Diastereoselective Additions of Allylmetal Reagents to Free and Protected *syn*-α,β-Dihydroxyketones Enable Efficient Synthetic Routes to Methyl Trioxacarcinoside A

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Supporting Information

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General Experimental Procedures

All reactions were performed in round-bottom flasks fitted with rubber septa under a positive pressure of argon, unless otherwise noted. Air- and moisture-sensitive liquids were transferred by syringe or stainless steel cannula. Organic solutions were concentrated by rotary evaporation (house vacuum, ca. 25−40 Torr) at ambient temperature, unless otherwise noted. Analytical thin-layer chromatography (TLC) was performed using glass plates pre-coated with silica gel (0.25 mm, 60 Å pore-size, 230−400 mesh, Merck KGA) impregnated with a fluorescent indicator (254 nm). TLC plates were visualized by exposure to ultraviolet light, then were stained by submersion in aqueous ceric ammonium molybdate (CAM) or potassium permanganate solutions followed by brief heating on a hot plate. Flash-column chromatography was performed as described by Still et al.,[1] employing silica gel (60 Å, 32-63 μM, standard grade, Dynamic

(1) Still, W. C.; Khan, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923−2925.

Adsorbents, Inc.). Tetrahydrofuran, dichloromethane, and ether were purified by the method of Pangborn et al.[2]

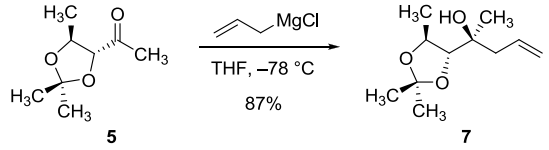
Instrumentation

Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded using Varian INOVA 500 (500 MHz) or Varian INOVA 600 (600 MHz) NMR spectrometers at 23 °C. Proton chemical shifts are expressed in parts per million (ppm, δ scale) and are referenced to residual protium in the NMR solvent ($CHCl_3$, δ 7.26 ppm; DMSO-d_5, δ 2.50 ppm). Data are represented as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet and/or multiple resonances), integration, coupling constant (*J*) in Hertz. Carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded using Varian Mercury 400 (100 MHz) or Varian INOVA 500 (125 MHz) NMR spectrometers at 23 °C. Carbon chemical shifts are expressed in parts per million (ppm, δ scale) and are referenced to the carbon resonances of the NMR solvent ($CDCl_3$, δ 77.0, DMSO-d_6, δ 39.52 ppm). Infrared (IR) spectra were obtained using a Shimadzu 8400S FT-IR spectrometer. Data are represented as follows: frequency of absorption (cm^{-1}), intensity of absorption (vs = very strong, s = strong, m = medium, w = weak, br = broad). High-resolution mass spectra were obtained at the Harvard University Mass Spectrometry Facility.

*(For clarity, intermediates that have not been assigned numbers in the text are numbered sequentially in the Supporting Information beginning with **25**.)*

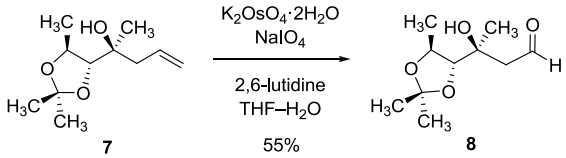
(2) Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometallics* **1996**, *15*, 1518–1520.

Initial Studies Toward Trioxacarcinose A



(*S*)-2-((4*R*,5*S*)-2,2,5-Trimethyl-1,3-dioxolan-4-yl)pent-4-en-2-ol (**7**).

Allylmagnesium chloride (2.0 M solution in tetrahydrofuran, 2.92 mL, 5.84 mmol, 2.2 equiv) was added dropwise to a solution of 1-((4*R*,5*S*)-2,2,5-trimethyl-1,3-dioxolan-4-yl)ethanone[3] **5** (420 mg, 2.66 mmol, 1 equiv) in tetrahydrofuran (25 mL) at –78 °C. After 10 min, saturated aqueous ammonium chloride solution (5 mL) was added carefully. The cooling bath was removed and the reaction flask was allowed to warm to 23 °C. The mixture was extracted with dichloromethane (3 × 30 mL). The organic layers were combined. The combined solution was dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated to provide (*S*)-2-((4*R*,5*S*)-2,2,5-trimethyl-1,3-dioxolan-4-yl)pent-4-en-2-ol (**7**) as a colorless oil (460 mg, 87%).[4] TLC: (30% ethyl acetate–hexanes) R_f = 0.59 (CAM); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 5.94–5.86 (m, 1H), 5.19–5.13 (m, 2H), 4.15–4.10 (m, 1H), 3.50 (d, 1H, *J* = 7.8 Hz), 2.35 (dd, 1H, *J* = 13.7, 6.8 Hz), 2.15 (dd, 1H, *J* = 13.7, 7.8 Hz), 1.97 (s, 1H), 1.41 (s, 3H), 1.40 (s, 3H), 1.35 (d, 3H, *J* = 5.9 Hz), 1.21 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 133.0, 118.7, 107.7, 87.4, 72.5, 71.3, 42.6, 27.3, 26.8, 23.5, 20.0; FTIR (neat), cm^{-1}: 3481 (br), 2984 (m), 1378 (s), 122 (s), 1174 (s), 1082 (s), 1055 (s), 916 (m); HRMS (ESI): Calcd for $(C_{11}H_{20}O_3+Na)^+$ 223.1305, found 223.1280.

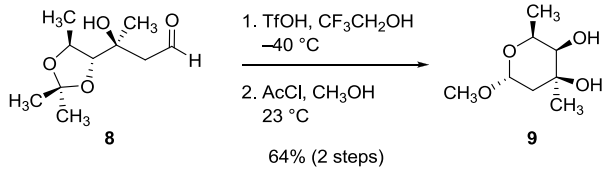


(*S*)-3-Hydroxy-3-((4*R*,5*S*)-2,2,5-trimethyl-1,3-dioxolan-4-yl)butanal (**8**).

2,6-Lutidine (341 μL, 2.95 mmol, 2.0 equiv) was added to a vigorously stirring suspension of (*S*)-2-((4*R*,5*S*)-2,2,5-trimethyl-1,3-dioxolan-4-yl)pent-4-en-2-ol **7** (295 mg, 1.47 mmol, 1 equiv),

(3) Smaltz, D. J.; Myers, A. G. *J. Org. Chem.* **2011**, *76*, 8554–8559.
(4) The product obtained in this procedure is a 4:1 mixture of diastereomers (epimeric tertiary alcohols); the major diastereomer is depicted in the equation above. The minor epimer was not easily separable by chromatography and was carried through as an impurity.

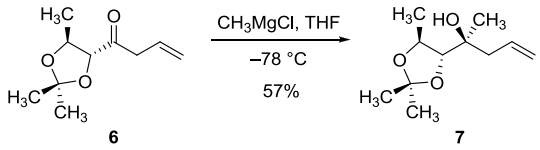
potassium osmate dihydrate (27 mg, 0.074 mmol, 0.05 equiv), and sodium periodate (1.26 g, 5.89 mmol, 4.0 equiv) in a mixture of tetrahydrofuran (20 mL) and water (10 mL). After 4 h, saturated aqueous sodium chloride solution was added (50 mL). The mixture was extracted with 1:1 ethyl acetate–hexanes (3 × 60 mL). The organic layers were combined. The combined solution was washed sequentially with saturated aqueous copper(II) sulfate solution (50 mL) then saturated aqueous sodium chloride solution (50 mL) and the washed solution was dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash-column chromatography (10% ethyl acetate–hexanes initially, grading to 30% ethyl acetate–hexanes) to provide (*S*)-3-hydroxy-3-((4*R*,5*S*)-2,2,5-trimethyl-1,3-dioxolan-4-yl)butanal (**8**) as a pale brown oil (166 mg, 56%). TLC: (30% ethyl acetate–hexanes) R_f = 0.26 (CAM); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 9.88 (m, 1H), 4.02 (m, 1H), 3.57 (d, 1H, *J* = 8.2 Hz), 2.88 (br, 1H), 2.75 (d, 1H, *J* = 16.0 Hz), 2.46 (dt, 1H, *J* = 16.5, 1.8 Hz), 1.38 (s, 3H), 1.37 (s, 3H), 1.32 (d, 3H, *J* = 6.0 Hz), 1.31 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 202.3, 108.4, 87.1, 72.8, 71.6, 50.8, 27.3, 26.9, 24.1, 20.0; FTIR (neat), cm^{-1}: 3475 (br) 2985 (m), 1718 (s), 1379 (s), 1217 (s), 1173 (s), 1077 (s), 862 (m); HRMS (ESI): Calcd for $(C_{10}H_{18}O_4+Na)^+$ 225.1113, found 225.1097.



Confirmation of Stereochemistry: Methyl 2,6-Dideoxy-3-*C*-methyl-L-*lyxo*-hexopyranoside (Methyl 3-*epi*-Axenoside, **9**).

Triflic acid (5% solution in 2,2,2-trifluoroethanol, 56 μL, 0.05 equiv) was added to a solution of (*S*)-3-hydroxy-3-((4*R*,5*S*)-2,2,5-trimethyl-1,3-dioxolan-4-yl)butanal **8** (128 mg, 0.633 mmol, 1 equiv) in 2,2,2-trifluoroethanol (9.9 mL) at –40 °C. After 40 min, triethylamine (10 μL) was added. The cooling bath was removed and the product solution was concentrated. ^{1}H NMR analysis of the residue established that the acetonide protective group had been removed. The residue was dissolved in methanol (6.3 mL). Acetyl chloride (451 μL, 6.35 mmol, 10 equiv) was added dropwise at 23 °C. After 20 min, silver carbonate (2.1 g, 7.62 mmol, 12 equiv) was added. After 10 min, the product mixture was filtered through a pad of Celite. The filtrate was concentrated. The residue was purified by flash-column chromatography (50% ethyl acetate–

hexanes) to provide the product (72 mg, 64% yield over two steps) as a colorless oil. ^{1}H NMR analysis revealed that the purified product was a mixture of α and β methyl glycosides. The most abundant component of the mixture exhibited ^{1}H NMR data in full agreement with those reported for methyl α-3-*epi*-axenoside (**9**)[5]: ^{1}H NMR (500 MHz, $CDCl_3$) δ: 4.74 (d, 1H, *J* = 4.4 Hz), 3.98 (q, 1H, *J* = 6.4 Hz), 3.31 (s, 3H), 3.19 (s, 1H), 2.67 (br, 1H), 2.28 (br, 1H), 1.75–1.87 (m, 2H), 1.39 (s, 3H), 1.28 (d, 3H, *J* = 6.4 Hz). Methyl β-axenoside was observed as a minor impurity (see S3, footnote 4): (^{1}H NMR δ: 4.61 (dd, 1H, *J* = 9.3, 2.4 Hz), 4.12 (q, 1H, *J* = 6.4 Hz)).[6]



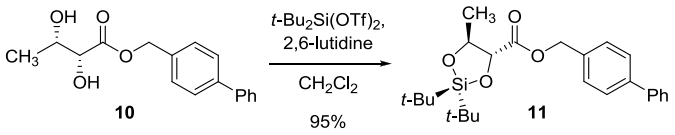
6 **7**

(*S*)-2-((4*R*,5*S*)-2,2,5-Trimethyl-1,3-dioxolan-4-yl)pent-4-en-2-ol (**7**).

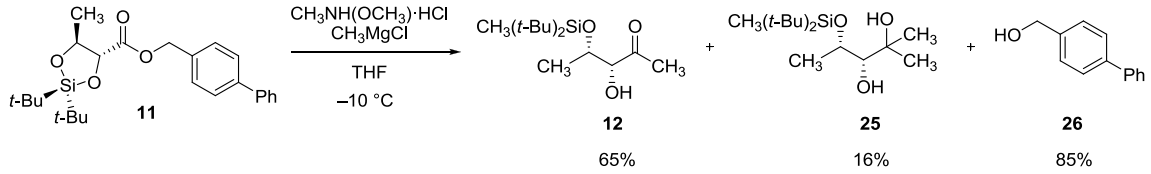
Methylmagnesium chloride (3.0 M solution in tetrahydrofuran, 288 μL, 0.863 mmol, 1.5 equiv) was added dropwise to a solution of 1-((4*R*,5*S*)-2,2,5-trimethyl-1,3-dioxolan-4-yl)but-3-en-1-one **6**[3] (106 mg, 0.575 mmol, 1 equiv) in tetrahydrofuran (6.0 mL) at –78 °C. After 45 min, a second portion of methylmagnesium chloride (3.0 M solution in tetrahydrofuran, 95 μL, 0.288 mmol, 0.5 equiv) was added. After 15 min, saturated aqueous ammonium chloride solution (2 mL) was added carefully. The cooling bath was removed and the reaction flask was allowed to warm to 23 °C. The mixture was extracted with dichloromethane (3 × 10 mL). The organic layers were combined. The combined solution was dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash-column chromatography (10% ethyl acetate–hexanes) to provide (*S*)-2-((4*R*,5*S*)-2,2,5-trimethyl-1,3-dioxolan-4-yl)pent-4-en-2-ol (**7**) as a colorless oil (65 mg, 57%). The product obtained in this procedure is a 4:1 mixture of diastereomers (epimeric tertiary alcohols); the major diastereomer is depicted in the equation above. See page S3 for characterization data.

(5) Roush, W.; Hagadorn, S. *Carbohyd. Res.* **1985**, *136*, 187–193.
(6) (a) Garegg, P. J.; Norberg, T. *Acta Chem. Scand.* **1975**, *29*, 506–513. (b) Giuliano, R. M.; Villani, F. J. J. *J. Org. Chem.* **1995**, *60*, 202–211.

Syntheses of Methyl Axenoside, Methyl Trioxacarcinoside A, and 1-*O*-Acetyl Trioxacarcinose A

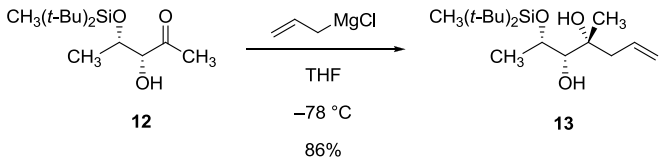


(4*R*,5*S*)-Biphenyl-4-ylmethyl 2,2-Di-*tert*-butyl-5-methyl-1,3,2-dioxasilolane-4-carboxylate (**11**). Di-*tert*-butylsilyl bis(trifluoromethanesulfonate) (12.6 mL, 34.6 mmol, 1.1 equiv) was added to a suspension of 2,6-lutidine (11.0 mL, 94.0 mmol, 3.0 equiv) and (2*R*,3*S*)-biphenyl-4-ylmethyl 2,3-dihydroxybutanoate[3] **10** (9.00 g, 31.4 mmol, 1 equiv) in dichloromethane (80 mL) at 23 °C. After 30 h, benzene (100 mL) was added and the solution was filtered through a column of silica gel, eluting with 10% ethyl acetate–hexanes. The filtrate was concentrated to provide (4*R*,5*S*)-biphenyl-4-ylmethyl 2,2-di-*tert*-butyl-5-methyl-1,3,2-dioxasilolane-4-carboxylate (**11**) as a colorless oil (12.71 g, 95%). TLC: (30% ethyl acetate–hexanes) R_f = 0.82 (CAM); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.59 (d, 4H, *J* = 7.8 Hz), 7.46–7.42 (m, 4H), 7.36 (t, 1H, *J* = 7.3 Hz), 5.31 (d, 1H, *J* = 12.2 Hz), 5.19 (d, 1H, *J* = 12.2 Hz), 4.18–4.10 (m, 2H), 1.44 (d, 3H, *J* = 5.9 Hz), 1.08 (s, 9H), 1.05 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 170.9, 141.2, 140.4, 134.3, 128.7, 128.6, 127.4, 127.2, 127.0, 80.2, 74.4, 66.4, 26.7, 26.7, 21.3, 21.0, 20.5; FTIR (neat), cm^{-1}: 2934 (m), 1759 (m), 1473 (m), 1279 (m), 1119 (s), 1090 (s), 928 (m), 826 (s); HRMS (ESI): Calcd for $(C_{25}H_{34}O_4Si+Na)^+$ 449.2119, found 449.2122.



(3*R*,4*S*)-4-(Di-*tert*-butyl(methyl)silyloxy)-3-hydroxypentan-2-one (**12**). Methylmagnesium chloride (3.0 M solution in tetrahydrofuran, 79.0 mL, 238 mmol, 8.0 equiv) was added dropwise through an addition funnel over 20 min to a suspension of *N*,*O*-dimethylhydroxylamine hydrochloride (3.63 g, 37.2 mmol, 1.25 equiv) and (4*R*,5*S*)-biphenyl-4-ylmethyl 2,2-di-*tert*-butyl-5-methyl-1,3,2-dioxasilolane-4-carboxylate **11** (12.71 g, 29.8 mmol, 1 equiv) in tetrahydrofuran (300 mL) at –10 °C. After 10 min, saturated aqueous ammonium chloride solution (50 mL) was added carefully. The cooling bath was removed and the reaction flask was allowed to warm to 23 °C. Water (200 mL) was added, and the mixture was extracted

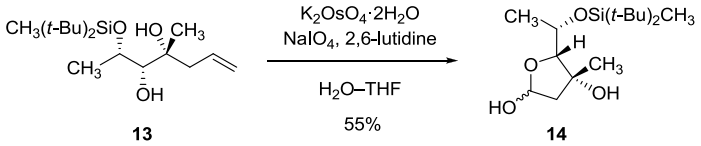
with ether (4 × 200 mL). The organic layers were combined. The combined solution was washed with saturated aqueous sodium chloride solution (100 mL) and the washed solution was dried over magnesium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash-column chromatography (5% ethyl acetate–hexanes initially, grading to 30% ethyl acetate–hexanes) to provide (3*R*,4*S*)-4-(Di-*tert*-butyl(methyl)silyloxy)-3-hydroxypentan-2-one (**12**) as a colorless oil (5.34 g, 65%). TLC: (20% ethyl acetate–hexanes) R_f = 0.60 (CAM); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 4.19 (m, 1H), 4.14 (m, 1H), 3.62 (d, 1H, *J* = 5.5 Hz), 2.31 (s, 3H), 1.05 (d, 1H, *J* = 6.4 Hz), 0.98 (s, 9H), 0.95 (s, 9H), 0.09 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 209.6, 80.4, 70.5, 27.8, 27.7, 27.6, 20.9, 20.1, 18.4, –8.9; FTIR (neat), cm^{-1}: 3482 (br), 2934 (m), 1715 (m), 1472 (m), 1256 (m), 1105 (s), 1007 (m), 824 (s); HRMS (ESI): Calcd for $(C_{14}H_{30}O_3Si+H)^+$ 275.2037, found 275.2034. In addition to the desired product, the tertiary alcohol byproduct, (3*R*,4*S*)-4-(di-*tert*-butyl(methyl)silyloxy)-2-methylpentane-2,3-diol (**25**), was obtained as a colorless oil (1.36 g, 16%). TLC: (20% ethyl acetate–hexanes) R_f = 0.38 (CAM); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 4.30–4.25 (m, 1H), 3.08–3.04 (m, 2H), 2.83 (s, 1H), 1.31 (d, 3H, *J* = 6.4 Hz), 1.26 (s, 6H), 1.02 (s, 9H), 0.99 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 80.1, 72.3, 69.8, 28.0, 27.8, 26.8, 26.1, 22.7, 21.2, 20.2, –6.8; FTIR (neat), cm^{-1}: 3470 (br), 2859 (m), 1471 (m), 1256 (m), 1128 (m), 1060 (s), 934 (s), 823 (s); HRMS (ESI): Calcd for $(C_{15}H_{34}O_3Si+H)^+$ 291.2350, found 291.2362. Finally, a fraction containing 4-phenylbenzyl alcohol **26** (90% purity) was collected. Recrystallization from dichloromethane–hexanes furnished pure 4-phenylbenzyl alcohol as a white solid (≥95% purity, 4.68 g, 85%).



(2*S*,3*R*,4*R*)-2-(Di-*tert*-butyl(methyl)silyloxy)-4-methylhept-6-ene-3,4-diol (**13**).

Allylmagnesium chloride (2.0 M solution in tetrahydrofuran, 19.8 mL, 39.6 mmol, 3.0 equiv) was added dropwise to a solution of (3*R*,4*S*)-4-(di-*tert*-butyl(methyl)silyloxy)-3-hydroxypentan-2-one **12** (3.62 g, 13.2 mmol, 1 equiv) in tetrahydrofuran (88 mL) at –78 °C. After 3 h, a second portion of allylmagnesium chloride (2.0 M solution in tetrahydrofuran, 6.6 mL, 13.2 mmol, 1.0 equiv) was added. After 1 h, the cooling bath was removed. After 10 min, aqueous ammonium chloride solution (50% saturated, 25 mL) was added slowly, and the reaction flask was allowed

to warm to 23 °C. Aqueous sodium chloride solution (25% saturated, 50 mL), and methyl *tert*-butyl ether (50 mL) were added. The layers were separated. The aqueous layer was extracted with methyl *tert*-butyl ether (2 × 100 mL). The organic layers were combined. The combined solution was washed with saturated aqueous sodium chloride solution (50 mL) and the washed solution was dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash-column chromatography (5% ethyl acetate–hexanes) to provide (2*S*,3*R*,4*R*)-2-(di-*tert*-butyl(methyl)silyloxy)-4-methylhept-6-ene-3,4-diol (**13**) as a colorless oil (3.59 g, 86%).[7] TLC: (20% ethyl acetate–hexanes) R_f = 0.60 (CAM); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 5.86 (m, 1H), 5.12 (m, 1H), 5.10 (t, 1H, *J* = 1.5 Hz), 4.3 (dq, 1H, *J* = 5.9, 3.9 Hz), 3.11 (dd, 1H, *J* = 6.8, 3.4 Hz), 3.05 (d, 1H, *J* = 6.8 Hz), 2.90 (s, 1H), 2.26 (m, 2H), 1.30 (d, 3H, *J* = 6.4 Hz), 1.20 (s, 3H), 1.02 (s, 9H), 0.99 (s, 9H), 0.17 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 134.0, 118.1, 77.9, 73.9, 69.6, 44.1, 28.0, 27.9, 23.2, 22.8, 21.3, 20.3, –6.7; FTIR (neat), cm^{-1}: 3503 (br), 2934 (m), 1472 (m), 1256 (m), 1065 (s), 928 (m), 824 (s); HRMS (ESI): Calcd for $(C_{17}H_{36}O_3Si+Na)^+$ 339.2326, found 339.2330.

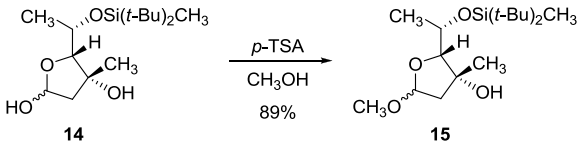


5-*O*-(Di-*tert*-butylmethylsilyl)-2,6-dideoxy-3-*C*-methyl-L-*xylo*-hexofuranose (**14**).

Potassium osmate dihydrate (209 mg, 0.567 mmol, 0.05 equiv) was added to a solution of (2*S*,3*R*,4*R*)-2-(di-*tert*-butyl(methyl)silyloxy)-4-methylhept-6-ene-3,4-diol **13** (3.59 g, 11.3 mmol, 1 equiv), sodium periodate (9.70 g, 45.4 mmol, 4.0 equiv), and 2,6-lutidine (2.64 mL, 22.7 mmol, 2.0 equiv) in a mixture of tetrahydrofuran (76 mL) and water (38 mL) at 23 °C. After 3 h, the product mixture was partitioned between saturated aqueous sodium chloride solution (100 mL), ethyl acetate (50 mL), and hexanes (50 mL). The layers were separated. The aqueous layer was extracted with 50% ethyl acetate–hexanes (2 × 100 mL). The organic layers were combined. The combined solution was washed with saturated aqueous copper(II) sulfate solution (100 mL) then saturated aqueous sodium chloride solution (100 mL) and the washed solution was dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The

(7) The product obtained in this procedure is a 13:1 mixture of diastereomers (epimeric tertiary alcohols); the major diastereomer is depicted in the equation above. The minor epimer was carried through as an impurity to the stage of the oxidative cleavage reaction (vide infra), where the diastereomeric products were easily separated.

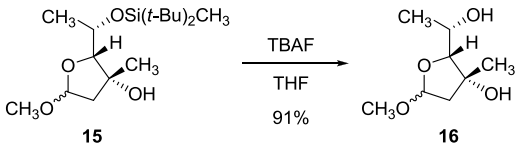
residue was purified by flash-column chromatography (10% ethyl acetate–hexanes initially, grading to 20% ethyl acetate–hexanes) to provide 5-*O*-(di-*tert*-butylmethylsilyl)-2,6-dideoxy-3-*C*-methyl-L-*xylo*-hexofuranose (**14**) as a 1:1.9 mixture of α- and β-anomers, respectively (1.97 g, 55%). TLC: (20% ethyl acetate–hexanes) R_f = 0.27 (CAM); ^{1}H NMR (500 MHz, $CDCl_3$) δ: α-anomer (minor): 5.66 (m, 1H), 4,35 (m, 1H) 4.17 (s, 1H), 3.79 (d, 1H, *J* = 3.9 Hz), 2.61 (br, 1H), 2.33 (dd, 1H, *J* = 13.7, 5.9 Hz), 1.92 (dd, 1H, *J* = 13.7, 3.4 Hz), 1.48 (s, 3H), 1.37 (d, 3H, *J* = 6.4 Hz), 1.01 (s, 9H), 0.98 (s, 9H), 0.16 (s, 3H); β-anomer (major): 5.41 (dd, 1H, *J* = 8.8, 4.9 Hz), 4.46 (s, 1H), 4.35 (m, 1H), 3.68 (d, 1H, *J* = 8.8 Hz), 3.48 (d, 1H, *J* = 4.4 Hz), 2.52 (s, 1H), 2.10 (d, 1H, *J* = 13.7 Hz), 2.02 (dd, 1H, *J* = 13.2, 4.9 Hz), 1.42 (s, 3H), 1.38 (d, 3H, *J* = 6.4 Hz), 1.03 (s, 9H), 1.00 (s, 9H), 0.18 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 97.8, 97.5, 89.0, 85.8, 79.2, 78.1, 70.7, 70.1, 50.1, 48.7, 27.9, 27.9, 27.8, 27.7, 27.3, 24.6, 21.2, 21.2, 20.9, 20.5, 20.3, 20.2, –7.1, –7.2; FTIR (neat), cm^{-1}: 3420 (br), 2934 (m), 1472 (m), 1256 (m), 1086 (s), 934 (m), 824 (s); HRMS (ESI): Calcd for $(C_{16}H_{34}O_4Si+Na)^+$ 341.2119, found 341.2129.



Methyl 5-*O*-(Di-*tert*-butylmethylsilyl)-2,6-dideoxy-3-*C*-methyl-L-*xylo*-hexofuranoside (**15**).

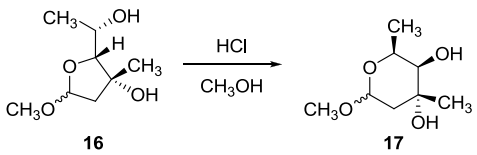
p-Toluenesulfonic acid monohydrate (353 mg, 1.86 mmol, 0.3 equiv) was added to a solution of (4*R*,5*R*)-5-((*S*)-1-(di-*tert*-butyl(methyl)silyloxy)ethyl)-4-methyltetrahydrofuran-2,4-diol **14** (1.97 g, 6.18 mmol, 1 equiv) in methanol (16 mL) at 23 °C. After 50 min, triethylamine (300 μL) was added and the product solution was concentrated. The residue was filtered through a short pad of silica gel (length: 2.5 cm, diameter: 3.5 cm), eluting with ethyl acetate (60 mL). The filtrate was concentrated to provide methyl 5-*O*-(di-*tert*-butylmethylsilyl)-2,6-dideoxy-3-*C*-methyl-L-*xylo*-hexofuranoside (**15**) as a 1:4.8 mixture of α- and β-anomers, respectively (1.84 g, 89%). TLC: (20% ethyl acetate–hexanes) R_f = 0.49, 0.69 (CAM); ^{1}H NMR (600 MHz, $CDCl_3$) δ: α-anomer (minor): 4.93 (dd, 1H, *J* = 4.4, 0.9 Hz), 4.05 (m, 1H), 3.54 (d, 1H, *J* = 7.0 Hz), 3.45 (s, 1H), 3.37 (s, 3H), 2.07–2.01 (m, 2H), 1.36 (s, 3H), 1.28 (d, 3H, *J* = 6.2 Hz), 1.00 (s, 9H), 0.96 (s, 9H), 0.11 (s, 3H); β-anomer (major): 5.06 (dd, 1H, *J* = 5.9, 2.9 Hz), 4.30 (dq, 1H, *J* = 6.4, 4.4 Hz), 3.80 (s, 1H), 3.64 (d, 1H, *J* = 4.1 Hz), 3.33 (s, 3H), 2.26 (dd, 1H, *J* = 13.7, 5.9 Hz), 1.92 (dd, 1H, *J* = 13.8, 2.6 Hz), 1.43 (s, 3H), 1.34 (d, 3H, *J* = 6.4 Hz), 1.00 (s, 9H), 0.96 (s, 9H), 0.13 (s, 3H); ^{13}C

NMR (100 MHz, $CDCl_3$) δ: 103.9, 103.7, 91.8, 85.6, 78.9, 77.0, 71.8, 70.3, 55.4, 55.1, 49.7, 48.5, 27.9, 27.9, 27.8, 27.7, 24.5, 21.5, 21.1, 21.0, 20.5, 20.3, 20.3, 20.2, –7.5, –8.1; FTIR (neat), cm^{-1}: 3482 (br), 2934 (m), 1472 (m), 1254 (m), 1105 (s), 1044 (s); HRMS (ESI): Calcd for $(C_{17}H_{36}O_4Si+Na)^+$ 355.2275, found 355.2266.



Methyl 2,6-Dideoxy-3-C-methyl-L-*xylo*-hexofuranoside (**16**).

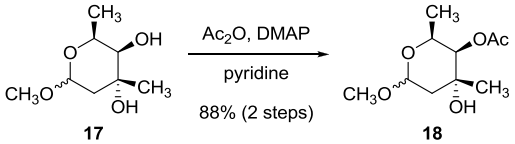
Tetra-*n*-butylammonium fluoride (1.0 M solution in tetrahydrofuran, 6.07 mL, 6.07 mmol, 1.1 equiv) was added to a solution of methyl 5-*O*-(di-*tert*-butylmethylsilyl)-2,6-dideoxy-3-*C*-methyl-L-*xylo*-hexofuranoside **15** (1.836 g, 5.52 mmol, 1 equiv) in tetrahydrofuran (37 mL) at 23 °C. After 16 h, the reaction mixture was partitioned between saturated aqueous sodium bicarbonate solution (10 mL) and ethyl acetate (50 mL). The layers were separated. The aqueous layer was extracted with ethyl acetate (3 × 50 mL). The organic layers were combined. The combined solution was dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash-column chromatography (10% ethyl acetate–hexanes initially, grading to 30% ethyl acetate–hexanes, then 80% ethyl acetate–hexanes, then ethyl acetate) to provide methyl 2,6-dideoxy-3-C-methyl-L-*xylo*-hexofuranoside (**16**) as a 1:5.0 mixture of α- and β-anomers, respectively (890 mg, 91%). TLC: (80% ethyl acetate–hexanes) R_f = 0.38 (CAM); ^{1}H NMR (500 MHz, $CDCl_3$) δ: α-anomer (minor): 5.02 (d, 1H, *J* = 4.9 Hz), 4.01 (m, 1H), 3.66 (s, 1H), 3.55 (s, 1H), 3.42 (s, 3H), 3.02 (d, 1H, *J* = 5.0 Hz), 2.17–2.08 (m, 2H), 1.38 (s, 3H), 1.28 (d, 3H, *J* = 6.4); β-anomer (major): 5.16 (dd, 1H, *J* = 5.9, 3.4 Hz), 4.11 (m, 1H), 3.73 (s, 1H), 3.56 (d, 1H, *J* = 1.5 Hz), 3.39 (s, 3H), 2.44 (d, 1H, *J* = 7.9 Hz), 2.30 (dd, 1H, *J* = 13.8, 5.6 Hz), 1.94 (dd, 1H, *J* = 13.8, 3.2 Hz), 1.39 (s, 3H), 1.36 (d, 3H, *J* = 6.7 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 104.1, 103.8, 90.2, 85.0, 79.1, 77.6, 67.2, 65.9, 55.3, 55.0, 49.6, 48.1, 25.4, 25.2, 21.4, 19.6; FTIR (neat), cm^{-1}: 3385 (br), 1375 (m), 1285 (w), 1198 (m), 1101 (s), 1028 (s), 970 (m); Calcd for $(C_8H_{16}O_4+Na)^+$ 199.0941, found 199.0932.



16 17

Methyl 2,6-Dideoxy-3-*C*-methyl-L-*xylo*-hexopyranoside (Methyl Axenoside, **17**).

Hydrochloric acid (1.0 M solution in methanol, 5.60 mL, 5.60 mmol, 1.1 equiv) was added to a solution of methyl 2,6-dideoxy-3-C-methyl-L-*xylo*-hexofuranoside **16** (890 mg, 5.05 mmol, 1 equiv) in methanol (45 mL) at 23 °C. After 22 h, silver carbonate (2.23 g, 8.08 mmol, 1.6 equiv) was added. After 30 min, the product mixture was filtered through a short pad of Celite, washing with methanol (50 mL). The filtrate was concentrated to provide the product, methyl 2,6-dideoxy-3-*C*-methyl-L-*xylo*-hexopyranoside (**17**), as a 1:1.8 mixture of α- and β-anomers, respectively, which was used directly in the next reaction without purification.[8] TLC: (5% methanol–dichloromethane) R_f = 0.26, 0.36 (CAM); ^{1}H NMR (500 MHz, $CDCl_3$) δ: α-anomer (minor): 4.80 (d, 1H, *J* = 3.9 Hz), 4.30 (q, 1H, *J* = 6.8 Hz), 4.02 (s, 1H), 3.38 (s, 3H), 3.14 (d, 1H, *J* = 7.8 Hz), 1.91 (dd, 1H, *J* = 14.7, 3.9 Hz), 1.73 (d, 1H, *J* = 8.3 Hz), 1.26 (d, 3H, *J* = 6.8 Hz), 1.24 (s, 3H); β-anomer (major): 4.62 (dd, 1H, *J* = 9.8, 2.4 Hz), 4.13 (dq, 1H, *J* = 6.8, 1.0 Hz), 3.50 (s, 3H), 2.98 (d, 1H, *J* = 10.3 Hz), 1.97 (d, 1H, *J* = 9.8 Hz), 1.69–1.57 (m, 2H), 1.34 (s, 3H), 1.27 (d, 3H, *J* = 6.8 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 100.4, 99.0, 74.6, 74.4, 72.5, 70.2, 68.9, 62.5, 56.5, 55.2, 39.1, 35.4, 27.8, 26.0, 16.7, 16.6; FTIR (neat), cm^{-1}: 3447 (br), 2934 (m), 1375 (m), 1121 (s), 1059 (s), 995 (s); Calcd for $(C_8H_{16}O_4+Na)^+$ 199.0941, found 199.0929.



17 18

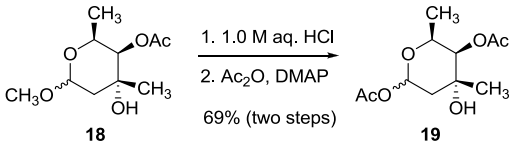
Methyl Trioxacarcinoside A (**18**).

Acetic anhydride (500 μL, 5.30 mmol, 1.05 equiv) was added to a solution of methyl 2,6-dideoxy-3-*C*-methyl-L-*xylo*-hexopyranoside **17** (1 equiv, see paragraph above) and 4-dimethylaminopyridine (1.23 g, 10.1 mmol, 2.0 equiv) in pyridine (50 mL) at 23 °C. After 20 h, a second portion of acetic anhydride (100 μL, 1.06 mmol, 0.2 equiv) was added. After 90 min, a third portion of acetic anhydride (150 μL, 1.59 mmol, 0.3 equiv) was added. After 40 min, the

(8) The product is a (presumably, thermodynamic) mixture of methyl pyranoside and furanoside isomers: (β-pyranoside: 62%, α-pyranoside: 34%, β-furanoside: 4%, α-furanoside: <1%). The furanosides were carried through as impurities to the stage of the acetylation reaction (vide infra), where the isomeric products were easily separated.

product solution was partitioned between ethyl acetate (150 mL) and saturated aqueous sodium bicarbonate solution (20 mL). The layers were separated. The organic layer was dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash-column chromatography (20% ethyl acetate–hexanes initially, grading to 60% ethyl acetate–hexanes) to provide methyl trioxacarcinoside A (**18**) as a 1:1.7 mixture of α- and β-anomers, respectively (970 mg, 88% yield over two steps). For characterization purposes, a sample of the product (~50 mg) was purified by flash-column chromatography (20% ethyl acetate–hexanes initially, grading to 60% ethyl acetate–hexanes) to provide separately α- and β-methyl trioxacarcinoside A, which were characterized by ^{1}H NMR, ^{13}C NMR, IR, and HRMS. Analytical data for the synthetic substances were in agreement with those reported in the literature.[9] α-anomer (minor): TLC: (50% ethyl acetate–hexanes) R_f = 0.63 (CAM); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 4.86 (d, 1H, *J* = 3.4 Hz), 4.70 (s, 1H), 4.32 (q, 1H, *J* = 6.4 Hz), 4.28 (s, 1H), 3.39 (s, 3H), 2.14 (s 3H), 1.93 (dd, 1H, *J* = 14.2, 3.9 Hz), 1.72 (dt, 1H, *J* = 14.7, 1.2 Hz), 1.13 (d, 3H, *J* = 6.4 Hz), 1.10 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 170.4, 99.1, 74.6, 68.8, 61.8, 55.2, 36.2, 25.7, 20.9, 16.6; FTIR (neat), cm^{-1}: 3507 (br, w), 2938 (w), 1748 (s), 1375 (m), 1233 (s), 1140 (m), 1121 (s), 1082 (m), 1047 (s), 1020 (m), 997 (s); HRMS (ESI): Calcd for $(C_{10}H_{18}O_5+Na)^+$ 241.1046, found 241.1050. β-anomer (major): $[\alpha]_D$ +13.3 (*c* 0.40, $CHCl_3$), lit.[9] $[\alpha]_D$ +14.5 (*c* 0.5, $CHCl_3$); TLC: (50% ethyl acetate–hexanes) R_f = 0.47 (CAM); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 4.67 (dd, 1H, *J* = 9.5, 2.7 Hz), 4.57 (d, 1H, *J* = 1.5 Hz), 4.15 (dq, 1H, *J* = 6.4, 1.5 Hz), 3.52 (s, 3H), 2.14 (s, 3H), 1.75–1.64 (m, 2H), 1.43 (s, 1H), 1.21 (s, 3H), 1.16 (d, 3H, *J* = 6.4 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 170.9, 99.9, 74.1, 71.3, 67.9, 56.5, 39.6, 27.1, 20.8, 16.5; FTIR (neat), cm^{-1}: 3468 (br), 2936 (w), 1745 (s), 1447 (m), 1373 (m), 1234 (s), 1169 (m), 1153 (m), 1119 (m), 1053 (s), 1011 (s), 922 (m); HRMS (ESI): Calcd for $(C_{10}H_{18}O_5+Na)^+$ 241.1046, found 241.1051.

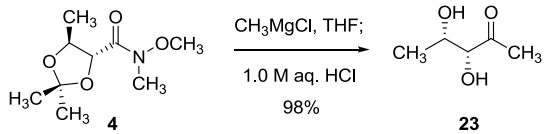
(9) Shirahata, K.; Iida, T.; Hirayama, N. *Symposium on the Chemistry of Natural Products* **1981**, 24, 199−206.



1-*O*-Acetyl Trioxacarcinose A (**19**).

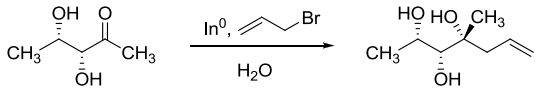
Methyl trioxacarcinoside A **18** (200 mg, 0.916 mmol, 1 equiv, 1:1.7 mixture of α- and β-anomers, respectively) was treated with 1.0 M aqueous hydrochloric acid (9.16 mL, 9.16 mmol, 10.0 equiv) at 23 °C. After 16 h, sodium bicarbonate (924 mg, 11.0 mmol, 12 equiv) was added, and the product solution was saturated with sodium chloride. The mixture was extracted with ethyl acetate (3 × 50 mL). The organic layers were combined. The combined solution was dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was dissolved in pyridine (13.9 mL). 4-Dimethylaminopyridine (170 mg, 1.39 mmol, 2.0 equiv) and acetic anhydride (69 μL, 0.73 mmol, 1.05 equiv) were added in sequence at 23 °C. After 15 h, a second portion of acetic anhydride (16 μL, 0.17 mmol, 0.25 equiv) was added. After 2.5 h, the product solution was partitioned between ethyl acetate (50 mL) and water (10 mL). The layers were separated. The organic layer was washed sequentially with 1.0 M aqueous hydrochloric acid solution (2 × 10 mL), saturated aqueous sodium bicarbonate solution (10 mL), then saturated aqueous sodium chloride solution (10 mL) and the washed solution was dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash-column chromatography (15% ethyl acetate–hexanes initially, grading to 40% ethyl acetate–hexanes) to provide 1-*O*-acetyl trioxacarcinose A (**19**) as a 1:3.4 mixture of α- and β-anomers, respectively (155 mg, 69%). For characterization purposes, a sample of the product (~50 mg) was further purified by flash-column chromatography (10% ethyl acetate–hexanes initially, grading to 30% ethyl acetate–hexanes) to provide the pure β-anomer, which was characterized by ^{1}H NMR, ^{13}C NMR, IR, and HRMS. TLC: (50% ethyl acetate–hexanes) R_f = 0.42 (CAM); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 5.99 (dd, 1H, J = 7.8, 4.9 Hz), 4.60 (s, 1H), 4.29 (q, 1H, J = 6.4 Hz), 2.25 (s, 1H), 2.13 (s, 3H), 2.08 (s, 3H), 1.76 (m, 2H), 1.20 (s, 3H), 1.13 (d, 3H, J = 6.4 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 170.7, 169.4, 91.8, 73.6, 71.0, 69.1, 38.4, 26.9, 21.1, 20.8, 16.4; FTIR (neat), cm^{-1}: 3482 (br), 2984 (m), 1734 (s), 1374 (m), 1233 (s), 1144 (s), 995 (s); HRMS (ESI): Calcd for $(C_{11}H_{18}O_6+Na)^+$ 269.0996, found 269.0994.

Second-Generation Synthesis of 1-*O*-Acetyl Trioxacarcinose A



(3*R*,4*S*)-3,4-Dihydroxypentan-2-one (**23**).

Methylmagnesium chloride (3.0 M solution in tetrahydrofuran, 86.0 mL, 257 mmol, 3.0 equiv) was added over 15 min to an ice-cooled solution of (4*R*,5*S*)-*N*-methoxy-*N*,2,2,5-tetramethyl-1,3-dioxolane-4-carboxamide **4**[3] (17.4 g, 86.0 mmol, 1 equiv) in tetrahydrofuran (570 mL). After 5 min, saturated aqueous ammonium chloride solution (80 mL) was added dropwise, and the reaction flask was allowed to warm to 23 °C. Aqueous hydrochloric acid solution (1.0 M, 570 mL) was added, a reflux condenser was affixed, and the reaction flask was heated at 60 °C. After 90 min of vigorous stirring, the reaction flask was allowed to cool to 23 °C. The product mixture was concentrated. Ethyl acetate (1 L) was added, and the suspension was dried over sodium sulfate. The dried suspension was filtered and the filtrate was concentrated to provide (3*R*,4*S*)-3,4-dihydroxypentan-2-one (**23**) as a colorless oil (9.89 g, 98%). Analytical data were in agreement with values previously reported.[10] TLC: (80% ethyl acetate–hexanes) R_f = 0.37 (CAM); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 4.18 (m, 1H), 3.98 (dd, 1H, *J* = 4.6, 2.3 Hz), 3.81 (d, 1H, *J* = 4.6 Hz), 2.44 (d, 1H, *J* = 9.2 Hz), 2.24 (s, 3H), 1.30 (d, 3H, *J* = 6.4 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 208.3, 80.4, 67.9, 25.5, 20.0; FTIR (neat), cm^{-1}: 3421 (br), 2934 (w), 1713 (s), 1360 (m), 1242 (m), 1134 (s), 1074 (s), 1009 (m); HRMS (ESI): Calcd for $(C_5H_{10}O_3+Na)^+$ 141.0522, found 141.0524.

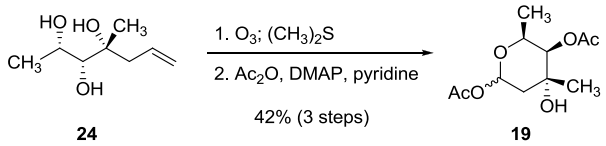


(2*S*,3*R*,4*R*)-4-Methylhept-6-ene-2,3,4-triol (**24**).

Allyl bromide (3.77 mL, 43.5 mmol, 1.5 equiv) was added to a mixture of (3*R*,4*S*)-3,4-dihydroxypentan-2-one **23** (3.43 g, 29.0 mmol, 1 equiv) and indium powder (5.00 g, 43.5 mmol, 1.5 equiv) in water (290 mL) at 23 °C. The reaction flask was sealed with a rubber septum. After 1 h of vigorous stirring, the product mixture was concentrated. Ethyl acetate (200 mL) was

(10) Zörb, A.; Brückner, R. *Eur. J. Org. Chem.* **2010**, 4785-4801.

added, and the suspension was dried over sodium sulfate. The dried suspension was filtered and the filtrate was concentrated. A small sample of the product (~50 mg) was purified by flash-column chromatography (60% ethyl acetate–hexanes initially, grading to 100% ethyl acetate) and the purified product was characterized by ^{1}H NMR, ^{13}C NMR, IR, and HRMS.[11] The balance of the product, (2*S*,3*R*,4*R*)-4-methylhept-6-ene-2,3,4-triol (**24**), was used directly in the next reaction without purification. TLC: (5% methanol–dichloromethane) R_f = 0.25 (CAM); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 5.88–5.79 (m, 1H), 5.01 (d, 1H, *J* = 4.9 Hz), 4.99 (d, 1H, *J* = 1.0 Hz), 4.45 (s, 1H), 4.40 (d, 1H, *J* = 4.9 Hz), 4.18 (d, 1H, *J* = 7.8 Hz), 3.95 (m, 1H), 2.91 (d, 1H, *J* = 7.8 Hz), 2.23 (m, 2H), 1.08 (d, 3H, *J* = 6.4 Hz), 1.06 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ: 135.5, 116.8, 76.8, 74.3, 65.5, 42.9, 24.1, 21.4; FTIR (neat), cm^{-1}: 3379 (br), 2934 (m), 1377 (m), 1124 (s), 997 (s), 916 (s); HRMS (ESI): Calcd for $(C_8H_{16}O_3+Na)^+$ 183.0992, found 183.0982.

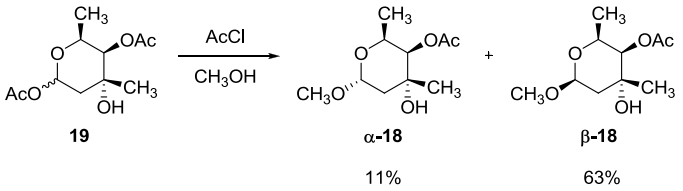


1-*O*-Acetyl Trioxacarcinose A (**19**).

Ozone was bubbled through a solution of (2*S*,3*R*,4*R*)-4-methylhept-6-ene-2,3,4-triol **24** (1 equiv, see paragraph above) in methanol (290 mL) at –78 °C. After 30 min, oxygen was bubbled through the blue-green solution. After 10 min, methyl sulfide (21.3 mL, 290 mmol, 10.0 equiv) was added, and the reaction flask was allowed to warm to 23 °C. After 16 h, the solution was concentrated. The residue was dissolved in pyridine (290 mL). Acetic anhydride (5.76 mL, 61.0 mmol, ~2.1 equiv) and 4-dimethylaminopyridine (7.45 g, 61.0 mmol, ~2.1 equiv) were added in sequence at 23 °C. After 2 h, a second portion of acetic anhydride (2.74 mL, 29.0 mmol, ~1.0 equiv) was added. After 45 min, saturated aqueous sodium bicarbonate solution (100 mL) was added, and the product mixture was concentrated. The residue was partitioned between ethyl acetate (800 mL) and saturated aqueous sodium bicarbonate solution (200 mL). The layers were separated. The aqueous layer was extracted with ethyl acetate (800 mL). The organic layers were combined. The combined solution was dried over sodium sulfate. The dried solution was filtered

(11) The product obtained in this procedure is a 15:1 mixture of diastereomers (epimeric tertiary alcohols); the major diastereomer is depicted in the equation above. The minor C4 epimer was carried through as an impurity to the stage of the acetylation reaction (vide infra), where the diastereomeric products were easily separated.

and the filtrate was concentrated. The residue was purified by flash-column chromatography (15% ethyl acetate–hexanes initially, grading to 40% ethyl acetate–hexanes) to provide the product, 1-*O*-acetyl trioxacarcinose A (**19**), as a 1:12.1 mixture of α- and β-anomers, respectively (2.97 g, 42% yield over 3 steps). For characterization purposes, a sample of the product (~50 mg) was further purified by flash-column chromatography (10% ethyl acetate–hexanes initially, grading to 30% ethyl acetate–hexanes) to provide the pure β-anomer, which was characterized by ^{1}H NMR, ^{13}C NMR, IR, and HRMS. See page S13 for characterization data.



19 α-**18** β-**18**

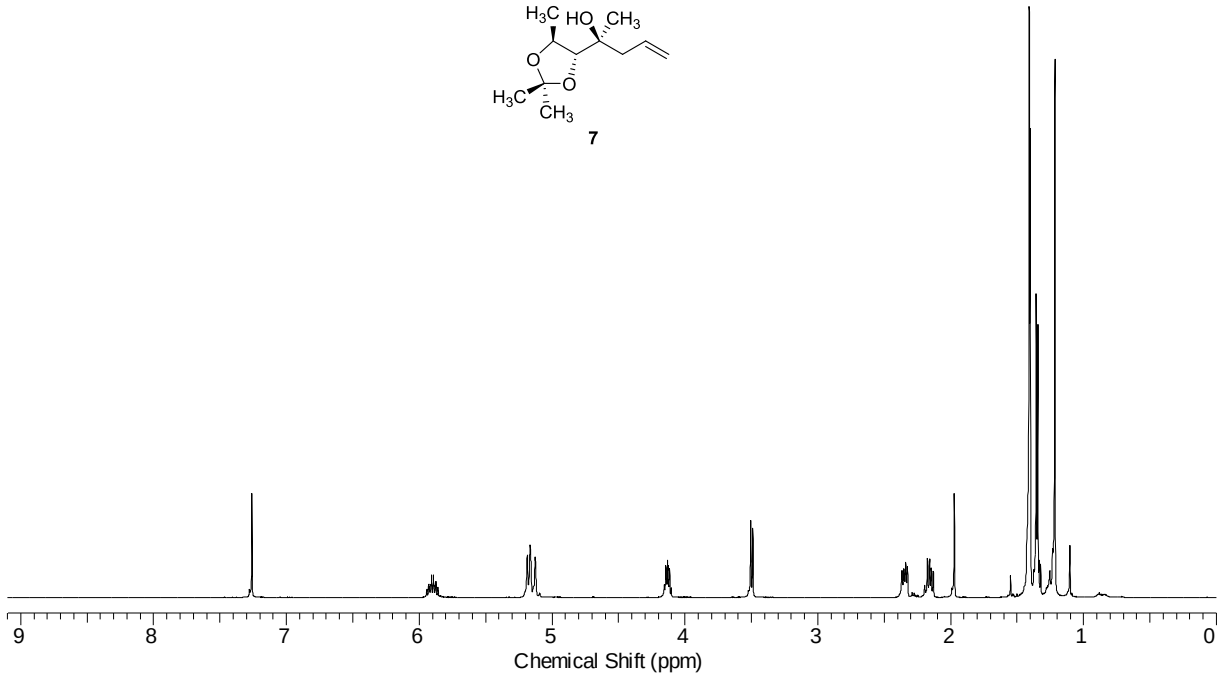
11% 63%

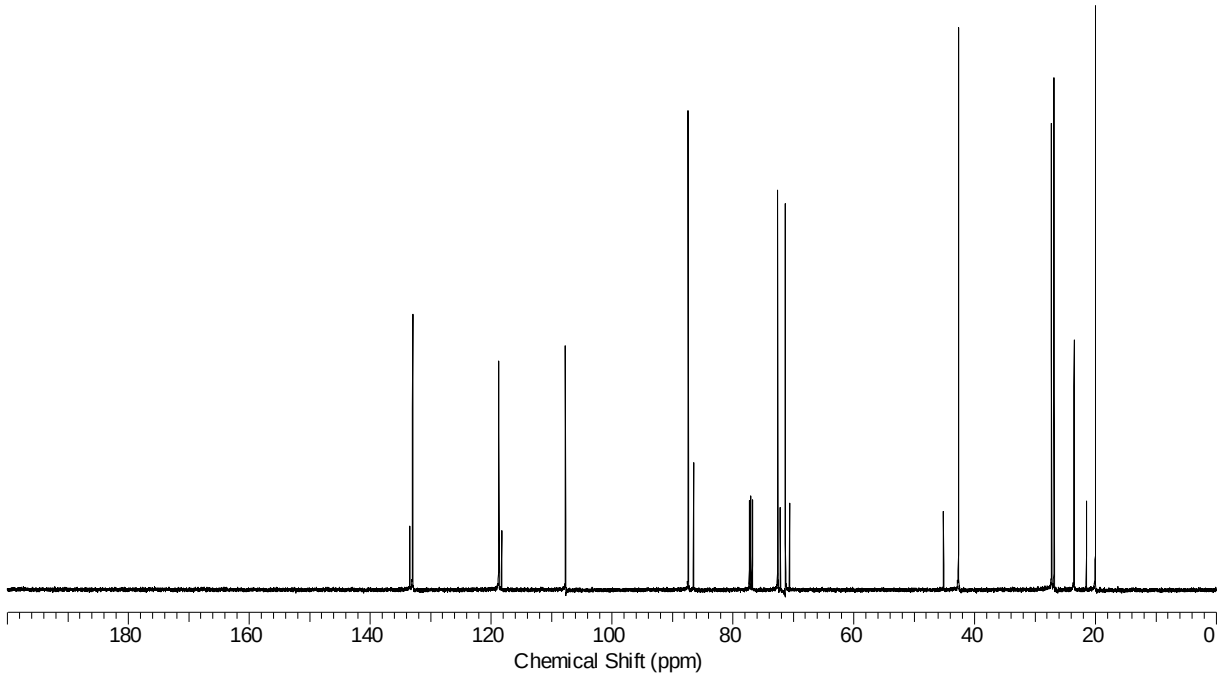
Conversion of 1-*O*-Acetyl Trioxacarcinose A (**19**) to Methyl Trioxacarcinoside A (**18**).

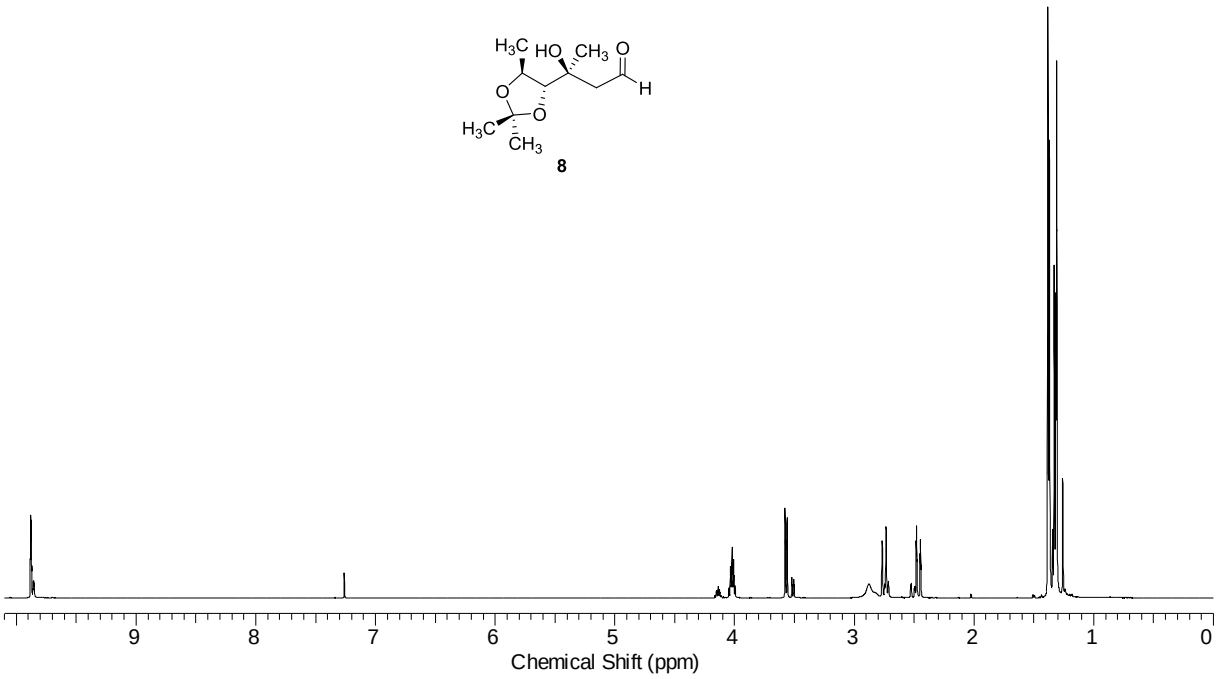
Acetyl chloride (289 μL, 4.06 mmol, 10.0 equiv) was added to a solution of 1-*O*-acetyl trioxacarcinose A **19** (100 mg, 406 μmol, 1 equiv, prepared from triol **24**) in methanol (4 mL) at 23 °C. After 10 min, sodium bicarbonate (341 mg, 4.06 mmol, 10.0 equiv) was added. The product mixture was filtered through a pad of Celite, washing with dichloromethane (40 mL). The filtrate was concentrated. The residue was purified by flash-column chromatography (20% ethyl acetate–hexanes initially, grading to 60% ethyl acetate–hexanes) to provide separately α- and β-methyl trioxacarcinoside A (**18**) (α-anomer: 10 mg, 11%; β-anomer: 56 mg, 63%). Analytical data for the synthetic substances were in agreement with those reported in the literature.[9] α-anomer: TLC: (50% ethyl acetate–hexanes) R_f = 0.63 (CAM); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 4.86 (d, 1H, *J* = 3.4 Hz), 4.70 (s, 1H), 4.32 (q, 1H, *J* = 6.4 Hz), 4.28 (s, 1H), 3.39 (s, 3H), 2.14 (s 3H), 1.93 (dd, 1H, *J* = 14.2, 3.9 Hz), 1.72 (dt, 1H, *J* = 14.7, 1.2 Hz), 1.13 (d, 3H, *J* = 6.4 Hz), 1.10 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 170.4, 99.1, 74.6, 68.8, 61.8, 55.2, 36.2, 25.7, 20.9, 16.6; FTIR (neat), cm^{-1}: 3507 (br), 2938 (w), 1748 (s), 1375 (m), 1233 (s), 1121 (s), 1082 (m), 1047 (s), 997 (s); HRMS (ESI): Calcd for $(C_{10}H_{18}O_5+Na)^+$ 241.1046, found 241.1050. β-anomer: TLC: (50% ethyl acetate–hexanes) R_f = 0.47 (CAM); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 4.67 (dd, 1H, *J* = 9.5, 2.7 Hz), 4.57 (d, 1H, *J* = 1.5 Hz), 4.15 (dq, 1H, *J* = 6.4, 1.5 Hz), 3.52 (s, 3H), 2.14 (s, 3H), 1.75-1.64 (m, 2H), 1.43 (s, 1H), 1.21 (s, 3H), 1.16 (d, 3H, *J* = 6.4 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 170.9, 99.9, 74.1, 71.3, 67.9, 56.5, 39.6, 27.1, 20.8, 16.5; FTIR

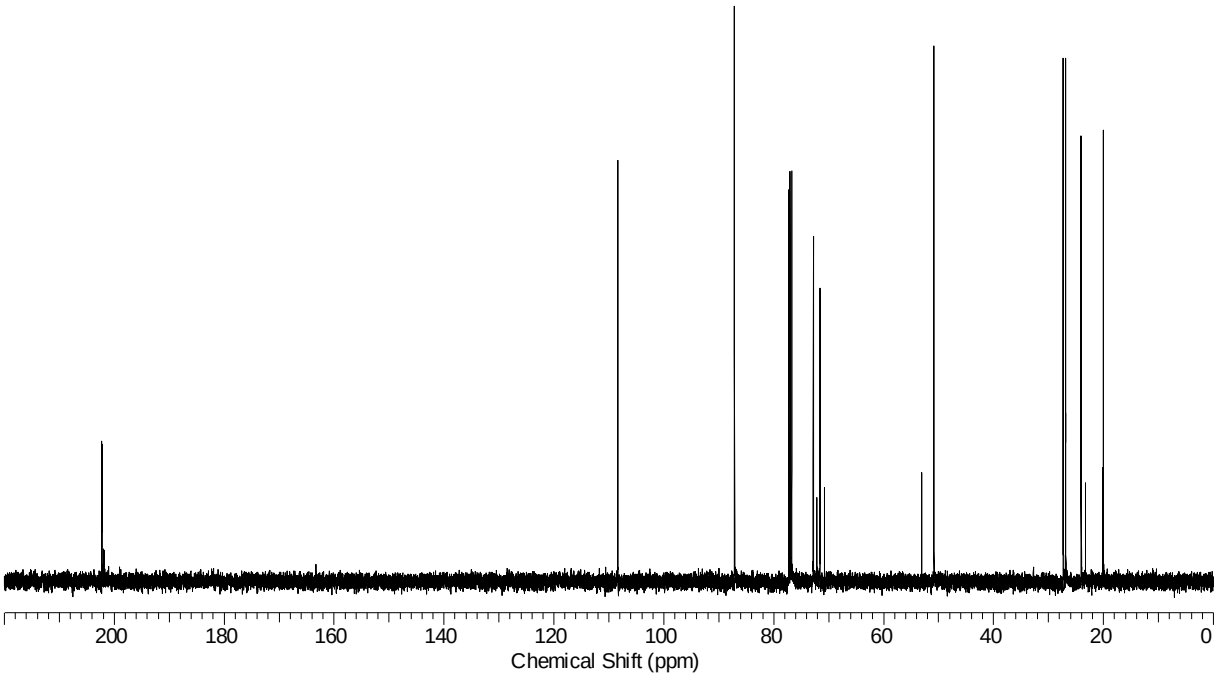
(neat), cm^{-1}: 3468 (br), 2936 (w), 1745 (s), 1447 (m), 1373 (m), 1234 (s), 1119 (m), 1053 (s), 1011 (s); HRMS (ESI): Calcd for $(C_{10}H_{18}O_5+Na)^+$ 241.1046, found 241.1051.

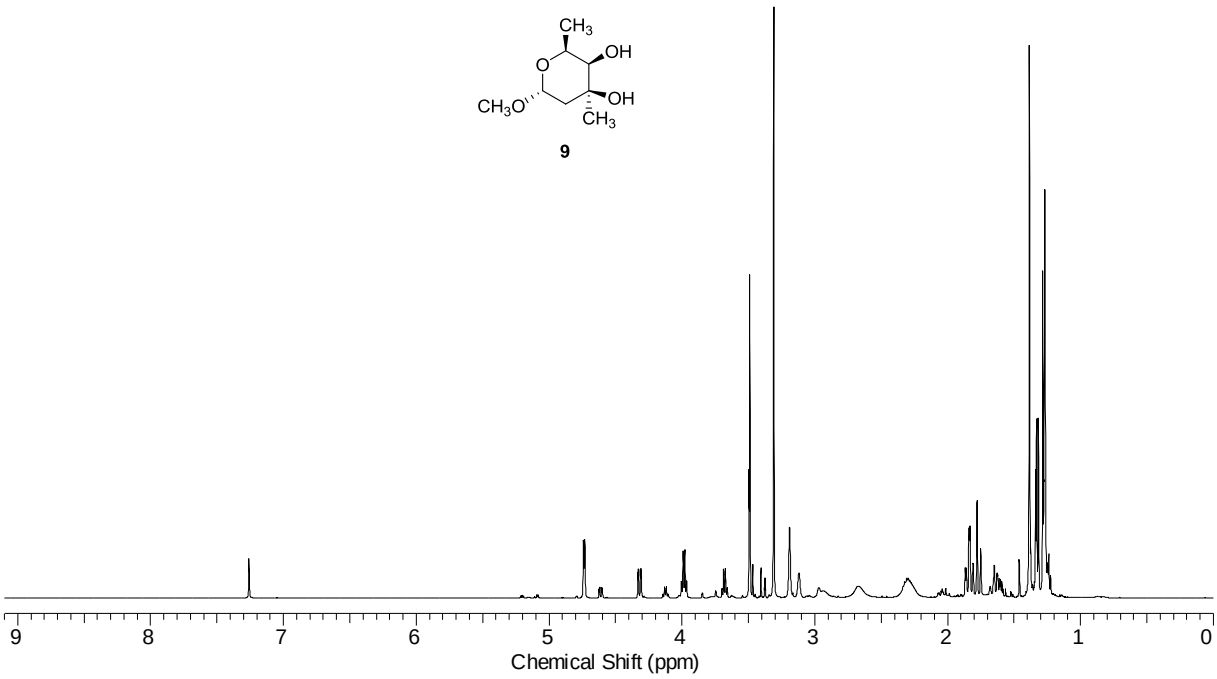
^{1}H and ^{13}C NMR Spectra

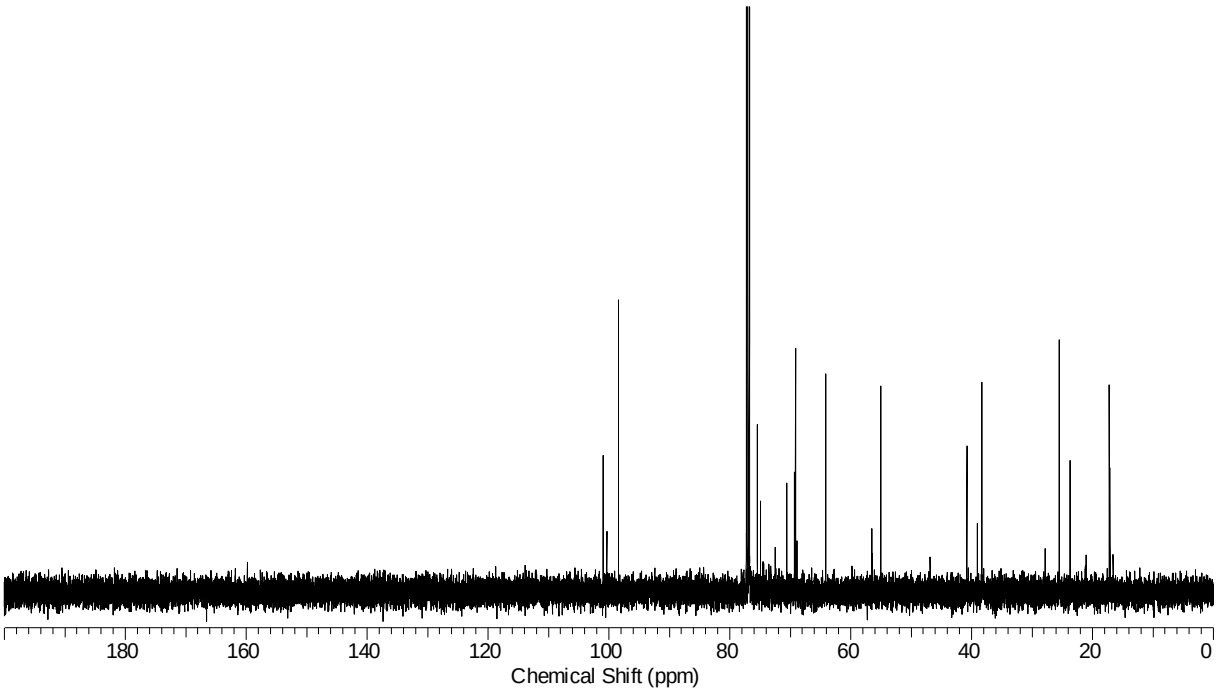


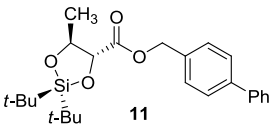



H3C HO CH3 O
O
H
O
H3C
CH3
8
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)


200
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

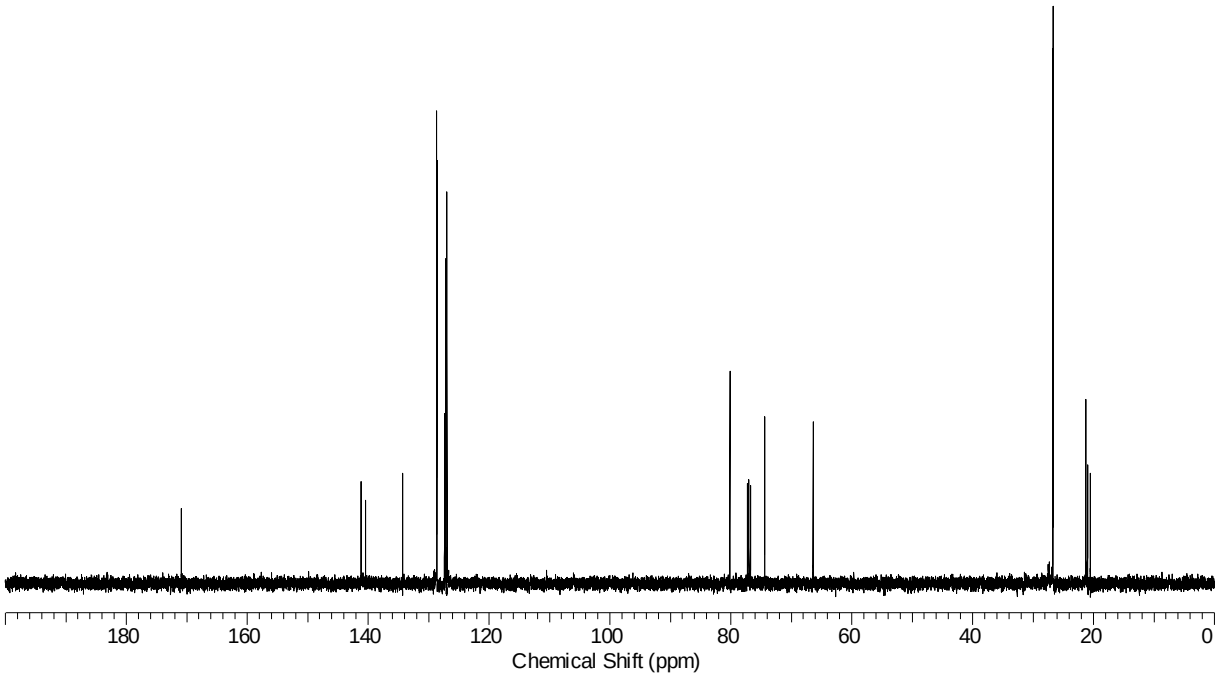

CH3
OH
O
OH
CH3O
CH3
9
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

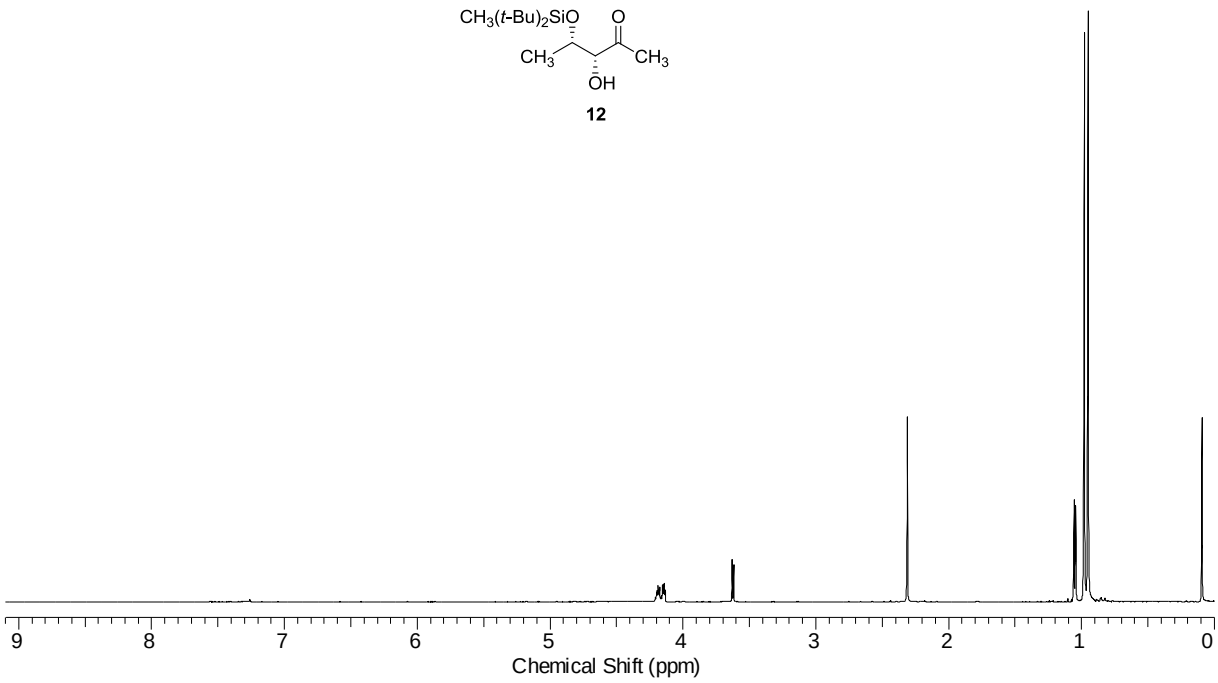

180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

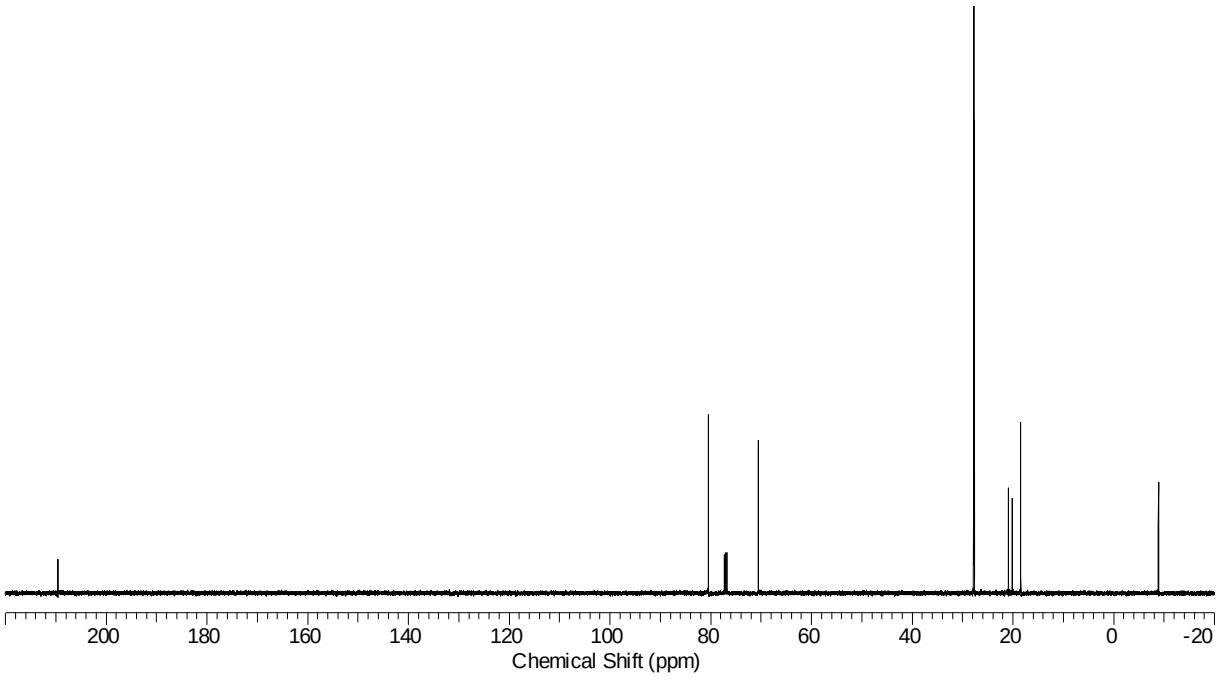

CH3
O
O
O
Si
O
t-Bu
t-Bu
Ph

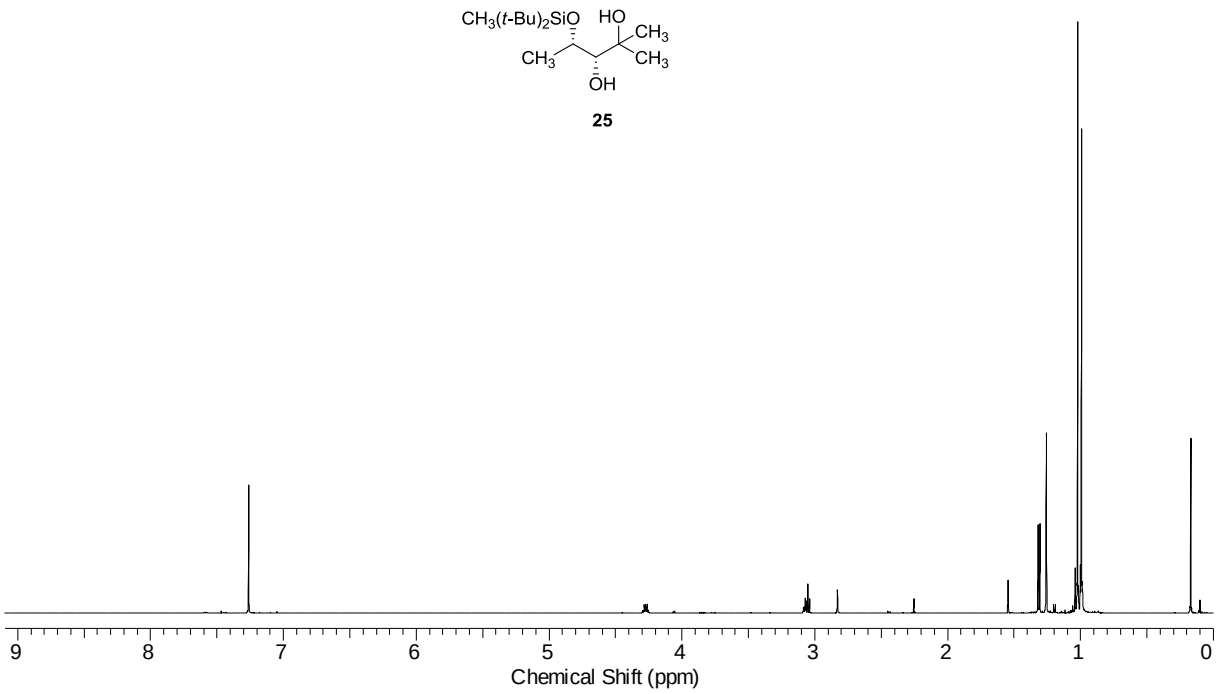
11

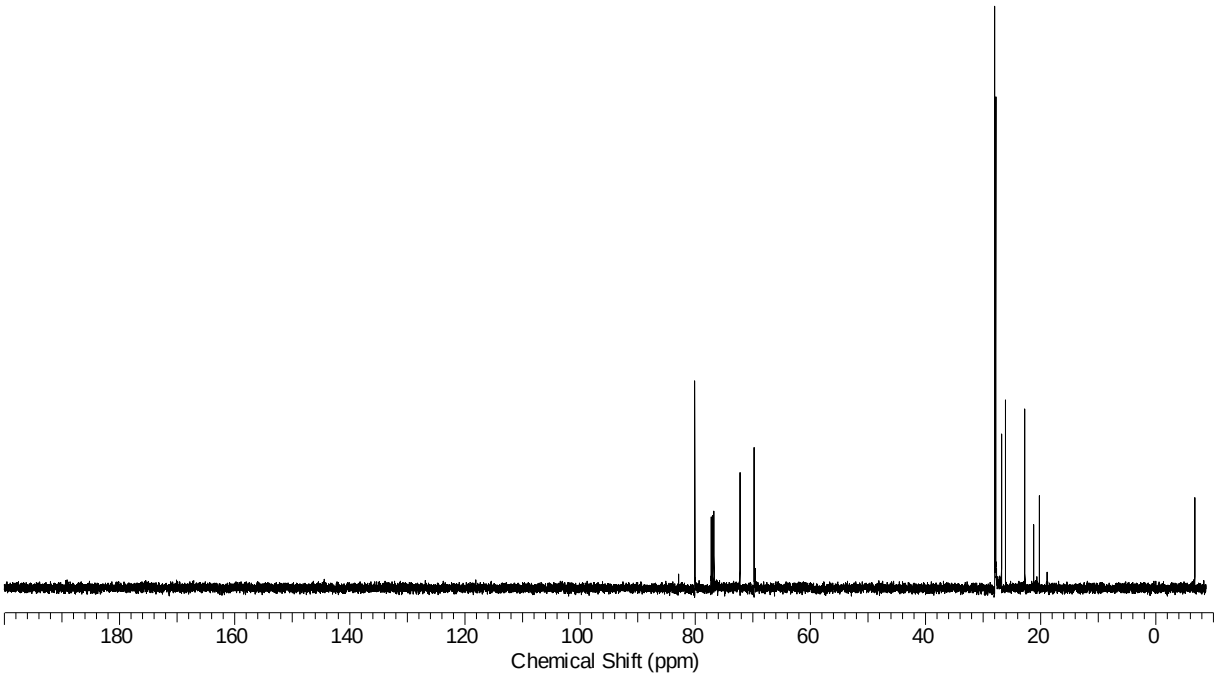
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

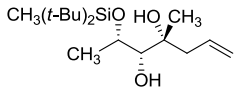

180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)


CH3(t-Bu)2SiO
O
CH3
CH3
OH
12
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)


200
180
160
140
120
100
80
60
40
20
0
-20
Chemical Shift (ppm)

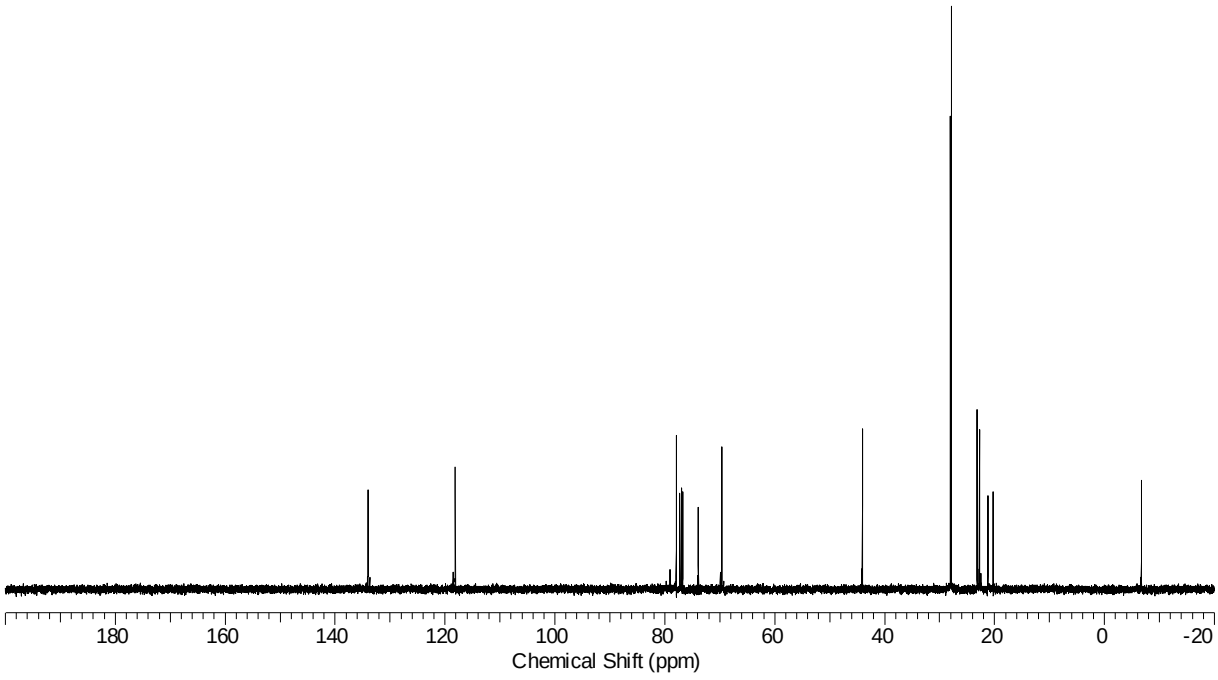

CH3(t-Bu)2SiO
HO
CH3
CH3
CH3
OH
25
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

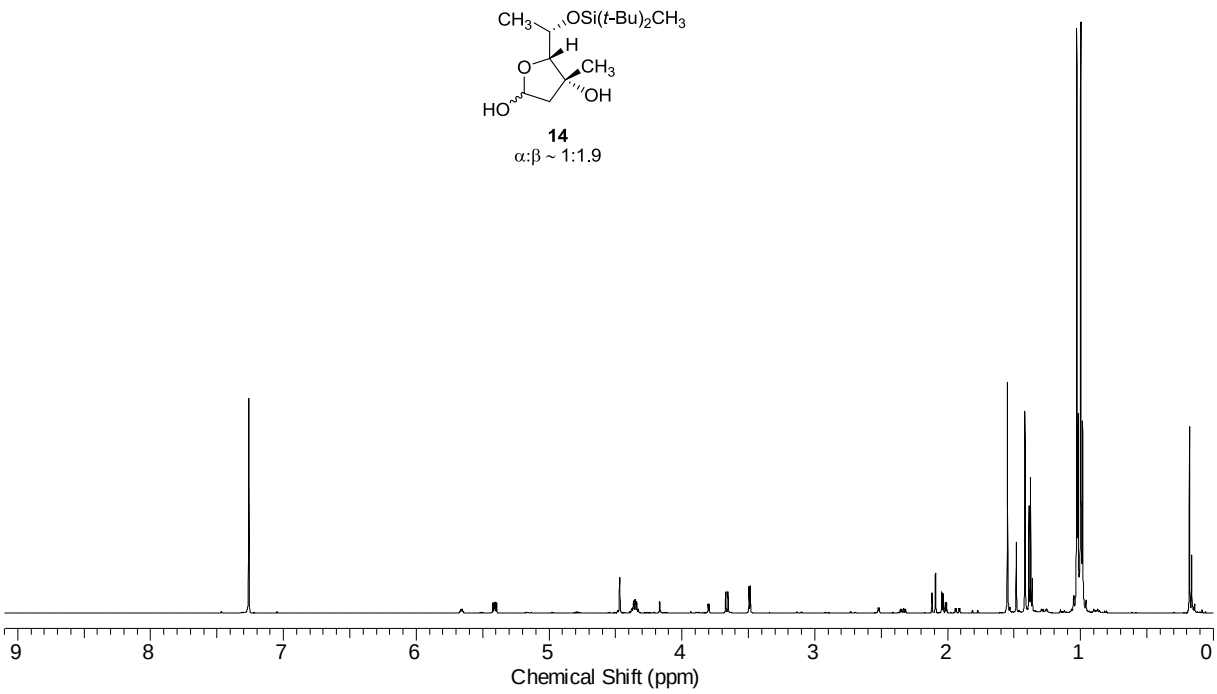

180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

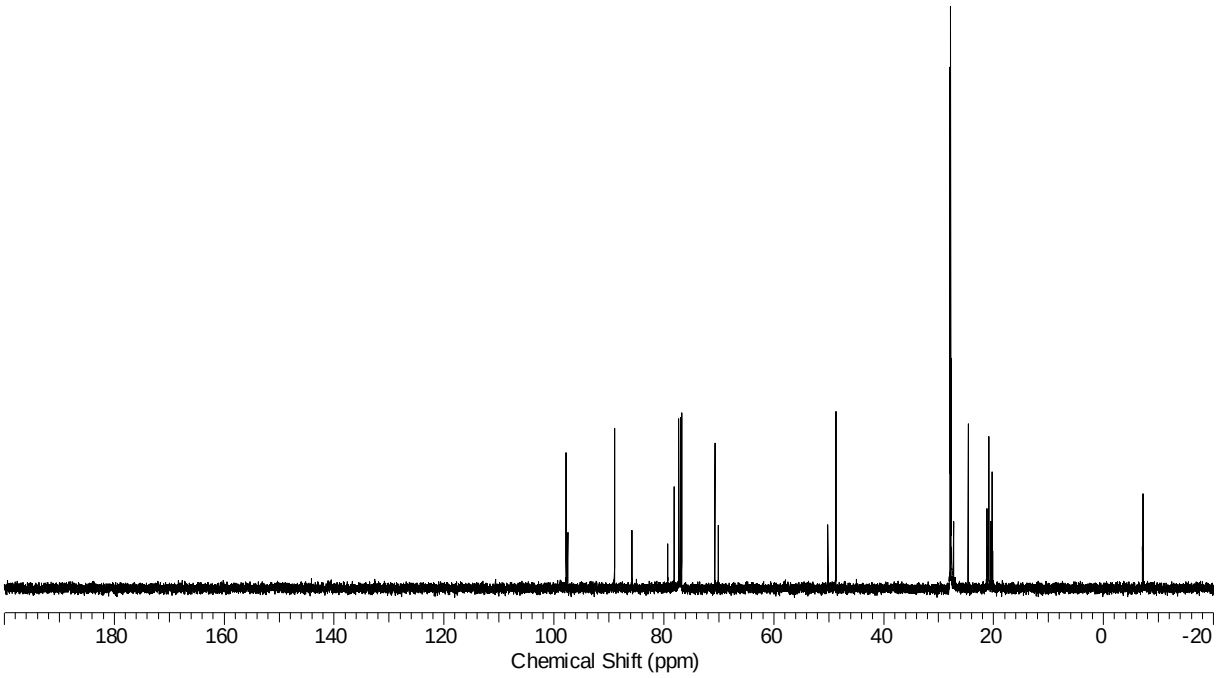

CH3(t-Bu)2SiO
HO
CH3
CH3
OH

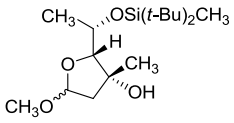
13

9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)


180
160
140
120
100
80
60
40
20
0
-20
Chemical Shift (ppm)


CH3
OSi(t-Bu)2CH3
H
O
CH3
OH
HO
14
α:β ~ 1:1.9
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

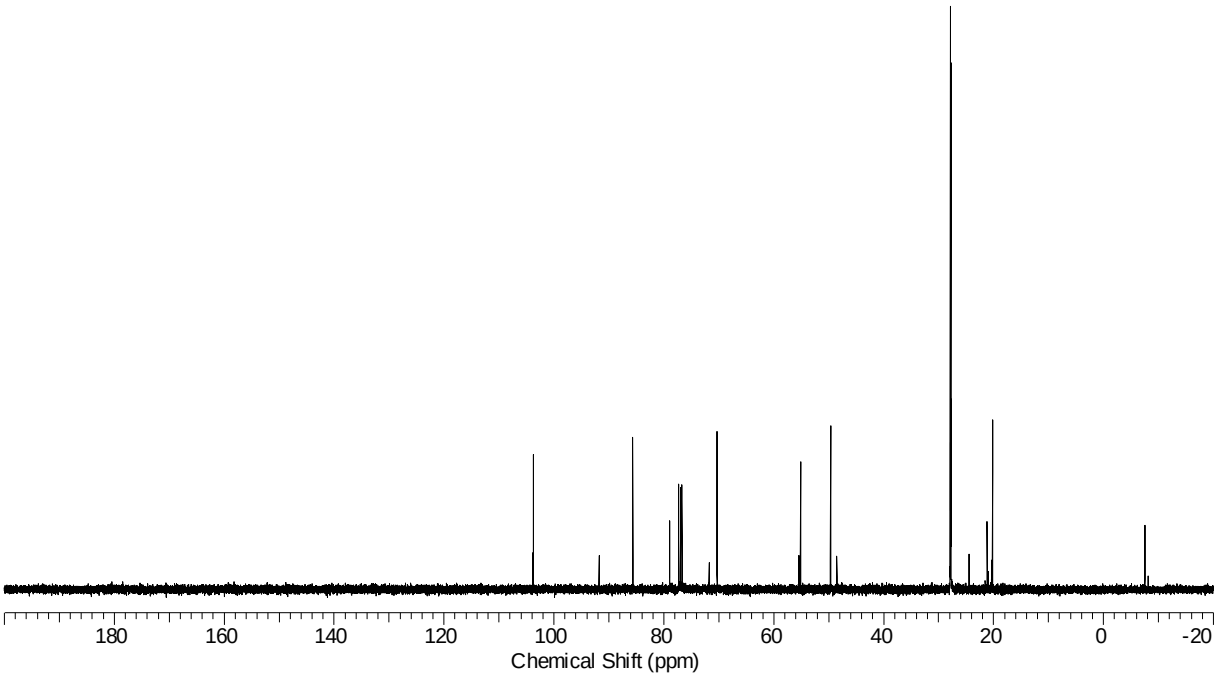

180
160
140
120
100
80
60
40
20
0
-20
Chemical Shift (ppm)

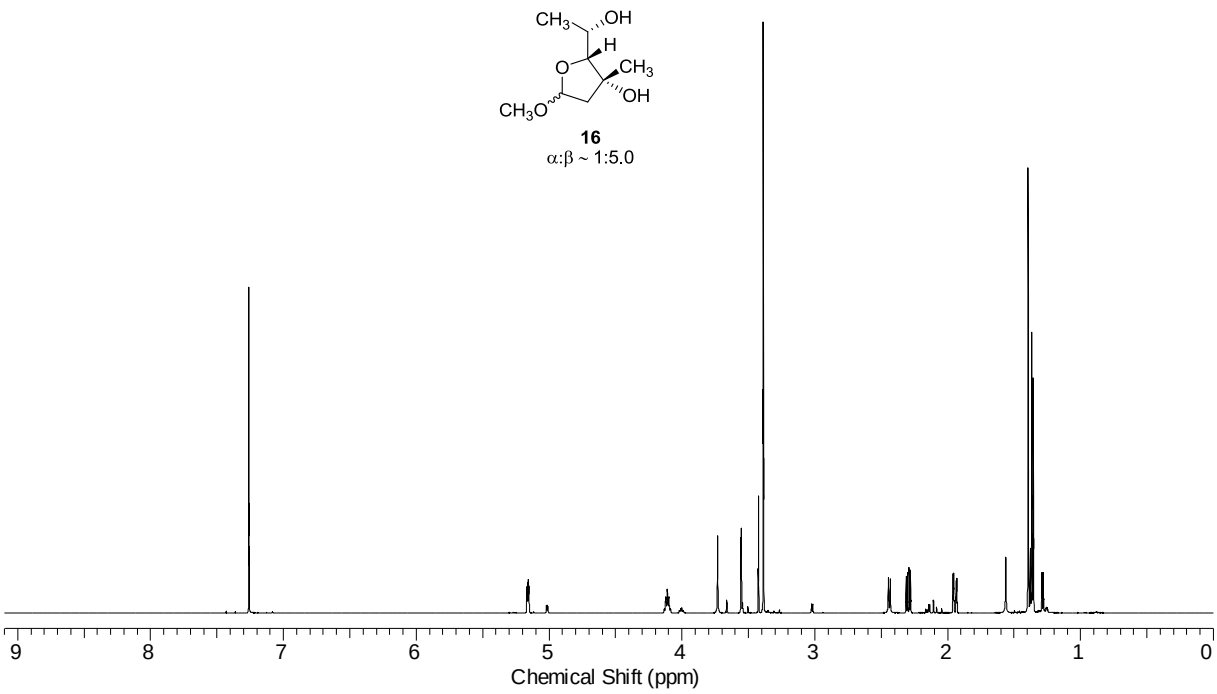

CH3
OSi(t-Bu)2CH3
H
O
CH3
OH
CH3O

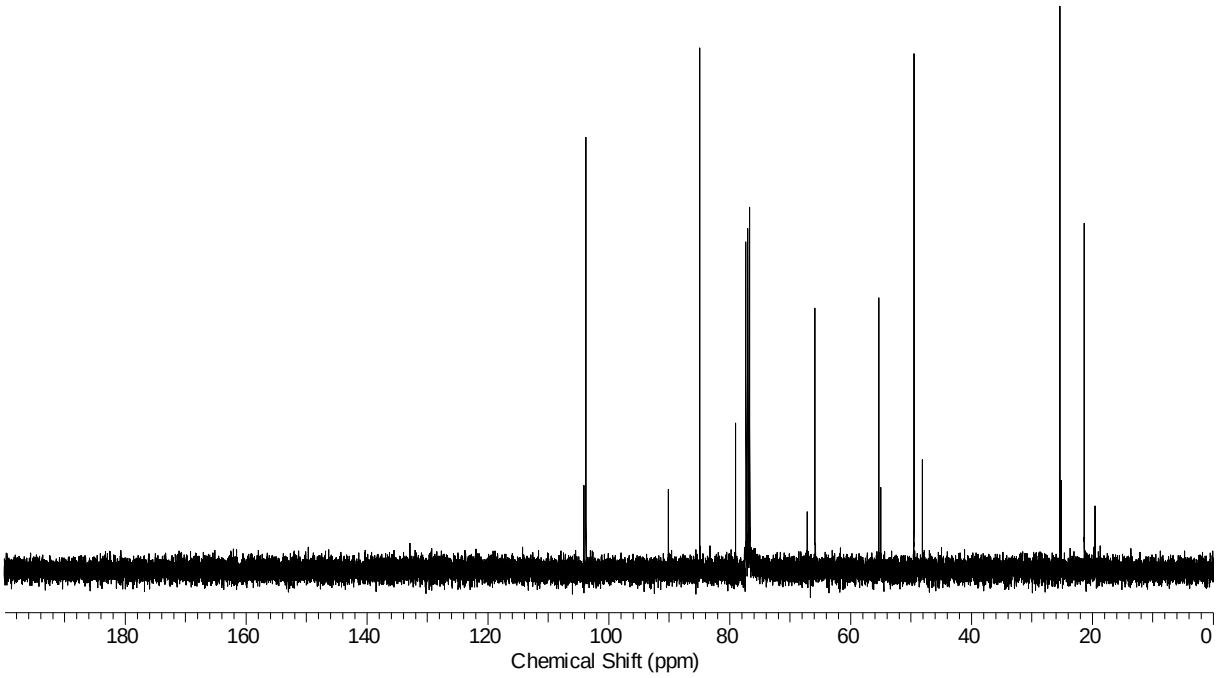
15

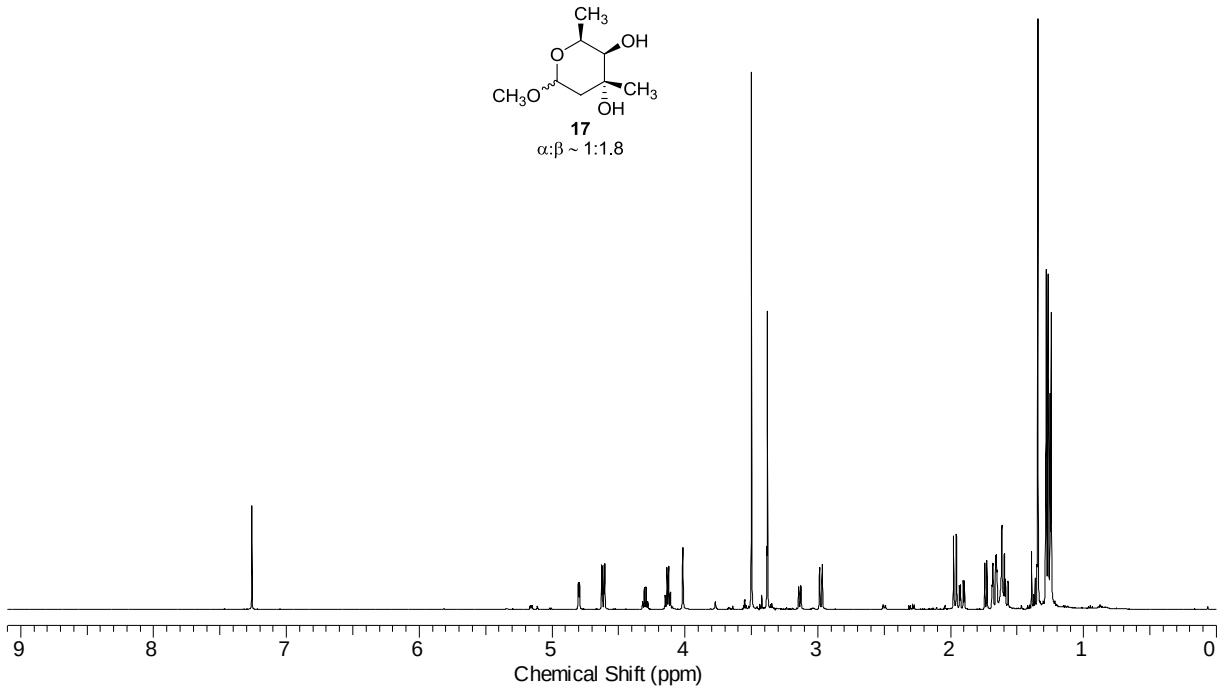
α:β ~ 1:4.8

9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)


180
160
140
120
100
80
60
40
20
0
-20
Chemical Shift (ppm)

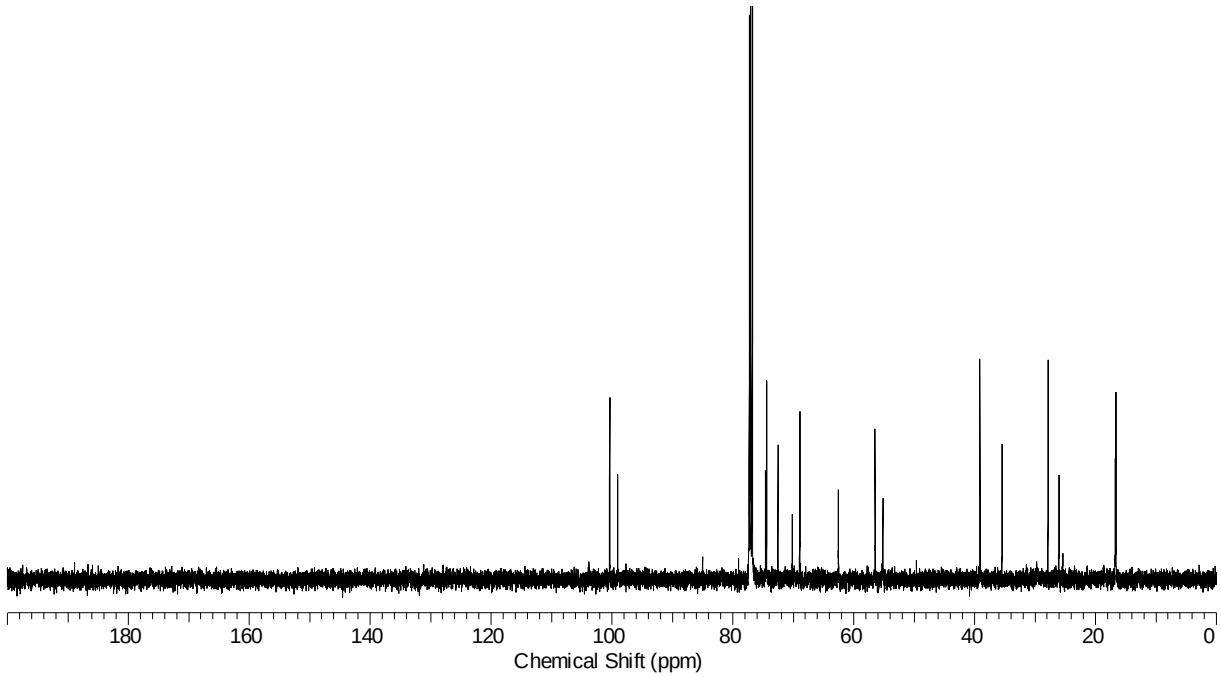

CH3
OH
H
O
CH3
OH
CH3O
16
α:β ~ 1:5.0
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

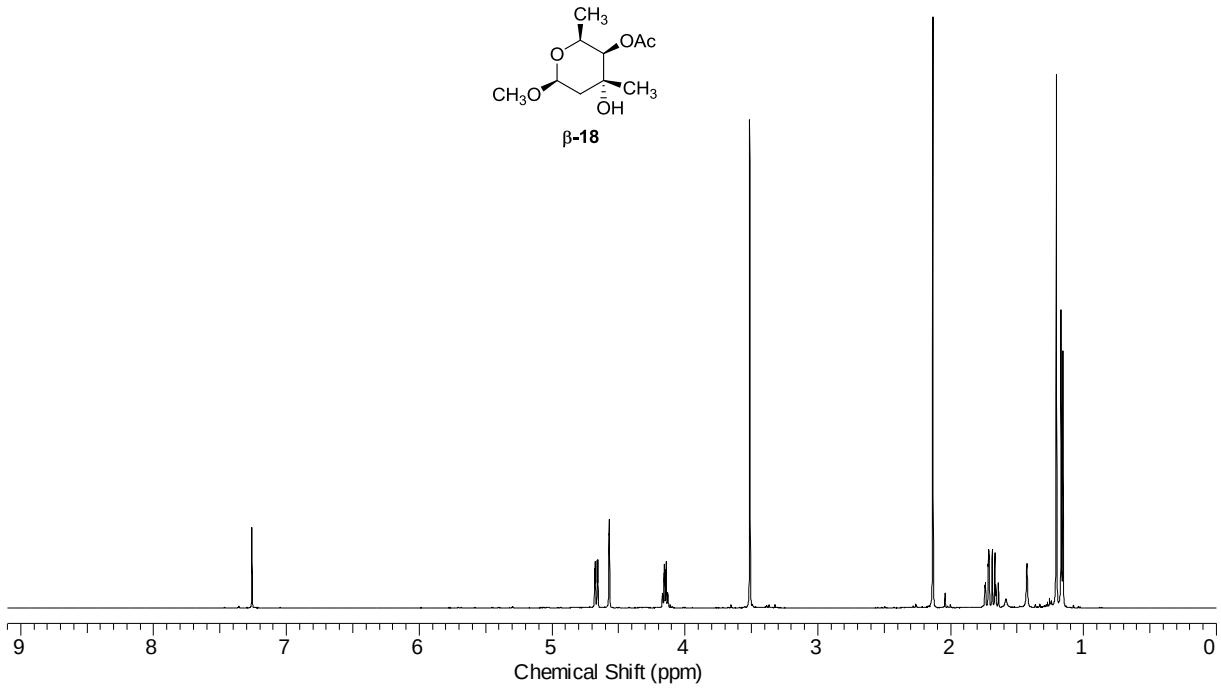

180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

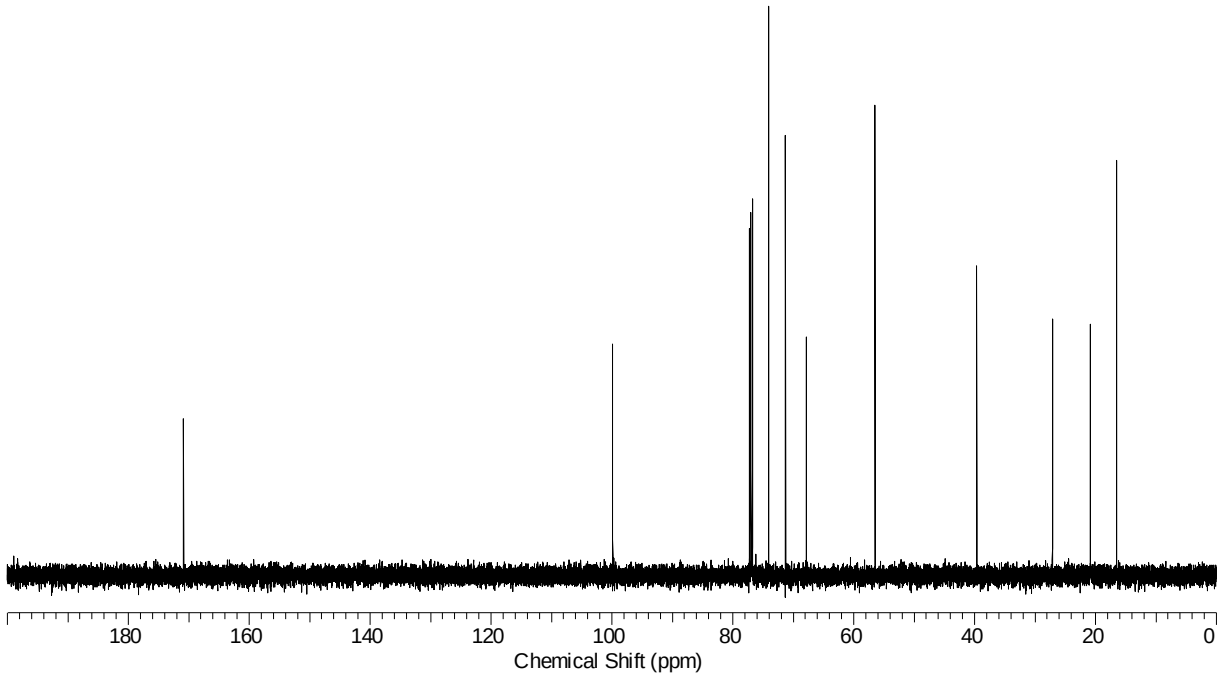

CH3
OH
O
CH3O
CH3
OH
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

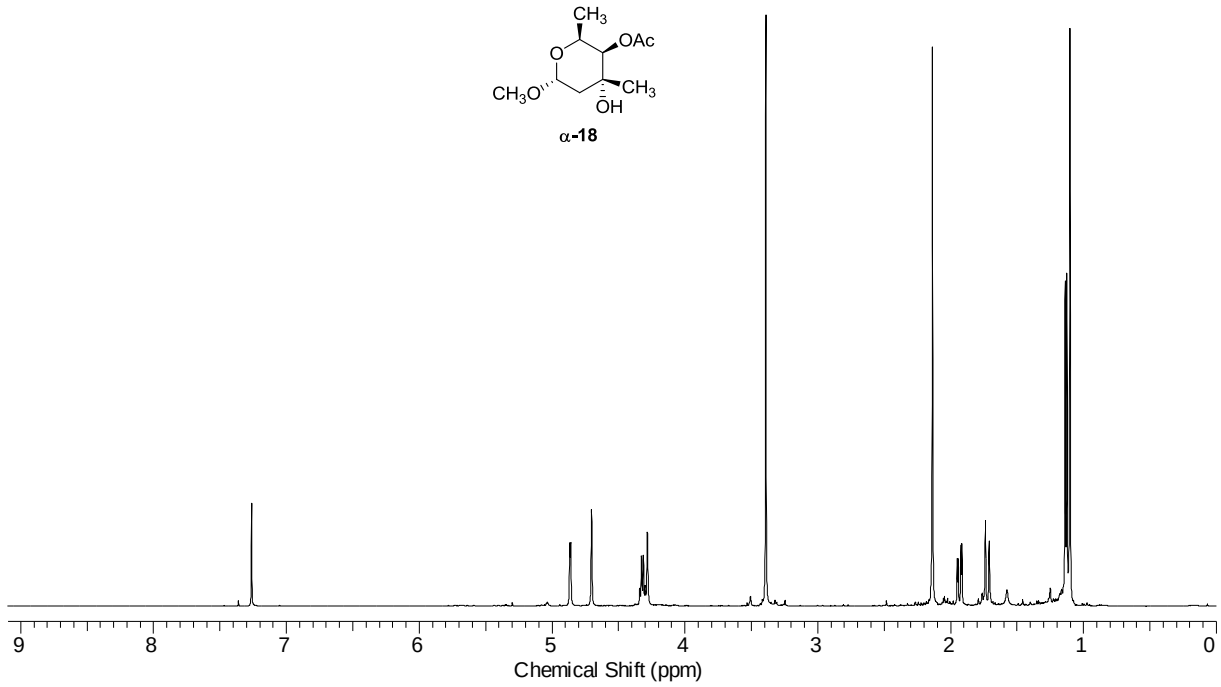
17

α:β ~ 1:1.8

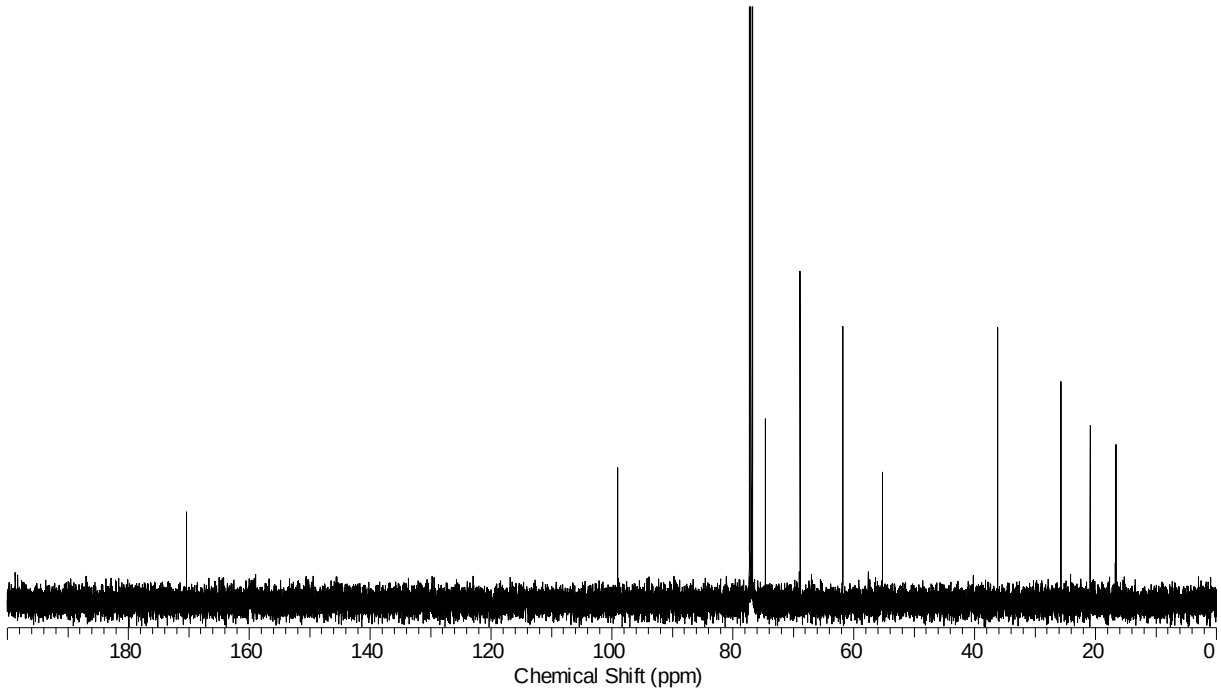

180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

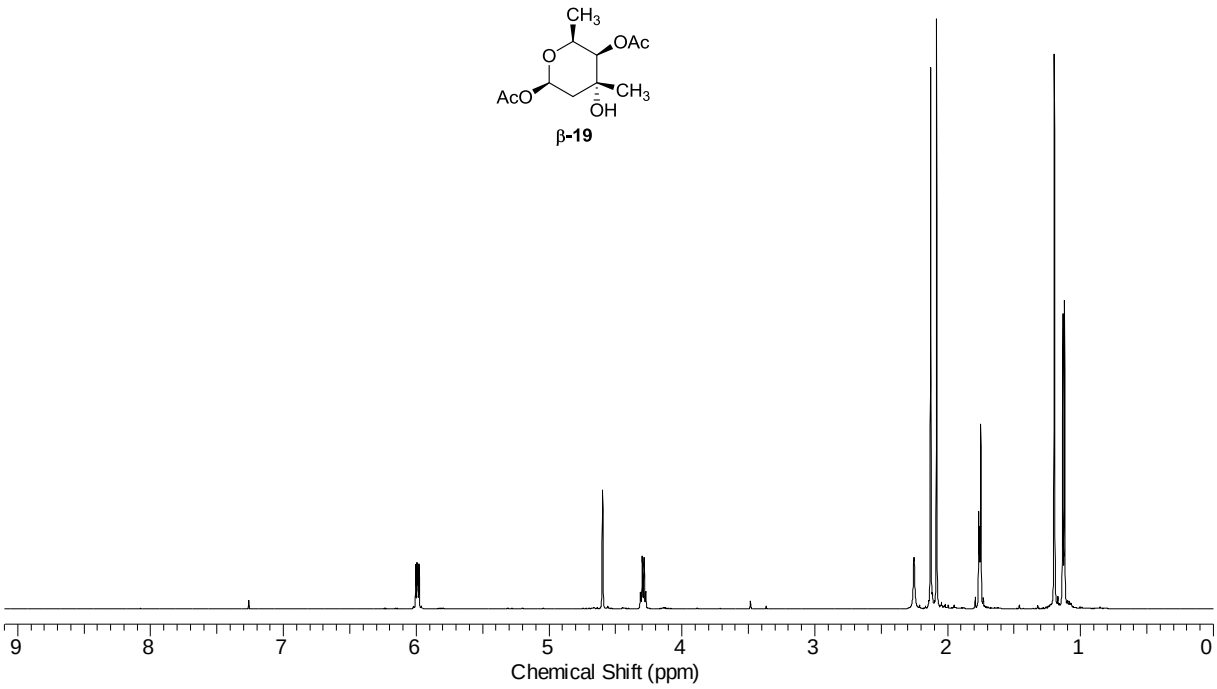

CH3
OAc
O
CH3O
CH3
OH
β-18
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

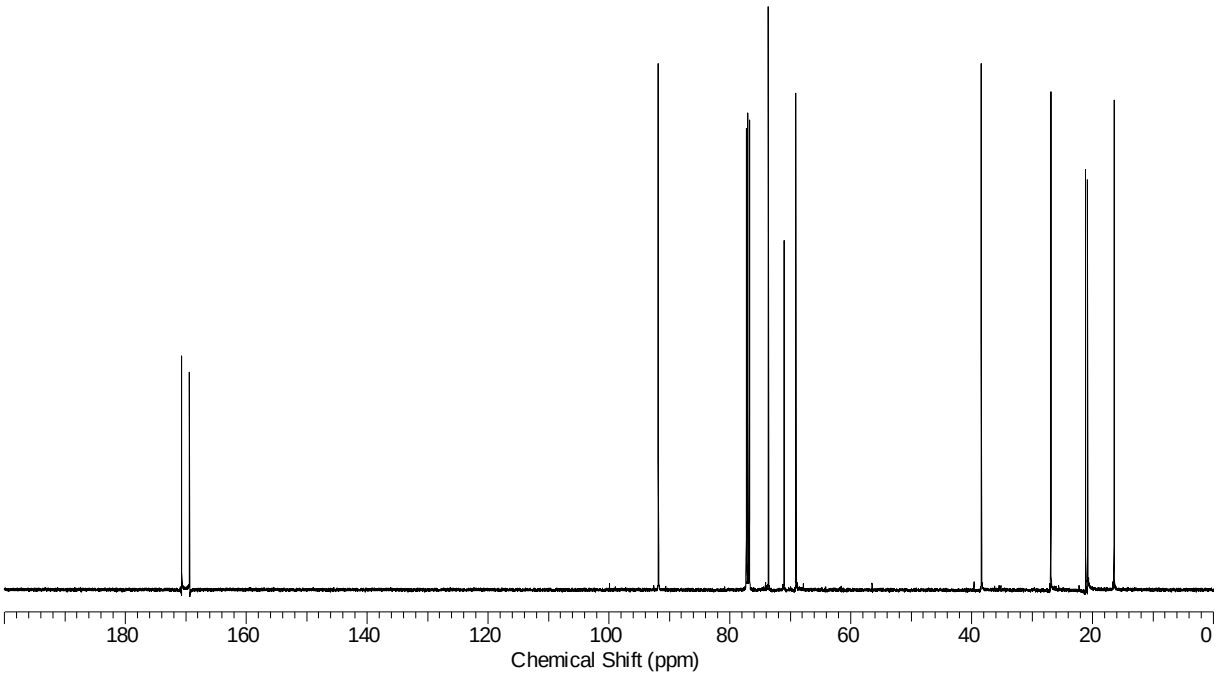

180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

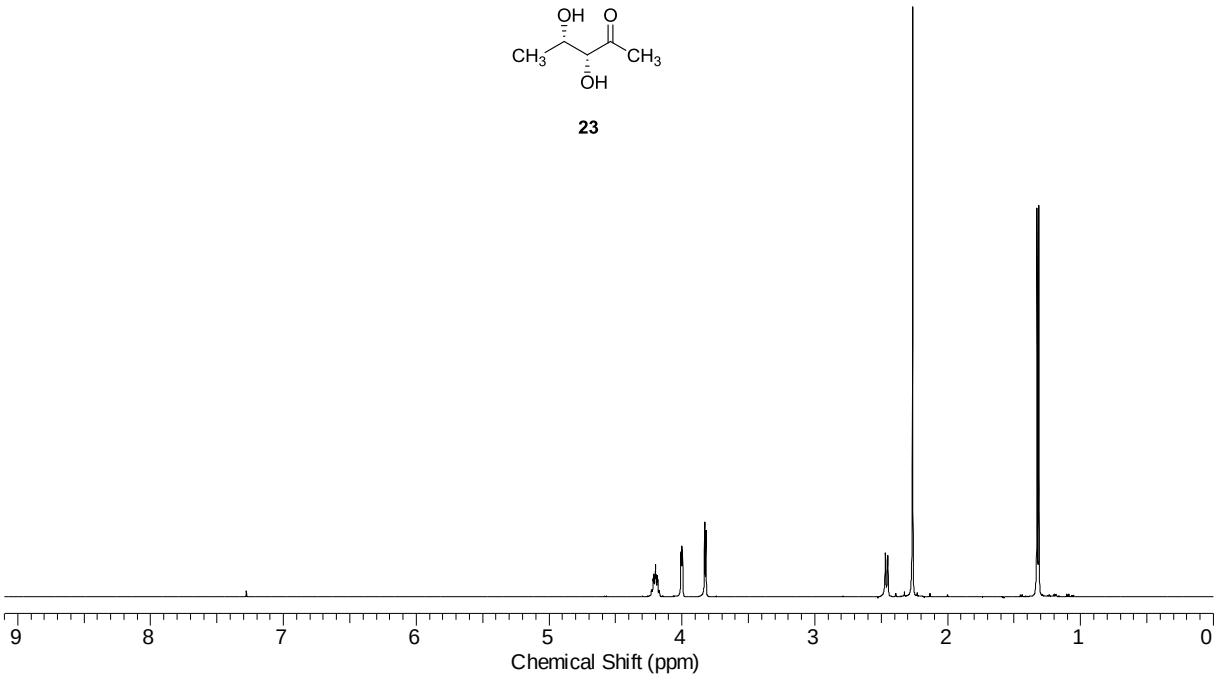

CH3
OAc
O
CH3O
CH3
OH
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

α-18

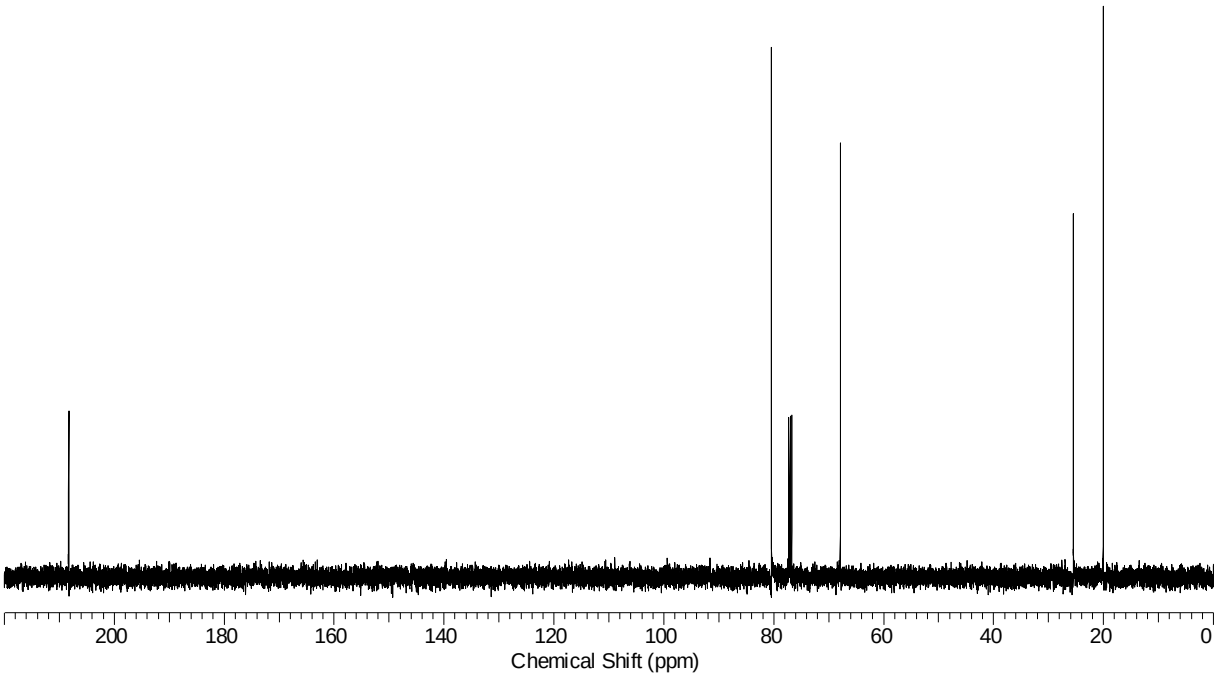

180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

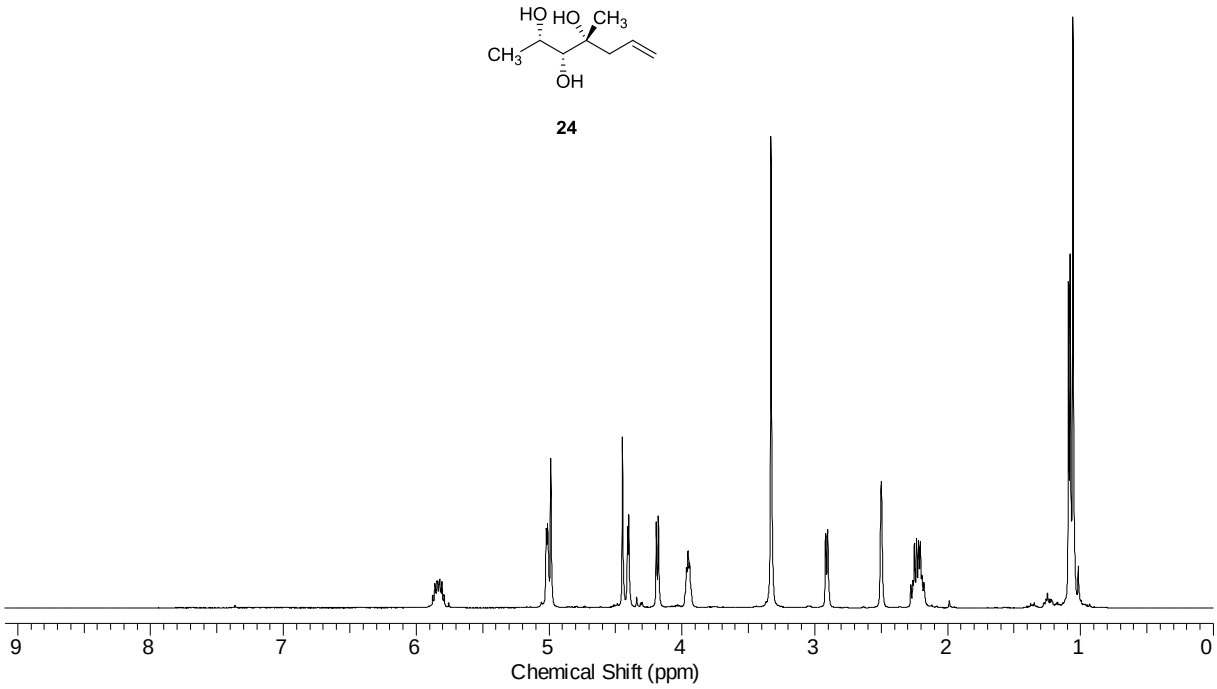

CH3
OAc
O
AcO
CH3
OH
β-19
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)


180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

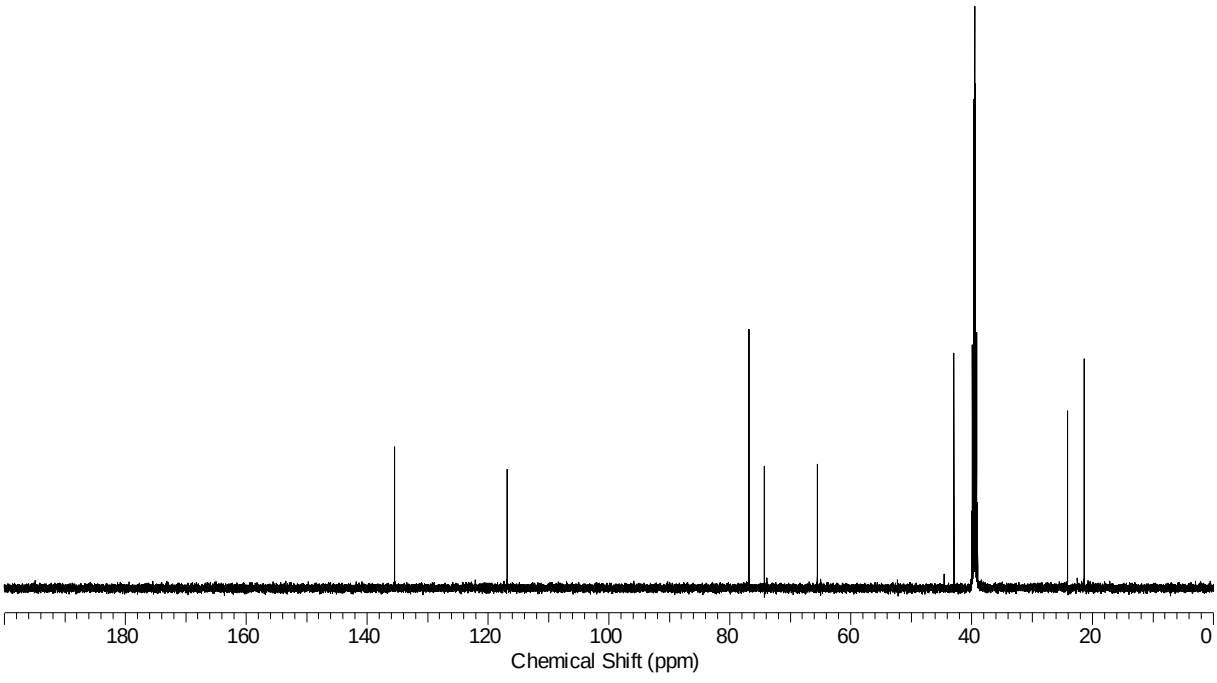

OH
O
CH3
CH3
OH
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

23


200
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)


HO
HO
CH3
CH3
OH
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

24


180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)