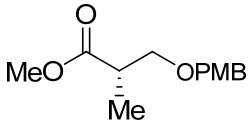
Supporting Information

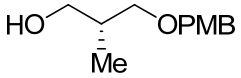
Total Synthesis, Assignment of the Relative and Absolute Stereochemistry, and Structural Reassignment of Phostriecin (aka Sultriecin)

Christopher P. Burke, Nadia Haq, and Dale L. Boger*

Department of Chemistry and the Skaggs Institute for Chemical Biology, The Scripps Research Institute, 10550 N. Torrey Pines Road, La Jolla, CA 92037

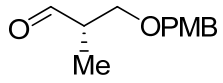


Methyl (*S*)-3-(4-Methoxybenzyloxy)-2-methylpropanoate (S1). A solution of 4-methoxybenzyl alcohol (44 g, 320 mmol) in 640 mL of Et_2O under N_2 at room temperature was treated with NaH (60% in oil, 1.3 g, 32 mmol). After stirring for 45 min, the solution was cooled to 0 °C, trichloroacetonitrile (46 g, 320 mmol) was added dropwise, and the mixture was allowed to warm to room temperature. The clear solution turned opaque orange. After 4 h, the mixture was concentrated under reduced pressure, and 124 mL of hexanes mixed with 0.84 mL of methanol was added to the mixture. The brown precipitate was removed by filtration, and the yellow filtrate was concentrated to a syrup and added to a solution of methyl (*S*)-3-hydroxy-2-methylpropanoate (**11**) (25 g, 212 mmol) in 1060 mL of CH_2Cl_2. The solution was then treated with (D,L)-10-camphorsulfonic acid (4.9 g, 21 mmol) and was stirred overnight. The reaction was quenched with the addition of saturated aqueous $NaHCO_3$, extracted with CH_2Cl_2, washed with H_2O, saturated aqueous NaCl, dried (Na_2SO_4), and concentrated. The trichloroacetamide solid that formed was removed by filtration with a hexanes wash, and the filtrate was concentrated to give the crude product which was taken to the next step without further purification. Analytically pure material was obtained by flash chromatography (SiO_2, 5% EtOAc/hexanes) providing the product as a colorless oil: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.26–7.22 (m, 2H), 6.89–6.85 (m, 2H), 4.48–4.42 (m, 2H), 3.80 (s, 3H), 3.69 (s, 3H), 3.63 (dd, J = 9.0, 7.5 Hz, 1H), 3.46 (dd, J = 9.0, 6.0 Hz, 1H), 2.81–2.72, (m, 1H), 1.17 (d, J = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 175.2, 159.1, 130.2, 129.1, 113.7, 72.7, 71.6, 55.2, 51.6, 40.1, 13.9.

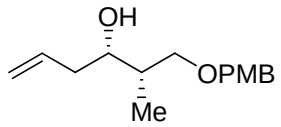


(*S*)-3-(4-Methoxybenzyloxy)-2-methylpropanol (12). A solution of methyl (*S*)-3-(4-methoxybenzyloxy)-2-methylpropanoate (**S1)** (from previous reaction, 212 mmol) in 120 mL of Et_2O was added slowly to a stirred suspension of lithium aluminum hydride (21.9 g, 577 mmol) in 940 mL of Et_2O at 0 °C under N_2. After 1 h, the reaction mixture was allowed to warm to room temperature and the mixture was stirred overnight. The solution was cooled to 0 °C and quenched by sequential *slow* addition of H_2O (20 mL), 15% aqueous NaOH (20 mL), and H_2O (60 mL). After allowing the mixture to warm to room temperature, the white solid was removed by filtration while washing with Et_2O. The filtrate was washed with saturated aqueous NaCl, dried (Na_2SO_4), and concentrated. The crude product was distilled (bp 130–133 °C @ 1.4 mm Hg, however all material

collected from 130–145 °C is usable in the next step) to give 40.3 g (91%, 2 steps) of **12** as a colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.23–7.18 (m, 2H), 6.87–6.83 (m, 2H), 4.42 (s, 2H), 3.78 (s, 3H), 3.61–3.53 (m, 2H), 3.50 (dd, J = 8.8, 4.8 Hz, 1H), 3.36 (dd, J = 8.8, 8.4 Hz, 1H), 2.35 (brs, 1H), 2.08–1.90 (m, 1H), 0.84 (d, J = 7.2 Hz, 3H); ^{13}C NMR (C_6D_6, 100 MHz) δ 159.3, 130.1, 129.2, 113.8, 75.2, 73.0, 68.0, 55.3, 35.5, 13.5; IR (film) ν_{max} 3406, 1511, 1243, 1031 cm^{-1}.



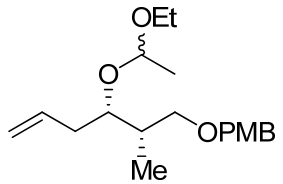
(*S*)-3-(4-Methoxybenzyloxy)-2-methylpropanal (S2). Oxalyl chloride (12.0 g, 94.5 mmol) was added slowly to a solution of DMSO (15.0 g, 191 mmol) in 224 mL of CH_2Cl_2 at –78 °C under N_2. After 20 min, **12** (10.0 g, 47.2 mmol) in 25 mL of CH_2Cl_2 was added slowly to the reaction mixture. After stirring for 20 min, 40 mL of Et_3N was slowly added, and the reaction mixture was allowed to warm to 0 °C over 1.5 h. The mixture was stirred at 0 °C for 15 min, quenched with the addition of saturated aqueous NH_4Cl, and extracted with Et_2O. The combined organic phases were washed with saturated aqueous NH_4Cl, H_2O, saturated aqueous NaCl, dried (Na_2SO_4), and concentrated to give the crude aldehyde as a yellow oil which was used immediately in the next step without further purification: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 9.71 (dd, J = 1.5, 1.0 Hz, 1H), 7.25–7.21 (m, 2H), 6.90–6.85 (m, 2H), 4.43 (s, 2H), 3.80 (s, 3H), 3.65(ddd, J = 9.5, 6.5, 1.0 Hz, 1H), 3.60 (ddd, J = 9.5, 5.5, 1.0 Hz, 1H), 2.64 (m, 1H), 1.12 (d, J = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 203.8, 159.2, 129.9, 129.1, 113.7, 72.8, 69.7, 55.2, 46.7, 10.6.



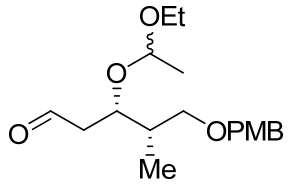
(2*S*,3*S*)-1-(4-Methoxybenzyloxy)-2-methylhex-5-en-3-ol (13).[1] A mixture of (–)-*B*-methoxydiisopinocampheylborane (33.2 g, 105 mmol) in 170 mL of Et_2O at –78 °C in a three-necked flask under N_2 was slowly treated with allylmagnesium bromide (1.0 M in Et_2O, 75 mL, 75 mmol). After stirring for 15 min at –78 °C, the cooling bath was removed, and the mixture was stirred for 1 h at room temperature during which time a white precipitate formed. The suspension was cooled to –100 °C (liquid N_2/EtOH bath), and (*S*)-3-(4-methoxybenzyloxy)-2-methylpropanal (**S2**) (from previous reaction, 47.2 mmol) in 80 mL of Et_2O (cooled to –78 °C) was added dropwise down the side of the reaction flask over 2 h via a jacketed addition funnel cooled to –78 °C (note: it is *critical* that the aldehyde solution is *COLD* when it hits the allyldiisopinocampheyl borane solution. It is therefore important to cool the aldehyde solution and add it dropwise *slowly* down the side of the flask). After addition of the aldehyde was complete, the reaction mixture was stirred for an additional 1 h at –78 °C before being quenched by the careful addition of MeOH (326 mL) followed by 3 N NaOH (30 mL) and 35% H_2O_2 (15

[1] (a) Racherla, U. S.; Brown, H. C. *J. Org. Chem.* **1991**, *56*, 401. (b) Nicolaou, K. C.; Patron, A. P.; Ajito, K.; Richter, P. K.; Khatuya, H.; Bertinato, P.; Miller, R. A.; Tomaszewski, M. J. *Chem. Eur. J.* **1996**, *2*, 847.

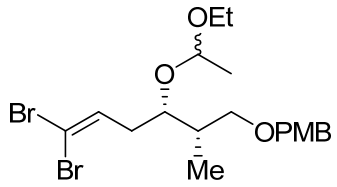
mL, exothermic). The mixture was stirred overnight at room temperature before saturated aqueous $Na_2S_2O_3$ (200 mL) was added. The mixture was diluted with Et_2O, and the phases were separated. The aqueous phase was extracted with Et_2O, and the combined organic phases were washed with saturated aqueous $Na_2S_2O_3$, H_2O, saturated aqueous NaCl, dried (Na_2SO_4), filtered, and concentrated. The crude syrup was then distilled under reduced pressure to remove most of the isopinocampheol by-product (bp 68–72 °C @ 3 mm Hg). The remaining oil was purified by flash chromatography (SiO_2, 5–40% EtOAc/hexanes gradient) to yield **13** as an oil and as a ~14:1 mixture of syn/anti diastereomers that contained some isopinocampheol. This mixture was used directly in the next step. For **13**: ^{1}H NMR (C_6D_6, 400 MHz) δ 7.15–7.10 (m, 2H), 6.80–6.74 (m, 2H), 5.87–5.75 (m, 1H), 5.08–4.98 (m, 2H), 4.22 (s, 2H), 3.81–3.76 (m, 1H), 3.38–3.24 (m, 2H), 3.28 (s, 3H), 2.28–2.17 (m, 1H), 2.12–2.03 (m, 2H), 1.82–1.68 (m, 1H), 0.93 (d, J = 7.2 Hz, 3H); ^{13}C NMR (C_6D_6, 125 MHz) δ 159.9, 136.2, 131.0, 129.6, 117.0, 114.3, 74.4, 73.3, 72.9, 54.9, 39.8, 38.3, 11.1; HRMS (ESI-TOF) calcd for $C_{15}H_{22}O_3 + Na^+$ 273.1461; found 273.1461.



(2*S*,3*S*)-3-(1-Ethoxyethoxy)-1-(4-methoxybenzyloxy)-2-methylhex-5-ene (14). A solution of **13** (from previous reaction, 47.2 mmol) in 470 mL of anhydrous CH_2Cl_2 under N_2 was treated with ethyl vinyl ether (51 g, 710 mmol) and PPTS (1.8 g, 7.1 mmol) at 25 °C. After 2 h, the reaction was quenched with the addition of saturated aqueous $NaHCO_3$, and the mixture was extracted with CH_2Cl_2. The combined organic phases were washed with H_2O, saturated aqueous NaCl, dried (Na_2SO_4), and concentrated. The crude product was isolated as a yellow oil along with the ethoxyethyl acetal of isopinocampheol and was used directly in the next reaction without further purification. Analytically pure material was obtained by flash chromatography (SiO_2, 5% EtOAc/hexanes) as a mixture of acetal isomers: $[\alpha]^{22}_D$ –2.8 (*c* 1.8, CH_2Cl_2); ^{1}H NMR (C_6D_6, 500 MHz) δ 7.26–7.18 (m, 4H), 6.82–6.76 (m, 4H), 5.91–5.81 (m, 1H), 5.79–5.69 (m, 1H), 5.10–4.97 (m, 4H), 4.66 (q, J = 5.5 Hz, 1H), 4.64 (q, J = 5.5 Hz, 1H), 4.42–4.27 (m, 4H), 3.88 (ddd, J = 3.5, 6.5, 9.5 Hz, 1H), 3.83 (ddd, J = 3.5, 6.0, 8.0 Hz, 1H), 3.59 (dd, J = 9.0, 7.0 Hz, 1H), 3.54–3.46 (m, 2H), 3.42 (dd, J = 9.0, 7.5 Hz, 1H), 3.39–3.31 (m, 3H), 3.29 (s, 6 H), 3.23 (dd, J = 9.0, 5.5 Hz, 1H), 2.55–2.48 (m, 1H), 2.39–2.29 (m, 2H), 2.28–2.18 (m, 1H), 2.12–2.00 (m, 1H), 1.26 (d, J = 5.5 Hz, 3H), 1.25 (d, J = 5.5 Hz, 3H), 1.12 (t, J = 7.0 Hz, 3H), 1.11 (t, J = 7.0 Hz, 3H), 1.07 (d, J = 7.0 Hz, 3H), 0.96 (d, J = 7.0 Hz, 3H); ^{13}C NMR (C_6D_6, 125 MHz) δ 159.7, 159.6, 136.0, 135.7, 131.4, 131.2 129.5, 129.3, 116.7, 116.4, 114.06, 114.03, 100.6, 99.0, 76.6, 75.6, 72.9, 72.4, 60.5, 60.1, 54.8, 54.7, 37.7, 37.3, 37.0, 36.7, 20.9, 20.6, 15.7, 15.6, 11.8, 11.2; IR (film) ν_{max} 1512, 1248, 1087 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{19}H_{30}O_4 + Na^+$ 345.2036; found 345.2020.

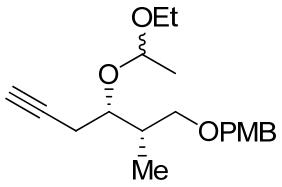


(3*S*,4*S*)-3-(1-Ethoxyethoxy)-5-(4-methoxybenzyloxy)-4-methylpentanal (15). A solution of **14** (all from previous reaction, 47.2 mmol) in THF/H_2O (2:1, 2430 mL) was treated with 2.5 wt% OsO_4 in *t*-BuOH (12.3 mL, 0.98 mmol), *N*-methylmorpholine *N*-oxide (22.1 g, 189 mmol) and $NaIO_4$ (40.4 g, 189 mmol) sequentially. A white precipitate formed within a few minutes, and the mixture was stirred for 18 h. The white precipitate was removed by filtration. Saturated aqueous $Na_2S_2O_3$ (300 mL) was added to the filtrate, and the mixture was stirred until it turned brown/black. The mixture was extracted with Et_2O, and the combined organic phases were washed with H_2O, saturated aqueous NaCl, dried (Na_2SO_4), and concentrated. The crude product was purified by flash chromatography (SiO_2, 5–10% EtOAc/hexanes gradient; the ethoxyethyl acetal of isopinocampheol is readily separated at this stage) to yield 11.24 g (73%, 4 steps; the yield typically ranges from 42–73%) of **15** as a pale yellow oil as a mixture of acetal isomers: $[\alpha]^{22}_D$ –3.8 (*c* 0.68, CH_2Cl_2); ^{1}H NMR (C_6D_6, 400 MHz) δ 9.62 (dd, *J* = 2.8, 1.6 Hz, 1H), 9.44 (dd, *J* = 2.4, 2.0 Hz, 1H), 7.24–7.17 (m, 4H), 6.83–6.77 (m, 4H), 4.60 (q, *J* = 5.2 Hz, 1H), 4.54 (q, *J* = 5.2 Hz, 1H), 4.32–4.22 (m, 4H), 4.22–4.15 (m, 2H), 3.49–3.40 (m, 2H), 3.33–3.17 (m, 5H), 3.29 (s, 6H), 3.14 (dd, *J* = 9.2, 5.6 Hz, 1H), 2.53 (ddd, *J* = 16.0, 7.6, 2.8 Hz, 1H), 2.34 (ddd, *J* = 16.8, 6.8, 2.4 Hz, 1H), 2.17 (ddd, *J* = 10.4, 4.8, 1.6 Hz, 1H), 2.13 (ddd, *J* = 10.8, 5.2, 1.6 Hz, 1H), 1.97–1.75 (m, 2H), 1.17 (d, *J* = 5.2 Hz, 3H), 1.15 (d, *J* = 5.2 Hz, 3H), 1.07 (t, *J* = 6.8 Hz, 3H), 1.06 (t, *J* = 7.2 Hz, 3H), 0.93 (d, *J* = 7.2 Hz, 3H), 0.81 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (C_6D_6, 125 MHz) δ 200.4, 200.0, 159.8, 159.7, 131.2, 131.0, 129.6, 129.4, 114.10, 114.07, 100.9, 99.4, 73.2, 72.89, 72.88, 72.1, 71.7, 60.8, 60.2, 54.79, 54.77, 47.6, 47.1, 38.7, 38.4, 20.6, 20.3, 15.5, 15.4, 12.7, 12.0; IR (film) ν_{max} 1723, 1612, 1513, 1248, 1087 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{18}H_{28}O_5 + Na^+$ 347.1829; found 347.1831.

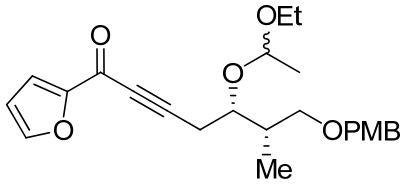


1-(((2*S*,3*S*)-6,6-Dibromo-3-(1-ethoxyethoxy)-2-methylhex-5-enyloxy)methyl)-4-methoxybenzene (16). Triphenylphosphine (17.3 g, 66.3 mmol) was added to a solution of CBr_4 (11.0 g, 33.1 mmol) in CH_2Cl_2 (138 mL) at 0 °C. After stirring for 15 min, **15** (6.50 g, 20.0 mmol) in 51 mL of CH_2Cl_2 was added. After stirring for 10 min, the mixture was concentrated under reduced pressure, and the resulting sludge was triturated repeatedly with hexanes. The combined hexanes mixture was concentrated, and the residue was purified by flash chromatography (SiO_2 pretreated with 2% Et_3N/hexanes, 5–20% EtOAc/hexanes gradient) to give 6.80 g (71%) of **16** as a mixture of acetal isomers as a yellow oil and 0.32 g (4%) of (2*S*,3*S*)-6,6-dibromo-1-(4-methoxybenzyloxy)-2-methylhex-5-en-3-ol, which could be reprotected with ethylvinyl ether and PPTS. For **16**: $[\alpha]^{25}_D$ –5.8 (*c* 0.99, $CHCl_3$); ^{1}H NMR (C_6D_6, 500 MHz) δ 7.24–7.17 m (4H), 6.83–

6.77 (m, 4H) 6.52 (t, J = 7.0 Hz, 1H), 6.25 (t, J = 7.0 Hz, 1H), 4.56–4.49 (m, 2H), 4.35–4.22 (m, 4H) 3.72 (td, J = 6.5, 4.5 Hz, 1H), 3.76 (td, J = 6.5, 4.0 Hz, 1H), 3.46–3.32 (m, 3H), 3.30 (s, 6H), 3.30–3.21 (m, 4H), 3.15 (dd, J = 5.5, 9.0 Hz, 1H), 2.38–2.10 (m, 4H), 1.86–1.80 (m, 1H), 1.80–1.73 (m, 1H), 1.95 (d, J = 5.5 Hz, 3H), 1.18 (d, J = 5.0 Hz, 3H), 1.11 (t, J = 7.0 Hz, 3H), 1.09 (t, J = 7.0 Hz, 3H), 1.01 (d, J = 7.0 Hz, 3H), 0.88 (t, J = 7.0 Hz, 3H); ^{13}C NMR (C_6D_6, 125 MHz) δ 159.8, 159.7, 136.9, 136.1, 131.2, 131.0, 129.6, 129.4, 114.11, 114.08, 100.9, 99.0, 90.1, 89.5, 75.8, 74.2, 73.0, 72.4, 71.9, 60.7, 60.4, 54.79, 54.77, 37.84, 37.79, 37.1, 36.0, 20.8, 20.4, 15.7, 15.6, 12.4, 11.8; IR (film) ν_{max} 1512, 1245, 1081, 1032 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{19}H_{28}Br_2O_4$ + Na^+ 501.0246; found 501.0236.

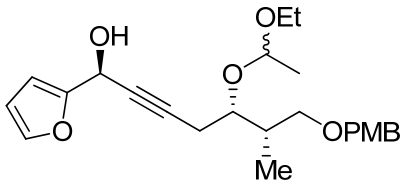


1-(((2*S*,3*S*)-3-(1-Ethoxyethoxy)-2-methylhex-5-ynyloxy)methyl)-4-methoxybenzene (10). *n*-BuLi (2.4 M in hexanes, 15.4 mL, 37.0 mmol) was added to a solution of **16** (8.12 g, 16.9 mmol) in 96 mL of THF at –78 °C. After stirring for 1 h, the solution was allowed to warm gradually to room temperature and was stirred overnight. H_2O was then slowly added and the phases were separated. The aqueous phase was extracted with Et_2O, and the combined organic phases were washed with saturated aqueous NaCl, dried (Na_2SO_4), and concentrated. The residue was purified by flash chromatography (SiO_2 pretreated with 2% Et_3N/hexanes, 5–10% EtOAc/hexanes gradient) giving 5.03 g (93%) of **10** as a colorless oil and as a mixture of acetal isomers: $[\alpha]^{25}_D$ +0.91 (*c* 0.55, $CHCl_3$); ^{1}H NMR (C_6D_6, 500 MHz) δ 7.24–7.16 (m, 4H), 6.81–6.75 (m, 4H), 4.69 (q, J = 5.0 Hz, 1H), 4.54 (q, J = 5.0 Hz, 1H), 4.36–4.23 (m, 4H), 4.03 (ddd, J = 7.5, 6.0, 4.0 Hz, 1H), 3.93 (ddd, J = 8.5, 5.0, 3.5 Hz, 1H), 3.52–3.22 (m, 8H,), 3.31 (s, 6H), 2.60 (ddd, J = 16.5, 5.0, 2.5 Hz, 1H), 2.47 (ddd, J = 16.5, 8.5, 2.5 Hz, 1H), 2.43–2.35 (m, 1H), 2.40 (ddd, J = 16.5, 6.0, 2.5 Hz, 1H), 2.33–2.26 (m, 1H), 2.30 (ddd, 16.5, 7.5, 3.0 Hz, 1H), 1.78–1.75 (m, 2H), 1.24 (d, J = 5 Hz, 3H), 1.17 (d, J = 5.0 Hz, 1H), 1.07 (t, J = 7.0 Hz, 3H), 1.05 (t, J = 7.0 Hz, 3H), 1.01 (d, J = 7.0 Hz, 1H), 0.94 (d, J = 7.0 Hz, 3H); ^{13}C NMR (C_6D_6, 125 MHz) δ 159.7, 159.6, 131.3, 131.1, 129.5, 129.3, 114.1, 114.0, 101.2, 99.3, 81.8, 81.7, 75.6, 74.1, 72.81, 72.80, 72.6, 72.2, 70.4, 70.3, 61.0, 60.3, 54.78, 54.76, 37.3, 36.4, 23.1, 22.5, 20.9, 20.4, 15.59, 1.56, 11.5, 10.8; IR (film) ν_{max} 3292, 1512, 1245 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{19}H_{28}O_4$ + Na^+ 343.188; found 343.187.



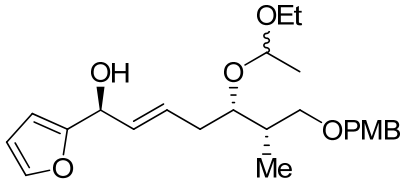
(5*S*,6*S*)-5-(1-Ethoxyethoxy)-1-(furan-2-yl)-7-(4-methoxybenzyloxy)-6-methylhept-2-yn-1-one (17). 2-Furoyl chloride (1.2 g, 9.5 mmol), $Pd(PPh_3)_2Cl_2$ (0.011 g, 0.015 mmol), and CuI (0.012 g, 0.065 mmol) were added to a stirred solution of **10** (2.40 g, 7.51 mmol)

in Et_3N (12 mL) under N_2 at room temperature. The mixture was stirred for 24 h before being diluted with Et_2O and filtered. The filtrate was concentrated, and the residue was purified by flash chromatography (SiO_2 pretreated with 2% Et_3N/hexanes, 10–20% EtOAc/hexanes gradient) to give 2.65 g (85%) of **17** as a yellow oil and as a mixture of acetal isomers: $[\alpha]^{25}_D$ –7.2 (*c* 0.12, $CHCl_3$); ^{1}H NMR (C_6D_6, 400 MHz) δ 7.25–7.17 (m, 4H), 7.12 (t, *J* = 1.2 Hz, 1H), 7.11 (t, *J* = 1.2 Hz, 1H), 6.84–6.82 (m, 2H), 6.82–6.77 (m, 4H), 5.79–5.76 (m, 2H), 4.74 (q, *J* = 5.2 Hz, 1H), 4.52 (q, *J* = 5.2 Hz, 1H), 4.35–4.21 (m 4H), 4.02 (td, *J* = 6.4, 4.0 Hz, 1H), 3.93–3.87 (m, 1H), 3.50–3.18 (m, 8H), 3.29 (s, 6H), 2.71 (dd, *J* = 17.4, 5.0 Hz, 1H), 2.55 (dd, *J* = 17.4, 7.8 Hz, 1H), 2.45 (dd, *J* = 17.4, 5.8 Hz, 1H), 2.35 (dd, *J* = 17.4, 6.6 Hz, 1H), 2.30–2.14 (m, 2H), 1.24 (d, *J* = 5.2 Hz, 3H), 1.17 (d, *J* = 5.2 Hz, 3H), 1.07 (t, *J* = 7.2 Hz, 3H), 1.06 (t, *J* = 7.2 Hz, 3H), 0.98 (d, *J* = 7.2 Hz, 3H), 0.09 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (C_6D_6, 125 MHz) δ 164.5, 164.4, 159.8, 159.7, 154.1, 147.21, 147.20, 131.1, 131.0, 129.6, 129.4, 119.7, 119.6, 114.11, 114.09, 112.29, 112.25, 101.4, 99.4, 91.8, 91.7, 81.23, 81.17, 75.5, 73.4, 72.9, 72.8, 72.2, 71.8, 61.0, 60.4, 54.8, 37.8, 37.0, 23.7, 23.1, 20.7, 20.3, 15.6, 11.9, 11.2; IR (film) ν_{max} 2209, 1634, 1461, 1013 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{24}H_{30}O_6$ + Na^+ 437.1934; found 437.1951.

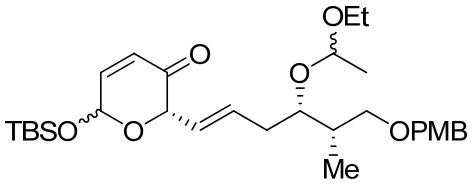


(1*S*,5*S*,6*S*)-5-(1-Ethoxyethoxy)-1-(furan-2-yl)-7-(4-methoxybenzyloxy)-6-methylhept-2-yn-1-ol (**S3**)**.** BH_3–Me_2S (2.0 M in THF, 8.5 mL, 17 mmol) was added dropwise over 15 min to a stirred solution of **17** (1.37 g, 3.31 mmol), methyl (*R*)-CBS-oxazaborolidine (1.0 M in toluene, 8.5 mL, 8.5 mmol), and powdered 4 Å molecular sieves (0.31 g) in THF (16.5 mL) at –40 °C. The mixture was stirred for 3 h at –40 °C before being warmed to 0 °C, and then MeOH (14 mL) was slowly added. The mixture was slowly warmed to room temperature and concentrated. The residue was purified by flash chromatography (SiO_2 pretreated with 2% Et_3N/hexanes, 10–20% EtOAc/hexanes gradient) to give a mixture of the product and residual CBS reagent as a colorless oil and as a mixture of acetal isomers which was taken to the next step without further purification. Analytically pure material was obtained as a mixture of acetal isomers by repetitive chromatography: $[\alpha]^{25}_D$ –2.3 (*c* 1.3, $CHCl_3$); ^{1}H NMR (C_6D_6, 500 MHz) δ 7.26–7.18 (m, 4H), 7.05–7.02 (m, 2H), 6.82–6.76 (m, 4H), 6.40–6.36 (m, 2H), 6.02–6.00 (m, 2H), 5.38–5.35 (m, 2H), 4.74 (q, *J* = 5.0 Hz, 1H), 4.56 (q, *J* = 5.0 Hz, 1H), 4.37–4.25 (m, 4H), 4.05 (ddd, *J* = 7.0, 5.5, 4.0 Hz, 1H), 3.94 (ddd, *J* = 8.5, 5.0, 3.5 Hz, 1H), 3.54–3.23 (m, 8H), 3.03 (s, 6H), 2.71 (ddd, *J* = 17, 5.0, 2.0 Hz, 1H), 2.53 (ddd, *J* = 17, 8.5, 2.5 Hz, 1H), 2.47 (ddd, *J* = 16.5, 5.5, 2.0 Hz, 1H), 2.42–2.26 (m, 2H), 2.37 (ddd, *J* = 16.5, 7.0, 2.0 Hz, 1H), 1.26 (d, *J* = 5.0 Hz, 3H), 1.19 (d, *J* = 5.0 Hz, 3H), 1.09 (t, *J* = 7.0 Hz, 3H), 1.08 (t, *J* = 7.0 Hz, 3H), 1.03 (d, *J* = 7.0 Hz, 3H), 0.95 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (C_6D_6, 125 MHz) δ 159.8, 159.7, 154.80, 154.75, 142.6, 131.3, 131.1, 129.6, 129.4, 114.10, 114.08, 110.50, 110.48, 107.4, 101.3, 99.3, 83.5, 83.4, 80.55, 80.51, 75.8, 74.1, 72.84, 72.81, 72.6, 72.1, 60.9, 60.4, 58.6, 54.80, 54.78, 37.4, 36.6, 23.4, 22.9, 20.9, 20.4,

15.60, 15.59, 11.6, 11.0; IR (film) ν_{max} 3397, 1512, 1246, 1007 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{24}H_{32}O_6 + Na^+$ 439.2091; found 439.2073.

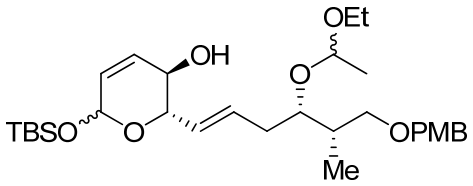


(1*S*,5*S*,6*S*,*E*)-5-(1-Ethoxyethyloxy)-1-(furan-2-yl)-7-(4-methoxybenzyloxy)-6-methylhept-2-en-1-ol (18). A $LiAlH_4$ solution (1.0 M in THF, 9.9 mL, 9.9 mmol) was added slowly to a solution of (1*S*,5*S*,6*S*)-5-(1-ethoxyethoxy)-1-(furan-2-yl)-7-(4-methoxybenzyloxy)-6-methylhept-2-yn-1-ol (**S3**) (from previous reaction, 3.3 mmol) in 22 mL of THF at 0 °C with stirring. The mixture was allowed to warm to room temperature and was stirred for 24 h at room temperature. The solution was cooled to 0 °C, and the reaction was quenched by slow addition of H_2O, and the mixture was extracted with EtOAc. The combined organic phases were dried (Na_2SO_4), concentrated, and purified by flash chromatography (SiO_2 pretreated with 2% Et_3N/hexanes, 20–50% EtOAc/hexanes gradient) to give 1.16 g (84%, 2 steps) of **18** as a colorless oil as a mixture of acetal isomers: $[\alpha]^{25}_D$ +16 (*c* 0.30, $CHCl_3$); ^1H NMR (C_6D_6, 500 MHz) δ 7.26–7.18 (m, 4H), 7.07–7.05 (m, 2H), 6.82–6.78 (m, 4H), 6.13–6.10 (m, 2H), 6.06–6.03 (m, 2H), 5.85–5.64 (m, 4H), 5.03 (d, *J* = 5.5 Hz, 1H), 5.00 (d, *J* = 5.0 Hz, 1H), 4.64 (q, *J* = 5.0 Hz, 1H), 4.62 (q, *J* = 5.5 Hz, 1H), 4.40–4.26 (m, 4H), 3.85 (td, *J* = 6.5, 3.5 Hz, 1H), 3.79 (ddd, *J* = 9.5, 6.0, 3.5 Hz, 2H), 3.58 (dd, *J* = 9.0, 7.0 Hz, 1H), 3.54–3.46 (m, 2H), 3.40 (dd, *J* = 9.0, 7.5 Hz, 1H), 3.37–3.30 (m, 3H), 3.30 (s, 6H), 3.20 (dd, *J* = 9.0, 5.5 Hz, 1H), 2.45 (td, *J* = 14.0, 6.0 Hz, 1H), 2.34–2.25 (m, 2H), 2.22–2.16 (m 1H), 2.10–1.98 (m, 2H), 1.65–1.52 (m, 2H), 1.24 (d, *J* = 5.5 Hz, 3H), 1.24 (d, *J* = 5.0 Hz, 3H), 1.12 (t, *J* = 7.0 Hz, 3H), 1.11 (t, *J* = 7.0 Hz, 3H), 1.06 (d, *J* = 7.0 Hz, 3H), 0.95 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (C_6D_6, 125 MHz) δ 159.8, 159.7, 157.0, 156.8, 142.0, 132.2, 131.9, 131.4, 131.2, 129.8, 129.6, 129.43, 129.41, 114.09, 114.06, 110.5, 110.4, 106.24, 106.21, 100.7, 99.0, 76.7, 75.6, 72.91, 72.86, 72.3, 68.7, 60.5, 60.3, 54.78, 54.76, 37.4, 36.8, 36.0, 35.3, 20.9, 20.6, 15.69, 15.67, 11.9, 11.3; IR (film) ν_{max} 3417, 3117, 1612, 1513, 1247, 1084 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{24}H_{34}O_6 + Na^+$ 441.2247; found 441.2252.



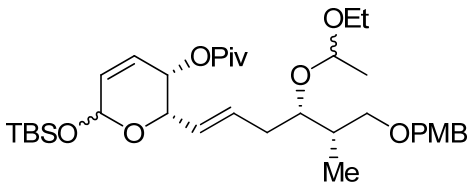
(*S*)-6-(*t*-Butyldimethylsilyloxy)-2-((4*S*,5*S*,*E*)-4-(1-ethoxyethoxy)-6-(4-methoxybenzyloxy)-5-methylhex-1-enyl)-2*H*-pyran-3-(6*H*)-one (20). *N*-Bromosuccinimide (1.25 g, 7.02 mmol) was added to a solution of **18** (2.44 g, 5.83 mmol), $NaHCO_3$ (0.98 g, 12 mmol), and NaOAc (0.46 g, 5.6 mmol) in THF (104 mL) and H_2O (27 mL) at 0 °C with stirring. After 1 h, the reaction was quenched by addition of saturated aqueous $NaHCO_3$, and the phases were separated. The aqueous layer was extracted with CH_2Cl_2, and the combined organic phases were washed with saturated aqueous NaCl, dried (Na_2SO_4), and concentrated to ~5% of the original volume (note:

complete concentration leads to decomposition as indicated by a color change from colorless/pale yellow to yellow/brown). The residue containing **19** was immediately dissolved in CH_2Cl_2/pyridine (1:1, 59 mL), and $AgNO_3$ (2.38 g, 14.0 mmol) was added followed by TBSCl (2.22 g, 14.7 mmol) at room temperature. After stirring for 15 min, the reaction mixture was diluted with Et_2O and filtered through a pad of Celite. The filtrate was concentrated, and the residue was used immediately in the next step. Purification of **20** by flash chromatography (SiO_2, 1–10% EtOAc/hexanes gradient) resulted in very low yields but gave access to analytically pure **20** as a mixture of isomers: $[\alpha]^{25}_D$ +18 (*c* 0.54, $CHCl_3$); ^{1}H NMR (C_6D_6, 500 MHz) δ 7.27–7.21 (m, 8H), 6.84–6.78 (m, 8H), 6.25 (dt, *J* = 10.5, 1.5 Hz, 2H), 6.12 (dt, *J* = 10.0, 3.0 Hz, 2H), 6.08–5.82 (m, 8H), 5.82–5.75 (m, 4H), 5.29 (d, *J* = 3.0 Hz, 1H), 5.28 (d, *J* = 3.0 Hz, 1H), 5.27–5.24 (m, 2H), 5.05–5.00 (m, 2H), 4.73–4.66 (m, 2H), 4.66–4.60 (m, 2H), 4.41–4.27 (m, 8H), 4.26–4.19 (m, 2H), 3.91–3.85 (m, 2H), 3.85–3.80 (m, 2H), 3.62–3.56 (m, 2H), 3.56–3.48 (m, 4H), 3.45–3.40 (m, 2H), 3.40–3.33 (m, 6H), 3.31 (s, 12H), 3.26–3.22 (m, 2H), 2.56–2.48 (m, 2H), 2.43–2.29 (m, 4H), 2.28–2.21 (m, 2H), 2.15–2.04 (m, 4H), 1.31 (t, *J* = 5.0 Hz, 6H), 1.255 (d, *J* = 5.5 Hz, 3H), 1.248 (d, *J* = 5.0 Hz, 3H), 1.16–1.05 (m, 18 H), 0.99–0.93 (m, 6H), 0.95 (s, 18H), 0.90 (s, 18H), 0.17–0.03 (m, 24H); ^{13}C NMR (C_6D_6, 125 MHz) δ 194.04, 194.02, 193.50, 193.46, 159.7, 159.6, 149.3, 149.2, 145.62, 145.58, 132.0, 131.9, 131.8, 131.7, 131.6, 131.5, 131.32, 131.30, 129.5, 129.3, 127.5, 126.9, 126.7, 126.13, 126.10, 125.9, 114.1, 114.0, 100.64, 100.62, 99.2, 91.6, 88.5, 79.53, 79.48, 76.7, 76.6, 75.92, 75.85, 74.94, 74.92, 72.85, 72.83, 72.80, 72.3, 60.65, 60.61, 60.32, 60.26, 54.77, 54.76, 37.58, 37.57, 36.77, 36.75, 36.23, 36.19, 35.7, 35.6, 25.9, 25.8, 21.0, 20.6, 18.20, 18.15, 15.7, 12.1, 11.5, –3.7, –4.4, –4.8, –5.39, –5.41; IR (film) ν_{max} 1697, 1513, 1249, 1096 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{30}H_{48}O_7Si + Na^+$ 571.3061; found 571.3074.

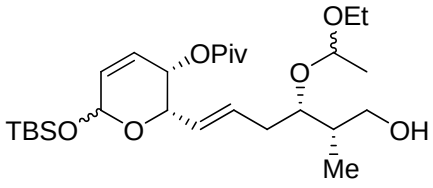


(2*S*,3*R*)-6-(*t*-Butyldimethylsilyloxy)-2-((4*S*,5*S*,*E*)-4-(1-ethoxyethoxy)-6-(4-methoxybenzyloxy)-5-methylhex-1-enyl)-3,6-dihydro-2*H*-pyran-3-ol (21). A stirred solution of **20** (from previous reaction, 5.83 mmol) in 58.3 mL of Et_2O was treated with a solution of $LiAlH_4$ (1.0 M in THF, 5.9 mL, 5.9 mmol) at –78 °C under N_2. The mixture was stirred at –50 °C for 3 h after which time the reaction was quenched by slow addition of H_2O. The mixture was extracted with Et_2O and the combined organic phases were washed with H_2O, saturated aqueous NaCl, dried (Na_2SO_4), and concentrated. The residue was purified by flash chromatography (SiO_2 pretreated with 2% Et_3N/hexanes, 10–20% EtOAc/hexanes) to give 1.63 g (51%, 3 steps) of **21** as a mixture of anomers and EE isomers as a colorless oil: $[\alpha]^{25}_D$ –7.0 (*c* 1.1, $CHCl_3$); ^{1}H NMR (C_6D_6, 500 MHz) see spectrum; ^{13}C NMR (C_6D_6, 125 MHz) δ 159.8, 159.7, 132.2, 132.14, 132.09, 131.8, 131.7, 131.6, 131.4, 131.3, 131.0, 130.7, 130.6, 130.3, 130.1, 130.0, 129.9, 129.7, 129.6, 129.5, 129.4, 128.8, 128.6, 114.09, 114.07, 101.0, 98.5, 93.6, 93.3, 93.2, 93.1, 89.71, 89.68, 80.8, 79.8, 76.8, 76.6, 76.5, 75.90, 75.85, 75.73, 75.70, 74.3, 73.4, 73.0, 72.93, 72.92, 72.9, 72.4, 72.3, 67.8, 67.6, 67.5, 67.3, 62.0, 61.9, 60.6, 60.5, 60.2, 54.79, 54.77,

37.9, 37.8, 37.50, 37.45, 37.0, 36.7, 36.6, 36.3, 35.5, 35.4, 26.1, 26.04, 26.00, 21.0, 20.83, 20.80, 20.78, 20.7, 20.6, 18.29, 18.26, 15.7, 15.64, 15.55, 12.1, 11.8, 11.7, 11.62, 11.58, 11.5, –3.4, –3.5, –3.9, –4.3, –4.4, –4.56, –4.60, –5.20, –5.24; IR (film) ν_{max} 3443, 1512, 1247, 1026 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{30}H_{50}O_7Si + Na^+$ 573.3218; found 573.3211.



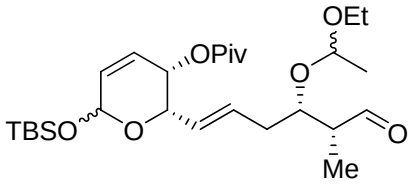
(2*S*,3*S*)-6-(*t*-Butyldimethylsilyloxy)-2-((4*S*,5*S*,*E*)-4-(1-ethoxyethoxy)-6-(4-methoxybenzyloxy)-5-methylhex-1-enyl)-3,6-dihydro-2*H*-pyran-3-yl Pivalate (22). A mixture of **21** (0.45 g, 0.82 mmol), PPh_3 (0.47 g, 1.8 mmol), and trimethylacetic acid (0.18 g, 1.8 mmol) was dried under vacuum for 1 h. THF (2.0 mL) was added, and the mixture was cooled to 0 °C while stirring. DIAD (0.36 g, 1.8 mmol) was added slowly, and the mixture was allowed to warm to room temperature while stirring overnight. The mixture was concentrated, and the residue was purified by flash chromatography (SiO_2 pretreated with 2% Et_3N/hexanes, 3% EtOAc/hexanes) [note: there are two difficult-to-separate product spots visible by TLC (R_f ~ 0.7 and 0.65, 25% EtOAc/hexanes, top spot is major); both are isomers of the **22** as shown by TBS and EE removal and oxidation to the lactone and are therefore not separated at this stage] affording 0.39 g (75%) of **22** as a yellow oil as a mixture of isomers: $[\alpha]^{25}_D$ +50 (*c* 0.25, $CHCl_3$); ^1H NMR (C_6D_6, 500 MHz) see spectrum; ^{13}C NMR (C_6D_6, 125 MHz) δ 177.3, 159.74, 159.66, 132.9, 131.5, 131.3, 130.7, 130.2, 130.0, 129.5, 129.3, 129.1, 128.7, 128.6, 124.4, 124.3, 114.1, 114.0, 100.7, 99.8, 99.0, 89.4, 76.7, 75.8, 73.0, 72.9, 72.5, 71.7, 70.2, 70.1, 65.2, 65.1, 60.5, 60.5, 60.1, 54.77, 54.76, 39.0, 37.3, 36.7, 36.3, 35.6, 27.4, 27.2, 26.1, 26.0, 25.9, 21.0, 20.5, 19.1, 18.2, 15.7, 11.9, 11.3, –4.09, –4.12, –5.3; IR (film) ν_{max} 1724, 1024, 836 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{35}H_{58}O_8Si + Na^+$ 657.3793; found 657.3770.



(2*S*,3*S*)-6-(*t*-Butyldimethylsilyloxy)-2-((4*S*,5*S*,*E*)-4-(1-ethoxyethoxy)-6-hydroxy-5-methylhex-1-enyl)-3,6-dihydro-2*H*-pyran-3-yl Pivalate (23). H_2O (5.8 mL) and DDQ (1.5 g, 6.5 mmol) were added to a solution of **22** (1.40 g, 22 mmol) in CH_2Cl_2 (103 mL) at 0 °C with stirring. After 1 h, saturated aqueous $NaHCO_3$ was added and the aqueous phase was extracted with CH_2Cl_2. The combined organic phases were washed with H_2O, saturated aqueous NaCl, dried (Na_2SO_4), and concentrated. The residue was purified by flash chromatography (SiO_2 pretreated with 2% Et_3N/hexanes, 10–20% EtOAc/hexanes gradient) to provide **23a** (0.43 g, 38%) along with some *p*-anisaldehyde as a colorless oil, **23b** (0.20 g, 18%) as a colorless oil, and a mixture of **23a** and **23b** (0.20 g, 18%) as a colorless oil [note: two product spots (**23a** and **23b**, R_f ~ 0.35 and 0.3 respectively, 25% EtOAc/hexanes) are isolated along with some *p*-anisaldehyde which co-elutes with **23a**.

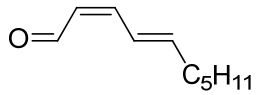
Each spot, **23a** and **23b**, is comprised of one major isomer and a small amount of a minor isomer]. Data for **23a** (major isomer): $[\alpha]^{25}_{D}$ +88 (*c* 0.06, $CHCl_3$); ^{1}H NMR (C_6D_6, 500 MHz) δ 5.93 (dd, *J* = 10.0, 5.5 Hz, 1H), 5.78–5.63 (m, 3H), 5.35 (d, *J* = 3.0 Hz, 1H), 5.00 (dd, *J* = 5.5, 2.5 Hz, 1H), 4.65–4.60 (m, 1H), 4.52 (q, *J* = 5.0 Hz, 1H), 3.91 (td, *J* = 7.0, 3.0 Hz, 1H), 3.80–3.70 (m, 1H), 3.65–3.55 (m, 1H), 3.28–3.17 (m, 2H), 3.07 (t, *J* = 7.0 Hz, 1H), 2.36–2.26 (m, 1H), 2.21–2.14 (m, 1H), 1.90–1.80 (m, 1H), 1.22–1.19 (m, 12 H), 1.07 (t, *J* = 7.0 Hz, 3H), 0.95 (s, 9H), 0.86 (d, *J* = 7.0 Hz, 3H), 0.14 (s, 3H), 0.09 (s, 3H); ^{13}C NMR (C_6D_6, 125 MHz) δ 177.4, 133.0, 129.8, 129.0, 124.2, 100.1, 89.4, 76.0, 70.1, 65.3, 65.0, 61.4, 39.0, 38.8, 35.9, 27.3, 25.9, 20.4, 18.2, 15.3, 10.2, –4.1, –5.3; IR (film) ν_{max} 3502, 1727, 1026 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{27}H_{50}O_7Si$ + Na^+ 537.3218; found 537.3216.

Data for **23b** (major isomer): $[\alpha]^{25}_{D}$ +59 (*c* 0.12, $CHCl_3$); ^{1}H NMR (C_6D_6, 500 MHz) δ 5.88 (dd, *J* = 9.5, 5.5 Hz, 1H), 5.81 (dt, *J* = 15.5, 7.0 Hz, 1H), 5.76–5.65 (m, 2H), 5.35 (d, *J* = 2.5 Hz, 1H), 5.01 (dd, *J* = 5.5, 2.5 Hz, 1H), 4.69 (q, *J* = 5.0 Hz, 1H), 4.66–4.61 (m, 1H), 3.71 (ddd, *J* = 7.5, 6.0, 3.5 Hz, 1H), 3.55–3.45 (m, 2H), 3.45–3.30 (m, 2H), 2.51–2.40 (m, 1H), 2.40–2.31 (m, 1H), 1.90–1.73 (m, 2H), 1.25 (d, 5.0 Hz, 3H), 1.20 (s, 9H), 1.12 (t, *J* = 7.0 Hz, 3H), 0.95 (s, 9H), 0.87 (d, *J* = 7.0 Hz, 3H), 0.15 (s, 3H), 0.10 (s, 3H); ^{13}C NMR (C_6D_6, 125 MHz) δ 177.7, 133.0, 130.3, 128.8, 124.2, 100.4, 89.4, 77.3, 70.4, 65.2, 60.2, 39.1, 38.3, 35.6, 27.3, 25.9, 20.4, 18.2, 15.6, 11.1, –4.1, –5.3; IR (film) ν_{max} 3501, 1726, 1024, 838 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{27}H_{50}O_7Si$ + Na^+ 537.3218; found 537.3222.

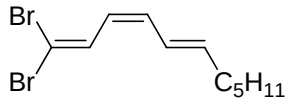


(2*S*,3*S*)-6-(*t*-Butyldimethylsilyloxy)-2-((4*S*,5*R*,*E*)-4-(1-ethoxyethoxy)-5-methyl-6-oxohex-1-enyl)-3,6-dihydro-2*H*-pyran-3-yl Pivalate (8). Dess–Martin periodinane (0.08 g, 0.20 mmol) was added to a solution of **23b** (0.064 g, 0.12 mmol) in CH_2Cl_2 (5.8 mL) at room temperature with stirring. After 1 h, saturated aqueous $NaHCO_3$ (1 mL), saturated aqueous $Na_2S_2O_3$ (1 mL), and Et_2O (10 mL) were added and the mixture was stirred vigorously for 15 min. The phases were separated and the aqueous phase was extracted with Et_2O. The combined organic phases were washed with saturated aqueous NaCl, dried (Na_2SO_4), and concentrated. The residue was purified through a short column (SiO_2, 5% EtOAc/hexanes) to give 0.059 g (92%; yield typically ranges from 83–92%) of **8b** as a colorless oil. Data for **8a** (major isomer): $[\alpha]^{25}_{D}$ +46 (*c* 0.87, $CHCl_3$); ^{1}H NMR (C_6D_6, 500 MHz) δ 9.70 (s, 1H), 5.93 (dd, *J* = 10.0, 5.5 Hz, 1H), 5.72 (dd, *J* = 10.0, 3.0 Hz, 1H), 5.70–5.58 (m, 2H), 5.34 (d, *J* = 2.5 Hz, 1H), 4.98 (dd, *J* = 5.5, 2.5 Hz, 1H), 4.63–4.53 (m, 2H), 4.02 (td, *J* = 7.0, 3.5 Hz, 1H), 3.35–3.26 (m, 1H), 3.26–3.17 (m, 1H), 2.32–2.20 (m, 2H), 2.15–2.07 (m, 1H), 1.19 (s, 9H), 1.70 (d, *J* = 5.5 Hz, 3H), 1.10 (d, *J* = 7.0 Hz, 3H), 1.07 (t, *J* = 7.0 Hz, 3H), 0.94 (s, 9H), 0.12 (s, 3H), 0.08 (s, 3H); ^{13}C NMR (C_6D_6, 125 MHz) δ 202.8, 177.3, 132.9, 129.8, 128.8, 124.2, 99.0, 89.4, 74.8, 70.0, 64.9, 59.7, 49.9, 39.0, 35.6, 27.3, 25.9, 20.3, 18.2, 15.4, 7.8, –4.2, –5.3; IR (film) ν_{max} 1725, 1025, 838 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{27}H_{48}O_7$ + Na^+ 535.3061; found 535.3056.

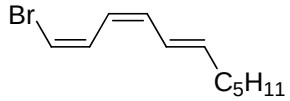
Data for **8b** (major isomer): $[\alpha]^{25}_{D}$ +45 (*c* 0.60, $CHCl_3$); ^1H NMR (C_6D_6, 500 MHz) δ 9.60 (s, 1H), 5.93 (dd, *J* = 10.0, 5.5 Hz, 1H), 5.77–5.67 (m, 2H), 5.62 (dd, *J* = 15.5, 5.5 Hz, 1H), 5.33 (d, *J* = 3.0 Hz, 1H), 4.97 (dd, *J* = 5.5, 2.5 Hz, 1H), 4.64–4.57 (m, 1H), 4.55 (q, *J* = 5.5 Hz, 1H), 3.95 (ddd, *J* = 8.0, 5.5, 4.0 Hz, 1H), 3.43–3.32 (m, 1H), 3.32–3.20 (m, 1H), 2.49–2.32 (m, 1H), 2.32–2.21 (m, 2H), 1.18 (s, 9H), 1.14 (d, *J* = 5.5 Hz, 3H), 1.08 (t, *J* = 7.0 Hz, 3H), 1.02 (d, *J* = 7.0 Hz, 3H), 0.93 (s, 9H), 0.11 (s, 3H), 0.07 (s, 3H); ^{13}C NMR (C_6D_6, 125 MHz) δ 202.7, 177.3, 132.9, 129.8, 129.1, 124.2, 100.1, 89.3, 75.1, 70.1, 65.0, 60.1, 49.7, 39.0, 36.4, 27.3, 25.9, 20.2, 18.2, 15.5, 7.8, –4.2, –5.3; IR (film) ν_{max} 1725, 1025, 838 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{27}H_{48}O_7$ + Na^+ 535.3061; found 535.3061.



(2*Z*,4*E*)-Deca-2,4-dienal (24). A solution of 1-iodopentane (3.03 g, 15.4 mmol) in 31 mL of anhydrous Et_2O was cooled under argon to −78 °C and was treated with *t*-BuLi (1.5 M in pentane, 25.3 mL, 38 mmol) slowly. After stirring for 1 h, the solution was allowed to warm to room temperature and was transferred via cannula to a suspension of pyrilium tetrafluoroborate[2] (2.0 g, 11.9 mmol) in THF (86 mL) at –78 °C. The reaction mixture was stirred for 4 h before saturated aqueous NH_4Cl was added, and the mixture was warmed to room temperature. The organic phase was extracted with Et_2O, washed with saturated aqueous NaCl, dried (Na_2SO_4), and carefully concentrated under reduced pressure. The residue was purified by flash chromatography (SiO_2 pretreated with 2% Et_3N/hexanes, 10% EtOAc/hexanes) to yield **24** as a volatile yellow liquid that was used immediately in the next step.

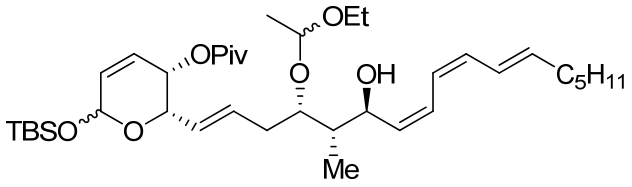


(3*Z*,5*E*)-1,1-Dibromoundeca-1,3,5-triene (25). PPh_3 (11.6 g, 44.2 mmol) was added to a solution of CBr_4 (17.6 g, 53.1 mmol) in 60 mL of anhydrous CH_2Cl_2 at 0 °C. After 5 min, Et_3N (16.7 g, 165 mmol) was added slowly followed by **24** (from previous reaction, 11.9 mmol) in 11 mL of anhydrous CH_2Cl_2. After 10 min, the mixture was concentrated, and the resulting sludge was triturated repeatedly with hexanes. The combined hexanes mixture was concentrated, and the residue was purified by flash chromatography (SiO_2 pretreated with 2% Et_3N/hexanes, hexanes) to give 3.12 g (85%, 2 steps) of **25** as a yellow oil: ^1H NMR (C_6D_6, 500 MHz) δ 7.26 (d, *J* = 9.9 Hz, 1H), 6.08–6.01 (m, 1H), 5.93–5.84 (m, 2H), 5.54 (dt, *J* = 15.0, 7.0 Hz, 1H), 1.89–1.81 (m, 2H), 1.20–1.15 (m, 6H), 0.82 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (C_6D_6, 125 MHz) δ 139.9, 133.6, 133.0, 126.0, 123.2, 92.2, 33.2, 31.7, 29.0, 22.9, 14.2; IR (film) ν_{max} 1548, 944, 818 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{11}H_{16}Br_2$ + Cl^- 340.9313; found 340.9310.



[2] Belosludtsev, Y. Y.; Borer, B. C.; Taylor, R. J. K. *Synthesis* **1991**, 320-322.

(1*Z*,3*Z*,5*E*)-1-Bromoundeca-1,3,5-triene (9). A solution of **25** (0.36 g, 1.2 mmol) in Et_2O (3.0 mL) at 0 °C was treated with $Pd(PPh_3)_4$ (0.15 g, 0.13 mmol) followed by Bu_3SnH (0.59 g, 2.0 mmol). After the reaction was complete as judged by TLC (~30 min; note: depending on the quality of Bu_3SnH, it is sometimes necessary to add a small amount of additional Bu_3SnH in order to achieve complete conversion), the mixture was concentrated, and the crude product was purified by flash chromatography (SiO_2 pretreated with 2% Et_3N/hexanes, hexanes) to provide 0.21 g (78%) of **9** as a colorless oil that was immediately diluted in ether and used in the next reaction. For **9**: ^{1}H NMR (C_6D_6, 400 MHz) δ 6.70 (dd, J = 10.8, 7.2, Hz, 1H), 6.35 (t, J = 10.8 Hz, 1H), 6.31–6.23 (m, 1H), 6.03 (t, J = 10.8 Hz, 1H), 5.83 (d, J = 7.2 Hz, 1H), 5.58 (dt, J = 15.2, 6.8 Hz, 1H), 1.93 (q, J = 7.2 Hz, 2H), 1.30–1.10 (m, 6H), 0.86 (t, J = 6.8 Hz, 3H); ^{13}C NMR (C_6D_6, 150 MHz) δ 140.6, 138.9, 133.7, 126.2, 122.6, 108.9, 33.3, 31.7, 29.0, 22.9, 14.2; IR (film) ν_{max} 1296, 947, 694, 638 cm^{-1}; GCMS calcd for $C_{11}H_{17}Br^+$ 228; found 228.

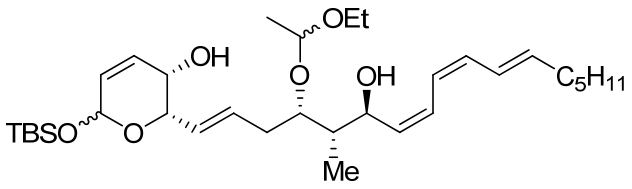


(2*S*,3*S*)-6-(*t*-Butyldimethylsilyloxy)-2-((1*E*,4*S*,5*S*,6*S*,7*Z*,9*Z*,11*E*)-4-(1-ethoxyethoxy)-6-hydroxy-5-methylheptadeca-1,7,9,11-tetraenyl)-3,6-dihydro-2*H*-pyran-3-yl Pivalate (26). *t*-BuLi (1.6 M in pentane, 0.90 mL, 1.43 mmol) was slowly added to a degassed solution of **9** (0.187 g, 0.816 mmol) in Et_2O (5.6 mL) with stirring at –78 °C under N_2. After 1.5 h, a solution of CuI–PBu_3[3] (0.126 g, 0.322 mmol) in 1.9 mL of Et_2O was added at –78 °C and the mixture was stirred for 15 min. A solution of **8b** (0.075 g, 0.146 mmol) in 4.6 mL of anhydrous Et_2O was added slowly to the mixture down the side of the flask over 15 min at –78 °C. After 1 h, the reaction was quenched by addition of saturated aqueous NH_4Cl/NH_4OH (pH 8, 2 mL) and warmed to room temperature. The mixture was extracted with Et_2O and the combined organic phases were washed with H_2O, saturated aqueous NaCl, dried (Na_2SO_4), and concentrated. The residue was purified by flash chromatography (SiO_2 pretreated with 2% Et_3N/hexanes, 10–20% EtOAc/hexanes gradient) to give 0.095 g (85%) of **26b** as a yellow oil. Data for **26a** (major isomer): $[\alpha]^{25}_D$ +43 (*c* 0.76, $CHCl_3$); ^{1}H NMR (C_6D_6, 500 MHz) δ 6.69 (t, J = 11.5 Hz, 1H), 6.57 (dd, J = 14.5, 11.5 Hz, 1H), 6.42 (t, J = 11.0 Hz, 1H), 6.00 (t, J = 11.5 Hz, 1H), 5.94 (dd, J = 9.5, 5.5 Hz, 1H), 5.80–5.65 (m, 4H), 5.60 (dt, J = 15.0, 7.5 Hz, 1H), 5.36 (d, J = 2.5 Hz, 1H), 5.00 (dd, J = 5.5, 2.5 Hz, 1H), 4.86 (t, J = 9.0 Hz, 1H), 4.64 (dd, J = 4.0, 2.5 Hz, 1H), 4.55 (q, J = 5.0 Hz, 1H), 4.22 (td, J = 7.0, 2.0 Hz, 1H), 3.98 (brs, 1H), 3.25 (q, J = 7.0 Hz, 2H), 2.44–2.36 (m, 1H), 2.26–2.18 (m, 1H), 1.98 (q, J = 7.0 Hz, 2H), 1.77–1.69 (m, 1H), 1.38–1.12 (m, 6H), 1.23 (d, J = 5.0 Hz, 3H), 1.21 (s, 9H), 1.09 (t, J = 7.0 Hz, 3H), 1.00 (d, J = 7.0 Hz, 3H), 0.97 (s, 9H), 0.85 (t, J = 7.0 Hz, 3H), 0.17 (s, 3H), 0.11 (s, 3H); ^{13}C NMR (C_6D_6, 150 MHz) δ 177.2, 136.8, 134.5, 133.0, 131.0, 129.5, 129.1, 126.1, 125.1, 124.2, 123.3, 100.2, 89.4, 75.2, 70.1, 68.8, 65.0, 61.9, 43.0, 39.0, 36.0, 33.3, 31.7, 29.3, 27.4, 25.9, 22.9, 20.4, 18.2, 15.3, 14.2, 9.9, –4.0, –5.3;

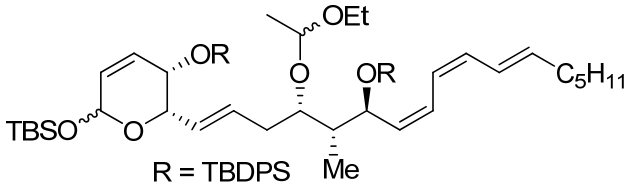
[3] Kauffman, G. B.; Teter, L. A. *Inorg. Synth.* **1963**, *7*, 9.

IR (film) ν_{max} 3468, 1726, 1025 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{38}H_{66}O_7Si + Na^+$ 685.4470; found 685.4460.

Data for **26b** (major isomer): $[\alpha]^{25}_D$ +32 (*c* 0.48, $CHCl_3$); ^1H NMR (C_6D_6, 500 MHz) δ 6.63 (t, *J* = 11.5 Hz, 1H), 6.57 (dd, *J* = 15.0, 12.5 Hz, 1H), 6.37 (t, *J* = 11.5 Hz, 1H), 6.05 (t, *J* = 11.0 Hz, 1H), 5.90 (dd, *J* = 10.0, 5.5 Hz, 1H), 5.80–5.67 (m, 3H), 5.65 (dt, *J* = 15.0, 7.0 Hz, 1H), 5.53 (t, *J* = 10.5 Hz, 1H), 5.35 (d, *J* = 2.5 Hz, 1H), 4.99 (dd, *J* = 5.5, 2.5 Hz, 1H), 4.84 (q, *J* = 5.5 Hz, 1H), 4.66–4.59 (m, 2H), 4.11 (ddd, *J* = 8.0, 5.5, 2.0 Hz, 1H), 3.60–3.53 (m, 1H), 3.42–3.50 (m, 1H), 2.67–2.59 (m, 1H), 2.42–2.33 (m, 1H), 2.00 (q, *J* = 7.0 Hz, 2H), 1.80–1.72 (m, 1H), 1.34 (d, *J* = 5.5 Hz, 3H), 1.33–1.15 (m, 6 H), 1.20 (s, 9H), 1.13 (t, *J* = 7.0 Hz, 3H), 0.97 (s, 9H), 0.97–0.94 (m, 3H), 0.87 (t, *J* = 7.0 Hz, 3H), 0.17 (s, 3H), 0.11 (s, 3H); ^{13}C NMR (C_6D_6, 125 MHz) δ 177.7, 137.4, 134.3, 133.0, 131.6, 130.2, 128.9, 125.9, 125.6, 124.2, 122.6, 100.5, 89.4, 76.2, 70.4, 68.8, 65.3, 60.3, 41.8, 39.1, 35.9, 33.3, 31.7, 29.3, 27.3, 26.0, 22.9, 20.6, 18.3, 15.6, 14.2, 10.1, –4.0, –5.3; IR (film) ν_{max} 3480, 1726, 1150, 1025, 837 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{38}H_{66}O_7Si + Na^+$ 685.4470; found 685.4470.

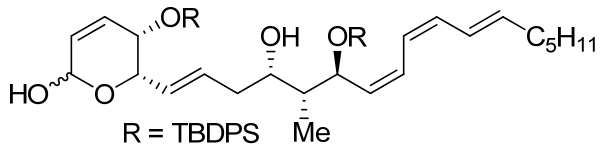


(2*S*,3*S*)-6-(*t*-Butyldimethylsilyloxy)-2-((1*E*,4*S*,5*S*,6*S*,7*Z*,9*Z*,11*E*)-4-(1-ethoxyethoxy)-6-hydroxy-5-methylheptadeca-1,7,9,11-tetraenyl)-3,6-dihydro-2*H*-pyran-3-ol (27). DIBAL (1.0 M in hexanes, 0.27 mL, 0.27 mmol) was added to a solution of **26b** (0.026 g, 0.039 mmol) in CH_2Cl_2 (0.33 mL) at –78 °C under N_2. After 2 h, the reaction was quenched by slow addition of saturated aqueous sodium potassium tartrate (2 mL). The mixture was extracted with EtOAc, and the combined organic phases were dried (Na_2SO_4) and concentrated under vacuum. Purification of **27** by silica gel chromatography resulted in very low yields, so the crude material was used directly in the next reaction. IR (film) ν_{max} 3394, 1000, 836, 779 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{33}H_{58}O_6Si + Na^+$ 601.3895; found 601.3898.

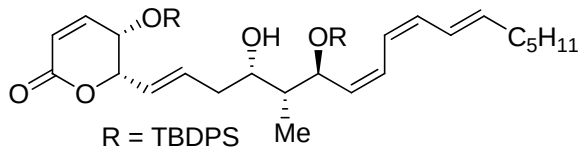


(5*S*,6*R*,7*S*)-7-((*E*)-3-((2*S*,3*S*)-6-(*t*-Butyldimethylsilyloxy)-3-(*t*-butyldiphenylsilyloxy)-3,6-dihydro-2*H*-pyran-2-yl)allyl)-2,2,6,9-tetramethyl-3,3-diphenyl-5-((1*Z*,3*Z*,5*E*)-undeca-1,3,5-trienyl)-4,8,10-trioxa-3-siladodecane (28). A solution of crude diol **27b** (from previous reaction, 0.039 mmol) in 1:1 CH_2Cl_2/pyridine (0.78 mL) was treated with TBDPSCl (0.11 g, 0.39 mmol) and $AgNO_3$ (0.06 g, 0.36 mmol) at room temperature with stirring. After stirring overnight, the mixture was diluted with Et_2O and filtered through Celite. The filtrate was concentrated and the residue purified by flash chromatography (SiO_2 pretreated with 2% Et_3N/hexanes, 3% EtOAc/hexanes) to give 0.033 g (80%, 2 steps) of **28b** as a colorless oil: (major isomer) $[\alpha]^{25}_D$ +34 (*c* 0.39, $CHCl_3$); ^1H NMR

(C_6D_6, 600 MHz) δ 7.94–7.70 (m, 8H), 7.30–7.18 (m, 12 H), 6.40–6.30 (m, 2H), 6.08 (dd, J = 15.6, 6.6 Hz, 1H), 5.90–5.82 (m, 3H), 5.66–5.59 (m, 3H), 5.56 (dt, J = 15.0, 7.2 Hz, 1H), 5.45 (d, J = 2.4 Hz, 1H), 4.90 (t, J = 9.0 Hz, 1H), 4.75 (q, J = 5.4 Hz, 1H), 4.56-4.52 (m, 1H), 4.26 (ddd, J = 8.4, 4.8, 3.0 Hz, 1H), 3.89 (dd, J = 4.8, 2.4 Hz, 1H), 3.46-3.40 (m, 2H), 2.87–2.81 (m, 1H), 2.62–2.54 (m, 1H), 2.19–2.12 (m, 1H), 1.94 (q, J = 7.2 Hz, 2H), 1.26–1.00 (m, 15H), 1.23 (s, 9H), 1.18 (s, 9H), 1.03 (s, 9H) 0.85 (t, J = 7.2 Hz, 3H), 0.30 (s, 3H), 0.18 (s, 3H); ^{13}C NMR (C_6D_6, 150 MHz) δ 137.1, 136.6, 136.5, 136.4, 136.1, 136.0, 135.9, 135.6, 135.3, 135.0, 134.9, 134.4, 134.3, 134.2, 133.0, 131.3, 130.9, 130.6, 130.0, 129.9, 129.81, 129.77, 129.4, 129.0, 127.5, 127.4, 126.0, 124.0, 122.6, 101.1, 89.6, 77.3, 72.7, 71.2, 66.2, 58.9, 43.4, 37.4, 33.3, 31.8, 31.2, 29.3, 27.6, 27.22, 27.15, 27.1, 26.8, 26.5, 26.1, 22.9, 20.5, 19.83, 19.79, 19.2, 18.3, 15.8, 14.2, 9.4, –3.6, –5.1; IR (film) ν_{max} 1110, 702 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{65}H_{94}O_6Si_3$ + Na^+ 1077.6250; found 1077.6267.

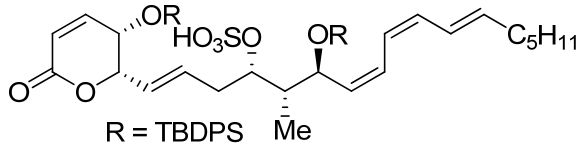


(5*S*,6*S*)-5-(*t*-Butyldiphenylsilyloxy)-6-((1*E*,4*S*,5*R*,6*S*,7*Z*,9*Z*,11*E*)-6-(*t*-butyldiphenylsilyloxy)-4-hydroxy-5-methylheptadeca-1,7,9,11-tetraenyl)-5,6-dihydro-2*H*-pyran-2-ol (S4). 0.5 M aqueous HCl (0.62 mL) was added to a solution of **28** (0.033 g, 0.031 mmol) in THF (12.7 mL) at room temperature, and the mixture was stirred overnight. The reaction was quenched by addition of saturated aqueous $NaHCO_3$, and the aqueous phase was extracted with EtOAc. The combined organic phases were washed with saturated aqueous NaCl, dried (Na_2SO_4), concentrated, and the residue was purified by flash chromatography (SiO_2, 10–30% EtOAc/hexanes gradient) to give 0.019 g (71%) of the lactol as a mixture of anomers as a glassy white solid: $[\alpha]^{25}_D$ +37 (*c* 0.20, $CHCl_3$); ^{1}H NMR (C_6D_6, 600 MHz) δ 7.89–7.76 (m, 8H), 7.29–7.16 (m, 12H), 6.34 (dd, J = 14.4, 11.4 Hz, 1H), 6.24 (t, J = 12.0 Hz, 1H), 6.06 (dd, J = 15.6, 7.2 Hz, 1H), 5.93 (dt, J = 14.4, 7.2 Hz, 1H), 5.80 (t, J = 10.8 Hz, 1H), 5.65 (t, J = 10.2 Hz, 1H), 5.62 (t, J = 11.4 Hz, 1H), 5.60–5.57 (m, 3H), 5.30 (s, 1H), 4.90 (dd, J = 9.0, 5.4 Hz, 1H), 4.50 (dd, J = 7.2, 1.8 Hz, 1H), 4.35–4.30 (m, 1H), 3.83 (dd, J = 4.2, 2.4 Hz, 1H), 2.73 (brs, 1H), 2.45–2.38 (m, 1H), 2.21–2.15 (m, 1H), 1.94 (q, J = 7.2 Hz, 1H), 1.79–1.70 (m, 1H), 1.28–1.12 (m, 6H), 1.20 (s, 9H), 1.17 (s, 9H), 1.08 (d, J = 7.2 Hz, 3H), 0.84 (t, J = 7.2 Hz, 3H); ^{13}C NMR (C_6D_6, 150 MHz) δ 137.2, 136.53, 136.47, 136.4, 136.3, 135.0, 134.3, 134.2, 133.9, 132.89, 132.85, 131.4, 130.9, 130.7, 130.08, 130.05, 129.911, 129.906, 129.3, 129.2, 125.9, 124.6, 122.1, 89.1, 73.7, 72.5, 70.7, 65.8, 44.7, 39.1, 33.2, 31.7, 29.4, 29.3, 27.4, 27.2, 22.9, 19.7, 14.2, 10.1; IR (film) ν_{max} 3417, 1107, 702 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{55}H_{72}O_5Si_2$ + Na^+ 891.4811; found 891.4804.

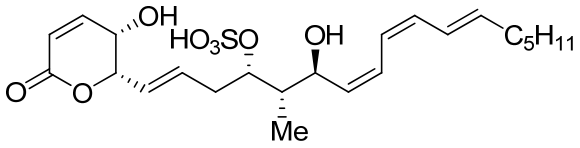


(5*S*,6*S*)-5-(*t*-Butyldiphenylsilyloxy)-6-((1*E*,4*S*,5*R*,6*S*,7*Z*,9*Z*,11*E*)-6-(*t*-butyldiphenylsilyloxy)-4-hydroxy-5-methylheptadeca-1,7,9,11-tetraenyl)-5,6-

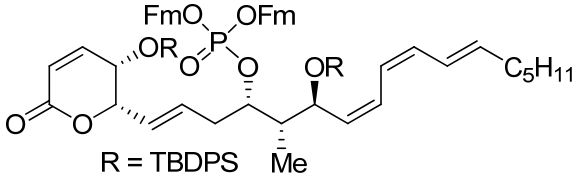
dihydro-2*H*-pyran-2-one (29). Ag_2CO_3 (~50% on Celite, 1.96 g, 3.55 mmol) was added in four portions over the course of 1 h to a solution of (5*S*,6*S*)-5-(*t*-butyldiphenylsilyloxy)-6-((1*E*,4*S*,5*R*,6*S*,7*Z*,9*Z*,11*E*)-6-(*t*-butyldiphenylsilyloxy)-4-hydroxy-5-methylheptadeca-1,7,9,11-tetraenyl)-5,6-dihydro-2*H*-pyran-2-ol (**S4**) (0.043 g, 0.049 mmol) in 4.9 mL of benzene at reflux. After the final addition, the mixture was stirred for 30 min before being cooled to room temperature and filtered through Celite while washing with EtOAc. The filtrate was concentrated and the residue was purified by flash chromatography (SiO_2, 10–20% EtOAc/hexanes gradient) to give 0.039 g (91%) of **29** as a glassy solid: $[\alpha]^{25}_D$ +20 (*c* 0.33, $CHCl_3$); ^{1}H NMR (C_6D_6, 600 MHz) δ 7.90–7.78 (m, 4H), 7.70–7.59 (m, 4H), 7.30–7.18 (m, 12 H), 6.34 (dd, *J* = 14.4, 12.0 Hz, 1H), 6.25 (t, *J* = 11.4 Hz, 1H), 5.94 (dd, *J* = 15.6, 7.2 Hz, 1H), 5.89–5.81 (m, 2H), 5.86 (dd, *J* = 9.6, 4.2 Hz, 1H), 5.70–5.65 (m, 1H), 5.67 (d, *J* = 9.6 Hz, 1H), 5.64–5.54 (m 2H), 4.86 (dd, *J* = 9.0, 5.4 Hz, 1H), 4.30–4.23 (m, 1H), 4.21 (dd, *J* = 6.6, 3.0 Hz, 1H), 3.84 (dd, *J* = 4.8, 3.0 Hz, 1H), 2.59 (brs, 1H), 2.39–2.31 (m, 1H), 2.08–2.01 (m, 1H), 1.95 (q, *J* = 7.2 Hz, 2H), 1.70–1.62 (m, 1H), 1.30–1.12 (m, 6H), 1.20 (s, 9H), 1.07 (s, 9H), 1.04 (d, *J* = 7.2 Hz, 3H), 0.84 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (C_6D_6, 150 MHz) δ 162.3, 144.2, 137.5, 136.51, 136.50, 136.21, 136.18, 134.1, 133.8, 133.63, 133.60, 133.2, 132.8, 131.7, 130.4, 130.3, 130.2, 130.0, 127.1, 125.8, 124.6, 122.5, 121.8, 81.2, 74.2, 70.5, 65.3, 44.6, 38.8, 33.2, 31.7, 29.4, 29.2, 27.3, 27.0, 22.9, 19.5, 14.2, 10.1; IR (film) ν_{max} 3512, 1732, 1109 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{55}H_{70}O_5Si_2$ + Na^+ 889.4654; found 889.4656.



(5*S*,6*S*)-5-(*t*-Butyldiphenylsilyloxy)-6-((1*E*,4*S*,5*S*,6*S*,7*Z*,9*Z*,11*E*)-6-(*t*-butyldiphenylsilyloxy)-5-methylheptadeca-1,7,9,11-tetraen-4-yl sulfate)-5,6-dihydro-2*H*-pyran-2-one (30). SO_3–pyridine complex (0.003 g, 0.016 mmol) was added to a solution of **29** (0.0064 g, 0.0074 mmol) in 0.31 mL of THF with stirring at room temperature. After 10 min, the mixture was transferred directly onto a short silica gel column and eluted with 15% MeOH/CH_2Cl_2. The product-containing fractions were concentrated to give 0.0056 g (80%) of **30** as a white solid: $[\alpha]^{25}_D$ +5.6 (*c* 0.14, MeOH); ^{1}H NMR (CD_3OD, 600 MHz) δ 7.75–7.60 (m, 8H), 7.49–7.29 (m, 12H), 6.54 (dd, *J* = 9.9, 5.4 Hz, 1H), 6.34 (dd, *J* = 14.4, 11.4 Hz, 1H), 6.24 (t, *J* = 11.4 Hz, 1H), 5.95 (d, *J* = 9.9 Hz, 1H), 5.78–5.62 (m, 4H), 5.55 (t, *J* = 11.4 Hz, 1H), 5.36 (t, *J* = 10.2 Hz, 1H), 4.81 (dd, *J* = 10.2, 6.0 Hz, 1H), 4.59–4.55 (m, 1H), 4.53 (dd, *J* = 6.6, 2.7 Hz, 1H), 4.19 (dd, *J* = 5.4, 2.7 Hz, 1H), 2.51–2.41 (m, 2H), 2.12–2.05 (m, 2H), 2.03–1.97 (m, 1H), 1.43–1.36 (m, 2H), 1.35–1.25 (m, 4H), 1.03 (s, 9H), 1.00 (m, 12H), 0.90 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (CD_3OD, 150 MHz) δ 178.1 165.8, 147.0, 138.0, 137.3, 137.2, 137.1, 135.9, 135.2, 134.6, 133.9, 132.9, 132.3, 131.5, 131.42, 131.35, 130.6, 130.5, 129.1, 129.0, 128.7, 128.53, 128.50, 128.2, 126.7, 126.4, 123.2, 122.8, 83.0, 79.7, 70.7, 66.1, 44.4, 37.0, 34.0, 32.7, 30.2, 29.8, 27.7, 27.5, 23.6, 20.2, 14.5, 10.4; IR (film) ν_{max} 3461, 1726, 1251, 1110 cm^{-1}.



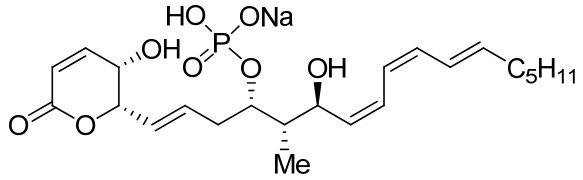
Sultriecin (1). A solution of HF–pyridine complex (0.27 mL) in 0.40 mL of THF was added to a solution of **30** (0.0056 g, 0.0059 mmol) in 0.40 mL of THF and 0.10 mL of pyridine with stirring at room temperature. After 96 h, the reaction mixture was carefully transferred to a mixture of saturated aqueous $NaHCO_3$ (6.3 mL) and EtOAc (2.4 mL). The mixture was extracted with EtOAc (5 × 4 mL), and the combined organic fractions were dried (Na_2SO_4) and concentrated under reduced pressure. The residue was purified by flash chromatography (SiO_2, 20% MeOH/CH_2Cl_2) to give 0.0017 g (60%) of sultriecin (**1**) as a white solid: $[\alpha]^{25}_D$ +9.0 (*c* 0.20, MeOH); ^{1}H NMR (CD_3OD, 600 MHz) δ 7.03 (dd, *J* = 9.6, 5.4 Hz, 1H), 6.59 (t, *J* = 12.0 Hz, 1H), 6.54 (dd, *J* = 14.4, 12.0 Hz, 1H), 6.21 (t, *J* = 12.0 Hz, 1H), 6.05 (d, *J* = 9.6 Hz, 1H), 6.02 (t, *J* = 12.0 Hz, 1H), 5.91 (dt, *J* = 15.6, 7.8 Hz, 1H), 5.83 (dd, *J* = 15.6, 7.2 Hz, 1H), 5.76 (dt, *J* = 14.4, 7.2 Hz, 1H), 5.38 (dd, *J* = 10.8, 9.6 Hz, 1H), 4.82 (ddd, *J* = 8.4, 6.6, 2.4 Hz, 1H), 4.61 (t, *J* = 9.6 Hz, 1H), 4.17 (dd, *J* = 5.4, 3.0 Hz, 1H), 2.80–2.74 (m, 1H), 2.50–2.43 (m, 1H), 2.13 (q, *J* = 7.2 Hz, 2H), 1.67–1.63 (m, 1H), 1.46–1.39 (m, 2H), 1.37–1.24 (m, 4H), 0.90 (t, *J* = 7.2 Hz, 3H), 0.83 (d, *J* = 7.2 Hz, 3H); ^{1}H NMR (DMSO-d_6, 600 MHz) δ 7.00 (dd, *J* = 9.6, 5.4 Hz, 1H), 6.56 (dd, *J* = 14.4, 10.8 Hz, 1H), 6.51 (t, *J* = 11.4 Hz, 1H), 6.09 (t, *J* = 10.8 Hz, 1H), 6.01 (t, *J* = 10.8 Hz, 1H), 5.98 (d, *J* = 9.6 Hz, 1H), 5.81–5.68 (m, 3H), 5.35 (t, *J* = 10.2 Hz, 1H), 4.97 (d, *J* = 4.2 Hz, 1H), 4.82 (dd, *J* = 6.6, 3.0 Hz, 1H), 4.51(ddd, *J* = 7.8, 5.4, 2.4 Hz, 1H), 4.32 (td, *J* = 9.0, 4.2 Hz, 1H), 4.15–4.09 (m, 1H), 4.08–4.04 (m, 1H), 2.63–2.57 (m, 1H), 2.32–2.26 (m, 1H), 2.11 (q, *J* = 7.2 Hz, 2H), 2.02–1.96 (m, 1H), 1.48–1.20 (m, 6H), 0.86 (t, *J* = 7.2 Hz, 3H), 0.66 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (DMSO-d_6, 150 MHz) δ 176.1, 163.3, 146.6, 136.8, 134.1, 131.3, 126.8, 125.5, 124.0, 122.3, 121.1, 80.9, 73.7, 66.9, 61.6, 41.2, 35.4, 32.2, 30.8, 28.3, 21.9, 13.9, 8.8; IR (film) ν_{max} 3426, 1720, 1253, 1042, 945 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{23}H_{34}O_8S - H^+$ 469.1902; found 469.1887.



Bis((9*H*-fluoren-9-yl)methyl)(1*E*,4*S*,5*S*,6*S*,7*Z*,9*Z*,11*E*)-6-(*t*-butyldiphenylsilyloxy)-1-((2*S*,3*S*)-3-(*t*-butyldiphenylsilyloxy)-6-oxo-3,6-dihydro-2*H*-pyran-2-yl)-5-methylheptadeca-1,7,9,11-tetraen-4-yl phosphate (31). *i*-$Pr_2NP(OFm)_2$[4] (0.035 g, 0.067 mmol) in CH_2Cl_2 (0.50 mL) was added at room temperature to a stirred solution of **29** (0.016 g, 0.018 mmol) and tetrazole (0.45 M in MeCN, 0.10 mL, 0.051 mmol) in anhydrous MeCN (0.39 mL) under N_2. After 1 h, aqueous H_2O_2 (35%, 0.10 mL, 0.8 mmol) was added, and the mixture was stirred vigorously for 15 min. Saturated aqueous $NaHCO_3$ (3.9 mL) was added, and the mixture was extracted with CH_2Cl_2. The

[4] (a) Lawhorn, B. G.; Boga, S. B.; Wolkenberg, S. E.; Colby, D. A.; Gauss, C.-M.; Swingle, M. R.; Amable, L.; Honkanen, R. E.; Boger, D. L. *J. Am. Chem. Soc.* **2006**, *128*, 16720. (b) Bialy, L.; Waldmann, H. *Chem. Eur. J.* **2004**, *10*, 2759. (c) Watanabe, Y.; Nakamura, T.; Mitsumoto, H. *Tetrahedron Lett.* **1997**, *38*, 7407.

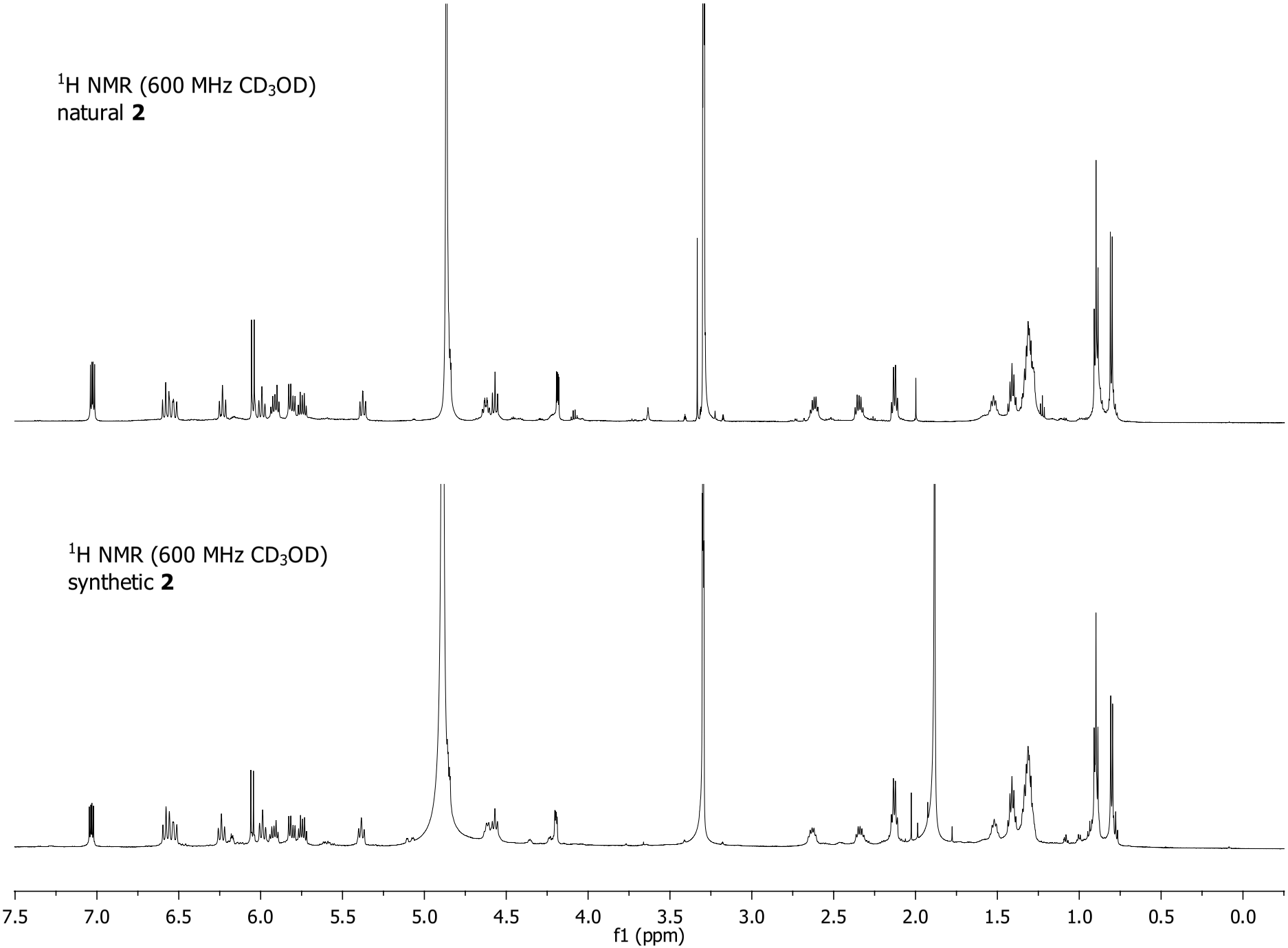
combined organic extracts were dried (Na_2SO_4), concentrated, and the residue was purified by flash chromatography (SiO_2, 25% EtOAc/hexanes) to give 0.023 g (96%) of **31** as a colorless oil: $[\alpha]^{25}_D$ +16 (*c* 0.24, $CHCl_3$); ^{1}H NMR (C_6D_6, 600 MHz) δ 7.97–7.85 (m, 4H), 7.67–7.58 (m, 4H), 7.56–7.43 (m, 8H), 7.35–7.07 (m, 20H), 6.27 (dd, *J* = 14.4, 10.8 Hz, 1H), 6.20 (t, *J* = 11.4 Hz, 1H), 5.96–5.88 (m, 2H), 5.85–5.72 (m, 2H), 5.76 (t, *J* = 10.8 Hz, 1H), 5.70 (d, *J* = 10.2 Hz, 1H), 5.57 (dt, *J* = 14.4, 7.2 Hz, 1H), 5.41 (t, *J* = 10.8 Hz, 1H), 5.18–5.11 (m, 1H), 5.04 (dd, *J* = 9.6, 7.8 Hz, 1H), 4.34–4.17 (m, 5H), 4.01 (t, *J* = 7.2 Hz, 1H), 3.97 (t, *J* = 6.6 Hz, 1H), 3.85 (dd, *J* = 4.8, 3.0 Hz, 1H), 2.70–2.63 (m, 1H), 2.54–2.46 (m, 1H), 2.15–2.07 (m, 1H), 1.93 (q, *J* = 7.2 Hz, 2H), 1.40–1.11 (m, 6H), 1.23 (s, 9H), 1.04 (s, 9H), 1.02 (d, *J* = 7.2 Hz, 3H), 0.85 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (C_6D_6, 150 MHz) δ 162.2, 144.0, 143.93, 143.89, 143.83, 143.76, 141.78, 141.77, 141.76, 137.3, 136.5, 136.4, 136.2, 136.1, 135.1, 134.2, 133.7, 133.1, 131.9, 131.0, 130.8, 130.5, 130.4, 129.9, 129.8, 128.6, 127.5, 127.42, 127.38, 127.23, 127.20, 126.0, 125.9, 125.72, 125.66, 125.63, 125.56, 122.7, 122.0, 120.24, 120.17, 80.8, 78.8, 78.7, 70.5, 69.44, 69.40, 69.22, 69.19, 65.1, 48.5, 48.42, 48.39, 37.32, 37.31, 33.3, 31.8, 29.4, 29.2, 27.4, 27.0, 22.9, 19.7, 19.5, 14.2, 9.9; ^{31}P NMR (C_6D_6, 160 MHz) δ –0.34; IR (film) ν_{max} 1732, 1108, 1006 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{83}H_{91}O_8PSi_2$ + Na^+ 1325.5882; found 1325.5894.



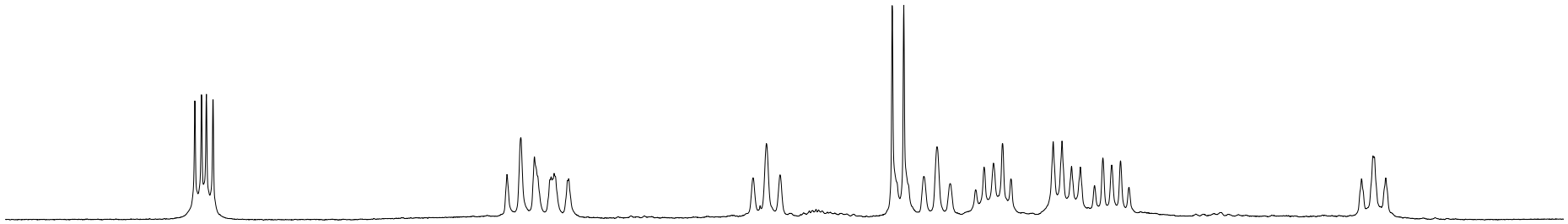
Phostriecin (2). HF–pyr (0.38 mL) in 0.57 mL of THF was added at room temperature to a solution of **31** (11.2 mg, 0.00859 mmol) in THF (0.57 mL) and pyridine (0.14 mL) and was stirred for 4 d in the dark. The reaction mixture was carefully transferred to a gently stirred mixture of saturated aqueous $NaHCO_3$ (9 mL) and EtOAc (3.5 mL) and was stirred until CO_2 evolution ceased. The phases were separated, and the aqueous phase was extracted with EtOAc (5 × 6 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated under vacuum. The crude residue of **32** was dissolved in MeCN (1.6 mL), and Et_3N (0.45 mL) was added at room temperature. The mixture was stirred overnight before toluene (1.9 mL) was added, and the mixture was concentrated under a stream of N_2. H_2O (2.7 mL) was added to the residue, and the mixture was washed with hexanes (5 × 3 mL). The aqueous layer was concentrated under reduced pressure, and the residue was dissolved in 1:1 MeCN/H_2O and passed through a short column of Dowex–Na^+ (2 cm × 1 cm, 1:1 MeCN/H_2O eluent). The product-containing fractions were then concentrated under reduced pressure (the H_2O was azeotoped with MeCN), and the remaining residue was further purified by flash column chromatography (C_{18} reverse phase SiO_2, 0–10% MeCN/H_2O gradient) to give 2.67 mg (63%) of **2** as a white solid: $[\alpha]^{25}_D$ +21 (*c* 0.12, MeOH; lit. $[\alpha]^{24}_D$ +23 (*c* 1.0, MeOH))[5]; ^{1}H NMR (CD_3OD, 600 MHz) δ 7.04 (dd, *J* = 9.6, 5.4 Hz, 1H), 6.60 (t, *J* = 11.4 Hz, 1H), 6.55 (dd, *J* = 15.0, 11.4 Hz, 1H), 6.25 (t, *J* = 11.4 Hz, 1H), 6.06 (d, *J* = 9.6 Hz, 1H), 6.01 (t, *J* = 11.4 Hz, 1H), 5.93 (dt, *J* = 15.6, 7.2 Hz, 1H), 5.82 (dd, *J* = 15.6, 7.2 Hz, 1H), 5.76 (dt, *J* =

[5] Ohkuma, H.; Naruse, N.; Nishiyama, Y.; Tsuno, T.; Hoshino, Y.; Sawada, Y.; Konishi, M.; Oki, T. *J. Antibiot.* **1992**, *45*, 1239.

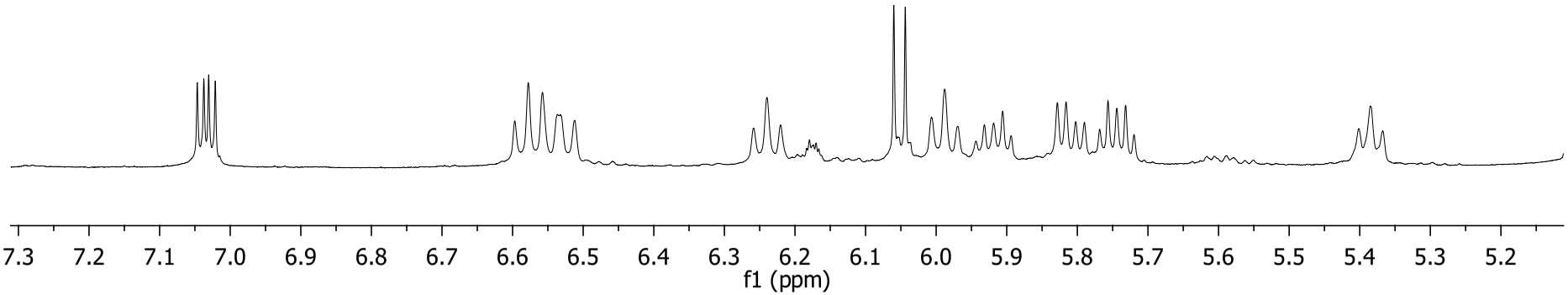
15.0, 7.2 Hz, 1H), 5.39 (dd, *J* = 10.8, 9.6 Hz, 1H), 4.86 (m, 1H), 4.64 (dddd, *J* = 9.6, 7.8, 7.2, 1.8 Hz, 1H), 4.58 (t, *J* = 9.6 Hz, 1H), 4.20 (dd, *J* = 5.4, 3.0 Hz, 1H), 2.67–2.59 (m, 1H), 2.40–2.32 (m, 1H), 2.14 (q, *J* = 7.2 Hz, 1H), 1.57–1.51 (m, 1H), 1.45–1.25 (m, 6H), 0.91 (t, *J* = 7.2 Hz, 3H), 0.82 (d, *J* = 7.2 Hz, 3H); ^{1}H NMR (DMSO-d_6, 600 MHz) δ 6.98 (dd, *J* = 9.6, 5.4 Hz, 1H), 6.55 (dd, *J*= 14.4, 11.1 Hz, 1H), 6.47 (t, *J* = 11.4 Hz, 1H), 6.14 (t, *J* = 11.4 Hz, 1H), 5.98 (t, *J* = 11.1 Hz, 1H), 5.95 (d, *J* = 9.6 Hz, 1H), 5.80–5.72 (m, 2H), 5.63 (dd, *J* = 15.6, 7.2 Hz, 1H), 5.34 (t, *J* = 10.2 Hz, 1H), 4.79 (dd, *J* = 7.2, 3.0 Hz, 1H), 4.49–4.39 (m, 1H), 4.28 (t, *J* = 9.6 Hz, 1H), 4.08 (dd, *J* = 6.0, 3.0 Hz, 1H), 2.35–2.26 (m, 1H), 2.12–2.04 (m, 3H), 1.40–1.32 (m, 2H), 1.32–1.16 (m, 5H), 0.86 (t, *J* = 6.6 Hz, 3H), 0.63 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (CD_3OD, 150 MHz) δ 178.1, 166.3, 147.4, 138.0, 133.77, 133.75, 132.0, 127.9, 126.8, 126.6, 123.6, 122.7, 83.4, 74.21, 74.17, 68.8, 63.7, 44.44, 44.41, 38.2, 34.0, 32.7, 30.2, 23.6, 14.4, 9.2; ^{31}P NMR (CD_3OD, 160 MHz) δ 3.4 (3.4–4.0, condition dependent); IR (film) ν_{max} 3414, 1719, 1662, 1088 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{23}H_{35}O_8P + Na^+$ 493.1962; found 493.1966.

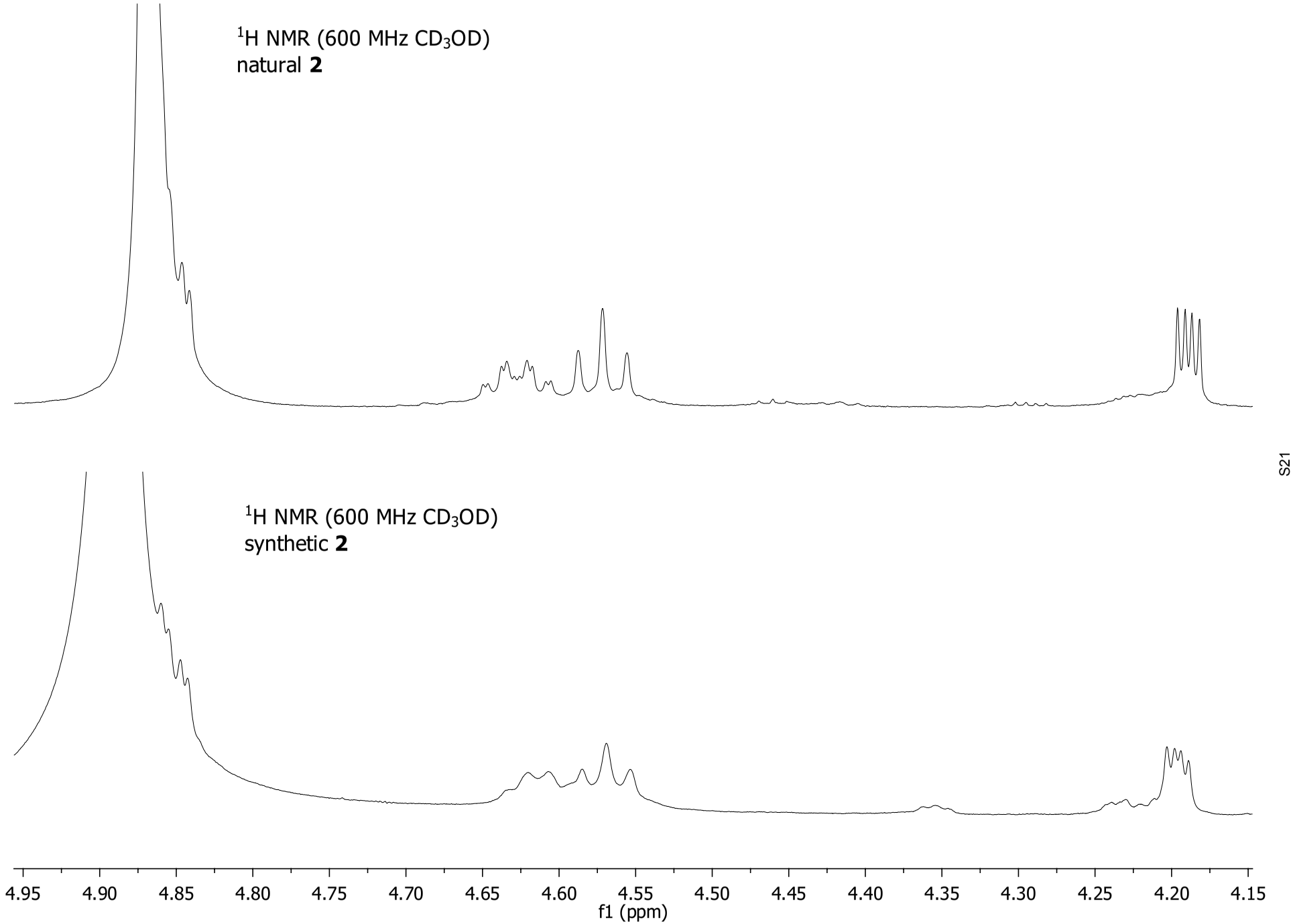

^{1}H NMR (600 MHz CD_3OD)
natural **2**
^{1}H NMR (600 MHz CD_3OD)
synthetic **2**
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

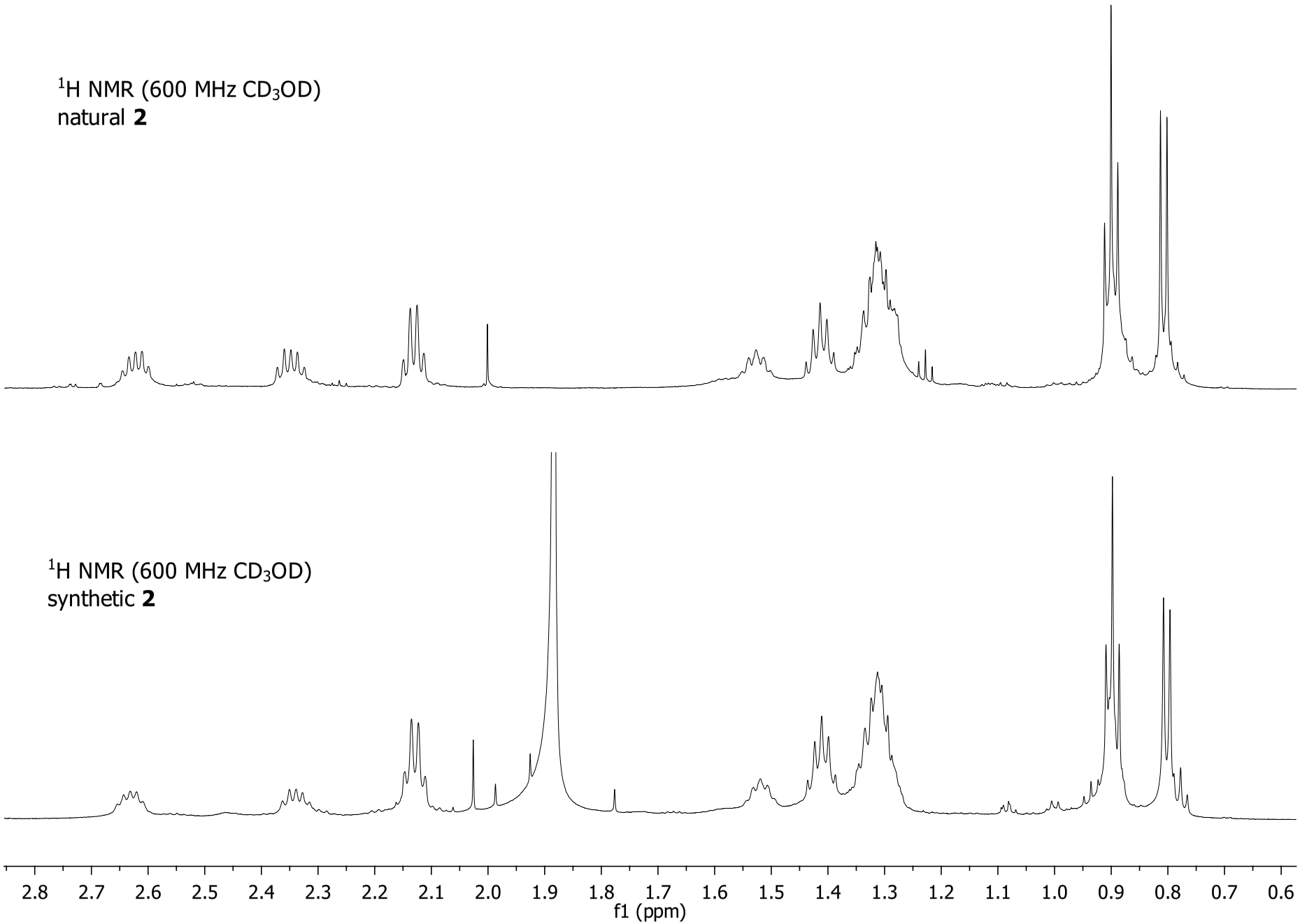
^{1}H NMR (600 MHz CD_3OD)
natural **2**

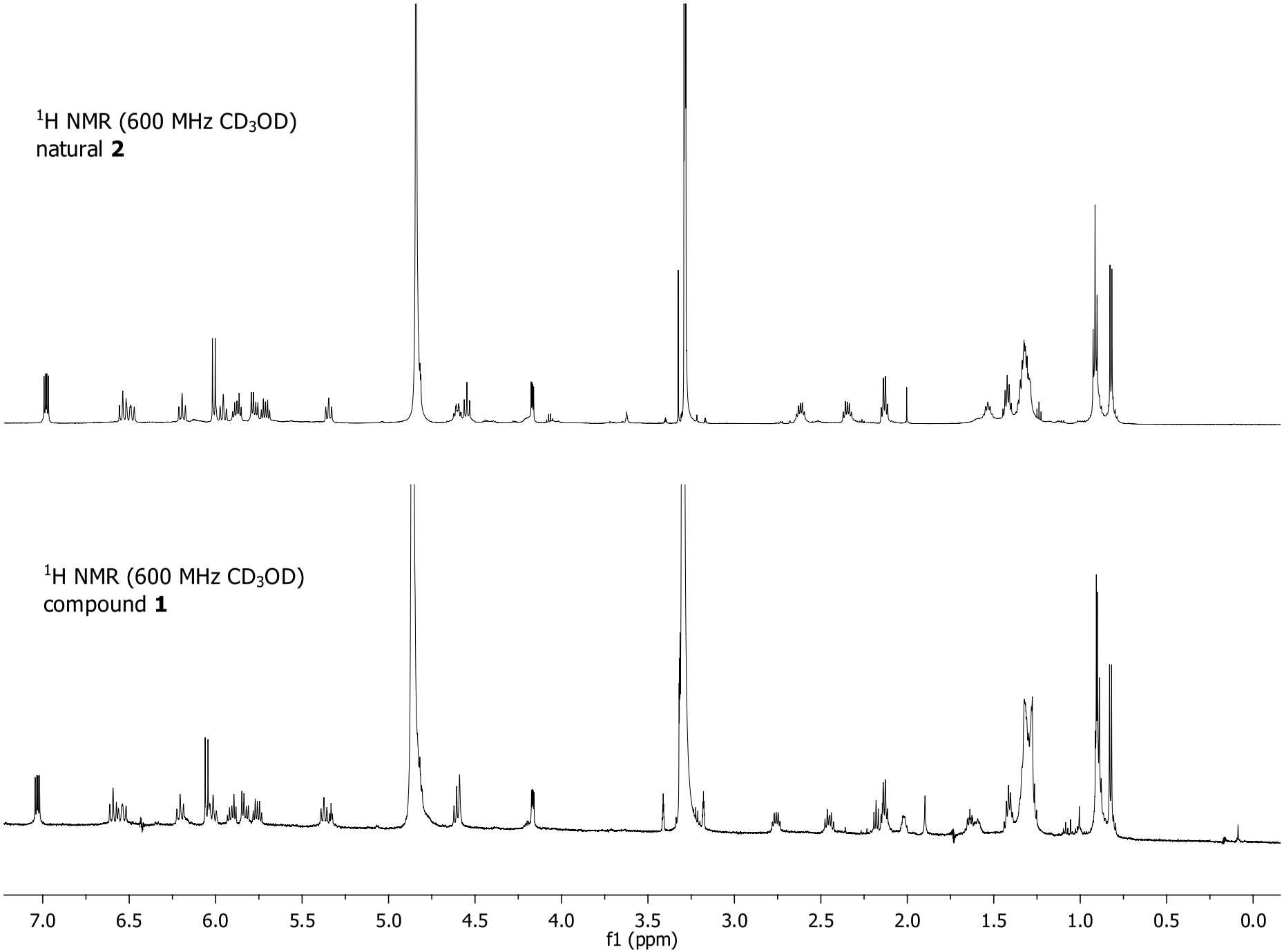


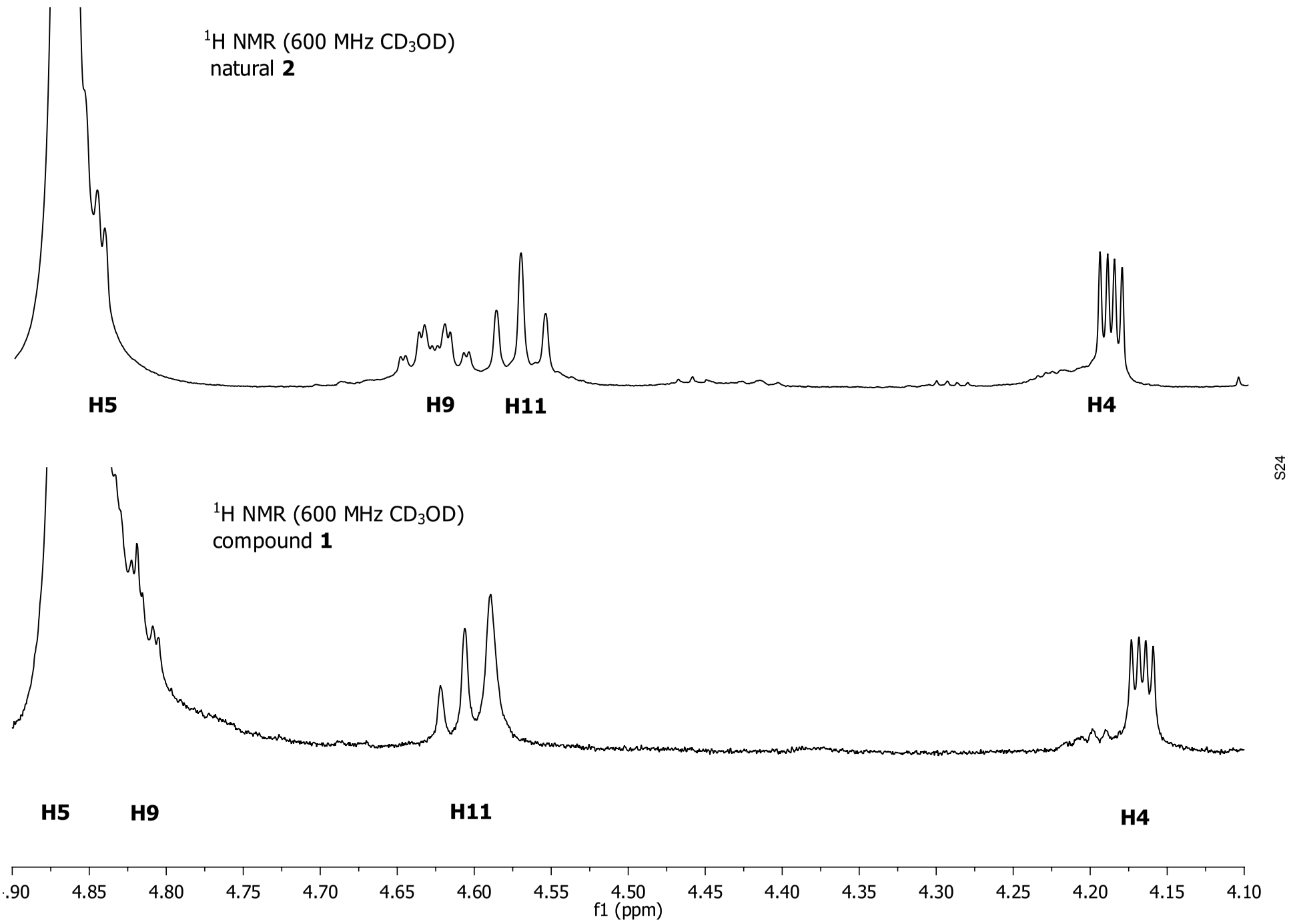
^{1}H NMR (600 MHz CD_3OD)
synthetic **2**



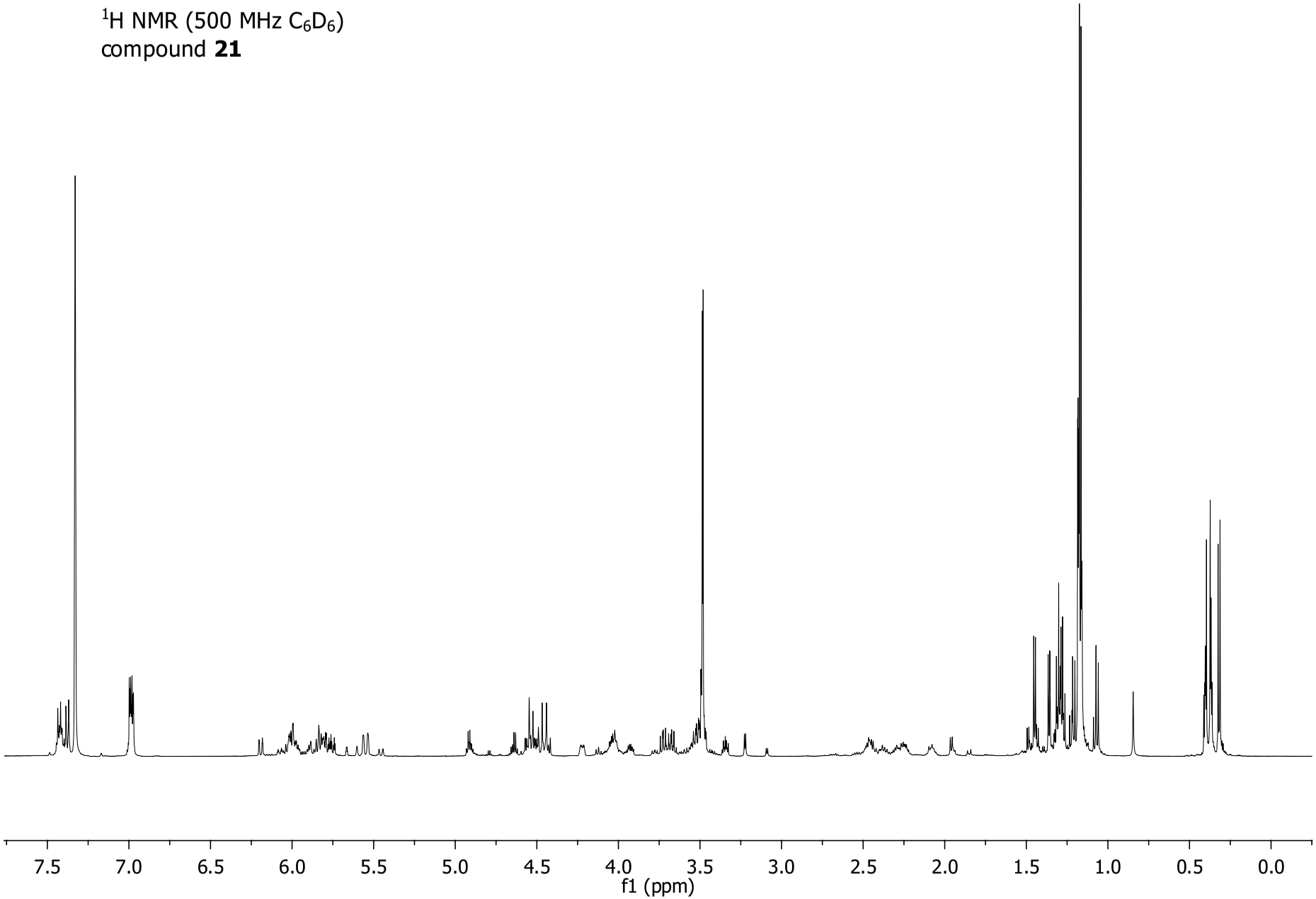

^{1}H NMR (600 MHz CD_3OD)
natural **2**
^{1}H NMR (600 MHz CD_3OD)
synthetic **2**
4.95
4.90
4.85
4.80
4.75
4.70
4.65
4.60
4.55
4.50
4.45
4.40
4.35
4.30
4.25
4.20
4.15
f1 (ppm)


^{1}H NMR (600 MHz CD_3OD)
natural **2**
^{1}H NMR (600 MHz CD_3OD)
synthetic **2**
2.8 2.7 2.6 2.5 2.4 2.3 2.2 2.1 2.0 1.9 1.8 1.7 1.6 1.5 1.4 1.3 1.2 1.1 1.0 0.9 0.8 0.7 0.6
f1 (ppm)


^{1}H NMR (600 MHz CD_3OD)
natural **2**
^{1}H NMR (600 MHz CD_3OD)
compound **1**
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


^{1}H NMR (600 MHz CD_3OD)
natural **2**
H5
H9
H11
H4
^{1}H NMR (600 MHz CD_3OD)
compound **1**
H5
H9
H11
H4
S24
.90 4.85 4.80 4.75 4.70 4.65 4.60 4.55 4.50 4.45 4.40 4.35 4.30 4.25 4.20 4.15 4.10
f1 (ppm)

^{1}H NMR (500 MHz C_6D_6)
compound **21**



S25

^{1}H NMR (500 MHz C_6D_6)
compound **22**