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Total Synthesis of Microsclerodermin E

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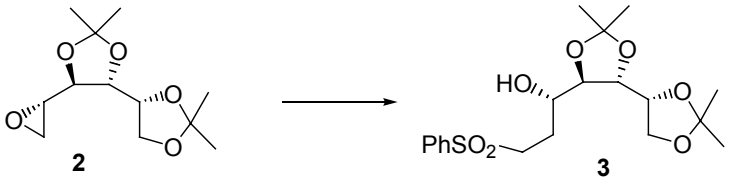
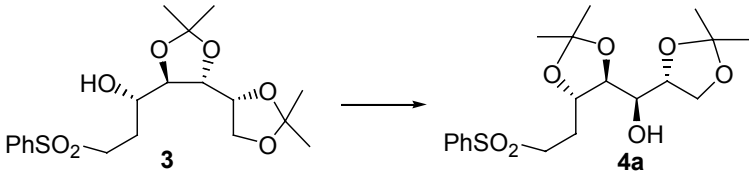
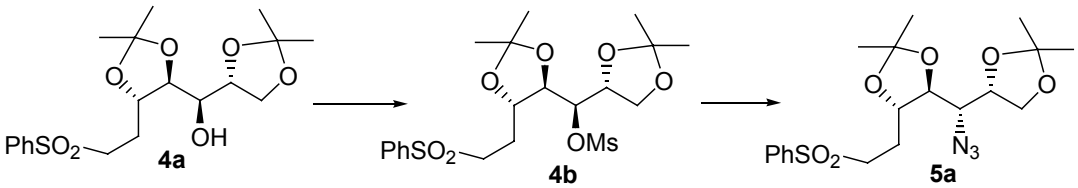
Experimental



γ-Hydroxyl sulphone 3. To a solution of methyl phenyl sulphone (150 mg, 0.96 mmol) in dry THF (4 mL) stirred under argon at -78 ^{o}C, *n*-butyllithium in hexane (1.6 M, 0.6 mL, 0.96 mmol) was added. The mixture was stirred at -78 ^{o}C for 30 min, whereupon it was added $BF_3 \cdot Et_2O$ (0.12 mL, 0.96 mmol), followed by a solution of **2** (196 mg, 0.80 mmol) in THF (2 mL). After 1 h at -78 ^{o}C, the mixture was allowed to warm to r.t. during 1.5 h, then aq. NH_4Cl was added and extracted with EtOAc. The organic phase was dried over Na_2SO_4 and evaporated and the residue was purified by flash chromatography on silica to give **3** (270 mg, 84%) as a white solid. $[\alpha]_D^{25}$ = -9.9 (*c* 0.8, $CHCl_3$); IR (film) 3550, 3479, 2990, 2932, 2881, 1446, 1370, 1216, 1152, 1068, 841 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.94 (d, *J* = 7.2 Hz, 2H), 7.67 (t, *J* = 7.2 Hz, 1H), 7.59 (t, *J* = 7.2 Hz, 2H), 4.15 (dd, *J* = 8.1, 5.7 Hz, 1H), 4.03-3.93 (m, 2H), 3.86-3.75 (m, 3H), 3.45 (m, 1H), 3.23 (m, 1H), 2.32 (d, *J* = 9.3 Hz, 1H), 2.02 (m, 1H), 1.39 (s, 6H), 1.37 (s, 3H), 1.34 (s, 3H); EI-MS *m/z* 385 $(M - CH_3)^+$, 327, 299, 281, 267, 241; Anal. Calcd. for $C_{19}H_{28}O_7S$ requires C: 56.98, H: 7.05, found C: 56.94, H: 7.06.

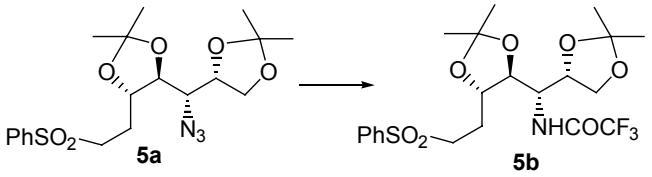


Acetonide 4a. A solution of **3** (8.5 g, 20.5 mmol) in THF (50 mL) and 1 N HCl (50 mL) was stirred for 5 h at 60 ^{o}C. The mixture was evaporated in vacuo to afford white solid. To the suspension of the residue in 2,2-dimethoxypropane (40 mL) and acetone (70 mL) was added TsOH (1.0 g, 5.3 mmol). The mixture was stirred overnight at room temperature, and then neutralized with solid Na_2CO_3 and filtered. The clear filtrate was evaporated in vacuo and the residue was subjected to flash chromatography on silica to give **4a** (5.7 g, 67%) as a colorless oil. $[\alpha]_D^{25}$ = -21.5 (*c* 1.1, $CHCl_3$); IR (film) 3541, 3508, 3480, 2992, 2937, 1452, 1372, 1308, 1145, 1068, 880 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.94 (d, *J* = 7.2 Hz, 2H), 7.68 (t, *J* = 7.2 Hz, 1H), 7.60 (t, *J* = 7.2 Hz, 2H), 4.13 (m, 1H), 3.99 (m, 3H), 3.86 (m, 2H), 3.36 (m, 1H), 3.23 (m, 1H), 2.28 (d, *J* = 8.1 Hz, 1H), 2.12 (m, 1H), 1.98 (m, 1H), 1.39 (s, 6H), 1.36 (s, 3H), 1.35 (s, 3H); EI-MS *m/z* 385 $(M - CH_3)^+$, 327, 309, 267, 241, 211, 143, 125, 101; Anal. Calcd. for $C_{19}H_{28}O_7S$ requires C: 56.98, H: 7.05, found C: 56.94, H: 6.81.



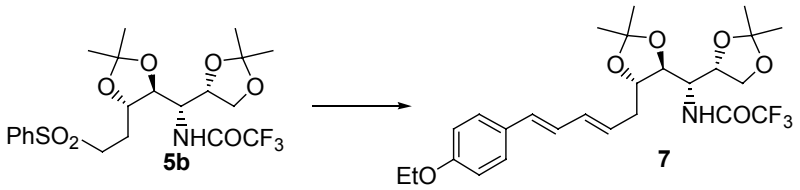
Azide 5a. A solution of **4a** (5.73 g, 14.3 mol) in dry CH_2Cl_2 (50 mL) was treated with Et_3N (2.6 mL, 18.6 mmol) and MsCl (1.3 mL, 17.3 mmol) successively at 0 ^oC. The mixture was stirred for 5 h and partitioned between CH_2Cl_2 (20 mL) and water (50 mL). The aqueous layer was further extracted with dichloromethane and the organic extracts were combined, dried over Na_2SO_4, evaporated in vacuo, and purified by flash chromatography on silica to give **4b** (6.61 g, 97%).

NaN_3 (8.0 g, 0.12 mol) was added to a solution of **4b** (6.61 g, 13.8 mmol) in DMF (50 mL). The mixture was stirred for 24 h at 120 ^oC, evaporated in vacuo, and partitioned between water (60 mL) and EtOAc (80 mL). The aqueous layer was seperated, and extracted with EtOAc. The organic layers were combined, washed with brine, dried over Na_2SO_4, evaporated in vacuo, and purified by flash chromatography on silica to give **5a** (4.86 g, 83%) as a colorless oil. $[\alpha]_D^{25}$ = -36.3 (*c* 2.2, $CHCl_3$); IR (film) 2989, 2937, 2114, 1448, 1373, 1309, 1258, 1216, 1152, 1068, 865 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.94 (d, *J* = 7.2 Hz, 2H), 7.68 (m, 1H), 7.59 (m, 2H), 4.21 (t, *J* = 6.1 Hz, 1H), 4.08 (dd, *J* = 8.7, 6.5 Hz, 1H), 4.00 (m, 1H), 3.90 (dd, *J* = 8.7, 6.6 Hz, 1H), 3.57 (t, *J* = 7.6 Hz, 1H), 3.39-3.22 (m, 3H), 2.30-2.22 (m, 1H), 1.97-1.89 (m, 1H), 1.44 (s, 3H), 1.35 (s, 3H), 1.33 (s, 3H), 1.31 (s, 3H); EI-MS *m/z* 410 $(M - CH_3)^+$, 382, 352, 269, 211, 101; Anal. Calcd. for $C_{19}H_{27}N_3O_6S$ requires C: 53.63, H: 6.40, N: 9.88, found C: 53.50, H: 6.45, N: 10.09.



Amide 5b. A suspension of 10% Pd/C (300 mg) in a solution of **5a** (4.86 g, 11.4 mmol) in methanol (50 mL) was stirred under H_2 (30 atm) at room temperature for 24 h. The mixture was filtered, and the filtrate was evaporated in vacuo. The residue was purified by flash chromatography on silica to give the free amine 2.83 g.

A solution of the above amine (2.83 g, 6.85 mmol) in dry CH_2Cl_2 (30 mL) was treated with pyridine (0.68 mL, 8.5 mmol) and trifluoroacetic anhydride (1.1 mL, 7.8 mmol) successively at 0 ^oC. The mixture was stirred for 2 h and partitioned between CH_2Cl_2 (20 mL) and water (30 mL). The aqueous layer was further extracted with dichloromethane and the organic extracts were combined, dried over Na_2SO_4, evaporated in vacuo, and purified by flash chromatography on silica to give **5b** (3.51 g, 62%) as a white solid. $[\alpha]_D^{25}$ = -25.8 (*c* 1.3, $CHCl_3$); IR (KBr) 3402, 2999, 2984, 2962, 2883, 1718, 1544, 1309, 1212, 1171, 1073 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.91 (d, *J* = 8.0 Hz, 2H), 7.67 (t, *J* = 7.5 Hz, 1H), 7.57 (t, *J* = 7.5 Hz, 2H), 6.64 (d, *J* = 9.6 Hz, 1H), 4.52 (t, *J* = 6.8 Hz, 1H), 4.12-4.05 (m, 2H), 3.97 (td, *J* = 8.0, 2.8 Hz, 1H), 3.75 (dd, *J* = 8.6, 7.3 Hz, 1H), 3.55 (dd, *J* = 8.8, 6.5 Hz, 1H), 3.35-3.29 (m, 1H), 3.20-3.14 (m, 1H), 2.04 (m, 2H), 1.45 (s, 3H), 1.36 (s, 3H), 1.35 (s, 3H), 1.33 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.0, 157.5, 138.8, 133.8, 129.3, 127.8, 109.8, 109.6, 79.1, 77.0, 73.1, 66.1, 52.74, 52.71, 27.1, 26.9, 26.7, 25.9, 24.4; EI-MS *m/z* 480 $(M - CH_3)^+$, 422, 380, 362, 336, 269, 211; Anal. Calcd. for $C_{21}H_{28}NO_7F_3S$ requires C: 50.90, H: 5.70, N: 2.83, found C: 50.99, H: 5.55, N: 2.84.

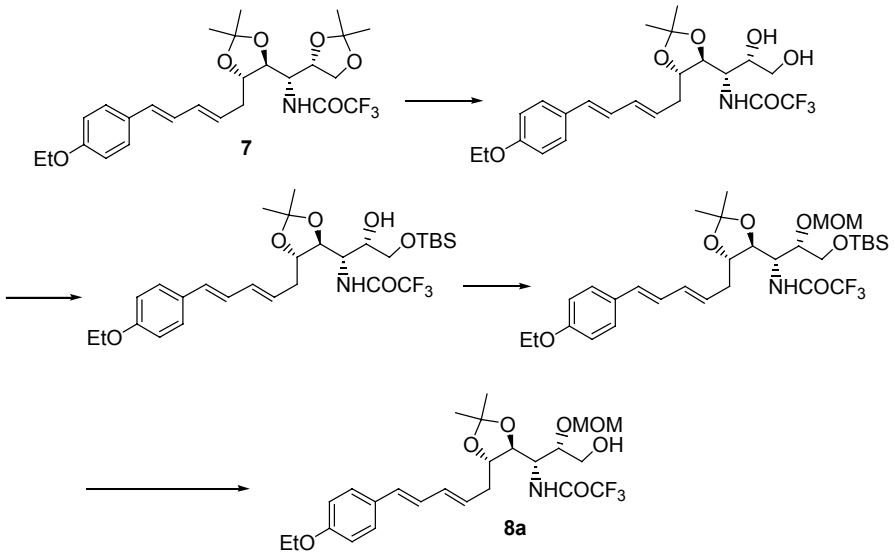


Julia olefination of 5b. To a solution of **5b** (5.15 g, 10.4 mmol) in dry THF (70 mL) stirred under argon at -78 ^oC, *n*-butyllithium in hexane (1.6 M, 14.3 mL, 22.9 mmol) was added. The mixture was stirred at -78 ^oC for 2 h, whereupon it was added a solution of **6** (4.03 g, 22.9 mmol) in THF (20 mL). After 20 min at -78 ^oC, aq. NH_4Cl (30 mL) was added and extracted with EtOAc. The organic phase was dried over Na_2SO_4, evaporated in vacuo and the residue was purified by flash chromatography on silica to give crude coupling product (6.96 g, 100%).

A solution of the above product (6.96 g, 10.4 mol) in dry CH_2Cl_2 (100 mL) was treated with Et_3N (3.6 mL, 26.0 mmol), DMAP (65 mg, 0.53 mmol) and PhCOCl (2.4 mL, 20.8 mmol) successively at room temperature. The mixture was stirred for 24 h and partitioned between CH_2Cl_2 (50 mL) and water (100 mL). The aqueous layer was further extracted with dichloromethane and the organic extracts were combined, washed with brine, dried over Na_2SO_4, evaporated in vacuo, and purified by flash chromatography on silica to

give acylation product (8.06 g, 100%).

A suspension of Na(Hg) (20.0 g, 52 mmol) in a solution of the above product (8.06 g, 10.4 mmol) in 120 mL of EtOAc/MeOH (1:2) was stirred at -20 ^{o}C for 4 h. The reaction was filtered through a plug of Celite, the plug was washed with EtOAc, and the filtrates were combined and evaporated in vacuo. The residue was partitioned between EtOAc (100 mL) and water (70 mL). The aqueous layer was further extracted with EtOAc and the organic extracts were combined, washed with brine, dried over Na_2SO_4, evaporated in vacuo, and purified by flash chromatography on silica to give **7** (4.26 g, 80%) as a pale yellow solid. $[\alpha]_D^{25}$ = -37.8 (*c* 1.1, $CHCl_3$); IR (KBr) 3359, 1716, 1606, 1546, 1510 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30 (d, *J* = 8.6 Hz, 2H), 6.84 (d, *J* = 8.5 Hz, 2H), 6.66-6.54 (m, 2H), 6.43 (d, *J* = 15.7 Hz, 1H), 6.22 (dd, *J* = 15.3, 10.3 Hz, 1H), 5.75-5.70 (m, 1H), 4.57 (t, *J* = 6.8 Hz, 1H), 4.13-4.00 (m, 5H), 3.81 (m, 1H), 3.56 (dd, *J* = 8.0, 6.7 Hz, 1H), 2.40 (m, 2H), 1.46-1.33 (m, 15H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.5, 133.8, 133.4, 131.7, 131.2, 129.9, 127.7, 127.6, 127.4, 126.4, 124.7, 121.4, 114.5, 109.8, 109.5, 78.9, 78.8, 73.2, 66.2, 63.4, 52.9, 37.5, 32.3, 27.3, 26.0, 24.5, 14.8; EI-MS *m/z* 513 (M^+), 498, 440, 414, 340, 282, 268; HRMS Calcd. for $C_{26}H_{34}F_3NO_6Na$ $(M + Na)^+$ requires 536.22359, found 536.22304.



Amide 8a. PPTs (1.51 g, 6.00 mmol) was added to a solution of **7** (2.05 g, 4.00 mmol) in dry methanol (20 mL). The mixture was stirred at 45 ^{o}C for 10 h, allowed to cool and neutralized with aqueous $NaHCO_3$. The methanol was removed in vacuo and the

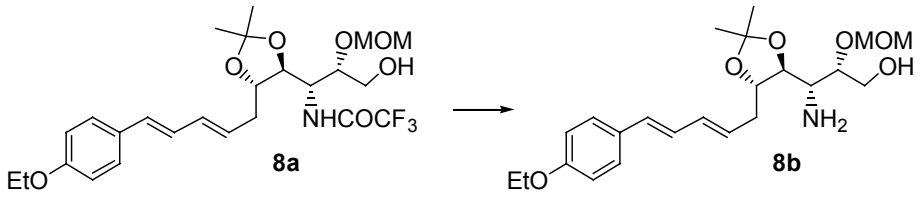
residue was extracted with EtOAc and the organic extracts were combined, washed with brine, dried over Na_2SO_4, evaporated in vacuo, and purified by flash chromatography on silica to give the diol (1.27g, 87%), along with the recovered **7** (476 mg). $[\alpha]_D^{25}$ = -24.6 (*c* 1.2, $CHCl_3$); IR (film) 3411, 2986, 2935, 1718, 1608, 1512, 1245, 1214, 1176, 1049 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.31 (d, *J* = 8.7 Hz, 2H), 7.01 (d, *J* = 8.9 Hz, 1H), 6.84 (d, *J* = 8.7 Hz, 2H), 6.63 (dd, *J* = 15.6, 10.2 Hz, 1H), 6.45 (d, *J* = 15.6 Hz, 1H), 6.27 (dd, *J* = 15.4, 10.6 Hz, 1H), 5.75 (m, 1H), 4.24-3.90 (m, 6H), 3.57 (m, 2H), 3.02 (s, 1H), 2.46 (m, 2H), 2.08 (s, 1H), 1.45-1.34 (m, 15H); ESI-MS *m/z* 496 $(M + Na)^+$, 474 $(M + H)^+$; HRMS Calcd. for $C_{23}H_{30}F_3NO_6Na$ $(M + Na)^+$ requires 496.19174, found 496.19312.

A solution of the above diol (1.27 g, 2.68 mmol) in dry DMF (10 mL) was treated with imidazole (200 mg, 2.95 mmol) and TBSCl (408 mg, 2.70 mmol) at 0 ^oC. The mixture was stirred overnight and evaporated in vacuo. The residue was partitioned between EtOAc (20 mL) and water (20 mL). The organic layer was washed with brine, dried over Na_2SO_4, evaporated in vacuo, and purified by flash chromatography on silica to give silyl ether (1.44 g, 91%). $[\alpha]_D^{25}$ = -30.3 (*c* 1.1, $CHCl_3$); IR (film) 3416, 1728, 1605, 1511, 1252, 1174 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.30 (d, *J* = 8.7 Hz, 2H), 7.02 (d, *J* = 9.2 Hz, 1H), 6.84 (d, *J* = 8.7 Hz, 2H), 6.62 (dd, *J* = 15.6, 10.5 Hz, 1H), 6.43 (d, *J* = 15.6 Hz, 1H), 6.22 (dd, *J* = 15.3, 10.5 Hz, 1H), 5.76 (m, 1H), 4.20-3.92 (m, 9H), 3.55 (d, *J* = 7.0 Hz, 2H), 2.95 (d, *J* = 3.0 Hz, 1H), 2.44 (m, 2H), 1.43 (s, 6H), 1.26 (t, *J* = 7.1 Hz, 3H), 0.88 (s, 9H), 0.06 (s, 6H); ESI-MS *m/z* 610 $(M + Na)^+$, 605 $(M + NH_4)^+$, 588 $(M + H)^+$; HRMS Calcd. for $C_{29}H_{44}F_3NO_6SiNa$ $(M + Na)^+$ requires 610.27822, found 610.27864.

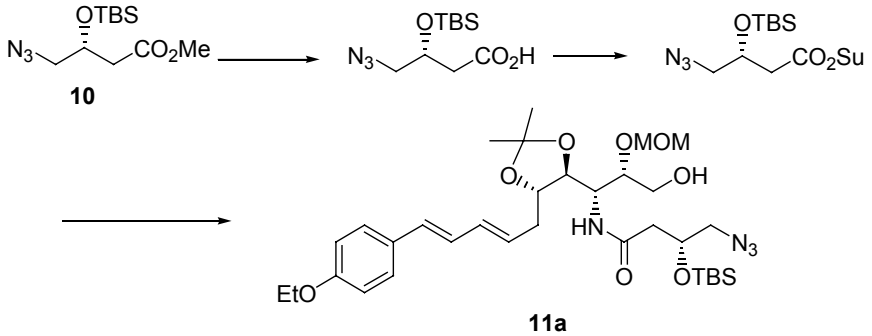
A solution of the above silyl ether (1.44 g, 2.45 mmol) in dry CH_2Cl_2 (15 mL) was treated with DIEA (0.98 mL, 5.64 mmol) and MOMCl (0.37 mL, 4.90 mmol) successively. The mixture was stirred overnight at room temperature and diluted with water (10 mL). The organic layer was seperated, washed with brine, dried over Na_2SO_4, evaporated in vacuo, and purified by flash chromatography on silica to give the MOM ether (1.54 g, 99%). $[\alpha]_D^{25}$ = -15.8 (*c* 1.1, $CHCl_3$); IR (film) 2687, 1730, 1512, 1251, 1173, 1035, 838, 779 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.30 (d, *J* = 8.4 Hz, 2H), 6.84 (d, *J* = 8.4 Hz, 2H), 6.65 (d, *J* = 9.9 Hz, 1H), 6.62 (dd, *J* = 15.6, 10.2 Hz, 1H), 6.42 (d, *J* = 15.6 Hz, 1H), 6.19 (dd, *J* = 15.3, 10.2 Hz, 1H), 5.76 (m, 1H), 4.74 (m, 2H), 4.36 (m, 1H), 4.15 (m, 2H), 4.05 (q, *J* = 7.0 Hz, 2H), 3.76 (m, 1H), 3.68 (dd, *J* = 9.9, 5.7 Hz, 1H), 3.39 (s, 3H), 3.37 (m, 1H), 2.37 (m, 2H), 1.42 (s, 9H), 0.88 (s, 9H), 0.04 (s, 6H); ESI-MS *m/z* 654 $(M + Na)^+$, 649 $(M + NH_4)^+$, 632 $(M + H)^+$; HRMS Calcd. for $C_{31}H_{48}F_3NO_7SiNa$ $(M + Na)^+$ requires 654.30444, found

654.30445.

To a solution of the above ether (804 mg, 1.27 mmol) in THF (5 mL) was added a solution of TBAF in THF (1.0 M, 1.5 mL, 1.50 mmol). The reaction was stirred for 2 h and partitioned between EtOAc (10 mL) and water (10 mL). The organic layer was dried over Na_2SO_4, evaporated in vacuo, and purified by flash chromatography on silica to give **8a** (656 mg, 100%) as a pale yellow solid. $[\alpha]_D^{25}$ = -9.4 (*c* 1.05, $CHCl_3$); IR (film) 3504, 3300, 1702, 1510, 1252, 1180 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.32 (d, *J* = 8.7 Hz, 2H), 6.86 (d, *J* = 8.7 Hz, 2H), 6.64 (dd, *J* = 15.3, 10.3 Hz, 1H), 6.61 (d, *J* = 10.5 Hz, 1H), 6.45 (d, *J* = 15.3 Hz, 1H), 6.22 (dd, *J* =15.3, 10.2 Hz, 1H), 5.73 (m, 1H), 4.77 (m, 2H), 4.20 (t, *J* = 9.3 Hz, 1H), 4.09 (m, 2H), 4.05 (q, *J* = 6.9 Hz, 2H), 3.78 (dd, *J* = 9.0, 6.9 Hz, 1H), 3.64 (m, 1H), 3.55 (m, 1H), 3.44 (s, 3H), 2.84 (m, 1H), 2.41 (m, 2H), 1.44 (t, *J* = 6.9 Hz, 3H), 1.43 (s, 6H); EI-MS *m/z* 517 (M^+), 272, 240, 210, 187; HRMS Calcd. for $C_{25}H_{34}F_3NO_7Na$ $(M + Na)^+$ requires 540.21851, found 540.21796.



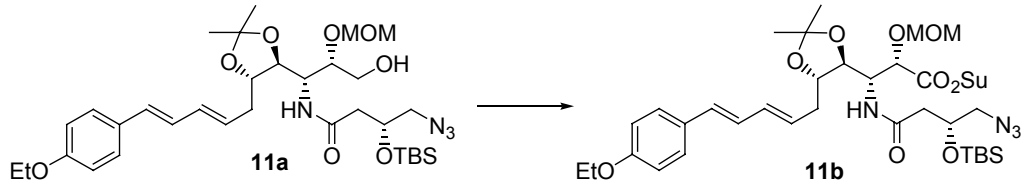
Amine 8b. $NaBH_4$ (73 mg, 1.93 mmol) was added to a solution of **8a** (333 mg, 0.64 mmol) in dry ethanol (3 mL). The mixture was stirred for 6 h and diluted with water (1 mL). The ethanol was removed in vacuo and the residue was partitioned between EtOAc (10 mL) and water (5 mL). The aqueous layer was further extracted with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4, evaporated in vacuo to give **8b** (270 mg, 100%) without further purification.



Dipeptide 11a. NaOH (287 mg, 7.20 mmol) was added in one portion to a stirred solution of the ester **10** (981 mg, 3.60 mmol) in CH_3OH/H_2O (4 : 1) (10 mL) at room temperature. The solution was stirred overnight and then acidified to pH 6 with 1 N HCl. After methanol was removed in vacuo, the residue was extracted with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4, evaporated in vacuo to give crude acid.

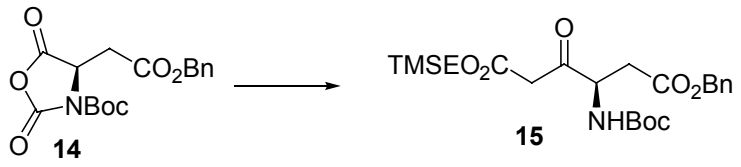
A solution of the above acid in dry CH_2Cl_2 (10 mL) was treated with HOSu (538 mg, 4.7 mmol) and EDCI (760 mg, 4.0 mmol) at room temperature. The mixture was stirred overnight and evaporated in vacuo. The residue was partitioned between EtOAc (10 mL) and water (10 mL). The organic layer was washed with brine, dried over Na_2SO_4, evaporated in vacuo, and purified by flash chromatography on silica to give activated ester (1.27 g, 99%). $[\alpha]_D^{25}$ = -7.3 (*c* 2.4, $CHCl_3$); IR (KBr) 2931, 2859, 2107, 1787, 1742, 1203, 1067, 838, 779 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.33 (m, 1H), 3.48 (dd, *J* = 12.8, 4.5 Hz, 1H), 3.35 (dd, *J* = 12.8, 5.0 Hz, 1H), 2.90 (m, 2H), 2.87 (s, 4H), 0.93 (s, 9H), 0.17 (s, 6H). ESI-MS *m/z* 379 $(M + Na)^+$, 374 $(M + NH_4)^+$, 357 $(M + H)^+$; HRMS Calcd. for $C_{14}H_{24}N_4O_5SiNa$ $(M + Na)^+$ requires 379.14082, found 379.14242.

A solution of the above activated ester (252 mg, 0.71 mmol) and **8b** (270 mg, 0.64 mmol) in ethyl acetate was added solid $NaHCO_3$ (108 mg, 1.29 mmol) and then refluxed for 6 h. The mixture was allowed to cool, evaporated in vacuo and the residue was purified by flash chromatography on silica to give **11a** (415 mg, 96%) as a pale yellow oil. $[\alpha]_D^{25}$ = -8.0 (*c* 0.6, $CHCl_3$); IR (film) 3347, 2105, 1655, 1606, 1511, 1252, 1101 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.31 (d, *J* = 8.7 Hz, 1H), 6.84 (d, *J* = 8.7 Hz, 1H), 6.64 (dd, *J* = 15.6, 10.3 Hz, 1H), 6.44 (d, *J* = 15.6 Hz, 1H), 6.24 (dd, *J* = 15.3, 10.3 Hz, 1H), 6.10 (d, *J* = 9.8 Hz, 1H), 5.78 (m, 1H), 4.75 (d, *J* = 6.7 Hz, 1H), 4.67 (d, *J* = 6.7 Hz, 1H), 4.25 (m, 2H), 4.07 (m, 4H), 3.70 (m, 2H), 3.42 (m, 2H), 3.38 (s, 3H), 3.28 (m, 1H), 2.59-2.41 (m, 4H), 1.41 (t, *J* = 7.0 Hz, 3H), 1.40 (s, 6H), 0.92 (s, 9H), 0.15 (s, 3H), 0.13 (s, 3H); ESI-MS *m/z* 685 $(M + Na)^+$, 663 $(M + H)^+$; HRMS Calcd. for $C_{33}H_{54}N_4O_8SiNa$ $(M + Na)^+$ requires 685.36031, found 685.36048.



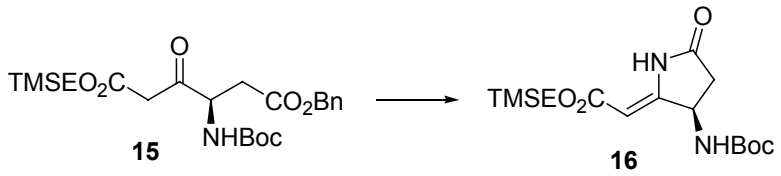
Activated ester 11b. To a solution of **11a** (2.00 g, 3.02 mmol) in dry CH_2Cl_2 (20 mL) was added Dess-Martin reagent (1.50 g, 3.56 mmol) at 0 ^oC. The mixture was stirred for 2 h before diluted with saturated $Na_2S_2O_3$ (10 mL). The organic layer was washed with 5% $NaHCO_3$ (5 mL) and brine, dried over Na_2SO_4, evaporated in vacuo and purified by flash chromatography on silica to give the aldehyde, which was dissolved in *t*-butyl alcohol (15 mL) and water (6 mL). After the resultant solution was added resorcinol (664 mg, 6.04 mmol), NaH_2PO_4 (1.88 g, 12.08 mmol) and sodium chlorite (80%, 510 mg, 4.53 mmol) at 0 ^oC, it was stirred for 2 h and then partitioned between EtOAc (50 mL) and water (20 mL). The aqueous layer was further extracted with EtOAc and the combined organic layers were washed with brine, dried (Na_2SO_4), evaporated in vacuo and purified by flash chromatography on silica to give the acid (1.51 g, 74%).

A solution of the resulting acid (1.51 g, 2.23 mmol) in dry CH_2Cl_2 (10 mL) was treated with HOSu (308 mg, 2.68 mmol) and EDCI (470 mg, 2.45 mmol) at room temperature. The mixture was stirred overnight and evaporated in vacuo. The residue was partitioned between EtOAc (20 mL) and water (20 mL). The organic layer was washed with brine, dried over Na_2SO_4, evaporated in vacuo, and purified by flash chromatography on silica to give **11b** (1.47 g, 85%) as a pale yellow solid. $[\alpha]_D^{25}$ = -16.8 (*c* 1.1, $CHCl_3$); IR (KBr) 3342, 2931, 2858, 2106, 1744, 1682, 1511, 1251, 1205, 1046, 780 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.30 (d, *J* = 8.4 Hz, 2H), 6.91 (d, *J* = 9.9 Hz, 1H), 6.84 (d, *J* = 8.4 Hz, 2H), 6.62 (dd, *J* = 15.9, 10.8 Hz, 1H), 6.41 (d, *J* = 15.9 Hz, 1H), 6.22 (dd, *J* = 14.7, 10.8 Hz, 1H), 5.75 (m, 1H), 5.05 (s, 1H), 4.77 (m, 3H), 4.28 (m, 1H), 4.14 (m, 1H), 4.03 (q, *J* = 6.9 Hz, 2H), 3.69 (dd, *J* = 9.6, 6.9 Hz, 1H), 3.42 (s, 3H), 3.35 (m, 2H), 2.82 (s, 4H), 2.60 (dd, *J* = 16.2, 6.0 Hz, 1H), 2.44 (m, 1H), 2.41 (m, 1H), 2.29 (m, 1H), 1.45 (s, 3H), 1.41 (s, 3H), 1.40 (t, *J* = 6.9 Hz, 3H), 0.95 (s, 9H), 0.18 (s, 3H), 0.14 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.5, 168.3, 166.6, 158.4, 133.5, 130.8, 130.0, 128.2, 127.7, 127.4, 126.7, 114.6, 109.2, 96.6, 79.1, 78.1, 72.1, 68.5, 63.4, 56.6, 56.5, 55.5, 53.6, 41.1, 37.3, 27.4, 27.1, 25.7, 25.5, 17.9, 14.8, -4.8, -5.0; ESI-MS *m/z* 796 $(M + Na)^+$, 774 $(M + H)^+$; HRMS Calcd. for $C_{37}H_{55}N_5O_{11}SiNa$ $(M + Na)^+$ requires 796.35596 found 796.35368.

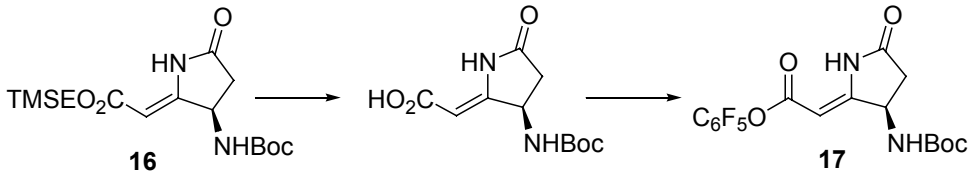


Keto ester 15. To a solution of trimethylsilylethyl acetate (918 mg, 5.74 mmol) in dry THF (3 mL) stirred under argon at -78 ^oC, LDA in THF (1.0 M, 5.74 mL, 5.74 mmol)

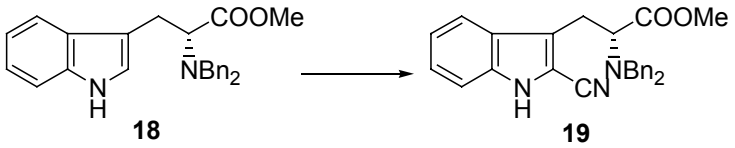
was added. The mixture was stirred at -78 ^{o}C for 1 h, whereupon it was added a solution of **14** (1.00 g, 2.87 mmol) in THF (5 mL). After 30 min at -78 ^{o}C, the mixture was added HOAc (0.5 mL, 8.61 mmol) and allowed to warm to rt. The mixture was partitioned between EtOAc (20 mL) and water (20 mL). The organic phase was dried over Na_2SO_4 and evaporated and the residue was purified by flash chromatography on silica to give **15** (1.06 g, 80%) as a colorless oil. $[\alpha]_D^{25}$ = +35.9 (*c* 1.7, $CHCl_3$); IR (film) 3367, 2956, 1719, 1500, 1251, 1168, 1053, 981, 861, 838, 753 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36 (s, 5H), 5.67 (d, *J* = 9.0 Hz, 1H), 5.14 (s, 2H), 4.61 (m, 1H), 4.23 (m, 2H), 3.62 (s, 2H), 3.08 (dd, *J* = 17.4, 5.4 Hz, 1H), 2.83 (dd, *J* = 17.4, 4.8 Hz, 1H), 1.45 (s, 9H), 1.03 (m, 2H), 0.06 (s, 9H); EI-MS *m/z* 466 $(M + H)^+$, 428, 410, 382, 338, 322, 278, 222, 178, 91, 57.



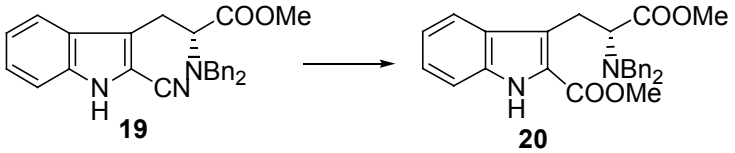
Pyrrolidinone 16. A suspension of 10% Pd/C (150 mg) in a solution of **15** (1.91 g, 4.12 mmol) in EtOAc (20 mL) was stirred under H_2 (1 atm) at room temperature for 3 h. The mixture was filtered, and the filtrate was evaporated in vacuo to give the crude acid, which was dissolved in dry THF (15 mL). To this solution NMM (0.56 mL, 5.08 mmol) and $ClCO_2{}^iBu$ (0.61 mL, 4.66 mmol) were added at 0 ^{o}C under argon. After 30 min, the mixture was added aqueous ammonia (5 mL) and stirred for another 30 min before diluted with 10 mL of water. The aqueous layer was extracted with ether and the combined organic layers were washed with brine, dried over Na_2SO_4 and evaporated in vacuo. The resulting hydroxypyrrolidinone was then dissolved in dry CH_2Cl_2 (15 mL) and treated with Et_3N (1.5 mL, 10.58 mmol) and MsCl (0.40 mL, 5.08 mmol) at 0 ^{o}C. The mixture was stirred for 4 h and then diluted with water (10 mL). The organic layer was washed with brine, dried over Na_2SO_4, evaporated in vacuo, and purified by flash chromatography on silica to give **16** (1.18 g, 81%) as a white solid. $[\alpha]_D^{25}$ = +58.9 (*c* 1.05, $CHCl_3$); IR (KBr) 3409, 3272, 2956, 1750, 1684, 1545, 1265, 1217, 1170, 1064, 867 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.76 (s, 1H), 5.19 (s, 1H), 4.98 (m, 2H), 4.23 (t, *J* = 8.7 Hz, 2H), 2.94 (dd, *J* = 21.0, 7.5 Hz, 1H), 2.42 (dd, *J* = 21.0, 4.8 Hz, 1H), 1.48 (s, 9H), 1.02 (t, *J* = 8.7 Hz, 2H), 0.07 (s, 9H); EI-MS *m/z* 356 (M^+), 300, 272, 257, 228, 213, 195, 183, 139, 73; Anal. Calcd. for $C_{16}H_{30}N_2O_6Si$ (M + H_2O) requires C: 51.31, H: 8.07, N: 7.48, found C: 51.27, H: 8.09, N: 7.39; HRMS Calcd. for $C_{16}H_{28}N_2O_5Si$ requires 356.17675 found 356.17358.



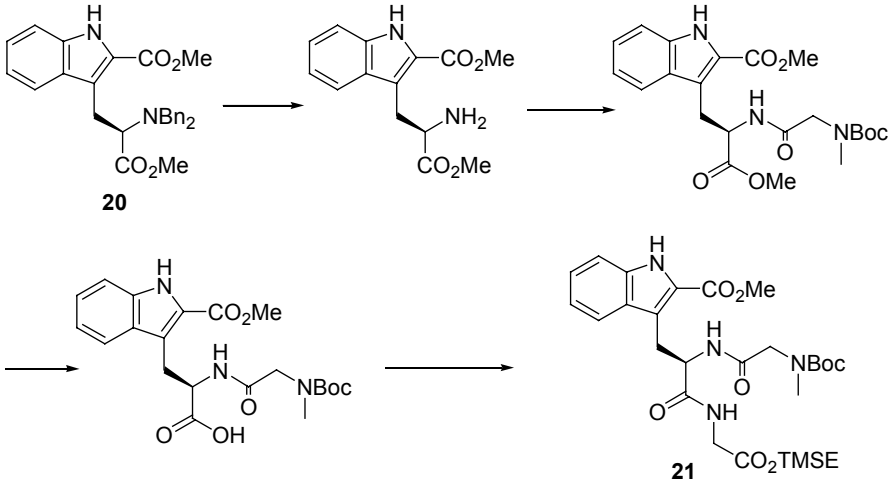
Activated ester 17. To a solution of **16** (201 mg, 0.56 mmol) and TsOH (215 mg, 1.13 mmol) in THF (0.5 mL) was added TBAF in THF (1 M, 3.4 mL, 3.4 mmol) at room temperature. The mixture was stirred for 24 h and evaporated in vacuo. The residue was purified by flash chromatography on silica to give the crude acid (119 mg, 82%) as a white solid. This acid (119 mg, 0.46 mmol) was dissolved in dry CH_2Cl_2 (3 mL) and treated with C_6F_5OH (93 mg, 0.51 mmol) and EDCI (98 mg, 0.51 mmol). The mixture was stirred overnight and evaporated in vacuo. The residue was purified by flash chromatography on silica to give **17** (175 mg, 89%) as a white solid. IR (KBr) 3381, 3342, 3252, 2984, 1693, 1663, 1523, 1174, 1122, 1008, 994 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.54 (s, 1H), 5.51 (s, 1H), 5.06 (m, 2H), 3.01 (dd, J = 17.4, 7.8 Hz, 1H), 2.51 (dd, J = 17.4, 5.7 Hz, 1H), 1.49 (s, 9H); ESI-MS *m/z* 445 $(M + Na)^+$; Anal. Calcd. for $C_{17}H_{15}F_5N_2O_5$ requires C: 48.35, H: 3.58, N: 6.63, found C: 48.02, H: 3.44, N: 6.38.



Amino ester 19. A solution of **18** (21.2 g, 53.3 mmol) in dry THF (150 mL) stirred under argon at -78 °C was treated with Et_3N (8.9 mL, 64.0 mmol) and *t*-BuOCl (7.7 mL, 64.0 mmol). After stirred for 1 h, the mixture was added TMSCN (10.6 mL, 80.0 mmol), followed by $BF_3 \cdot Et_2O$ (10.1 mL, 80 mmol). The reaction was allowed to warm to rt, stirred overnight and then diluted with 5% $NaHCO_3$ (100 mL). The aqueous layer was extracted with EtOAc, and the combined organic layers were washed with brine, dried (Na_2SO_4), evaporated in vacuo, and purified by flash chromatography on silica to give **19** (20.0 g, 89%) as a pale yellow oil. $[\alpha]_D^{25}$ = +157.1 (*c* 0.7, $CHCl_3$); IR (film) 3326, 3030, 2223, 1733, 1495, 1454, 1245, 1173, 745, 699 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.47 (s, 1H), 7.38-7.20 (m, 12H), 6.96 (d, J = 3.1 Hz, 2H), 4.00 (d, J = 13.7 Hz, 2H), 3.85 (dd, J = 8.8, 6.1 Hz, 1H), 3.74 (s, 3H), 3.57 (d, J = 13.7 Hz, 2H), 3.51 (dd, J = 14.2, 8.8 Hz, 1H), 3.23 (dd, J = 14.2, 6.1 Hz, 1H); EI-MS *m/z* 424 $(M + H)^+$, 364 $(M - CO_2Me)^+$, 268, 181, 155, 91.



Diester 20. To a solution of **19** (2.15 g, 5.1 mmol) in methanol (30 mL) was added 6 N KOH (10 mL). The solution was heated to reflux for 24 h, allowed to cool and then acidified to pH 3 with 6 N HCl. The methanol was evaporated in vacuo, and the residue was extracted with $CHCl_3$. The combined organic layers were dried (Na_2SO_4), evaporated in vacuo to give the dicarboxylic acid, which was dissolved in dry DMF (20 mL). To this solution were added $KHCO_3$ (1.8 g, 18.0 mmol) and CH_3I (2.6 g, 18.0 mmol). The mixture was stirred overnight and then evaporated in vacuo. The residue was partitioned between EtOAc (50 mL) and water (50 mL). The organic layer was washed with brine, dried over Na_2SO_4, evaporated in vacuo and purified by flash chromatography on silica to give **20** (1.65 g, 71%) as a white solid. $[\alpha]_D^{25} = +121.6$ (*c* 1.2, $CHCl_3$); IR (KBr) 3344, 2951, 1727, 1684, 1456, 1257, 740, 698 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.76 (s, 1H), 7.41-7.30 (m, 3H), 7.14-6.95 (m, 1H), 4.02 (d, *J* = 14.0 Hz, 2H), 3.95 (dd, *J* = 8.9, 6.6 Hz, 1H), 3.71 (s, 3H), 3.64 (dd, *J* = 14.0, 8.9 Hz, 1H), 3.58 (s, 3H), 3.54 (d, *J* = 14.0 Hz, 2H), 3.44 (dd, *J* = 14.0, 6.6 Hz, 1H); EI-MS *m/z* 456 (M^+), 397, 306, 268, 181, 156, 128, 91; Anal. Calcd. for $C_{28}H_{28}N_2O_4$ requires C: 73.66, H: 6.18, N: 6.14, found C: 73.98, H: 5.99, N: 6.08.

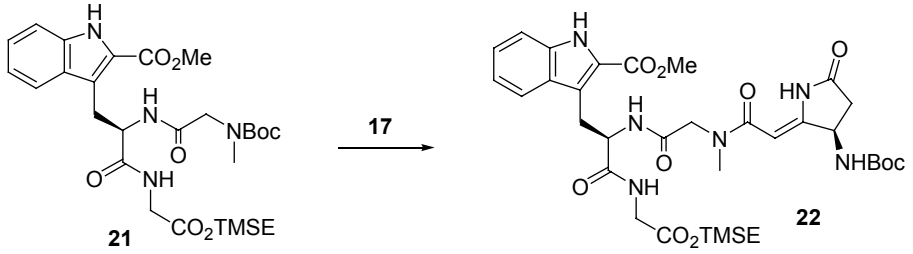


Tripeptide 21. A suspension of $Pd(OH)_2$ (100 mg) in a solution of **20** (850 mg, 1.86 mmol) in methanol (10 mL) was stirred under H_2 (40 atm) at room temperature for 24 h. The mixture was filtered, and the filtrate was evaporated in vacuo. The residue was purified by flash chromatography on silica to give the free amine (361 mg, 70%).

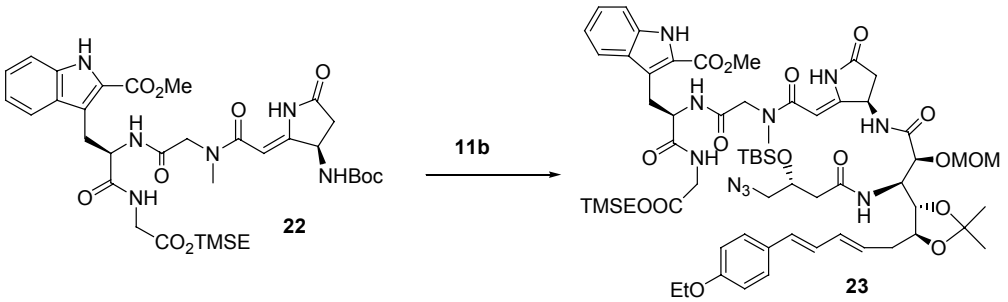
A solution of the above amine (361 mg, 1.31 mmol) and Boc-*N*-Me-Gly-OH (297 mg, 1.57 mmol) in 5.0 mL of dry CH_2Cl_2 was treated with DIEA (0.46 mL, 2.62 mmol),

HOBt (212 mg, 1.57 mmol), and EDCI (301 mg, 1.57 mmol) at 0 ^{o}C. The mixture was stirred for overnight at r.t. and evaporated in vacuo. The residue was partitioned between EtOAc (10 mL) and water (10 mL). The organic layer was washed with brine, dried over Na_2SO_4, evaporated in vacuo and purified by flash chromatography on silica to give the dipeptide (564 mg, 96%) as a colorless solid. $[\alpha]_D^{25}$ = -21.6 (*c* 1.0, $CHCl_3$); IR (KBr) 3335, 2954, 1745, 1702, 1549, 1450, 1251, 1151, 1099 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.90 (s, 1H), 7.71 (d, *J* = 7.8 Hz, 1H), 7.36 (m, 2H), 7.19 (t, *J* = 8.1 Hz, 1H), 7.07 (br s, 1H), 4.81 (m, 1H), 4.01 (s, 3H), 3.81 (m, 1H), 3.69 (s, 3H), 3.61 (m, 3H), 2.78 (s, 3H), 1.40 (s, 9H); EI-MS *m/z* 447 (M^+), 374, 347, 304, 288, 259; HRMS Calcd. for $C_{22}H_{29}N_3O_7Na$ $(M + Na)^+$ requires 470.19032, found 470.18977.

A solution of the above dipeptide (1.40 g, 3.13 mmol) in methanol (16 mL) was treated with 1 N LiOH (4.1 mL, 4.1 mmol) at 0 ^{o}C. The mixture was stirred overnight, and acidified to pH 5 with 1 N HCl. The methanol was removed in vacuo and the residue was extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, evaporated in vacuo to give the crude acid, which was dissolved in 20 mL of dry CH_2Cl_2. To this solution were added H-Gly-OTMSE (657 mg, 3.75 mmol), DIEA (1.1 mL, 6.26 mmol), HOBt (506 mg, 3.75 mmol), and EDCI (720 mg, 3.75 mmol) at 0 ^{o}C, respectively. The mixture was stirred for overnight at r.t. and evaporated in vacuo. The residue was partitioned between EtOAc (30 mL) and water (20 mL). The organic layer was washed with brine, dried over Na_2SO_4, evaporated in vacuo and purified by flash chromatography on silica to give **21** (1.63 g, 88%) as a colorless solid. $[\alpha]_D^{25}$ = +14.0 (*c* 0.8, $CHCl_3$); IR (KBr) 3327, 3062, 2955, 1700, 1656, 1545, 1251, 1178, 1151 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.13 (s, 1H), 7.66 (d, *J* = 7.5 Hz, 1H), 7.28 (m, 2H), 7.09 (t, *J* = 7.5 Hz, 1H), 7.06 (s, 1H), 6.88 (s, 1H), 4.77 (dd, *J* = 14.7, 7.5 Hz, 1H), 4.10 (t, *J* = 8.4 Hz, 2H), 3.98 (s, 3H), 3.87 (m, 2H), 3.84 (d, *J* = 16.5 Hz, 1H), 3.66 (d, *J* = 16.5 Hz, 1H), 3.52 (m, 2H), 2.76 (s, 3H), 1.42 (s, 9H), 0.93 (t, *J* = 8.4 Hz, 2H), 0.00 (s, 9H); ESI-MS *m/z* 613 $(M + Na)^+$, 591 $(M + H)^+$; HRMS Calcd. for $C_{28}H_{42}N_4O_8SiNa$ $(M + Na)^+$ requires 613.26641, found 613.26521.

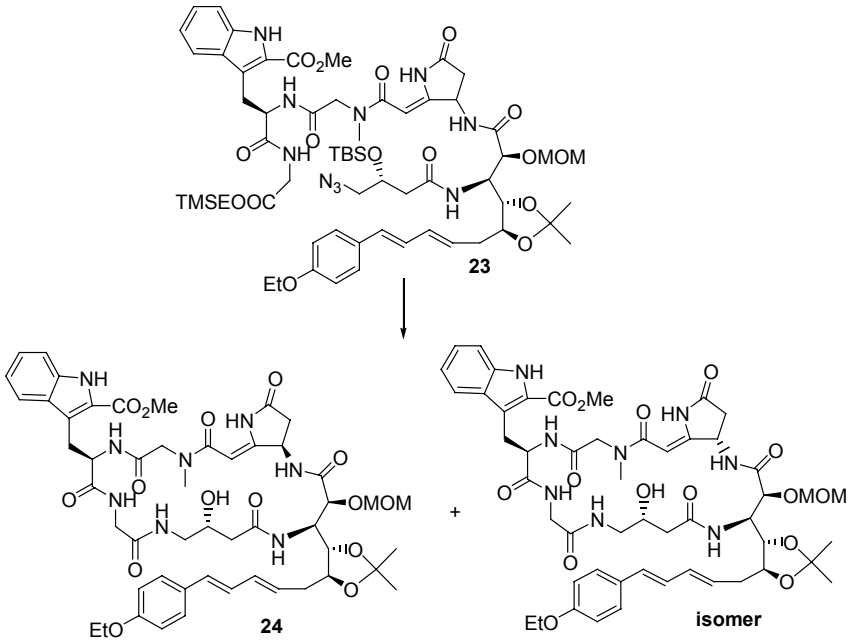


Tetrapeptide 22. A solution of **21** (200 mg, 0.34 mmol) in dry CH_2Cl_2 (2.5 mL) was treated with CF_3CO_2H (0.5 mL) at 0 ^oC. The mixture was stirred for 2.5 h and then evaporated in vacuo to give the amine salt, which was dissolved in in 2 mL of dry DMF. To this solution were added **17** (156 mg, 0.37 mmol) and $NaHCO_3$ (143 mg, 1.70 mmol). The reaction mixture was stirred for 10 h at 40 ^oC, evaporated in vacuo, and purified by flash chromatography on silica to give **22** (199 mg, 81%) as a white solid. $[\alpha]_D^{25} = +28.6$ (*c* 0.9, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 10.47 (s, 1H), 9.40 (s, 1H), 7.71 (t, *J* = 7.8 Hz, 1H), 7.33 (m, 2H), 7.14 (t, *J* = 5.4 Hz, 1H), 6.98 (s, 1H), 6.82 (s, 1H), 5.37 (s, 1H), 5.20 (d, *J* = 9.0 Hz, 1H), 4.93 (m, 1H), 4.71 (m, 1H), 4.22 (m, 2H), 4.01 (s, 3H), 3.96 (m, 2H), 3.87 (m, 1H), 3.64 (m, 2H), 3.55 (m, 1H), 2.89 (s, 3H), 2.70 (m, 1H), 2.37 (m, 1H), 1.48 (s, 9H), 1.00 (m, 2H), 0.06 (s, 9H); ESI-MS *m/z* 767 $(M + K)^+$, 751 $(M + Na)^+$, 729 $(M + H)^+$; HRMS Calcd. for $C_{34}H_{48}N_6O_{10}SiNa$ $(M + Na)^+$ requires 751.31245, found 751.30934.



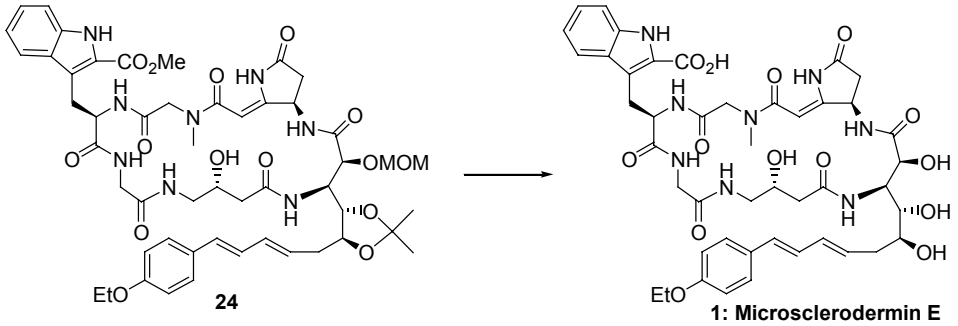
Coupling tetrapeptide 22 with dipeptide 11b. A solution of **22** (180 mg, 0.25 mmol) in dry CH_2Cl_2 (3.0 mL) was treated with CF_3CO_2H (0.6 mL) at 0 ^oC. The mixture was stirred for 2.5 h and then evaporated in vacuo at 0 ^oC to give the amine salt, which was dissolved in 4 mL of dry CH_3CN. To this solution were added 11b (160 mg, 0.21 mmol) and $NaHCO_3$ (83 mg, 0.99 mmol). The reaction mixture was stirred for 10 h at 70 ^oC, evaporated in vacuo, and purified by flash chromatography on silica to give **23** (224 mg, 84%) as a pale yellow solid. ^1H NMR (300 MHz, $CDCl_3$) δ 10.58 (s, 1H), 9.40 (s, 1H), 7.71 (d, *J* = 7.8 Hz, 1H), 7.49 (m, 1H), 7.40-7.24 (m, 4H), 7.12 (m, 3H), 6.94 (m, 1H), 6.84 (m, 2H), 6.57 (m, 1H), 6.39 (m, 1H), 6.23 (m, 1H), 5.72 (m, 1H), 5.43 (s, 1H), 5.17 (m, 1H),

5.04 (m, 1H), 4.85-4.65 (m, 4H), 4.51 (m, 1H), 4.28-4.20 (m, 3H), 4.17-3.93 (m, 9H), 3.76-3.57 (m, 3H), 3.42 (s, 3H), 3.29 (m, 2H), 2.89 (s, 3H), 2.52 (m, 2H), 2.38 (m, 3H), 2.02 (m, 1H), 1.45-1.37 (m, 9H), 1.03 (m, 2H), 0.95 (m, 9H), 0.18-0.05 (m, 15H); ESI-MS *m/z* 1287 $(M + H)^+$, 1305 $(M + NH_4)^+$, 1309 $(M + Na)^+$; HRMS Calcd. for $C_{62}H_{90}N_{10}O_{16}Si_2Na$ $(M + Na)^+$ requires 1309.59670, found 1309.59451.

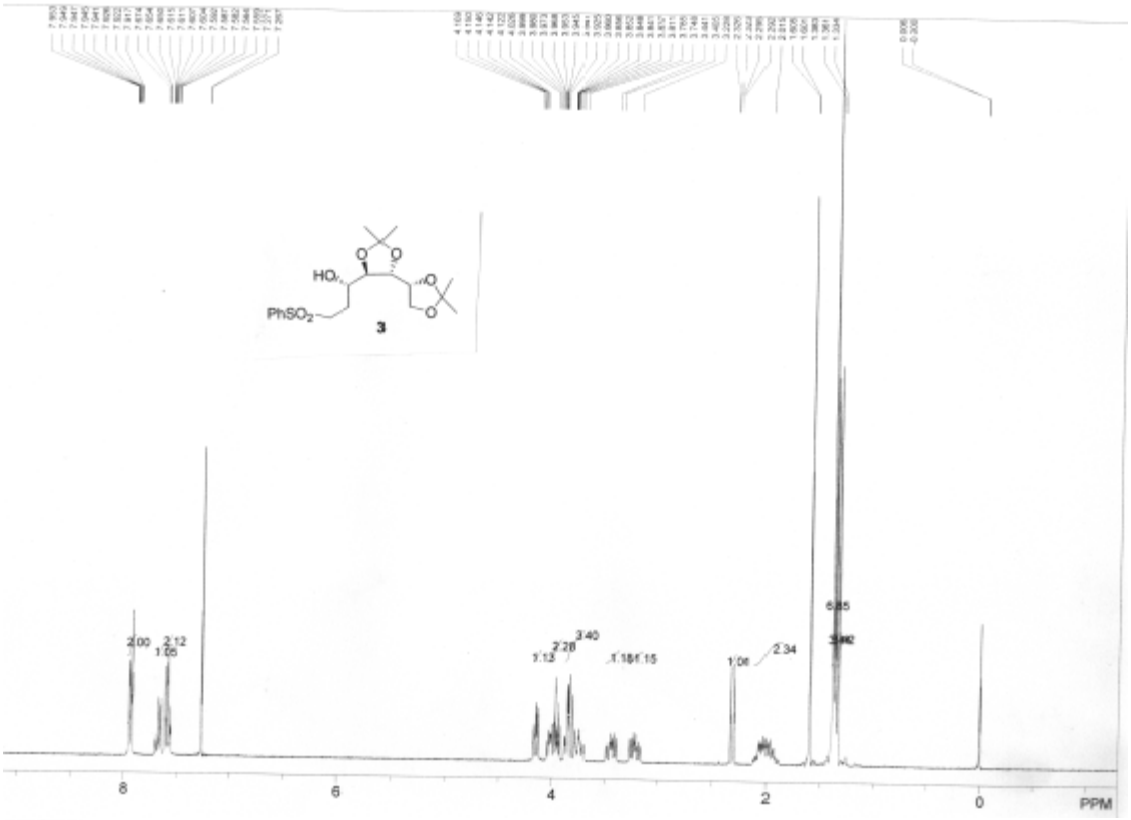


Lactam 24. A solution of **23** (200 mg, 0.156 mmol) in THF (1.0 mL) was treated with TsOH (59 mg, 0.312 mmol) and TBAF in THF (1 M, 0.94 mL) at room temperature. The mixture was stirred for 24 h, diluted with $CHCl_3$ (10 mL) and washed with water. The organic phase was dried over Na_2SO_4 and evaporated in vacuo. The resultant acid was dissolved in THF (3 mL) and treated with Me_3P in THF (1 M, 1.6 mL, 1.6 mmol) under argon. After 2 h, water (100 μL) was added and the mixture was stirred overnight, and evaporated in vacuo. Toluene (2 mL) was added to the residue and evaporated in vacuo to remove the remained water. The residue was dissolved in dry DMF (100 mL), cooled at 0 ^oC and treated with $NaHCO_3$ (131 mg, 1.56 mmol) and DPPA (215 mg, 0.78 mmol) under argon. The mixture was stirred for 3 days at 0 ^oC, allowed to warm to rt and stirred for 10 days. The solvent was evaporated in vacuo, and the residue was partitioned between EtOAc (10 mL) and water (5 mL). The organic phase was washed with brine, dried over Na_2SO_4, evaporated in vacuo, and purified by flash chromatography on silica to give **24** (63.2 mg, 40%) as a colorless solid and its isomer (15.1 mg, 9%). **24**: $[\alpha]_D^{25}$ = -73.2 (*c* 1.6, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 10.33 (s, 1H), 9.01 (s, 1H), 8.72 (s, 1H), 7.92 (m, 1H), 7.79 (d, *J* = 7.8 Hz, 1H), 7.56 (m, 2H), 7.41 (m, 2H), 7.30 (d, *J* = 6.9 Hz, 2H), 7.16 (m, 2H), 6.82 (d, *J* = 6.9 Hz, 2H), 6.60 (dd, *J* = 15.9, 10.8 Hz, 1H), 6.39 (d, *J* = 15.9 Hz, 1H), 6.22 (dd, *J* = 15.6, 10.8 Hz, 1H), 5.74 (m, 1H), 5.48 (s, 1H), 5.45 (m, 1H), 4.99 (m, 1H), 4.71 (m,

3H), 4.55 (s, 1H), 4.44 (m, 1H), 4.33 (dd, J = 17.1, 8.4 Hz, 1H), 4.13 (m, 3H), 4.02 (s, 3H), 3.99 (m, 3H), 3.66 (m, 3H), 3.40 (s, 3H), 3.34 (m, 1H), 3.30 (s, 3H), 2.83 (m, 2H), 2.42 (m, 3H), 2.21 (m, 3H), 1.44 (s, 3H), 1.40 (s, 3H), 1.27 (t, J = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.8, 172.0, 171.3, 170.9, 169.7, 163.8, 158.3, 156.9, 135.9, 133.5, 130.7, 129.9, 129.3, 128.4, 127.4, 127.3, 126.7, 123.5, 121.0, 120.7, 119.9, 114.5, 112.0, 109.3, 97.0, 89.6, 79.7, 77.6, 77.4, 76.6, 67.8, 63.4, 60.4, 57.7, 56.6, 52.6, 45.9, 42.4, 40.9, 39.3, 34.8, 29.6, 27.4, 27.1, 21.0, 14.8, 14.1; ESI-MS m/z 1051 $(M + Na)^+$, 1067 $(M + K)^+$; HRMS Calcd. for $C_{51}H_{64}N_8O_{15}Na$ $(M + Na)^+$ requires 1051.43834, found 1051.43396.



Microsclerodermin E 1. A solution of **24** (15.7 mg, 15.3 μmol) in methanol/THF (2 : 3, 0.5 mL) was treated with aqueous LiOH (1 M, 92 μL, 92 μmol) at 0 ^{o}C. The mixture was stirred for 5 h, acidified with 1 N HCl, and evaporated in vacuo. A suspension of Amberlyst-15 (100 mg) in a solution of the resulting acid in methanol/THF (4 : 1, 2.5 mL) was heated to 70 ^{o}C and stirred for 24 h. The mixture was filtered and the resin was washed with methanol. The combined filtrates was evaporated in vacuo, and the residue was purified by flash chromatography on silica eluting with methanol/$CHCl_3$ (1 : 2) to give **1** (8.7 mg, 61%) as a white solid. $[\alpha]_D^{25}$ = -22.7 (c 0.4, 1 : 1 MeOH/0.1 N NH_4HCO_3 (aq); lit. reported: $[\alpha]_D^{25}$ = -24 (c 0.4, 1 : 1 MeOH/0.1N NH_4HCO_3 (aq)); ^{1}H NMR (300 MHz, DMF-d_7 with trace of TFA) δ 11.58 (s, 1H), 10.60 (s, 1H), 8.88 (d, J = 4.8 Hz, 1H), 8.62 (d, J = 8.7 Hz, 1H), 8.49 (t, J = 6.2 Hz, 1H), 7.72 (d, J = 7.8 Hz, 1H), 7.59 (br, 1H), 7.54 (d, J = 8.1 Hz, 1H), 7.40 (d, J = 8.7 Hz, 2H), 7.35 (m, 1H), 7.31 (t, J = 7.8 Hz, 1H), 7.16 (t, J = 7.8 Hz, 1H), 6.91 (d, J = 8.7 Hz, 2H), 6.73 (dd, J = 15.9, 10.8 Hz, 1H), 6.45 (d, J = 15.9 Hz, 1H), 6.24 (dd, J = 15.0, 10.8 Hz, 1H), 5.83 (m, 1H), 5.45 (s, 1H), 5.42 (m, 1H), 4.68 (s, 1H), 4.64 (d, J = 15.9 Hz, 1H), 4.33 (m, 1H), 4.27 (m, 1H), 4.05 (q, J = 5.7 Hz, 2H), 3.95 (br, 1H), 3.73 (m, 1H), 3.68 (m, 2H), 3.61 (m, 2H), 3.47 (d, J = 15.9 Hz, 1H), 3.45 (m, 2H), 3.07 (s, 3H), 2.91 (m, 2H), 2.59 (dd, J = 18.9, 4.8 Hz, 1H), 2.48 (d, J = 13.5 Hz, 1H), 2.39 (m, 2H), 2.21 (m, 1H), 1.35 (t, J = 5.7 Hz, 3H); negative ESI-MS m/z 929 $(M - H)^-$.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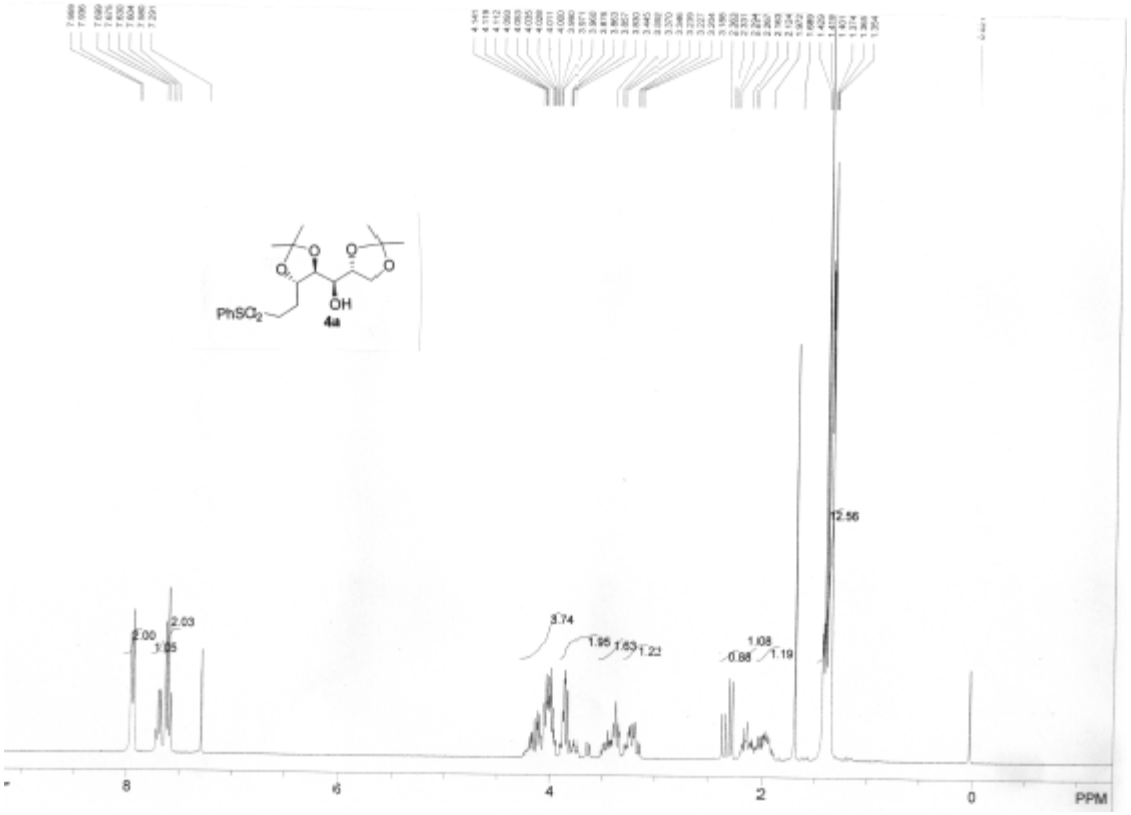
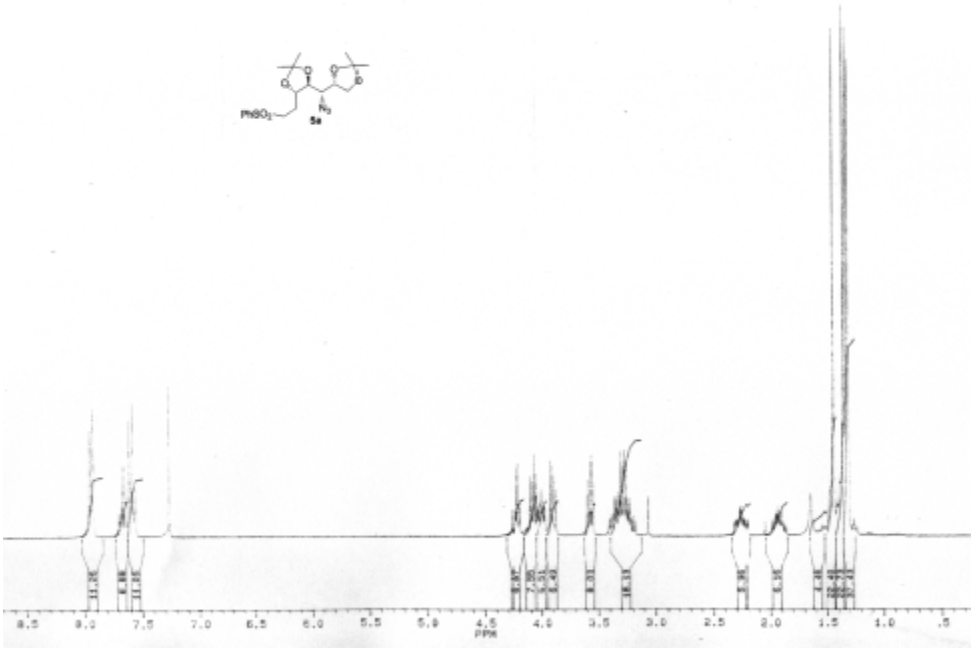
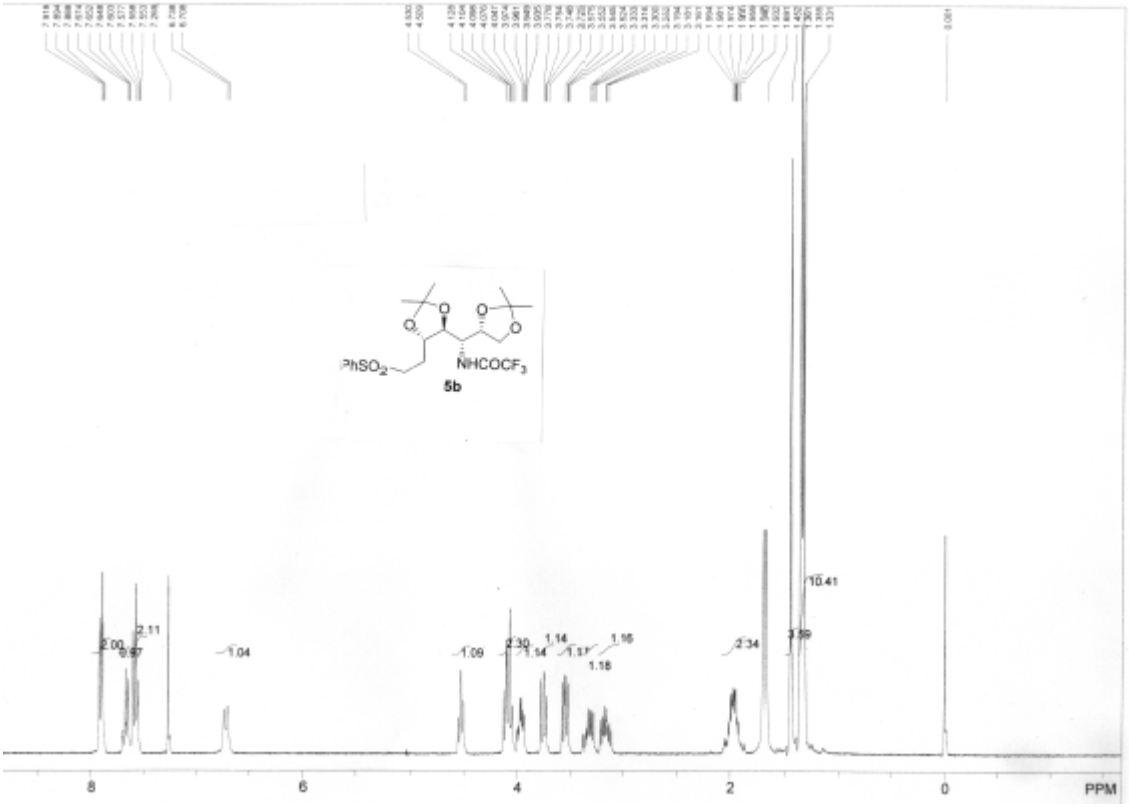
2.12
1.05
3.40
2.28
1.13
1.15
1.06
2.34
6.85
8
6
4
2
0
PPM


PhSO2
OH
4a
2.00
2.03
1.05
3.74
1.95
1.63
1.22
1.08
0.88
1.19
12.56
8
6
4
2
0
PPM

4a


PhSO2
5a
PPM

5a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NHCOCF3
5b
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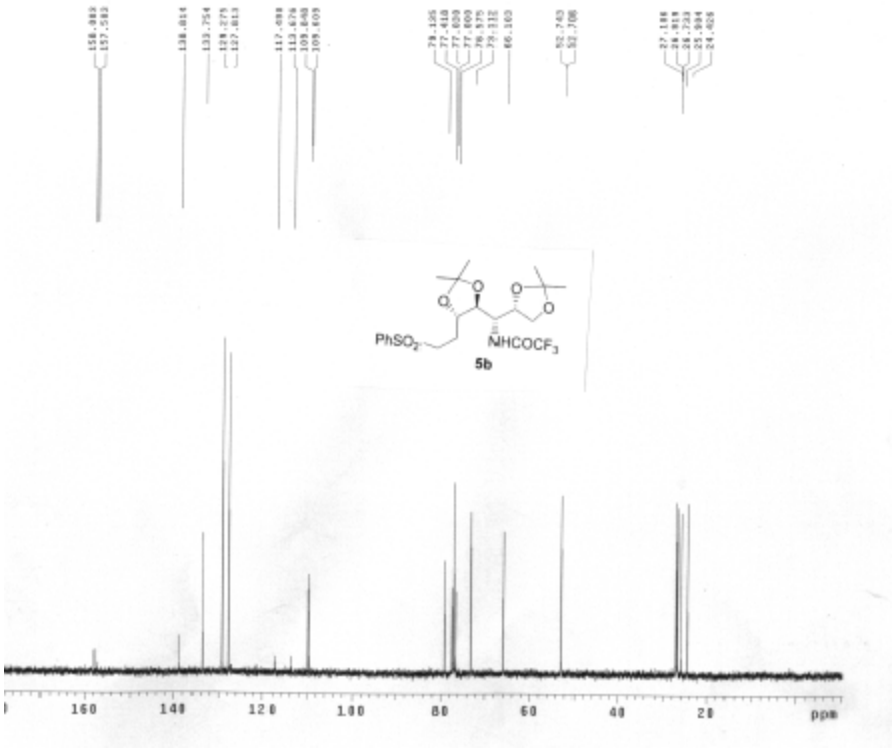
2.11
1.04
1.09
2.30
1.14
1.16
1.18
2.34
8
6
4
2
0
PPM

5b-H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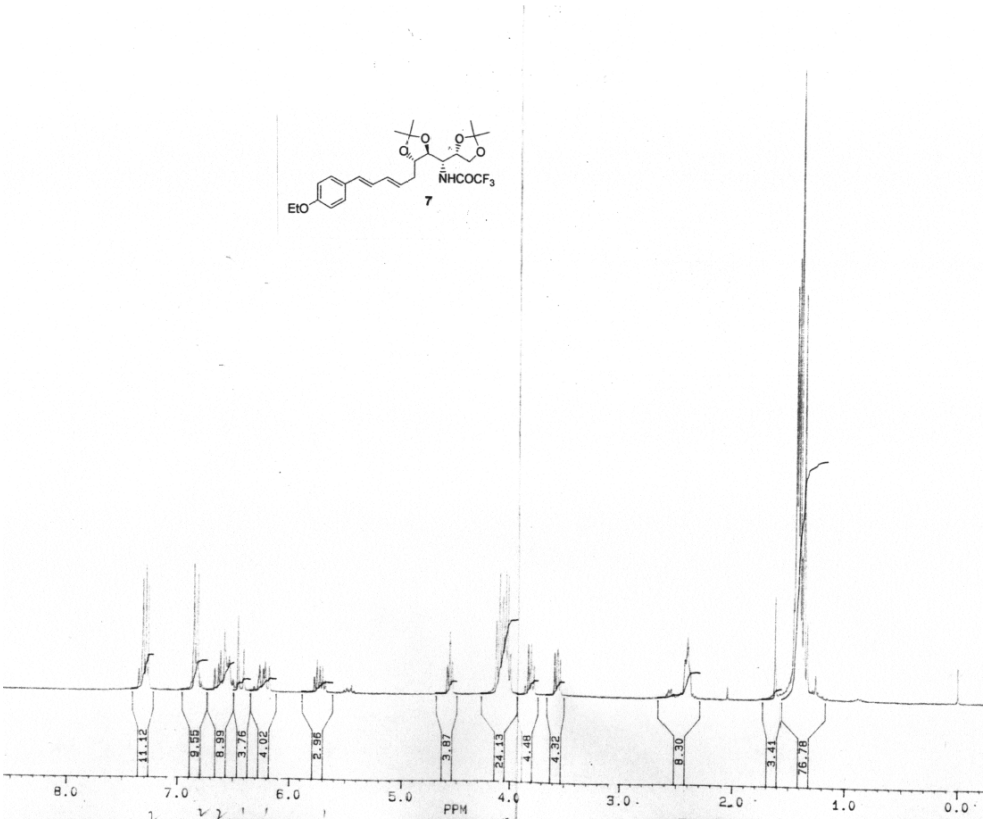
140
120
100
80
60
40
20
ppm

5b-C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NHCOCF3
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11.12
9.55
8.99
3.76
4.02
2.96
3.87
24.13
4.48
4.32
8.30
3.41
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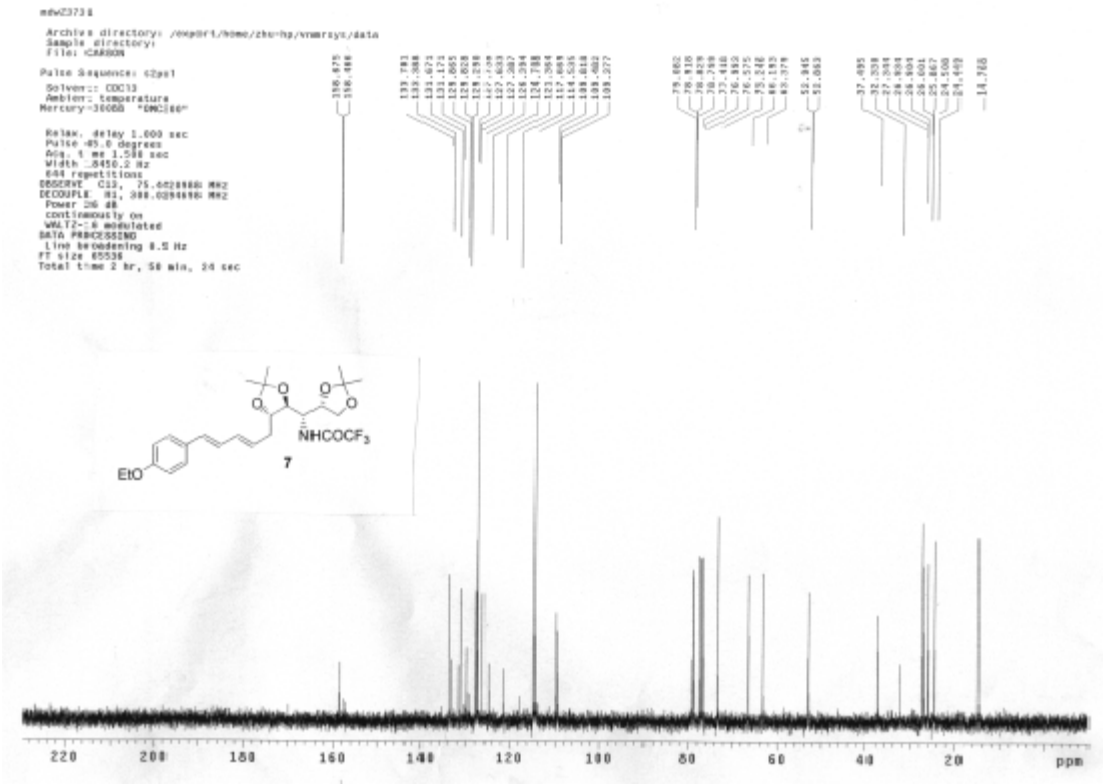
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
PPM

7-H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EtO
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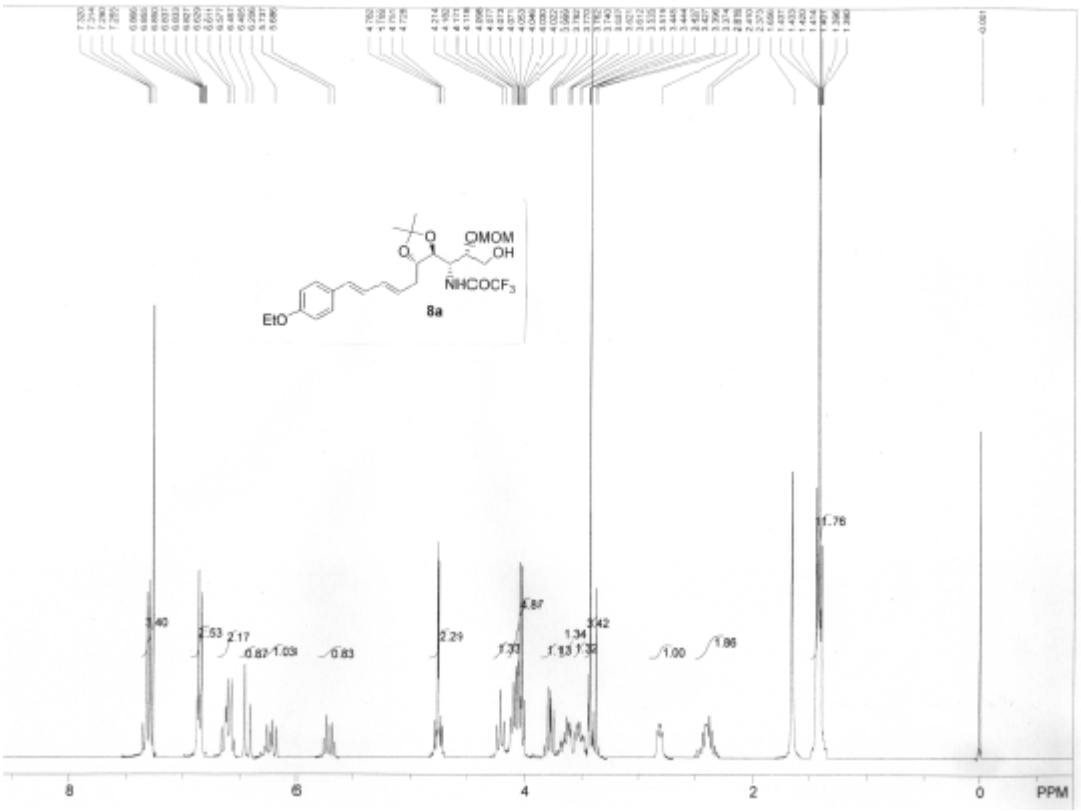
200
180
160
140
120
100
80
60
40
20
ppm

7-C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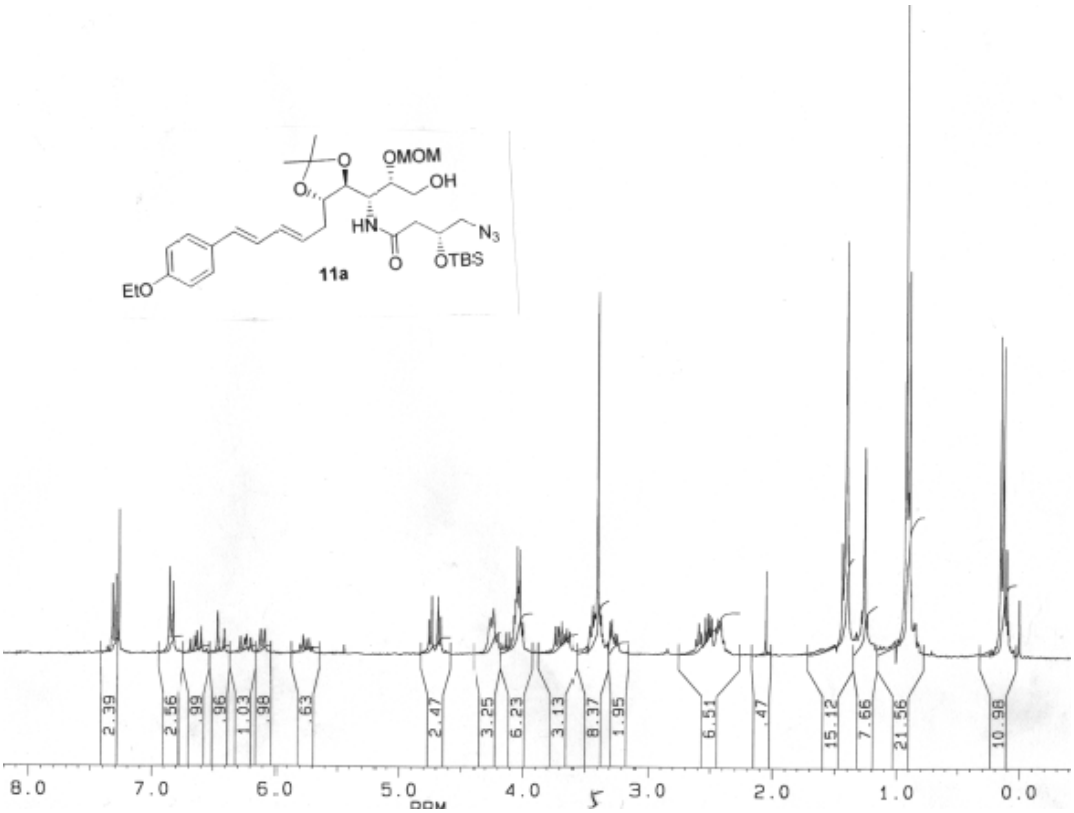
EtO
8a
8
6
4
2
0
PPM

8a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HN
N3
OTBS
EtO
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.99
.96
1.03
.98
.63
2.47
3.25
6.23
3.13
8.37
1.95
6.51
.47
15.12
7.66
21.56
10.98
8.0
7.0
6.0
5.0
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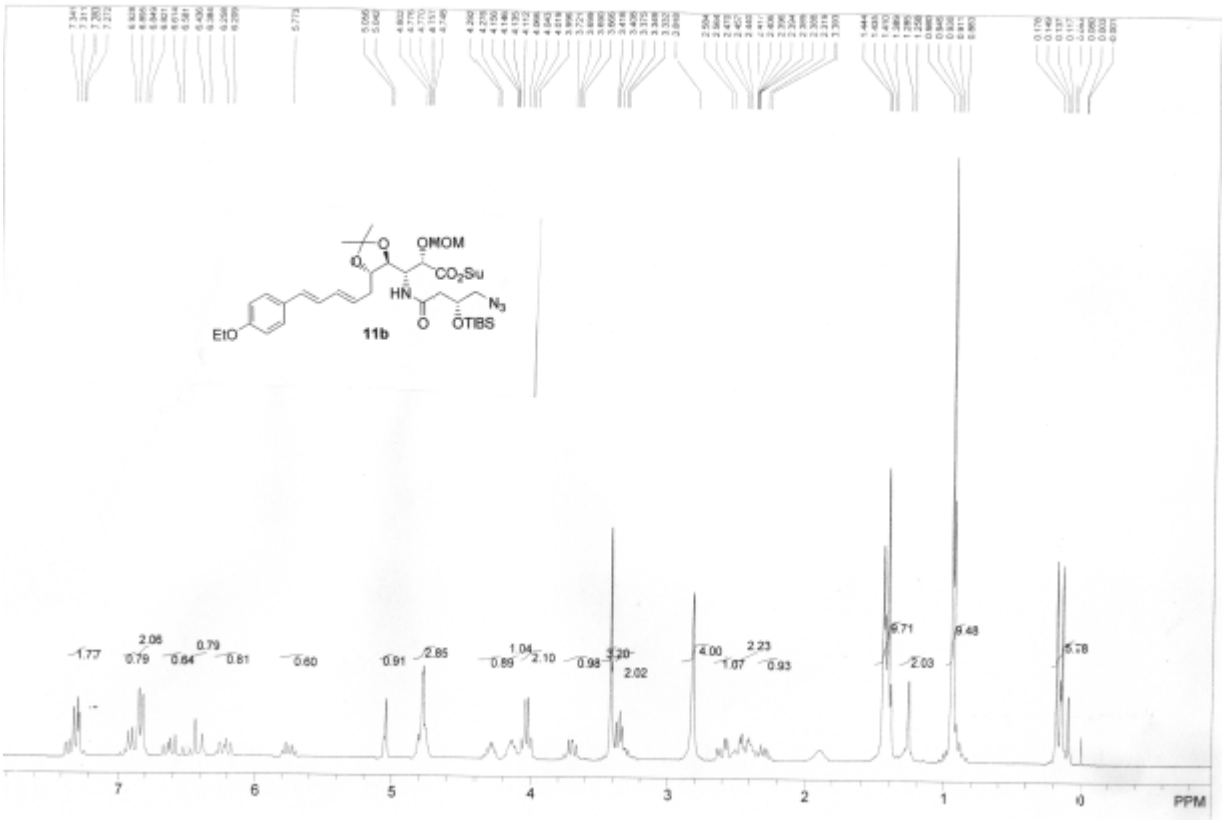
3.0
2.0
1.0
0.0

11a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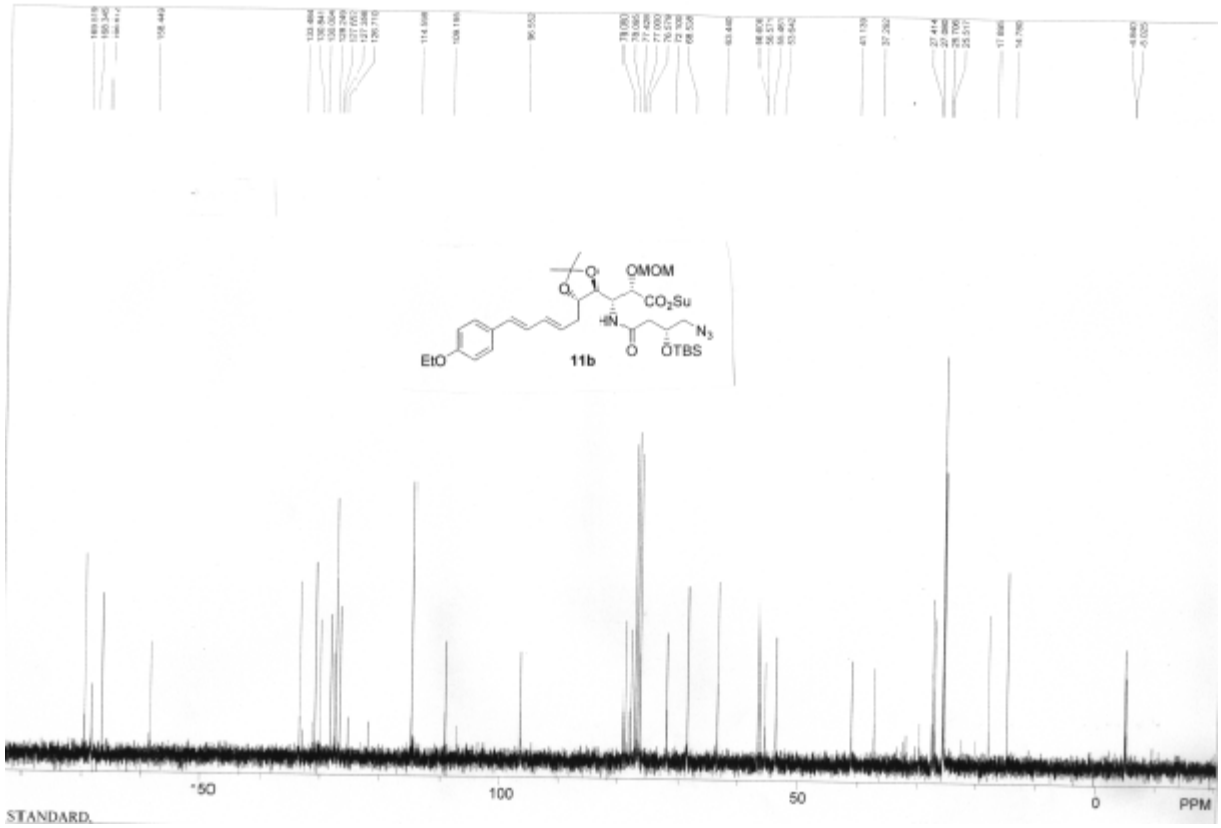
CO2Siu
HN
N3
OTBS
EtO
11b
1.77
2.06
0.79
0.84
0.79
0.81
0.60
0.91
2.85
1.04
0.89
2.10
0.98
3.20
2.02
4.00
1.07
2.23
0.93
6.71
2.03
9.48
5.78
7
6
5
4
3
2
1
0
PPM

11b-H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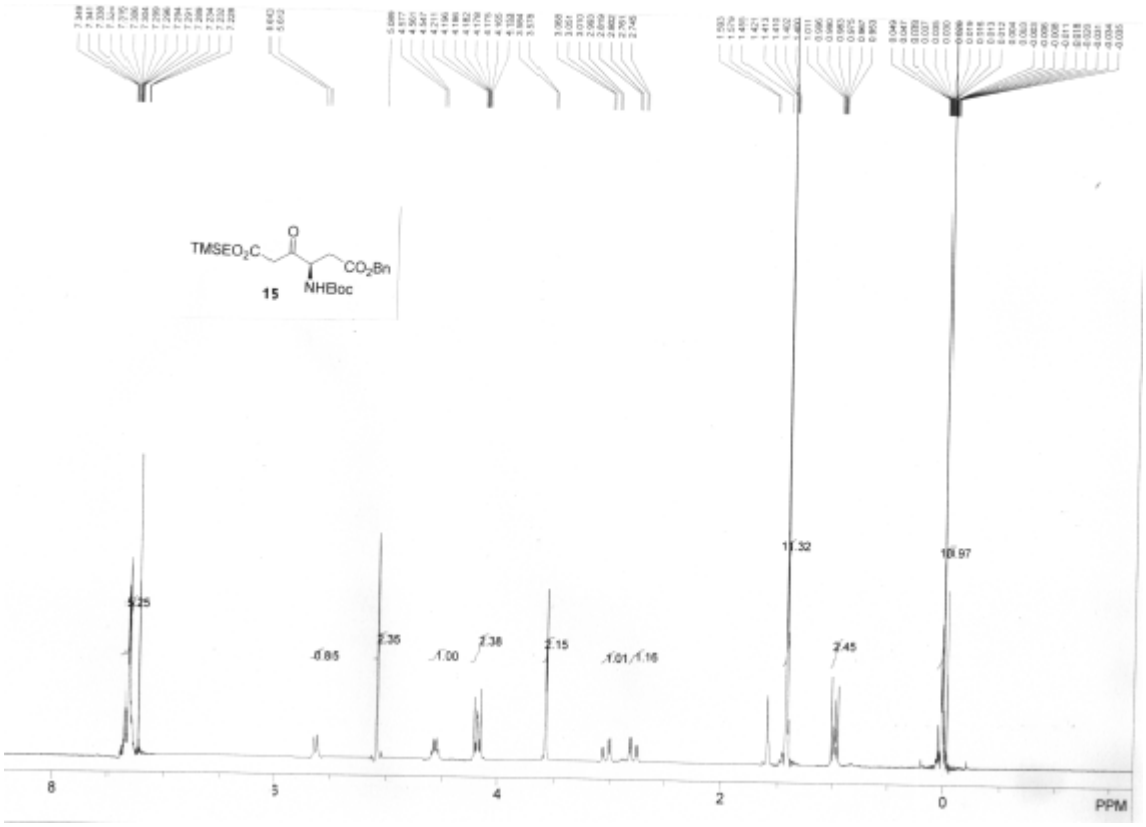
CO_2Su
N_3
OTBS
EtO
11b
150
100
50
0
PPM
STANDARD

11b-C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NHBoc
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2.35
1.00
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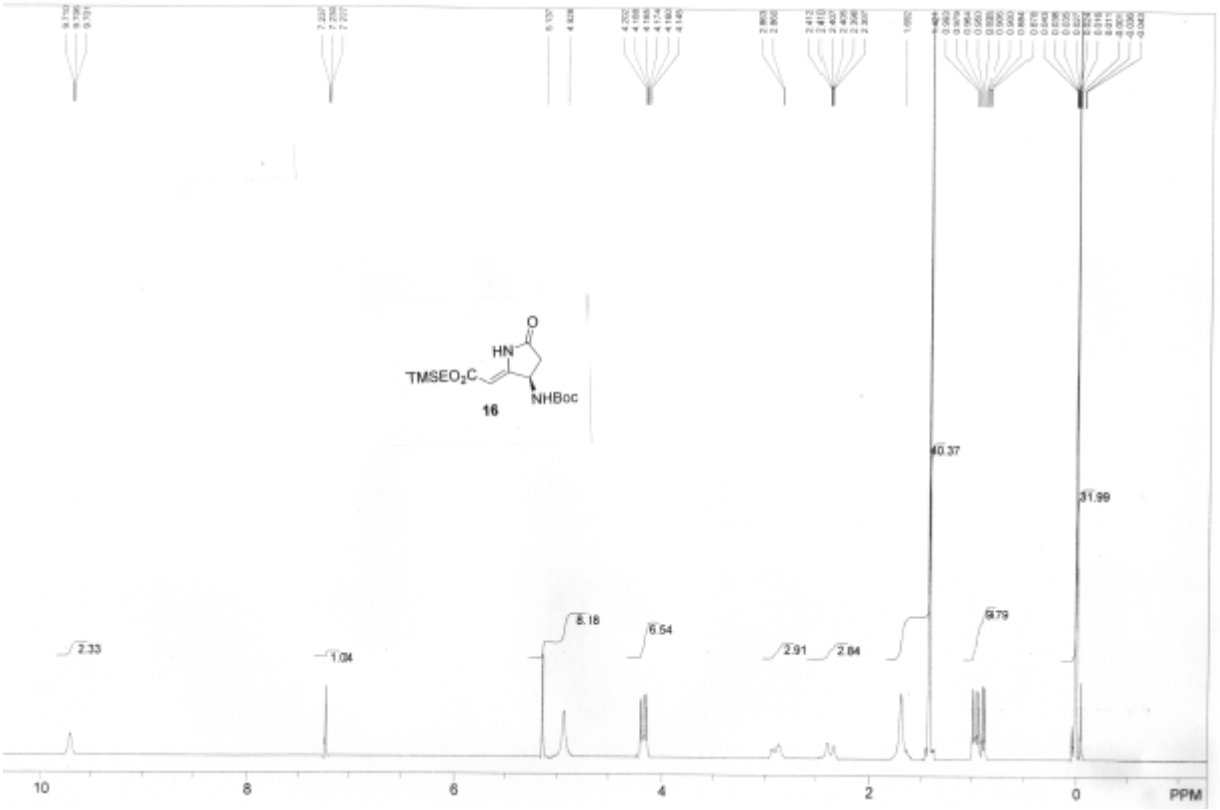
1.01
1.16
11.32
10.97
2.45
8
5
4
2
0
PPM

15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HN
O
NHBoc
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31.99
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1.04
5.18
6.54
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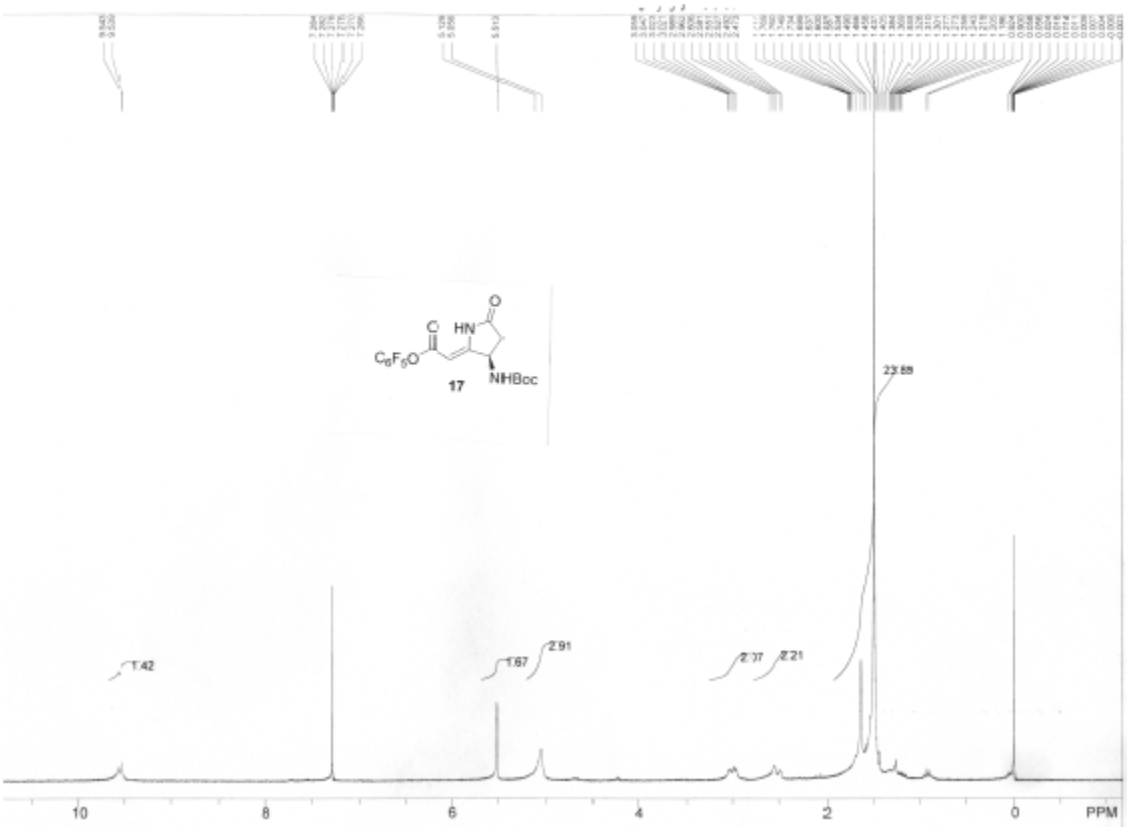
0.79
10
8
6
4
2
0
PPM

16


C6F5O
HN
O
NHBoc
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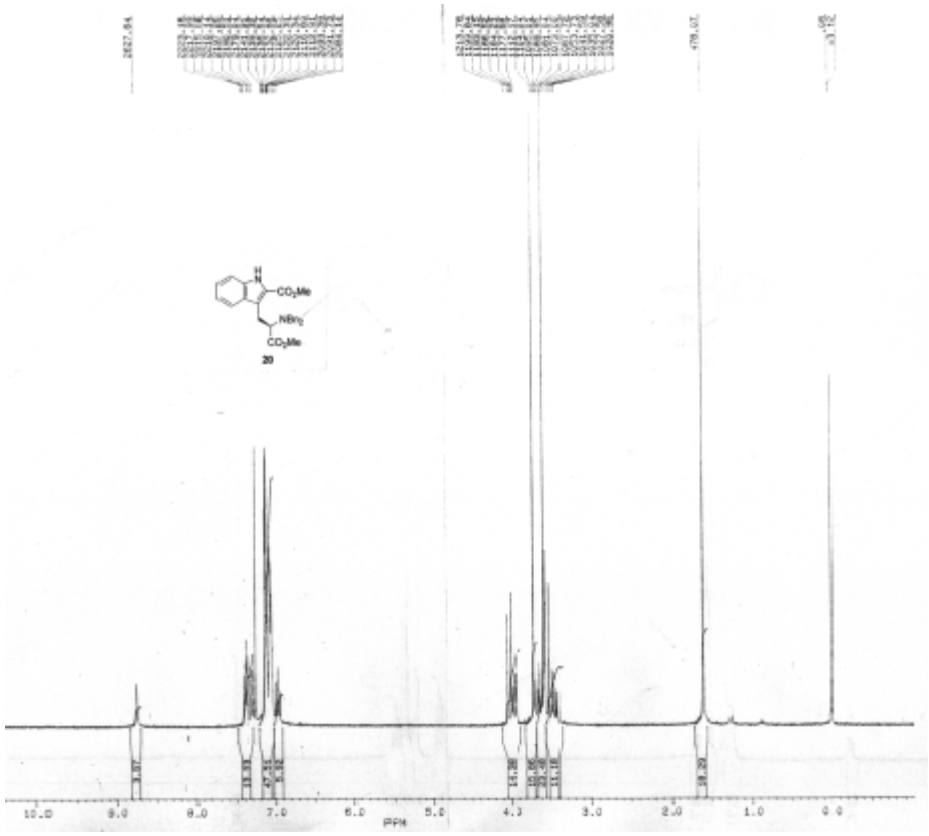
2.37
2.21
10
8
6
4
2
0
PPM

17



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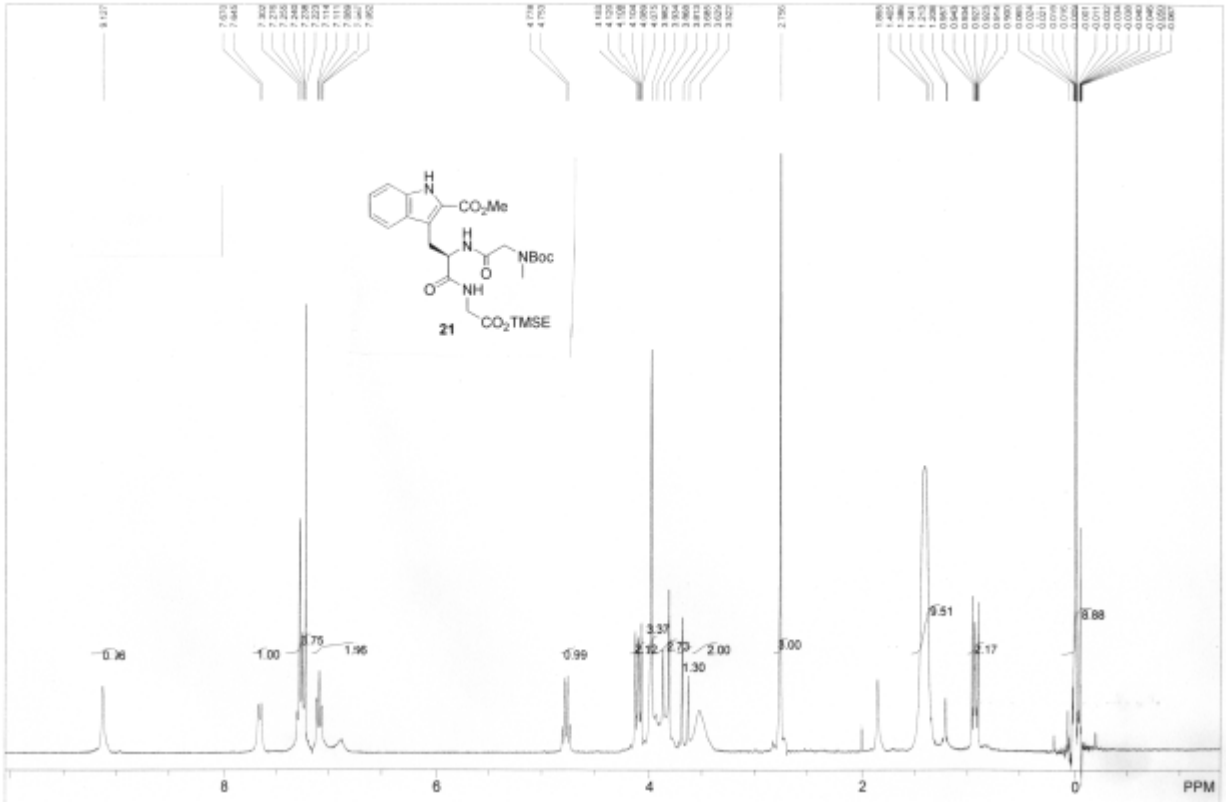

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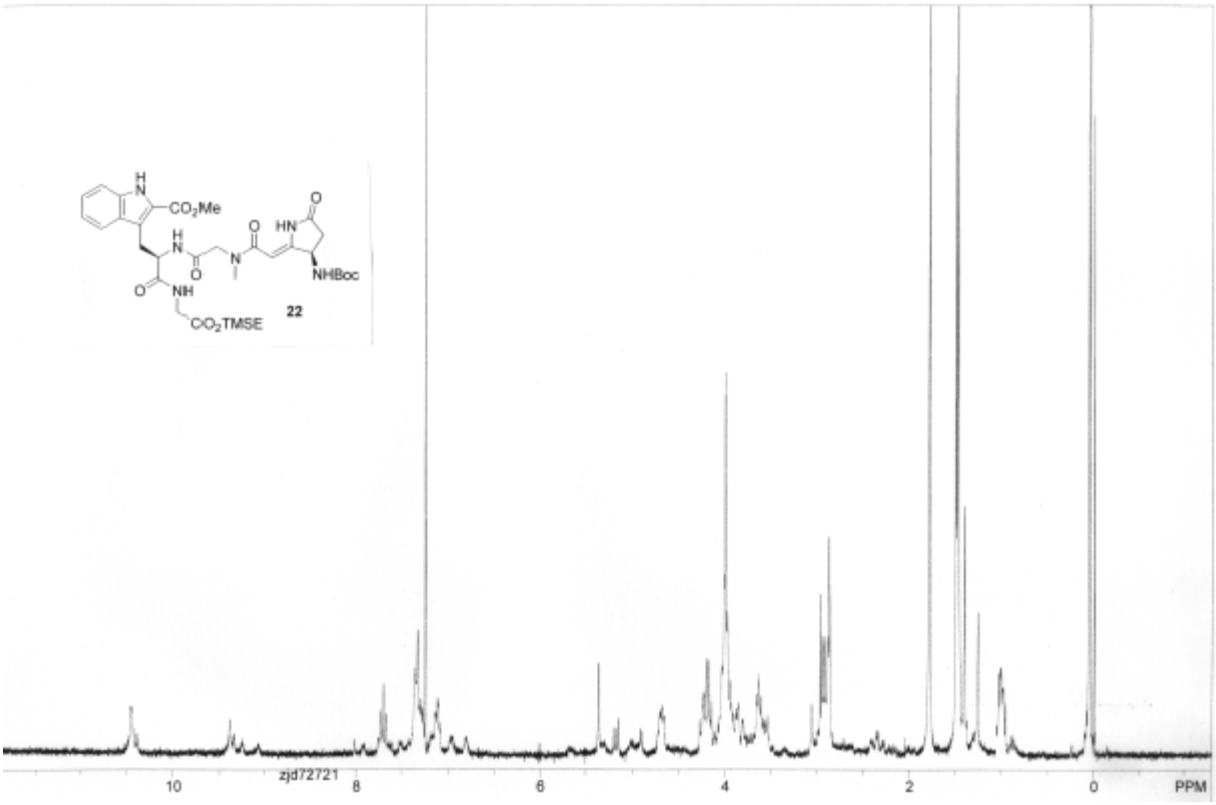
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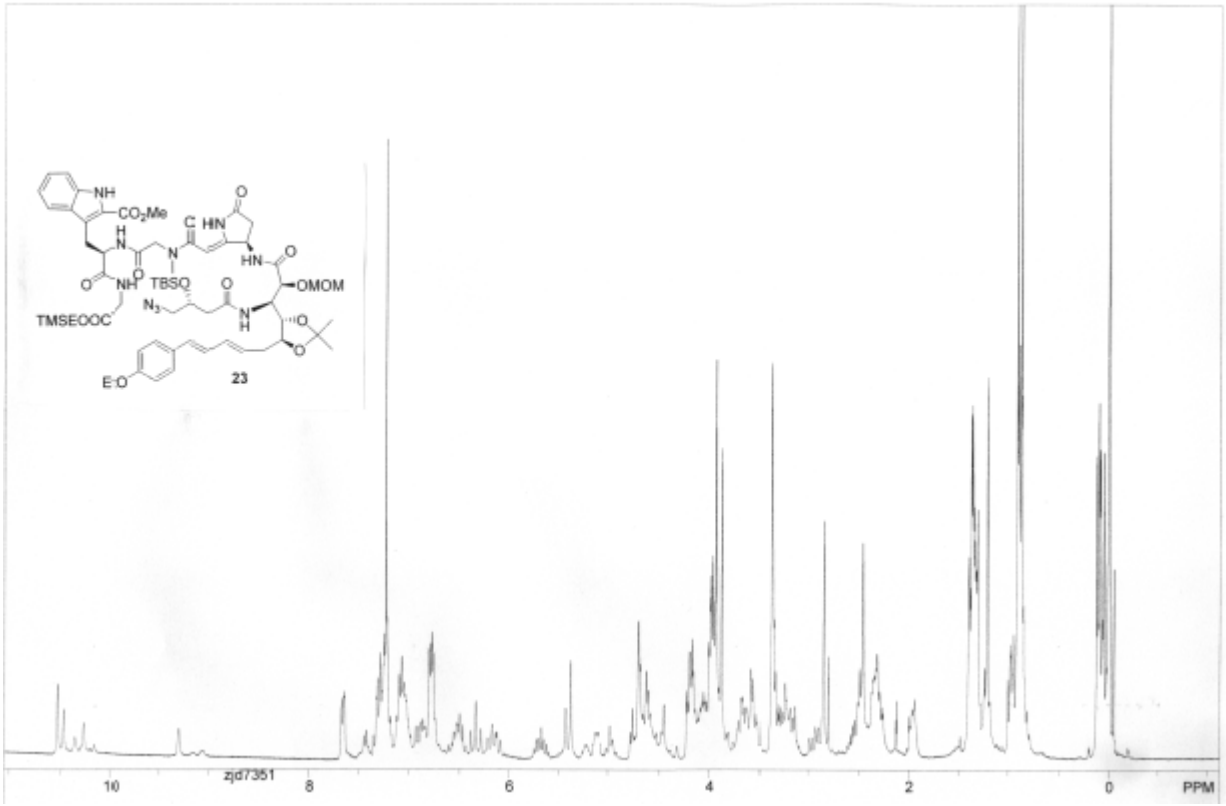
zjd72721
10
8
6
4
2
0
PPM

22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TBSO
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TMSEOOC
23
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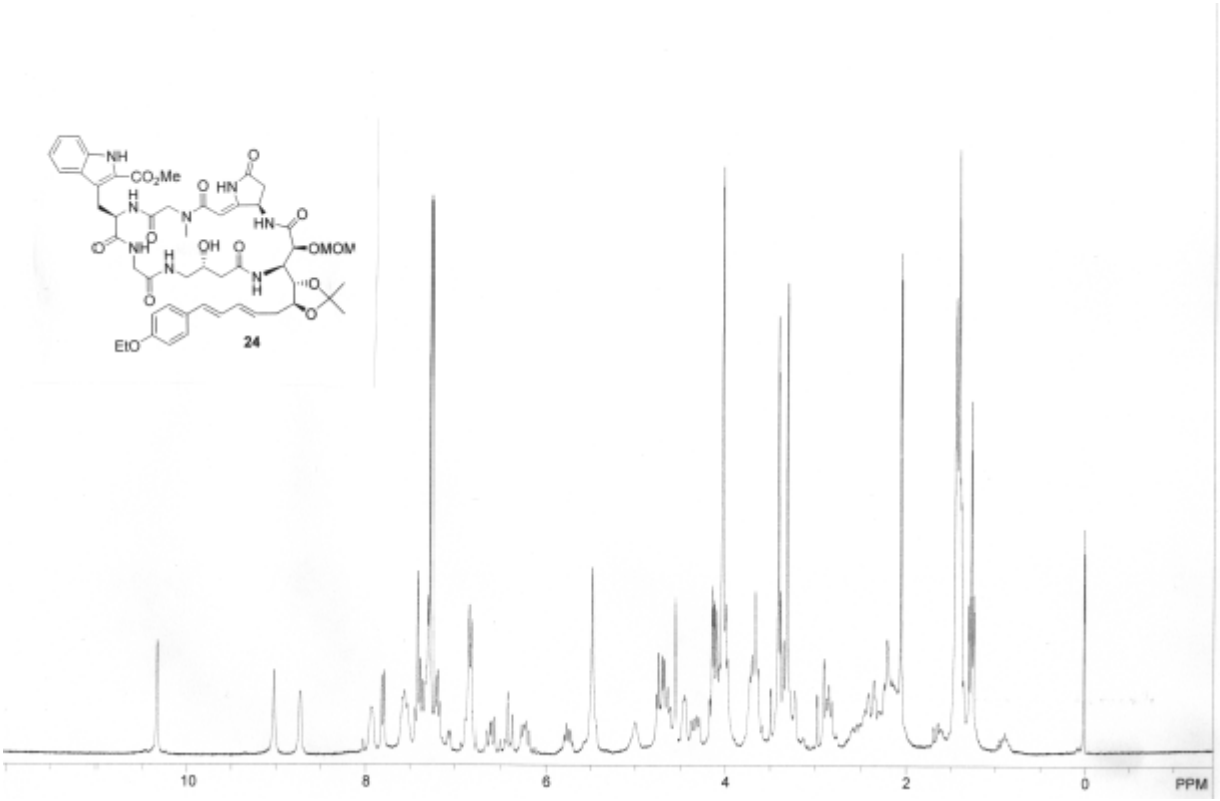
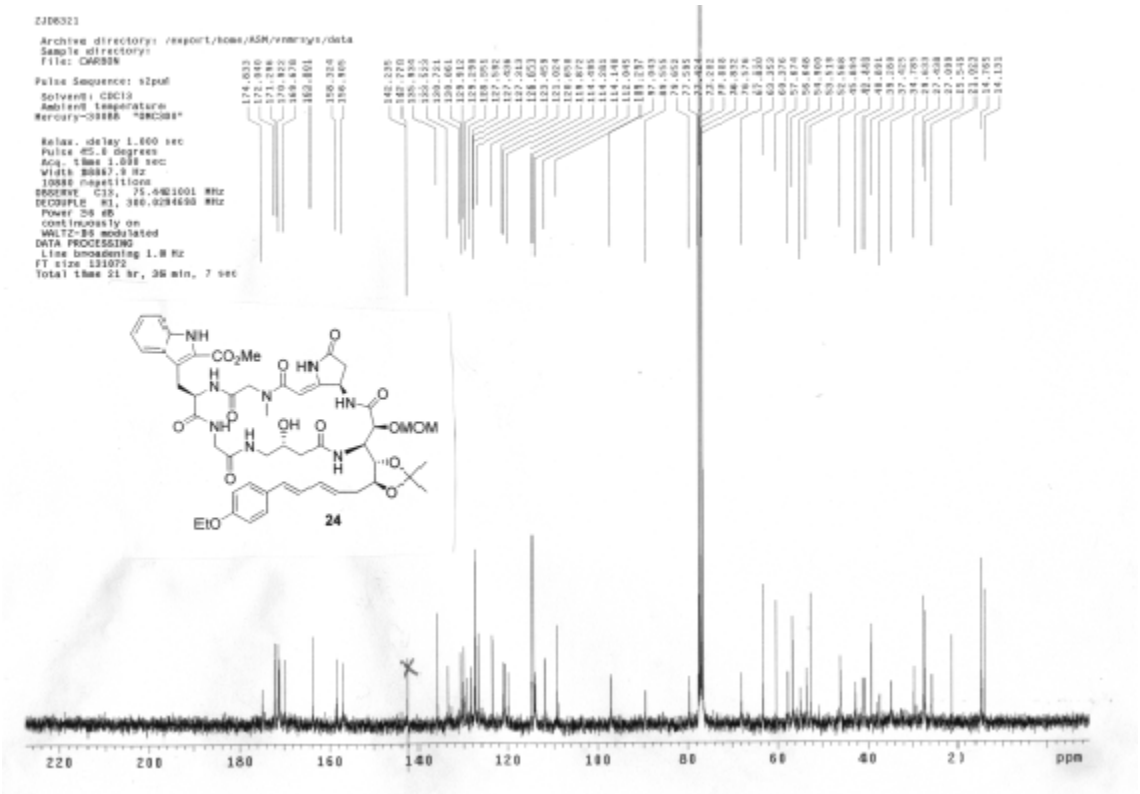
10
8
6
4
2
0
PPM

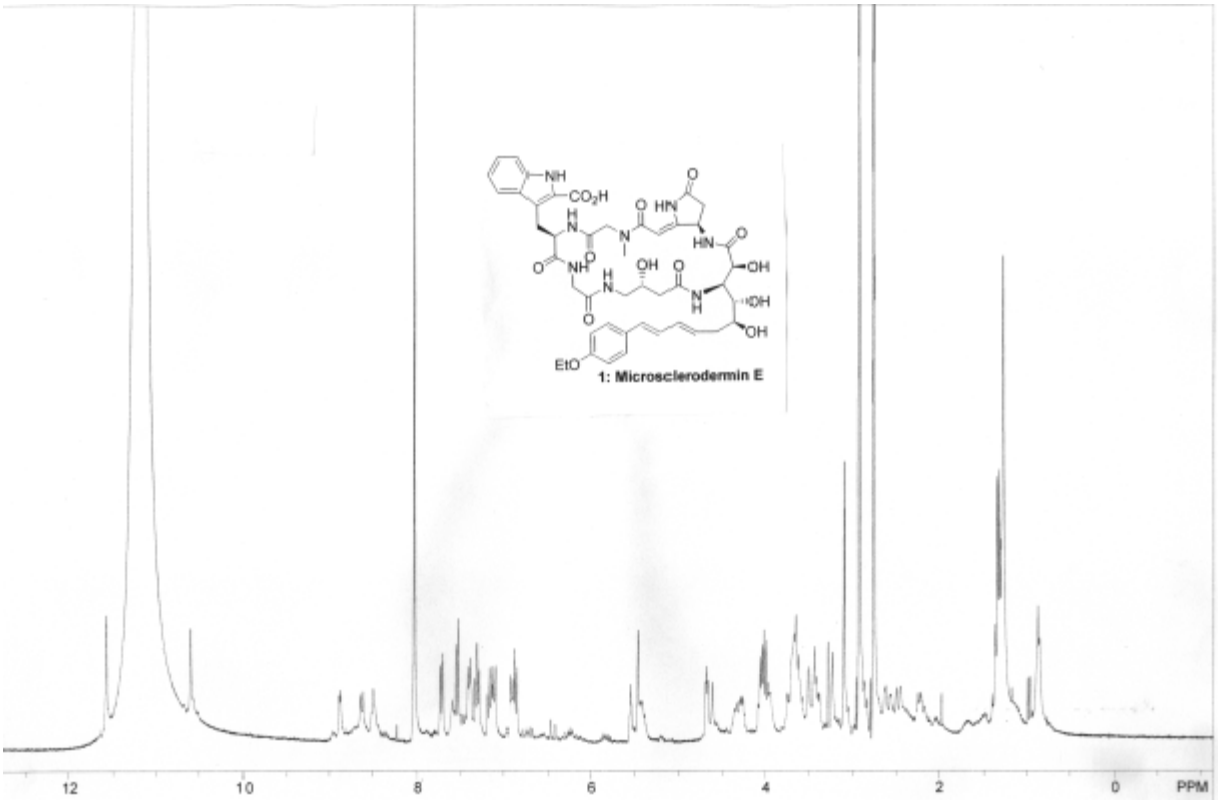
23


NH
CO2Me
O HN
HN
OMOM
OH
EtO
24
10
8
6
4
2
0
PPM

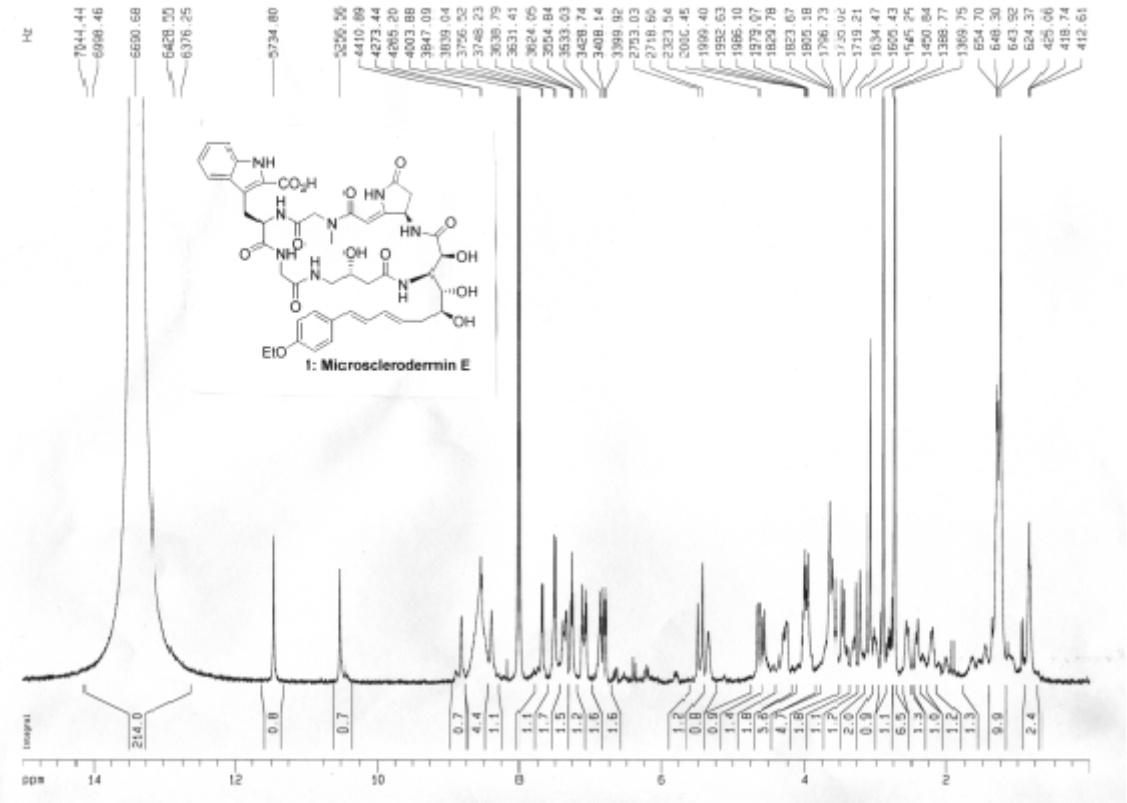
24-H


NH
CO2Me
O HN
HN
OMOM
OH
EtO
24
220
200
180
160
140
120
100
80
60
40
20
ppm

24-C


1: Microsclerodermin E
12
10
8
6
4
2
0
PPM

1-300M


1: Microsclerodermin E
ppm
14
12
10
8
6
4
2

1-500M