Stereoselective Synthesis of Higher Sugars by Homologation of Carbohydrate-Derived Enals with Nonracemic γ-(Silyloxy) Allylic Stannanes and Substrate-Directed Hydroxylation

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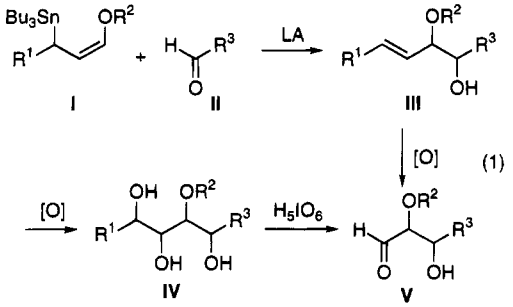
A strategy is described for the chain extension of carbohydrate derivatives utilizing sequential Horner–Emmons condensation and then reduction–oxidation to prepare the enal homologue **VII**, which is converted to the corresponding dienyl bis-OTBS derivative **IX** upon condensation with a γ-(silyloxy) allylic stannane **VI** and subsequent silylation. Dihydroxylation of dienes **IX** with OsO_4–NMO leads to *syn,anti,syn,anti,syn* hexol derivatives **X** with excellent diastereoselectivity. These hexols undergo selective oxidative cleavage with H_5IO_6 to yield γ-lactols **XI**. The methodology has been used to prepare the octonic lactone **15** from (*S,S*)-dimethyl tartrate and the undeconic lactone **32** from D-mannitol.

In recent years an increasing awareness of the important biological functions of so-called "higher sugars" has stimulated the quest for efficient synthetic routes to various 7–11-carbon carbohydrates.[1] In view of the ready availability of many natural 4–6-carbon monosaccharides and their derivatives, strategies based on chain elongation of appropriate aldoses are of particular interest.[1] In that connection, we have directed our attention to the use of nonracemic γ-oxygenated allylic stannanes **I** as homologation reagents (eq 1). The adduct **III**, a

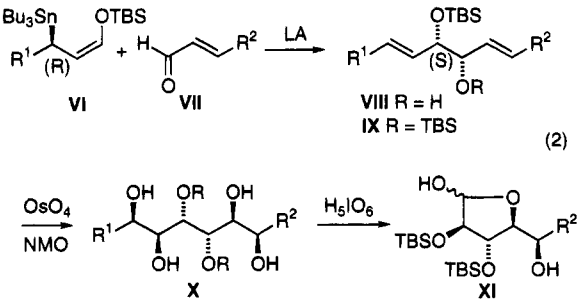


R^1 = alkyl, R^2 = alkyl or silyl, R^3 = carbohydrate residue, LA = Lewis acid (BF_3•OEt_2 or $MgBr_2$•OEt_2), [O] = OsO_4 or O_3

monoprotected 1,2-diol, can be further transformed to a tetrol derivative **IV** or the hydroxy aldehyde **V**.[2]

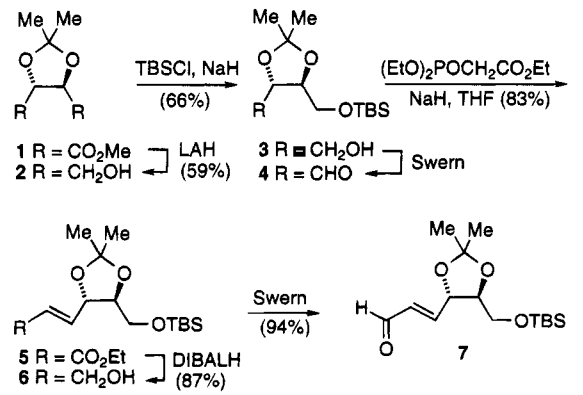
The present study was undertaken to explore the reaction of carbohydrate-derived enals **VII** with γ-(silyloxy) allylic stannanes **VI**[3] as a route to bis-silylated *syn*-1,2-diols **IX** whose subsequent hydroxylation would afford *syn,anti,syn,anti,syn* hexol derivatives as outlined in eq 2. Polyol derivatives such as **X** are of intrinsic interest as carbohydrate analogues.

A key feature of the strategy is the remarkable *anti* directing effect of the *syn* bis-OTBS moiety of dienyl diethers **IX**.[4] It was also of interest to explore the



possibility of a regioselective cleavage of tetrol **X** to produce a lactol such as **XI**.

An appropriate enal was prepared from the known diol **2**[5] available through reduction of the acetonide of (*S,S*)-dimethyl tartrate. Selective silylation of diol **2** afforded the mono TBS ether **3**.[6] Swern oxidation[7] and subsequent Horner–Emmons condensation[8] gave the (*E*)-conjugated ester **5** in 83% yield for the two steps. Conversion to the enal **7** was effected by sequential reduction with DIBALH and Swern oxidation.



The (*R*)-allylic OTBS stannane **9** was prepared as previously described for the racemic analogue through

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(1) Secrist, J. A., III; Barnes, K. O.; Wu, S.-R. In *Trends in Synthetic Carbonhydrate Chemistry*; Horton, D., Hawkins, L. D., McGarvey, G. J., Eds.; ACS Symposium Series 386; American Chemical Society: Washington, DC, 1989; Chapter 5. For other pertinent references and a preliminary account of a portion of this work, see: Marshall, J. A.; Beaudoin, S.; Lewinski, K. *J. Org. Chem.* **1993**, *58*, 5876.

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(3) Marshall, J. A.; Welmaker, G. S. *J. Org. Chem.* **1992**, *57*, 7158.

(4) Saito, S.; Morikawa, Y.; Moriwake, T. *J. Org. Chem.* **1990**, *55*, 5424. Saito, S.; Narahara, O.; Ishikawa, T.; Asahara, M.; Moriwake, T. *J. Org. Chem.* **1993**, *58*, 6292.

(5) Feit, P. W. *J. Med. Chem.* **1964**, *7*, 14.

(6) McDougal, P. G.; Rico, J. G.; Oh, Y.-I.; Condon, B. D. *J. Org. Chem.* **1986**, *51*, 3388.

(7) Mancuso, A. J.; Swern, D. *Synthesis* **1981**, 165.

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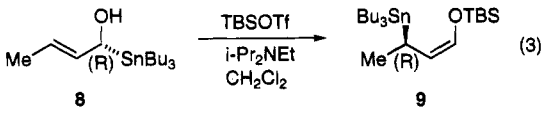
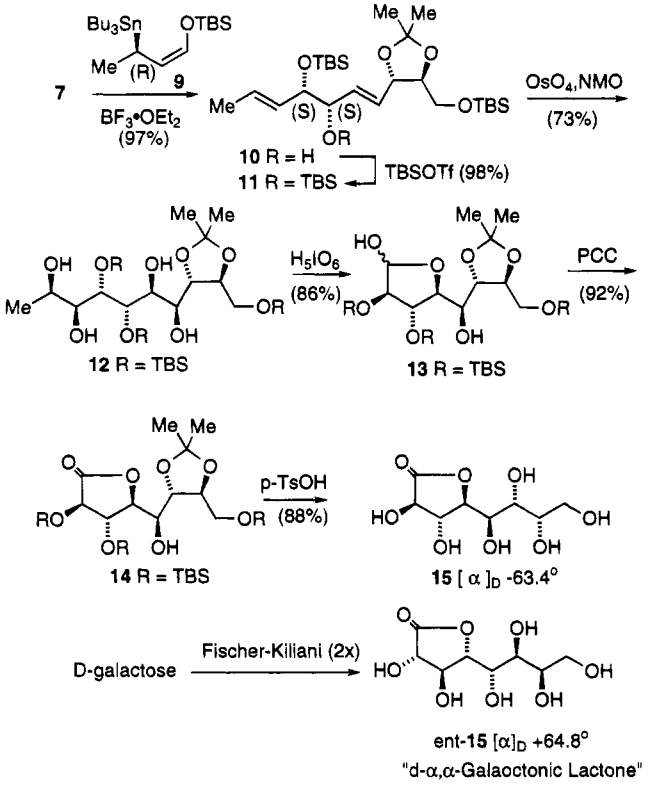
brief exposure of the (*R*)-α-hydroxystannane **8**[9] to TBSOTf in the presence of Hunig's base (eq 3).[3]



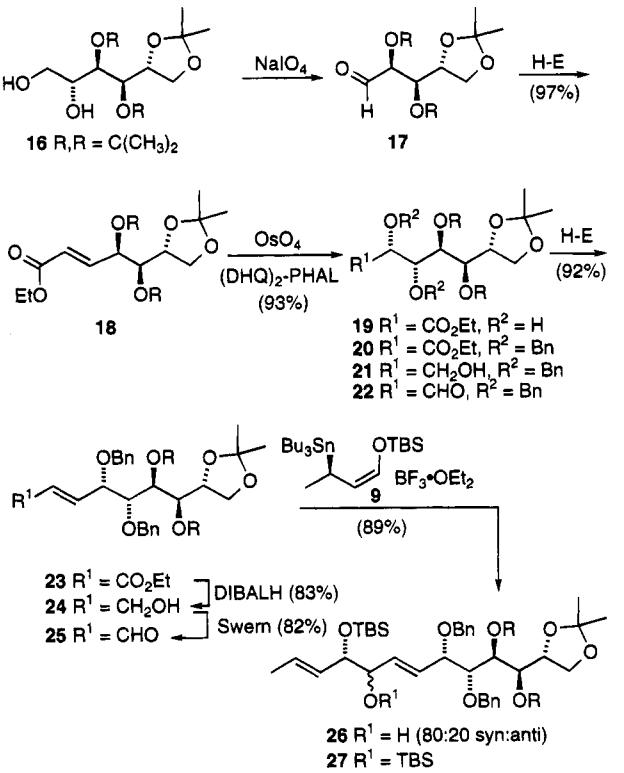
Upon treatment with $BF_3{\cdot}OEt_2$ in CH_2Cl_2 at -78 °C, stannane **9** smoothly added to aldehyde **7** to give the *syn* diol derivative **10** as the sole detectable product in 97% yield. Silylation with TBSOTf afforded the bis-TBS ether **11**. As expected, hydroxylation of this dienyl ether proceeded with high diastereoselectivity, affording tetrol **12** in 73% yield.[10]



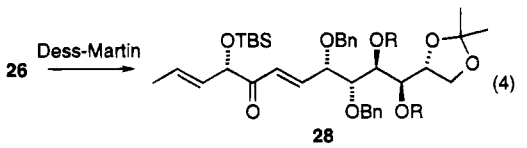
With the feasibility of the carbohydrate chain extension methodology established, we were in a position to examine the proposed selective diol cleavage. Treatment of tetrol **12** with periodic acid[11] gave rise to an epimeric mixture of lactols judged to be **13** from the ^1H NMR spectrum. Oxidation of this mixture with PCC led to a single lactone **14** in high yield.[12] Removal of all protective groups was achieved with *p*-TsOH. The resulting product exhibited mp and optical rotation consistent with its formulation as the enantiomer of *d*-α,α-galaoctonic lactone, *ent*-**15**, first prepared by Fischer from D-galactose nearly a century ago.[13]

A further test of the foregoing strategy was initiated with aldehyde **17** secured by periodate cleavage of the mannitol bis-acetonide **16**.[14] Our ultimate goal in this exercise was lactone **32**, previously prepared by Ikemoto and Schreiber as an intermediate in their synthesis of (−)-hikizimycin.[15]

Horner–Emmons homologation of aldehyde **17**, as before, gave the expected (*E*)-conjugated ester **18**. Hydroxylation with OsO_4–NMO led to a 2:1 mixture of diols favoring **19**. However, when the Sharpless protocol was employed (AD-mix-α), diol **19** was obtained as the sole product.[16] The dibenzylated derivative **20** was subjected to sequential reduction with DIBALH and Swern oxidation, as described above for ester **5**, leading to aldehyde **22**. Repetition of the Horner–Emmons, DIBALH reduction, Swern oxidation sequence afforded enal **25** in high overall yield.



Addition of silyloxy stannane **9** to enal **25** in the presence of $BF_3{\cdot}OEt_2$ proceeded efficiently, but in this case an 80:20 mixture of *syn* and *anti* alcohol adducts was obtained. Separation proved difficult, so the mixture was used directly for the subsequent steps. The *syn*/*anti* relationships of the two alcohol adducts was ascertained through oxidation of the mixture to ketone **28** (eq 4).



Hydroxylation of the dienyl bis-TBS ether **27** with OsO_4–NMO proceeded smoothly, as before, affording a single tetrol **29**. Selective cleavage of the less hindered diol led to the lactol **30** as an epimeric mixture in 76%

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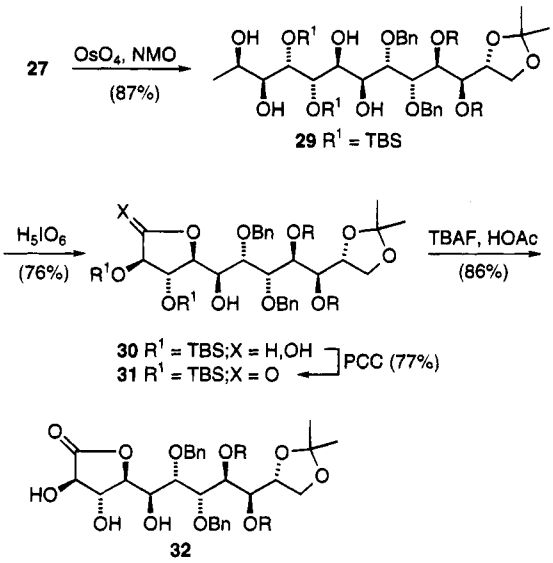
(15) Ikemoto, N.; Schreiber, S. *J. Am. Chem. Soc.* **1992**, *114*, 2524.
(16) Sharpless, K. B.; Amberg, W.; Bennani, Y. L.; Crispino, G. A.; Hartung, J.; Heong, K.-S.; Kwong, H.-L.; Morikawa, K.; Wang, Z.-M.; Xu, D.; Zhang, X.-L. *J. Org. Chem.* **1992**, *57*, 2768. Morikawa, K.; Sharpless, K. B. *Tetrahedron Lett.* **1993**, *34*, 5575.

yield. Oxidation of this mixture and subsequent TBS removal afforded lactone **32** whose identity with the Schreiber intermediate was ascertained through comparison of optical rotation and spectral data.[15]



In conclusion, we have developed a direct sequence for the four-carbon homologation of carbohydrate-derived enals to *syn,anti,syn,anti,syn* hexol derivatives which can be regioselectively cleaved to perhydroxylated γ-lactols with a *syn,anti,syn* disposition of the newly created stereocenters (eq 2). Use of the (*R*)-stannane **9** leads to products with the 2*R*,3*S*,4*S*,5*R* configuration as in **XI** via **X**. The enantiomeric stannane could be employed to prepare the 2*S*,3*R*,4*R*,5*S* (enantiomer of **XI**). The methodology benefits from the high degree of enantioselectivity exhibited in the BF_3-promoted addition of OTBS allylic stannane **9** to enals, the strong facial bias of *syn* additions to the derived bis-TBS allylic ethers, and the highly selective cleavage of the less hindered 1,2-diol moiety of the resultant tetrol. It would be of interest to modify the approach to access other stereoisomeric homologation products. Studies along these lines are currently under way.

Experimental Section[17]

(2*S*,3*S*)-2,3-*O*-(1-Methylethylidene)-1,4-butanediol (2). To a suspension of LAH (13.3 g, 0.35 mol) in Et_2O (150 mL) at 0 °C was added diester **1** (45.5 g, 0.18 mol) in Et_2O (150 mL). After the addition, the reaction mixture was refluxed for 3 h, cooled to 0 °C, and then quenched with H_2O (13.3 mL), 15% NaOH (13.3 mL), and H_2O (39.9 mL). The mixture was stirred to granulate the salts, which were then filtered and washed with hot THF (200 mL). The filtrate was concentrated, and the residue was distilled under vacuum (114–116 °C, 0.9 mmHg) to afford diol **2** (17.6 g, 59%) as a pale yellow oil.[5]

(2*S*,3*S*)-4-[(*tert*-Butyldimethylsilyl)oxy]-2,3-*O*-(1-methylethylidene)-1-butanol (3). To a suspension of sodium hydride (1.29 g, 53.8 mmol) in THF (25 mL) at room temperature was added dropwise diol **2** (4.36 g, 26.8 mmol) in THF (25 mL). After 45 min, *tert*-butyldimethylchlorosilane (4.04 g, 26.8 mmol) was added. The reaction mixture was stirred for 2.5 h, diluted with Et_2O (200 mL), washed with 10% Na_2CO_3 (100 mL) and brine (100 mL), and dried over Na_2SO_4. Purification by flash chromatography on silica gel (4:1, hexanes–EtOAc) afforded alcohol **3** (1.12 g, 66%) as a colorless oil: $[\alpha]_D$ +17.6 (*c* 1.15; $CHCl_3$); IR (film, cm^{-1}) 3476; ^1H NMR (300 MHz, $CDCl_3$) δ 0.05 (6 H, s), 0.88 (9 H, s), 1.37 (3 H, s), 1.39 (3 H, s), 2.39 (1 H, bs), 3.60–3.77 (3 H, m), 3.81–3.87 (2 H, m), 3.93–3.99 (1 H, m); ^{13}C NMR ($CDCl_3$, 125 MHz) δ −5.54, −5.50, 18.28, 25.83, 26.88, 27.01, 62.70, 63.64, 78.02, 80.07, 109.07. Anal. Calcd for $C_{13}H_{28}O_4$: C, 56.48; H, 10.21. Found: C, 56.31; H, 10.28.

(*E*)-(4*S*,5*S*)-Ethyl 6-[(*tert*-Butyldimethylsilyl)oxy]-4,5-*O*-(1-methylethylidene)-2-hexenoate (5). To a solution of oxalyl chloride (1.6 mL, 18.2 mmol) in CH_2Cl_2 (50 mL) at −78 °C was added 2.6 mL (36.4 mmol) of DMSO. After 5 min, alcohol **3** (4.55 g, 16.5 mmol) in CH_2Cl_2 (50 mL) was added dropwise. The reaction mixture was stirred at −78 °C for 15 min, and then 11.4 mL (81.8 mmol) of Et_3N was added and the solution was allowed to warm to 0 °C. The reaction mixture was extracted with 10% HCl (50 mL), H_2O (50 mL), and brine (50 mL) and dried over Na_2SO_4. The crude aldehyde was used without further purification.

To a suspension of sodium hydride (591 mg, 24.6 mmol) in THF (50 mL) at 0 °C was added dropwise 5.52 g (24.6 mmol) of triethyl phosphonoacetate. After 15 min at 0 °C, the above aldehyde in THF (50 mL) was added dropwise. The reaction mixture was allowed to warm to room temperature over a period of 2 h and then diluted with Et_2O (200 mL), washed with H_2O (50 mL), and brine (50 mL) and dried over Na_2SO_4. Purification by flash chromatography on silica gel (9:1, hexanes–Et_2O) afforded ester **5** (4.68 g, 83%) as a light yellow oil: $[\alpha]_D$ −2.6 (*c* 1.01; $CHCl_3$); IR (film, cm^{-1}) 1725; ^1H NMR (300 MHz, $CDCl_3$) δ 0.05 (3 H, s), 0.06 (3 H, s), 0.88 (9 H, s), 1.27 (3 H, t, J = 7.1 Hz), 1.40 (3 H, s), 1.41 (3 H, s), 3.72–3.81 (3 H, m), 4.18 (2 H, q, J = 7.1 Hz), 4.47–4.53 (1 H, m), 6.10 (1 H, dd, J = 1.6, 15.7 Hz), 6.93 (1 H, dd, J = 5.1 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ −5.51, −5.45, 14.18, 18.22, 25.80 (3C), 26.74, 26.87, 60.40, 62.69, 80.69, 109.79, 121.83, 144.66, 166.01. Anal. Calcd for $C_{17}H_{32}O_5Si$: C, 59.27; H, 9.36. Found: C, 59.31; H, 9.29.

(*E*)-(4*S*,5*S*)-6-[(*tert*-Butyldimethylsilyl)oxy]-4,5-*O*-(1-methylethylidene)-2-hexen-1-ol (6). To a solution of ester **5** (4.68 g, 13.6 mmol) in THF (30 mL) at −78 °C was added dropwise 30 mL (30.0 mmol) of 1.0 M DIBALH in toluene. After 2 h at −78 °C, the reaction was quenched with saturated Rochelle's salt (100 mL), allowed to warm to room temperature, and stirred for 1.5 h. The aqueous phase was extracted with CH_2Cl_2 (3 × 50 mL), and the combined organic layers were dried over Na_2SO_4. Purification by flash chromatography on silica gel (3:2 hexanes–Et_2O) afforded alcohol **6** (3.57 g, 87%) as a colorless oil: $[\alpha]_D$ −3.5 (*c* 0.99; $CHCl_3$); IR (film, cm^{-1}) 3417; ^1H NMR (300 MHz, $CDCl_3$) δ 0.04 (3 H, s), 0.05 (3 H, s), 0.87 (9 H, s), 1.39 (3 H, s), 1.41 (3 H, s), 1.52 (1 H, bs), 3.69–3.76 (3 H, m), 4.16 (2 H, dd, J = 1.5, 5.1 Hz), 4.36 (1 H, t, J = 7.2 Hz), 5.73 (1 H, ddt, J = 1.5, 7.2, 15.5 Hz), 5.96 (1 H, dt, J = 5.1, 15.5 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ −5.08, −4.97, 18.67, 26.23 (3C), 27.26, 27.43, 62.65, 62.89, 78.66, 81.70, 109.37, 128.44, 133.96. Anal. Calcd for $C_{15}H_{30}O_4Si$: C, 59.56; H, 10.00. Found: C, 59.31; H, 9.29.

(*E*)-(4*S*,5*S*)-6-[(*tert*-Butyldimethylsilyl)oxy]-4,5-*O*-(1-methylethylidene)-2-hexenal (7). The procedure described for aldehyde **5** was employed with 1.0 g (3.31 mmol) of alcohol **6**. Purification by flash chromatography on silica gel (80:20 hexanes–Et_2O) afforded aldehyde **7** (0.932 g, 94%) as a light yellow oil: $[\alpha]_D$ −4.3 (*c* 1.02; $CHCl_3$); IR (film, cm^{-1}) 1698; ^1H NMR (300 MHz, $CDCl_3$) δ 0.06 (3 H, s), 0.07 (3 H, s), 0.88 (9 H, s), 1.41 (3 H, s), 1.43 (3 H, s), 3.70–3.87 (3 H, m), 4.59–4.63 (1 H, m), 6.37 (1 H, ddd, J = 1.5, 7.9, 15.7 Hz), 6.82 (1 H, dd, J = 4.8, 15.7 Hz), 9.57 (1 H, d, J = 7.9 Hz). Anal. Calcd for $C_{15}H_{28}O_4Si$: C, 59.96; H, 9.39. Found: C, 59.73; H, 9.35.

(*Z*)-(3*R*)-1-[(*tert*-Butyldimethylsilyl)oxy]-3-(tri-*n*-butylstannyl)-1-butene (9). The (*R*)-γ-(silyloxy)stannane **9** was obtained from the known (*R*)-α-(silyloxy)stannane[9] as previously described for the racemate[3] (22–41% overall yield): $[\alpha]_D$ −170.4 (*c* 1.13, CH_2Cl_2).

(2*E*,6*E*)-(4*S*,5*S*,8*S*,9*S*)-4,5,10-Tris[(*tert*-butyldimethylsilyl)oxy]-8,9-*O*-(1-methylethylidene)-2,6-decadien-5-ol (10). To a solution of aldehyde **7** (682 mg, 2.27 mmol) and (*R*)-stannane **9** (1.19 g, 2.50 mmol) in CH_2Cl_2 (30 mL) at −78 °C was added dropwise 0.37 mL (3.02 mmol) of $BF_3{\cdot}Et_2O$. After being stirred at −78 °C for 1.5 h, the mixture was quenched with saturated $NaHCO_3$ (10 mL), allowed to warm to room

(17) For typical experimental protocols, see: Marshall, J. A.; Wang, X.-j. *J. Org. Chem.* **1991**, *56*, 960.

temperature, and then diluted with Et_2O (100 mL), washed with water (20 mL) and brine (20 mL), and dried over Na_2SO_4. Purification by flash chromatography on silica gel (hexanes then hexanes:Et_2O 4:1) afforded alcohol **10** (1.07 g, 97%) as a colorless oil: $[\alpha]_D$ −12.0 (*c* 0.98; $CHCl_3$); IR (film, cm^{-1}) 3477, 1672; ^1H NMR (300 MHz, $CDCl_3$) δ 0.01 (3 H, s), 0.04 (6 H, s), 0.05 (3 H, s), 0.87 (9 H, s), 0.89 (9 H, s), 1.40 (6 H, s), 1.67 (3 H, dd, J = 1.5, 6.5 Hz), 2.58 (1 H, d, J = 3.8 Hz), 3.58−3.75 (3 H, m), 3.80−3.92 (2 H, m), 4.30−4.40 (1 H, m), 5.37 (1 H, ddd, J = 1.6, 7.5, 15.4 Hz), 5.62 (1 H, qd, J = 6.5, 15.4 Hz), 5.76−5.78 (2 H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ −5.06, −4.95, −4.43, −3.58, 18.07, 18.49, 18.70, 26.22 (3C), 26.26 (3C), 27.32, 27.43, 62.52, 75.09, 77.92, 78.57, 81.85, 109.35, 129.49, 129.54, 130.98, 132.60. Anal. Calcd for $C_{25}H_{50}O_5Si_2$: C, 61.68; H, 10.35. Found: C, 61.51; H, 10.32.

(2*E*,6*E*)-(4*S*,5*S*,8*S*,9*S*)-4,5,10-Tris[(*tert*-butyldimethylsilyl)oxy]-8,9-*O*-(1-methylethylidene)-2,6-decadiene (11). To a solution of alcohol **10** (1.0 g, 2.05 mmol) and 2,6-lutidine (0.49 g, 4.55 mmol) in CH_2Cl_2 (30 mL) at 0 °C was added 0.83 mL (3.61 mmol) of TBSOTf. The reaction mixture was stirred at 0 °C for 1 h, diluted with ether (100 mL), extracted with 10% HCl (20 mL), saturated $NaHCO_3$ (20 mL), H_2O (20 mL), and brine (20 mL), and dried over Na_2SO_4. Purification by flash chromatography on silica gel (95:5 hexanes−Et_2O) afforded silyl ether **11** (1.21 g, 98%) as a colorless oil: $[\alpha]_D$ −45.4 (*c* 1.16; $CHCl_3$); IR (film, cm^{-1}) 1672; ^1H NMR (500 MHz, $CDCl_3$) δ −0.01 (3 H, s), 0.01 (3 H, s), 0.02 (3 H, s), 0.03 (3 H, s), 0.04 (3 H, s), 0.05 (3 H, s), 0.86 (9 H, s), 0.87 (9 H, s), 0.88 (9 H, s), 1.40 (6 H, s), 1.64 (3 H, ddd, J = 1.2, 1.2, 6.4 Hz), 3.62−3.65 (2 H, m), 3.72−3.76 (1 H, m), 3.98−4.06 (2 H, m), 4.36 (1 H, dd, J = 7.3, 7.3 Hz), 5.40 (1 H, qdd, J = 1.2, 5.8, 15.3 Hz), 5.52 (1 H, ddd, J = 1.2, 6.4, 15.3 Hz), 5.61 (1 H, ddd, J = 1.4, 7.0, 15.6 Hz), 5.76 (1 H, ddd, J = 0.8, 5.1, 15.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ −5.44, −5.31, −4.74, −4.71, −4.52, −4.49, 17.77, 18.14, 18.19, 18.37, 17.77, 18.14, 18.19, 18.37, 25.88 (6C), 25.93 (3C), 26.95, 27.03, 61.93, 75.52, 76.01, 78.12, 81.79, 108.91, 126.76, 128.59, 129.94, 132.87. Anal. Calcd for $C_{31}H_{64}O_5Si_3$: C, 61.94; H, 10.73. Found: C, 61.78; H, 10.69.

(2*R*,3*S*,4*S*,5*R*,6*R*,7*R*,8*R*,9*S*)-4,5,10-Tris[(*tert*-butyldimethylsilyl)oxy]-8,9-*O*-(1-methylethylidene)-2,3,6,7-decanetetrol (12). To a solution of diene **11** (1.14 g, 1.89 mmol) and *N*-methylmorpholine *N*-oxide (1.11 g, 9.41 mmol) in acetone (70 mL) was added 3.8 mL (0.38 mmol) of 0.1 M OsO_4 in H_2O. After 16 h at room temperature, the reaction mixture was quenched with saturated $NaHSO_3$ (50 mL) and stirred for 1 h. The acetone was removed under reduced pressure, and the aqueous phase was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were washed with H_2O (50 mL) and then dried over Na_2SO_4. Purification by flash chromatography on silica gel (80:20 hexanes−EtOAc) afforded tetrol **12** (0.922 g, 73%) as a foam: $[\alpha]_D$ −30.2 (*c* 1.06; $CHCl_3$); IR (film, cm^{-1}) 3480; ^1H NMR (300 MHz, $CDCl_3$) δ 0.07 (6 H, s), 0.16 (3 H, s), 0.17 (3 H, s), 0.18 (6 H, s), 0.87 (9 H, s), 0.88 (18 H, s), 1.26 (3 H, d, J = 6.6 Hz), 1.33 (3 H, s), 1.38 (3 H, s), 2.02 (1 H, d, J = 11.1 Hz), 2.87 (1 H, d, J = 7.8 Hz), 3.54 (1 H, t, J = 8.1 Hz), 3.71−4.19 (11 H, m); ^{13}C NMR (125 MHz, C_6D_6) δ −5.33, −5.30, −5.05, −4.94, −4.24, −4.06, 18.15 (2C), 18.55, 20.47, 25.89 (6C), 26.11 (3C), 27.41 (2C), 65.06, 65.68, 72.06, 72.22, 72.28, 72.87, 75.72, 77.37, 81.69, 109.50. Anal. Calcd for $C_{31}H_{68}O_9Si_3$: C, 55.65; H, 10.24. Found: C, 55.53; H, 10.22.

(2*R*,3*S*,4*S*,5*R*,6*R*,7*S*)-2,3,8-Tris[(*tert*-Butyldimethylsilyl)oxy]-6,7-*O*-(1-methylethylidene)-5-hydroxyoctanoic Acid γ-Lactone (14). To a solution of tetrol **12** (500 mg, 0.75 mmol) in THF (15 mL) at 0 °C was added 188 mg (0.82 mmol) of periodic acid. After being stirred at 0 °C for 1 h, the reaction mixture was diluted with Et_2O (50 mL), washed with saturated $NaHCO_3$ (10 mL), H_2O (10 mL), and brine (10 mL), and dried over Na_2SO_4. Flash chromatography on silica gel (4:1 hexanes−Et_2O) afforded lactol **13** (400 mg, 86%) as a colorless oil: IR (film, cm^{-1}) 3441. Anal. Calcd for $C_{29}H_{62}O_8Si_3$: C, 55.90; H, 10.03. Found: C, 56.02; H, 10.06.

To a suspension of the above lactol **13** (54 mg, 0.09 mmol) and 3 Å molecular sieves (150 mg) in CH_2Cl_2 (2 mL) was added 44 mg (0.20 mmol) of PCC. The reaction mixture was stirred at room temperature for 4 h and then filtered through silica gel (9:1, hexanes−Et_2O). After solvent removal under reduced pressure, the residue was purified by flash chromatography (9:1 hexanes−Et_2O) to afford lactone **14** (50 mg, 92%) as a colorless oil: $[\alpha]_D$ −2.6 (*c* 0.96, $CHCl_3$); IR (film, cm^{-1}) 3420, 1803; ^1H NMR (300 MHz, $CDCl_3$) δ 0.09 (6 H, s), 0.11 (3 H, s), 0.12 (6 H, s), 0.18 (3 H, s), 0.88 (18 H, s), 0.92 (9 H, s), 1.35 (3 H, s), 1.36 (3 H, s), 3.58−3.75 (3 H, m) 3.88−3.95 (3 H, m), 4.23 (1 H, d, J = 7.9 Hz), 4.34 (1 H, d, J = 3.8 Hz), 4.50 (1 H, t, J = 8.1 Hz); ^{13}C NMR (125 MHz; $CDCl_3$) δ −5.26, −5.16, −4.57, −4.39, −4.07, −3.62, 18.17, 18.61, 18.65, 26.06 (3C), 26.13 (3C), 26.17 (3C), 27.11, 27.22, 69.37, 74.16, 77.16, 79.59, 79.94, 80.97, 109.88, 173.24. Anal. Calcd for $C_{29}H_{60}O_8Si_3$: C, 56.09; H, 9.74. Found: C, 56.26; H, 9.81.

(2*R*,3*S*,4*S*,5*R*,6*R*,7*S*)-2,3,5,6,7,8-Hexahydroxyoctanoic Acid γ-Lactone (15). A solution of lactone **14** (211 mg, 0.34 mmol) and TsOH·H_2O (6 mg, 0.03 mmol) in MeOH (5 mL) was heated at 60 °C for 40 h and then cooled at 0 °C for 30 min. The solid was filtered and washed with MeOH, affording hydroxy lactone **15** (71 mg, 88%) as a white solid: mp 219 °C (glacial acetic acid, dec); $[\alpha]_D$ −63.4 (*c* 0.83; H_2O); IR (KBr, cm^{-1}) 3334, 1765; ^1H NMR (D_2O, 500 MHz) δ 3.70 (1 H, dd, J = 1.4, 9.8 Hz), 3.71 (2 H, d, J = 6.4 Hz), 3.92 (1 H, dd, J = 1.2, 9.8 Hz), 3.99 (td, J = 1.4, 6.4 Hz), 4.44 (1 H, t, J = 9.1 Hz), 4.61 (1 H, dd, J = 1.2, 9.1 Hz), 4.67 (1 H, d, J = 9.1 Hz). Anal. Calcd for $C_8H_{14}O_8$: C, 40.34; H, 5.92. Found: C, 40.24; H, 5.90. Reported for the (+)-enantiomer: $[\alpha]_D$ +64.8 (*c* 0.8, H_2O), +64.0; mp 219−220 °C (dec), 225−228 °C (dec).[13]

(4*R*,5*S*,6*R*)-Ethyl 4,5:6,7-Bis-*O*-(1-methylethylidene)-2-heptenoate (18). The procedure described for ester **5** was employed on 3.15 g (13.7 mmol) of aldehyde **17**. Purification by flash chromatography on silica gel (4:1 hexanes−Et_2O) gave the ester **18** (3.99 g, 97%) as a light yellow oil: $[\alpha]_D$ −2.1 (*c* 1.17, $CHCl_3$); IR (film, cm^{-1}) 1724, 1663; ^1H NMR (300 MHz, $CDCl_3$) δ 1.27 (3 H, t, J = 7.1 Hz), 1.32 (3 H, s), 1.39 (6 H, s), 1.40 (3 H, s), 3.66 (1 H, t, J = 7.7 Hz), 3.89−3.96 (1 H, m), 4.06−4.15 (2 H, m), 4.51 (1 H, ddd, J = 1.6, 4.5, 7.8 Hz), 4.18 (2 H, ABX_3, qd, J_{AB} = 1.0, J_{AX} = 7.1 Hz), 6.14 (1 H, dd, J = 1.6, 15.7 Hz), 6.98 (1 H, dd, J = 4.5, 15.7 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.15, 25.11, 26.63, 26.67, 26.88, 60.32, 67.43, 76.93, 78.87, 81.11, 109.75, 110.15, 121.32, 144.94, 166.08. Anal. Calcd for $C_{15}H_{24}O_6$: C, 59.98; H, 8.05. Found: C, 60.24; H, 8.09.

(2*R*,3*S*,4*R*,5*S*,6*R*)-Ethyl 4,5:6,7-Bis-*O*-(1-methylethylidene)-2,3-dihydroxyheptanoate (19). To a solution of $K_3Fe(CN)_6$ (8.12 g, 24.7 mmol), K_2CO_3 (3.44 g, 24.9 mmol), $CH_3SO_2NH_2$ (0.78 g, 8.20 mmol), and $(DHQ)_2$−PHAL (0.32 g, 0.41 mmol) in H_2O (40 mL) at 0 °C was added 0.8 mL (0.08 mmol) of 0.1 M OsO_4 in H_2O, followed by unsaturated ester **17** (2.48 g, 8.20 mmol) in *t*-BuOH (40 mL). After 25 h, 8.26 g (65.5 mmol) of Na_2SO_3 was added. After 30 min, the reaction mixture was allowed to warm to room temperature and diluted with EtOAc (80 mL), and the phases were separated. The aqueous layer was extracted with EtOAc (3 × 30 mL), and the combined extracts were dried over $MgSO_4$. Flash chromatography on silica gel (2:1 Et_2O−hexanes) gave diol **19** (2.56 g, 93%) as a white solid: mp 52−54 °C; $[\alpha]_D$ −10.0 (*c* 1.28, $CHCl_3$); IR (film, cm^{-1}) 3454, 1741; ^1H NMR (400 MHz, $CDCl_3$) δ 1.30 (3 H, t, J = 7.1 Hz), 1.33, (3 H, s), 1.37 (3 H, s), 1.38 (3 H, s), 1.42 (3 H, s), 3.02 (1 H, d, J = 8.0 Hz), 3.74−3.78 (2 H, m), 3.86−3.88 (1 H, m), 3.97−4.01 (3 H, m), 4.05 (1 H, ddd, J = 5.4, 5.4, 8.7 Hz), 4.28 (2 H, qd, J = 7.1, 7.1 Hz), 4.38 (1 H, d, J = 8.1 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.11, 24.97, 26.22, 26.90, 61.65, 67.68, 70.78, 73.63, 76.30, 78.73, 81.00, 109.84, 110.19, 173.13.

(2*R*,3*S*,4*R*,5*S*,6*R*)-Ethyl 2,3-Bis(benzyloxy)-4,5:6,7-bis-*O*-(1-methylethylidene)heptanoate (20). To a suspension of NaH (69 mg, 2.88 mmol) in THF (1.5 mL) at 0 °C was added dropwise diol **19** (502 mg, 1.50 mmol) in THF (1 mL). After 1 h, Bu_4NI (111 mg, 0.3 mmol), dibenzo-18-C-6 (2 mg, 5.5 μmol), and BnBr (496 mg, 2.90 mmol) were added. After being stirred at room temperature for 3 h, the reaction mixture was diluted with Et_2O (15 mL), washed with H_2O (2 mL) and brine (2 mL), and dried over $MgSO_4$. Flash chromatography on silica gel (3:1 then 1:1 hexanes−Et_2O) gave dibenzyl ether **20** (354 mg, 48%) and a mixture of the two monobenzyl ethers (157 mg, 25%).

20: $[\alpha]_D$ +23.8 (*c* 1.39, $CHCl_3$); IR (film, cm^{-1}) 1749; ^1H NMR (400 MHz, $CDCl_3$) δ 1.27 (3 H, t, J = 7.2 Hz), 1.33 (6 H, s), 1.34 (6 H, s), 3.85 (1 H, dd, J = 7.0, 8.1 Hz), 3.94–4.04 (3 H, m), 4.11 (1 H, t, J = 5.5 Hz), 4.14–4.25 (3 H, m), 4.24 (1 H, d, J = 3.8 Hz), 4.52, 4.80 (2 H, ABq, J_{AB} = 11.6 Hz), 4.56, 4.71 (2 H, ABq, J_{AB} = 11.1 Hz), 7.24–7.37 (10 H, m); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.19, 25.35, 26.36, 27.55, 27.60, 61.10, 65.67, 73.39, 74.07, 76.24, 77.24, 78.66, 79.63, 81.13, 109.36, 110.00, 127.84, 128.14, 128.26, 128.31, 128.38, 137.41, 137.70, 171.30. Anal. Calcd for $C_{24}H_{38}O_8$: C, 67.69; H, 7.44. Found: C, 67.76; H, 7.49.

(2*S*,3*S*,4*R*,5*R*,6*R*)-2,3-Bis(benzyloxy)-4,5:6,7-bis-*O*-(1-methylethylidene)-1-heptanol (21). To a solution of ester **20** (328 mg, 0.64 mmol) in THF (5 mL) at 0 °C was added 1.6 mL (1.6 mmol) of 1.0 M DIBAL-H in hexanes. After 1 h, the reaction mixture was quenched with saturated potassium sodium tartrate (5 mL) and stirred at room temperature for 4 h. The aqueous phase was extracted with CH_2Cl_2 (3 × 10 mL), and the combined extracts were dried over $MgSO_4$. Flash chromatography on silica gel (2:1 Et_2O–hexanes) gave alcohol **21** (285 mg, 95%) as a colorless oil: $[\alpha]_D$ +13.8 (*c* 1.30, $CHCl_3$); IR (film, cm^{-1}) 3480; ^1H NMR (400 MHz, $CDCl_3$) δ 1.29 (3 H, s), 1.33 (3 H, s), 1.35 (3 H, s), 1.39 (3 H, s), 2.05 (1 H, bs), 3.67–3.82 (4 H, m), 3.90 (1 H, dd, J = 6.3, 8.1 Hz), 4.04–4.13 (3 H, m), 4.17 (1 H, dd, J = 6.3, 13.0 Hz), 4.60, 4.73 (2 H, ABq, J_{AB} = 11.5 Hz), 4.72, 4.79 (2 H, ABq, J_{AB} = 11.1 Hz), 7.26–7.34 (10 H, m); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 25.38, 26.42, 27.26, 27.33, 61.83, 66.88, 73.51, 75.09, 76.94, 78.45, 79.66, 80.04, 80.68, 109.54, 127.69, 127.75, 127.99, 128.00, 128.35, 128.42, 138.36, 138.48. Anal. Calcd for $C_{27}H_{36}O_7$: C, 68.62; H, 7.68. Found: C, 68.55; H, 7.70.

(2*R*,3*S*,4*R*,5*R*,6*R*)-2,3-Bis(benzyloxy)-4,5:6,7-bis-*O*-(1-methylethylidene)heptanal (22). To a solution of alcohol **21** (279 mg, 0.59 mmol) in CH_2Cl_2 (5 mL) was added 451 mg (1.06 mmol) of Dess–Martin periodinane reagent.[18] After 30 min, $Na_2S_2O_3$ (1.18 g, 7.46 mmol), saturated $NaHCO_3$ (10 mL), and Et_2O (7 mL) were added. After 10 min, the phases were separated, and the organic layer was washed with saturated $NaHCO_3$ (5 mL), H_2O (5 mL), and brine (5 mL) and dried over $MgSO_4$. Flash chromatography on silica gel (2:1 hexanes–Et_2O) gave the aldehyde **22** (248 mg, 89%) as a colorless oil: $[\alpha]_D$ +20.6 (*c* 1.13, $CHCl_3$); IR (film, cm^{-1}) 1732; ^1H NMR (300 MHz, $CDCl_3$) δ 1.29 (3 H, s), 1.30 (3 H, s), 1.34 (6 H, s), 3.85 (1 H, dd, J = 5.6, 7.9 Hz), 3.95–4.15 (6 H, m), 4.53, 4.58 (2 H, ABq, J_{AB} = 11.5 Hz), 4.63, 4.73 (2 H, ABq, J_{AB} = 12.0 Hz), 7.28–7.33 (10 H, m), 9.76 (1 H, d, J = 0.8 Hz). Anal. Calcd for $C_{27}H_{34}O_7$: C, 68.92; H, 7.28. Found: C, 68.81; H, 7.18.

(4*S*,5*R*,6*R*,7*R*,8*R*)-Ethyl 2,3-Bis(benzyloxy)-4,5:6,7-bis-*O*-(1-methylethylidene)-2-nonenoate (23). The procedure described for ester **5** was employed with 245 mg (0.52 mmol) of aldehyde **22**. Flash chromatography on silica gel (2:1 hexanes–Et_2O) gave the ester **23** (260 mg, 92%) as a colorless oil: $[\alpha]_D$ +33.5 (*c* 1.12, $CHCl_3$); IR (film, cm^{-1}) 1721, 1656; ^1H NMR (400 MHz, $CDCl_3$) δ 1.29 (3 H, t, J = 7.1 Hz), 1.29 (3 H, s), 1.31 (6 H, s), 1.34 (3 H, s), 3.69 (1 H, dd, J = 4.6, 6.2 Hz), 3.85–3.90 (1 H, m), 4.01–4.23 (4 H, m), 4.21 (2 H, ABX_3, qd, J_{AB} = 0.9, J_{AX} = 7.1 Hz), 4.29 (1 H, ddd, J = 1.3, 6.2, 6.2), 4.44, 4.62 (2 H, ABq, J_{AB} = 11.8 Hz), 4.66, 4.80 (2 H, ABq, J_{AB} = 11.1 Hz), 6.15 (1 H, dd, J = 1.3, 15.8 Hz), 7.00 (1 H, J = 6.2, 15.8 Hz), 7.26–7.31 (10 H, m); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.28, 25.40, 26.40, 27.26, 27.28, 60.48, 66.99, 71.87, 75.34, 76.82, 78.19, 78.94, 79.54, 82.17, 109.41, 109.54, 123.56, 127.68, 127.90, 128.04, 128.28, 128.32, 137.90, 138.13, 145.22, 166.08. Anal. Calcd for $C_{31}H_{40}O_8$: C, 68.87; H, 7.46. Found: C, 68.80; H, 7.45.

(4*S*,5*R*,6*R*,7*R*,8*R*)-2,3-Bis(benzyloxy)-4,5:6,7-bis-*O*-(1-methylethylidene)-2-nonen-1-ol (24). The procedure described for alcohol **21** was employed with 255 mg (0.47 mmol) of ester **23**. Flash chromatography on silica gel (2:1 Et_2O–hexanes) gave alcohol **24** (195 mg, 83%) as a colorless oil: $[\alpha]_D$ +26.2 (*c* 1.22, $CHCl_3$); IR (film, cm^{-1}) 3413; ^1H NMR (400 MHz, $CDCl_3$) δ 1.28 (3 H, s), 1.30 (3 H, s), 1.32 (3 H, s), 1.35 (3 H, s), 3.65 (1 H, dd, J = 4.7, 6.2 Hz), 3.90 (1 H, dd, J = 6.5, 8.1 Hz), 4.00–4.21 (8 H, m), 4.43, 4.60 (2 H, ABq, J_{AB} = 12.0 Hz), 4.69, 4.81 (2 H, ABq, J_{AB} = 11.3 Hz), 5.72 (1 H, dd, J = 7.5, 15.6 Hz), 5.92 (1 H, td, J = 5.2, 15.6 Hz), 7.23–7.34 (10 H, m); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 25.48, 26.41, 27.31, 62.76, 66.63, 70.85, 75.25, 76.75, 78.06, 79.43, 79.78, 82.57, 109.22, 109.49, 127.44, 127.58, 127.85, 128.03, 128.23, 128.26, 128.42, 133.68, 138.48, 138.53. Anal. Calcd for $C_{29}H_{38}O_7$: C, 69.86; H, 7.68. Found: C, 69.79; H, 7.71.

(4*S*,5*R*,6*R*,7*R*,8*R*)-2,3-Bis(benzyloxy)-4,5:6,7-bis-*O*-(1-methylethylidene)-2-nonenal (25). The procedure described for aldehyde **7** was employed with 194 mg (0.39 mmol) of alcohol **24** . Flash chromatography on silica gel (7:3 hexanes–Et_2O) gave aldehyde **25** (159 mg, 82%) as a colorless oil: $[\alpha]_D$ +27.4 (*c* 0.99, $CHCl_3$); IR (film, cm^{-1}) 1694; ^1H NMR (400 MHz, $CDCl_3$) δ 1.29 (3 H, s), 1.30 (3 H, s), 1.32 (3 H, s), 1.34 (3 H, s), 3.74 (1 H, dd, J = 4.7, 6.0 Hz), 3.85–3.92 (1 H, m), 4.04–4.10 (3 H, m), 4.14–4.17 (1 H, m), 4.37 (1 H, dd, J = 4.8, 6.0 Hz), 4.48, 4.59 (2 H, ABq, J_{AB} = 11.8 Hz), 4.70, 4.76 (2 H, ABq, J_{AB} = 11.3 Hz), 6.36 (1 H, ddd, J = 1.2, 7.9, 15.8 Hz), 6.84 (1 H, dd, J = 6.0, 15.8 Hz), 7.24 (10 H, m), 9.54 (1 H, d, J = 7.9 Hz, CHO); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 25.38, 26.42, 27.29, 27.30, 67.05, 72.30, 75.19, 76.83, 78.27, 79.04, 79.61, 81.65, 109.63, 109.65, 127.87, 127.89, 127.97, 128.11, 128.38, 128.40, 133.39, 137.51, 137.88, 154.07, 193.26. Anal. Calcd for $C_{29}H_{36}O_7$: C, 70.14; H, 7.31. Found: C, 70.13; H, 7.35.

(4*S*,5*S*,8*S*,9*R*,10*R*,11*R*,12*R*)-8,9-Bis(benzyloxy)-4-[(*tert*-butyldimethylsilyl)oxy]-10,11:12,13-bis-*O*-(1-methylethylidene)-2,6-tridecadien-5-ol (26). The procedure described for alcohol **10** was employed with 145 mg (0.29 mmol) of aldehyde **25** and 180 mg (0.38 mmol) of (*R*)-stannane **9.** Flash chromatography on silica gel (3:2 hexanes–Et_2O) gave alcohol **26** (177 mg, 89%) as an 81:19 *syn*/*anti* mixture according to integration of the ^1H NMR spectrum: $[\alpha]_D$ +27.4 (*c* 0.99, $CHCl_3$); IR (film, cm^{-1}) 3479; ^1H NMR (400 MHz, $CDCl_3$) δ 0.03 (3 H, s), 0.06 (3 H, s), 0.89 (9 H, s), 1.26 (3 H, s), 1.27 (3 H, s), 1.31 (3 H, s), 1.33 (3 H, s), 1.67 (3 H, dd, J = 1.3, 6.5 Hz), 2.61 (1 H, bs), 3.64 (1 H, dd, J = 4.3, 6.6 Hz), 3.85–4.18 (8 H, m), 4.39, 4.61 (2 H, ABq, J_{AB} = 12.0 Hz), 4.66, 4.87 (2 H, ABq, J_{AB} = 11.1 Hz), 5.38 (1 H, qdd, J = 1.3, 7.6, 15.3 Hz), 5.62 (1 H, qd, J = 6.5, 15.3 Hz), 5.76–5.78 (2 H, m), 7.22–7.34 (10 H, m); ^{13}C NMR ($CDCl_3$, 100 MHz) δ −4.72, −3.86, 17.82, 18.16, 25.54, 25.89, 26.36, 27.25, 27.37, 66.91, 70.49, 75.30, 75.43, 76.79, 77.75, 78.01, 79.61, 79.79, 82.72, 109.06, 109.42, 127.33, 127.44, 127.82, 127.89, 128.18, 129.22, 129.67, 130.73, 133.41, 138.63, 138.65.

Minor isomer (partial spectrum): ^{13}C NMR ($CDCl_3$, 100 MHz) δ −4.77, −4.10, 13.62, 17.51, 18.20, 25.51, 26.84, 27.31, 27.85, 66.73, 76.69, 76.91, 79.45, 82.83, 127.37, 127.74, 127.92, 128.51, 129.44, 129.87, 133.09.

(4*S*,5*S*,8*S*,9*R*,10*R*,11*R*,12*R*)-8,9-Bis(benzyloxy)-4,5-bis-[(*tert*-butyldimethylsilyl)oxy]-10,11:12,13-bis-*O*-(1-methylethylidene)-2,6-tridecadiene (27). The procedure described for silyl ether **11** was employed with 152 mg (0.22 mmol) of alcohol **26**. Flash chromatography on silica gel (85:15 hexanes–Et_2O) gave disilyl ether **27** (160 mg, 90%) as an 81:19 *syn*/*anti* mixture according to integration of the ^1H NMR spectrum: $[\alpha]_D$ +1.1 (*c* 1.08, $CHCl_3$); IR (film, cm^{-1}) 1498; ^1H NMR (400 MHz, $CDCl_3$) δ 0.03 (3 H, s), 0.05 (3 H, s), 0.06 (3 H, s), 0.08 (3 H, s), 0.89 (9 H, s), 0.90 (9 H, s), 1.20 (3 H, s), 1.24 (3 H, s), 1.29 (3 H, s), 1.33 (3 H, s), 1.64 (3 H, d, J = 6.2 Hz), 3.68 (1 H, dd, J = 3.4, 7.5 Hz), 3.84–4.15 (8 H, m), 4.38, 4.60 (2 H, ABq, J_{AB} = 12.2 Hz), 4.69, 4.93 (2 H, ABq, J_{AB} = 11.3 Hz), 5.48–5.65 (3 H, m), 5.85 (1 H, dd, J = 5.0, 15.7 Hz), 7.21–7.35 (10 H, m); ^{13}C NMR ($CDCl_3$, 100 MHz) δ −4.68, −4.66, −4.52, −4.48, 17.89, 18.20, 18.25, 25.57, 25.88, 25.97, 26.03, 26.31, 27.11, 27.16, 67.14, 69.81, 75.55, 75.58, 75.88, 76.58, 75.88, 76.77, 77.41, 79.89, 80.14, 82.58, 108.57, 109.42, 126.29, 127.28, 127.72, 127.93, 127.98, 128.13, 128.18, 130.08, 135.33, 138.83, 139.06. Anal. Calcd for $C_{45}H_{72}O_8Si_2$: C, 67.80; H, 9.10. Found: C, 67.68; H, 9.06.

Minor isomer (partial spectrum): ^{13}C NMR ($CDCl_3$, 100 MHz) δ −4.42, −4.36, −4.20, 17.76, 18.32, 25.48, 26.03, 26.34, 27.26, 27.31, 66.93, 70.20, 75.64, 76.95, 78.06, 78.42, 79.46, 83.28, 108.95, 127.10, 127.43, 127.88, 127.89, 131.71, 135.38, 138.72, 138.74.

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(2*E*,6*E*)-(4*S*,8*S*,9*R*,10*R*,11*R*,12*R*)-8,9-Bis(benzyloxy)-4-[(*tert*-butyldimethylsilyl)oxy]-10,11:12,13-bis-*O*-(methylethylidene)-2,6-tridecadien-5-one (28). To a solution of alcohol **26** (18 mg, 26.6 μmol) in CH_2Cl_2 (1 mL) was added 23 mg (54.2 μmol) of Dess–Martin periodinane.[18] After 30 min, 60 mg (0.38 mmol) of sodium thiosulfate was added, followed by saturated $NaHCO_3$ (1 mL). After 10 min, the reaction mixture was diluted with Et_2O (10 mL), washed with H_2O (1 mL) and brine (1 mL), and dried over $MgSO_4$. Flash chromatography on silica gel (3:2 hexanes–Et_2O) gave ketone **28** (17 mg, 92%) as a colorless oil: ^1H NMR (400 MHz, $CDCl_3$) δ 0.04 (3 H, s), 0.05 (3 H, s), 0.88 (9 H, s), 1.28 (6 H, s), 1.30 (3 H, s), 1.32 (3 H, s), 1.68 (3 H, d, J = 6.6 Hz), 3.63 (1 H, t, J = 5.5 Hz), 3.85–3.88 (2 H, m), 3.99–4.03 (2 H, m), 4.07–4.12 (2 H, m), 4.35 (1 H, td, ABq, J = 1.3, 4.2 Hz), 4.44, 4.63 (2 H, ABq, J = 11.1 Hz), 4.57, 4.76 (2 H, ABq, J = 11.8 Hz), 5.43 (1 H, qdd, J = 1.7, 5.8, 15.1 Hz), 5.84 (1 H, qd, J = 6.6, 15.1 Hz), 6.87 (1 H, dd, J = 1.3, 15.9 Hz), 7.06 (1 H, dd, J = 5.4, 15.9 Hz), 7.24–7.29 (10 H, m).

(2*R*,3*S*,4*S*,5*R*,6*R*,7*R*,8*R*,9*S*,10*S*,11*R*,12*R*)-8,9-Bis(benzyloxy)-4,5-bis[(*tert*-butyldimethylsilyl)oxy]-10,11:12,13-bis-*O*-(1-methylethylidene)-2,3,5,6-tridecanetetrol (29). The procedure described for tetrol **12** was employed with 150 mg (0.19 mmol) of diene **27**. Flash chromatography on silica gel (1:1 hexanes–Et_2O) gave tetrol **29** (143 mg, 87%) as a colorless oil: $[\alpha]_D$ −25.1 (*c* 0.99, $CHCl_3$); IR (film, cm^{-1}) 3475; ^1H NMR (400 MHz, $CDCl_3$) δ .0.10 (3 H, s), 0.17 (3 H, s), 0.18 (3 H, s), 0.19 (3 H, s), 0.84 (9 H, s), 0.84 (9 H, s), 1.24 (3 H, d, J = 6.6 Hz_3), 1.26 (3 H, s), 1.35 (3 H, s), 1.38 (6 H, s), 2.02 (1 H, bs), 2.76 (1 H, d, J = 11.2 Hz), 3.66 (1 H, d, J = 8.5 Hz), 3.75–4.15 (13 H, m), 4.29–4.32 (1 H, m), 4.67, 4.75 (2 H, ABq, J_{AB} = 11.2 Hz), 4.71, 4.87 (2 H, ABq, J_{AB} = 11.2 Hz), 7.25–7.34 (10 H, m); ^{13}C NMR ($CDCl_3$, 100 MHz) δ −5.26, −5.13, −4.27, −4.14, 20.40, 25.42, 25.71, 25.77, 26.28, 27.36, 27.44, 65.30, 66.33, 69.09, 71.20, 71.63, 72.34, 74.81, 74.89, 75.56, 76.58, 78.48, 78.60, 78.80, 81.46, 109.22, 109.53, 127.40, 127.52, 127.57, 128.11, 128.21, 128.27, 138.63, 138.68. Anal. Calcd for $C_{45}H_{76}O_{12}Si_2$: C, 62.47; H, 8.85. Found: C, 62.59; H, 8.91.

(2*R*,3*S*,4*R*,5*R*,6*R*,7*S*,8*S*,9*R*,10*R*)-6,7-Bis(benzyloxy)-2,3-bis[(*tert*-butyldimethylsilyl)oxy]-8,9:10,11-bis-*O*-(1-methylethylidene)-5-hydroxyundecanoic Acid γ-Lactone (31). The procedure described for lactone **14** was employed with 121 mg (0.14 mmol) of tetrol **29**. Flash chromatography on silica gel (7:3 hexanes–Et_2O) gave lactol **30** (87 mg, 76%) as a colorless oil.

Oxidation of lactol **30** (87 mg, 0.11 mmol) was achieved as described for lactone **14**. Flash chromatography on silica gel (3:1 hexanes–Et_2O) gave lactone **31** (87 mg, 77%) as a glassy solid: mp 46–48 °C; $[\alpha]_D$ −9.8 (*c* 0.97, $CHCl_3$); IR (CCl_4 film, cm^{-1}) 3406, 1803; ^1H NMR (400 MHz, $CDCl_3$) δ 0.07 (3 H, s), 0.11 (3 H, s), 0.12 (3 H, s), 0.18 (3 H, s), 0.87 (9 H, s), 0.92 (9 H, s), 1.33 (3 H, s), 1.35 (3 H, s), 1.38 (3 H, s), 1.48 (3 H, s), 3.12 (1 H, d, J = 10.5 Hz), 3.74–3.76 (2 H, m), 3.90–3.94 (2 H, m), 4.06–4.11 (2 H, m), 4.19 (1 H, t, J = 6.9 Hz), 4.31–4.43 (3 H, m), 4.50 (1 H, t, J = 5.1 Hz), 4.58, 4.81 (2 H, ABq, J_{AB} = 11.6 Hz), 4.78 (2 H, s), 7.22–7.29 (10 H, m); ^{13}C NMR ($CDCl_3$, 100 MHz) δ −4.66, −4.61, −4.42, −4.05, 17.76, 18.23, 25.35, 25.71, 25.74, 26.24, 27.22, 67.19, 68.26, 74.30, 74.59, 75.59, 76.20, 76.95, 78.14, 78.46, 79.52, 79.58, 81.98, 109.20, 110.41, 127.50, 127.55, 127.68, 128.29, 138.23, 138.32, 172.96. Anal. Calcd for $C_{43}H_{68}O_{11}Si_2$: C, 63.12; H, 8.50. Found: C, 63.20; H, 8.47.

(2*R*,3*S*,4*R*,5*R*,6*R*,7*S*,8*S*,9*R*,10*R*)-6,7-Bis(benzyloxy)-2,3-bis-[(*tert*-butyldimethylsilyl)oxy]-8,9:10,11-bis-*O*-(1-methylethylidene)-2,3,5-trihydroxyundecanoic Acid γ-Lactone (32). To a solution of lactone **31** (61 mg, 0.07 mmol) in THF (1 mL) was added 11 mL (0.19 mmol) of glacial AcOH, followed by 0.19 mL (0.19 mmol) of 1.0 M TBAF in THF. After 24 h, the reaction mixture was concentrated under reduced pressure. Flash chromatography on silica gel (2:1 EtOAc–hexanes) gave lactone **32** (38 mg, 86%) as a glassy solid: $[\alpha]_D$ −38.0 (*c* 2.93, $CHCl_3$) [lit.[15] $[\alpha]_D$ −35.7 (*c* 3.34, CHCl3)]; IR (CCl_4 film, cm^{-1}) 3423, 1784; ^1H NMR (500 MHz, $CDCl_3$) δ 1.18 (3 H, s), 1.19 (3 H, s), 1.21 (3 H, s), 1.24 (3 H, s), 2.23 (1 H, bs), 3.78–3.81 (2 H, m), 3.88–3.95 (3 H, m), 4.01 (1 H, bs), 4.04–4.12 (2 H, m), 4.19 (1 H, t, J = 6.7 Hz), 4.25–4.28 (1 H, m), 4.41 (1 H, t, J = 5.9 Hz), 4.44–4.45 (2 H, m), 4.54, 4.76 (2 H, ABq, J_{AB} = 11.2 Hz), 4.74, 4.75 (2 H, ABq, J_{AB} = 11.0 Hz), 7.22–7.31 (10 H, m); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 25.29, 26.24, 27.20, 27.25, 67.00, 68.54, 73.11, 74.69, 74.72, 75.05, 78.09, 78.32, 79.17, 79.84, 80.87. The spectra were essentially superimposable on those of an authentic sample provided by Prof. Shreiber.[15]

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Supplementary Material Available: Copies of ^1H and ^{13}C NMR spectra of key intermediates (22 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.