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BonSuk Koo

Part 1. Synthesis of the Branched *C*-Glycoside Substructure of Altromycin B.

Part 2. Fischer Carbene Catalysis of the Alkynol Cycloisomerization: Application to the Synthesis of the Altromycin B Disaccharide.

By

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BonSuk Koo

B. A., Hanyang University, 1999

M. S., Hanyang University, 2001

Adviser: Frank E. McDonald

An Abstract of

A dissertation submitted to the Faculty of the Graduate School of Emory University in partial fulfillment Of the requirements for the degree of

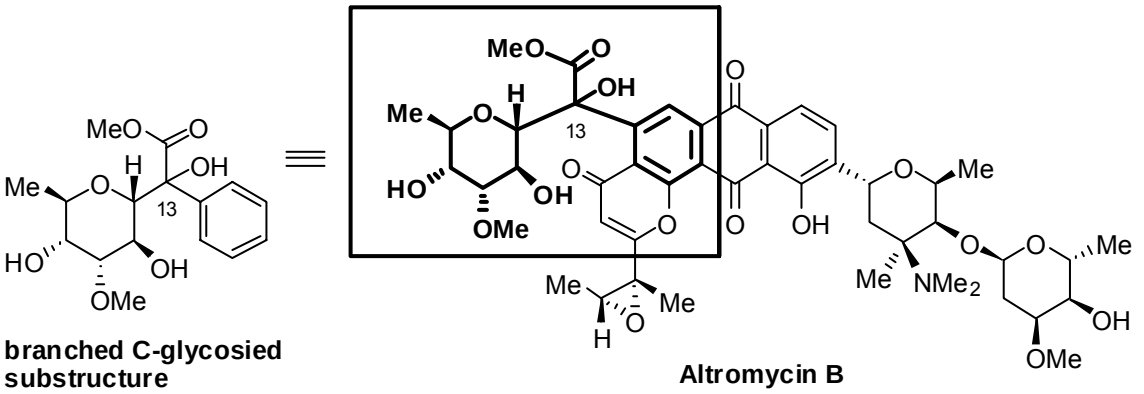
Doctor of Philosophy

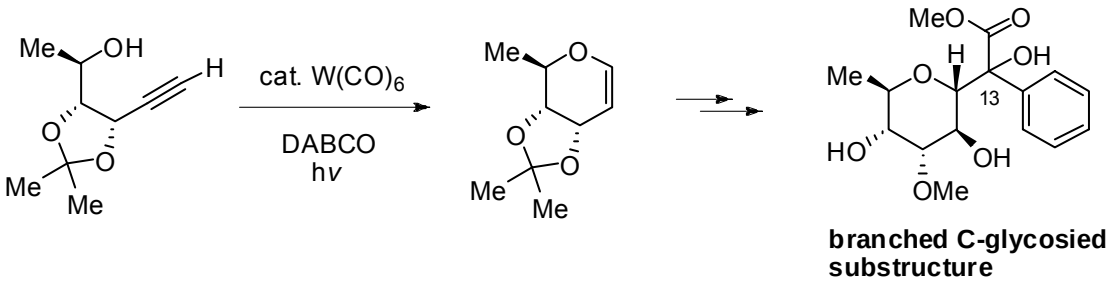
Department of Chemistry

2007

Abstract

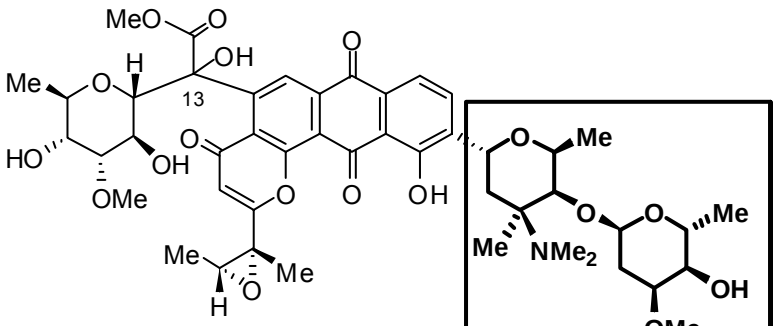
Part 1. Synthesis of the Branched *C*-Glycoside Substructure of Altromycin B.



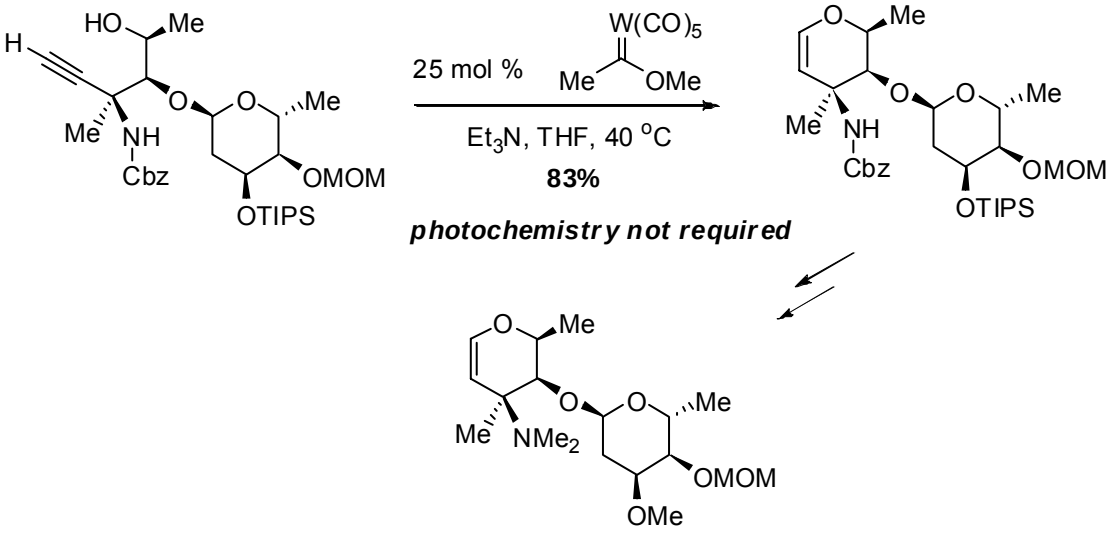


Tungsten-catalyzed cycloisomerization of alkynyl alcohol provides only the endocyclic enol ether as a key intermediate for the branched *C*-glycoside substructure of altromycin B. A sequence of Stille cross-coupling reaction and regio- and stereoselective functional group transformations affords each C13-diastereomer of the branched *C*-arylglycoside.

Part 2. Fischer Carbene Catalysis of the Alkynol Cycloisomerization: Application to the Synthesis of the Altromycin B Disaccharide.



Altromycin B



disaccharide substructure of altromycin B

The tungsten-catalyzed cycloisomerization of alkynols can be conducted without using photochemistry, using a stable tungsten Fischer carbene as the precatalyst for this transformation. A variety of alkynyl alcohols undergo cycloisomerization under these conditions to provide endocyclic enol ethers of 5, 6, and 7-membered ring sizes. The utility of this method is further demonstrated in the stereoselective synthesis of the disaccharide substructure of altromycin B.

Part 1. Synthesis of the Branched *C*-Glycoside Substructure of Altromycin B. Part 2. Fischer Carbene Catalysis of the Alkynol Cycloisomerization: Application to the Synthesis of the Altromycin B Disaccharide.

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Abbreviations

Ac	acetyl
Anal. Calcd.	analysis calculated
aq	aqueous
Ar	aryl
BINAP	2,2'-bis(diphenylphosphino)-1,1'-binaphthyl
Bn	benzyl
Bz	benzoyl
CAN	ceric ammonium nitrate
Cbz	carbobenzyloxycarbonyl
CSA	camphor sulfonic acid
CuTC	copper(I) thiophene-2-carboxylate
d	doublet
DABCO	1,4-diazabicyclo[2,2,2]octane
Dba	dibenzylideneacetone
DDQ	2,3-dichloro-5,6-cyano-1,4-benzoquinone
DHP	dihydropyran
DIBAL	diisobutylaluminum hydride
DIPT	diisopropyl tartrate
DMAP	*N, N*-dimethylaminopyridine
DMF	*N, N*-dimethylformamide
DMM	dimethoxymethane
DMSO	dimethylsulfoxide

equiv	equivalent
HMPA	hexamethylphosphoric triamide
HRMS	high-resolution mass spectroscopy
LAH	lithium aluminum hydride
m	multiplet
mL	milliliter
mmol	millimole
MOM	methoxymethyl
n-BuLi	*n*-butyllithium
NIS	*N*-iodosuccinimide
NMP	*N*-methylpyrrolidinone
NMR	nuclear magnetic resonance
Ph	phenyl
PMB	*para*-methoxybenzyl
PMP	*para*-methoxyphenyl
p-TsOH	*para*-toluenesulfonic acid
Pyr	pyridine
q	quartet
rt	room temperature
s	singlet
t	triplet
TBAF	tetrabutylammonium fluoride
TBS	*tert*-butyldimethylsilyl

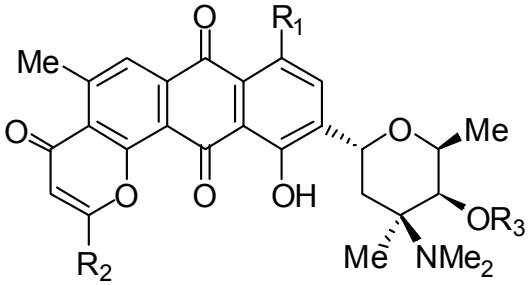
t-BuLi	*tert*-butyllithium
t-BuOOH	*tert*-butylhydroperoxide
TEA	triethylamine
TFP	trifurylphosphine
THF	tetrahydrofuran
TIPS	triisopropylsilyl
TMS	trimethylsilyl
Ts	*para*-toluenesulfonyl

Part 1. Synthesis of the Branched *C*-Glycoside Substructure of Altromycin B.

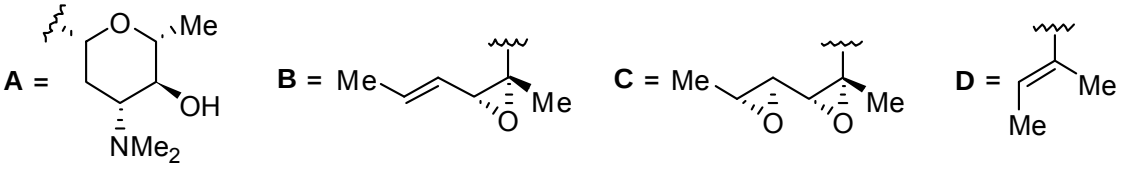
1.1 Introduction and background

The anthraquinone-derived glycosidic natural products are a large family of natural products exhibiting a wide variety of biological activities.[1,2] For instance, pluramycins display a range of structures from the simple aglycone pluramycins to the heavily glycosylated compounds, and exhibit antibiotic, antimicrobial and anticancer activity (Figure 1).[2-5]

Figure 1. Classical pluramycins.



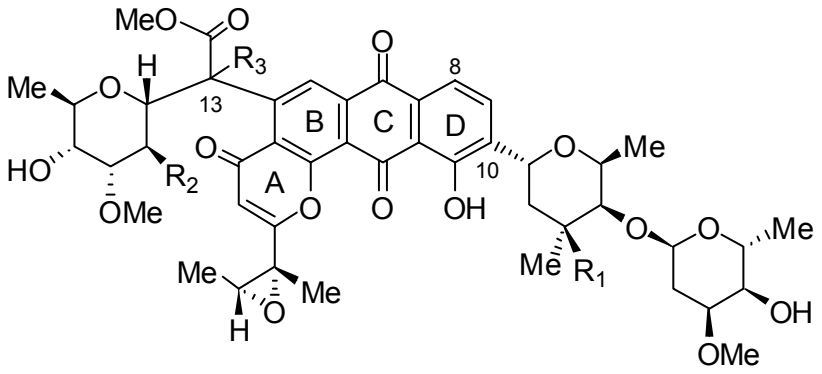
Classical Pluramycins



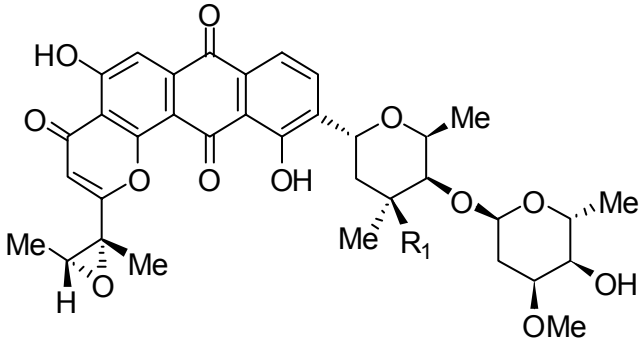
1	Pluramycin	R_1 = A	R_2 = B	R_3 = COMe
2	Neopluramycin	R_1 = A	R_2 = D	R_3 = COMe
3	Hedamycin	R_1 = A	R_2 = C	R_3 = H
4	Kidamycin	R_1 = A	R_2 = D	R_3 = H
5	Ankinomycin	R_1 = H	R_2 = C	R_3 = H

Hedamycin (**3**),[6] kidamycin (**4**)[7-9] and ankinomycin (**5**),[10,11] classical members of pluramycins, have been reported to have activity against colon, lung, and ovarian tumors and also reported to exhibit cytotoxicity as a result of DNA binding and inhibition of DNA synthesis.[12-14]

Figure 2. Structures of altromycin natural products.



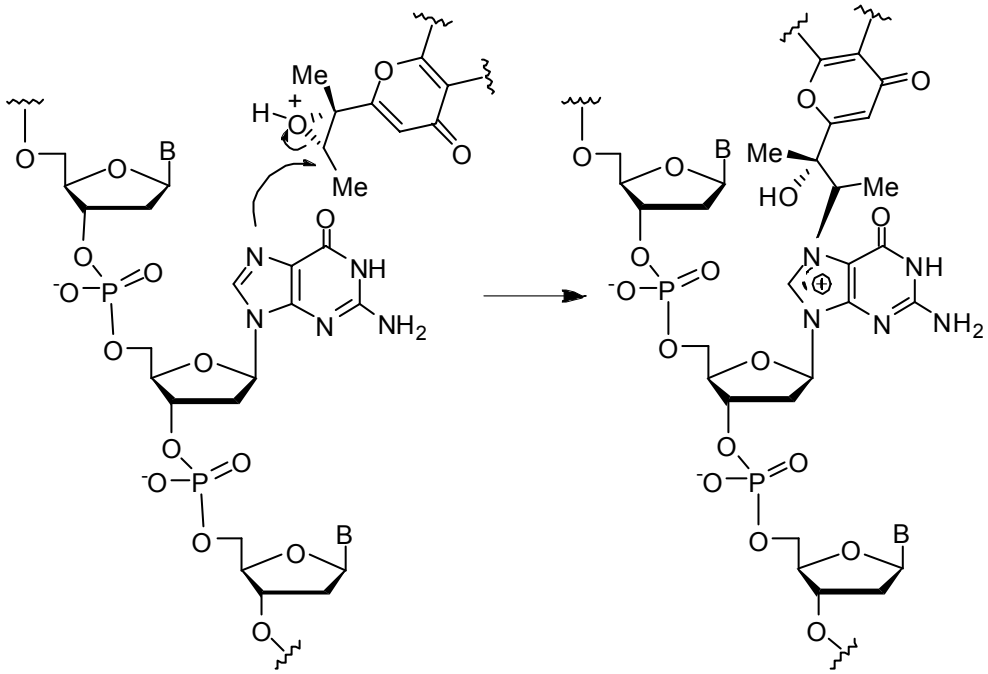
6	Altromycin A	$R_1 = NHCH_3$	$R_2 = OH$	$R_3 = OH$
7	Altromycin B	$R_1 = N(CH_3)_2$	$R_2 = OH$	$R_3 = OH$
8	Altromycin C	$R_1 = NHCH_3$	$R_2 = H$	$R_3 = OH$
9	Altromycin D	$R_1 = N(CH_3)_2$	$R_2 = H$	$R_3 = OH$
10	Altromycin E	$R_1 = NHCH_3$	$R_2 = OH$	$R_3 = H$
11	Altromycin F	$R_1 = N(CH_3)_2$	$R_2 = OH$	$R_3 = H$
12	Altromycin G	$R_1 = NH_2$	$R_2 = OH$	$R_3 = OH$



13	Altromycin H	$R_1 = NHCH_3$
14	Altromycin I	$R_1 = N(CH_3)_2$

Altromycins (**6** – **14**) (Figure 2) are new members of the family of pluramycin antibiotics, and altromycins A – D were first reported in 1990,[15,16] while altromycins E – I were reported in 1994. The altromycins were isolated from a South African bushveld soil.[17] Structurally, altromycins (A – G) have the common aglycone of classical pluramycins, but the unusual disaccharide unit on C10 of the D ring as well as the substitution of C13 on the B ring with a neutral *C*-glycoside differ from the classical pluramycins. All altromycins (A – I) were reported to have selective antibiotic activities against Gram-positive bacteria and anticancer activity including in vivo activity against P388 leukemia, as well as colon, lung, and ovarian tumors.[15-17]

Scheme 1. Mechanism of DNA alkylation.

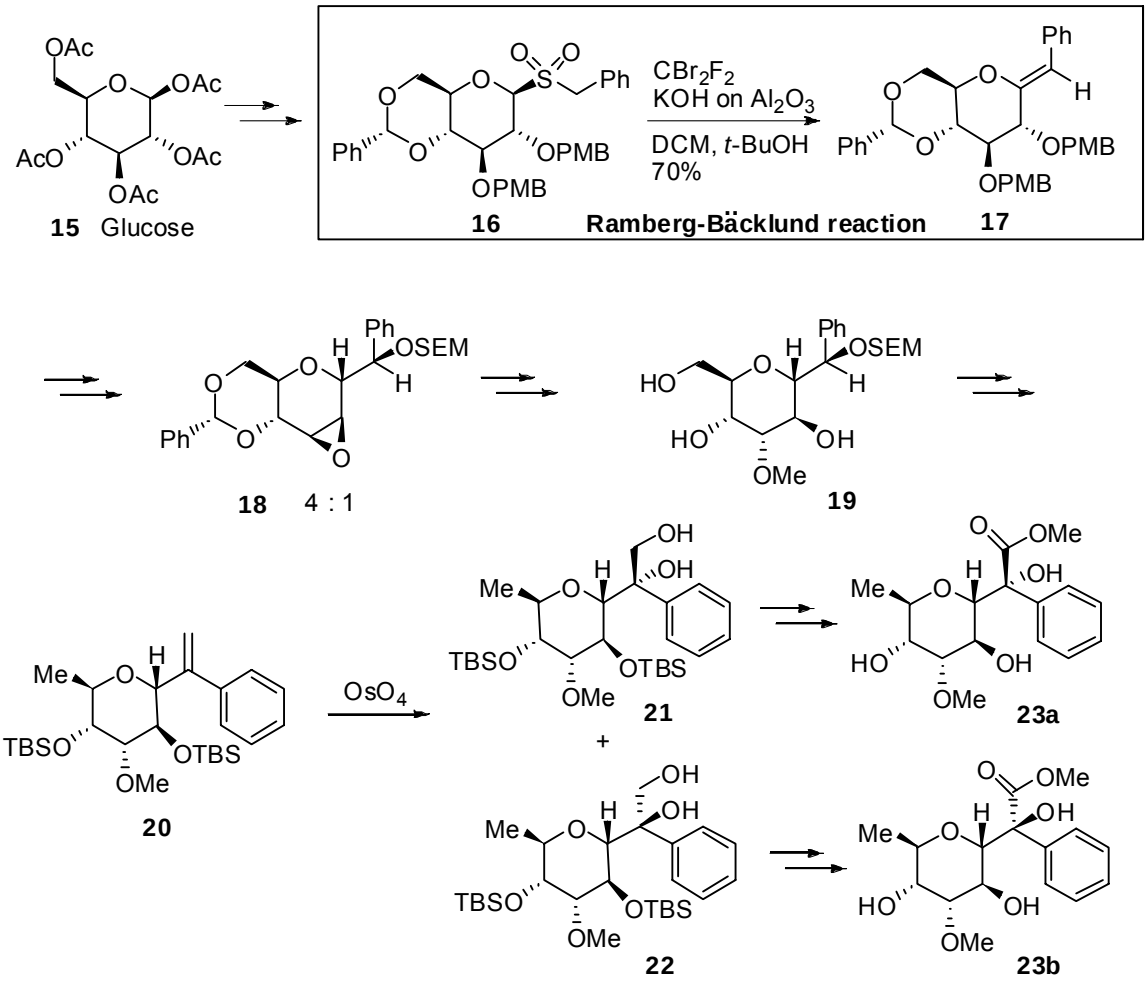


It has been also demonstrated that altromycins form a complex with DNA by covalently binding to the N-7 guanine via nucleophilic attack of the guanine nitrogen to the epoxide (Scheme 1).[12,13,18-21] Along with the studies on the biological activities, interactions between altromycins with DNA and its metal complex have been reported.[22-24] The structures of altromycins have been determined primarily by NMR spectroscopy, and the absolute stereochemistry of each of the widely separated chiral subunits has not been unambiguously assigned. Specifically, the stereochemistry of C13 hydroxyl group, the epoxide moiety and the disaccharide relative to each other has not been clearly elucidated.[16] Despite the attractive biological activity of altromycins, none of the altromycin natural products have been prepared by total synthesis. Only one example for the synthesis of the branched *C*-glycoside substructure of altromycin B (**7**) was reported prior to our studies in this area.[25]

Pasetto and Franck recently reported the synthesis of both possible C13 isomers (**23a**, **23b**) of the northwest quadrant of altromycin B (**7**) by utilizing the Ramberg-Bäcklund reaction[26] as a key step to form a *C*-glycoside linkage (Scheme 2). Starting from D-glucose **15** as starting material, several transformations including protection and deprotection reactions provided sulfone **16**, which was used for the Ramberg- Bäcklund reaction to give *exo* glucal **17** in 70% yield. The *exo* glucal **17** was then further transformed to the epoxide **18** and regioselective diaxial ring opening of epoxide **18** with NaOMe at the C-4 position provided all the required stereocenters in the sugar moiety **19**. Further asymmetric transformations provided alkene **21** and subsequent

dihydroxylation[27] produced both separable diols **21** and **22**, which were then individually elaborated to both possible diastereomers **23a** and **23b** of the branched glycoside of altromycin B (**7**).

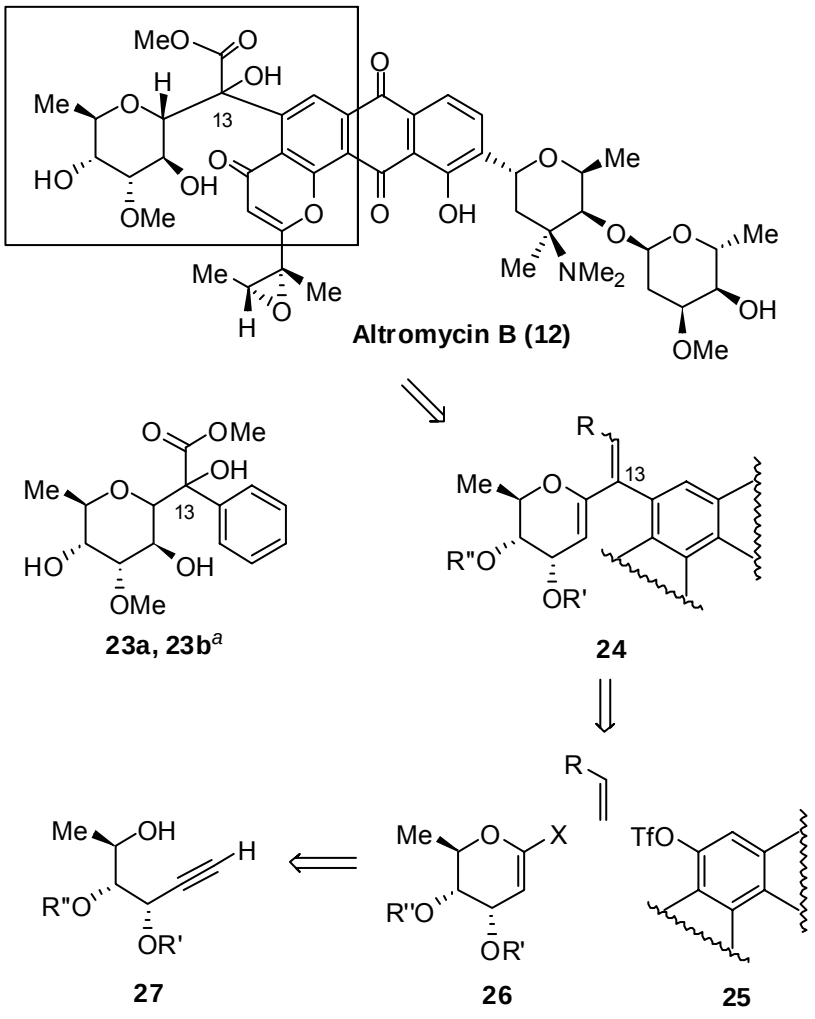
Scheme 2. Franck's synthesis of the branched substructures of altromycin B.



As a different approach for the west branched *C*-glycoside substructure synthesis, we envisioned that formation of *C*-glycosyl linkage **24** could be accomplished by a transition metal-catalyzed cross-coupling reaction of aromatic

derivative **25** and sugar moiety **26**, which would be derived from tungsten-catalyzed *endo*-selective cycloisomerization of alkynyl alcohol **27** (Figure 3).[28]

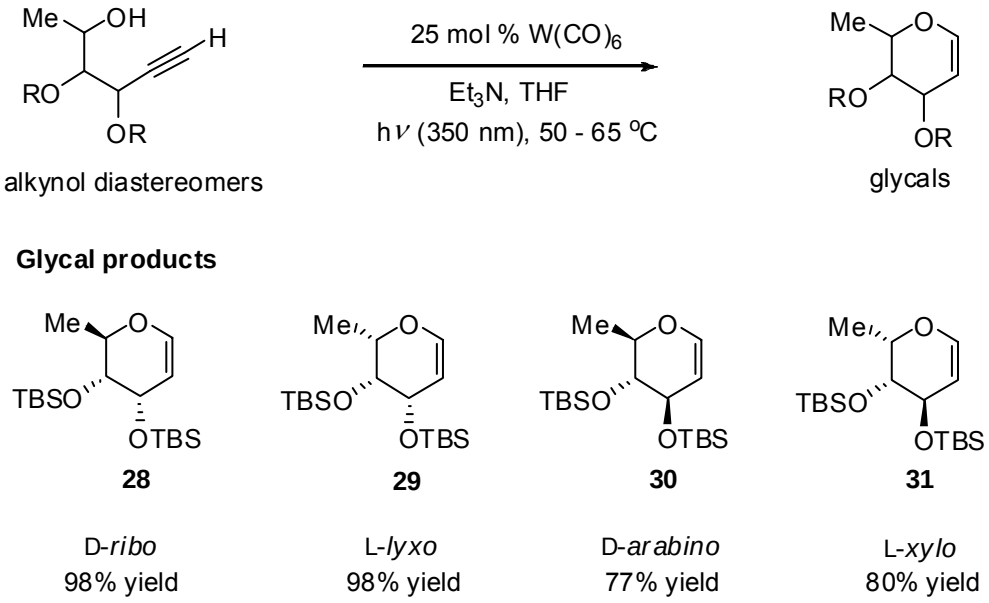
Figure 3. Retrosynthesis of the branched *C*-glycoside substructure of altromycin B.



The McDonald laboratory first reported the tungsten-catalyzed *endo*-selective alkynol cycloisomerization in 2000 (Scheme 3).[28,29] This single step and high

yielding protocol was utilized for the stereoselective synthesis of 6-deoxy-1,2-glycals (**28** – **31**).

Scheme 3. Stereoselective synthesis of 6-deoxy-1,2-glycals via tungsten-catalyzed alkynol cycloisomerization.

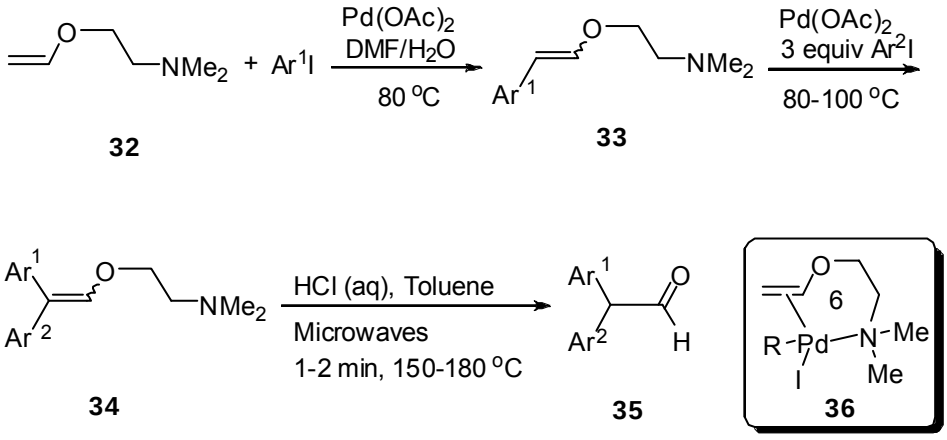


This methodology could provide efficiency in the synthesis of the west altrose substructure by constructing all the required stereocenters before cycloisomerization.

For the formation of *C*-glycoside linkage, transition metal-catalyzed cross-coupling reactions using glycal **26** and aromatic derivative **25** were considered. In 2001, Hallberg's group reported a regioselective multiple Heck reaction utilizing dimethylamine-tethered enolether **32** (Scheme 4).[30,31] The coordinating amine was believed to form a 6-membered intermediate **36** to facilitate diarylated

product **34** with the control of regiochemistry. The cleavage of dimethylamino-tethering group was conducted under acidic microwave conditions to give aldehyde **35**.

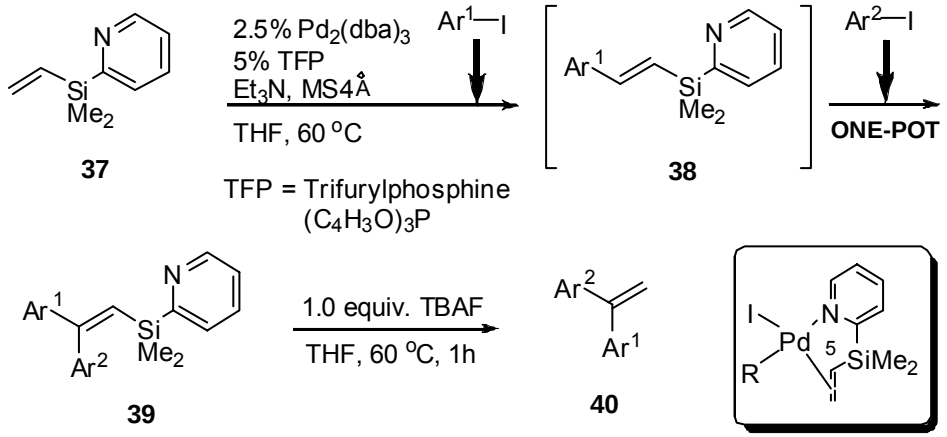
Scheme 4. Regioselective sequential Heck arylations of vinyl ethers.



32 **33** **34** **35** **36**

Yoshida's group reported regioselective multiple Heck reaction using 2-pyridyl-dimethyl(vinyl)silane **37** as a versatile platform for highly substituted olefin synthesis (Scheme 5).[32-34]

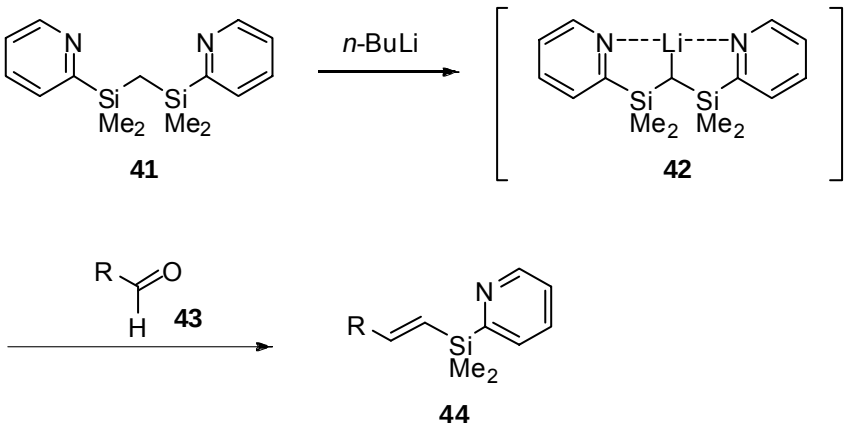
Scheme 5. Regioselective sequential Heck arylations of vinyl silane.



37 **38** **39** **40**

The nitrogen in the pyridine provided a 5-membered metallocyclic intermediate and facilitated control of the regioselectivity in the multiple Heck reaction. The first coupling reaction of vinylsilane derivative **37** with aryliodide in the presence of palladium catalyst produced monoarylated vinylic silane **38** followed by addition of the second aryl iodide into reaction mixture provided diarylated product **39** in one-pot process. The 2-pyridyldimethylsilyl group in **39** was easily cleaved by TBAF to give diarylated alkene **40**. Yoshida's group also reported a Peterson-type olefination of aldehyde using bis(2-pyridyldimethyl)silane **41** (Scheme 6).[35] This method provided the *trans*-monosubstituted vinylic silane derivative **44**, which is similar to **38** prepared by cross-coupling reactions.

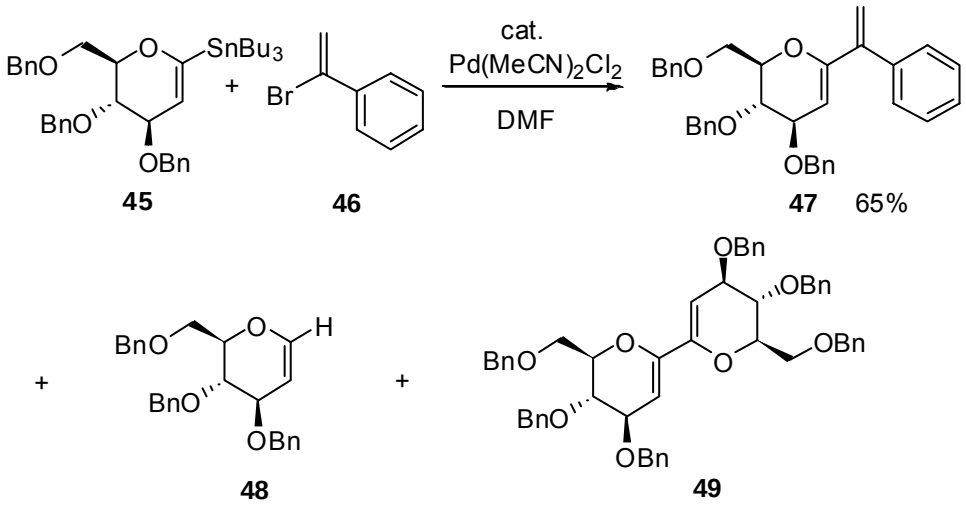
Scheme 6. Peterson-type olefination of aldehyde.



As a straightforward method for the formation of the *C*-glycosidic linkage, the Stille cross-coupling reaction was considered.[36-38] The Quayle group reported the synthesis of sugar containing dienes **47** via Stille cross-coupling reaction (Scheme 7).[39,40] In their synthesis, stannylated glycal **45** and bromo styrene **46** were used as coupling partners in the presence of palladium catalyst. After

screening the reaction conditions, the desired diene **47** was obtained in 65% yield along with undesired destannylated product **48** and homocoupling product **49**.

Scheme 7. Stille cross-coupling reaction of stannylated glycal and vinyl iodide.



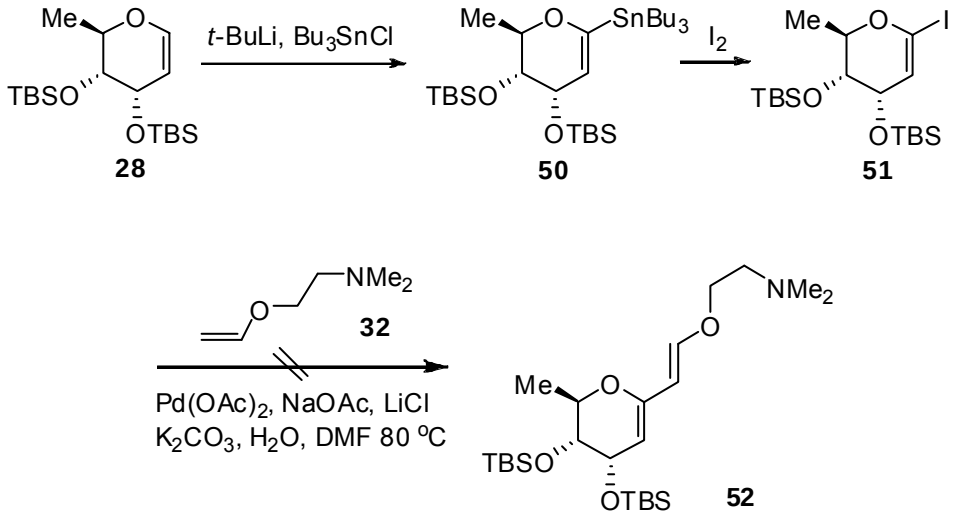
1. 2. Results and Discussion

1. 2. 1. Experiments for the formation of C-glycoside linkage (Hallberg's multiple Heck reaction).

Our initial plan for the synthesis of the west *C*-glycoside model system of atromycin B (**12**) was envisioned by sequential Heck type β,β-diarylation reaction reported by the Hallberg group (Scheme 8).[30,31] The coupling partner, iodoglycal **51**, was prepared through stannylation of known glycal **28** followed by iodination of the stannylated glycal **50**.[41] The light sensitive iodoglycal **51** was then immediately used for the first Heck reaction. However, all our efforts to obtain

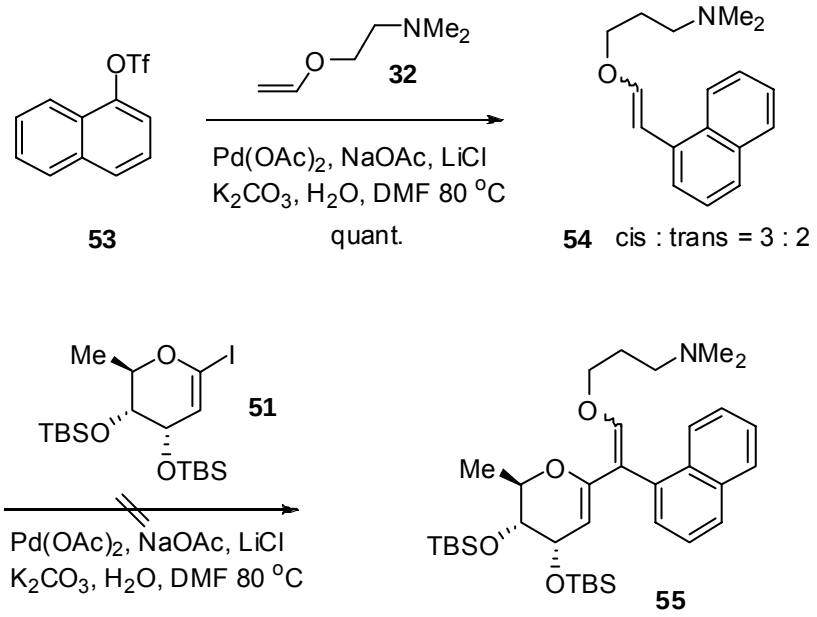
coupling product **52** were unsuccessful and all reaction conditions provided complex mixtures.

Scheme 8. Heck reaction of iodoglycal **51** and vinylether **32**.



In an attempt to obtain the desired product, we decided to change the coupling order in the sequential Heck reaction (Scheme 9). Naphthyltriflate **53** was first treated under the Heck reaction conditions and produced known mono aryl-substituted vinylic ether product **54** (cis:trans = 3:2) in quantitative yield.[30] However, the second Heck reaction with iodoglycal **51** provided none of the desired disubstituted product **55**. We assumed that the stability of iodoglycal **51** could be problematic and caused decomposition under the reaction conditions.

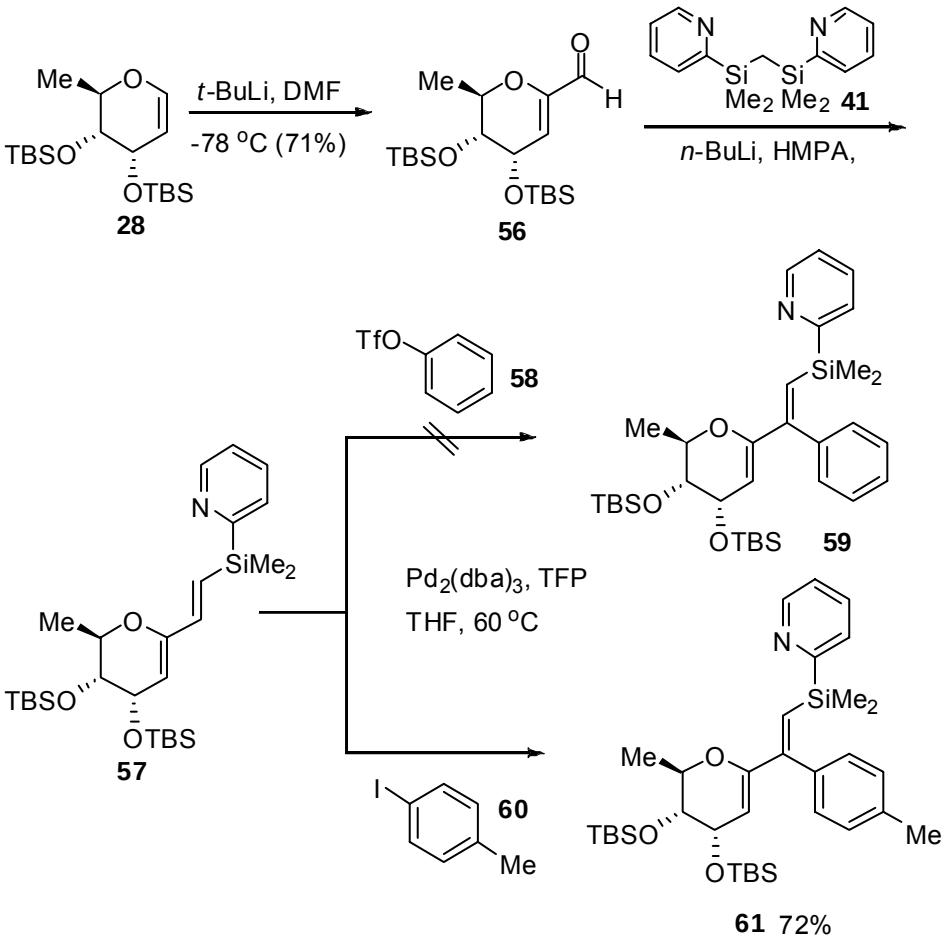
Scheme 9. Sequential Heck reaction of naphthyl triflate **53** and iodoglycal **51**.



1. 2. 2. The formation of C-glycoside linkage (Yoshida's multiple Heck reaction).

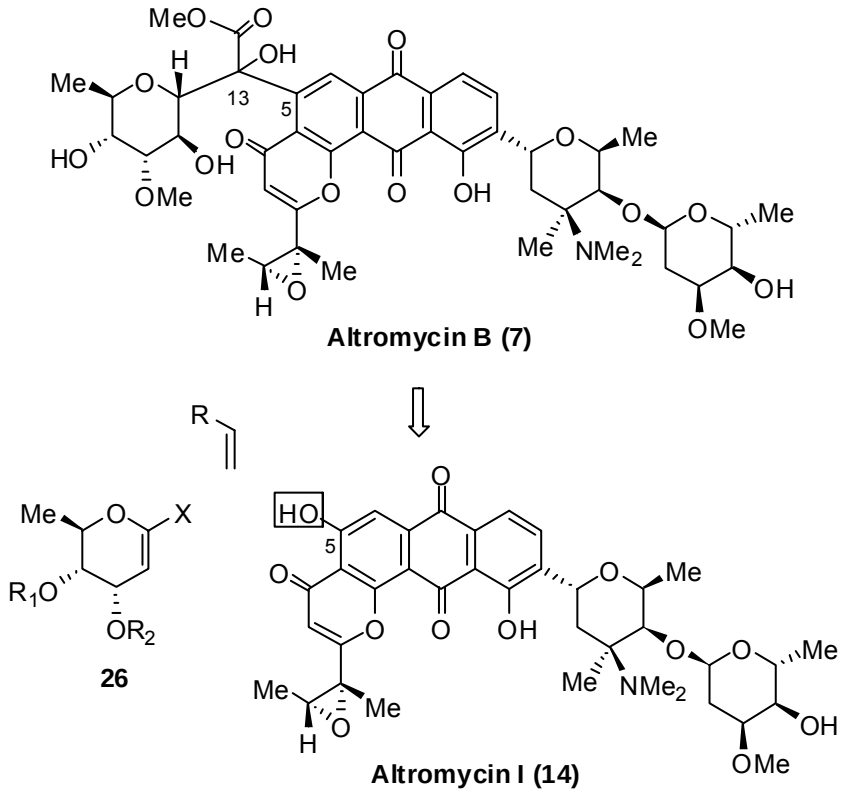
As an alternative of the Hallberg's protocol, Yoshida's multiple Heck reaction was considered (Scheme 10).[33] In this reaction, we decided to use the Peterson-type olefination reaction[35] for the preparation of glycal substituted vinyl silane **57**, rather than using the Heck reaction, due to the instability of iodoglycal as well as the difficulties in the preparation of iodoglycal. Lithiation of glycal **28** by *t*-butyllithium and subsequent quench with DMF gave aldehyde **56** in 71% yield. Peterson-type olefination was conducted with bis(2-pyridyldimethyl)silane **41** in the presence of *n*-butyllithium and HMPA to give glycal-substituted vinylsilane **57** in 82% yield.

Scheme 10. Olefination and Heck reaction.



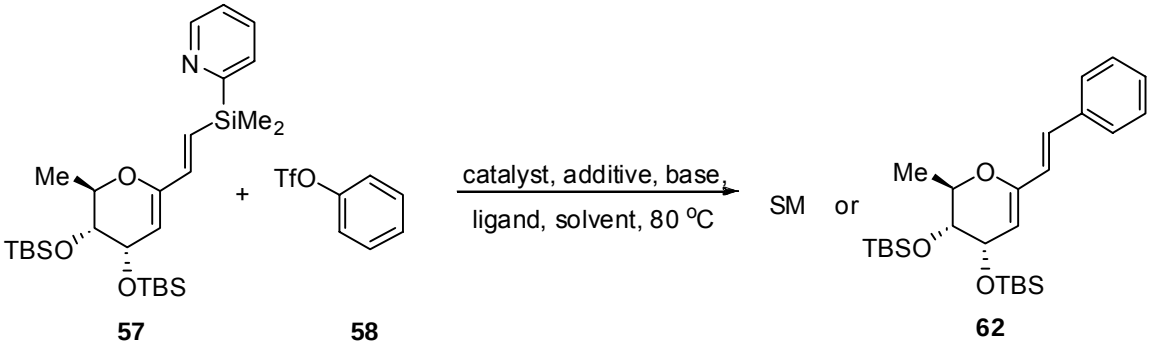
The Heck reaction was conducted with phenyltriflate **58** in the presence of 10 mol % of $Pd_2(dba)_3$ and 20 mol % of TFP (trifurylphosphine) in THF, but only starting materials were recovered. However, when phenyliodide **60** was used as a cross-coupling partner, 72% of the desired product **61** was obtained. Encouraged by the partial success in the formation of disubstituted compound **61** with aryl iodide **62**, we focused our attention to the optimization of reaction conditions using vinyl triflate as a coupling partner.

Figure 4. Synthetic plan for altromycin B.



Based on our synthetic plan for the total synthesis of altromycin B (**7**), aryl triflate was considered as a practical coupling partner than aryl iodide because the aromatic portion in the altromycin B (**7**) could be derived from altromycin I (**14**) in which hydroxyl group at C5 position can be easily transformed to aryl triflate (Figure 4). Several different reaction conditions for the reaction beween glycal substituted vinylsilane **57** and phenyl triflate **58** were screened as shown in table 1. However, all efforts including changing ligand, base and additives did not provide desired β, β-disubstituted product. Only starting materials or the Hiyama type coupling product **62** were obtained.[42]

Table 1. Heck reaction of vinylsilane **57** and phenyl triflate **62**.



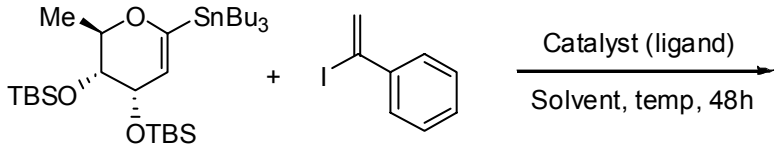
57 **58** **62**

cat (20 mol%)	ligand	base	additive	product
$Pd(OAc)_2$	none	K_2CO_3, NaOAc	LiCl	Starting materials
		Et_3N, NaOAc		
		Et_3N		
		K_2CO_3	TBACl	**62**
	BINAP		TBACl	**62** (81%)
	PPh_3		TBACl	**62**

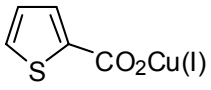
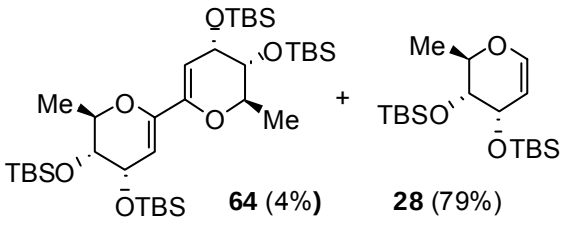
1. 2. 3. Experiments for the formation of C-glycoside linkage (Stille cross coupling reaction).

As our third choice for the formation of *C*-glycosidic linkage, Stille cross coupling between stannylated glycal **50** and α-iodo styrene **63** was conducted (Table 2).[39,40] Despite the similar examples in the literature, a variety of different reaction conditions proved ineffective.

Table 2. Stille reaction of stannylated glycal **50** and vinyl iodide **63**.



50 **63**

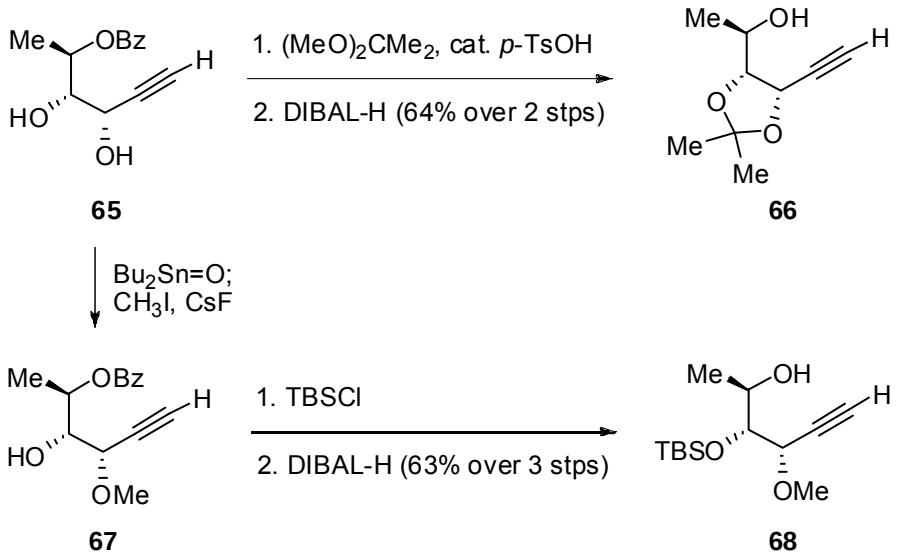
Catalyst (ligand)	Solvent	Temp	Product (analyzed by ^{1}H NMR)
$Pd(CH_3CN)_2Cl_2$	DMF	40 °C	Starting materials
	NMP	60 °C	
	THF	rt	
$Pd_2(dba)_3CHCl_3$ ($As(PPh_3)_3$), CuI	NMP	60 °C	No major spot on TLC complex ^{1}H NMR
CuTC (2 equiv.) 	DMF	0 °C	 **64** (4%) + **28** (79%)
	NMP	0 °C	

Starting materials were recovered in most cases and undesired homocoupling product **64** and destannylated glycal **28** were obtained when excess of CuTc (copper(I) thiophene-2-carboxylate) was used instead of palladium catalyst.[43] We assumed that the poor solubility of bis-TBS protected stannylated glycal **51** in polar solvents (DMF or NMP) could be problematic in the reaction.

1. 2. 4. Synthesis of branched *C*-Glycoside substructure of altromycin B**.**

To increase the polarity of the stannylated glycal, we decided to change the bis-TBS protecting group in alkynol to acetonide **66** or methyl ether **68** (Scheme 11).

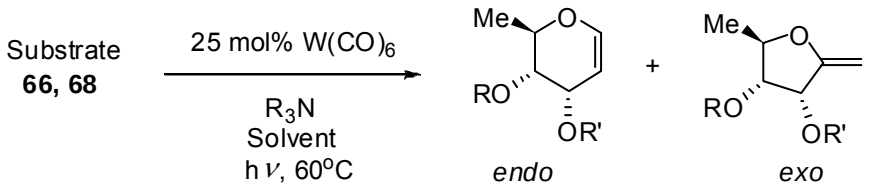
Scheme 11. Preparation of alkynyl alcohol **66** and **68**.



The acetonide protected alkynol **66** was prepared from the known diol **65**[28] through the sequence of acetonide protection followed by DIBAL reduction of the benzoate ester. Alternatively, regioselective methylation[44] followed by TBS protection of the free hydroxyl group and DIBAL reduction produced C4 methyl-protected alkynol **68**. Both alkynyl alchohols were tested for the tungsten-catalyzed cycloisomerization (Table 3). The alkynyl alcohol **68** gave poor *endo* selectivity as well as poor combined yields in the glycal formation. The crude ^{1}H

NMR of the product mixture suggested the formation of a minor amount of the *exo*cyclic product **72**, but this byproduct could not be isolated due to its stability.[45]

Table 3. Tungsten-catalyzed cycloisomerization of alkynol **66** and **68**.



endo *exo*

69 R, R' = Me_2C **70**
71 R = TBS, R' = Me **72**

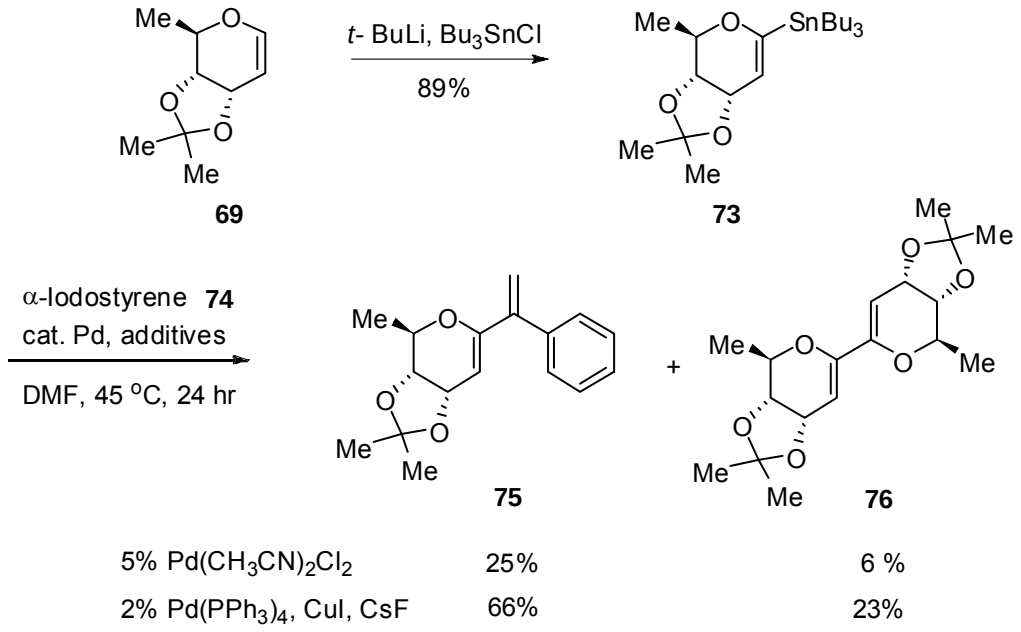
substrate	R_3N	solvent	product (ratio)[a]	combined yield (%)
66	Et_3N	THF	**69, 70** (7:1)	52
66	DABCO	THF	**69, 70** (10:1)	68
66	Et_3N	toluene	**69, 70** (8:1)	64
66	DABCO	toluene	**69** (*endo* only)	72[b]
68	DABCO	THF	**71, 72** (4:1)	33

[a] determined by ^1H NMR (400 MHz). [b] Isolated yield with 10 mol % $W(CO)_6$.

Even though the C4-methoxy substituted alkynyl alcohol can provide convenience in the synthesis of the west *C*-glycoside synthesis, the poor yields of the cycloisomerization made the synthesis less practical. However, cycloisomerization of acetonide protected alkynol **66** provided much better results. The choice of DABCO as the base and toluene as the solvent[46-48] in the presence of 10 mol% of $W(CO)_6$ provided only the *endo* glycal **69** in 72% isolated yield. The acetonide protective group in glycal **69** also proved ideal for conversion into the stannylated glycal **73** due to the tolerance of the acetonide

upon reaction with *t*-butyllithium, as well as solubility for subsequent transformations, relative to silyl ether protected glycals including **69**.

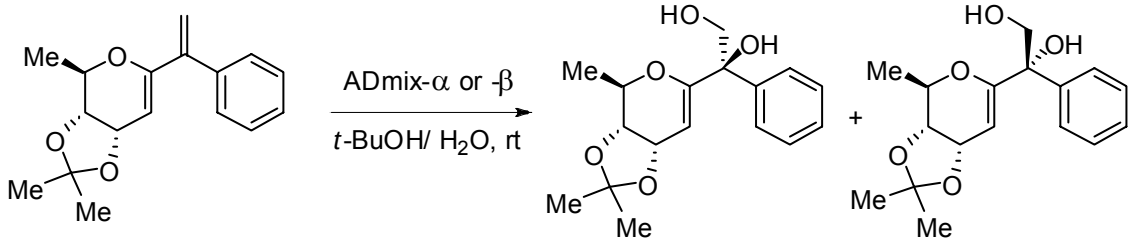
Scheme 12. Formation of *C*-glycosyl linkage via Stille cross coupling reaction.



Glycal **69** was treated with *t*-butyllithium and Bu_3SnCl to afford stannylated glycal **73** in 89% yield (Scheme 12). The Stille cross coupling reaction was initially conducted with 5 mol % of $Pd(CH_3CN)_2Cl_2$ as a catalyst in the presence of α-iodostyrene **74**.[40] The reaction was very sluggish and produced desired α-disubstituted diene **75** in 25% yield along with 6% of undesired homocoupling product **76**. Along with the low yielding process, this reaction conditions were not reproducible especially in large-scale reaction conditions. Under the optimization of the reaction conditions, satisfactory results were obtained by implementing

Baldwin's conditions.[49] The synergistic effect of CuI[49-52] and CsF in the presence of 2 mol % of $Pd(PPh_3)_4$ in the reaction dramatically increased reactivity and produced desired product **75** in 66% yield along with 23% of undesired dimer product **76**. The reaction conditions provide a robust solution for this important transformation in our synthesis even for large-scale reaction.

Scheme 13. Preparation of diol **77** and **78**.

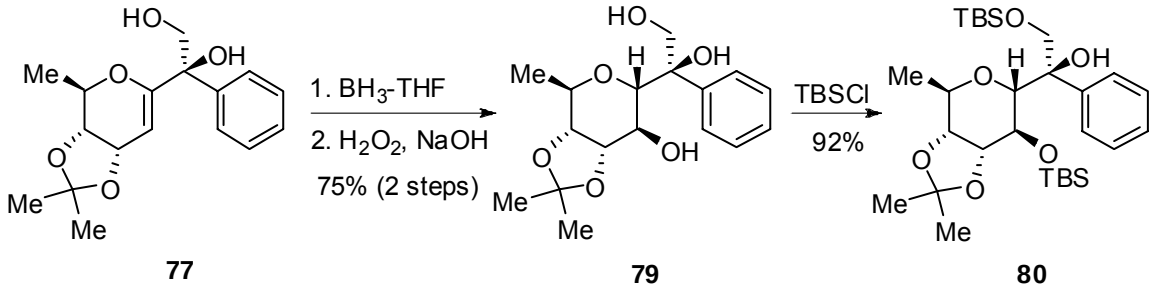


75 **77** **78**

ADmix-α	92%	0.9	:	1.0
ADmix-β	93%	3.6	:	1.0

α-Disubstituted diene **75** was used for the next regioselective dihydroxylation reaction (Scheme 13).[53] Both AD-mix α and β proved to be effective and the reaction occurred only in the less hindered alkene to provide both separable diol **77** and **78** in 0.9 : 1.0 ratio with AD-mix α, and 3.6 : 1.0 with AD-mix β. Since the stereochemistry of C13 hydroxyl group has not been conclusively determined, both diastereomers were used for the further transformations. The absolute stereochemistry of both C13 hydroxyl diastereomers **76** and **77** was confirmed by X-ray crystallography and nOe studies in the later stage of the synthesis.

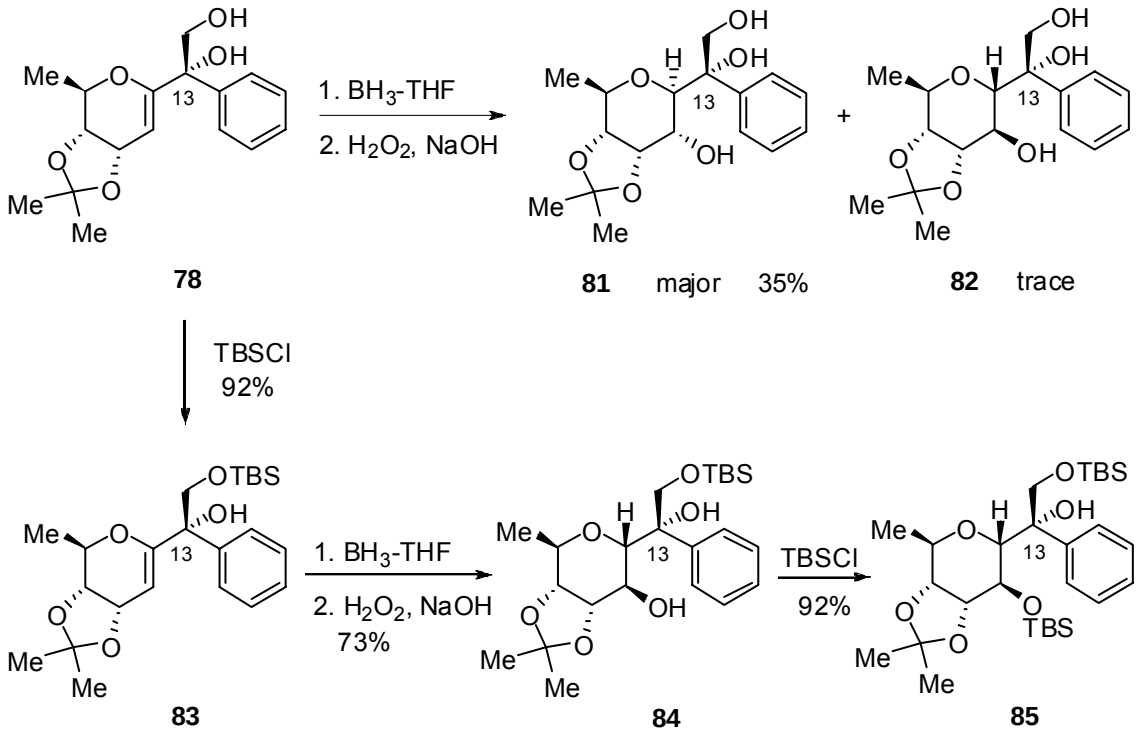
Scheme 14. Synthesis of bis-TBS protected alcohol **80**.



77 **79** **80**

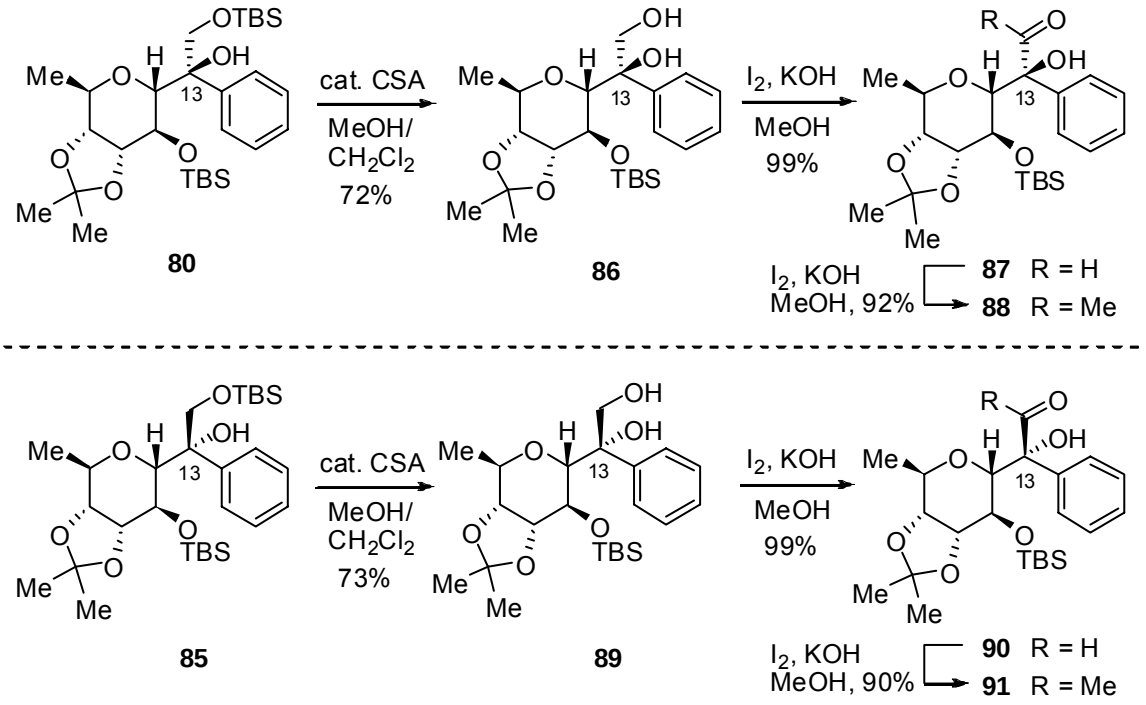
Treatment of diol **77** with borane-THF followed by $NaOH/H_2O$ provided triol product **79** in which the newly produced hydroxyl group has the opposite stereochemistry relative to the adjacent acetonide protected group (Scheme 14). The prepared triol **79** was then treated with TBSCl to give bis-TBS protected alcohol **80**. However, when the other diol isomer**78** was subjected in the same reaction conditions, undesired product **81** was obtained in 35% yield as a major product along with a trace amount of desired product **82** as a minor product (Scheme 15). We postulated that the primary hydroxyl group might affect the stereochemistry of hydroboration by forming 6-membered boracyclic transition state.[54-56] Under this assumption, we decided to protect the primary hydroxyl group in diol **78** as a silylether to prevent the interaction between primary hydroxyl group and borane reagent. Hydroboration-oxidation of TBS ether **83** gave desired stereoisomer **84** consistent with sterically controlled addition in good yield under normal reaction conditions. The diol **84** was then treated with TBSCl to produce bis-TBS protected alcohol **85**.

Scheme 15. Synthesis of bis-TBS protected alcohol **85**.



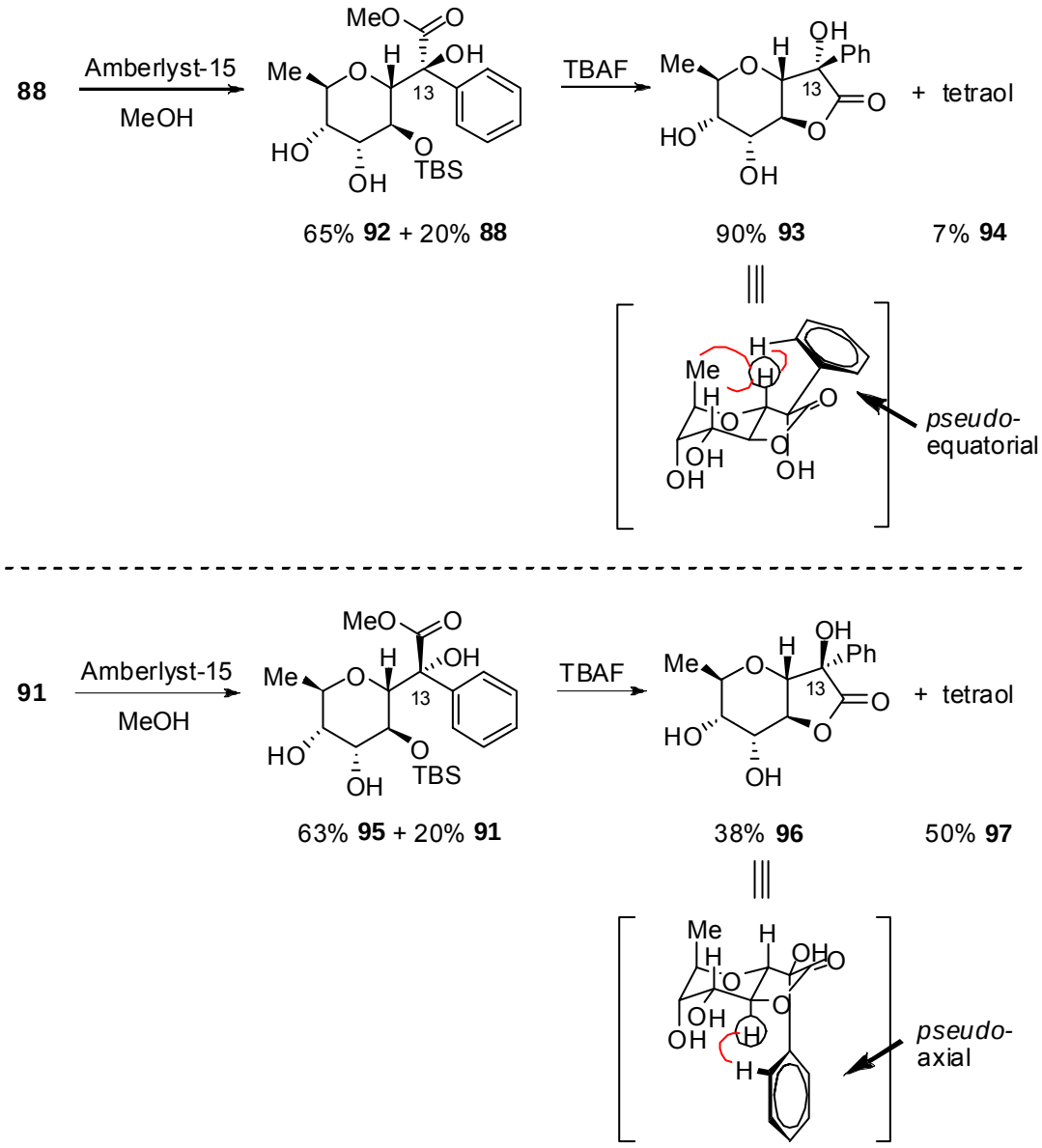
Both compound **80** and **85** were separately used for the same sequences for the methyl ester formation (Scheme 16). The bis-TBS protected alcohol **80** and **85** underwent selective deprotection process in the presence of 10 mol % of CSA in a mixture of MeOH and CH_2Cl_2 at 0 ^oC to produce primary alcohols **86** and **89**.[57] Parikh-Doering oxidation[58] of alcohol to aldehydes **87** and **90** followed by further oxidation by I_2/KOH under MeOH gave methyl esters **88** and **91**.[59]

Scheme 16. Synthesis of esters **88** and **91**.



Removal of acetonide protecting group in **88** and **91** under acidic conditions produced both acetonide deprotected diastereomers **92** and **95** in 65% and 63% yield along with 20 % of unreacted starting materials in both cases (Scheme 17). Removal of the TBS protecting group with TBAF provided a mixture of 5-6 fused lactones **93** and **96**.

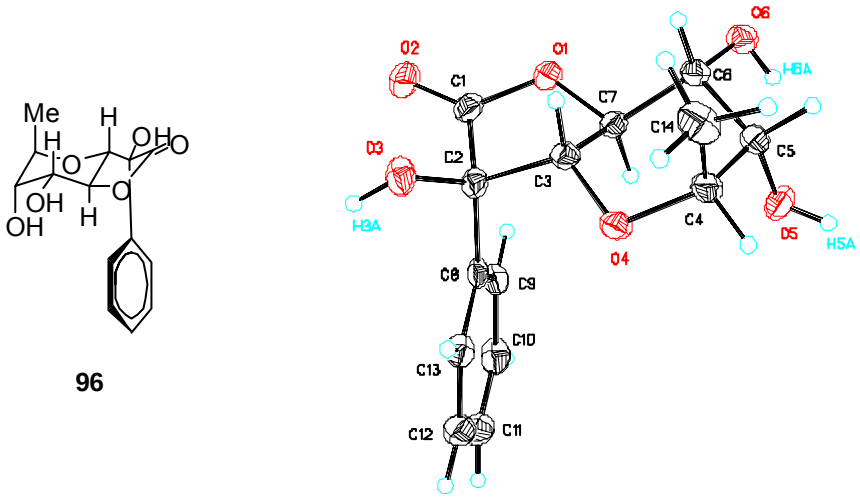
Scheme 17. Synthesis of bicyclic lactones **93** and **96**.



However, the reactivity of two diastereomers **92** and **95** in the lactonization step was significantly different. Treatment of **92** under simple TBAF-mediated desilylation condition produced 5-6-fused lactone **93** in 90% yield along with 6% of simply deprotected tetraol **94**. The high yield in this lactonization process was

presumed by the favorable configuration of the lactone product **93** in which the large phenyl group is placed in the *pseudo* equatorial position. In the case of the other lactone diastereomer **96**, the large phenyl group is in the *pseudo* axial position and disfavored the formation of lactone. As a result, tetraol **97** was obtained in 50% as a major product.

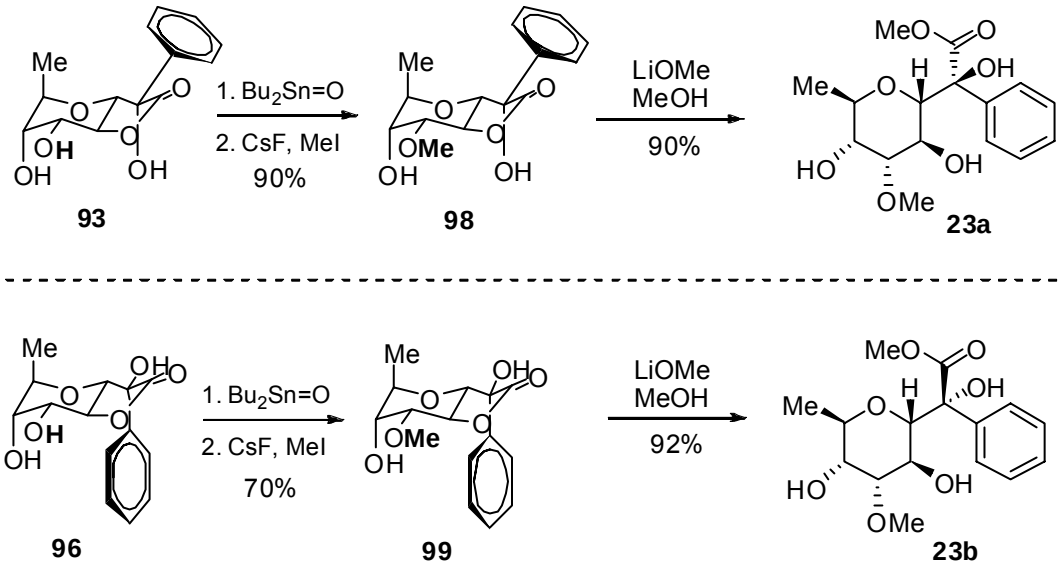
Figure 5. X-ray crystal structure of compound **96**.



The lactone formation step in this synthesis is very important because these two equatorial and axial hydroxyl groups in both lactone **93** and **96** can be differentiated in the next methylation step. With the importance of the formation of lactone in mind, we tried to convert the tetraol **97** to lactone **96**. However, all our efforts under various acidic or basic conditions were unsuccessful. In this stage, we could unambiguously determine the absolute stereochemistry of both C13 diastereomers by nOe for compound **93**, and X-ray crystallography experiments for compound **96**. The obtained lactones **93** and **96** were utilized for

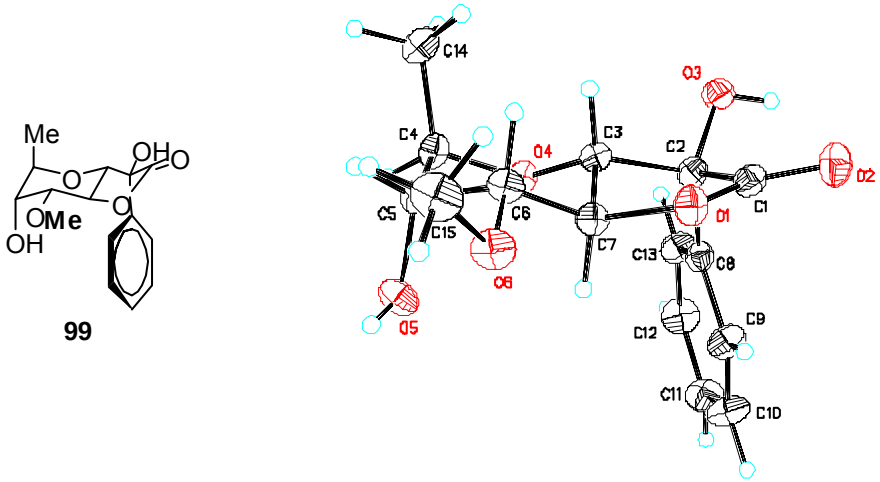
the final products through a sequence of regioselective methylation at C4 equatorial hydroxyl group via tin acetal formation followed by methyl addition.[44]

Scheme 18. Completion of synthesis.



The syntheses of both possible altromycin branched glycoside substructures **23a** and **23b** were completed by regioselective methylation of the equatorial hydroxyl group, followed by methanolysis of lactones **98** and **99**. Opening of the lactones **98** and **99** to the methyl ester of target compounds **23a** and **23b** were initially accomplished by acidic methanolysis (Amberlyst-15, MeOH),[60] but better yields were consistently obtained by basic methanolysis.[61] The ^{1}H NMR spectra for our synthetic compounds **23a** and **23b** matched the data published by Pasetto and Franck for these two compounds.[25]

Figure 6. X-ray crystal structure of compound **99**.



1. 3. Conclusions.

Both possible diastereomers of the west *C*-glycoside substructures **23a** and **23b** of altromycin B (**7**) were successfully synthesized. Tungsten-catalyzed alkynol cycloisomerization was utilized as a key step for the preparation of the altrose moiety in high yield and with high *endo* selectivity. The Stille cross couping reaction was applied to the formation of *C*-glycosyl linkage between aromatic portion and altrose glycal. The stereochemistry of the west *C*-glycoside substructures **23a** and **23b** of altromycin B (**7**) was unambiguously determined by ^{1}H, ^{13}C NMR, X-ray crystallography and nOe experiments.

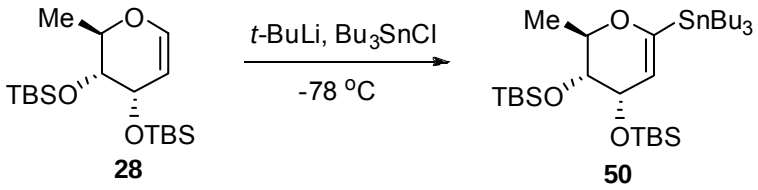
1. 4. Experimental Section.

General: ^{1}H NMR and ^{13}C NMR spectra were recorded on a Varian INOVA-400 spectrometer (400 MHz for ^{1}H, 100 MHz for ^{13}C), or on an INOVA-600 spectrometer (600 MHz for ^{1}H, 150 MHz for ^{13}C). NMR spectra were recorded on solutions in deuterated chloroform ($CDCl_3$), with residual chloroform (δ 7.26 ppm for ^{1}H NMR and δ 77.0 ppm for ^{13}C NMR) or deuterated methyl sulfoxide (DMSO-d_6), with residual methyl sulfoxide (δ 2.50 ppm for ^{1}H NMR and δ 35.0 ppm for ^{13}C NMR) 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; q, quartet; m, multiplet. IR spectra were collected on a Mattson Genesis II FT-IR spectrometer 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. Elemental analyses were performed by Atlantic Microlab Inc, P. O. Box 2288, Norcross, Georgia. Melting points were determined with a Fisher-Johns melting point apparatus. Optical rotations were measured at 23°C (concentration in g/100 mL) using a Perkin-Elmer 341 polarimeter. Analytical Thin Layer Chromatography (TLC) was performed on precoated glass backed plates purchased from Whatman (silica gel $60F_{254}$; 0.25mm thickness). Flash column chromatography was carried out with silica gel 60 (230-400 mesh ASTM) from EM Science.

All reactions were carried out with anhydrous solvents in oven-dried or flame-dried and nitrogen- or argon-charged glassware. All anhydrous solvents except

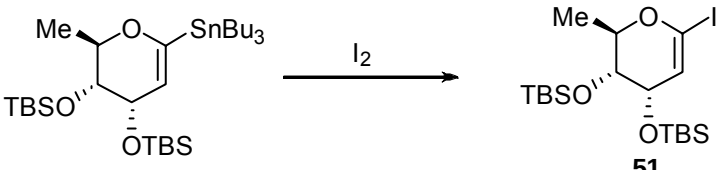
as mentioned were dried with 3 or 4 Å molecular sieves (beads) purchased from Aldrich and tested for trace water content with Coulometric KF Titrator from Denver Instruments. All solvents used in extraction procedures and chromatography were used as received from commercial suppliers without prior purification. 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 Aldrich or Strem Chemicals.

Preparation of iodoglycal 51.



Stannylated glycal 51. The known glycal **28**[28] (0.25 g, 0.70 mmol) was dissolved in THF (3 mL), cooled to -78°C, and *t*-BuLi (1.44 mL, 1.7 M solution in pentane) was added dropwise over 10 minutes at -78°C. The reaction mixture was stirred at -78°C for additional 30 minutes and then stirred for 30 minutes at 0°C. The resulting mixture was cooled to -78°C and Bu_3SnCl (0.60 mL, 2.4 mmol) was added and the mixture was stirred for additional 1 hour at -78°C. The resulting mixture was diluted with Et_2O (3 mL) and quenched with water (3 mL). After extraction with Et_2O (3 × 5 mL), the combined organic layers were dried over Na_2SO_4 and evaporated. Chromatography (hexanes : EtOAc = 80 : 1 to 40 : 1) afforded tributylstannyl glycal **50** (0.38 g, 84%) as a colorless oil. ^{1}H NMR

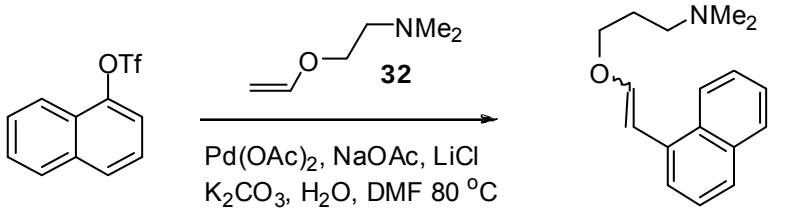
(400 MHz, $CDCl_3$) δ 4.78 (d, *J* = 5.6 Hz, 1H), 3.98 (dq, *J* = 6.4, 9.6 Hz, 1H), 3.90 (dd, *J* = 5.6, 9.2 Hz, 1H), 1.55-1.47 (m, 6H), 1.36-1.26 (m, 15H), 1.22 (d, *J* = 6.4 Hz, 3H), 0.99-1.39 (s, 3H), 0.07 (s, 6H), 0.06 (s, 3H), 0.05 (s, 3H).



50 **51**

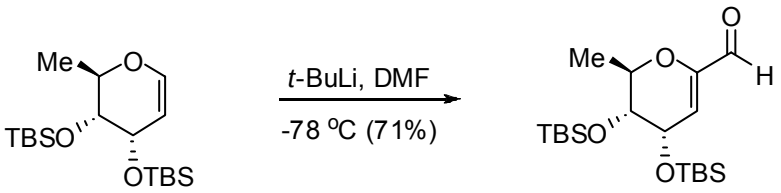
Iodo glycal 51. To a solution of stannylated glycal **50** (0.18 g, 0.27 mmol) in dry CH_2Cl_2 (5 mL) was added I_2 (0.77 g, 0.29 mmol) in dry CH_2Cl_2 (3 mL) dropwise at 0 ^oC. The reaction mixture was stirred for 1 hr at 0 ^oC and then quenched with sat. aq $Na_2S_2O_4$ (2 mL). The resulting mixture was extracted with Et_2O (3 × 5 mL) and the combined organic layers were dried over $MgSO_4$ and evaporated. Chromatography (hexanes : EtOAc = 80 : 1 to 40 : 1) afforded iodo glycal **51** (0.10 g, 76%) as a yellowish oil. ^1H NMR (400 MHz, $CDCl_3$) δ 5.28 (d, *J* = 6.4 Hz, 1H), 4.39 (dq, *J* = 6.4, 9.6 Hz, 1H), 3.88 (dd, *J* = 3.6, 6.4 Hz, 1H), 3.55 (dd, *J* = 6.4, 10.2 Hz, 1H), 1.31 (d, *J* = 6.4 Hz, 3H), 0.90 (s, 9H), 0.88 (s, 9H), 0.08 (s, 6H), 0.07 (s, 3H), 0.06 (s, 3H).

Heck reaction of 53 with 32.



53 **54** cis : trans = 3 : 2

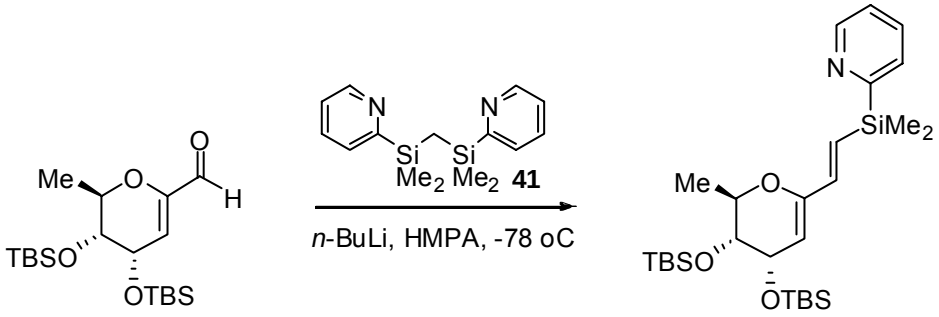
Compound 54. Naphthyl triflate **53** (0.10 g, 0.36 mmol) and vinylether **32** (0.083 g, 0.72 mmol) were dissolved in dry DMF (1.5 mL) and $Pd(OAc)_2$ (10 mg, 0.045 mmol), NaOAc (36 mg, 0.43 mmol), LiCl (30 mg, 0.72 mmol), K_2CO_3 (60 mg, 0.43 mmol) and H_2O (0.20 ml) were added in order. The mixture was then degassed by three cycles of the standard freeze-thaw method. The flask was sealed and the reaction mixture was stirred for 24 hours at 80 ^oC. After cooling, the reaction mixture was diluted with Et_2O (2 mL) and then washed with 0.1 M NaOH (2 × 0.5 mL). The organic layer was separated and the aqueous layer was extracted with Et_2O (3 × 3 mL). The organic layer was dried over K_2CO_3 and volatile components were removed under reduced pressure. The coupling product **54** (0.12 g) was obtained inseparable mixture of *cis* and *trans* (*cis* : *trans* = 3 : 2) as a yellowish oil. ^1H data is same as the known compound.[30]



28 **56**

Aldehyde 56. To a solution of glycal **28** (0.65 g, 1.81 mmol) in dry THF (2 mL) was added *t*-BuLi (2.66 ml, 1.7 M in pentane) at –78 ^oC dropwise. The reaction mixture was stirred at -78^oC for additional 30 minutes and then stirred for 30 minutes at 0 ^oC. The resulting mixture was cooled to –78 ^oC, DMF (5.0 mL) quickly added, and the mixture was stirred for additional 1 hour at 0 ^oC. The reaction was diluted with Et_2O (3.0 mL) and then quenched with aq. sat. NH_4Cl (2.0 mL). The organic layer was separated and the aqueous layer was extracted with Et_2O (3 × 3.0 mL). The organic layer was dried over Na_2SO_4 and volatile

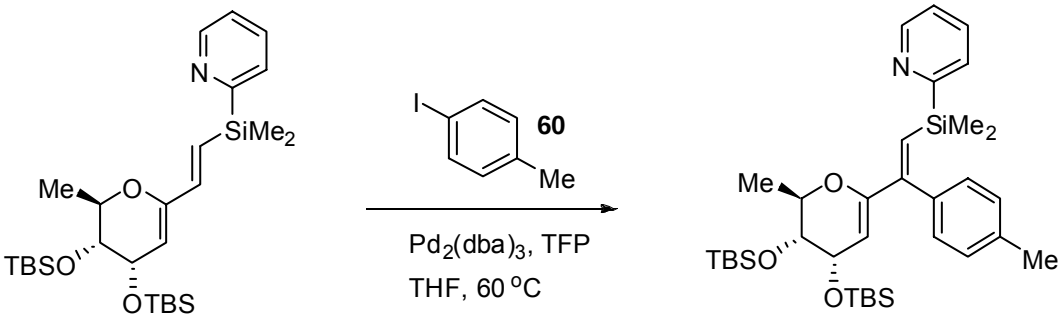
components were removed under reduced pressure. Chromatography (hexanes : EtOAc = 10 : 1) gave the aldehyde **56** (0.50 g, 71%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.20 (s, 1H), 5.73 (d, *J* = 5.6 Hz, 1H), 4.30-4.24 (m, 2H), 3.56 (dd, *J* = 3.6, 8.8 Hz, 1H), 1.38 (d, *J* = 6.4 Hz, 3H), 0.91 (s, 9H), 0.89 (s, 9H), 0.11 (s, 3H), 0.10 (s, 3H), 0.09 (s, 6H).



56 **57**

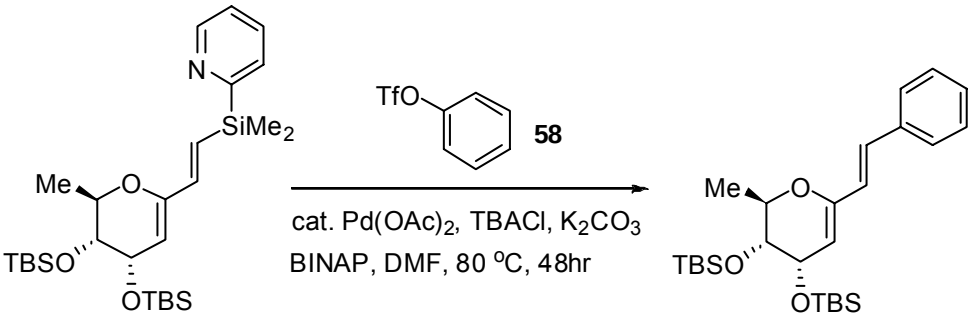
Compound 57. Bis(2-pyridyldimethyl)silane **41** (0.48 g, 1.67 mmol) was dissolved in dry THF (2 mL) and HMPA (0.46 ml, 2.58 mmol) was added and then cooled to –78 ^{o}C. *n*-BuLi (0.97 ml, 1.6 M in hexane) was added dropwise at –78 ^{o}C and then stirred for 1 hr. The reaction mixture was slowly cannulated to the cold (–78 ^{o}C) THF (2 mL) solution containing aldehyde **56** (0.50 g, 1.29 mmol). The reaction mixture was stirred for 30 min at –78 ^{o}C and then slowly warmed to room temperature and stirred for 1 h. The reaction mixture was diluted with Et_2O (4.0 mL) and quenched with aq. sat. NH_4Cl (4.0 mL). The organic layer was separated and the aqueous layer was extracted with Et_2O (3 × 5.0 mL). The organic layer was dried over Na_2SO_4 and volatile components were removed under reduced pressure. Chromatography (Hexanes : EtOAc = 15 : 1) gave product **57** (0.54 g, 81%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.79 (d, *J* = 4.4 Hz, 1H), 7.59 (t, *J* = 7.2 Hz, 1H), 7.53 (d, *J* = 7.2 Hz, 1H), 7.21 (t, *J* = 5.6

Hz, 1H), 6.43 (d, *J* = 18.8 Hz, 1H), 6.30 (d, *J* = 18.8 Hz, 1H), 4.87 (d, *J* = 5.6 Hz, 1H), 4.18 (dq, *J* = 6.4, 9.6 Hz, 1H), 4.07 (dd, *J* = 3.6, 6.0 Hz, 1H), 3.50 (dd, *J* = 3.6, 6.0 Hz, 1H), 1.33 (d, *J* = 6.4 Hz, 3H), 0.91 (s, 9H), 0.87 (s, 9H), 0.43 (s, 6H), 0.06 (s, 9H), 0.05 (s, 3H).



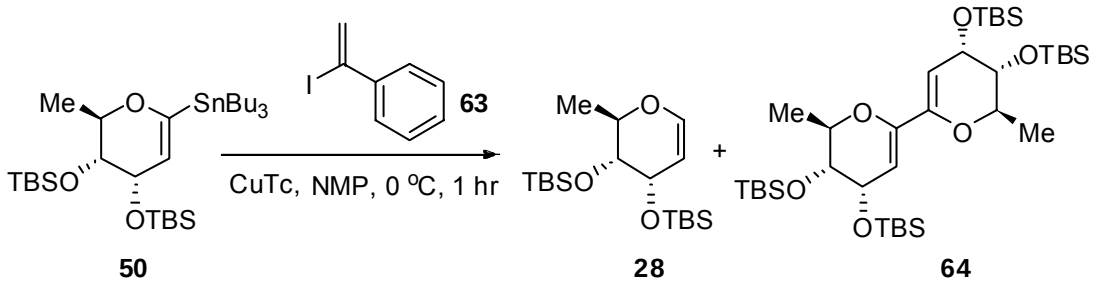
Compound 61. To a dry solution of $Pd_2(dba)_3$ (2.7 mg, 2.5 μmol) and TFP (2.4 mg 10 μmol) in dry THF (0.5 mL) was added 4-iodotoluene (14 mg, 60 μmol), compound **57** (25 mg, 50 μmol) and Et_3N (8 μL, 75 μmol). The mixture was then degassed by three cycles of the standard freeze-thaw method. The flask was sealed and the reaction mixture was stirred for 48 h at 60 ^oC. After cooling, the reaction mixture was diluted with Et_2O (2 mL) and then filtered through celite. The filtrate was washed with water and then extracted with Et_2O (3 × 3.0 mL). The organic layer was dried over $MgSO_4$ and volatile components were removed under reduced pressure. Chromatography (Hexanes : EtOAc = 15 : 1) gave the coupling product **61** as a colorless oil (25 mg, 72%). ^1H NMR (300 MHz, $CDCl_3$) δ 8.78 (d, *J* = 4.5 Hz, 1H), 7.58-7.54 (m, *J* = 7.2 Hz, 2H), 7.30-7.27 (m, 2H), 6.03 (s, 1H), 4.77 (d, *J* = 6.0 Hz, 1H), 4.03 (dq, *J* = 6.3, 9.6 Hz, 1H), 3.93 (dd, *J* = 3.3, 5.7 Hz, 1H), 3.70 (dd, *J* = 3.3, 9.6 Hz, 1H), 2.35 (s, 3H), 1.02 (d, *J* = 6.3 Hz, 3H),

0.88 (s, 9H), 0.86 (s, 9H), 0.49 (s, 3H), 0.47 (s, 3H), 0.05 (s, 3H), 0.04 (s, 3H), -0.02 (s, 3H), -0.05 (s, 3H).



Compound 62. Compound **57** (50 mg, 96 μmol) and phenyl triflate **58** (32 mg, 0.14 mmol) were dissolved in dry DMF (1.0 mL) and $Pd(OAc)_2$ (2.2 mg, 9.6 μmol), TBACl (27 mg, 96 μmol), K_2CO_3 (33 mg, 0.24 mmol) and BINAP (11 mg, 19 μmol) were added in order. The mixture was then degassed by three cycles of the standard freeze-thaw method. The flask was sealed and the reaction mixture was stirred for 48 h at 80 °C. After cooling, the reaction mixture was diluted with Et_2O (2 mL) and then filtered through celite. The organic layer was separated and the aqueous layer was extracted with Et_2O (3 × 3.0 mL). The organic layer was dried over $MgSO_4$ and volatile components were removed under reduced pressure. Chromatography (Hexanes : EtOAc = 15 : 1) gave the coupling product **62** as a colorless oil (35 mg, 81%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43-7.40 (m, 2H), 7.33-7.30 (m, 2H), 7.25-7.21 (m, 1H), 6.92 (d, *J* = 16.0 Hz, 1H), 6.40 (d, *J* = 16.0 Hz, 1H), 4.94 (d, *J* = 5.6 Hz, 1H), 4.25 (dq, *J* = 6.4, 10.0 Hz, 1H), 4.12 (dd, *J* = 3.6, 5.6 Hz, 1H), 3.55 (dd, *J* = 7.2, 9.6 Hz, 1H), 1.39 (d, *J* = 6.4 Hz, 3H), 0.93 (s, 9H), 0.88 (s, 9H), 0.10 (s, 3H), 0.09 (s, 3H), 0.08 (s, 3H), 0.07 (s, 3H).

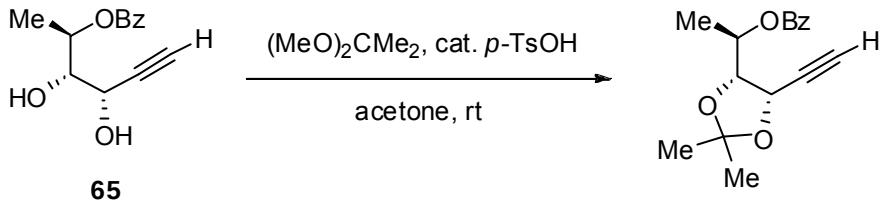
Stille coupling reaction between 50 and 63.



50 **28** **64**

Compound 28 and 64. To a solution of stannylated glycal **50** (0.11 g, 0.18 mmol) and iodostyrene **63** (52 mg, 0.21 mmol) in dry NMP (1.0 mL) was added Copper(I) thiocarboxylate (CuTc) (50 mg, 0.26 mmol) at 0°C. The reaction mixture was stirred for 1 h at 0 °C. The reaction was diluted with Et_2O (1.0 mL) and then filtered through a short pad of alumina. All volatiles were removed under reduced pressure and chromatography (Hexanes : EtOAc = 15 : 1) gave separable known glycal **28** (50 mg, 79%) and homocoupling product **64** (5 mg, 4%). ^{1}H NMR for compound **59**: (400 MHz, $CDCl_3$) δ 5.29 (d, *J* = 5.6 Hz, 1H), 4.17 (dq, *J* = 6.4, 9.2 Hz, 1H), 4.10 (dd, *J* = 3.6, 5.6 Hz, 1H), 3.49 (dd, *J* = 3.6, 9.6 Hz, 1H), 1.31 (d, *J* = 6.4 Hz, 3H), 0.90 (s, 9H), 0.87 (s, 9H), 0.07 (s, 3H), 0.06 (s, 3H), 0.05 (s, 6H).

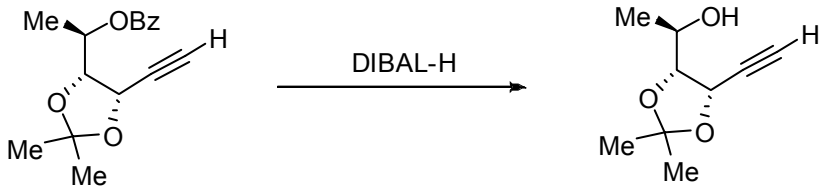
Preparation of alkynyl alcohol 66



65

Protection of diol 65. The alkynyl diol **65**[28] (11.3 g, 45.7 mmol) was dissolved in dry acetone (100 mL), and while stirring at room temperature 2,2-dimethoxypropane (28.0 mL, 228 mmol) was added followed by a catalytic

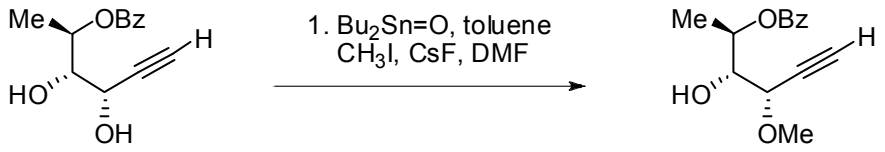
amount of *para*-toluenesulfonic acid (*p*-TsOH, 0.870 g, 4.57 mmol). The reaction mixture was stirred overnight at room temperature. The resulting mixture was quenched with triethylamine (2 mL) and volatile components were removed under reduced pressure. Chromatography (hexanes : EtOAc = 20 : 1) gave the acetonide protected benzoate ester (10.7 g, 85%) as a colorless oil. $[\alpha]^{23}_{D}$ = -43.6 (*c* = 0.96, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01-7.99 (m, 2H), 7.57-7.53 (m, 1H), 7.45-7.41 (m, 2H), 5.37 (dq, *J* = 6.4, 8.0 Hz, 1H), 4.94 (dd, *J* = 2.4, 6.4 Hz, 1H), 4.28 (dd, *J* = 6.4, 8.0 Hz, 1H), 1.56 (s, 3H), 1.51 (d, *J* = 6.0 Hz, 1H), 1.39 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.31, 132.91, 130.19, 129.63, 129.51, 128.29, 110.81, 79.47, 78.93, 76.08, 70.95, 68.07, 27.28, 25.80, 17.32; IR (neat) 2988, 2937, 2879, 2119, 1969, 1941, 1721cm^{-1}; HRMS (FAB$^+$) Calcd. For $C_{16}H_{18}O_4Li$ [$(M+Li)^+$] 281.1365, Found 281.1378; Anal. Calcd for $C_{16}H_{18}O_4$: C, 70.06; H, 6.61; O, 23.33. Found: C, 69.88; H, 6.64; O, 23.55.



66

Alkynyl alcohol 66. The benzoate ester prepared above (10.7 g, 38.8 mmol) was dissolved in CH_2Cl_2 (40 mL), cooled to -78^{o}C, and DIBAL-H (78 mL, 1M solution in CH_2Cl_2) was added dropwise over 30 minutes at -78^{o}C. The reaction mixture was stirred for additional 30 minutes at -78^{o}C. The reaction mixture was then quenched with a -78^{o}C solution of EtOAc (150 mL) and poured into a cold aqueous solution of Rochelle's salt (150 mL). The resulting mixture was stirred until two layers were clearly separated, and then extracted with EtOAc (3 × 50

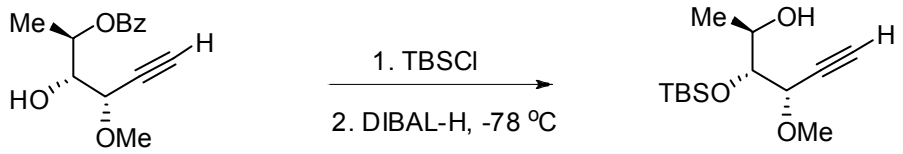
mL). The combined organic layers were dried over Na_2SO_4 and evaporated, and chromatography (hexanes : EtOAc = 10 : 1) afforded alkynyl alcohol **66** (4.95 g, 75%) as a colorless oil. $[\alpha]^{23}_D$ = -28.1 (*c* = 0.94, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.89 (dd, *J* = 2.0, 5.6 Hz, 1H), 4.10 (dq, *J* = 6.4, 8.0 Hz, 1H), 3.89 (dd, *J* = 5.6, 8.0 Hz, 1H), 2.64 (d, *J* = 4.4 Hz, -OH), 1.48 (s, 3H), 1.31 (s, 3H), 1.29 (d, *J* = 2.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 110.56, 81.62, 80.04, 76.24, 67.83, 67.39, 27.37, 25.74, 20.16; IR (neat) 3436 (br), 3289, 2922, 2851, 2114, 1372, 1229, 1070 cm^{-1}; HRMS (FAB^+) Calcd. For $C_9H_{15}O_3$, $[(M+H)^+]$ 171.1021, Found 171.1026. Anal. Calcd for $C_9H_{14}O_3$: C, 63.51; H, 8.29; O, 28.20. Found: C, 61.21; H, 8.06; O, 28.86.



65 **67**

Compound 67. Dean-Stark column was fitted into 100 mL round bottom flask containing a solution of known diol **65**[28] (2.30 g, 9.82 mmol) and dibutyltin oxide (3.08 g, 10.8 mmol) in toluene (50 mL). The reaction mixture was refluxed for 5 hours and then cooled to room temperature. Solvent was removed under reduced pressure and refilled with dry DMF (50 mL). CsF (2.98 g, 19.6 mmol) and MeI (3.05 mL, 49.1 mmol) were added and stirred vigorously for 48 hours at room temperature. The reaction mixture was extracted with Et_2O (3 × 20 mL) and washed with brine (2 × 20 mL). Combined organic layer was dried over $MgSO_4$

and chromatography (Hexanes : EtOAc = 4 : 1) gave monomethylated compound **67** as a colorless oil (2.04 g, 84% yield).



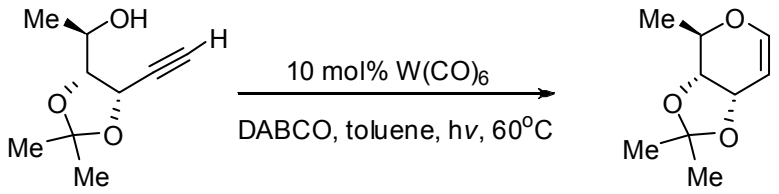
67 **68**

TBS protection of alcohol 67. To a solution of monomethylated compound 67 (1.16 g, 4.67 mmol) in DMF (5 mL) was added imidazole (1.91 g, 28.0 mmol) and TBSCl (2.10 g, 14.0 mmol) were added, and the reaction mixture was stirred for 5 hours at room temperature. The resulting mixture was diluted with Et_2O (2 mL) and extracted with Et_2O (3 $\times$ 10 mL). The combined organic layers were dried over Na_2SO_4 and evaporated. Chromatography (hexanes : EtOAc = 20 : 1) gave TBS protected ester (1.50 g, 85% yield) as a colorless oil.

Alkynyl alcohol 68. Following the same procedure for alkynyl alcohol **66**, ester (1.50 g, 3.98 mmol) in dry CH_2Cl_2 (5 mL), and DIBAL-H (9.95 mL, 1 M in CH_2Cl_2) gave alkynyl alcohol **68** (0.719 g, 70% yield) as a colorless oil.

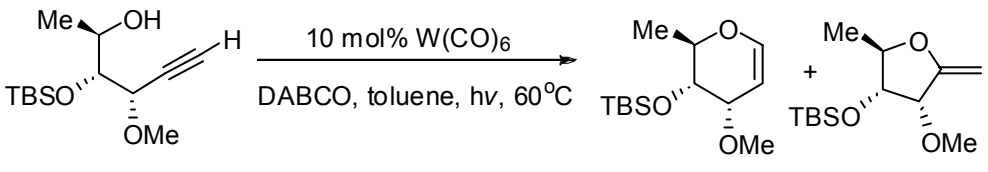
^{1}H NMR (400 MHz, $CDCl_3$) δ 4.06 (dd, *J* = 2.0, 4.8 Hz, 1H), 3.91 (app h, *J* = 6.4 Hz, 1 H), 3.67 (t, *J* = 5.2 Hz, 1H), 3.41 (s, 3H), 2.46 (d, *J* = 2.0 Hz, 1H), 1.21 (d, *J* = 6.4 Hz, 3H), 0.91 (s, 9H), 0.14 (s, 3H), 0.10 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 80.67, 77.62, 75.66, 73.50, 69.28, 56.64, 25.96, 18.26, -4.10, -4.48; IR (neat) 3410 (br), 2930, 2114, 1252, 1090 cm^{-1}; HRMS (FAB^+) Calcd for $C_{13}H_{26}O_3SiLi$ [$(M+Li)^+$] 265.1811, Found 265.1802; Anal. Calcd for $C_{13}H_{26}O_3Si$: C, 60.31; H, 10.24. Found: C, 60.38; H, 10.30.

Cycloisomerizations of alkynyl alcohols 66 and 68



66 **70**

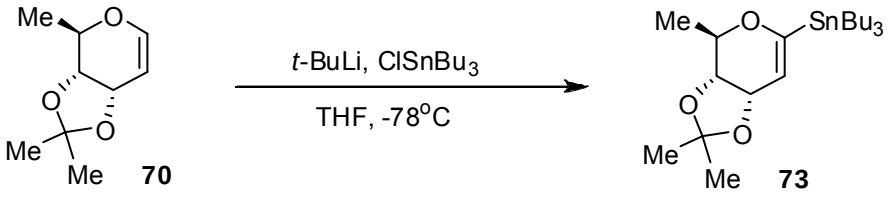
Glycal 70. Alkynyl alcohol **66** (9.74 g, 57.2 mmol) was dissolved in toluene (50 mL) with stirring, and $W(CO)_6$ (2.0 g, 0.97 mmol) and DABCO (12.8 g, 114 mmol) were added. The flask was fitted with reflux condenser and then placed into Rayonet photoreactor under an atmosphere of argon. The reaction mixture was irradiated at 350 nm at 60 ^oC for 12 h, with stirring. The resulting solution was then directly applied to a silica gel chromatography column (pentanes : ether = 8 : 1) and removal of solvent under reduced pressure at 10 ^oC gave volatile glycal **70** (7.01 g, 72%) as a colorless oil. $[\alpha]^{23}_D$ = +184.4 (*c* = 1.07, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 6.56 (d, *J* = 5.6 Hz, 1H), 5.08 (dd, *J* = 5.6 Hz, 1H), 4.40 (dd, *J* = 5.6 Hz, 1H), 3.69 (dd, *J* = 5.6, 6.4 Hz, 1H), 3.45 (dq, *J* = 6.4, 12.4Hz, 1H), 1.44 (s, 3H), 136 (s, 3H), 1.34 (d, *J* = 2.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.24, 108.15, 99.09, 75.81, 71.96, 67.76, 28.53, 25.71, 16.91; IR (neat) 3067, 2985, 2935, 2876, 2116, 1911, 1851, 1642, 1373, 1062 cm^{-1}; HRMS (EI) Calcd. For $C_9H_{14}O_3$ [M^+] 170.09429, Found 170.09413; Anal. Calcd for $C_9H_{14}O_3$: C, 63.51; H, 8.29; O, 28.20. Found: C, 63.52; H, 8.41; O, 27.99.



68 **71** **72**

Glycal 71. Alkynyl alcohol **68** (1.38 g, 5.34 mmol) was dissolved in dry THF (10 mL) with stirring, and $W(CO)_6$ (0.47 g, 1.3 mmol) and DABCO (1.20 g, 10.68 mmol) were added. The Pyrex flask was fitted with a reflux condenser and irradiated at 350 nm (Rayonet photoreactor) at 60ºC for 12 hours under argon, with stirring. Evaporation of solvent followed by silica gel chromatography (hexanes : ethyl acetate (95:5, 1% Et_3N) gave glycal **71** (0.45 g, 33%) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.38 (d, *J* = 6.0 Hz, 1H), 4.92 (t, *J* = 6.0 Hz, 1H), 4.07 (dq, *J* = 6.4, 10 Hz, 1 H), 3.61 (dd, *J* = 3.6, 10.0 Hz, 1H), 3.56 (dd, *J* = 3.6, 5.6 Hz, 1H), 3.43 (s, 1H), 1.30 (d, *J* = 6.0 Hz, 3H), 0.93 (s, 9H), 0.12 (s, 3H), 0.11 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.30, 98.63, 73.87, 72.30, 71.19, 56.95, 25.86, 18.20, 17.83, -4.16, -4.76; IR (neat) 3064, 2955, 2930, 2858, 1642, 1242, 1142, 1090, 837 cm^{-1}; HRMS (FAB$^+$) Calcd for $C_{13}H_{26}O_3SiLi$ [(M+Li)$^+$] 265.1811, Found 265.1800; Anal. Calcd for $C_{13}H_{26}O_3Si$: C, 60.31; H, 10.24. Found: C, 60.42; H, 10.31.

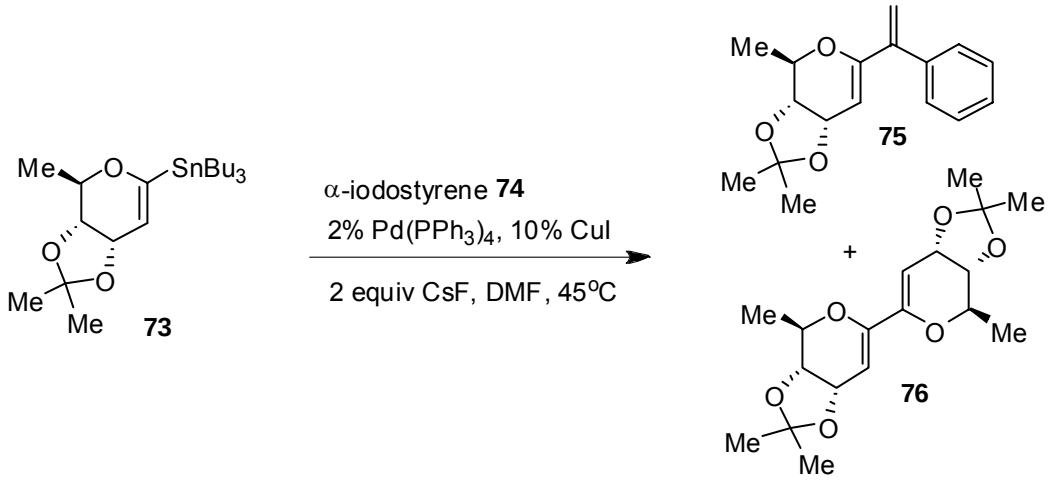
Synthesis of diols 77 and 78



Stannylated glycal 73. The glycal **70** (7.01 g, 38.8 mmol) was dissolved in THF (50 mL), cooled to -78ºC, and *t*-BuLi (34.2 mL, 1.7 M solution in pentane) was added dropwise over 30 minutes at -78ºC. The reaction mixture was stirred at -78ºC for additional 30 minutes and then stirred for 30 minutes at 0ºC. The resulting mixture was cooled to -78ºC, Bu_3SnCl (16.8 mL, 62.1 mmol) was added,

and the mixture was stirred for additional 1 hour at -78°C. The resulting mixture was extracted with Et_2O (3 × 40 mL) and the combined organic layers were dried over Na_2SO_4 and evaporated. Chromatography (hexanes : EtOAc = 80 : 1 to 40 : 1) afforded tributylstannyl glycal **73** (15.9 g, 89%) as a colorless oil. $[\alpha]^{23}_D$ = -43.6 (*c* = 1.06, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.17 (d, *J* = 4.0 Hz, 1H), 4.32 (dd, *J* = 4.8 Hz, 1H), 3.64 (dd, *J* = 5.6, 9.6 Hz, 1H), 3.28 (dq, *J* = 6.4, 12.6 Hz, 1H), 1.54-1.47 (m, 6H), 1.44 (s, 3H), 1.36 (m, 3H), 1.34-1.25 (m, 9H), 0.94 (t, J = 8.4 Hz, 9H), 0.87 (t, *J* = 7.2 Hz, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.78, 109.72, 107.36, 76.20, 71.82, 67.84, 28.86, 28.54, 27.13, 25.77, 17.14, 13.66, 9.65 ; IR (neat) 2957, 2928, 2871, 2855, 1597, 1462, 1374,1248, 1060 cm^{-1}; HRMS (FAB^+) Calcd. For $C_{21}H_{39}O_3Sn$ [$(M+H)^+$] 459.1921, Found 459.1935; Anal. Calcd for $C_{21}H_{39}O_3Sn$: C, 54.92; H, 8.78; O, 10.45. Found: C, 55.14; H, 8.93; O, 10.63.

Stille cross coupling reaction

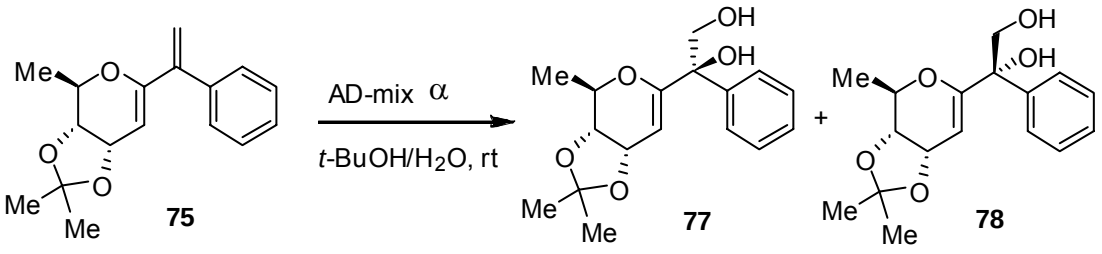


***gem*-Disubstituted diene 75.** Tributylstannyl glycal **73** (10.0 g, 21.8 mmol) and *alpha*-iodostyrene **74** (5.9 g, 24 mmol) were dissolved in DMF (30 mL), and

oven-dried CsF (6.6 g, 44 mmol), $Pd(PPh_3)_4$ (0.51 g, 0.44 mmol), and CuI (0.42 g, 2.2 mmol) were added. The mixture was then degassed by three cycles of the standard freeze-thaw method. The flask was sealed and the reaction mixture was stirred for 24 hours at 45°C. After cooling, the reaction mixture was diluted with CH_2Cl_2 (100 mL), EtOAc (100 mL) and H_2O (10 mL) and then stirred vigorously for 1 hour at room temperature. The resulting mixture was filtered through Celite and the filtrate was extracted with EtOAc (3 × 40 mL). The combined organic layers were dried over Na_2SO_4 and $MgSO_4$, and evaporated. Chromatography (hexanes : EtOAc = 40 : 1) afforded *gem*-disubstituted diene **75** (3.9 g, 66% yield) as a colorless oil along with undesired homodimerized glycal **76** (1.5 g, 20% yield) as a yellowish solid.

Compound 75: $[\alpha]^{23}_D$ = +115.1 (*c* = 1.00, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (s, 5H), 5.77 (d, *J* = 1.6 Hz, 1H), 5.10 (d, *J* = 4.4 Hz, 1H), 4.52 (dd, *J* = 5.6 Hz, 1H), 3.80 (dd, *J* = 5.6, 9.6 Hz, 1H), 3.61 (dq, *J* = 9.6, 12.8 Hz, 1H), 1.46 (s, 3H), 1.46 (d, *J* = 6.4 Hz, 3H), 1.37 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.99, 143.95, 139.30, 128.82, 127.96, 127.63, 116.43, 108.26, 100.29, 75.89, 72.66, 69.23, 28.41, 25.64, 17.06; IR (neat) 2984, 2933, 2873, 1950, 1827, 1378, 1248, cm^{-1}; Anal. Calcd for $C_{17}H_{20}O_3$: C, 74.97; H, 7.40; O, 17.62. Found: C, 74.61; H, 7.38; O, 17.47.

Compound 76: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.72 (d, *J* = 4.4 Hz, 2H), 4.53 (t, *J* = 4.4 Hz, 2H), 3.74 (dd, *J* = 6.0, 10.0 Hz, 2H), 3.44 (dq, *J* = 6.4, 10.0 Hz, 1H), 1.43 (s, 6H), 1.39 (d, *J* = 6.4 Hz, 6H), 1.38 (s, 6H)



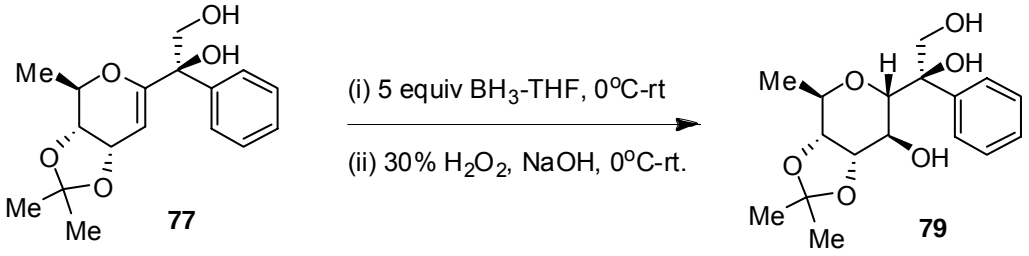
Diol 77 and 78. A homogeneous solution of AD-mix α (17.0 g, 1.4 g/mmol) in a mixture of *t*-BuOH (60 mL) and H_2O (60 mL) was poured into a flask containing *gem*-disubstituted diene **75** (3.40 g, 12.5 mmol). The reaction mixture was stirred for 24 hours at room temperature. The resulting solution was cooled to 0°C, and sodium sulfite (30 g) was added and then stirred for 3 hours at room temperature. The solution was diluted with CH_2Cl_2 (60 mL) and extracted with CH_2Cl_2 (2 × 40 mL) and EtOAc (2 × 40 mL). The combined organic layers were dried over Na_2SO_4 and $MgSO_4$, and evaporated. Two cycles of careful chromatography (Hexanes : EtOAc = 4 : 1 to 3 : 1) gave both diol diastereomers **77** (1.9 g, 49%) and **78** (1.7 g, 43%), each as a white crystals.

77: $[\alpha]^{23}_D$ = +74.9 (*c* = 1.02, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51-7.48 (m, 2H), 7.36-7.27 (m, 3H), 5.44 (d, *J* = 4.8 Hz, 1H), 4.52 (dd, *J* = 4.8, 5.2 Hz, 1H), 4.11 (dd, *J* = 4.8, 10.0 Hz, 1H), 3.74 (dd, *J* = 5.6, 9.4 Hz, 2H), 3.45 (dq, *J* = 5.6, 12.6 Hz, 1H), 3.24 (s, -OH), 2.12 (t, *J* = 6.4 Hz, -OH), 1.41 (s, 3H), 1.37 (s, 3H), 1.36 (d, *J* = 6.0, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.26, 140.91, 128.23, 127.72, 125.56, 108.39, 96.96, 77.14, 75.63, 73.01, 68.56, 67.60, 28.32, 25.64, 16.91; IR (KBr pellet) 3341(br), 2987, 2935, 2878, 1976, 1873, 1805, 1731, 1668, 1216, 1108 cm^{-1}; HRMS (FAB^+) Calcd. For $C_{17}H_{23}O_5$, $[(M+H)^+]$ 307.1545, Found

307.1540; Anal. Calcd for $C_{17}H_{22}O_5$: C, 66.65; H, 7.24; O, 26.11. Found: C, 66.71; H, 7.27; O, 25.83; mp = 135-136°C.

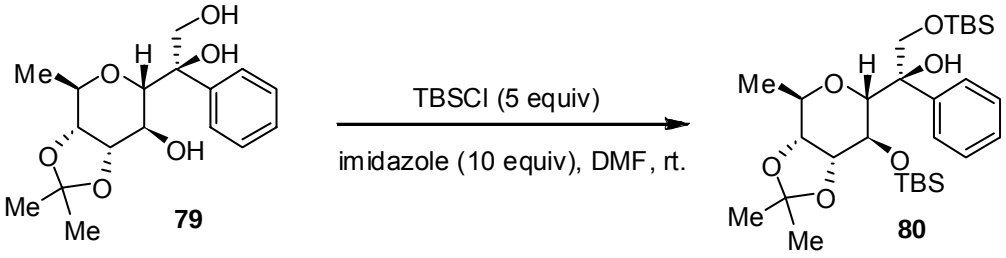
78: $[\alpha]^{23}_D$ = +91.6 (*c* = 1.00, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53-7.50 (m, 2H), 7.37-7.27 (m, 3H), 5.45 (d, *J* = 4.4 Hz, 1H), 4.50 (dd, *J* = 4.4, 5.6 Hz, 1H), 4.08 (dd, *J* = 6.4, 7.6 Hz, 1H), 3.73 (ddd, *J* = 1.6, 6.0, 8.8 Hz, 2H), 3.56 (dq, *J* = 6.4, 9.2 Hz, 1H), 3.29 (s, -OH), 2.21 (t, *J* = 6.4 Hz, -OH), 1.45 (s, 3H), 1.38 (s, 3H), 1.33 (d, *J* = 6.0, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.79, 140.87, 128.20, 127.76, 125.69, 108.51, 96.82, 77.41, 75.50, 73.12, 68.65, 67.84, 28.38, 25.72, 16.87; IR (KBr pellet) 3451 (br), 2984, 2934, 2880, 2248, 1954, 1882, 1815, 1449, 1379, 1062 cm^{-1}; HRMS (FAB^+) Calcd. For $C_{17}H_{23}O_5$, [$(M+H)^+$] 307.1545, Found 307.1548; Anal. Calcd for $C_{17}H_{22}O_5$: C, 66.65; H, 7.24; O, 26.11. Found: C, 66.59; H, 7.22; O, 25.90; mp = 103-104°C.

Synthesis of diols 86 and 89



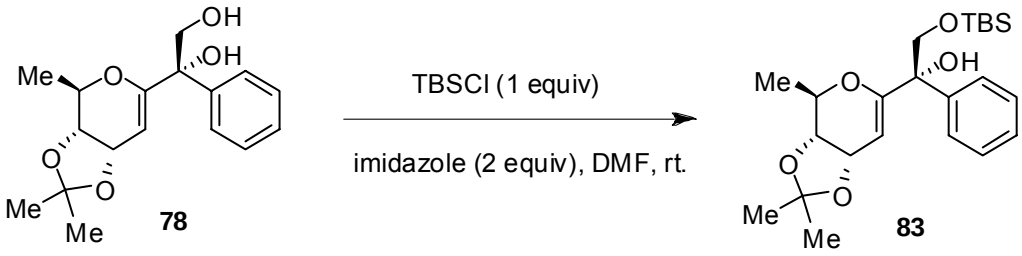
Triol 79. Diol **77** (0.52 g, 1.7 mmol) was dissolved in THF (5 mL) and cooled to 0 °C. While stirring, BH_3·THF (8.5 mL, 1.0 M solution in THF) was added dropwise over 30 minutes. The reaction mixture was stirred for 3 hours at 0°C and then for 24 hours at room temperature. The reaction mixture was then cooled to 0°C, NaOH (3 mL, 3 M solution in H_2O) and 30% H_2O_2 (3 mL) were carefully added at 0°C, and the reaction mixture was stirred for an additional 24 hours at room

temperature. The resulting mixture was diluted with EtOAc (10 mL) and then extracted with EtOAc (4 × 20 mL). The combined organic layers were dried over Na_2SO_4 and evaporated. Chromatography (hexanes : EtOAc = 2 : 1 to 1 : 1) gave triol **79** (0.41 g, 75%) as a white foamy solid. $[\alpha]^{23}_D$ = +1.5 (*c* = 1.36, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54-7.52 (m, 2H), 7.37-7.28 (m, 3H), 4.28 (s, -OH), 4.13 (dd, *J* = 7.2 Hz, 1H), 4.08 (dd, *J* = 11.6 Hz, 1H), 3.89 (dd, *J* = 6.8 Hz, 1H), 3.81 (d, *J* = 10.0 Hz, 1H), 3.69 (dd, *J* = 3.6, 11.6 Hz, 1H), 3.64 (dd, *J* = 8.0, 10.4 Hz, 1H), 3.45 (dq, *J* = 6.4, 9.2 Hz, 1H), 1.28 (s, 3H), 1.27 (s, 3H), 1.20 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.47, 128.20, 127.66, 125.86, 109.54, 78.81, 78.40, 77.49, 72.87, 70.23, 69.47, 67.02, 27.08, 25.04, 18.21; IR (KBr pellet) 3394(br), 2983, 2931, 2248, 1959, 1893, 1822, 1447, 1381, 1057 cm^{-1}; HRMS (FAB^+) Calcd. For $C_{17}H_{25}O_6$, $[(M+H)^+]$ 325.1651, Found 325.1646; Anal. Calcd for $C_{17}H_{24}O_6$: C, 62.95; H, 7.46; O, 29.59. Found: C, 63.23; H, 7.62; O, 29.42; mp = 104 - 106 °C.



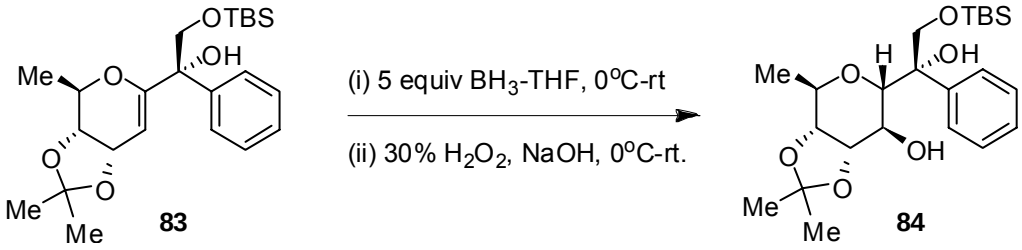
Bissilyl ether 80. Triol **79** (0.20 g, 0.65 mmol) was dissolved in DMF (2 mL), imidazole (0.44 g, 6.5 mmol) and TBSCl (0.49 g, 3.2 mmol) were added, and the reaction mixture was stirred for 24 hours at room temperature. The resulting mixture was diluted with Et_2O (2 mL) and extracted with Et_2O (3 × 10 mL). The combined organic layers were dried over Na_2SO_4 and evaporated.

Chromatography (hexanes : EtOAc = 40 : 1) gave alcohol **80** (0.33 g, 93%) as a colorless oil. $[\alpha]^{23}_{D}$ = -3.5 (*c* = 0.48, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, *J* = 5.6, 2H), 7.32-7.23 (m, 3H), 4.10 (dd, *J* = 1.6, 8.0 Hz, 1H), 4.08 (dd, *J* = 6.8 Hz, 1H), 4.00 (d, *J* = 1.2 Hz, 1H), 3.94 (d, *J* = 9.6 Hz, 1H), 3.91 (dd, *J* = 5.2, 6.4 Hz, 1H), 3.75 (d, *J* = 6.8 Hz, 1H), 3.73 (dq, *J* = 6.8, 12.6 Hz, 1H), 3.49 (d, *J* = 10.4 Hz, 1H), 1.29 (s, 3H), 1.28 (d, *J* = 6.0 Hz, 3H), 1.27 (s, 3H), 0.90 (s, 9H), 0.89 (s, 9H), 0.07 (s, 3H), 0.05 (s, 3H), 0.04 (s, 3H), -0.12 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.80, 127.57, 127.14, 126.85, 108.78, 78.90, 78.70, 77.54, 72.66, 71.41, 69.15, 68.57, 27.36, 26.21, 26.02, 25.50, 18.19, 17.69, -4.00, -5.15, -5.41, -5.45; IR (neat) 3484(br), 2953, 2930, 2857, 1471, 1382, 1251, 1092 cm^{-1}; HRMS (FAB^+) Calcd. For $C_{29}H_{52}O_6Si_2Li$, [$(M+Li)^+$] 559.3463, Found 559.3438; Anal. Calcd for $C_{29}H_{53}O_6Si_2$: C, 63.00; H, 9.48. Found: C, 63.71; H, 9.76.

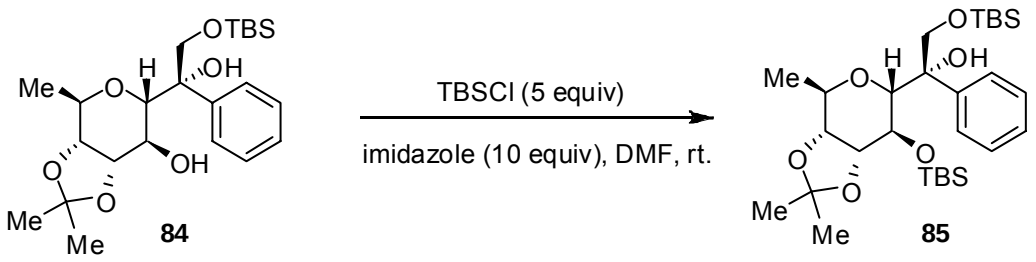


Monosilyl ether 83. The diol **78** (1.4 g, 4.6 mmol) was dissolved in DMF (6 mL), imidazole (0.63 g, 9.2 mmol) and TBSCl (0.69 g, 4.6 mmol) were added, and the reaction mixture was stirred for 1 hour at room temperature. The resulting mixture was extracted with Et_2O (3 × 20 mL) and the combined organic layers were dried over Na_2SO_4 and evaporated. Chromatography (hexanes : EtOAc = 10 : 1) provided alcohol **83** (1.8 g, 95%) as a colorless oil. $[\alpha]^{23}_{D}$ = +67.2 (*c* = 1.50, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55-7.53 (m, 2H), 7.35-7.30 (m, 2H), 7.27-7.23 (m, 1H), 4.09 (d, *J* = 6.0 Hz, 1H), 4.08 (t, *J* = 6.8 Hz, 1H), 3.97-3.90 (m, 2H),

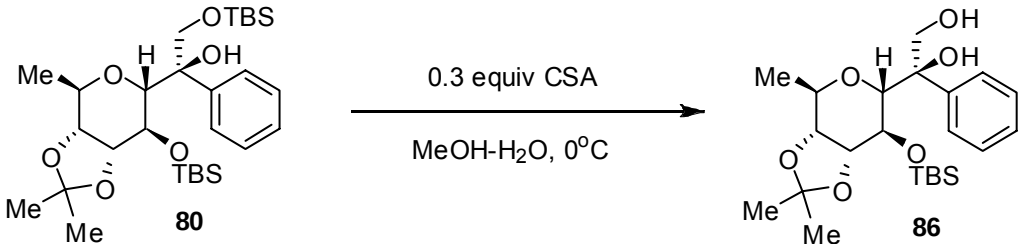
3.67 (d, *J* = 9.6 Hz, 1H), 2.74 (d, *J* = 1.6 Hz, 1H), 1.49 (s, 3H), 1.32 (s, 3H), 1.19 (d, *J* = 6.0, 3H), 0.78 (s, 9H), -0.01 (s, 3H), -0.11 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.00, 128.04, 127.35, 125.72, 109.44, 78.31, 78.02, 77.53, 76.61, 70.01, 69.96, 69.94, 27.44, 25.21, 18.42, 18.09, -5.52, -5.67; IR (neat) 3451(br), 2952, 2931, 2885, 2857, 2247, 1950, 1883, 1793, 1379, 1255, 1084, 838 cm^{-1}; HRMS (FAB$^+$) Calcd. For $C_{23}H_{36}O_5Li$ [(M+Li)$^+$] 427.2492, Found 427.2479.



Diol 84. Following the same procedure used for the conversion of **77** into **79**, compound **83** (1.63 g, 3.88 mmol) afforded diol **84** (1.26 g, 73%) as a colorless oil. $[\alpha]^{23}_D$ = -9.1 (*c* = 0.88, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55-7.23 (m, 2H), 7.35-7.30 (m, 2H), 7.27-7.23 (m, 1H), 4.17 (dq, *J* = 2.4, 9.6 Hz, 1H), 4.09 (d, *J* = 6.0 Hz, 1H), 4.08 (dd, *J* = 6.8 Hz, 1H), 3.97-3.90 (m, 2H), 3.67 (d, *J* = 9.6 Hz, 1H), 2.74 (d, *J* = 1.6 Hz, 1H), 1.49 (s, 3H), 1.32 (s, 3H), 1.19 (d, *J* = 6.0 Hz, 3H), 0.78 (s, 9H), -0.01(s, 3H), -0.11 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.00, 128.04, 127.35, 125.72, 109.44, 78.31, 78.02, 77.53, 76.61, 70.01, 69.96, 69.94, 27.44, 25.21, 18.42, 18.09, -5.52, -5.67; IR (neat) 3450(br), 2951, 2931, 2885, 2857, 2246, 1949, 1882, 1793, 1379, 1255, 1084, 838 cm^{-1}; HRMS (FAB$^+$) Calcd. For $C_{23}H_{38}O_6SiLi$ [(M+Li)$^+$] 445.2598, Found 445.2594.

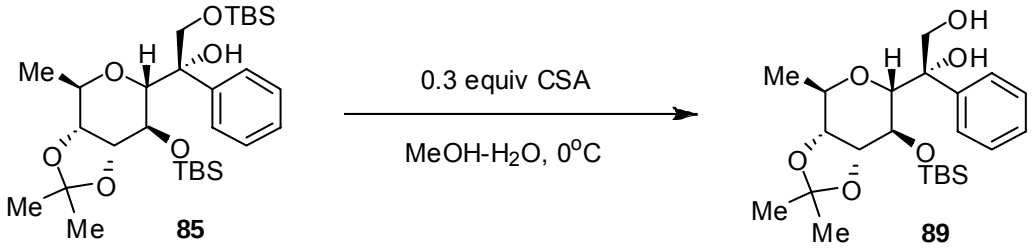


Bissilyl ether 85. Following the same procedure used for the conversion of **79** into **81**, compound **84** (0.95 g, 2.2 mmol) afforded bissilyl ether **85** (1.10 g, 92%) as a colorless oil. $[\alpha]^{23}_{D}$ = -6.5 (*c* = 1.48, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65-7.62 (m, 2H), 7.31-7.27 (m, 2H), 7.24-7.20 (m, 1H), 4.25 (d, *J* = 2.8 Hz, 1H), 4.14 (dd, *J* = 3.6, 6.4 Hz, 1H), 4.11 (s, 1H), 4.08 (dq, *J* = 2.8, 6.8 Hz, 1H), 4.00 (dd, *J* = 2.8 Hz, 1H), 3.98 (d, *J* = 9.2 Hz, 1H), 3.91 (dd, *J* = 3.2, 6.4 Hz, 1H), 3.55 (d, *J* = 9.2 Hz, 1H), 1.54 (s, 3H), 1.37 (d, *J* = 6.4 Hz, 3H), 1.34 (s, 3H), 0.84 (s, 9H), 0.78 (s, 9H), -0.03 (s, 3H), -0.08 (s, 3H), -0.22 (s, 3H), -0.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.10, 127.74, 126.90, 126.67, 209.24, 77.45, 76.95, 75.94, 75.92, 26.86, 25.83, 25.71, 25.58, 18.17, 17.82, 16.77, -4.77, -5.64, -5.82; IR (neat) 3478(br), 2953, 2953, 2931, 2887, 2857, 1462, 1380, 1254, 1099, 838 cm^{-1}; HRMS (FAB$^+$) Calcd. For $C_{29}H_{53}O_6Si_2$ [$(M+H)^+$] 553.3381, Found 553.3384; Anal. Calcd for $C_{29}H_{53}O_6Si_2$: C, 63.00; H, 9.48. Found: C, 63.36; H, 9.48.



Diol 86. Bissilyl ether **80** (0.95 g, 1.7 mmol) was dissolved in a mixture of MeOH (8 mL) and CH_2Cl_2 (12 mL), cooled to 0°C, and 10-camphorsulfonic acid (0.12 g, 0.52 mmol) was added. The reaction mixture was stirred for 5 hours at 0°C.

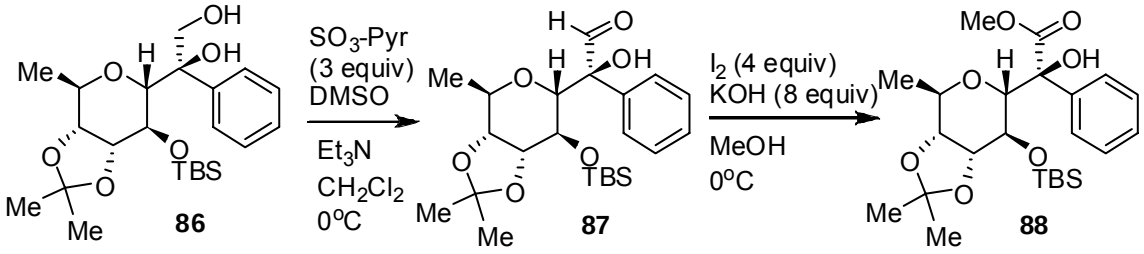
The resulting mixture was quenched by addition of sat. aq. $NaHCO_3$. Extraction with CH_2Cl_2 (3 × 20 mL) and chromatography (hexanes : EtOAc = 10 : 1) provided diol **86** (0.54 g, 72%) as a foamy solid. $[\alpha]^{23}_D$ = -11.6 (*c* = 1.05, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64-7.62 (m, 2H), 7.34-7.31 (m, 2H), 7.28-7.25 (m, 1H), 4.68 (d, *J* = 1.6 Hz, 1H), 4.08 (dd, *J* = 1.6, 7.6 Hz, 1H), 4.04 (d, *J* = 7.2 Hz, 1H), 3.93 (ddd, *J* = 5.6, 6.4 Hz, 1H), 3.90 (d, *J* = 6.4 Hz, 1H), 3.78 (dq, *J* = 6.4 Hz, 1H), 3.65 (dd, *J*= 6.8, 10.4 Hz, 1H), 3.51 (dd, *J* = 3.6, 10.4 Hz, 1H), 2.40 (dd, *J* = 3.6, 10.4 Hz, 1H), 1.31 (d, *J* = 6.8 Hz, 3H), 1.28 (s, 3H), 1.27 (s, 3H), 0.92 (s, 9H), 0.09 (s, 3H), -0.14 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.14, 127.82, 127.41, 126.41, 108.94, 78.91, 78.47, 77.57, 73.48, 71.42, 69.17, 67.67, 27.31, 26.17, 25.42, 18.12, 17.58, -3.89, -5.70; IR (KBr) 3465(br), 2983, 2932, 2859, 1471, 1380, 1250, 1069, 838 cm^{-1}; HRMS (FAB^+) Calcd. For $C_{23}H_{38}O_6Si_1Li$ [$(M+Li)^+$] 445.2598, Found 445.2579; mp = 81 - 83 °C.



Diol 89. Following the same procedure used for the conversion of **80** into **86**, compound **85** (2.07 g, 3.74 mmol) afforded diol **89** (1.12 g, 73%) as a foamy solid. $[\alpha]^{23}_D$ = +8.5 (*c* = 1.50, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56-7.53 (m, 2H), 7.36-7.32 (m, 2H), 7.27-7.23 (m, 1H), 4.40 (s, 1H), 4.13 (dd, *J* = 4.4, 6.4 Hz, 1H), 4.10-4.03 (m, 4H), 3.91 (dd, *J* = 2.8, 6.4 Hz, 1H), 3.76 (dd, *J* = 8.4, 11.6 Hz, 1H), 1.54 (s, 3H), 1.34 (s, 3H), 1.32 (d, *J* = 7.2, 3H), 0.78 (s, 9H), -0.15 (s, 3H), -0.40

(s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.94, 128.29, 127.32, 126.16, 109.39, 79.93, 77.14, 76.03, 75.92, 72.18, 68.64, 66.59, 27.01, 25.66, 25.56, 17.79, 16.76, -4.78, -5.90; IR (neat) 3455(br), 2932, 2896, 2858, 2248, 1953, 1889, 1819, 1463, 1374, 1251, 1056, 839 cm^{-1}; HRMS (FAB$^+$) Calcd. For $C_{23}H_{38}O_6Si_1Li$ [(M+Li)$^+$] 445.2598, Found 445.2603.

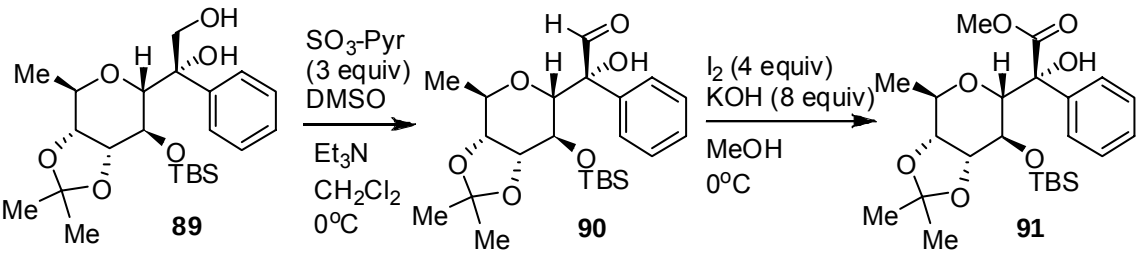
Synthesis of corresponding altromycin branched *C*-glycoside substructures 23a and 23b



Aldehyde 87. The diol **86** (0.50 g, 1.1 mmol) was dissolved in CH_2Cl_2 (7 mL), anhydrous Et_3N (2 mL) was added, and the mixture was cooled to 0°C with stirring. A mixture of SO_3-pyridine complex (0.56 g, 3.4 mmol) dissolved in anhydrous DMSO (4 mL) was added, and the reaction mixture was stirred for 1 hour at 0°C. Removal of solvent under reduced pressure followed by chromatography (Hexanes : EtOAc = 10 : 1) gave aldehyde **87** (0.50 g, 99%) as a colorless oil. $[\alpha]^{23}_D$ = -68.2 (*c* = 0.88, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.61 (d, *J* = 1.2 Hz, 1H), 7.57-7.54 (m, 2H), 7.42-7.38 (m, 2H), 7.33-7.29 (m, 1H), 4.26 (d, *J* = 1.2 Hz, 1H), 4.22 (dq, *J* = 3.6, 6.8 Hz, 1H), 3.98 (ddd, *J* = 6.4, 1H), 3.91 (m, 1H), 1.47 (s, 3H), 1.32 (s, 3H), 1.40 (d, *J* = 6.0 Hz, 3H), 0.92 (s, 9H), 0.16 (s, 3H), 0.08 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.49, 136.88, 128.60, 127.79, 126.09, 109.14, 83.13, 78.65, 77.62, 76.64, 71.08, 70.01, 27.32, 26.34, 25.24,

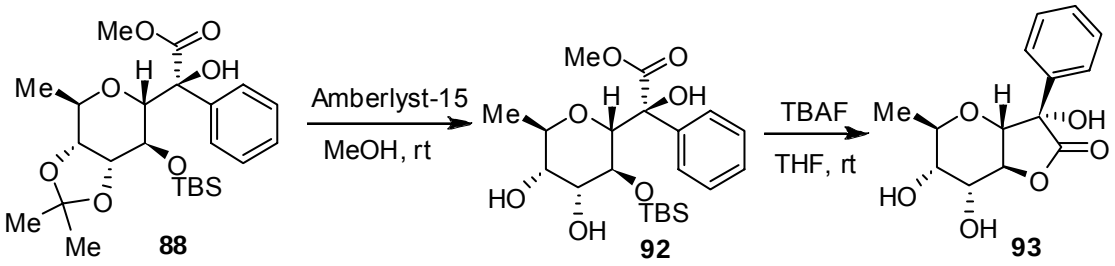
18.35, 17.94, -3.53, -4.68; IR (neat) 3465(br), 2932, 2895, 2858, 1720, 1257, 1069, 839 cm^{-1}; HRMS (FAB^+) Calcd. For $C_{23}H_{38}O_6Si_1Li$ $[(M+Li)^+]$ 443.2441, Found 443.2435.

Ester 88. Aldehyde **87** (0.50 g, 1.1 mmol) was dissolved in MeOH (10 mL) and cooled to 0 ^oC with stirring. A solution of KOH (0.51 g, 9.11 mmol) in MeOH (10 mL) was added to the reaction mixture and then I_2 (1.16 g, 4.58 mmol) was immediately added. The reaction mixture warmed to room temperature and stirred overnight. The resulting solution was quenched by addition of sat. aq. $Na_2S_2O_3$ and then extracted with CH_2Cl_2 (3 $\times$ 20 mL). The combined organic layers were dried over $MgSO_4$ and then evaporated. Chromatography on silica gel (Hexanes : EtOAc = 10 : 1) gave ester **88** (0.49 g, 92%) as a colorless oil. $[\alpha]^{23}_D$ = +10.9 (*c* = 1.12, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.66-7.63 (m, 2H), 7.36-7.32 (m, 2H), 7.30-7.27 (m, 1H), 4.39 (d, *J* = 8.0 Hz, 1H), 4.38 (s, 1H), 4.17 (t, *J* = 6.0 Hz, 1H), 4.11 (dd, *J* = 6.0, 7.6 Hz, 1H), 3.91 (d, *J* = 6.0 Hz, 1H), 3.90 (dq, *J* = 6.4, 11.2 Hz, 1H), 3.74 (s, 3H), 1.44 (s, 3H), 1.31 (s, 3H), 1.14 (d, *J* = 6.4 Hz, 3H), 0.92 (s, 9H), 0.14 (s, 3H), 0.07 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.97, 139.68, 127.76, 127.52, 126.25, 109.18, 79.78, 78.39, 77.43, 75.85, 71.08, 70.07, 53.04, 27.40, 26.20, 25.58, 18.35, 17.48, -3.99, -4.41; IR (neat) 3496(br), 2952, 2931, 2856, 1732, 1380, 1257, 1070, 839 cm^{-1}; HRMS (FAB^+) Calcd. For $C_{24}H_{38}O_7Si_1Li$ $[(M+Li)^+]$ 473.2547, Found 473.2545.



Aldehyde 90. Following the same procedure used for the oxidation of alchol **86** to aldehyde **87**, the diol **89** (1.1 g, 2.5 mmol) was converted into the corresponding aldehyde **90** (1.05 g, 99%) as a white solid. $[\alpha]^{23}_{D}$ = +37.7 (*c* = 2.50, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.62 (s, 1H), 7.61-7.59 (m, 2H), 7.37-7.34 (m, 2H), 7.29-7.24 (m, 1H), 4.59 (s, 1H), 4.54 (d, *J* = 4.2 Hz, 1H), 4.15 (dd, *J* = 4.8, 6.6 Hz, 1H), 4.10 (dd, *J* = 4.8 Hz, 1H), 4.02 (dq, *J* = 3.6, 14.4 Hz, 1H), 3.92 (dd, *J* = 3.6, 6.6, 1H), 1.54 (s, 3H), 1.34 (s, 3H), 1.33 (d, *J* = 7.2 Hz, 3H), 0.69 (s, 9H), -0.19 (s, 3H), -0.51 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 200.32, 135.94, 128.67, 128.09, 126.59, 109.35, 82.92, 79.24, 76.53, 76.16, 72.57, 66.02, 26.88, 25.65, 25.39, 17.77, 16.90, -4.72, -5.80; IR (KBr) 3459(br), 2978, 2932, 2896, 2856, 2035, 1955, 1889, 1731, 1380, 1251, 1071, 838 cm^{-1}; HRMS (FAB^+) Calcd. For $C_{23}H_{38}O_6Si_1Li$ [$(M+Li)^+$] 443.2441, Found 443.2438; mp = 95 - 96°C.

Ester 91. As described for **88**, aldehyde **90** (1.05 g, 2.40 mmol) was converted into ester **91** (1.01 g, 90%) as a colorless oil. $[\alpha]^{23}_{D}$ = +25.0 (*c* = 1.23, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74-7.71 (m, 2H), 7.33-7.29 (m, 2H), 7.27-7.23 (m, 1H), 4.57 (d, *J* = 4.4 Hz, 1H), 4.34 (s, 1H), 4.14 (dd, *J* = 4.4, 6.4 Hz, 1H), 4.09 (dq, *J* = 2.8, 6.4 Hz, 1H), 4.03 (dd, *J* = 4.4 Hz, 1H), 3.92 (dd, *J* = 2.8, 6.4 Hz, 1H), 3.71 (s, 3H), 1.53 (s, 3H), 1.36 (d, *J* = 6.4 Hz, 3H), 1.32 (s, 3H), 0.70 (s, 9H), -0.22 (s, 3H), -0.59 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.82, 137.82, 128.21, 127.95, 126.66, 109.18, 80.41, 79.35, 76.67, 76.07, 72.68, 65.89, 52.87, 26.94, 25.70, 25.34, 17.79, 16.79, -4.69, -5.91; IR (neat) 3486(br), 2977, 2951, 2252, 2034, 1950, 1889, 1736, 1375, 1071, 839 cm^{-1}; HRMS (FAB^+) Calcd. For $C_{24}H_{38}O_7Si_1Li$ [$(M+H)^+$] 467.2454, Found 467.2465.

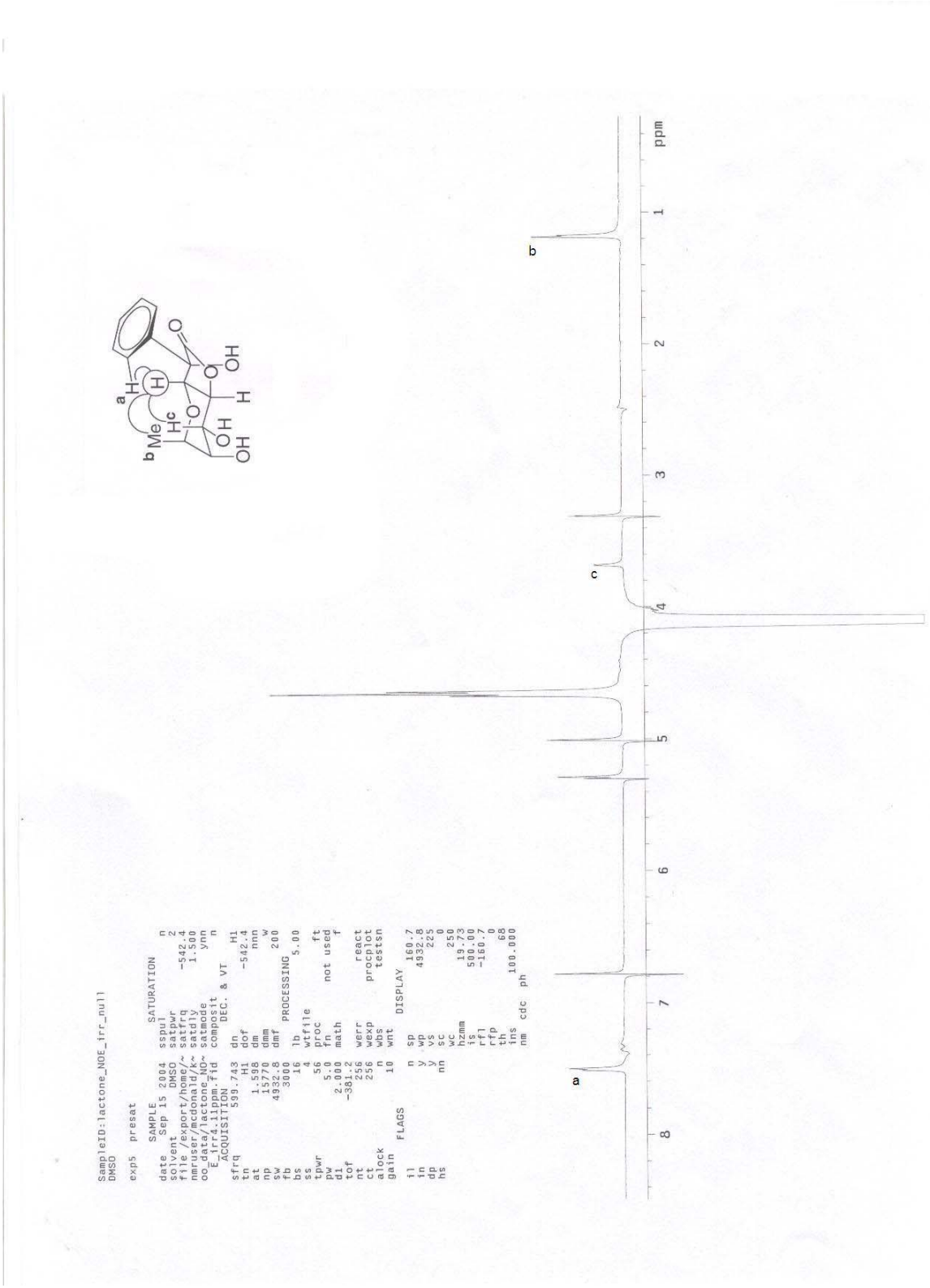


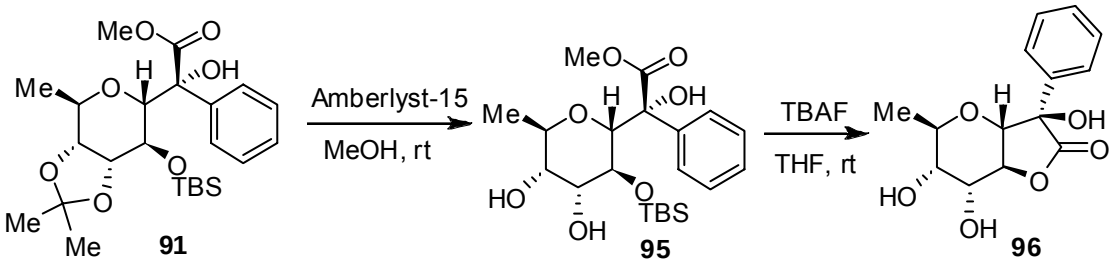
Triol 92. The acetonide-ester **88** (0.49 g, 1.1 mmol) was dissolved in MeOH (15 mL) with stirring, Amberlyst-15 (0.25 g) was added, and the reaction mixture stirred for 24 hours at room temperature. The resulting mixture was filtered through Celite using CH_2Cl_2, and the solvent was evaporated. Chromatography on silica gel (Hexanes : EtOAc = 2 : 1) gave triol-ester **92** (0.29 g, 65%) as a foamy solid and starting acetonide-ester **88** (0.09 g, 20%) as a colorless oil. $[\alpha]^{23}_D$ = +21.2 (*c* = 0.98, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.60-7.58 (m, 2H), 7.39-7.36 (m, 2H), 7.32-7.30 (m, 1H), 5.01 (s, 1H), 4.58 (d, *J* = 1.8 Hz, 1H), 4.47 (d, *J* = 7.8 Hz, 1H), 4.01 (dd, *J* = 2.4, 3.6 Hz, 1H), 3.84 (m, 1H), 3.83 (s, 3H), 3.78 (s, 1H), 3.50 (dq, *J* = 3.6, 6.6 Hz, 1H), 2.49 (d, *J* = 9.6 Hz, 1H), 1.30 (d, *J* = 6.6 Hz, 3H), 0.91 (s, 9H), 0.12 (s, 3H), 0.11 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.35, 134.39, 124.17, 123.89, 121.37, 77.81, 76.70, 67.58, 66.75, 66.41, 64.67, 49.68, 21.65, 13.89, 13.31, -8.77, -8.82; IR (KBr) 3325(br), 2953, 2931, 2246, 1732, 1450, 1253, 1094 cm^{-1}; HRMS (FAB^+) Calcd. For $C_{21}H_{34}O_7Si_1Li$ $[(M+Li)^+]$ 433.2234, Found 433.2226; mp = 60 - 61°C.

Lactone 93. This triol-ester **92** (63 mg, 0.15 mmol) was dissolved in THF (15 mL), TBAF (1.36 mL, 1 M in THF) was added, and the reaction mixture was stirred for 30 minutes at room temperature. The resulting mixture was extracted with EtOAc (3 × 20 mL) and washed with brine. The combined organic layer was dried over

Na_2SO_4 and then evaporated. Chromatography on silica gel (Hexanes : EtOAc = 1 : 2) gave lactone **93** (37 mg, 90%) as a white solid. $[\alpha]^{23}_D$ = -26.6 (*c* = 0.64, THF); ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.52 (d, *J* = 6.4, 2H), 7.40-7.31 (m, 3H), 6.80 (s, 1H), 5.32 (d, *J* = 6.4 Hz, 1H), 5.04 (d, *J* = 4.8 Hz, 1H), 4.66 (dd, *J* = 10.0 Hz, 1H), 4.17-4.08 (m, 3H), 3.67 (s, 1H), 1.19 (d, *J* = 10.8 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 173.92, 138.84, 128.06, 126.72, 78.07, 77.54, 76.70, 76.66, 73.12, 68.37, 15.43; IR (KBr) 3423(br), 3336, 1770, 1190, 1144, 1041 cm^{-1}; HRMS (FAB^+) Calcd. For $C_{14}H_{16}O_6Li$ $[(M+Li)^+]$ 287.1107, Found 287.1120; mp = 251 - 252^{o}C.

1D Noe spectra for lactone **93**.





Triol 95. Following the same procedure as described for the conversion of acetonide-ester **88** to triol-ester **92**, the acetonide-ester **91** (1.01 g, 2.17 mmol) afforded the corresponding triol-ester **95** (0.58 g, 63%) as a foamy solid and starting ester **91** (0.18 g, 20%) was recovered as a colorless oil. For the triol-ester: $[\alpha]^{23}_{D}$ = +30.7 (*c* = 1.10, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.69-7.67 (m, 2H), 7.41-7.38 (m, 2H), 7.36-7.33 (m, 1H), 5.06 (s, 1H), 4.85 (d, *J* = 11.4 Hz, 1H), 4.00 (dq, *J* = 6.0, 9.6 Hz, 1H), 3.92 (s, 3H), 3.76 (d, *J* = 2.4 Hz, 1H), 3.63 (ddd, *J* = 3.6 Hz, 1H), 3.46 (ddd, *J* = 3.6, 9.6 Hz, 1H), 2.47 (d, *J* = 10.2 Hz, 1H), 1.28 (d, *J* = 6.0 Hz, 3H), 0.77 (s, 9H), -0.24 (s, 3H), -0.34 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.13, 137.06, 128.92, 126.21, 83.43, 83.15, 70.48, 70.04, 69.48, 69.24, 54.55, 25.82, 18.87, 17.96, -5.04, -5.13; IR (KBr) 3339(br), 2953, 2931, 2247, 1743, 1446, 1253, 1093 cm^{-1}; HRMS (FAB^+) Calcd. For $C_{21}H_{34}O_7Si_1Li$, $[(M+Li)^+]$ 433.2234, Found 433.2243; mp = 62 - 63°C.

Lactone 96. As described for **93**, this triol-ester **95** (0.29 g, 0.68 mmol) was converted into lactone **96** (72 mg, 38%) as a white solid. $[\alpha]^{23}_{D}$ = -2.3 (*c* = 1.10, THF); ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.41-7.35 (m, 3H), 7.29-7.27 (m, 2H), 6.76 (s, 1H), 5.30 (d, *J* = 7.2 Hz, 1H), 4.90 (d, *J* = 3.6 Hz, 1H), 4.07 (d, *J* = 9.0 Hz, 1H), 4.04 (dd, *J* = 7.2, 15.0 Hz, 1H), 4.00 (dq, *J* = 3.6, 6.6 Hz, 1H), 3.93 (dd, *J* = 10.2 Hz, 1H), 3.59 (dd, *J* = 3.0 Hz, 1H), 1.26 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (150

MHz, DMSO-d_6) δ 173.92, 138.84, 128.06, 126.72, 78.07, 77.54, 76.70, 76.66, 73.12, 68.37, 15.43; IR (KBr) 3371(br), 2975, 2936, 2877, 1791, 1046 cm^{-1}; HRMS (ESI^+)Calcd. For $C_{14}H_{15}O_5$ $[(M+H-H_2O)^+]$ 263.09140, Found 263.09133; mp = 251 - 252°C.

The structure of lactone **96** was confirmed by single crystal X-ray analysis. Thermal ellipsoid diagram for lactone **96**:

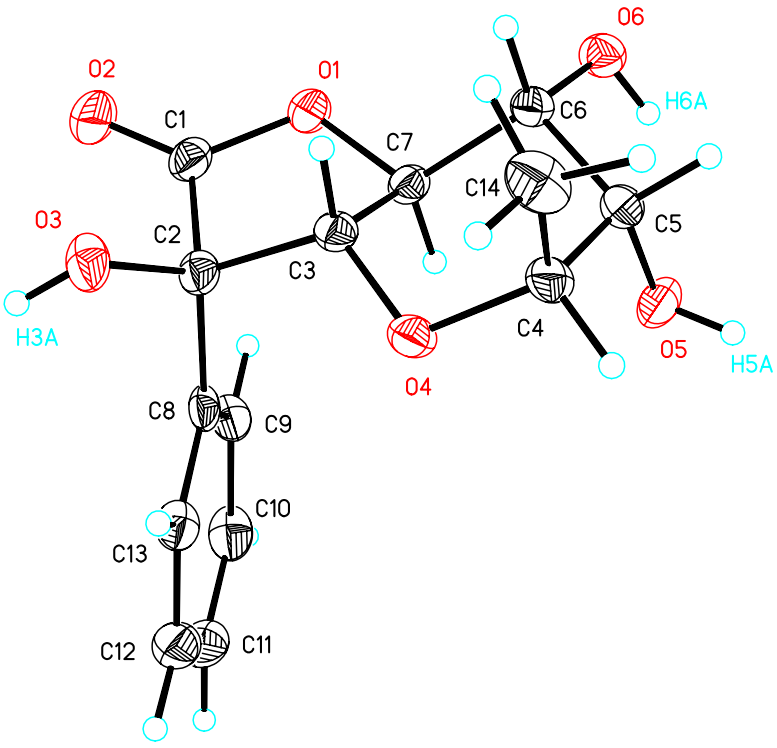


Table 4. Crystal data and structure refinement for **96**.

Identification code	BK01s	
Empirical formula	C14 H16 O6	
Formula weight	280.27	
Temperature	173(2) K	
Wavelength	1.54178 Å	
Crystal system	Orthorhombic	
Space group	P2(1)2(1)2(1)	
Unit cell dimensions	a = 7.5660(14) Å	α = 90°.
	b = 12.748(2) Å	β = 90°.
	c = 13.632(3) Å	γ = 90°.
Volume	1314.8(4) $Å^3$	
Z	4	
Density (calculated)	1.416 Mg/m^3	
Absorption coefficient	0.941 mm^{-1}	
F(000)	592	
Crystal size	0.80 x 0.16 x 0.15 mm^3	
Theta range for data collection	4.75 to 67.38°.	
Index ranges	-9<=h<=8, -12<=k<=15, -14<=l<=14	
Reflections collected	7147	
Independent reflections	2181 [R(int) = 0.0434]	
Completeness to theta = 67.38°	95.2 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.8717 and 0.5198	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2181 / 0 / 194	
Goodness-of-fit on F^2	1.148	
Final R indices [I>2sigma(I)]	R1 = 0.0336, wR2 = 0.0814	
R indices (all data)	R1 = 0.0366, wR2 = 0.0842	
Absolute structure parameter	-0.07(18)	
Largest diff. peak and hole	0.253 and -0.270 $e.Å^{-3}$	

Table 5. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for **96**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
C(1)	3541(3)	10453(1)	1323(1)	23(1)
C(2)	1644(2)	10096(1)	1054(1)	20(1)
C(3)	1146(2)	9618(1)	2043(1)	18(1)
C(4)	-553(2)	8512(1)	3040(1)	23(1)
C(5)	1152(2)	8096(1)	3502(1)	21(1)
C(6)	2734(2)	8840(1)	3422(1)	19(1)
C(7)	2869(2)	9104(1)	2348(1)	19(1)
C(8)	1603(2)	9307(1)	219(1)	19(1)
C(9)	3105(2)	8769(1)	-91(1)	23(1)
C(10)	3001(3)	8069(1)	-877(1)	28(1)
C(11)	1406(3)	7918(2)	-1352(1)	30(1)
C(12)	-86(3)	8450(1)	-1050(1)	28(1)
C(13)	-1(2)	9131(1)	-261(1)	22(1)
C(14)	-1495(3)	9322(2)	3672(1)	30(1)
O(1)	4194(2)	9885(1)	2083(1)	23(1)
O(2)	4347(2)	11160(1)	952(1)	34(1)
O(3)	576(2)	10977(1)	853(1)	27(1)
O(4)	-256(2)	8902(1)	2048(1)	22(1)
O(5)	1734(2)	7152(1)	3026(1)	27(1)
O(6)	4269(2)	8384(1)	3850(1)	24(1)

Table 6. Bond lengths [Å] and angles [°] for **96**.

C(1)-O(2)	1.201(2)
C(1)-O(1)	1.357(2)
C(1)-C(2)	1.550(3)
C(2)-O(3)	1.411(2)
C(2)-C(8)	1.519(2)
C(2)-C(3)	1.527(2)
C(3)-O(4)	1.399(2)
C(3)-C(7)	1.517(2)
C(4)-O(4)	1.458(2)
C(4)-C(14)	1.523(3)
C(4)-C(5)	1.531(3)
C(5)-O(5)	1.436(2)
C(5)-C(6)	1.531(2)
C(6)-O(6)	1.424(2)
C(6)-C(7)	1.505(2)
C(7)-O(1)	1.459(2)
C(8)-C(9)	1.393(2)
C(8)-C(13)	1.397(3)
C(9)-C(10)	1.396(2)
C(10)-C(11)	1.382(3)
C(11)-C(12)	1.380(3)
C(12)-C(13)	1.384(3)
O(2)-C(1)-O(1)	122.53(18)
O(2)-C(1)-C(2)	126.23(18)
O(1)-C(1)-C(2)	111.18(14)
O(3)-C(2)-C(8)	111.74(14)
O(3)-C(2)-C(3)	110.35(14)
C(8)-C(2)-C(3)	113.11(13)
O(3)-C(2)-C(1)	110.06(13)
C(8)-C(2)-C(1)	112.99(14)
C(3)-C(2)-C(1)	97.83(14)
O(4)-C(3)-C(7)	111.58(13)
O(4)-C(3)-C(2)	116.83(14)
C(7)-C(3)-C(2)	101.69(13)
O(4)-C(4)-C(14)	111.44(15)
O(4)-C(4)-C(5)	111.74(14)

C(14)-C(4)-C(5)	113.35(15)
O(5)-C(5)-C(4)	111.24(14)
O(5)-C(5)-C(6)	104.32(13)
C(4)-C(5)-C(6)	114.49(13)
O(6)-C(6)-C(7)	115.79(15)
O(6)-C(6)-C(5)	110.80(13)
C(7)-C(6)-C(5)	105.13(14)
O(1)-C(7)-C(6)	116.10(14)
O(1)-C(7)-C(3)	103.13(13)
C(6)-C(7)-C(3)	107.75(14)
C(9)-C(8)-C(13)	119.21(15)
C(9)-C(8)-C(2)	122.46(16)
C(13)-C(8)-C(2)	118.32(16)
C(8)-C(9)-C(10)	120.08(17)
C(11)-C(10)-C(9)	119.85(18)
C(12)-C(11)-C(10)	120.38(16)
C(11)-C(12)-C(13)	120.15(18)
C(12)-C(13)-C(8)	120.33(17)
C(1)-O(1)-C(7)	107.66(13)
C(3)-O(4)-C(4)	110.13(12)

Symmetry transformations used to generate equivalent atoms

Table 7. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for **96**. 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)	31(1)	18(1)	19(1)	-2(1)	6(1)	-4(1)
C(2)	26(1)	16(1)	18(1)	0(1)	2(1)	2(1)
C(3)	21(1)	18(1)	16(1)	-3(1)	2(1)	-1(1)
C(4)	24(1)	29(1)	16(1)	0(1)	3(1)	-8(1)
C(5)	27(1)	22(1)	15(1)	-1(1)	3(1)	-3(1)
C(6)	21(1)	19(1)	18(1)	-2(1)	-1(1)	0(1)

C(7)	21(1)	18(1)	18(1)	-1(1)	2(1)	-4(1)
C(8)	28(1)	15(1)	13(1)	4(1)	4(1)	1(1)
C(9)	26(1)	23(1)	20(1)	2(1)	0(1)	3(1)
C(10)	37(1)	23(1)	25(1)	0(1)	8(1)	9(1)
C(11)	45(1)	24(1)	21(1)	-6(1)	5(1)	-4(1)
C(12)	35(1)	27(1)	22(1)	-1(1)	0(1)	-6(1)
C(13)	25(1)	21(1)	20(1)	1(1)	4(1)	2(1)
C(14)	23(1)	43(1)	24(1)	-2(1)	5(1)	2(1)
O(1)	23(1)	23(1)	23(1)	2(1)	1(1)	-8(1)
O(2)	44(1)	28(1)	30(1)	6(1)	4(1)	-13(1)
O(3)	40(1)	19(1)	21(1)	1(1)	5(1)	11(1)
O(4)	23(1)	27(1)	16(1)	-1(1)	0(1)	-6(1)
O(5)	35(1)	18(1)	27(1)	-1(1)	8(1)	-6(1)
O(6)	25(1)	22(1)	24(1)	-1(1)	-3(1)	2(1)

Table 8. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for **96**.

	x	y	z	U(eq)
H(3)	873	10198	2513	22
H(4)	-1372	7899	2979	27
H(5)	929	7942	4211	26
H(6)	2448	9498	3788	23
H(7)	3060	8449	1959	23
H(9)	4202	8878	233	28
H(10)	4023	7699	-1086	34
H(11)	1338	7445	-1889	36
H(12)	-1174	8348	-1384	33
H(13)	-1038	9481	-45	26
H(14A)	-2523	9595	3318	45
H(14B)	-683	9900	3822	45
H(14C)	-1886	8993	4285	45

H(6A)	4290(30)	7740(20)	3730(17)	50(7)
H(3A)	640(30)	11163(16)	260(20)	41(7)
H(5A)	1190(30)	6673(19)	3282(18)	42(7)

Table 9. Torsion angles [°] for **96**.

O(2)-C(1)-C(2)-O(3)	-38.7(2)
O(1)-C(1)-C(2)-O(3)	138.65(14)
O(2)-C(1)-C(2)-C(8)	87.0(2)
O(1)-C(1)-C(2)-C(8)	-95.68(17)
O(2)-C(1)-C(2)-C(3)	-153.73(17)
O(1)-C(1)-C(2)-C(3)	23.57(16)
O(3)-C(2)-C(3)-O(4)	85.13(17)
C(8)-C(2)-C(3)-O(4)	-40.9(2)
C(1)-C(2)-C(3)-O(4)	-160.02(13)
O(3)-C(2)-C(3)-C(7)	-153.17(14)
C(8)-C(2)-C(3)-C(7)	80.84(17)
C(1)-C(2)-C(3)-C(7)	-38.32(14)
O(4)-C(4)-C(5)-O(5)	-68.72(18)
C(14)-C(4)-C(5)-O(5)	164.35(15)
O(4)-C(4)-C(5)-C(6)	49.22(19)
C(14)-C(4)-C(5)-C(6)	-77.71(19)
O(5)-C(5)-C(6)-O(6)	-56.95(17)
C(4)-C(5)-C(6)-O(6)	-178.75(14)
O(5)-C(5)-C(6)-C(7)	68.85(16)
C(4)-C(5)-C(6)-C(7)	-52.96(18)
O(6)-C(6)-C(7)-O(1)	-62.7(2)
C(5)-C(6)-C(7)-O(1)	174.71(13)
O(6)-C(6)-C(7)-C(3)	-177.64(13)
C(5)-C(6)-C(7)-C(3)	59.72(16)
O(4)-C(3)-C(7)-O(1)	167.46(13)
C(2)-C(3)-C(7)-O(1)	42.19(15)
O(4)-C(3)-C(7)-C(6)	-69.25(17)
C(2)-C(3)-C(7)-C(6)	165.48(13)

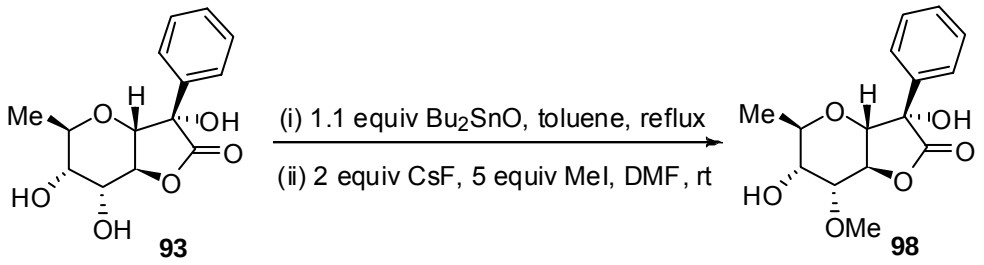
O(3)-C(2)-C(8)-C(9)	140.16(16)
C(3)-C(2)-C(8)-C(9)	-94.60(19)
C(1)-C(2)-C(8)-C(9)	15.4(2)
O(3)-C(2)-C(8)-C(13)	-38.8(2)
C(3)-C(2)-C(8)-C(13)	86.43(19)
C(1)-C(2)-C(8)-C(13)	-163.58(15)
C(13)-C(8)-C(9)-C(10)	0.4(2)
C(2)-C(8)-C(9)-C(10)	-178.52(15)
C(8)-C(9)-C(10)-C(11)	0.5(3)
C(9)-C(10)-C(11)-C(12)	-0.3(3)
C(10)-C(11)-C(12)-C(13)	-0.7(3)
C(11)-C(12)-C(13)-C(8)	1.6(3)
C(9)-C(8)-C(13)-C(12)	-1.5(2)
C(2)-C(8)-C(13)-C(12)	177.50(14)
O(2)-C(1)-O(1)-C(7)	179.64(16)
C(2)-C(1)-O(1)-C(7)	2.22(17)
C(6)-C(7)-O(1)-C(1)	-145.30(15)
C(3)-C(7)-O(1)-C(1)	-27.74(16)
C(7)-C(3)-O(4)-C(4)	63.04(17)
C(2)-C(3)-O(4)-C(4)	179.42(14)
C(14)-C(4)-O(4)-C(3)	76.06(17)
C(5)-C(4)-O(4)-C(3)	-51.89(17)

Symmetry transformations used to generate equivalent atoms:

Table 10. Hydrogen bonds for **96** [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
O(6)-H(6A)...O(5)	0.83(3)	2.29(3)	2.7222(19)	113(2)
O(6)-H(6A)...O(2)#1	0.83(3)	2.31(3)	3.0341(19)	146(2)
O(3)-H(3A)...O(6)#2	0.84(3)	2.01(3)	2.8513(19)	179(2)
O(5)-H(5A)...O(3)#3	0.81(2)	1.99(3)	2.7622(18)	158(2)

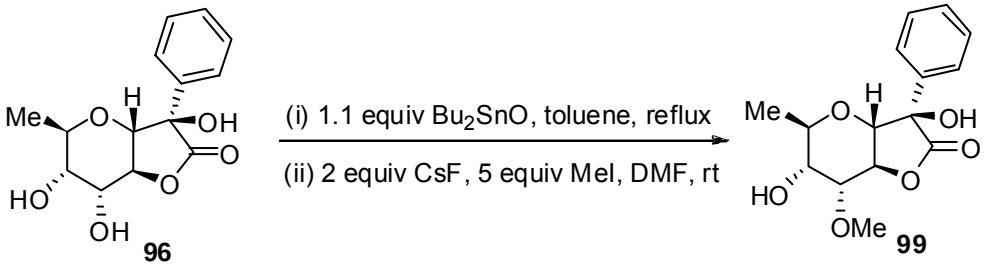
Symmetry transformations used to generate equivalent atoms:
#1 -x+1,y-1/2,-z+1/2 #2 -x+1/2,-y+2,z-1/2 #3 -x,y-1/2,-z+1/2



93 **98**

Methyl ether-lactone 98. The lactone **93** (18 mg, 0.064 mmol) was dissolved in toluene (15 mL) with stirring, dibutyltin oxide (18 mg, 0.071 mmol) was added, and the mixture was heated at reflux with Dean-Stark column for 6 hours. The resulting mixture was then cooled to room temperature and solvent was removed under reduced pressure. CsF (19 mg, 0.13 mmol) was added to the resulting white solid and then dried under high vacuum for 3 hours. DMF (4 mL) and MeI (0.019 mL, 0.32 mmol) were added and the reaction mixture was stirred for 48 hours at room temperature. The resulting mixture was extracted with EtOAc (3 × 10 mL) and washed with brine. The combined organic layers were dried with Na_2SO_4, evaporated, and the residue was purified by chromatography (Hexanes : EtOAc = 1 : 1) to afford methyl ether-lactone **98** (16 mg, 90%) as a yellowish oil. $[\alpha]^{23}_D$ = -8 (*c* = 0.25, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59-7.56 (m, 3H), 7.45-7.38 (m, 2H), 4.91 (dd, *J* = 9.6 Hz, 1H), 4.49 (ddd, *J* = 1.2, 7.2, 13.2 Hz, 1H), 4.03 (dd, *J* = 1.2, 3.6 Hz, 1H), 3.99 (d, *J* = 9.6 Hz, 1H), 3.77 (dd, *J* = 3.6, 10.0 Hz, 1H), 1.34 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ

171.97, 136.92, 129.01, 126.31, 77.87, 77.36, 76.59, 76.12, 75.79, 71.70, 58.17, 15.60; IR (neat) 3399(br), 2922, 2851, 1790, 1135, 1049 cm^{-1}; HRMS ($APCI^+$) Calcd. For $C_{15}H_{17}O_5$ [$(M+H-H_2O)^+$] 277.10705, Found 277.10700.



Methyl ether-lactone 99. Following the procedure described above for the preparation of **98**, the lactone **96** (50 mg, 0.68 mmol) afforded methyl ether-lactone **99** (37 mg, 70%) as a white solid. $[\alpha]^{23}_D$ = +18.9 (*c* = 0.88, THF); ^{1}H NMR (600 MHz, DMSO-*d*$_6$) δ 7.41-7.35 (m, 3H), 7.29-7.27 (m, 2H), 6.76 (s, 1H), 5.30 (d, *J* = 7.2 Hz, 1H), 4.90 (d, *J* = 3.6 Hz, 1H), 4.07 (d, *J* = 9.0 Hz, 1H), 4.04 (dd, *J* = 7.2, 15.0 Hz, 1H), 4.00 (dq, *J* = 3.6, 6.6 Hz, 1H), 3.93 (dd, *J* = 10.2 Hz, 1H), 3.59 (dd, *J* = 3.0 Hz, 1H), 1.26 (d, *J* = 7.2 Hz; ^{13}C NMR (150 MHz, DMSO-*d*$_6$) δ 171.65, 130.64, 124.01, 123.61, 122.99, 74.80, 73.05, 72.95, 72.61, 70.89, 64.38, 51.45, 10.71; IR (KBr) 3386(br), 2919, 2849, 1791, 1046 cm^{-1}; HRMS ($APCI^+$) Calcd. For $C_{15}H_{17}O_5$ [$(M+H)^+$] 295.15400, Found 295.15411; mp = 205 - 206°C.

The structure of lactone **99** was confirmed by single crystal X-ray analysis.

Thermal ellipsoid diagram for lactone **94**:

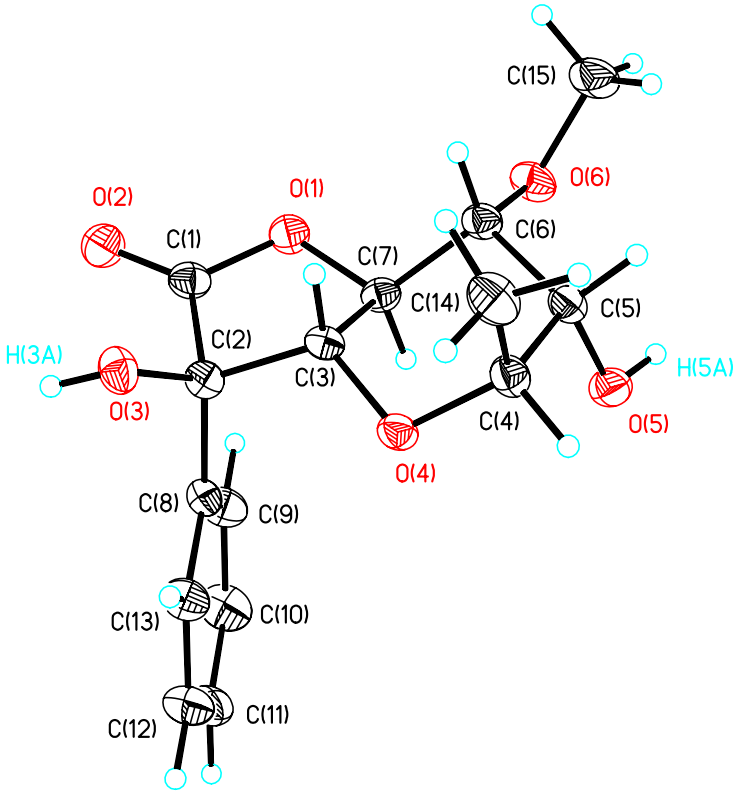


Table 11. Crystal data and structure refinement for **99**.

Identification code	BK021m	
Empirical formula	C16 H22 O7	
Formula weight	326.34	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P2(1)2(1)2(1)	
Unit cell dimensions	a = 8.2807(5) Å	α = 90°.
	b = 12.6741(8) Å	β = 90°.
	c = 15.0669(9) Å	γ = 90°.
Volume	1581.28(17) $Å^3$	
Z	4	
Density (calculated)	1.371 Mg/m^3	
Absorption coefficient	0.108 mm^{-1}	
F(000)	696	
Crystal size	0.43 x 0.13 x 0.11 mm^3	
Theta range for data collection	2.10 to 28.40°.	
Index ranges	-11<=h<=11, -16<=k<=16, -20<=l<=20	
Reflections collected	22205	
Independent reflections	3948 [R(int) = 0.0497]	
Completeness to theta = 28.40°	99.8 %	
Absorption correction	None	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3948 / 0 / 216	
Goodness-of-fit on F^2	1.012	
Final R indices [I>2sigma(I)]	R1 = 0.0375, wR2 = 0.0835	
R indices (all data)	R1 = 0.0408, wR2 = 0.0849	
Absolute structure parameter	-0.3(7)	
Largest diff. peak and hole	0.283 and -0.240 $e.Å^{-3}$	

Table 12. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for **99**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
C(1)	-798(2)	4375(1)	3625(1)	22(1)
C(2)	874(2)	4283(1)	4083(1)	20(1)
C(3)	279(2)	3995(1)	5004(1)	18(1)
C(4)	586(2)	3772(1)	6528(1)	21(1)
C(5)	-1123(2)	4214(1)	6671(1)	21(1)
C(6)	-2225(2)	4147(1)	5839(1)	20(1)
C(7)	-1263(2)	4621(1)	5100(1)	19(1)
C(8)	1819(2)	5314(1)	4048(1)	20(1)
C(9)	1099(2)	6284(1)	3884(1)	27(1)
C(10)	2001(2)	7197(1)	3887(1)	33(1)
C(11)	3639(2)	7154(1)	4056(1)	31(1)
C(12)	4368(2)	6195(1)	4214(1)	32(1)
C(13)	3466(2)	5276(1)	4211(1)	26(1)
C(14)	663(2)	2575(1)	6561(1)	30(1)
C(15)	-4913(2)	4107(1)	6361(1)	32(1)
O(1)	-1990(1)	4539(1)	4222(1)	24(1)
O(2)	-1076(1)	4276(1)	2848(1)	30(1)
O(3)	1737(1)	3429(1)	3733(1)	24(1)
O(4)	1312(1)	4184(1)	5722(1)	20(1)
O(5)	-961(1)	5291(1)	6927(1)	26(1)
O(6)	-3666(1)	4722(1)	5971(1)	26(1)
O(1S)	2959(2)	3812(1)	2148(1)	41(1)
C(1S)	2303(2)	3368(1)	1377(1)	38(1)

Table 13. Bond lengths [Å] and angles [°] for **99**.

C(1)-O(2)	1.1988(17)	C(14)-H(14B)	0.9800
C(1)-O(1)	1.3522(17)	C(14)-H(14C)	0.9800
C(1)-C(2)	1.5520(18)	C(15)-O(6)	1.4205(17)
C(2)-O(3)	1.3998(15)	C(15)-H(15A)	0.9800
C(2)-C(3)	1.5170(18)	C(15)-H(15B)	0.9800
C(2)-C(8)	1.5247(19)	C(15)-H(15C)	0.9800
C(3)-O(4)	1.4001(15)	O(3)-H(3A)	0.8400
C(3)-C(7)	1.5100(17)	O(5)-H(5A)	0.8400
C(3)-H(3)	1.0000	O(1S)-C(1S)	1.4004(19)
C(4)-O(4)	1.4519(15)	O(1S)-H(1S)	0.83(2)
C(4)-C(14)	1.5190(19)	C(1S)-H(1S1)	0.9800
C(4)-C(5)	1.5372(19)	C(1S)-H(1S2)	0.9800
C(4)-H(4)	1.0000	C(1S)-H(1S3)	0.9800
C(5)-O(5)	1.4244(17)		
C(5)-C(6)	1.5540(18)	O(2)-C(1)-O(1)	121.76(13)
C(5)-H(5)	1.0000	O(2)-C(1)-C(2)	126.69(13)
C(6)-O(6)	1.4126(16)	O(1)-C(1)-C(2)	111.48(11)
C(6)-C(7)	1.4949(18)	O(3)-C(2)-C(3)	108.97(10)
C(6)-H(6)	1.0000	O(3)-C(2)-C(8)	112.81(10)
C(7)-O(1)	1.4565(16)	C(3)-C(2)-C(8)	113.87(10)
C(7)-H(7)	1.0000	O(3)-C(2)-C(1)	110.22(11)
C(8)-C(13)	1.3867(19)	C(3)-C(2)-C(1)	97.77(10)
C(8)-C(9)	1.3878(19)	C(8)-C(2)-C(1)	112.21(10)
C(9)-C(10)	1.377(2)	O(4)-C(3)-C(7)	110.65(10)
C(9)-H(9)	0.9500	O(4)-C(3)-C(2)	117.87(10)
C(10)-C(11)	1.381(2)	C(7)-C(3)-C(2)	103.65(10)
C(10)-H(10)	0.9500	O(4)-C(3)-H(3)	108.1
C(11)-C(12)	1.378(2)	C(7)-C(3)-H(3)	108.1
C(11)-H(11)	0.9500	C(2)-C(3)-H(3)	108.1
C(12)-C(13)	1.384(2)	O(4)-C(4)-C(14)	111.63(12)
C(12)-H(12)	0.9500	O(4)-C(4)-C(5)	111.55(11)
C(13)-H(13)	0.9500	C(14)-C(4)-C(5)	113.47(12)
C(14)-H(14A)	0.9800	O(4)-C(4)-H(4)	106.6

C(14)-C(4)-H(4)	106.6	C(12)-C(13)-H(13)	119.9
C(5)-C(4)-H(4)	106.6	C(8)-C(13)-H(13)	119.9
O(5)-C(5)-C(4)	107.49(11)	C(4)-C(14)-H(14A)	109.5
O(5)-C(5)-C(6)	109.02(11)	C(4)-C(14)-H(14B)	109.5
C(4)-C(5)-C(6)	114.06(11)	H(14A)-C(14)-H(14B)	109.5
O(5)-C(5)-H(5)	108.7	C(4)-C(14)-H(14C)	109.5
C(4)-C(5)-H(5)	108.7	H(14A)-C(14)-H(14C)	109.5
C(6)-C(5)-H(5)	108.7	H(14B)-C(14)-H(14C)	109.5
O(6)-C(6)-C(7)	110.39(11)	O(6)-C(15)-H(15A)	109.5
O(6)-C(6)-C(5)	110.72(10)	O(6)-C(15)-H(15B)	109.5
C(7)-C(6)-C(5)	105.41(10)	H(15A)-C(15)-H(15B)	109.5
O(6)-C(6)-H(6)	110.1	O(6)-C(15)-H(15C)	109.5
C(7)-C(6)-H(6)	110.1	H(15A)-C(15)-H(15C)	109.5
C(5)-C(6)-H(6)	110.1	H(15B)-C(15)-H(15C)	109.5
O(1)-C(7)-C(6)	115.25(10)	C(1)-O(1)-C(7)	108.30(10)
O(1)-C(7)-C(3)	103.01(10)	C(2)-O(3)-H(3A)	109.5
C(6)-C(7)-C(3)	108.12(11)	C(3)-O(4)-C(4)	109.40(9)
O(1)-C(7)-H(7)	110.1	C(5)-O(5)-H(5A)	109.5
C(6)-C(7)-H(7)	110.1	C(6)-O(6)-C(15)	112.92(10)
C(3)-C(7)-H(7)	110.1	C(1S)-O(1S)-H(1S)	115.1(13)
C(13)-C(8)-C(9)	119.02(13)	O(1S)-C(1S)-H(1S1)	109.5
C(13)-C(8)-C(2)	117.91(12)	O(1S)-C(1S)-H(1S2)	109.5
C(9)-C(8)-C(2)	123.05(11)	H(1S1)-C(1S)-H(1S2)	109.5
C(10)-C(9)-C(8)	120.70(13)	O(1S)-C(1S)-H(1S3)	109.5
C(10)-C(9)-H(9)	119.6	H(1S1)-C(1S)-H(1S3)	109.5
C(8)-C(9)-H(9)	119.6	H(1S2)-C(1S)-H(1S3)	109.5
C(9)-C(10)-C(11)	120.01(14)		
C(9)-C(10)-H(10)	120.0	Symmetry transformations used to generate equivalent atoms	
C(11)-C(10)-H(10)	120.0		
C(12)-C(11)-C(10)	119.80(14)		
C(12)-C(11)-H(11)	120.1		
C(10)-C(11)-H(11)	120.1		
C(11)-C(12)-C(13)	120.34(14)		
C(11)-C(12)-H(12)	119.8		
C(13)-C(12)-H(12)	119.8		
C(12)-C(13)-C(8)	120.12(14)		

Table 14. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for **99**. 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)	22(1)	20(1)	24(1)	4(1)	-1(1)	-3(1)
C(2)	19(1)	20(1)	21(1)	2(1)	0(1)	1(1)
C(3)	15(1)	18(1)	21(1)	1(1)	0(1)	-1(1)
C(4)	17(1)	27(1)	20(1)	3(1)	0(1)	2(1)
C(5)	18(1)	23(1)	22(1)	1(1)	3(1)	-2(1)
C(6)	14(1)	22(1)	25(1)	-1(1)	0(1)	1(1)
C(7)	15(1)	21(1)	22(1)	0(1)	-3(1)	0(1)
C(8)	20(1)	22(1)	18(1)	1(1)	3(1)	-2(1)
C(9)	22(1)	27(1)	34(1)	6(1)	-1(1)	1(1)
C(10)	33(1)	21(1)	46(1)	6(1)	3(1)	3(1)
C(11)	30(1)	25(1)	38(1)	1(1)	5(1)	-8(1)
C(12)	21(1)	35(1)	39(1)	1(1)	0(1)	-4(1)
C(13)	22(1)	24(1)	31(1)	4(1)	0(1)	1(1)
C(14)	30(1)	27(1)	32(1)	8(1)	3(1)	2(1)
C(15)	16(1)	37(1)	43(1)	-5(1)	6(1)	-2(1)
O(1)	18(1)	31(1)	23(1)	0(1)	-3(1)	1(1)
O(2)	29(1)	39(1)	22(1)	2(1)	-4(1)	-4(1)
O(3)	28(1)	21(1)	24(1)	1(1)	6(1)	2(1)
O(4)	15(1)	26(1)	20(1)	3(1)	-1(1)	-2(1)
O(5)	19(1)	28(1)	30(1)	-8(1)	2(1)	-1(1)
O(6)	14(1)	29(1)	35(1)	0(1)	4(1)	3(1)
O(1S)	27(1)	67(1)	28(1)	4(1)	2(1)	-17(1)
C(1S)	31(1)	39(1)	42(1)	-6(1)	0(1)	-4(1)

Table 15. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for **99**.

	x	y	z	U(eq)
H(3)	-7	3228	5004	22
H(4)	1260	4035	7033	25
H(5)	-1646	3818	7167	25
H(6)	-2481	3393	5702	24
H(7)	-1007	5375	5237	23
H(9)	-28	6319	3769	33
H(10)	1496	7856	3773	40
H(11)	4260	7784	4063	38
H(12)	5496	6165	4326	38
H(13)	3976	4617	4320	31
H(14A)	-103	2280	6132	44
H(14B)	385	2333	7159	44
H(14C)	1759	2342	6412	44
H(15A)	-5263	3563	5941	48
H(15B)	-5829	4564	6509	48
H(15C)	-4506	3771	6903	48
H(3A)	2017	3568	3209	36
H(5A)	-1829	5502	7153	39
H(1S1)	2724	2652	1299	56
H(1S2)	2602	3800	863	56
H(1S3)	1124	3343	1429	56
H(1S)	3900(20)	4027(15)	2100(12)	45

Table 16. Torsion angles [°] for **99**.

O(2)-C(1)-C(2)-O(3)	-42.19(18)
O(1)-C(1)-C(2)-O(3)	134.88(11)
O(2)-C(1)-C(2)-C(3)	-155.76(13)
O(1)-C(1)-C(2)-C(3)	21.31(13)
O(2)-C(1)-C(2)-C(8)	84.45(17)
O(1)-C(1)-C(2)-C(8)	-98.48(12)
O(3)-C(2)-C(3)-O(4)	87.24(13)
C(8)-C(2)-C(3)-O(4)	-39.66(15)
C(1)-C(2)-C(3)-O(4)	-158.19(11)
O(3)-C(2)-C(3)-C(7)	-150.14(10)
C(8)-C(2)-C(3)-C(7)	82.95(13)
C(1)-C(2)-C(3)-C(7)	-35.58(12)
O(4)-C(4)-C(5)-O(5)	-72.42(13)
C(14)-C(4)-C(5)-O(5)	160.46(11)
O(4)-C(4)-C(5)-C(6)	48.57(16)
C(14)-C(4)-C(5)-C(6)	-78.55(15)
O(5)-C(5)-C(6)-O(6)	-50.00(14)
C(4)-C(5)-C(6)-O(6)	-170.13(11)
O(5)-C(5)-C(6)-C(7)	69.39(13)
C(4)-C(5)-C(6)-C(7)	-50.75(15)
O(6)-C(6)-C(7)-O(1)	-66.90(14)
C(5)-C(6)-C(7)-O(1)	173.49(10)
O(6)-C(6)-C(7)-C(3)	178.51(10)
C(5)-C(6)-C(7)-C(3)	58.90(13)
O(4)-C(3)-C(7)-O(1)	166.66(9)
C(2)-C(3)-C(7)-O(1)	39.38(12)
O(4)-C(3)-C(7)-C(6)	-70.92(13)
C(2)-C(3)-C(7)-C(6)	161.81(10)
O(3)-C(2)-C(8)-C(13)	-37.75(17)
C(3)-C(2)-C(8)-C(13)	87.13(15)
C(1)-C(2)-C(8)-C(13)	-162.97(12)
O(3)-C(2)-C(8)-C(9)	144.01(13)
C(3)-C(2)-C(8)-C(9)	-91.11(15)
C(1)-C(2)-C(8)-C(9)	18.79(18)

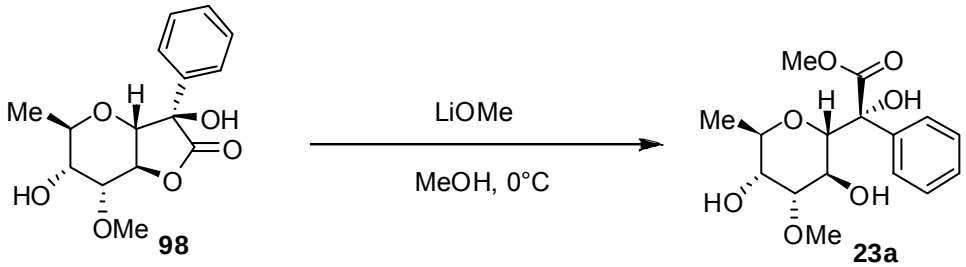
C(13)-C(8)-C(9)-C(10)	-0.3(2)
C(2)-C(8)-C(9)-C(10)	177.94(13)
C(8)-C(9)-C(10)-C(11)	-0.2(2)
C(9)-C(10)-C(11)-C(12)	0.5(3)
C(10)-C(11)-C(12)-C(13)	-0.5(2)
C(11)-C(12)-C(13)-C(8)	0.0(2)
C(9)-C(8)-C(13)-C(12)	0.3(2)
C(2)-C(8)-C(13)-C(12)	-177.98(12)
O(2)-C(1)-O(1)-C(7)	179.81(12)
C(2)-C(1)-O(1)-C(7)	2.57(14)
C(6)-C(7)-O(1)-C(1)	-143.38(11)
C(3)-C(7)-O(1)-C(1)	-25.88(12)
C(7)-C(3)-O(4)-C(4)	66.04(13)
C(2)-C(3)-O(4)-C(4)	-174.97(11)
C(14)-C(4)-O(4)-C(3)	73.95(13)
C(5)-C(4)-O(4)-C(3)	-54.16(14)
C(7)-C(6)-O(6)-C(15)	154.64(12)
C(5)-C(6)-O(6)-C(15)	-89.02(14)

Symmetry transformations used to generate equivalent atoms:

Table 17. Hydrogen bonds for **99** [Å and °].

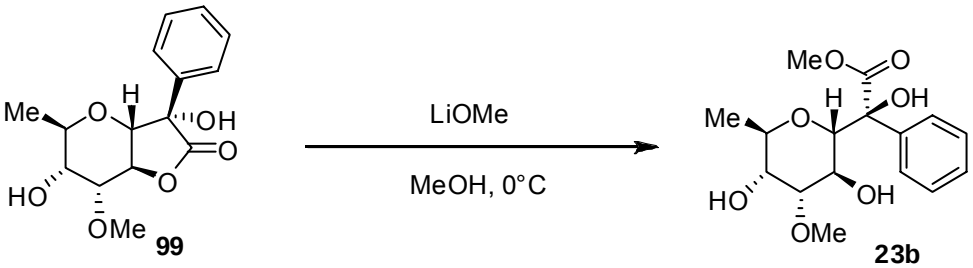
D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
O(3)-H(3A)...O(1S)	0.84	1.81	2.6378(15)	170.3
O(5)-H(5A)...O(2)#1	0.84	2.05	2.8725(14)	168.1
O(1S)-H(1S)...O(5)#2	0.83(2)	1.93(2)	2.7536(15)	172.0(18)

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



98 **23a**

Compound 23a. The lactone **98** (6 mg, 0.02 mmol) was dissolved in MeOH (1 mL), cooled to 0°C with stirring, and LiOMe (0.06 mL, 1 M in MeOH) was added. The reaction mixture was stirred for 5 min at 0 °C. The resulting mixture was then quenched with sat. aq. NH_4Cl and extracted with EtOAc (3 × 10 mL). The combined organic layers were dried over Na_2SO_4 and then evaporated. Chromatography on silica gel using an eluent of EtOAc gave compound **23a** (6 mg, 90%) as a white solid. $[\alpha]^{23}_D$ = -34.2 (*c* = 0.4, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.60 (d, *J* = 7.8 Hz, 2H), 7.60 (t, *J* = 7.8 Hz, 2H), 7.24 (t, *J* = 7.8 Hz, 2H), 4.47 (ddd, *J* = 2.4, 6.4 Hz, 1H), 3.84 (s, 2H), 3.68 (s, 3H), 3.59 (s, 3H), 3.48 (dd, *J* = 2.0, 6.4 Hz, 1H), 1.11 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 172.96, 140.55, 127.77, 127.33, 126.09, 81.42, 78.36, 75.42, 73.07, 69.75, 66.75, 58.00, 52.89, 14.25.; IR (KBr) 3447(br), 2930, 2245, 1737, 1253, 1073, 730 cm^{-1}; HRMS (PESI$^+$) Calcd. For $C_{16}H_{22}O_7$ Na [(M+^{23}Na)$^+$] 349.12577, Found 349.12602; mp = 161 - 163 °C.



99 **23b**

Compound 23b: Following the same procedure described for the preparation of compound **23a**, the lactone **99** (15 mg, 0.68 mmol) afforded compound **23b** (15 mg, 92%) as a white solid. $[\alpha]^{23}_{D}$ = -3.5 (*c* = 0.75, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82-7.79 (m, 2H), 7.40-7.36 (m, 2H), 7.34-7.30 (m, 1H), 4.37 (d, *J* = 9.6 Hz, 1H), 4.27 (dq, *J* = 1.6, 7.2 Hz, 1H), 4.13 (ddd, *J* = 2.8, 8.8 Hz, 1H), 4.01 (s, 1H), 3.89 (ddd, *J* = 1.6, 3.2 Hz, 1H), 3.80 (s, 3H), 3.43 (s, 3H), 3.37 (dd, *J* = 3.6, 9.2 Hz, 1H), 2.57 (d, *J* = 2.0 Hz, 1H), 1.31 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.47, 137.30, 128.40, 128.23, 125.87, 80.60, 79.75, 76.87, 73.21, 68.88, 67.02, 57.81, 53.13, 14.86; IR (neat) 3468(br), 2929, 2248, 1740, 1238, 1142, 728 cm^{-1}; HRMS ($PESI^+$) Calcd. For $C_{16}H_{22}O_7Na$ $[(M+^{23}Na)^+]$ 349.12577, Found 349.12589; mp = 158 - 160°C.

1. 5. References.

1. Levy, D. E.; Tang, C. *The Chemistry of C-glycosides*; Pergamon Press, Oxford, 1995.
2. Hacksell, U.; Daves, G. D. *Prog. Med. Chem.* **1985**, *22*, 1.
3. Thiericke, R. *Nat. Prod. Rep.* **1992**, 103.
4. Hansen, M. R.; Hurley, L. H. *Acc. Chem. Res.* **1995**, *29*, 249.
5. Sequin, U. *Prog. Chem. Org. Nat. Prod.* **1986**, *50*, 57.
6. Zehnder, M.; Sequin, U.; Nadig, H. *Helv. Chim. Acta.* **1979**, *62*, 2525.
7. Kanda, N.; Kono, M.; Asano, K. *J. Antibiot.* **1972**, *25*, 553.
8. Kanda, N. *J. Antibiot.* **1972**, *24*, 599.

9. Kanda, N. *J. Antibiot.* **1972**, *25*, 557.

10. Ishii, S.; Satoh, Y.; Tsuruo, T. *Cancer Chemother. Pharmacol.* **1993**, *32*, 173.

11. Satoh, Y.; Watabe, H.; Nakazawa, T.; Shomura, T.; Yamamoto, H.; Sezaki, M.; Kono, S. *J. Antibiot.* **1989**, *42*, 149.

12. Hansen, M. R.; Hurley, L. H. *Acc. Chem. Res.* **1996**, *1996*, 249.

13. Bililign, T.; Griffith, B. R.; Thorson, J. S. *Nat. Prod. Rep.* **2005**, *22*, 742.

14. Furukawa, M.; Hayakawa, I.; Ohta, G. *Tetrahedron* **1975**, *31*, 2989.

15. Jackson, M.; Karwowski, J. P.; Theriault, R. J.; Hardy, D. J.; Swanson, S. J.; Barlow, G. J.; Tillis, P. M.; McAlpine, J. B. *J. Antibiot.* **1990**, *43*, 223.

16. Brill, G. M.; McAlpine, J. B.; Whittern, D. N.; Buko, A. M. *J. Antibiot.* **1990**, *43*, 229.

17. Gregory, M. B.; Marianna, J.; Whittern, D. N.; Buko, A. M.; Hill, P.; Chen, R. H.; McAlpine, J. B. *J. Antibiot.* **1994**, *47*, 1160.

18. Sun, D.; Hansen, M.; Clement, J. J.; Hurley, L. H. *Biochemistry* **1993**, *32*, 1068.

19. Nakatani, K.; Okamoto, A.; Matsuno, T.; Saito, I. *J. Am. Chem. Soc.* **1998**, *120*, 11219.

20. Hansen, M.; Yun, S.; Hurley, L. *Chem. Biol.* **1995**, *2*, 229.

21. Hansen, M.; Hurley, L. *J. Am. Chem. Soc.* **1995**, *117*, 2421.

22. Menidiatis, C.; Methenitis, C.; Nikolis, N.; Peumatikakis, G. *J. Inorg. Biochem.* **2004**, *98*, 1795.

23. Nikolis, N.; Methenitis, C.; Pneumatikakis, G. *J. Inorg. Biochem.* **2003**, *95*,

177.

24. Nikolis, N.; Methenitis, C.; Peumatikakis, G.; Fiallo, M. L. *J. Inorg. Biochem.* **2002**, *89*, 131.

25. Pasetto, P.; Franck, R. W. *J. Org. Chem.* **2003**, *68*, 8042.

26. Ramberg, L.; Bäcklund, B. *Ark. Kemi Mineral. Geol.* **1940**, *13A*, no. 27.

27. Schröder, M. *Chem. Rev.* **1980**, *80*, 187.

28. McDonald, F. E.; Reddy, K. S.; Díaz, Y. *J. Am. Chem. Soc.* **2000**, *122*, 4304.

29. Sheng, Y.; Musaev, D. G.; Reddy, K. S.; McDonald, F. E.; Morokuma, K. *J. Am. Chem. Soc.* **2002**, *124*, 4149.

30. Nilsson, P.; Larhed, M.; Hallberg, A. *J. Am. Chem. Soc.* **2001**, *123*, 8217.

31. Nilsson, P.; Larhed, M.; Hallberg, A. *J. Am. Chem. Soc.* **2003**, *125*, 3430.

32. Itami, K.; Nokami, T.; Ishimura, Y.; Mitsudo, K.; Kamei, T.; Yoshida, J. i. *J. Am. Chem. Soc.* **2001**, *123*, 11577.

33. Itami, K.; Mineno, M.; Muraoka, N.; Yoshida, J. *J. Am. Chem. Soc.* **2004**, *126*, 11778.

34. Vallin, K. S. A.; Larhed, M.; Hallberg, A. *J. Org. Chem.* **2001**, *66*, 4340.

35. Itami, K.; Nokami, T.; Yoshida, J. i. *Org. Lett.* **2000**, *2*, 1299.

36. Yin, L. X.; Liebscher, J. *Chem. Rev.* **2007**, *107*, 133.

37. Stille, J. K. *Angew. Chem. Int. Ed. Engl.* **1986**, *25*, 508.

38. Stille, J. K. *Pure. Appl. Chem.* **1985**, *57*, 1771.

39. MacLeod, D.; Moorcroft, D.; Quayle, P.; Dorrity, M. R. J.; Malone, J. F.; Davies, G. M. *Tetrahedron Lett.* **1990**, *31*, 6077.

40. Abas, A.; Beddoes, R. L.; Conway, J. C.; Quayle, P.; Urch, C. J. *Synlett* **1995**, *12*, 1264.

41. Tius, M. A.; Gomez-Galeno, J.; Gu, X. Q.; Zaidi, J. H. *J. Am. Chem. Soc.* **1991**, *113*, 5775.

42. Hatanaka, Y.; Hiyama, T. *Synlett* **1991**, 845.

43. Allred, G. D.; Liebeskind, L. S. *J. Am. Chem. Soc.* **1996**, *118*, 2748.

44. Grindley, T. B. *Adv. Carbohydr. Chem. Biochem.* **1998**, *53*, 17.

45. Wipf, P.; Graham, T. H. *J. Org. Chem.* **2003**, *68*, 8798.

46. Iwasawa, N.; Maeyama, K.; Kusama, H. *Org. Lett.* **2001**, *3*, 3871.

47. Kusama, H.; Yamabe, H.; Iwasawa, N. *Org. Lett.* **2002**, *4*, 2569.

48. Maeyama, K.; Iwasawa, N. *J. Am. Chem. Soc.* **1998**, *120*, 1928.

49. Mee, P. H.; Lee, V.; Baldwin, J. E. *Angew. Chem. Int. Ed.* **2004**, *43*, 1132.

50. (a) Kapadia, V. F. S.; Krishnan, B. M.; Wang, C.; Liebeskind, L. S. *J. Org. Chem.* **1994**, *59*, 1047. (b) Liebeskind, L. S.; Fengl, R. W. *J. Org. Chem.* **1990,** *55*, 5359.

51. Casado, A. L.; Espinet, P. *Organometallics* **2003**, *22*, 1305.

52. Han, X.; Stoltz, B. M.; Corey, E. J. *J. Am. Chem. Soc.* **1999**, *121*, 7600.

53. Kolb, H. C.; VanNieuwenhze, M. S.; Sharpless, K. B. *Chem. Rev.* **1994**, *94*, 2483.

54. Evans, D. A.; Fu, G. C.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1998**, *110*, 6917.

55. Evans, D. A.; Fu, G. C. *J. Am. Chem. Soc* **1991**, *113*, 4042.

56. Smith, A. B.; Yokoyama, Y.; Huryn, D. M.; Dunlap, N. K. *Tetrahedron Lett.*

1987, *28*, 3659.

57. Paterson, I.; Florence, G. J.; Gerlach, K.; Scott, J. P.; Sereinig, N. *J. Am. Chem. Soc* **2001**, *123*, 9535.

58. Parikh, J.; Doering, W. *J. Am. Chem. Soc* **1967**, *89*, 5505.

59. Yamada, S. M., D.; Yamamoto, K. *Tetrahedron Lett.* **1992**, *33*, 4329.

60. Anand, R. C.; Selvapalam, N. *Synth. Commun.* **1994**, *24*, 2743.

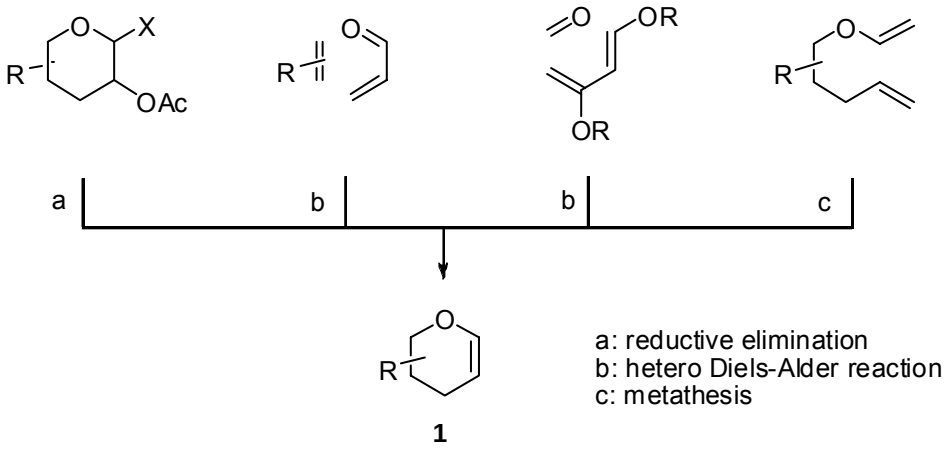
61. Kamenecka, T. M.; Danishefsky, S. J. *Chem. Eur. J.* **2001**, *7*, 41.

Part 2. Fischer Carbene Catalysis of the Alkynol Cycloisomerization: Application to the Synthesis of the Altromycin B Disaccharide.

2.1 Introduction and background

The importance of glycals in synthetic organic chemistry has been demonstrated in several contexts, including the efficient synthesis of a variety of biologically important carbohydrate and oligosaccharide-containing natural products, in which carbohydrate-derived glycals are valuable electrophilic partners for a variety of glycoside synthesis processes.[1-5]

Scheme 1. Representative examples of glycal synthesis.

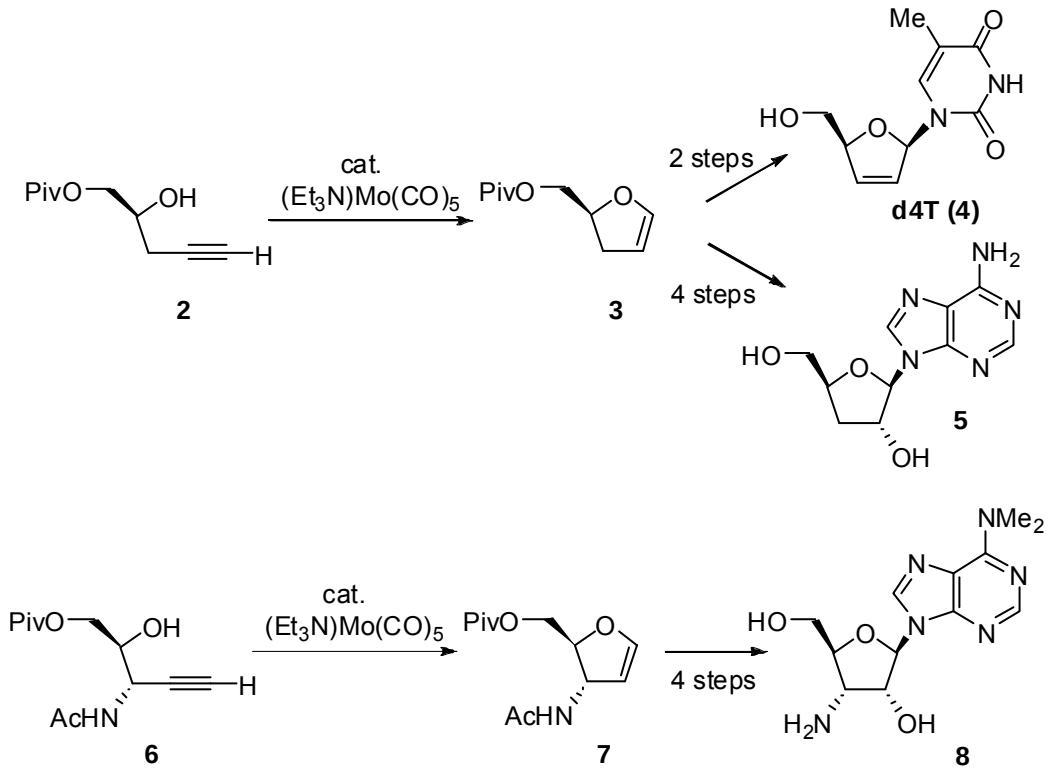


Several methods for the preparation of glycals have been reported (Scheme 1). In 1914, Emil Fischer reported the first synthesis of a 1,2-glycal via reductive elimination of a 2-(acyloxy)glycosyl halide.[6] Later, hetero Diels-Alder

reactions,[7-9] and more recently, ring closing metathesis[10-12] have been introduced for the preparation of glycals.

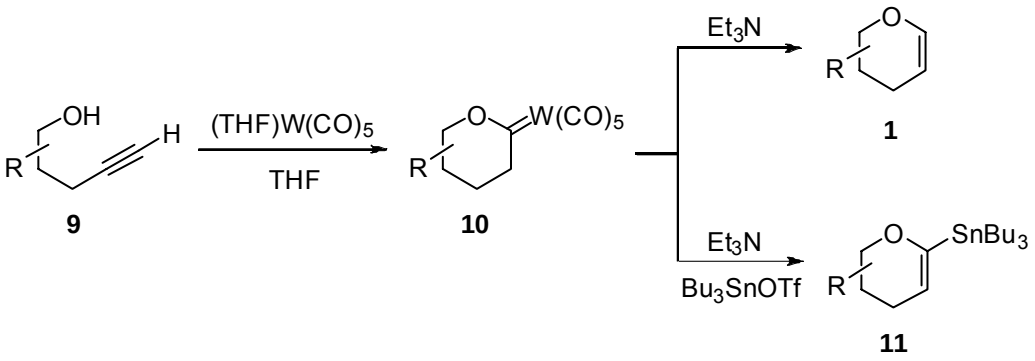
As a novel approach to the glycal synthesis, the McDonald laboratory has reported alkynyl alcohol cycloisomerization utilizing group VI transition metals. $Mo(CO)_5 \cdot Et_3N$ proved to be an effective catalyst for the formation of 5-membered cyclic enol ether, and this methodology was utilized for the stereoselective synthesis of a bioactive glycoconjugate represented by the anti-AIDS nucleoside, d4T **(4)** (Scheme 2).[13-15]

Scheme 2. Synthesis of glycoconjugates via $(Et_3N)Mo(CO)_5$ catalyzed alkynol cycloisomerization.



The McDonald laboratory has also demonstrated that $(THF)W(CO)_5$ is effective for the formation of stable 6-membered cyclic tungsten Fischer carbenes (Scheme 3). The generated carbene **10** was further converted into the corresponding dihydropyran **1** in the presence of Et_3N.[16-18] The tungsten-mediated cyclic Fischer carbene formation was further utilized for the preparation of synthetically useful α-stannyl glycals under relatively mild conditions. Treatment of tungsten carbene **10** with Et_3N and Bu_3SnOTf at room temperature provided α-stannyl glycal **11** in high yield.[16-18]

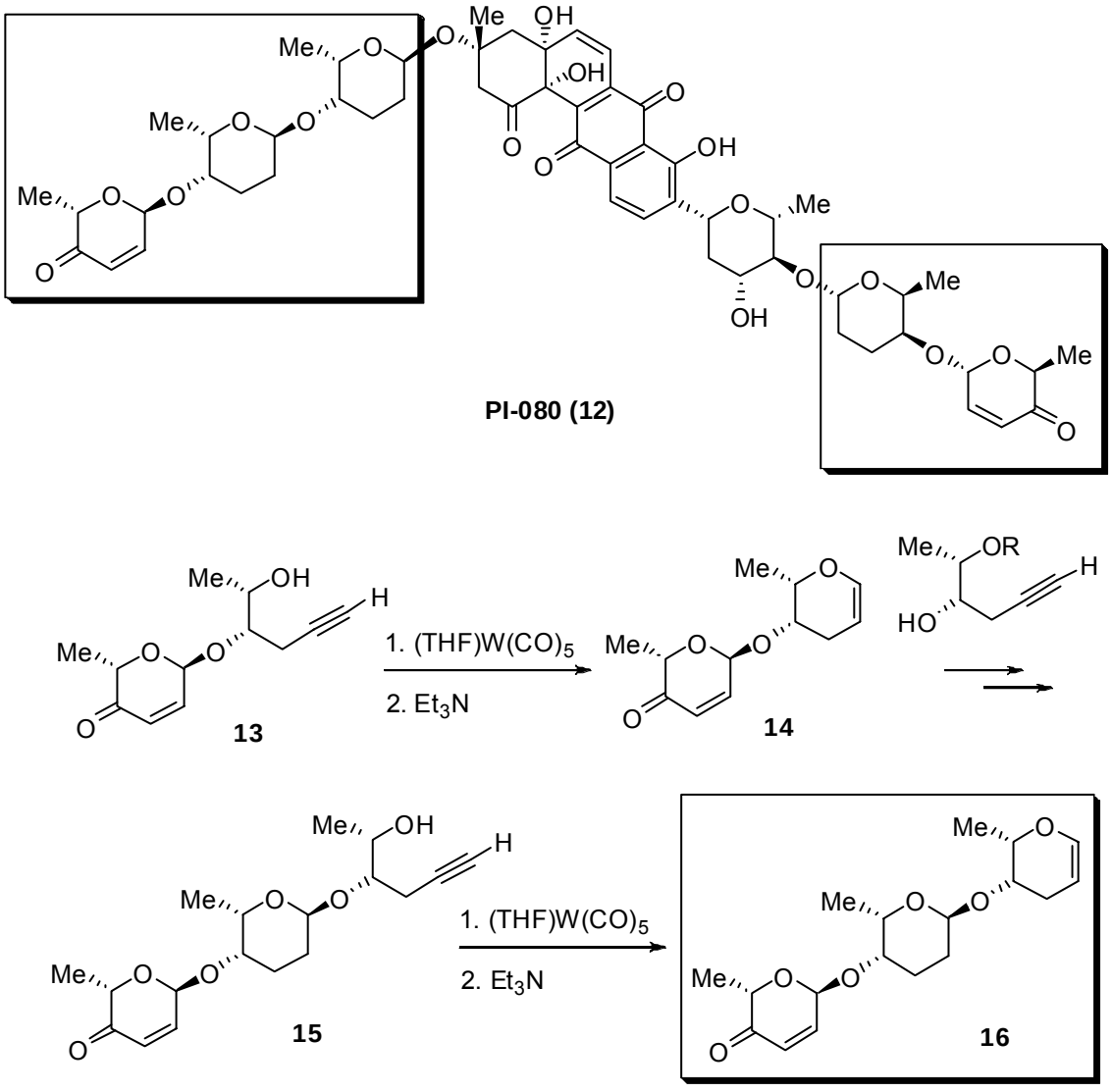
Scheme 3. Synthesis of glycal and α-stannyl glycal via $W(CO)_6$ mediated alkynol cycloisomerization.



9 **10** **1** **11**

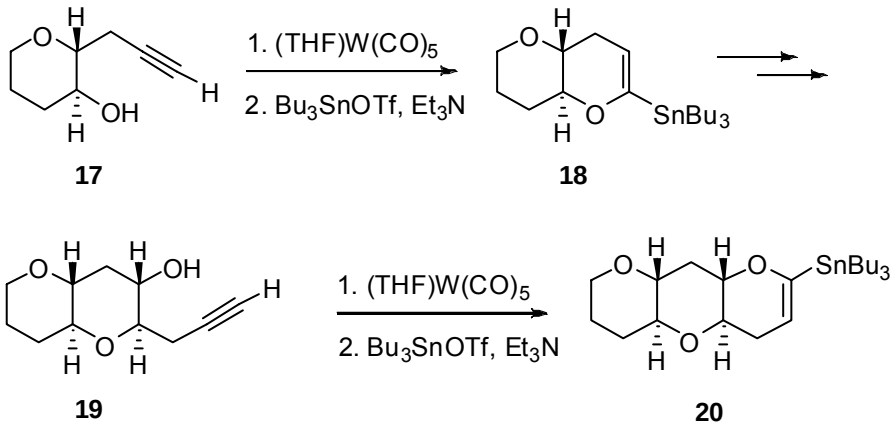
The efficiency of novel 6-membered glycal formation reaction was well demonstrated in the synthesis of of trisaccharide *O*-glycoside substructure **16** of antibiotic PI-080 **(12)** through the iteration of cycloisomerization and stereoselective glycosylation (Scheme 4).[19-21]

Scheme 4. Iterative approach for the synthesis of trisaccharide substructure of PI-080.



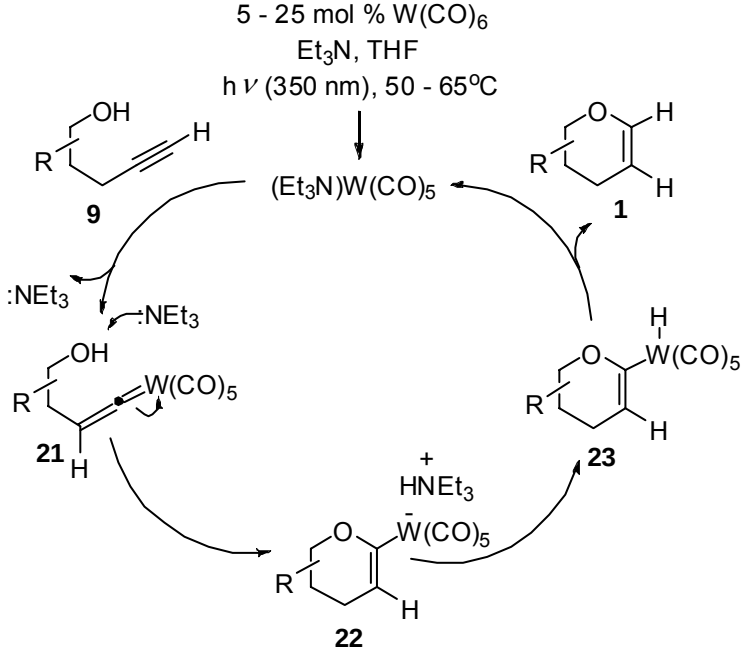
The iterative strategy of α-stannyl glycal formation reaction also provided a straightforward procedure for the construction of fused pyran rings commonly found in marine natural products (Scheme 5).[22]

Scheme 5. Iterative approach for the synthesis of poly-cyclic ether.



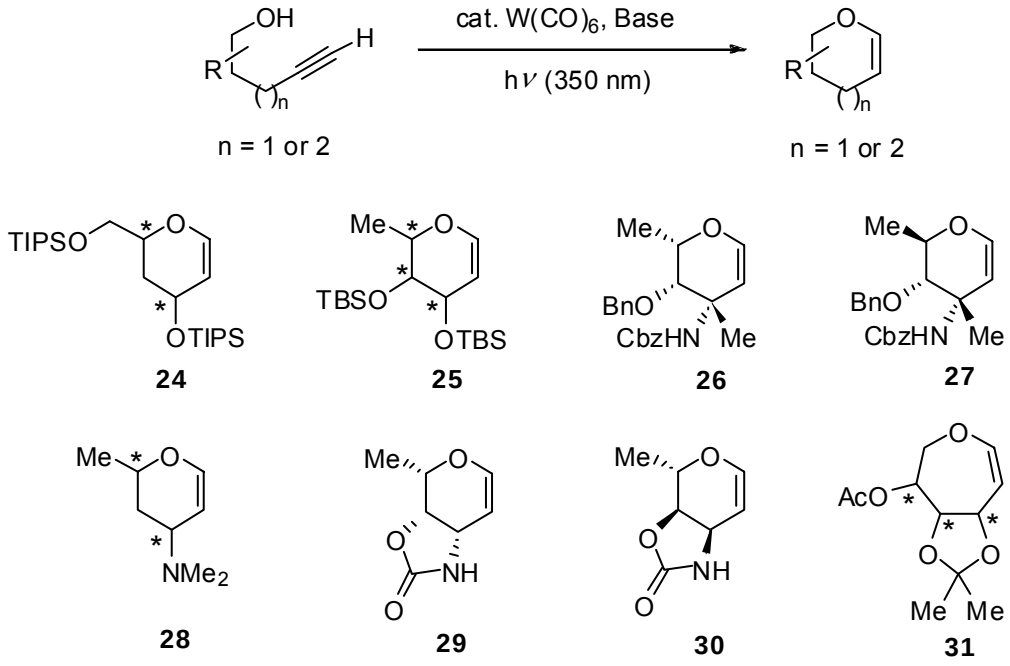
In 2000, the McDonald laboratory successfully optimized the two-step glycal formation sequence to one-pot catalysis upon continuous photoirradiation (350 nm) of alkynol in the presence of 5 to 25 mol% of $W(CO)_6$ and base (Scheme 6).[21,23]

Scheme 6. Proposed mechanism of tungsten-catalyzed cycloisomerization.



The *in situ* generated $(Et_3N)W(CO)_5$ reacts with alkynol **9** to provide tungsten vinylidene intermediate **21**, followed by regioselective nucleophilic addition of hydroxyl to the terminal carbon atom afforded the vinyl tungsten anion **22**. Proton transfer to tungsten anion, followed by reductive elimination produces glycal **1** and regenerates $(Et_3N)W(CO)_5$. This methodology provided and efficient way to prepare structurally diverse glycals exemplified by **24**[24,25], **25**[23] including amino glycals **26** – **30**,[26-29] and seven-membered glycals **31**[30] (Figure 1).

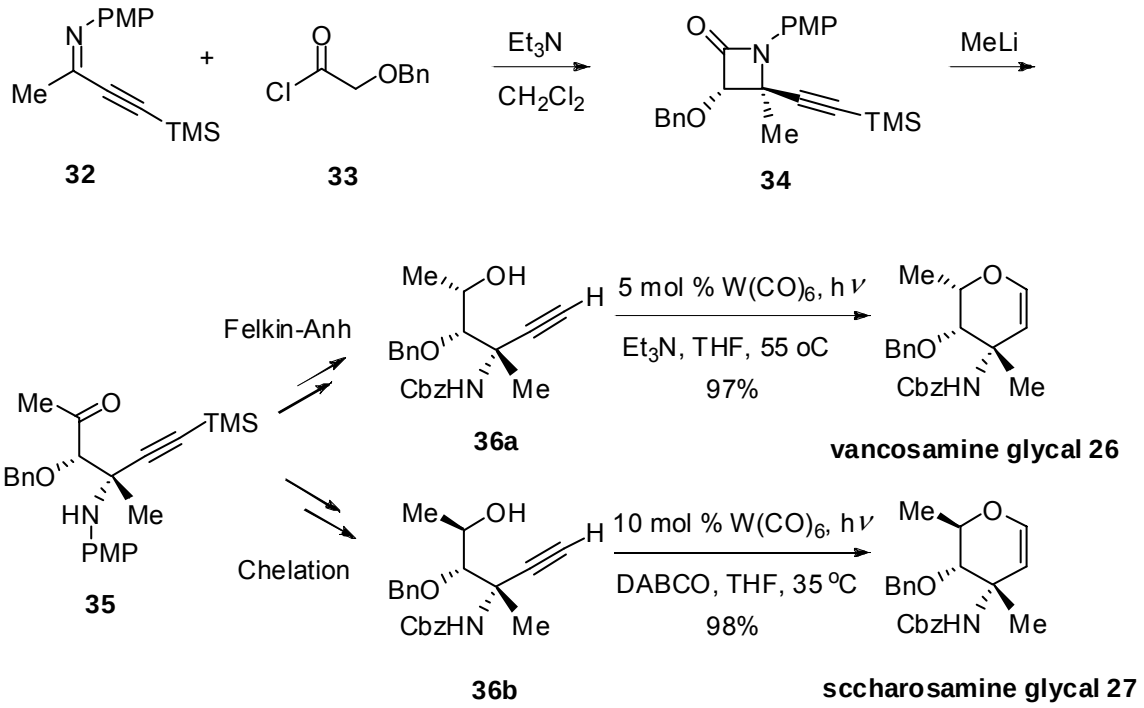
Figure 1. Variety of glycals prepared by tungsten catalyzed cycloisomerization.



Cutchins and McDonald have demonstrated that only 5 – 10 mol % of catalyst loading is required in the cycloisomerization process to produce vancosamine **26** and saccharosamine **27** glycals over 97% isolated yield

(Scheme 7).[26] Each alkynyl alcohols **36a** and **36b** was efficiently prepared by the sequence of formation of *beta*-lactam **34** and ring opening to methyl ketone **35**, followed by stereoselective reduction of ketone.

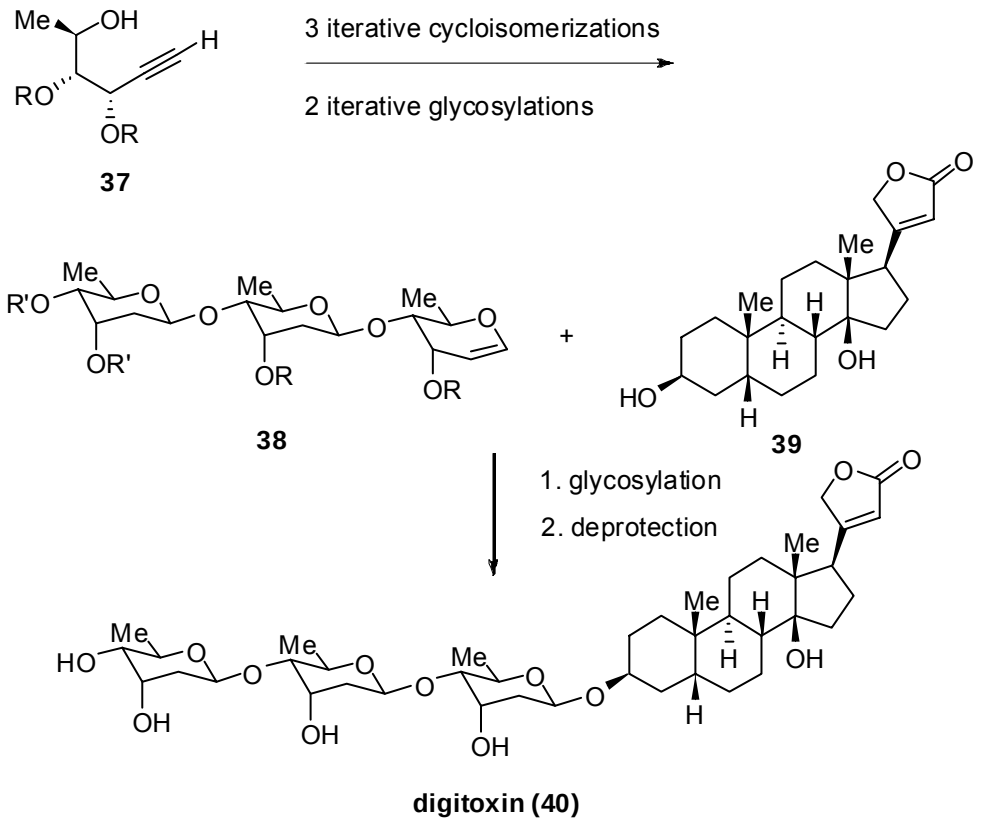
Scheme 7. Synthesis of vancosamine- and saccharosamine-glycals **26** and **27**.



The efficiency of this one-pot high yielding process was highlighted in the total synthesis of digitoxin **(40)** (Scheme 8).[31] The iterative strategy of tungsten-catalyzed cycloisomerization and acid-catalyzed stereoselective glycosylation provided trisaccharide glycal **38**. The final acid-catalyzed glycosylation of the tri-saccharide glycal **38** with digitoxigenin aglycone **39**, followed by deprotection produced digitoxin **(40)** in a highly convergent and stereoselective manner. Later,

this strategy was applied to the preparation of oligosaccharide stereoisomers of digitoxin.[32]

Scheme 8. Total synthesis of digitoxin **(40)**.



As a similar approach to tungsten-catalyzed cycloisomerization, the Trost group reported Ru catalyzed alkynol cycloisomerization in 2002 and later, Rh was also proved to be effective in this process.[33,34]

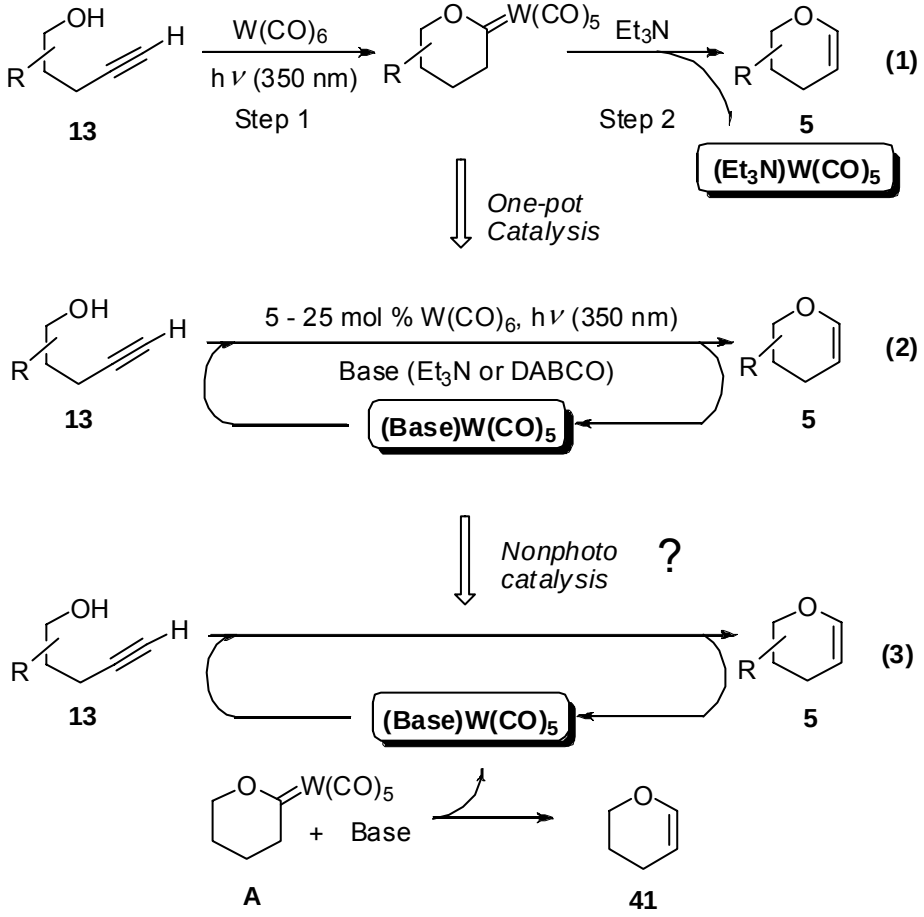
Along with our interests in developing an efficient synthetic method for glycal synthesis, we have continued to explore tungsten cycloisomerizations from non-carbohydrate alkynol substrates.

1. 2. Results and Discussion

2. 2. 1. Design and hypothesis of Fischer carbene catalysis.

In our earlier studies, we reported a two-step glycal synthesis via generation of stable cyclic tungsten Fischer oxacarbene by photolysis of $W(CO)_6$, followed by base promoted demetalation (eq 1 in Scheme 9).[16-18,35] Later, this two-step sequence was optimized to one-pot catalysis by generating active catalytic species, $(Base)W(CO)_5$, upon continuous photoirradiation (350 nm) of alkynol and 5 - 25 mol% of $W(CO)_6$ in the presence of base (eq 2).[23]

Scheme 9. Design of Fischer carbene catalyzed cycloisomerization.

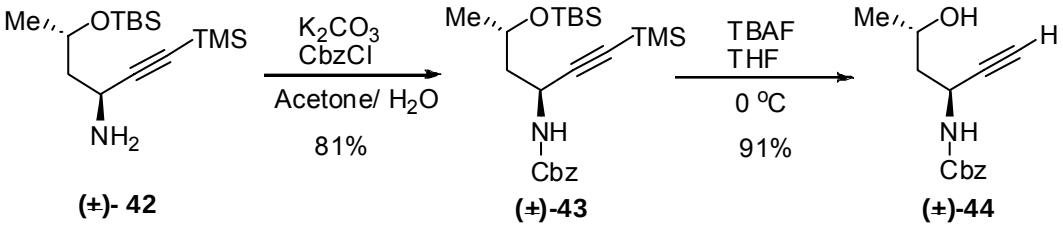


On the basis of our mechanistic rationale, we envisioned that a cyclic tungsten Fischer carbene **A** could be utilized as a precatalyst for the alkynol cycloisomerization, in which the active catalytic source, (Base)$W(CO)_5$, could be generated via base promoted demetalation of tungsten Fischer carbene **A** in the absence of photoirradiation (eq 3).[36-39]

2. 2. 2. Optimization of reaction conditions.

Our initial study of Fischer carbene catalyzed alkynol cycloisomerization was tested with alkynol (±)-**44**, which was prepared from known amine (±)-**42**[27] through Cbz protection followed by desilylations (Scheme 10).

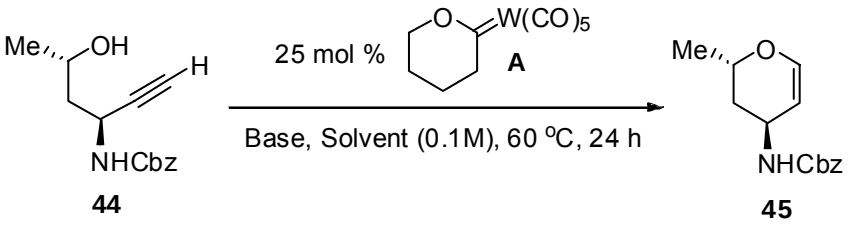
Scheme 10. Preparation of alkynyl alcohol (±)-**44**.



The reactions were screened under different combinations of base and solvent in the presence of alkynol (±)-**44** and 25 mol % of cyclic tungsten Fischer carbene **A**, prepared by photolysis of 4-pentyn-1-ol and stoichiometric $W(CO)_6$ (Table 1).[16] The best result was obtained by subjecting alkynol (±)-**44** to the mixture of Et_3N in THF at 60 °C for 24 hours, and this reaction conditions provided the only *endo* glycal (±)-**45** in 92% isolated yield. The choice of Et_3N as base was critically

important to success of this transformation , as the use of DABCO resulted in low conversion under the reaction conditions.

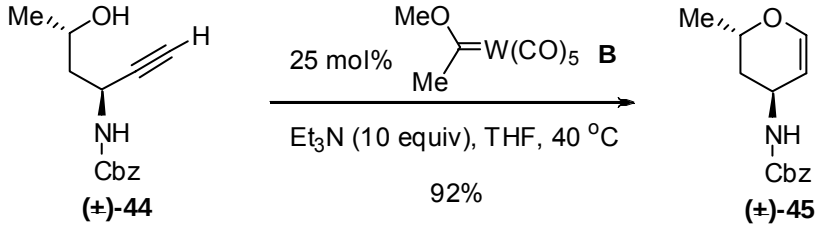
Table 1. Optimization of reaction conditions.



R_3N (eq)	Solvent (0.1M)	yield (%)
DABCO (2 eq)	THF	32% (52% **44)**
DABCO (2 eq)	Toluene	49% (36% **44)**
Et_3N (20 eq)	**THF**	**92%**
Et_3N (20 eq)	Toluene	90%

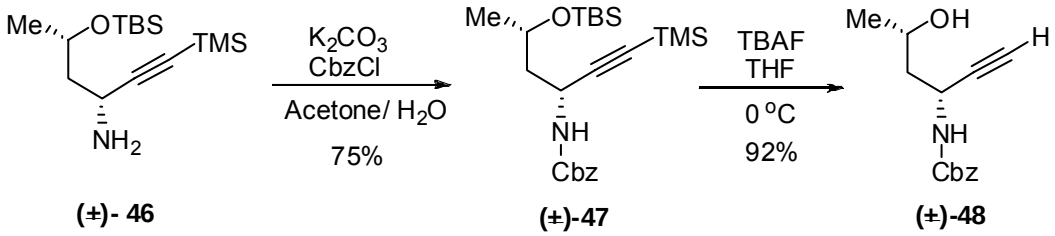
Encouraged by the initial success, we endeavored to find an exclusive non-photochemical environment, in which both the preparation of precatalyst as well as the cycloisomerization process would not require photoirradiation, so that our procedure would be usable by laboratories without access to photochemical equipment. The simple tungsten Fischer carbene, $(OC)_5W=C(OMe)(Me)$ **B**,[40-42] was chosen as a precatalyst due to its structural similarity as cyclic carbene **A** as well as its facile preparation and the stability. The tungsten carbene **B** proved to be also effective for the cycloisomerization. In the presence of 25 mol % of **B**, and 10 equiv. of Et_3N under THF at 40 °C, alkynol (±)-**44** provided only the *endo* glycal (±)-**45** in 92 % yield (Scheme 11).

Scheme 11. Fischer carbene **B** catalyzed alkynol cycloisomerization.



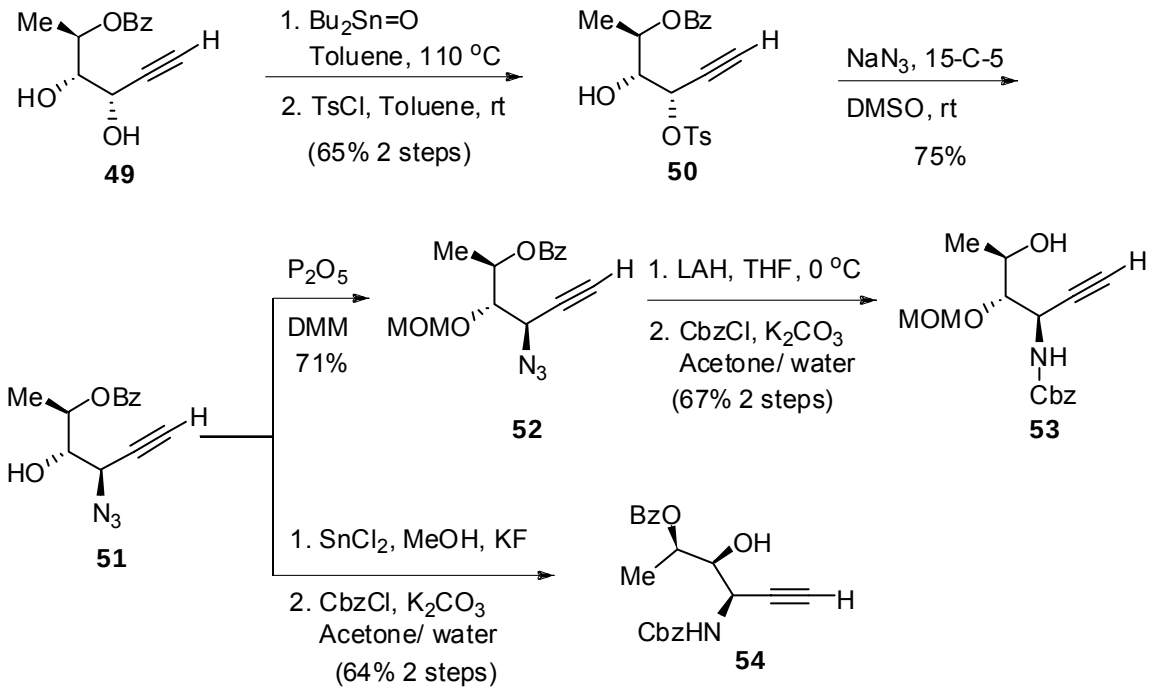
To test the versatility of the reaction conditions, a variety of alkynyl alcohols were synthesized.

Scheme 12. Preparation of alkynyl alcohol (±)-**48**.



The *cis* amino alkynyl alcohol (±)-**48** was prepared from known amine (±)-**46**[27] with the same sequence as the *trans* diastereomer (±)-**44** (Scheme 12). The amino alkynols **53** and **54** were prepared from the known diol **49**[23] (Scheme 13). Selective tosylation was initially conducted with pyridine and tosyl chloride, but better yield and selectivity were obtained with tin acetal formation[43] followed by tosylation. The mono-tosylated alcohol **50** underwent azide displacement to give azido alcohol **51**.

Scheme 13. Synthesis of alkynol **53** and **54**.



The alkynyl alcohol **53** was obtained through the sequence of MOM protection, LAH reduction of azide **52** followed by Cbz protection. The alkynol **54** was synthesized from the common intermediate **51** through reduction of azide followed by Cbz protection of amine. The other alkynols **26**, **27**, **55** and **56** were prepared by known procedures in the literature.[26,30]

Figure 2. Substrates for the Fischer carbene catalyzed cycloisomerization.

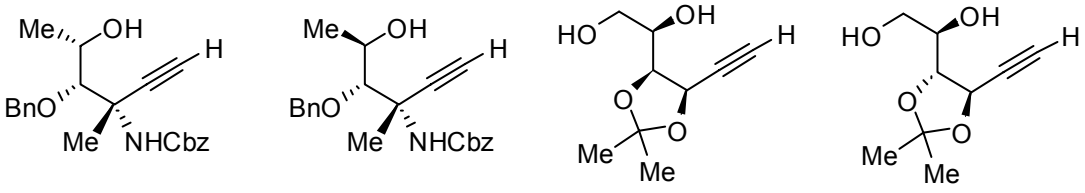
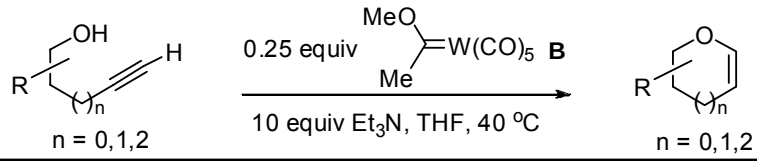
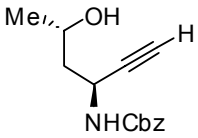
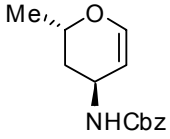
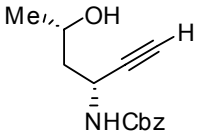
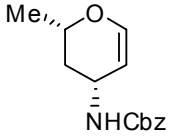
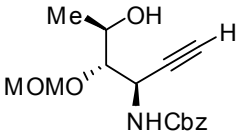
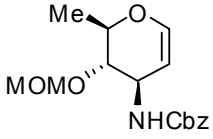
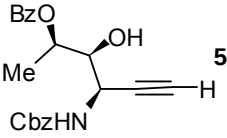
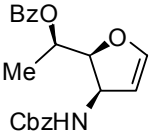
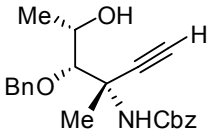
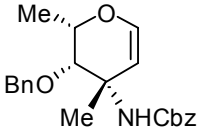
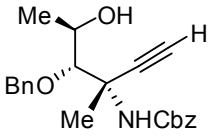
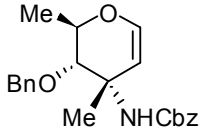
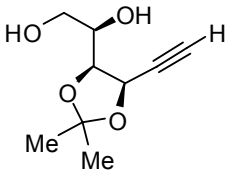
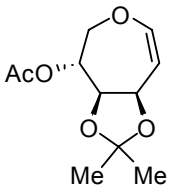
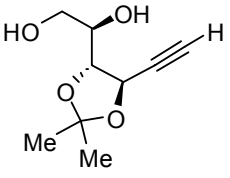
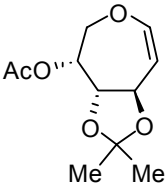


Table 2. Fischer carbene catalyzed cycloisomerization.



Entry	Alkynol		Product		rxn time	% Yield
1		**44**		**57**	12 h	92
2		**50**		**58**	12 h	95
3		**53**		**59**	12 h	95
4		**54**		**60**	12 h	77
5		**26**		**61**	12 h	84
6		**27**		**62**	12 h	94
7		**55**		**63**	24 h[a]	82[c]
8		**56**		**64**	24 h[a]	82[b, c]

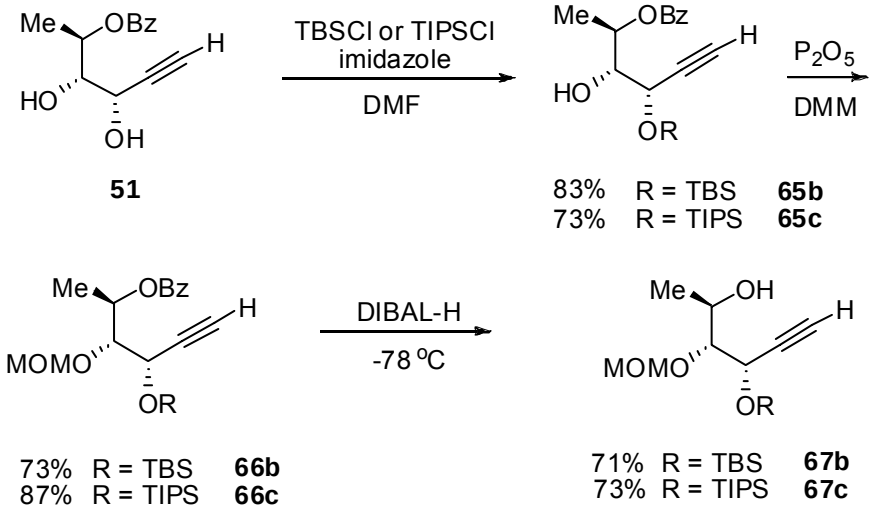
[a] reaction was conducted at 60 °C. [b] 0.4 equiv of catalyst was used. [c] 2 step yield after acyl protection.

The prepared alkynols were treated with tungsten Fischer carbene **B** under optimized conditions, and all alkynols (entries 1-8) provided 5- to 7-membered glycals in good to excellent yields (Table 1). The substrates containing carbamate group at the propargylic position (entries 1-6) showed excellent *endo* selectivity as well as higher reactivity. However, oxygen containing alkynol substrates (entries 7 and 8) required higher temperature (60 ^{o}C), longer reaction time (24 hr) and higher loading of precatalyst **B** (40 mol %, entry 8).

2. 2. 3. Comparison of non-photochemical and photochemical procedures.

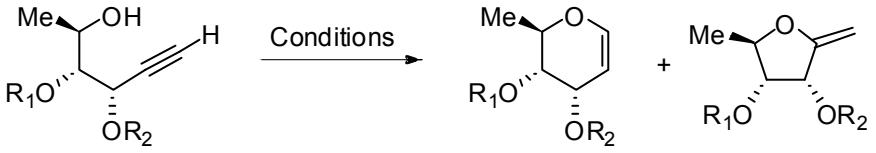
The efficiency of this non-photochemical procedure was examined by comparison with known photochemical reaction conditions using three different alkynols **67a - c**.

Scheme 14. Preparation of alkynol **67b** and **67c**.



The alkynols **67b** and **67c** were prepared from known diol **51**[23] through the same sequence of selective silyl protection of diol, MOM protection, and DIBAL reduction of ester (Scheme 14). Alkynyl alcohol substrates with propargylic oxygen substituents **67** utilized in our digitoxin synthesis[31] required additional optimization relative to the photochemical procedure (Table 3).

Table 3. Comparison of non-photochemical and photochemical procedures.



endo *exo*

67 a R_1, R_2 = TBS; b R_1 = MOM, R_2 = TBS; c R_1 = MOM, R_2 = TIPS

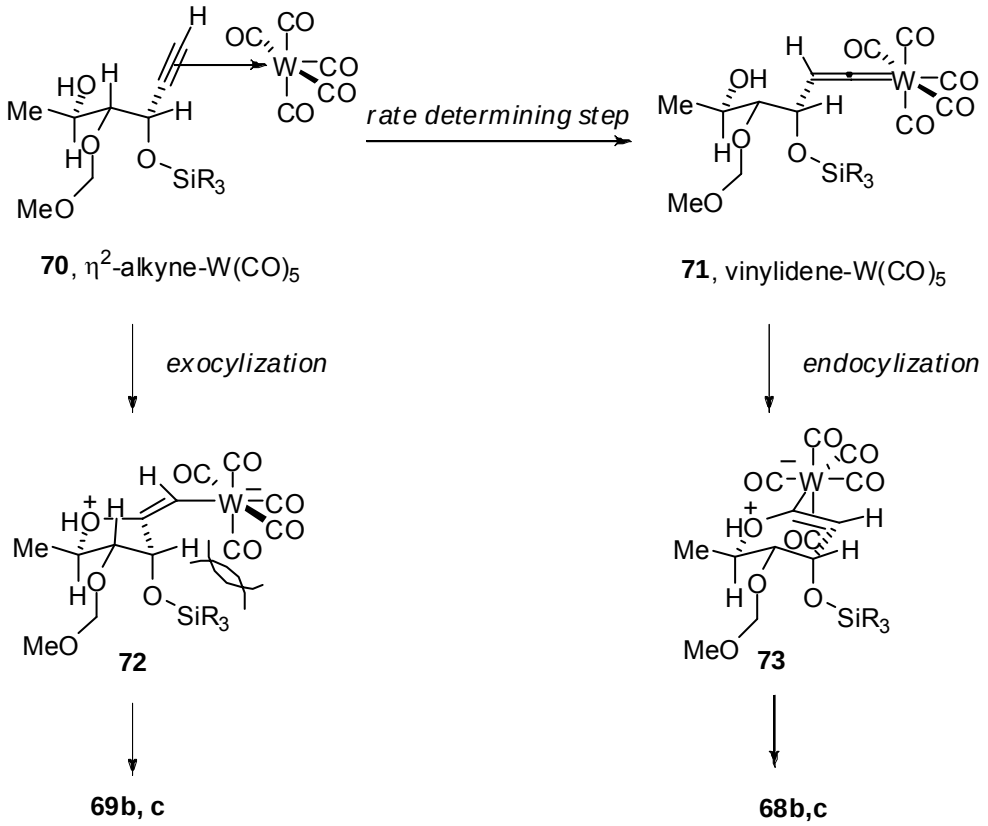
68 **69**

entry	substrate	conditions[a]	%yield **68**	%yield **69**
1	**67a**	A	53[b]	0[b]
2	**67a**	B	92	0
3	**67b**	A	53	35
4	**67b**	B	65	20
5	**67b**	C	75	15
6	**67c**	A	85	9
7	**67c**	B	88	7
8	**67c**	C	88	6

[a] A: 40 mol% **B**, 10 equiv. Et_3N, THF, 24 h
B: 25 mol% $W(CO)_6$, 10 equiv. Et_3N, THF, hν (350 nm), 60 ^oC, 6 h
C: 25 mol% $W(CO)_6$, 2 equiv. DABCO, THF, hν (350 nm), 60 ^oC, 6 h
[b] 30% of **67a** was recovered

Specifically, the sensitivity of cycloisomerization regioselectivity noted by others[25,44] was more pronounced. These results with substrate family **67** show that sterically bulky substituents are required for high *endo*-regioselectivity, and reduced steric bulk in one substituent requires increasing the steric bulk of the other substituent (compare **67b** with **67c**) in order to obtain good *endo*-regioselectivity.

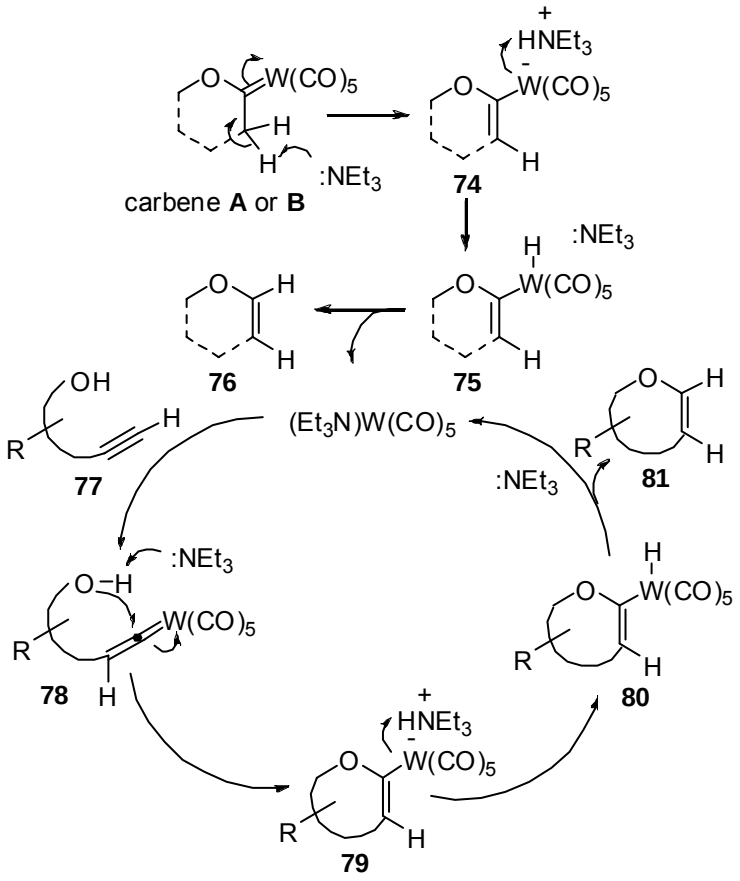
Figure 3. Proposal for substituent effects on regioselectivity.



We propose that steric bulk at the propargylic position causes steric interaction with the tungsten pentacarbonyl reactant, facilitating rearrangement of the η^2-alkyne-tungsten complex **70** to the tungsten vinylidene **71** (Figure 3), which is the likely rate determining step for *endo*-regioselectivity in these cycloisomerization transformations to favor **68c** with R = isopropyl.[45-47] From substrate **67b** with the TBS protective group, we propose that the tungsten pentacarbonyl can promote Lewis acid-promoted cyclization to **72** as the precursor to **69b**, but steric bulk disfavors formation of **72** relative to rearrangement to vinylidene intermediate **71**.

2. 2. 4. Proposed mechanism for the Fischer carbene catalysis.

Scheme 15. Proposed mechanism for the Fischer carbene catalysis.

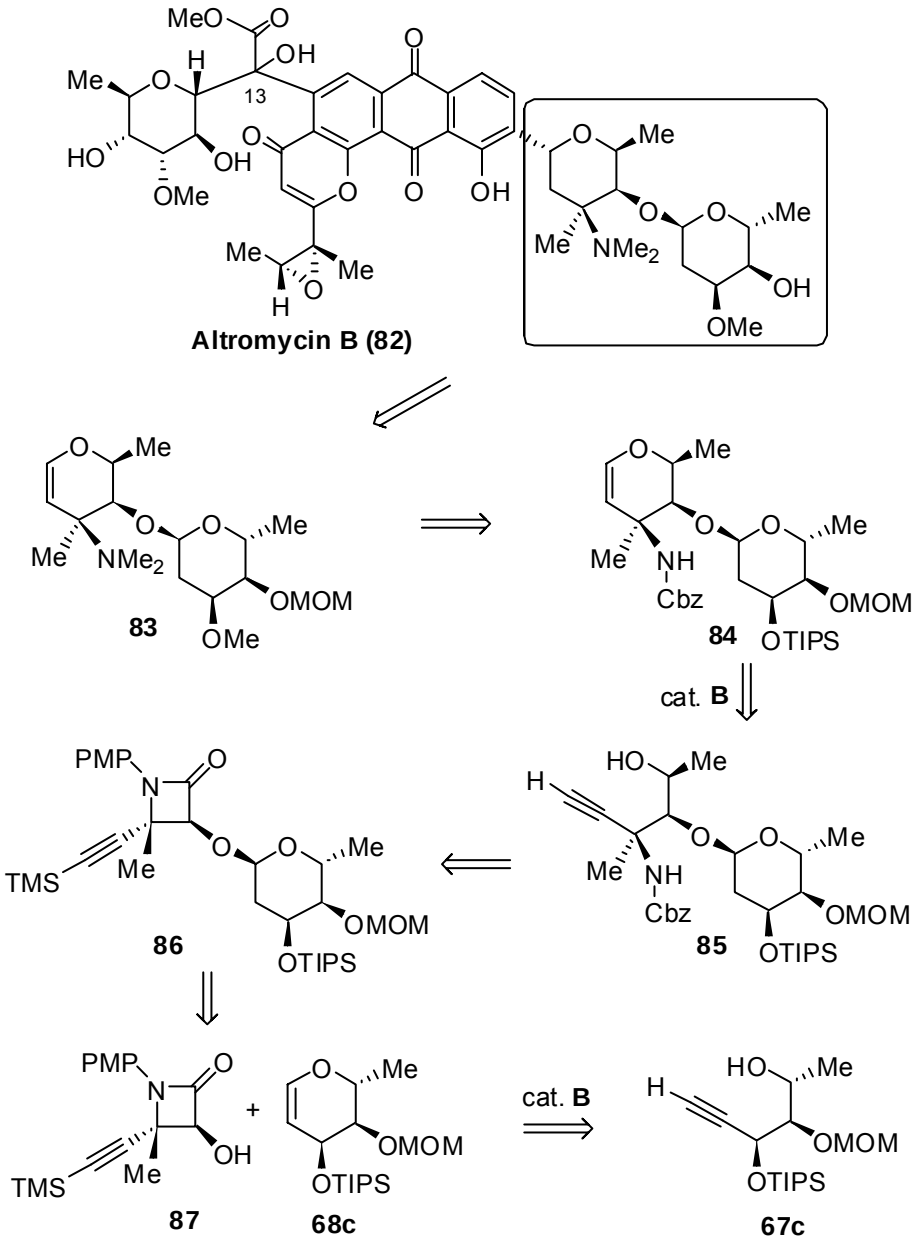


A plausible mechanism for this non-photochemical catalysis procedure is described in Scheme 15. The active catalytic source, $(Et_3N)W(CO)_5$, generated through the precatalytic cycles via reaction between tungsten Fischer carbene **A** or **B** and Et_3N, reacts with the alkynol **77** to provide tungsten vinylidene intermediate **78**. Regioselective nucleophilic addition of hydroxyl to the terminal carbon atom of vinylidene, followed by proton transfer to tungsten anion **79** to produce **80** and reductive elimination provides *endo* glycal product **81**, and regenerates $(Et_3N)W(CO)_5$ for further catalysis.

2. 2. 5. Synthesis of the east disaccharide substructure of altromycin B.

The utility of this new reaction condition is further demonstrated in the synthesis of the east disaccharide *O*-glycoside substructure of altromycin B **(82)**. Altromycin B **(82)** was first isolated in the early 1990's and reported to have anticancer activity including *in vivo* activities against P388 leukemia, as well as colon, lung, and ovarian tumors.[48,49] Our synthetic plan is shown in figure 5. We envisioned the east disaccharide *O*-glycoside substructure **83** by functional group transformations of compound **84**, which in turn would be derived by Fischer carbene catalysis of alkynol **85**. As it was already demonstrated in the synthesis of vancosamine glycal by Cutchins and McDonald,[26] the alkynol **85** was envisioned from the *beta*-lactam **86**, arising from the glycosylation of hydroxyl *beta*-lactam **87** and the cycloisomerization product **68c** of alkynol **67c**.

Figure 5. Retrosynthetic analysis of the east substructure of altromycin B.



The enantiomerically pure hydroxyl *beta*-lactam (+)-**87** was obtained by resolution of (±)-**87**[26]. NIS-mediated glycosylation[50] of (±)-**87** and known glycal **67a**[23] produced separable mixture of diastereomers **89** and **90**. Both compounds

89 and **90** were separately treated with MeLi to give (+)-**87** and (–)-**87**, along with **67a**. The absolute stereochemistry of (+)-**87** was initially confirmed by comparison with the known compound[28] after further transformations, and later reconfirmed by X-ray crystallography of (+)-**87**. The enantiomerically pure (+)-**87** was utilized for the disaccharide substructure of altromycin B.

Scheme 16. Resolution of racemic *beta*-lactam (±)-**87**.

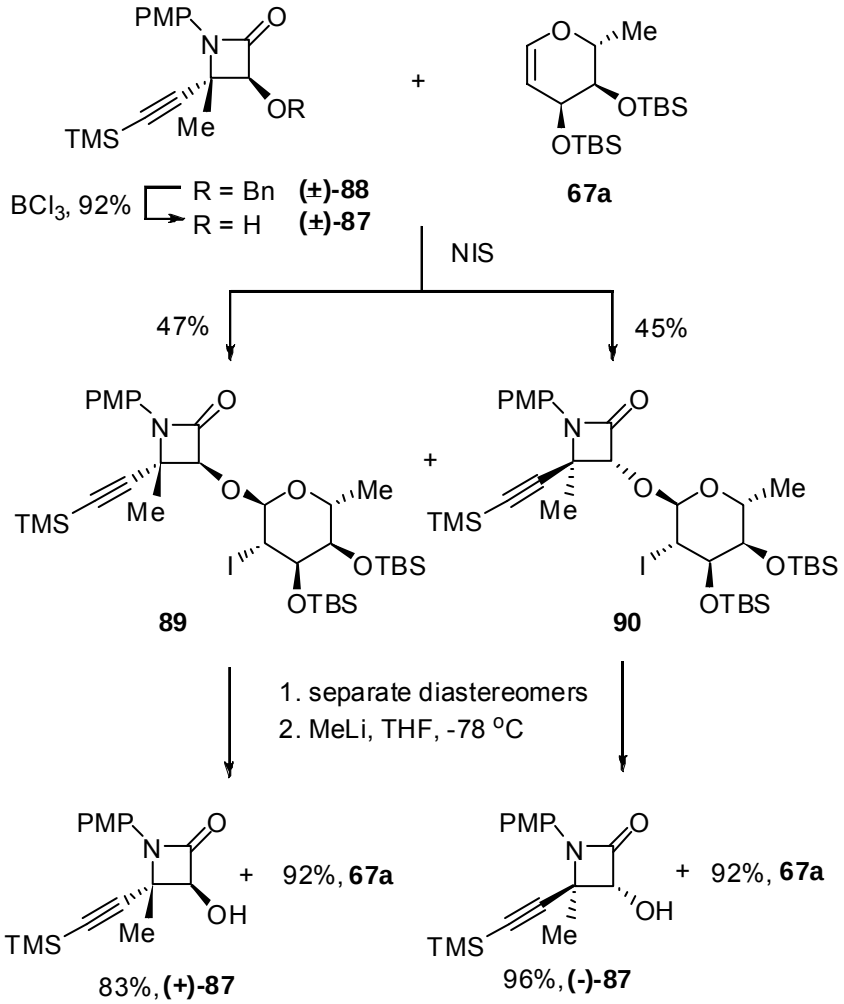
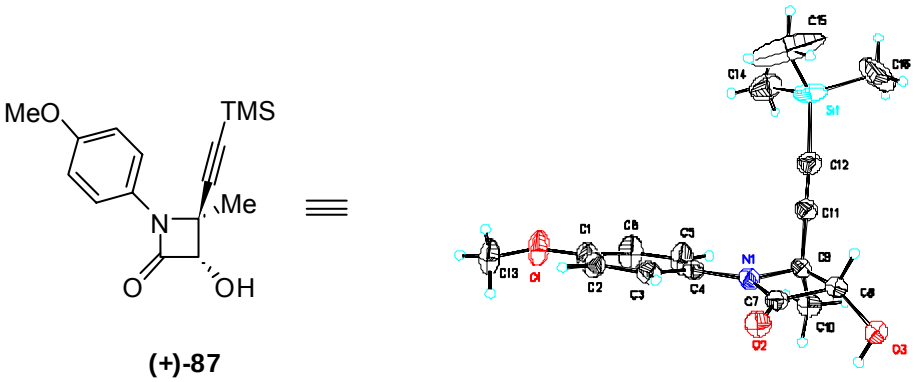
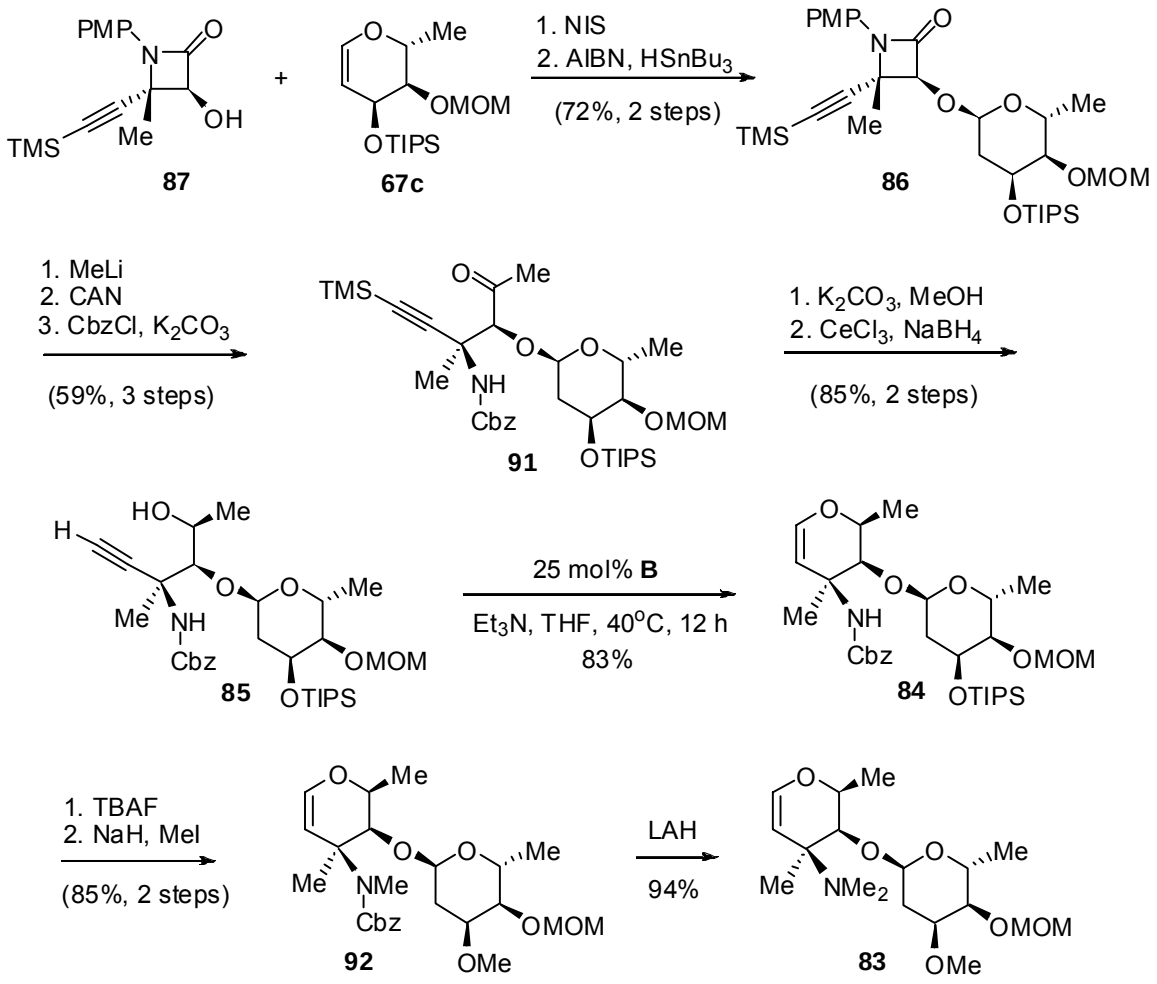


Figure 6. X-ray crystal structure of compound **96**.



The synthesis commenced with glycal **67c**, obtained by tungsten Fischer carbene catalyzed cycloisomerization. NIS-mediated glycosylation[50] between hydroxy *beta*-lactam **80** and glycal **67c**, and subsequent removal of iodide under radical conditions produced a single diastereomer **86**, which was then treated with methyllithium, followed by replacement of *N*- protective group from PMP to less basic Cbz to produce ketone **91**. Alkyne desilylation followed by Felkin-Anh controlled reduction under Luche conditions provided alkynyl alcohol **85**. The cycloisomerization proceeded smoothly in the presence of 25 mol% of precatalyst **B** and 10 equiv of Et_3N at 40°C for 12 hours and produced disaccharide glycal **84** in excellent yield. Finally, the synthesis of the east disaccharide substructure **83** was completed through the sequence of removal of TIPS, methylation and LAH reduction.

Scheme 17. Synthesis of the disaccharide substructure **33** of altromycin B.



While each of the transformations described herein also proceeds by the photochemical method (in some cases with lower catalytic loading), these new conditions now mean that photochemical equipment is no longer required for tungsten-catalyzed cycloisomerization. In addition, the tungsten-catalyzed cycloisomerization procedure requires neither expensive transition metals nor specialized ligands, and is compatible with a broad range of functional groups.

2.3 Conclusions.

We have demonstrated the first use of tungsten Fischer carbene as a precatalyst in the non-photochemical alkynol cycloisomerization, and iterative application of this method to the stereoselective synthesis of disaccharide *O*-glycoside substructure of altromycin B. In combination with mechanistic studies of this method, further studies directed toward the total synthesis of the altromycin natural products are in progress.

2. 4. Experimental Section.

General: ^{1}H NMR and ^{13}C NMR spectra were recorded on a Varian INOVA-400 spectrometer (400 MHz for ^{1}H, 100 MHz for ^{13}C), or on an INOVA-600 spectrometer (600 MHz for ^{1}H, 150 MHz for ^{13}C). NMR spectra were recorded on solutions in deuterated chloroform ($CDCl_3$), with residual chloroform (δ 7.26 ppm for ^{1}H NMR and δ 77.0 ppm for ^{13}C NMR) or deuterated methyl sulfoxide (DMSO-d_6), with residual methyl sulfoxide (δ 2.50 ppm for ^{1}H NMR and δ 35.0 ppm for ^{13}C NMR) 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; q, quartet; m, multiplet. IR spectra were collected on a Mattson Genesis II FT-IR spectrometer 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. Melting points were determined with a Fisher-Johns melting point apparatus. Optical rotations were measured at 23°C (concentration

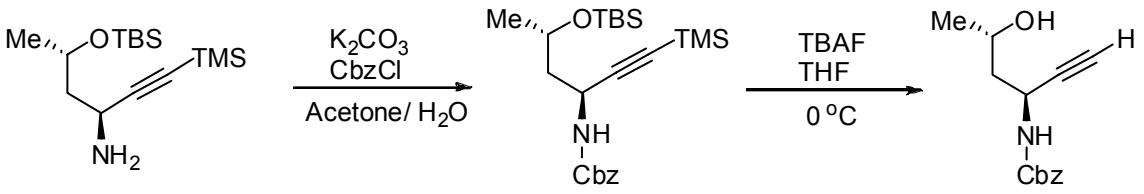
in g/100 mL) using a Perkin-Elmer 341 polarimeter. Analytical thin layer chromatography (TLC) was performed on precoated glass backed plates purchased from Whatman (silica gel $60F_{254}$; 0.25mm thickness). Flash column chromatography was carried out with silica gel 60 (230-400 mesh ASTM) from EM Science.

All reactions were carried out with anhydrous solvents in oven-dried or flame-dried and nitrogen- or argon-charged glassware. All anhydrous solvents except as mentioned were dried with 3 or 4 Å molecular sieves (beads) purchased from Aldrich and tested for trace water content with coulometric KF titrator from Denver Instruments.

All solvents used in extraction procedures and 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 Aldrich or Strem Chemicals.

Representative examples of alkynyl alcohol synthesis and cycloisomerizations

Preparation of alkynyl alcohol (±)-44



(±)-42 **(±)-43** **(±)-44**

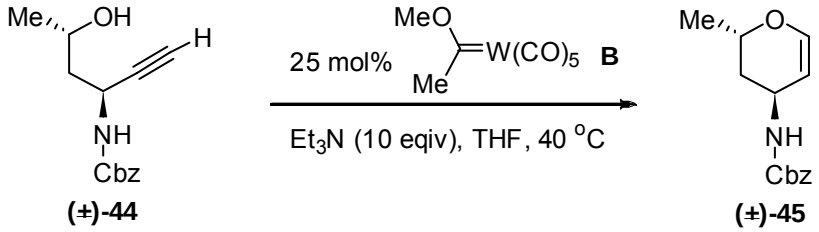
Cbz protection: The known amine (±)-**42**[27] (0.380 g, 1.26 mmol) was dissolved in a mixture of acetone (3 mL) and water (3 mL), K_2CO_3 (17.4 mg, 0.126 mmol) and CbzCl (0.266 mL, 1.89 mmol) were added quickly. The mixture was stirred at room temperature for 10 min, and then water (3 mL) was added and the reaction mixture diluted with CH_2Cl_2 (3 mL). The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic layer was dried over $MgSO_4$ and evaporated under reduced pressure. Chromatography (hexanes : EtOAc = 15 : 1) gave Cbz protected compound (±)-**43** as a white crystal (0.367 g, 81% yield). MP = 100 – 101 ºC; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.36-7.11 (m, 5H), 5.11 (s, 2H), 4.96 (brs, 1H), 4.64 (brs, 1H), 4.01 (brs, 1H), 1.85 (brs, 1H), 1.60 (ddd, *J* = 3.0, 10.8 Hz, 1H), 1.18 (d, *J* = 6.6 Hz, 3H), 0.84 (s, 9H), 0.08 (s, 9H), 0.02 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 155.31, 136.61, 128.75, 128.37, 105.16, 88.45, 67.06, 66.23, 46.15, 42.26, 26.11, 24.38, 18.24, 0.14, 0.09, -3.92, -4.67; IR (KBr) 3286, 2958, 2930, 2895, 2857, 2171, 1693, 1538, 1251, 840 cm^{-1}; HRMS [M+H] Calcd. for $C_{23}H_{40}O_3N_1{}^{28}Si_2$, 434.25413, Found. 434.25389.

Desilylation: Compound (±)-**43** (0.367 g, 1.02 mmol) was dissolved in THF (6 mL), cooled to 0 °C, and TBAF (4.10 mL, 1 M in THF) was added and then stirred for 1 hour. The reaction was quenched with water and diluted with EtOAc (5 mL), and then brine (5 mL) was added. The organic layer was separated and the

aqueous layer was extracted with EtOAc (3 × 10 mL). The combined organic layer was dried over $MgSO_4$ and evaporated under reduced pressure. Chromatography (hexanes : EtOAc = 2 : 1 to 1 : 1) gave the alkynyl alcohol (±)-**44** as a colorless oil (0.229 g, 91% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36-7.30 (m, 5H), 5.19 (brs, 1H), 5.11 (s, 2H), 4.66 (d, *J* = 7.2 Hz, 1H), 4.03 (dqd, *J* = 3.6, 6.0, 10.0 Hz, 1H), 2.34 (d, *J* = 2.0 Hz, 1H), 2.05 (brs, 1H), 1.89-1.76 (m, 2H), 1.24 (d, *J* = 6.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.65, 136.36, 128.76, 128.44, 88.14, 72.12, 67.29, 65.57, 44.94, 41.53, 24.12; IR (neat) 3402 (brs), 2965, 2925, 1689, 1530, 1249 cm^{-1}; HRMS Calcd [M+H]. for $C_{14}H_{18}O_3N_1$, 248.12812, Found. 248.12800.

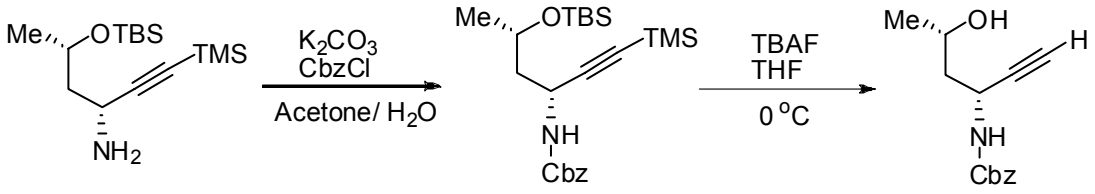
General procedure for alkynyl alcohol cycloisomerizations:

The alkynyl alcohol (0.1 mmol) was dissolved in dry THF (1.0 mL) in a 5 mL conical vial, and then Et_3N (0.14 mL, 1.0 mmol) and tungsten cabene **B** (9.6 mg, 0.025 mmol) were added under argon atmosphere. The vial was sealed with a Teflon cap, and then stirred for 12 h at 40 °C, after which time the reaction mixture was cooled to room temperature. Solvent was removed by rotary evaporation. The yellowish crude oil was purified by chromatography (hexanes : EtOAc = 20 : 1 with 1% Et_3N) to give pure product glycal.



Synthesis of glycal (±)-45: Following the general procedure for alkynyl alcohol cycloisomerization, alkynyl alcohol (±)-**44** (0.025 g, 0.10 mmol) afforded glycal (±)-**45** as a white crystal (23 mg, 92 % yield). MP = 92-93 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.30 (m, 5H), 6.49 (d, *J* = 6.4 Hz, 1H), 5.13 (d, *J* = 12.4 Hz, 1H), 5.06 (d, *J* = 12.4 Hz, 1H), 4.83 (brs, 1H), 4.75 (dt, *J* = 1.6, 6.0 Hz, 1H), 4.14 (d, *J* = 6.0 Hz, 1H), 3.86 (dqd, *J* = 1.6, 6.0, 12.4 Hz, 1H), 1.95 (d, *J* = 14.4 Hz, 1H), 1.67 (ddd, *J* = 4.4, 12.4 Hz, 1H), 1.31 (d, *J* = 6.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.24, 147.69, 136.61, 128.78, 128.42, 99.75, 68.19, 66.89, 41.82, 36.84, 20.98; IR (KBr) 1680, 1528, 1239 1070 cm^{-1}; HRMS [M+H] Calcd. for $C_{14}H_{18}O_3N_1$, 248.12812, Found. 248.12793.

Preparation of alkynyl alcohol (±)-48



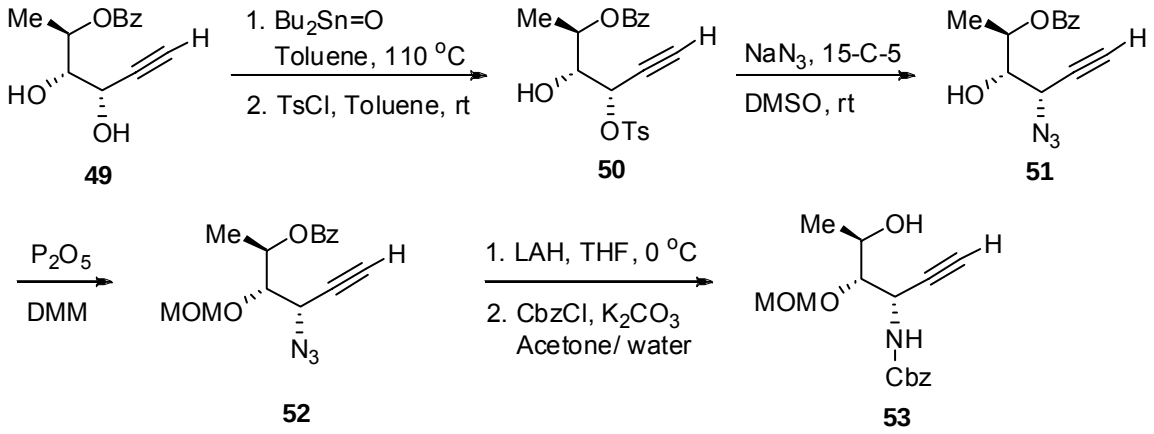
(±)-46 **(±)-47** **(±)-48**

Cbz protection: The procedure as described above for (±)-**45** was followed with the known amine (±)-**46**[1] (0.210 g, 0.701 mmol) and CbzCl (0.148 mL, 1.05 mmol), giving Cbz-protected compound (±)-**47** as a colorless oil (0.230 g, 75 % yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35-7.28 (m, 5H), 5.81 (d, *J* = 8.4 Hz, 1H), 5.11 (s, 2H), 4.58 (brs, 1H), 4.25 (brs, 1H), 1.82-1.73 (m, 2H), 1.18 (d, *J* = 6.0 Hz, 3H), 0.90 (s, 9H), 0.15 (s, 9H), 0.12 (s, 3H), 0.09 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.54, 136.87, 128.62, 128.13, 128.04, 104.91, 87.84, 66.92, 66.80, 43.77, 42.40, 26.12, 24.19, 18.19, 0.15, -3.88, -4.75; IR (neat) 3289, 2957, 2930,

2171, 1729, 1500, 1251, 841 cm^{-1}; HRMS [M+H] Calcd. for $C_{23}H_{40}O_3N_1{}^{28}Si_2$, 434.25413, Found. 434.25432.

Desilylation: The procedure as described above for (±)-**45** was followed with compound (±)-**47** (0.230 g, 0.701 mmol) and TBAF (2.80 mL, 1 M in THF), giving the alkynyl alcohol (±)-**48** as a colorless oil (0.158 g, 92% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38-7.30 (m, 5H), 5.59 (d, *J* = 8.0 Hz, 1H), 5.11 (s, 2H), 4.71 (m, 1H), 4.01 (m, 1H), 2.97 (d, *J* = 4.0 Hz, 1H), 1H), 2.32 (d, *J* = 2.4 Hz, 1H), 1.83-1.70 (m, 2H) 1.21 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.59, 136.27, 128.76, 128.49, 128.42, 82.88, 71.89, 64.46, 66.44, 44.96, 41.24, 23.41; IR (neat) 3390 (brs), 1704, 1537, 1256 cm^{-1}; HRMS [M+H] Calcd. for $C_{14}H_{18}O_3N_1$, 248.12812, Found. 248.12809.

Preparation of alkynyl alcohol 53



Selective tosylation: A Dean-Stark column was fitted into a 50 mL round bottom flask containing a solution of known diol **49**[23] (1.00 g, 4.27 mmol) and dibutyltin oxide (1.34 g, 1.34 mmol) in toluene (20 mL). The reaction mixture was refluxed for 5 h, and then cooled to room temperature. *p*-Toluenesulfonyl chloride (1.22 g, 6.40 mmol) was added, and the reaction mixture was stirred vigorously for 24 h

at room temperature. Solvent was removed by rotary evaporation, and chromatography (hexanes : EtOAc = 4 : 1) gave monotosylated compound **50** as a colorless oil (1.08 g, 65% yield). $[\alpha]^{23}_{D}$ = +39.2 (*c* = 2.07, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02-7.99 (m, 2H), 7.82-7.80 (m, 2H), 7.59 (dt, *J* = 2.4, 7.6 Hz, 1H), 7.46 (dt, *J* = 1.6, 8.0 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 5.31 (dd, *J* = 2.0, 3.6 Hz, 1H), 5.18 (dt, *J* = 6.4, 13.6 Hz, 1H), 4.11 (dq, *J* = 3.6, 6.4 Hz, 1H), 2.71 (d, *J* = 6.4 Hz, 1H), 2.46 (d, *J* = 2.4 Hz, 1H), 2.43 (s, 3H), 1.46 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.64, 145.57, 133.54, 133.34, 130.03, 129.90, 128.70, 128.39, 78.95, 75.23, 75.18, 72.02, 71.16, 21.93, 16.65; IR (neat) 3503 (brs), 3281, 2127, 1717, 1275, 1177 cm^{-1}; HRMS [M+H] Calcd. for $C_{20}H_{21}O_6{}^{32}S_1$ 389.10534, Found 389.10454.

Azide substitution: The tosylate **50** (0.480 g, 1.24 mmol) was dissolved in dry DMSO (4 mL), 15-Crown-5 (0.4 mL) and NaN_3 (0.403 g, 6.20 mmol) were added, and the reaction mixture was stirred overnight at room temperature. The reaction mixture was diluted with Et_2O (5 mL) and quenched with water (5 mL). The organic layer was separated and the aqueous layer was extracted with Et_2O (3 × 5 mL). The combined organic layer was dried over $MgSO_4$ and solvent removed by rotary evaporation. Chromatography (hexanes : EtOAc = 5 : 1) provided azido alcohol **51** as a white solid (0.240 g, 75% yield). MP = 69-70 ^{o}C; $[\alpha]^{23}_{D}$ = -123.8 (*c* = 1.47, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05-8.01 (m, 2H), 7.58 (dt, *J* = 2.4, 7.2 Hz, 1H), 7.47-7.43 (m, 2H), 5.31 (dq, *J* = 6.4, 12.8 Hz, 1H), 4.25 (dd, *J* = 2.4, 5.2 Hz, 1H), 3.97 (t, *J* = 5.2 Hz, 1H), 2.70 (d, *J* = 2.4 Hz, 1H), 2.58 (brs, 1H), 1.46 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.78, 133.48, 130.13, 129.88,

128.68, 77.56, 76.52, 75.68, 70.95, 54.57, 15.93; IR (KBr) 3467 (brs), 3295, 2112, 1713, 1275, 713 cm^{-1}; HRMS [M+H] Calcd. for $C_{13}H_{14}O_3N_3$ 260.10297, Found 260.10251.

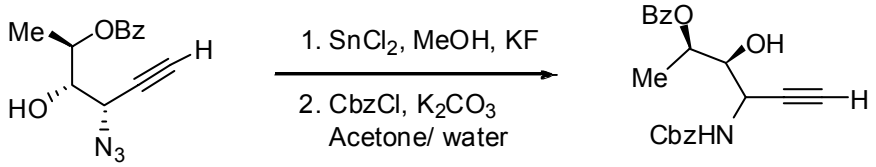
MOM protection: The azido alcohol **51** (0.216 g, 0.833 mmol) was dissolved in dimethoxymethane (4 mL), and P_2O_5 (0.125 g, 0.833 mmol) was added. The reaction mixture was stirred for 30 min at room temperature, and additional P_2O_5 (0.125 g, 0.833 mmol) was added and then stirred for 30 min. The reaction mixture was diluted with CH_2Cl_2 (5 mL) and poured into a solution of cold saturated aq. $NaHCO_3$ (20 mL). The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layer was dried over $MgSO_4$ and evaporated under reduced pressure. Chromatography (hexanes : EtOAc = 10 : 1) gave MOM-protected compound **52** as a colorless oil (0.180 g, 71% yield). $[\alpha]^{23}_D$ = -58.95 (*c* = 3.2, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05-8.02 (m, 2H), 7.56 (dt, *J* = 2.8, 7.2 Hz, 1H), 7.47-7.42 (m, 2H), 5.40 (dq, *J* = 4.8, 6.4 Hz, 1H), 4.93 (d, *J* = 6.8 Hz, 1H), 4.81 (d, *J* = 5.6 Hz, 1H), 4.20 (dd, *J* = 2.4, 5.2 Hz, 1H), 4.00 (dd, *J* = 4.8, 5.2 Hz, 1H), 3.44 (s, 3H), 2.70 (d, *J* = 2.0 Hz, 1H), 1.45 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.70, 133.35, 130.24, 129.81, 128.62, 98.02, 80.56, 77.57, 76.79, 70.95, 56.62, 53.78, 15.54; IR (neat) 2112, 1720, 1273, 1037 cm^{-1}; HRMS [M+H] Calcd. for $C_{15}H_{18}O_4N_3$ 304.12918, Found 304.12836.

Reduction of azide: The azide **52** (0.180 g, 0.590 mmol) was dissolved in dry THF (4 mL) and the solution was cooled to 0 ^oC. Lithium aluminum hydride (1.80 mL, 1 M in THF, 1.8 mmol) was added dropwise to the 0 ^oC solution, and the

reaction mixture was stirred for 3 h at 0 °C. The reaction mixture was quenched by careful addition of water (0.1 mL) and 15% NaOH (0.3 mL), and then stirred for 1 h at room temperature. The resulting clear solution with white solid was treated with $MgSO_4$ and filtered through Celite. After rotary evaporation of the organic layer, the amino alcohol was obtained as a yellowish oil, which was directly used for the next step without further purification.

Cbz protection: The procedure as described above for (±)-**45** and (±)-**48** was followed with crude amino alcohol**,** K_2CO_3 (17.4mg, 0.126 mmol) and CbzCl (0.266 mL, 1.89 mmol) in a mixture of acetone (3 mL)/water (3 mL), and gave alkynyl alcohol **53** as a colorless oil (0.120 g, 67 % yield over 2 steps) after chromatography (hexanes : EtOAc = 5 : 1). $[\alpha]^{23}_D$ = +21.4 (*c* = 1.4, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.31 (m, 5H), 5.54 (d, *J* = 8.4 Hz, 1H), 4.88 (d, *J* = 6.8 Hz, 2H), 3.88 (br d, *J* = 6.0 Hz, 1H), 3.50 (dd, *J* = 3.2, 5.2 Hz, 1H), 3.42 (s, 3H), 3.11 (d, *J* = 4.4 Hz, 1H), 2.33 (d, *J* = 3.6 Hz, 1H), 1.27 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.55, 136.19, 128.78, 128.53, 128.45, 98.21, 84.38, 81.43, 72.63, 67.62, 67.08, 56.68, 44.61, 19.55; IR (neat) 3410 (brs), 2926, 1709, 1514, 1252, 1030 cm^{-1}; HRMS [M+H] Calcd. for $C_{16}H_{22}O_5N_1$ 308.14925, Found 308.14896.

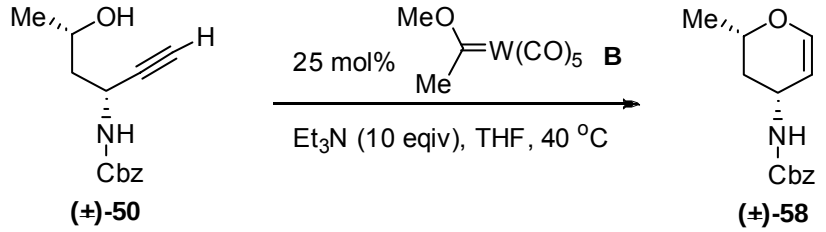
Preparation of alkynyl alcohol 54



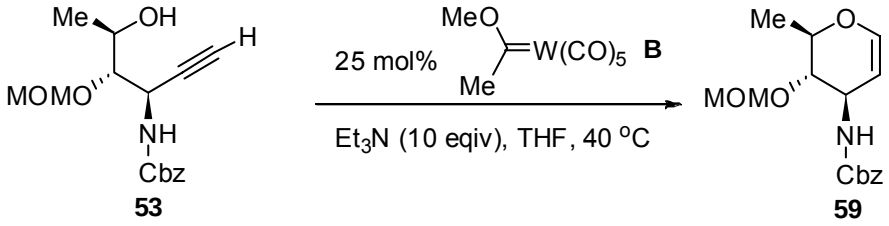
51 **54**

Reduction of azide: The azido alcohol **51** (0.16 g, 0.62 mmol) was dissolved in MeOH (6 mL), and $SnCl_2$ (0.18 g, 0.93 mmol) was added. The reaction mixture was stirred at room temperature for 24 h. Solvent was removed by rotary evaporation, and the crude material was dissolved in EtOAc (6 mL). Aqueous KF (3 mL, 5 M) was added and the reaction mixture was stirred at room temperature for 5 h. The organic layer was separated and the aqueous layer was extracted with EtOAc (3 × 5 mL). The combined organic layer was dried over $MgSO_4$, and solvents removed by rotary evaporation. The yellowish crude amino alcohol was used for the next step without further purification.

Cbz protection: The procedure as described above for (±)-**45**, (±)-**46** and **53** was followed with crude amino alcohol**,** K_2CO_3 (8.7 mg, 0.062 mmol) and CbzCl (0.13 mL, 0.93 mmol) in a mixture of acetone (2 mL) / water (2 mL), and gave the alkynyl alcohol **54** as a colorless oil (0.146 g, 64% yield over 2 steps) after chromatography (hexanes : EtOAc = 5 : 1). $[\alpha]^{23}_{D}$ = +45.4 (*c* = 2.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 7.6 Hz, 2H), 7.55 (dt, *J* = 2.8, 7.6 Hz 1H), 7.43-7.39 (m, 2H), 7.31 (br s, 5H), 5.41 (d, *J* = 9.2 Hz, 1H), 5.24 (ddd, *J* = 2.4, 4.8 Hz, 1H), 5.05 (s, 2H), 4.75 (d, *J* = 3.2 Hz, 1H), 3.98 (d, *J* = 4.4 Hz, 1H), 3.07 (d, *J* = 3.6 Hz, 1H), 2.39 (d, *J* = 2.0 Hz, 1H), 1.45 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166. 02, 156.12, 136.14, 133.35, 130.21, 129.86, 128.71, 128.62, 128.41, 80.95, 75.74, 73.18, 71.03, 67.52, 45.57, 16.28; IR (neat) 3406 (brs), 2926, 2252, 2120, 1968, 1713, 1524, 1275, 1116 cm^{-1}; HRMS [M+H] Calcd. for $C_{21}H_{22}O_5N_1$ 368.14925, Found 368.14822.

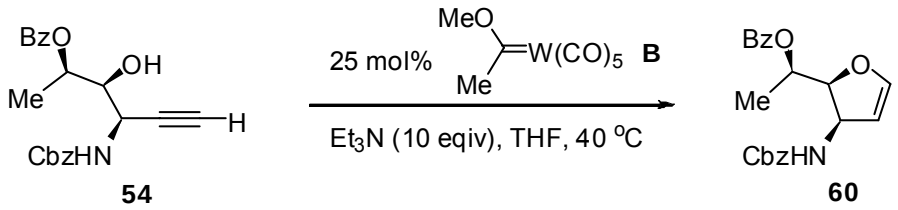


Synthesis of glycal (±)-58: Following the general procedure for alkynyl alcohol cycloisomerization, substrate (±)-**50** (25 mg, 0.1 mmol) afforded glycal (±)-**58** as a white crystal (24 mg, 95% yield). MP = 92-93 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36-7.30 (m, 5H), 6.38 (dd, *J* = 1.2, 6.0 Hz, 1H), 5.10 (s, 2H), 4.65 (d, *J* = 7.2 Hz, 1H), 4.58 (dt, *J* = 2.0, 6.4 Hz, 1H), 4.30 (ddd, *J* = 8.8 Hz, 1H), 4.08 (dqd, *J* = 6.0 Hz, 1H), 2.26 (dd, *J* = 6.4, 12.8 Hz, 1H), 1.41 (ddd, *J* = 11.2, 13.2 Hz, 1H) 1.28 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.09, 146.27, 136.65, 128.77, 128.39, 102.58, 71.77, 66.92, 44.26, 37.59, 21.18; IR (KBr) 1683, 1234, 746 cm^{-1}; HRMS [M+H] Calcd. for $C_{14}H_{18}O_3N_1$, 248.12812, Found. 248.12801.

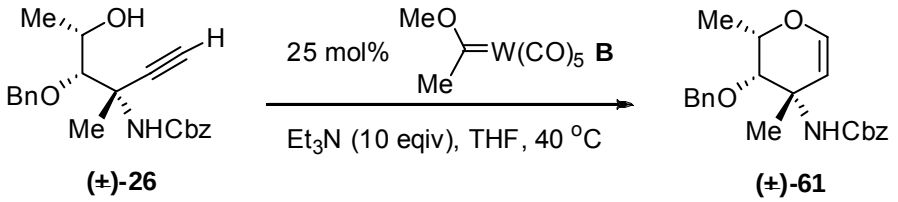


Synthesis of glycal 59: Following the general procedure for alkynyl alcohol cycloisomerization, substrate **53** (30.7 mg, 0.10 mmol) afforded glycal **59** as a white crystal (29.4 mg, 95% yield). MP = 102-103 °C; $[\alpha]^{23}_{D}$ = -74.2 (*c* = 0.99, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36-7.30 (m, 5H), 6.31 (dd, *J* = 1.6, 6.4 Hz, 1H), 5.11 (s, 2H), 5.06 (brs, 1H), 4.73 (s, 1H), 4.72 (d, *J* = 6.8 Hz, 1H), 4.67 (d, *J* = 6.8 Hz, 1H), 4.29 (m, 1H), 3.98 (dq, *J* = 6.4, 8.4 Hz, 1H), 3.36 (dd, *J* = 8.4, 1H),

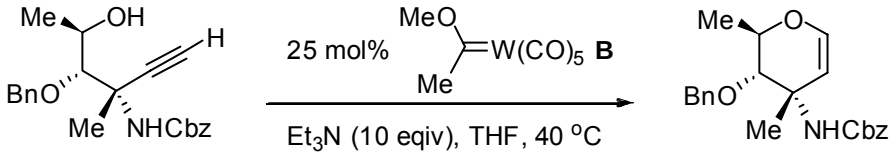
3.21 (s, 3H), 1.35 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.33, 144.44, 136.67, 128.73, 128.37, 101.51, 97.38, 78.85, 74.55, 66.94, 56.12, 50.36, 17.41; IR (KBr) 1693, 1553, 1234, 1047 cm^{-1}; HRMS [M+H] Calcd. for $C_{16}H_{22}O_5N_1$, 308.14925, Found. 308.14847.



Synthesis of glycal 60: Following the general procedure for alkynyl alcohol cycloisomerization, substrate **54** (37 mg, 0.10 mmol) afforded glycal **60** as colorless oil (28 mg, 77% yield). $[\alpha]^{23}_D$ = +77.3 (*c* = 1.49, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04-8.02 (m, 2H), 7.55 (dt, *J* = 2.8, 7.6 Hz, 1H), 7.42 (t, *J* = 7.6 Hz, 2H), 7.33-7.28 (m, 3H), 7.23-7.22 (m, 2H), 6.52 (dd, *J* = 1.2, 2.4 Hz, 1H), 5.46 (dq, *J* = 6.4 Hz, 1H), 5.18-5.14 (m, 1H), 5.08 (t, *J* = 3.2 Hz, 1H), 4.85 (d, *J* = 12.4 Hz, 1H), 4.76 (d, *J* = 10.0 Hz, 1H), 4.66 (d, *J* = 12.4 Hz, 1H), 4.44 (dd, *J* = 7.6 Hz, 1H), 1.48 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166. 12, 155.50, 149.45, 136.74, 133.55, 130.69, 130.32, 129.01, 128.69, 128.65, 102.98, 84.59, 68.71, 67.35, 54.50, 18.09; IR (KBr) 2925, 1716, 1524, 1266, 1059, 712 cm^{-1}; HRMS [M+H] Calcd. for $C_{21}H_{22}O_5N_1$ 368.14925, Found 368.14801.

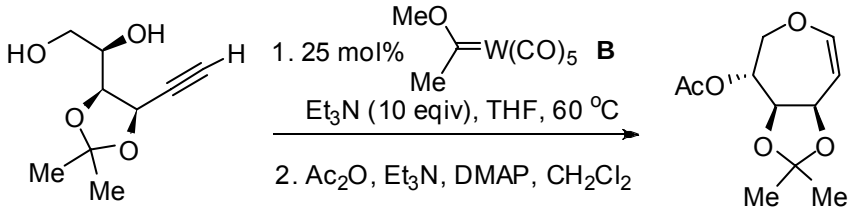


Synthesis of glycal (±)-61: Following the general procedure for alkynyl alcohol cycloisomerization, the known alkynyl alcohol substrate (±)-**31** (0.037 g, 0.10 mmol) afforded the known glycal (±)-**61** as a white crystal (0.031 g, 84% yield). All spectroscopic data for compounds (±)-**31** and (±)-**61** match the reported data. [26]



(±)-27 **(±)-62**

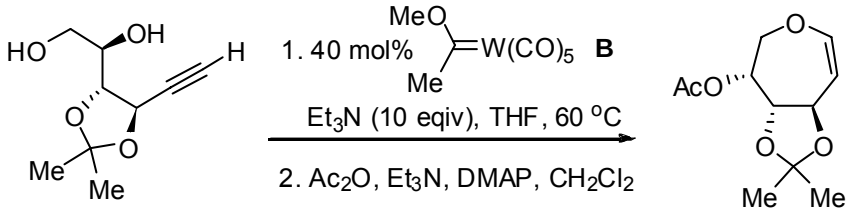
Synthesis of glycal (±)-62: Following the general procedure for alkynyl alcohol cycloisomerization, the known alkynyl alcohol substrate (±)-**32** (37 mg, 0.10 mmol) afforded known glycal (±)-**62** as a white crystal (35 mg, 94% yield). All spectroscopic data for compounds (±)-**32** and (±)-**62** match with reported data.[26]



55 **63**

Synthesis of glycal 63: Following the general procedure for alkynyl alcohol cycloisomerization, the known substrate **55** (15 mg, 0.10 mmol) underwent reaction at 60 °C. Acetylation (acetic anhydride, 0.010 mL; Et_3N, 0.020 mL and DMAP, 1 crystal in 1.5 ml of dry CH_2Cl_2) of the crude material gave the known

glycal **63** as a white crystal (15 mg, 82% yield over two steps). All spectroscopic data for compounds **55** and **63** match with reported data.[30]

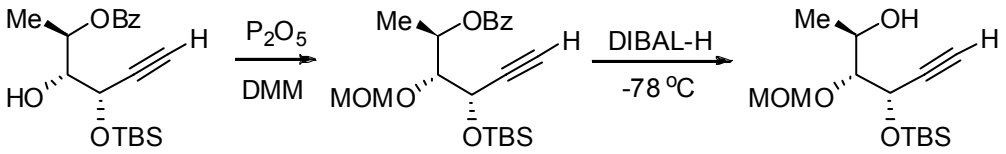


56 **64**

Synthesis of glycal 19: Following the general procedure for alkynyl alcohol cycloisomerization, the known substrate **18** (15 mg, 0.10 mmol) underwent reaction using 40 mol % of **3** at 60 °C. Acetylation (acetic anhydride, 0.010 mL; Et_3N, 0.020 mL and DMAP, 1 crystal in 1.5 ml of dry CH_2Cl_2) of the crude material gave the known glycal **63** as a white crystal (15 mg, 82% yield over two steps). All spectroscopic data for compounds **55** and **63** match with reported data. [30]

Comparisons of non-photochemical procedure vs. photochemical procedures

Preparation of alkynyl alcohol 67b



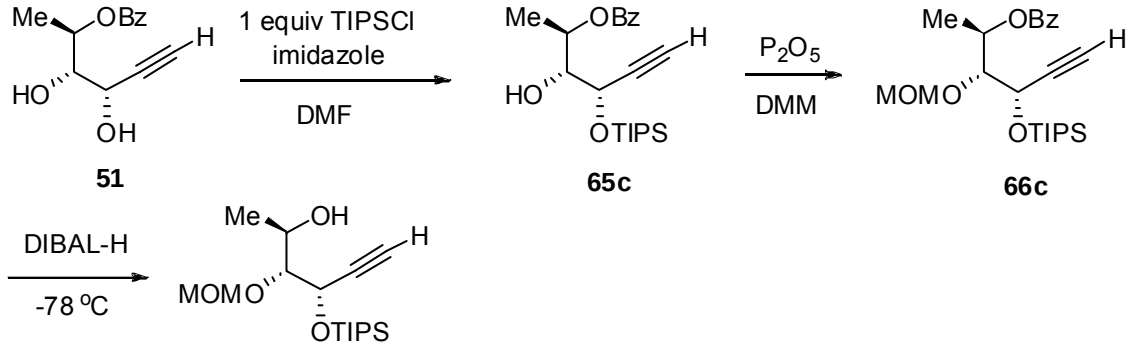
65b **66b** **67b**

MOM protection: The procedure as described above for alkynyl alcohol **52** was followed with known mono-TBS protected alkynyl alcohol **65b**[2] (0.28 g, 0.80 mmol) and P_2O_5 (0.23 g, 1.60 mmol) in DMM (3 mL), and produced MOM-protected product **66b** as a colorless oil (0.23 g, 73% yield) after chromatography (hexanes : EtOAc = 15 : 1). $[\alpha]^{23}_D$ = +34.3 (*c* = 0.7, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06-8.03 (m, 2H), 7.58-7.54 (m, 1H), 7.46-7.42 (m, 2H), 5.43 (dq, *J* = 4.0, 6.4 Hz, 1H), 4.96 (d, *J* = 6.4 Hz, 1H), 4.81 (d, *J* = 6.8 Hz, 1H), 4.51 (dd, *J* = 2.4, 5.6 Hz, 1H), 3.96 (dd, *J* = 4.0, 5.6 Hz, 1H), 3.43 (s, 3H), 2.46 (d, *J* = 2.4 Hz, 1H), 1.43 (d, *J* = 6.4 Hz, 3H), 0.92 (s, 9H), 0.17 (s, 3H), 0.15 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.81, 133.15, 130.68, 129.83, 128.57, 97.72, 82.83, 81.43, 74.41, 71.20, 64.30, 56.46, 25.91, 18.33, 15.24, -4.26, -5.03; IR (neat) 2954, 2931, 2894, 2858, 2116, 1721, 1274, 839 cm^{-1}; HRMS [M+Na] Calcd. for $C_{21}H_{32}O_5{}^{23}Na_1{}^{28}Si_1$ 415.19112, Found 415.19090.

Alkynyl alcohol 67b: The MOM-protected alkyne **66b** (0.23 g, 0.59 mmol) was dissolved in dry CH_2Cl_2 (3 mL), and cooled to -78 ^{o}C. DIBAL-H (1.2 mL, 1.2 mmol) was added dropwise at –78 ^{o}C, and the reaction mixture was stirred for 1 hr at –78 ^{o}C. Cold EtOAc (6 mL) was added to quench the reaction, followed by Rochelle's salt (5 mL). The reaction mixture was stirred until two layers were clearly separated. The organic layer was separated and the aqueous layer was extracted with EtOAc (3 × 5 mL). The combined organic layer was dried over $MgSO_4$ and solvent removed by rotary evaporation. Chromatography (hexanes : EtOAc = 10 :1) gave alkynyl alcohol **67b** as a colorless oil (0.12 g, 71% yield). $[\alpha]^{23}_D$ = +105.8 (*c* = 2.3, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.82 (d, *J* = 6.4 Hz,

1H), 4.74 (d, *J* = 6.4 Hz, 1H), 4.40 (dd, *J* = 2.4, 6.0 Hz, 1H), 3.98 (dq, *J* = 6.4, 9.6 Hz, 1H), 3.59 (dd, *J* = 4.4, 6.4 Hz, 1H), 3.43 (s, 3H), 2.96 (d, *J* = 8.0 Hz, 1H), 2.44 (d, *J* = 2.4 Hz, 1H), 1.20 (d, *J* = 6.4 Hz, 3H), 0.88 (s, 9H), 0.15 (s, 3H), 0.11 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 98.59, 86.56, 83.47, 73.97, 67.08, 64.40, 56.41, 25.84, 18.22, 18.14, -4.22, -5.09; IR (neat) 3454 (brs), 3310, 2955, 2931, 2897, 2858, 2115, 1253, 1153, 1104, 1033, 839 cm^{-1}; HRMS Calcd. [M+H] for $C_{14}H_{29}O_4{}^{28}Si_1$ 289.18296, Found 289.18288.

Preparation of alkynyl alcohol 67c



Selective TIPS protection of diol: The known diol **51**[2] (1.06 g, 4.53 mmol) was dissolved in dry DMF (5 mL), imidazole (0.616 g, 9.05 mmol) and TIPSCl (1.05 mL, 4.98 mmol) were added, and the reaction mixture was stirred for 1 h at room temperature. The reaction was quenched with water (3 mL) and diluted with ethyl ether (5 mL). The organic layer was separated and the aqueous layer was extracted with ethyl ether (3 × 5 mL). The combined organic layer was dried over $MgSO_4$ and evaporated under reduced pressure. Chromatography (hexanes : EtOAc = 15 :1) gave mono-TIPS protected alkynyl alcohol **65c** as a colorless oil (1.30 g, 73% yield). $[\alpha]^{23}_D$ = -22.7 (*c* = 1.14, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ

8.03-8.00 (m, 2H), 7.57 (dt, *J* = 2.4, 7.6 Hz, 1H), 7.44 (t, *J* = 7.6 Hz, 2H), 5.29 (dq, *J* = 6.4, 7.6 Hz, 1H), 4.72 (dd, *J* = 2.4, 3.6 Hz, 1H), 3.91 (ddd, *J* = 3.6, 7.6 Hz, 1H), 2.67 (d, *J* = 3.6 Hz, 1H), 2.45 (d, *J* = 2.4 Hz, 1H), 1.49 (d, *J* = 6.4 Hz, 3H), 1.22-1.03 (m, 21H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.56, 133.26, 130.53, 129.78, 128.62, 80.98, 76.58, 75.29, 71.66, 64.78, 18.19, 18.17, 17.94, 16.71, 12.36; IR (neat) 3514 (brs), 3308, 2943, 2866, 1720, 1274, 1113, 1067 cm^{-1}; HRMS [M+H] Calcd. for $C_{22}H_{35}O_4{}^{28}Si_1$ 391.22991, Found 392.22853.

MOM protection: The procedure as described above for alkynyl alcohol **52** was followed with TIPS-protected alkynyl alcohol **65c** (1.30 g, 3.33 mmol) and P_2O_5 (1.87 g, 6.66 mmol) in dimethoxymethane (5 mL), and gave MOM-protected alkyne **66c** as a colorless oil (1.25 g, 87% yield) after chromatography (hexanes : EtOAc = 15 : 1). $[\alpha]^{23}_D$ = +25.7 (*c* = 2.6, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05-8.03 (m, 2H), 7.56 (dt, *J* = 2.8, 7.6 Hz, 1H), 7.43 (t, *J* = 7.6 Hz, 2H), 5.41 (dq, *J* = 6.4, 7.2 Hz, 1H), 5.04 (d, *J* = 7.2 Hz, 1H), 4.82 (d, *J* = 7.2 Hz, 1H), 4.69 (dd, *J* = 2.0, 4.4 Hz, 1H), 3.99 (dd, *J* = 4.4, 5.6 Hz, 1H), 3.45 (s, 3H), 2.47 (d, *J* = 2.4 Hz, 1H), 1.46 (d, *J* = 6.4 Hz, 3H), 1.21-1.08 (m, 21H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.70, 133.17, 130.60, 129.83, 128.54, 97.77, 82.49, 81.76, 74.66, 71.17, 64.87, 56.49, 18.23, 18.22, 15.97, 12.44; IR (neat) 2943, 2867, 1721, 1273, 1112, 1036, 712 cm^{-1}; HRMS [M+H] Calcd. for $C_{24}H_{39}O_5{}^{28}Si_1$ 435.25613, Found 435.25507.

Alkynyl alcohol 67c: The tri-*O*-protected alkyne **66c** (1.25 g, 2.88 mmol) was dissolved in dry CH_2Cl_2 (10 mL), cooled to -78 ^{o}C, and DIBAL-H (5.76 mL, 5.76 mmol) was added dropwise at -78 ^{o}C. The reaction mixture was stirred for 1 h at –78 ^{o}C after which time cold EtOAc (30 mL) was added to quench the reaction,

followed by Rochelle's salt (20 mL). The reaction mixture was stirred until two layers were clearly separated. The organic layer was separated and the aqueous layer was extracted with EtOAc (3 × 10 mL). The combined organic layer was dried over $MgSO_4$ and evaporated under reduced pressure. Chromatography (hexanes : EtOAc = 10 :1) gave alkynyl alcohol **67c** as a colorless oil (0.699 g, 73% yield). $[\alpha]^{23}_D$ = +89.7 (*c* = 0.73, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.89 (d, *J* = 6.4 Hz, 1H), 4.76 (d, *J* = 6.4 Hz, 1H), 4.62 (dd, *J* = 2.4, 5.6 Hz, 1H), 4.02 (dq, *J* = 6.4, 12.6 Hz, 1H), 3.62 (t, *J* = 4.8 Hz, 1H), 3.44 (s, 3H), 2.73 (d, *J* = 7.2 Hz, 1H), 2.47 (d, *J* = 2.4 Hz, 1H), 1.27 (d, *J* = 6.4 Hz, 3H), 1.21-1.08 (m, 21H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 98.48, 86.55, 83.38, 74.33, 67.38, 64.91, 56.46, 18.84, 18.25, 12.51; IR (neat) 3436 (brs), 3310, 2943, 2867, 2115, 1463, 1105, 1033 cm^{-1}; HRMS Calcd. for $C_{17}H_{35}O_4{}^{28}Si_1$ 331.22991, Found 331.22895.

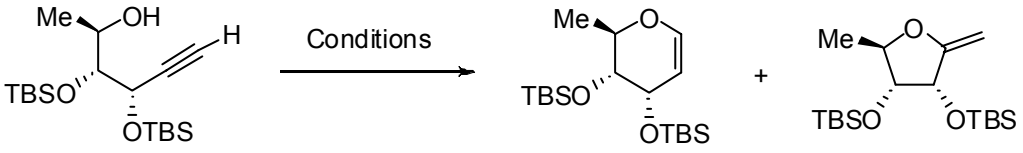
Cycloisomerization Conditions

Condition A: The alkynyl alcohol substrate (0.10 mmol) was dissolved in dry THF (1.0 mL) in a conical vial. Et_3N (0.14 mL, 1.0 mmol) and tungsten Fischer carbene **B** (15.3 mg, 0.040 mmol) were added under argon atmosphere. The vial was sealed with a Teflon cap, and then stirred for 24 hours at 60 ^oC, after which time the reaction mixture was cooled to room temperature and solvent was removed by rotary evaporation. Chromatography (hexanes : EtOAc = 20 : 1 with 1% Et_3N) gave pure product.

Condition B: The alkynyl alcohol (0.10 mmol) was dissolved in dry THF (1 mL) with stirring, and $W(CO)_6$ (8.8 mg, 0.025 mmol) and Et_3N (0.14 mL, 1.0 mmol)

were added. The flask was fitted with a reflux condenser and then placed into Rayonet photoreactor under an atmosphere of argon. The reaction mixture was irradiated at 350 nm at 60 ^{o}C for 6 h, with stirring. Solvent was removed by rotary evaporation, and chromatography (hexanes : EtOAc = 20 : 1 with 1% Et_3N) gave pure product.

Condition C: Condition B, except DABCO (22 mg, 0.20 mmol) was used instead of Et_3N.



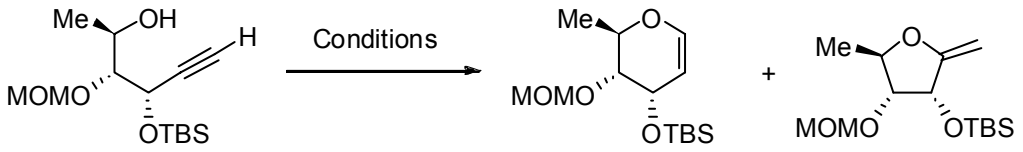
67a **68a** **69a**

Cycloisomerizations of alkynyl alcohol 67a: Following the general procedure for alkynyl cycloisomerization with the conditions described above, the known alkynyl alcohol **67a** (36 mg, 0.10 mmol) afforded known *endo* glycal **68a**.[2]

Condition A: **68a** (19 mg, 53% yield) and **67a** (11 mg, 30%) was recovered

Condition B: **68a** (33 mg, 92% yield).

All spectroscopic data for compounds **67a** and **68a** match the reported data.[2]



67b **68b** **69b**

Cycloisomerizations of alkynyl alcohol 67b: Following the conditions described for cycloisomerization of **67a**, the alkynyl alcohol substrate **67b** (29 mg, 0.10 mmol) afforded *endo* glycal **68b** and *exo* product **69b**.

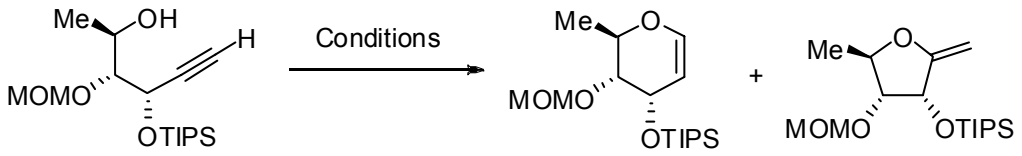
Condition A: **68b** (15 mg, 53% yield) and **69b** (10 mg, 35% yield).

Condition B: **68b** (21 mg, 65% yield) and **69b** (6.6 mg, 20% yield).

Condition C: **68b** (22 mg, 75% yield) and **69b** (4.4 mg, 15% yield).

68b: $[\alpha]^{23}_{D}$ = +297.2 (*c* = 1.48, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.31 (d, *J* = 6.0 Hz, 1H), 4.81 (d, *J* = 6.4 Hz, 1H), 4.76 (dd, *J* = 6.0 Hz, 1H), 4.61 (d, *J* = 6.4 Hz, 1H), 4.25 (dd, *J* = 3.6, 5.2 Hz, 1H), 4.17 (dq, *J* = 3.6, 6.4 Hz, 1H), 3.51 (dd, *J* = 3.2, 9.2 Hz, 1H 3.40 (s, 3H), 3.34 (d, *J* = 6.4 Hz), 1.28 (d, *J* = 6.4 Hz, 3H), 0.89 (s, 9H), 0.08 (s, 3H), 0.07 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.17, 101.98, 94.72, 76.13, 70.01, 61.17, 55.90, 26.08, 18.39, 17.84, -3.75, -4.26; IR (neat) 2953, 2929, 2857, 1642, 1472, 1240, 1149, 1119, 835 cm^{-1}; HRMS Calcd. [M+H] for $C_{14}H_{29}O_4{}^{28}Si_1$ 289.18296, Found 289.18292.

69b: ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.74 (d, *J* = 7.2 Hz, 1H), 4.68 (d, *J* = 6.4 Hz, 1H), 4.56 (d, *J* = 4.4 Hz, 1H), 4.38 (dq, *J* = 5.2, 6.4 Hz, 1H), 4.33 (dd, *J* = 1.6 Hz, 1H), 4.05 (dd, *J* = 1.2, 1.6 Hz, 1H), 3.71 (dd, *J* = 4.4 Hz, 1H), 3.39 (s, 3H), 1.32 (d, *J* = 6.8 Hz, 3H), 0.92 (s, 9H), 0.14 (s, 3H), 0.12 (s, 3H); IR (neat) 2917, 2853, 1462, 1052 cm^{-1}; HRMS Calcd. [M+H] for $C_{14}H_{29}O_4{}^{28}Si_1$ 289.18296, Found 289.18285.



67c **68c** **69c**

Cycloisomerizations of alkynyl alcohol 67c: Following the conditions described for cycloisomerization of **67a**, the alkynyl alcohol substrate **67c** (33 mg, 0.10 mmol) afforded *endo* glycal **68c** and *exo* product **69c**.

Condition A: **68c** (28 mg, 85% yield) and **69c** (3.0 mg, 9% yield).

Condition B: **68c** (29 mg, 88% yield) and **69c** (2.3 mg, 7% yield).

Condition C: **68c** (29 mg, 88% yield) and **9c** (2.0 mg, 6% yield).

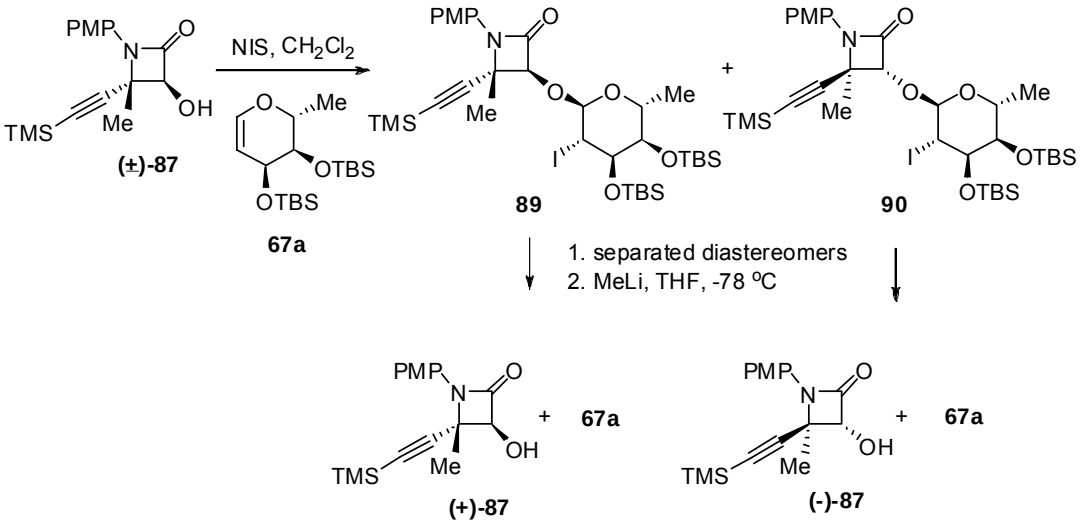
68c: $[\alpha]^{23}_{D}$ = +279.4 (*c* = 1.2, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.31 (d, *J* = 6.0 Hz, 1H), 4.85 (d, *J* = 6.8 Hz, 1H), 4.83 (dd, *J* = 5.6, 6.0 Hz, 1H), 4.63 (d, *J* = 7.2 Hz, 1H), 4.39 (dd, *J* = 3.6, 5.2 Hz, 1H), 4.23 (dq, *J* = 6.4, 8.8 Hz, 1H), 3.54 (dd, *J* = 3.6, 8.8 Hz, 1H), 3.41 (s, 3H), 1.34 (d, *J* = 6.8 Hz, 3H), 1.07-1.06 (m, 21H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.07, 101.97, 94.85, 76.27, 70.19, 61.32, 55.92, 18.37, 17.90, 12.93; IR (neat) 2941, 1641, 1240, 1041, 1005 cm^{-1}; HRMS [M+H] Calcd. for $C_{17}H_{35}O_4{}^{28}Si_1$ 331.22991, Found 331.22919.

69c: $[\alpha]^{23}_{D}$ = -69.8 (*c* = 1.8, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.77 (d, *J* = 6.8 Hz, 1H), 4.70 (d, *J* = 2.0 Hz, 1H), 4.69 (d, *J* = 6.8 Hz, 1H), 4.40 (dq, *J* = 4.8, 6.8 Hz, 1H), 4.33 (dd, *J* = 1.6 Hz, 1H), 4.13 (dd, *J* = 1.6 Hz, 1H), 3.71 (dd, *J* = 4.4 Hz, 1H), 3.39 (s, 3H), 1.31 (d, *J* = 6.4 Hz, 3H), 1.15-1.07 (m, 21H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.18, 96.26, 83.27, 81.22, 79.03, 71.45, 55.93, 18.98, 18.28,

18.26, 12.78; IR (neat) 2942, 2867, 1463, 1147, 1052, 996 cm^{-1}; HRMS [M+H] Calcd. for $C_{17}H_{35}O_4{}^{28}Si_1$ 331.22991, Found 331.22979.

Synthesis of the altromycin disaccharide 83

Enantiomer resolution of (±)-87



NIS mediated glycosylation: Racemic hydroxyl *beta*-lactam (±)-**87**[3] (2.25 g, 7.42 mmol) and bis-TBS protected glycal **67a** (2.40 g, 6.67 mmol) were dissolved in CH_2Cl_2 (40 mL), and cooled to 0 °C. NIS (1.59 g, 7.05 mmol) was added, and the mixture was slowly warmed to room temperature and stirred overnight at room temperature in the dark. The reaction mixture was diluted with CH_2Cl_2 (10 mL) and quenched with sat. aq. $Na_2S_2O_4$ (20 mL). The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layer was dried over $MgSO_4$ and solvent was removed by rotary evaporation. Chromatography (hexanes : EtOAc = 30 :1) gave each separable glycosylated *beta*-lactam **89** (2.50 g, 47% yield) as a foam and **90** (2.39 g, 45% yield) as a colorless oil.

Compound 89: $[\alpha]^{23}_{D}$ = +114.22 (*c* = 6.6, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (d, *J* = 8.8 Hz, 2H), 6.86 (d, *J* = 8.8 Hz, 2H), 5.19 (s, 1H), 4.96 (s, 1H), 4.63 (brs, 1H), 4.29 (d, *J* = 2.4 Hz, 1H), 4.15 (d, *J* = 10.0 Hz, 1H), 4.12 (s, 1H), 3.78 (s, 1H), 1.65 (s, 3H), 1.30 (d, *J* = 6.4 Hz, 3H), 0.91 (s, 9H), 0.87 (s, 9H), 0.16 (s, 9H), 0.14 (s, 3H), 0.10 (s, 3H), 0.07 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.73, 156.64, 129.85, 119.58, 114.39, 104.17, 102.43, 92.51, 86.57, 74.66, 70.08, 65.15, 57.47, 55.62, 29.27, 26.23, 25.92, 20.52, 18.23, 18.17, 17.98, -0.09, -3.42, -3.59, -4.34, -4.67; IR (neat) 2953, 2932, 2896, 2858, 2253, 2162, 1764, 1513, 1250, 1093, 976, 839 cm^{-1}; HRMS [M+H] Calcd. for $C_{34}H_{59}O_6N_1{}^{127}I_1{}^{28}Si_3$ 788.26895, Found 788.26923.

Compound 90: $[\alpha]^{23}_{D}$ = +8.1 (*c* = 2.78, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, *J* = 8.8 Hz, 2H), 6.88 (d, *J* = 9.2 Hz, 2H), 5.27 (s, 1H), 4.84 (s, 1H), 4.38 (d, *J* = 2.4 Hz, 1H), 4.30 (m, 1H), 4.16-4.13 (m, 2H), 3.80 (s, 1H), 1.67 (s, 3H), 1.25 (d, *J* = 6.4 Hz, 3H), 0.92 (s, 9H), 0.88 (s, 9H), 0.17 (s, 9H), 0.14 (s, 3H), 0.13 (s, 3H), 0.11 (s, 3H), 0.06 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.26, 156.78, 129.71, 119.78, 114.47, 104.59, 103.87, 92.52, 89.12, 74.89, 69.96, 65.37, 58.50, 55.68, 29.36, 26.31, 26.10, 20.97, 18.35, 18.32, 17.83, -0.05, -3.35, -3.73, -4.26, -4.56; IR (neat) 2954, 2931, 2896, 2858, 2164, 1761, 1513, 1250, 838 cm^{-1}; HRMS [M+H] Calcd. for $C_{34}H_{59}O_6N_1{}^{127}I_1{}^{28}Si_3$ 788.26895, Found 788.26893.

Enantiomerically pure hydroxyl beta lactam (+)-87: The glycosylated *beta*-lactam **89** (2.50 g, 3.17 mmol) was dissolved in dry THF (50 mL), and cooled to -78 ^{o}C. MeLi (2.18 mL, 1.6 M in Et_2O) was added dropwise at -78 ^{o}C. The

reaction mixure was stirred for 10 min at -78 ^{o}C and quenched with aq. sat. NH_4Cl (10 mL). The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layer was dried over $MgSO_4$ and solvent removed by rotary evaporation. Chromatography (hexanes : EtOAc = 30 :1 to 10 : 1) gave each separable bis-TBS protected glycal **67a** (1.05 g, 92% yield) as a colorless oil, and enantiomerically pure hydroxyl beta lactam (+)-**87** (0.83 g, 87%) as a white solid. MP = 116 ^{o}C; $[\alpha]^{23}_{D}$ = +193.5 (*c* = 1.2, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, *J* = 9.2 Hz, 2H), 6.82 (d, *J* = 9.2 Hz, 2H), 5.04 (s, 1H), 3.78 (s, 3H), 1.73 (s, 3H), 0.17 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.68, 156.93, 129.42, 119.94, 114.37, 104.06, 92.53, 83.37, 59.04, 55.56, 19.96, -0.09; IR (KBr) 3368 (brs), 2168, 1756, 1032, 941; HRMS [M+H] Calcd. for $C_{16}H_{22}O_3{}^{28}Si_1$ 304.13640, Found 304.13562.

(-)-87: The procedure as described above for preparation of (+)-**87** was followed with compound **O** (2.39 g, 3.03 mmol) and MeLi (2.18 mL, 1.6 M in Et_2O) in THF (50 mL), affording each separable bis-TBS protected glycal **671a** (1.05 g, 96%) as a colorless oil and (-)-**87** (0.85 g, 92%) as a white solid.

Crystal structure of (+)-87: The absolute stereochemistry of hydroxyl *beta*-lactam (+)-**87** was confirmed by single crystal X-ray analysis, with absolute structure parameter 0.08(3). Thermal ellipsoid diagram for (+)-**87** is shown below:

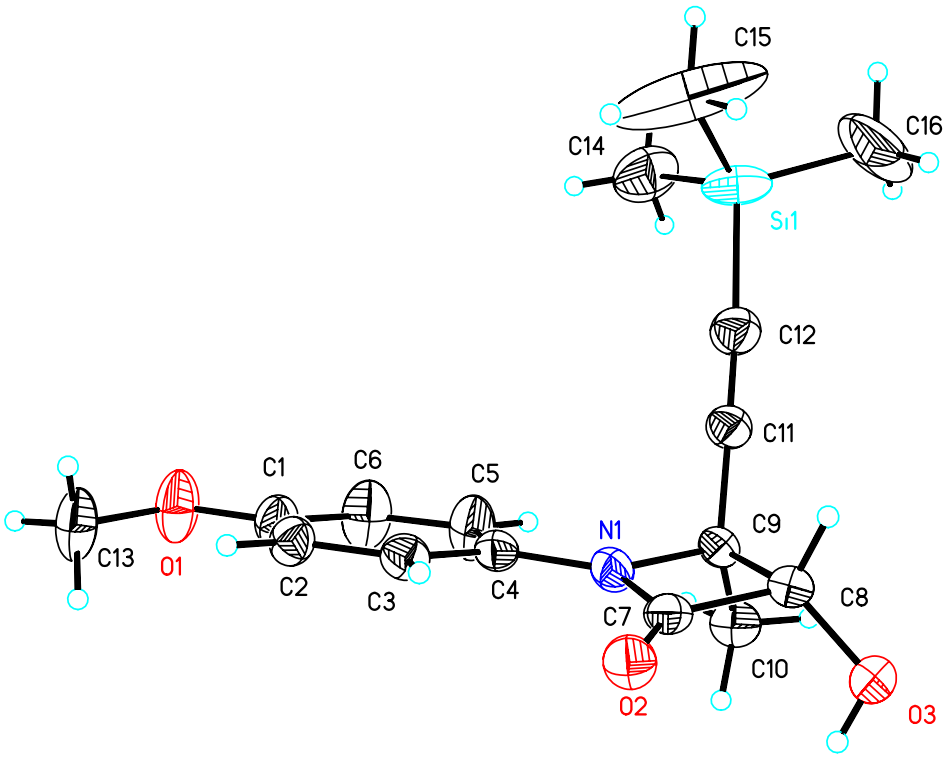


Table 1. Crystal data and structure refinement for (+)-**87**.

Identification code	(+)-**87**
Empirical formula	C_{16} H_{21} N O_3 Si
Formula weight	303.43
Temperature	173(2) K

Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	P2(1)	
Unit cell dimensions	a = 10.6408(8) Å	α = 90°.
	b = 6.0649(5) Å	β = 101.346(4)°.
	c = 13.6002(10) Å	γ = 90°.
Volume	860.54(11) $Å^3$	
Z	2	
Density (calculated)	1.171 Mg/m^3	
Absorption coefficient	1.280 mm^{-1}	
F(000)	324	
Crystal size	0.40 x 0.13 x 0.06 mm^3	
Theta range for data collection	3.31 to 65.71°.	
Index ranges	-8<=h<=12, -6<=k<=6, -16<=l<=15	
Reflections collected	6072	
Independent reflections	2403 [R(int) = 0.0200]	
Completeness to theta = 65.71°	94.2 %	
Max. and min. transmission	0.9272 and 0.6285	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2403 / 1 / 196	
Goodness-of-fit on F^2	1.016	
Final R indices [I>2sigma(I)]	R1 = 0.0279, wR2 = 0.0716	
R indices (all data)	R1 = 0.0293, wR2 = 0.0729	
Absolute structure parameter	0.08(3)	
Largest diff. peak and hole	0.142 and -0.168 $e.Å^{-3}$	

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3) for (+)-**87**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
C(1)	5502(2)	7544(3)	1477(1)	34(1)
C(2)	4509(2)	8835(3)	963(1)	31(1)
C(3)	3249(2)	8357(3)	1027(1)	30(1)
C(4)	2967(2)	6597(3)	1602(1)	28(1)
C(5)	3968(2)	5346(4)	2129(2)	45(1)
C(6)	5218(2)	5802(4)	2056(2)	48(1)
C(7)	529(2)	6735(3)	1114(1)	28(1)
C(8)	-216(2)	5464(3)	1785(1)	29(1)
C(9)	1143(2)	4575(3)	2334(1)	28(1)
C(10)	1336(2)	2131(4)	2175(1)	36(1)
C(11)	1537(2)	5257(3)	3389(1)	31(1)
C(12)	1866(2)	5846(4)	4242(2)	39(1)
C(13)	7079(2)	9459(4)	785(2)	51(1)
C(14)	4095(2)	5972(5)	5974(2)	64(1)
C(15)	2338(5)	9966(6)	5432(3)	158(3)
C(16)	1368(3)	5873(8)	6331(2)	100(2)
N(1)	1684(1)	6074(3)	1646(1)	29(1)
O(1)	6774(1)	7846(3)	1464(1)	50(1)
O(2)	236(1)	7902(2)	371(1)	33(1)
O(3)	-1143(1)	3965(2)	1341(1)	37(1)
Si(1)	2425(1)	6909(1)	5522(1)	48(1)

Table 3. Bond lengths [Å] and angles [°] for (+)-**87**.

C(1)-O(1)	1.369(2)	C(5)-C(4)-N(1)	120.36(17)
C(1)-C(6)	1.386(3)	C(3)-C(4)-N(1)	120.85(16)
C(1)-C(2)	1.388(3)	C(6)-C(5)-C(4)	120.37(19)
C(2)-C(3)	1.391(2)	C(5)-C(6)-C(1)	120.97(19)
C(3)-C(4)	1.391(3)	O(2)-C(7)-N(1)	131.87(16)
C(4)-C(5)	1.388(3)	O(2)-C(7)-C(8)	134.99(16)
C(4)-N(1)	1.413(2)	N(1)-C(7)-C(8)	93.14(14)
C(5)-C(6)	1.381(3)	O(3)-C(8)-C(7)	118.49(14)
C(7)-O(2)	1.223(2)	O(3)-C(8)-C(9)	119.07(16)
C(7)-N(1)	1.358(2)	C(7)-C(8)-C(9)	85.47(13)
C(7)-C(8)	1.530(3)	C(11)-C(9)-N(1)	111.54(15)
C(8)-O(3)	1.389(2)	C(11)-C(9)-C(10)	113.15(16)
C(8)-C(9)	1.585(2)	N(1)-C(9)-C(10)	115.01(14)
C(9)-C(11)	1.473(3)	C(11)-C(9)-C(8)	114.98(15)
C(9)-N(1)	1.500(2)	N(1)-C(9)-C(8)	85.79(13)
C(9)-C(10)	1.518(3)	C(10)-C(9)-C(8)	113.67(15)
C(11)-C(12)	1.198(3)	C(12)-C(11)-C(9)	178.9(2)
C(12)-Si(1)	1.842(2)	C(11)-C(12)-Si(1)	176.16(19)
C(13)-O(1)	1.425(3)	C(7)-N(1)-C(4)	133.78(15)
C(14)-Si(1)	1.852(3)	C(7)-N(1)-C(9)	95.29(13)
C(15)-Si(1)	1.860(4)	C(4)-N(1)-C(9)	130.92(15)
C(16)-Si(1)	1.832(3)	C(1)-O(1)-C(13)	116.84(15)
O(1)-C(1)-C(6)	115.82(17)	C(16)-Si(1)-C(12)	108.99(13)
O(1)-C(1)-C(2)	125.08(17)	C(16)-Si(1)-C(14)	110.98(14)
C(6)-C(1)-C(2)	119.10(17)	C(12)-Si(1)-C(14)	108.46(11)
C(1)-C(2)-C(3)	119.91(18)	C(16)-Si(1)-C(15)	110.7(2)
C(2)-C(3)-C(4)	120.84(17)	C(12)-Si(1)-C(15)	106.50(14)
C(5)-C(4)-C(3)	118.78(16)	C(14)-Si(1)-C(15)	111.09(18)

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for (+)-**87**. 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)	27(1)	41(1)	34(1)	6(1)	2(1)	-4(1)
C(2)	33(1)	29(1)	31(1)	4(1)	5(1)	-3(1)
C(3)	30(1)	33(1)	27(1)	1(1)	3(1)	3(1)
C(4)	28(1)	35(1)	21(1)	-1(1)	3(1)	-2(1)
C(5)	35(1)	56(2)	41(1)	25(1)	1(1)	-3(1)
C(6)	29(1)	59(2)	53(1)	27(1)	-3(1)	4(1)
C(7)	30(1)	29(1)	23(1)	-4(1)	3(1)	0(1)
C(8)	30(1)	33(1)	25(1)	-5(1)	7(1)	-3(1)
C(9)	31(1)	33(1)	21(1)	0(1)	8(1)	-5(1)
C(10)	40(1)	34(1)	33(1)	0(1)	6(1)	1(1)
C(11)	35(1)	34(1)	24(1)	1(1)	6(1)	-3(1)
C(12)	42(1)	41(1)	32(1)	0(1)	6(1)	-6(1)
C(13)	30(1)	58(2)	65(1)	20(1)	12(1)	-6(1)
C(14)	55(1)	71(2)	57(2)	-8(1)	-8(1)	-4(1)
C(15)	248(6)	46(2)	120(3)	-25(2)	-115(4)	27(3)
C(16)	78(2)	192(5)	34(1)	-23(2)	19(1)	14(2)
N(1)	30(1)	35(1)	22(1)	2(1)	6(1)	-2(1)
O(1)	25(1)	61(1)	62(1)	25(1)	5(1)	-2(1)
O(2)	32(1)	37(1)	29(1)	5(1)	3(1)	2(1)
O(3)	33(1)	45(1)	33(1)	-6(1)	7(1)	-10(1)
Si(1)	64(1)	44(1)	30(1)	-11(1)	-9(1)	5(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for (+)-**87**.

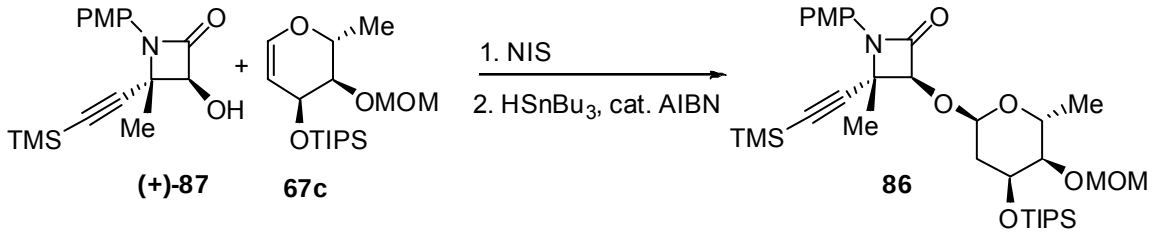
	x	y	z	U(eq)
H(2)	4686	10019	577	37
H(3)	2587	9225	680	36
H(5)	3797	4193	2534	54
H(6)	5879	4928	2400	58
H(8)	-569	6479	2222	35
H(10A)	2210	1743	2445	54
H(10B)	1144	1809	1470	54
H(10C)	777	1296	2507	54
H(13A)	6601	9163	123	76
H(13B)	7979	9402	781	76
H(13C)	6861	10898	994	76
H(14A)	4138	4399	5907	95
H(14B)	4368	6371	6666	95
H(14C)	4646	6659	5583	95
H(15A)	2935	10484	5038	237
H(15B)	2548	10593	6092	237
H(15C)	1486	10401	5118	237
H(16A)	495	6228	6039	150
H(16B)	1596	6547	6980	150
H(16C)	1460	4303	6397	150
H(3A)	-921	3396	855	55

Table 6. Hydrogen bonds for (+)-**87** [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
O(3)-H(3A)...O(2)#1	0.82	1.97	2.7663(17)	163.6

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

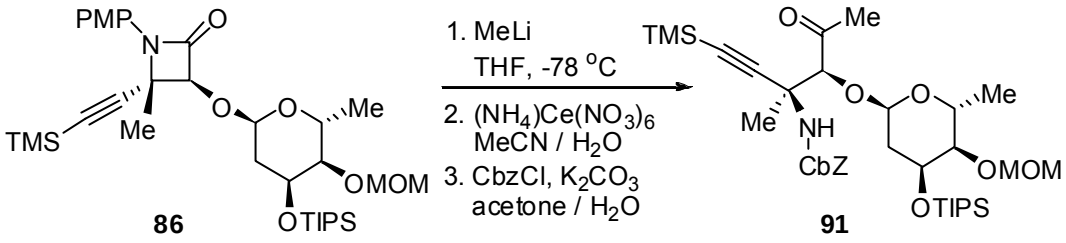
Preparation of glycosylated *beta*-lactam 29



NIS mediated glycosylation: The hydroxyl *beta*-lactam (+)-**87** (0.411 g, 1.36 mmol) and glycal **67c** (0.407 g, 1.23 mmol) were dissolved in CH_2Cl_2 (8 mL), and cooled to 0 ^oC. NIS (0.290 g, 1.29 mmol) was added at 0 ^oC. The mixture was slowly warmed to room temperature and then stirred overnight in the dark. The resulting solution was diluted with CH_2Cl_2 (5 mL) and quenched with sat. aq. $Na_2S_2O_4$ (10 mL). The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layer was dried over $MgSO_4$ and solvent removed by rotary evaporation. Chromatography (hexanes : EtOAc = 15 :1) gave iodoglycal *beta*-lactam as a colorless oil (0.766 g, 82% yield). $[\alpha]^{23}_D$ = +132.9 (*c* = 3.45, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, *J* = 9.2 Hz, 2H), 6.87 (d, *J* = 9.2 Hz, 2H), 5.23 (s, 1H), 4.97 (s, 1H), 4.71 (d, *J* = 6.4 Hz, 1H), 4.68 (dq, *J* = 6.4, 9.6 Hz, 1H), 4.59 (d, *J* = 7.2 Hz, 1H), 4.40 (t, *J* = 2.4 Hz, 1H), 4.36 (d, *J* = 2.4 Hz, 1H), 4.04 (dd, *J* = 2.0, 9.6 Hz, 1H), 3.79 (s, 3H), 3.42 (s, 3H), 1.64 (s, 3H), 1.38 (d, *J* = 6.4 Hz, 3H), 1.06 (s, 21H), 0.16 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.18, 156.67, 129.87, 119.63, 114.43, 104.15, 102.47, 95.56, 92.58, 86.67, 74.16, 72.55, 64.10, 57.52, 56.36, 55.66, 29.33, 20.54, 18.22, 18.13, 17.86, 12.76, -0.09; IR (neat) 2942, 2252, 2162, 2057, 1950, 1871, 1760, 1513, 1373, 1247, 844 cm^{-1}; HRMS [M+H] Calcd. for $C_{33}H_{55}O_7N_1{}^{127}I_1{}^{28}Si_2$ 760.25564, Found 760.25794.

Deiodination: Iodo-glycoside (0.550g, 0.754 mmol) was dissolved in toluene (25 mL), and $HSnBu_3$ (1.00 mL, 3.77 mmol) and AIBN (12.4 mg, 0.075 mmol) were added. Air was removed through vacuum-argon exchange (3 times). The reaction mixture was heated to 80 ^oC and stirred for 5 h. The reaction mixture was cooled to room temperature, and solvent was removed by rotary evaporation. Chromatography (hexanes : EtOAc = 40 : 1, gradient to 30 : 1 and to 20 : 1) gave compound **86** as a colorless oil (0.416 g, 88% yield). $[\alpha]^{23}_D$ = +114.3 (*c* = 1.8, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, *J* = 9.2 Hz, 2H), 6.87 (d, *J* = 9.2 Hz, 2H), 5.02 (s, 1H), 4.93 (dd, *J* = 2.0, 4.8 Hz, 1H), 4.76 (d, *J* = 7.2 Hz, 1H), 4.59 (d, *J* = 7.2 Hz, 1H), 4.55 (dq, *J* = 6.4, 8.8 Hz, 1H), 4.26 (ddd, *J* = 3.2, 4.8 Hz, 1H), 3.79 (s, 3H), 3.40 (s, 3H), 3.37 (dd, *J* = 2.8, 8.4 Hz, 1H), 2.19 (ddd, *J* = 2.4, 4.8, 14.4 Hz, 1H), 1.92 (ddd, *J* = 3.2, 4.8, 14.4 Hz, 1H), 1.63 (s, 3H), 1.34 (d, *J* = 6.4 Hz, 3H), 1.06 (s, 21H), 0.15 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.30, 156.56, 130.10, 119.60, 114.40, 104.62, 97.70, 95.28, 92.14, 86.97, 78.40, 65.76, 64.66, 57.53, 56.05, 55.68, 36.69, 20.54, 18.32, 18.27, 12.76, -0.05; IR (neat) 2941, 2866, 2162, 1763, 1512, 1248 cm^{-1}; HRMS Calcd. [M+H] for $C_{33}H_{56}O_7N_1{}^{28}Si_2$ 634.35899, Found 634.35891.

Preparation of alkynyl ketone 30



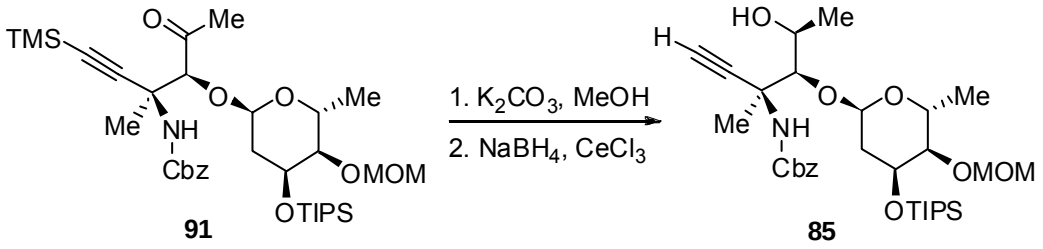
MeLi addition: *Beta*-lactam compound **86** (0.416 g, 0.733 mmol) was dissolved in dry THF (10 mL) and cooled to -78 ^{o}C. MeLi (0.687 mL, 1.10 mmol, 1.6 M in Et_2O) was added dropwise at –78 ^{o}C. The reaction mixture was stirred for 30 min at –78 ^{o}C and quenched with aq. sat. $NaHCO_3$ (5 mL). The organic layer was separated and the aqueous layer was extracted with Et_2O (3 × 10 mL). The combined organic layer was dried over $MgSO_4$ and solvent removed by rotary evaporation. Chromatography (hexanes : EtOAc = 10 :1) gave ketone as a colorless oil (0.425 g, 90% yield). $[\alpha]^{23}_{D}$ = +80.5 (*c* = 2.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.03 (d, *J* = 9.2 Hz, 2H), 6.76 (d, *J* = 9.2 Hz, 2H), 4.94 (dd, *J* = 4.0 Hz, 1H), 4.78 (d, *J* = 6.8 Hz, 1H), 4.62 (d, *J* = 6.8 Hz, 1H), 4.24-4.17 (m, 2H), 4.00 (s, 1H), 3.99 (d, *J* = 4.0 Hz, 1H), 3.76 (s, 3H), 3.39 (s, 3H), 3.38 (dd, *J* = 2.8, 6.0 Hz, 1H), 2.35 (s, 3H), 2.27 (ddd, *J* = 4.0, 6.4, 14.0 Hz, 1H), 1.94 (ddd, *J* = 4.0, 14.4 Hz, 1H), 1.42 (s, 3H), 1.17 (d, *J* = 6.8 Hz, 3H), 1.10 (s, 21H), 0.13 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 209.60, 154.83, 138.33, 122.63, 114.11, 107.10, 99.91, 95.90, 90.53, 87.80, 78.19, 66.61, 65.99, 56.42, 55.98, 55.72, 36.65, 29.17, 24.27, 18.39, 18.34, 17.74, 12.72, -0.04; IR (neat) 2942, 2867, 2166, 1712, 1510, 1248, 1035, 842 cm^{-1}; HRMS Calcd. [M+H] for $C_{34}H_{60}O_7N_1{}^{28}Si_2$ 650.39029, Found 650.38986.

Removal of PMP: The ketone (0.425g, 0.660 mmol) was dissolved in a mixture of CH_3CN (12 mL) and water (6 mL), and cooled to 0 ^{o}C. Ceric ammonium nitrate (0.724 g, 1.32 mmol) dissolved in water (6 mL) was added dropwise at 0 ^{o}C, and the reaction mixture was slowly warmed to room temperature and stirred for 1 h. The resulting solution was quenched with aq. sat. $NaHCO_3$ (20 mL) and then

stirred for 1 h at room temperature. The solution was filtered through Celite using EtOAc as eluent and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 × 10 mL), the combined organic layer was dried over $MgSO_4$, and solvents were removed by rotary evaporation, to afford crude amine which was used in the next step without further purification.

Cbz protection: The procedure as described above for (±)-**45,** (±)-**58, 59** and **60** was followed with crude amine, K_2CO_3 (9.1 mg, 0.066 mmol) and CbzCl (0.14 mL, 0.99 mmol) in acetone (6 mL) and water (6 mL), to provide ketone **91** as a colorless oil (0.29 g, 65 % over 2 steps) after chromatography (hexanes : EtOAc = 5 : 1). $[\alpha]^{23}_{D}$ = +87.8 (*c* = 3.5, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.26 (m, 5H), 5.67 (s, 1H), 5.07 (s, 2H), 4.81 (dd, *J* = 3.2, 5.2 Hz, 1H), 4.74 (d, *J* = 6.8 Hz, 1H), 4.58 (d, *J* = 6.8 Hz, 1H), 4.12 (ddd, *J* = 3.2, 6.0 Hz, 1H), 4.11 - 4.07 (m, 2H), 3.37 (s, 3H), 3.31 (dd, *J* = 2.8, 8.0 Hz, 1H), 2.35 (s, 3H), 2.16 (ddd, *J* = 2.8, 5.6, 14.0 Hz, 1H), 1.85 (ddd, *J* = 3.6, 5.2, 14.0 Hz, 1H), 1.65 (s, 3H), 1.12 (d, *J* = 6.8 Hz, 3H), 1.06 (s, 21H), 0.13 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.41, 154.58, 136.71, 128.60, 128.32, 128.16, 109.96, 99.91, 95.60, 88.94, 86.10, 78.11, 66.62, 65.79, 65.70, 55.97, 52.80, 36.54, 30.24, 24.29, 18.29, 18.23, 17.70, 12.63, -0.03; IR (neat) 2943, 2867, 2173, 1726, 1504, 1248, 1036, 843 cm^{-1}; HRMS [M+Na] Calcd. for $C_{35}H_{59}O_8N_1{}^{23}Na_1{}^{28}Si_2$ 700.36715, Found 700.36652.

Preparation of alkynyl alcohol 31

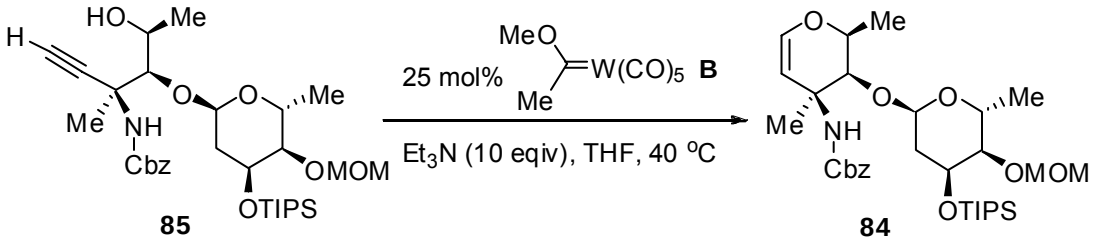


91 **85**

Desilylation: The alkynylsilane compound **91** (0.15 g, 0.22 mmol) was dissolved in MeOH (8 mL), K_2CO_3 (6.0 mg, 0.044 mmol) was added, and the reaction mixture was stirred overnight at room temperature. The reaction was quenched with aq. sat. NH_4Cl (5 mL) and diluted with CH_2Cl_2 (10 mL). The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic layer was dried over $MgSO_4$ and solvent was removed by rotary evaporation. Chromatography (hexanes : EtOAc = 10 :1) gave terminal alkyne as a colorless oil (0.13 g, 95% yield). $[\alpha]^{23}_D$ = +86.5 (*c* = 2.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36-7.27 (m, 5H), 5.75 (s, 1H), 5.16-5.03 (m, 2H), 4.85 (dd, *J* = 3.2, 5.2 Hz, 1H), 4.75 (d, *J* = 7.2 Hz, 1H) , 4.58 (d, *J* = 7.2 Hz, 1H), 4.17 (ddd, *J* = 3.2, 6.0 Hz, 1H), 4.14-4.07 (m, 2H), 3.37 (s, 3H), 3.20 (dd, *J* = 3.5, 8.0 Hz, 1H), 2.44 (s, 1H), 2.36 (s, 3H), 2.18 (ddd, *J* = 3.6, 6.0, 14.4 Hz, 1H), 1.88 (ddd, *J* = 3.6, 4.8, 14.4 Hz, 1H), 1.66 (s, 3H), 1.13 (d, *J* = 6.4 Hz, 3H), 1.05 (s, 21H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.07, 154.76, 136.54, 128.63, 128.43, 128.24, 100.09, 95.61, 85.70, 83.39, 78.03, 72.68, 66.77, 65.86, 65.73, 56.00, 52.19, 36.49, 30.50, 24.15, 18.38, 18.29, 18.22, 17.79, 12.63; IR (neat) 2943, 2867, 2173, 1726, 1504, 1248, 1036, 843 cm^{-1}; HRMS [M+Na] Calcd. for $C_{32}H_{51}O_8N_1{}^{23}Na_1{}^{28}Si_1$ 628.32762, Found 628.32721.

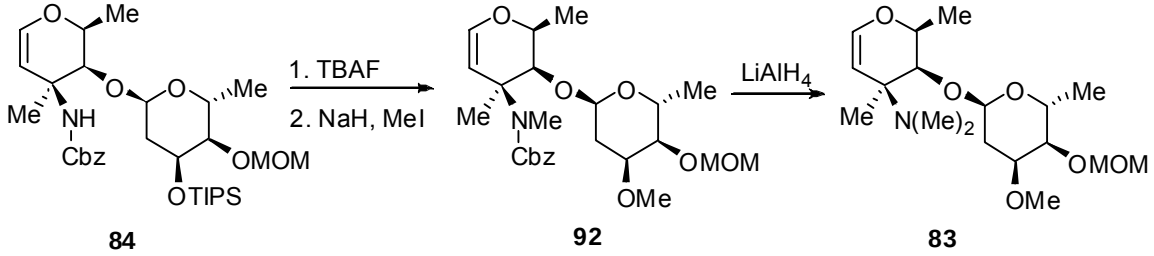
Diastereoselective reduction of ketone: Terminal alkyne (0.13 g, 0.21 mmol) was dissolved in a mixture of CH_2Cl_2 (4 mL) and MeOH (2 mL), and $CeCl_3 \cdot 7H_2O$ (0.16 g, 0.42 mmol) was added. The reaction mixture was stirred for 20 min at room temperature and then cooled to –78 ^oC. $NaBH_4$ (8.0 mg, 0.21 mmol) was added to the reaction mixture and then stirred for 1 h at –78 ^oC. An additional portion of $NaBH_4$ (8.0 mg, 0.21 mmol) was added and then stirred for 1 hr at –78 ^oC. The reaction mixture was quenched with aq. sat. $NaHCO_3$ (4 mL) and then diluted with CH_2Cl_2 (5 mL). The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic layer was dried over $MgSO_4$ and solvent was removed by rotary evaporation. Chromatography (hexanes : EtOAc = 10 :1) gave alkynyl alcohol **85** as a colorless oil (0.11 g, 89 % yield). $[\alpha]^{23}_D$ = +93.2 (*c* = 1.2, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35-7.27 (m, 5H), 6.12 (s, 1H), 5.13-5.01 (m, 3H), 4.79 (d, *J* = 6.8 Hz, 1H), 4.60 (d, *J* = 7.2 Hz, 1H), 4.26 (ddd, *J* = 6.8, 14.0 Hz, 1H), 4.23-4.12 (m, 2H), 3.66 (d, *J* = 1.2 Hz, 1H), 3.40 (s, 3H), 3.38 (dd, *J* = 3.6, 7.6 Hz, 1H), 2.84 (d, *J* = 10.4 Hz, 1H), 2.37 (s, 1H), 2.23 (ddd, *J* = 3.6, 6.0, 14.0 Hz, 1H), 1.94 (ddd, *J* = 3.6, 7.6, 14.0 Hz, 1H), 1.64 (s, 3H), 1.28 (d, *J* = 6.4 Hz, 3H), 1.26 (d, *J* = 6.4 Hz, 3H), 1.06 (s, 21H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.09, 136.69, 128.61, 128.35, 128.20, 99.25, 95.70, 84.87, 77.75, 71.52, 66.63, 66.21, 65.99, 65.95, 56.13, 55.10, 36.78, 23.73, 22.85, 18.31, 18.19, 17.82, 12.69; IR (neat) 2943, 1726, 1514, 1249, 1035 cm^{-1}; HRMS [M+Na] Calcd. for $C_{32}H_{53}O_8N_1{}^{23}Na_1{}^{28}Si_1$ 630.34327, Found 630.34292.

Synthesis of disaccharide glycal 84 via alkynyl alcohol cycloisomerization



Disaccharide glycal 84: Following the general procedure for alkynyl alcohol cycloisomerization, substrate **85** (114 mg, 0.188 mmol) afforded disaccharide glycal **84** as a colorless oil (95 mg, 83 % yield). $[\alpha]^{23}_{D}$ = +78.7 (*c* = 3.3, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-7.28 (m, 5H), 6.18 (d, *J* = 6.4 Hz, 1H), 5.35 (s, 1H), 5.08-5.01 (m, 3H), 4.88 (dd, *J* = 3.2, 5.2 Hz, 1H), 4.76 (d, *J* = 7.2 Hz, 1H), 4.59 (d, *J* = 7.2 Hz, 1H), 4.31-4.21 (m, 2H), 4.15 (ddd, *J* = 3.2, 5.2 Hz, 1H), 3.71 (d, *J* = 3.6 Hz, 1H), 3.39 (s, 3H), 3.34 (dd, *J* = 2.4, 3.6 Hz, 1H), 2.14 (ddd, *J* = 3.2, 5.6, 14.0 Hz, 1H), 1.83 (ddd, *J* = 3.6, 14.0 Hz, 1H), 1.48 (s, 3H), 1.38 (d, *J* = 6.8 Hz, 1H), 1.23 (d, *J* = 6.8 Hz, 1H), 1.04 (s, 21H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.14, 141.69, 136.91, 128.63, 128.28, 128.15, 104.14, 99.81, 95.67, 80.44, 78.23, 71.67, 66.37, 65.95, 65.38, 56.02, 51.24, 36.84, 27.03, 18.32, 18.22, 15.20, 2.65; IR (neat) 2940, 2867, 1726, 1495, 1035 cm^{-1}; HRMS [M+Na] Calcd. for $C_{32}H_{53}O_8N_1{}^{23}Na_1{}^{28}Si_1$ 630.34327, Found 630.34292.

Synthesis of disaccharide glycal 83



Desilylation: Silyl ether **84** (60 mg, 0.099 mmol) was dissolved in dry THF (3 mL), and TBAF (0.2 mL, 1M in THF, 0.2 mmol) was added. The reaction mixture was stirred for 30 min at room temperature. The reaction was diluted with EtOAc (2 mL) and quenched with water (3 mL). The organic layer was separated and the aqueous layer was extracted with EtOAc (3 × 5 mL) and washed with brine. The combined organic layer was dried over $MgSO_4$ and solvent removed by rotary evaporation. The crude material was used for the next step without further purification.

***N*,*O*-Dimethylation:** The crude amino alcohol was dissolved in dry DMF (3 mL), and cooled to 0 ^oC. Sodium hydride (16 mg, 0.40 mmol) was added, and the mixture was slowly warmed to room temperature and stirred for 20 min. Iodomethane (31 μL, 0.50 mmol) was added to the reaction mixture and then stirred for 1 h at room temperature. The reaction mixture was carefully quenched with water (1 mL) and then diluted with EtOAc. The organic layer was separated and the aqueous layer was extracted with EtOAc (3 × 5 mL). The combined organic layer was dried over $MgSO_4$ and solvent removed by rotary evaporation. Chromatography (hexanes : EtOAc = 5 : 1) gave *N*- and *O*-methylated product **92** as a colorless oil (42 mg, 85 % over 2 steps). $[\alpha]^{23}_D$ = +6.4 (*c* = 1.4, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.29-7.18 (m, 5H), 6.19 (d, *J* = 6.4 Hz, 1H), 5.09 (d, *J* = 12.0 Hz, 1H), 4.89 (d, *J* = 12.4 Hz, 1H), 4.63 (d, *J* = 6.8 Hz, 1H), 4.62 (dd, *J* = 2.4, 6.4 Hz, 1H), 4.56 (dd, *J* = 3.6, 4.4 Hz, 1H), 4.54 (d, *J* = 6.8 Hz, 1H), 4.18 (ddd, *J* = 2.8, 14.0 Hz, 1H), 4.03 (brs, 1H), 3.98 (d, *J* = 2.4 Hz, 1H), 3.39 (brs, 1H), 3.27 (s, 3H), 3.22 (dd, *J* = 3.2, 7.6 Hz, 1H), 3.20 (s, 3H), 2.93 (s, (3H), 1.89 (d, *J* =

12.0 Hz, 1H), 1.53 (s, 3H), 1.40-1.29 (m, 1H), 1.23 (d, *J* = 6.8 Hz, 1H), 1.06 (d, *J* = 6.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.96, 128.22, 128.42, 127.98, 104.78, 97.45, 95.53, 77.84, 77.31, 73.34, 71.78, 66.70, 65.23, 58.81, 55.91, 55.38, 31.10, 17.61; IR (neat) 2932, 1964, 1345, 1105, 1040 cm^{-1}; HRMS [M+Na] Calcd. for $C_{25}H_{37}O_8N_1{}^{23}Na_1$ 502.24114, Found 502.24075.

$LiAlH_4$ reduction: Compound **92** obtained above (42 mg, 0.084 mmol) was dissolved in dry Et_2O (3 mL) and cooled to 0 ^{o}C. $LiAlH_4$ (0.25 mL, 1 M solution in Et_2O) was added dropwise at 0 ^{o}C. The reaction mixture was slowly warmed to room temperature and stirred for 5 h. The reaction mixture was diluted with Et_2O (2 mL), quenched with water (0.05 mL) and 3 M NaOH (0.1 mL), and then stirred for additional 1 hour. The solution was then dried over $MgSO_4$ and solvent removed by rotary evaporation. Chromatography (hexanes : EtOAc = 5 : 1, gradient to 2 : 1 and to 1 : 1) gave the disaccharide glycal **83** as a yellowish oil (28 mg, 94 % yield). $[\alpha]^{23}_D$ = +83.6 (*c* = 1.2, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.27 (d, *J* = 6.4 Hz, 1H), 5.23 (dd, *J* = 1.6, 4.8 Hz, 1H), 4.78 (d, *J* = 6.8 Hz, 1H), 4.68-4.66 (m, 2H), 4.30 (dq, *J* = 6.6, 8.8 Hz, 1H), 4.16 (dq, *J* = 2.4, 6.4 Hz, 1H), 3.72 (dd, *J* = 2.8, 7.2 Hz, 1H), 3.58 (dd, *J* = 2.4 Hz, 1H), 3.41 (s, 3H), 3.40 (s, 3H), 3.34 (dd, *J* = 2.8, 8.8 Hz, 1H), 2.37 (ddd, *J* = 2.0, 4.4, 14.8 Hz, 1H), 2.30 (s, 6H), 1.70 (ddd, *J* = 2.8, 4.8, 14.8 Hz, 1H), 1.41 (d, *J* = 6.0 Hz, 3H), 1.22 (d, *J* = 6.8 Hz, 1H), 1.11 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.73, 104.57, 97.30, 95.75, 78.86, 78.60, 73.56, 73.24, 64.22, 56.21, 55.73, 40.62, 31.13, 22.97, 18.14, 17.27; IR (neat) 2929, 1111, 1042, 985 cm^{-1}; [M+H] Calcd. for $C_{18}H_{34}O_6N_1$ 360.23806, Found 360.23788.

2. 5 References

1. Danishefsky, S. J.; Bilodeau, M. T. *Angew. Chem. Int. Ed.* **1996**, *35*, 1380.
2. Danishefsky, S. J.; Roberge, J. Y. *Pure Appl. Chem.* **1995**, *67*, 1647.
3. Seeberger, P. H.; Bilodeau, M. T.; Danishefsky, S. J. *Aldrichimica Acta* **1997**, *30*, 75.
4. Williams, L. J.; Garbaccio, R. M.; Danishefsky, S. J. *Carbohydrates in Chemistry and Biology* **2000**, *1*, 61.
5. Priebe, W.; Grynkiewicz, G. *Glycoscience* **2001**, *1*.
6. Fischer, E. *Ber* **1914**, *47*, 196.
7. Smith, C. W.; Norton, D. G.; Ballard, S. A. *J. Am. Chem. Soc.* **1951**, *73*, 5270.
8. Danishefsky, S.; Kerwin, J. F.; Kobayashi, S. *J. Am. Chem. Soc.* **1982**, *104*, 358.
9. Danishefsky, S. J.; Pearson, W. H.; Harvey, D. F.; Maring, C. J.; Springer, J. P. *J. Am. Chem. Soc.* **1985**, *107*, 1256.
10. Sturino, C. F.; Wong, J. C. Y. *Tetrahedron Lett.* **1998**, *39*, 9623.
11. Gurjar, M. K.; Krishna, L. M.; Reddy, B. S.; Chorghade, M. S. *Synthesis* **2000**, *4*, 557.
12. Adam, J.-M.; de Fays, L.; Laguerre, M.; Ghosez, L. *Tetrahedron* **2004**, *60*, 7325.
13. McDonald, F. E.; Gleason, M. M. *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 350.

14. McDonald, F. E.; Gleason, M. M. *J. Am. Chem. Soc.* **1996**, *118*, 6648.

15. McDonald, F. E.; Connolly, C. B.; Gleason, M. M.; Towne, T. B.; Treiber, K. D. *J. Org. Chem.* **1993**, *58*, 6952.

16. McDonald, F. E.; Bowman, J. L. *Tetrahedron Lett.* **1996**, *37*, 4675.

17. McDonald, F. E.; Zhu, H. Y. H. *Tetrahedron* **1997**, *53*, 11061.

18. McDonald, F. E.; Schultz, C. C.; Chatterjee, A. K. *Organometallics* **1995**, *14*, 3628.

19. McDonald, F. E.; Zhu, H. Y. H. *J. Am. Chem. Soc.* **1998**, *120*, 4247.

20. McDonald, F. E. *Chem. Eur. J.* **1999**, *5*, 3103.

21. McDonald, F. E.; Reddy, K. S. *J. Organometal. Chem.* **2001**, *617-618*, 444.

22. Bowman, J. L.; McDonald, F. E. *J. Org. Chem.* **1998**, *63*, 3680.

23. McDonald, F. E.; Reddy, K. S.; Díaz, Y. *J. Am. Chem. Soc.* **2000**, *122*, 4304.

24. Burova, S. A. Ph. D. dissertation. Emory University **2003**.

25. Moilanen, S. B.; Tan, D. S. *Org. Biomol. Chem.* **2005**, *3*, 798.

26. Cutchins, W. W.; McDonald, F. E. *Org. Lett.* **2002**, *4*, 749.

27. Davidson, M. H.; McDonald, F. E. *Org. Lett.* **2004**, *6*, 1601.

28. Parker, K. A.; Chang, W. *Org. Lett.* **2003**, *5*, 3891.

29. Parker, K. A.; Chang, W. *Org. Lett.* **2005**, *7*, 1785.

30. Alcázar, E.; Pletcher, J. M.; McDonald, F. E. *Org. Lett.* **2004**, *6*, 3877.

31. McDonald, F. E.; Reddy, K. S. *Angew. Chem. Int. Ed. Engl.* **2001**, *40*, 3653.

32. McDonald, F. E.; Wu, M. *Org. Lett.* **2002**, *4*, 3979.

33. Trost, B. M.; Rhee, Y. H. *J. Am. Chem. Soc.* **2003**, *125*, 7482.

34. Trost, B. M.; Rhee, Y. H. *J. Am. Chem. Soc.* **2002**, *124*, 2528.

35. McDonald, F. E.; Schultz, C. C.; Chatterjee, A. K. *Organometallics* **1995**, *14*, 3628.

36. Fischer, E. O.; Plabst, D. *Chem. Ber.* **1974**, *107*, 3326.

37. Bernasconi, C. F. *Chem. Soc. Rev.* **1997**, *26*, 299.

38. Kreiter, C. G. *Angew. Chem. Int. Ed.* **1968**, *7*, 390.

39. Casey, C. P.; Anderson, R. L. *Chem. Soc. Chem. Commun.* **1975**, 895.

40. Fischer, E. O.; Maasböl, A. *Angew. Chem. Int. Ed.* **1964**, *3*, 850.

41. Lam, C. T.; Malkiewich, C. D.; Senoff, C. V. *Inorg. Synth.* **1977**, *17*, 95.

42. Matsuyama, H.; Nakamura, T.; Iyoda, M. J. *J. Org. Chem.* **2000**, *65*, 4796.

43. Grindley, T. B. *Adv. Carbohydr. Chem. Biochem.* **1998**, *53*, 17.

44. Wipf, P.; Graham, T. H. *J. Org. Chem.* **2003**, *68*, 8798.

45. Sheng, Y.; Musaev, D. G.; Reddy, K. S.; McDonald, F. E.; Morokuma, K. *J. Am. Chem. Soc.* **2002**, *124*, 4149.

46. Nowroozi-Isfahani, T.; Musaev, D. G.; McDonald, F. E.; Morokuma, K. *Organometallics* **2005**, *24*, 2921.

47. Sordo, T.; Campomanes, P.; Diéguez, A.; Rodriguez, F.; Fañanás, F. J. *J. Am. Chem. Soc.* **2005**, *127*, 944.

48. Brill, G. M.; McAlpine, J. B.; Whittern, D. N.; Buko, A. M. *J. Antibiot.* **1990**, *43*, 229.

49. Jackson, M.; Karwowski, J. P.; Theriault, R. J.; Hardy, D. J.; Swanson, S.

J.; Barlow, G. J.; Tillis, P. M.; McAlpine, J. B. *J. Antibiot.* **1990**, *43*, 223.

50. Thiem, J.; Ossowski, P.; Schwentner, J. *J. Chem. Ber.* **1980**, *113*, 955.