# Simple Designs for the Construction of Complex *Trans*-Fused Polyether Toxin Frameworks. A Linear Strategy Based on Entropically Favored Oxirane Ring Enlargement in Epoxycycloalkenes Followed by Carbon–Carbon or Carbon–Oxygen Bond-Forming Cyclizations†

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A successful design for the construction of *trans*-fused medium-size cyclic ethers is described. The key features of the synthesis are as follows: (i) intramolecular oxirane ring expansion in cycloalkenes to give bridged oxabicyclic systems and (ii) linear, one- or two-directional synthetic operations which generate external oxocycles in single reaction steps. The general approach involves the intramolecular addition of a stable γ-alkoxy-substituted allylstannane to an aldehyde carbonyl group, and the entire reaction is conducted in a one-pot process which includes the following: (i) *vic*-diol fragmentation from the bridged oxabicyclic precursor and (ii) Lewis acid-induced cyclization of the resulting aldehyde–allylic tin system. While the present strategy was mostly developed around racemic models, the potential for adoption of enantioselective features is immediate. The versatility, scope, limitations, and potential applications of the present technology are discussed in detail.

## Introduction

Marine dinoflagellates are attracting more and more attention as a source of compounds with unique structures possessing useful biological activity.[1] Many of them are polyethers, which have become valuable reagents in biomedical research, e.g., okadaic acid,[2] halichondrins,[3] brevetoxins,[4] and ciguatoxins.[5]

Hemibrevetoxin B (**1**)[4f] and brevetoxin B (**2**)[4a] and A (**3**)[4d] (Figure 1) are three examples of potent lipid-soluble neurotoxins with *trans*-fused polyether structures found in cultured cells of the extremely deleterious organism *Gymnodinium breve* (= *Ptychodiscus brevis*).[4] This toxic dinoflagellate is the causative organism of the red tides along the Gulf coast of Florida, which accompany massive fish kills and human intoxications.[6] Ciguatoxin (**4**),[5d] a toxin causing food poisoning by ingestion of certain coastal fishes which inhibit subtropical and tropical seas,[7] is closely related to these substances, at least as far as its ladder-shaped structural organization and toxicity are concerned. Just like the toxic polyethers from *G. breve*,[8] ciguatoxin (**4**) is a powerful activator of the $Na^+$ channels[9] that mediate the electrical excitability of nerve, heart, and skeletal muscle and is thus of particular interest in medicinal studies. Maitotoxin (**5**)[10] (Figure 2), the largest and most potent nonproteinaceous toxin known, is a related polyether extracted from cultured cells of *Gambierdiscus toxicus*. Although scarcity of material has impeded full pharmacological studies, maitotoxin, like okadaic acid,[11] is involved in $Ca^{2+}$-dependent mechanisms in a wide range of cell types.[12]

† Dedicated to Professor Sir Derek Barton on the occasion of his 75th birthday.

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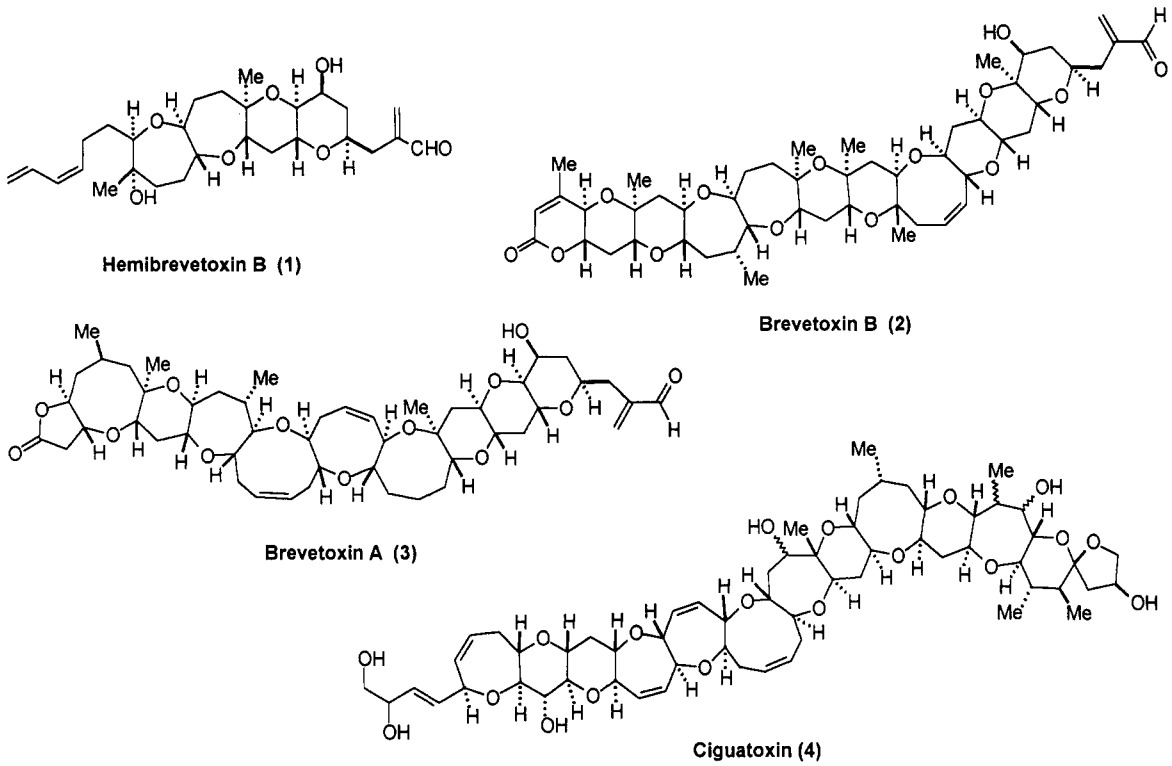


**Figure 1.** Examples of *trans*-fused polyether toxins from marine origin.

The structural complexity of these molecules and the novelty of their polyether systems make them most attractive from the synthetic point of view, and a considerable effort is presently being devoted to the preparation in the laboratory of simplified models[13a-v] and the total synthesis[13w,x] of some of these substances. Furthermore, the difficulty in isolating significant quantities of these polyether toxins has hampered extensive pharmacological investigations of this class of compounds; hence, the development of efficient strategies for their synthesis will make these interesting molecules available for further testing.

Toxicological studies[5-7] reveal an increasing lethal potency against mice in the sequence **1** ≪ **2** ≪ **3** ≪ **4** indicating that the toxicity of these molecules is associated with two main structural factors: (i) the molecular size of the polyether and (ii) its conformational mobility. The former factor accounts for the low toxicity of hemibrevetoxin B (**1**) and the latter for the lower activity of brevetoxin B (**2**) which has, compared with brevetoxin A (**3**) and ciguatoxin (**4**), a more rigid conformation mainly imposed by the *trans*-fused sequence of oxane rings. Both **3** and **4** possess flexible conformations associated with their oxepane, oxocane, and oxonane rings and endocyclic unsaturated carbons (Figure 1).

Although this can be considered an oversimplified view and other features may also be involved, the construction by synthesis of more accessible structural models which comply with the requisites of size and conformational mobility is not only an important objective for further biomedical studies but also presents an unusual and formidable synthetic challenge, particularly with regard to the generation of their *trans*-fused medium-size ring system. In addition, the structural analysis of selected synthetic fragments may provide useful topochemical information for the identification of the common structural features needed for toxin action.

## Background

These novel structures do indeed require the development of new methods of synthesis and the careful design

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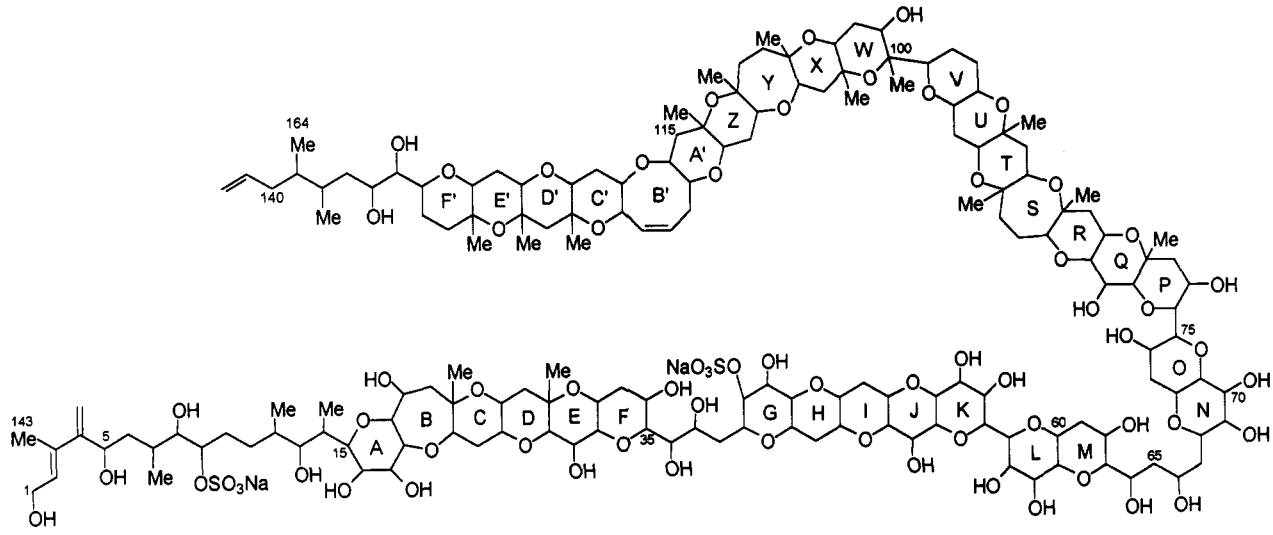

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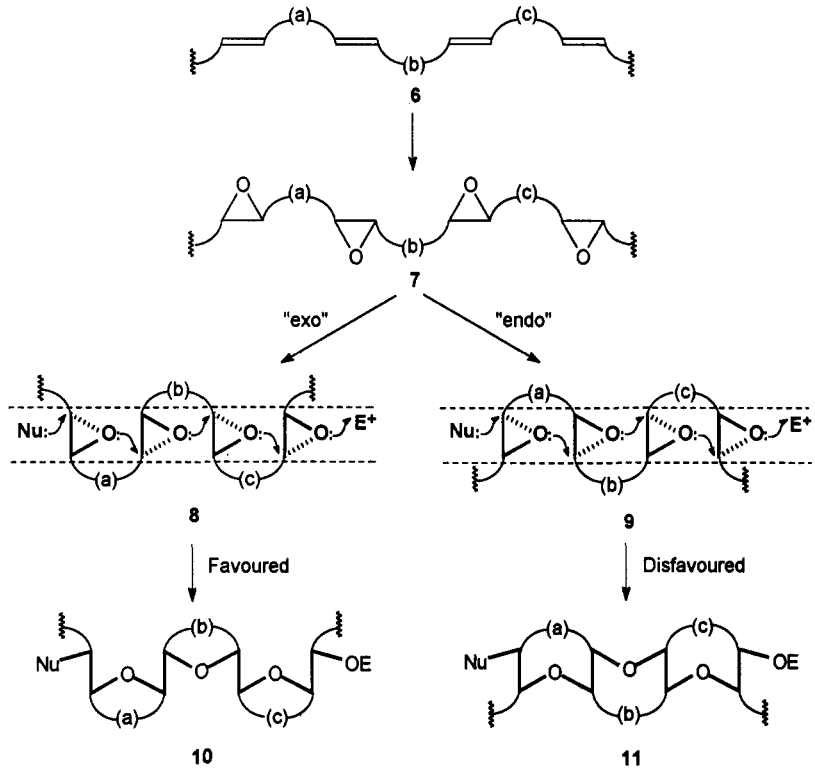
**Figure 2.** Structure of maitotoxin. Most of the ether rings are *trans*-fused except for rings L/M and N/O which are *cis*-fused.

**Scheme 1. Polyene → Polyepoxide → Polyether Sequences in Isolated and Fused Polyether Biosynthesis**



of the strategy to be adopted, before their total synthesis can be undertaken with any expectation of success. Virtually all the stereocenters in the brevetoxins and related substances are contained in vicinally oxygenated carbons, which suggests that the stereocontrolled functionalization of a polyolefin precursor may be involved in their biosynthesis.[14] The polyene → polyepoxide → polyether hypothesis[15] (Scheme 1) for the construction of the characteristic cyclic ether skeleton of these polyethers is important from a biosynthetic[14] as well as a synthetic[13a,j] point of view.

In ring-forming reactions by intramolecular cyclization, the formation of favored and less favored products can be understood in terms of the geometric and kinetic features that the reactants encounter along the reaction coordinate.[16] In general, favored cyclization pathways are those in which the length and nature of the linking chain enable the terminal atoms to achieve the proper geometry for reaction, whereas unfavored cases require severe distortion

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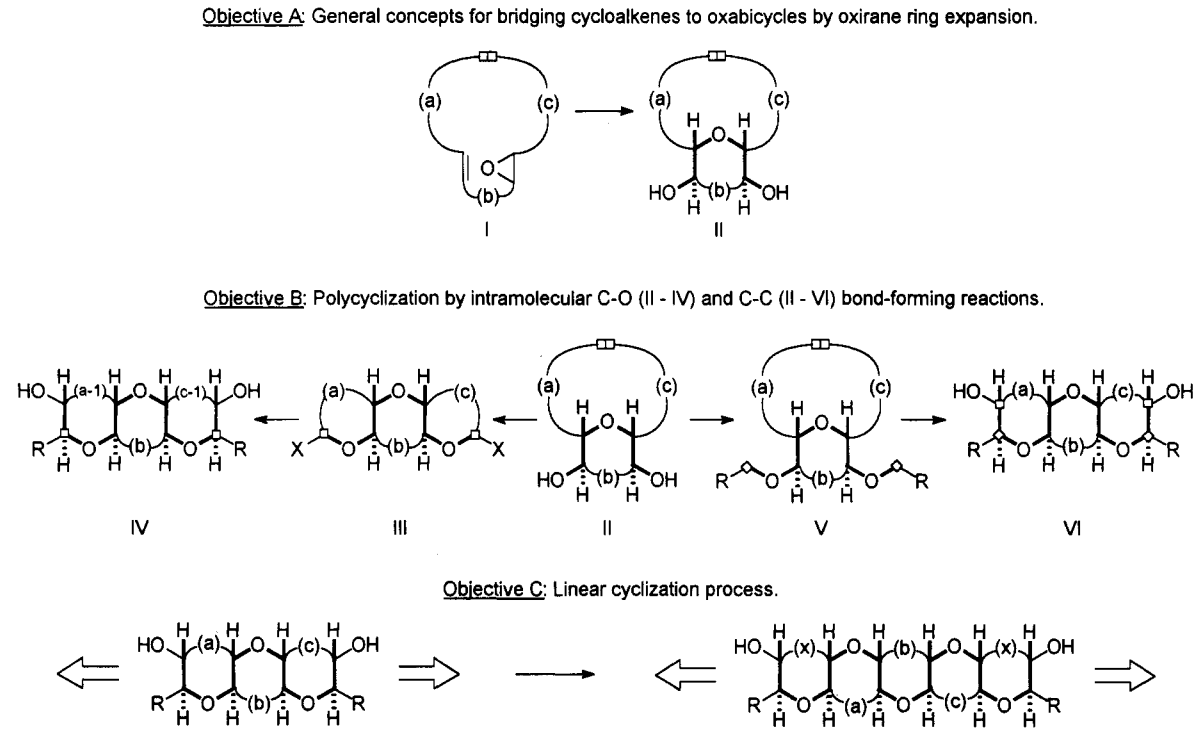
**Scheme 2**




of bond angles. Experimental evidence shows that, in accordance with Baldwin's rules,[17] the "exo" mode of cyclization in the polyepoxide **7** (Scheme 1) is the kinetically preferred pathway yielding the *isolated* polyether **10**.[18] The alternative "endo" cyclization to the apparently unfavored *fused* polyether **11** should overcome the energy barriers and the strain necessary to bring the epoxide oxygen into a geometry that allows the nucleophilic attack in the appropriate C–O bond direction.[19] The geometry of the possible transition states for intramolecular oxirane-ring expansion is restricted to those restraints imposed by the connecting chain. This structural requirement must be the essential feature for the endocyclic restriction since formally identical stereoelectronic behavior can be presumed to operate in both the "endo" and "exo" reaction processes (**8** and **9**, Scheme 1).

## Synthetic Rationale

Our general synthetic objectives are set out in Scheme 2.[20] Objective A refers in general to the intramolecular oxirane ring expansion in cycloalkenes **I** to give bridged oxabicyclic systems **II**. Because of the severe difficulties involved in synthesizing fused medium-size ring polyethers by cyclization reactions, our design for entry into these systems was based on epoxide ring enlargement on a carbocyclic framework, since the generated electrophilic carbon in **I** can be appropriately oriented for intramolecular capture by the nearby nucleophilic oxygen giving rise to the bridged oxabicyclic system **II**.

Objective B (Scheme 2) consists of the preliminary steps toward a synthetic two-way development involving the reaction sequences shown as **II** → **III** → **IV** and **II** → **V** → **VI** depending on whether the synthetic operations permit the simultaneous formation of carbon–oxygen bonds (**II** → **IV**) or carbon–carbon bonds (**II** → **VI**). In either case the end result has been the creation of *trans*-fused oxatricyclic substructures which are differentiated by the number of carbon atoms of the newly created external heterocycles. Both subunits **IV** or **VI** should be capable of increasing their number of oxacycles either by convergent processes through intermolecular couplings or by one- or two-way linear sequences which generate external oxacycles in single reaction steps (objective C, Scheme 2). In this paper we examine the scope and limitations of this synthetic strategy and offer mechanistic explanations for the observed results.

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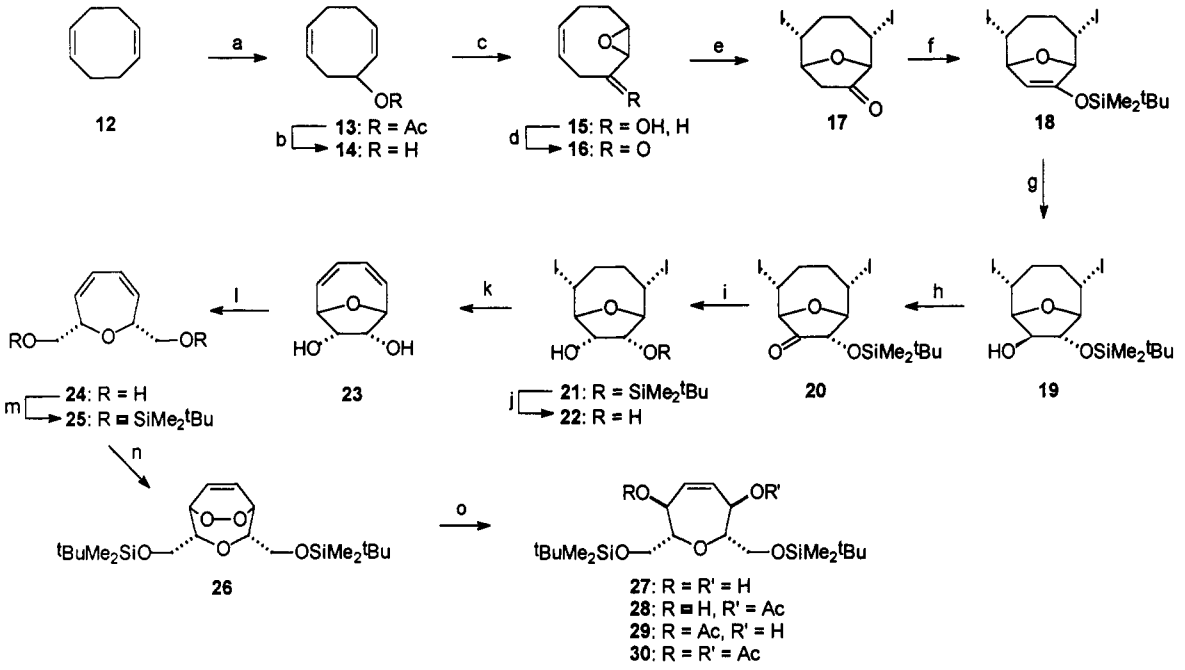
**Scheme 3**[a]




[a] Key: (a) 0.2 equiv of *t*-BuOOH, 0.8 equiv of AcOH, $Cu_2Cl_2$ catalyst, isooctane, 80 °C, 52 h (82%); (b) 0.2 equiv of $K_2CO_3$, MeOH, 25 °C, 12 h (100%); (c) 1.1 equiv of *t*-BuOOH, $VO(acac)_2$ catalyst, benzene, 25 °C, 2 h (79%); (d) 4.0 equiv of $SO_3$·pyr, 6.0 equiv of $Et_3N$, DMSO–$CH_2Cl_2$ (1:6), 0 °C, 2 h (85%); (e) 1.2 equiv of $I_2$, $CH_2Cl_2$, 25 °C, 12 h (85%); (f) 2.0 equiv of *t*-BuMe$_2$SiOTf, 6.0 equiv of $Et_3N$, $CH_2Cl_2$, 25 °C, 9 h (98%); (g) 1.2 equiv of $BH_3$·$Me_2S$, THF, 25 °C, 12 h, then excess of $H_2O_2$, excess of NaOH, 40 °C, 2 h (82%); (h) 3.0 equiv of $(COCl)_2$, 9.0 equiv of DMSO, 15.0 equiv of $Et_3N$, $CH_2Cl_2$, −78 to 0 °C, 1 h (98%); (i) 4.5 equiv of $NaBH_4$, THF, 25 °C, 12 h (90%); (j) 1.5 equiv of *n*-$Bu_4NF$, THF, 0 °C, 1 h (75%); (k) 6.0 equiv of DBU, THF, 60 °C, 12 h (75%); (l) 1.5 equiv of $NaIO_4$, MeOH–$H_2O$ (4:1), 0 °C, 30 min, then 3.0 equiv of $NaBH_4$, 0–25 °C, 30 min (68%); (m) 1.2 equiv of *t*-BuMe$_2$SiCl, 2.2 equiv of imidazole, DMF, 0 °C, 12 h (100%); (n) $O_2$, h$\nu$, TPP catalyst, $CHCl_3$, 25 °C, 32 h (74%); (o) $H_2$, Lindlar catalyst, quinoline, MeOH, 25 °C, 12 h (98%).

## Discussion and Results

**Transannular Ring Expansion of Epoxycycloalkenes to Bridged Oxabicyclic Systems. Generation of the $C_8$ *trans,syn,trans*-Substituted Oxepenyl Subunit 27.** To exemplify the initial concepts involved in these syntheses, we detail here the construction of the meso $C_8$ *trans,syn,trans* subunit **27** starting from (*Z,Z*)-cycloocta-1,5-diene (**12**) (Scheme 3). The efficiency of the synthesis of the optically pure monoacetates **28** and **29** by enzymatic asymmetrization[21] makes this compound an interesting starting point for the synthesis of *trans*-fused polyether targets including ciguatoxin (**4**) and related substances.[5]

Although there are several general approaches to the preparation of oxepanes[22] even in a form suitable for incorporation into synthetic schemes of fused polyethers,[13b,e,g,k] we were interested in a conceptually simple approach to the synthesis of **27** using transannular ring expansion of the epoxycycloalkene chemistry to achieve stereochemical control of the ring appendages.[20e,f] The requisite precursor, the oxabicyclic compound **17**, was prepared in 47% overall yield on a reasonable scale (>200 g) as described elsewhere.[20e] Selective enolization of **17** to the silyl ether **18**, followed by hydroboration, gave **19** after oxidative workup. Swern oxidation[23] of the alcohol **19** yielded ketone **20** which was submitted to selective facial reduction with $NaBH_4$ to give **21**. Fluoride-induced deprotection in **21** gave the *cis* diol **22** (56% overall yield from **17**). Treatment of **22** with DBU in THF produced the diene **23** which was fragmented by reaction with $NaIO_4$, and the resulting dialdehyde further reduced quantitatively to the dienyl derivative **24**. Protection of the primary hydroxyl groups of **24** with *tert*-butyldimethylsilyl chloride gave **25** which was submitted to singlet oxygen addition to generate the endoperoxide **26**. Hydrogenation of **26** with Lindlar catalyst in MeOH cleanly produced the meso compound **27** with the required *trans,syn,trans* stereochemistry.

Enzymatic reactions using prochiral and meso substrates for the production of chiral synthons is well-documented[24] and can be particularly effective, as, in theory, all the substrate may be processed to a single enantiomer. Transesterification of the prochiral diol **27** with isoprenyl acetate[25] promoted by *Pseudomonas* lipase proceeds stereoselectively to give the optically active monoacetate (−)-**28**, $[\alpha]^{25}_D$ = −48.3°. A suitable condition for this

(21) (a) Margolin, A. L. *CHEMTECH* **1991**, 160. (b) Nakamura, K.; Takebe, Y.; Kitayama, T.; Ohno, A. *Tetrahedron Lett.* **1991**, *32*, 4941. (c) Xie, Z.-F. *Tetrahedron: Asymmetry* **1991**, *2*, 733. (d) Klibanov, A. *Acc. Chem. Res.* **1990**, *23*, 114. (e) Wong, C.-H. *Science* **1989**, *244*, 1145. (f) Chen, C.-S.; Sih, C. J. *Angew. Chem., Int. Ed. Engl.* **1985**, *28*, 695. (g) Toone, E. J.; Simon, E. S.; Bednarski, M. D.; Whitesides, G. M. *Tetrahedron* **1989**, *45*, 5365.

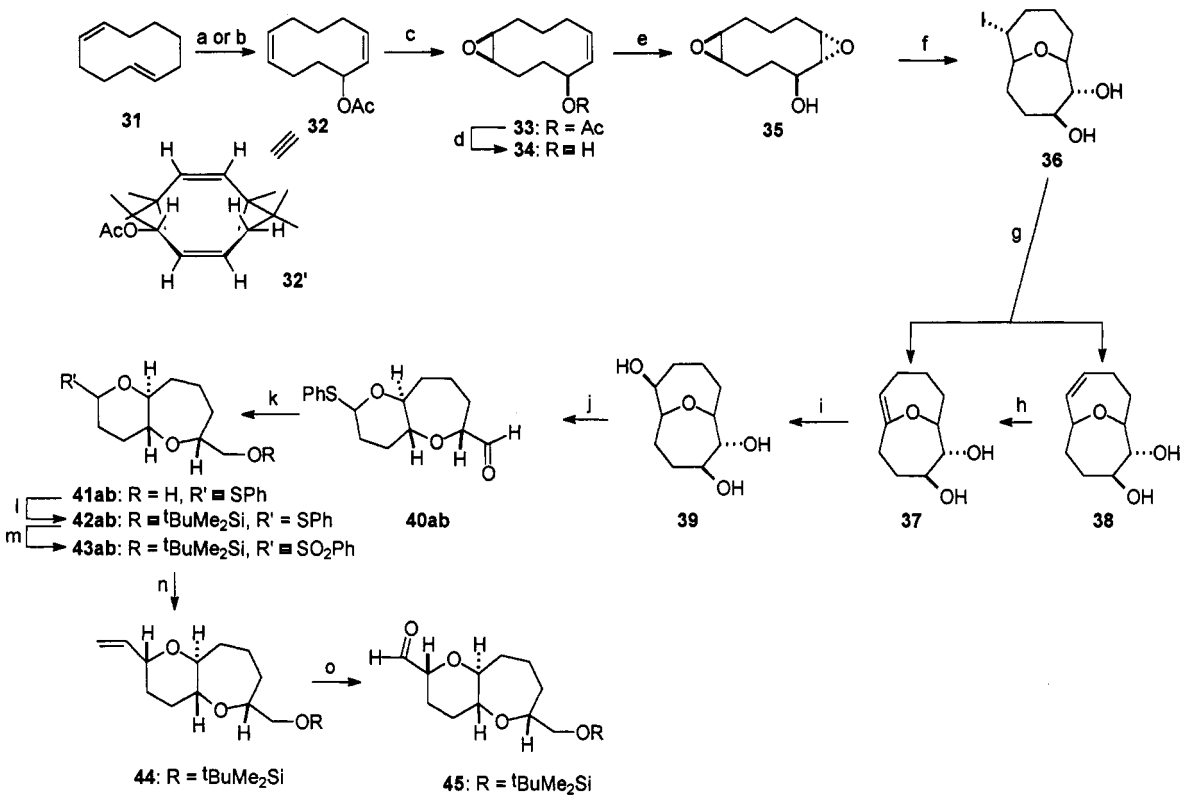
(22) For a brief review of the synthesis and chemistry of seven-membered ring ethers, see: Boyd, D. R. In *Comprehensive Heterocyclic Chemistry*; Katritzky, A. R., Rees, C. W., Lwowski, W., Eds.; Pergamon Press: Oxford, 1985; Vol. 7, Chapter 5.17.

(23) (a) Hwang, S. L.; Mancuso, A. J.; Swern, D. *J. Org. Chem.* **1978**, *63*, 2480. (b) Omura, K.; Swern, D. *Tetrahedron* **1978**, *34*, 1651.

(24) (a) Ohno, M. In *Organic Synthesis, An Interdisciplinary Challenge*; Proceeding of the 5th IUPAC Symposium on Organic Synthesis; Streith, J., Prinzbach, H., Schill, H., Eds.; Blackwells: Oxford, England, 1984; pp 189–204. (b) Francis, C. J.; Jones, J. D. *J. Chem. Soc., Chem. Commun.* **1984**, 579. (c) Seebach, D.; Eberle, M. *Chimia* **1986**, *40*, 315. (d) Mohr, P.; Walspe-Sacrevic, N.; Tamm, C. *Helv. Chim. Acta* **1984**, *66*, 250. (e) Hemmerle, H.; Gais, H. J. *Tetrahedron Lett.* **1987**, *30*, 3471. (f) Whitesides, G. M.; Wong, C.-H. *Angew. Chem., Int. Ed. Engl.* **1985**, *97*, 613. (g) Hultin, P. G.; Muesler, F.-J.; Jones, J. B. *J. Org. Chem.* **1991**, *56*, 5375. (h) Johnson, C. R.; Golebiowski, A.; Steensma, D. H. *J. Am. Chem. Soc.* **1992**, *114*, 9414.

(25) Harris, K. J.; Gu, Q.; Shih, Y.; Girdaukas, G.; Sih, C. J. *Tetrahedron Lett.* **1991**, *32*, 3941.

**Scheme 4**[a]




[a] Key: (a) (i) Na–$Al_2O_3$ catalyst, $CH_2Cl_2$, 12 h, 25 °C; (ii) 0.2 equiv of *t*-BuOOH, 0.8 equiv of AcOH, $Cu_2Cl_2$ catalyst, isooctane, 80 °C, 42 h (78%); (b) (i) 1.1 equiv of *m*-CPBA, EtOAc, 25 °C, 30 min (93%); (ii) 1.5 equiv of PhLi, $Et_2O$, reflux, 12 h (92%); (iii) 2.0 equiv of $Ac_2O$, 2.5 equiv of $Et_3N$, DMAP catalyst, 1 h (98%); (c) 1.1 equiv of *m*-CPBA, $CH_2Cl_2$, 0 °C, 5 h (80%); (d) 0.1 equiv of $K_2CO_3$, MeOH, 25 °C, 3 h (98%); (e) 1.5 equiv of *m*-CPBA, $CH_2Cl_2$, 0–25 °C, 12 h (80%); (f) 1.5 equiv of $I_2$, 0.2 equiv of Ti(O-*i*-Pr)$_4$, $CH_2Cl_2$, 25 °C, 3 h (64%); (g) 5.0 equiv of DBN, xylene, 140 °C, 5 h (87%) (**37**:**38** = 7:1); (h) 3.2 equiv of KO-*t*-Bu, DMSO, THF, 50 °C, 4 h (63%); (i) 1.5 equiv of $BH_3$·$Me_2S$ complex, THF, 25 °C, 12 h (76%); (j) 2.0 equiv of $NaIO_4$, MeOH, 25 °C, 2 h, then 1.2 equiv of PhSH, CSA catalyst, $CH_2Cl_2$, 25 °C, 6 h (68%) (2*S**:2*R** = 3:1); (k) 10.0 equiv of $NaBH_4$, MeOH, 0 °C, 10 min (96%) (2*S**:2*R** = 3:1); (l) 2.0 equiv of *t*-BuMe$_2$SiCl, 2.5 equiv of imidazole, DMF, 40 °C, 6 h (88%) (2*S**:2*R** = 3:1); (m) 3.0 equiv of *m*-CPBA, 3.0 equiv of $NaHCO_3$, EtOAc, 12 h (96%) (2*S**:2*R** = 3:1); (n) 5.0 equiv of $CH_2$=CHMgBr, 2.5 equiv of $ZnBr_2$, THF, 25 °C, 30 min, then **43ab** in THF, 25 °C, 6 h (92%); (o) (i) 2.0 equiv of NMO, 0.02 equiv of $OsO_4$, THF:$H_2O$ (1:1), 25 °C, 6 h (100%); (ii) 3.0 equiv of $NaIO_4$, MeOH:$H_2O$ (5:1), 25 °C, 20 min (83%).

reaction was to use an equivalent weight of crude Amano AK lipase and neat isoprenyl acetate as solvent and acyl donor. After the reaction mixture was stirred at 25 °C for 72 h and purified by silica gel chromatography, monoacetate **28** was isolated in enantiomerically pure form (determined by its Mosher[26,27] derivative) in 85% yield (ca. 40% overall from oxepadiene **24**).

Enzymatic hydrolysis[28,29] of diacetate **30** prepared from **27** in the conventional manner was carried out in the presence of the four enzymatic systems resulting in the enantioselective generation of monoacetate (+)-**29**, $[\alpha]^{25}_D$ = +47.3°. Hydrolytic reactions were performed in 10% MeOH–0.1 M phosphate buffer (pH 7.0) at 25 °C keeping the pH constant by continuous addition of NaOH (0.5 N). Of the enzymes used, esterase from porcine liver and lipase AK derived from *Pseudomonas sp* were the most active in the selective hydrolysis of the meso diacetate **30**. In all cases, the ee > 98% of the enantiomeric monoacetates (−)-**28** and (+)-**29** were determined by $^1$H-NMR spectroscopy (400 MHz) after conversion into their corresponding Mosher esters.[26,27]

**Heterocyclization by Intramolecular C–O Bond-Forming Reactions. Stereocontrolled Preparation of the *Trans*-Fused Oxane–Oxepanyl Ring System 45.** As an extension of the work directed toward the selective construction of *ortho*-condensed polycycles following the ideas outlined in Scheme 2 (objective B), we will now detail the synthesis of the 6,7-*trans*-fused ring system **45** starting from the commercially available cycloalkene (*E*,*Z*)-1,5-cyclodecadiene (**31**) (Scheme 4),[30] as an example that involves intramolecular carbon–oxygen bond-forming cyclization.[20l] The most convenient preparation of the allylic acetate **32** on the required scale was achieved from **31** via selective epoxidation of the *trans* double bond

(26) (a) Dale, J. A.; Dull, D. L.; Mosher, H. S. *J. Org. Chem.* **1969**, *34*, 2543. (b) Dale, J. A.; Mosher, H. S. *J. Am. Chem. Soc.* **1973**, *95*, 512. (c) Sullivan, G. R.; Dale, J. A.; Mosher, H. S. *J. Org. Chem.* **1973**, *38*, 2143. (d) Yamaguchi, S.; Yasuhara, F.; Kabuto, K. *Tetrahedron* **1976**, *32*, 1363.

(27) For an advanced Mosher's method using high-field FT-NMR spectroscopy, see: Ohtani, I.; Kusumi, T.; Kashman, Y.; Kakisawa, H. *J. Am. Chem. Soc.* **1991**, *113*, 4092. Ohtani, I.; Kusumi, T.; Kashman, Y.; Kakisawa, H. *J. Org. Chem.* **1991**, *56*, 1296. Ohtani, I.; Kusumi, T.; Ishitsuk, M. O.; Kakisawa, H. *Tetrahedron Lett.* **1989**, *30*, 3147.

(28) (a) Ohno, M.; Otsuka, M. *Org. React.* **1989**, *37*, 1. (b) Zhu, L.-M.; Tedford, C. *Tetrahedron* **1990**, *46*, 6587.

(29) Some recent references are: (a) Hultin, P. G.; Mueseler, F.-j.; Jones, J. B. *J. Org. Chem.* **1991**, *56*, 5375. (b) Mori, K.; Bernotas, R. *Tetrahedron: Asymmetry* **1990**, *2*, 87. (c) Naemura, K.; Matsumura, T.; Komatsu, M.; Hirose, Y.; Chikamatsu, H. *Bull. Chem. Soc. Jpn.* **1989**, *62*, 3523. (d) Ganey, M. V.; Padykula, R. E.; Berchtold, G. A. *J. Org. Chem.* **1989**, *54*, 2787. (e) Fouque, E.; Rousseau, G. *Synthesis* **1989**, 661. (f) Luyten, M.; Muller, S.; Herzog, B.; Keese, R. *Helv. Chim. Acta* **1987**, *70*, 1250. (g) Deardorff, D. R.; Matthews, A. J.; Mc Meekin, D. S.; Craney, C. L. *Tetrahedron Lett.* **1986**, *27*, 1255. (h) Lam, L. K. P.; Hu, R. A. H. F.; Jones, J. B. *J. Org. Chem.* **1986**, *51*, 2047.

(30) (*E*,*Z*)-1,5-Cyclododecadiene (98% pure) was obtained by reduced pressure distillation of a hydrocarbon mixture (90%) provided by Aldrich Chemical Co. and by cyclooligomerization of 1,3-butadiene and ethylene with nickel bis-1,5-cyclooctadiene catalyst (Wilke, G. *Angew. Chem., Int. Ed. Engl.* **1963**, *2*, 105).

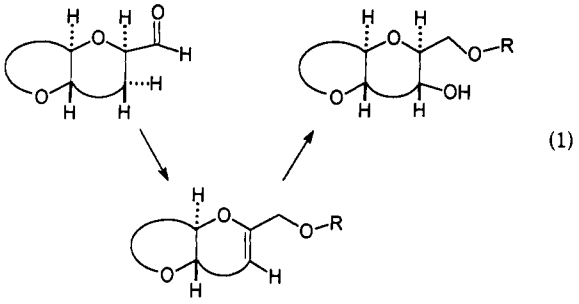
followed by treatment with phenyllithium in refluxing ether which gave, after acetylation, compound **32** in 84% overall yield.[31] Alternatively, sodium–alumina catalyzed isomerization of **31** to give (*Z,Z*)-1,6-cyclodecadiene,[32] followed by allylic acyloxylation,[33] furnished **32** in 77% yield. The *syn*-epoxy acetate **33** was prepared from **32** via facial epoxidation in 80% yield. Base hydrolysis of **33**gave **34** which was treated with *m*-chloroperbenzoic acid to afford the *trans*-bisepoxide **35** in good yield (87%). As far as we can determine, this facially controlled double oxidation of **32** gave rise to the bis-epoxide **35** in high stereochemical purity, and further transformation of **35** did not reveal the presence of significant amounts of diastereoisomers of **35** (*vide infra*). Molecular mechanics calculations predict that the conformation of **32** containing a pseudoequatorial acetoxy group (**32'**) will be of the least energy.[34] It is clear from this view that the two faces of the olefinic $\pi$ system in **32'** are sterically very different. Since one face of the $\pi$-systems is severely hindered by the disposition of the allylic C–C bonds as well as by transannular methylene groups, it is to be expected that various addition reactions would occur largely or perhaps exclusively from the less hindered, peripheral faces of the olefinic linkages.

Treatment of **35** with $I_2$–Ti(O-*i*-Pr)$_4$ in methylene chloride resulted in an efficient conversion (64%) to the expanded ether **36**. The effect of Ti on the observed chemoselective transannular ring expansion can be attributed to the anchimerically assisted opening of the oxirane imposed on the intermediate in which the hydroxy and epoxy oxygens are both coordinated to the Ti catalyst. Base-induced elimination converted **36** into a mixture of **37** and **38** (87%, **37**:**38** ca. 7:1). The undesired isomer **38** was isomerized to the required enol ether **37** (63%) under basic conditions.

The next operation required regio- and stereoselective attack of a hydroborating agent from the exo side of **37**. Ample regiochemical precedent,[35] as well as MM2 calculations and modeling, predicted such a scenario. Hydroboration of **37** followed by oxidative workup did indeed result in a single stereoisomer (76% yield) which has been proven to have the assumed structure **39**. Transformation of **39** to **40** required two steps: $NaIO_4$-induced cleavage of the *vic*-diol system and acid-induced mixed ketalization in the presence of thiophenol. Because of the anomeric effect, the phenylthio substituent in **40** assumed an axial position preferentially as revealed by the vicinal $^1$HNMR coupling constant data ($J$ = 3.4, 2.8 Hz). $NaBH_4$ reduction of **40** gave the primary alcohol **41** which, after silyl protection to **42**, was oxidized to yield the benzenesulfonyl derivative **43** as a 3:1 mixture of stereoisomers.[36]

Optimum yields for the direct nucleophilic displacement of the sulfone moiety[37] in **43** to give **44** were obtained by treatment of the filtered solutions of the vinylzinc reagent in dry THF with the sulfone for several hours at 40 °C (92% yield). Compound **44** was converted to the aldehyde **45** (71% yield) by conventional methods via the *vic*-diol intermediate as summarized in Scheme 4.

At the outset of this undertaking, we had little data to draw on about whether $\alpha$ or $\beta$ C-linked aldehydes at the anomeric position would serve as precursors to endocyclic hydroxymethyl enol ethers, which would be hydrated to the desired *trans,syn,trans*-substituted oxacycles (eq 1).




(1)

We will review some of these studies here because they provide some definition of the scope and limitations of our approach to the synthesis of multigram quantities of these useful precursors.[38] Scheme 5 outlines the general concepts that led to the development of the present technology to give the *trans,syn,trans*-substituted $C_7$-tetrahydropyranyl derivative **57** in 18–22% overall yield (depending on the scale) starting from tri-*O*-acetyl-D-glucal (**46**). Direct dehydrogenation of the $\alpha$-linked C-glycosyl aldehyde **53** to **55** was achieved in high yield by the reaction of the *E,Z*-silyl enol ether mixture **54** with $Pd^{II}(OAc)_2$ in acetonitrile.[39] Compound **56** (R = *t*-BuMe$_2$Si) was regioselectively hydroborated with oxidative workup to give a 5:2 mixture of **57** and **58** (R = *t*-BuMe$_2$Si). The ratio was improved to 8:1 by hydroboration of the benzyl ether derivative of **56**, R = Bzl. The structure of compound **57** was determined by decoupling studies on **57** (R = *t*-BuMe$_2$-Si) and (R = Bzl) where coupling constants of 8.4 and 9.00 Hz for $H_a/H_b$ established the respective vicinal/trans diaxial relationships. Furthermore, ROESY experiments confirmed the $H_b/H_c$ and $H_a/H_d$ syn relationship and thus the stereochemistry of **57**.

**Heterocyclization by Intramolecular C–C Bond-Forming Reactions.** We have studied the development of new syntheses of *trans*-fused common and medium-ring oxacycles involving construction of the heterocyclic

(31) (a) Traynham, J. G.; Franzen, G. R.; Knesel, G. A.; Northington, D. J., Jr. *J. Org. Chem.* **1967**, *32*, 3285. (b) Taylor, S. K.; Rose, C. B. *J. Org. Chem.* **1977**, *42*, 2175.

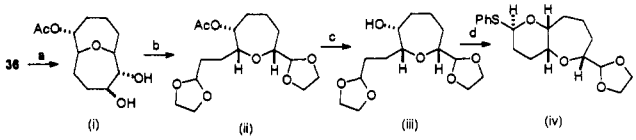
(32) Haag, W. O.; Pines, H. *J. Am. Chem. Soc.* **1960**, *82*, 387.

(33) Walling, C.; Zavitsas, A. *J. Am. Chem. Soc.* **1963**, *85*, 2084.

(34) The program PCMODEL-PI was employed for these calculations.

(35) Brown, H. C.; Negishi, E. *Synthesis* **1974**, 77.

(36) We have also assembled in cis the oxane–oxepanyl ring system as illustrated below using the type a methodology



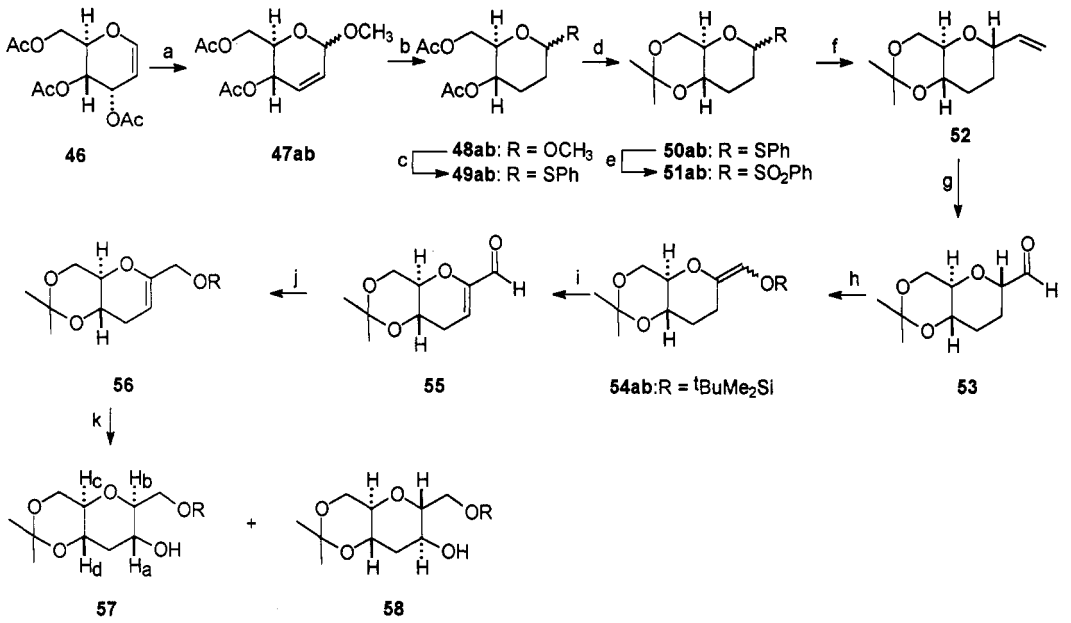

**Reagents and conditions**: (a) 1.5 equiv of AgOAc, AcOH:$CHCl_3$ (1:4), 25 °C, 6 h (70%); (b) 1.5 equiv of $NaIO_4$, MeOH:$H_2O$ (4:1), 25 °C, 4 h, then benzene:$(CH_2OH)_2$ (1:1), 0.2 equiv of CSA, reflux, 12 h (93%); (c) 0.1 equiv of $K_2CO_3$, MeOH, 25 °C, 3 h (98%); (d) 2.5 equiv of PhSH, CSA catalyst, $CH_2Cl_2$, 25 °C, 12 h (96%). (Experimental data for these compounds are included in the supplementary material).

(37) Ley, S. V.; Lygo, B.; Wonnacott, A. *Tetrahedron Lett.* **1985**, *26*, 535. Beau, J.-M.; Sinay, P. *Tetrahedron Lett.* **1985**, *26*, 6185, 6189, 6193. Grek, C.; Grice, S. V.; Ley, S. V.; Wonnacott, A. *Tetrahedron Lett.* **1986**, *27*, 5277. Ley, S. V.; Lygo, B.; Sternfeld, F.; Wonnacott, A. *Tetrahedron* **1986**, *42*, 4333. Brown, S. D.; Ley, S. V. *Tetrahedron Lett.* **1988**, *29*, 4869. Crich, D.; Ritchie, J. T. *J. Chem. Soc., Chem. Commun.* **1988**, 985. Brown, S. D.; Bruno, M.; Davenport, J. R.; Ley, S. V. *Tetrahedron* **1989**, *45*, 4293. Crich, D.; Lim, L. B. L. *Tetrahedron Lett.* **1990**, *31*, 1897. Brown, S. D.; Ley, S. V.; Vile, S.; Thompson, M. *Tetrahedron* **1991**, *47*, 1329. Ley, S. V.; Amstrong, A.; Díez-Martín, D.; Ford, M. J.; Grice, P.; Knight, J. G.; Kolb, H. C.; Madin, A.; Marby, C. A.; Mukherjee, S.; Shaw, A. N.; Slawin, A. M. Z.; Vile, S.; White, A. D.; Williams, D. J.; Woods, M. *J. Chem. Soc., Perkin Trans. 1* **1991**, 667.

(38) The practical aspects of this reaction as a general convergent approach to *trans*-fused polyethers will be described in due course (Alvarez, E.; Díaz, M. T.; Rico, M.; Rodríguez, R. M.; Martín, J. D. Unpublished work).

(39) Ito, Y.; Hirao, T.; Saegusa, T. *J. Org. Chem.* **1978**, *43*, 1011.

**Scheme 5**[a]

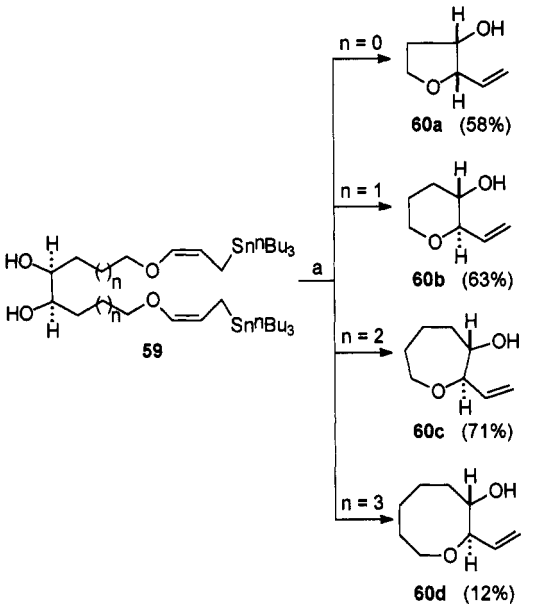



[a] Key: (a) 1.1 equiv of $SnCl_4$, 1.1 equiv of MeOH, $CH_2Cl_2$, −78 °C, 10 min (83%) [ca. $\alpha$:$\beta$ (6:1) stereoselectivity]; (b) $H_2/PtO_2$, THF, 25 °C, 4 h (95%); (c) 1.5 equiv of $PhSSiMe_3$, 1.2 equiv of $Me_3SiOSO_2CF_3$, $CH_2Cl_2$, 0–25 °C, 10 h, (86%) [ca. $\alpha$:$\beta$ (4:1) stereoselectivity]; (d) (i) 0.1 equiv of $K_2CO_3$, MeOH, 25 °C, 1 h (100%); (ii) 2.0 equiv of $Me_2C(OMe)_2$, $POCl_3$ cat., $CH_2Cl_2$, 25 °C, 12 h, (92%); (e) 3.0 equiv of *m*-CPBA, 3.0 equiv of $NaHCO_3$, EtOAc, 0–25 °C, 5 h (94%); (f) 2.5 equiv of $CH_2$=$CHMgBr$, 1.5 equiv of $ZnBr_2$, THF, 25–40 °C, 12 h (84%); (g) (i) 2.0 equiv of NMO, 0.01 equiv of $OsO_4$, THF:$H_2O$ (1:1), 25 °C, 12 h (100%); (ii) 3.0 equiv of $NaIO_4$, MeOH:$H_2O$ (4:1), 25 °C, 30 min, (84%); (h) 2.0 equiv of *t*-$BuMe_2SiOTf$, 2.0 equiv of $Et_3N$, $CH_2Cl_2$, 0–25 °C, 12 h, (72%) [*E*:*Z* (3:1) stereoselectivity]; (i) 1.1 of $Pd(OAc)_2$, $CH_3CN$, 25 °C, 12 h, (80%); (j) (i) 2.0 equiv of DIBAL, $Et_2O$, 25 °C, 3 h (95%) (**56**, R = H); (ii) 1.1 equiv of *t*-$BuMe_2SiCl$, 2.2 equiv of imidazole, DMF, 0 °C, 6 h, (100%) (**56**, R = *t*-$BuMe_2Si$); (k) 1.5 equiv of $BH_3$·$Me_2S$, THF, 25 °C, 12 h, then excess NaOH, excess $H_2O_2$, 0 °C, 1 h, (72%) (**57**, R = *t*-$BuMe_2Si$), (18%) (**58**, R = *t*-$BuMe_2Si$).

rings by intramolecular C–O[20l] or C–C[20m] bond-forming reactions. In many cases, the carbon–carbon approach offers notable advantages over cyclization strategies involving carbon–oxygen bond formation, particularly with regard to regiochemical and stereochemical control.[13n,o,40] One of the most important classes of carbon–carbon bond-forming reactions of this type is the addition of allylic organometallic reagents to aldehydes and acetals,[41] the power and utility of this reaction deriving from the mild conditions and high degree of stereocontrol with which these processes occur.[42]

The objective of our efforts in this area was the development of a cyclization reaction that would (a) assemble ether rings of various sizes from simple acyclic precursors and (b) directly install a $\beta$-hydroxy group and an $\alpha$-alkenyl appendage in the cyclic ether products in a *trans*-relationship that is found in natural fused polyethers.[1]

**Scheme 6**[a]




[a] Key: (a) 1.2 equiv of *n*-$Bu_4NIO_4$, $CH_2Cl_2$, 0–25 °C, 3–4 h, then add 2.0 equiv of $BF_3$·$OEt_2$ at −78 °C, 5–10 min.

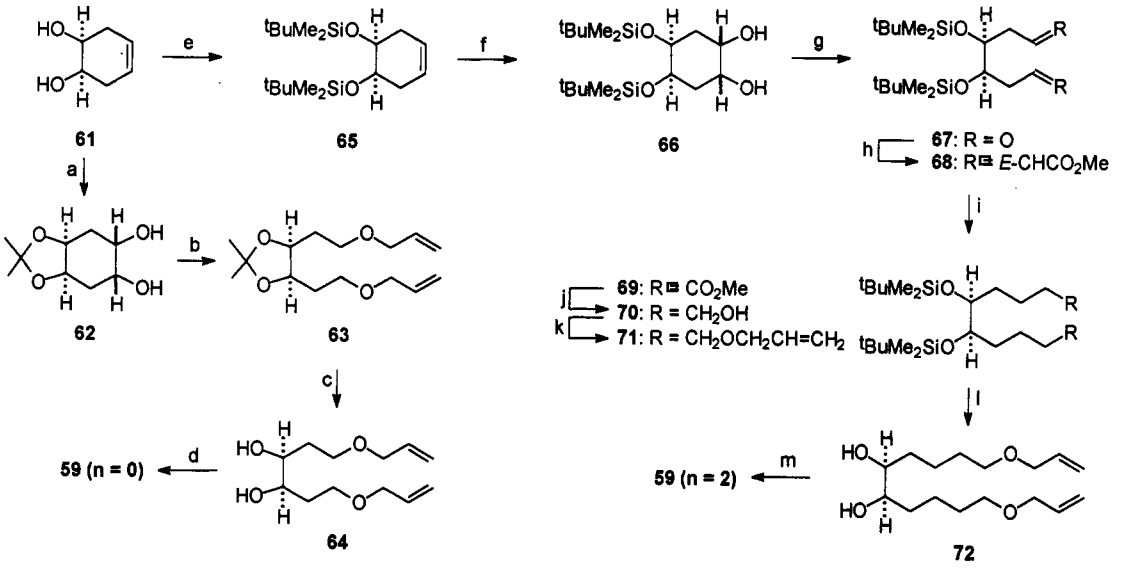
As shown in Scheme 6, the general approach involves the intramolecular addition of a stable $\gamma$-alkoxy-substituted allylstannane to an aldehyde carbonyl group.[13±,42] The entire reaction is conducted in a one-pot process which

(40) For selected recent syntheses of cyclic ethers involving C–C bond-forming reactions, see: Berger, D.; Overman, L. E. *Synlett* **1992**, 811. Fu, G. C.; Grubbs, R. H. *J. Am. Chem. Soc.* **1992**, *114*, 5426. Etter, J. B.; Harring, L. S.; Molander, G. A.; Thorel, P.-J. *J. Am. Chem. Soc.* **1991**, *113*, 8036. Brown, M. J.; Harrison, T.; Overman, L. E. *J. Am. Chem. Soc.* **1991**, *113*, 5375. Hopkins, M. H.; Overman, L. E.; Rishton, G. M. *J. Am. Chem. Soc.* **1991**, *113*, 5354. Blumenkopf, T. A.; Bratz, M.; Castañeda, A.; Look, G. C.; Overman, L. E.; Rodríguez, D.; Thompson, A. S. *J. Am. Chem. Soc.* **1990**, *112*, 4386. Ayra, P.; Chan, T.-H. *J. Chem. Soc., Chem. Commun.* **1990**, 967. Guyot, B.; Migniac, L.; Pornet, J. *J. Organomet. Chem.* **1989**, *373*, 279. Hiemstra, H.; Lolkema, L. D. M.; Mooiweer, H. H.; Speckamp, W. N. *Tetrahedron Lett.* **1988**, *29*, 6365. Trost, B. M.; Verhoeven, T. R. *J. Am. Chem. Soc.* **1980**, *102*, 4743.

(41) For recent reviews see: (a) Hoffmann, R. W. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 555; (b) **1987**, *26*, 489. (c) Yamamoto, Y. *Acc. Chem. Res.* **1987**, *20*, 243. (d) Yamamoto, Y. *Aldrichim. Acta* **1987**, *30*, 45. (e) Roush, W. R. In *Comprehensive Organic Synthesis*; Trost, B., Ed.; Pergamon Press: Oxford, 1991; Vol. 2, p 1. (f) Fleming, I. *Ibid.* 564. (g) Marshall, J. A. *Chemtracts* **1992**, *5*, 75.

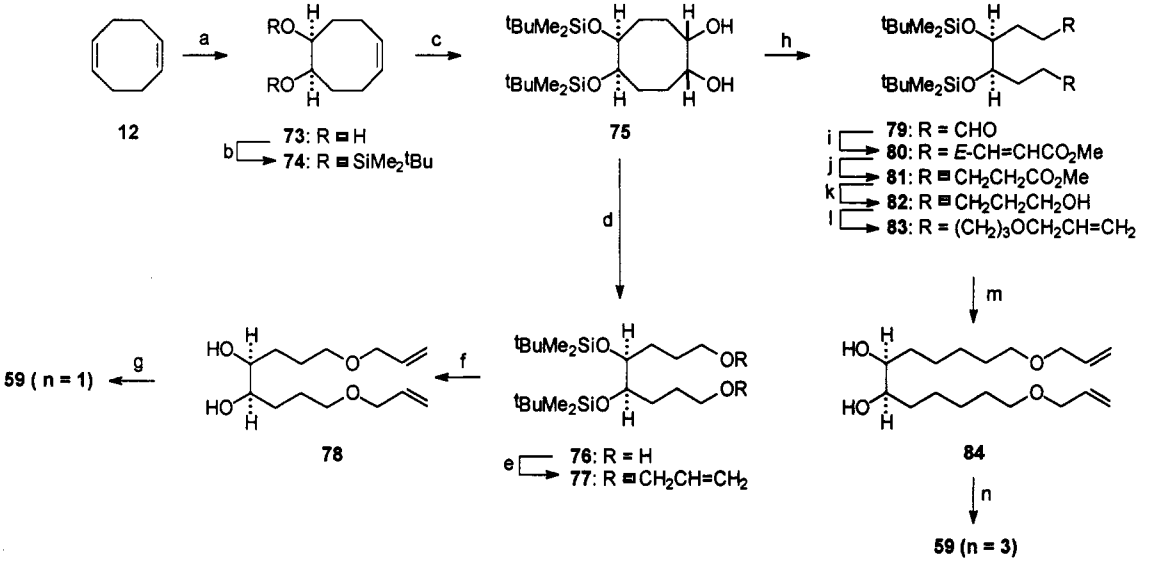
(42) $\alpha$-Alkoxy stannanes and allylic stannanes have played a useful role as nucleophilic reagents in intramolecular C–C bond-forming reactions. For selected syntheses, see: Gevorgyan, V.; Kadota, I.; Yamamoto, Y. *Tetrahedron Lett.* **1993**, *34*, 1313. Yamada, J.-i.; Asano, T.; Kadota, I.; Yamamoto, Y. *J. Org. Chem.* **1990**, *55*, 6066. Marshall, J. A.; Welmaker, G. S.; Gung, B. W. *J. Am. Chem. Soc.* **1991**, *113*, 647. Marshall, J. A.; Gung, W. Y. *Tetrahedron Lett.* **1988**, *29*, 1657. Marshall, J. A.; Markwalder, J. A. *Tetrahedron Lett.* **1988**, *29*, 4811. Marshall, J. A.; Gung. W. Y. *Tetrahedron Lett.* **1989**, *30*, 2183.

**Scheme 7**[a]



[a] Key: (a) (i) 1.5 equiv of 2,2-dimethoxypropane, 0.05 equiv of CSA, $CH_2Cl_2$, 25 °C, 15 min (97%); (ii) 1.3 equiv of NMO, 0.03 equiv of $OsO_4$, THF:$H_2O$ (1:1), 25 °C, 12 h (90%); (b) (i) 1.0 equiv of $NaIO_4$, acetone:$H_2O$ (4:1), 0–25 °C, 3 h; (ii) 2.2 equiv of DIBAL, diethyl ether, 0 °C, 1 h (96%); (iii) 2.6 equiv of NaH, 4.4 equiv of allyl bromide, DMF, 0–25 °C, 15 min (97%); (c) 0.03 equiv of CSA, MeOH, 25 °C, 15 min (97%); (d) 4.4 equiv of *s*-BuLi, 2.2 equiv of *n*-$Bu_3SnCl$, THF, −78 °C, 10 min (62%); (e) 2.4 equiv of *t*-$BuMe_2SiCl$, 5.0 equiv of imidazole, $CH_2Cl_2$, 25 °C, 12 h (98%); (f) 5.0 equiv of NMO, $OsO_4$ catalyst, THF:$H_2O$ (1:1), 25 °C, 4 h (90%); (g) 1.0 equiv of $NaIO_4$, acetone:$H_2O$ (4:1), 0–25 °C, 2.5 h; (h) 3.8 equiv of NaH, 4.0 equiv of $(MeO)_2P(O)CH_2CO_2Me$, benzene, 25 °C, 30 min (83%); (i) $H_2$, Adams' catalyst, EtOAc, 25 °C, 3 h (100%); (j) 4.2 equiv of DIBAL, diethyl ether, 0 °C, 1.5 h (77%); (k) 2.6 equiv of NaH, 4.4 equiv of allyl bromide, DMF, 0–25 °C, 3 h (95%); (l) 4.4 equiv of *n*-$Bu_4NF$, THF, 25 °C, 3 h (90%); (m) 4.2 equiv of *s*-BuLi, 2.2 equiv of *n*-$Bu_3SnCl$, THF, −78 °C, 15 min (65%).

**Scheme 8**[a]



[a] Key: (a) 1.0 equiv of NMO, $OsO_4$ catalyst, THF:acetone:$H_2O$ (1:1:1), 25 °C, 12 h (93%); (b) 2.4 equiv of *t*-$BuMe_2SiCl$, 5.0 equiv of imidazole, DMF, 25 °C, 12 h (96%); (c) 5.0 equiv of NMO, $OsO_4$ catalyst, THF:acetone (1:1), 25 °C, 12 h (97%); (d) (i) 1.0 equiv of $NaIO_4$, acetone:$H_2O$ (4:1), 0–25 °C, 1.5 h; (ii) 2.0 equiv of DIBAL, diethyl ether, 0 °C, 1 h (83%); (e) 2.4 equiv of NaH, 4.4 equiv of allyl bromide, DMF, 0–25 °C, 3 h (95%); (f) 4.0 equiv of *n*-$Bu_4NF$, THF, 25 °C, 3 h (95%); (g) 4.3 equiv of *s*-BuLi, 2.2 equiv of *n*-$Bu_3SnCl$, THF, −78 °C, 10 min (65%); (h) 1.2 equiv of $NaIO_4$, acetone:$H_2O$ (4:1), 0–25 °C, 3 h (91%); (i) 4.0 equiv of NaH, 4.0 equiv of $(MeO)_2P(O)CH_2CO_2Me$, benzene, 25 °C, 1 h (82%); (j) $H_2$, Adams' catalyst, EtOAc, 25 °C, 3 h (100%); (k) 4.0 equiv of DIBAL, diethyl ether, 0 °C, 1 h (79%); (l) 2.6 equiv of NaH, 4.4 equiv of allyl bromide, DMF, 0–25 °C, 3.5 h (94%); (m) 4.0 equiv of *n*-$Bu_4NF$, THF, 25 °C, 2.5 h (95%); (n) 4.2 equiv of *s*-BuLi, 2.2 equiv of *n*-$Bu_3SnCl$, THF, −78 °C, 10 min (60%).

includes *vic*-diol fragmentation and Lewis acid-induced cyclization of the resulting aldehyde–allylic tin system.

The syntheses of a γ-alkoxy allylstannanes (**59**) are summarized in Schemes 7 and 8. Experimental data for these compounds are included in the supplementary material.

The depicted stereochemistry for compounds **60a–d** was supported by the coupling constants between the C-2 and C-3 protons determined by analysis of the $^1H$ NMR spectra of their *p*-bromobenzoate derivatives. The formation of the trans-substituted oxepane (**60c**) and oxane (**60b**) was further confirmed by $^1H$ NMR studies on their reaction products **92–94** and **104–106**, respectively. The coupling constants $J_{ab}$ are given in Table 1.

The foregoing examples reflect conformational preferences in the $S_{E'}$ transition state which are a composite of conformational constraints and electronic effects.[43] Although the reason for the observed *cis*-stereoselectivity

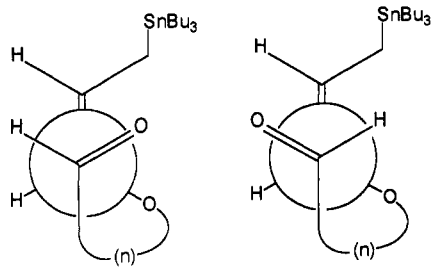
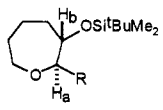
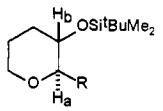



**Figure 3.** Predicted stereochemical course of syn $S_{E'}$ intramolecular addition of γ-alkoxy-substituted allylstannane to an aldehyde carbonyl group.

**Table 1. $^1$H-NMR Data: Coupling Constants**

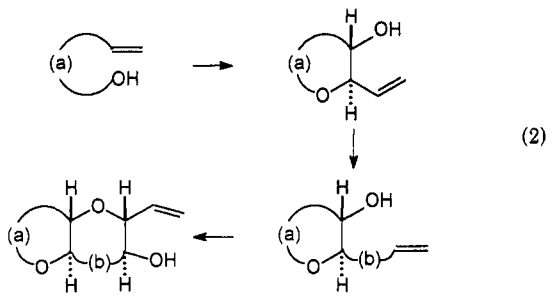



| compd | $J_{ab}$ (Hz) | compd | $J_{ab}$ (Hz) |
|---|---|---|---|
| **92**: R = $CH_2OH$ | 7.5 | **104**: R = $CH_2OH$ | 8.5 |
| **93**: R = $CH_2I$ | 7.0 | **105**: R = $CH_2I$ | 8.5 |
| **94**: R = $(CH_2)_2$-CH=$CH_2$ | 7.2 | **106**: R = $(CH_2)_2$-CH=$CH_2$ | 8.9 |

between the α-vinyl and β-hydroxy groups in oxolane **60a** is not fully understood, the thermodynamically more stable *trans* hydroxy–vinyl arrangement observed in the series **60b–d** indicates a marked preference for the less crowded and more flexible synclinal transition state of type B (Figure 3).[44] The transition-state structure required for the intramolecular reaction seems then to be fundamentally related to the length of the connecting chain.

This reaction was of particular interest to us in the context of *trans*-fused polyether synthesis as is shown in eq 2 since the resulting cyclization compound is a latent version of what one starts with. That is, if one inspects the monocyclic compound in eq 2, it can readily be seen that protection of the free hydroxyl group followed by homologation of the vinyl appendage regenerates the initial conditions for continuing with the cyclization process.




(2)

**One-Directional Polycyclization Strategy.** In order to explore the scope of the ideas outlined above in the construction of bicyclic systems, we synthesized the substrates shown in Schemes 9 and 10 and investigated their acid-catalyzed cyclizations. The results are quite interesting and led to the selective syntheses of the *trans*-fused oxepane–oxepanyl and oxane–oxepanyl substructures **101** (Scheme 9) and **113** (Scheme 10), respectively. The synthesis of **101** started with the acetate of 5-hexen-1-ol which was oxidized at the terminal double bond to its corresponding *vic*-diol and converted to the acetonide **85** in 86% yield. Base-hydrolysis and subsequent allylation gave the allyl ether **87**. Hydrolysis of the acetonide followed by lithiation and trapping with *n*-$Bu_3SnCl$ gave **89** in 49% yield. Cyclization, after *n*-$Bu_4NIO_4$ fragmentation, proceeded smoothly in the presence of $BF_3$·$OEt_2$ to give **60c** in 70% yield. Alkenyl **94** was prepared from **60c** in five straightforward steps via silylation of the free hydroxyl group in **60c** to give **90**, vinyl fragmentation continued by reduction of the resulting aldehyde from **90** to yield **92** via **91**, and iodination[45] followed by the Keck allyl radical coupling procedure[46] to afford the two-carbon homologated alkenyl **94** (30% overall yield from **60c**). Transformation of the alkenyl side chain in **94** and allylation of the ring hydroxyl by iterative application of the already described methodology gave **100** which was cyclized to the fused oxepane–oxepanyl system **101** in 98% yield. The syn relationship of the newly implanted $H_b$ proton with the $H_c$ was assigned on the basis of NOE studies of their *p*-bromobenzoate (**101**, X = BrBz), prepared under standard conditions. Thus, irradiation of the proton $H_b$ signal (400 MHz, $CDCl_3$, δ 4.13) resulted in a 12% enhancement of the $H_c$ proton signal (δ 3.51). The trans stereochemistry of the $H_a/H_b$ junction in **101**, X = BrBz, was based on the coupling constant $J_{a,b}$ = 6.6 Hz determined by $^1$HNMR decoupling experiments.

A similar procedure was followed for the synthesis of the *trans*-fused oxane–oxepanyl system **113** (Scheme 10). Tri-*O*-acetyl-D-glucal (**46**) was converted into diol **102** according to the literature procedure.[13o] Racemic diol **102** was also easily formed from **60b** via vinyl fragmentation followed by reduction of the resulting aldehyde. Selective silyl deprotection of the primary hydroxyl gave **104** which was iodinated and submitted to allyl radical coupling to afford **106**. Alkenyl **106** was transformed to compounds **107–112** by methods analogous to those employed in the previously described oxepanyl homologues. Acid-induced cyclization of **112** to **113** was finally accomplished in 70% yield. The *trans,syn,trans* stereochemistry shown in **113** was assigned by one-dimensional NOE difference techniques (NOE between $H_b$ and $H_c$ protons ca. 20%, $J_{ab}$ = 7.3 Hz).

These results demonstrate the viability of utilizing this methodology in a reiterative manner since the required *trans,syn,trans* stereochemistry is generated through the more favorable transition state of type B (Figure 3), independently of the size of the ring (6 or 7) supporting the cyclized appendages. Applications of this technology to substructures of *trans*-fused marine natural toxins have, therefore, considerable potential. Similar results have been published recently by Yamamoto et al.[13u]

**Two-Directional Polycyclization Strategy.** As an extension of this methodology in a two-directional way,

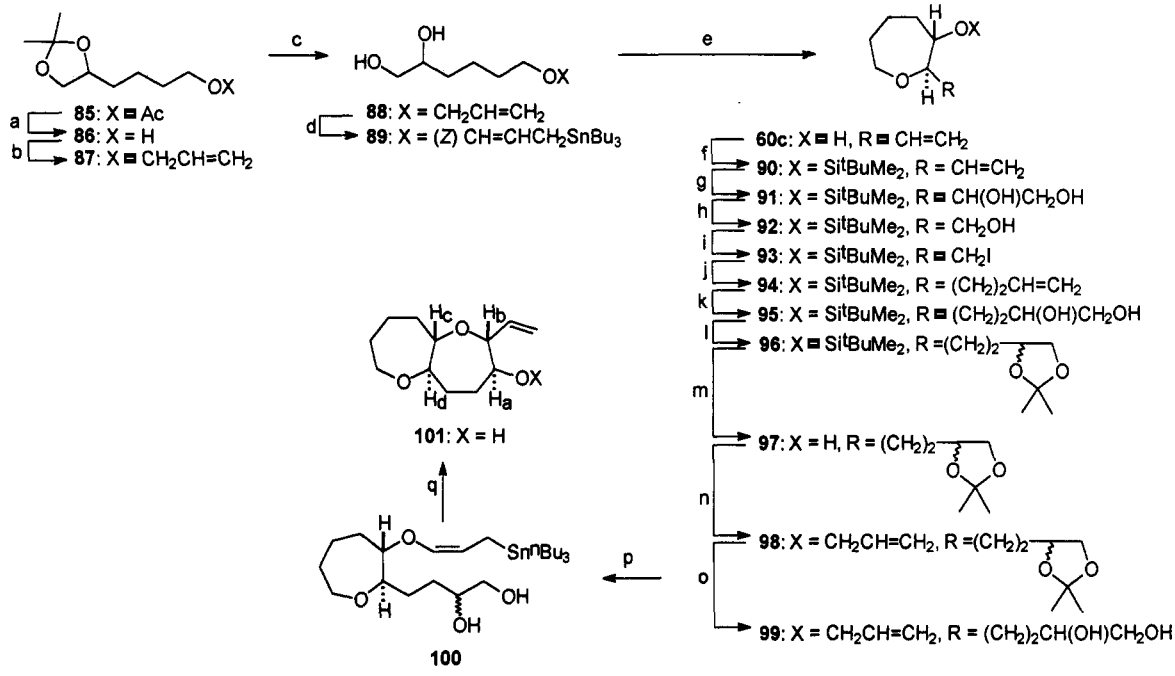
(43) For mechanistic investigation on $S_{E'}$ additions of allyltin to aldehydes, see: Gung, B. W.; Peat, A. J.; Snook, B. M.; Smith, D. T. *Tetrahedron Lett.* **1991**, *32*, 453. Ganis, P.; Furlani, D.; Marton, D.; Tagliavili, G.; Valle, G. *J. Organomet. Chem.* **1985**, *293*, 207. Denmark, S. E.; Weber, E. J. *J. Am. Chem. Soc.* **1984**, *106*, 7970. Dumartin, G.; Quintard, J. P.; Pereyre, M. *J. Organomet. Chem.* **1983**, *252*, 37. Wickham, G.; Young, D.; Kitching, W. *J. Org. Chem.* **1982**, *47*, 4884. Yamamoto, Y.; Yatagai, H.; Naruta, Y.; Muruyama, K. *J. Am. Chem. Soc.* **1980**, *102*, 7107.

(44) For the transition-state geometry for intramolecular allylic tin cyclization, see: Denmark, S. E.; Wilson, T. M. In *Selectivities in Lewis Acid Promoted Reactions*; Schinzer, E., Ed.; NATO ASI Series; Klumer Academic Publishers: Dodrecht, 1989; p 247. Denmark, S. E.; Wilson, T. M. *J. Am. Chem. Soc.* **1989**, *111*, 3475.

(45) Garegg, P. J.; Samuelson, D. *J. Chem. Soc., Perkin Trans. 1* **1980**, 2866.

(46) Keck, G. E.; Enholm, E. J.; Yates, J. B.; Wiley, M. R. *Tetrahedron* **1985**, *41*, 4079.

**Scheme 9**[a]




[a] Key: (a) 2.0 equiv of $K_2CO_3$, acetone:MeOH (4:1), 25 °C, 3 h (96%); (b) 1.3 equiv of NaH, 2.2 equiv of allyl bromide, DMF, 25 °C, 3 h (89%); (c) CSA catalyst, MeOH, 25 °C, 15 min (97%); (d) 3.2 equiv of *s*-BuLi, 1.1 equiv of $Bu_3SnCl$, THF, −78 °C, 15 min (50%); (e) 1.5 equiv of *n*-$Bu_4NIO_4$, $CH_2Cl_2$, 0–25 °C, 3 h, then add 2.0 equiv of $BF_3{\cdot}OEt_2$, −78 °C, 5 min (70%); (f) 1.4 equiv of *t*-$BuMe_2SiOTf$, 2.0 equiv of $Et_3N$, $CH_2Cl_2$, 0 °C, 15 min (70%); (g) 3.0 equiv of 4-methylmorpholine *N*-oxide, $OsO_4$ catalyst, THF:acetone (1:1), 25 °C, 4 h (85%); (h) 1.5 equiv of $NaIO_4$, MeOH:$H_2O$ (8:1), 0 °C, 10 min, then add 4.0 equiv of $NaBH_4$, 25 °C, 30 min (77%); (i) 2.0 equiv of $I_2$, 3.0 equiv of $Ph_3P$, 1.2 equiv of imidazole, 10 °C, 3 h (95%); (j) 2.0 equiv of allyltributyltin, 0.3 equiv of AIBN, benzene, reflux, 5 h (70%); (k) 3.0 equiv of NMO, $OsO_4$ catalyst, THF:acetone (1:1), 25 °C, 5 h (85%); (l) 4.0 equiv of 2,2-dimethoxypropane, CSA catalyst, $CH_2Cl_2$, 25 °C, 15 min (90%); (m) 2.0 equiv of $Bu_4NF$, THF, 25 °C, 3 h (87%); (n) 1.3 equiv of NaH, 2.2 equiv of allyl bromide, DMF, 0–25 °C, 15 min (85%); (o) CSA catalyst, MeOH, 25 °C, 15 min (95%); (p) 3.2 equiv of *s*-BuLi, 1.1 equiv of $Bu_3SnCl$, THF, −78 °C, 10 min (70%); (q) 1.5 equiv of *n*-$Bu_4NIO_4$, $CH_2Cl_2$, 0–25 °C, 2.5 h, then add 2.0 equiv of $BF_3{\cdot}OEt_2$, −78 °C, 3 min (98%).

we describe in Scheme 11 the synthesis of the conveniently functionalized oxocene–oxane–oxepane subunit **135** by two simultaneous one-carbon homologations culminating in the generation of both external rings of the tricyclic system by a one-pot double carbon–carbon bond-forming strategy. The stereocontrolled preparation of these materials via simultaneous heterocyclization in two directions is attractive since the number of transformations can be reduced in relation to the one-directional cyclization process. However, the termini of the newly synthesized oxacycles will require chemical differentiation.

Scheme 11 depicts our adopted strategy, which relies on the premise of final differentiation of the two hydroxy groups in **135**. Selective transformations led efficiently to the intermediate **136** or **138** equipped with suitable features for further heterocyclization in one- or two-directional ways in accordance with the methodology described above.

Iodine-induced cyclization of the readily available epoxy acetate **119**, prepared from the triene **118**,[20c] followed by base-induced hydrolysis gave the iodo ether **120** in 66% yield. Treatment of the oxa-bridged bicycle **120** with AgOAc in a refluxing mixture of 1% AcOH in chloroform furnished the diacetate **124** in 89% yield, which possesses an oxygenated pattern identical with that found in trans-fused polyether toxins. The replacement of iodine by oxygen with concomitant five- to six-O-ring enlargement was based on previous observations in these laboratories[20j] and is believed to take place through the intermediation of the two consecutive oxocarbenium ions **121** and **123**.[20j]

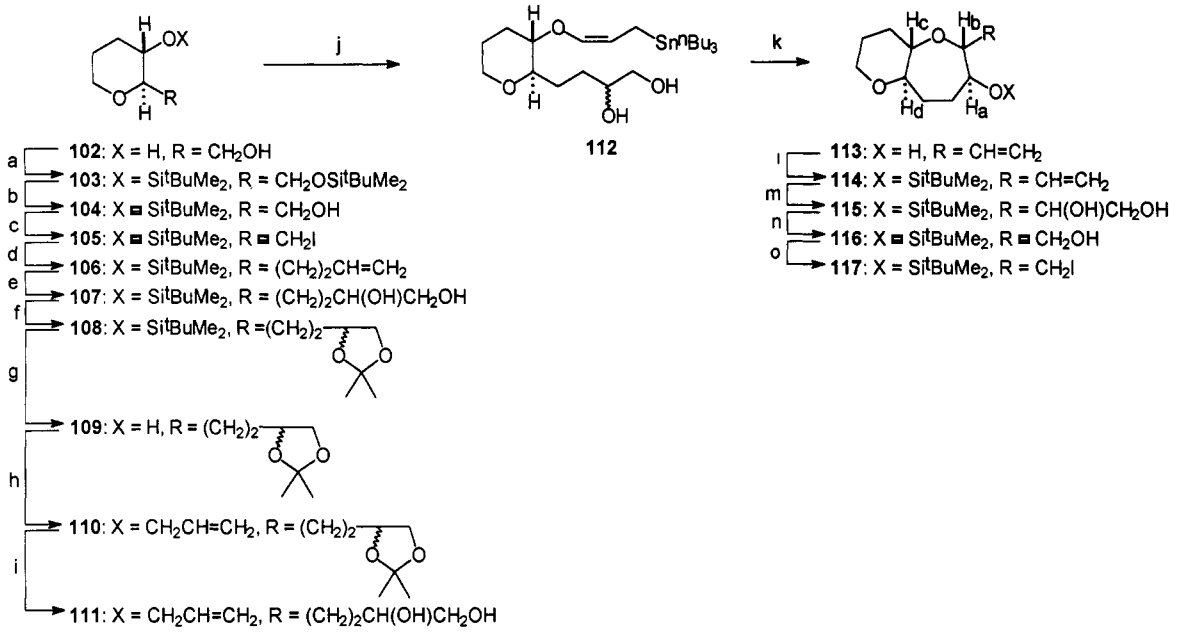
The subsequent synthetic operations required the following: (i) mesylation of the hydroxyl group in **124** to give **125**, (ii) mild hydrolysis of the acetyl group in **125** to afford **126**, and (iii) silylation of **126** to give **127**. *cis*-Hydroxylation with $OsO_4$–NMO converted **127** into a 3:1 mixture of $\alpha$:$\beta$ *vic*-diols **128ab** which was submitted to base-induced removal of the methanesulfonate to give **129a,b**, further converted to the acetonide **130a,b**. Removal of the silyl groups and subsequent allylation gave the allyl ether **132a,b**. Hydrolysis of the acetonide in **132a,b** followed by lithiation and trapping with *n*-$Bu_3SnCl$ gave **134a,b**. The double intramolecular alkylation to give **135** was accomplished by *vic*-diol fragmentation with *n*-$BuNIO_4$ followed by treatment with $BF_3{\cdot}OEt_2$ to afford **135** in 63% yield. The different steric environment of the two hydroxyl groups in **135** allowed selective acylation to yield the mono *p*-bromobenzoate **136**. Mild hydrolysis of the bis-*p*-bromobenzoate **137** gave the mono ester **138** exclusively.

The manner of fusion and stereochemistry of the ether rings in **135** were clarified on the basis of ROESY data (Figure 4) and $J_{H,H}$ (Table 2) determined on the bis(*p*-bromobenzoate) **137**. Prominent cross peaks in the ROESY of **137** were observed on $H_3/H_8$, $H_7/H_{11}$, $H_{10}/H_{16}$, and $H_{11}/H_{14\beta}$. Coupling constants between angular methines ($H_3/H_4$, $H_7/H_8$, $H_{10}/H_{11}$, and $H_{15}/H_{16}$) were around 9 Hz (Table 2), which was the typical value for interaction between antiperiplanar oxymethines, indicating a *trans*-fusing manner for all ether rings.

## Conclusion

We have pointed out in this paper that transannular epoxide-ring enlargements on epoxide-ring enlargements

**Scheme 10**[a]




[a] Key: (a) 2.2 equiv of *t*-BuMe$_2$SiCl, 2.5 equiv of imidazole, DMF, 45 °C, 12 h (92%); (b) 14.0 equiv of trifluoroacetic acid, THF:H$_2$O (1:1), 0 °C, 5 min (72%); (c) 2.0 equiv of I$_2$, 3.0 equiv of Ph$_3$P, 1.2 equiv of imidazole, 10 °C, 3.5 h (95%); (d) 2.0 equiv of allyltributyltin, 0.3 equiv of AIBN, benzene, reflux, 5.5 h (70%); (e) 3.0 equiv of NMO, OsO$_4$ catalyst, THF:acetone (1:1), 25 °C, 6 h (90%); (f) 4.0 equiv of 2,2-dimethoxypropane, CSA catalyst, CH$_2$Cl$_2$, 25 °C, 20 min (90%); (g) 2.1 equiv of Bu$_4$NF, THF, 25 °C, 3.5 h (85%); (h) 1.3 equiv of NaH, 2.2 equiv of allyl bromide, DMF, 0–25 °C, 15 min (85%); (i) CSA catalyst, MeOH, 25 °C, 15 min (70%); (j) 3.2 equiv of *s*-BuLi, 1.1 equiv of Bu$_3$SnCl, THF, −78 °C, 12 min (66%); (k) 1.5 equiv of *n*-Bu$_4$NIO$_4$, CH$_2$Cl$_2$, 0–25 °C, 3 h, then add 2.0 equiv of BF$_3$·OEt$_2$, −78 °C, 3 min (65%); (l) 1.5 equiv of *t*-BuMe$_2$SiOTf, 2.0 equiv of Et$_3$N, CH$_2$Cl$_2$, 0 °C, 15 min (96%); (m) 3.0 equiv of 4-methylmorpholine *N*-oxide, OsO$_4$ catalyst, THF:acetone (1:1), 25 °C, 3.5 h (92%); (n) 1.5 equiv of NaIO$_4$, MeOH:H$_2$O (8:1), 0 °C, 10 min, then add 4.0 equiv of NaBH$_4$, 25 °C, 30 min (82%); (o) 2.0 equiv of I$_2$, 3.0 equiv of Ph$_3$P, 1.2 equiv of imidazole, 10 °C, 3.5 h (97%).

on epoxycycloalkenes represent a powerful approach to the construction of bridged oxacyclic molecules. The details given here demonstrate the power of this methodology in the particular synthesis of *trans*-fused O-heterocyclic systems present in many bioactive natural products, including ciguatoxin and brevetoxins. The syntheses include new technologies for the construction of medium-size oxacycles via organostannanes and follow a highly economical strategy.

In seeking to apply the two-directional pathway, one quickly realizes that few compounds of interest have the symmetry required for the strict application of this advantage, but it can undoubtedly be a useful tool for the synthesis of elaborated *subunits* of general applicability in the convergent synthesis of natural polyethers. It is expected that the reported methodology will be usefully applied to the synthesis of natural and designed molecules. Such applications are currently being tested in these laboratories.

## Experimental Section

**General Methods.** NMR spectra were recorded on a Bruker WP 200SY or AMX-400 MHz instrument. IR spectra were recorded on a Perkin-Elmer 257 or 1605 Series FT-IR infrared spectrophotometer UV spectra were taken on a Perkin-Elmer 402 instrument. High-resolution mass spectra (HRMS) were recorded on a VG Micromass ZAB-2F spectrometer. Melting points were determined on a Buchi 241 apparatus and are uncorrected. Optical rotations were measured on a Perkin-Elmer Model 241 polarimeter. GLC was carried out using an HP Model 5790A or 5890 gas chromatograph, SGE capillary column, OV-101, 25- × 0.22-mm i.d.

Flash column chromatography was carried out with E. Merck silica gel (60, particle size 0.040–0.063 mm). All chromatographic separations were monitored by TLC analyses, conducted on 0.25-nm E. Merck silica gel plates (60F-254) using UV light (254 nm) and 10% ethanolic phosphomolybdic acid or H$_2$O:H$_2$SO$_4$:EtOAc (1:4:20) solution and heat as developing agent. Preparative thin-layer chromatography was performed on 0.5 or 0.25-mm × 20-cm × 20-cm E. Merck silica gel plates (60F-254). Yields are reported for chromatographically and spectroscopically ($^1$H- and $^{13}$C-NMR) pure compounds.

Lipase AK derived from *Pseudomonas sp* (PR-14) was obtained from Amano International Enzyme Co., Frankfurt (Germany), and PLE esterase (EC 3.1.1.1), lot no 29F8055, was purchased from Sigma Corp., St. Louis, MO, and both were used as received. Preparative-scale enzyme-mediated hydrolysis was made with the aid of a pH-stat.

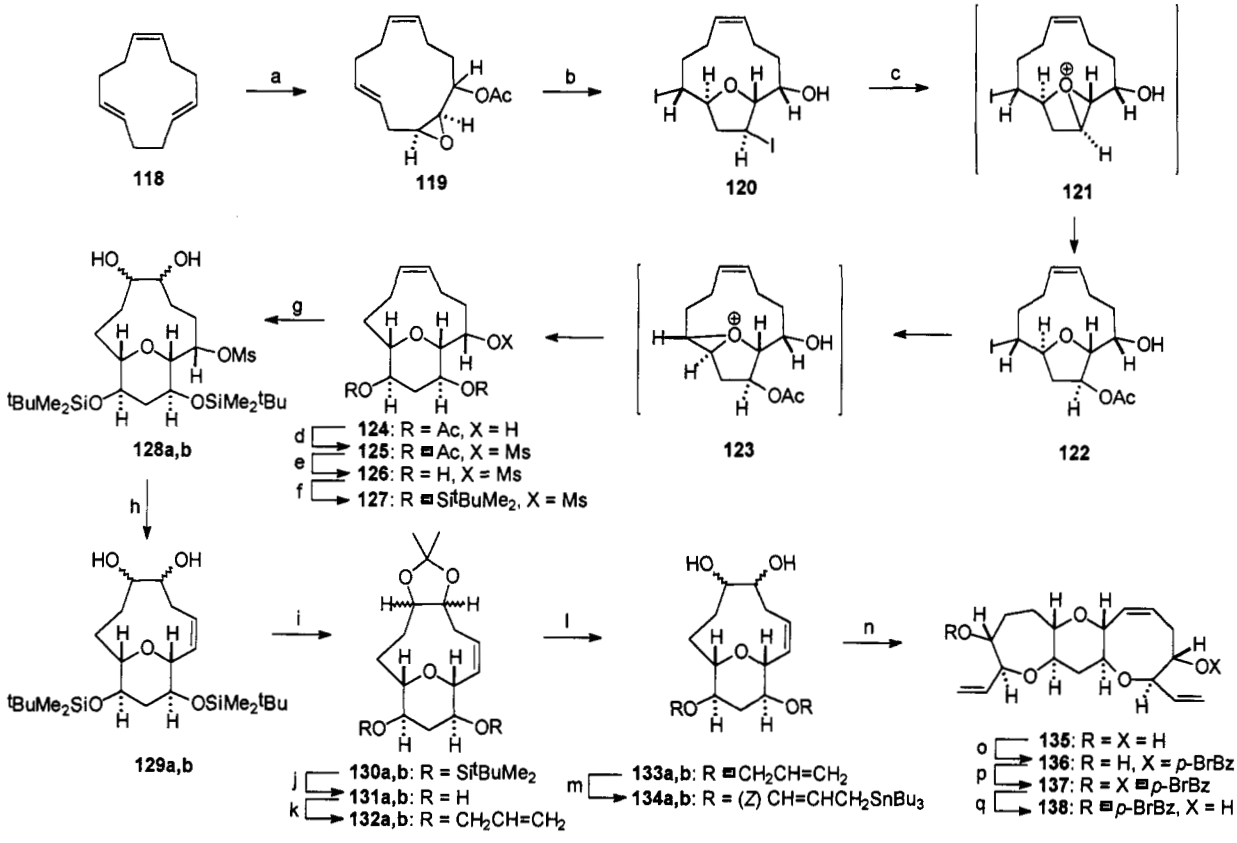
All reactions were carried out under argon atmosphere with dry, freshly distilled solvents under anhydrous conditions unless otherwise stated.

Experimental procedures for compounds **59** ($n$ = 0–3) and **61–84** are given in the supplementary material.

**2,6-Cyclooctadien-1-ol (14).**[47] In a preparative-scale experiment 172 mL (1.4 mol) of 1,5-cyclooctadiene, 48 mL (0.8 mol) of AcOH, 56 mL (0.28 mol) of *t*-BuOOH in isooctane (5 M), and 280 mg (2.8 mmol) of copper(I) chloride were refluxed gently for 52 h. Gas–liquid chromatographic analysis showed *t*-BuOH and an 82% yield of 2,6-cyclooctadien-1-yl acetate (**13**). Dilution with ether (200 mL) followed by washing with H$_2$O (2 × 60 mL) and brine (60 mL), drying (MgSO$_4$), and concentration gave an oil which was treated with K$_2$CO$_3$ (41 g, 0.3 mol) and MeOH (250 mL) and stirred at 25 °C for 12 h. Dilution with ether (400 mL) and petroleum ether (400 mL) followed by filtration through a Celite pad and concentration gave the dienol **14** (142.4 g, 100%) (82% overall from **12**). **14**: oil; $R_f$ = 0.42 (silica, 15% ether in petroleum ether); $^1$H NMR (200 MHz, CDCl$_3$) δ 5.56 (m, 4H), 4.88 (m, 1H), 2.71 (m, 2H), 2.26 (m, 4H), 1.83 (m, 1H); $^{13}$C NMR (CDCl$_3$) δ 133.4 (d), 129.0 (d), 128.9 (d), 125.9 (d), 69.0 (d), 37.0 (t), 27.9 (t), 27.6 (t). Anal. Calcd for C$_8$H$_{12}$O: C, 77.42; H, 9.68. Found: C, 77.54; H, 10.01.

(47) Walling, C.; Zaritsas, A. *J. Am. Chem. Soc.* **1963**, *85*, 2084. Cantrell, T. S.; Salomon, J. S. *J. Am. Chem. Soc.* **1970**, *92*, 4656.

**Scheme 11**[a]




[a] Key: (a) ref 20c; (b) (i) 2.4 equiv of $I_2$, $CH_2Cl_2$, 25 °C, 6 h; (ii) 2.0 equiv of $K_2CO_3$, MeOH:acetone (1:1), 25 °C, 1 h (66%); (c) 2.5 equiv of AgOAc, $CHCl_3$:AcOH (110:1), reflux, 12 h (89%); (d) 2.0 equiv of MsCl, pyridine, 0–40 °C, 4 h (90%); (e) 3.0 equiv of $K_2CO_3$, MeOH:acetone (1:10), 25 °C, 1 h (96%); (f) 2.8 equiv of *t*-BuMe$_2$SiOTf, 4.0 equiv of $Et_3N$, $CH_2Cl_2$, 0 °C, 30 min (97%); (g) 33.8 (equiv of 4-methylmorpholine *N*-oxide, $OsO_4$ catalyst, THF:acetone (1:1), 12 h, 25 °C (90%) [ca. **128a** (5*S**,6*R** isomer):**128b** (5*R**,6*S** isomer), 3:1, stereoselectivity]; (h) 10.0 equiv of DBU, toluene, reflux, 12 h (79%); (i) 4.0 equiv of 2,2-dimethoxypropane, CSA catalyst, $CH_2Cl_2$, 25 °C, 15 min (99%); (j) 4.0 equiv of $Bu_4NF$, THF, 25 °C, 3 h (98%); (k) 2.6 equiv of NaH, DMF, 4.4 equiv of allyl bromide, 0–25 °C, 3 h (98%); (l) CSA catalyst, MeOH, 25 °C, 15 min (100%); (m) 4.4 equiv of *s*-BuLi, 2.4 equiv of $Bu_3SnCl$, THF, −78 °C, 40 min (79%); (n) (i) 2.0 equiv of $Bu_4NIO_4$, $CH_2Cl_2$, 25 °C, 3.5 h; (ii) 4.0 equiv of $BF_3$·$Et_2O$, $CH_2Cl_2$, −78 °C, 5 min (63%); (o) 2.0 equiv of BrBzCl, 3.0 equiv of DMAP, $CH_2Cl_2$, 25 °C, 3 h (77%); (p) 4.2 equiv of BrBzCl, 4.0 equiv of DMAP, $CH_2Cl_2$, 25 °C, 30 h (85%); (q) 0.5 equiv of $K_2CO_3$, MeOH, 25 °C, 1.5 h (96%).

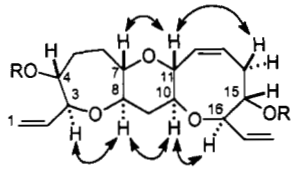



**Figure 4.** Structure of **137**. Arrows indicate the protons giving NOEs around the ether linkages by ROESY and NOE difference spectra in $CDCl_3$.

**(1*S**,2*S**,8*R**)-9-Oxabicyclo[6.1.0]non-4-en-2-ol (15).** In a preparative-scale experiment, *t*-BuOOH in isooctane (5 M) (240 mL, 1.2 mol) was added dropwise over a 30-min period to a stirred solution of the dienol **14** (124.0 g, 1.0 mol) and $VO(acac)_2$ (40 mg) in dry benzene (400 mL) at 25 °C. The mixture was allowed to react at 40 °C, and after 2 h the solvent was removed in vacuo and the residue was chromatographed (silica, 20% diethyl acetate in *n*-hexane) to afford the epoxylated alcohol **15** (110.6 g, 79%). **15**: oil; $R_f$ = 0.15 (silica, 30% EtOAc–hexane); IR ($CHCl_3$) $\nu_{max}$ 3578, 3025, 3013, 2947, 2902, 1698, 1662, 1487, 1456, 1431, 1404, 1373, 1036 cm$^{-1}$; $^1$H NMR (200 MHz, $CDCl_3$) $\delta$ 5.51 (m, 2H), 4.05 (br d, $J$ = 11.3 Hz, 1H), 3.21 (m, 2H), 2.49, 2.12 (m, 6H); $^{13}$C NMR ($CDCl_3$) $\delta$ 130.7 (d), 124.0 (d), 69.9 (d), 59.2 (d), 58.5 (d), 30.6 (t), 27.2 (t), 23.8 (t); MS *m/e* (rel intensity) 140 (M$^+$, 1), 122 (1), 96 (11), 79 (36), 71 (84), 57 (100); HRMS calcd for $C_8H_{10}O$ (M − $H_2O$)$^+$ 122.0732, found 122.0717.

**(1*S**,8*R**)-9-Oxabicyclo[6.1.0]non-4-en-2-one (16).** In a preparative-scale experiment. $SO_3$–py complex (240 g, 1.5 mol) was added to a stirred mixture of the epoxy alcohol **15** (100 g, 0.72 mol), triethylamine (660 mL, 4.7 mol), dry DMSO (480 mL, 6.8 mol), and $CH_2Cl_2$ (800 mL) at 0 °C. After 2 h, the reaction mixture was diluted with ether (500 mL), washed with $H_2O$ (3 × 200 mL) and brine (200 mL), dried ($MgSO_4$), and concentrated to furnish ketone **16** (83.8 g, 85%). **16**: oil; $R_f$ = 0.34 (silica, 10% EtOAc–hexane); IR ($CHCl_3$) $\nu_{max}$ 3020, 2945, 1692, 1460, 1415, 1365, 1295 cm$^{-1}$; $^1$H NMR (200 MHz, $CDCl_3$) $\delta$ 5.65 (m, 1H), 5.47 (ddd, $J$ = 10.4, 6.6, 6.6 Hz, 1H), 3.47 (ddd, $J$ = 14.1, 6.6, 1.5 Hz, 1H), 3.42 (dd, $J$ = 5.0, 0.9 Hz, 1H), 3.32 (ddd, $J$ = 5.0, 3.1, 3.0 Hz, 1H), 2.94 (dd, $J$ = 14.1, 6.6 Hz, 1H), 2.44–1.88 (m, 4H); $^{13}$C NMR ($CDCl_3$) $\delta$ 204.5 (s), 130.9 (d), 122.1 (d), 59.6 (d), 56.6 (d), 38.6 (t), 26.1 (t), 20.2 (t); MS *m/e* (rel intensity) 138 (M$^+$, 2), 121 (1), 109 (6), 95 (12), 81 (26), 67 (27), 54 (100); HRMS calcd for $C_8H_{10}O_2$ (M$^+$) 138.0681, found 138.0676. Anal. Calcd for $C_8H_{10}O_2$: C, 69.56; H, 7.25. Found: C, 69.42; H, 7.36.

**(1*R**,2*R**,5*S**,6*S**)-2,5-Diiodo-9-oxabicyclo[4.2.1]nonan-7-one (17).** In a preparative-scale experiment, resublimated iodine (182.7 g, 0.72 mol) was added to a stirred solution of ketone **16** (83.0 g, 0.6 mol) in dry $CH_2Cl_2$ (500 mL). After 12 h at 25 °C the reaction mixture was washed with $H_2O$ (2 × 100 mL) and brine (200 mL), dried ($MgSO_4$), and concentrated. The residue was chromatographed (silica, 8% ether in petroleum ether) to afford compound **17** (200.4 g, 85%). **17**: crystalline solid; mp 142–143 °C (hexane/EtOAc); IR (KBr) $\nu_{max}$ 3000, 2944, 2920, 1755, 1450, 1430, 1402, 1355, 1250, 1175, 1149, 1098, 1042 cm$^{-1}$; $^1$H NMR (200 MHz, $CDCl_3$) $\delta$ 4.90 (dddd, $J$ = 8.2, 4.0, 4.0, 1.2 Hz, 1H), 4.54 (dddd, $J$ = 8.5, 6.0, 3.0, 1.0 Hz, 1H), 4.42 (ddd, $J$ = 11.2, 4.2, 4.0 Hz, 1H), 4.02 (d, $J$ = 8.5 Hz, 1H), 2.88 (dd, $J$ = 19.5, 4.0 Hz, 1H), 2.80 (dd, $J$ = 19.5, 8.2 Hz, 1H), 2.48 (m, 1H), 2.36 (m, 1H), 2.22 (m, 1H), 1.93 (dddd, $J$ = 14.2, 11.2, 11.2, 1.2 Hz, 1H); $^{13}$C NMR

**Table 2. Selected $^1$H- and $^{13}$C-NMR Chemical Shifts ($\delta$)[a] and Coupling Constants[a] of 137**

| positn | $^1$H (pattern)[b] | $^{13}$C (pat.)[b] | positn | $^1$H (pattern) | $^{13}$C (pat.) | positn | $^1$H (pattern) | $^{13}$C (pat.) |
|---|---|---|---|---|---|---|---|---|
| 1 | 5.36 (br d, 17.2)<br>5.17 (br d, 10.6) | 116.5 (t) | 7 | 3.19 (9.6, 9.2, 4.4) | 81.4 (d) | 13 | 5.71 (br dd, 11.6, 9.4) | 125.7 (d) |
| 2 | 5.89 (17.2, 10.6, 5.3) | 136.4 (d) | 8 | 3.41 (13.5, 9.2, 4.4) | 79.3 (d) | 14 | 2.85 (13.6, 9.4, 3.5), 2.50 (br d, 13.6) | 24.8 (t) |
| 3 | 4.21 (5.3, 5.3) | 83.5 (d) | 9 | 2.53 (12.0, 4.6, 4.4)<br>1.73 (13.5, 13.2, 12.0) | 39.5 (t) | 15 | 5.12 (10.0, 4.0, 3.5) | 77.6 (d) |
| 4 | 5.23 (m)[c] | 76.8 (d) | 10 | 3.32 (13.2, 9.2, 4.6) | 80.5 (d) | 16 | 4.14 (10.0, 5.0) | 80.1 (d) |
| 5 | 2.00 (m)[c]<br>2.00 (m)[c] | 30.3 (t) | 11 | 4.02 (11.6, 9.2) | 79.7 (d) | 17 | 5.80 (16.8, 10.4, 5.0) | 136.6 (d) |
| 6 | 1.90 (m)[c]<br>1.88 (m)[c] | 27.4 (t) | 12 | 5.84 (br dd, 11.6, 11.6) | 135.5 (d) | 18 | 5.28 (br d, 16.8)<br>5.10 (br d, 10.4) | 116.4 (t) |

[a] $^1$H- and $^{13}$C-NMR spectra were measured with a 400-MHz spectrometer in $CDCl_3$. [b] Multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet) and coupling constants in Hz. [c] Couplings could not be assigned due to heavy signal overlapping.

($CDCl_3$) $\delta$ 209.9 (s), 80.3 (d), 78.7 (d), 39.2 (t), 38.1 (t), 32.8 (t), 31.6 (d), 24.6 (d); MS *m/e* (rel intensity) 392 ($M^+$, 45), 265 (100), 137 (52), 109 (50), 81 (55), 67 (80); HRMS calcd for $C_8H_{10}I_2O_2$ ($M^+$) 391.8688, found 391.8642. Anal. Calcd for $C_8H_{10}I_2O_2$: C, 24.49; H, 2.55. Found: C, 24.63; H, 2.70.

**(1*R**,2*R**,5*S**,6*S**)-7-(*tert*-Butyldimethylsiloxy)-2,5-diiodo-9-oxabicyclo[4.2.1]non-7-ene (18).** To a stirred mixture of the ketone 17 (777 mg, 2.0 mmol), triethylamine (1.66 mL, 11.8 mmol), and dry $CH_2Cl_2$ (10 mL) was added TBDMSOTf (1.0 mL, 4.4 mmol). After 9 h at 25 °C the reaction was quenched with ether (25 mL) followed by washing with $H_2O$ (2 × 25 mL) and brine (25 mL). Drying ($MgSO_4$), concentration, and flash chromatography (silica, 5% ether in petroleum ether) gave the vinyl silyl ether 18 (981 mg, 98%). 18: oil; $R_f$ = 0.63 (silica, 5% EtOAc–hexane); IR ($CHCl_3$) $\nu_{max}$ 3006, 2957, 2931, 2899, 2859, 1655, 1256, 1238, 1051, 1011 cm$^{-1}$; $^1$H NMR (200 MHz, $CDCl_3$) $\delta$ 5.27 (d, *J* = 2.1 Hz, 1H), 4.91 (dd, *J* = 5.9, 2.3 Hz, 1H), 4.49 (m, 2H), 4.28 (m, 1H), 2.32 (m, 4H), 0.99 (s, 9H), 0.32 (s, 3H), 0.27 (s, 3H); $^{13}$C NMR ($CDCl_3$) $\delta$ 154.0 (s), 103.6 (d), 84.6 (d), 84.0 (d), 37.3 (d), 34.7 (d), 34.0 (d), 26.1 (d), 26.0 (q), 18.2 (s), −4.5 (q), −4.7 (q); MS *m/e* (rel intensity) 506 ($M^+$, 1), 449 (10), 379 (96), 322 (4), 224 (4), 189 (22), 147 (95), 73 (100); HRMS calcd for $C_{10}H_{16}I_2O_2Si$ (M + H − *t*-Bu)$^+$ 449.9009, found 449.9008.

**(1*S**,2*S**,5*R**,6*R**,7*S**,8*R**)-8-(*tert*-Butyldimethylsiloxy)-2,5-diiodo-9-oxabicyclo[4.2.1]nonan-7-ol (19).** To a stirred solution of the cyclic enol ether 18 (318 mg, 0.63 mmol) in dry THF (1 mL) at 0 °C was added $BH_3$·$Me_2S$ (0.38 mL, 0.75 mmol, 2 M in THF) dropwise over a 5-min period. After the solution was stirred for 12 h at 25 °C, the excess borane was quenched carefully with $H_2O$ (0.5 mL). Dropwise addition of a mixture of 3 N NaOH (0.7 mL, 2.10 mmol) and 30% $H_2O_2$ (0.20 mL, 3.1 mmol) over 5 min and continued stirring for 2 h at 40 °C resulted in a white heterogeneous mixture. Dilution with ether (20 mL), followed by washing with $H_2O$ (2 × 20 mL) and brine (20 mL), drying ($MgSO_4$), concentration, and flash chromatography (silica, 15–20% ether in petroleum ether) produced alcohol 19 (270 mg, 82%). 19: noncrystalline solid; $R_f$ = 0.33 (silica, 10% EtOAc–hexane); IR ($CHCl_3$) $\nu_{max}$ 3592, 2952, 2930, 2857, 1462, 1361, 1214, 1132 cm$^{-1}$; $^1$H NMR (200 MHz, $C_6D_6$) $\delta$ 4.59 (m, 1H), 4.45 (m, 2H), 4.04 (dd, *J* = 6.1, 3.6 Hz, 1H), 3.90 (dd, *J* = 6.1, 3.2 Hz, 1H), 3.69 (br d, *J* = 11.5 Hz, 1H), 2.12 (m, 1H), 1.89 (m, 3H), 1.02 (s, 9H), 0.21 (s, 3H), 0.19 (s, 3H); $^{13}$C NMR ($C_6D_6$) $\delta$ 87.7 (d), 84.1 (d), 82.6 (d), 80.7 (d), 38.5 (t), 33.7 (t), 30.6 (d), 26.4 (q), 23.6 (d), 18.5 (s), −3.9 (q), −4.4 (q); MS *m/e* (rel intensity) 467 [(M − *t*-Bu)$^+$, 6], 340 (8), 213 (14), 75 (100); HRMS calcd for $C_{10}H_{18}I_2O_3Si$ (M + H − *t*-Bu)$^+$ 467.9115, found 467.9124.

**(1*S**,2*S**,5*R**,6*R**,8*S**)-8-(*tert*-Butyldimethylsiloxy)-2,5-diiodo-9-oxabicyclo[4.2.1]nonan-7-one (20).** To a cold (−78 °C) stirred solution of oxalyl chloride (11.5 mL, 131.5 mmol) in $CH_2Cl_2$ (120 mL) freshly distilled from $CaH_2$ under argon was added DMSO (28 mL, 395 mmol. After the solution was stirred for 10 min, the alcohol 19 (23.0 g, 43.9 mmol) in $CH_2Cl_2$ (100 mL) was added dropwise at −78 °C, and the mixture was stirred at that temperature for 30 min. Triethylamine (92 mL, 658.4 mmol) was then added dropwise, and the reaction mixture was allowed to warm to 0 °C while being stirred. After 20 min, the reaction mixture was poured onto a mixture of saturated aqueous $NH_4Cl$ solution (500 mL) and ether (1 L). Shaking and separation of the organic layer were followed by washing with $H_2O$ (2 × 500 mL) and brine (500 mL) and drying ($MgSO_4$). Evaporation of the solvent under vacuum afforded essentially pure ketone 20 (22.4 g, 98%) which was used for the next step without further purification. 20: crystalline solid, mp 53–54 °C (*n*-hexane); $R_f$ = 0.61 (silica, 5% EtOAc–hexane); IR ($CHCl_3$) $\nu_{max}$ 2953, 2930, 2858, 1774, 1463, 1362, 1260, 1215, 1150, 1133 cm$^{-1}$; $^1$H NMR (200 MHz, $CDCl_3$) $\delta$ 4.79 (dd, *J* = 7.7, 2.8 Hz, 1H), 4.60 (dd, *J* = 7.7, 1.4 Hz, 1H), 4.44 (ddd, *J* = 7.7, 5.7, 4.2 Hz, 1H), 4.33 (dd, *J* = 5.7, 1.4 Hz, 1H), 4.14 (ddd, *J* = 12.0, 6.0, 2.8 Hz, 1H), 2.41 (m, 2H), 2.19 (m, 2H), 0.98 (s, 9H), 1.98, 0.22 (s, 3H each); $^{13}$C NMR ($CDCl_3$) $\delta$ 210.4 (s), 78.9 (d), 77.6 (d), 75.3 (d), 38.2 (t), 32.9 (t), 26.4 (q), 23.2 (d), 22.5 (d), 18.7 (s), −4.05 (q), −4.2 (q); MS *m/e* (rel intensity) 523 (M − 1, 2), 465 (16), 380 (1), 338 (87), 281 (5), 183 (50), 155 (22), 73 (100); HRMS calcd for $C_{14}H_{25}I_2O_3Si_2$ (M − H)$^+$ 522.9654, found 522.9681.

**(1*S**,2*S**,5*R**,6*R**,7*R**,8*R**)-7-(*tert*-Butyldimethylsiloxy)-2,5-diiodo-9-oxabicyclo[4.2.1]nonan-7-ol (21).** To a stirred solution of ketone 20 (20.0 g, 38.3 mmol) in THF (40 mL) was added $NaBH_4$ (6.5 g, 172.3 mmol). When monitoring of the reaction by TLC indicated that all starting material had been consumed (ca. 12 h at 25 °C), the quenched reaction mixture was taken with 5% aqueous HCl solution (100 mL) and the separated aqueous phase was extracted with ether (3 × 50 mL). The combined organic layers were washed with 5% $NaHCO_3$ solution (150 mL) and water (150 mL). The organic phase was dried over $MgSO_4$ and concentrated to give 21 (18.4 g, 90%). 21: noncrystalline solid; $R_f$ = 0.33 (silica, 5% EtOAc–hexane); IR ($CHCl_3$) $\nu_{max}$ 3494, 3008, 2954, 2931, 2859, 1471, 1464, 1391, 1363, 1256, 1161, 1131, 1046, 1012 cm$^{-1}$; $^1$H NMR (200 MHz, $CDCl_3$) $\delta$ 4.63 (dd, *J* = 7.4, 4.0 Hz, 1H), 4.53 (dd, *J* = 6.1, 2.8 Hz, 1H), 4.42 (m, 2H), 4.33 (ddd, *J* = 8.6, 7.0, 4.0 Hz, 1H), 4.04 (ddd, *J* = 12.5, 4.0, 2.8 Hz, 1H), 2.79 (d, *J* = 1.7 Hz, 1H), 2.39 (m, 4H), 0.95 (s, 9H), 0.26, 0.19 (s, 3H each); $^{13}$C NMR ($CDCl_3$) $\delta$ 84.2 (d), 81.2 (d), 72.7 (d), 69.1 (d), 36.9 (t), 35.5 (t), 26.3 (q), 26.0 (d), 24.4 (d), 18.4 (s), −4.2 (q), −5.1 (q); MS *m/e* (rel intensity) 525 (M + 1, 0.2) 467 (34), 449 (4), 339 (12), 265 (8), 195 (20), 185 (22), 75 (100); HRMS calcd for $C_{14}H_{27}I_2O_3Si$ (M + H)$^+$ 524.9819, found 524.9821.

**(1*S**,2*S**,5*R**,6*R**,7*R**,8*R**)-2,5-Diiodo-9-oxabicyclo[4.2.1]nonane-7,8-diol (22).** A mixture of the silyl ether 21 (27.6 g, 52.8 mmol), *n*-$Bu_4NF$ (20.7 g, 79.1 mmol), and THF (100 mL) was stirred at 0 °C for 1 h. Concentration and flash chromatography (silica, 20–40% ether in petroleum ether) gave the diol 22 (16.3 g, 75%). 22: crystalline solid, mp 138 °C (*n*-hexane/ether); $R_f$ = 0.36 (silica, 30% EtOAc–hexane); IR ($CHCl_3$) $\nu_{max}$ 3598, 3530, 3007, 2946, 1454, 1162, 1128, 1045, 1008 cm$^{-1}$; $^1$H NMR (200 MHz, $CDCl_3$ + $CD_3OD$) $\delta$ 4.56 (ddd, *J* = 12.3, 6.2, 2.5 Hz, 2H), 4.46 (dd, *J* = 5.1, 2.5 Hz, 2H), 4.25 (m, 2H), 2.63, 2.33 (m, 4H); $^{13}$C NMR ($CDCl_3$) $\delta$ 83.1 (d), 70.5 (d), 36.8 (t), 25.7 (d); MS *m/e* (rel intensity) 411 (M + 1, 6), 393 (1), 283 (29), 265 (20), 155 (53), 137 (87), 81 (100); HRMS calcd for $C_8H_{13}I_2O_3$ (M + H)$^+$ 410.8949, found 410.8961. Anal. Calcd for $C_8H_{12}I_2O_3$: C, 23.41; H, 2.93. Found: C, 23.12; H, 3.04.

**(1*R**,2*S**,7*S**,8*R**)-9-Oxabicyclo[4.2.1]nonane-2,4-diene-7,8-diol (23).** To a stirred solution of the diiodide 22 (15.0 g, 36.6 mmol) in dry THF (400 mL) at 25 °C was added dropwise DBU (33.0 mL, 219 mmol). After being stirred at 60 °C for 12 h, the solvent was evaporated and the residue subjected to flash chromatography (silica, 70% EtOAc in *n*-hexane) to give the diene 23 (4.2 g, 75%). 23: oil; $R_f$ = 0.29 (silica, 75% EtOAc–hexane); IR ($CHCl_3$) $\nu_{max}$ 3517, 3013, 3023, 1623, 1596, 1399, 1229, 1113, 1070, 973, 912 cm$^{-1}$; $^1$H NMR (200 MHz, $CDCl_3$) $\delta$ 6.07

(ddd, $J$ = 12.6, 3.4, 3.0 Hz, 2H), 5.95 (m, 2H), 4.88 (dd, $J$ = 7.5, 5.2 Hz, 2H), 4.20 (dd, $J$ = 5.2, 1.7 Hz, 2H), 2.84 (br s, 2H); $^{13}$C NMR ($CDCl_3$) $\delta$ 135.0 (d), 127.9 (d), 80.5 (d), 77.4 (d); MS $m/e$ (rel intensity) 154 ($M^+$, 6), 137 (10), 127 (27), 107 (10), 86 (52), 77 (35), 55 (100); HRMS calcd for $C_8H_{10}O_3$ ($M^+$) 154.0630, found 154.0658. Anal. Calcd for $C_8H_{10}O_3$: C, 62.34; H, 6.49. Found: C, 62.12; H, 6.53.

***meso*-2,7-Bis(hydroxymethyl)-2,7-dihydrooxepane (24).** A stirred solution of diol **23** (2.5 g, 16.2 mmol) in MeOH:$H_2O$ (8:1) (160 mL) at 0 °C was treated with $NaIO_4$ (5.2 g, 24.3 mmol). After 30 min, when monitoring of the reaction by TLC indicated that all starting material had been consumed, $NaBH_4$ (1.8 g, 48.7 mmol) was added, and the reaction mixture was allowed to reach 25 °C. After 30 min the reaction was quenched with 15% aqueous NaOH solution (50 mL). Dilution with ether (500 mL) followed by washing with water (2 × 200 mL), 5% aqueous HCl solution (2 × 100 mL), saturated $NaHCO_3$ (100 mL), and brine (100 mL), drying ($MgSO_4$), concentration, and flash chromatography (silica, 50% ether in petroleum ether) afforded the *meso*-oxepadienyl derivative **24** (1.74, 68%). **24**: oil; $R_f$ = 0.33 (silica, EtOAc); IR ($CHCl_3$) $\nu_{max}$ 3382, 3022, 3012, 2928, 2874, 1624, 1456, 1430, 1401, 1130, 1097, 1052 cm$^{-1}$; UV (EtOH) $\lambda_{max}$ 255 nm (1080); $^1$H NMR (200 MHz, $CDCl_3$) $\delta$ 5.90 (m, 2H), 5.69 (m, 2H), 4.53 (m, 2H), 3.72 (br d, $J$ = 15.5 Hz, 2H), 3.68 (br dd, $J$ = 15.5, 11.8 Hz, 2H); $^{13}$C NMR ($CDCl_3$) $\delta$ 134.8 (d), 126.1 (d), 81.0 (d), 64.5 (t); MS $m/e$ (rel intensity) 157 (M + 1, 1), 139 (8), 126 (18), 108 (28), 95 (16), 81 (100); HRMS calcd for $C_8H_{12}O_3$ ($M^+$) 156.0783, found 156.0802. Anal. Calcd for $C_8H_{12}O_3$: C, 61.54; H, 7.69. Found: C, 61.43; H, 7.82.

***meso*-2,7-Bis[(*tert*-butyldimethylsiloxy)methyl]-2,7-dihydrooxepane (25).** TBDMSCl (812 mg, 5.4 mmol) was added to a stirred solution of diol **24** (350 mg, 2.24 mmol) and imidazole (764 mg, 11.2 mmol) in anhydrous $CH_2Cl_2$ (5 mL) at 25 °C. After being stirred for 12 h at 25 °C the reaction mixture was quenched with 25 mL of water and extracted with ether (3 × 15 mL). The combined organic layers were washed with 5% aqueous HCl (2 × 25 mL) and with saturated $NaHCO_3$ solution (2 × 25 mL) prior to drying ($MgSO_4$). The ether solution was chromatographed (silica, $n$-hexane) to yield **25** (860 mg, 100%). **25**: oil; $R_f$ = 0.53 (silica, 2% EtOAc–hexane); IR ($CHCl_3$) $\nu_{max}$ 3004, 2956, 2929, 2884, 2857, 1472, 1463, 1389, 1361, 1256, 1115, 1075 cm$^{-1}$; $^1$H NMR (200 MHz, $CDCl_3$) $\delta$ 5.93 (m, 4H), 4.41 (dd, $J$ = 7.0, 6.4 Hz, 2H), 3.82 (dd, $J$ = 10.0, 6.4 Hz, 2H), 3.55 (dd, $J$ = 10.0, 7.0 Hz, 2H), 0.89 (s, 18H), 0.06 (s, 12H); $^{13}$C NMR ($CDCl_3$) $\delta$ 136.1 (d), 125.8 (d), 80.9 (d), 65.4 (t), 26.1 (q), 25.9 (q), 18.5 (s), 18.3 (s), −2.8 (q), −5.1 (q), −5.2 (q); MS $m/e$ (rel intensity) 384 ($M^+$, 1), 327 (27), 297 (4), 235 (9), 195 (30), 73 (100); HRMS calcd for $C_{20}H_{40}O_3Si$ ($M^+$) 384.2524, found 384.2516.

***meso*-2,7-Bis[(*tert*-butyldimethylsiloxy)methyl]-3,6-epidioxy-4,5-didehydrooxepane (26).** To a solution of oxepadienyl derivative **25** (300 mg, 0.78 mmol) in dry $CHCl_3$ (200 mL) was added 0.5 mg of tetraphenylporphyrin. The resultant deep purple solution was irradiated with a 500-W tungsten halogen lamp at 25 °C for 32 h while oxygen was continuously bubbled through it. The solvent was removed on the rotary evaporator and the residue submitted to chromatographic purification in Sephadex LH-20 to yield the endoperoxide **26** (240 mg, 74%). **26**: oil; $R_f$ = 0.44 (silica, 5% EtOAc–hexane); IR ($CHCl_3$) $\nu_{max}$ 2956, 2930, 2883, 2858, 1472, 1463, 1389, 1362, 1257, 1118 cm$^{-1}$; UV (EtOH) $\lambda_{max}$ 249 (1455); $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 6.43 (dd, $J$ = 5.3, 3.3 Hz, 2H), 4.82 (dd, $J$ = 5.3, 3.3 Hz, 2H), 3.91 (dd, $J$ = 8.0, 4.6 Hz, 2H), 3.69 (dd, $J$ = 10.5, 4.6 Hz, 2H), 3.38 (dd, $J$ = 10.5, 8.0 Hz, 2H), 0.87 (s, 18H), 0.04 (s, 12H); $^{13}$C NMR ($CDCl_3$) $\delta$ 127.5 (d), 81.5 (d), 80.5 (d), 62.9 (t), 25.8 (q), 18.2 (s), −5.4 (q); MS $m/e$ (rel intensity) 359 ([M − $t$-Bu]$^+$, 5), 325 (2), 255 (10), 213 (22), 117 (80), 73 (100); HRMS calcd for $C_{16}H_{31}O_5Si_2$ (M − $t$-Bu)$^+$ 359.1710, found 359.1699.

***meso*-3,6-Dihydroxy-2,7-bis[(*tert*-butyldimethylsiloxy)methyl]-4,5-didehydrooxepane (27).** To a stirred solution of the endoperoxide **26** (50 mg, 0.12 mmol) in MeOH (5 mL) were added Lindlar catalyst (1.5 mg) and quinoline (0.05 mL). A $H_2$ atmosphere was introduced by using a $H_2$-filled balloon (repeated evacuation with aspirator). After 12 h of vigorous stirring, the $H_2$ was replaced by argon. The reaction mixture was filtered through a Celite pad, and the filtrate was concentrated, followed by flash chromatography (silica, 60% ether in petroleum ether), to afford the enediol **27** (49 mg, 98%). **27**: crystalline solid, mp 89.9–90.2 °C ($n$-hexane–$CH_2Cl_2$); $R_f$ = 0.22 (silica, 20% EtOAc–hexane); IR ($CHCl_3$) $\nu_{max}$ 3465, 2970, 2950, 2780, 1466, 1390, 1360 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 5.59 (s, 2H), 4.28 (br d, $J$ = 8.4 Hz, 2H), 3.82 (dd, $J$ = 10.3, 5.2 Hz, 2H), 3.69 (dd, $J$ = 10.3, 6.7 Hz, 2H), 3.45 (ddd, $J$ = 8.4, 6.7, 5.2 Hz, 2H), 0.88 (s, 18H), 0.07 (s, 12H); $^{13}$C NMR ($CDCl_3$) $\delta$ 132.5 (d), 83.0 (d), 73.4 (d), 66.3 (t), 25.9 (q), 18.3 (s), −5.4 (q); MS $m/e$ (rel intensity) 361 ([M − $t$-Bu]$^+$, 2), 325 (1), 251 (2), 211 (6), 199 (3), 193 (4), 185 (3), 183 (4), 169 (20), 117 (55), 89 (46), 81 (13), 75 (100); HRMS calcd for $C_{16}H_{33}O_5Si_2$ (M − $t$-Bu)$^+$ 361.1866, found 361.1867; calcd for $C_{16}H_{29}O_3Si_2$ (M − $t$-Bu − 2 × $H_2O$)$^+$ 325.1655, found 325.1653. Anal. Calcd for $C_{20}H_{42}O_5Si_2$: C, 57.42; H, 10.05. Found: C, 57.62; H, 9.87.

***meso*-3,6-Diacetoxy-2,7-bis[(*tert*-butyldimethylsiloxy)methyl]-4,5-didehydrooxepane (30).** Diol **27** (418 mg, 1.0 mmol) and triethylamine (0.5 mL, 4.0 mmol) in $CH_2Cl_2$ (10 mL) at 0 °C containing a catalytic amount of DMAP (10 mg) were slowly treated with $Ac_2O$ (0.5 mL, 5.3 mmol). The cooling bath was removed and stirring continued for 1 h at 25 °C. The solution was then diluted with ether (50 mL) and washed with 1 M HCl (3 × 20 mL), saturated aqueous $Na_2CO_3$ (3 × 20 mL), and brine (10 mL). The organic layer was dried ($MgSO_4$) and evaporated. Flash column chromatography (silica, 10% EtOAc in $n$-hexane) of the residue gave diacetate **30** (497 mg, 99%). **30**: crystalline solid, mp 46–46.5 °C ($n$-hexane); $R_f$ = 0.65 (silica, 20% EtOAc–hexane); IR ($CHCl_3$) $\nu_{max}$ 2940, 2890, 2860, 1738, 1464, 1370 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 5.78 (d, $J$ = 1.9 Hz, 2H), 5.43 (br d, $J$ = 7.2 Hz, 2H), 3.90 (ddd, $J$ = 7.2, 5.1, 3.8 Hz, 2H), 3.69 (dd, $J$ = 10.9, 5.1 Hz, 2H), 3.64 (dd, $J$ = 10.9, 3.8 Hz, 2H), 2.10 (s, 6H), 0.96 (s, 18H), 0.12 (s, 6H), 0.09 (s, 6H); $^{13}$C NMR ($CDCl_3$) $\delta$ 169.8 (s), 130.1 (d), 82.0 (d), 71.2 (d), 64.3 (t), 26.2 (q), 21.4 (q), 18.6 (s), −5.02 (q); MS $m/e$ (rel intensity) 445 ([M − $t$-Bu]$^+$, 6), 385 (4), 325 (23), 251 (43), 169 (23), 117 (100), 73 (65); HRMS calcd for $C_{20}H_{37}O_7Si_2$ (M − $t$-Bu)$^+$ 445.2078, found 445.2081; calcd for $C_{18}H_{33}O_5Si_2$ (M − $t$-Bu − AcOH)$^+$ 385.1866, found 385.1863. Anal. Calcd for $C_{24}H_{46}O_7Si_2$: C, 57.37; H, 9.16. Found: C, 57.12; H, 9.20.

**(2*S*,3*R*,6*S*,7*R*)-3-Acetoxy-6-hydroxy-2,7-bis[(*tert*-butyldimethylsiloxy)methyl]-4,5-didehydrooxepane (28).** To diol **27** (209 mg, 0.5 mmol) in isopropenyl acetate (20 mL) was added crude Amano AK lipase (200 mg). The reaction mixture was stirred at 25 °C for 72 h. The enzyme was removed by filtration, and the filtrate was concentrated in vacuo. The residue was chromatographed (silica, 2:1 petroleum ether/EtOAc) to give monoacetate (+)-**28** (196 mg, 85%). (−)-**28**: crystalline solid, mp 51.1–51.6 °C ($n$-hexane); $R_f$ = 0.41 (silica, 20% EtOAc–hexane); $[\alpha]^{25}_D$ = −48.3° ($c$ 8.4, $CHCl_3$); IR ($CHCl_3$) $\nu_{max}$ 3475, 2945, 2880, 1737, 1600, 1463, 1392, 1370, 1220, 1090 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 5.75 (ddd, $J$ = 13.0, 2.3, 2.3 Hz, 1H), 5.56 (ddd, $J$ = 13.0, 2.6, 2.6 Hz, 1H), 5.38 (ddd, $J$ = 8.6, 2.6, 2.3 Hz, 1H), 4.43 (br dd, $J$ = 8.9, 2.6 Hz, 1H), 3.99 (dd, $J$ = 10.2, 4.7 Hz, 1H), 3.78 (dd, $J$ = 10.2, 7.7 Hz, 1H), 3.72 (ddd, $J$ = 8.6, 5.4, 3.1 Hz, 1H), 3.62 (m, 2H), 2.11 (s, 3H), 0.95 (s, 9H), 0.93 (s, 9H), 0.16, 0.15, 0.09, 0.08 (s, 3H each); $^{13}$C NMR ($CDCl_3$) $\delta$ 170.2 (s), 134.5 (d), 128.5 (d), 84.2 (d), 82.0 (d), 74.5 (d), 71.8 (d), 67.0 (t), 64.3 (t), 26.2 (q), 21.6 (q), 18.7 (s), −5.0 (q), −5.2 (q); MS $m/e$ (rel intensity) 403 ([M − $t$-Bu]$^+$, 5), 343 (11), 271 (29), 251 (13), 211 (28), 193 (16), 183 (14), 169 (78), 159 (11), 149 (12), 119 (20), 117 (100), 107 (20), 95 (84), 83 (96), 73 (99); HRMS calcd for $C_{18}H_{35}O_6Si_2$ (M − $t$-Bu)$^+$ 403.1972, found 403.1970. **Preparation of (*R*)- and (*S*)-MTPA Esters of (−)-28.** To a solution of monoacetate (−)-**28** (12.2 mg, 26.5 μmol) and DMAP (9.7 mg, 79.5 μmol) in 1.0 mL of dry $CH_2Cl_2$ were added triethylamine (3.12 mg, 4.3 μL, 30.8 μmol) and (*R*)-(−)-α-methoxy-α-(trifluoromethyl)phenylacetyl chloride (13.4 mg, 9.9 μL, 53.0 μmol), and the solution was allowed to stand at 25 °C for 3 h. After removal of the solvent, the residue was chromatographed (silica, 50% EtOAc–hexane) to yield the (*R*)-MTPA ester of (−)-**28** (14.3 mg, 80%): HRMS calcd for $C_{28}H_{42}F_3O_8Si_2$ (M − $t$-Bu)$^+$ 619.2370, found 619.2371. (*S*)-MTPA ester of (−)-**28**: HRMS calcd for $C_{28}H_{42}F_3O_8Si_2$ (M − $t$-Bu)$^+$ 619.2370, found 619.2340. The $^1$H NMR spectral data for (*R*)- and (*S*)-MTPA esters of (−)-**28** are listed in the supplementary material.

**PLE-Catalyzed Hydrolyses. General Procedure. (2*R*,3*S*,6*R*,7*S*)-3-Acetoxy-6-hydroxy-2,7-bis[(*tert*-butyldimethylsiloxy)methyl]-4,5-didehydrooxepane (29).** The following basic method was used for all enzyme-promoted hydrolyses. The diacetate **30** (502 mg, 1.0 mmol) was suspended in MeOH (3 mL) and aqueous phosphate buffer (0.1 M, pH 7.0, 30 mL) and treated with PLE (200 μL, 1200 units). The pH was kept at 7.00 by the pH-stat-controlled addition of 0.5 N NaOH. The reaction was stopped after 1 equiv of the base had been added (24 h). Workup by extraction with EtOAc (5 × 50 mL) at pH 7.0 yielded a mixture of starting diacetate **30** and monoacetate **29** which were isolated by column chromatography (silica, 10% EtOAc in *n*-hexane) to yield **30** (226 mg, 0.45 mmol) and (+)-**29** (250.6 mg, 0.54 mmol). ()-**29**: crystalline solid, mp 50.8–52 °C (*n*-hexane); $R_f$ = 0.41 (silica, 20% EtOAc–hexane); $[\alpha]^{25}_D$ = +47.2° (*c* 5.3, $CHCl_3$). This optically active monoacetate showed IR, NMR, and MS spectra identical to those of the opposite enantiomer: (−)-**28**. **Preparation of (*R*)- and (*S*)-MTPA Esters of (+)-29.** To a solution of monoacetate (+)-**29** (11.96 mg, 26.0 μmol) and DMAP (9.5 mg, 7.8 μmol) in 1.0 mL of dry $CH_2Cl_2$ were added triethylamine (3.0 mg, 4.2 μL, 30.0 μmol) and (*R*)-(−)-α-methoxy-α-(trifluoromethyl)phenylacetyl chloride (13.2 mg, 9.7 μL, 52.0 μmol), and the solution was allowed to stand at 25 °C for 3 h. After removal the solvent, the residue was chromatographed (silica, 50% EtOAc–hexane) to yield (+)-**29** (*R*)-MTPA ester (13.9 mg, 78%): HRMS calcd for $C_{28}H_{42}F_3O_8Si_2$ (M − *t*-Bu)$^+$ 619.2370, found 619.2396; calcd for $C_{26}H_{38}F_3O_6Si_2$ (M − *t*-Bu − AcOH)$^+$ 559.2159, found 559.2155. (*S*)-MTPA ester of (+)-**29**: HRMS calcd for $C_{28}H_{42}F_3O_8Si_2$ (M − *t*-Bu)$^+$ 619.2370, found 619.2372. The $^1H$ NMR spectral data for (*R*)- and (*S*)-MTPA esters of (+)-**29** are listed in supplementary material.

**Preparation of (*Z*,*Z*)-1-Acetoxy-2,7-cyclodecadiene (32). Method A.** To a stirred solution of (*E*,*Z*)-1,5-cyclodecadiene (**31**) (20.0 g, 147 mmol) in dry $CH_2Cl_2$ (200 mL) at 0 °C was slowly added 8% Na-on-alumina (54 g). The reaction mixture was stirred under argon for 12 h at 25 °C before dilution with ether (1 L), filtered, washed with $H_2O$ (2 × 300 mL) and brine (300 mL), and dried ($MgSO_4$). Concentration followed by flash chromatography (silica, *n*-hexane) afforded (*Z*,*Z*)-1,6-cyclodecadiene[32] (18.4 g, 92%) which was treated with a 5 M solution of *t*-BuOOH in isooctane (5.6 mL, 28 mmol), AcOH (4.8 mL, 80 mmol), and a catalytic amount of copper(I) chloride and stirred for 42 h at 80 °C. Dilution with ether (200 mL) followed by washing with $H_2O$ (3 × 100 mL) and brine (100 mL), drying ($MgSO_4$), and concentration gave an oil which was purified by chromatography (silica, 5% ether in petroleum ether) to yield **32** (22.0 g, 84%) (78% overall from **31**). **32**: oil; $R_f$ = 0.80 (silica, 20% EtOAc in *n*-hexane); IR ($CHCl_3$) $\nu_{max}$ 3009, 2927, 2857, 1736, 1452, 1372, 1246, 1020, 962 cm$^{-1}$; $^1H$ NMR (200 MHz, $CDCl_3$) δ 5.58–5.21 (m, 5H), 2.42–2.06 (m, 4H), 1.99 (s, 3H), 2.06–1.73 (m, 6H); $^{13}C$ NMR ($CDCl_3$) δ 169.8 (s), 134.2 (d), 129.9 (d), 129.5 (d), 128.6 (d), 70.0 (d), 31.5 (t), 25.7 (t), 24.5 (t), 23.2 (t), 23.2 (t), 21.3 (q); MS *m*/*e* (rel intensity) 195 (M + 1, 5), 193 (12), 180 (25), 167 (70), 165 (38), 149 (64), 135 (100), 91 (37), 79 (34), 67 (46), 43 (91); HRMS calcd for $C_{12}H_{19}O_2$ (M + H)$^+$ 195.1385, found 195.1383.

**Method B.** To a stirred solution of **31** (20.6 g, 0.15 mol) in dry EtOAc (20 mL) at 20 °C was added *m*-CPBA (34.4 g, 0.17 mol). The reaction mixture was stirred for 30 min at 25 °C by external cooling before dilution with ether (50 mL) and washing with aqueous saturated $NaHCO_3$ (2 × 50 mL) and brine (100 mL) and then dried ($MgSO_4$). Concentration followed by flash column chromatography (silica, 30% ether in petroleum ether) gave *trans*-5,6-epoxy-*cis*-cyclodecene[31a] as an oil (21.0 g, 93%): $R_f$ = 0.40 (silica, 2% EtOAc in *n*-hexane); $^1H$ NMR (200 MHz, $CDCl_3$) δ 5.37 (m, 2H), 2.69 (ddd, *J* = 9.8, 3.9, 3.9 Hz, 1H), 2.46 (ddd, *J* = 10.0, 3.9, 3.9 Hz, 1H), 2.11 (m, 5H), 1.57 (m, 5H), 0.83 (m, 2H); MS *m*/*e* (rel intensity) 152 (M$^+$, 4), 134 (5), 123 (9), 109 (16), 93 (33), 79 (51), 67 (100), 55 (71). A solution of *trans*-5,6-epoxy-*cis*-cyclodecene (20.0 g, 137.6 mmol) in dry ether (20 mL) was added dropwise to a freshly prepared 1 M solution of phenyllithium in ether (206 mL, 206 mmol). After 12 h of reflux the reaction mixture was diluted with ether (500 mL), washed with $H_2O$ (2 × 500 mL) and brine (500 mL), and dried ($MgSO_4$). Concentration followed by flash chromatography of the residue (silica, 10% ether in petroleum ether) afforded (*E*,*E*)-2,7-cyclodecadienol[31b] (18.5 g, 92%): $R_f$ = 0.42 (silica, 20% EtOAc in *n*-hexane); crystalline solid, mp 84–86 °C (ether/*n*-hexane); IR ($CHCl_3$) $\nu_{max}$ 3601, 3453, 3009, 2926, 2857, 1437, 1373, 1039 cm$^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 5.45 (m, 2H), 5.34 (ddd, *J* = 9.6, 9.6, 1.5 Hz, 1H), 5.27 (dd, *J* = 11.3, 4.0 Hz, 1H), 4.52 (ddd, *J* = 10.9, 9.6, 4.4 Hz, 1H), 2.29 (m, 3H), 1.90 (m, 4H), 1.56 (m, 3H); $^{13}C$ NMR ($CDCl_3$) δ 133.2 (d), 132.3 (d), 130.3 (d), 129.6 (d), 67.4 (d), 34.7 (t), 26.0 (t), 25.7 (t), 24.6 (t), 23.9 (t); MS *m*/*e* (rel intensity) 152 (M$^+$, 22), 135 (13), 129 (19), 105 (39), 55 (100); HRMS calcd for $C_{10}H_{16}O$ (M$^+$) 152.1201, found 152.1199; calcd for $C_{10}H_{15}O$ 151.1123, found 151.1124; calcd for $C_{10}H_{14}$ (M − $H_2O$)$^+$ 134.1095, found 134.1092. To a cold solution of (*E*,*E*)-2,7-cyclodecadienol (10 g, 65.7 mmol), triethylamine (22.9 mL, 164.2 mmol), and a catalytic amount of DMAP in dry $CH_2Cl_2$ (200 mL) at 0 °C was added dropwise $Ac_2O$ (12.4 mL, 131.3 mmol). The reaction mixture was allowed to reach 25 °C and stirred for 1 h before dilution with MeOH (10 mL) and ether (500 mL). The mixture was washed with aqueous saturated $NH_4Cl$ solution (2 × 100 mL) and $H_2O$ (2 × 100 mL) and then dried ($MgSO_4$). Concentration followed by flash column chromatography (silica, 5% EtOAc in *n*-hexane) gave acetate **32** (13.2 g, 98%) (84% overall from **31**), which was shown to be identical in all respects (IR, NMR, and MS spectra) with those of compound **32** prepared by method A.

**(1*S**,7*S**,8*R**)-Acetoxy-7,8-epoxy-2-cyclodecene (33).** A solution of *m*-CPBA acid (14.4 g, 68.64 mmol) in $CH_2Cl_2$ (75 mL) at 0 °C was added dropwise to a stirred solution of acetate **32** (12.0 g, 57.2 mmol) in $CH_2Cl_2$ (25 mL). The reaction mixture was stirred at 0 °C for 5 h, quenched with an aqueous saturated $Na_2SO_3$ solution, and extracted with ether (3 × 100 mL). The combined ethereal phases were washed with 1 N NaOH (2 × 50 mL) and brine (50 mL) prior to drying ($MgSO_4$) and solvent evaporation. Purification of the residue by chromatography on silica gel (elution 5% EtOAc in *n*-hexane) gave **33** (9.60 g, 80%). **33**: oil; $R_f$ = 0.55 (silica, 20% EtOAc in *n*-hexane); IR ($CHCl_3$) $\nu_{max}$ 3010, 2970, 2929, 2865, 1728, 1451, 1373, 1253, 1023 cm$^{-1}$; $^1H$ NMR (200 MHz, $CDCl_3$) δ 5.52 (m, 2H), 5.29 (ddd, *J* = 8.8, 8.8, 1.4 Hz, 1H), 2.94 (dd, *J* = 13.6, 3.3 Hz, 1H), 2.85 (dd, *J* = 13.6, 3.3 Hz, 1H), 2.44 (m, 2H), 2.01 (s, 3H), 2.2–1.6 (m, 6H), 1.19 (m, 2H); $^{13}C$ NMR ($CDCl_3$) δ 170.0 (s), 133.8 (d), 128.2 (d), 68.5 (d), 58.0 (d), 57.6 (d), 30.6 (t), 25.5 (t), 24.1 (t), 23.1 (t), 22.1 (t), 21.1 (q); MS *m*/*e* (rel intensity) 211 (M + 1, 7), 210 (1), 183 (6), 151 (78), 133 (85), 121 (47), 107 (46), 91 (100), 79 (83), 67 (84), 55 (59); HRMS calcd for $C_{12}H_{19}O_3$ (M + H)$^+$ 211.1334, found 211.1344.

**(1*S**,7*S**,8*R**)-7,8-Epoxy-2-cyclodecenol (34).** A mixture of acetate **33** (9.5 g, 45.3 mmol), $K_2CO_3$ (630 mg, 4.5 mmol), and MeOH (50 mL) was stirred at 25 °C for 3 h. Dilution with ether (100 mL) and *n*-hexane (100 mL) followed by filtration through a Celite pad and concentration gave the alcohol **34** (7.5 g, 98%). **34**: noncrystalline solid; $R_f$ = 0.65 (silica, 75% EtOAc in *n*-hexane); IR ($CHCl_3$) $\nu_{max}$ 3691, 3601, 2934, 2860, 1718, 1601, 909 cm$^{-1}$; $^1H$ NMR (200 MHz, $CDCl_3$) δ 5.40 (m, 2H), 4.57 (ddd, *J* = 10.0, 10.0, 4.1 Hz, 1H), 2.95 (dd, *J* = 10.9, 3.8 Hz, 1H), 2.83 (dd, *J* = 10.0, 3.6 Hz, 1H), 2.59 (m, 2H), 2.0–1.5 (m, 6H), 1.22 (m, 2H); $^{13}C$ NMR ($CDCl_3$) δ 132.9 (d), 131.8 (d), 66.1 (d), 58.3 (d), 58.2 (d), 33.7 (t), 25.6 (t), 24.5 (t), 23.1 (t), 22.6 (t); MS *m*/*e* (rel intensity) 168 (M$^+$, 1), 149 (6), 139 (15), 110 (10), 93 (25), 83 (56), 70 (62), 55 (100); HRMS calcd for $C_{10}H_{16}O_2$ (M$^+$) 168.1150, found 168.1148.

**(1*S**,2*S**,3*S**,7*S**,8*R**)-2,3;7,8-Diepoxycyclodecanol (35).** To a cold (0 °C) solution of the epoxy alcohol **34** (10.0 g, 59.5 mmol) in $CH_2Cl_2$ (100 mL) was added dropwise a solution of *m*-CPBA acid (15.4 g, 89.2 mmol) in $CH_2Cl_2$ (50 mL, buffered with 300 mg of $NaHCO_3$). The reaction mixture was stirred at 25 °C for 12 h, quenched with saturated $Na_2SO_3$ solution, and extracted with ether (2 × 100 mL). The combined ethereal phases were washed with 1 N NaOH (2 × 50 mL) and brine (50 mL) prior to drying ($MgSO_4$) and solvent evaporation. Concentration followed by flash chromatography yielded the diepoxide **35** (8.76 g, 80%). **35**: crystalline solid, mp 120–122 °C (*n*-hexane); $R_f$ = 0.42 (silica, 75% EtOAc in *n*-hexane); IR ($CHCl_3$) $\nu_{max}$ 3587, 3475, 3019, 2963, 2933, 2867, 1718, 1602, 1454, 1043, 1000, 933 cm$^{-1}$; $^1H$ NMR (200 MHz, $CDCl_3$) δ 3.51 (ddd, *J* = 11.4, 9.2, 4.4 Hz, 1H), 3.02 (ddd, *J* = 10.7, 3.8, 1.2 Hz, 1H), 2.86 (m, 3H), 1.8 (m, 7H), 1.3 (m, 3H); $^{13}C$ NMR ($CDCl_3$) δ 65.8 (d), 60.7 (d), 58.5 (d), 57.1 (d), 57.0 (d), 30.5 (t), 23.8 (t), 22.7 (t), 21.7 (t), 20.5 (t); MS *m*/*e* (rel intensity) 184 (M$^+$, 1) 183 (8), 137 (2), 105 (11), 95 (21), 83 (51), 67 (66), 57 (88), 55 (100); HRMS calcd for $C_{10}H_{16}O_3$ (M$^+$)

184.1099, found 184.1095; calcd for $C_8H_{11}O_2$ 139.0759, found 139.0756; calcd for $C_8H_9$ 105.0704, found 105.0704.

**(1*R**,2*R**,3*S**,6*R**,7*R**)-7-Iodo-11-oxabicyclo[4.4.1]undecane-2,3-diol (36).** To a stirred solution of diepoxide **35** (920 mg, 5.0 mmol) in dry $CH_2Cl_2$ (100 mL) and titanium(IV) isopropoxide (0.3 mL, 1.0 mmol) was added freshly sublimated iodine (1.52 g, 1.0 mmol). When monitoring of the reaction by TLC indicated that all starting material has been consumed (3 h), the quenched reaction mixture was taken with saturated $Na_2SO_3$ solution and 15% aqueous tartaric acid solution (20 mL) and extracted with ether (2 × 100 mL). The combined ethereal phases were washed with 0.5 N NaOH (2 × 50 mL) and brine (50 mL) prior to drying ($MgSO_4$) and solvent evaporation. Purification of the residue by chromatography on silica gel (elution with 60% EtOAc in *n*-hexane) yielded **36** (994 mg, 64%). **36**: crystalline solid, mp 173–175 °C (*n*-hexane/ether); $R_f$ = 0.30 (75% EtOAc in *n*-hexane); IR ($CHCl_3$) $\nu_{max}$ 3690, 3610, 3022, 3011, 2939, 1733, 1602, 1442, 1222, 1053, 1018 $cm^{-1}$; $^1H$ NMR (200 MHz, $CDCl_3$) $\delta$ 4.16 (ddd, $J$ = 8.4, 4.5, 0.5 Hz, 1H), 4.06 (m, 1H), 3.84 (ddd, $J$ = 6.3, 4.8, 1.6 Hz, 1H), 3.48 (m, 1H), 3.38 (dd, $J$ = 9.0, 4.8 Hz, 1H), 2.35 (m, 2H), 1.96 (m, 3H), 1.48 (m, 5H); $^{13}C$ NMR ($CDCl_3/CD_3OD$) $\delta$ 80.6 (d), 78.1 (d), 77.8 (d), 73.3 (d), 38.2 (t), 33.4 (d), 29.3 (t), 29.2 (t), 26.6 (t), 23.0 (t); MS *m/e* (rel intensity) 313 (M + 1, 3), 258 (4), 256 (10), 186 (41), 131 (17), 93 (36), 55 (100); HRMS calcd for $C_{10}H_{18}IO_3$ $(M + H)^+$ 313.0301, found 313.0304; calcd for $C_{10}H_{18}O_3$ $(M + H - 1)^+$ 186.1256, found 186.1241; calcd for $C_{10}H_{11}$ 131.0861, found 131.0856.

**Preparation of Compounds (1*R**,2*S**,3*R**)-2,3-Dihydroxy-11-oxabicyclo[4.4.1]undec-6-ene (37) and (1*R**,2*S**,3*R**)-2,3-Dihydroxy-11-oxabicyclo[4.4.1]undec-7-ene (38).** DBN (1.47 mL, 11.9 mmol) was added to a stirred solution of iodide **36** (1.0 g, 2.38 mmol) in dry mixed xylenes (10 mL). The flask was equipped with a reflux condenser and lowered into a preheated oil bath at 150 °C. The reaction was heated for 5 h and allowed to cool to rt, and the entire reaction mixture was preadsorbed onto silica gel (7 g). Flash chromatography gave a 7:1 mixture of **37** and **38** (380 mg, 87%). Acetylation of the mixture in the usual way followed by chromatographic purification (silica, 30% EtOAc in *n*-hexane) yielded **37** (diacetate) (470.5 mg) and **38** (diacetate) (80.2 mg). **37** (diacetate): crystalline solid, mp 67–69 °C (ether/*n*-hexane); $R_f$ = 0.65 (silica, 30% EtOAc in *n*-hexane); IR ($CHCl_3$) $\nu_{max}$ 3024, 2945, 1735, 1466, 1370, 1248, 1135, 1036 $cm^{-1}$; $^1H$ NMR (200 MHz, $CDCl_3$) $\delta$ 5.17 (m, 2H), 4.93 (m, 1H), 4.35 (m, 1H), 2.34 (m, 3H), 2.02 (s, 3H), 2.01 (s, 3H), 2.05–1.50 (m, 5H), 1.23 (m, 1H), 0.82 (m, 1H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 170.1 (s), 169.9 (s), 150.5 (s), 113.0 (d), 76.0 (d), 75.1 (d), 70.9 (d), 28.5 (t), 28.1 (t), 25.7 (t), 24.9 (t), 21.2 (q), 20.9 (q), 18.2 (t); MS *m/e* (rel intensity) 268 ($M^+$, 3), 226 (1), 208 (20), 166 (35), 120 (40), 83 (72), 55 (100); HRMS calcd for $C_{14}H_{20}O_5$ ($M^+$) 268.1311, found 268.1320; calcd for $C_{12}H_{16}O_3$ 208.1099, found 208.1111; calcd for $C_9H_{10}O_3$ 166.0630, found 166.0624. **38** (diacetate) crystalline solid, mp 62–66 °C (ether/*n*-hexane); $R_f$ = 0.55 (silica, 30% EtOAc in *n*-hexane); IR ($CHCl_3$) $\nu_{max}$ 3025, 2948, 1738, 1672, 1602, 1372, 1233, 1042 $cm^{-1}$; $^1H$ NMR (200 MHz, $CDCl_3$) $\delta$ 5.66 (m, 2H), 5.07 (m, 2H), 4.31 (m, 1H), 4.10 (m, 1H), 2.33 (m, 2H), 2.10 (m, 1H), 2.02 (s, 6H), 2.00–1.50 (m, 5H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 170.1 (s), 170.0 (s), 133.9 (d), 129.2 (d), 80.0 (d), 75.8 (d), 75.3 (d), 74.6 (d), 32.8 (t), 29.4 (t), 27.3 (t), 27.2 (t), 21.3 (q), 21.1 (q); MS *m/e* (rel intensity) 269 (M + 1, 25), 268 (2), 225 (3), 208 (16), 166 (36), 148 (40), 122 (67), 55 (100); HRMS calcd for $C_{14}H_{21}O_5$ $(M + H)^+$ 269.1389, found 269.1393; calcd for $C_{14}H_{20}O_5$ ($M^+$) 268.1311, found 268.1329. A stirred solution of the olefin **38** (diacetate) (268 mg, 1.0 mmol), potassium *tert*-butoxide (619 mg, 5.0 mmol), and dry DMSO (20 mL) was heated at 50 °C for 4 h. The cooled reaction mixture was diluted with $H_2O$ (20 mL) and extracted with ether (5 × 100 mL). The combined organic products were washed with brine (2 × 50 mL), dried ($MgSO_4$), and concentrated, and the resulting residue was submitted to acetylation to give, after chromatographic purification, the enol ether **37** (diacetate) (168 mg, 63%) and the starting allyl ether **38** (diacetate) (42 mg, 16%), which could be further recycled.

**(1*R**,2*S**,3*R**,6*R**,7*S**)-11-Oxabicyclo[4.4.1]undecane-2,3,7-triol (39).** To a cooled (0 °C) and stirred solution of **37** (314.6 mg, 1.71 mmol) in dry THF (20 mL) was slowly added $BH_3$·$Me_2S$ complex (1.28 mL, 2.56 mmol) of a 2.0 M solution in THF. The reaction mixture was allowed to warm to 25 °C and was stirred for 12 h before being quenched with $H_2O$ (385 μL) and aqueous 3 N NaOH solution (900 μL) and dropwise addition of 30% $H_2O_2$ (900 μL). After being stirred for 10 min the mixture was diluted with ether (50 mL), washed with $H_2O$ (2 × 20 mL) and brine (30 mL), and then dried ($MgSO_4$). Solvent evaporation *in vacuo* followed by chromatography (Sephadex LH-20, *n*-hexane:$CHCl_3$:MeOH (2:1:1)) gave triol **39** (262 mg, 76%). **39**: noncrystalline solid; $R_f$ = 0.40 (silica, 10% MeOH in EtOAc); IR ($CHCl_3$) $\nu_{max}$ 3508, 3438, 3011, 2935, 1726, 1603, 1375, 1054, 1036 $cm^{-1}$; $^1H$ NMR (200 MHz, $CD_3OD$) $\delta$ 3.85 (m, 2H), 3.64 (d, $J$ = 2.7 Hz, 1H), 3.52 (ddd, $J$ = 9.4, 9.4, 3.6 Hz, 1H), 3.52 (dd, $J$ = 9.4, 5.0 Hz, 1H), 2.03 (m, 1H), 1.88 (m, 1H), 1.51 (m, 7H), 0.87 (m, 1H); $^{13}C$ NMR ($CD_3OD$) $\delta$ 81.7 (d), 79.8 (d), 78.9 (d), 74.5 (d), 72.8 (d), 34.4 (t), 31.1 (t), 31.0 (t), 27.8 (t), 20.6 (t); MS *m/e* (rel intensity) 203 (M + 1, 7), 185 (9), 166 (5), 149 (5), 122 (10), 97 (31), 84 (42), 70 (63), 57 (100); HRMS calcd for $C_{10}H_{19}O_4$ $(M + H)^+$ 203.1283, found 203.1274; calcd for $C_{10}H_{14}O_2$ $(M - 2H_2O)^+$ 166.0994, found 166.1003.

**(2*R**/2*S**,4a*R**,6*R**,9a*S**)-2-(Phenylthio)-6-formylpyrano[2,3-*b*]oxepane (40ab).** An excess of $NaIO_4$ (212 mg, 0.99 mmol) was added under argon to a stirred solution of triol **39** (100 mg, 0.49 mmol) in MeOH (5 mL) at 25 °C. The reaction mixture, after being stirred for 2 h at 25 °C, was filtered through a Celite pad, and the solution concentrated *in vacuo*. The solid residue was suspended in $CH_2Cl_2$ (20 mL), filtered, and treated with crushed 3-Å molecular sieves (2.0 g), thiophenol (60 μL, 65.2 mg, 0.6 mmol), and a catalytic amount of CSA (2 mg). After the mixture was vigorously stirred for 12 h at 25 °C, the solvent was evaporated and the crude oil flash chromatographed (silica, 30% ether in petroleum ether) to afford a diastereomeric mixture of mixed ketals **40ab** (2*S**:2*R**, 3:1) (98 mg, 0.33 mmol, 68%). **40ab**: oil; $R_f$ = 0.40 (silica, 20% EtOAc in *n*-hexane); IR ($CHCl_3$) $\nu_{max}$ 3009, 2942, 2871, 1737, 1584, 1440, 1223, 1086, 1026 $cm^{-1}$. The data for **40a** and **40b** were determined from the mixture: $^1H$ NMR (400 MHz, $CDCl_3$) **40a** (2*S** isomer) $\delta$ 9.73 (s, 1H), 7.35 (m, 2H), 7.31 (m, 3H), 5.56 (dd, $J$ = 3.4, 2.8 Hz, 1H), 4.14 (m, 2H), 3.34 (m, 1H), 2.19–1.90 (m, 6H), 1.79 (m, 2H), 1.52 (m, 2H); **40b** (2*R** isomer) $\delta$ 203.3 (d), 135.9 (s), 131.4 (2C, d), 129.3 (2C, d), 127.2 (d), 84.5 (d), 83.3 (d), 78.9 (d), 73.9 (d), 34.7 (t), 29.8 (t), 27.9 (t), 19.5 (t); (2*R** isomer) $\delta$ 202.8 (d), 131.4 (2C, d), 129.2 (2C, d), 127.5 (d), 82.9 (d), 78.1 (d), 34.9 (t), 32.0 (t), 31.6 (t), 29.7 (t), 19.3 (t); MS *m/e* (rel intensity) 292 ($M^+$, 4), 263 (4), 199 (8), 183 (70), 169 (22), 139 (48), 109 (54), 81 (40), 67 (43), 55 (100); HRMS calcd for $C_{16}H_{20}O_3S$ ($M^+$) 292.1133, found 292.1131.

**(2*R**/2*S**,4a*R**,6*R**,9a*S**)-2-(Phenylthio)-6-(hydroxymethyl)pyrano[2,3-*b*]oxepane (41ab).** A mixture of compounds **40ab** (100 mg, 0.34 mmol) and $NaBH_4$ (32.5 mg, 0.85 mmol) was stirred together in a solution of MeOH (20 mL) at 0 °C for 10 min. After to filtration through a pad of Celite the solvent was removed by *in vacuo* evaporation. Silica gel chromatography (40% EtOAc in *n*-hexane) afforded **41a** (2*S** isomer) (72.5 mg, 0.25 mmol) and **41b** (2*R** isomer) (24.1 mg, 0.08 mmol). **41a** (2*S** isomer): oil; $R_f$ = 0.70 (silica, 50% EtOAc in *n*-hexane); IR ($CHCl_3$) $\nu_{max}$ 3689, 3587, 2940, 2873, 1088, 1019 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 7.50 (m, 2H), 7.30 (m, 3H), 5.56 (dd, $J$ = 3.4, 2.8 Hz, 1H), 4.03 (ddd, $J$ = 9.6, 9.6, 4.4 Hz, 1H), 3.84 (ddd, $J$ = 12.4, 12.4, 6.3 Hz, 1H), 3.51 (m, 2H), 3.24 (ddd, $J$ = 11.1, 9.4, 4.6 Hz, 1H), 2.16 (m, 2H), 2.01 (m, 2H), 1.77–1.52 (m, 6H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 136.0 (s), 131.4 (2C, d), 129.2 (2C, d), 127.1 (d), 84.6 (d), 80.2 (d), 80.1 (d), 74.4 (d), 66.5 (t), 34.2 (t), 31.2 (t), 30.6 (t), 28.0 (t), 19.9 (t); MS *m/e* (rel intensity) 294 ($M^+$, 1), 276 (43), 264 (5), 201 (8), 185 (73), 167 (33), 141 (48), 109 (58), 81 (50), 67 (40), 55 (100); HRMS calcd for $C_{16}H_{22}O_3S$ ($M^+$) 294.1289, found 294.1290. **41b** (2*R** isomer): oil; $R_f$ = 0.65 (silica, 50% EtOAc in *n*-hexane); $^1H$ NMR (400 MHz, $CDCl_3$) (selected signals) $\delta$ 4.80 (dd, $J$ = 11.6, 2.1 Hz, 1H, H-2); $^{13}C$ NMR ($CDCl_3$) $\delta$ 131.4 (2C, d), 129.2 (2C, d), 127.5 (d), 83.4 (d), 80.3 (d), 80.1 (d), 79.4 (d), 74.4 (d), 66.6 (t), 34.4 (t), 32.1 (t), 31.7 (t), 30.6 (t), 19.8 (t); MS *m/e* (rel intensity) 294 ($M^+$, 0.1), 276 (59), 264 (10), 201 (10), 185 (93), 167 (28), 141 (39), 109 (60), 81 (60), 67 (48), 55 (100); HRMS calcd for $C_{16}H_{22}O_3S$ ($M^+$) 294.1289, found 294.1293.

**(2*R**/2*S**,4a*R**,9a*S**)-2-(Phenylthio)-6-[(*tert*-butyldimethylsiloxy)methyl]pyrano[2,4-*b*]oxepane (42ab).** To a stirred mixture of the alcohols **41ab** (96 mg, 0.32 mmol), imidazole (54 mg, 0.80 mmol), and dry DMF (5 mL) at 0 °C was added TBDMSCl (96 mg, 0.64 mmol). After 6 h at 40 °C the reaction

was quenched with ether (50 mL) followed by washing with $H_2O$ (2 × 50 mL) and brine (50 mL). Drying ($MgSO_4$), concentration, and flash chromatography (silica, 10% ether in petroleum ether) gave the silyl ethers **42ab** (2*S**:2*R**, 3:1) (115 mg, 0.28 mmol, 88%). **42ab**: oil; $R_f$ = 0.60 (2% EtOAc in *n*-hexane). The data for **42a** and **42b** were determined from the mixture: $^1$H NMR (400 MHz, $CDCl_3$) (2*S** isomer) δ 7.52 (m, 2H), 7.30 (m, 3H), 5.56 (d, *J* = 2.0 Hz, 1H), 4.02 (ddd, *J* = 9.4, 9.4, 4.5 Hz, 1H), 3.77 (dd, *J* = 11.8, 5.9 Hz, 1H), 3.65 (dd, *J* = 10.3, 6.2 Hz, 1H), 3.49 (dd, *J* = 10.3, 6.1 Hz, 1H), 3.24 (dd, *J* = 9.4, 5.4 Hz, 1H), 2.16 (m, 2H), 2.02 (m, 1H), 1.89 (m, 1H), 1.70 (m, 4H), 1.54 (m, 1H), 1.31 (m, 1H), 0.95 (s, 9H), 0.13 (s, 6H); (2*R** isomer) (selected signals) δ 4.81 (dd, *J* = 11.5, 2.1 Hz, 1H); $^{13}$C NMR ($CDCl_3$) (2*S** isomer) δ 136.2 (s), 131.4 (2C, d), 129.2 (2C, d), 127.1 (d), 84.7 (d), 80.2 (d), 76.6 (d), 74.7 (d), 66.5 (t), 34.5 (t), 31.4 (t), 30.4 (t), 28.1 (t), 26.4 (3C, q), 19.3 (t), −4.7 (q); (2*R** isomer) δ 131.3 (2C, d), 129.2 (2C, d), 127.4 (d), 84.6 (d), 83.7 (d), 80.3 (d), 78.7 (d), 66.5 (t), 34.5 (t), 32.2 (t), 31.9 (t), 30.5 (t), 26.3 (2C, q), 19.3 (t), −4.73 (q), −4.88 (q).

**(2*R**/2*S**,4a*R**,6*R**,9a*S**)-2-(Phenylsulfonyl)-6-[(*tert*-butyldimethylsiloxy)methyl]pyrano[2,3-*b*]oxepane (43ab).** A stirred solution of the mixed ketal **42ab** (115 mg, 0.28 mmol) in dry EtOAc (5.0 mL) at 25 °C was treated with *m*-CPBA (145 mg, 0.84 mmol) and $NaHCO_3$ (70.0 mg, 0.84 mmol). After 12 h the reaction mixture was diluted with ether (50 mL) and filtered through a pad of Celite. The filtrate was washed with water (2 × 10 mL), brine (20 mL), and dried ($MgSO_4$). Concentration and flash chromatography (silica, 20% EtOAc in *n*-hexane) furnished **43ab** (116 mg, 0.26 mmol, 96%). **43ab**: oil; $R_f$ = 0.35 (silica, 10% EtOAc in *n*-hexane). The data for **43a** and **43b** were determined from the mixture: $^1$H NMR (400 MHz, $CDCl_3$) (2*S** isomer) δ 7.94 (m, 2H), 7.69 (m, 1H), 7.61 (m, 2H), 4.61 (d, *J* = 6.6 Hz, 1H), 3.72 (ddd, *J* = 9.7, 9.7, 4.7 Hz, 1H), 3.72 (ddd, *J* = 6.0, 6.0, 6.0 Hz, 1H), 3.63 (dd, *J* = 10.3, 6.0 Hz, 1H), 3.46 (dd, *J* = 10.3, 6.0 Hz, 1H), 3.20 (ddd, *J* = 9.6, 9.6, 4.4 Hz, 1H), 2.78 (m, 1H), 2.19 (m, 1H), 2.03 (m, 2H), 1.90 (m, 1H), 1.66 (m, 4H), 1.34 (m, 1H), 0.94 (s, 9H), 0.11 (s, 6H); (2*R** isomer) (selected signals) δ 4.18 (dd, *J* = 11.6, 2.3 Hz, 1H), 3.57 (dd, *J* = 10.4, 6.2 Hz, 1H), 3.41 (dd, *J* = 10.4, 6.0 Hz, 1H); $^{13}$C NMR ($CDCl_3$) (2*S** isomer) δ 134.2 (d), 129.4 (2C, d), 129.2 (2C, d), 88.8 (d), 80.4 (d), 78.5 (d), 77.7 (d), 66.4 (t), 34.5 (t), 30.3 (t), 27.2 (t), 26.3 (3C, q), 22.3 (t), 19.0 (t), −4.8 (q), −4.9 (q); (2*R** isomer) (selected signals) δ 91.2 9d), 83.8 (d), 80.1 (d), 77.7 (d), 66.3 (t), 34.2 (t), 30.2 (t), 26.4 (t), 26.3 (3C, q), 23.9 (t), 18.8 (t).

**(2*R**,4a*R**,6*R**,9a*S**)-6-[(*tert*-Butyldimethylsiloxy)methyl]-2-vinylpyrano[2,3-*b*]oxepane (44).** A freshly prepared 1.0 M solution of vinylmagnesium bromide (5 mL, 5.0 mmol) in dry THF was treated with a 1.0 M solution of $ZnBr_2$ in THF (2.5 mL, 2.5 mmol), and the reaction mixture was stirred for 30 min under argon at 25 °C to afford the organozinc species. The clear decanted solution (0.30 M of vinylzinc bromide) (1.33 mL, 0.4 mmol) was filtered and slowly added through a cannula to a stirred solution of the sulfone **43ab** (3:1 mixture, 2*S**:2*R**) (44 mg, 0.1 mmol) in dry THF (10 mL). The reaction mixture was stirred at 25 °C for 6 h, diluted with ether (30 mL), and washed with a saturated solution of $NaHCO_3$ (3 × 20 mL) and water (2 × 20 mL). The organic layer was dried ($MgSO_4$) and concentrated *in vacuo*. Chromatography of the residue on silica gel (10% EtOAc in *n*-hexane) yielded the vinyl derivative **44** as a single diastereoisomer (30.1 mg, 0.092 mmol, 92%). **44**: oil; $R_f$ = 0.80 (silica, 10% EtOAc in *n*-hexane); IR ($CHCl_3$) $\nu_{max}$ 3002, 2932, 2859, 1632, 1602, 1462, 1375, 1264, 1098, 1045, 1028 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ 5.94 (ddd, *J* = 17.5, 10.9, 4.2 Hz, 1H), 5.23 (m, 2H), 4.37 (dd, *J* = 4.2, 2.2 Hz, 1H), 3.68 (ddd, *J* = 6.1, 6.1, 6.1 Hz, 1H), 3.56 (dd, *J* = 10.2, 6.1 Hz, 1H), 3.39 (dd, *J* = 10.2, 6.1 Hz, 1H), 3.32 (ddd, *J* = 9.6, 9.6, 4.6 Hz, 1H), 3.10 (ddd, *J* = 11.0, 9.4, 4.3 Hz, 1H), 1.86 (m, 3H), 1.67–1.40 (m, 5H), 1.25 (m, 2H), 0.88 (s, 9H), 0.04 (m, 6H); $^{13}$C NMR ($CDCl_3$) δ 137.9 (d), 117.3 (t), 80.2 (d), 80.0 (d), 75.8 (d), 72.9 (d), 66.5 (t), 34.9 (t), 30.5 (t), 27.8 (t), 27.4 (t), 26.3 (3C, q), 19.3 (t), −4.78 (q), −4.92 (q); MS *m/e* (rel intensity) 326 ($M^+$, 0.5) 229 (10), 269 (2), 242 (23), 211 (31), 171 (15), 149 (53), 117 (30), 105 (28), 745 (100); HRMS calcd for $C_{18}H_{34}O_3Si$ ($M^+$) 326.2277, found 326.2283.

**(2*R**,4a*R**,6*R**,9a*S**)-2-Formyl-6-[(*tert*-butyldimethylsiloxy)methyl]pyrano[2,3-*b*]oxepane (45).** To a stirred solution of 4-methylmorpholine *N*-oxide (82.0 mg, 0.6 mmol) and $OsO_4$ (0.75 mg, 0.003 mmol) in THF:$H_2O$ (8.0 mL) was added compound **44** (100 mg, 0.31 mmol) in THF (2 mL). After being stirred for 6 h at 25 °C, the reaction was quenched with an aqueous saturated $Na_2SO_3$ solution and extracted with ether (3 × 20 mL). The combined ethereal phases were washed with 0.1 N NaOH (2 × 20 mL) and brine (50 mL) prior to drying ($MgSO_4$) and solvent evaporation. The residue (112 mg, 0.30 mmol) was dissolved in MeOH:$H_2O$ (5:1) (10 mL) and treated with $NaIO_4$ (130 mg, 0.6 mmol). The reaction mixture was stirred at 25 °C for 20 min, concentrated *in vacuo*, diluted with EtOAc (10 mL), and filtered through a Celite pad. The solution was diluted with ether (20 mL) and washed with a saturated solution of $NaHCO_3$ (3 × 10 mL) and water (2 × 10 mL). The organic layer was dried ($MgSO_4$) and concentrated *in vacuo*. Chromatography of the residue on silica gel (10% EtOAc in *n*-hexane) furnished the aldehyde **45** (84.4 mg, 0.25 mmol, 83%). **45**: oil; $R_f$ = 0.50 (silica, 10% EtOAc in *n*-hexane); IR ($CHCl_3$) $\nu_{max}$ 2931, 2858, 1732, 1602, 1462, 1255, 1113, 1045 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ 9.84 (s, 1H), 4.09 (d, *J* = 6.4 Hz, 1H), 3.68 (ddd, *J* = 6.3, 6.1, 5.8 Hz, 1H), 3.54 (dd, *J* = 10.4, 6.3 Hz, 1H), 3.39 (dd, *J* = 10.4, 5.8 Hz, 1H), 3.23 (ddd, *J* = 9.2, 9.2, 4.7 Hz, 1H), 3.09 (ddd, *J* = 11.1, 9.2, 4.4 Hz, 1H), 2.25 (m, 1H), 2.12 (m, 1H), 1.94 (m, 1H), 1.66 (m, 4H), 1.25 (m, 3H), 0.88 (s, 9H), 0.03 (s, 6H); $^{13}$C NMR ($CDCl_3$) δ 205.1 (s), 80.4 (d), 80.3 (d), 79.0 (d), 78.9 (d), 66.5 (t), 34.8 (t), 30.5 (t), 28.5 (t), 26.3 (3C, q), 23.6 (t), 19.2 (t), −4.8 (q), −4.9 (q); MS *m/e* (rel intensity) 299 ($M^+$ − CHO, 2), 271 (14), 177 (14), 171 (20), 149 (65), 117 (42), 105 (33), 75 (100); HRMS calcd for $C_{16}H_{31}O_3Si$ (M − CHO)$^+$ 299.2042, found 299.2038.

**Methyl 4,6-Di-*O*-acetyl-2,3-didehydro-2,3-dideoxy-α,β-D-*erythro*-pyranoside (47ab).** To a stirred solution of tri-*O*-acetyl-D-glucal (**46**) (20.0 g, 73.5 mmol) in dry $CH_2Cl_2$ (300 mL) at −78 °C was added, under argon, dry MeOH (3.27 mL, 80.8 mmol) dropwise, followed by addition of $SnCl_4$ (9.09 mL, 80.8 mmol). After 10 min at −78 °C, the reaction mixture was diluted with ether (500 mL), washed with aqueous saturated $NaHCO_3$ solution (2 × 300 mL) and water (2 × 300 mL), and then dried ($MgSO_4$). Concentration followed by flash chromatography (silica, 20% EtOAc in *n*-hexane) gave **47ab** (14.9 g, 61.0 mmol, 83%) as a 6:1 mixture of α:β anomers. The α-*anomer* was isolated by successive chromatographic purifications (silica, 10% EtOAc in *n*-hexane) as a colorless syrup (2.4 g) with $[\alpha]^{25}_D$ = +143° (*c* 1.5, $CHCl_3$); $R_f$ = 0.30 (silica, 20% EtOAc in *n*-hexane); IR ($CHCl_3$) $\nu_{max}$ 3030, 2957, 2933, 2908, 2832, 1744, 1451, 1371, 1242, 1048, 965, 910 cm$^{-1}$; $^1$H NMR (200 MHz, $CDCl_3$) δ 5.82 (m, 2H), 5.28 (dd, *J* = 9.6, 1.2 Hz, 1H), 4.89 (s, 1H), 4.17 (m, 2H), 4.04 (ddd, *J* = 9.6, 5.2, 2.5 Hz, 1H), 3.42 (s, 3H), 2.07 (s, 3H), 2.05 (s, 3H); $^{13}$C NMR ($CDCl_3$) δ 170.7 (s), 170.3 (s), 129.3 (d), 127.8 (d), 95.5 (d), 67.0 (d), 65.4 (d), 63.0 (t), 55.9 (q), 20.9 (q), 20.7 (q); MS *m/e* (rel intensity) 213 ($M^+$ − OMe, 3) 153 (4), 142 (15), 111 (15), 100 (100), 71 (17); HRMS calcd for $C_{10}H_{13}O_5$ (M − OMe)$^+$ 213.0763, found 213.0771. β-*Anomer* (from α+β mixture): $^{13}$C NMR ($CDCl_3$) δ 170.7 (s), 170.3 (s), 130.3 (d), 126.4 (d), 96.1 (d), 72.9 (d), 64.4 (d), 63.5 (t), 55.3 (q), 21.0 (q), 20.8 (q).

**Methyl 4,6-Di-*O*-acetyl-2,3-dideoxy-α,β-D-*erythro*-pyranoside (48ab).** $PtO_2$ catalyst (50 mg) was added to a stirred solution of the mixture **46ab** (α:β anomers, 6:1) (14.9 g, 61.0 mmol) in THF at 25 °C under $H_2$ atmosphere. After the mixture was stirred for 6 h at 25 °C, the catalyst was filtered off and the solvent was removed under vacuo to give essentially pure **47ab** (α:β anomers, 6:1) (12.8 g, 52.4 mmol, 95%). Chromatography of the crude residue on silica gel (eluant: 10% EtOAc in *n*-hexane containing 1 mL/L of pyridine) first gave **48a** (α anomer) as a colorless oil: $R_f$ = 0.3 (silica, 20% EtOAc in *n*-hexane); $[\alpha]^{25}_D$ = +83° (*c* 0.5, $CHCl_3$); IR (neat) $\nu_{max}$ 2958, 1737, 1438, 1369, 1245, 1052 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ 4.76 (m, 2H), 4.29 (dd, *J* = 12.0, 5.3 Hz, 1H), 4.15 (dd, *J* = 12.0, 2.3 Hz, 1H), 3.94 (ddd, *J* = 10.0, 5.3, 2.3 Hz, 1H), 3.41 (s, 3H), 2.13 (s, 3H), 2.08 (s, 3H), 2.01 (m, 1H), 1.86 (m, 3H); $^{13}$C NMR ($CDCl_3$) δ 170.7 (s), 169.9 (s), 97.6 (d), 68.7 (d), 67.9 (d), 63.3 (t), 54.6 (q), 28.8 (t), 24.1 (q), 21.0 (q), 20.8 (q); MS *m/e* (rel intensity) 215 ($M^+$ − OMe, 12), 173 (4), 144 (12), 126 (8), 113 (8), 84 (29), 71 (14), 58 (100); HRMS calcd for $C_{10}H_{15}O_5$ (M−OMe)$^+$ 215.0919, found 215.0920. Further elution gave **48b** (β anomer) as a colorless oil; $R_f$ = 0.26 (silica, 20% EtOAc in *n*-hexane); IR ($CHCl_3$) $\nu_{max}$ 2935, 2854, 1738, 1459, 1370, 1242, 1062 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ 4.75 (m, 1H), 4.46 (dd, *J* = 8.4, 2.1 Hz, 1H), 4.29 (dd, *J* = 11.9, 5.3 Hz, 1H),

4.20 (dd, $J$ = 11.9, 3.1 Hz, 1H), 3.69 (ddd, $J$ = 8.6, 5.3, 3.1 Hz, 1H), 3.51 (s, 3H), 2.25 (m, 1H), 2.11 (s, 3H), 2.07 (s, 3H), 1.94 (m, 1H), 1.69 (m, 1H), 1.59 (m, 1H); $^{13}$C NMR ($CDCl_3$) $\delta$ 171.2 (s), 170.4 (s), 102.8 (d), 75.2 (d), 67.9 (d), 63.7 (t), 56.8 (q), 29.7 (t), 26.9 (t), 21.4 (q), 21.2 (q); MS $m/e$ (rel intensity) 246 ($M^+$, 1), 215 (3), 173 (14), 144 (13), 115 (14), 99 (23), 84 (34), 69 (34), 58 (100); HRMS calcd for $C_{11}H_{18}O_6$ ($M^+$) 246.1103, found 246.1101.

**Phenyl 4,6-Di-*O*-acetyl-2,3-dideoxy-1-thio-$\alpha$,$\beta$-*erythro*-pyranoside (49ab).** To a stirred solution of **48ab** ($\alpha$:$\beta$ anomers, 6:1) (10.0 g, 40.6 mmol) in dry $CH_2Cl_2$ (120 mL) was added, under argon atmosphere, $PhSSiMe_3$ (11.5 mL, 60.9 mmol) followed by addition of TMSOTf (9.4 mL, 48.7 mmol). After 10 h at 25 °C, the mixture was diluted with ether (100 mL) and quenched with an aqueous solution of $Ba(OH)_2$ (1 M, 100 mL). Dilution with ether (100 mL) and sequential washing with $H_2O$ (2 × 50 mL) and brine (50 mL), drying ($MgSO_4$), and concentration yielded a crude mixture of **49ab** ($\alpha$:$\beta$ anomers, 4:1) (11.70 g, 36.13 mmol, 86%) which was separated into the $\alpha$ and $\beta$ anomers by column chromatography (silica, 20% EtOAc in $n$-hexane). **49a** ($\alpha$ anomer): crystalline solid; mp 96–98 °C (ether/$n$-hexane); $R_f$ = 0.45 (20% EtOAc in $n$-hexane); $[\alpha]^{25}_D$ = +244° ($c$ 0.3, $CHCl_3$); IR ($CHCl_3$) $\nu_{max}$ 2916, 2285, 1737, 1456, 1373, 1212, 1096, 995 cm$^{-1}$; $^1$H NMR (200 MHz, $CDCl_3$) $\delta$ 7.45 (m, 2H), 7.25 (m, 3H), 5.56 (d, $J$ = 4.9 Hz, 1H), 4.74 (ddd, $J$ = 10.0, 10.0, 4.5 Hz, 1H), 4.45 (ddd, $J$ = 10.0, 5.7, 2.3 Hz, 1H), 4.26 (dd, $J$ = 11.9, 5.7 Hz, 1H), 4.05 (dd, $J$ = 11.9, 2.3 Hz, 1H), 2.03 (s, 3H), 2.00 (s, 3H), 2.2–1.8 (m, 4H); $^{13}$C NMR ($CDCl_3$) $\delta$ 169.8 (s), 169.2 (s), 134.2 (s), 130.8 (2C, d), 128.4 (2C, d), 126.6 (d), 83.5 (d), 68.8 (d), 67.5 (d), 62.5 (t), 29.2 (t), 25.1 (t), 20.4 (q), 20.1 (q); MS $m/e$ (rel intensity) 324 ($M^+$, 2), 215 (100), 155 (39), 135 (4), 113 (28), 109 (23), 95 (49), 67 (34); HRMS calcd for $C_{16}H_{19}O_5S$ ($M - H$)$^+$ 323.0953, found 323.0973; calcd for $C_9H_{11}O_4S$ 215.0378, found 215.0381; calcd for $C_6H_7O$ 95.0497, found 95.0497. **49b** ($\beta$ anomer): colorless syrup; $R_f$ = 0.35 (silica, 20% EtOAc in $n$-hexane); $[\alpha]^{25}_D$ = +50.0° ($c$ 0.4, $CHCl_3$); IR (neat) $\nu_{max}$ 2953, 2916, 2848, 1738, 1455, 1372, 1252, 1212, 1058, 991, 908 cm$^{-1}$; $^1$H NMR (200 MHz, $CDCl_3$) $\delta$ 7.50 (m, 2H), 7.30 (m, 3H), 4.78 (dd, $J$ = 11.2, 2.3 Hz, 1H), 4.68 (ddd, $J$ = 9.9, 9.9, 4.5 Hz, 1H), 4.20 (d, $J$ = 4.4 Hz, 2H), 3.67 (ddd, $J$ = 9.4, 4.4, 4.4 Hz, 1H), 2.30 (m, 1H), 2.07 (s, 3H), 2.04 (s, 3H), 1.88 (m, 1H), 1.75 (m, 1H), 1.60 (m, 1H); $^{13}$C NMR ($CDCl_3$) $\delta$ 170.7 (s), 169.8 (s), 134.0 (s), 131.4 (2C, d), 128.7 (2C, d), 127.3 (d), 84.5 (d), 77.9 (d), 67.4 (d), 63.4 (t), 30.4 (t), 29.6 (t), 20.9 (q), 20.7 (q); MS $m/e$ (rel intensity) 324 ($M^+$, 3), 215 (100), 155 (40), 113 (41), 109 (33), 95 (78), 83 (22), 67 (50); HRMS calcd for $C_{16}H_{20}O_5S$ ($M^+$) 324.1031, found 324.1028.

**Phenyl 4,6-Di-*O*-isopropylidene-2,3-dideoxy-1-thio-$\alpha$-D-*erythro*-pyranoside (50).** A mixture of **49a** ($\alpha$ anomer) (10.0 g, 30.8 mmol) and $K_2CO_3$ (420 mg, 3.0 mmol) in MeOH (50 mL) was stirred at 25 °C for 1 h. Dilution with ether (50 mL) followed by filtration through a Celite pad and concentration gave a residue which was diluted with ether (200 mL) and washed with $H_2O$ (2 × 150 mL) and brine (150 mL) and dried ($MgSO_4$). Concentration followed by flash column chromatography (silica, 80% EtOAc in $n$-hexane) yielded the corresponding diol (7.4 g, 30.7 mmol, 100%) which was dissolved in dry $CH_2Cl_2$ (20 mL) and further treated with 2,2-dimethoxypropane (7.58 mL, 61.6 mmol) and a catalytic amount of $POCl_3$. After 12 h of continuous stirring at 25 °C, the reaction mixture was poured directly into ether (200 mL) and a saturated aqueous solution of $NaHCO_3$ (100 mL). After shaking and separation, the organic portion was dried ($MgSO_4$) and concentrated to yield, after chromatographic purification (silica, 20% EtOAc in $n$-hexane) compound **50** (7.93 g, 28.3 mmol, 92%). **50**: oil; $R_f$ = 0.65 (silica, 20% EtOAc in $n$-hexane); $[\alpha]^{25}_D$ = +241° ($c$ 0.3, $CHCl_3$); IR (neat) $\nu_{max}$ 2996, 2952, 2341, 1584, 1480, 1384, 1208, 1153, 1084, 1044, 865, 744, 726 cm$^{-1}$; $^1$H NMR (200 MHz, $CDCl_3$) $\delta$ 7.44 (m, 2H), 7.28 (m, 3H), 5.51 (d, $J$ = 4.8 Hz, 1H), 4.18 (ddd, $J$ = 9.2, 9.2, 6.6 Hz, 1H), 3.69 (m, 3H), 2.17 (m, 2H), 1.85 (m, 2H), 1.51 (s, 3H), 1.43 (s, 3H); $^{13}$C NMR ($CDCl_3$) $\delta$ 135.2 (s), 131.3 (2C, d), 129.0 (2C, d), 127.0 (d), 99.3 (s), 84.4 (d), 70.7 (d), 67.0 (d), 62.6 (t), 30.7 (t), 29.4 (q), 25.8 (t), 19.3 (q); MS $m/e$ (rel intensity) 280 ($M^+$, 10), 265 (18), 205 (7), 171 (98), 135 (13), 123 (13), 113 (100), 69 (83), 55 (55); HRMS calcd for $C_{15}H_{20}O_3S$ ($M^+$) 280.1133, found 280.1142.

**Phenyl 4,6-Di-*O*-isopropylidene-2,3-dideoxy-1-sulfonyl-$\alpha$-D-*erythro*-pyranoside (51).** A stirred solution of mixed ketal **50** (6.5 g, 23.2 mmol) in dry EtOAc (200 mL) at 0 °C was treated with $m$-CPBA (12.0 g, 69.6 mmol) and $NaHCO_3$ (5.84 g, 69.6 mmol). After 5 h of stirring at 25 °C, the reaction mixture was diluted with ether (100 mL) and filtered through a pad of Celite. The filtrate was washed with water (2 × 100 mL) and brine (100 mL) and dried ($MgSO_4$). Concentration and flash chromatography (silica, 20% EtOAc in $n$-hexane) furnished compound **51** (6.8 g, 21.8 mmol, 94%) as a colorless syrup. **51**: oil; $R_f$ = 0.45 (silica, 30% EtOAc in $n$-hexane); $[\alpha]^{25}_D$ = +87° ($c$ 0.2, $CHCl_3$); IR ($CHCl_3$) $\nu_{max}$ 2848, 1722, 1615, 1375, 1305, 1216, 1148, 1079, 774 cm$^{-1}$; $^1$H NMR (200 MHz, $CDCl_3$) $\delta$ 7.93 (m, 2H), 7.62 (m, 3H), 4.60 (dd, $J$ = 6.3, 3.2 Hz, 1H), 4.33 (ddd, $J$ = 9.9, 5.1, 5.1 Hz, 1H), 3.60 (m, 3H), 2.82 (m, 1H), 2.18 (m, 1H), 1.89 (m, 1H), 1.48 (s, 3H), 1.42 (s, 3H), 1.30 (m, 1H); $^{13}$C NMR ($CDCl_3$) $\delta$ 136.9 (s), 133.6 (d), 128.8 (2C, d), 128.4 (2C, d), 99.2 (s), 87.6 (d), 69.23 (d), 69.19 (d), 62.1 (t), 28.8 (q), 24.5 (t), 21.2 (t), 18.7 (q); MS $m/e$ (rel intensity) 313 ($M^+ - 1$, 4), 297 (20), 171 (37), 155 (17), 125 (59), 113 (100), 95 (22), 83 (43), 69 (54), 43 (39); HRMS calcd for $C_{15}H_{21}O_5S$ ($M + H$)$^+$ 313.1109, found 313.1102.

**(4a*R*,6*R*,8a*S*)-Perhydro-2,2-dimethyl-6-vinylpyrano[2,3-*d*]-1,3-dioxin (52).** A freshly prepared 1.0 M solution of vinylmagnesium bromide (40.0 mL, 40.0 mmol) in dry THF was treated with a 1.0 M solution of $ZnBr_2$ in THF (24.0 mL, 24.0 mmol), and the reaction mixture was stirred for 40 min under argon at 25 °C to afford the organozinc compound. The clear decanted solution was filtered and slowly added through a cannula to a stirred solution of the sulfone **51** (5.0 g, 16.0 mmol) in dry THF (40 mL). The reaction mixture was stirred under argon for 12 h at 40 °C, diluted with ether (200 mL), and washed with a saturated aqueous solution of $NaHCO_3$ (3 × 100 mL) and water (2 × 100 mL). The organic layer was dried ($MgSO_4$) and concentrated *in vacuo*. Chromatography of the residue on silica gel (5% EtOAc in $n$-hexane) yielded the vinyl derivative **52** (2.7 g, 13.4 mmol, 84%). **52**: oil; $R_f$ = 0.45 (10% EtOAc in $n$-hexane); $[\alpha]^{25}_D$ = +53.6° ($c$ 0.3 $CHCl_3$); IR ($CHCl_3$) $\nu_{max}$ 3086, 3009, 2949, 2801, 2455, 1732, 1641, 1460, 1375, 1121, 1088, 939, 885, 840 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 5.96 (ddd, $J$ = 17.5, 10.8, 4.2 Hz, 1H), 5.28 (m, 2H), 4.43 (m, 1H), 3.78 (dd, $J$ = 10.8, 5.3 Hz, 1H), 3.67 (dd, $J$ = 10.8, 10.8 Hz, 1H), 3.63 (ddd, $J$ = 10.9, 9.8, 4.3 Hz, 1H), 3.50 (ddd, $J$ = 9.8, 9.8, 5.2 Hz, 1H), 1.98 (m, 1H), 1.94 (m, 1H), 1.75 (m, 1H), 1.64 (m, 1H), 1.50 (s, 3H), 1.39 (s, 3H); $^{13}$C NMR ($CDCl_3$) $\delta$ 137.6 (t), 117.8 (d), 99.8 (s), 73.6 (d), 71.7 (d), 68.7 (d), 63.6 (t), 29.8 (q), 27.8 (t), 25.6 (t), 19.7 (q); MS $m/e$ (rel intensity) 198 ($M^+$, 2), 184 (2), 183 (15), 155 (2), 140 (5), 123 (8), 97 (100), 79 (55), 69 (41), 55 (46); HRMS calcd for $C_{11}H_{18}O_3$ ($M^+$) 198.1256, found 198.1249.

**(4a*R*,6*R*,8a*S*)-Perhydro-2,2-dimethyl-6-formylpyrano[2,3-*d*]-1,3-dioxin (53).** To a stirred solution of 4-methylmorpholine $N$-oxide (2.70 g, 20.0 mmol) and $OsO_4$ (25 mg, 0.1 mmol) in THF:$H_2O$ (1:1) (100 mL) was added dropwise a solution of compound **52** (1.98 g, 10.0 mmol) in THF (15.0 mL). After being stirred for 12 h at 25 °C, the reaction was quenched with a saturated solution of $Na_2SO_3$ (200 mL) and extracted with ether (2 × 200 mL). The combined ethereal phases were washed with 0.1 N NaOH (2 × 100 mL) and brine (100 mL) prior to drying ($MgSO_4$) and solvent evaporation. The residue was dissolved in MeOH:$H_2O$ (4:1) (30 mL), treated with $NaIO_4$ (4.27 g, 20.0 mmol), and stirred at 25 °C for 30 min. The MeOH was evaporated in vacuo and the residue diluted with ether (200 mL), filtered through a Celite pad, and then sequentially washed with $H_2O$ (3 × 50 mL) and brine (50 mL). Drying ($MgSO_4$), concentration, and flash chromatography (silica, 5% EtOAc in $n$-hexane) afforded the $\alpha$-C-glycosyl aldehyde **53** (1.68 g, 84 mmol, 84%). **53**: crystalline solid, mp 56–58 °C (ether/$n$-hexane); $R_f$ = 0.20 (silica, 10% EtOAc in $n$-hexane); $[\alpha]^{25}_D$ = +62.0° ($c$ 0.2 $CHCl_3$); IR ($CHCl_3$) $\nu_{max}$ 2998, 2945, 2883, 1732, 1384, 1270, 1230, 1200, 1088, 1047 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 9.82 (s, 1H), 4.14 (d, $J$ = 6.1 Hz, 1H), 3.91 (dd, $J$ = 10.8, 5.2 Hz, 1H), 3.72 (dd, $J$ = 10.8, 10.8 Hz, 1H), 3.60 (ddd, $J$ = 11.2, 9.6, 4.1 Hz, 1H), 3.56 (ddd, $J$ = 9.6, 9.6, 5.2 Hz, 1H), 2.31 (dd, $J$ = 14.1, 2.9 Hz, 1H), 1.82 (m, 2H), 1.49 (s, 3H), 1.39 (m, 1H), 1.36 (s, 3H); $^{13}$C NMR ($CDCl_3$) $\delta$ 204.2 (s), 100.0 (s), 79.3 (d), 72.6 (d), 70.2 (d), 63.1 (t), 29.6 (q), 26.5 (t), 23.4 (t), 19.5 (q); MS $m/e$ (rel intensity) 201 ($M^+ + 1$, 42), 200 (1), 185 (100), 171 (71), 142 (20), 125 (47), 113 (51), 95 (49), 83 (37), 69 (84), 59 (63); HRMS calcd for $C_{10}H_{17}O_4$ ($M + H$)$^+$ 201.1127, found 201.1144; calcd for $C_9H_{13}O_4$ ($M - Me$)$^+$ 185.0814, found 185.0814; calcd for $C_9H_{15}O_3$ ($M - CHO$)$^+$ 171.1021, found 171.1027.

**(4a*R*,8a*S*)-2,2-Dimethyl-6[(*E*/*Z*)-(*tert*-butyldimethylsiloxy)methylidene]pyrano[2,3-*d*]-1,3-dioxin [54a(*E*) and 54b(*Z*)].** To a stirred solution of the α-C-glycosyl aldehyde **53** (500.2 mg, 2.5 mmol), TEA (556 mg, 5.5 mmol), and dry $CH_2Cl_2$ (30 mL) was added TBDMSOTf (1.32 g, 5.0 mmol). After 12 h at 25 °C the reaction was quenched with ether (100 mL) followed by washing with an aqueous saturated solution of $NaHCO_3$ (2 × 50 mL) and $H_2O$ (2 × 50 mL). Drying ($MgSO_4$), concentration and flash chromatography (silica, 5% EtOAc in petroleum ether) gave the vinyl ether **54** as a 3:1 mixture of *E*:*Z* isomers (565 mg, 1.8 mmol, 72%). **54a** (*E* isomer): oil; $R_f$ = 0.60 (silica, 10% EtOAc in *n*-hexane); $^1$H NMR (200 MHz, $CDCl_3$) δ 6.36 (d, *J* = 2.0 Hz, 1H), 3.9–3.7 (m, 4H), 3.25 (ddd, *J* = 9.5, 9.5, 5.4 Hz, 1H), 2.88 (m, 1H), 2.15–1.95 (m, 2H), 1.53 (s, 3H), 1.41 (s, 3H), 0.92 (s, 6H), 0.90 (s, 3H), 0.12 (s, 3H), 0.11 (s, 3H). **54b** (*Z* isomer): oil; $R_f$ = 0.55 (silica, 10% EtOAc in *n*-hexane); $^1$H NMR (200 MHz, $CDCl_3$) δ 5.65 (d, *J* = 1.7 Hz, 1H), 3.95 (dd, *J* = 10.6, 5.5 Hz, 1H), 3.84 (d, *J* = 10.6 Hz, 1H), 3.75 (m, 1H), 3.35 (m, 1H), 2.19 (m, 2H), 1.93 (m, 1H), 1.53 (s, 3H), 1.42 (s, 3H), 0.92 (s, 9H), 0.12 (s, 3H), 0.11 (s, 3H); MS *m*/*e* (rel intensity) 315 (M + 1, 2), 297 (14), 171 (63), 125 (49), 113 (100), 77 (67), 71 (82). HRMS calcd for $C_{16}H_{31}O_4Si$ (M + H)$^+$ 315.1991, found 315.1998.

**(4a*R*,8a*S*)-4,4a,8,8a-Tetrahydro-2,2-dimethyl-6-formylpyrano[2,3-*d*]-1,3-dioxin (55).** To a stirred mixture of compounds **54ab** (*E*:*Z*, 3:1) (100.0 mg, 0.32 mmol) in acetonitrile (3.0 mL) at 0 °C was added $Pd^{II}(OAc)_2$ (79.2 mg, 0.35 mmol). After 12 h at 25 °C the mixture was filtered through a Celite pad, diluted with ether (50 mL), washed with $H_2O$ (2 × 20 mL) and brine (20 mL), and dried ($MgSO_4$). Concentration followed by flash chromatography (silica, 20% EtOAc in *n*-hexane) afforded the α,β-unsaturated aldehyde **55** (51.2 mg, 80%). **55**: noncrystalline solid; $R_f$ = 0.65 (silica, 50% EtOAc in *n*-hexane); IR ($CHCl_3$) 2998, 2960, 2926, 2851, 1698, 1631, 1257, 1154, 1099, 1072, 1042 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ 9.21 (s, 1H), 5.93 (dd, *J* = 5.7, 2.8 Hz, 1H), 4.19 (dd, *J* = 11.1, 5.4 Hz, 1H), 4.03 (ddd, *J* = 9.6, 9.6, 6.0 Hz, 1H), 3.96 (dd, *J* = 11.1, 11.1 Hz, 1H), 3.70 (ddd, *J* = 9.8, 9.8, 5.3 Hz, 1H), 2.61 (ddd, *J* = 18.7, 5.8, 5.8 Hz, 1H), 2.43 (ddd, *J* = 18.7, 9.8, 2.8 Hz, 1H), 1.59 (s, 3H), 1.48 (s, 3H); $^{13}$C NMR ($CDCl_3$) δ 186.0 (s), 121.0 (d), 98.4 (s), 72.0 (d), 66.8 (d), 62.4 (t), 29.5 (q), 28.8 (t), 19.5 (q); MS *m*/*e* (rel intensity) 199 (M$^+$ + 1, 1), 183 (3), 165 (2), 115 (7), 97 (19), 81 (26), 69 (30), 57 (66), 55 (100); HRMS calcd for $C_{10}H_{15}O_4$ (M + H)$^+$ 199.0970, found 199.0972; calcd for $C_{10}H_{14}O_4$ (M$^+$) 198.0892, found 198.0902; calcd for $C_9H_{11}O_4$ (M − Me)$^+$ 183.0657, found 183.0656.

**(4a*R*,8a*S*)-4,4a,8,8a-Tetrahydro-2,2-dimethyl-6-(hydroxymethyl)pyrano[2,3-*d*]-1,3-dioxin (56, R = H).** DIBAL (0.24 mL, 1 M in hexanes, 0.24 mmol) was added dropwise dropwise to a stirred solution of the aldehyde **55** (39.6 mg, 0.20 mmol) in dry ether (5.0 mL) at −78 °C over a 5-min period. After 3 h of stirring at 25 °C, the mixture was diluted with ether (50 mL) and washed with saturated aqueous sodium potassium tartrate solution (20 mL). Drying ($MgSO_4$) and concentration followed by flash chromatography (silica, 30% EtOAc in *n*-hexane) afforded the allylic alcohol **56**, R = H (38.2 mg, 0.19 mmol, 95%). **56, R = H**: oil; $R_f$ = 0.45 (silica, 50% EtOAc in *n*-hexane); $[\alpha]^{25}_D$ = +49° (*c* 0.1, $CHCl_3$); IR ($CHCl_3$) $\nu_{max}$ 3690, 3607, 2998, 2932, 1733, 1677, 1602, 1375, 1100, 1073 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ 4.84 (dd, *J* = 5.4, 2.1 Hz, 1H), 4.02 (m, 4H), 3.87 (dd, *J* = 10.7, 10.7 Hz, 1H), 3.70 (ddd, *J* = 9.9, 9.8, 5.4 Hz, 1H), 2.28 (ddd, *J* = 16.1, 5.7, 5.7 Hz, 1H), 2.17 (ddd, *J* = 16.1, 9.8, 1.7 Hz, 1H), 1.59 (s, 3H), 1.48 (s, 3H); $^{13}$C NMR ($CDCl_3$) δ 99.6 (s), 98.2 (s), 96.2 (d), 71.4 (d), 67.4 (d), 62.9 (t), 62.4 (t), 29.3 (q), 27.1 (t), 19.2 (q); MS *m*/*e* (rel intensity) 200 (M$^+$, 26), 185 (26), 125 (21), 111 (33), 101 (47), 81 (40), 69 (94), 55 (100); HRMS calcd for $C_{10}H_{16}O_4$ (M$^+$) 200.1048, found 200.1085; calcd for $C_9H_{13}O_4$ (M − Me)$^+$ 185.0814, found 185.0831.

**(4a*R*,8a*S*)-4,4a,8,8a-Tetrahydro-2,2-dimethyl-6-[(*tert*-butyldimethylsiloxy)methyl]pyrano[2,3-*d*]dioxin (56, R = $^t$BuMe$_2$Si).** TBDMSCl (90.4 mg, 0.60 mmol) was added in one portion to a cooled (0 °C) and stirred solution of **56** (R = H) (100 mg, 0.5 mmol) and imidazole (51.0 mg, 0.75 mmol) in dry THF (10.0 mL) under an argon atmosphere. The reaction mixture was stirred for 6 h before dilution with ether (50 mL), washing with aqueous saturated $NH_4Cl$ solution (2 × 20 mL) and brine (20 mL), and drying ($MgSO_4$). Concentration followed by flash chromatography (silica, 20% EtOAc in *n*-hexane) gave compound **56**, R = $^t$BuMe$_2$Si (156.4 mg, 0.5 mmol). **56, R = $^t$BuMe$_2$Si**: oil; $R_f$ = 0.48 (silica, 10% ether in petroleum ether); $[\alpha]^{25}_D$ = +12° (*c* 0.4 $CHCl_3$); IR (neat) $\nu_{max}$ 3050, 3000, 2940, 2860, 1675, 1595, 1465, 1430, 1375, 1320, 1265, 1240, 1185, 1100, 940 cm$^{-1}$; $^1$H NMR (200 MHz, $CDCl_3$) δ 4.80 (br s, 1H), 3.98 (m, 3H), 3.93 (m, 1H), 3.80 (dd, *J* = 10.5, 10.5 Hz, 1H), 3.62 (ddd, *J* = 10.5, 9.7, 5.5 Hz, 1H), 2.22 (m, 1H), 2.21 (m, 1H), 1.53 (s, 3H), 1.40 (s, 3H), 0.90 (s, 9H), 0.11 (s, 6H); $^{13}$C NMR ($CDCl_3$) δ 153.0 (s), 99.8 (s), 94.5 (d), 71.4 (d), 67.9 (d), 62.8 (t), 62.7 (t), 29.6 (q), 27.4 (t), 26.3 (q), 19.5 (q), −4.9 (q); MS *m*/*e* (rel intensity) 315 (M + 1, 0.5), 299 (12), 258 (100), 237 (22), 199 (97), 179 (32), 143 (96), 121 (98), 60 (49); HRMS calcd for $C_{16}H_{31}O_4Si$ (M + H)$^+$ 315.1991, found 315.2001.

**2,6-Anhydro-1-*O*-(*tert*-butyldimethylsilyl)-4-deoxy-5,7-*O*-isopropylidene-D-*allo*-heptitol (57, R = $^t$BuMe$_2$Si) and 2,6-Anhydro-7-*O*-(*tert*-butyldimethylsilyl)-4-deoxy-1,3-isopropylidene-D-*manno*-heptitol (58, R = $^t$BuMe$_2$Si).** To a stirred solution of the cyclic enol ether **56**, R = $^t$BuMe$_2$Si (156 mg, 0.5 mmol) in dry THF (2.0 mL) at 0 °C was added $BH_3$·Me$_2$S (0.38 mL, 0.75 mmol, 2M in THF) dropwise over a 5-min period. After the mixture was stirred for 12 h at 25 °C, the excess borane was quenched carefully with $H_2O$ (0.5 mL). Dropwise addition of a mixture of 3 N NaOH (0.7 mL, 2.10 mmol) and 30% $H_2O_2$ (0.20 mL, 3.1 mmol) over 5 min, removal of the cooling bath, and continued stirring for 30 min resulted in a white heterogeneous mixture. Dilution with ether (20 mL), followed by washing with $H_2O$ (2 × 20 mL) and brine (20 mL), drying ($MgSO_4$), concentration, and flash chromatography (silica, 10–20% EtOAc in *n*-hexane), produced the desired alcohol **57** (R = $^t$BuMe$_2$Si) (119.5 mg, 0.36 mmol, 72%) and its diastereomer **58** (R = $^t$BuMe$_2$Si) (30.0 mg, 0.09 mmol, 18%) (less polar component). **57 (R = $^t$BuMe$_2$Si)**: oil; $R_f$ = 0.25 (silica, 25% EtOAc in *n*-hexane); $[\alpha]^{25}_D$ = +9.9° (*c* 0.21 $CHCl_3$); IR (neat) $\nu_{max}$ 3450, 3080, 3050, 2950, 2860, 1595, 1480, 1427, 1380, 1365, 1275, 1200, 1010, 825, 740 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ 3.94 (dd, *J* = 10.0, 4.7 Hz, 1H), 3.86 (dd, *J* = 10.8, 5.2 Hz, 1H), 3.77 (ddd, *J* = 10.0, 8.4, 4.8 Hz, 1H), 3.68 (dd, *J* = 10.0, 8.4 Hz, 1H), 3.64 (dd, *J* = 10.8, 10.6 Hz, 1H), 3.56 (m, 1H), 3.34 (ddd, *J* = 8.4, 8.4, 4.7 Hz, 1H), 3.19 (ddd, *J* = 10.6, 9.6, 5.2 Hz, 1H), 2.31 (ddd, *J* = 11.6, 4.8, 4.5 Hz, 1H), 1.6 (m, 1H), 1.49 (s, 3H), 1.42 (s, 3H), 0.91 (s, 9H), 0.08 (s, 6H); $^{13}$C NMR ($CDCl_3$) δ 99.6 (s), 79.6 (d), 74.4 (d), 70.8 (d), 69.0 (d), 66.4 (d), 63.0 (t), 37.8 (t), 30.1 (s), 29.6 (q), 19.5 (q), −5.2 (q), −5.3 (q); MS *m*/*e* (rel intensity) 317 (M$^+$ − Me, 31) 275 (4), 259 (2), 239 (4), 217 (100), 199 (16), 187 (25), 137 (28), 169 (14), 157 (14), 147 (14), 143 (22), 131 (38), 129 (22), 117 (70), 105 (20), 75 (82); HRMS calcd for $C_{15}H_{29}O_5Si$ (M − Me)$^+$ 317.1874, found 317.1777; calcd for $C_{12}H_{23}O_5Si$ (M − $^t$Bu)$^+$ 275.1315, found 275.12984. **58 (R = $^t$BuMe$_2$Si)**: oil; $R_f$ = 0.32 (silica, 25% EtOAc in *n*-hexane); $[\alpha]^{25}_D$ = +6.3° (*c* 0.55, $CHCl_3$); IR (neat) $\nu_{max}$ 3450, 3075, 3000, 2940, 1595, 1480, 1470, 1380, 1210, 1185, 1100, 865 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ 4.20 (br s, 1H), 4.05 (ddd, *J* = 11.7, 9.8, 4.5 Hz, 1H), 3.80 (m, 4H), 3.71 (dd, *J* = 10.5, 10.5 Hz, 1H), 3.46 (ddd, *J* = 10.5, 9.8, 5.3 Hz, 1H), 2.04 (m, 1H), 1.82 (m, 1H), 1.49 (s, 3H), 1.40 (s, 3H), 0.90 (s, 9H), 0.10 (s, 6H); $^{13}$C NMR ($CDCl_3$) δ 100.1 (s), 80.0 (d), 69.8 (d), 67.6 (d), 66.8 (d), 63.6 (t), 62.3 (t), 33.5 (t), 30.1 (s), 29.7 (q), 26.3 (q), 19.7 (q); MS *m*/*e* (rel intensity) 317 (M$^+$ − Me, 35), 275 (43), 239 (5), 217 (16), 199 (22), 169 (17), 145 (69), 117 (82), 75 (100); HRMS calcd for $C_{15}H_{29}O_5Si$ (M − Me)$^+$ 317.1784, found 317.1787; calcd for $C_{12}H_{23}O_5Si$ (M − $^t$Bu)$^+$ 275.1315, found 275.1315.

**(4a*R*,8a*S*)-4,4a,8,8a-Tetrahydro-6-[(benzyloxy)methyl]-2,2-dimethylpyrano[2,3-*d*]-1,3-dioxin (56, R = Bzl).** A stirred solution of the enol **56**, R = H (38 mg, 0.19 mmol), in dry THF (5 mL) was treated with NaH (5.5 mg, 0.23 mmol), BnBr (49 mg, 0.28 mmol), and a catalytic amount of *n*-$Bu_4NBr$. After 30 min of vigorous stirring at 25 °C, the reaction mixture was diluted with ether (30 mL), washed with a saturated aqueous solution of $NaHCO_3$ (3 × 20 mL) and $H_2O$ (3 × 20 mL), and dried ($MgSO_4$). Concentration in vacuo followed by flash chromatography (silica, 5% EtOAc in *n*-hexane) yielded the benzyl ether **56** (R = Bzl) (47.6 mg, 0.16 mmol, 86%). **56 (R = Bzl)**: noncrystalline solid; $[\alpha]^{25}_D$ = +1.4° (*c* 0.32, $CHCl_3$); IR ($CHCl_3$) $\nu_{max}$ 3000, 2940, 2890, 1675, 1450, 1380, 1240, 1205, 1105, 945 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.38 (m, 2H), 7.33 (m, 3H), 4.87 (dd, *J* = 5.4, 2.0 Hz, 1H), 4.5 (d, *J* = 3.7 Hz, 2H), 4.07 (dd, *J* = 10.8, 5.4 Hz, 1H), 3.98 (ddd, *J* = 9.7, 9.7, 6.1 Hz, 1H), 3.89 (t, *J* = 12.8 Hz, 2H), 3.88 (t,

$J$ = 10.8 Hz, 1H), 3.68 (ddd, $J$ = 9.7, 9.7, 5.4 Hz, 1H), 2.28 (ddd, $J$ = 16.2, 5.8, 5.8 Hz, 1H), 2.16 (ddd, $J$ = 16.2, 9.9, 2.0 Hz, 1H), 1.58 (s, 3H), 1.44 (s, 3H); $^{13}$C NMR ($CDCl_3$) $\delta$ 128.5 (2C, d), 128.0 (2C, d), 127.8 (d), 99.6 (s), 98.0 (d), 72.4 (t), 71.3 (d), 69.7 (t), 67.3 (d), 62.5 (t), 29.3 (q), 27.3 (t), 19.3 (q).

**2,6-Anhydro-1-*O*-benzyl-4-deoxy-5,7-*O*-isopropylidene-D-*allo*-heptitol (57, R = Bzl) and 2,6-Anhydro-7-*O*-benzyl-4-deoxy-1,3-*O*-isopropylidene-D-*manno*-heptitol (58, R = Bzl).** To a stirred solution of the benzyl ether **56**, R = Bzl (58.0 mg, 0.2 mmol), in dry THF (2.0 mL) at 0 °C was added $BH_3$·$Me_2S$ (0.19 mL, 0.37 mmol, 2M in THF). After the solution was stirred for 3 h at 25 °C, the excess of borane was quenched with cold $H_2O$ (0.5 mL). Dropwise addition of a mixture of 3 N NaOH (0.34 mL, 1.0 mmol) and 30% $H_2O_2$ (0.08 mL, 1.2 mmol) and continued stirring for 30 min at 25 °C gave a white heterogeneous mixture. Dilution with ether (30 mL), followed by washing with $H_2O$ (2 × 20 mL) and brine (20 mL), drying ($MgSO_4$), concentration, and flash chromatography (silica, 10% EtOAc in *n*-hexane), gave the alcohol **57** (R = Bzl) (53.1 mg, 0.17 mmol, 85%) together with its less polar diastereomer **58** (R = Bzl) (6.6 mg, 0.022 mol, 10%). **57 (R = Bzl)**: oil; $R_f$ = 0.25 (silica, 30% EtOAc in *n*-hexane); $[\alpha]^{25}_D$ = +9.1° (*c* 0.34 $CHCl_3$); $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.33 (m, 5H), 4.59 (d, $J$ = 12.0 Hz, 1H), 4.54 (d, $J$ = 12.0 Hz, 1H), 3.88 (dd, $J$ = 10.7, 5.2 Hz, 1H), 3.75 (m, 2H), 3.67 (dd, $J$ = 10.7, 9.8 Hz, 1H), 3.64 (ddd, $J$ = 11.4, 9.0, 4.4 Hz, 1H), 3.58 (ddd, $J$ = 11.6, 9.8, 4.0 Hz, 1H), 3.39 (ddd, $J$ = 9.0, 5.1, 5.0 Hz, 1H), 3.18 (ddd, $J$ = 9.8, 9.8, 5.2 Hz, 1H), 2.30 (ddd, $J$ = 11.4, 4.4, 4.0 Hz, 1H), 1.53 (dd, $J$ = 11.6, 11.4 Hz, 1H), 1.48 (s, 3H), 1.41 (s, 3H); $^{13}$C NMR ($CDCl_3$) $\delta$ 137.9 (s), 129.0 (2C, d), 128.4 (d), 128.3 (2C, d), 99.6 (s), 81.4 (d), 74.6 (d), 74.2 (t), 71.5 (t), 69.1 (d), 68.9 (d), 63.0 (t), 38.2 (t), 29.6 (q), 19.5 (q); MS *m/e* (rel intensity) 309 ($M^+$ + 1, 19), 293 (9), 253 (5), 116 (24), 97 (11), 91 (100), 85 (15), 71 (21), 57 (32); HRMS calcd for $C_{17}H_{24}O_5$ ($M^+$) 308.1624, found 308.1604. **58 (R = Bzl)**: oil; $R_f$ = 0.30 (silica, 30% EtOAc in *n*-hexane); $[\alpha]^{25}_D$ = +4.02° (*c* 0.24, $CHCl_3$); $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.36 (m, 5H), 4.59 (d, $J$ = 12.1 Hz, 1H), 4.54 (d, $J$ = 12.1 Hz, 1H), 4.13 (br s, 1H), 4.60 (ddd, $J$ = 11.6, 9.7, 4.4 Hz, 1H), 3.99 (dd, $J$ = 6.5, 6.4 Hz, 1H), 3.82 (dd, $J$ = 10.7, 5.3 Hz, 1H), 3.72 (dd, $J$ = 10.7, 9.9 Hz, 1H), 3.71 (d, $J$ = 10 Hz, 1H), 3.63 (dd, $J$ = 10.0, 6.5 Hz, 1H), 3.45 (ddd, $J$ = 9.9, 9.7, 5.3 Hz, 1H), 2.03 (ddd, $J$ = 13.2, 4.4, 3.2 Hz, 1H), 1.77 (ddd, $J$ = 13.2, 11.6, 3.2 Hz, 1H), 1.52 (s, 3H), 1.40 (s, 3H); $^{13}$C NMR ($CDCl_3$) $\delta$ 138.0 (s), 128.9 (2C, d), 128.3 (d), 128.1 (2C, d), 100.1 (s), 78.5 (d), 73.9 (t), 69.4 (d), 68.5 (t), 68.0 (d), 66.8 (d), 66.5 (t), 33.6 (t), 29.7 (q), 19.7 (q); MS *m/e* (rel intensity) 308 ($M^+$, 8), 293 830), 279 (7), 267 (4), 199 (8), 181 (7), 171 (16), 167 (15), 157 (13), 149 (42), 145 (17), 116 (61), 107 (35), 91 (100), 70 (35); HRMS calcd for $C_{17}H_{24}O_5$ ($M^+$) 308.1624, found 308.1613; calcd for $C_{16}H_{21}O_5$ ($M - Me)^+$ 293.1389, found 293.1407.

**General Procedure for Allylstannane–Aldehyde Cyclization. Preparation of (2*R**,3*R**)-2-Ethenyltetrahydrofuran-3-yl *p*-Bromobenzoate (60a-*p*-BrBz) from 1,6-Bis[[(3′-(tributylstannyl)propenyl]oxy]hexane-3,4-diol (59, *n* = 0).** To a stirred solution of the allylstannane **59**, $n$ = 0 (1.4 g, 1.7 mmol), in dry $CH_2Cl_2$ (17 mL) at 0 °C was added *n*-$Bu_4NIO_4$ (1.5 g, 3.5 mmol). The cooling bath was removed, and the reaction mixture was stirred at 25 °C. TLC indicated the reaction was complete in 3 h. The homogeneous solution was recooled to −78 °C and treated dropwise with $BF_3$·$OEt_2$ (1.0 mL, 3.5 mmol), and the resulting mixture was stirred vigorously for 5 min. The reaction mixture was slowly warmed to −10 °C over a 5-min period and then poured onto a stirred mixture of $CH_2Cl_2$ (50 mL) and saturated aqueous $NaHCO_3$ (100 mL). After separation, the organic portion was washed with water (2 × 50 mL) and dried ($MgSO_4$). After filtration and removal the solvent in vacuo, the resulting oil (**60a**) was treated in dry $CH_2Cl_2$ (15 mL) at 0 °C with DMAP (1.5 g, 7.0 mmol) and *p*-bromobenzoyl chloride (1.7 g, 6.0 mmol). After being stirred for 3 h at 25 °C, the reaction mixture was diluted with ether (100 mL), washed with water (2 × 50 mL) and brine (50 mL), and dried ($MgSO_4$). Concentration and flash chromatography (silica, 10% ether in petroleum ether) furnished **60a-*p*-BrBz** (0.29 g, 58%). **60a-*p*-BrBz**: noncrystalline solid; $R_f$ = 0.7 (silica, 20% EtOAc in hexane); IR ($CHCl_3$) $\nu_{max}$ 3100, 2900, 2850, 2329, 1715, 1590, 1480, 1390, 1110, 1100, 1010 cm$^{-1}$; $^1$H NMR (200 MHz, $CDCl_3$) $\delta$ 7.88 (d, $J$ = 8.6 Hz, 2H), 7.59 (d, $J$ = 8.6 Hz, 2 H), 5.93 (ddd, $J$ = 17.1, 10.5, 5.1 Hz, 1H), 5.40 (dd, $J$ = 17.1, 1.5 Hz, 1H), 5.27 (ddd, $J$ = 5.9, 5.8, 1.9 Hz, 1H), 5.23 (dd, $J$ = 10.5, 1.5 Hz, 1H), 4.53 (dd, $J$ = 5.1, 1.9 Hz, 1H), 4.14 (ddd, $J$ = 8.4, 8.4, 2.9 Hz, 1H), 4.05 (ddd, $J$ = 9.0, 9.0, 6.5 Hz, 1H), 2.31 (m, 1H), 2.11 (m, 1H); $^{13}$C NMR ($CDCl_3$) $\delta$ 136.0 (d), 132.2 (d), 131.6 (d), 116.9 (t), 84.6 (d), 79.7 (d), 67.6 (t), 32.0 (t); MS *m/e* (rel intensity) 271, 269 ($M^+ - C_2H_3$, 0.3), 241, 239 (0.6), 185, 183 (100), 157, 155 (80), 113 (100), 104 (21), 96 (100), 83 (17), 76 (80); HRMS calcd for $C_{10}H_9{}^{81}BrO_2$ ($M - C_3H_4O)^+$ 241.9765, found 241.9760; calcd for $C_6H_9O_2$ ($M - C_7H_4BrO)^+$ 113.0602, found 113.0607. Anal. Calcd for $C_{13}H_{13}BrO_3$: C, 52.52; H, 4.38. Found: C, 52.73; H, 4.21.

**(2*R**,3*S**)-2-Ethenyltetrahydropyran-3-yl *p*-Bromobenzoate (60b-*p*-BrBz) from 1,8-Bis[[(3′-(tributylstannyl)propenyl]oxy]octane-4,5-diol (59, *n* = 1).** Prepared from **59**, $n$ = 1, as described above for **60a-*p*-BrBz** from **59**, $n$ − 0. **60b-*p*-BrBz**: oil; $R_f$ = 0.6 (silica, 20% EtOAc in hexane); IR ($CHCl_3$) $\nu_{max}$ 3100, 2925, 2850, 1715, 1590, 1480, 1390, 1260, 1110, 1100, 1010 cm$^{-1}$; $^1$H NMR (200 MHz, $CDCl_3$) $\delta$ 7.87 (d, $J$ = 8.5 Hz, 2H), 7.58 (d, $J$ = 8.5 Hz, 2H), 5.85 (ddd, $J$ = 17.2, 10.5, 6.6 Hz, 1H), 5.34 (dd, $J$ = 17.2, 1.1 Hz, 1H), 5.19 (dd, $J$ = 10.5, 1.1 Hz, 1H), 4.84 (ddd, $J$ = 9.5, 9.4, 4.6 Hz, 1H), 4.03 (dddd, $J$ = 11.5, 2.2, 2.0, 2.0 Hz, 1H), 3.85 (dd, $J$ = 9.4, 6.6 Hz, 1H), 3.49 (ddd, $J$ = 11.5, 11.5, 2.8 Hz, 1H), 2.31 (m, 1H), 1.80 (m, 2H), 1.65 (m, 1H); $^{13}$C NMR ($CDCl_3$) $\delta$ 165.3 (s), 135.7 (d), 132.1 (d), 131.5 (d), 129.6 (s), 128.5 (s), 118.7 (t), 81.1 (d), 72.6 (d), 67.9 (t), 29.7 (t), 25.4 (t); MS *m/e* (rel intensity) 312, 310 ($M^+$, 2), 285, 283 (2), 242, 240 (3), 185, 183 (100), 157, 155 (92), 127 (80), 110 (100), 104 (29), 85 (13), 78 (34), 72 (34), 71 (100), 57 (43); HRMS calcd for $C_{12}H_{12}{}^{81}BrO_3$ ($M^+ - C_2H_3$) 284.9949, found 284.9957. Anal. Calcd for $C_{14}H_{15}BrO_3$: C, 54.02; H, 4.82. Found: C, 54.14; H, 5.11.

**(2*R**,3*S**)-2-Vinyloxepan-3-yl *p*-Bromobenzoate (60c-*p*-BrBz) from 1,10-Bis[[(3′-tributylstannyl)propenyl]oxy]-decane-5,6-diol (59, *n* = 2).** Prepared from **59**, $n$ = 2, as described above for **60a-*p*-BrBz** from **59**, $n$ = 0. **60c-*p*-BrBz**: noncrystalline solid, $R_f$ = 0.7 (silica, 20% EtOAc in hexane); IR ($CHCl_3$) $\nu_{max}$ 2925, 2850, 1725, 1590, 1490, 1380, 1260, 1110, 1100, 1020 cm$^{-1}$; $^1$H NMR (200 MHz, $CDCl_3$) $\delta$ 7.90 (d, $J$ = 8.6 Hz, 2H), 7.56 (d, $J$ = 8.6 Hz, 2H), 5.88 (ddd, $J$ = 16.0, 10.5, 6.0 Hz, 1H), 5.31 (dd, $J$ = 16.0, 1.5 Hz, 1H), 5.15 (dd, $J$ = 10.5, 1.5 Hz, 1H), 5.12 (ddd, $J$ = 7.2, 7.0, 3.5 Hz, 1H), 4.09 (dd, $J$ = 7.0, 6.0 Hz, 1H), 4.05 (ddd, $J$ = 12.4, 4.0, 4.0 Hz, 1H), 3.69 (ddd, $J$ = 12.0, 4.0, 4.0 Hz, 1H), 2.06 (m, 1H), 1.94 (m, 1H), 1.79 (m, 2H), 1.71 (m, 2H); $^{13}$C NMR ($CDCl_3$) $\delta$ 165.3 (s), 137.0 (d), 132.3 (d), 132.2 (d), 131.5 (d), 129.8 (s), 128.5 (s), 116.7 (t), 83.4 (d), 78.0 (d), 70.9 (t), 31.6 (t), 31.2 (t), 21.7 (t); MS *m/e* (rel intensity) 326, 324 ($M^+$, 1), 296, 294 (0.8), 185, 183 (100), 157, 155 (44), 141 (57), 124 (31), 104 (15), 98 (16), 85 (100), 76 (27), 57 (38); HRMS calcd for $C_{15}H_{17}{}^{81}BrO_3$ ($M^+$) 326.0341, found 326.0337; calcd for $C_{15}H_{17}{}^{79}BrO_3$ ($M^+$) 324.0361, found 324.0359.

**(2*R**,3*S**)-2-Vinyloxocan-3-yl *p*-Bromobenzoate (60d-*p*-BrBz) from 1,12-Bis[[(3′-(tributylstannyl)propenyl]oxy]-decane-6,7-diol (59, *n* = 3).** Prepared from **59**, $n$ = 2 as described above for **60a-*p*-BrBz** from **59**, $n$ = 0. **60d-*p*-BrBz**: noncrystalline solid; $R_f$ = 0.5 (silica, 20% EtOAc in hexane); IR ($CHCl_3$) $\nu_{max}$ 2900, 2850, 1710, 1585, 1260, 1110, 1100, 1015 cm$^{-1}$; $^1$H NMR (200 MHz, $CDCl_3$) $\delta$ 7.92 (d, $J$ = 8.4 Hz, 2H), 7.58 (d, $J$ = 8.4 Hz, 2H), 5.80 (ddd, $J$ = 17.2, 10.6, 6.5 Hz, 1H), 5.29 (d, $J$ = 17.2 Hz, 1H), 5.23 (d, $J$ = 10.6 Hz, 1H), 5.16 (ddd, $J$ = 8.2, 8.2, 2.6 Hz, 1H), 3.95 (dd, $J$ = 6.5, 2.6 Hz, 1H), 3.68 (m, 1H), 3.40 (m, 1H), 2.04 (m, 1H), 1.79–1.35 (m, 7H); $^{13}$C NMR ($CDCl_3$) $\delta$ 165.9 (s), 135.3 (d), 132.1 (d), 131.7 (d), 129.7 (s), 128.4 (s), 118.4 (s), 79.2 (d), 76.4 (d), 68.0 (t), 30.2 (t), 29.6 (t), 26.3 (t), 25.2 (t); MS *m/e* (rel intensity) 340, 338 ($M^+$, 0.2), 324, 322 (0.7), 252, 250 (2), 224, 222 (7), 185, 183 (68), 155 (18), 139 (15), 105 (100), 77 (18); HRMS calcd for $C_{16}H_{19}{}^{81}BrO_3$ ($M^+$) 340.0497, found 340.0502; calcd for $C_{16}H_{19}{}^{79}BrO_3$ ($M^+$) 338.0517, found 338.0501.

**4-(2,2′-Dimethyl-1′,3-dioxolan-4′-yl)butyl Acetate (85).** To a stirred mixture of 4-methylmorpholine *N*-oxide (66.1 g, 489.3 mmol) and water (270 mL) at 25 °C was added $OsO_4$ (12.7 mg, 0.07 mmol), followed by addition of hex-5-enyl acetate (23.16 g, 163.1 mmol) in THF:acetone (1:1) (540 mL). Stirring was continued for 5 h at 25 °C, and the reaction mixture was quenched by treatment with an aqueous saturated solution of $Na_2SO_3$ (100 mL). Extractive workup with ether gave a crude oil, which was chromatographed on silica gel using 50% EtOAc–hexane as eluent to afford 25.8 g (90%) of the desired diol as an oil: $R_f$ = 0.2 (silica,

60% EtOAc–hexane); IR ($CHCl_3$) $\nu_{max}$ 3590, 3020, 2945, 2870, 1728, 1460, 1435, 1390, 1365, 1250, 1210, 1040 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 4.04 (t, $J$ = 6.6 Hz, 2H), 3.67 (m, 1H), 3.60 (dd, $J$ = 11.1, 2.8 Hz, 1H), 3.40 (dd, $J$ = 11.1, 4.6 Hz, 1H), 2.02 (s, 3H), 1.62 (m, 2H), 1.53–1.34 (m, 4H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 171.8 (s), 72.4 (d), 67.1 (t), 64.7 (t), 33.0 (t), 29.0 (t), 22.4 (t), 21.4 (q); MS $m/e$ (rel intensity) 177 ($M^+$ + 1, 1), 145 (1), 117 (4), 99 (6), 85 (100), 81 (15), 67 (75), 61 (83), 57 (100); HRMS calcd for $C_8H_{17}O_4$ $(M + H)^+$ 177.1127, found 177.1135. To a solution of the above diol (25.8 g, 146.6 mmol) in dry $CH_2Cl_2$ (730 mL) was added, under argon atmosphere, 2,2-dimethoxypropane (72.1 mL, 586.4 mmol) and a catalytic amount of CSA. After 15 min of continuous stirring at 25 °C the reaction mixture was poured into $CH_2Cl_2$ (300 mL) and a saturated solution of $NaHCO_3$ (200 mL). After shaking and separation, the organic portion was dried ($MgSO_4$) and concentrated to give, after chromatographic purification (silica, 20% EtOAc–hexane), compound **85** (29.9 g, 95%). **85**: oil; $R_f$ = 0.8 (silica, 20% EtOAc–hexane); IR ($CHCl_3$) $\nu_{max}$ 3000, 2990, 2870, 1731, 1455, 1435, 1380, 1370, 1160, 1060 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 4.05 (m, 4H), 3.49 (dd, $J$ = 7.2, 7.2 Hz, 1H), 2.03 (s, 3H), 1.71–1.44 (m, 6H), 1.39, 1.33 (s, 3H each); $^{13}C$ NMR ($CDCl_3$) $\delta$ 171.5 (s), 109.1 (s), 76.2 (d), 69.8 (t), 64.6 (t), 33.6 (t), 29.0 (t), 27.3 (q), 26.1 (q), 22.7 (t), 21.3 (q); MS $m/e$ (rel intensity) 201 ($M^+$ – Me, 63), 159 (8), 141 (7), 117 (5), 99 (42), 86 (11), 81 (100), 72 (100), 57 (46), 55 (57); HRMS calcd for $C_{10}H_{17}O_4$ $(M - Me)^+$ 201.1127, found 201.1127.

**4-(2′,2′-Dimethyl-1′,3′-dioxolan-4′-yl)butan-1-ol (86).** A mixture of acetate **85** (29.9 g, 138.4 mmol) and $K_2CO_3$ (35.7 g, 276.8 mmol) in acetone:MeOH (4:1) (690 mL) was stirred at 25 °C for 3 h. Dilution with EtOAc (200 mL) followed by filtration through a Celite pad and concentration gave a residue which was diluted with ether (200 mL), washed with $H_2O$ (2 × 200 mL), and dried ($MgSO_4$). Concentration followed by flash column chromatography (silica, 10%–20% EtOAc–hexane) afforded the alcohol **86** (23.1 g, 96%). **86**: oil; $R_f$ = 0.2 (silica, 20% EtOAc–hexane); IR ($CHCl_3$) $\nu_{max}$ 3625, 2460, 2990, 2490, 2440, 1875, 1475, 1455, 1435, 1380, 1370, 1230, 1155, 1055 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 4.09 (ddd, $J$ = 12.4, 7.4, 6.4 Hz, 1H), 4.05 (dd, $J$ = 7.4, 6.0 Hz, 1H), 3.65 (t, $J$ = 6.4 Hz, 2H), 3.50 (dd, $J$ = 7.4, 7.4 Hz, 1H), 1.70–1.43 (m, 6H), 1.40 (s, 3H), 1.34 (s, 3H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 190.1 (s), 76.4 (d), 69.8 (t), 63.1 (t), 33.7 (t), 33.0 (t), 27.4 (q), 26.1 (q), 22.5 (t); MS $m/e$ (rel intensity) 159 ($M^+$ – Me, 39), 117 (10), 101 (44), 99 (36), 86 (3), 81 (100), 72 (47), 69 (11); HRMS calcd for $C_8H_{15}O_3$ $(M - Me)^+$ 159.1021, found 159.1023. Anal. Calcd for $C_9H_{18}O_3$: C, 62.07; H, 10.34. Found: C, 61.81; H, 10.52.

**4-[4-(Allyloxy)butyl]-2,2-dimethyl-1,3-dioxolane (87).** To a stirred mixture of the alcohol **86** (23.1 g, 132.7 mmol) and dry *N*,*N*-dimethylformamide (265 mL) at 0 °C was added NaH (5.17 g, 172.5 mmol, 80% dispersion in mineral oil). After 15 min at 0 °C allyl bromide (25.3 mL, 291.9 mmol) was added, the cooling bath removed, and the reaction mixture stirred for 3 h. The excess of NaH was carefully quenched at 0 °C with $H_2O$ (500 mL). Dilution with ether (750 mL), followed by washing with $H_2O$ (3 × 500 mL), drying ($MgSO_4$), concentration, and flash column chromatography (silica, 5%–10% EtOAc–hexane), gave the allyl derivative **87** (25.2 g, 89%). **87**: oil; $R_f$ = 0.5 (silica, 10% EtOAc–hexane); IR ($CHCl_3$) $\nu_{max}$ 3010, 2990, 2865, 1455, 1435, 1420, 1380, 1370, 1230, 1160, 1095 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 5.88 (dddd, $J$ = 17.2, 10.4, 5.6, 5.6 Hz, 1H), 5.23 (dq, $J$ = 17.2, 1.5 Hz, 1H), 5.14 (dq, $J$ = 10.4, 1.5 Hz, 1H), 4.05 (m, 1H), 4.00 (dd, $J$ = 7.2, 6.0 Hz, 1H), 3.93 (dt, $J$ = 5.6, 1.5 Hz, 2H), 3.50 (t, $J$ = 7.2 Hz, 1H), 3.40 (t, $J$ = 6.5 Hz, 2H), 1.69–1.36 (m, 6H), 1.36 (s, 3H), 1.32 (s, 3H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 135.4 (d), 117.1 (t), 109.0 (s), 76.3 (d), 72.2 (t), 60.5 (t), 69.8 (t), 33.8 (t), 30.1 (t), 27.4 (q), 26.1 (q), 22.9 (t); MS $m/e$ (rel intensity) 199 ($M^+$ – Me, 59), 157 (3), 139 (6), 99 (23), 85 (5), 81 (100), 71 (15), 69 (9), 59 (12), 57 (12), 55 (16); HRMS calcd for $C_{11}H_{19}O_3$ $(M - Me)^+$ 199.1334, found 199.1339.

**6-(Allyloxy)hexane-1,2-diol (88).** The acetonide **87** (26.4 g, 117.8 mmol) together with a catalytic amount of CSA in MeOH (589 mL) was stirred at 25 °C for 15 min. Triethylamine (12.0 mL) was added dropwise at 0 °C and the solution stirred for 10 min and then poured onto a mixture of aqueous saturated $NH_4Cl$ (250 mL), water (100 mL), and ether (300 mL). The organic phase was separated, washed with $H_2O$ (2 × 200 mL), and dried ($MgSO_4$). Removal of the solvent followed by flash column chromatography (silica, 50%–60% EtOAc–hexane) gave diol **88** (19.9 g, 97%). **88**: oil; $R_f$ = 0.2 (silica, 60% EtOAc–hexane); IR ($CHCl_3$) $\nu_{max}$ 3415, 3010, 2940, 2865, 1645, 1460, 1420, 1400, 1345, 1235, 1190, 1095, 995 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 5.87 (dddd, $J$ = 17.2, 10.5, 5.7, 5.7 Hz, 1H), 5.23 (dq, $J$ = 17.2, 1.0 Hz, 1H), 5.14 (dq, $J$ = 10.5, 1.0 Hz, 1H), 3.94 (dt, $J$ = 5.7, 1.0 Hz, 2H), 3.65 (m, 1H), 3.57 (m, 1H), 3.41 (m, 3H), 1.59 (m, 2H), 1.52 (m, 2H), 1.47 (m, 2H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 135.3 (d), 117 (t), 72.5 (d), 72.2 (t), 70.6 (t), 67.1 (t), 33.2 (t), 30.0 (t), 22.7 (t); MS $m/e$ (rel intensity) 175 ($M^+$ + 1, 3), 157 (1), 143 (6), 115 (18), 99 (27), 85 (100), 81 (94), 71 (23), 67 (70), 57 (100); HRMS calcd for $C_9H_{19}O_3$ $(M + H)^+$ 175.1334, found 175.1333. Anal. Calcd for $C_9H_{18}O_3$: C, 62.07; H, 10.34. Found: C, 62.10; H, 10.23.

**6-[[3′-(Tributylstannyl)propenyl]oxy]hexane-1,2-diol (89).** *s*-BuLi (281.6 mL, 366.1 mmol, 1.3 M in cyclohexane) was added under an argon atmosphere at –78 °C to a solution of **88** (19.9 g, 114.4 mmol) in dry THF (863 mL). To the resulting solution was added tributyltin chloride (33.9 mL, 125.8 mmol) at –78 °C over 15 min. The resulting mixture was maintained at –78 °C for 10 min, aqueous $NH_4Cl$ (300 mL) was then added, and the resulting aqueous suspension was saturated with NaCl and extracted with ether (2 × 250 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated, and the residue was purified by flash column chromatography (silica, 50%–60% EtOAc–hexane) to yield **89** (26.4 g, 50%). **89**: oil; $R_f$ = 0.4 (silica, 60% EtOAc–hexane); IR ($CHCl_3$) $\nu_{max}$ 3420, 2910, 2850, 1650, 1455, 1380, 1095, 950 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 5.74 (d, $J$ = 6.0 Hz, 1H), 4.50 (ddd, $J$ = 9.0, 9.0, 6.0 Hz, 1H), 3.64 (t, $J$ = 6.4 Hz, 2H), 3.55 (m, 2H), 3.32 (dd, $J$ = 11.2, 8.0 Hz, 1H), 1.63 (d, $J$ = 9.0 Hz, 2H), 1.60 (m, 12H), 1.40 (m, 12H), 0.80 (m, 9H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 141.8 (d), 106.0 (d), 72.5 (d), 72.0 (t), 67.1 (t), 33.2 (t), 30.2 (t), 29.5 (t), 29.4 (t), 28.2 (t), 27.7 (t), 22.4 (t), 14.1 (q), 14.0 (q), 13.9 (q), 9.5 (q), 6.3 (t).

**(2*R**,3*S**)-2-Ethenyl-3-oxepanol (60c).** To a stirred solution of the allylstannane **89** (26.4 g, 57.1 mmol) in dry $CH_2Cl_2$ (570 mL) at 0 °C was added *n*-$Bu_4NIO_4$ (37.1 g, 85.6 mmol). The cooling bath was removed, and the reaction mixture was stirred at 25 °C. TLC indicated the reaction was complete after 3 h. The homogeneous solution was recooled to –78 °C and treated dropwise with $BF_3{\cdot}OEt_2$ (14.0 mL, 117.0 mmol) and the resulting mixture stirred vigorously for 5 min. The reaction was slowly warmed to –10 °C over a 5-min period and then poured onto a mixture of $CH_2Cl_2$ (200 mL) and saturated aqueous $NaHCO_3$ (200 mL). After separation, the organic portion was washed with $H_2O$ (2 × 100 mL), dried ($MgSO_4$), and concentrated, and the residue was purified by flash column chromatography (silica, 10%–15% EtOAc–hexane) to give **60c** (5.67 g, 70%). **60c**: oil; $R_f$ = 0.2 (silica, 20% EtOAc–hexane); $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 5.93 (dddd, $J$ = 17.3, 10.5, 6.5, 1.0 Hz, 1H), 5.39 (ddd, $J$ = 17.3, 1.7, 1.0 Hz, 1H), 5.25 (ddd, $J$ = 10.5, 1.0, 1.0 Hz, 1H), 3.96 (ddd, $J$ = 12.3, 6.0, 6.0 Hz, 1H), 3.65 (m, 2H), 3.57 (ddd, $J$ = 12.0, 8.0, 4.0 Hz, 1H), 2.53 (br s, 1H), 2.04 (m, 1H), 1.78 (m, 1H), 1.64 (m, 2H), 1.48 (m, 1H), 1.29 (m, 1H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 138.1 (d), 117.3 (t), 86.0 (d), 74.8 (d), 70.5 (t), 35.6 (t), 30.6 (t), 21.1 (t). The *p*-bromobenzoate of **60c** prepared in the usual way furnished **60c-*p*-BrBz**, which was shown to be identical in all respects (IR, NMR, and MS spectra) with those of the compound hereafter described generated by cyclization of **59**, $n$ = 2.

**(2*R**,3*S**)-2-Ethenyl-3-(*tert*-butyldimethylsiloxy)oxepane (90).** To a stirred solution of the alcohol **60c** (5.67 g, 39.9 mmol), triethylamine (8.4 mL, 79.8 mmol), and dry $CH_2Cl_2$ (200 mL) at 0 °C was added TBDMSOTf (12.8 mL, 55.9 mmol). After 15 min the reaction mixture was diluted with $CH_2Cl_2$ (100 mL) and washed with $H_2O$ (2 × 100 mL). Drying ($MgSO_4$) and concentration followed by flash column chromatography (silica, 15% EtOAc–hexane) afforded **90** (7.15 g, 70%). **90**: oil; $R_f$ = 0.8 (silica, 20% EtOAc–hexane); IR ($CHCl_3$) $\nu_{max}$ 3025, 2955, 2920, 2860, 1650, 1470, 1255, 1110, 1070 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 5.90 (ddd, $J$ = 17.1, 10.7, 6.0 Hz, 1H), 5.28 (d, $J$ = 17.1 Hz, 1H), 5.12 (d, $J$ = 10.7 Hz, 1H), 3.96 (ddd, $J$ = 12.6, 5.08, 4.4 Hz, 1H), 3.76 (dd, $J$ = 7.0, 6.0 Hz, 1H), 3.66 (m, 2H), 1.87 (m, 1H), 1.78 (m, 1H), 1.68 (m, 3H), 1.55 (m, 1H), 0.89 (s, 9H), 0.04 (s, 6H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 138.5 (d), 115.2 (t), 86.3 (d), 76.4 (d), 70.7 (t), 35.3 (t), 31.3 (t), 26.2 (q), 21.0 (t), 18.4 (s), –4.0 (q), –4.2 (q); MS $m/e$ (rel intensity) 258 ($M^+$, 0.2), 199 ($M^+$ – $^t$Bu, 6), 189 (3), 171 (2), 157 (3), 149 (6), 147 (41), 141 (7), 133 (10), 73 (100), 67

(10), 59 (34); HRMS calcd for $C_{10}H_{17}O_2Si$ (M − $^t$Bu)$^+$ 197.0998, found 197.1011.

**(2*S**,3*S**)-2-[3′-(tert-Butyldimethylsiloxy)-2′-oxepanyl]-1,2-ethanediol (91).** To a stirred solution mixture of 4-methylmorpholine *N*-oxide (11.3 g, 83.7 mmol) and water (139 mL) at 25 °C was added $OsO_4$ (25.4 mg, 0.1 mmol) followed by slow addition of **90** (7.15 g, 27.9 mmol) in THF:acetone (1:1) (278 mL). After 4 h at 25 °C the reaction mixture was treated with an aqueous saturated solution of $Na_2SO_4$ (75 mL), diluted with EtOAc (500 mL), washed with $H_2O$ (2 × 100 mL), and dried ($MgSO_4$). Concentration followed by flash column chromatography (silica, 60% EtOAc–hexane) afforded **91** (6.88 g, 85%). **91**: oil; $R_f$ = 0.2 (silica, 60% EtOAc–hexane); IR ($CHCl_3$) $\nu_{max}$ 3565, 3385, 2950, 2935, 2860, 1470, 1465, 1390, 1260, 1110, 1090, 1070, 1005 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 3.93 (ddd, $J$ = 11.8, 6.0, 6.0 Hz, 1H), 3.84 (ddd, $J$ = 8.4, 7.3, 4.0 Hz, 1H), 3.73 (m, 2H), 3.62 (ddd, $J$ = 11.8, 7.6, 5.0 Hz, 1H), 3.43 (dd, $J$ = 7.3, 5.6 Hz, 1H), 3.23 (d, $J$ = 5.6 Hz, 1H), 2.47 (m, 1H), 1.93 (m, 1H), 1.76 (m, 1H), 1.69 (m, 2H), 1.60 (m, 1H), 1.52 (m, 1H), 0.88 (s, 9H), 0.09 (s, 6H); $^{13}$C NMR ($CDCl_3$) $\delta$ 85.8 (d), 75.1 (d), 72.7 (d), 71.7 (t), 63.7 (t), 36.5 (t), 30.4 (t), 26.2 (q), 20.4 (t), 18.3 (s), −3.6 (q), −4.4 (q); MS $m/e$ (rel intensity) 291 (M$^+$ + H, 0.5), 259 (1), 233 (4), 215 (20), 173 (5), 159 (10), 131 (37), 123 (45), 117 (48), 105 (26), 97 (41), 85 (100), 77 (35), 75 (100); HRMS calcd for $C_{13}H_{27}O_3Si$ (M − $CH_2OH$)$^+$ 259.1729, found 259.1727. Anal. Calcd for $C_{14}H_{30}O_4Si$: C, 57.93; H, 10.34. Found: C, 58.14; H, 10.19.

**(2*R**,3*S**)-3-(*tert*-Butyldimethylsiloxy)-2-(hydroxymethyl)oxepane (92).** To a stirred solution of diol **91** (6.88 g, 23.7 mmol) in MeOH:$H_2O$ (8:1) (237 mL) at 0 °C was added under argon an excess of $NaIO_4$ (7.6 g, 35.5 mmol). The reaction mixture, after being stirred for 10 min at 0 °C, was treated with $NaBH_4$ (0.89 g, 23.7 mmol) and stirred at 25 °C. When monitoring of the reaction by TLC indicated that all the aldehyde had been reduced (30 min), the quenched reaction mixture was taken with $H_2O$ (500 mL) and extracted with ether (2 × 300 mL). The combined organic layers were washed with 5% $NaHCO_3$ aqueous solution (2 × 200 mL) and water (2 × 200 mL). The organic phase was dried ($MgSO_4$) and concentrated to give compound **92** (4.74 g, 77%), after chromatographic purification (silica, 15% EtOAc–hexane). **92**: oil; $R_f$ = 0.4 (silica, 20% EtOAc–hexane); IR ($CHCl_3$) $\nu_{max}$ 3580, 3015, 2930, 1860, 1470, 1465, 1390, 1360, 1260, 1110, 1070, 1040 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 4.03 (ddd, $J$ = 12.1, 5.4, 5.4 Hz, 1H), 3.73 (ddd, $J$ = 11.1, 8.8, 3.4 Hz, 1H), 3.63 (m, 2H), 3.47 (ddd, $J$ = 11.1, 7.6, 3.8 Hz, 1H), 3.37 (ddd, $J$ = 7.6, 7.5, 3.4 Hz, 1H), 2.16 (dd, $J$ = 8.8, 3.8 Hz, 1H), 1.88 (m, 1H), 1.76 (m, 4H), 1.52 (m, 1H), 0.88 (s, 9H), 0.04 (s, 6H); $^{13}$C NMR ($CDCl_3$) $\delta$ 85.9 (d), 73.5 (d), 72.0 (t), 64.9 (t), 36.3 (t), 31.0 (t), 26.2 (q), 20.6 (t), 18.3 (s), −3.9 (q), −4.5 (q). Anal. Calcd for $C_{13}H_{28}O_3Si$: C, 60.00; H, 10.77. Found: C, 59.78; H, 11.02.

**(2*R**,3*S**)-3-(*tert*-Butyldimethylsiloxy)-2-(iodomethyl)oxepane (93).** To a cold (10 °C) stirred solution of alcohol **91** (4.74 g, 18.2 mmol), triphenylphosphine (14.3 g, 54.6 mmol), and imidazole (1.49 g, 21.8 mmol) in dry benzene (180 mL) under argon was added iodine (9.24 g, 36.4 mmol). When monitoring of the reaction by TLC indicated that all starting material had been consumed (ca. 3 h at 10 °C), the reaction was filtered through a Celite pad and the solvent evaporated *in vacuo* to give a residue which was further purified by flash column chromatography (silica, 5% EtOAc–hexane) to afford **93** (6.4 g, 95%). **93**: oil; $R_f$ = 0.7 (silica, 5% EtOAc–hexane); IR ($CHCl_3$) $\nu_{max}$ 3005, 2930, 2860, 1470, 1485, 1420, 1375, 1260, 1100, 1080, 1060 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 3.99 (ddd, $J$ = 11.8, 5.7, 5.7 Hz, 1H), 3.62 (m, 2H), 3.46 (dd, $J$ = 14.6, 7.6 Hz, 1H), 3.19 (ddd, $J$ = 7.6, 7.5, 7.0 Hz, 1H), 3.17 (dd, $J$ = 14.6, 7.0 Hz, 1H), 1.90 (m, 1H), 1.79 (m, 1H), 1.65 (m, 2H), 1.56 (m, 1H), 1.53 (m, 1H), 0.87 (s, 9H), 0.06 (s, 6H); $^{13}$C NMR ($CDCl_3$) $\delta$ 84.4 (d), 76.2 (d), 71.6 (t), 36.7 (t), 30.7 (t), 26.3 (q), 20.5 (t), 18.3 (s), 11.4 (t), −3.7 (q), −4.2 (q); MS $m/e$ (rel intensity) 370 (M$^+$, 0.8), 355 (12), 313 (100), 295 (46), 271 (90), 243 (100), 239 (70), 213 (90), 199 (89); HRMS calcd for $C_{13}H_{27}IO_2Si$ (M$^+$) 370.0785, found 370.0792.

**(2′*R**,3′*S**)-4-[3′-(*tert*-Butyldimethylsiloxy)-2′-oxepanyl]-1-butene (94).** According to the general procedure of Keck,[46] iodide **93** (6.4 g, 17.3 mmol) was dissolved in dry benzene (34 mL) and charged with allyltributyltin (10.8 mL, 34.6 mmol) and AIBN (0.85 g, 5.19 mmol). The resulting solution was heated in the dark at reflux for 5 h, allowed to cool to 23 °C, concentrated *in vacuo*, diluted with ether (300 mL), washed with $H_2O$ (2 × 100 mL), dried ($MgSO_4$), and concentrated. Purification of the residue by flash column chromatography (silica, 1%–2% EtOAc–hexane) gave **94** (3.44 g, 70%). **94**: oil; $R_f$ = 0.6 (silica, 2.5% EtOAc–hexane); IR ($CHCl_3$) $\nu_{max}$ 3030, 3020, 2925, 1643, 1380, 1265, 1100, 1010 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 5.82 (m, 1H), 5.02 (d, $J$ = 17.1 Hz, 1H), 4.95 (d, $J$ = 9.8 Hz, 1H), 3.95 (ddd, $J$ = 12.0, 6.3, 5.3 Hz, 1H), 3.53 (m, 2H), 3.19 (ddd, $J$ = 7.2, 7.2, 2.0 Hz, 1H), 2.24 (m, 1H), 2.09 (m, 1H), 1.86 (m, 1H), 1.72 (m, 3H), 1.55 (m, 2H), 1.44 (m, 1H), 1.30 (m, 1H), 0.89 (s, 9H), 0.04 (s, 6H); $^{13}$C NMR ($CDCl_3$) $\delta$ 139.3 (d), 114.8 (t), 85.2 (d), 76.7 (t), 71.4 (t), 36.1 (t), 33.8 (t), 31.4 (t), 30.4 (t), 26.4 (q), 20.7 (t), 18.4 (s), −3.4 (q), −4.3 (q); MS $m/e$ (rel intensity) 284 (M$^+$, 1), 229 (3), 227 (37), 185 (68), 159 (8), 143 (42), 135 (13), 131 (34), 115 (13), 101 (28), 93 (33), 85 (29), 75 (100), 67 (65); HRMS calcd for $C_{16}H_{33}O_2Si$ (M + H)$^+$ 285.2250, found 285.2266.

**(2′*R**,3′*S**)-4-[3′-(*tert*-Butylsiloxy)-2′-oxepanyl]-1,2-butanediol (95).** Diol **95** was prepared from **94** (4.91 g, 36.3 mmol) by the same procedure used to convert **90** to **91** described above. Flash column chromatography (silica, 40% EtOAc–hexane) afforded **95** (3.27 g, 85%). **95**: oil; $R_f$ = 0.2 (silica, 40% EtOAc–hexane); IR ($CHCl_3$) $\nu_{max}$ 3565, 3495, 2930, 2860, 1470, 1465, 1390, 1360, 1260, 1200, 1110, 1090 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 4.00 (ddd, $J$ = 12.0, 6.0, 4.4 Hz, 1H), 3.61 (m, 4H), 3.45 (m, 1H), 3.21 (ddd, $J$ = 7.0, 6.8, 3.0 Hz, 1H), 1.87–1.45 (m, 10H), 0.88 (s, 9H), 0.04 (s, 6H); $^{13}$C NMR ($CDCl_3$) $\delta$ 86.7 (d), 76.6 (d), 72.7 (d), 71.7 (t), 67.4 (t), 35.8 (t), 31.0 (t), 30.1 (t), 26.2 (q), 20.6 (t), 18.4 (s), −3.8 (q), −4.3 (q); MS $m/e$ (rel intensity) 319 (M$^+$ + 1, 0.2), 287 (9), 269 (6), 261 (2), 243 (34), 225 (19), 213 85), 187 (15), 169 (40), 159 (60), 155 (80), 131 (84), 101 (96), 97 (100). HRMS calcd for $C_{16}H_{35}O_4Si$ (M + H)$^+$ 319.2305, found 319.2306; calcd for $C_{16}H_{33}O_3$ (M − $OH_2$)$^+$ 301.2199, found 301.2194; calcd for $C_{12}H_{25}O_4Si$ (M − $^t$Bu)$^+$ 261.1522, found 261.1511.

**(2′*R**,3′*S**)-2-[2′-(2″,2″-Dimethyl-1″,3″-dioxolan-4″-yl)-ethyl]-3-(*tert*-butyldimethylsiloxy)oxepane (96).** To a stirred mixture of the diol **95** (3.27 g, 10.3 mmol) and 2,2-dimethoxypropane (5.07 mL, 41.2 mmol) in dry $CH_2Cl_2$ (50 mL) was added a catalytic amount of CSA. After 15 min at 25 °C the reaction mixture was treated with triethylamine (5 mL), poured onto an aqueous saturated $NH_4Cl$ solution (150 mL), washed with $H_2O$ (2 × 100 mL), and dried ($MgSO_4$). Removal of the solvent followed by flash column chromatography (silica, 10% EtOAc–hexane) gave acetonide **96** (3.32 g, 90%). **96**: oil; $R_f$ = 0.6 (silica, 10% EtOAc–hexane); IR ($CHCl_3$) $\nu_{max}$ 2990, 2930, 2860, 1470, 1463, 1380, 1370, 1260, 1200, 1110, 1060, 840 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 4.07 (m, 1H), 4.03 (m, 1H), 3.94 (m, 2H), 3.50 (m, 3H), 3.15 (m, 1H), 1.89–1.45 (m, 9H), 1.38 (s, 3H), 1.32 (s, 3H), 0.86 (s, 9H), 0.03 (s, 6H); $^{13}$C NMR ($CDCl_3$) $\delta$ 109.0 (s), 86.0, 85.9 (d), 77.7 (d), 76.6 (d), 76.3 (d), 71.5 (t), 69.9, 69.7 (t), 35.9, 35.8 (t), 31.2 (t), 30.8, 30.6 (t), 30.2, 30.1 (t), 27.4, 27.3 (q), 26.3 (q), 20.7 (q), 18.3 (s), −3.8 (q), −4.3 (q); MS $m/e$ (rel intensity) 358 (M$^+$, 0.2), 343 (10), 301 (7), 243 (30), 185 (18), 151 (22), 101 (18), 75 (100). HRMS calcd for $C_{18}H_{35}O_4Si$ (M − Me)$^+$ 343.2304, found 343.2323. Anal. Calcd for $C_{19}H_{38}O_4Si$: C, 63.69; H, 10.61. Found: C, 63.41; H, 10.72.

**(2*R**,3*S**)-2-[2′-(2″,2″-Dimethyl-1″,3″-dioxolan-4″-yl)-ethyl]oxepan-3-ol (97).** A mixture of **96** (3.23 g, 9.27 mmol), *n*-$Bu_4NF$ (18.5 mL, 18.5 mmol, 1 M in THF), and THF (18 mL) was stirred at 25 °C for 3 h. The reaction was diluted with EtOAc (250 mL), washed with an aqueous saturated NaCl solution (100 mL) and $H_2O$ (100 mL), and dried ($MgSO_4$). Concentration followed by flash chromatography (silica, 25% EtOAc–hexane) afforded **97** (1.98 g, 87%). **97**: oil; $R_f$ = 0.2 (silica, 30% EtOAc–hexane); IR ($CHCl_3$) $\nu_{max}$ 3620, 3465, 3000, 2990, 2870, 1455, 1380, 1370, 1230, 1105 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 4.09 (m, 1H), 4.02 (m, 1H), 3.95 (m, 1H), 3.51 (m, 3H), 3.13 (m, 1H), 1.97–1.47 (m, 10H), 1.38, 1.32 (s, 3H each); $^{13}$C NMR ($CDCl_3$) $\delta$ 109.1 (s), 85.5, 85.3 (d), 76.8, 76.5 (d), 76.0, 75.9 (d), 71.7, 71.6 (t), 69.9, 69.8 (t), 36.6, 36.5 (t), 31.0, 30.8 (t), 30.4, 30.3 (t), 30.0 (t), 27.3 (q), 26.2 (q), 21.1, 21.0 (t); MS $m/e$ (rel intensity) 229 (M$^+$ − Me, 12), 210 (1) 185 (6), 169 (3), 151 (6), 142 (77), 101 (29), 100 (49), 86 (13), 85 (90), 72 (24), 58 (28), 57 (100); HRMS calcd for $C_{13}H_{24}O_4$ (M$^+$) 244.1675, found 244.1686.

**(2*R**,3*S**)-3-(Allyloxy)-2-[2′-(2″,2″-dimethyl-1″,3″-dioxolan-4″-yl)ethyl]oxepane (98).** Allyl ether **98** was prepared from **97** (1.98 g, 8.1 mmol) by the same procedure used to convert **86** to

87 described above. Flash column chromatography (silica, 20%–30% EtOAc–hexane) gave **98** (1.96, 85%). **98**: oil; $R_f$ = 0.8 (silica, 30% EtOAc–hexane); IR ($CHCl_3$) $\nu_{max}$ 3085, 3020, 2990, 2865, 1645, 1455, 1380, 1370, 1236, 1195, 1110 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 5.86 (dddd, $J$ = 17.2, 10.4, 5.6, 5.6 Hz, 1H), 5.22 (d, $J$ = 17.2 Hz, 1H), 5.11 (d, $J$ = 10.4 Hz, 1H), 3.99 (m, 4H), 3.81 (dd, $J$ = 12.6, 5.8 Hz, 1H), 3.45 (m, 2H), 3.22 (m, 2H), 1.84–1.55 (m, 8H), 1.52 (m, 2H), 1.36, 1.31 (s, 3H each); $^{13}C$ NMR ($CDCl_3$) $\delta$ 135.5 (d), 117.0 (t), 109.0 (s), 84.7, 84.6, (d), 83.7, 83.6 (d), 76.7, 76.3 (d), 72.4, 72.2 (t), 70.4 (t), 69.9, 69.7 (t), 31.7 (t), 31.3 (t), 30.7, 30.6 (t), 40.3, 30.3 (t), 27.3 (q), 26.1 (q), 21.2, 21.0 (t); MS *m/e* (rel intensity) 269 ($M^+$ – Me, 6), 227 (3), 209 (1), 169 (7), 151 (7), 142 (6), 101 (22), 86 (10), 85 (100), 72 (39), 57 (93); HRMS calcd for $C_{16}H_{28}O_4$ ($M^+$) 284.1988, found 284.2020.

**(2′*R**,3′*S**)-4-[3′-(Allyloxy)oxepan-2′-yl]-1,2-butanediol (99).** Diol **99** was prepared from **98** (1.96 g, 6.90 mmol) by the same procedure used to convert **87** to **88** described above. Flash column chromatography (silica, 50% EtOAc–hexane) afforded **99** (1.6 g, 95%). **99**: oil; $R_f$ = 0.2 (silica, 50% EtOAc–hexane); IR ($CHCl_3$) $\nu_{max}$ 3585, 3410, 3010, 2935, 2865, 1645, 1445, 1365, 1230, 1225, 1195, 1105 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 5.88 (dddd, $J$ = 17.2, 10.4, 5.4, 5.4 Hz, 1H), 5.24 (d, $J$ = 17.2 Hz, 1H), 5.14 (d, $J$ = 10.4 Hz, 1H), 4.03 (m, 2H), 3.84 (dd, $J$ = 12.5, 5.4 Hz, 1H), 3.67 (m, 1H), 3.56 (br d, $J$ = 11.4 Hz, 1H), 3.43 (m, 2H), 3.30 (m, 2H), 1.83–1.46 (m, 10H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 135.4, 135.3 (d), 117.3, 117.2 (t), 85.2, 85.1 (d), 83.5, 83.2 (d), 72.6, 72.5 (d), 72.4, 72.3 (t), 70.4 (t), 67.3, 67.1 (t), 31.6, 31.5 (t), 31.1, 31.0 (t), 30.4, 30.3 (t), 30.2, 30.1 (t), 21.1, 20.1 (t); MS *m/e* (rel intensity) 245 ($M^+$ + 1, 6), 227 (1), 187 (18), 169 (4), 155 (14), 124 (13), 111 (25), 101 (43), 97 (23), 83 (62), 81 (20), 69 (60), 57 (100); HRMS calcd for $C_{13}H_{25}O_4$ $(M + H)^+$ 245.1753, found 245.1737.

**(2*R**,3*S**)-2-[2′-(2″,2″-Dimethyl-1″,3″-dioxolan-4″-yl)-ethyl]oxepan-3-ol (100).** To a cooled (–78 °C) solution of compound **99** (1.6 g, 6.57 mmol) in dry THF (65 mL) was added *s*-BuLi (16.2 mL, 21.0 mmol, 1.3 M in cyclohexane). The resulting solution was maintained at –78 °C for 30 min, at which time tributyltin chloride (2.13 mL, 7.89 mmol) was slowly added. The mixture was then maintained at –78 °C for 10 min, whereupon the reaction was quenched with aqueous $NH_4Cl$ solution (100 mL) and extracted with ether (2 × 100 mL). The combined organic extracts were washed with $H_2O$ (2 × 100 mL), dried ($MgSO_4$), and concentrated. Purification of the residue by flash column chromatography (silica, 50% EtOAc–hexane) gave **100** (2.4 g, 70%). **100**: oil; $R_f$ = 0.4 (silica, 50% EtOAc–hexane); IR ($CHCl_3$) $\nu_{max}$ 3585, 3450, 2935, 2860, 1645, 1465, 1390, 1110, 1080 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) (selected signals) $\delta$ 5.71 (d, $J$ = 6.2 Hz, 1H), 4.52 (ddd, $J$ = 9.0, 9.0, 6.2 Hz, 1H), 4.05 (m, 1H), 3.80–3.30 (m, 6H), 1.87–1.55 (m, 10H), 1.51 (m, 2H); $^{13}C$ NMR ($CDCl_3$) (selected signals) $\delta$ 140.6 (d), 107.1 (d), 85.6, 85.3 (d), 84.9, 84.8 (d), 72.7 (t), 72.4, 72.2 (t), 67.4, 67.2 (t), 32.1, 31.8 (t), 31.5, 31.4 (t), 30.5, 30.1 (t), 29.6 (t), 27.8 (t), 14.1 (q), 9.8 (t).

**(2*R**,3*S**,5a*R**,10a*S**)-2-Vinyldecahydrodioxaheptalen-3-ol (101) and Its *p*-Bromobenzoate (101, X = *p*-BrBz).** To a cooled (0 °C) solution of the allylstannane **100** (2.4 g, 4.5 mmol) in dry $CH_2Cl_2$ (45 mL) was added *n*-$Bu_4NIO_4$ (2.9 g, 6.69 mmol). The resulting solution was maintained at 25 °C for 3 h, at which time the reaction mixture was allowed to cool to –78 °C, and a solution of $BF_3{\cdot}OEt_2$ (1.1 mL, 9.0 mmol) was added. The mixture was allowed to warm to –10 °C over a 5-min period and then poured onto a stirred mixture of $CH_2Cl_2$ (100 mL) and aqueous saturated $NaHCO_3$ solution (200 mL). After separation, the organic portion was washed with $H_2O$ (2 × 50 mL), dried ($MgSO_4$), and concentrated. Purification of the residue by flash chromatography (silica, 30–40% EtOAc–hexane) afforded **101** (934 mg, 98%). **101**: oil; $R_f$ = 0.55 (silica, 50% EtOAc–hexane); $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 5.91 (ddd, $J$ = 17.2, 10.5, 6.1 Hz, 1H), 5.33 (d, $J$ = 17.2, 1H), 5.21 (d, $J$ = 10.5 Hz, 1H), 3.80 (m, 1H), 3.70 (m, 2H), 3.56 (m, 1H), 3.41 (m, 2H), 2.12 (m, 1H), 1.78–1.44 (m, 9H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 138.2 (d), 116.7 (t), 87.7 (d), 81.4 (d), 74.5 (d), 69.6 (t), 35.9 (t), 30.8 (t), 24.1 (t), 23.4 (t), 21.3 (t). Anal. Calcd for $C_{12}H_{20}O_3$: C, 67.92; H, 9.43. Found: C, 67.73; H, 9.12. Benzoylation of **101** (930 mg, 4.4 mmol) with *p*-BrBzCl (1.93 g, 8.8 mmol) and DMAP (1.07 g, 8.8 mmol) under standard conditions (see above) gave **101**, X = *p*-BrBz (1.6 g, 95%). **101**, X = *p*-BrBz: noncrystalline solid; $R_f$ = 0.8 (silica, 20% EtOAc–hexane); IR ($CHCl_3$) $\nu_{max}$ 3020, 3005, 2935, 2860, 1715, 1485, 1455, 1265, 1115, 1105, 1070, 1010, 990 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 7.89 (d, $J$ = 8.6 Hz, 2H), 7.59 (d, $J$ = 8.6 Hz, 2H), 5.86 (ddd, $J$ = 17.2, 10.6, 5.4 Hz, 1H), 5.32 (ddd, $J$ = 17.2, 1.6, 1.6 Hz, 1H), 5.13 (ddd, $J$ = 10.6, 1.6, 1.6 Hz, 1H), 5.09 (ddd, $J$ = 6.6, 6.4, 3.4 Hz, 1H), 4.13 (ddd, $J$ = 6.6, 5.4, 1.6 Hz, 1H), 3.87 (ddd, $J$ = 12.0, 6.8, 6.8 Hz, 1H), 3.69 (ddd, $J$ = 12.0, 6.0, 6.0 Hz, 1H), 3.51 (ddd, $J$ = 8.8, 8.8, 5.0 Hz, 1H), 3.37 (ddd, $J$ = 8.8, 8.8, 5.0 Hz, 1H), 2.11 (m, 1H), 2.06–1.85 (m, 6H), 1.81–1.53 (m, 3H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 165.3 (s), 137.0 (d), 132.2 (d), 131.5 (d), 129.6 (s), 128.6 (s), 116.3 (t), 86.0 (d), 83.7 (d), 82.4 (d), 77.5 (d), 70.1 (t), 35.8 (t), 29.7 (t), 29.0 (t), 25.7 (t), 21.1 (t); MS *m/e* (rel intensity) 397, 395 ($M^+$ + 1, 1), 213, 211 (2), 194 (39), 185, 183 (100), 177 (5), 155 (100), 149 (15), 137 (52), 124 (93), 111 (100), 104 (26), 95 (60), 85 (100); HRMS calcd for $C_{19}H_{23}{}^{81}BrO_4$ ($M^+$) 396.0759, found 396.0759; calcd for $C_{19}H_{23}{}^{79}BrO_4$ ($M^+$) 394.0779, found 394.0766.

**1,5-Anhydro-4,6-bis(*tert*-butyldimethylsilyl)-2,3-dideoxy-D-*erythro*-hexitol (103).** To a stirred solution of the diol **102**[13o] (30 g, 228 mmol), imidazole (38.6 g, 568 mmol), and dry THF (200 mL) at 0 °C was added TBDMSCl (75.3 g, 500 mmol). After 12 h at 45 °C, the reaction mixture was diluted with ether (600 mL) and MeOH (30 mL). The mixture was washed with aqueous saturated $NH_4Cl$ solution (2 × 150 mL) and $H_2O$ (3 × 150 mL) and then dried ($MgSO_4$). Concentration followed by flash column chromatography (silica, 10% EtOAc in hexane) gave compound **103** (75.2 g, 92%) as a colorless oil. Spectral data were identical to those reported for **103**.[13o]

**1,5-Anhydro-4-*O*-(*tert*-butyldimethylsilyl)-2,3-dideoxy-D-*erythro*-hexitol (104).** To a stirred solution of compound **103** (75.2 g, 208 mmol) in THF:$H_2O$ (1:1) (400 mL) at 0 °C was added TFA (200 mL). The reaction mixture was maintained at 0 °C for 5 min and then poured into a saturated aqueous $NaHCO_3$ solution (300 mL) and extracted with ether (3 × 100 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated. Purification of the residue by flash column chromatography (silica, 20% EtOAc in hexane) afforded **104** (37.0 g, 72%) as a colorless oil. Spectral data were identical to those reported for **104**.[13o]

**(2*S*,3*S*)-3-(*tert*-Butyldimethylsiloxy)-3,4,5,6-tetrahydro-2*H*-pyran-2-iodomethane (105).** Iodide **105** was prepared from **104** (12.3 g, 50.0 mmol) by the same procedure used to convert **92** to **93** described above. Flash column chromatography (silica, 5% EtOAc–hexane) gave **105** (16.9 g, 95%). **105**: oil; $R_f$ = 0.75 (silica, 5% EtOAc–hexane); $[\alpha]^{25}_D$ = +47.82° (*c* 1.38, $CHCl_3$); IR ($CHCl_3$) $\nu_{max}$ 3006, 2955, 2858, 1463, 1217, 1111, 838 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 3.97 (ddd, $J$ = 11.4, 4.4, 2.8 Hz, 1H), 3.50 (dd, $J$ = 10.4, 2.7 Hz, 1H), 3.40 (m, 2H), 3.34 (dd, $J$ = 10.4, 5.8 Hz, 1H), 2.83 (ddd, $J$ = 8.5, 5.8, 2.7 Hz, 1H), 2.03 (br dd, $J$ = 12.5, 4.7, 2.8 Hz, 1H), 1.67 (m, 2H), 1.50 (ddd, $J$ = 12.8, 10.6, 4.7 Hz, 1H), 0.89 (s, 9H), 0.12 (s, 3H), 0.09 (s, 3H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 81.3 (d), 71.6 (d), 68.4 (t), 33.6 (t), 26.0 (q), 25.8 (t), 18.3 (s), 9.8 (t), –3.4 (q), –4.1 (q); MS *m/e* (rel intensity) 357 ($M^+$ + 1, 2), 299 (100), 255 (9), 215 (15), 195 (14), 185 (46), 171 (31), 145 (7), 115 (10), 105 (13), 101 (16), 97 (21); HRMS calcd for $C_8H_{16}IO_2Si$ $(M - t\text{-}Bu)^+$ 298.9964, found 298.9970.

**(2*R*,3*S*)-3-(*tert*-Butyldimethylsiloxy)-3,4,5,6-tetrahydro-2*H*-pyran-2-butene (106).** Compound **106** was prepared from **105** (16.9 g, 47.8 mmol) by the same procedure used to convert **93** to **94** described above. Flash column chromatography (silica, 1–2% EtOAc–hexane) afforded **106** (9.06 g, 70%). **106**: oil; $R_f$ = 0.80 (silica, 5% EtOAc–hexane); $[\alpha]^{25}_D$ = +38.16° (*c* 2.01, $CHCl_3$); IR ($CHCl_3$) $\nu_{max}$ 3003, 2930, 2857, 1640, 1463, 1362, 1258, 1223, 1097, 915 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 5.84 (dddd, $J$ = 17.2, 10.3, 6.6, 6.6 Hz, 1H), 5.02 (dd, $J$ = 17.2, 1.7 Hz, 1H), 4.94 (d, $J$ = 10.3 Hz, 1H), 3.87 (ddd, $J$ = 10.7, 2.0, 2.0 Hz, 1H), 3.30 (m, 2H), 3.01 (ddd, $J$ = 8.9, 8.9, 2.4 Hz, 1H), 2.24 (m, 1H), 2.11 (m, 1H), 1.99 (m, 1H), 1.91 (m, 1H), 1.63 (m, 2H), 1.30 (m, 2H), 0.88 (s, 9H), 0.05 (s, 6H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 139.3 (d), 114.7 (t), 82.4 (d), 71.8 (d), 68.1 (t), 34.1 (t), 31.9 (t), 30.0 (2xt), 26.2 (q), 18.4 (s), –3.6 (q), –4.3 (q); MS *m/e* (rel intensity) 270 ($M^+$, 0.2), 213 (16), 195 (2), 171 (42), 145 (11), 131 (8), 121 (15), 105 (10), 101 (29), 93 (29), 75 (100); HRMS calcd for $C_{11}H_{21}O_2Si$ $(M - t\text{-}Bu)^+$ 213.1311, found 213.1312. Anal. Calcd for $C_{15}H_{30}O_2Si$: C, 66.67; H, 11.11. Found: C, 66.80; H, 11.18.

**(2*R*,3*S*)-4-[3-(*tert*-Butyldimethylsiloxy)-3,4,5,6-tetrahydro-2*H*-pyran-2-yl]butane-1,2-diol (107).** Compound **107** was prepared from **106** (9.04 g, 33.5 mmol) by the same procedure

used to convert **90** to **91** described above. Flash column chromatography (silica, 60% EtOAc–hexane) gave the diol **107** (9.2 g, 90%). **107**: oil; $R_f$ = 0.25 (silica, 50% EtOAc–hexane); IR ($CHCl_3$) $\nu_{max}$ 3395, 3008, 2930, 1463, 1389, 1361, 1253, 1100, 839 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 3.85 (m, 1H), 3.68 (m, 1H), 3.57 (br d, $J$ = 11.0 Hz, 1H), 3.43 (m, 1H), 3.30 (m, 2H), 3.02 (ddd, $J$ = 9.1, 9.1, 2.0 Hz, 1H), 2.09–1.90 (m, 2H), 1.68–1.34 (m, 6H), 0.85 (s, 9H), 0.04 (s, 6H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 83.7, 83.3 (d), 72.8, 72.3 (d), 71.6, 71.1 (d), 68.2, 68.1 (t), 67.3, 67.1 (t), 33.9 (t), 30.4, 29.7 (t), 29.0, 28.0 (t), 26.2 (q), 26.1, 26.0 (t), 18.3 (s), –3.6 (q), –4.3 (q); MS $m/e$ (rel intensity) 305 ($M^+$ + 1, 0.1), 273 (2), 229 (8), 175 (7), 157 (11), 155 (20), 145 (15), 137 (23), 131 (13), 119 (9), 83 (24), 75 (100); HRMS calcd for $C_{15}H_{33}O_4Si$ ($M + H)^+$ 305.2148, found 305.2154.

**(2*R*,3*S*)-3-(*tert*-Butyldimethylsiloxy)-2-[2′-(2″,2″-dimethyl-1″,3″-dioxolan-4″-yl)ethyl]-3,4,5,6-tetrahydro-2*H*-pyran (108).** Compound **108** was prepared from **107** (9.18 g, 30.15 mmol) by the same procedure used to convert **95** to **96** described above. Flash column chromatography (silica, 10% EtOAc–hexane) afforded **108** (9.33 g, 90%). **108**: oil; $R_f$ = 0.72 (silica, 10% EtOAc–hexane); IR ($CHCl_3$) $\nu_{max}$ 2931, 2858, 1463, 1371, 1253, 1096 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 4.10 (m, 1H), 4.02 (m, 1H), 3.86 (br d, $J$ = 7.4 Hz, 1H), 3.53 (br dd, $J$ = 7.6, 7.6 Hz, 1H), 3.30 (m, 2H), 2.98 (br dd, $J$ = 8.8, 8.8 Hz, 1H), 2.0 (m, 1H), 1.85 (m, 1H), 1.71 (m, 1H), 1.67 (m, 2H), 1.53 (m, 1H), 1.45 (m, 2H), 1.41 (s, 3H), 1.35 (s, 3H), 0.89 (s, 9H), 0.06 (s, 6H); MS $m/e$ (rel intensity) 329 ($M^+$ – Me, 10), 287 (3), 229 (29), 211 (15), 187 (16), 171 (32), 161 (5), 157 (10), 145 (17), 137 (45), 131 (26), 101 (49), 75 (100); HRMS calcd for $C_{17}H_{33}O_4Si$ (M – Me)$^+$ 329.2148, found 329.2148.

**(2*R*,3*S*)-2-[2′-(2″,2″-Dimethyl-1″,3″-dioxolan-4″-yl)ethyl]-3,4,5,6-tetrahydro-2*H*-pyran-3-ol (109).** Compound **109** was prepared from **108** (9.3 g, 27.0 mmol) by the same procedure used to convert **96** to **97** described above. Flash column chromatography (silica, 30–40% EtOAc–hexane) gave **109** (5.28 g, 85%). **109**: oil; $R_f$ = 0.3 (silica, 30% EtOAc–hexane); IR ($CHCl_3$) $\nu_{max}$ 3668, 3618, 3450, 3008, 2940, 1453, 1381, 1228, 1090 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 4.05 (m, 1H), 3.98 (m, 1H), 3.83 (br d, $J$ = 11.9 Hz, 1H), 3.48 (ddd, $J$ = 7.5, 7.5, 3.2 Hz, 1H), 3.25 (m, 2H), 2.94 (m, 1H), 2.03 (m, 1H), 1.96 (m, 1H), 1.79 (m, 2H), 1.55 (m, 3H), 1.48 (m, 1H), 1.36 (s, 3H), 1.30 (s, 3H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 109.1 (s), 82.7, 82.3 (d), 76.7, 76.4 (d), 70.6, 70.4 (d), 69.7 (t), 67.9 (t), 33.2 (t), 29.8, 29.2 (t), 28.6, 28.3 (t), 27.3, 27.2 (q), 26.1 (t), 26.0 (q); MS $m/e$ (rel intensity) 215 ($M^+$ – Me, 32), 212 (4), 173 (4), 159 (3), 155 (13), 142 (3), 137 (13), 119 (3), 84 (33), 73 (11), 71 (100), 67 (23); HRMS calcd for $C_{11}H_{19}O_4$ (M – Me)$^+$ 215.1283, found 215.1290.

**(2*R*,3*S*)-3-(Allyloxy)-2-[2′-(2″,2″-dimethyl-1″,3″-dioxolan-4″-yl)ethyl]-3,4,5,6-tetrahydro-2*H*-pyran (110).** Compound **110** was prepared from **109** (5.2 g, 22.6 mmol) by the same procedure used to convert **86** to **87** described above. Flash column chromatography (silica, 20–30% EtOAc–hexane) furnished **110** (5.19 g, 85%). **110**: oil; $R_f$ = 0.8 (silica, 30% EtOAc–hexane); IR ($CHCl_3$) $\nu_{max}$ 3009, 2940, 2859, 1640, 1455, 1371, 1232, 1095 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 5.91 (ddd, $J$ = 17.2, 10.3, 5.8 Hz, 1H), 5.26 (dd, $J$ = 17.2, 1.6 Hz, 1H), 5.16 (d, $J$ = 10.3 Hz, 1H), 4.11 (m, 1H), 4.09 (m, 1H), 4.05 (dd, $J$ = 7.2, 6.0 Hz, 1H), 3.93 (dd, $J$ = 12.5, 5.8 Hz, 1H), 3.87 (dddd, $J$ = 11.4, 4.4, 2.4, 2.4 Hz, 1H), 3.53 (dd, $J$ = 13.8, 7.2 Hz, 1H), 3.31 (ddd, $J$ = 11.4, 11.4, 2.6 Hz, 1H), 3.07 (m, 1H), 3.00 (m, 1H), 2.20 (m, 1H), 2.02 (m, 1H), 1.87 (m, 1H), 1.70–15.0 (m, 3H), 1.40 (s, 3H), 1.35 (s, 3H), 1.31 (m, 1H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 135.5 (d), 117.2 (t), 109.0 (s), 81.2, 81.1 (d), 77.6, 77.5 (d), 76.7, 76.5 (d), 70.2, 70.1 (t), 69.9, 69.8 (t), 68.0 (t), 30.3, 30.0 (t), 29.8, 29.7 (t), 28.9, 28.5 (t), 27.3 (q), 26.2 (q), 25.8 (t); MS $m/e$ (rel intensity) 270 ($M^+$, 0.2), 255 (12), 212 (9), 155 (12), 154 (25), 141 (12), 137 (15), 111 (32), 101 (20), 98 (27), 97 (41), 84 (91), 71 (100); HRMS calcd for $C_{15}H_{26}O_4$ ($M^+$) 270.1831, found 270.1797; calcd for $C_{14}H_{23}O_4$ (M – Me)$^+$ 255.1596, found 255.1601.

**(2*R*,3*S*)-4-[3-(Allyloxy)-3,4,5,6-tetrahydro-2*H*-pyran-2-yl]-butane-1,2-diol (111).** Compound **111** was prepared from **110** (5.1 g, 18.9 mmol) by the same procedure used to convert **87** to **88** described above. Flash column chromatography (silica, 50% EtOAc–hexane) gave **111** (3.04 g, 70%). **111**: oil; $R_f$ = 0.15 (silica, 50% EtOAc–hexane); IR ($CHCl_3$) $\nu_{max}$ 3580, 3404, 3010, 2943, 2862, 1640, 1463, 1344, 1239, 1086 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 5.90 (ddd, $J$ = 17.2, 5.7, 5.6 Hz, 1H), 5.26 (d, $J$ = 17.2 Hz, 1H), 5.17 (d, $J$ = 10.7, 1H), 4.08 (ddd, $J$ = 12.6, 5.6, 1.2 Hz, 1H), 3.86 (m, 1H), 3.65 (m, 1H), 3.75 (m, 1H), 3.41 (m, 1H), 3.31 (ddd, $J$ = 11.5, 11.5, 2.6 Hz, 1H), 3.13 (m, 1H), 3.00 (m, 1H), 2.78 (m, 1H), 2.04 (m, 1H), 1.60–1.42 (m, 6H), 1.29 (m, 1H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 135.4, 135.3 (d), 117.5, 117.4 (t), 81.7, 81.6 (d), 77.5, 77.1 (d), 72.7, 72.5 (d), 70.3, 70.2 (t), 68.1 (t), 67.3, 67.1 (t), 30.2, 29.7 (t), 29.6 (t), 28.9, 28.2 (t), 25.7, 25.6 (t); MS $m/e$ (rel intensity) 231 ($M^+$ + 1, 1), 199 (3), 154 (5), 141 (13), 129 (5), 126 (2), 111 (7), 103 (3), 101 (23), 97 (41), 84 (32), 71 (95), 55 (100); HRMS calcd for $C_{12}H_{23}O_4$ ($M + H)^+$ 231.1596, found 231.1596.

**(2*R**,3*S**)-4-[3-[[3-(Tributylstannyl)propenyl]oxy]-3,4,5,6-tetrahydro-2*H*-pyran-2-yl]butane-1,2-diol (112).** Compound **112** was prepared from **111** (3.0 g, 13.0 mmol) by the same procedures used to convert **99** to **100** described above. Flash column chromatography (silica, 50% EtOAc–hexane) yielded **112** (4.45 g, 66%). **112**: oil; $R_f$ = 0.35 (silica, 50% EtOAc–hexane); IR ($CHCl_3$) $\nu_{max}$ 3591, 3394, 3011, 2927, 2871, 1649, 1464, 1356, 1252, 1094 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) (selected signals) $\delta$ 5.78 (d, $J$ = 6.0 Hz, 1H), 4.51 (ddd, $J$ = 9.0, 9.0, 6.0 Hz, 1H), 3.93 (m, 1H), 3.65 (m, 1H), 3.60 (m, 1H), 3.43 (m, 1H), 3.35 (m, 1H), 3.18 (m, 2H), 2.25–1.97 (m, 3H); $^{13}C$ NMR ($CDCl_3$) (selected signals) $\delta$ 140.5 (d), 106.8 (d), 81.8, 81.4 (d), 79.5, 79.1 (d), 72.8, 72.2 (d), 68.2 (t), 67.4, 67.1 (t).

**(4a*S*,6*R*,7*S*,9a*R*)-6-Vinyl-2,3,4,4a,8,9-hexahydropyran[3,2-*b*]oxepan-7-ol (113).**[13u] Compound **113** was prepared from **112** (4.4 g, 8.5 mmol) by the same procedure used to convert **100** to **101** described above. Flash column chromatography (silica, 20–30% EtOAc–hexane) gave **113** (1.09 g, 65%). **113**: oil; $R_f$ = 0.2 (silica, 30% EtOAc–hexane); $[\alpha]^{25}_D$ = +20.8° (*c* 0.77, $CHCl_3$); IR ($CHCl_3$) $\nu_{max}$ 3690, 3608, 3009, 2944, 2856, 1645, 1331, 1086, 1037, 961 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 5.87 (ddd, $J$ = 17.2, 10.5, 5.7 Hz, 1H), 5.29 (ddd, $J$ = 17.2, 1.6, 1.6 Hz, 1H), 5.14 (ddd, $J$ = 10.5, 1.6, 1.6 Hz, 1H), 3.84 (br d, $J$ = 12.2 Hz, 1H), 3.77 (dd, $J$ = 7.3, 5.7 Hz, 1H), 3.71 (m, 1H), 3.30 (ddd, $J$ = 12.5, 12.2, 4.8 Hz, 1H), 3.20 (ddd, $J$ = 12.8, 9.2, 4.3 Hz, 1H), 2.99 (ddd, $J$ = 12.8, 9.2, 4.8 Hz, 1H), 2.06 (m, 1H), 1.82 (m, 4H), 1.64 (m, 2H), 1.42 (m, 1H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 138.2 (d), 116.1 (t), 86.7 (d), 83.6 (d), 82.5 (d), 73.9 (d), 68.2 (t), 31.8 (t), 30.1 (t), 27.8 (t), 26.7 (t); MS $m/e$ (rel intensity) 198 ($M^+$, 2), 141 (97), 124 (13), 123 (15), 112 (6), 106 (6), 97 (100), 85 (38), 81 (75), 71 (57); HRMS calcd for $C_{11}H_{18}O_3$ ($M^+$) 198.1256, found 198.1255. Anal. Calcd for $C_{11}H_{18}O_3$: C, 66.67; H, 9.09. Found: C, 66.83; H, 9.00.

**(4a*S*,6*R*,7*S*,9a*R*)-7-(*tert*-Butyldimethylsiloxy)-6-vinyl-2,3,4,4a,8,9-hexahydropyrano[3,2-*b*]oxepane (114).** Compound **114** was prepared from **113** (1.0 g, 5.1 mmol) by the same procedure used to convert **60c** to **90** described above. Flash column chromatography (silica, 10–20% EtOAc–hexane) afforded **114** (1.53 g, 96%). **114**: oil; $R_f$ = 0.9 (silica, 20% EtOAc–hexane); $[\alpha]^{25}_D$ = +34.1° (*c* 0.39, $CHCl_3$); IR ($CHCl_3$) $\nu_{max}$ 2953, 2856, 1471, 1256, 1085, 1061 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 5.82 (ddd, $J$ = 16.5, 10.5, 5.6 Hz, 1H), 5.27 (ddd, $J$ = 16.5, 1.6, 1.6 Hz, 1H), 5.10 (ddd, $J$ = 10.5, 1.6, 1.6 Hz, 1H), 3.88 (dd, $J$ = 5.6, 5.0 Hz, 1H), 3.86 (br d, $J$ = 11.4 Hz, 1H), 3.31 (ddd, $J$ = 11.4, 7.3, 4.8 Hz, 1H), 3.28 (ddd, $J$ = 10.5, 9.5, 4.5 Hz, 1H), 3.00 (ddd, $J$ = 13.6, 9.5, 4.0 Hz, 1H), 2.07 (m, 1H), 1.75 (m, 3H), 1.63 (m, 2H), 1.40 (m, 1H), 0.98 (s, 9H), 0.04 (s, 6H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 138.2 (d), 115.2 (t), 87.1 (d), 83.1 (d), 80.6 (d), 75.1 (d), 68.1 (t), 32.0 (t), 28.7 (t), 27.2 (t), 26.4 (t), 26.2 (q), 18.4 (s), –4.1 (q), –4.2 (q); MS $m/e$ (rel intensity) 255 ($M^+$ – *t*-Bu, 14), 237 (3), 199 (14), 187 (8), 171 (37), 163 (13), 157 (5), 149 (6), 141 (17), 135 (6), 123 (43), 115 (16), 101 (69), 97 (67), 85 (27), 75 (100); HRMS calcd for $C_{17}H_{32}O_5Si$ ($M^+$) 312.2121, found 312.2134; calcd for $C_{13}H_{23}O_3Si$ (M – *t*-Bu)$^+$ 255.1417, found 255.1419.

**(4a*S*,6*R*,7*S*,9a*S*)-[7-(*tert*-Butyldimethylsiloxy)-2,3,4,4a,8,9-hexahydropyrano[3,2-*b*]oxepan-6-yl]ethane-1,2-diol (115).** Compound **115** was prepared from **114** (1.5 g, 4.8 mmol) by the same procedure used to convert **90** to **91** described above. Flash column chromatography (silica, 50–60% EtOAc–hexane) gave **115** (1.53 g, 92%). **115**: oil; $R_f$ = 0.25 (silica, 60% EtOAc–hexane); IR ($CHCl_3$) $\nu_{max}$ 3488, 2931, 2857, 1636, 1484, 1437, 1388, 1257, 1087, 1050 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 4.05 (m, 1H), 3.84 (br d, $J$ = 10.4 Hz, 1H), 3.67 (m, 2H), 3.54 (m, 2H), 3.26 (ddd, $J$ = 10.4, 10.2, 4.5 Hz, 1H), 3.17 (ddd, $J$ = 10.5, 9.7, 4.5 Hz, 1H), 2.92 (ddd, $J$ = 10.2, 9.7, 4.3 Hz, 1H), 2.03 (m, 1H), 1.94 (m, 1H), 1.73 (m, 3H), 1.60 (m, 2H), 1.30 (m, 1H), 0.87 (s, 9H), 0.04 (s, 6H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 88.7 (d), 82.6 (d), 81.7 (d), 72.7 (d), 72.2 (d),

68.0 (t), 64.0 (t), 31.8 (t), 29.0 (t), 27.0 (t), 26.2 (q), 26.1 (t), 18.3 (s) -3.9 (q), -4.4 (q); MS *m/e* (rel intensity) 315 (M + 1, 1), 289 (10), 253 (5), 215 (2), 197 (17), 179 (29), 171 (12), 161 (14), 153 (15), 143 (12), 131 (26), 117 (56), 101 (60), 97 (100), 75 (100); HRMS calcd for $C_{16}H_{31}O_4Si$ (M - $CH_2OH$)$^+$ 315.1992, found 315.1999; calcd for $C_{13}H_{25}O_5Si$ (M - *t*-Bu)$^+$ 289.1471, found 289.1470.

**(4a*S*,6*R*,7*S*,9a*S*)-7-(*tert*-Butyldimethylsiloxy)-6-(hydroxymethyl)-2,3,4,4a,8,9-hexahydropyrano[3,2-*b*]oxepane (116).** Compound **116** was prepared from **115** (1.5 g, 4.3 mmol) by the same procedure to convert **91** to **92** described above. Flash column chromatography (silica, 25% EtOAc–hexane) afforded **116** (1.12 g, 82%). **116**: oil; $R_f$ = 0.5 (silica, 20% EtOAc–hexane); $[\alpha]^{25}_D$ = +39.58° (*c* 0.48, $CHCl_3$); IR (KBr) $\nu_{max}$ 3476, 2934, 2856, 1472, 1437, 1370, 1252, 1093, 1060 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 3.87 (br d, *J* = 11.4 Hz, 1H), 3.71 (m, 1H), 3.62 (br d, *J* = 10.6 Hz, 1H), 3.52 (ddd, *J* = 8.4, 5.0, 4.0 Hz, 1H), 3.41 (dd, *J* = 10.6, 8.4 Hz, 1H), 3.31 (ddd, *J* = 11.4, 8.0, 7.6 Hz, 1H), 3.20 (ddd, *J* = 10.7, 10.0, 4.4 Hz, 1H), 2.97 (ddd, *J* = 10.0, 10.0, 3.5 Hz, 1H), 2.08 (m, 1H), 1.92 (br dd, *J* = 11.6, 10.0 Hz, 1H), 1.77 (m, 2H), 1.66 (m, 3H), 1.42 (m, 1H), 0.88 (s, 9H), 0.03 (s, 6H); $^{13}$C NMR ($CDCl_3$) $\delta$ 87.5 (d), 83.1 (d), 82.2 (d), 71.8 (d), 68.0 (t), 64.8 (t), 31.8 (t), 29.9 (t), 27.3 (t), 26.3 (t), 26.1 (q), 18.3 (s), -4.0 (q), -4.5 (q); MS *m/e* (rel intensity) 259 (M$^+$ - *t*-Bu, 6), 241 (16), 211 (2), 197 (3), 171 (8), 157 (19), 147 (10), 143 (10), 131 (25), 123 (18), 121 (16), 117 (19), 101 (29), 97 (89), 75 (100); HRMS calcd for $C_{12}H_{33}O_4Si$ (M - *t*-Bu)$^+$ 259.1366, found 259.1373.

**(4a*S*,6*R*,7*S*,9a*S*)-[7-(*tert*-Butyldimethylsiloxy)-2,3,4,4a,8,9-hexahydropyrano[3,2-*b*]oxepan-6-yl]iodomethane (117).** Compound **117** was prepared from **116** (1.1 g, 3.48 mmol) by the same procedure used to convert **92** to **93** described above. Flash column chromatography (silica, 5% EtOAc–hexane) gave **117** (178 g, 97%). **117**: oil; $R_f$ = 0.7 (silica, 5% EtOAc–hexane); $[\alpha]^{25}_D$ = +22.19° (*c* 0.32, $CHCl_3$); IR (KBr) 2934, 2855, 1471, 1361, 1257, 1089, 1060, 984, 835, 775 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 3.86 (br d, *J* = 11.5 Hz, 1H), 3.77 (ddd, *J* = 6.2, 3.2, 3.2 Hz, 1H), 3.43 (ddd, *J* = 8.2, 6.2, 3.5 Hz, 1H), 3.35 (dd, *J* = 10.2, 3.5 Hz, 1H), 3.31 (ddd, *J* = 11.5, 8.6, 5.9 Hz, 1H), 3.17 (ddd, *J* = 11.1, 9.2, 4.4 Hz, 1H), 3.11 (dd, *J* = 10.2, 8.2 Hz, 1H), 2.97 (ddd, *J* = 9.5, 9.2, 3.2 Hz, 1H), 2.19 (m, 1H), 1.88 (m, 1H), 1.80 (m, 3H), 1.66 (m, 2H), 1.45 (m, 1H), 0.88 (s, 9H), 0.07 (s, 6H); $^{13}$C NMR ($CDCl_3$) $\delta$ 86.8 (d), 83.3 (d), 83.2 (d), 74.8 (d), 68.2 (t), 31.4 (t), 30.7 (t), 27.4 (t), 26.3 (t), 26.2 (q), 18.3 (s), 10.0 (t), -3.8 (q), -4.3 (q); MS *m/e* (rel intensity) 369 (M$^+$ - *t*-Bu, 33), 299 (8), 281 (7), 255 (3), 185 (10), 171 (25), 167 (36), 157 (10), 149 (19), 141 (21), 131 (13), 123 (33), 115 (24), 101 (23), 97 (89), 89 (16), 73 (100); HRMS calcd for $C_{16}H_{31}O_3Si$ (M - I)$^+$ 299.2043, found 299.2043.

**(1*R**,2*S**,5*Z*,9*R**,10*S**,12*S**)-9,12-Diiodo-13-oxabicyclo[8.2.1]-tridec-5-en-2-ol (120).** To a stirred solution of the epoxy acetate **119** (23.6 g, 0.1 mol) in dry $CH_2Cl_2$ (250 mL), iodine (31.7 f, 0.12 mol) in $CH_2Cl_2$ (100 mL) was added dropwise. The mixture was stirred at 25 °C for 6 h before quenching with a saturated $Na_2SO_3$ aqueous solution (200 mL). The organic phase was washed with 0.5 N NaOH (2 × 100 mL) and brine (2 × 100 mL) prior to drying ($MgSO_4$) and solvent evaporation. Purification of the residue by chromatography on silica gel (elution with 20% EtOAc in *n*-hexane) yielded **120** (acetate) (33.3 g, 68%) which was dissolved in a 10:1 mixture of MeOH:acetone (100 mL). An excess of $K_2CO_3$ (13.8 g, 0.1 mol) was added and the reaction mixture stirred at 25 °C for 4 h. The mixture was diluted with water (200 mL) and ether (300 mL) and the organic phase washed with $H_2O$ (2 × 100 mL) and brine (100 mL) and then dried ($MgSO_4$). Solvent evaporation under vacuo followed by flash column chromatography (silica, 20% EtOAc in *n*-hexane) gave alcohol **120** (29.6 g, 66%). **120**: mp 119 °C (*n*-hexane); $R_f$ = 0.42 (silica, 15% EtOAc in *n*-hexane); IR (KBr) $\nu_{max}$ 3250, 2990, 2950, 1732, 1454, 1441, 1427, 1348, 1311, 1240, 1037, 924, 850 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 5.40 (ddd, *J* = 11.0, 10.8, 2.4 Hz, 1H), 5.20 (ddd, *J* = 11.4, 11.0, 2.6 Hz, 1H), 4.27 (ddd, *J* = 12.0, 7.4, 7.4 Hz, 1H), 4.03 (br s, 1H), 3.95 (ddd, *J* = 12.0, 12.0, 4.0 Hz, 1H), 3.79 (ddd, *J* = 10.6, 7.5, 7.3 Hz, 1H), 3.67 (br d, *J* = 10.6, 1H), 2.97 (m, 1H), 2.91 (ddd, *J* = 13.6, 7.4, 7.3 Hz, 1H), 2.48 (m, 2H), 2.34 (dddd, *J* = 13.5, 12.0, 3.0, 3.0 Hz, 1H), 2.08 (m, 1H), 2.06 (ddd, *J* = 13.6, 7.5, 7.4 Hz, 1H), 1.72 (m, 2H), 1.55 (dddd, *J* = 14.4, 10.8, 3.4, 0.5 Hz, 1H); $^{13}$C NMNR ($CDCl_3$) $\delta$ 132.7 (d), 127.6 (d), 85.9 (d), 84.2 (d), 65.8 (d), 47.3 (t), 42.1 (t), 36.9 (d), 35.7 (t), 29.2 (t), 20.3 (t), 19.6 (d); MS *m/e* (rel intensity) 448 (M$^+$, 1), 321 (27), 303 (23), 257 (2), 193 (30), 175 (39), 157 (25), 147 (27), 133 (23), 129 (10), 119 (25), 109 (12), 96 (24), 91 (40), 79 (60), 67 (100); HRMS calcd for $C_{12}H_{18}I_2O_2$ (M$^+$) 447.9318, found 447.9336.

**(1*R**,2*S**,5*Z*,10*S**,12*S**)-12-Acetoxy-9-iodo-13-oxabicyclo-[8.2.1]tridec-5-en-2-ol (122) and (1*R**,2*S**,5*Z*,9*S**,10*R**,12*S**)-10,12-Diacetoxy-13-oxabicyclo[7.3.1]tridec-5-en-2-ol (124).** To a stirred solution of diiodide **120** (28.5 g, 63.6 mmol) in dry $CHCl_3$ (220 mL) were added AgOAc (26.6 gr, 159 mmol) and AcOH (2 mL). The reaction mixture was refluxed for 4 h, the solvent was partially removed under vacuo, and the residue was diluted with ether (500 mL). Washing with aqueous $NaHCO_3$ solution (3 × 100 mL), $H_2O$ (2 × 100 mL), and brine (100 mL) followed by drying ($MgSO_4$), evaporation, and flash column chromatography (silica, 20% ether in petroleum ether) gave **122** (fast moving, 8.4 g, 22.1 mmol, 34.7%) and **124** (slow moving, 11.0 g, 35.3 mmol, 55.5%).

Treatment of monoacetate **122** (8.3 g, 21.8 mmol) in $CHCl_3$ (80 mL) with AgOAc (3.7 g, 22.0 mmol) and AcOH (0.5 mL), refluxing the reaction mixture (12 h), and extraction following the procedure above indicated gave diacetate **124** (6.8 g, 99%). **122**: crystalline solid, mp 168–170 °C (*n*-hexane); $R_f$ = 0.55 (silica, 15% EtOAc in *n*-hexane); IR (KBr) $\nu_{max}$ 3487, 2990, 2920, 2865, 1738, 1437, 1336, 1284, 1255, 1132, 1070, 1033, 1008, 775 cm$^{-1}$; $^1$H NMR (200 MHz, $CDCl_3$) $\delta$ 5.43 (m, 2H), 5.03 (ddd, *J* = 7.0, 3.0, 3.0 Hz, 1H), 4.02 (ddd, *J* = 11.7, 10.0, 4.1 Hz, 1H), 3.48 (dd, *J* = 8.2, 5.2 Hz, 1H), 3.38 (dd, *J* = 11.7, 10.0, 2.3 Hz, 1H), 3.27 (dd, *J* = 7.4, 2.8 Hz, 1H), 2.65 (m, 1H), 2.51 (m, 2H), 2.27 (ddd, *J* = 14.8, 3.0, 2.3 Hz, 1H), 2.09 (m, 1H), 2.08 (s, 3H), 2.04 (m, 1H), 1.78 (m, 2H), 1.73 (ddd, *J* = 14.8, 10.0, 3.0 Hz, 1H), 1.47 (m, 1H); $^{13}$C NMR ($CDCl_3$) $\delta$ 169.9 (s), 132.5 (d), 126.9 (d), 79.5 (d), 75.2 (d), 71.6 (d), 66.4 (d), 43.4 (t), 35.1 (t), 34.0 (d), 29.7 (t), 26.7 (t), 22.5 (t), 21.4 (q); MS *m/e* (rel intensity) 380 (55), 320 (11), 253 (73), 193 (81), 175 (46), 131 (41), 123 (10), 119 (35), 111 (13), 105 (32), 97 (52), 93 (43), 91 (55), 83 (34), 81 (60), 77 (25), 67 (100); HRMS calcd for $C_{14}H_{21}IO_4$ (M$^+$) 380.0443, found 380.0444. **124**: noncrystalline solid; $R_f$ = 0.24 (silica, 20% EtOAc in *n*-hexane); IR (KBr) $\nu_{max}$ 2991, 2937, 2912, 1728, 1450, 1375, 1250, 1234, 1184, 1105, 1064, 1028, 986, 816 cm$^{-1}$; $^1$H NMR (200 MHz, $CDCl_3$) $\delta$ 5.42 (m, 2H), 4.89 (ddd, *J* = 11.0, 10.0, 5.0 Hz, 1H), 4.69 (ddd, *J* = 10.5, 10.5, 5.0 Hz, 1H), 3.71 (m, 1H), 3.20 (m, 1H), 2.97 (d, *J* = 10.0 Hz, 1H), 2.62 (*J* = 11.5, 5.0, 5.0 Hz, 1H), 2.50 (m, 3H), 2.03 (s, 3H), 2.01 (s, 3H), 1.90–1.50 (m, 5H), 1.45 (ddd, *J* = 11.5, 11.0, 10.5 Hz, 1H); $^{13}$C NMR ($CDCl_3$) $\delta$ 169.8 (s), 169.7 (s), 133.2 (d), 126.8 (d), 82.3 (d), 78.7 (d), 70.6 (d), 66.9 (d), 65.9 (d), 35.6 (t), 35.4 (t), 29.2 (t), 22.2 (t), 20.8 (t), 20.8 (2xq); MS *m/e* (rel intensity) 312 (M$^+$, 1), 279 (2), 210 (9), 192 (47), 174 (18), 131 (11), 121 (17), 107 (34), 97 (20), 94 (65), 91 (19), 81 (100), 79 (33), 67 (45); HRMS calcd for $C_{16}H_{24}O_6$ (M$^+$) 312.1573, found 312.1564.

**(1*R**,2*S**,5*Z*,9*S**,10*R**,12*S**)-10,12-Diacetoxy-13-oxabicyclo-[7.3.1]tridec-5-en-2-yl Methanesulfonate (125).** MsCl (1.99 mL, 25.6 mmol) was added to a cooled (0 °C) and stirred solution of the alcohol **124** (4.0 g, 12.8 mmol) in dry pyridine (42 mL) under an argon atmosphere. After 1 h the reaction mixture was allowed to warm to 40 °C (ca. 20 min) and the stirring continued for 4 h. The reaction mixture was diluted with ether (300 mL), washed with aqueous 2% HCl (2 × 100 mL) and aqueous saturated $NaHCO_3$ solutions (2 × 100 mL) and $H_2O$ (2 × 100 mL), and dried ($MgSO_4$). Concentration followed by flash chromatography (silica, 5% ether in petroleum ether) afforded **125** (4.49 g, 90%). **125**: crystalline solid, mp 123.5 °C (*n*-hexane); $R_f$ = 0.72 (silica, 30% EtOAc in *n*-hexane); IR (KBr) $\nu_{max}$ 3528, 3462, 2936, 2922, 1736, 1450, 1246, 1130, 1043, 1024, 970, 954, 860cm$^{-1}$; $^1$H NMR (200 MHz, $CDCl_3$) (selected signals) $\delta$ 5.39 (m, 2H), 4.81 (dd, *J* = 3.2, 3.2 Hz, 1H), 4.78 (m, 2H), 3.07, 2.03, 2.01 (s, 3H each); $^{13}$C NMR ($CDCl_3$) $\delta$ 169.6 (s), 132.7 (d), 127.0 (d), 81.6 (d), 78.7 (d), 74.3 (d), 70.6 (d), 66.4 (d), 38.7 (q), 35.6 (t), 34.2 (t), 29.2 (t), 22.0 (t), 21.1 (t), 20.8 (q), 20.8 (q); MS *m/e* (rel intensity) 390 (M$^+$, 1) 331 (2), 311 (48), 270 (3), 251 (9), 209 (18), 191 (100), 174 (11), 163 (8), 147 (16), 145 (22), 91 (15), 81 (23), 79 (33), 67 (25).

**(1*R**,2*S**,5*Z*,9*S**,10*R**,12*S**)-10,12-Dihydroxy-13-oxabicyclo-[3.7.1]tridec-5-en-yl Methanesulfonate (126).** A mixture of diacetate **125** (5.62 g, 14.4 mmol) and $K_2CO_3$ (6.3 g, 48.8 mmol) in acetone:MeOH (10:1) (50 mL) was stirred at 25 °C for 4 h. The reaction mixture was diluted with ether (300 mL) and washed with water (2 × 100 mL) and brine (2 × 100 mL). Drying ($MgSO_4$)

followed by concentration and flash chromatography (silica, 60% EtOAc in *n*-hexane) gave diol **126** (4.23 g, 96%). **126**: colorless needles (ether–hexane), mp 100–101 °C; $R_f$ = 0.25 (silica, 90% EtOAc in *n*-hexane); IR ($CHCl_3$) $\nu_{max}$ 3690, 3600, 3020, 2970, 2930, 2875, 1265, 1170, 1110, 1030 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 5.41 (m, 2H), 5.06 (dd, $J$ = 3.2, 3.2 Hz, 1H), 3.69 (ddd, $J$ = 11.0, 9.3, 4.8 Hz, 1H), 3.51 (m, 1H), 3.11 (s, 3H), 2.91 (m, 1H), 2.82 (d, $J$ = 9.3 Hz, 1H), 2.71 (br s, 1H), 2.57 (m, 1H), 2.45 (ddd, $J$ = 12.0, 4.8, 4.8 Hz, 1H), 2.38 (ddd, $J$ = 15.7, 9.4, 3.5 Hz, 1H), 1.98 (ddd, $J$ = 13.2, 6.6, 5.2 Hz, 1H), 1.87 (m, 1H), 1.87 (m, 1H), 1.64 (m, 1H), 1.59 (m, 2H), 1.44 (m, 2H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 132.8 (d), 127.7 (d), 84.6 (d), 81.2 (d), 76.1 (d), 71.3 (d), 65.7 (d), 42.2 (t), 38.8 (q), 34.5 (t), 29.8 (t), 24.3 (t), 22.6 (t); MS *m/e* (rel intensity) 306 ($M^+$, 0.9), 227 (4), 210 (100), 192 (81), 174 (25), 118 (24), 100 (48), 93 (100), 83 (100), 41 (100); HRMS calcd for $C_{12}H_{18}O_3$ (M – MsOH)$^+$ 210.1256, found 210.1257.

**(1*R**,2*S**,5*Z*,9*S**,10*R**,12*S**)-10,12-Bis(*tert*-Butyldimethylsiloxy)-13-oxabicyclo[7.3.1]tridec-5-en-2-yl Methanesulfonate (127).** To a stirred solution of the diol **126** (4.22 g, 13.8 mmol), triethylamine (7.7 mL, 55.2 mmol), and dry $CH_2Cl_2$ (135 mL) at 0 °C was added TBDMSOTf (8.9 mL, 38.6 mmol). After 30 min the reaction mixture was diluted with ether (300 mL) and washed with $H_2O$ (50 mL) and brine (50 mL). Drying ($MgSO_4$) and concentration followed by flash column chromatography (silica, 10% EtOAc in *n*-hexane) afforded compound **127** (7.10 g, 97%). **127**: colorless needles, mp 82–83 °C (ether–hexane); $R_f$ = 0.8 (silica, 30% EtOAc in *n*-hexane); IR ($CHCl_3$) $\nu_{max}$ 3025, 3000, 2955, 2885, 1650, 1470, 1455, 1390, 1255, 1230, 1170, 1085 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 5.39 (m, 2H), 5.03 (dd, $J$ = 2.9, 2.9 Hz, 1H), 3.69 (ddd, $J$ = 11.8, 11.6, 4.9 Hz, 1H), 3.42 (ddd, $J$ = 11.8, 9.8, 4.9 Hz, 1H), 3.05 (s, 3H), 2.89 (m, 2H), 2.80 (d, $J$ = 11.8 Hz, 1H), 2.55 (m, 1H), 2.47 (ddd, $J$ = 13.2, 9.4, 4.0 Hz, 1H), 2.29 (ddd, $J$ = 12.1, 4.9, 4.9 Hz, 1H), 1.88 (m, 3H), 1.57 (m, 1H), 1.50 (ddd, $J$ = 11.6, 11.6, 5.6 Hz, 1H), 1.37 (ddd, $J$ = 12.1, 11.8, 11.6 Hz, 1H), 0.87 (s, 18H), 0.11 (s, 3H), 0.08 (s, 3H), 0.04 (s, 6H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 132.5 (d), 127.9 (d), 84.8 (d), 81.3 (d), 76.9 (d), 71.3 (d), 66.6 (d), 44.8 (t), 39.8 (q), 34.2 (t), 30.2 (t), 26.1 (q), 22.6 (t), 21.3 (t), 18.4 (s), –3.3 (q), –3.9 (q), –4.2 (q), –4.3 (q); MS *m/e* (rel intensity) 534 ($M^+$, 2), 477 (1), 438 (5), 381 (5), 307 (47), 249 (42), 191 (55), 173 (39), 115 (5), 96 (5), 73 (100), 57 (7), 41(13); HRMS calcd for $C_{24}H_{46}O_3Si_2$ (M – MsOH)$^+$ 438.2985, found 438.2993.

**(1*S**,2*S**,5*S**/*R**,6*R**/*S**,9*S**,10*R**,12*S**)-5,6-Dihydroxy-10,12-bis(*tert*-butyldimethylsiloxy)-13-oxabicyclo[7.3.1]tridecan-2-yl Methanesulfonate (128a,b).** To a stirred mixture of 4-methylmorpholine *N*-oxide (60.7 g, 449 mmol) and water (40 mL) at 25 °C was added $OsO_4$ (12.7 mg, 0.07 mmol), followed by addition of **127** (7.0 g, 13.2 mmol) in THF:acetate (1:1) (80 mL). After 12 h at 25 °C the reaction mixture was treated with an aqueous saturated solution of $Na_2SO_3$ (40 mL), diluted with EtOAc (300 mL), washed with $H_2O$ (2 × 100 mL) and brine (50 mL), and dried ($MgSO_4$). Concentration followed by flash chromatography (silica, 80% EtOAc in *n*-hexane) afforded a 3:1 mixture of diastereomeric diols **128a,b** by $^1H$ NMR analysis (6.79 g, 90%). The major diastereomer **128a** (5*S**,6*R**): colorless oil; $R_f$ = 0.30 (silica, 60% EtOAc in *n*-hexane); IR ($CHCl_3$) $\nu_{max}$ 3670, 3450, 2950, 2930, 2885, 2855, 1470, 1465, 1390, 1360, 1315, 1170 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 5.04 (m, 1H), 3.71 (m, 2H), 3.36 (ddd, $J$ = 10.5, 9.8, 4.8 Hz, 1H), 3.30 (m, 1H), 3.01 (s, 3H), 2.99 (d, $J$ = 9.2 Hz, 1H), 2.88 (m, 1H), 2.63 (br s, 1H), 2.51 (br s, 1H), 2.39 (m, 1H), 2.34 (m, 1H), 2.28 (ddd, $J$ = 12.2, 4.8, 4.8 Hz, 1H), 1.90 (m, 2H), 1.79 (m, 1H), 1.64 (m, 1H), 1.56 (m, 1H), 1.40 (ddd, $J$ = 12.2, 10.5, 10.5 Hz, 1H), 1.24 (ddd, $J$ = 14.8, 7.2, 7.2 Hz, 1H), 0.86 (s, 9H), 0.85 (s, 9H), 0.10 (s, 3H), 0.07 (s, 3H), 0.04 (s, 3H), 0.03 (s, 3H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 84.8 (d), 79.9 (d), 76.7 (2 × d), 76.6 (d), 75.9 (d), 72.4 (d), 65.9 (d), 44.7 (t), 40.0 (q), 31.1 (t), 29.2 (t), 28.4 (t), 26.1 (q), 25.1 (t), 18.3 (s), –3.4 (q), –3.8 (q), –4.3 (q); MS *m/e* (rel intensity) 472 ($M^+$ – MsOH, 23), 454 (35), 397 (37), 301 (42), 265 (68), 147 (100), 73 (100); HRMS calcd for $C_{24}H_{48}O_5Si_2$ (M – MsOH)$^+$ 472.3040, found 472.3017. Anal. Calcd for $C_{25}H_{52}O_8SSi_2$: C, 52.82; H, 9.15. Found: C, 53.12; H, 9.24.

**(1*S**,4*S**,5*R**,7*Z*,9*R**,10*S**,12*R**)-10,12-Bis(*tert*-butyldimethylsiloxy)-13-oxabicyclo[7.3.1]tridec-7-ene-4,5-diol (129a) and (1*S**,4*R**,5*S**,7*Z*,9*R**,10*S**,12*R**)-10,12-Bis(*tert*-butyldimethylsiloxy)-13-oxabicyclo[7.3.1]tridec-7-ene-4,5-diol (129b).** To a stirred solution of **128a,b** (3:1 diastereomeric mixture of *syn* diols) (6.79 g, 11.9 mmol) in dry toluene (40 mL) at 25 °C was added dropwise DBU (178 mL, 119 mmol). The flask was equipped with a reflux condenser and the reaction mixture refluxed for 12 h, allowed to cool rt, and preadsorbed onto silica gel (25 g). Flash chromatography (silica gel, 50% EtOAc in *n*-hexane) gave **129a,b** (4.5 g, 79%) as a colorless oil, which was shown to be a 3:1 mixture of the diastereomeric *syn* diols **129a** (4*S**,5*R** isomer) and **129b** (4*R**,5*S** isomer), respectively. Careful separation by flash chromatography (silica, 35% EtOAc in *n*-hexane) provided pure samples of each diastereomer. **129a (4*S**,5*R** isomer)**: colorless needles; mp 119–120 °C (ether–hexane); $R_f$ = 0.7 (silica, 60% EtOAc–hexane); IR ($CHCl_3$) $\nu_{max}$ 3400, 2950, 2850, 1460, 1380, 1355, 1125, 1220, 1090 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 5.89 (ddd, $J$ = 10.8, 7.8, 7.8 Hz, 1H), 5.79 (dd, $J$ = 10.8, 3.0 Hz, 1H), 3.82 (m, 2H), 3.74 (m, 1H), 3.53 (ddd, $J$ = 10.0, 10.0, 4.0 Hz, 1H), 3.42 (ddd, $J$ = 10.3, 8.5, 4.5 Hz, 1H), 3.11 (ddd, $J$ = 8.5, 5.0, 5.0 Hz, 1H), 2.59 (ddd, $J$ = 11.2, 4.5, 4.0 Hz, 1H), 2.33 (m, 1H), 2.19 (ddd, $J$ = 11.2, 4.5, 4.0 Hz, 1H), 1.93 (m, 1H), 1.77 (m, 1H), 1.68 (m, 1H), 1.56 (m, 1H), 1.48 (ddd, $J$ = 11.2, 10.3, 10.0 Hz, 1H), 1.27 (s, 18H), 0.08 (s, 12H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 130.0 (2 × d), 81.9 (d), 78.6 (d), 76.1 (d), 74.3 (d), 71.6 (d), 67.2 (d), 45.0 (t), 28.9 (t), 28.0 (t), 27.8 (t), 26.0 (q), 18.6 (s), 18.3 (s), –3.8 (q), –4.3 (q), –4.4 (q), –4.6 (q); MS *m/e* (rel intensity) 472 ($M^+$, 8), 454 (3), 415 (9), 397 (28), 379 (4), 301 (49), 283 (20), 265 (27), 247 (14), 191 (24), 147 (40), 73 (100), 41 (7); HRMS calcd for $C_{24}H_{48}O_5Si_2$ ($M^+$) 472.3040, found 472.3058. **129b (4*R**,5*S** isomer)**: noncrystalline solid; $R_f$ = 0.60 (silica, 60% EtOAc–hexane); IR ($CHCl_3$) $\nu_{max}$ 3610, 3425, 3030, 2955, 2860, 1470, 1390, 1360, 1220, 1090 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 5.88 (ddd, $J$ = 10.5, 10.1, 2.2 Hz, 1H), 5.75 (dd, $J$ = 10.5, 2.6 Hz, 1H), 3.97 (m, 2H), 3.66 (br d, $J$ = 9.6 Hz, 1H), 3.48 (ddd, $J$ = 10.7, 9.6, 4.5 Hz, 1H), 3.35 (ddd, $J$ = 10.7, 10.0, 4.6 Hz, 1H), 3.05 (ddd, $J$ = 10.7, 10.7, 2.9 Hz, 1H), 2.50 (ddd, $J$ = 12.7, 10.1, 7.1 Hz, 1H), 2.19 (ddd, $J$ = 11.3, 4.6, 4.5 Hz, 1H), 2.02 (m, 2H), 1.76 (m, 1H), 1.59 (m, 1H), 1.48 (ddd, $J$ = 11.3, 10.7, 10.0 Hz, 1H), 1.24 (m, 1H), 0.89 (s, 18H), 0.09 (s, 6H), 0.06 (s, 6H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 132.9 (d), 130.9 (d), 83.6 (d), 78.5 (2 × d), 76.8 (d), 71.6 (d), 70.2 (d), 44.3 (t), 34.2 (t), 31.5 (t), 28.4 (t), 26.3 (q), 18.4 (s), 18.3 (s), –3.7 (q), –3.9 (q), –4.3 (2 × q); MS *m/e* (rel intensity) 473 ($M^+$ + 1, 1), 454 (1), 415 (12), 379 (2), 323 (8), 301 (21), 283 (32), 265 (18), 247 (9), 209 (18), 197 (24), 191 (26), 173 (17), 99 (17), 73 (100); HRMS calcd for $C_{24}H_{48}O_5Si_2$ ($M^+$) 472.3040, found 472.3039.

**(1*S**,4*S**/*R**,8*R**/*S**,10*Z*,12*R**,13*R**,15*R**)-13,15-Bis(*tert*-butyldimethylsiloxy)-6,6-dimethyl-5,7,16-trioxatricyclo-[10.3.1.0$^{4,8}$]hexadec-10-ene (130a,b).** To a stirred solution of diol **129a** (4*S**,5*R** isomer) (4.4 g, 9.4 mmol) in dry $CH_2Cl_2$ (180 mL) was added, under argon atmosphere, 2,2-dimethoxypropane (4.62 mL, 37.6 mmol) and a catalytic amount of CSA. After 15 min of continuous stirring at 25 °C the reaction mixture was poured into $CH_2Cl_2$ (200 mL) and a saturated aqueous solution of $NaHCO_3$ (100 mL). After shaking and separation, the organic portion was dried ($MgSO_4$) and concentrated to yield, after chromatographic purification (silica, 5% EtOAc–hexane), compound **130a** (4*S**,8*R** isomer) (4.83, 99%). **130a**: amorphous solid; $R_f$ = 0.9 (silica, 10% EtOAc–hexane); IR ($CHCl_3$) $\nu_{max}$ 3020, 2955, 2930, 2860, 1475, 1455, 1370, 1250, 1094 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 5.88 (ddd, $J$ = 11.3, 7.7, 7.7 Hz, 1H), 5.72 (ddd, $J$ = 11.3, 4.0, 1.7 Hz, 1H), 4.08 (m, 2H), 3.67 (dd, $J$ = 8.9, 4.0 Hz, 1H), 3.45 (m, 2H), 3.17 (ddd, $J$ = 8.4, 5.0, 5.0 Hz, 1H), 2.93 (ddd, $J$ = 7.7, 7.2, 1.7 Hz, 1H), 2.18 (ddd, $J$ = 11.5, 4.3, 4.3 Hz, 1H), 1.94 (m, 1H), 1.91 (m, 1H), 1.88 (m, 1H), 1.82 (m, 1H), 1.49 (ddd, $J$ = 11.5, 11.5, 11.5 Hz, 1H), 1.44 (s, 3H), 1.32 (s, 3H), 1.29 (m, 1H), 0.88 (s, 18H), 0.06 (s, 12H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 130.9 (d), 129.2 (d), 106.5 (s), 82.0 (d), 81.4 (d), 79.8 (d), 78.5 (d), 71.5 (d), 69.2 (d), 43.8 (t), 32.2 (t), 28.7 (q), 27.7 (t), 26.4 (q), 26.0 (q), 24.6 (t), 18.3 (s), –3.8 (q), –3.9 (q), –4.3 (q), –4.4 (q); MS *m/e* (rel intensity) 512 ($M^+$, 7), 497 (4), 454 (6), 439 (2), 397 (22), 379 (7), 301 (22), 283 (1), 265 (41), 247 (25), 191 (32), 173 (30), 147 (67), 115 (18), 73 (100), 57 (26); HRMS calcd for $C_{27}H_{52}O_5Si_2$ ($M^+$) 512.3353, found 512.3351. **130b (4*R**,8*S** Isomer).** This was prepared in similar manner from **129b** (4*R**,5*S** isomer) (3.2 g, 6.8 mmol) in 98% yield (3.4 g, 6.8 mmol). **130b**: colorless foam; $R_f$ = 0.9 (silica, 10% EtOAc–hexane); IR ($CHCl_3$) $\nu_{max}$ 2925, 2860, 1460, 1355, 1225, 1115, 1090 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 5.94 (ddd, $J$ = 11.0, 10.5, 7.8 Hz, 1H), 5.70 (br d, $J$ = 10.5 Hz,

1H), 3.97 (m, 2H), 3.62 (br d, $J$ = 9.5 Hz, 1H), 3.46 (ddd, $J$ = 9.7, 9.5, 4.5 Hz, 1H), 3.32 (ddd, $J$ = 10.5, 10.5, 4.6 Hz, 1H), 3.03 (ddd, $J$ = 11.5, 10.5, 3.1 Hz, 1H), 2.58 (ddd, $J$ = 13.3, 11.0, 7.7 Hz, 1H), 2.18 (ddd, $J$ = 12.4, 4.6, 4.5 Hz, 1H), 2.05 (m, 2H), 1.92 (m, 1H), 1.76 (m, 1H), 1.46 (ddd, $J$ = 12.4, 10.5, 9.7 Hz, 1H), 1.40 (s, 3H), 1.29 (s, 3H), 1.22 (m, 1H), 0.86 (s, 18H), 0.07, 0.06, 0.04, 0.03 (s, 3H each); $^{13}$C NMR ($CDCl_3$) $\delta$ 133.9 (d), 128.7 (d), 106.3 (s), 83.9 (d), 82.8 (d), 82.4 (d), 80.8 (d), 71.8 (d), 69.8 (d), 44.5 (t), 31.5 (t), 30.6 (t), 30.1 (t), 29.2 (q), 26.4 (q), 26.1 (q), 18.4 (s), 18.3 (s), −4.1 (q), −4.2 (q), −4.3 (q), −4.4 (q).

**(1*S**,4*S**/*R**,8*R**/*S**,10*Z*,12*R**,13*S**,15*R**)-6,6-Dimethyl-5,7,16-trioxatricyclo[10.3.1.0$^{4,8}$]hexadec-10-en-13,15-diol (131a,b).** A mixture of silyl ether **130a** (4*S**,8*R** isomer) (4.8 g, 9.4 mmol), $n$-$Bu_4NF$ (37.6 mL, 378.6 mmol, 1 M in THF), and THF (50 mL) was stirred at 25 °C for 3 h. Concentration and flash chromatography (silica, 40% → 80% EtOAc–hexane) gave diol **131a** (4*S**,8*R** isomer) (2.6 g, 98%). **131a**: noncrystalline solid; $R_f$ = 0.25 (silica, 75% EtOAc in hexane); IR ($CHCl_3$) $\nu_{max}$ 3690, 3600, 3020, 2940, 1380, 1370, 1225, 1200, 1165, 1110 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 5.94 (ddd, $J$ = 11.0, 7.7, 7.7 Hz, 1H), 5.81 (ddd, $J$ = 11.0, 4.0, 1.7 Hz, 1H), 4.07 (m, 2H), 3.69 (dd, $J$ = 9.0, 4.0 Hz, 1H), 3.53 (m, 2H), 3.21 (ddd, $J$ = 8.4, 5.0, 5.0 Hz, 1H), 2.87 (ddd, $J$ = 7.7, 7.2, 1.7 Hz, 1H), 2.40 (ddd, $J$ = 11.5, 4.3, 4.3 Hz, 1H), 2.03 (m, 1H), 1.96 (m, 1H), 1.89 (m, 1H), 1.81 (m, 1H), 1.48 (ddd, $J$ = 11.5, 11.4, 11.4 Hz, 1H), 1.43 (s, 3H), 1.32 (s, 3H), 1.25 (m, 1H); $^{13}$C NMR ($CDCl_3$) $\delta$ 132.4 (d), 128.3 (d), 106.7 (s), 82.2 (d), 81.4 (d), 79.3 (d), 78.4 (d), 71.1 (d), 68.2 (d), 42.0 (t), 32.0 (t), 28.6 (q), 27.6 (t), 26.7 (q), 24.8 (t); MS $m/e$ (rel intensity) 284 ($M^+$, 3), 269 (0.4), 251 (0.9), 226 (94), 208 (48), 191 (22), 173 (15), 118 (6), 100 (12), 93 (21), 83 (47), 57 (51), 43 (100); HRMS calcd for $C_{15}H_{24}O_5$ ($M^+$) 284.1623, found 284.1657. Anal. Calcd for $C_{15}H_{24}O_5$: C, 63.38; H, 8.45. Found: C, 63.18; H, 8.25. **131b** (4*R**,8*S** Isomer): this was prepared in the same was from **130b** (4*R**,8*S** isomer) (3.2 g, 6.3 mmol) in 99% yield (1.77 g, 6.24 mmol). **131b**: oil; $R_f$ = 0.2 (silica, 75% EtOAc in hexane); IR ($CHCl_3$) $\nu_{max}$ 3690, 3400, 2900, 2850, 1355, 1110 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 5.98 (dddd, $J$ = 10.5, 10.4, 7.2, 2.4 Hz, 1H), 5.79 (dd, $J$ = 10.5, 2.3 Hz, 1H), 4.01 (m, 2H), 3.65 (d, $J$ = 10.1 Hz, 1H), 3.50 (ddd, $J$ = 10.1, 10.1, 4.5 Hz, 1H), 3.39 (ddd, $J$ = 10.5, 10.3, 4.5 Hz, 1H), 3.08 (ddd, $J$ = 11.5, 10.3, 3.2 Hz, 1H), 2.65 (ddd, $J$ = 13.2, 10.4, 6.6 Hz, 1H), 2.50 (m, 2H), 2.37 (ddd, $J$ = 12.2, 4.5, 4.5 Hz, 1H), 2.09 (m, 2H),1.93 (br dd, $J$ = 14.7, 8.5 Hz, 1H), 1.79 (br ddd, $J$ = 14.7, 9.0, 9.0 Hz, 1H), 1.46 (ddd, $J$ = 12.2, 10.5, 10.1 Hz, 1H), 1.42 (s, 3H), 1.34 (m, 1H), 1.31 (s, 3H); $^{13}$C NMR ($CDCl_3$) $\delta$ 134.4 (d), 128.2 (d), 106.6 (s), 83.5 (d), 82.6 (d), 81.5 (d), 79.1 (d), 71.0 (d), 69.3 (d), 42.3 (t), 31.4 (t), 30.0 (t), 29.7 (t), 28.7 (q), 26.6 (q). Anal. Calcd for $C_{15}H_{24}O_5$: C, 63.38; H, 8.45. Found: C, 63.26; H, 8.22.

**(1*S**,4*S**/*R**,8*R**/*S**,10*Z*,12*R**,13*S**,15*R**)-13,15-Bis(Allyloxy)-6,6-dimethyl-5,7,16-trioxatricyclo[10.3.1.0$^{4,8}$]hexadec-10-ene (132a,b).** To a stirred mixture of the alcohol **131a** (4*S**,8*R** isomer) (5.2 g, 18.4 mmol) and dry DMF (45 mL) at 0 °C was added NaH (1.44 g, 47.8 mmol, 80% dispersion in mineral oil). After 15 min at 0 °C allyl bromide (7.0 mL, 81.0 mmol) was added, the cooling bath removed, and the reaction mixture stirred for an additional 3 h. The excess NaH was carefully quenched at 0 °C with water (50 mL). Dilution with ether (200 mL), followed by washing with water (100 mL), drying ($MgSO_4$), concentration, and flash chromatography (silica, 10% EtOAc in hexane), furnished the bis-allyl derivative **132a** (4*S**,8*R** isomer) (6.4 g, 98%). **132a**: colorless needles; mp 120–121 °C (ether–hexane); $R_f$ = 0.9 (silica, 10% EtOAc–hexane); IR ($CHCl_3$) $\nu_{max}$ 3020, 2930, 1380, 1225, 1215, 1200, 1110, 930 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 5.89 (m, 3H), 5.81 (ddd, $J$ = 14.0, 3.8, 1.2 Hz, 1H), 5.25 (ddd, $J$ = 17.3, 4.0, 1.2 Hz, 2H), 5.18 (d, $J$ = 10.2 Hz, 2H), 4.10 (m, 4H), 3.95 (m, 2H), 3.75 (dd, $J$ = 9.2, 3.8 Hz, 1H), 3.28 (ddd, $J$ = 9.4, 4.5, 4.5 Hz, 1H), 3.20 (m, 2H), 2.90 (ddd, $J$ = 7.2, 7.0, 7.0 Hz, 1H), 2.58 (ddd, $J$ = 12.0, 4.2, 4.2 Hz, 1H), 1.97 (m, 2H), 1.86 (m, 3H), 1.40 (s, 3H), 1.35 (m, 1H), 1.32 (s, 3H); $^{13}$C NMR ($CDCl_3$) $\delta$ 135.2 (2 × d), 131.1 (d), 129.0 (d), 117.7 (t), 117.5 (t), 166.5 (s), 82.1 (d), 81.4 (d), 78.1 (d), 77.9 (d), 76.8 (d), 70.5 (t), 70.4 (t), 36.0 (t), 32.0 (t), 28.7 (q), 27.9 (t), 26.7 (q), 25.0 (t); MS $m/e$ (rel intensity) 364 ($M^+$, 6), 349 (3), 306 (2), 265 (10), 247 (3), 206 (7), 191 (4), 189 (4), 173 (3), 118 (3), 100 (4), 93 (13), 83 (19), 57 (27), 41 (100); HRMS calcd for ($M^+$) $C_{21}H_{32}O_5$ 364.2249, found 364.2216. **132b** (4*R**,8*S** isomer): this was prepared as described above from **131b** (4*R**,8*S** isomer) (3.5 g, 12.3 mmol) in 98% yield (4.38 g, 12.1 mmol). **132b**: colorless foam; $R_f$ = 0.8 (silica, 10% EtOAc–hexane); IR ($CHCl_3$) $\nu_{max}$ 3400, 3020, 2900, 2850, 1380, 1100 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 5.99 (ddd, $J$ = 10.5, 10.1, 2.5 Hz, 1H), 5.89 (m, 2H), 5.78 (dd, $J$ = 10.5, 2.5 Hz, 1H), 5.28 (dddd, $J$ = 17.2, 1.6, 1.6, 1.6 Hz, 2H), 5.19 (dd, $J$ = 10.4, 1.2 Hz, 2H), 4.13 (dd, $J$ = 12.6, 5.5 Hz, 1H), 4.10 (dd, $J$ = 12.6, 6.4 Hz, 1H), 3.98 (m, 4H), 3.73 (br d, $J$ = 10.2 Hz, 1H), 3.24 (ddd, $J$ = 12.5, 10.2, 4.3 Hz, 1H), 3.13 (ddd, $J$ = 10.0, 9.0, 3.2 Hz, 1H), 3.09 (ddd, $J$ = 10.0, 9.0, 4.5 Hz, 1H), 2.61 (m, 2H), 2.18 (ddd, $J$ = 10.0, 8.4, 3.0 Hz, 1H), 2.06 (dd, $J$ = 12.9, 7.2 Hz, 1H), 1.95 (dd, $J$ = 14.8, 8.4 Hz, 1H), 1.78 (m, 1H), 1.43 (s, 3H), 1.33 (ddd, $J$ = 12.6, 12.5, 10.0 Hz, 1H), 1.31 (s, 3H), 1.29 (m, 1H, H-2); $^{13}$C NMR ($CDCl_3$) $\delta$ 135.2 (2 × d), 133.1 (d), 129.9 9d), 117.7 (d), 117.5 (t), 82.2 (d), 76.8 (2 × d), 76.7 (d), 76.3 (2 × d), 70.7 (t), 70.5 (t), 36.4 (t), 34.1 (t), 31.6 (2 × t), 28.5 (2 × q).

**(1*S**,4*S**,5*R**/*S**,7*Z*,9*R**,10*S**,12*R**)-10,12-Bis(Allyloxy)-13-oxabicyclo[7.3.1]tridec-7-ene-4,5-diol (133a,b).** The acetonide **132a** (4*S**,4*R** isomer) (3.27 g, 9.0 mmol) together with a catalytic amount of CSA in MeOH (125 mL) was stirred at 25 °C for 15 min. Triethylamine (2.0 mL) was then added dropwise at 0 °C, stirred for 5 min, and poured onto a mixture of aqueous saturated $NH_4Cl$ solution (20 mL), water (100 mL), and ether (200 mL). The organic phase was separated, washed with $H_2O$ (2 × 50 mL), and dried ($MgSO_4$). Removal of the solvent followed by flash column chromatography (silica, 20% → 60% EtOAc–hexane) gave diol **133a** (4*S**,5*R** isomer) (2.91 g, 100%). **133a**: colorless plates; mp 123–124 °C (ether–hexane); $R_f$ = 0.4 (silica, 70% EtOAc–hexane); IR ($CHCl_3$) $\nu_{max}$ 3690, 3600, 3020, 2930, 2860, 1340, 1225, 1110, 1080, 940 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 5.89 (m, 4H), 5.28 (dd, $J$ = 17.2, 1.3 Hz, 2H), 5.19 (dd, $J$ = 10.3, 1.3 Hz, 2H), 4.10 (m, 2H), 4.05 (m, 2H), 3.98 (m, 2H), 3.84 (m, 3H), 3.26 (m, 3H), 2.60 (ddd, $J$ = 12.2, 4.2, 4.2 Hz, 1H), 2.46 (m, 1H), 1.36 (ddd, $J$ = 12.2, 10.0, 10.0 Hz, 1H); $^{13}$C NMR ($CDCl_3$) $\delta$ 135.1 (d), 134.9 (d), 129.9 (d), 117.7 (2xt), 80.6 (d), 79.3 (d), 77.3 (d), 75.8 (d), 74.3 (d), 73.2 (d), 71.0 (t), 70.3 (t), 37.5 (t), 29.0 (t), 28.1 (t), 27.9 (t); MS $m/e$ (rel intensity) 324 ($M^+$, 13), 306 (1), 265 (46), 247 (2), 229 (1), 207 (27), 191 (10), 173 (5), 118 (12), 100 (21), 93 (50), 83 (95), 57 (100); HRMS calcd for $C_{18}H_{28}O_5$ ($M^+$) 324.1936, found 324.1927. **133b (4*R**,5*S** Isomer).** This was prepared in the same way from **132b** (4*R**,8*S** isomer) (4.30 g, 11.9 mmol) in 100% yield (3.85 g, 11.9 mmol). **133b**: noncrystalline solid; $R_f$ = 0.4 (silica, 70% EtOAc–hexane); IR ($CHCl_3$) $\nu_{max}$ 3690, 3600, 3400, 2930, 2560, 1090 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 5.91 (m, 3H), 5.80 (dd, $J$ = 10.5, 2.7 Hz, 1H), 5.28 (dddd, $J$ = 17.2, 5.8, 1.6, 1.6 Hz, 2H), 5.18 (ddd, $J$ = 9.1, 1.6, 1.2 Hz, 2H), 4.14 (dddd, $J$ = 11.0, 4.1, 4.1, 1.4, 1.4 Hz, 1H), 4.09 (ddd, $J$ = 12.6, 5.5, 1.3 Hz, 1H), 3.96 (m, 4H), 3.76 (br d, $J$ = 10.7 Hz, 1H), 3.23 (ddd, $J$ = 10.7, 10.7, 4.5 Hz, 1H), 3.15 (ddd, $J$ = 9.0, 9.0, 2.8 Hz, 1H), 3.10 (ddd, $J$ = 10.7, 9.0, 4.5 Hz, 1H), 2.60 (ddd, $J$ = 12.2, 4.5, 4.5 Hz, 1H), 2.50 (ddd, $J$ = 13.0, 9.8, 6.7 Hz, 1H), 2.08 (m, 2H), 1.95 (m, 1H), 1.79 (m, 1H), 1.73 (m, 1H), 1.60 (br s, 1H), 1.32 (ddd, $J$ = 12.2, 10.7, 10.7 Hz, 1H), 1.28 (m, 1H); $^{13}$C NMR ($CDCl_3$) $\delta$ 135.2 (d), 135.1 (d), 133.2 (d), 129.8 (d), 117.7 (t), 117.6 (t), 82.2 (d), 77.7 (d), 77.5 (d), 77.6 (d), 76.5 (d), 76.4 (d), 70.7 (t), 70.5 (t), 36.4 (t), 34.2 (t), 31.6 (t), 28.4 (t). Anal. Calcd for $C_{18}H_{28}O_5$: C, 66.67; H, 8.64. Found: C, 67.00; H, 8.81.

**(1*S**,4*S**/*R**,5*R**/*S**,7*Z*,9*R**,10*S**,12*R**)-10,12-Bis[[3′-(tributylstannyl)propenyl]oxy]-13-oxabicyclo[7.3.1]tridec-7-ene-4,5-diol (134a,b).** $s$-BuLi (30.4 mL, 39.6 mmol, 1.3 M in cyclohexane) was added under argon atmosphere at −78 °C to a solution of **133a** (4*S**,5*R** isomer) (2.9 g, 9.0 mmol) in dry THF (90 mL). To the resulting solution was added $n$-$Bu_3SnCl$ (5.86 mL, 7.03 g, 21.6 mmol) at −78 °C over 10 min. The resulting mixture was maintained at −78 °C for 40 min, aqueous $NH_4Cl$ (50 mL) was then added, and the resulting aqueous suspension was saturated with NaCl and extracted with ether (2 × 100 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated, and the residue was purified by flash chromatography (silica, 50% EtOAc–hexane) to give **134a** (4*S**,5*R** isomer) (6.41 g, 79%). **134a**: colorless oil; $R_f$ = 0.5 (silica, 40% EtOAc–hexane); IR ($CHCl_3$) $\nu_{max}$ 3480, 2906, 2850, 1640, 1620, 1460, 1370, 1250, 1095, 955 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) (selected signals) $\delta$ 5.93 (m, 1H), 5.85 (m, 1H), 5.81 (d, $J$ = 5.8 Hz, 1H), 5.78 (d, $J$ = 5.9 Hz, 1H), 4.57 (m, 2H), 3.88 (m, 3H), 3.50 (m, 1H), 3.44 (m, 1H), 3.34 (br s, 1H), 2.56 (m, 1H), 2.48 (m, 1H), 2.04 (m, 1H), 1.86

(m, 2H), 1.55 (m, 4H); $^{13}$C NMR ($CDCl_3$) δ 140.2 (d), 140.1 (d), 129.4 (2 × d), 107.6 (2 × d), 77.7 (d), 77.6 (d), 77.4 (d), 77.1 (d), 70.0 (d), 37.8 (t), 33.2 (t), 29.5 (t), 28.4 (t), 28.2 (t), 27.8 (t), 27.2 (t), 17.9 (t), 14.2 (q), 14.0 (q), 9.8 (t), 6.3 (t). **134b (4*R**,5*S** Isomer).** This was prepared as described above from **133b** (4*R**,5*S** isomer) (3.8 g, 11.7 mmol) in 80% yield (8.47 g, 9.4 mmol), oil, $R_f$ = 0.5 (silica, 40% EtOAc–hexane), which was used for the next reaction without further purification.

**(2*S**,3*R**,5a*S**,13a*R**,12a*S**,6a*R**,7*Z*,10*S**,11*R**)-2,11-Divinyl-2,3,4,5,5a,6a,9,10,11,12a,13,13a-dodecahydro-1,6,12-trioxacyclohepta[4,5]benzo[1,2]cyclooctene-3,10-diol (135).** To a stirred solution of the bis(allylstannane) **134a** (4*S**,5*R** isomer) (6.40 g, 7.1 mmol) in dry $CH_2Cl_2$ (70 mL) at 0 °C was added *n*-$Bu_4NIO_4$ (6.6 g, 14.2 mmol). The cooling bath was removed, and the reaction mixture was stirred at 25 °C. TLC indicated the reaction was complete after 3.5 h. The homogeneous solution was recooled to −78 °C and treated dropwise with $BF_3$·$OEt_2$ (3.4 mL, 28.4 mmol), and the resulting mixture was stirred vigorously for 5 min. The reaction was slowly warmed to −10 °C over a 5-min period and then poured onto a stirred mixture of $CH_2Cl_2$ (100 mL) and saturated aqueous $NaHCO_3$ (50 mL). After separation, the organic portion was washed with $H_2O$ (2 × 50 mL), dried ($MgSO_4$), and concentrated, and the residue was purified by flash column chromatography (silica, 30% EtOAc–hexane) to give the cyclized compound **135** (1.5 g, 63%). Compound **135** was prepared in a similar manner from **134b** (4*R**,5*S** isomer) (8.4 g, 9.8 mmol) in 63% yield (1.89 g, 5.88 mmol). **135**: amorphous solid; $R_f$ = 0.30 (silica, 40% EtOAc–hexane); $^1$H NMR (400 MHz, $CDCl_3$) δ 5.93 (ddd, *J* = 11.6, 10.5, 5.6 Hz, 1H), 5.88 (ddd, *J* = 11.6, 10.5, 5.5 Hz, 1H), 5.76 (m, 2H), 5.33 (d, *J* = 10.5 Hz, 1H), 5.29 (d, *J* = 10.5 Hz, 1H), 5.19 (d, *J* = 11.6 Hz, 2H), 3.94 (br d, *J* = 9.1 Hz, 1H), 3.78 (m, 3H), 3.72 (m, 1H), 3.30 (ddd, *J* = 14.0, 9.1, 5.0 Hz, 1H), 3.26 (ddd, *J* = 13.5, 9.5, 4.4 Hz, 1H), 3.10 (m, 1H), 2.74 (ddd, *J* = 14.0, 9.4, 2.5 Hz, 1H), 2.43 (ddd, *J* = 11.9, 5.0, 4.4 Hz, 1H), 2.34 (br d, *J* = 14.0 Hz, 1H), 1.92 (m, 4H), 1.64 (ddd, *J* = 14.0, 13.5, 11.9 Hz, 1H).

**(2*S**,3*R**,5a*S**,13a*R**,12a*S**,6a*R**,7*Z*,10*S**,11*R**)-10-[(4-Bromobenzoyl)oxy]-2,11-divinyl-3-hydroxy-2,3,4,5,5a,6a,9,10,11,12a,13,13a-dodecahydro-1,6,12-trioxacyclohepta[4,5]benzo[1,2]cyclooctene (136).** To a stirring mixture of the diol **135** (1.0 g, 3.1 mmol) in dry $CH_2Cl_2$ (30 mL) and DMAP (4.02 g, 9.3 mmol) at 0 °C was added 4-bromobenzoyl chloride (1.44 g, 6.2 mmol). After 3 h at 25 °C the reaction mixture was diluted with ether (100 mL) and washed with water (2 × 50 mL). Drying ($MgSO_4$) and concentration, followed by flash column chromatography (silica, 30% EtOAc–hexane), gave **136** (1.2 g, 77%). **136**: colorless foam; $R_f$ = 0.50 (silica, 30% EtOAc–hexane); IR ($CHCl_3$) $\nu_{max}$ 3650, 3020, 2925, 2855, 1720, 1465, 1270, 1115, 1085, 1010, 935 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.85, 7.58 (d, *J* = 6.7 Hz, 2H each), 5.90 (ddd, *J* = 17.2, 10.6, 5.6 Hz, 1H), 5.83 (br dd, *J* = 11.0, 5.3 Hz, 1H), 5.80 (ddd, *J* = 16.0, 10.6, 5.4 Hz, 1H), 5.71 (br ddd, *J* = 11.0, 10.6, 6.6 Hz, 1H), 5.33 (d, *J* = 17.2 Hz, 1H), 5.27 (ddd, *J* = 16.0, 1.6, 1.6 Hz, 1H), 5.20 (d, *J* = 10.6 Hz, 1H), 5.11 (ddd, *J* = 9.7, 3.5, 3.1 Hz, 1H), 5.09 (ddd, *J* = 10.6, 1.6, 1.6 Hz, 1H), 4.13 (dd, *J* = 9.7, 5.4 Hz, 1H), 3.99 (dd, *J* = 7.2, 5.3 Hz, 1H), 3.80 (m, 2H), 3.33 (m, 2H), 3.12 (m, 1H), 2.84 (ddd, *J* = 14.0, 10.6, 3.5 Hz, 1H), 2.50 (ddd, *J* = 14.0, 6.6, 3.1 Hz, 1H), 2.48 (ddd, *J* = 11.8, 4.7, 4.7 Hz, 1H), 1.92 (m, 4H), 1.70 (ddd, *J* = 12.0, 11.8, 11.8 Hz, 1H); MS *m*/*e* (rel intensity) 449, 447 ($M^+$ − $C_3H_5O$, 2), 367, 365 (4), 341, 339 (2), 185 (100), 157, 155 (20), 111, 109 (13), 104 (25), 97 (22); HRMS calcd for $C_{22}H_{24}{}^{81}BrO_5$ (M − $C_3H_5O$)$^+$ 449.0786, found 449.0786; calcd for $C_{22}H_{24}{}^{79}BrO_5$ (M − $C_3H_5O$)$^+$ 447.0807, found 447.0797. Anal. Calcd for $C_{25}H_{29}BrO_6$: C, 59.41; H, 5.74. Found: C, 59.72; H, 6.00.

**(2*S**,3*R**,5a*S**,13a*R**,12a*S**,6a*R**,7*Z*,10*S**,11*R**)-3,10-Bis[(4-bromobenzoyl)oxy]-2,11-divinyl-2,3,4,5,5a,6a,9,10,11,12a,13,13a-dodecahydro-1,6,12-trioxacyclohepta[4,5]benzo[1,2]cyclooctene (137).** To a stirring mixture of the diol **135** (1.54 g, 4.77 mmol) in dry $CH_2Cl_2$ (45 mL) and DMAP (8.2 g, 19.0 mmol) at 0 °C was added 4-bromobenzoyl chloride (4.58 g, 20.9 mmol). After 30 h at 25 °C the reaction mixture was diluted with ether (200 mL) and washed with water (2 × 50 mL). Drying ($MgSO_4$) and concentration gave the bis(4-bromobenzoate) **137** which was further purified by flash column chromatography (silica, 10% EtOAc–hexane) (2.7 g, 85%). **137**: amorphous solid; $R_f$ = 0.35 (silica, 15% EtOAc–hexane); IR ($CHCl_3$) $\nu_{max}$ 3015, 2955, 2930, 2915, 2845, 1720, 1485, 1445, 1400, 1360, 1340, 1270, 1230, 1100, 1070 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.90, 7.85, 7.61, 7.58 (d, *J* = 8.5 Hz, 2H each), 5.89 (ddd, *J* = 17.2, 10.6, 5.3 Hz, 1H), 5.84 (br dd, *J* = 11.6, 11.6 Hz, 1H), 5.80 (ddd, *J* = 16.8, 10.4, 5.0 Hz, 1H), 5.71 (br dd, *J* = 11.6, 9.4 Hz, 1H), 5.36 (br d, *J* = 17.2 Hz, 1H), 5.28 (br d, *J* = 16.8 Hz, 1H), 5.23 (m, 1H), 5.17 (br d, *J* = 10.6 Hz, 1H), 5.12 (ddd, *J* = 10.0, 4.0, 3.5 Hz, 1H), 5.10 (d, *J* = 10.4 Hz, 1H), 4.21 (dd, *J* = 5.3, 5.3 Hz, 1H), 4.14 (dd, *J* = 10.0, 5.0 Hz, 1H), 4.02 (dd, *J* = 11.6, 9.2 Hz, 1H), 3.41 (ddd, *J* = 13.5, 9.2, 4.4 Hz, 1H), 3.32 (ddd, *J* = 13.2, 9.2, 4.6 Hz, 1H), 3.19 (ddd, *J* = 9.6, 9.2, 4.4 Hz, 1H), 2.85 (ddd, *J* = 13.6, 9.4, 3.5 Hz, 1H), 2.53 (ddd, *J* = 12.0, 4.6, 4.4 Hz, 1H), 2.50 (br d, *J* = 13.6 Hz, 1H), 2.00 (m, 2H), 1.90 (m, 1H), 1.88 (m, 1H), 1.73 (ddd, *J* = 13.5, 13.2, 12.0 Hz, 1H); $^{13}$C NMR ($CDCl_3$) (selected signals) δ 136.6 (d), 136.4 (d), 135.5 (d), 125.7 (d), 116.5 (t), 116.4 (t), 83.5 (d), 81.4 (d), 80.5 (d), 80.1 (d), 79.7 (d), 79.3 (d), 77.6 (d), 76.8 (d), 39.5 (t), 30.3 (t), 27.4 (t), 24.8 (t); MS *m*/*e* (rel intensity) 690, 688, 686 ($M^+$, 0.5, 1.0, 0.5), 488, 486 (4.6, 4.6), 449, 447 (17, 17), 367, 365 (58, 58), 311, 309 (5, 5), 247 (13), 202 (8), 190 (2), 185 (100), 184 (35), 183 (100), 177 (4), 165 (12), 161 (2), 157 (36), 155 (36), 147 (12), 137 (10), 133 (8), 122 (17), 121 (20), 111 (11), 104 (79), 97 (26), 95 (25, 93 (27); HRMS calcd for $C_{25}H_{27}{}^{81}BrO_5$ (M − BrBzOH)$^+$ 488.1021, found 488.1021; calcd for $C_{25}H_{27}{}^{79}BrO_5$ 486.1042, found 486.1048. Anal. Calcd for $C_{32}H_{32}Br_2O_7$: C, 55.81; H, 4.65. Found: C, 55.73; H, 4.59.

**(2*S**,3*R**,5a*S**,13a*R**,12a*S**,6a*R**,7*Z*,10*S**,11*R**)-3-[(4-Bromobenzoyl)oxy]-2,11-divinyl-10-hydroxy-2,3,4,5,5a,6a,9,10,-11,12a,13,13a-dodecahydro-1,6,12-trioxacyclohepta[4,5]benzo-[1,2]cyclooctene (138).** A mixture of **137** (1.38 g, 2.0 mmol) and $K_2CO_3$ (276 mg, 2.0 mmol) in MeOH (25 mL) was stirred at 25 °C for 1.5 h. Dilution with ether (50 mL) followed by filtration through a Celite pad and concentration gave a residue which was diluted with ether (50 mL), washed with water (2 × 50 mL), 2% HCl aqueous solution (2 × 50 mL), and water (50 mL), and dried ($MgSO_4$). Concentration followed by flash column chromatography (silica, 30% EtOAc–hexane) yielded the mono *p*-bromobenzoate **138** (0.97 g, 96%). **138**: noncrystalline solid; $R_f$ = 0.65 (silica, 30% EtOAc–hexane); IR ($CHCl_3$) $\nu_{max}$ 3685, 3020, 2925, 2855, 1720, 1640, 1485, 1465, 1400, 1380, 1345, 1265, 1230, 1115, 1095, 1010 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.90, 7.61 (d, *J* = 8.4 Hz, 2H each), 5.95 (ddd, *J* = 16.0, 10.6, 5.6 Hz, 1H), 5.83 (ddd, *J* = 17.0, 10.3, 5.2 Hz, 1H), 5.80 (m, 2H), 5.36 (d, *J* = 17.0 Hz, 1H), 5.30 (d, *J* = 16.0 Hz, 1H), 5.22 (m, 1H), 5.19 (d, *J* = 10.6 Hz, 1H), 5.16 (d, *J* = 10.6 Hz, 1H), 4.19 (dd, *J* = 5.2, 4.7 Hz, 1H), 3.97 (dd, *J* = 9.0, 3.5 Hz, 1H), 3.37 (ddd, *J* = 12.3, 11.4, 4.8 Hz, 1H), 3.27 (ddd, *J* = 13.6, 9.0, 4.8 Hz, 1H), 3.16 (ddd, *J* = 13.6, 11.4, 4.8 Hz, 1H), 2.75 (m, 1H), 2.46 (ddd, *J* = 12.3, 4.8, 4.8 Hz, 1H), 2.37 (m, 1H), 2.09–1.84 (m, 4H), 165 (ddd, *J* = 13.6, 12.3, 12.3 Hz, 1H); MS *m*/*e* (rel intensity) 506, 504 ($M^+$, 0.4), 449, 447 (2), 304 (2), 247 (6), 185, 183 (100), 177 (2), 165 (4), 157, 155 (20), 135, 133 (4), 111 (13), 104 (14); HRMS calcd for $C_{22}H_{24}{}^{81}BrO_5$ (M − $C_3H_5O$)$^+$ 449.0786, found 449.0778; calcd for $C_{22}H_{24}{}^{79}BrO_5$ (M − $C_3H_5O$)$^+$ 447.0807, found 447.0803. Anal. Calcd for $C_{25}H_{29}BrO_6$: C, 59.41; H, 5.74. Found: C, 59.32; H, 5.96.

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**Supplementary Material Available:** Experimental procedures and characterization data for **59** *n* = 0–3, **61–84**, and **i–iv**, $^1$H NMR assignments of (*R*)- and (*S*)-MTPA esters of (−)-**28** and (+)-**29**, and $^{13}$C NMR spectra of new compounds (173 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.