthetic material did not match that of muzitone (**49**) as reported by Kashman, we were intrigued by the coupling constant values of the C22 proton for the synthetic and natural materials. Our ^{1}H NMR of the synthetic *ent*-muzitone (***ent*-49**) shows that the chemical shift of the C22 proton is 4.24 ppm (600 MHz, C_6D_6) and is a doublet of doublets with coupling constants of 2.4 and 6.0 Hz (for instructive comparison, the shift of this proton in the precursor, ***ent*-73**, was 3.49 ppm (400 MHz, $CDCl_3$) with coupling constants of 5.2 and 11.6 Hz). This C22 proton in Kashman's data has a chemical shift of 3.88 ppm (500 MHz, C_6D_6) and coupling constants of 5.3 and 11.3 Hz. Considering the conformational freedom achieved upon oxidative cleavage of the tetrasubstituted alkene, our data seems more consistent with the expected conformational change. Kashman's coupling constant data is more

consistent with a rigid cyclic system, as observed in our characterization of ***ent*-73**. Based on these considerations, we were led to believe the stereochemical and/or structural assignment of Kashman's muzitone (**49**) was incorrect (Figure 3).

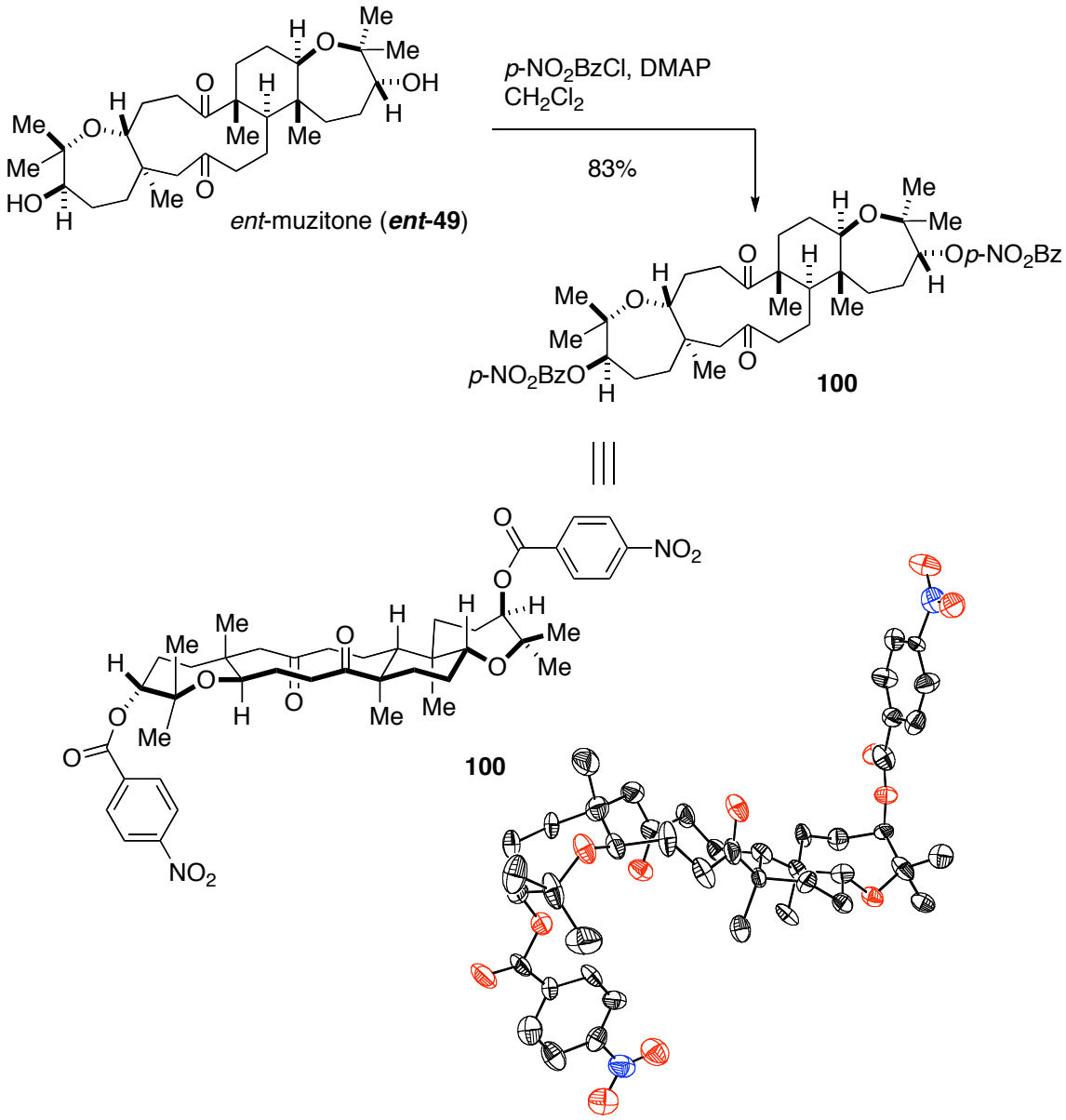
Figure 3. Comparison of synthetic *ent*-muzitone and "natural" muzitone



After many unsuccessful attempts to grow single crystals of ***ent*-49**, we elected to protect the free alcohols in an attempt to improve the crystallinity of the compound. With the undesired transannular aldol reaction in mind, our plan was to ester-protect the alcohols of ***ent*-73** followed by oxidative cleavage in order to avoid potential problems with base-promoted alcohol protection of ***ent*-49**. However, we were surprised to find that exposure of ***ent*-49** to DMAP-catalyzed *para*-nitrobenzoyl ester protection led to a very clean conversion to the desired di-*para*-nitrobenzoyl ester **100**. More importantly, recrystallization of **100** afforded white needle-like crystals that were suitable for X-ray analysis. The thermal

ellipsoid of **100** gave absolute proof to our structural assignment, thus proving Kashman's proposed structure of muzitone was incorrect (Scheme 35).

Scheme 35. Di-*para*-nitrobenzoyl ester protection of *ent*-49 to 100; thermal ellipsoid of 100



In conclusion, we have completed the total synthesis of the proposed structure of *ent*-muzitone (***ent*-49**) using a biomimetic strategy that featured a tandem oxa/ carbacyclization cascade to build the proposed biosynthetic intermediate pentacyclic tetrasubsituted alkene ***ent*-73**. The key HI-catalyzed isomerization of the trisubstituted alkene to ***ent*-73** was profoundly critical in allowing for synthetic investigation of the final biomimetic alkene oxidation. We found that $NaBH_4$ reduction of the stable cyclic osmate ester derived from the tetrasubstituted alkene was key in achieving a successful dihydroxylation. The biomimetic oxidation of the tetrasubstituted alkene gave considerable insight into the reactivity of the tetrasubstituted alkene, a relatively unexplored functionality in synthetic chemistry. Ultimately, our bioinspired total synthesis of the proposed structure of *ent*-muzitone (***ent*-49**) revealed a structural misassignment that has implications beyond this synthetic achievement. Muzitone (**49**) was thought to arise biosynthetically from abudinol B. Thus, the biogenetic link between muzitone (**49**) and abudinol B (**50**) was discredited by our completion of the total synthesis of *ent*-muzitone (***ent*-50**). This synthesis further demonstrates the power of total synthesis as a vehicle by which a postulated biogenesis can be empirically tested.

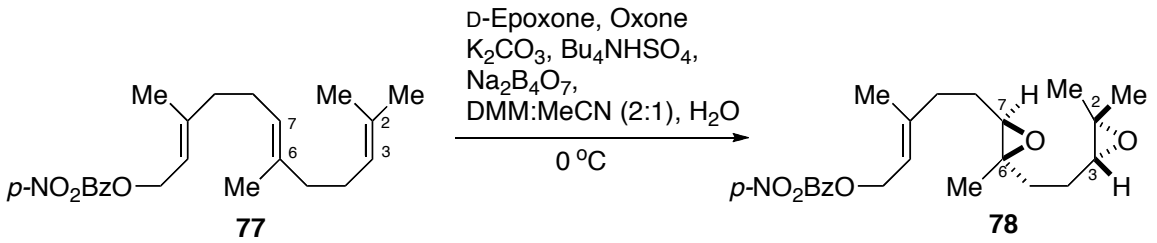
2.3. Experimental Details

General information: ^{1}H and ^{13}C NMR spectra were recorded on a Varian INOVA-400 spectrometer (400 MHz for ^{1}H, 100 MHz for ^{13}C), or an INOVA-600 spectrometer (600 MHz for ^{1}H, 150 MHz for ^{13}C). NMR spectra were recorded as solutions in deuterated chloroform ($CDCl_3$) with residual chloroform (7.27 ppm for ^{1}H NMR and 77.23 ppm for ^{13}C NMR) taken as the internal standard, deuterated methanol (CD_3OD) with residual methanol (4.78 ppm for ^{1}H, 49.15 ppm for ^{13}C) taken as the internal standard, deuterated benzene (C_6D_6) with residual benzene (7.16 ppm for ^{1}H, 128.39 ppm for ^{13}C) taken as the internal standard, deuterated dichloromethane (CD_2Cl_2) with residual dichloromethane (5.35 ppm ^{1}H, 54.00 ppm for ^{13}C) taken as the internal standard, or deuterated tetrahydrofuran (C_4D_8O) with residual tetrahydrofuran taken as the internal standard (67.57 ppm for ^{13}C) and were reported in parts per million (ppm). Abbreviations for signal coupling are as follows: s, singlet; d, doublet; t, triplet; dd, doublet of doublets; dt, doublet of triplets; qt, quartet of triplets; dtd, doublet of triplet of doublets; ddt, doublet of doublet of triplets; ddd, doublet of doublet of doublets; m, multiplet. IR spectra were collected on a Mattson Genesis II FT-IR spectrometer with samples as neat films. Mass spectra (high resolution FAB or EI) were recorded on a VG 70-S Nier Johason mass spectrometer or a Thermo Finnigan LTQ FT spectrometer. Optical rotations were recorded at 23 ^{o}C with a Perkin-Elmer Model 341 polarimeter (concentration in g/100mL). Analytical thin layer chromatography (TLC) was performed on precoated glass backed plates purchased from Whatman (silica gel 60 F_{254}; 0.25 mm thickness). Flash column

chromatography was carried out with silica gel 60 (230-400 mesh ASTM) from EM Science.

All reactions except as mentioned were conducted with anhydrous solvents in oven - dried or flame - dried and argon - charged glassware. All anhydrous solvents were dried over 3Å or 4Å molecular sieves (beads). Trace water content was tested with Coulometric KF titrator from Denver Instruments. All solvents used in workup, extraction and column chromatography were used as received from commercial suppliers without prior purification. During reaction workup, the reaction mixture was usually diluted to three times the original volume, and washed with an equal volume of water and/or aqueous solutions as needed. All reagents were purchased from Sigma-Aldrich.

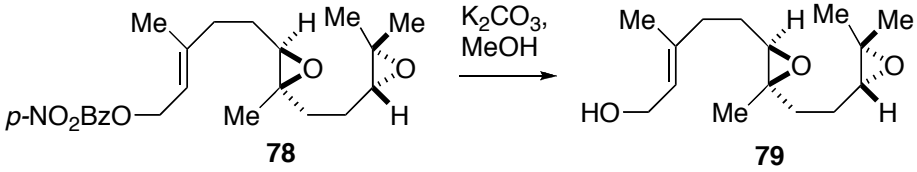
Synthesis of *para* - nitrobenzoyl diepoxy farnesol 78



trans,trans-Farnesol *para*-nitrobenzoate **78**[81] (20 g, 54 mmol) was transferred into a three neck 3.0 L flask. Then DMM:MeCN (2:1) (0.10 M, 500 mL) and $Na_2B_4O_7$ (0.05 M soln. in $4x10^{-4}$ M Na_2EDTA) (0.15 M, 350 mL) were added, followed by the addition of Bu_4NHSO_4 (1.8 g, 5.4 mmol). D-Epoxone (7.0 g, 27 mmol) was added. The flask was equipped with a mechanical stirrer and two addition funnels. To one addition funnel was added Oxone (140 g, 220 mmol) dissolved in $4x10^{-4}$ M Na_2EDTA (400 mL). To the other addition funnel was added K_2CO_3 (112 g, 810 mmol) dissolved in distilled H_2O (400 mL). The flask was cooled to 0 °C and the Oxone and K_2CO_3 solutions were added dropwise over a 1.25 hour period. After the additions were complete, EtOAc (500 mL) was added to the reaction and transferred to a 3.0 L separatory funnel. After the layers were separated, the aqueous was extracted with EtOAc (750 mL). The organic extracts were combined and dried with $MgSO_4$. After filtration, the volatiles were removed under reduced pressure. Chromatography (4:1→2:1 hexanes:EtOAc) provided diepoxide **78** (d.r. = 4:1) as a pale yellow oil (10.6 g, 49%), along with the monoepoxide (mixture of the 6,7- and 10,11-epoxides) (5.93 g, 28%). This procedure was repeated x 3. The monoepoxide from each reaction was collected and subjected to the same reaction conditions using only

2.0 equiv. of oxone and 8.0 equiv. of K_2CO_3. The combined reactions gave 50.9 g of the diepoxide **78**. $[\alpha]_D^{23}$ = + 8.8 (c 1.40, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.29 (d, *J* = 8.8 Hz, 2H), 8.22 (d, *J* = 8.8 Hz, 2H), 5.52 (t, *J* = 7.2 Hz, 1H), 4.90 (d, *J* = 6.8 Hz, 2H), 2.75 (t, *J* = 6.0 Hz, 1H), 2.71 (m, 1H), 2.24 (m, 2H), 1.81 (s, 3H), 1.79-1.56 (m, 6H), 1.31 (s, 3H), 1.29 (s, 3H), 1.27 (s, 3H); (100 MHz, $CDCl_3$) δ 164.9, 150.7, 142.5, 135.9, 130.9 (x2), 123.7 (x2), 118.5, 63.9, 62.8, 60.5, 58.6, 36.4, 35.4, 27.1, 25.0 (x2), 24.7, 18.4, 16.9, 16.8; IR (KBr) 2962, 1724, 1606, 1529, 1456, 1381, 1348, 1271, 1101, 1014, 874, 721 cm^{-1}; HRMS (ESI) $[M+H^+]$ Calcd. for $C_{22}H_{29}N_1O_6$ 404.20676, found 404.20717.

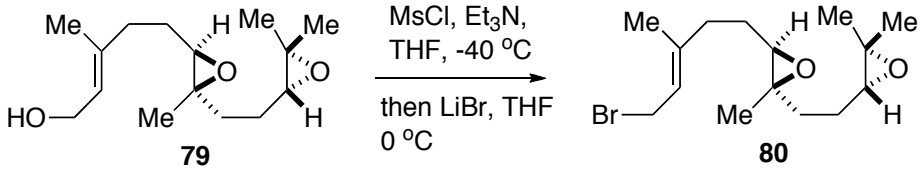
Synthesis of diepoxy allylic alcohol 79.



Diepoxy *para*-nitrobenzoate **78** (23 g, 57 mmol) was dissolved in MeOH (0.50 M, 115 mL). Then K_2CO_3 (3.9 g, 29 mmol) was added all at once. The reaction was stirred for 15 minutes. After dilution with Et_2O (100 mL), and the reaction was quenched by the addition of a saturated solution of NH_4Cl (250 mL). The layers were separated. The aqueous layer was extracted with EtOAc (250 mL x 2). The organic extracts were combined and dried with $MgSO_4$. After filtration, the volatiles were removed under reduced pressure. Chromatography (4:1→0:1 hexanes:EtOAc) then gave diepoxy allylic alcohol **79** as an oil (12.8 g, 88%). When loading the crude mixture on silica, EtOAc was used to dissolve the *para*-nitrobenzoate methyl ester byproduct. This did not affect the separation. This

procedure was also used on a second batch of diepoxide **78** (27.8 g) to give additional diepoxy allylic alcohol **79** (15.1 g, 86%). $[\alpha]_D^{23}$ = + 11.0 (c 0.965, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 5.46 (m, 1H), 4.16 (d, *J* = 6.6 Hz, 2H), 2.76-2.71 (m, 2H), 2.21 (m, 1H), 2.16 (m, 1H), 1.79 (m, 1H), 1.70 (s, 3H), 1.68 (m, 3H), 1.60 (m, 3H), 1.60 (m, 3H), 1.31 (s, 3H), 1.28 (s, 3H), 1.27 (s, 3H); (150 MHz, $CDCl_3$) δ 138.5, 124.3, 64.1, 62.9, 60.5, 59.4, 58.7, 36.4, 35.3, 27.0, 24.9, 24.7, 18.8, 16.9, 16.4; IR (KBr) 3437, 2924, 1666, 1454, 1385, 1250, 1119, 1011, 872 cm^{-1}; HRMS (APCI) [M+H$^+$] Calcd. for $C_{15}H_{27}O_3$ 255.19547, found 255.19552.

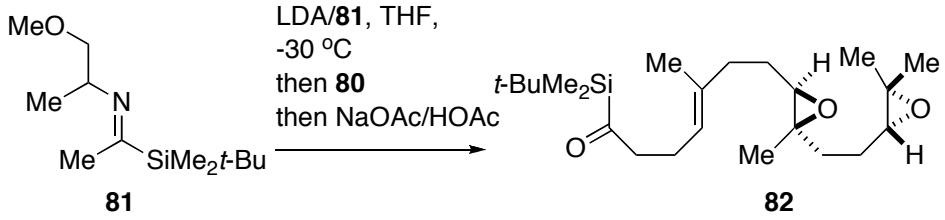
Synthesis of diepoxy allylic bromide 80



The diepoxy allylic alcohol **79** (12.8 g, 50 mmol) was dissolved in THF (0.30 M, 170 mL). The solution was cooled to -40 °C. Et_3N (10.5 mL, 76 mmol) was then added all at once. MsCl (4.71 mL, 60 mmol) was then added all at once. The reaction was stirred for 30 minutes at -40 °C. After warming to 0 °C, flame-dried LiBr (13.1 g, 150 mmol) dissolved in THF (5.0 M, 30 mL) was added all at once. The reaction was stirred for an additional 15 minutes. Then the reaction was quenched by the addition of H_2O (200 mL). Et_2O (200 mL) was added. After the layers were separated, the aqueous layer was extracted with Et_2O (100 mL). The organic extracts were combined and dried with $MgSO_4$. After filtration, the volatiles were removed under reduced pressure. To the crude mixture was

added hexanes (100 mL), and the solids were filtered. After removal of the volatiles under reduced pressure, the analytically pure allylic bromide (15.3 g, 96%) was taken on to the next step. * We elected not to subject this sensitive allylic bromide to chromatography, as significant decomposition occurred (even with Et_3N buffering). Once made, the allylic bromide was immediately used. This procedure was also used on a second batch of diepoxy allylic alcohol **79** (15.1 g) to give additional diepoxy allylic bromide **80** (16.9 g, 90%). $[\alpha]_D^{23}$ = + 4.9 (c 0.85, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 5.59 (t, *J* = 8.4 Hz, 1H), 4.02 (d, *J* = 7.8 Hz, 2H), 2.73 (m, 2H), 2.24 (m, 1H), 2.18 (m, 1H), 1.76 (s, 3H), 1.68 (m, 3H), 1.61 (m, 3H), 1.32 (s, 3H), 1.29 (s, 3H), 1.28 (s, 3H); (150 MHz, $CDCl_3$) δ 142.6, 121.3, 63.9, 62.7, 60.5, 58.7, 36.4, 35.3, 29.4, 26.9, 25.0, 24.7, 18.8, 16.9, 16.1; IR (KBr) 2962, 1655, 1454, 1381, 1203, 1122, 876 cm^{-1}; HRMS (APCI) $[M+H^+]$ Calcd. for $C_{15}H_{26}O_2Br_1$ 317.11107, found 317.11115.

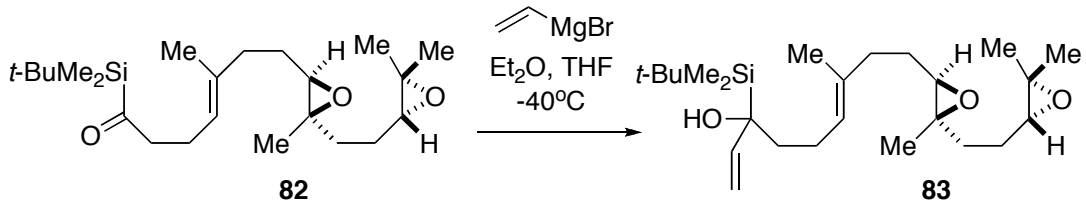
Synthesis of diepoxy acyl silane 82



Anhydrous diisopropylamine (DIPA) (12 mL, 85 mmol) was added to THF (0.75 M, 71 mL). After cooling to -30 °C, *n*-BuLi (2.5 M solution in hexanes, 34 mL, 85 mmol) was added via syringe pump over a 30 minute period. After stirring for 10 minutes at -30 °C, silyl imine **81**[82] (18 g, 80 mmol) was slowly added via syringe pump over a 30 minute period. During this time, the solution became light yellow in color. The reaction was then allowed to warm to -10 °C over a 30 minute

period. After cooling to -30 °C, diepoxy allylic bromide **80** dissolved in THF (2.0 M, 20 mL) was added via syringe pump over a 45 minute period. The reaction was then warmed to -10 °C over a 1 hour period. After dilution with Et_2O (100 mL), the reaction contents were poured into half saturated NH_4Cl (250 mL). After separation of layers, the aqueous layer was extracted with Et_2O (300 mL). The organic extracts were combined and dried with $MgSO_4$. After filtration, the volatiles were removed under reduced pressure. The crude mixture was dissolved in pentane (300 mL). Then a NaOAc/HOAc buffer (200 mL) (made by mixing 56 g NaOAc, 126 mL HOAc, and 540 mL distilled H_2O) was added. The biphasic mixture was stirred for 1 hour. Et_2O (200 mL) was added, and the layers were separated. The organic layer was washed with saturated $NaHCO_3$. Care must be taken to add additional solid $NaHCO_3$ until the aqueous layer is basic. After drying with $MgSO_4$, the volatiles were removed under reduced pressure. Chromatography (20:1→4:1 hexanes:EtOAc) afforded acyl silane **82** as a yellow oil (15.6 g, 74%). This procedure was also used on a second batch of diepoxy allylic bromide **80** (13.4 g) to give additional acyl silane **82** (12.6 g, 75%). $[\alpha]_D^{23}$ = + 10.4 (c 1.25, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 5.11 (t, *J* = 6.8 Hz, 1H), 2.70 (t, *J* = 6.0 Hz, 1H), 2.63 (t, *J* = 7.2 Hz, 1H), 2.20 (dd, *J* = 6.8, 14.4 Hz, 1H), 2.10 (m, 1H), 1.78 (m, 3H), 1.63 (s, 3H), 1.61 (m, 9H), 1.32 (s, 3H), 1.27 (s, 3H), 0.93 (s, 9H), 0.19 (s, 3H); (100 MHz, $CDCl_3$) δ 247.4, 135.0, 123.9, 64.0, 63.1, 60.5, 58.6, 50.3, 36.5, 35.5, 27.4, 26.6 (x3), 25.0, 24.8, 20.8, 18.8, 16.9, 16.7, 16.1, -6.80 (x2); IR (KBr) 2929, 2858, 1641, 1464, 1385, 1250, 1122, 837, 775, 673 cm^{-1}; HRMS (ESI) [M+H^+] Calcd. for $C_{23}H_{42}O_3Si_1$ 395.29760, found 395.29775.

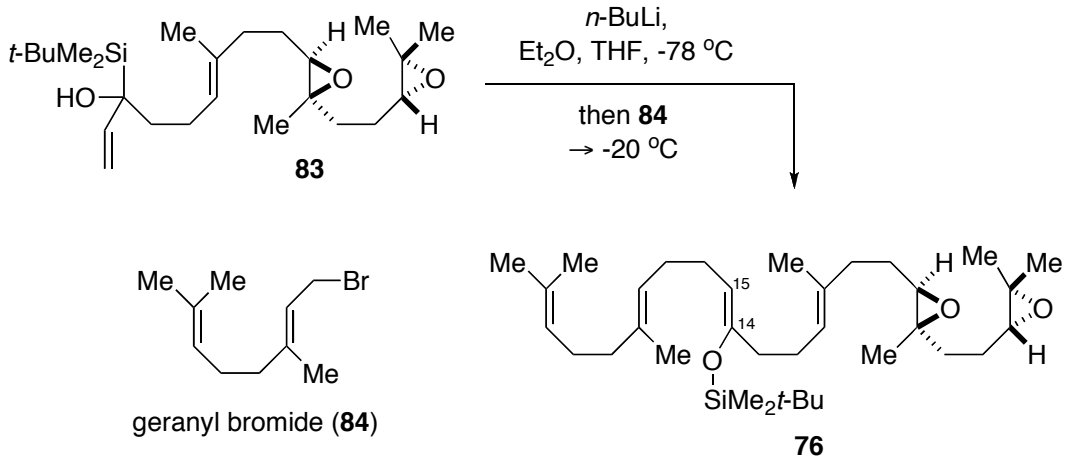
Synthesis of α-silyl allylic alcohol 83



82 **83**

Acyl silane **82** (12.6 g, 32 mmol) was dissolved in Et_2O (0.50 M, 70 mL). The solution was cooled to -40 °C. Then vinyl magnesium bromide (1.0 M solution in THF, 64 mL, 64 mmol) was added via syringe pump over a 45 minute period. After the addition was complete, the reaction was stirred at -40 °C for 1.5 hours. After dilution with Et_2O (100 mL), the reaction was quenched by the addition of a saturated solution of NH_4Cl (200 mL). The biphasic mixture was stirred for 20 minutes. After the layers were separated, the aqueous layer was extracted with Et_2O (150 mL). The organic extracts were combined and dried with $MgSO_4$. After concentration, α-silyl allylic alcohol **83** was obtained as an analytically pure oil (13.2 g, quant.). $[\alpha]_D^{23}$ = + 6.5 (c 1.08, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 5.95 (dd, *J* = 10.8, 17.2 Hz, 1H), 5.19 (t, *J* = 7.6 Hz, 1H), 5.06 (m, 2H), 2.72 (t, *J* = 6.0 Hz, 2H), 2.11 (m, 4H), 1.90-1.76 (m, 4H), 1.64 (m, 5H), 1.61 (s, 3H), 1.31 (s, 3H), 1.27 (s, 6H), 0.96 (s, 9H), 0.009 (s, 3H), 0.002 (s, 3H); (100 MHz, $CDCl_3$) δ 143.7, 134.6, 125.5, 110.2, 74.1, 64.0, 63.1, 60.5, 58.6, 37.3, 36.5, 35.5, 78.0, 27.3, 25.0, 24.8, 21.3, 18.8, 18.4, 16.9, 16.3, -7.49, -7.62; IR (KBr) 3500, 2958, 2858, 1626, 1464, 1385, 1248, 1119, 999, 903, 833, 769, 673 cm^{-1}; HRMS (APCI) [M+H$^+$] Calcd. for $C_{25}H_{46}O_3Si_1$ 423.32890, found 423.32925.

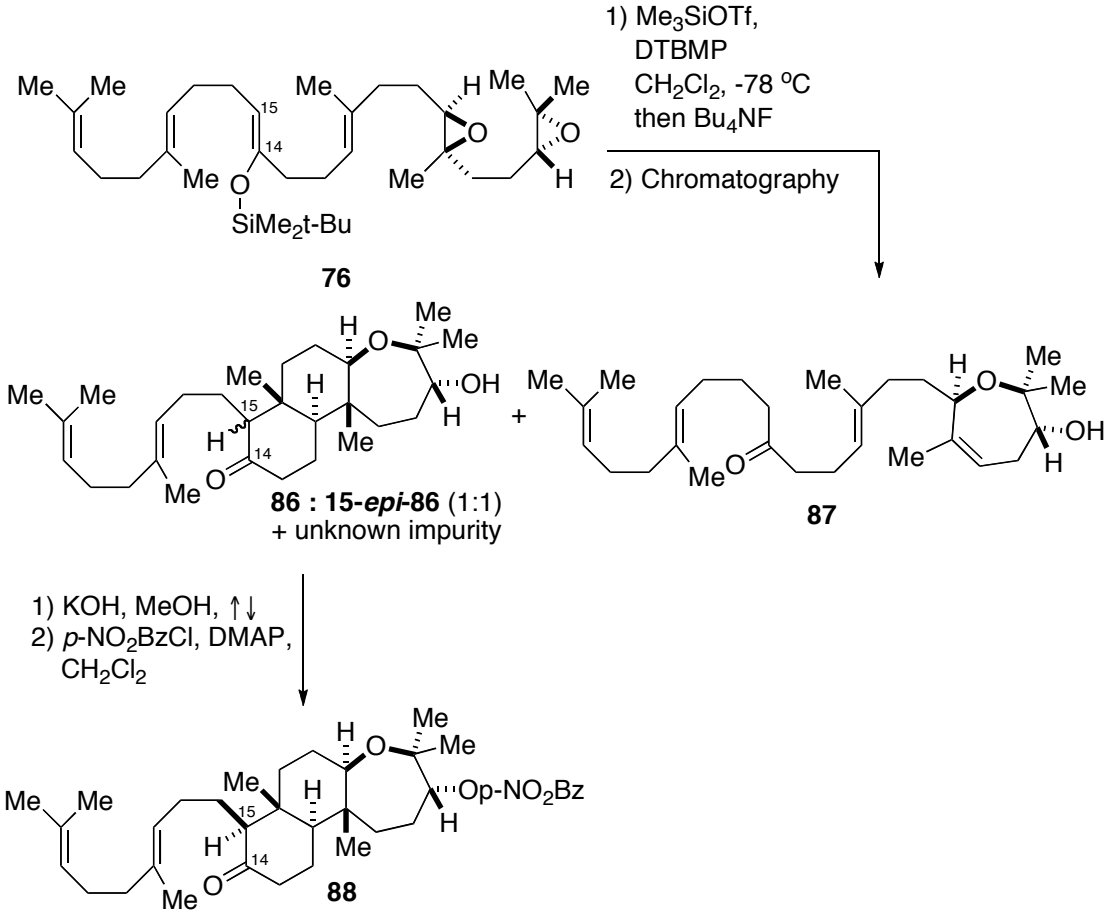
Fragment coupling: Synthesis of enolsilane 76



A 250 mL round bottom flask was pre-cooled to -78 °C. Then *n*-BuLi (2.5 M in hexanes, 15.5 mL, 39 mmol) was added to the flask. **83** (13.2 g, 32 mmol) was dissolved in a mixture of THF (6.0 mL) and Et_2O (30 mL). The solution was then added to the pre-cooled *n*-BuLi via syringe pump over a 30 minute period. Then THF (64 mL) was slowly added via syringe pump over a 45 minute period. The reaction was stirred for 1.5 hours. Then geranyl bromide (**84**) (9.62 mL, 48 mmol) dissolved in THF (4.0 M, 10 mL) was added via syringe pump over a 30 minute period. After the addition was complete, the flask was tightly sealed and place into a -20 °C freezer without stirring. After 17 hours, the reaction was diluted with Et_2O (100 mL) and quenched by the addition of H_2O (150 mL). After separation of layers, the aqueous layer was extracted with Et_2O (100 mL). The organics were combined and dried with $MgSO_4$. After filtration, the volatiles were removed under reduced pressure. Chromatography (30:1→9:1 hexanes:EtOAc + 0.5 % Et_3N) gave enol silane **76** as an oil (7.01 g, 39%). $[\alpha]_D^{23}$ = + 6.1 (c 1.39, CH_2Cl_2); ^1H NMR (400 MHz, C_6D_6) δ 5.39 (m, 1H), 5.27 (m, 2H), 4.65 (t, *J* = 6.4

Hz, 1H), 2.65 (t, *J* = 6.4 Hz, 1H), 2.54 (t, *J* = 6.8 Hz, 1H), 2.33 (m, 4H), 2.23-2.03 (m, 11H), 1.70 (s, 3H), 1.66 (s, 3H), 1.59 (s, 3H), 1.58 (s, 3H), 1.57 (m, 5H), 1.16 (s, 3H), 1.13 (s, 3H), 1.11 (s, 3H), 1.04 (s, 9H), 0.18 (s, 6H); (100 MHz, $CDCl_3$) δ 150.1, 135.1, 134.6, 131.4, 124.6 , 124.6 (x2), 108.1, 64.1, 63.2, 60.5, 58.6, 39.9, 36.9, 36.5, 35.5, 28.5, 27.5, 26.9, 26.0 (x3), 25.1, 18.8, 18.5, 17.9, 16.9, 16.2, -3.77 (x2); IR (KBr) 2958, 2929, 2858, 1672, 1462, 1379, 1254, 837, 779 cm^{-1}; HRMS (APCI) [M+H^+] Calcd. for $C_{35}H_{62}O_3Si_1$ 559.45410, found 559.45470.

Synthesis of *para*-nitrobenzoyl tricyclic ketone 88



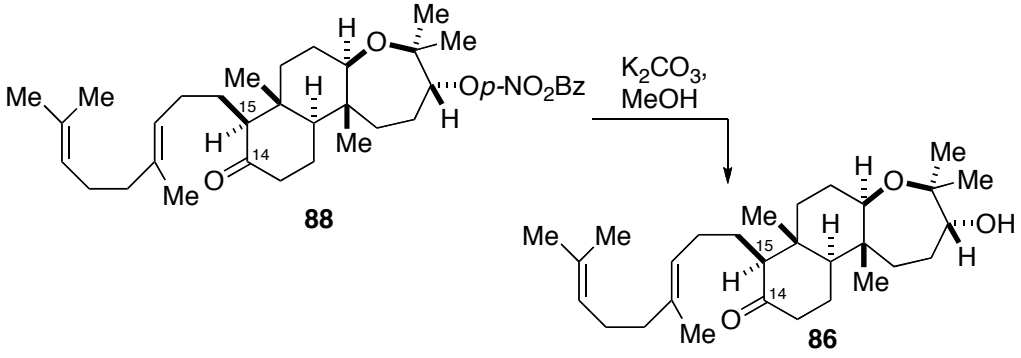
Enol silane **76** (7.01 g, 12.5 mmol) was dissolved in CH_2Cl_2 (0.02 M, 630 mL). Then DTBMP (1.28 g, 6.3 mmol) was added all at once. The mixture was then

cooled to -78 °C. Me_3SiOTf (2.49 mL, 14 mmol) was quickly added, and the reaction was allowed to stir at -78 °C for 1 hour. Then the reaction was poured into a saturated solution of $NaHCO_3$ (500 mL). The layers were separated. The aqueous layer was extracted with Et_2O (300 mL). The organic extracts were combined and dried with $MgSO_4$. After filtration, the volatiles were removed under reduced pressure. The crude mixture was dissolved in THF (0.10 M, 125 mL), and Bu_4NF (1.0 M solution in THF, 25 mL, 25 mmol) was added all at once. The reaction was stirred for 14 hours. After dilution with Et_2O (200 mL), H_2O (200 mL) was added. The layers were separated. The aqueous layer was extracted with Et_2O (200 mL). The organic extracts were combined and dried with $MgSO_4$. After filtration, the volatiles were removed under reduced pressure. Chromatography (9:1→6:1→4:1 hexanes:EtOAc) gave impure tricyclic ketone **86** as an oil (1.6 g, 1:1 mixture of C15 epimers) and monocyclic **87** as an oil (400 mg, 7.3 %). The impure tricyclic ketone **86** was then dissolved in MeOH (100 mL). Then KOH (10 g) was added to the solution, which was then refluxed under argon for 3 hours. After this time, the reaction was cooled to r.t. and diluted with H_2O (200 mL) and EtOAc (200 mL). The layers were separated, and the aqueous layer was extracted with EtOAc (200 mL). The organic extracts were combined and dried with $MgSO_4$. After filtration, the volatiles were removed under reduced pressure. ^1H NMR of the crude mixture indicated complete epimerization to the pseduoequatorial C15 epimer. The impurity from the previous step was still present, thus the crude mixture was dissolved in CH_2Cl_2 (36 mL). Then DMAP (880 mg) and *para*-nitrobenzoyl chloride (800 mg) were

successively added to the solution. After 30 minutes of stirring, the reaction was diluted with Et_2O (75 mL), then poured into a saturated solution of $NaHCO_3$ (150 mL). The layers were separated, and the aqueous layer was extracted with Et_2O (150 mL). The organic extracts were combined and dried with $MgSO_4$. After filtration, the volatiles were removed under reduced pressure. Chromatography (9:1 hexanes:EtOAc) gave *para*-nitrobenzoyl tricyclic ketone as an oil (1.32 g, 18% over 4 steps). Characterization for monocyclic **87**: $[\alpha]_D^{23}$ = - 28.3 (c 0.75, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 5.49 (m, 1H), 5.09 (m, 3H), 3.95 (d, *J* = 9.6 Hz, 1H), 3.40 (dd, *J* = 3.6, 10.8 Hz, 1H), 2.46-2.37 (m, 7H), 2.26 (m, 4H), 2.18-1.87 (m, 10H), 1.68 (s, 3H), 1.64 (s, 3H), 1.61 (s, 3H), 1.59 (s, 3H), 1.58 (s, 3H), 1.26 (s, 3H), 1.16 (s, 3H); (150 MHz, $CDCl_3$) δ 211.3, 136.1, 136.0, 135.7, 131.6, 124.5, 123.8, 123.4, 119.4, 76.8, 72.6, 71.8, 42.9, 42.4, 39.9, 36.5, 29.9, 29.7, 27.5, 26.9, 26.8, 25.9, 25.6, 24.2, 24.1, 22.6, 20.1, 17.9, 16.2; IR (KBr) 3487, 2929, 1712, 1448, 1377, 1078 cm^{-1}; HRMS (APCI) [$M+H^+$] Calcd. for $C_{29}H_{48}O_3$ 445.36762, found 445.36788. Characterization for *para*-nitrobenzoyl tricyclic ketone **88**: $[\alpha]_D^{23}$ = + 28.3 (c 1.27, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 8.37 (d, *J* = 9.0 Hz, 2H), 8.25 (d, *J* = 9.0 Hz, 2H), 5.25 (d, *J* = 7.2 Hz, 1H), 5.09 (m, 2H), 3.57 (dd, *J* = 4.8, 12.0 Hz, 1H), 2.39 (m, 1H), 2.26 (m, 1H), 2.16-1.99 (m, 9H), 1.87-1.70 (m, 4H), 1.65 (s, 3H), 1.58 (s, 6H), 1.42 (m, 3H), 1.34 (m, 3H), 1.29 (s, 3H), 1.28 (s, 3H), 1.20 (m, 1H), 0.94 (s, 3H), 0.76 (s, 3H); (150 MHz, $CDCl_3$) δ 211.7, 163.9, 150.9, 135.8, 131.6, 130.7, 124.5, 124.5, 124.1, 81.6, 78.1, 77.9, 63.5, 55.9, 42.5, 42.4, 41.7, 39.9, 37.9, 37.0, 29.1, 27.5, 26.9, 25.9, 23.7, 23.5, 22.1, 21.9, 17.9, 16.3, 15.0, 13.8; IR (KBr) 2943, 1714, 1606, 1529,

1444, 1348, 1277, 1101, 719 cm^{-1}; HRMS (APCI) [M+H^+] Calcd. for $C_{36}H_{51}N_1O_6$ 594.37892, found 594.37925. Characterization for monocyclic **87**: $[\alpha]_D^{23}$ = - 28.3 (c 0.75, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 5.49 (m, 1H), 5.09 (m, 3H), 3.95 (d, *J* = 9.6 Hz, 1H), 3.40 (dd, *J* = 3.6, 10.8 Hz, 1H), 2.46-2.37 (m, 7H), 2.26 (m, 4H), 2.18-1.87 (m, 10H), 1.68 (s, 3H), 1.64 (s, 3H), 1.61 (s, 3H), 1.59 (s, 3H), 1.58 (s, 3H), 1.26 (s, 3H), 1.16 (s, 3H); (150 MHz, $CDCl_3$) δ 211.3, 136.1, 136.0, 135.7, 131.6, 124.5, 123.8, 123.4, 119.4, 76.8, 72.6, 71.8, 42.9, 42.4, 39.9, 36.5, 29.9, 29.7, 27.5, 26.9, 26.8, 25.9, 25.6, 24.2, 24.1, 22.6, 20.1, 17.9, 16.2; IR (KBr) 3487, 2929, 1712, 1448, 1377, 1078 cm^{-1}; HRMS (APCI) [M+H^+] Calcd. for $C_{29}H_{48}O_3$ 445.36762, found 445.36788.

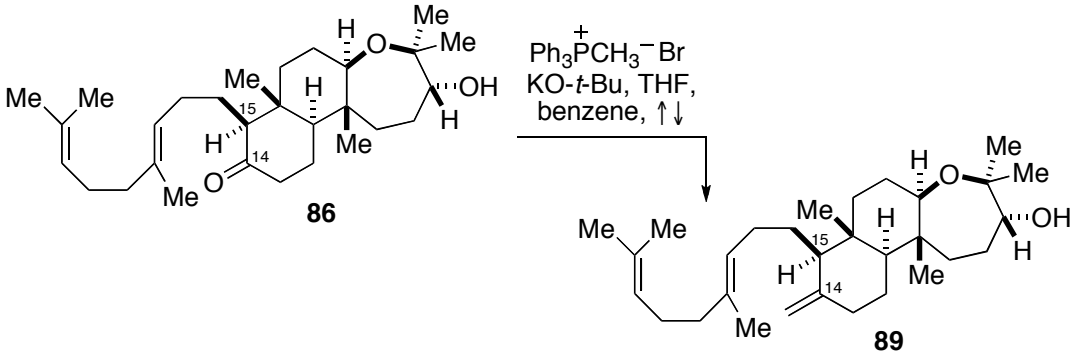
Synthesis of ketoalcohol 86



The *para*-nitrobenzoyl tricyclic ketone **88** (1.06 g, 1.8 mmol) was dissolved in MeOH:THF (4:1) (0.07 M, 25 mL). Then K_2CO_3 was added all at once. The reaction was allowed to stir for 2 hours. After dilution with Et_2O (50 mL) and EtOAc (100 mL) the reaction was quenched by the addition of a saturated solution of NH_4Cl (75 mL). The layers were separated. The organic layer was dried with $MgSO_4$. After filtration, the volatiles were removed under reduced pressure. Chromatography (9:1→4:1 hexanes:EtOAc) gave tricyclic ketoalcohol

86 as an oil (704 mg, 89%). $[\alpha]_D^{23}$ = + 31.6 (c 1.02, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 5.11 (t, *J* = 6.0 Hz, 1H), 5.07 (t, *J* = 6.0 Hz, 1H), 3.84 (d, *J* = 6.6 Hz, 1H), 3.63 (dd, *J* = 4.8, 11.4 Hz, 1H), 2.39 (m, 1H), 2.28 (m, 1H), 2.08-1.98 (m, 8H), 1.78-1.51 (m, 13H), 1.70 (s, 3H), 1.62 (s, 3H), 1.56 (s, 3H), 1.29 (s, 3H), 1.14 (s, 3H), 0.88 (s, 3H), 0.73 (s, 3H); (150 MHz, $CDCl_3$) δ 212.4, 135.8, 131.5, 124.6, 124.5, 78.1, 77.1, 76.9, 63.2, 55.2, 42.6, 42.6, 41.7, 39.9, 37.6, 35.8, 29.1, 27.6, 27.4, 26.9, 25.9, 25.8, 23.7, 21.9, 21.7, 17.9, 16.2, 15.0, 13.8; IR (KBr) 3479, 2939, 1712, 1446, 1385, 1159, 1064, 918, 860, 735 cm^{-1}; HRMS (APCI) [M $+H^+$] Calcd. for $C_{29}H_{48}O_3$ 445.36762, found 445.36785.

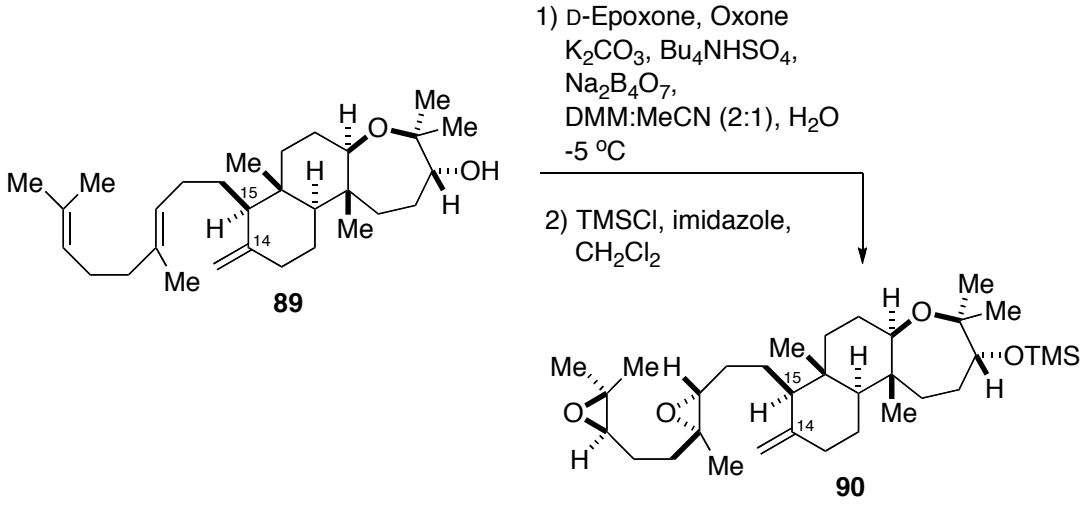
Synthesis of triene 89.



Methyl triphenylphosphonium bromide (5.69 g, 16 mmol) was suspended in benzene (0.15 M, 11 mL). Then KO-*t*-Bu (1.0 M solution in THF, 16 mL, 16 mmol) was added all at once. The reaction was then warmed to 70 °C over a 20 minute period. After cooling to 35 °C (internal temperature), the tricyclic ketoalcohol **86** (704 mg, 1.6 mmol) dissolved in benzene (0.50 M, 5 mL) was added to the flask. After stirring for 1 hour, the reaction was cooled to r.t. and diluted with Et_2O (75 mL). The mixture was then poured into H_2O (150 mL). After the layers were separated, the aqueous layer was extracted with EtOAc

(150 mL). The organic extracts were combined and dried with $MgSO_4$. After filtration, the volatiles were removed under reduced pressure. Chromatography (9:1→4:1 hexanes:EtOAc) gave triene alcohol **89** as an oil (570 mg, 81 %). * An alternative work-up that involved filtration of the reaction mixture through a short silica column followed by removal of the volatiles and chromatography resulted in a slightly lower yield of **89** (71%). The previous sequence (starting from acyl silane) was repeated to provide 700 mg of additional triene alcohol **89**, giving a total of 1.27 g for the subsequent double Shi epoxidation. $[\alpha]_D^{23}$ = - 7.19 (c 0.70, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 5.11 (m, 2H), 4.83 (s, 1H), 4.54 (s, 1H), 3.81 (m, 1H), 3.53 (dd, *J* = 4.8, 12.0 Hz, 1H), 2.38 (m, 1H), 2.07 (m, 3H), 1.99 (m, 4H), 1.82 (m, 1H), 1.75 (s, 3H), 1.70 (s, 3H), 1.62 (s, 3H), 1.56 (s, 3H), 1.52-1.29 (m, 9H), 1.28 (s, 3H), 1.15 (m, 2H), 1.13 (s, 3H), 0.84 (s, 3H), 0.68 (s, 3H); (150 MHz, $CDCl_3$) δ 148.6, 135.2, 131.5, 125.2, 124.6, 106.5, 77.9, 77.3, 77.3, 56.4, 56.1, 41.6, 39.9, 39.3, 38.5, 37.7, 35.8, 29.2, 27.9, 26.9, 26.9, 25.9, 25.8, 24.2, 24.1, 21.7, 17.9, 16.2, 14.8, 13.9; IR (KBr) 3464, 2935, 1643, 1446, 1381, 1084 cm^{-1}; HRMS (APCI) [M+H^+] Calcd. for $C_{30}H_{50}O_2$ 443.38836, found 443.38978.

Double Shi epoxidation: Synthesis of diepoxy trimethylsilyl ether 90



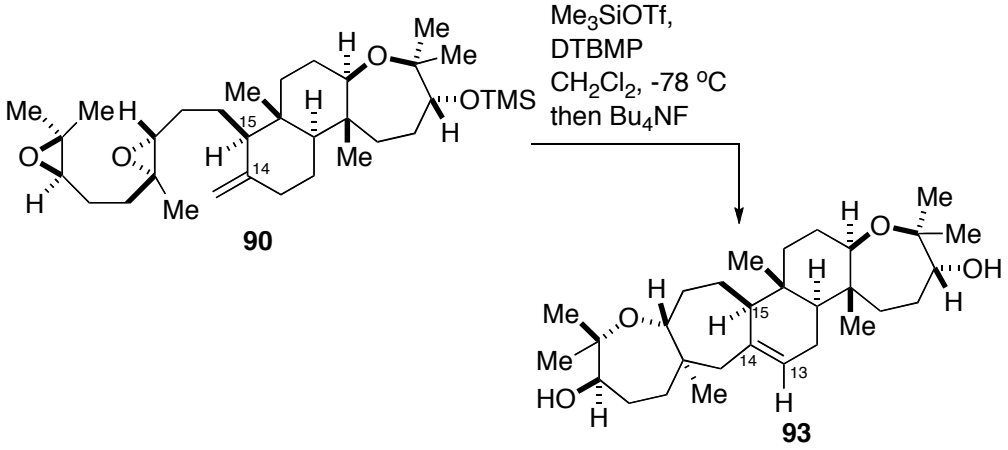
Triene alcohol **89** (1.27 g, 2.9 mmol) was transferred into a 100 mL single neck round bottom flask that was mounted in an ethylene glycol:H_2O (2:1) bath that was equipped with a cryostat. Then DMM:MeCN (2:1) (0.13 M, 22 mL) and $Na_2B_4O_7$ (0.05 M soln. in $4x10^{-4}$ M Na_2EDTA) (0.19 M, 15 mL) were added, followed by the addition of Bu_4NHSO_4 (110 mg, 0.29 mmol). D-Epoxone (370 mg, 1.43 mmol) was then added. The cryostat was used to maintain a constant bath temperature between - 4 °C and - 5 °C. Then Oxone (4.94 g, 8.0 mmol) was dissolved in $4x10^{-4}$ M Na_2EDTA (20 mL) and transferred to a syringe. K_2CO_3 (3.16 g, 23 mmol) was dissolved in distilled H_2O (20 mL) and transferred to a syringe. The Oxone and K_2CO_3 solutions were then added via syringe pump over a 1 hour period. Extensive use of TLC was used to ensure a successful outcome, as competitive epoxidation of the 1,1-disubstituted alkene was problematic. Thus, a TLC was taken at least every 2-5 minutes as the additions occurred. Only 14 mL of each solution was added. The reaction was quenched as soon as the intensity of the diepoxide was substantial on TLC, which

subsequently also marks the appearance of the triepoxide in the reaction mixture. Then Et_2O (100 mL) and H_2O (50 mL) were added. The layers were separated. The aqueous layer was extracted with Et_2O (75 mL). The organic extracts were combined and dried with $MgSO_4$. After filtration, the volatiles were removed under reduced pressure. Chromatography (4:1→2:1 hexanes:EtOAc) provided the diepoxide that was contaminated with D-epoxone, along with a mixture of triene alcohol **89** and monoepoxide. Thus, the triene alcohol **89** and monoepoxide were subjected to a recycle using the following reaction conditions: triene alcohol **89** + monoepoxide (930 mg), D-epoxone (270 mg, 1.1 mmol), Oxone (3.62 g, 5.9 mmol) in $4x10^{-4}$ M Na_2EDTA (20 mL), K_2CO_3 (2.32 g, 17 mmol) in distilled H_2O (15 mL), Bu_4NHSO_4 (82 mg, 0.21 mmol), DMM:MeCN (2:1) (18 mL), and $Na_2B_4O_7$ (0.05 M soln. in $4x10^{-4}$ M Na_2EDTA) (13 mL). Using the same technique, the reaction was frequently monitored and only 5 mL of each solution was added. After work-up and chromatography, the mixture of diepoxide and D-epoxone was collected. Another recycle was performed on the triene alcohol **89** (very minor component) + monoepoxide using the following reaction conditions: triene alcohol **89** + monoepoxide (500 mg), D-epoxone (150 mg, 0.57 mmol), Oxone (1.39 g, 2.3 mmol) in $4x10^{-4}$ M Na_2EDTA (12 mL), K_2CO_3 (940 mg, 6.8 mmol) in distilled H_2O (12 mL), Bu_4NHSO_4 (43 mg, 0.11 mmol), DMM:MeCN (2:1) (15 mL), and $Na_2B_4O_7$ (0.05 M soln. in $4x10^{-4}$ M Na_2EDTA) (10 mL). Using the same technique, the reaction was frequently monitored and only 2.5 mL of each solution was added. After work-up and chromatography, the mixture of diepoxide and D-epoxone was collected. Another recycle was

performed on the triene alcohol **89** (very minor component) + monoepoxide using the following reaction conditions: triene alcohol **89** + monoepoxide (200 mg), D-epoxone (87 mg, 0.34 mmol), Oxone (840 mg, 1.4 mmol) in $4x10^{-4}$ M Na_2EDTA (8 mL), K_2CO_3 (560 mg, 4.1 mmol) in distilled H_2O (8 mL), Bu_4NHSO_4 (26 mg, 0.068 mmol), DMM:MeCN (2:1) (10 mL), and $Na_2B_4O_7$ (0.05 M soln. in $4x10^{-4}$ M Na_2EDTA) (5 mL). After work-up and chromatography, the mixture of diepoxide and D-epoxone was collected. After combining the diepoxide and D-epoxone impurity, 1.26 g of the crude mixture was obtained. For purification purposes, the mixture was dissolved in CH_2Cl_2 (27 mL). Then imidazole (720 mg, 11 mmol) was added, followed by the addition of Me_3SiCl (0.67 mL, 5.3 mmol). The reaction was stirred for 5 minutes. Then the reaction was poured into a saturated solution of $NaHCO_3$ (50 mL). The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (30 mL). The organic extracts were combined and dried with $MgSO_4$. After filtration, the volatiles were removed under reduced pressure. Chromatography (10:1→6:1 hexanes:EtOAc) afforded pure diepoxy trimethylsilyl ether **90** (615 mg, 39% combined yield over 2 steps). $[\alpha]_D^{23}$ = - 4.2 (c 0.90, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 4.83 (s, 1H), 4.47 (s, 1H), 3.70 (d, *J* = 6.8 Hz, 1H), 3.56 (dd, *J* = 4.8, 12.0 Hz, 1H), 2.72 (m, 2H), 2.38 (m, 1H), 2.02-1.90 (m, 2H), 1.81-1.32 (m, 15H), 1.31 (s, 3H), 1.28 (s, 3H), 1.26 (s, 3H), 1.25 (m, 2H), 1.15 (s, 3H), 1.10 (s, 3H), 1.05 (m, 2H), 0.81 (s, 3H), 0.68 (s, 3H), 0.11 (s, 9H); (100 MHz, $CDCl_3$) δ 148.5, 106.3, 78.3, 77.7, 76.6, 64.1, 60.3, 58.6, 56.8, 56.4, 41.4, 39.5, 38.5, 37.7, 35.9, 35.5, 29.1, 28.1, 27.8, 26.5, 25.0, 24.8, 24.2, 22.6, 21.0, 18.9, 16.9, 14.7, 13.9, 0.23 (x3); IR (KBr) 2943, 1645, 1446,

1381, 1250, 1101, 874, 841 cm^{-1}; HRMS (APCI) [M+H+] Calcd. for $C_{33}H_{58}O_4Si_1$ 547.41772, found 547.41765.

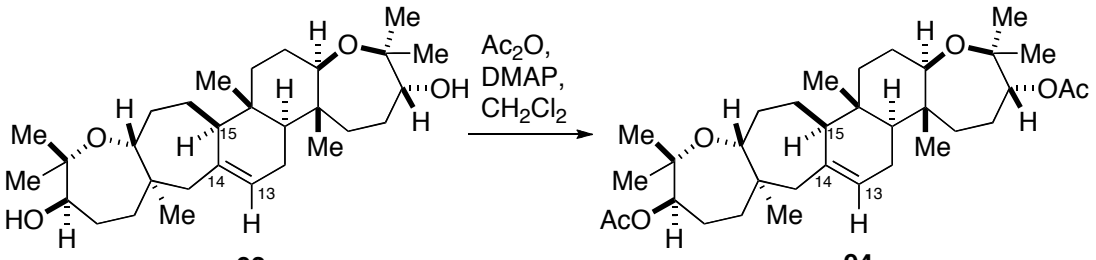
Second-stage bicyclization: synthesis of pentacyclic diol trisubstituted alkene 93



The diepoxy alkene **90** (615 mg, 1.1 mmol) was dissolved in CH_2Cl_2 (0.01 M, 112 mL). DTBMP (460 mg, 2.3 mmol) was added to the solution. The solution was then cooled to -78 °C. After stirring for 5 minutes, Me_3SiOTf (0.22 mL, 1.2 mmol) was quickly added. The reaction was allowed to stir for 1 hour, after which time Bu_4NF (1.0 M solution in THF, 2.5 mL, 2.5 mmol) was added to the reaction. After stirring for 5 minutes, the mixture was poured into a saturated solution of $NaHCO_3$ (200 mL). The layers were separated. The aqueous layer was then extracted with CH_2Cl_2 (200 mL). The organic extracts were combined and dried with $MgSO_4$. After filtration, the volatiles were removed under reduced pressure. The crude oil was then dissolved in THF (0.11 M, 10 mL). Bu_4NF (1.0 M solution in THF, 2.5 mL, 2.5 mmol) was then added, and the reaction was stirred for 15 hours. After dilution with EtOAc (50 mL), the reaction was poured into H_2O (100

mL). The layers were separated. The aqueous layer was extracted with Et_2O (100 mL). The organic extracts were combined and dried with $MgSO_4$. After filtration, the volatiles were removed under reduced pressure. Chromatography (4 : 1 hexanes : EtOAc) gave pentacyclic trisubstituted alkene diol **93** as a white solid (226 mg, 43%). mp 230-232 ^oC; $[\alpha]_D^{23}$ = + 26.8 (c 0.30, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 5.36 (bs, 1H), 3.80 (dd, *J* = 3.2, 6.4 Hz, 1H), 3.77 (dd, *J* = 3.6, 6.8 Hz, 1H), 3.52-3.47 (m, 2H), 2.23 (m, 1H), 2.11-1.84 (m, 6H), 1.78-1.64 (m, 8H), 1.54-1.41 (m, 6H), 1.28 (s, 3H), 1.25 (s, 3H), 1.13 (s, 3H), 1.12 (s, 3H), 1.08 (m, 3H), 0.89 (s, 3H), 0.84 (s, 3H), 0.66 (s, 3H); (100 MHz, CD_3OD) δ 138.3, 124.1, 79.9 (x2), 79.6, 78.5, 77.5, 77.5, 58.4, 52.8, 49.8, 49.6, 49.2, 42.4, 41.7, 39.4, 38.9, 38.7, 36.5, 29.8, 29.5, 28.6, 27.3, 26.8, 25.3, 22.5, 21.8, 17.6, 14.2, 13.7; IR (KBr) 3437, 2974, 2929, 1443, 1381, 1157, 1061, 756 cm^{-1}; HRMS (APCI) [M+H$^+$] Calcd. for $C_{30}H_{50}O_4$ 475.37819, found 475.37846.

Synthesis of pentacyclic diacetoxy trisubstituted alkene 94



Pentacyclic trisubstituted alkene diol **93** (226 mg, 0.48 mmol) was dissolved in CH_2Cl_2 (0.10 M, 4.8 mL). DMAP (171 mg, 1.4 mmol) was added to the solution, followed by the addition of Ac_2O (0.11 mL, 1.2 mmol). The reaction was stirred for 1 hour, at which point the reaction was diluted with Et_2O (25 mL) and poured into a saturated solution of $NaHCO_3$ (50 mL). The layers were separated. The

aqueous layer was extracted with Et_2O (100 mL). The organic extracts were combined and dried with $MgSO_4$. After filtration, the volatiles were removed under reduced pressure. The crude mixture was dissolved in Et_2O (10 mL) and then passed through a plug of silica gel contained within a Pasteur pipette. After thoroughly rinsing the plug with Et_2O, the volatiles were removed under reduced pressure giving diacetate **94** as a white solid (243 mg, 91%). mp 190-193 ^oC; $[\alpha]_D^{23}$ = - 11.5 (c 0.84, $CHCl_3$); ^1H NMR (600 MHz, C_6D_6) δ 5.46 (bs, 1H), 5.09 (d, *J* = 6.6 Hz, 1H), 5.06 (d, *J* = 6.6 Hz, 1H), 3.48-3.43 (m, 2H), 2.27 (m, 1H), 2.10 (m, 1H), 1.98-1.88 (m, 7H), 1.84 (d, *J* = 15 Hz, 1H), 1.76 (s, 3H), 1.72 (m, 1H), 1.65 (s, 3H), 1.61 (dd, *J* = 3.0, 7.2 Hz, 1H), 1.60 (m, 1H), 1.57-1.46 (m, 3H), 1.39-1.26 (m, 4H), 1.19 (s, 3H), 1.16 (s, 3H), 1.12 (s, 3H), 1.09 (s, 3H), 1.03 (s, 3H), 0.99 (s, 3H), 0.93-0.87 (m, 2H), 0.72 (s, 3H); (150 MHz, C_6D_6) δ 169.7, 169.6, 137.5, 123.8, 79.5, 79.4, 79.3, 77.9, 77.7, 77.4, 57.3, 52.2, 48.9, 41.8, 41.3, 39.4, 38.1, 37.8, 36.7, 36.3, 29.6, 29.5, 28.3, 24.9, 24.3, 23.9, 22.1, 21.8, 21.5, 20.9 (x2), 17.5, 14.2, 13.6; IR (KBr) 2976, 2931, 1739, 1443, 1363, 1242, 1057, 1032, 756 cm^{-1}; HRMS (APCI) [$M+H^+$] Calcd. for $C_{34}H_{54}O_6$ 559.39932, found 559.40001.

Compound **94** was dissolved in Et_2O. Upon evaporation of the solvent over an extended period of time, the resulting crystals were suitable for structural characterization by X-ray crystallography, resulting in the thermal ellipsoid diagram below:

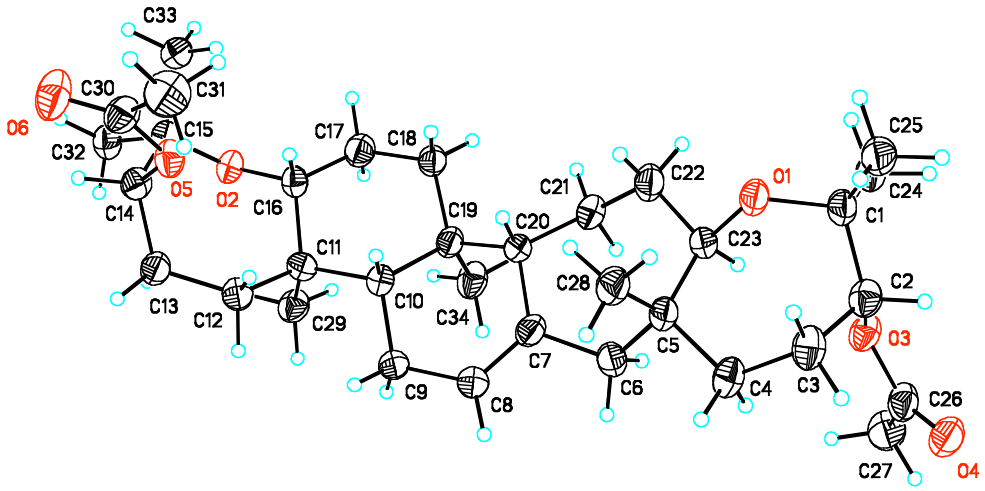

C33
C30
C31
O6
C32
C15
O5
O2
C16
C17
C18
C14
C19
C20
C21
C22
O1
C25
C24
C1
C23
C11
C28
C2
C13
C12
C29
C10
C34
C5
O3
C7
C6
C4
C3
C26
C9
C8
C27
O4

Table 1. Crystal data and structure refinement for **94**.

Identification code	b103_6_237s	
Empirical formula	C34 H54 O6	
Formula weight	558.77	
Temperature	173(2) K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	P2(1)	
Unit cell dimensions	a = 13.2539(17) Å	α= 90°.
	b = 7.4121(9) Å	β= 101.349(6)°.
	c = 16.7467(18) Å	γ = 90°.
Volume	1613.0(3) $Å^3$	
Z	2	
Density (calculated)	1.150 Mg/m^3	
Absorption coefficient	0.610 mm^{-1}	
F(000)	612	
Crystal size	0.33 x 0.31 x 0.16 mm^3	
Theta range for data collection	2.69 to 66.71°.	
Index ranges	-15<=h<=12, -8<=k<=8, -19<=l<=19	
Reflections collected	10661	
Independent reflections	4737 [R(int) = 0.0338]	
Completeness to theta = 66.71°	92.6 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9088 and 0.8242	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4737 / 1 / 362	
Goodness-of-fit on F^2	1.131	
Final R indices [I>2sigma(I)]	R1 = 0.0608, wR2 = 0.1614	
R indices (all data)	R1 = 0.0980, wR2 = 0.2206	
Absolute structure parameter	-0.1(4)	
Extinction coefficient	0.0180(17)	
Largest diff. peak and hole	0.396 and -0.331 $e.Å^{-3}$	

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for **94** (b103_6_237s). U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor

	x	y	z	U(eq)
C(1)	6137(4)	1781(8)	12190(3)	44(1)
C(2)	6168(4)	-154(8)	12530(3)	43(1)
C(3)	5649(5)	-1546(9)	11920(3)	50(1)
C(4)	6329(4)	-2283(8)	11343(3)	46(1)
C(5)	6613(4)	-1012(7)	10687(3)	41(1)
C(6)	7504(4)	-2005(8)	10394(3)	45(1)
C(7)	7757(4)	-1547(7)	9567(3)	43(1)
C(8)	7854(4)	-2923(8)	9069(3)	48(1)
C(9)	8162(5)	-2727(7)	8260(3)	48(1)
C(10)	8193(4)	-766(7)	7987(3)	39(1)
C(11)	8608(4)	-598(7)	7169(3)	40(1)
C(12)	7864(4)	-1650(8)	6507(3)	44(1)
C(13)	7922(4)	-1306(7)	5613(3)	43(1)
C(14)	7570(4)	540(7)	5263(3)	38(1)
C(15)	8371(4)	2031(7)	5470(3)	40(1)
C(16)	8578(4)	1432(7)	6944(3)	37(1)
C(17)	9140(4)	2615(8)	7627(3)	46(1)
C(18)	8663(4)	2438(7)	8385(3)	41(1)
C(19)	8669(4)	511(7)	8705(3)	38(1)
C(20)	7932(4)	386(7)	9337(3)	38(1)
C(21)	8254(4)	1589(8)	10090(3)	46(1)
C(22)	7372(4)	2181(8)	10503(3)	48(1)
C(23)	6992(4)	831(7)	11063(3)	39(1)
C(24)	5108(5)	2633(9)	12225(3)	54(2)
C(25)	6996(5)	2965(8)	12642(3)	51(2)
C(26)	7421(5)	-2051(8)	13349(3)	48(1)
C(27)	8530(5)	-2542(10)	13515(3)	60(2)
C(28)	5679(4)	-798(8)	9997(3)	49(1)
C(29)	9703(4)	-1339(8)	7210(3)	47(1)
C(30)	5786(4)	1499(8)	5018(3)	47(1)
C(31)	4895(5)	1770(11)	5429(4)	67(2)

C(32)	9081(4)	1929(8)	4854(3)	46(1)
C(33)	7887(5)	3920(8)	5447(3)	50(1)
C(34)	9759(4)	-48(9)	9130(3)	50(1)
O(1)	6156(3)	1739(5)	11330(2)	45(1)
O(2)	9044(2)	1722(5)	6238(2)	41(1)
O(3)	7236(3)	-639(5)	12838(2)	45(1)
O(4)	6758(3)	-2820(6)	13628(2)	56(1)
O(5)	6627(3)	943(5)	5561(2)	44(1)
O(6)	5782(3)	1724(7)	4313(2)	70(1)

Table 3. Bond lengths [Å] and angles [°] for **94 (**b103_6_237s)

C(1)-O(1)	1.444(5)	C(9)-C(10)	1.526(7)
C(1)-C(24)	1.515(8)	C(9)-H(9A)	0.9900
C(1)-C(25)	1.517(8)	C(9)-H(9B)	0.9900
C(1)-C(2)	1.541(8)	C(10)-C(19)	1.562(7)
C(2)-O(3)	1.454(6)	C(10)-C(11)	1.579(6)
C(2)-C(3)	1.518(8)	C(10)-H(10A)	1.0000
C(2)-H(2A)	1.0000	C(11)-C(29)	1.541(7)
C(3)-C(4)	1.545(8)	C(11)-C(12)	1.542(7)
C(3)-H(3A)	0.9900	C(11)-C(16)	1.549(7)
C(3)-H(3B)	0.9900	C(12)-C(13)	1.536(7)
C(4)-C(5)	1.549(7)	C(12)-H(12A)	0.9900
C(4)-H(4A)	0.9900	C(12)-H(12B)	0.9900
C(4)-H(4B)	0.9900	C(13)-C(14)	1.525(8)
C(5)-C(28)	1.525(7)	C(13)-H(13A)	0.9900
C(5)-C(23)	1.546(7)	C(13)-H(13B)	0.9900
C(5)-C(6)	1.550(7)	C(14)-O(5)	1.464(6)
C(6)-C(7)	1.527(7)	C(14)-C(15)	1.524(7)
C(6)-H(6A)	0.9900	C(14)-H(14A)	1.0000
C(6)-H(6B)	0.9900	C(15)-O(2)	1.432(6)
C(7)-C(8)	1.340(8)	C(15)-C(32)	1.530(7)
C(7)-C(20)	1.513(7)	C(15)-C(33)	1.537(8)
C(8)-C(9)	1.497(7)	C(16)-O(2)	1.453(5)
C(8)-H(8A)	0.9500	C(16)-C(17)	1.515(7)

C(16)-H(16A)	1.0000	C(29)-H(29C)	0.9800
C(17)-C(18)	1.531(6)	C(30)-O(6)	1.191(6)
C(17)-H(17A)	0.9900	C(30)-O(5)	1.356(6)
C(17)-H(17B)	0.9900	C(30)-C(31)	1.492(8)
C(18)-C(19)	1.525(7)	C(31)-H(31A)	0.9800
C(18)-H(18A)	0.9900	C(31)-H(31B)	0.9800
C(18)-H(18B)	0.9900	C(31)-H(31C)	0.9800
C(19)-C(34)	1.537(7)	C(32)-H(32A)	0.9800
C(19)-C(20)	1.578(7)	C(32)-H(32B)	0.9800
C(20)-C(21)	1.535(7)	C(32)-H(32C)	0.9800
C(20)-H(20A)	1.0000	C(33)-H(33A)	0.9800
C(21)-C(22)	1.536(7)	C(33)-H(33B)	0.9800
C(21)-H(21A)	0.9900	C(33)-H(33C)	0.9800
C(21)-H(21B)	0.9900	C(34)-H(34A)	0.9800
C(22)-C(23)	1.523(7)	C(34)-H(34B)	0.9800
C(22)-H(22A)	0.9900	C(34)-H(34C)	0.9800
C(22)-H(22B)	0.9900		
C(23)-O(1)	1.442(6)	O(1)-C(1)-C(24)	103.9(4)
C(23)-H(23A)	1.0000	O(1)-C(1)-C(25)	110.5(4)
C(24)-H(24A)	0.9800	C(24)-C(1)-C(25)	109.4(5)
C(24)-H(24B)	0.9800	O(1)-C(1)-C(2)	110.2(4)
C(24)-H(24C)	0.9800	C(24)-C(1)-C(2)	109.4(5)
C(25)-H(25A)	0.9800	C(25)-C(1)-C(2)	113.0(4)
C(25)-H(25B)	0.9800	O(3)-C(2)-C(3)	110.6(5)
C(25)-H(25C)	0.9800	O(3)-C(2)-C(1)	108.3(4)
C(26)-O(4)	1.215(7)	C(3)-C(2)-C(1)	114.1(4)
C(26)-O(3)	1.343(7)	O(3)-C(2)-H(2A)	107.9
C(26)-C(27)	1.487(8)	C(3)-C(2)-H(2A)	107.9
C(27)-H(27A)	0.9800	C(1)-C(2)-H(2A)	107.9
C(27)-H(27B)	0.9800	C(2)-C(3)-C(4)	114.8(5)
C(27)-H(27C)	0.9800	C(2)-C(3)-H(3A)	108.6
C(28)-H(28A)	0.9800	C(4)-C(3)-H(3A)	108.6
C(28)-H(28B)	0.9800	C(2)-C(3)-H(3B)	108.6
C(28)-H(28C)	0.9800	C(4)-C(3)-H(3B)	108.6
C(29)-H(29A)	0.9800	H(3A)-C(3)-H(3B)	107.6
C(29)-H(29B)	0.9800	C(3)-C(4)-C(5)	118.8(5)

C(3)-C(4)-H(4A)	107.6	C(29)-C(11)-C(16)	109.6(4)
C(5)-C(4)-H(4A)	107.6	C(12)-C(11)-C(16)	109.6(4)
C(3)-C(4)-H(4B)	107.6	C(29)-C(11)-C(10)	114.8(4)
C(5)-C(4)-H(4B)	107.6	C(12)-C(11)-C(10)	107.5(4)
H(4A)-C(4)-H(4B)	107.1	C(16)-C(11)-C(10)	106.9(4)
C(28)-C(5)-C(23)	111.5(4)	C(13)-C(12)-C(11)	117.9(5)
C(28)-C(5)-C(4)	109.0(4)	C(13)-C(12)-H(12A)	107.8
C(23)-C(5)-C(4)	110.7(4)	C(11)-C(12)-H(12A)	107.8
C(28)-C(5)-C(6)	111.4(4)	C(13)-C(12)-H(12B)	107.8
C(23)-C(5)-C(6)	110.0(5)	C(11)-C(12)-H(12B)	107.8
C(4)-C(5)-C(6)	103.9(4)	H(12A)-C(12)-H(12B)	107.2
C(7)-C(6)-C(5)	119.9(4)	C(14)-C(13)-C(12)	117.0(4)
C(7)-C(6)-H(6A)	107.4	C(14)-C(13)-H(13A)	108.1
C(5)-C(6)-H(6A)	107.4	C(12)-C(13)-H(13A)	108.1
C(7)-C(6)-H(6B)	107.4	C(14)-C(13)-H(13B)	108.1
C(5)-C(6)-H(6B)	107.4	C(12)-C(13)-H(13B)	108.1
H(6A)-C(6)-H(6B)	106.9	H(13A)-C(13)-H(13B)	107.3
C(8)-C(7)-C(20)	121.6(4)	O(5)-C(14)-C(15)	112.2(4)
C(8)-C(7)-C(6)	117.4(5)	O(5)-C(14)-C(13)	105.6(4)
C(20)-C(7)-C(6)	120.9(4)	C(15)-C(14)-C(13)	114.6(4)
C(7)-C(8)-C(9)	124.5(5)	O(5)-C(14)-H(14A)	108.1
C(7)-C(8)-H(8A)	117.8	C(15)-C(14)-H(14A)	108.1
C(9)-C(8)-H(8A)	117.8	C(13)-C(14)-H(14A)	108.1
C(8)-C(9)-C(10)	113.1(4)	O(2)-C(15)-C(14)	111.8(4)
C(8)-C(9)-H(9A)	109.0	O(2)-C(15)-C(32)	103.9(4)
C(10)-C(9)-H(9A)	109.0	C(14)-C(15)-C(32)	107.7(4)
C(8)-C(9)-H(9B)	109.0	O(2)-C(15)-C(33)	110.5(4)
C(10)-C(9)-H(9B)	109.0	C(14)-C(15)-C(33)	112.7(4)
H(9A)-C(9)-H(9B)	107.8	C(32)-C(15)-C(33)	109.7(4)
C(9)-C(10)-C(19)	112.1(4)	O(2)-C(16)-C(17)	107.7(4)
C(9)-C(10)-C(11)	111.7(4)	O(2)-C(16)-C(11)	110.3(4)
C(19)-C(10)-C(11)	117.6(4)	C(17)-C(16)-C(11)	113.2(4)
C(9)-C(10)-H(10A)	104.6	O(2)-C(16)-H(16A)	108.5
C(19)-C(10)-H(10A)	104.6	C(17)-C(16)-H(16A)	108.5
C(11)-C(10)-H(10A)	104.6	C(11)-C(16)-H(16A)	108.5
C(29)-C(11)-C(12)	108.4(4)	C(16)-C(17)-C(18)	110.8(4)

C(16)-C(17)-H(17A)	109.5	O(1)-C(23)-C(5)	109.3(4)
C(18)-C(17)-H(17A)	109.5	C(22)-C(23)-C(5)	116.7(4)
C(16)-C(17)-H(17B)	109.5	O(1)-C(23)-H(23A)	108.6
C(18)-C(17)-H(17B)	109.5	C(22)-C(23)-H(23A)	108.6
H(17A)-C(17)-H(17B)	108.1	C(5)-C(23)-H(23A)	108.6
C(19)-C(18)-C(17)	113.4(4)	C(1)-C(24)-H(24A)	109.5
C(19)-C(18)-H(18A)	108.9	C(1)-C(24)-H(24B)	109.5
C(17)-C(18)-H(18A)	108.9	H(24A)-C(24)-H(24B)	109.5
C(19)-C(18)-H(18B)	108.9	C(1)-C(24)-H(24C)	109.5
C(17)-C(18)-H(18B)	108.9	H(24A)-C(24)-H(24C)	109.5
H(18A)-C(18)-H(18B)	107.7	H(24B)-C(24)-H(24C)	109.5
C(18)-C(19)-C(34)	110.7(5)	C(1)-C(25)-H(25A)	109.5
C(18)-C(19)-C(10)	108.9(4)	C(1)-C(25)-H(25B)	109.5
C(34)-C(19)-C(10)	113.2(4)	H(25A)-C(25)-H(25B)	109.5
C(18)-C(19)-C(20)	109.2(4)	C(1)-C(25)-H(25C)	109.5
C(34)-C(19)-C(20)	108.9(4)	H(25A)-C(25)-H(25C)	109.5
C(10)-C(19)-C(20)	105.7(4)	H(25B)-C(25)-H(25C)	109.5
C(7)-C(20)-C(21)	111.9(4)	O(4)-C(26)-O(3)	123.8(5)
C(7)-C(20)-C(19)	111.9(4)	O(4)-C(26)-C(27)	125.2(5)
C(21)-C(20)-C(19)	114.1(4)	O(3)-C(26)-C(27)	111.0(5)
C(7)-C(20)-H(20A)	106.1	C(26)-C(27)-H(27A)	109.5
C(21)-C(20)-H(20A)	106.1	C(26)-C(27)-H(27B)	109.5
C(19)-C(20)-H(20A)	106.1	H(27A)-C(27)-H(27B)	109.5
C(20)-C(21)-C(22)	115.0(5)	C(26)-C(27)-H(27C)	109.5
C(20)-C(21)-H(21A)	108.5	H(27A)-C(27)-H(27C)	109.5
C(22)-C(21)-H(21A)	108.5	H(27B)-C(27)-H(27C)	109.5
C(20)-C(21)-H(21B)	108.5	C(5)-C(28)-H(28A)	109.5
C(22)-C(21)-H(21B)	108.5	C(5)-C(28)-H(28B)	109.5
H(21A)-C(21)-H(21B)	107.5	H(28A)-C(28)-H(28B)	109.5
C(23)-C(22)-C(21)	117.6(5)	C(5)-C(28)-H(28C)	109.5
C(23)-C(22)-H(22A)	107.9	H(28A)-C(28)-H(28C)	109.5
C(21)-C(22)-H(22A)	107.9	H(28B)-C(28)-H(28C)	109.5
C(23)-C(22)-H(22B)	107.9	C(11)-C(29)-H(29A)	109.5
C(21)-C(22)-H(22B)	107.9	C(11)-C(29)-H(29B)	109.5
H(22A)-C(22)-H(22B)	107.2	H(29A)-C(29)-H(29B)	109.5
O(1)-C(23)-C(22)	104.6(4)	C(11)-C(29)-H(29C)	109.5

H(29A)-C(29)-H(29C)	109.5	C(15)-C(33)-H(33A)	109.5
H(29B)-C(29)-H(29C)	109.5	C(15)-C(33)-H(33B)	109.5
O(6)-C(30)-O(5)	123.3(5)	H(33A)-C(33)-H(33B)	109.5
O(6)-C(30)-C(31)	126.0(5)	C(15)-C(33)-H(33C)	109.5
O(5)-C(30)-C(31)	110.7(4)	H(33A)-C(33)-H(33C)	109.5
C(30)-C(31)-H(31A)	109.5	H(33B)-C(33)-H(33C)	109.5
C(30)-C(31)-H(31B)	109.5	C(19)-C(34)-H(34A)	109.5
H(31A)-C(31)-H(31B)	109.5	C(19)-C(34)-H(34B)	109.5
C(30)-C(31)-H(31C)	109.5	H(34A)-C(34)-H(34B)	109.5
H(31A)-C(31)-H(31C)	109.5	C(19)-C(34)-H(34C)	109.5
H(31B)-C(31)-H(31C)	109.5	H(34A)-C(34)-H(34C)	109.5
C(15)-C(32)-H(32A)	109.5	H(34B)-C(34)-H(34C)	109.5
C(15)-C(32)-H(32B)	109.5	C(23)-O(1)-C(1)	119.0(4)
H(32A)-C(32)-H(32B)	109.5	C(15)-O(2)-C(16)	117.7(4)
C(15)-C(32)-H(32C)	109.5	C(26)-O(3)-C(2)	117.4(4)
H(32A)-C(32)-H(32C)	109.5	C(30)-O(5)-C(14)	118.6(4)
H(32B)-C(32)-H(32C)	109.5		

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for **94** (b103_6_237s). 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}
C(1)	52(3)	49(3)	29(2)	-1(2)	8(2)	6(3)
C(2)	38(3)	54(3)	37(3)	3(2)	5(2)	6(3)
C(3)	48(4)	67(4)	34(3)	-1(3)	4(2)	-2(3)
C(4)	45(3)	60(4)	32(3)	3(2)	4(2)	-5(3)
C(5)	50(4)	44(3)	29(2)	2(2)	7(2)	5(2)
C(6)	54(4)	47(3)	35(3)	-4(2)	8(2)	9(3)
C(7)	52(3)	42(3)	32(2)	6(2)	3(2)	-3(3)
C(8)	68(4)	37(3)	40(3)	-1(2)	12(3)	-5(3)
C(9)	75(4)	32(3)	39(3)	1(2)	17(3)	-10(3)
C(10)	47(3)	40(3)	30(2)	1(2)	8(2)	2(2)

C(11)	44(3)	35(3)	39(3)	-1(2)	9(2)	5(2)
C(12)	52(4)	42(3)	38(3)	-2(2)	10(2)	-4(3)
C(13)	46(3)	47(3)	35(3)	3(2)	6(2)	4(3)
C(14)	37(3)	44(3)	38(3)	3(2)	17(2)	4(2)
C(15)	46(3)	42(3)	30(2)	1(2)	6(2)	2(2)
C(16)	41(3)	43(3)	30(2)	-2(2)	11(2)	-1(2)
C(17)	48(4)	52(4)	40(3)	4(2)	11(2)	4(3)
C(18)	51(3)	38(3)	33(2)	-1(2)	8(2)	-8(2)
C(19)	41(3)	43(3)	29(2)	3(2)	6(2)	3(2)
C(20)	49(3)	33(3)	30(2)	1(2)	5(2)	6(2)
C(21)	54(3)	52(3)	32(2)	5(2)	5(2)	1(3)
C(22)	60(4)	51(3)	34(2)	-3(2)	10(2)	-10(3)
C(23)	49(3)	39(3)	32(2)	-1(2)	12(2)	6(2)
C(24)	61(4)	61(4)	41(3)	7(3)	11(3)	23(3)
C(25)	71(4)	51(3)	31(2)	-2(2)	7(3)	3(3)
C(26)	52(4)	61(4)	31(2)	5(3)	7(2)	12(3)
C(27)	55(4)	68(4)	51(3)	5(3)	1(3)	18(3)
C(28)	55(4)	55(4)	35(3)	3(2)	2(2)	8(3)
C(29)	42(3)	55(3)	42(3)	6(2)	5(2)	11(3)
C(30)	42(3)	54(4)	45(3)	6(3)	5(3)	4(3)
C(31)	50(4)	81(5)	73(4)	4(4)	21(3)	14(4)
C(32)	50(3)	52(3)	37(2)	-3(2)	12(2)	-5(3)
C(33)	63(4)	45(3)	41(3)	4(2)	11(3)	11(3)
C(34)	41(3)	68(4)	38(3)	5(3)	2(2)	9(3)
O(1)	55(2)	53(2)	29(2)	4(2)	10(2)	10(2)
O(2)	42(2)	50(2)	30(2)	4(2)	8(1)	-1(2)
O(3)	44(2)	56(2)	33(2)	9(2)	3(2)	6(2)
O(4)	65(3)	61(3)	45(2)	12(2)	16(2)	6(2)
O(5)	41(2)	58(2)	34(2)	-4(2)	10(2)	4(2)
O(6)	61(3)	105(4)	42(2)	5(2)	2(2)	16(3)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for **94 (**b103_6_237s)

	x	y	z	U(eq)
H(2A)	5805	-151	13001	52
H(3A)	5024	-999	11587	60
H(3B)	5426	-2571	12223	60
H(4A)	5976	-3348	11060	56
H(4B)	6980	-2719	11685	56
H(6A)	8136	-1805	10811	55
H(6B)	7352	-3313	10394	55
H(8A)	7717	-4104	9240	58
H(9A)	7670	-3403	7846	57
H(9B)	8851	-3271	8292	57
H(10A)	7455	-396	7838	47
H(12A)	7981	-2954	6616	53
H(12B)	7153	-1380	6572	53
H(13A)	8645	-1484	5554	51
H(13B)	7502	-2236	5276	51
H(14A)	7388	428	4657	46
H(16A)	7843	1827	6806	45
H(17A)	9105	3888	7446	56
H(17B)	9874	2258	7763	56
H(18A)	9047	3220	8821	49
H(18B)	7944	2877	8254	49
H(20A)	7248	848	9048	45
H(21A)	8593	2682	9927	56
H(21B)	8770	932	10493	56
H(22A)	7595	3282	10824	58
H(22B)	6780	2522	10071	58
H(23A)	7554	615	11547	47
H(24A)	4552	1866	11935	81
H(24B)	5065	3826	11969	81
H(24C)	5040	2758	12795	81

H(25A)	7662	2395	12635	77
H(25B)	6914	3119	13206	77
H(25C)	6969	4147	12376	77
H(27A)	8646	-3561	13895	89
H(27B)	8940	-1506	13755	89
H(27C)	8734	-2882	13004	89
H(28A)	5456	-1987	9775	74
H(28B)	5863	-43	9567	74
H(28C)	5118	-225	10208	74
H(29A)	9902	-1175	6681	70
H(29B)	9719	-2626	7346	70
H(29C)	10187	-686	7629	70
H(31A)	4297	2178	5029	100
H(31B)	5072	2681	5858	100
H(31C)	4731	628	5670	100
H(32A)	9370	712	4857	69
H(32B)	9641	2805	5002	69
H(32C)	8688	2207	4309	69
H(33A)	8433	4825	5583	74
H(33B)	7434	3981	5844	74
H(33C)	7487	4156	4900	74
H(34A)	10225	45	8744	75
H(34B)	9749	-1296	9321	75
H(34C)	9999	751	9594	75

Table 6. Torsion angles [°] for **94** (b103_6_237s)

O(1)-C(1)-C(2)-O(3)	92.1(5)
C(24)-C(1)-C(2)-O(3)	-154.3(4)
C(25)-C(1)-C(2)-O(3)	-32.1(5)
O(1)-C(1)-C(2)-C(3)	-31.4(6)
C(24)-C(1)-C(2)-C(3)	82.2(5)
C(25)-C(1)-C(2)-C(3)	-155.6(5)
O(3)-C(2)-C(3)-C(4)	-39.1(6)
C(1)-C(2)-C(3)-C(4)	83.3(6)
C(2)-C(3)-C(4)-C(5)	-69.5(6)

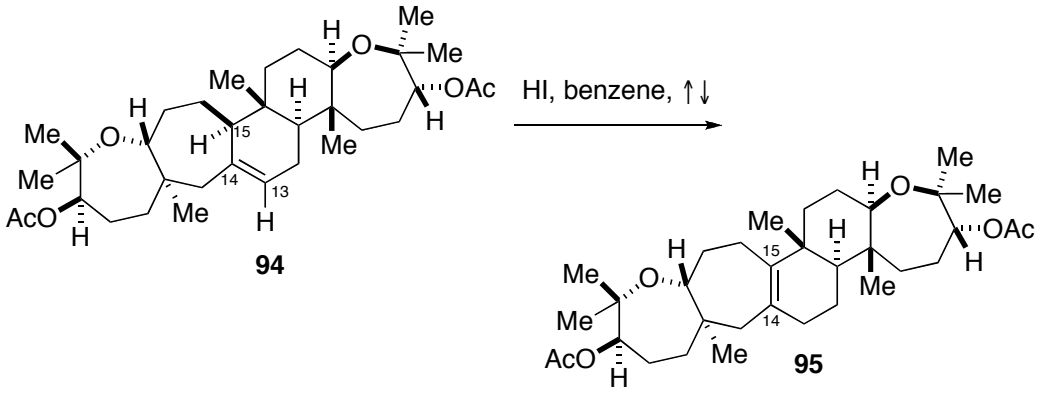
C(3)-C(4)-C(5)-C(28)	-75.6(6)
C(3)-C(4)-C(5)-C(23)	47.5(6)
C(3)-C(4)-C(5)-C(6)	165.5(4)
C(28)-C(5)-C(6)-C(7)	41.9(7)
C(23)-C(5)-C(6)-C(7)	-82.3(5)
C(4)-C(5)-C(6)-C(7)	159.2(5)
C(5)-C(6)-C(7)-C(8)	-130.6(6)
C(5)-C(6)-C(7)-C(20)	51.7(7)
C(20)-C(7)-C(8)-C(9)	1.6(9)
C(6)-C(7)-C(8)-C(9)	-176.1(5)
C(7)-C(8)-C(9)-C(10)	-9.3(8)
C(8)-C(9)-C(10)-C(19)	40.9(7)
C(8)-C(9)-C(10)-C(11)	175.4(5)
C(9)-C(10)-C(11)-C(29)	-59.6(6)
C(19)-C(10)-C(11)-C(29)	72.1(6)
C(9)-C(10)-C(11)-C(12)	61.1(6)
C(19)-C(10)-C(11)-C(12)	-167.2(5)
C(9)-C(10)-C(11)-C(16)	178.6(5)
C(19)-C(10)-C(11)-C(16)	-49.6(6)
C(29)-C(11)-C(12)-C(13)	-71.0(6)
C(16)-C(11)-C(12)-C(13)	48.6(6)
C(10)-C(11)-C(12)-C(13)	164.4(4)
C(11)-C(12)-C(13)-C(14)	-68.7(7)
C(12)-C(13)-C(14)-O(5)	-42.8(6)
C(12)-C(13)-C(14)-C(15)	81.2(6)
O(5)-C(14)-C(15)-O(2)	90.6(5)
C(13)-C(14)-C(15)-O(2)	-29.8(6)
O(5)-C(14)-C(15)-C(32)	-155.8(4)
C(13)-C(14)-C(15)-C(32)	83.8(5)
O(5)-C(14)-C(15)-C(33)	-34.7(5)
C(13)-C(14)-C(15)-C(33)	-155.1(4)
C(29)-C(11)-C(16)-O(2)	49.5(5)
C(12)-C(11)-C(16)-O(2)	-69.3(5)
C(10)-C(11)-C(16)-O(2)	174.4(4)
C(29)-C(11)-C(16)-C(17)	-71.2(5)
C(12)-C(11)-C(16)-C(17)	169.9(4)

C(10)-C(11)-C(16)-C(17)	53.7(5)
O(2)-C(16)-C(17)-C(18)	177.7(4)
C(11)-C(16)-C(17)-C(18)	-60.1(6)
C(16)-C(17)-C(18)-C(19)	58.4(6)
C(17)-C(18)-C(19)-C(34)	73.9(5)
C(17)-C(18)-C(19)-C(10)	-51.1(6)
C(17)-C(18)-C(19)-C(20)	-166.2(4)
C(9)-C(10)-C(19)-C(18)	-179.5(5)
C(11)-C(10)-C(19)-C(18)	49.0(6)
C(9)-C(10)-C(19)-C(34)	56.9(6)
C(11)-C(10)-C(19)-C(34)	-74.6(6)
C(9)-C(10)-C(19)-C(20)	-62.2(5)
C(11)-C(10)-C(19)-C(20)	166.2(4)
C(8)-C(7)-C(20)-C(21)	-154.5(5)
C(6)-C(7)-C(20)-C(21)	23.1(7)
C(8)-C(7)-C(20)-C(19)	-25.1(7)
C(6)-C(7)-C(20)-C(19)	152.5(5)
C(18)-C(19)-C(20)-C(7)	170.1(4)
C(34)-C(19)-C(20)-C(7)	-68.9(6)
C(10)-C(19)-C(20)-C(7)	53.0(5)
C(18)-C(19)-C(20)-C(21)	-61.7(5)
C(34)-C(19)-C(20)-C(21)	59.4(6)
C(10)-C(19)-C(20)-C(21)	-178.7(4)
C(7)-C(20)-C(21)-C(22)	-78.3(6)
C(19)-C(20)-C(21)-C(22)	153.5(4)
C(20)-C(21)-C(22)-C(23)	79.6(6)
C(21)-C(22)-C(23)-O(1)	-178.1(4)
C(21)-C(22)-C(23)-C(5)	-57.2(6)
C(28)-C(5)-C(23)-O(1)	55.8(5)
C(4)-C(5)-C(23)-O(1)	-65.8(5)
C(6)-C(5)-C(23)-O(1)	179.9(4)
C(28)-C(5)-C(23)-C(22)	-62.6(6)
C(4)-C(5)-C(23)-C(22)	175.8(5)
C(6)-C(5)-C(23)-C(22)	61.5(6)
C(22)-C(23)-O(1)-C(1)	-130.5(4)
C(5)-C(23)-O(1)-C(1)	103.8(5)

C(24)-C(1)-O(1)-C(23)	-173.6(5)
C(25)-C(1)-O(1)-C(23)	69.1(6)
C(2)-C(1)-O(1)-C(23)	-56.5(6)
C(14)-C(15)-O(2)-C(16)	-54.0(5)
C(32)-C(15)-O(2)-C(16)	-169.9(4)
C(33)-C(15)-O(2)-C(16)	72.5(5)
C(17)-C(16)-O(2)-C(15)	-132.6(4)
C(11)-C(16)-O(2)-C(15)	103.5(5)
O(4)-C(26)-O(3)-C(2)	-7.6(8)
C(27)-C(26)-O(3)-C(2)	171.8(4)
C(3)-C(2)-O(3)-C(26)	-71.7(5)
C(1)-C(2)-O(3)-C(26)	162.7(4)
O(6)-C(30)-O(5)-C(14)	-2.1(8)
C(31)-C(30)-O(5)-C(14)	177.7(5)
C(15)-C(14)-O(5)-C(30)	103.9(5)
C(13)-C(14)-O(5)-C(30)	-130.6(5)

Symmetry transformations used to generate equivalent atoms:

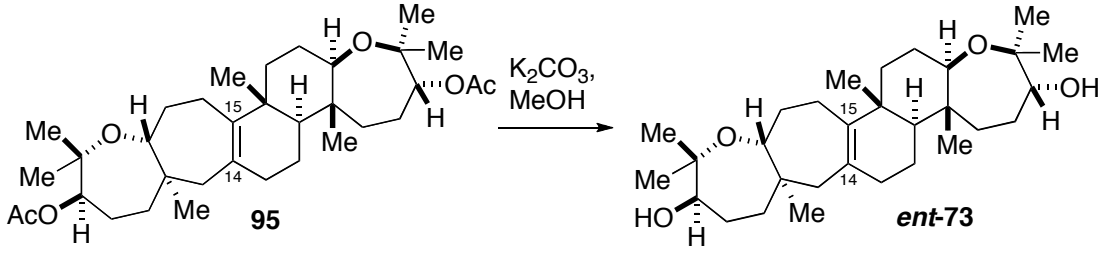
Alkene isomerization to tetrasubstituted alkene 95



Diacetoxy trisubstituted alkene **94** (137 mg, 0.24 mmol) was dissolved in benzene (0.010 M, 18 mL). Then HI (47% solution in H_2O, 40 µL, 0.14 mmol) was added all at once. A reflux condenser was placed on the flask, and the reaction was heated at 70 °C for 1 hour. The reaction was then cooled to r.t. After dilution with CH_2Cl_2 (25 mL), the reaction was washed with a 10 % solution of $NaHSO_3$ (50 mL). The layers were separated. The aqueous layer was extracted with CH_2Cl_2 (50 mL). The organic extracts were combined and washed with a saturated solution of $NaHCO_3$ (50 mL). The organic layer was then dried with $MgSO_4$. After filtration, the volatiles were removed under reduced pressure giving diacetoxy tetrasubstituted alkene **95** as a white solid (137 mg, quant.). mp 90 - 93 °C; $[\alpha]_D^{23}$ = - 29.2 (c 0.60, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 4.95 (d, *J* = 6.4 Hz, 1H), 4.92 (d, *J* = 7.2 Hz, 1H), 3.43 (dd, *J* = 4.8, 11.6 Hz, 1H), 3.35 (dd, *J* = 4.8, 11.6 Hz, 1H), 2.19 (m, 1H), 2.14 (s, 3H), 2.12 (s, 3H), 2.07 (dd, *J* = 7.2, 14.4 Hz, 1H), 1.98 (m, 3H), 1.86-1.77 (m, 4H), 1.63 (m, 3H), 1.49 (m, 3H), 1.39 (m, 2H), 1.31-1.26 (m, 4H), 1.20 (s, 3H), 1.18 (s, 3H), 1.15 (s, 6H), 1.14 (s, 3H), 1.02 (d, *J* = 11.4 Hz, 1H), 0.98 (d, *J* = 6.6 Hz, 1H), 0.92 (s, 3H), 0.87 (s, 3H), 0.85

(s, 3H); (150 MHz, C_6D_6) δ 169.7, 169.6, 142.9, 129.1, 80.2, 79.5, 79.3, 78.0, 77.7, 77.5, 54.1, 45.5, 41.5, 39.7, 38.9, 38.8, 36.9, 36.9, 35.5, 32.8, 29.5, 29.3, 28.2, 24.4, 23.9, 23.8, 22.2, 21.8, 20.9, 20.8, 20.3, 19.9, 16.7, 14.4; IR (KBr) 2933, 1741, 1444, 1362, 1242, 1163, 1061, 1028 cm^{-1}; HRMS (APCI) [M+H$^+$] Calcd. for $C_{34}H_{54}O_6$ 559.39932, found 559.39996.

Deacetylation of 95: Synthesis of *ent*-73.



Diacetoxy tetrasubstituted alkene **95** (96 mg, 0.17 mmol) was dissolved in MeOH (5.0 mL, 0.034 M). K_2CO_3 (506 mg, 3.7 mmol) was added. After 18.5 hours, the TLC indicated the presence of monoacetate, so the reaction flask was fitted with a reflux condenser and heated to reflux for 15 minutes. TLC then indicated completion of the reaction. The reaction was cooled to r.t. and diluted with Et_2O (40 mL). The mixture was poured into H_2O (50 mL). The layers were separated. The aqueous layer was extracted with Et_2O (25 mL). The organic extracts were combined and dried with $MgSO_4$. After filtration, the volatiles were removed under reduced pressure giving the tetrasubstituted alkene diol ***ent*-73** (81 mg, quant.). mp 205 - 208 ^oC; $[\alpha]_D^{23}$ = -14.8 (c 0.795, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 3.80 (d, *J* = 6.8 Hz, 1H), 3.76 (d, *J* = 6.4 Hz, 1H), 3.49 (dd, *J* = 5.2, 11.6 Hz, 2H), 2.19 (d, *J* = 14.0 Hz, 1H), 2.11-1.89 (m, 6H), 1.79-1.63 (m, 9H), 1.59-1.33 (m, 9H), 1.26 (s, 3H), 1.25 (s, 3H), 1.13 (s, 3H), 1.10 (s, 3H), 0.89 (s,

3H), 0.84 (s, 3H), 0.83 (s, 3H); (150 MHz, CD_3OD) δ 143.6, 130.3, 81.1, 80.0, 79.9, 78.6, 77.5, 77.4, 54.5, 46.2, 42.1, 40.3, 39.4, 38.8, 37.6, 36.5, 36.1, 33.5, 29.7, 29.4, 28.6, 27.4, 26.8, 24.4, 22.6, 22.1, 20.4, 20.2, 16.7, 14.5; IR (KBr) 3419, 2931, 1444, 1379, 1157, 1061 cm^{-1}; HRMS (APCI) [$M+H^+$] Calcd. for $C_{30}H_{50}O_4$ 475.37819, found 475.37840.

Slow recrystallization of compound ***ent*-73** from a mixture of hexanes and ether provided crystals suitable for structural characterization by X-ray crystallography, resulting in the thermal ellipsoid diagram below:

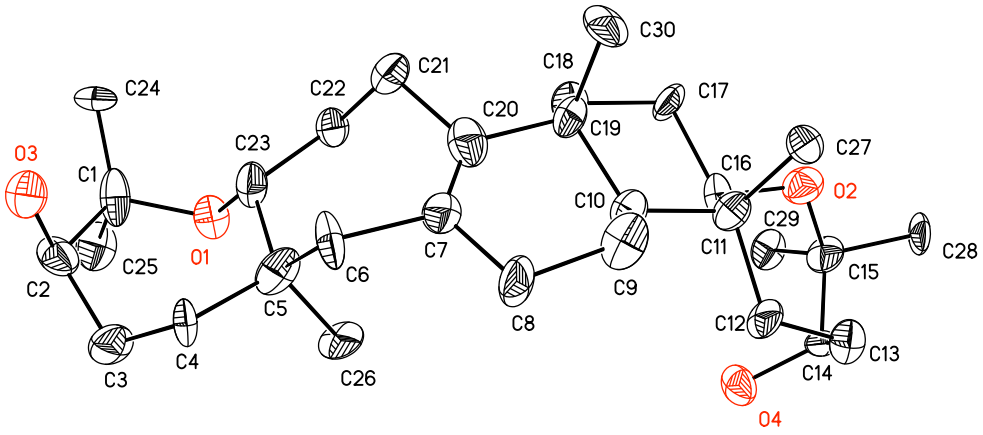


Table 7. Crystal data and structure refinement for ***ent*-73**

Identification code	b103_7_65s	
Empirical formula	C30 H50 O4	
Formula weight	474.70	
Temperature	173(2) K	
Wavelength	1.54178 Å	
Crystal system	Orthorhombic	
Space group	P2(1)2(1)2(1)	
Unit cell dimensions	a = 12.194(3) Å	a= 90°.
	b = 17.305(4) Å	b= 90°.
	c = 25.660(6) Å	g = 90°.
Volume	5415(2) $Å^3$	
Z	8	
Density (calculated)	1.165 Mg/m^3	
Absorption coefficient	0.583 mm^{-1}	
F(000)	2096	
Crystal size	0.38 x 0.06 x 0.05 mm^3	
Theta range for data collection	3.08 to 66.46°.	
Index ranges	-14<=h<=11, -15<=k<=19, -28<=l<=26	
Reflections collected	18408	
Independent reflections	8555 [R(int) = 0.1354]	
Completeness to theta = 66.46°	92.8 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9714 and 0.8089	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	8555 / 0 / 614	
Goodness-of-fit on F^2	1.003	
Final R indices [I>2sigma(I)]	R1 = 0.0803, wR2 = 0.0952	
R indices (all data)	R1 = 0.2062, wR2 = 0.1295	
Absolute structure parameter	0.2(4)	
Extinction coefficient	0.000152(11)	
Largest diff. peak and hole	0.248 and -0.287 $e.Å^{-3}$	

Table 8. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for ***ent*-73** (b103_7_65s). U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor

	x	y	z	U(eq)
C(1)	2467(7)	2965(5)	3296(3)	47(2)
C(2)	1572(6)	3017(5)	3729(3)	44(2)
C(3)	2049(7)	3211(4)	4258(3)	47(2)
C(4)	2289(6)	4080(5)	4353(3)	45(2)
C(5)	3233(6)	4457(5)	4060(3)	37(2)
C(6)	3033(6)	5354(4)	4128(3)	44(2)
C(7)	4012(6)	5884(5)	4014(3)	47(2)
C(8)	4376(6)	6336(5)	4495(3)	56(3)
C(9)	5279(6)	6934(5)	4361(3)	50(2)
C(10)	6083(6)	6559(5)	3984(3)	39(2)
C(11)	7238(6)	6925(5)	3975(3)	40(2)
C(12)	7667(6)	6872(5)	4545(3)	43(2)
C(13)	8913(6)	6958(5)	4628(3)	45(2)
C(14)	9661(7)	6313(5)	4413(3)	43(2)
C(15)	9883(7)	6400(5)	3827(3)	44(2)
C(16)	7957(6)	6427(5)	3619(3)	37(2)
C(17)	7454(6)	6312(5)	3082(3)	43(2)
C(18)	6303(6)	5948(4)	3105(3)	38(2)
C(19)	5505(6)	6409(5)	3455(3)	37(2)
C(20)	4468(6)	5943(5)	3557(3)	44(2)
C(21)	3945(7)	5534(4)	3090(3)	45(2)
C(22)	4005(6)	4648(4)	3126(3)	41(2)
C(23)	3184(6)	4255(5)	3480(3)	41(2)
C(24)	2031(6)	3194(4)	2751(3)	48(2)
C(25)	2927(6)	2150(4)	3289(3)	49(2)
C(26)	4349(6)	4212(5)	4308(3)	52(3)
C(27)	7275(6)	7787(4)	3809(3)	48(2)
C(28)	10871(6)	6962(4)	3763(3)	47(2)
C(29)	10166(6)	5625(4)	3572(3)	44(2)
C(30)	5164(6)	7158(4)	3150(3)	49(2)
C(1B)	-2548(7)	3218(5)	3804(4)	52(3)

C(2B)	-3406(7)	3098(5)	3354(3)	51(3)
C(3B)	-2867(6)	2859(5)	2838(3)	48(2)
C(4B)	-2538(6)	2004(5)	2775(3)	47(2)
C(5B)	-1562(7)	1698(5)	3103(3)	40(2)
C(6B)	-1529(6)	801(4)	3021(3)	46(2)
C(7B)	-528(6)	377(5)	3226(3)	39(2)
C(8B)	200(6)	13(5)	2803(3)	48(2)
C(9B)	1115(6)	-494(5)	3030(3)	43(2)
C(10B)	1605(6)	-113(4)	3510(3)	34(2)
C(11B)	2761(6)	-416(5)	3683(3)	39(2)
C(12B)	3549(6)	-308(5)	3227(3)	41(2)
C(13B)	4785(6)	-383(5)	3331(3)	51(3)
C(14B)	5312(7)	272(5)	3638(3)	48(2)
C(15B)	5128(7)	197(5)	4236(3)	50(3)
C(16B)	3141(6)	94(5)	4136(3)	39(2)
C(17B)	2316(5)	142(4)	4579(3)	37(2)
C(18B)	1212(6)	447(5)	4385(3)	42(2)
C(19B)	717(6)	-48(5)	3944(3)	36(2)
C(20B)	-305(6)	344(5)	3716(3)	37(2)
C(21B)	-1091(6)	694(5)	4107(3)	49(3)
C(22B)	-1033(6)	1586(5)	4095(3)	42(2)
C(23B)	-1756(6)	1948(5)	3674(3)	41(2)
C(24B)	-3014(7)	3090(5)	4335(3)	61(3)
C(25B)	-2116(6)	4057(4)	3747(3)	62(3)
C(26B)	-460(6)	2050(5)	2884(3)	46(2)
C(27B)	2774(6)	-1293(4)	3830(3)	45(2)
C(28B)	6039(6)	-325(4)	4451(3)	51(2)
C(29B)	5159(6)	984(5)	4514(3)	53(3)
C(30B)	314(5)	-834(4)	4174(3)	47(2)
O(1)	3409(4)	3436(3)	3427(2)	39(1)
O(2)	9008(4)	6774(3)	3554(2)	39(2)
O(3)	725(4)	3564(3)	3595(2)	52(2)
O(4)	9178(4)	5569(3)	4519(2)	49(2)
O(1B)	-1570(4)	2772(3)	3708(2)	43(2)
O(2B)	4142(4)	-202(3)	4364(2)	38(1)
O(3B)	-4246(4)	2565(3)	3496(2)	56(2)

O(4B)	4865(4)	973(3)	3426(2)	53(2)

Table 9. Bond lengths [Å] and angles [°] for ***ent*-73** (b103_7_65s)

C(1)-O(1)	1.447(9)
C(1)-C(25)	1.518(10)
C(1)-C(24)	1.549(10)
C(1)-C(2)	1.560(10)
C(2)-O(3)	1.443(9)
C(2)-C(3)	1.513(9)
C(2)-H(2A)	1.0000
C(3)-C(4)	1.553(10)
C(3)-H(3A)	0.9900
C(3)-H(3B)	0.9900
C(4)-C(5)	1.522(9)
C(4)-H(4A)	0.9900
C(4)-H(4B)	0.9900
C(5)-C(23)	1.530(9)
C(5)-C(26)	1.561(9)
C(5)-C(6)	1.582(10)
C(6)-C(7)	1.533(9)
C(6)-H(6A)	0.9900
C(6)-H(6B)	0.9900
C(7)-C(20)	1.304(10)
C(7)-C(8)	1.527(10)
C(8)-C(9)	1.549(10)
C(8)-H(8A)	0.9900
C(8)-H(8B)	0.9900
C(9)-C(10)	1.522(9)
C(9)-H(9A)	0.9900
C(9)-H(9B)	0.9900
C(10)-C(11)	1.545(10)
C(10)-C(19)	1.554(9)
C(10)-H(10A)	1.0000
C(11)-C(16)	1.532(10)

C(11)-C(27)	1.551(10)
C(11)-C(12)	1.555(9)
C(12)-C(13)	1.542(9)
C(12)-H(12A)	0.9900
C(12)-H(12B)	0.9900
C(13)-C(14)	1.544(9)
C(13)-H(13A)	0.9900
C(13)-H(13B)	0.9900
C(14)-O(4)	1.441(9)
C(14)-C(15)	1.534(10)
C(14)-H(14A)	1.0000
C(15)-O(2)	1.431(9)
C(15)-C(29)	1.532(10)
C(15)-C(28)	1.557(9)
C(16)-O(2)	1.426(8)
C(16)-C(17)	1.523(9)
C(16)-H(16A)	1.0000
C(17)-C(18)	1.541(9)
C(17)-H(17A)	0.9900
C(17)-H(17B)	0.9900
C(18)-C(19)	1.546(9)
C(18)-H(18A)	0.9900
C(18)-H(18B)	0.9900
C(19)-C(20)	1.522(10)
C(19)-C(30)	1.570(10)
C(20)-C(21)	1.531(10)
C(21)-C(22)	1.537(9)
C(21)-H(21A)	0.9900
C(21)-H(21B)	0.9900
C(22)-C(23)	1.514(9)
C(22)-H(22A)	0.9900
C(22)-H(22B)	0.9900
C(23)-O(1)	1.450(8)
C(23)-H(23A)	1.0000
C(24)-H(24A)	0.9800
C(24)-H(24B)	0.9800

C(24)-H(24C)	0.9800
C(25)-H(25A)	0.9800
C(25)-H(25B)	0.9800
C(25)-H(25C)	0.9800
C(26)-H(26A)	0.9800
C(26)-H(26B)	0.9800
C(26)-H(26C)	0.9800
C(27)-H(27A)	0.9800
C(27)-H(27B)	0.9800
C(27)-H(27C)	0.9800
C(28)-H(28A)	0.9800
C(28)-H(28B)	0.9800
C(28)-H(28C)	0.9800
C(29)-H(29A)	0.9800
C(29)-H(29B)	0.9800
C(29)-H(29C)	0.9800
C(30)-H(30A)	0.9800
C(30)-H(30B)	0.9800
C(30)-H(30C)	0.9800
C(1B)-O(1B)	1.442(9)
C(1B)-C(24B)	1.492(10)
C(1B)-C(25B)	1.551(11)
C(1B)-C(2B)	1.573(10)
C(2B)-O(3B)	1.425(9)
C(2B)-C(3B)	1.534(10)
C(2B)-H(2BA)	1.0000
C(3B)-C(4B)	1.540(10)
C(3B)-H(3B1)	0.9900
C(3B)-H(3B2)	0.9900
C(4B)-C(5B)	1.551(10)
C(4B)-H(4B1)	0.9900
C(4B)-H(4B2)	0.9900
C(5B)-C(23B)	1.547(10)
C(5B)-C(6B)	1.568(10)
C(5B)-C(26B)	1.578(9)
C(6B)-C(7B)	1.518(10)

C(6B)-H(6BA)	0.9900
C(6B)-H(6BB)	0.9900
C(7B)-C(20B)	1.288(10)
C(7B)-C(8B)	1.537(9)
C(8B)-C(9B)	1.534(9)
C(8B)-H(8BA)	0.9900
C(8B)-H(8BB)	0.9900
C(9B)-C(10B)	1.520(8)
C(9B)-H(9BA)	0.9900
C(9B)-H(9BB)	0.9900
C(10B)-C(19B)	1.558(9)
C(10B)-C(11B)	1.568(9)
C(10B)-H(10B)	1.0000
C(11B)-C(12B)	1.526(9)
C(11B)-C(16B)	1.531(9)
C(11B)-C(27B)	1.564(10)
C(12B)-C(13B)	1.536(9)
C(12B)-H(12C)	0.9900
C(12B)-H(12D)	0.9900
C(13B)-C(14B)	1.523(10)
C(13B)-H(13C)	0.9900
C(13B)-H(13D)	0.9900
C(14B)-O(4B)	1.437(8)
C(14B)-C(15B)	1.555(10)
C(14B)-H(14B)	1.0000
C(15B)-O(2B)	1.425(9)
C(15B)-C(28B)	1.534(9)
C(15B)-C(29B)	1.538(10)
C(16B)-O(2B)	1.448(8)
C(16B)-C(17B)	1.520(9)
C(16B)-H(16B)	1.0000
C(17B)-C(18B)	1.529(8)
C(17B)-H(17C)	0.9900
C(17B)-H(17D)	0.9900
C(18B)-C(19B)	1.543(9)
C(18B)-H(18C)	0.9900

C(18B)-H(18D)	0.9900
C(19B)-C(20B)	1.534(10)
C(19B)-C(30B)	1.561(9)
C(20B)-C(21B)	1.516(10)
C(21B)-C(22B)	1.545(10)
C(21B)-H(21C)	0.9900
C(21B)-H(21D)	0.9900
C(22B)-C(23B)	1.529(9)
C(22B)-H(22C)	0.9900
C(22B)-H(22D)	0.9900
C(23B)-O(1B)	1.445(8)
C(23B)-H(23B)	1.0000
C(24B)-H(24D)	0.9800
C(24B)-H(24E)	0.9800
C(24B)-H(24F)	0.9800
C(25B)-H(25D)	0.9800
C(25B)-H(25E)	0.9800
C(25B)-H(25F)	0.9800
C(26B)-H(26D)	0.9800
C(26B)-H(26E)	0.9800
C(26B)-H(26F)	0.9800
C(27B)-H(27D)	0.9800
C(27B)-H(27E)	0.9800
C(27B)-H(27F)	0.9800
C(28B)-H(28D)	0.9800
C(28B)-H(28E)	0.9800
C(28B)-H(28F)	0.9800
C(29B)-H(29D)	0.9800
C(29B)-H(29E)	0.9800
C(29B)-H(29F)	0.9800
C(30B)-H(30D)	0.9800
C(30B)-H(30E)	0.9800
C(30B)-H(30F)	0.9800
O(3)-H(3C)	0.8400
O(4)-H(4E)	0.8400
O(3B)-H(3BB)	0.8400

O(4B)-H(4BB)	0.8400
O(1)-C(1)-C(25)	103.5(7)
O(1)-C(1)-C(24)	109.8(7)
C(25)-C(1)-C(24)	110.6(7)
O(1)-C(1)-C(2)	110.9(7)
C(25)-C(1)-C(2)	108.7(7)
C(24)-C(1)-C(2)	112.9(7)
O(3)-C(2)-C(3)	110.2(7)
O(3)-C(2)-C(1)	111.6(7)
C(3)-C(2)-C(1)	112.5(7)
O(3)-C(2)-H(2A)	107.4
C(3)-C(2)-H(2A)	107.4
C(1)-C(2)-H(2A)	107.4
C(2)-C(3)-C(4)	115.3(7)
C(2)-C(3)-H(3A)	108.4
C(4)-C(3)-H(3A)	108.4
C(2)-C(3)-H(3B)	108.4
C(4)-C(3)-H(3B)	108.4
H(3A)-C(3)-H(3B)	107.5
C(5)-C(4)-C(3)	118.6(7)
C(5)-C(4)-H(4A)	107.7
C(3)-C(4)-H(4A)	107.7
C(5)-C(4)-H(4B)	107.7
C(3)-C(4)-H(4B)	107.7
H(4A)-C(4)-H(4B)	107.1
C(4)-C(5)-C(23)	110.7(7)
C(4)-C(5)-C(26)	110.0(7)
C(23)-C(5)-C(26)	111.6(7)
C(4)-C(5)-C(6)	104.4(6)
C(23)-C(5)-C(6)	109.0(7)
C(26)-C(5)-C(6)	110.8(7)
C(7)-C(6)-C(5)	116.5(6)
C(7)-C(6)-H(6A)	108.2
C(5)-C(6)-H(6A)	108.2
C(7)-C(6)-H(6B)	108.2

C(5)-C(6)-H(6B)	108.2
H(6A)-C(6)-H(6B)	107.3
C(20)-C(7)-C(8)	124.4(8)
C(20)-C(7)-C(6)	123.3(8)
C(8)-C(7)-C(6)	112.3(7)
C(7)-C(8)-C(9)	111.7(7)
C(7)-C(8)-H(8A)	109.3
C(9)-C(8)-H(8A)	109.3
C(7)-C(8)-H(8B)	109.3
C(9)-C(8)-H(8B)	109.3
H(8A)-C(8)-H(8B)	107.9
C(10)-C(9)-C(8)	108.3(7)
C(10)-C(9)-H(9A)	110.0
C(8)-C(9)-H(9A)	110.0
C(10)-C(9)-H(9B)	110.0
C(8)-C(9)-H(9B)	110.0
H(9A)-C(9)-H(9B)	108.4
C(9)-C(10)-C(11)	115.0(7)
C(9)-C(10)-C(19)	109.6(7)
C(11)-C(10)-C(19)	118.0(6)
C(9)-C(10)-H(10A)	104.2
C(11)-C(10)-H(10A)	104.2
C(19)-C(10)-H(10A)	104.2
C(16)-C(11)-C(10)	107.5(7)
C(16)-C(11)-C(27)	111.1(7)
C(10)-C(11)-C(27)	115.1(7)
C(16)-C(11)-C(12)	109.5(6)
C(10)-C(11)-C(12)	105.6(6)
C(27)-C(11)-C(12)	107.8(7)
C(13)-C(12)-C(11)	117.2(7)
C(13)-C(12)-H(12A)	108.0
C(11)-C(12)-H(12A)	108.0
C(13)-C(12)-H(12B)	108.0
C(11)-C(12)-H(12B)	108.0
H(12A)-C(12)-H(12B)	107.2
C(12)-C(13)-C(14)	117.5(7)

C(12)-C(13)-H(13A)	107.9
C(14)-C(13)-H(13A)	107.9
C(12)-C(13)-H(13B)	107.9
C(14)-C(13)-H(13B)	107.9
H(13A)-C(13)-H(13B)	107.2
O(4)-C(14)-C(15)	110.2(7)
O(4)-C(14)-C(13)	109.7(7)
C(15)-C(14)-C(13)	112.6(7)
O(4)-C(14)-H(14A)	108.1
C(15)-C(14)-H(14A)	108.1
C(13)-C(14)-H(14A)	108.1
O(2)-C(15)-C(29)	110.7(6)
O(2)-C(15)-C(14)	113.1(7)
C(29)-C(15)-C(14)	111.9(7)
O(2)-C(15)-C(28)	104.0(7)
C(29)-C(15)-C(28)	109.1(7)
C(14)-C(15)-C(28)	107.6(7)
O(2)-C(16)-C(17)	108.0(6)
O(2)-C(16)-C(11)	110.4(7)
C(17)-C(16)-C(11)	112.6(6)
O(2)-C(16)-H(16A)	108.6
C(17)-C(16)-H(16A)	108.6
C(11)-C(16)-H(16A)	108.6
C(16)-C(17)-C(18)	112.7(6)
C(16)-C(17)-H(17A)	109.1
C(18)-C(17)-H(17A)	109.1
C(16)-C(17)-H(17B)	109.1
C(18)-C(17)-H(17B)	109.1
H(17A)-C(17)-H(17B)	107.8
C(17)-C(18)-C(19)	112.6(7)
C(17)-C(18)-H(18A)	109.1
C(19)-C(18)-H(18A)	109.1
C(17)-C(18)-H(18B)	109.1
C(19)-C(18)-H(18B)	109.1
H(18A)-C(18)-H(18B)	107.8
C(20)-C(19)-C(18)	110.4(7)

C(20)-C(19)-C(10)	108.4(7)
C(18)-C(19)-C(10)	108.0(6)
C(20)-C(19)-C(30)	107.7(6)
C(18)-C(19)-C(30)	107.7(6)
C(10)-C(19)-C(30)	114.6(7)
C(7)-C(20)-C(19)	123.4(8)
C(7)-C(20)-C(21)	119.5(8)
C(19)-C(20)-C(21)	117.2(7)
C(20)-C(21)-C(22)	113.2(7)
C(20)-C(21)-H(21A)	108.9
C(22)-C(21)-H(21A)	108.9
C(20)-C(21)-H(21B)	108.9
C(22)-C(21)-H(21B)	108.9
H(21A)-C(21)-H(21B)	107.8
C(23)-C(22)-C(21)	116.9(7)
C(23)-C(22)-H(22A)	108.1
C(21)-C(22)-H(22A)	108.1
C(23)-C(22)-H(22B)	108.1
C(21)-C(22)-H(22B)	108.1
H(22A)-C(22)-H(22B)	107.3
O(1)-C(23)-C(22)	105.0(7)
O(1)-C(23)-C(5)	107.8(7)
C(22)-C(23)-C(5)	117.1(7)
O(1)-C(23)-H(23A)	108.9
C(22)-C(23)-H(23A)	108.9
C(5)-C(23)-H(23A)	108.9
C(1)-C(24)-H(24A)	109.5
C(1)-C(24)-H(24B)	109.5
H(24A)-C(24)-H(24B)	109.5
C(1)-C(24)-H(24C)	109.5
H(24A)-C(24)-H(24C)	109.5
H(24B)-C(24)-H(24C)	109.5
C(1)-C(25)-H(25A)	109.5
C(1)-C(25)-H(25B)	109.5
H(25A)-C(25)-H(25B)	109.5
C(1)-C(25)-H(25C)	109.5

H(25A)-C(25)-H(25C)	109.5
H(25B)-C(25)-H(25C)	109.5
C(5)-C(26)-H(26A)	109.5
C(5)-C(26)-H(26B)	109.5
H(26A)-C(26)-H(26B)	109.5
C(5)-C(26)-H(26C)	109.5
H(26A)-C(26)-H(26C)	109.5
H(26B)-C(26)-H(26C)	109.5
C(11)-C(27)-H(27A)	109.5
C(11)-C(27)-H(27B)	109.5
H(27A)-C(27)-H(27B)	109.5
C(11)-C(27)-H(27C)	109.5
H(27A)-C(27)-H(27C)	109.5
H(27B)-C(27)-H(27C)	109.5
C(15)-C(28)-H(28A)	109.5
C(15)-C(28)-H(28B)	109.5
H(28A)-C(28)-H(28B)	109.5
C(15)-C(28)-H(28C)	109.5
H(28A)-C(28)-H(28C)	109.5
H(28B)-C(28)-H(28C)	109.5
C(15)-C(29)-H(29A)	109.5
C(15)-C(29)-H(29B)	109.5
H(29A)-C(29)-H(29B)	109.5
C(15)-C(29)-H(29C)	109.5
H(29A)-C(29)-H(29C)	109.5
H(29B)-C(29)-H(29C)	109.5
C(19)-C(30)-H(30A)	109.5
C(19)-C(30)-H(30B)	109.5
H(30A)-C(30)-H(30B)	109.5
C(19)-C(30)-H(30C)	109.5
H(30A)-C(30)-H(30C)	109.5
H(30B)-C(30)-H(30C)	109.5
O(1B)-C(1B)-C(24B)	113.0(8)
O(1B)-C(1B)-C(25B)	101.8(7)
C(24B)-C(1B)-C(25B)	110.7(8)
O(1B)-C(1B)-C(2B)	110.7(8)

C(24B)-C(1B)-C(2B)	113.5(8)
C(25B)-C(1B)-C(2B)	106.3(7)
O(3B)-C(2B)-C(3B)	110.8(7)
O(3B)-C(2B)-C(1B)	112.1(7)
C(3B)-C(2B)-C(1B)	112.6(7)
O(3B)-C(2B)-H(2BA)	107.0
C(3B)-C(2B)-H(2BA)	107.0
C(1B)-C(2B)-H(2BA)	107.0
C(2B)-C(3B)-C(4B)	117.4(7)
C(2B)-C(3B)-H(3B1)	107.9
C(4B)-C(3B)-H(3B1)	107.9
C(2B)-C(3B)-H(3B2)	107.9
C(4B)-C(3B)-H(3B2)	107.9
H(3B1)-C(3B)-H(3B2)	107.2
C(3B)-C(4B)-C(5B)	118.1(7)
C(3B)-C(4B)-H(4B1)	107.8
C(5B)-C(4B)-H(4B1)	107.8
C(3B)-C(4B)-H(4B2)	107.8
C(5B)-C(4B)-H(4B2)	107.8
H(4B1)-C(4B)-H(4B2)	107.1
C(23B)-C(5B)-C(4B)	107.5(7)
C(23B)-C(5B)-C(6B)	114.1(7)
C(4B)-C(5B)-C(6B)	106.6(6)
C(23B)-C(5B)-C(26B)	111.1(7)
C(4B)-C(5B)-C(26B)	109.2(7)
C(6B)-C(5B)-C(26B)	108.2(7)
C(7B)-C(6B)-C(5B)	116.9(7)
C(7B)-C(6B)-H(6BA)	108.1
C(5B)-C(6B)-H(6BA)	108.1
C(7B)-C(6B)-H(6BB)	108.1
C(5B)-C(6B)-H(6BB)	108.1
H(6BA)-C(6B)-H(6BB)	107.3
C(20B)-C(7B)-C(6B)	122.0(8)
C(20B)-C(7B)-C(8B)	123.3(8)
C(6B)-C(7B)-C(8B)	114.7(6)
C(9B)-C(8B)-C(7B)	112.7(6)

C(9B)-C(8B)-H(8BA)	109.0
C(7B)-C(8B)-H(8BA)	109.0
C(9B)-C(8B)-H(8BB)	109.0
C(7B)-C(8B)-H(8BB)	109.0
H(8BA)-C(8B)-H(8BB)	107.8
C(10B)-C(9B)-C(8B)	110.3(7)
C(10B)-C(9B)-H(9BA)	109.6
C(8B)-C(9B)-H(9BA)	109.6
C(10B)-C(9B)-H(9BB)	109.6
C(8B)-C(9B)-H(9BB)	109.6
H(9BA)-C(9B)-H(9BB)	108.1
C(9B)-C(10B)-C(19B)	109.7(6)
C(9B)-C(10B)-C(11B)	116.0(7)
C(19B)-C(10B)-C(11B)	116.6(6)
C(9B)-C(10B)-H(10B)	104.3
C(19B)-C(10B)-H(10B)	104.3
C(11B)-C(10B)-H(10B)	104.3
C(12B)-C(11B)-C(16B)	108.7(6)
C(12B)-C(11B)-C(27B)	107.3(7)
C(16B)-C(11B)-C(27B)	111.9(7)
C(12B)-C(11B)-C(10B)	108.0(6)
C(16B)-C(11B)-C(10B)	107.1(6)
C(27B)-C(11B)-C(10B)	113.7(6)
C(11B)-C(12B)-C(13B)	118.3(6)
C(11B)-C(12B)-H(12C)	107.7
C(13B)-C(12B)-H(12C)	107.7
C(11B)-C(12B)-H(12D)	107.7
C(13B)-C(12B)-H(12D)	107.7
H(12C)-C(12B)-H(12D)	107.1
C(14B)-C(13B)-C(12B)	116.2(7)
C(14B)-C(13B)-H(13C)	108.2
C(12B)-C(13B)-H(13C)	108.2
C(14B)-C(13B)-H(13D)	108.2
C(12B)-C(13B)-H(13D)	108.2
H(13C)-C(13B)-H(13D)	107.4
O(4B)-C(14B)-C(13B)	105.7(6)

O(4B)-C(14B)-C(15B)	112.9(7)
C(13B)-C(14B)-C(15B)	112.8(7)
O(4B)-C(14B)-H(14B)	108.4
C(13B)-C(14B)-H(14B)	108.4
C(15B)-C(14B)-H(14B)	108.4
O(2B)-C(15B)-C(28B)	104.1(7)
O(2B)-C(15B)-C(29B)	110.0(7)
C(28B)-C(15B)-C(29B)	109.6(7)
O(2B)-C(15B)-C(14B)	113.0(7)
C(28B)-C(15B)-C(14B)	107.4(7)
C(29B)-C(15B)-C(14B)	112.3(7)
O(2B)-C(16B)-C(17B)	106.0(6)
O(2B)-C(16B)-C(11B)	111.0(6)
C(17B)-C(16B)-C(11B)	113.5(6)
O(2B)-C(16B)-H(16B)	108.7
C(17B)-C(16B)-H(16B)	108.7
C(11B)-C(16B)-H(16B)	108.7
C(16B)-C(17B)-C(18B)	111.0(6)
C(16B)-C(17B)-H(17C)	109.4
C(18B)-C(17B)-H(17C)	109.4
C(16B)-C(17B)-H(17D)	109.4
C(18B)-C(17B)-H(17D)	109.4
H(17C)-C(17B)-H(17D)	108.0
C(17B)-C(18B)-C(19B)	113.0(7)
C(17B)-C(18B)-H(18C)	109.0
C(19B)-C(18B)-H(18C)	109.0
C(17B)-C(18B)-H(18D)	109.0
C(19B)-C(18B)-H(18D)	109.0
H(18C)-C(18B)-H(18D)	107.8
C(20B)-C(19B)-C(18B)	110.6(7)
C(20B)-C(19B)-C(10B)	108.9(6)
C(18B)-C(19B)-C(10B)	107.0(6)
C(20B)-C(19B)-C(30B)	105.9(6)
C(18B)-C(19B)-C(30B)	109.3(6)
C(10B)-C(19B)-C(30B)	115.2(6)
C(7B)-C(20B)-C(21B)	119.6(8)

C(7B)-C(20B)-C(19B)	124.4(8)
C(21B)-C(20B)-C(19B)	116.0(7)
C(20B)-C(21B)-C(22B)	111.0(7)
C(20B)-C(21B)-H(21C)	109.4
C(22B)-C(21B)-H(21C)	109.4
C(20B)-C(21B)-H(21D)	109.4
C(22B)-C(21B)-H(21D)	109.4
H(21C)-C(21B)-H(21D)	108.0
C(23B)-C(22B)-C(21B)	113.4(7)
C(23B)-C(22B)-H(22C)	108.9
C(21B)-C(22B)-H(22C)	108.9
C(23B)-C(22B)-H(22D)	108.9
C(21B)-C(22B)-H(22D)	108.9
H(22C)-C(22B)-H(22D)	107.7
O(1B)-C(23B)-C(22B)	105.7(6)
O(1B)-C(23B)-C(5B)	108.0(7)
C(22B)-C(23B)-C(5B)	117.8(7)
O(1B)-C(23B)-H(23B)	108.3
C(22B)-C(23B)-H(23B)	108.3
C(5B)-C(23B)-H(23B)	108.3
C(1B)-C(24B)-H(24D)	109.5
C(1B)-C(24B)-H(24E)	109.5
H(24D)-C(24B)-H(24E)	109.5
C(1B)-C(24B)-H(24F)	109.5
H(24D)-C(24B)-H(24F)	109.5
H(24E)-C(24B)-H(24F)	109.5
C(1B)-C(25B)-H(25D)	109.5
C(1B)-C(25B)-H(25E)	109.5
H(25D)-C(25B)-H(25E)	109.5
C(1B)-C(25B)-H(25F)	109.5
H(25D)-C(25B)-H(25F)	109.5
H(25E)-C(25B)-H(25F)	109.5
C(5B)-C(26B)-H(26D)	109.5
C(5B)-C(26B)-H(26E)	109.5
H(26D)-C(26B)-H(26E)	109.5
C(5B)-C(26B)-H(26F)	109.5

H(26D)-C(26B)-H(26F)	109.5
H(26E)-C(26B)-H(26F)	109.5
C(11B)-C(27B)-H(27D)	109.5
C(11B)-C(27B)-H(27E)	109.5
H(27D)-C(27B)-H(27E)	109.5
C(11B)-C(27B)-H(27F)	109.5
H(27D)-C(27B)-H(27F)	109.5
H(27E)-C(27B)-H(27F)	109.5
C(15B)-C(28B)-H(28D)	109.5
C(15B)-C(28B)-H(28E)	109.5
H(28D)-C(28B)-H(28E)	109.5
C(15B)-C(28B)-H(28F)	109.5
H(28D)-C(28B)-H(28F)	109.5
H(28E)-C(28B)-H(28F)	109.5
C(15B)-C(29B)-H(29D)	109.5
C(15B)-C(29B)-H(29E)	109.5
H(29D)-C(29B)-H(29E)	109.5
C(15B)-C(29B)-H(29F)	109.5
H(29D)-C(29B)-H(29F)	109.5
H(29E)-C(29B)-H(29F)	109.5
C(19B)-C(30B)-H(30D)	109.5
C(19B)-C(30B)-H(30E)	109.5
H(30D)-C(30B)-H(30E)	109.5
C(19B)-C(30B)-H(30F)	109.5
H(30D)-C(30B)-H(30F)	109.5
H(30E)-C(30B)-H(30F)	109.5
C(1)-O(1)-C(23)	114.9(6)
C(16)-O(2)-C(15)	115.0(6)
C(2)-O(3)-H(3C)	109.5
C(14)-O(4)-H(4E)	109.5
C(1B)-O(1B)-C(23B)	114.1(6)
C(15B)-O(2B)-C(16B)	116.6(6)
C(2B)-O(3B)-H(3BB)	109.5
C(14B)-O(4B)-H(4BB)	109.5

Symmetry transformations used to generate equivalent atoms:

Table 10. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for ***ent*-73** (b103_7_65s). 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}
C(1)	41(6)	52(6)	46(5)	-10(5)	5(5)	4(5)
C(2)	26(5)	60(6)	46(5)	0(5)	-1(4)	-6(5)
C(3)	44(6)	56(7)	40(5)	5(5)	5(4)	2(5)
C(4)	32(5)	67(6)	37(5)	1(5)	3(4)	-3(5)
C(5)	32(5)	49(6)	30(4)	-7(4)	4(4)	-4(4)
C(6)	31(5)	55(6)	44(5)	-13(5)	0(4)	-8(5)
C(7)	31(5)	61(7)	49(5)	-14(5)	-6(5)	-7(5)
C(8)	35(6)	84(8)	49(5)	-27(6)	5(4)	-1(5)
C(9)	33(6)	59(7)	56(6)	-21(5)	-1(4)	0(5)
C(10)	30(5)	46(6)	42(5)	-3(4)	9(4)	1(4)
C(11)	25(5)	64(7)	31(4)	-5(5)	-2(4)	2(5)
C(12)	30(5)	55(6)	45(5)	-10(5)	1(4)	2(4)
C(13)	47(6)	48(6)	41(5)	-4(4)	4(4)	-5(5)
C(14)	43(6)	52(6)	36(5)	-1(5)	-9(4)	7(5)
C(15)	26(5)	49(6)	57(6)	1(5)	-5(5)	-2(4)
C(16)	38(5)	36(5)	36(5)	-1(4)	-1(4)	1(4)
C(17)	33(5)	52(6)	44(5)	1(5)	-6(4)	7(5)
C(18)	37(6)	46(6)	33(4)	2(4)	1(4)	3(4)
C(19)	18(4)	49(6)	45(5)	-3(4)	-2(4)	5(4)
C(20)	35(5)	51(6)	45(5)	-7(5)	-7(4)	3(5)
C(21)	41(6)	53(6)	42(5)	4(5)	-1(4)	-6(5)
C(22)	29(5)	61(6)	32(4)	-7(4)	-10(4)	-1(5)
C(23)	28(5)	55(6)	41(5)	-1(5)	-7(4)	-10(4)
C(24)	44(6)	48(6)	53(6)	3(5)	-12(5)	-12(5)
C(25)	48(6)	44(6)	56(6)	-7(5)	-2(5)	5(5)
C(26)	31(5)	77(7)	49(5)	4(5)	-4(4)	12(5)
C(27)	40(6)	42(6)	64(6)	-6(5)	-4(5)	-8(4)
C(28)	38(6)	46(6)	56(5)	-6(5)	-2(5)	-9(5)
C(29)	39(5)	39(6)	55(5)	-1(5)	3(5)	-1(4)
C(30)	48(6)	38(6)	62(6)	0(5)	-6(5)	-2(5)
C(1B)	32(6)	57(7)	67(6)	6(5)	-15(5)	4(5)

C(2B)	35(6)	40(6)	77(7)	-12(5)	-18(5)	0(5)
C(3B)	28(5)	65(7)	50(5)	9(5)	-15(4)	-9(5)
C(4B)	36(6)	55(7)	51(5)	5(5)	-1(4)	1(5)
C(5B)	28(5)	57(6)	35(5)	-2(4)	-9(4)	-2(4)
C(6B)	36(6)	65(7)	36(5)	-1(5)	-1(4)	-7(5)
C(7B)	30(5)	42(6)	45(5)	-2(4)	4(4)	-3(4)
C(8B)	32(5)	73(7)	38(5)	-9(5)	-2(4)	5(5)
C(9B)	37(5)	48(6)	44(5)	-2(4)	5(4)	2(4)
C(10B)	25(5)	43(5)	33(4)	0(4)	1(4)	-3(4)
C(11B)	33(5)	52(6)	31(4)	0(4)	1(4)	1(4)
C(12B)	39(5)	48(6)	37(5)	-7(4)	10(4)	-1(5)
C(13B)	51(6)	57(7)	46(5)	-11(5)	18(5)	7(5)
C(14B)	40(6)	63(7)	41(5)	2(5)	2(4)	-3(5)
C(15B)	33(6)	67(7)	49(6)	2(5)	-5(4)	10(5)
C(16B)	34(5)	52(6)	29(4)	-8(4)	2(4)	-9(5)
C(17B)	30(5)	44(6)	37(4)	-5(4)	-5(4)	6(4)
C(18B)	29(5)	60(6)	36(4)	1(5)	0(4)	-1(4)
C(19B)	33(5)	37(5)	37(4)	4(4)	1(4)	5(4)
C(20B)	30(5)	33(5)	47(5)	0(4)	7(4)	0(4)
C(21B)	25(5)	82(8)	40(5)	12(5)	0(4)	6(5)
C(22B)	35(5)	61(6)	31(4)	-1(4)	-5(4)	6(5)
C(23B)	18(5)	48(6)	57(6)	7(5)	1(4)	3(4)
C(24B)	64(7)	70(7)	48(6)	-7(5)	-11(5)	7(6)
C(25B)	58(7)	41(6)	87(7)	-17(6)	-21(6)	-1(5)
C(26B)	34(6)	64(7)	40(5)	-3(5)	-2(4)	-8(5)
C(27B)	37(6)	55(6)	44(5)	2(5)	4(4)	-4(5)
C(28B)	22(5)	65(7)	64(6)	10(5)	4(5)	6(5)
C(29B)	46(6)	48(6)	64(6)	-8(5)	-4(5)	-11(5)
C(30B)	24(5)	68(7)	48(5)	19(5)	9(4)	11(5)
O(1)	30(3)	42(4)	45(3)	-4(3)	-2(3)	2(3)
O(2)	24(3)	50(4)	43(3)	8(3)	-2(3)	2(3)
O(3)	29(4)	64(4)	63(4)	-11(4)	4(3)	6(3)
O(4)	41(4)	61(4)	43(3)	10(3)	-11(3)	-9(3)
O(1B)	35(4)	44(4)	49(4)	-7(3)	-5(3)	2(3)
O(2B)	23(3)	43(4)	47(3)	3(3)	4(3)	-3(3)
O(3B)	29(4)	55(4)	84(5)	1(4)	-2(3)	-3(3)

O(4B)	47(4)	54(4)	57(4)	9(3)	-8(3)	-7(3)

Table 11. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for ***ent-73*** (b103_7_65s)

	x	y	z	U(eq)
H(2A)	1220	2497	3758	53
H(3A)	2741	2919	4301	56
H(3B)	1533	3029	4529	56
H(4A)	1614	4372	4269	54
H(4B)	2428	4149	4731	54
H(6A)	2422	5507	3896	52
H(6B)	2791	5448	4491	52
H(8A)	4659	5972	4760	67
H(8B)	3736	6608	4646	67
H(9A)	4947	7397	4200	60
H(9B)	5666	7095	4683	60
H(10A)	6205	6031	4132	47
H(12A)	7294	7276	4752	52
H(12B)	7441	6365	4689	52
H(13A)	9048	7001	5008	54
H(13B)	9145	7453	4469	54
H(14A)	10379	6341	4600	52
H(16A)	8056	5909	3786	44
H(17A)	7942	5976	2872	52
H(17B)	7406	6819	2904	52
H(18A)	6364	5413	3240	46
H(18B)	5998	5919	2748	46
H(21A)	4320	5704	2767	54
H(21B)	3167	5691	3064	54
H(22A)	3913	4436	2770	49
H(22B)	4751	4506	3245	49
H(23A)	2428	4362	3348	50
H(24A)	2629	3163	2496	73

H(24B)	1746	3723	2762	73
H(24C)	1442	2839	2649	73
H(25A)	3485	2109	3015	74
H(25B)	2334	1782	3218	74
H(25C)	3259	2033	3627	74
H(26A)	4464	3657	4255	78
H(26B)	4338	4325	4682	78
H(26C)	4947	4501	4142	78
H(27A)	7004	7837	3451	73
H(27B)	8032	7975	3828	73
H(27C)	6811	8092	4043	73
H(28A)	10698	7457	3929	70
H(28B)	11013	7046	3391	70
H(28C)	11522	6737	3927	70
H(29A)	9556	5264	3621	67
H(29B)	10829	5413	3733	67
H(29C)	10294	5703	3199	67
H(30A)	4820	7013	2819	74
H(30B)	5817	7472	3081	74
H(30C)	4644	7457	3360	74
H(2BA)	-3769	3608	3293	61
H(3B1)	-2201	3178	2790	57
H(3B2)	-3378	2991	2552	57
H(4B1)	-2364	1916	2403	57
H(4B2)	-3188	1685	2859	57
H(6BA)	-2186	576	3190	55
H(6BB)	-1589	697	2643	55
H(8BA)	-262	-304	2569	57
H(8BB)	534	430	2591	57
H(9BA)	813	-1006	3124	52
H(9BB)	1694	-572	2765	52
H(10B)	1740	433	3401	40
H(12C)	3416	211	3078	50
H(12D)	3352	-690	2955	50
H(13C)	4913	-872	3522	62
H(13D)	5166	-425	2991	62

H(14B)	6119	266	3569	58
H(16B)	3281	627	4001	46
H(17C)	2602	488	4854	44
H(17D)	2214	-378	4733	44
H(18C)	1310	983	4258	50
H(18D)	691	462	4681	50
H(21C)	-906	508	4461	59
H(21D)	-1848	526	4026	59
H(22C)	-1260	1789	4439	50
H(22D)	-263	1745	4036	50
H(23B)	-2540	1844	3764	49
H(24D)	-2438	3166	4597	91
H(24E)	-3298	2562	4360	91
H(24F)	-3610	3458	4397	91
H(25D)	-1566	4158	4017	93
H(25E)	-2727	4420	3786	93
H(25F)	-1783	4122	3403	93
H(26D)	-462	2612	2935	69
H(26E)	-399	1934	2511	69
H(26F)	164	1824	3070	69
H(27D)	3516	-1443	3937	68
H(27E)	2551	-1601	3527	68
H(27F)	2263	-1385	4118	68
H(28D)	5952	-378	4829	76
H(28E)	6755	-94	4374	76
H(28F)	5993	-835	4287	76
H(29D)	5051	908	4889	79
H(29E)	4575	1315	4376	79
H(29F)	5872	1230	4453	79
H(30D)	940	-1117	4319	70
H(30E)	-26	-1142	3897	70
H(30F)	-224	-736	4450	70
H(3C)	108	3353	3627	78
H(4E)	9188	5486	4841	73
H(3BB)	-4859	2786	3480	84
H(4BB)	5281	1345	3498	79

Table 12. Torsion angles [°] for ***ent*-73** (b103_7_65s)

O(1)-C(1)-C(2)-O(3)	98.2(8)
C(25)-C(1)-C(2)-O(3)	-148.7(7)
C(24)-C(1)-C(2)-O(3)	-25.5(10)
O(1)-C(1)-C(2)-C(3)	-26.3(10)
C(25)-C(1)-C(2)-C(3)	86.8(9)
C(24)-C(1)-C(2)-C(3)	-150.0(7)
O(3)-C(2)-C(3)-C(4)	-44.0(10)
C(1)-C(2)-C(3)-C(4)	81.3(10)
C(2)-C(3)-C(4)-C(5)	-70.6(10)
C(3)-C(4)-C(5)-C(23)	47.8(10)
C(3)-C(4)-C(5)-C(26)	-76.1(9)
C(3)-C(4)-C(5)-C(6)	164.9(7)
C(4)-C(5)-C(6)-C(7)	162.8(6)
C(23)-C(5)-C(6)-C(7)	-78.9(9)
C(26)-C(5)-C(6)-C(7)	44.4(9)
C(5)-C(6)-C(7)-C(20)	63.4(12)
C(5)-C(6)-C(7)-C(8)	-117.1(8)
C(20)-C(7)-C(8)-C(9)	5.7(13)
C(6)-C(7)-C(8)-C(9)	-173.8(7)
C(7)-C(8)-C(9)-C(10)	-41.5(10)
C(8)-C(9)-C(10)-C(11)	-157.1(7)
C(8)-C(9)-C(10)-C(19)	67.2(9)
C(9)-C(10)-C(11)-C(16)	174.4(7)
C(19)-C(10)-C(11)-C(16)	-53.8(10)
C(9)-C(10)-C(11)-C(27)	-61.2(9)
C(19)-C(10)-C(11)-C(27)	70.6(10)
C(9)-C(10)-C(11)-C(12)	57.5(9)
C(19)-C(10)-C(11)-C(12)	-170.6(7)
C(16)-C(11)-C(12)-C(13)	46.3(10)
C(10)-C(11)-C(12)-C(13)	161.8(7)
C(27)-C(11)-C(12)-C(13)	-74.7(9)
C(11)-C(12)-C(13)-C(14)	-67.2(10)
C(12)-C(13)-C(14)-O(4)	-42.2(9)

C(12)-C(13)-C(14)-C(15)	80.9(9)
O(4)-C(14)-C(15)-O(2)	93.7(8)
C(13)-C(14)-C(15)-O(2)	-29.1(10)
O(4)-C(14)-C(15)-C(29)	-32.1(9)
C(13)-C(14)-C(15)-C(29)	-155.0(7)
O(4)-C(14)-C(15)-C(28)	-151.9(6)
C(13)-C(14)-C(15)-C(28)	85.2(8)
C(10)-C(11)-C(16)-O(2)	174.5(6)
C(27)-C(11)-C(16)-O(2)	47.7(8)
C(12)-C(11)-C(16)-O(2)	-71.3(8)
C(10)-C(11)-C(16)-C(17)	53.7(9)
C(27)-C(11)-C(16)-C(17)	-73.1(9)
C(12)-C(11)-C(16)-C(17)	167.9(7)
O(2)-C(16)-C(17)-C(18)	-179.3(6)
C(11)-C(16)-C(17)-C(18)	-57.2(10)
C(16)-C(17)-C(18)-C(19)	55.0(9)
C(17)-C(18)-C(19)-C(20)	-168.1(6)
C(17)-C(18)-C(19)-C(10)	-49.7(9)
C(17)-C(18)-C(19)-C(30)	74.6(8)
C(9)-C(10)-C(19)-C(20)	-54.1(9)
C(11)-C(10)-C(19)-C(20)	171.7(7)
C(9)-C(10)-C(19)-C(18)	-173.7(7)
C(11)-C(10)-C(19)-C(18)	52.1(10)
C(9)-C(10)-C(19)-C(30)	66.2(9)
C(11)-C(10)-C(19)-C(30)	-68.0(9)
C(8)-C(7)-C(20)-C(19)	6.6(15)
C(6)-C(7)-C(20)-C(19)	-174.0(8)
C(8)-C(7)-C(20)-C(21)	-172.7(8)
C(6)-C(7)-C(20)-C(21)	6.7(14)
C(18)-C(19)-C(20)-C(7)	135.7(9)
C(10)-C(19)-C(20)-C(7)	17.6(12)
C(30)-C(19)-C(20)-C(7)	-107.0(10)
C(18)-C(19)-C(20)-C(21)	-44.9(10)
C(10)-C(19)-C(20)-C(21)	-163.1(7)
C(30)-C(19)-C(20)-C(21)	72.4(9)
C(7)-C(20)-C(21)-C(22)	-67.6(11)

C(19)-C(20)-C(21)-C(22)	113.0(8)
C(20)-C(21)-C(22)-C(23)	78.4(9)
C(21)-C(22)-C(23)-O(1)	178.5(6)
C(21)-C(22)-C(23)-C(5)	-61.9(10)
C(4)-C(5)-C(23)-O(1)	-67.7(8)
C(26)-C(5)-C(23)-O(1)	55.2(9)
C(6)-C(5)-C(23)-O(1)	178.0(6)
C(4)-C(5)-C(23)-C(22)	174.3(7)
C(26)-C(5)-C(23)-C(22)	-62.8(10)
C(6)-C(5)-C(23)-C(22)	60.0(9)
O(1B)-C(1B)-C(2B)-O(3B)	100.5(8)
C(24B)-C(1B)-C(2B)-O(3B)	-27.7(11)
C(25B)-C(1B)-C(2B)-O(3B)	-149.7(7)
O(1B)-C(1B)-C(2B)-C(3B)	-25.1(10)
C(24B)-C(1B)-C(2B)-C(3B)	-153.4(8)
C(25B)-C(1B)-C(2B)-C(3B)	84.7(9)
O(3B)-C(2B)-C(3B)-C(4B)	-46.7(10)
C(1B)-C(2B)-C(3B)-C(4B)	79.7(10)
C(2B)-C(3B)-C(4B)-C(5B)	-70.3(10)
C(3B)-C(4B)-C(5B)-C(23B)	49.3(10)
C(3B)-C(4B)-C(5B)-C(6B)	171.9(7)
C(3B)-C(4B)-C(5B)-C(26B)	-71.4(9)
C(23B)-C(5B)-C(6B)-C(7B)	-71.8(9)
C(4B)-C(5B)-C(6B)-C(7B)	169.7(6)
C(26B)-C(5B)-C(6B)-C(7B)	52.4(9)
C(5B)-C(6B)-C(7B)-C(20B)	64.9(12)
C(5B)-C(6B)-C(7B)-C(8B)	-113.7(8)
C(20B)-C(7B)-C(8B)-C(9B)	8.8(13)
C(6B)-C(7B)-C(8B)-C(9B)	-172.6(7)
C(7B)-C(8B)-C(9B)-C(10B)	-40.7(9)
C(8B)-C(9B)-C(10B)-C(19B)	63.7(8)
C(8B)-C(9B)-C(10B)-C(11B)	-161.7(7)
C(9B)-C(10B)-C(11B)-C(12B)	57.8(9)
C(19B)-C(10B)-C(11B)-C(12B)	-170.7(7)
C(9B)-C(10B)-C(11B)-C(16B)	174.7(6)
C(19B)-C(10B)-C(11B)-C(16B)	-53.8(9)

C(9B)-C(10B)-C(11B)-C(27B)	-61.2(9)
C(19B)-C(10B)-C(11B)-C(27B)	70.3(8)
C(16B)-C(11B)-C(12B)-C(13B)	50.3(10)
C(27B)-C(11B)-C(12B)-C(13B)	-70.9(9)
C(10B)-C(11B)-C(12B)-C(13B)	166.2(7)
C(11B)-C(12B)-C(13B)-C(14B)	-71.6(10)
C(12B)-C(13B)-C(14B)-O(4B)	-43.2(9)
C(12B)-C(13B)-C(14B)-C(15B)	80.7(9)
O(4B)-C(14B)-C(15B)-O(2B)	91.6(9)
C(13B)-C(14B)-C(15B)-O(2B)	-28.2(11)
O(4B)-C(14B)-C(15B)-C(28B)	-154.2(7)
C(13B)-C(14B)-C(15B)-C(28B)	86.0(9)
O(4B)-C(14B)-C(15B)-C(29B)	-33.6(10)
C(13B)-C(14B)-C(15B)-C(29B)	-153.4(7)
C(12B)-C(11B)-C(16B)-O(2B)	-70.6(8)
C(27B)-C(11B)-C(16B)-O(2B)	47.7(8)
C(10B)-C(11B)-C(16B)-O(2B)	172.9(6)
C(12B)-C(11B)-C(16B)-C(17B)	170.1(6)
C(27B)-C(11B)-C(16B)-C(17B)	-71.5(9)
C(10B)-C(11B)-C(16B)-C(17B)	53.7(9)
O(2B)-C(16B)-C(17B)-C(18B)	-179.8(6)
C(11B)-C(16B)-C(17B)-C(18B)	-57.7(9)
C(16B)-C(17B)-C(18B)-C(19B)	57.6(9)
C(17B)-C(18B)-C(19B)-C(20B)	-172.3(6)
C(17B)-C(18B)-C(19B)-C(10B)	-53.9(8)
C(17B)-C(18B)-C(19B)-C(30B)	71.5(8)
C(9B)-C(10B)-C(19B)-C(20B)	-52.2(9)
C(11B)-C(10B)-C(19B)-C(20B)	173.5(7)
C(9B)-C(10B)-C(19B)-C(18B)	-171.7(6)
C(11B)-C(10B)-C(19B)-C(18B)	53.9(9)
C(9B)-C(10B)-C(19B)-C(30B)	66.6(8)
C(11B)-C(10B)-C(19B)-C(30B)	-67.8(9)
C(6B)-C(7B)-C(20B)-C(21B)	3.7(14)
C(8B)-C(7B)-C(20B)-C(21B)	-177.8(7)
C(6B)-C(7B)-C(20B)-C(19B)	-177.5(7)
C(8B)-C(7B)-C(20B)-C(19B)	1.0(15)

C(18B)-C(19B)-C(20B)-C(7B)	138.1(9)
C(10B)-C(19B)-C(20B)-C(7B)	20.8(12)
C(30B)-C(19B)-C(20B)-C(7B)	-103.6(10)
C(18B)-C(19B)-C(20B)-C(21B)	-43.1(10)
C(10B)-C(19B)-C(20B)-C(21B)	-160.3(7)
C(30B)-C(19B)-C(20B)-C(21B)	75.2(9)
C(7B)-C(20B)-C(21B)-C(22B)	-73.4(10)
C(19B)-C(20B)-C(21B)-C(22B)	107.7(8)
C(20B)-C(21B)-C(22B)-C(23B)	84.6(8)
C(21B)-C(22B)-C(23B)-O(1B)	-178.1(6)
C(21B)-C(22B)-C(23B)-C(5B)	-57.3(10)
C(4B)-C(5B)-C(23B)-O(1B)	-72.3(8)
C(6B)-C(5B)-C(23B)-O(1B)	169.8(6)
C(26B)-C(5B)-C(23B)-O(1B)	47.2(8)
C(4B)-C(5B)-C(23B)-C(22B)	168.2(7)
C(6B)-C(5B)-C(23B)-C(22B)	50.2(10)
C(26B)-C(5B)-C(23B)-C(22B)	-72.4(9)
C(25)-C(1)-O(1)-C(23)	-177.8(6)
C(24)-C(1)-O(1)-C(23)	64.0(9)
C(2)-C(1)-O(1)-C(23)	-61.4(9)
C(22)-C(23)-O(1)-C(1)	-127.1(7)
C(5)-C(23)-O(1)-C(1)	107.3(7)
C(17)-C(16)-O(2)-C(15)	-130.0(7)
C(11)-C(16)-O(2)-C(15)	106.5(7)
C(29)-C(15)-O(2)-C(16)	71.8(8)
C(14)-C(15)-O(2)-C(16)	-54.7(9)
C(28)-C(15)-O(2)-C(16)	-171.2(6)
C(24B)-C(1B)-O(1B)-C(23B)	68.3(10)
C(25B)-C(1B)-O(1B)-C(23B)	-172.9(6)
C(2B)-C(1B)-O(1B)-C(23B)	-60.2(9)
C(22B)-C(23B)-O(1B)-C(1B)	-122.0(7)
C(5B)-C(23B)-O(1B)-C(1B)	111.0(7)
C(28B)-C(15B)-O(2B)-C(16B)	-170.5(6)
C(29B)-C(15B)-O(2B)-C(16B)	72.1(8)
C(14B)-C(15B)-O(2B)-C(16B)	-54.3(9)
C(17B)-C(16B)-O(2B)-C(15B)	-132.5(7)

C(11B)-C(16B)-O(2B)-C(15B)	103.8(7)

Symmetry transformations used to generate equivalent atoms:

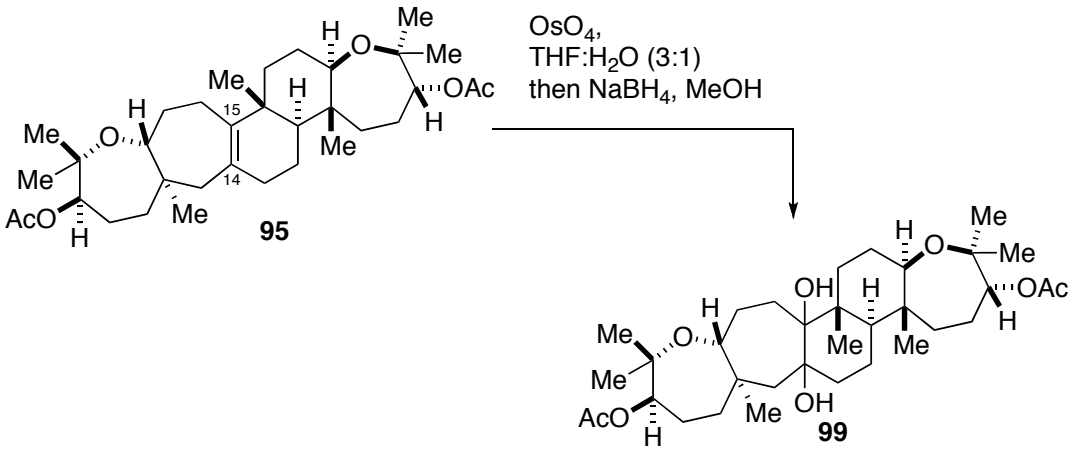
Table 13. Hydrogen bonds for ***ent-73*** (b103_7_65s) [Å and °]

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
O(3)-H(3C)...O(1B)	0.84	2.29	3.130(7)	179.6
O(4)-H(4E)...O(2B)#1	0.84	2.10	2.936(7)	175.6
O(3B)-H(3BB)...O(1)#2	0.84	2.40	3.237(7)	178.9
O(4B)-H(4BB)...O(3B)#3	0.84	2.19	2.966(8)	153.8

Symmetry transformations used to generate equivalent atoms:

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

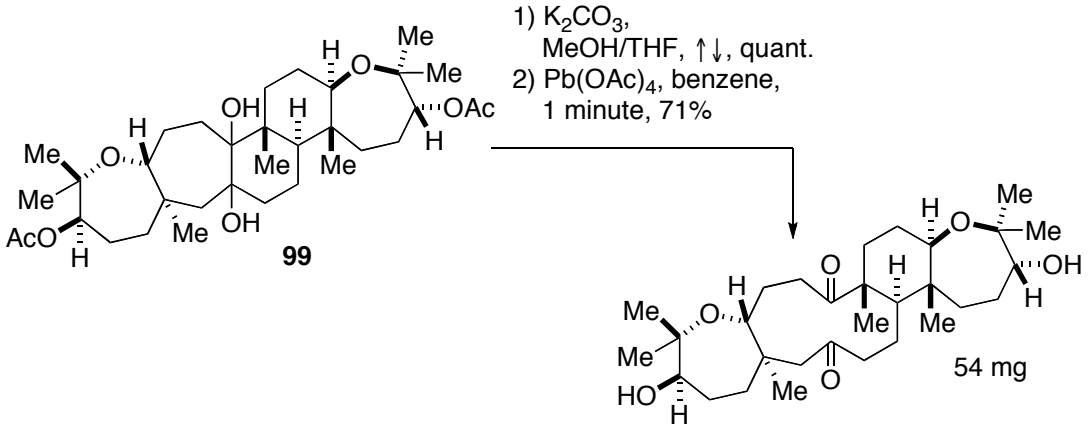
Dihydroxylation of diacetoxy tetrasubstituted alkene 95: synthesis of diacetoxy diol 99



The diacetoxy tetrasubstituted alkene **95** (137 mg, 0.25 mmol) was dissolved in THF:H_2O (3:1) (0.063 M, 4.0 mL). Then OsO_4 (125 mg, 0.50 mmol) was added. The reaction was allowed to stir for 5 hours at r.t. After dilution with Et_2O (20 mL), a 10% solution of $NaHSO_3$ (15 mL) was added. After stirring for 10 minutes, the layers were separated, and the aqueous layer was extracted with Et_2O (25 mL). The organic extracts were combined and dried with $MgSO_4$. After filtration, the volatiles were removed under reduced pressure. The crude osmate ester was immediately dissolved in MeOH (10 mL). $NaBH_4$ (95 mg, 2.5 mmol) was added all at once. After 10 minutes, the reaction was diluted with Et_2O (30 mL) and quenched by a careful addition of a half-saturated solution of NH_4Cl (25 mL). The layers were separated. The aqueous layer was extracted with Et_2O (30 mL). The organic extracts were combined and dried with $MgSO_4$. After filtration, the volatiles were removed under reduced pressure. Chromatography (2:1 hexanes:EtOAc) afforded the diacetoxy diol **99** as a white solid (95 mg, 64%, 80% based on recovered **95**) and recovered **95** (20 mg). mp 240-243 ^oC; $[\alpha]_D^{23}$ =

+ 10.8 (c 0.635, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 4.95 (d, *J* = 6.6 Hz, 1H), 4.91 (d, *J* = 7.2 Hz, 1H), 3.41 (dd, *J* = 3.0, 11.4 Hz, 1H), 3.35 (dd, *J* = 4.2, 11.4 Hz, 1H), 3.06 (s, 1H), 2.35 (m, 1H), 2.24 (s, 1H), 2.14 (s, 3H), 2.12 (s, 3H), 2.06-1.89 (m, 3H), 1.84-1.53 (m, 9H), 1.46-1.39 (m, 6H), 1.35-1.23 (m, 3H), 1.21 (s, 3H), 1.19 (s, 3H), 1.16 (s, 3H), 1.14 (s, 3H), 1.06 (s, 3H), 0.91 (s, 3H), 0.97 (s, 3H); (150 MHz, CD_2Cl_2) δ 170.6, 170.4, 79.8, 79.6, 79.6, 78.6, 78.2, 77.7, 77.6, 77.5, 51.7, 44.9, 43.9, 41.7, 41.4, 40.5, 39.6, 36.8, 32.8, 31.3, 29.7, 29.3, 29.2, 27.3, 23.7, 23.4, 21.9, 21.7, 21.5, 21.4, 19.1, 19.0, 18.5, 13.8; IR (KBr) 3475, 2943, 1732, 1446, 1365, 1250, 1049 cm^{-1}; HRMS (ESI) [M+H$^+$] Calcd. for $C_{34}H_{57}O_8$ 593.40480, found 593.40549.

$Pb(OAc)_4$-promoted oxidative cleavage: completion of the proposed structure of *ent*-muzitone (*ent*-49)



ent-muzitone (***ent*-49**)

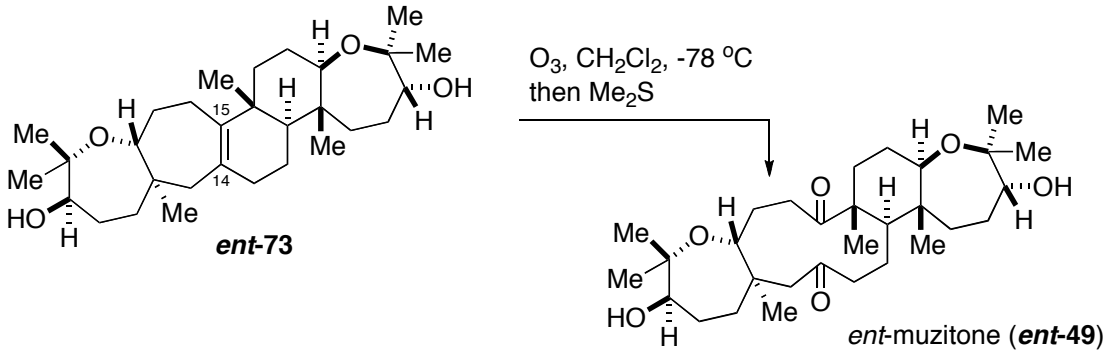
The diacetoxy diol **99** (95 mg, 0.16 mmol) was dissolved in MeOH:THF (2.5:1) (7.0 mL, 0.023 M). K_2CO_3 (310 mg, 2.2 mmol) was added all at once. The reaction flask was equipped with a reflux condenser, and the reaction was refluxed for 2.75 hours. After that time, the reaction was cooled to r.t. and diluted

with Et_2O (50 mL). The reaction mixture was then poured into H_2O (40 mL). The layers were separated, and the aqueous layer was extracted with Et_2O (30 mL). The organic extracts were combined and dried with $MgSO_4$. After filtration, the volatiles were removed under reduced pressure, which afforded tetraol **A** as a white solid (82 mg, quant.). mp 200-203 ^oC; $[\alpha]_D^{23}$ = + 43.3 (c 0.41, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 3.74 (m, 2H), 3.46 (m, 2H), 2.85 (s, 1H), 2.35 (s, 1H), 2.24 (m, 1H), 1.96 (m, 2H), 1.84 (m, 1H), 1.78-1.48 (m, 13H), 1.43-1.35 (m, 8H), 1.23 (s, 6H), 1.17 (s, 3H), 1.09 (s, 6H), 1.00 (s, 3H), 0.87 (s, 3H); (150 MHz, THF-d8) δ 79.7, 78.5, 78.4 (x2), 77.5, 77.2, 76.9 (x2), 52.9, 44.7, 44.4, 42.3, 42.1, 40.6, 39.9, 36.4, 32.5, 31.9, 30.6, 29.8, 29.7, 28.2, 27.1, 27.0, 22.5, 22.1, 19.7, 19.4, 19.2, 14.4; IR (KBr) 3433, 2931, 1446, 1381, 1161, 1057, 918, 733 cm^{-1}; HRMS (APCI) [$M+H^+-H_2O$] Calcd. for $C_{30}H_{51}O_5$ 491.37310, found 491.37356.

Tetraol **A** (77 mg, 0.15 mmol) was dissolved in benzene (0.0068 M, 22 mL). $Pb(OAc)_4$ (87 mg, 0.20 mmol) was added all at once. Upon addition of $Pb(OAc)_4$, a TLC of the reaction mixture was immediately performed (spotted 30 seconds after addition of $Pb(OAc)_4$) and indicated complete consumption of the starting material. Thus, after 3 minutes from the point of addition of $Pb(OAc)_4$, the reaction was diluted with Et_2O (25 mL) and poured into a saturated solution of $NaHCO_3$ (50 mL). Additional Et_2O (50 mL) was added to the mixture, and the layers were separated. The aqueous layer was extracted with Et_2O (35 mL). The organic extracts were combined, washed with brine (30 mL), then dried with $MgSO_4$. After filtration, the volatiles were removed under reduced pressure.

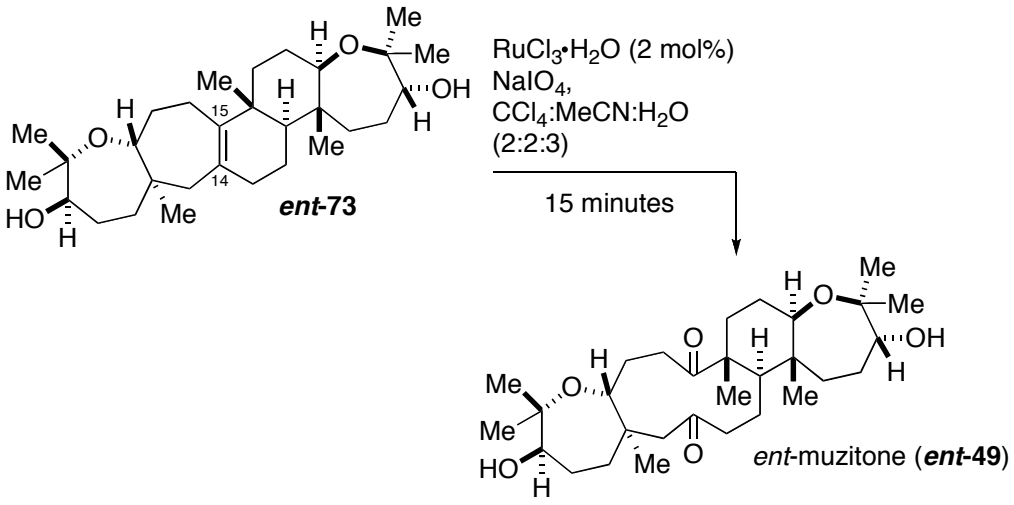
Chromatography (2:1→1:1 hexanes:EtOAc) gave the proposed structure of *ent*-muzitone (***ent*-49**) as a white solid (54 mg, 71%).

Ozonolysis of *ent*-73: total synthesis of the proposed structure of *ent*-muzitone (*ent*-49)



Ent*-73** (31 mg, 0.066 mmol) was dissolved in CH_2Cl_2 (0.001 M, 80 mL). The flask was capped with a teflon coated septum. After cooling to -78 °C, O_3 was bubbled through the solution for 5 minutes until a faint blue color was achieved in the reaction mixture. Me_2S (49 μL, 0.66 mmol) was added all at once. After stirring for 20 minutes, additional Me_2S (49 μL, 0.66 mmol) was added. The acetone/dry ice bath was removed, and the solution was allowed to 3 hours. The volatiles were removed under reduced pressure. Chromatography (2:1→1:1 hexanes:EtOAc) gave the proposed structure of *ent*-muzitone (ent*-49**) as a white solid (6.6 mg, 21%).

RuO_4-catalyzed cleavage of *ent*-73: completion of the proposed structure of *ent*-muzitone (*ent*-49)



Ent*-73** (11 mg, 0.023 mmol) was dissolved in CCl_4:MeCN:H_2O (2:2:3) (0.023 M, 1.0 mL) with vigorous stirring. $NaIO_4$ (20 mg, 0.092 mmol) was added all at once. Then $RuCl_3$•H_2O (2 mg, 0.001 mmol) was added and the solution became black in color. The reaction was stirred for 15 minutes. After dilution with Et_2O (2 mL), saturated $NaHCO_3$ (2 mL) was added. The layers were separated. The aqueous layer was extracted with Et_2O (2 x 2 mL). The organic extracts were combined and dried with $MgSO_4$. After filtration, the volatiles were removed under reduced pressure. Chromatography (2:1→1:1 hexanes:EtOAc) gave the proposed structure of *ent*-muzitone (ent*-49**) as a white solid (2.8 mg, 24%).

Characterization data for the proposed structure of *ent*-muzitone (*ent*-49)

mp 210 - 213 °C; $[\alpha]_D^{23}$ = + 22.9 (c 0.095, MeOH); ^{1}H NMR (600 MHz, C_6D_6) δ 4.24 (dd, *J* = 2.4, 6.0 Hz, 1H), 3.67 (dd, *J* = 4.8, 12.0 Hz, 1H), 3.52 (m , 1H), 3.36 (d, *J* = 6.0 Hz, 1H), 2.53 (dd, *J* = 8.4, 16.8 Hz, 1H), 2.43 (d, *J* = 17.4 Hz, 1H), 2.22 (m, 2H), 2.16 (dd, *J* = 9.6, 17.4 Hz, 1H), 2.04 (m, 2H), 1.92 (d, *J* = 18.0 Hz,

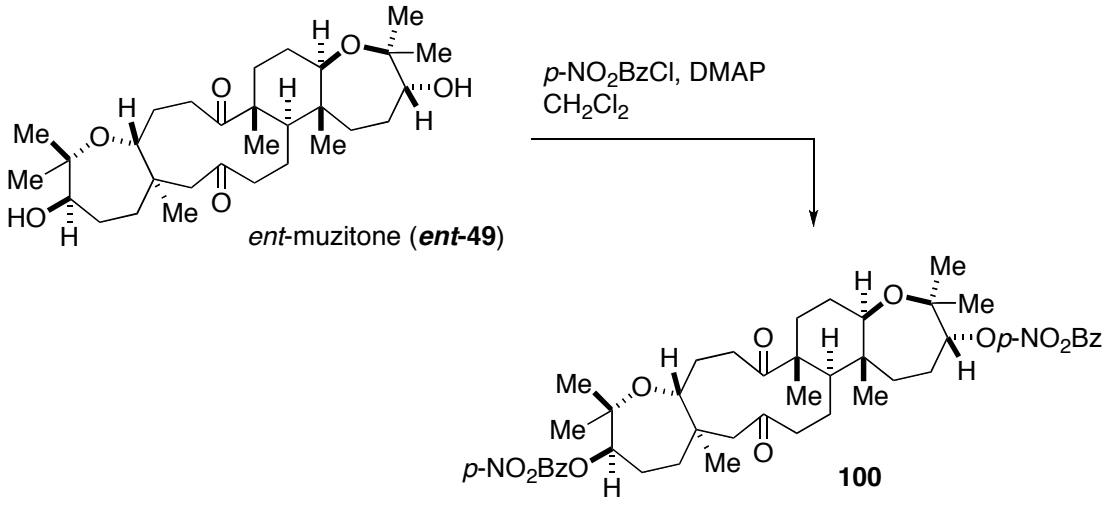
1H), 1.86 (m, 6H), 1.74 (at, *J* = 13.2 Hz, 1H), 1.68-1.54 (m, 5H), 1.43 (m, 5H), 1.49 (s, 3H), 1.22 (s, 3H), 1.18 (s, 3H), 1.16 (s, 3H), 1.13 (m, 2H), 1.05 (s, 3H), 1.01 (s, 3H), 0.98 (s, 3H); ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.03 (m, 1H), 3.78 (d, *J* = 6.6 Hz, 1H), 3.65 (m, 1H), 3.58 (dd, *J* = 3.6, 10.2 Hz, 1H), 2.67 (dd, *J* = 8.4, 18.0 Hz, 1H), 2.55 (d, *J* = 18.6 Hz, 1H), 2.36 (dd, *J* = 10.2, 18.0 Hz, 1H), 2.32 (dd, *J* = 8.4, 16.8 Hz, 1H), 2.23 (d, *J* = 18.0, 2H), 2.13 (dd, *J* = 10.8, 15.6 Hz, 2H), 2.06 (dd, *J* = 7.8, 15.6 Hz, 1H), 1.98 (m, 1H), 1.91 (at, *J* = 10.8 Hz, 2H), 1.80 (dd, *J* = 9.0, 15.6 Hz, 1H), 1.73 (m, 2H), 1.62 (m, 4H), 1.49 (m, 3H), 1.44 (m, 3H), 1.35 (s, 3H), 1.31 (s, 3H), 1.25 (s, 3H), 1.14 (s, 3H), 1.11 (s, 3H), 0.94 (s, 3H), 0.89 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 217.3 (quaternary), 212.4 (quaternary), 78.4 (quaternary), 78.2 (quaternary), 77.9 (CH), 76.9 (CH), 76.4 (CH), 76.2 (CH), 53.4 (CH_2), 51.9 (quaternary), 50.9 (CH), 43.8 (CH_2), 42.7 (quaternary), 40.1 (quaternary), 37.9 (CH_2), 35.9 (CH_2), 35.6 (CH_2), 33.8 (CH_2), 29.3 (CH_3), 29.1 (CH_3), 28.1 (CH_2), 26.7 (CH_2), 26.1 (CH_2), 25.9 (CH_2), 21.7 (CH_3), 21.6 (CH_3), 20.7 (CH_3), 19.7 (CH_2), 17.6 (CH_3), 13.7 (CH_3); ^{13}C NMR(150 MHz, C_6D_6) δ 216.3, 211.6, 78.6, 78.3, 78.1, 76.7, 76.9, 76.9, 53.7, 52.2, 51.2, 43.9, 43.2, 40.7, 38.3, 36.3, 35.7, 34.7, 29.9, 29.5, 29.0, 27.4, 26.9, 26.4, 22.3, 22.1, 21.3, 20.3, 17.9, 14.3; IR (KBr) 3450, 2926, 1703, 1452, 1061 cm^{-1}; HRMS (APCI) [$M+H^+$] Calcd. for $C_{30}H_{51}O_6$ 507.36802, found 507.36883.

Comparative characterization data for *ent*-muzitone (***ent*-49**)

Natural muzitone	**Synthetic *ent*-muzitone**
oil	white crystalline solid, mp 210-213 ^{o}C
$[\alpha]_D$ = - 14.2 (c 0.1, MeOH)	$[\alpha]_D$ = + 22.9 (c 0.095, MeOH)
IR (neat, cm $^{-1}$)	IR (neat, cm $^{-1}$)
3410 2950 1715 1450 -	3450 2926 1703 1452 1061
^{1}H NMR (500 MHz, C_6D_6, δ)	^{1}H NMR (600 MHz, C_6D_6, δ)
3.88 (dd, *J* = 5.3, 11.3 Hz) 3.56 (dd, *J* = 5.0, 11.5 Hz) 3.37 (d, *J* = 6.7 Hz) 3.28 (d, *J* = 7.2 Hz) 2.12 (m) 2.10 (m) 1.95 (m) 1.76 (m) 1.74 (m) 1.66 (m) 1.65 (m) 1.58 (m) 1.52 (m) 1.45 (m) 1.44 (m) 1.38 (m) 1.33 (m) 1.08 (m) 0.90 (m) 1.14 (s, 3H) 1.13 (s, 3H) 1.05 (s, 3H) 1.02 (s, 3H) 0.95 (s, 3H) 0.90 (s, 3H) 0.80 (s, 3H)	4.24 (dd, *J* = 2.4, 6.0 Hz) 3.67 (dd, *J* = 4.8, 12.0 Hz) 3.52 (m, 1H) 3.36 (d, *J* = 6.0 Hz) 2.53 (dd, *J* = 8.4, 16.8 Hz, 1H) 2.43 (d, *J* = 17.4 Hz, 1H) 2.22 (m, 2H) 2.16 (dd, *J* = 9.6, 17.4 Hz, 1H) 2.04 (m, 2H) 1.92 (d, *J* = 18.0 Hz, 1H) 1.86 (m, 6H) 1.74 (at, *J* = 13.2 Hz, 1H) 1.68-1.54 (m, 5H) 1.43 (m, 5H) 1.49 (s, 3H) 1.22 (s, 3H) 1.18 (s, 3H) 1.16 (s, 3H) 1.13 (m, 2H) 1.05 (s, 3H) 1.01 (s, 3H) 0.98 (s, 3H)

Natural	Synthetic	
^{13}C NMR (not reported, C_6D_6, δ)	^{13}C NMR (150 MHz, C_6D_6, δ)	^{13}C NMR (150 MHz, $CDCl_3$, δ)
218.0 (quaternary)	216.3	217.3 (quaternary)
207.0 (quaternary)	211.6	212.4 (quaternary)
77.0 (quaternary)	78.6	78.4 (quaternary)
76.9 (CH)	78.3	78.2 (quaternary)
76.5 (CH)	78.1	77.9 (CH)
76.1 (CH)	76.7	76.9 (CH)
76.0 (quaternary)	76.9	76.4 (CH)
73.0 (CH)	76.9	76.2 (CH)
54.1 (CH)	53.7	53.4 (CH_2)
53.2 (CH_2)	52.2	51.9 (quaternary)
48.0 (quaternary)	51.2	50.9 (CH)
41.3 (quaternary)	43.9	43.8 (CH_2)
41.2 (quaternary)	43.2	42.7 (quaternary)
38.9 (CH_2)	40.7	40.1 (quaternary)
35.7 (CH_2)	38.3	37.9 (CH_2)
33.9 (CH_2)	36.3	35.9 (CH_2)
30.6 (CH_2)	35.7	35.6 (CH_2)
30.2 (CH_2)	34.7	33.8 (CH_2)
28.9 (CH_2)	29.9	29.3 (CH_3)
28.8 (CH_3)	29.5	29.1 (CH_3)
27.6 (CH_3)	29.0	28.1 (CH_2)
25.5 (CH_2)	27.4	26.7 (CH_2)
25.3 (CH_2)	26.9	26.1 (CH_2)
21.9 (CH_3)	26.4	25.9 (CH_2)
21.6 (CH_3)	22.3	21.7 (CH_3)
21.2 (CH_2)	22.1	21.6 (CH_3)
18.1 (CH_2)	21.3	20.7 (CH_3)
17.3 (CH_3)	20.3	19.7 (CH_2)
15.7 (CH_3)	17.9	17.6 (CH_3)
13.8 (CH_3)	14.3	13.7 (CH_3)
HRMS (EI) [M^+] Calcd. for $C_{30}H_{50}O_6$ 506.3594, found 506.3586	HRMS (APCI) [$M+H^+$] Calcd. for $C_{30}H_{51}O_6$ 507.36802, found 507.36883	

Synthesis of di-*para*-nitrobenzoyl 100



***ent*-49** (23 mg, 0.045 mmol) was dissolved in CH_2Cl_2 (0.045 M, 1.0 mL). DMAP (17 mg, 0.14 mmol) was added and allowed to dissolve. Then *p*-NO_2BzCl (18 mg, 0.099 mmol) was added all at once. After 20 minutes, TLC indicated complete consumption of the starting material. After dilution with Et_2O (2 mL), the reaction was quenched by the addition of a saturated solution of $NaHCO_3$ (2 mL). After separation of layers, the aqueous layer was extracted with Et_2O (2 x 2 mL). The organic extracts were combined and dried with $MgSO_4$. After filtration, the volatiles were removed under reduced pressure. The crude mixture was dissolved in CH_2Cl_2 and passed through a short plug of silica gel in a Pasteur pipette to remove trace DMAP. The volatiles were then removed under reduced pressure giving **100** as a white crystalline solid (30 mg, 83%). mp 143-146 ^oC; $[\alpha]_D^{23}$ = + 32.6 (c 0.60, $CHCl_3$); ^1H NMR (600 MHz, C_6D_6) δ 8.64 (d, J = 9.0 Hz, 2H), 8.08 (d, J = 9.0 Hz, 2H), 7.98 (d, J = 9.0 Hz, 2H), 7.78 (d, J = 8.4 Hz, 2H), 5.34 (d, J = 7.2 Hz, 1H), 5.24 (d, J = 6.0 Hz, 1H), 4.44 (d, J = 7.2 Hz, 1H), 3.61 (dd, J = 4.2, 11.6 Hz, 1H), 2.71 (dd, J = 8.4, 18.6 Hz, 1H), 2.54 (d, J = 19.2 Hz,

1H), 2.51 (dd, J = 7.8, 15.0 Hz, 1H), 2.38 (at, J = 13.2, 1H), 2.11 (dd, J = 10.2, 16.8 Hz, 1H), 2.08 (m, 1H), 2.01-1.89 (m, 5H), 1.78 (m, 1H), 1.74 (d, J = 18.6 Hz, 1H), 1.63 (m, 2H), 1.53 (dd, J = 10.8, 15.0 Hz, 1H), 1.46 (m, 2H), 1.41 (s, 3H), 1.39-1.33 (m, 3H), 1.28 (s, 3H), 1.23 (dd, J = 9.0, 14.4 Hz, 1H), 1.16 (s, 3H), 1.14 (s, 3H), 1.11 (s, 3H), 0.97 (s, 3H), 0.90 (s, 3H), 0.73 (m, 1H); ^{13}C NMR (150 MHz, C_6D_6) δ 215.8, 211.1, 164.5, 164.1, 151.3, 151.2, 136.1, 135.7, 131.9 (x2), 130.7 (x2), 124.3 (x2), 123.9 (x2), 81.5, 80.9, 78.8, 78.1, 78.0, 77.9, 53.6, 52.5, 51.8, 43.9, 42.9, 40.2, 39.6, 37.6, 36.9, 33.7, 29.2, 29.0, 27.3, 27.2, 24.5, 23.8, 22.8, 22.1, 20.5, 19.6, 17.8, 14.0; IR (KBr) 2924, 2854, 1724, 1531, 1454, 1350, 1278, 1103 cm^{-1}; HRMS (APCI) [M+H$^+$] Calcd. for $C_{44}H_{57}O_{12}N_2$ 805.39060, found 805.39147.

Compound **100** was dissolved in C_6D_6. Upon evaporation of the solvent under reduced pressure, an oily residue was obtained to which was added Et_2O. Needle-like crystals began to form instantly. Hexane was then added to induce additional crystal growth overnight (16 hours). The resulting crystals were suitable for structural characterization by X-ray crystallography, resulting in the thermal ellipsoid diagram below:

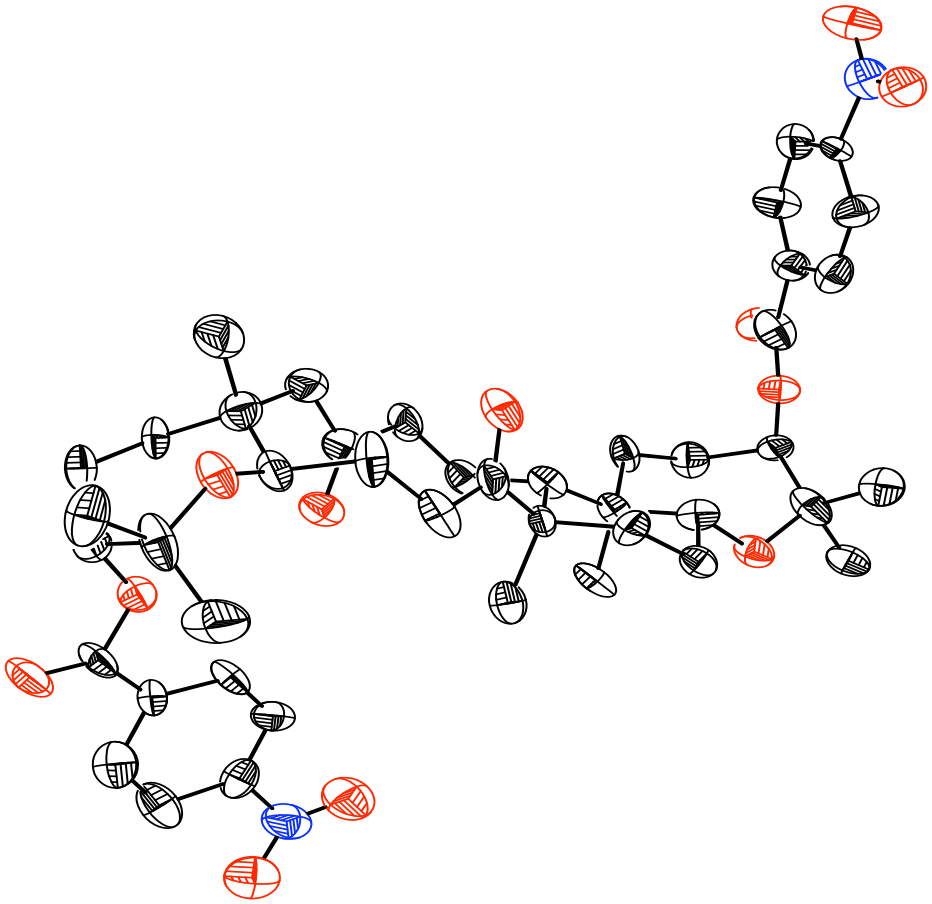


Table 14. Crystal data and structure refinement for **100**

Identification code	b103_7_189	
Empirical formula	C44 H56 N2 O12	
Formula weight	804.91	
Temperature	173(2) K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	P2(1)	
Unit cell dimensions	a = 16.924(14) Å	α= 90°.
	b = 7.236(6) Å	β= 98.926(10)°.
	c = 39.64(3) Å	γ = 90°.
Volume	4796(7) $Å^3$	
Z	4	
Density (calculated)	1.115 Mg/m^3	
Absorption coefficient	0.666 mm^{-1}	
F(000)	1720	
Crystal size	0.18 x 0.04 x 0.01 mm^3	
Theta range for data collection	8.29 to 66.42°.	
Index ranges	-19<=h<=16, -8<=k<=7, -43<=l<=45	
Reflections collected	27071	
Independent reflections	11876 [R(int) = 0.1748]	
Completeness to theta = 66.42°	83.6 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9934 and 0.8895	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	11876 / 1 / 1047	
Goodness-of-fit on F^2	0.989	
Final R indices [I>2sigma(I)]	R1 = 0.0905, wR2 = 0.1472	
R indices (all data)	R1 = 0.2107, wR2 = 0.1804	
Absolute structure parameter	0.4(4)	
Extinction coefficient	0.00022(10)	
Largest diff. peak and hole	0.287 and -0.253 $e.Å^{-3}$	

Table 15. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for **100** (b103_7_189). U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor

	x	y	z	U(eq)
C(1)	-2720(9)	1719(17)	-7201(4)	75(4)
C(2)	-1875(10)	1495(18)	-7087(4)	100(5)
C(3)	-1435(9)	566(18)	-7304(4)	93(5)
C(4)	-1832(8)	-45(17)	-7626(3)	64(4)
C(5)	-2634(8)	207(16)	-7712(3)	70(4)
C(6)	-3085(9)	1131(17)	-7509(3)	73(4)
C(7)	-1299(8)	-1001(18)	-7816(3)	71(4)
C(8)	-1274(8)	-2623(17)	-8355(3)	69(4)
C(9)	-1380(7)	-1613(16)	-8695(3)	78(4)
C(10)	-2197(6)	-776(16)	-8836(3)	72(4)
C(11)	-2881(8)	-2199(19)	-8960(4)	81(4)
C(12)	-2947(7)	-3550(18)	-8691(3)	74(4)
C(13)	-1656(8)	-4775(18)	-8379(5)	100(5)
C(14)	-1975(9)	-5490(20)	-8040(3)	131(7)
C(15)	-973(8)	-5879(17)	-8497(3)	109(5)
C(16)	-3709(7)	-4730(13)	-8747(3)	79(4)
C(17)	-4317(8)	-4306(16)	-8505(3)	83(5)
C(18)	-5045(8)	-3167(18)	-8659(4)	81(4)
C(19)	-5606(7)	-2203(16)	-8463(3)	56(3)
C(20)	-5987(7)	-498(13)	-8642(3)	57(3)
C(21)	-5370(7)	1009(14)	-8660(3)	65(4)
C(22)	-4840(7)	827(18)	-8926(3)	86(5)
C(23)	-4064(9)	-183(15)	-8804(4)	79(5)
C(24)	-3668(7)	-1169(19)	-9088(3)	81(4)
C(25)	-2686(8)	-3130(20)	-9291(3)	117(6)
C(26)	-5174(6)	-1957(14)	-8078(3)	75(4)
C(27)	-6235(8)	-3722(16)	-8439(3)	77(4)
C(28)	-6970(7)	-3028(15)	-8277(3)	70(4)
C(29)	-7345(7)	-1325(15)	-8491(3)	60(3)
C(30)	-6752(7)	237(14)	-8509(3)	59(3)
C(31)	-6603(6)	1279(15)	-8155(3)	80(4)

C(32)	-7176(6)	1551(15)	-8785(3)	65(4)
C(33)	-7996(7)	2283(16)	-8756(3)	78(4)
C(34)	-8689(8)	895(16)	-8821(3)	67(4)
C(35)	-8737(8)	-344(19)	-8530(4)	84(5)
C(36)	-9135(7)	-2283(16)	-8633(3)	83(4)
C(37)	-9226(7)	540(16)	-8255(3)	80(4)
C(38)	-8834(8)	628(18)	-9413(4)	85(5)
C(39)	-8873(7)	-605(17)	-9720(3)	69(4)
C(40)	-8910(7)	-2611(17)	-9659(3)	77(4)
C(41)	-8985(8)	-3811(17)	-9942(3)	81(4)
C(42)	-9055(6)	-3003(18)	-10252(3)	61(3)
C(43)	-9023(7)	-1106(19)	-10321(3)	85(4)
C(44)	-8960(7)	73(16)	-10041(3)	80(4)
C(1B)	-6911(10)	450(20)	-5689(4)	86(5)
C(2B)	-6326(9)	1350(20)	-5825(4)	89(5)
C(3B)	-6157(8)	721(19)	-6142(4)	86(4)
C(4B)	-6654(8)	-739(16)	-6309(3)	57(3)
C(5B)	-7249(8)	-1540(15)	-6175(3)	60(4)
C(6B)	-7399(8)	-900(17)	-5847(4)	77(4)
C(7B)	-6483(9)	-1267(18)	-6649(4)	80(5)
C(8B)	-6982(8)	-2961(15)	-7189(3)	80(4)
C(9B)	-7757(8)	-2341(15)	-7393(3)	78(4)
C(10B)	-8548(9)	-2618(16)	-7270(3)	80(4)
C(11B)	-8871(8)	-4512(14)	-7263(3)	65(4)
C(12B)	-8244(7)	-5744(15)	-7046(3)	57(3)
C(13B)	-6866(7)	-5098(16)	-7160(3)	63(3)
C(14B)	-6437(7)	-5747(16)	-6819(3)	86(4)
C(15B)	-6376(7)	-5572(15)	-7438(3)	73(4)
C(16B)	-9107(7)	-5299(15)	-7636(3)	85(4)
C(17B)	-8542(7)	-7697(14)	-6949(3)	71(4)
C(18B)	-8649(8)	-7805(16)	-6562(3)	76(4)
C(19B)	-9482(8)	-7653(16)	-6485(4)	69(4)
C(20B)	-9612(8)	-7328(16)	-6115(3)	65(4)
C(21B)	-10408(8)	-6292(13)	-6112(3)	61(4)
C(22B)	-10368(7)	-4206(15)	-6208(3)	65(3)
C(23B)	-10386(7)	-3819(18)	-6605(3)	82(4)

C(24B)	-9647(8)	-3896(18)	-6750(5)	96(6)
C(25B)	-9654(8)	-4374(16)	-7106(3)	79(4)
C(26B)	-8861(6)	-6312(15)	-5912(3)	68(4)
C(27B)	-9696(7)	-9310(15)	-5980(3)	70(4)
C(28B)	-9960(8)	-9415(17)	-5635(3)	86(4)
C(29B)	-10784(8)	-8503(15)	-5659(3)	61(3)
C(30B)	-10770(7)	-6446(13)	-5787(3)	59(4)
C(31B)	-11699(7)	-5944(15)	-5868(3)	67(4)
C(32B)	-12271(8)	-6291(15)	-5608(3)	77(4)
C(33B)	-12445(7)	-8272(17)	-5551(3)	69(4)
C(34B)	-11796(10)	-9245(16)	-5312(3)	77(4)
C(35B)	-11844(8)	-11317(14)	-5345(3)	98(5)
C(36B)	-11880(8)	-8800(18)	-4931(3)	98(5)
C(37B)	-13315(12)	-9600(20)	-6019(4)	99(6)
C(38B)	-13345(11)	-10689(18)	-6363(4)	80(4)
C(39B)	-12645(8)	-11521(17)	-6445(4)	79(4)
C(40B)	-12618(9)	-12462(18)	-6744(4)	93(5)
C(41B)	-13386(12)	-12425(18)	-6938(4)	95(6)
C(42B)	-14057(10)	-11700(20)	-6863(4)	108(6)
C(43B)	-14033(9)	-10840(20)	-6571(4)	98(5)
C(44B)	-10375(6)	-5260(13)	-5471(3)	74(4)
N(1)	-3223(11)	2690(19)	-6964(4)	106(6)
N(2)	-9215(7)	-4284(17)	-10559(3)	86(4)
N(1B)	-7110(9)	1175(16)	-5349(3)	93(5)
N(2B)	-13366(11)	-13432(17)	-7292(4)	116(6)
O(1)	-2842(7)	3238(13)	-6677(3)	118(4)
O(2)	-3899(8)	2826(16)	-7064(3)	124(5)
O(3)	-614(5)	-1362(14)	-7747(2)	102(3)
O(4)	-1703(5)	-1588(10)	-8123(2)	72(2)
O(5)	-9221(6)	-5877(15)	-10487(2)	106(3)
O(6)	-9305(5)	-3554(13)	-10841(2)	97(3)
O(7)	-8987(5)	2296(12)	-9455(2)	87(3)
O(8)	-8623(5)	-167(9)	-9110(2)	62(2)
O(9)	-7973(5)	-767(10)	-8310(2)	68(2)
O(10)	-5224(5)	-3257(10)	-8978(2)	83(3)
O(11)	-3743(5)	-160(10)	-8508(2)	75(3)

O(12)	-2266(5)	-4892(10)	-8672(2)	78(3)
O(1B)	-6676(6)	2266(18)	-5209(3)	148(5)
O(2B)	-7726(8)	605(15)	-5252(3)	124(5)
O(3B)	-5921(6)	-729(14)	-6777(2)	101(4)
O(4B)	-7072(5)	-2360(11)	-6818(2)	81(3)
O(5B)	-7607(5)	-6067(10)	-7247(2)	64(2)
O(6B)	-8987(5)	-3471(9)	-6560(2)	71(2)
O(7B)	-10064(5)	-7979(10)	-6701(2)	75(3)
O(8B)	-10999(6)	-8584(10)	-5327(2)	78(3)
O(9B)	-12557(6)	-9312(12)	-5863(2)	87(3)
O(10B)	-13883(7)	-9082(18)	-5912(3)	150(6)
O(11B)	-12725(9)	-14126(15)	-7343(3)	141(6)
O(12B)	-14019(8)	-13516(17)	-7474(3)	176(7)

Table 16. Bond lengths [Å] and angles [°] for **100** (b103_7_189)

C(1)-C(6)	1.349(16)
C(1)-C(2)	1.441(17)
C(1)-N(1)	1.534(19)
C(2)-C(3)	1.395(16)
C(2)-H(2A)	0.9500
C(3)-C(4)	1.418(16)
C(3)-H(3A)	0.9500
C(4)-C(5)	1.360(14)
C(4)-C(7)	1.441(15)
C(5)-C(6)	1.368(14)
C(5)-H(5A)	0.9500
C(6)-H(6A)	0.9500
C(7)-O(3)	1.177(13)
C(7)-O(4)	1.366(12)
C(8)-O(4)	1.463(12)
C(8)-C(9)	1.522(14)
C(8)-C(13)	1.683(17)
C(8)-H(8A)	1.0000
C(9)-C(10)	1.534(13)
C(9)-H(9A)	0.9900

C(9)-H(9B)	0.9900
C(10)-C(11)	1.570(15)
C(10)-H(10A)	0.9900
C(10)-H(10B)	0.9900
C(11)-C(12)	1.465(16)
C(11)-C(24)	1.541(15)
C(11)-C(25)	1.554(15)
C(12)-O(12)	1.499(12)
C(12)-C(16)	1.534(14)
C(12)-H(12A)	1.0000
C(13)-O(12)	1.434(14)
C(13)-C(15)	1.537(16)
C(13)-C(14)	1.608(19)
C(14)-H(14A)	0.9800
C(14)-H(14B)	0.9800
C(14)-H(14C)	0.9800
C(15)-H(15A)	0.9800
C(15)-H(15B)	0.9800
C(15)-H(15C)	0.9800
C(16)-C(17)	1.542(15)
C(16)-H(16A)	0.9900
C(16)-H(16B)	0.9900
C(17)-C(18)	1.527(15)
C(17)-H(17A)	0.9900
C(17)-H(17B)	0.9900
C(18)-O(10)	1.258(13)
C(18)-C(19)	1.491(15)
C(19)-C(20)	1.516(13)
C(19)-C(27)	1.543(14)
C(19)-C(26)	1.595(13)
C(20)-C(21)	1.519(13)
C(20)-C(30)	1.564(14)
C(20)-H(20A)	1.0000
C(21)-C(22)	1.492(14)
C(21)-H(21A)	0.9900
C(21)-H(21B)	0.9900

C(22)-C(23)	1.516(15)
C(22)-H(22A)	0.9900
C(22)-H(22B)	0.9900
C(23)-O(11)	1.215(12)
C(23)-C(24)	1.567(16)
C(24)-H(24A)	0.9900
C(24)-H(24B)	0.9900
C(25)-H(25A)	0.9800
C(25)-H(25B)	0.9800
C(25)-H(25C)	0.9800
C(26)-H(26A)	0.9800
C(26)-H(26B)	0.9800
C(26)-H(26C)	0.9800
C(27)-C(28)	1.569(14)
C(27)-H(27A)	0.9900
C(27)-H(27B)	0.9900
C(28)-C(29)	1.573(13)
C(28)-H(28A)	0.9900
C(28)-H(28B)	0.9900
C(29)-O(9)	1.431(12)
C(29)-C(30)	1.521(14)
C(29)-H(29A)	1.0000
C(30)-C(32)	1.539(12)
C(30)-C(31)	1.579(13)
C(31)-H(31A)	0.9800
C(31)-H(31B)	0.9800
C(31)-H(31C)	0.9800
C(32)-C(33)	1.507(14)
C(32)-H(32A)	0.9900
C(32)-H(32B)	0.9900
C(33)-C(34)	1.535(15)
C(33)-H(33A)	0.9900
C(33)-H(33B)	0.9900
C(34)-O(8)	1.397(12)
C(34)-C(35)	1.473(16)
C(34)-H(34A)	1.0000

C(35)-O(9)	1.474(12)
C(35)-C(36)	1.582(16)
C(35)-C(37)	1.602(15)
C(36)-H(36A)	0.9800
C(36)-H(36B)	0.9800
C(36)-H(36C)	0.9800
C(37)-H(37A)	0.9800
C(37)-H(37B)	0.9800
C(37)-H(37C)	0.9800
C(38)-O(7)	1.241(13)
C(38)-O(8)	1.331(14)
C(38)-C(39)	1.503(15)
C(39)-C(44)	1.348(14)
C(39)-C(40)	1.474(15)
C(40)-C(41)	1.409(14)
C(40)-H(40)	0.9500
C(41)-C(42)	1.347(14)
C(41)-H(41A)	0.9500
C(42)-C(43)	1.403(16)
C(42)-N(2)	1.522(15)
C(43)-C(44)	1.393(15)
C(43)-H(43A)	0.9500
C(44)-H(44A)	0.9500
C(1B)-C(6B)	1.365(16)
C(1B)-C(2B)	1.368(17)
C(1B)-N(1B)	1.532(18)
C(2B)-C(3B)	1.406(16)
C(2B)-H(2BA)	0.9500
C(3B)-C(4B)	1.446(16)
C(3B)-H(3BA)	0.9500
C(4B)-C(5B)	1.342(14)
C(4B)-C(7B)	1.471(18)
C(5B)-C(6B)	1.439(15)
C(5B)-H(5BA)	0.9500
C(6B)-H(6BA)	0.9500
C(7B)-O(3B)	1.208(15)

C(7B)-O(4B)	1.364(13)
C(8B)-C(9B)	1.499(14)
C(8B)-C(13B)	1.561(14)
C(8B)-O(4B)	1.563(13)
C(8B)-H(8BA)	1.0000
C(9B)-C(10B)	1.507(15)
C(9B)-H(9B1)	0.9900
C(9B)-H(9B2)	0.9900
C(10B)-C(11B)	1.478(14)
C(10B)-H(10C)	0.9900
C(10B)-H(10D)	0.9900
C(11B)-C(12B)	1.543(13)
C(11B)-C(25B)	1.551(15)
C(11B)-C(16B)	1.579(14)
C(12B)-O(5B)	1.455(12)
C(12B)-C(17B)	1.568(14)
C(12B)-H(12B)	1.0000
C(13B)-O(5B)	1.430(12)
C(13B)-C(14B)	1.505(13)
C(13B)-C(15B)	1.521(14)
C(14B)-H(14D)	0.9800
C(14B)-H(14E)	0.9800
C(14B)-H(14F)	0.9800
C(15B)-H(15D)	0.9800
C(15B)-H(15E)	0.9800
C(15B)-H(15F)	0.9800
C(16B)-H(16C)	0.9800
C(16B)-H(16D)	0.9800
C(16B)-H(16E)	0.9800
C(17B)-C(18B)	1.577(14)
C(17B)-H(17C)	0.9900
C(17B)-H(17D)	0.9900
C(18B)-C(19B)	1.491(15)
C(18B)-H(18A)	0.9900
C(18B)-H(18B)	0.9900
C(19B)-O(7B)	1.222(13)

C(19B)-C(20B)	1.536(16)
C(20B)-C(21B)	1.543(15)
C(20B)-C(27B)	1.545(15)
C(20B)-C(26B)	1.577(14)
C(21B)-C(30B)	1.515(15)
C(21B)-C(22B)	1.561(14)
C(21B)-H(21C)	1.0000
C(22B)-C(23B)	1.593(14)
C(22B)-H(22C)	0.9900
C(22B)-H(22D)	0.9900
C(23B)-C(24B)	1.455(16)
C(23B)-H(23A)	0.9900
C(23B)-H(23B)	0.9900
C(24B)-O(6B)	1.284(12)
C(24B)-C(25B)	1.453(17)
C(25B)-H(25D)	0.9900
C(25B)-H(25E)	0.9900
C(26B)-H(26D)	0.9800
C(26B)-H(26E)	0.9800
C(26B)-H(26F)	0.9800
C(27B)-C(28B)	1.506(14)
C(27B)-H(27C)	0.9900
C(27B)-H(27D)	0.9900
C(28B)-C(29B)	1.533(14)
C(28B)-H(28C)	0.9900
C(28B)-H(28D)	0.9900
C(29B)-O(8B)	1.422(11)
C(29B)-C(30B)	1.573(14)
C(29B)-H(29B)	1.0000
C(30B)-C(44B)	1.581(13)
C(30B)-C(31B)	1.597(14)
C(31B)-C(32B)	1.541(14)
C(31B)-H(31D)	0.9900
C(31B)-H(31E)	0.9900
C(32B)-C(33B)	1.488(15)
C(32B)-H(32C)	0.9900

C(32B)-H(32D)	0.9900
C(33B)-O(9B)	1.436(12)
C(33B)-C(34B)	1.509(15)
C(33B)-H(33C)	1.0000
C(34B)-O(8B)	1.441(14)
C(34B)-C(35B)	1.506(14)
C(34B)-C(36B)	1.572(15)
C(35B)-H(35A)	0.9800
C(35B)-H(35B)	0.9800
C(35B)-H(35C)	0.9800
C(36B)-H(36D)	0.9800
C(36B)-H(36E)	0.9800
C(36B)-H(36F)	0.9800
C(37B)-O(10B)	1.168(17)
C(37B)-O(9B)	1.350(18)
C(37B)-C(38B)	1.572(19)
C(38B)-C(43B)	1.322(16)
C(38B)-C(39B)	1.411(16)
C(39B)-C(40B)	1.373(16)
C(39B)-H(39A)	0.9500
C(40B)-C(41B)	1.403(18)
C(40B)-H(40C)	0.9500
C(41B)-C(42B)	1.327(19)
C(41B)-N(2B)	1.585(19)
C(42B)-C(43B)	1.311(17)
C(42B)-H(42A)	0.9500
C(43B)-H(43B)	0.9500
C(44B)-H(44B)	0.9800
C(44B)-H(44C)	0.9800
C(44B)-H(44D)	0.9800
N(1)-O(2)	1.157(15)
N(1)-O(1)	1.277(14)
N(2)-O(5)	1.188(12)
N(2)-O(6)	1.224(12)
N(1B)-O(1B)	1.159(13)
N(1B)-O(2B)	1.237(15)

N(2B)-O(12B)	1.224(16)
N(2B)-O(11B)	1.240(16)

C(6)-C(1)-C(2)	122.8(14)
C(6)-C(1)-N(1)	118.7(14)
C(2)-C(1)-N(1)	118.5(15)
C(3)-C(2)-C(1)	117.3(14)
C(3)-C(2)-H(2A)	121.4
C(1)-C(2)-H(2A)	121.4
C(2)-C(3)-C(4)	118.9(14)
C(2)-C(3)-H(3A)	120.6
C(4)-C(3)-H(3A)	120.6
C(5)-C(4)-C(3)	120.0(13)
C(5)-C(4)-C(7)	127.9(13)
C(3)-C(4)-C(7)	111.9(12)
C(4)-C(5)-C(6)	122.9(13)
C(4)-C(5)-H(5A)	118.5
C(6)-C(5)-H(5A)	118.5
C(1)-C(6)-C(5)	117.9(13)
C(1)-C(6)-H(6A)	121.0
C(5)-C(6)-H(6A)	121.0
O(3)-C(7)-O(4)	118.6(14)
O(3)-C(7)-C(4)	131.2(13)
O(4)-C(7)-C(4)	110.3(11)
O(4)-C(8)-C(9)	108.1(10)
O(4)-C(8)-C(13)	106.6(10)
C(9)-C(8)-C(13)	113.7(11)
O(4)-C(8)-H(8A)	109.4
C(9)-C(8)-H(8A)	109.4
C(13)-C(8)-H(8A)	109.4
C(8)-C(9)-C(10)	119.2(11)
C(8)-C(9)-H(9A)	107.5
C(10)-C(9)-H(9A)	107.5
C(8)-C(9)-H(9B)	107.5
C(10)-C(9)-H(9B)	107.5
H(9A)-C(9)-H(9B)	107.0

C(9)-C(10)-C(11)	115.8(10)
C(9)-C(10)-H(10A)	108.3
C(11)-C(10)-H(10A)	108.3
C(9)-C(10)-H(10B)	108.3
C(11)-C(10)-H(10B)	108.3
H(10A)-C(10)-H(10B)	107.4
C(12)-C(11)-C(24)	113.8(13)
C(12)-C(11)-C(25)	112.1(11)
C(24)-C(11)-C(25)	102.6(11)
C(12)-C(11)-C(10)	110.2(11)
C(24)-C(11)-C(10)	110.1(11)
C(25)-C(11)-C(10)	107.8(12)
C(11)-C(12)-O(12)	108.8(11)
C(11)-C(12)-C(16)	115.0(11)
O(12)-C(12)-C(16)	105.6(10)
C(11)-C(12)-H(12A)	109.1
O(12)-C(12)-H(12A)	109.1
C(16)-C(12)-H(12A)	109.1
O(12)-C(13)-C(15)	101.6(12)
O(12)-C(13)-C(14)	111.5(12)
C(15)-C(13)-C(14)	117.1(12)
O(12)-C(13)-C(8)	108.8(11)
C(15)-C(13)-C(8)	101.4(11)
C(14)-C(13)-C(8)	115.1(13)
C(13)-C(14)-H(14A)	109.5
C(13)-C(14)-H(14B)	109.5
H(14A)-C(14)-H(14B)	109.5
C(13)-C(14)-H(14C)	109.5
H(14A)-C(14)-H(14C)	109.5
H(14B)-C(14)-H(14C)	109.5
C(13)-C(15)-H(15A)	109.5
C(13)-C(15)-H(15B)	109.5
H(15A)-C(15)-H(15B)	109.5
C(13)-C(15)-H(15C)	109.5
H(15A)-C(15)-H(15C)	109.5
H(15B)-C(15)-H(15C)	109.5

C(12)-C(16)-C(17)	115.3(10)
C(12)-C(16)-H(16A)	108.5
C(17)-C(16)-H(16A)	108.5
C(12)-C(16)-H(16B)	108.5
C(17)-C(16)-H(16B)	108.5
H(16A)-C(16)-H(16B)	107.5
C(18)-C(17)-C(16)	115.8(12)
C(18)-C(17)-H(17A)	108.3
C(16)-C(17)-H(17A)	108.3
C(18)-C(17)-H(17B)	108.3
C(16)-C(17)-H(17B)	108.3
H(17A)-C(17)-H(17B)	107.4
O(10)-C(18)-C(19)	118.4(13)
O(10)-C(18)-C(17)	115.3(13)
C(19)-C(18)-C(17)	125.7(13)
C(18)-C(19)-C(20)	113.3(11)
C(18)-C(19)-C(27)	101.6(10)
C(20)-C(19)-C(27)	111.2(9)
C(18)-C(19)-C(26)	108.4(10)
C(20)-C(19)-C(26)	117.0(9)
C(27)-C(19)-C(26)	103.8(9)
C(19)-C(20)-C(21)	111.2(9)
C(19)-C(20)-C(30)	115.7(10)
C(21)-C(20)-C(30)	112.5(9)
C(19)-C(20)-H(20A)	105.5
C(21)-C(20)-H(20A)	105.5
C(30)-C(20)-H(20A)	105.5
C(22)-C(21)-C(20)	117.6(10)
C(22)-C(21)-H(21A)	107.9
C(20)-C(21)-H(21A)	107.9
C(22)-C(21)-H(21B)	107.9
C(20)-C(21)-H(21B)	107.9
H(21A)-C(21)-H(21B)	107.2
C(21)-C(22)-C(23)	113.8(11)
C(21)-C(22)-H(22A)	108.8
C(23)-C(22)-H(22A)	108.8

C(21)-C(22)-H(22B)	108.8
C(23)-C(22)-H(22B)	108.8
H(22A)-C(22)-H(22B)	107.7
O(11)-C(23)-C(22)	122.5(14)
O(11)-C(23)-C(24)	121.6(13)
C(22)-C(23)-C(24)	115.8(11)
C(11)-C(24)-C(23)	115.4(11)
C(11)-C(24)-H(24A)	108.4
C(23)-C(24)-H(24A)	108.4
C(11)-C(24)-H(24B)	108.4
C(23)-C(24)-H(24B)	108.4
H(24A)-C(24)-H(24B)	107.5
C(11)-C(25)-H(25A)	109.5
C(11)-C(25)-H(25B)	109.5
H(25A)-C(25)-H(25B)	109.5
C(11)-C(25)-H(25C)	109.5
H(25A)-C(25)-H(25C)	109.5
H(25B)-C(25)-H(25C)	109.5
C(19)-C(26)-H(26A)	109.5
C(19)-C(26)-H(26B)	109.5
H(26A)-C(26)-H(26B)	109.5
C(19)-C(26)-H(26C)	109.5
H(26A)-C(26)-H(26C)	109.5
H(26B)-C(26)-H(26C)	109.5
C(19)-C(27)-C(28)	113.3(10)
C(19)-C(27)-H(27A)	108.9
C(28)-C(27)-H(27A)	108.9
C(19)-C(27)-H(27B)	108.9
C(28)-C(27)-H(27B)	108.9
H(27A)-C(27)-H(27B)	107.7
C(27)-C(28)-C(29)	107.9(10)
C(27)-C(28)-H(28A)	110.1
C(29)-C(28)-H(28A)	110.1
C(27)-C(28)-H(28B)	110.1
C(29)-C(28)-H(28B)	110.1
H(28A)-C(28)-H(28B)	108.4

O(9)-C(29)-C(30)	111.2(9)
O(9)-C(29)-C(28)	102.6(9)
C(30)-C(29)-C(28)	113.2(9)
O(9)-C(29)-H(29A)	109.9
C(30)-C(29)-H(29A)	109.9
C(28)-C(29)-H(29A)	109.9
C(29)-C(30)-C(32)	104.8(8)
C(29)-C(30)-C(20)	110.4(9)
C(32)-C(30)-C(20)	106.9(9)
C(29)-C(30)-C(31)	109.2(10)
C(32)-C(30)-C(31)	109.2(9)
C(20)-C(30)-C(31)	115.8(9)
C(30)-C(31)-H(31A)	109.5
C(30)-C(31)-H(31B)	109.5
H(31A)-C(31)-H(31B)	109.5
C(30)-C(31)-H(31C)	109.5
H(31A)-C(31)-H(31C)	109.5
H(31B)-C(31)-H(31C)	109.5
C(33)-C(32)-C(30)	119.8(10)
C(33)-C(32)-H(32A)	107.4
C(30)-C(32)-H(32A)	107.4
C(33)-C(32)-H(32B)	107.4
C(30)-C(32)-H(32B)	107.4
H(32A)-C(32)-H(32B)	106.9
C(32)-C(33)-C(34)	116.5(10)
C(32)-C(33)-H(33A)	108.2
C(34)-C(33)-H(33A)	108.2
C(32)-C(33)-H(33B)	108.2
C(34)-C(33)-H(33B)	108.2
H(33A)-C(33)-H(33B)	107.3
O(8)-C(34)-C(35)	109.1(10)
O(8)-C(34)-C(33)	109.9(10)
C(35)-C(34)-C(33)	113.6(10)
O(8)-C(34)-H(34A)	108.0
C(35)-C(34)-H(34A)	108.0
C(33)-C(34)-H(34A)	108.0

C(34)-C(35)-O(9)	116.1(12)
C(34)-C(35)-C(36)	114.2(10)
O(9)-C(35)-C(36)	105.6(10)
C(34)-C(35)-C(37)	112.8(11)
O(9)-C(35)-C(37)	100.2(9)
C(36)-C(35)-C(37)	106.6(11)
C(35)-C(36)-H(36A)	109.5
C(35)-C(36)-H(36B)	109.5
H(36A)-C(36)-H(36B)	109.5
C(35)-C(36)-H(36C)	109.5
H(36A)-C(36)-H(36C)	109.5
H(36B)-C(36)-H(36C)	109.5
C(35)-C(37)-H(37A)	109.5
C(35)-C(37)-H(37B)	109.5
H(37A)-C(37)-H(37B)	109.5
C(35)-C(37)-H(37C)	109.5
H(37A)-C(37)-H(37C)	109.5
H(37B)-C(37)-H(37C)	109.5
O(7)-C(38)-O(8)	124.2(13)
O(7)-C(38)-C(39)	119.2(14)
O(8)-C(38)-C(39)	116.6(11)
C(44)-C(39)-C(40)	120.8(12)
C(44)-C(39)-C(38)	122.1(12)
C(40)-C(39)-C(38)	116.7(12)
C(41)-C(40)-C(39)	118.5(11)
C(41)-C(40)-H(40)	120.7
C(39)-C(40)-H(40)	120.7
C(42)-C(41)-C(40)	116.2(12)
C(42)-C(41)-H(41A)	121.9
C(40)-C(41)-H(41A)	121.9
C(41)-C(42)-C(43)	127.1(12)
C(41)-C(42)-N(2)	116.4(12)
C(43)-C(42)-N(2)	116.5(11)
C(44)-C(43)-C(42)	116.3(12)
C(44)-C(43)-H(43A)	121.9
C(42)-C(43)-H(43A)	121.9

C(39)-C(44)-C(43)	120.8(12)
C(39)-C(44)-H(44A)	119.6
C(43)-C(44)-H(44A)	119.6
C(6B)-C(1B)-C(2B)	125.7(15)
C(6B)-C(1B)-N(1B)	116.8(16)
C(2B)-C(1B)-N(1B)	117.0(14)
C(1B)-C(2B)-C(3B)	117.2(14)
C(1B)-C(2B)-H(2BA)	121.4
C(3B)-C(2B)-H(2BA)	121.4
C(2B)-C(3B)-C(4B)	117.6(14)
C(2B)-C(3B)-H(3BA)	121.2
C(4B)-C(3B)-H(3BA)	121.2
C(5B)-C(4B)-C(3B)	123.5(12)
C(5B)-C(4B)-C(7B)	121.2(12)
C(3B)-C(4B)-C(7B)	115.3(13)
C(4B)-C(5B)-C(6B)	117.9(12)
C(4B)-C(5B)-H(5BA)	121.0
C(6B)-C(5B)-H(5BA)	121.0
C(1B)-C(6B)-C(5B)	117.8(14)
C(1B)-C(6B)-H(6BA)	121.1
C(5B)-C(6B)-H(6BA)	121.1
O(3B)-C(7B)-O(4B)	123.0(16)
O(3B)-C(7B)-C(4B)	125.3(13)
O(4B)-C(7B)-C(4B)	111.6(14)
C(9B)-C(8B)-C(13B)	115.2(10)
C(9B)-C(8B)-O(4B)	102.7(10)
C(13B)-C(8B)-O(4B)	103.5(10)
C(9B)-C(8B)-H(8BA)	111.6
C(13B)-C(8B)-H(8BA)	111.6
O(4B)-C(8B)-H(8BA)	111.6
C(8B)-C(9B)-C(10B)	122.1(12)
C(8B)-C(9B)-H(9B1)	106.8
C(10B)-C(9B)-H(9B1)	106.8
C(8B)-C(9B)-H(9B2)	106.8
C(10B)-C(9B)-H(9B2)	106.8
H(9B1)-C(9B)-H(9B2)	106.6

C(11B)-C(10B)-C(9B)	118.7(12)
C(11B)-C(10B)-H(10C)	107.6
C(9B)-C(10B)-H(10C)	107.6
C(11B)-C(10B)-H(10D)	107.6
C(9B)-C(10B)-H(10D)	107.6
H(10C)-C(10B)-H(10D)	107.1
C(10B)-C(11B)-C(12B)	108.8(10)
C(10B)-C(11B)-C(25B)	106.9(11)
C(12B)-C(11B)-C(25B)	111.8(10)
C(10B)-C(11B)-C(16B)	110.8(10)
C(12B)-C(11B)-C(16B)	111.5(10)
C(25B)-C(11B)-C(16B)	106.9(10)
O(5B)-C(12B)-C(11B)	107.0(10)
O(5B)-C(12B)-C(17B)	106.4(9)
C(11B)-C(12B)-C(17B)	115.9(9)
O(5B)-C(12B)-H(12B)	109.1
C(11B)-C(12B)-H(12B)	109.1
C(17B)-C(12B)-H(12B)	109.1
O(5B)-C(13B)-C(14B)	110.3(10)
O(5B)-C(13B)-C(15B)	105.7(10)
C(14B)-C(13B)-C(15B)	109.9(10)
O(5B)-C(13B)-C(8B)	111.9(10)
C(14B)-C(13B)-C(8B)	114.4(10)
C(15B)-C(13B)-C(8B)	104.2(10)
C(13B)-C(14B)-H(14D)	109.5
C(13B)-C(14B)-H(14E)	109.5
H(14D)-C(14B)-H(14E)	109.5
C(13B)-C(14B)-H(14F)	109.5
H(14D)-C(14B)-H(14F)	109.5
H(14E)-C(14B)-H(14F)	109.5
C(13B)-C(15B)-H(15D)	109.5
C(13B)-C(15B)-H(15E)	109.5
H(15D)-C(15B)-H(15E)	109.5
C(13B)-C(15B)-H(15F)	109.5
H(15D)-C(15B)-H(15F)	109.5
H(15E)-C(15B)-H(15F)	109.5

C(11B)-C(16B)-H(16C)	109.5
C(11B)-C(16B)-H(16D)	109.5
H(16C)-C(16B)-H(16D)	109.5
C(11B)-C(16B)-H(16E)	109.5
H(16C)-C(16B)-H(16E)	109.5
H(16D)-C(16B)-H(16E)	109.5
C(12B)-C(17B)-C(18B)	111.9(10)
C(12B)-C(17B)-H(17C)	109.2
C(18B)-C(17B)-H(17C)	109.2
C(12B)-C(17B)-H(17D)	109.2
C(18B)-C(17B)-H(17D)	109.2
H(17C)-C(17B)-H(17D)	107.9
C(19B)-C(18B)-C(17B)	116.7(11)
C(19B)-C(18B)-H(18A)	108.1
C(17B)-C(18B)-H(18A)	108.1
C(19B)-C(18B)-H(18B)	108.1
C(17B)-C(18B)-H(18B)	108.1
H(18A)-C(18B)-H(18B)	107.3
O(7B)-C(19B)-C(18B)	121.9(14)
O(7B)-C(19B)-C(20B)	118.5(13)
C(18B)-C(19B)-C(20B)	119.1(12)
C(19B)-C(20B)-C(21B)	109.6(10)
C(19B)-C(20B)-C(27B)	102.9(10)
C(21B)-C(20B)-C(27B)	108.7(11)
C(19B)-C(20B)-C(26B)	109.6(11)
C(21B)-C(20B)-C(26B)	113.9(10)
C(27B)-C(20B)-C(26B)	111.5(9)
C(30B)-C(21B)-C(20B)	116.0(10)
C(30B)-C(21B)-C(22B)	108.6(9)
C(20B)-C(21B)-C(22B)	113.4(11)
C(30B)-C(21B)-H(21C)	106.0
C(20B)-C(21B)-H(21C)	106.0
C(22B)-C(21B)-H(21C)	106.0
C(21B)-C(22B)-C(23B)	114.6(10)
C(21B)-C(22B)-H(22C)	108.6
C(23B)-C(22B)-H(22C)	108.6

C(21B)-C(22B)-H(22D)	108.6
C(23B)-C(22B)-H(22D)	108.6
H(22C)-C(22B)-H(22D)	107.6
C(24B)-C(23B)-C(22B)	119.7(11)
C(24B)-C(23B)-H(23A)	107.4
C(22B)-C(23B)-H(23A)	107.4
C(24B)-C(23B)-H(23B)	107.4
C(22B)-C(23B)-H(23B)	107.4
H(23A)-C(23B)-H(23B)	106.9
O(6B)-C(24B)-C(25B)	120.2(15)
O(6B)-C(24B)-C(23B)	118.8(15)
C(25B)-C(24B)-C(23B)	120.9(12)
C(24B)-C(25B)-C(11B)	121.7(11)
C(24B)-C(25B)-H(25D)	106.9
C(11B)-C(25B)-H(25D)	106.9
C(24B)-C(25B)-H(25E)	106.9
C(11B)-C(25B)-H(25E)	106.9
H(25D)-C(25B)-H(25E)	106.7
C(20B)-C(26B)-H(26D)	109.5
C(20B)-C(26B)-H(26E)	109.5
H(26D)-C(26B)-H(26E)	109.5
C(20B)-C(26B)-H(26F)	109.5
H(26D)-C(26B)-H(26F)	109.5
H(26E)-C(26B)-H(26F)	109.5
C(28B)-C(27B)-C(20B)	114.7(10)
C(28B)-C(27B)-H(27C)	108.6
C(20B)-C(27B)-H(27C)	108.6
C(28B)-C(27B)-H(27D)	108.6
C(20B)-C(27B)-H(27D)	108.6
H(27C)-C(27B)-H(27D)	107.6
C(27B)-C(28B)-C(29B)	108.4(11)
C(27B)-C(28B)-H(28C)	110.0
C(29B)-C(28B)-H(28C)	110.0
C(27B)-C(28B)-H(28D)	110.0
C(29B)-C(28B)-H(28D)	110.0
H(28C)-C(28B)-H(28D)	108.4

O(8B)-C(29B)-C(28B)	106.5(10)
O(8B)-C(29B)-C(30B)	110.9(9)
C(28B)-C(29B)-C(30B)	111.7(10)
O(8B)-C(29B)-H(29B)	109.2
C(28B)-C(29B)-H(29B)	109.2
C(30B)-C(29B)-H(29B)	109.2
C(21B)-C(30B)-C(29B)	111.8(9)
C(21B)-C(30B)-C(44B)	117.3(10)
C(29B)-C(30B)-C(44B)	106.5(9)
C(21B)-C(30B)-C(31B)	109.1(10)
C(29B)-C(30B)-C(31B)	102.5(9)
C(44B)-C(30B)-C(31B)	108.6(9)
C(32B)-C(31B)-C(30B)	122.0(10)
C(32B)-C(31B)-H(31D)	106.8
C(30B)-C(31B)-H(31D)	106.8
C(32B)-C(31B)-H(31E)	106.8
C(30B)-C(31B)-H(31E)	106.8
H(31D)-C(31B)-H(31E)	106.7
C(33B)-C(32B)-C(31B)	114.7(10)
C(33B)-C(32B)-H(32C)	108.6
C(31B)-C(32B)-H(32C)	108.6
C(33B)-C(32B)-H(32D)	108.6
C(31B)-C(32B)-H(32D)	108.6
H(32C)-C(32B)-H(32D)	107.6
O(9B)-C(33B)-C(32B)	112.1(10)
O(9B)-C(33B)-C(34B)	106.4(10)
C(32B)-C(33B)-C(34B)	113.8(11)
O(9B)-C(33B)-H(33C)	108.1
C(32B)-C(33B)-H(33C)	108.1
C(34B)-C(33B)-H(33C)	108.1
O(8B)-C(34B)-C(35B)	111.5(12)
O(8B)-C(34B)-C(33B)	114.5(10)
C(35B)-C(34B)-C(33B)	112.7(12)
O(8B)-C(34B)-C(36B)	101.3(11)
C(35B)-C(34B)-C(36B)	105.9(11)
C(33B)-C(34B)-C(36B)	110.0(11)

C(34B)-C(35B)-H(35A)	109.5
C(34B)-C(35B)-H(35B)	109.5
H(35A)-C(35B)-H(35B)	109.5
C(34B)-C(35B)-H(35C)	109.5
H(35A)-C(35B)-H(35C)	109.5
H(35B)-C(35B)-H(35C)	109.5
C(34B)-C(36B)-H(36D)	109.5
C(34B)-C(36B)-H(36E)	109.5
H(36D)-C(36B)-H(36E)	109.5
C(34B)-C(36B)-H(36F)	109.5
H(36D)-C(36B)-H(36F)	109.5
H(36E)-C(36B)-H(36F)	109.5
O(10B)-C(37B)-O(9B)	124.2(18)
O(10B)-C(37B)-C(38B)	123.9(19)
O(9B)-C(37B)-C(38B)	111.9(15)
C(43B)-C(38B)-C(39B)	120.8(14)
C(43B)-C(38B)-C(37B)	119.2(17)
C(39B)-C(38B)-C(37B)	120.0(16)
C(40B)-C(39B)-C(38B)	123.5(13)
C(40B)-C(39B)-H(39A)	118.3
C(38B)-C(39B)-H(39A)	118.3
C(39B)-C(40B)-C(41B)	108.2(15)
C(39B)-C(40B)-H(40C)	125.9
C(41B)-C(40B)-H(40C)	125.9
C(42B)-C(41B)-C(40B)	129.6(15)
C(42B)-C(41B)-N(2B)	121.0(16)
C(40B)-C(41B)-N(2B)	109.4(17)
C(43B)-C(42B)-C(41B)	118.4(14)
C(43B)-C(42B)-H(42A)	120.8
C(41B)-C(42B)-H(42A)	120.8
C(42B)-C(43B)-C(38B)	119.5(16)
C(42B)-C(43B)-H(43B)	120.2
C(38B)-C(43B)-H(43B)	120.2
C(30B)-C(44B)-H(44B)	109.5
C(30B)-C(44B)-H(44C)	109.5
H(44B)-C(44B)-H(44C)	109.5

C(30B)-C(44B)-H(44D)	109.5
H(44B)-C(44B)-H(44D)	109.5
H(44C)-C(44B)-H(44D)	109.5
O(2)-N(1)-O(1)	128(2)
O(2)-N(1)-C(1)	116.2(16)
O(1)-N(1)-C(1)	115.9(15)
O(5)-N(2)-O(6)	129.4(14)
O(5)-N(2)-C(42)	113.9(12)
O(6)-N(2)-C(42)	116.7(11)
O(1B)-N(1B)-O(2B)	125.4(16)
O(1B)-N(1B)-C(1B)	116.4(16)
O(2B)-N(1B)-C(1B)	118.1(13)
O(12B)-N(2B)-O(11B)	128.0(18)
O(12B)-N(2B)-C(41B)	113.9(17)
O(11B)-N(2B)-C(41B)	118.0(16)
C(7)-O(4)-C(8)	119.2(10)
C(38)-O(8)-C(34)	117.3(9)
C(29)-O(9)-C(35)	114.4(9)
C(13)-O(12)-C(12)	116.9(9)
C(7B)-O(4B)-C(8B)	116.9(11)
C(13B)-O(5B)-C(12B)	119.0(9)
C(29B)-O(8B)-C(34B)	115.3(10)
C(37B)-O(9B)-C(33B)	117.5(12)

Symmetry transformations used to generate equivalent atoms:

Table 17. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for **100** (b103_7_189). 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}
C(1)	72(13)	65(8)	96(12)	-1(8)	37(10)	9(8)
C(2)	88(13)	77(10)	125(13)	-17(10)	-18(12)	-9(9)
C(3)	76(12)	79(9)	126(13)	-8(9)	23(11)	32(9)
C(4)	41(10)	77(9)	75(9)	0(7)	7(8)	-13(7)

C(5)	51(10)	78(9)	70(9)	-4(8)	-25(8)	6(7)
C(6)	91(13)	73(9)	53(8)	4(7)	2(8)	-7(8)
C(7)	47(10)	89(9)	68(10)	-3(8)	-22(8)	13(8)
C(8)	59(10)	84(9)	65(9)	-18(7)	15(7)	0(7)
C(9)	39(9)	82(9)	114(12)	0(9)	14(8)	3(7)
C(10)	40(9)	78(8)	98(10)	-3(8)	13(8)	-21(7)
C(11)	66(11)	95(10)	84(11)	9(9)	17(9)	18(9)
C(12)	45(9)	87(9)	89(10)	-30(8)	2(8)	-4(8)
C(13)	43(10)	83(10)	166(16)	-29(11)	-8(11)	12(8)
C(14)	128(16)	167(16)	96(12)	23(12)	13(11)	84(13)
C(15)	70(11)	84(10)	182(15)	15(10)	48(11)	26(9)
C(16)	36(9)	40(7)	162(13)	-25(8)	25(9)	13(6)
C(17)	60(10)	52(7)	125(12)	-5(8)	-26(9)	0(7)
C(18)	57(11)	87(10)	97(11)	-25(9)	9(9)	-34(8)
C(19)	34(8)	82(8)	55(8)	-26(7)	10(6)	-14(6)
C(20)	62(9)	39(6)	64(8)	-2(6)	-8(7)	9(6)
C(21)	66(10)	43(7)	79(9)	1(6)	-9(8)	-8(6)
C(22)	44(10)	118(11)	89(10)	32(9)	-14(8)	1(8)
C(23)	111(13)	43(7)	77(10)	18(7)	-9(10)	-39(8)
C(24)	71(11)	105(10)	65(9)	5(8)	6(8)	9(9)
C(25)	101(13)	145(14)	105(12)	-45(11)	12(10)	-15(11)
C(26)	50(9)	67(8)	107(11)	0(8)	5(8)	12(6)
C(27)	78(11)	89(10)	70(9)	7(7)	24(8)	-25(9)
C(28)	74(10)	74(8)	59(8)	-23(7)	6(7)	-22(7)
C(29)	71(10)	51(7)	59(8)	-2(6)	14(7)	24(7)
C(30)	52(9)	47(7)	70(8)	-4(6)	-10(7)	-1(6)
C(31)	73(10)	76(8)	75(9)	-12(7)	-35(7)	-1(7)
C(32)	40(8)	60(7)	88(9)	17(7)	-10(7)	-4(6)
C(33)	70(10)	70(8)	89(10)	15(7)	4(8)	4(8)
C(34)	80(11)	74(8)	43(7)	23(7)	0(7)	-17(7)
C(35)	61(11)	92(10)	92(11)	-42(9)	-10(9)	10(8)
C(36)	76(11)	84(9)	92(10)	-7(8)	21(8)	27(8)
C(37)	78(10)	88(9)	67(9)	7(7)	-15(8)	16(8)
C(38)	86(12)	53(8)	110(13)	-17(9)	-1(9)	2(8)
C(39)	76(11)	69(8)	60(9)	-5(7)	8(7)	-10(7)
C(40)	54(10)	87(9)	90(11)	30(9)	15(8)	15(8)

C(41)	109(13)	76(9)	65(9)	-6(8)	30(9)	-5(9)
C(42)	48(9)	96(10)	36(7)	-14(7)	-2(6)	-16(7)
C(43)	81(12)	95(10)	79(10)	4(9)	10(8)	-23(9)
C(44)	116(13)	56(8)	63(9)	0(7)	-2(9)	2(8)
C(1B)	107(15)	72(10)	68(10)	2(9)	-19(10)	-4(9)
C(2B)	87(13)	85(10)	85(12)	11(9)	-17(10)	3(9)
C(3B)	74(11)	99(10)	80(10)	-14(9)	-1(9)	-13(8)
C(4B)	63(11)	53(7)	57(8)	-11(7)	20(8)	19(7)
C(5B)	72(11)	58(7)	49(8)	6(6)	3(7)	14(7)
C(6B)	71(11)	65(8)	99(11)	44(8)	23(9)	7(8)
C(7B)	46(11)	66(9)	120(15)	7(9)	-13(10)	-2(8)
C(8B)	89(12)	57(8)	89(11)	-3(7)	1(9)	8(7)
C(9B)	102(12)	53(7)	75(10)	-11(7)	-2(9)	20(8)
C(10B)	87(12)	75(9)	78(10)	24(7)	16(8)	1(9)
C(11B)	74(10)	46(7)	72(9)	-7(6)	1(8)	-18(7)
C(12B)	45(9)	66(8)	58(8)	-6(7)	0(7)	-4(7)
C(13B)	50(9)	70(8)	68(9)	12(7)	11(7)	-6(7)
C(14B)	82(11)	77(8)	93(10)	7(8)	-4(8)	14(8)
C(15B)	59(10)	74(8)	96(10)	-13(7)	40(8)	8(7)
C(16B)	106(12)	71(8)	71(9)	5(7)	-8(8)	17(8)
C(17B)	72(10)	54(7)	85(10)	11(7)	7(8)	20(7)
C(18B)	77(11)	58(8)	93(11)	11(7)	13(9)	15(7)
C(19B)	38(10)	53(7)	125(14)	18(8)	36(9)	-5(7)
C(20B)	59(10)	67(8)	71(9)	7(7)	16(8)	11(7)
C(21B)	71(10)	44(6)	65(9)	-9(6)	-2(8)	-1(7)
C(22B)	59(9)	77(8)	57(8)	7(7)	8(7)	3(7)
C(23B)	13(8)	106(11)	128(12)	20(9)	9(8)	4(7)
C(24B)	25(9)	86(10)	166(17)	-15(10)	-19(10)	-3(7)
C(25B)	85(12)	77(9)	68(9)	-38(8)	-11(8)	-23(8)
C(26B)	49(9)	79(8)	70(8)	18(7)	-9(7)	27(7)
C(27B)	46(9)	73(8)	94(10)	-4(8)	14(8)	2(7)
C(28B)	80(12)	75(8)	112(12)	12(8)	46(10)	24(8)
C(29B)	72(10)	70(8)	46(7)	-1(6)	23(7)	8(7)
C(30B)	52(9)	32(6)	87(10)	-3(6)	-6(8)	5(6)
C(31B)	67(10)	59(7)	68(9)	7(7)	-12(7)	-1(7)
C(32B)	90(12)	47(7)	93(10)	-12(7)	11(9)	-2(7)

C(33B)	63(10)	94(10)	47(8)	1(7)	-1(7)	17(8)
C(34B)	97(13)	49(7)	93(11)	-4(7)	33(10)	-1(8)
C(35B)	162(15)	47(7)	82(10)	-3(7)	10(9)	25(8)
C(36B)	113(13)	107(11)	87(10)	33(9)	53(9)	40(9)
C(37B)	103(19)	107(13)	99(13)	-6(10)	50(12)	-47(12)
C(38B)	83(13)	64(9)	100(12)	-1(8)	37(10)	-22(9)
C(39B)	65(11)	60(8)	108(13)	24(8)	-6(9)	0(8)
C(40B)	109(14)	97(11)	68(10)	-19(9)	-2(10)	0(10)
C(41B)	144(18)	58(9)	70(11)	-8(8)	-25(12)	10(10)
C(42B)	82(13)	100(12)	126(15)	-40(11)	-32(11)	25(10)
C(43B)	77(12)	93(11)	112(14)	-18(10)	-27(11)	19(9)
C(44B)	79(10)	45(6)	96(10)	-1(7)	6(8)	-5(7)
N(1)	134(16)	92(9)	83(12)	8(8)	-8(12)	-37(11)
N(2)	77(9)	81(8)	97(10)	4(9)	5(8)	11(8)
N(1B)	132(15)	62(8)	76(10)	-25(7)	-12(9)	13(8)
N(2B)	171(19)	57(8)	112(13)	29(9)	-5(13)	14(10)
O(1)	149(11)	84(7)	118(9)	7(7)	15(8)	7(7)
O(2)	134(11)	121(9)	113(10)	-28(7)	6(9)	-9(9)
O(3)	71(7)	141(8)	80(7)	-16(6)	-28(6)	10(6)
O(4)	62(7)	83(6)	70(6)	8(5)	5(5)	-5(5)
O(5)	123(9)	104(7)	94(8)	-15(7)	29(6)	-31(8)
O(6)	114(8)	98(7)	71(6)	-18(6)	-12(6)	44(6)
O(7)	96(8)	88(6)	77(6)	10(5)	17(5)	14(6)
O(8)	81(7)	53(4)	51(5)	-4(4)	7(5)	10(4)
O(9)	55(6)	79(5)	65(5)	-6(5)	-3(5)	19(5)
O(10)	64(6)	73(5)	105(7)	-27(6)	-6(5)	0(5)
O(11)	92(7)	57(5)	68(6)	13(5)	-10(5)	-9(5)
O(12)	52(6)	63(5)	111(7)	-13(5)	-10(5)	11(4)
O(1B)	109(9)	208(12)	121(9)	-80(9)	-3(7)	-49(9)
O(2B)	180(14)	91(8)	108(9)	-8(6)	45(9)	-29(8)
O(3B)	96(9)	99(7)	104(8)	-21(6)	3(7)	-18(7)
O(4B)	65(7)	83(6)	98(7)	-16(5)	18(5)	-16(5)
O(5B)	66(7)	64(5)	64(5)	-9(4)	14(5)	-5(5)
O(6B)	78(7)	63(5)	73(6)	9(4)	17(5)	7(5)
O(7B)	75(7)	58(5)	88(7)	-18(5)	-1(5)	-15(5)
O(8B)	89(8)	60(5)	84(7)	-5(5)	8(6)	11(5)

O(9B)	74(7)	96(6)	84(7)	-18(5)	-10(6)	-4(5)
O(10B)	91(11)	183(12)	186(12)	-83(10)	53(9)	-26(9)
O(11B)	220(17)	91(8)	116(9)	18(7)	36(10)	48(9)
O(12B)	179(12)	167(11)	140(11)	-30(9)	-108(9)	52(9)

Table 18. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^{2}x 10^3) for **100** (b103_7_189)

	x	y	z	U(eq)
H(2A)	-1627	1961	-6872	120
H(3A)	-880	347	-7237	111
H(5A)	-2893	-280	-7924	84
H(6A)	-3638	1351	-7582	88
H(8A)	-693	-2676	-8258	83
H(9A)	-1239	-2488	-8869	94
H(9B)	-981	-602	-8676	94
H(10A)	-2132	42	-9030	86
H(10B)	-2370	5	-8656	86
H(12A)	-2912	-2891	-8467	89
H(14A)	-2171	-6756	-8075	196
H(14B)	-2410	-4684	-7992	196
H(14C)	-1537	-5452	-7847	196
H(15A)	-1125	-7184	-8522	164
H(15B)	-488	-5759	-8328	164
H(15C)	-870	-5397	-8717	164
H(16A)	-3553	-6047	-8720	94
H(16B)	-3976	-4556	-8985	94
H(17A)	-4509	-5493	-8424	100
H(17B)	-4036	-3639	-8304	100
H(20A)	-6170	-884	-8883	68
H(21A)	-5657	2201	-8697	78
H(21B)	-5025	1081	-8435	78
H(22A)	-4715	2077	-9004	104
H(22B)	-5134	157	-9125	104

H(24A)	-4056	-2064	-9207	97
H(24B)	-3562	-230	-9257	97
H(25A)	-3104	-4029	-9373	176
H(25B)	-2169	-3760	-9242	176
H(25C)	-2663	-2183	-9466	176
H(26A)	-4746	-1038	-8070	113
H(26B)	-4946	-3142	-7992	113
H(26C)	-5565	-1539	-7936	113
H(27A)	-5977	-4756	-8300	93
H(27B)	-6428	-4203	-8670	93
H(28A)	-6796	-2658	-8036	84
H(28B)	-7372	-4027	-8281	84
H(29A)	-7575	-1734	-8727	72
H(31A)	-7116	1687	-8096	120
H(31B)	-6260	2355	-8172	120
H(31C)	-6341	440	-7978	120
H(32A)	-6821	2630	-8795	78
H(32B)	-7214	905	-9007	78
H(33A)	-8115	3316	-8920	93
H(33B)	-7981	2800	-8524	93
H(34A)	-9200	1609	-8868	80
H(36A)	-8838	-2904	-8794	125
H(36B)	-9691	-2098	-8741	125
H(36C)	-9124	-3047	-8428	125
H(37A)	-8991	1738	-8179	120
H(37B)	-9200	-290	-8058	120
H(37C)	-9785	715	-8358	120
H(40)	-8882	-3083	-9434	92
H(41A)	-8987	-5117	-9917	98
H(43A)	-9042	-651	-10547	102
H(44A)	-8980	1373	-10075	96
H(2BA)	-6046	2369	-5711	107
H(3BA)	-5732	1234	-6242	103
H(5BA)	-7561	-2499	-6293	72
H(6BA)	-7824	-1398	-5745	92
H(8BA)	-6513	-2346	-7268	95

H(9B1)	-7799	-2952	-7619	94
H(9B2)	-7705	-1000	-7434	94
H(10C)	-8497	-2110	-7036	96
H(10D)	-8951	-1857	-7416	96
H(12B)	-8020	-5069	-6832	69
H(14D)	-6401	-7098	-6819	129
H(14E)	-6734	-5347	-6638	129
H(14F)	-5898	-5217	-6778	129
H(15D)	-6281	-6908	-7439	110
H(15E)	-5862	-4922	-7395	110
H(15F)	-6668	-5193	-7661	110
H(16C)	-8625	-5425	-7743	128
H(16D)	-9481	-4449	-7771	128
H(16E)	-9361	-6511	-7626	128
H(17C)	-8152	-8646	-6996	85
H(17D)	-9060	-7971	-7094	85
H(18A)	-8423	-8995	-6469	91
H(18B)	-8326	-6807	-6437	91
H(21C)	-10803	-6870	-6296	73
H(22C)	-9870	-3672	-6081	77
H(22D)	-10824	-3556	-6133	77
H(23A)	-10762	-4716	-6732	99
H(23B)	-10619	-2575	-6654	99
H(25D)	-9999	-3456	-7244	95
H(25E)	-9928	-5582	-7144	95
H(26D)	-8379	-7039	-5926	102
H(26E)	-8930	-6177	-5672	102
H(26F)	-8808	-5087	-6011	102
H(27C)	-10087	-9991	-6146	84
H(27D)	-9174	-9945	-5967	84
H(28C)	-9570	-8766	-5463	103
H(28D)	-9990	-10721	-5564	103
H(29B)	-11181	-9224	-5821	73
H(31D)	-11734	-4612	-5925	80
H(31E)	-11921	-6620	-6079	80
H(32C)	-12036	-5735	-5387	93

H(32D)	-12782	-5646	-5688	93
H(33C)	-12951	-8343	-5450	83
H(35A)	-11779	-11678	-5577	147
H(35B)	-12366	-11741	-5298	147
H(35C)	-11419	-11882	-5181	147
H(36D)	-11895	-7457	-4900	147
H(36E)	-11422	-9316	-4779	147
H(36F)	-12375	-9348	-4878	147
H(39A)	-12167	-11425	-6286	95
H(40C)	-12160	-13039	-6808	111
H(42A)	-14544	-11802	-7018	130
H(43B)	-14506	-10323	-6509	118
H(44B)	-9807	-5576	-5414	111
H(44C)	-10644	-5525	-5274	111
H(44D)	-10430	-3943	-5527	111

Table 19. Torsion angles [°] for **100** (b103_7_189)

C(6)-C(1)-C(2)-C(3)	-2(2)
N(1)-C(1)-C(2)-C(3)	178.4(12)
C(1)-C(2)-C(3)-C(4)	2.1(19)
C(2)-C(3)-C(4)-C(5)	-2.8(19)
C(2)-C(3)-C(4)-C(7)	-179.1(12)
C(3)-C(4)-C(5)-C(6)	4(2)
C(7)-C(4)-C(5)-C(6)	179.4(12)
C(2)-C(1)-C(6)-C(5)	3(2)
N(1)-C(1)-C(6)-C(5)	-177.6(11)
C(4)-C(5)-C(6)-C(1)	-3.9(19)
C(5)-C(4)-C(7)-O(3)	-174.8(15)
C(3)-C(4)-C(7)-O(3)	1(2)
C(5)-C(4)-C(7)-O(4)	3.3(19)
C(3)-C(4)-C(7)-O(4)	179.3(10)
O(4)-C(8)-C(9)-C(10)	-40.3(14)
C(13)-C(8)-C(9)-C(10)	77.9(14)
C(8)-C(9)-C(10)-C(11)	-70.0(15)
C(9)-C(10)-C(11)-C(12)	52.7(16)

C(9)-C(10)-C(11)-C(24)	178.9(11)
C(9)-C(10)-C(11)-C(25)	-69.9(15)
C(24)-C(11)-C(12)-O(12)	160.6(10)
C(25)-C(11)-C(12)-O(12)	44.7(14)
C(10)-C(11)-C(12)-O(12)	-75.3(12)
C(24)-C(11)-C(12)-C(16)	42.4(15)
C(25)-C(11)-C(12)-C(16)	-73.5(15)
C(10)-C(11)-C(12)-C(16)	166.5(10)
O(4)-C(8)-C(13)-O(12)	95.3(14)
C(9)-C(8)-C(13)-O(12)	-23.8(16)
O(4)-C(8)-C(13)-C(15)	-158.1(10)
C(9)-C(8)-C(13)-C(15)	82.9(13)
O(4)-C(8)-C(13)-C(14)	-30.7(14)
C(9)-C(8)-C(13)-C(14)	-149.7(11)
C(11)-C(12)-C(16)-C(17)	-109.4(13)
O(12)-C(12)-C(16)-C(17)	130.6(10)
C(12)-C(16)-C(17)-C(18)	102.7(12)
C(16)-C(17)-C(18)-O(10)	24.5(15)
C(16)-C(17)-C(18)-C(19)	-164.4(11)
O(10)-C(18)-C(19)-C(20)	-38.1(15)
C(17)-C(18)-C(19)-C(20)	151.1(11)
O(10)-C(18)-C(19)-C(27)	81.2(14)
C(17)-C(18)-C(19)-C(27)	-89.6(13)
O(10)-C(18)-C(19)-C(26)	-169.8(10)
C(17)-C(18)-C(19)-C(26)	19.4(16)
C(18)-C(19)-C(20)-C(21)	-67.3(12)
C(27)-C(19)-C(20)-C(21)	179.0(10)
C(26)-C(19)-C(20)-C(21)	60.0(14)
C(18)-C(19)-C(20)-C(30)	162.8(9)
C(27)-C(19)-C(20)-C(30)	49.1(12)
C(26)-C(19)-C(20)-C(30)	-69.9(12)
C(19)-C(20)-C(21)-C(22)	78.3(13)
C(30)-C(20)-C(21)-C(22)	-150.1(10)
C(20)-C(21)-C(22)-C(23)	-91.4(12)
C(21)-C(22)-C(23)-O(11)	-29.2(16)
C(21)-C(22)-C(23)-C(24)	154.3(11)

C(12)-C(11)-C(24)-C(23)	54.4(15)
C(25)-C(11)-C(24)-C(23)	175.7(10)
C(10)-C(11)-C(24)-C(23)	-69.7(15)
O(11)-C(23)-C(24)-C(11)	3.8(17)
C(22)-C(23)-C(24)-C(11)	-179.7(11)
C(18)-C(19)-C(27)-C(28)	-173.6(10)
C(20)-C(19)-C(27)-C(28)	-52.7(13)
C(26)-C(19)-C(27)-C(28)	74.0(11)
C(19)-C(27)-C(28)-C(29)	55.9(12)
C(27)-C(28)-C(29)-O(9)	-177.1(9)
C(27)-C(28)-C(29)-C(30)	-57.2(12)
O(9)-C(29)-C(30)-C(32)	-76.5(11)
C(28)-C(29)-C(30)-C(32)	168.7(9)
O(9)-C(29)-C(30)-C(20)	168.7(8)
C(28)-C(29)-C(30)-C(20)	53.9(12)
O(9)-C(29)-C(30)-C(31)	40.4(11)
C(28)-C(29)-C(30)-C(31)	-74.5(12)
C(19)-C(20)-C(30)-C(29)	-49.9(12)
C(21)-C(20)-C(30)-C(29)	-179.3(9)
C(19)-C(20)-C(30)-C(32)	-163.4(9)
C(21)-C(20)-C(30)-C(32)	67.3(11)
C(19)-C(20)-C(30)-C(31)	74.7(12)
C(21)-C(20)-C(30)-C(31)	-54.6(12)
C(29)-C(30)-C(32)-C(33)	54.1(13)
C(20)-C(30)-C(32)-C(33)	171.4(9)
C(31)-C(30)-C(32)-C(33)	-62.7(13)
C(30)-C(32)-C(33)-C(34)	-71.4(14)
C(32)-C(33)-C(34)-O(8)	-44.6(13)
C(32)-C(33)-C(34)-C(35)	78.0(15)
O(8)-C(34)-C(35)-O(9)	93.5(12)
C(33)-C(34)-C(35)-O(9)	-29.5(16)
O(8)-C(34)-C(35)-C(36)	-29.7(15)
C(33)-C(34)-C(35)-C(36)	-152.7(10)
O(8)-C(34)-C(35)-C(37)	-151.6(10)
C(33)-C(34)-C(35)-C(37)	85.4(14)
O(7)-C(38)-C(39)-C(44)	9(2)

O(8)-C(38)-C(39)-C(44)	-169.8(12)
O(7)-C(38)-C(39)-C(40)	-163.5(12)
O(8)-C(38)-C(39)-C(40)	17.4(17)
C(44)-C(39)-C(40)-C(41)	4(2)
C(38)-C(39)-C(40)-C(41)	177.0(12)
C(39)-C(40)-C(41)-C(42)	-2.9(19)
C(40)-C(41)-C(42)-C(43)	3(2)
C(40)-C(41)-C(42)-N(2)	-174.5(11)
C(41)-C(42)-C(43)-C(44)	-4(2)
N(2)-C(42)-C(43)-C(44)	173.5(11)
C(40)-C(39)-C(44)-C(43)	-5(2)
C(38)-C(39)-C(44)-C(43)	-177.8(12)
C(42)-C(43)-C(44)-C(39)	5.1(19)
C(6B)-C(1B)-C(2B)-C(3B)	-7(2)
N(1B)-C(1B)-C(2B)-C(3B)	-178.2(11)
C(1B)-C(2B)-C(3B)-C(4B)	4.6(19)
C(2B)-C(3B)-C(4B)-C(5B)	-1.6(19)
C(2B)-C(3B)-C(4B)-C(7B)	176.4(11)
C(3B)-C(4B)-C(5B)-C(6B)	0.2(18)
C(7B)-C(4B)-C(5B)-C(6B)	-177.7(10)
C(2B)-C(1B)-C(6B)-C(5B)	5(2)
N(1B)-C(1B)-C(6B)-C(5B)	176.9(10)
C(4B)-C(5B)-C(6B)-C(1B)	-1.9(17)
C(5B)-C(4B)-C(7B)-O(3B)	-173.6(14)
C(3B)-C(4B)-C(7B)-O(3B)	8(2)
C(5B)-C(4B)-C(7B)-O(4B)	10.6(17)
C(3B)-C(4B)-C(7B)-O(4B)	-167.4(10)
C(13B)-C(8B)-C(9B)-C(10B)	68.9(16)
O(4B)-C(8B)-C(9B)-C(10B)	-42.9(14)
C(8B)-C(9B)-C(10B)-C(11B)	-70.5(15)
C(9B)-C(10B)-C(11B)-C(12B)	55.8(15)
C(9B)-C(10B)-C(11B)-C(25B)	176.7(10)
C(9B)-C(10B)-C(11B)-C(16B)	-67.1(14)
C(10B)-C(11B)-C(12B)-O(5B)	-73.0(12)
C(25B)-C(11B)-C(12B)-O(5B)	169.2(8)
C(16B)-C(11B)-C(12B)-O(5B)	49.5(12)

C(10B)-C(11B)-C(12B)-C(17B)	168.5(11)
C(25B)-C(11B)-C(12B)-C(17B)	50.7(13)
C(16B)-C(11B)-C(12B)-C(17B)	-69.0(14)
C(9B)-C(8B)-C(13B)-O(5B)	-17.1(17)
O(4B)-C(8B)-C(13B)-O(5B)	94.2(11)
C(9B)-C(8B)-C(13B)-C(14B)	-143.4(12)
O(4B)-C(8B)-C(13B)-C(14B)	-32.1(14)
C(9B)-C(8B)-C(13B)-C(15B)	96.7(14)
O(4B)-C(8B)-C(13B)-C(15B)	-152.1(9)
O(5B)-C(12B)-C(17B)-C(18B)	134.7(9)
C(11B)-C(12B)-C(17B)-C(18B)	-106.5(12)
C(12B)-C(17B)-C(18B)-C(19B)	101.6(12)
C(17B)-C(18B)-C(19B)-O(7B)	21.3(16)
C(17B)-C(18B)-C(19B)-C(20B)	-166.9(10)
O(7B)-C(19B)-C(20B)-C(21B)	-35.8(15)
C(18B)-C(19B)-C(20B)-C(21B)	152.2(10)
O(7B)-C(19B)-C(20B)-C(27B)	79.8(13)
C(18B)-C(19B)-C(20B)-C(27B)	-92.3(13)
O(7B)-C(19B)-C(20B)-C(26B)	-161.5(10)
C(18B)-C(19B)-C(20B)-C(26B)	26.4(14)
C(19B)-C(20B)-C(21B)-C(30B)	159.3(10)
C(27B)-C(20B)-C(21B)-C(30B)	47.5(13)
C(26B)-C(20B)-C(21B)-C(30B)	-77.5(13)
C(19B)-C(20B)-C(21B)-C(22B)	-74.1(12)
C(27B)-C(20B)-C(21B)-C(22B)	174.1(9)
C(26B)-C(20B)-C(21B)-C(22B)	49.1(13)
C(30B)-C(21B)-C(22B)-C(23B)	-153.6(10)
C(20B)-C(21B)-C(22B)-C(23B)	75.9(13)
C(21B)-C(22B)-C(23B)-C(24B)	-84.6(15)
C(22B)-C(23B)-C(24B)-O(6B)	-30.1(18)
C(22B)-C(23B)-C(24B)-C(25B)	152.3(12)
O(6B)-C(24B)-C(25B)-C(11B)	4.0(19)
C(23B)-C(24B)-C(25B)-C(11B)	-178.4(11)
C(10B)-C(11B)-C(25B)-C(24B)	-68.3(15)
C(12B)-C(11B)-C(25B)-C(24B)	50.6(15)
C(16B)-C(11B)-C(25B)-C(24B)	172.9(11)

C(19B)-C(20B)-C(27B)-C(28B)	-170.9(11)
C(21B)-C(20B)-C(27B)-C(28B)	-54.6(14)
C(26B)-C(20B)-C(27B)-C(28B)	71.8(14)
C(20B)-C(27B)-C(28B)-C(29B)	60.7(14)
C(27B)-C(28B)-C(29B)-O(8B)	-178.4(10)
C(27B)-C(28B)-C(29B)-C(30B)	-57.2(13)
C(20B)-C(21B)-C(30B)-C(29B)	-47.5(13)
C(22B)-C(21B)-C(30B)-C(29B)	-176.4(9)
C(20B)-C(21B)-C(30B)-C(44B)	75.9(12)
C(22B)-C(21B)-C(30B)-C(44B)	-53.1(13)
C(20B)-C(21B)-C(30B)-C(31B)	-160.2(9)
C(22B)-C(21B)-C(30B)-C(31B)	70.8(11)
O(8B)-C(29B)-C(30B)-C(21B)	170.2(10)
C(28B)-C(29B)-C(30B)-C(21B)	51.6(13)
O(8B)-C(29B)-C(30B)-C(44B)	40.9(13)
C(28B)-C(29B)-C(30B)-C(44B)	-77.7(12)
O(8B)-C(29B)-C(30B)-C(31B)	-73.0(12)
C(28B)-C(29B)-C(30B)-C(31B)	168.4(10)
C(21B)-C(30B)-C(31B)-C(32B)	169.2(9)
C(29B)-C(30B)-C(31B)-C(32B)	50.5(13)
C(44B)-C(30B)-C(31B)-C(32B)	-61.8(12)
C(30B)-C(31B)-C(32B)-C(33B)	-70.3(14)
C(31B)-C(32B)-C(33B)-O(9B)	-40.8(15)
C(31B)-C(32B)-C(33B)-C(34B)	80.0(14)
O(9B)-C(33B)-C(34B)-O(8B)	91.3(12)
C(32B)-C(33B)-C(34B)-O(8B)	-32.6(16)
O(9B)-C(33B)-C(34B)-C(35B)	-37.5(16)
C(32B)-C(33B)-C(34B)-C(35B)	-161.4(12)
O(9B)-C(33B)-C(34B)-C(36B)	-155.4(10)
C(32B)-C(33B)-C(34B)-C(36B)	80.7(15)
O(10B)-C(37B)-C(38B)-C(43B)	9(3)
O(9B)-C(37B)-C(38B)-C(43B)	-169.9(13)
O(10B)-C(37B)-C(38B)-C(39B)	-169.6(18)
O(9B)-C(37B)-C(38B)-C(39B)	11.1(18)
C(43B)-C(38B)-C(39B)-C(40B)	2(2)
C(37B)-C(38B)-C(39B)-C(40B)	-178.6(12)

C(38B)-C(39B)-C(40B)-C(41B)	0.0(19)
C(39B)-C(40B)-C(41B)-C(42B)	-2(2)
C(39B)-C(40B)-C(41B)-N(2B)	177.7(10)
C(40B)-C(41B)-C(42B)-C(43B)	2(3)
N(2B)-C(41B)-C(42B)-C(43B)	-178.1(13)
C(41B)-C(42B)-C(43B)-C(38B)	1(2)
C(39B)-C(38B)-C(43B)-C(42B)	-3(2)
C(37B)-C(38B)-C(43B)-C(42B)	178.0(14)
C(6)-C(1)-N(1)-O(2)	1(2)
C(2)-C(1)-N(1)-O(2)	-179.3(15)
C(6)-C(1)-N(1)-O(1)	-179.1(12)
C(2)-C(1)-N(1)-O(1)	0.2(19)
C(41)-C(42)-N(2)-O(5)	-3.5(18)
C(43)-C(42)-N(2)-O(5)	178.5(13)
C(41)-C(42)-N(2)-O(6)	177.7(12)
C(43)-C(42)-N(2)-O(6)	-0.3(17)
C(6B)-C(1B)-N(1B)-O(1B)	177.1(12)
C(2B)-C(1B)-N(1B)-O(1B)	-10.7(19)
C(6B)-C(1B)-N(1B)-O(2B)	-5.0(19)
C(2B)-C(1B)-N(1B)-O(2B)	167.2(14)
C(42B)-C(41B)-N(2B)-O(12B)	-2(2)
C(40B)-C(41B)-N(2B)-O(12B)	177.9(13)
C(42B)-C(41B)-N(2B)-O(11B)	-178.1(16)
C(40B)-C(41B)-N(2B)-O(11B)	2(2)
O(3)-C(7)-O(4)-C(8)	-0.6(19)
C(4)-C(7)-O(4)-C(8)	-179.0(10)
C(9)-C(8)-O(4)-C(7)	-123.8(11)
C(13)-C(8)-O(4)-C(7)	113.5(11)
O(7)-C(38)-O(8)-C(34)	9(2)
C(39)-C(38)-O(8)-C(34)	-171.5(10)
C(35)-C(34)-O(8)-C(38)	158.4(11)
C(33)-C(34)-O(8)-C(38)	-76.4(13)
C(30)-C(29)-O(9)-C(35)	103.1(11)
C(28)-C(29)-O(9)-C(35)	-135.6(9)
C(34)-C(35)-O(9)-C(29)	-48.8(14)
C(36)-C(35)-O(9)-C(29)	78.8(13)

C(37)-C(35)-O(9)-C(29)	-170.6(9)
C(15)-C(13)-O(12)-C(12)	-163.7(10)
C(14)-C(13)-O(12)-C(12)	70.8(14)
C(8)-C(13)-O(12)-C(12)	-57.3(16)
C(11)-C(12)-O(12)-C(13)	109.4(13)
C(16)-C(12)-O(12)-C(13)	-126.6(12)
O(3B)-C(7B)-O(4B)-C(8B)	1.8(19)
C(4B)-C(7B)-O(4B)-C(8B)	177.7(9)
C(9B)-C(8B)-O(4B)-C(7B)	-125.4(11)
C(13B)-C(8B)-O(4B)-C(7B)	114.4(11)
C(14B)-C(13B)-O(5B)-C(12B)	67.5(12)
C(15B)-C(13B)-O(5B)-C(12B)	-173.8(8)
C(8B)-C(13B)-O(5B)-C(12B)	-61.0(13)
C(11B)-C(12B)-O(5B)-C(13B)	104.6(10)
C(17B)-C(12B)-O(5B)-C(13B)	-130.9(9)
C(28B)-C(29B)-O(8B)-C(34B)	-132.1(10)
C(30B)-C(29B)-O(8B)-C(34B)	106.2(11)
C(35B)-C(34B)-O(8B)-C(29B)	77.9(13)
C(33B)-C(34B)-O(8B)-C(29B)	-51.5(14)
C(36B)-C(34B)-O(8B)-C(29B)	-169.8(8)
O(10B)-C(37B)-O(9B)-C(33B)	-1(3)
C(38B)-C(37B)-O(9B)-C(33B)	177.9(10)
C(32B)-C(33B)-O(9B)-C(37B)	-97.0(14)
C(34B)-C(33B)-O(9B)-C(37B)	138.0(13)

Symmetry transformations used to generate equivalent atoms:

Appendix 1

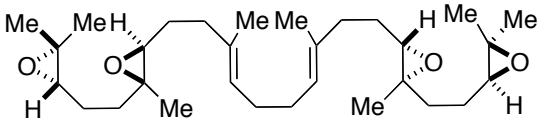
Appendix 1

Total synthesis of (3*R*,6*R*,7*R*,18*R*,19*R*,22*R*)-squalene tetraepoxide

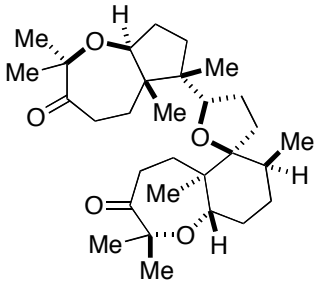
A1.1. Introduction and Background

Squalene tetraepoxide (**1**) has been implicated as the biogenetic precursor to a number of oxaterpenoid natural products, some of which have interesting biological activities.[71] Representative members of this family of polycyclic ether terpenoid natural products, such as yardenone (**2**), sodwanone M (**3**), and raspacionin (**4**) are all characterized by highly compact and complex molecular architectures. We were intrigued by the great structural diversity of these compounds and thus became interested in developing a synthetic route to squalene tetraepoxide (**1**) to test the biomimetic cyclization behavior to gain potential access to the core structures of these complex natural products.

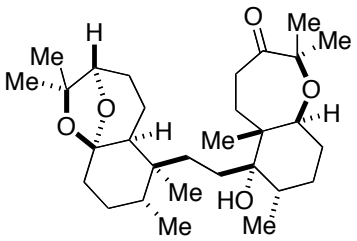
Figure 1. Representative squalene tetraepoxide-derived polycyclic ether natural products



(3*S*,6*S*,7*S*,18*S*,19*S*,22*S*)-squalene tetraepoxide (**1**)

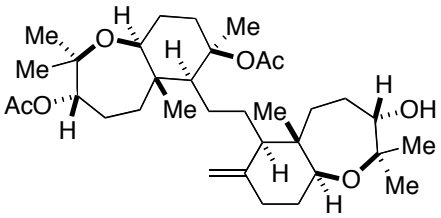


yardenone (**2**)



sodwanone M (**3**)

1 mg/mL cytotoxicity
P-388 murine leukemia cells

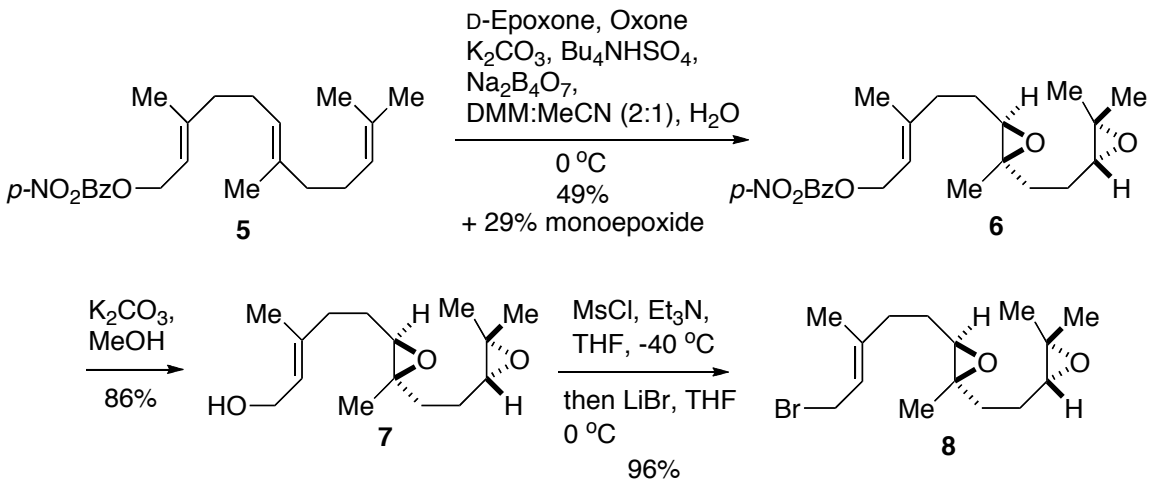


raspacionin (**4**)

A1.2. Results and Discussion

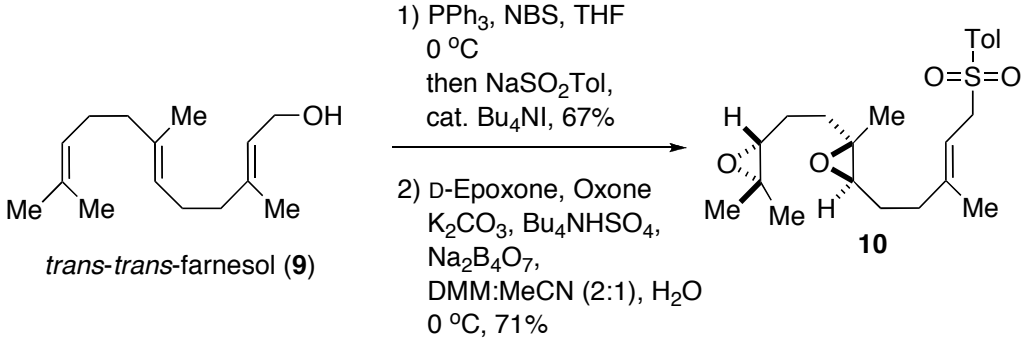
In 2008, Dr. Rongbiao Tong of the McDonald laboratory developed a clever asymmetric synthesis of (3*R*,6*R*,7*R*,18*R*,19*R*,22*R*)-squalene tetraepoxide (***ent*-1**) (121 mg), which was later optimized by Matthew Boone to give provide more material (944 mg). The synthesis commenced by the construction of the two key coupling fragments, diepoxy allylic bromide **8** and diepoxy allylic sulfone **10**. The synthesis of diepoxy allylic bromide **8** began with the double Shi epoxidation of *trans*-*trans*-farnesol *para*-nitrobenzoate **5** to the corresponding diepoxy *para*-nitrobenzoate **6**, followed by de-esterification to the diepoxy allylic alcohol **7**. Diepoxy allylic alcohol **7** was smoothly converted to the diepoxy allylic bromide **8** using a mesylation/bromination sequence.

Scheme 1. Double Shi epoxidation to diepoxy allylic bromide 8



Diepoxy allylic sulfone was made in three steps from *trans-trans*-farnesol (**9**). The synthesis began with conversion of t*rans-trans*-farnesol (**9**) to 1-farnesyl *para*-tolyl sulfone. A double Shi epoxidation of 1-farnesyl *para*-tolyl sulfone gave the diepoxy allylic sulfone **10**.

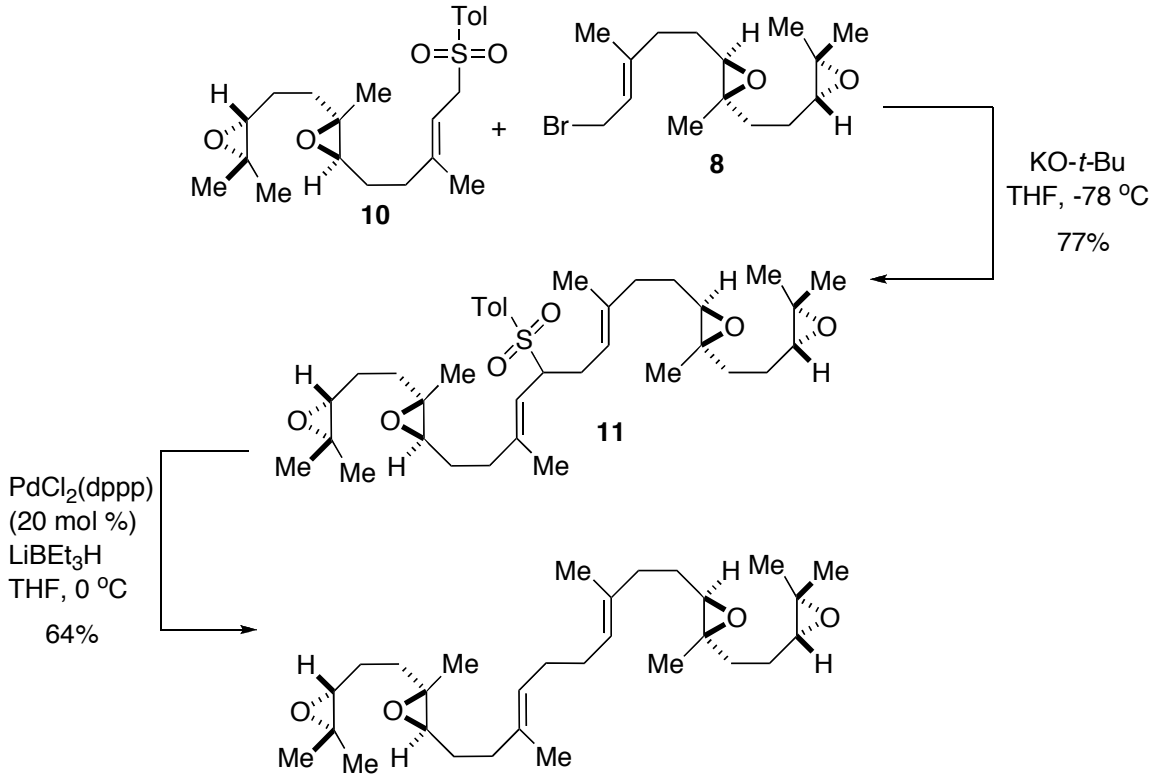
Scheme 2. Double Shi epoxidation to diepoxy allylic sulfone 10



The fragment coupling of diepoxy allylic bromide **8** and diepoxy allylic sulfone **10** was a relatively straightforward transformation to the tetraepoxy allylic sulfone **11**. This coupling simply required mixing the two coupling partners in THF followed by addition of KO-*t*-Bu at -78 °C. The tetraepoxy allylic sulfone **11** was then converted to squalene tetraepoxide (***ent*-1**) via a reductive sulfonylation

using $PdCl_2$(dppp) and lithium triethylborohydride ($LiEt_3BH$). The multiple epoxides of **11** were compatible with the use of the hydride reagent, so long as the reaction was closely monitored to prevent over-reduction (Scheme 3).

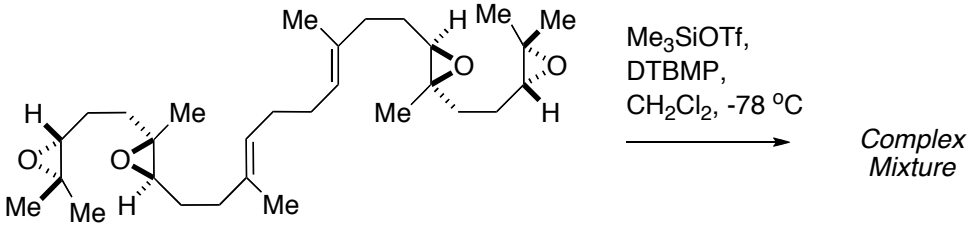
Scheme 3. Anionic fragment coupling and reductive desulfonylation to (3*R*,6*R*,7*R*,18*R*,19*R*,22*R*)-squalene tetraepoxide (*ent*-1)



(3*R*,6*R*,7*R*,18*R*,19*R*,22*R*)-squalene tetraepoxide (***ent*-1**)

Having synthetic squalene tetraepoxide (***ent*-1**), we turned our attention to the biomimetic cyclization of the material. Thus, we subjected **e*nt*-1** to trimethylsilyltriflate (Me_3SiOTf) activation in the presence of 2,6-di-*tert*-butyl-4-methylpyridine (DTBMP). Unfortunately, a complex mixture of products was observed in the reaction mixture (≥ 20 products by TLC visualization) (Scheme 4).

Scheme 4. Attempted biomimetic polycyclization of (3*R*,6*R*,7*R*,18*R*,19*R*, 22*R*)-squalene tetraepoxide (*ent*-1)



(3*R*,6*R*,7*R*,18*R*,19*R*,22*R*)-squalene tetraepoxide (***ent*-1**)

In conclusion, we have successfully demonstrated the synthesis of (3R,6R, 7R,18R,19R,22R)-squalene tetraepoxide (***ent*-1**) using an anionic coupling of the diepoxy allylic bromide **8** and diepoxy allylic sulfone **10**. This synthesis was a remarkable example that highlights the importance of the Shi epoxidation for the generation of such complex epoxy-ene frameworks. While we do not currently understand the abiological cyclization behavior of our synthetic squalene tetraepoxide (***ent*-1**), further optimization and synthetic investigation of cyclization conditions could open new possibilities of accessing highly complex natural product core structures from a readily available precursor.

A1.3. Experimental Details

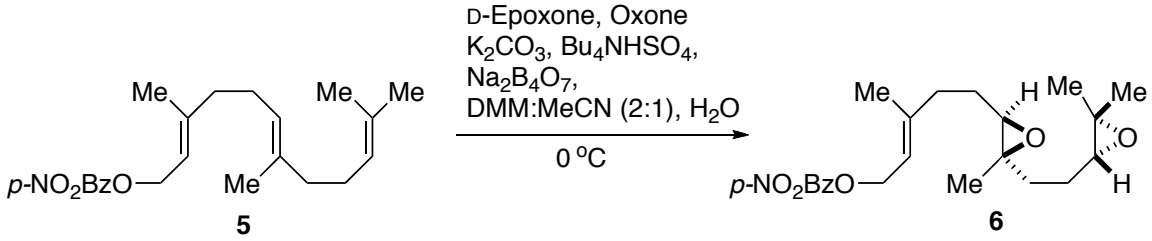
General information: ^{1}H and ^{13}C NMR spectra were recorded on a Varian INOVA-400 spectrometer (400 MHz for ^{1}H, 100 MHz for ^{13}C), or an INOVA-600 spectrometer (600 MHz for ^{1}H, 150 MHz for ^{13}C). NMR spectra were recorded as solutions in deuterated chloroform ($CDCl_3$) with residual chloroform (7.27 ppm for ^{1}H NMR and 77.23 ppm for ^{13}C NMR) taken as the internal standard and were reported in parts per million (ppm). Abbreviations for signal coupling are as follows: s, singlet; d, doublet; t, triplet; dd, doublet of doublets; m, multiplet. IR spectra were collected on a Mattson Genesis II FT-IR spectrometer with samples as neat films. Mass spectra (high resolution FAB or EI) were recorded on a VG 70-S Nier Johason mass spectrometer or a Thermo Finnigan LTQ FT spectrometer. Optical rotations were recorded at 23 ^{o}C with a Perkin-Elmer Model 341 polarimeter (concentration in g/100mL). Analytical thin layer chromatography (TLC) was performed on precoated glass backed plates purchased from Whatman (silica gel 60 F_{254}; 0.25 mm thickness). Flash column chromatography was carried out with silica gel 60 (230-400 mesh ASTM) from EM Science.

All reactions except as mentioned were conducted with anhydrous solvents in oven - dried or flame - dried and argon - charged glassware. All anhydrous solvents were dried over 3Å or 4Å molecular sieves (beads). Trace water content was tested with Coulometric KF titrator from Denver Instruments. All solvents used in work-up, extraction and column chromatography were used as received from commercial suppliers without prior purification. During reaction

workup, the reaction mixture was usually diluted to three times the original volume, and washed with an equal volume of water and/or aqueous solutions as needed. All reagents were purchased from Sigma-Aldrich.

*Compounds **10**, **11**, and ***ent*-1** were fully characterized by Dr. Rongbiao Tong. Matthew Boone obtained the optical rotation values for compounds **10** and **11**.

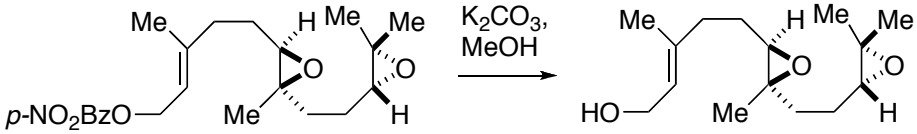
Synthesis of *para* - nitrobenzoyl diepoxy farnesol 6.



trans,trans-Farnesol *para*-nitrobenzoate **5**[79] (20 g, 54 mmol) was transferred into a three-neck 3.0 L flask. Then DMM:MeCN (2:1) (0.10 M, 500 mL) and $Na_2B_4O_7$ (0.05 M soln. in $4x10^{-4}$ M Na_2EDTA) (0.15 M, 350 mL) were added, followed by the addition of Bu_4NHSO_4 (1.8 g, 5.4 mmol). D-Epoxone (7.0 g, 27 mmol) was added. The flask was equipped with a mechanical stirrer and two addition funnels. To one addition funnel was added Oxone (140 g, 220 mmol) dissolved in $4x10^{-4}$ M Na_2EDTA (400 mL). The other addition funnel was added K_2CO_3 (112 g, 810 mmol) dissolved in distilled H_2O (400 mL). The flask was cooled to 0 °C and the Oxone and K_2CO_3 solutions were added dropwise over a 1.25 hour period. After the additions were complete, EtOAc (500 mL) was added to the reaction and transferred to a 3.0 L separatory funnel. After the layers were separated, the aqueous was extracted with EtOAc (750 mL). The organic extracts were combined and dried with $MgSO_4$. After filtration, the volatiles were

removed under reduced pressure. The crude oil was then chromatographed (4:1→2:1 hexanes:EtOAc) to provide diepoxide **6** (d.r. = 4:1) as a pale yellow oil (10.6 g, 49%), along with the monoepoxide (mixture of the 6,7- and 10,11-epoxides) (5.93 g, 28%). This procedure, along with monoepoxide recycling, was repeated to give sufficient material for the next step. $[\alpha]_D^{23}$ = + 8.8 (c 1.40, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.29 (d, *J* = 8.8 Hz, 2H), 8.22 (d, *J* = 8.8 Hz, 2H), 5.52 (t, *J* = 7.2 Hz, 1H), 4.90 (d, *J* = 6.8 Hz, 2H), 2.75 (t, *J* = 6.0 Hz, 1H), 2.71 (m, 1H), 2.24 (m, 2H), 1.81 (s, 3H), 1.79-1.56 (m, 6H), 1.31 (s, 3H), 1.29 (s, 3H), 1.27 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.9, 150.7, 142.5, 135.9, 130.9 (x2), 123.7 (x2), 118.5, 63.9, 62.8, 60.5, 58.6, 36.4, 35.4, 27.1, 25.0 (x2), 24.7, 18.4, 16.9, 16.8; IR (KBr) 2962, 1724, 1606, 1529, 1456, 1381, 1348, 1271, 1101, 1014, 874, 721 cm^{-1}; HRMS (ESI) $[M+H^+]$ Calcd. for $C_{22}H_{29}N_1O_6$ 404.20676, found 404.20717.

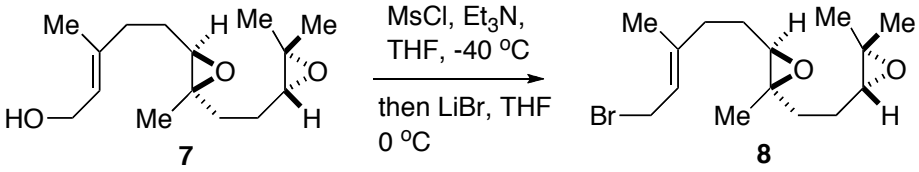
Synthesis of diepoxy allylic alcohol 7.



para-Nitrobenzoate diepoxide **6** (23 g, 57 mmol) was dissolved in MeOH (0.50 M, 115 mL). Then K_2CO_3 (3.9 g, 29 mmol) was added all at once. The reaction was stirred for 15 minutes. After dilution with Et_2O (100 mL), and the reaction was quenched by the addition of a saturated solution of NH_4Cl (250 mL). The layers were separated. The aqueous layer was extracted with EtOAc (250 mL x 2). The organic extracts were combined and dried with $MgSO_4$. After filtration, the

volatiles were removed under reduced pressure. Chromatography (4:1→0:1 hexanes:EtOAc) then gave diepoxy allylic alcohol **7** as an oil (12.8 g, 88%). When loading the crude mixture on silica, EtOAc was used to dissolve the *para*-nitrobenzoate methyl ester byproduct. This did not affect the separation. $[\alpha]_D^{23}$ = + 11.0 (c 0.965, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 5.46 (m, 1H), 4.16 (d, *J* = 6.6 Hz, 2H), 2.76-2.71 (m, 2H), 2.21 (m, 1H), 2.16 (m, 1H), 1.79 (m, 1H), 1.70 (s, 3H), 1.68 (m, 3H), 1.60 (m, 3H), 1.60 (m, 3H), 1.31 (s, 3H), 1.28 (s, 3H), 1.27 (s, 3H); (150 MHz, $CDCl_3$) δ 138.5, 124.3, 64.1, 62.9, 60.5, 59.4, 58.7, 36.4, 35.3, 27.0, 24.9, 24.7, 18.8, 16.9, 16.4; IR (KBr) 3437, 2924, 1666, 1454, 1385, 1250, 1119, 1011, 872 cm^{-1}; HRMS (APCI) [M+H$^+$] Calcd. for $C_{15}H_{27}O_3$ 255.19547, found 255.19552.

Synthesis of diepoxy allylic bromide 8.

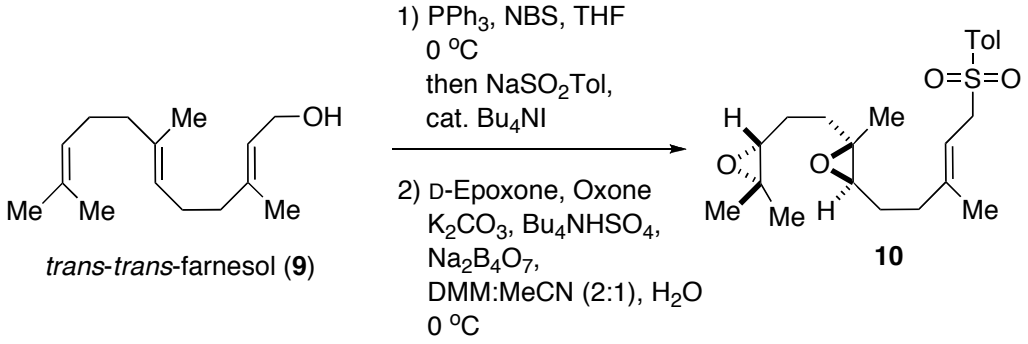


7 **8**

The diepoxy allylic alcohol **7** (12.8 g, 50 mmol) was dissolved in THF (0.30 M, 170 mL). The solution was cooled to -40 °C. Et_3N (10.5 mL, 76 mmol) was then added all at once. MsCl (4.71 mL, 60 mmol) was then added all at once. The reaction was stirred for 30 minutes at -40 °C. After warming to 0 °C, flame-dried LiBr (13.1 g, 150 mmol) dissolved in THF (5.0 M, 30 mL) was added all at once. The reaction was stirred for an additional 15 minutes. Then the reaction was quenched by the addition of H_2O (200 mL). Et_2O (200 mL) was added. After the layers were separated, the aqueous layer was extracted with Et_2O (100 mL).

The organic extracts were combined and dried with $MgSO_4$. After filtration, the volatiles were removed under reduced pressure. To the crude mixture was added hexanes (100 mL), and the solids were filtered. After removal of the volatiles under reduced pressure, the analytically pure allylic bromide **8** (15.3 g, 96%) was obtained. * We elected not to subject this sensitive allylic bromide to chromatography, as significant decomposition occurred (even with Et_3N buffering). Once made, the allylic bromide was immediately used. $[\alpha]_D^{23}$ = + 4.9 (c 0.85, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 5.59 (t, *J* = 8.4 Hz, 1H), 4.02 (d, *J* = 7.8 Hz, 2H), 2.73 (m, 2H), 2.24 (m, 1H), 2.18 (m, 1H), 1.76 (s, 3H), 1.68 (m, 3H), 1.61 (m, 3H), 1.32 (s, 3H), 1.29 (s, 3H), 1.28 (s, 3H); (150 MHz, $CDCl_3$) δ 142.6, 121.3, 63.9, 62.7, 60.5, 58.7, 36.4, 35.3, 29.4, 26.9, 25.0, 24.7, 18.8, 16.9, 16.1; IR (KBr) 2962, 1655, 1454, 1381, 1203, 1122, 876 cm^{-1}; HRMS (APCI) [M +H^+] Calcd. for $C_{15}H_{26}O_2Br_1$ 317.11107, found 317.11115.

Synthesis of diepoxy allylic sulfone 10



trans-trans-farnesol (**9**)

10

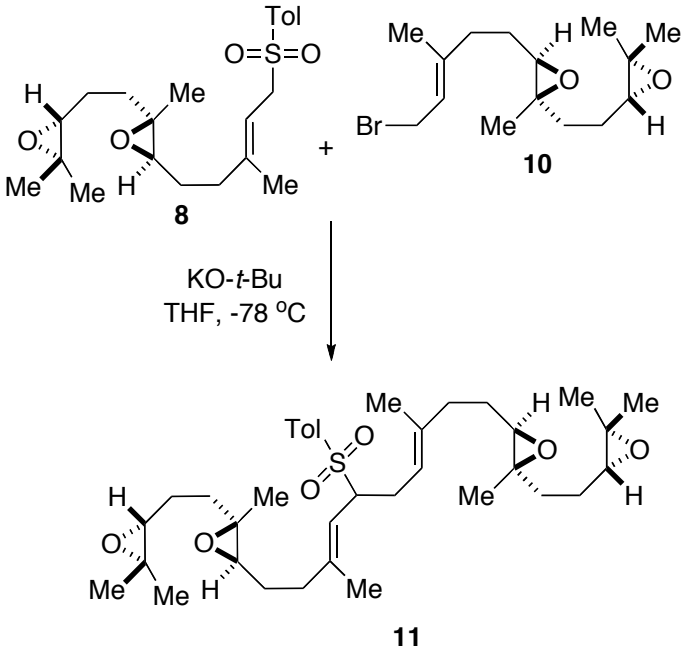
trans-trans-Farnesol (**9**) (10.0 g, 45 mmol) was dissolved in dry THF (0.22 M, 200 mL) and then cooled to 0 °C. Triphenylphosphine (PPh_3) (14.7 g, 56 mmol) was then added. *N*-Bromosuccinimide (NBS) (9.23 g, 51.6 mmol) was slowly added in ten batches over 20 minutes. The light yellow reaction mixture was stirred for

1.5 hours at 0 °C until complete conversion was achieved. Then, Bu_4NI (1.70 g, 4.5 mmol) and *p*-toluenesulfinic acid sodium salt ($NaSO_2Tol$) (12 g, 68 mmol) were subsequently added. The light yellow suspension was warmed to room temperature and stirred for 16 hours. During this time, the reaction became light brown in color. The reaction was quenched with saturated $NaHSO_3$ (200 mL). The layers were separated. The aqueous layer was extracted with Et_2O (2 x 100 mL). The combined organic extracts were washed with saturated $NaHCO_3$ (100 mL), brine (100 mL), and dried with anhydrous $MgSO_4$. After filtration, the volatiles were removed under reduced pressure. Chromatography (9:1 hexanes:EtOAc) gave 1-farnesyl *para*-tolyl sulfone **A** (10.8 g, 67%), which was used for the Shi epoxidation in the next step.

A (3.6 g, 10 mmol) was transferred to a three-neck 1.0 L flask to which was added DMM:acetonitrile (2:1), (0.067 M, 150 mL). $Na_2B_4O_7$ (0.05 M soln. in $4x10^{-4}$ M Na_2EDTA) (0.091 M, 110 mL) were added, followed by the addition of Bu_4NHSO_4 (0.34 g, 1.0 mmol). D-Epoxone (1.3 g, 5.0 mmol) was added. The solution was cooled to 0 °C and vigorously stirred. The flask was equipped with two addition funnels. To one addition funnel was added Oxone (17 g, 28 mmol) dissolved in $4x10^{-4}$ M Na_2EDTA (140 mL). To the other addition funnel was added K_2CO_3 (15 g, 110 mmol) dissolved in distilled H_2O (140 mL). The oxone and K_2CO_3 solutions were added dropwise over a 2 hour period. Upon completion of the additions, the reaction was allowed to stir for an additional 20 minutes, at which time H_2O (100 mL) and Et_2O (200 mL) were added. The layers were separated. The aqueous layer was extracted with Et_2O (2 x 100 mL). The

organic extracts were dried with $MgSO_4$. After filtration, the volatiles were removed under reduced pressure. Chromatography (2:1→1:1 hexanes:EtOAc) gave the diepoxy allylic sulfone **10** (d.r. = 5:1) as a yellow oil (2.8 g, 71%). $[\alpha]_D^{23}$ = + 2.8 (c 1.01, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 8.0 Hz, 2H), 7.31 (d, *J* = 8.4 Hz, 2H), 5.21 (t, *J* = 8.0 Hz, 1H), 3.78 (d, *J* = 8.0 Hz, 2H), 2.69 (m, 2H), 2.43 (s, 3H), 2.14 (m, 2H), 1.78-1.50 (m, 6H), 1.38 (s, 3H), 1.30 (s, 3H), 1.27 (s, 3H), 1.26 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.5, 144.7, 135.9, 129.8 (x2), 128.6 (x2), 111.2, 64.0, 62.7, 60.5, 58.6, 56.2, 36.5, 35.3, 27.1, 25.0, 24.7, 21.8, 18.8, 16.8, 16.4; IR (KBr) cm^{-1} 2962, 2926, 1664, 1597, 1452, 1383, 1313, 1149, 1088, 744; HRMS (ESI) [M+H$^+$] Calcd. for $C_{22}H_{33}O_4S_1$ 393.20941, found 393.20941.

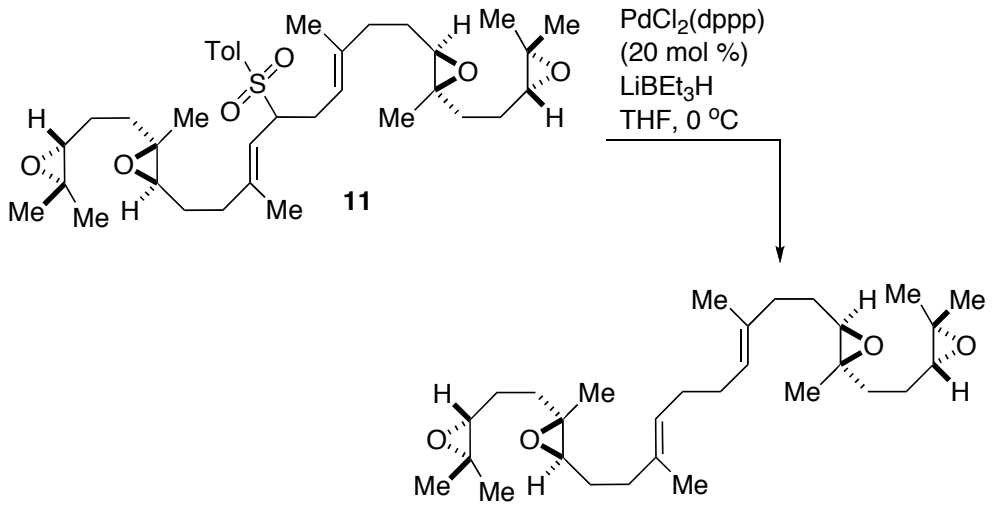
Fragment coupling: Synthesis of tetraepoxy allylic sulfone 11



The diepoxy allylic bromide **8** (1.8 g, 5.7 mmol) and diepoxy allylic sulfone **10** (1.6 g, 4.0 mmol) were dissolved in THF (0.05 M, 81 mL). The solution was then

cooled to -78 °C. Then KO-*t*-Bu (1.0 M solution in THF, 5.3 mL, 5.3 mmol) was added via syringe pump over a 30 minute period. The reaction was stirred for 2 hours at -78 °C. Then saturated $NaHCO_3$ (200 mL) was added. The layers were separated. The aqueous layer was extracted with Et_2O (200 mL). The organic extracts were combined and dried with $MgSO_4$. After filtration, the volatiles were removed under reduced pressure. Chromatography (9:1→1.5:1 hexanes:EtOAc + 0.5% Et_3N) gave the tetraepoxy allylic sulfone **11** as an oil (1.96 g, 77%). $[\alpha]_D^{23}$ = + 13.8 (c 0.745, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 7.6 Hz, 2H), 7.30 (d, *J* = 7.3 Hz, 2H), 5.01 (m, 2H), 3.73 (m, 1H), 2.69 (m, 4H), 2.44 (s, 3H), 2.40-2.24 (m, 2H), 2.20-2.00 (m, 4H), 1.80-1.50 (m, 12H), 1.62 (s, 6H), 1.31 (s, 3H), 1.30 (s, 3H), 1.28 (s, 3H), 1.27 (s, 3H), 1.26 (s, 3H), 1.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.6 (x2), 137.8, 135.3, 129.6 (x2), 129.3 (x2), 119.5, 117.8, 64.9, 64.2, 64.0 (x2), 62.9, 62.7, 60.5, 58.6, 36.5, 35.8, 35.4, 35.3, 29.9, 27.5, 27.4, 27.0, 25.0 (x3), 24.8 (x2), 21.8, 18.9, 16.8 (x2), 16.6; IR (KBr) cm^{-1} 2960, 2926, 2856, 1597, 1456, 1381, 1300, 1144, 1059, 1250, 874; HRMS (ESI) [M+H^+] Calcd. for $C_{37}H_{57}O_6S_1$ 629.38704, found 629.38761.

Synthesis of (3*R*,6*R*,7*R*,18*R*,19*R*,22*R*)-squalene tetraepoxide (*ent*-1)



(3*R*,6*R*,7*R*,18*R*,19*R*,22*R*)-squalene tetraepoxide (***ent*-1**)

Tetraepoxy sulfone **11** (1.96 g, 3.1 mmol) was dissolved in THF (0.10 M, 31 mL). The solution was cooled to 0 °C. Then $PdCl_2$(dppp) (370 mg, 0.62 mmol) was added. Lithium triethylborohydride ($LiBEt_3H$) (1.0 M solution in THF, 6.2 mL, 6.2 mmol) was added dropwise to the solution over a 15 minute period. The reaction was stirred for an additional 40 minutes at 0 °C. Then Et_2O (40 mL) was added, followed by the addition of saturated NH_4Cl (50 mL). The layers were separated. The aqueous layer was extracted with Et_2O (50 mL). The organic extracts were combined and dried with $MgSO_4$. After filtration, the volatiles were removed under reduced pressure. Chromatography (9:1→2:1→1:1 hexanes:EtOAc + 0.5% Et_3N) gave squalene tetraepoxide (***ent*-1**) as a clear oil (944 mg, 64%, 72% based on recovered **11**) and **11** (218 mg). $[\alpha]_D^{23}$ = + 15.1 (c 0.81, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 5.18 (bs, 2H), 2.72 (m, 4H), 2.18-2.13 (m, 2H), 2.10-2.07 (m, 2H), 2.02 (m, 4H), 1.78 (m, 2H), 1.70-1.54 (m, 10H), 1.62 (s, 6H), 1.31 (s, 6H), 1.28 (s, 6H), 1.27 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 134.5,

125.0, 64.1, 63.2, 60.5, 58.6, 36.5, 35.5, 28.4, 27.5, 25.1, 24.9, 18.9, 16.9, 16.3; IR (KBr) cm^{-1} 2960, 2926, 2858, 1452, 1379, 1323, 1250, 1120, 874; HRMS (ESI) [M+H^+] Calcd. for $C_{30}H_{51}O_4$ 475.37819, found 475.37829.

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