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Supporting Information

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SUPPORTING INFORMATION

Total Synthesis of Theopederin D

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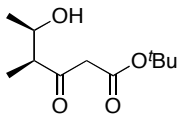
General Experimental

Proton (^{1}H NMR) and carbon (^{13}C NMR) nuclear magnetic resonance were recorded on Bruker Avance 300 spectrometers at (300 MHz and 75 MHz, respectively), Bruker Avance 500 spectrometers at (500 MHz and 125 MHz, respectively) Bruker Avance 600 spectrometers at (600 MHz and 150 MHz, respectively), and a Bruker Avance 600 spectrometer equipped with a 5mm cryoprobe (600 MHz, and 150 MHz, respectively). The chemical shifts are given in parts per million (ppm) on the delta (δ) scale. The solvent peak was used as reference values. For ^{1}H NMR: $CDCl_3$=7.27 ppm, C_6D_6=7.15. For ^{13}C NMR: $CDCl_3$=77.00 ppm, C_6D_6=128.00 ppm. For proton data: app=apparent; s=singlet; d=doublet; t=triplet; q=quartet; p=pentet; dd=doublet of doublets; dt=doublet of triplets; ddd=doublet of doublet of doublets; dddd=doublet of doublet of doublet of doublets; ddt=doublet of doublet of triplets; ddq=doublet of doublet of quartets; qd=quartet of doublets; br=broad; m=multiplet. High resolution and low resolution mass spectra were recorded on a VG 7070 spectrometer. Infrared (IR) spectra were collected on a Mattson Cygnus 100 spectrometer. Samples for IR were prepared as a thin film on NaCl plates. Analytical high performance liquid chromatography (HPLC) was performed on a Hewlett Packard 1100 liquid chromatograph equipped with a variable wavelength UV detector (deuterium lamp, 190-600 nm) using a Daicel Chiralpak^{TM} AD column (250 x 4.6 mm) (Daicel Inc.) and HPLC-grade isopropanol and hexanes as the eluting solvents. Optical rotations were measured on a Perkin-Elmer 241 polarimeter. Analytical thin layer chromatography (TLC) was performed on E. Merck pre-coated (25 nm) silica gel 60F-254 plates. Visualization was done under UV (254 nm). Flash column chromatography was performed using ICN SiliTech 32-63 60Å silica gel. Preparatory thin layer chromatography (PTLC) was performed on Sorbent Technologies pre-coated (25 nm) silica gel HL UV254 plates. Reagent grade ethyl acetate, hexanes (commercial mixture), ether, dichloromethane, benzene, acetone, and toluene were purchased from EM Science and used as is for chromatography. Reagent grade methylene chloride (CH_2Cl_2) and 1, 2-dichloroethane (DCE) were distilled from CaH_2 under N_2. Diethyl ether (Et_2O) was dried by passing through an aluminum drying column. THF was dried by passing through an aluminum drying column, except where noted. In these cases THF, was distilled from sodium benzophenone under N_2. Anhydrous methanol (MeOH) was purchased from Aldrich and used as is. All reactions were conducted under argon or nitrogen atmosphere, in oven or flame dried glassware with magnetic stirring except were noted.

(3*S* ,4*R*)-3,4-dimethyloxetan-2-one

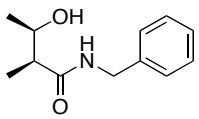
To a solution of $LiClO_4$ (1.61 g, 15.1 mmol) in Et_2O (50 mL) was added TMS-quinidine[1] (2.00 g, 5.0 mmol) in CH_2Cl_2 (100 mL). The mixture was cooled to –78 °C whereupon ^{i}Pr$_2$NEt (21.9 mL, 126 mmol) and acetaldehyde (3.8 mL, 67 mmol) were added. To this reaction mixture was added a solution of propionyl chloride (8.8 mL, 101 mmol) in CH_2Cl_2 (25 mL) dropwise over 3 hours. After the addition was complete, the reaction continued to stir at –78 °C overnight. Et_2O (40 mL) was then added to the mixture at –78 °C. The solution was warmed to room temperature then filtered through a short pad of Celite. The filtrate was concentrated to 1/3 of its original volume under reduced pressure at 0 °C and was used crude without further purification. ***Alternatively***, the filtrate can be concentrated under reduced pressure at 0 °C and purified via flash column chromatography (pentane to 10% Et_2O in pentane to 20% Et_2O in pentane) to afford the desired product as a low boiling colorless liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.77 (m, 1H), 3.75 (m, 1H), 1.46 (d, J = 6.3 Hz, 3H), 1.28 (d, J = 7.8 Hz, 3H).



(4*S*, 5*R*)-*tert*-butyl 5-hydroxy-4-methyl-3-oxohexanoate (8)

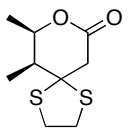
To a freshly prepared solution of LDA (150 mL, 1 M in THF) at –78 °C was added *t*-butyl acetate (17.53 g, 20.34 mL, 150.9 mmol) dropwise. The reaction mixture was stirred for 10 minutes, then the crude β-lactone in Et_2O/CH_2Cl_2 (prepared in the previous step) was slowly added dropwise at -78 °C. After 30 minutes, aqueous NH_4Cl (150 mL) was added, and the reaction was warmed to room temperature. The reaction mixture was extracted with EtOAc (3 x 50 mL), and the combined organic layers were washed with brine (50 mL). The organic extracts were dried (Na_2SO_4), filtered, and concentrated under reduced pressure to afford a crude yellow oil. The crude residue was purified via flash column chromatography (30% EtOAc in hexanes to 70% EtOAc in hexanes to 100% EtOAc to 5% MeOH in EtOAc) to afford the desired product as an 8:1 inseparable mixture with its tautomer (5.15 g, 76%). *Underlined values correspond to assignable tautomer peaks*. ^{1}H (300 MHz, $CDCl_3$): δ <u>12.4</u> (br s, 1H), <u>4.94</u> (s, 1H), 4.18 (m, 1H), 3.50 (d, J = 15.3 Hz, 1H), 3.43 (d, J = 15.6 Hz, 1H) 2.72 (qd, J = 3.3, 7.2 Hz, 1H), 2.53 (br s, 1H), <u>1.49</u> (s, 9H), 1.47 (s, 9H), 1.18 (d, J = 6.6 Hz, 3H), 1.17 (d, J = 7.2 Hz, 3H).

To determine the ee of the β-lactone, the ring was opened with benzylamine and the amide product was analyzed by HPLC.



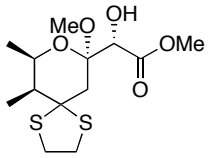
(2*S*, 3*R*)-*N*-benzyl-3-hydroxy-2-methylbutanamide

To a solution of the β-lactone (0.15 g, 1.5 mmol) in CH_3CN (5.0 mL) at room temperature was added catalytic DMAP followed by benzylamine (0.16 g, 1.5 mmol). After 4 hours, the reaction was cooled to 0 °C and 3% Et_3N in Et_2O (2 mL) was added to the reaction mixture, followed by addition of H_2O (2 mL). The reaction mixture was extracted with Et_2O (3 x 5 mL), and the organic layers were combined. The combined organic extracts were washed with brine (5 mL), dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The crude residue was purified via flash column chromatography to afford the desired product as a white solid. ^{1}H (300 MHz, $CDCl_3$): δ 7.37-7.25 (m, 5H), 6.50 (br s, 1H), 4.43 (s, 1H), 4.41 (s, 1H), 4.06 (qd, *J* = 4.1, 6.4 Hz, 1H), 3.45 (br s, 1H), 2.32 (qd, *J* = 3.0, 7.1 Hz, 1H), 1.17 (d, *J* = 7.2 Hz, 3H), 1.14 (d, *J* = 6.5 Hz, 3H).



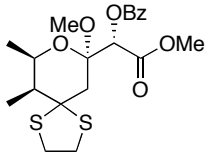
(9*R*, 10*S*)-9,10-dimethyl-8-oxa-1,4-dithiaspiro[4.5]decan-7-one[2]

To a solution of **8** (2.50 g, 11.6 mmol) in CH_2Cl_2 (69.0 mL) at –40 °C were sequentially added 1,2-ethanedithiol (3.00 mL, 34.7 mmol) and $BF_3{\cdot}Et_2O$ (7.30 mL, 57.8 mmol). The reaction was warmed to room temperature. After 48 hours, the reaction mixture was carefully poured into a 0 °C solution of saturated aqueous $NaHCO_3$ (100 mL). The reaction mixture was extracted with CH_2Cl_2 (3 x 50 mL), and the combined organic layers were washed with saturated aqueous $NaHCO_3$ (20 mL) and brine (20 mL), then dried (Na_2SO_4), filtered, and concentrated under reduced pressure to afford a crude orange residue. The material was purified via flash column chromatography (hexanes to 20% EtOAc in hexanes) to afford the desired product and its C_2 diastereomer (~10:1) as a yellow solid. The solid was recrystallized from 30% EtOAc in hexanes to afford the desired product (1.60 g, 64%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.89 (qd, *J* = 2.7, 6.3, 1H), 3.45-3.29 (m, 4H), 3.14 (d, *J* = 19.2 Hz, 1H), 3.06 (d, *J* = 19.2 Hz, 1H), 2.17 (qd, *J* = 2.7, 6.9, 1H), 1.38 (d, *J* = 6.3 Hz, 3H), 1.2 (d, *J* = 6.9 Hz, 3H), $[\alpha]^{27}_D$ +99.8 (*c* 1.10, $CHCl_3$), lit. $[\alpha]^{27}_D$ +106.7 (*c* 1.10, $CHCl_3$).



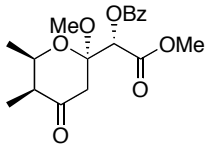
(*S*)-methyl 2-hydroxy-2-((7*R*, 9*R*, 10*S*)-7-methoxy-9,10-dimethyl-8-oxa-1,4-dithiaspiro[4.5]decan-7-yl)acetate[2]

To a flame dried flask under argon atmosphere was added ^{i}Pr$_2$NEt (2.9 mL, 21 mmol) and freshly distilled THF (42 mL). The flask was evacuated and purged with argon three times, then cooled to –78 °C. ^{n}BuLi (1.6 M in hexanes, 12.5 mL) was slowly added dropwise. The reaction was warmed to 0 °C for 15 minutes, then cooled to –78 °C. To the reaction mixture was slowly added a solution of the methyl 2-methoxypropyloxyglycolate (3.36 g, 20.7 mmol) in freshly distilled THF (21.0 mL) (*separately prepared and evacuated and backfilled with argon*) dropwise over 10 minutes. The reaction mixture was stirred for 1 hour, then freshly distilled HMPA (5.2 mL, 30.1 mmol, *evacuated and backfilled with argon*) was added slowly dropwise over 8 minutes. The reaction was stirred for an additional 15 minutes, then $ZnCl_2$ (20.7 mL, 1 M in Et_2O) was slowly added dropwise over 15 minutes. The reaction mixture was stirred at –78 °C for 2 hours. After 2 hours, the lactone (0.40 g, 1.8 mmol) in freshly distilled THF (10.8 mL) (*evacuated and backfilled with argon*) was slowly added to the reaction mixture dropwise over 4 minutes. The reaction was stirred at –78 °C for 2 hours, then warmed to –40 °C. After 12 hours at –40 °C, saturated aqueous NH_4Cl (aq., satd., 30 mL) was added, and the mixture was extracted with EtOAc (3 x 20 mL). The organic layers were combined and washed with aqueous NH_4Cl (20 mL), $NaHCO_3$ (20 mL), and brine (20 mL), then dried (Na_2SO_4), filtered, and concentrated under reduced pressure to afford a crude yellow oil. The crude material was diluted with CH_2Cl_2 (26 mL) and MeOH (26 mL). To this mixture was added trimethyl orthoformate (10 mL) and camphorsulfonic acid (0.55 g, 2.4 mmol). The solution was stirred at room temperature for 3 hours then poured into a separatory funnel containing ice water (20 mL). The reaction mixture was extracted with Et_2O (3 x 30 mL). The combined organic layers were washed with $NaHCO_3$ (20 mL), and brine (20 mL), then dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The crude residue was purified via flash column chromatography (30% EtOAc in hexanes) to afford the desired product as a yellow oil (0.35 g, 60% isolated, 70% brsm) and recovered lactone (0.06 g, 10%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.38 (qd, *J* = 1.8, 6.6 Hz, 1H), 4.29 (d, *J* = 5.7 Hz, 1H), 3.82 (s, 3H), 3.37-3.1 (m, 4H), 3.33 (s, 3H), 2.81 (d, *J* = 5.7 Hz, 1H), 2.33 (d, *J* = 14.7, 1H), 2.26 (d, *J* = 14.7 Hz, 1H), 1.69 (br q, *J* = 6 Hz, 1H), 1.20 (d, *J* = 6.3 Hz, 3H), 1.00 (d, *J* = 6.9 Hz, 3H); $[\alpha]^{23}_D$ +63.0 (*c* 0.60, $CHCl_3$), lit. $[\alpha]^{28}_D$ +102.8 (*c* 1.04, $CHCl_3$).



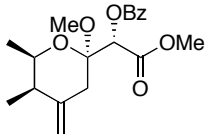
(*S*)-2-methoxy-1-((7*R* ,9*R*, 10*S*)-7-methoxy-9,10-dimethyl-8-oxa-1,4-dithiaspiro[4.5]decan-7-yl)-2-oxoethyl benzoate[2]

To a solution of the alcohol (0.13 g, 0.42 mmol) in pyridine (4.50 mL) at 0 °C was added benzoyl chloride (0.35 mL, 3.00 mmol) and a few crystals of DMAP. The solution was stirred at 0 °C for 10 minutes then warmed to room temperature. After 17 hours, the reaction was cooled to 0 °C and benzoyl chloride (0.35 mL, 3.0 mmol) and a few crystals of DMAP were added. The reaction was stirred for 10 minutes at 0 °C then warmed to room temperature and stirrred overnight. The reaction was cooled to 0 °C and 10% tartaric acid (aq., w/v, 10 mL) was added to the reaction mixture. The mixture was stirred vigorously for 10 minutes at 0 °C, then was extracted with EtOAc (3 x 5 mL). The organic layers were combined, washed with 10% tartaric acid (aq.) (w/v) (10 mL), $NaHCO_3$ (satd., aq., 5 mL), brine (5 mL), dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The crude residue was purified via column chromatography (10% EtOAc in hexanes to 20% EtOAc in hexanes) to afford the desired product as a white solid (0.17 g, 94%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.07-8.04 (m, 2H), 7.61-7.56 (m, 1H), 7.47-7.40 (m, 2H), 5.38 (s, 1H), 4.40 (qd, *J* = 1.9, 6.3 Hz, 1H), 3.79 (s, 3H), 3.34-3.315 (m, 4H), 3.30 (s, 3H), 2.84 (d, *J* = 14.7 Hz, 1H), 2.40 (d, *J* = 14.7 Hz, 1H), 1.67 (br q, *J* = 6.9 Hz, 1H), 1.19 (d, *J* = 6.6 Hz, 3H), 1.01 (d, *J* = 6.9 Hz, 3H); $[\alpha]^{22}_D$ +84.0 (*c* 0.81, $CHCl_3$), lit. $[\alpha]^{28}_D$ +87.9 (*c* 1.29, $CHCl_3$).



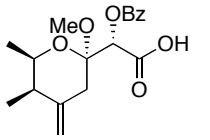
(*S*)-2-methoxy-1-((2*R*, 5*S*, 6*R*)-2-methoxy-5,6-dimethyl-4-oxotetrahydro-2H-pyran-2-yl)-2-oxoethyl benzoate[2]

To a solution of the dithiolane (0.070 g, 0.16 mmol) in CH_3CN (3.6 mL) and H_2O (0.5 mL) at –5 °C was added $PhI(OTFA)_2$ (0.21 g, 0.49 mmol). The reaction was stirred at –5 °C for 50 minutes then warmed to room temperature. After 20 minutes, the reaction mixture was poured into aqueous $NaHCO_3$ (5 mL) and the mixture was extracted with EtOAc (3 x 5 mL). The organic layers were combined, washed with brine (5 mL), dried (Na_2SO_4), filtered, and concentrated under reduced pressure to afford a crude yellow oil. The crude residue was purified via flash column chromatography (20% EtOAc in hexanes to 30% EtOAc in hexanes) to afford the desired product (0.04 g, 63%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.07-8.04 (m, 2H), 7.64-7.58 (m, 1H), 7.50-7.45 (m, 2H), 5.49 (s, 1H), 4.20 (qd, *J* = 3.0, 6.6 Hz, 1H), 3.84 (s, 3H), 3.29 (s, 3H), 3.27 (d, *J* = 15.6 Hz, 1H), 2.66 (dd, *J* = 0.9, 15.6 Hz, 1H), 2.36 (br qd, *J* = 2.7, 7.2 Hz, 1H), 1.26 (d, *J* = 6.6 Hz, 3H), 1.08 (d, *J* = 7.2 Hz, 3H) $[\alpha]^{23}_D$ +94.6 (*c* 0.84, $CHCl_3$), lit. $[\alpha]^{28}_D$ +114.4 (*c* 1.23, $CHCl_3$).



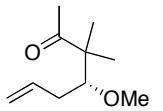
(*S*)-2-methoxy-1-((2*R*, 5*R*, 6*R*)-2-methoxy-5,6-dimethyl-4-methylenetetrahydro-2H-pyran-2-yl)-2-oxoethyl benzoate[2]

To a solution of the ketone (0.12 g, 0.34 mmol) in THF (6.2 mL) at room temperature was slowly added freshly prepared Takai-Nozaki olefination reagent[2] dropwise (5.1 mL). After the addition was complete, the reaction was poured into 0 °C aqueous $NaHCO_3$ (10 mL), and the reaction mixture was extracted with EtOAc (3 x 10 mL). The organic layers were combined and washed with $NaHCO_3$ (10 mL), and brine (10 mL), then dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The crude residue was purified via flash column chromatography (30% EtOAc in hexanes - **NOTE**: the purification was carried out quickly using a short pad of silica gel to minimize decomposition on the column) to afford the desired product (0.01 g, 85%) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.11-8.08 (m, 2H), 7.63-7.58 (m, 1H), 7.50-7.49 (m, 2H) 5.43 (s, 1H), 4.88 (br t, *J* = 1.8 Hz, 1H), 4.81 (br t, *J* = 1.8 Hz, 1H), 3.92 (qd, *J* = 2.4, 6.6 Hz, 1H), 3.82 (s, 3H), 3.28 (s, 3H), 2.91 (d, *J* = 14.4 Hz, 1H), 2.47 (d, *J* = 14.7 Hz, 1H), 2.24 (br qd, *J* = 2.4, 7.2 Hz, 1H), 1.16 (d, *J* = 6.3 Hz, 3H), 0.961 (d, *J* = 6.9 Hz, 3H); $[\alpha]^{23}_D$ +104.6 (*c* 2.65, CH_2Cl_2), lit. $[\alpha]^{28}_D$ +112.5 (*c* 0.51, CH_2Cl_2).



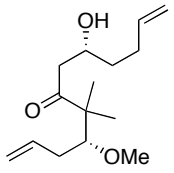
(*S*)-2-(benzoyloxy)-2-((2*R*, 5*R*, 6*R*)-2-methoxy-5,6-dimethyl-4-methylenetetrahydro-2H-pyran-2-yl)acetic acid (9)

To a solution of the methyl ester (0.08 g, 0.22 mmol) in 1, 2-dichloroethane (12.3 mL) was added Me_3SnOH (0.20 g, 1.11 mmol). The reaction was stirred at 80 °C. for 4 hours. The reaction was cooled to room temperature and aqueous $NaHSO_4$ (10 mL, 0.01 M) was added. The reaction mixture was extracted with EtOAc (3 x mL). The organic layers were combined, washed with brine (10 mL), dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The crude residue was purified via flash column chromatography (30% EtOAc in hexanes to 100% EtOAc to 10% MeOH in EtOAc) to afford the desired product (0.06 g, 82%). ^{1}H (300 MHz, $CDCl_3$) δ 8.12 (d, *J* = 8.5 Hz, 2H), 7.65-7.60 (m, 1H), 7.51-7.46 (m, 2H), 5.67 (s, 1 H), 4.94 (s, 1H), 4.86 (s, 1H), 4.09 (qd, *J* = 2.7, 6.6 Hz, 1H), 3.28 (s, 3H), 2.67 (d, *J* = 14.4 Hz, 1H), 2.55 (d, *J* = 14.4 Hz, 1H), 2.36-2.32 (m, 1H), 1.26 (d, *J* = 6.3 Hz, 3H), 1.05 (d, *J* = 7.2 Hz, 3H). $[\alpha]^{21}_D$ +133.7 (*c* 0.40, CH_2Cl_2), (lit. (antipode)[3] $[\alpha]^{25}_D$ –93.1 (*c* 1.00, CH_2Cl_2).



(*R*)-4-methoxy-3,3-dimethylhept-6-en-2-one

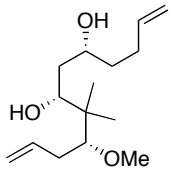
To a solution of **6** (2.03 g, 13.0 mmol) in CH_2Cl_2 (13.0 mL) at 0 °C was added 2,6-di-*tert*-butyl pyridine (4.3 mL, 19.5 mmol) and MeOTf (1.9 mL, 16.9 mmol), sequentially, and the reaction was subsequently warmed to room temperature. After 12 hours, the reaction was cooled to 0 °C and 2,6-di-*tert*-butyl pyridine (4.3 mL, 19.5 mmol) and MeOTf (1.9 mL, 16.9 mmol) were added again, and the reaction was subsequently warmed to room temperature. After 12 hours, H_2O (15 mL) was added, and the reaction was extracted with CH_2Cl_2 (3 x 15 mL). The organic layers were combined and washed with $NaHCO_3$ (satd., aq., 20 mL), brine (20 mL), dried (Na_2SO_4), filtered, and *carefully concentrated* under reduced pressure at 0 °C. The crude residue was purified via flash column chromatography (CH_2Cl_2) to afford the desired product (2.01 g, 91%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.96-5.82 (m, 1H), 5.15-5.08 (m, 1H), 5.06-5.03 (m, 1H), 3.43 (dd, *J* = 6.5, 5.5 Hz, 1H), 3.39 (s, 3H), 2.21-2.25 (m, 2H), 2.17 (s, 3H), 1.16 (s, 3H), 1.09 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 212.9, 136.0, 116.4, 86.0, 59.9, 52.4, 36.7, 26.5, 10.9, 20.2; IR (neat) 2977, 2827, 1704, 1469, 1100 cm^{-1}; LRMS (EI) *m/z* calcd. for $C_7H_{13}O_2$ $[M–C_3H_5]^+$ 129, found 129, calcd for C_5H_9O $[M–C_5H_9O]^+$ 85, found 85; $[\alpha]^{24}_D$ –9.72 (*c* 1.19, $CHCl_3$).



(4*R*, 8*R*)-8-hydroxy-4-methoxy-5,5-dimethyldodeca-1,11-dien-6-one (10)

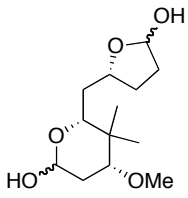
To a solution of (+)-DIP-Cl (2.83 g, 8.81 mmol) in Et_2O (6.0 mL) at 0 °C was added Et_3N (1.4 mL, 10 mmol), followed by the β-methoxy ketone (1.00 g, 5.87 mmol). The reaction mixture was stirred at 0 °C for 30 minutes, then cooled to –78 °C. 4-Pentenal (1.7 mL, 17.61 mmol) was slowly added dropwise. After 15 minutes, pH 7 (phosphate) buffer solution (16 mL), MeOH (8 mL), and hydrogen peroxide solution (aq., 30%, 8 mL) were added to the reaction at –78 °C, and the reaction was subsequently warmed to room temperature. After stirring for 20 minutes at room temperature, the reaction mixture was extracted with EtOAc (3 x 20 mL) and the organic layers were combined. The combined organic extracts were washed with brine (20 mL), aqueous Na_2SO_3 (20 mL), dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The crude residue was purified via flash column chromatography (30% EtOAc in hexanes) to afford the desired product as a yellow oil (0.93 g, 62%). ^{1}H NMR (300 MHz,

$CDCl_3$): δ 5.91-5.75 (m, 2H), 5.15-4.95 (m, 4H), 4.05-3.97 (m, 1H), 3.41 (dd, *J* = 5.4, 6.6 Hz, 1H), 3.35 (s, 3H), 3.27 (d, *J* = 3 Hz, 1H), 2.70 (dd, *J* = 2.7, 18 Hz, 1H), 2.56, (dd, *J* = 9, 18 Hz, 1H), 2.23-2.12 (m, 4 H), 1.70-1.40 (m, 2 H), 1.16 (s, 3 H), 1.09 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 217.0, 138.3, 136.0, 116.9, 114.8, 86.2, 67.1, 60.0, 52.5, 45.3, 35.6, 35.4, 29.8, 21.4, 19.8; IR (neat) 3526, 3079, 2978, 2936, 1694, 1640 cm^{-1}; HRMS (EI) *m/z* calcd. for $C_{15}H_{25}O_2$ [M–OH]$^+$ 237.1854, found 237.1843; $[\alpha]^{24}_D$ –21.0 (*c* 0.80, $CHCl_3$).



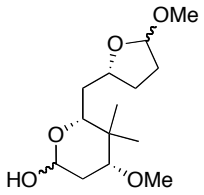
(5*R*, 7*R*, 9*R*)-9-methoxy-8,8-dimethyldodeca-1,11-diene-5,7-diol

To a solution of **10** (2.09 g, 8.2 mmol) in THF (82 mL) and MeOH (8.2 mL) at –78 °C was added Et_2BOMe (1.13 mL, 9.04 mmol). After 1 hour, $NaBH_4$ (0.93 g, 24.7 mmol) was added at –78 °C. After one hour, hydrogen peroxide solution (aq., 30%, 31.0 mL) was added *carefully dropwise*. After addition, the reaction was warmed to room temperature. After 3 hours the reaction mixture was extracted with EtOAc (3 x 40 mL), and the combined organic layers were washed with brine (50 mL) and aqueous Na_2SO_3 (40 mL). The reaction mixture was dried (Na_2SO_4), filtered and concentrated under reduced pressure to afford a crude residue. The material was purified via flash column chromatography (20% EtOAc in hexanes) to afford the desired product (1.63 g, 77%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.90-5.77 (m, 2H), 5.17- 4.95 (m, 4H), 4.46 (d, *J* = 2.3 Hz, 1H), 4.38 (s, 1H), 3.87-3.80 (m, 2H), 3.45 (s, 3H), 3.17 (dd, *J* = 3.8, 7.6 Hz, 1H), 2.43-2.13 (m, 4H), 1.66-1.40 (m, 4H), 0.98 (s, 3H), 0.86 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.3, 136.0, 116.3, 114.1, 89.6, 77.8, 71.7, 59.9, 41.4, 36.9, 36.6, 34.7, 29.4, 21.2, 20.2, IR (neat): 3440, 2977, 2253, 1641, 1470, 1389 cm^{-1}; HRMS (ESI) *m/z* calcd. For $C_{15}H_{28}O_3Na$ [M+Na]$^+$ 279.1936, found 279.1911; $[\alpha]^{24}_D$ +2.0 (*c* 0.85, $CHCl_3$).



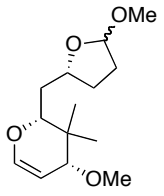
(4*R*, 6*R*)-6-(((*R*)-5-hydroxytetrahydrofuran-2-yl)methyl)-4-methoxy-5, 5-dimethyltetrahydro-2H-pyran-2-ol (6)

To a solution of the diol (0.92 g, 3.6 mmol) in *p*-dioxane (18 mL) and H_2O (18 mL) at room temperature were added 2,6-lutidine (0.77 g, 7.2 mmol), OsO_4 (0.02 g, 0.07 mmol), and $NaIO_4$ (3.08 g, 14.4 mmol). After 4 h, the chalky reaction mixture was extracted with EtOAc (3 x 50 mL). The aqueous layer was separated and extracted again with EtOAc (2 x 200 mL). The organic layers were combined, dried (Na_2SO_4), filtered and concentrated under reduced pressure to afford a crude residue. The material was purified via flash chromatography (30% EtOAc in hexanes to 50% EtOAc in hexanes to 70% EtOAc in hexanes to 100% EtOAc to 10% MeOH in EtOAc) to afford a diastereomeric mixture of the desired product as a viscous oil (0.77 g, 82%); ^{13}C (75 MHz): δ 98.6, 98.4, 97.9, 94.6, 94.5, 91.8, 91.6, 83.3, 80.1, 80.0, 79.8, 79.7, 79.3, 78.4, 78.1, 74.7, 73.8, 60.2, 57.1, 57.1, 56.9, 38.8, 38.7, 38.0, 35.7, 34.7, 34.3, 33.6, 33.3, 33.1, 32.2, 32.1, 30.8, 30.6, 30.3, 30.1, 29.3, 22.3, 22.2, 20.8, 14.0, 12.9, 12.0; IR (neat): 3404, 2962, 1737, 1443, 1244 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{13}H_{24}O_5Na$ [M+Na]$^+$ 283.1521, found 283.1537; $[\alpha]^{23}_D$ +16.6 (*c* 0.79, MeOH).



(4*R*, 6*R*)-4-methoxy-6-(((*R*)-5-methoxytetrahydrofuran-2-yl)methyl)-5, 5-dimethyltetrahydro-2H-pyran-2-ol

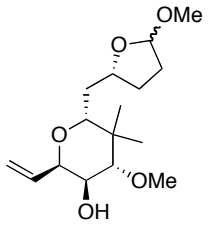
To a solution of **6** (0.60 g, 2.31 mmol) in THF (12.0 mL) and MeOH (12.0 mL) at room temperature was added PPTS (0.17 g, 0.69 mmol). After 40 minutes the reaction was cooled to 0 °C and aqueous $NaHCO_3$ (10 mL) was added. The mixture was subsequently warmed to room temperature then extracted with EtOAc (3 x 10 mL). The combined organic layers were washed with brine (10 mL), dried (Na_2SO_4), filtered, and concentrated under reduced pressure to afford a viscous yellow residue which was used without further purification. ^{13}C NMR (75 MHz, $CDCl_3$): δ 104.8, 104.8, 104.7, 104.6, 94.6, 91.9, 83.6, 83.5, 80.0, 79.9, 79.1, 78.8, 78.12, 78.06, 76.0, 75.7, 72.9, 72.8, 57.2, 57.1, 54.5, 54.4, 54.3, 38.7, 38.6, 37.9, 37.9, 35.5, 35.2, 34., 34.1, 34.0, 33.1, 33.0, 31.9, 31.0, 29.0, 28.8, 28.6, 28.5, 22.4, 22.3, 22.3, 22.2, 13.0, 13.0, 12.1, 12.1; IR (neat): 34.11, 2962, 2829, 2246, 1733, 1443, 1367, 1244 cm^{-1}; HRMS (EI) *m/z* calcd. for $C_{14}H_{26}O_5Na$ [M+Na]$^+$ 297.1678, found 297.1705; $[\alpha]^{23}_D$ +30.1 (*c* 0.60, MeOH).



(2*R*,4*R*)-4-methoxy-2-(((*R*)-5-methoxytetrahydrofuran-2-yl)methyl)-3,3-dimethyl-3,4-dihydro-2H-pyran (11)

Crude hemiacetal (0.6 g, 2.31 mmol) was dissolved in CH_2Cl_2 (14 mL) and cooled to –78 °C, whereupon ^{i}Pr$_2$NEt (2.5 mL, 14 mmol) and trifluoroacetic anhydride (0.69 mL, 4.9 mmol) were added, sequentially. The reaction mixture was stirred for 10 minutes at –78 °C then warmed to 0 °C and stirred for 1 hour. The reaction was heated to 40 °C. After 2 hours, the mixture was cooled to room temperature and brine was added (10 mL). The reaction mixture was extracted with CH_2Cl_2 (3 x 12 mL), and the combined organic layers were washed with aqueous $NaHCO_3$ (10 mL) and brine (15 mL), then dried (Na_2SO_4), filtered and concentrated under reduced pressure. The crude residue was purified via flash chromatography (the column was washed with 3% Et_3N in hexanes, eluent: 30% EtOAc in hexanes) to afford the desired product as a mixture of inseparable isomers (0.55 g, 92%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.33 (d, *J* = 6.3 Hz, 1H), 5.04 (dd, *J* = 1.8, 5.1 Hz, 0.5H), 4.96 (d, *J* = 4.2 Hz, 0.5H), 4.81 (ddd, *J* = 2.4, 4.8, 6.3 Hz, 1H), 4.31-4.21 (m, 1 H), 3.61 (d, *J* = 10.8 Hz, 1H), 3.46 (br s, 1H), 3.37 (s, 3H), 3.35 (s, 1.5H), 3.34 (s, 1.5H), 2.19-1.80 (m, 4H), 1.72-1.4 (m, 2H), 0.96 (s, 3H), 0.89 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 143.8, 104.7, 104.6, 100.0, 100.0, 80.3, 80.2, 80.1, 78.1, 75.3, 56.9, 54.4, 54.1, 35.4, 35.2, 35.1, 33.5, 33.0, 31.9, 28.7, 28.4, 23.4, 13.7; IR (neat): 3056, 2979, 2934, 2825,

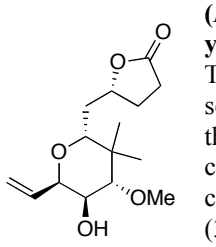
1648, 1464, 1367, 1266, 1195, 1100, 1042 cm^{-1}; HRMS (EI) *m/z* calcd. for $C_{14}H_{24}O_4$ $[M]^+$ 256.1675, found 256.1675; $[\alpha]^{23}_D$ -30.0 (*c* 1.02, $CHCl_3$).



(2*R*, 3*S*, 4*S*, 6*R*)-4-methoxy-6-(((*R*)-5-methoxytetrahydrofuran-2-yl)methyl)-5, 5-dimethyl-2-vinyltetrahydro-2H-pyran-3-ol

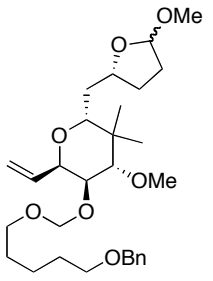
To a solution of **11** (0.47 g, 1.9 mmol) in CH_2Cl_2 (19 mL) at 0 °C was slowly added a solution of dimethyl dioxirane[4] (0.07 M in CH_2Cl_2, 75.0 mL) in 3 portions. After the final addition was complete, the reaction was concentrated under reduced pressure at 0 °C, (using argon to backfill the rotary evaporator after the vacuum was removed), until approximately 5 mL of solvent remained. The crude solution was diluted in CH_2Cl_2 (31.0 mL) and added dropwise over 15 minutes to a stirring solution of trivinylalane[5] (0.1 M, 111 mL) at -78 °C. The reaction was stirred for 2 hours at –78 °C, then warmed to room temperature and stirred for an additional 30 minutes. Afterwards, H_2O (30 mL) and aqueous Na K tartrate (100 mL) were added and the reaction mixture was stirred for 2 hours at room temperature. The resulting mixture was extracted with CH_2Cl_2 (3 x 40 mL), and the combined organic layers were washed with brine (30 mL), dried (Na_2SO_4), filtered, and concentrated under reduced pressure to afford the desired product in quantitative yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.21-6.12 (m, 1H), 5.51-5.41 (m, 2H), 5.03 (br d, *J* = 3.3 Hz, 0.5H), 4.94 (br d, *J* = 3.9 Hz, 0.5H), 4.56-4.501 (m, 1H) 4.3-4.19 (m , 1H), 3.91-3.80 (m, 1H), 3.60 (s, 3H), 3.44-3.34 (m, 4H), 2.82 (d, *J* = 9.9 Hz, 1H), 2.08-1.62 (m, 6H), 0.95 (s, 1.5H), 0.94 (s, 1.5H), 0.89 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 132.5, 132.3, 119.3, 119.1, 104.7, 104.5, 87.2, 87.1, 78.2, 75.8, 75.8, 75.7, 74.5, 74.1, 69.4, 67.7, 62.3, 54.3, 54.1, 41.2, 41.1, 36.5, 34.5, 33.0, 31.8, 28.9, 28.5, 25.4, 23.2, 23.1, 13.7, 13.6; HRMS (EI) *m/z* calcd. for $C_{15}H_{25}O_4$ $[M–OMe]^+$ 269.1752, found 269.1745.

The following reaction was conducted to confirm the stereoselectivity of the epoxidation/nucleophilic opening sequence.



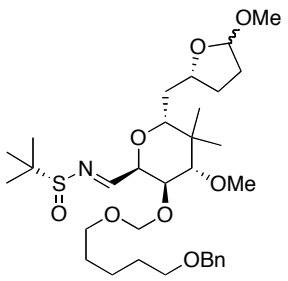
(*R*)-5-(((2*R*,4*S*,5*S*,6*R*)-5-hydroxy-4-methoxy-3, 3-dimethyl-6-vinyltetrahydro-2H-pyran-2-yl)methyl)dihydrofuran-2(3H)-one

To a solution of the vinyl tetrahydropyran (0.02 g, 0.07 mmol) in CH_2Cl_2 (1.34 mL) at 0 °C were sequentially added *m*-CPBA (0.02 g, 0.09 mmol) and $BF_3{\cdot}Et_2O$ (0.018 mL, 0.15 mmol). After 2 minutes, the reddish-orange reaction mixture was warmed to room temperature. After 20 minutes, the reaction was cooled to 0 °C, and Et_3N (0.050 mL) was added. The reaction was stirred at 0 °C for 10 minutes then concentrated under reduced pressure. The crude residue was purified via flash column chromatography (30% hexanes in EtOAc) to afford the desired product. ^{1}H NMR (300 MHz, $CDCl_3$): 6.23-6.12 (m, 1H), 5.45 (d, 1H, *J* = 9.6 Hz), 5.43 (d, *J* = 18.3 Hz, 1H), 4.71-4.65 (m, 1H), 4.49 (dd, *J*=5.4, 6.3 Hz, 1H), 3.89 (dd, 6.6, 9.6 Hz, 1H), 3.60 (s, 3H), 3.44 (app. d, *J* = 10.5 Hz, 1H), 2.85 (d, *J* = 9.9 Hz, 1H), 2.57-2.52 (m, 2H), 2.36-2.26 (m, 1 H), 2.09-1.83 (m, 2H), 1.63-1.59 (m, 2H), 0.96 (s, 3H), 0.91 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 177.0, 132.2, 120.5, 87.1, 78.8, 75.9, 73.0, 69.5, 62.6, 41.2, 34.1, 28.8, 27.3, 23.5, 14.1; HRMS (EI) *m/z* calcd. for $C_{15}H_{24}O_5$ $[M]^+$ 284.1624, found 284.1621



(2*R*, 4*S*, 5*S*, 6*R*)-5-((4-(benzyloxy)butoxy)methoxy)-4-methoxy-2-(((R)-5-methoxytetrahydrofuran-2-yl)methyl)-3, 3-dimethyl-6-vinyltetrahydro-2H-pyran

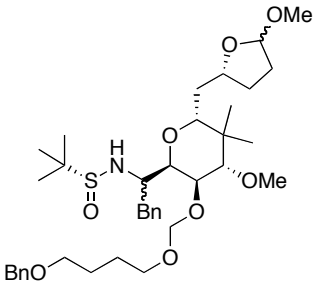
To a solution of the vinyl tetrahydropyran (0.042 g, 0.14 mmol) in 1,2-dichloroethane (0.5 mL) was added ^{i}Pr$_2$NEt (0.06 mL, 0.35 mmol). The solution was stirred for 30 minutes, then a heterogeneous mixture of benzyloxybutoxymethyl chloride[6] (0.08 g, 0.35 mmol) and KI (0.06 g, 0.35 mmol) in 1,2-dichloroethane (0.5 mL) was added. The reaction was heated to 50 °C and stirred overnight. The mixture was cooled to room temperature, and H_2O (1 mL) was added. The reaction mixture was extracted with EtOAc (3 x 2 mL), and the combined organic layers were washed with brine (2 mL), dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The crude residue was purified via flash chromatography (10 to 40% EtOAc in hexanes) to afford the desired product (0.053 g, 77%) ^{1}H NMR (300 MHz, $CDCl_3$): 7.25-.7.21 (m, 5H), 6.11-6.05 (m, 1H), 5.48-5.37 (m, 2H), 5.04-5.03 (m, 0.5H), 4.95-4.93 (m, 0.5H), 4.80 (d, *J* = 6.6 H, 1H), 4.73 (d *J* = 6.6 Hz, 1H), 4.60-4.51 (m, 4H), 4.31-.4.15 (m, 1H), 3.79-3.74 (m, 1H), 3.56-3.38 (m, 6H), 3.31-3.24 (m, 4H), 2.81-2.76 (m, 1H), 2.03-1.20 (m, 10H), 0.83 (s, 6H), ^{13}C NMR (75 MHz, $CDCl_3$): δ 138.5, 133.5, 133.2, 128.2, 127.5, 127.4, 119.1, 119.0, 104.8, 104.6, 95.7, 85.7, 85.6, 78.3, 76.3, 75.8, 74.9, 74.4, 74.0, 72.7, 70.0, 67.8, 61.9, 54.5, 54.2, 41.5, 41.4, 36.8, 34.8, 33.1, 31.9, 29.1, 28.7, 26.4, 26.3, 23.0, 22.9, 13.8, 13.7; IR (neat) 3019, 2400, 1215, 1100, 1040, 757 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{28}H_{44}O_7Na$ $[M+Na]^+$ 515.2985, found 515.2963; $[\alpha]^{24}_D$ +32.6 (*c* 1.00, $CHCl_3$).



(E)-*N*-(((2*R*,3*R*,4*S*,6*R*)-3-((4-(benzyloxy)butoxy)methoxy)-4-methoxy-6-(((*R*)-5-methoxytetrahydrofuran-2-yl)methyl)-5,5-dimethyltetrahydro-2H-pyran-2-yl)methylene)-2-methylpropane-2-sulfinamide (12)

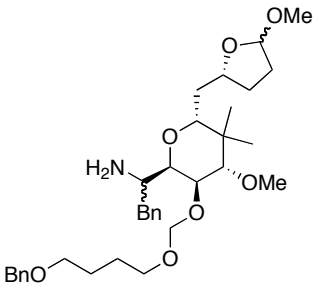
O_3 was bubbled into a solution of the protected vinyl tetrahydropyran (0.50 g, 1.02 mmol) in CH_2Cl_2 (10 mL) at –78 °C in 20 second intervals until all starting material was observed to be consumed by TLC (approximately 3 minutes total bubbling time). The solution was aerated with N_2 for 10 minutes, then PPh_3 (0.80 g, 3.1 mmol) was added to the reaction mixture at –78 °C. The solution was subsequently warmed to room temperature. After stirring for 1 hour at room temperature, the reaction mixture was concentrated under reduced pressure and then dissolved in

THF (13.4 mL). To this solution at room temperature was added $Ti(O^iPr)_4$ (1.56 mL, 5.20 mmol), followed by (*R*)-*tert*-butylsulfinamide (0.37 g, 3.06 mmol). The reaction was stirred overnight. The following morning, brine (20 mL) was added to the reaction mixture. The heterogeneous mixture was filtered through a short pad of Celite, and the filter cake was washed with EtOAc. The filtrate was washed with brine (10 mL), dried (Na_2SO_4), and concentrated under reduced pressure. The crude yellow to translucent oil was purified via flash column chromatography (30 to 50% EtOAc in hexanes) to afford the desired product as a pale yellow oil (0.34 g, 55%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.37 (d, *J* = 2.7 Hz, 1H), 7.38-7.29 (m, 5H), 5.03-5.00 (m, 0.57H), 4.93 (app. d, 0.43 H), 4.84 (d, *J* = 6.9 Hz, 1H), 4.79-4.73 (m, 1H), 4.77 (d, *J* = 6.9 Hz, 1H), 4.50 (s, 2H), 4.65-4.23 (m, 1H), 4.05-3.98 (m, 1H), 3.70-3.6 (m, 1H), 3.55-3.45 (m, 7H), 3.33 (m, 3H), 2.81-2.76 (m, 1H), 2.2-1.4 (m, 10H), 1.27-1.22 (m, 9H), 0.90 (s, 6H);^{13}C NMR (75 MHz, $CDCl_3$): δ 166.6, 166.5, 138.5, 128.2, 127.4, 127.3, 104.8, 104.7, 96.0, 86.2, 86.2, 78.2, 76.5, 76.3, 76.0, 75.9, 75.4, 70.7, 69.8, 68.1, 62.0, 57.1, 57.1, 54.5, 54.2, 41.4, 41.3, 36.8, 34.8, 33.0, 32.0, 29.6, 29.3, 28.9, 26.4, 26.3, 22.7, 22.5, 22.3, 13.4; IR (neat): 3052, 2933, 2248, 1620, 1454, 1364, 1265, 1100, 1039, 909 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{31}H_{51}NO_8NaS$ $[M+Na]^+$ 620.3233, found 620.3267; $[\alpha]^{24}_D$ –10.7 (*c* 0.58, $CHCl_3$).



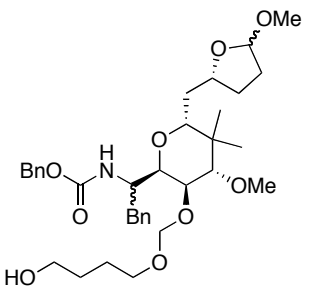
_N_-(1-((2R,3*R*,4*S*,6*R*)-3-((4-(benzyloxy)butoxy)methoxy)-4-methoxy-6-(((R)-5-methoxytetrahydrofuran-2-yl)methyl)-5, 5-dimethyltetrahydro-2H-pyran-2-yl)-2-phenylethyl)-2-methylpropane-2-sulfinamide

To a solution of **12** (0.78 g, 1.31 mmol) in CH_2Cl_2 (33.0 mL) at –78 °C was slowly added benzylmagnesium choride (18.0 mL, 1M in Et_2O) dropwise. After addition was complete, H_2O (20 mL) was added to the reaction mixture and the solution was warmed to 0 °C. The reaction mixture was extracted with CH_2Cl_2 (3 x 20 mL). The combined organic extracts were washed with brine (20 mL), dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The crude residue was purified via flash column chromatography (30% EtOAc in hexanes to 100% EtOAc) to afford the desired product as a ~1:1 mixture of inseparable isomers (0.66 g, 73%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.34-7.18 (m, 10H), 5.30-5.19 (m, 1H), 5.03-4.95 (m, 1H), 4.77-4.67 (m, 2H), 4.6-4.5 (m, 1H), 4.49 (s, 2H), 4.38-4.2 (m, 1H), 4.31 (m, 1H), 3.95-3.80 (m, 2H), 3.54-3.23 (m, 9H), 3.19-3.03 (m, 2H), 2.90-2.75 (m, 1H), 2.38-1.78 (m, 4H), 1.68-1.26 (m, 7H), 1.21-0.80 (m, 15H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 138.4, 138.2, 138.0, 136.8, 136.7, 130.6, 129.6, 129.4, 129.3, 128.1, 127.6, 127.4, 126.2, 126.0, 104.9, 104.7, 104.6, 96.4, 95.3, 84.1, 84.0, 78.8, 78.4, 78.2, 76.4, 75.6, 73.8, 72.7, 72.1, 71.8, 71.0, 69.8, 68.4, 68.3, 68.0, 61.5, 60.5, 59.7, 55.7, 55.5, 55.3, 55.2, 54.5, 54.2, 54.1, 41.2, 41.0, 39.1, 37.3, 37.1, 36.3, 36.1, 35.3, 34.3, 33.8, 33.0, 31.9, 31.8, 29.1, 29.1, 29.0, 25.9, 2.6, 23.8, 23.6, 22.4, 22.1 ;IR (neat): 3252, 3029, 2947, 2360, 1454, 1364, 1268, 1042, 953 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{38}H_{59}NO_8NaS$ $[M+Na]^+$ 712.3859, found 712.2859; $[\alpha]^{25}_D$ –22.6. (*c* 0.53, $CHCl_3$).



1-((2*R*, 3*R*, 4*S*, 6*R*)-3-((4-(benzyloxy)butoxy)methoxy)-4-methoxy-6-(((*R*)-5-methoxytetrahydrofuran-2-yl)methyl)-5, 5-dimethyltetrahydro-2H-pyran-2-yl)-2-phenylethanamine

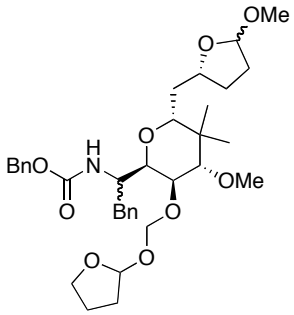
To a solution of the sulfinamide (1.60 g, 2.39 mmol) in MeOH (120 mL) at 0 °C was added 4M HCl in *p*-dioxane (6.0 mL, 24 mmol). The reaction was stirred for 10 minutes at 0 °C then was warmed to room temperature. After 40 minutes the reaction was cooled to 0 °C and 10% NaOH (aq. w/v) was added until precipitation occurred. The reaction mixture was extracted with EtOAc (3 x 40 mL), and the combined organic layers were washed with brine (30 mL). The organic extracts were dried (Na_2SO_4), filtered and concentrated under reduced pressure. The crude residue was purified via flash column chromatography (the column was washed in 3% Et_3N in hexanes, eluent: 50% EtOAc in hexanes to 100% EtOAc) to afford the desired product (1.13 g, 80%). ^{1}H NMR (300 MHz, $CDCl_3$): 7.34-7.21 (m, 10H), 5.03-5.01 (m, 0.64H), 4.94 (app d, 0.36H), 4.83 (d, *J* = 6.6 Hz, 1H), 4.77-4.48 (m, 3H), 4.49-4.48 (m, 2H), 4.32-4.28 (m, 1H), 4.01-3.55 (m, 5H), 3.49-3.45 (m, 3H), 3.34-3.29 (m, 3H), 3.22-3.17 (m, 1H), 3.08-3.04 (m, 1H), 2.6-1.4 (m, 12H), 1.14-1.07 (m, 3H), 0.95-0.93 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 139.4, 139.3, 139.2, 139.1, 138.3, 129.5, 129.2, 129.0, 129.0, 128.2, 128.1, 127.8, 127.3, 127.2, 126.0, 125.6, 104.8, 104.7, 104.6, 104.5, 95.4, 95.3, 95.1, 84.8, 84.3, 84.1, 78.7, 78.2, 77.2, 76.3, 75.7, 74.9, 74.5, 74.2, 73.7, 73.3, 73.5, 72.5, 69.7, 69.7, 68.1, 60.7, 60.4, 60.1, 54.5, 54.3, 54.1, 52.2, 51.0, 50.9, 40.1, 39.9, 39.1, 38.4, 36.4, 34.5, 33.0, 31.7, 29.7, 29.2, 28.9, 28.8, 28.6, 26.3, 26.2, 25.6, 25.1, 24.6, IR (neat): 3364, 2941, 2830, 2525, 1651, 1454, 1098, 1029 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{34}H_{52}NO_7$ $[M+H]^+$ 586.3744, found 586.3719; $[\alpha]^{23}_D$ +6.15 (*c* 0.54, $CHCl_3$).



Benzyl 1-((2*R*, 3*R*, 4*S*, 6*R*)-3-((4-hydroxybutoxy)methoxy)-4-methoxy-6-(((R)-5-methoxytetrahydrofuran-2-yl)methyl)-5, 5-dimethyltetrahydro-2H-pyran-2-yl)-2-phenylethylcarbamate (13)

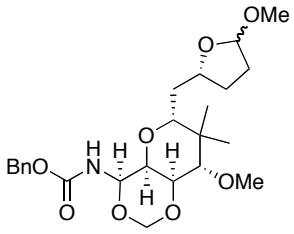
To a solution of the amine (0.13 g, 0.22 mmol), in MeOH (20 mL) was added glacial acetic acid (0.10 mL, 1.7 mmol) and Pd/C (0.10 mg, 10 wt. %). The reaction vessel was evacuated, and then placed under H_2 (1 atm). After stirring overnight the reaction mixture was filtered through a pad of celite, and the filter cake was rinsed copiously with EtOAc. The organic filtrate was washed with aqueous $NaHCO_3$ (10 mL) and brine (20 mL). The aqueous layers were combined and back-extracted with EtOAc (3 x 20 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated under reduced pressure. To a solution of crude amino alcohol (0.11 g,

0.22 mmol) in THF/H_2O (1:1, 4.0 mL) were sequentially added $NaHCO_3$ (0.22 g, 0.27 mmol) and benzyl chloroformate (0.05 g, 0.27 mmol). After 2 hours the reaction mixture was diluted with EtOAc (10 mL) and H_2O (3 mL). The reaction mixture was extracted with EtOAc (3 x 5 mL). The combined organic layers were washed with brine (5 mL), dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The crude residue was purified via flash column chromatography (50 to 70% EtOAc in hexanes to 100% EtOAc) to afford the desired product (0.080 g, 70%, 2 steps) ^{1}H (300 MHz, $CDCl_3$): δ 7.31-7.13 (m, 10H), 6.42 (br s, 0.32, 1H), 5.98 (br s, 0.68H), 5.46 (app d, 0.62H), 5.35 (app d, 0.38H), 5.13-5.06 (m, 0.66H), 5.02-4.91 (m, 2.85H), 4.82-4.74 (m, 1.22H), 4.65-4.63 (m, 1.5H), 4.57-4.42 (m, 1.36H), 4.40-4.29 (m, 0.41H), 4.26-4.05 (m, 1.07H), 3.92-3.77 (m, 1.15H), 3.67-3.54 (m, 2.53H), 3.46-3.27 (m, 6.06H), 3.20-3.00 (m, 1.43H), 3.00-2.72 (m, 1.76H), 2.70-2.14 (m, 1.22H), 2.12-1.78 (m, 3.15H), 1.63-1.31 (m, 5.63H), 1.25 (s, 1.35H), 1.09 (s, 1.07H), 1.00 (s, 0.96H), 0.90-0.85 (m, 2.62H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 156.2, 156.0, 155.7, 137.6, 137.5, 137.1, 136.8, 130.0, 130.0, 129.6, 129.6, 129.0, 129.0, 128., 128.2, 128.1, 127.9, 127.8, 127.7, 127.7, 126.2, 126.1, 104.9, 104.7, 96.1, 96.0, 95.1, 84.4, 84.0, 83.9, 83.7, 80.0, 78.6, 77.1, 75.7, 68.6, 68.1, 66.1, 65.9, 62.3, 62.2, 60.8, 59.9, 59.7, 54.5, 54.2, 54.1, 51.8, 51.2, 39.8, 38.3, 37.7, 37.0, 36.6, 35.1, 34.6, 34.0, 33.1, 32.7, 31.8, 31.5, 29.8, 29.5, 29.4, 29.4, 39.3, 39.3, 29.2, 28.9, 28.8, 26.2, 26.1, 24.5, IR (neat): 3432, 2936, 2360, 1702, 1496, 1453, 1365, 1096, 1038 cm^{-1}; HRMS (ESI) calcd. for $C_{35}H_{51}NO_9Na$ $[M+Na]^+$ 652.3462, found 652.3436; $[\alpha]^{21}_D$ +19.6 (*c*, 1.40 $CHCl_3$).



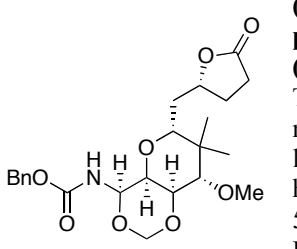
Benzyl 1-((2*R*,3*R*,4*S*,6*R*)-4-methoxy-6-(((*R*)-5-methoxytetrahydrofuran-2-yl)methyl)-5, 5-dimethyl-3-((tetrahydrofuran-2-yloxy)methoxy)tetrahydro-2H-pyran-2-yl)-2-phenylethylcarbamate (14)

To a solution of the hydroxy carbamate (0.13 g, 0.21 mmol) in cyclohexane (14.0 mL) at room temperature were added (diacetoxyiodo)benzene (0.150, 0.46 mmol) and I_2 (0.04 g, 0.33 mmol). The reaction was stirred vigorously for 20 minutes, and then irradiated (medium pressure Hg lamp, Pyrex filtration). After 2 hours the reaction mixture was diluted with EtOAc (14.0 mL) and washed with $Na_2S_2O_3$ (satd., aq., 15 mL) followed by brine (15 mL). The aqueous layers were combined and back-extracted with EtOAc (3 x 10 mL). The combined organic layers were dried (Na_2SO_4) filtered, and concentrated under reduced pressure to afford a crude yellow oil. The crude residue was purified via flash column chromatography (the column was washed with 3% Et_3N in hexanes, then eluted with 30 to 50% EtOAc in hexanes) to afford the desired product (0.10 g, 80%).



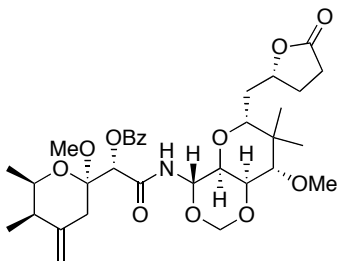
2-((4a*S*, 6*R*, 8*S*, 8a*R*)-8-methoxy-6-(((*R*)-5-methoxytetrahydrofuran-2-yl)methyl)-7, 7-dimethylhexahydropyrano[3,2-d][1,3]dioxin-4-ylamino)-1-phenylethanone (17)

To a solution of **14** (44 mg, 70 μmol) in 1,2-dichloroethane (9.0 mL) and toluene (1.4 mL) at room temperature was added $NMQPF_6$ (0.001 mg, 4.2 μmol), NaOAc (88 mg), $Na_2S_2O_3$ (88 mg) and powdered 4Å mol. sieves (88 mg). The reaction mixture was stirred at room temperature for 30 minutes, and then irradiated (medium pressure Hg lamp, Pyrex filtration) for 4 hours while air was gently bubbled through the solution. *CAUTION: While we have never had a problem with this reaction, appropriate precautions should be taken any time that oxygen is used in the presence of a powerful lamp.* The crude reaction mixture was then filtered through a short pad of Celite, and the filter cake was washed copiously with EtOAc. The filtrate was concentrated under reduced pressure and the crude residue was purified via flash column chromatography (20% to 50% EtOAc in hexanes) to afford the desired product as a 2:1 mixture of inseparable diastereomers (24 mg, 73%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.39-7.30 (m, 5H), 6.85 (d, *J* = 7.8 Hz, 0.33H), 6.73 (d, *J* = 8.1 Hz, 0.67H), 5.18-5.07 (m, 4.5H), 4.93 (d, *J* = 3.9 Hz, 0.5H), 4.85 (d, *J* = 6.6 Hz, 1H), 4.12-4.02 (m, 1H), 3.83-3.64 (m, 3H), 3.39 (s, 3H), 3.16 (s, 3H), 2.93 (d, *J*=2.4 Hz, 1H), 2.40-1.40 (m, 6H), 1.24 (s, 3H), 0.92 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.8, 136.3, 136.1, 128.5, 128.4, 105.1, 105.0, 91.3, 83.8, 83.7, 81.6, 81.5, 80.6, 80.0, 77.7, 77.2, 72.9, 67.1, 66.9, 61.4, 61.3, 59.4, 59.3, 54.4, 54.3, 36.7, 36.6, 34.7, 32.9, 31.6, 29.9, 29.8, 27.7, 27.6; IR (neat): 3054, 2986, 2306, 1729, 1512, 1422, 1265 cm^{-1}; HRMS (ESI) calcd. for $C_{24}H_{35}NO_8Na$ $[M+Na]^+$ 488.2260, found 488.2268. $[\alpha]^{23}_D$ −8.5 (*c* 0.61, $CHCl_3$).



(5*R*)-5-(((4a*S*, 6*R*, 8*S*, 8a*R*)-8-methoxy-7, 7-dimethyl-4-(2-oxo-2-phenylethylamino)hexahydropyrano[3,2-d][1,3]dioxin-6-yl)methyl)dihydrofuran-2(3H)-one (18)

To a solution of **17** (0.13 g, 0.27 mmol) in acetone (5 mL) at 0 °C was added Jones reagent (0.20 mL, 2.67M). After addition, the reaction was complete by TLC analysis. The reaction mixture was loaded directly onto a column and purified via flash column chromatography (50 to 70% EtOAc in hexanes) to afford the desired product (80 mg, 64%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.60-7.0 (m, 5H), 6.16 (d, *J* = 9.0 Hz, 0.88H), 5.95 (d, *J* = 10.2 Hz, 0.12, 1H) 5.21-5.09 (m, 4 H), 4.89 (d, *J* = 6.6 Hz, 0.16H), 4.83 (d, *J* = 6.6 Hz, 0.84H), 4.54-4.44 (m, 0.74H), 4.38-4.25 (m, 0.26H), 3.75 (br s, 2H), 3.66 (dd, *J* = 2.7, 12.3 Hz, 1H), 3.91 (s, 2.59H), 2.98 (s, 0.41H), 2.95 (d, *J* = 2.1 Hz, 1H), 2.65-2.59 (m, 1H), 2.52-2.47 (m, 2H), 2.41-2.29 (m, 1H), 1.93-1.79 (m, 1H), 1.16-1.58 (m, 1H), 1.26 (s, 1.13H), 1.24 (s, 1.87H), 0.94 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 176.6, 155.5, 136.1, 128.7, 128.5, 128.1, 91.4, 83.4, 79.7, 79.5, 79.2, 78.8, 72.6, 67.2, 61.7, 59.3, 36.4, 33.4, 28.6, 28.1, 27.3, 22.5; IR (neat) 3019, 2400, 1771, 1730, 1514, 1423, 1024, 929 cm^{-1}; HRMS (ESI) calcd. for $C_{23}H_{31}NO_8Na$ $[M+Na]^+$ 472.1947, found 472.1914, $[\alpha]^{23}_D$ −1.4 (*c* 0.63, $CHCl_3$).



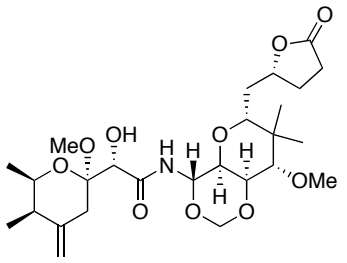
C_7-Benzoyl Theopederin D (19)

To a solution of **18** (0.016 g, 0.037 mmol) in EtOAc at room temperature was added Pd/C (3 mg, 10 wt%). The reaction vessel was evacuated and backfilled with H_2 (g) 3 times before being left under H_2 (g) atmosphere. After 40 minutes, the reaction was complete by TLC. The reaction mixture was filtered through a short pad of celite and the filter cake was washed several times with EtOAc. The filtrate was concentrated under reduced pressure to afford a colorless oil which was used immediately without further purification.

To a solution of **8** (0.025 g, 0.075 mmol) in CH_2Cl_2 (1.60 mL) was added pyridine (0.31 mL, 0.62 M in CH_2Cl_2, dried over $MgSO_4$) and $SOCl_2$ (0.31 mL, 0.48 M, dried over $MgSO_4$) at room temperature. The reaction was stirred for 20 minutes then concentrated under reduced pressure. The material was used immediately and without further purification.

The crude acid chloride was dissolved in CH_2Cl_2 (0.75 mL) and cooled to 0 °C. DMAP (0.009 g, 0.075 mmol) was added, and the reaction was stirred for 5 minutes. A solution of the crude amino trioxadecalin in CH_2Cl_2 (0.37 mL) was added to the reaction mixture. The reaction was stirred at 0 °C for 5 minutes and then warmed to room temperature. After 4 hours the reaction mixture was directly purified via PTLC (50% EtOAc in hexanes) followed by a second prep plate, (20% EtOAc in benzene, 2 elutions) to afford the desired products as a 1:1 mixture of separable diastereomers at the C_{10} position (0.008 g, 40%). C_7-benzoyl-theopederin D (**19**, faster eluting): ^{1}H NMR (600 MHz, C_6D_6): δ 8.25 (dd, *J* = 1.5, 8.1 Hz, 2H), 7.09-7.00 (m, 3H), 5.84 (s, 1H), 5.76 (app t, *J* = 9.6 Hz, 1H), 4.82 (br s, 1H), 4.79 (br s, 1H), 4.58 (d, *J* = 6.6 Hz, 1H), 4.56-4.52 (m, 1H), 4.50 (d, *J* = 6.6 Hz, 1H), 4.22 (dd, *J* = 6.6, 10.2 Hz, 1H), 3.81 (qd, *J* = 3.0, 6.0 Hz, 1H), 3.65 (dd, *J* = 7.2, 10.2 Hz, 1H), 3.26 (s, 3H), 3.16 (d, *J* = 10.2 Hz, 1H), 2.93 (d, *J* = 10.2 Hz, 1H), 2.92 (s, 3H), 2.77 (br d, *J* = 13.8 Hz, 1H), 2.71 (d, *J* = 13.8 Hz, 1H), 2.45-2.37 (m, 1H), 2.33 (dt, *J* = 11.4, 16.8 Hz, 1H), 2.14 (ddd, *J* = 3.0, 9.0, 12.6 Hz, 1H), 1.93-1.85 (m, 1H), 1.90 (qd, *J* = 2.4, 7.2 Hz, 1H), 1.21-1.17 (m, 2H), 1.04 (d, *J* = 7.2 Hz, 3H), 0.89 (d, *J* = 6.6 Hz, 3H), 0.75 (s, 3H), 0.68 (s, 3H); ^{13}C NMR (150 MHz, C_6D_6): δ 175.9, 167.0, 165.4, 144.9, 133.6, 130.1, 129.8, 127.6, 111.5, 99.8, 86.6, 78.7, 78.0, 75.2, 74.9, 74.1, 73.0, 71.9, 69.9, 61.3, 48.4, 41.4, 41.2, 45.6, 34.6, 28.8, 28.2, , 22.8, 17.6, 12.2; IR (neat): 3354, 2962, 2924, 2854, 2360, 2339, 1770, 1727, 1526, 1453, 1413, 1261 cm^{-1}; HRMS (ES) calcd. for $C_{33}H_{45}NO_{11}Na$ $[M+Na]^+$ 654.2890 found 654.2877; $[\alpha]^{22}_D$ +29.0 (*c*, 0.1, EtOAc).

C_7-*O*-Bz-C_{10}-*epi*-theopederin D **(20,** slower eluting): ^{1}H NMR (300 MHz, C_6D_6): δ 8.36-8.33 (m, 2 H), 8.13 (d, *J* = 9.3 Hz, 1 H), 7.08-6.97 (m, 3 H), 6.20 (s, 1 H), 5.23 (dd, *J* = 1.8, 9.3 Hz, 1 H), 4.87 (br t, *J* = 1.8 Hz, 1 H), 4.84 (d, *J* = 6.3 Hz, 1 H), 4.83 (br t, *J* = 1.8 Hz, 1 H), 4.32 (d, *J* = 6.6 Hz, 1 H), 4.31-4.27 (m, 1 H), 4.11-4.00 (m, 1 H), 4.00 (qd, *J* = 2.7, 6.6 Hz, 1 H), 3.42 (dd, *J* = 2.7, 11.4 Hz, 1 H), 3.17 (s, 3 H), 3.14 (br s , 1 H), 3.05 (br d, *J* = 14.7 Hz, 1 H), 2.90 (s, 3 H), 2.84 (d, *J* = 14.1 Hz, 1 H), 2.66 (d, *J* = 1.8 Hz, 1 H), 2.30 (ddd, *J* = 3.6, 7.5, 15.0, Hz, 2 H), 2.09 (qd, *J* = 2.7, 7.2 Hz, 1 H), 2.00 (d, *J* = 10.2 Hz, 1 H), 1.64-1.54 (m, 1 H) 1.98 (dd, *J* = 1.5 Hz, 9.6 Hz, 1 H), 1.39-1.15 (m, 2 H), 1.31-1.29 (m, 6 H), 1.11 (d, *J* = 6.3 Hz, 3 H), 0.76 (s, 3 H); ^{13}C NMR (75 MHz) δ 175.9, 167.3, 166.3, 146.9, 133.4, 130.8, 110.8, 100.3, 91.7, 84.1, 80.2, 79.9, 78.2, 73.2, 72.4, 70.2, 61.7, 59.0, 48.5, 42.5, 36.9, 35.1, 33.4, 32.3, 29.0, 28.5, 28.0, 23.4, 18.5, 14.7, 14.6, 12.6, 1.6; IR (neat): 3608. 3593, 3376, 2924, 1774, 1730, 1703, 1522, 1453, 1270, 1148, 1091, 1027 cm^{-1}; HRMS (ESI) calcd. for $C_{33}H_{45}NO_{11}Na$ $[M+Na]^+$ 654.2890 found 654.2901; $[\alpha]^{23}_D$ +24.5 (*c*, 0.22, $CHCl_3$).



Theopederin D (2)

To a solution of **17** (0.002 g, 0.004 mmol) in MeOH (0.500 mL) at room temperature was added K_2CO_3 (0.001 g, 0.006 mmol). After 10 minutes, the reaction was complete as determined by TLC. H_2O (1.00 mL) was added and the reaction mixture was extracted with EtOAc (3 x 3 mL). The organic layers were combined, dried (Na_2SO_4), filtered and concentrated under reduced pressure. The crude resiude was purified via flash column chromatography (50% EtOAc in hexanes to 100% EtOAc) to afford the desired product (1.1 mg, 66%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.55 (d, *J* = 9.6 Hz, 1H), 5.83 (dd, *J* = 9.3, 9.6 Hz, 1H), 5.15 (d, *J* = 6.9 Hz, 1H), 4.89 (d, *J* = 6.9 Hz, 1H), 4.88 (br s, 1 H), 4.76 (br s, 1H), 4.50-4.41 (m, 1H), 4.29 (d, *J* = 3.3 Hz, 1H), 4.22 (dd, *J* = 6.6, 9.9 Hz, 1H), 4.16 (d, *J* = 3.3 H, 1H), 4.04 (qd, *J* = 2.7, 6.3 Hz, 1H), 3.83 (dd, *J* = 6.3, 9.0 Hz, 1H), 3.58 (s, 3H), 3.45 (d, *J* = 9.6 Hz, 1H), 3.43 (d, *J* = 9.3 Hz, 1H), 3.32 (s, 3H), 2.53-2.49 (m, 1H), 2.46-2.33 (m, 2H), 2.36 (d, *J* = 13.8 Hz, 1H); 2.28-2.18 (m, 2H), 2.05-1.95 (m, 1H), 1.80-1.60 (m, 2H), 1.21 (d, *J* = 6.3 Hz, 3H), 1.03 (s, 3H), 1.02 (d, *J* = 7.2 Hz, 3H), 0.89 (s, 3H); ^{13}C (150 MHz) δ 177.5, 172.3, 145.0, 111.0, 99.8, 86.5, 79.5, 76.1, 74.0, 73.7, 71.6, 69.5, 61.7, 48.5, 41.3, 35.0, 33.3, 28.7, 28.0, 22.7, 18.1, 14.1, 12.0; IR (neat): 3541, 3164, 3060, 2999, 2943, 2292, 2252, 1735, 1627, 1442, 1375, 1270, 1039, 919 cm^{-1}; HRMS (ES) calcd. for $C_{26}H_{41}NO_{10}Na$ $[M+Na]^+$ 550.2528, found 550.2655, lit. $[\alpha]^{28}_D$ +7.6 (*c* 0.14, $CHCl_3$).

References

1. C. Chu, X. Shen, S. G. Nelson, *J. Am. Chem. Soc.* **2004**, *126*, 5352.
2. N. S. Trotter, S. Takahashi, T. Nakata, *Org. Lett.* **1999**, *1*, 957.
3. B. M. Trost, H. Yang, G. D. Probst, *J. Am. Chem. Soc.* **2004**, *126*, 48.
4. (a) R. W. Murray, T. Jeyaraman, *J. Org. Chem*. **1985**, *50*, 2847. (b) M. Gilbert, G. Ferrer, F. Sanchez-Baeza, A. Messeguer, *Tetrahedron* **1997**, *53*, 8643.
5. M. G. Saulnier, J. F. Kadow, M. M. Tun, D. R. Langley, D. M. Vyas, *J. Am. Chem. Soc*. **1989**, *111*, 8320.
6. J. C. Rech, P. E. Floreancig, *Org. Lett.* **2003**, *5*, 1495.

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9
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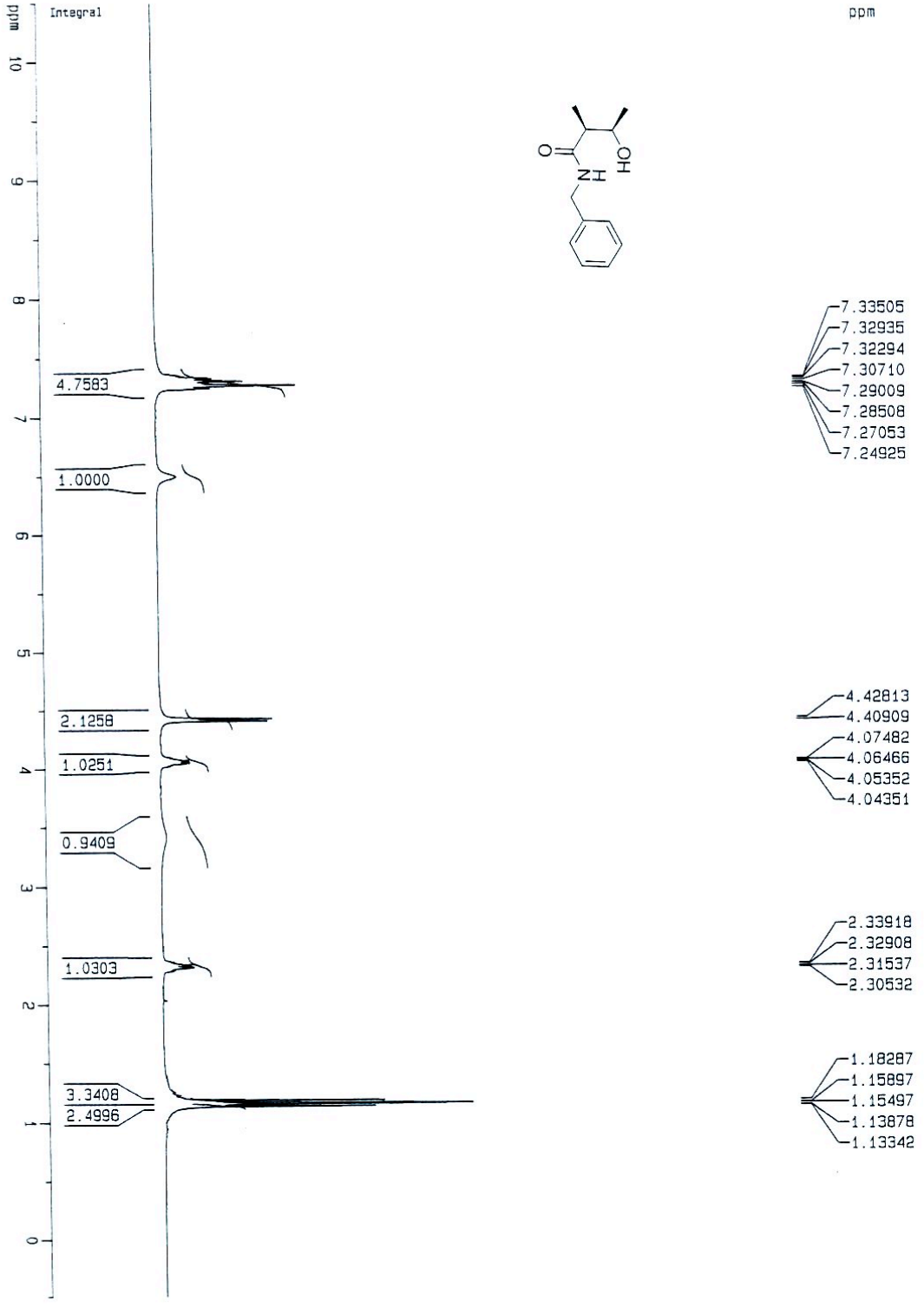
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OBz
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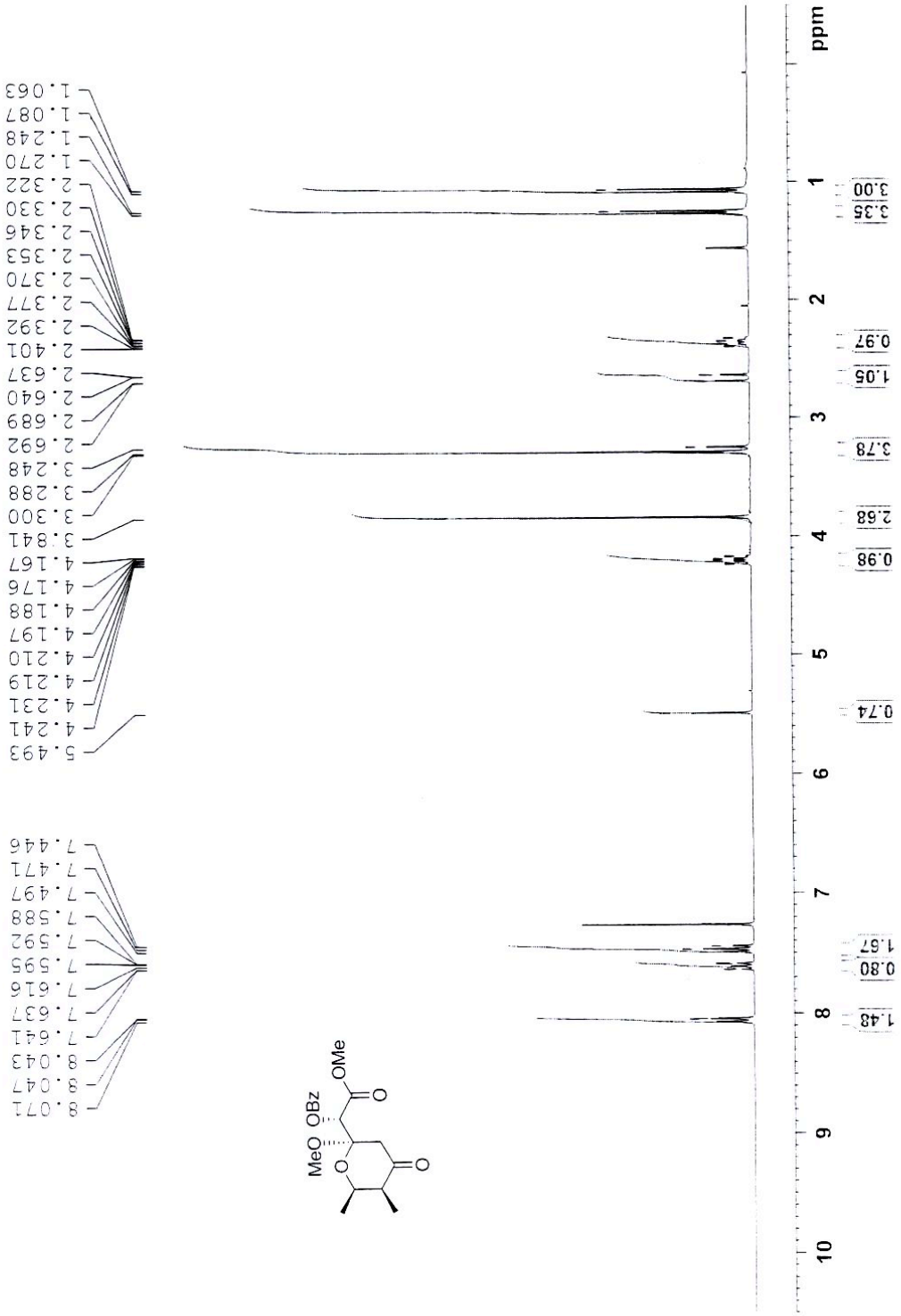
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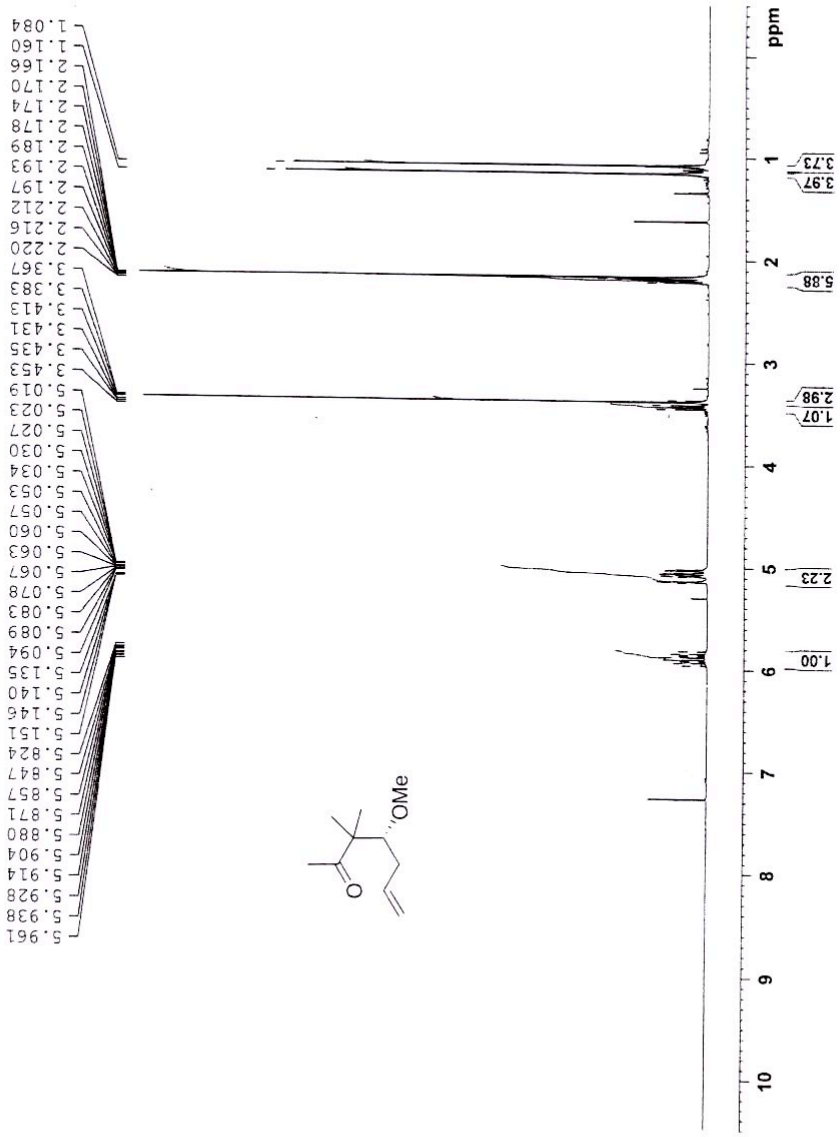
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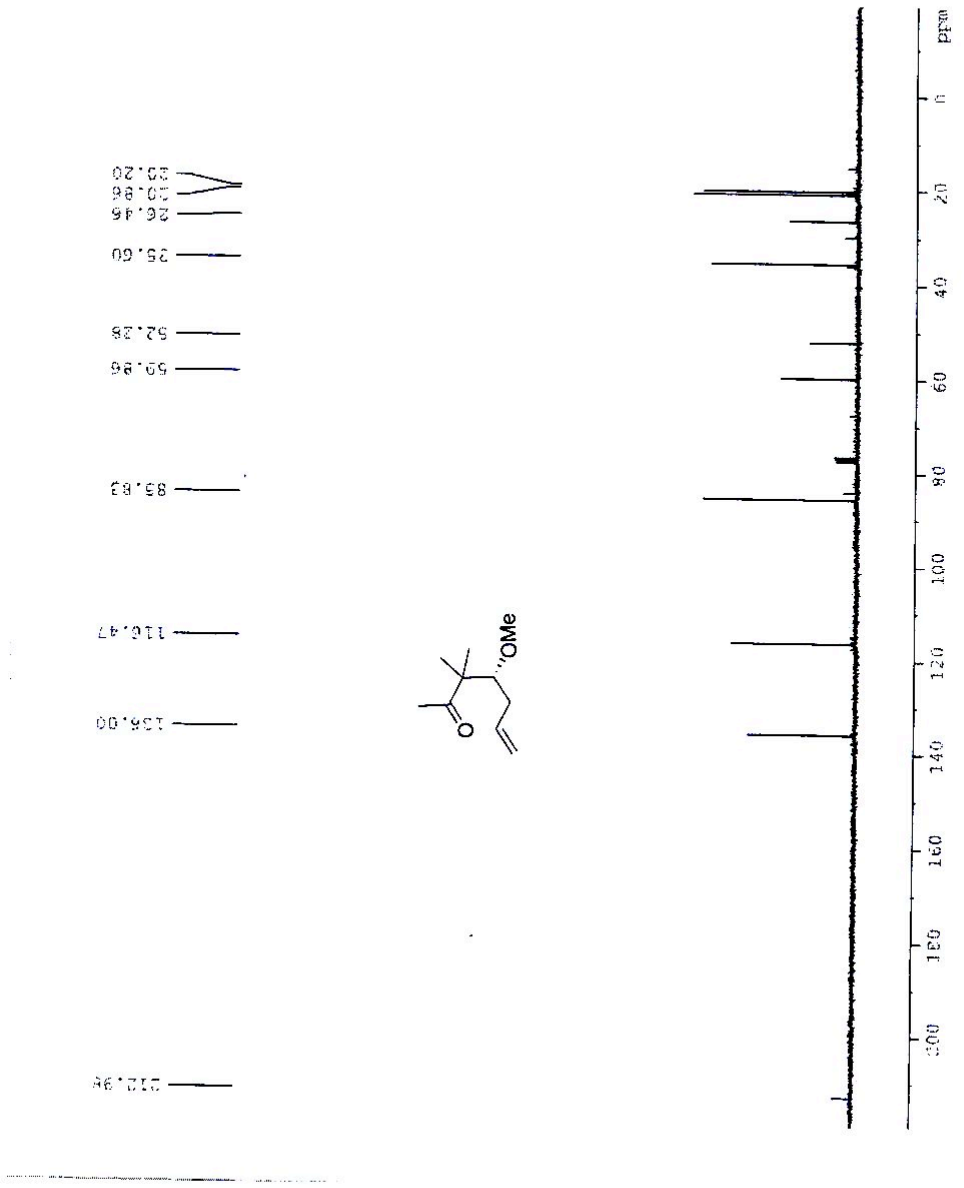
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OMe
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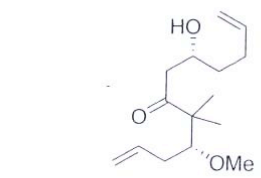

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ppm

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19.09
18.18
17.21
OMe
O
O
145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15 10 5 ppm

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O
O
OMe
HO
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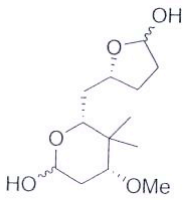

6

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OMe
OMe
HO
O
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20
10
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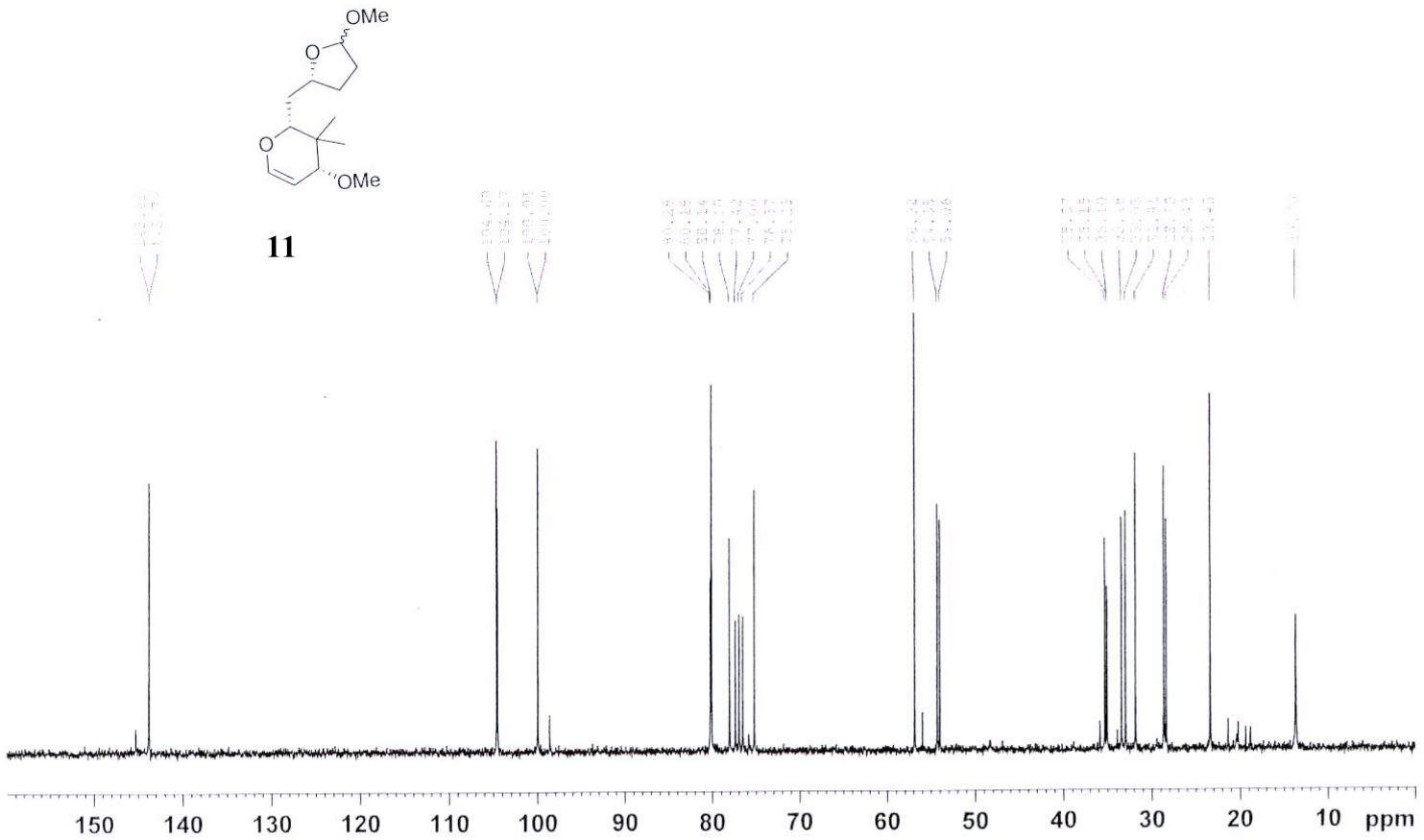

11

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OMe
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OMe
OMe
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80
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ppm

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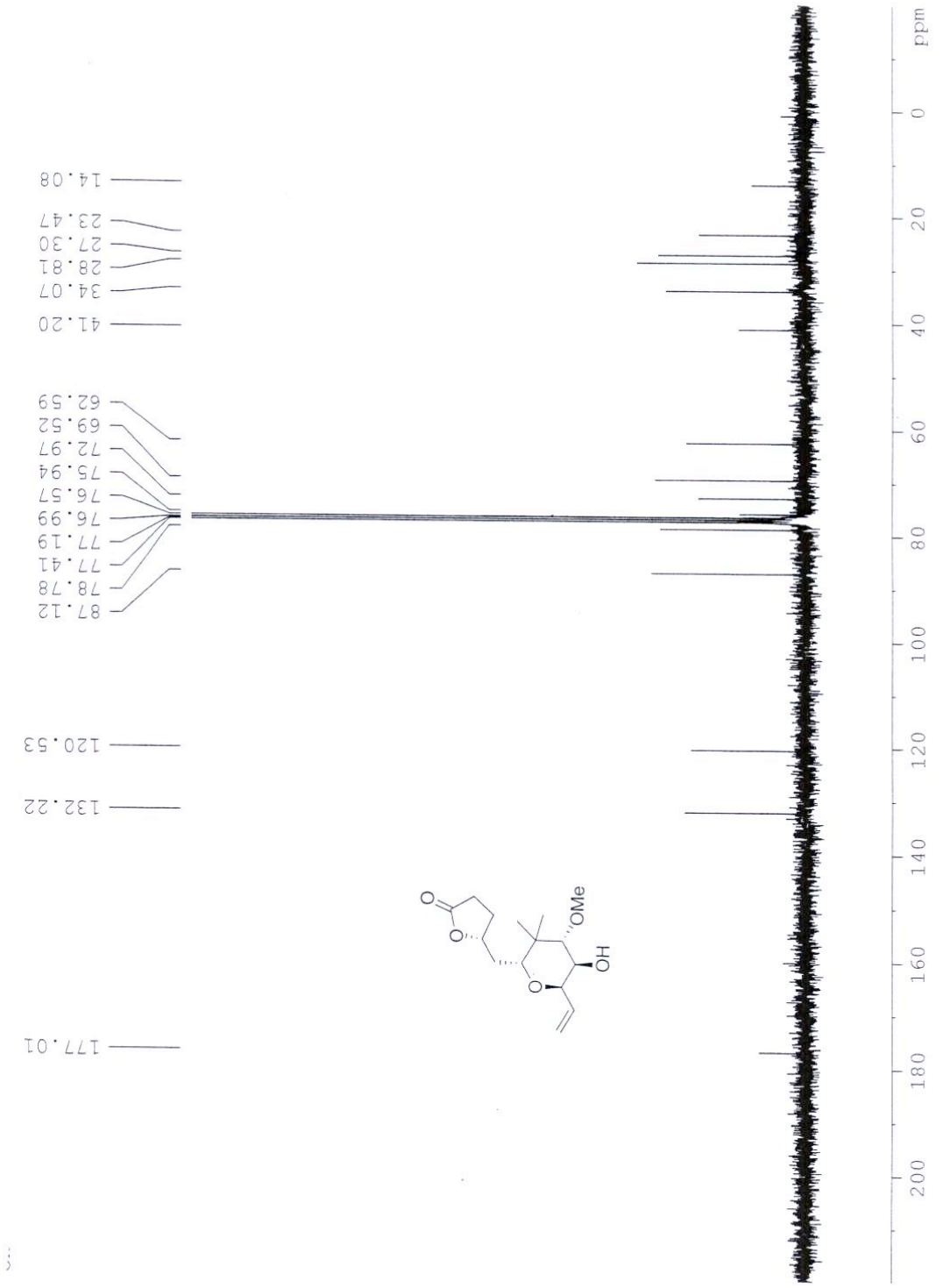
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OH
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O
O
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20
40
60
80
100
120
140
160
180
200

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0.82535

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OMe
BnO
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130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

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5.009
5.003
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4.783
4.773
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4.728
4.503
4.022
4.012
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1.816
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1.221
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OMe
N
S
O
O
H
O
O
BnO
12
ppm
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7
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5
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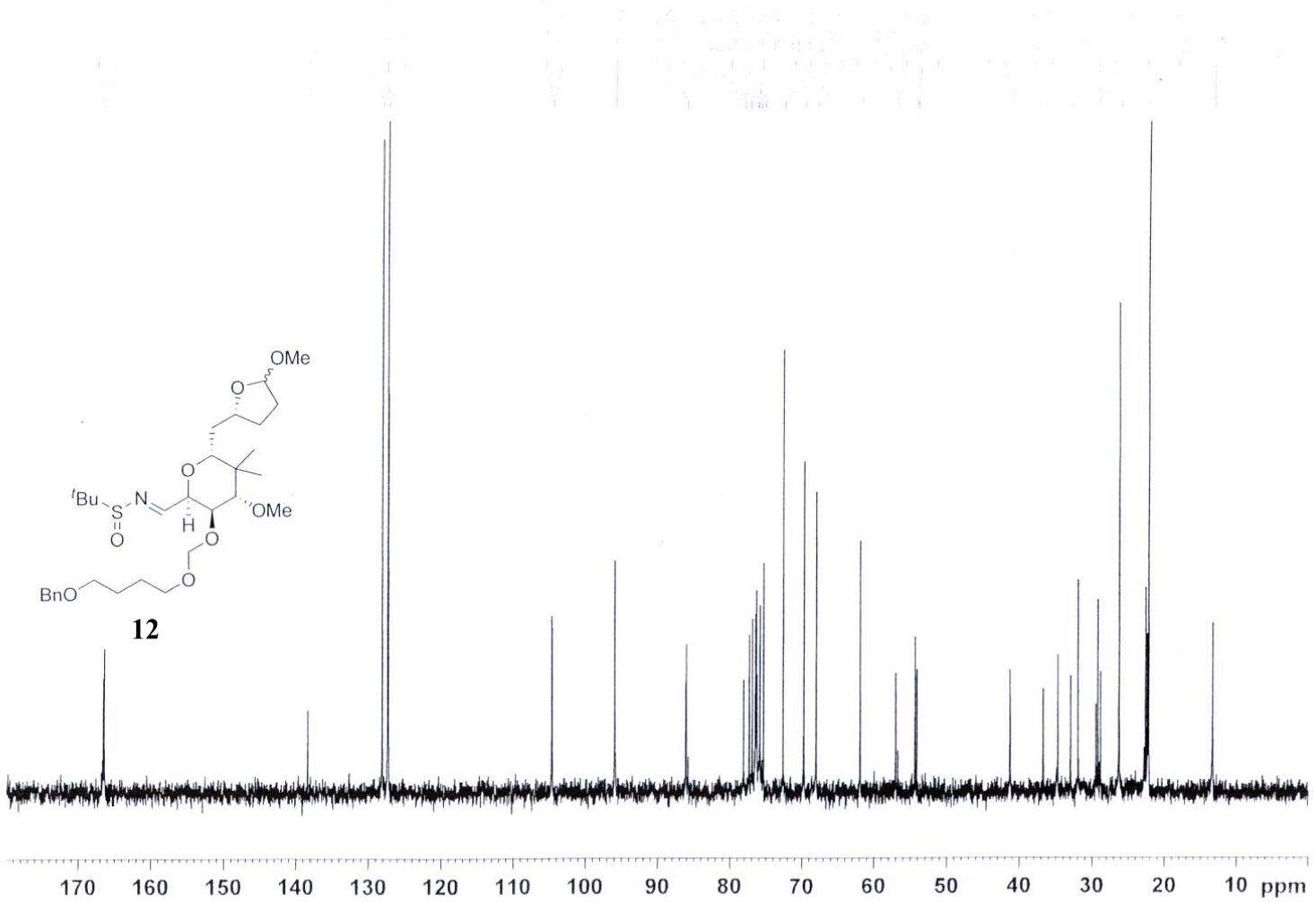
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110
100
90
80
70
60
50
40
30
20
10
ppm

12

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3.540
3.499
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2.857
2.816
2.055
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1.863
1.680
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1.500
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1.80
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8.17
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OMe
O
O
O
H
Bn
N
H
S
O
O
tBu
O
O
BnO

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OMe
Bn
BnO
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160
140
120
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80
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OMe
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O
H
Bn
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O
BnO
ppm
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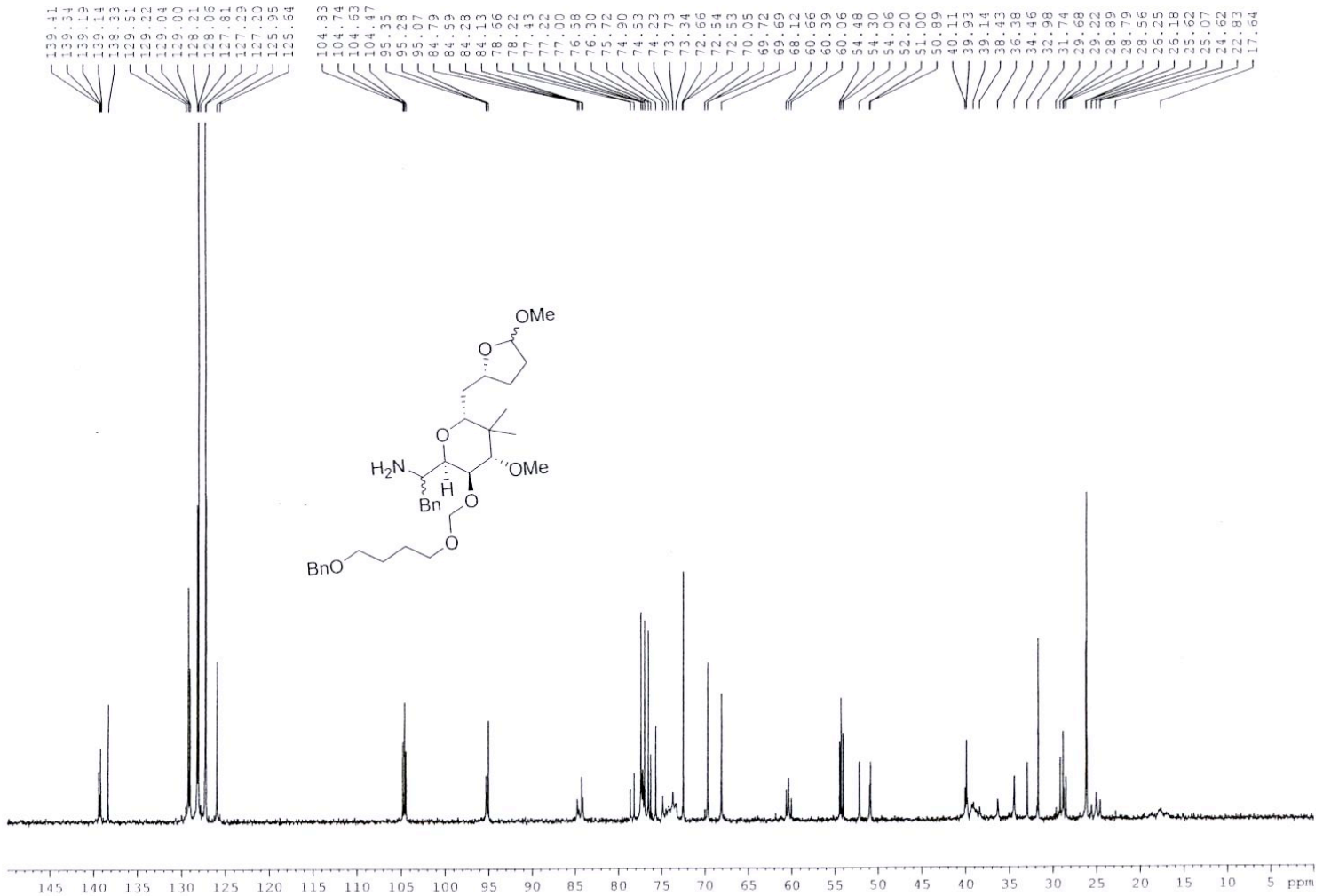
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Bn
H
OMe
O
O
BnO
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3.331
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3.095
3.067
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BnO
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O
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O
O
HO
ppm
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8
7
6
5
4
3
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OMe
Bn
BnO
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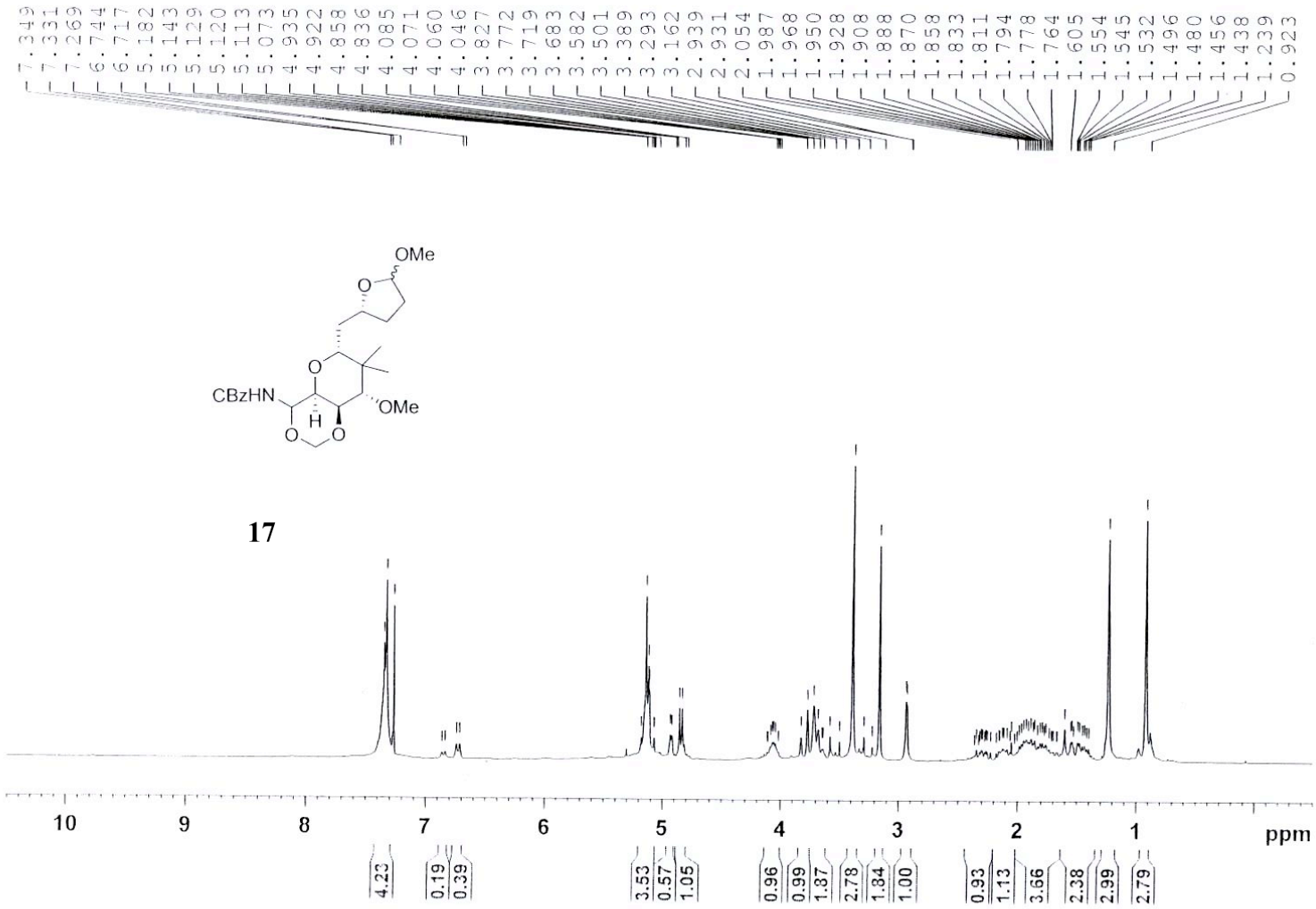
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CBzHN
H
OMe
O
O
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8
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6
5
4
3
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1
ppm
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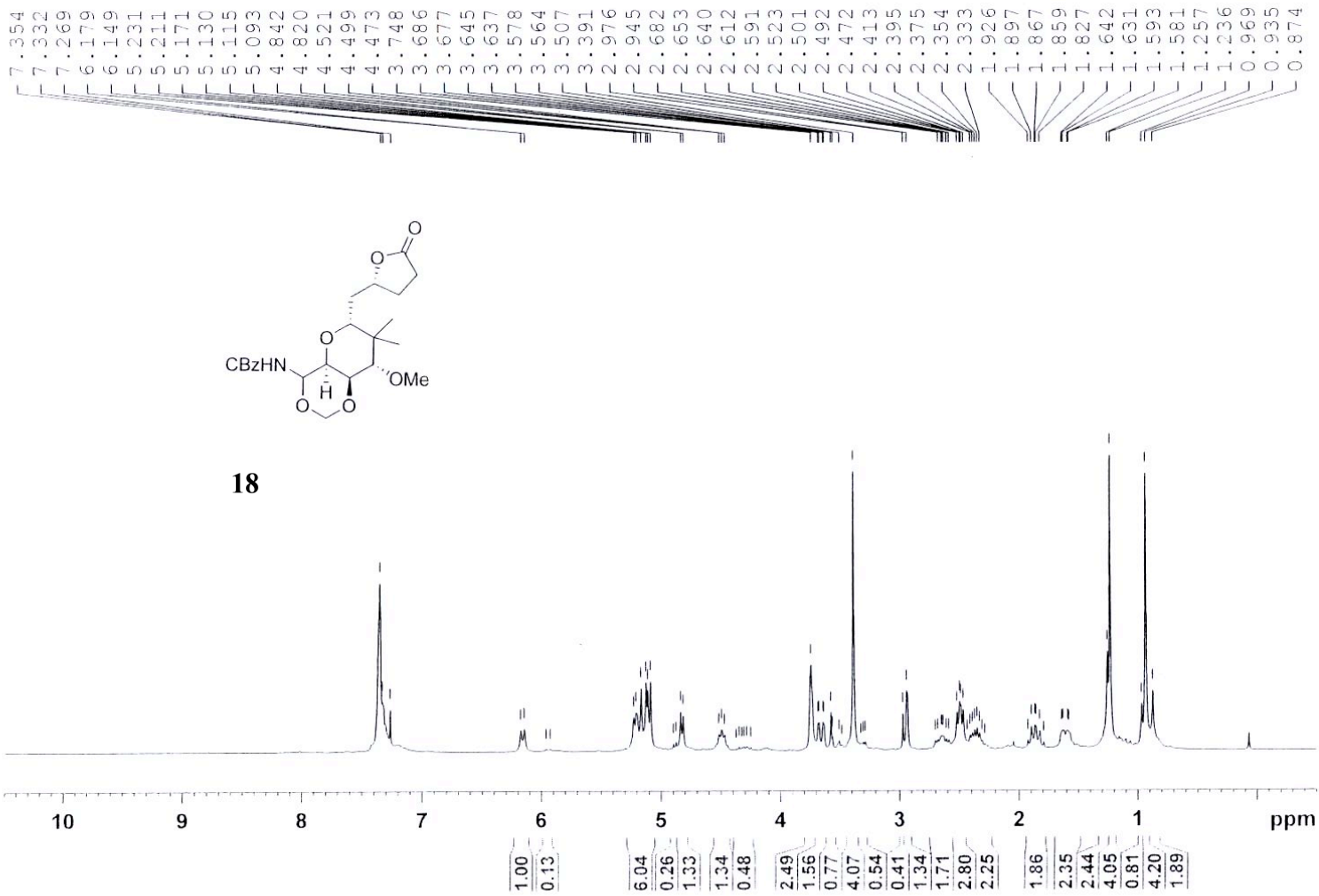
17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OMe
H
O
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9
8
7
6
5
4
3
2
1
ppm
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0.13
6.04
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1.34
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2.49
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4.07
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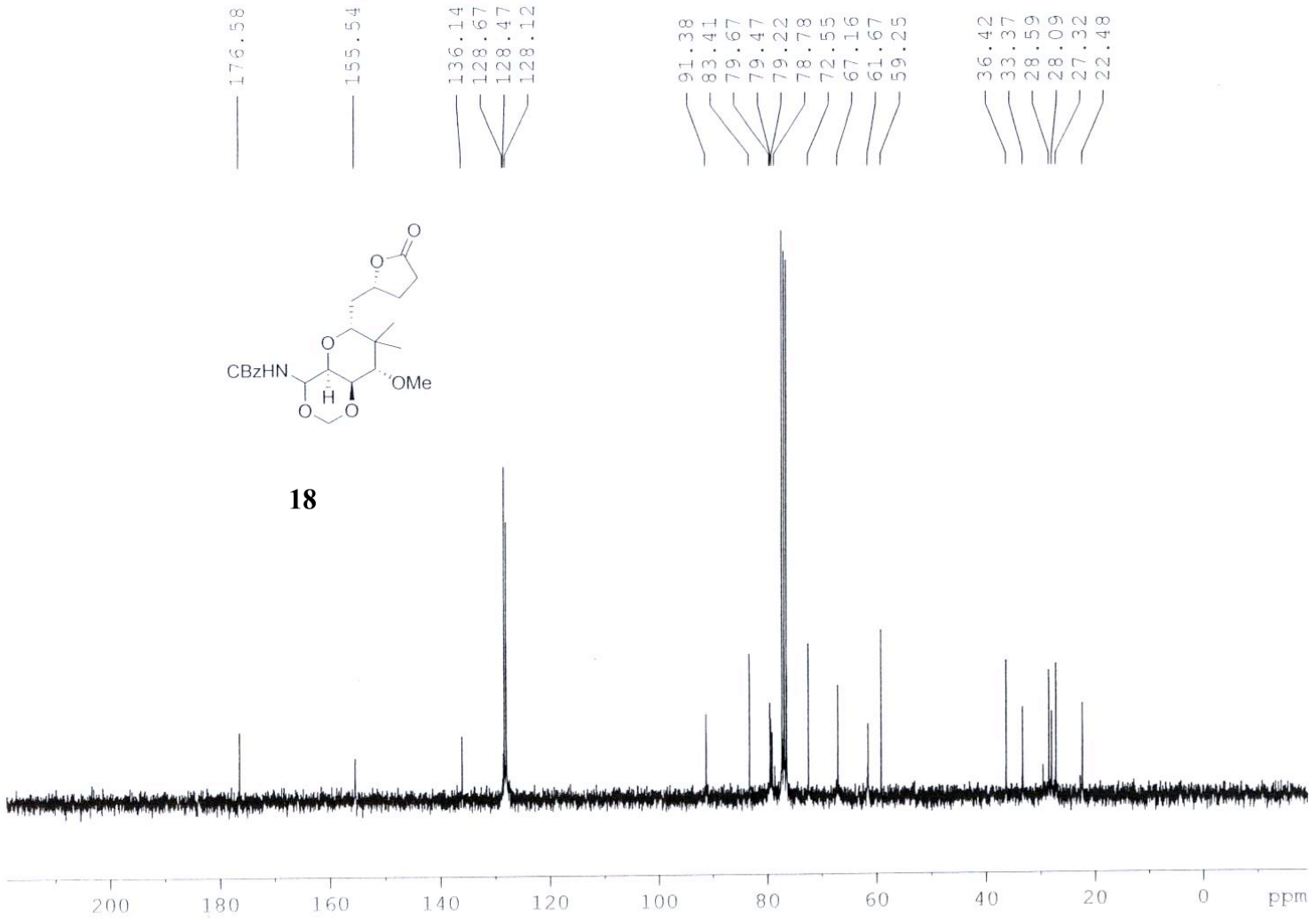
18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67.16
61.67
59.25
36.42
33.37
28.59
28.09
27.32
22.48
CBzHN
OMe
H
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O
O
O
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20
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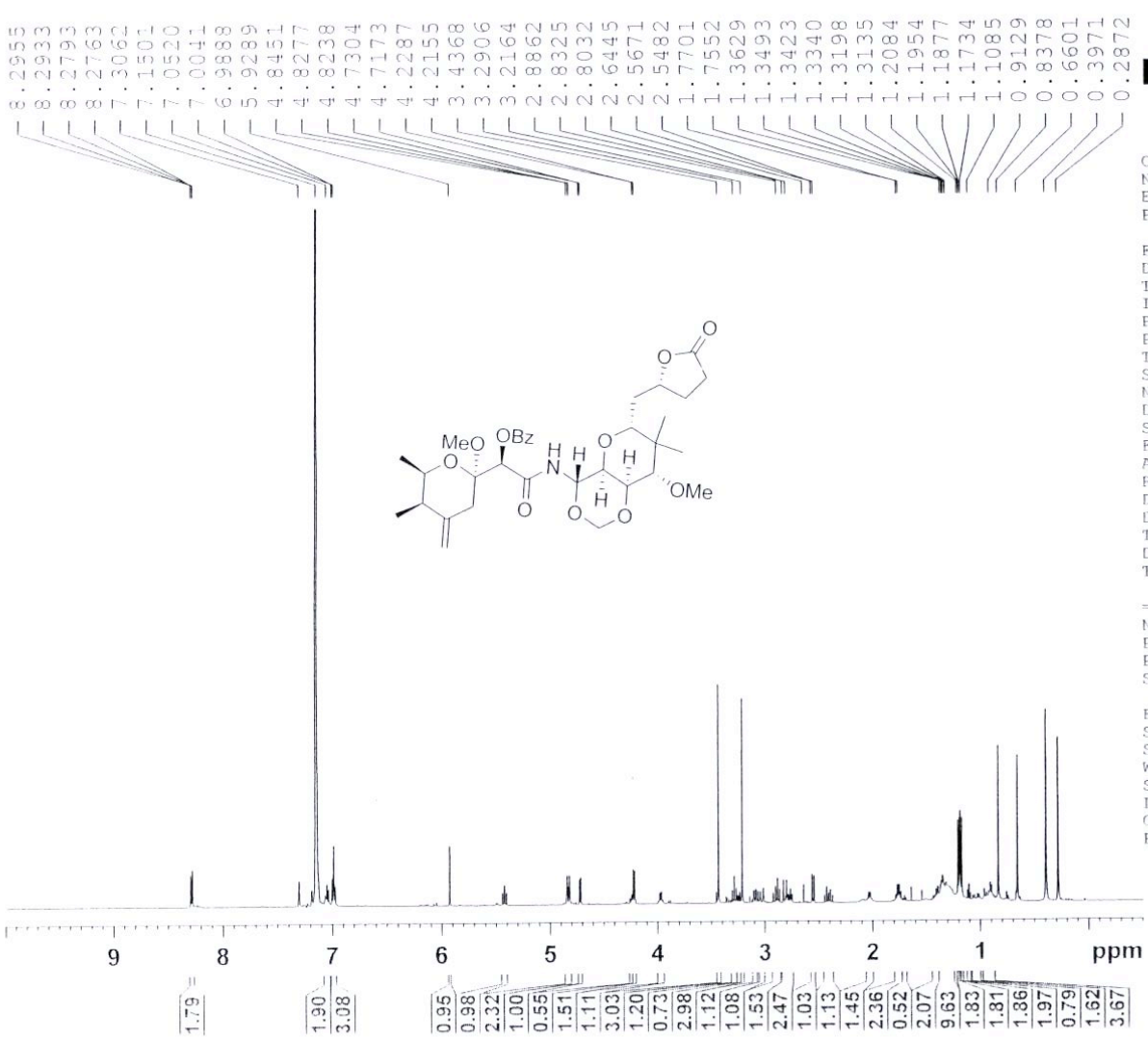
ppm

18



BRUKER

Current Data Parameters
NAME MG02070801
EXPNO 2
PROCNO 1

F2 - Acquisition Parameters
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Time 11.27
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PULPROG zg
TD 65536
SOLVENT C6D6
NS 16
DS 2
SWH 10330.578 Hz
FIDRES 0.157632 Hz
AQ 3.1719923 sec
RG 181
DW 48.400 usec
DE 6.00 usec
TE 298.2 K
D1 1.00000000 sec
TD0 1

======== CHANNEL f1 ========
NUC1 1H
P1 9.00 usec
PL1 0.00 dB
SFO1 500.1330885 MHz

F2 - Processing parameters
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SF 500.1300622 MHz
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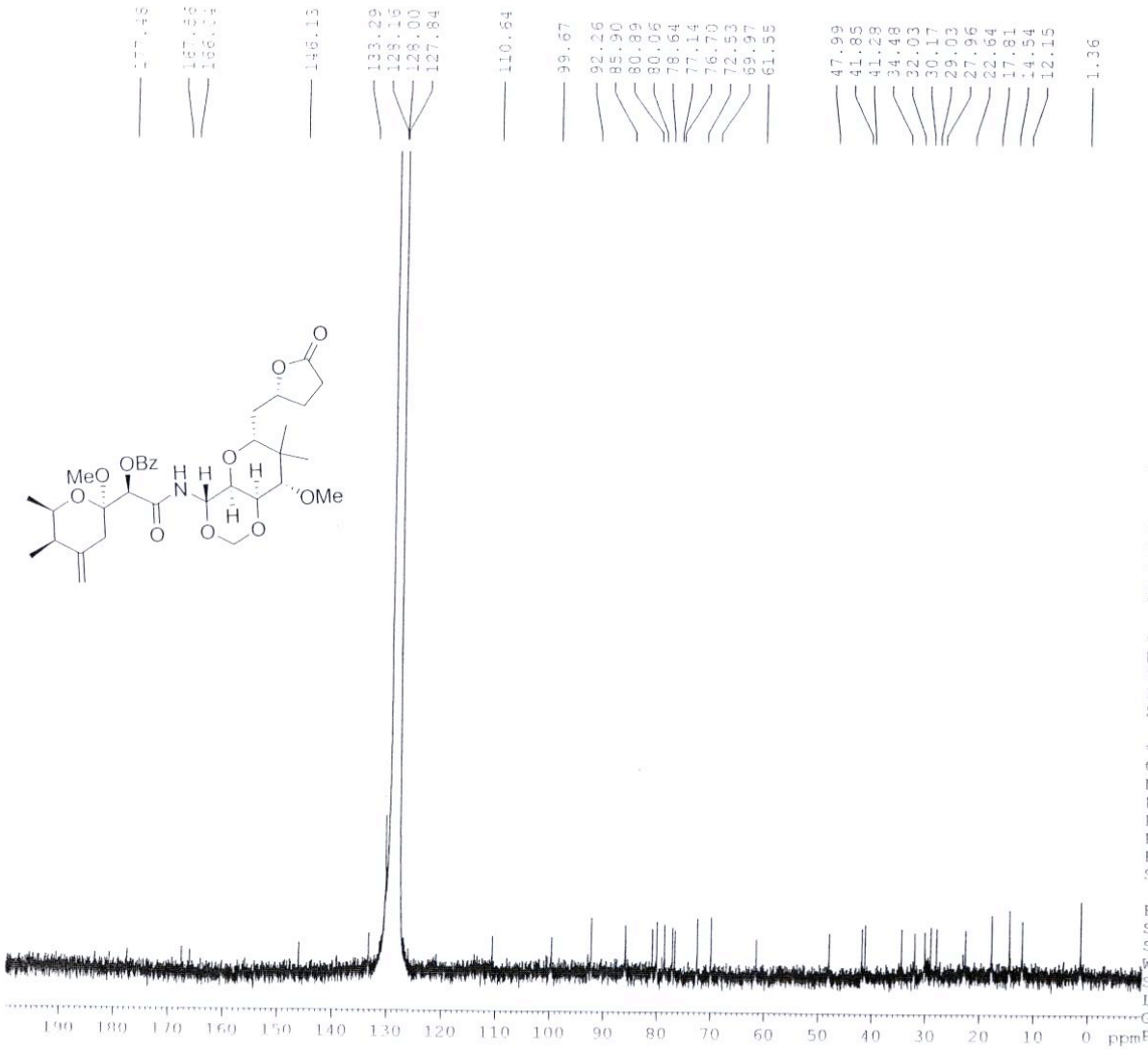
SSB 0
LB 0.30 Hz
GB 0
PC 0.80



BRUKER

Current Data Parameters
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EXPNO 2
PROCNO 1

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Time 18.20
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PULPROG zgpg
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SOLVENT C6D6
NS 40745
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SWH 36231.883 Hz
FIDRES 0.552855 Hz
AQ 0.9044606 sec
RG 6502
DW 13.800 usec
DE 6.00 usec
TE 294.2 K
D1 5.00000000 sec
d11 0.03000000 sec
DELTA 4.90000010 sec
TD0 1

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PL1 -1.00 dB
SFO1 151.1039906 MHz

======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 8.00 dB
PL12 29.68 dB
PL13 27.10 dB
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F2 - Processing parameters
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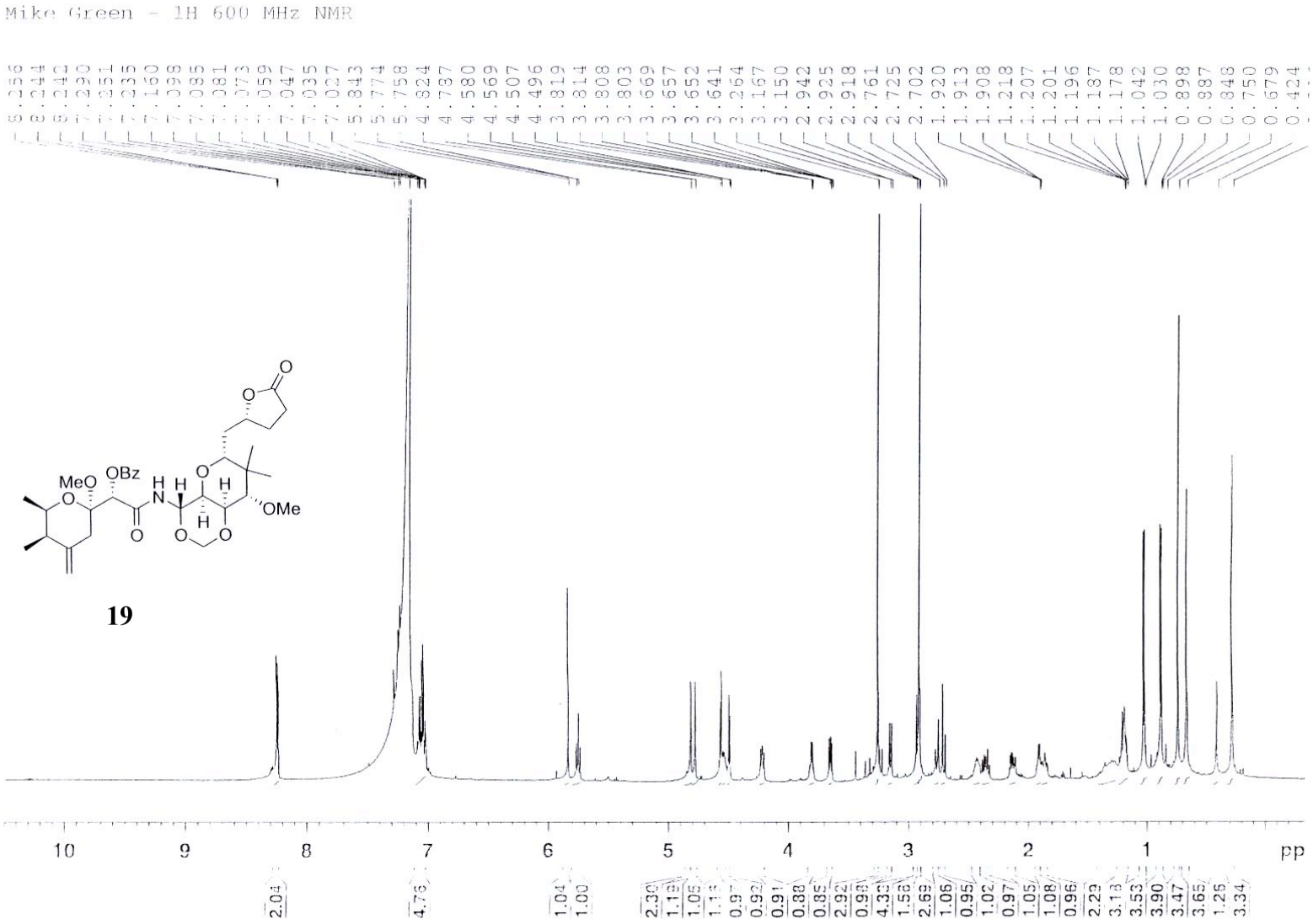
PC 1.00


Mike Green - 1H 600 MHz NMR
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OBz
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H
O
H
H
O
O
OMe
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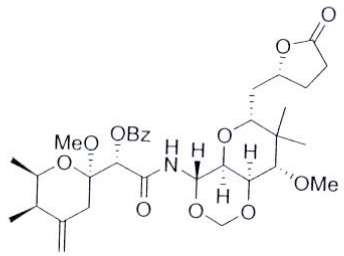
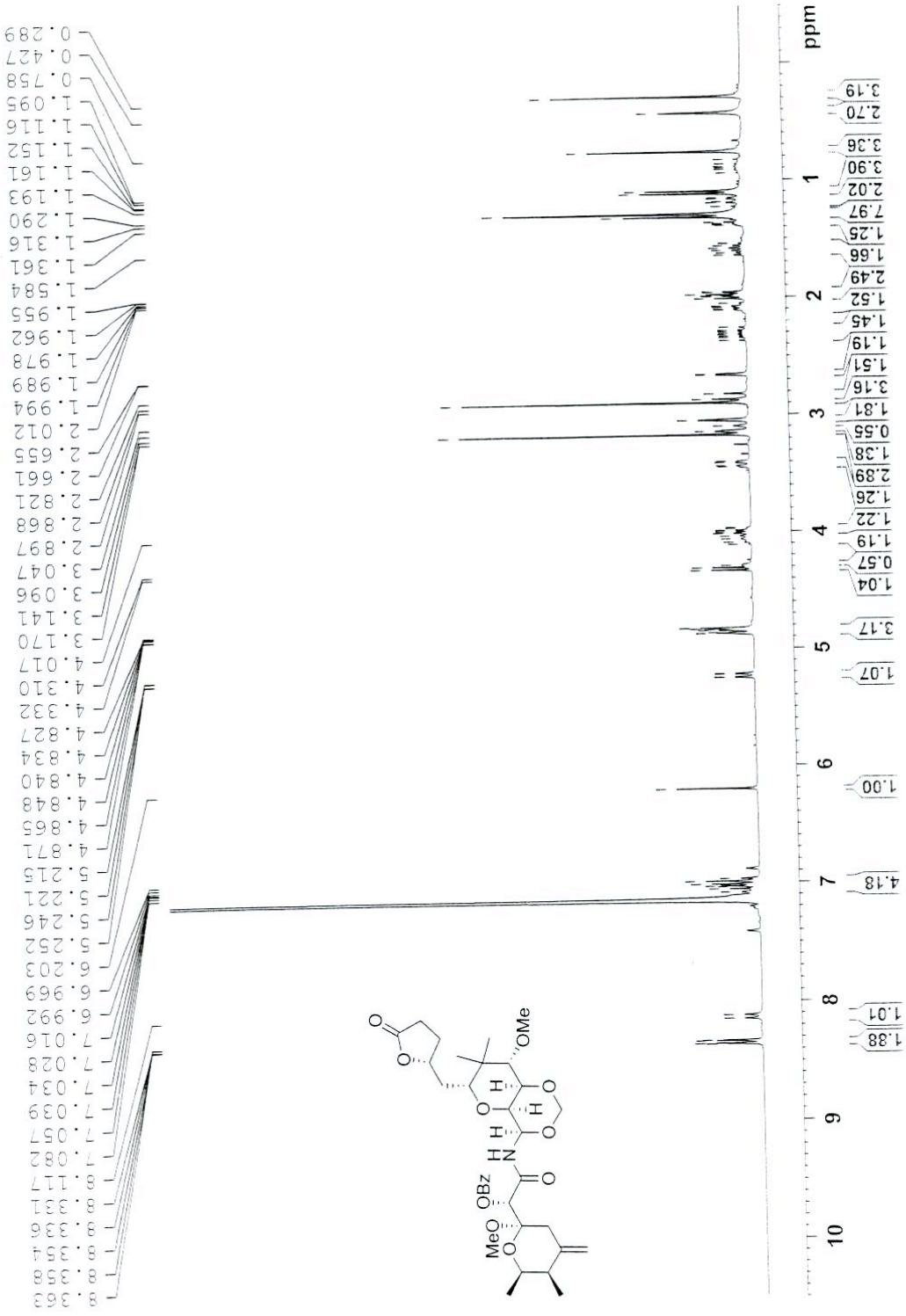
O
19
10
9
8
7
6
5
4
3
2
1
pp

Mike Green - 13C 600 MHz NMR



19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OMe
OBz
MeO
8.363
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8.117
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7.057
7.039
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35.13
33.38
32.30
29.00
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18.50
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ppm
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80
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100
110
120
130
140
150
160
170
180
190
OMe
OBz
MeO
H
N
O

2
ppm
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9
8
7
6
5
4
3
2
1
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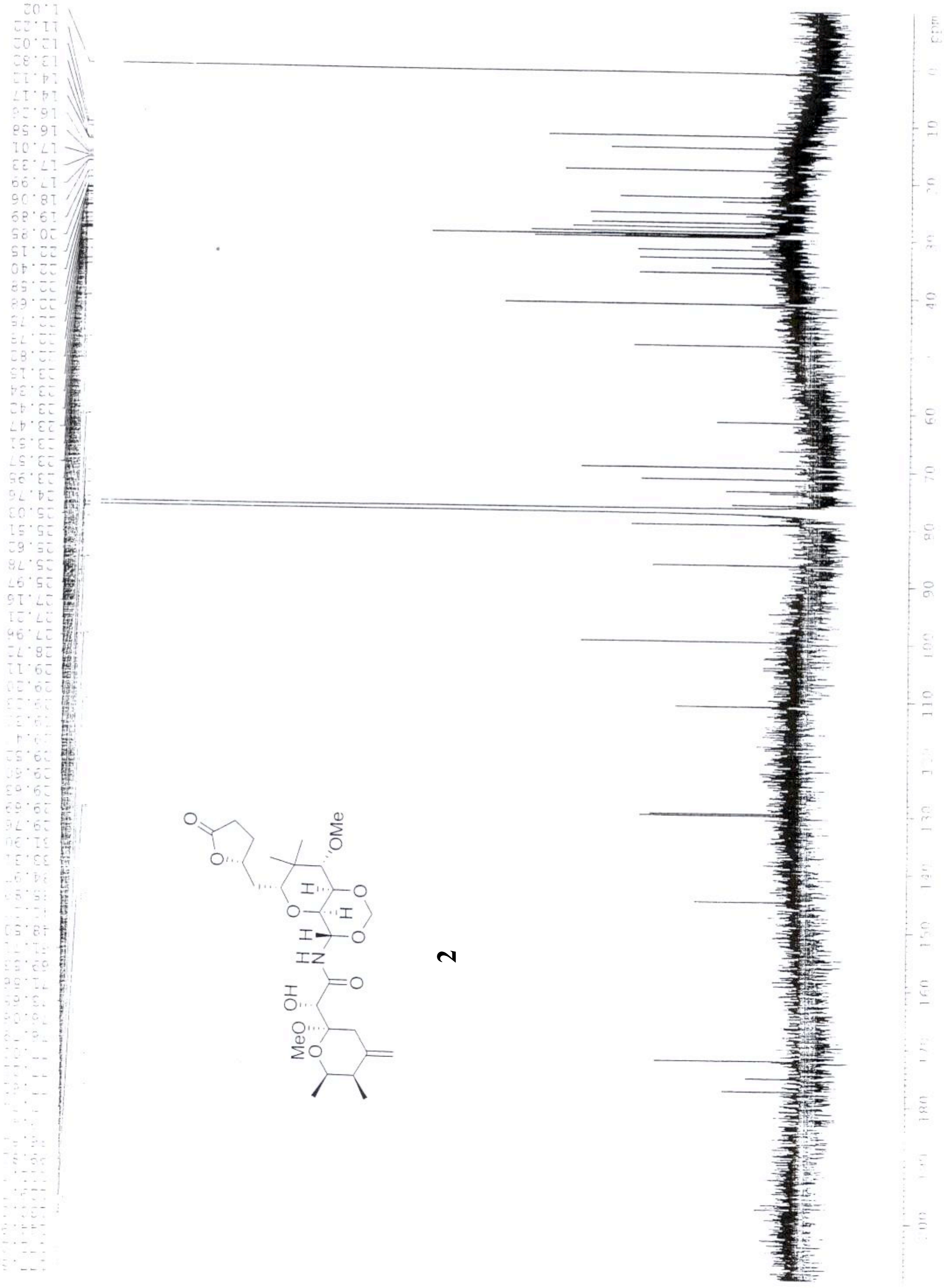
2