Total Synthesis of Bryostatin 9

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Supporting Information

Contents

General Methods

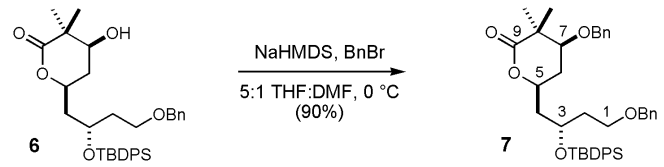
Unless otherwise noted, all reactions were run under a nitrogen atmosphere in flame or oven dried glassware. Reactions were stirred using Teflon-coated magnetic stirrer bars. Reactions were monitored using thin layer silica gel chromatography (TLC) using 0.25 mm silica gel 60F plates with fluorescent indicator from Merck. Plates were visualized by treatment with UV, acidic *p*-anisaldehyde stain, or $KMnO_4$ stain with gentle heating. Products were purified by column chromatography using the solvent systems indicated. Silica gel 60, 230-400 mesh, was purchased from EM.

When necessary, solvents and reagents were purified before use. Tetrahydrofuran (THF) was distilled from sodium benzophenone ketyl under N_2. Ethyl ether (Et_2O) and dichloromethane (CH_2Cl_2) were passed through an alumina drying column (*Solv-Tek Inc.*) using nitrogen pressure. Toluene was dried by either of the aforementioned methods. Anhydrous dimethylformamide (DMF) and dimethyl sufoxide (DMSO) were obtained from Acros Organics. Ethyl acetate (EtOAc), petroleum ether, pentane, hexanes, and methanol (MeOH) were obtained from Fisher Scientific. Powdered 4Å molecular sieves (< 5 micron) were purchased from Aldrich and stored/activated as indicated. Amine bases (Et_3N, pyridine, diisopropylamine) were distilled from CaH_2 under nitrogen. All other reagents were purchased from commercial suppliers (Aldrich, Acros, Strem) and were either used as received without additional purification or were purified using standard methods. Preparative HPLC was carried out using an acetonitrile (MeCN)/H_2O gradient using a Shimadzu Prominence system equipped with a Restek 18 column (5 μm, 21 x 250 mm).

NMR spectra were measured on a Varian INOVA 500 (^{1}H at 500 MHz, ^{13}C at 125 MHz), a Varian 400 (^{1}H at 400 MHz, ^{13}C at 100 MHz), or a Varian INOVA 600 MHz (^{1}H at 500 MHz, ^{13}C at 150 MHz) magnetic resonance spectrometer, as noted. ^{1}H chemical shifts are reported relative to the residual solvent peak (chloroform = 7.26 ppm; benzene = 7.15 ppm; methanol = 3.31 ppm)[1] as follows: chemical shift (δ), (multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, b = broad, *app* = apparent), integration, coupling constant(s) in Hz, proton ID [when available, designated by carbon number]). Proton assignments were made via 2D spectroscopy (COSY, HSQC and/or HMBC) or analogy. ^{13}C chemical shifts are reported relative to the residual deuterated solvent ^{13}C signals ($CDCl_3$ = 77.16 ppm, C_6D_6 = 128.06 ppm)[1]. nOe's are reported in percent, relative to the intensity of the irradiated signal, set at -100%. ROESY enhancements are reported in percent, relative to the enhancement observed for designated geminal protons at 100%. Infrared spectra were recorded on a Perkin-Elmer 1600 Series Fourier transform spectrometer (FTIR) and are reported in wavenumbers (cm^{-1}). Optical rotation data were obtained using a JASCO DIP are reported as $[\boldsymbol{\alpha}]_D^T$ (*c* = grams/100 mL), where D indicates the sodium D line (589 nm) and T indicates temperature (when noted, all optical rotation values were obtained at ambient temperature, ca. 22 – 25 °C). Unless otherwise indicated, optical rotations are the average (± standard deviation) of 10 individual measurements. Optical rotations were not recorded for isomeric mixtures. High resolution mass spectra were obtained at the Vincent Coates Mass Spectrometry Laboratory, Stanford, CA 94305.

[1] Gottlieb, H. E.; Kotlyar, V.; Nudelman, A. *J. Org. Chem.* **1997**, *62*, 7512-7515.

Experimental Procedures and Characterization Data



Procedure for benzyl lactone 7

Hydroxylactone **6** (2.38 g, 4.24 mmol) was dissolved in THF (55 mL) and DMF (11 mL), and the resulting solution was cooled in an ice water bath. Once cold (~20 min), NaHMDS (1.0 M in THF, 4.7 mL, 4.7 mmol) was added dropwise via syringe over 2 min. Benzyl bromide (1.0 mL, 8.5 mmol) was then added dropwise via syringe over 30 s. The reaction was stirred at 0 ºC for 20 min, by which time the mixture was cloudy with salts. The reaction was quenched with 0.2 N HCl (150 mL), and the resulting biphasic mixture was diluted with Et_2O (100 mL). The phases were separated, and the aqueous phase was extracted with Et_2O (100 mL). The organic phase was washed with H_2O (2 x 50 mL) and brine (50 mL), dried over $MgSO_4$, filtered, and concentrated to afford a crude residue. Purification by silica gel chromatography (15 % EtOAc in petroleum ether) gave 2.48 g of lactone **7** (90%) as a colorless oil.

Characterization data for Lactone **7**:

^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.69 (m, 4H), 7.42 (m, 2H), 7.39-7.26 (m, 14H), 4.57 (d, 1H, *J* = 11.8 Hz, C7-OBn), 4.39 (bs, 2H, C1-OBn), 4.35 (d, 1H, *J* = 11.8 Hz, C7-OBn), 4.24 (m, 1H, C3), 4.03 (dddd, 1H, *J* = 3.4, 3.4, 8.7, 12.0 Hz, C5), 3.51 (m, 2H, C1, C1), 3.19 (dd, 1H, *J* = 3.8, 11.2 Hz, C7), 1.90-1.79 (m, 4H, C2, C2, C4, C6), 1.69 (ddd, 1H, *J* = 3.6, 8.3, 14.2 Hz, C4), 1.47 (dt, 1H, *J* = 11.4, 13.3 Hz, C6), 1.24 (s, 3H, C8-CH_3), 1.18 (s, 3H, C8-CH_3), 1.06 (s, 9H, -TBDPS) ppm.

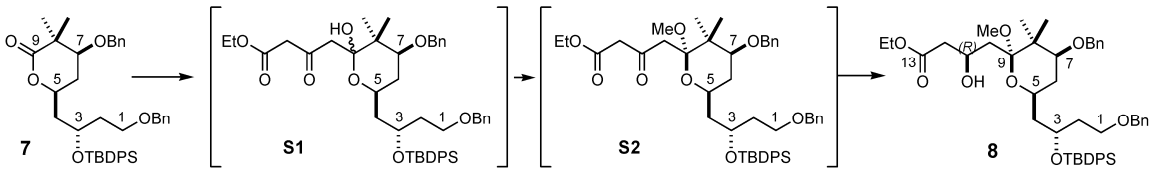
^{13}C NMR ($CDCl_3$, 125 MHz): δ = 176.5, 138.5, 138.1, 136.1, 136.0, 134.2, 133.9, 129.9, 129.8, 128.5, 128.5, 127.9, 127.8, 127.8, 127.7, 127.6, 127.6, 78.7, 73.3, 73.0, 71.4, 67.9, 66.6, 44.4, 44.2, 37.8, 30.8, 27.2, 23.8, 21.3, 19.6 ppm.

IR: 3030, 2932, 2857, 1732, 1454, 1427, 1382, 1361, 1260, 1156, 1110, 1028, 912, 821, 737, 702 cm^{-1}

HRMS (TOF MS ES+): Calculated for $C_{41}H_{50}O_5SiNa^+$: 673.3320; Found: 673.3318.

$[\alpha]_D^{23.2}$ = + 28.5 ± 0.1 ° (*c* 2.72, CH_2Cl_2)

R_f = 0.36 (15% EtOAc in petroleum ether), one grey spot, *p*-anisaldehyde stain.



Procedure for hydroxyester 8

A solution of diisopropylamine (2.56 mL, 18.3 mmol) in THF (50 mL) was cooled in an ice water bath. *n*-BuLi (1.6 M in pentane, 11.4 mL, 18.2 mmol) was added dropwise via syringe over 3 min. The resulting solution was stirred for 10 min and was cooled to –78 ºC in a CO_2/acetone bath. Once cold (~10 min), ethyl acetoacetate (1.14 mL, 9.0 mmol) was added dropwise over 1.5 min, resulting in a pale yellow solution. After stirring for 5 min, this solution was warmed to 0 ºC in an ice water bath. After an additional 7 min, the bright yellow solution was re-cooled in a CO_2/acetone bath to –78 ºC. Once cold (~10 min), lactone **7**

(1.92 g, 2.95 mmol) was added via canula as a solution in THF (10 mL) over 6 min. Three additional washings of THF (1 x 5 mL, 2 x 2.5 mL) were added in the same manner to ensure quantitative transfer. The resulting solution was stirred for 40 min and was then quenched with 0.2 N HCl (50 mL) and allowed to warm to ambient temperature. The resulting biphasic mixture was diluted with Et_2O (100 ml). The layers were separated, and the organic phase was washed with 0.2 N HCl (2 x 50 mL). The combined aqueous phase was acidified with 2 N HCl and was extracted with Et_2O (40 mL). The combined organic phase was dried over $MgSO_4$, filtered, and concentrated to afford crude **S1** as a yellow oil that was used directly in the subsequent step.

The product from the previous step was dissolved in MeOH (85 mL). Pyridinium *para*-toluenesulfonate (PPTS) (890 mg, 3.5 mmol) was added in one portion, and the resulting solution was stirred for 3 h in a 45 ºC oil bath. The reaction was then concentrated to ~30 mL *in vacuo* and was diluted with Et_2O (200 mL) and petroleum ether (100 mL). The mixture was washed with H_2O (100 ml) and brine (100 mL) and was dried over $MgSO_4$. Filtration and concentration provided a crude residue that was purified by silica gel chromatography (12% EtOAc in petroleum ether) to afford 1.96 g of ketoester **S2** (84% over 2 steps).

Ketoester **S2** (1.63 g, 2.05 mmol) was dissolved in absolute EtOH (75 mL) and the resulting solution was cooled via NaCl:ice slush to –20 ºC. Once cold (~10 min), $NaBH_4$ (1.24 g, 32.8 mmol) was added in one portion. The reaction was stirred for 5 min and was moved to a freezer at –15 ºC. After standing 15 h, the reaction mixture was carefully quenched into a stirred biphasic mixture of Et_2O (200 mL) and saturated NH_4Cl (100 mL). The resulting mixture was diluted with 0.1 N HCl (100 mL), H_2O (100 mL), and petroleum ether (100 mL). The layers were separated, and the organic layer was washed with 0.1 N HCl (100 mL), H_2O (100 mL), and brine (100 mL). The combined organic phase was dried over $MgSO_4$, filtered, and concentrated to afford a crude residue that was passed through a short silica gel column (15% EtOAc in petroleum ether) to afford 1.43 g of a diastereomeric mixture (78:22 *R*:*S*) of hydroxyesters (88% combined yield). This mixture was purified by silica gel chromatography (11 → 13% EtOAc in petroleum ether) to provide 990 mg of C11-(*R*)-hydroxyester **8** (61%) as a colorless oil.

Characterization data for C11-(R)-hydroxyester **8**:

^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.66 (m, 4H), 7.43-7.25 (m, 16H), 4.48 (d, 1H, *J* = 11.7 Hz, C7-OBn), 4.39 (s, 2H, C1-OBn), 4.36 (m, 1H, C11), 4.33 (d, 1H, *J* = 11.7 Hz, C7-OBn), 4.14 (m, 2H, C13-OEt), 4.02 (m, 1H, C3), 3.57-3.50 (m, 3H, C1, C1, C7), 3.49 (d, 1H, *J* = 1.2 Hz, C11-OH), 3.45 (dddd, 1H, *J* = 3.0, 6.2, 6.2, 12.1 Hz, C5), 3.00 (s, 3H, C9-OMe), 2.50 (dd, 1H, *J* = 6.4, 15.4 Hz, C12), 2.33 (dd, 1H, *J* = 7.0, 15.4 Hz, C12), 1.90 (dd, 1H, *J* = 10.2, 15.6 Hz, C10), 1.85-1.78 (m, 3H, C2, C2, C4), 1.76 (dd, 1H, *J* = 1.6, 15.6 Hz, C10), 1.54 (dt, 1H, *J* = 5.5, 13.8 Hz, C4), 1.48 (ddd, 1H, *J* = 3.0, 4.6, 12.8 Hz, C6), 1.26 (t, 3H, *J* = 7.2 Hz, C13-OEt), 1.04 (s, 9H, -TBDPS), 0.98 (m, 1H, C6), 0.94 (s, 3H, C8-CH_3), 0.89 (s, 3H, C8-CH_3) ppm.

^{13}C NMR ($CDCl_3$, 125 MHz): δ = 171.7, 139.4, 138.6, 136.0, 136.0, 134.3, 134.2, 129.8, 129.8, 128.4, 128.3, 127.7[2], 127.7, 127.5, 127.4, 127.3, 104.7, 78.0, 73.0, 71.5, 69.0, 66.9, 66.8, 65.9, 60.6, 48.8, 44.2, 43.1, 42.0, 39.5, 37.5, 32.7, 27.1, 20.6, 19.4, 17.3, 14.3 ppm.

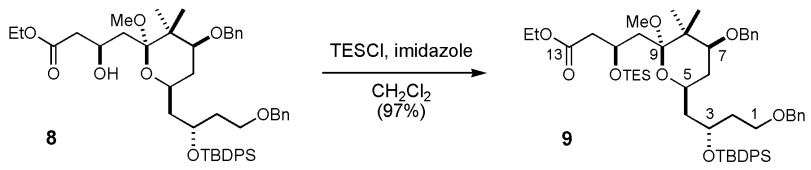
IR: 3543, 3030, 2943, 2857, 1732, 1454, 1427, 1362, 1256, 1157, 1104, 1026, 945, 822, 737, 702 cm^{-1}

HRMS (TOF MS ES+): Calculated for $C_{48}H_{64}O_8SiNa^+$: 819.4263; Found: 819.4273.

$[\alpha]_D^{23.0}$ = + 41.1 ± 0.2 ° (*c* 0.987, CH_2Cl_2)

R_f = 0.35 (20 % EtOAc in petroleum ether), one purple spot, *p*-anisaldehyde stain.

[2] Two aryl signals fail to resolve at this resonance.



Procedure for silyl ether 9

Hydroxyester **8** (243 mg, 0.305 mmol) was dissolved in CH_2Cl_2 under ambient atmosphere. Imidazole (100 mg, 1.47 mmol) was added in one portion. Once all solids had dissolved, TES-Cl (67 µL, 1.3 mmol) was added in one portion. The resulting solution was stirred for 2 h at ambient temperature and was then loaded directly onto a silica gel column, eluting with 2 → 5% EtOAc in pentane to afford 271 mg of triethylsilyl ether **9** (97%) as a clear, colorless oil.

Characterization data for silyl ether **9:**

^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.69 (m, 4H), 7.47-7.26 (m, 16H), 4.51 (d, 1H, *J* = 11.8 Hz, C7-OBn), 4.41 (s, 2H, C1-Bn), 4.36 (d, 1H, *J* = 11.8 Hz, C7-OBn), 4.31 (dddd, 1H, *J* = 4.0, 4.0, 8.2, 12.1 Hz, C11), 4.11 (m, 2H, C13-OEt), 4.00 (p, 1H, *J* = 5.7 Hz, C3), 3.55 (m, 2H, C1, C1), 3.50 (dd, 1H, *J* = 4.7, 11.6 Hz, C7), 3.34 (dddd, 1H, *J* = 2.8, 6.1, 6.1, 12.0 Hz, C5), 2.84 (s, 3H, C9-OMe), 2.78 (dd, 1H, *J* = 3.7, 14.8 Hz, C12), 2.33 (dd, 1H, *J* = 7.9, 14.8 Hz, C12), 1.92-1.74 (m, 5H, C2, C2, C4, C10, C10), 1.59 (dt, 1H, *J* = 5.7, 13.9 Hz, C4), 1.48 (ddd, 1H, *J* = 2.9, 4.5, 12.6 Hz, C6), 1.27 (t, 3H, *J* = 7.2 Hz, C13-OEt), 1.06 (s, 9H, -TBDPS), 1.02 (m, 1H, C6), 1.01 (s, 3H, C8-CH_3), 0.97 (s, 3H, C8-CH_3), 0.96 (t, 9H, *J* = 7.9 Hz, -TES), 0.61 (m, 6H, -TES) ppm.

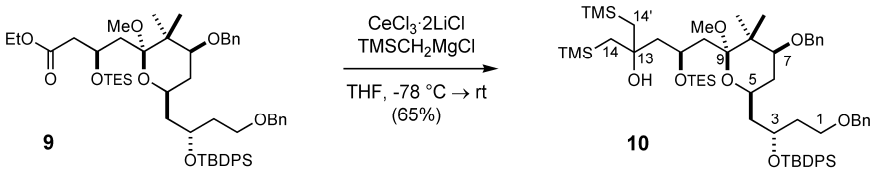
^{13}C NMR ($CDCl_3$, 125 MHz): δ = 172.0, 139.5, 138.6, 136.0, 136.0, 134.3, 134.2, 129.8[3], 128.4, 128.3, 127.7, 127.7, 127.6, 127.5, 127.3, 127.3, 103.8, 78.5, 72.9, 71.4, 69.0, 67.1, 66.9, 66.4, 60.2, 47.7, 44.6, 44.2, 43.5, 39.3, 37.7, 32.6, 27.1, 20.8, 19.4, 16.9, 14.3, 7.0, 5.1 ppm.

IR: 3031, 2953, 2876, 1737, 1455, 1428, 1361, 1316, 1239, 1171, 1110, 1067, 1028, 821, 737, 702 cm^{-1}

HRMS (TOF MS ES+): Calculated for $C_{54}H_{78}O_8Si_2Na^+$: 933.5127; Found: 933.5127.

$[\alpha]_D^{23.2}$ = + 26.5 ± 0.3 ° (*c* 0.888, CH_2Cl_2)

$\mathbf{R}_f$ = 0.30 (5 % EtOAc in petroleum ether), one magenta/red spot, *p*-anisaldehyde stain



Procedure for tertiary alcohol 10

Preparation of the Grignard reagent

Magnesium metal granules (235 mg, 9.6 mmol) were stirred in Et_2O (7.0 mL) in a 2-neck flask fitted with a reflux condenser and rubber septum. $TMSCH_2Cl$ (1.1 mL, 7.9 mmol) was added in one portion. The mixture was stirred vigorously and heated briefly to reflux, at which time the reaction initiated and active heating was discontinued. As the reaction proceeded, its exothermicity maintained a gentle reflux. After reflux ceased (10-15 min), the grey, turbid mixture was stirred for an additional 15 min. Solids were

[3] Two aryl signals fail to resolve at this chemical shift.

allowed to settle for ~2 h, affording a clear, grey supernatant that was used on the same day as its preparation (maximum titre of $TMSCH_2MgCl$ = 0.94 M).

To a N_2-purged Schlenk flask was added a solution of $CeCl_3 \cdot 2LiCl$[4] (~0.33 M in THF, 11.2 mL, 3.70 mmol). The bronze solution was cooled in a CO_2/acetone bath for 5 min and $TMSCH_2MgCl$ (0.94 M in Et_2O, 3.9 mL, 3.7 mmol) was added dropwise over 3 min, resulting in a tan suspension. This mixture was stirred at −78 ºC for 70 min, at which time ester **9** (337 mg, 0.370 mmol) was added by canula as a solution in THF (4 mL) over 4 min. Additional portions of THF (2 x 2 mL) were used to ensure complete transfer. The reaction mixture was then warmed to ambient temperature and stirred for 70 h. The reaction was quenched with saturated aqueous sodium potassium tartrate solution (30 mL) and the biphasic mixture was stirred vigorously for 1 h to afford a yellow aqueous layer. The mixture was diluted with EtOAc (50 mL) and H_2O (50 mL), and the layers were separated. The aqueous phase was extracted with EtOAc (2 x 100 mL), and the combined organic phase was dried over $MgSO_4$, filtered, and concentrated to afford a crude residue. Purification by silica gel chromatography (4% → 10% EtOAc in petroleum ether) gave 249 mg of tertiary alcohol **10** (65%) as a colorless oil.

Characterization data for tertiary alcohol **10**:

^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.67 (m, 4H), 7.41 (m, 2H), 7.38-7.23 (m, 14H), 4.43 (dd, 1H, *J* = 11.7 Hz, C7-OBn), 4.38 (s, 2H, C1-OBn), 4.29 (m, 1H, C11), 4.28 (dd, 1H, *J* = 11.7 Hz, C7-OBn), 4.09 (s, 1H, C13-OH), 3.90 (m, 1H, C3), 3.56 (m, 2H, C1, C1), 3.44 (dd, 1H, *J* = 4.7, 11.6 Hz, C7), 3.26 (m, 1H, C5), 2.95 (s, 3H, C9-OMe), 2.06 (dd, 1H, *J* = 2.1, 14.2 Hz, C12[5]), 1.89 (dd, 1H, *J* = 2.6, 15.2 Hz, C10[6]), 1.86-1.70 (m, 4H, C2, C2, C4, C10[6]), 1.62 (dd, 1H, *J* = 9.8, 14.4 Hz, C12[5]), 1.56 (ddd, 1H, *J* = 4.4, 8.9, 13.3 Hz, C4), 1.43 (ddd, 1H, *J* = 2.9, 4.5, 12.7 Hz, C6), 1.23 (d, 1H, *J* = 14.5 Hz, C14), 1.12 (d, 1H, *J* = 14.6 Hz, C14'), 1.04 (s, 9H, -TBDPS), 0.98 (s, 3H, C8-Me), 0.98 (t, 9H, *J* = 7.9 Hz, -TES), 0.97 (m, 1H, C14'), 0.94 (s, 3H, C8-Me), 0.83 (d, 1H, *J* = 14.5 Hz, C14), 0.82 (ddd, 1H, *J* = 12.3, 12.3, 12.3 Hz, C6), 0.67 (q, 6H, *J* = 7.9 Hz, -TES), 0.09 (s, 9H, -TMS), 0.08 (s, 9H, -TMS) ppm.

^{13}C NMR ($CDCl_3$, 125 MHz): δ = 139.5, 138.6, 136.1, 134.2, 134.2, 129.9, 129.8, 128.4, 128.3, 127.7, 127.7, 127.7, 127.6, 127.4, 127.3, 104.1, 78.4, 75.9, 73.1, 71.2, 69.8, 68.4, 66.8, 66.5, 52.4, 48.0, 43.9, 43.7, 40.8, 37.2, 34.8, 32.0, 31.6, 27.2, 20.9, 19.5, 17.1, 7.1, 5.9, 1.2, 1.1 ppm.

IR: 3501, 3069, 3031, 2952, 2878, 1455, 1427, 1361, 1245, 1110, 1029, 1004, 916, 837, 738, 700 cm^{-1}

HRMS (TOF MS ES+): Calculated for $C_{60}H_{96}O_7Si_4Na^+$: 1063.6125; Found: 1063.6119.

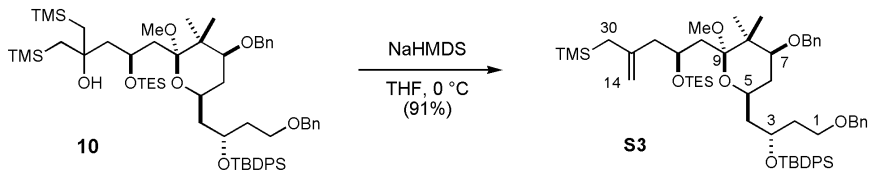
$[\alpha]_D^{24.0}$ = + 12.6 ± 0.2 ° (*c* 1.53, CH_2Cl_2)

R_f = 0.47 (7 % EtOAc in petroleum ether), one purple spot, *p*-anisaldehyde stain.

[4] Krasovskiy, A.; Kopp, F.; Knochel, P. "Soluble Lanthanide Salts ($LnCl_3 \cdot 2LiCl$) for the Improved Addition of Organomagnesium Reagents to Carbonyl Compounds" *Angew. Chem. Int. Ed.* **2006**, *45*, 497-500.

[5] Or C10, the assignment of these protons is ambiguous

[6] Or C12, the assignment of these protons is ambiguous



Procedure for allylsilane S3

Tertiary alcohol **10** (420 mg, 0.40 mmol) was dissolved in THF (8 mL) and the solution was cooled in an ice water bath. Once cold (~10 min), NaHMDS (1.0 M, 500 µL, 0.050 mmol) was added as a solution in THF over 30 s. The reaction was stirred for 40 min and was quenched with saturated aqueous NH_4Cl (5 mL). The biphasic mixture was diluted with Et_2O (10 mL) and H_2O (10 mL), and the layers were separated. The aqueous layer was extracted with Et_2O (2 x 20 mL), and the combined organic phase was dried over $MgSO_4$, filtered, and concentrated to afford a crude residue. Purification by silica gel chromatography (4% Et_2O in petroleum ether) gave 350 mg of allylsilane **S3** (91%) as a colorless oil.

Characterization data for allylsilane **S3**:

^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.67 (m, 4H), 7.40 (m, 2H), 7.36-7.24 (m, 14H), 4.63 (m, 1H, C14), 4.56 (m, 1H, C14), 4.45 (d, 1H, *J* = 11.7 Hz, C7-OBn), 4.38 (s, 2H, C1-OBn), 4.31 (d, 1H, *J* = 11.7 Hz, C7-OBn), 4.12 (m, 1H, C11), 3.94 (m, 1H, C3), 3.55 (m, 2H, C1, C1), 3.46 (dd, 1H, *J* = 4.6, 11.6 Hz, C7), 3.29 (m, 1H, C5), 2.91 (s, 3H, C9-OMe), 2.16 (dd, 1H, *J* = 7.0, 13.3 Hz, C12), 2.05 (dd, 1H, *J* = 5.9, 13.3 Hz, C12), 1.91-1.74 (m, 5H, C2, C2, C4, C10, C10), 1.58 (ddd, 1H, *J* = 4.4, 7.4, 13.5 Hz, C4), 1.50 (bs, 2H, C30, C30), 1.43 (ddd, 1H, *J* = 2.7, 4.5, 12.6 Hz, C6), 1.03 (s, 9H, -TBDPS), 1.01 (s, 3H, C8-CH_3), 0.95 (t, 9H, *J* = 8.0 Hz, -TES), 0.91 (m, 1H, C6), 0.89 (s, 3H, C8-CH_3), 0.59 (q, 6H, *J* = 8.0 Hz, -TES), 0.03 (s, 9H, -$SiMe_3$) ppm.

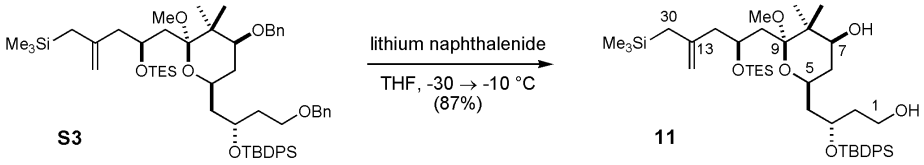
^{13}C NMR ($CDCl_3$, 125 MHz): δ = 144.6, 139.6, 138.7, 136.1, 136.1, 134.4, 134.3, 129.8, 129.7, 128.4, 128.3, 127.7, 127.7[7], 127.6, 127.3, 127.3, 110.5, 104.3, 78.9, 73.0, 71.4, 69.0, 68.6, 67.0, 66.1, 48.5, 48.1, 44.2, 43.2, 39.9, 37.4, 32.4, 27.5, 27.2, 21.1, 19.5, 17.1, 7.2, 5.6, -1.3 ppm.

IR: 3069, 2952, 2875, 1631, 1454, 1427, 1361, 1247, 1104, 1007, 854, 736, 700 cm^{-1}

HRMS (TOF MS ES+): Calculated for $C_{57}H_{86}O_6Si_3Na^+$: 973.5624; Found: 973.5659.

$[\alpha]_D^{23.0}$ = + 23.1 ± 0.4 ° (*c* 0.845, CH_2Cl_2)

R_f = 0.20 (5 % EtOAc in petroleum ether), one red spot, *p*-anisaldehyde stain



Procedure for diol 11

Preparation of the lithium naphthalenide reagent

Naphthalene (2.33 g, 18.2 mmol) and high-sodium lithium granules (104 mg, 15 mmol) were added to a dry Schlenk flask. The flask was purged twice with N_2, and freshly distilled THF (12.5 mL) was added via syringe. Sonication for 1 h yielded the lithium naphthalenide reagent (ca. 1 M) as a thick, deep green solution in which no pieces of unreacted Li metal were visible. The solution was stirred at room

[7] Two aryl signals fail to resolve at this chemical shift.

temperature for an additional hour and was stored in at −15 ºC until use. When stored this way, no appreciable loss in activity was observed over the course of several months.

A solution of the lithium naphthalenide reagent (ca. 1 M in THF, 8.75 mL, 8.75 mmol) was cooled in a CO_2/MeCN bath maintained at –30 ºC. Bis-benzyl ether **S3** (81 mg, 0.085 mmol) was added as a solution in THF (1 mL) via canula over 30 s. Two additional portions of THF (1 mL each) were added in the same manner to ensure quantitative transfer. The resulting deep green solution was stirred for 30 min, by which time the cold bath had reached –10 ºC. The reaction was stirred for an additional 30 min, maintaining the cold bath at –10 ºC by periodic addition of CO_2. The reaction was then quenched with saturated aqueous NH_4Cl (15 mL), and the resulting colorless biphasic mixture was diluted with Et_2O (50 mL) and H_2O (20 mL). The layers were separated, and the aqueous layer was extracted with Et_2O (20 mL). The combined organic phase was dried over $MgSO_4$, filtered, and concentrated to afford a crude solid that was purified by silica gel chromatography (5 → 15 → 30% EtOAc in pentane) to afford 34.2 mg of clean diol **11** and 25.5 mg of a slightly impure product. Re-purification of the impure material by silica gel chromatography (15 → 30% EtOAc in pentane) gave an additional 22.6 mg of diol **11** (87% total yield) as a white solid.

Characterization data for diol **11:**

^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.69 (m, 4H, -TBDPS), 7.44 (m, 2H, -TBDPS), 7.39 (m, 4H, -TBDPS), 4.63 (m, 1H, C14), 4.58 (m, 1H, C14), 4.11 (m, 1H), 3.99 (m, 1H), 3.83 (ddd, 1H, *J* = 4.2, 8.6, 11.2 Hz), 3.73 (dd, 1H, *J* = 4.8, 11.5 Hz), 3.72 (m, 1H), 3.23 (m, 1H), 2.93 (s, 3H), 2.28 (bs, 1H), 2.10 (dd, 1H, *J* = 7.4, 13.2 Hz), 2.07 (dd, 1H, *J* = 5.6, 13.2 Hz), 1.97-1.87 (m, 2H), 1.84 (dd, 1H, *J* = 4.2, 15.9 Hz), 1.75 (dd, 1H, *J* = 6.9, 15.9 Hz), 1.72-1.64 (m, 2H), 1.55 (ddd, 1H, *J* = 3.9, 7.1, 13.7 Hz), 1.50 (m, 2H), 1.24 (ddd, 1H, *J* = 2.8, 4.6, 12.4 Hz), 1.06 (s, 9H, -TBDPS), 0.97 (s, 3H, C8-Me), 0.95 (t, 9H, *J* = 7.9 Hz), 0.87 (q, 1H, *J* = 12.0 Hz), 0.79 (s, 3H, C8-Me), 0.59 (q, 6H, *J* = 7.9 Hz), 0.03 (s, 9H) ppm.

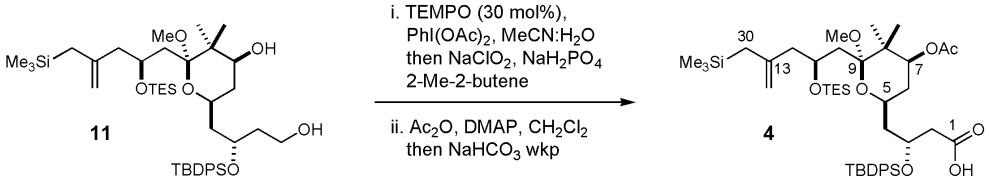
^{13}C NMR ($CDCl_3$, 125 MHz): δ = 144.6, 136.1, 136.0, 133.8, 133.7, 130.0, 130.0, 127.9, 127.8, 110.5, 104.3, 71.0, 70.7, 68.6, 66.0, 59.7, 48.5, 48.2, 43.1, 42.8, 40.0, 38.3, 35.6, 27.5, 27.1, 20.7, 19.3, 15.9, 7.2, 5.6, -1.3 ppm.

IR: 3401, 3071, 2953, 2878, 1632, 1471, 1427, 1385, 1361, 1298, 1248, 1187, 1147, 1110, 1072, 1007, 853, 822, 739, 702, 612 cm^{-1}

HRMS (TOF MS ES+): Calculated for $C_{43}H_{74}O_6Si_3Na^+$: 793.4685; Found: 793.4669.

$[\alpha]_D^{25.9} = -1.00 \pm 0.07°$ (*c* 3.42, CH_2Cl_2)

R_f = 0.37 (30 % EtOAc in petroleum ether), one magenta spot, *p*-anisaldehyde stain



Procedure for carboxylic acid northern fragment 4

To a solution of diol **11** (56 mg, 0.073 mmol) in MeCN (3.9 mL) was added H_2O (615 µL). TEMPO (3.2 mg, 0.020 mmol) and $PhI(OAc)_2$ (70.1 mg, 0.218 mmol) were added in one portion. The resulting mixture was stirred vigorously at ambient temperature for 80 min, at which time 2-methyl-2-butene (1.0 mL), H_2O (400 µL) and NaH_2PO_4 (87 mg, 0.73 mmol) were added. The resulting mixture was cooled in an ice water bath. Once cold (~10 min), $NaClO_2$ (80% tech. grade, 52 mg, 0.58 mmol) was added in one

portion, inducing a red color. The biphasic mixture was stirred vigorously for 30 min, at which time additional $NaClO_2$ (16 mg, 0.18 mmol) was added in one portion. The reaction was stirred an additional 15 min, at which time it was quenched by the addition of saturated aqueous $Na_2S_2O_3$ (5 mL). The resulting mixture was diluted with Et_2O (20 mL) and brine (10 mL), and the phases were separated. The aqueous phase was extracted with Et_2O (2 x 15 mL), and the combined organic phase was dried over Na_2SO_4. Filtration and concentration gave a crude residue that was used directly in the following step.

The crude product (max. 0.073 mmol) from the previous step was dissolved in CH_2Cl_2 (600 µL). DMAP (107 mg, 0.88 mmol) was added in one portion, and the resulting solution was cooled in an ice water bath. Once cold (~10 min), acetic anhydride (68 µL, 0.72 mmol) was added in one portion. After 15 min, the reaction was quenched by the addition of saturated aqueous $NaHCO_3$ (600 µL). The biphasic mixture was removed from the ice water bath and was vigorously stirred at room temperature for 18 h. The mixture was diluted with Et_2O (10 mL) and saturated aqueous NH_4Cl (10 ml). The layers were separated, and the aqueous phase was extracted with Et_2O (2 x 10 mL). The combined organic phase was dried over $MgSO_4$, filtered, and concentrated to provide a crude residue that was purified by silica gel chromatography (15 → 25% EtOAc in pentane) to afford 34.5 mg acid **4** (57 % over 2 steps) as a colorless residue.

Characterization data for carboxylic acid **4**:

^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.67 (m, 4H, -TBDPS), 7.42 (m, 6H, -TBDPS), 4.95 (dd, 1H, *J* = 4.8, 11.8 Hz, C7), 4.62 (bs, 1H, C14), 4.58 (bs, 1H, C14), 4.11 (m, 2H, C3, C11), 3.25 (dddd, 1H, *J* = 2.7, 6.5, 6.5, 12.3 Hz, C5), 2.94 (s, 3H, C9-OMe), 2.68 (dd, 1H, *J* = 4.2, 15.3 Hz, C2), 2.54 (dd, 1H, *J* = 6.2, 15.3 Hz, C2), 2.11 (dd, 1H, *J* = 5.0, 13.1 Hz, C12), 2.05 (dd, 1H, *J* = 8.0, 13.1 Hz, C12), 2.01 (s, 3H, C7-OAc), 1.85 (m, 2H, C4, C10), 1.72 (dd, 1H, *J* = 7.6, 16.1 Hz, C10), 1.56 (ddd, 1H, *J* = 3.5, 6.3, 13.9 Hz, C4), 1.51 (d, 1H, *J* = 13.2 Hz, C30), 1.46 (d, 1H, *J* = 13.2 Hz, C30), 1.30 (ddd, 1H, *J* = 2.6, 4.6, 12.2 Hz, C6), 1.03 (s, 9H, -TBDPS), 0.94 (t, 9H, *J* = 8.0 Hz, -TES), 0.93 (m, 1H, C6), 0.88 (s, 3H, C8-CH_3), 0.88 (s, 3H, C8-CH_3), 0.57 (q, 6H, *J* = 8.0 Hz, -TES), 0.02 (s, 9H, -$SiMe_3$) ppm.

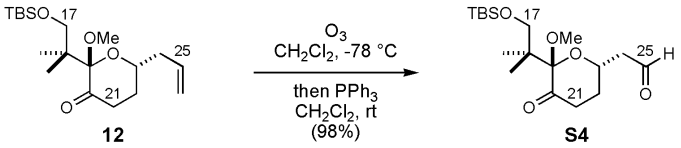
^{13}C NMR ($CDCl_3$, 125 MHz): δ = 176.2, 170.8, 144.3, 136.0, 136.0, 133.8, 133.2, 130.0, 129.9, 127.8, 127.8, 110.7, 104.4, 74.0, 68.9, 68.3, 65.5, 48.6, 48.3, 43.4, 42.5, 41.9, 39.7, 32.6, 27.4, 27.0, 21.4, 20.9, 19.4, 17.2, 7.2, 5.6, -1.3 ppm.

IR: 3072, 2954, 1742, 1713, 1428, 1366, 1246, 1111, 1081, 1018, 854, 739, 702 cm^{-1}

HRMS (TOF MS ES+): Calculated for $C_{45}H_{74}O_8Si_3Na^+$: 849.4584; Found: 849.4567.

$[\alpha]_D^{23.2}$ = + 19.7 ± 0.4 ° (*c* 0.60, CH_2Cl_2)

R_f = 0.45 (30 % EtOAc in petroleum ether), one blue streak, *p*-anisaldehyde stain



Procedure for ketoaldehyde S4

A solution of olefin **12** (825 mg, 2.30 mmol) in CH_2Cl_2 (50 mL) was cooled under ambient atmosphere to −78 ºC in a CO_2/acetone bath. O_3 was bubbled through this solution via glass pipet at a rate of 1.5 LPM until a faint blue color developed. The mixture was stirred for 5 min while TLC analysis indicated complete consumption of starting material. N_2 was bubbled through the solution until the blue color dissipated, and PPh_3 (780 mg, 3.0 mmol) was added in one portion. The mixture was stirred at ambient temperature for 2.5 h, and additional PPh_3 (780 mg, 3.0 mmol) was added in one portion. The resulting solution was stirred for

1.75 h and was concentrated *in vacuo*. The resulting crude yellow residue was dissolved in $PhCH_3$ and loaded onto a slurry-packed (10% EtOAc in petroleum ether) silica gel column. Elution with 10 → 35 % EtOAc in petroleum ether gave 814 mg of aldehyde **S4** (98%) a viscous yellow oil.

Characterization data for ketoaldehdye **S4**:

^{1}H NMR (C_6D_6, 400 MHz): δ = 9.40 (dd, 1H, *J* = 1.4, 2.4 Hz, C25), 3.91 (dddd, 1H, *J* = 2.4, 4.3, 7.9, 10.6 Hz, C23), 3.76 (d, 1H, *J* = 9.8 Hz, C17), 3.51 (d, 1H, *J* = 9.8 Hz, C17), 3.12 (s, 3H, C19-OMe), 2.34 (ddd, 1H, *J* = 2.7, 6.6, 18.0 Hz, C21), 2.14 (ddd, 1H, *J* = 2.5, 8.0, 16.5 Hz, C24), 2.00 (ddd, 1H, *J* = 7.4, 11.2, 18.0 Hz, C21), 1.82 (ddd, 1H, *J* = 1.4, 4.3, 16.5 Hz, C24), 1.47 (dddd, 1H, *J* = 6.6, 11.2, 11.2, 20.0 Hz, C22), 1.23 (s, 3H, C18-Me), 1.22 (m, 1H, C22), 1.07 (s, 3H, C18-Me), 0.92 (s, 9H, -OTBS), 0.02 (s, 3H, -OTBS), 0.00 (s, 3H, -OTBS) ppm.

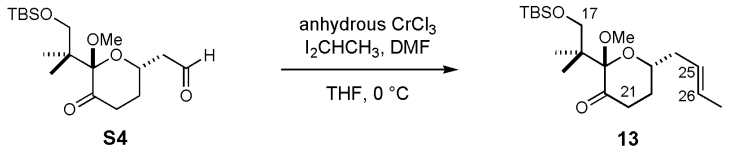
^{13}C NMR ($CDCl_3$, 100 MHz): δ = 204.0, 198.6, 103.8, 69.3, 68.6, 52.2, 49.2, 46.0, 37.8, 29.2, 26.2, 20.6, 20.2, 18.7, -5.3, -5.4 ppm.

IR: 2954, 2931, 2888, 2857, 1727, 1471, 1392, 1361, 1254, 1187, 1117, 1091, 1048, 963, 942, 837, 777, 669 cm^{-1}

HRMS (TOF MS ES+): Calculated for $C_{18}H_{34}O_5SiNa^+$: 381.2068; Found: 381.2072.

$[\alpha]_D$ = + 1.5 ± 0.3 ° (*c* 1.55, CH_2Cl_2)

R_f = 0.67 (30% EtOAc in petroleum ether), one streaky grey spot, *p*-anisaldehyde stain.



Procedure for olefin 13

In a glovebox, anhydrous $CrCl_2$ (2.69 g, 21.9 mmol) was added to a dry round-bottomed flask containing a Teflon-coated stirbar. The flask was sealed with a septum cap, removed from the glovebox, and fitted with a N_2 inlet. Anhydrous THF (25 mL) was added, and the resulting light green suspension was stirred at ambient temperature for 10 min to achieve an even consistency. The flask was cooled to 0 ºC in an ice water bath. After 10 min, diiodoethane[8] (1.8 g, 6.4 mmol) was added dropwise over 30 s. Aldehyde **S4** (775 mg, 2.16 mmol) was then added via canula as a solution in anhydrous THF (5 mL) over 3 min. Two additional portions of THF (2.5 mL each) were used to ensure complete transfer. After 5 min, DMF (1.7 mL, 21.9 mmol) was added dropwise in three roughly equal portions. As DMF was added, the reaction darkened in color and some aggregation of solids was observed. The mixture was stirred vigorously at 0 ºC for 2.5 h, and was diluted with H_2O (100 mL) and petroleum ether (100 mL). The resulting dark green emulsion was partially separated, and brine (25 mL) was used to aid layer separation. The aqueous phase was extracted twice with petroleum ether (75 mL each), again using brine to aid layer separation. The combined organic phase was dried over $MgSO_4$, filtered through a short pad of celite, and concentrated *in vacuo*. The resulting crude residue was purified by silica gel chromatography (0 → 4 → 6% EtOAc in petroleum ether) to afford 607 mg of olefin **13** (76%) as a yellow oil. The C25/C26-*E*:*Z* ratio was determined by ^{1}H NMR analysis to be of 92.5:7.5.

[8] Prepared from acetaldehyde via iodination of its hydrazone, see: Friedrich, E. C.; Falling, S. N.; Lyons, D. E. "A Convenient Synthesis of Ethylidine Iodide" *Syn. Comm.* **1975**, *5*, 33-36. For an alternative preparation, see: Letsinger, R. L.; Kammeyer, C. W. "The Preparation of Ethylidene Iodide" *J. Am. Chem. Soc.* **1951**, *73*, 4476.

Characterization data for C25/C26-*E* -olefin **13**:

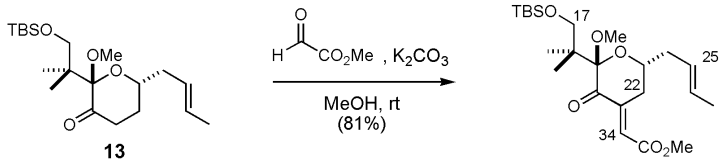
^{1}H NMR (C_6D_6, 600 MHz): δ = 5.48-5.36 (m, 2H, C25, C26), 3.90 (d, 1H, *J* = 9.8 Hz, C17), 3.64 (d, 1H, *J* = 9.8 Hz, C17), 3.57 (dddd, 1H, *J* = 2.5, 5.9, 5.9, 10.9 Hz, C23), 3.14 (s, 3H, C19-OMe), 2.40 (ddd, 1H, *J* = 3.0, 6.8, 17.8 Hz, C21), 2.17 (m, 1H, C24), 2.09-2.01 (m, 2H, C21, C24), 1.65-1.56 (m, 1H, C22), 1.59 (m, 3H, C27), 1.38-1.33 (m, 1H, C22), 1.33 (s, 3H, C18-Me), 1.20 (s, 3H, C18-Me), 0.95 (s, 9H, -OTBS), 0.05 (s, 3H, -OTBS), 0.04 (s, 3H, -OTBS).

^{13}C NMR ($CDCl_3$, 125 MHz): δ = 205.0, 128.0, 127.1, 103.8, 73.7, 68.6, 52.0, 46.0, 39.3, 38.0, 28.7, 26.2, 20.6, 20.4, 18.7, 18.2, -5.3, -5.4 ppm.

IR: 1954, 2931, 2857, 1725, 1471, 1392, 1361, 1254, 1186, 1116, 1090, 1052, 1005, 966, 836, 776, 668 cm^{-1}

HRMS (TOF MS ES+): Calculated for $C_{20}H_{38}O_4SiNa^+$: 393.2432; Found: 393.2427.

R_f = 0.38 (5% EtOAc in petroleum ether), one red spot, *p*-anisaldehyde stain.



Procedure for enone S5

To a solution of ketone **13** (435 mg, 1.17 mmol, ~92.5:7.5 C25/C26-*E:Z*) in anhydrous MeOH (10.6 mL) was added a solution of methyl glyoxylate in THF[9] (ca. 2 M, 3.5 mL, 7.0 mmol). K_2CO_3 (970 mg, 7.0 mmol) was added in one portion, and the resulting suspension was stirred for 35 min at ambient temperature. The orange mixture was poured into saturated aqueous NH_4Cl (20 mL), and the resulting biphasic mixture was diluted with 1:1 Et_2O:petroleum ether (20 mL). The phases were separated, and the aqueous phase was extracted with 1:1 Et_2O:petroleum ether (2 x 20 mL) and once with petroleum ether (20 mL). The combined organic phase was dried over $MgSO_4$, filtered and concentrated. The resulting crude residue was purified by silica gel chromatography (10% Et_2O in petroleum ether) to afford 420 mg of enone **S5** (81%) as a bright yellow oil. The C25/C26-*E*:*Z* ratio was determined by ^{1}H NMR analysis to be 92:8; these isomers were found to be inseparable by standard chromatographic means.

Characterization data for C25/C26-*E* enone **S5**:

^{1}H NMR (C_6D_6, 400 MHz): δ = 6.94 (dd, 1H, *J* = 1.4, 3.3 Hz, C34), 5.53-5.34 (m, 2H, C25, C26), 3.91 (d, 1H, *J* = 9.8 Hz, C17), 3.65 (dddd, 1H, *J* = 1.9, 5.7, 5.7, 12.3 Hz, C23), 3.53 (d, 1H, *J* = 9.8 Hz, C17), 3.52 (ddd, 1H, *J* = 1.7, 1.7, 17.9 Hz, C22), 3.31 (s, 3H, -CO_2Me), 3.13 (s, 3H, C19-OMe), 2.81 (ddd, 1H, *J* = 3.3, 12.5, 17.9 Hz, C22), 2.13 (m, 2H, C24, C24), 1.55 (m, 3H, C27), 1.29 (s, 3H, C18-Me), 1.16 (s, 3H, C18-Me), 0.91 (s, 9H, -OTBS), 0.02 (s, 3H, -OTBS), 0.00 (s, 3H, -OTBS) ppm.

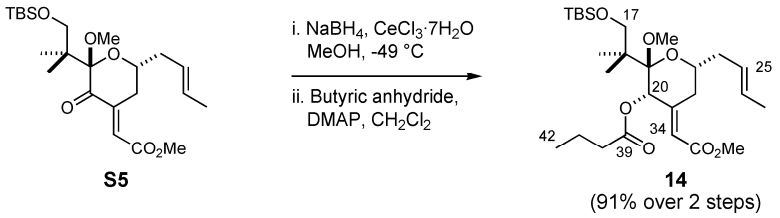
^{13}C NMR ($CDCl_3$, 125 MHz): δ = 196.3, 166.5, 147.9, 129.0, 125.7, 122.5, 103.9, 72.5, 68.2, 51.9, 51.8, 46.5, 38.6, 34.1, 26.0, 20.0, 19.6, 18.6, 18.1, -5.5, -5.6 ppm.

IR: 2953, 2931, 2857, 1726, 1709, 1631, 1471, 1435, 1359, 1253, 1204, 1175, 1128, 1040, 1063, 1007, 967, 937, 837, 779 cm^{-1}

HRMS (TOF MS ES+): Calculated for $C_{23}H_{40}O_6SiNa^+$: 463.2486; Found: 463.2473.

R_f = 0.44 (7% EtOAc in petroleum ether), one red spot, *p*-anisaldehyde stain.

[9] Kelly, T. R.; Schmidt, T. E.; Haggerty, J. G. "A Convenient Preparation of Methyl and Ethyl Glyoxylate" *Synthesis*, **1972**, *1972*, 544-545.



Procedure for ester 14

To a solution of enone **S5** (87.4 mg, 0.198 mmol, ~8% C25/C26 *Z*-olefin) in MeOH (2.7 mL) was added $CeCl_3 \cdot 7H_2O$ (72 mg, 0.19 mmol). The mixture was stirred at ambient temperature until all solids dissolved, and the resulting solution was cooled in a CO_2/MeCN bath to −49 ºC (ext. temperature). Once cold (~10 min), $NaBH_4$ (32.8 mg, 0.867 mmol) was added in one portion. The mixture was stirred for 14 min and was then carefully quenched with saturated aqueous NH_4Cl (2 mL). The mixture was diluted with Et_2O (10 mL), petroleum ether (10 mL), sat. NH_4Cl (10 mL), and H_2O (10 mL). The phases were separated, and the aqueous phase was extracted with 1:1 Et_2O:petroleum ether (20 mL). The combined organic phase was dried over $MgSO_4$, filtered and concentrated to a crude residue that was used directly in the next step.

The crude residue from the previous step (max. 0.198 mmol) was dissolved in CH_2Cl_2 (1.9 mL). DMAP was added in one portion (74 mg, 0.61 mmol) and, once all solids had dissolved, butyric anhydride (49 μL, 0.30 mmol) was added in one portion. The reaction was stirred for 18 h and was then concentrated under a stream of N_2. The crude residue was loaded directly onto a slurry-packed silica gel column, and elution with 5% EtOAc in petroleum ether provided 93 mg of butyrate ester **14** (91% over 2 steps) as a clear, colorless residue. HNMR demonstrated a ~92:8 *E*:*Z* mixture of olefin isomers.

Characterization data for C25/C26-*E* butyrate ester **14**:

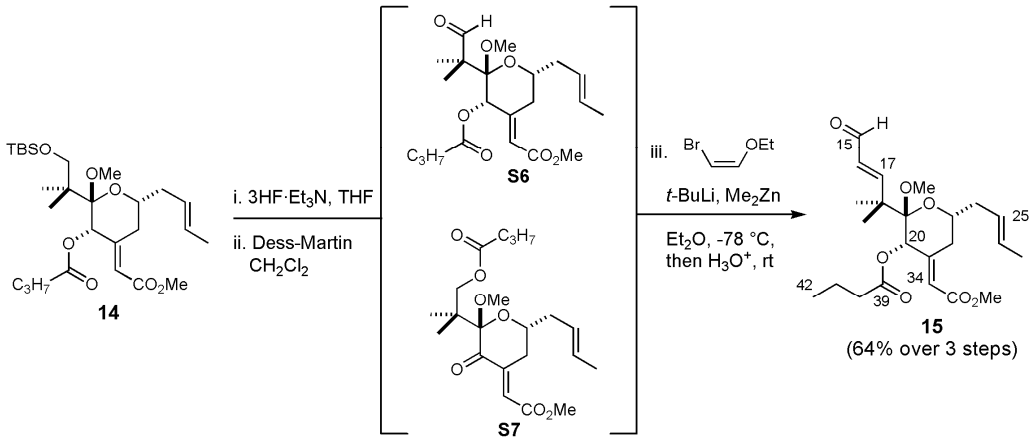
^{1}H NMR (C_6D_6, 600 MHz): δ = 6.18 (m, 1H, C34), 5.96 (s, 1H, C20), 5.46 (m, 1H), 5.39 (m, 1H), 3.87 (d, 1H, *J* = 9.4 Hz, C17), 3.82 (d, 1H, *J* = 9.4 Hz, C17), 3.71 (m, 1H, C23), 3.49 (bd, 1H, *J* = 17.0 Hz, C22), 3.35 (s, 3H, -OMe), 3.17 (s, 3H, -OMe), 2.65 (dd, 1H, *J* = 12.1, 17.0 Hz, C22), 2.18-2.01 (m, 4H), 1.56 (m, 3H), 1.55-1.47 (m, 2H), 1.30 (s, 3H), 1.26 (s, 3H), 0.98 (s, 9H, -TBS), 0.75 (t, 3H, *J* = 7.5 Hz, C42), 0.09 (s, 3H, -TBS), 0.08 (s, 3H, -TBS) ppm.

^{13}C NMR (C_6D_6, 125 MHz): δ = 171.4, 166.4, 154.6, 128.4, 126.5, 115.8, 103.3, 71.6, 71.4, 67.9, 50.7, 50.4, 47.8, 39.0, 36.3, 33.7, 26.2, 21.0, 20.9, 18.7, 18.5, 18.2, 13.7, -5.2, -5.2 ppm.

IR: 2954, 2857, 1747, 1722, 1666, 1467, 1435, 1389, 1361, 1252, 1220, 1157, 1080, 836, 776 cm^{-1}

HRMS (TOF MS ES+): Calculated for $C_{27}H_{48}O_7SiNa^+$: 535.3062; Found: 535.3052.

R_f = 0.58 (15 % EtOAc in petroleum ether), one blue spot, *p*-anisaldehyde stain



Procedure for enal 15

In a polypropylene vial, silyl ether **14** (93 mg, 0.18 mmol) was dissolved in THF (1.8 mL). 3HF·Et_3N (400 µL) was added dropwise via syringe over 1 min. The reaction mixture was stirred at ambient temperature for 20.5 h and was quenched by its dropwise addition to a stirred mixture of saturated aqueous $NaHCO_3$ (35 mL) and Et_2O (20 mL). The resulting biphasic mixture was diluted with Et_2O (10 mL) and saturated $NaHCO_3$ (10 mL). The organic and aqueous phases were separated, and the aqueous phase was extracted with Et_2O (2 x 30 mL). The combined organic phase was dried over $MgSO_4$, filtered, and concentrated to afford a crude product that was used immediately in the following step.

The crude residue from the previous step (max. 0.18 mmol) was dissolved in CH_2Cl_2 (3.5 mL). Dess-Martin periodinane was added (187 mg, 0.44 mmol) in one portion. The cloudy white suspension was stirred at ambient temperature for 30 min and was then quenched by the addition of saturated aqueous $Na_2S_2O_3$ (5 mL). The mixture was stirred for 5 min until all solids dissolved and was diluted with Et_2O (20 mL), brine (5 mL), and saturated aqueous $NaHCO_3$ (5 mL). The phases were separated, and the cloudy white aqueous layer was extracted with Et_2O (2 x 20 mL). The combined organic phase was dried over $MgSO_4$, filtered, and concentrated to afford a crude residue. Purification by silica gel chromatography (8% EtOAc in petroleum ether) gave 56.8 mg of desired aldehyde product **S6** contaminated with 4.5 mol % of **S7**, the oxidation product derived from C20 → C17 acyl migration in the previous step. This mixture was used directly in the following step.

A solution of *cis*-1-bromo-2-ethyoxyethylene (85% technical grade, 86 µL, 0.74 mmol) in Et_2O (3.0 mL) was cooled to −78 ºC in a CO_2/acetone bath. Once cold (~10 min), *t*-BuLi (1.6 M in pentane, 870 µL, 1.4 mmol) was added dropwise via syringe over 1 min. After 20 min, Me_2Zn (1.2 M in $PhCH_3$, 620 µL, 0.74 mmol) was added dropwise via syringe over 1 min. After an additional 30 min, the mixture's appearance was cloudy white and aldehyde **S6** (72 mg, 0.18 mmol, contaminated with 4.5 mol % **S7**) was added as a solution in Et_2O (1.0 mL) via canula. Two additional portions of Et_2O (1.0 mL each) were used to ensure complete transfer. The resulting yellow-colored reaction was stirred for 100 min and was quenched with 1 N HCl (4.5 mL, 4.5 mmol). The resulting biphasic mixture was warmed to ambient temperature and was vigorously stirred for 20 h. The mixture was then diluted with Et_2O (20 mL) and H_2O (20 mL), and the phases were separated. The aqueous phase was extracted with Et_2O (2 x 20 mL), and the combined organic phase was dried over $MgSO_4$, filtered, and concentrated. Purification of the crude residue by silica gel chromatography (10% EtOAc in hexanes) gave 63.2 mg of enal **15** as a colorless residue (82%; 64% over three steps from **14**). HNMR demonstrated a ~92:8 *E*:*Z* mixture of C25/C26-olefin isomers that was inseparable using standard chromatographic means.

Characterization data for C25/C26-*E* enal **15**:

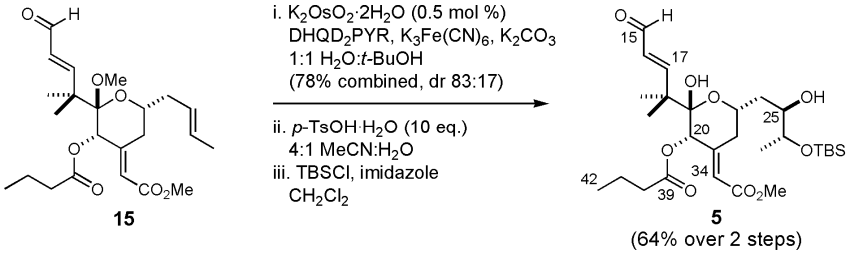
^{1}H NMR (C_6D_6, 500 MHz): δ = 9.5 (d, 1H, *J* = 7.6 Hz, C15), 7.17 (d, 1H, *J* = 16.1 Hz, C17), 6.11 (m, 1H, C34), 5.94 (dd, 1H, *J* = 7.6, 16.1 Hz, C16), 5.69 (s, 1H, C20), 5.46-5.35 (m, 2H, C25, C26), 3.58 (m, 2H, C22, C23), 3.32 (s, 3H, -OMe), 3.04 (s, 3H, -OMe), 2.50 (dd, 1H, *J* = 12.5, 16.3 Hz, C22), 2.17-2.04 (m, 2H, C24, C24), 1.93-1.81 (m, 2H, C40, C40), 1.56 (bd, 3H, C27), 1.46-1.36 (m, 2H, C41, C41), 1.02 (s, 3H), 0.98 (s, 3H), 0.72 (t, 3H, *J* = 7.4 Hz, C42) ppm.

^{13}C NMR (C_6D_6, 125 MHz): δ = 193.3, 171.3, 166.3, 165.5, 153.1, 128.7, 127.6, 126.2, 117.1, 102.8, 72.1, 71.0, 50.8, 50.7, 47.5, 38.9, 36.1, 32.7, 23.3, 22.2, 18.3, 18.1, 13.5 ppm.

IR: 2967, 1745, 1720, 1688, 1627, 1460, 1436, 1382, 1362, 1302, 1250, 1219, 1159, 1103, 1079, 1042, 970, 940, 912, 881 cm^{-1}

HRMS (TOF MS ES+): Calculated for $C_{23}H_{34}O_7Na^+$: 445.2197; Found: 445.2195.

R_f = 0.35 (15% EtOAc in petroleum ether), one black spot, *p*-anisaldehyde stain.



Procedure for southern fragment 5

Preparation of the dihydroxylation reagent mixture

Potassium osmate dihydrate (2.5 mg, 0.0068 mmol), $(DHQD)_2PYR$ (16 mg, 0.018 mmol), K_2CO_3 (700 mg, 5.1 mmol) and $K_3Fe(CN)_6$ (1.67 g, 5.1 mmol) were dissolved in H_2O (8.4 mL) and *t*-BuOH (8.4 mL). The resulting yellow/orange biphasic mixture (ca. 0.35 mM in osmium) was stirred vigorously at ambient temperature for 2 h prior to use.

Neat olefin **15** (65.3 mg, 0.155 mmol as a 92:8 mixture of *E*:*Z* C25/C26 olefin isomers) was isolated in a glass vial and was cooled in an ice water bath. An aliquot of the dihydroxylation reagent mixture (2.1 mL, ca. 0.5 mol % osmium) was added in one portion and the resulting biphasic mixture was allowed to stir in the ice water bath for 5 min, effecting precipitation of orange salts. The heterogeneous mixture was then moved to a cold room at 4 °C and was stirred vigorously for 23 h. The reaction mixture was then diluted with H_2O (25 mL) and EtOAc (25 mL). The phases were separated, and the yellow aqueous phase was extracted with EtOAc (2 x 25 mL). The combined organic phase was dried over Na_2SO_4, filtered, and concentrated. Purification by flash chromatography (15 → 70 → 100% EtOAc in pentane) gave 55.2 mg of an inseparable mixture of (*R,R*) and (*S,S*) diols (d.r. 83:17) as a colorless residue (78% combined yield).

The diol mixture (55.2 mg, 0.12 mmol) from the previous step was dissolved in 4:1 MeCN:H_2O (12 mL). *p*-TsOH·H_2O (236 mg, 1.24 mmol) was added in one portion. The resulting solution was stirred at ambient temperature for 45 h and was then diluted with EtOAc (30 mL), saturated $NaHCO_3$ (30 mL), and H_2O (5 mL). The phases were separated, and the aqueous phase was extracted with EtOAc (2 x 30 mL). The combined organic phase was dried over Na_2SO_4, filtered, and concentrated to afford a crude hemiketal product that was used directly in the subsequent step.

The crude product (ca. 0.12 mmol) from the previous step was dissolved in CH_2Cl_2 (370 µL). Imidazole (34.5 mg, 0.51 mmol) was added in one portion. Once all solids had dissolved, a solution of TBS-Cl (1.0 M in CH_2Cl_2, 180 µL, 0.18 mmol) was added in one portion via syringe. The reaction was stirred at ambient temperature for 6 h, by which time the mixture was turbid with salts. The reaction was diluted with Et_2O (1.5 mL) and saturated aqueous NH_4Cl (1.5 mL). The phases were separated, and the aqueous phase was extracted with Et_2O (4 x 1.5 mL). The combined organic phase was dried over $MgSO_4$, filtered, and concentrated. Purification by flash chromatography (27 → 32% EtOAc in hexanes) gave 43.1 mg of recognition domain **5** as a single diastereomer (64% over two steps; 50% over three steps. Yields not adjusted for starting material diastereomeric/geometric ratios).

Characterization data for southern fragment **5**:

^{1}H NMR (C_6D_6, 500 MHz): δ = 9.60 (d, 1H, *J* = 7.6 Hz, C15), 7.37 (d, 1H, *J* = 16.1 Hz, C17), 6.30 (d, 1H, *J* = 1.7 Hz, C34), 6.00 (dd, 1H, *J* = 7.7, 16.1 Hz, C16), 5.45 (s, 1H, C20), 4.74 (s, 1H, C19-OH), 4.44 (tt, 1H, *J* = 2.1, 11.0 Hz, C23), 4.07 (dd, 1H, *J* = 2.0, 13.9 Hz, C22), 3.87 (m, 1H, C25), 3.59 (dq, 1H, *J* = 4.5, 6.2 Hz, C26), 3.40 (bs, 1H, C25-OH), 3.34 (s, 3H, -OMe), 2.30 (ddd, 1H, *J* = 1.7, 11.7, 14.0 Hz, C22), 1.88 (m, 2H, C40, C40), 1.73 (ddd, 1H, *J* = 1.7, 10.9, 13.7 Hz, C24), 1.59 (ddd, 1H, *J* = 2.1, 11.1, 13.7 Hz, C24), 1.41 (m, 2H, C41, C41), 1.13 (s, 3H, C18-Me), 1.11 (s, 3H, C18-Me), 1.08 (d, 3H, *J* = 6.2 Hz, C27), 0.93 (s, 9H, -TBS), 0.72 (t, 3H, *J* = 7.4 Hz, C42), 0.03 (s, 3H, -TBS), 0.02 (s, 3H, -TBS) ppm.

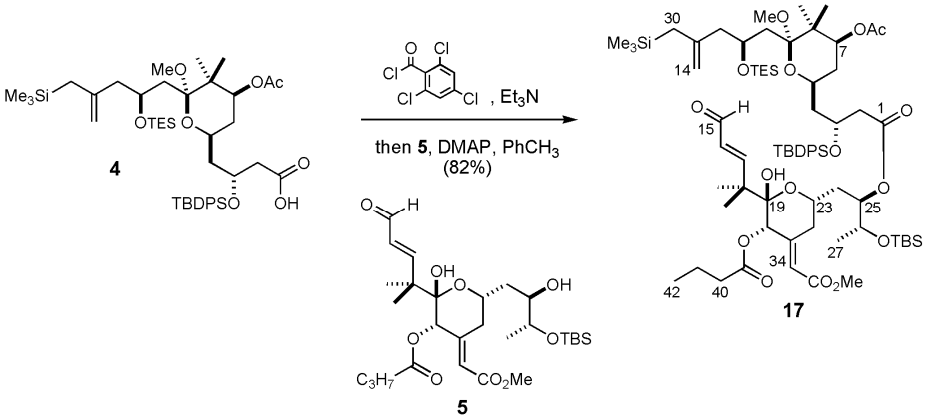
^{13}C NMR (C_6D_6, 125 MHz): δ = 193.6, 171.3, 166.5, 165.3, 151.1, 128.3, 121.1, 100.3, 73.2, 71.8, 71.8, 67.4, 51.0, 46.0, 39.1, 36.4, 31.9, 26.0, 23.3, 20.3, 19.4, 18.3, 18.3, 13.4, -4.3, -4.7 ppm.

IR: 3427 (broad), 2954, 2884, 2858, 1744, 1722, 1688, 1627, 1468, 1436, 1382, 1293, 1253, 1158, 1082, 994, 943, 878, 836, 777 cm^{-1}

HRMS (TOF MS ES+): Calculated for $C_{28}H_{48}O_9SiNa^+$: 579.2960; Found: 579.2956.

$[\alpha]_D^{23.5} = -46.29 \pm 0.08$ ° (*c* 4.31, CH_2Cl_2)

R_f = 0.33 (40 % EtOAc in petroleum ether), one purple spot, *p*-anisaldehyde stain



Procedure for macrocyclization precursor 17

Carboxylic acid **4** (34 mg, 0.041 mmol) was dissolved in $PhCH_3$ (1.5 mL). Triethylamine (35 µL, 0.25 mmol) was added in one portion followed by 2,4,6-trichlorobenzoyl chloride (10.3 µL, 0.062 mmol). The resulting solution was stirred at ambient temperature for 4.5 hr, by which time the mixture was turbid with salts. Alcohol **5** (23.5 mg, 0.042 mmol) and DMAP (14.8 mg, 0.121 mmol) were added as a solution in $PhCH_3$ (0.50 mL) in one portion via canula. Two additional washings of $PhCH_3$ (0.50 mL each) were used to ensure quantitative transfer. The resulting mixture was stirred for 30 min and was then loaded directly

onto a slurry-packed (12% EtOAc in pentane) silica gel column. Elution with 12% → 15% EtOAc in pentane provided 45.8 mg of ester **17** (82%) as a clear, colorless residue.

Characterization data for macrocyclization precursor **17**:

^{1}H NMR ($CDCl_3$, 600 MHz): δ = 9.55 (d, 1H, *J* = 7.8 Hz, C15), 7.66 (m, 4H, -TBDPS), 7.44 (d, 1H, *J* = 16.1 Hz, C17), 7.42-7.33 (m, 6H, -TBDPS), 6.00 (d, 1H, *J* = 1.7 Hz, C34), 5.95 (dd, 1H, *J* = 7.8, 16.1 Hz, C16), 5.17 (*app*-dd, 1H, *J* = 4.3, 10.7 Hz, C25), 5.12 (s, 1H, C20), 4.93 (dd, 1H, *J* = 4.8, 11.7 Hz, C7), 4.61 (bs, 1H, C14), 4.56 (bs, 1H, C14), 4.12 (m, 2H), 3.86 (dq, 1H, *J* = 4.4, 6.3 Hz, C26), 3.78 (m, 1H), 3.66 (m, 1H, C22), 3.64 (s, 3H, -CO_2Me), 3.32 (m, 1H), 3.14 (s, 1H, C19-OH), 2.94 (s, 3H, C9-OMe), 2.57-2.48 (m, 2H, C2, C2), 2.12-2.03 (m, 4H, C12, C12, C22, C40), 2.01 (s, 3H, C7-OAc), 2.02-1.96 (m, 2H, C24, C40), 1.85-1.79 (m, 2H, C4, C10), 1.75-1.64 (m, 2H, C10, C24), 1.56-1.45 (m, 5H, C4, C30, C30, C41, C41), 1.28 (m, 1H, C6), 1.20 (s, 3H, -CH_3), 1.16 (s, 3H, -CH_3), 1.13 (d, 3H, *J* = 6.3 Hz, C27), 0.98 (s, 9H), 0.93 (t, 9H, *J* = 8.0 Hz, -TES), 0.91 (s, 9H), 0.88 (s, 3H, -CH_3), 0.86 (s, 3H, -CH_3), 0.85 (t, 3H, *J* = 7.4 Hz, C42), 0.84 (m, 1H, C6), 0.56 (q, 6H, *J* = 8.0 Hz, -TES), 0.07 (s, 3H, -TBS), 0.06 (s, 3H, -TBS), 0.03 (s, 9H, -$SiMe_3$) ppm.

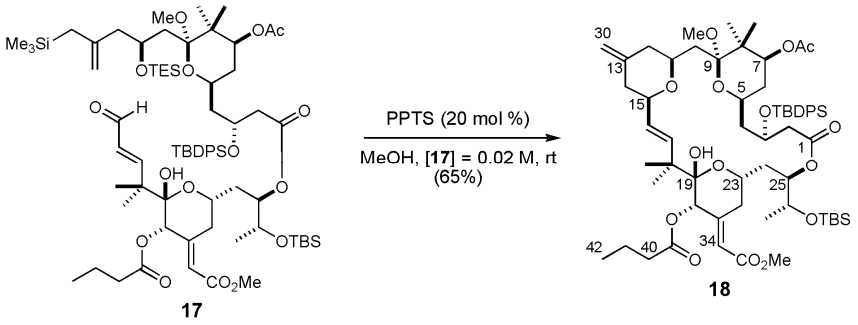
^{13}C NMR ($CDCl_3$, 125 MHz): δ = 194.9, 172.3, 171.7, 170.8, 167.0, 166.5, 150.8, 144.3, 136.1, 135.9, 134.0, 133.3, 130.0, 129.8, 127.8, 127.7, 127.4, 120.9, 110.7, 104.3, 99.6, 74.1, 73.4, 72.6, 68.4, 68.3, 68.1, 66.3, 65.2, 51.3, 48.6, 48.3, 45.9, 43.2, 42.5, 41.9, 39.7, 36.5, 34.5, 32.4, 31.1, 27.4, 27.0, 25.9, 23.1, 21.4, 20.8, 20.0, 19.4, 18.2, 18.2, 18.1, 17.1, 13.6, 7.2, 5.6, -1.3, -4.4, -4.8 ppm.

IR: 3490, 2954, 2882, 2858, 1742, 1724, 1690, 1630, 1469, 1429, 1383, 1366, 1248, 1157, 1109, 1022, 878, 854, 838, 739, 704 cm^{-1}

HRMS (TOF MS ES+): Calculated for $C_{73}H_{120}O_{16}Si_4Na^+$: 1387.7546; Found: 1387.7576.

$[\alpha]_D^{23.5} = -19.2 \pm 0.2$ ° (*c* 2.15, CH_2Cl_2)

R_f = 0.57 (20% EtOAc in petroleum ether), one blue spot, *p*-anisaldehyde stain



Procedure for bryopyran 18

Neat macrocyclization precursor **17** (21.5 mg, 0.0157 mmol) was dissolved in a solution of pyridinium *para*-toluenesulfonate (PPTS) in anhydrous MeOH (4 mM, 790 μL, 0.0032 mmol). The reaction was stirred under ambient atmosphere in a Teflon-capped vial for 20 h, at which time the solution was diluted with Et_2O (1.5 mL), pentane (1.5 mL), H_2O (1 mL) and brine (1 mL). The phases were separated, and the aqueous phase was extracted with 1:1 Et_2O:pentane (4 x 1.5 mL). The combined organic phase was dried over $MgSO_4$, filtered, and concentrated to afford a crude residue that was purified via silica gel chromatography (2.5 → 6% Et_2O:CH_2Cl_2) to afford 12.1 mg of bryopyran **18** (65%) as a clear, colorless residue.

Characterization data for bryopyran **18**:

^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.69-7.60 (m, 4H, -TBDPS), 7.42-7.33 (m, 6H, -TBDPS), 5.99 (d, 1H, *J* = 1.8 Hz, C34), 5.91 (d, 1H, *J* = 16.1 Hz, C17), 5.53 (dd, 1H, *J* = 7.1, 16.1 Hz, C16), 5.18 (dd, 1H, *J* = 5.0, 11.7 Hz, C7), 5.13 (s, 1H, C20), 5.08 (ddd, 1H, *J* = 1.2, 4.4, 11.4 Hz, C25), 4.80 (s, 2H, C30, C30), 4.57 (m, 1H), 3.97 (ddd, 1H, *J* = 1.9, 7.2, 11.1 Hz, C15), 3.80 (m, 1H, C5), 3.69 (s, 3H, -CO_2Me), 3.67 (tt, 1H, *J* = 2.0, 11.3 Hz, C23), 3.64-3.57 (m, 2H, C22, C26), 3.53 (m, 1H, C11), 2.69 (s, 3H, C9-OMe), 2.61 (s, 1H, C19-OH), 2.58 (dd, 1H, *J* = 4.1, 17.3 Hz, C2), 2.35-2.20 (m, 3H, C2, C40, C40), 2.12 (m, 1H, C14), 2.09 (m, 1H, C13), 2.04 (s, 3H, C7-OAc), 2.06-1.92 (m, 3H, C10, C14, C22), 1.89 (bt, 1H, *J* = 12.6 Hz, C13), 1.74 (ddd, 1H, *J* = 1.2, 11.6, 14.0 Hz, C24), 1.67-1.58 (m, 4H, C6, C24, C41, C41), 1.53 (m, 1H, C4), 1.52 (bd, 1H, *J* = 16.0 Hz, C10), 1.45 (ddd, 1H, *J* = 1.7, 9.6, 13.9 Hz, C4), 1.32 (*app*-q, 1H, *J* = 12.1 Hz, C6), 1.17 (s, 3H, -Me), 1.01 (s, 9H, -TBDPS), 1.00 (s, 3H, -Me), 0.94-0.91 (m, 9H, C42, C27, -Me), 0.86 (s, 9H, -TBS), 0.81 (s, 3H, -Me), 0.01 (s, 3H, -TBS), -0.01 (s, 3H, -TBS) ppm.

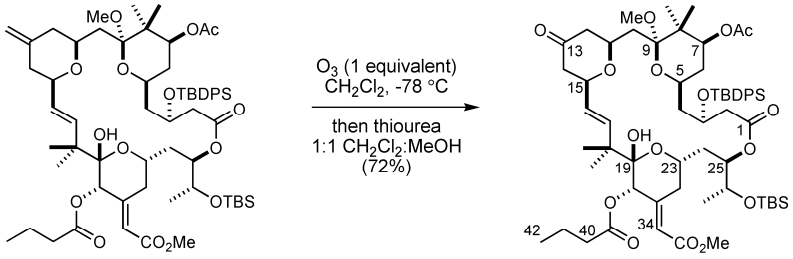
^{13}C NMR ($CDCl_3$, 125 MHz): δ = 172.1, 171.0, 170.2, 167.0, 151.7, 145.0, 135.9, 135.8, 135.3, 134.8, 134.2, 133.8, 129.8, 129.8, 127.8, 127.8, 119.9, 108.7, 102.9, 98.1, 78.5, 74.1[10], 73.1, 72.0, 68.4, 67.4, 65.1, 64.7, 51.3, 48.1, 45.4, 45.0, 42.8, 41.7, 41.6, 40.8, 39.9, 36.6, 34.5, 33.6, 31.3, 27.1, 26.0, 24.1, 22.5, 21.5, 20.4, 20.1, 19.4, 18.3, 18.2, 17.5, 13.8, -4.7, -4.7 ppm.

IR: 3508, 3071, 2953, 2858, 1738, 1731, 1667, 1471, 1428, 1385, 1365, 1249, 1161, 1104, 1049, 1022, 1004, 986, 885, 835, 777, 739, 704 cm^{-1}

HRMS (TOF MS ES+): Calculated for: $C_{64}H_{96}O_{15}Si_2Na^+$: 1183.6180; Found: 1183.6165.

$[\alpha]_D^{22.7}$ = + 13.4 ± 0.5 ° (*c* 0.67, CH_2Cl_2)

R_f = 0.48 (20% EtOAc in petroleum ether), one purple spot, *p*-anisaldehyde stain



Procedure for ketone S8

A solution of O_3 in CH_2Cl_2 (ca. 25 mM) was prepared by bubbling O_3 (2 LPM) for ~5 min through ~50 mL CH_2Cl_2 at −78 ºC (CO_2/acetone bath). The resulting bright blue solution was used immediately.

A solution of olefin **18** (10.8 mg, 9.30 µmol) in CH_2Cl_2 (400 µL) was cooled under ambient atmosphere to −78 ºC in a CO_2/acetone bath. An aliquot of the previously described O_3 solution (~25 mM, 370 µL, ~9.30 µmol) was added in one portion. After stirring for 7 min, thiourea (13.7 mg, 0.180 mmol) was added in one portion. The resulting suspension was removed from the cold bath and was diluted with MeOH (770 µL). After 19.5 h, the reaction mixture was then concentrated under a gentle stream of N_2 and directly loaded onto a slurry-packed silica gel column. Elution with 17% EtOAc in pentane provided 7.8 mg of ketone **S5** (72%) as a clear, colorless residue.

Characterization data for ketone **S8**:

[10] Two signals failed to resolve at this chemical shift

^{1}H NMR (C_6D_6, 500 MHz): δ = 7.66 (m, 4H, -TBDPS), 7.35 (m, 1H, -TBDPS), 7.28-7.19 (m, 5H, -TBDPS), 6.33 (d, 1H, *J* = 1.8 Hz, C34), 6.32 (dd, 1H, *J* = 0.7, 16.1 Hz, C17), 5.73 (dd, 1H, *J* = 6.5, 16.1 Hz, C16), 5.59 (dd, 1H, *J* = 4.9, 11.7 Hz, C7), 5.58 (s, 1H, C20), 5.39 (ddd, 1H, *J* = 1.0, 5.0, 11.4 Hz, C25), 4.67 (m, 1H, C3), 4.51 (ddd, 1H, *J* = 2.0, 6.4, 11.5 Hz, C15), 4.27 (dd, 1H, *J* = 2.2, 13.9 Hz, C22), 4.12 (tt, 1H, *J* = 1.8, 11.3 Hz, C23), 3.98 (*app*-t, 1H, *J* = 10.6 Hz, C5), 3.75 (ddd, 1H, *J* = 2.0, 9.0, 11.2 Hz, C11), 3.57 (dq, 1H, *J* = 5.0, 6.2 Hz, C26), 3.13 (s, 3H, -CO_2Me), 2.85 (dd, 1H, *J* = 3.7, 17.3 Hz, C2), 2.76 (s, 1H, C19-OH), 2.54 (s, 3H, C9-OMe), 2.38 (ddd, 1H, *J* = 1.9, 1.9, 14.0 Hz, C14), 2.36 (ddd, 1H, *J* = 1.9, 11.3, 13.6 Hz, C22), 2.31 (dd, 1H, *J* = 9.6, 17.3 Hz, C2), 2.10 (ddd, 1H, *J* = 1.9, 1.9, 14.0 Hz, C12), 2.07 (dd, 1H, *J* = 11.9, 13.9 Hz, C14), 2.03 (dd, 1H, *J* = 8.9, 16.3 Hz, C10), 2.02-1.87 (m, 3H, C40, C40, C24), 1.82 (dd, 1H, *J* =12.2, 13.9 Hz, C12), 1.70 (s, 3H, C7-OAc), 1.67 (m, 2H, C6, C24), 1.53 (ddd, 1H, *J* = 1.3, 9.8, 14.1 Hz, C4), 1.49 (s, 3H, -Me), 1.51-1.31 (m, 4H, C4, C6, C41, C41), 1.28 (d, 1H, *J* = 16.2 Hz, C10), 1.20 (s, 3H, -Me), 1.14 (s, 3H, -Me), 1.09 (s, 9H, -TBDPS), 1.02 (s, 3H, -Me), 0.91 (s, 9H, -TBS), 0.87 (d, 3H, *J* = 6.2 Hz, C27), 0.68 (t, 3H, *J* = 7.4 Hz, C42), -0.02 (s, 3H, -TBS), -0.03 (s, 3H, -TBS) ppm.

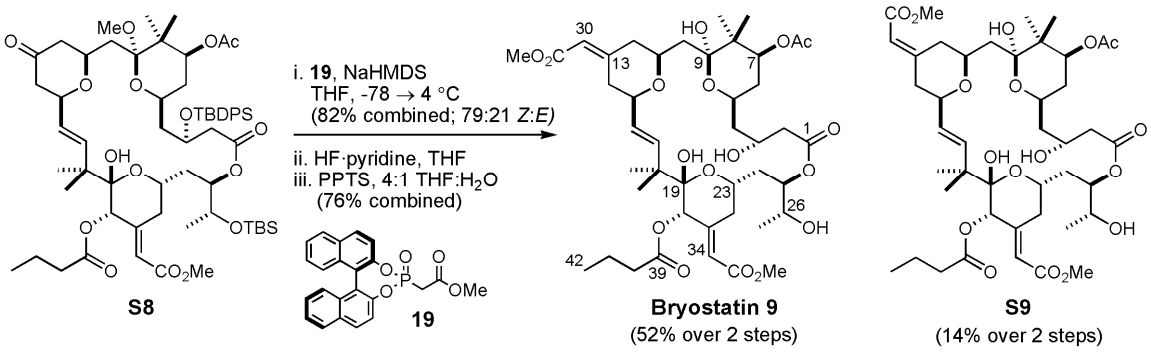
^{13}C NMR (C_6D_6, 125 MHz): δ = 204.8, 171.5, 170.7, 169.8, 166.4, 151.3, 136.3, 136.2, 136.0, 134.9, 133.9, 133.3, 130.5, 130.3, 128.1, 128.0, 121.0, 103.0, 98.9, 77.0, 74.4, 73.8, 72.7, 72.1, 69.0, 67.1, 65.7, 64.8, 50.7, 48.6, 48.1, 47.7, 45.3, 45.2, 43.0, 42.1, 39.7, 36.4, 35.3, 33.9, 31.8, 27.2, 26.0, 24.2, 20.8, 20.7, 20.6, 19.4, 18.8, 18.5, 18.2, 17.7, 13.6, -4.6, -4.7 ppm.

IR: 3518, 1956, 2858, 1729, 1665, 1469, 1430, 1384, 1365, 1248, 1157, 1106, 1020, 833, 705 cm^{-1}

HRMS (TOF MS ES+): Calculated for $C_{63}H_{94}O_{16}Si_2Na^+$: 1185.5973; Found: 1185.5984.

$[\alpha]_D^{23.6}$ = + 17.2 ± 0.6 ° (*c* 0.75, CH_2Cl_2).

R_f = 0.63 (30% EtOAc in petroleum ether), one brown spot, *p*-anisaldehyde stain.



Procedure for bryostatin 9 and its C13-C30 geometric isomer S9

(R)-BINOL derived phosphonoacetate **19**[11] (34 mg, 0.084 mmol) was dissolved in THF (700 µL) and the resulting solution was cooled in a –78 ºC bath. Once cold (~10 min), NaHMDS (1.0 M in THF, 76 µL, 0.076 mmol) was added dropwise via microsyringe over 15 s. The resulting solution was stirred for 20 min and was then moved to an ice water bath. After 30 min at 0 ºC, the solution was re-cooled in a –78 ºC bath, where the reagent (~0.1 M in sodium phosphonoacetate) was stored prior to its immediate use.

To a septa-sealed vial containing neat ketone **S8** (3.5 mg, 0.0030 mmol) cooled in a –78 ºC bath was added an aliquot of the above phosphonoacetate anion solution (~0.1 M THF, 600 µL, 0.06 mmol). The resulting solution was stirred at –78 ºC for 15 min and was then moved to an ice water bath. After 10 min at

[11] Tanaka, K.; Ohta, Y.; Fuji, K. "Differentiation of Enantiotopic Carbonyl Groups by the Horner-Wadsworth-Emmons Reaction" *Terahedron Lett.* **1993**, *34*, 4071-4074.

0 ºC, the septa cap was quickly replaced with a Teflon-lined screw-cap and the reaction was moved to a cold room at 4 ºC. After 20 h at 4 ºC, the reaction was quenched with saturated aqueous NH_4Cl (1.5 mL) and was diluted with Et_2O (1.0 mL). The phases were separated, and the aqueous phase was extracted with Et_2O (4 x 1 mL). The cloudy organic layer was dried over $MgSO_4$ and filtered through a short pad of Celite. Concentration of the resulting solution gave a crude residue that was purified by silica gel chromatography (15% EtOAc in pentane) to provide 3.0 mg of a 79:21 *Z*:*E* mixture of B-ring enoate products (82% combined yield).

In a polypropylene vial, the enoate mixture from the previous step (3.0 mg, 0.0025 mmol) was dissolved in THF (1.0 mL). HF·pyridine (250 μL) was added dropwise over 30 s, and the resulting solution was stirred for 90 h. The reaction was then quenched by its dropwise addition to a stirred mixture of saturated aqueous $NaHCO_3$ (15 mL) and EtOAc (10 mL). The biphasic mixture was further diluted with EtOAc (10 mL), and the phases were separated. The basic aqueous phase was extracted with EtOAc (2 x 10 mL), and the combined organic phase was washed with 0.2 N HCl (15 mL). The acidic aqueous phase was extracted with EtOAc (2 x 10 mL), and the combined organic phase was dried over Na_2SO_4, filtered, and concentrated to a crude residue that was used without further purification.

The crude residue from the previous step (max. 0.0025 mmol) was dissolved in a 0.05 M solution of pyridinium *para*-toluenesulfonate (PPTS) in 20% H_2O:THF (390 μL, 0.02 mmol). The resulting solution was stirred for 48 h at ambient temperature and was then diluted with H_2O (1 mL) and Et_2O (1 mL). The phases were separated, and the aqueous phase was extracted with Et_2O (4 x 1 mL). The combined organic phase was dried over $MgSO_4$, filtered, and concentrated to afford a crude residue that was partially purified by silica gel chromatography (50% → 70% EtOAc in pentane) to afford 1.6 mg of a 80:20 mixture of bryostatin 9 and its C13-30 stereoisomer (76% combined yield). These isomers were separated via reverse-phase HPLC (Restek 5 μm C18, 21x250 mm, 75 → 100% MeCN in H_2O) to afford 1.1 mg of bryostatin 9 as a white solid film (52% yield) along with 0.3 mg of its C13-30 stereoisomer as a white film (14% yield).

Characterization data for synthetic bryostatin 9:[12]

^{1}H NMR (CD_3OD, 600 MHz): δ = 5.91 (d, 1H, *J* = 15.8 Hz, C17), 5.91 (d, 1H, *J* = 1.9 Hz, C34), 5.78 (bs, 1H, C30), 5.37 (dd, 1H, *J* = 8.5, 15.8 Hz, C16), 5.26 (dd, 1H, *J* = 4.9, 11.7 Hz, C7), 5.25 (ddd, 1H, *J* = 3.0, 4.1, 12.1 Hz, C25), 5.14 (s, 1H, C20), 4.28 (tt, 1H, *J* = 2.9, 11.7 Hz, C5), 4.18-4.12 (m, 2H, C3, C15), 4.02 (tt, 1H, *J* = 2.2, 11.4 Hz, C23), 3.99 (m, 1H, C11), 3.87 (dq, 1H, *J* = 4.3, 6.5 Hz, C26), 3.72 (s, 3H, -CO_2Me), 3.71 (s, 3H, -CO_2Me), 3.67 (dd, 1H, *J* = 2.2, 13.9 Hz, C22), 3.66 (dd, 1H, *J* = 1.9, 13.9 Hz, C14), 2.62-2.58 (m, 2H, C2, C2), 2.42-2.30 (m, 2H, C40, C40), 2.21 (m, 2H, C12, C12), 2.12-2.07 (m, 2H, C10, C22), 2.06 (s, 3H, C7-OAc), 2.01 (ddd, 1H, *J* = 2.6, 12.5, 13.9 Hz, C24), 1.95-1.81 (m, 3H, C5, C14, C24), 1.78-1.71 (m, 3H, C4, C6, C10), 1.69 (dd, 1H, *J* = 3.3, 7.4 Hz, C41), 1.66 (dd, 1H, *J* = 3.0, 7.4 Hz, C41), 1.50 (*app*-q,1H, *J* = 12.0 Hz, C6), 1.23 (s, 3H, -CH_3), 1.19 (d, 3H, *J* = 6.5 Hz, C27), 1.05 (bs, 6H, -CH_3, -CH_3), 0.96 (t, 3H, *J* = 7.3 Hz, C42), 0.96 (s, 3H, -CH_3) ppm.

^{13}C NMR ($CDCl_3$, 125 MHz): δ = 172.4, 172.2, 171.1, 167.2, 166.9, 156.7, 152.0, 139.3, 129.6, 119.8, 114.5, 102.0, 99.0, 79.3, 74.4, 73.9, 72.9, 71.6, 70.3, 68.6, 65.9, 64.8, 51.3, 51.2, 45.0, 44.3, 42.5, 42.1, 41.1, 39.9, 36.7, 36.5, 36.0, 33.4, 31.3, 24.7, 21.3, 21.2, 20.0, 19.9, 18.4, 17.0, 13.8 ppm.

[12] As has been reported for bryostatin 1, we observed that several ^{1}H NMR chemical shifts for bryostatin 9 are strongly concentration-dependent in certain aprotic solvents ($CDCl_3$, C_6D_6). This was not observed in CD_3OD, in which excellent spectral overlay was obtained between the synthetic and authentic material. See: (a) Pettit, G. R.; Leet, J. E.; Herald, C. L.; Kamano, Y.; Boettner, F. E.; Baczynskyj, L.; Nieman, R. A. *J. Org. Chem.* **1987**, *52*, 2854-2860. (b) Keck, G. E.; Poudel, Y. B.; Cummins, T. J.; Rudra, A.; Covel, J. A. *J. Am. Chem. Soc.* **2011**, *133*, 744-747.

IR (thin film): 3465, 3350, 2974, 2949, 1722, 1658, 1435, 1377, 1366, 1282, 1247, 1159, 1098, 1079, 1058, 1002, 987, 859 cm^{-1}

HRMS (TOF MS ES+): Calculated for $C_{43}H_{64}O_{17}Na^{+}$: 875.4036; Found: 875.4044.

$[\alpha]_D^{22.8} = +77.5 \pm 0.7$ º (*c* 0.20 MeOH).

$\mathbf{R}_f$ = 0.30 (60% EtOAc in petroleum ether), one purple spot, *p*-anisaldehyde stain.

Observed and Reported[13] Characterization data for authentic Bryostatin 9

Observed ^{1}H NMR (CD_3OD, 600 MHz): δ = 5.91 (d, 1H, *J* = 15.8 Hz, C17), 5.91 (d, 1H, *J* = 1.8 Hz, C34), 5.78 (s, 1H, C30), 5.37 (dd, 1H, *J* = 8.5, 15.8 Hz, C16), 5.26 (dd, 1H, *J* = 5.2, 11.9 Hz, C7), 5.25 (ddd, 1H, *J* = 3.0, 4.0, 12.2 Hz, C25), 5.14 (s, 1H, C20), 4.28 (tt, 1H, *J* = 2.7, 11.6 Hz, C5), 4.18-4.12 (m, 2H, C3, C15), 4.02 (tt, 1H, *J* = 2.1, 11.2 Hz, C23), 3.99 (m, 1H, C11), 3.72 (s, 3H, -CO_2Me), 3.71 (s, 3H, -CO_2Me), 3.70-3.64 (m, 2H, C14, C22), 2.62-2.58 (m, 2H, C2, C2), 2.42-2.30 (m, 2H, C40, C40), 2.24-2.19 (m, 2H, C12, C12), 2.13-2.06 (m, 2H, C10, C22), 2.06 (s, 3H, C7-OAc), 2.01 (ddd, 1H, *J* = 2.4, 12.2, 13.9 Hz, C24), 1.95-1.81 (m, 3H, C5, C14, C24), 1.78-1.71 (m, 3H, C4, C6, C10), 1.69 (dd, 1H, *J* = 3.3, 7.3 Hz, C41), 1.66 (dd, 1H, *J* = 3.1, 7.3 Hz, C41), 1.50 (*app*-q, 1H, *J* = 12.0 Hz, C6), 1.23 (s, 3H, -CH_3), 1.19 (d, 3H, *J* = 6.5 Hz, C27), 1.05 (bs, 6H, -CH_3, -CH_3), 0.98-0.95 (m, 6H, C42, -CH_3) ppm.[14]

Observed IR (thin film): 3466, 3350, 2951, 2930, 1722, 1435, 1408, 1380, 1367, 1281, 1247, 1163, 1098, 1080, 1002, 987, 860 cm^{-1}

Reported IR (KBr): 3465, 3440, 2975-2940, 1735, 1725, 1655-1645, 1440, 1380, 1365, 1290, 1240, 1160, 1100, 1080, 1070, 1045, 1000, 870 cm^{-1}

Reported $[\alpha]_D^{28} = +87.31$ º (*c* 0.04, MeOH)

Characterization data for the *E*-C13-C30 isomer **S9**:

^{1}H NMR (CD_3OD, 600 MHz): δ =5.88 (d, 1H, *J* = 15.9 Hz, C17), 5.88 (d, 1H, *J* = 1.9 Hz, C34), 5.76 (bs, 1H, C30), 5.31 (dd, 1H, *J* = 8.5, 15.9 Hz, C16), 5.24 (d, 1H, *J* = 4.9, 11.8 Hz, C7), 5.21 (ddd, 1H, *J* = 3.0, 4.0, 12.3 Hz, C25), 5.10 (s, 1H, C20), 4.25 (tt, 1H, *J* = 2.9, 11.6 Hz, C5), 4.19 (ddd, 1H, *J* = 2.4, 8.5, 11.0 Hz, C15), 4.10 (m, 1H, C3), 3.99 (tt, 1H, *J* = 2.3, 11.3 Hz, C23), 3.92 (ddd, 1H, *J* = 2.1, 6.7, 11.1 Hz, C11), 3.84 (dq, 1H, *J* = 4.3, 6.5 Hz, C26), 3.70 (m, 1H, C12), 3.69 (s, 3H, CO_2Me), 3.69 (s, 3H, CO_2Me), 3.64 (dd, 1H, *J* = 2.2, 14.0 Hz, C22), 2.61-2.54 (m, 2H, C2, C2), 2.35 (dt, 1H, *J* = 7.2, 15.8 Hz, C40), 2.29 (dt, 1H, *J* =7.3, 15.8 Hz, C40), 2.17 (m, 1H, C14), 2.12-2.04 (m, 3H, C10, C14, C22), 2.03 (s, 3H, -OAc), 1.99 (ddd, 1H, *J* = 2.4, 12.4, 14.1 Hz, C24), 1.94 (m, 1H, C12), 1.85 (ddd, 1H, *J* = 2.5, 11.9, 14.6 Hz, C4), 1.80 (m, 1H, C24), 1.77 (d, 1H, *J* = 15.5 Hz, C10), 1.70 (m, 2H, C4, C6), 1.67-1.60 (m, 2H, C41, C41), 1.47 (*app*-q, 1H, *J* = 12.1 Hz, C6), 1.18 (s, 3H, -CH_3), 1.16 (d, 3H, *J* = 6.5 Hz, C27), 1.03 (s, 3H, -CH_3), 1.01 (s, 3H, -CH_3), 0.95 (s, 3H, -CH_3), 0.93 (t, 3H, *J* = 7.5 Hz, C42) ppm.

^{13}C NMR ($CDCl_3$, 125 MHz): δ = 172.4, 172.1, 170.9, 167.2, 167.1, 156.8, 151.8, 138.7, 129.3, 119.8, 114.5, 101.9, 99.0, 79.9, 74.3, 73.7, 72.9, 71.5, 70.3, 68.7, 65.9, 64.8, 51.3, 51.2, 45.0, 43.2, 42.5, 42.2, 41.2, 40.0, 37.6, 36.7, 35.9, 33.5, 31.3, 24.7, 21.3, 21.2, 20.0, 19.8, 18.4, 16.9, 13.8 ppm

IR: 3466, 3325, 2976, 2951, 1731, 1715, 1667, 1435, 1408, 1367, 1242, 1157, 1098, 1079, 1002, 883, 860, 813, 735 cm^{-1}

HRMS (TOF MS ES+): Calculated for $C_{43}H_{64}O_{17}Na^{+}$: 875.4036; Found: 875.4032.

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[13] Pettit, G.R.; Kamano, Y.; Herald, C. L. "Antineoplastic Agents, 118. Isolation and Structure of Bryostatin 9" *J. Nat. Prod.* **1986**, *49*, 661-664.

[14] Minor variation between the synthetic and authentic sample HNMR data is ascribed to the presence of an unidentified minor impurity in the authentic sample (see p. S21 for HPLC analysis). Proton assignments were independently made in both cases by 2D-COSY NMR analysis (see p. S24).

$[\alpha]_D^{24.7} = -9.7 \pm 0.8$ ° (*c* 0.11, MeOH)

$\mathbf{R}_f$ = 0.42 (60% EtOAc in petroleum ether), one maroon spot, *p*-anisaldehyde stain.

HPLC comparison of synthetic and authentic bryostatin 9

Agilent Zorbax C18, 5 micron, 3 x 150 mm; 30 to 95% MeCN in water, 1 mL/min

```
Print of all graphic windows
Data File  : C:\CHEM32\1\DATA\SCHRIER\DEF_LC 2011-02-11 13-34-59\090211000004.D
Sample Name : Bryo 9 Auth + Syth
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Acq. Operator   : Schrier                       Seq. Line :   1
Acq. Instrument : Instrument 1                   Location : Vial 23
                                                      Inj :   1
                                                Inj Volume : 20.0 µl
Different Inj Volume from Sequence !     Actual Inj Volume : 90.0 µl
Acq. Method     : C:\CHEM32\1\DATA\SCHRIER\DEF_LC 2011-02-11 13-34-59\PICOLOG.M

Analysis Method : C:\CHEM32\1\DATA\SCHRIER\DEF_LC 2011-02-11 13-34-59\090211000004.D\DA.M (
                  PICOLOG.M)

Method Info     : 30-95% in 30 min
Current Chromatogram(s)
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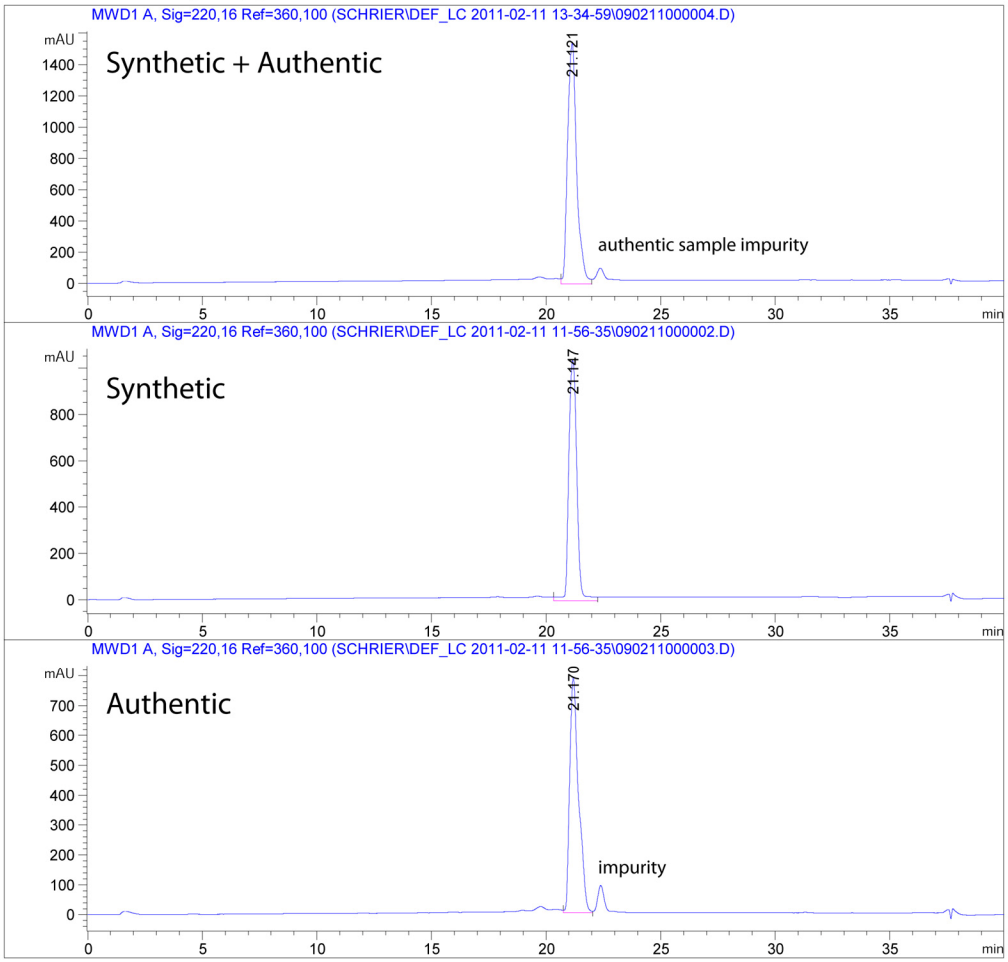
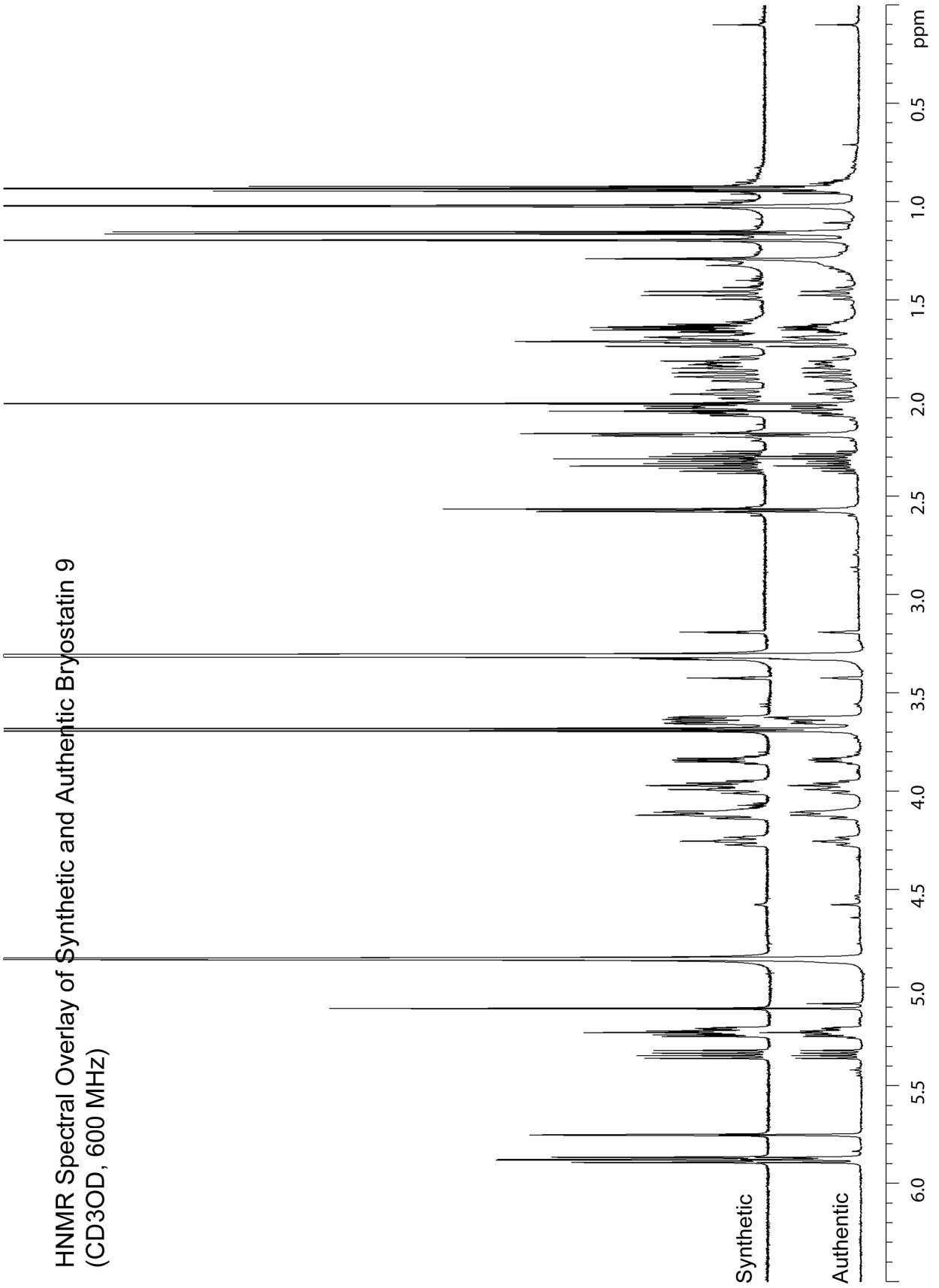
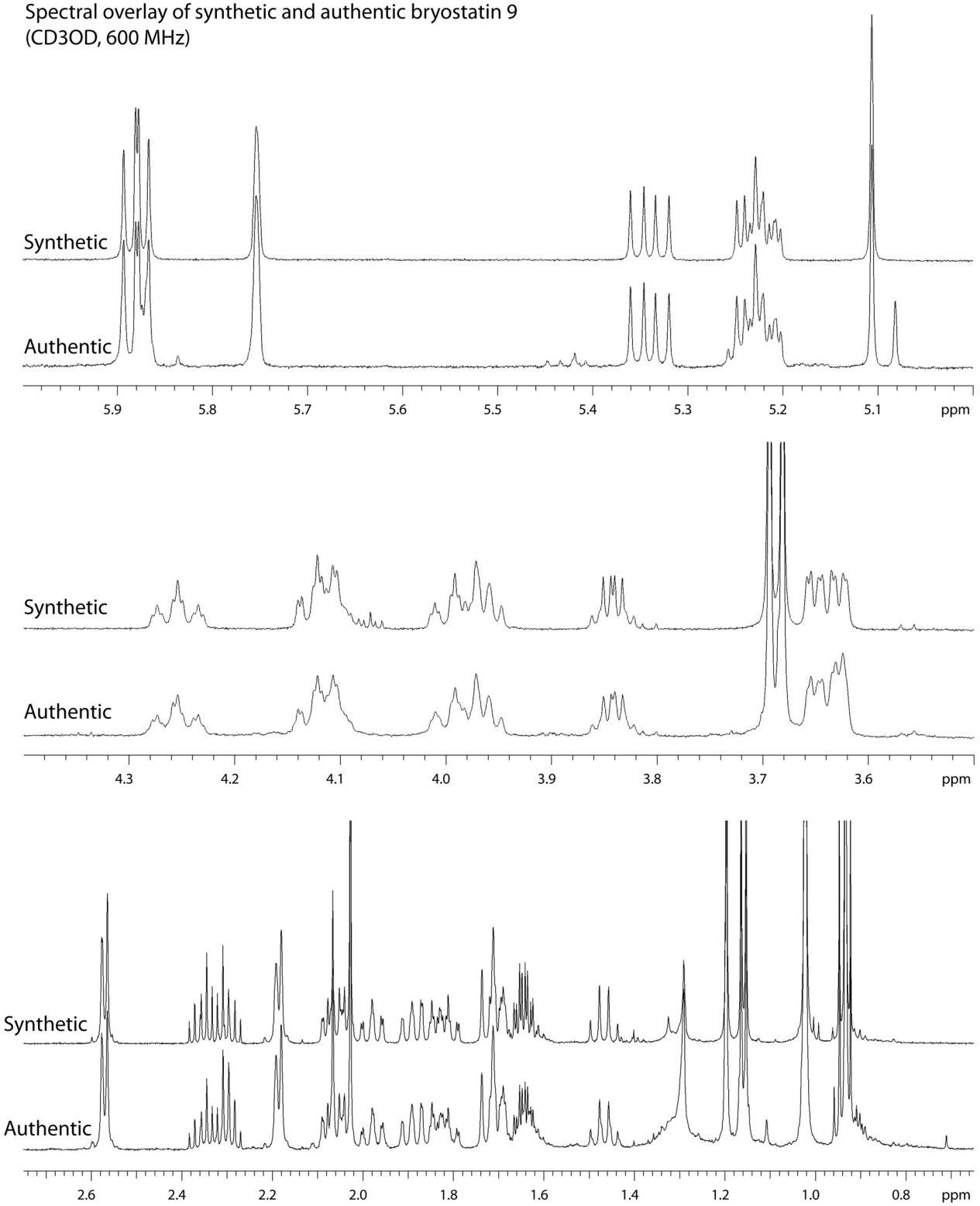
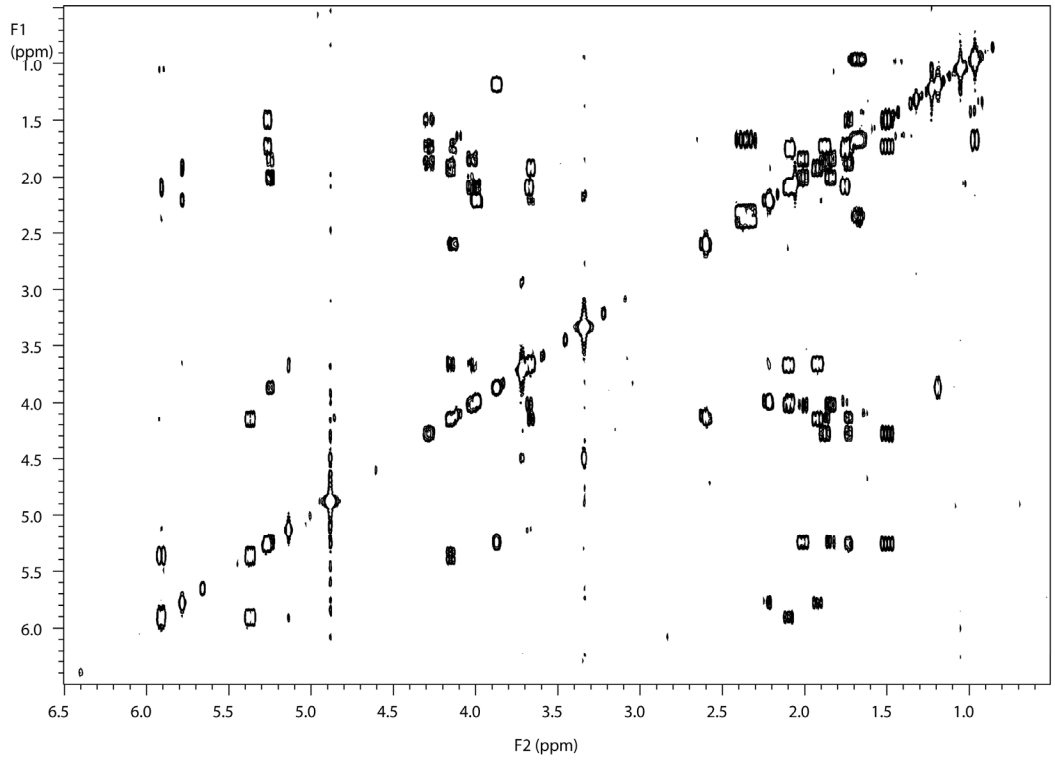



HNMR Spectral Overlay of Synthetic and Authentic Bryostatin 9
(CD3OD, 600 MHz)
Synthetic
Authentic
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm

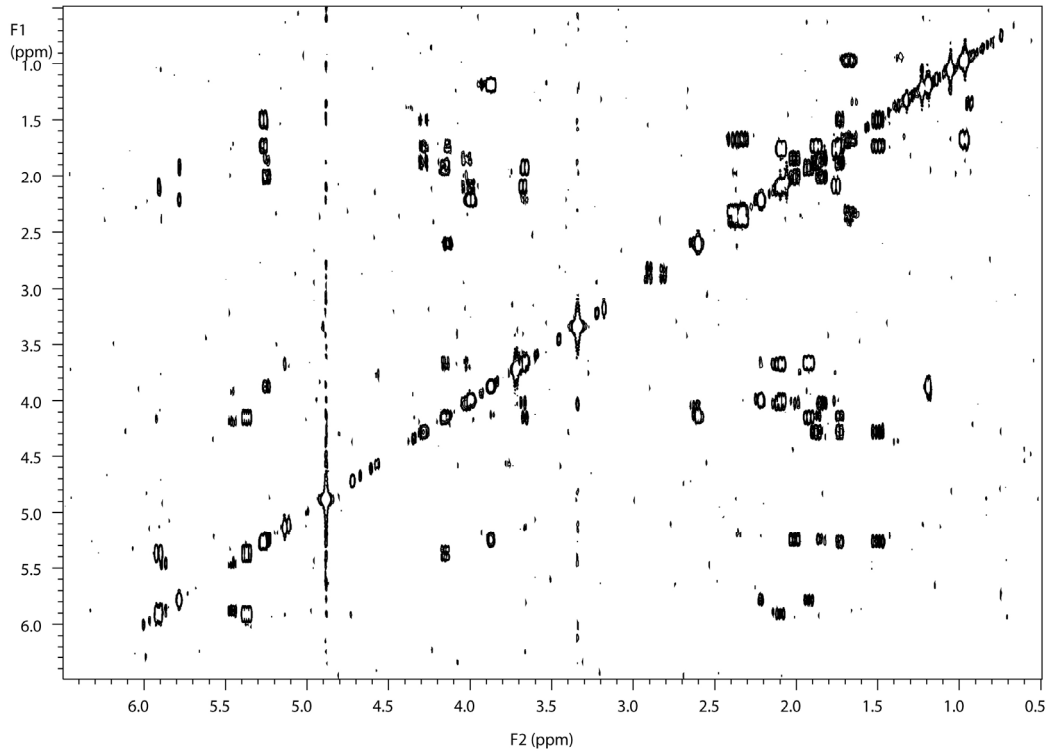
Spectral overlay of synthetic and authentic bryostatin 9
(CD3OD, 600 MHz)



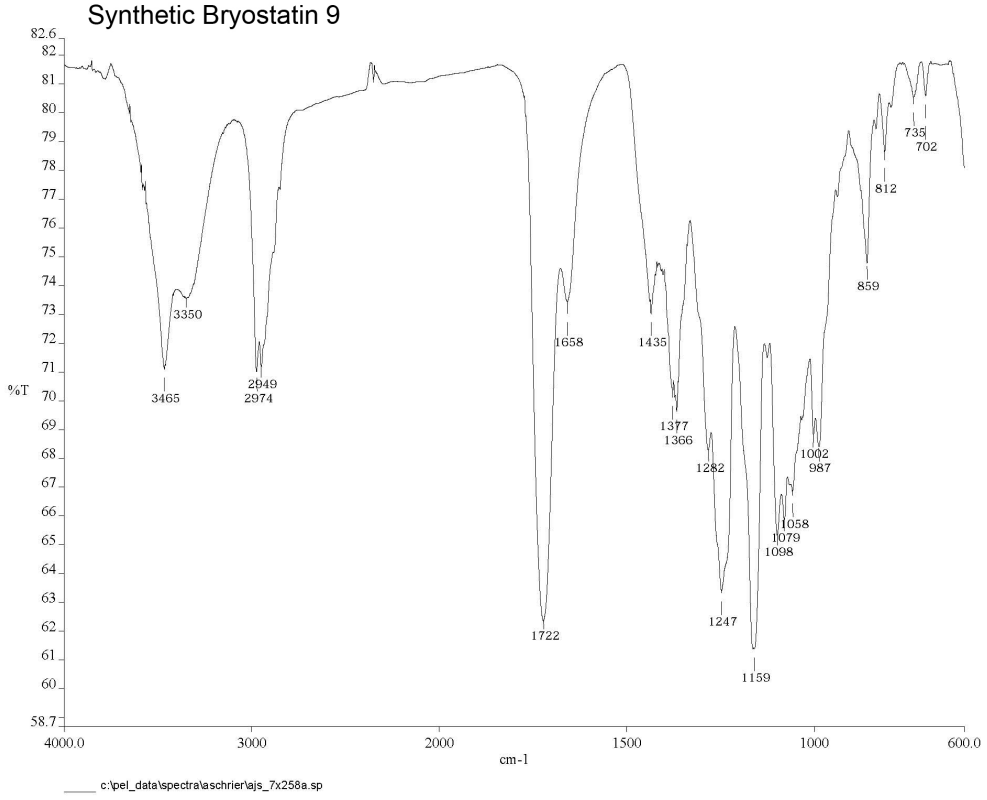
Synthetic Bryostatin 9 - COSY, CD3OD, 600 MHz



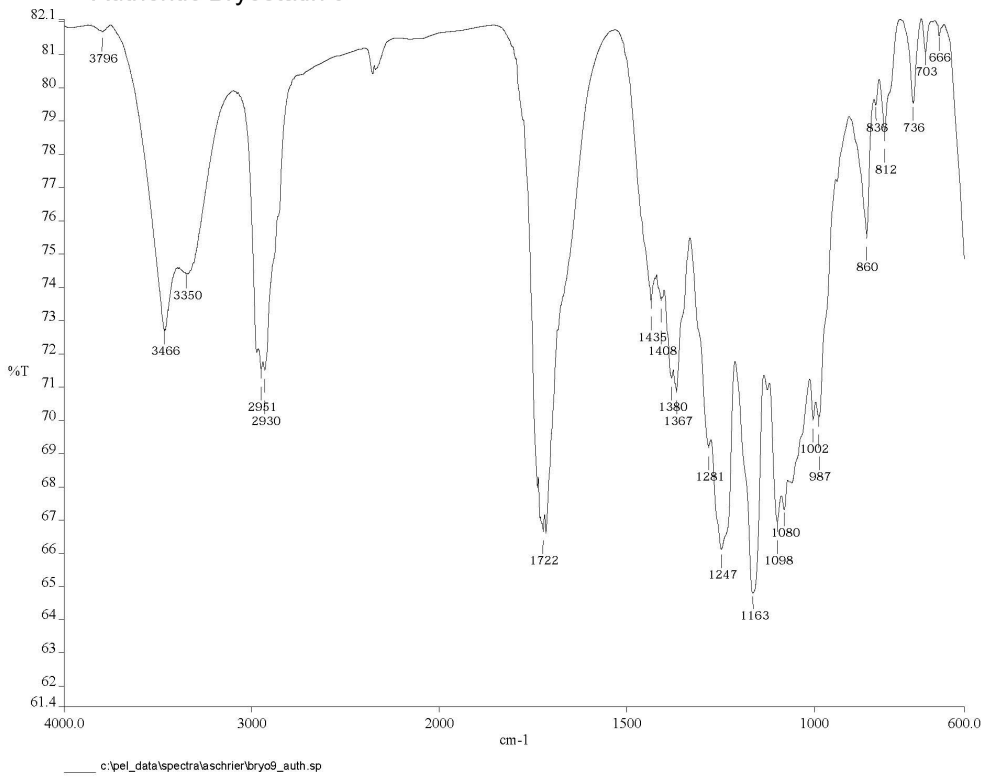
Authentic Bryostatin 9 - COSY, CD3OD, 600 MHz



Synthetic Bryostatin 9



Authentic Bryostatin 9



STANDARD PROTON PARAMETERS

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Solvent: CDCl3

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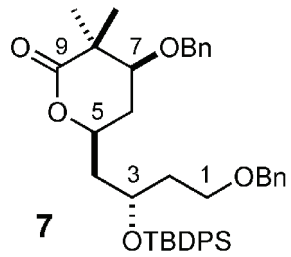
FT size 131072
Total time 17 min



7

5x111

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Sample directory:

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Solvent: CDCl3

User: 1-15-87

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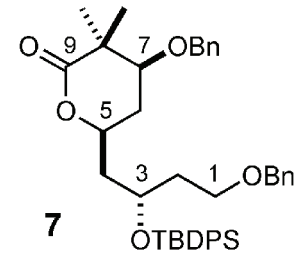
296 repetitions
OBSERVE C13, 125.6618663 MHz
DECOUPLE H1, 499.7505605 MHz
Power 43 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 131072
Total time 34 min



7

220 200 180 160 140 120 100 80 60 40 20 0 -20 ppm

5x122 Product A

Archive directory:
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File: 5x122A

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Solvent: CDCl3

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Width 8000.0 Hz
16 repetitions
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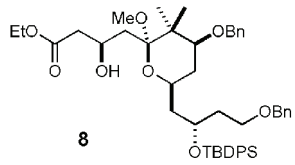
Total time 17 min



8

C13par

Archive directory:
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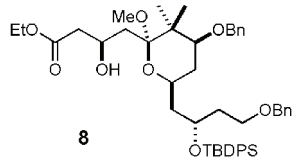
Sample directory:

File: 5x122A_C



8

Pulse Sequence: s2pul
Solvent: CDCl3

User: 1-15-87

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Acq. time 1.500 sec
Width 33003.3 Hz
160 repetitions
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DECOUPLE H1, 499.7505605 MHz
Power 43 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 131072
Total time 34 min

220 200 180 160 140 120 100 80 60 40 20 0 -20 ppm

5x123

Archive directory:
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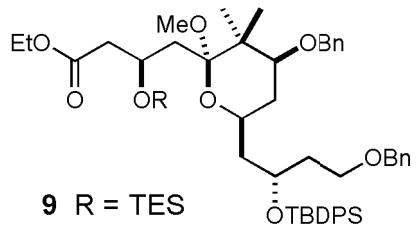
Sample directory:

File: 5x123

Pulse Sequence: s2pul
Solvent: CDCl3



9 R = TES

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12 repetitions
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DATA PROCESSING
FT size 131072
Total time 17 min

C13par

Archive directory:
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Sample directory:

File: 5x123_C

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Solvent: CDCl3

User: 1-15-87

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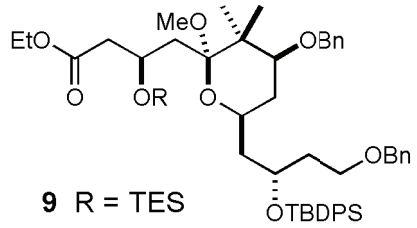
FT size 131072
Total time 34 min



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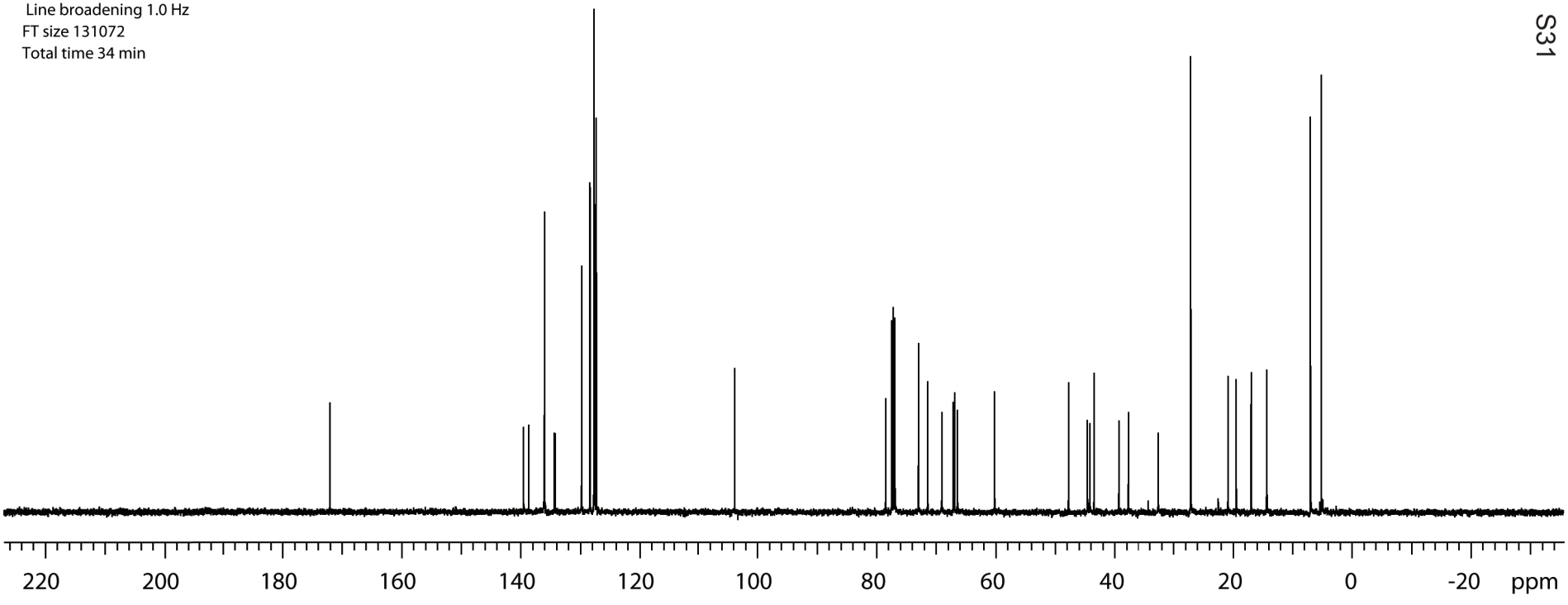

5x124 Characterization Sample

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Sample directory:

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Solvent: CDCl3

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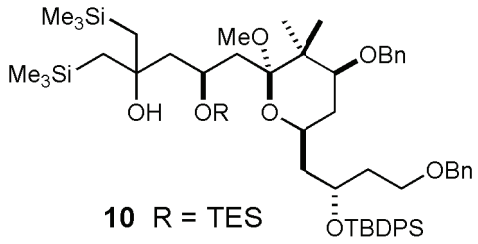
Total time 17 min



10 R = TES

C13par

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Sample directory:

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Solvent: CDCl3

User: 1-15-87

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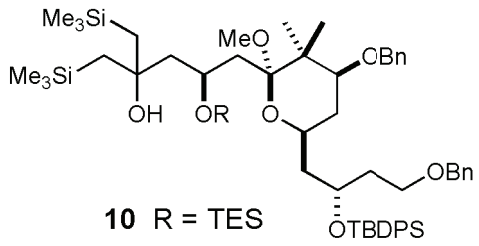
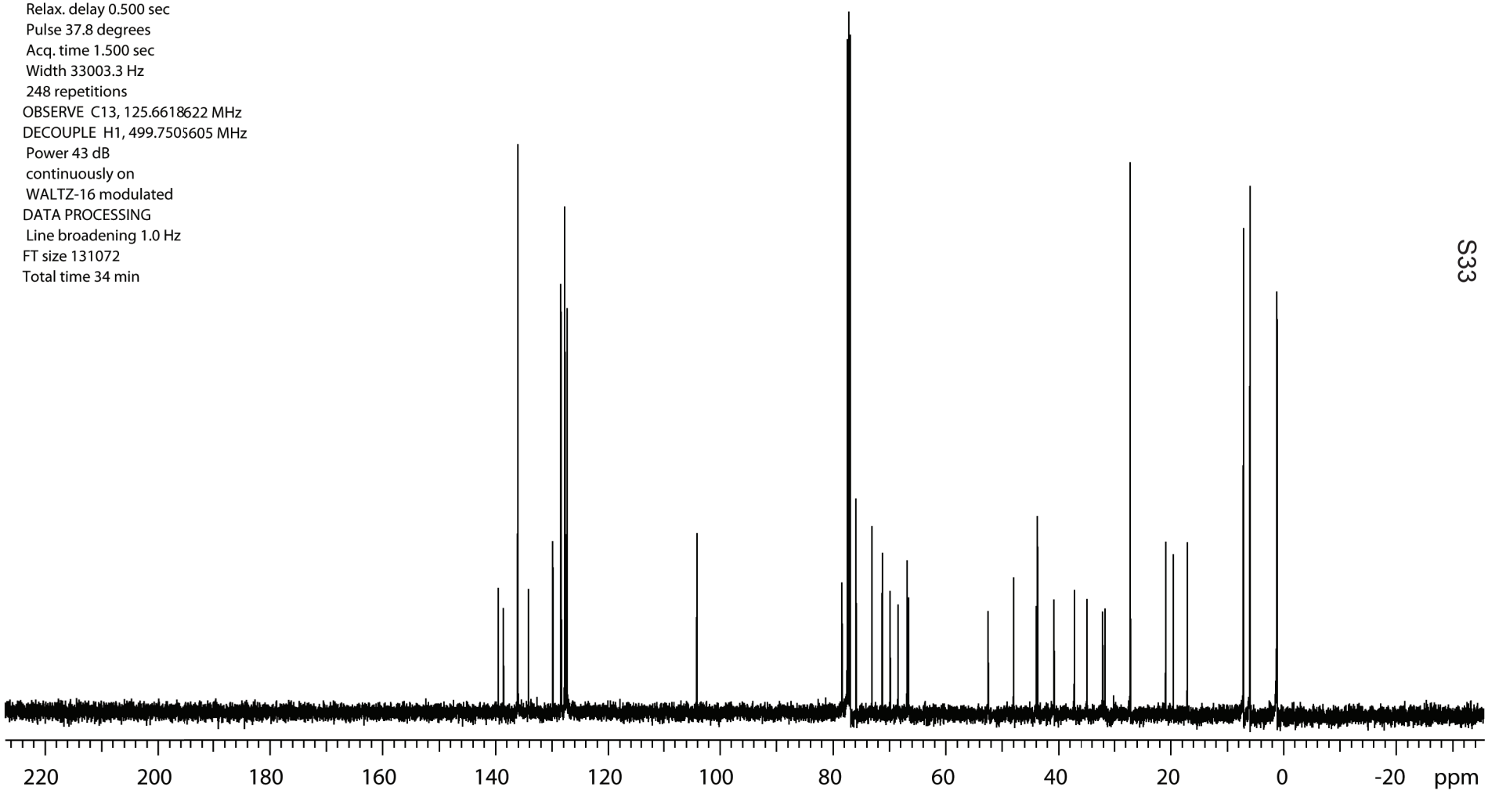
248 repetitions
OBSERVE C13, 125.6618622 MHz
DECOUPLE H1, 499.7505605 MHz
Power 43 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 131072
Total time 34 min



10 R = TES



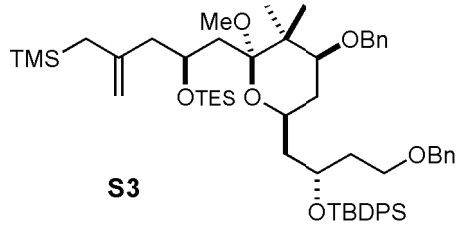
5x13o repurified

Archive directory:
/export/home/schrier/vnmrsys/data
Sample directory:

File: 5x130_CH

Pulse Sequence: s2pul
Solvent: CDCl3

Pulse 48.0 degrees
Acq. time 4.000 sec
Width 8000.0 Hz
20 repetitions
OBSERVE H1, 499.7485738 MHz
DATA PROCESSING
FT size 131072
Total time 17 min



S3

5x130

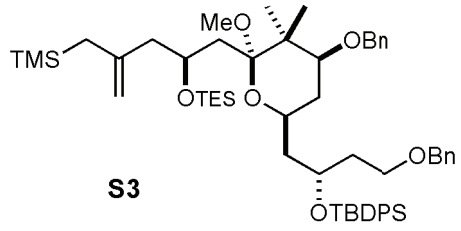
Archive directory:
/export/home/schrier/vnmrsys/data
Sample directory:

File: 5x130_CH_C

Pulse Sequence: s2pul
Solvent: CDCl3

User: 1-15-87

Relax. delay 0.500 sec
Pulse 37.8 degrees
Acq. time 1.500 sec
Width 33003.3 Hz
708 repetitions
OBSERVE C13, 125.6618607 MHz
DECOUPLE H1, 499.7505605 MHz
Power 43 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 131072
Total time 34 min



S3

220 200 180 160 140 120 100 80 60 40 20 0 -20 ppm

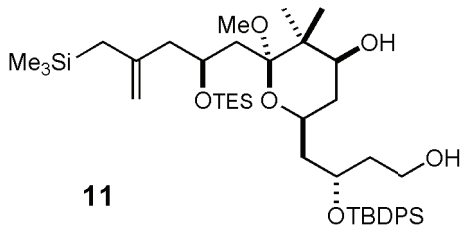
STANDARD PROTON PARAMETERS

Archive directory:
/export/home/schrier/vnmrsys/data
Sample directory:

File: 6x034_CH

Pulse Sequence: s2pul
Solvent: CDCl3

Pulse 48.0 degrees
Acq. time 4.000 sec
Width 8000.0 Hz
28 repetitions
OBSERVE H1, 499.7485738 MHz
DATA PROCESSING
FT size 131072
Total time 17 min



11

C13par

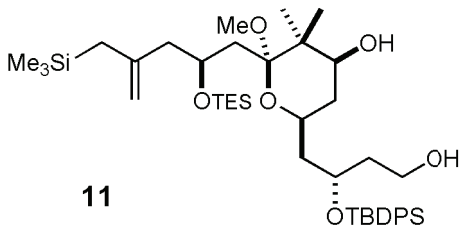
Archive directory:
/export/home/schrier/vnmrsys/data
Sample directory:

File: 6x034_C

Pulse Sequence: s2pul
Solvent: CDCl3

User: 1-15-87

Relax. delay 0.500 sec
Pulse 37.8 degrees
Acq. time 1.500 sec
Width 33003.3 Hz
96 repetitions
OBSERVE C13, 125.6618627 MHz
DECOUPLE H1, 499.7505605 MHz
Power 43 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 2.0 Hz
FT size 131072
Total time 34 min



11

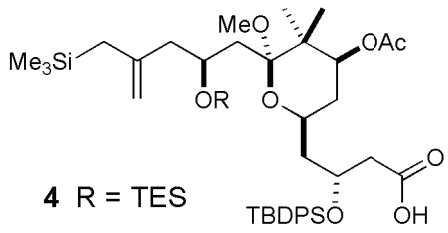
7x140

Archive directory:
/export/home/schrier/vnmrsys/data
Sample directory:

File: 7x140

Pulse Sequence: s2pul
Solvent: CDCl3

Pulse 30.5 degrees
Acq. time 4.000 sec
Width 8000.0 Hz
8 repetitions
OBSERVE H1, 499.7485737 MHz
DATA PROCESSING
FT size 65536
Total time 17 min



4 R = TES

C13par

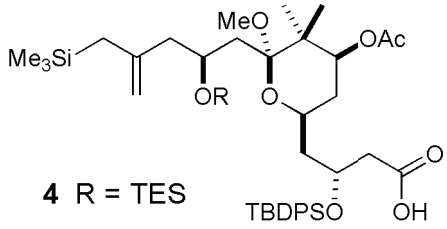
Archive directory:
/export/home/schrier/vnmrsys/data
Sample directory:

File: 7x140_C

Pulse Sequence: s2pul
Solvent: CDCl3

User: 1-15-87

Relax. delay 0.500 sec
Pulse 38.3 degrees
Acq. time 1.500 sec
Width 33003.3 Hz
452 repetitions
OBSERVE C13, 125.6618622 MHz
DECOUPLE H1, 499.7505605 MHz
Power 43 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 2.0 Hz
FT size 131072
Total time 34 min



4 R = TES

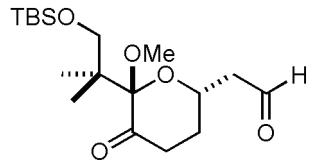
STANDARD 1H OBSERVE

Archive directory:
/export/home/schrier/vnmrsys/data
Sample directory:

File: 6x280_CH

Pulse Sequence: s2pul
Solvent: Benzene

Relax. delay 0.500 sec
Pulse 56.8 degrees
Acq. time 4.002 sec
Width 4997.5 Hz
16 repetitions
OBSERVE H1, 400.1115597 MHz
DATA PROCESSING
FT size 65536
Total time 19 min



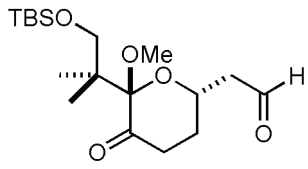
S4

13C OBSERVE

Archive directory:
/export/home/schrier/vnmrsys/data
Sample directory:

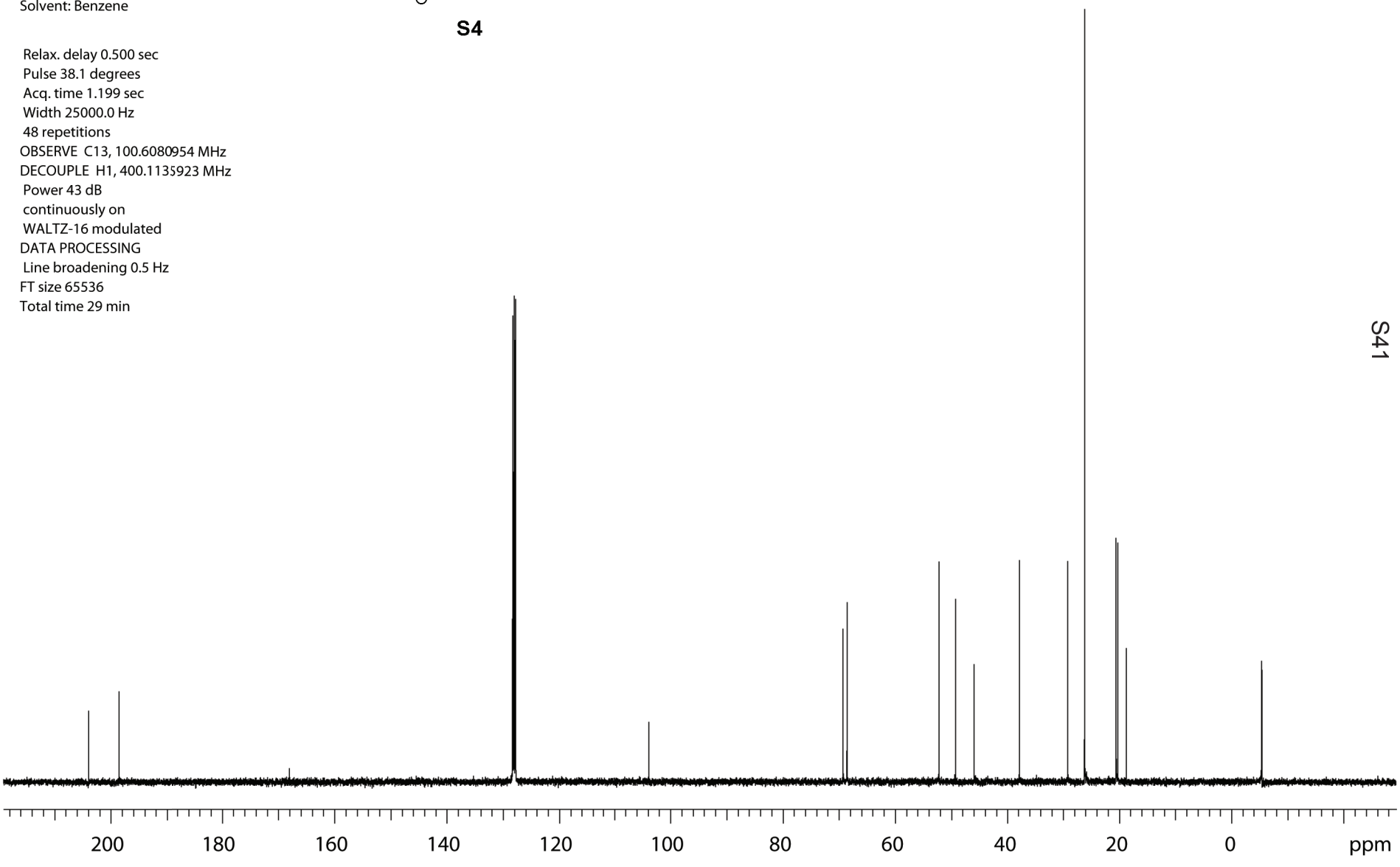
File: 6x280_CH_C

Pulse Sequence: s2pul
Solvent: Benzene



S4

Relax. delay 0.500 sec
Pulse 38.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
48 repetitions
OBSERVE C13, 100.6080954 MHz
DECOUPLE H1, 400.1135923 MHz
Power 43 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 29 min



STANDARD PROTON PARAMETERS

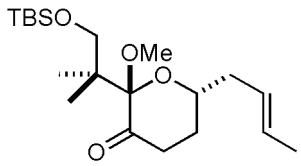
Archive directory:
/export/home/schrier/vnmrsys/data
Sample directory:

File: 7x253

Pulse Sequence: s2pul
Solvent: Benzene

Temp. 25.0 C / 298.1 K
User: 1-15-87

Relax. delay 0.500 sec
Pulse 50.8 degrees
Acq. time 4.000 sec
Width 8000.0 Hz
80 repetitions
OBSERVE H1, 599.7973227 MHz
DATA PROCESSING
FT size 65536
Total time 19 min



13

C13par

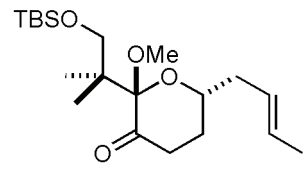
Archive directory:
/export/home/schrier/vnmrsys/data
Sample directory:

File: 7x253_C

Pulse Sequence: s2pul
Solvent: Benzene

User: 1-15-87

Relax. delay 0.500 sec
Pulse 38.3 degrees
Acq. time 1.500 sec
Width 33003.3 Hz
140 repetitions
OBSERVE C13, 125.6618397 MHz
DECOUPLE H1, 499.7506055 MHz
Power 43 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 2.0 Hz
FT size 131072
Total time 8 min



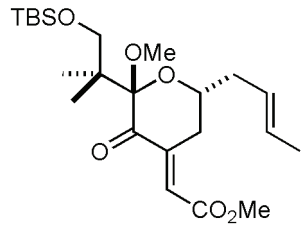
13

STANDARD 1H OBSERVE

Archive directory:
/export/home/schrier/vnmrsys/data
Sample directory:

File: 6x286

Pulse Sequence: s2pul
Solvent: Benzene



S5

Relax. delay 0.500 sec
Pulse 56.8 degrees
Acq. time 4.002 sec
Width 4997.5 Hz
8 repetitions
OBSERVE H1, 400.1115602 MHz
DATA PROCESSING
FT size 65536
Total time 19 min

C13par

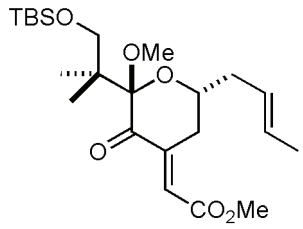
Archive directory:
/export/home/schrier/vnmrsys/data
Sample directory:

File: 6x286_C

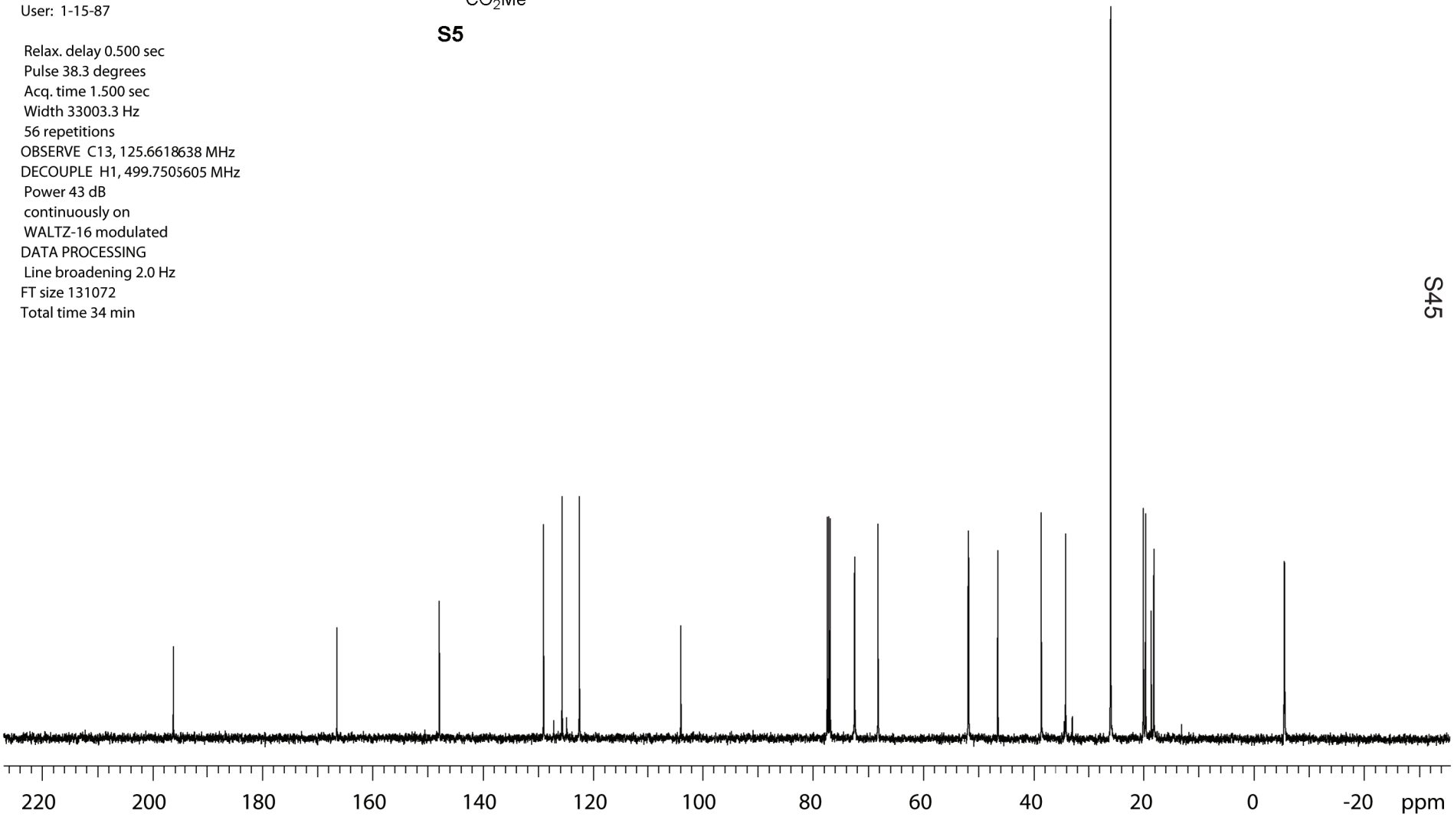
Pulse Sequence: s2pul
Solvent: CDCl3

User: 1-15-87

Relax. delay 0.500 sec
Pulse 38.3 degrees
Acq. time 1.500 sec
Width 33003.3 Hz
56 repetitions
OBSERVE C13, 125.6618638 MHz
DECOUPLE H1, 499.7505605 MHz
Power 43 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 2.0 Hz
FT size 131072
Total time 34 min



S5



STANDARD PROTON PARAMETERS

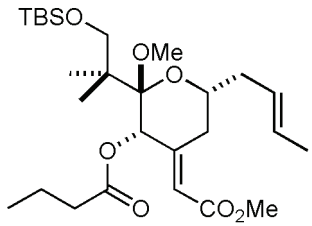
Archive directory:
/export/home/schrier/vnmrsys/data
Sample directory:

File: 6x292

Pulse Sequence: s2pul
Solvent: Benzene

Temp. 25.0 C / 298.1 K
User: 1-15-87

Relax. delay 0.500 sec
Pulse 37.0 degrees
Acq. time 4.000 sec
Width 8000.0 Hz
12 repetitions
OBSERVE H1, 599.7973237 MHz
DATA PROCESSING
FT size 65536
Total time 19 min



14

C13par

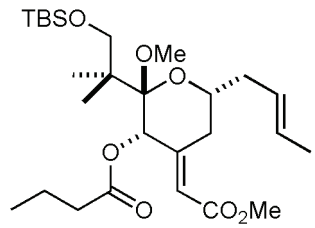
Archive directory:
/export/home/schrier/vnmrsys/data
Sample directory:

File: 7x068_C

Pulse Sequence: s2pul
Solvent: Benzene

User: 1-15-87

Relax. delay 0.500 sec
Pulse 38.3 degrees
Acq. time 1.500 sec
Width 33003.3 Hz
96 repetitions
OBSERVE C13, 125.6618387 MHz
DECOUPLE H1, 499.7506055 MHz
Power 43 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 2.0 Hz
FT size 131072
Total time 34 min



14

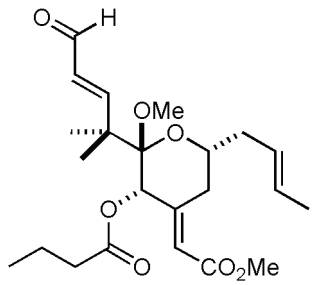
STANDARD PROTON PARAMETERS

Archive directory:
/export/home/schrier/vnmrsys/data
Sample directory:

File: 7x031

Pulse Sequence: s2pul
Solvent: Benzene

Pulse 30.5 degrees
Acq. time 4.000 sec
Width 8000.0 Hz
16 repetitions
OBSERVE H1, 499.7486026 MHz
DATA PROCESSING
FT size 65536
Total time 17 min



15

C13par

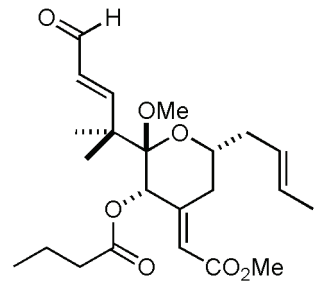
Archive directory:
/export/home/schrier/vnmrsys/data
Sample directory:

File: 7x031_C

Pulse Sequence: s2pul
Solvent: Benzene

User: 1-15-87

Relax. delay 0.500 sec
Pulse 38.3 degrees
Acq. time 1.500 sec
Width 33003.3 Hz
260 repetitions
OBSERVE C13, 125.6618407 MHz
DECOUPLE H1, 499.7506055 MHz
Power 43 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 2.0 Hz
FT size 131072
Total time 34 min



15

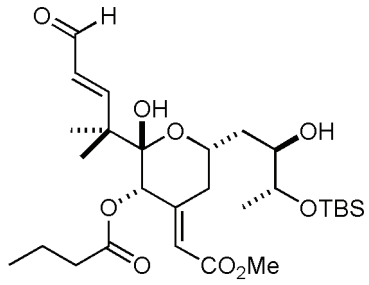
7x101

Archive directory:
/export/home/schrier/vnmrsys/data
Sample directory:

File: 7x101

Pulse Sequence: s2pul
Solvent: Benzene

Pulse 30.5 degrees
Acq. time 4.000 sec
Width 8000.0 Hz
12 repetitions
OBSERVE H1, 499.7486023 MHz
DATA PROCESSING
FT size 65536
Total time 17 min



5

C13par

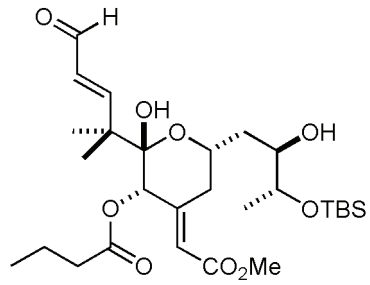
Archive directory:
/export/home/schrier/vnmrsys/data
Sample directory:

File: 7x101_C

Pulse Sequence: s2pul
Solvent: Benzene

User: 1-15-87

Relax. delay 0.500 sec
Pulse 38.3 degrees
Acq. time 1.500 sec
Width 33003.3 Hz
96 repetitions
OBSERVE C13, 125.6618407 MHz
DECOUPLE H1, 499.7506055 MHz
Power 43 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 131072
Total time 34 min



5

220 200 180 160 140 120 100 80 60 40 20 0 ppm

STANDARD PROTON PARAMETERS

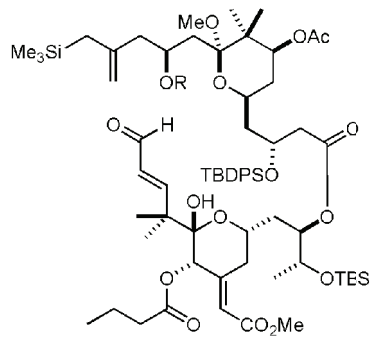
Archive directory:
/export/home/schrier/vnmrsys/data
Sample directory:

File: 7x141_600

Pulse Sequence: s2pul
Solvent: CDCl3

Temp. 25.0 C / 298.1 K
User: 1-15-87

Relax. delay 0.500 sec
Pulse 37.0 degrees
Acq. time 4.000 sec
Width 8000.0 Hz
8 repetitions
OBSERVE H1, 599.7972892 MHz
DATA PROCESSING
FT size 65536
Total time 19 min



17 R = TES

C13par

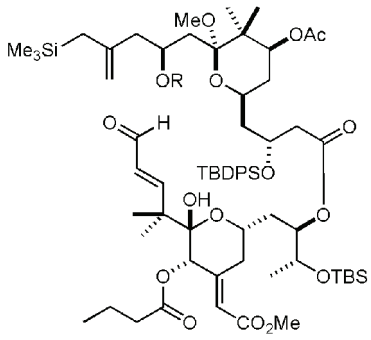
Archive directory:
/export/home/schrier/vnmrsys/data
Sample directory:

File: 7x141_C

Pulse Sequence: s2pul
Solvent: CDCl3

User: 1-15-87

Relax. delay 0.500 sec
Pulse 38.3 degrees
Acq. time 1.500 sec
Width 33003.3 Hz
260 repetitions
OBSERVE C13, 125.6618627 MHz
DECOUPLE H1, 499.7505605 MHz
Power 43 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 2.0 Hz
FT size 131072
Total time 34 min



17 R = TES

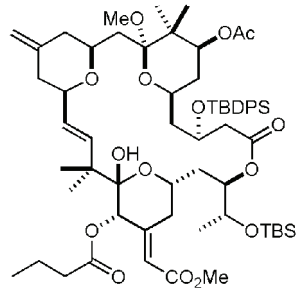
STANDARD PROTON PARAMETERS

Archive directory:
/export/home/schrier/vnmrsys/data
Sample directory:

File: 7x230_CH

Pulse Sequence: s2pul
Solvent: CDCl3

Pulse 30.5 degrees
Acq. time 4.000 sec
Width 8000.0 Hz
24 repetitions
OBSERVE H1, 499.7485737 MHz
DATA PROCESSING
FT size 65536
Total time 17 min



18

C13par

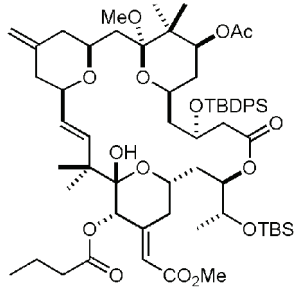
Archive directory:
/export/home/schrier/vnmrsys/data
Sample directory:

File: 7x230_C

Pulse Sequence: s2pul
Solvent: CDCl3

User: 1-15-87

Relax. delay 0.500 sec
Pulse 38.3 degrees
Acq. time 1.500 sec
Width 33003.3 Hz
640 repetitions
OBSERVE C13, 125.6618612 MHz
DECOUPLE H1, 499.7505605 MHz
Power 43 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 2.0 Hz
FT size 131072
Total time 5 hr, 34 min



18

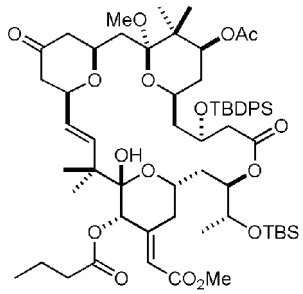
7x154

Archive directory:
/export/home/schrier/vnmrsys/data
Sample directory:

File: 7x154

Pulse Sequence: s2pul
Solvent: Benzene

Pulse 30.5 degrees
Acq. time 4.000 sec
Width 8000.0 Hz
84 repetitions
OBSERVE H1, 499.7486026 MHz
DATA PROCESSING
Resol. enhancement -0.0 Hz
FT size 65536
Total time 17 min



S8

C13par

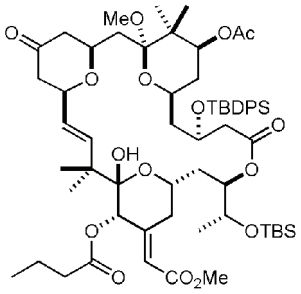
Archive directory:
/export/home/schrier/vnmrsys/data
Sample directory:

File: 7x154_C

Pulse Sequence: s2pul
Solvent: Benzene

User: 1-15-87

Relax. delay 0.900 sec
Pulse 38.3 degrees
Acq. time 1.500 sec
Width 33003.3 Hz
1896 repetitions
OBSERVE C13, 125.6618412 MHz
DECOUPLE H1, 499.7506055 MHz
Power 43 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.5 Hz
FT size 131072
Total time 669 hr, 9 min



S8

STANDARD PROTON PARAMETERS

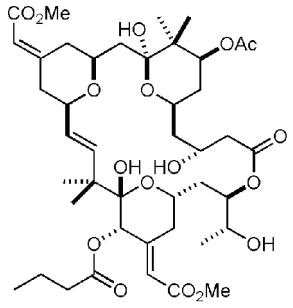
Archive directory:
/export/home/schrier/vnmrsys/data
Sample directory:

File: 7x258_159E

Pulse Sequence: s2pul
Solvent: CD3OD

Temp. 25.0 C / 298.1 K
User: 1-15-87

Relax. delay 0.500 sec
Pulse 52.5 degrees
Acq. time 4.000 sec
Width 8000.0 Hz
52 repetitions
OBSERVE H1, 599.7996488 MHz
DATA PROCESSING
FT size 65536
Total time 19 min



S9

8 7 6 5 4 3 2 1 0 ppm

C13par

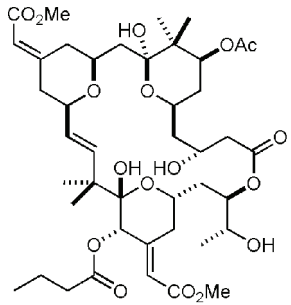
Archive directory:
/export/home/schrier/vnmrsys/data
Sample directory:

File: 7x158E_C

Pulse Sequence: s2pul
Solvent: CDCl3

User: 1-15-87

Relax. delay 1.000 sec
Pulse 38.3 degrees
Acq. time 1.500 sec
Width 33003.3 Hz
14196 repetitions
OBSERVE C13, 125.6618602 MHz
DECOUPLE H1, 499.7505605 MHz
Power 43 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 2.0 Hz
FT size 131072
Total time 6969 hr, 19 min



S9

STANDARD PROTON PARAMETERS

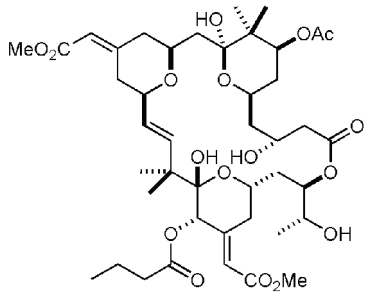
Archive directory:
/export/home/schrier/vnmrsys/data
Sample directory:

File: 7x159A_CD3OD_1mg_mL

Pulse Sequence: s2pul
Solvent: CD3OD

Temp. 25.0 C / 298.1 K
User: 1-15-87

Relax. delay 0.500 sec
Pulse 50.8 degrees
Acq. time 4.000 sec
Width 8000.0 Hz
72 repetitions
OBSERVE H1, 599.7996308 MHz
DATA PROCESSING
FT size 65536
Total time 19 min



Bryostatin 9

S60

8 7 6 5 4 3 2 1 0 ppm

Bryo 9 at 1 mg/mL in CD3OD

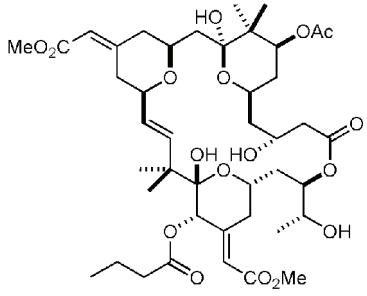
Archive directory:
/export/home/schrier/vnmrsys/data
Sample directory:

File: Bryo9_CD3OD_1mg_mL

Pulse Sequence: s2pul
Solvent: CD3OD

Temp. 25.0 C / 298.1 K
User: 1-15-87

Relax. delay 0.500 sec
Pulse 50.8 degrees
Acq. time 4.000 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 599.7996488 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 65536
Total time 19 min



Bryostatin 9
(Authentic)

8 7 6 5 4 3 2 1 0 ppm

Bryostatin 9

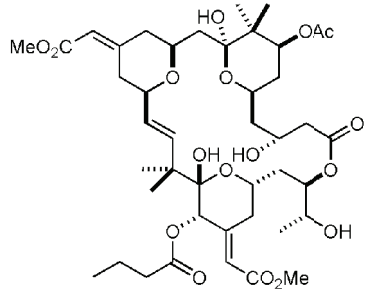
Archive directory:
/export/home/schrier/vnmrsys/data
Sample directory:

File: 7x159A_C

Pulse Sequence: s2pul
Solvent: CDCl3

User: 1-15-87

Relax. delay 0.900 sec
Pulse 38.3 degrees
Acq. time 1.500 sec
Width 33003.3 Hz
15184 repetitions
OBSERVE C13, 125.6618607 MHz
DECOUPLE H1, 499.7505605 MHz
Power 43 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 2.0 Hz
FT size 131072
Total time 6691 hr, 32 min



Bryostatin 9