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Stereoselectivity of electrophile-promoted oxacyclizations of 1,4-dihydroxy-5-alkenes to 3-hydroxytetrahydropyrans

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Dedicated to Professor Paul A. Wender with heartiest congratulations on his receipt of the 2012 Tetrahedron Prize for Creativity in Organic Chemistry

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ABSTRACT

Stereoinduction from the allylic hydroxyl group of 1,4-dihydroxy-5-alkenes has been systematically explored with various alkene substitution patterns and electrophilic reagents. For formation of *erythro*-diastereomers of 2-substituted 3-hydroxytetrahydropyrans, mercuric trifluoroacetate-promoted cyclizations of *cis*- and (*Z*)-alkenyldiols generally give the highest diastereoselectivities. For the corresponding 1,4-dihydroxy-5-alkyne, mercuric triflate-catalyzed cyclization followed by triethylsilane reduction affords an alternative route to the *erythro*-diastereomer.

1. Introduction

trans–syn–trans Polycyclic ether natural products have long been the subject of considerable interest by the synthetic community,[1] both in terms of target-directed total synthesis and development of synthetic methods inspired by the common stereochemistry of the ring fusions, exemplified by the structure of brevanal (**1**, Fig. 1).[2] Our laboratory has explored several approaches to these compounds, including iterative alkynol cycloisomerizations and polyepoxide cyclizations.[3,4] These synthetic methods have focused on mechanistic design to favor *endo*-mode cyclization motifs.[5] On the other hand, a few strategies for fused polycyclic ether structures from other laboratories have utilized *exo*-cyclizations (**2**→**3**, **5**→**6**, Fig. 2) followed by solvolytic ring expansion to products corresponding to *endo*-mode cyclization (i.e., **4**, **7**).[6,7]

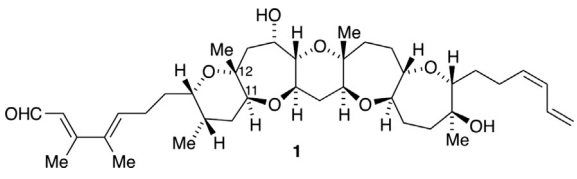

Fig. 1. Structure of brevenal.

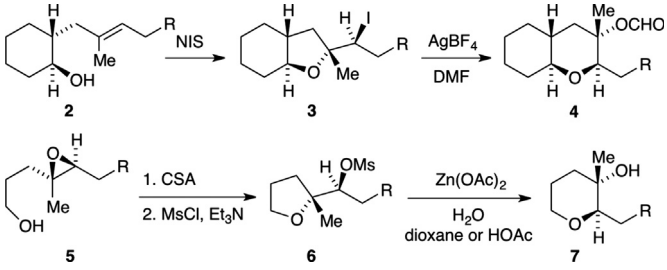

Fig. 2. *exo*-Mode cyclization followed by stereospecific ring expansion.

Herein we describe preliminary studies toward a variation on this approach, in which 1,4-dihydroxy-5-alkenes **8** bearing an allylic alcohol in the tether will undergo 6-*exo*-mode cyclization with stereoinduction from the chiral allylic alcohol, so that the ether

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oxygen in product structures **9** or **10** will be *erythro* or *threo*, respectively, with reference to the chiral alcohol (Fig. 3). In this new approach, subsequent rearrangement will not be required if the regio- and stereoselectivity are properly controlled. Although extensive studies of 5-*exo*-mode cyclizations have been reported, especially for electrophile-promoted lactonizations,[8,9] fewer studies have been described for 6-*exo*-mode cyclizations to forming 3-hydroxytetrahydropyrans. The most relevant studies utilized compounds bearing additional substituents and chiral centers in the tether, so that stereoinduction from the chiral allylic alcohol was not isolated from other factors.[10,11]

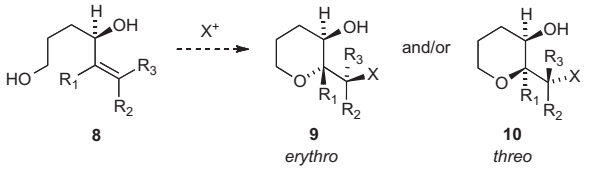


Fig. 3. Oxacyclization with stereoinduction from the chiral allylic alcohol.

Chamberlin and Hehre have proposed a reactive conformational model for a variety of cyclization reactions with stereoinduction from allylic alcohol substituents.[9] The essential features of this model predict that intramolecular electrophilic additions generally occur via conformation **A**, in which the electrophile forms a π-complex on the face *syn*- to the carbinol hydrogen, with the allylic hydroxyl in the plane of the alkene (Fig. 4). In contrast to intermolecular electrophilic additions, the internal nucleophile will add to the electrophile-activated alkene before the π-complex can transform into an onium ion. Applying this model to the formation of six-membered rings from 1,4-dihydroxy-5-alkenes **8** predicts the formation of the *threo*-diastereomer **10**. However, the synthetic application of this transformation to the *trans*-fused polycyclic ethers will require the opposite *erythro*-diastereomer **9**. To this end, the Chamberlin–Hehre model predicts that the *erythro*-diastereomer **9** will arise from 1,4-dihydroxy-5-alkene **8** with a *cis*-alkene ($R_3 \neq H$), in which the hydroxyl-in-plane conformer **A** is destabilized by steric interaction with R_3. The alternate conformer **B** has the sterically small carbinol hydrogen in the plane of the alkene, so that intramolecular nucleophilic addition occurs on the opposite face of the activated alkene. In this paper, we will systematically report the patterns of stereoinduction in cyclizations with a variety of di- and trisubstituted 1,4-dihydroxy-5-alkenes as well as a related transformation with a dihydroxyalkyne congener, with the goal of finding generally applicable methods to prepare the *erythro*-diastereomers required for the synthesis of *trans*-fused polycyclic ether natural products.

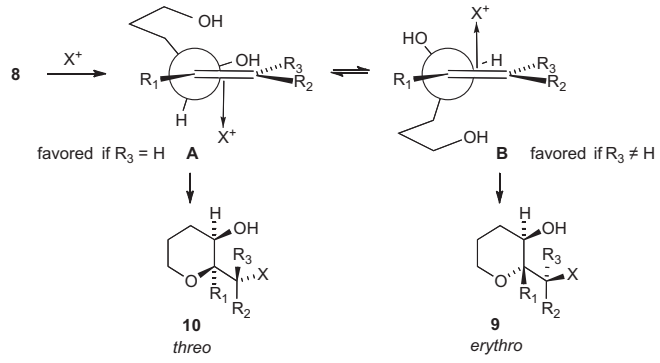


Fig. 4. Conformational models for oxacyclizations with stereoinduction from a chiral allylic alcohol.

2. Results and discussion

2.1. Preparation of 1,4-dihydroxy-5-alkene substrates

By design, all substrates had an additional oxygen protected as a benzyl or silyl ether, to mimic the presence of additional oxygens as a model system for future tandem cyclization processes. Most of the required substrates were prepared by nucleophilic addition to 4-silyloxybutanal (**11**).[12] For instance, the terminal alkyne of **12** was deprotonated with *n*-butyllithium,[13] followed by addition to aldehyde **11** to provide the propargylic alcohol **14**, with deprotection of the silyl ether affording the 1,4-dihydroxy-5-alkyne substrate **15**. P2-nickel hydrogenation[14] afforded reduction to give the *cis*-alkene predominantly, whereas the *trans*-alkene isomer **17** was prepared by hydroxyl-directed reduction with Red-Al (Fig. 5).[15] The 1,1-disubstituted alkene of **21** was synthesized from halogen-metal exchange of **19**,[16] with addition to tetrahydro-2-furanol (**20**, Fig. 6).[17]

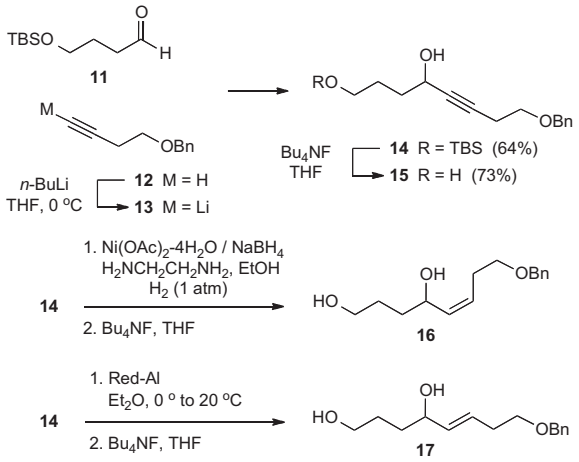


Fig. 5. Preparation of dihydroxyalkyne substrate **15**, and the *cis*- and *trans*-1,2-disubstituted dihydroxyalkenes **16** and **17**.

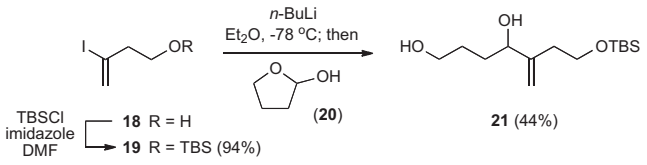


Fig. 6. Preparation of 1,1-disubstituted dihydroxyalkene **21**.

To avoid the difficulty of selectively deprotecting only one of two TBS ethers in subsequent substrates, the trisubstituted dihydroxyalkenes **24** and **30** were protected as the triisopropylsilyl (TIPS) ethers. Thus the known vinylic iodide **22**[18] underwent halogen–metal exchange and addition of the vinyllithium intermediate **23** to the TBS-protected aldehyde **11**, from which the TBS ether was selectively deblocked under acidic conditions to afford the (*Z*)-alkene substrate **24** (Fig. 7). For the (*E*)-isomer **30**, the (*E*)-vinylic iodide **26** was prepared by hydrotitanation–iodination of 2-butyn-1-ol (**25**).[19,20] After protection as the TIPS ether **27**, the same sequence of halogen–metal exchange and addition to aldehyde **11** followed by selective hydrolysis of the TBS ether provided compound **30** (Fig. 8).

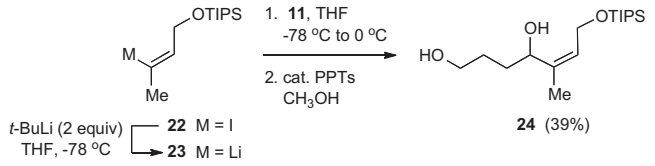


Fig. 7. Preparation of (*Z*)-trisubstituted dihydroxyalkene **24**.

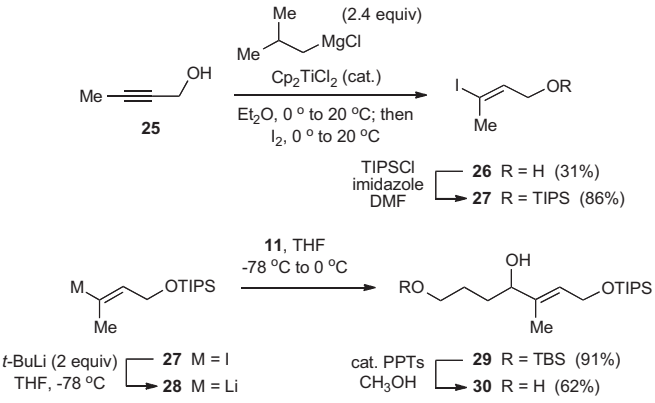


Fig. 8. Preparation of (*E*)-trisubstituted dihydroxyalkene **30**.

2.2. Stereoselectivity of electrophile-promoted oxacyclizations of 1,2-disubstituted alkenes

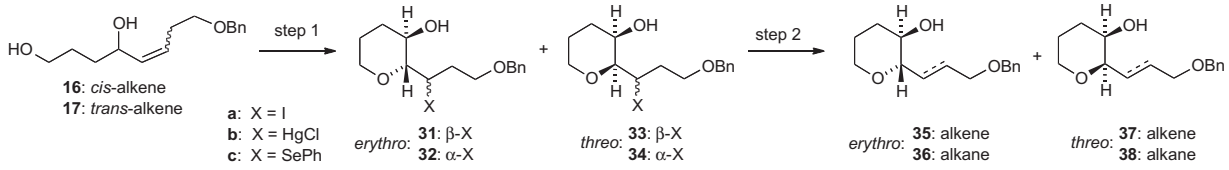
We began our studies by evaluating typical conditions for iodocyclizations of the *cis*- and *trans*-alkenes **16** and **17**, as well as mercury- and selenium-promoted cyclizations. The first experiments with iodine in dichloromethane or in acetonitrile afforded dehydrative cyclization to the 2-alkenyltetrahydrofuran. As this undesired reaction pathway was presumably acid-catalyzed, we added sodium bicarbonate but failed to inhibit the dehydrative cyclization, until we changed the solvent to tetrahydrofuran. Under these conditions, iodocyclization of *cis*-alkene **16** provided the six-membered cyclic iodoether product structures, but without appreciable diastereoselectivity, providing both diastereomers **31a** and **34a** (Table 1, entry 1). Stereochemical assignments were confirmed by conversion of each iodoether into the corresponding alkenes **35** and **37** and comparing the coupling constants for the hydrogens at the adjacent chiral centers. Thus the coupling constant of 8.4 Hz[21] was consistent with the *erythro*-stereochemistry of **35** (depicted as the diequatorial conformer), whereas the coupling constant of 1.2 Hz indicated the *threo*-stereochemistry assigned to **37**(Fig. 9). Moreover, the structure of the *threo*-diastereomer **34a** was unambiguously confirmed by X-ray crystallography (Fig. 10).

In contrast, the mercury-promoted cyclization of **16** more closely followed the Chamberlin–Hehre model (Fig. 4),[9] to provide primarily the desired *erythro*-diastereomer (81:19 ratio before separation), which was isolated as compound **36** after reduction of the organomercury intermediate (Table 1, entry 2). Our ^{1}H and ^{13}C NMR data for compound **36** closely matched the tabulated data previously reported for this compound.[22]

The corresponding phenylselenium-mediated cyclization of **16** proceeded with somewhat lower diastereoselectivity and yield (Table 1, entry 3), and was best evaluated after oxidation and elimination giving a mixture of the same alkenes **35** and **37** obtained from the iodocyclization and elimination protocol. Iodocyclization of the *trans*-alkene **17** afforded only the *threo*-diastereomer **33a** (Table 1, entry 4), consistent with the Chamberlin–Hehre stereoinduction model. The mercury- and selenium-promoted cyclizations of the *trans*-alkene **17** proceeded with poor diastereoselectivity and could not be optimized to favor the desired *erythro*-diastereomer (Table 1, entries 5 and 6).

At this stage, we can only speculate on the reasons for superior diastereoselectivity with the mercury-promoted procedure when compared with iodocyclization, but the predicted hydrogen-in-plane conformation **B** may be complemented by chelation or electrostatic attraction between the Lewis acidic mercuric ion and a non-bonding electron pair from the allylic hydroxyl (**B′**, Fig. 11), thus providing a higher degree of conformational organization than might be expected from the conformational model **B** depicted in

Table 1
Oxacyclization of 1,2-disubstituted alkenes **16** and **17**



Entry	Alkene	(Steps) Reagents and conditions	*erythro*-Product, isolated yield	*threo*-Product, isolated yield
1[a]	**16**	(1) I_2, $NaHCO_3$, THF, 0° to 20 °C (2) DBU, CH_2Cl_2, 20 °C	**31a**, X=I, 26% **35**, 33%[c]	**34a**, X=I, 30% **37**, 46%[d]
2[b]	**16**	(1) Hg $(O_2CCF_3)_2$, THF, 20 °C; then satd aq KCl, 20 °C (2) Bu_3SnH, cat. AIBN, toluene, 74 °C	**36**:**38** [81:19 ratio], 65% combined yield (two steps)[e]	
3[b]	**16**	(1) PhSeNPhth, *p*-TsOH–H_2O, CH_2Cl_2, 20 °C (2) H_2O_2, HOAc, THF, 0 °C	**35**:**37** [70:30 ratio], 41% combined yield (two steps)[f]	
4	**17**	(1) I_2, $NaHCO_3$, THF, 0° to 20 °C (2) DBU, CH_2Cl_2, 20 °C	(Not observed)	**33a**, X=I, 69% **37**, 60%
5	**17**	(1) Hg $(O_2CCF_3)_2$, THF, 20 °C; then satd aq KCl, 20 °C (2) then Bu_3SnH, cat. AIBN, toluene, 77 °C	**36**:**38** [34:66 ratio], 50% combined yield (two steps)[e]	
6	**17**	(1) PhSeNPhth, *p*-TsOH–H_2O, CH_2Cl_2, 20 °C (2) H_2O_2, HOAc, THF, 0 °C	**35**:**37** [56:44 ratio], 62% combined yield (two steps)[f]	

[a] Compound **16** was used as the pure *cis*-isomer.
[b] Compound **16** was used as an 88:12 mixture of *cis*- and *trans*-isomers.
[c] Starting material was also recovered.
[d] Starting material was also recovered, contaminated by an enol ether isomer of **37**.
[e] The organomercury intermediates were not isolated. Pure samples of **36** and **38** could be obtained by careful chromatographic separation.
[f] The organoselenium intermediates were not isolated. However, crude NMR showed the *erythro*-selenoethers **31c** (entry 3) and **32c** (entry 6) mixed with *threo*-alkene **37** at the conclusion of step 1. Mixtures of diastereomeric alkenes **35** and **37** were inseparable.

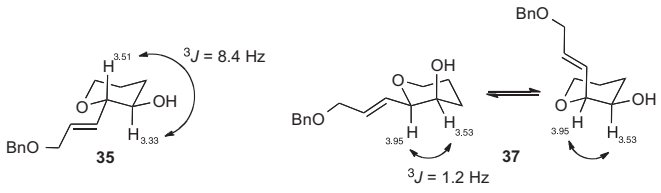


Fig. 9. Coupling constants for diastereomers **35** and **37**.

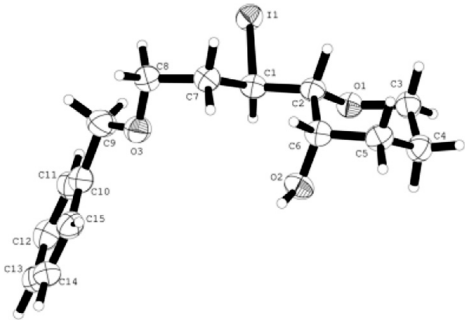


Fig. 10. Thermal ellipsoid map for *threo*-**34a**.

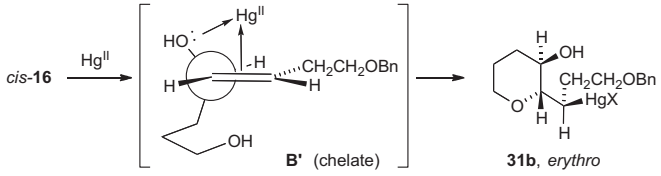


Fig. 11. Conformational model for $Hg(O_2CCF_3)_2$-promoted oxacyclization of *cis*-**16**, giving *erythro*-**31b** as the major diastereomer.

Fig. 4. Moreover, the different diastereoselectivities observed could arise from different degrees of π-complex versus onium ion formation, depending on the choice of electrophile.

2.3. Mercury-catalyzed reductive cyclization of 1,4-dihydroxy-5-alkyne

We then explored oxacyclizations of the 1,4-dihydroxy-5-alkyne **15**, followed by reduction of the cyclization product. Mercuric trifluoroacetate was poorly reactive with the dihydroxyalkyne **15**, but substoichiometric mercuric triflate induced the rapid reaction of dihydroxyalkyne **15**.[23,24] We could not isolate the expected cycloisomerization product **39**, but instead recovered a compound with structural characteristics consistent with the cyclic hemiacetal **41** (Fig. 12). Recognizing the likely intermediacy of the oxonium ion **40** in the presence of triflic acid (which was probably also responsible for catalytic turnover of the initial vinylmercury intermediate), we quenched the cycloisomerization reaction mixture with excess triethylsilane.[25] This protocol provided compound **36** in excellent yield and high selectivity for the *erythro*-diastereomer; in fact the *threo*-diastereomer **37** was not observed when the triethylsilane reduction stage was conducted at −15 °C.[26] Compound **36** generated by this method was indistinguishable from the product described earlier, from mercuric trifluoroacetate-promoted cyclization of *cis*-alkene **16** followed by tributyltin hydride (Table 1, entry 2).

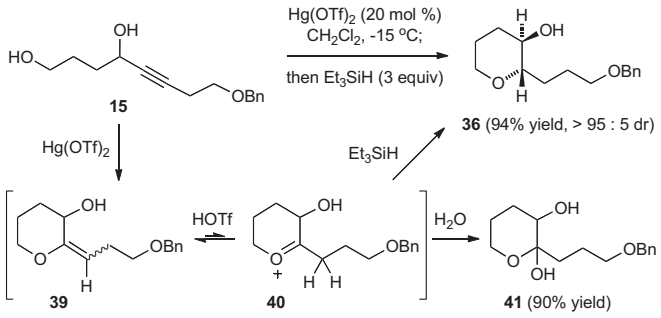


Fig. 12. Reductive oxacyclization of dihydroxyalkyne **15**.

The cycloisomerization stage of this transformation (**15**→**39**) involved protiodemercuration of the initial mercury-containing exocyclic enol ether, providing a mechanism for catalytic turnover of the mercuric triflate catalyst. Moreover, hydride delivery to the oxonium ion **40** proceeded with axial addition, consistent with many literature precedents.[4,25,27] However, addition of triethylsilane to the reaction mixture immediately reduced mercuric triflate to Hg(0), so that its activity for cycloisomerization was destroyed in the reduction step, and thus the mercuric triflate-catalyzed cycloisomerization could not be conducted in the presence of triethylsilane. Nonetheless, this one-pot procedure gave superior yield and diastereoselectivity when compared with the corresponding cyclizations of the 1,4-dihydroxy-5-alkene substrates.

2.4. Stereoselectivity of electrophile-promoted oxacyclization of 1,1-disubstituted 1,4-dihydroxy-5-alkene

For the formation of the cyclic ether bearing a methyl substituent at the reactive carbon, we first envisioned an approach, in which the 1,1-disubstituted dihydroxyalkene **21** would undergo cyclization via the generally favored hydroxyl-in-plane conformation **A** (Fig. 13). The Chamberlin–Hehre model would predict formation of the *threo*-diastereomer, but if the carbon bearing the X group were transformed into the methyl group and the R_1 substituent was the ethanyl ether structure mimicking a longer-chain substituent, this would also provide a cyclic ether substructure with the desired stereochemistry. Iodocyclization of **21** gave stereoselective formation of the iodoether as a mixture of the diol **42a** and silyl ether **43a**, which was desilylated to maximize the isolated yield of **42a** (Table 2, entry 1). Compound **42a** was isolated in crystalline form and unambiguously characterized by X-ray crystallography (Fig. 14). Radical deiodination of **42a** afforded compound **44** with the axial methyl group at the quaternary center, corresponding to the relative stereochemistry of C_{11} and C_{12} of brevenal (Fig. 1). Mercury- and phenylselenium-promoted cyclizations of **21** proceeded without loss of the silyl ether to provide predominantly **45**, albeit with poorer yields (Table 2, entries 2, 3). The identity of **45** was confirmed by desilylation to provide the diol **44**.

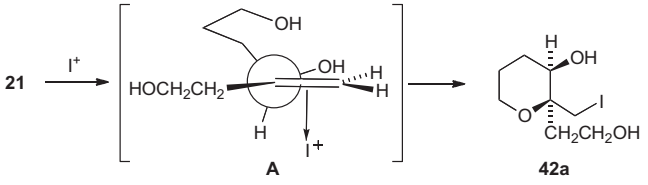
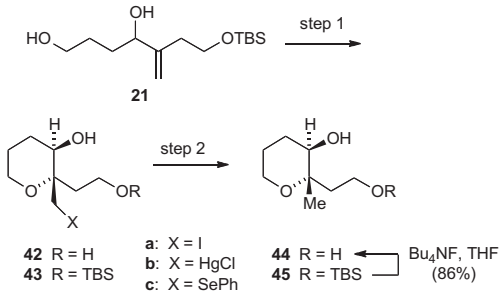


Fig. 13. Conformational model for iodine-promoted oxacyclization of **21**, giving *threo*-**42a** as the major diastereomer.

2.5. Stereoselectivity of electrophile-promoted oxacyclizations of trisubstituted 1,4-dihydroxy-5-alkenes

With the *Z*-trisubstituted alkene **24**, iodocyclization favored formation of the *threo*-diastereomer **49a** (Table 3, entry 1), but the

Table 2
Oxacyclization of 1,1-disubstituted alkene **21**



Entry	(Steps) Reagents and conditions	Products, isolated yield
1	(1) I_2, $NaHCO_3$, THF, 0 °C–20 °C; then cat. PPTS, MeOH (2) Bu_3SnH, cat. AIBN, toluene, 80 °C	**42a**, 70% **44**, 74%
2	(1) $Hg(O_2CCF_3)_2$, THF, 20 °C; then satd aq KCl, 20 °C (2) Bu_3SnH, cat. AIBN, toluene, 74 °C	**45**, 38% (two steps)[a]
3	(1) PhSeNPhth, *p*-TsOH, CH_2Cl_2, 0 °C (2) Bu_3SnH, cat. AIBN, toluene, 70 °C	**43c**, 23% **45**, 90%

[a] Compound **45** was accompanied by 7% of the diastereomer. The organomercury intermediates were not isolated.

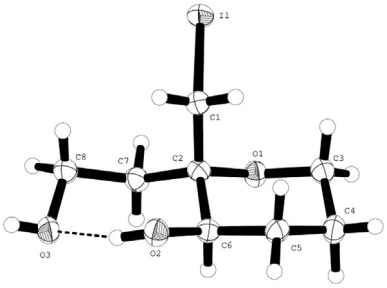


Fig. 14. Thermal ellipsoid map for **42a**.

corresponding reaction with mercuric trifluoroacetate gave only the desired *erythro*-diastereomer **46b**, which was further confirmed upon reductive demercuration to **50** (Table 3, entry 2). The *erythro*-stereochemistry of **46b** was confirmed by observing NOE interactions between a side-chain hydrogen and the carbinol hydrogen (Fig. 15), whereas the *O*-acetyl derivative **52** (from the *threo*-compound **49a**) exhibited NOE interactions showing the methyl substituent on the ether ring *cis*- to the carbinol hydrogen. Moreover, desilylation of *erythro*-**50** provided compound **44**, equivalent to the product arising from iodocyclization and deiodination of the 1,1-disubstituted alkene **21**, thus demonstrating an alternative synthetic approach to the relative stereochemistry at C_{11} and C_{12} of brevenal. However, the selenium-mediated reaction of **24** provided ca. 1:1 mixture of *erythro*-**46c** and *threo*-**49c** (confirmed by desilylation and O-acetylation to afford the separable diastereomers **53** and **54**, which were analyzed for NOE interactions, Fig. 15). The corresponding reactions of the (*E*)-alkene **30** with iodine, mercury and selenium reagents uniformly favored formation of the *threo*-diastereomers (i.e., *threo*-**48a**, Fig. 15) and were not further optimized (Table 3, entries 4–6).

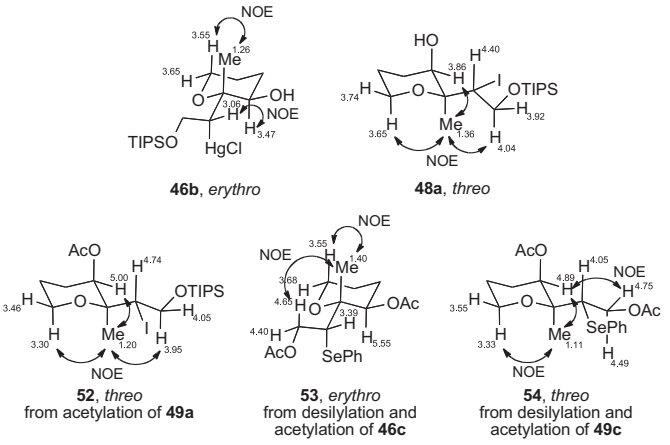
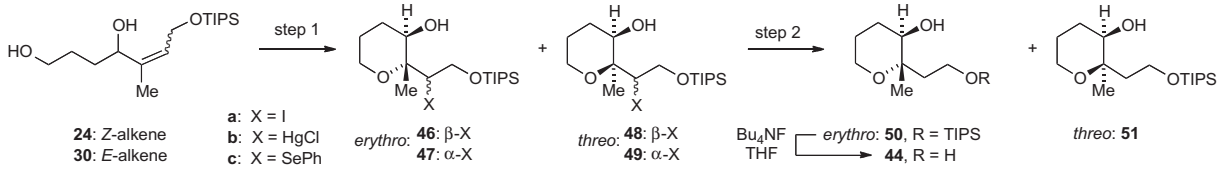


Fig. 15. Assignments of relative stereochemistry by NOE interactions in *erythro*- and *threo*-diastereomers.

Table 3
Oxacyclizations of trisubstituted alkenes **24** and **30**



Entry	Alkene	(Steps) Reagents and conditions	*erythro*-Product, isolated yield	*threo*-Product, isolated yield
1	**24**	(1) I_2, $NaHCO_3$, THF, 0° to 20 °C (2) Bu_3SnH, cat. AIBN, toluene, 70 °C	**46a**, X=I, 11%[a] **50**, 67% (from minor isomer **46a**)	**49a**, 51%[a] (not conducted from **49a**)
2	**24**	(1) $Hg(O_2CCF_3)_2$, THF, 20 °C; then satd aq KCl, 0° to 20 °C (2) Bu_3SnH, cat. AIBN, toluene, 70 °C	**46b**, X=HgCl, 54% **50**, 90%	(Not observed)
3	**24**	(1) PhSeNPhth, *p*-TsOH–H_2O, CH_2Cl_2, 0 °C	**46c**:**49c** [X=SePh, 47:53 ratio], 78% combined yield[b]	
4	**30**	(1) I_2, $NaHCO_3$, THF, 20 °C (2) Bu_3SnH, cat. AIBN, toluene, 70 °C	(Not observed)	**48a**, X=I, 76% **51**, 99%
5	**30**	(1) $Hg(O_2CCF_3)_2$, THF, 0 °C, 30 min; then satd aq KCl, 0 °C (2) Bu_3SnH, cat. AIBN, toluene, 75 °C	**50**, 13% (two steps)	**51**, 48% (two steps)
6	**30**	(1) PhSeNPhth, *p*-TsOH–H_2O, CH_2Cl_2, 0° to 20 °C (2) Bu_3SnH, cat. AIBN, toluene, 75 °C	**50**, 8% (two steps)[c]	**51**, 50% (two steps)[c]

[a] Pure samples of **46a** and **49a** were obtained by careful chromatographic separation.
[b] Diastereomers **46c** and **49c** were inseparable. Due to the low diastereoselectivity, the reduction (step 2) was not conducted.
[c] A pure sample of **51** was obtained by careful chromatographic separation.

Thus the behavior of (*Z*)-**24** was similar to that of the *cis*-alkene **16**, so that only the mercuric trifluoroacetate-promoted cyclization afforded the *erythro*-diastereomer predicted by the Chamberlin–Hehre model. The divergent behavior observed between iodocyclization and mercuriocyclization may be explained by Hg(II) uniquely interacting with the allylic hydroxyl oxygen in the π-complex **B′** (Fig. 16).

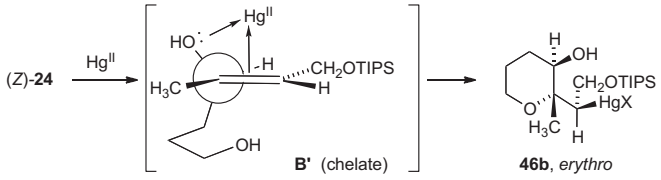


Fig. 16. Conformational model for $Hg(O_2CCF_3)_2$-promoted oxacyclization of (*Z*)-**24**, giving *erythro*-**46b** as the major diastereomer.

3. Conclusions

In summary, these results have demonstrated several oxacyclization pathways to the desired *erythro*-stereochemistry required for *trans–syn–trans* polypyran structures:

(a) $Hg(O_2CCF_3)$-promoted cyclizations are generally consistent with the Chamberlin–Hehre model, so that the *cis*-alkene **16** and the (*Z*)-alkene **24** both favor the *erythro*-diastereomers **36** and **50**, respectively.
(b) The $Hg(OTf)_2$-catalyzed cyclization of the 1,4-dihydroxy-5-alkyne **15** coupled with acid-catalyzed hydride reduction also favors the *erythro*-diastereomer **36**.
(c) Although the iodocyclization of the 1,1-disubstituted alkene **21** is formally *threo*-selective, the product is easily transformed by deiodination into the same diastereomer produced by *erythro*-selective mercuriocyclization of the (*Z*)-alkene **24**.

Generally, iodocyclizations of 1,4-dihydroxy-5-alkenes to the six-membered cyclic ethers generally exhibit a preference for producing the *threo*-diastereomers, regardless of the substitution pattern of the alkene. Although the *threo*-selectivity is diminished for the *cis*-alkene **16** and (*Z*)-alkene **24**, the conformer **B** predicted by the Chamberlin–Hehre model is apparently not favored for iodocyclizations of these substrates. Although the mechanistic significance of these findings awaits more thorough experimental and/or theoretical study, this work does establish the viability of several oxacyclization pathways to produce the relative stereochemistry of hydroxyl and side-chain substituents corresponding to the stereochemistry of many fused polycyclic ether natural products.

4. Experimental section

4.1. General information

^1H and ^{13}C NMR spectra were recorded on an Inova-400 spectrometer (400 MHz for ^1H, 100 MHz for ^{13}C), or an Inova-600 spectrometer (600 MHz for ^1H, 150 MHz for ^{13}C). NMR spectra were reported in deuterated solvents with the following reference peaks for ^1H NMR: $CDCl_3$, 7.26 ppm; C_6D_6, 7.16 ppm; $(CD_3)_2C{=}O$, 2.05 ppm; and for ^{13}C NMR: $CDCl_3$, 77.00 ppm; C_6D_6, 128.39 ppm; $(CD_3)_2C{=}O$, 206.68 or 29.92 ppm. Abbreviations for signal couplings are as follows: s, singlet; d, doublet; t, triplet; q, quartet; dd, doublet of doublets; dt, doublet of triplets; td, triplet of doublets; qt, quartet of triplets; ddd, doublet of doublet of doublets; ddt, doublet of doublet of triplets; dtd, doublet of triplet of doublets; tdd, triplet of doublet of doublets; dddd, doublet of doublet of doublet of doublets; m, multiplet; br, broad. IR spectra were collected on a Mattson Genesis II FT-IR spectrometer, with samples as neat films. Mass spectra (high resolution FAB) were recorded on a VG 70-S Nier Johason Mass Spectrometer or a Thermo Finnigan LTQ FT spectrometer. Optical rotations were recorded at 23 °C with a Perkin–Elmer Model 341 polarimeter (concentration in g/100 mL). Melting points were recorded on Fisher-Johns melting point apparatus. Analytical thin layer chromatography (TLC) was performed on precoated glass backed plates purchased from Whatman (silica gel 60 F_{254}; 0.25 mm thickness). Flash column chromatography was carried out with silica gel 60 (230–400 mesh ASTM) from EM Science. All reactions were conducted with anhydrous solvents in oven-dried or flame-dried and argon-charged glassware. All anhydrous solvents were dried over 3 Å or 4 Å molecular sieves, and trace water content was tested with Coulometric KF Titrator from Denver Instruments. Solvents used in workup, extraction and column chromatography were used as received from commercial suppliers without prior purification. All reagents were purchased from Sigma–Aldrich.

4.2. Preparation of 1,4-dihydroxy-5-alkene substrates

4.2.1. Alkynyldiol ***15***

4.2.1.1. Preparation of alkynyl alcohol ***14***. The terminal alkyne **12** (5.76 g, 36.0 mmol)[13] was dissolved in THF (90 mL), cooled to 0 °C, and *n*-butyllithium (1.55 M in hexane, 21.3 mL, 33.0 mmol) was added slowly. The reaction mixture was stirred at 0 °C for 5 min, and then a solution of aldehyde **11** (6.06 g, 30.0 mmol)[12] in THF (30 mL) was added. The reaction mixture was stirred for 2 h at 0 °C, and then quenched with pH 7 buffer solution. The mixture was extracted with ethyl acetate (three times), the combined organic layers were washed with brine and dried over magnesium sulfate, and solvent was removed by rotary evaporation. The residue was purified by silica gel flash chromatography (hexanes/ethyl acetate=90/10 to 80/20) to give the propargylic alcohol **14** (6.94 g, 19.2 mmol, 64% yield); ν_{max} (liquid film) 3427, 3031, 2953, 2928, 2858, 2238, 1740, 1471, 1389, 1362, 1254, 1101, 1028, 836, 777, 737 cm^{-1}; δ_H ($CDCl_3$, 600 MHz) 7.37–7.26 (5H, m), 4.55 (2H, s), 4.44–4.38 (1H, m), 3.71–3.62 (2H, m), 3.58 (2H, t, *J*=7.2 Hz), 3.00 (1H, d, *J*=6.0 Hz (OH)), 2.53 (2H, t, *J*=7.2 Hz), 1.82–1.73 (3H, m), 1.71–1.62 (1H, m), 0.90 (9H, s), 0.07 (6H, s); δ_C ($CDCl_3$, 150 MHz) 138.0, 128.4, 127.7 (2C), 82.4, 81.6, 72.9, 68.4, 63.2, 62.2, 35.5, 28.6, 25.9, 20.1, 18.3, −5.4 (2C); HRMS (APCI) calcd for $C_{21}H_{35}O_3Si$ $[M+H]^+$ 363.23500, found 363.23523.

4.2.1.2. Desilylation of ***14*** *to alkynyldiol* ***15***. Compound **14** (6.76 g, 17.8 mmol) was dissolved in THF (180 mL), cooled to 0 °C, and tetrabutylammonium fluoride (1 M in THF, 26.75 mL, 26.75 mmol) was added dropwise. The resulting solution was allowed to warm to room temperature. After 2 h, the reaction mixture was quenched with saturated aqueous ammonium chloride. The mixture was extracted with ethyl acetate (five times), the combined organic layers were washed with brine and dried over magnesium sulfate, filtered, and solvent was removed by rotary evaporation. The residue was purified by silica gel flash chromatography (hexanes/ethyl acetate=30/70) to give the alkynyldiol **15** (3.21 g, 13.0 mmol, 73% yield) as a pale yellow oil; ν_{max} (liquid film) 3345, 2930, 2865, 1453, 1363, 1093, 1027, 735, 697 cm^{-1}; δ_H ($CDCl_3$, 600 MHz) 7.38–7.29 (5H, m), 4.53 (2H, s), 4.38 (1H, m), 3.92 (1H, broad (OH)), 3.64–3.58 (2H, m), 3.56 (2H, t, *J*=6.8 Hz), 3.17 (1H, broad (OH)), 2.50 (2H, td, *J*=6.9, 2.0 Hz), 1.90–1.51 (4H, m); δ_C ($CDCl_3$, 100 MHz) 137.9, 128.5, 127.8 (2C), 82.4, 81.9, 72.9, 68.4, 62.3, 62.0, 35.0, 28.4, 20.1; HRMS (ESI) calcd for $C_{15}H_{20}O_3Na$ $[M+Na]^+$ 271.13047, found 271.13043.

4.2.2. cis-Alkenyldiol ***16***. $Ni(OAc)_2{\cdot}4H_2O$ (179.0 mg, 0.719 mmol) was suspended in ethanol (3 mL), and $NaBH_4$ (26.7 mg, 0.705 mmol) was added to give a black suspension. The flask was purged with hydrogen gas. Ethylenediamine (100 μL, 1.50 mmol) was added followed by a solution of propargylic alcohol **14** (2.20 g, 6.08 mmol) in ethanol (4 mL). The reaction mixture was stirred under a balloon pressure of H_2 for 3 h. The reaction mixture was filtered through filter paper, and washed with dichloromethane. The organic layer was washed with brine, dried over magnesium sulfate, and the solvent was removed by rotary evaporation. The residue was diluted with THF (60 mL). Tetrabutylammonium fluoride (1 M in THF, 9 mL, 9 mmol) was added to the solution. The reaction mixture was stirred overnight at room temperature, and quenched by addition of saturated aqueous ammonium chloride. The product mixture was extracted with ethyl acetate (three times), the combined organic layers were washed with brine and dried over magnesium sulfate, and solvents were removed under rotary evaporation. The residue was purified by silica gel flash chromatography (hexanes/ethyl acetate=50/50 to 0/100 with 1% Et_3N) to give *cis*-alkenyldiol **16** (876.1 mg, 3.50 mmol, 58% yield (two steps)); ν_{max} (liquid film) 3365, 2939, 2864, 1454, 1362, 1096, 1005, 739 cm^{-1}; δ_H ($CDCl_3$, 600 MHz) 7.37–7.26 (5H, m), 5.62 (1H, ddd, *J*=10.8, 8.4, 1.2 Hz), 5.58–5.52 (1H, m), 4.52 (2H, s), 4.43 (1H, q, *J*=6.6 Hz), 3.72–3.57 (2H, m), 3.55 (1H, dt, *J*=9.0, 5.4 Hz), 3.43 (1H, td, *J*=9.0, 4.2 Hz), 2.61–2.51 (1H, m), 2.30–2.24 (1H, m), 1.74–1.55 (4H, m); δ_C ($CDCl_3$, 150 MHz) 137.6, 135.2, 128.61, 128.63, 128.5, 127.8, 73.2, 68.8, 66.6, 62.9, 34.0, 29.2, 28.4; HRMS (APCI) calcd for $C_{15}H_{23}O_3$ $[M+H]^+$ 251.16417, found 251.16420. A separate run on similar scale (1.8 g of **14**) produced an inseparable 88:12 mixture of **16** and **17**.

4.2.3. trans-Alkenyldiol ***17***. The propargylic alcohol **14** (1.76 g, 4.86 mmol) was dissolved in Et_2O (25 mL), and cooled to 0 °C. Red-Al® (sodium bis(2-methoxyethoxy)aluminate, >65% in toluene, 4.4 mL, 14.7 mmol) was slowly added, and the reaction mixture stirred at 0 °C for 2 h, then gradually warmed to room temperature and stirred overnight. The reaction mixture was cooled to 0 °C, and was quenched with saturated aqueous Rochelle's salt. The mixture was extracted with ethyl acetate (four times), the combined organic layers were washed with brine and dried over magnesium sulfate, and solvents were removed by rotary evaporation. Without further purification, the crude allylic alcohol was dissolved in THF (50 mL), and tetrabutylammonium fluoride (1 M in THF, 7.3 mL, 7.3 mmol) was added. The reaction mixture was stirred overnight, and then quenched with saturated aqueous ammonium chloride. The mixture was extracted with ethyl acetate (three times), the combined organic layers were washed with brine and dried over magnesium sulfate, and solvents were removed by rotary evaporation. The residue was purified by silica gel flash chromatography (ethyl acetate with 1% Et_3N) to give the *trans*-alkenyldiol **12** (1.08 g, 4.32 mmol, 89% yield (two steps)); ν_{max} (liquid film) 3364, 2934, 2860, 1737, 1454, 1362, 1095, 1077, 1062, 971, 738 cm^{-1}; δ_H ($CDCl_3$, 600 MHz) 7.38–7.26 (5H, m), 5.69 (1H, dt, *J*=15.6, 6.6 Hz), 5.58 (1H, dd, *J*=15.6, 6.6 Hz), 4.51 (2H, s), 4.15–4.10 (1H, m), 3.70–3.62 (2H, m), 3.52 (2H, t, *J*=6.6 Hz), 2.36 (2H, q, *J*=6.6 Hz), 2.00 (1H, broad), 1.96 (1H, broad), 1.70–1.58 (4H, m); δ_C ($CDCl_3$, 150 MHz) 138.3, 134.8, 128.4, 128.0, 127.7, 127.6, 72.8, 72.6, 69.6, 62.8, 34.2, 32.6, 28.8; HRMS (APCI) calcd for $C_{15}H_{23}O_3$ $[M+H]^+$: 251.16417, found 251.16428.

4.2.4. 1,1-Disubstituted alkenyldiol ***21***

4.2.4.1. Preparation of vinylic iodide ***19***. The iodoalcohol **18** (597 mg, 3.00 mmol, prepared from 3-butyn-1-ol)[16] was dissolved in DMF (15 mL) and cooled to 0 °C, imidazole (542 mg, 7.96 mmol) and TBSCl (600 mg, 3.98 mmol) were added, and the reaction mixture gradually warmed to room temperature. After the mixture was stirred for 8 h, water was added. The mixture was extracted with ethyl acetate (two times), the combined organic layers were washed with brine and dried over magnesium sulfate, and the solvent was removed by rotary evaporation. The residue was purified by silica gel flash chromatography (hexanes/ethyl acetate=90/10) to give the silyl ether **19** (881 mg, 2.82 mmol, 94% yield); ν_{max} (liquid film) 2954, 2929, 2857, 1617, 1255, 1108, 836, 776 cm^{-1}; δ_H ($CDCl_3$, 400 MHz) 6.08 (1H, q, *J*=1.2 Hz), 5.76 (1H, d, *J*=1.2 Hz), 3.72 (2H, t, *J*=6.4 Hz), 2.59 (2H, td, *J*=6.4, 0.8 Hz), 0.89 (9H, s), 0.07 (6H, s); δ_C ($CDCl_3$, 100 MHz) 127.4, 107.6, 61.7, 48.4, 25.9, 18.3, −5.2; HRMS (APCI) calcd for $C_{10}H_{22}OISi$ $[M+H]^+$ 313.04792, found 313.04810.

4.2.4.2. Preparation of the alkenyldiol ***21***. Compound **19** (3.12 g, 10.0 mmol) was dissolved in ether (30 mL) and cooled to −78 °C, and a 1.6 M hexane solution of *n*-butyllithium (6.3 mL, 10 mmol) was added slowly. The reaction mixture was stirred at −78 °C for 45 min. A solution of the lactol **20** and ethyl acetate (**20**:EtOAc=78:22, ca. 450 mg of **20**, 4.0 mmol, prepared from butyrolactone)[17] in Et_2O (20 mL) was added slowly, the reaction mixture gradually warmed to 0 °C, and was stirred for 3.5 h. The reaction mixture was quenched by addition of saturated aqueous ammonium chloride. The mixture was extracted with diethyl ether (three times), the combined organic layers were washed with brine and dried over magnesium sulfate, and the solvent was removed by rotary evaporation. The residue was purified by silica gel flash chromatography (hexanes/ethyl acetate=70/30 to 60/40) to give the alkenyldiol **21** (438 mg, 1.77 mmol, 44% yield). ν_{max} (liquid film) 3351, 2953, 2930, 2858, 1646, 1255, 1095, 836 cm^{-1}; δ_H ($CDCl_3$, 600 MHz) 5.05 (1H, s), 4.91 (1H, s), 4.12–4.08 (1H, m), 3.82 (1H, dt, *J*=10.8, 5.4 Hz), 3.74–3.62 (3H, m), 2.41 (1H, ddd, *J*=14.4, 9.0, 5.4 Hz), 2.24 (1H, dt, *J*=14.4, 4.8 Hz), 1.71–1.62 (4H, m), 0.90 (9H, s), 0.079 (3H, s), 0.076 (3H, s); δ_C ($CDCl_3$, 150 MHz) 149.7, 112.8, 75.0, 64.3, 62.9, 34.6, 33.4, 29.5, 25.8, 18.3, −5.48, −5.53; HRMS (ESI) calcd for $C_{14}H_{30}O_3NaSi$ $[M+Na]^+$ 297.18564, found 297.18570.

4.2.5. (Z)-Trisubstituted alkenyldiol ***24***. The iodoalkene **22** (1.06 g, 2.99 mmol)[18] was dissolved in THF (15 mL), cooled to −78 °C, and *tert*-butyllithium (1.59 M in pentane, 3.8 mL, 6.0 mmol) was added slowly. The reaction mixture was stirred at −78 °C for 75 min, and then a solution of aldehyde **11** (512 mg, 2.53 mmol)[12] in THF (15 mL) was added. The reaction mixture gradually warmed to 0 °C over 2 h, and was stirred at 0 °C for 40 min. The reaction was then quenched with saturated aqueous ammonium chloride. The mixture was extracted with ether (three times), the combined organic layers were washed with brine and dried over magnesium sulfate, and solvent was removed by rotary evaporation. Without further purification, the residue was dissolved in methanol (60 mL), and pyridinium *p*-toluenesulfonate (73.9 mg, 0.294 mmol) was added. The reaction mixture was stirred at room temperature for 5 h, and then quenched by addition of saturated aqueous sodium bicarbonate. The mixture was extracted with ethyl acetate (three times), the combined organic layers were washed with brine and dried over magnesium sulfate, and solvent was removed by rotary evaporation. The residue was purified by silica gel flash chromatography (hexanes/ethyl acetate=70/30 to 60/40) to give the alkenyldiol **24** (310.4 mg, 0.980 mmol, 39% yield); ν_{max} (liquid film) 3351, 2943, 2866, 1463, 1381, 1059, 1011, 883, 774 cm^{-1}; δ_H ($CDCl_3$, 600 MHz) 5.49 (1H, t, *J*=6.6 Hz), 4.49 (1H, dd, *J*=7.8, 4.2 Hz), 4.32 (1H, ddd, *J*=12.6, 6.6, 1.2 Hz), 4.21 (1H, ddd, *J*=12.6, 6.6, 1.2 Hz), 3.71 (1H, dt, *J*=11.4, 5.4 Hz), 3.66 (1H, dt, *J*=11.4, 6.0 Hz), 1.74 (3H, s), 1.73–1.60 (4H, m), 1.15–1.04 (21H, m); δ_C ($CDCl_3$, 150 MHz) 140.2, 126.5, 70.2, 62.7, 59.0, 32.0, 29.5, 18.1, 17.9, 11.9; HRMS (APCI) calcd for $C_{17}H_{37}O_3Si$ $[M+H]^+$ 317.25065, found 317.25081.

4.2.6. (E)-Trisubstituted alkenyldiol ***30***

4.2.6.1. Preparation of vinylic iodide ***27***. Isobutylmagnesium chloride (0.75 M in ether, 64 mL, 48 mmol) was cooled to 0 °C, and titanocene dichloride (257 mg, 1.03 mmol) was added. The reagent

mixture was stirred for 10 min at 0 °C, and then 2-butyn-1-ol (**25**, 1.42 g, 20.3 mmol) in ether (6 mL) was added. The reaction mixture was gradually warmed to room temperature, and was then stirred for 4 h. The reaction mixture was then cooled to 0 °C, iodine (13.2 g, 52.0 mmol) was added, and the mixture was stirred overnight while gradually warming to room temperature.[19] The reaction was quenched by addition of saturated aqueous sodium thiosulfate. The mixture was extracted with ethyl acetate (three times), the combined organic layers were washed with brine (twice) and dried over magnesium sulfate, and the solvent was removed by rotary evaporation. The residue was purified by silica gel flash chromatography (hexanes/ethyl acetate=90/10 to 80/20) to give (*E*)-3-iodobut-2-en-1-ol (**26**, 1.25 g, 6.31 mmol) in 31% yield. The spectral data matched the literature values.[20] Compound **26** (1.25 g, 6.31 mmol) was dissolved in DMF (6 mL), cooled to 0 °C, and imidazole (752 mg, 11.0 mmol) and TIPSCl (1.4 mL, 6.5 mmol) were added. The reaction mixture was stirred at 0 °C for 3 h, and then quenched by addition of pH 7 buffer solution. The mixture was extracted with ether (three times), the combined organic layers were washed with brine and dried over magnesium sulfate, and solvents were removed by rotary evaporation. The residue was purified by silica gel flash chromatography (hexanes/ethyl acetate=100/0 to 95/5) to give silyl ether **27** (1.92 g, 5.42 mmol, 86% yield). ν_{max} (liquid film) 2942, 2866, 1638, 1463, 1381, 1370, 1254, 1108, 1042, 882, 771 cm^{-1}; δ_H ($CDCl_3$, 600 MHz) 6.32 (1H, tq, *J*=6.0, 1.2 Hz), 4.20 (2H, dd, *J*=6.0, 0.6 Hz), 2.41 (3H, s), 1.13–1.04 (2H, m); δ_C ($CDCl_3$, 150 MHz) 141.0, 95.4, 61.0, 28.2, 17.9, 12.0; HRMS (APCI) calcd for $C_{13}H_{28}OISi$ $[M+H]^+$ 355.09487, found 355.09476.

*4.2.6.2. Preparation of **29**.* The iodoalkene **27** (886 mg, 2.50 mmol) was dissolved in THF (12.5 mL), cooled to −78 °C, and *tert*-butyllithium (1.59 M in pentane, 3.1 mL, 4.9 mmol) was added slowly. The reaction mixture was stirred at −78 °C for 85 min, and then a solution of aldehyde **11** (425 mg, 2.10 mmol)[12] in THF (12.5 mL) was added. The reaction mixture gradually warmed to 0 °C, and was stirred at 0 °C for 3 h. The reaction was then quenched with saturated ammonium chloride. The mixture was extracted with ether (three times), the combined organic layers were washed with brine and dried over magnesium sulfate, and solvent was removed by rotary evaporation. The residue was purified by silica gel flash chromatography (hexanes/ethyl acetate=90/10) to give the alcohol **29** (982 mg, 2.28 mmol, 91% yield); ν_{max} (liquid film) 3396, 2947, 2865, 1463, 1386, 1254, 1102, 1058, 1011, 836, 776 cm^{-1}; δ_H ($CDCl_3$, 600 MHz) 5.58 (1H, t, *J*=5.4 Hz), 4.34–4.26 (2H, m), 4.04–4.00 (1H, m), 3.65 (2H, t, *J*=6.0 Hz), 2.31 (1H, d, *J*=3.0 Hz (OH)), 1.70–1.53 (4H, m), 1.61 (3H, s), 1.14–1.04 (21H, m), 0.90 (9H, s), 0.06 (6H, s); δ_C ($CDCl_3$, 150 MHz) 137.8, 126.3, 76.9, 63.2, 60.2, 32.0, 29.0, 25.9, 18.3, 18.0, 12.0, 11.9, −5.4; HRMS (ESI) calcd for $C_{23}H_{50}NaO_3Si_2$ $[M+Na]^+$ 453.31962, found 453.31922; HRMS (ESI) calcd for $C_{23}H_{50}KO_3Si_2$ $[M+K]^+$ 469.29356, found 469.29317.

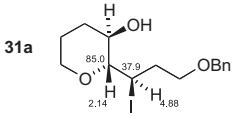
*4.2.6.3. Preparation of **30**.* Compound **29** (167 mg, 0.388 mmol) was dissolved in methanol (8 mL) and cooled to 0 °C, and pyridinium *p*-toluenesulfonate (12.2 mg, 0.0485 mmol) was added. The reaction mixture was stirred at 0 °C for 8 h, and then quenched by addition of saturated aqueous sodium bicarbonate. The mixture was extracted with ethyl acetate (three times), the combined organic layers were washed with brine and dried over magnesium sulfate, and solvent was removed by rotary evaporation. The residue was purified by silica gel flash chromatography (hexanes/ethyl acetate=80/20 to 50/50) to give the alkenyldiol **30** (76.0 mg, 0.240 mmol, 62% yield); ν_{max} (liquid film) 3345, 2941, 2865, 1670, 1463, 1384, 1258, 1115, 1083, 1057, 1011, 882, 779 cm^{-1}; δ_H ($CDCl_3$, 600 MHz) 5.58 (1H, t, *J*=6.0 Hz), 4.32–4.25 (2H, m), 4.06–4.02 (1H, m), 3.70–3.61 (2H, m), 1.68–1.59 (4H, m), 1.61 (3H, s), 1.14–1.03 (21H, m); δ_C ($CDCl_3$, 150 MHz) 138.0, 126.2, 77.0, 62.8, 60.1, 31.9, 29.2, 18.0, 12.0; HRMS (ESI) calcd for $C_{17}H_{36}O_3NaSi$ $[M+Na]^+$ 339.23259, found 339.23267.

4.3. Oxacyclizations of 1,2-disubstituted alkenes 16 and 17

*4.3.1. Iodocyclization of cis-alkenyldiol **16***

*4.3.1.1. Formation of **31a** and **34a**.* The *cis*-alkenyldiol **16** (70.0 mg, 0.280 mmol) was dissolved in THF (3 mL), the solution was cooled to 0 °C, and sodium bicarbonate (70.7 mg, 0.842 mmol) and iodine (214.4 mg, 0.845 mmol) were added. The reaction mixture gradually warmed to room temperature while stirring for 24 h. The reaction was quenched with saturated aqueous sodium thiosulfate. The mixture was extracted with ethyl acetate (three times), the combined organic layers were washed with brine and dried over magnesium sulfate, and the solvent was removed by rotary evaporation. The residue was purified by silica gel flash chromatography (hexanes/ethyl acetate=90/10 to 80/20) to give the *erythro*-product **31a** (27.9 mg, 0.0742 mmol, 26% yield), and *threo*-product **34a** (31.3 mg, 0.0832 mmol, 30% yield).

*4.3.1.1.1. Data for **31a**.* ν_{max} (liquid film) 3427, 2937, 2856, 2228, 1692, 1454, 1364, 1270, 1095, 945, 739 cm^{-1}; δ_H ($CDCl_3$, 600 MHz) 7.37–7.26 (5H, m), 4.76 (1H, ddd, *J*=9.6, 4.8, 1.8 Hz), 4.55 (1H, d, *J*=12.0 Hz), 4.51 (1H, d, *J*=12.0 Hz), 3.99 (1H, dd, *J*=11.4, 4.8 Hz), 3.67–3.58 (3H, m), 3.39 (1H, td, *J*=11.4, 2.4 Hz), 2.35 (1H, tq, *J*=9.6, 4.8 Hz), 2.15 (1H, dd, *J*=8.4, 1.8 Hz), 2.15–2.04 (2H, m), 1.77 (1H, qt, *J*=13.2, 4.2 Hz), 1.70–1.63 (1H, m), 1.58–1.50 (1H, m); δ_H (acetone-d_6, 600 MHz) 7.38–7.24 (5H, m), 4.88 (1H, dd, *J*=10.2, 5.4 Hz), 4.52 (2H, s), 3.90–3.84 (1H, m), 3.68–3.58 (2H, m), 3.51–3.44 (1H, m), 3.44–3.37 (1H, m), 2.31–2.24 (1H, m), 2.14 (1H, d, *J*=7.8 Hz), 2.12–2.03 (2H, m), 1.67–1.59 (2H, m), 1.59–1.49 (1H, m); δ_C ($CDCl_3$, 150 MHz) 138.3, 128.4, 127.8, 127.6, 83.6, 73.1, 71.4, 69.2, 67.9, 37.8, 35.2, 32.3, 25.3; δ_C (acetone-d_6, 150 MHz) 140.3, 129.6, 128.9, 128.7, 85.0, 73.9, 71.8, 70.5, 68.7, 39.6, 37.9, 33.8, 26.7; HRMS (APCI) calcd for $C_{15}H_{22}O_3I$ $[M+H]^+$ 377.06082, found 377.06098. The unusual chemical shifts for the proton resonances of the iodoether were confirmed by HMQC spectroscopy (values in acetone-d_6):



*4.3.1.1.2. Data for **34a**.* Mp 81–89 °C (recrystallized from toluene/hexanes); ν_{max} (liquid film) 3475, 2940, 2854, 1720, 1453, 1357, 1206, 1131, 1096, 1061, 999, 883, 738, 697 cm^{-1}; δ_H ($CDCl_3$, 400 MHz) 7.38–7.26 (5H, m), 4.54 (1H, d, *J*=11.6 Hz), 4.51 (1H, d, *J*=11.6 Hz), 4.37 (1H, td, *J*=9.2, 3.2 Hz), 4.12–4.05 (1H, m), 4.04 (1H, broad), 3.76 (1H, dt, *J*=10.0, 5.6 Hz), 3.66 (1H, ddd, *J*=9.2, 7.2, 5.6 Hz), 3.50 (1H, dd, *J*=12.0, 2.0 Hz), 3.44 (1H, d, *J*=9.2 Hz), 2.20–1.80 (4H, m), 1.62–1.51 (1H, m), 1.36–1.44 (1H, m); δ_C ($CDCl_3$, 100 MHz) 138.2, 128.4, 127.7, 127.6, 84.1, 73.1, 69.9, 69.2, 64.8, 34.8, 34.4, 30.6, 20.1; HRMS (APCI) calcd for $C_{15}H_{22}O_3I$ $[M+H]^+$ 377.06082, found 377.06081. The structure of **34a** was confirmed by X-ray crystallography, as described in the Supplementary data.

*4.3.1.2. Dehydrohalogenation of **31a**–**35**.* The iodoether **31a** (20.5 mg, 0.0545 mmol) was dissolved in CH_2Cl_2 (1 mL), and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU, 16 μL, 0.11 mmol) was added. After stirring for 2 days, the solvent was removed by rotary evaporation, and the residue was purified by silica gel flash chromatography (hexanes/ethyl acetate=85/15 to 75/25) to give the alkene **35** (4.5 mg, 0.018 mmol, 33% yield), along with 46% recovered **31a** (9.3 mg, 0.025 mmol); ν_{max} (liquid film) 3429, 3030, 2936, 2854, 1724, 1454, 1361, 1264, 1208, 1093, 972, 739 cm^{-1}; δ_H ($CDCl_3$, 600 MHz) 7.37–7.26 (5H, m), 5.97 (1H, dtd, *J*=15.6, 5.4, 0.6 Hz), 5.81 (1H, ddt, *J*=15.6, 7.2, 1.2 Hz), 4.53 (2H, s), 4.07 (2H, dd,

J=5.4, 1.2 Hz), 3.94 (1H, ddt, J=10.8, 3.6, 1.8), 3.51 (1H, br t, J=8.4 Hz), 3.39 (1H, td, J=10.8, 3.6 Hz), 3.33 (1H, ddd, J=10.8, 8.4, 4.8 Hz), 2.18–2.10 (1H, m), 1.80–1.66 (2H, m), 1.50–1.38 (1H, m); δ_C ($CDCl_3$, 100 MHz) 138.1, 131.3, 130.3, 128.4, 127.72, 127.65, 83.0, 72.4, 70.0, 69.7, 67.4, 31.6, 25.4; HRMS (APCI) calcd for $C_{15}H_{21}O_3$ $[M+H]^+$ 249.14852, found 249.14856.

*4.3.1.3. Dehydrohalogenation of **34a**–**37**.* The iodoether **34a** (17.5 mg, 0.0466 mmol) was dissolved in CH_2Cl_2 (1 mL), and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU, 14 μL, 0.094 mmol) was added. After stirring for 2 days, the solvent was removed by rotary evaporation, and the residue was purified by silica gel flash chromatography (hexanes/ethyl acetate=85/15 to 75/25) to give the alkene **37** (5.4 mg, 0.022 mmol, 47% yield), along with a trisubstituted enol ether byproduct (9.4 mg, contaminated with **34a**); ν_{max} (liquid film) 3452, 3030, 2927, 2852, 1723, 1454, 1361, 1101, 1081, 1056, 999, 970, 895, 737 cm^{-1}; δ_H ($CDCl_3$, 600 MHz) 7.36–7.26 (5H, m), 5.94 (1H, dtd, J=15.6, 5.4, 1.2 Hz), 5.80 (1H, dd, J=15.6, 4.8 Hz), 4.52 (2H, s), 4.06 (2H, dt, J=4.8, 1.2 Hz), 4.07–4.02 (1H, m), 3.95 (1H, dt, J=4.8, 1.2 Hz), 3.73 (1H, br m), 3.53 (1H, td, J=11.4, 2.4 Hz), 2.04–1.92 (2H, m), 1.74–1.66 (1H, m), 1.43–1.37 (1H, m); δ_C ($CDCl_3$, 100 MHz) 138.2, 130.2, 129.1, 128.4, 127.7, 127.6, 79.3, 72.2, 70.1, 68.3, 66.9, 30.0, 19.9; HRMS (APCI) calcd for $C_{15}H_{21}O_3$ $[M+H]^+$ 249.14852, found 249.14849.

*4.3.2. Mercury-promoted cyclization of cis-alkenyldiol **16** to form **36** and **38**.* The alkenyldiol **16** (53.0 mg, 0.212 mmol) was dissolved in THF (2 mL), the solution was cooled to 0 °C, and a solution of mercuric trifluoroacetate (139.8 mg, 0.328 mmol) in THF (2 mL) was added slowly. The reaction mixture gradually warmed to room temperature while stirring for 2 h. Saturated aqueous potassium chloride (0.14 mL) was added, and the mixture was stirred for 1.5 h at room temperature. The reaction mixture was diluted with ethyl acetate, the organic layer was washed with water (twice) and brine, dried over magnesium sulfate, and the solvent was removed by rotary evaporation. The residue was diluted with toluene (6 mL), tributyltin hydride (0.26 mL, 0.97 mmol) and AIBN (5.6 mg) were added, and the reaction mixture was heated at 74 °C for 2 h. The reaction mixture cooled to room temperature, the solvent was removed by rotary evaporation, and the residue was purified by flash chromatography on silica gel support mixed with 10% KF (hexanes/ethyl acetate=90/10 to 50/50) to give pure samples of diastereomers **36** and **38** along with fractions containing both diastereomers, which in total corresponded to an 81:19 mixture of diastereomers **36** and **38** (34.2 mg, 0.137 mmol, 65% combined yield). The data for compound **36** closely matched the tabulated data previously reported for this compound.[22]

*4.3.2.1. Data for **36**.* ν_{max} (liquid film) 3433, 2935, 2853, 1720, 1454, 1361, 1270, 1205, 1095, 940, 737 cm^{-1}; δ_H ($CDCl_3$, 400 MHz) 7.36–7.24 (5H, m), 4.51 (2H, s), 3.91–3.84 (1H, m), 3.51 (2H, t, J=6.0 Hz), 3.34–3.24 (2H, m), 3.00 (1H, td, J=8.8, 2.8 Hz), 2.11–2.03 (1H, m), 2.03–1.80 (3H, m), 1.74–1.61 (2H, m), 1.55–1.44 (1H, m), 1.43–1.31 (1H, m); δ_C ($CDCl_3$, 150 MHz) 138.5, 128.3, 127.7, 127.5, 82.1, 72.8, 70.4, 70.2, 67.5, 32.7, 28.6, 25.6, 25.3; HRMS (APCI) calcd for $C_{15}H_{23}O_3$ $[M+H]^+$ 251.16417, found 251.16425.

*4.3.2.2. Data for **38**.* ν_{max} (liquid film) 3452, 2942, 2852, 1718, 1496, 1454, 1362, 1275, 1206, 1095, 992, 907, 738 cm^{-1}; δ_H ($CDCl_3$, 400 MHz) 7.37–7.24 (5H, m), 4.50 (2H, s), 4.00–3.92 (1H, m), 3.63 (1H, broad), 3.54–3.38 (3H, m), 3.28 (1H, t, J=6.2 Hz), 2.12–1.80 (3H, m), 1.80–1.50 (4H, m), 1.44–1.34 (1H, m); δ_C ($CDCl_3$, 150 MHz) 138.5, 128.3, 127.6, 127.5, 79.8, 72.8, 70.2, 68.5, 66.6, 30.6, 28.5, 25.7, 20.2; HRMS (APCI) calcd for $C_{15}H_{23}O_3$ $[M+H]^+$ 251.16417, found 251.16425.

*4.3.3. Selenium-promoted cyclization of cis-alkenyldiol **16** to form **35** and **37**.* The alkenyldiol **16** (50.1 mg, 0.200 mmol) was dissolved in CH_2Cl_2 (3 mL), the solution was cooled to 0 °C, and toluenesulfonic acid (5.7 mg, 0.030 mmol) and *N*-phenylselenophthalimide (75.8 mg, 0.251 mmol) were added. The reaction mixture gradually warmed to 20 °C over 6.5 h. The mixture was then diluted with chloroform, the organic phase was washed with 0.2 M aqueous KOH (three times) followed by brine, dried over magnesium sulfate, and the solvent was removed by rotary evaporation. The crude NMR spectrum at this stage showed that the phenylselenyl compound **31c** was present, along with elimination product **37**. Without separating these compounds, the mixture was dissolved in THF (2 mL) and cooled to 0 °C, acetic acid (64 μL) and 30% hydrogen peroxide (0.27 mL) were added. The reaction mixture was stirred for 45 min, and then quenched with saturated aqueous sodium bicarbonate (20 mL). The mixture was extracted with diethyl ether (three times), the combined organic layers were washed with brine and dried over magnesium sulfate, and solvents were removed by rotary evaporation. The residue was purified by silica gel flash chromatography (hexanes/ethyl acetate=70/30 to 60/40) to give an inseparable mixture of **35** and **37** (70:30, 20.6 mg, 41% combined yield). The mixture exhibited spectroscopic characteristics consistent with **35** and **37** arising from dehydrohalogenation of the corresponding iodoethers **31a** and **34a**, respectively.

*4.3.4. Iodocyclization of trans-alkenyldiol **17***

*4.3.4.1. Formation of **33a**.* The *trans*-alkenyldiol **17** (104.4 mg, 0.418 mmol) was dissolved in THF (4 mL), the solution was cooled to 0 °C, and sodium bicarbonate (100.8 mg, 1.20 mmol) and iodine (303.8 mg, 1.20 mmol) were added. The reaction mixture gradually warmed to room temperature while stirring for 7.5 h. The reaction was quenched with saturated aqueous sodium thiosulfate. The mixture was extracted with ethyl acetate (three times), the combined organic layers were washed with brine and dried over magnesium sulfate, and the solvent was removed by rotary evaporation. The residue was purified by silica gel flash chromatography (hexanes/ethyl acetate=90/10 to 80/20) to give the *threo*-product **33a** (108.2 mg, 0.288 mmol, 69% yield); ν_{max} (liquid film) 3346, 2943, 2854, 1454, 1365, 1210, 1093, 998, 892, 736 cm^{-1}; δ_H ($CDCl_3$, 600 MHz) 7.38–7.25 (5H, m), 4.53 (2H, s), 4.37 (1H, td, J=9.0, 3.0 Hz), 4.29 (1H, dt, J=9.6, 3.0 Hz), 3.98 (1H, dd, J=11.4, 4.8 Hz), 3.69 (1H, ddd, J=9.0, 6.6, 4.2 Hz), 3.62 (1H, ddd, J=9.0, 7.8, 5.4 Hz), 3.44 (1H, d, J=9.0 Hz), 3.46–3.40 (1H, m), 2.47 (1H, dddd, J=15.0, 7.8, 6.6, 3.0 Hz), 2.03–1.94 (2H, m), 1.89 (1H, d, J=9.6 Hz), 1.87 (1H, qt, J=13.8, 4.2 Hz), 1.67 (1H, tdd, J=13.8, 4.8, 3.0 Hz), 1.36–1.31 (1H, m); δ_C ($CDCl_3$, 150 MHz) 138.4, 128.3, 127.7, 127.5, 82.9, 73.0, 69.7, 69.1, 66.3, 35.4, 32.0, 30.9, 19.9; HRMS (APCI) calcd for $C_{15}H_{22}O_3I$ $[M+H]^+$ 377.06082, found 377.06085.

*4.3.4.2. Dehydrohalogenation of **33a** to **37**.* The iodoether **33a** (47.3 mg, 0.126 mmol) was dissolved in CH_2Cl_2 (1.5 mL), and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU, 36 μL, 0.241 mmol) was added. After stirring for 1 day, the solvent was removed by rotary evaporation, and the residue was purified by silica gel flash chromatography (hexanes/ethyl acetate=70/30) to give the alkene **37** (18.9 mg, 0.0762 mmol, 60% yield). Spectroscopic data matched that of compound **37** obtained by dehydrohalogenation of **34a**.

*4.3.5. Mercury-promoted cyclization of trans-alkenyldiol **17** to form **36** and **38**.* The alkenyldiol **17** (53.1 mg, 0.212 mmol) was dissolved in THF (2 mL), the solution was cooled to 0 °C, and a solution of mercuric trifluoroacetate (139.9 mg, 0.328 mmol) in THF (2 mL) was added slowly. The reaction mixture gradually warmed to room temperature while stirring for 2 h. Saturated aqueous potassium chloride (0.14 mL) was added, and the mixture was stirred for 1.5 h at room temperature. The reaction mixture was diluted with ethyl acetate, the organic layer was washed with water (twice) and brine, dried over magnesium sulfate, and the solvent was removed by

rotary evaporation. The residue was diluted with toluene (6 mL), tributyltin hydride (0.26 mL, 0.97 mmol) and AIBN (6.0 mg) were added, and the reaction mixture was heated at 77 °C for 2 h. The reaction mixture cooled to room temperature, the solvent was removed by rotary evaporation, and the residue was purified by flash chromatography on silica gel support mixed with 10% KF (hexanes/ethyl acetate=90/10 to 50/50) to give pure samples of diastereomers **36** and **38** along with fractions containing both diastereomers, which in total corresponded to a 34:66 mixture of diastereomers **36** and **38** (26.3 mg, 0.105 mmol, 50% combined yield). Compounds **36** and **38** exhibited spectroscopic characteristics consistent with compounds arising from mercury-promoted cyclization of **16** followed by reductive demercuration.

*4.3.6. Selenium-promoted cyclization of trans-alkenyldiol **17** to form **35** and **37**.* The alkenyldiol **17** (49.0 mg, 0.196 mmol) was dissolved in CH_2Cl_2 (3 mL), the solution was cooled to 0 °C, and toluenesulfonic acid (3.1 mg, 0.016 mmol) and *N*-phenylselenophthalimide (73.8 mg, 0.244 mmol) were added. The reaction mixture gradually warmed to 20 °C over 14.5 h. The mixture was then diluted with chloroform, the organic phase was washed with 0.2 M aqueous KOH (three times) followed by brine, dried over magnesium sulfate, and the solvent was removed by rotary evaporation. The crude NMR spectrum at this stage showed that the phenylselenyl compound **32c** was present, along with elimination product **37**. Without separating these compounds, the mixture was dissolved in THF (2 mL) and cooled to 0 °C, acetic acid (64 mL) and 30% hydrogen peroxide (0.27 mL) were added. The reaction mixture was stirred for 25 min, and then quenched with saturated aqueous sodium bicarbonate (20 mL). The mixture was extracted with diethyl ether (three times), the combined organic layers were washed with brine and dried over magnesium sulfate, and solvents were removed by rotary evaporation. The residue was purified by silica gel flash chromatography (hexanes/ethyl acetate=70/30 to 60/40) to give an inseparable mixture of **35** and **37** (56:44, 30.2 mg, 62% combined yield). The mixture exhibited spectroscopic characteristics consistent with **35** and **37** arising from dehydrohalogenation of the corresponding iodoethers **31a** and **33a**/**34a**, respectively.

4.4. Mercury-catalyzed oxacyclizations of 15

*4.4.1. Mercury-catalyzed oxacyclization and hydration to **41**.* Mercuric triflate (508 mg, 1.01 mmol) was dissolved in CH_2Cl_2 (8 mL) and the solution was cooled to −20 °C. A solution of the alkynyldiol **15** (505 mg, 2.03 mmol) in CH_2Cl_2 (2 mL) was added dropwise to the catalyst solution. After stirring for 15 min, the reaction mixture was quenched with triethylamine (100 μL) and filtered through a pad of silica gel. Solvents were removed by rotary evaporation, and the crude off-white powder was purified by silica gel flash chromatography (hexanes/ethyl acetate=90/10) to afford compound **41** as a white powder (452 mg, 90% yield); δ_H ($CDCl_3$, 600 MHz) 7.41–7.17 (5H, m), 4.52 (2H, s), 3.93 (1H, t, *J*=3.0 Hz), 3.86 (1H, dd, *J*=11.7, 5.0 Hz), 3.63 (1H, td, *J*=12.5, 2.6 Hz), 3.53 (2H, t, *J*=6.2 Hz), 2.00–1.67 (8H, m), 1.26 (1H, broad (OH)), 1.20 (1H, m); δ_C ($CDCl_3$, 100 MHz) 138.5, 128.2, 127.5, 127.4, 95.1, 72.6, 70.5, 64.5, 63.9, 29.3, 26.2, 22.1, 19.1.

*4.4.2. Mercury-catalyzed reductive cyclization to **36**.* Mercuric triflate (19 mg, 0.038 mmol) was dissolved in CH_2Cl_2 (2 mL) and the solution was cooled to −20 °C. A solution of the alkynyldiol **15** (54.1 mg, 0.21 mmol) in CH_2Cl_2 (1 mL) was added dropwise to the catalyst solution. After stirring for 15 min, the reaction mixture was quenched with triethylsilane (130 μL, 0.81 mmol) and filtered through a pad of silica gel. Solvents were removed by rotary evaporation, and the crude oil was purified by silica gel flash chromatography (hexanes/ethyl acetate=90/10 to 80/20) to afford compound **36** (50.7 mg, 94% yield). Spectroscopic data matched that of compound **36** produced by mercuric trifluoroacetate-promoted cyclization of *cis*-**16** followed by tributyltin hydride demercuration.

4.5. Oxacyclizations of 1,1-disubstituted alkene 21

*4.5.1. Iodocyclization of **21***

*4.5.1.1. Formation of **42a**.* The alkenyldiol **21** (54.7 mg, 0.199 mmol) was dissolved in THF (2 mL), the solution was cooled to 0 °C, and sodium bicarbonate (50.7 mg, 0.604 mmol) and iodine (150.0 mg, 0.591 mmol) were added. The reaction mixture gradually warmed to room temperature while stirring overnight. The reaction was quenched with saturated aqueous sodium thiosulfate. The mixture was extracted with ethyl acetate (three times), the combined organic layers were washed with brine and dried over magnesium sulfate, and the solvent was removed by rotary evaporation. As TLC and crude NMR analysis of the product mixture revealed that the silyl ether **43a** was largely deprotected under the iodocyclization conditions, the residue was diluted with MeOH (4 mL), pyridinium *p*-toluenesulfonate (7.0 mg, 0.028 mmol) was added, and the mixture was stirred at room temperature for 20 h, to complete the desilylation process. The reaction was quenched with saturated aqueous sodium bicarbonate. The mixture was extracted with ethyl acetate (three times), the combined organic layers were washed with brine and dried over magnesium sulfate, and the solvent was removed by rotary evaporation. The residue was purified by silica gel flash chromatography (hexanes/ethyl acetate=70/30 to 60/40) to give the iododiol **42a** (39.9 mg, 0.139 mmol, 70% yield). The product was recrystallized from hexanes and ethyl acetate to provide crystals suitable for X-ray analysis; mp 119–120 °C (decomposed); ν_{max} (liquid film) 3235, 3155, 2931, 2871, 1425, 1335, 1073, 1064, 1046, 998, 785, 705 cm^{-1}; δ_H ($CDCl_3$, 600 MHz) 3.86 (1H, ddd, *J*=8.4, 5.4, 3.6 Hz), 3.84–3.75 (2H, m), 3.79 (1H, d, *J*=12.0 Hz), 3.69–3.64 (1H, m), 3.47 (1H, d, *J*=12.0 Hz), 3.39 (1H, td, *J*=12.0, 4.2 Hz), 2.03 (1H, ddd, *J*=15.0, 5.4, 2.4 Hz), 1.95–1.88 (2H, m), 1.74–1.54 (4H, m); δ_C ($CDCl_3$, 150 MHz) 76.3, 70.0, 60.7, 58.3, 41.4, 27.2, 24.8, 9.8; HRMS (APCI) calcd for $C_8H_{16}O_3I$ $[M+H]^+$ 287.01387, found 287.01396.

*4.5.1.2. Reductive deiodination of **42a** to **44**.* The iodide **42** (29.5 mg, 0.103 mmol) was dissolved in toluene (3 mL), tributyltin hydride (0.10 mL, 0.37 mmol) and AIBN (3.1 mg) were added, and the reaction mixture was heated at 80 °C for 3.5 h. The reaction mixture cooled to room temperature, solvent was removed by rotary evaporation, and the residue was purified by flash chromatography on silica gel support mixed with 10% KF (eluted with ethyl acetate) to give the diol **44** (12.3 mg, 0.0768 mmol, 74% yield); ν_{max} (liquid film) 3376, 2940, 2871, 1666, 1443, 1376, 1082, 1058, 987 cm^{-1}; δ_H ($CDCl_3$, 600 MHz) 3.86–3.76 (2H, m), 3.63–3.51 (3H, m), 3.34 (1H, broad, (OH)), 3.29 (1H, broad, (OH)), 1.89–1.80 (3H, m), 1.71–1.54 (3H, m), 1.22 (3H, s); δ_C ($CDCl_3$, 150 MHz) 78.2, 72.0, 60.4, 59.0, 42.4, 27.5, 25.4, 14.3; HRMS calcd for $C_8H_{17}O_3$ $[M+H]^+$ 161.11722, found 161.11707.

*4.5.2. Mercury-promoted cyclization of **21***

*4.5.2.1. Formation of **45**.* The alkenyldiol **21** (48.1 mg, 0.194 mmol) was dissolved in THF (2 mL), the solution was cooled to 0 °C, and a solution of mercuric trifluoroacetate (137.0 mg, 0.321 mmol) in THF (2 mL) was added slowly. The reaction mixture gradually warmed to room temperature while stirring for 2 h. Saturated aqueous potassium chloride (0.14 mL) was added, and the mixture was stirred for 1.5 h at room temperature. The reaction mixture was diluted with ethyl acetate, the organic layer was washed with water (twice) and brine, dried over magnesium

sulfate, and the solvent was removed by rotary evaporation. The residue was diluted with toluene (6 mL), tributyltin hydride (0.26 mL, 0.97 mmol) and AIBN (5.3 mg) were added, and the reaction mixture was heated at 74 °C for 2 h. The reaction mixture cooled to room temperature, the solvent was removed by rotary evaporation, and the residue was purified by flash chromatography on silica gel support mixed with 10% KF (hexanes/ethyl acetate=90/10 to 70/30) to give the cyclic ether **45** (20.4 mg, 0.0743 mmol, 38% yield), and a minor diastereomer (3.6 mg, 0.013 mmol, 7% yield).

*4.5.2.1.1. Data for **45**.* ν_{max} (liquid film) 3433, 2953, 2858, 1471, 1254, 1089, 1003, 836, 777 cm^{-1}; δ_H ($CDCl_3$, 400 MHz) 4.46 (1H, d, *J*=3.2 Hz, OH), 3.81 (1H, ddd, *J*=10.8, 5.2, 4.0 Hz), 3.71 (1H, ddd, *J*=11.2, 9.2, 2.8 Hz), 3.52–3.63 (2H, m), 3.47 (1H, ddd, *J*=10.8, 4.4, 2.8 Hz), 1.88–1.47 (6H, m), 1.17 (3H, s), 0.90 (9H s), 0.10 (3H, s), 0.09 (3H, s); δ_C ($CDCl_3$, 100 MHz) 72.2, 60.4, 59.5, 45.6, 26.7, 25.8, 25.5, 25.2, 18.2, 13.8, −5.5, −5.6; HRMS (APCI) calcd for $C_{14}H_{31}O_3Si$ $[M+H]^+$ 275.20370, found 275.20378.

4.5.2.1.2. Partial data for the minor diastereomer. δ_H ($CDCl_3$, 400 MHz) 3.82–3.64 (4H, m), 3.44 (1H, td, *J*=6.4, 2.8 Hz), 2.15 (1H, ddd, *J*=14.4, 10.0, 4.4 Hz), 1.94–1.80 (2H, m), 1.80–1.69 (1H, m), 1.64 (1H, ddd, *J*=14.8, 4.8, 3.2 Hz), 1.54–1.44 (1H, m), 1.27 (3H, s), 0.91 (9H, s), 0.10 (3H, s), 0.09 (3H, s).

*4.5.2.2. Desilylation of **45** to **44**.* The silyl ether **45** (15.8 mg, 0.0638 mmol) was dissolved in THF (0.6 mL), and tetrabutylammonium fluoride (1 M in THF, 0.10 mL, 0.10 mmol) was added. The reaction mixture was stirred for 6.5 h, after, which the solvent was removed by rotary evaporation. The residue was purified by silica gel flash chromatography (eluted with ethyl acetate) to give the diol **44** (8.8 mg, 0.055 mmol, 86% yield). The spectroscopic data matched that of compound **44** obtained by reductive deiodination of **42a**.

*4.5.3. Selenium-promoted cyclization of **21***

*4.5.3.1. Formation of **43c**.* The alkenyldiol **21** (49.1 mg, 0.198 mmol) was dissolved in CH_2Cl_2 (3 mL), the solution was cooled to 0 °C, and toluenesulfonic acid (5.3 mg, 0.028 mmol) and *N*-phenylselenophthalimide (74.3 mg, 0.246 mmol) were added. The reaction mixture was stirred for 8 h at 0 °C. The mixture was then diluted with chloroform, the organic phase was washed with 0.2 M aqueous KOH (three times) followed by brine, dried over magnesium sulfate, and the solvent was removed by rotary evaporation. The crude product contained many compounds, but the principal component was isolated by silica gel flash chromatography (hexanes/ethyl acetate=95/5 to 90/10) to give selenoether **43c** (19.2 mg, 0.0447 mmol, 23% yield); ν_{max} (liquid film) 3396, 3071, 3057, 2953, 2933, 2858, 1579, 1475, 1437, 1256, 1081, 1057, 837, 779, 736 cm^{-1}; δ_H ($CDCl_3$, 400 MHz) 7.55–7.50 (2H, m), 7.30–7.20 (3H, m), 4.95 (1H, d, *J*=2.4 Hz, OH), 3.80 (1H, ddd, *J*=11.2, 5.2, 4.0 Hz), 3.76–3.68 (2H, m), 3.68–3.58 (2H, m), 3.52–3.44 (1H, m), 3.16 (1H, d, *J*=12.8 Hz), 2.18 (1H, ddd, *J*=15.2, 4.8, 1.6 Hz), 1.94–1.86 (1H, m), 1.80 (1H, ddd, *J*=14.0, 10.4, 2.0 Hz), 1.72–1.56 (3H, m), 0.89 (9H, s), 0.10 (3H, s), 0.07 (3H, s); δ_C ($CDCl_3$, 100 MHz) 132.6, 130.6, 129.0, 126.7, 78.4, 72.5, 61.0, 59.6, 42.9, 28.0, 26.5, 25.8, 25.2, 18.2, −5.5, −5.7; HRMS (ESI) calcd for $C_{20}H_{33}O_3SeSi$ $[M-H]^+$ 429.13587, found. 429.13623.

*4.5.3.2. Reductive deselenylation of **43c** to **45**.* Compound **43** (17.7 mg, 0.0412 mmol) was dissolved in toluene (3 mL). Tributyltin hydride (0.10 mL, 0.37 mmol) and AIBN (3.9 mg) were added, and the reaction mixture was heated to 70 °C for 2 h, after which the solvent was removed by rotary evaporation. The residue was purified by flash chromatography on silica gel support mixed with 10% KF (hexanes/ethyl acetate=90/10) to give the product **45** (10.2 mg, 0.0372 mmol) in 90% yield. The spectroscopic data matched that of **45** obtained by mercury-promoted cyclization of **21** followed by reductive demercuration.

4.6. Oxacyclizations of trisubstituted alkenes 24 and 30

*4.6.1. Iodocyclization of (Z)-alkenyldiol **24***

*4.6.1.1. Formation of **46a** and **49a**.* The *Z*-alkenyldiol **24** (113.4 mg, 0.358 mmol) was dissolved in THF (3.6 mL), the solution was cooled to 0 °C, and sodium bicarbonate (91.4 mg, 1.09 mmol) was added. Iodine (184.1 mg, 0.725 mmol) was then added in several portions. The reaction mixture was stirred at 0 °C for 4 h, and at room temperature for 20.5 h. The reaction was quenched with saturated aqueous sodium thiosulfate. The mixture was extracted with ethyl acetate (three times), the combined organic layers were washed with brine and dried over magnesium sulfate, and the solvent was removed by rotary evaporation. The residue was purified by silica gel flash chromatography (hexanes/ethyl acetate=95/5 to 80/20) to give pure samples of diastereomers **46a** and **49a** along with fractions containing both diastereomers, which in total corresponded to a 17:83 mixture of diastereomers **46a** and **49a** (97.7 mg, 0.221 mmol, 62% combined yield).

*4.6.1.1.1. Data for **46a**.* ν_{max} (liquid film) 3428, 2943, 2866, 1463, 1381, 1276, 1257, 1087, 986, 822, 782 cm^{-1}; δ_H ($CDCl_3$, 600 MHz) 4.95 (1H, d, *J*=3.6 Hz, OH), 4.30 (1H, dd, *J*=11.4, 3.6 Hz), 4.26 (1H, dd, *J*=9.6, 3.0 Hz), 4.04 (1H, dd, *J*=11.4, 10.2 Hz), 3.69–3.63 (1H, m), 3.61 (1H, dt, *J*=10.2, 4.2 Hz), 3.50 (1H, dt, *J*=12.0, 7.2 Hz), 1.94–1.87 (1H, m), 1.66–1.53 (3H, m), 1.29 (3H, s), 1.20–1.02 (21H, m); δ_C ($CDCl_3$, 150 MHz) 78.4, 70.2, 67.3, 61.1, 49.1, 28.1, 25.1, 17.80, 17.76, 13.0, 11.8; HRMS (APCI) calcd for $C_{17}H_{36}O_3ISi$ $[M+H]^+$ 443.14730, found. 443.14752.

*4.6.1.1.2. Data for **49a**.* ν_{max} (liquid film) 3415, 2941, 2866, 1463, 1383, 1262, 1214, 1116, 1089, 1058, 1032, 995, 882, 799 cm^{-1}; δ_H ($CDCl_3$, 600 MHz) 4.72 (1H, dd, *J*=9.0, 3.0 Hz), 4.27 (1H, dd, *J*=11.4, 3.0 Hz), 4.01 (1H, dd, *J*=11.4, 9.0 Hz), 3.95 (1H, d, *J*=7.2 Hz (OH)), 3.75–3.64 (3H, m), 1.96–1.84 (2H, m), 1.84–1.77 (1H, m), 1.49–1.42 (1H, m), 1.38 (3H, s), 1.20–1.11 (3H, m), 1.11–1.04 (18H, m); δ_C ($CDCl_3$, 150 MHz) 77.4, 68.8, 67.3, 61.3, 43.5, 27.5, 21.9, 20.3, 17.9, 11.8; HRMS (APCI) calcd for $C_{17}H_{36}O_3ISi$ $[M+H]^+$ 443.14730, found 443.14850.

*4.6.1.2. Reductive deiodination of **46a** to **50**.* Iodide **46a** (9.6 mg, 0.0217 mmol) was dissolved in toluene (3 mL), tributyltin hydride (0.10 mL, 0.37 mmol) and AIBN (3.2 mg) were added, and the reaction mixture was heated at 70 °C for 2 h. The reaction mixture then cooled to room temperature, solvent was removed by rotary evaporation, and the residue was purified by flash chromatography on silica gel support mixed with 10% KF (hexanes/ethyl acetate=90/10) to give compound **50** (4.6 mg, 0.015 mmol, 67% yield); ν_{max} (liquid film) 3420, 2941, 2866, 1463, 1380, 1089, 997, 883, 729 cm^{-1}; δ_H ($CDCl_3$, 600 MHz) 4.59 (1H, d, *J*=3.0 Hz, OH), 3.88 (1H, ddd, *J*=10.8, 5.4, 3.6 Hz), 3.83 (1H, td, *J*=10.8, 2.4 Hz), 3.62–3.54 (2H, m), 3.51 (1H, ddd, *J*=10.8, 4.2, 2.4 Hz), 1.88–1.81 (2H, m), 1.76–1.71 (1H, m), 1.68–1.62 (2H, m), 1.58–1.50 (1H, m), 1.19 (3H, s), 1.18–1.04 (21H, m); δ_C ($CDCl_3$, 150 MHz) 72.2, 60.4, 59.8, 45.9, 26.7, 25.6, 25.2, 17.88, 17.86, 13.8, 11.8; HRMS (APCI) calcd for $C_{17}H_{37}O_3Si$ $[M+H]^+$ 317.25065, found 317.25056.

*4.6.1.3. Acetylation of **49a** to **52**.* Iodide **49a** (23.0 mg, 0.0520 mmol) was dissolved in dichloromethane (2 mL), and acetic anhydride (49 μL, 0.52 mmol), pyridine (84 μL, 1.0 mmol), and dimethylaminopyridine (1.4 mg, 0.011 mmol) were added successively. The mixture was stirred at room temperature for 20.5 h, the solvent was removed by rotary evaporation, and the residue was purified by silica gel chromatography (hexanes/ethyl acetate=90/10) to provide the acetate ester **52** (24.9 mg, 0.0514 mmol, 99% yield); ν_{max} (liquid film) 2942, 2866, 1741, 1463, 1373, 1236, 1090, 883, 807 cm^{-1}; δ_H (benzene-d_6, 600 MHz) 5.00 (1H, dd, *J*=4.8, 3.0 Hz), 4.74 (1H, dd, *J*=7.8, 4.2 Hz), 4.05 (1H, dd, *J*=12.0, 4.2 Hz), 3.95 (1H, dd, *J*=12.0, 7.8 Hz), 3.46 (1H, dt, *J*=11.4, 3.0 Hz), 3.30 (1H,

td, J=11.4, 3.0 Hz), 1.69 (3H, s), 1.63–1.57 (1H, m), 1.55–1.46 (1H, m), 1.46–1.35 (1H, m), 1.20 (3H, s), 1.17–1.07 (21H, m), 0.82 (1H, dt, J=13.2, 3.6 Hz); δ_C (benzene-d_6, 100 MHz) 169.5, 75.3, 70.8, 66.5, 61.3, 47.8, 25.2, 21.4, 21.1, 20.3, 18.7, 12.7; HRMS (APCI) calcd for $C_{19}H_{38}O_4ISi$ $[M+H]^+$ 485.15787, found 485.15816.

4.6.2. Mercury-promoted cyclization of (Z)-alkenyldiol **24**

*4.6.2.1. Formation of **46b**.* The (*Z*)-alkenyldiol **24** (31.4 mg, 0.0992 mmol) was dissolved in THF (1 mL), the solution was cooled to 0 °C, and a solution of mercuric trifluoroacetate (69.0 mg, 0.162 mmol) in THF (1 mL) was added slowly. The reaction mixture gradually warmed to room temperature while stirring for 1.5 h. Saturated aqueous potassium chloride (69 μL) was added, and the mixture was stirred for 2 h at room temperature. The reaction mixture was diluted with ethyl acetate, the organic layer was washed with water (twice) and brine, dried over magnesium sulfate, and the solvent was removed by rotary evaporation. The residue was purified by silica gel flash chromatography (hexanes/ethyl acetate=90/10 to 80/20) to provide the *erythro*-product **46b** (29.5 mg, 0.0535 mmol, 54% yield); melting point 100–103 °C; ν_{max} (liquid film) 3260, 2939, 2863, 1459, 1082, 1063, 1001, 982, 882, 791, 681, 671, 654, 640 cm^{-1}; δ_H ($CDCl_3$, 600 MHz) 4.18 (1H, d, J=2.4 Hz (OH)), 4.09 (1H, dd, J=11.4, 4.8 Hz), 4.04 (1H, t, J=10.8 Hz), 3.67–3.62 (1H, m), 3.57–3.52 (1H, m), 3.47 (1H, ddd, J=11.4, 4.2, 2.4 Hz), 3.06 (1H, dd, J=10.8, 4.8 Hz), 1.93–1.86 (1H, m), 1.67–1.58 (2H, m), 1.56–1.46 (1H, m), 1.26 (3H, s), 1.17–1.04 (21H, m); δ_C ($CDCl_3$, 150 MHz) 79.7, 73.8, 70.1, 62.0, 61.3, 28.0, 25.6, 18.0, 15.7, 11.8; HRMS (ESI, negative) calcd for $C_{17}H_{35}Cl_2HgO_3Si$ $[M+Cl]^-$ 587.14388, found 587.14507.

*4.6.2.2. Reductive demercuration of **46b** to **50**.* Compound **46b** (17.7 mg, 0.0412 mmol) was dissolved in toluene (3 mL), tributyltin hydride (0.10 mL, 0.37 mmol) and AIBN (2.8 mg) were added, and the reaction mixture was heated at 70 °C for 2 h. After the reaction mixture had cooled to room temperature, the solvent was removed by rotary evaporation, and the residue was purified by flash chromatography on silica gel support mixed with 10% KF (hexanes/ethyl acetate=90/10) to give **50** (15.0 mg, 0.0474 mmol, 90% yield). Spectroscopic characteristics were identical to those of **50** arising from reductive deiodination of **46a**.

*4.6.2.3. Desilylation of **50** to **44**.* The silyl ether **50** (19.3 mg, 0.0610 mmol) was dissolved in THF (1 mL), and tetrabutylammonium fluoride (1 M in THF, 0.10 mL, 0.10 mmol) was added. The reaction mixture was stirred for 4 h, after which the solvent was removed by rotary evaporation. The residue was purified by silica gel flash chromatography (eluted with ethyl acetate) to give the diol **44** (6.1 mg, 0.038 mmol, 38% yield). The spectroscopic data matched that of compound **44** obtained by reductive deiodination of **42a**.

4.6.3. Selenium-promoted cyclization of (Z)-alkenyldiol **24**

*4.6.3.1. Formation of **46c** and **49c**.* The (*Z*)-alkenyldiol **24** (32.8 mg, 0.104 mmol) was dissolved in CH_2Cl_2 (1.5 mL), the solution was cooled to 0 °C, and toluenesulfonic acid (2.4 mg, 0.013 mmol) and *N*-phenylselenophthalimide (38.8 mg, 0.128 mmol) were added. The reaction mixture was stirred at 0 °C for 7 h. The mixture was then diluted with chloroform, the organic phase was washed with 0.2 M aqueous KOH (three times) followed by brine, dried over magnesium sulfate, and the solvent was removed by rotary evaporation. The residue was purified by silica gel flash chromatography (hexanes/ethyl acetate=90/10) to give an inseparable mixture of **46c** and **49c** (47:53, 30.8 mg, 78% combined yield); Data for the mixture: ν_{max} (liquid film) 3395, 3070, 3057, 2941, 2866, 2240, 1579, 1463, 1382, 1257, 1082, 1024, 883, 801, 740 cm^{-1}; δ_H ($CDCl_3$, 400 MHz) 7.68–7.63 (2H, m), 7.34–7.23 (3H, m), 5.10 (0.44H, d, J=3.2 Hz), 4.63 (0.56H, d, J=7.6 Hz), 4.01–3.50 (6H, m), 2.01–1.51 (4H, m), 1.37 (1.68H, s), 1.30 (1.32H, s), 0.96–0.84 (21H, m); δ_C ($CDCl_3$, 150 MHz) 136.2, 135.9, 129.2, 129.0, 128.8, 128.7, 128.05, 127.98, 79.8, 78.6, 72.2, 71.1, 64.4, 64.1, 61.2, 60.8, 58.7, 53.0, 27.4, 27.1, 25.1, 22.7, 19.2, 17.73, 17.69, 11.6, 11.5, 11.4; HRMS (ESI) calcd for $C_{23}H_{39}O_3SeSi$ $[M-H]^+$ 471.18282, found 471.18316.

*4.6.3.2. Desilylation and acetylation of **46c** and **49c** to provide **53** and **54**.* The mixture of **46c** and **49c** (37.4 mg, 0.0793 mmol) was dissolved in THF (0.8 mL), and tetrabutylammonium fluoride (1 M in THF, 0.12 mL, 0.12 mmol) was added. The reaction was stirred for 1.5 h. The solvent was then removed by rotary evaporation, and the residue was purified by silica gel flash chromatography (hexanes/ethyl acetate=50/50 to 0/100) to give an inseparable mixture of diol diastereomers (22.9 mg, 0.0726 mmol, 92% combined yield). This mixture was dissolved in dichloromethane (4 mL), and acetic anhydride (103 μL, 1.09 mmol), pyridine (0.18 mL, 2.23 mmol), and dimethylaminopyridine (3.6 mg, 0.029 mmol) were added successively. The mixture was stirred for 17 h. The solvent was then removed by rotary evaporation, and the residue was purified by silica gel flash chromatography (hexanes/ethyl acetate=90/10) to provide the *erythro*-product **53** (10.4 mg, 0.0260 mmol, 36% yield), and the *threo*-product **54** (12.7 mg, 0.0318 mmol, 44% yield).

*4.6.3.2.1. Data for **53**.* ν_{max} (liquid film) 3056, 2959, 2872, 1731, 1746, 1578, 1477, 1438, 1373, 1234, 1079, 1038, 990, 894, 742 cm^{-1}; δ_H ($CDCl_3$, 400 MHz) 7.62–7.56 (2H, m), 7.29–7.22 (3H, m), 5.55 (1H, dd, J=10.0, 4.4 Hz), 4.65 (1H, dd, J=12.0, 6.4 Hz), 4.40 (1H, dd, J=12.0, 6.4 Hz), 3.68 (1H, br d, J=11.6 Hz), 3.55 (1H, td, J=11.6, 2.8 Hz), 3.39 (1H, t, J=6.4 Hz), 2.15–2.05 (1H, m), 1.97 (3H, s), 1.91 (3H, s), 1.84–1.56 (3H, m), 1.40 (3H, s); δ_C ($CDCl_3$, 150 MHz) 170.8, 170.0, 134.7, 130.3, 129.0, 127.5, 76.6, 72.7, 65.1, 61.1, 53.8, 24.4, 24.2, 21.2, 20.8, 16.2; HRMS (ESI) calcd for $C_{18}H_{24}O_5NaSe$ $[M+Na]^+$ 423.06812, found. 423.06834.

*4.6.3.2.2. Data for **54**.* ν_{max} (liquid film) 3071, 3056, 2955, 2869, 1746, 1731, 1578, 1477, 1438, 1373, 1234, 1093, 1081, 1049, 1022, 912, 742 cm^{-1}; δ_H (benzene-d_6, 600 MHz) 7.71–7.66 (2H, m), 6.97–6.90 (3H, m), 4.89 (1H, t, J=3.0 Hz), 4.75 (1H, dd, J=12.0, 6.0 Hz), 4.49 (1H, dd, J=12.0, 7.8 Hz), 4.05 (1H, dd, J=7.8, 6.0 Hz), 3.55 (1H, br d, J=12.0 Hz), 3.33 (1H, td, J=12.0, 2.4 Hz), 1.78 (3H, s), 1.77–1.70 (1H, m), 1.66–1.56 (1H, m), 1.60 (3H, s), 1.45–1.39 (1H, m), 1.11 (3H, s), 0.85–0.79 (1H, m); δ_C (benzene-d_6, 100 MHz) 170.4, 170.0, 135.3, 131.2, 129.6, 127.9, 77.1, 71.8, 65.9, 61.6, 53.6, 24.5, 21.3, 20.80, 20.77, 18.4; HRMS (ESI) calcd for $C_{18}H_{24}O_5NaSe$ $[M+Na]^+$ 423.06812, found 423.06842.

4.6.4. Iodocyclization of (E)-alkenyldiol **30**

*4.6.4.1. Formation of **48a**.* The (*E*)-alkenyldiol **30** (31.2 mg, 0.0985 mmol) was dissolved in THF (1 mL), the solution was cooled to 0 °C, and sodium bicarbonate (25.5 mg, 0.304 mmol) and iodine (74.2 mg, 0.292 mmol) were added. The reaction mixture gradually warmed to room temperature while stirring for 3 h. The reaction was quenched with saturated aqueous sodium thiosulfate. The mixture was extracted with ethyl acetate (three times), the combined organic layers were washed with brine and dried over magnesium sulfate, and the solvent was removed by rotary evaporation. The residue was purified by silica gel flash chromatography (hexanes/ethyl acetate=95/5 to 90/10) to give the *threo*-product **48a** (33.2 mg, 0.0750 mmol, 76% yield); mp 108–110 °C; ν_{max} (liquid film) 3298, 2914, 2864, 1461, 1380, 1215, 1096, 1053, 1036, 994, 882, 804, 685, 639 cm^{-1}; δ_H ($CDCl_3$, 400 MHz) 4.40 (1H, dd, J=8.4, 3.2 Hz), 4.04 (1H, dd, J=10.8, 3.2 Hz), 3.92 (1H, dd, J=10.8, 8.4 Hz), 3.86 (1H, dt, J=7.6, 3.6 Hz), 3.74 (1H, br dd, J=11.2, 4.0 Hz), 3.65 (1H, td, J=11.6, 2.8 Hz), 2.05 (1H, d, J=7.6 Hz, OH), 2.02–1.76 (3H, m), 1.36 (3H, s), 1.33–1.20 (1H, m), 1.20–1.00 (21H, m); δ_C ($CDCl_3$, 150 MHz) 76.3, 69.4, 64.8, 62.5, 44.6, 25.9, 19.5, 18.1, 16.0, 12.0; HRMS (APCI) calcd for $C_{17}H_{36}O_3ISi$ $[M+H]^+$ 443.14730, found 443.14764.

*4.6.4.2. Reductive deiodination of **48a** to **51**.* Iodide **48a** (20.3 mg, 0.0459 mmol) was dissolved in toluene (3 mL), tributyltin hydride (0.10 mL, 0.37 mmol) and AIBN (3.5 mg) were added, and the reaction mixture was heated at 70 °C for 2 h. The reaction mixture then cooled to room temperature, solvent was removed by rotary evaporation, and the residue was purified by flash chromatography on silica gel support mixed with 10% KF (hexanes/ethyl acetate=90/10) to give compound **51** (16.9 mg, 0.0534 mmol, 99% yield); ν_{max} (liquid film) 3433, 2941, 2866, 2721, 1463, 1382, 1088, 995, 883, 731 cm^{-1}; δ_H ($CDCl_3$, 600 MHz) 3.86 (1H, dt, *J*=10.8, 4.2 Hz), 3.83–3.78 (2H, m), 3.66 (2H, t, *J*=5.4 Hz), 3.47 (1H, td, *J*=6.6, 3.0 Hz), 2.20 (1H, ddd, *J*=14.4, 9.6, 4.2 Hz), 1.91–1.82 (2H, m), 1.77–1.70 (1H, m), 1.64 (1H, ddd, *J*=15.0, 5.4, 3.6 Hz), 1.53–1.45 (1H, m), 1.28 (3H, s), 1.16–1.05 (21H, m); δ_C ($CDCl_3$, 150 MHz) 76.3, 70.9, 60.9, 59.7, 38.4, 26.9, 22.8, 22.1, 17.9, 11.8; HRMS (APCI) calcd for $C_{17}H_{37}O_3Si$ $[M+H]^+$ 317.25065, found 317.25054.

*4.6.5. Mercury-promoted cyclization of (E)-alkenyldiol **30** to **50** and **51**.* The (*E*)-alkenyldiol **30** (33.9 mg, 0.107 mmol) was dissolved in THF (1 mL), the solution was cooled to 0 °C, and a solution of mercuric trifluoroacetate (66.3 mg, 0.155 mmol) in THF (1 mL) was added slowly. The reaction mixture was stirred at 0 °C for 30 min. Saturated aqueous potassium chloride (69 μL) was added, and the mixture was stirred for 2 h at 0 °C. The reaction mixture was diluted with ethyl acetate, the organic layer was washed with water (twice) and brine, dried over magnesium sulfate, and the solvent was removed by rotary evaporation. The residue was diluted with toluene (3 mL), tributyltin hydride (0.13 mL, 0.48 mmol) and AIBN (4.3 mg) were added, and the reaction mixture was heated at 75 °C for 2 h. After the reaction mixture cooled to room temperature, the solvent was removed by rotary evaporation, and the residue was purified by flash chromatography on silica gel support mixed with 10% KF (hexanes/ethyl acetate=95/5 to 80/20) to give the *erythro*-diastereomer **50** (4.5 mg, 0.0142 mmol, 13% yield), and the *threo*-diastereomer **51** (16.3 mg, 0.0515 mmol, 48% yield). The spectroscopic data matched that observed for compounds **50** and **51** arising from reductive deiodinations of **46a** and **48a**, respectively.

*4.6.6. Selenium-promoted cyclization of (E)-alkenyldiol **30** to **50** and **51**.* The (*E*)-alkenyldiol **30** (63.7 mg, 0.201 mmol) was dissolved in CH_2Cl_2 (3 mL), the solution was cooled to 0 °C, and toluenesulfonic acid (4.2 mg, 0.022 mmol) and *N*-phenylselenophthalimide (78.5 mg, 0.260 mmol) were added. The reaction mixture gradually warmed to 20 °C over 15 h. The mixture was then diluted with chloroform, the organic phase was washed with 0.2 M aqueous KOH (three times) followed by brine, dried over magnesium sulfate, and the solvent was removed by rotary evaporation. The residue was dissolved in toluene (6 mL), tributyltin hydride (0.26 mL, 0.97 mmol) and AIBN (7.6 mg) were added. The reaction mixture was heated at 70 °C for 2 h, additional tributyltin hydride (0.52 mL, 1.93 mmol) and AIBN (14.3 mg) were added, and the reaction mixture was heated at 70 °C for two additional hours. The mixture was allowed to cool to room temperature, solvents were removed by rotary evaporation, and the residue was purified by flash chromatography on silica gel support mixed with 10% KF (hexanes/ethyl acetate=90/10 to 80/20) to give primarily the *threo*-diastereomer **51** (24.1 mg, 0.0761 mmol, 38% yield), and mixture fractions containing both *erythro*-**50** and *threo*-**51** (40:60 ratio, 13 mg total, 20% combined yield). The spectroscopic data matched that observed for compounds **50** and **51** arising from reductive deiodinations of **46a** and **48a**, respectively.

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Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.tet.2013.04.138.

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