Total Synthesis of (+)-Cylindramide A

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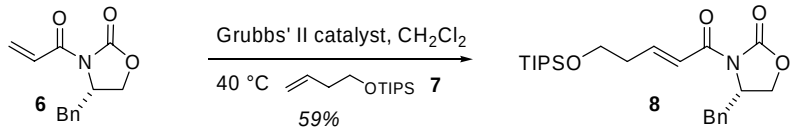
SUPPORTING INFORMATION

General Experimental Procedures.
^{1}H and ^{13}C NMR spectra were recorded at 25 ^{o}C on a Varian Inova spectrometer at 500 and 125 MHz, respectively, using $CDCl_3$ as the solvent and internal reference. Inverse detect spectra were obtained with a Varian 3mm PFG indirect detect probe with *jnxh*=8.3Hz and $^1J_{CH}$ = 130Hz . Coupling constants are reported in hertz, Hz. All non-aqueous reactions were run in flame-dried glassware under a dry N_2 atmosphere. Toluene, THF, CH_2Cl_2, and Et_2O were obtained from Aldrich (Pure-Pac) and further dried by passage through activated alumina as described by Bergman and Grubbs.[1] All flash chromatography was performed with normal phase silica gel (Sorbent Technologies, 32-63 um particle size, 60 A pore size), following the general protocol of Still.[2]

4-Benzyl-3-(5-triisopropylsilanyloxy-pent-2-enoyl)-oxazolidin-2-one, 8



The acryloyl oxazolidinone **6**[3] (37 mg, 0.160 mmol) and triisopropylsilyl 3-buten-1-ol **7** (47 mg, 0.208 mmol) were dissolved in CH_2Cl_2 (0.8 mL) in a flame-dried flask under $N_{2(g)}$. Grubbs' 2nd generation catalyst (7.0 mg, 0.008 mmol) was added in one portion, and the reaction was heated at 40 °C for 20 h. An additional 3% catalyst was added, and the reaction temperature was maintained at 40 °C for an additional 4h. The completed reaction was cooled to rt and the solvent removed *in vacuo*. The residue was purified by flash column chromatography (10% EtOAc/Hex) to provide **8** (41 mg, 59%) as an oil.

$[\alpha]_D$ +21.6 (*c* 0.765, $CHCl_3$); **IR** (thin film): 2937.34, 2867.08, 1775.43, 1683.56, 1640.33, 1353.91, 1197.18, 1110.72 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.30 (m, 7H), 4.72 (ddt, 1H, *J* = 12.0, 9.5, 4.0 Hz), 4.17 (m, 2H), 3.83 (t, 2H, *J* = 8.5 Hz), 3.31 (dd, 1H, *J* = 17.0, 4.0 Hz), 2.77 (dd, 1H, *J* = 16.5, 11.5), 2.53 (q, 2H, *J* = 8.0 Hz), 1.05 (s, 18H), 1.04 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 164.79, 153.35, 148.61, 135.30, 129.41, 128.87, 127.23, 121.69, 66.01, 61.88, 55.20, 37.76, 36.37, 17.94, 11.87; **MS** (EI): *m/z* 432.2 (M^++H), 430.2 (M^+-H), 388.2 (M^+-^{i}Pr); **HRMS** (EI): calculated for $C_{24}H_{36}NO_4Si$ (M^+-H) 430.2414, found 430.2411

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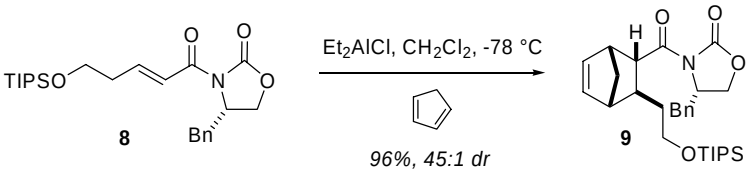
[1] a) Alaimo, P. J.; Peters, D.W.; Arnold, J.; Bergman, R.G. *J. Chem. Educ.* **2001** *78* 64. b) Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R.K.; Timmers, F. J. *Organometallics* **1996,** *15*, 151.
[2] Still, W.C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.
[3] Evans, D. A.; Chapman, K. T.; Bisaha, J. *J. Am. Chem. Soc.***1988**,*110*, 1238.

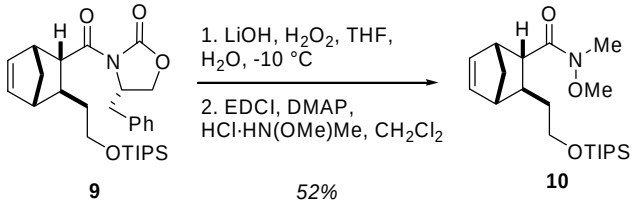
4-Benzyl-3-[3-(2-triisopropylsilanyloxy-ethyl)-bicyclo[2.2.1]hept-5-ene-2-carbonyl]-oxazolidin-2-one, 9



4-Benzyl-3-(5-triisopropylsilanyloxy-pent-2-enoyl)-oxazolidin-2-one **8** (17.2 g, 39.8 mmol) was dissolved in CH_2Cl_2 (250 mL) in a flame-dried round bottom flask under $N_{2(g)}$. The solution was cooled to -78 °C. Freshly distilled cyclopentadiene (32.8 mL, 398.5 mmol) was added. Lastly, Et_2AlCl (7.0 mL, 55.7 mmol) was slowly added over 10 min. The reaction was stirred at -78 °C for 12 h. The reaction was cautiously quenched at -78 °C with 1M HCl. After warming to room temperature, the mixture was extracted with CH_2Cl_2 (100 mL x 2). The combined organic layers were washed successively with H_2O (100 mL), saturated aqueous $NaHCO_3$ (100 mL), and saturated aqueous NaCl (100 mL). The combined organic layers were dried over Na_2SO_4, vacuum filtered through a plug of silica gel, and concentrated *in vacuo* to provide **9** (19.3 g, 96%, 45:1 dr) as an oil which needed no further purification.

$[\alpha]_D$ +62.7 (*c* 0.130, $CHCl_3$); **IR** (thin film): 3055.28, 2937.16, 2860.95, 1782.59, 1694.95, 1454.89, 1378.68, 1195.78, 1108.14 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.24 (m, 5H), 6.38 (dd, 1H, *J* = 5.5, 3.0 Hz), 5.83 (dd, 1H, *J* = 5.5, 2.5 Hz), 4.61 (m, 1H), 4.13 (d, 2H, *J* = 6.0 Hz), 3.70 (m, 2H), 3.66 (t, 1H, *J* = 4.0 Hz), 3.35 (s, 1H), 3.20 (dd, 1H, *J* = 13.0, 3.0 Hz), 2.72 (s, 1H), 2.65 (dd, 1H, *J* = 13.0, 10.0 Hz), 2.13 (m, 1H), 1.70 (q, 2H, *J* = 6.5 Hz), 1.68 (d, 1H, *J* = 10.0 Hz), 1.48 (dd, 1H, *J* = 8.5, 1.5 Hz), 1.02 (s, 21H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 173.90, 153.32, 139.57, 135.35, 131.01, 129.45, 129.37, 127.29, 66.04, 62.81, 50.32, 47.95, 47.61, 47.22, 39.47, 38.61, 38.10, 26.33, 18.01, 11.95; **MS** (EI): *m/z* 454.2 (M^+-^{i}Pr), 388.2 (M^+-C_5H_6); **HRMS** (EI): calculated for $C_{26}H_{36}NO_4Si$ (M^+-^{i}Pr) 454.2414, found 454.2417

3-(2-Triisopropylsilanyloxy-ethyl)-bicyclo[2.2.1]hept-5-ene-2-carboxylic acid methoxy-methyl-amide, 10



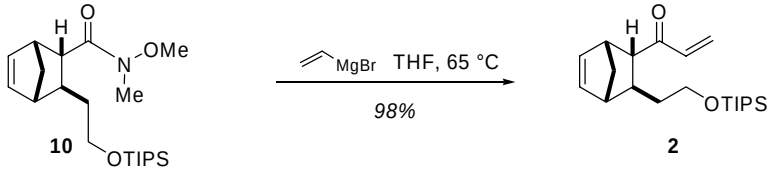
4-Benzyl-3-[3-(2-triisopropylsilanyloxy-ethyl)-bicyclo[2.2.1]hept-5-ene-2-carbonyl]-oxazolidin-2-one **9** (11.6 g, 19.5 mmol) was dissolved in a mixture of THF (300 mL) and H_2O (100 mL) and cooled to -10 °C. H_2O_2 (7.4 mL, 30% solution, 78.0 mmol) was added. LiOH (885 mg, 39.0 mmol) was slowly added so that the internal temperture did not exceed 0 °C, and the reaction was stirred at -10 °C for 2 hs. The reaction was slowly quenched at -10 °C with Na_2SO_3 (11 g in 60 mL H_2O, 4 eq), followed by addition of 150 mL saturated aqueous $NaHCO_3$ and allowed to warm to room temperature. After acidifying to pH 3 with 3 M HCl, the mixture was extracted with EtOAc (100 mL x 4). The combined

organic layers were dried over Mg_2SO_4, filtered, and concentrated *in vacuo*. The solution was triturated with Et_2O (80 mL) and filtered to remove the oxazolidinone. After concentration of the organics *in vacuo*, the carboxylic acid was isolated as an oil. The carboxylic acid was immediately used in the next reaction without any further purification.

The crude 3-(2-triisopropylsilanyloxy-ethyl)-bicyclo[2.2.1]hept-5-ene-2-carboxylic acid (19.5 mmol) was dissolved in CH_2Cl_2 (70 m) in a flame-dried round bottom flask under $N_{2(g)}$. DMAP (238 mg, 1.95 mmol) and *N*-methoxy-*N*-methylamine hydrochloride (2.85 g, 29.3 mmol) were added. Lastly, EDCI (5.6 g, 29.3 mmol) was added and the reaction was stirred for 10 h. The reaction was quenched with saturated aqueous NH_4Cl (40 mL) and extracted with CH_2Cl_2 (2 x 40 mL). The combined organic layers were washed with saturated aqueous NaCl (60 mL), dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The oil was purified by flash column chromatography (10-25% EtOAc/Hex) to yield **10** (4.70 g, 52% over 2 steps).

$[\alpha]_D$ +54.4 (*c* 0.210, $CHCl_3$); **IR** (thin film): 2962.66, 2935.96, 2867.32, 1669.85, 1463.91, 1380.01, 1109.25 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$): δ 6.25 (dd, 1H, *J* = 5.5, 3.0 Hz), 5.88 (dd, 1H, *J* = 6.0, 3.0 Hz), 3.69 (s, 3H), 3.66 (m, 2H), 3.13 (s, 3H), 3.08 (s, 1H), 2.74 (m, 1H), 2.66 (d, 1H, *J* = 1.5 Hz), 1.87 (dq, 1H, *J* = 6.0, 1.5 Hz), 1.75 (m, 1H), 1.69 (m, 1H), 1.57 (d, 1H, *J* = 8.5 Hz), 1.42 (dd, 1H, *J* = 8.5, 1.5 Hz), 1.03 (s, 18H), 1.02 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 175.26, 137.97, 132.26, 62.85, 61.28, 48.24, 47.29, 46.28, 39.52, 39.09, 32.54, 18.02, 11.94; **MS** (LSIMS): *m/z* 382.3 (M^++H), 350.62 (M^+-CH_3), 338.2 (M^+-CH_3), 321.2 (M^+-$N(OCH_3)CH_3$), 272.1 (M^+-C_5H_6-^{i}Pr); **HRMS** (LSIMS): calculated for $C_{21}H_{39}NO_3Si$ (M^+) 381.2699, found 381.2700

1-[3-(2-Triisopropylsilanyloxy-ethyl)-bicyclo[2.2.1]hept-5-en-2-yl]-propenone, 2

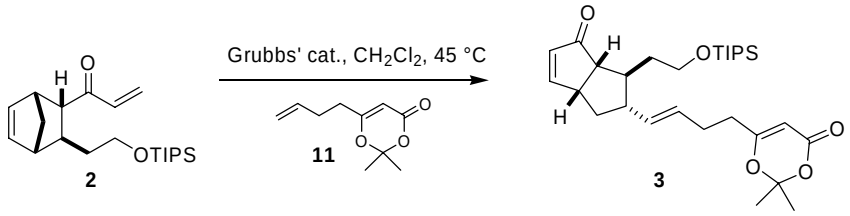


3-(2-Triisopropylsilanyloxy-ethyl)-bicyclo[2.2.1]hept-5-ene-2-carboxylic acid methoxy-methyl-amide **10** (616 mg, 1.61 mmol) was dissolved in THF (16 mL) in a round bottom flask under $N_{2(g)}$. The solution was heated to reflux, and vinyl magnesium bromide (4.0 mL, 1.0 M in THF, 4.03 mmol) was added. The reaction was heated to reflux for 15 min, then cooled to room temperature. The reaction was diluted with Et_2O (10 mL) and quenched with saturated aqueous NH_4Cl (10 mL). The mixture was extracted with Et_2O (2 x 10 mL) and washed with saturated aqueous NaCl (10 mL). The combined organic layers were dried over $MgSO_4$ and vacuum filtered through a plug of silica gel. The solution was concentrated *in vacuo* to yield **2** (557 mg, 99%) as an oil which could be used without further purification.

$[\alpha]_D$ +48.2 (*c* 0.175, $CHCl_3$); **IR** (thin film): 2956.45, 2941.64, 2871.32, 1698.00, 1457.41, 1098.39 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ6.46 (dd, 1H, *J* = 17.5, 10.5 Hz), 6.22 (d, 1H, *J* = 17.5 Hz), 6.21 (m, 1H), 5.80 (dd, 1H, *J* = 5.5, 2.5 Hz), 5.67 (d, 1H, *J* = 10.5 Hz), 3.68 (m, 1H), 3.13 (s, 1H), 2.81 (t, 1H, *J* = 4.0 Hz), 2.66 (s, 1H), 1.95 (q, 1H, *J* = 4.5 Hz), 1.72 (nonet, 2H, *J* = 4.5 Hz), 1.60 (d, 1H, *J* = 8.5 Hz), 1.45 (d, 1H, *J* = 8.5 Hz), 1.02 (s, 18H), 1.01 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 200.16, 138.29, 135.40, 132.27, 127.35, 62.74, 57.64, 47.39, 46.87, 46.53, 39.11, 38.08, 18.02, 11.94; **MS** (FAB): *m/z*

349.2 (M^++H), 305.1 (M^+-^{i}Pr), 239.1 (M^+-C_5H_6-iPr); **HRMS** (FAB): calculated for $C_{21}H_{37}O_2Si$ (M^++H) 349.2563, found 349.2551

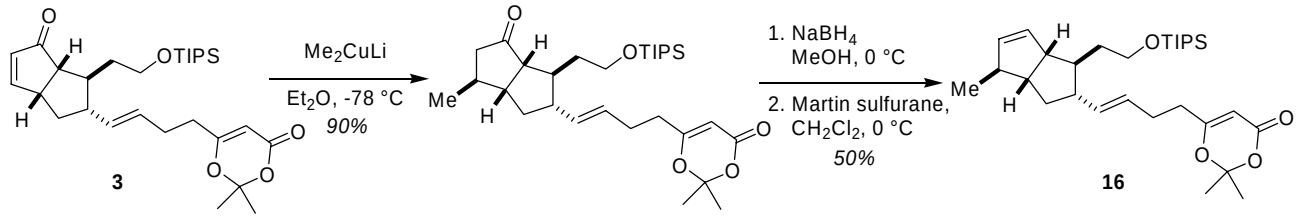
2,2-Dimethyl-6-{4-[4-oxo-3-(2-triisopropylsilanyloxy-ethyl)-1,2,3,3a,4,6a-hexahydro-pentalen-2-yl]-but-3-enyl}-[1,3]dioxin-4-one, 3



Enone **2** (34.6 mg, 0.0993 mmol) was dissolved in anhydrous CH_2Cl_2 (10 mL) in a flame-dried round bottom flask equipped with a condenser under $N_{2(g)}$. 6-But-3-enyl-2,2-dimethyl-[1,3]dioxin-4-one **11** (54.0 mg, 0.298 mmol) was added followed by Grubbs' catalyst (3.3 mg, 0.004 mol dissolved in 100 μL CH_2Cl_2). The reaction was heated at 45 °C for 6 h. After cooling to rt, the solvent was removed *in vacuo*. The crude oil contained a 2:1 mixture of diastereisomers **163** (57.3 mg, 59%) which were separated by FCC (20-40% Et_2O/Pet. Et_2O) to give pure (*E*)-**3**.

$[\alpha]_D$ -29.9 (*c* 0.5800, $CHCl_3$); **IR** (thin film): 2937.09, 2864.97, 1733.18, 1699.89, 1633.32, 1461.33, 1383.66, 1272.70, 1211.67, 1089.62 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.56 (dd, 1H, *J* = 5.5, 2.5 Hz), 5.90 (dd, 1H, *J* = 5.5, 1.5 Hz), 5.38 (dt, 1H, *J* = 15.5, 6.5 Hz), 5.26 (dd, 1H, *J* = 15.5, 8.0 Hz), 5.19 (s, 1H), 3.92 (td, 1H, *J*= 9.5, 5.5 Hz), 3.75 (ddd, 1H, *J* = 10.0, 9.0, 6.0 Hz), 3.36 (m, 1H), 2.50 (t, 1H, *J* = 7.5 Hz), 2.40 (m, 1H), 2.17 – 2.31 (m, 4H), 2.06 (ddd, 1H, *J* = 14.5, 8.5, 6.5 Hz), 1.84 (m, 1H), 1.65 (s, 3H), 1.64 (s, 3H), 1.40 – 1.60 (m, 2 H), 1.09 (m, 1H), 1.04 (s, 18H), 1.03 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 211.34, 171.09, 166.07, 161.27, 134.01, 131.49, 128.36, 106.33, 93.43, 62.17, 56.18, 53.79, 46.80, 43.65, 37.32, 37.11, 33.45, 29.68, 28.55, 25.04, 18.03, 11.95; **MS** (ESI): *m/z* 525 (M^++Na), 467 (M^++Na-C_3H_6O); **HRMS** (ESI): *m/z* calculated for $C_{29}H_{46}O_5SiNa$ (M^++Na) 525.3007, found 525.3033.

2,2-Dimethyl-6-{4-[4-methyl-1-(2-triisopropylsilanyloxy-ethyl)-1,2,3,3a,4,6a-hexahydro-pentalen-2-yl]-but-3-enyl}-[1,3]dioxin-4-one, 16:



Dioxenone **3** (66 mg, 0.131 mmol) was dissolved in anhydrous Et_2O (2 mL) and cooled to -78 °C in a flame-dried round bottom flask under $N_{2(g)}$. Freshly prepared Me_2CuLi (1 mL, 0.262 mmol, 0.26 M Et_2O) was added. After 10 min, the cold reaction was poured directly into a separatory funnel containing saturated aqueous NH_4Cl and EtOAc (20 mL). The reaction was extracted with EtOAc (2 x 5 mL) and the combined organic layers were washed with saturated aqueous NaCl, dried over $MgSO_4$, and

vacuum filtered through a short pad of silica gel. The solvent was removed *in vacuo* to provide **16** (61 mg, 90%).

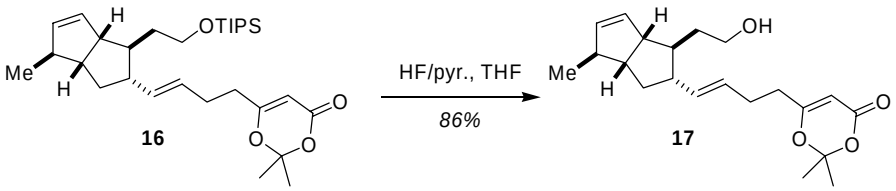
$[\alpha]_D$: -41.5 (*c* 1.6800, $CHCl_3$); **IR** (thin film): 2935.45, 2861.06, 1739.58, 1630.86, 1470.65, 1390.54, 1367.65, 1270.38, 1207.44, 1098.73 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 5.33 (m, 2H), 5.19 (s, 1H), 3.79 (ddd, 1H, *J* = 10.4, 8.8, 5.6 Hz), 3.69 (ddd, 1H, *J* = 10.0, 8.4, 6.4 Hz), 2.52 (dd, 1H, *J* = 18.0, 7.6 Hz), 2.37 (m, 2H), 2.10 – 2.30 (m, 5H), 2.03 (m, 2H), 1.87 (dd, 1H, *J* = 18.0, 4.8 Hz), 1.76 (m, 1H), 1.64 (s, 6H), 1.59 (m, 2H), 1.14 (dd, 1H, *J* = 11.2, 8.8 Hz), 1.03 (m, 25H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 220.99, 171.16, 161.27, 134.52, 127.89, 106.31, 93.38, 62.06, 57.05, 51.83, 48.81, 45.53, 44.88, 39.47, 37.48, 33.73, 33.53, 28.59, 25.04, 25.02, 21.61, 18.00, 11.92; **MS**(ESI): *m/z* 541 (M^++Na), 483 (M^++Na-C_3H_6O); **HRMS** (ESI): *m/z* calculated for $C_{30}H_{50}O_5SiNa$ (M^++Na) 541.3320, found 541.3310.

The intermediate ketone (256 mg, 0.493 mmol) was stirred in wet MeOH (5 mL) and cooled to -10 °C. $NaBH_4$ (28 mg, 0.739 mmol) was added in one portion and the reaction continued for 10 min. The cold reaction was poured into a separatory funnel containg saturated aqueous NH_4Cl and Et_2O (20 mL). After extracting with Et_2O (3 x 10 mL), the combined organic layers were washed with saturated aqueous NaCl (15 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo*. The crude oil was used without further purification.

The crude mixture of diastereoisomeric alcohols obtained above was stirred in 4 mL dry CH_2Cl_2 at 0 °C in a flame-dried round bottom flask under $N_{2(g)}$. Martin sulfurane was added and the reaction allowed to warm to rt over 8 h. The reaction was quenched with saturated aqueous NH_4Cl (10 mL) and extracted with EtOAc (3 x 10 mL). The combined organic layers were washed with saturated aqueous NaCl (20 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo*. The crude oil was purified by FCC (5% EtOAc/Hex to remove the Martin sulfurane byproducts and 10-20% Et_2O/Hex to isolate the desired material) to yield **16** (124 mg, 50%).

$[\alpha]_D$ +56.9 (*c* 0.4850, $CHCl_3$); **IR** (thin film): 2948.77, 2858.40, 1740.12, 1627.17, 1463.38, 1389.96, 1378.66, 1271.35, 1209.22, 1101.91 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 5.53 (dt, 1H, *J* = 5.6, 1.6 Hz), 5.43 (dt, 1H, *J* = 5.6, 2.0 Hz), 5.33 (m, 1H), 5.26 (dd, 1H, *J* = 15.2, 7.2 Hz), 5.18 (s, 1H), 3.74 (ddd, 1H, *J* = 9.6, 8.4, 5.2 Hz), 3.67 (dt, 1H, *J* = 9.2, 7.6 Hz), 2.78 (m, 1H), 2.36 (m, 1H), 2.06 – 2.26 (m, 5H), 1.92 (m, 2H), 1.76 (m, 1H), 1.63 (s, 6H), 1.36 (m, 1H), 1.22 (m, 1H), 1.06 (m, 1H), 1.02 (s, 18H), 1.01 (s, 3H), 0.95 (d, 3H, *J* = 6.8 Hz); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 171.31, 161.28, 135.34, 134.11, 133.45, 127.15, 106.25, 93.32, 62.55, 56.58, 50.79, 49.31, 48.00, 46.41, 40.74, 37.52, 33.63, 28.64, 25.04, 24.97, 21.72, 17.99, 11.92; **HRMS** (ESI): *m/z* calculated for $C_{30}H_{50}O_4SiNa$ (M^++Na) 525.3376, found 525.3764.

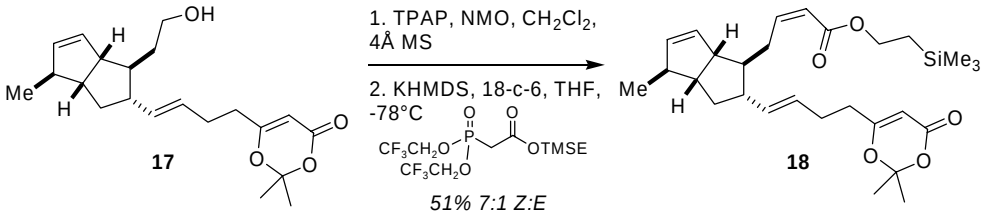
6-{4-[1-(2-Hydroxy-ethyl)-4-methyl-1,2,3,3a,4,6a-hexahydro-pentalen-2-yl]-but-3-enyl}-2,2-dimethyl-[1,3]dioxin-4-one, 17



Dioxenone **16** (137 mg, 0.273 mmol) was stirred in dry THF (2.7 mL) in a round bottom flask under $N_{2(g)}$. HF/pyr. (0.1 mL, 0.681 mmol) was added and the reaction stirred at rt for 2.5 h at which time, additionol HF/pyr. 0.1 mL) was added. After stirring 90 min, the reaction was diluted with EtOAc (5 mL) and slowly quenched with saturated aqueous $NaHCO_3$. Extraction with EtOAc (3 x 5 mL) was followed by washing of the combined organic layers with saturated aqueous NaCl (10 mL). Subsequent drying of the organic layer over $MgSO_4$. filtering and removing the solvents *in vacuo* provided an oil which could be purified by FCC (25-50% EtOAc/Hex) to provide **17** (81 mg, 86%) as an oil.

$[\alpha]_D$ +76.0 (*c* 0.2100, $CHCl_3$); **IR** (thin film): 3448.20, 3044.56, 2947.92, 2919.49, 2862.64, 1725.64, 1634.68, 1384.54, 1276.52, 1208.30 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 5.54 (dt, 1H, *J* = 5.6, 1.6 Hz), 5.47 (dt, 1H, *J* = 5.6, 2.0 Hz), 5.30 (m, 2H), 5.21 (s, 1H), 3.72 (ddd, 1H, *J* = 10.4, 8.8, 5.2 Hz), 3.61 (dt, 1H, *J* = 10.4, 7.2 Hz), 2.78 (m, 1H), 2.39 (m, 1H), 2.20 – 2.30 (m, 5H), 2.13 (m, 1H), 1.97 (m, 2H), 1.88 (br s, 1H), 1.75 (dddd, 1H, *J* = 12.8, 8.8, 7.2, 4.0 Hz), 1.66 (s, 6H), 1.39 (m, 1H), 1.19 (m, 1H), 1.07 (m, 1H), 0.97 (d, 3H, *J* = 7.2 Hz); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 171.31, 161.61, 135.65, 134.52, 133.11, 127.37, 106.35, 93.70, 61.89, 56.67, 49.36, 48.06, 46.46, 40.75, 37.36, 33.44, 28.51, 25.17, 24.89, 21.71; **MS** (ESI): *m/z* 370 (M^++H+Na), 369 (M^++Na); **HRMS** (ESI): *m/z* calculated for $C_{21}H_{30}O_4Na$ (M^++Na) 369.2036, found 369.2043.

4-{2-[4-(2,2-Dimethyl-6-oxo-6*H*-[1,3]dioxin-4-yl)-but-1-enyl]-4-methyl-1,2,3,3a,4,6a-hexahydro-pentalen-1-yl}-but-2-enoic acid 2-trimethylsilanyl-ethyl ester, 4

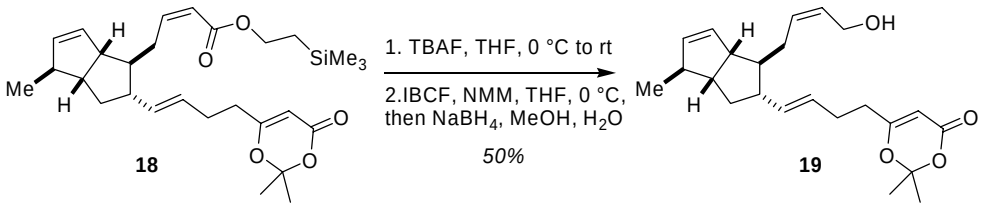


Alcohol **17** (92 mg, 0.264 mmol) was stirred in dry CH_2Cl_2 (2 mL) in a flame-dried round bottom flask under $N_{2(g)}$. Freshly dried and powdered 4 Å molecular sieves were added followed by NMO (96 mg, 0.820 mmol). After stirring for 10 min, TPAP (5 mg, 0.0132 mmol) was added. The black slurry was stirred for 20 min and diluted with CH_2Cl_2 (5 mL). The reaction was vacuum filtered through a short plug of silica gel with 30% Et_2/CH_2Cl_2. The solvent was removed *in vacuo* and the crude aldehyde used immediately in the ensuing olefination.

[Bis-(2,2,2-trifluoroethoxy)phosphoryl] acetic acid (2-trimethylsilyl)ethyl ester[4] (171 mg, 0.449 mmol) was stirred in anhydrous THF (2 mL) in a flame-dried round bottom flask under $N_{2(g)}$. Following the addition of 18-crown-6 (349 mg, 1.32 mmol), the mixture was cooled to -78 °C. KHMDS (0.49 mL, 0.449 mmol, 0.91 M THF) was slowly added and the yellow solution was stirred 15 min. The aldehyde synthesized above was slowly added in dry CH_2Cl_2 (0.6 mL). After stirring for 2 h at -78 °C, the reaction was poured into a separatory funnel containing saturated aqueous NH_4Cl/EtOAc (10 mL). The reaction was extracted with EtOAc (3 x 5 mL) and the combined organic layers were washed with saturated aqueous NaCl, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude oil was purified by FCC (10% EtOAc/Pet. Et_2O) to provide (*Z*)-**4** (67.0 mg, 51%) and (E)-**4** (8.4 mg).

$[\alpha]_D$ +176.2 (*c* 0.0250, $CHCl_3$); **IR** (thin film): 3034.57, 2953.15, 2924.07, 2865.91, 1731.83, 1720.19, 1632.96, 1394.51, 1365.43, 1173.51 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$): δ 6.20 (ddd, 1H, *J* = 9.2, 6.8, 5.2 Hz), 5.76 (d, 1H, *J* = 9.2 Hz), 5.51 (dt, 1H, *J* = 4.8, 1.6 Hz), 5.44 (dt, 1H, *J* = 4.4, 1.6 Hz), 5.35 (dt, 1H, *J* = 12.0, 4.8 Hz), 5.28 (dd, 1H, *J* = 12.0, 5.6 Hz), 5.20 (s, 1H), 4.17 (m, 2H), 2.62 – 2.86 (m, 3H), 2.37 (m, 1H), 2.18 – 2.28 (m, 4H), 2.12 (m, 1H), 2.01 (m, 2H), 1.64 (s, 3H), 1.63 (s, 3H), 1.27 (m, 1H), 1.07 (m, 1H), 0.95 (d, 3H, *J* = 5.6 Hz), 0.02 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 171.26, 166.66, 161.28, 149.28, 139.91, 134.49, 133.00, 127.75, 120.26, 106.29, 93.42, 61.94, 56.01, 51.35, 50.55, 49.15, 46.60, 40.58, 33.58, 32.81, 28.68, 25.09, 25.02, 21.70, 17.31, -1.50; **MS** (ESI): *m/z* 509 (M^++Na), 451 (M^++Na-C_3H_6O); **HRMS** (ESI): *m/z* calculated for $C_{28}H_{42}O_5SiNa$ (M^++Na) 509.2694, found 509.2701.

6-{4-[1-(4-Hydroxy-but-2-enyl)-4-methyl-1,2,3,3a,4,6a-hexahydro-pentalen-2-yl]-but-3-enyl}-2,2-dimethyl-[1,3]dioxin-4-one, 19



Ester **18** (57 mg, 0.1171 mmol) was stirred in dry THF (1.2 mL) in a flame-dried round bottom flask under $N_{2(g)}$ and cooled to 0 °C. TBAF (0.35 mL, 0.3513 mmol, 1.0 M THF) was added and the reaction was allowed to warm to rt over 4.5 h. The reaction was quenched with NH_4Cl and extracted with EtOAc (4 x 5 mL). The combined organic layers were washed with 1 M HCl (10 mL) and saturated aqueous NaCl (10 mL). After drying over $MgSO_4$ and filtering, the solvent was removed *in vacuo*. The carboxylic acid could be used without further purification.

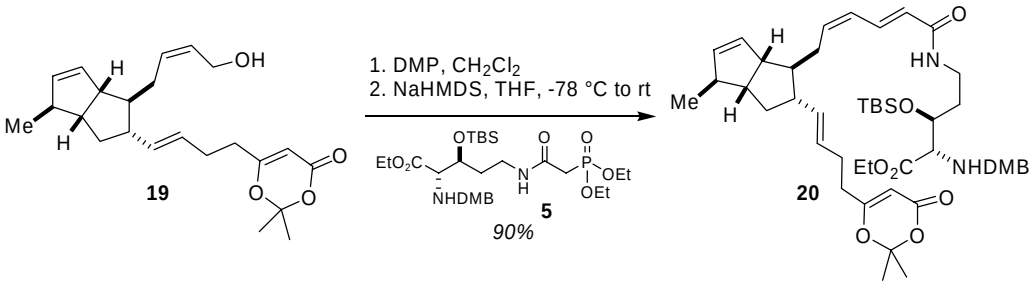
The carboxylic acid (24 mg, 0.0617 mmol) was dissolved in dry THF (0.5 mL) in a flame-dried round bottom flask under $N_{2(g)}$ and cooled to 0 °C. NMM (20 μL, 0.1851 mmol) was added followed by the addition of IBCF (16 μL, 0.1235 mmol). Salts immediately precipitated out, however the reaction was allowed to stir for 10 min [anhydride formation monitored by TLC (30% EtOAc/Pet. Et_2O)]. The salts were removed by filtration and washed twice with dry THF. The solution was recooled to 0 °C and $CeCl_3$ (23 mg, 0.0617 mmol) was added. The reaction was diluted with MeOH (0.3 mL) and H_2O (0.3 mL). $NaBH_4$ (7 mg, 0.1851 mmol) was added and the reaction stirred at 0 °C for 15 min. The reaction

[4] Boger, D. L.; Sakya, S. M.; Yohannes, D. *J. Org. Chem.*, **1991**, *56*, 4204.

was quenched with saturated aqueous NH_4Cl and exhaustively extracted with EtOAc. The combined organic layers were washed with saturated aqueous NaCl, dried over $MgSO_4$, filtered and concentrated *in vacuo*. FCC (25-50% EOAc/Pet. Et_2O) provided **19** (12 mg, 50% over 2 steps).

$[\alpha]_D$ +73.2 (*c* 0.2300, $CHCl_3$); **IR** (thin film): 3419.21, 2951.00, 2917.56, 2861.82, 1735.87, 1629.97, 1395.86, 1367.99, 1267.66, 1206.35 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$): δ 5.64 (m, 1H), 5.57 (m, 1H), 5.53 (dt, 1H, *J* = 4.4, 1.6 Hz), 5.45 (dt, 1H, *J* = 12.0, 4.8 Hz), 5.27 (dd, 1H, *J* = 12.0, 5.6 Hz), 5.21 (s, 1H), 4.17 (d, 2H, *J* = 5.2 Hz), 2.75 (m, 1H), 2.37 (m, 1H), 2.25 (m, 5H), 2.10 (m, 1H), 1.97 (m, 3H), 1.65 (s, 6H), 1.51 (br s, 1H), 1.19 (m, 1H), 1.06 (m, 1H), 0.96 (d, 3H, *J* = 5.6 Hz); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 171.29, 161.45, 135.24, 134.45, 133.13, 131.48, 129.10, 127.58, 106.39, 93.54, 58.62, 56.06, 51.53, 50.42, 49.16, 46.61, 40.66, 33.61, 31.12, 28.59, 25.11, 25.06, 21.74; **HRMS** (ESI): *m/z* calculated for $C_{23}H_{32}O_4Na$ (M^++Na) 395.2193, found 395.2207.

3-(*tert*-Butyl-dimethyl-silanyloxy)-2-(2,4-dimethoxy-benzylamino)-5-(6-{2-[4-(2,2-dimethyl-6-oxo-6*H*-[1,3]dioxin-4-yl)-but-1-enyl]-4-methyl-1,2,3,3a,4,6a-hexahydro-pentalen-1-yl}-hexa-2,4-dienoylamino)-pentanoic acid ethyl ester, 20



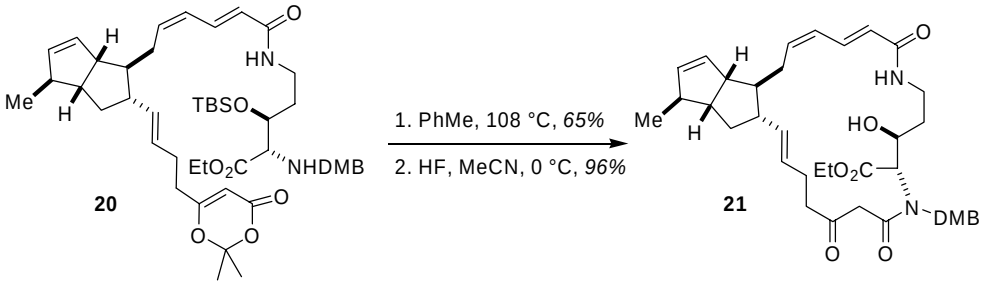
Allylic alcohol **19** (5 mg, 0.0134 mmol) was dissolved in CH_2Cl_2. Dess-Martin periodinane (6.8 mg, 0.0161 mmol) was added and the reaction stirred for 10 min. The reaction was quenched for with $Na_2S_2O_3$ doped $NaHCO_3$. Once two clear layers were evident, the mixture was extracted with EtOAc (3 x 5 mL) and washed with saturated aqueous NaCl (10 mL). The organics were dried over $MgSO_4$, filtered and concentrated *in vacuo*. The enal was used immediately without any additional purification.

The phosphonate **5** (10 mg, 0.0161 mmol) was dissolved in dry THF (0.25 mL) and cooled to -78 °C in a flame-dried round bottom flask under $N_{2(g)}$. NaHMDS (0.12 mL, 0.0168 mmol, 0.135 M THF) was slowly added and the bright yellow solution was stirred for 15 min. The enal was added slowly in THF (0.15 mL) and the reaction was stirred at -78 °C for 30 min. The dry ice was removed from the bath and the reaction warmed slowly for 30 min, followed by removing the bath for 15 min prior to quenching. The reaction was poured into half-saturated aqueous NH_4Cl (5 mL) and EtOAc (5 mL). The mixture was extracted with EtOAc (3 x 5mL) and the combined organic layers were dried over $MgSO_4$, filtered and concentrated *in vacuo* to provide pure **20** (10 mg, 90%).

$[\alpha]_D$ +70.0 (*c* 0.105, $CHCl_3$); **IR** (thin film): 3303.51, 2955.86, 2928.51, 2854.30, 1733.22, 1662.91, 1635.57, 1616.04, 1467.60, 1377.76, 1201.98 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.49 (dd, 1H, *J* = 15.0, 11.5 Hz), 7.44 (br s, 1H), 7.06 (d, 1H, *J* = 8.0 Hz), 6.41 (m, 2H), 6.02 (t, 1H, *J* = 11.5), 5.74 (m, 1H), 5.43 (m, 1H), 5.35 (dt, 1H, *J* = 15.5, 6.0 Hz), 5.27 (dd, 1H, *J* = 15.0, 7.5 Hz), 5.22 (s, 1H), 4.08 (q, 2H, *J* = 7.5 Hz), 3.94 (m, 1H), 3.78 (s, 3H), 3.77 (s, 3H), 3.68 (AB, 2H, J_{AB} = 12.5 Hz), 3.40 (m, 1H), 3.32 (m, 1H), 3.29 (d, 1H, *J* = 6.5 Hz), 2.76 (m, 1H), 2.37 (m, 2H), 2.18 – 2.30 (m, 6H), 2.11 (m, 1H),

1.99 (m, 4H), 1.85 (m, 1H), 1.77 (m, 1H), 1.65 (s, 6H), 1.06 (m, 1H), 0.95 (d, 3H, *J* = 7.0 Hz), 0.83 (s, 9H), 0.02 (s, 3H), -0.05 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 171.38, 165.96, 161.33, 160.46, 158.62, 137.91, 135.02, 134.83, 133.10, 130.76, 128.27, 127.24, 124.64, 106.26, 103.72, 98.50, 93.39, 72.32, 60.78, 55.88, 55.30, 55.19, 51.37, 50.50, 49.05, 47.66, 46.55, 40.60, 35.27, 33.92, 33.53, 31.98, 29.64, 28.65, 25.60, 25.00, 22.64, 21.67, 17.80, 14.14, -4.59, -5.21; **MS** (ESI): *m/z* 857 (M^++Na), 835 (M^++H), 799 (M^++Na-C_3H_6O); **HRMS** (ESI): *m/z* calculated for $C_{47}H_{70}N_2O_9SiNa$ (M^++Na) 857.4743, found 857.4774.

Macrocycle 21



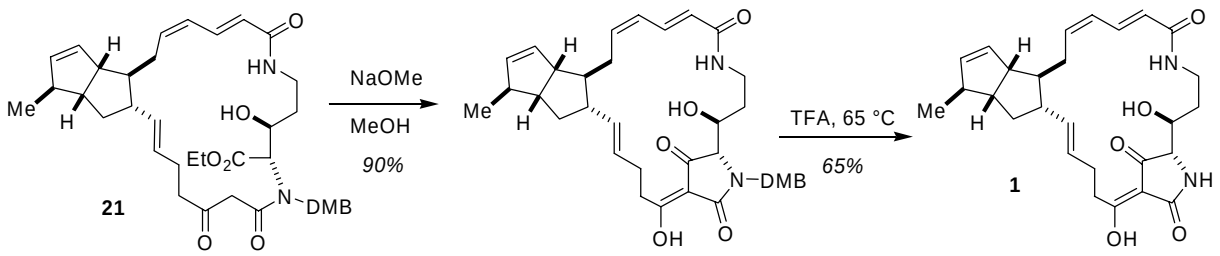
Amino-dioxenone **20** (8 mg, 0.0101 mmol) was dissolved in dry PhMe (1.0 mL) in a flame-dried round bottom flask equipped with a cold finger. The solution was heated to reflux for 2 h. After cooling to rt and concentration *in vacuo*, the oil was purified by FCC (50% EtOAc/Hex) to yield the macrocycle (5 mg, 65%).

The macrocycle (19 mg, 0.0243 mmol) was stirred in MeCN (0.5 mL) at 0 °C. 3 drops aqueous HF (~0.0365 mmol) was added and stirring continued at 0 °C for 7 h. The reaction was diluted with H_2O (5 mL) and EtOAc (5 mL) and transferred to a separatory funnel. The reaction was extracted with EtOAc (3 x 5 mL) and the combined organic layers were washed with saturated aqueous NaCl (2 x 10 mL), dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purification of the oil was accomplished with FCC (100% EtOAc) to yield **21** (16 mg, 90%).

$[\alpha]_D$ +122.5 (*c* 0.1550, $CHCl_3$); **IR** (thin film): 3370.11, 2954.22, 2923.42, 2857.95, 1733.79, 1725.58, 1717.38, 1655.82, 1635.30, 1617.52, 1456.26, 1294.53, 1275.28, 1209.81 cm^{-1}; **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.45 (dd, 1H, *J* = 15.2, 11.6 Hz), 7.15 (d, 1H, *J* = 7.6 Hz), 6.44 (m, 2H), 6.16 (t, 1H, *J* = 10.8 Hz), 5.88 (td, 1H, *J* = 10.8, 5.2 Hz), 5.79 (d, 1H, *J* = 15.2 Hz), 5.75 (t, 1H, *J* = 6.0 Hz), 5.62 (d, 1H, *J* = 5.6 Hz), 5.50 (d, 1H, *J* = 5.6 Hz), 5.17 (d, 2H, *J* = 4.0 Hz), 4.65 (d, 1H, *J* = 15.6 Hz), 4.50 (t, 1H, *J* = 8.8 Hz), 4.21 (d, 1H, *J* = 15.6 Hz), 4.03 (m, 2H), 3.94 (m, 1H), 3.86 (d, 1H, *J* = 14.4 Hz), 3.82 (s, 3H), 3.81 (s, 3H), 3.70 (m, 1H), 3.51 (d, 1H, *J* = 14.4 Hz), 3.44 (d, 1H, *J* = 8.4 Hz), 3.22 (m, 1H), 3.02 (m, 1H), 2.52 – 2.72 (m, 3H), 2.40 (m, 1H), 2.20 – 2.34 (m, 4H), 1.40 (m, 1H), 1.06 (m, 1H), 1.00 (d, 3H, *J* = 7.2 Hz); **^{13}C NMR**[5] ($CDCl_3$, 100 MHz): δ 204.42, 174.59, 167.77, 167.48, 161.54, 159.20, 159.16, 135.95, 134.92, 133.42, 132.76, 131.43, 130.06, 128.11, 124.25, 103.82, 98.80, 65.88, 63.89, 61.52, 55.63, 55.34, 53.93, 50.94, 50.57, 49.45, 48.82, 47.08, 43.38, 40.73, 36.00, 28.48, 32.14, 30.27, 27.40, 22.05, 14.16; **HRMS** (ESI): *m/z* calculated for $C_{38}H_{50}N_2O_8Na$ (M^++Na) 685.3459, found 685.3457.

[5] Due to small quantities of material, ^{13}C NMR data was extrapolated from HSQC and HMBC data.

Cylindramide A, 1



Freshly prepared NaOMe/MeOH (2.8 mL, 0.0706 mmol, 0.025 M) was added to the macrocycle **21** (16 mg, 0.0235 mmol) stirring in a flame-dried round bottom flask under $N_{2(g)}$. The reaction was vigourously stirred for 2 min and poured into a separatory funnel containing 1/1 pH 4 adjusted H_2O and EtOAc (10 mL). The mixture was extracted with EtOAc (3 x 5 mL) and concentrated *in vacuo* to provide DMB-protected tetramic acid (13.0 mg, 90%) as a white solid.

$[\alpha]_D$ +121.0 (*c* 0.1000, MeOH); **IR** (thin film): 3604.44, 3577.20, 2950.72, 2928.93, 2841.77, 1730.45, 1665.08, 1599.70, 1468.96, 1283.74 cm^{-1}; **^{1}H NMR** ($CDCl_3/CD_3OD$, 400 MHz): δ 7.34 (dd, 1H, *J* = 12.4, 12.4 Hz), 7.14 (d, 1H, *J* = 12.4 Hz), 6.41 (m, 2H), 6.14 (t, 1H, *J* = 10.8 Hz), 5.89 (td, 1H, *J* = 10.0, 5.6 Hz), 5.82 (d, 1H, *J* = 15.2 Hz), 5.60 (d, 1H, *J* = 5.6 Hz), 5.46 (d, 1H, *J* = 5.6 Hz),5.25 (m, 2H), 5.02 (d, 1H, *J* = 14.4 Hz), 4.31 (d, 1H, *J* = Hz), 3.99 (d, 1H, *J* = Hz), 3.78 (s, 1H), 3.75 (s, 3H), 3.74 (s, 3H), 3.53 (d, 1H, *J* =), 2.98 (m, 2H), 2.52 (m, 1H), 1.50 – 1.80 (m, 11H), 1.25 (m, 1H), 1.05 (m, 1H), 0.97 (d, 3H, *J* = 7.2 Hz); **^{13}C NMR**[6] ($CDCl_3/CD_3OD$, 100 MHz): δ 168.18, 160.74, 158.64, 136.63, 136.03, 135.33, 133.97, 132.74, 131.64, 130.26, 128.40, 123.86, 104.82, 98.83, 70.41, 69.94, 55.71, 54.28, 52.05, 49.68, 49.49, 47.50, 40.59, 40.09, 36.59, 34.40, 30.88, 30.63, 28.70, 22.16; **MS** (ESI): *m/z* 663 (M^++2Na+H), 662 (M^++2Na), 661 (M^++2Na-H), 607 (M^++Na-CH_3O-H); **HRMS** (ESI): *m/z* calculated for $C_{36}H_{44}N_2O_7Na_2$ (M^++2Na) 662.3041, found 662.3055.

To the DMB-protected tetramic acid (6.5 mg, 0.0105 mmol) in a flame-dried round bottom flask equipped with a cold finger under $N_{2(g)}$ was added TFA (1 mL) and the solution was immediately placed in a 67 °C bath. After 10 min, the bright pink solution was concentrated *in vacuo* to provide a solid that was purified by trituration (3 x 500 μL Et_2O) and reverse-phase preparative HPLC (Zorbax SB-C18 column, 21.2 mm I.D., 25 cm length, MeCN/H_2O) to give cylindramide A (3.2 mg, 65%).

$[\alpha]_D$ +128.0 (*c* 0.08, $CHCl_3$); +152.0 (*c* 0.08, MeOH); **IR** (thin film): 2953.30, 2926.73, 2841.69, 2767.29, 2746.03, 2845.60, 1688.38, 1683.07, 1603.35, 1470.48, 1204.74, 1135.65 cm^{-1}; **^{1}H NMR** (CD_3OD, 600 MHz): 7.46 (dd, 1H, *J* = 14.4, 12.0 Hz), 6.24 (t, 1H, *J* = 10.8 Hz), 5.96 (m, 1H), 5.95 (d, 1H, *J* = 15.0 Hz), 5.68 (d, 1H, *J* = 5.4 Hz), 5.51 (d, *J* = 5.4 Hz), 5.35 (dt, 1H, *J* = 15.0, 7.2 Hz), 5.16 (dd, 1H, *J* = 15.0, 8.4 Hz), 4.01 (d, 1H, *J* = 7.8 Hz), 3.85 (d, 1H, *J* = 2.4 Hz), 3.52 (d, 1H, *J* = 13.8 Hz), 3.06 (q, 1H, *J* = 7.2 Hz), 3.04 (t, 1H, *J* = 8.4 Hz), 2.92 (t, 1H, *J* = 13.2 Hz), 2.68 (td, 1H, *J* = 12.6, 6.0 Hz), 2.41 (m, 1H), 2.35 (m, 1H), 2.30 (m, 1H), 2.13 (m, 2H), 2.07 (m, 1H), 2.06 (m, 1H), 2.02 (m, 1H), 1.65 (m, 1H), 1.39 (m, 1H), 1.34 (m, 1H), 1.09 (q, 1H, *J* = 11.4 Hz), 1.02 (d, 3H, *J* = 7.2 Hz); **^{13}C NMR** (CD_3OD, 100 MHz): δ 195.26, 176.13, 169.10, 135.83, 135.66, 132.32, 132.22, 132.12, 128.00, 123.47,

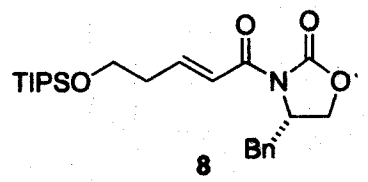
[6] Due to small quantities of material, ^{13}C NMR data was extrapolated from HSQC and HMBC data.

69.56, 66.88, 53.63, 52.13, 50.04, 49.47, 48.55, 40.56, 38.25, 36.20, 31.10, 29.86, 27.66, 21.29; **MS** (ESI): *m/z* 511 (M^++2Na-H), 491 (M^++Na+2H); **HRMS** (ESI): *m/z* calculated for $C_{27}H_{33}N_2O_5Na_2$ (M+2Na-H^+) 511.2282, found 511.2447.

Table. Comparison of data for synthetic and natural cylindramde A

	Natural ($CDCl_3$/CD_3OD)		Synthetic (CD_3OD)	
	^{1}H δ (mult, *J*)	^{13}C δ	^{1}H δ (mult, *J*)	^{13}C δ[7]
1	-	194.3	-	195.26
2	3.97 (s)	68.8	3.85 (d, 2.4)	66.88
3	3.96 (d, 7.7)	70.0	4.01 (d, 7.8)	69.56
4a	1.55 (ddd, 14.3, 11.6, 3.0)	31.3	1.65 (m)	31.10
4b	1.43 (m)		1.39 (m)	
5a	3.51 (dt, 13.7, 3.7)	36.7	3.52 (d, 13.8)	36.20
5b	2.94 (ddd, 13.7, 11.6, 1.9)		2.95 (t, 13.2)	
6	-	-	-	-
7	-	168.4	-	169.10
8	5.87 (d)	123.9	5.95 (d, 15.0)	123.47
9	7.48 (dd, 11.0, 15.0)	136.6	7.46 (dd, 14.4, 12.0)	135.66
10	6.19 (t, 11.0)	128.7	6.24 (t, 10.8)	128.00
11	5.91 (dt, 11.0, 5.4)	136.6	5.96 (m)	135.66
12a	2.59 (ddd, 14.5, 11.0, 6.0)	28.6	2.68 (td, 12.6, 6.0)	27.66
12b	2.29 (m)		2.35 (m)	
13	1.33 (qdd, 8.5, 6.0, 3.0)	52.4	1.34 (m)	52.13
14	3.01 (tq, 9.5, 2.2)	54.4	3.06 (q, 7.2)	53.63
15	5.62 (dt, 5.6, 2.1)	132.8	5.68 (d, 5.4)	132.32
16	5.47 (dt, 5.6, 2.8)	135.4	5.51 (d, 5.4)	135.83
17	2.39 (qq, 7.0, 2.0)	47.9	2.41 (m)	48.55
17-CH_3	0.98 (d, 7.0)	22.2	1.02 (d, 7.2)	21.29
18	2.11 (tdd, 9.5, 7.8, 2.7)	50.0	2.13 (m)	49.47
19a	1.06 (q, 10.8)	40.9	1.09 (q, 11.4)	40.56
19b	1.99 (dd, 11.0, 7.8)		2.02 (m)	
20	2.06 (q, 8.5)	49.5	2.06 (m)	50.04
21	5.21 (d, 15.1, 8.5)	133.8	5.16 (dd, 15.0, 8.4)	132.12
22	5.29 (ddd, 15.1, 8.4, 5.7)	131.3	5.35 (dt, 15.0, 7.2)	132.22
23a	2.25 (m)	30.9	2.13 (m)	29.86
23b	2.07 (m)		2.07 (m)	
24a	3.08 (t, 11.4)	35.4	3.04 (t, 8.4)	38.25
24b	2.25 (m)		2.30 (m)	
25	-	190.5	-	-
26	-	101.2	-	-
27	-	176.7	-	176.13

[7] Due to limited sample, this data was obtained by HSQC and HMBC experiments.



8

8 7 6 5 4 3 2 1 0 ppm

Relax. delay 1.500 sec
Pulse 19.7 degrees
Acq. time 3.000 sec
Width 7200.1 Hz
14 repetitions

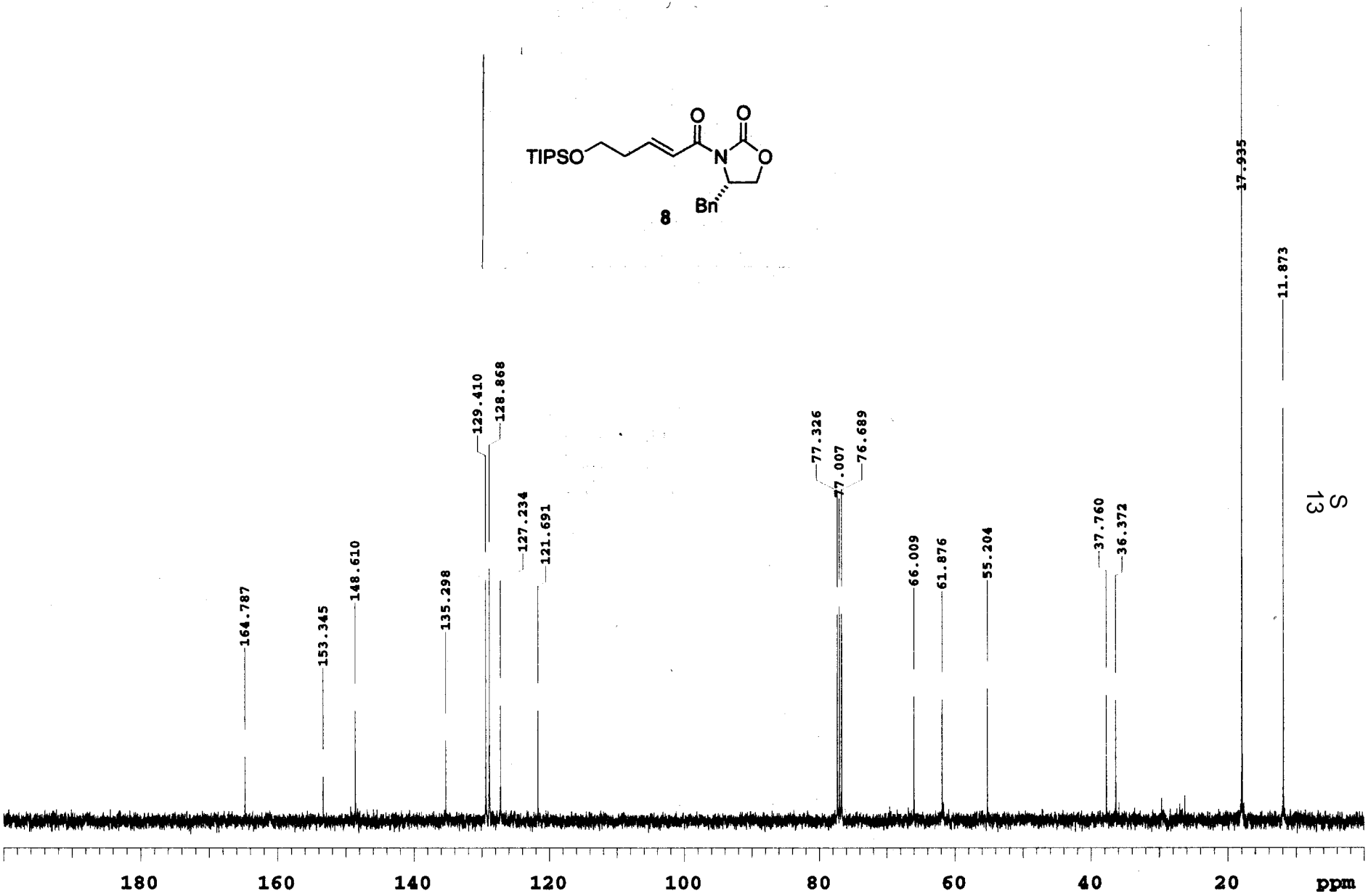
OBSERVE H1, 500.3674489

DATA PROCESSING
Line broadening 0.1 Hz
FT size 131072
Total time 1 minute

Solvent: CDC13
Ambient temperature
File: ach-zz21-150-2

Data Acquired: Sep 19 2003

University of Colorado at Boulder NMR



S 13

Relax. delay 1.500 sec
Pulse 45.0 degrees
Acq. time 1.311 sec
Width 25000.0 Hz
31 repetitions

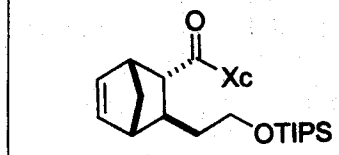
OBSERVE C13, 100.6189918
DECOUPLE H1, 400.1574807
Power 38 dB
continuously on
WALTZ-16 modulated

DATA PROCESSING
Line broadening 1.2 Hz
FT size 131072
Total time 1 minute

Solvent: CDCl3
Ambient temperature
File: ach-2-131-c13

Data Acquired: Jan 28 2005

University of Colorado at Boulder NMR



9

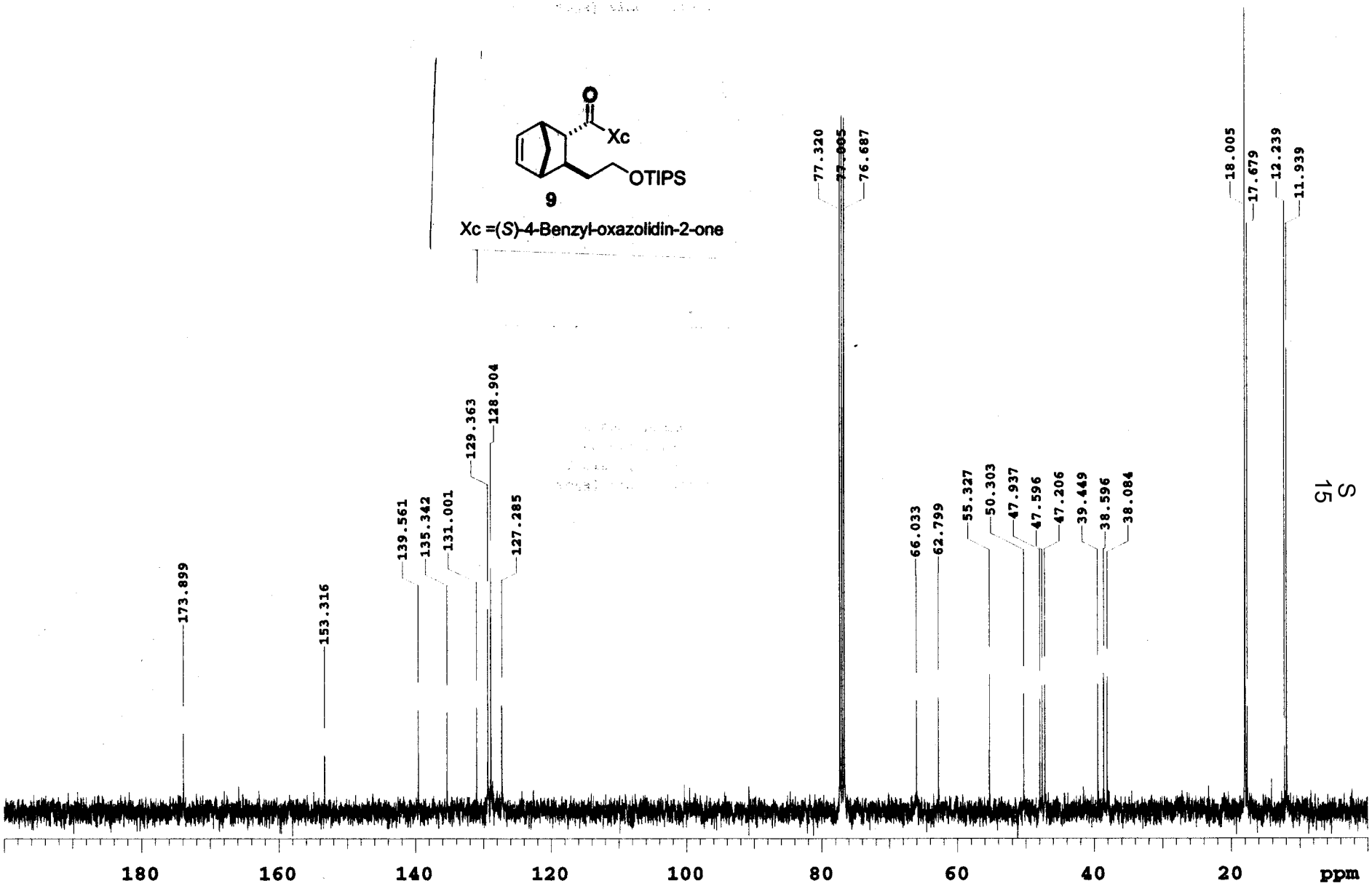
Xc =(*S*)-4-Benzyl-oxazolidin-2-one

Relax. delay 1.500 sec
Pulse 26.5 degrees
Acq. time 3.000 sec
Width 7200.1 Hz
17 repetitions

OBSERVE H1, 500.3674484

DATA PROCESSING
Line broadening 0.1 Hz
FT size 131072
Total time 1 minute

Solvent: CDCl3
Ambient temperature
File: ach-zz21-dielsalder-9

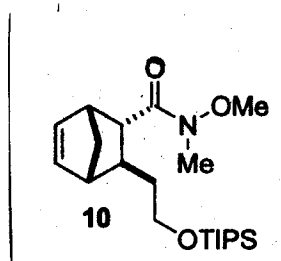


Relax. delay 1.500 sec
Pulse 45.0 degrees
Acq. time 1.311 sec
Width 25000.0 Hz
149 repetitions

OBSERVE C13, 100.6189882
DECOUPLE H1, 400.1574807
Power 38 dB
continuously on
WALTZ-16 modulated

DATA PROCESSING
Line broadening 1.5 Hz
FT size 131072
Total time 7 minutes

Solvent: CDCl3
Ambient temperature
File: ach-zz20-dielsalder-13C



Relax. delay 1.000 sec
Pulse 26.5 degrees
Acq. time 3.000 sec
Width 7200.1 Hz
17 repetitions

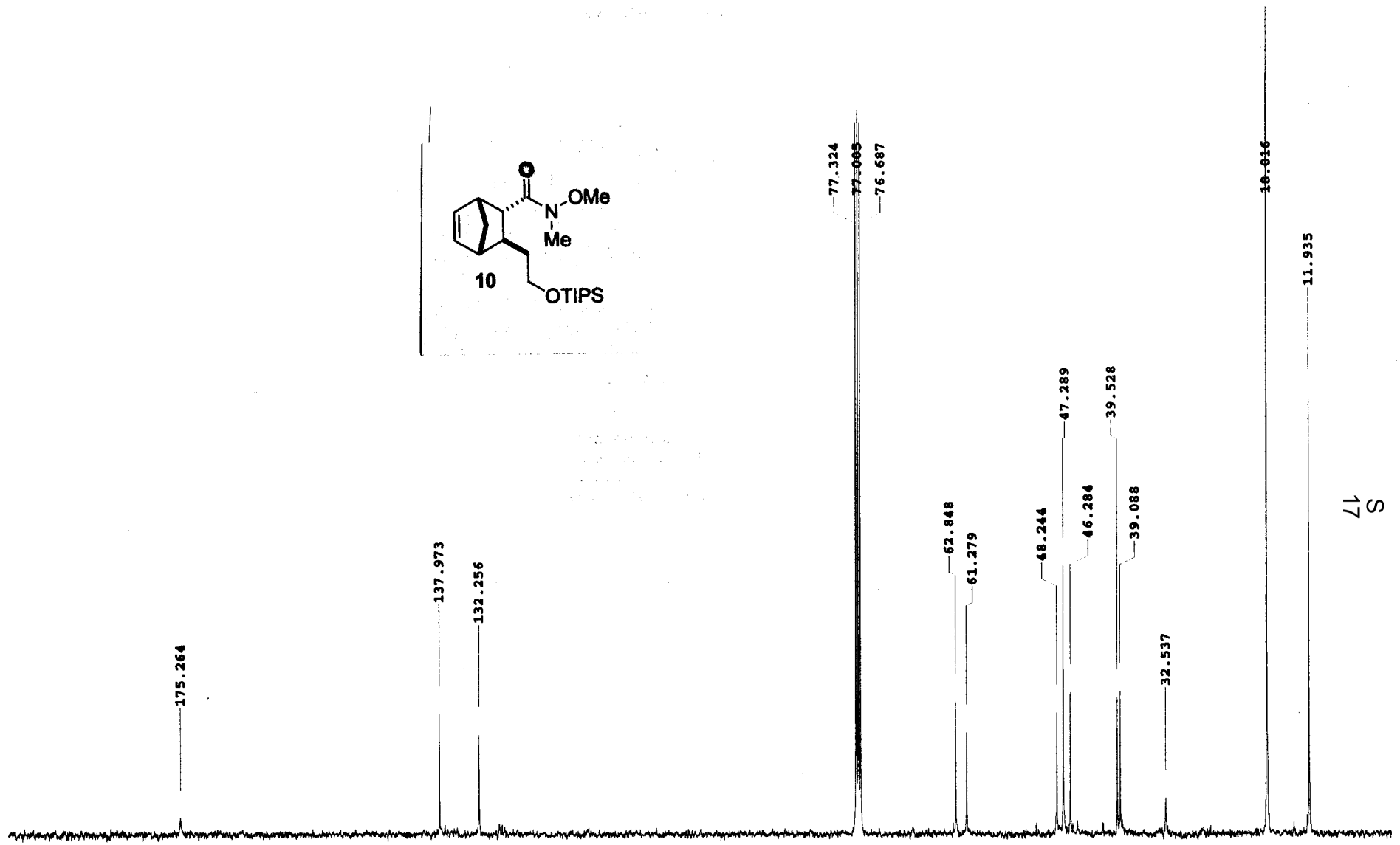
OBSERVE H1, 500.3674482

DATA PROCESSING
Line broadening 0.1 Hz
FT size 131072
Total time 1 minute

Solvent: CDCl3
Ambient temperature
File: ach-zz21-weinrabamide-1H

Data Acquired: Jan 6 2005

University of Colorado at Boulder NMR



Relax. delay 1.500 sec
Pulse 45.0 degrees
Acq. time 1.311 sec
Width 25000.0 Hz
941 repetitions

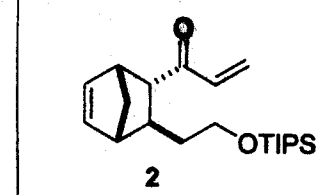
OBSERVE C13, 100.6189878
DECOUPLE H1, 400.1574807
Power 38 dB
continuously on
WALTZ-16 modulated

DATA PROCESSING
Line broadening 4.0 Hz
FT size 131072
Total time 44 minutes

Solvent: CDCl3
Ambient temperature
File: ach-zz21-weinrebamide-13C

Data Acquired: Jan 11 2005

University of Colorado at Boulder NMR



2

Relax. delay 1.500 sec
Pulse 28.2 degrees
Acq. time 3.000 sec
Width 6000.6 Hz
17 repetitions

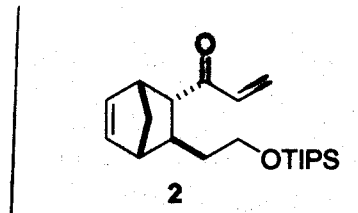
OBSERVE H1, 400.1547356

DATA PROCESSING
Line broadening 0.1 Hz
FT size 131072
Total time 1 minute

Solvent: CDCl3
Ambient temperature
File: ach-zz21-044-1H

Data Acquired: Jan 11 2005

University of Colorado at Boulder NMR



2

Relax. delay 1.500 sec
Pulse 45.0 degrees
Acq. time 1.311 sec
Width 28001.4 Hz
305 repetitions

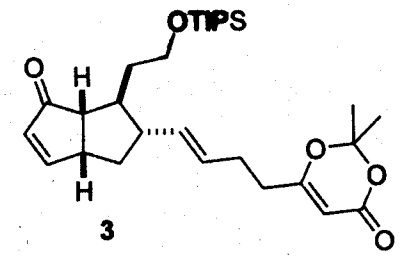
OBSERVE C13, 100.6189874
DECOUPLE H1, 400.1574807
Power 38 dB
continuously on
WALTZ-16 modulated

DATA PROCESSING
Line broadening 1.2 Hz
FT size 131072
Total time 14 minutes

Solvent: CDCl3
Ambient temperature
File: ach-zz21-044-13C

Data Acquired: May 5 2005

University of Colorado at Boulder NMR



3

Relax. delay 1.500 sec
Pulse 19.7 degrees
Acq. time 3.000 sec
Width 7199.4 Hz
23 repetitions

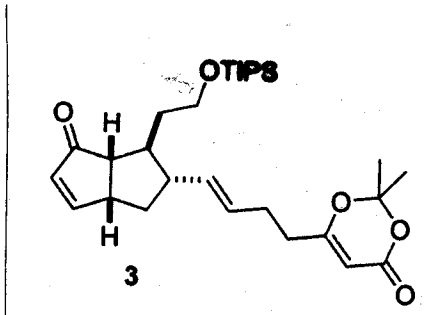
OBSERVE H1, 500.3674488

DATA PROCESSING
Line broadening 0.1 Hz
FT size 131072
Total time 1 minutes

Solvent: CDCl3
Ambient temperature
File: ach-zz23-116-eisomer

Data Acquired: May 6 2005

University of Colorado at Boulder NMR



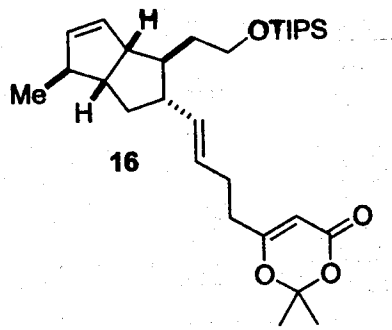
S 21

Relax. delay 1.500 sec
Pulse 45.0 degrees
Acq. time 1.311 sec
Width 26999.7 Hz
1218 repetitions

OBSERVE C13, 100.6189623
DECOUPLE H1, 400.1574807
Power 38 dB
continuously on
WALTZ-16 modulated

DATA PROCESSING
Line broadening 1.2 Hz
FT size 131072
Total time 57 minutes

Solvent: CDCl3
Ambient temperature
File: ach-zz23-116-eisomer-13c



16

7 6 5 4 3 2 1 0 ppm

Relax. delay 1.500 sec
Pulse 28.2 degrees
Acq. time 3.000 sec
Width 6000.6 Hz
17 repetitions

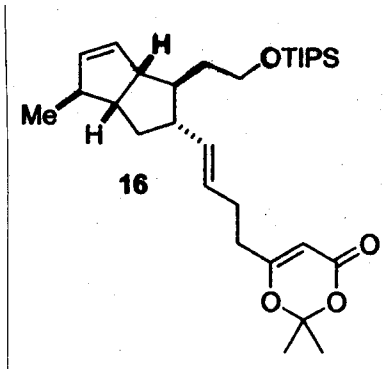
OBSERVE H1, 400.1547355

DATA PROCESSING
Line broadening 0.1 Hz
FT size 131072
Total time 1 minute

Solvent: CDCl3
Ambient temperature
File: ach-zz23-064-3-1H

Data Acquired: Apr 17 2005

University of Colorado at Boulder NMR



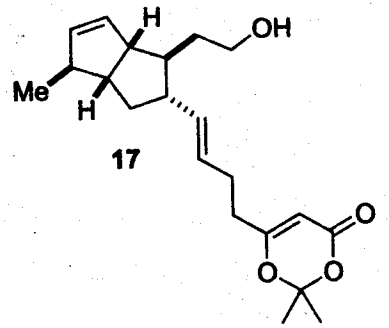
S 23

Relax. delay 1.500 sec
Pulse 45.0 degrees
Acq. time 1.311 sec
Width 25000.0 Hz
87 repetitions

OBSERVE C13, 100.6189912
DECOUPLE H1, 400.1574807
Power 38 dB
continuously on
WALTZ-16 modulated

DATA PROCESSING
Line broadening 2.0 Hz
FT size 131072
Total time 4 minutes

Solvent: CDCl3
Ambient temperature
File: ach-zz23-064-13C



17

Relax. delay 1.500 sec
Pulse 28.2 degrees
Acq. time 2.999 sec
Width 6002.4 Hz
16 repetitions

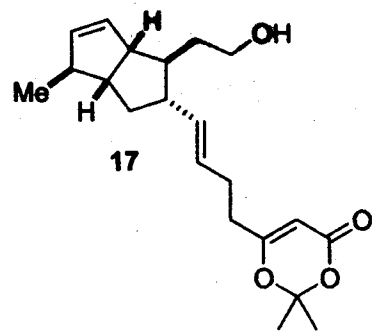
OBSERVE H1, 400.1547354

DATA PROCESSING
Line broadening 0.1 Hz
FT size 131072
Total time 1 minute

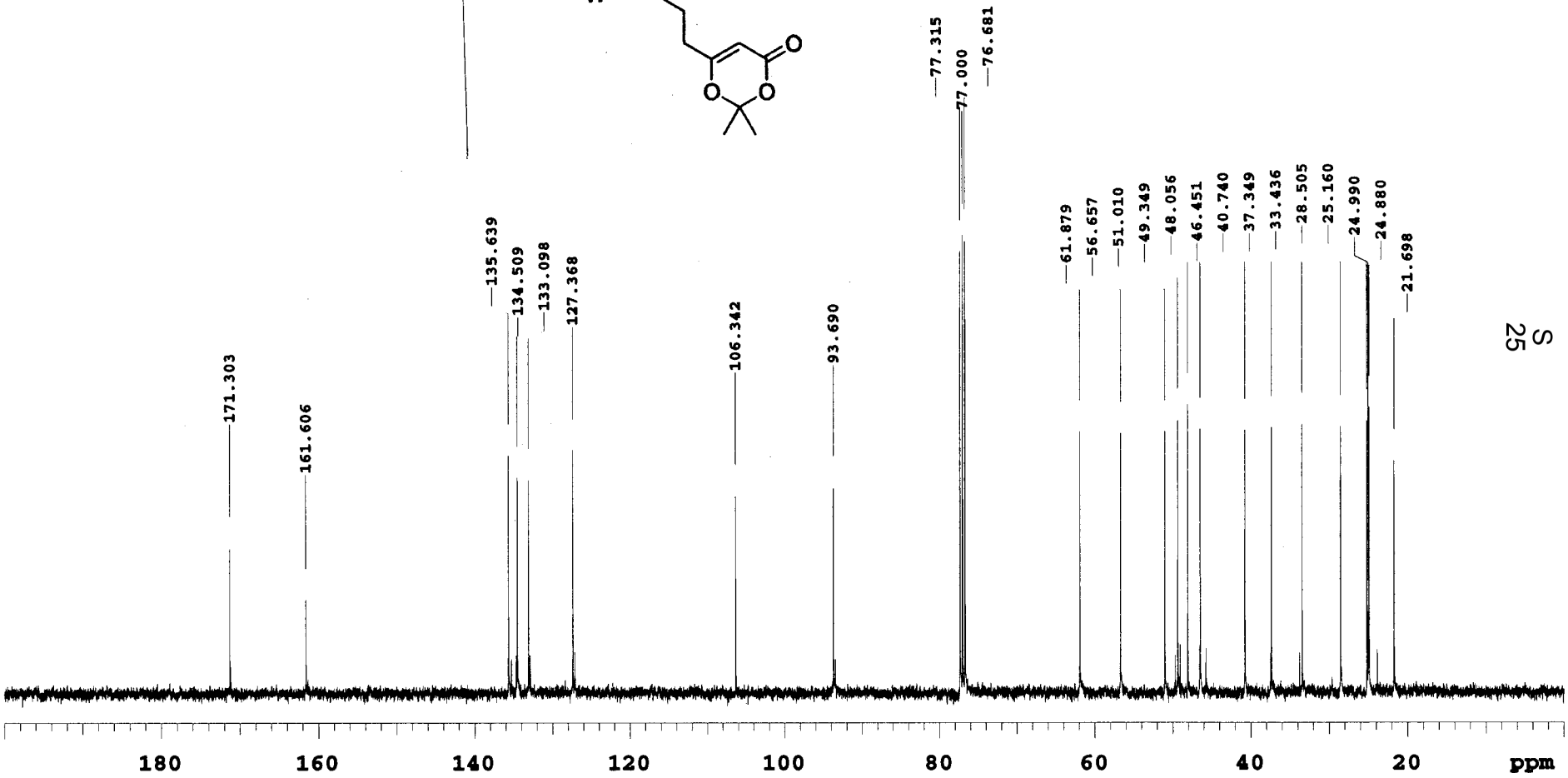
Solvent: CDCl3
Ambient temperature
File: ach-zz22-013-1H

Data Acquired: Mar 29 2005

University of Colorado at Boulder NMR



17



Relax. delay 1.500 sec
Pulse 45.0 degrees
Acq. time 1.310 sec
Width 25007.8 Hz
287 repetitions

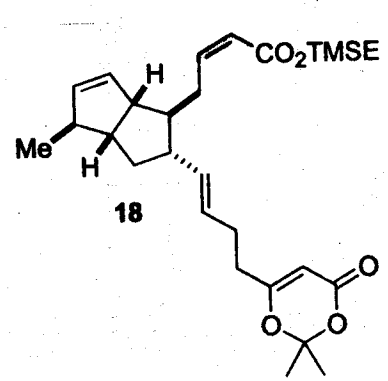
OBSERVE C13, 100.6189912
DECOUPLE H1, 400.1574807
Power 38 dB
continuously on
WALTZ-16 modulated

DATA PROCESSING
Line broadening 1.2 Hz
FT size 131072
Total time 13 minutes

Solvent: CDCl3
Ambient temperature
File: ach-zz22-013-c13

Data Acquired: Mar 30 2005

University of Colorado at Boulder NMR



18

S 26

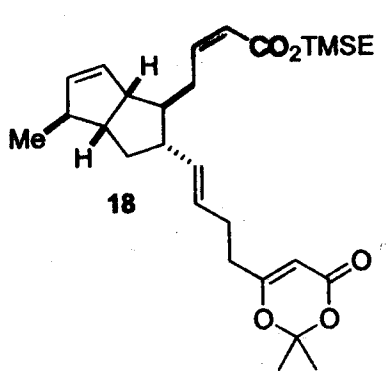
8 7 6 5 4 3 2 1 0 ppm

Relax. delay 1.500 sec
Pulse 19.7 degrees
Acq. time 3.000 sec
Width 7199.4 Hz
16 repetitions

OBSERVE H1, 500.3674489

DATA PROCESSING
Line broadening 0.1 Hz
FT size 131072
Total time 1 minute

Solvent: CDCl3
Ambient temperature
File: ach-zz22-150-2



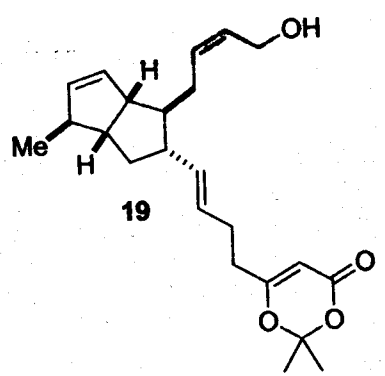
18

Relax. delay 1.500 sec
Pulse 45.0 degrees
Acq. time 1.310 sec
Width 25007.8 Hz
149 repetitions

OBSERVE C13, 100.6189884
DECOUPLE H1, 400.1574807
Power 38 dB
continuously on
WALTZ-16 modulated

DATA PROCESSING
Line broadening 1.2 Hz
FT size 131072
Total time 7 minutes

Solvent: CDCl3
Ambient temperature
File: ach-zz22-150-13C



19

8 7 6 5 4 3 2 1 0 ppm

Relax. delay 1.500 sec
Pulse 19.7 degrees
Acq. time 3.000 sec
Width 7199.4 Hz
18 repetitions

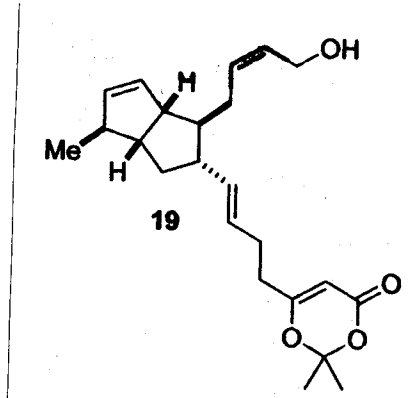
OBSERVE H1, 500.3674488

DATA PROCESSING
Line broadening 0.1 Hz
FT size 131072
Total time 1 minute

Solvent: CDCl3
Ambient temperature
File: ach-zz23-024-col2-high

Data Acquired: Apr 5 2005

University of Colorado at Boulder NMR



19

Relax. delay 1.500 sec
Pulse 45.0 degrees
Acq. time 1.311 sec
Width 25000.0 Hz
880 repetitions

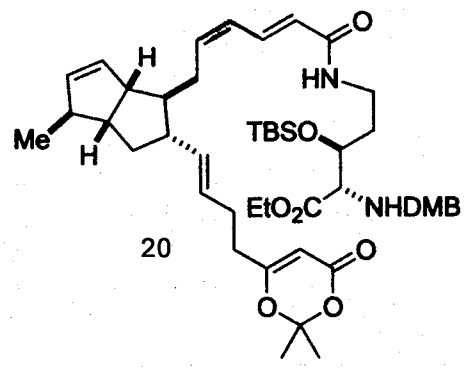
OBSERVE C13, 100.6189870
DECOUPLE H1, 400.1574807
Power 38 dB
continuously on
WALTZ-16 modulated

DATA PROCESSING
Line broadening 2.0 Hz
FT size 131072
Total time 41 minutes

Solvent: CDCl3
Ambient temperature
File: ach-zz23-024-col2-13C

Data Acquired: Sep 26 2004

University of Colorado at Boulder NMR



20

S 30

8 7 6 5 4 3 2 1 0 ppm

Relax. delay 1.000 sec
Pulse 26.5 degrees
Acq. time 3.000 sec
Width 7200.1 Hz
74 repetitions

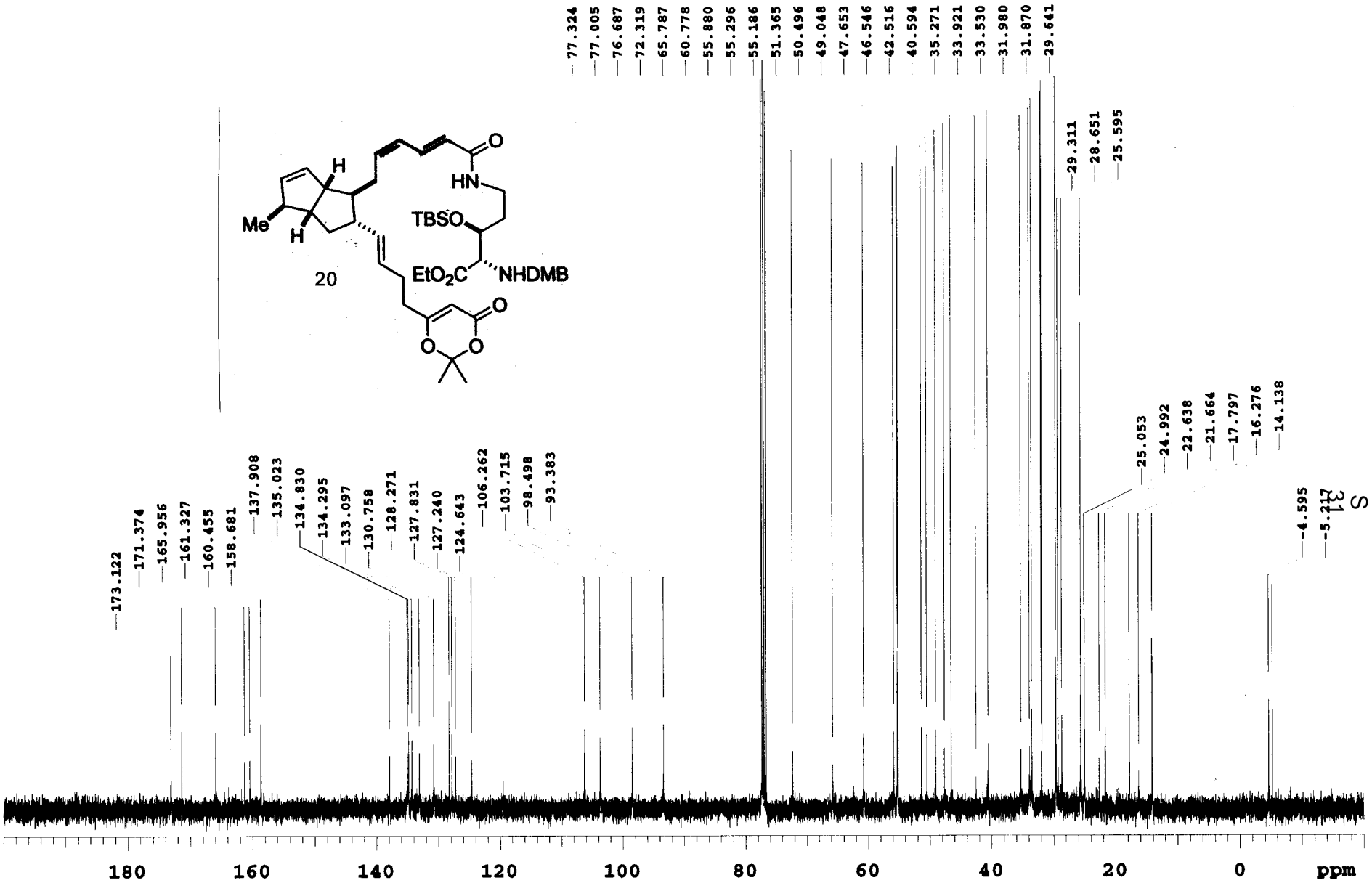
OBSERVE H1, 500.3674483

DATA PROCESSING
Line broadening 0.1 Hz
FT size 65536
Total time 4 minutes

Solvent: CDCl3
Ambient temperature
File: ach-zz19-040-hplc-2

Data Acquired: May 12 2005

University of Colorado at Boulder NMR

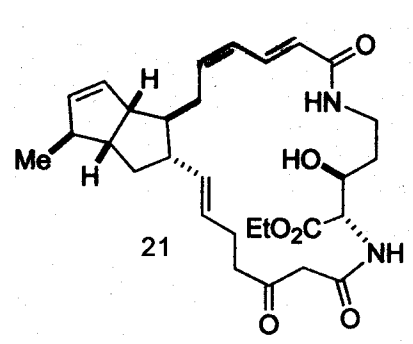


Relax. delay 1.500 sec
Pulse 45.0 degrees
Acq. time 1.311 sec
Width 25000.0 Hz
448 repetitions

OBSERVE C13, 100.6189908
DECOUPLE H1, 400.1574807
Power 38 dB
continuously on
WALTZ-16 modulated

DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 21 minutes

Solvent: CDCl3
Ambient temperature
File: ach-zz23-139-13c



8 7 6 5 4 3 2 1 0 ppm

Relax. delay 0.500 sec
Pulse 45.0 degrees
Acq. time 3.500 sec
Width 6000.6 Hz
64 repetitions

OBSERVE H1, 400.1547353

DATA PROCESSING
Line broadening 0.2 Hz
FT size 131072
Total time 4 minutes

Solvent: CDCl3
Ambient temperature
File: ach-zz23-099-prepTLC-spot7-1h3

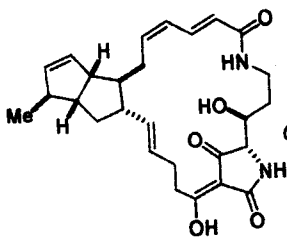
UCB Varian Inova-500
Standard Proton Parameters
NALORAC 4N Probe

Pulse Sequence: s2pul

File: cylindramide.fid (Varian Data)
Date: May 26 2005

Acquisition Parameters:
Nucleus: H1 at 500.372 MHz
Solvent: CD3OD
tof 273.7
sw 7200.1 Hz (14.389 ppm)
pw 2.10 usec
d1 1.500 sec
np 43200
at 3.000 sec
bs/ss 4/0
nt/ct 1024/127

Processing Parameters:
lb 0.50
fn 131072
lp/rp -27.3/164.7
ppm/cm 0.40



Cylindramide A, 1