Synthetic Studies on the Polyene Macrolide Antibiotics. Development of *syn*- and *anti*-1,3-Diol Subunits and Assembly of the Polyacetate Region of Amphotericin B

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The synthesis of *syn*- and *anti*-1,3-diol subunits from thiol ester oxazoline **4** has been described. The key features of these synthetic sequences include the stereodivergent allylation of an asymmetric β-amino aldehyde (**7**) and the stereospecific transformation of a vicinal amino alcohol to an epoxide. The resultant diasteromeric silyl-protected epoxy alcohols (**10s** and **10a**) serve as convenient precursors to the isomeric diol aldehyde derivatives **13**, **13-ent**, and **16**. One of these fragments, compound **13**, has been exploited in a highly convergent synthesis of the C1–C13 polyacetate segment of amphotericin B.

I. Introduction

The polyene macrolide antibiotics have received considerable attention as a result of their selective cytotoxic properties.[1] Several of these compounds, notably amphotericin B and nystatin, have gained clinical prominence for their potent antifungal activities.[2] Unfortunately, their value as drugs for this purpose has been attenuated by accompanying toxicity, especially in the treatment of serious human mycoses. This has spurred efforts to define the chemical basis of the mechanism by which selective fungal toxicity is expressed by some members of this family of compounds.[3] With evidence to date indicating that aggregates of polyene macrolide–sterol complexes in cell membranes are the basis of this toxicity,[3,4] attention has been focused toward understanding the structural features contributing to selective polyene macrolide–sterol complexation.[5]

As indicated by the representative examples (Figure 1), the structures of these compounds are characterized by large macrolactone rings bearing clearly defined hydrophilic polyol and hydrophobic olefinic regions.[1] To date, the stereostructures of only a handful of the over 200 members of this class of compounds have been established. Plagued by problems of noncrystallinity, only two structures, amphotericin B (**1**)[6] and roxaticin (**2**),[7] have succumbed to single crystal X-ray diffraction.

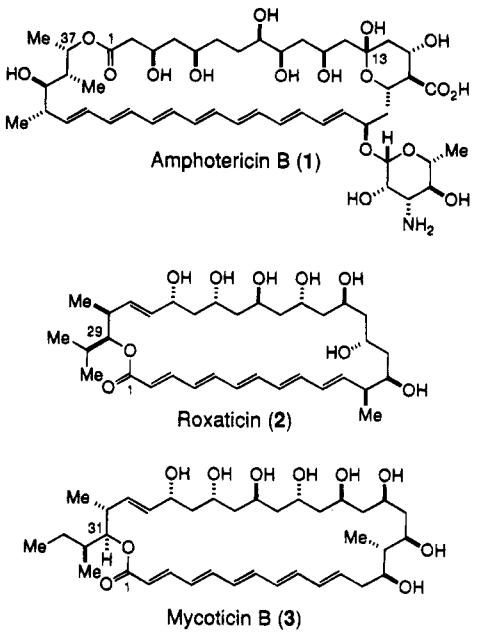

Figure 1.

An important alternative approach to structure determination has emerged which combines the powerful tools of NMR spectroscopy and chemical synthesis. These methods have been instrumental in establishing the structures of nystatin A_1,[8] mycoticins A and B (**3**),[9] pimaricin,[10] pentamycin,[11] candidin,[12] vacidin,[13] and roflamycoin,[14] as well as the partial structure of lienomycin.[15]

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As a consequence of the interest in the structural and biological features of the polyene macrolide antibiotics, they have become appealing targets for synthetic studies. A conspicuous synthetic challenge is found in the 1,3-polyol regions that are ubiquitous to this family of compounds.[16] Herein, we report on our efforts to develop synthons for *syn*- and *anti*-1,3-diols from a readily available amino acid and the application of these results to the synthesis of the C1–C13 polyacetate region of amphotericin B (**1**).

II. Background

Studies addressing the synthesis of the polyene macrolide antibiotics have documented remarkable successes in recent years. The total syntheses of amphotericin B (**1**),[17] mycoticin A,[18] and both the natural (**2**)[19] and unnatural enantiomers[20] of roxaticin, as well as the aglycon of pimaricin,[21] have been reported. A key structural issue effectively confronted by each of these syntheses is the prominent occurrence of asymmetric 1,3-diols on a conformationally flexible carbon framework. The resultant synthetic technology has found important applications in studies to elucidate the structures of other members of this class of compounds. In this vein, the stereocontrolled synthesis of the polyol fragments of nystatin A_1,[12ac,22] pentamycin,[11,23] and roflamycoin[14] have been described.

These richly asymmetric polyoxygenated structures, along with the questions still at large regarding the structural details of their biological action, continue to offer an important challenge to synthetic chemistry.[24] In an effort to develop an efficient and general solution to these structures, we have examined a strategy that seeks to apply *a single key intermediate to the establishment of all the asymmetric centers* of the dominant 1,3-oxygenation pattern on the macrocyclic skeleton. Consistent with this goal, we have previously reported on the

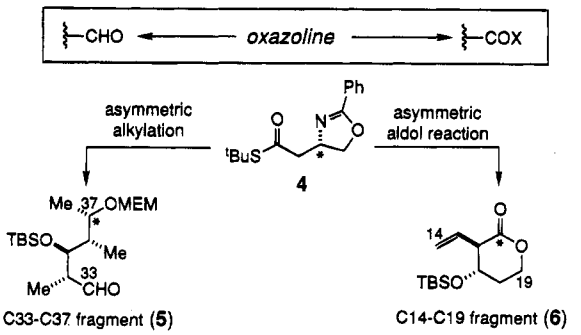
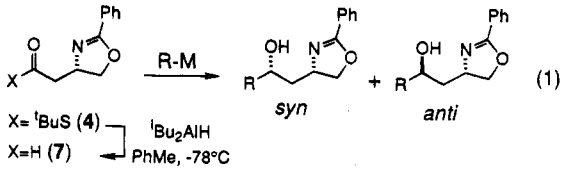


Figure 2.

exploitation of thiol ester oxazoline **4**, which is readily available from L-aspartic acid, for the synthesis of the C14–C19 (**6**)[25] and C33–C37 (**5**)[26] regions of amphotericin B (Figure 2). The successful synthesis of these fragments by this strategy required the exercise of effective substrate control in the key intermediate **4** and the efficient unmasking of the chiral oxazoline as an aldehyde (for **5**) and a carboxylic acid derivative (for **6**).[27] In this way, the asymmetric amine center (starred position in **4**) acts as a *pro-carbonyl* center that both directs the formation of new stereocenters in polypropionate (**5**) and branched propionate skeletons (**6**) and results in the establishment of the necessary 1,3-oxygenation pattern (see starred positions in **5** and **6**, Figure 2).[28]

Our attention was next turned to the application of this key intermediate **4** to the assembly of the *all-syn*-polyacetate segment of amphotericin B. Unlike fragments **5** and **6**, which feature contiguous stereocenters, this fragment demands the proper installation of 1,3-stereorelationships. It was envisioned that addition reactions on the easily available aldehyde **7** could be controlled for this purpose (eq 1). In order to fully exploit



this stereoselective addition, it became an additional objective of these studies to develop an asymmetric N → O operation that retains the stereochemical information resident in the oxazoline ring. We have previously reported in preliminary form our successful realization of some of these goals through stereoselective allylation reactions and the conversion of the asymmetric oxazoline into an asymmetric epoxide with complete inversion of the asymmetric center.[29] The complete details of these

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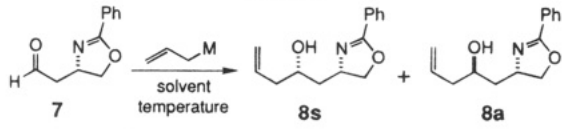
Table 1



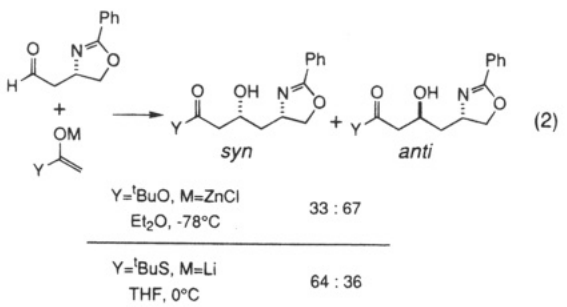
entry	M	solvent temp, °C	**8s:8a**[a] (% yield[b])
1	MgBr	ether/−78	59:41
2	ZnCl/LiCl	ether/−78	70:30
3	ZnCl/MgBr	ether/−78	76:24
4	ZnCl/MgBr	THF/−78	84:16 (82)
5	ZnCl/MgBr	THF/0	92:8
6	Zn(allyl)/LiCl	THF/0	98:2 (70)
7	$AlMe_3MgBr$	ether/−78	44:56
8	$AlMe_3Li$	ether/−78	16:84 (78)
9	$SnBu_3/BF_3$	CH_2Cl_2/−78	80:20 (70)

[a] Determined by ^1H NMR. [b] Isolated yield after chromatographic purification.

studies and their exploitation for the assembly of the C1−C13 fragment of amphotericin B will be described in the following section.

III. Results and Discussion

A. 1,3-Diol Synthon Studies. In an effort to secure a general solution to the polyacetate problem, the elaboration of key intermediate **4** into both *syn*- and *anti*-diols was an important objective. It was anticipated that the appropriate 1,3-stereochemical relationship could be realized through stereocontrolled addition reactions to aldehyde **7**, which is readily available through $^iBu_2AlH$ reduction in toluene of the key intermediate **4** (95%, see eq 1).[25] In an attempt to directly install the appropriate oxygenation pattern, substrate control using achiral enolates was examined first.[30] Perhaps not surprisingly, a study of various acetate enolate species resulted in disappointingly low levels of stereoselection as the course of the reaction could be influenced to favor either the *syn* or *anti* isomer by ratios of 64:36 and 67:33, respectively (eq 2).[31]



Our search for higher levels of substrate control led to an examination of the addition reactions of various allyl anions with the results described in Table 1. While the addition of simple allylmagnesium bromide in diethyl ether proceeded in virtually stereorandom fashion (entry 1), the corresponding allylzinc anion resulted in pronounced *syn* selectivity (entries 2−6). Further investigation revealed that stereoselection was improved by using

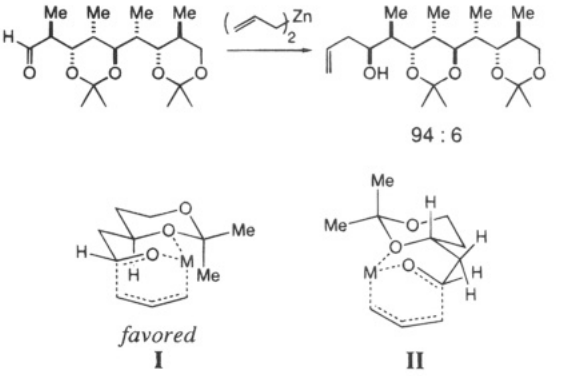
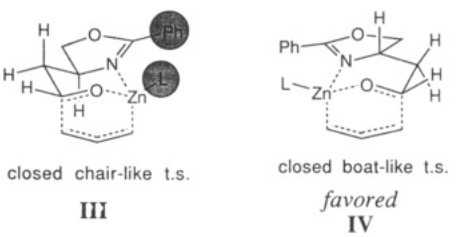


Figure 3.

the allylzinc anion generated from $ZnCl_2$ exchange with allylmagnesium bromide rather than allyllithium (entries 2 and 3), employing THF rather than Et_2O (entries 3 and 4), and carrying out the reaction at slightly elevated temperatures (entries 4 and 5). Substrate control was ultimately optimized for the *syn* isomer through the use of diallylzinc in THF at 0 °C (entry 6). It is noteworthy that Kishi previously observed that diallylzinc addition to β-alkoxy aldehydes favors the formation of the *anti* isomer and that the degree of selectivity was dependent upon the purity of the zinc reagent (Figure 3).[32] This selectivity was explained as resulting from a chelated/closed transition state that favored the *trans*-decalin-like geometry **I** as opposed to the corresponding boat structure **II**. It seems likely that the allylzinc additions to the β-imino aldehyde **7** also favor a chelated closed transition state. However, in this instance the preferred *syn* isomer is correctly predicted by the boatlike geometry **IV**. We speculate that the sp^2 nature of the nitrogen center makes this geometry more energetically accessible relative to the chair form **III**. In addition, a significant $A^{1,3}$-like interaction appears to exist between the phenyl ring and the ligand associated with the zinc center. This interaction is relieved in the boat geometry.



Relevant to the objectives of this study, it was found that allyltrimethylaluminate reagents favored formation of the *anti*-isomer (entries 7 and 8). As indicated, the degree of selectivity was found to be very sensitive to the nature of the counterion in these reagents. This appears consistent with the intervention of an *open* chair-like transition state such as **V**.[33] The counterion selectivity may be explained by a kinetic or thermodynamic preference for a lithium chelate relative to a magnesium halide chelate in this geometry.

Finally, it is of note that respectable levels of *syn* selection were observed in the $BF_3{\cdot}OEt_2$-mediated addi-

(30) These results are taken from the dissertation of J. Michael Williams, University of Virginia, 1986.

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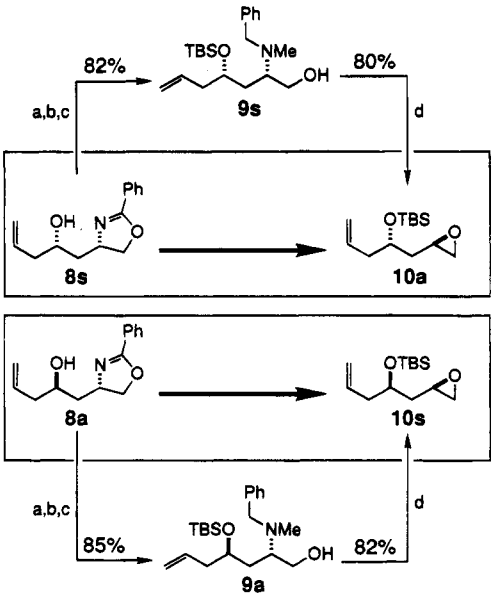
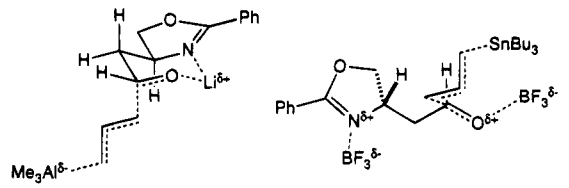
(33) This facial selectivity is predicted by attack that leads to the energetically favored chair-like product chelate, rather the twist-boat chelate.

Scheme 1[a]



[a] Reagents: (a) ^{t}BuMe$_2$SiOTf, Et$_3$N, 0 °C; (b) DIBAL, PhCH$_3$, 0 °C; (c) HCHO, PhH, Dean–Stark (−H$_2$O); DIBAL, PhCH$_3$, −78 °C; (d) CHCl$_3$, 50% NaOH(aq), Bu$_4$NI(cat.).

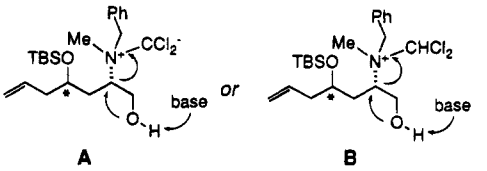
tions of tri-*n*-butylallylstannane (entry 9). This result is consistent with previous suggestions that an extended transition state of the type **VI** is in operation in this instance.[34]



V **VI**

This divergent stereocontrol (see entries 6 and 8) coupled with straightforward separation of these diastereomers by simple flash chromatography results in practical access to the isomerically pure homoallyl alcohols **8s** and **8a**.[35] Our attention was then turned to the stereoselective replacement of nitrogen by oxygen to result in the desired 1,3-oxygenation pattern. We had previously reported such an interconversion using sodium nitroprusside under mildly basic aqueous conditions.[36] Unfortunately, this method proved to be quite substrate dependent and was ill-suited to our present needs. In the course of our investigations, we were pleased to find that the methodology reported by Castedo and co-workers for the conversion of vicinal amino alcohols to epoxides provided an excellent solution to this problem.[37] In the case at hand, the diastereomeric homoallylic alcohols **8s** and **8a** were routinely protected as their *tert*-butyldimethylsilyl ethers at which time the oxazoline may be reductively cleaved to a benzylamino alcohol for subsequent reductive methylation to afford tertiary amino alcohols **9s** and **9a** in 82% and 85% yield, respectively (Scheme 1). Exposure of these compounds to dichlorocarbene generated under the conditions described by Castedo and co-workers smoothly yielded the desired epoxy ethers **10a** and **10s** with complete stereochemical control (in 80% and 82% yields, respectively).[38]

This remarkably effective epoxide-forming reaction apparently proceeds via intramolecular substitution with clean inversion either on the initially formed ylide adduct **A** or through the protonated tetraalkylammonium intermediate **B**. A noteworthy feature of this N → O exchange reaction is its selectivity. Potential competitive side reactions, including dichlorocarbene insertion into the benzylic C–H bonds or the carbon–carbon double bond, were not observed under conditions leading to epoxide formation.[39]



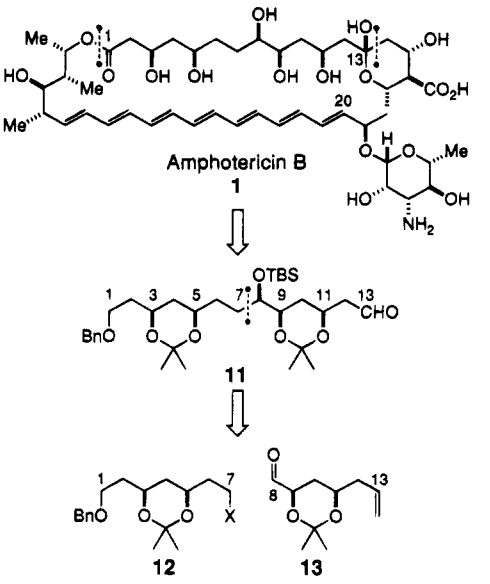


Figure 4.

B. Synthesis of the C1–C13 Fragment of Amphotericin B. Having access to chiral 1,3-diol synthons **10a** and **10s** from a common precursor, we turned our attention to their exploitation in the synthesis of amphotericin B. In particular, the C1–C13 fragment of amphotericin B poses the synthetic challenges attending polyacetate-derived carbon skeletons, a problem seemingly well served by these epoxy ethers. We felt that the C1–C13 polyacetate region of amphotericin B (**1**) was well-represented by the protected polyhydroxy aldehyde **11** for eventual incorporation into the intact macrolide structure (Figure 4). Further simplification of the synthetic objective was realized by dictating the assembly of the carbon framework by formation of the C7–C8 carbon bond. As a result, a convergent synthesis of the

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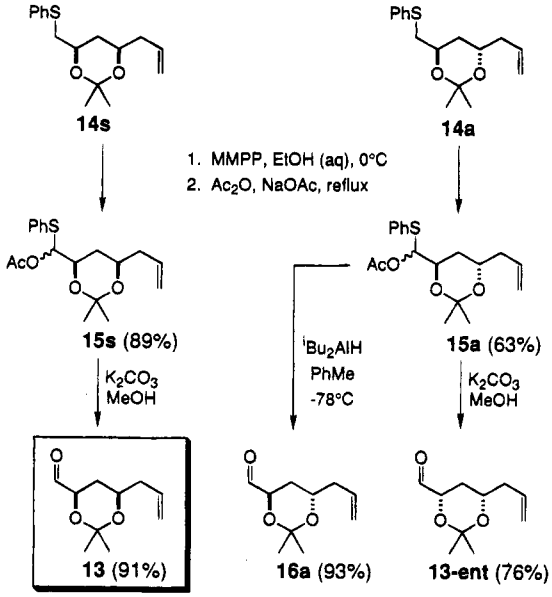
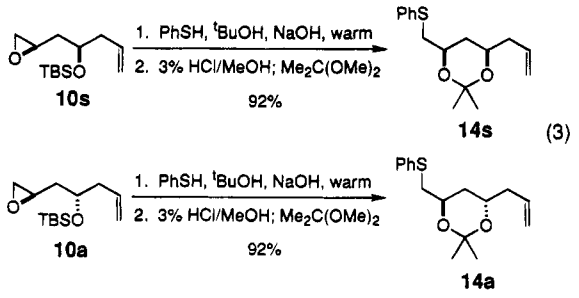
(39) Kirmse, W. *Carbene Chemistry*; Academic Press: New York, 1971.

Scheme 2



polyacetate region was envisioned from *syn*-1,3-diol subunits **12** and **13**, both of which appeared available from the *syn*-epoxy ether **10s**.

Guided by this plan, we examined the ring-opening reactions of epoxides **10s** and **10a** that would lead to asymmetric fragments suitable for use in synthesis of complex polyols. In first considering aldehyde **13**, it becomes necessary to open the *syn*-epoxide **10s** in a manner consistent with installation of an aldehyde at the C8 position. It was felt that the protocols developed by Masamune and Sharpless for their monosaccharide syntheses would serve this purpose well.[40] In the event, epoxides **10s** and **10a** were readily opened in the presence of PhSNa to provide the corresponding isomeric diols for subsequent protection as acetonides **14s** and **14a** in 92% overall yield (eq 3).



The requisite aldehydes were acquired through application of Pummerer methodology as described in Scheme 2.[40] Treatment of the isomeric acetonides with magnesium monoperoxyphthalate (MMPP) afforded the expected sulfoxides which smoothly underwent the Pummerer rearrangement in the presence of Ac_2O and NaOAc to yield diastereomeric mixtures of the *syn*- (**15s**) and *anti*-acetoxy sulfides (**15a**) in 89% and 63%, respectively. Simple hydrolysis of **15s** unmasks the desired aldehyde to give required intermediate **13** in excellent overall yield from the epoxide **10s**.

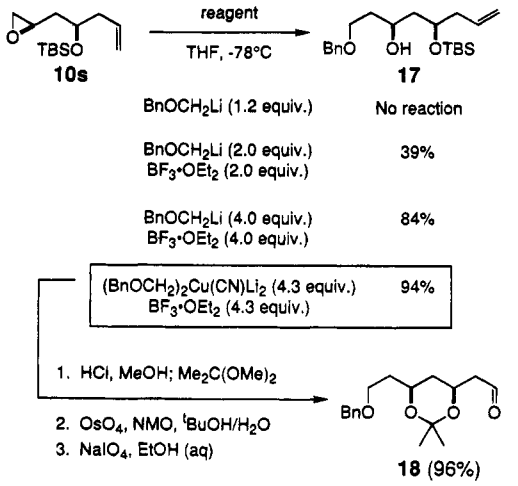


Figure 5.

Other polyol stereochemistries are served by the *anti*-acetonide **15a**. The *anti*-diol aldehyde **16a** is cleanly produced by reductive cleavage of the mixed acetal.[40] Alternatively, exposure to basic conditions leads to acetate hydrolysis and epimerization of the resultant aldehyde to afford the *syn* compound **13-ent** (the enantiomer of **13**).[40] In this fashion, three of the four possible stereoisomers of this useful 1,3-diol building block have been effectively prepared from readily available L-aspartic acid.

Having the C8–C13 fragment in hand, the realization of the C1–C7 unit was pursued. Toward this end, ring opening of epoxide **10s** was examined with α-oxygenated carbon nucleophiles to install C1 of the macrocycle. This conceptually attractive approach to the construction of 1,3-diols has found only limited use to date.[41] In practice, this reaction was found to be exquisitely sensitive to the reaction conditions (Figure 5). [(Benzyloxy)methyl]-lithium, prepared through tin → lithium exchange of the tri-*n*-butylstannane precursor, was an ineffective nucleophile in the absence of $BF_3{\cdot}OEt_2$ catalysis. However, good yields of the desired product **17** could be realized through the use of an excess of both of these reagents. Further study revealed that excellent and reproducible yields (94%) of **17** were obtainable through exposure of epoxide **10** to an excess of the CuCN-derived higher order cuprate in the presence of equimolar amounts of $BF_3{\cdot}OEt_2$. Straightforward protection of the resultant diol and oxidative cleavage of the double bond affords an aldehyde **18** poised for completion of the assembly of the polyacetate fragment **11**.

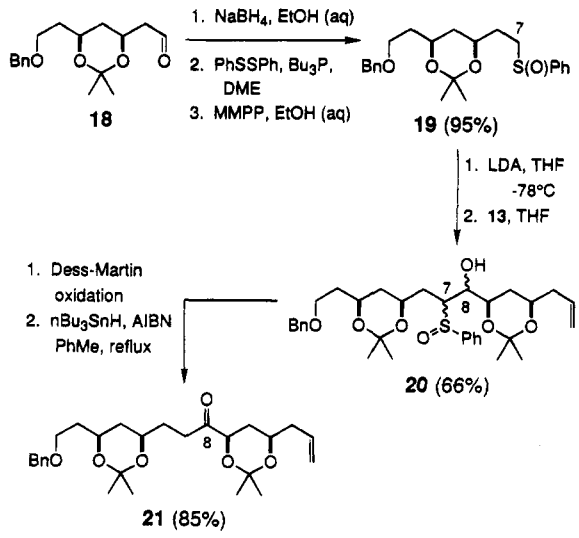
Several strategies were considered for the formation of the C7–C8 bond. Among the most expedient was the conversion of the aldehyde **18** to its corresponding dithiane for subsequent deprotonation and addition to aldehyde **13**.[42] Unfortunately, the polyfunctional nature of **18** frustrated our attempts in this regard, complicating the formation of the dithiane[43] and, more importantly, proving to be a poor carbanion precursor for the addition reaction.[44] As a result, other bond-forming strategies were pursued. A significant improvement was found in

(40) (a) Ko, S. Y.; Lee, A. W. M.; Masamune, S.; Reed, L. A., III, Sharpless, K. B.; Walker, F. J. *Science* **1983**, *220*, 949–951. (b) Katsuki, T.; Lee, A. W. M.; Ma, P.; Martin, V. S.; Masamune, S.; Sharpless, K. B.; Tuddenham, D.; Walker, F. J. *J. Org. Chem.* **1982**, *47*, 1373–1378. (c) Lee, A. W. M.; Martin, V. S.; Masamune, S.; Sharpless, K. B.; Walker, F. J. *J. Am. Chem. Soc.* **1982**, *104*, 3515–3516.

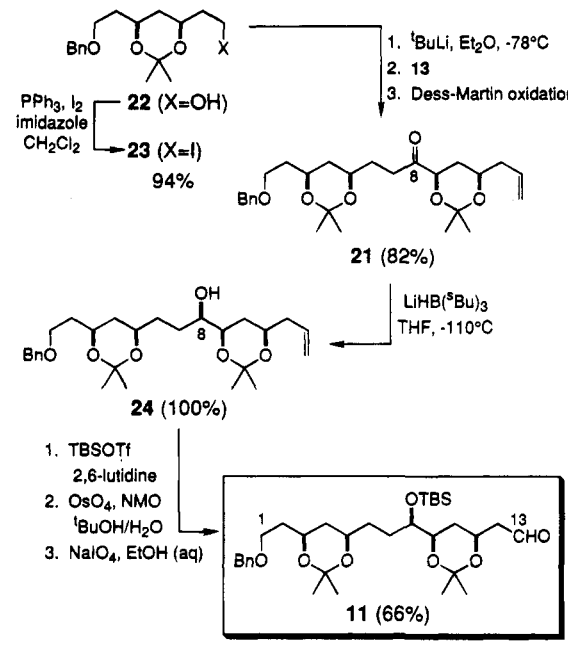
(41) (a) Prandi, J.; Audin, C.; Beau, J.-M. *Tetrahedron Lett.* **1991**, *32*, 769–772. (b) Rychnovsky, S. D.; Griesgraber, G.; Zeller, S.; Skalitzky, D. J. *J. Org. Chem.* **1991**, *56*, 5161–5169. See also ref 14.

(42) This approach bears resemblance to the strategy employed by Solladié in his construction of the C1–C12 segment of amphotericin B: Sollodié, G.; Hunt, J. *Tetrahedron Lett.* **1987**, *28*, 797–800.

Scheme 3



Scheme 4



the use of a sulfoxide as a carbanion stabilizing substituent (Scheme 3).[45] Aldehyde **18** was reduced and the resultant alcohol converted to a phenyl sulfide using the Hatta methodology.[46] Oxidation using MMPP gave **19** in excellent overall yield as a mixture of sulfoxide diastereomers. The crucial carbon–carbon bond was formed through condensation of the resultant lithium anion with aldehyde **13** to afford the intact carbon skeleton **20** as a mixture of diastereomers at C7 and C8. Cognizant of Nicolaou's report that the stereochemistry at C8 could be cleanly established through reduction of a ketone precursor,[17c] the isomeric nature of this product was not a concern as it could be efficiently converted to ketone **21** through sequential oxidation of the C8 alcohol[47] and tin-mediated desulfurization at C7.[48]

In the course of bringing more material through this sequence to ketone **21**, the sulfoxide-mediated coupling reaction proved to be capricious, often proceeding in significantly depressed yields when applied on preparatively useful scale. Consequently, a more reliable coupling reaction was sought. A solution to this problem was found in the utilization of iodide **23**, which was easily accessible from alcohol **22**, as a precursor to an organolithium intermediate through halogen–metal exchange (Scheme 4). A more concise and reproducibly high yielding synthesis of ketone **21** (82% overall yield) became available through sequential treatment of iodide **23** with ^{t}BuLi (2 equiv) and aldehyde **13**, followed by Dess–Martin periodinane oxidation.[47] The completion of the synthesis of the C1–C13 fragment **11** followed in straightforward fashion. The reduction conditions of Nicolaou quantitatively yielded the correct C8 stereochemistry to furnish alcohol **24** having all the stereocenters properly established. Routine protection of the alcohol followed by oxidative cleavage of the double bond provides the desired fragment **11**.

IV. Conclusion

We have reported a reproducible and efficient synthesis of the C1–C13 polyacetate region of the polyene macrolide antibiotic amphotericin B that uses L-aspartic acid as the sole source of chirality. In the course of this investigation, general approaches to the asymmetric synthesis of 1,3-polyols have been developed that feature the exploitation of substrate control to make accessible multiple stereochemical series from a common precursor. An important facet of this study was the observation that clean N → O exchange may be carried out under mild conditions using the procedure originally reported by Castedo and co-workers. As a result, the stereochemical information in the starting amino acid may be retained and used for further asymmetric transformation, thus rendering the chiral oxazoline intermediate even more synthetically useful. This transformation promises to elevate the synthetic utility of other readily available α-amino acids for the preparation of asymmetric polyoxygenated compounds. With the availability of suitable quantities of crucial intermediate **11**, the completion of the synthesis of amphotericin B is under investigation and will be reported in due course.

Experimental Section

General. Chemicals used were reagent grade and used as purchased unless otherwise noted. $BF_3{\cdot}OEt_2$ was distilled under argon at atmospheric pressure just prior to use. Tetrahydrofuran (THF), diethyl ether (Et_2O), and dimethoxyethane (DME) were distilled from Na^0 and benzophenone under N_2 prior to use. The remaining solvents, including CH_2Cl_2, $CHCl_3$, benzene, and toluene, as well as the amines Et_3N and $^iPr_2NH$, were distilled from CaH_2 under N_2 at atmospheric pressure. Alkyllithium reagents and Grignard reagents were titrated using a standardized solution of ^{i}PrOH in xylenes with 1,10-

(43) Owing to problems associated with deketalization, standard conditions could not be used for the formation of the dithiane of aldehyde **18** (e.g., 1,3-propane dithiol, $ZnCl_2$, CH_2Cl_2). Satifactory results were obtained using the conditions of Soderquist and Miranda which yielded the desired dithiane in 72% yield, along with 27% of the free diol dithiane. See: Soderquist, J. A.; Miranda, E. I. *Tetrahedron Lett.* **1986**, *27*, 478–481.

(44) Deprotonation of this dithiane proved to be difficult in our hands, and the resulting addition reactions generally resulted in extensive decompostion.

(45) This approach bears resemblance to a strategy examined by Masamune during his studies that led to a successful synthesis of amphoteronolide B.[17e] See: Masamune, S. *Ann. N.Y. Acad. Sci.* **1988**, *544*, 168–179.

(46) Cleary, D. G. *Synth. Commun.* **1989**, *19*, 737–744.

(47) Dess, D. B.; Martin, J. C. *J. Org. Chem.* **1983**, *48*, 4155–4156.

(48) Smith, A. B., III; Hale, K. J.; McCauley, J. P. *Tetrahedron Lett.* **1989**, *30*, 5579–5582.

(49) Hutchinson, D. K.; Fuchs, P. L. *J. Am. Chem. Soc.* **1987**, *109*, 4930–4939.

phenanthroline as an indicator. All reactions were carried out under argon or N_2 atmospheres and concentrations under reduced pressure carried out using a rotary evaporator or a vacuum pump.

Melting points are uncorrected. ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ at 300 and 75 MHz, respectively. Mass spectra, IR, and optical rotations were obtained on commercially available instrumentation.

Analytical thin-layer chromatography was performed on E. Merck silica gel 60 F_{254} plates (0.25 mm). Column chromatography was carried out using the flash technique described by Still[35] using E. Merck silica gel 60 (200–425 mesh). Radial chromatography was performed using a model 7924 Chromatotron from Harrison Research. Microanalyses were performed by Atlanta Microlab, Norcross, GA.

(4*S*)-4-(2′-Oxoethyl)-2-phenyloxazoline (7). To a solution of thiolate **4** (3.00 g, 10.8 mmol) in CH_2Cl_2 (10 mL) at −78 °C was added $^iBu_2AlH$ (14.1 mL, 12.9 mmol, 0.91 M in hexanes) by slow dropwise addition. After the addition was complete, the reaction mixture was quenched by careful addition of ethyl acetate (2 mL) and the result allowed to warm to room temperature. The reaction mixture was partitioned between ether (50 mL) and 1.0 M aqueous sodium potassium tartrate (150 mL) and then shaken vigorously until a viscous emulsion was obtained. The layers were separated and the aqueous layer was further extracted with Et_2O (3 × 20 mL). The organic extracts were combined, washed with brine, dried ($MgSO_4$), and filtered through a pad of Celite. The solvent was removed under reduced pressure to give a slightly yellow oil. The oil was subjected to high vacuum (0.1 mmHg) for 6 h to give the aldehyde **7** as a pale yellow crystalline solid (1.95 g, 95%): R_f 0.28 (SiO_2; 1:3 Et_2O:CH_2Cl_2); IR (neat) 2980–2840, 1725, 1645, 1360, 1065, 785, 698 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.71 (dd, 1H, J = 8.1, 18.0 Hz), 3.11 (dd, 1H, J = 4.5, 18.0 Hz), 4.02 (m, 1H), 4.68 (m, 2H), 7.46 (m, 3H), 7.95 (m, 2H), 9.89 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 49.64, 61.04, 72.40, 127.03, 127.94, 128.02, 131.21, 164.09, 200.05

2-Phenyl-4(*S*)-(2(*R*)-hydroxypent-4-enyl)-2-oxazoline (8a). To a solution of tri-*n*-butylallylstannane (4.88 mL, 15.7 mmol) in Et_2O (20 mL) at 0 °C was added *n*-butyllithium (6.1 mL, 2.44 M in hexane). This solution was allowed to warm to room temperature where it was kept for 30 min and then cooled to −78 °C. Trimethylaluminum in hexane (7.5 mL, 2.0 M) was introduced and the result allowed to warm to 0 °C. After once again cooling to −78 °C, aldehyde **7** (1.42 g, 7.5 mmol) in Et_2O (10 mL) was introduced and the resulting mixture allowed to warm to room temperature over 6 h. At this time, the reaction was quenched with excess methanol and the resulting mixture partitioned between Et_2O and H_2O. The layers were separated, and the aqueous solution was extracted with Et_2O (4 × 20 mL). The organic extracts were combined, washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure. The resulting oil was chromatographed using a gradient elution (SiO_2; 1:2 to 1:1 Et_2O:hexane) to give the isomerically pure homoallylic alcohol **8a** as a clear oil (1.00 g, 59%): R_f 0.22 (SiO_2; 1:1 Et_2O:hexanes); IR (neat) 3400, 2910, 1645, 1365, 1070, 1365, 1070, 790, 200 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.85 (m, 2H), 2.36 (broad t, 2H, J = 6.8 Hz), 4.01 (m, 1H), 4.05 (t, 1H, J = 7.0 Hz), 4.55 (m, 1H), 4.59 (t, 1H, J = 7.1 Hz), 5.12 (dd, 1H, J = 1.5, 10.1 Hz), 5.17 (dd, 1H, J = 1.5, 17.5 Hz), 5.86 (ddt, 1H, J = 7.2, 10.1, 17.5 Hz), 7.45 (m, 3H), 7.87 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 41.76, 41.94, 63.67, 68.78, 73.24, 117.74, 127.25, 128.24, 128.29, 134.83, 164.04.

(2R,4′S)-2-[[Dimethyl(2-methyl-2-propyl)silyl]oxy]-1-[4′-(2′-phenyloxazolinyl)]-4-pentene. A solution of homoallyl alcohol **8a** (1.02 g, 4.41 mmol) and NEt_3 (1.22 mL, 8.80 mmol) in CH_2Cl_2 (10 mL) at 0 °C was treated with *tert*-butyldimethylsilyl triflate (1.21 mL, 5.26 mmol). After 5 min, the reaction was quenched with excess saturated aqueous $NaHCO_3$. The resulting mixture was diluted with Et_2O, and the layers were separated. The organic layer was extracted three times with water, dried ($MgSO_4$), and filtered through a short column of silica gel. Evaporation of the solvent under reduced pressure afforded the product as a slightly green oil (1.52 g, 100%): R_f 0.75 (SiO_2; 50% Et_2O:hexane); $[\alpha]^{22}_D$ = −63.80° (*c* 1.0, $CHCl_3$); IR (film) 3053, 1652, 1368, 1284 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.125 (s, 6H), 0.919 (s, 9H), 1.65 (m, 1H), 1.89 (m, 1H), 2.28 (t, 2H, J = 6.81 Hz), 4.05 (t, 1H, J = 8.14 Hz), 4.10 (m, 1H), 4.33 (m, 1H), 4.51 (dd, 1H, J = 8.15, 9.30 Hz), 5.05 (m, 2H), 5.82 (m, 1H), 7.41 (m, 3H), 7.93 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ −3.86, 18.53, 26.39, 43.23, 43.83, 64.88, 70.51, 74.12, 128.67, 131.54, 1 34.89, 163.58. Anal. Calcd for $C_{20}H_{31}NO_2Si$: C, 69.52; H, 9.04; N, 4.05. Found: C, 68.86; H, 9.40; N, 3.72.

(2S,4R)-2-(*N*-Benzylamino)-4-[[dimethyl(2-methyl-2-propyl)silyl]oxy]-6-hepten-1-ol. To a solution of the *anti*-silyl ether oxazoline (1.38 g, 3.99 mmol) in toluene (30 mL) at −5 °C was added $^iBu_2AlH$ (21.9 mL, 19.9 mmol, 0.91 M in hexane) in a dropwise fashion. The result was kept at 0 °C for 5 min at which time the reaction was quenched with ethyl acetate (6 mL) and the result allowed to warm to room temperature. The yellow solution was diluted with ether (100 mL) and shaken with 1.0 M aqueous potassium sodium tartrate (150 mL). The layers were separated, and the aqueous layer was extracted with ether (4 × 50 mL). The organic extracts were combined, dried ($MgSO_4$), and concentrated under reduced pressure to give a yellow oil. The oil was purified by flash chromatography (SiO_2; 5% methanol:CH_2Cl_2) to afford the product as a colorless oil (1.28 g, 92%): R_f 0.34 (SiO_2; 8% methanol:CH_2Cl_2); $[\alpha]^{23}_D$ = −7.1° (*c* 1.0, $CHCl_3$); IR (film) 1257, 1472, 2932, 3390 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.06 (s, 6H), 0.93 (s, 9H), 1.51 (m, 1H), 1.78 (m, 1H), 2.18 (m, 2H), 2.87 (m, 1H), 3.28 (m, 1H), 3.72 (m, 3H), 3.87 (m, 1H), 5.02 (m, 2H), 5.74 (m, 1H), 7.3 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ −4.26, −4.03, 18.43, 26.23, 26.27, 37.95, 41.78, 51.31, 55.39, 63.48, 70.83, 117.85, 127.76, 129.30, 134.90. Anal. Calcd for $C_{20}H_{35}NO_2Si$: C, 68.72; H, 10.09; N, 4.01. Found: C, 68.60; H, 10.15; N, 3.96.

(2R,4′S)-*N*′-Benzyl-2-[[dimethyl(2-methyl-2-propyl)-silyl]oxy]-1-(4′-oxazolidinyl)-4-pentene. A solution of the *anti*-amino alcohol (927 mg, 2.65 mmol) in benzene (50 mL) at room temperature was treated with formaldehyde (0.24 mL, 3.18 mmol, 13.34 M in water). The result was heated to reflux under Dean–Stark conditions for 30 min. After being allowed to cool to room temperature, the solution was concentrated under reduced pressure to give the product as a chromatographically pure (TLC), colorless oil (958 mg, 100%): R_f 0.76 (SiO_2; 20% hexane:Et_2O); $[\alpha]^{23}_D$ = −15.29° (*c* 1.0, $CHCl_3$); IR (film) 774, 835, 1005, 1042, 1095, 1255, 2857, 2884, 2929, 2955 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.051 (s, 3H), 0.078 (s, 3H), 0.898 (s, 9H), 1.45 (m, 1H), 1.73 (m, 1H), 2.23 (m, 2H), 3.20 (p, 1H, J = 5.96 Hz), 3.40 (dd, 1H, J = 5.07, 7.77 Hz), 3.70 (q, 2H, J = 13.05 Hz), 3.92 (m, 1H), 4.06 (t, 1H, J = 7.22 Hz), 4.23 (s, 2H), 5.03 (m, 2H), 5.80 (m, 1H), 7.35 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ -4.05, −3.65, 18.51, 26.34, 26.41, 41.40, 42.96, 58.69, 61.75, 70.36, 70.43, 85.27, 117.64, 127.60, 128.81, 129.19, 134.99, 139.75. Anal. Calcd for $C_{21}H_{35}NO_2Si$: C, 69.75; H, 9.76; N, 3.87. Found: C, 69.96; H, 9.82; N, 3.96.

(2S,4R)-2-(*N*-Benzyl-*N*-methylamino)-4-[[dimethyl(2-methyl-2-propyl)silyl]oxy]-6-hepten-1-ol (9a). A solution of the *anti*-(silyloxy)oxazolidine (601 mg, 1.66 mmol) in toluene (10 mL) at −60 °C under argon was treated with $^iBu_2AlH$ (2.0 mL, 1.83 mmol, 0.91 M in hexane). After 5 min, the reaction was quenched by addition of ethyl acetate (1 mL) and the mixture allowed to warm to room temperature. The resulting solution was diluted with Et_2O (50 mL) then shaken with 1.0 M aqueous potassium sodium tartrate (100 mL). The resulting layers were separated, and the aqueous layer was extracted three times with Et_2O. The organic extracts were combined, washed with brine, dried ($MgSO_4$), filtered through a bed of Celite, and evaporated under reduced pressure to give amino alcohol **9a** as a colorless oil (572 mg, 95%): R_f 0.32, (streak, SiO_2; 50% Et_2O:hexane); $[\alpha]^{23}_D$ = +4.5° (*c* 1.0, $CHCl_3$); IR (film) 913, 1040, 1258, 2800, 2885, 3448 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.051 (s, 3H), 0.076 (s, 3H), 0.908 (s, 9H), 1.24 (m, 1H), 1.86 (m, 1H), 2.15 (s, 3H), 2.25 (t, 2H, J = 6.23 Hz), 3.54 (m, 4H), 3.76 (p, 1H), 5.06 (m, 2H), 5.82 (m, 1H), 7.32 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ −4.11, −3.98, −3.90, −3.77, 18.51, 26.33, 26.39, 32.30, 36.33, 42.45, 58.37. 61.49, 62.25, 70.92, 117.88, 127.59, 128.83, 129.20, 134.89, 139.55.

(4*R*,6*S*)-4-[[Dimethyl(2-methyl-2-propyl)silyl]oxy]-6,7-epoxyheptene (10a). A solution of *trans*-amino alcohol **9s** (467 mg, 1.28 mmol) and tetra-*n*-butylammonium chloride (18 mg, 0.064 mmol) in $CHCl_3$ (30 mL) was vigorously stirred with 50% aqueous sodium hydroxide (10 mL). After 90 min, the stirring was ceased and the mixture was allowed to stand undisturbed to allow the layers to separate. The $CHCl_3$ layer was separated, dried ($MgSO_4$), and filtered through a short plug of silica gel. The result was then carefully concentrated under reduced pressure to give a yellow oil. This oil was purified by radial chromatography (SiO_2; 10% Et_2O:hexanes) to give the *anti*-epoxy ether **10a** as a colorless oil (164 mg, 52%): R_f 0.77 (SiO_2; 50% Et_2O:hexane); $[\alpha]^{23}_D = +27.86°$ (*c* 1.0, $CHCl_3$); IR (film) 2954, 2857, 1256, 1090, 836, 775 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.053 (s, 6H), 0.83 (s, 9H), 1.60 (m, 2H), 2.25 (dd, 2H, J = 5.93, 6.89 Hz), 2.46 (dd, 1H, J = 2.72, 5.11 Hz), 2.7 (t, 1H, J = 4.07 Hz), 3.00 (m, 1H), 3.94 (m, 1H), 5.02 (m, 2H), 5.78 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ −4.28, −4.04, 18.47, 26.21, 26.28, 40.36, 43.01, 48.18, 50.24, 70.07, 117.76, 134.88.

2-Phenyl-4(*S*)-(2(*S*)-hydroxypent-4-enyl)-2-oxazoline (8s). Solid anhydrous $ZnCl_2$ (14.7 g, 0.108 mol) was fused three times under reduced pressure (0.1 mmHg), cooled under N_2, and dissolved in sufficient THF to give a 1.0 M, solution. Allylmagnesium bromide (54 mL, 1.0 M in Et_2O) was added at 0 °C, and the resulting suspension was warmed at room temperature for 5 min. After cooling to 0 °C, aldehyde **7** (2.04 g, 10.8 mmol) as a 2 M solution in THF was introduced by dropwise addition. After 3 h, the reaction was quenched by the addition of saturated aqueous $NaHCO_3$ followed by sufficient water to dissolve all solids. The layers were separated, and the aqueous layer extracted with Et_2O (3 × 20 mL). The organic extracts were combined, washed with brine, dried ($NaSO_4$), and concentrated under reduced pressure. The residue was chromatographed (SiO_2; 1:1 Et_2O:hexanes) to give the isomerically pure homoallylic alcohol **8s** as a clear oil (1.66 g, 68%): R_f 0.2 (SiO_2; 1:1 Et_2O:hexanes); IR (neat) 3400, 2910, 1645, 1365, 1070, 1365, 1070, 790, 200 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.61 (dt, 2H, J = 12.2, 13.7 Hz), (ddd, 1H, J = 2.3, 4.1, 13.5 Hz), 2.25 (m, 1H), 2.35 (m, 1H), 4.02 (t, 1H, J = 8.1 Hz), 4.08 (ddt, 1H, J = 2.2, 6.3, 10.4 Hz), 4.45 (dt, 1H, J = 4.0, 9.5 Hz), 4.60 (dd, 1H, J = 8.1, 9.5 Hz), 4.86 (broad s, 1H), 5.09 (dd, 1H, J = 1.8, 11.2 Hz), 5.13 (dd, 1H, J = 1.8, 7.1 Hz), 5.89 (ddt, H, J = 7.4, 10.1, 17.1 Hz), 7.45 (m, 3H), 7.87 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 41.73, 42.06, 65.92, 70.59, 72.89, 116.95, 126.80, 128.01, 131.37, 134.64, 163.50. Anal. Calcd for $C_{14}H_{17}NO_2$: C, 72.70; H, 7.41. Found: C, 72.76; H, 7.43.

(2*S*,4′*S*)-2-[[Dimethyl(2-methyl-2-propyl)silyl]oxy]-1-[4′-(2′-phenyloxazolinyl)]-4-pentene. A solution of homoallyl alcohol **8s** (407 mg, 1.76 mmol) and NEt_3 (0.49 mL, 3.52 mmol) in CH_2Cl_2 (10 mL) at 0 °C was treated with *tert*-butyldimethylsilyl triflate (0.48 mL, 2.11 mmol). After 5 min, the reaction was quenched with excess saturated aqueous $NaHCO_3$. The resulting mixture was diluted with Et_2O and shaken, and the layers were separated. The organic layer was extracted three times with water, dried ($MgSO_4$), and filtered through a short column of silica gel. Evaporation of the solvent under reduced pressure gave the silyl ether as a colorless oil (608 mg, 100%): R_f 0.76 (SiO_2; 50% Et_2O:hexane); $[\alpha]^{22}_D$ = −17.49° (*c* 1.0, $CHCl_3$); IR (film) 2957, 2857, 1652, 1256, 1091, 836, 775, 694 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.049, 0.075 (singlets, 6H), 0.898 (s, 9H), 1.65 (m, 1H), 2.06 (m, 1H), 2.34 (m, 2H), 3.92 (p, 1H, J = 5.29 Hz), 4.07 (t, 1H, J = 7.31 Hz), 4.45 (m, 2H), 5.05 (m, 2H), 5.82 (m, 1H), 7.40 (m, 3H), 7.93 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ −4.12, −3.97, 18.49, 26.28, 26.35, 42.25, 43.13, 63.79, 69.82, 73.44, 117.83, 128.32, 128.63, 131.61, 135.01, 163.92. Anal. Calcd for $C_{20}H_{31}NO_2Si$: C, 69.52; H, 9.04. Found: C, 68.90; H, 9.17.

(2*S*,4′*S*)-2-(*N*-Benzylamino-4-[[dimethyl(2-methyl-2-propyl)silyl]oxy]-6-hepten-1-ol. To a solution the *syn*-silyl ether oxazoline (100 mg, 0.289 mmol) in toluene (2.8 mL) at 0 °C was introduced $^iBu_2AlH$ (1.59 mL, 1.45 mmol, 0.91 M in hexane) in a dropwise fashion. After 5 min, the reaction was quenched with ethyl acetate (excess) and allowed the mixture to warm to room temperature. The resulting yellow solution was diluted with ether (15 mL) and shaken with 1.0 M aqueous sodium potassium tartrate (20 mL), and the resulting layers were separated. The aqueous layer was extracted with ether (4 × 5 mL), and the organic extracts were combined, dried ($MgSO_4$), and evaporated under reduced pressure to give the product as a pale yellow oil (99 mg, 99%) that was judged greater than 95% pure (300 MHz NMR) and was used without further purification: R_f 0.12−0.42 (streak, SiO_2; ethyl acetate); ^1H NMR ($CDCl_3$, 300 MHz) δ 0.04 (s, 3H), 0.07 (s, 3H), 0.85 (s, 9H), 1.62 (m, 2H), 2.18 (m, 1H), 2.25 (t, 2H, J = 6.84 Hz), 2.87 (m, 1H), 3.34 (dd, 1H, J = 5.30, 10.79 Hz), 3.67 (dd, 1H), 3.78 (d, 2H, J = 3.29 Hz), 3.83 (m, 1H), 5.04 (m, 2H), 5.78 (m, 1H), 7.33 (s, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ −4.17, −3.78, 18.44, 26.24, 26.30, 39.30, 42.74, 51.41, 55.94, 63.45, 70.38, 117.87, 127.54, 128.55, 129.02, 134.80, 140.51.

(2*S*,4′*S*)-2-[[Dimethyl(2-methyl-2-propyl)silyl]oxy]-1-[4′-(2′-phenyloxazolinyl)]-4-pentene. A solution of the *syn*-amino alcohol (407 mg, 1.76 mmol) in benzene (25 mL) at room temperature was treated with formaldehyde (0.15 mL, 2.11 mmol, 13.34 M in water). The solution was heated to reflux under Dean−Stark conditions for 30 min. After allowing to cool to room temperature, the solution was concentrated under reduced pressure to give the product as a chromatographically pure (TLC), colorless oil (608 mg, 100%): R_f 0.76 (SiO_2; 50% Et_2O:hexane); $[\alpha]^{22}_D$ = −17.49° (*c* 1.0, $CHCl_3$); IR (film) 2957, 2857, 1652, 1256, 1091, 836, 775, 694 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.049, 0.075 (singlets, 6H), 0.898 (s, 9H), 1.65 (m, 1H), 2.06 (m, 1H), 2.34 (m, 2H), 3.92 (p, 1H, J = 5.29 Hz), 4.07 (t, 1H, J = 7.31 Hz), 4.45 (m, 2H), 5.05 (m, 2H), 5.82 (m, 1H), 7.40 (m, 3H), 7.93 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ −4.12, −3.97, 18.49, 26.28, 26.35, 42.25, 43.13, 63.79, 69.82, 73.44, 117.83, 128.32, 128.63, 131.61, 135.01, 163.92. Anal. Calcd for $C_{20}H_{31}NO_2Si$: C, 69.52; H, 9.04. Found: C, 68.90; H, 9.17.

(2*S*,4*S*)-2-(*N*-Benzyl-*N*-methylamino)-4-[[dimethyl(2-methyl-2-propyl)silyl]oxy]-6-hepten-1-ol (9s). A solution of the *syn*-(silyloxy)oxazolidine (954 mg, 2.64 mmol) in CH_2Cl_2 (5 mL) at −23 °C was treated with $^iBu_2AlH$ (3.19 mL, 2.90 mmol, 0.91 M in hexanes). After 5 min, the reaction was quenched by addition of excess ethyl acetate and the mixture allowed to warm to room temperature. The resulting solution was diluted with Et_2O (30 mL) and shaken with 1.0 M aqueous potassium sodium tartrate (50 mL). The layers were separated, and the aqueous layer was extracted with additional Et_2O (2 × 10 mL). The organic extracts were combined, washed with brine, dried ($MgSO_4$), filtered through a bed of Celite, and evaporated under reduced pressure to give amino alcohol **9s** as a colorless oil (787 mg, 82%, >95% pure by NMR): R_f 0.11−0.40 (streak, SiO_2; 50% Et_2O:hexane); ^1H NMR ($CDCl_3$, 300 MHz) δ 0.048, 0.062 (singlets, 6H), 0.87 (s, 9H), 1.29 (m, 1H), 1.74 (m, 1H), 2.14 (s, 3H), 2.24 (m, 2H), 3.03 (m, 1H), 3.3−3.8 (m, 5H), 5.04 (m, 2H), 5.78 (m, 1H), 7.34 (m, 5H).

(4*R*,6*R*)-4-[[Dimethyl(2-methyl-2-propyl)silyl]oxy]-6,7-epoxyheptene (10s). A solution of the *anti*-amino alcohol **9a** (358 mg, 0.985 mmol) and tetra-*n*-butylammonium chloride (5 mg, 0.064 mmol) in $CHCl_3$ (30 mL) was vigorously stirred with 50% aqueous sodium hydroxide (10 mL) at room temperature. After 45 min, stirring was ceased and the mixture was allowed to stand undisturbed to allow two layers to separate. At this time the $CHCl_3$ layer was removed, dried ($MgSO_4$), and filtered through a short plug of silica gel. The $CHCl_3$ was then carefully evaporated under reduced pressure (taking care to maintain the temperature below room temperature) to give the *syn*-epoxy ether **10s** as a colorless oil (179 mg, 75%, >95% pure by NMR): R_f 0.77 (SiO_2; 50% Et_2O: hexane); $[\alpha]^{23}_D$ = −6.33° (*c* 1.0, $CHCl_3$); IR (film) 2954, 2857, 1256, 1090, 836, 775 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.057 (s, 6H), 0.67 (s, 6H), 0.893 (s, 9H), 1.66 (m, 2H), 2.32 (m, 2H), 2.44 (dd, 1H, J = 2.72, 5.07 Hz), 2.75 (t, 1H, J = 4.35 Hz), 3.03 (m, 1H), 3.91 (p, 1H, J = 5.8 Hz), 5.06 (m, 2H), 5.81 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ −4.35, −3.95, 26.20, 26.26, 40.15, 42.31, 47.23, 49.89, 70.55, 117.69, 128.78, 135.22. Anal. Calcd for $C_{13}H_{26}O_2Si$: C, 64.41; H, 10.81. Found: C, 64.35; H, 10.68.

(2*R*,4*R*)-4-[[Diphenyl(2-methyl-2-propyl)silyl]oxy]-1-(phenylthio)-6-hepten-2-ol. To a solution of epoxide **10s** (1.0

g, 2.73 mmol) in *tert*-butyl alcohol (25 mL) and 0.5 N aqueous NaOH (25 mL) at room temperature was added thiophenol (0.35 mL, 3.41 mmol). This mixture was warmed to 60–70 °C where it was maintained for 1 h. The reaction mixture was allowed to cool to room temperature and partitioned between ether (75 mL) and saturated aqueous NH_4Cl (75 mL), the layers were separated, and the organic layer was washed with 10% aqueous NaOH (3 × 20 mL), water, and brine and dried ($MgSO_4$). After filtering through a short plug of silica gel, the solvent was removed under reduced pressure to give the phenylthio ether as a colorless oil (1.30 g, 100%): R_f 0.40 (SiO_2; 20% Et_2O:hexane); $[\alpha]^{23}_D = -6.92°$ (*c* 1.04, $CHCl_3$); IR (film) 3350, 3060, 2910 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.03 (s, 9H), 1.72 (m, 2H), 2.15 (m, 2H), 2.83 (m, 2H), 2.96 (dd, 1H, J = 4.69, 13.55 Hz), 3.88 (oct, 1H, J = 3.89 Hz), 3.97 (p, 1H, J = 5.12 Hz), 4.79 (dd, 1H, J = 1.08, 17.07 Hz), 4.91 (dd, 1H, J = 0.86, 10.15 Hz), 5.59 (m, 1H), 7.36 (m, 11H), 7.68 (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 19.69, 27.29, 27.61, 41.29, 41.59, 42.04, 66.91, 71.71, 118.02, 126.51, 128.12, 128.25, 128.52, 129.25, 129.79, 130.12, 130.40, 133.78, 134.26, 134.35, 136.23, 136.54. Anal. Calcd for $C_{29}H_{36}O_2SSi$: C, 73.06; H, 7.61. Found: C, 72.96; H, 7.62.

(2*R*,4*R*)-2,4-*O*-Isopropylidene-1-(phenylthio)-6-heptene-2,4-diol (14s). The *syn*-phenyl sulfide adduct (60.7 mg, 0.177 mmol) was treated with of 5% concentrated HCl/methanol (1 mL) and allowed to stir at room temperature for 5 min. The result was then concentrated under reduced pressure to a residue which was then dissolved in 2,2-dimethoxypropane (1 mL). After stirring for 20 min at room temperature, the solution was evaporated under reduced pressure to a colorless oil. This oil was dissolved in 50% Et_2O:hexane, filtered through a 3 × 1 cm silica gel plug, and concentrated under reduced pressure to give the product **14s** as a colorless oil (40 mg, 100%): R_f 0.84 (SiO_2; 50% Et_2O:hexane); $[\alpha]^{23}_D = +32.00°$ (*c* 0.825, $CHCl_3$); IR (film) 730, 1370, 1430, 1472, 1573, 2980, 3030 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.16 (q, 1H, J = 12.0 Hz), 1.40 (s, 6H), 1.74 (dt, 1H, J = 12.9, 2.4 Hz), 2.15 (p, 1H, J = 6.9 Hz), 2.30 (p, 1H, J = 6.9 Hz), 2.87 (dd, 1H, J = 6.6, 13.2 Hz), 3.10 (dd, 1H, J = 6.6, 13.2 Hz), 3.85 (m, 1H), 3.97 (m, 1H), 5.07 (m, 2H), 5.77 (m, 1H), 7.24 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 20.22, 30.48, 36.17, 39.89, 41.18, 68.80, 68.97, 99.40, 117.70, 126.44, 129.32, 129.59, 134.39, 136.88.

(2*R*,4*S*)-4-[[Dimethyl(2-methyl-2-propyl)silyl]oxy]-1-(phenylthio)-6-hepten-2-ol. To a solution of epoxide **10a** (100 mg, 0.412 mmol) in *tert*-butyl alcohol (2 mL) and 0.5 M aqueous NaOH (2 mL) at room temperature was added thiophenol (0.05 mL, 0.516 mmol). This mixture was warmed to 55–60 °C where it was maintained for 1 h. The reaction mixture was allowed to cool to room temperature and partitioned between Et_2O (20 mL) and saturated aqueous NH_4Cl (20 mL), the layers were separated, and the aqueous layer was extracted with additional portions of Et_2O (3 × 5 mL). The organic extracts were combined, washed with 10% aqueous NaOH (2 × 5 mL), water, and brine, and dried ($MgSO_4$). Removal of the solvent under reduced pressure gave a colorless oil which was then purified by radial chromatography (SiO_2; 15% Et_2O:hexanes) to give the thioether as a colorless oil (134 mg, 92%): R_f 0.36 (SiO_2; 20% Et_2O/hexane); $[\alpha]^{23}_D = +8.00°$ (*c* 1.0, $CHCl_3$); IR (film) 775, 835, 1075, 1256, 2928, 3474 (br) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.05 (s, 3H), 0.10 (s, 3H), 0.85 (s, 9H), 1.63 (m, 2H), 2.27 (t, 2H, J = 6.65 Hz), 2.97 (m, 2H), 3.95 (m, 1H), 4.05 (m, 1H), 5.04 (m, 2H), 5.73 (m, 1H), 7.30 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ −4.40, −3.91, 18.39, 26.20, 26.27, 41.56, 42.12, 42.43, 66.65, 70.45, 117.97, 126.85, 129.43, 130.35, 134.76, 135.88. Anal. Calcd for $C_{19}H_{32}O_2SSi$: C, 64.72; H, 9.15. Found: C, 64.55; H, 9.19.

(2*R*,4*S*)-2,4-*O*-Isopropylidene-1-(phenylthio)-6-heptene-2,4-diol (14a). The *anti*-phenyl sulfide adduct (100 mg, 0.284 mmol) was treated with 5% concentrated HCl/methanol (2 mL) at room temperature for 15 min. At this time, the solution was concentrated under reduced pressure to afford a colorless residue which then dissolved in 2,2-dimethoxypropane (2 mL). After sirring for 20 min at room temperature, the solution was again concentrated under reduced pressure to afford a colorless oil. This oil was dissolved in 50% Et_2O:hexane and passed through a 4 × 1 cm silica gel plug, and the result concentrated under reduced pressure to give the product **14a** as a colorless oil (64 mg, 100%): R_f 0.80 (SiO_2; 50% Et_2O:hexane); $[\alpha]^{23}_D = +50.23°$ (*c* 1.0, $CHCl_3$); IR (film) 680, 737, 911, 1224, 1378, 1439, 1481, 2928, 2988 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.33 (s, 3H), 1.36 (s, 3H), 1.72 (m, 2H), 2.24 (m, 2H), 2.96 (dd, 1H, J = 5.99, 13.10 Hz), 3.10 (dd, 1H, J = 5.99, 13.10 Hz), 3.88 (m, 1H), 3.97 (m, 1H), 5.06 (m, 2H), 5.78 (m, 1H), 7.27 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 25.17, 25.38, 37.70, 39.76, 40.48, 66.31, 66.66, 101.14, 117.49, 126.55, 129.32, 129.91, 134.66, 136.78.

(2*R*,4*R*)-2,4-*O*-Isopropylidene-1-(phenylsulfinyl0-6-heptene-2,4-diol. To a solution of the *syn*-isopropylidene sulfide **14s** (1.35 g, 5.96 mmol) in ethanol (14 mL) at 0 °C was introduced a solution of magnesium monoperoxyphthalate (1.62 g, 3.28 mmol) in water (14 mL) by dropwise addition. Immediately following this addition, the resulting mixture was partitioned between CH_2Cl_2 (25 mL) and water (75 mL). The layers were separated, and the aqueous layer was extracted with additional portions of CH_2Cl_2 (3 × 15 mL). The organic extracts were combined, dried ($MgSO_4$), and filtered through a short plug of silica gel. Removal of the solvent under reduced pressure yielded the diastereomeric sulfoxides as a colorless oil (1.44 g, 100%): R_f 0.24 (SiO_2; 50% Et_2O:hexane); IR (film) 3010, 3000, 1010 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.19 (m, 1H), 1.27, 1.31, 1.44, 1.53 (singlets, 6H), 1.68 (m, 1H), 2.15 (m, 1H), 2.27 (m, 1H), 2.78, 3.15 (multiplets, 2H), 3.82, 3.93 (multiplets, 2H), 4.11, 4.48 (multiplets, 1H), 5.06 (m, 2H), 5.73 (m, 1H), 7.49 (m, 3H), 7.64 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 20.04, 20.29, 30.36, 30.41, 36.08, 36.32, 41.02, 53.87, 63.30, 63.88, 64.26, 65.43, 68.70, 68.76, 99.36, 99.73, 117.82, 117.88, 124.15, 124.75, 128.63, 129.53, 129.70, 131.33, 131.51, 134.12, 143.93, 145.24. Anal. Calcd for $C_{16}H_{22}O_3S$: C, 65.28; H, 7.53. Found: C, 65.20; H, 7.56.

(2*R*,4*R*)-1-Acetoxy-2,4-*O*-isopropylidene-1-(phenylthio)-6-heptene-2,4-diol (15s). A solution of the *syn*-sulfoxides (126 mg, 0.449 mmol) in acetic anhydride (3 mL) at room temperature was treated with excess sodium acetate (126 mg) in one portion. The resulting heterogeneous mixture was warmed to reflux where it was maintained for 3 h. After the reaction mixture was allowed to cool to room temperature, it was concentrated *in vacuo*. The resulting residue was passed through a plug of silica gel using 50% Et_2O:hexanes. Concentration of the filtrate under reduced pressure gave the product **15s** as a pale yellow oil (135 mg, 89%): R_f 0.64 (SiO_2; 50% Et_2O:hexane); IR (film) 3020, 2960, 1730, 1360, 1200 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.30 (m), 1.40 (s), 1.60 (dt, J = 2.48, 12.70 Hz), 1.68 (dt, J = 2.31, 12.80 Hz), 2.05 (s), 2.06 (s), 2.25 (m), 3.85 (m), 4.04 (dq, J = 2.74, 4.74, 11.49 Hz), 4.12 (dq, J = 2.39, 5.52, 11.72 Hz), 5.08 (m), 5.79 (m), 6.05 (d, J = 4.77 Hz), 6.11 (d, J = 5.53 Hz), 7.30 (m), 7.50 (m); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.56, 20.04, 21.40, 21.47, 23.09, 30.35, 32.02, 32.40, 32.96, 41.10, 68.66, 68.74, 70.50, 71.04, 83.05, 83.37, 99.65, 117.81, 128.62, 128.70, 129.36, 129.45, 132.57, 133.69, 134.11, 134.25, 170.12, 170.23. Anal. Calcd for $C_{18}H_{24}O_4S$: C, 64.26; H, 7.19. Found: C, 64.07; H, 7.21.

(2*R*,4*R*)-2,4-Dihydroxy-2,4-*O*-isopropylidene-6-heptenal (13). A solution of thioacetals **15s** (400 mg, 1.40 mmol) in methanol (10 mL) at room temperature was treated with potassium carbonate (213 mg, 1.54 mmol) in one portion. After stirring an additional 45 min, this yellow reaction mixture was partitioned between $CHCl_3$ (25 mL) and saturated aqueous NH_4Cl (25 mL), the layers were separated, and the aqueous layer was extracted with additional portions of $CHCl_3$ (3 × 10 mL). The organic extracts were combined and dried ($MgSO_4$), and the result was concentrated under reduced pressure to give a yellow oil. This oil was purified by radial chromatography (SiO_2; 20% Et_2O:hexanes) to give aldehyde **13** as a slightly yellow oil (236 mg, 91%): (This compound is very prone to hydration, which is reflected in the IR data and the difficulty in obtaining accurate elemental analysis and optical rotation.) R_f ca. 0.34 (streak, SiO_2; 50% Et_2O:hexane); IR (film) 3410, 3060, 2970, 1730 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.28 (q, 1H, J = 11.99 Hz), 1.47 (s, 6H), 1.75 (dt, 1H, J = 2.63, 13.05 Hz), 2.26 (dp, 2H, J = 6.61, 30.72 Hz), 3.94 (m, 1H), 4.28 (dd, 1H, J = 2.93, 12.23 Hz), 5.10 (m, 2H), 5.79 (m, 1H), 9.58 (s,

1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 20.02, 30.32, 40.98, 68.45, 71.74, 74.40, 99.09, 118.11, 134.35, 201.93.

(2*R*,4*S*)-2,4-*O*-Isopropylidene-1-(phenylsulfinyl)-6-heptene-2,4-diol. To a solution of the *anti*-isopropylidene sulfide **14a** (175 mg, 0.630 mmol) in THF (10 mL) at 0 °C was introduced a solution of magnesium monoperoxyphthalate (171 mg, 0.347 mmol) in water (10 mL) by dropwise addition. Immediately following this addition, the resulting mixture was partitioned between CH_2Cl_2 (30 mL) and water (30 mL). The layers were separated, and the aqueous layer was extracted with additional portions of CH_2Cl_2 (3 × 10 mL). The organic extracts were combined, dried ($MgSO_4$), and filtered through a plug of silica gel. Removal of the solvent *in vacuo* affords the diastereomeric sulfoxides as a colorless oil (167 mg, 90%): R_f 0.36 and R_f 0.45 (SiO_2; 20% hexane:Et_2O); IR (film) 3400 (w), 3050, 2290, 2920, 1430, 1370 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.26, 1.31, 1.40, 1.47 (singlets, 6H), 1.70 (m, 2H), 2.22 (m, 2H), 2.81, 2.83, 3.18 (doublets of doublets, 2H), 3.90 (m, 1H), 4.03 (m, 1H), 4.45 (m, 1H), 5.07 (m, 2H), 5.78 (m, 1H), 7.60 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 24.98, 25.28, 25.36, 25.41, 25.45, 37.40, 37.47, 37.53, 40.35, 61.47, 62.26, 64.53, 64.59, 66.39, 66.56, 101.20, 101.56, 117.67, 124.18, 124.89, 129.67, 131.33, 131.65, 134.38, 134.43, 144.12, 145.19.

(2*R*,4*S*)-1-Acetoxy-2,4-*O*-isopropylidene-1-(phenylthio)-6-heptene-2,4-diol (15a). A solution of the *anti*-sulfoxides (30.6 mg, 0.104 mmol) in acetic anhydride (1 mL) at room temperature was treated with sodium acetate (31 mg) and the result brought to a reflux. After 1 h at reflux, the reaction mixture was allowed to cool to room temperature, and the excess acetic anhydride was removed *in vacuo*. The resulting residue was suspended in 50% Et_2O:hexanes and then filtered through a short plug of silica gel. Concentration of the filtrate under reduced pressure gave the product **15a** as a colorless oil (22 mg, 63%): R_f 0.74 (SiO_2; 80% Et_2O:hexane); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.32, 1.35, 1.38 (singlets, 6H), 1.65−1.87 (m, 2H), 2.06, 2.065 (singlets, 3H), 2.23 (m, 2H), 3.88 (m, 1H), 4.09 (m, 1H), 5.08 (m, 2H), 5.78 (m, 1H), 6.10, 6.13 (singlets, 1H), 7.30, 7.48 (multiplets, 5H).

(2*S*,4*S*)-2,4-Dihydroxy-2,4-*O*-isopropylidene-6-heptenal (13-ent). A solution of thioacetals **15a** (47 mg, 0.165 mmol) in methanol (2 mL) at room temperature was treated with potassium carbonate (50 mg, 0.363 mmol) in one portion. After stirring an additional 1 h, this mixture was partitioned between ether (10 mL) and water (10 mL), the layers were separated, and the aqueous layer was extracted with additional portions of ether (3 × 1 mL). The organic extracts were combined and dried ($MgSO_4$), and the result was concentrated under reduced pressure to give a yellow oil. This oil was purified by radial chromatography (SiO_2; 10% Et_2O: hexane) to give aldehyde **13-ent** as a colorless oil (22.8 mg, 76%): R_f 0.36 (streak, SiO_2; 50% Et_2O:hexane); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.27 (q, 1H, J = 12.01 Hz), 1.45 (s, 6H), 1.72 (dt, 1H, J = 2.72, 12.97 Hz), 2.24 (dp, 2H, J = 6.57, 31.01 Hz), 3.90 (m, 1H), 4.25 (dd, 1H, J = 2.87, 12.27 Hz), 5.07 (m, 2H), 5.79 (m, 1H), 9.55 (s, 1H).

(2*R*,4*S*)-2,4-Dihydroxy-2,4-*O*-isopropylidene-6-heptenal (16a). A solution of thioacetals **15a** (50 mg, 0.149 mmol) in toluene (2 mL) at −78 °C under argon was treated with ^{i}Bu$_2$AlH (0.14 mL, 0.123 mmol, 0.91 M in hexanes). After 5 min, the reaction was quenched with water and the mixture allowed to warm to room temperature. The resulting mixture was partitioned between Et_2O (5 mL) and 1.0 M aqueous sodium potassium tartrate (5 mL), the layers were separated, and the aqueous layer was extracted with additional portions of ether (3 × 1 mL). The organic extracts were combined and dried ($MgSO_4$), and the result was filtered through a short plug of silica gel. Evaporation of the solvent under reduced pressure gave the product **16a** as a colorless oil (13 mg, 93%): R_f 0.52 (streak, SiO_2; 66% ether:hexane); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.33, 1.35 (singlets, 6H), 1.67 (m, 2H), 2.25 (m, 2H), 3.85 (m, 1H), 4.29 (dd, 1H), 5.08 (m, 2H), 5.78 (m, 1H), 9.87 (s, 1H).

(3*S*,5*R*)-1-(Benzyloxy)-5-[[dimethyl(2-methyl-2-propyl)silyl]oxy]-7-octen-3-ol (17). Copper(I) cyanide (159 mg, 1.77 mmol) was repeatedly (three times) subjected to azeotropically dehydration by slurrying the salt with toluene (1.0 mL), then concentrating *in vacuo* (at ca. 0.5 mm). The dry copper cyanide was then suspended in THF (5.0 mL), cooled to −78 °C, and stored under argon. In a separate vessel, *n*-butyllithium (1.37 mL, 3.37 mmol, 2.45 M in hexanes) was introduced dropwise to a cold (−78 °C) solution of [(benzyloxy)methyl]tri-*n*-butylstannane[49] (1.26 g, 3.46 mmol) in THF (5.0 mL). After an additional 20 min at −78 °C, the resulting bright yellow solution was transferred via a cooled cannula to the suspension of copper(I) cyanide. The resultant mixture was stirred at −78 °C for 30 min. To the freshly prepared cuprate reagent was added dropwise via a solution of epoxide **10s** (100 mg, 0.412 mmol) in THF (1.0 mL). After stirring an additional 2 min at −78 °C, the yellow solution was treated with boron trifluoride etherate (0.22 mL, 1.77 mmol) by slow dropwise addition. After stirring at −78 °C for 1 h, the mixture was allowed to warm to room temperature. The resulting black mixture was diluted with CH_2Cl_2 (20 mL) and poured into a vigorously stirred solution prepared from saturated aqueous NH_4Cl (20 mL) and concentrated aqueous NH_4OH (20 mL). After stirring for 1 h, the layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2 × 20 mL). The organic extracts were combined, dried ($MgSO_4$), and evaporated to give a colorless oil. The oil was purified by flash chromatography (SiO_2; gradient from 100% pentane to 20% Et_2O:pentane) to give adduct **17** as a colorless oil (142 mg, 94%): R_f 0.28 (SiO_2; 20% Et_2O:hexane); $[\alpha]^{23}_D$ = −12.48° (*c* 1.0, $CHCl_3$); IR (film) 698, 736, 776, 837, 1096, 1256, 2858, 2930, 3518 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.103 (s, 6H), 0.901 (s, 9H), 1.62 (m, 2H), 1.75 (m, 2H), 2.27 (m, 2H), 3.65 (m, 2H), 3.95 (m, 1H), 4.52 (s, 2H), 5.05 (m, 2H), 5.78 (m, 1H), 7.32 (s, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ −4.656, −4.081, −3.231, 18.423, 25.887, 26.674, 37.591, 42.682, 43.697, 68.618, 69.302, 72.051, 73.628, 117.793, 127.708, 128.442, 129.191, 134.672, 134.931, 138.695.

(3*S*,5*R*)-1-(Benzyloxy)-3,5-*O*-isopropylidene-7-octene-3,5-diol. The silyl ether alcohol **17** (38 mg, 0.104 mmol) was treated with 5% concentrated HCl/methanol (1 mL) and the mixture allowed to stir at room temperature for 5 min. This solution was then concentrated to an oil under reduced pressure and diluted with 2,2-dimethoxypropane (1 mL) at room temperature. After 20 min, the reaction mixture was concentrated under reduced pressure and the resulting colorless oil dissolved in 50% Et_2O:hexane. This solution was filtered through a 3 × 1 cm silica gel plug and concentrated under reduced pressure to give the isopropylidene as a colorless oil (30 mg, 100%): R_f 0.73 (SiO_2; 50% Et_2O:hexane); $[\alpha]^{23}_D$ = −12.58° (*c* 0.785, $CHCl_3$); IR (film) 729, 908, 1090, 1372, 2850, 2928, 2990 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.15 (q, 1H, J = 12.7 Hz), 1.38, 1.43 (singlets, 6H), 1.52 (dt, 1H, J = 2.43, 12.9 Hz), 1.75 (m, 2H), 2.15 (p, 1H, J = 7.0 Hz), 2.30 (p, 1H, J = 6.29 Hz), 3.56 (m, 2H), 3.86 (m, 1H), 4.07 (m, 1H), 4.50 (d, 2H, J = 1.8 Hz), 5.07 (m, 2H), 5.78 (m, 1H), 7.33 (s, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 20.31, 30.66, 36.98, 37.02, 41.29, 66.48, 66.65, 69.09, 73.42, 98.97, 117.48, 128.07, 128.79, 134.65, 138.98. Anal. Calcd for $C_{18}H_{26}O_3$: C, 74.45; H, 9.02. Found: C, 74.36; H, 8.99.

(3*S*,5*S*)-7-(Benzyloxy)-3,5-dihydroxy-3,5-*O*-isopropylideneheptanal (18). To a solution of the isopropylidene olefin (25 mg, 0.086 mmol) and 4-methylmorpholine-*N*-oxide (50 mg, 0.43 mmol) in 50% aqueous *tert*-butyl alcohol(2 mL) at room temperature was introduced a solution of osmium tetroxide in ^{t}BuOH (0.05 mL, 0.004 mmol, 0.0773 M in ^{t}BuOH). After stirring for 12 h at room temperature, the reaction mixture was treated with an excess of saturated aqueous Na_2SO_3 and the result allowed to stir for an additional 45 min. This mixture was partitioned between ethyl acetate (10 mL) and water (10 mL), the layers were separated, and the aqueous layer was extracted with additional portions of ethyl acetate (3 × 5 mL). The organic extracts were combined, dried (Na_2SO_4), and filtered through a short plug of Florisil. The filtrate was concentrated under reduced pressure to give the diol (29 mg) as a colorless oil [R_f 0.41 (SiO_2; ethyl acetate)]. Without purification, the diol was dissolved in ethanol (1 mL), cooled to 0 °C, and treated dropwise with a solution of $NaIO_4$ (92 mg, 0.43 mmol) in water (1 mL). After 10 min, the excess periodate was quenched by the addition of ethylene glycol (ca. 0.2 mL)

followed by stirring for an additional 10 min at room temperature. The mixture was partitioned between CH_2Cl_2 (10 mL) and water (10 mL), the layers were separated, and the resultant aqueous layer was extracted with CH_2Cl_2 (3 × 5 mL). The organic extracts were combined, dried ($MgSO_4$), filtered through a short plug of silica gel, and concentrated to give aldehyde **18** as a colorless oil (24 mg, 96%): R_f 0.32 (SiO_2; 50% Et_2O:hexane); $[\alpha]^{23}_D = -12.60°$ (*c* 1.0, $CHCl_3$); IR (film) 3000, 2900, 2720, 1730, 1450, 1380, 1120, 740, 700 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.26 (m, 1H), 1.36, 1.45 (singlets, 6H), 1.57 (m, 2H), 1.75 (m, 1H), 2.45 (m, 1H), 2.60 (m, 1H), 3.55 (m, 2H), 4.08 (m, 1H), 4.41 (m, 1H), 4.50 (d, 2H, J = 1.7 Hz), 7.33 (m, 5H), 9.78 (t, 1H, J = 1.82 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 20.20, 30.49, 36.88, 37.16, 50.23, 65.14, 66.32, 66.46, 73.43, 99.26, 128.01, 128.08, 128.80, 138.91, 201.39.

(3*S*,5*S*)-7-(Benzyloxy)-3,5-*O*-isopropylideneheptane-1,3,5-triol (22). To a solution of aldehyde **18** (834 mg, 2.85 mmol) in ethanol (20 mL) at room temperature was added a solution of $NaBH_4$ (55 mg, 1.47 mmol) in water (3 mL). At completion of the addition, the reaction was quenched by the addition of concentrated aqueous NH_3 (1 mL) and the result allowed to stir for 1 h. This mixture was partitioned between ether (50 mL) and water (50 mL), the layers were separated, and the aqueous layer was extracted with additional portions of Et_2O (3 × 15 mL). The organic extracts were combined, dried ($MgSO_4$), and filtered through a short plug of silica gel. The filtrate was concentrated under reduced pressure to give the alcohol product **22** as a colorless oil (828 mg, 99%): R_f 0.18 (SiO_2; 50% Et_2O:hexane); $[\alpha]^{23}_D = -9.00°$ (*c* 1.0, $CHCl_3$); IR (film) 3420, 3000, 2970, 1380, 1100, 740, 700 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.30 (m, 1H), 1.37, 1.45 (singlets, 6H), 1.49 (m, 1H), 1.72 (m, 4H), 2.55 (s (broad), 1H), 3.55 (m, 2H), 3.77 (m, 2H), 4.08 (m, 2H), 4.51 (d, 2H, J = 1.71 Hz), 7.38 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 20.34, 30.66, 36.91, 37.24, 38.58, 61.12, 66.45, 66.53, 69.64, 73.44, 99.10, 128.01, 128.10, 128.80, 138.89.

(3*S*,5*S*)-7-(Benzyloxy)-3,5-*O*-isopropylidene-1-(phenylthio)heptane-3,5-diol. A solution of alcohol **22** (528 mg, 1.79 mmol) and diphenyldisulfide (1.95 g, 8.95 mmol) in DME (25 mL) at room temperature under argon was treated with tri-*n*-butylphosphine (2.23 mL, 8.95 mmol). The resulting colorless solution was warmed to reflux where it was maintained for 24 h. This mixture was allowed to cool to room temperature at which time the solvent was removed under reduced pressure to give a colorless residue. This residue was purified by flash chromatography (SiO_2, gradient from 20% Et_2O: hexanes to 80% Et_2O:hexanes) to give the phenylthio ether as a nearly colorless, waxy solid (677 mg, 97%): mp 28–30 °C; R_f 0.38 (SiO_2; 20% Et_2O:hexane); $[\alpha]^{23}_D = +10.70°$ (*c* 1.0, $CHCl_3$); IR (film) 3000, 2920, 1100 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.17 (q, 1H, J = 11.69 Hz), 1.37, 1.41 (singlets, 6H), 1.46 (m, 1H), 1.75 (m, 4H), 3.01 (m, 2H), 3.55 (m, 2H), 4.04 (m, 2H), 4.50 (s, 2H), 7.32 (m, 10H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 20.30, 29.57, 30.64, 36.25, 37.00, 37.29, 66.46, 66.60, 67.78, 73.44, 99.07, 126.21, 128.00, 128.10, 128.80, 129.30, 129.40, 137.05, 138.95. Anal. Calcd for $C_{23}H_{30}O_3S$: C, 71.47; H, 7.82. Found: C, 71.56; H, 7.85.

(3*S*,5*S*)-7-(Benzyloxy)-3,5-*O*-isopropylidene-1-(phenylsulfinyl)heptane-3,5-diol (19). To a solution of phenyl sulfide (242 mg, 0.626 mmol) in ethanol (2 mL) at 0 °C was introduced a solution of magnesium monoperoxyphthalate (170 mg, 0.344 mmol) in water (2 mL) in a dropwise fashion. At completion of this addition, the reaction mixture was partitioned between CH_2Cl_2 (20 mL) and water (20 mL), the layers was separated, and the aqueous layer extracted with additional portions of CH_2Cl_2 (3 × 5 mL). The organic extracts were combined, dried ($MgSO_4$), and filtered through a short plug of silica gel, and the filtrate was concentrated under reduced pressure to give sulfoxides **19** as a colorless oil (251 mg, 99%, a mixture of sulfoxide isomers as judged by NMR): R_f 0.18 (SiO_2; 66% Et_2O:hexane); IR (film) 3000, 2940, 2890, 1060, 1010, 705, 670 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.08 (m, 1H), 1.25, 1.28, 1.32 (singlets, 6H), 1.41 (m, 1H), 1.8 (m, 4H), 2.9 (m, 2H), 3.5 (m, 2H), 3.8 (m, 1H), 4.0 (m, 1H), 4.5 (d, 2H), 7.3, 7.5, 7.6 (multiplets, 10H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 20.17, 20.46, 28.74, 29.53, 30.39, 30.70, 36.91, 37.18, 37.29, 53.54, 53.72, 53.86, 66.27, 66.35, 66.50, 67.85, 67.92, 68.40, 68.50, 73.45, 99.14, 124.32, 124.60, 127.93, 128.24, 128.63, 128.80, 129.46, 129.83, 131.19, 131.51, 138.90. Anal. Calcd for $C_{23}H_{30}O_4S$: C, 68.63; H, 7.51. Found: C, 68.89; H, 7.71.

(3*S*,5*S*,7*RS*,8*RS*,9*R*,11*R*)-1-(Benzyloxy)-3,5:9,11-di-*O*-isopropylidene-7-(phenylsulfinyl)-13-tetradecene-3,5,8,9,11-pentol (20). A solution of diisopropylamine (0.15 mL, 1.06 mmol) in THF (7 mL) at 0 °C was treated with *n*-butyllithium (0.40 mL, 2.40 M in hexanes, 0.973 mmol) and the result allowed to stir for an additional hour. At this time, the solution was cooled to −78 °C and treated with a solution of the sulfoxides **19** (356 mg, 0.885 mmol) in THF (2 mL). The resulting bright yellow solution was warmed to −60 °C where it was maintained for an additional hour. The solution was then cooled to −78 °C and treated with a solution of aldehyde **13** (81.5 mg, 0.442 mmol) in THF (1 mL). After 30 min, the reaction was quenched by the addition of saturated aqueous NH_4Cl (2 mL), and the result was allowed to warm to room temperature. This mixture was partitioned between CH_2Cl_2 (20 mL) and water (20 mL), the layers were separated, and the aqueous layer was extracted with additional portions of CH_2Cl_2 (3 × 10 mL). The organic extracts were combined, dried ($MgSO_4$), and concentrated under reduced pressure to yield a nearly colorless oil. This oil was purified by radial chromatography (SiO_2, gradient from 20% ethyl acetate: hexanes to 50% ethyl acetate:hexanes) to give the desired product **20** as a colorless oil (171 mg, 66%, mixture of diastereomers): R_f 0.28–0.44 (SiO_2; 50% ethyl acetate:hexane); IR (film) 3400, 3080, 3000, 2880, 1450, 1380, 1100, 750, 700 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.0 (m), 1.21, 1.28, 1.34, 1.37, 1.38, 1.43 (singlets), 1.5 (m), 1.75 (m), 2.2 (m), 2.94 (m), 3.15 (m), 3.55 (m), 3.8 (m), 4.08 (m), 4.5 (m), 5.03 (m), 5.74 (m), 7.3 (m), 7.6 (m), 7.7 (m); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.63, 19.99, 20.18, 20.29, 20.41, 21.47, 29.40, 30.33, 30.39, 30.47, 30.58, 30.64, 31.06, 32.16, 32.71, 33.97, 34.07, 36.82, 36.99, 37.50, 37.63, 41.20, 41.37, 60.07, 60.80, 60.94, 64.57, 66.12, 66.41, 66.50, 68.22, 68.57, 68.66, 69.00, 69.28, 69.93, 73.23, 73.45, 73.51, 73.59, 73.71, 76.26, 98.80, 98.92, 98.97, 99.20, 99.56, 117.69, 124.68, 125.08, 125.75, 125.97, 126.36, 128.06, 128.81, 129.39, 129.47, 129.63, 131.22, 131.39, 131.50, 131.72, 131.82, 134.25, 134.31, 134.41, 138.86, 141.91. Anal. Calcd for $C_{33}H_{46}O_7S$: C, 67.55; H, 7.90. Found: C, 67.96; H, 8.06.

(3*S*,5*S*,7*RS*,9*R*,11*R*)-1-(Benzyloxy)-3,5:9,11-di-*O*-isopropylidene-8-oxo-7-(phenylsulfinyl)-13-tetradecene-3,5,9,11-tetrol. A solution of alcohol **20** (64.6 mg, 0.110 mmol) in CH_2Cl_2 (2 mL) at room temperature was treated with a solution of the Dess–Martin periodinane[47] (51 mg, 0.121 mmol) in CH_2Cl_2 (3 mL) by dropwise addition. The resulting mixture was allowed to stir for 1 h, at which time it was diluted with Et_2O (15 mL), and then poured into 1.3 M aqueous NaOH (10 mL). After stirring vigorously for 10 min, the layers were separated and the organic layer was sequentially washed with 1.3 M aqueous NaOH (5 mL), water, and brine. The solution was dried ($MgSO_4$) and concentrated under reduced pressure to give a colorless oil which was subjected to purification by radial chromatography (SiO_2; 60% ethyl acetate:hexanes) to give the product ketone as a colorless oil (61.1 mg, 95%): R_f 0.47 (SiO_2; 50% ethyl acetate:hexane); IR (film) 3030, 3010, 2990, 2850, 1710, 1100, 740, 690 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.76, 0.90, 1.10 (multiplets), 1.23, 1.24, 1.26, 1.29, 1.30, 1.36, 1.38, 1.41, 1.44, 1.45 (singlets), 1.60–1.80 (multiplets), 1.90–2.25 (multiplets), 3.50 (m), 3.6–4.0 (m), 4.1–4.4 (doublets, J = 2.94 Hz), 4.54 (singlets), 4.6–4.7 (multiplets), 5.05 (m), 5.75 (m), 7.30 (m), 7.55 (m); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 19.60, 19.63, 19.78, 19.98, 20.09, 20.29, 20.35, 20.41, 29.84, 30.15, 30.30, 30.45, 30.50, 30.63, 31.20, 31.56, 31.90, 32.00, 32.07, 32.31, 36.49, 36.59, 36.87, 37.10, 37.14, 37.31, 37.39, 37.51, 40.71, 40.95, 41.19, 64.94, 65.24, 66.29, 66.35, 66.42, 66.45, 67.97, 68.65, 68.81, 68.89, 73.43, 75.24, 75.39, 75.48, 98.80, 99.04, 99.14, 99.55, 99.68, 117.69, 118.00, 125.14, 125.26, 125.67, 125.85, 126.07, 127.90, 128.23, 128.63, 128.78, 128.97, 129.38, 129.45, 129.64, 129.72, 131.75, 131.88, 132.00, 132.25, 133.89, 134.21, 134.34, 138.87, 141.23, 141.91, 142.43, 202.76, 203.26, 204.70. Anal. Calcd for $C_{33}H_{44}O_7S$: C, 67.78; H, 7.58. Found: C, 67.47; H, 7.49.

(3S,5S,9R,11R)-1-(Benzyloxy)-3,5:9,11-di-O-isopropylidene-8-oxo-13-tetradecene-3,5,9,11-tetraol (21, via the Sulfoxide Route). A solution of keto sulfoxide **20** (61.1 mg, 0.104 mmol) and tri-*n*-butyltin hydride (0.1 mL, 0.418 mmol) in toluene (3 mL) was brought to reflux then treated with 2,2'-azobisisobutryronitrile (10 mg, 0.061 mmol). After 5 min, the solution was treated with an additional portion of 2,2'-azobisisobutryronitrile (9 mg, 0.055 mmol). Following a total of 10 min at reflux, the solution was allowed to cool to room temperature, at which time the solvent was removed under reduced pressure to give a colorless oil. This oil was purified by radial chromatography (SiO_2; gradient from 20% Et_2O: hexanes to 50% Et_2O:hexanes) to give ketone **21** as a colorless oil (43.0 mg, 89%): R_f 0.71 (SiO_2; 50% ethyl acetate:hexane); $[\alpha]^{23}_D = +13.0°$ (*c* 1.0, $CHCl_3$); IR (film) 3060, 3020, 2980, 2910, 2860, 1710, 1375, 730, 685 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.08–1.33 (m, 2H), 1.35, 1.39, 1.45, 1.46 (singlets, 12H), 1.57–1.83 (m, 6H), 2.17 (p, 1H, J = 6.9 Hz), 2.30 (p, 1H, J = 6.43 Hz), 2.65 (m, 2H), 3.55 (m, 2H), 3.75–4.05 (m, 3H), 4.28 (dd, 1H, J = 2.83, 12.11 Hz), 4.49 (d, 2H, J = 1.9 Hz), 5.08 (m, 2H), 5.79 (m, 2H), 7.35 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.04, 15.71, 17.94, 19.90, 20.33, 27.27, 28.28, 30.00, 30.40, 30.62, 32.78, 33.68, 37.00, 37.40, 41.09, 66.27, 66.45, 66.61, 68.59, 68.88, 73.41, 75.15, 98.94, 99.35, 127.97, 128.05, 128.77, 134.00, 138.97, 210.61. Anal. Calcd for $C_{27}H_{40}O_6$: C, 70.41; H, 8.75. Found: C, 70.56; H, 8.62.

(3S,5S)-7-(Benzyloxy)-1-iodo-3,5-isopropylideneheptane-3,5-diol (23). To a solution of CH_2Cl_2 (5 mL) and iodine (360 mg, 1.38 mmol) at 0 °C was added triphenylphosphine (362 mg, 1.38 mmol). The resultant red solution was stirred an additional 10 min at 0 °C. To this solution was added imidazole (187 mg, 2.75 mmol), the result was stirred for 2 min, and then the alcohol **22** (444 mg, 1.10 mmol) in CH_2Cl_2 (1 mL) was introduced in a dropwise manner via cannula over a 5 min period (an additional 1 mL of CH_2Cl_2 was use to ensure complete addition). The resulting solution was stirred at 0 °C until the reaction was judged (by TLC) complete (3 h). At this time, the reaction was quenched at 0 °C by sequential dropwise addition of 3 mL each of saturated aqueous $NaHCO_3$ solution, saturated aqueous $Na_2S_2O_3$, and H_2O. The resulting biphasic mixture was stirred for 30 min at room temperature, then the layers were separated, and the aqueous was extracted with several portions of CH_2Cl_2 (4 × 10 mL). The organic layers were combined and dried ($MgSO_4$), and the resulting solution was carefully concentrated under reduced pressure to afford a yellow solid which was diluted with Et_2O and filtered through silica gel. The Et_2O was removed under reduced pressure and the residue subjected to flash chromatography (SiO_2, hexane to 4:1 hexane:Et_2O) to yield the desired iodide **23** as a clear oil (380 mg, 87%) (note: this product decomposed slowly at −20 °C): R_f 0.78 (SiO_2; 90% hexanes: Et_2O,); $[\alpha]^{23}_D = +12.1°$ (*c* 0.415, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz) δ 1.22 (m, 2H), 1.37 (s, 3H), 1.45 (s, 3H), 1.77 (m, 2H), 1.90 (m, 2H), 3.25 (m, 2H), 3.54 (m, 2H), 3.94 (m, 1H) 4.06 (m, 1H), 4.51 (s, 2H), 7.34 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 3.05, 20.33, 30.60, 36.86, 36,99, 40.08, 66.48, 66.58, 69.03, 73.47, 99.16, 128.03, 129.41, 128.82, 138.95. HLPC characterization t_R = 13.20 min; econosil (9:1 hexane:EtOH), 3 mL/min. Anal. Calcd for $C_{17}H_{25}O_3I$: C, 50.51; H, 6.23; Found: C, 51.0; H, 6.47.

(3S,5S,9R,11R)-1-(Benzyloxy)-3,5:9,11-di-O-isopropylidene-8-oxo-13-tetradecene-3,5,9,11-tetraol (21, via the Iodide Route). A solution of the iodide **23** (584 mg, 1.45 mmol) in Et_2O (8 mL) was cooled to −78 °C and then treated to dropwise addition of ^{t}BuLi in hexanes (1.92 mL, 1.51 M). After allowing the transmetalation to proceed at −78 °C for 30 min, a portion of freshly distilled aldehyde **13** (191 mg, 1.04 mmol) in Et_2O (3 mL) at −78 °C was introduced by dropwise addition via cannula (several small rinses with Et_2O ensured complete transfer). The resulting reaction mixture was stirred an additional 15 min at −78 °C and then allowed to warm to room temperature over 1 h. This mixture was cooled to 0 °C and quenched by careful dropwise addition of saturated aqueous NH_4Cl. The resultant layers were separated and the aqueous layer was extracted with several portions of CH_2Cl_2 (4 × 10 mL). The organic layers were combined, dried ($MgSO_4$), filtered through a short plug of silica gel, and concentrated under reduced pressure to afford a light yellow oil. This oil (580 mg) was then dissolved in CH_2Cl_2 (5 mL) and introduced (via cannula) to a stirred solution of the Dess–Martin periodinane[47] (666 mg, 1.5 mmol) in CH_2Cl_2 (15 mL) at 0 °C. The reaction was judged complete in 2 h (TLC), at which time a solution of $Na_2S_2O_3$/$NaHCO_3$ was introduced and the resultant biphasic mixture stirred for an additional hour. The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL). The organic layers were combined, dried ($MgSO_4$), and concentrated under reduced pressure to a light yellow oil. This oil was chromatographed (SiO_2) to give ketone **21** (390 mg, 82%).

(3S,5S,8R,9R,11R)-1-(Benzyloxy)-3,5:9,11-di-O-isopropylidene-13-tetradecene-3,5,8,9,11-pentol (24). A solution of ketone **21** (147 mg, 0.319 mmol) in THF (7 mL) at −110 °C was treated to a slow dropwise addition of lithium tri-*sec*-butylborohydride (0.70 mL, 0.70 mmol, 1.0 M in THF). At completion of the addition, the reaction mixture was allowed to warm to 0 °C and then treated with a solution of sodium perborate tetrahydrate (324 mg, 2.10 mmol) in water (7 mL). The resultant mixture was allowed to warm to room temperature and stirred an additional 2 h. This mixture was partitioned between CH_2Cl_2 (20 mL) and water (20 mL), the layers were separated, and the aqueous layer was extracted with additional portions of CH_2Cl_2 (3 × 5 mL). The organic extracts were combined, dried ($MgSO_4$), and filtered through a short plug of silica gel. Concentration of the filtrate under reduced pressure afforded the diastereomerically pure product **24** as a colorless oil (147 mg, 100%): R_f 0.29 (SiO_2, 50% Et_2O: hexane); $[\alpha]^{23}_D = +1.0°$ (*c* 1.0, $CHCl_3$); IR (film) 3400, 2990, 2920, 1370, 1190, 730, 690 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.10–1.31 (m, 2H), 1.36, 1.39, 1.41, 1.43 (singlets, 12H), 1.48–1.62 (m, 2H), 1.67–1.90 (m, 6H), 2.18, 2.32 (multiplets, 2H), 2.73 (d, 1H, J = 3.83Hz), 3.40 (m, 1H), 3.55 (m, 2H), 3.72 (m, 2H), 3.85 (m, 1H), 4.03 (m, 1H), 4.48 (d, 2H, J = 1.80 Hz), 5.07 (m, 2H), 5.80 (m, 1H), 7.32 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 20.33, 20.34, 27.96, 28.28, 30.13, 30.49, 30.64, 32.49, 32.55, 37.01, 37.47, 41.28, 66.52, 66.63, 68.67, 69.15, 72.44, 73.42, 74.17, 98.96, 99.19, 117.66, 127.97, 128.07, 128.78, 134.45. Anal. Calcd for $C_{27}H_{42}O_6$: C, 70.10; H, 9.15. Found: C, 70.23; H, 9.27.

(3S,5S,8R,9R,11R)-1-(Benzyloxy)-3,5:9,11-di-O-isopropylidene-8-[[Dimethyl(2-methyl-2-propyl)silyl]oxy]-13-tetradecene-3,5,9,11-tetrol. To a solution of alcohol **24** (131 mg, 0.283 mmol) and 2,6-lutidene (0.071 mL, 0.311 mmol) in CH_2Cl_2 (2.5 mL) at 0 °C was introduced *tert*-butyldimethylsilyl trifluoromethanesulfonate (0.071 mL, 0.311 mmol) by slow dropwise addition. After 2 min, the reaction was quenched by the addition of saturated aqueous $NaHCO_3$ (2 mL). The resulting mixture was diluted with ether (20 mL) and sequentially extracted with saturated aqueous $CuSO_4$ (2 × 5 mL), saturated aqueous $NaHCO_3$ (5 mL), and brine. This solution was dried ($MgSO_4$) and concentrated under reduced pressure to give a colorless residue. This oil was subjected to purification by flash chromatography (SiO_2, 20% Et_2O:hexanes) to give the product as a colorless oil (129 mg, 80%): R_f 0.43 (SiO_2; 20% Et_2O:hexane); $[\alpha]^{23}_D = +3.0°$ (*c* 1.0, $CHCl_3$); IR (film) 2980, 2940, 2840, 1370, 1100, 900, 830, 730 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.04 (s, 6H), 0.88 (s, 9H), 1.10–1.35 (m, 2H), 1.36, 1.38, 1.40,1.41 (singlets, 12H), 1.35–1.55 (m, 6H), 1.75 (p, 2H, J = 6.91 Hz), 2.23 (dp, 2H, J = 6.60 Hz), 3.54 (m, 2H), 3.66–3.90 (m, 3H), 4.02 (m, 1H), 4.50 (s, 2H), 5.08 (m, 2H), 5.81 (m, 1H), 7.34 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ −4.24, −3.59, 18.76, 20.11, 20.56, 26.43, 27.88, 30.50, 30.69, 32.03, 32.13, 37.07, 37.49, 41.42, 66.51, 66.69, 68.88, 69.37, 72.76, 73.43, 75.16, 98.85, 98.89, 117.43, 127.98, 128.08,128.79, 134.71, 138.99. Anal. Calcd for $C_{33}H_{56}O_6Si$: C, 68.71; H, 9.78. Found: C, 68.77; H, 9.86.

(3S,5S,8R,9R,11R)-1-(Benzyloxy)-3,5:9,11-di-O-isopropylidene-8-[[dimethyl(2-methyl-2-propyl)silyl]-oxy]-13-oxotridecane-3,5,9,11-tetrol (11). To a solution of silyl-protected **24** (103 mg, 0.179 mmol) and 4-methylmorpholine-*N*-oxide (104 mg, 0.893 mmol) in 50% aqueous *tert*-butyl alcohol (4 mL) at room temperature was introduced osmium tetroxide in *tert*-butyl alcohol (0.12 mL, 0.009 mmol, 0.0773

M). After stirring for 4 h at room temperature, the reaction was quenched by the addition of saturated aqueous $Na_2S_2O_3$ (4 mL) and stirring an additional 45 min. This mixture was next partitioned between ethyl acetate (20 mL) and water (20 mL), the layers were separated, and the aqueous layer was extracted with several portions of ethyl acetate (3 × 5 mL). The organic extracts were combined, dried ($MgSO_4$), and filtered through a short plug of Florisil. Concentration of the filtrate under reduced pressure yielded a colorless oil (100 mg). This residue was dissolved in ethanol (2 mL), cooled to 0 °C, and then treated by slow dropwise addition with sodium periodate (175 mg, 0.818 mmol, 0.5 M in water). At the completion of the addition, the reaction was quenched by treatment with excess ethylene glycol followed by stirring for 10 min. The resultant mixture was partitioned between CH_2Cl_2 (10 mL) and water (10 mL), the layers were separated, and the aqueous layer was extracted with fresh CH_2Cl_2 (3 × 2 mL). The organic extracts were combined, dried ($MgSO_4$), and filtered through a short plug of silica gel. Concentration of the filtrate under reduced pressure yielded aldehyde **11** as a colorless oil (85 mg, 82%): R_f 0.68 (SiO_2; 50% ethyl acetate: hexane); $[\alpha]^{23}_D$ = +2.0° (*c* 1.0, $CHCl_3$); IR (film) 2990, 2920, 2840, 1720, 1100, 730 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.46 (s, 6H), 0.87 (s, 9H), 1.05–1.34 (m, 2H), 1.35, 1.36, 1.41, 1.43 (singlets, 12H), 1.35–1.55 (m, 6H), 1.75 (m, 2H), 2.53 (m, 2H), 3.55 (m, 3H), 3.76 (m, 2H), 4.03 (m, 1H), 4.37 (m, 1H), 4.50 (d, 2H, J = 1.31 Hz), 7.32 (m, 5H), 9.77 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ −4.23, −3.62, 15.71, 18.71, 19.99, 20.35, 26.40, 27.87, 30.13, 30.33, 30.69, 32.15, 37.06, 37.47, 50.36, 65.00, 66.28, 66.49, 66.67, 69.36, 72.59, 73.42, 74.93, 98.86, 99.23, 127.97, 128.07, 128.78, 138.99, 201.42. Anal. calcd for $C_{32}H_{54}O_7Si$: C, 66.40; H, 9.40. Found: C, 66.33; H, 9.31.

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