Supporting Information

Total Synthesis of (-)-2-*Epi*-Peloruside A

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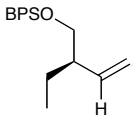
I. Materials and Methods

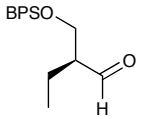
Except as otherwise indicated, all reactions were carried out under an argon atmosphere in flame- or oven-dried glassware, and solvents were freshly distilled. The argon was deoxygenated and dried by passage through an OXICLEAR™ filter from Aldrich and Drierite tube, respectively. Diethyl ether (Et_2O) and tetrahydrofuran (THF) were distilled from sodium/benzophenone-ketyl. Dichloromethane (CH_2Cl_2) was distilled from calcium hydride. All other reagents were purchased from Aldrich or Acros and used as received. Reactions were monitored by thin layer chromatography (TLC) with 0.25-mm E. Merck pre-coated silica gel plates. Silica gel for flash chromatography (particle size 0.040-0.063 mm) was supplied by Bodman, Silicycle and Sorbent Technologies. Yields refer to chromatographically and spectroscopically pure compounds unless otherwise noted. ^{1}H and ^{13}C spectra were recorded on a Bruker AMX-500 spectrometer. Chemical shifts are reported as δ values relative to internal chloroform (δ 7.26) or benzene (δ 7.15) for ^{1}H and either chloroform (δ 77.0) or benzene (δ 128.0) for ^{13}C. Infrared spectra were recorded on either a Perkin-Elmer model 283B, Perkin-Elmer model 1600 FTIR, or Jasco FTIR-480plus spectrometer. Optical rotations were measured on a Perkin-Elmer model 241 polarimeter in the solvent indicated. High resolution mass spectra were measured at the University of Pennsylvania Mass Spectrometry Center by Dr. Rakesh Kohli or Mr. John Dykins on either a VG Micromass 70/70H or VG ZAB-E spectrometer.

II. Experimental procedure



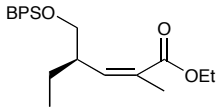
(-)-**SI 1**

Olefin (-)-SI 1: To a solution of alcohol (+)-**5** (850 mg, 8.48 mmol) in DCM (8.5 mL) at rt. was added BPSCl (2.6 mL, 10.2 mmol), NEt_3 (3.54 mL, 25.4 mmol) and DMAP (100 mg, 0.85 mmol). The reaction mixture was stirred for 15 h and quenched with water (20 mL). The layers were separated and the water layer extracted with DCM (3 x 25 mL), dried over anhydrous Na_2SO_4, filtered and concentrated. Flash chromatography (40:1 hexanes/ethyl acetate) afforded olefin (-)-**SI 1** as a colorless oil (2.46 g, 86%). $[\alpha]^{20}_D$ -13.76° (*c* 1.09, $CHCl_2$); IR (film) 3071 (m), 2960 (m), 2930 (m), 2857 (m), 1112 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.99-7.95 (m, 4H), 7.66-7.58 (m, 6H), 5.98-5.90 (m, 1H), 5.32 (s, 1H), 5.31-5.29 (m, 1H), 3.90 (s, 1H), 3.89 (s, 1H), 1.94-1.86 (m, 1H), 1.63-1.54 (m, 1H), 1.37 (s, 9H), 1.13 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 145.9, 141.6, 139.8, 135.5, 133.6, 121.6, 72.9, 54.2, 32.7, 29.5, 25.2, 17.5; high resolution mass spectrum (CI+) *m/z* 337.1988 [(M+); calcd for $C_{22}H_{29}OSi$: 337.1992]



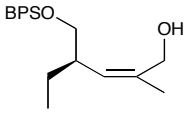
(+)-**6**

Aldehyde (+)-6: To a solution of olefin (-)-**SI 1** (2.3 g, 6.79 mmol) in DCM (7 mL) at –78 °C was bubbled O_3 at a flow of 2.1 and 90 volts for 0.5 hr. The reaction mixture was quenched with a solution of PPh_3 (205 mg, 7.81 mmol) in DCM (2 mL) slowly over 5 min. and the PPh_3 flask rinsed with DCM (0.5 mL) and added. The reaction was warmed to rt. over 0.5 h and concentrated. Flash chromatography (40:1 hexanes/ethyl acetate) afforded aldehyde (+)-**6** as a colorless oil (2.05 g, 89%). $[\alpha]^{20}_D$ +21.5 (c 0.95, $CHCl_3$); IR (film) 3071 (m), 2966 (s), 2931 (s), 2855 (s), 2710 (m), 1743 (s), 1589 (m), 1473 (s), 1428 (s), 1113 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.77 (d, *J* = 2.4 Hz, 1H), 7.68 (m, 4H), 7.46-7.35 (m, 6H), 3.92 (m, 2H), 2.40 (m, 1H), 1.75 (m, 1H), 1.55 (m, 1H), 1.07 (s, 9H), 0.91 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 204.6, 135.5, 133.2, 133.1, 129.8, 127.7, 62.3, 55.8, 26.7, 19.2, 18.5, 11.4; high resolution mass spectrum (ES+) *m/z* 363.1752 [$(M+Na)^+$; calcd for $C_{21}H_{28}O_2SiNa^+$: 363.1756].



(-)-**8**

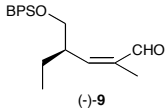
(*Z*)-α,β-Unsaturated Ester (-)-8. To a solution of ethyl {bis(2,2,2-trifluoroethyl)phosphono}-propionate **7** (19.8 g, 57.2 mmol, 1.0 equiv.) and 18-crown-6 (53.0 g, 286.3 mmol, 3.5 equiv.) in THF (270 mL) was added dropwise potassium hexamethyldisilazide (114.5 mL, 57.2 mmol, 0.5 M in THF, 1.0 equiv.) at –78 ^{0}C. After the reaction mixture was stirred for 10 min at –78 ^{o}C, a solution of aldehyde (+)-**6** in THF (30 mL) was added at –78 ^{o}C *via* cannula. The resulting mixture was stirred for 2 h at –78 ^{o}C, poured into saturated aqueous NH_4Cl (200 mL), and then extracted with EtOAc (350 mL). The organic layers were washed with brine (300 mL), dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purification by flash chromatography on silica gel (5/1, hexanes/EtOAc) gave (*Z*)-α,β-unsaturated ester (-)-**8** (21.7 g, 89% yield) as a colorless oil: $[\alpha]_D^{20}$ -36.0 (*c* 0.75, $CHCl_3$); IR (film) 2960 (m), 1719 (s), 1457 (m), 1428 (m), 1218 (s), 1112 (s) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.66-7.60 (m, 4H), 7.44-7.30 (m, 6H), 5.76 (dd, *J* = 10.2, 1.4 Hz, 1H), 4.17 (q, *J* = 7.1 Hz, 2H), 3.61 (m, 2H), 3.24 (m, 1H), 1.92 (d, *J* = 1.3 Hz, 3H), 1.62 (m, 1H), 1.33 (m, 1H), 1.27 (t, *J* = 7.1 Hz, 3H), 1.04 (s, 9H), 0.86 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.1, 144.2, 135.6, 133.9, 129.4, 128.3, 127.5, 66.6, 60.0, 42.9, 26.8, 24.4, 20.9, 19.3, 14.2, 11.6; high resolution mass spectrum (ES+) *m/z* 447.2336 [(M+Na)$^{+}$; calcd for $C_{26}H_{36}O_3SiNa^{+}$: 447.2331].



(-)-**SI 2**

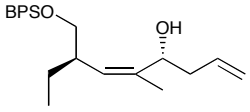
Allyl Alcohol (-)-SI 2. To a solution of ester (-)-**8** (5.20 g, 12.2 mmol) in CH_2Cl_2 (100 mL) was added dropwise diisobutylaluminum hydride (30.6 mL, 30.6 mmol, 1.0 M in hexanes, 2.5 equiv.) at –40 ^{o}C. The reaction mixture was stirred for 1 h at –40 ^{o}C, water (20 mL) and 1 N aqueous HCl (20 mL) were added dropwise, and then the resulting mixture was extracted with EtOAc (100 mL). The organic layers were washed with brine (300 mL), dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purification by flash chromatography on silica gel (3/1, hexanes/EtOAc) gave allyl alcohol (-)-**SI 2** (4.40 g, 94% yield) as a colorless oil: $[\alpha]_D^{20}$ -14.1 (*c* 0.45, $CHCl_3$); IR (film) 3388 (m), 2960 (s), 2858 (s), 1473 (m), 1428 (s), 1113 (s), 1007 (m) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.68-

7.64 (m, 4H), 7.44-7.37 (m, 6H), 5.00 (d, *J* = 10.1 Hz, 1H), 4.17 (d, *J* = 11.9 Hz, 1H), 3.94 (d, *J* = 11.9 Hz, 1H), 3.57 (dd, *J* = 9.7, 5.3 Hz, 1H), 3.35 (dd, *J* = 9.6, 8.2 Hz, 1H), 2.66 (m, 1H), 1.85 (d, *J* = 1.3 Hz, 3H), 1.44 (m, 1H), 1.07 (m, 1H), 1.05 (s, 9H), 0.82 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.2, 135.6, 135.6, 133.4, 130.7, 129.7, 127.7, 127.6, 67.6, 62.2, 42.4, 26.8, 24.5, 22.1, 19.1, 11.7; high resolution mass spectrum (ES+) *m/z* 405.2242 [$(M+Na)^+$; calcd for $C_{24}H_{34}O_2SiNa^+$: 405.2226].



(-)-**9**

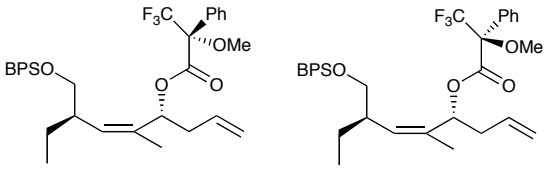
Aldehyde (-)-9. To a solution of alcohol (-)-**SI 2** (300 mg, 0.784 mmol) in CH_2Cl_2 (7.0 mL) was added pyridine (0.32 mL, 3.92 mmol, 5.0 equiv.) and Dess-Martin periodinane (499 mg, 1.176 mmol, 1.5 equiv.) at 0 °C. The reaction mixture was stirred for 10 min at room temperature, and poured into 1:1 mixture (20 mL) of saturated aqueous $NaHSO_3$ and saturated aqueous $NaHCO_3$. The resulting mixture was stirred for 15 min at room temperature, and extracted with EtOAc (30 mL). The organic layers were washed with brine (30 mL), dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purification by flash chromatography on silica gel (5/1, hexanes/EtOAc) gave aldehyde (-)-**9** (260 mg, 87% yield) as a colorless oil: $[\alpha]_D^{20}$ -35.4 (*c* 1.09, $CHCl_3$); IR (film) 2960 (m), 2858 (m), 1685 (s), 1472 (m), 1427 (m), 1112 (s) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.00 (s, 1H), 7.67-7.60 (m, 4H), 7.46-7.33 (m, 6H), 6.23 (dd, *J* = 10.9, 1.4 Hz, 1H), 3.69 (dd, *J* = 10.0, 5.3 Hz, 1H), 3.53 (dd, *J* = 10.0, 7.3 Hz, 1H), 3.18 (m, 1H), 1.81 (d, *J* = 1.3 Hz, 3H), 1.60 (m, 1H), 1.26 (m, 1H), 1.03 (s, 9H), 0.86 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 191.9, 151.3, 137.8, 135.6, 135.5, 133.4, 133.4, 129.7, 127.7, 127.7, 66.7, 41.0, 26.8, 24.3, 19.1, 16.6, 11.7; high resolution mass spectrum (ES+) *m/z* 403.2056 [$(M+Na)^+$; calcd for $C_{24}H_{32}O_2SiNa^+$: 403.2069].



(-)-**10**

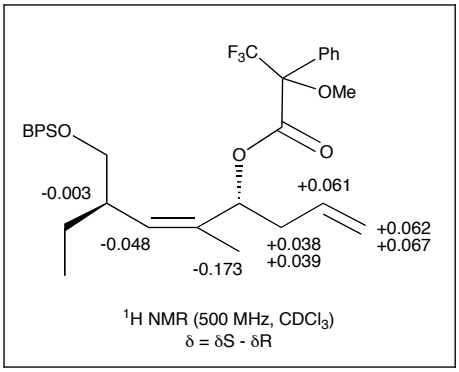
Homoallyl Alcohol (-)-10. To a solution of (+)-$Ipc_2B(OMe)$ (10.3 g, 32.5 mmol, 1.8 equiv.) in Et_2O (150 mL) was added dropwise vinylmagnesium bromide (32.5 mL, 32.5 mmol, 1.0 M in Et_2O, 1.8 equiv.) at –78 °C *via* syringe. The reaction mixture was stirred for 15 min at –78 °C, and for 1 h at room temperature. The reaction

mixture was cooled to –78 °C, and a solution of aldehyde (-)-**9** (6.98 g, 18.34 mmol) in Et_2O (30 mL) was added dropwise via cannula. The resulting mixture was stirred for 1 h at –78 °C, poured into 1:1 solution (50 mL) of 1 M aqueous NaOH and 30% aqueous hydrogen peroxide. The resulting mixture was stirred for 30 min at room temperature, and extracted with CH_2Cl_2 (300 mL). The organic layers were washed with brine (300 mL), dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purification by flash chromatography on silica gel (20/1, hexanes/EtOAc) gave homoallyl alcohol (-)-**10** (6.0 g, 77% yield) as a colorless oil: $[\alpha]_D^{20}$ -29.1 (*c* 0.85, $CHCl_3$); IR (film) 3433 (m), 3072 (m), 2931 (s), 2858 (s), 1641 (m), 1589 (m), 1473 (s), 1429 (s), 1263 (m), 1188 (m), 1112 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.67-7.65 (m, 4H), 7.45-7.36 (m, 6H), 5.72 (m, 1H), 5.07 (dd, *J* = 17.1, 1.5 Hz, 1H), 5.00 (app t, *J* = 9.5 Hz, 2H), 4.44 (dd, *J* = 8.0, 5.4 Hz, 2H), 3.52 (dd, *J* = 9.7, 6.2 Hz, 1H), 3.41 (dd, *J* = 9.7, 6.8 Hz, 1H), 2.68 (m, 1H), 2.33 (m, 1H), 2.23 (m, 1H), 1.74 (d, *J* = 1.0 Hz, 3H), 1.59 (m, 1H), 1.18 (m, 1H), 1.05 (s, 9H), 0.87 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.3, 135.7, 135.7, 135.6, 134.9, 133.7, 133.6, 129.8, 129.6, 127.6, 127.6, 117.3, 70.5, 67.4, 41.5, 40.2, 26.8, 24.7, 19.2, 19.1, 11.7; high resolution mass spectrum (ES+) *m/z* 445.2542 [$(M+Na)^+$; calcd for $C_{27}H_{38}O_2SiNa^+$: 445.2539].



(*R*)-MTPA Ester of (-)-**10**

(*S*)-MTPA Ester of (-)-**10**

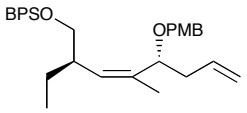


^1H NMR (500 MHz, $CDCl_3$)
$\delta = \delta S - \delta R$

The (*S*)-MTPA Ester of (-)-10. To a solution of (-)-**10** (5 mg, 0.0118 mmol) and 4-(*N,N*-dimethylamino)pyridine (6 mg, 0.0473 mmol, 4.0 equiv.) in CH_2Cl_2 (0.3 μL) was added (*R*)-(-)-α-methoxy-α-trifluoromethylphenylacetyl chloride [(*R*)-MTPACl, 4.5 μL, 0.0237 mmol, 2.0 equiv.). After 3 h, direct purification by Preparative-TLC (5/1, hexanes/EtOAc, 500 μm plate) gave the (*S*)-MTPA ester of (-)-**10** (6.1 mg, 81% yield) as a colorless oil: ^1H NMR (500 MHz, $CDCl_3$) δ 7.65 (m, 4H), 7.52 (d, *J* = 7.2 Hz, 2H), 7.45-7.34 (m, 9H), 5.88 (dd, *J* = 8.3, 6.2 Hz, 1H), 5.48 (m, 1H), 5.13 (d, *J* = 10.3 Hz, 1H), 4.98 (dd, *J* = 17.0, 1.4 Hz, 1H), 4.91 (d, *J* = 10.2 Hz,

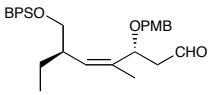
1H), 3.55 (s, 3H), 3.50 (m, 2H), 2.68 (m, 1H), 2.47 (m, 1H), 2.25 (m, 1H), 1.75 (m, 2H), 1.52 (s, 3H), 1.05 (s, 9H), 0.87 (t, J = 7.5 Hz, 3H).

The (*R*)-MTPA Ester of (-)-10. In similar fashion, the (*R*)-MTPA ester of (-)-**10** was obtained as a colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65 (m, 4H), 7.49 (d, J = 7.2 Hz, 2H), 7.45-7.30 (m, 9H), 5.95 (dd, J = 8.2, 6.2 Hz, 1H), 5.42 (m, 1H), 5.18 (d, J = 10.3 Hz, 1H), 4.91 (dd, J = 17.1, 1.4 Hz, 1H), 4.84 (d, J = 10.1 Hz, 1H), 3.60-3.45 (m, 2H), 3.52 (s, 3H), 2.69 (m, 1H), 2.43 (m, 1H), 2.22 (m, 1H), 1.70 (m, 2H), 1.70 (s, 3H), 1.05 (s, 9H), 0.82 (t, J = 7.5 Hz, 3H).



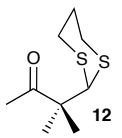
(-)-**SI 3**

PMB Ether (-)-SI 3. To a suspension of sodium hydride (189 mg, 4.73 mmol, 65% wt., 2.0 equiv.) in THF (12 mL) was added dropwise a solution of homoallyl alcohol (-)-**10** (1.0 g, 2.37 mmol) in DMF (12 mL) at 0 °C *via* cannula. After the reaction mixture was stirred for 10 min at 0 °C, *p*-methoxybenzyl chloride (0.64 mL, 4.73 mmol, 2.0 equiv.) and tetra-*n*-butylammonium iodide (874 mg, 2.37 mmol, 1.0 equiv.) was added at 0 °C. The resulting mixture was stirred for 12 h at room temperature, poured into water (30 mL), and then extracted with EtOAc (100 mL). The organic layers were washed with brine (100 mL), dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purification by flash chromatography on silica gel (10/1 to 5/1, hexanes/EtOAc) gave allyl alcohol (-)-**SI 3** (1.00 g, 78% yield) as a pale yellow oil: $[\alpha]_D^{20}$ -15.3 (*c* 1.02, $CHCl_3$); IR (film) 3070 (m), 2966 (m), 2931 (m), 2858 (m), 1784 (s), 1700 (s), 1472 (m), 1428 (m), 1390 (s), 1349 (s), 1211 (s), 1112 (s) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70-7.65 (m, 4H), 7.45-7.35 (m, 6H), 7.26 (d, J = 8.6 Hz, 2H), 6.89 (d, J = 8.6 Hz, 2H), 5.57 (m, 1H), 5.23 (d, J = 9.7 Hz, 1H), 4.93 (dd, J = 3.3, 1.4 Hz, 1H), 4.83 (m, 1H), 4.41 (d, J = 11.3 Hz, 1H), 4.17 (m, 2H), 3.81 (s, 3H), 3.53 (dd, J = 9.8, 4.9 Hz, 1H), 3.43 (dd, J = 9.8, 7.3 Hz, 1H), 2.40 (m, 2H), 2.12 (m, 1H), 1.81 (m, 1H), 1.71 (d, J = 1.3 Hz, 3H), 1.31 (m, 1H), 1.07 (s, 9H), 0.92 (t, J = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.1, 135.8, 135.6, 135.6, 135.1, 134.0, 133.9, 131.7, 131.1, 129.5, 129.5, 129.1, 127.6, 116.4, 113.8, 76.5, 69.6, 67.3, 55.3, 41.4, 38.5, 26.9, 24.9, 19.3, 17.7, 11.8; high resolution mass spectrum (ES+) *m/z* 565.3118 [(M+Na)$^+$; calcd for $C_{35}H_{46}O_3SiNa^+$: 565.3114].



(-)-**11**

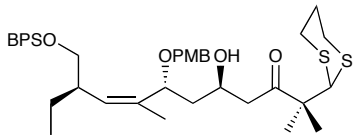
Aldehyde (-)-11. To a solution of PMB ether (-)-**SI 3** (100 mg, 0.184 mmol) in 1,4-dioxane (1.2 mL) and water (0.4 mL) was added 2,6-lutidine (42 μL, 0.368 mmol, 2.0 equiv.), osmium tetraoxide (23 μL, 3.68 μmol, 4% in water), and $NaIO_4$ (158 mg, 0.737 mmol) at room temperature. The reaction mixture was stirred for 1.5 h at room temperature, poured into water, and then extracted with EtOAc (5.0 mL). The organic layers were washed with brine (100 mL), dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purification by flash chromatography on silica gel (10/1, hexanes/EtOAc) gave aldehyde (-)-**11** (85.2 mg, 85% yield) as a pale yellow oil: $[\alpha]^{20}_D$ –26.0 (*c* 0.82, $CHCl_3$); IR (film) 2958 (s), 2931 (s), 2855 (s), 1727 (s), 1512 (s), 1428 (m), 1248 (s), 1112 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.53 (dd, *J* = 2.9, 1.3 Hz, 1H), 7.64-7.60 (m, 4H), 7.43-7.33 (m, 6H), 7.21 (d, *J* = 8.6 Hz, 2H), 6.87 (d, *J* = 8.6 Hz, 2H), 5.22 (d, *J* = 10.1 Hz, 1H), 4.73 (dd, *J* = 10.1, 3.4 Hz, 1H), 4.39 (d, *J* = 11.2 Hz, 1H), 4.17 (d, *J* = 11.2 Hz, 1H), 3.80 (s, 3H), 3.49 (dd, *J* = 10.2, 6.4 Hz, 1H), 3.44 (dd, *J* = 9.8, 5.8 Hz, 1H), 2.68 (ddd, *J* = 16.3, 10.2, 3.0 Hz, 1H), 2.48 (m, 1H), 2.11 (ddd, *J* = 16.3, 3.4, 1.4 Hz, 1H), 1.71 (s, 3H), 1.70 (m, 1H), 1.27 (m, 1H), 1.04 (s, 9H), 0.92 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.8, 159.3, 135.6, 135.6, 134.8, 133.8, 133.4, 132.5, 130.4, 129.6, 129.6, 129.2, 127.6, 113.8, 71.6, 69.9, 67.4, 55.3, 47.8, 41.7, 26.8, 24.9, 19.3, 17.8, 11.8; high resolution mass spectrum (ES+) *m/z* 567.2897 [$(M+Na)^+$; calcd for $C_{34}H_{44}O_4SiNa^+$: 567.2907].



12

Ketone 12. To a solution of known dithiane aldehyde[1] (4.95 g, 26 mmol) in THF (86 mL) at –15 °C was added MeMgBr (26 mL, 78 mmol of a 3.0 M solution in ether) over 0.5 h, warmed to 0 °C and stirred for 0.5 hr. The reaction mixture was quenched with saturated aq. NH_4Cl (30 mL) and warmed to rt. The layers were separated and the aqueous layer extracted with CH_2Cl_2 (3 x 25 mL), dried over Na_2SO_4, filtered and concentrated in vacuo. The resulting alcohol was azeotroped with benzene (2 x 10 mL) and used without purification. To a solution of crude alcohol in CH_2Cl_2 (52 mL) at –15 °C was added DMSO (11.07 mL, 156 mmol), DIEA (13.6 mL, 78 mmol) and stirred for 10 min. To the reaction mixture was added SO_3•pyridine in one portion and slowly warmed to 0 °C over 0.5 h. The reaction mixture was quenched with saturated aq. NH_4Cl (30 mL) and warmed to rt. The

layers were separated and the aqueous layer extracted with CH_2Cl_2 (3 x 25 mL), dried over anhydrous Na_2SO_4, filtered and concentrated. Flash chromatography (6:1, hexanes/ethyl acetate) afforded ketone **12** as a white solid (4.39 g, 83%, 2 steps). Mp 82-83 °C; IR (film) 2978 (m), 2929 (m), 2890 (m), 2828 (m), 1700 (s), 1280 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.23 (s, 1H), 2.77-2.71 (m, 2H), 2.66-2.62 (m, 2H), 1.98 (s, 3H), 1.91-1.87 (m, 1H), 1.62-1.53 (m, 1H), 1.02 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 215.1, 62.4, 57.6, 36.7, 31.4, 30.9, 27.5; high resolution mass spectrum (CI+) *m/z* 204.0647 [(M+); calcd for $C_9H_{16}OS_2$: 204.0643].

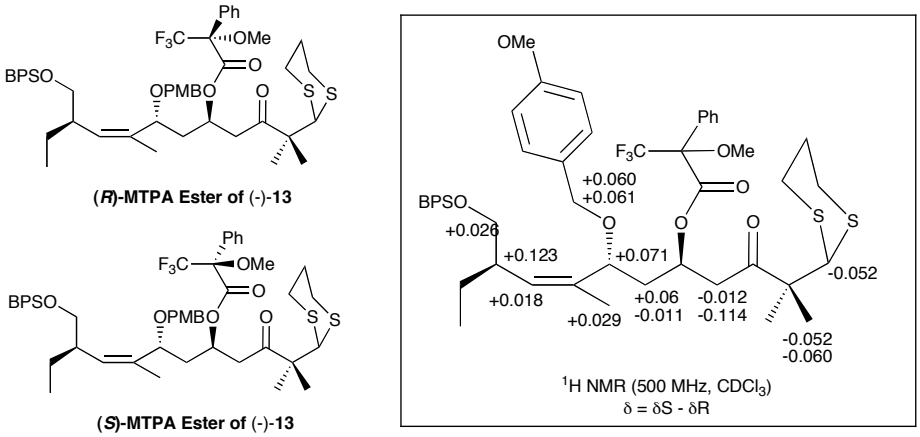


(-)-**13**

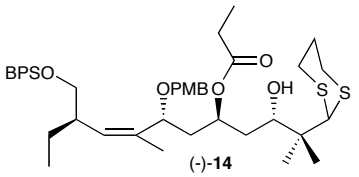
Mukaiyama-aldol Product (-)-13. To a solution of ketone **12** (225 mg, 1.1 mmol, 1.2 equiv.) in THF (11 mL) was added dropwise lithium hexamethyldisilazide (2.2 mL, 2.2 mmol, 1.0 M in THF, 2.4 equiv.) at 0 °C. After the reaction mixture was stirred for 30 min at 0 °C, trimethylsilyl chloride (0.21 mL, 1.65 mmol, 1.8 equiv.) was added dropwise at 0 °C *via* syringe. The resulting mixture was stirred for the additional 1 h at 0 °C, poured into saturated aq. $NaHCO_3$ (5.0 mL), and then extracted with Et_2O (3 x10 mL). The organic layers were washed with brine (10 mL), dried over $MgSO_4$, filtered, and concentrated *in vacuo* to give the corresponding silyl enol ether.

To a solution of the crude silyl enol ether and aldehyde **(-)-11** (500 mg, 0.92 mmol) in CH_2Cl_2 (11 mL) was added dropwise borone trifluoride-diethyl ether complex (128 μL, 1.0 mmol, 1.1 equiv.) at –78 °C *via* syringe. The reaction mixture was stirred for 11 h at -78 °C, poured into saturated aqueous $NaHCO_3$ (5.0 mL), and then extracted with CH_2Cl_2 (3 x 10 mL). The organic layers were washed with brine (10 mL), dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purification by flash chromatography on silica gel (10/1 to 5/1, hexanes/EtOAc) gave aldol product (-)-**13** (645 mg, 86% yield) as a pale yellow oil: $[\alpha]_D^{20}$ –19.70 (*c* 0.66, $CHCl_3$); IR (film) 3510 (m), 2955 (s), 1698 (m), 1513 (m), 1247 (m), 1108 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.67 (m, 4H), 7.45-7.30 (m, 6H), 7.26 (d, *J* = 8.5 Hz, 2H), 6.87 (d, *J* = 8.5 Hz, 2H), 5.21 (d, *J* = 10.1 Hz, 1H), 4.55 (d, *J* = 10.5 Hz, 1H), 4.39 (d, *J* = 11.0 Hz, 1H), 4.37 (s, 1H), 4.30 (m, 1H), 4.18 (d, *J* = 11.0 Hz, 1H), 3.80 (s, 3H), 3.54 (dd, *J* = 9.6, 5.4 Hz, 1H), 3.48 (dd, *J* = 9.6, 6.1 Hz, 1H), 3.05 (br, 1H), 2.90-2.75 (m, 4H), 2.64 (dd, *J* = 17.8, 2.9 Hz, 1H), 2.55 (m, 2H), 2.06 (m, 1H), 1.85-1.65 (m, 3H), 1.73 (s, 3H), 1.42 (m, 1H), 1.25 (m, 1H), 1.23 (s, 3H), 1.22 (s, 3H), 1.05 (s, 9H), 0.90 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 213.1, 159.2, 136.4, 135.7, 135.7,

134.0, 134.0, 131.3, 130.9, 129.5, 129.5, 129.4, 127.6, 127.6, 113.9, 73.8, 70.1, 67.3, 65.0, 56.9, 55.3, 52.2, 44.7, 41.3, 41.1, 31.3, 27.0, 25.9, 24.9, 22.1, 22.0, 19.4, 18.1, 14.2, 11.8; high resolution mass spectrum (ES+) *m/z* 771.3532 [(M+Na)$^+$; calcd for $C_{43}H_{60}O_5S_2SiNa^+$: 771.3549].

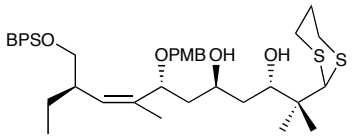


The MTPA Esters of (-)-13. In similar fashion described above, the (*S*)- and (*R*)-MTPA ester of (-)-**13** was obtained as a pale yellow oil, respectively: **(*S*)-MTPA Ester of (-)-13:** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.63 (dd, *J* = 7.8, 1.3 Hz, 4H), 7.49 (d, *J* = 7.2 Hz, 2H), 7.42-7.25 (m, 13H), 6.85 (d, *J* = 8.6 Hz, 2H), 5.80 (m, 1H), 5.25 (d, *J* = 10.1 Hz, 1H), 4.35-4.25 (m, 3H), 4.09 (d, *J* = 10.8 Hz, 1H), 3.78 (s, 3H), 3.48 (m, 2H), 3.40 (s, 3H), 2.98 (dd, *J* = 17.7, 7.2 Hz, 1H), 2.90-2.70 (m, 4H), 2.67 (dd, *J* = 17.7, 5.2 Hz, 1H), 2.38 (m, 1H), 2.04 (m, 1H), 1.78 (m, 1H), 1.71 (s, 3H), 1.60 (m, 1H), 1.35-1.20 (m, 3H), 1.13 (s, 3H), 1.10 (s, 3H), 1.05 (s, 9H), 0.85 (t, *J* = 7.4 Hz, 3H). **(*R*)-MTPA Ester of** (-)-**13:** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65 (dd, *J* = 7.8, 1.3 Hz, 4H), 7.48 (d, *J* = 7.6 Hz, 2H), 7.45-7.25 (m, 13H), 6.86 (d, *J* = 8.6 Hz, 2H), 5.76 (m, 1H), 5.23 (d, *J* = 10.3 Hz, 1H), 4.36 (s, 1H), 4.25 (d, *J* = 10.6 Hz, 1H), 4.20 (d, *J* = 10.6 Hz, 1H), 4.03 (d, *J* = 10.6 Hz, 1H), 3.45 (m, 2H), 3.42 (s, 3H), 3.40 (s, 3H), 2.99 (dd, *J* = 17.7, 7.2 Hz, 1H), 2.90-2.75 (m, 5H), 2.26 (m, 1H), 2.05 (m, 1H), 1.98 (m, 1H), 1.90-1.50 (m, 3H), 1.69 (s, 3H), 1.30 (m, 1H), 1.18 (s, 3H), 1.16 (s, 3H), 1.05 (s, 9H), 0.84 (t, *J* = 7.4 Hz, 3H).



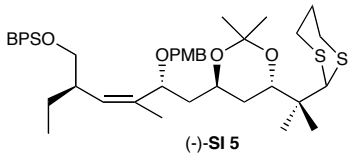
Alcohol (-)-14: To a solution of keto-alcohol (-)-**13** (2.38 g, 3.18 mmol) in THF (32 mL) at –10 °C was added freshly distilled EtCHO (1.15 mL, 15.88 mmol), followed by freshly prepared SmI_2 (6.35 mL of a 0.1 M

solution in THF, 0.635 mmol),[2] dropwise over a period of 5 min. The reaction mixture was stirred for 1 h, quenched with saturated aq. $NaHCO_3$ (30 mL). The layers were separated and the aq. phase extracted with CH_2Cl_2 (3 x 25 mL), dried over anhydrous Na_2SO_4, filtered and concentrated. Flash chromatography (10:1 to 5:1 hexanes/ethyl acetate) afforded alcohol (-)-**14** as a colorless oil (2.56 g, 97%). $[\alpha]_D^{20}$ -27.08° (*c* 0.325, $CHCl_2$); IR (film) 3057 (m), 2958 (m), 2931 (m), 2857 (m), 1715 (s), 1197 (m), 1112 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.71-7.68 (m, 4H), 7.44-7.38 (m, 6H), 7.28 (d, *J* = 8.4 Hz, 2H), 6.88 (d, *J* = 8.3 Hz, 2H), 5.48-5.43 (m, 1H), 5.24 (d, *J* = 10.0 Hz, 1H), 4.40 (d, *J* = 11.0 Hz, 1H), 4.35 (s, 1H), 4.29 (d, *J* =10.6 Hz, 1H), 4.12 (d, *J* = 11.0 Hz, 1H), 3.79 (s, 3H), 3.69 (dd, *J* = 7.1, 5.5 Hz, 1H), 3.58-3.50 (m, 2H), 3.09 (br s, 1H), 2.92-2.82 (m, 4H), 2.48 (ddd, *J* = 14.3, 9.3, 5.2 Hz, 1H), 3.44-2.21 (m, 2H), 2.08-2.05 (m, 1H), 1.94 (ddd, *J* = 13.9, 11.2, 2.1 Hz, 1H), 1.86-1.78 (m, 1H), 1.76 (s, 3H), 1.70 (ddd, *J* = 20.2, 12.7, 7.4 Hz, 1H), 1.60 (dd, *J* = 10.5, 10.5 Hz, 1H), 1.53 (dd, *J* = 6.9, 5.7 Hz, 1H), 1.30 (ddd, *J* = 21.3, 15.4, 7.6 Hz, 1H), 1.13 (t, *J* = 7.5 Hz, 3H), 1.10 (s, 3H), 1.09 (s, 9H), 1.00 (s, 3H), 0.94 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.3, 159.0, 136.3, 135.5, 135.4, 133.6, 133.6, 131.1, 130.3, 129.4, 129.4, 127.5, 127.4, 113.6, 72.6, 69.9, 69.9, 69.2, 67.1, 59.0, 55.0, 41.9, 41.5, 40.4, 37.0, 31.3, 31.2, 27.6, 26.8, 26.7, 26.7, 26.6, 26.3, 24.7, 20.5, 19.7, 19.1, 17.8, 11.8, 9.3; high resolution mass spectrum (ES+) *m/z* 829.3986 [(M+Na)$^+$; calcd for $C_{46}H_{66}O_6S_2SiNa$: 829.3968].

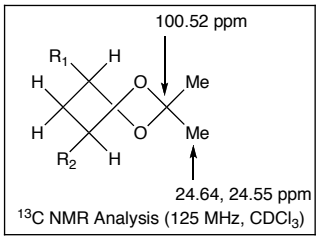


(-)-**SI 4**

***Anti*-diol (-)-SI 4.** $[\alpha]^{20}_D$ –5.26 (*c* 1.05, $CHCl_3$); IR (film) 3501 (m), 2957 (s), 1248 (s), 1111 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.64 (m, 4H), 7.43-7.35 (m, 6H), 7.23 (d, *J* = 8.6 Hz, 2H), 6.87 (d, *J* = 8.6 Hz, 2H), 5.22 (d, *J* = 10.0 Hz, 1H), 4.53 (dd, *J* = 9.7, 3.1 Hz, 1H), 4.39 (d, *J* = 11.1 Hz, 1H), 4.20 (s, 1H), 4.15 (d, *J* = 11.1 Hz, 1H), 4.07 (m, 1H), 3.99 (dd, *J* = 10.1, 2.0 Hz, 1H), 3.80 (s, 3H), 3.51 (m, 2H), 2.92-2.83 (m, 4H), 2.50 (m, 1H), 2.08 (m, 1H), 1.83 (m, 4H), 1.75 (d, *J* = 1.1 Hz, 3H), 1.70 (m, 1H), 1.50-1.40 (m, 3H), 1.28 (m, 1H), 1.05 (s, 9H), 1.03 (s, 3H), 0.97 (s, 3H), 0.91 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.2, 136.4, 135.6, 135.6, 133.9, 133.9, 131.5, 130.6, 129.6, 129.6, 129.3, 127.6, 127.6, 113.9, 74.3, 72.3, 69.9, 67.3, 66.8, 59.4, 55.3, 42.4, 41.4, 41.3, 37.4, 31.5, 31.4, 26.9, 26.4, 24.9, 21.1, 20.0, 19.3, 18.2, 11.8; high resolution mass spectrum (ES+) *m/z* 773.3741 [(M+Na)$^+$; calcd for $C_{43}H_{62}O_5S_2SiNa^+$: 773.3706].

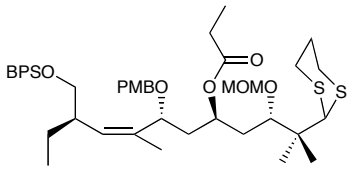


(-)-**SI 5**



^{13}C NMR Analysis (125 MHz, $CDCl_3$)

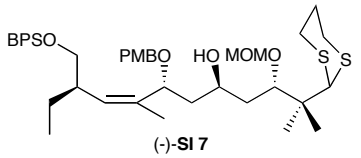
Acetonide (-)-SI 5. $[\alpha]^{20}_D$ –2.38 (*c* 0.78, $CHCl_3$); IR (film) 2929 (s), 2856 (s), 1247 (s), 1111 (s) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67 (m, 4H), 7.41-7.35 (m, 6H), 7.24 (d, *J* = 8.6 Hz, 2H), 6.86 (d, *J* = 8.6 Hz, 2H), 5.17 (d, *J* = 9.9 Hz, 1H), 4.47 (d, *J* = 9.1 Hz, 1H), 4.35 (d, *J* = 10.6 Hz, 1H), 4.20 (s, 1H), 4.11 (d, *J* = 10.7 Hz, 1H), 4.03 (dd, *J* = 9.9, 6.4 Hz, 1H), 3.94 (m, 1H), 3.79 (s, 3H), 3.53 (dd, *J* = 9.7, 5.1 Hz, 1H), 3.47 (dd, *J* = 9.7, 6.3 Hz, 1H), 2.95-2.85 (m, 4H), 2.56 (m, 1H), 2.07 (m, 1H), 1.84-1.62 (m, 4H), 1.70 (d, *J* = 1.1 Hz, 3H), 1.37-1.18 (m, 3H), 1.29 (s, 3H), 1.26 (s, 3H), 1.062 (s, 3H), 1.058 (s, 3H), 0.93 (s, 9H), 0.92 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.4, 136.8, 135.7, 134.0, 131.0, 130.9, 129.6, 129.5, 127.6, 127.6, 113.9, 100.5, 73.5, 70.4, 69.3, 67.4, 63.6, 58.6, 55.3, 41.5, 41.4, 41.0, 33.3, 31.5, 29.7, 26.9, 26.5, 25.0, 24.6, 24.6, 20.1, 19.4, 19.3, 18.0, 14.2, 11.9; high resolution mass spectrum (ES+) *m/z* 813.4028 [(M+Na)$^+$; calcd for $C_{46}H_{66}O_5S_2SiNa^+$: 813.4019].



(-)-**SI 6**

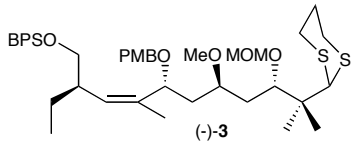
Dithiane (-)-SI 6: To a solution of alcohol (-)-**14** (650 mg, 0.8 mmol) in DMF (8 mL) was added DIEA (0.561 mL, 3.22 mmol), followed by MOMCl (0.122 mL, 1.61 mmol). The reaction mixture was stirred for 48 h, quenched with water (15 mL) and CH_2Cl_2 (15 mL), the layers were separated and the aq. phase extracted with CH_2Cl_2 (3 x 20 mL), dried over anhydrous Na_2SO_4, filtered and concentrated. Flash chromatography (5:1, hexanes/ethyl acetate) afforded dithiane (-)-**SI 6** as a colorless oil (720 mg, 99%). $[\alpha]^{20}_D$ -20.79° (*c* 0.380, $CHCl_2$); IR (film) 2958 (s), 2932 (s), 2895 (m), 2856 (m), 1734 (s), 1612 (m), 1111 (s), 1037 (s) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.74-7.71 (m, 4H), 7.42-7.35 (m, 8H), 6.87 (d, *J* = 8.4 Hz, 2H), 5.52-5.46 (m, 1H), 5.24 (d, *J* = 9.6 Hz, 1H), 4.82 (d, *J* = 6.1 Hz, 1H), 4.74 (d, *J* = 6.1 Hz, 1H), 4.40-4.34 (m, 3H), 4.21 (d, *J* = 10.5 Hz, 1H), 3.84 (d, *J* = 7.9 Hz, 1H), 3.73 (s, 3H), 3.62-3.55 (m, 3H), 3.37 (s, 3H), 2.90-2.77 (m, 4H), 2.35-2.28 (m, 2H), 2.04-1.98 (m, 2H), 1.79 (s, 3H), 1.79-1.58 (m, 5H), 1.32 (ddd, *J* = 20.0, 12.7, 6.5 Hz, 1H), 1.16 (t, *J* = 7.5 Hz, 3H), 1.12 (s, 12H),

1.05 (s, 3H), 0.96 (t, J = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.8, 159.1, 136.8, 135.6, 135.6, 133.8, 130.9, 130.8, 129.6, 127.7, 127.7, 113.6, 98.8, 80.3, 77.7, 73.8, 70.4, 69.8, 67.4, 59.0, 55.8, 55.0, 42.9, 41.7, 41.0, 37.6, 31.4, 31.3, 27.9, 27.0, 26.5, 24.9, 20.8, 20.6, 19.3, 18.1, 12.0, 9.5; high resolution mass spectrum (ES+) *m/z* 873.4200 [(M+Na)$^+$; calcd for $C_{46}H_{70}O_7S_2SiNa$: 873.4230].



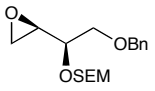
(-)-**SI 7**

Alcohol (-)-SI 7: To a solution of dithiane (-)-**SI 6** (670 mg, 0.787 mmol) in DCM (8 mL) at -78 °C was added DIBALH (1.57 mL, of a 1.0 M solution in hexanes, 1.57 mmol). The reaction mixture was stirred for 30 min., quenched with solid Na_2SO_4-H_2O (2 g) in 0.5 g portions over 10 min., diluted with CH_2Cl_2 (15 mL), dried over anhydrous Na_2SO_4, filtered and concentrated. Flash chromatography (10:1 hexanes/ethyl acetate) afforded alcohol (-)-**SI 7** as a colorless oil (597 mg, 95%). $[\alpha]_D^{20}$ -28.94° (*c* 1.55, $CHCl_2$); IR (film) 3493 (bd), 2956 (s), 2932 (s), 2896 (m), 2856 (m), 1513 (m), 1612 (m), 1111 (s), 1071 (s), 1033 (s) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71-7.69 (m, 4H), 7.47-7.39 (m, 6H), 7.28 (d, J = 8.4 Hz, 2H), 6.88 (d, J = 8.3 Hz, 2H), 5.27 (d, J = 10.1 Hz, 1H), 4.89 (d, J = 6.6 Hz, 1H), 4.72 (d, J = 6.6 Hz, 1H), 4.65 (d, J = 9.0 Hz, 1H), 4.46 (d, J = 11.1 Hz, 1H), 4.22 (d, J = 11.1 Hz, 1H), 4.16 (s, 1H), 4.10 (dd, J = 9.5, 9.5 Hz, 1H), 4.04 (dd, J = 10.1, 2.6 Hz, 1H), 3.80 (s, 3H), 3.60 (dd, J = 9.7, 5.4 Hz, 1H), 3.54 (dd, J = 9.6, 5.8 Hz, 1H), 3.39 (s, 3H), 2.93 (bs, 1H), 2.89-2.82 (m, 4H), 2.61 (ddd, J = 14.7, 10.5, 5.4 Hz, 1H), 2.06 (ddd, J = 14.1, 6.1, 2.9 Hz, 1H), 1.88-1.81 (m, 2H), 1.80 (s, 3H), 1.72 (ddd, J = 20.1, 12.6, 7.0 Hz, 1H), 1.53-1.29 (m, 4H), 1.12 (s, 3H), 1.09 (s, 9H), 1.02 (s, 3H), 0.96 (t, J = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.1, 136.7, 135.7, 135.6, 133.9, 133.9, 131.1, 131.0, 129.5, 129.5, 129.2, 127.6, 127.6, 113.7, 99.2, 81.0, 73.9, 70.0, 67.4, 64.5, 59.2, 56.3, 55.2, 43.1, 42.2, 41.3, 38.0, 31.5, 31.4, 27.0, 26.4, 24.9, 21.0, 21.0, 19.4, 18.2, 11.9; high resolution mass spectrum (ES+) *m/z* 817.3981 [(M+Na)$^+$; calcd for $C_{45}H_{66}O_6S_2SiNa$: 817.3968].



(-)-**3**

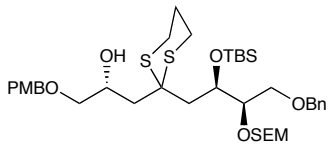
Dithiane (-)-3: To a solution of alcohol (-)-**SI 7** (1.22 g, 1.54 mmol) in THF (15.4 mL) at 0 °C was added 95% NaH (177 mg, 7.7 mmol), followed by 15-crown-5 (0.336 mL, 1.69 mmol) and MeI (0.863 mL, 13.86 mmol). The reaction mixture was warmed to rt. stirred for 22 h, cooled to 0 °C, quenched with saturated aq. NH_4Cl (10 mL) and warmed to rt. The layers were separated and the aqueous layer extracted with diethyl ether (3 x 20 mL). The combined organic layers were washed with water (1 x 20 mL), dried over anhydrous $MgSO_4$, filtered and concentrated. Flash chromatography (10:1, hexanes/ethyl acetate) afforded dithiane (-)-**3** as a colorless oil (1.13 g, 89%). $[\alpha]_D^{23}$ -22.7° (*c* 0.44, $CHCl_2$); IR (film) 2958 (s), 2931 (s), 2895 (s), 2857 (s), 1111 (s), 1037 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.70-7.67 (m, 4H), 7.47-7.37 (m, 6H), 7.30 (d, *J* = 8.5 Hz, 2H), 6.88 (d, *J* = 8.5 Hz, 2H), 5.27 (d, *J* = 10.1 Hz, 1H), 4.81 (d, *J* = 6.3 Hz, 1H), 4.74 (d, *J* = 6.3 Hz, 1H), 4.43 (d, *J* = 12.4 Hz, 1H), 4.40 (d, *J* = 11.2 Hz, 1H), 4.29 (s, 1H), 4.19 (d, *J* = 10.9 Hz, 1H), 3.95 (dd, *J* = 8.5, 2.3 Hz, 1H), 3.80 (s, 3H), 3.73 (ddd, *J* = 12.2, 8.2, 4.2 Hz, 1H), 3.60 (dd, *J* = 9.7, 5.1 Hz, 1H), 3.52 (dd, *J* = 9.6, 6.0 Hz, 1H), 3.37 (s, 3H), 3.25 (s, 3H), 2.94-2.86 (m, 4H), 2.57 (ddd, *J* = 14.7, 10.5, 5.4 Hz, 1H), 2.08 (ddd, *J* = 10.4, 6.3, 3.1 Hz, 1H), 1.88-1.81 (m, 1H), 1.80-1.71 (m, 1H), 1.76 (s, 3H), 1.63-1.52 (m, 4H), 1.34 (ddd, *J* = 22.3, 16.3, 8.6 Hz, 1H), 1.10 (s, 3H), 1.09 (s,9H), 1.02 (s, 3H), 0.95 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.9, 136.6, 135.5, 135.5, 133.7, 130.9, 129.4, 129.4, 129.1, 127.5, 127.5, 113.5, 98.7, 80.9, 77.2, 74.8, 74.3, 69.8, 67.2, 59.1, 55.8, 55.7, 55.1, 42.8, 41.3, 39.7, 36.8, 31.5, 31.2, 26.8, 26.3, 24.8, 20.9, 20.6, 19.2, 18.0, 11.8; high resolution mass spectrum (ES+) *m/z* 831.4154 [$(M+Na)^+$; calcd for $C_{46}H_{68}O_6S_2SiNa$: 831.4125].



(+)-**16**

SEM Ether (+)-16. To a suspension of sodium hydride (1.48 g, 40.2 mmol, 65% wt., 1.3 equiv.) in THF (200 mL) was added a solution of alcohol (-)-**15**[3] (6.0 g, 30.9 mmol) in THF (50 mL) at 0 °C *via* cannula. After the reaction mixture was stirred for 20 min at 0 °C, (trimethylsilyl)ethoxymethyl chloride (6.56 mL, 37.1 mmol, 1.2 equiv.) was added at 0 °C *via* syringe. The resulting mixture was stirred for an additional 12 h, poured into water (100 mL), and then extracted with EtOAc (250 mL). The organic layers were washed with brine (200 mL), dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purification by flash chromatography on silica gel (5/1, hexanes/EtOAc) gave SEM ether (+)-**16** (8.51 g, 85% yield) as a pale yellow oil: $[\alpha]_D^{20}$ +17.1 (*c* 1.08, $CHCl_3$); IR

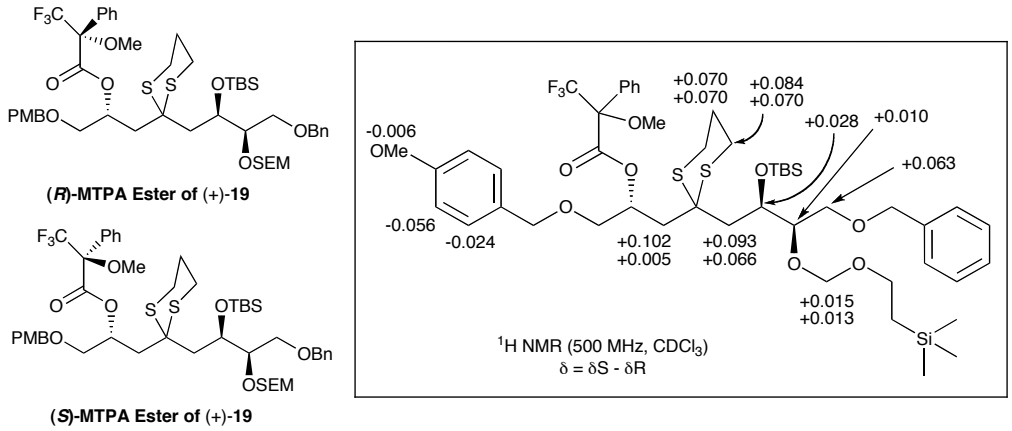
(film) 2952 (s), 2871 (s), 1455 (m), 1249 (s), 1029 (s), 836 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.40-7.25 (m, 5H), 4.85 (d, *J* = 6.8 Hz, 1H), 4.79 (d, *J* = 6.8 Hz, 1H), 4.58 (d, *J* = 12.1 Hz, 1H), 4.54 (d, *J* = 12.1 Hz, 1H), 3.70-3.55 (m, 5H), 3.12 (m, 1H), 2.77 (t, *J* = 4.7 Hz, 1H), 2.63 (dd, *J* = 5.0, 2.7 Hz, 1H), 0.93 (m, 2H), 0.01 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.0, 128.3, 127.6, 127.5, 94.1, 76.2, 73.4, 70.3, 65.3, 52.8, 43.8, 18.0, -1.5; high resolution mass spectrum (ES+) *m/z* 347.1649 [$(M+Na)^+$; calcd for $C_{17}H_{28}O_4SiNa^+$: 347.1655].



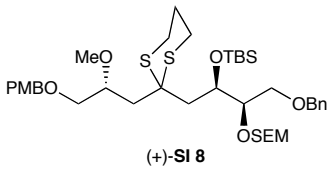
(+)-**19**

TBS-dithiane Linchpin Product (+)-19. To a solution of TBS-dithiane **17** (87 mg, 0.371 mmol, 1.2 equiv.) in Et_2O (2.5 mL) was added dropwise *tert*-butyllithium (0.25 mL, 1.5 M in pentane, 1.2 equiv.) at –78 °C. The resulting solution was stirred for 1 h at –78 °C, warmed to –45 °C over 1 h, and then cooled back to –78 °C. A solution of epoxide (+)-**16** (100 mg, 0.308 mmol) in Et_2O (0.5 mL) was added dropwise to the reaction mixture at –78 °C *via* cannula. The resultant solution was stirred for 30 min at –78 °C, warmed to –45 °C over 2 h, and then cooled to –78 °C. A solution of PMB ether of glycidol [(+)-**18**] (90 mg, 0.463 mmol, 1.5 equiv.) in THF (1.0 mL) and HMPA (0.4 mL) was added dropwise to the reaction mixture at –78 °C *via* cannula. After 10 min, the reaction vessel was transferred to 0 °C-bath and stirred for 12 h at 0 °C. The resulting mixture was poured into saturated aqueous $NaHCO_3$ (5 mL) and extracted with EtOAc (10 mL). The organic layers were washed with brine (10 mL), dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purification by flash chromatography on silica gel (20/1 to 3/1, hexanes/EtOAc) gave linchpin product (+)-**19** (151 mg, 65% yield) as a pale yellow oil: **Linchpin product (+)-19:** $[\alpha]_D^{20}$ +10.2 (*c* 1.06, $CHCl_3$); IR (film) 3457 (m), 2951 (s), 2929 (s), 2857 (s), 1612 (m), 1513 (s), 1362 (m) 1249 (s), 1104 (s), 1032 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.33-7.24 (m, 5H), 7.25 (d, *J* = 8.5 Hz, 2H), 6.86 (d, *J* = 8.5 Hz, 2H), 4.87 (d, *J* = 6.7 Hz, 1H), 4.75 (d, *J* = 6.8 Hz, 1H), 4.54 (d, *J* = 12.1 Hz, 1H), 4.51-4.46 (m, 3H), 4.30 (m, 1H), 4.23 (m, 1H), 3.94 (m, 1H), 3.81-3.52 (m, 4H), 3.80 (s, 3H), 3.41-3.33 (m, 2H), 2.88-2.70 (m, 4H), 2.55 (d, *J* = 5.1 Hz, 1H), 2.22 (d, *J* = 15.3 Hz, 1H), 2.12-1.88 (m, 4H), 0.94 (m, 2H), 0.86 (s, 9H), 0.17 (s, 3H), 0.14 (s, 3H), 0.00 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.1, 138.4, 130.4, 129.3, 128.3, 128.3, 127.4, 113.7, 94.4,

77.6, 74.3, 73.4, 73.0, 72.8, 70.5, 69.8, 66.9, 65.3, 55.2, 51.9, 43.2, 38.5, 26.2, 26.1, 25.7, 25.1, 18.1, 18.0, -1.4, -3.5, -4.2; high resolution mass spectrum (ES+) *m/z* 775.3537 [$(M+Na)^+$; calcd for $C_{38}H_{64}O_7S_2Si_2Na^+$: 775.3530].

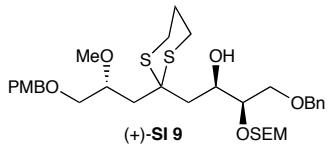


The MTPA Esters of (+)-19. In similar fashion as described above, the (*S*)- and (*R*)-MTPA ester of (+)-**19** was obtained as a pale yellow oil, respectively: **(*S*)-MTPA Ester of (+)-19:** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.58 (d, *J* = 7.5 Hz, 2H), 7.40-7.30 (m, 8H), 7.17 (d, *J* = 8.6 Hz, 2H), 6.82 (d, *J* = 8.6 Hz, 2H), 5.79 (m, 1H), 4.86 (d, *J* = 6.7 Hz, 1H), 4.75 (d, *J* = 6.7 Hz, 1H), 4.54 (d, *J* = 12.2 Hz, 1H), 4.46 (d, *J* = 12.2 Hz, 1H), 4.44 (d, *J* = 11.3 Hz, 1H), 4.37 (d, *J* = 11.3 Hz, 1H), 4.20 (dd, *J* = 7.5, 4.6 Hz, 1H), 3.91 (m, 1H), 3.79 (s, 3H), 3.75-3.60 (m, 4H), 3.53 (d, *J* = 5.1 Hz, 1H), 3.51 (s, 3H), 3.48 (dd, *J* = 10.1, 8.5 Hz, 1H), 2.92 (ddd, *J* = 14.0, 10.8, 3.2 Hz, 1H), 2.84 (ddd, *J* = 14.0, 10.3, 3.0 Hz, 1H), 2.68 (ddd, *J* = 14.3, 6.2, 3.0 Hz, 1H), 2.63 (d, *J* = 14.2 Hz, 1H), 2.59 (m, 1H), 2.34 (dd, *J* = 16.3, 4.2 Hz, 1H), 2.14 (dd, *J* = 16.3, 5.4 Hz, 1H), 1.95 (m, 1H), 1.85 (m, 1H), 1.70 (dd, *J* = 15.0, 8.3 Hz, 1H), 0.94 (t, *J* = 8.5 Hz, 2H), 0.79 (s, 9H), 0.10 (s, 3H), 0.07 (s, 3H), -0.01 (s, 9H). **(*R*)-MTPA Ester of (+)-19:** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60 (d, *J* = 7.5 Hz, 2H), 7.45-7.30 (m, 8H), 7.23 (d, *J* = 8.6 Hz, 2H), 6.85 (d, *J* = 8.6 Hz, 2H), 5.75 (m, 1H), 4.84 (d, *J* = 6.7 Hz, 1H), 4.74 (d, *J* = 6.7 Hz, 1H), 4.58-4.45 (m, 4H), 4.18 (dd, *J* = 7.1, 4.6 Hz, 1H), 3.87 (m, 1H), 3.80 (s, 3H), 3.75-3.55 (m, 5H), 3.56 (s, 3H), 3.47 (dd, *J* = 10.1, 8.4 Hz, 1H), 2.84 (ddd, *J* = 14.0, 10.0, 2.8 Hz, 1H), 2.62 (m, 2H), 2.53 (d, *J* = 14.2 Hz, 1H), 2.52 (m, 1H), 2.24 (dd, *J* = 16.2, 4.0 Hz, 1H), 2.13 (dd, *J* = 16.2, 5.5 Hz, 1H), 1.88 (m, 1H), 1.78 (m, 1H), 1.63 (dd, *J* = 15.0, 8.1 Hz, 1H), 0.92 (t, *J* = 8.5 Hz, 2H), 0.81 (s, 9H), 0.10 (s, 3H), 0.08 (s, 3H), -0.01 (s, 9H).



(+)-**SI 8**

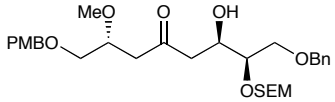
Methyl Ether (+)-SI 8. To a suspension of sodium hydride (956 mg, 23.9 mmol, 65% wt., 2.0 equiv.) in THF (100 mL) was added drowise a solution of alcohol (+)-**19** (9.0 g, 11.9 mmol) in THF (20 mL) at 0 °C *via* cannula. After the reaction mixture was stirred for 15 min at 0 °C, methyl iodide (1.49 mL, 23.9 mmol, 2.0 equiv.) and 15-crown-5 (4.75 mL, 23.9 mmol, 2.0 equiv.) were added dropwise. The resulting mixture was stirred for 3 h at room temperature, poured into saturated aqueous NH_4Cl (100 mL) and then extracted with EtOAc (200 mL). The organic layers were washed with brine (200 mL), dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purification by flash chromatography on silica gel (5/1, hexanes/EtOAc) gave methyl ether (+)-**SI 8** (9.05 g, 99% yield) as a pale yellow oil: $[\alpha]_D^{20}$ +4.32 (*c* 0.74, $CHCl_3$); IR (film) 2951 (s), 2928 (s), 1612 (m). 1514 (s), 1456 (m), 1362 (m), 1248 (s), 1106 (s), 1033 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.35-7.24 (m, 5H), 7.27 (d, *J* = 8.5 Hz, 2H), 6.86 (d, *J* = 8.5 Hz, 2H), 4.87 (d, *J* = 6.7 Hz, 1H), 4.77 (d, *J* = 6.7 Hz, 1H), 4.58-4.55 (m, 4H), 4.21 (m, 1H), 3.96 (m, 1H), 3.80 (s, 3H), 3.78-3.60 (m, 4H), 3.55 (t, 1H), 3.46 (m, 2H), 3.40 (s, 3H), 2.92-2.82 (m, 2H), 2.71-2.63 (m, 2H), 2.14 (dd, *J* = 15.6, 2.6 Hz, 1H), 1.97-1.80 (m, 4H), 1.73 (dd, *J* = 15.1, 8.0 Hz, 1H), 0.95 (m, 2H), 0.84 (s, 9H), 0.122 (s, 3H), 0.120 (s, 3H), 0.00 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 141.0, 138.5, 130.5, 129.2, 128.2, 127.4, 127.4, 113.6, 94.2, 77.4, 77.1, 73.2, 72.8, 72.0, 69.7, 69.7, 65.2, 57.1, 55.2, 52.9, 43.4, 41.5, 36.0, 26.1, 26.0, 25.8, 24.9, 18.1, 17.9, -1.4, -3.7, -4.1; high resolution mass spectrum (ES+) *m/z* 789.3685 [$(M+Na)^+$; calcd for $C_{39}H_{66}O_7S_2Si_2Na^+$: 789.3686].



(+)-**SI 9**

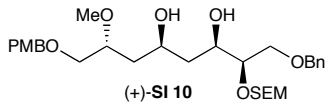
Alcohol (+)-SI 9. To a solution of methyl ether (+)-**SI 8** (10.5 g, 13.7 mmol) in THF (100 mL) was added tetra-*n*-butylammonium fluoride (27.4 mL, 27.4 mmol, 1.0 M in THF, 2.0 equiv.) at room temperature. The reaction mixture was stirred for 4 h at the same temperature, poured into saturated aqueous NH_4Cl (100 mL), and then extracted with EtOAc (200 mL). The organic layers were washed with brine (200 mL), dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purification by flash chromatography on silica gel (3/1, hexanes/EtOAc) gave

alcohol (+)-**SI 9** (8.35 g, 93% yield) as a yellow oil: $[\alpha]_D^{20}$ +8.89 (*c* 0.90, $CHCl_3$); IR (film) 3419 (br m), 2949 (s), 2899 (s), 1612 (m), 1512 (s), 1420 (m), 1365 (m), 1248 (s), 1101 (s), 1033 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.32 (m, 5H), 7.25 (d, *J* = 8.7 Hz, 2H), 6.87 (d, *J* = 8.7 Hz, 2H), 4.86 (d, *J* = 6.8 Hz, 1H), 4.76 (d, *J* = 6.8 Hz, 1H), 4.56 (d, *J* = 12.0 Hz, 1H), 4.52 (d, *J* = 12.0 Hz, 1H), 4.48 (s, 2H), 4.12 (m, 1H), 4.09 (d, *J* = 5.0 Hz, 1H), 3.80 (s, 3H), 3.75-3.60 (m, 5H), 3.50 (dd, *J* = 9.5, 5.0 Hz, 2H), 3.41 (m, 1H), 3.40 (s, 3H), 2.90-2.70 (m, 4H), 2.37 (d, *J* = 15.2 Hz, 1H), 2.31 (dd, *J* = 15.5, 8.4 Hz, 1H), 2.26 (d, *J* = 15.0 Hz, 1H), 2.17 (dd, *J* = 15.3, 9.0 Hz, 1H), 1.96 (m, 2H), 0.94 (m, 2H), 0.00 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.2, 138.4, 130.1, 129.2, 128.3, 127.5, 127.4, 113.8, 94.9, 79.0, 77.2, 73.3, 73.0, 71.2, 70.6, 67.9, 65.4, 57.4, 55.2, 51.5, 41.2, 40.6, 26.0, 25.9, 25.2, 18.1, -1.4; high resolution mass spectrum (ES+) *m/z* 675.2825 [$(M+Na)^+$; calcd for $C_{33}H_{52}O_7S_2SiNa^+$: 675.2821].



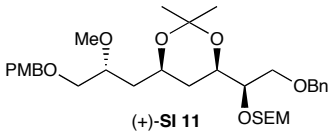
(+)-**20**

Ketone (+)-20. To a solution of alcohol (+)-**SI 9** (5.8 g, 8.88 mmol) in THF (80 mL) and water (8.0 mL) was added 2,6-lutidine (5.17 mL, 44.4 mmol, 5.0 equiv.) and $Hg(ClO_4)_2$-H_2O (7.10 g, 17.8 mmol, 2.0 equiv.) at 0 °C. The reaction mixture was stirred for 15 min at room temperature, filtered through a pad of Celite, and then extracted with EtOAc (100 mL). The organic layers were washed with 1 N aqueous HCl (100 mL) and brine (200 mL), dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purification by flash chromatography on silica gel (3/1, hexanes/EtOAc) gave alcohol (+)-**20** (8.35 g, 93% yield) as a yellow oil: $[\alpha]_D^{20}$ +2.80 (*c* 1.32, $CHCl_3$); IR (film) 3457 (br m), 2951 (s), 2897 (s), 1713 (s), 1612 (m), 1514 (s), 1454 (m), 1366 (m), 1249 (s), 1101 (s), 1033 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.31 (m, 5H), 7.23 (d, *J* = 8.7 Hz, 2H), 6.86 (d, *J* = 8.7 Hz, 2H), 4.79 (d, *J* = 7.0 Hz, 1H), 4.74 (d, *J* = 7.0 Hz, 1H), 4.55 (d, *J* = 12.0 Hz, 1H), 4.49 (d, *J* = 12.0 Hz, 1H), 4.46 (d, *J* = 11.7 Hz, 1H), 4.43 (d, *J* = 11.7 Hz, 1H), 4.26 (m, 1H), 3.87 (m, 1H), 3.79 (s, 3H), 3.70-3.58 (m, 5H), 3.46 (dd, *J* = 4.7, 1.8 Hz, 2H), 3.36 (s, 3H), 3.14 (m, 1H), 2.73 (dd, *J* = 16.5, 7.5 Hz, 2H), 2.70 (dd, *J* = 16.6, 8.8 Hz, 2H), 0.91 (t, *J* = 8.5 Hz, 2H), 0.00 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 208.5, 159.2, 137.8, 130.1, 129.3, 128.4, 127.7, 127.6, 113.7, 95.1, 78.5, 75.9, 73.4, 73.0, 70.5, 70.0, 68.0, 65.6, 57.6, 55.2, 46.7, 45.7, 18.0. –1.5; high resolution mass spectrum (ES+) *m/z* 585.2875 [$(M+Na)^+$; calcd for $C_{30}H_{46}O_8SiNa^+$: 585.2860].



(+)-**SI 10**

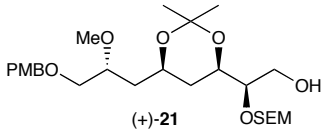
***Syn*-diol (+)-SI 10.** To a solution of ketone (+)-**20** (4.35 g, 7.72 mmol) in THF (60 mL) and MeOH (15 mL) was added diethyl methoxyborane (8.5 mL, 8.50 mmol, 1.1 equiv.) at –78 °C. After the reaction mixture was stirred for 15 min at –78 °C, sodium borohydride (322 mg, 8.50 mmol, 1.1. equiv.) was added. The resulting mixture was stirred for an additional 2 h at –78 °C, poured into water, and then extracted with EtOAc (100 mL). The organic layers were washed with brine (100 mL), dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purification by flash chromatography on silica gel (2/1, hexanes/EtOAc) gave *syn*-diol (+)-**SI 10** (3.68 g, 84% yield) as a yellow oil: $[\alpha]_D^{20}$ +1.71 (*c* 0.88, $CHCl_3$); IR (film) 3444 (br m), 2950 (s), 1612 (m), 1513 (s), 1453 (m), 1370 (m), 1248 (s), 1100 (s), 1033 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.32 (m, 5H), 7.25 (d, *J* = 8.5 Hz, 2H), 6.87 (d, *J* = 8.5 Hz, 2H), 4.80 (d, *J* = 7.0 Hz, 1H), 4.76 (d, *J* = 7.0 Hz, 1H), 4.55 (d, *J* = 12.0 Hz, 1H), 4.49 (d, *J* = 12.0 Hz, 1H), 4.48 (s, 2H), 4.09 (m, 1H), 4.02 (m, 1H), 3.94 (br s, 1H), 3.78 (s, 3H), 3.70-3.55 (m, 7H), 3.48 (m, 2H), 3.43 (s, 3H), 1.70-1.50 (m, 4H), 0.92 (t, *J* = 8.5 Hz, 2H), 0.00 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.2, 137.8, 130.2, 129.2, 128.4, 127.7, 127.6, 113.7, 95.1, 79.8, 77.4, 73.5, 73.0, 72.5, 71.6, 70.0, 69.0, 65.7, 57.9, 55.2, 39.7, 39.4, 18.0, -1.5; high resolution mass spectrum (ES+) *m/z* 587.3011 [$(M+Na)^+$; calcd for $C_{30}H_{48}O_8SiNa^+$: 587.3016].



(+)-**SI 11**

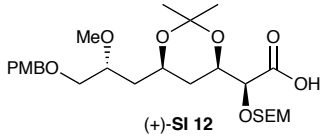
Acetonide (+)-SI 11. To a solution of diol (+)-**SI 10** (3.68 g, 6.52 mmol) in CH_2Cl_2 (50 mL) was added 2,2-dimethoxypropane (1.60 mL, 13.03 mmol, 2.0 equiv.) and pyridinium *p*-toluenesulfonate (327 mg, 1.30 mmol, 0.2 equiv.) at room temperature. The reaction mixture was stirred for 2 h at room temperature, poured into brine, and then extracted with EtOAc (100 mL). The organic layers were washed with brine (100 mL), dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purification by flash chromatography on silica gel (3/1, hexanes/EtOAc) gave acetonide (+)-**SI 11** (3.30 g, 84% yield) as a yellow oil: $[\alpha]_D^{20}$ +12.70 (*c* 0.74, $CHCl_3$); IR (film) 2950 (s), 2893 (s), 1612 (m), 1512 (s), 1465 (m), 1378 (m), 1249 (s), 1200 (m), 1101 (s), 1034 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.32 (m, 5H), 7.25 (d, *J* = 8.3 Hz, 2H), 6.87 (d, *J* = 8.3 Hz, 2H), 4.81 (d, *J* = 7.0 Hz, 1H), 4.77 (d, *J* = 7.0 Hz, 1H),

4.55 (d, *J* = 12.1 Hz, 1H), 4.50 (d, *J* = 12.1 Hz, 1H), 4.48 (s, 2H), 4.11 (m, 1H), 4.05 (m, 1H), 3.80 (s, 3H), 3.70-3.60 (m, 4H), 3.60-3.45 (m, 3H), 3.42 (s, 3H), 3.39 (m, 1H), 1.65-1.25 (m, 4H), 1.42 (s, 3H), 1.36 (s, 3H), 0.91 (dd, *J* = 9.1, 7.9 Hz, 2H), 0.00 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.1, 138.2, 130.4, 129.3, 129.1, 128.3, 127.6, 127.5, 113.7, 98.6, 94.9, 77.8, 76.3, 73.3, 72.9, 72.2, 69.5, 69.4, 65.3, 65.1, 58.2, 55.2, 39.3, 32.8, 30.2, 19.8, 18.0, -1.5; high resolution mass spectrum (ES+) *m/z* 627.3306 [(M+Na)$^+$; calcd for $C_{33}H_{52}O_8SiNa^+$: 627.3329].



(+)-**21**

Alcohol (+)-21. To a solution of acetonide (+)-**SI 11** (69 mg, 0.114 mmol) in EtOH (1.5 mL) and 1-methyl-1,4-cyclohexadiene (0.8 mL) was added calcium carbonate (114 mg, 1.14 mmol, 10.0 equiv.) and palladium hydroxide on carbon (35 mg). The reaction mixture was stirred for 2 h at 75 °C, filtered through a pad of Celite, and then the filtrate was concentrated *in vacuo*. Purification by flash chromatography on silica gel (2/1, hexanes/EtOAc) gave alcohol (+)-**21** (49 mg, 84% yield) as a yellow oil: $[\alpha]_D^{20}$ +32.07 (*c* 1.35, $CHCl_3$); IR (film) 3463 (m), 2951 (s), 1613 (m), 1513 (s), 1465 (m), 1379 (s), 1249 (s), 1201 (m), 1102 (s), 1059 (s), 1035 (s) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.15 (d, *J* = 8.6 Hz, 2H), 6.77 (d, *J* = 8.6 Hz, 2H), 4.73 (d, *J* = 6.9 Hz, 1H), 4.62 (d, *J* = 6.9 Hz, 1H), 4.38 (s, 2H), 3.96 (m, 2H), 3.70 (s, 3H), 3.64 (m, 2H), 3.58-3.42 (m, 4H), 3.40 (dd, *J* = 10.2, 3.8 Hz, 1H), 3.32 (s, 3H), 3.30 (m, 1H), 2.85 (br s, 1H), 1.54-1.40 (m, 2H), 1.40-1.20 (m, 2H), 1.33 (s, 3H), 1.27 (s, 3H), 0.86 (t, *J* = 8.5 Hz, 2H), -0.08 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.2, 130.5, 129.2, 128.3, 113.7, 98.7, 95.5, 81.6, 76.2, 73.0, 72.1, 70.5, 65.7, 65.2, 62.3, 58.2, 55.2, 39.3, 32.5, 30.1, 19.7, 18.1, -1.5; high resolution mass spectrum (ES+) *m/z* 537.2875 [(M+Na)$^+$; calcd for $C_{26}H_{46}O_8SiNa^+$: 537.2860].

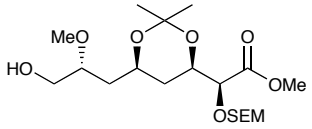


(+)-**SI 12**

Carboxylic Acid (+)-SI 12. To a solution of alcohol (+)-**21** (138 mg, 0.267 mmol) in CH_2Cl_2 (2.5 mL) was added dropwise DMSO (0.19 mL, 2.67 mmol, 10.0 equiv.) and diisopropylethylamine (0.14 mL, 0.802 mmol, 3.0 equiv.) at –15 °C. After 15 min, sulfur trioxide-pyridine complex (125 mg, 0.802 mmol, 3.0 equiv.) was added.

The reaction mixture was stirred for 30 min at –15 °C, poured into brine (20 mL), and then extracted with Et_2O (20 mL). The organic layers were washed with brine (20 mL), dried over $MgSO_4$, filtered, and concentrated *in vacuo* to give crude aldehyde as a yellow oil, which was used in the next reaction without further purification.

To a solution of the crude aldehyde in *t*-BuOH (2.5 mL) and 2-methyl-2-butene (0.2 mL) was added a solution of $NaClO_2$ (121 mg, 1.34 mmol, 5.0 equiv.) and NaH_2PO_4 (417 mg, 2.67 mmol, 10.0 equiv.) in water (0.8 mL) at room temperature. The raction mixture was stirred for 30 min at same temperature, poured into saturated aqueous NH_4Cl (10 mL), and then extracted with EtOAc (20 mL). The organic layers were washed with brine (20 mL), dried over $MgSO_4$, filtered, and concentrated *in vacuo* to give crude carboxylic acid (+)-**SI 12** as a pale yellow oil, which was used to the next reaction without further purification: $[\alpha]_D^{20}$ +1.71 (*c* 1.05, $CHCl_3$); IR (film) 3404 (s), 2925 (s), 2360 (s), 1734 (m), 1652 (m), 1514 (m), 1249 (s), 1066 (s) cm^{-1}; high resolution mass spectrum (ES+) *m/z* 551.2664 [$(M+Na)^+$; calcd for $C_{26}H_{44}O_9SiNa^+$: 551.2652].

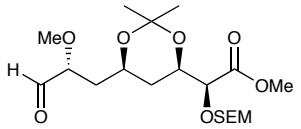


(-)-**22**

Alcohol (-)-22. To a solution of the crude carboxylic acid (+)-**SI 12** in MeOH (0.5 mL) and benzene (2.0 mL) was added dropwise trimethylsilyldiazomethane (0.20 mL, 0.40 mmol, 2.0 M in hexane, 1.5 equiv.) at room temperature. After the reaction mixture was stirred for 20 min at the same temperature, AcOH was added until the yellow color disappeared. The resulting mixture was poured into saturated aqueous $NaHCO_3$ (20 mL), and extracted with EtOAc (20 mL). The organic layers were washed with brine (20 mL), dried over $MgSO_4$, filtered, and concentrated *in vacuo* to give crude methyl ester as a pale yellow oil, which was used to the next reaction without further purification.

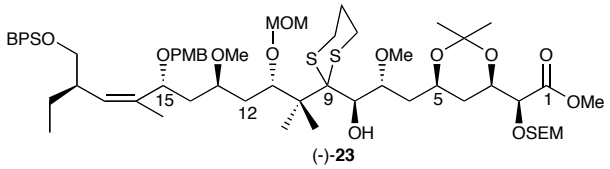
To a solution of the crude methyl ester in CH_2Cl_2 (2.5 mL) and pH 7.0 buffer (0.25 mL) was added DDQ (91 mg, 0.40 mmol, 3.0 equiv.) at 0 °C. The reaction mixture was stirred for 1 h at room temperature, poured into saturated aqueous $NaHCO_3$ (20 mL), and then extracted with EtOAc (20 mL). The organic layers were washed with saturated aqueous $NaHCO_3$ (20 mL) and brine (20 mL), dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purification by flash chromatography on silica gel (2/1, hexanes/EtOAc) gave alcohol (-)-**22** (84 mg, 74% yield over 4 steps) as a yellow oil: $[\alpha]_D^{20}$ –14.19 (*c* 1.16, $CHCl_3$); IR (film) 3420 (m), 2952 (s), 1749 (s), 1436 (m),

1381 (m), 1250 (s), 1201 (s), 1165 (s), 1114 (s), 1064 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.76 (d, *J* = 7.1 Hz, 1H), 4.73 (d, *J* = 7.1 Hz, 1H), 4.26 (ddd, *J* = 11.8, 4.8, 2.4 Hz, 1H), 4.12 (d, *J* = 4.8 Hz, 1H), 4.02 (m, 1H), 3.73 (s, 3H), 3.72 (m, 1H), 3.65 (m, 2H), 3.45 (m, 2H), 3.39 (s, 3H), 2.18 (br s, 1H), 1.67 (m, 1H), 1.52 (m, 2H), 1.41 (s, 3H), 1.37 (s, 3H), 1.33 (dt, *J* = 12.7, 2.4 Hz, 1H), 0.88 (t, *J* = 8.5 Hz, 2H), 0.00 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.7, 99.1, 94.7, 78.2, 77.7, 70.1, 65.8, 65.6, 64.0, 57.7, 51.9, 38.6, 32.4, 29.9, 19.5, 18.0, -1.5; high resolution mass spectrum (ES+) *m/z* 445.2240 [$(M+Na)^+$; calcd for $C_{19}H_{38}O_8SiNa^+$: 445.2234].



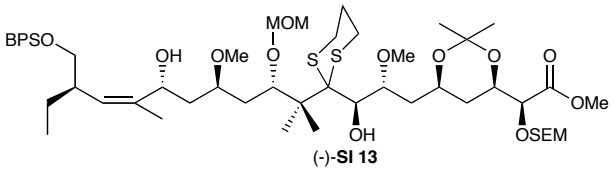
(+)-**4**

Aldehyde (+)-4. To a solution of alcohol (-)-**22** (100 mg, 0.237 mmol) in CH_2Cl_2 (2.5 mL) was added dropwise DMSO (0.18 mL, 2.37 mmol, 10.0 equiv.) and diisopropylethylamine (0.12 mL, 0.710 mmol, 3.0 equiv.) at –15 °C. After 15 min, sulfur trioxide-pyridine complex (111 mg, 0.710 mmol, 3.0 equiv.) was added. The reaction mixture was stirred for 30 min at –15 °C, poured into brine (20 mL), and then extracted with Et_2O (20 mL). The organic layers were washed with brine (20 mL), dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purification by flash chromatography on silica gel (5/1, hexanes/EtOAc plus 3% triethylamine) gave aldehyde (+)-**4** (87 mg, 87% yield) as a yellow oil: $[\alpha]_D^{20}$ +1.25 (*c* 0.75, $CHCl_3$); IR (film) 2952 (s), 1736 (s), 1381 (m), 1250 (m), 1201 (s), 1113 (m), 1066 (s), 1026 (s) cm^{-1}, ^1H NMR (500 MHz, $CDCl_3$) δ 9.63 (d, *J* = 1.6 Hz, 1H), 4.77 (d, *J* = 7.1 Hz, 1H), 4.75 (d, *J* = 7.1 Hz, 1H), 4.28 (ddd, *J* = 11.8, 4.8, 2.4 Hz, 1H), 4.14 (d, *J* = 4.8 Hz, 1H), 4.08 (m, 1H), 3.83 (ddd, *J* = 9.8, 3.7, 1.6 Hz, 1H), 3.75 (s, 3H), 3.64 (dd, *J* = 17.2, 7.8 Hz, 2H), 3.45 (s, 3H), 1.81 (ddd, *J* = 13.8, 9.6, 3.8 Hz, 1H), 1.61 (ddd, *J* = 14.1, 9.8, 2.8 Hz, 1H), 1.55 (m, 1H), 1.41 (s, 3H), 1.38 (s, 3H), 1.35 (m, 1H), 0.89 (t, *J* = 8.5 Hz, 2H), 0.00 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.6, 99.3, 94.7, 82.3, 77.6, 70.0, 65.8, 64.4, 58.8, 52.0, 36.7, 32.2, 29.9, 19.5, 18.0, -1.4; high resolution mass spectrum (ES+) m/z 443.2088 [$(M+Na)^+$; calcd for $C_{19}H_{36}O_8SiNa^+$: 443.2077].



(-)-**23**

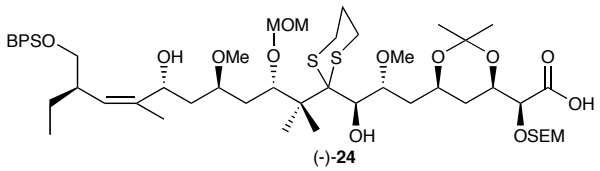
Coupling Product (-)-23. To a solution of dithiane (-)-**3** (61 mg, 0.0785 mmol, 1.5 equiv.) in THF (5.0 mL) was added *tert*-butyllithium (52 μL, 0.0785 mmol, 1.5 M in pentane, 1.5 equiv.) and HMPA (39 μL, 0.156 mmol, 4.5 equiv.) at –78 °C. After the reaction mixture was stirred for 30 min at –78 °C, a solution of aldehyde (+)-**4** (22 mg, 0.0523 mmol) in 5 mL of THF was added dropwise *via* cannula. The resulting mixture was stirred for 4 h at –78 °C, poured into saturated aqueous $NaHCO_3$ (30 mL), and then extracted with EtOAc (30 mL). The organic layers were washed with brine (30 mL), dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purification by Preparative-TLC (4/1, hexanes/EtOAc, 500 μm plate) gave coupling product (-)-**23** (64.3 mg, 40% yield) as a yellow oil: $[\alpha]_D^{20}$ –12.56 (*c* 0.52, MeOH); IR (film) 3402 (m), 2929 (s), 1749 (m), 1700 (m), 1652 (m), 1458 (m), 1248 (s), 1109 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.81 (m, 4H), 7.40-7.25 (m, 8H), 6.87 (d, *J* = 8.3 Hz, 2H), 5.24 (d, *J* = 10.0 Hz, 1H), 4.80 (d, *J* = 7.0 Hz, 1H), 4.69 (d, *J* = 7.0 Hz, 1H), 4.65-4.50 (m, 6H), 4.32 (m, 1H), 4.29 (d, *J* = 11.0 Hz, 1H), 4.25 (m, 1H), 4.20 (d, *J* = 4.8 Hz, 1H), 3.95 (m, 2H), 3.72-3.55 (m, 4H), 3.52 (s, 3H), 3.35 (s, 3H), 3.343 (s, 3H), 3.342 (s, 3H), 3.14 (s, 3H), 2.80-2.50 (m, 4H), 2.40 (m, 1H), 2.28 (m, 2H), 1.98 (m, 1H), 1.85 (m, 2H), 1.78 (s, 3H), 1.70-1.20 (m, 7H), 1.62 (s, 3H), 1.44 (s, 3H), 1.42 (s, 3H), 1.37 (s, 3H), 1.21 (s, 9H), 0.97 (t, *J* = 7.4 Hz, 3H), 0.89 (t, *J* = 8.5 Hz, 2H), 0.00 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.6, 159.7, 137.8, 136.1, 136.1, 134.3, 134.2, 131.7, 131.0, 130.0, 130.0, 129.5, 128.5, 127.5, 114.0, 99.2, 98.9, 95.1, 79.5, 78.9, 75.6, 74.6, 70.9, 70.3, 67.8, 66.1, 65.7, 57.3, 56.4, 56.0, 54.8, 52.2, 51.2, 41.9, 40.9, 40.0, 39.6, 33.3, 30.3, 30.2, 27.2, 27.0, 25.4, 23.7, 22.1, 19.8, 19.6, 18.3, 18.1, 12.2, -1.3; high resolution mass spectrum (ES+) *m/z* 1251.6268 [$(M+Na)^+$; calcd for $C_{65}H_{104}O_{14}S_2Si_2Na^+$: 1251.6304].



(-)-**SI 13**

Diol (-)-SI 13: To a solution of alcohol (-)-**23** (19 mg, 0.0155 mmol) in CH_2Cl_2 (1.54 mL) and pH 7.0 phosphate buffer (0.077 mL) at 0 °C was added DDQ (6.3 mg, 0.278 mmol). The reaction mixture was stirred for 3 h at 0 °C, quenched with saturated aq. $NaHCO_3$ (1 mL), diluted with water (2 mL) and DCM (2 mL). The layers were separated and the aqueous layer extracted with CH_2Cl_2 (3 x 5 mL), dried over anhydrous Na_2SO_4, filtered and concentrated. Preparative thin layer chromatography (2:1, hexanes/ethyl acetate, 3% TEA)[4] afforded diol (-)-

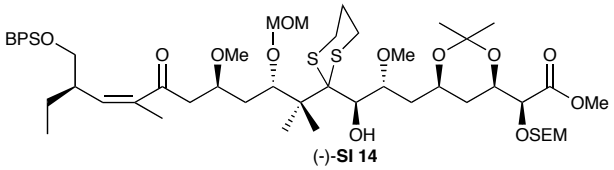
SI 13 as a colorless oil (15.6 mg, 91%). $[\alpha]_D^{24}$ -21.9° (*c* 4.07, C_6H_6); IR (film) 3457 (br), 2957 (s), 2932 (s), 2895 (s), 2857 (s), 1751 (s), 1112 (s), 1036 (s) cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ 7.81-7.78 (m, 4H), 7.33-7.25 (m, 6H), 5.01 (d, *J* = 13.3 Hz, 1H), 4.98 (d, *J* = 10.4 Hz, 1H), 4.79 (d, *J* = 7.0 Hz, 1H), 4.69 (d, *J* = 7.0 Hz, 1H), 4.63-4.57 (m, 2H), 4.53 (d, *J* = 10.4 Hz, 1H), 4.31 (ddd, *J* = 7.5, 5.3, 2.2 Hz, 1H), 4.21-4.17 (m, 2H), 4.00 (bs, 1H), 3.88-3.84 (m, 1H), 3.70-3.57 (m, 4H), 3.52 (s, 3H), 3.36 (s, 3H), 3.30 (s, 3H), 3.18 (s, 3H), 3.08 (bs, 1H), 2.88-2.50 (m, 6H), 2.45-2.42 (m, 1H), 2.19 (dd, *J* = 24.7, 13.5 Hz, 1H), 2.03 (ddd, *J* = 18.0, 14.5, 4.1 Hz, 1H), 1.85 (d, *J* = 1.1 Hz, 3H), 1.71 (dd, *J* = 24.2, 12.0 Hz, 1H), 1.65-1.51 (m, 5H), 1.60 (s, 3H), 1.46 (s, 3H), 1.41 (s, 3H), 1.36 (s, 3H), 1.26-1.17 (m, 2H), 1.19 (s, 9H), 0.93 (t, *J* = 7.4 Hz, 3H), 0.89 (t, *J* = 8.9 Hz, 2H), -0.02 (s, 9H); ^{13}C NMR (125 MHz, C_6D_6) δ 170.5, 140.2, 136.1, 136.1, 134.2, 134.1, 130.0, 129.9, 128.5, 128.3, 128.1, 128.1, 127.9, 99.4, 98.9, 95.1, 79.3, 78.0, 77.8, 76.6, 70.9, 68.3, 68.0, 67.1, 66.0, 65.7, 57.3, 56.3, 55.9, 52.0, 51.2, 42.1, 39.5, 39.3, 33.2, 30.3, 27.3, 27.2, 27.0, 25.2, 24.8, 23.3, 22.2, 19.8, 19.5, 19.1, 18.1, 12.0, -1.3; high resolution mass spectrum (ES+) *m/z* 1131.5771 [(M+Na)$^+$; calcd for $C_{57}H_{96}O_{13}S_2Si_2Na$: 1131.5729].



(-)-**24**

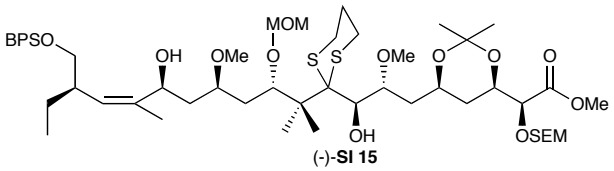
Seco-acid (-)-24: To a solution of diol (-)-**SI 13** (8.5 mg, 0.0077 mmol) in THF (0.5 mL) and water (0.175 mL) at rt was added LiOH (1.8 mg, 0.077 mmol). The reaction mixture was stirred for 20 h, diluted with EtOAc (2 mL) and acidified to pH 5 with 1 M HCl. The layers were separated and the aqueous layer extracted with EtOAc (5 x 5 mL), dried over anhydrous Na_2SO_4, filtered and concentrated to yield (-)-**24** as a colorless oil (8.4 mg, 99%) that was used without further purification. $[\alpha]_D^{23}$ -26.2° (*c* 0.210, C_6H_6); IR (film) 3445 (br), 3053 (m), 2929 (s), 2895 (s), 2857 (s), 1739 (s), 1112 (s), 1036 (s) cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ 7.82-7.80 (m, 4H), 7.33-7.23 (m, 6H), 5.03 (d, *J* = 10.2 Hz, 1H), 4.99 (d, *J* = 10.1 Hz, 1H), 4.72 (d, *J* = 6.9 Hz, 1H), 4.67 (d, *J* = 6.4 Hz, 1H), 4.62-4.55 (m, 4H), 4.32 (br, *J* = 10.8 Hz, 1H), 4.21 (dd, *J* = 10.4, 10.4 Hz, 1H), 4.13 (d, *J* = 4.4 Hz, 1H), 4.05 (br s, 1H), 3.89 (br s, 1H), 3.63-3.57 (m, 5H), 3.53 (s, 3H), 3.44-3.33 (m, 1H), 3.34 (s, 3H), 3.22 (s, 3H), 3.02 (br s, 1H), 2.90-2.81 (m, 2H), 2.65 (br s, 1H), 2.59-2.57 (m, 1H), 2.48-2.43 (m, 1H), 2.20-2.18 (m, 1H), 2.10-2.03 (m, 1H), 1.86 (s, 3H), 1.79-1.16 (m, 7H), 1.62 (s, 3H), 1.48 (s, 3H), 1.40 (s, 3H), 1.35 (s, 3H), 1.20 (s, 9H), 0.95 (t, *J* = 7.3 Hz, 3H),

0.89 (t, *J* = 8.5 Hz, 2H), -0.01 (s, 9H); ^{13}C NMR (125 MHz, C_6D_6) δ 172.2, 140.1, 136.1, 136.1, 134.2, 134.1, 130.0, 129.0, 128.5, 128.5, 128.3, 128.1, 128.1, 127.5, 99.5, 99.1, 95.3, 79.6, 78.9, 77.8, 76.6, 70.7, 68.4, 68.0, 67.0, 66.1, 65.9, 57.3, 56.3, 56.0, 52.0, 42.1, 39.5, 39.4, 39.2, 33.3, 32.3, 30.1, 30.0, 29.8, 27.4, 27.3, 27.2, 27.1, 26.9, 25.2, 24.7, 23.2, 23.1, 22.2, 19.7, 19.5, 19.1, 18.1, 12.0, -1.3; high resolution mass spectrum (ES+) *m/z* 1117.5508 [(M+Na)$^+$; calcd for $C_{56}H_{94}O_{13}S_2Si_2Na$: 1117.5572].



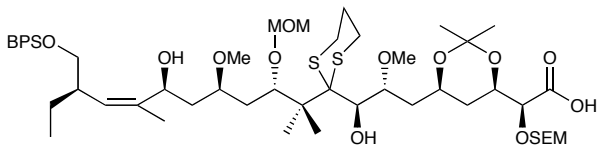
(-)-**SI 14**

Enone (-)-SI 14: To a solution of alcohol (-)-**SI 13** in CH_2Cl_2 (2.82 mL) at –10 °C was added DMSO (0.09 mL, 1.27 mmol), DIEA (0.11 mL, 0.633 mmol) and stirred for 10 min. To the reaction mixture was added SO_3•pyridine (67 mg, 0.424 mmol) in one portion and slowly warmed to 0 °C over 0.5 h. The reaction mixture was quenched with saturated aq. $NaHCO_3$ (5 mL) diluted with 40% EtOAc/heptane (10 mL) and warmed to rt. The layers were separated and the aqueous layer extracted with 40% EtOAc/heptane (3 x 5 mL). The combined organic layers were washed with water (1 x 10 mL) and brine (1 x 10 mL), dried over anhydrous Na_2SO_4, filtered, concentrated, and used without further purification. $[\alpha]_D^{24}$ -21.1° (*c* 3.94, C_6H_6); IR (film) 3448 (br), 2954 (s), 2860 (s), 1751 (s), 1690 (m), 1108 (s), 1068 (s), 1028 (s) cm^{-1}; ^{1}H NMR (500 MHz, C_6D_6) δ 7.79-7.75 (m, 4H), 7.29-7.24 (m, 6H), 5.34 (dd, *J* = 10.3, 1.3 Hz, 1H), 4.79 (d, *J* = 7.0 Hz, 1H), 4.68 (d, *J* = 7.0 Hz, 1H), 4.64-4.62 (m, 2H), 4.59 (d, *J* = 6.5 Hz, 1H), 4.54 (d, *J* = 10.5 Hz, 1H), 4.30 (ddd, *J* = 7.3, 5.1, 2.2 Hz, 1H), 4.21 (bd, *J* = 9.6 Hz, 1H), 4.19 (d, *J* = 5.2 Hz, 1H), 3.98 (bs, 1H), 3.69-3.59 (m, 4H), 3.52 (s, 3H), 3.40-3.31 (m, 1H), 3.35 (s, 3H), 3.28 (s, 3H), 3.27 (s, 3H), 3.19-3.05 (m, 2H), 2.84 (dd, *J* = 16.7, 5.4 Hz, 1H), 2.66-2.57 (m, 2H), 2.51 (dd, *J* = 16.6, 6.3 Hz, 1H), 2.38-2.34 (m, 1H), 2.32-2.21 (m, 2H), 1.77-1.70 (m, 1H), 1.73 (d, *J* = 1.1 Hz, 3H), 1.67-1.59 (m, 2H), 1.60 (s, 3H), 1.56-1.44 (m, 3H), 1.41 (s, 6H), 1.36 (s, 3H), 1.34-1.25 (m, 2H), 1.22-1.19 (m, 1H), 1.17 (s, 9H), 0.91 (t, *J* = 7.4 Hz, 3H), 0.88 (t, *J* = 8.3 Hz, 2H), -0.02 (s, 9H); ^{13}C NMR (125 MHz, C_6D_6) δ 203.1, 170.6, 139.4, 137.7, 136.1, 136.0, 136.0, 134.2, 134.1, 129.9, 128.5, 128.3, 128.1, 127.9, 99.4, 98.8, 95.0, 79.4, 78.9, 77.4, 74.4, 70.8, 67.5, 66.0, 65.7, 57.3, 56.7, 56.2, 51.9, 51.2, 47.2, 43.4, 40.5, 39.5, 33.2, 30.3, 30.1, 27.2, 27.1, 27.0, 26.9, 25.1, 24.9, 23.6, 22.0, 20.8, 19.8, 19.5, 18.1, 11.9, -1.3; high resolution mass spectrum (ES+) *m/z* 1129.5595 [(M+Na)$^+$; calcd for $C_{57}H_{94}O_{13}S_2Si_2Na$: 1129.5572].



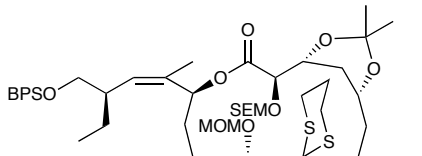
(-)-**SI 15**

Diol (-)-SI 15: To a solution of BH_3•THF (0.157 mL, of a 1 M solution in THF, 0.157 mmol) in THF (0.982 mL) at 0 °C was added (*R*)-2-methyl-CBS-oxazaborolidine (0.157 mL, of a 1 M solution in toluene, 0.157 mmol) over 5 min, stirred for 15 min, warmed to rt and stirred for 3 h. To a solution of the above enone (-)-**SI 14** in THF (4.24 mL) at –30 °C was added the above solution (0.873 mL, 0.106 mmol) slowly down the side of the flask and stirred for 48 h at –30 °C. To the reaction mixture was added MeOH (1 mL), warmed to rt and diluted with 0.5 M HCl (5 mL) and EtOAc (5 mL). The layers were separated and the aqueous layer extracted with EtOAc (3 x 5 mL). The combined organic layers were washed with water (2 x 5 mL) and brine (1 x 5 mL), dried over anhydrous Na_2SO_4, filtered and concentrated. Preparative thin layer chromatography (2:1 hexanes/ethyl acetate, 3% TEA)[4] afforded diol (-)-**SI 15** as a 10:1 mixture at C(15) (43 mg, 91% for 2 steps). $[\alpha]_D^{26}$ -14.0° (*c* 2.15, C_6H_6); IR (film) 3448 (br), 2957 (s), 2932 (s), 2895 (s), 1751 (s), 1112 (s), 1023 (s) cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ 7.81-7.78 (m, 4H), 7.33-7.24 (m, 6H), 4.93 (d, *J* = 10.3 Hz, 1H), 4.83 (dd, *J* = 10.0, 2.2 Hz, 1H), 4.79 (d, *J* = 7.0 Hz, 1H), 4.69-4.60 (m, 2H), 4.68 (d, *J* = 7.0 Hz, 1H), 4.55 (d, *J* = 10.3 Hz, 1H), 4.30 (ddd, *J* = 7.6, 5.4, 2.3 Hz, 1H), 4.24-4.18 (m, 1H), 4.18 (d, *J* = 5.3 Hz, 1H), 4.01 (br s, 1H), 3.83-3.76 (m, 1H), 3.71-3.58 (m, 4H), 3.54-3.51 (m, 1H), 3.52 (s, 3H), 3.40 (s, 3H), 3.27 (s, 3H), 3.22 (s, 3H), 3.17 (br s, 1H), 2.82-2.75 (m, 1H), 2.65-2.52 (m, 4H), 2.42-2.36 (m, 1H), 2.30-2.20 (m, 2H), 2.08 (br s, 1H), 1.83 (d, *J* = 1.1 Hz, 3H), 1.69 (dd, *J* = 24.2, 12.0 Hz, 1H), 1.61 (s, 3H), 1.58-1.49 (m, 3H), 1.46 (s, 3H), 1.41 (s, 3H), 1.36 (s, 3H), 1.20-1.15 (m, 3H), 1.19 (s, 9H), 0.93 (t, *J* = 7.4 Hz, 3H), 0.88 (ddd, *J* = 9.5, 6.9, 2.6 Hz, 2H), -0.02 (s, 9H); ^{13}C NMR (125 MHz, C_6D_6) δ 170.6, 140.3, 136.1, 134.1, 134.0, 130.0, 129.4, 128.5, 128.4, 128.3, 127.9, 99.4, 98.8, 95.1, 79.4, 79.0, 77.4, 76.2, 70.8, 68.1, 67.0, 65.0, 65.7, 64.6, 57.3, 56.1, 55.4, 52.0, 51.2, 46.8, 42.1, 39.6, 39.2, 39.0, 33.2, 30.3, 27.2, 27.1, 26.9, 26.5, 25.5, 25.1, 24.8, 24.7, 23.7, 22.0, 19.8, 19.7, 19.5, 18.4, 18.1, 12.2, -1.3; high resolution mass spectrum (ES+) *m/z* 1131.5809 [$(M+Na)^+$; calcd for $C_{57}H_{96}O_{13}S_2Si_2Na$: 1131.5789].



(-)-**25**

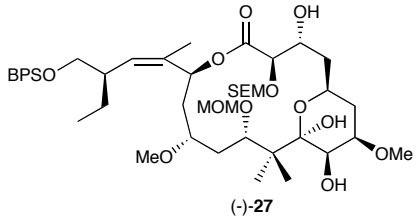
Seco-acid (-)-25: To a solution of diol (-)-**SI 16** (43 mg, 0.0387 mmol) in THF (2.58 mL) and water (0.86 mL) at rt was added LiOH (27.8 mg, 1.16 mmol). The reaction mixture was stirred for 24 h, diluted with EtOAc (5 mL) and acidified to pH 5 with 1 M HCl. The layers were separated and the aqueous layer extracted with EtOAc (5 x 5 mL), dried over anhydrous Na_2SO_4, filtered and concentrated to yield (-)-**25** as a colorless oil (42 mg, 99%) that was used without further purification. $[\alpha]_D^{22}$ -21.9° (*c* 2.10, C_6H_6); IR (film) 3440 (br), 2957 (s), 2932 (s), 2895 (s), 1733 (s), 1112 (s), 1060 (s) cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ 7.82-7.80 (m, 4H), 7.34-7.25 (m, 6H), 4.96 (d, *J* = 9.4 Hz, 1H), 4.84 (dd, *J* = 9.7, 2.5 Hz, 1H), 4.77 (d, *J* = 6.8 Hz, 1H), 4.70 (d, *J* = 6.6 Hz, 1H), 4.67-4.65 (m, 2H), 4.57 (d, *J* = 10.4 Hz, 1H), 4.37 (ddd, *J* = 7.6, 5.4, 2.3 Hz, 1H), 4.24 (dd, *J* = 10.8, 10.8 Hz, 1H), 4.17 (d, *J* = 4.5 Hz, 1H), 4.07 (br s, 1H), 3.81 (br s, 1H), 3.69-3.60 (m, 4H), 3.55 (dd, *J* = 9.8, 6.8 Hz, 1H), 3.53 (s, 3H), 3.30 (s, 3H), 3.26 (s, 3H), 3.06 (br s, 1H), 2.77 (ddd, *J* = 15.5, 11.2, 6.3 Hz, 1H), 2.62-2.53 (m, 3H), 2.45-2.42 (m, 1H), 2.29-2.17 (m, 2H), 1.84 (d, *J* = 1.2 Hz, 3H), 1.73 (dd, *J* = 24.1, 11.9 Hz, 1H), 1.62 (s, 3H), 1.60-1.51 (m, 4H), 1.47 (s, 3H), 1.41 (s, 3H), 1.40 (s, 3H), 1.37-1.23 (m, 4H), 1.19 (s, 9H), 1.19-1.11 (m, 2H), 0.98-0.86 (m, 5H), 0.00 (s, 9H); ^{13}C NMR (125 MHz, C_6D_6) δ 173.1, 140.2, 136.1, 134.1, 130.0, 130.0, 129.3, 128.5, 128.3, 128.1, 99.3, 99.0, 95.1, 79.8, 78.9, 77.7, 76.5, 70.8, 68.1, 67.2, 66.0, 66.0, 57.3, 56.1, 55.5, 52.0, 42.1, 39.4, 38.3, 39.2, 33.4, 30.2, 30.1, 27.3, 27.2, 27.2, 26.9, 25.2, 25.1, 24.6, 24.5, 24.4, 23.6, 23.1, 22.1, 19.8, 19.5, 18.5, 18.1, 12.2, 12.0, -1.3; high resolution mass spectrum (ES+) *m/z* 1117.5618 [(M+Na)$^+$; calcd for $C_{56}H_{94}O_{13}S_2Si_2Na$: 1117.5571].



(-)-**26**

Macrocycle (-)-26: To a solution of seco-acid (-)-**25** (30 mg, 0.274 mmol) in THF (2.74 mL) at 0 °C was added DIEA (0.286 mL, 1.64 mmol) and 2,4,6-trichlorobenzoyl chloride (0.085 mL, 0.548 mmol) dropwise, slowly warmed to rt and stirred for 16 h. The reaction was diluted with toluene (7.82 mL) and added via syringe pump

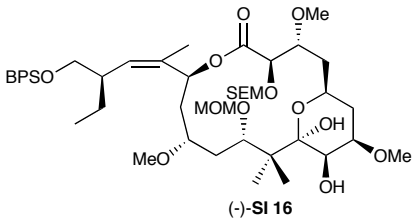
over a period of 8 h to a 90 °C solution of DMAP (167 mg, 1.37 mmol) in toluene (40.26 mL). The seco-acid flask was rinsed with toluene (2 x 2.74 mL) and added to the DMAP solution over 5 h for each rinse. The reaction was stirred for an additional 6 h and cooled to rt, diluted with EtOAc (25 mL) and quenched with saturated aq. $NaHCO_3$ (20 mL) and water (20 mL). The layers were separated and the aqueous layer extracted with EtOAc (3 x 20 mL). The combined organic layers were washed with 1 M HCl (2 x 10 mL) and brine (1 x 10 mL), dried over anhydrous Na_2SO_4, filtered and concentrated. Preparative thin layer chromatography (10:1 hexanes/ethyl acetate, 3% TEA)[4] afforded macrocycle (-)-**26** as a colorless oil (21 mg, 71%). $[\alpha]_D^{23}$ -2.56° (*c* 0.39, C_6H_6); IR (film) 3309 (bd), 2957 (s), 2932 (s), 2895 (s), 2857 (m), 1750 (s), 1105 (s), 1035 (s) cm^{-1}; ^1H NMR (500 MHz, C_6D_6, 363 K) δ 7.85-7.81 (m, 4H), 7.34-7.26 (m, 6H), 6.14-6.11 (m, 1H), 5.29 (d, *J* = 10.1 Hz, 1H), 4.89-4.82 (m, 3H), 4.77 (d, *J* = 5.7 Hz, 1H), 4.58-4.55 (m, 2H), 4.43-4.40 (m, 1H), 4.11 (br s, 1H), 3.94-3.86 (m, 4H), 3.77 (dd, *J* = 9.8, 6.2 Hz, 1H), 3.73-3.68 (m, 1H), 3.32-3.31 (m, 1H), 3.28 (s, 3H), 3.28-3.24 (m, 1H), 3.24 (s, 3H), 3.23 (s, 3H), 3.12-2.97 (m, 1H), 2.77 (br s, 1H), 2.66 (br s, 1H), 2.41-2.28 (m, 4H), 2.17-2.13 (m, 3H), 1.92-1.83 (m, 2H), 1.79-1.75 (m, 1H), 1.74 (d, *J* = 1.1 Hz, 3H), 1.57 (s, 6H), 1.52 (s, 3H), 1.52-1.43 (m, 2H), 1.43 (s, 3H), 1.38-1.26 (m, 3H), 1.21 (s, 9H), 0.96-0.92 (m, 5H), 0.00 (s, 9H); ^{13}C NMR (125 MHz, C_6D_6, 363 K) δ 168.6, 136.1, 134.7, 134.7, 133.8, 132.7, 129.8, 128.8, 128.5, 128.3, 127.9, 99.5, 98.3, 94.8, 82.5, 81.2, 77.1, 76.8, 71.7, 68.6, 67.3, 65.9, 65.6, 56.3, 55.8, 55.0, 53.0, 49.3, 41.8, 39.2, 38.8, 36.3, 32.6, 30.2, 30.1, 30.1, 28.4, 27.4, 27.2, 25.2, 23.8, 23.6, 22.6, 21.9, 20.0, 19.8, 18.9, 18.4, 11.7, -1.2; high resolution mass spectrum (ES+) *m/z* 1099.5515 [$(M+Na)^+$; calcd for $C_{56}H_{92}O_{12}S_2Si_2Na$: 1099.5467].



(-)-**27**

Pyran (-)-27: To a solution of macrocycle (-)-**26** (6 mg, 0.0055 mmol) in acetonitrile (1.55 mL) and water (0.155 mL) at 0 °C was added $PhI(O_2CCF_3)_2$ (6 mg, 0.014 mmol) and stirred for 30 min. The reaction was warmed to rt and stirred for an additional 6 h, diluted with EtOAc (2 mL) and quenched with saturated aq. $NaHCO_3$ (2 mL). The layers were separated and the aqueous layer extracted with EtOAc (4 x 5 mL). The combined organic layers were washed with brine (1 x 10 mL), dried over anhydrous Na_2SO_4, filtered and concentrated.

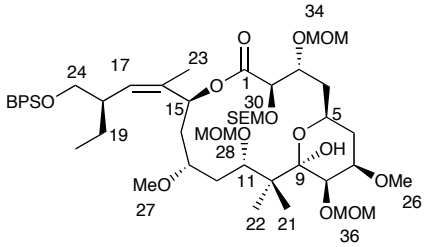
Preparative thin layer chromatography (1:1 hexanes/ethyl acetate, 3% TEA)[4] afforded pyran (-)-**27** as a colorless oil (3.7 mg, 70%). $[\alpha]_D^{22}$ -18.4° (*c* 0.185, C_6H_6); IR (film) 3407 (br), 2957 (s), 2930 (s), 2894 (s), 2858 (m), 1748 (s), 1092 (s), 1057 (s), 1028 (s); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.68-7.63 (m, 4H), 7.41-7.33 (m, 6H), 5.76 (br s, 1H), 5.18 (d, *J* = 10.5 Hz, 1H), 4.75 (d, *J* = 7.0 Hz, 1H), 4.70 (d, *J* = 7.1 Hz, 1H), 4.67 (d, *J* = 7.0 Hz, 1H), 4.49 (d, *J* = 7.1 Hz, 1H), 4.35 (br s, 1H), 4.27 (s, 1H), 4.06 (br s, 1H), 3.94 (d, *J* = 2.4 Hz, 1H), 3.81-3.74 (m, 4H), 3.72-3.62 (m, 2H), 3.58-3.49 (m, 4H), 3.43-3.40 (m, 1H), 3.40 (s, 3H), 3.35 (s, 3H), 3.30 (br s, 3H), 2.72 (br s, 1H), 2.65 (br s, 1H), 2.17-2.11 (m, 1H), 2.04 (dd, *J* = 15.7, 4.6 Hz, 1H), 1.90 (dd, *J* = 15.6, 9.6 Hz, 1H), 1.74-1.61 (m, 3H), 1.66 (s, 3H), 1.35-1.26 (m, 2H), 1.12 (s, 3H), 1.05 (s, 9H), 1.04 (s, 3H), 0.93-0.85 (m, 2H), 0.83 (t, *J* = 7.5 Hz, 3H), -0.10 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.4, 135.7, 135.6, 134.2, 134.2, 134.1, 130.6, 129.4, 129.4, 127.5, 127.5, 98.9, 95.0, 78.0, 77.7, 77.6, 76.2, 70.4, 69.5, 68.2, 66.4, 66.1, 66.0, 61.8, 56.9, 56.2, 55.9, 47.0, 41.2, 37.7, 37.7, 34.8, 29.7, 27.0, 26.9, 24.5, 21.8, 19.4, 18.9, 18.5, 18.0, 11.7, 11.6, -1.4; high resolution mass spectrum (ES+) *m/z* 969.5174 [(M+Na)$^+$; calcd for $C_{50}H_{82}O_{13}Si_2Na$: 969.5192].



(-)-**SI 16**

Pyran (-)-SI 16: To a solution of pyran (-)-**27** (8.8 mg, 0.0093 mmol) in CH_2Cl_2 (5.9 mL) at 0 °C was added 2,6-di-*tert*-buty-4-methy-pyridine (398 mg, 1.94 mmol), followed by Me_3OBF_4 (206 mg, 1.76 mmol) and stirred for 10 hr. at 0 °C. The reaction was diluted with CH_2Cl_2 (5 mL) and quenched with saturated aq. $NaHCO_3$ (3 mL). The layers were separated and the aqueous layer extracted with CH_2Cl_2 (4 x 5 mL). The combined organic layers were washed with 1 M HCl (2 x 5 mL), brine (1 x 10 mL), dried over anhydrous Na_2SO_4, filtered and concentrated. Preparative thin layer chromatography (2:1, hexanes/ethyl acetate, 3% TEA)[4] afforded pyran (-)-**SI 16** as a colorless oil (7.6 mg, 85%). $[\alpha]_D^{22}$ -21.1° (*c* 0.38, C_6H_6); IR (film) 3401 (bd), 2945 (s), 2927 (s), 2854 (s), 2809 (m), 1745 (s), 1192 (s), 1101 (s) cm^{-1}; ^{1}H NMR (500 MHz, C_6D_6) δ 7.89-7.84 (m, 4H), 7.36-7.24 (m, 6H), 6.19 (d, *J* = 10.0 Hz, 1H), 5.16 (d, *J* = 10.5 Hz, 1H), 4.84 (s, 1H), 4.81 (d, *J* = 7.0 Hz, 1H), 4.79 (d, *J* = 7.0 Hz, 1H), 4.53 (d, *J*

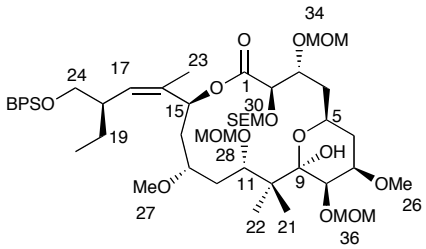
= 6.4 Hz, 1H), 4.49 (br s, 1H), 4.24 (br s, 1H), 4.15 (s, 1H), 4.00-3.91 (m, 3H), 3.84 (br s, 1H), 3.74 (dd, *J* = 9.7, 6.8 Hz, 1H), 3.69 (br s, 1H), 3.60 (br s, 1H), 3.54 (dd, *J* = 17.5, 7.9 Hz, 1H), 3.35 (s, 3H), 3.19 (s, 3H), 3.10 (br s, 6H), 3.00 (br s, 1H), 2.54 (br s, 1H), 2.03-1.82 (m, 5H), 1.76-1.64 (m, 1H), 1.71 (s, 6H), 1.46-1.34 (m, 5H), 1.21 (s, 12H), 0.97-0.84 (m, 5H), -0.02 (s, 9H); ^{13}C NMR (125 MHz, C_6D_6) δ 169.7, 136.1, 136.1, 135.2, 134.5, 134.4, 130.6, 129.8, 129.1, 128.3, 128.1, 101.8, 99.2, 94.1, 78.1, 76.8, 76.1, 74.4, 69.0, 67.0, 65.9, 65.4, 57.0, 56.2, 55.3, 55.2, 47.6, 42.0, 38.6, 36.5, 34.7, 30.9, 30.4, 30.1, 27.2, 25.1, 22.0, 19.7, 19.0, 18.2, 12.0, -1.3; high resolution mass spectrum (ES+) *m/z* 983.5300 [(M+Na)$^+$; calcd for $C_{51}H_{84}O_{13}Si_2Na$: 983.5348].



(-)-**SI 17**

Tri-MOM (-)-SI 17: To a solution of crude pyran (-)-**27** (4.34 mg, 0.0045 mmol) in DMF (0.5 mL) at rt was added DIEA (0.012 mL, 0.07 mmol), followed by MOMCl (0.003, 0.036 mmol). The reaction mixture was stirred for 24 h, diluted with CH_2Cl_2 (5 mL) and quenched with water (3 mL). The layers were separated and the aqueous layer extracted with CH_2Cl_2 (4 x 2 mL). The combined organic layers were washed with water (1 x 5 mL), dried over anhydrous Na_2SO_4, filtered and concentrated. Preparative thin layer chromatography (5:1, hexanes/ethyl acetate, 3% TEA)[4] afforded tri-MOM (-)-**SI 17** as a colorless oil (3 mg, 65% for 2 steps). $[\alpha]_D^{23}$ -23.3° (*c* 0.15, C_6H_6); IR (film) 3415 (bd), 2953 (s), 2912 (s), 2879 (s), 2837 (m), 1746 (s), 1152 (s), 1099 (s) cm^{-1}; ^{1}H NMR (500 MHz, C_6D_6) δ 7.89-7.84 (m, 4H), 7.35-7.25 (m, 6H), 6.25 (dd, *J* = 7.3, 4.0 Hz, 1H), 5.14 (d, *J* = 10.6 Hz, 1H), 5.09 (d, *J* = 6.1 Hz, 1H), 4.89 (d, *J* = 6.1 Hz, 1H), 4.85 (br, *J* = 12.0 Hz, 1H), 4.84 (d, *J* = 7.0 Hz, 1H), 4.83 (d, *J* = 7.0 Hz, 1H), 4.78 (s, 1H), 4.77 (d, *J* = 6.7 Hz, 1H), 4.69 (d, *J* = 6.7 Hz, 1H), 4.61 (d, *J* = 6.1 Hz, 1H), 4.58 (d, *J* = 6.9 Hz, 1H), 4.48 (s, 1H), 4.15 (d, *J* = 1.7 Hz, 1H), 4.06-4.00 (m, 3H), 3.93 (q, *J* = 8.1 Hz, 1H), 3.83-3.78 (m, 1H), 3.72 (dd, *J* = 9.8, 6.9 Hz, 1H), 3.67 (d, *J* = 7.2 Hz, 1H), 3.57 (q, *J* = 8.1 Hz, 1H), 3.32 (s, 3H), 3.31 (s, 3H), 3.18 (s, 3H), 3.14 (s, 3H), 3.05-3.00 (m, 1H), 3.00 (s, 3H), 2.99-2.93 (m, 1H), 2.89-2.83 (m, 1H), 2.16-1.93 (m, 3H), 1.83-1.64 (m, 4H), 1.69 (d, *J* = 1.3 Hz, 3H), 1.67 (s, 3H), 1.46 (s, 3H), 1.43-1.39 (m, 1H), 1.21 (s, 9H), 0.91 (t, *J* = 8.1 Hz, 2H), 0.86 (t, *J* = 7.4 Hz, 3H), -0.03 (s, 9H); ^{13}C NMR (125 MHz, C_6D_6) δ 169.7, 136.1, 136.1, 135.1, 134.5, 134.3,

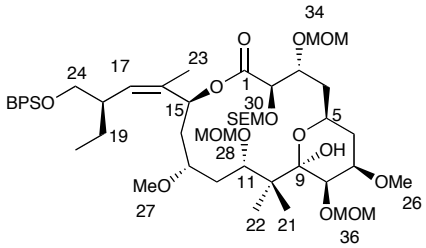
130.5, 129.9, 128.3, 128.1, 127.9, 101.7, 99.1, 98.3, 94.8, 94.2, 84.5, 77.7, 77.4, 76.3, 75.7, 72.3, 68.9, 67.0, 65.5, 65.1, 57.3, 56.7, 55.7, 55.4, 55.1, 47.8, 42.1, 38.9, 38.9, 38.5, 34.2, 32.6, 27.3, 25.1, 21.4, 19.7, 19.0, 18.1, 17.7, 12.0, -1.3; high resolution mass spectrum (ES+) *m/z* 1057.5671 [(M+Na)$^+$; calcd for $C_{54}H_{90}O_{15}Si_2Na$: 1057.5716].



(-)-**SI 17**

Summary of COSY Spectrum for (-)-**SI 17.**

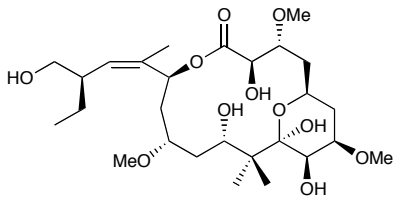
1. Protons at 6.25 ppm C(15) show cross peaks with protons at 1.83-1.64 ppm C(14).
2. Protons at 5.14 ppm C(17) show cross peaks with protons at 2.99-2.93 ppm C(18), 1.69 ppm C(23).
3. Protons at 4.85 ppm C(3) show cross peaks with protons at 2.89-2.83 ppm C(4), 2.16-1.93 ppm C(4).
4. Protons at 4.15 ppm C(8) show cross peaks with protons at 4.06-4.00 ppm C(7).
5. Protons at 4.06-4.00 ppm C(7) show cross peaks with protons at 2.16-1.93 ppm C(6), 1.83-1.64 ppm C(6).
6. Protons at 4.06-4.00 ppm C(5) show cross peaks with protons at 2.16-1.93 ppm C(6), 1.83-1.64 ppm C(6), 2.16-1.93 ppm C(4).
7. Protons at 4.06-4.00 ppm, 3.72 C(24) show cross peaks with protons at 2.99-2.93 ppm C(18).
8. Protons at 2.99-2.93 ppm C(18) show cross peaks with protons at 2.16-1.93 ppm C(19), 1.43-1.39 ppm C(19).
9. Protons at 2.16-1.93 ppm, 1.43-1.39 C(19) show cross peaks with protons at 0.86 ppm C(20).
10. Protons at 3.67 ppm C(11) show cross peaks with protons at 1.83-1.64 ppm C(12).
11. Protons at 3.83-3.78 ppm C(13) show cross peaks with protons at 3.05-3.00 ppm C(12), 2.16-1.93 ppm C(14).



(-)-**SI 17**

Summary of NOESY Spectrum of (-)**-SI 17.**

1. Protons at 6.25 ppm C(15) show NOE cross peaks with protons at 2.99-2.93 ppm C(18), 3.18 ppm C(27).
2. Protons at 5.14 ppm C(17) show NOE cross peaks with protons at 1.69 ppm C(23), 3.72 ppm C(24), 1.43-1.39 C(19), 0.86 ppm C(20).
3. Protons at 0.86 ppm C(20) show NOE cross peaks with protons at 3.18 ppm C(27), 2.99-2.93 ppm C(18).
4. Protons at 4.58 ppm C(28) show NOE cross peaks with protons at 1.67 ppm C(21), 1.46 ppm C(22), 3.67 ppm C(11).
5. Protons at 4.15 ppm C(8) show NOE cross peaks with protons at 1.46 ppm C(22), 4.48 ppm C(9)OH, 3.83-3.78 ppm C(13), 4.58 ppm C(28).
6. Protons at 3.67 ppm C(11) show NOE cross peaks with protons at 1.46 ppm C(22), 4.48 ppm C(9)OH, 3.83-3.78 ppm C(13), 4.58 ppm C(28).
7. Protons at 4.48 ppm C(9)OH show NOE cross peaks with protons at 3.67 ppm C(11), 4.06-4.00 ppm C(5), C(7), 3.18 ppm C(27).
8. Protons at 5.09 ppm, 4.89 ppm C(36) show NOE cross peaks with protons at 3.00 ppm C(26).
9. Protons at 3.83-3.78 ppm C(13) show NOE cross peaks with protons at 3.18 ppm C(27).
10. Protons at 4.85 ppm C(3) show NOE cross peaks with protons at 3.05 ppm C(12), 4.77, 4.69 ppm C(34), 4.06-4.00 ppm C(15), 1.67 ppm C(21), 4.78 ppm C(2).
11. Protons at 4.78 ppm C(2) show NOE cross peaks with protons at 1.69 ppm C(23), 4.84 ppm C(30).



2-*epi*-peloruside A (-)-**28**

2-*epi*-peloruside A (-)-28: To a solution of pyran (-)-**SI 16** (8 mg, 0.0083 mmol) in MeOH (2.4 mL) was added 4 M HCl (2.4 mL) over a period of 1 h. The reaction was stirred for 2 h, cooled to 0 °C, diluted with EtOAc (2 mL) and quenched with saturated aq. $NaHCO_3$ until pH 8.0. The layers were separated and the aqueous layer extracted with EtOAc (5 x 5 mL), dried over anhydrous Na_2SO_4, filtered and concentrated. Flash chromatography (ethyl acetate) afforded 2-*epi*-peloruside A (-)-**28** as an amorphous solid (3.0 mg, 66%). $[\alpha]_D^{23}$ -37.8° (*c* 0.045, CH_2Cl_2); IR (film) 3398 (br), 2919 (s), 2857 (m), 1731 (s), 1461 (m), 1379 (m), 1262 (m), 1201 (m), 1089 (s), 1064 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_6$) δ 5.82 (dd, *J* = 6.8, 2.6 Hz, 1H), 5.01 (d, *J* = 10.5 Hz, 1H), 4.50 (s, 1H), 4.10-4.08 (m, 1H), 3.98 (d, *J* = 2.8 Hz, 1H), 3.80-3.73 (m, 2H), 3.69-3.61 (m, 2H), 3.57-3.53 (m, 1H), 3.42 (s, 3H), 3.41-3.31 (m, 2H), 3.39 (s, 3H), 3.30 (s, 3H), 2.81 (br s, 1H), 2.78-2.70 (m, 1H), 2.52 (br s, 1H), 2.32-2.20 (m, 1H), 2.08-1.99 (m, 2H), 1.83-1.70 (m, 3H), 1.68 (d, *J* = 0.6 Hz, 3H), 1.49-1.39 (m, 3H), 1.21 (s, 3H), 1.20-1.09 (m, 2H), 1.02 (s, 3H), 1.00-0.96 (m, 1H), 0.87 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_6$) δ 173.4, 136.0, 131.9, 101.9, 78.8, 76.5, 72.5, 70.8, 70.8, 70.6, 66.8, 66.2, 65.0, 57.6, 56.1, 55.8, 47.2, 42.5, 39.8, 35.9, 34.3, 29.9, 28.3, 25.1, 22.3, 22.3, 18.2, 11.9; high resolution mass spectrum (ES+) *m/z* 571.3116 [$(M+Na)^+$; calcd for $C_{27}H_{48}O_{11}Na$: 571.3095].

III. Computational Studies

Conformational searches of (-)-**26** and the 2-epi-**26** were performed using with MMFF force field as implemented in Macromodel 7.2[1]. For each structure 35000 steps of Monte Carlo searches were performed with MCMM keyword in 5000 steps batches starting from different initial structures until no new low energy conformation families were obtained and the global minimum structures were found more than one time. The solvent effect has been modeled with a Generalized Born/Surface Area (GB/SA) model in chloroform. Lowest energy structures within 50 kj/mol were clustered based on the ring torsions with XCluster[2] software. Lowest energy representative structures of the clustered families were subjected to PM3[3] geometry optimizations. The energy difference between the lowest energy structures of (-)-**26** and the desired epimer were calculated to be 11.4 kcal/mol at the

PM3 level. The two lowest energy structures were further given into geometry optimization at B3LYP/6-31G (d,p) level[4] using Gaussian 03[5] software on 64-node Linux cluster[6] running on Red Hat 9. Each optimization was calculated on 8 nodes of dual 2.8GHz Xeon processors with 2GB memory and were completed in 10 days. The undesired isomer (-)-**26** is found to be the thermodynamically more stable product with 1.802 kcal/mol energy difference. The coordinate files can be obtained from author upon request.

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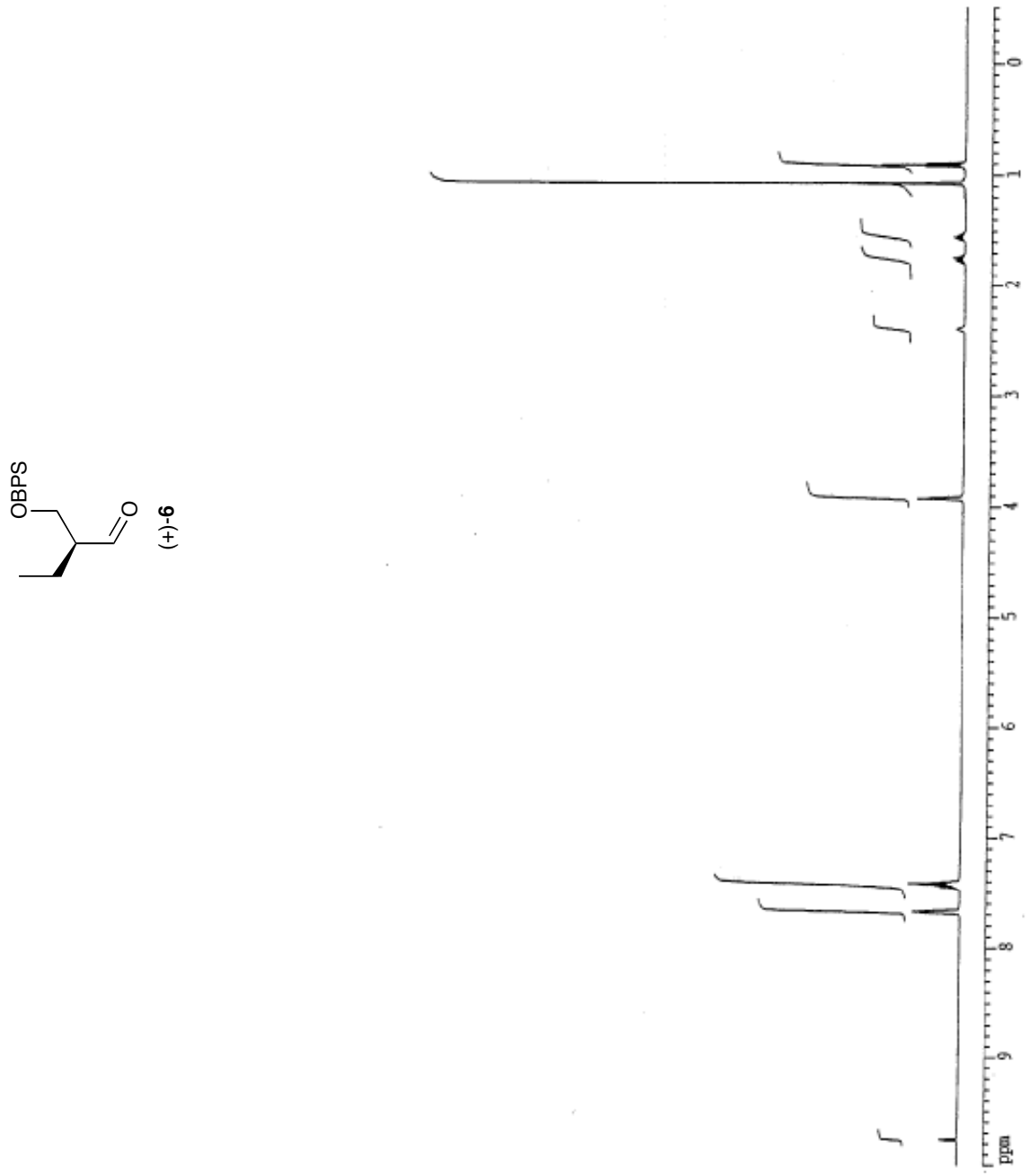
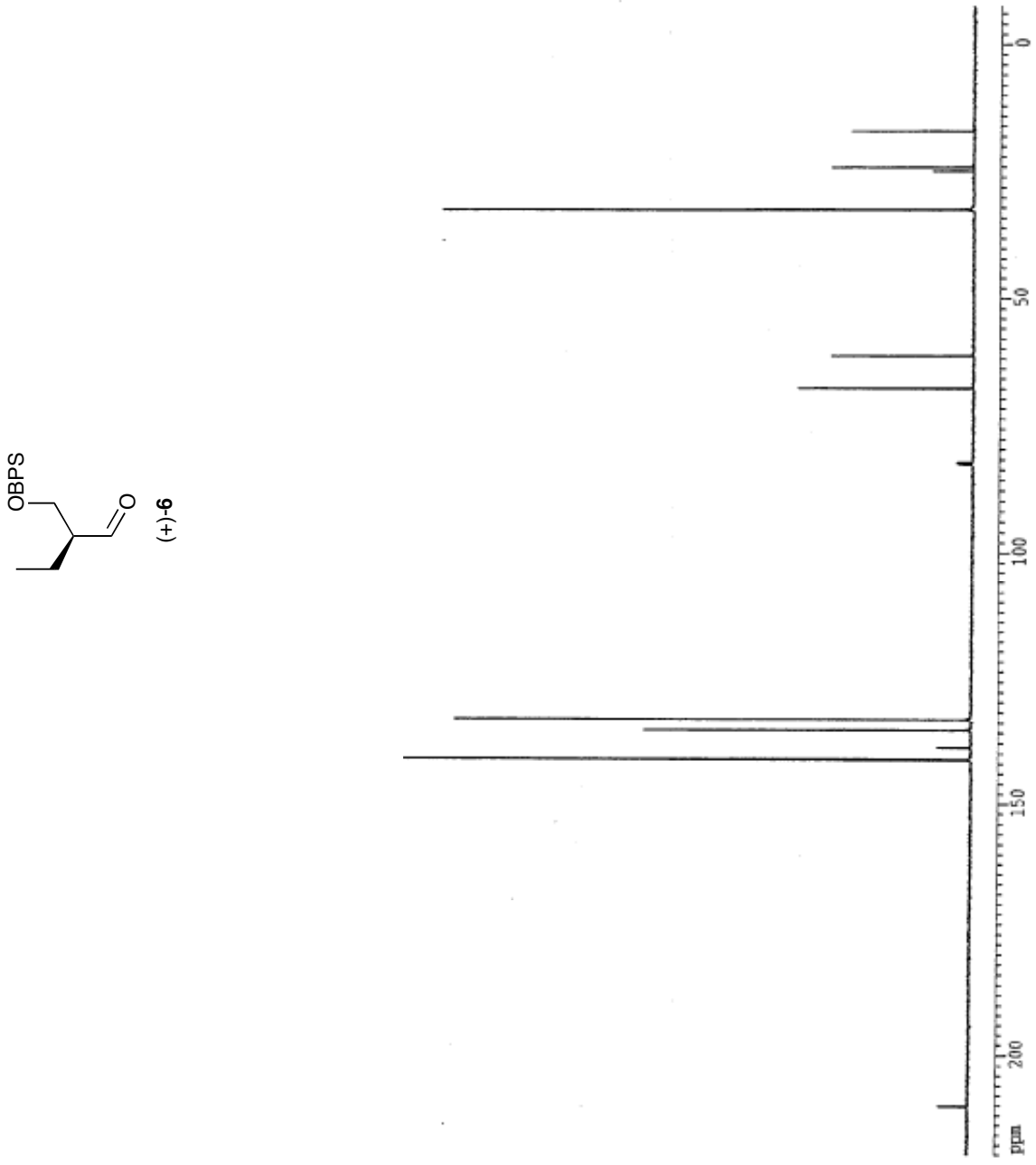
(6) This material is based upon work supported by the National Science Foundation under Grant No. 0131132.

IV. Spectra

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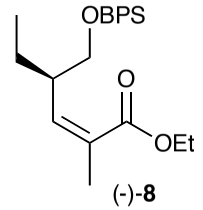

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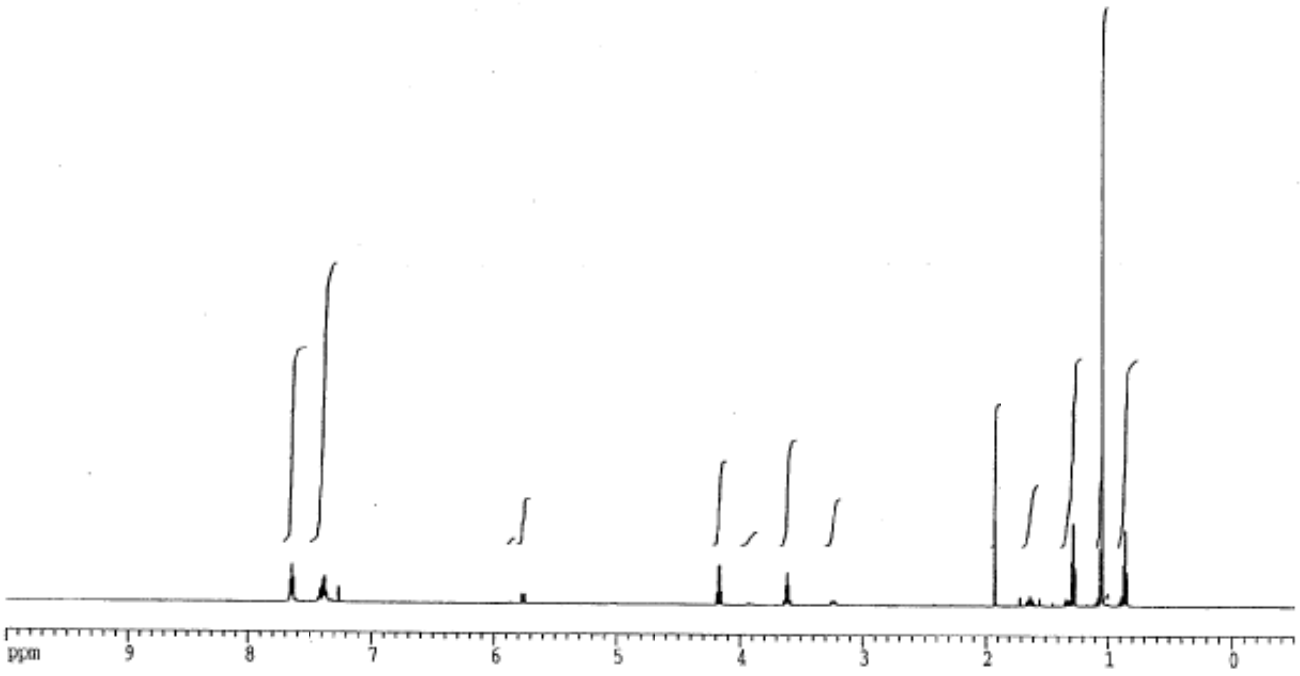

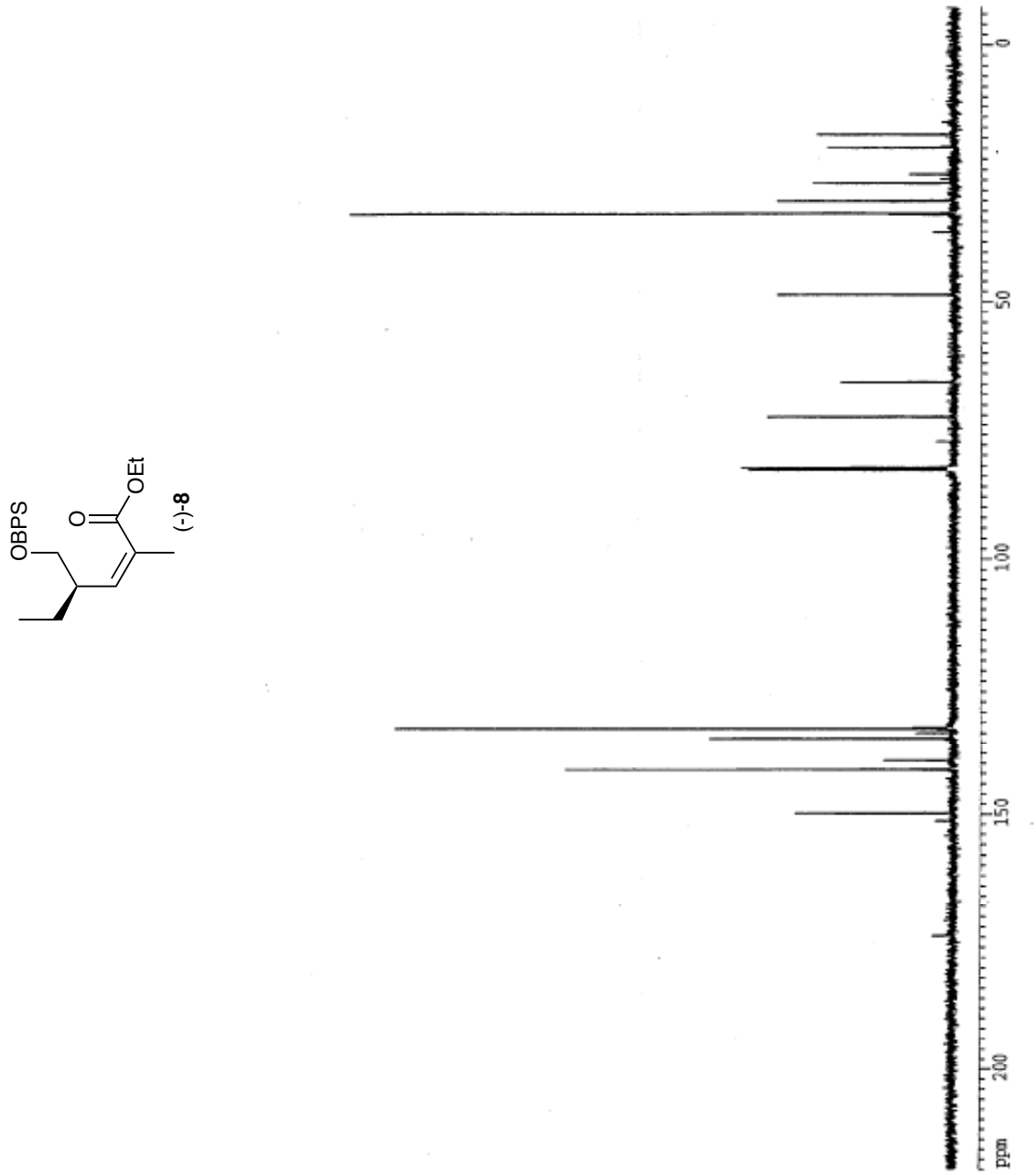
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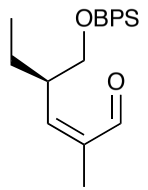

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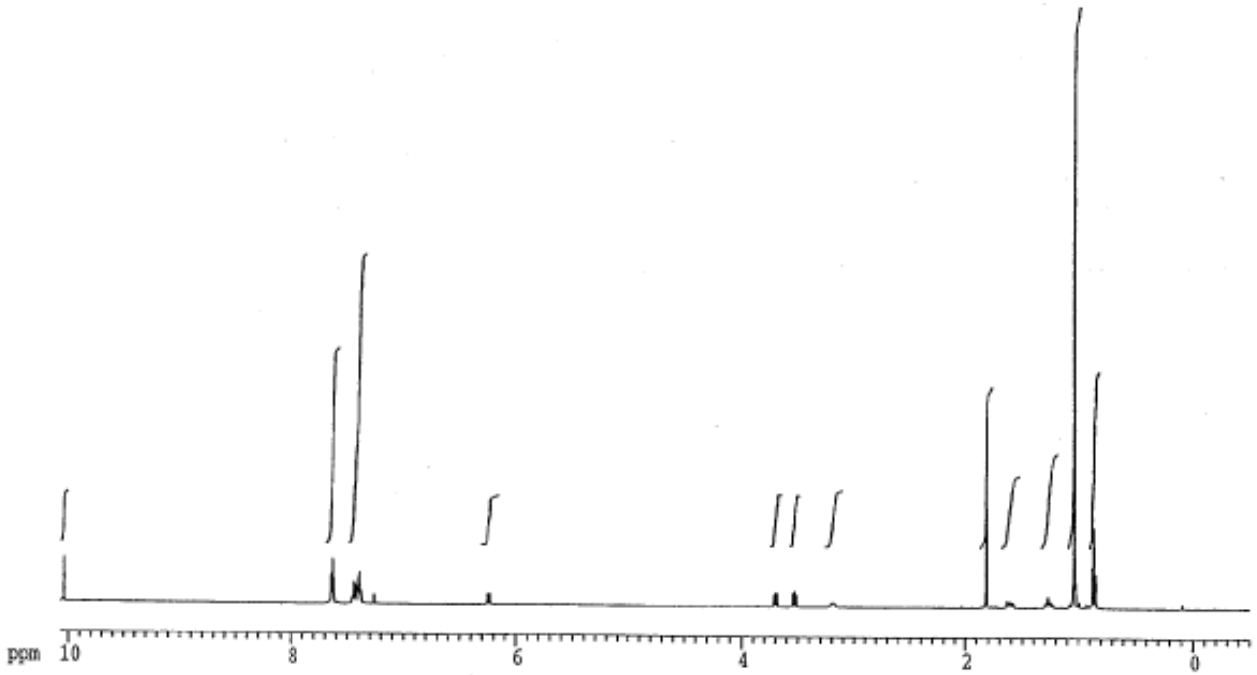

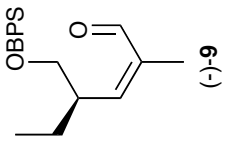

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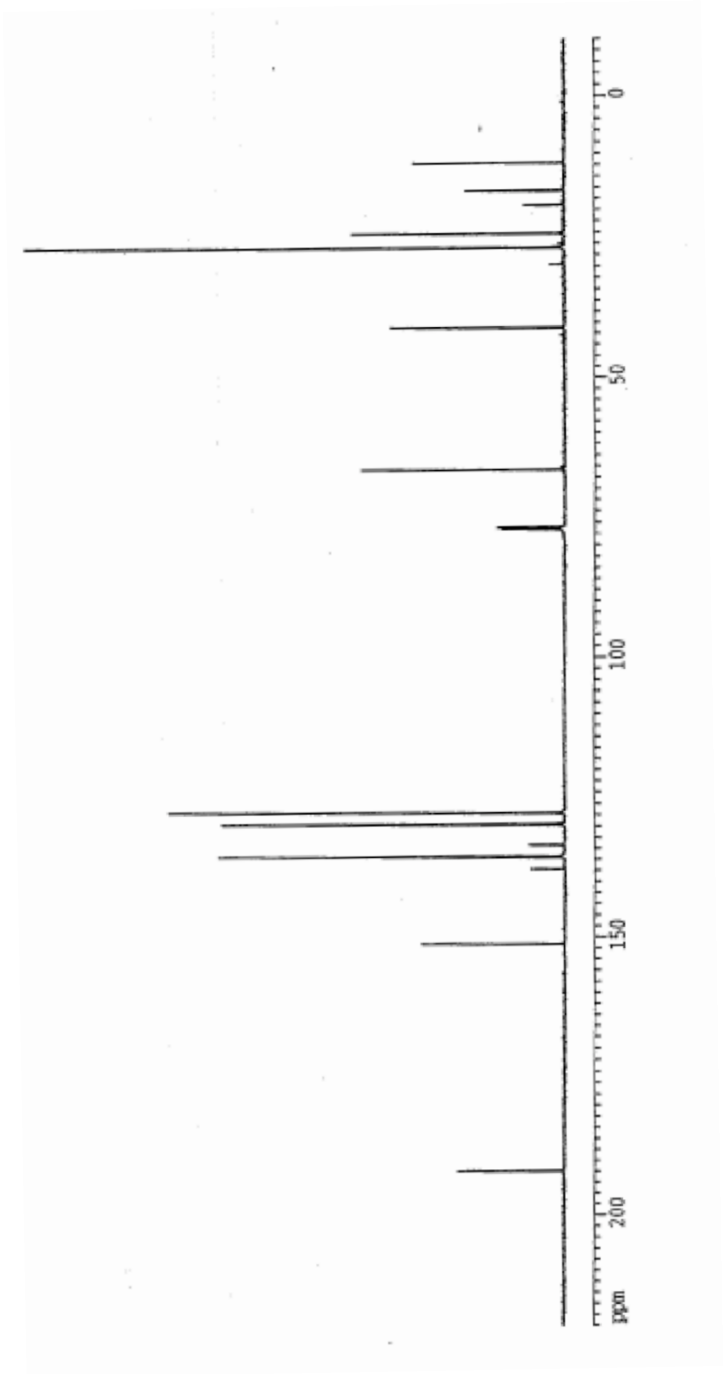

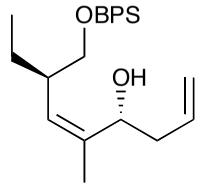

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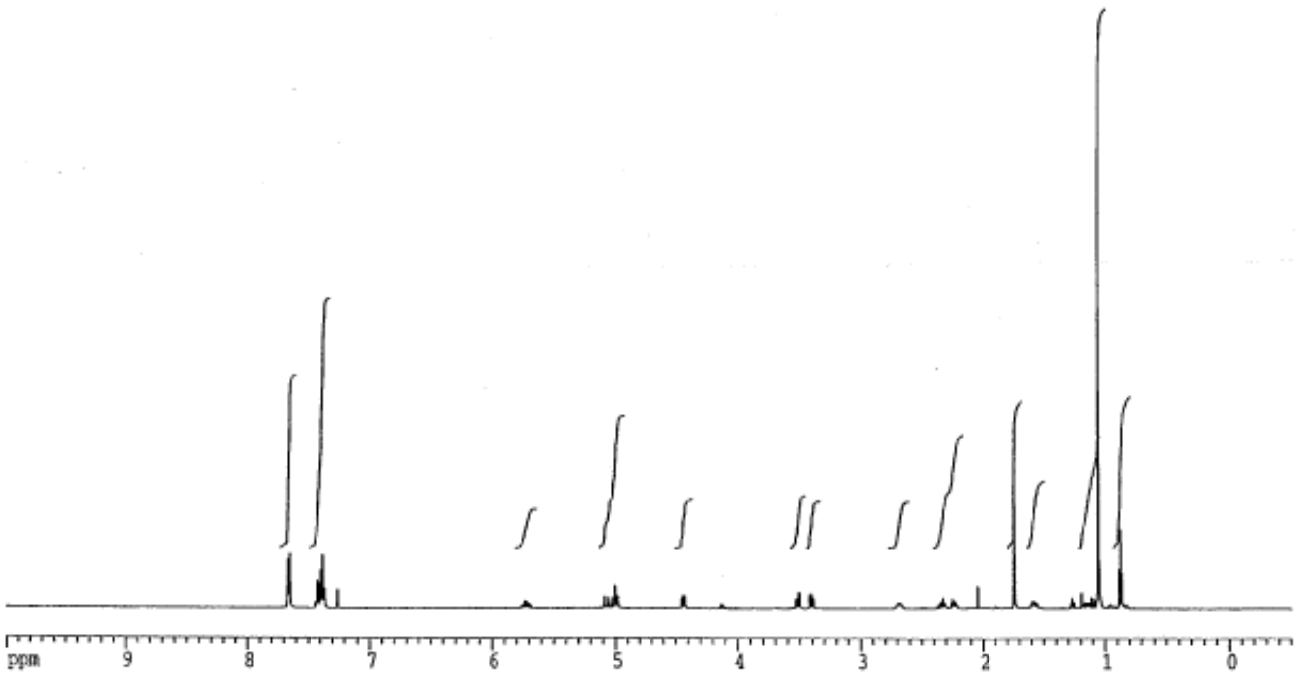

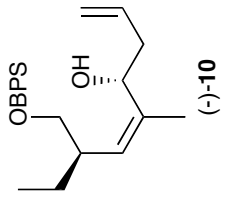

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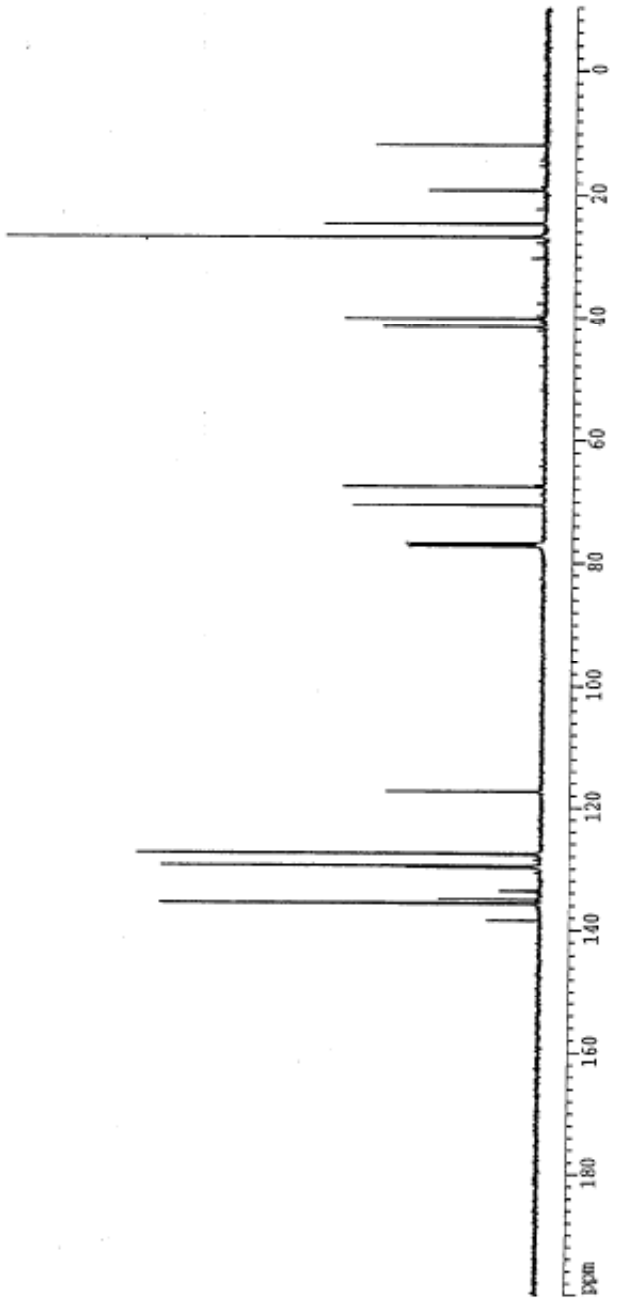

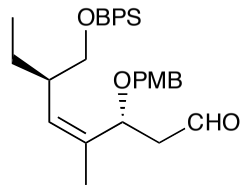

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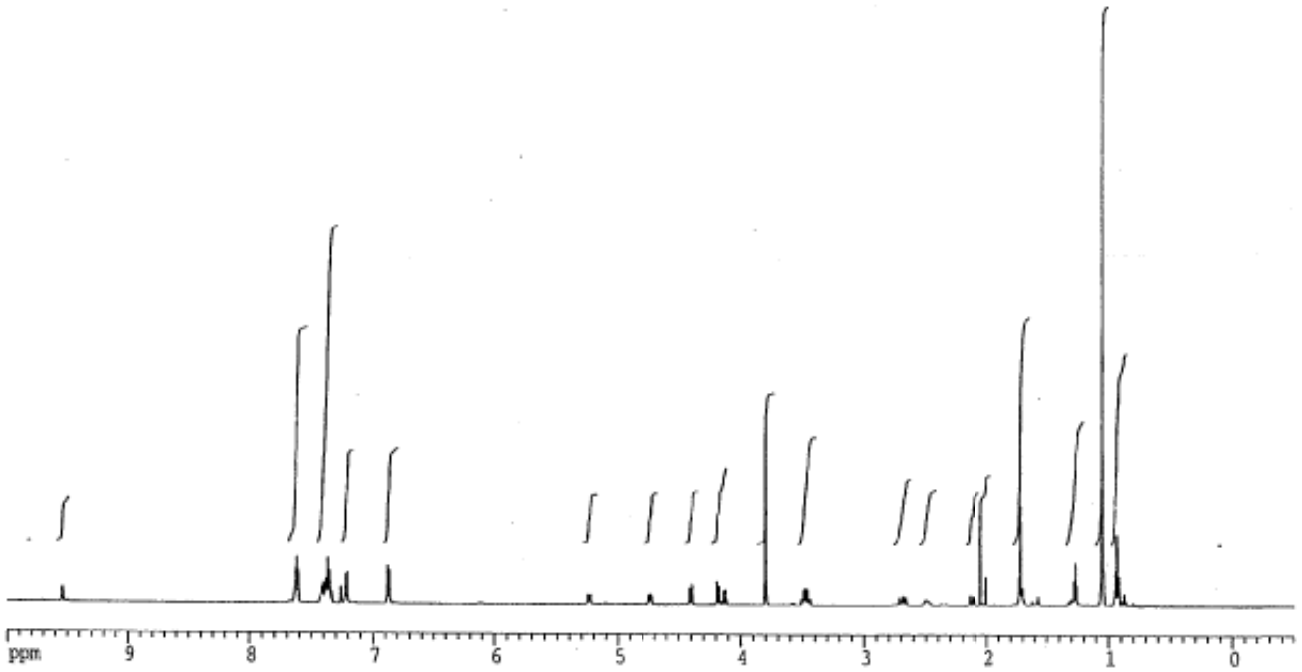

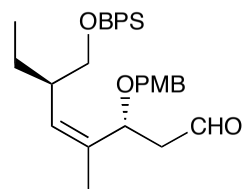

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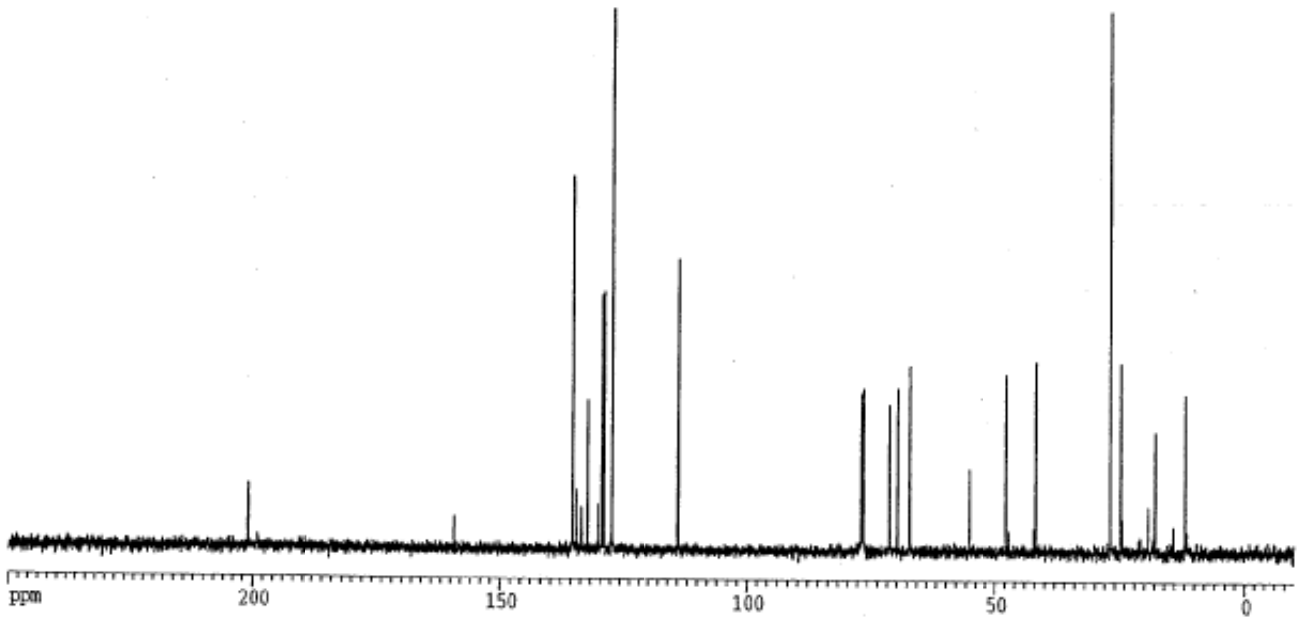

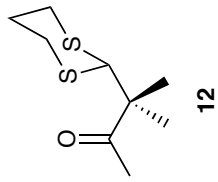

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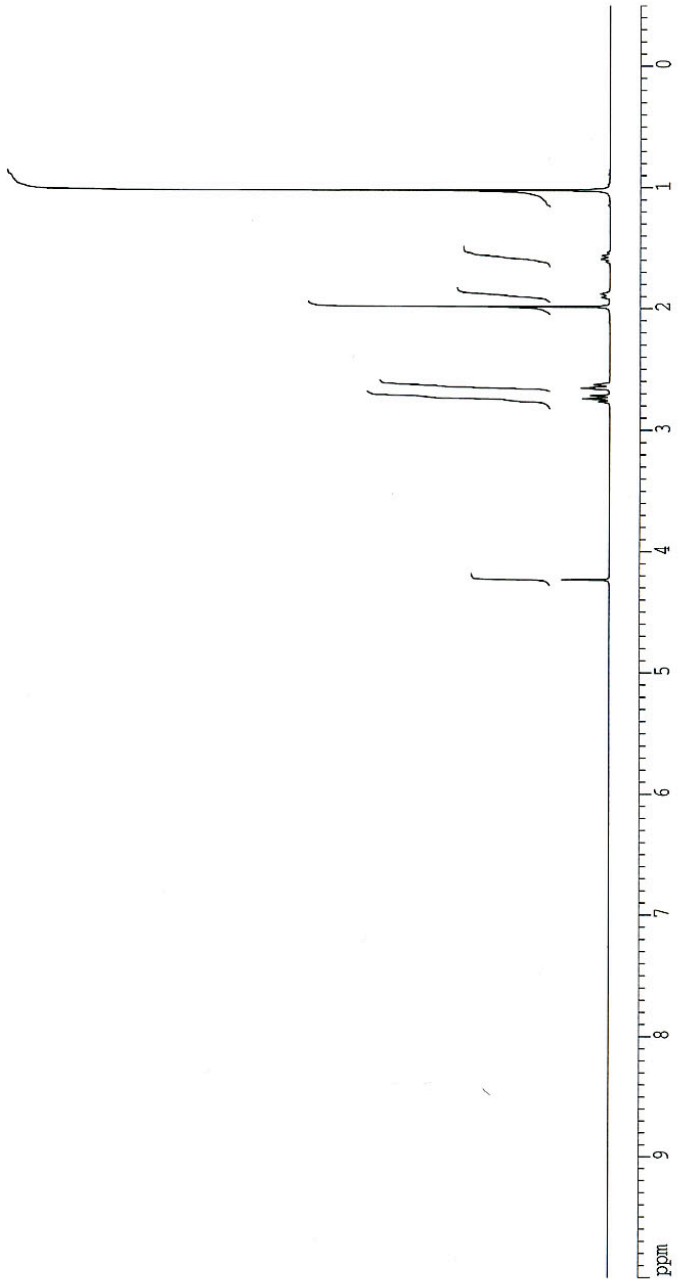

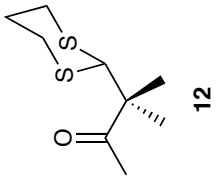

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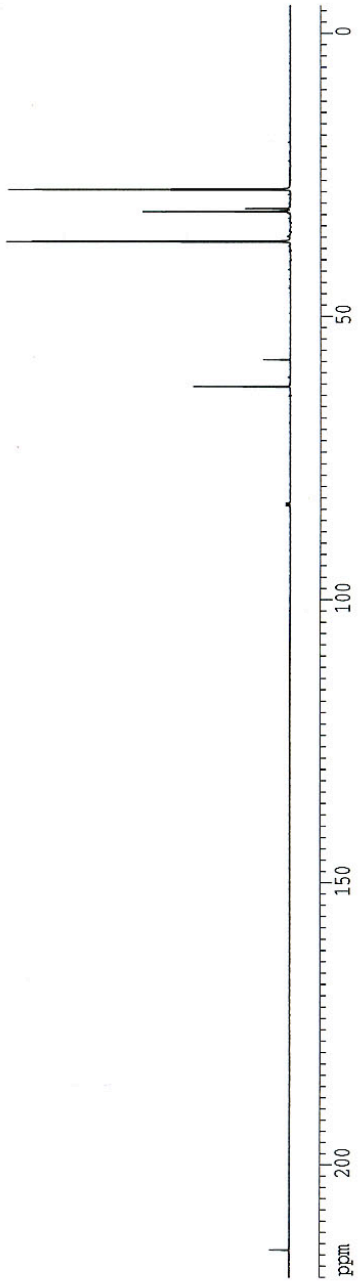

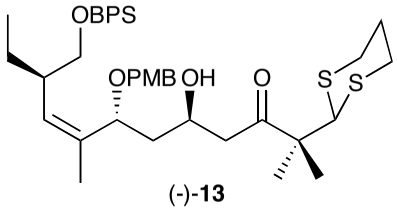

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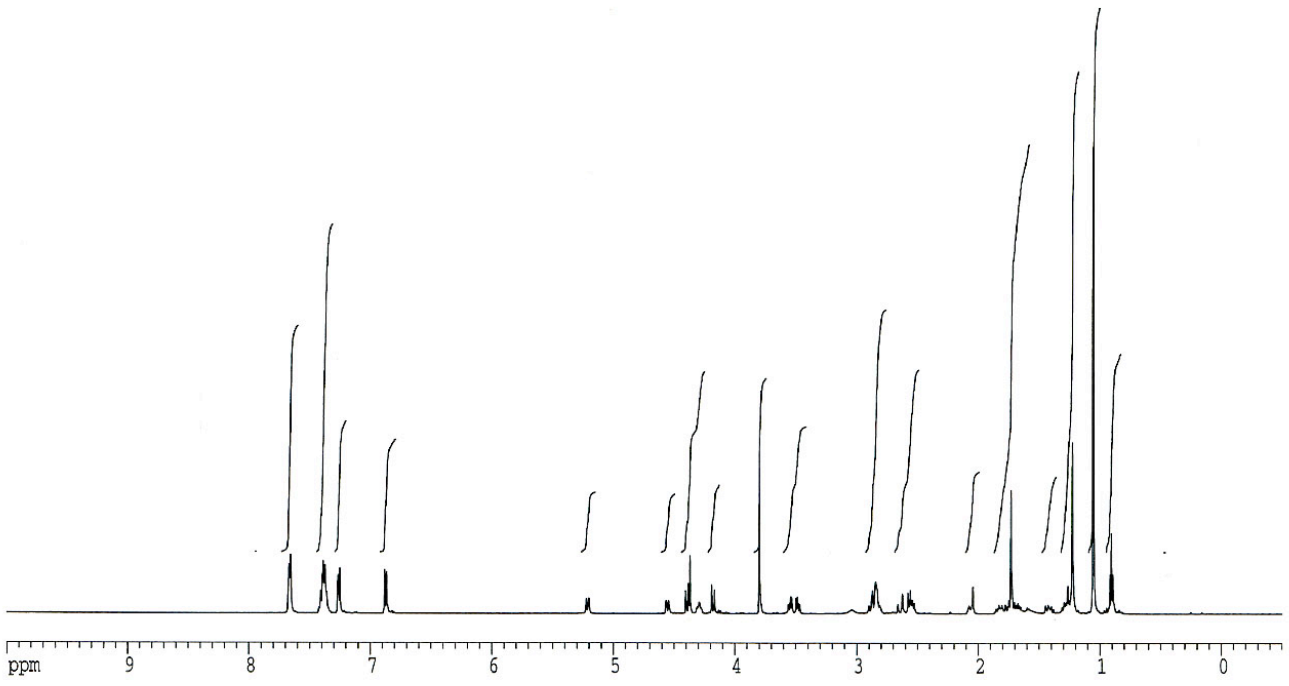

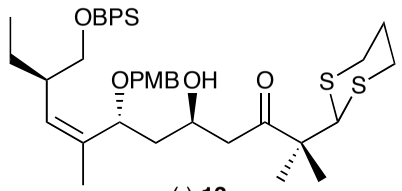

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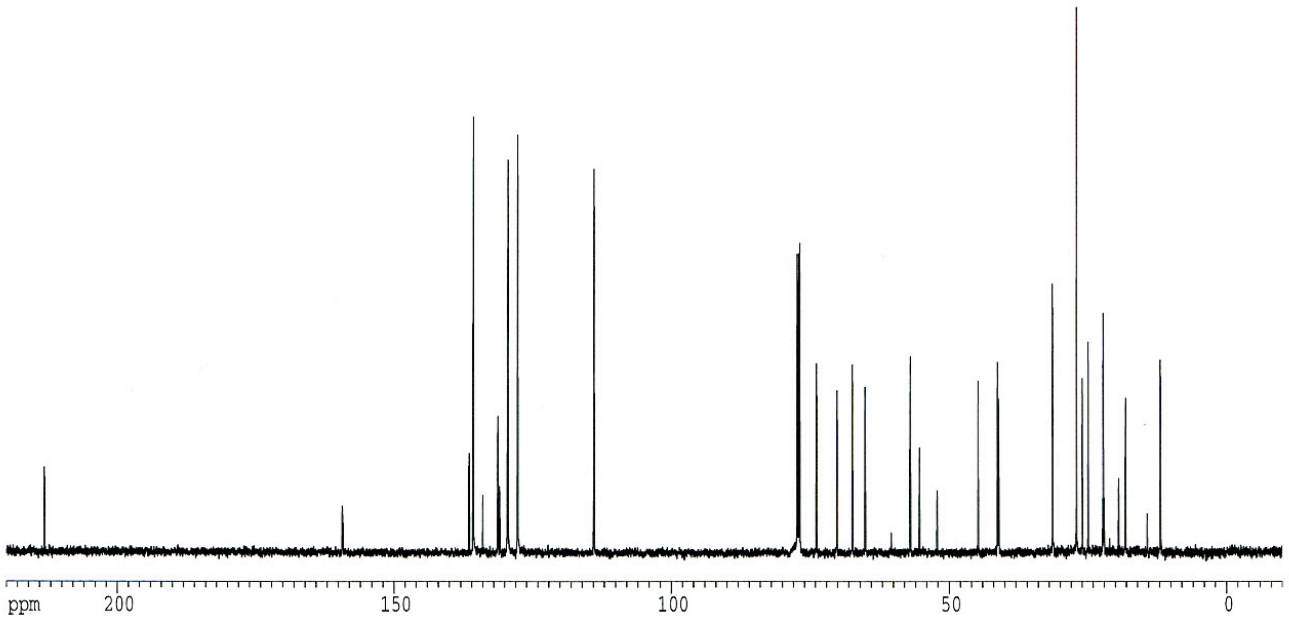

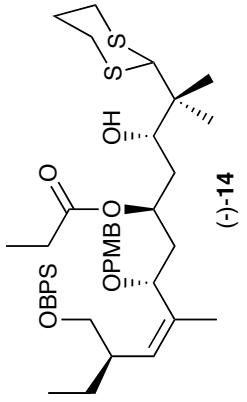

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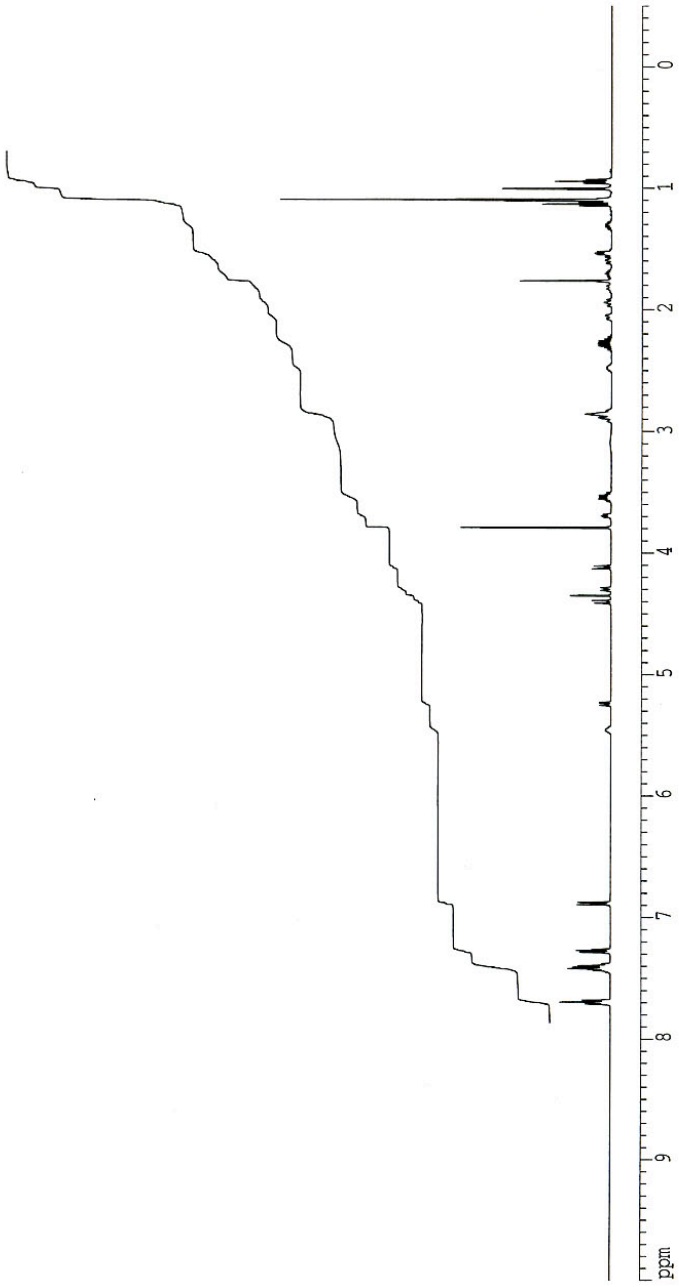

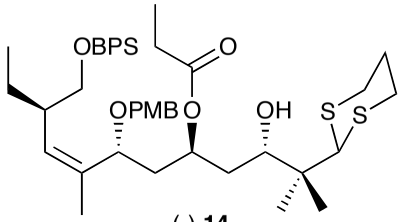

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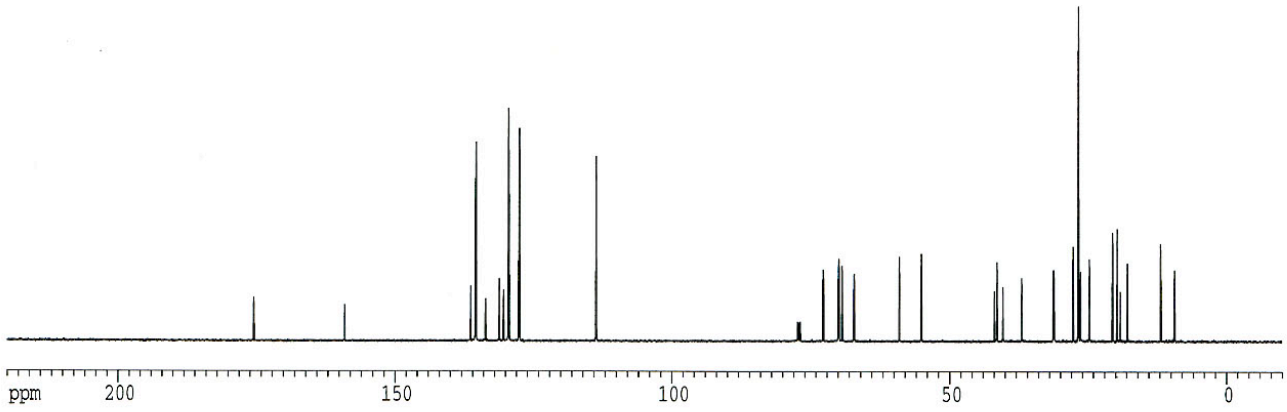

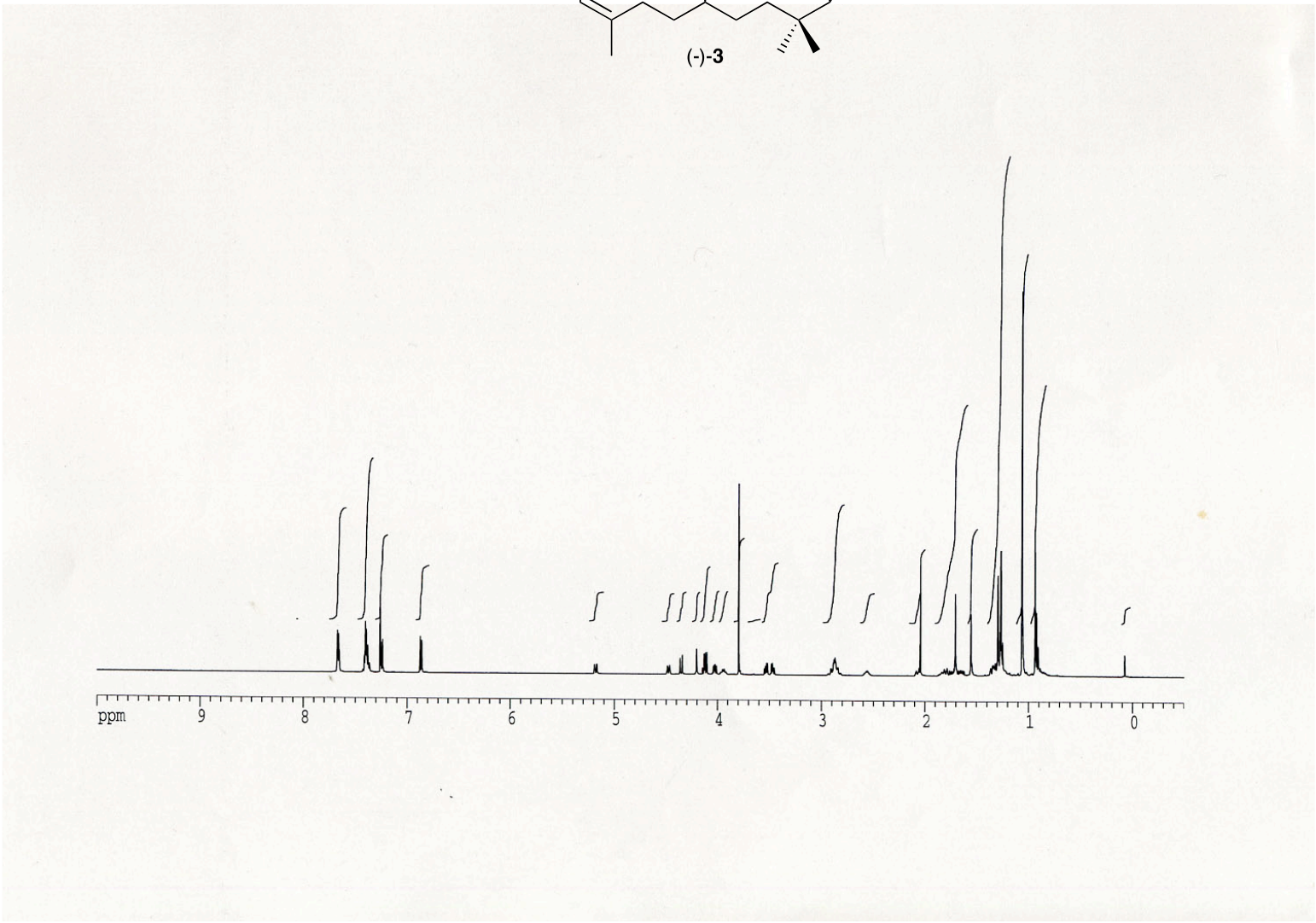
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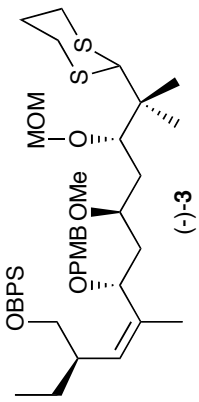
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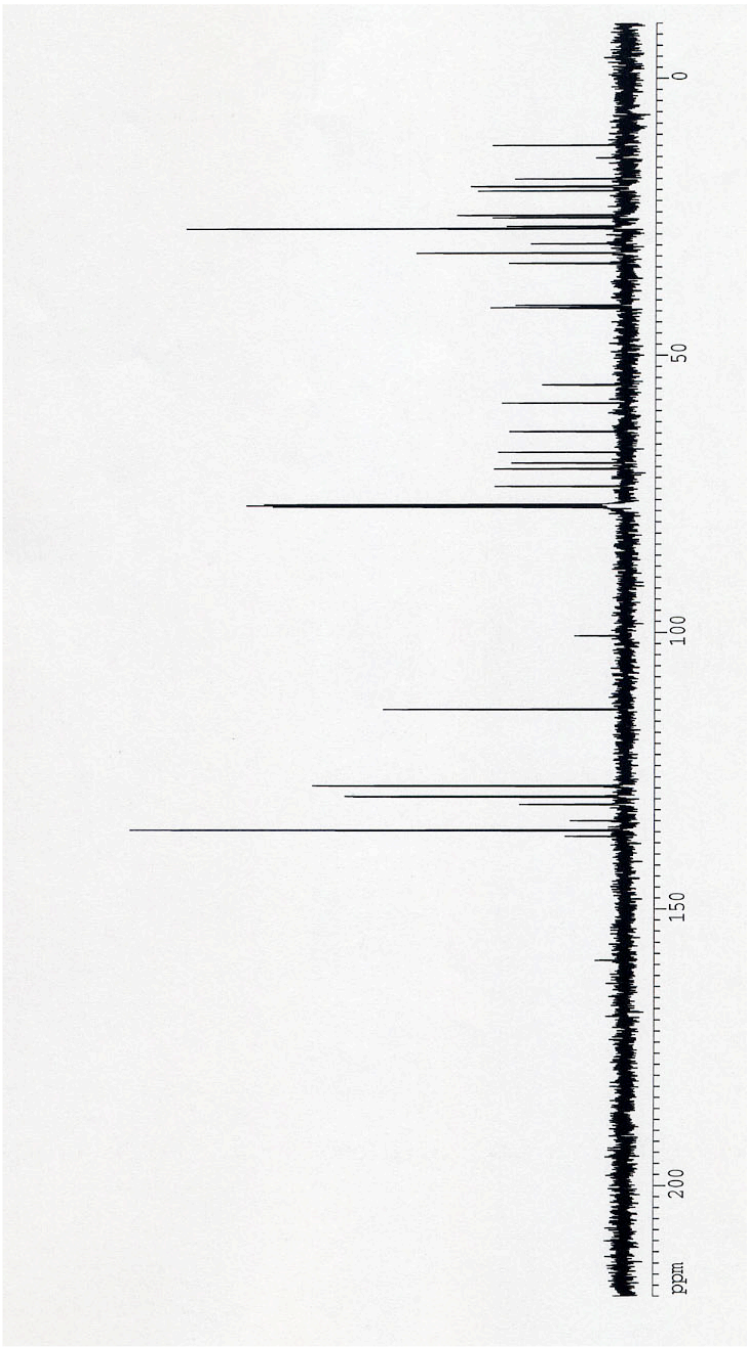
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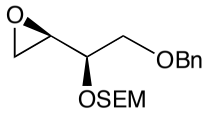

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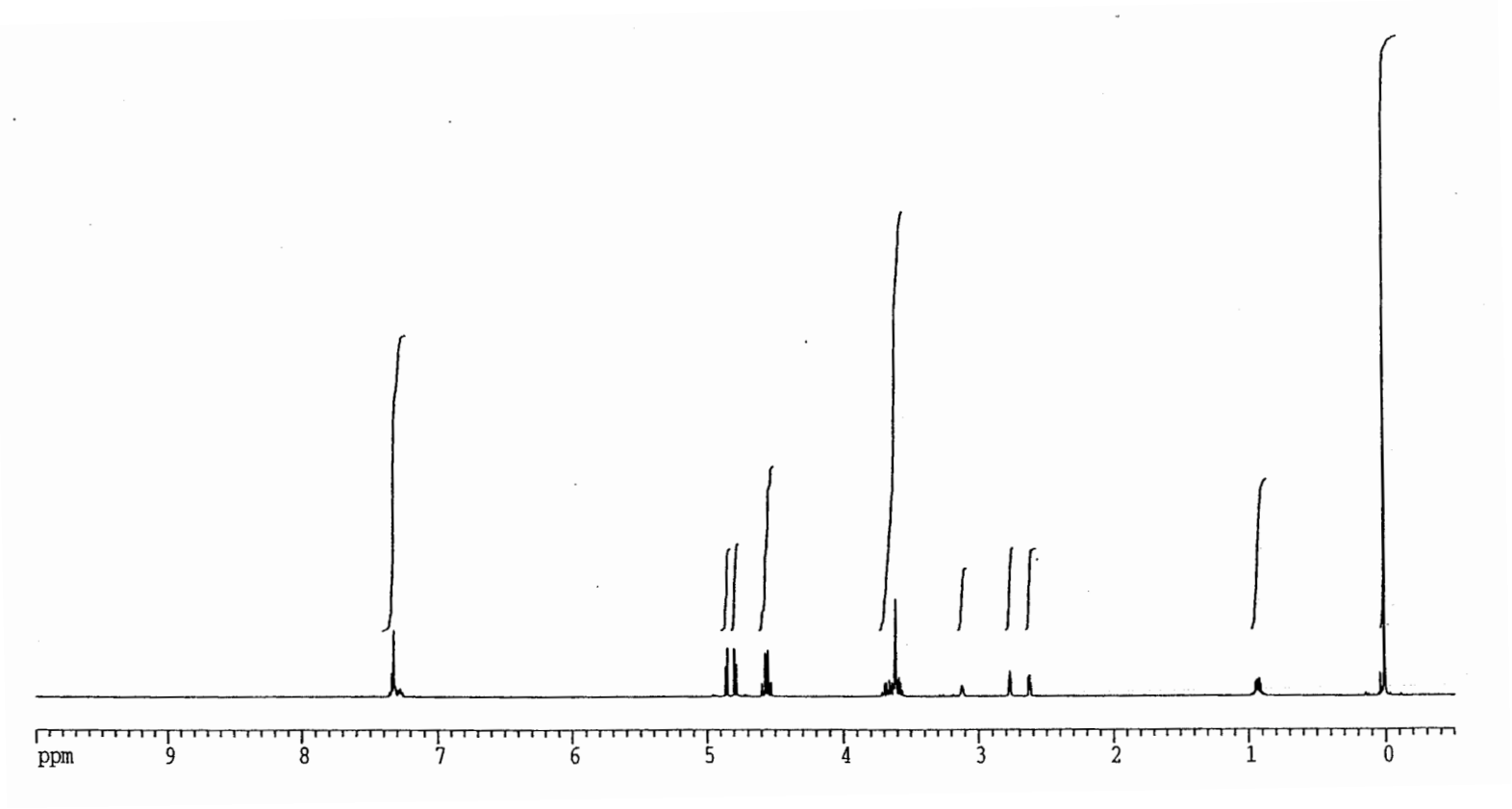

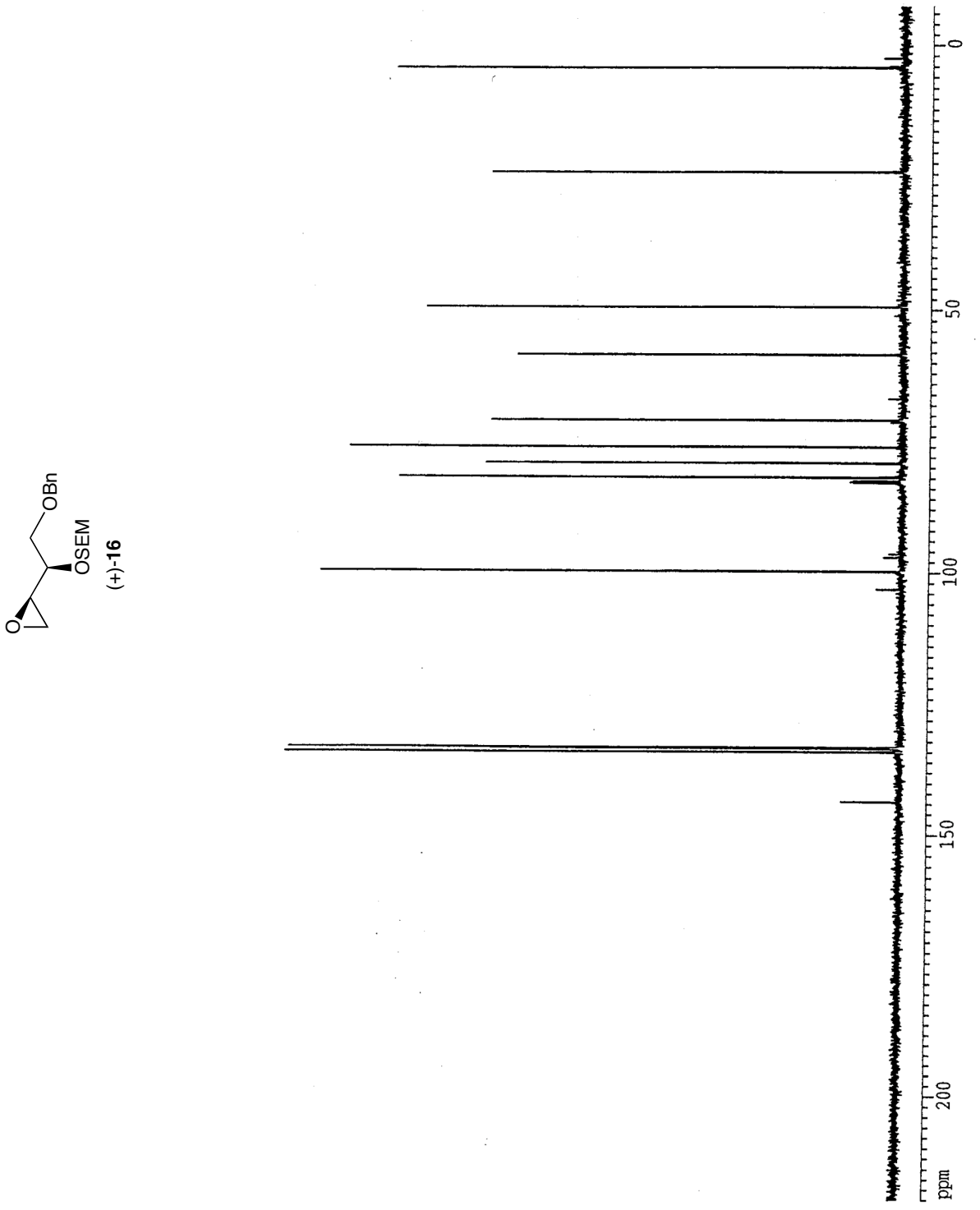
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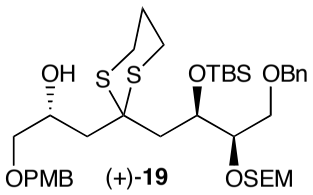
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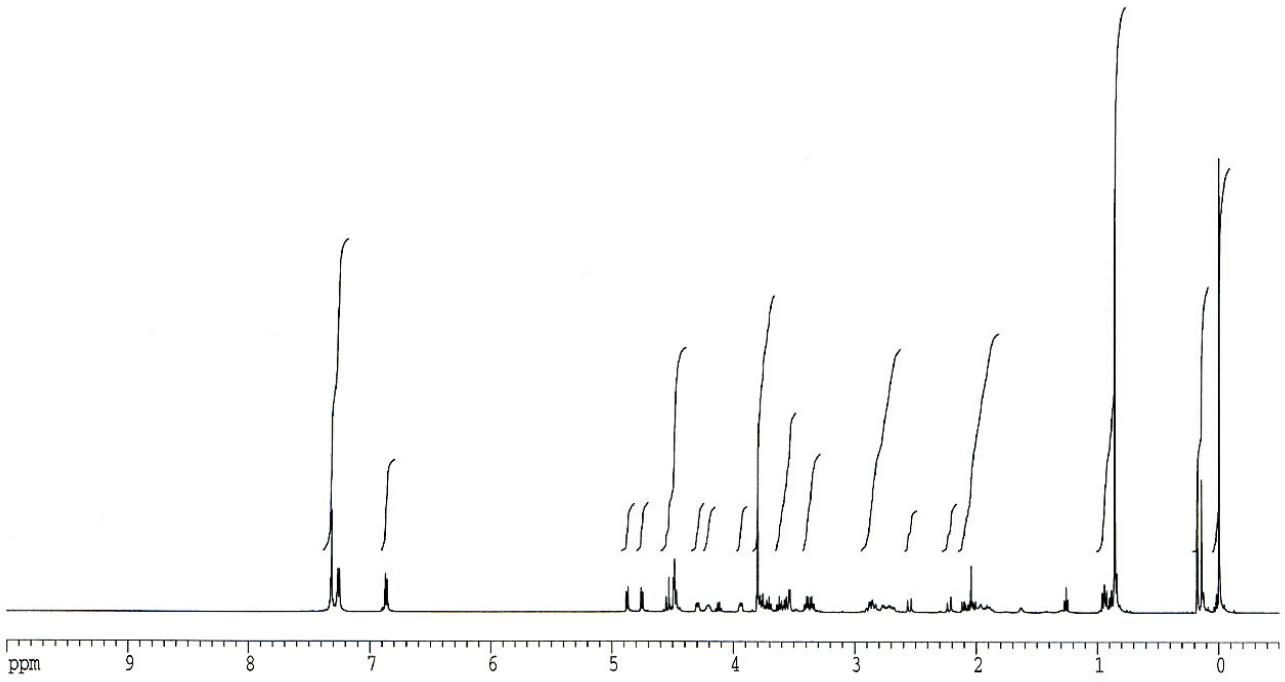
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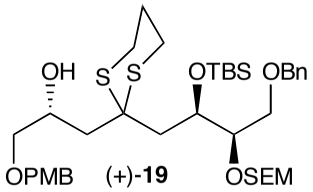
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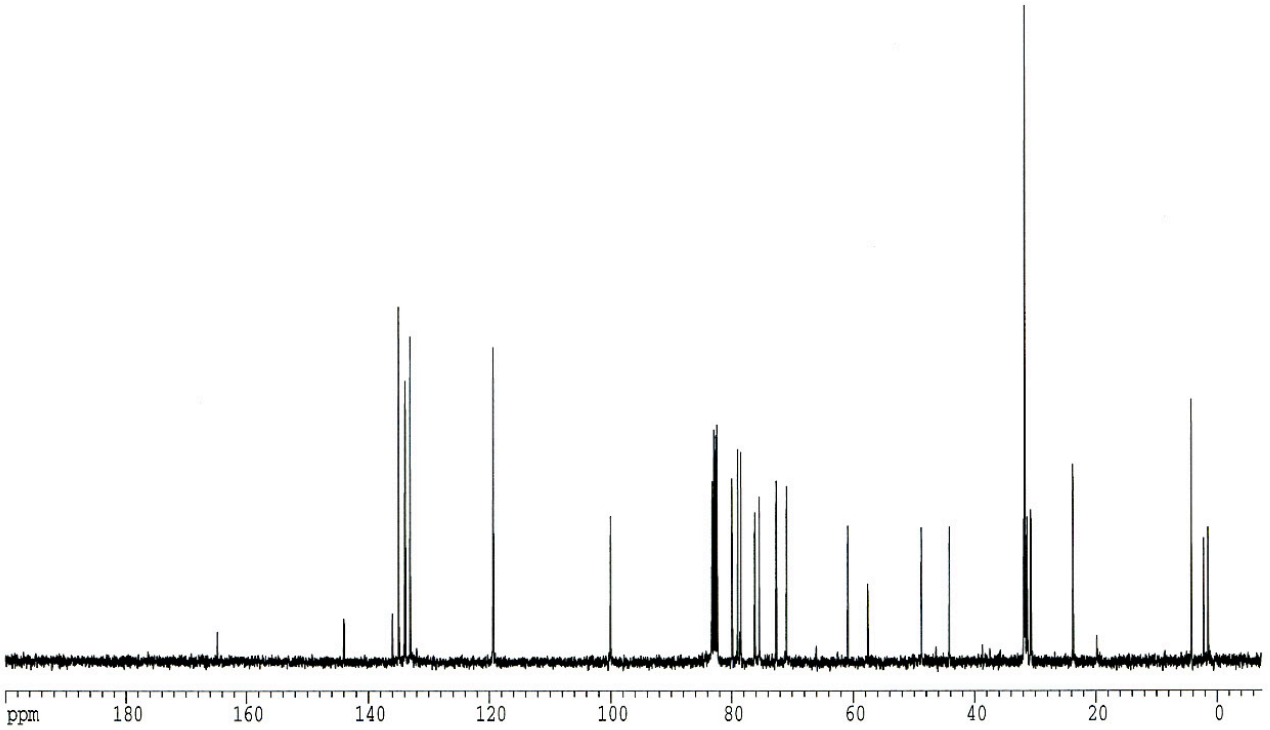
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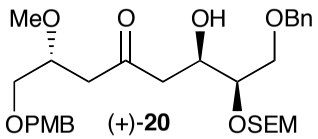
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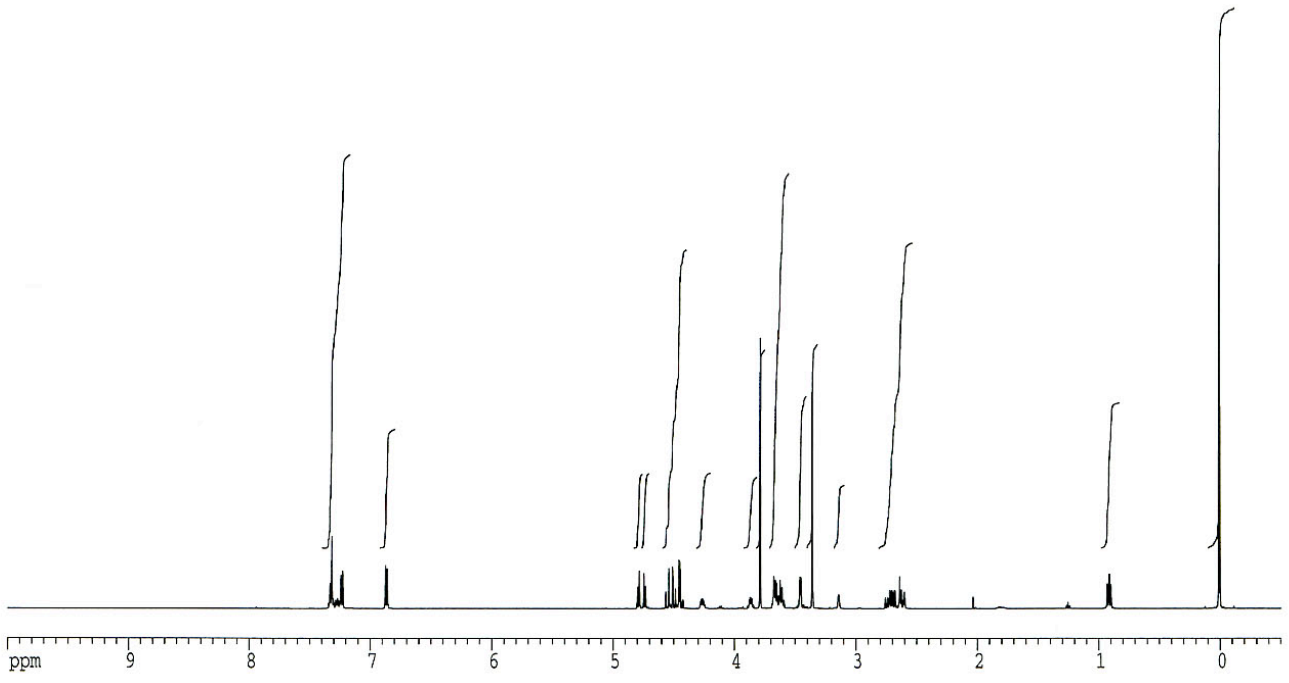
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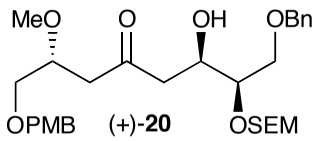
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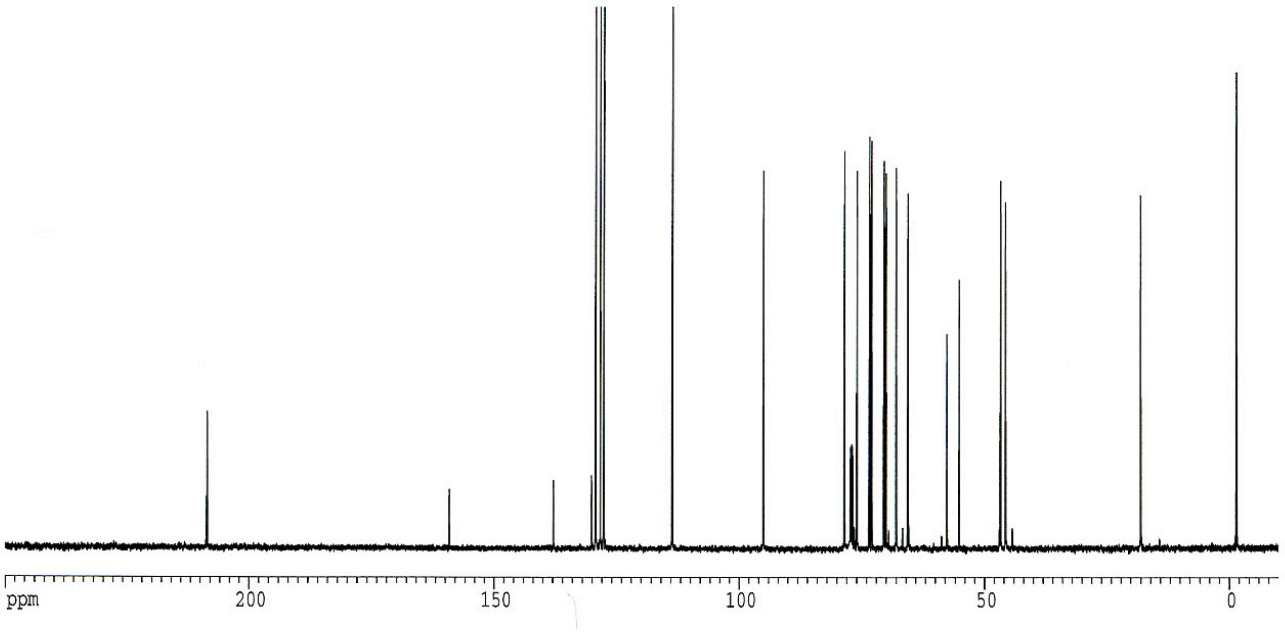
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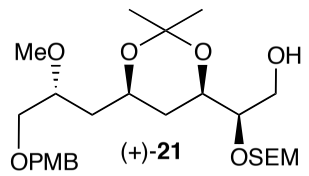
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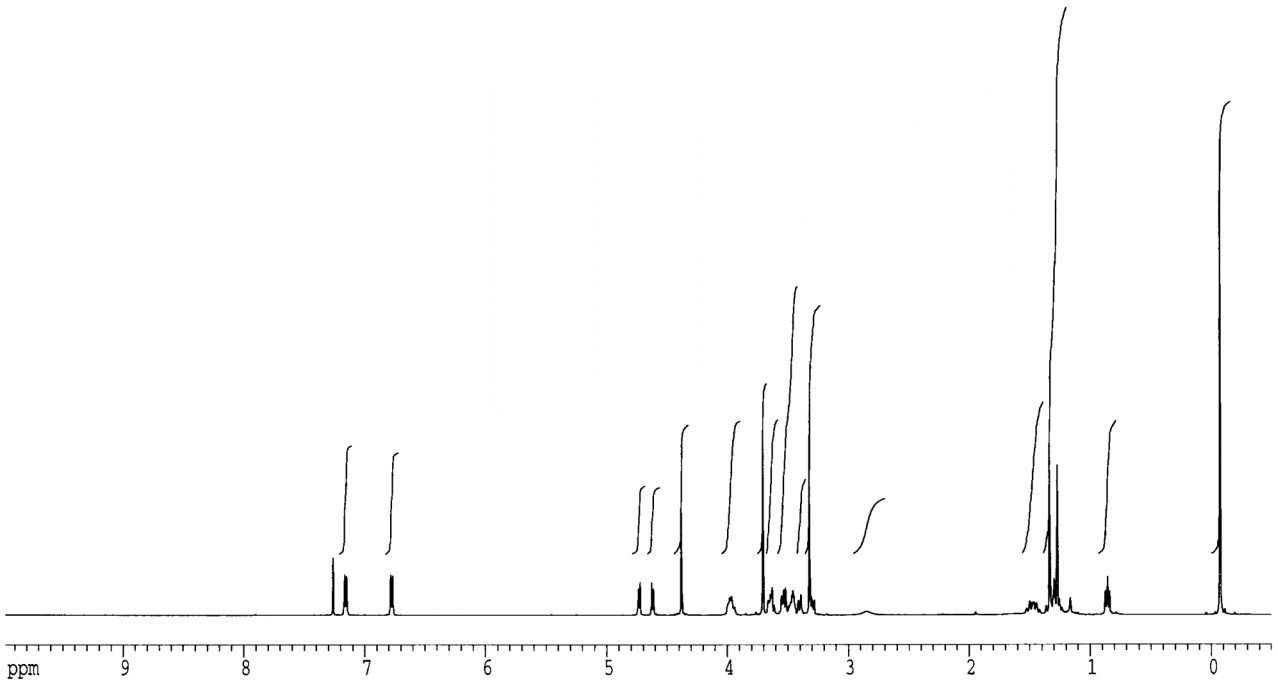
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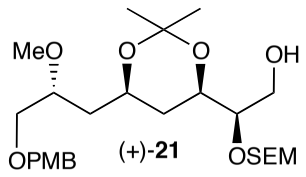
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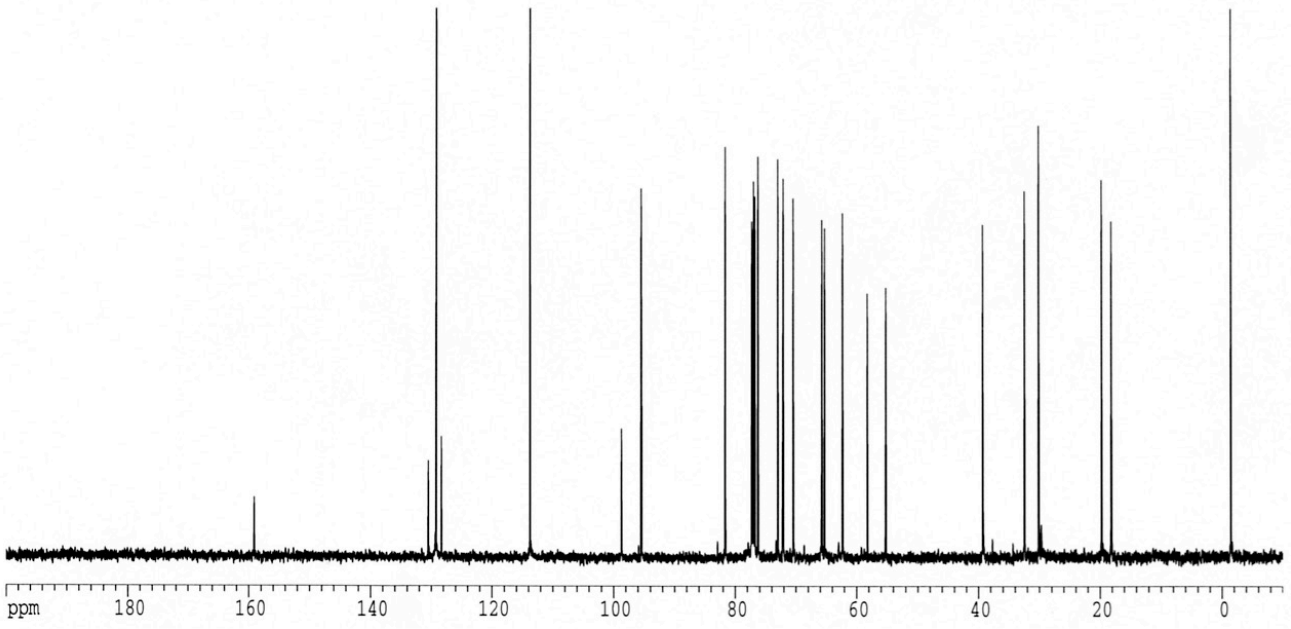
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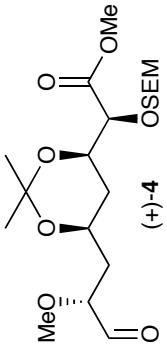

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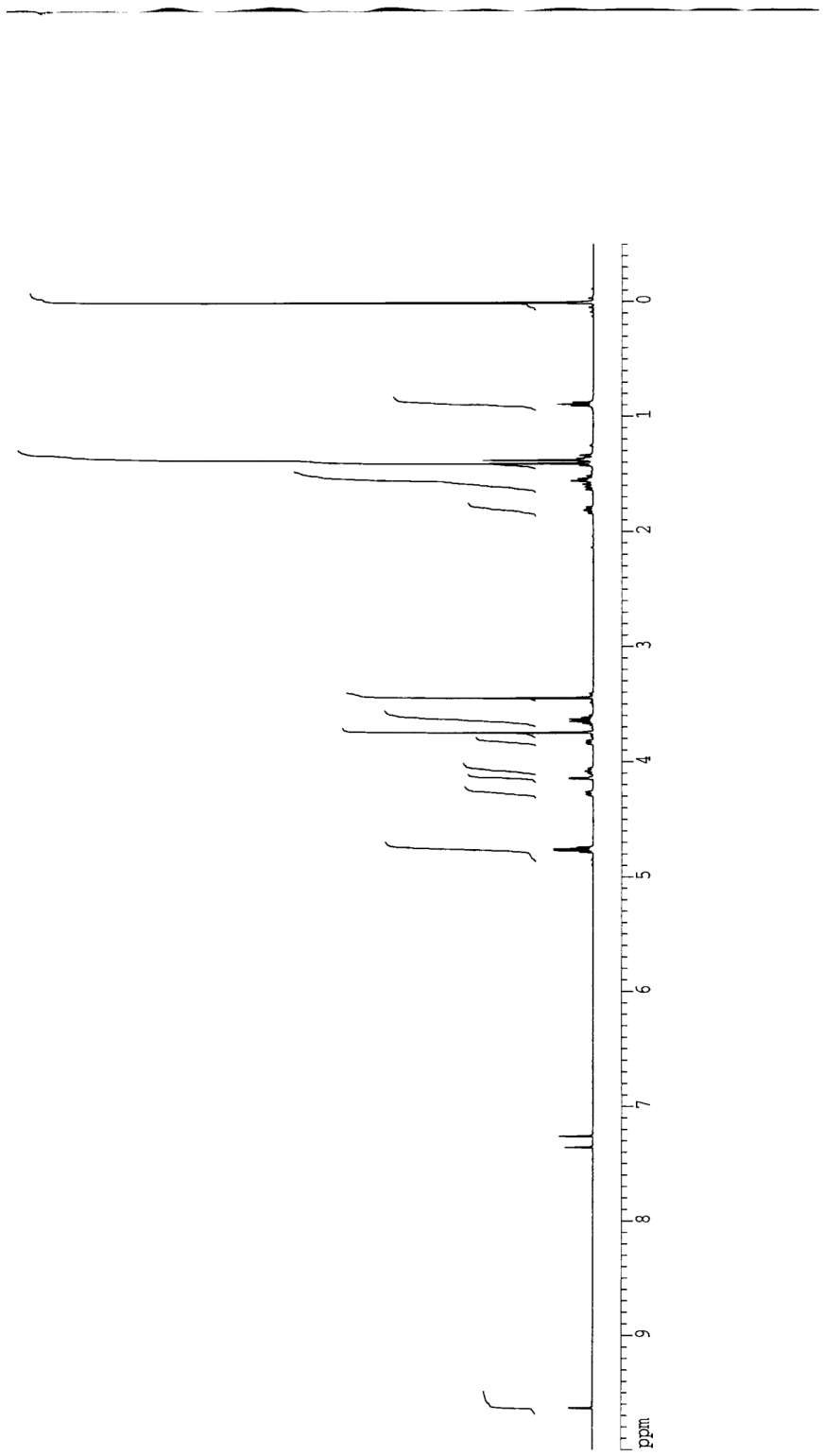

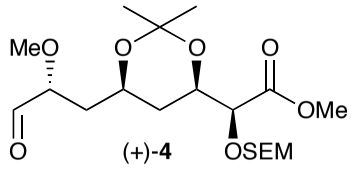

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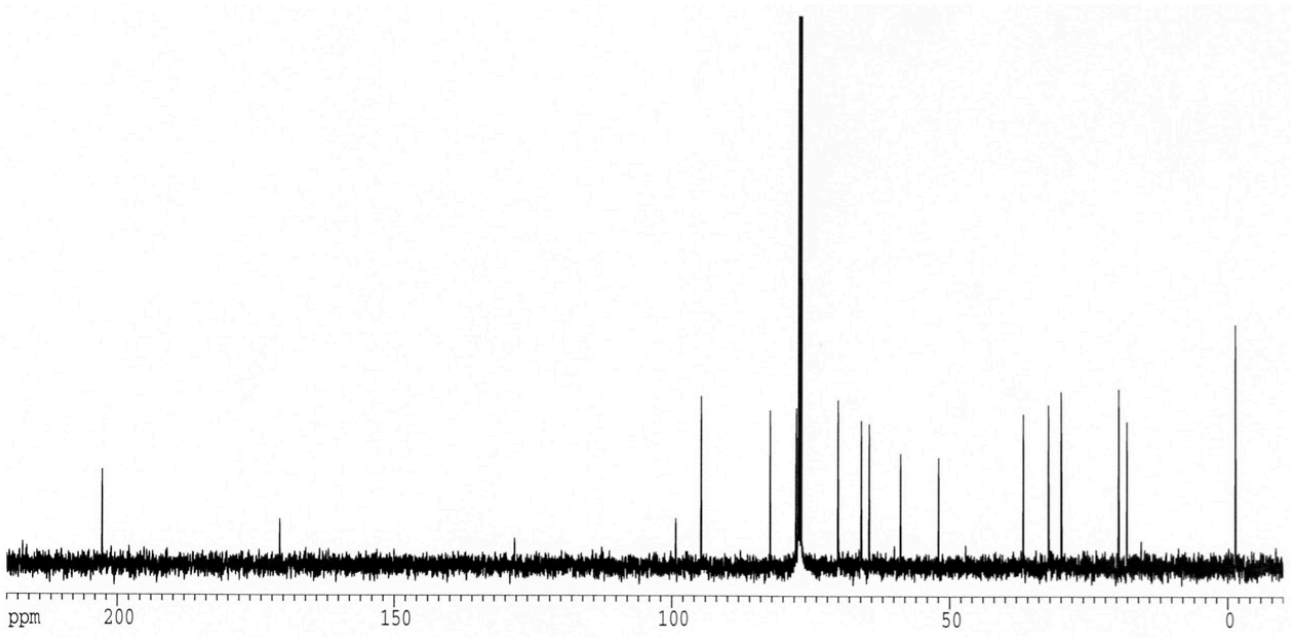

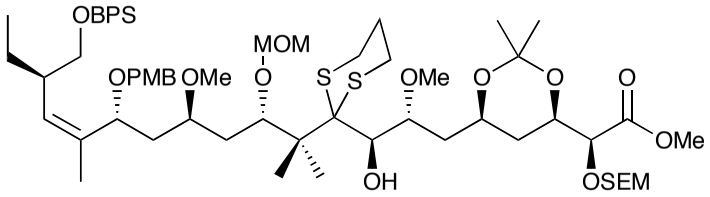

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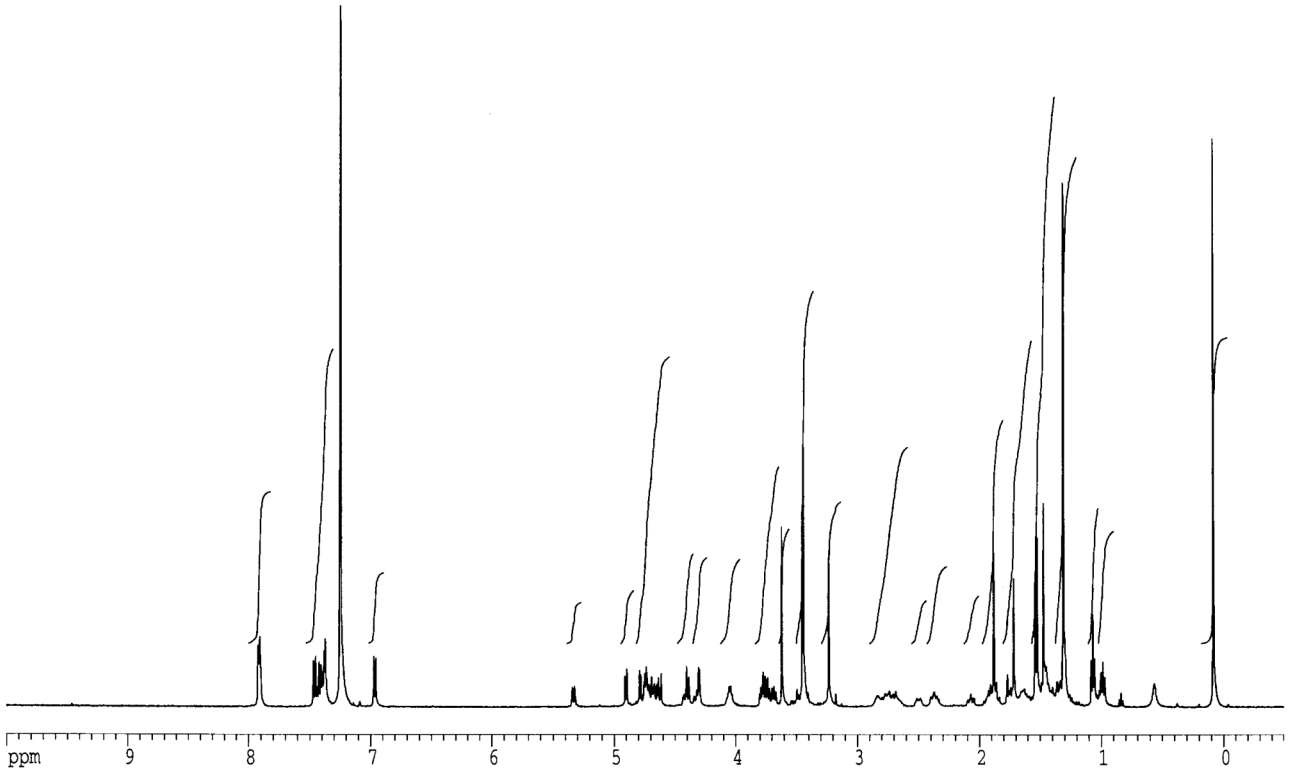

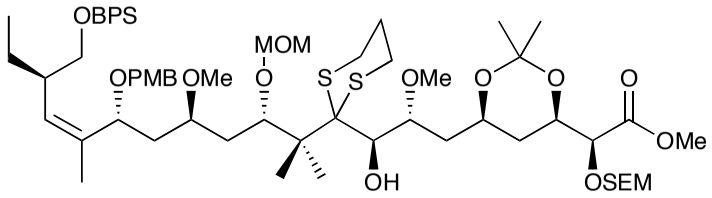
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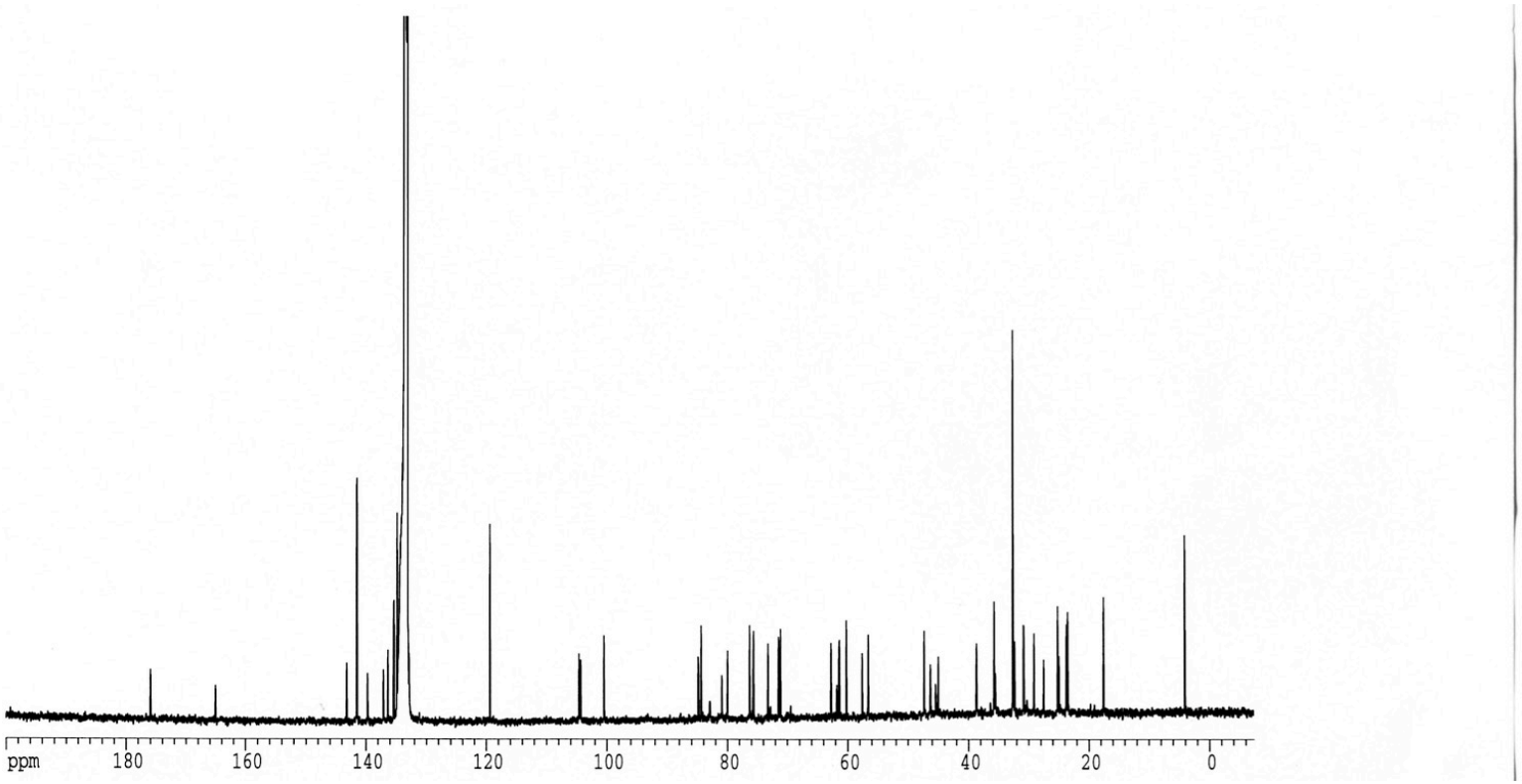
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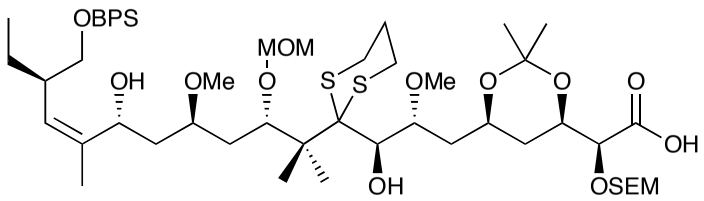

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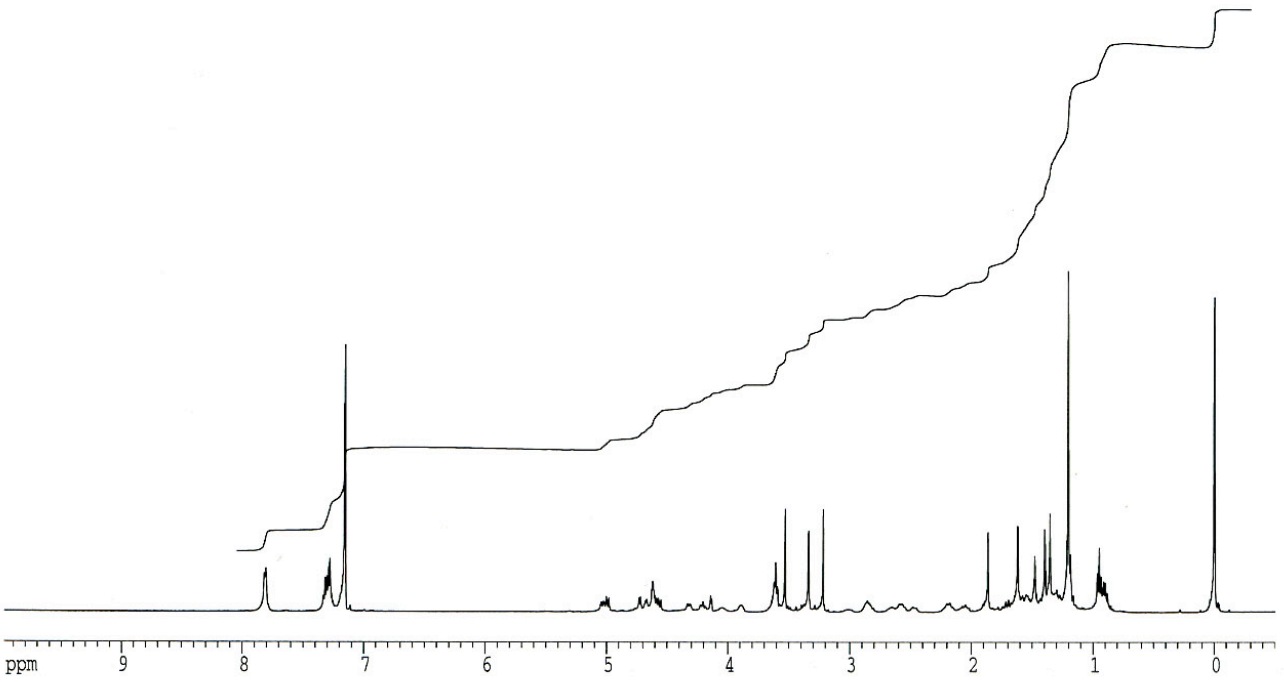

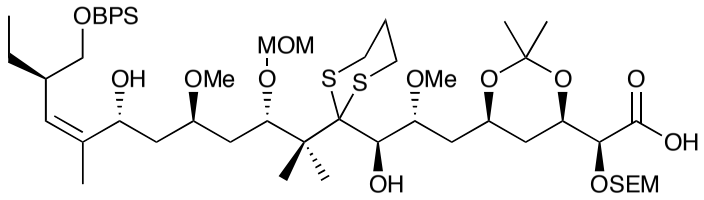

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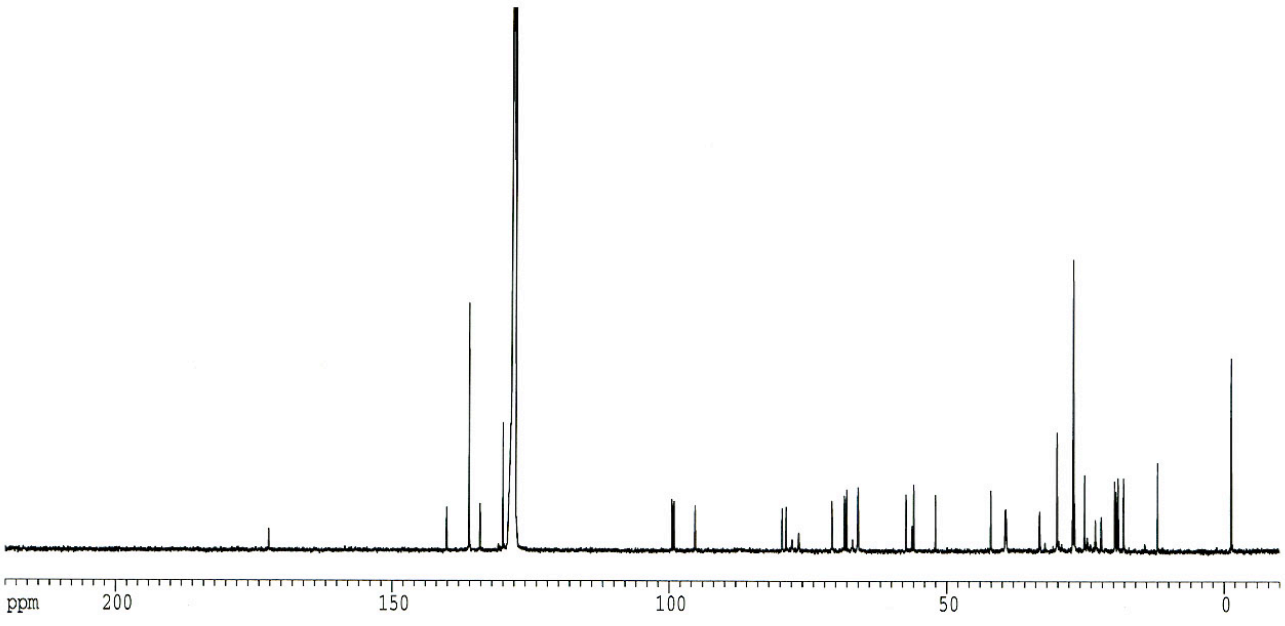

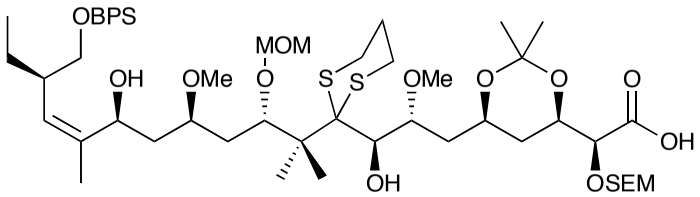

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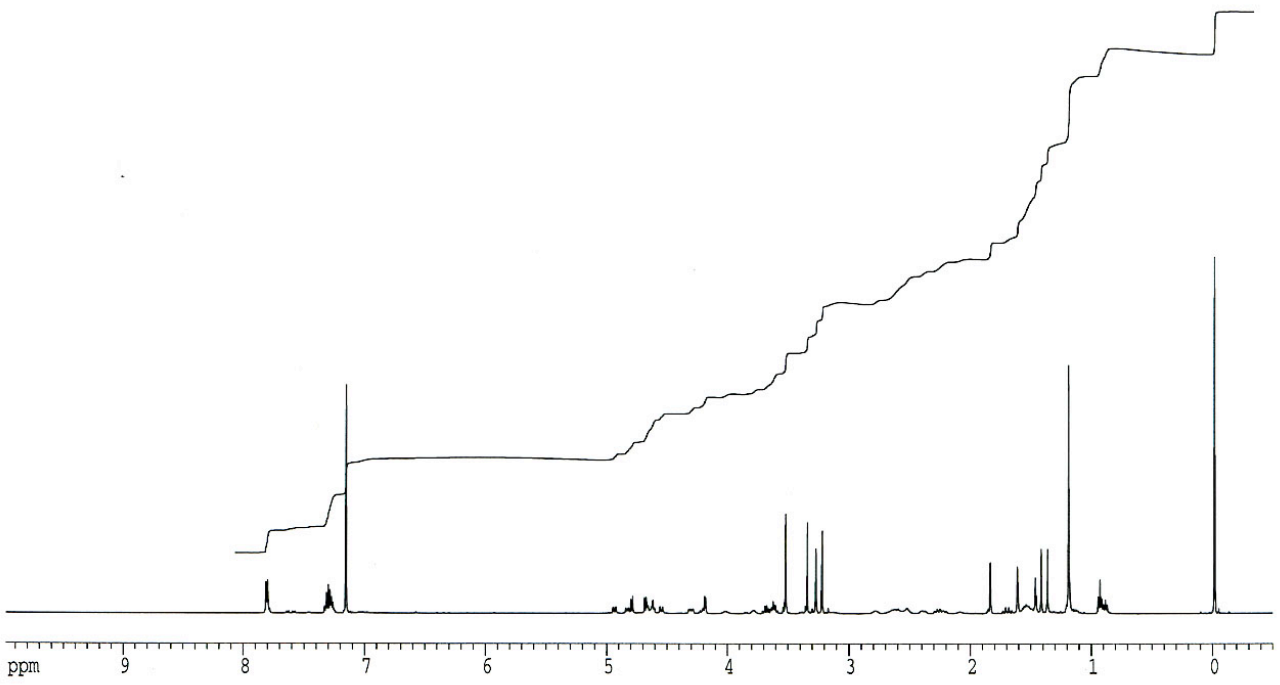

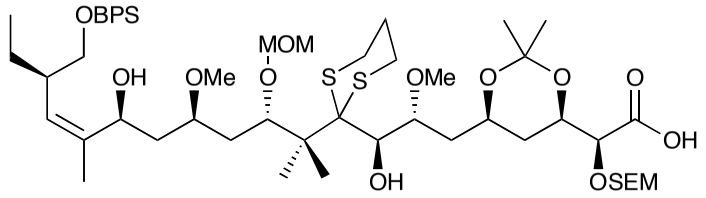

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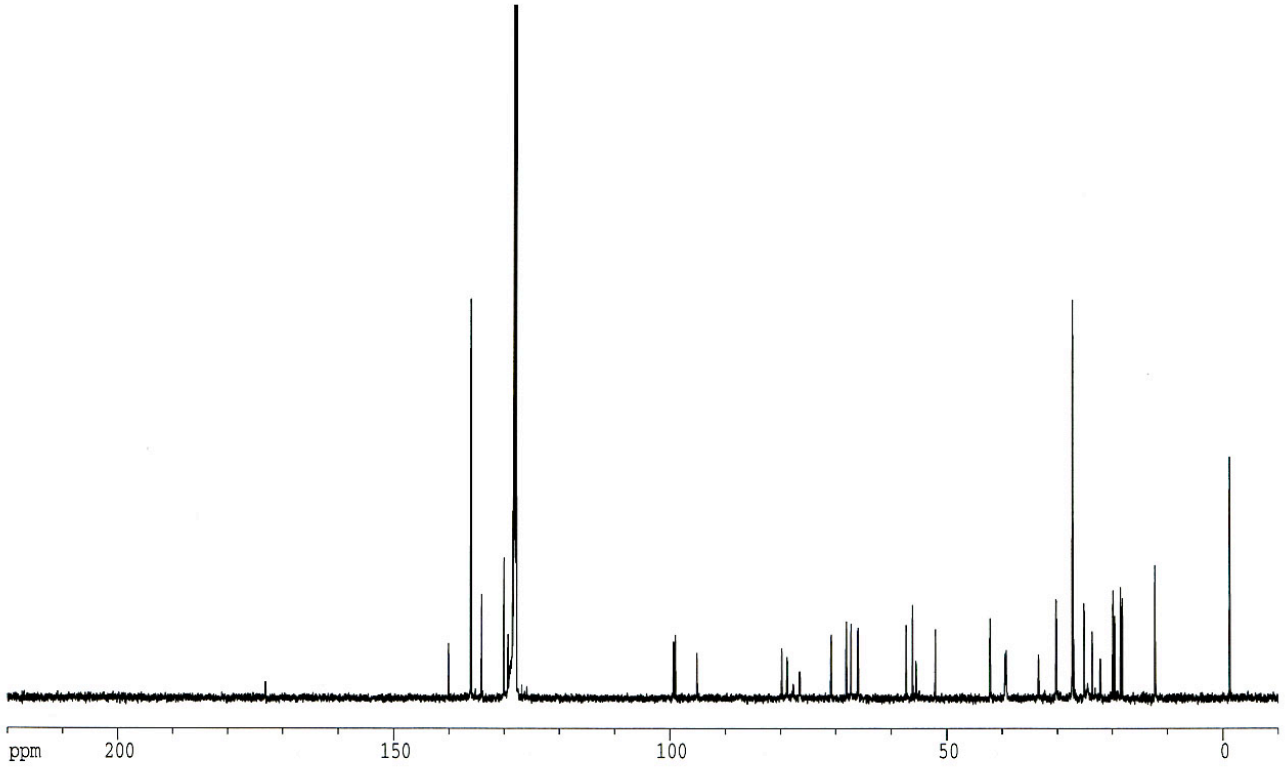

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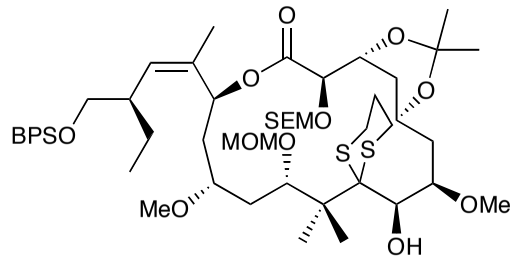

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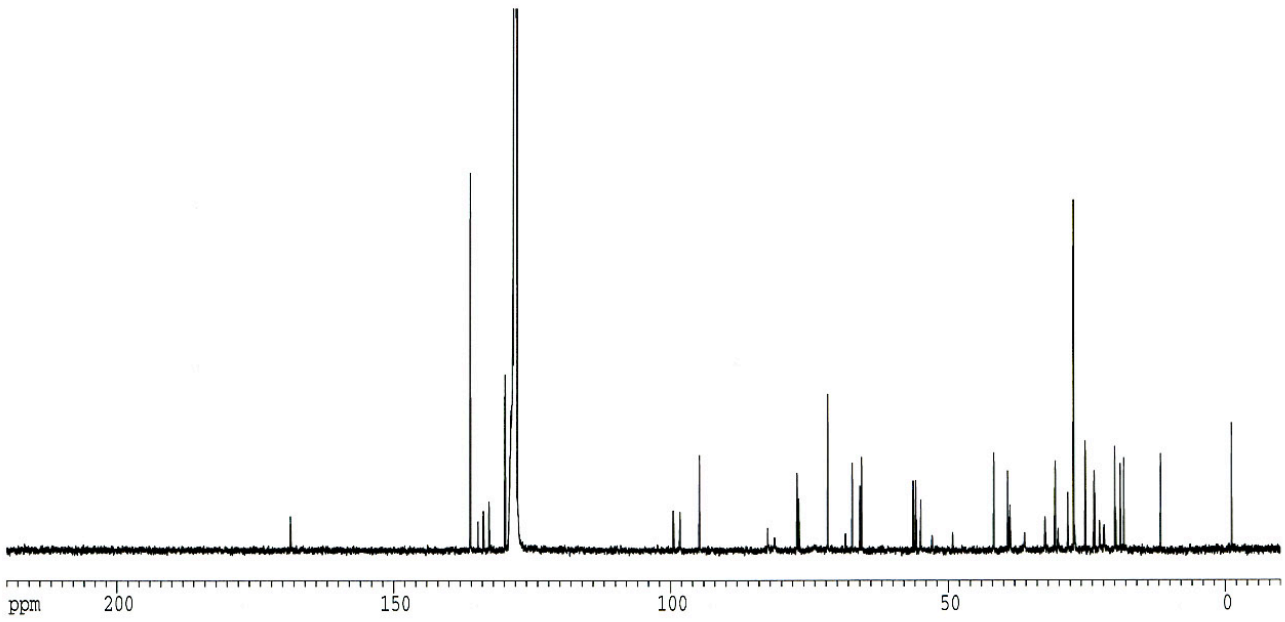

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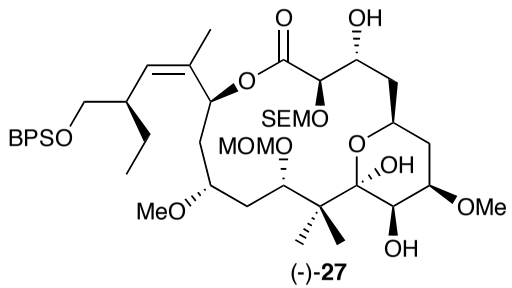

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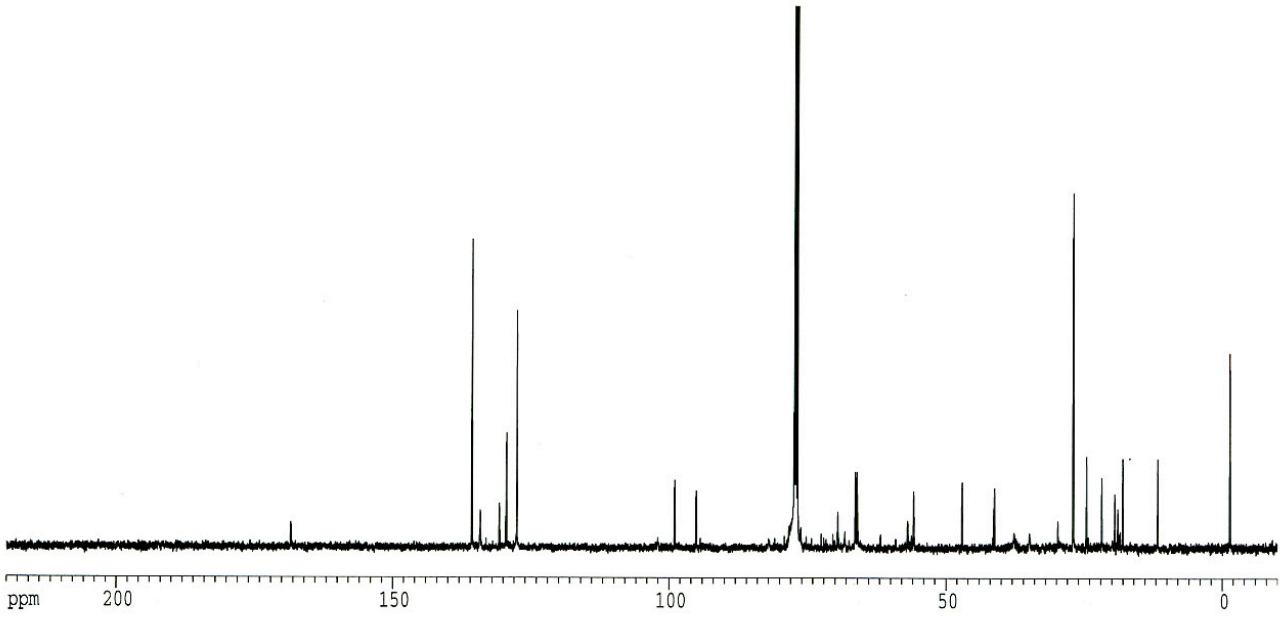

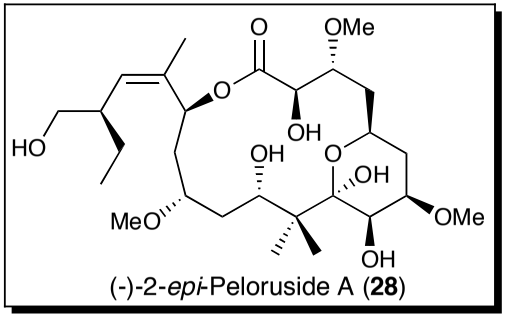

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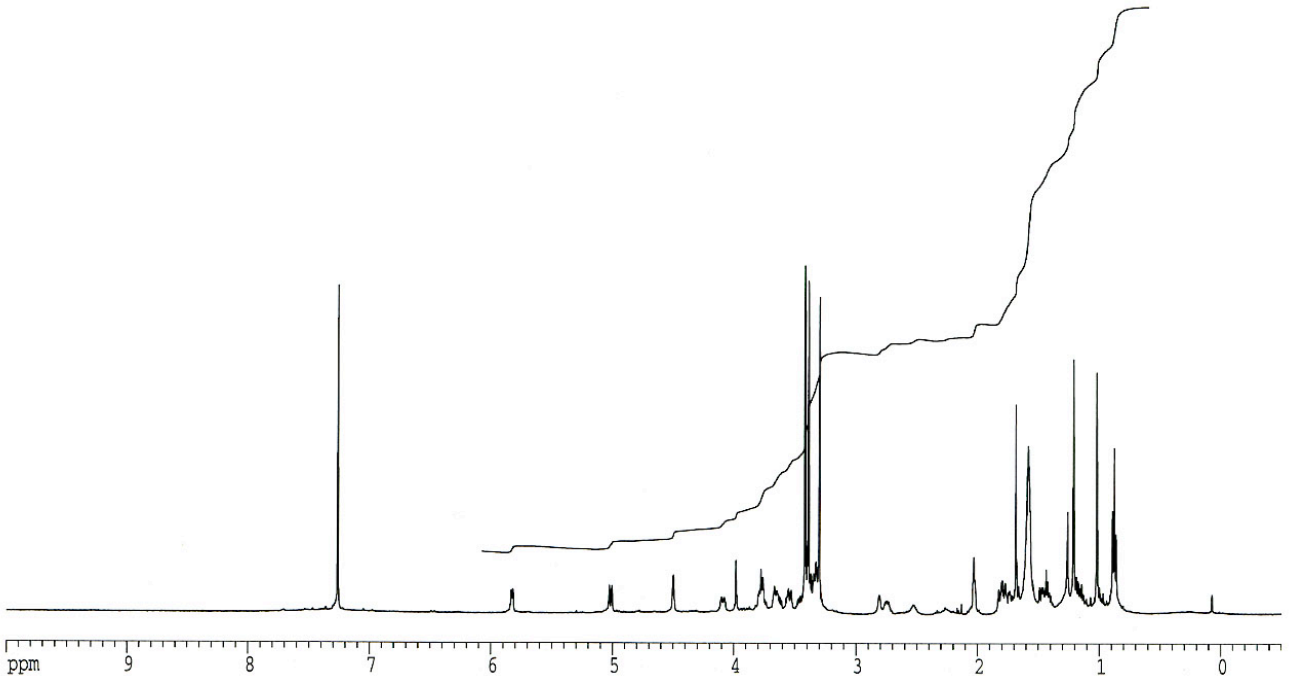

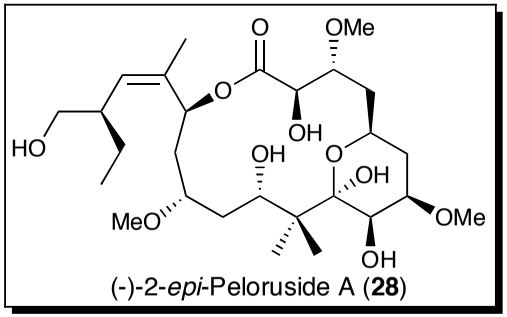

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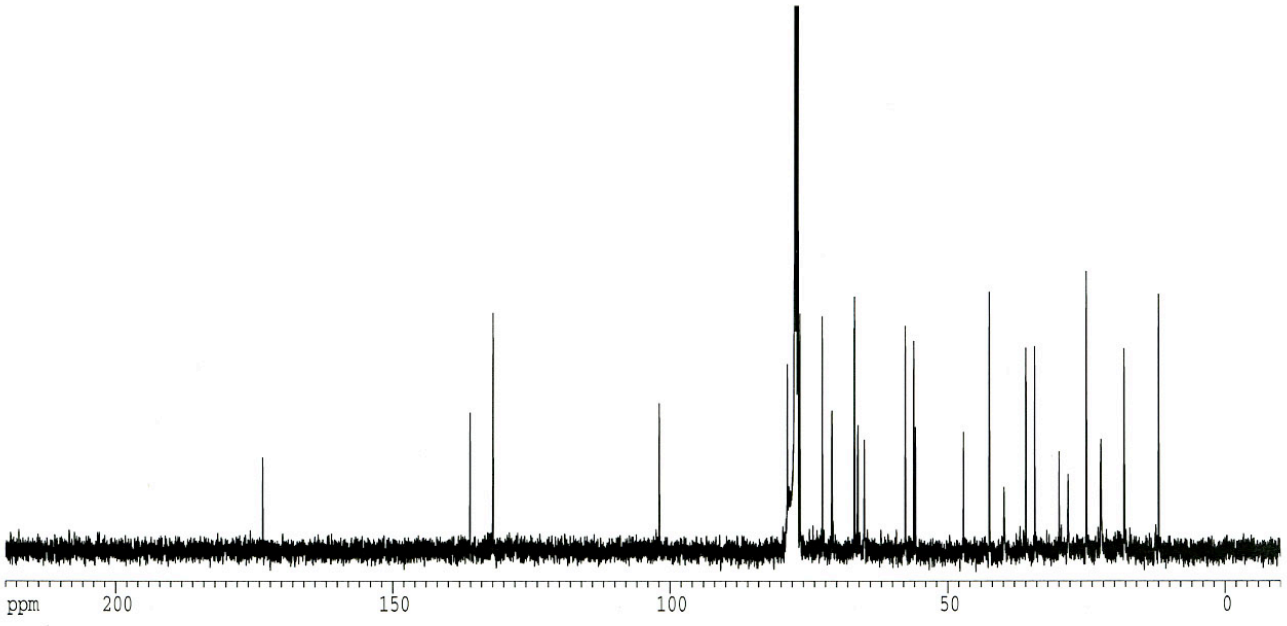

IV. References

(1) Smith, A. B., III; Friestad, G. K; Barbosa, J.; Bertounesque, E.; Hull, K. G.; Iwashima, M.; Qiu, Y.; Salvatore, B. A.; Spoors, G.; Duan, J. J.-W. *J. Am. Chem. Soc.* **1999**, *121*, 10468.

(2) Smith, A. B., III; Lee, D.; Adams, C. M.; Kozlowski, M. C. *Org. Lett.* **2002**, *4*, 4539.

(3) Hungerbühler, E.; Seebach, D. *Helv. Chim. Acta*. **1981**, *64*, 687.

(4) The preparative TLC plates were pre treated with the same solvent system and allowed to dry for 30 min. before using.