Supporting Methods

All reaction solvents were purified before use. Tetrahydrofuran, dichloromethane, acetonitrile, toluene, and benzene were purified by passing through a solvent column composed of activated A-1 alumina, as described (1). *tert*-Amyl alcohol, dioxane, and ethylenediamine were purified by distillation from sodium. Dioxane was also purchased anhydrous from Aldrich and used as received. DMSO, *i*-Pr_2NEt, and trichloroacetonitrile were purified by distillation from calcium hydride. Methanol was purified by distillation from magnesium turnings. TMS-Br was distilled prior to use. Trimethylphosphine, thallium ethoxide, and $Pd(Ph_3P)_4$ were purchased from Strem Chemicals (Newburyport, MA) and used without further purification. A 0.5-M solution of KHMDS in toluene was purchased from Aldrich. LiCl was flame-dried prior to use. DBU and pyridine were distilled from calcium hydride. Trimethyl phosphonoacetate, DIBAL, $TrBF_4$, TBAF, CBr_4, Ph_3P, triphenylphosphoranylidne-2-propanone, $SnCl_2$, $AgClO_4$, triphenylphosphoryl azide, $K_2OsO_4(OH)_4$, $(DHQD)_2$•pyr, TBSCl, Ac_2O, SO_3•pyr, diethylphosphonoacetic acid, guanidinium nitrate, Tris•(trimethylsilyl)silane, methyl(triphenylphosphoranylidene)acetate, benzenethiol, sodium cyanoborohydride, sodium hydride, methyl iodide, carbon disulfide, pentafluorophenyl chlorothionoformate, tributyltin hydride, triethyl borane, AIBN, and DMAP were purchased from Aldrich and used as received. HF•pyridine and 18-crown-6 were purchased from Acros Organics (Geel, Belgium) and used without further purification. We purchased 1,1'-thiocarbonyldiimidazole from Lancaster Synthesis and used it as received.

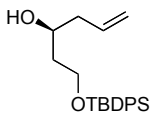
All reactions sensitive to moisture or oxygen were conducted under a nitrogen or argon atmosphere using flame-dried (under vacuum) or oven-dried (170°C, overnight) glassware. House nitrogen was used without further purification. Argon was purchased from Cryogenic Gases and used without further purification. Removal of solvents was accomplished on a rotary evaporator at reduced pressure. Crushed 4-Å molecular sieves were activated by thorough flame-drying under high vacuum immediately prior to use.

Physical Properties and Spectroscopic Measurements. Proton NMR (^{1}H NMR) spectra were recorded on a VXR-400 spectrometer (Varian) at 400 MHz or on a Inova-500 spectrometer (Varian) at 500 MHz. Carbon-13 NMR (^{13}C NMR) spectra were recorded on the aforementioned instruments at 100 and 125 MHz, respectively. The proton signal of residual, nondeuterated solvent (δ 7.26 ppm for $CHCl_3$, δ 7.15 ppm for C_6HD_5) was used as an internal reference for ^{1}H spectra measured in these solvents. For ^{13}C spectra, chemical shifts are reported relative to the δ 77.0 ppm resonance of $CDCl_3$ and δ 128.0 ppm for C_6D_6. Coupling constants are reported in Hz.

IR spectra were recorded as thin films on a Spectrum 1000 Fourier transform infrared (FRIR) (Perkin–Elmer). Optical rotations were measured on an Autopol III polarimeter (Rudolph Instruments, Fairfield, NJ) by using a quartz cell with a 1-ml capacity and a 10-cm path length. Mass spectra were recorded on a VG 70-250-S spectrometer manufactured by Micromass (Manchester, U.K.).

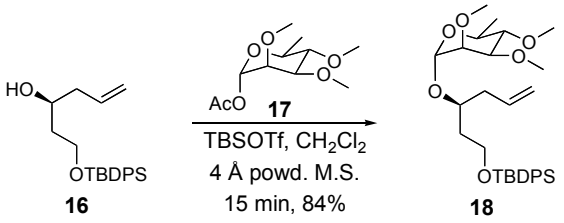
Analytical TLC was performed on Kieselgel 60 F_{254} glass plates precoated with a 0.25 mm thickness of silica gel. The TLC plates were visualized with UV light and/or by staining with Hanessian solution (a mixture of ceric sulfate and ammonium molybdate in aqueous sulfuric acid). Column chromatography was generally performed according to the method of Still (2) by using Kieselgel 60 (230–400 mesh) silica gel. Unless noted otherwise, all compounds isolated by chromatography were sufficiently pure by ^{1}H NMR analysis for use in subsequent reactions. The amount of silica gel used for purification was a 50:1 to 100:1 weight ratio of silica/crude product.

HPLC purifications were performed by using an HPLC system composed of two HPXL Rainin (Oakland, CA) pumps connected to various axial compression columns Dynamax (Houston, TX) packed with 60-Å irregular silica gel (Rainin). Samples were loaded into the system with a 2-ml 7125 injector (Rheodyne, Cotati, CA) and were detected by using either a UV-C detector (Rainin, Dynamax) or a RI-1 detector (Rainin, Dynamax). Integration of the various signals was performed by using the reprocessing program within the HPLC Method Manager (Dynamax).



16

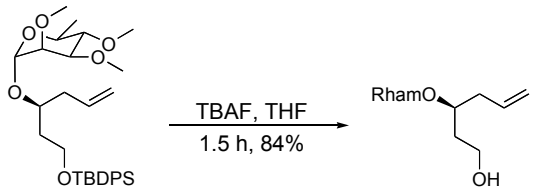
(3*S*)-1-(*tert*-Butyldiphenylsiloxy)hex-5-en-3-ol (16). This known compound was synthesized by published procedures (3, 4): $[\alpha]_D^{24.0}$-3.3° (*c* 4.4, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.71–7.68 (m, 4 H), 7.47–7.39 (m, 6 H), 5.86 (ddt, *J* = 17.1, 10.3, 7.1 Hz, 1 H), 5.15–5.11 (m, 1 H), 5.11–5.09 (m, 1 H), 4.01–3.95 (m, 1 H), 3.92–3.82 (m, 2 H), 3.28 (br s, 1 H), 2.34–2.23 (m, 2 H), 1.78–1.66 (m, 2 H), 1.07 (s, 9 H); IR (thin film) 3,455, 3,072, 3,051, 2,931, 2,858, 1,641, 1,590, 1,487, 1,472, 1,463, 1,428, 1,390, 1,362, 1,331, 1,308, 1,262, 1,190, 1,112, 1,083, 998, 939, 915, 876, 823, 738, 702, 688, 614 cm^{-1}; HRMS (ES) calcd for $C_{22}H_{30}O_2Si$ $[M + Na]^+$ 377.1913, found 377.1904 *m*/*z*.



16 **18**

(3*S*)-*tert*-Butyldiphenyl{3-[(6-Deoxy-2,3,4-trimethyl-*O*-methyl-α-L-mannopyranosyl)-oxy]-hex-5-enyloxy}silane (18). Powdered molecular sieves (4 Å, 29 mg) were flame-dried under vacuum in a 2-ml reaction vial. The vial was vented to argon and acceptor **16** (75 mg, 0.21 mmol), donor **17** (105 mg, 0.42 mmol), and CH_2Cl_2 (0.84 ml) were added. TBSOTf (24 μl, 0.1 mmol) was then added. The reaction turned yellow and then brown. The mixture was stirred for 5 min, at which point TLC analysis indicated the disappearance of **16**. Et_3N (0.5 ml) was added, and the reaction color dissipated. This mixture was poured into a 1:1 mixture of EtOAc and saturated $NaHCO_3$ (10 ml each). The layers were separated, and the aqueous layer was extracted twice with EtOAc (20 ml total). The combined organics were dried over $MgSO_4$, filtered, and concentrated, yielding a yellow oil. Purification of this oil by column chromatography (1:1 hexanes/Et_2O) afforded α-glycoside **18** (96 mg, 84%) as a clear oil. An analytical sample of **18** was prepared by preparative HPLC (2:1 hexanes/EtOAc): $[\alpha]_D^{23.7}$–4.3°

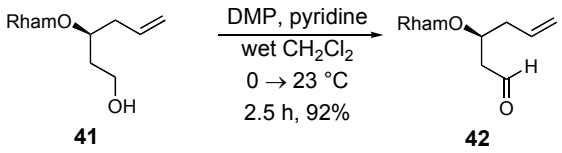
(*c* 2.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67–7.74 (m, 4 H), 7.45–7.36 (m, 6 H), 5.83–5.74 (m, 1 H), 5.06 (d, *J* = 1.0 Hz, 1 H), 5.05–5.02 (m, 1 H), 4.91 (d, *J* = 1.5 Hz, 1 H), 3.95–3.89 (m, 1 H), 3.78–3.70 (m, 2 H), 3.67 (dq, *J* = 9.3, 6.1 Hz, 1 H), 3.54 (s, 3 H), 3.46 (s, 3 H), 3.44–3.42 (m, 1 H), 3.41–3.39 (m, 1 H), 3.40 (s, 3 H), 3.11 (dd, *J* = 9.3, 9.3 Hz, 1 H), 2.32 (br dd, *J* = 5.9, 5.9 Hz, 2 H), 1.78–1.66 (m, 2 H), 1.27 (d, *J* = 6.1 Hz, 3 H), 1.05 (s, 9 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.5, 135.4, 134.5, 133.7, 133.6, 129.6, 127.6, 117.2, 96.8, 82.2, 81.1, 77.8, 75.2, 68.0, 60.8, 60.3, 58.8, 57.7, 39.7, 36.5, 26.8, 19.2, 17.6; IR (thin film) 3,072, 2,931, 2,858, 2,824, 1,641, 1,590, 1,472, 1,428, 1,389, 1,288, 1,194, 1,142, 1,106, 1,054, 1,038, 998, 915, 879, 823, 703, 614; HRMS (ES) calcd for $C_{31}H_{46}O_6Si$ $[M + Na]^+$ 565.2961, found 565.2959 *m*/z.



18 **41**

(3*S*)-3-[(6-Deoxy-2,3,4-trimethyl-*O*-methyl-α-L-mannopyranosyl)oxy]hex-5-en-1-ol (41). Silyl ether **18** (467 mg, 0.86 mmol) was dissolved in THF (8 ml) and cooled to 0°C. TBAF (1.7 ml, 1.7 mmol, 1.0 M solution in THF) was added. The reaction was warmed to ambient temperature and stirred for 1.25 h, at which point **18** had been consumed, as judged by TLC analysis. The reaction mixture was diluted with Et_2O (30 ml) and washed with saturated NH_4Cl (10 ml) and saturated $NaHCO_3$ (10 ml). The organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure affording a clear oil. Purification of this material by column chromatography (40 × 80 mm silica, 1:4 hexanes/EtOAc) afforded **41** (220 mg, 84%) as a light yellow oil: $[\alpha]_D^{23.8}$–18.3° (*c* 4.8, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$; partial) δ 5.78 (ddt, *J* = 17.3, 10.5, 7.3 Hz, 1 H), 5.11–5.07 (m, 1 H), 4.96 (d, *J* = 1.7 Hz, 1 H), 3.87 (br dddd, *J* = 6.6, 6.6 , 6.6 , 6.6 Hz, 1 H), 3.78–3.70 (m, 2 H), 3.66 (dq, *J* = 9.5, 6.4 Hz, 1 H), 3.54 (s, 3 H), 3.51 (dd, *J* = 3.2, 2.2 Hz, 1 H), 3.48 (s, 3 H), 3.43 (dd, *J* = 9.0, 3.2 Hz, 1 H), 3.12 (dd, *J* = 9.3, 9.3 Hz, 1 H), 2.43–2.30 (m, 2 H), 1.84–1.78 (m, 1 H), 1.75–1.68 (m, 2

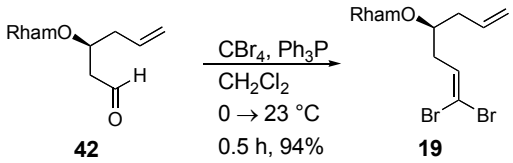
H), 1.26 (d, J = 6.4 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 134.1, 117.3, 96.6, 81.9, 80.7, 77.7, 75.8, 67.9, 60.5, 59.1, 58.7, 57.5, 39.4, 35.9, 17.5; IR (thin film) 3,475, 3,076, 2,976, 2,934, 2,827, 1,642, 1,449, 1,386, 1,346, 1,289, 1,196, 1,140, 1,118, 1,054, 997, 914, 880, 839, 777, 671 cm^{-1}; HRMS (ES) calcd for $C_{15}H_{28}O_6$ $[M + Na]^+$ 327.1784, found 327.1780 m/z.



41 **42**

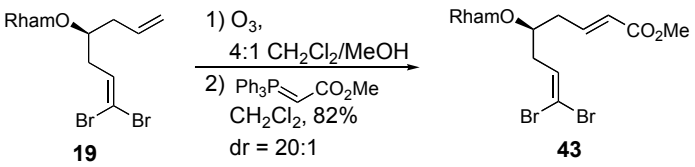
(3*S*)-3-[(6-Deoxy-2,3,4-trimethyl-*O*-methyl-α-L-mannopyranosyl)oxy]hex-5-enal (42). Alcohol **41** (207 mg, 0.68 mmol) was dissolved in CH_2Cl_2 (3.8 ml) and pyridine (0.28 ml, 3.5 mmol) was added. This mixture was cooled to 0°C, and Dess–Martin periodinane (434 mg, 1.0 mmol) was added in one portion. The reaction was stirred for 10 min, and wet CH_2Cl_2 (1.9 ml, generated by shaking a biphasic mixture of CH_2Cl_2 and H_2O in a separatory funnel) was added. The reaction mixture was then warmed to ambient temperature and stirred for 2 h, at which point TLC analysis indicated the complete consumption of **41**. The reaction was diluted with Et_2O (40 ml) and transferred to an Erlynmeyer flask containing a 1:1 mixture of 1 M $Na_2S_2O_3$ and saturated $NaHCO_3$ (30 ml total). After this biphasic mixture was vigorously stirred for 45 min, the layers were separated, and the organic layer was washed with saturated $NaHCO_3$ and brine, dried over $MgSO_4$, filtered, and concentrated yielding a yellow oil. Purification of this material by column chromatography (25 × 150 mm silica, 1:1 hexanes/EtOAc) afforded **42** (190 mg, 92%) as a yellow oil: $[\alpha]_D^{23.9}$–44.7° (c 0.6, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.80 (t, J = 1.7 Hz, 1 H), 5.81–5.73 (m, 1 H), 5.13 (m, 1 H), 5.11–5.09 (m, 1 H), 5.01 (d, J = 2.0 Hz, 1 H), 4.20 (dddd, J = 5.1, 5.1, 9.8, 9.8 Hz, 1 H), 3.62 (dq, J = 9.8, 6.4 Hz, 1 H), 3.54 (s, 3 H), 3.49 (s, 3 H), 3.49–3.46 (m, 2 H), 3.47 (s, 3 H), 3.44 (dd, J = 3.2, 2.0 Hz, 1 H), 3.39 (dd, J = 9.5, 3.4 Hz, 1 H), 3.12 (dd, J = 9.5, 9.5 Hz, 1 H), 2.69 (ddd, A of AB system, J = 17.1, 7.6, 2.0 Hz, 1 H), 2.60 (ddd, B of AB system, J = 17.1, 4.2, 1.2 Hz, 1 H), 2.47–2.41 (m, A of AB system, 1 H), 2.39–2.33 (m, B of AB system, 1 H), 1.27 (d, J = 6.4 Hz, 1 H); ^{13}C NMR (125 MHz,

$CDCl_3$) δ 200.4, 133.4, 118.5, 97.2, 82.0, 80.9, 77.6, 73.3, 68.4, 60.9, 58.9, 57.7, 47.9, 39.8, 17.6; IR (thin film) 3,078, 2,978, 2,933, 2,827, 2,729, 1,725, 1,642, 1,447, 1,386, 1,346, 1,322, 1,289, 1,197, 1,173, 1,141, 1,120, 1,104, 1,053, 997, 916, 879, 839, 792, 662 cm^{-1}; HRMS (ES) calcd for $C_{15}H_{26}O_6$ $[M + Na]^+$ 325, 1,627, found 325.1622 *m*/*z*.



1-[(1 *S*)-Allyl-4,4-dibromobut-3-enyloxy]-2,3,4-trimethyl-α-L-rhamnose (19). Ph_3P (567 mg, 2.2 mmol) was dissolved in CH_2Cl_2 (4.8 ml). CBr_4 (358 mg, 1.1 mmol) was added and the resulting orange mixture was stirred for 15 min and then cooled to 0°C. Aldehyde **42** (163 mg, 0.54 mmol) was added as a solution in CH_2Cl_2 (1 ml). The flask originally containing **42** was rinsed with CH_2Cl_2 (1 ml), and this wash was added to the reaction mixture. This orange mixture was stirred for 20 min, at which point TLC analysis indicated the complete consumption of **42**. The reaction mixture was then poured into a mixture of Et_2O (10 ml), EtOAc (10 ml), and saturated $Na_2S_2O_3$ (15 ml) in a separatory funnel, and this mixture was agitated. The layers were separated, and the organic layer was washed with saturated $Na_2S_2O_3$ and brine. The organic layer was dried over $MgSO_4$, filtered, and concentrated yielding a white solid. Purification of this crude material by column chromatography (4:1 hexanes/EtOAc) afforded **19** (231 mg, 94%) as a yellow oil. An analytical sample of **19** was prepared by preparative HPLC (45% EtOAc in hexanes): $[\alpha]_D^{23.8}$–39.2° (*c* 3.2, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 6.44 (t, *J* = 7.6 Hz, 1 H), 5.78 (ddt, *J* = 17.3, 10.5, 7.1 Hz, 1 H), 5.13–5.10 (m, 1 H), 5.10–5.08 (m, 1 H), 4.91 (d, *J* = 1.7 Hz, 1 H), 3.81 (dddd, *J* = 6.2, 6.2, 6.2, 6.2 Hz, 1 H), 3.63 (dq, *J* = 9.5, 6.4 Hz, 1 H), 3.55 (s, 3 H), 3.53 (dd, *J* = 3.4, 2.0 Hz, 1 H), 3.50 (s, 3 H), 3.50 (s, 3 H), 3.44 (dd, *J* = 9.3, 3.2 Hz, 1 H), 3.11 (dd, *J* = 9.3, 9.3 Hz, 1 H), 2.38–2.24 (m, 4 H), 1.26 (d, *J* = 6.1 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 134.3, 133.8, 118.0, 95.9, 90.8, 82.0, 80.9, 77.7, 75.0, 68.2, 60.9, 59.1, 57.7, 39.4, 36.8, 17.6; IR (thin film) 3,077, 2,977, 2,931, 2,825, 1,642, 1,444, 1,385, 1,345, 1,321,

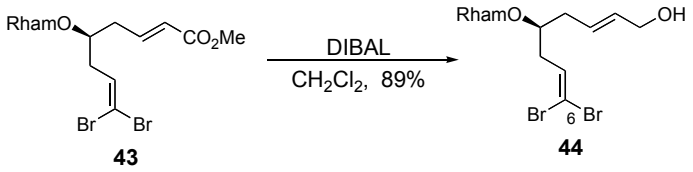
1,289, 1,196, 1,172, 1,141, 1,120, 1,105, 1,051, 996, 916, 879, 838, 780, 661 cm^{-1}; HRMS (ES) calcd for $C_{16}H_{26}Br_2O_5$ $[M + Na]^+$ 479.0045, found 479.0043 *m*/*z*.



(5*S*)-5-[(6-Deoxy-2,3,4-trimethyl-*O*-methyl-α-L-mannopyranosyl)oxy]-8,8-dibromo-octa-2,7-dienoic Acid Methyl Ester (43). Diene **19** (290 mg, 0.63 mmol) was dissolved in CH_2Cl_2 (3.3 ml). MeOH (0.9 ml) was added, followed by a catalytic amount of $KHCO_3$. The reaction mixture was cooled to –78°C and a stream of O_3 in O_2 was bubbled through the solution by using a 5.75-inch pipette. When the first trace of a faint yellow color was observed, ozone introduction was stopped and the reaction mixture was immediately purged with N_2 for 5 min. Ph_3P (258 mg, 0.98 mmol) was then added. The faint yellow color dissipated and the resulting clear reaction was allowed to warm to ambient temperature. This mixture was stirred for 2 h after which it was concentrated under reduced pressure, yielding aldehyde **43** as a pale yellow oil. This crude material was used immediately in the next reaction.

Crude **43** (theoretically, 0.6 mmol) was dissolved in CH_2Cl_2, and methyl(triphenylphosphoranylidene)acetate (318 mg, 0.95 mmol) was added. The resulting pale yellow reaction was stirred for 12 h, at which point TLC analysis indicated that the crude aldehyde had been consumed. Direct purification of this reaction mixture by column chromatography (3:7 hexanes/ Et_2O) afforded **43** (267 mg, 82% from **19**) as a pale yellow oil. An analytical sample of **43** was prepared by preparative HPLC (45% EtOAc in hexanes): $[\alpha]_D^{23.9}$–37.7° (*c* 4.0, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 6.91 (dt, *J* = 15.6, 7.3 Hz, 1 H), 6.43 (t, *J* = 7.3 Hz, 1 H), 5.91 (dt, *J* = 15.6, 1.5 Hz, 1 H), 4.89 (d, *J* = 2.0 Hz, 1 H), 3.90 (dddd, *J* = 6.1, 6.1, 6.1, 6.1 Hz, 1 H), 3.74 (s, 3 H), 3.57 (dq, *J* = 9.3, 6.4 Hz, 1 H), 3.54 (s, 3 H), 3.53 (dd, *J* = 3.2, 2.0 Hz, 1 H), 3.51 (s, 3 H), 3.51 (s, 3 H), 3.42 (dd, *J* = 9.3, 3.4 Hz, 1 H), 3.12 (dd, *J* = 9.3, 9.3 Hz, 1 H), 2.52–2.40 (m, 2 H), 2.35–2.31 (m, 2 H), 1.26 (d, *J* = 6.1

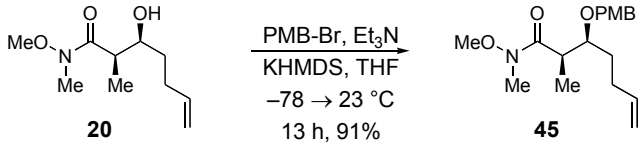
Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.3, 144.0, 133.7, 123.9, 96.4, 91.5, 81.9, 80.7, 77.7, 74.5, 68.5, 60.7, 59.1, 57.8, 51.5, 37.7, 37.3, 17.6; IR (thin film) 2,977, 2,932, 2,826, 1,724, 1,660, 1,437, 1,385, 1,321, 1,274, 1,199, 1,171, 1,141, 1,118, 1,104, 1,039, 916, 880, 838, 789, 656 cm^{-1}; HRMS (ES) calcd for $C_{18}H_{28}Br_2O_7$ $[M + Na]^+$ 537.0099, found 537.0098 *m*/*z*.



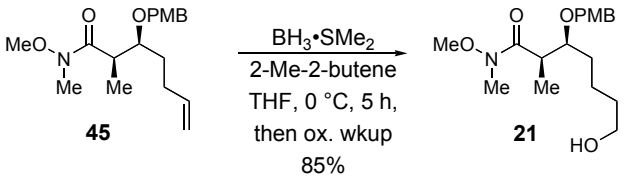
43 **44**

(5*S*)-5-[(6-Deoxy-2,3,4-trimethyl-*O*-methyl-α-L-mannopyranosyl)oxy]-8,8-dibromo-octa-2,7-dien-1-ol (44). Enoate **43** (113 mg, 0.22 mmol) was dissolved in CH_2Cl_2 (3.7 ml), and this mixture was cooled to –78°C. DIBAL (0.88 ml, 0.88 mmol, 1.0 M solution in hexanes) was added dropwise to the reaction mixture. This mixture was stirred for 1.25 h at –78°C, at which point **43** had been consumed, as judged by TLC analysis. The reaction was warmed to 0°C and then saturated $NaKC_4H_4O_6$ (Rochelle's salt) was added. Gas evolution was observed. Et_2O (13 ml) was added, and the biphasic mixture was warmed to ambient temperature and stirred vigorously for 12 h. The layers were separated, and the aqueous layer was extracted with Et_2O (20 ml). The combined organics were dried over $MgSO_4$, filtered, and concentrated under reduced pressure affording a clear oil. Purification of this crude material by column chromatography (3:7 hexanes/EtOAc) gave **44** (95 mg, 89%) as a clear oil. An analytical sample was prepared by preparative HPLC (85% EtOAc in hexanes): $[\alpha]_D^{24.0}$ –48.5° (*c* 5.7, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.44 (t, *J* = 7.6 Hz, 1 H), 5.76–5.70 (m, 1 H), 5.63–5.56 (m, 1 H), 4.97 (d, *J* = 1.7 Hz, 1 H), 4.12–4.04 (m, 2 H), 3.82 (dq, *J* = 7.8, 5.1 Hz, 1 H), 3.66 (dq, *J* = 9.5, 6.4 Hz, 1 H), 3.55 (s, 3 H), 3.52 (dd, *J* = 3.4, 2.0 Hz, 1 H), 3.50 (s, 3 H), 3.50 (s, 3 H), 3.49 (dd, *J* = 9.3, 3.4 Hz, 1 H), 3.11 (dd, *J* = 9.5, 9.5 Hz, 1 H), 2.37–2.33 (m, 2 H), 2.28–2.22 (m, 2 H), 1.75 (br s, 1 H), 1.26 (d, *J* = 6.4 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 134.0, 133.4, 128.0, 94.3, 91.0, 82.4, 80.9, 77.3, 72.5, 67.7, 63.4, 61.0, 59.1, 57.7, 37.7, 36.6, 17.7; IR (thin film) 3,460, 2,976,

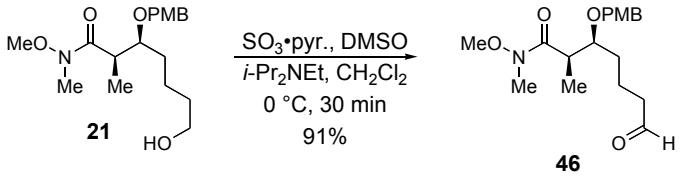
2,931, 2,827, 1,621, 1,446, 1,386, 1,346, 1,322, 1,290, 1,196, 1,172, 1,140, 1,118, 1,103, 1,046, 974, 914, 881, 837, 781, 656 cm^{-1}; HRMS (ES) calcd for $C_{17}H_{28}Br_2O_6$ $[M + Na]^+$ 509.0150, found 509.0140 *m*/*z*.



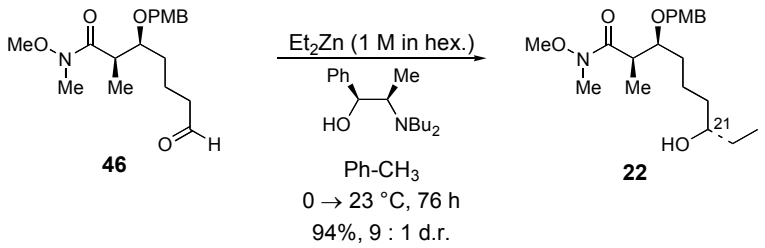
(2*R*,3*S*)-3-(4-Methoxybenzyloxy)-2-methylhept-6-enoic Acid *N*-methoxy-*N*-methylamide (45). The known alcohol **20** (5) (765 mg, 3.8 mmol) was dissolved in THF (18.5 ml) under N_2. Et_3N (2.4 ml, 17.2 mmol) was added, followed by *p*-methoxybenzyl bromide (2.68 g, 13.3 mmol). This mixture was cooled to –78°C, and then KHMDS (9.6 ml, 4.8 mmol, 0.5 M in $PhCH_3$) was added dropwise. The reaction mixture was stirred at –78°C for 2.5 h and then allowed to warm to ambient temperature overnight, at which point the starting material was consumed as judged by TLC analysis. The reaction was diluted with saturated NH_4Cl, followed by CH_2Cl_2. The layers were separated, and the aqueous layer was extracted three times with CH_2Cl_2. The combined organics were washed with saturated $NaHCO_3$, brine, dried over Na_2SO_4, filtered, and concentrated yielding a yellow oil. Purification of this oil by column chromatography (50x60 mm silica, 2:1 hexanes/EtOAc) provided **45** (1.11 g, 91%) as a light yellow oil: $[\alpha]_D^{26.2}$–20.3° (*c* 2.4, CH_2Cl_2); ^1H NMR (500 MHz, $CDCl_3$) δ 7.30–7.27 (m, 2 H), 6.89–6.86 (m, 2 H), 5.81 (dddd, *J* = 17.1, 10.3, 6.8, 6.8 Hz, 1 H), 5.03–4.99 (m, 1 H), 4.96–4.93 (m, 1 H), 4.52–2.48 (m, 2 H), 3.80 (s, 3 H), 3.66, (s, 3 H), 3.64 (m, *J* = 7.6, 3.9 Hz, 1 H), 3.18 (s, 3 H), 3.14–3.08 (m, 1 H), 2.27–2.18 (m, 1 H), 2.17–2.08 (m, 1 H), 1.68–1.55 (m, 2 H), 1.25 (d, *J* = 7.1 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.0, 159.0, 138.3, 130.4, 129.3, 114.3, 113.5, 79.8, 72.4, 61.2, 55.0, 39.8, 32.2, 31.9, 29.4, 14.1; IR (thin film) 3,075, 2,937, 2,838, 1,660, 1,613, 1,586, 1,514, 1,461, 1,417, 1,384, 1,302, 1,249, 1,210, 1,174, 1,110, 1,063, 1,036, 995, 913, 822 cm^{-1}; HRMS (ES) calcd for $C_{18}H_{27}NO_4$ $[M + Na]^+$ 344.1838, found 344.1836 *m*/*z*.



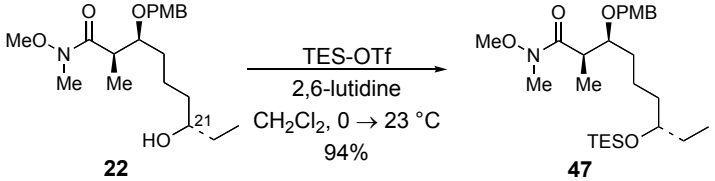
(2*R*,3*S*)-7-Hydroxy-3-(4-methoxybenzyloxy)-2-methylheptanoic Acid *N*-methoxy-*N*-methylamide (21). THF (1.4 ml) was added to 2-methyl-2-butene (0.94 ml, 1.9 mmol) in a 5-ml conical vial. This mixture was cooled to 0°C, and BH_3•SMe_2 (92 μl, 0.96 mmol) was added dropwise. After being stirred for 2.25 h, this borane mixture was added to a solution of **45** (97 mg, 0.30 mmol) in THF at 0°C. The reaction mixture was placed in a 0°C refrigerator for 2 h, at which point the starting olefin **45** was consumed, as judged by TLC analysis. The reaction was quenched by addition of a mixture of 35% H_2O_2 (2 ml) and saturated $NaHCO_3$ (5 ml). The resulting white slurry was stirred vigorously for 1.25 h while being allowed to warm to ambient temperature. The reaction mixture was diluted with EtOAc and saturated aqueous Na_2SO_3. Vigorous gas evoluation was observed. [Caution: on larger scales, the addition of Na_2SO_3 (or $Na_2S_2O_3$) should be done at 0°C because it is very exothermic.] The layers were separated and the aqueous layer was extracted twice with EtOAc. The combined organics were tested with peroxide detection strips to verify the absence of peroxides. The combined organics were then washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure, yielding a light yellow oil. This oil was purified by column chromatography (40 × 60 mm silica, 2:1 hexanes/acetone), which afforded **21** (87 mg, 85%) as a clear oil: $[\alpha]_D^{26.4}$–22.7° (*c* 0.8, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29–7.26 (m, 2 H), 6.89–6.85 (m, 2 H), 4.52–4.48 (m, 2 H), 3.80 (s, 3 H), 3.67 (s, 3 H), 3.64–3.59 (m, 2 H), 3.61 (dd, *J* = 6.3, 6.3 Hz, 1 H), 3.18 (s, 3 H), 3.14–3.08 (m, 1 H), 1.60–1.36 (m, 7 H), 1.24 (d, *J* = 7.1 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.3, 159.1, 130.6, 129.5, 113.7, 80.5, 72.6, 62.5, 61.4, 55.2, 45.5, 40.0, 32.9, 32.1, 21.4, 14.4; IR (thin film) 3,436 (br), 2,938, 2,867, 1,655, 1,613, 1,586, 1,514, 1,460, 1,421, 1,387, 1,302, 1,249, 1,174, 1,109, 1,060, 1,034, 994, 822 cm^{-1}; HRMS (ES) calcd for $C_{18}H_{29}NO_5$ $[M + Na]^+$ 362.1943, found 362.1947 *m*/*z*.



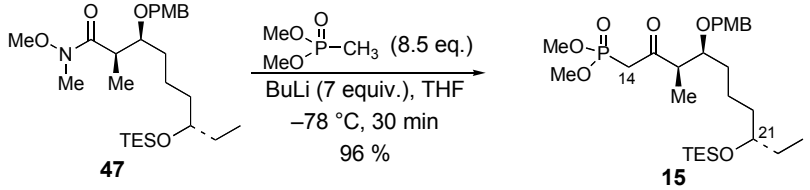
(2*R*,3*S*)-7-Hydroxy-3-(4-methoxybenzyloxy)-2-methyl-7-oxoheptanoic Acid *N*-methoxy-*N*-methylamide (46). Alcohol **21** was azeotropically dried by coevaporation from benzene. The dry residue was dissolved in CH_2Cl_2 (10 ml) and *i*-Pr_2NEt (0.81 ml, 4.7 mmol) was added, followed by DMSO (2.8 ml, 39.5 mmol). The reaction mixture was cooled to 0°C and SO_3•pyr (485 mg, 3.1 mmol) was added. The mixture was stirred for 20 min at 0°C, at which point **21** had been consumed, as judged by TLC analysis. Saturated $NaHCO_3$ (≈8 ml) was added, and the reaction was allowed to warm to ambient temperature with vigorous stirring. This mixture was then diluted with EtOAc, the layers were separated, and the aqueous layer was extracted twice with EtOAc. The combined organics were washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure, yielding a light yellow, odorous oil. Purification of this residue by column chromatography (50 × 60 mm silica, 2:1 hexanes/acetone) afforded **46** (305 mg, 91%) as a light yellow oil: $[\alpha]_D^{28.0}$–24.1° (*c* 2.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.72 (t, *J* = 1.7 Hz, 1 H), 7.29–7.26 (m, 2 H), 6.89–6.86 (m, 2 H), 4.52 (d, A of AB system, *J* = 10.7 Hz, 1 H), 4.48 (d, B of AB system, *J* = 10.7 Hz, 1 H), 3.80 (s, 3 H), 3.67 (s, 3 H), 3.62 (ddd, *J* = 7.3, 7.3, 4.2, 1 H), 3.18 (s, 3 H), 3.14–3.08 (m, 1 H), 2.40 (app ddd, *J* = 7.3, 7.3, 1.7 Hz, 2 H), 1.84–1.74 (m, 1 H), 1.71–1.48 (m, 3 H), 1.24 (d, *J* = 6.8 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.4, 176.1, 159.2, 130.5, 129.5, 113.8, 80.1, 72.6, 61.4, 55.2, 43.8, 39.9, 32.3, 32.1, 17.9, 14.5; IR (thin film) 3,497, 2,939, 2,876, 2,838, 2,724, 1,722, 1,656, 1,613, 1,586, 1,514, 1,460, 1,420, 1,386, 1,302, 1,249, 1,210, 1,175, 1,149, 1,110, 1,060, 1,034, 993, 822 cm^{-1}; HRMS (ES), calcd for $C_{18}H_{27}NO_5$ $[M + Na]^+$ 360.1787, found 360.1798 *m/z*.



(2*R*,3*S*,7*S*)-7-Hydroxy-3-(4-methoxybenzyloxy)-2-methyl-7-oxononanoic Acid *N*-methoxy-*N*-methylamide (22). Aldehyde **46** (81 mg, 0.24 mmol) was dissolved in toluene (0.5 ml) under argon and (–)-*N,N*-dibutylnorephedrine (15 μl, 0.054 mmol) was added. This mixture was stirred for 30 min and cooled to 0°C, and diethylzinc (1.0 ml, 1.0 mmol, 1.0 M solution in hexanes) was added dropwise. After the addition was complete, the reaction was allowed to warm to ambient temperature and was then stirred for 76 h. At this point, **46** had been consumed, as judged by TLC analysis. The reaction was cooled to 0°C and saturated NaCl was added (NH_4Cl can also be used). This mixture was further diluted with EtOAc, the layers were separated, and the aqueous layer was extracted with EtOAc. The combined organics were washed with saturated $NaHCO_3$ and brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure yielding a clear oil. Purification of this material by column chromatography (25 × 90 mm silica, 3:2 hexanes/acetone) provided **22** (83 mg, 94%) as a clear oil: $[\alpha]_D^{26.0}$–18.1° (*c* 1.5, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30–7.27 (m, 2 H), 6.89–6.85 (m, 2 H), 4.52–4.48 (m, 2 H), 3.80 (s, 3 H), 3.66 (s, 3 H), 3.64–3.60 (m, 1 H), 3.50–3.46 (m, 1 H), 3.18 (s, 3 H), 3.14–3.06 (m, 1 H), 1.60–1.33 (m, 9 H), 1.25 (d, *J* = 6.8 Hz, 3 H), 0.93 (t, *J* = 7.3 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.3, 159.2, 130.7, 129.5, 113.7, 80.4, 72.9, 72.6, 61.4, 55.2, 40.1, 37.0, 33.1, 32.1, 30.1, 21.4, 14.4, 9.9; IR (thin film) 3,452, 2,936, 2,874, 1,656, 1,613, 1,586, 1,514, 1,461, 1,421, 1,385, 1,302, 1,249, 1,174, 1,110, 1,062, 1,035, 994, 936, 822, 757, 736 cm^{-1}; HRMS (ES), calcd for $C_{20}H_{33}NO_5$ $[M + Na]^+$ 390.2256, found 390.2251 *m*/*z*.

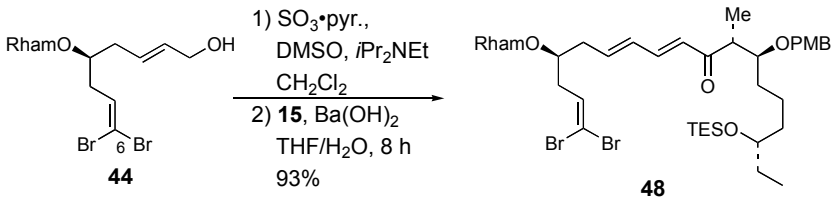


(2*R*,3*S*,7*S*)-7-Hydroxy-3-(4-methoxybenzyloxy)-2-methyl-7-triethylsiloxy-nonanoic Acid *N*-methoxy-*N*-methylamide (47). Alcohol **22** (190 mg, 0.52 mmol) was azeotropically dried by coevaporation from benzene, then was dissolved in CH_2Cl_2 (5.2 ml) and 2,6-lutidine (0.2 ml, 1.7 mmol) was added. The reaction mixture was then cooled to 0°C. TESOTf (0.23 ml, 1.0 mmol) was added slowly, and the reaction was stirred at 0°C for 1 h, at which point TLC analysis indicated the disappearance of **22**. The reaction mixture was diluted with saturated $NaHCO_3$ (≈4 ml) and stirred vigorously while being warmed to ambient temperature. The reaction was further diluted with EtOAc, the mixture was agitated, and the layers were separated. The aqueous layer was extracted with EtOAc. The combined organics were then washed with brine, dried over Na_2SO_4, filtered, and concentrated, yielding a bronze oil. Purification of this material by column chromatography (40 × 100 mm silica, 7:3 hexanes/EtOAc) afforded **47** (235 mg, 94%) as a light bronze oil: $[\alpha]_D^{27.2}$–15.3° (*c* 2.3, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29–7.26 (m, 2 H), 6.88–6.84 (m, 2 H), 4.52–4.47 (m, 2 H), 3.79 (s, 3 H), 3.65 (s, 3 H), 3.63–3.59 (m, 1 H), 3.55 (dddd, *J* = 5.4, 5.4, 5.4, 5.4 Hz, 1 H), 3.17 (s, 3 H), 3.12–3.04 (m, 1 H), 1.58–1.28 (m, 8 H), 1.23 (d, *J* = 7.1 Hz, 3 H), 0.95 (t, *J* = 8.1 Hz, 9 H), 0.85 (t, *J* = 7.3 Hz, 3 H), 0.58 (q, *J* = 8.1 Hz, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.1, 159.0, 130.5, 129.3, 113.5, 80.4, 73.2, 72.4, 61.1, 54.9, 39.9, 36.6, 33.3, 31.9, 29.5, 21.2, 14.0, 9.4, 6.7, 4.9; IR (thin film) 2,956, 2,938, 2,912, 2,876, 1,663, 1,614, 1,587, 1,514, 1,461, 1,415, 1,381, 1,302, 1,248, 1,173, 1,111, 1,063, 1,038, 1,008, 892, 822, 741, 671, 620 cm^{-1}; HRMS (ES), calcd for $C_{26}H_{47}NO_5Si$ $[M + Na]^+$ 504.3121, found 504.3124 *m*/*z*.



(3*R*,4*S*,8*S*)-[4-(4-Methoxybenzyloxy)-3-methyl-2-oxo-8-triethylsiloxy-decyl]phosphonic Acid Dimethyl Ester (15). Dimethyl methylphosphonate (527 mg, 4.2 mmol) was dissolved in THF (6

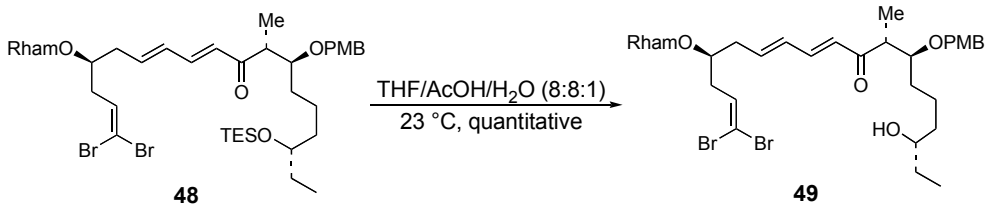
ml). This solution was cooled to –78°C, and BuLi (2.3 ml, 3.57 mmol, 1.55 M in hexanes) was added slowly over 5 min. The resulting mixture was stirred at –78°C for 1.25 h and then **47** (232 mg, 0.48 mmol) was added as a solution in THF (2 ml). The flask originally containing **47** was rinsed with 0.6 ml THF and twice with 0.5 ml of THF; these rinses were added to the reaction mixture. The reaction was stirred at –78°C for 1.5 h, at which point TLC analysis indicated **47** had been consumed. The reaction flask was placed in a 0°C bath, stirred for 2 min, diluted slowly with saturated NH_4Cl, and then stirred vigorously while warming to 0°C. This mixture was diluted with EtOAc, the layers were separated, and the aqueous layer was extracted with EtOAc. The combined organics were washed with brine, dried over Na_2SO_4, filtered, and concentrated yielding a bronze oil. This material was purified by column chromatography (40 × 120 mm silica, 3:2 hexanes/acetone) affording **15** (250 mg, 96%) as a light bronze oil: $[\alpha]_D^{25.0}$–97.4° (*c* 1.8, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29–7.26 (m, 2 H), 6.89–6.85 (m, 2 H), 4.62 (d, A of AB system, *J* = 11.0 Hz, 1 H), 4.45 (d, B of AB system, *J* = 11.0 Hz, 1 H), 3.80 (s, 3 H), 3.76 (d, *J* = 11.2 Hz, 3 H), 3.73 (d, *J* = 11.2 Hz, 3 H), 3.56–3.50 (m, 2 H), 3.48 (dd, *J* = 23.0, 13.7 Hz, 1 H), 3.24 (app dq, *J* = 7.1, 4.4 Hz, 1 H), 2.98 (dd, *J* = 22.2, 13.7Hz , 1 H), 1.64–1.18 (m, 8 H), 1.08 (d, *J* = 7.1 Hz, 3 H), 0.95 (t, *J* = 8.1 Hz, 9 H), 0.85 (t, *J* = 7.6 Hz, 3 H), 0.58 (q, *J* = 7.8 Hz, 6 H); ^{13}C (125 MHz, $CDCl_3$) δ 204.0 (d, *J* = 26 Hz), 159.1, 129.9, 129.4, 113.5, 80.2, 73.0, 71.2, 55.0 (d, *J* = 16 Hz), 52.6 (d, *J* = 82 Hz), 49.0, 41.6, 40.6, 36.2, 31.4, 29.6, 21.8, 11.7, 9.4, 6.8, 4.9; IR (thin film), 3,483, 2,955, 2,913, 2,876, 1,710, 1,613, 1,586, 1,515, 1,461, 1,414, 1,401, 1,379, 1,302, 1,250, 1,180, 1,110, 1,035, 884, 812, 743, 671; HRMS (ES), calcd for $C_{27}H_{49}O_7PSi$ $[M + Na]^+$ 567.2883, found 567.2907 *m*/*z*.



(3*S*,7*S*,8*R*,10*E*,12*E*,15*S*)-18,18-Dibromo-7-(4-methoxybenzyloxy)-8-methyl-3-triethylsiloxy-15-[(6-deoxy-2,3,4-trimethyl-*O*-methyl-α-L-mannopyranosyl)oxy]octadeca-10,12,17-trien-9-one (48). Alcohol **44** (100 mg, 0.20 mmol) was azeotropically dried by coevaporation from benzene. The dry residue was dissolved in CH_2Cl_2 (2.1 ml) and *i*Pr_2NEt (0.25 ml, 7.2 mmol) was added, followed by DMSO (0.15 ml, 10.6 mmol). This mixture was cooled to 0°C, and SO_3•pyr. (128 mg, 0.80 mmol) was added. The reaction mixture was stirred at 0°C for 20 min, at which point **44** had been consumed as judged by TLC analysis. Saturated $NaHCO_3$ was added, the ice bath was removed, and the biphasic mixture was stirred vigorously for 20 min. This mixture was then diluted with EtOAc, the layers were separated, and the organic layer was extracted with EtOAc. The combined organics were washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure yielding aldehyde **14** as a bronze, odorous oil. Residual pyridine was removed from **14** by coevaporation from benzene, followed by placement of the resulting oil under high vacuum for 1 h. This crude material was used directly in the subsequent Horner–Wadsworth–Emmons reaction.

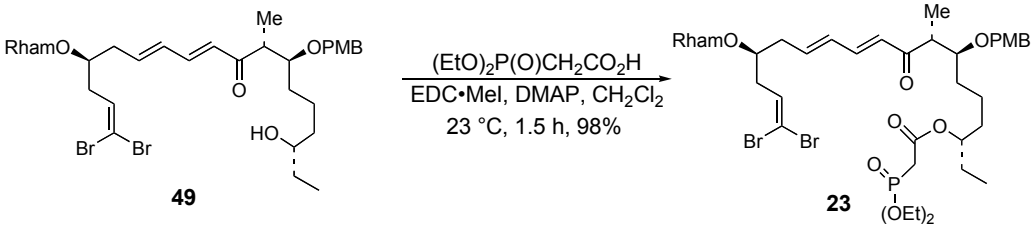
$Ba(OH)_2$•$8H_2O$ was activated by heating at 140°C under a stream of N_2 with a bleed needle for 2 h. Phosphonate **15** (128 mg, 0.23 mmol) was dissolved in THF (1.0 ml), and a portion of the activated $Ba(OH)_2$ (42 mg, 0.22 mmol) was added. The resulting slurry was stirred vigorously for 70 min, and then the crude aldehyde prepared above (**14**, theoretically, 0.20 mmol) was added as a solution in 40:1 THF/H_2O (0.5 ml). The flask that had contained **14** was rinsed twice with 0.35 ml of 40:1 THF/H_2O, and these rinses were added to the reaction mixture. This mixture became very viscous after 10 min, and the stirring velocity was increased. This vigorous stirring was continued for 6.5 h, at which point TLC analysis indicated that aldehyde **14** had been consumed. The reaction mixture was diluted with saturated $NaHCO_3$, followed by EtOAc. The layers were separated, and the aqueous layer was extracted with EtOAc. The combined organics were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure, yielding a bronze oil. This material was purified by

column chromatography (50 × 120 mm silica, 7:3 hexanes/EtOAc) affording diene **48** (168 mg, 93%) as a clear oil: $[\alpha]_D^{26.2}$–41.4° (*c* 0.57, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.26–7.23 (m, 2 H), 7.16 (dd, *J* = 15.1, 10.7 Hz, 1 H), 6.88–6.84 (m, 2 H), 6.43 (dd, *J* = 7.6, 7.6 Hz, 1 H), 6.26–6.20 (m, 1 H), 6.23 (d, *J* = 15.4 Hz, 1 H), 6.13–6.07 (m, 1 H), 4.90 (d, *J* = 2.0 Hz, 1 H), 4.49–4.44 (m, 2 H), 3.85 (dddd, *J* = 5.9, 5.9, 5.9, 5.9 Hz, 1 H), 3.80 (s, 3 H), 3.64 (q, *J* = 5.6 Hz, 1 H), 3.60–3.50 (m, 3 H), 3.53 (s, 3 H), 3.51 (s, 3 H), 3.50 (s, 3 H), 3.43 (dd, *J* = 9.3, 3.4 Hz, 1 H), 3.11 (dd, *J* = 9.3, 9.3 Hz, 1 H), 2.82–2.67 (m, 1 H), 2.50–2.37 (m, 2 H), 2.32 (dd, *J* = 7.3, 5.6 Hz, 2 H), 1.52–1.26 (m, 8 H), 1.25 (d, *J* = 6.4 Hz, 3 H), 1.16 (d, *J* = 7.1 Hz, 3 H), 0.95 (t, *J* = 8.1 Hz, 9 H), 0.85 (t, *J* = 7.6 Hz, 3 H), 0.58 (q, *J* = 8.3 Hz, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.4, 159.1, 141.8, 139.4, 133.9, 131.9, 130.5, 129.4, 128.1, 113.6, 96.4, 91.2, 81.8, 80.8, 80.3, 77.6, 75.0, 73.3, 72.0, 68.4, 60.8, 59.0, 57.7, 55.1, 48.6, 38.6, 37.1, 36.6, 32.9, 29.7, 21.6, 17.7, 12.6, 9.5, 6.9, 5.0; IR (thin film) 2,935, 2,876, 2,835, 1,684, 1,657, 1,636, 1,613, 1,594, 1,514, 1,459, 1,368, 1,347, 1,302, 1,248, 1,196, 1,173, 1,141, 1,119, 1,105, 1,038, 915, 881, 823, 782, 743, 659 cm^{-1}; HRMS (ES) calcd for $C_{42}H_{68}Br_2O_9Si$ $[M + Na]^+$ 925.2897, found 925.2896 *m*/*z*.



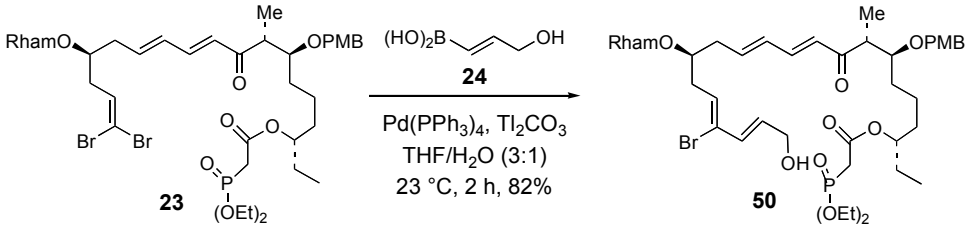
(3*S*,7*S*,8*R*,10*E*,12*E*,15*S*)-18,18-Dibromo-3-hydroxy-7-(4-methoxybenzyloxy)-8-methyl-15-[(6-deoxy-2,3,4-trimethyl-*O*-methyl-α-L-mannopyranosyl)oxy]octadeca-10,12,17-trien-9-one (49). Triene **48** (465 mg, 0.51 mmol) was dissolved in THF (11 ml). AcOH (11 ml) was added, followed by H_2O (1.45 ml). The reaction mixture was stirred at ambient temperature for 2 h, at which point **48** was consumed, as judged by TLC analysis. The reaction mixture was transferred by pipette to a vigorously stirred biphasic mixture of EtOAc, saturated $NaHCO_3$, and solid $NaHCO_3$. This mixture was stirred vigorously until gas evolution ceased and then transferred to a separatory funnel. The layers were

separated, and the aqueous layer was extracted twice with EtOAc (50 ml each). The combined organics were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure, yielding a yellow oil. This material was purified by column chromatography (40 × 105 mm silica, 7:3 hexanes/acetone) affording **49** (403 mg, quantitative) as a yellow oil: $[\alpha]_D^{25.6}$–33.2° (*c* 0.71, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27–7.23 (m, 2 H), 7.16 (dd, *J* = 15.4, 10.7 Hz, 1 H), 6.88–6.84 (m, 2 H), 6.42 (dd, *J* = 7.3, 7.3 Hz, 1 H), 6.23 (dd, *J* = 15.1, 10.7 Hz, 1 H), 6.22 (d, *J* = 15.1 Hz, 1 H), 6.14–6.08 (m, 1 H), 4.89 (d, *J* = 1.7 Hz, 1 H), 4.48 (d, A of AB system, *J* = 11.0 Hz, 1 H), 4.44 (d, B of AB system, *J* = 11.0 Hz, 1 H), 3.84 (dddd, *J* = 5.6, 5.6, 5.6, 5.6 Hz, 1 H), 3.79 (s, 3 H), 3.67–3.63 (m, 1 H), 3.56 (dq, *J* = 9.3, 6.1 Hz, 1 H), 3.53 (s, 3 H), 3.50 (s, 3 H), 3.50 (s, 3 H), 3.50–3.44 (m, 1 H), 3.42 (dd, *J* = 9.3, 3.2 Hz, 1 H), 3.11 (dd, *J* = 9.3, 9.3 Hz, 1 H), 2.96 (app quint., *J* = 6.8 Hz, 1 H), 2.49–2.37 (m, 2 H), 2.32 (dd, *J* = 7.3, 5.6 Hz, 2 H), 1.58–1.29 (m, 10 H), 1.25 (d, *J* = 6.1 Hz, 3 H), 1.17 (d, *J* = 6.8 Hz, 3 H), 0.92 (t, *J* = 7.6 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.6, 142.0, 139.6, 133.9, 131.9, 130.5, 129.5, 113.7, 96.4, 91.3, 81.9, 80.8, 80.1, 77.6, 75.0, 73.0, 72.0, 68.4, 60.8, 59.1, 57.7, 55.2, 48.5, 38.6, 37.2, 36.8, 32.6, 30.1, 21.7, 17.7, 12.8, 9.8; IR (thin film) 3,490, 2,934, 2,835, 1,682, 1,656, 1,635, 1,613, 1,593, 1,514, 1,460, 1,347, 1,302, 1,248, 1,196, 1,174, 1,140, 1,118, 1,103, 1,037, 1,002, 915, 881, 822, 782, 733, 654; HRMS (ES) calcd for $C_{36}H_{54}Br_2O_9$ $[M + Na]^+$ 811.2032, found 811.2032 *m*/*z*.



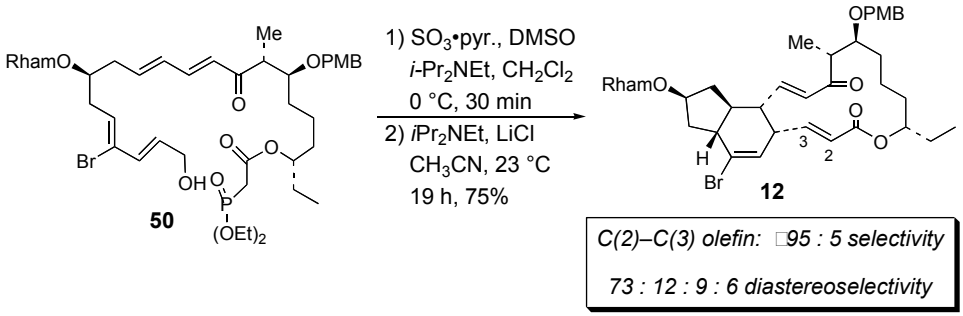
(1*S*,5*S*,6*R*,8*E*,10*E*,13*S*)-(Diethoxyphosphoryl)acetic Acid 16,16-Dibromo-1-ethyl-5-(4-methoxybenzyloxy)-6-methyl-7-oxo-13-[(6-deoxy-2,3,4-trimethyl-*O*-methyl-α-L-mannopyranosyl)oxy]hexadeca-8,10,15-trienyl Ester (23). Alcohol **49** (100 mg, 0.13 mmol) was azeotropically dried by coevaporation from benzene. Diethylphosphonoacetic acid (185 mg, 0.94

mmol) was added and this mixture was dissolved in CH_2Cl_2 (5.1 ml). EDC•MeI (217 mg, 0.73 mmol) was added, followed by a catalytic amount of DMAP. The resulting bright yellow solution became warm and then turned orange. This orange solution was stirred for 1.5 h, at which point TLC analysis indicated that **49** had been consumed. The reaction mixture was diluted with ≈5 ml of hexanes, and the resulting slurry was purified directly by chromatography (40 × 100 mm silica, 3:1 hexanes/acetone → 2:1 hexanes/acetone) affording **23** (121 mg, 98%) as a yellow oil. An analytical sample of **23** was prepared by preparative HPLC: $[\alpha]_D^{26.6}$–47.4° (*c* 0.55, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$; partial) δ 7.27–7.22 (m, 2 H), 7.16 (dd, *J* = 15.1, 10.7 Hz, 1 H), 6.88–6.84 (m, 2 H), 6.43 (dd, *J* = 7.3, 7.3 Hz, 1 H), 6.28–6.20 (m, 1 H), 6.24 (d, *J* = 15.4 Hz, 1 H), 6.14–6.08 (m, 1 H), 4.90 (d, *J* = 1.7 Hz, 1 H), 4.84–4.78 (m, 1 H), 4.48 (d, A of AB system, *J* = 11.0 Hz, 1 H), 4.42 (d, B of AB system, *J* = 11.0 Hz, 1 H), 3.85 (dddd, *J* = 5.7, 5.7, 5.7, 5.7 Hz, 1 H), 3.80 (s, 3 H), 3.65–3.60 (m, 1 H), 3.56 (dq, *J* = 9.3, 6.1 Hz, 1 H), 3.53 (s, 3 H), 3.51 (s, 3 H), 3.50 (s, 3 H), 3.42 (dd, *J* = 9.3, 3.4 Hz, 1 H), 3.11 (dd, *J* = 9.3, 9.3 Hz, 1 H), 2.95–2.91 (m, 1 H), 2.93 (dd, *J* = 21.7, 3.4 Hz, 2 H), 2.50–2.38 (m, 2 H), 2.32 (dd, *J* = 7.3, 5.9 Hz, 2 H), 1.61–1.42 (m, 9 H), 1.33 (t, *J* = 7.1 Hz, 6 H), 1.24 (d, *J* = 6.4 Hz, 3 H), 1.16 (d, *J* = 7.1 Hz, 3 H), 0.88 (t, *J* = 7.3 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.2, 165.4, 141.8, 139.5, 133.8, 131.7, 130.3, 129.3, 113.6, 96.3, 91.1, 81.7, 80.7, 79.9, 77.5, 76.6, 74.9, 71.9, 68.3, 60.6, 59.0, 57.6, 55.1, 48.5, 38.5, 37.1, 34.9, 33.6, 33.2, 32.3, 26.6, 21.3, 17.6, 16.2, 16.1, 12.6, 9.3; IR (thin film) 2,974, 2,934, 2,835, 1,682, 1,656, 1,636, 1,612, 1,594, 1,514, 1,460, 1,386, 1,368, 1,348, 1,273, 1,250, 1,205, 1,173, 1,140, 1,118, 1,104, 1,031, 972, 913, 836, 783; HRMS (ES) calcd for $C_{42}H_{65}Br_2O_{13}P$ [M + Na]$^+$ 989.2427, found 989.2432 *m*/*z*.



(1*S*,5*S*,6*R*,8*E*,10*E*,13*S*,14*R*,15*Z*,17*E*)-(Diethoxyphosphoryl)acetic Acid 16-Bromo-1-ethyl-19-hydroxy-5-(4-methoxybenzyloxy)-6-methyl-7-oxo-13-[(6-deoxy-2,3,4-trimethyl-*O*-methyl-α-L-mannopyranosyl)oxy]hexadeca-8,10,15-tetraenyl Ester (50). THF and H_2O were degassed separately by means of the freeze–pump–thaw method (three cycles, vent to argon). Vinyl boronic acid **24** (45 mg, 0.44 mmol) was transferred in MeOH to a flask containing **23** (80 mg, 0.083 mmol), and this mixture was concentrated under reduced pressure, placed under high vacuum, and vented to argon. The evacuate/vent cycle was repeated three times and then degassed THF (2.1 ml) was added, followed by degassed H_2O (0.7 ml). $Pd(PPh_3)_4$ (70 mg, 0.061 mmol) was added, and the resulting yellow suspension was stirred for 5 min, at which point Tl_2CO_3 (80 mg, 0.17 mmol) was added. The resulting yellow, heterogeneous reaction was protected from light with aluminum foil and stirred under argon for 1 h. At this point, additional $Pd(PPh_3)_4$ (30 mg, 0.026 mmol), and a small amount of Tl_2CO_3 was added. Stirring was continued for an additional 1 h, at which point phosphonate **23** was consumed, as judged by TLC analysis. The pale yellow reaction mixture was diluted with Et_2O, followed by 1 M $NaHSO_4$. The resulting bright yellow biphasic mixture was stirred vigorously for 10 min and then filtered through Celite, rinsing with EtOAc. The layers were separated, and the aqueous layer was extracted with EtOAc. The combined organics were washed with brine, dried over Na_2SO_4, filtered, and concentrated, yielding a yellow solid. Purification of this material by column chromatography (25 × 120 mm silica, 2:3 hexanes/acetone) afforded **50** (64 mg, 82%) as a yellow oil. An analytic sample of **50** was prepared by preparative HPLC (EtOAc): $[\alpha]_D^{24.0}$–39.0° (*c* 1.5, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$; partial) δ 7.25–7.22 (m, 2 H), 7.15 (dd, *J* = 15.1, 10.5 Hz, 1 H), 6.88–6.84 (m, 2 H), 6.32 (d, *J* = 14.7 Hz, 1 H), 6.25–6.10 (m, 4 H), 5.96 (dd, *J* = 7.3, 7.3 Hz, 1 H), 4.93 (d, *J* = 1.7 Hz, 1 H), 4.84–4.78 (m, 1 H) 4.48 (d, A of AB system, *J* = 11.0 Hz, 1 H), 4.42 (d, B of AB system, *J* = 11.0 Hz, 1 H), 3.88 (dddd, *J* = 5.9, 5.9, 5.9, 5.9 Hz, 1 H), 3.79 (s, 3 H), 3.65–3.60 (m, 1 H), 3.56 (dq, *J* = 9.8, 6.4 Hz, 1 H), 3.52 (s, 3 H), 3.50 (dd, *J* = 3.2, 2.0 Hz, 1 H) 3.49 (s, 3 H), 3.46 (s, 3 H), 3.42 (dd, *J* = 9.3, 3.2 Hz,

1 H), 3.10 (dd, J = 9.5, 9.5 Hz, 1 H), 2.95–2.89 (m, 1 H), 2.92 (dd, J = 21.7, 3.4 Hz, 2 H), 2.55 (dd, J = 6.1, 6.1 Hz, 2 H), 2.49–2.38 (m, 2 H), 1.71 (br s, 1 H), 1.58–1.40 (m, 7 H), 1.25 (d, J = 6.1 Hz, 3 H), 1.16 (d, J = 6.8 Hz, 3 H), 0.89 (t, J = 7.3 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.5, 165.5 (d, J = 25.5 Hz), 159.2, 142.2, 140.3, 133.7, 131.7, 130.5, 129.1, 128.7, 127.9, 127.1, 113.7, 95.9, 82.0, 80.9, 80.1, 72.7, 75.4, 72.1, 68.4, 62.6 (d, J = 14.0 Hz), 62.6 (d, J = 14.0 Hz), 62.3, 60.8, 59.0, 57.7 (d, J = 6.5 Hz), 55.2, 48.7, 38.6, 35.6, 35.0, 33.9, 33.4, 32.5, 26.7, 21.4, 17.7, 16.3, 16.3, 12.8, 9.4; IR (thin film) 3,418, 2,974, 2,934, 2,836, 1,732, 1,682, 1,655, 1,634, 1,613, 1,591, 1,514, 1,456, 1,386, 1,368, 1,274, 1,250, 1,206, 1,174, 1,104, 1,030, 974, 914, 837, 785, 756, 653; HRMS (ES) calcd for $C_{45}H_{70}BrO_{14}P$ [M + Na]$^+$ 967.3584, found 967.3574 m/z.

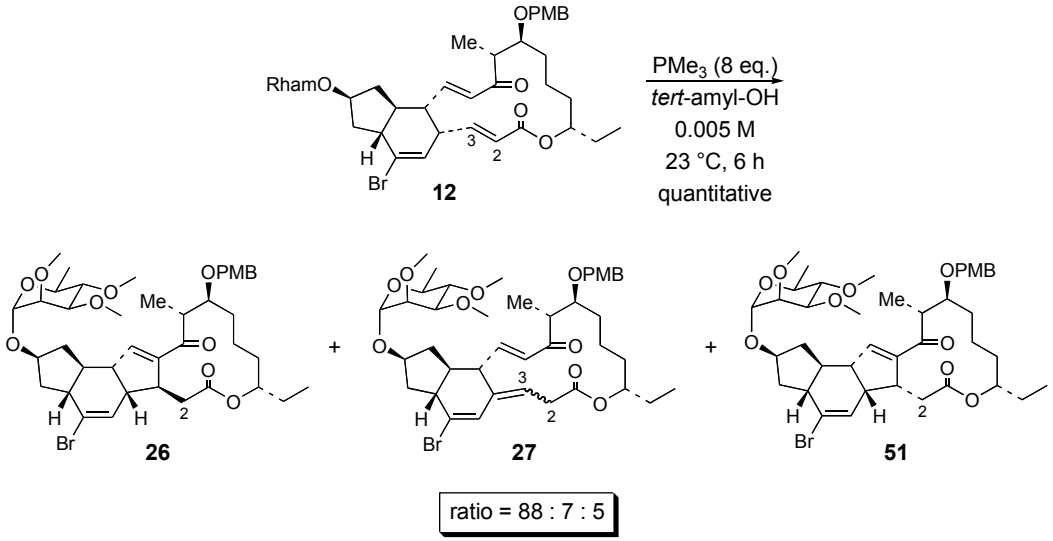


(1*R*,2*S*,3a*S*,4*S*,5*E*,8*R*,9*S*,13*S*,16*E*,18*R*,20a*S*)-20-Bromo-13-ethyl-9-(4-methoxybenzyl-oxy)-8-methyl-2-[(6-deoxy-2,3,4-trimethyl-*O*-methyl-α-L-mannopyranosyl)oxy]-2,3,3a,4,18,20a-hexahydro-1*H*-indeno[5,4-*e*]oxacyclopentadeca-5,16-diene-7,15-dione (12). Alcohol **50** (155 mg, 0.16 mmol) was azeotropically dried by coevaporation from benzene. The dry residue was dissolved in CH_2Cl_2 (8.0 ml). i-Pr_2NEt (0.20 ml, 1.2 mmol) was added, followed by DMSO (0.10 ml, 1.4 mmol). The reaction mixture was cooled to 0°C and SO_3•pyr (104 mg, 0.65 mmol) was added. The resulting reaction mixture was stirred at 0°C for 25 min, at which point TLC analysis indicated the disappearance of **50**. The reaction mixture was diluted with saturated $NaHCO_3$ (≈6 ml), the ice bath was removed, and the biphasic mixture was stirred vigorously for 5 min. This mixture was diluted with EtOAc, the layers were separated, and the aqueous layer was extracted with EtOAc. The combined organics were washed with brine, dried over Na_2SO_4, filtered, and concentrated, yielding aldehyde **25**

as a yellow/orange oil. Residual pyridine was removed from **25** by coevaporation from benzene and the resulting residue was used directly in the next reaction.

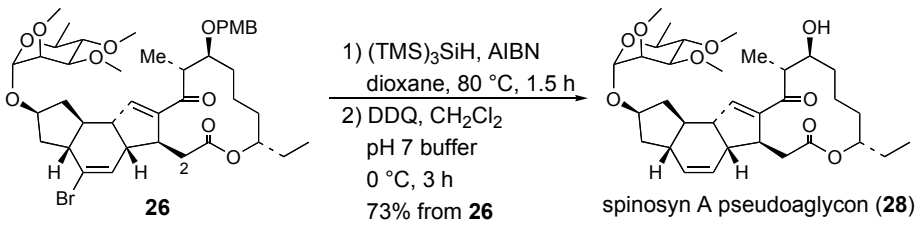
The crude aldehyde **25** (theoretically, 0.16 mmol) was dissolved in CH_3CN (160 ml) under argon. Dry LiCl (255 mg, 6.0 mmol) was added and the resulting heterogeneous mixture was stirred slowly for 5 min to allow the stir bar to grind the LiCl. *i*-Pr_2NEt (0.95 ml, 5.5 mmol) was added and the slow stirring was continued until the LiCl was very finely ground. The stirring velocity was then increased, and the reaction mixture was stirred for 12 h, at which point ESMS analysis indicated that the starting aldehyde had been consumed. The reaction mixture was poured into a biphasic mixture of EtOAc (250 ml) and 1 M $NaHSO_4$ (75 ml). The reaction flask was rinsed with EtOAc (50 ml) and this rinse was added to the biphasic mixture. The mixture was agitated, the layers were separated, and the aqueous layer was extracted with EtOAc. The combined organics were washed with brine, dried over Na_2SO_4, filtered, and concentrated to yield a yellow oil. Purification of this material by column chromatography (25 × 90 mm silica, 1:1 hexanes/EtOAc) afforded **12** (96 mg, 75%, 73:12:9:6 mixture of diastereomers) as a clear oil. Partial separation of the minor diastereomers from **12** could be achieved by preparative HPLC (2:3 hexanes/EtOAc), affording **12** as an 88:7:5 mixture of diastereomers (alternatively, **12** could be used in the subsequent MBH reaction without HPLC purification, and this protocol was typically used). Data for **12**: $[\alpha]_D^{24.4}$ –164.1° (*c* 1.1, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$; partial) δ 7.27–7.22 (m, 2 H), 6.90–6.86 (m, 2 H), 6.65 (dd, *J* = 16.6, 4.4 Hz, 1 H), 6.46 (dd, *J* = 15.6, 9.0 Hz, 1 H), 6.09 (dd, *J* = 16.6, 2.0 Hz, 1 H), 5.77 (dd, *J* = 4.6, 2.9 Hz, 1 H), 5.71 (dd, *J* = 15.6, 0.7 Hz, 1 H), 4.90–4.85 (m, 1 H), 4.86 (d, *J* = 1.7 Hz, 1 H), 4.48 (d, A of AB system, *J* = 10.7 Hz, 1 H), 4.42 (d, B of AB system, *J* = 10.7 Hz, 1 H), 4.39–4.35 (m, 1 H), 3.80 (s, 3 H), 3.54 (s, 3 H), 3.52–3.47 (m, 3 H), 3.51 (s, 3 H), 3.48 (s, 3 H), 3.41 (dd, *J* = 9.5, 3.4 Hz, 1 H), 3.37–3.32 (m, 1 H), 3.11 (dd, *J* = 9.3, 9.3 Hz, 1 H), 3.09–3.03 (m, 1 H), 2.84–2.79 (m, 1 H), 2.69 (quint., *J* = 7.1 Hz, 1 H), 2.69–2.61 (m, 1 H), 1.77 (dq, *J* = 11.5, 6.4 Hz, 1 H), 1.69–1.26 (m, 10 H), 1.28 (d, *J* =

6.4 Hz, 3 H), 1.18 (d, *J* = 6.8 Hz, 1 H), 0.88 (t, *J* = 7.6 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.7, 165.2, 159.2, 145.2, 145.1, 131.2, 130.4, 129.5, 128.6, 123.8, 113.8, 95.4, 82.2, 81.4, 81.0, 77.6, 76.6, 73.5, 71.4, 68.1, 60.9, 59.1, 57.7, 55.3, 48.1, 46.6, 45.2, 43.2, 42.7, 38.3, 37.4, 33.5, 32.2, 27.5, 21.2, 17.8, 15.3, 9.9; IR (thin film) 2,969, 2,934, 2,835, 1,713, 1,662, 1,615, 1,586, 1,514, 1,456, 1,382, 1,360, 1,301, 1,269, 1,251, 1,197, 1,173, 1,139, 1,118, 1,104, 1,060, 1,035, 984, 913, 832, 786, 755, 666 cm^{-1}; HRMS (ES), calcd for $C_{41}H_{57}BrO_{10}Si$ $[M + Na]^+$ 811.3033, found 811.3048 *m*/*z*.



(3*R*,4*S*,8*S*,11a*S*,11b*R*,13a*S*,14*R*,15*S*,16a*S*,16b*S*,)-13-bromo-14-8-ethyl-4-(4-methoxy-benzyloxy)-3-methyl-15-[(6-deoxy-2,3,4-trimethyl-*O*-methyl-α-L-mannopyranosyl)oxy]-11a,11b,13a,14,15,16,16a,16b-octahydro-*as*-indaceno[3,2-*d*]oxacyclododeca-2,10-dione (26). *tert*-Amyl alcohol was degassed by bubbling argon through the solvent for 90 min. We azeotropically dried **12** (16 mg, 0.02 mmol) by coevaporation from benzene. This dry residue was placed under high vacuum and then vented to argon. This high vacuum/vent cycle was repeated three times. The resulting residue was dissolved in degassed *tert*-amyl alcohol (5.0 ml) under argon. A 0.3-M stock solution of Me_3P in degassed *tert*-amyl alcohol was prepared. A portion of the Me_3P stock solution (200 µl, 0.06 mmol) was added to the solution of **12**. This solution was stirred for 2.5 h, and then 130 µl (0.04 mmol) of the stock Me_3P solution was added. Stirring was continued for 1.75 h, and then 130 µl (0.04

mmol) of the Me_3P solution was added. After 1 h, 65 μl (0.02 mmol) of the stock Me_3P solution was added. Stirring was continued for 30 min, at which point TLC analysis indicated that **12** had been consumed. The reaction mixture was poured into a biphasic mixture of EtOAc and 1 M $NaHSO_4$. This mixture was agitated, the layers were separated, and the aqueous layer was extracted with EtOAc. The combined organics were washed with brine, dried over Na_2SO_4, filtered, and concentrated, yielding a yellow oil. Residual *tert*-amyl alcohol was removed by coevaporation from benzene. Purification of this material by column chromatography (25 × 55 mm silica, 35% EtOAc in hexanes) afforded an 88:7:5 mixture of **26**, **27**, and **51** (16 mg, quantitative) as a yellow oil. An analytical sample of **26** was prepared by preparative HPLC (55% EtOAc in hexanes): $[\alpha]_D^{28.0}$ –121.5° (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28–7.24 (m, 2 H), 6.89–6.86 (m, 2 H), 6.69 (br s, 1 H), 6.13 (dd, *J* = 3.2, 3.2 Hz, 1 H), 4.85 (d, *J* = 1.7 Hz, 1 H), 4.70–4.64 (m, 1 H), 4.52 (d, A of AB system, *J* = 11.0 Hz, 1 H), 4.38 (d, B of AB system, *J* = 11.0 Hz, 1 H), 4.29 (app. q, *J* = 7.3 Hz, 1 H), 3.80 (s, 3 H), 3.63–3.58 (m, 1 H), 3.55 (s, 3 H), 3.55–3.49 (m, 3 H), 3.55 (s, 3 H), 3.50 (s, 3 H), 3.50 (s, 3 H), 3.44 (dd, *J* = 9.3, 3.4 Hz, 1 H), 3.28 (dq, *J* = 9.5, 6.8 Hz, 1 H), 3.11 (dd, *J* = 9.5 Hz, 9.5 1 H), 3.09 (ddt, *J* = 11.2, 4.6, 2.4 Hz, 1 H), 2.61–2.54 (m, 1 H), 2.40–2.32 (m, 2 H), 2.02 (dd, *J* = 12.9, 6.6 Hz, 1 H), 1.70–1.64 (m, 1 H), 1.69–1.40 (m, 10 H), 1.38–1.30 (m, 1 H), 1.27 (d, *J* = 6.1 Hz, 1 H), 1.24 (d, *J* = 6.8 Hz, 1 H), 1.13–1.06 (m, 1 H), 0.82 (t, *J* = 7.6 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.8, 172.2, 159.2 145.8, 144.2, 130.6, 129.6, 129.5, 123.8, 113.8, 95.5, 82.2, 81.1, 80.2, 77.6, 76.4, 74.2, 71.6, 68.0, 61.0, 59.1, 57.7, 55.3, 48.3, 47.7, 46.8, 46.7, 44.6, 38.1, 37.6, 34.0, 31.7, 30.6, 28.0, 20.5, 17.8, 17.5, 9.4; IR (thin film) 2,968, 2,933, 2,834, 1,719, 1,662, 1,612, 1,586, 1,514, 1,458, 1,373, 1,302, 1,248, 1,216, 1,170, 1,140, 1,118, 1,103, 1,033, 928, 909, 877, 836, 736, 660; HRMS (ES), calcd for $C_{41}H_{57}BrO_{10}Si$ $[M + Na]^+$ 811.3033, found 811.3033 *m*/*z*.

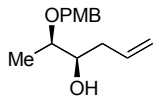


(3*R*,4*S*,8*S*,11a*S*,11b*R*,13a*S*,15*S*,16a*S*,16b*S*)-8-Ethyl-4-hydroxy-3-methyl-15-[(6-deoxy-2,3,4-trimethyl-*O*-methyl-α-L-mannopyranosyl)oxy]-11a,11b,13a,14,15,16,16a,16b-octahydro-*as*-indaceno[3,2-*d*]oxacyclododeca-2,10-dione (Spinosyn A Pseudoaglycon 28). Tetracycle **26** (16 mg, 20 μmol) was dissolved in dioxane in a 5-ml conical vial. $(TMS)_3SiH$ (155 μl, 500 μmol) was added (6, 7). A 0.05-M stock solution of AIBN in dioxane was prepared, and 21 μl (1.0 μmol) was added to the reaction mixture. The vial was sealed with a teflon-coated cap and heated in an 80–85°C oil bath for 30 min. The reaction mixture was cooled to ambient temperature, and AIBN solution was added as described above. The vial was sealed, and the reaction was heated for 20 min. The recharging process was repeated as described above, and the reaction was heated for 20 min more, at which point ESMS analysis indicated all of **26** had been consumed. This mixture was purified directly by column chromatography (25 × 90 mm silica, 1:9 hexanes/EtOAc → 2:3 hexanes/EtOAc), affording des-bromo **26**, which was still contaminated with $(TMS)_3SiH$. This semipure material was used directly in the next reaction.

Des-bromo **26** (theoretically, 20 μmol) was dissolved in CH_2Cl_2 (1.2 ml). pH 7 buffer (0.12 ml) was added and the biphasic reaction mixture was cooled to 0°C. Recrystallized DDQ (5.2 mg, 0.023 mmol) was added. The resulting mixture was stirred vigorously and monitored by TLC analysis. After 1.5 h, an additional 3 mg (0.013 mmol) of DDQ was added. Vigorous stirring was continued and after 50 min an additional 2mg (0.008 mmol) of DDQ was added. After 20 min more, TLC analysis indicated that a trace amount of starting material remained. A trace quantity of DDQ was added. The reaction was stirred for an additional 15 min and then diluted with saturated $NaHCO_3$. The ice bath was removed, and the reaction was stirred vigorously for 2 min. This mixture was then poured into a

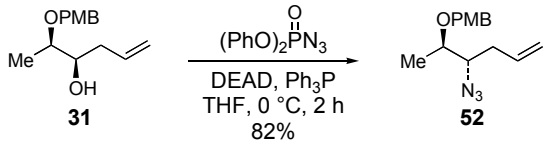
biphasic mixture of EtOAc and saturated $NaHCO_3$. This biphasic mixture was agitated, the layers were separated, and the aqueous layer was extracted with EtOAc. The combined organics were washed with brine, dried over Na_2SO_4, filtered, and concentrated yielding a maroon oil. Purification of this residue by column chromatography (25x75 mm silica, 1:3 hexanes/EtOAc) afforded the spinosyn A pseudoaglycon **28** (8.5 mg, 73% from **26**) as a clear oil. An analytical sample of **28** was prepared by preparative HPLC (EtOAc): $[\alpha]_D^{30.0}$–217.0° (*c* 0.1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.78 (s, 1 H), 5.88 (d, *J* = 9.8 Hz, 1 H), 5.80 (dt, *J* = 9.8, 2.8 Hz, 1 H), 4.85 (d, *J* = 1.6 Hz, 1 H), 4.73–4.68 (m, 1 H), 4.32 (app q, *J* = 6.7 Hz, 1 H), 3.71–3.66 (m, 1 H), 3.57–3.53 (m, 1 H), 3.56 (s, 3 H), 3.51–3.44 (m, 4 H), 3.50 (s, 3 H), 3.46 (dd, *J* = 9.4, 3.3 Hz, 1 H), 3.21 (dq, *J* = 8.8, 6.7 Hz, 1 H), 3.12 (dd, *J* = 9.5, 9.5 Hz, 1 H), 3.02 (m, 1 H), 2.87 (ddt, *J* = 11.4, 5.2, 2.6 Hz, 1 H), 2.42 (dd, *J* = 13.6, 3.3 Hz, 1 H), 2.28 (m, 1 H), 2.17 (m, 1 H), 1.93 (dd, *J* = 13.5, 7.2 Hz, 1 H), 1.72–1.24 (m, 10 H), 1.28 (d, *J* = 6.4 Hz, 3 H), 1.22 (d, *J* = 6.8 Hz, 3 H), 0.92 (dq, *J* = 11.7, 6.7 Hz, 1 H), 0.82 (t, *J* = 7.5 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.7, 172.7, 147.5, 144.4, 129.4, 128.7, 95.4, 82.3, 81.0, 77.7, 77.0, 76.1, 72.7, 67.9, 61.0, 59.0, 57.7, 49.4, 48.1, 47.6, 45.9, 41.5, 41.2, 37.4, 36.3, 34.9, 34.0, 30.0, 28.4, 21.6, 17.8, 15.7, 9.4; IR (thin film) 3,483, 2,930, 1,720, 1,659, 1,608, 1,457, 1,373, 1,313, 1,288, 1,260, 1,215, 1,141, 1,118, 1,104, 1,056, 1,036, 998, 909, 879, 838, 787, 736, 657 cm^{-1}; HRMS (ES), calcd for $C_{33}H_{50}O_9$ $[M + Na]^+$ 613.3353, found 613.3353 *m/z*. TLC co-spot with natural (–)-spinosyn A pseudoaglycon, R_f 0.36 (1:3 hexanes/EtOAc), 0.19 (3:1 hexanes/acetone), 0.71 (19:1 EtOAc/MeOH), 0.57 (7:3 CH_2Cl_2/acetone).

Tabulated comparative NMR data for synthetic spinosyn pseudoaglycone (**28**) vs. natural pseudoaglycone and data reported by Evans and Black (5) and Paquette *et al*. (8) are presented in Tables 1 and 2.



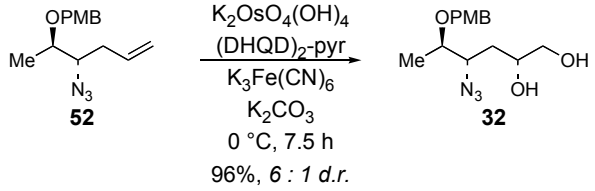
31

(2*R*,3*R*)-2-(4-Methoxybenzyloxy)-hex-5-en-3-ol (31). This compound was prepared according to the procedure in ref. 9. Partial data for **31**: $[\alpha]_D^{26.0}$–48.2° (*c* 8.0, CH_2Cl_2); literature $[\alpha]_D^{26.0}$+48.2° (*c* 1.0, CH_2Cl_2) for *ent*-**31** (9); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28–7.25 (m, 2 H), 6.90–6.87 (m, 2 H), 5.92–5.83 (m, 1 H), 5.13–5.08 (m, 1 H), 5.09–5.07 (m, 1 H), 4.60 (d, A of AB system, *J* = 11.0 Hz, 1 H), 4.37 (d, B of AB system, *J* = 11.2 Hz, 1 H), 3.81 (s, 3 H), 3.53–3.49 (m, 1 H), 3.42 (q, *J* = 6.1 Hz, 1 H), 2.53 (d, *J* = 3.7 Hz, 1 H), 2.37–2.31 (m, 1 H), 2.23–2.16 (m, 1 H), 1.19 (d, *J* = 6.1 Hz, 3 H).



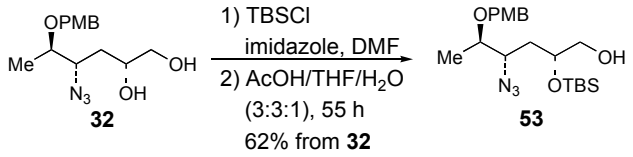
1-[(1*R*,2*S*)-2-Azido-1-methylpent-4-enyloxymethyl]-4-methoxy Benzene (52). Alcohol **31** (505 mg, 2.1 mmol) was dissolved in THF (7 ml) under argon. Triphenyl phosphine was added and the reaction mixture was cooled to 0°C. Diphenylphosphoryl azide (0.56 ml, 2.6 mmol) was added slowly. DEAD (1.27 ml, 2.8 mmol, 40% solution in toluene) was then added slowly over 5 min. The resulting yellow solution was stirred at 0°C for 2 h at which point **31** had been consumed as judged by ESMS analysis. The reaction mixture was poured into a biphasic mixture of Et_2O and 5% aqueous $NaHCO_3$. The layers were separated and the organic layer was washed with brine, dried over Na_2SO_4, filtered, and concentrated yielding a yellow oil. Purification of this crude material by column chromatography (40x140 mm silica, 9:1 hexanes/Et_2O) provided **52** (456 mg, 82%) as a clear oil: $[\alpha]_D^{24.0}$+0.3° (*c* 2.4, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28–7.25 (m, 2 H), 6.90–6.86 (m, 2 H), 5.81 (ddt, *J* = 17.1, 10.3, 7.1 Hz, 1 H), 5.16 (dq, *J* = 17.1, 1.7 Hz, 1 H), 5.14–5.10 (m, 1 H), 4.55 (d, A of AB system, *J* = 11.2 Hz, 1 H), 4.45 (d, B of AB system, *J* = 11.2 Hz, 1 H), 3.81 (s, 3 H), 3.57 (dq, *J* = 6.4, 4.6 Hz, 1 H), 3.47–3.43 (m, 1 H), 2.35–2.24 (m, 2 H), 1.22 (d, *J* = 6.4 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.5, 134.5, 130.5, 129.5, 118.2, 114.1, 76.5, 70.8, 65.5, 55.5, 34.9, 15.5; IR (thin film) 3,078, 2,980, 2,937, 2,907, 2,837, 2,104, 1,643, 1,613, 1,587, 1,514, 1,465, 1,442, 1,379, 1,348, 1,302, 1,249, 1,174,

1,095, 1,036, 920, 822, 756, 704 cm^{-1}; HRMS (ES) calcd for $C_{14}H_{19}N_3O_2$ $[M + Na]^+$ 284.1375, found 284.1368 *m*/*z*.



(2*R*,4*S*,5*R*)-4-Azido-5-(4-methoxybenzyloxy)hexane-1,2-diol (32). $K_2OsO_4(OH)_4$ (7.7 mg, 0.023 mmol), $(DHQD)_2$-pyr (31 mg, 0.035 mmol), $K_3Fe(CN)_6$ (1.18 g, 3.58 mmol), and K_2CO_3 (481 mg, 3.48 mmol) were suspended in *tert*-BuOH (4 ml) and H_2O (6 ml). This heterogeneous mixture was stirred until it was essentially homogeneous, and then it was cooled to 0°C. Azide **52** (300 mg, 1.15 mmol) was added as a solution in *tert*-BuOH (1 ml). The flask containing **52** was rinsed twice with *tert*-BuOH (0.5 ml each) and these rinses were added to the reaction mixture. The resulting orange slurry was stirred at 0°C for 7 h at which point ESMS analysis indicated the complete consumption of **52**. Na_2SO_3 (1.8 g) was added, the ice bath was removed, and the resulting mixture was stirred vigorously for 1.5 h. The layers were separated and the aqueous layer was extracted twice with EtOAc. At this point an emulsion had formed. Brine was added to break up the emulsion, and the aqueous layer was extracted two additional times with EtOAc. The combined organics were dried over $MgSO_4$, filtered, and concentrated yielding a yellow oil. Purification of this material by column chromatography (40x80 mm silica, 3:2 hexanes/acetone) afforded **32** (325 mg, 96%, 6:1 mixture of inseparable diastereomers) as a clear oil. Data for major diastereomer **32**: $[\alpha]_D^{25.0}$–23.5° (*c* 2.6, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28–7.25 (m, 2 H), 6.90–6.87 (m, 2 H), 4.57 (d, A of AB system, *J* = 11.2 Hz, 1 H), 4.48 (d, B of AB system, *J* = 11.2 Hz, 1 H), 3.81 (s, 3 H), 3.70–3.61 (m, 3 H), 3.49 (dd, *J* = 11.0, 6.6 Hz, 1 H), 1.67–1.64 (m, 1 H), 1.65 (t, *J* = 5.9 Hz, 1 H), 1.24 (d, *J* = 6.4 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.2, 129.8, 129.2, 113.8, 76.7, 70.6, 69.9, 66.2, 63.2, 55.2, 33.3, 15.3; IR (thin film) 3,386, 2,936, 2,838, 2,500, 2,105, 1,613, 1,586, 1,514, 1,464, 1,380, 1,347, 1,302,

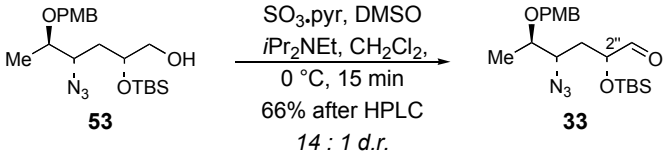
1,249, 1,175, 1,072, 1,034, 935, 822, 755, 637 cm^{-1}; HRMS (ES) calcd for $C_{14}H_{21}N_3O_4$ $[M + Na]^+$ 318.1430, found 318.1428 *m*/*z*.



(2*R*,4*S*,5*R*)-4-Azido-2-(*tert*-butyldimethylsiloxy)-5-(4-methoxybenzyloxy)hexan-1-ol (53). Diol **32** (105 mg, 0.36 mmol) was dissolved in DMF (0.7 ml) and imidazole (87 mg, 3.55 mmol) was added. TBSCl (132 mg, 2.43 mmol) was then added. The reaction mixture was stirred for 4 h at which point **32** was consumed as judged by ESMS analysis. The reaction mixture was diluted with Et_2O and washed four times with H_2O, once with saturated $NaHCO_3$, and once with brine. The organic layer was then dried over Na_2SO_4, filtered, and concentrated yielding a clear oil. This crude material was used directly in the next reaction.

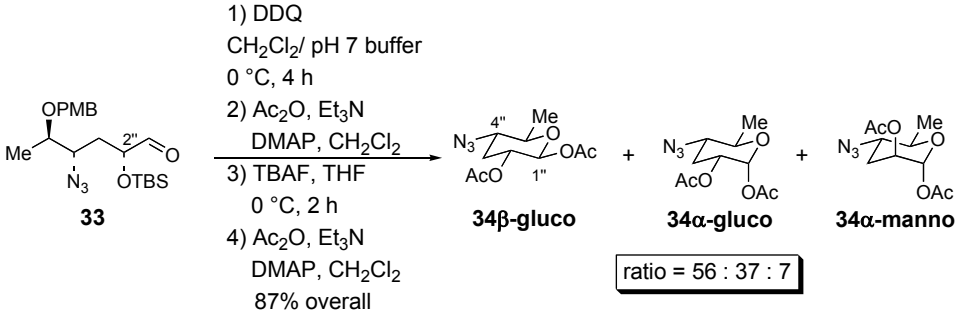
A mixture of the crude bis-silyl ether (theoretically 0.36 mmol) in THF (3.75 ml), HOAc (3.75 ml) and H_2O (1.25 ml) was stirred vigorously and the progress of the reaction was monitored by ESMS analysis. After 55 h, the reaction mixture was transferred portionwise via pipette into a vigorously stirring, triphasic mixture of EtOAc, saturated $NaHCO_3$, and solid $NaHCO_3$. The resulting mixture was stirred until gas evolution ceased and then the layers were separated. The aqueous layer was extracted twice with EtOAc. The organic layer was washed with saturated $NaHCO_3$, brine, dried over Na_2SO_4, filtered, and concentrated yielding a clear oil. Purification of this crude material by column chromatography (25 × 70 mm silica, 3:1 hexanes/EtOAc) gave **53** (91 mg, 62% from **32**, 6:1 mixture of diastereomers) as a clear oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29–7.26 (m, 2 H), 6.90–6.87 (m, 2 H), 4.55 (d, A of AB system, *J* = 11.5 Hz, 1 H), 4.48 (d, B of AB system, *J* = 11.5 Hz, 1 H), 3.96–3.91 (m, 1 H), 3.81 (s, 3 H), 3.63–3.59 (m, 2 H), 3.56–3.51 (m, 2 H), 1.71 (ddd, *J* = 11.0, 7.8, 3.2 Hz, 1 H), 1.59 (ddd, *J* = 14.5, 10.3, 4.2 Hz, 1 H), 1.20 (d, *J* = 6.4 Hz, 3 H), 0.90 (s, 9 H), 0.09 (s, 3 H), 0.09 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.1, 130.2, 129.1, 113.7, 70.4, 70.1, 69.6, 65.1, 61.4, 55.2, 33.7,

25.7, 18.0, 14.9, –4.7, –4.8; $[\alpha]_D^{24.2}$–25.4° (*c* 1.4, $CHCl_3$); IR (thin film) 3,460, 2,955, 2,931, 2,885, 2,858, 2,105, 1,614, 1,587, 1,515, 1,464, 1,443, 1,380, 1,361, 1,348, 1,303, 1,251, 1,174, 1,085, 1,038, 1,007, 974, 939, 836, 778, 679, 638 cm^{-1}; HRMS (ES) calcd for $C_{20}H_{35}N_3O_4Si$ $[M + Na]^+$ 432.2295, found 432.2294 *m*/*z*.



(2*R*,4*S*,5*R*)-4-Azido-2-(*tert*-butyldimethylsiloxy)-5-(4-methoxybenzyloxy)hexanal (33). Alcohol **53** (220 mg, 0.54 mmol) was azeotropically dried by coevaporation from benzene. The dry material was dissolved in CH_2Cl_2 (5.5 ml). *i*-Pr_2NEt (0.37 ml, 2.12 mmol) was added, followed by DMSO (0.27 ml, 3.80 mmol). The reaction mixture was cooled to 0°C and SO_3•pyr (215 mg, 1.35 mmol) was added. This mixture was stirred for 15 min at which point TLC analysis indicated that **53** had been consumed. The reaction mixture was diluted with saturated $NaHCO_3$, the ice bath was removed, and the biphasic mixture was stirred vigorously for 10 min. The layers were separated and the aqueous layer was extracted twice with EtOAc. The combined organics were washed once with saturated $NaHCO_3$, twice with 1 M $NaHSO_4$, and once with brine. The organic layer was then dried over Na_2SO_4, filtered, and concentrated yielding a yellow odorous oil. Purification of this material by column chromatography (25 × 50 mm silica, 3:2 hexanes/EtOAc) afforded **33**. Partial separation of the C(2′′) diastereomers was achieved by preparative HPLC (5:1 hexanes/EtOAc) affording **33** (145 mg, 66%, 14:1 mixture of diastereomers) as a light yellow oil: ^1H NMR (500 MHz, $CDCl_3$) δ 9.67 (d, *J* = 1.0 Hz, 1 H), 7.27–7.24 (m, 2 H), 6.89–6.86 (m, 2 H), 4.54 (d, A of AB system, *J* = 11.2 Hz, 1 H), 4.46 (d, B of AB system, *J* = 11.5 Hz, 1 H), 4.15–4.12 (m, 1 H), 3.81 (s, 3 H), 3.68 (dt, *J* = 9.5, 3.9 Hz, 1 H), 3.59 (dq, *J* = 6.4, 4.2 Hz, 1 H), 1.91–1.86 (m, 2 H), 1.20 (d, *J* = 6.4 Hz, 3 H), 0.93 (s, 9 H), 0.12 (s, 3 H), 0.08 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.1, 159.0, 130.0, 129.0, 113.6, 76.5, 74.7, 70.3, 60.6, 55.0, 34.2, 25.6, 18.0, 15.3, –4.9, –5.2; $[\alpha]_D^{25.0}$–21.8° (*c* 1.1, $CHCl_3$); IR (thin film) 2,955, 2,932,

2,885, 2,858, 2,115, 1,737, 1,614, 1,590, 1,514, 1,471, 1,464, 1,443, 1,382, 1,362, 1,303, 1,251, 1,173, 1,153, 1,111, 1,037, 1,008, 940, 838, 780, 675, 638 cm^{-1}; HRMS (ES) calcd for $C_{20}H_{33}N_3O_4Si$ [M + Na+ MeOH]$^+$ 462.2400, found 462.2392 *m*/*z*.



1-Acetoxy-3,4,6-trideoxy-2-acetoxy-4-azidoglucopyranoside (34). Aldehyde **33** (450 mg, 1.10 mmol) was dissolved in CH_2Cl_2 (11 ml) and pH 7 buffer (1.1 ml) was added. This biphasic reaction mixture was cooled to 0°C and DDQ (282 mg, 1.24 mmol, recrystallized from 4:1 chloroform/benzene) was added. The reaction mixture immediately turned green. After 2 h, an additional 100 mg (0.44 mmol) of DDQ was added. Stirring was continued for an additional 1 h at which point EMSM analysis indicated that a trace of **33** remained. An additional 13 mg (0.057 mmol) of DDQ was added. The reaction mixture was stirred for an additional 1 h and then diluted with saturated $NaHCO_3$. CH_2Cl_2 was added, the ice bath was removed, and the mixture was stirred vigorously for 15 min. EtOAc was added, the layers were separated, and the aqueous layer was extracted with EtOAc. The combined organics were washed with brine, dried over $MgSO_4$, filtered, and concentrated yielding a maroon oil. Baseline impurities were removed by filtration of this crude material through a plug of silica (50 × 30 mm silica) affording the desired lactol as a clear oil. This semipure lactol was used directly in the next reaction.

The semipure lactol (theoretically, 1.10 mmol) was dissolved in CH_2Cl_2 (11 ml). Et_3N (0.47 ml, 3.37 mmol) was added, followed by Ac_2O (0.21 ml, 2.22 mmol). A catalytic amount of DMAP was added and the reaction mixture was stirred for 12 h, at which point TLC analysis indicated that the starting lactol had been consumed. EtOAc (30 ml) was added and the reaction mixture was poured into

saturated $NaHCO_3$ (20 ml). The resulting biphasic mixture was stirred vigorously for 15 min. The layers were separated and the aqueous layer was extracted with EtOAc. The combined organics were washed with 1 M $NaHSO_4$, brine, dried over Na_2SO_4, filtered, and concentrated yielding the desired acetate as a yellow oil. This crude material was used directly in the next experiment.

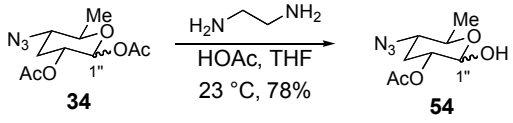
The crude acetate (theoretically, 1.10 mmol) was dissolved in THF and this mixture was cooled to 0°C. TBAF (1.5 ml, 1.5 mmol, 1.0 M solution in THF) was added slowly. The resulting yellow reaction mixture was stirred at 0°C for 1 h at which point the crude acetate starting material had been consumed as judged by TLC analysis. The reaction mixture was diluted with saturated NH_4Cl and EtOAc, the ice bath was reomoved, and the mixture was stirred vigorously for 10 min. The layers were separated and the aqueous layer was extracted with EtOAc. The combined organics were washed with brine, dried over Na_2SO_4, filtered, and concentrated yielding a brown oil. This crude material was used directly in the next experiment.

The crude alcohol (theoretically 1.10 mmol) from the previous experiment was dissolved in CH_2Cl_2 (11 ml). Et_3N (0.50 ml, 3.59 mmol) was added, followed by Ac_2O (0.22 ml, 2.33 mmol). A catalytic amount of DMAP was added and the resulting mixture was stirred for 18 h at which point the crude alcohol starting material had been consumed as judged by TLC analysis. EtOAc was added and the mixture was poured into saturated $NaHCO_3$. The resulting biphasic mixture was stirred vigorously for 15 min. The layers were separated and the aqueous layer was extracted with EtOAc. The combined organics were washed with 1 M $NaHSO_4$ and brine, dried over Na_2SO_4, filtered, and concentrated yielding a brown oil. This crude material was dissolved in 1:1 Et_2O/hexanes (8 ml total) and saturated $NaHSO_3$ was added. The resulting biphasic mixture was stirred vigorously for 2 h and then filtered through a medium-pore frit funnel. The filter cake was washed with a small amount of 1:1 Et_2O/hexanes and these rinses were combined with the biphasic mixture. The layers were separated and the aqueous layer was extracted twice with 1:1 Et_2O/hexanes. The combined organics were dried over Na_2SO_4, filtered, and concentrated, yielding a light yellow oil. Purification of this mixture by

column chromatography (40 × 100 mm silica, 3:1 hexanes/EtOAc) afforded bis-acetate **34** (247 mg, 87%, 14:1 mixture of C(2") diastereomers; 1. 7:1 mixture of β- and α-anomers) as a clear oil. This mixture was utilized in subsequent glycosidation reactions; however, partial separation of this mixture was achieved by preparative HPLC (3:1 hexanes/EtOAc) which afforded pure **34α-gluco** as well as a mixture of **34β-gluco** and **34α-manno**. Data for **34α-gluco**: $[\alpha]_D^{24.8}$+166.0° (*c* 0.2, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.15 (d, *J* = 3.4 Hz, 1 H), 4.97 (ddd, *J* = 12.2, 4.9, 3.4 Hz, 1 H), 3.69 (dq, *J* = 10.0, 6.1 Hz, 1 H), 3.20 (ddd, *J* = 14.4, 10.0, 4.4 Hz, 1 H), 2.30 (m, 1 H), 2.16 (s, 3 H), 2.04 (s, 3 H), 1.96 (dd *J* = 12.2, 12.2 Hz, 1 H), 1.28 (d, *J* = 6.3 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.9, 169.3, 88.4, 69.3, 67.0, 60.6, 29.0, 21.0, 20.8, 18.0; IR (thin film) 2,983, 2,940, 2,105, 1,756, 1,456, 1,370, 1,323, 1,243, 1,220, 1,149, 1,104, 1,059, 1,013, 991, 972, 945, 921, 869, 832, 670 cm^{-1}; HRMS (ES) calcd for $C_{10}H_{15}N_3O_5$ $[M + Na]^+$ 280.0909, found 280.0899 *m*/*z*.

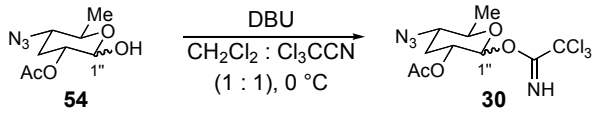
Partial data for **34β-gluco**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.63 (d, *J* = 8.1 Hz, 1 H), 4.81 (ddd, *J* = 13.2, 8.3, 4.9 Hz, 1 H), 3.50 (dq, *J* = 9.8, 6.1 Hz, 1 H), 3.20 (m, 1 H), 2.59 (ddd, *J* = 12.5, 4.9, 4.9 Hz, 1 H), 2.11 (s, 3 H), 2.06 (s, 3 H), 1.64 (dd, *J* = 12.2, 11.7 Hz, 1 H), 1.33 (d, *J* = 5.9 Hz, 3 H).

Partial data for **34α-manno**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.93 (br s, 1 H), 4.96 (m, 1 H), 4.91 (m, 1 H), 3.69 (m, 2 H), 3.38 (m, 1 H), 3.20 (m, 1 H).

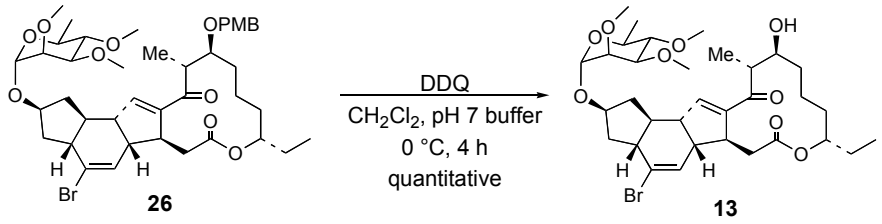


(3*R*,5*S*,6*R*)-Acetic Acid 5-Azido-2-hydroxy-6-methyltetrahydropyran-3-yl Ester (54). Ethylenediamine (23 μl, 0.34 mmol, distilled from Na) was dissolved in THF and HOAc (24 μl, 0.42 mmol) was added. A white precipitate was immediately observed. Bis-acetate **34** (44 mg, 0.17 mmol) was added as a solution in THF (1 ml) to this heterogeneous mixture. The flask initially containing **34** was rinsed three times with THF (0.5 ml each), and these rinses were added to the reaction mixture. The mixture was stirred and monitored by TLC analysis. After 24 h, it appeared that the reaction had

stalled. At this point, the mixture was diluted with H_2O and the resulting homogeneous mixture was poured into a biphasic solution of CH_2Cl_2 and H_2O. The layers were separated and the aqueous layer was extracted with CH_2Cl_2. The combined organics were washed with 0.1 M HCl, saturated $NaHCO_3$, dried over Na_2SO_4, filtered, and concentrated, yielding a yellow oil. Purification of this crude material by column chromatography (25 × 130 mm silica, 2:1 hexanes/EtOAc → 1:1 hexanes/EtOAc) gave **54** (29 mg, 78%, 1.5:1 mixture of anomeric lactols) as a clear oil. Partial data for **54** (major lactol): ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.26 (br s, 1 H), 4.84 (ddd, *J* = 12.2, 4.9, 3.7 Hz, 1 H), 3.88 (dq, *J* = 9.8, 6.1 Hz, 1 H), 3.15–3.09 (m, 1 H), 2.69–2.63 (m, 1 H), 2.24 (ddd, *J* = 11.2, 4.4, 4.4 Hz, 1 H), 2.11 (s, 3 H), 2.04 (dd, *J* = 12.0, 11.0 Hz, 1 H), 1.26 (d, *J* = 6.1 Hz, 3 H).

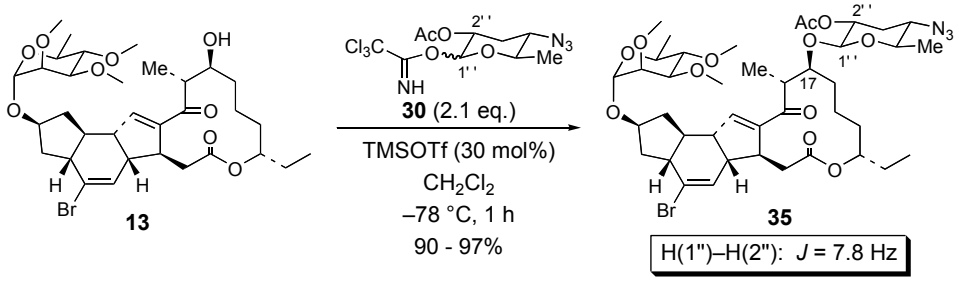


(α,β)-3,4,6-Trideoxy-2-acetoxy-4-azidoglucopyranosyl Trichloroacetimidate (30). Lactol **54** (4 mg, 19 μmol) was dried azeotropically by coevaporation from benzene. The dry residue was dissolved in CH_2Cl_2 (195 μl) and cooled to 0°C. Cl_3CCN (195 μl, distilled from CaH_2) was added, followed by DBU (0.9 μl, 6 μmol). The resulting bright yellow reaction mixture was stirred for 1.5 h, at which point TLC analysis indicated **54** was nearly consumed. The reaction mixture was concentrated and residual Cl_3CCN was removed by coevaporation from CH_2Cl_2. Purification of this crude material by filtration through a short Davisil silica gel plug (3:1 hexanes/EtOAc) afforded a ≈3:1 to 6:1 mixture of **30** and **54** because of decomposition of **30**. Imidate **30** was isolated as a >20:1 mixture diastereomers at C(2") and as a 5:1 mixture of of β/α anomers. This mixture was used immediately in subsequent glycosidation reactions. Partial data for **30**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.65 (br s, 1 H), 5.79 (d, *J* = 8.1 Hz, 1 H), 5.01 (ddd, *J* = 13.2, 8.1, 5.1 Hz, 1 H), 3.58 (dq, *J* = 9.3, 6.1 Hz, 1 H), 3.27 (ddd, *J* = 14.2, 9.5, 4.6 Hz, 1 H), 2.61 (ddd, *J* = 12.7, 5.1, 5.1 Hz, 1 H), 2.04 (s, 3 H), 1.75–1.58 (m, 1 H), 1.38 (d, *J* = 6.4 Hz, 3 H).



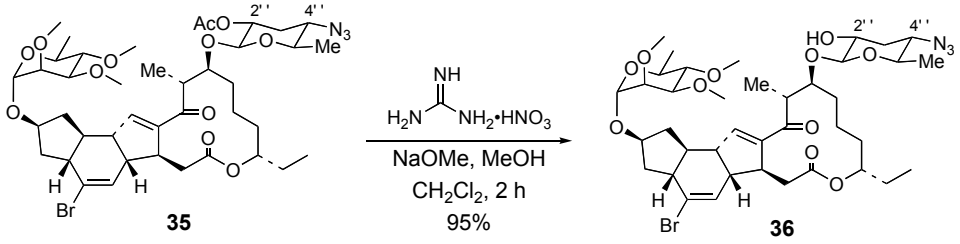
(3*R*,4*S*,8*S*,11a*S*,11b*R*,13a*S*,15*S*,16a*S*,16b*S*,)-13-Bromo-8-ethyl-4-hydroxy-3-methyl-15-[(6-deoxy-2,3,4-trimethyl-*O*-methyl-α-L-mannopyranosyl)oxy]-11a,11b,13a,14,15,16,16a,16b-octahydro-*as*-indaceno[3,2-*d*]oxacyclododeca-2,10-dione (13). PMB ether **26** (22 mg, 0.028 mmol) was dissolved in CH_2Cl_2 (2.0 ml). pH 7 buffer (200 μl) was added and the biphasic reaction mixture was cooled to 0°C. Recrystallized DDQ (10 mg, 0.044 mmol) was added and the resulting mixture was stirred vigorously and monitored by TLC analysis. After 1 h, an additional 2 mg (0.008 mmol) of DDQ was added. Vigorous stirring was continued and after 45 min the recharging process was repeated as above. After 40 additional minutes **26** was consumed as judged by TLC analysis (Note: The anisaldehyde produced in this reaction nearly TLC co-spots with **26**). The reaction mixture was diluted with saturated $NaHCO_3$, the ice bath was removed, and the reaction was stirred vigorously for 5 min. This mixture was then poured into a biphasic mixture of EtOAc and saturated $NaHCO_3$. The biphasic mixture was agitated, the layers were separated, and the aqueous layer was extracted with EtOAc. The combined organics were washed with brine, dried over Na_2SO_4, filtered, and concentrated yielding a dark red oil. Purification of this residue by column chromatography (25 × 80 mm silica, 1:2 hexanes/EtOAc) afforded alcohol **13** (19 mg, quantitative) as a clear oil. An analytical sample of **13** was prepared by preparative TLC (2:3 hexanes/EtOAc): $[\alpha]_D^{25.0}$–292.6° (*c* 0.27, $CHCl_3$); ^{1}H NMR δ 6.71 (s, 1 H), 6.15 (dd, *J* = 3.4, 3.4 Hz, 1 H), 4.85 (d, *J* = 1.6 Hz, 1 H), 4.73–4.68 (m, 1 H), 4.30 (app q, *J* = 7.3 Hz, 1 H), 3.70–3.65 (m, 1 H), 3.62–3.53 (m, 1 H), 3.56 (s, 3 H), 3.53–3.49 (m, 1 H), 3.51 (s, 3 H), 3.51 (s, 3 H), 3.45 (dd, *J* = 9.3, 3.4 Hz, 1 H), 3.18 (dq, *J* = 9.0, 6.8 Hz, 1 H), 3.15–3.07 (m, 2 H), 3.12 (dd, *J* = 9.3, 9.3 Hz, 1 H), 2.85 (ddt, *J* = 11.5, 5.4, 2.7 Hz, 1 H), 2.64–2.55 (m, 1 H), 2.41–2.35 (m, 2 H), 2.03 (dd, *J* = 13.4, 6.8 Hz, 1 H), 1.70–1.40 (m, 11 H), 1.32–1.24 (m, 2 H), 1.28 (d, *J* = 6.1

Hz, 3 H), 1.21 (d, J = 6.8 Hz, 3 H), 0.82 (t, J = 7.3 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.4, 172.5, 147.5, 146.0, 144.7, 129.4, 124.0, 95.6, 82.2, 81.1, 77.6, 74.3, 72.7, 68.1, 61.0, 59.1, 57.7, 48.3, 48.2, 47.3, 46.9, 46.8, 44.7, 38.1, 37.6, 34.9, 33.5, 30.0, 28.4, 21.6, 17.8, 15.7, 9.4; IR (thin film) 3,463, 2,972, 2,925, 1,716, 1,659, 1,457, 1,372, 1,287, 1,215, 1,157, 1,137, 1,116, 1,101, 1,037, 1,003, 998, 910, 840, 754 cm^{-1}; HRMS (ES), calcd for $C_{33}H_{49}BrO_9$ $[M + Na]^+$ 691.2458, found 691.2451 m/z.



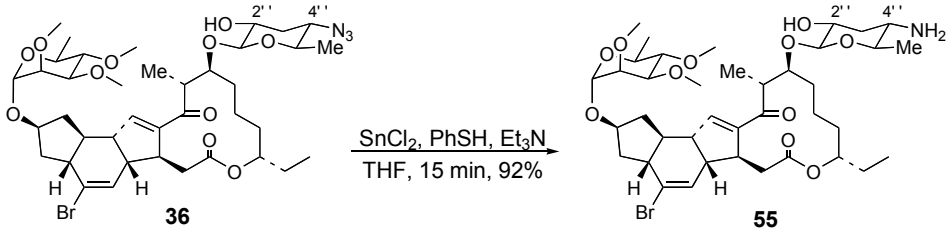
(3*R*,4*S*,8*S*,11a*S*,11b*R*,13a*S*,15*S*,16a*S*,16b*S*,)-13-Bromo-4-[(3,4,6-trideoxy-2-acetoxy-4-azido-D-glucopyranosyl)oxy]-8-ethyl-3-methyl-15-[(6-deoxy-2,3,4-trimethyl-*O*-methyl-α-L-mannopyranosyl)oxy]-11a,11b,13a,14,15,16,16a,16b-octahydro-*as*-indaceno[3,2-*d*]oxa-cyclododeca-2,10-dione (35). Acceptor **13** and donor **30** were combined and azeotropically dried by coevaporation from benzene. The dry mixture was dissolved in CH_2Cl_2 (170 μl) under argon and cooled to –78°C. TMSOTf (0.7 μl, 3.9 μmol) was added via a 10-μl syringe (the needle tip was submerged in the reaction mixture prior to addition). This mixture was stirred at –78°C for 1 h, at which point TLC analysis indicated the consumption of **13**. Et_3N (60 μl) was added and then the reaction was slowly diluted with dry CH_2Cl_2 (200 μl). This mixture was stirred and warmed to ambient temperature at which point the mixture was diluted with EtOAc and poured into a biphasic mixture of EtOAc and saturated $NaHCO_3$. The layers were separated and the aqueous layer was extracted with EtOAc. The combined organics were washed with brine, dried over Na_2SO_4, filtered, and concentrated yielding a yellow oil. Purification of this crude material by preparative TLC afforded **35** (11 mg, 97%) as a clear oil (Note: purification of this material by column chromatography was not effective due to coelution of trichloroacetamide with **35**): $[\alpha]_D^{24.2}$–155.0° (*c* 0.3, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$)

δ 6.71 (s, 1 H), 6.14 (dd, *J* = 3.2. 3.2 Hz, 1 H), 4.85 (d, *J* = 1.7 Hz, 1 H), 4.71–4.64 (m, 1 H), 4.47 (d, *J* = 7.8 Hz, 1 H), 4.29 (app q, *J* = 7.1 Hz, 1 H), 3.65–3.56 (m, 2 H), 3.56 (s, 3 H), 3.52–3.49 (m, 2 H), 3.51 (s, 3 H), 3.50 (s, 3 H), 3.45 (dd, *J* = 9.3, 3.4 Hz, 1 H), 3.34 (dq, *J* = 9.8, 6.1 Hz, 1 H), 3.28 (dq, *J* = 10.0, 6.6 Hz, 1 H), 3.17–3.06 (m, 3 H), 3.12 (dd, *J* = 9.3, 9.3 Hz, 1 H), 2.86 (ddt, *J* = 11.5, 5.0, 2.5 Hz, 1 H), 2.64–2.55 (m, 1 H), 2.52 (dt, *J* = 12.2, 4.9, Hz, 1 H), 2.40–2.33 (m, 2 H), 2.03 (dd, *J* = 13.7, 6.8 Hz, 1 H), 1.72–1.65 (m, 1 H), 1.64–1.32 (m, 11 H), 1.28 (d, *J* = 6.1 Hz, 3 H), 1.28 (d, *J* = 6.4 Hz, 1 H), 1.21 (d, *J* = 6.8 Hz, 3 H), 1.16–1.08 (m, 1 H), 0.81 (t, *J* = 7.6 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.3, 172.2, 169.6, 146.2, 144.2, 129.4, 123.9, 103.2, 95.6, 82.2, 81.7, 81.1, 77.6, 76.6, 74.3, 74.3, 69.9, 68.1, 61.0, 60.8, 59.1, 57.7, 48.3, 47.5, 47.4, 46.8, 44.7, 38.1, 37.6, 34.3, 33.8, 33.7, 30.3, 28.3, 21.1, 21.0, 18.2, 17.8, 16.3, 9.4; IR (thin film) 2,970, 2,934, 2,826, 2,104, 1,744, 1,720, 1,661, 1,610, 1,458, 1,375, 1,322, 1,282, 1,236, 1,215, 1,167, 1,137, 1,118, 1,105, 1,072, 1,042, 1,007, 963, 905, 878, 838, 800, 755, 737, 692, 665 cm^{-1}; HRMS (ES), calcd for $C_{41}H_{60}BrN_3O_{12}$ $[M + Na]^+$ 888.3258, found 888.3267 *m/z*.



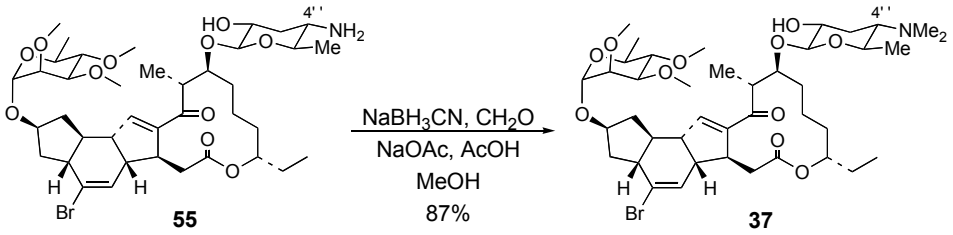
(3*R*,4*S*,8*S*,11a*S*,11b*R*,13a*S*,15*S*,16a*S*,16b*S*,)-13-Bromo-4-[(3,4,6-trideoxy-2-hydroxy-4-azido-D-glucopyranosyl)oxy]-8-ethyl-3-methyl-15-[(6-deoxy-2,3,4-trimethyl-*O*-methyl-α-L-mannopyranosyl)oxy]-11a,11b,13a,14,15,16,16a,16b-octahydro-*as*-indaceno[3,2-*d*]oxacyclo-dodeca-2,10-dione (36). MeOH (10 ml) was cooled to 0°C, and sodium metal (228mg, 10 mmol) was added in three small chunks. This mixture was stirred until the disappearance of sodium was observed and then the homogeneous mixture was warmed to ambient temperature, providing a 1 M NaOMe solution. In a separate flask, guanidinium nitrate (622 mg, 5.1 mmol) was dissolved in MeOH (45 ml), and then CH_2Cl_2 (5 ml) was added. The initially heterogeneous mixture was stirred until all the solid

had dissolved and then 1 ml of the 1 M NaOMe solution was added. This mixture was stirred for 5 min, affording a stock solution of guanidine/guanidinium nitrate. Acetate **35** (11 mg, 0.013 mmol) was then dissolved in 0.78 ml of this stock solution. The resulting mixture was stirred for 2 h, at which point **35** had been consumed, as judged by TLC analysis. The reaction mixture was poured into a biphasic mixture of CH_2Cl_2 (5 ml), saturated NH_4Cl (5 ml) and H_2O (1 ml). The reaction vial was rinsed with CH_2Cl_2 and these rinses were added to the biphasic mixture. This mixture was agitated, the layers were separated, and the aqueous layer was extracted twice with CH_2Cl_2. The combined organics were dried over Na_2SO_4, filtered, and concentrated yielding a yellow oil. This crude material was purified by preparative TLC (250 μm thickness silica plate, 2:3 hexanes/EtOAc) affording **36** (10 mg, 95%) as a clear oil: $[\alpha]_D^{25.0}$–138.7° (*c* 1.4, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.69 (s, 1 H), 6.14 (dd, *J* = 3.2, 3.2 Hz, 1 H), 4.85 (d, *J* = 2.0 Hz, 1 H), 4.72–4.65 (m, 1 H), 4.30 (app q, *J* = 7.1 Hz, 1 H), 4.29 (d, *J* = 7.6 Hz, 1 H), 3.73–3.68 (m, 1 H), 3.65–3.59 (m, 1 H), 3.56 (s, 3 H), 3.55–3.49 (m, 3 H), 3.51 (s, 3 H), 3.50 (s, 3 H), 3.45 (dd, *J* = 9.5, 3.4 Hz, 1 H), 3.38–3.30 (m, 2 H), 3.13–3.06 (m, 3 H), 3.12 (dd, *J* = 9.3, 9.3 Hz, 1 H), 2.86 (ddt, *J* = 11.2, 4.9, 2.4 Hz, 1 H), 2.61–2.54 (m, 1 H), 2.44–2.30 (m, 4 H), 2.03 (dd, *J* = 13.7, 7.1 Hz, 1 H), 1.72–1.37 (m, 11 H), 1.28 (d, *J* = 6.1 Hz, 3 H), 1.28 (d, *J* = 6.4 Hz, 1 H), 1.23 (d, *J* = 6.8 Hz, 3 H), 1.23–1.14 (m, 1 H), 0.81 (t, *J* = 7.6 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.1, 172.4, 146.0, 144.3, 129.4, 123.3, 105.2, 95.5, 82.2, 81.1, 80.5, 77.5, 76.7, 74.3, 74.3, 74.2, 69.1, 68.0, 61.2, 61.0, 59.1, 57.7, 48.3, 47.4, 46.9, 46.8, 46.8, 38.1, 37.6, 35.2, 33.6, 33.5, 30.4, 28.3, 21.1, 18.2, 17.8, 16.3, 9.3; IR (thin film) 2,970, 3,484, 3,051, 2,970, 2,934, 2,828, 2,103, 1,719, 1,661, 1,610, 1,458, 1,381, 1,319, 1,284, 1,260, 1,232, 1,216, 1,166, 1,135, 1,118, 1,104, 1,069, 1,032, 1,005, 962, 927, 905, 878, 838, 799, 786, 754, 737, 703, 666 cm^{-1}; HRMS (ES), calcd for $C_{39}H_{58}BrN_3O_{11}$ $[M + Na]^+$ 846.3152, found 846.3143 *m*/*z*.



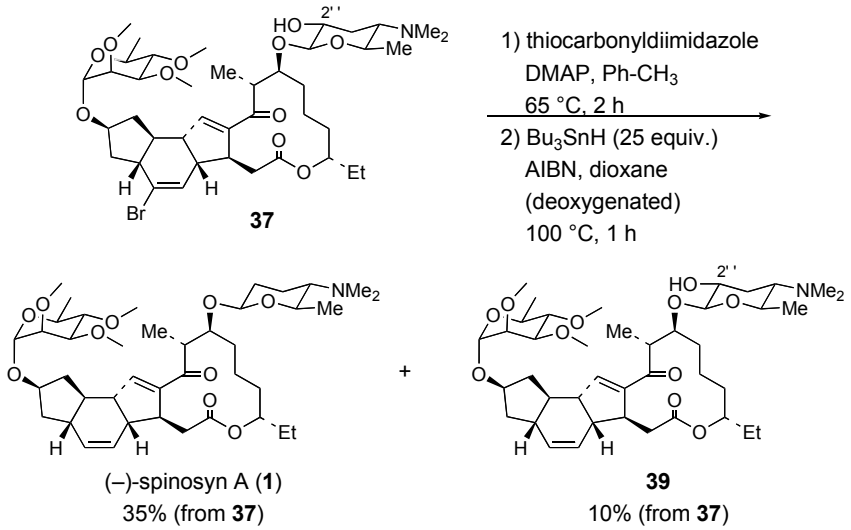
(3*R*,4*S*,8*S*,11a*S*,11b*R*,13a*S*,15*S*,16a*S*,16b*S*,)-13-Bromo-4-[(3,4,6-trideoxy-2-hydroxy-4-amino-D-glucopyranosyl)oxy]-8-ethyl-3-methyl-15-[(6-deoxy-2,3,4-trimethyl-*O*-methyl-α-L-mannopyranosyl)oxy]-11a,11b,13a,14,15,16,16a,16b-octahydro-*as*-indaceno[3,2-*d*]oxa-cyclododeca-2,10-dione (55). $SnCl_2$ (5.2 mg, 0.027 mmol) was suspended in THF (0.6 ml) under argon. PhSH (8.9 μl, 0.087 mmol) was added, followed by Et_3N (12.5 μl, 0.09 mmol). A white precipitate was immediately observed. In a separate flask, **36** (9 mg, 0.011 mmol) was azeotropically dried by coevaporation from benzene. The dry material was was then added to the reaction mixture as a solution in THF (300 μl). The flask containing **36** was rinsed twice with THF (100 μl each) and these rinses were added to the reaction mixture. The resulting reaction mixture was stirred for 15 min at which point TLC analysis indicated that **36** had been consumed. The reaction mixture was poured into a biphasic mixture of CH_2Cl_2 and saturated $NaHCO_3$. The mixture was agitated and the layers were separated. The aqueous layer was extracted three times with CH_2Cl_2. The combined organics were dried over Na_2SO_4, filtered, and concentrated yielding a yellow, odorous oil. This oil was dissolved in 5 ml MeOH, stirred for 1 h, and concentrated. Purification of this material by column chromatography (13x60mm silica, CH_2Cl_2 → 9:1 CH_2Cl_2/MeOH with 0.5% NH_4OH) afforded amine **55** (8 mg, 92%) as a white solid: $[\alpha]_D^{25.0}$–141.2° (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.70 (s, 1 H), 6.14 (dd, *J* = 2.9, 2.9 Hz, 1 H), 4.85 (d, *J* = 1.5 Hz, 1 H), 4.72–4.65 (m, 1 H), 4.30 (app q, *J* = 7.1 Hz, 1 H), 4.28 (d, *J* = 7.3 Hz, 1 H), 3.72 (app q, *J* = 7.1 Hz, 1 H), 3.65–3.59 (m, 1 H), 3.56 (s, 3 H), 3.55–3.48 (m, 3 H), 3.51 (s, 3 H), 3.50 (s, 3 H), 3.45 (dd, *J* = 9.3, 3.2 Hz, 1 H), 3.38–3.32 (m, 1 H), 3.21–3.15 (m, 1 H), 3.14–3.06 (m, 2 H), 3.12 (dd, *J* = 9.3, 9.3 Hz, 1 H), 2.89–2.83 (m, 1 H), 2.61–2.54 (m, 2 H), 2.40–2.34 (m, 2 H), 2.24 (dt, *J* = 12.2, 4.4 Hz, 1 H), 2.03 (dd, *J* = 13.7, 7.1 Hz, 1 H), 1.72–1.64 (m, 1 H), 1.64–

1.34 (m, 11 H), 1.28 (d, J = 6.1 Hz, 3 H), 1.25 (d, J = 6.8 Hz, 1 H), 1.24 (d, J = 7.1 Hz, 3 H), 1.24–1.15 (m, 1 H), 0.81 (t, J = 7.3 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.2, 172.4, 146.0, 144.3, 129.5, 123.9, 105.7, 95.5, 82.2, 81.1, 80.5, 77.6, 74.3, 69.8, 68.1, 60.1, 59.1, 57.7, 52.8, 48.3, 47.5, 47.1, 46.8, 44.7, 38.1, 33.8, 33.7, 30.4, 28.3, 21.2, 18.0, 17.8, 16.5, 9.4; IR (thin film) 3,500, 2,969, 2,933, 1,721, 1,661, 1,610, 1,456, 1,374, 1,287, 1,259, 1,216, 1,165, 1,118, 1,102, 1,041, 1,006, 904, 877, 838, 800, 753, 736, 702, 661 cm^{-1}; HRMS (ES), calcd for $C_{39}H_{58}BrNO_{11}$ $[M + Na]^+$ 820.3247, found 820.3264 *m/z*.



(3*R*,4*S*,8*S*,11a*S*,11b*R*,13a*S*,15*S*,16a*S*,16b*S*,)-13-Bromo-4-[(3,4,6-trideoxy-2-hydroxy-4-*N*,*N*,-dimethylamino-D-glucopyranosyl)oxy]-8-ethyl-3-methyl-15-[(6-deoxy-2,3,4-trimethyl-*O*-methyl-α-L-mannopyranosyl)oxy]-11a,11b,13a,14,15,16,16a,16b-octahydro-*as*-indaceno[3,2-*d*]-oxacyclododeca-2,10-dione (37). NaOAc (1.84 g, 22 mmol) was dissolved in H_2O (5 ml) and HOAc (1.3 ml, 23 mmol) was added. Aqueous formaldehyde (5.7 ml of a 37% solution) was added to prepare a buffered formaldehyde solution. In a separate flask, **55** (10 mg, 12.5 μmol) was dissolved in MeOH (1.6 ml) and 0.8 ml of the buffered formaldehyde solution was added. The resulting mixture was stirred for 15 min and then $NaBH_3CN$ (≈5 mg, 0.08 mmol) was added. After 10 min, an additional 5 mg (0.08 mmol) of $NaBH_3CN$ was added. This recharging process was repeated twice more at 15 min intervals at which point ESMS analysis indicated that **55** had been consumed. The reaction mixture was then poured into a biphasic mixture of CH_2Cl_2 (20 ml) and saturated $NaHCO_3$ (20 ml). The layers were separated and the aqueous layer was extracted three times with CH_2Cl_2. The combined organics were dried over Na_2SO_4, filtered through cotton on top of a fritted funnel, and concentrated yielding a bronze oil. Purification of the crude material by column chromatography (13x120 mm silica, 19:1

EtOAc/MeOH → 10:1 EtOAc/MeOH) afforded **37** (9 mg, 87%) as a clear oil: $[\alpha]_D^{26.8}$–146.5° (*c* 0.8, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.69 (s, 1 H), 6.14 (dd, *J* = 3.2, 3.2 Hz, 1 H), 4.85 (d, *J* = 1.5 Hz, 1 H), 4.71–4.65 (m, 1 H), 4.30 (app q, *J* = 6.8 Hz, 1 H), 4.23 (d, *J* = 7.3 Hz, 1 H), 3.72–3.68 (m, 1 H), 3.65–3.59 (m, 1 H), 3.56 (s, 3 H), 3.53–3.44 (m, 4 H), 3.51 (s, 3 H), 3.50 (s, 3 H), 3.45 (dd, *J* = 9.3, 3.4 Hz, 1 H), 3.35 (dq, *J* = 10.0, 6.6 Hz, 1 H), 3.12–3.07 (m, 2 H), 3.12 (dd, *J* = 9.3, 9.3 Hz, 1 H), 2.86 (ddt, *J* = 11.0, 4.5, 2.5 Hz, 1 H), 2.62–2.54 (m, 1 H), 2.40–2.34 (m, 3 H), 2.25 (br s, 6 H), 2.16–2.10 (m, 1 H), 2.03 (dd, *J* = 13.7, 7.3 Hz, 1 H), 1.74–1.64 (m, 1 H), 1.63–1.38 (m, 11 H), 1.28 (d, *J* = 6.4 Hz, 3 H), 1.28 (d, *J* = 6.4 Hz, 1 H), 1.25–1.16 (m, 1 H), 1.23 (d, *J* = 6.8 Hz, 3 H), 0.81 (t, *J* = 7.3 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.2, 172.4, 146.0, 144.3, 129.5, 123.9, 105.7, 95.5, 82.2, 81.1, 80.3, 77.5, 74.2, 73.6, 70.5, 68.0, 64.6, 61.0, 59.1, 57.7, 48.3, 47.4, 47.1, 46.8, 46.8, 44.7, 40.8, 38.1, 37.6, 33.7, 30.4, 28.3, 26.1, 21.2, 18.4, 17.8, 16.4, 9.3; IR (thin film) 3,501, 2,969, 2,934, 2,827, 2,785, 1,721, 1,661, 1,610, 1,456, 1,374, 1,286, 1,259, 1,216, 1,166, 1,119, 1,093, 1,061, 1,031, 962, 904, 877, 838, 800, 754, 737, 702, 665, 628 cm^{-1}; HRMS (ES), calcd for $C_{41}H_{64}BrNO_{11}$ $[M + H]^+$ 820.3247, found 820.3264 *m/z*.



(–)-Spinsoyn A (1). Alcohol **37** (8 mg, 9.7 μmol) was azeotropically dried by coevaporation from benzene. The dry material was dissolved in toluene under argon and DMAP (15 mg, 123 μmol) was added. Thiocarbonyldiimidazole (32 mg, 180 μmol) was added. The reaction vial was sealed with

a Teflon-lined cap and heated in a 65°C oil bath for 2 h at which point ESMS analysis indicated only a trace of **37** remained. The reaction mixture was diluted with CH_2Cl_2 and washed twice with aqueous HCl (0.1 M). The aqueous layer was then extracted twice with CH_2Cl_2. The combined organics were washed twice with saturated $NaHCO_3$ and the aqueous layer was back-extracted twice with CH_2Cl_2. The combined organics were dried over a mixture of Na_2SO_4 and K_2CO_3, filtered through cotton on a fritted funnel, and concentrated yielding **38** as a light yellow oil. This unstable intermediate was used immediately in the subsequent deoxygenation reaction.

Dioxane was degassed via three freeze–pump–thaw cycles (vent to argon). The crude thionoimidazole derivative **38** (theoretically 9.7 μmol) was dissolved in degassed dioxane (0.87 ml). In a separate vial, Bu_3SnH (58 μl, 0.22 mmol) was dissolved in 50 μl of degassed dioxane. A 0.04 M solution of AIBN in degassed dioxane was prepared and 3 μl (0.11 μmol AIBN) of this solution was added to the Bu_3SnH solution. After this solution was prepared, the reaction vial containing **38** was heated in a 100°C oil bath. When sporadic boiling of this solution was observed, the Bu_3SnH/AIBN solution was added rapidly via syringe. The resulting mixture was heated for 20 min at which point ESMS analysis indicated the complete consumption of **38**. The reaction mixture was cooled to ambient temperature, diluted with EtOAc, and concentrated yielding a clear oil. Nonpolar impurities were removed from this crude mixture by column chromatography (13x120 mm silica, EtOAc → 9:1 EtOAc/MeOH) affording a mixture of (–)-spinosyn A (**1**) and alcohol **39**. This mixture was further purified by reverse phase HPLC (C18, elution with a gradient solvent system of 35:35:30 MeOH/CH_3CN/H_2O buffered with 0.5% NH_4OAc → 45:45:10 MeOH/CH_3CN/H_2O buffered with 0.5% NH_4OAc) (10) affording **1** (2.5 mg, 35%) and alcohol **39** (≈10% based on HPLC integration). An analytical sample of **1** was prepared by preparative TLC (9:1 EtOAc/MeOH. This material was free of trace impurities; however, it was contaminated with grease. Repurification of this material by reverse phase HPLC as above (glass-distilled solvents) afforded analytically pure (–)-spinosyn A (**1**). Data for

1: ^{1}H NMR (500 MHz, $CDCl_3$ over anhydrous K_2CO_3) δ 6.76 (br s, 1 H), 5.88 (d, A of AB system *J* = 10.0 Hz, 1 H), 5.80 (dt, B of AB system, *J* = 10.0, 2.9 Hz, 1 H), 4.85 (d, *J* = 1.7 Hz, 1 H), 4.70–4.64 (m, 1 H), 4.46–4.30 (m, 1 H), 4.31 (app q, *J* = 6.4 Hz, 1 H), 3.66–3.61 (m, 1 H), 3.56 (s, 3 H), 3.54 (dd, *J* = 9.3, 6.4 Hz, 1 H), 3.52–3.45 (m, 2 H), 3.50 (s, 3 H), 3.50 (s, 3 H), 3.46 (dd, *J* = 9.3, 3.4 Hz, 1 H), 3.29 (dq, *J* = 9.5, 6.8 Hz, 1 H), 3.14–3.11 (m, 1 H), 3.12 (dd, *J* = 9.3, 9.3 Hz, 1 H), 2.87 (ddt, *J* = 11.2, 4.5, 2.7 Hz, 1 H), 2.40 (dd, *J* = 13.4, 3.2 Hz, 1 H), 2.29–2.23 (m, 1 H), 2.24 (br s, 6 H), 2.20–2.13 (m, 1 H), 2.01–1.96 (m, 1 H), 1.93 (dd, *J* = 13.2, 7.1 Hz, 1 H), 1.88–1.82 (m, 1 H), 1.81–1.75 (m, 1 H), 1.60–1.42 (m, 7 H), 1.40–1.24 (m, 4 H), 1.28 (d, *J* = 6.1 Hz, 3 H), 1.28 (d, *J* = 6.1 Hz, 1 H), 1.18 (d, *J* = 6.6 Hz, 3 H), 0.82 (t, *J* = 7.3 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.4, 147.7, 144.1, 129.4, 128.7, 95.5, 82.3, 81.2, 81.1, 77.7, 77.2, 76.9, 76.6, 76.1, 68.0, 65.2, 61.0, 59.0, 57.7, 49.5, 47.6, 47.5, 46.1, 41.5, 41.2, 37.4, 36.3, 34.3, 34.2, 30.1, 29.7, 28.4, 21.5, 17.8, 16.2, 9.4; $[\alpha]_D^{24.8}$–157.1° (*c* 0.035, $CHCl_3$); IR (thin film) 2,955, 2,931, 2,872, 2,782, 1,767, 1,721, 1,661, 1,609, 1,457, 1,375, 1,314, 1,288, 1,283, 1,214, 1,163, 1,142, 1,121, 1,106, 1,069, 1,038, 990, 905, 878, 841, 786, 718, 670 cm^{-1}; HRMS (ES), calcd for $C_{41}H_{65}NO_{10}$ $[M + H]^+$ 732.4686, found 732.4688 *m*/*z*. TLC co-spot with natural (–)-spinosyn A, R_f 0.28 (9:1 EtOAc/MeOH. Tabulated comparisons of ^{1}H and ^{13}C NMR data for synthetic and natural **1** are presented in Tables 3 and 4.

References

1. Pangborn, A. B., Giardello, M. A., Grubbs, R. H., Rosen, R. K. & Timmers, F. J. (1996) *Organometallics* **15,** 1518.
2. Still, W. C., Kahn, M. & Mitra, A. (1978) *J. Org. Chem.* **43,** 2923.
3. Smith, A. B., III, Safonov, I. G. & Corbett, R. M. (2002) *J. Am. Chem. Soc.* **124,** 11102.
4. Smith, A. B., III, Lin, Q., Nakayama, K., Boldi, A. M., Brook, C. S., McBriar, M. D., Moser, W. H., Sobukawa, M. & Zhuang, L. (1997) *Tetrahedron Lett.* **38,** 8675.
5. Evans, D. A. & Black, W. C. (1993) *J. Am. Chem. Soc.* **115,** 4497.
6. Ballestri, M., Chatgilialoglu, C., Clark, K. B., Griller, D., Giese, B. & Kopping, B. (1991) *J. Org. Chem.* **56,** 678.
7. Chatgilialoglu, C. (1992) *Acc. Chem. Res.* **25,** 188.
8. Paquette, L. A., Collado, I. & Purdie, M. (1998) *J. Am. Chem. Soc.* **120,** 2553.
9. Roush, W. R., Bennett, C. E. & Roberts, S. E. (2001) *J. Org. Chem.* **66,** 6389.

10. Kirst, H. A., Michel, K. H., Chio, E. H., Yao, R. C., Nakatsukasa, W. M., Boeck, L., Occolowitz, J. L., Paschal, J. W., Deeter, J. B. & Thompson, G. D. (1991) in *Microbial Metabolites*, ed. Nash, C. (William C. Brown, Dubuque, IA), Vol. 32, pp. 109.