10 Hz, 1 H, H-5), 3.09 (br t, J = 11.5 Hz, 1 H, H-18), 2.92 (s, 3 H, OCH_3), 2.47 (m, 1 H, H-34), 2.41 (t, J = 10.5 Hz, 1 H, H-16), 2.41 (dd, J = 16.9, 6.8 Hz, 1 H, H-2), 2.30 (dd, J = 13.0, 4.9 Hz, 1 H, H-14), 2.24 (br d, J = 12 Hz, 1 H, H-18), 2.12 (dd, J = 17.1, 5.7 Hz, 1 H, H-2), 2.06, 2.03, 1.98 (singlets, 3 H each, $CH_3C(O)O$), 1.96 (m, 1 H, H-36), 1.40 (br t, J = 12 Hz, 1 H, H-14), 1.10 (m, 1 H, H-10), 0.95 (m, 1 H, H-4), 1.15 (d, J = 6.4 Hz, 3 H, *Me*-37), 0.94 (d, J = 6.5 Hz, 3 H, *Me*-34), 0.87 (d, J = 7.0 Hz, 3 H, *Me*-36), 1.80–1.15 (m, 8 H total, H-4, H-6, H-7, H-10, H-12); HRMS calcd for $C_{55}H_{78}O_{17}$ 1010.5239, found 1010.5274. Phase-sensitive ^{1}H COSY spectra of **36a** and **36b** were collected by the TPPI method: 512 experiments of 16 scans each; relaxation delay of 1.5 s; size 1 K data points; spectral width in F1 and F2 6000 Hz; no zero filling in F2, and to 1 K in F1, apodization in both dimensions squared sinebell.

Acknowledgment. We wish to express our many thanks to Dr. C. Cimarusti, The Squibb Institute for Medical Research, for generous samples of amphotericin B and to Professor K. Nakanishi, Columbia University, for his assistance in the CD studies. Our thanks are also due to John Dykins of this department for his superb mass spec assistance and helpful comments. This work was financially supported by the National Institutes of Health, Merck Sharp & Dohme, and Hoffman-La Roche, Inc.

Total Synthesis of Amphoteronolide B and Amphotericin B. 1. Strategy and Stereocontrolled Construction of Key Building Blocks†

K. C. Nicolaou,* R. A. Daines, J. Uenishi, W. S. Li, D. P. Papahatjis, and T. K. Chakraborty

Contribution from the Department of Chemistry, University of Pennsylvania, Philadelphia, Pennsylvania 19104. *Received October 19, 1987*

Abstract: The retrosynthetic analysis and strategy for the total synthesis of amphotericin B (**1**) and amphoteronolide B (**2**) is discussed. Focusing on subtle and repeated structural units, a retrosynthetic scheme was constructed that led to the recognition of readily available and enantiomerically related compounds as starting materials for the total synthesis of **1** and **2**. Thus, the four key building blocks **8–11** were defined as subtargets and synthesized in optically active forms. Segments **8** and **11** were derived from epoxide **15**, which is readily available from (+)-DET. Segments **9** and **10** were obtained from (+)- and (−)-xylose, respectively, or from the prostereogenic allylic alcohol **14** and (−)- and (+)-DET, respectively, via a stereocontrolled sequence based on the Sharpless asymmetric epoxidation reaction. This latter sequence provides a general and flexible entry into the 1,3,5,···$(2n + 1)$ polyol series of compounds, reminiscent of substructures occurring in polyene macrolide antibiotics.

Amphotericin B (**1**) and its aglycon amphoteronolide B (**2**) represent important synthetic targets,[1] providing unique opportunities for the development of both new and existing synthetic technologies. Accomplishments in this area may have broad applications to the problem of structure elucidation and eventual total synthesis of the biomedically important polyene macrolide antibiotics. In the preceding paper[2] we described some chemistry of amphotericin B (**1**) culminating in its conversion[3,4] to its aglycon amphoteronolide B (**2**). In this series of papers we describe the total synthesis of both amphoteronolide B (**2**) and amphotericin B (**1**). In the present paper we describe the general synthetic strategy and the stereocontrolled construction of the requisite key building blocks[5] for this undertaking.

Results and Discussion

Strategy and Retrosynthetic Analysis. Our general strategy for the construction of amphotericin B (**1**) and its aglycon (**2**) is presented in Scheme I. The heptaenone **3** was recognized as the key intermediate from which both **1** and **2** could be derived. Thus, stereocontrolled reduction of the carbonyl group of **3**, or of a compound derived from **3**, was expected to lead to an amphoteronolide B derivative from which target **2** could be liberated. Glycosidation of amphoteronolide B derivatives derived from **3** with a mycosamine equivalent followed by functional group manipulations was projected as the final sequence toward amphotericin B (**1**). CPK models of **3** and analogous structures pointed to a stereoselective reduction by peripheral attack, although it was not a priori possible to predict with confidence which of the two possible C-19 epimers would result.[2] However, if necessary, inversion of configuration at C-19 would correct the situation at that stage. Despite the plethora of macrolide-forming reactions[6] currently at our disposal, the construction of the heptaenone **3**, due to its size and complexity, presented a rather formidable problem. Inspection of **3** revealed two rather obvious strategic bonds for disconnection in the retrosynthetic sense, on the basis of a macrocyclization reaction, namely the lactone linkage and the C-20 double bond.

† This paper is dedicated with respect and affection to Professor E. J. Corey on the occasion of his 60th birthday.

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(4) Nicolaou, K. C.; Daines, R. A.; Ogawa, Y.; Chakraborty, T. K. *J. Am. Chem. Soc.*, accompanying paper in this issue.

(5) Preliminary communication: Nicolaou, K. C.; Daines, R. A.; Uenishi, J.; Li, W. S.; Papahatjis, D. P.; Chakraborty, T. K. *J. Am. Chem. Soc.* **1987**, *109*, 2205.

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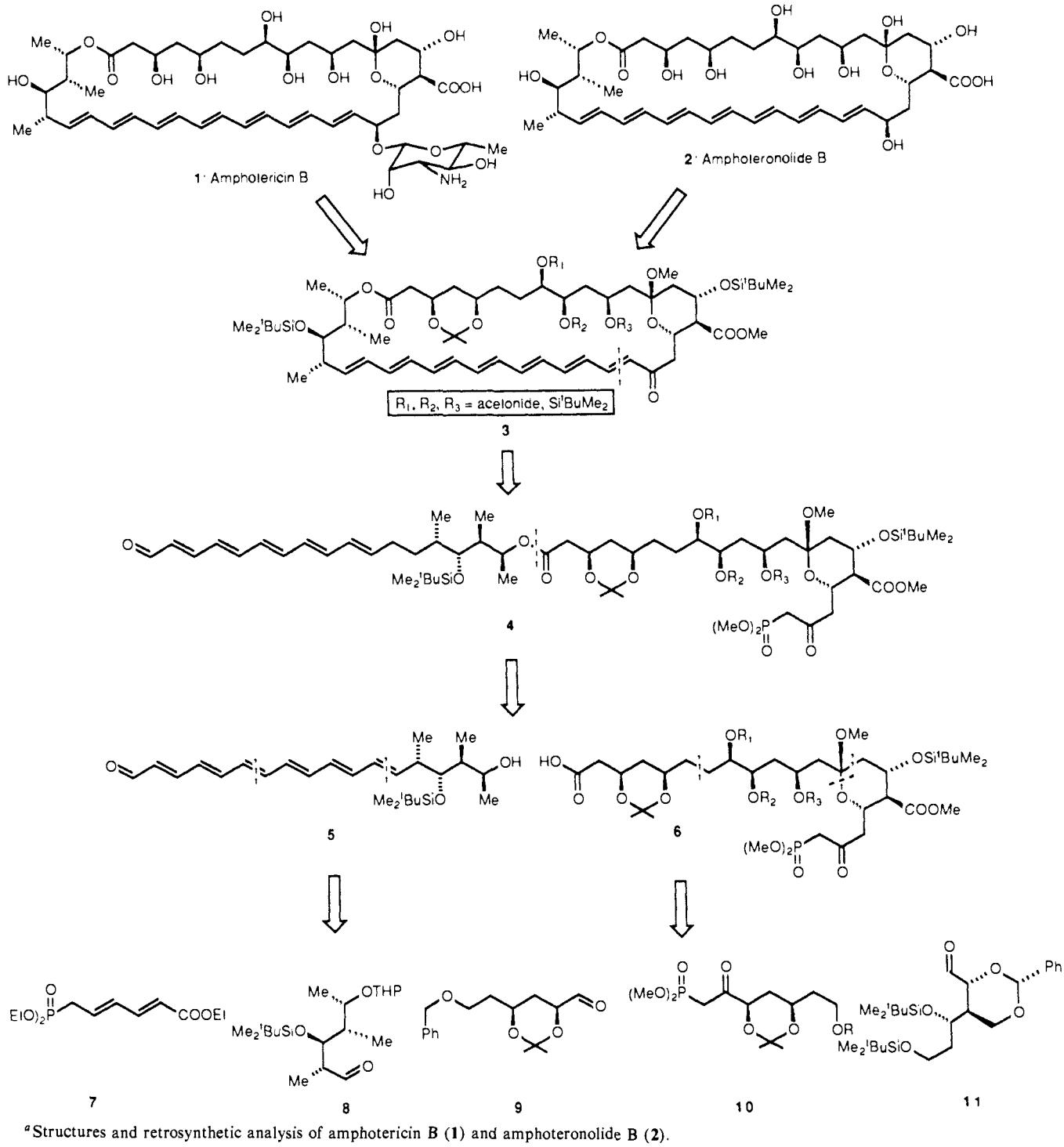
Scheme I[a]



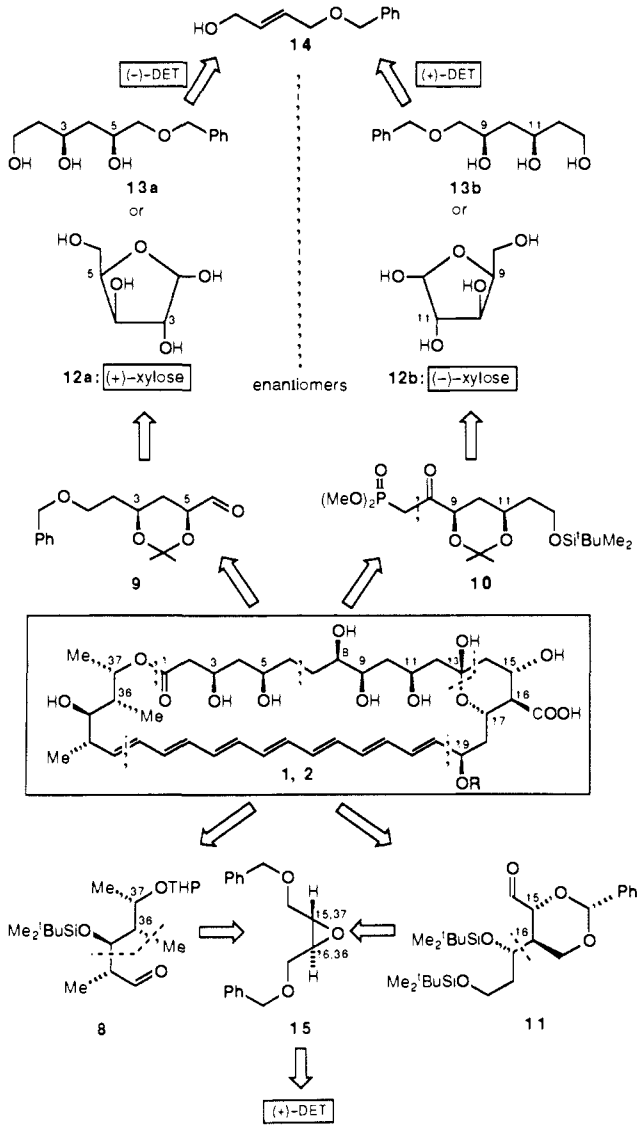
[a] Structures and retrosynthetic analysis of amphotericin B (**1**) and amphoteronolide B (**2**).

On the basis of our past experiences in the macrolide field, and particularly in the 16-membered ring series exemplified by tylosin,[7] we projected a keto phosphonate aldehyde condensation as the key macrocyclization step for the construction of **3**. Thus, disconnection of **3** as indicated by the dotted line unravels the long-chain keto phosphonate aldehyde **4** as a potential precursor to **3**. The presence of the rather rigid polyene system, the numerous substituents as well as the pyran, and the two acetonide rings in **4** was expected to facilitate the cyclization reaction by decreasing the degrees of rotational freedom in this precursor. Proceeding with the retrosynthetic analysis, compound **4** can then be dissected at the indicated ester bond, leading to the two advanced intermediates, hydroxy aldehyde **5** and keto phosphonate acid **6**, and precipitating a convergent strategy. The convergency of the sequence is amplified by the remaining disconnections indicated in Scheme I, leading to the key building blocks **7**–**11**. Thus, sequential coupling of **8** with two molecules of **7** followed by simple functional group manipulations was expected to lead to **5**, whereas sequential coupling of **9** with **10** and then **11** with appropriate manipulations was to provide the requisite advanced intermediate **6**. A requirement we set for the projected strategy was that it should provide the target molecules in their naturally occurring enantiomeric forms.

In the selection of optically active starting materials for the total syntheses at hand, the recognition of important, but subtle symmetry in the molecules of amphotericin B (**1**) and amphoteronolide B (**2**) played a crucial role. Scheme II presents a

(7) Nicolaou, K. C.; Seitz, S. P.; Pavia, M. R. *J. Am. Chem. Soc.* **1982**, *104*, 2030.

Scheme II[a]

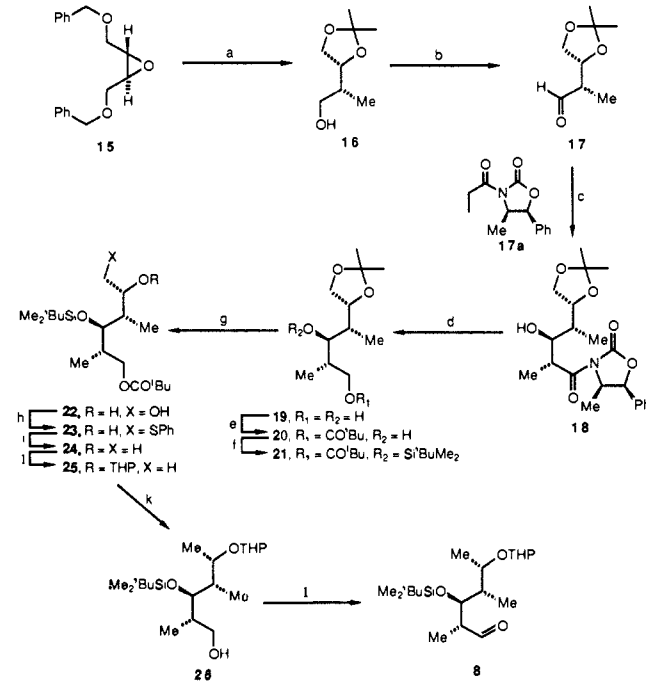


[a] Symmetry recognition and retrosynthetic analysis of amphotericin B(**1**) and amphoteronolide B(**2**).

retrosynthetic analysis of subtargets **8–11**, which focuses on these symmetry elements, allowing the design of a synthetic strategy that utilizes the readily available enantiomers of xylose and tartaric acid as starting materials and/or chiral auxiliaries to secure optically active materials. Thus, following the indicated disconnections in Scheme II, the initially generated key intermediates **8–11** were further traced back to epoxide **15** (**8**, **11** ⇒ **15**), (+)-xylose (**12a**) (**9** ⇒ **12a**), and (−)-xylose (**12b**) (**10** ⇒ **12b**). Alternatively, intermediates **9** and **10** may be traced back to the enantiomeric tetraol derivatives **13a** and **13b**, respectively. It was further recognized that enantiomerically pure epoxide **15** is readily available from (+)-DET (diethyltartrate), whereas (−)- and (+)-DET can be used as chiral auxiliaries to build the requisite absolute stereochemistry in intermediates **13a** and **13b**, respectively, from the prochiral starting material **14** via a Sharpless asymmetric epoxidation.[8] The numbering in the structures of Scheme II traces the origin of selected carbon centers of amphotericin B (**1**) and amphoteronolide B (**2**).

Construction of Building Blocks 8 and 11. Scheme III outlines the stereocontrolled construction of building block **8** from the readily available epoxide **15**.[9] Thus, **15** was converted to acetonide

Scheme III[a]



[a] *Synthesis of building block* **8**. *Reagents and Conditions*: (a) Reference 1; (b) 2.0 equiv of PCC, 4 Å MS, CH_2Cl_2, 2.5 h, 94%; (c) 0.8 equiv of **17a**, 0.84 equiv of n-Bu_2BOTf, 0.96 equiv of i-Pr_2EtN, CH_2Cl_2, 0 °C, 0.5 h, then −78 °C, add **17**, 1.5 h, 72%; (d) 2.2 equiv of $LiBH_4$, THF, −40 to −30 °C, 4 h, 100%; (e) 2.0 equiv of t-BuCOCl, pyridine, 0–25 °C, 4 h, 90%; (f) 1.5 equiv of t-$BuMe_2OTf$, 2.0 equiv of 2,6-lutidine, CH_2Cl_2, 0–25 °C, 0.5 h, 97%; (g) AcOH–THF–H_2O, 45 °C, 45 h, 72%; (h) 1.55 equiv of PhSSPh, 1.5 equiv of n-Bu_3P, 0–25 °C, 6 h, 95%; (i) Raney Ni, EtOH, 25 °C, 2 h, 98%; (j) 1.1 equiv of dihydropyran, CSA catalyst, CH_2Cl_2, 0 °C, 0.5 h, 96%; (k) 2.5 equiv of DIBAL, CH_2Cl_2, −78 °C, 0.5 h, 98%; (l) 2.0 equiv of PCC, 5.0 equiv of NaOAc, 4 Å MS, CH_2Cl_2, 25 °C, 2.5 h, 75%.

alcohol **16** according to our previously described sequence[9] and thence to aldehyde **17** by oxidation (PCC, 94% yield). Aldehyde **17** was then condensed with the boronenolate derived from oxazolidone **17a** according to Evans' procedure[10] (n-Bu_2BOTf, i-Pr_2EtN) to give adduct **18** in 72% yield and ca. 11:1 stereoselectivity.[11] Reduction of this mixture (**18**) to the diol **19** ($LiBH_4$) followed by selective pivaloate ester formation (t-BuCOCl–Pyr) led to compound **20** in 90% overall yield as a mixture of diastereoisomers. At this stage the major product (**20**) was chromatographically separated from the minor diastereoisomer (silica, 50% ether in petroleum ether, R_fs 0.45 (major) and 0.32 (minor)). The structure of the major aldol product was as expected on the basis of Evans' results[12] and was confirmed by its conversion to intermediate **24**, identical with a sample obtained from amphotericin B (**1**) by degradation.[1] Thus, silylation of **20** (t-$BuMe_2SiOTf$, 2,6-lutidine) gave **21** (97%), followed by sequential deacetonization (AcOH–THF–H_2O, 2:1:1), selective phenylsulfide formation (PhSSPh–n-Bu_3P) and desulfurization (Raney Ni) to give compounds **22** (72%), **23** (95%), and **24** (98%), respectively. The tetrahydropyranyl (THP) ether **25** was then prepared from **24** (dihydropyran, CSA) in 96% yield. Finally, deprotection of the primary alcohol of **25** by DIBAL reduction (98%) followed by PCC oxidation (75%) led to the desired building block **8** via intermediate **26**.

(8) For excellent recent reviews on the Sharpless asymmetric epoxidation reaction see: Rossiter, B. E. (pp 193) and Finn, M. G.; Sharpless, K. B. (pp 247) In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic: New York, 1985; Vol. 5.

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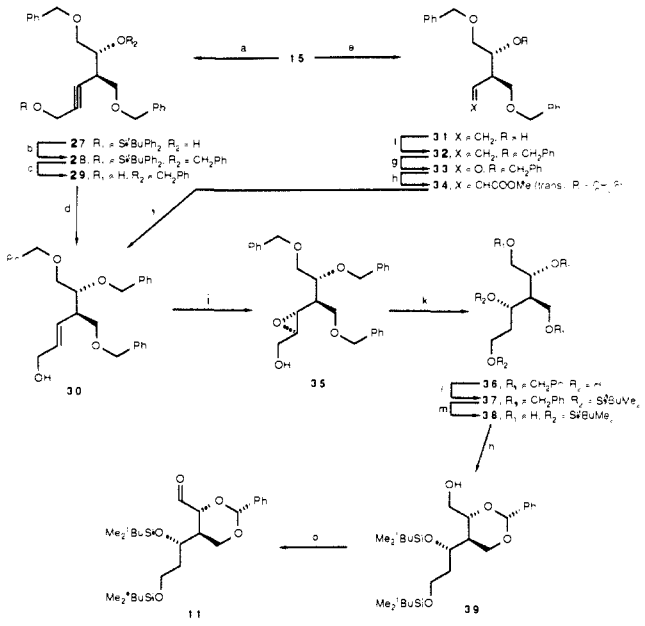
(11) Precise stereochemistry of the minor isomer of **18** was not assigned.

(12) For an excellent review on the Evans stereoselective aldol condensation, see: Evans, D. A.; Nelson, J. V.; Taber, T. J. In *Topics in Stereochemistry*; Allinger, N. L., Eliel, E. L., Wilen, S. H., Eds.; 1982; Vol. 13, p 1.

(13) Suzuki, T.; Saimoto, H. I.; Tomioka, H.; Oshima, K.; Nozaki, H. *Tetrahedron Lett.* **1982**, *23*, 3597.

Scheme IV[a]



[a] *Synthesis of building block* **11**. *Reagents and Conditions*: (a) 2.5 equiv of $Et_2AlC{\equiv}CCH_2OSi$-*t*-$BuPh_2$, hexane–toluene, −78 → 0 °C, 0.5 h, 85%; (b) 1.2 equiv of NaH, 1.2 equiv of $PhCH_2Br$, THF, 0–25 °C, 16 h, 95%; (c) 1.5 equiv of Bu_4NF, THF, 0–25 °C, 3 h, 87%; (d) 1.7 equiv of Red-Al, Et_2O, 0–25 °C, 3 h, 93%; (e) 2.3 equiv of $CH_2{=}CHMgBr$, 1.0 equiv of CuI, THF, −78 → 0 °C, 1 h, 91%; (f) 1.3 equiv of NaH, 1.3 equiv of $PhCH_2Br$, THF, 0 → 25 °C, 16 h, 93%; (g) O_3, CH_2Cl_2, 0.3 equiv MeOH, −78 °C and then 10 equiv of Me_2S, −78 → 25 °C, 3 h, and then 0.5 equiv of Ph_3P, 25 °C, 0.5 h, 100%; (h) 1.5 equiv of $Ph_3P{=}CHCOOEt$, benzene, 25 °C, 16 h, 85% (trans); (i) 2.2 equiv of DIBAL, CH_2Cl_2, −78 °C, 0.5 h, 93%; (j) 1.5 equiv of (−)-DET, 2.2 equiv of TBHP, 1.2 equiv of $Ti(i\text{-}PrO)_4$, CH_2Cl_2, −20 °C, 16 h and then tartaric acid, 75%; (k) 3.5 equiv of Red-Al, THF, 0 °C, 4 h, 96%; (l) 2.9 equiv of *t*-$BuMe_2SiCl$, 3.0 equiv of imidazole, DMF, 0–25 °C, 12 h, 92%; (m) H_2, 20% $Pd(OH)_2$–C, EtOH, 25 °C, 0.5 h, 95%; (n) 2.5 equiv of $PhCH(OMe)_2$, CSA catalyst, benzene, 25 °C, 1 h, 80%; (o) 6.0 equiv of SO_3·pyr, 10.0 equiv of Et_3N, DMSO, CH_2Cl_2, 25 °C, 4 h, 94%.

The synthesis of building block **11** from epoxide **15**[9] was effectively accomplished as shown in Scheme IV. The key intermediate **30** was reached via two alternative pathways. In the first approach the epoxide **15** was reacted with [[(*tert*-butyldiphenylsilyl)oxy]propargyl]diethylalane ($Et_2AlC{\equiv}CCH_2OSi$-*t*-$BuPh_2$)[13] to afford acetylenic alcohol **27** in 85% yield, which was benzylated (NaH, $PhCH_2Br$, 91%) and subsequently desilylated (*n*-Bu_4NF, 95%) leading to **29** via **28**. Stereoselective reduction of **29** with excess Red-Al (Aldrich) led to the trans allylic alcohol **30** in 97% yield. The second approach to intermediate **30** began with opening of epoxide **15** by employing vinylmagnesium bromide in the presence of cuprous iodide to afford hydroxy olefin **31** in quantitative yield. Benzylation of this alcohol (NaH, $PhCH_2Br$, 90%) followed by ozonolysis–reduction (O_3 then Me_2S and Ph_3P, 100%) led to aldehyde **33** via intermediate **32**. Without purification, aldehyde **33** was subjected to a Wittig olefination ($Ph_3P{=}CHCOOEt$) to give the *E*-α,β-unsaturated ester **34** in 85% yield. The accompanying *Z* isomer of **34** (ca. 15% yield) was conveniently separated from **34** at this stage by chromatography. With compound **30** in hand, conversion to subtarget **11** was effected as follows. Reduction of **34** with DIBAL led cleanly (93% yield) to the desired intermediate **30**. Sharpless asymmetric epoxidation of **30** [(−)-DET] smoothly furnished epoxide **35** in 82% yield (single isomer isolated). Regioselective epoxide opening of **35** with Red-Al[14] (97%) followed by silylation (*t*-$BuMe_2SiCl$–imidazole, 89%) and debenzylation led to compound **38** via intermediates **36** and **37**. The key engagement of the 1,3-diol system in **38** as a six-membered benzylidene[15] was carried out with $PhCH(OMe)_2$ under acid catalysis (CSA) in benzene solution, giving **39** (80%), which was then smoothly oxidized to the subtarget **11** by means of SO_3·Pyr–Et_3N–DMSO in CH_2Cl_2 (94% yield).

Construction of Building Blocks 9 and 10. The Carbohydrate Approach. As the retrosynthetic analysis of Scheme II shows, a potential route to building blocks **9** and **10** involves (+)- and (−)-xylose (**12a** and **12b**, respectively) as starting materials. The required transformations involve proper functionalization of the carbohydrate framework and deoxygenation at C-3 as detailed in Scheme V. Thus, **12a** was converted to its monoacetonide **40a** by diacetonization followed by selective removal of the more labile six-membered ring acetonide,[16] in 50% overall yield, and thence to the monosilyl ether **41a** by exposure to slightly over stoichiometric amounts of *t*-$BuPh_2SiCl$ in the presence of imidazole in DMF (96% yield). Deoxygenation of **41a** at C-3 was then achieved by one of two ways. The first method involved preparation of derivative **42a** (PhOC(S)Cl–Pyr, DMAP, 94%) and its radical-mediated deoxygenation[17] (*n*-Bu_3SnH–AIBN) to afford **43a** (77% yield). The second method for the conversion of **41a** to **43a** involved reductive cleavage (Superhydride, 90% yield) of iodide **59a** (Scheme V) prepared from **41a** via the corresponding triflate[18] (80% overall yield). The liberation of lactol **44** from **43a** required the use of BCl_3[19] at −78 °C (90%). Subsequent condensation of lactol **44** with methylenetriphenylphosphorane ($Ph_3P{=}CH_2$, generated from $CH_3PPh_3{}^+Br^-$ and *n*-BuLi in THF) to form olefin **45** proceeded in optimum yield (67%) when **44** was first treated with NaH (1.0 equiv). Engagement of the 1,3-diol system of **45** as an acetonide furnished **46** in 90% yield, while hydroboration–oxidation (Sia_2BH–$NaOH/H_2O_2$) of the terminal olefin in **46** gave primary alcohol **47** (88% yield). Installment of a benzyl ether in **47** (KH–$PhCH_2Br$, 85%) followed by desilylation (*n*-Bu_4NF, 96%) led to compound **49** via **48**. Finally, oxidation of **49** with SO_3·Pyr–Et_3N–DMSO system led to the desired building block **9** in 75% yield.

The synthesis of key intermediate **10** from (−)-xylose (**12b**) proceeded, in its initial stages, along similar lines as the above described construction of **9**. Thus, **12b** was converted to **43b** via intermediates **40b–42b** exactly as described for **12a** → **43a**. By use of standard chemistry, the silyl protecting group in **43b** was exchanged for a benzyl group, leading to intermediate **51** via **50** (96 × 95%). Deacetonization of **51** under acid conditions (HCl–H_2O/DME) gave lactol **52** in 75% yield, which was subjected to the methylenation–acetonization reaction sequence described above for the conversion **44** → **46**, to afford olefin acetonide **54** via 1,3-diol **53** (67–90%). Hydroboration of **54** as described above for **46** → **47** led to primary alcohol **55** in 88% yield. Standard methods then allowed the formation of silyl ether **56** (92%), alcohol **57** (H_2, 10% Pd–C, 98% yield), and methyl ester **58** ($NaIO_4$–RuO_4 catalyst, CH_3CN–CCl_4–H_2O[20] and then CH_2N_2, 76% overall yield). Finally, reaction of methyl ester **58** with $LiCH_2P(O)(OMe)_2$ furnished the desired keto phosphonate **10** in 96% yield.

Construction of Building Blocks 9 and 10. The Sharpless Asymmetric Epoxidation Approach. Inspection of the structures of several members of the polyene macrolide class,[21] including amphotericin B (**1**), reveals molecular fragments belonging to the series of 1,3,5,···(2*n* + 1) polyols. In order to provide a general and flexible solution to the problem of constructing such com-

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(16) Levene, P. A.; Raymond, A. L. *J. Biol. Chem.* **1933**, *102*, 317.

(17) Robins, M. J.; Wilson, J. S. *J. Am. Chem. Soc.* **1981**, *103*, 932.

(18) Binkley, R. W.; Ambrose, M. G.; Hehemann, D. G. *J. Org. Chem.* **1980**, *45*, 4387.

(19) Tewson, T. J.; Welch, M. J. *J. Org. Chem.* **1978**, *43*, 1090.

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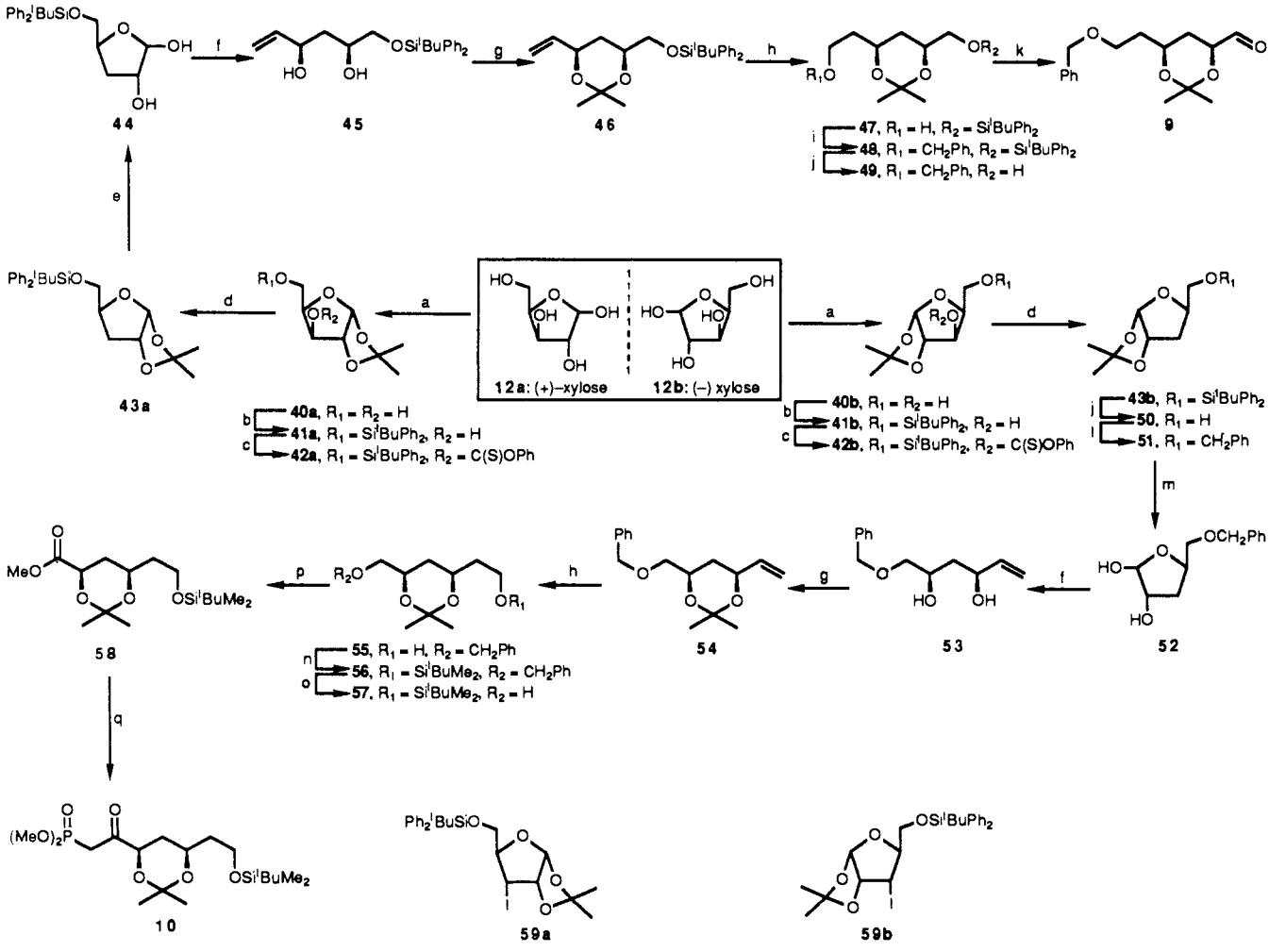
(21) See for example: *Macrolide Antibiotics, Chemistry, Biology and Practice*; Omura, S., Ed.; Academic: New York, 1984.

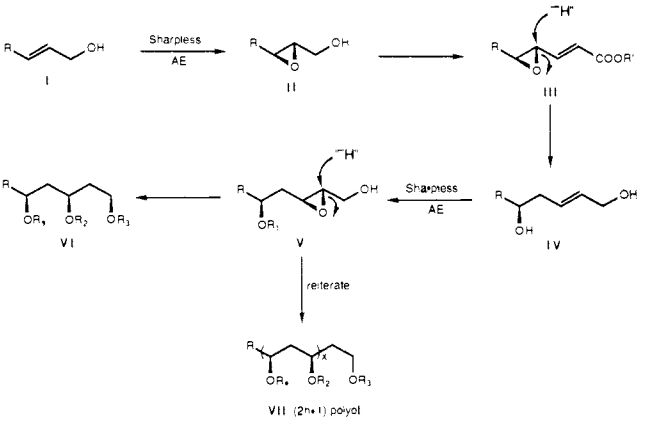
Scheme V[a]



[a] *Construction of building blocks* **9** *and* **10** *from* (+)- *and* (−)-*xylose* **12a** *and* **12b**. *Reagents and Conditions*: (a) Reference 15; (b) 1.1 equiv of t-$BuPh_2SiCl$, 4.0 equiv of imidazole, DMF, 0–25 °C, 1 h, 94%; (c) 1.5 equiv of PhOC(S)Cl, 2.6 equiv of pyr, DMAP catalyst, CH_2Cl_2, 0–25 °C, 15 h, 94%; (d) 1.1 equiv of n-Bu_3SnH, AIBN catalyst, toluene, 80 °C, 1 h, 77%; (e) 1.0 equiv of BCl_3, CH_2Cl_2–hexane (1:2), −78 °C, 10 min, 90%; (f) 1.0 equiv of NaH, and then 3.0 equiv of $Ph_3P{=}CH_2$ (from $CH_3PPh_3{}^+Br^-$ and n-BuLi in THF), THF, −20 → 25 °C, 3.5 h, 67–70%; (g) $Me_2C(OMe)_2$, CSA catalyst 25 °C, 1 h, 88–90%; (h) 2.2 equiv of Sia_2BH, THF, 0 °C, 1.5 h, and then $NaOH$–H_2O_2 workup, 86–93%; (i) 1.3 equiv of KH, 1.3 equiv of $PhCH_2Br$, THF, 0–25 °C, 14 h, 85%; (j) 1.1 equiv of n-Bu_4NF, THF, 0–25 °C, 0.5 h, 92%; (k) 5.0 equiv of SO_3·pyr, 5.0 equiv of Et_3N, 0.3 M in DMSO–CH_2Cl_2 (2:1), 25 °C, 30 min, 92%; (l) 1.3 equiv of NaH, 1.1 equiv of $PhCH_2Br$, 0.01 equiv of n-Bu_4NI, THF, 0–25 °C, 2 h, 95%; (m) dilute HCl, DME–H_2O (2:1), reflux, 1 h, 95%; (n) 1.1 equiv of t-$BuMe_2SiCl$, 4.0 equiv of imidazole, DMF, 0–25 °C, 1 h, 92%; (o) H_2, 20% Pd–C, EtOH, 25 °C, 98%; (p) 5.0 equiv of $NaIO_4$, RuO_4 catalyst, CH_3CN–CCl_4–H_2O (2:2:3), 25 °C, 6 h, and then CH_2N_2, 76% overall; (q) 2.2 equiv of $(MeO)_2P(O)CH_2Li$, THF, −78 → 0 °C, 1 h, 96%.

pounds with stereochemical control, we set out to engineer a sequence based on the powerful asymmetric epoxidation reaction developed by Sharpless.[8] We expected such a sequence to be useful, not only for attacking the problem at hand, but also in other structural and synthetic studies, particularly in the polyene macrolide series. Scheme VI outlines the designed sequence,[22] starting from readily available allylic alcohols (I). Thus Sharpless asymmetric epoxidation (AE) on I would lead to epoxide II (or its enantiomer, if so desired), which could easily be transformed to compound III by oxidation–olefination. This latter operation was anticipated to differentiate between the two epoxide carbons, rendering the one adjacent to the double bond more susceptible to nucleophilic attack by hydride. Thus reductive opening of III as indicated in Scheme VI was to lead, upon concomitant ester reduction, to diol IV. Protection of the secondary hydroxyl in IV, followed by a second Sharpless AE reaction would then furnish epoxide V (or its epimer, at will). Regio- and stereocontrolled reductive opening at V, utilizing Red-Al as reducing agent, followed by appropriate manipulations, was finally expected to form 1,3,5 polyol systems VI (or any of its stereoisomers, at will). Reiteration would form higher homologues VII, as desired. This

Scheme VI[a]

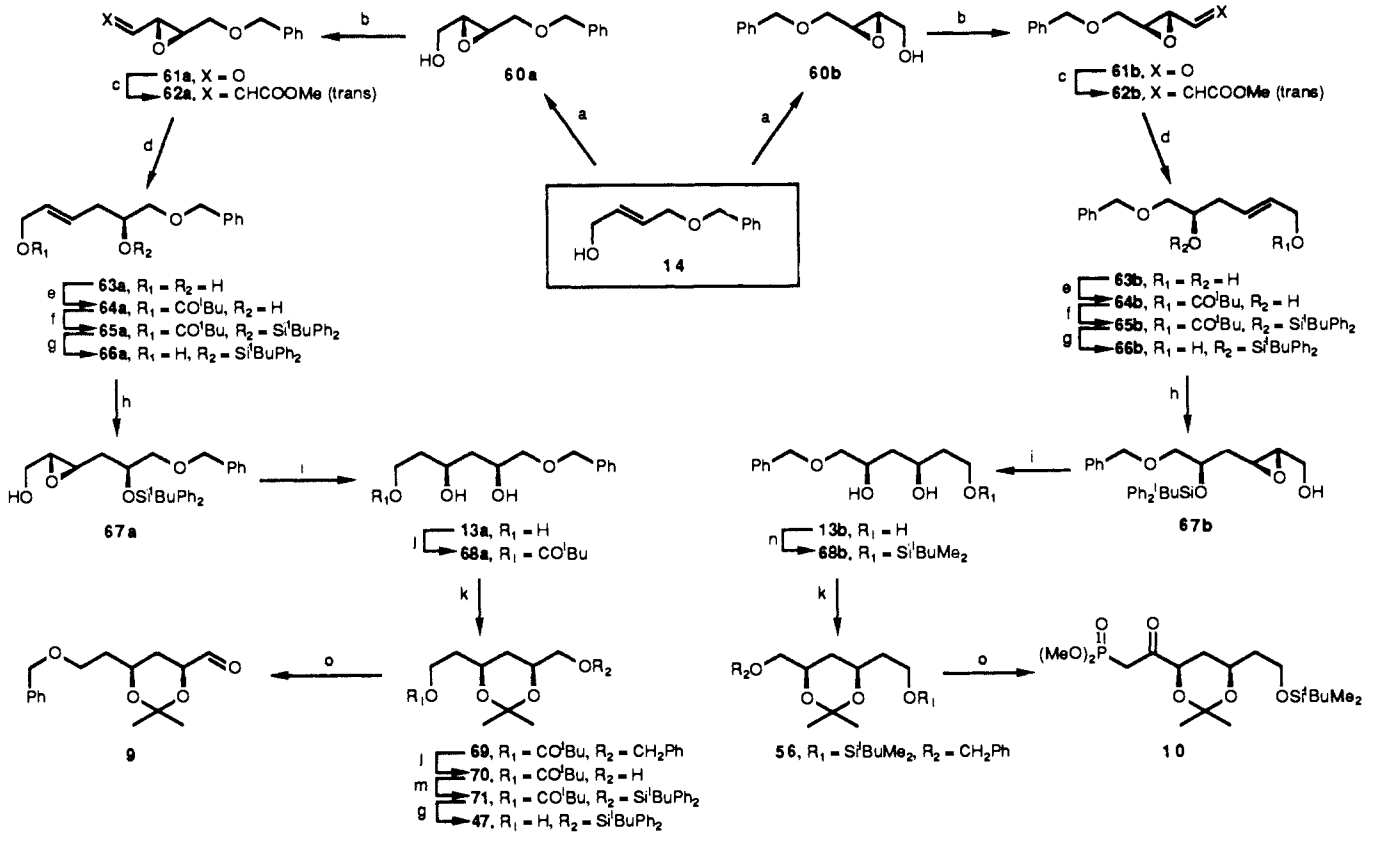


[a] General approach to $(2n + 1)$ polyol systems.

scheme proved to be a highly flexible and viable entry into a variety of such systems, including the requisite fragments **9** and **10** for the total synthesis of amphoteronolide B (**2**) and amphotericin B (**1**).

(22) Preliminary communication: Nicolaou, K. C.; Uenishi, J. *J. Chem. Soc., Chem. Commun.* **1982**, 1292.

Scheme VII[a]



[a] *Construction of building blocks* **9** *and* **10** *from butanediol derivative* **14**. *Reagents and Conditions*: (a) 1.1 equiv of (−)-DET, 1.1 equiv of $Ti(O\text{-}i\text{-}Pr)_4$, 2.1 equiv of TBHP, CH_2Cl_2, −23 °C, 5 h, and then Me_2S, tartaric acid, 75%; (b) $(COCl)_2$, DMSO, CH_2Cl_2, −78 °C, 15 min and then NEt_3, 98%; (c) 1.1 equiv of $Ph_3P{=}CHCOOMe$, benzene, 16 h, 77%; (d) 5.9 equiv of DIBAL, CH_2Cl_2–hexane, −78 °C, 0.5 h, and then MeOH, 82%; (e) 1.2 equiv of *t*-BuCOCl, pyridine, 0 °C, 3 h, 95%; (f) 1.3 equiv of *t*-$BuPh_2SiCl$, 5.3 equiv of imidazole, DMF, 25 °C, 1.5 h, 96%; (g) 1.4 equiv of DIBAL, CH_2Cl_2–hexane, −78 °C, 0.5 h, 87–91%; (h) 1.1 equiv of (−)-DET, 1.1 equiv of $Ti(O\text{-}i\text{-}Pr)_4$, 2.0 equiv of TBHP, CH_2Cl_2, −20 °C, 16 h, 60% (9:1 mixture of isomers); (i) 2.0 equiv of Red-Al, THF, 25 °C, 3 h, 85%; (j) 1.4 equiv of *t*-BuCOCl, DMAP catalyst, pyridine, 25 °C, 5 h, 88%; (k) $Me_2C(OMe)_2$, CSA catalyst 25 °C, 05 h, 93–95%; (l) H_2, 10% Pd–C, CH_2Cl_2, 25 °C, 4 h; (m) 1.1 equiv of *t*-$BuPh_2SiCl$, 4.5 equiv of imidazole, DMF, 25 °C, 3 h, 73% from **69**; (n) 1.0 equiv of *t*-$BuMe_2SiCl$, 4.2 equiv of imidazole, DMF, 25 °C, 2 h, 90%; (o) see Scheme V.

Scheme VII details the constructions of **9** and **10** according to the above general method. The allylic alcohol **14** on Sharpless asymmetric epoxidation ((−)-DET) gave epoxide **60a**[23,24] in 75% yield and 99:1 enantioselectivity. Swern oxidation ($(COCl)_2$–DMSO–Et_3N, 98%) of **60a**, followed by Wittig reaction, gave olefin **62a** (93% yield, *E*:*Z* = 84:16) via aldehyde **61a**. The crucial regioselective epoxide opening (attack at carbon adjacent to double bond), necessary for the success of this method, was cleanly effected with DIBAL, leading to the monoprotected intermediate **66a** via (i) temporary protection of the primary hydroxyl as a pivaloate ester (**63a** → **64a**, *t*-BuCOCl–Pyr, 95%), (ii) silylation of the secondary hydroxyl (**64a** → **65a**, *t*-$BuPh_2SiCl$–imidazole, 96%), and (iii) DIBAL-induced deprotection of the primary OH group (**65a** → **66a**, 90%). Reiteration of the Sharpless asymmetric epoxidation reaction on allylic alcohol **66a** ((−)-DET) led to epoxide **67a** (60% yield, ca. 91:9 stereoselectivity). Regioselective opening of epoxide **67a** with Red-Al, then led directly to the free triol **13a** (85%). Selective pivaloate ester formation (slightly over stoichiometric amounts of *t*-BuCOCl–Pyr, 88%) at the primary alcohol in **13a** led to **68a**, which was then converted to acetonide **69** ($(MeO)_2CMe_2$, 93%) and thence to **70** (debenzylation, 85%), **71** (silylation, 85%), and **47** (pivaloate cleavage, 91%). Compound **47** was then converted to key building block **9** according to the sequence described above (Scheme V). With use of (+)-DET as the chiral auxiliary in the Sharpless asymmetric epoxidation and via the same sequence described above, **13b**, the enantiomer of **13a**, was synthesized from the same prostereogenic allylic alcohol **14** via intermediates **60b**–**67b** as shown in Scheme VII. Silylation (*t*-$BuMe_2SiCl$–imidazole, 90%) of **13b** followed by acetonization ($(MeO)_2CMe_2$, 95%) gave compound **56** via **68b**. Building block **10** was then generated from **56** according to the sequence described above (Scheme V).

Conclusion

In this paper, amphotericin B (**1**) and amphoteronolide B (**2**) are discussed as synthetic targets. With the focus on subtle and repeated structural units, a retrosynthetic scheme was devised that led to the recognition of readily available and enantiomerically related compounds as starting points for a total synthesis of both amphotericin B (**1**) and amphoteronolide B (**2**). Thus, four key building blocks (**8**–**11**) were defined as subtargets and synthesized in optically active forms. Fragments **8** and **11** were derived from epoxide **15**, itself available from (+)-DET. Fragments **9** and **10** were obtained from (+)- and (−)-xylose, respectively, or from the prostereogenic allylic alcohol **14** and (−)- and (+)-DET, respectively, via a sequence based on the Sharpless asymmetric epoxidation reaction.

The latter sequence was engineered so as to provide a flexible entry into the 1,3,5,···(2*n* + 1) polyol series of compounds reminiscent of segments occurring in polyene macrolide antibiotics. The method, which, in principle, could provide all possible stereoisomers of any member of the above series, may be useful in constructing such segments for synthetic and/or structural studies in this field.

The described chemistry set the stage for the total synthesis of both amphotericin B (**1**) and its aglycon, amphoteronolide B (**2**). The following two papers[3,4] describe the completion of these two projects.

(23) Klunder, J. M.; Ko, S. Y.; Sharpless, K. B. *J. Org. Chem.* **1986**, *51*, 3710.

(24) Hungerbuhler, E.; Seebach, D. *Helv. Chim. Acta* **1981**, *64*, 687.

Experimental Section

General Methods. See ref 2.

[*R*-(*R*S**)]-α,2,2-Trimethyl-1,3-dioxolane-4-acetaldehyde (17).** [*R*-(*R***R**)]-α,2,2-Trimethyl-1,3-dioxolane-4-ethanol (**16**) (1.4 g, 8.75 mmol) was dissolved in freshly distilled CH_2Cl_2 (44 mL). Dry 4A molecular sieves (1.5 g) were added, followed by freshly recrystallized PCC (3.76 g, 17.50 mmol), and the reaction mixture was stirred for 2.5 h. The resulting mixture was then poured onto dry ether (300 mL) and filtered through Florisil. The solid residue was thoroughly washed with dry ether. The ether was removed in vacuo at 0 °C, and the resulting aldehyde **17** (1.3 g, 94%, essentially pure) was utilized in the next step without further purification. **17**: colorless oil; R_f 0.44 (silica, 50% ether in petroleum ether); $[\alpha]^{25}_D$ +22.8° (*c* 5.2, $CHCl_3$); IR (film) ν_{max} 2995, 2940, 2880, 2730, 1730 (CHO), 1460, 1382, 1373, 1255, 1215, 1160, 855, 790, 730 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 9.79 (d, *J* = 2.0 Hz, 1 H, C*H*O), 4.26 (m, 1 H, C*H*O), 4.13 (dd, *J* = 8.0, 6.0 Hz, 1 H, CH_2O), 3.73 (dd, *J* = 8.0, 7.0 Hz, 1 H, CH_2O), 2.60 (m, 1 H, C*H*), 1.42, 1.37 (singlets, 3 H each, acetonides), 1.08 (d, *J* = 7.5 Hz, 3 H, CH_3); HRMS (CI) calcd for $C_8H_{15}O_3$ + H 159.1177, found 159.1157 (M + H).

(4*R*,5*S*)-3-[2,4-Dideoxy-2,4-dimethyl-5,6-*O*-(1-methylethylidene)-L-altronoyl]-4-methyl-5-phenyl-2-oxazolidinone (18). (4*R*,5*S*)-3-Propionyl-4-methyl-5-phenyloxazolidone (**17a**)[10] (1.53 g, 6.57 mmol) was dissolved in dry CH_2Cl_2 (13 mL) under an argon atmosphere, and the solution was cooled to 0 °C. Freshly prepared *n*-Bu_2BOTf (1.9 g, 6.93 mmol) was slowly added with stirring, followed by the addition of *i*-Pr_2EtN (1.02 g ≡ 1.37 mL, 7.88 mmol), and the mixture was stirred at 0 °C for 0.5 h to ensure complete enolization. This solution was then cooled to −78 °C, and a solution of aldehyde **17** (1.30 g, 8.23 mmol) in dry CH_2Cl_2 (4 mL) was added dropwise. Stirring was continued for 0.5 h at −78 °C and for 1.5 h at room temperature. The reaction was then quenched by addition of pH 7 phosphate buffer (10 mL). The mixture was extracted with ether (2 × 150 mL), and the combined ether extracts were washed with brine (2 × 30 mL) and concentrated in vacuo. The crude oil, so obtained, was dissolved in methanol (20 mL) and cooled to 0 °C. Hydrogen peroxide (30%, 7 mL) was added, and stirring was continued for 2 h at the same temperature. Water (15 mL) was added, and the milky mixture was concentrated in vacuo to remove most of the methanol. The residue was extracted with ether (2 × 150 mL), washed with 5% aqueous $NaHCO_3$ (2 × 50 mL) and brine (50 mL), and dried ($MgSO_4$). Evaporation and purification by flash column chromatography (50% ether in petroleum ether) afforded the pure aldol adduct **18** (1.85 g, 72%). **18**: colorless foam; R_f 0.39 (silica, 75% ether in petroleum ether); $[\alpha]^{25}_D$ +14.1° (*c* 0.32, $CHCl_3$); IR (film) ν_{max} 3470, 3060, 3030, 2980, 2930, 2880, 1780, 1695, 1450, 1365, 1340, 1220, 1190, 1145, 1115, 1060, 1020, 980, 955, 855, 760, 725, 693 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.51–7.29 (m, 5 H, aromatic), 5.72 (d, *J* = 9.0 Hz, 1 H, PhC*H*O), 4.77 (m, 1 H, NC*H*CH$_3$), 4.20–3.60 (m, 6 H, C*H*, C*H*O, CH_2O, O*H*), 1.82 (m, 1 H, C*H*), 1.42, 1.37 (singlets, 3 H each, acetonide), 1.22 (d, *J* = 7.0 Hz, 3 H, CH_3), 0.93 (d, *J* = 7.0 Hz, 3 H, CH_3), 0.89 (d, *J* = 6.0 Hz, 3 H, CH_3); HRMS (CI) calcd for $C_{21}H_{29}O_6$ + H 392.2073, found 392.2078 (M + H).

2,4-Dideoxy-2,4-dimethyl-5,6-*O*-(1-methylethylidene)-L-altritol (19). Aldol adduct **18** (2.74 g, 7.0 mmol) was dissolved in freshly distilled THF (23.4 mL) and was stirred under an argon atmosphere while being cooled to −40 °C. $LiBH_4$ (336 mg, 15.4 mmol) was added in one portion, and stirring was continued at −40 °C for 4 h, after which the reaction was quenched by the addition of H_2O (5 mL). The reaction mixture was concentrated in vacuo to remove most of the THF. The residue was extracted with EtOAc (3 × 150 mL), and the organic phase was washed with H_2O (2 × 20 mL) and brine (50 mL) and dried ($MgSO_4$). Filtration and evaporation gave crude diol **19** (1.53 g, 100%), which was used for the next step without purification. **19**: colorless oil; R_f 0.26 (silica, ether); $[\alpha]^{25}_D$ +3.33° (*c* 0.3, $CHCl_3$); IR (film) ν_{max} 3405, 2995, 2930, 1455, 1380, 1370, 1260, 1215, 1157, 1057, 985, 857, 790, 700 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 4.22–3.55 (m, 7 H, C*H*O, CH_2O, O*H*), 2.72 (br s, 1 H, O*H*), 1.68 (m, 2 H, C*H*), 1.37, 1.33 (singlets, 3 H each, acetonide), 0.92 (d, *J* = 6.0 Hz, 3 H, CH_3), 0.68 (d, *J* = 7.0 Hz, 3 H, CH_3); HRMS (CI) calcd for $C_{11}H_{22}O_4$ + H 219.1597, found 219.1596 (M + H).

2,4-Dideoxy-2,4-dimethyl-5,6-*O*-(1-methylethylidene)-L-altritol 2,2-Dimethylpropanoate (20). Diol **19** (1.53 g, 7.0 mmol) was dissolved in dry pyridine (8.7 mL), flushed with argon, and stirred at 0 °C. Trimethylacetyl chloride (1.69 g ≡ 1.73 mL, 14.0 mmol) was slowly added, the cooling bath was removed, and stirring was continued for 4 h at room temperature. The reaction mixture was diluted with ice–water (50 mL) and transferred to a separatory funnel. The aqueous phase was extracted with ether (3 × 100 mL), and the combined extract solution was washed with saturated aqueous $CuSO_4$ (3 × 50 mL), H_2O (50 mL), saturated $NaHCO_3$ (2 × 50 mL), and brine (50 mL). Drying over $MgSO_4$, filtration, evaporation, and purification by flash column chromatography (silica, 40% ether in petroleum ether) yielded pivaloate ester **20** (1.90 g, 90%). **20**: colorless oil; R_f 0.45 (silica, 50% ether in petroleum ether); $[\alpha]^{25}_D$ +11.0° (*c* 0.69, $CHCl_3$); IR (film) ν_{max} 3520, 2970, 2930, 2870, 1725 (s, C=O), 1477, 1455, 1395, 1375, 1365, 1280, 1210, 1155, 1055, 990, 855 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 4.15–3.52 (m, 7 H, C*H*O, CH_2O, O*H*), 1.99 (m, 1 H, C*H*), 1.75 (m, 1 H, C*H*), 1.42, 1.36 (singlets, 3 H each, acetonide), 1.18 (s, 9 H, *t*-*Bu*), 0.89 (d, *J* = 6.0 Hz, 3 H, CH_3), 0.72 (d, *J* = 7.0 Hz, 3 H, CH_3); HRMS (CI) calcd for $C_{16}H_{30}O_5$ + H 303.2171, found 303.2175 (M + H). Anal. Calcd for $C_{16}H_{30}O_5$: C, 63.55; H, 9.99. Found: C, 63.37; H, 10.08.

2,4-Dideoxy-3-*O*-[(1,1-dimethylethyl)dimethylsilyl]-2,4-dimethyl-5,6-*O*-(1-methylethylidene)-L-altritol 2,2-Dimethylpropanoate (21). Alcohol **20** (2.9 g, 9.6 mmol) and dry 2,6-lutidine (2 mL, 19.2 mmol) were dissolved in dry CH_2Cl_2 (10 mL), under argon, and the solution was cooled to 0 °C. To this stirred solution, was slowly added, *t*-$BuMe_2SiOTf$ (3.8 g ≡ 3.3 mL, 14.4 mmol), the cooling bath was removed, and stirring was continued at room temperature for 0.5 h. The reaction mixture was then diluted with ether (250 mL) and washed with 5% aqueous $NaHCO_3$ solution (30 mL), H_2O (2 × 30 mL), and brine (2 × 50 mL). Drying ($MgSO_4$) followed by concentration and purification by flash column chromatography (silica, 10% ether in petroleum ether) gave silyl ether **21** (3.87 g, 97%). **21**: colorless oil; R_f 0.48 (silica, 20% ether in petroleum ether); $[\alpha]^{25}_D$ +2.5° (*c* 0.6, $CHCl_3$); IR (film) ν_{max} 2960, 2930, 2885, 2860, 1730 (s, C=O), 1480, 1470, 1460, 1380, 1370, 1280, 1250, 1210, 1155, 1060, 1050, 1035, 850, 835, 770, 735, 670 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 4.06–3.80 (m, 5 H, C*H*O, CH_2O), 4.60 (m, 1 H, C*H*O), 2.09 (m, 1 H, C*H*), 1.93 (m, 1 H, C*H*), 1.38, 1.33 (singlets, 3 H each, acetonide), 1.22 (s, 9 H, *t*-*Bu*), 0.91 (d, *J* = 6.0 Hz, 3 H, CH_3), 0.91 (s, 9 H, Si-*t*-*Bu*), 0.87 (d, *J* = 7.0 Hz, 3 H, CH_3), 0.06 (s, 6 H, $SiMe_2$); HRMS (CI) calcd for $C_{22}H_{44}O_5Si$ + H 417.3036, found 417.3051 (M + H).

2,4-Dideoxy-3-*O*-[(1,1-dimethylethyl)dimethylsilyl]-2,4-dimethyl-L-altritol 2,2-Dimethylpropanoate (22). Acetonide **21** (1.7 g, 4.1 mmol) was dissolved in AcOH–THF–H_2O (2:1:1, 50 mL) and stirred at 45 °C under argon for 4.5 h. The reaction mixture was then diluted with CH_2Cl_2 (150 mL), and the organic phase was washed with 50% aqueous $NaHCO_3$ (5 × 50 mL), H_2O (2 × 50 mL), and brine (50 mL). Drying ($MgSO_4$) followed by concentration and flash column chromatography (silica, 50% ether in petroleum ether) provided diol **22** (1.11 g, 72%). **22**: colorless oil; R_f 0.14 (silica, 50% ether in petroleum ether); $[\alpha]^{25}_D$ +16.2° (*c* 0.13, $CHCl_3$); IR (film) ν_{max} 3440, 2960, 2930, 2890, 2860, 1727 (s, C=O), 1480, 1460, 1390, 1360, 1285, 1250, 1155, 1105, 1050, 1030, 940, 912, 835, 770, 730, 670 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 4.00 (dd, *J* = 11.0, 6.0 Hz, 1 H, CH_2O), 3.88 (dd, *J* = 10.0, 9.0 Hz, 1 H, CH_2O), 3.84–3.44 (m, 5 H, C*H*O, CH_2O, O*H*), 2.64 (br s, 1 H, O*H*), 2.04 (m, 1 H, C*H*), 1.88 (m, 1 H, C*H*), 1.22 (s, 9 H, *t*-*Bu*), 0.95 (d, *J* = 7.0 Hz, 3 H, CH_3), 0.93 (s, 9 H, Si-*t*-*Bu*), 0.86 (d, *J* = 6.0 Hz, 3 H, CH_3), 0.14, 0.10 (s, 3 H each, $SiMe_2$); HRMS (CI) calcd for $C_{19}H_{40}O_5Si$ + H 377.2724, found 377.2734 (M + H).

2,4-Dideoxy-3-*O*-[(1,1-dimethylethyl)dimethylsilyl]-2,4-dimethyl-6-*S*-phenyl-6-thio-L-altritol 2,2-Dimethylpropanoate (23). Diol **22** (774 mg, 2.0 mmol) was dissolved in freshly distilled THF (2.6 mL). Phenyl disulfide (696 mg, 3.1 mmol) was added and the mixture was cooled to 0 °C under argon. *n*-Bu_3P (607 mg ≡ 0.747 mL, 3.0 mmol) was added with stirring, the cooling bath was removed, and the reaction mixture was stirred at room temperature for 6 h. Evaporation of the solvent followed by flash column chromatography (silica, 10% ether in petroleum ether) gave sulfide **23** (920 mg, 95%). **23**: colorless oil; R_f 0.42 (silica, 20% ether in petroleum ether); $[\alpha]^{25}_D$ +71.0° (*c* 0.1, $CHCl_3$); IR (film) ν_{max} 3510, 3060, 2960, 2930, 2860, 1727 (s, C=O), 1585, 1485, 1465, 1390, 1285, 1255, 1155, 1105, 1045, 1025, 935, 835, 770, 730, 670 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.44–7.15 (m, 5 H, aromatic), 4.04–3.60 (m, 4 H, C*H*O, CH_2O), 3.30 (dd, *J* = 14.0, 9.0 Hz, 1 H, CH_2S), 2.88 (dd, *J* = 14.0, 9.0 Hz, 1 H, CH_2S) 2.03 (m, 1 H, C*H*), 1.91 (m, 1 H, C*H*), 1.20 (s, 9 H, *t*-*Bu*), 0.95–0.86 (15 H, Si-*t*-*Bu*, CH_3), 0.07 (s, 6 H, $SiMe_2$); HRMS (CI) calcd for $C_{25}H_{44}O_4SSi$ 468.2724, found 468.2720 (M^+). Anal. Calcd for $C_{25}H_{44}O_4SSi$: C, 64.06; H, 9.46; S, 6.84. Found: C, 64.12; H, 9.52; S, 6.72.

(2*S*,3*R*,4*S*,5*S*)-3-[[(1,1-Dimethylethyl)dimethylsilyl]oxy]-2,4-dimethyl-1,5-hexanediol 1-(2,2-Dimethylpropanoate) (24). Compound **23** (637 mg, 1.36 mmol) was dissolved in absolute EtOH (5.3 mL) and stirred at 60 °C under argon. Freshly prepared Raney Ni (2 g in 15 mL EtOH) was added in portions, and stirring was continued for 2 h. After cooling, the catalyst was filtered off (Celite) and washed thoroughly with ethanol and dry ether. Evaporation of the solvents gave essentially pure **24** (480 mg, 98%). **24**: colorless oil; R_f 0.23 (silica, 20% ether in petroleum ether); $[\alpha]^{25}_D$ +11.8° (*c* 3.22, $CHCl_3$); IR (film) ν_{max} 3490, 2960, 2930, 2900, 2860, 1720 (s, C=O), 1480, 1460, 1395, 1385, 1360, 1285, 1250, 1150, 1030, 940, 830, 810, 770, 665 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 4.07–3.65 (m, 4 H, C*H*O, CH_2O), 3.09 (br s, 1 H, O*H*), 2.0

(m, 1 H, C*H*), 1.64 (m, 1 H, C*H*), 1.20 (s, 9 H, *t-Bu*), 1.14 (d, J = 6.0 Hz, 3 H, CH_3), 0.93 (d, J = 7.0 Hz, 3 H, CH_3), 0.91 (s, 9 H, Si-*t-Bu*), 0.82 (d, J = 7.5 Hz, 3 H, CH_3), 0.11, 0.09 (s, 3 H each, $SiMe_2$); HRMS (CI) calcd for $C_{19}H_{40}O_4Si$ + H 361.2774, found 361.2758 (M + H). Anal. Calcd for $C_{19}H_{40}O_4Si$: C, 63.28; H, 11.18. Found: C, 63.10; H, 11.37.

(2*S*,3*R*,4*S*,5*S*)-3-[[(1,1-Dimethylethyl)dimethylsilyl]oxy]-2,4-dimethyl-5-[(tetrahydro-2*H*-pyran-2-yl)oxy]-1-hexanol 1-(2,2-Dimethylpropanoate) (25). To a solution of alcohol **24** (3.61 g, 10 mmol) and freshly distilled dihydropyran (0.925 g ≡ 1.0 mL, 11 mmol) in dry CH_2Cl_2 (20 mL) at 0 °C under argon was added camphorsulfonic acid (CSA, 116 mg, 0.5 mmol). After being stirred for 0.5 h at 0 °C, the reaction mixture was quenched with saturated aqueous $NaHCO_3$ solution (20 mL) and extracted with ether (30 mL). The organic extract was washed with brine (20 mL), dried ($MgSO_4$), filtered, and concentrated. Flash column chromatography (silica, 10% ether in petroleum ether) gave tetrahydropyranyl ether **25** as a mixture of two anomers (4.27 g, 96%). **25** (mixture of anomers, ca. 1:1): colorless oil; R_f 0.32 and 0.37 (silica, 10% ether in petroleum ether); $[\alpha]^{20}_D$ +30.2° (c 2.48, $CHCl_3$); IR ($CHCl_3$) ν_{max} 2960, 2930, 2860, 1725 (s, C=O), 1485, 1380, 1290, 1260, 1160, 1030, 840 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 4.63, 4.53 (multiplets, ca. 1:1 ratio, 1 H, OC*H*O), 4.01–3.38 (m, 6 H, CH_2O, C*H*O), 2.10–0.95 (m, 8 H, CH_2, C*H*), 1.18 (s, 9 H, *t-Bu*), 1.10, 1.00 (doublets, J = 6.4 Hz, ca. 1:1 ratio, 3 H, CH_3), 0.89, 0.88, 0.85 (singlets, 12 H total, CH_3, Si-*t-Bu*), 0.79 (d, J = 7.1 Hz, 3 H, CH_3), 0.04, 0.03 (singlets, ca. 1:1 ratio, 6 H total, $SiMe_2$); HRMS (CI) calcd for $C_{24}H_{48}O_5Si$ + H 445.3349, found 445.3282 (M + H).

(2*S*,3*R*,4*S*,5*S*)-3-[[(1,1-Dimethylethyl)dimethylsilyl]oxy]-2,4-dimethyl-5-[(tetrahydro-2*H*-pyran-2-yl)oxy]-1-hexanol (26). To a stirred solution of pivaloate ester **25** (4.0 g, 9.0 mmol) in dry CH_2Cl_2 (20 mL) at −78 °C was added DIBAL (22.5 mL, 1 M solution in hexane, 22.5 mmol) dropwise under argon. The reaction was stirred at −78 °C for 0.5 h before quenching with MeOH (1 mL). The reaction mixture was diluted with ether (50 mL) and shaken with saturated aqueous sodium–potassium tartrate solution (40 mL) until the organic layer became clear. The organic phase was then washed with brine (40 mL), dried ($MgSO_4$), filtered, and concentrated. Flash column chromatography (silica, 40% ether in petroleum ether) gave alcohol **26** as a mixture of two anomers (3.18 g, 98%). **26** (mixture of anomers, ca. 1:1): colorless oil; R_f 0.27 and 0.34 (silica, 40% ether in petroleum ether); $[\alpha]^{20}_D$ +4.4° (c 3.62, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3450, 3000, 2960, 2940, 2900, 2860, 1475, 1470, 1385, 1255, 1130, 1080, 1025, 840 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 4.60–3.30 (m, 8 H, CH_2O, C*H*O, O*H*), 1.95–0.95 (m, 8 H, CH_2, C*H*), 1.14, 1.08 (doublets, J = 6.1 Hz, ca. 1:1 ratio, 3 H, CH_3), 0.89–0.78 (m, 15 H, Si-*t-Bu*, CH_3), 0.06, 0.05, 0.04 (singlets, 6 H total, $SiMe_2$); HRMS (CI) calcd for $C_{19}H_{40}O_4Si$ + H 361.2774, found 361.2762 (M + H).

(2*S*,3*R*,4*S*,5*S*)-3-[[(1,1-Dimethylethyl)dimethylsilyl]oxy]-2,4-dimethyl-5-[(tetrahydro-2*H*-pyran-2-yl)oxy]-1-hexanol (8). To a stirred solution of alcohol **26** (3.065 g, 8.5 mmol) in dry CH_2Cl_2 (42 mL) were added sequentially powdered and freshly dried 4A molecular sieves (3.6 g), anhydrous NaOAc (3.486 g, 42.5 mmol), and freshly recrystallized PCC (3.664 g, 17 mmol) at 25 °C under argon. After being stirred for 2.5 h at room temperature, the reaction mixture was poured onto dry ether (200 mL) and filtered through Florisil. The filter cake was washed thoroughly with dry ether. The filtrate was concentrated in vacuo, and the residue was flash chromatographed (silica, 20% ether in petroleum ether) to give the rather labile aldehyde **8** as a mixture of two anomers (2.285 g, 75%), which was used immediately in the next step. **8** (mixture of anomers, ca. 1:1): colorless oil; R_f 0.35 and 0.42 (silica, 20% ether in petroleum ether); $[\alpha]^{20}_D$ −70.0° (c 2.56, $CHCl_3$); IR ($CHCl_3$) ν_{max} 2960, 2940, 2900, 2860, 1730 (s, C=O), 1470, 1390, 1260, 1150, 1080, 1030, 840 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 9.67, 9.66 (singlets, ca. 1:1 ratio, 1 H, C*H*O), 4.60–3.35 (m, 5 H, CH_2O, C*H*O), 2.60–2.40 (m, 1 H, C*H*C(O)), 2.00–1.30 (m, 7 H, CH_2, C*H*), 1.18–1.06 (m, 6 H, CH_3), 0.88–0.82 (m, 12 H, Si-*t-Bu*, CH_3), 0.04 to −0.05 (singlets, 6 H, total, $SiMe_2$).

(2*R*,3*R*)-6-[[(1,1-Dimethylethyl)silyl]oxy]-2-(phenylmethoxy)-3-[(phenylmethoxy)methyl]-4-hexyn-2-ol (27). To a solution of (*tert*-butyldiphenylsilyl)propargyl ether (1.47 g, 5 mmol) in dry hexane (10 mL) was added *n*-BuLi (3.13 mL, 1.6 M solution in hexane, 5 mmol), and the mixture was stirred at −78 °C under argon. Diethylaluminum chloride (2.8 mL, 25% solution in toluene, 5 mmol) was added dropwise to the reaction mixture, and the resulting milky white solution was warmed to −40 °C. Epoxide **15** (0.568 g, 2 mmol) in 3 mL toluene was added via syringe. After 30 min, the reaction was quenched with saturated aqueous $NaHCO_3$ solution and diluted with ether (20 mL) and H_2O (10 mL). The organic phase was separated, and the aqueous layer was extracted with ether (2 × 20 mL). The combined organic solution was washed with saturated $NaHCO_3$ (10 mL) and brine (10 mL), dried ($MgSO_4$), and concentrated. Purification by flash column chromatography (silica, 10% EtOAc in petroleum ether) gave pure alcohol **27** (0.989 g, 85%). **27**: colorless oil; R_f 0.32 (silica, 20% EtOAc in petroleum ether); $[\alpha]^{20}_D$ −8.6° (c 2.5, MeOH); IR (film) ν_{max} 3480, 3060, 3020, 2920, 2840, 2240, 1580, 1500, 1470, 1460, 1420, 1360, 1250, 1200, 1100, 1000, 900, 820, 720, 690 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$, TMS) δ 7.71–7.20 (m, 20 H, aromatic), 4.54 (m, 4 H, PhCH_2O), 4.29 (d, J = 1.5 Hz, 2 H, CH_2O), 3.90–3.51 (m, 5 H, CH_2O, C*H*O), 3.02 (d, J = 2.2 Hz, 1 H, O*H*), 2.87 (m, 1 H, C*H*), 1.04 (s, 9 H, Si-*t-Bu*); HRMS (CI) calcd for $C_{37}H_{42}O_4Si$ + NH_4 596.3197, found 596.3166 (M + NH_4).

(4*R*,5*R*)-2-[[(1,1-Dimethylethyl)dimethylsilyl]oxy]-5,6-bis(phenylmethoxy)-4-[(phenylmethoxy)methyl]-2-hexyne (28). NaH (80 mg, 50% dispersion in oil, 1.66 mmol) was portionwise added to a solution of alcohol **27** (0.80 g, 1.38 mmol) in dry THF (3 mL) at 0 °C under argon. The cooling bath was removed, and stirring was continued at room temperature for 0.5 h. The mixture was again cooled to 0 °C, and benzylbromide (0.28 g ≡ 0.197 mL, 1.66 mmol) was added dropwise. Stirring was continued at room temperature for 16 h, and then the reaction was quenched by pouring onto precooled saturated aqueous NH_4Cl solution (10 mL) and ether (10 mL). The organic phase was separated, and the aqueous phase was extracted with ether (3 × 10 mL). The combined organic layer was washed with brine (10 mL), dried ($MgSO_4$), and concentrated. Flash column chromatography (silica, 5% EtOAc in petroleum ether) gave ether **28** (0.88 g, 95%). **28**: colorless oil; R_f 0.38 (silica, 10% EtOAc in petroleum ether); $[\alpha]^{20}_D$ +0.26° (c 3.2, MeOH); IR (film) ν_{max} 3060, 3020, 2920, 2840, 1600, 1500, 1475, 1470, 1450, 1425, 1365, 1200, 1100, 1020, 820, 730, 690, 670 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$, TMS) δ 7.70 (dd, J = 8.0, 1.6 Hz, 4 H, aromatic), 7.40–7.21 (m, 21 H, aromatic), 4.70 (d, J = 11.6 Hz, 1 H, PhCH_2O), 4.50 (m, 5 H, PhCH_2O), 4.31 (d, J = 2.0 Hz, 2 H, CH_2O), 3.79–3.58 (m, 5 H, CH_2O), 2.99 (m, 1 H, C*H*), 1.04 (s, 9 H, Si-*t-Bu*); HRMS (CI) calcd for $C_{44}H_{48}O_4Si$ + NH_4 686.3666, found 686.3658 (M + NH_4).

(4*R*,5*R*)-5,6-Bis(phenylmethoxy)-4-[(phenylmethoxy)methyl]-2-hexyn-1-ol (29). *n*-Bu_4NF (1.95 mL, 1 M solutions in THF, 1.95 mmol) was slowly added to a solution of **28** (0.87 g, 1.3 mmol) in THF (1.3 mL) at 0 °C. The cooling bath was removed, and stirring was continued at room temperature for 3 h. The reaction was quenched with saturated aqueous NH_4Cl solution (5 mL) and diluted with ether (10 mL). The organic phase was separated, and the aqueous phase was extracted with ether (3 × 10 mL). The combined organic solution was washed with saturated aqueous NH_4Cl (5 mL) and brine (5 mL) and dried ($MgSO_4$). Concentration followed by flash column chromatography (silica, 30% EtOAc in petroleum ether) gave alcohol **29** (0.49 g, 87%). **29**: colorless oil; R_f 0.33 (silica, 30% EtOAc in petroleum ether); $[\alpha]^{20}_D$ −3.5° (c 1.5, MeOH); IR (film) ν_{max} 3410, 3060, 3020, 2900, 2860, 2220, 1500, 1450, 1360, 1200, 1100, 1050, 910, 730, 690 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$, TMS) δ 7.40–7.25 (m, 15 H, aromatic), 4.68 (d, J = 11.6 Hz, 1 H, PhCH_2O), 4.54 (m, 5 H, PhCH_2O), 4.13 (d, J = 1.7 Hz, 2 H, CH_2O), 3.80–3.61 (m, 5 H, CH_2O, C*H*O), 3.03 (m, 1 H, C*H*), 2.24 (br s, 1 H, O*H*); HRMS (CI) calcd for $C_{28}H_{30}O_4$ + H 431.2220, found 431.2200 (M + H).

(4*R*,5*R*)-5,6-Bis(phenylmethoxy)-4-[(phenylmethoxy)methyl]-2-hexen-1-ol (30). To a solution of Red-Al (0.5 mL, 3.4 M solution in toluene, 1.7 mmol) in Et_2O (0.3 mL) was slowly added alcohol **29** (0.43 g, 1.0 mmol) in Et_2O (0.5 mL) at 0 °C under argon. The reaction mixture was gradually warmed up to room temperature over 3 h with stirring and then quenched with 1 N HCl (4 mL) and diluted with Et_2O (10 mL). The organic phase was separated, and the aqueous phase extracted with Et_2O (3 × 10 mL). The combined organic solution was washed with saturated aqueous $NaHCO_3$ (2 × 5 mL) and brine (5 mL), dried ($MgSO_4$), and concentrated. Purification by flash column chromatography (silica, 30% EtOAc in petroleum ether) gave olefin **30** (0.42 g, 93%). **30**: colorless oil; R_f 0.18 (silica, 30% EtOAc in petroleum ether); $[\alpha]^{20}_D$ −9.0° (c 1.0, MeOH); IR (film) ν_{max} 3600, 3440, 3100, 3080, 3040, 2915, 2860, 1610, 1590, 1500, 1480, 1460, 1360, 1210, 1100, 1030, 970, 910, 735, 700, 680 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$, TMS) δ 7.40–7.20 (m, 15 H, aromatic), 5.68 (m, 2 H, olefinic), 4.73 (d, J = 11.5 Hz, 1 H, PhCH_2O), 4.54 (d, J = 11.5 Hz, 1 H, PhCH_2O), 4.53 (s, 2 H, PhCH_2O), 4.44 (s, 2 H, PhCH_2O), 4.02 (t, J = 4.3 Hz, CH_2O), 3.76–3.50 (m, 5 H, CH_2O, C*H*O), 2.68 (m, 1 H, C*H*), 1.4 (t, J = 4.3 Hz, 1 H, O*H*); HRMS (CI) calcd for $C_{28}H_{32}O_4$ + H 433.2379, found 433.2350 (M + H).

(2*R*,3*R*)-2-(Phenylmethoxy)-3-[(phenylmethoxy)methyl]-4-penten-2-ol (31). Dry CuI (17.5 g, 39.5 mmol) was added to a solution of epoxide **15** (11.0 g, 40.0 mmol) in dry THF (160 mL), and the mixture was stirred at −78 °C under argon. Vinylmagnesium bromide (92 mL, 1 M solution in THF, 92 mmol) was dropwise added over a period of 30 min. The cooling bath was removed, and the stirred reaction mixture was allowed to reach 0 °C (0.5 h) and then poured onto precooled saturated aqueous NH_4Cl solution (200 mL) and ether (100 mL). The organic phase was separated, and the aqueous phase was extracted with ether (3

× 150 mL). The combined organic solution was washed with saturated aqueous NH_4Cl solution (100 mL) and brine (100 mL), dried ($MgSO_4$), and concentrated. Purification by flash column chromatography (silica, 10% EtOAc in petroleum ether) gave pure olefin **31** (11.4 g, 91%). **31**: colorless oil; R_f 0.33 (silica, 20% EtOAc in petroleum ether); $[\alpha]^{20}_D$ −29.1° (*c* 1.0, $CHCl_3$); IR (film) ν_{max} 3530, 3400, 3060, 3020, 2900, 2860, 1640, 1600, 1500, 1450, 1360, 1200, 1100, 1020, 910, 730, 690 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$, TMS) δ 7.32 (m, 10 H, aromatic), 5.75 (ddd, *J* = 17.5, 10.0, 7.3 Hz, 1 H, olefinic), 5.15 (dd, *J* = 17.5, 2.2 Hz, 1 H, olefinic), 5.12 (dd, *J* = 10.0, 2.2 Hz, 1 H, olefinic), 4.60–4.50 (m, 4 H, PhCH_2O), 3.92 (m, 1 H, C*H*O), 3.62 (dd, *J* = 7.6, 3.3 Hz, 2 H, CH_2O), 3.55 (dd, *J* = 10.0, 3.3 Hz, 1 H, CH_2O), 3.45 (dd, *J* = 10.0, 8.2 Hz, 1 H, CH_2O), 3.10 (d, *J* = 3.3 Hz, 1 H, O*H*), 2.55 (m, 1 H, C*H*); HRMS (CI) calcd for $C_{20}H_{25}O_3$ + H 313.1804, found 313.1777 (M + H).

(3*R*,4*R*)-4,5-Bis(phenylmethoxy)-3-[(phenylmethoxy)methyl]-1-pentene (32). A solution of alcohol **31** (43.7 g, 140 mmol) in dry THF was slowly added over a period of 1 h to a stirred suspension of NaH (8.4 g, 50% dispersion in oil, 182 mmol) in dry THF (280 mL) at 0 °C and under argon. The cooling bath was removed, and stirring was continued at room temperature for an additional 1 h. The mixture was recooled to 0 °C, and benzylbromide (28.7 g ≡ 20 mL; 175 mmol) was added dropwise. Stirring was continued at room temperature for 16 h, and then the reaction was quenched by pouring onto precooled saturated aqueous NH_4Cl solution (150 mL) and ether (100 mL). The organic solution was separated, and the aqueous phase was extracted with ether (3 × 150 mL). The combined organic phase was washed with brine (100 mL), dried ($MgSO_4$), and concentrated. Flash column chromatography (silica, 5% EtOAc in petroleum ether) gave compound **32** (52.34 g, 93%). **32**: colorless oil; R_f 0.37 (silica, 10% EtOAc in petroleum ether); $[\alpha]^{20}_D$ −5.8° (*c* 1.0, MeOH); IR (film) ν_{max} 3060, 3020, 2900, 2860, 1640, 1600, 1500, 1450, 1355, 1200, 1100, 1020, 910, 730, 690, 670 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$, TMS) δ 7.32 (m, 15 H, aromatic), 5.85 (ddd, *J* = 17.5, 10.0, 7.3 Hz, 1 H, olefinic), 5.15 (dd, *J* = 17.5, 2.2 Hz, 1 H, olefinic), 5.12 (dd, *J* = 10.0, 2.2 Hz, 1 H, olefinic), 4.75 (d, *J* = 10.0 Hz, 1 H, PhCH_2O), 4.55 (d, *J* = 10.0 Hz, 1 H, PhCH_2O), 4.52 (s, 2 H, PhCH_2O), 4.48 (s, 2 H, CH_2Ph), 3.80–3.48 (m, 5 H, CH_2O, C*H*O), 2.75–2.60 (m, 1 H, C*H*); HRMS (CI) calcd for $C_{27}H_{30}O_3$ + H 403.2273, found 403.2236 (M + H). Anal. Calcd for $C_{27}H_{30}O_3$: C, 80.55; H, 7.51. Found C, 80.84; H, 7.74.

(2*R*,3*R*)-3,4-Bis(phenylmethoxy)-2-[(phenylmethoxy)methyl]-1-butanal (34) via 33. Terminal olefin **32** (50 g, 122 mmol) was dissolved in dry CH_2Cl_2 (500 mL) and MeOH (1.6 mL, 36.6 mmol) and cooled to −78 °C. Ozone was passed through the solution until a faint blue color appeared. Dimethyl sulfide (Me_2S, 1.8 mL, 12.2 mmol) was added at −78 °C, and the reaction mixture was allowed to reach room temperature and stirred for 3 h, and, then Ph_3P (10 g, 38.1 mmol) was portionwise added to complete the ozonide reduction. Concentration of the mixture followed by azeotropic drying with benzene (2 × 100 mL) and addition of benzene (200 mL) gave a solution of aldehyde **33**, which was reacted, without purification, with $Ph_3P{=}CHCOOEt$ (63.7 g, 183 mmol) at room temperature and under argon. After stirring for 16 h, the reaction mixture was diluted with 5% ether in petroleum ether (300 mL). The precipitate was filtered off and thoroughly washed with 5% ether in petroleum ether (400 mL). The filtrate was concentrated, and the residue was flash chromatographed (silica, 10% EtOAc in petroleum ether) to give olefin **34** (49.9 g, 85%). **34**: colorless oil; R_f 0.19 (silica, 10% EtOAc in petroleum ether); $[\alpha]^{20}_D$ −8.6° (*c* 1.0, MeOH); IR (film) ν_{max} 3060, 3020, 2900, 2860, 1720, 1650, 1600, 1580, 1500, 1450, 1430, 1355, 1260, 1200, 1170, 1100, 1020, 900, 730, 690, 670 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$, TMS) δ 7.32–7.21 (m, 15 H, aromatic), 6.97 (dd, *J* = 15.6, 8.9 Hz, 1 H, olefinic), 5.92 (d, *J* = 15.6 Hz, 1 H, olefinic), 4.68 (d, *J* = 11.6 Hz, 1 H, PhCH_2O), 4.50 (d, *J* = 11.6 Hz, 1 H, PhCH_2O), 4.48 (s, 2 H, PhCH_2O), 4.44 (s, 2 H, PhCH_2O), 3.70 (s, 3 H, OCH_3), 3.82–3.45 (m, 5 H, C*H*O, CH_2O), 2.91–2.78 (m, 1 H, C*H*); HRMS (CI) calcd $C_{29}H_{32}O_5$ + H 461.2328, found 461.2412 (M + H). Anal. Calcd for $C_{29}H_{32}O_5$: C, 75.61; H, 7.00. Found: C, 75.47; H, 7.03.

Preparation of Compound 30 from 34. Ester **34** (54 g, 111 mmol) was dissolved in dry CH_2Cl_2 (350 mL) under argon and cooled to −78 °C. To the stirred solution was added DIBAL (244 mL; 1 M solution in toluene; 244 mmol) dropwise, and stirring was continued for 30 min. The reaction mixture was quenched with MeOH (10 mL) and poured into a separatory funnel containing saturated sodium potassium tartrate solution (300 mL). After shaking, the organic phase was separated and the aqueous phase was extracted with EtOAc (2 × 150 mL). The combined organic extract was washed with brine (100 mL), dried ($MgSO_4$), and concentrated. Flash column chromatography (silica, 30% EtOAc in petroleum ether) gave allylic alcohol **30** (44.6 g, 93%). This material was identical with the compound obtained via acetylenic intermediate **27** by the usual criteria.

4,5-Anhydro-3-deoxy-3-[(phenylmethoxy)methyl]-1,2-bis-*O*-(phenylmethyl)galactitol (35). Allylic alcohol **30** (12.5 g, 28.7 mmol) was dissolved in anhydrous CH_2Cl_2 (287 mL) and cooled to −20 °C under argon. To this stirred solution were sequentially added (−)-diethyltartrate (8.88 g ≡ 9.14 mL, 43.1 mmol), Ti(O-*i*-Pr)$_4$ (9.79 g ≡ 10.2 mL, 34.4 mmol), and *t*-BuOOH (5.68 g ≡ 21.0 mL, 3.4 M solution in CH_2Cl_2, 63.1 mmol). The reaction mixture was kept at −20 °C for 16 h, quenched at that temperature with 10% aqueous tartaric acid solution (75 mL), and vigorously stirred for 1 h at −20 °C and then for 1 h at 25 °C. The resulting precipitate was filtered off (Celite), and the filtrate was dried over Na_2SO_4. Filtration followed by concentration gave an oily residue, which was diluted with ether (250 mL), cooled to 0 °C, and treated with NaOH solution (1 N, 80 mL). The two-phase mixture was vigorously stirred at 0 °C for 30 min, and the organic phase was then separated and washed with aqueous HCl (1 N, 30 mL), saturated aqueous $NaHCO_3$ (2 × 25 mL), and finally brine (50 mL). Drying ($MgSO_4$), concentration, and flash column chromatography (silica, 30% EtOAc in petroleum ether) gave epoxide **35** (9.65 g, 75%). **35**: colorless oil; R_f 0.31 (silica, 40% EtOAc in petroleum ether); $[\alpha]^{20}_D$ +13.6° (*c* 0.73, MeOH); IR (film) ν_{max} 3460, 3080, 3060, 3030, 2940, 2860, 1600, 1580, 1500, 1480, 1450, 1360, 1200, 1100, 1020, 900, 730, 690, 670 cm^{-1}; ^1H NMR (250 MHz, benzene-d_6, TMS) δ 7.40–7.05 (m, 15 H, aromatic), 4.82 (d, *J* = 11.6 Hz, 1 H, PhCH_2O), 4.56 (d, *J* = 11.6 Hz, 1 H, PhCH_2O), 4.37 (s, 2 H, PhCH_2O), 4.19 (s, 2 H, PhCH_2O), 4.05 (m, 1 H, C*H*O), 3.75–3.50 (m, 5 H, C*H*O, CH_2O), 3.40–3.34 (m, 1 H, C*H*O), 3.06 (dd, *J* = 8.6, 2.1 Hz, 1 H, C*H* epoxide), 2.83 (m, 1 H, C*H* epoxide), 1.89–1.81 (m, 1 H, C*H*), 1.61 (br s, 1 H, O*H*); HRMS (CI) calcd for $C_{28}H_{32}O_5$ + H 449.2328, found 449.2321 (M + H).

3,5-Dideoxy-3-[(phenylmethoxy)methyl]-1,2-bis-*O*-(phenylmethyl)-L-*arabino*-hexitol (36). A solution of epoxide **35** (20 g, 44.3 mmol) in dry THF (50 mL) was slowly added to a cold (0 °C) stirred solution of Red-Al (46 mL, 3.4 M solution in toluene, 156 mmol) in dry THF (80 mL) under argon. Stirring was continued at 0 °C for 4 h, and the reaction mixture was quenched with aqueous HCl (2 N, 71 mL). The solution was diluted with ether (200 mL), the organic phase was separated, and the aqueous phase was reextracted with EtOAc (3 × 100 mL). The combined organic extract was washed with saturated aqueous $NaHCO_3$ solution (2 × 50 mL) and brine (50 mL), dried ($MgSO_4$), and concentrated. Flash column chromatography (silica, 40% EtOAc in petroleum ether) gave diol **36** (19.0 g, 96%). **36**: colorless oil; R_f 0.14 (silica, 40% EtOAc in petroleum ether); $[\alpha]^{20}_D$ −5.7° (*c* 0.87, MeOH); IR (film) ν_{max} 3500, 3080, 3060, 3020, 2920, 2860, 1600, 1580, 1500, 1450, 1360, 1200, 1100, 1020, 730, 700 cm^{-1}; ^1H NMR (250 MHz, benzene-d_6, TMS), δ 7.27–7.04 (m, 15 H, aromatic), 4.67 (d, *J* = 11.6 Hz, 1 H, PhCH_2O), 4.48 (d, *J* = 11.6 Hz, 1 H, PhCH_2O), 4.31 (s, 2 H, PhCH_2O), 4.23 (d, *J* = 12.0 Hz, 1 H, PhCH_2O), 4.17 (d, *J* = 12.0 Hz, 1 H, PhCH_2O), 4.15–4.03 (m, 2 H, PhCH_2O), 3.95 (d, *J* = 5.3 Hz, 1 H, C*H*O), 3.84–3.48 (m, 6 H, C*H*O, CH_2O), 2.94 (dd, *J* = 5.9, 3.8 Hz, 1 H, O*H*), 2.14 (m, 1 H, C*H*), 1.75 (m, 1 H, CH_2), 1.56 (m, 1 H, CH_2); HRMS (CI) calcd for $C_{28}H_{34}O_5$ + H 451.2484, found 451.2480 (M + H). Anal. Calcd for $C_{28}H_{34}O_5$: C, 74.66; H, 7.65. Found C, 75.08; H, 7.85.

3,5-Dideoxy-4,6-bis-*O*-[(1,1-dimethylethyl)dimethylsilyl]-3-[(phenylmethoxy)methyl]-1,2-bis-*O*-(phenylmethyl)-L-*arabino*-hexitol (37). *t*-BuMe$_2$SiCl (5.9 g, 39.2 mmol) was portionwise added to a stirred solution of diol **36** (6.1 g, 13.5 mmol) and imidazole (2.8 g, 41.1 mmol) in dry DMF (40 mL) at room temperature under argon. The reaction mixture was stirred at ambient temperature for 16 h and then it was diluted with ether (200 mL) and H_2O (60 mL). After shaking, the organic phase was separated and washed with H_2O (30 mL) and brine (50 mL) and dried ($MgSO_4$). Concentration followed by flash column chromatography (silica, 2% EtOAc in petroleum ether) gave silyl ether **37** (9.5 g, 92%). **37**: colorless oil; R_f 0.43 (silica, 5% EtOAc in petroleum ether); $[\alpha]^{20}_D$ −7.0° (*c* 0.73, MeOH); IR (film) ν_{max} 3080, 3060, 3020, 2940, 2920, 2850, 1600, 1560, 1500, 1485, 1475, 1470, 1460, 1390, 1360, 1250, 1100, 1040, 1020, 940, 830, 770, 730, 700, 670 cm^{-1}; ^1H NMR (250 MHz, benzene-d_6, TMS) δ 7.35–7.05 (m, 15 H, aromatic), 4.70 (d, *J* = 11.5 Hz, 1 H, PhCH_2O), 4.53 (d, *J* = 11.5 Hz, 1 H, PhCH_2O), 4.40 (s, 2 H, PhCH_2O), 4.31 (s, 2 H, PhCH_2O), 3.92 (m, 2 H, CH_2O), 3.83–3.66 (m, 6 H, C*H*O, CH_2O), 2.40 (m, 1 H, C*H*), 1.9 (m, 2 H, CH_2), 0.95 (s, 18 H, Si-*t*-*Bu*), 0.13, 0.08, 0.04, and 0.02 (singlets, 12 H total, Si*Me*$_2$); HRMS (CI) calcd for $C_{40}H_{62}O_5Si_2$ + H 679.4215, found 679.4246 (M + H).

3,5-Dideoxy-4,6-bis-*O*-[(1,1-dimethylethyl)dimethylsilyl]-3-(hydroxymethyl)-L-*arabino*-hexitol (38). Tribenzyl ether **37** (7.3 g, 10.7 mmol) was dissolved in absolute EtOH (50 mL), and $Pd(OH)_2$–C (1.0 g, Pearlman's catalyst) was added with stirring at 25 °C. The reaction mixture was degassed by aspirator suction and argon flushing, and then hydrogen was introduced via a balloon. Stirring for 0.5 h followed by filtration through a Celite pad (washing with ether, 300 mL) gave a

solution of the product, which was washed with H_2O (20 mL) and brine (30 mL). Drying (Na_2SO_4) followed by concentration gave essentially pure triol **38** (4.1 g, 95%). **38**: colorless oil; R_f 0.21 (silica, 40% EtOAc in petroleum ether); $[\alpha]^{20}_D$ −14.7° (*c* 1.0, MeOH); IR (film) ν_{max} 3400 (s, OH), 3080, 3060, 3040, 2950, 2930, 2880, 2860, 1470, 1460, 1380, 1360, 1250, 1100, 1030, 1000, 830, 770, 700, 670 cm^{-1}; ^1H NMR (250 MHz, benzene-d_6, TMS) δ 4.20–3.60 (m, 8 H, C*H*O, CH_2O), 3.85 (br s, 1 H, O*H*), 3.00 (br s, 1 H, O*H*), 1.82 (m, 3 H, CH_2, C*H*), 1.64 (br s, 1 H, O*H*), 0.89 (s, 18 H, Si-*t-Bu*), 0.11–0.05 (singlets, 12 H total, SiMe_2); HRMS (CI) calcd for $C_{19}H_{44}O_5Si_2$ + H 409.2806, found 409.2799 (M + H). Anal. Calcd for $C_{19}H_{44}O_5Si_2$: C, 55.84; H, 10.86. Found: C, 56.13; H, 11.00.

[2*R*-[2α,4α,5β,5(*S)]]-5-[1,3-Bis[[(1,1-dimethylethyl)dimethylsilyl]-oxy]propyl]-2-phenyl-1,3-dioxane-4-methanol (39).** To a stirred solution of triol **38** (3.0 g, 7.4 mmol) in dry benzene (28 mL) under argon was sequentially added benzaldehyde dimethylacetal (2.8 mL, 18.4 mmol) and camphorsulfonic acid (46 mg, 0.07 mmol) at room temperature. The reaction mixture was stirred at ambient temperature for 30 min and then diluted with ether (150 mL). The solution was washed with saturated aqueous $NaHCO_3$ (2 × 30 mL) and brine (30 mL) and then dried ($MgSO_4$). Concentration followed by flash chromatography (silica, 10% EtOAc in petroleum ether) gave alcohol **39** (2.9 g, 80%). **39**: colorless oil; R_f 0.33 (silica, 20% EtOAc in petroleum ether); $[\alpha]^{20}_D$ −41.0° (*c* 0.86, MeOH); IR (film) ν_{max} 3580, 3480, 3080, 3060, 3040, 2960, 2940, 2880, 2850, 1470, 1465, 1385, 1360, 1255, 1215, 1080, 1030, 990, 940, 840, 800, 770, 690, 675 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$, TMS) δ 7.43 (m, 2 H, aromatic), 7.32 (m, 3 H, aromatic), 5.43 (s, 1 H PhCH_2O), 4.29 (dd, *J* = 11.4, 4.6 Hz, 1 H, CH_2O), 3.90 (m, 1 H, C*H*O), 3.78 (m, 2 H, C*H*O, CH_2O), 3.61 (m, 2 H, CH_2O), 2.21 (m, 1 H, C*H*), 1.56 (m, 2 H, CH_2), 0.85 (s, 18 H, Si-*t-Bu*), 0.07, 0.02, 0.01 (singlets, 12 H total, SiMe_2); HRMS (CI) calcd for $C_{26}H_{48}O_5Si$ + H 497.3119, found 497.3123 (M + H). Anal. Calcd for $C_{26}H_{48}O_5Si_2$: C, 62.85; H, 9.81. Found: C, 62.55; H, 9.93.

[2*R*-[2α,4α,5β,5(*S)]]-5-[1,3-Bis[[(1,1-dimethylethyl)dimethylsilyl]-oxy]propyl]-2-phenyl-1,3-dioxane-4-carboxaldehyde (11).** Dry triethylamine (1.7 mL, 12 mmol) was added to a solution of alcohol **39** (580 mg, 1.2 mmol) in freshly distilled DMSO (3 mL) and CH_2Cl_2 (3 mL) and the solution was stirred under argon at 25 °C. SO_3·pyr complex (1.1 g, 7.2 mmol) was added portionwise, and the mixture was stirred for 4 h, diluted with ether (50 mL), and poured onto ice–water (50 mL). The organic phase was separated, and the aqueous phase was extracted with ether (3 × 75 mL). The combined organic solution was washed with H_2O (30 mL) and brine (20 mL), dried ($MgSO_4$), and concentrated, giving essentially pure aldehyde **11** (550 mg, 94%). **11**: colorless oil; R_f 0.33 (silica, 20% EtOAc in petroleum ether); $[\alpha]^{20}_D$ −30.9° (*c* 1.0, $CHCl_3$); IR (film) ν_{max} 3080, 3060, 3020, 2950, 2920, 2880, 2850, 1735, 1470, 1460, 1385, 1375, 1360, 1250, 1220, 1100, 1030, 1000, 930, 835, 770, 690, 670 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$, TMS) δ 9.68 (s, 1 H, C*H*O), 7.52 (m, 2 H, aromatic), 7.37 (m, 3 H, aromatic), 5.52 (s, 1 H, PhC*H*O), 4.43 (dd, *J* = 11.3, 4.6 Hz, 1 H, CH_2O), 4.24 (d, *J* = 10.9 Hz, 1 H, C*H*O), 4.08 (m, 1 H, C*H*O), 3.90 (t, *J* = 11.3 Hz, 1 H, CH_2O), 3.66 (m, 2 H, CH_2O), 2.36 (m, 1 H, C*H*), 1.66 (m, 2 H, CH_2), 0.91 (s, 18 H, Si-*t-Bu*), 0.08, 0.06 (singlets, 12 H total, SiMe_2); HRMS (CI) calcd for $C_{26}H_{46}O_5Si$ − H 493.2807, found 493.2865 (M − H).

5-*O*-[(1,1-Dimethylethyl)diphenylsilyl]-1,2-*O*-(1-methylethylidene)-α-D-xylofuranose (41a). To a magnetically stirred solution of the acetonide **40a** (obtained from (+)-xylose (**12a**)[15] (26.7 g, 0.14 mol) and imidazole (38.0 g, 0.56 mol) in DMF (200 mL) at 0 °C was added dropwise *t*-BuPh_2SiCl (42.0 g ≡ 39 mL, 0.15 mol) over 10 min. The reaction mixture was allowed to reach room temperature and stirred for 1 h. Ether (400 mL) and water (50 mL) were then added to the mixture, and the organic phase was separated and washed with water (3 × 50 mL) and brine (50 mL). Drying ($MgSO_4$), concentration, and purification by recrystallization (10% ether in hexane) gave pure silyl ether **41a** (57.0 g, 94%), **41a**: colorless crystals; mp 93.0–93.5 °C; $[\alpha]^{20}_D$ −2.3° (*c* 2.5, $CHCl_3$); IR (KBr) ν_{max} 3480, 2990, 2965, 2935, 2880, 2860, 1430, 1250, 1220, 1170, 1118, 1073, 1052, 1010, 990, 915, 865, 820, 709 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.77–7.65 (m, 4 H, aromatic), 7.52–7.33 (m, 6 H, aromatic), 6.00 (d, *J* = 3.7 Hz, 1 H, H-1), 4.55 (d, *J* = 3.7 Hz, 1 H, H-2), 4.37 (m, 1 H, H-4), 4.11 (m, 3 H, H-3, H-5), 4.07 (d, *J* = 3.1 Hz, O*H*), 1.47, 1.33 (singlets, 3 H each, acetonide), 1.05 (s, 9 H, Si-*t-Bu*). Anal. Calcd for $C_{24}H_{32}O_5Si$: C, 67.49; H, 7.67. Found: C, 67.26; H, 7.67.

5-*O*-[(1,1-Dimethylethyl)diphenylsilyl]-1,2-*O*-(1-methylethylidene)-α-D-xylofuranose 3-(*O*-Phenylthiocarbonate) (42a). To a magnetically stirred mixture of alcohol **41a** (32.1 g, 75.0 mmol), pyridine (16.0 mL, 198 mmol), and DMAP (460 mg, 3.75 mmol) in dry CH_2Cl_2 (500 mL) at 0 °C was added dropwise PhOC(S)Cl (19.4 g ≡ 15.7 mL, 112 mmol) in CH_2Cl_2 (60 mL). The reaction mixture was stirred overnight at ambient temperature and then poured into ice water (150 mL). The organic layer was separated, washed with water (3 × 20 mL), saturated aqueous $CuSO_4$ (2 × 20 mL), and brine (20 mL), dried ($MgSO_4$), and concentrated. Flash column chromatography (silica, 8% ether in petroleum ether) gave pure **42a** (39.8 g, 94%). **42a**: colorless oil; $[\alpha]^{20}_D$ +1.5° (*c* 2.4, $CHCl_3$); IR (film) ν_{max} 2960, 2935, 2895, 2860, 1492, 1430, 1385, 1375, 1310, 1272, 1202, 1165, 1110, 1105, 1065, 786, 761, 700 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.80–7.60 (m, 4 H, aromatic), 7.50–7.20 (m, 9 H, aromatic), 7.02 (dd, *J* = 8.0, 0.8 Hz, 2 H, aromatic), 5.97 (d, *J* = 3.8 Hz, 1 H, H-1), 5.78 (d, *J* = 3.1 Hz, 1 H, H-3), 4.79 (d, J = 3.8 Hz, 1 H, H-2), 4.56 (dt, *J* = 7.0, 3.1 Hz, 1 H, H-4), 3.96 (d, *J* = 7.0 Hz, 2 H, H-5), 1.56, 1.35 (singlets, 3 H each, acetonide), 1.07 (s, 9 H, Si-*t-Bu*); HRMS (CI) calcd for $C_{31}H_{36}O_6SSi$ + H 565.2078, found 565.2131 (M + H).

3-Deoxy-5-*O*-[(1,1-dimethylethyl)diphenylsilyl]-1,2-*O*-(1-methylethylidene)-α-D-xylofuranose (43a). Ester **42a** (40.0 g, 71.0 mmol) and AIBN (350 mg, 2.5 mmol) were dissolved in dry toluene (500 mL) and degassed by passing argon through the solution with stirring (30 min). *n*-Bu_3SnH (21.7 g, 74.0 mmol) was added. After being stirred for 1 h at 80 °C, the reaction mixture was cooled to room temperature and the solvent was removed in vacuo. The product was purified by recrystallization from hexane to give deoxy sugar **43a** (42.7 g, 77%). **43a**: colorless crystalline solid; R_f 0.13 (silica, 50% CH_2Cl_2 in hexane); $[\alpha]^{20}_D$ −8.3° (*c* 2.7, $CHCl_3$); IR (KBr) ν_{max} 2990, 2955, 2935, 2915, 2890, 2858, 1428, 1386, 1380, 1370, 1166, 1136, 1110, 1100, 1058, 1035, 1000, 708 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.75–7.65 (m, 4 H, aromatic), 7.60–7.30 (m, 6 H, aromatic), 5.83 (d, *J* = 3.6 Hz, 1 H, H-1), 4.75 (dd, *J* = 4.6, 3.6 Hz, 1 H, H-2), 4.33 (m, 1 H, H-4), 3.77 (m, 2 H, H-5), 2.08 (dd, *J* = 13.4, 4.6 Hz, 1 H, H-3), 1.88 (ddd, *J* = 13.4, 10.3, 4.6 Hz, 1 H, H-3), 1.51, 1.33 (singlets, 3 H each, acetonide), 1.05 (s, 9 H, Si-*t-Bu*); HRMS (CI) calcd for $C_{24}H_{32}O_4Si$ + H 413.2146, found 413.2078 (M + H). Anal. Calcd for $C_{24}H_{32}O_4Si$: C, 69.87; H, 7.71. Found: C, 70.01; H, 7.82.

Preparation of Deoxy Sugar 43a from 41a via Iodide 59a. To a magnetically stirred solution of **41a** (428 mg, 1.00 mmol) and pyridine (131 μL, 1.50 mmol) in CH_2Cl_2 (5 mL) at −10 °C was slowly added $(CF_3SO_2)_2O$ (186 μL, 1.10 mmol). Stirring was continued for 15 min at −10 °C. The mixture was diluted with Et_2O (30 mL), and the organic phase was washed with H_2O (10 mL), 5% aqueous HCl (10 mL), saturated aqueous $NaHCO_3$ (10 mL), and brine (10 mL), dried ($MgSO_4$), and concentrated to give crude triflate **41a**. This triflate was dissolved in dry benzene (5 mL) and *n*-Bu_4NI (739 mg, 2.00 mmol) was added. The resulting mixture was heated at reflux for 12 h, and then the solvent was removed in vacuo. The crude product was dissolved in Et_2O (30 mL) and washed with 10% $NaHSO_3$ (10 mL), saturated aqueous $NaHCO_3$ (10 mL), H_2O (10 mL), and brine (10 mL). Purification by flash column chromatography (silica, 10% ether in petroleum ether) gave iodide **59a** (323 mg, 60%). The iodide **59a** obtained above was dissolved in THF (3 mL), and $LiEt_3BH$ (1 M in THF, 1.20 mL, 1.20 mmol) was added. The resulting solution was refluxed for 12 h and then cooled to room temperature and quenched with saturated aqueous NH_4Cl (2 mL). The product was extracted with ether (2 × 20 mL), and the combined extract was washed with H_2O (5 × 10 mL) and brine (10 mL). Drying ($MgSO_4$) followed by concentration and purification by flash column chromatography afforded deoxy sugar **43a** (212 mg, 95%), which was identical with the product derived from **42a** as described above.

3-Deoxy-5-*O*-[(1,1-dimethylethyl)diphenylsilyl]-D-xylofuranose (44). To a magnetically stirred solution of deoxy sugar **43a** (20.0 g, 48.5 mmol) in dry CH_2Cl_2 (194 mL) at −78 °C was added BCl_3 (1 M solution in hexane, 63.0 mL, 63.0 mmol). The reaction mixture was stirred for 10 min at −78 °C and then poured into a pH7 buffer solution (1 M phosphate buffer, 630 mL) and vigorously stirred at room temperature for 1 h. The reaction mixture was diluted with EtOAc (400 mL), and the organic phase was separated and washed with H_2O (50 mL) and brine (50 mL) and dried ($MgSO_4$). The crude product was purified by flash column chromatography (silica, 70% ether in petroleum ether) to afford lactol **44** (α/β = 57/43, 16.2 g, 90%). **44** (α,β mixture 57/43 ratio): R_f 0.33 (silica, ether); $[\alpha]^{20}_D$ +8.8° (*c* 2.9, $CHCl_3$); IR (film) ν_{max} 3410, 2935, 2860, 1429, 1110, 1040, 945, 820, 790, 740, 700 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$, α anomer) δ 7.75–7.65 (m, 4 H, aromatic), 7.50–7.30 (m, 6 H, aromatic), 5.19 (d, *J* = 7.3 Hz, 1 H, H-1), 4.49 (m, 1 H, H-4), 4.24 (m, 1 H, H-2), 3.84 (dd, *J* = 10.9, 3.0 Hz, 1 H, H-5), 3.72 (d, *J* = 7.3 Hz, 1 H, O*H*), 3.50 (dd, *J* = 10.9, 2.9 Hz, 1 H, H-5), 2.76 (d, *J* = 5.9, 1 H, O*H*), 2.27–1.91 (m, 2 H, H-3), 1.07 (s, 9 H, Si-*t-Bu*); HRMS (CI) calcd for $C_{21}H_{28}O_4Si$ − OMe 341.1572, found 341.1564 (M − OMe).

(2*S*,4*R*)-7-[[(1,1-Dimethylethyl)diphenylsilyl]oxy]-5-hexene-2,4-diol (45). To a stirred suspension of $[Ph_3PCH_3]^+Br^-$ (30.5 g, 85.4 mmol) in dry THF (160 mL) was added *n*-BuLi (1.6 M solution in hexane, 53.4 mL, 85.4 mmol) at −20 °C under an argon atmosphere. The mixture was stirred for 20 min at −20 °C and for 25 min at 0 °C and then cooled

back to −20 °C. Lactol **40** (10.6 g, 28.5 mmol) was dissolved in dry THF (90 mL), NaH (50% in mineral oil, 1.37 g, 28.5 mmol) was added at −10 °C under an argon atmosphere, and the mixture was stirred at the same temperature for 20 min. The ylide solution prepared above was then added dropwise at −20 °C over a 5-min period, and stirring was continued for 20 min at −20 °C and 3 h at room temperature. The reaction mixture was quenched with saturated aqueous NH_4Cl (50 mL) and diluted with ether (300 mL). The organic layer was separated and washed with water (50 mL) and brine. Drying ($MgSO_4$), evaporation, and flash column chromatography (silica, 70% ether in petroleum ether) gave pure diol **45** (7.39 g, 70%). **45**: R_f 0.63 (silica, ether); $[\alpha]^{20}_D$ −1.3° (*c* 2.6, $CHCl_3$); IR (film) ν_{max} 3390, 2960, 2935, 2860, 1471, 1461, 1429, 1390, 1361, 1115, 1075, 910, 825, 735, 701 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.70–7.60 (m, 4 H, aromatic), 7.50–7.35 (m, 6 H, aromatic), 5.82 (ddd, *J* = 17.4, 10.4, 5.9 Hz, 1 H, H-5), 5.25 (dt, *J* = 17.4, 1.4 Hz, 1 H, H-6), 5.09 (dt, *J* = 10.4, 1.4 Hz, 1 H, H-6), 4.37 (m, 1 H, H-4), 3.98 (m, 1 H, H-2), 3.62 (dd, *J* = 10.2, 4.2 Hz, 1 H, H-1), 3.43 (dd, *J* = 10.2, 7.0 Hz, 1 H, H-1), 3.30 (d, *J* = 1.7 Hz, 1 H, O*H*), 3.04 (d, *J* = 3.0 Hz, 1 H, O*H*), 1.61 (m, 2 H, H-3), 1.07 (s, 9 H, Si-*t*-*Bu*); HRMS (CI) calcd for $C_{22}H_{30}O_3Si$ − OH − H_2O 335.1829, found 335.1786 (M − OH − H_2O).

[4*S*-(4β,6β)]-6-Ethenyl-4-[[[(1,1-Dimethylethyl)diphenylsilyl]oxy]methyl]-2,2-dimethyl-1,3-dioxane (46). A mixture of diol **45** (12.5 g, 33.8 mmol) and CSA (75 mg, 0.32 mmol) in 2,2-dimethoxypropane (70 mL) was stirred for 1 h under an argon atmosphere. The reaction mixture was diluted with ether (300 mL), and the organic layer was separated, washed with saturated aqueous $NaHCO_3$ (50 mL), water (50 mL), and brine (50 mL), dried ($MgSO_4$), and concentrated. Purification by flash column chromatography (silica, 5% ether in petroleum ether) gave acetonide **46** (12.2 g, 88%). **46**: R_f 0.22 (silica, 10% ether in petroleum ether); $[\alpha]^{20}_D$ +2.7° (*c* 2.7, $CHCl_3$); IR (film) ν_{max} 2995, 2960, 2935, 2860, 1430, 1380, 1275, 1201, 1176, 1130, 1115, 1030, 997, 987, 920, 821, 735, 700 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.75–7.65 (m, 4 H, aromatic), 7.47–7.33 (m, 6 H, aromatic), 5.83 (ddd, *J* = 17.1, 10.4, 6.0 Hz, 1 H, olefinic), 5.27 (dt, *J* = 17.1, 1.2 Hz, 1 H, olefinic), 5.14 (t, *J* = 10.4, 1.2 Hz, 1 H, olefinic), 4.34 (m, 1 H, H-6), 4.02 (m, 1 H, H-4), 3.72 (dd, *J* = 10.1, 5.2 Hz, 1 H, C*H*$_2$O), 3.55 (dd, *J* = 10.1, 6.1 Hz, 1 H, C*H*$_2$O), 1.68 (dt, *J* = 12.9, 2.5 Hz, 1 H, H-5), 1.46, 1.40 (singlets, 3 H each, acetonide), 1.29 (m, 1 H, H-5), 1.06 (s, 9 H, Si-*t*-*Bu*); HRMS (CI) calcd for $C_{25}H_{34}O_3Si$ − Me 395.2041, found 395.2072 (M − Me).

2,3-Dideoxy-6-*O*-[(1,1-dimethylethyl)diphenylsilyl]-3,5-*O*-(1-methylethylidene)-D-*erythro*-hexitol (47). To a magnetically stirred solution of 2-methyl-2-butene (7.02 g ≡ 10.6 mL, 100 mmol) in dry THF (100 mL) at 0 °C was added a BH_3·THF solution (1 M, 50.0 mL, 50.0 mmol). After the mixture was stirred for 1 h at 0 °C, a solution of olefin **46** (10.0 g, 24.4 mmol) in THF (50 mL) was added dropwise and stirring was continued at 0 °C for 2 h. The excess reagent was quenched with H_2O (5 mL), and 6 N NaOH (50 mL, 300 mmol) was slowly added followed by 30% H_2O_2 (35 mL). The mixture was vigorously stirred at room temperature for 30 min and then diluted with ether (300 mL). The organic phase was separated and washed with H_2O (2 × 50 mL), 10% aqueous $NaHSO_3$ (50 mL), saturated aqueous $NaHCO_3$ (50 mL), and brine (50 mL) and dried ($MgSO_4$). The solution was concentrated in vacuo, and the residue was purified by flash column chromatography (silica, 60% ether in petroleum ether) to afford alcohol **47** (8.99 g, 86%). **47**: colorless oil; R_f 0.39 (silica, 85% ether in petroleum ether); $[\alpha]^{20}_D$ −13.4° (*c* 1.9, $CHCl_3$); IR (film) ν_{max} 3440, 2935, 2860, 1470, 1461, 1429, 1380, 1200, 1140, 1105, 1050, 820, 737, 700 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 4.12 (m, 1 H, H-3), 3.99 (m, 1 H, H-5), 3.76 (m, 2 H, H-1), 3.71 (dd, *J* = 10.2, 5.2 Hz, 1 H, H-6), 3.54 (dd, *J* = 10.2, 6.0 Hz, 1 H, H-6), 2.59 (t, *J* = 4.8 Hz, 1 H, O*H*), 1.73 (dt, *J* = 5.6, 5.5, 2 H, Hz, H-2), 1.58 (dt, *J* = 12.9, 2.5 Hz, 1 H, H-4), 1.44, 1.37 (singlets, 3 H each, acetonide), 1.30 (ddd, *J* = 12.9, 11.5, 10.8 Hz, 1 H, H-4), 1.06 (s, 9 H, Si-*t*-*Bu*); HRMS (CI) calcd for $C_{25}H_{36}O_4Si$ + H 429.2459, found 429.2436 (M + H).

2,4-Dideoxy-6-*O*-[(1,1-dimethylethyl)diphenylsilyl]-3,5-*O*-(1-methylethylidene)-1-*O*-(phenylmethyl)-D-*erythro*-hexitol (48). To a stirred suspension of KH (1.40 g, 25% in mineral oil, 8.78 mmol) in dry THF (10 mL) at 0 °C was added, under argon, alcohol **47** (3.00 g, 7.02 mmol) in THF (15 mL) over 10 min. The reaction mixture was allowed to reach room temperature and stirred for an additional 10 min. Benzyl bromide (1.50 g, 8.78 mmol) was added, and the mixture was stirred for 14 h at room temperature. The resulting mixture was diluted with ether (150 mL), washed with saturated aqueous NH_4Cl (50 mL), water (30 mL), and brine (30 mL), dried ($MgSO_4$), and concentrated. Purification by flash column chromatography (silica, 5% ether in petroleum ether) afforded benzyl ether **48** (3.09 g, 85%). **48**: colorless oil; R_f 0.80 (silica, 50% ether in petroleum ether); $[\alpha]^{20}_D$ −12.7° (*c* 2.5, $CHCl_3$); IR (film) ν_{max} 2990, 2935, 2860, 1470, 1450, 1425, 1379, 1197, 1168, 1108, 994, 818, 735, 697 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.77–7.65 (m, 4 H, aromatic), 7.46–7.27 (m, 6 H, aromatic), 7.33 (s, 5 H, aromatic), 4.51 (d, *J* = 12.6 Hz, 1 H, PhC*H*$_2$O), 4.49 (d, *J* = 12.6 Hz, 1 H, PhC*H*$_2$O), 4.00 (m, 2 H, H-3, H-5), 3.71 (dd, *J* = 10.4, 5.2 Hz, 1 H, H-6), 3.55 (m, 2 H, H-1), 3.53 (dd, *J* = 10.4, 5.6 Hz, 1 H, H-6), 1.77 (m, 2 H, H-2), 1.59 (m, 1 H, H-4), 1.40, 1.35 (singlets, 3 H each, acetonide), 1.25 (m, 1 H, H-4), 1.07, 1.05 (singlets, 9 H total, Si-*t*-*Bu*); HRMS (CI) calcd for $C_{32}H_{42}O_4Si$ + H 519.2928, found 519.2950.

2,4-Dideoxy-3,5-*O*-(1-methylethylidene)-1-*O*-(phenylmethyl)-D-*erythro*-hexitol (49). *n*-Bu_4NF (1 M in THF, 30 mL, 30.0 mmol) was slowly added to silyl ether **48** (13.0 g, 25.0 mmol) in dry THF (120 mL) at room temperature, and the reaction mixture was stirred for 1 h. This mixture was diluted with ether (100 mL), washed with water (5 × 30 mL) and brine (30 mL), and dried ($MgSO_4$). Concentration, followed by flash column chromatography (silica, 20 → 70% ether in petroleum ether), gave alcohol **49** (6.75 g, 96%). **49**: colorless oil; R_f 0.24 (silica, 60% ether in petroleum ether); $[\alpha]^{20}_D$ −14.6° (*c* 0.26, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3600 (OH), 3000, 2970, 2920, 2870, 1450, 1380, 1200, 1165, 1100, 700 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.40–7.20 (m, 5 H, aromatic), 4.53, 4.47 (doublets, *J* = 12.1 Hz, 1 H each, PhC*H*$_2$O), 4.05 (m, 2 H, C*H*O), 3.55 (m, 4 H, C*H*$_2$O), 2.02 (dd, *J* = 7.2, 5.4 Hz, 1 H, C*H*$_2$), 1.75 (m, 2 H, C*H*$_2$), 1.44, 1.39 (singlets, 3 H each, acetonide), 1.30 (m, 1 H, C*H*$_2$); HRMS (CI) calcd for $C_{14}H_{24}O_4$ + H 281.1753, found 281.1745 (M + H). Anal. Calcd for $C_{14}H_{24}O_4$: C, 68.54; H, 8.63. Found: C, 68.57; H, 8.62.

3,5-Dideoxy-2,4-*O*-(1-methylethylidene)-6-*O*-(phenylmethyl)-L-*erythro*-hexose (9). To a magnetically stirred solution of alcohol **49** (5.9 g, 21.1 mmol), DMSO (50.0 mL), and triethylamine (1.50 mL, 106 mmol) in CH_2Cl_2 (25 mL) was added SO_3·Pyr complex (16.8 g, 106 mmol), and stirring was continued for 0.5 h. The mixture was then diluted with ether (200 mL) and washed with H_2O (2 × 25 mL), 5% aqueous HCl (25 mL), saturated aqueous $NaHCO_3$ (25 mL), and brine (25 mL). Drying ($MgSO_4$) and concentration followed by flash column chromatography (silica, 60% ether in petroleum ether) gave pure aldehyde **9** (5.4 g, 92%). **9**: colorless oil; R_f 0.22 (silica, 60% ether in petroleum ether); $[\alpha]^{20}_D$ −62.5° (*c* 0.40, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3000, 2885, 1740 (s, C=O), 1455, 1385, 1200, 1170, 1105, 700 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 9.60 (s, 1 H, C*H*O), 7.38–7.26 (m, 5 H, aromatic), 4.53, 4.47 (doublets, *J* = 12.2 Hz, 1 H each, PhC*H*$_2$O), 4.30 (dd, *J* = 12.2, 3.0 Hz, 1 H, C*H*C(O), 4.13 (m, 1 H, C*H*O), 3.60 (m, 2 H, C*H*$_2$O), 1.80 (m, 3 H, C*H*$_2$), 1.46 (s, 6 H, acetonide), 1.35 (m, 1 H, C*H*$_2$); HRMS (CI) calcd for $C_{16}H_{22}O_4$ + H 279.1596, found 279.1615 (M + H).

3-Deoxy-1,2-*O*-(1-methylethylidene)-α-L-xylofuranose (43b). Compound **43b** was prepared by the same sequence as compound **43a** except that (−)-xylose was used as the starting material. Compound **43b** was identical with **43a** except for the $[\alpha]^{20}_D$, which was +8.0° (*c* 2.4, $CHCl_3$).

3-Deoxy-1,2-*O*-(1-methylethylidene)-α-L-xylofuranose (50). To a magnetically stirred solution of silyl ether **43b** (23.0 g, 55.8 mmol) in dry THF (55 mL) was added dropwise *n*-Bu_4NF (1 M in THF, 60.0 mL, 60.0 mmol), and the reaction mixture was stirred for 30 min. The mixture was concentrated to one-third of its original volume and directly subjected to flash chromatography (silica, 80% ether in petroleum ether) to give crystalline alcohol **50** (8.94 g, 92%). **50**: colorless crystalline solid; mp 78–79 °C (ether–hexane); R_f 0.28 (silica, ether); $[\alpha]^{20}_D$ +12.5° (*c* 3.5, $CHCl_3$); IR (KBr) ν_{max} 3490, 3390, 2995, 2970, 2940, 1380, 1371, 1265, 1210, 1165, 1110, 1065, 1058, 1049, 1030 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 5.83 (d, *J* = 3.7 Hz, 1 H, H-1), 4.76 (dd, *J* = 4.6, 3.7 Hz, 1 H, H-2), 4.35 (m, 1 H, H-4), 3.89 (m, 1 H, H-5), 3.56 (m, 1 H, H-5), 2.21 (br s, 1 H, O*H*), 2.00 (dd, *J* = 13.5, 4.6 Hz, 1 H, H-3), 1.84 (ddd, *J* = 13.5, 10.8, 4.6 Hz, 1 H, H-3), 1.52, 1.33 (singlets, 3 H each, acetonide). Anal. Calcd for $C_8H_{14}O_4$: C, 55.16; H, 8.10. Found: C, 55.32; H, 8.07.

3-Deoxy-1,2-*O*-(1-methylethylidene)-5-*O*-(phenylmethyl)-α-L-xylofuranose (51). To a magnetically stirred solution of alcohol **50** (40.7 g, 234 mmol) in dry THF (240 mL) at 0 °C was added NaH (12.0 g, 60% in mineral oil, 304 mmol), the mixture was allowed to warm to room temperature, and stirring was continued for 20 min. *n*-Bu_4NI (865 mg, 2.34 mmol) was added, and the mixture was cooled to 0 °C before benzyl bromide (31.0 mL, 257 mmol) was added slowly. The resulting mixture was then allowed to stir for 1 h at room temperature, after which time saturated aqueous NH_4Cl (60 mL) and ether (400 mL) were added. The organic phase was separated, washed with H_2O (50 mL) and brine (50 mL), dried ($MgSO_4$), and concentrated. Purification by flash column chromatography (silica, 30% ether in petroleum ether) gave benzyl ether **51** (58.7 g, 95%). **51**: colorless oil; R_f 0.56 (silica, 60% in petroleum ether); IR (film) ν_{max} 3035, 2990, 2940, 2910, 2865, 1382, 3373, 1213, 1165, 1130, 1100, 1061, 1020, 738, 695 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.40–7.25 (m, 5 H, aromatic), 5.84 (d, *J* = 3.8 Hz, 1 H, H-1), 4.73 (dd, *J* = 4.6, 3.8 Hz, 1 H, H-2), 4.58 (s, 2 H, PhC*H*$_2$O), 4.41 (m, 1 H, H-4), 3.64 (dd, *J* = 10.7, 3.5 Hz, 1 H, H-5), 3.54 (dd, *J* = 10.7,

5.0 Hz, 1 H, H-5), 2.06 (dd, J = 13.4, 4.6 Hz, 1 H, H-3), 1.76 (ddd, J = 13.4, 10.8, 4.6 Hz, 1 H, H-3), 1.51, 1.33 (singlets, 3 H each, acetonide); HRMS (CI) calcd for $C_{15}H_{20}O_4$ + H 265.1406, found 265.1439 (M + H).

3-Deoxy-5-*O*-(phenylmethyl)-L-xylofuranose (52). A mixture of acetonide **51** (12.6 g, 48.0 mmol), aqueous HCl (1.2 N, 24 mL, 28.8 mmol), water (105 mL), and DME (200 mL) was heated under reflux for 1 h. After being cooled to room temperature, the mixture was neutralized with $NaHCO_3$ (ca. 2.5 g), concentrated to ca. 50 mL, and extracted with ether (5 × 50 mL). The combined organic phase was washed with water (10 mL) and brine (10 mL) and dried ($MgSO_4$). Concentration followed by flash column chromatography (silica, 2% MeOH in ether) gave diol **52** (10.2 g, 95%). **52**: colorless oil; R_f 0.41 (silica, 2.5% EtOH in ether); $[\alpha]^{20}_D$ −5.5° (c 2.1, $CHCl_3$, α/β = 67/33); IR (film) ν_{max} 3400, 3040, 2940, 2868, 1452, 795, 735, 695 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$, α anomer) δ 7.50–7.30 (m, 5 H, aromatic), 5.17 (d, J = 8.0 Hz, 1 H, H-1), 4.64, 4.57 (doublets, J = 11.7 Hz, 1 H each, $PhCH_2O$), 4.45 (m, 1 H, H-4), 4.22 (m, 1 H, H-2), 3.81, 3.77 (singlets, 1 H each, O*H*), 3.68 (dd, J = 10.0, 2.7 Hz, 1 H, H-5), 3.43 (dd, J = 10.0, 3.0 Hz, 1 H, H-5), 2.33, 2.03 (multiplets, 1 H each, H-3); HRMS (CI) calcd for $C_{12}H_{16}O_4$ − OH 207.1020, found 207.1017 (M − OH).

(2*R*,4*S*)-1-[(Phenylmethoxy)methyl]-5-hexene-2,4-diol (53). Compound **53** was prepared from **52** in the same manner as described for **45** from **44** (67% yield). **52**: colorless oil; R_f 0.63 (silica, 2.5% EtOH in ether); $[\alpha]^{20}_D$ +0.86° (c 2.3, $CHCl_3$); IR (film) ν_{max} 3400, 2918, 2965, 1452, 1362, 1095, 990, 920 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.32 (s, 5 H, aromatic), 5.84 (ddd, J = 17.2, 10.4, 6.0 Hz, 1 H, H-5), 5.24 (ddd, J = 17.2, 1.4, 1.3 Hz, 1 H, H-6), 5.08 (ddd, J = 10.4, 1.4, 1.3 Hz, 1 H, H-6), 4.54 (s, 2 H, $PhCH_2O$), 4.35 (m, 1 H, H-4), 4.05 (m, 1 H, H-2), 3.46 (s, 1 H, O*H*), 3.41 (m, 2 H, CH_2O), 3.35 (s, 1 H, O*H*), 1.63 (m, 2 H, H-3); HRMS (CI) calcd for $C_{13}H_{18}O_3$ + H 223.1333, found 223.1321 (M + H).

[4*R*-(4α,5α)]-4-[(Phenylmethoxy)methyl]-6-ethenyl-2,2-dimethyl-1,3-dioxane (54). Compound **54** was prepared from **53** in the same manner as described for **46** from **45** (90% yield). **54**: colorless oil; R_f 0.30 (silica, 10% ether in petroleum ether); $[\alpha]^{20}_D$ +1.48° (c 2.3, $CHCl_3$); IR (film) ν_{max} 2995, 2940, 2910, 2865, 1451, 1379, 1255, 1200, 1173, 1101, 985, 920, 861, 735, 694 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.43–7.27 (m, 5 H, aromatic), 5.82 (ddd, J = 17.2, 10.5, 5.9 Hz, 1 H, olefinic), 5.25 (ddd, J = 17.2, 1.3, 1.4 Hz, 1 H, olefinic), 5.12 (ddd, J = 10.5, 1.3, 1.2 Hz, 1 H, olefinic), 4.60, 4.54 (doublets, J = 12.2 Hz, 1 H each, $PhCH_2O$), 4.37 (m, 1 H, H-6), 4.14 (m, 1 H, H-4), 3.52 (dd, J = 9.9, 5.8 Hz, 1 H, CH_2O), 3.38 (dd, J = 9.9, 5.0 Hz, 1 H, CH_2O), 1.60 (dt, J = 12.9, 2.9 Hz, 1 H, H-5), 1.50, 1.45 (singlets, 3 H each, acetonide), 1.34 (dt, J = 12.9, 11.7 Hz, 1 H, H-5); HRMS (CI) calcd for $C_{16}H_{22}O_3$ + H 263.1646, found 263.1636 (M + H).

3,5-Dideoxy-2,4-*O*-(1-methylethylidene)-1-*O*-(phenylmethyl)-D-*erythro*-hexitol (55). Compound **55** was prepared from **54** in the same manner as described for **47** from **46** (93% yield). **55**: colorless oil; R_f 0.14 (silica, 60% ether in petroleum ether); $[\alpha]^{20}_D$ +22.9° (c 2.5, $CHCl_3$); IR (film) ν_{max} 3450, 2945, 2920, 2870, 1380, 1200, 1165, 1105, 1050, 737, 695 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.33 (s, 5 H, aromatic), 4.57, 4.54 (doublets, J = 12.2 Hz, 1 H each, $PhCH_2O$), 4.10 (m, 2 H, H-2, H-4), 3.74 (m, 2 H, H-6), 3.50 (dd, J = 9.9, 5.8 Hz, 1 H, H-1), 3.37 (dd, J = 9.9, 4.9 Hz, 1 H, H-1), 2.65 (t, J = 4.9 Hz, 1 H, O*H*), 1.71 (m, 2 H, H-5), 1.51 (ddd, J = 12.9, 2.6, 2.8 Hz, 1 H, H-3), 1.48, 1.41 (singlets, 3 H each, acetonide), 1.33 (dt, J = 12.9, 11.7 Hz, 1 H, H-3); HRMS (CI) calcd for $C_{16}H_{24}O_4$ + H 281.1751, found 281.1753 (M + H).

3,5-Dideoxy-6-*O*-[(1,1-dimethylethyl)dimethylsilyl]-2,4-*O*-(1-methylethylidene)-1-*O*-(phenylmethyl)-D-*erythro*-hexitol (56). Compound **56** was prepared from **55** in the same manner as described for **68b** from **13b** (92% yield). **56**: colorless oil; R_f 0.8 (silica, 60% ether in petroleum ether); $[\alpha]^{20}_D$ +17.6° (c 2.5, $CHCl_3$); IR (film) ν_{max} 2950, 2925, 2885, 1380, 1256, 1200, 1100, 835, 772 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.38–7.25 (m, 5 H, aromatic), 4.60, 4.54 (doublets, J = 12.2 Hz, 1 H each, $PhCH_2O$), 4.08 (m, 2 H, H-2, H-4), 3.72 (ddd, J = 10.1, 7.5, 5.7 Hz, 1 H, H-6), 3.63 (dd, J = 10.1, 5.3 Hz, 1 H, H-6), 3.50 (dd, J = 9.9, 5.7 Hz, 1 H, H-1), 3.37 (dd, J = 9.9, 4.9 Hz, 1 H, H-1), 1.65 (m, 2 H, H-5), 1.54 (ddd, J = 12.8, 2.5, 2.4 Hz, 1 H, H-3), 1.45, 1.40 (singlets, 3 H each, acetonide), 1.22 (dt, J = 12.8, 11.7 Hz, 1 H, H-3), 0.89 (s, 9 H, Si-*t*-*Bu*), 0.04 (s, 6 H, $SiMe_2$); HRMS (CI) calcd for $C_{22}H_{38}O_4Si$ 395.2616, found 395.2611.

3,5-Dideoxy-6-*O*-[(1,1-dimethylethyl)dimethylsilyl]-2,4-*O*-(1-methylethylidene)-D-*erythro*-hexitol (57). Benzyl ether **56** (2.45 g, 6.20 mmol) was dissolved in EtOH (30 mL) and stirred under a hydrogen atmosphere in the presence of 10% Pd–C (500 mg) at room temperature for 1 h. The catalyst was filtered off, and the solvent was removed in vacuo. Purification by flash column chromatography gave pure alcohol **57** (1.85 g, 98%). **57**: colorless oil; R_f 0.20 (silica, 40% ether in petroleum ether); $[\alpha]^{20}_D$ +10.2° (c 0.40, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3600 (OH), 2960, 2930, 2880, 2860, 1470, 1465, 1380, 1260, 1100, 840 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 4.05 (m, 2 H, CH_2O), 3.78–3.45 (m, 4 H, CH_2O, C*H*O), 2.05 (dd, J = 7.1, 5.4 Hz, 1 H, CH_2), 1.67 (m, 2 H, CH_2), 1.45, 1.44 (singlets, 3 H each, acetonide), 1.35 (m, 1 H, CH_2), 0.89 (s, 9 H, Si-*t*-*Bu*), 0.05 (s, 6 H, $SiMe_2$); HRMS (CI) calcd for $C_{15}H_{32}O_4Si$ + H 305.2148, found 305.2088 (M + H). Anal. Calcd for $C_{15}H_{32}O_4Si$: C, 59.69; H, 10.59. Found: C, 59.45; H, 10.62.

Methyl 3,5-Dideoxy-6-*O*-[(1,1-dimethylethyl)dimethylsilyl]-2,4-*O*-(1-methylethylidene)-D-*erythro*-hexonate (58). To a magnetically stirred solution of alcohol **57** (304 mg, 1.00 mmol) and $NaIO_4$ (1.07 g, 5.00 mmol) in MeCN (2 mL), CCl_4 (2 mL), and H_2O (3 mL) was added a catalytic amount of ruthenium(IV) oxide hydrate (3 mg). The mixture was vigorously stirred for 6 h (TLC monitoring) and then diluted with CH_2Cl_2 (50 mL) and H_2O (30 mL). The organic phase was separated, and the aqueous phase was extracted with CH_2Cl_2 (3 × 20 mL). The combined extract was concentrated, dissolved in ether (5 mL), and cooled to 0 °C. Excess ethereal diazomethane was added to this solution, and after the completion of esterification (TLC) argon was bubbled through the solution to remove the excess diazomethane (20 min). This solution was diluted with ether (50 mL), dried ($MgSO_4$), and concentrated. Flash column chromatography (silica, 20% ether in petroleum ether) afforded pure methyl ester **58** (253 mg, 76%). **58**: colorless oil; R_f 0.20 (silica, 20% ether in petroleum ether); $[\alpha]^{20}_D$ +20.4° (c 4.9, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3000, 2960, 2950, 2860, 1755 (s, C=O), 1470, 1460, 1440, 1380, 1260, 1140, 1100, 830 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 4.50 (dd, J = 12.1, 2.8 Hz, 1 H, OC*H*C(O)), 4.10 (m, 1 H, C*H*O), 3.74 (s, 3 H, OCH_3), 3.66 (m, 2 H, CH_2O), 1.85 (dt, J = 13.0, 2.7 Hz, 1 H, CH_2), 1.70–1.40 (m, 3 H, CH_2), 1.45, 1.44 (singlets, 3 H each, acetonide), 0.86 (s, 9 H, Si-*t*-*Bu*), 0.02 (s, 6 H, $SiMe_2$); HRMS (CI) calcd for $C_{16}H_{32}O_5Si$ + H 333.2097, found 333.2052. Anal. Calcd for $C_{16}H_{32}O_5Si$: C, 57.59; H, 9.70. Found: C, 58.00; H, 9.95.

Dimethyl [[[(4*R*,6*R*)-6-[2-[[(1,1-Dimethylethyl)dimethylsilyl]oxy]ethyl]-2,2-dimethyl-*m*-dioxan-4-yl]carbonyl]methyl]phosphonate (10). To a magnetically stirred solution of dimethyl methylphosphonate (236 mg ≡ 0.270 mL, 2.50 mmol) in dry THF (25 mL) was added *n*-BuLi (1.6 M in hexane, 1.56 mL, 2.50 mmol) at −78 °C, and the mixture was stirred for 30 min at the same temperature. A solution of methyl ester **58** (332 mg, 1.00 mmol) in dry THF (5 mL) was slowly added, and stirring was continued for 30 min. The reaction mixture was quenched at −78 °C with saturated aqueous NH_4Cl (5 mL) and then allowed to warm to room temperature, diluted with ether (100 mL), washed with H_2O (10 mL) and brine (10 mL), dried ($MgSO_4$), and concentrated. Purification by flash column chromatography (silica, ether → 2.5% MeOH in ether) gave pure keto phosphonate **10** (407 mg, 96%). **10**: colorless oil; R_f 0.16 (silica, ether); $[\alpha]^{20}_D$ +48.1° (c 3.6, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3020, 2980, 2960, 2870, 1730 (s, C=O), 1480, 1470, 1380, 1255, 1045, 840 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 4.36 (dd, J = 11.9, 2.9 Hz, 1 H, OC*H*C(O)), 4.06 (m, 1 H, C*H*O), 3.770 (d, J = 11.1 Hz, 3 H, $POCH_3$), 3.768 (d, J = 11.3 Hz, 3 H, $POCH_3$), 3.64 (m, 2 H, CH_2O), 3.47 (dd, J = 22.6, 14.3 Hz, 1 H, $PCH_2C(O)$), 3.16 (dd, J = 21.9, 14.3 Hz, 1 H, $PCH_2C(O)$), 1.79 (dt, J = 13.1, 2.7 Hz, 1 H, CH_2), 1.63 (m, 2 H, CH_2), 1.44, 1.42 (singlets, 3 H each, acetonide), 1.30 (dt, J = 13.0, 11.9 Hz, 1 H, CH_2), 0.86 (s, 9 H, Si-*t*-*Bu*), 0.01 (s, 6 H, $SiMe_2$); HRMS (CI) calcd for $C_{18}H_{37}O_7PSi$ + H 425.2124, found 425.2134 (M + H). Anal. Calcd for $C_{18}H_{37}O_7PSi$: C, 50.92; H, 8.78; P, 7.30. Found: C, 50.75; H, 8.77; P, 7.42.

[2*R*-(2β,3α)]-3-[(Phenylmethoxy)methyl]oxiranemethanol (60a). D-(−)-Diethyltartrate (22.7 g, 0.11 mol) in dry CH_2Cl_2 (25 mL) was slowly added to a stirred solution of $Ti(O\text{-}i\text{-}Pr)_4$ (31.2 g, 0.11 mol) in CH_2Cl_2 (800 mL) at −23 °C under argon. Stirring was continued at −23 °C for 15 min, and then allylic alcohol **14** (17.8 g, 0.10 mol) in CH_2Cl_2 (100 mL) was slowly added, followed by *t*-BuOOH (4 M in CH_2Cl_2, 57.5 mL, 0.23 mol). The reaction mixture was stirred for 5 h at −23 °C, and then it was quenched with Me_2S (2 mL) and 10% aqueous tartaric acid (100 mL). After being stirred at −23 °C for 0.5 h and then at room temperature for 1 h, the solution was diluted with CH_2Cl_2 (500 mL) and the organic phase was separated. Washing of the organic phase with water (100 mL) and brine (100 mL) followed by drying ($MgSO_4$), concentration, and flash column chromatography (silica, 80% ether in petroleum ether) gave epoxide **60a** (1.45 g, 75%). **60a**: colorless oil; R_f 0.17 (silica, ether); $[\alpha]^{25}_D$ +21.8° (c 6.5, $CHCl_3$); IR (film) ν_{max} 3430, 3060, 3025, 2980, 2920, 2860, 1492, 1452, 1362, 1310, 1240, 1203, 1100, 1025, 867 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.45–7.28 (m, 5 H, aromatic), 4.60, 4.57 (doublets, J = 11.9 Hz, 1 H each, $PhCH_2O$), 3.93 (ddd, J = 12.8, 5.7, 2.4 Hz, 1 H, CH_2O), 3.77 (dd, J = 11.5, 3.0 Hz, 1 H, CH_2O), 3.64 (ddd, J = 12.8, 7.3, 4.4 Hz, 1 H, CH_2O), 3.53 (dd, J = 11.5, 5.5 Hz, 1 H, CH_2O), 3.24 (m, 1 H, C*H* epoxide), 3.10 (m, 1 H, C*H* epoxide), 1.99 (dd, J = 7.3, 5.7 Hz, 1 H, O*H*); HRMS (CI) calcd for

$C_{11}H_{14}O_3$ 194.0943, found 194.0955 (M^+).

[2*R*-(2β,3α)]-3-[(Phenylmethoxy)methyl]oxiranecarboxaldehyde (61a). To a cold (−78 °C) stirred solution of oxalyl chloride (5.35 g ≡ 3.60 mL, 42.1 mmol) in CH_2Cl_2 (100 mL) was slowly added DMSO (4.38 g ≡ 4.0 mL, 56.2 mmol). After the mixture was stirred at −78 °C for 10 min, epoxy alcohol **60a** (8.16 g, 42.5 mmol) in CH_2Cl_2 (30 mL) was added, and the reaction mixture was stirred at that temperature for 15 min. Triethylamine (14.1 g ≡ 13.2 mL, 140 mmol) was slowly added, and the reaction mixture was stirred at −78 °C for 30 min and then the cooling bath was removed and stirring was continued for an additional 30 min. Dilution with CH_2Cl_2 (300 mL), washing with dilute aqueous HCl (100 mL), water (100 mL), and brine (100 mL), followed by drying ($MgSO_4$) and evaporation, gave essentially pure aldehyde **61a** (8.00 g, 98%). Further purification could be effected by flash column chromatography (silica, 30% ether in petroleum ether): R_f 0.24 (silica, 50% ether in petroleum ether); $[\alpha]^{25}_D$ −9.4° (*c* 1.8, $CHCl_3$); IR (film) ν_{max} 3022, 2920, 2920, 2860, 1730 (s, C=O), 1493, 1452, 1361, 1210, 1098, 1025, 859, 736, 695 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 9.05 (d, *J* = 6.2 Hz, 1 H, C*H*O), 7.34 (s, 5 H, aromatic), 4.59 (s, 2 H, PhCH_2O), 3.85 (dd, *J* = 11.8, 2.6 Hz, 1 H, CH_2O), 3.59 (dd, *J* = 11.8, 5.2 Hz, 1 H, CH_2O), 3.48 (m, 1 H, C*H* epoxide), 3.34 (dd, *J* = 6.2, 1.8 Hz, 1 H, C*H* epoxide); HRMS (CI) calcd for $C_{11}H_{12}O_3$ + H 193.0864, found 193.0826 (M + H).

[2*R*-(2β,3α,*E*)]-3-[(Phenylmethoxy)methyl]oxiranepropenoic Acid Methyl Ester (62a). A mixture of aldehyde **61a** (5.10 g, 26.6 mmol) and Ph_3P=CHCOOMe (10.0 g, 29.9 mmol) in dry benzene (30 mL) was stirred at room temperature under argon for 16 h. Concentration followed by flash column chromatography (silica, 20% ether in petroleum ether) gave, in order of elution, the *Z* isomer of **62a** (955 mg, 14.5%) and *E* olefin **62a** (5.05 g, 77%). *E* olefin **62a**: colorless oil; R_f 0.42 (silica, 50% ether in petroleum ether) (R_f for the *Z* isomer of **62a** in same system was 0.51); $[\alpha]^{25}_D$ +17.9° (*c* 1.5, $CHCl_3$); IR (film) ν_{max} 3060, 3025, 2995, 2950, 2860, 1725, 1660, 1492, 1451, 1433, 1360, 1305, 1275, 1195, 1180, 1140, 1098, 1025, 973, 882, 850, 740, 697 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.34 (s, 5 H, aromatic), 6.68 (dd, *J* = 15.8, 7.3 Hz, 1 H, olefinic), 6.16 (d, *J* = 15.8 Hz, 1 H, olefinic), 4.57 (s, 2 H, PhCH_2O), 3.79 (dd, *J* = 12.0, 9.5 Hz, 1 H, CH_2O), 3.75 (s, 3 H, COOCH_3), 3.58 (dd, *J* = 12.0, 5.0 Hz, 1 H, CH_2O), 3.42 (dd, *J* = 7.3, 1.7 Hz, 1 H, C*H* epoxide), 3.15 (m, 1 H, C*H* epoxide); HRMS (CI) calcd for $C_{14}H_{16}O_4$ + H 249.1126, found 249.1133 (M + H).

(*S*)-6-(Phenylmethoxy)-2-hexene-1,5-diol (63a). To a stirred solution of epoxy ester **62a** (*E* isomer, 4.80 g, 19.4 mmol) in dry CH_2Cl_2 (190 mL) was slowly added DIBAL (114 mL, 1 M solution in hexane, 114 mmol) at −78 °C under argon. The reaction mixture was stirred at −78 °C for 30 min and then quenched with MeOH (5 mL) and water (10 mL). The mixture was diluted with CH_2Cl_2 (300 mL) and washed with dilute aqueous HCl (100 mL), water (100 mL), and brine (100 mL). Drying ($MgSO_4$) followed by concentration and flash column chromatography (silica, ether) gave pure allylic alcohol **63a** (3.53 g, 82%). **63a**: colorless oil; R_f 0.31 (silica, 2.5% EtOH in ether); $[\alpha]^{25}_D$ +2.7° (*c* 1.5, $CHCl_3$); IR (film) ν_{max} 3390, 3030, 2920, 2865, 1496, 1455, 1365, 1207, 1102, 1093, 1030, 1000, 972, 738, 697 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.34 (s, 5 H, aromatic), 5.70 (m, 2 H, olefinic), 4.55 (s, 2 H, PhCH_2O), 4.09 (m, 2 H, CH_2OH), 3.87 (m, 1 H, C*H*O), 3.73 (dd, *J* = 9.2, 7.4 Hz, 1 H, CH_2O), 3.50 (dd, *J* = 9.2, 3.3 Hz, 1 H, CH_2O), 2.55 (br s, 1 H, O*H*), 2.25 (m, 2 H, CH_2), 1.73 (br s, 1 H, O*H*); HRMS (CI) calcd for $C_{13}H_{18}O_3$ + H 223.1333, found 223.1364 (M + H).

(*S*)-6-(Phenylmethoxy)-2-hexene-1,5-diol 1-(2,2-Dimethylpropanoate) (64a). To a stirred solution of diol **63a** (4.50 g, 20.3 mmol) in dry pyridine (2.2 mL) was added trimethylacetyl chloride (2.93 g ≡ 3.0 mL, 24.3 mmol) at 0 °C under argon. The reaction mixture was stirred at 0 °C for 3 h and then quenched with water (10 mL) and extracted with ether (100 mL). The organic phase was washed with dilute aqueous HCl (25 mL), water (25 mL), and brine (25 mL) and dried ($MgSO_4$). Concentration followed by flash column chromatography (silica, 50% ether in petroleum ether) gave pivaloate ester **64a** (5.89 g, 95%). **64a**: colorless oil; R_f 0.68 (silica, 85% ether in petroleum ether); $[\alpha]^{25}_D$ +2.8° (*c* 1.7, $CHCl_3$); IR (film) ν_{max} 3460, 3020, 2985, 2930, 2900, 2870, 1730, 1492, 1480, 1452, 1395, 1363, 1280, 1150, 1110, 1098, 1025, 970, 765, 730, 693 cm^{-1}; ^{H} NMR (250 MHz, $CDCl_3$) δ 7.32 (s, 5 H, aromatic), 5.76 (dt, *J* = 15.4, 6.8 Hz, 1 H, olefinic), 5.63 (dt, *J* = 15.4, 5.7 Hz, 1 H, olefinic), 4.53 (s, 2 H, PhCH_2O), 4.50 (d, *J* = 5.7 Hz, 2 H, CH_2OC(O)), 3.84 (m, 1 H, C*H*O), 3.47 (dd, *J* = 9.6, 3.3 Hz, 1 H, CH_2O), 3.35 (dd, *J* = 9.6, 7.0 Hz, 1 H, CH_2O), 2.71 (br s, 1 H, O*H*), 2.25 (dd, *J* = 6.8, 6.3 Hz, 2 H, allylic CH_2), 1.19 (s, 9 H, *t-Bu*); HRMS (CI) calcd for $C_{18}H_{26}O_4$ + H 307.1908, found 307.1903 (M + H).

(*S*)-5-[[(1,1-Dimethylethyl)diphenylsilyl]oxy]-6-(phenylmethoxy)-2-hexen-1-ol 2,2-Dimethylpropanoate (65a). *t*-$BuPh_2SiCl$ (4.12 g ≡ 3.9 mL, 15.0 mmol) was added to a stirred solution of alcohol **64a** (3.50 g, 11.4 mmol) and imidazole (4.08 g, 60 mmol) in DMF (15 mL) at room temperature under argon. The reaction mixture was stirred for 1.5 h and then it was diluted with ether (100 mL) and washed with water (3 × 10 mL) and brine (10 mL). Drying ($MgSO_4$) followed by concentration and flash column chromatography (silica, 5% ether in petroleum ether) gave compound **65a** (5.97 g, 96%). **65a**: colorless oil; R_f 0.28 (silica, 10% ether in petroleum ether); $[\alpha]^{25}_D$ +1.7° (*c* 1.0, $CHCl_3$); IR (film) ν_{max} 3065, 3040, 3025, 2960, 2930, 2890, 2859, 1730, 1585, 1478, 1470, 1460, 1452, 1425, 1392, 1388, 1360, 1280, 1150, 1110, 1025, 1005, 995, 970, 819, 735, 698, 602 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.70–7.15 (m, 15 H, aromatic), 5.77 (dt, *J* = 15.4, 7.4 Hz, 1 H, olefinic), 5.42 (dt, *J* = 15.4, 5.5 Hz, 1 H, olefinic), 4.44 (d, *J* = 5.5 Hz, 2 H, CH_2OC(O)), 4.34 (s, 2 H, PhCH_2O), 3.93 (m, 1 H, C*H*O), 3.37 (d, *J* = 5.9 Hz, 2 H, CH_2O), 2.28 (m, 2 H, allylic CH_2), 1.19 (s, 9 H, *t-Bu*), 1.05 (s, 9 H, Si-*t-Bu*).

(*S*)-5-[[(1,1-Dimethylethyl)diphenylsilyl]oxy]-6-(phenylmethoxy)-2-hexen-1-ol (66a). DIBAL (8.0 mL, 1 M solution in hexane, 8.0 mmol) was added to a cold (−78 °C) stirred solution of pivaloate ester **65a** (3.2 g, 5.9 mmol) in CH_2Cl_2 (20 mL) under argon. Stirring was continued for 0.5 h, and then the solution was diluted with CH_2Cl_2 (50 mL) and washed with dilute aqueous HCl solution (25 mL), water (25 mL), and brine (10 mL). Drying ($MgSO_4$) followed by concentration and flash column chromatography (silica, 50% ether in petroleum ether) gave allylic alcohol **66a** (2.7 g, 87%). **66a**: colorless oil; R_f 0.5 (silica, 85% ether in petroleum ether) $[\alpha]^{20}_D$ −3.7° (*c* 1.8, $CHCl_3$); IR (film) ν_{max} 3380, 2925, 2885, 1428, 1390, 1360, 1105, 995, 970, 820, 735, 700 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.70–7.20 (m, 15 H, aromatic), 5.55 (m, 2 H, olefinic), 4.36 (s, 2 H, PhCH_2O), 3.96 (m, 2 H, CH_2OH), 3.93 (m, 1 H, C*H*O), 3.39 (m, 2 H, CH_2O), 2.28 (m, 2 H, allylic CH_2), 1.05 (s, 9 H, Si-*t-Bu*); HRMS (CI) calcd for $C_{29}H_{36}O_3Si$ 460.2432, found 460.2410.

2,3-Anhydro-5-*O*-[(1,1-dimethylethyl)diphenylsilyl]-6-*O*-(phenylmethyl)-D-*arabino*-hexitol (67a). To a stirred solution of Ti(*i*-PrO)$_4$ (1.37 g, 4.83 mmol) in CH_2Cl_2 (15 mL) was added D-(−)-diethyltartrate (996 mg, 4.83 mmol) in CH_2Cl_2 (2 mL) under argon at −20 °C. After stirring for 10 min at −20 °C, allylic alcohol **66a** (2.0 g, 4.35 mmol) in CH_2Cl_2 (3 mL) and *t*-BuOOH (3.2 mL, 3 M in toluene, 9.7 mmol) were sequentially added, and the mixture was kept at −20 °C for 16 h. The reaction mixture was processed as described above for the conversion **14** → **60a**, and the product was purified by flash column chromatography (silica, 40% ether in petroleum ether) leading to epoxide **67a** (1.24 g, 60%, *ca* 9:1 ratio of isomers). **67a**: colorless oil; R_f 0.23 (silica, 50% ether in petroleum ether); $[\alpha]^{25}_D$ −1.2° (ca. 9:1 mixture, *c* 1.6, $CHCl_3$); IR (film) ν_{max} 3430, 2930, 2890, 2855, 1427, 1428, 1390, 1360, 1190, 1110, 1070, 905, 818, 730 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ (for major isomer only) 7.23–7.15 (m, 15 H, aromatic), 4.40, 4.34 (doublets, *J* = 11.8 Hz, 1 H each, PhCH_2O), 4.05 (m, 1 H, C*H*O), 3.76 (m, 1 H, CH_2O), 3.46 (m, 1 H, CH_2O), 3.45 (m, 2 H, CH_2OH), 2.81 (m, 1 H, C*H* epoxide), 2.79 (m, 1 H, C*H* epoxide), 1.84 (m, 1 H, CH_2), 1.77 (m, 1 H, CH_2), 1.06 (s, 9 H, Si-*t-Bu*); HRMS (CI) calcd for $C_{29}H_{36}O_4Si$-*t*-Bu 419.1677, found 419.1719 (M − *t*-Bu).

2,4-Dideoxy-6-*O*-(phenylmethyl)-D-*erythro*-hexitol (13a). Epoxide **67a** (900 mg, 1.89 mmol) was dissolved in dry THF (30 mL), and Red-Al (1 M in THF, 1.89 mL, 1.89 mmol) was added dropwise with stirring at room temperature under an argon atmosphere. After stirring for 1 h another portion of Red-Al (1.89 mL, 1.89 mmol) was added, and stirring was continued for an additional 2 h. The reaction mixture was diluted with ether (100 mL) and H_2O (10 mL) and then acidified with 10% aqueous HCl to pH 3. The organic phase was washed with H_2O (3 mL), saturated aqueous $NaHCO_3$ (3 mL) and brine (3 mL). The combined aqueous phase was neutralized and subjected to continuous extraction with ether for 12 h. The combined extract was dried ($MgSO_4$), concentrated, and purified by flash column chromatography (silica, 20% acetone in ether) to give triol **13a** (386 mg, 85%). **13a**: colorless oil; R_f 0.19 (silica, 2.5% EtOH in ether); $[\alpha]^{20}_D$ −4.9° (*c* 1.7, $CHCl_3$); IR (film) ν_{max} 3360, 3090, 2940, 2915, 2860, 1453, 1365, 1205, 1100, 840, 740, 735 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.33 (s, 5 H, aromatic), 4.55 (s, 2 H, PhCH_2O), 4.30–3.00 (br s, 3 H, O*H*), 4.13 (m, 2 H, C*H*O), 3.82 (m, 2 H, CH_2OH), 3.45 (dd, *J* = 9.4, 3.9 Hz, 1 H, CH_2O), 3.38 (dd, *J* = 9.4, 7.1 Hz, 1 H, CH_2O), 1.69 (m, 2 H, CH_2), 1.58 (m, 2 H, CH_2); HRMS (CI) calcd for $C_{13}H_{20}O_4$ + H 241.1439, found 241.1429 (M + H).

2,4-Dideoxy-6-*O*-(phenylmethyl)-D-*erythro*-hexitol 1-(2,2-Dimethylpropanoate) (68a). A mixture of triol **13a** (176 mg, 0.73 mmol), 4-(dimethylamino)pyridine (DMAP, 5 mg, 0.04 mmol) and trimethylacetyl chloride (121 mg ≡ 0.12 mL, 1.0 mmol) in pyridine (7.3 mL) was stirred at room temperature under argon for 5 h. The mixture was diluted with ether (50 mL) and washed with water (2 × 5 mL) and brine (5 mL). Drying ($MgSO_4$) and concentration followed by flash column chromatography (silica, 60% ether in petroleum ether) gave ester **68a** (208 mg, 88%). **68a**: colorless oil; R_f 0.48 (silica, ether); $[\alpha]^{22}_D$ −3.1° (*c* 1.6,

$CHCl_3$); IR (film) ν_{max} 3440, 2965, 2935, 2910, 2870, 1726, 1481, 1455, 1400, 1365, 1285, 1162, 1108, 853, 735 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.43-7.23 (m, 5 H, aromatic), 4.55 (s, 2 H, $PhCH_2O$), 4.31 (ddd, J = 11.3, 7.5, 6.1 Hz, 1 H, $CH_2OC(O)$), 4.13 (ddd, J = 11.3, 5.6, 5.0 Hz, 1 H, $CH_2OC(O)$), 4.08 (m, 1 H, CHO), 3.92 (m, 1 H, CHO), 3.69 (s, 1 H, OH), 3.43 (m, 2 H, CH_2O), 3.26 (s, 1 H, OH), 1.76 (m, 2 H, CH_2), 1.61 (m, 2 H, CH_2), 1.19 (s, 9 H, Si-*t*-*Bu*); HRMS (CI) calcd for $C_{18}H_{28}O_5$ + H 325.2013, found 325.2006 (M + H).

2,4-Dideoxy-3,5-*O*-(1-methylethylidene)-6-*O*-(phenylmethyl)-D-*erythro*-hexitol 1-(2,2-Dimethylpropanoate) (69). Diol **68a** (196 mg, 0.6 mmol) and camphorsulfonic acid (CSA, 3 mg, 0.012 mmol) were dissolved in 2,2-dimethoxypropane (2 mL) at room temperature under argon. The reaction mixture was stirred at that temperature for 30 min and then it was diluted with ether (30 mL) and washed with 10% aqueous $NaHCO_3$ solution (2 mL) and brine (2 mL). Drying ($MgSO_4$) followed by flash column chromatography (silica, 10% ether in petroleum ether) gave acetonide **69** (204 mg, 93%). **69**: colorless oil; R_f 0.25 (silica, 10% ether in petroleum ether); $[\alpha]^{20}_D$ -21.0° (*c* 2.3, $CHCl_3$); IR (film) ν_{max} 2970, 2955, 2935, 2910, 2870, 1728, 1495, 1479, 1455, 1378, 1365, 1281, 1261, 1200, 1158, 1110, 735, 695 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.36 (s, 5 H, aromatic), 4.60, 4.55 (doublets, J = 12.2 Hz, 1 H each, $PhCH_2O$), 4.15 (t, J = 6.3 Hz, 2 H, $CH_2OC(O)$), 4.09 (m, 1 H, CHO), 3.98 (m, 1 H, CHO), 3.51 (dd, J = 9.8, 5.7 Hz, 1 H, CH_2O), 3.37 (dd, J = 9.8, 5.0 Hz, 1 H, CH_2O), 1.78 (dt, J = 6.3, 6.0 Hz, 2 H, CH_2), 1.54 (dt, J = 12.8, 2.5 Hz, 1 H, CH_2), 1.44, 1.40 (singlets, 3 H each, acetonide), 1.33 (dt, J = 12.8, 11.7 Hz, 1 H, CH_2), 1.19 (s, 9 H, *t*-*Bu*); HRMS (CI) calcd for $C_{21}H_{32}O_5$ + H 365.2326, found 365.2279.

2,4-Dideoxy-6-*O*-[(1,1-dimethylethyl)diphenylsilyl]-3,5-*O*-(1-methylethylidene)-D-*erythro*-hexitol 1-(2,2-Dimethylpropanoate) (71) via Alcohol 70. Benzyl ether **69** (481 mg, 1.34 mmol) was dissolved in CH_2Cl_2 (10 mL), and 10% Pd-C (30 mg) was added. The mixture was vigorously stirred under a H_2 atmosphere at ambient temperature for 4 h (TLC monitoring). Removal of the catalyst by filtration followed by evaporation of the solvent gave essentially pure alcohol **70**, which was dissolved in dry DMF (3 mL) and silylated without further purification as follows. Imidazole (408 mg, 6 mmol) and *t*-$BuPh_2SiCl$ (412 mg ≡ 0.40 mL, 1.5 mmol) were sequentially added under argon at 25 °C, and the reaction mixture was stirred at that temperature for 3 h. The reaction mixture was then diluted with ether (50 mL) and washed with water (2 × 10 mL) and brine (5 mL). The organic phase was dried ($MgSO_4$) and concentrated to give an oily residue, which was flash chromatographed (silica, 10% ether in petroleum ether) to give derivative **71** (500 mg, 73%). **71**: colorless oil; R_f 0.30 (silica, 20% ether in petroleum ether); IR (film) ν_{max} 3070, 3045, 2960, 2930, 2860, 1729, 1480, 1471, 1462, 1427, 1380, 1283, 1200, 11445, 1110, 1055, 1040, 1005, 995, 739, 700 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.73-7.65 (m, 4 H, aromatic), 7.45-7.32 (m, 6 H, aromatic), 4.15 (m, 2 H, $CH_2OC(O)$), 3.97 (m, 2 H, CHO), 3.71 (dd, J = 10.1, 5.2 Hz, 1 H, CH_2O), 3.54 (dd, J = 10.1, 6.1 Hz, 1 H, CH_2O), 1.78 (dt, J = 6.4, 6.4 Hz, 2 H, CH_2), 1.62 (dt, J = 12.5, 2.4 Hz, 1 H, CH_2), 1.39, 1.35 (singlets, 3 H each, acetonide), 1.21 (dt, J = 12.5, 11.8 Hz, 1 H, CH_2), 1.20, 1.06 (singlets, 9 H each, *t*-*Bu*).

Preparation of Compound 47 from 71. Compound **47** was prepared from pivaloate ester **71** by DIBAL reduction as described above for the preparation of **66a** from **65a**. Used, **71** (285 mg, 0.56 mmol); obtained, **47** (211 mg, 91%). The spectral data of this material were identical with those of a sample obtained from (+)-xylose as described above.

3,5-Dideoxy-6-*O*-[(1,1-dimethylethyl)dimethylsilyl]-1-*O*-(phenylmethyl)-D-*erythro*-hexitol (68b). To a stirred solution of triol **13b** (344 mg, 1.43 mmol) in DMF (2.5 mL) was added imidazole (408 mg, 6.00 mmol) and *t*-$BuMe_2SiCl$ (226 mg, 1.50 mmol). Stirring was continued for 2 h at ambient temperature, and then the reaction mixture was diluted with ether (50 mL). The organic phase was washed with water (3 × 5 mL) and brine (5 mL), dried ($MgSO_4$), and concentrated. Purification by flash column chromatography (silica, 70% ether in petroleum ether) gave pure diol **68b** (457 mg, 90%). **68b**: R_f 0.21 (70% ether in petroleum ether); $[\alpha]^{20}_D$ -3.7° (*c* 2.8, $CHCl_3$); IR (film) ν_{max} 3420, 3035, 2955, 2930, 2860, 1470, 1460, 1452, 1390, 1360, 1309, 1255, 1092, 1028, 1005, 938, 835 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.33 (s, 5 H, aromatic), 4.56 (s, 2 H, $PhCH_2O$), 4.08 (m, 3 H, CHO, OH), 3.87 (m, 3 H, H-1, OH), 3.44 (m, 2 H, H-6), 1.64 (m, 4 H, CH_2), 0.89 (s, 9 H, Si-*t*-*Bu*), 0.08 (s, 6 H, $SiMe_2$); HRMS (CI) calcd for $C_{19}H_{34}O_4Si$ + H 355.2303, found 355.2313 (M + H).

3,5-Dideoxy-6-*O*-[(1,1-dimethylethyl)dimethylsilyl]-2,4-*O*-(1-methylethylidene)-1-*O*-(phenylmethyl)-D-*erythro*-hexitol (56). Compound **56** was prepared (95%) in the same manner as described for **69** from **68a** and was identical by the usual criteria with a sample obtained from (-)-xylose.

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Total Synthesis of Amphoteronolide B and Amphotericin B. 2. Total Synthesis of Amphoteronolide B†

K. C. Nicolaou,* R. A. Daines, T. K. Chakraborty, and Y. Ogawa

Contribution from the Department of Chemistry, University of Pennsylvania, Philadelphia, Pennsylvania 19104. *Received October 19, 1987*

Abstract: The efficient coupling of building blocks **4-8** by four aldehyde-phosphonate type condensation reactions and an esterification reaction leading to advance intermediate keto phosphonate aldehyde **39** are reported. The intramolecular keto phosphonate-aldehyde condensation leading to heptaenone **3** and its elaboration to amphoteronolide B (**1**) are also described.

In the preceding paper[1] we discussed the significance and retrosynthetic analysis of amphotericin B (**1**) and amphoteronolide B (**2**) (Scheme I) and the stereocontrolled construction of key building blocks **5-8** required for the total synthesis of these targets. In this paper we describe (a) the coupling of these building blocks and their elaboration to the cyclic heptaenone **3** (Scheme I), a key intermediate for the synthesis of both amphoteronolide B (**2**) and amphotericin B (**1**), and (b) the total synthesis of amphoteronolide B (**2**).[2,3]

Results and Discussion

Synthesis of Advanced Key Intermediate, Hydroxy Aldehyde 15. The plan for the synthesis of advanced intermediate **15** from aldehyde **5** involved construction of the polyene chain by sequential reaction with two units of phosphonate **4** (Scheme I). The details of the execution of this strategy are presented in Scheme II. Thus, condensation of **5** with the lithio derivative of (*E*,*E*)-$(EtO)_2P(O)CH_2CH{=}CHCH{=}CHCOOEt$ (**4**)[4] led predominantly to the

† This paper is dedicated with respect and affection to Professor E. J. Corey on the occasion of his 60th birthday.

(1) Nicolaou, K. C.; Daines, R. A.; Uenishi, J.; Li, W. S.; Papahatjis, D. P.; Chakraborty, T. K. *J. Am. Chem. Soc.*, preceding paper in this issue.

(2) Preliminary communication: Nicolaou, K. C.; Daines, R. A.; Chakraborty, T. K. *J. Am. Chem. Soc.* **1987**, *109*, 2208. Apparently migration of the acetonide group occurred under the reaction conditions (**27** → **28** → **29**). We thank Professor S. Masamune for bringing this possibility to our attention in the form of a manuscript: Kennedy, R. M.; Abiko, A.; Masamune, S. *Tetrahedron Lett.* **1988**, *29*, 447. See also: Kennedy, R. M.; Abili, A.; Takemasa, T.; Okumoto, H.; Masamune, S. *Tetrahedron Lett.* **1988**, *29*, 451.

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