1.29 (s, 3 H, $CH_3$), 1.26 (s, 3 H, $CH_3$), 1.24 (s, 3 H, $CH_3$), 0.09 (s, 9 H, $(CH_3)_3Si$); MS *m/e* (rel intensity) 535 (M + 1, 90), 504 (8), 452 (12), 396 (100), 344 (51), 317 (70), 287 (54), 182 (100), 136 (100); HRMS calcd for $C_{30}H_{51}O_6Si$ (M + 1) 535.3455, found 535.3419.

**(2*S*,3*R*,4a*S*,6*R*,7*S*,8a*R*)-7-[(Benzyloxy)methoxy]-2-(2-iodoethyl)-6-(4-methyl-3-pentenyl)-2,4a,6-trimethyl-3-(trimethylsiloxy)perhydropyrano[3,2-*b*]pyran (33).** To a stirred heterogeneous mixture of alcohol **32** (2.6 g, 4.9 mmol), triphenylphosphine (3.8 g, 14.7 mmol), imidazole (1.0 g, 14.7 mmol), and dry benzene (50 mL) at 10 °C was added, in one portion, iodine (2.4 g, 9.8 mmol). After 20 min, the iodine color dissipated, and the clear benzene solution was decanted from the orange residue. The residue was washed with benzene (2 × 2 mL), and the benzene fractions were combined. Concentration and flash chromatography (silica, 3% ether in petroleum ether) gave the iodide **33** (2.8 g, 89%). **33**: oil; $R_f$ = 0.61 (silica, 5% ether in petroleum ether); $[\alpha]^{21}_D$ +36.7° (*c* 1.65, $CHCl_3$); IR (neat) $\nu_{max}$ 3030, 2990, 2960, 2900, 1460, 1385, 1270, 1260, 1180, 1140, 1100, 1050, 990, 920, 890, 750, 740, 700 $cm^{-1}$; $^1H$ NMR (250 MHz, $CDCl_3$) $\delta$ 7.40–7.28 (m, 5 H, Ar), 5.08 (br t, *J* = 7.0 Hz, 1 H, *H*C=C), 4.85, 4.72 (2 × d, *J* = 7.1 Hz, 2 × 1 H, $CH_2Ar$), 4.61 (br s, 2 H, $OCH_2O$), 3.72 (dd, *J* = 11.3, 4.7 Hz, 1 H, -*H*CO), 3.65 (dd, *J* = 1.3, 5.2 Hz, 1 H, -*H*CO), 3.23 (dd, *J* = 7.7, 7.5 Hz, 2 H, $CH_2I$), 3.18 (dd, *J* = 12.0, 3.1 Hz, 1 H, -*H*CO ring juncture), 2.30–1.45 (m, 10 H, $CH_2$), 1.66, 1.58 (2 × s, 2 × 3 H, $(CH_3)_2C$=C), 1.26 (s, 3 H, $CH_3$), 1.24 (s, 3 H, $CH_3$), 1.12 (s, 3 H, $CH_3$), 0.10 (s, 9 H, $(CH_3)_3Si$); MS *m/e* (intensity) 644 (M, 7), 506 (57), 424 (32), 397 (74), 284 (100); HRMS calcd for $C_{30}H_{49}O_5SiI$ (M) 644.2394, found 644.2369.

**(2*S*,3*R*,4a*S*,6*R*,7*S*,8a*R*)-7-[(Benzyloxy)methoxy]-6-(3-hydroxypropyl)-2-(2-iodoethyl)-2,4a,6-trimethyl-3-(trimethylsiloxy)perhydropyrano[3,2-*b*]pyran (34).** Ozone was passed through a solution of the olefin **33** (1.0 g, 1.6 mmol) in dichloromethane (20 mL) at −78 °C until a blue coloration persisted. The excess ozone was removed with a stream of oxygen, followed by addition of $BH_3{\cdot}SMe_2$ (3.0 mL, 2 M in THF, 6.0 mmol). The cooling bath was removed and the reaction mixture was stirred for 30 min. The excess $BH_3{\cdot}SMe_2$ was carefully quenched at 25 °C by dropwise addition of $H_2O$ (2.0 mL). Dilution with ether (60 mL) followed by washing with $H_2O$ (50 mL) and brine (20 mL), drying ($MgSO_4$), and concentration gave a crude oil. Flash chromatography (silica, 35% ether in petroleum ether) furnished the alcohol **34** (0.85 g, 86%). **34**: oil; $R_f$ = 0.37 (silica, 50% ether in petroleum ether); $[\alpha]^{21}_D$ +46.6° (*c* 0.60, $CHCl_3$); IR (neat) $\nu_{max}$ 3450 (s, OH), 2990, 2960, 2900, 1470, 1460, 1385, 1270, 1260, 1180, 1100, 1050, 990, 890, 850, 740, 700 $cm^{-1}$; $^1H$ NMR (250 MHz, $CDCl_3$) $\delta$ 7.42-7.30 (m, 5 H, Ar), 4.87, 4.75 (2 × d, *J* = 7.1 Hz, 2 × 1 H, $CH_2Ar$), 4.62 (br s, 2 H, $OCH_2O$), 3.71–3.50 (m, 4 H, $-CH_2O$ and -*H*CO), 3.24 (dd, *J* = 10.3, 7.3 Hz, 1 H, $CH_2I$), 3.20 (m, 1 H, -*H*CO ring juncture), 2.57 (br s, 1 H, O*H*), 2.30–1.96 (m, 3 H, $CH_2$), 1.89–1.50 (m, 7 H, $CH_2$), 1.29 (s, 3 H, $CH_3$), 1.25 (s, 3 H, $CH_3$), 1.12 (s, 3 H, $CH_3$), 0.09 (s, 9 H, $(CH_3)_3Si$); MS *m/e* (rel intensity) 621 (M + 1, 68), 573 (20), 513 (85), 483 (80), 387 (42), 354 (100), 284 (64), 215 (100); HRMS calcd for $C_{27}H_{46}O_6ISi$ (M) 621.2051, found 621.2022. Anal. Calcd for $C_{27}H_{46}O_6ISi$: C, 52.17; H, 7.46. Found: C, 52.31; H, 7.24.

**(2*S*,3*R*,4a*S*,6*R*,7*S*,8a*R*)-7-[(Benzyloxy)methoxy]-6-[3-(*tert*-butyldimethylsiloxy)propyl]-2-(2-iodoethyl)-2,4a,6-trimethyl-3-(trimethylsiloxy)perhydropyrano[3,2-*b*]pyran (35).** A stirred mixture of alcohol **34** (0.85 g, 1.4 mmol), imidazole (380 mg, 4.2 mmol), and dry DMF (5 mL) at 0 °C was treated with *tert*-butyldimethylsilyl chloride (310 mg, 2.1 mmol). After 1 h the reaction mixture was diluted with ether (20 mL) and washed with $H_2O$ (2 × 5 mL) and brine (5 mL). Drying (MgSO4) and concentration followed by flash chromatography (silica, 3% ether in petroleum ether) gave the bis silyl ether **35** (1.0 g, 98%). **35**: oil; $R_f$ = 0.23 (silica, 5% ether in petroleum ether); $[\alpha]^{21}_D$ +34.1° (*c* 0.51, $CHCl_3$); IR (neat) $\nu_{max}$ 3000, 2960, 2900, 2870, 1480, 1470, 1385, 1270, 1260, 1180, 1100, 1050, 1035, 890, 845, 780, 735, 700 $cm^{-1}$; $^1H$ NMR (250 MHz, $CDCl_3$) $\delta$ 7.38–7.28 (m, 5 H, Ar), 4.83, 4.72 (2 × d, *J* = 7.1 Hz, 2 × 1 H, $CH_2Ar$), 4.61 (br s, 2 H, $OCH_2O$), 3.75–3.53 (m, 4 H, $CH_2O$ and -*H*CO), 3.28–3.12 (m, 3 H, $CH_2I$, -O*CH*- ring juncture), 2.30–1.42 (m, 10 H, $CH_2$), 1.26 (s, 3 H, $CH_3$), 1.23 (s, 3 H, $CH_3$), 1.11 (s, 3 H, $CH_3$), 0.88 (s, 9 H, $(CH_3)_3CSi$), 0.03 (s, 6 H, $(CH_3)_2Si$); MS *m/e* (rel intensity) 735 (M + 1, 4), 647 (43), 597 (37), 539 (15), 449 (17), 354 (100), 284 (100), 215 (100); HRMS calcd for $C_{33}H_{60}IO_6Si_2$ (M + 1) 735.2912, found 735.2973.

**3,7:6,10-Dianhydro-9-*O*-[(benzyloxy)methyl]-13-*O*-(*tert*-butyldimethylsilyl)-1,2,5,8,11,12-hexadeoxy-3,6,10-tri-*C*-methyl-4-*O*-(trimethylsilyl)-1-(triphenylphosphonio)-D-*erythro*-D-*allo*-tridecitol Iodide (1).** A stirred mixture of iodide **35** (1.0 g, 1.3 mmol), triphenylphosphine (2.7 g, 10.4 mmol), and dry $CH_3CN$ (3.0 mL) was heated at 90 °C for 24 h. After cooling, the excess triphenylphosphine was removed by washing with hexanes (10 × 15 mL). The remaining solvents were removed in vacuo to afford the phosphoinium salt **1** (1.3 g, 100%). **1**: amorphous solid; $R_f$ = 0.31 (silica, 10% methanol in EtOAc); $[\alpha]^{21}_D$ +33.6° (*c* 0.99, $CHCl_3$); IR (neat) $\nu_{max}$ 3060, 3040, 3000, 2960, 2900, 2870, 1595, 1470, 1460, 1445, 1390, 1270, 1260, 1220, 1190, 1160, 1110, 1040, 1000, 890, 845, 780, 740, 700 $cm^{-1}$; $^1H$ NMR (250 MHz, $CDCl_3$) $\delta$ 7.90–7.22 (m, 20 H, Ar), 4.84, 4.72 (2 × d, *J* = 7.0 Hz, 2 × 1 H, $CH_2Ar$), 4.61 (s, 2 H, $OCH_2O$), 3.68 (dd, *J* = 11.3, 4.7 Hz, 1 H, -*H*CO), 3.58 (m, 3 H, $CH_2O$ and $CH_2P$), 3.45 (dd, *J* = 11.2, 5.2 Hz, 1 H, -*H*CO), 3.32 (m, 1 H, $CH_2P$), 3.20 (dd, *J* = 11.0, 3.0 Hz, 1 H, -*H*CO ring juncture), 2.13–1.45 (m, 10 H, $CH_2$), 1.27 (s, 3 H, $CH_3$), 1.26 (s, 3 H, $CH_3$), 1.19 (s, 3 H, $CH_3$), 0.86 (s, 9 H, $(CH_3)_3CSi$), 0.10 (s, 6 H, $(CH_3)_2Si$), −0.08 (s, 9 H, $(CH_3)_3Si$); HRMS calcd for $C_{51}H_{74}O_6PSi_2$ (M − 1) 869.476, found 869.481. Anal. Calcd for $C_{51}H_{74}O_6PSi_2$: C, 61.43; H, 7.48. Found: C, 61.62; H, 7.27.

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**Supplementary Material Available:** ORTEP drawing and X-ray crystallographic analysis data for compound **30** (7 pages). Ordering information is given on any current masthead page.

# Synthesis of the Brevetoxin B IJK Ring System

**K. C. Nicolaou,* C.-K. Hwang,[1] and M. E. Duggan**

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**Abstract:** A stereoselective synthesis of a functionalized system representing the IJK ring framework of brevetoxin B is reported. The synthesis begins with D-mannose pentaacetate and proceeds through intermediates **24** and **38**, which serve as key cyclization precursors. The stereochemistry of the optically active target molecule **1** was confirmed by an X-ray crystallographic analysis of the crystalline derivative **42**.

In a preceding paper,[2] we described a retrosynthetic analysis of brevetoxin B in which three fragments containing the tetrahydropyran rings, ABC, FG, and IJK (**1**) were defined as subtargets for an eventual total synthesis. We also described stereoselective syntheses of fragments ABC[2] and FG.[3] In this article, we report a stereocontrolled construction of the IJK ring framework of brevetoxin B as the dithio ketal aldehyde **1** (Scheme

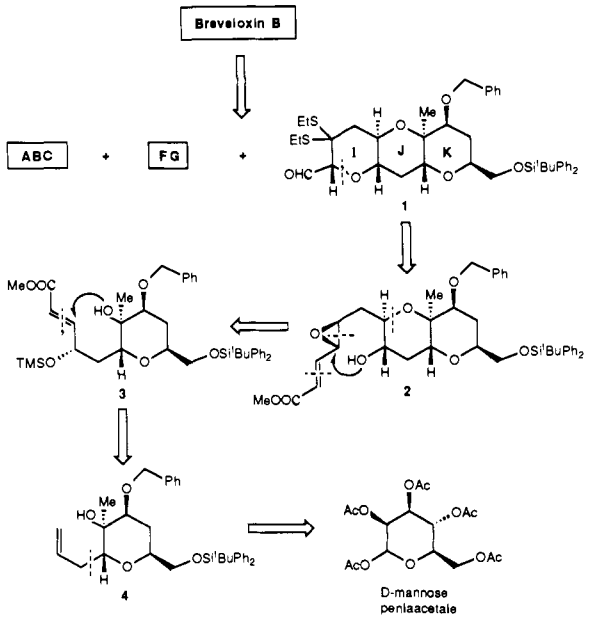
(1) Taken in part from the Ph.D. Thesis of C.-K. H., Department of Chemistry, University of Pennsylvania, 1986.

(2) Nicolaou, K. C.; Duggan, M. E.; Hwang, C.-K. *J. Am. Chem. Soc.*, first of three papers in this issue.

(3) Nicolaou, K. C.; Duggan, M. E.; Hwang, C.-K. *J. Am. Chem. Soc.*, second of three papers in this issue.

0002-7863/89/1511-6682$01.50/0 

**Scheme I**[a]




[a] Retrosynthetic analysis of the IJK ring system **1** of brevetoxin B.

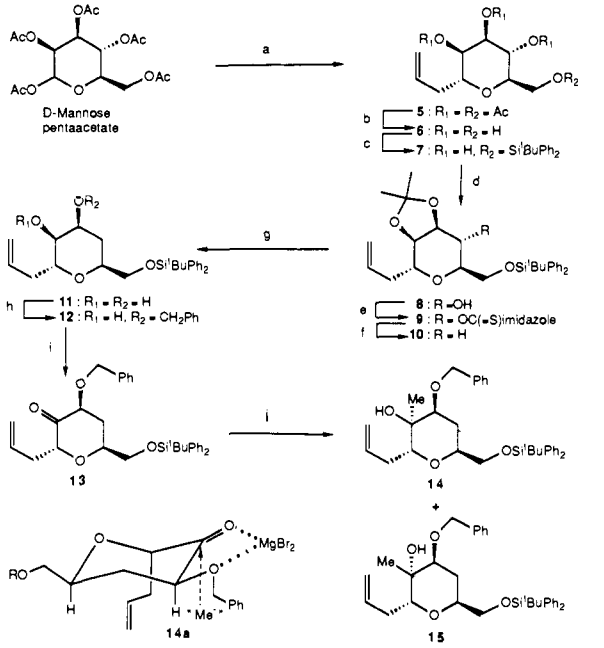
I). As is the case of fragments ABC and FG, this construction also utilized a key operation, the 6-endo activation method[4] for tetrahydropyran synthesis from hydroxy epoxides.

## Results and Discussion

**Retrosynthetic Analysis.** A retrosynthetic analysis of the IJK ring system (**1**) of brevetoxin B is shown in Scheme I. Thus, disconnection of the indicated C–O bond in structure **1** accompanied by a number of standard functional group manipulations leads to hydroxy epoxide **2** as a potential precursor to this tricycle. Disassembling the second ring via a second C–O bond rupture as indicated in **2** and further retromanipulations then reveals the $\alpha,\beta$-unsaturated ester **3** as a potential intermediate to deliver **2** (Michael reaction). The stereochemical outcome of the synthetic Michael reaction was expected to be as desired leading to the isomer with an equatorial side chain presumed to be the thermodynamically most stable one. Further disconnections of **3** traced a possible origin for it in the *C*-glycoside **4**, which, in turn, may arise from D-mannose pentaacetate as presented in Scheme I. The advantages of a stragegy based on the above retrosynthetic analysis include initiation of the sequence with an optically active starting material and flexibility to manipulate the ends of the intermediate, if needed, for further elaborations.

**Synthesis of the IJK Ring System (1) of Brevetoxin B.** As indicated above, the synthesis of the subtarget **1** began with D-mannose pentaacetate as shown in Scheme II. Thus, C-glycosidation[5] of D-mannose pentaacetate (mixture of anomers) with allyltrimethylsilane in the presence of $BF_3{\cdot}Et_2O$ (1.0 equiv) and TMSOTf (Tf = triflate, 0.2 equiv)[6] in $CH_3CN$ at 0 °C afforded the *C*-glycoside **5** in good yield ($\alpha$:$\beta$ anomers ca. 6.8:1). Deacetylation of this product with NaOMe in MeOH at 25 °C gave tetraol **6** in 75% overall yield (anomeric mixture). This mixture was carried through and separated at the convenient stage of alcohol **8** (vide infra). Selective protection of tetraol **6** was accomplished in one pot by reaction with stoichiometric amounts of *tert*-butyldiphenylsilyl chloride in the presence of imidazole followed by in situ acetonide formation using 2-methoxypropene and camphorsulfonic acid (CSA) catalyst to afford compound **8** via triol **7** (82% overall yield). The required deoxygenation of intermediate **8** was carried out in two steps. Reaction of **8** with

**Scheme II**[a]




[a] Reagents and conditions: (a) 1.3 equiv of (allyltrimethyl)silane, 2.0 equiv of $BF_3$–$Et_2O$, 0.2 equiv of TMSOTf, $CH_3CN$, 0 °C, 16 h, 75% ($\alpha$:$\beta$ ca. 6.8:1 by $^1H$ NMR); (b) 0.5 equiv of NaOMe, MeOH, 25 °C, 2 h, 100%; (c) 1.0 equiv of *t*-$BuPh_2SiCl$, 1.1 equiv of imidazole, DMF, 0 °C, 30 min; then (d) 0.2 equiv of CSA, 1.5 equiv of 2-methoxypropene, 1 h, 82% overall; (e) 1.2 equiv of S=C(imidazole)$_2$, toluene, 110 °C, 3 h, 92%; (f) 1.5 equiv of *n*-$Bu_3SnH$, 0.01 equiv of AIBN, toluene, 110 °C, 3 h, 72%; (g) Amberlyst-15 ($H^+$), MeOH, 60 °C, 4 h, 72%; (h) 1.0 equiv of *n*-$Bu_2SnO$, MeOH, 60 °C, 1 h, then 1.5 equiv of $PhCH_2Br$, DMF, 100 °C, 4 h, 74%; (i) 1.5 equiv of $(COCl)_2$, 2.0 equiv of DMSO, $CH_2Cl_2$, −78 °C, 30 min, then 4.0 equiv of $Et_3N$, 0 °C, 30 min, 100%; (j) 1.3 equiv of $MgBr_2$–$Et_2O$, 3.0 equiv of $AlMe_3$, $CH_2Cl_2$, −50 °C, 10 min, then 0 °C, 3 h, **14** (61%), **15** (20%).

**Table I.** Methylation of Ketone **14**

| entry[a] | conditions | yield, % | ratio (**14**:**15**, ca.)[b] |
|---|---|---|---|
| 1 | MeLi (1.2 equiv), $Et_2O$, −78 °C | 85 | 0:1 |
| 2 | Me(O-*i*-Pr)$_3$Ti (1.2 equiv), $CH_2Cl_2$, −78 °C | 76 | 0:1 |
| 3 | MeMgI (1.2 equiv), $Et_2O$, −78 °C | 92 | 1:3 |
| 4 | $AlMe_3$ (1.0 equiv), $CH_2Cl_2$, 0 °C | 86 | 2:3 |
| 5 | $AlMe_3$ (3.0 equiv), $CH_2Cl_2$, 0 °C | 82 | 5:4 |
| 6 | $AlMe_3$ (3.0 equiv), $MgBr_2$–$Et_2O$ (1.3 equiv), $CH_2Cl_2$, −50 to 0 °C | 81 | 3:1 |

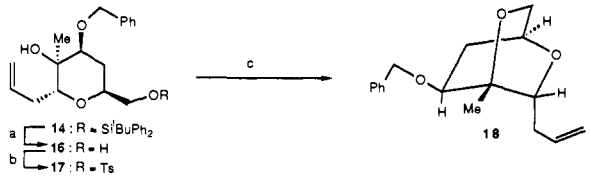
[a] Reactions were carried out on 1.0 mmol scale. [b] Ratio was determined by $^1H$ NMR spectroscopy.

thiocarbonyldiimidazole[7] in refluxing toluene gave the thiocarbonylimidazolide **9** (92%), which was reacted with *n*-$Bu_3SnH$ hydride in the presence of AIBN in refluxing toluene to afford the deoxygenated product **10** in 72% yield. The acetonide was then removed from **10** by exposure to amberlyst-15 ($H^+$) in methanol at 60 °C leading to the diol **11** (72% yield), which was then monobenzylated selectively by the method of Nashed.[8] Thus, treatment of **11** with *n*-$Bu_2SnO$ in methanol followed by exchange of the solvent with DMF and addition of benzyl bromide led to benzyl ether **12** in 74% yield. Swern oxidation[9] of **12** then furnished the desired ketone **13** in quantitative yield.

The next operation in the sequence required addition of a methyl group to ketone **13** from the $\alpha$-face, delivering compound **14**. Examination of molecular models of **13** revealed a serious torsional interaction between the axial allyl group and the incoming nucleophile from the $\alpha$-face (see structure **14a**, Scheme II). Prior

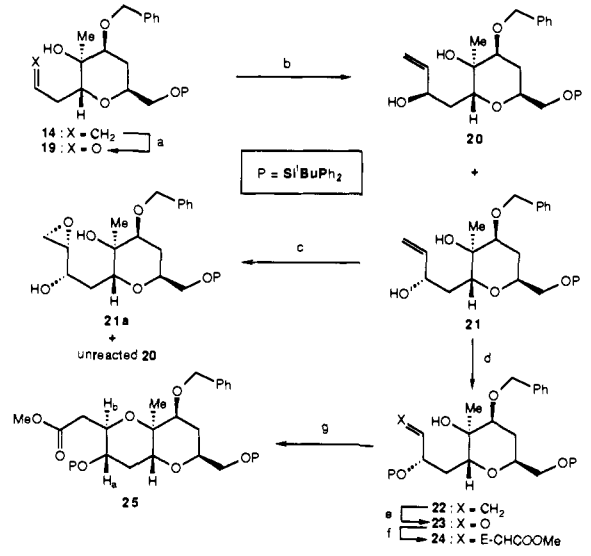
(4) Nicolaou, K. C.; Prasad, C. V. C.; Somers, K. P.; Hwang, C.-K. *J. Am. Chem. Soc.*, in press.
(5) For similar C-glycosidation reactions see: Lewis, M. D.; Cha, J. K.; Kishi, Y. J. *J. Am. Chem. Soc.* **1982**, *104*, 4976.
(6) This combination of reagents was found to be highly effective and most convenient to use for large-scale operations.
(7) Pullukat, T. J.; Urry, G. *Tetrahedron Lett.* **1967**, *20*, 1953.
(8) Nashed, M. *Carbohydr. Res.* **1978**, *60*, 200.
(9) Hwang, S. L.; Mancuso, A. J.; Swern, D. J. *Org. Chem.* **1978**, *63*, 2480. Omura, K.; Swern, D. *Tetrahedron* **1978**, *34*, 1651.

**Scheme III**[a]



[a] Reagents and conditions: (a) 1.2 equiv of $n$-$Bu_4NF$, THF, 25 °C, 4 h, 99%; (b) 1.1 equiv of TsCl, 1.5 equiv of DMAP, $CH_2Cl_2$, 0 °C, 3 h, 85%; (c) 1.0 equiv of NaOMe, MeOH, 80 °C, 16 h, 71%.

**Scheme IV**[a]

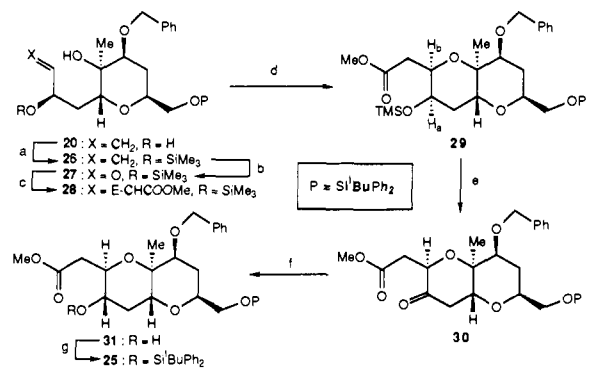


[a] Reagents and conditions: (a) $O_3$, $CH_2Cl_2$, −78 °C, 2 h, 5.0 equiv of $Me_2S$ and 1.0 equiv of $Ph_3P$, then (b) 2.2 equiv of vinylmagnesium bromide, THF, 0 °C, 30 min, **20** (45%), **21** (44%); (c) 1.4 equiv of (−)DET, 1.4 equiv of $Ti(O\text{-}i\text{-}Pr)_4$, 2.0 equiv of $t$-BuOOH, $CH_2Cl_2$, −20 °C, 12 h, **21a** (42%), unreacted **20** (47%); (d) 1.2 equiv of $t$-$BuPh_2SiCl$, 2.0 equiv of imidazole, DMF, 25 °C, 16 h, 88%; (e) same as (a), then (f) 1.2 equiv of $Ph_3P$=CHCOOMe, benzene, 25 °C, 6 h, 89% overall; (g) 1.0 equiv of NaH, THF, 25 °C, 5 h, 92%.

complexation, however, to the β-benzyloxy substituent in **13** would hinder the top face to a varying degree so that attack from the bottom side would compete favorably. A thorough investigation of this reaction was, therefore, undertaken to determine the best conditions for the requisite preference. Table I summarizes some of the results obtained. As seen, most reagents and conditions favored the product of attack from the top face (leading to compound **15**). The addition of $MgBr_2 \cdot Et_2O$ prior to addition of $AlMe_3$, however, resulted in good selectivity (**14**:**15** ca. 3:1) and yield (81%). Diagram **14a** (Scheme II) represents our hypothesis of complexation to explain this stereochemical outcome by preferential attack of "$Me^-$" from the bottom side of the molecule. Compounds **14** and **15** were distinguished by the successful conversion of **14** to the bridged bicyclic system **18** via diol **16** and tosylate **17** (Scheme III). This sequence proved the syn disposition of the tertiary hydroxy and the hydroxymethyl groups in compounds **14**, **16**, and **17**. The tosylate derived from **15**, on the other hand, failed to produce a cyclic ether under similar conditions. Scheme IV summarizes the next phase of the construction leading to the bicyclic system **25** from olefin **14**. Thus, ozonolysis of **14** followed by $Ph_3P$ workup gave the aldehyde **19**, which reacted with vinylmagnesium bromide in THF to afford diols **20** and **21** in 89% total yield (ca. 1:1 ratio by chromatographic separation). Determination of stereochemistry of the two isomers was tentatively based on the Sharpless kinetic resolution results.[10] Thus, a mixture of **20** and **21** was reacted under Sharpless kinetic resolution conditions[10] by using (−)-diethyl tartrate, leading to

(10) Martin, V. S.; Woodard, S. S.; Katsuki, T.; Yamada, Y.; Ikada, M.; Sharpless, K. B. *J. Am. Chem. Soc.* **1981**, *103*, 6237.

**Scheme V**[a]



[a] Reagents and conditions: (a) 1.1 equiv of TMS-imidazole, $CH_2Cl$, 0 °C, 10 min, 85%; (b) $O_3$, $CH_2Cl_2$, −78 °C, 2 h, 5.0 equiv of $Me_2S$ and 1.0 equiv of $Ph_3P$, then (c) 1.2 equiv of $Ph_3P$=CHCOOMe, benzene, 25 °C, 6 h, 85% overall; (d) 1.0 equiv of NaH, THF, 25 °C, 5 h, 72%; (e) Jones' oxidation, 0 °C, 30 min, 69%; (f) 1.0 equiv of $NaBH_4$, MeOH, 0 °C, 10 min, 85%; (g) 1.2 equiv of $t$-$BuPh_2SiCl$, 2.0 of equiv imidazole, DMF, 25 °C, 16 h, 89%.

42% yield of epoxide **21a** and 47% unreacted allylic alcohol **20** suggesting the designated stereochemistries. An X-ray crystallographic analysis on an advanced intermediate (vide infra) confirmed this assignment. The correct stereoisomer **21** was taken to **25** as follows. Monosilylation under standard conditions (88%) followed by ozonolysis gave aldehyde **23** (98%) via silyl ether **22**. Condensation of aldehyde **23** with the stabilized phosphorane $Ph_3P$=CHCOOMe in benzene furnished, in 89% yield, the $E$-α,β-unsaturated ester **24**. Finally, exposure of **24** to NaH at 25 °C in THF for 1 h gave the bicyclic system **25** in 92% yield as a single stereoisomer. The stereochemistry of the newly formed stereocenter in **25** was based on a $J$ value for $H_a/H_b$ of 10.5 Hz, indicating a trans-diaxial relationship for these protons. Dreiding models confirmed the more comfortable diequatorial positions for the two appendages on the newly formed ring.

A sequence was then developed to funnel back into the synthesis the epimeric allylic alcohol **20**. Scheme V presents the seven-step conversion of **20** to **25**. Thus, protection of **20** as a trimethylsilyl ether followed by a similar sequence for the conversion of **21** to **25** (Scheme IV) led to compound **29** in 52% overall yield via compounds **26**–**28**. A coupling constant ($J$) for $H_a/H_b$ of <1 Hz supported the assigned stereochemistry for compound **29**. Jones' oxidation of **29** at 0 °C led directly to ketone **30** in 69% yield. From molecular modeling it was anticipated that hydride attack on the carbonyl group of compound **30** would occur from the axial direction (top face) leading to the required equatorial hydroxy group. Indeed, reduction of **30** with sodium borohydride at 0 °C furnished a single compound (**31**, 85%), which upon silylation with *tert*-butyldiphenylsilyl chloride proved to be identical with the previously obtained compound **25** (89% yield).

The fusion of the third ring (ring I of brevetoxin B) onto the bicyclic system **25** was then undertaken (Scheme VI). DIBAL reduction of **25** at −78 °C produced the aldehyde **32**[11] (92%) which was subjected to Wittig olefination to afford the $E$-α,β-unsaturated ester **33** in 86% yield. A second DIBAL reduction at −78 °C produced the allylic alcohol **34** in 88% yield. Sharpless asymmetric epoxidation of **34** under various conditions gave poor selectivity. Surprisingly, however, high stereoselectivity was observed in the mCPBA epoxidation of **34** leading to the desired epoxide **35** as the major product (87% yield, ca. 10:1 ratio of isomers). At this juncture the stereochemistry of the major epoxide **35** was based on its ability to cyclize to a tetrahydrofuran system, whereas the minor isomer did not (vide infra). This assignment was later confirmed by an X-ray crystallographic analysis of a derivative (vide infra). Swern oxidation of the epoxy alcohol **35** (95%)

(11) The ability of this substrate to deliver cleanly the aldehyde **32** rather than the corresponding alcohol in this DIBAL reduction is presumably due to the presence of the β-alkoxy function, which stabilized the initially formed aluminum complex.

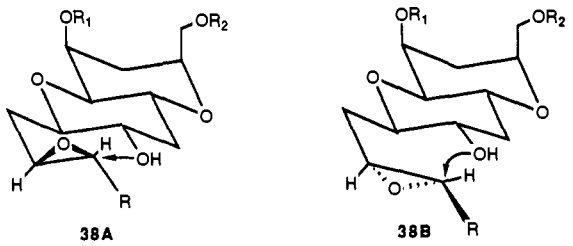
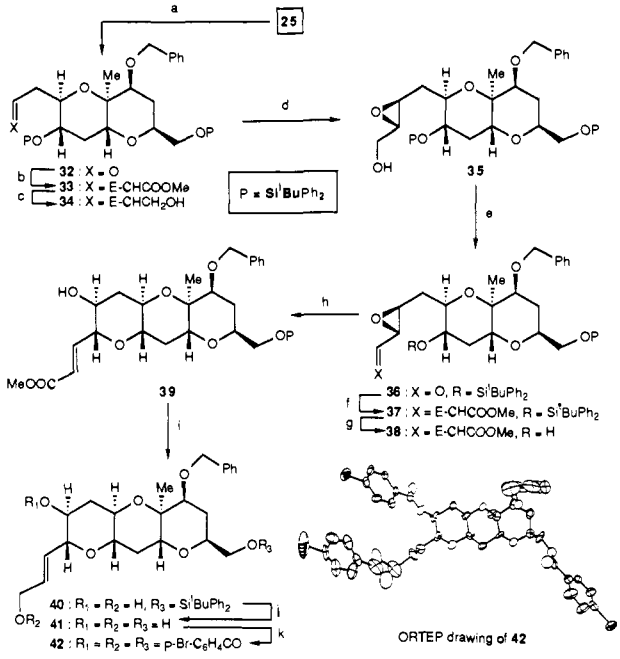



**Figure 1.** Transition states **38A** and **38B** required for the cyclization of **38** and its epimer to tricyclic systems.

**Scheme VI**[a]



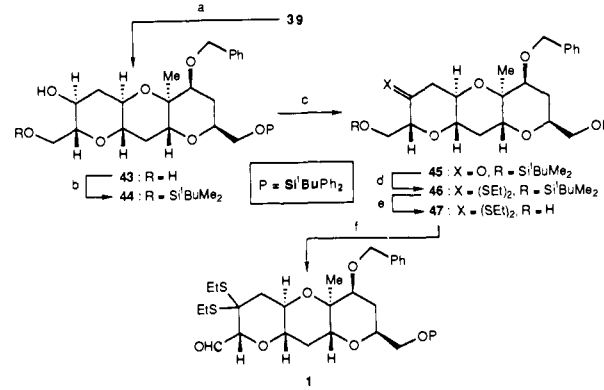

[a] Reagents and conditions: (a) 1.5 equiv of DIBAL, $CH_2Cl_2$, −78 °C, 15 min, then (b) 1.3 equiv of $Ph_3P{=}CHCOOMe$, benzene, 25 °C, 2 h, 75% overall; (c) 2.2 equiv of DIBAL, $CH_2Cl_2$, −78 °C, 30 min, 88%; (d) 1.2 equiv of mCPBA, $CH_2Cl_2$, 0 °C, 30 min, 88% ($\beta$:$\alpha$ 10:1); (e) 1.5 equiv of $(COCl)_2$, 2.0 equiv of DMSO, $CH_2Cl_2$, −78 °C, 30 min, then 4.0 equiv of $Et_3N$, then (f) same as (b), 72% overall; (g) 1.2 equiv of *n*-$Bu_4NF$, THF, 25 °C, 3 h, 89%; (h) 0.2 equiv of CSA, $CH_2Cl_2$, 25 °C, 3 h, 70%; (i) 3.5 equiv of DIBAL, $CH_2Cl_2$, −78 °C, 10 min, 95%; (j) same as (g), 100%; (k) 3.0 equiv of *p*-$BrC_6C_4COCl$, 3.3 equiv of DMAP, $CH_2Cl_2$, 0 °C, 30 min, 92%.

followed by olefination (82%) gave the 6-endo activated epoxide **37** via aldehyde **36**. Selective desilylation using just over stoichiometric amounts of fluoride then produced the hydroxy epoxide **38** in 89% yield ready for ring closure. Small amounts of bis(desilylated) product (ca. 5–7%) produced in this reaction were separated chromatographically and could be recycled.

Cyclization of hydroxy epoxide **38** with camphorsulfonic acid (CSA) afforded smoothly the tricycle **39**. Interestingly, the minor isomer of **35** failed to cyclize under these conditions and, therefore, this step served to separate the two epoxide isomers as well as to accomplish the construction of the desired tricyclic framework. The yield of **39** from a 10:1 mixture of **38** was 71% (single stereoisomer). The difference in the reactivity of the two epoxides toward ring closure is reflected in the required transition states **38A** and **38B** (Figure 1). As can be seen from these models, **38A** is able to assume a comfortable, chairlike conformation, whereas **38B** has to go through a high-energy boatlike arrangement before it reaches a tricyclic skeleton.

The structure of the tricyclic system **39** was confirmed by an X-ray crystallographic analysis of a crystalline derivative. Thus, DIBAL reduction of **39** afforded diol **40** in 95% yield. Desilylation of **40** using fluoride (98%) followed by reaction with *p*-bromobenzoyl chloride and DMAP furnished the highly crystalline tribenzoate **42** (92%), mp 175–177 °C (from ether–hexane), via

**Scheme VII**[a]



[a] Reagents and conditions: (a) $O_3$, $CH_2Cl_2$, −78 °C, 30 min, 5.0 equiv of $Me_2S$ and 1.0 equiv of $Ph_3P$, then 4.0 equiv of $NaBH_4$, MeOH, 25 °C, 1 h, 95%; (b) 1.1 equiv of *t*-$BuMe_2SiCl$, 1.5 equiv of imidazole, DMF, 0 °C, 30 min, 91%; (c) 1.5 equiv of $(COCl)_2$, 2.0 equiv of DMSO, $CH_2Cl_2$, −78 °C, 30 min, then 4.0 equiv of $Et_3N$, 98%; (d) 1.0 equiv of $Zn(OTf)_2$, 10.0 equiv of EtSH, $CH_2Cl_2$, 25 °C, 30 min, then (e) 0.2 equiv of CSA, MeOH, 25 °C, 15 min, 78% overall; (f) 5.0 equiv of $SO_3$–pyr., 5.0 equiv of $Et_3N$, $CH_2Cl_2$–DMSO (1:1), 0 °C, 1.5 h, 83%.

the triol **41**. An X-ray crystallographic analysis[12] on **42** proved the assigned stereochemistry (see the ORTEP drawing in Scheme VI).

The last phase of the synthesis was designed to prepare the IJK fragment (Scheme VII) of brevetoxin B for a coupling reaction with the FG ring system and the formation of the requisite oxocene system via our hydroxy dithio ketal technology.[13] To this end, the olefin **39** was subjected to ozonolysis followed by sequential reduction with $Ph_3P$ and $NaBH_4$ to afford diol **43** in 95% overall yield. Monosilylation of **43** with *tert*-butyldimethylsilyl chloride (91%) followed by Swern oxidation[9] furnished ketone **45** (98% yield). Treatment of ketone **45** with excess EtSH in $CH_2Cl_2$ in the presence of $Zn(OTf)_2$ followed by addition of methanol and camphorsulfonic acid (CSA) led to the hydroxy dithio ketal **47** via compound **46** (78% overall yield). Finally, oxidation of **47** with $SO_3$·pyridine complex in $CH_2Cl_2$–DMSO (1:1) furnished the targeted aldehyde **1** in 83% yield.

## Conclusion

A fully functionalized tricyclic system (**1**) corresponding to the IJK ring framework of brevetoxin B has been synthesized in optically active form from D-mannose pentaacetate. The described construction involves a stereocontrolled intramolecular Michael type reaction and a stereospecific cyclization of a 6-endo activated hydroxy epoxide. This synthesis represents another demonstration of the power of the 6-endo activation method[4] for the construction of complex tetrahydropyran systems and is expected to facilitate an eventual total synthesis of the brevetoxins.

## Experimental Section

**General Methods.** See the Experimental Section of ref 2.

**2,6-Anhydro-7,8,9-trideoxy-D-*glycero*-D-*manno*-non-8-enitol Tetraacetate (5).** To a magnetically stirred mixture of mannose pentaacetate (39.00 g, 0.1 mol) and allyltrimethylsilane (13.68 g, 0.12 mol) in acetonitrile (500 mL) at 0 °C were sequentially and dropwise added $BF_3$·$Et_2O$ (27.20 g, 0.2 mol) and TMSOTf (4.44 g, 0.02 mol). After stirring for 1 h, the reaction mixture was allowed to warm to 25 °C, and stirring was continued for another 16 h. The reaction mixture was poured onto a mixture of saturated aqueous $NaHCO_3$ solution (400 mL) and ether (1.5 L), and, after shaking, the organic layer was separated and washed with additional $NaHCO_3$ solution (400 mL), $H_2O$ (500 mL), and brine (300 mL) and dried over anhydrous $MgSO_4$. Solvent evaporation, followed by flash column chromatography (silica, 40% ether in petroleum ether) gave the *C*-glycoside **5** (27.90 g, 75%, $\alpha$:$\beta$ ca. 6.8:1 by $^1H$ NMR). **5**: oil; $R_f$ = 0.61 (silica, 80% ether in petroleum ether); $[\alpha]^{17}_D$ +6.83°

(12) We thank Dr. Patrick Carroll of this Department for this X-ray crystallographic analysis.

(13) Nicolaou, K. C.; Duggan, M. E.; Hwang, C.-K. *J. Am. Chem. Soc.* **1986**, *108*, 2468.

(*c* 1.2, $CH_2Cl_2$); IR (neat) $\nu_{max}$ 3080, 2984, 2958, 1760, 1751, 1745, 1648, 1436, 1375, 1232, 1056, 926, 740, 705 $cm^{-1}$; $^1H$ NMR (250 MHz, $CDCl_3$) $\delta$ 5.78 (m, 1 H, CH=$CH_2$), 5.20 (m, 5 H, C*H*-OAc, CH=C$H_2$), 4.30 (dd, $J$ = 12.0, 6.0 Hz, 1 H, C$H_2$-OAc), 4.10 (dd, $J$ = 12.0, 3.0 Hz, 1 H, C$H_2$-OAc), 4.02 (m, 1 H, C*H*-O), 3.88 (m, 1 H, C*H*-O), 2.60–2.30 (m, 2 H, C$H_2$—CH=$CH_2$), 2.06, 2.04, 2.03, 2.01 (4 × s, 4 × 3 H, 4 × OCOC$H_3$); MS *m/e* (rel intensity) 373 (M + 1, 65), 331 (48), 313 (100), 253 (5), 229 (5), 211 (17), 193 (61), 169 (100), 151 (35), 127 (32), 109 (62), 97 (20), 83 (35); HRMS calcd for $C_{17}H_{25}O_9$ (M + 1) 373.1499, found 373.1505.

**2,6-Anhydro-7,8,9-trideoxy-D-*glycero*-D-*manno*-non-8-enitol (6).** Sodium methoxide (2.40 g, 0.05 mol) was added to a stirred solution of compound **5** (37.21 g, 0.1 mol) in methanol (200 mL) at 25 °C. After stirring for 2 h at 25 °C, the solvent was removed under reduced pressure and the residue was flash chromatographed (silica, 10% MeOH in EtOAc) to furnish tetraol **6** (20.40 g, 100%). **6**: oil; $R_f$ = 0.15 (silica, 10%, MeOH in EtOAc); $[\alpha]^{17}_D$ +24.30° (*c* 2.65, MeOH); IR (neat) $\nu_{max}$ 3400 (s, OH) 2984, 2938, 1648, 1421, 1272, 1073, 923, 845, 785, 743 $cm^{-1}$; $^1H$ NMR (250 MHz, $CD_3OD$) $\delta$ 5.82 (m, 1 H, C*H*=$CH_2$), 5.08 (m, 2 H, CH=C$H_2$), 3.88 (t, $J$ = 7.0 Hz, 1 H, C*H*-O), 3.79–3.55 (m, 5 H, C*H*-O, C$H_2$-O), 3.42 (m, 1 H, C$H_2$-O), 2.53–2.23 (m, 2 H, C$H_2$—CH=$CH_2$); HRMS calcd for $C_9H_{10}O_5$ (M) 204.0998, found 204.0993.

**2,6-Anhydro-1-*O*-(*tert*-butyldiphenylsilyl)-7,8,9-trideoxy-4,5-*O*-isopropylidene-D-*glycero*-D-*manno*-non-8-enitol (8).** *tert*-Butyldiphenylsilyl chloride (27.49 g, 0.1 mol) was added to a stirred solution of alcohol **6** (20.40 g, 0.1 mol) and imidazole (7.48 g, 0.11 mol) in anhydrous DMF (500 mL) at 0 °C. After stirring for 30 min at 0 °C, the reaction mixture was treated with camphorsulfonic acid (CSA, 4.65 g, 0.02 mol), and 2-methoxypropene (10.8 g, 0.15 mol) was added. Stirring was continued for another 1 h at 0 °C, and then the reaction mixture was poured onto saturated aqueous $NaHCO_3$ solution 400 mL and ether (1.5 L). After shaking, the organic layer was separated and washed with $H_2O$ (2 × 400 mL) and brine (400 mL) and dried over anhydrous $MgSO_4$. Solvent removal followed by flash column chromatography gave compound **8** (39.52 g, 82%). **8**: oil; $R_f$ = 0.70 (silica, 50% ether in petroleum ether); $[\alpha]^{17}_D$ −5.83° (*c* 1.2, $CH_2Cl_2$); IR (neat) $\nu_{max}$ 3450 (s, OH), 3095, 3078, 3037, 2995, 2938, 2860, 1648, 1592, 1485, 1430, 1385, 1221, 1115, 1070, 920, 825, 745, 705, 680 $cm^{-1}$; $^1H$ NMR (250 MHz, $CDCl_3$) $\delta$ 7.70 (m, 4 H, Ar), 7.40 (m, 6 H, Ar), 5.82 (m, 1 H, C*H*=$CH_2$), 5.10 (m, 2 H, CH=C$H_2$), 4.10 (m, 3 H, C*H*-O), 3.87 (d, $J$ = 5.0 Hz, 2 H, C$H_2$-O), 3.87 (m, 1 H, C*H*-O), 3.50 (m, 1 H, C*H*-O), 2.82 (d, $J$ = 3.0 Hz, 1 H, O*H*), 2.36 (m, 2 H, C$H_2$—CH=$CH_2$), 1.50, 1.38 (2 × s, 2 × 3 H, acetonide), 1.02 (s, 9 H, SiC($CH_3$)$_3$); MS m/e (rel intensity) 500 (M + $NH_4$, 8), 467 (13), 425 (100), 405 (100), 380 (55), 329 (28), 289 (59), 269 (42), 241 (64), 221 (27), 199 (61), 163 (39); HRMS calcd for $C_{28}H_{42}O_5SiN$ (M + $NH_4$) 500.2832, found 500.2813.

**2,6-Anhydro-1-*O*-(*tert*-butyldiphenylsilyl)-7,8,9-trideoxy-4,5-*O*-isopropylidene-D-*glycero*-D-*manno*-non-8-enitol Imidazole-1-carbothioate (9).** A mixture of the hydroxy compound **8** (48.22 g, 0.1 mol) and 1,1′-thiocarbonyldiimidazole (21.39 g, 0.12 mol) in toluene (200 mL) was refluxed for 3 h. The solvent was then removed under vacuum, and the product was purified by flash column chromatography (silica, 50% ether in petroleum ether) furnishing derivative **9** (54.46 g, 92%). **9**: oil; $R_f$ = 0.65 (silica, ether); $[\alpha]^{18}_D$ −9.50° (*c* 4.4, $CH_2Cl_2$); IR (neat) $\nu_{max}$ 3138, 3092, 3078, 3059, 2990, 2938, 2860, 1533, 1533, 1485, 1432, 1395, 1335, 1290, 1290, 1240, 1118, 995, 828, 708, 682, 656 $cm^{-1}$; $^1H$ NMR (250 MHz, $CDCl_3$) $\delta$ 8.30 (s, 1 H, imidazole), 7.70–7.30 (m, 11 H, imidazole, Ar), 7.05 (s, 1 H, imidazole), 6.10 (t, $J$ = 6.0 Hz, 1 H, C*H*-OC(S)-), 5.90 (m, 1 H, C*H*=$CH_2$), 5.18 (m, 2 H, CH=C$H_2$), 4.40 (t, $J$ = 5.0 Hz, 1 H, C*H*-O), 4.08 (t, $J$ = 6.0 Hz, 1 H, C*H*-O), 3.90 (m, 3 H, C*H*-O), 3.78 (m, 1 H, C*H*-O), 2.40 (m, 2 H, C$H_2$), 1.44, 1.35 (2 × s, 2 × 3 H, acetonide), 1.02 (s, 9 H, SiC($CH_3$)$_3$); MS *m/e* (rel intens ity) 591 (M + 1, 87), 535 (100), 475 (67), 381 (100), 349 (100), 309 (100), 241 (100), 199 (100), 163 (100), 135 (100), 105 (100), 81 (100); HRMS calcd for $C_{32}H_{41}O_5SiSN_2$ (M + 1) 593.2505, found 593.2491.

**2,6-Anhydro-1-*O*-(*tert*-butyldiphenylsilyl)-3,7,8,9-tetradeoxy-4,5-*O*-isopropylidene-D-*altro*-non-8-enitol (10).** A mixture of the thioimidazolide **9** (59.22 g, 0.1 mol), *n*-$Bu_3SnH$ (43.65 g, 0.15 mol), and AIBN (200 mg, 1.20 mmol) in toluene (500 mL) was heated to 110 °C for 3 h under an argon atmosphere. The solvent was then removed, and the product was purified by flash column chromatography (silica, 20% ether in petroleum ether) giving compound **10** (33.60 g, 72%). **10**: oil; $R_f$ = 0.31 (silica, 30% ether in petroleum ether); $[\alpha]^{21}_D$ +14.12° (*c* 4.3, $CH_2Cl_2$); IR (neat) $\nu_{max}$ 3400 (s, OH), 3075, 3050, 3000, 2938, 2862, 1648, 1475, 1432, 1318, 1270, 1115, 1000, 920, 823, 742, 705, 618 $cm^{-1}$; $^1H$ NMR (250 MHz, $CDCl_3$) $\delta$ 7.66 (m, 4 H, Ar), 7.19 (m, 6 H, Ar), 5.81 (m, 1 H, C*H*=$CH_2$), 5.10 (m, 2 H, CH=C$H_2$), 4.03–3.50 (m, 6 H, C*H*-O, C$H_2$-O), 2.85 (br s, 1 H, OH), 2.34 (t, $J$ = 7.0 Hz, 2 H, C$H_2$CH=C$H_2$), 1.96 (m, 1 H, C$H_2$), 1.65 (m, 2 H, C$H_2$, OH), 1.02 (s, 9 H, SiC($CH_3$)$_3$); MS *m/e* (rel intensity) 484 (M + $NH_4$, 36) 451 (18), 409 (100), 389 (100), 351 (48), 331 (38), 273 (60), 241 (89), 221 (27), 199 (43), 181 (22), 163 (28); HRMS calcd for $C_{28}H_{42}O_4SiN$ (M + $NH_4$) 484.2883, found 484.2942.

**2,6-Anhydro-1-*O*-(*tert*-butyldiphenylsilyl)-3,7,8,9-tetradeoxy-4,5-*O*-isopropylidene-D-*altro*-non-8-enitol (11).** The acetonide **10** (46.62, g, 0.1 mol) together with amberlyst-15 ($H^+$, 7.0 g) in methanol (500 mL) was heated to 60 °C for 4 h. Removal of the catalyst by filtration followed by concentration and flash column chromatography (silica, 50% ether in petroleum ether) gave pure diol **11** (30.69 g, 72%). **11**: oil; $R_f$ = 0.25 (silica, 70% ether in petroleum ether); $[\alpha]^{21}_D$ +13.62° (*c* 0.9, $CH_2Cl_2$); IR (neat) $\nu_{max}$ 3400 (s, OH), 3075, 3050, 3000, 2938, 2862, 1648, 1475, 1432, 1318, 1270, 1115, 1000, 920, 823, 742, 705, 618 $cm^{-1}$; $^1H$ NMR (250 MHz, $CDCl_3$) $\delta$ 7.66 (m, 4 H, Ar), 7.19 (m, 6 H, Ar), 5.81 (m, 1 H, C*H*=$CH_2$), 5.10 (m, 2 H, CH=C$H_2$), 4.03–3.50 (m, 6 H, C*H*-O, C$H_2$-O), 2.83 (br s, 1 H, O*H*), 2.34 (t, $J$ = 7.0 Hz, 2 H, C$H_2$CH=C$H_2$), 1.96 (m, 1 H, C$H_2$), 1.65 (m, 2 H, C$H_2$, O*H*), 1.02 (s, 9 H, SiC($CH_3$)$_3$); MS *m/e* (rel intensity) 444 (M + $NH_4$, 24), 427 (M + 1, 18), 409 (11), 391 (42), 349 (28), 331 (100), 313 (20), 291 (100), 273 (100), 253 (100), 221 (100), 201 (100), 181 (97), 135 (100), 117 (100), 91 (100); HRMS calcd for $C_{25}H_{38}O_4SiN$ (M + $NH_4$) 444.2570, found 444.2476. Anal. Calcd for $C_{25}H_{34}O_4Si$: C, 70.38; H, 8.03. Found: C, 70.25; H, 8.25.

**2,6-Anhydro-4-*O*-benzyl-1-*O*-(*tert*-butyldiphenylsilyl)-3,7,8,9-tetradeoxy-D-*altro*-non-8-enitol (12).** A mixture of the diol **11** (42.62 g, 0.1 mol) and *n*-$Bu_2SnO$ (24.90 g, 0.1 mol) in absolute methanol (1.0 L) was heated under argon at 60 °C for 1 h. The solvent was then removed under vacuum, and the residue was dried azeotropically with benzene (2 × 200 mL) and dissolved in dry DMF (500 mL). Benzyl bromide (25.65 g, 0.15 mol) was added, and the mixture was heated at 100 °C for 4 h before dilution with ether (2.0 L) and washing with $H_2O$ (2 × 500 mL) and brine (300 mL). Drying of the organic layer ($MgSO_4$) followed by concentration and flash column chromatography (silica, 20% ether in petroleum ether) gave pure monobenzyl ether **12** (38.20 g, 74%). **12**: oil; $R_f$ = 0.65 (silica, 50% ether in petroleum ether); $[\alpha]^{19}_D$ +25.13° (*c* 0.8, $CH_2Cl_2$); IR (neat) $\nu_{max}$ 3450 (s, OH), 3088, 3039, 2962, 2935, 2860, 1432, 1120, 1010, 916, 827, 742, 704, 618 $cm^{-1}$; $^1H$ NMR (250 MHz, $CDCl_3$) $\delta$ 7.70–7.30 (m, 15 H, Ar), 5.80 (m, 1 H, C*H*=$CH_2$), 5.06 (m, 2 H, CH=C$H_2$), 4.64, 4.54 (2 × d, $J$ = 12.0 Hz, 2 × 1 H, benzylic), 3.94–3.60 (m, 6 H, C*H*-O, C$H_2$-O), 2.40 (d, $J$ = 5.0 Hz, 1 H, O*H*), 2.32 (m, 2 H, C$H_2$—CH=$CH_2$), 1.88 (m, 2 H, C$H_2$), 1.05 (s, 9 H, SiC($CH_3$)$_3$); HRMS calcd for $C_{32}H_{40}O_4Si$ (M) 516.2696, found 516.2686.

**(2*R*,4*S*,6*S*)-2-Allyl-4-(benzyloxy)-6-[(*tert*-butyldiphenylsiloxy)methyl]dihydro-2*H*-pyran-3(4*H*)-one (13).** To a cold (−78 °C) stirred solution of oxalyl chloride (6.5 mL, 75 mmol) in methylene chloride (500 mL) under argon was added dimethyl sulfoxide (7.09 mL, 100 mmol). After stirring for 10 min, the alcohol **12** (25.71 g, 50 mmol) in methylene chloride (50 mL) was dropwise added at −78 °C, and the mixture was stirred at that temperature for 1 h. Triethylamine (27.88 mL, 200 mmol) was then dropwise added, and the reaction mixture was allowed to warm to 0 °C with stirring. After 10 min, the reaction mixture was poured onto a mixture of saturated aqueous $NH_4Cl$ solution (400 mL) and ether (2.0 L). Shaking and separation of the organic layer were followed by washing with $H_2O$ (2 × 400 mL) and brine (300 mL) and drying ($MgSO_4$). Evaporation of the solvent under vacuum afforded essentially pure product **13** (25 g, 100%), which was used for the next step without further purification. **13**: oil; $R_f$ = 0.75 (silica, 40% ether in petroleum ether); $[\alpha]^{20}_D$ +18.58° (*c* 7.2, $CH_2Cl_2$); IR (neat) $\nu_{max}$ 3075, 3039, 2960, 2938, 2862, 1742 (s, C=O), 1474, 1430, 1117, 825, 742, 704, 682, 615 $cm^{-1}$; $^1H$ NMR (250 MHz, $CDCl_3$) $\delta$ 7.68–7.30 (m, 1k H, Ar), 5.77 (m, 1 H, C*H*=$CH_2$), 5.10 (m, 2 H, CH=C$H_2$), 4.88, 4.58 (2 × d, $J$ = 12.0 Hz, 2 × 1 H, benzylic), 4.38 (dd, $J$ = 7.0, 7.0 Hz, 1 H, C*H*-O), 4.28 (dd, $J$ = 13.5, 5.0 Hz, 1 H, C*H*-O), 4.15 (m, 1 H, C*H*-O), 3.70 (m, 2 H, C$H_2$-O), 2.48–2.0 (m, 4 H, C$H_2$), 1.02 (s, 9 H, SiC($CH_3$)$_3$); HRMS Calcd for $C_{32}H_{38}O_4Si$ (M) 514.2550, found 514.2529.

**2,6-Anhydro-4-*O*-benzyl-1-*O*-(*tert*-butyldiphenylsilyl)-3,7,8,9-tetradeoxy-5-*C*-methyl-D-*altro*-non-8-enitol (14) and 4,8-Anhydro-6-*O*-benzyl-9-*O*-(*tert*-butyldiphenylsilyl)-1,2,3,7-tetradeoxy-5-*C*-methyl-D-*ido*-non-1-enitol (15).** A mixture of ketone **13** (53.03 g, 0.1 mol) and $MgBr_2$·$Et_2O$ (33.57 g, 0.13 mol) in methylene chloride (350 mL) was cooled to −50 °C under an argon atmosphere and stirred for 15 min before $AlMe_3$ (150 mL of 2 M hexane solution, 0.3 mol) was dropwise added. The reaction mixture was brought up to 0 °C and allowed to stir for 4 h before being quenched with methanol (100 mL) and diluted with ethyl acetate (1.5 L). The mixture was washed with saturated aqueous solution of potassium sodium tartrate (2 × 500 mL), water (500 mL), and brine (400 mL) and then dried ($MgSO_4$). Evacuation of the solvent followed by flash column chromatography (silica, 3% ethyl acetate in benzene) gave alcohols **14** (slow moving, 32.60 g, 61%) and **15** (fast moving, 10.68 g, 20%). **14**: oil; $R_f$ = 0.22 (silica, 4% ethyl acetate in benzene); $[\alpha]^{24}_D$ +56.06° (*c* 1.7, $CH_2Cl_2$); IR (neat) $\nu_{max}$ 3450 (s, OH),

3078, 3036, 2960, 2935, 2860, 1430, 1362, 1110, 916, 825, 730, 702, 615 $cm^{-1}$; $^1H$ NMR (250 MHz, $CDCl_3$) $\delta$ 7.68–7.20 (m, 15 H, Ar), 5.80 (m, 1 H, C*H*=$CH_2$), 5.01 (m, 2 H, CH=C*H*$_2$), 4.64, 4.39 (2 × d, $J$ = 12.0 Hz, 2 × 1 H, benzylic), 3.95–3.77 (m, 2 H, C*H*–O), 3.65 (m, 2 H, C*H*$_2$–O), 3.45 (dd, $J$ = 6.0, 4.0 Hz, 1 H, C*H*–O), 2.67 (m, 1 H, O*H*), 2.25 (m, 2 H, C*H*$_2$—CH=$CH_2$), 1.18 (s, 3 H, C*H*$_3$), 1.02 (s, 9 H, SiC(C*H*$_3$)$_3$); HRMS calcd for $C_{33}H_{42}O_4Si$ (M) 530.2842, found 530.2841. Anal. Calcd for $C_{33}H_{42}O_4Si$: C, 74.68; H, 7.98. Found: C, 74.52; H, 8.26. **15**: oil; $R_f$ = 0.26 (silica, 4% ethyl acetate in benzene); $[\alpha]^{24}_D$ +49.96° (*c* 2.3, $CH_2Cl_2$); IR (neat) $\nu_{max}$ 3480 (s, OH), 3095, 3088, 3040, 2938, 2865, 1432, 1365, 1120, 913, 826, 742, 705, 682, 617 $cm^{-1}$; $^1H$ NMR (250 MHz, $CDCl_3$) $\delta$ 7.67–7.27 (m, 1 H, Ar), 5.83 (m, 1 H, C*H*=$CH_2$), 5.05 (m, 2 H, CH=C*H*$_2$), 4.64, 4.45 (2 × d, $J$ = 12.01 Hz, 2 × 1 H, benzylic), 3.38–3.55 (m, 5 H, C*H*–O, C*H*$_2$–O), 2.38 (m, 2 H, C*H*$_2$—CH=$CH_2$), 2.30 (s, 1 H, –O*H*), 2.03 (m, 1 H, C*H*$_2$), 1.59 (m, 1 H, C*H*$_2$), 1.29 (s, 3 H, –C*H*$_3$), 1.03 (s, 9 H, SiC(C*H*$_3$)$_3$); HRMS calcd for $C_{33}H_{42}O_4Si$ (M) 530.2842, found 530.2842.

**2,6-Anhydro-4-*O*-benzyl-3,7,8,9-tetradeoxy-5-*C*-methyl-D-*altro*-non-8-enitol (16).** Tetra-*n*-butylammonium fluoride (1.2 mL, 1 M in THF, 1.2 mmol) was added to a solution of silyl ether **14** (530 mg, 1 mmol) in dry THF (5 mL) at 25 °C. After stirring for 4 h, the solvent was removed, and the residue was flash chromatographed (silica, ether) giving diol **16** (290 mg, 99%). **16**: oil; $R_f$ = 0.30 (silica, ether); $[\alpha]^{20}_D$ +64.36° (*c* 1.4, $CH_2Cl_2$); IR (neat) $\nu_{max}$ 3540 (s, OH), 3078, 3020, 2982, 2842, 2881, 1602, 1461, 1372, 1268, 1181, 1100, 981, 821, 712, 705, 680 $cm^{-1}$; $^1H$ NMR (250 MHz, $CDCl_3$) $\delta$ 7.34 (m, 5 H, Ar), 5.82 (m, 1 H, C*H*=$CH_2$), 5.10 (m, 2 H, CH=C*H*$_2$), 4.65, 4.44 (2 × d, $J$ = 12.0 Hz, 2 × 1 H, benzylic), 3.96–3.40 (m, 5 H, C*H*–O, C*H*$_2$–O), 2.68 (br s, 1 H, O*H*), 2.43–1.72 (m, 5 H, C*H*$_2$, OH), 1.20 (s, 3 H, C*H*$_3$); MS *m/e* (rel intensity) 310 (M + $NH_4$, 100), 293 (M + 1, 32), 275 (100), 247 (22), 223 (20), 205 (9), 183 (22), 167 (82), 155 (48), 143 (28), 125 (58); HRMS calcd for $C_{17}H_{28}O_4N$ (M + $NH_4$) 310.2018, found 310.2037.

**2,6-Anhydro-4-*O*-benzyl-3,7,8,9-tetradeoxy-5-*C*-methyl-D-*altro*-non-8-enitol 1-*p*-Toluenesulfonate (17).** *p*-Toluenesulfonyl chloride (210 mg, 1.1 mmol) was added in one portion to a cold (0 °C) and stirred solution of alcohol **16** (290 mg, 1.0 mmol) and 4-(dimethylamino)pyridine (183 mg, 1.5 mmol) in dry $CH_2Cl_2$ (5 mL) under an argon atmosphere. The reaction mixture was allowed to reach room temperature and was stirred for 3 h before dilution with methanol (0.5 mL) and ether (50 mL). The mixture was washed with aqueous saturated $NH_4Cl$ solution (10 mL), $H_2O$ (10 mL), and brine (10 mL) and then dried ($MgSO_4$). Concentration followed by flash column chromatography (silica, 50% ether in petroleum ether) gave compound **17** (379 mg, 85%). **17**: oil; $R_f$ = 0.25 (silica, 50% ether in petroleum ether); $[\alpha]^{20}_D$ +67.53° (*c* 1.5, $CH_2Cl_2$); IR (neat) $\nu_{max}$ 3430 (s, OH), 3065, 3040, 2982, 2880, 1458, 1378, 1271, 1100, 1032, 921, 740, 705 $cm^{-1}$; $^1H$ NMR (250 MHz, $CDCl_3$) $\delta$ 7.77–7.28 (m, 9 H, Ar), 5.74 (m, 1 H, C*H*=$CH_2$), 5.02 (m, 2 H, CH=C*H*$_2$), 4.65, 4.41 (2 × d, $J$ = 12.0 Hz, 2 × 1 H, benzylic), 4.38–3.46 (m, 5 H, C*H*–O, C*H*$_2$–O), 2.62 (s, 1 H, O*H*), 2.45 (s, 3 H, $C_6H_4$–C*H*$_3$), 2.42–1.82 (m, 4 H, C*H*$_2$), 1.17 (s, 3 H, C*H*$_3$); MS *m/e* (rel intensity) 446 (M, 43), 355 (16), 322 (11), 281 (100), 257 (9), 233 (14), 184 (25), 155 (54), 131 (58), 114 (32); HRMS calcd for $C_{24}H_{30}L_6S$ (M) 446.1763, found 446.1830.

**1,5:2,6-Dianhydro-4-*O*-benzyl-3,7,8,9-tetradeoxy-5-*C*-methyl-D-*altro*-non-8-enitol (18).** A mixture of the tosylate **17** (270 mg, 0.61 mmol) and sodium methoxide (33 mg, 0.61 mmol) in absolute methanol (10 mL) was refluxed for 16 h. The solvent was then removed under vacuum, and the product purified by flash column chromatography (silica, 40% ether in petroleum ether) furnishing tricyclic compound **18** (118 mg, 71%). **18**: oil; $R_f$ = 0.45 (silica, 50% ether in petroleum ether); $[\alpha]^{20}_D$ +115.89° (*c* 1.8, $CH_2Cl_2$); IR (neat) $\nu_{max}$ 3078, 2928, 2941, 2878, 1640, 1458, 1351, 1212, 1175, 1115, 1000, 924, 865, 818, 738, 704 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 7.33 (m, 5 H, Ar), 5.82 (m, 1 H, C*H*=$CH_2$), 5.07 (m, 2 H, CH=C*H*$_2$), 4.72, 4.48 (2 × d, $J$ = 12.5 Hz, 2 × 1 H, benzylic), 4.30–3.64 (m, 5 H, C*H*–O, C*H*$_2$–O), 2.48–1.69 (s, 4 H, C*H*$_2$), 1.15 (s, 3 H, C*H*$_3$); MS *m/e* (rel intensity) 292 (M + $NH_4$, 44), 275 (M + 1, 95), 257 (8), 233 (16), 202 (11), 183 (13), 167 (34), 143 (12), 127 (15); HRMS calcd for $C_{17}H_{26}O_{3N}$ (M + $NH_4$) 292.1913, found 292.1881. Anal. Calcd for $C_{17}H_{22}O_3$: C, 74.42; H, 8.08. Found: C, 74.21; H, 8.08.

**5,9-Anhydro-7-*O*-benzyl-10-*O*-(*tert*-butyldiphenylsilyl)-1,2,4,8-tetradeoxy-6-*C*-methyl-D-*glycero*-L-*allo*-dec-1-enitol (21) and 5,9-Anhydro-7-*O*-benzyl-10-*O*-(*tert*-butyldiphenylsilyl)-1,2,4,8-tetradeoxy-6-*C*-methyl-D-*glycero*-L-*altro*-dec-1-enitol (20).** Ozone was passed through a solution of compound **14** (28.02 g, 50 mmol) in methylene chloride (500 mL) at –78 °C until a blue coloration persisted (ca. 2 h). The excess ozone was removed by a stream of oxygen before dimethyl sulfide (10 mL) was added slowly followed by triphenylphosphine (13.1 g, 50 mmol) both at –78 °C. The cooling was removed, and the reaction mixture was stirred for 3 h before the solvent was removed under vacuum and below 10 °C to afford the corresponding aldehyde (**19**), which was immediately subjected to the next reaction without purification. To this crude aldehyde (**19**) in anhydrous THF (300 mL) at 0 °C was added dropwise vinylmagnesium bromide (110 mL of 1 M solution in THF, 110 mmol) with stirring and under an argon atmosphere. After stirring at 0 °C for 30 min, the reaction mixture was quenched with saturated aqueous $NH_4Cl$ solution (50 mL) and diluted with ether (800 mL). After shaking and separation, the organic phase was washed with $H_2O$ (2 × 300 mL) and brine (300 mL) and dried ($MgSO_4$). Concentration followed by flash column chromatography (silica, 40% ether in petroleum ether) gave the two allylic alcohols **21** (fast moving, 12.6 g, 45%) and **20** (slow moving, 12.3 g, 44%). **21**: oil; $R_f$ = 0.35 (silica, 60% ether in petroleum ether); $[\alpha]^{22}_D$ + 52.75° (*c* 4.0, $CH_2Cl_2$); IR (neat) $\nu_{max}$ 3500 (s, OH), 3090, 3075, 3038, 2960, 2938, 2862, 1482, 1432, 1120, 925, 824, 722, 705, 682, 618 $cm^{-1}$; $^1H$ NMR (250 MHz, $CDCl_3$) $\delta$ 7.75–7.20 (m, 15 H, Ar), 5.88 (ddd, $J$ = 16.0, 11.0, 6.0 Hz, 1 H, C*H*=$CH_2$), 5.28 (d, $J$ = 16.0 Hz, 1 H, CH=C*H*$_2$), 5.07 (d, $J$ = 11.0 Hz, 1 H, CH=C*H*$_2$), 4.60, 4.36 (2 × d, $J$ = 12.0 Hz, 2 × 1 H, benzylic), 4.30 (m, 1 H, $CH_2$=CH—C*H*—O), 4.15–3.90 (m, 3 H, C*H*–O or C*H*$_2$–O), 3.68 (br s, 1 H, O*H*), 3.61 (dd, $J$ = 10.0, 4.0 Hz, 1 H, –C*H*$_2$–O), 3.47 (dd, $J$ = 4.0, 4.0 Hz, 1 H, C*H*–O), 2.78 (s, 1 H, –O*H*), 1.90 (t, $J$ = 4.0 Hz, 2 H, C*H*$_2$), 1.88–1.64 (m, 2 H, C*H*$_2$), 1.20 (s, 3 H, C*H*$_3$), 1.06 (s, 9 H, SiC(C*H*$_3$)$_3$); MS *m/e* (rel intensity): 501 (M + 1, 23), 543 (29), 465 (46), 407 (44), 339 (64), 297 (90), 263 (100), 229 (100), 199 (100), 161 (62), 135 (86); HRMS calcd for $C_{34}H_{45}O_5Si$ (M + 1) 561.3036, found 561.3070. **20**: oil; $R_f$ = 0.30 (silica, 60% ether in petroleum ether); $[\alpha]^{22}_D$ +35.49° (*c* 3.5, $CH_2Cl_2$); IR (neat) $\nu_{max}$ 3460 (s, OH), 3094, 3078, 3039, 2960, 2936, 2862, 1482, 1430, 1115, 825, 825, 722, 705, 680, 617 $cm^{-1}$; $^1H$ NMR (250 MHz, $CDCl_3$) $\delta$ 7.65–7.17 (m, 15 H, Ar), 5.85 (ddd, $J$ = 16.0, 10.5, 5.0 Hz, 1 H, C*H*=$CH_2$), 5.23 (ddd, $J$ = 16.0, 1.0, 1.0 Hz, 1 H, CH=C*H*$_2$), 5.04 (ddd, $J$ = 10.5, 1.0 Hz, 1 H, CH=C*H*$_2$), 4.57, 4.32 (2 × d, $J$ = 12.0 Hz, 2 × 1 H, benzylic), 4.35 (m, 1 H, $CH_2$=CH—C*H*—O), 4.00 (m, 2 H, C*H*–O, C*H*$_2$–O), 3.85 (m, 1 H, C*H*–O), 3.55 (dd, $J$ = 11.0, 5.0 Hz, 1 H, C*H*$_2$–O), 3.42 (dd, $J$ = 4.5, 4.5 Hz, 1 H, C*H*–O), 3.05 (br s, 1 H, O*H*), 2.71 (s, 1 H, O*H*), 1.85–1.65 (m, 4 H, C*H*$_2$), 1.15 (s, 3 H, C*H*$_3$), 1.01 (s, 9 H, SiC(C*H*$_3$)$_3$); MS *m/e* (rel intensity) 561 (M + 1, 28), 543 (33), 435 (47), 431 (62), 407 (64), 377 (18), 339 (28), 289 (16), 263 (63), 235 (29), 199 (100), 163 (33), 135 (74), 91 (100); HRMS calcd for $C_{36}H_{45}O_5Si$ (M + 1) 561.3036, found 561.3003.

**1,2:5,9-Dianhydro-7-*O*-benzyl-10-*O*-(*tert*-butyldiphenylsilyl)-4,8-dideoxy-6-*C*-methyl-D-*threo*-L-*altro*-decitol (21a).** *tert*-Butyl hydroperoxide (0.2 mL, 4.93 M in $CH_2ClCH_2Cl$, 1.0 mmol) was added dropwise to a mixture of alcohols **20** and **21** (ca. 1:1 mixture, 280 mg, 0.5 mmol), diethyl L-tartrate (0.12 mL, 0.7 mmol), and titanium(IV) isopropoxide (0.21 mL, 0.7 mmol) in dry $CH_2Cl_2$ (5 mL) at –20 °C. The mixture was stirred for 12 h before quenching with 10% tartaric acid (2 mL) and dilution with ether (50 mL). The organic phase was separated and washed with $H_2O$ (2 × 10 mL) and brine (10 mL). Drying ($MgSO_4$) followed by solvent evaporation and flash column chromatography (silica, 50% ether in petroleum ether) gave epoxide alcohol **21a** (slow moving, 120 mg, 42%) and unreacted alcohol **20** (fast moving, 132 mg, 47%). **21a**: oil; $R_f$ = 0.30 (silica, 60% ether in petroleum ether); $[\alpha]^{20}_D$ +20.56° (*c* 0.9, $CH_2Cl_2$); IR (neat) $\nu_{max}$ 3496 (s, OH), 3078, 3057, 3005, 2962, 2938, 2860, 1431, 1362, 1265, 1117, 825, 745, 702, 614 $cm^{-1}$; $^1H$ NMR (250 MHz, $CDCl_3$) $\delta$ 7.67–7.16 (m, 15 H, Ar), 4.59, 4.35 (2 × d, $J$ = 12.5 Hz, 2 × 1 H, benzylic), 4.18–3.46 (m, 6 H, C*H*–O, C*H*$_2$–O), 3.78 (br s, 1 H, O*H*), 2.96 (m, 1 H, epoxide), 2.80 (dd, $J$ = 5.0, 4.5 Hz, 1 H, epoxide), 2.76 (s, 1 H, O*H*), 2.71 (dd, $J$ = 5.0, 2.5 Hz, 1 H, epoxide), 2.07–1.30 (m, 5 H, C*H*$_2$, O*H*) 1.24 (s, 3 H, C*H*$_3$), 1.09 (s, 9 H, SiC(C*H*$_3$)$_3$); MS *m/e* (rel intensity) 577 (M + 1, 18), 519 (10), 441 (21), 393 (18), 367 (10), 333 (33), 303 (36), 263 (60), 235 (59), 199 (100), 135 (100); HRMS calcd for $C_{34}H_{45}O_6Si$ (M + 1) 577.2985, found 577.3013.

**5,9-Anhydro-7-*O*-benzyl-3,10-bis[*O*-(*tert*-butyldiphenylsilyl)]-1,2,4,8-tetradeoxy-6-*C*-methyl-D-*glycero*-L-*allo*-dec-1-enitol (22).** *tert*-Butyldiphenylsilyl chloride (8.25 g, 30.0 mmol) was added in one portion to a cooled (0 °C) and stirred solution of alcohol **21** (14.0 g, 25.0 mmol) and imidazole (3.4 g, 50.0 mmol) in dry DMF (50 mL) under an argon atmosphere. The reaction mixture was allowed to reach room temperature and was stirred for 16 h before dilution with methanol (20 mL) and ether (500 mL). The mixture was washed with aqueous saturated $NH_4Cl$ solution (300 mL), $H_2O$ (2 × 300 mL) and brine (200 mL) and then dried ($MgSO_4$). Concentration followed by flash column chromatography (silica, 20% ether in petroleum ether) gave compound **22** (17.56 g, 88%). **22**: oil; $R_f$ = 0.25 (silica, 30% ether in petroleum ether); $[\alpha]^{22}_D$ +34.33° (*c* 2.7, $CH_2Cl_2$); IR (neat) $\nu_{max}$ 3450 (m, OH), 3092, 3078, 3040, 2962, 2939, 2895, 2893, 1433, 1365, 1118, 927, 825, 742, 705, 680, 617 $cm^{-1}$; $^1H$ NMR (250 MHz, $CDCl_3$) $\delta$ 7.70–7.23 (m, 25 H, Ar), 5.93 (ddd, $J$ = 16.0, 11.0, 5.0 Hz, 1 H, C*H*=$CH_2$), 5.09 (m, 2 H, CH=C*H*$_2$), 4.65, 4.43 (2 × d, $J$ = 12.0 Hz, 2 × 1 H, benzylic), 4.22 (m, 1 H,

$CH_2$=CH—C*H*—O), 3.69 (dd, $J$ = 11.0, 3.0 Hz, 1 H, C*H*–O), 3.50 (m, 2 H, $CH_2$–O), 3.23 (dd, $J$ = 9.0, 5.0 Hz, 1 H, C*H*–O), 2.96 (m, 1 H, C*H*–O), 2.53 (s, 1 H, O*H*), 1.81–1.50 (m, 4 H, $CH_2$), 1.10 (s, 3 H, $CH_3$), 1.06, 1.03 (2 × s, 2 × 9 H, $SiC(CH_3)_3$); HRMS calcd for $C_{50}H_{62}O_5Si_2$ (M) 798.4220, found 798.4240.

**Methyl (*E*)-6,10-Anhydro-8-*O*-benzyl-4,11-bis[*O*-(*tert*-butyldiphenylsilyl)]-2,3,5,9-tetradeoxy-7-*C*-methyl-D-*glycero*-L-*allo*-undec-2-enonate (24).** The terminal olefin **22** (17.56 g, 22.0 mmol) was ozonized to the corresponding aldehyde by using the procedure described above for the conversion of **14** to its corresponding aldehyde. The crude aldehyde (**23**) so obtained (16.82 g, 19.6 mmol) was dissolved in dry benzene (50 mL), and methyl (triphenylphosphoranylidene)acetate (8.36 g, 25 mmol) was added at 25 °C. After stirring for 6 h, the solvent was removed, and the product was purified by flash column chromatography (silica, 30% ether in petroleum ether) furnishing pure **24** (14.98 g, 89% from **22**). **24**: oil; $R_f$ = 0.20 (silica, 30% ether in petroleum ether); $[\alpha]^{22}_D$ +14.5° (*c* 4.0, $CH_2Cl_2$); IR (neat) $\nu_{max}$ 3430 (m, OH), 3095, 3078, 3038, 2960, 2939, 2862, 1730 (s, COOMe), 1665 (m, CH=CHCOOMe), 1482, 1430, 1302, 1275, 916, 825, 723, 1302, 1275, 916, 825, 723, 705, 680, 616 $cm^{-1}$; $^1H$ NMR (250 MHz, $CDCl_3$) δ 7.70–7.24 (m, 25 H, Ar), 7.08 (dd, $J$ = 16.0, 5.0 Hz, 1 H, olefinic), 6.08 (d, $J$ = 16.0 Hz, 1 H, olefinic), 4.64, 4.42 (2 × d, $J$ = 12.0 Hz, 2 × 1 H, benzylic), 4.45 (m, 1 H, CH=CH—C*H*—O, 3.70 (m, 1 H, C*H*–O), 3.68 (s, 3 H, $COOCH_3$), 3.50 (d, $J$ = 5.0 Hz, 2 H, $CH_2$–O), 3.15 (dd, $J$ = 10.0, 5.0 Hz, 1 H, C*H*–O), 2.83 (m, 1 H, C*H*–O), 2.48 (s, 1 H, O*H*), 1.78–1.50 (m, 4 H, $CH_2$), 1.07, 1.03 (2 × s, 2 × 9 H, 2 × $SiC(CH_3)_3$), 1.05 (s, 3 H, $CH_3$); HRMS calcd for $C_{52}H_{65}O_7Si_2$ (M + 1) 857.428, found 857.423. Anal. Calcd for $C_{52}H_{64}O_7Si_2$: C, 72.86; H, 7.53. Found: C, 72.98; H, 7.64.

**Methyl 3,7:6,10-Dianhydro-8-*O*-benzyl-4,11-bis[*O*-(*tert*-butyldiphenylsilyl)]-2,5,9-trideoxy-7-*C*-methyl-D-*threo*-L-*allo*-undeconate (25).** Sodium hydride (0.4 g, 60% oil dispersion, 10.0 mmol) was added in one portion to a solution of hydroxy ester **24** (8.56 g, 10.0 mmol) in dry THF (50 mL) with cooling (0 °C) and stirring. The reaction mixture was stirred at 25 °C for 5 h and then was quenched with methanol (20 mL) and ether (300 mL). Washing with $H_2O$ (2 × 100 mL) and brine (100 mL) followed by drying ($MgSO_4$), concentration, and flash column chromatography (silica, 20% ether in petroleum ether) afforded bicyclic compound **25** (7.87 g, 92%). **25**: oil; $R_f$ = 0.45 (silica, 20% ether in petroleum ether); $[\alpha]^{22}_D$ +39.41° (*c* 2.4, $CH_2Cl_2$); IR (neat) $\nu_{max}$ 3083, 3064, 3030, 2951, 2931, 2882, 2855, 1750 (s, COOMe), 1471, 1427, 1278, 1100, 1060, 820, 738, 700, 675, 610 $cm^{-1}$; $^1H$ NMR (250 MHz, $CDCl_3$) δ 7.82–7.22 (m, 25 H, Ar), 4.75, 4.53 (2 × d, $J$ = 12.0 Hz, 2 × 1 H, benzylic), 4.17–3.97 (m, 3 H, C*H*–O), 3.80 (m, 1 H, C*H*–O), 3.72 (s, 3 H, $COOCH_3$), 3.52 (br s, 2 H, $CH_2$–O), 2.62 (br d, $J$ = 13.5 Hz, 1 H, $CH_2$–COOMe), 2.20 (dd, $J$ = 13.5, 10.0 Hz, 1 H, $CH_2$COOMe), 2.10–1.65 (m, 4 H, $CH_2$), 1.28 (s, 3 H, $CH_3$), 1.11, 1.09 (2 × s, 2 × 9 H, 2 × $SiC(CH_3)_3$); HRMS calcd for $C_{52}H_{65}O_7Si_2$ (M + 1) 857.428, found 857.423.

**5,9-Anhydro-7-*O*-benzyl-10-*O*-(*tert*-butyldiphenylsilyl)-1,2,4,8-tetradeoxy-6-*C*-methyl-3-*O*-(trimethylsilyl)-D-*glycero*-L-*altro*-dec-1-enitol (26).** 1-(Trimethylsilyl)imidazole (1.54 g, 11.0 mmol) was added dropwise to a solution of alcohol **20** (5.6 g, 10.0 mmol) in $CH_2Cl_2$ (50 mL) at 0 °C. After stirring for 10 min, the reaction mixture was diluted with methanol (5.0 mL) and ether (300 mL). Washing with $H_2O$ (2 × 100 mL) and brine (100 mL) followed by drying ($MgSO_4$), concentration, and flash column chromatography (silica, 30% ether in petroleum ether) gave compound **26** (5.37 g, 85%). **26**: oil; $R_f$ = 0.24 (silica, 30% ether in petroleum ether); $[\alpha]^{23}_D$ +51.13° (*c* 1.9 $CH_2Cl_2$); IR (neat) $\nu_{max}$ 3460 (m, OH), 3095, 3080, 3040, 2962, 2938, 2862, 1432, 1365, 1250, 1118, 1032, 925, 850, 733, 705, 681, 617 $cm^{-1}$; $^1H$ NMR (250 MHz, $CDCl_3$) δ 7.67–7.30 (m, 15 H, Ar), 5.83 (ddd, $J$ = 16.0, 10.0, 5.0 Hz, 1 H, C*H*=$CH_2$), 5.15 (d, $J$ = 16.0 Hz, 1 H, CH=C*H*$_2$), 5.01 (d, $J$ = 10.0 Hz, 1 H, CH=C*H*$_2$), 4.74, 4.46 (2 × d, $J$ = 12.0 Hz, 2 × 1 H, benzylic), 4.19 (m, 1 H, $CH_2$=CH—C*H*—O), 3.90, 3.43 (m, 5 H, C*H*–O, $CH_2$–O), 2.64 (s, 1 H, O*H*), 1.94 (m, 2 H, $CH_2$), 1.59 (m, 2 H, $CH_2$), 1.19 (s, 3 H, $CH_3$), 1.04 (s, 9 H, $SiC(CH_3)_3$), 0.01 (s, 9 H, –$SiC(CH_3)_3$); MS *m/e* (rel intensity) 633 (M + 1, 51), 615 (92), 543 (33), 507 (52), 465 (54), 357 (69), 317 (68), 263 (100), 207 (100), 135 (100), 92 (100); HRMS calcd for $C_{37}H_{53}O_5Si$ (M + 1) 633.3432, found 633.3410.

**Methyl (*E*)-6,10-Anhydro-8-*O*-benzyl-11-*O*-(*tert*-butyldiphenylsilyl)-2,3,5,9-tetradeoxy-7-*C*-methyl-4-*O*-(trimethylsilyl)-D-*glycero*-L-*altro*-undec-2-enonate (28).** The α,β-unsaturated ester **28** was prepared from terminal olefin **26** (15.38 g, 24.32 mmol) by the same procedure used to convert **22** to **24** described above. Flash column chromatography (silica, 30% ether in petroleum ether) afforded pure **28** (14.27 g, 85%). **28**: oil; $R_f$ = 0.20 (silica, 30% ether in petroleum ether); $[\alpha]^{22}_D$ +44.34° (*c* 1.8, $CH_2Cl_2$); IR (neat) $\nu_{max}$ 3450 (m, OH), 3084, 3066, 3030, 2848, 2928, 2858, 1725 (s, COOMe), 1658 (m, CH=CHCOOMe), 1478, 1427, 1250, 1165, 1108, 1026, 972, 840, 748, 701, 675, 611 $cm^{-1}$; $^1H$ NMR (250 MHz, $CDCl_3$) δ 7.68–7.32 (m, 15 H, Ar), 6.92 (dd, $J$ = 16.0, 5.0 Hz, 1 H, olefinic), 5.96 (dd, $J$ = 16.0, 1.0 Hz, 1 H, olefinic), 4.73, 4.54 (2 × d, $J$ = 12.0 Hz, 2 × 11 H, benzylic), 4.34 (m, 1 H, CH=CH—C*H*—O), 3.88–3.42 (m, 5 H, C*H*–O, $CH_2$–O), 2.61 (s, 1 H, O*H*), 1.94 (m, 2 H, $CH_2$), 1.60 (m, 2 H, $CH_2$), 1.16 (s, 3 H, $CH_3$), 1.06 (s, 9 H, $SiC(CH_3)_3$), 0.02 (s, 9 H, $Si(CH_3)_3$); MS *m/e* (rel intensity) 691 (M + 1, 24), 633 (61), 565 (9), 525 (23), 435 (16), 375 (21), 241 (46), 187 (100), 135 (62), 91 (100); HRMS calcd for $C_{39}H_{55}O_7Si_2$ (M + 1) 691.3486, found 691.3461.

**Methyl 3,7:6,10-Dianhydro-8-*O*-benzyl-11-*O*-(*tert*-butyldiphenylsilyl)-2,5,9-trideoxy-7-*C*-methyl-4-*O*-(trimethylsilyl)-D-*threo*-L-*gluco*-undeconate (29).** The preparation of **29** from **28** (14.27 g, 20.68 mmol) was carried out as described above for the conversion of **24** to **25**. After flash column chromatography (silica, 20% ether in petroleum ether) the cyclized product **29** (10.27 g, 72%) was obtained. **29**: oil; $R_f$ = 0.31 (silica, 20% ether in petroleum ether); $[\alpha]^{22}_D$ +39.00° (*c* 2.5, $CH_2Cl_2$); IR (neat) $\nu_{max}$ 3096, 3078, 3040, 2960, 2900, 2862, 1745 (s, COOMe), 1432, 1300, 1255, 1120, 1071, 845, 742, 705, 681, 613 $cm^{-1}$; $^1H$ NMR (250 MHz, $CDCl_3$) δ 7.68–7.24 (m, 15 H, Ar), 4.98, 4.53 (2 × d, $J$ = 12.0 Hz, 2 × 1 H, benzylic), 4.57 (m, 1 H, TMSOC*H*, equatorial), 4.17–3.54 (m, 6 H, C*H*–O, $CH_2$–O), 3.70 (s, 3 H, $COOCH_3$), 2.58 (m, 2 H, $CH_2COOCH_3$), 2.20–1.77 (m, 4 H, $CH_2$), 1.28 (s, 3 H, $CH_3$), 1.04 (s, 9 H, $SiC(CH_3)_3$), 0.09 (s, 9 H, $SiC(CH_3)_3$); MS *m/e* (rel intensity) 691 (M + 1, 20), 659 (9), 525 (100), 465 (35), 435 (100), 375 (11), 331 (13), 259 (100), 207 (100), 141 (100), 91 (100); HRMS calcd for $C_{39}H_{55}O_7Si_2$ (M + 1) 691.3486, found 691.3567.

**Methl 3,7:6,10-Anhydro-8-*O*-benzyl-11-*O*-(*tert*-butyldiphenylsilyl)-2,5,9-trideoxy-7-*C*-methyl-D-*glycero*-L-*allo*-4-undeculosonate (30).** Jones' reagent (15 mL of a solution prepared from 11.1 g of $CrO_3$, 9.7 mL of concentrated $H_2SO_4$, and 25 mL of $H_2O$) was added dropwise to a cold (0 °C) and stirred solution of compound **29** (6.9 g, 10.0 mmol) in acetone (50 mL). After stirring at 0 °C for 30 min, the reaction mixture was quenched with isopropyl alcohol (10 mL) and then was diluted with ether (500 mL). Washing with $H_2O$ (2 × 100 mL) and brine (100 mL) followed by drying ($MgSO_4$), evaporation, and flash column chromatography (silica, 20% ether in petroleum ether) gave ketone **30** (4.25 g, 69%). **30**: oil; $R_f$ = 0.32 (silica, 40% ether in petroleum ether); $[\alpha]^{21}_D$ +35.85° (*c* 1.4, $CH_2Cl_2$); IR (neat) $\nu_{max}$ 3091, 3075, 3038, 2958, 2938, 2890, 2861, 1748 (s, COOMe), 1730 (s, CO), 1430, 1355, 1280, 1178, 1118, 825, 752, 705, 680, 618 $cm^{-1}$; $^1H$ NMR (250 MHz, $CDCl_3$) δ 7.72–7.24 (m, 15 H, Ar), 4.78, 4.58 (2 × d, $J$ = 12.0 Hz, 2 × 1 H, benzylic), 4.43–3.66 (m, 6 H, C*H*–O, $CH_2$–O), 3.60 (s, 3 H, $COOCH_3$), 2.88 (d, $J$ = 5.0 Hz, 2 H, $CH_2$–CO), 2.80 (dd, $J$ = 16.0, 5.0 Hz, 1 H, $CH_2$–CO), 2.50 (dd, $J$ = 16.0, 12.0 Hz, 1 H, $CH_2$–CO), 2.14 (m, 2 H, $CH_2$), 1.39 (s, 3 H, $CH_3$), 1.12 (s, 9 H, $SiC(CH_3)_3$); MS *m/e* (rel intensity) 634 (M + $NH_4$, 9), 559 (34), 451 (38), 391 (11), 361 (15), 275 (45), 241 (42), 207 (100), 168 (53), 135 (32), 91 (100); HRMS calcd for $C_{36}H_{48}O_7SiN$ (N + $NH_4$) 634.3200, found 634.3254.

**Methyl 3,7:6,10-Anhydro-8-*O*-benzyl-11-*O*-(*tert*-butyldiphenylsilyl)-2,5,9-trideoxy-7-*C*-methyl-D-*threo*-L-*allo*-undeculosonate (31).** Sodium borohydride (0.38 g, 10.0 mmol) was added in one portion to a cold (0 °C) stirred solution of ketone **30** (6.16 g, 10.0 mmol) in absolute methanol (50 mL). Upon completion (~10 min) the reaction mixture was diluted with ether (500 mL) and then washed with aqueous saturated $NH_4Cl$ solution (2 × 100 mL), $H_2O$ (2 × 100 mL), and brine (100 mL). Drying ($MgSO_4$), concentration, and flash column chromatography (silica, 40% ether in petroleum ether) gave pure **31** (5.25 g, 85%). **31**: oil; $R_f$ = 0.25 (silica, 60% ether in petroleum ether); $[\alpha]^{21}_D$ +55.81° (*c* 2.7, $CH_2Cl_2$); IR (neat) $\nu_{max}$ 3440 (s, OH), 3086, 3068, 3030, 2950, 2886, 2881, 1750 (s, COOMe), 1428, 1110, 1050, 1000, 820, 728, 700, 678, 611 $cm^{-1}$; $^1H$ NMR (250 MHz, $CDCl_3$) δ 7.76–7.28 (m, 15 H, Ar), 4.80, 4.57 (2 × d, $J$ = 12.0 Hz, 2 × 1 H, benzylic), 4.23–3.33 (m, 7 H, C*H*–O, $CH_2$–O), 2.84 (dd, $J$ = 15.5, 4.5 Hz, 1 H, $CH_2$–CO), 2.50 (dd, $J$ = 15.5, 7.4 Hz, 1 H, $CH_2$–CO), 2.47 (br s, 1 H, O*H*), 2.07 (m, 3 H, $CH_2$), 1.64 (m, 1 H, $CH_2$), 1.14 (s, 9 H, $SiC(CH_3)_3$); MS *m/e* (rel intensity) 636 (M + $NH_4$, 6), 561 (7), 453 (18), 393 (10), 361 (5), 241 (25), 207 (68), 168 (25), 141 (22), 91 (100); HRMS calcd for $C_{36}H_{50}O_7SiN$ (M + $NH_4$) 636.3357, found 636.3381.

**Silylation of 31 to 25.** The silylation of **31** (3.2 g, 5.0 mmol) to compound **25** was performed exactly in the same manner as that of **21** to **22** described above. After flash column chromatography (silica, 20% ether in petroleum ether), pure **25** (3.8 g, 89%) exhibited identical chromatographic and spectroscopic properties as described above.

**Methyl (*E*)-5,9:8,12-Dianhydro-10-*O*-benzyl-6,13-bis[*O*-(*tert*-butyldiphenylsilyl)]-2,3,4,7,11-pentadeoxy-9-*C*-methyl-D-*threo*-L-*allo*-tridec-2-enonate (33).** DIBAL (15.0 mL, 1 M solution in $CH_2Cl_2$, 15.0 mmol) was dropwise added to a cold (−78 °C) and stirred solution of ester **25** (8.56 g, 10.0 mmol) in dry $CH_2Cl_2$ (50 mL) under argon. After stirring at −78 °C for 15 min, the reaction mixture was quenched with methanol (20 mL), diluted with ethyl acetate (500 mL), and washed with aqueous

saturated potassium sodium tartrate solution (2 × 200 mL), $H_2O$ (200 mL), and brine (100 mL). Drying ($MgSO_4$) followed by filtration and concentration gave crude aldehyde **32** (8.20 g), which was condensed directly with methyl (triphenylphosphoranylidene)acetate (4.35 g, 12 mmol) according to the procedure described above for the preparation of **24** from **23**. After flash chromatography, the α,β-unsaturated ester **33** (6.62 g, 75% overall from **25**) was obtained. **33**: oil; $R_f$ = 0.68 (silica, 30% ether in petroleum ether); $[\alpha]^{23}_D$ +40.85° (*c* 1.7, $CH_2Cl_2$); IR (neat) $\nu_{max}$ 3100, 3080, 3042, 3004, 2960, 2941, 2900, 2864, 1730 (s, COOMe), 1662 (s, CH=CHCOOMe), 1482, 1431, 1278, 1112, 828, 742, 705, 680, 615 $cm^{-1}$; $^1H$ NMR (250 MHz, $CDCl_3$) δ 7.74–7.15 (m, 25 H, Ar), 6.95 (dd, *J* = 15.5, 6.5 Hz, 1 H, olefinic), 5.80 (d, *J* = 15.5 Hz, 1 H, olefinic), 4.70, 4.48 (2 × d, *J* = 12.0 Hz, 2 × 1 H, benzylic), 4.05–3.42 (m, 7 H, C*H*–O, $CH_2$–O), 3.72 (s, 3 H, $COOCH_3$), 2.70 (dd, *J* = 15.0, 6.5 Hz, 1 H, $CH_2$–CH=C), 2.14–1.62 (m, 5 H, $CH_2$), 1.22 (s, 3 H, $CH_3$), 1.07, 1.03 (2 × s, 2 × 9 H, 2 × $SiC(CH_3)_3$); HRMS calcd for $C_{54}H_{67}O_7Si_2$ (M + 1) 883.443, found 883.451.

**(*E*)-2,6:5,9-Dianhydro-4-*O*-benzyl-1,8-bis[*O*-(*tert*-butyldiphenylsilyl)]-3,7,10,11,12-pentadeoxy-5-*C*-methyl-D-*erythro*-L-*altro*-tridec-11-enitol (34).** DIBAL (22.0 mL, 1 M solution in $CH_2Cl_2$, 22.0 mmol) was added dropwise to a cold (−78 °C) and stirred solution of ester **33** (8.83 g, 10.0 mmol) in dry $CH_2Cl_2$ (50 mL) under argon. After stirring at −78 °C for 30 min, methanol (20 mL) was added, and the reaction mixture was worked up as described above for the DIBAL reduction of **25** to **32**. After flash column chromatography (silica, 40% ether in petroleum ether), pure compound **34** was obtained (7.51 g, 88%). **34**: oil; $R_f$ = 0.33 (silica, 50% ether in petroleum ether); $[\alpha]^{23}_D$ +28.00° (*c* 1.5, $CH_2Cl_2$); IR (neat) $\nu_{max}$ 3450 (s, OH), 3090, 3078, 3040, 3000, 2962, 2938, 2900, 2860, 1590, 1475, 1431, 1365, 1196, 1110, 1000, 827, 742, 710, 680, 615 $cm^{-1}$; $^1H$ NMR (250 MHz, $CDCl_3$) δ 7.75–7.18 (m, 25 H, Ar), 5.60 (m, 2 H, olefinic), 4.80, 4.54 (2 × d, *J* = 12.0 Hz, 2 × 1 H, benzylic), 4.11–3.50 (m, 7 H, C*H*–O, $CH_2$–O), 2.59 (br d, *J* = 15.5 Hz, 1 H, $CH_2$—CH=C), 2.25–1.68 (m, 5 H, $CH_2$), 1.28 (s, 3 H, $CH_3$), 1.13, 1.07 (2 × s, 2 × 9 H, 2 × $SiC(CH_3)_3$); HRMS calcd for $C_{53}H_{67}O_6Si_2$ (M + 1) 855.488, found 855.482. Anal. Calcd for $C_{53}H_{66}O_6Si_2$: C, 74.43; H, 7.78. Found: C, 74.32, H, 8.01.

**2,6:5,9:8,12-Trianhydro-10-*O*-benzyl-6,13-bis[*O*-(*tert*-butyldiphenylsilyl)]-4,7,11-trideoxy-9-*C*-methyl-D-*talo*-L-*altro*-tridecitol (35).** *m*-Chloroperoxybenzoic acid (mCPBA, 2.58 g, 85% pure, 12.0 mmol) was added in one portion to a cold (0 °C) and stirred solution of allylic alcohol **34** (8.54 g, 10.0 mmol) in $CH_2Cl_2$ (50 mL). After stirring for 30 min at 0 °C, the reaction mixture was quenched with $Me_2S$ (2 mL) followed by $Et_3N$ (2 mL). Evaporation of the solvents followed by flash column chromatography (silica, 40% ether in petroleum ether) gave epoxide **35** (7.40 g, 88%, mixture of two isomers, β:α ≥ 10:1 by $^1H$ NMR, ratio of signals at δ 4.50 and 4.45 for one of the benzylic protons). **35**: oil; $R_f$ = 0.30 (silica, 50% ether in petroleum ether); IR (neat) $\nu_{max}$ 3450 (m, OH), 3450, 3100, 3078, 3049, 2962, 2938, 2896, 2862, 1432, 1118, 828, 743, 709, 680, 615 $cm^{-1}$; $^1H$ NMR (250 MHz, $CDCl_3$) (signals corresponding to the major product **35**) δ 7.69–7.14 (m, 25 H, Ar), 4.69, 4.50 (2 × d, *J* = 12.0 Hz, 2 × 1 H, benzylic), 4.04–3.45 (m, 7 H, C*H*–O, $CH_2$–O), 2.99 (m, 1 H, epoxide), 2.89 (m, 1 H, epoxide), 2.08–1.60 (m, 6 H, $CH_2$), 1.22 (s, 3 H, $CH_3$), 1.04, 1.01 (2 × s, 2 × 9 H, 2 × $SiC(CH_3)_3$); HRMS calcd for $C_{53}H_{67}O_7Si_2$ (M + 1) 871.443, found 871.448.

**Methyl (*E*)-4,5:7,11:10,14-Trianhydro-12-*O*-benzyl-8,15-bis[*O*-(*tert*-butyldiphenylsilyl)]-2,3,6,9,13-pentadeoxy-11-*C*-methyl-D-*talo*-L-*altro*-pentadec-2-enonate (37).** Oxalyl chloride (1.31 mL, 15.0 mmol) was slowly added to a cold (−78 °C) and stirred solution of dimethyl sulfoxide (1.42 mL, 20.0 mmol) in dry $CH_2Cl_2$ (50 mL) under argon. After stirring for 10 min, the alcohol **35** (8.7 g, mixsture, ca. 10:1 β:α epoxide isomers, 10 mmol) in $CH_2Cl_2$ (10 mL) was dropwise added at −78 °C, and stirring was continued at that temperature for 1 h. Triethylamine (5.6 mL, 40 mmol) was then dropwise added at −78 °C and the reaction mixture was allowed to reach 0 °C, stirred for an additional 10 min and then poured onto a mixture of aqueous saturated $NH_4Cl$ solution (50 mL) and ether (300 mL). The organic phase was separated, washed with $H_2O$ (2 × 50 mL) and brine (30 mL), and dried ($MgSO_4$). The crude aldehyde **36** obtained after removal of the solvents was immediately reacted with methyl (triphenylphosphoranylidene)acetate (4.01 g, 12 mmol) in dry benzene (30 mL) at 25 °C (3 h) to afford, after removal of the solvent and flash column chromatography (silica, 50% ether in petroleum ether), compound **37** (6.65 g, 72% overall from **35**, ca. 10:1 mixture of β:α epoxide isomers). **37**: oil; $R_f$ = 0.5 (silica, 40% ether in petroleum ether); IR (neat) $\nu_{max}$ 3096, 3075, 3052, 3038, 2960, 2936, 2892, 2860, 1726 (s, COOMe), 1662 (m, CH=CHCOOMe), 1428, 1268, 1110, 823, 735, 700, 678, 609 $cm^{-1}$; $^1H$ NMR (250 MHz, $CDCl_3$) δ 7.70–7.10 (m, 25 H, Ar), 5.62 (dd, *J* = 15.0, 7.0 Hz, 1 H, olefinic), 6.10 (d, *J* = 15.0 Hz, 1 H, olefinic), 4.66, 4.49 (2 × d, *J* = 12.0 Hz, 2 × 1 H, benzylic), 4.02–3.44 (m, 7 H, C*H*–O, $CH_2$–O), 3.77 (s, 3 H, $COOCH_3$), 3.16 (br d, *J* = 7.0 Hz, 1 H, epoxide), 2.94 (m, 1 H, epoxide), 2.08–1.58 (m, 6 H, $CH_2$), 1.22 (s, 3 H, $CH_3$), 1.08, 1.02 (2 × s, 2 × 9 H, 2 × $SiC(CH_3)_3$); HRMS calcd for $C_{56}H_{69}O_8Si_2$ (M + 1) 925.454, found 925.458.

**Methyl (*E*)-4,5:7,11:10,14-Trianhydro-12-*O*-benzyl-8-hydroxy-15-*O*-(*tert*-butyldiphenylsilyl)-2,3,6,9,13-pentadeoxy-11-*C*-methyl-D-*talo*-L-*altro*-pentadec-2-enonate (38).** Tetra-*n*-butylammonium fluoride (12.0 mL, 1 M in THF, 12.0 mmol) was added to a solution of bissilyl ether **37** (9.24 g, mixture, ca. 10:1 β:α epoxide isomers, 10.0 mmol) in dry THF (50 mL) at 25 °C. After stirring for 3 h, the solvent was removed, and the residue was flashed chromatographed (silica, ethyl acetate) giving **38** (6.11 g, 89%) and the corresponding desilylated product (314 mg, 7%). **38**: oil; $R_f$ = 0.45 (silica, 80% ether in petroleum ether); IR (neat) $\nu_{max}$ 3450 (s, OH), 3058, 3047, 2960, 2937, 2862, 1732 (s, COOMe), 1665 (m, CH=CHCOOMe), 1432, 1310, 1269, 1192, 1115, 1048, 828, 740 706, 618 $cm^{-1}$; $^1H$ NMR (250 MHz, $CDCl_3$) δ 7.70–7.18 (m, 15 H, Ar), 6.58 (dd, *J* = 15.5, 6.5 Hz, 1 H, olefinic), 6.10 (d, *J* = 15.5 Hz, 1 H, olefinic), 4.72, 4.56 (2 × d, *J* = 12.5 Hz, 2 × 1 H, benzylic), 4.20–3.42 (m, 7 H, C*H*$_2$–O), 3.23 (dd, *J* = 6.5, 3.0 Hz, 1 H, epoxide), 2.98 (m, 1 H, epoxide), 2.16–1.48 (m, 6 H, $CH_2$), 1.22 (s, 3 H, $CH_3$), 1.08 (s, 9 H, $SiC(CH_3)_3$); HRMS calcd $C_{40}H_{50}O_8SiNa$ (*M* + Na) 709.3173, found 709.3134. The corresponding diol exhibited the following data: oil; $R_f$ = 0.20 (silica, ethyl acetate); IR (neat) $\nu_{max}$ 3430 (s, OH), 3092, 3060, 3036, 1725 (s, COOMe), 1662 (m, CH=CHCOOMe), 1440, 1350, 1311, 1268, 1200, 1110, 1048, 852, 742, 700 $cm^{-1}$; $^1H$ NMR (250 MHz, $CDCl_3$) δ 7.30 (m, 5 H, Ar), 6.57 (dd, *J* = 16.0, 7.0 Hz, 1 H, olefinic), 6.11 (d, *J* = 16.0 Hz, 1 H, olefinic), 4.85, 4.63 (2 × d, *J* = 12.0 Hz, 2 × 1 H, benzylic), 4.30–3.44 (m, 7 H, C*H*–O, $CH_2$–O), 3.78 (s, 3 H, $COOCH_3$), 3.26 (br d, *J* = 7.0 Hz, epoxide), 3.06 (m, 1 H, epoxide), 2.69 (br s, 2 H, O*H*), 2.28–1.58 (m, 6 H, $CH_2$), 1.32 (s, 3 H, $CH_3$); MS *m/e* (rel intensity): 449 (M + 1, 38); 417 (8), 324 (100), 293 (12), 255 (28), 225 (21), 199 (83), 169 (44), 141 (70), 92 (100); HRMS calcd for $C_{24}H_{33}O_8$ (M + 1) 449.2175, found 449.2163. Anal. Calcd for $C_{24}H_{32}O_8$: C, 64.27; H, 7.19. Found: C, 64.08; H, 7.52.

**Methyl (*E*)-4,8:7,11:10,14-Trianhydro-12-*O*-benzyl-15-*O*-(*tert*-butyldiphenylsilyl)-2,3,6,9,13-pentadeoxy-11-*C*-methyl-D-*talo*-L-*allo*-pentadec-2-enonate (39).** Camphorsulfonic acid (464 mg, 2 mmol) was added portionwise to a cold (0 °C) and stirred solution of epoxide alcohol **38** (6.86 g, 10 mmol, mixture, ca. 10:1 β:α epoxide isomers) in dry $CH_2Cl_2$ (100 mL). The reaction mixture was allowed to reach room temperature, and stirring was continued until completion (ca. 3 h) before quenching with triethylamine (1 mL). The solution was diluted with $CH_2Cl_2$ (150 mL), washed with $H_2O$ (50 mL) and brine (50 mL), and then dried ($MgSO_4$). Removal of the solvent followed by flash column chromatography (silica, ether) gave the pure cyclized product **39** (4.80 g, 70%, single isomer, only β epoxide cyclized). **39**: oil; $R_f$ = 0.40 (silica, 70% ether in petroleum ether); $[\alpha]^{22}_D$ +28.00° (*c* 8.0, $CH_2Cl_2$); IR (neat) $\nu_{max}$ 3450 (s, OH), 3092, 3075, 3038, 3000, 2962, 2938, 2894, 2860, 1730 (s, COOMe), 1665 (m, CH=CHCOOMe), 1483, 1432, 1310, 1116, 829, 746, 706, 680 $cm^{-1}$; $^1H$ NMR (250 MHz, $CDCl_3$) δ 7.68–7.25 (m, 15 H, Ar), 7.08 (dd, *J* = 16.0, 5.0 Hz, 1 H, olefinic), 6.18 (dd, *J* = 16.0, 1.0 Hz, 1 H, olefinic), 4.75, 4.54 (2 × d, *J* = 12.0 Hz, 2 × 1 H, benzylic), 4.22–3.85 (m, 9 H, C*H*–O, $CH_2$–O), 3.76 (s, 3 H, $COOCH_3$), 2.50 (br s, 1 H, OH), 2.36–1.40 (m, 6 H, $CH_2$), 1.27 (s, 3 H, $CH_3$), 1.05 (s, 9 H, $SiC(CH_3)_3$); HRMS calcd for $C_{40}H_{50}O_8SiNa$ (M + Na) 709.3173, found 709.3195.

**(*E*)-4,8:7,11:10,14-Trianhydro-1,5-dihydroxy-12-*O*-benzyl-15-*O*-(*tert*-butyldiphenylsilyl)-2,3,6,9,13-pentadeoxy-11-*C*-methyl-D-*talo*-L-*allo*-pentadec-2-enitol (40).** DIBAL (0.7 mL, 1 M in hexane, 0.7 mmol) was added dropwise to a solution of compound **39** (137 mg, 0.2 mmol) in dry $CH_2Cl_2$ (2 mL) and −78 °C. The reaction mixture was stirred for 10 min at that temperature before dilution with methanol (1 mL) and ethyl acetate (20 mL). The mixture was washed with potassium sodium tartrate (2 × 4 mL), $H_2O$ (2 × 5 mL), and brine (5 mL) and then dried ($MgSO_4$). Concentration followed by flash column chromatography (silica, ether) gave diol **40** (125 mg, 95%). **40**: oil, $R_f$ = 0.52 (silica, ethyl acetate); $[\alpha]^{23}_D$ +32.41° (*c* 3.2, $CH_2Cl_2$); IR (neat) $\nu_{max}$ 3368 (s, OH), 3072, 3051, 2956, 2929, 2860, 1468, 1430, 1268, 1110, 1051, 1008, 827, 740, 705, 617 $cm^{-1}$; $^1H$ NMR (250 MHz, $CDCl_3$) δ 7.70–7.23 (m, 15 H, Ar), 6.04 (ddd, *J* = 16.0, 5.0, 5.0 Hz, 1 H, =C*H*—$CH_2$—O), 5.73 (dd, *J* = 16.0, 6.0 Hz, 1 H, =C*H*—$CH_2$—O), 4.75, 4.54 (2 × d, *J* = 12.5 Hz, 2 × 1 H, benzylic), 4.20–2.86 (m, 11 H, C*H*–O, $CH_2$–O), 2.75 (br s, 1 H, O*H*), 2.46 (br s, 1 H, OH), 2.18–1.38 (m, 6 H, $CH_2$), 1.24 (s, 3 H, $CH_3$), 1.04 (s, 9 H, $SiC(CH_3)_3$); MS *m/e* (rel intensity): 659 (M + 1, 7), 641 (20), 601 (100), 565 (14), 523 (18), 493 (100), 433 (100), 397 (66), 319 (35), 241 (100), 207 (100), 163 (60), 135 (55); HRMS calcd for $C_{39}H_{51}O_7Si$ (M + 1) 659.3404, found 659.3480.

**(*E*)-4,8:7,11:10,14-Trianhydro-1,5,15-trihydroxy-12-*O*-benzyl-2,3,6,9,13-pentadeoxy-11-*C*-methyl-D-*talo*-L-*allo*-pentadec-2-enitol (41).** Tetra-*n*-butylammonium fluoride (0.15 mL, 1 M in THF, 0.15 mmol)

was added into a solution of compound **40** (66 mg, 0.01 mmol) in THF (2 mL) at 25 °C. The reaction mixture was stirred for 6 h at that temperature, and then the solvent was removed under vacuum followed by flash column chromatography (silica, 5% methanol in ethyl acetate) giving triol **41** (42 mg, 100%). **41**: oil; $R_f$ = 0.35 (silica, 5% methanol in ethyl acetate); $[\alpha]^{23}_D$ +39.48° (*c* 2.7, $CH_2Cl_2$); IR (neat) $\nu_{max}$ 3400 (s, OH), 3061, 3024, 2940, 2878, 1642, 1452, 1381, 1350, 1275, 1208, 1131, 1048, 908, 735, 695, 647 $cm^{-1}$; $^1H$ NMR (250 MHz, $CDCl_3$) $\delta$ 7.36 (m, 5 H, Ar), 6.02 (ddd, *J* = 15.5, 4.5, 4.5 Hz, 1 H, olefinic), 5.71 (dd, *J* = 15.5, 5.0 Hz, 1 H, olefinic), 4.86, 4.57 (2 × d, *J* = 12.5 Hz, 2 × 1 H, benzylic), 4.28–3.05 (m, 11 H, C*H*–O, $CH_2$–O), 2.75–1.42 (m, 9 H, $CH_2$, O*H*), 1.28 (s, 3 H, $CH_3$); MS *m/e* (rel intensity) 421 (M + 1, 12), 315 (35), 297 (16), 279 (8), 242 (7), 207 (24), 171 (23), 142 (100), 127 (25); HRMS calcd for $C_{23}H_{33}O_7$ (M + 1) 421.2226, found 421.2216.

**(*E*)-4,8:7,11:10,14-Trianhydro-12-*O*-benzyl-2,3,6,9,13-pentadeoxy-11-*C*-methyl-D-*talo*-L-*allo*-pentadec-2-ene 1,5,15-Tris(*p*-bromobenzoate) (42).** To a cold (0 °C) stirred solution of compound **41** (42 mg, 0.1 mmol) and 4-(dimethylamino)pyridine (40 mg, 0.33 mmol) in dry $CH_2Cl_2$ (2 mL) was added 4-bromobenzoyl chloride (66 mg, 0.3 mmol) in one portion. The reaction mixture was stirred at that temperature for 30 min before dilution with methanol (1 mL) and ether (15 mL). The mixture was washed with $H_2O$ (2 × 5 mL) and brine (5 mL) and then dried ($MgSO_4$). Concentration followed by flash column chromatography (silica, 30% ether in petroleum ether) gave tribenzoate **42** (89 mg, 92%). **42**: crystalline solid; mp 175–177 °C (from ether, hexane); $R_f$ = 0.50 (silica, 50% ether in petroleum ether); $[\alpha]^{23}_D$ +93.39° (*c*, 6.9, $CH_2Cl_2$); IR ($CH_2Cl_2$) $\nu_{max}$ 3092, 3065, 3037, 2958, 2882, 1760 (s, benzoate), 1751 (s, benzoate), 1592, 1487, 1400, 1271, 1177, 1103, 1014, 911, 849, 757, 733, 685, 650, 609 $cm^{-1}$; $^1H$ NMR (250 MHz, $CDCl_3$) $\delta$ 7.96–7.25 (m, 17 H, Ar), 6.04 (ddd, *J* = 16.0, 5.0, 5.0 Hz, 1 H, olefinic), 5.84 (dd, *J* = 16.0, 5.0 Hz, 1 H, olefinic), 5.36–3.24 (m, 11 H, C*H*–O, $CH_2$–O), 2.58–1.58 (m, 6 H, $CH_2$), 1.29 (s, 3 H, $CH_3$); HRMS calcd for $C_{44}H_{42}O_{10}Br_3$ (M + 1): 967.0328, found 967.0366.

**2,6:5,9:8,12-Trianhydro-4-*O*-benzyl-1-*O*-(*tert*-butyldiphenylsilyl)-3,7,10-trideoxy-5-*C*-methyl-D-*allo*-D-*altro*-tridecitol (43).** Ozone was passed through a cold (−78 °C) solution of the $\alpha,\beta$-unsaturated ester **39** (1.37 g, 2.0 mmol) in $CH_2Cl_2$ (30 mL) until a blue coloration persisted. The excess of ozone was removed with a stream of oxygen and then $Me_2S$ (1 mL) and $Ph_3P$) 525 mg, 2.0 mmol) were sequentially added. The reaction mixture was allowed to reach room temperature with stirring and then treated with methanol (10 mL) and $NaBH_4$ (304 mg, 8.0 mmol). After stirring at room temperature for 1 h, the reaction mixture was diluted with ethyl acetate (200 mL), washed with aqueous saturated $NH_4Cl$ solution (2 × 50 mL), $H_2O$ (2 × 50 mL), and brine (50 mL), and then dried ($MgSO_4$). Solvent removal followed by flash column chromatography (silica, ethyl acetate) gave pure diol **43** (1.20 g, 95%). **43**: oil; $R_f$ = 0.62 (silica, ethyl acetate); $[\alpha]^{22}_D$ +39.91° (*c* 2.3, $CH_2Cl_2$); IR (neat) $\nu_{max}$ 3410 (s, OH), 3092, 3078, 3039, 2940, 2884, 2860, 1483, 1432, 1100, 1050, 827, 742, 705, 680, 615 $cm^{-1}$; $^1H$ NMR (250 MHz, $CDCl_3$) $\delta$ 7.79–7.25 (m, 15 H, Ar), 4.75, 4.52 (2 × d, *J* = 12.0 Hz, 2 × 1 H, benzylic), 4.20–2.84 (m, 11 H, C*H*–O, $CH_2$–O), 2.33–1.10 (m, 8 H, $CH_2$, O*H*), 1.26 (s, 3 H, $CH_3$), 1.08 (s, 9 H, $SiC(CH_3)_3$); MS *m/e* (rel intensity) 575 (M − $C(CH_3)_3$, 100), 545 (10), 497 (16), 467 (72), 407 (100), 359 (24), 331 (19), 241 (100), 207 (100), 163 (58), 135 (52); HRMS calcd for $C_{33}H_{39}O_7Si$ (M − $C(CH_3)_3$) 575.2465, found 575.2441.

**2,6:5,9:8,12-Trianhydro-4-*O*-benzyl-13-*O*-(*tert*-butyldimethylsilyl)-1-*O*-(*tert*-butyldiphenylsilyl)-3,7,10-trideoxy-5-*C*-methyl-D-*allo*-D-*altro*-tridecitol (44).** *tert*-Butyldimethylsilyl chloride (331 mg, 2.2 mmol) was added in one portion to a cold (0 °C) and stirred solution of imidazole (204 mg, 3.0 mmol) and diol **43** (1.26, 2.0 mmol) in dry DMF (7 mL). After stirring at 0 °C for 30 min, the reaction mixture was quenched with methanol (1 mL), diluted with ether (30 mL), and washed with aqueous saturated $NH_4Cl$ solution (2 × 5 mL), $H_2O$ (2 × 5 mL), and brine (5 mL). Drying ($MgSO_4$) followed by concentration and flash column chromatography (silica, 50% ether in petroleum ether) gave compound **44** (1.36 g, 91%). **44**: oil; $R_f$ = 0.45 (silica, 50% ether in petroleum ether); $[\alpha]^{22}_D$ +28.42° (*c* 2.4, $CH_2Cl_2$); IR (neat) $\nu_{max}$ 3450 (s, OH), 3072, 3050, 3028, 2930, 2882, 2857, 1464, 1430, 1255, 1118, 1070, 910, 838, 780, 735, 702, 616 $cm^{-1}$; $^1H$ NMR (250 MHz, $CDCl_3$) $\delta$ 7.69–7.26 (m, 15 H, Ar), 4.77, 4.54 (2 × d, *J* = 12.0 Hz, 2 × 1 H, benzylic), 4.21–2.83 (m, 11 H, C*H*–O, $CH_2$–O), 2.35–1.37 (m, 7 H, $CH_2$, O*H*), 1.25 (s, 3 H, $CH_3$), 1.09, 0.95 (2 × s, 2 × 9 -, 2 × $SiC(CH_3)_3$), 0.09 (s, 6 H, $Si(CH_3)_2$); HRMS calcd for $C_{43}H_{63}O_7Si_2$ (M + 1) 747.4112, found 747.4082.

**2,6:5,9:8,12-Trianhydro-10-*O*-benzyl-1-*O*-(*tert*-butyldimethylsilyl)-13-*O*-(*tert*-butyldiphenylsilyl)-4,7,11-trideoxy-9-*C*-methyl-D-*threo*-L-*allo*-L-*glycero*-3-trideculose (45).** The oxidation of alcohol **44** to ketone **45** was carried out in exactly the same way as described above for the oxidation of compound **12** to **13**. Thus, **44** (1.49 g, 2.0 mmol) gave, after flash column chromatography (silica, 20% ether in petroleum ether) ketone **45** (1.46 g, 98%). **45**: oil; $R_f$ = 0.75 (silica, 40% ether in petroleum ether; $[\alpha]^{22}_D$ +33.63° (*c* 3.0, $CH_2Cl_2$); IR (neat) $\nu_{max}$ 3092, 3078, 3038, 2960, 2936, 2884, 2861, 1730 (s, CO), 1432, 1358, 1358, 1116, 1070, 840, 782, 705, 682, 618 $cm^{-1}$; $^1H$ NMR (250 MHz, $CDCl_3$) $\delta$ 7.70–7.20 (m, 15 H, Ar), 4.70, 4.55 (2 × d, *J* = 12.0 Hz, 2 × 1 H, benzylic), 4.24–3.13 (m, 10 H, C*H*–O), 2.80 (dd, *J* = 16.0, 5.0 Hz, 1 H, $CH_2$–CO), 2.26 (dd, *J* = 16.0, 11.0 Hz, 1 H, $CH_2$–CO), 2.12–1.35 (m, 4 H, $CH_2$), 1.28 (s, 3 H, $CH_3$), 1.05, 0.92 (2 × s, 2 × 9 H, 2 × $SiC(CH_3)_3$), 0.09, 0.08 (2 × s, 2 × 3 H, $Si(CH_3)_2$); HRMS calcd for $C_{43}H_{61}O_7Si_2$ (M + 1) 745.3956, found 745.3904.

**2,6:5,9:8,12-Trianhydro-10-*O*-benzyl-10-*O*-(*tert*-butyldiphenylsilyl)-4,7,11-trideoxy-9-*C*-methyl-D-*threo*-L-*allo*-L-*glycero*-3-trideculose Diethyl Mercaptole (47).** Zinc triflate ($Zn(OTf)_2$, 726 mg, 2.0 mmol) was added in one portion to a cold (0 °C) and stirred solution of the ketone **45** (1.49 g, 2.0 mmol) and EtSH (2 mL) in dry $CH_2Cl_2$ (10 mL). The cooling was stopped and stirring was continued for 30 min (completion of thioketalization by TLC) before addition of methanol (5 mL) and CSA (100 mg). Monodesilylation was complete in 15 min (TLC), at which time $Et_3N$ (1 mL) was added and the reaction mixture was diluted with ether (100 mL). Washing of the reaction mixture with water (2 × 20 mL) and brine (20 mL) followed by drying, concentration, and flash column chromatography (silica, 50% ether in petroleum ether) gave the hydroxy dithio ketal **47** (1.16 g, 78%). **47**: oil; $R_f$ = 0.42 (silica, 50% ether in petroleum ether); $[\alpha]^{22}_D$ +41.33° (*c* 2.7, $CH_2Cl_2$); IR (neat) $\nu_{max}$ $\delta$ 3480 (s, OH), 3082, 3063, 3050, 2980, 2851, 2875, 1462, 1121, 1070, 917, 741, 713, 622 $cm^{-1}$; $^1H$ NMR (250 MHz, $CDCl_3$) $\delta$ 7.69–7.22 (m, 15 H, Ar), 4.74, 4.54 (2 × d, *J* = 12.0 Hz, 2 × 1 H, benzylic), 4.23–2.85 (m, 10 H, C*H*–O, $CH_2$–O), 2.84 (m, 4 H, 2 × $SCH_3CH_3$), 2.33, 1.60 (multiplets, 6 H, $CH_2$), 1.29 (s, 3 H, $CH_3$), 1.27 (m, 6 H, 2 × $SCH_2CH_3$), 1.09 (s, 9 H, $SiC(CH_3)_3$); HRMS calcd for $C_{39}H_{51}O_6SiS$ (M − $SC_2H_5$) 675.3176, found 675.3138. Anal. Calcd for $C_{40}H_{56}O_6SiS_2$: C, 66.80; H, 7.66. Found: C, 66.96; H, 7.74.

**2,6:5,9:8,12-Trianhydro-10-*O*-benzyl-10-*O*-(*tert*-butyldiphenylsilyl)-4,7,11-trideoxy-9-*C*-methyl-1-aldehyde-D-*threo*-L-*allo*-L-*glycero*-3-trideculose Diethyl Mercaptole (1).** The hydroxy dithio ketal **47** (1.47 g, 2.0 mmol) was dissolved in dry $CH_2Cl_2$ (10 mL) and DMSO (10 mL) and cooled to 0 °C. Triethylamine (1.39 mL, 10 mmol) and $SO_3$·pyr complex (1.59 g, 10 mmol) were successively added at 0 °C with stirring, and the reaction was allowed to proceed at that temperature. Upon completion of the reaction (1.5 h, TLC), the reaction mixture was poured onto saturated $NH_4Cl$ solution (10 mL) and extracted with ether (100 mL). The organic phase was washed with saturated $NH_4Cl$ solution (10 mL), $H_2O$ (10 mL), and brine (10 mL) before drying ($MgSO_4$) and evaporation. The same oxidation (**47** → **1**) was carried out with similar results using Swern conditions as described above for the oxidation of **34** to the corresponding aldehyde. Flash column chromatography (silica, 30% ether in petroleum ether) of the crude product furnished pure aldehyde **1** (1.22 g, 83%). **1**: oil; $R_f$ = 0.30 (silica, 30% ether in petroleum ether); $[\alpha]^{20}_D$ +50.21° (*c* 2.0, $CH_2Cl_2$); IR (neat) $\nu_{max}$ 3082, 3040, 2958, 2922, 2850, 1738 (s, CHO), 1451, 1428, 1368, 1265, 1112, 1064, 822, 736, 700, 612 $cm^{-1}$; $^1H$ NMR (250 MHz, $CDCl_3$) $\delta$ 9.76 (s, 1 H, CHO), 7.70–7.20 (m, 15 H, Ar), 4.70, 4.56 (2 × d, *J* = 12.5 Hz, 2 × 1 H, benzylic), 4.20–3.77 (m, 5 H, CH–O, $CH_2$–O), 4.07 (s, 1 H, OCH–C(O)H), 3.55 (m, 1 H, CH–O), 2.94 (m, 1 H, CH–O), 2.70 (m, 4 H, 2 × $SCH_2CH_3$), 2.38–1.59 (m, 6 H, $CH_2$), 1.29 (s, 3 H, $CH_3$), 1.27 (m, 6 H, 2 × $SCH_2CH_3$), 1.04 (s, 9 H, $SiC(CH_3)_3$); HRMS calcd for $C_{41}H_{55}O_6SiS_2$ (M + 1) 735.3209, found 735.3190.

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**Supplementary Material Available:** X-ray crystallographic analysis data for compound **42** and $^{13}C$ NMR data for compounds **16**, **18**, **39** (P = H), **39**, and **47** (14 pages). Ordering information is given on any current masthead page.