Electronic Supplementary Material (ESI) for Chemical Communications

A Concise Route to the Macrocyclic Core of the Rakicidins

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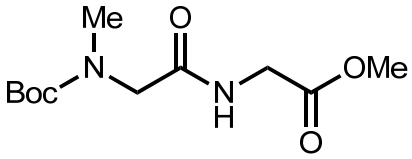
Supporting Information

Contents

General Procedures and Materials. All reactions were carried out under anhydrous conditions under an atmosphere of argon, unless specifically stated. Dry dichloromethane (CH_2Cl_2), dry tetrahydrofuran (THF), dry acetonitrile (CH_3CN) were obtained by passing pre-dried solvents through activated alumina. Dry 1,2-dichloroethane (DCE) and dry chloroform ($CHCl_3$) were obtained by drying of HPLC-grade formulations over activated 4A molecular sieves. Yields refer to compounds that homogenous by TLC and ^{1}H NMR. If not specifically stated reagents were used as received from commercial suppliers. For flash chromatography (FC), silica gel was purchased from Iatron Laboratories Inc. (Iatrobeads 6RS-8060) or from Sigma (Silica gel 60, 230-400 mesh). Analytical thin layer chromatography (TLC) was performed using pre-coated aluminium-backed plates (Merck Kieselgel 60 F254) and visualized by ultraviolet irradiation, $KMnO_4$ or CAM dip. Melting points were recorded on a Büchi B-540 apparatus and are uncorrected. Infrared (IR) spectra were acquired on a Perkin Elmer Spectrum Two™ UATR spectrometer. UV-vis spectra were acquired on a Varian Cary® 100 Bio spectrometer. Nuclear magnetic resonance (NMR) spectra were acquired on a Varian AS 400 spectrometer, running at 400 and 100 MHz for ^{1}H and ^{13}C, respectively. Chemical shifts (δ) are reported in ppm relative to residual solvent signals ($CDCl_3$: 7.26 ppm for ^{1}H NMR, 77.16 ppm for ^{13}C NMR; DMSO-d_6: 2.50 ppm for ^{1}H NMR, 39.52 ppm for ^{13}C NMR; CD_3CN: 1.94 ppm for ^{1}H NMR, 1.32 ppm for ^{13}C NMR). Multiplicities are indicated using the following abbreviations: s = singlet, d = dublet, t = triplet, q = quartet, m = multiplet, br = broad, a = apparent. ^{13}C NMR spectra were acquired on a broad band decoupled mode. Mass spectra were recorded on a micromass LCT spectrometer using electrospray (ES^+) ionization techniques. Monte Carlo conformational searches were carried out using the Maestro/Macromodel (vers. 9.1.107) software package. The force field employed was MMFF94S, the number of iterations in each conformational search was 10000, and the solvent employed in the calculation was water.

Synthetic Protocols and Characterization Data

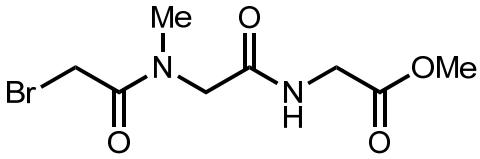
Methyl 2-(2-((tert-butoxycarbonyl)(methyl)amino)acetamido)acetate (8):



A dried round bottom flask equipped with a magnetic stirring bar was charged with *N*-Boc sarcosine (1.89 g, 10 mmol, 1.0 equiv) and glycine methyl ester hydrochloride (1.26 g, 10 mmol, 1.0 equiv). The flask was evacuated and backfilled with argon. Dry CH_2Cl_2 (50 mL) was added and the mixture was cooled to 0 ^oC. Then HOBt-hydrate (1.84 g, 12 mmol, 1.2 equiv) was added followed by EDCI (2.30 g, 12 mmol, 1.2 equiv). Finally *N*-ethyldiisopropylamine (4.4 mL, 25 mmol, 2.5 equiv) was added, and the mixture was allowed to warm to room temperature and the stirring was continued under argon for 14 h. The reaction was diluted with CH_2Cl_2 (100 mL). The combined organics were washed with 1N aq. HCl (75 mL) and the organic phase was separated. To the heavy precipitate remaining was added H_2O (60 mL) and $CHCl_3$ (60 mL) and the mixture was shaken vigorously. The organic phase was combined with the first organic extract. The combined organics were washed sequentially with 1N aq. HCl (40 mL), sat. aq. $NaHCO_3$ (40 mL), and brine (40 mL). Following drying over Na_2SO_4 the mixture was concentrated *in vacuo*. The product was obtained after FC (SiO_2, 9x4 cm) eluting with EtOAc/pentane 3:1 to 100:0 as a viscous colourless oil (2.49 g, 8.31 mmol, 83%). R_f = 0.26, EtOAc/pentane 3:1, $KMnO_4$ dip.

^1H NMR ($CDCl_3$, 400 MHz) δ 6.57 (br s, 1H), 4.04 (d, *J* = 5.6 Hz, 2H), 3.89 (s, 2H), 3.73 (s, 3H), 2.93 (s, 3H), 1.45 (s, 9H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.0, 169.6, 80.8, 52.8, 52.2, 40.9, 35.7, 28.2. HRMS calc.: $C_{11}H_{20}N_2NaO_5$ 283.1270; found: 283.1271.

Methyl 2-(2-(2-bromo-N-methylacetamido)acetamido)acetate (9):



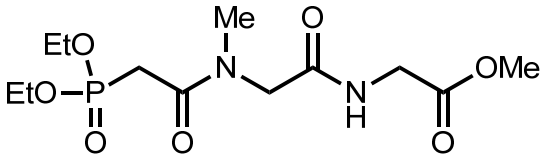
Boc-Sar-Gly-OMe (**8**) (0.599 g, 2.00 mmol, 1.0 equiv) was placed in a round bottom flask equipped with a magnetic stirring bar. The material was azeotroped with dry benzene and placed under high vacuum for ca. 30 min. The flask was backfilled with argon and then a solution of 4M HCl (g) in 1,4-dioxane (10 mL) was added by syringe. The mixture was stirred at room temperature under argon for 3 h at which time TLC (EtOAc) indicated full consumption of the starting material. The mixture was concentrated *in vacuo* and co-evaporated with Et_2O two times and placed under high vacuum. The hydrochloride salt was then re-dissolved in dry $CHCl_3$ (12 mL) under argon, triethylamine (836 μL, 6.00 mmol, 3.0 equiv) was added, and the mixture was cooled to -78 ^oC. A solution of bromo acetylbromide (270 μL. 3.00 mmol, 1.5 equiv.) in $CHCl_3$ (4 mL) was added dropwise over ca. 5 min. The reaction was maintained at -78 ^oC for 0.5 h and was then allowed to warm to

0 °C over a period of 3 h. The reaction was diluted with CH_2Cl_2 (100 mL), and washed with 1N aq. HCl (30 mL). The aqueous phase was back-extracted with $CHCl_3$ (20 mL). The combined organics were washed with brine (40 mL), and the aqueous phase was back-extracted with $CHCl_3$ (20 mL). The combined organics were dried over Na_2SO_4 and concentrated *in vacuo*. The bromoacetamide derivative **9** was obtained after FC (SiO_2, 8x3 cm) eluting with EtOAc as a viscous yellow oil (455 mg, 1.62 mmol, 81% (2 steps)). R_f = 0.42, MeOH/EtOAc 1:9, $KMnO_4$ dip.

The compound was found to exist as a 2/1 mixture of rotamers in CD_3CN at room temperature. Data below is for the major rotamer.

^{1}H NMR (CD_3CN, 400 MHz) δ 6.80 (br s, 1H), 4.04 (s, 2H), 3.99 (s, 2H), 3.90 (d, J = 6 Hz, 2H), 3.67 (s, 3H), 3.08 (s, 3H). ^{13}C NMR (CD_3CN, 100 MHz) δ 171.2, 169.5, 168.2, 52.7, 52.0, 41.5, 37.7, 28.4. HRMS calc.: $C_8H_{13}BrN_2NaO_4$ 302.9956; found: 302.9947.

Methyl 2-(2-(2-(diethoxyphosphoryl)-N-methylacetamido)acetamido)acetate (10):

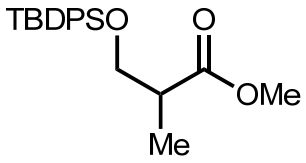


Bromoacetamide **9** (107 mg, 0.38 mmol, 1.0 equiv) was added to a roundbottom flask equipped with a magnetic stirring bar. The material was azeotroped with dry benzene, placed under high vacuum, and backfilled with argon. Dry dichloroethane (0.45 mL) was added, followed by $P(OEt)_3$ (130 µL, 0.76 mmol, 2.0 equiv). A reflux condenser was fitted and the reaction was heated to reflux (bath temperature 90 °C) under argon for 13 h at which time TLC (MeOH/EtOAC 1/9) showed full conversion of the starting material. The mixture was concentrated *in vacuo* and placed under high vacuum. The residue was purified by FC (SiO_2, 11x1 cm) eluting with MeOH/EtOAc 0/100 to 10/90 to afford the phosphonate ester **10** as a viscous colourless oil (127 mg, 0.38 mmol, 100%). R_f = 0.18, MeOH/EtOAc 1:9, $KMnO_4$ dip.

The compound was found to exist as a 6/1 mixture of rotamers in $CDCl_3$ at room temperature. Data below is for the major rotamer.

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.73 (br s, 1H), 4.23-4.13 (m, 4H), 4.16 (s, 2H), 4.05 (d, J = 6.0 Hz, 2H), 3.71 (s, 3H), 3.23 (s, 3H), 3.15 (d, J = 22 Hz, 2H), 1.35 (t, J = 6.8 Hz, 6H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.0, 168.9, 166.0 (d, J_{CP} = 6 Hz), 63.2 (d, J = 7 Hz), 52.1, 51.7, 40.9, 37.9, 33.6 (d, J = 128 Hz), 16.3 (d, J_{CP} = 6 Hz). HRMS calc.: $C_{12}H_{23}N_2NaO_7P$ 361.1141; found: 361.1145.

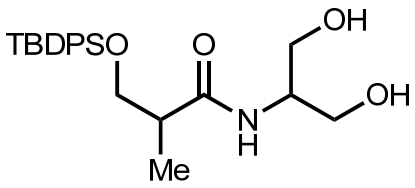
Methyl 3-((tert-butyldiphenylsilyl)oxy)-2-methylpropanoate (12):



Methyl 3-hydroxy-2-methyl propionate (0.773 g, 6.54 mmol, 1.0 equiv) was added to a dry roundbottom flask equipped with a magnetic stirring bar. Dry CH_2Cl_2 (26 mL) was added followed by imidazole (1.367 g, 13.1 mmol, 2.0 equiv) and TBDPSCl (1.888 g, 6.87 mmol, 1.79 mL) in that order. The reaction was stirred at room temperature under argon for 12 h at which time TLC (EtOAc/pentane 15/85) shows full conversion of the starting material. Sat. aq. NH_4Cl (25 mL) was added to the reaction and the organic phase was separated. The aqueous phase was extracted with $CHCl_3$ (3 x 30 mL), and the combined organics were dried over $MgSO_4$ and concentrated *in vacuo*. The silyl ether product **12** was obtained after FC (SiO_2, 15x4 cm) eluting with an EtOAc/pentane gradient (0/100 to 10/90) as a colourless oil (2.30 g, 6.45 mmol, 99%). R_f = 0.72, EtOAc/pentane 15/85, $KMnO_4$ dip.

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.65 (m, 4 H), 7.45-7.35 (m, 6H), 3.82 (dd, *J* = 7.2, 10 Hz, 1H), 3.72 (dd, J = 6.0, 10 Hz, 1H), 3.68 (s, 3H), 2.72 (m, 1H), 1.15 (d, *J* = 7.2 Hz, 3H), 1.03 (s, 9H). ^{13}C NMR ($CDCl_3$, 100 MHZ) δ 175.4, 135.6, 133.5, 129.6, 127.6, 65.9, 51.5, 42.,4, 26.7, 19.2, 13.5. HRMS calc.: $C_{21}H_{28}NaO_3Si$ 379.1705; found: 379.1703.

3-((tert-butyldiphenylsilyl)oxy)-N-(1,3-dihydroxypropan-2-yl)-2-methylpropanamide (13):

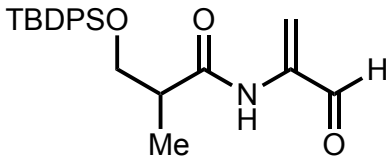


The TBDPS-ether (**12**) (2.30 g, 6.45 mmol, 1.0 equiv) was added to a roundbottom flask equipped with a magnetic stirring bar. The material was dissolved in EtOH (11 mL) and then 1N aq. NaOH (7.0 mL, 7.0 mmol, 1.08 equiv) was added. The reaction mixture was stirred vigorously at room temperature for 14 h at which time TLC (EtOAc/pentane 15/85) shows full conversion of the starting material. The reaction was concentrated in vacuo and re-dissolved in 10% aq. HCl (30 mL). The aqueous solution was extracted with $CHCl_3$ (3x30 mL) and the combined organics were dried over $MgSO_4$. Following concentration the crude carboxylic acid product was obtained. This material was then azeotroped with dry benzene and placed under high vacuum. The dry acid was re-dissolved in CH_2Cl_2 (30 mL) under argon and serinol (0.626 g, 6.87 mmol, 1.05 equiv) was added. The suspension was cooled to 0 ^oC and then HOBt-hydrate (1.20 g, 7.85 mmol, 1.2 equiv) was added followed by EDCI (1.50 g, 7.85 mmol, 1.2 equiv). Finally, *N*-ethyldiisopropylamine (1.35 mL, 7.85 mmol, 1.2 equiv) was added, and the mixture was allowed to warm to room temperature and the stirring was continued under argon for 14 h. The reaction was diluted with CH_2Cl_2 (50 mL). The combined organics were washed with 1N aq. HCl (35 mL) and the organic phase was separated. To the heavy precipitate remaining was added H_2O (30 mL) and $CHCl_3$ (30 mL) and the mixture

was shaken vigorously. The organic phase was combined with the first organic extract. The combined organics were washed sequentially with 1N aq. HCl (20 mL), sat. aq. $NaHCO_3$ (20 mL), and brine (20 mL). Following drying over Na_2SO_4 the mixture was concentrated *in vacuo*. The amido diol product **13** was obtained after FC (SiO_2, 11x4 cm) eluting with EtOAc/pentane 3/1 to 100/0 and then with MeOH/EtOAc 2/98 as a white solid (1.74 g, 4.19 mmol, 64% (2 steps)). R_f = 0.23, EtOAc/pentane 3:1, KMnO4 dip. m.p. 103 °C.

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.65 (m, 4H), 7.45-7.36 (m, 6H), 6.87 (br d, *J* = 7.2 Hz, 1H), 3.97 (m, 1H), 3.84-3.68 (m, 6H), 3.02 (br s, 2H), 2.49 (m, 1H), 1.07 (d, *J* = 7.2 Hz, 3H), 1.06 (s, 9H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 176.0, 135.5 (2 signals), 133.1, 133.0, 129.9, 127.8, 66.2, 63.1, 52.7, 43.4, 26.8, 19.2, 13.7. HRMS calc.: $C_{23}H_{33}NNaO_4Si$ 438.2077; found: 438.2070.

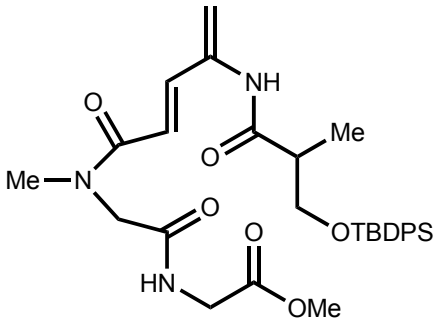
3-((tert-butyldiphenylsilyl)oxy)-2-methyl-N-(3-oxoprop-1-en-2-yl)propanamide (14):



A dry round bottom flask equipped with a magnetic stirring bar under argon was charged with CH_2Cl_2 (2.0 mL). Oxalyl chloride (170 µL, 2.00 mmol, 2.0 equiv) was added and the solution was cooled to -78 °C. 1400 µL of a 1/1 solution of dry CH_2Cl_2 and dry DMSO was added dropwise. Following the addition, the mixture was stirred 10 min at -78 °C. Then amido diol **13** (415 mg, 1.00 mmol, 1.0 equiv) dissolved in 1800 µL of 2/1 DMSO/CH_2Cl_2 was added dropwise. The reaction was stirred at -78 °C for 20 min and then NEt_3 (700 µL) was added. Reaction was maintained at -78 °C for another 5 min and then allowed to gradually (ca. 60 min) warm to -15 °C and then quenched by addition of water (3.0 mL). The reaction was diluted with water (20 mL) and CH_2Cl_2 (20 mL) and the organic phase separated. The aqueous phase was extracted with $CHCl_3$ (2x20 mL). The combined organics were washed with 10% aq. citric acid (20 mL), water (20 mL), and brine (20 mL). Following drying over Na_2SO_4, the mixture was concentrated *in vacuo* to afford a viscous yellow oil. The enal product **14** was obtained after FC (SiO_2, 8x3 cm) eluting with EtOAc/pentane 1/1 as a viscous slightly yellow oil (340 mg, 0.86 mmol, 86%). R_f = 0.75, EtOAc/pentane 3/1, UV and KMnO4 dip. The material remained stable when stored under argon at -20 °C for at least 4 weeks.

^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.17 (s, 1H), 8.29 (br s, 1H), 7.64 (m, 4H), 7.46-7.36 (m, 6H), 7.22 (s, 1H), 5.58 (s, 1H), 3.73 (dd, *J* = 10.4, 8.0 Hz, 3H), 2.58 (m 1H), 1.08 (d, *J* = 7.2 Hz, 3H), 1.04 (s, 9H) ^{13}C NMR ($CDCl_3$, 100 MHZ) δ 188.9, 174.0, 139.9, 135.6, 135.5, 133.0, 132.8, 129.8 (2 signals), 127.8, 127.7, 118.2, 66.1, 44.4, 26.7, 19.1, 13.2 HRMS calc.: $C_{23}H_{29}NNaO_3Si$ 418.1814; found: 418.1815.

(*E*)-methyl 2,2,6,13-tetramethyl-9-methylene-7,12,15-trioxo-3,3-diphenyl-4-oxa-8,13,16-triaza-3-silaoctadec-10-en-18-oate (15):

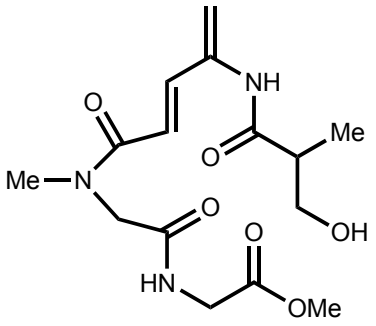


In a round bottom flask equipped with a magnetic stirring bar was added LiCl (8.5 mg, 0.20 mmol, 2.0 equiv). The salt was heated under vacuum at 140 ^{o}C overnight. After cooling, the flask was backfilled with argon. A solution (0.30 M, 0.50 mL, 0.15 mmol, 1.5 equiv) of phosphonate ester **10** in dry CH_3CN was added to the flask by syringe and the resulting mixture was stirred for 5 minutes at room temperature. Then DBU (30 μL, 0.20 mmol, 2.0 equiv) was added and the mixture was stirred for an additional 10 minutes. Finally a solution (0.20M, 0.50 mL, 0.10 mmol, 1.0 equiv) of aldehyde **14** in dry CH_2Cl_2 was added dropwise by syringe and the stirring continued for 4 hours at room temperature. At this time TLC (MeOH/EtOAc 10/90) indicated full conversion of the aldehyde with concomitant formation of an intense UV spot. The mixture was co-evaporated with 10 mL of THF to remove most of the CH_3CN and concentrated to a volume of ca. 1.0 mL. This solution was loaded directly on a column packed with iatrobeads (1 x 8 cm) equilibrated with EtOAc. The column was eluted with EtOAc to afford diene **15** as a viscous colourless oil along with traces of solvent (34.7 mg, 0.060 mmol, 60%). R_f = 0.50, MeOH/EtOAc 10/90, UV and $KMnO_4$ dip. The compound was immediately advanced to the next step.

The compound was found to exist as a 2/1 mixture of rotamers in DMSO-d_6 at room temperature. Data below is for the major rotamer.

^{1}H NMR (DMSO-d_6, 400 MHz) δ 9.13 (br s, 1H), 8.36 (br t, *J* = 5.6 Hz, 1H), 7.63-7.58 (m, 4H), 7.48-7.38 (m, 6H), 6.95 (d, *J* = 16 Hz, 1H), 6.85 (d, *J* = 16 Hz, 1H), 5.99 (s, 1H), 5.25 (s, 1H), 4.09 (d , *J* = 16 Hz, 1H), 4.03 (d, *J* = 16 Hz, 1H), 3.86 (d, J = 6 Hz, 2H), 3.80 (m, 2H), 3.63 (s, 3H), 3.08 (s, 3H), 2.96 (m, 1H) 1.02 (d, *J* = 6.4 Hz, 3H), 0.96 (s, 9H). ^{13}C NMR (DMSO-d_6, 100 MHz) δ 173.7, 170.2, 168.7, 165.5, 139.5, 139.0, 138.0, 135.0, 132.9, 129.8, 127.8, 117.6, 66.2, 51.7, 50.1, 42.8, 40.4, 36.1, 26.5, 18.8, 13.8 HRMS calc.: $C_{31}H_{41}N_3NaO_6$ 602.2662; found: 602.2664.

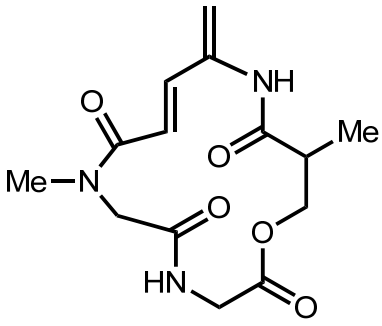
(*E*)-methyl 2-(2-(4-(3-hydroxy-2-methylpropanamido)-N-methylpenta-2,4-dienamido)acetamido)acetate (16):



Silyl ether **15** (32 mg, 0.055 mmol, 1,0 equiv) was co-evaporated with dry THF (2 x 3 mL). The mixture was concentrated to a volume of ca. 1.0 mL and then placed under argon. A dry magnet was added. Then NEt_3 (153 µL, 1.10 mmol, 20 equiv) was added followed by $3HF{\cdot}NEt_3$ (126 µL, 0.77 mmol, 14 equiv). The mixture was stirred under argon at room temperature for 90 minutes at which time TLC (MeOH/EtOAc 10/90) indicated complete conversion of the starting material. The mixture was loaded directly on a column packed with iatrobeads (1 x 6 cm) equilibrated with MeOH/EtOAc (5/95). The column was eluted with MeOH/EtOAc 5/95 to 10/90, which afforded alcohol **16** as a white powder (13 mg, 0.038 mmol, 69%). R_f = 0.35, MeOH/EtOAc 15:85, UV and $KMnO_4$ dip. The compound was found to exist as a 2/1 mixture of rotamers in DMSO-d_6 at room temperature. Data below is for the major rotamer.

^{1}H NMR (DMSO-d_6, 400 MHz) δ 9.03 (br s, 1H), 8.35 (br t, *J* = 5.6 Hz, 1H), 6.93 (d, *J* = 15 Hz, 1H), 6.81 (d, *J* = 15 Hz, 1H), 5.89 (s, 1H), 5.22 (s, 1H), 4.88 (br t, *J* = 4.8 Hz, 1H), 4.06 (s, 2H), 3.85 (d, J = 6.0 Hz, 2H), 3.63 (s, 3H), 3.37 (m, 2H), 2.67 (m, 1H), 3.10 (s, 3H), 1.00 (d, J = 6.0 Hz, 3H). ^{13}C NMR (DMSO-d_6, 100 MHz) δ 174.1, 170.2, 168.7, 165.5, 139.5, 139.0, 138.2, 117.7, 63.7, 51.7, 50.2, 42.9, 40.4, 36.2, 14.1. HRMS calc.: $C_{15}H_{23}N_3NaO_6$ 364.1485; found: 364.1484.

(*E*)-7,14-dimethyl-11-methylene-1-oxa-4,7,12-triazacyclopentadec-9-ene-2,5,8,13-tetraone (5):

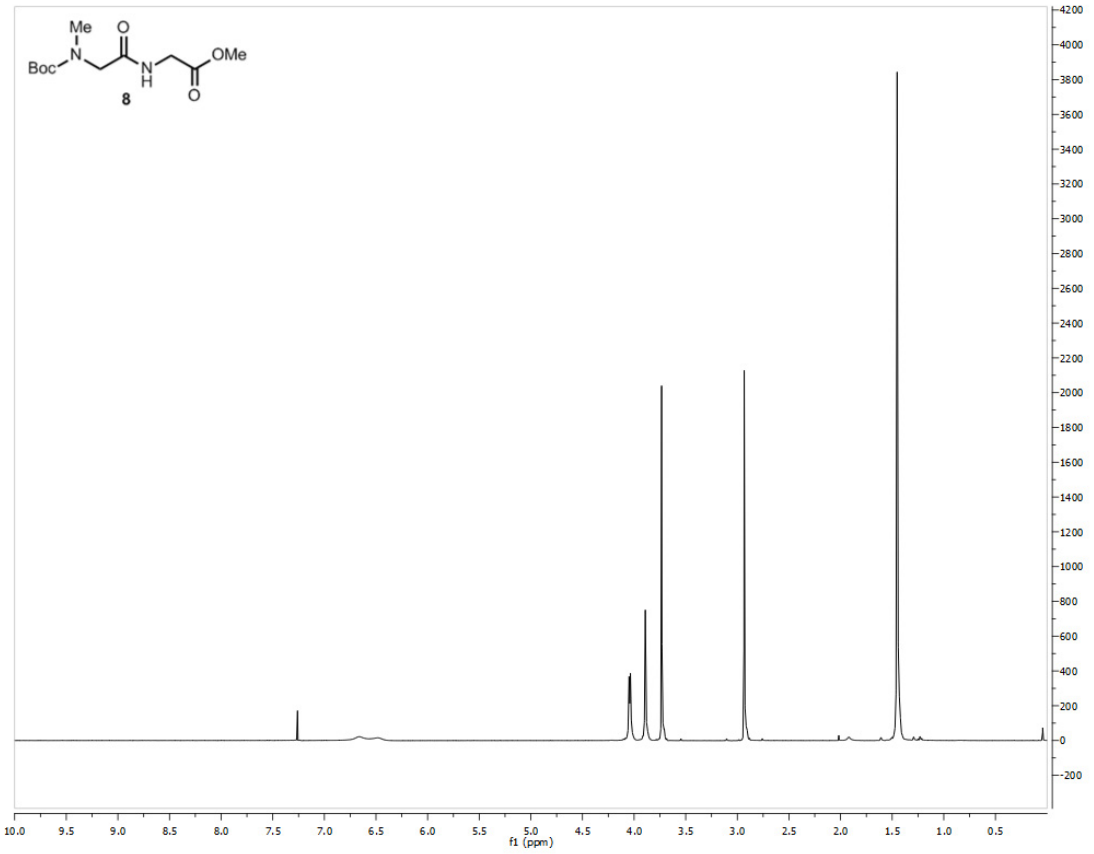


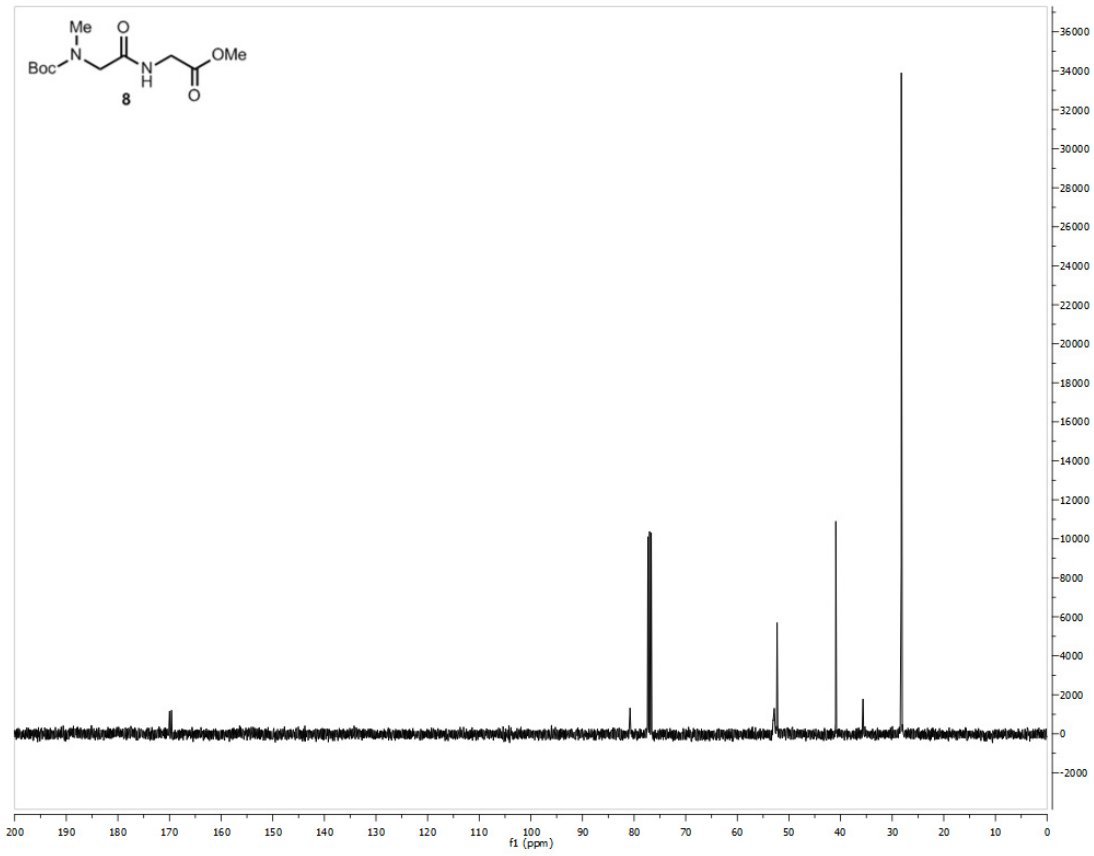
Alcohol **16** (13.0 mg, 0.038 mmol, 1,0 equiv) was placed briefly on the high vacuum line and then dissolved in dry CH_3CN under argon. A dry magnet was added. Then DBU (15 µL. 0.10 mmol, 2.6 equiv) was added and the mixture stirred at room temperature. After ca. 20 minutes a heavy precipitate develops. The mixture was stirred for additional of 70 minutes at which time TLC (MeOH/EtOAc 15/85) indicates full conversion of the alcohol spot into a slightly more polar spot. 10 mL of Et_2O was added and the mixture filtered. The resulting white powder was washed with Et_2O (10 mL) and pentane (5 mL). After drying under high vacuum, macrocycle **5** was obtained as a white powder (9.9 mg, 0.032 mmol, 84%). R_f = 0.27, MeOH/EtOAc 15:85, UV and $KMnO_4$ dip. m.p. 240 ^{o}C (decomp).

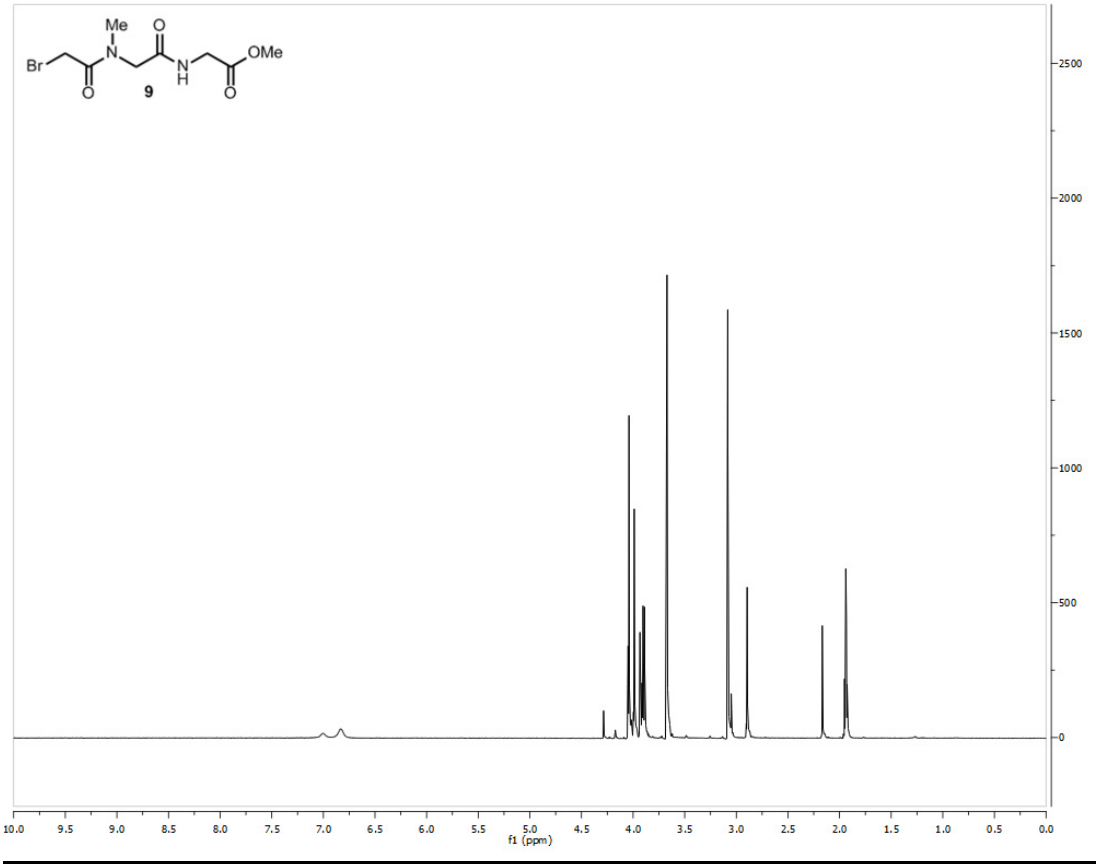
IR (neat) ν_{max} /cm^{-1} 3361, 3278, 1720, 1669, 1646, 1609, 1591, 1553, 1508, 1400, 1308, 1256, 1008, 973, 862. UV λ_{max}(EtOH)/nm 255 (ε/dm^3 mol^{-1} cm^{-1} 7600). ^{1}H NMR (DMSO-d$_6$, 400 MHz) δ 9.27 (br s, 1H), 8.62 (br t, *J* = 6.0 Hz, 1H), 6.98 (d, *J* = 15.2 Hz, 1H), 6.08 (d, *J* = 15.2 Hz, 1H), 5.50 (s, 1H), 5.28 (s, 1H), 4.16 (d, *J* = 18.0 Hz, 1H), 4.07-3.96 (m, 3H), 3.89 (d, *J* = 6.8 Hz, 2H), 3.88 (d, *J* = 18.0 Hz, 1H), 2.91 (s, 3H), 2.76 (m, 1H), 1.05 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (DMSO-d$_6$, 100 MHz) δ 172.2, 169.3, 168.4, 166.2, 139.2, 138.1, 120.5, 117.9, 66.9, 52.3, 41.1, 38.6, 35.6, 14.0. HRMS calc.: $C_{14}H_{19}N_3NaO_5$ 332.1222; found: 332.1235.

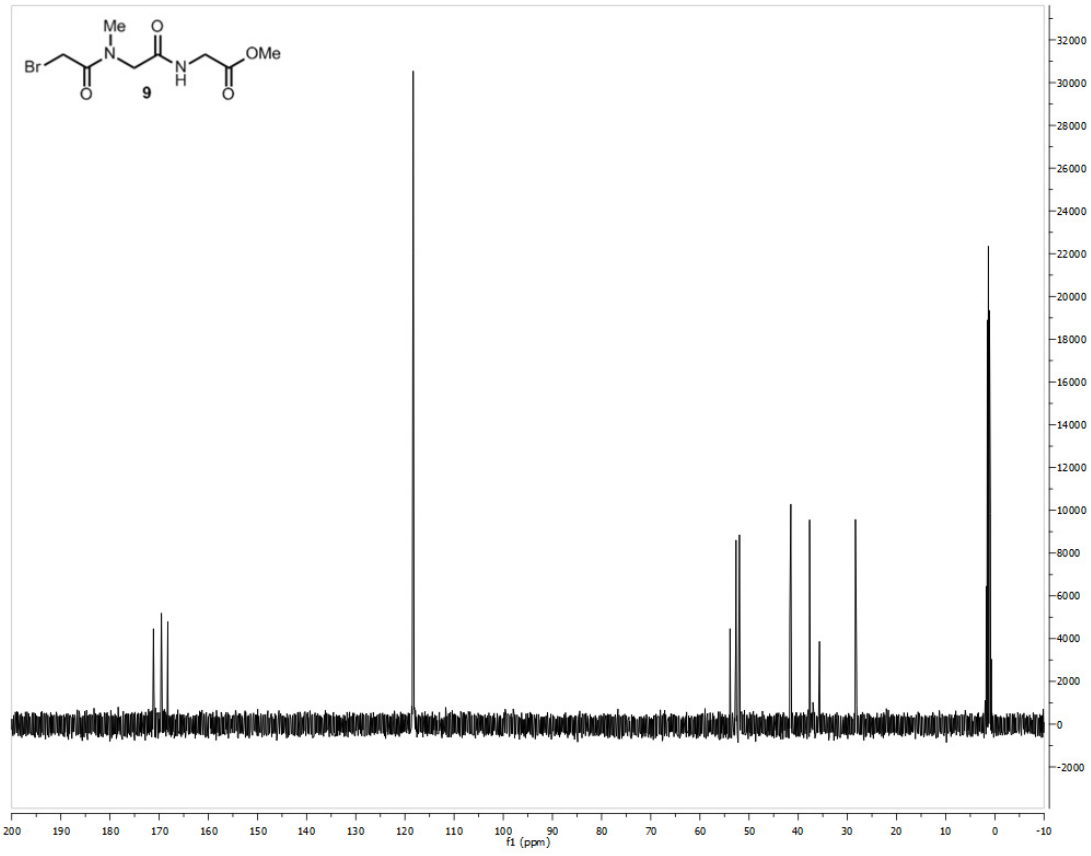
For NOE experiments, see spectra attached below.

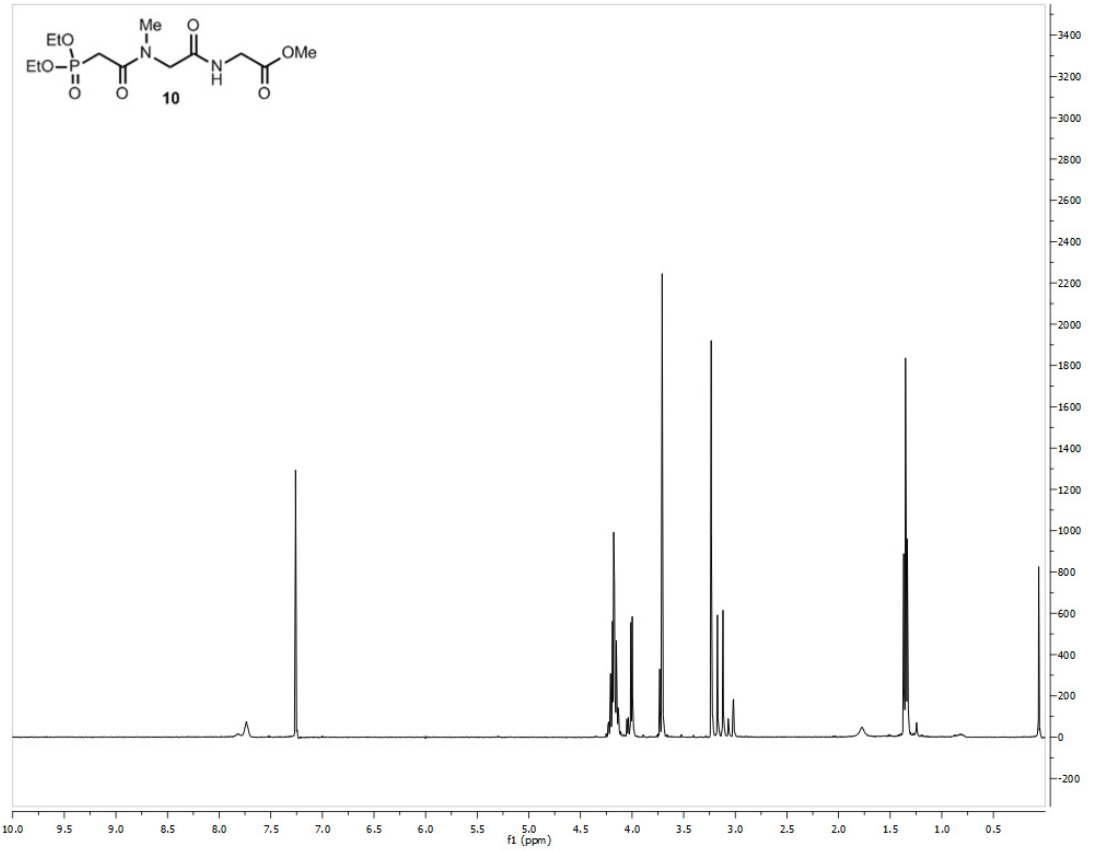
Spectra

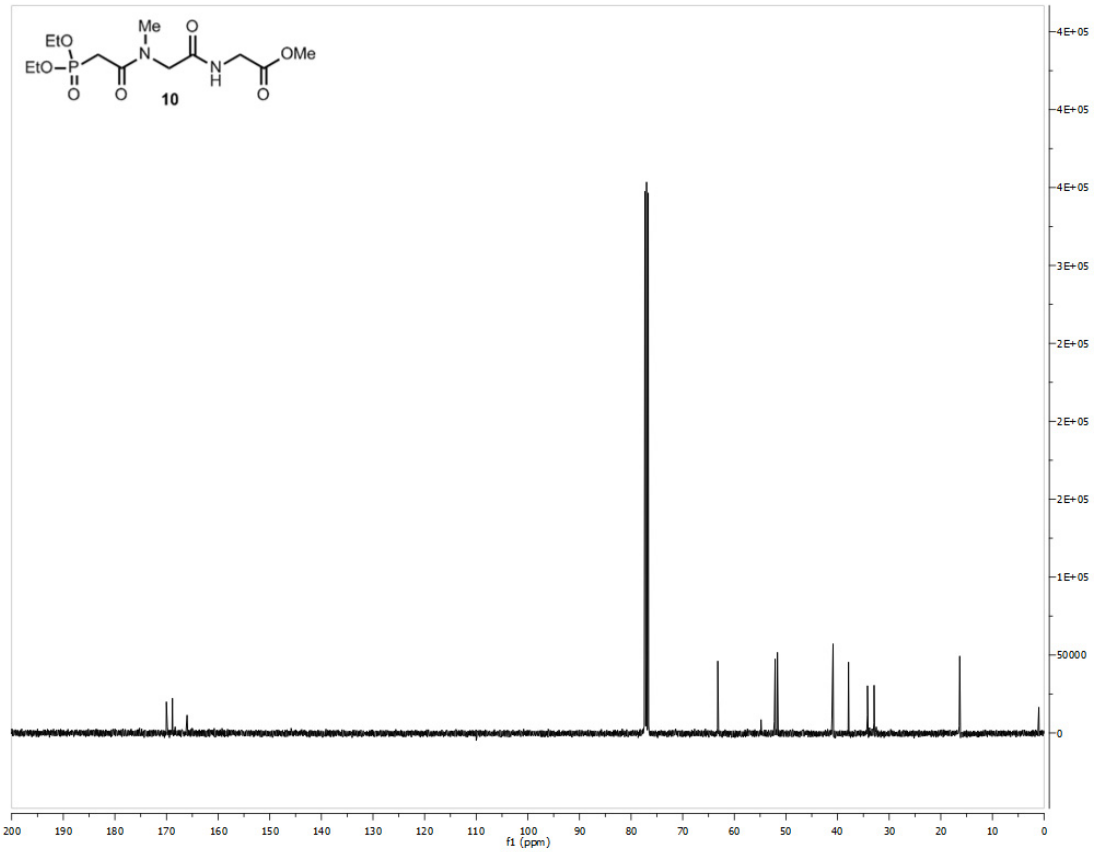


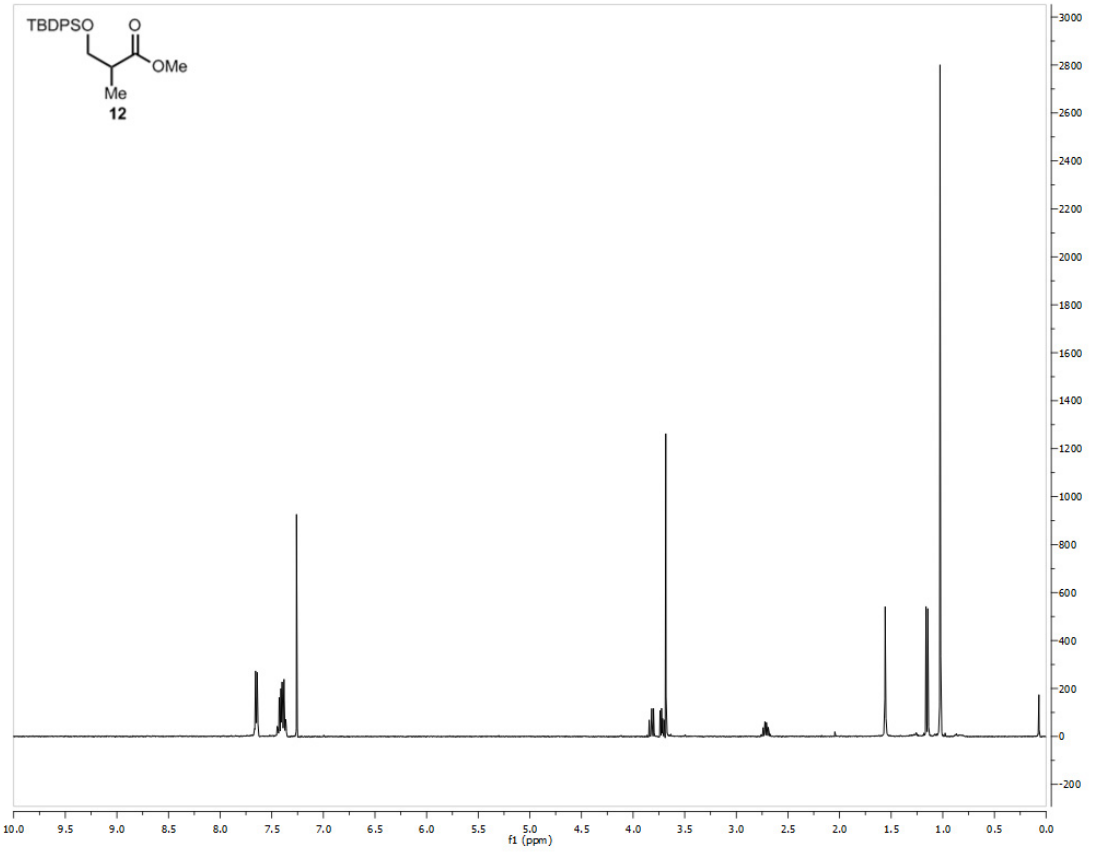


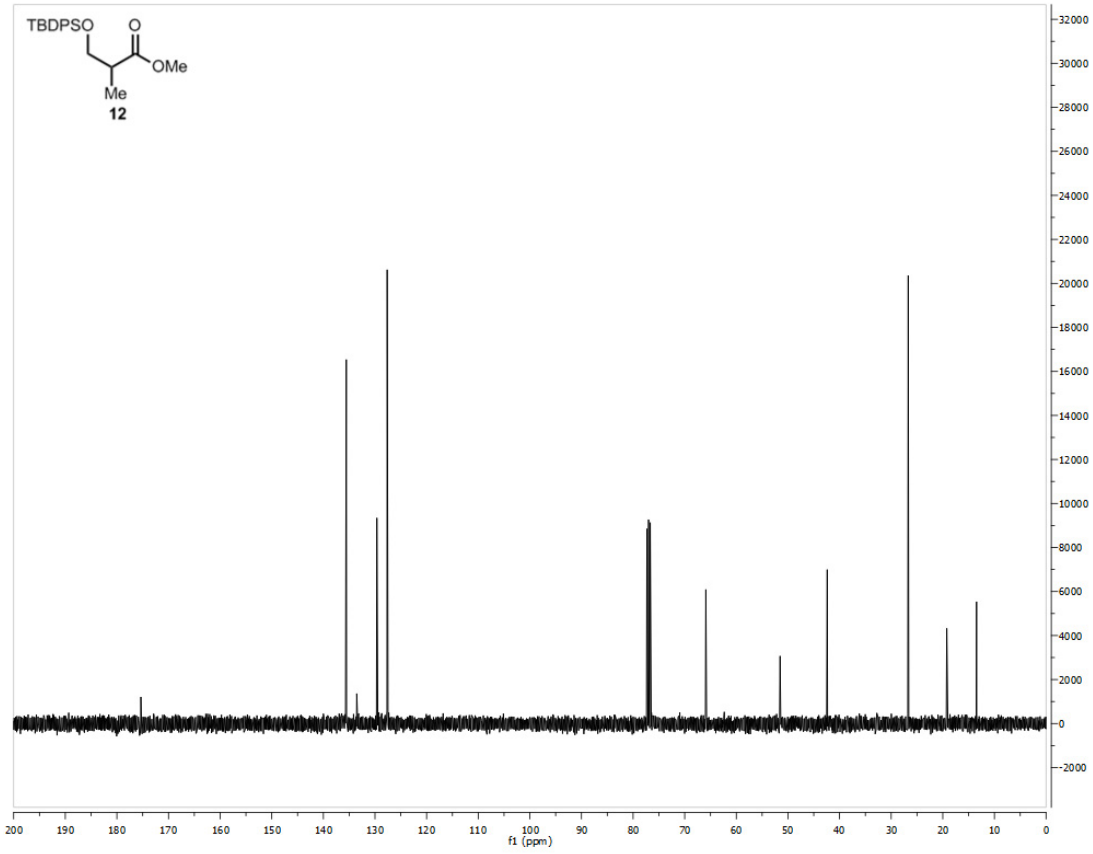

Me
O
Br
N
N
H
OMe
O
O
9
2500
2000
1500
1000
500
0
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

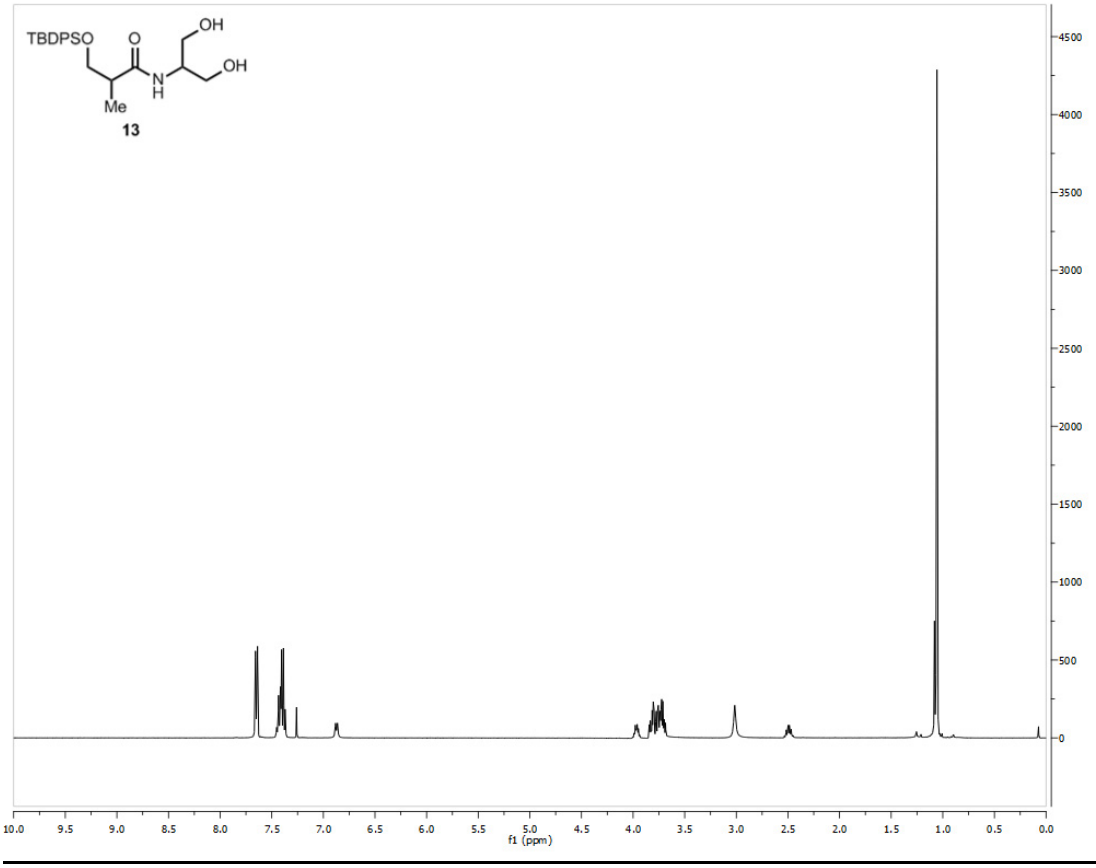

Me
O
Br
N
N
H
OMe
O
O
9
32000
30000
28000
26000
24000
22000
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
-2000
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

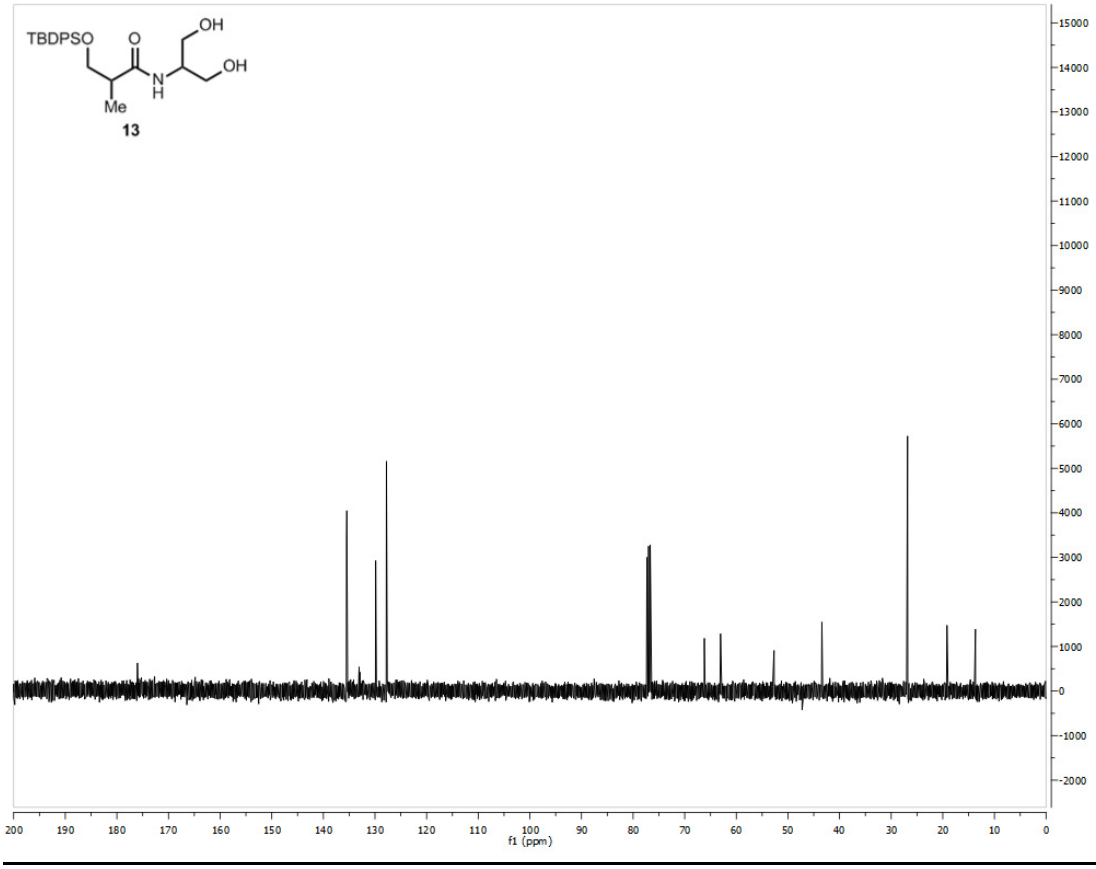

EtO
EtO
P
O
Me
N
O
O
N
H
O
OMe
O
10
3400
3200
3000
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
-200
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

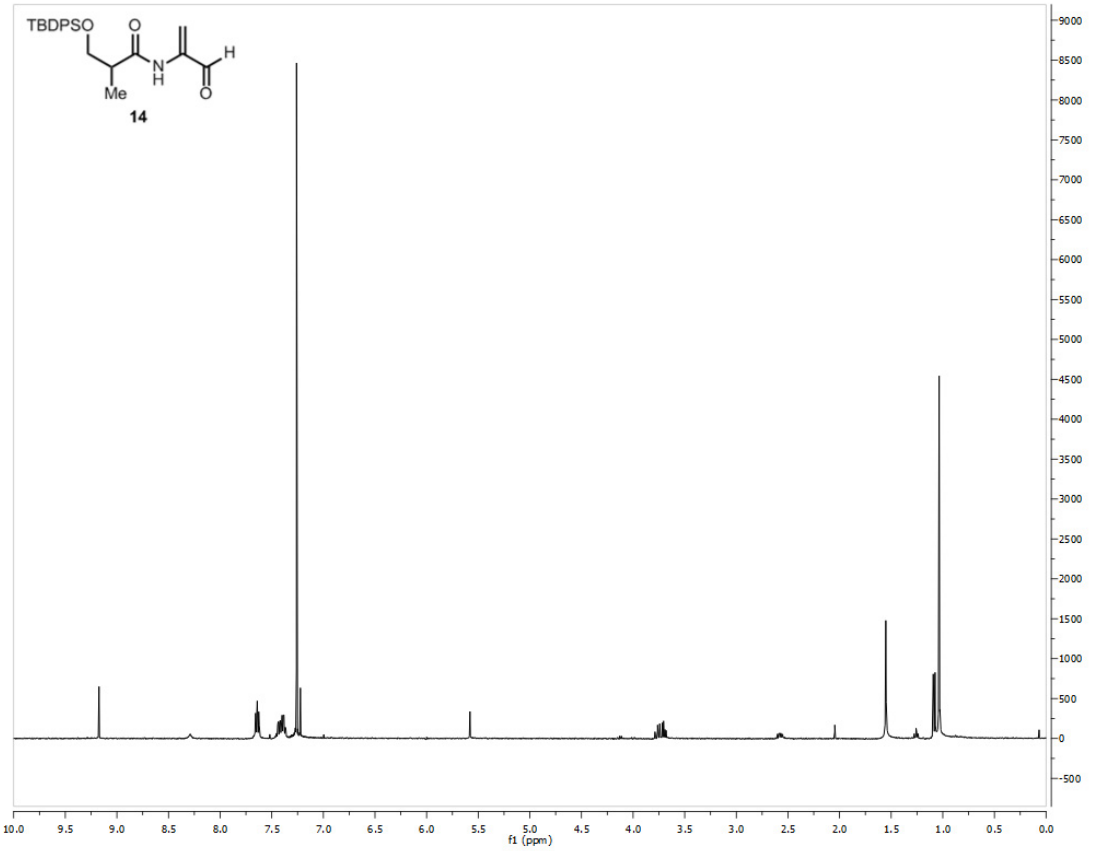

EtO
EtO
P
O
Me
N
O
O
N
H
O
OMe
O
10
4E+05
4E+05
4E+05
3E+05
2E+05
2E+05
2E+05
1E+05
50000
0
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

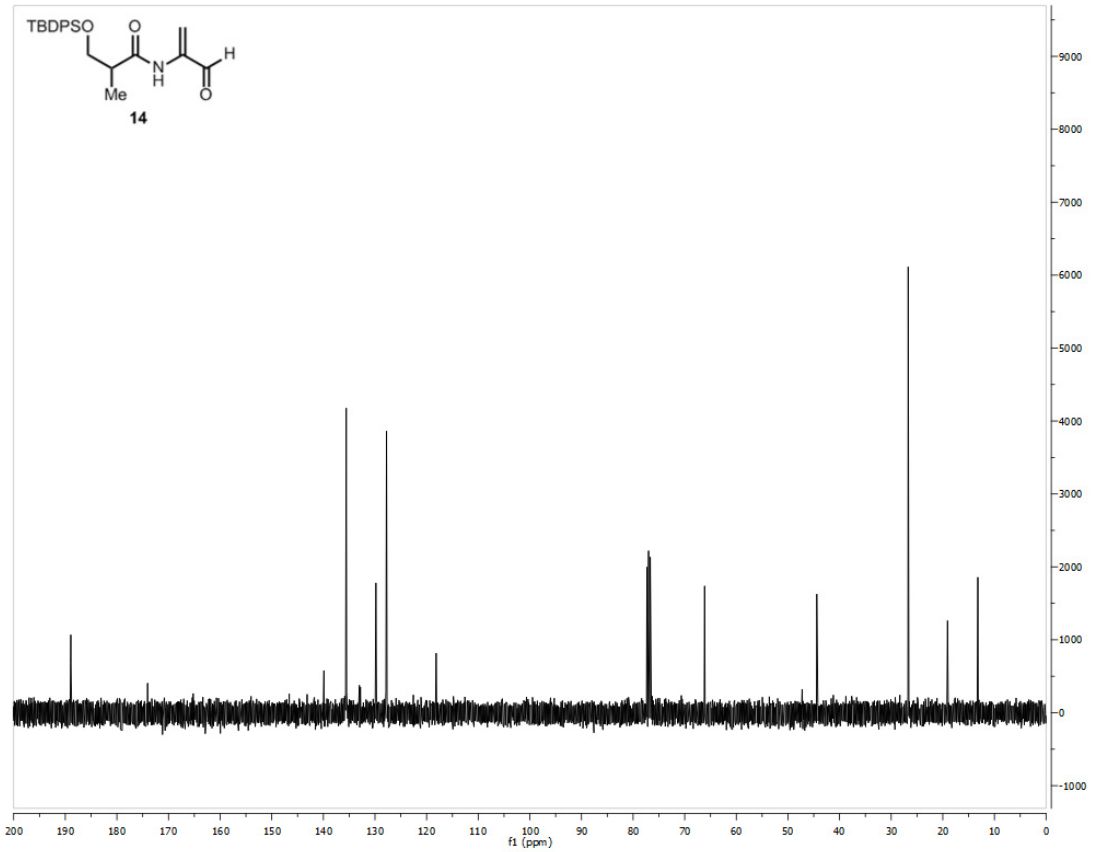

TBDPSO
O
OMe
Me
12
f1 (ppm)

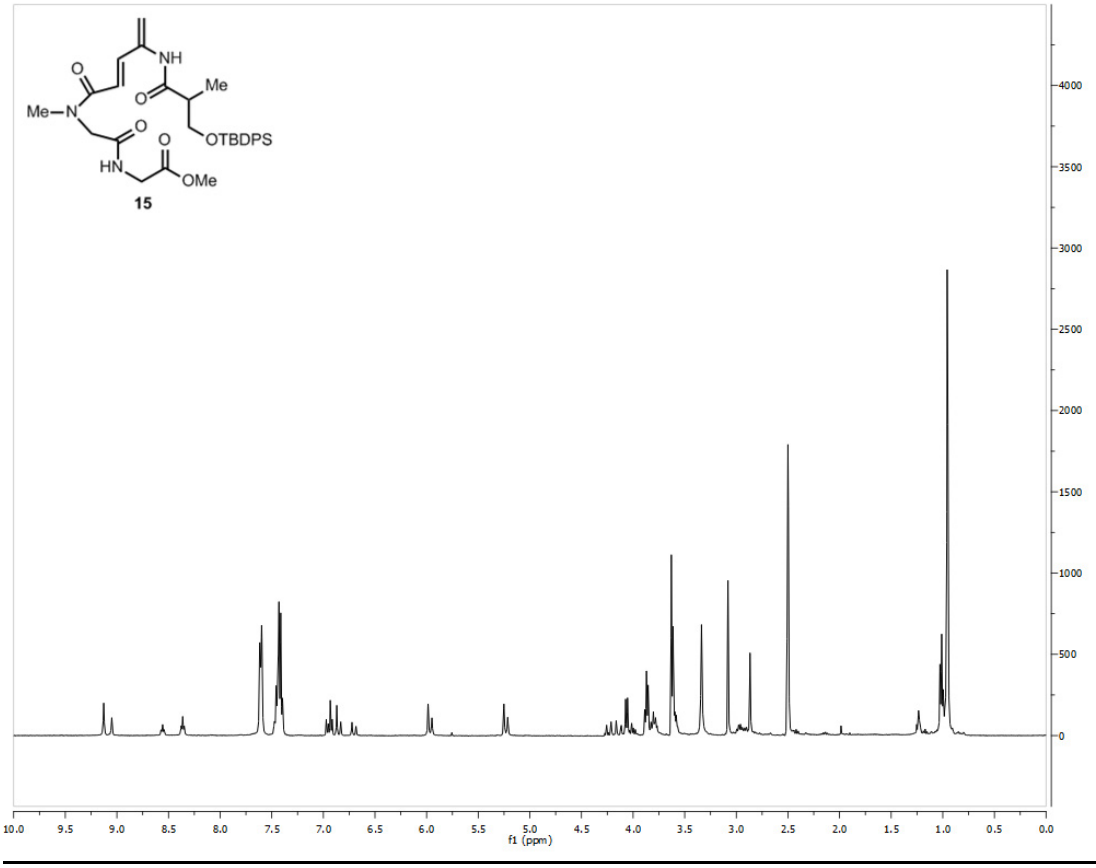

TBDPSO
O
OMe
Me
12
f1 (ppm)

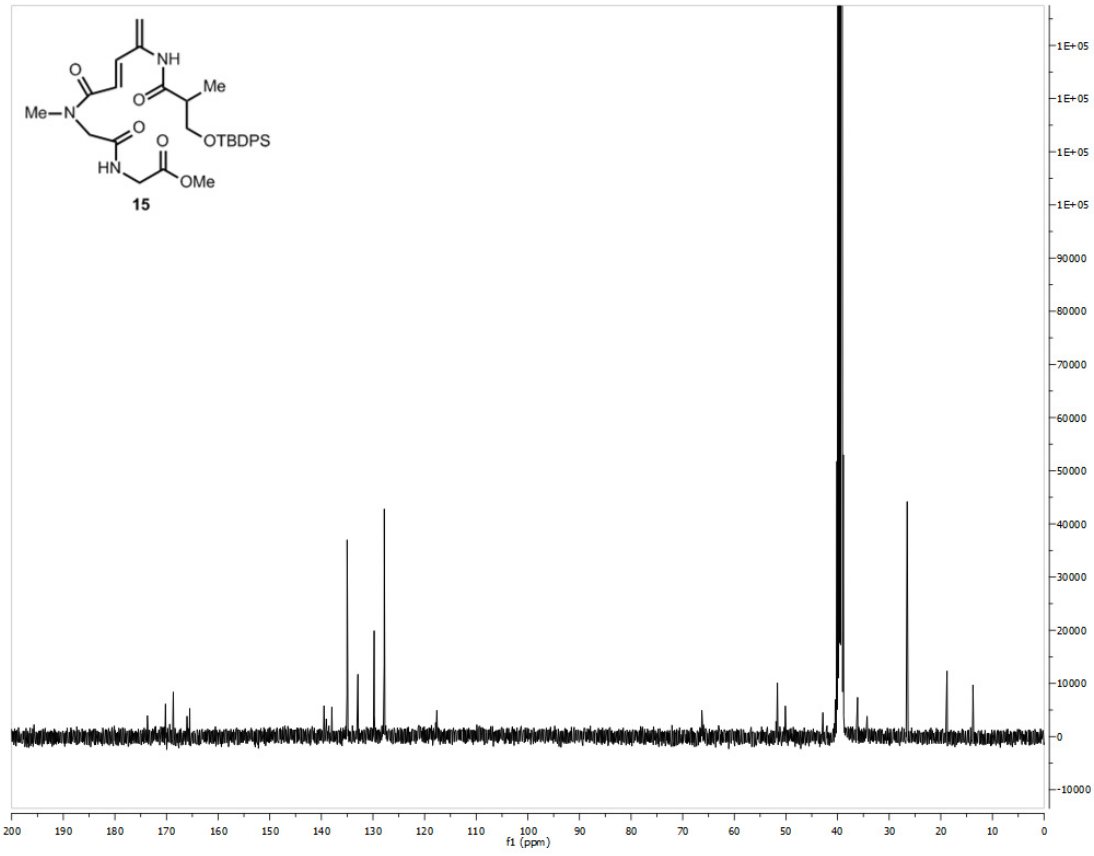

TBDPSO
O
OH
OH
N
H
Me
13
f1 (ppm)

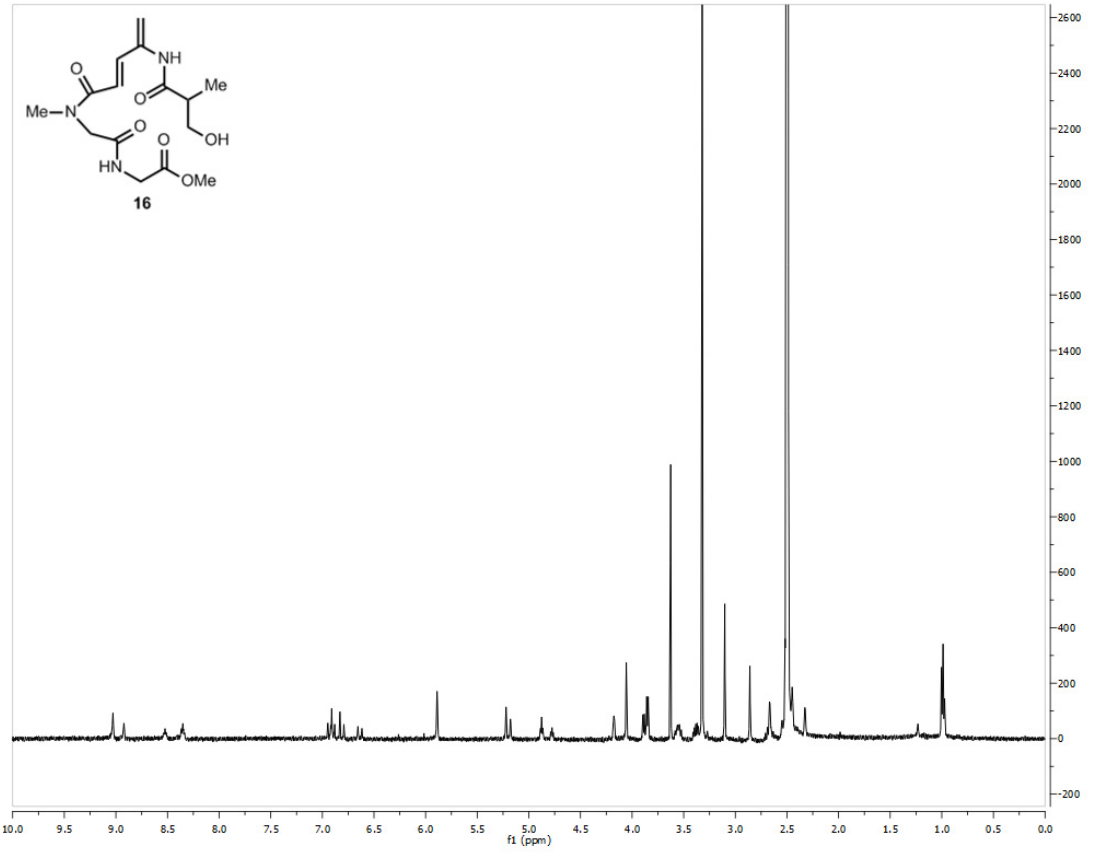

TBDPSO
O
OH
OH
N
H
Me
13
f1 (ppm)

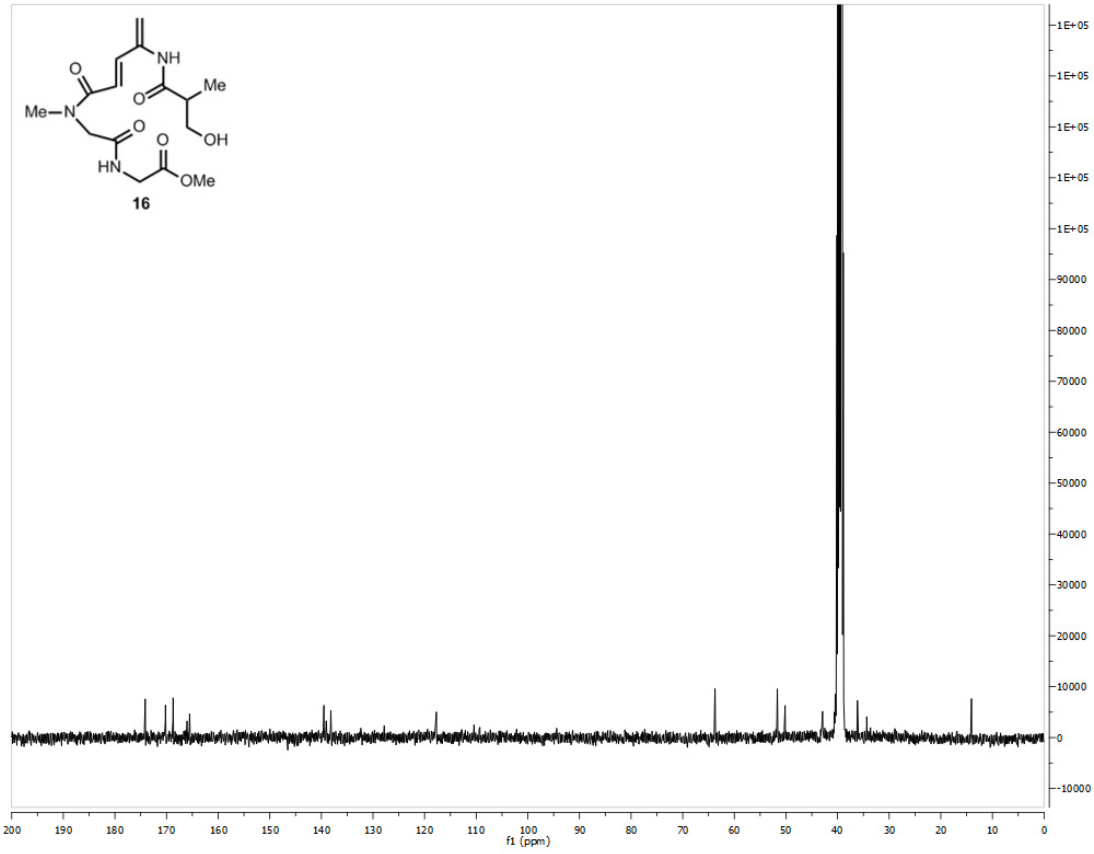

TBDPSO
O
N
H
H
O
Me
14
f1 (ppm)

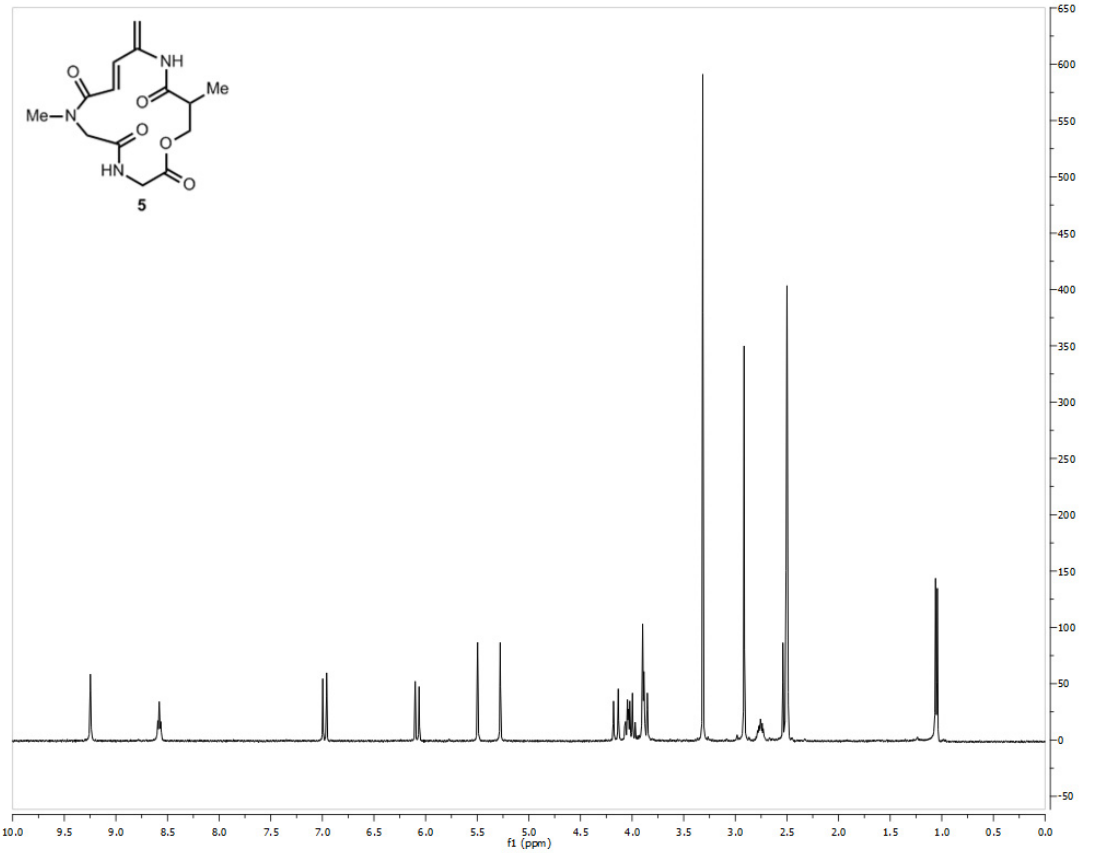

TBDPSO
O
N
H
H
O
Me
14
f1 (ppm)

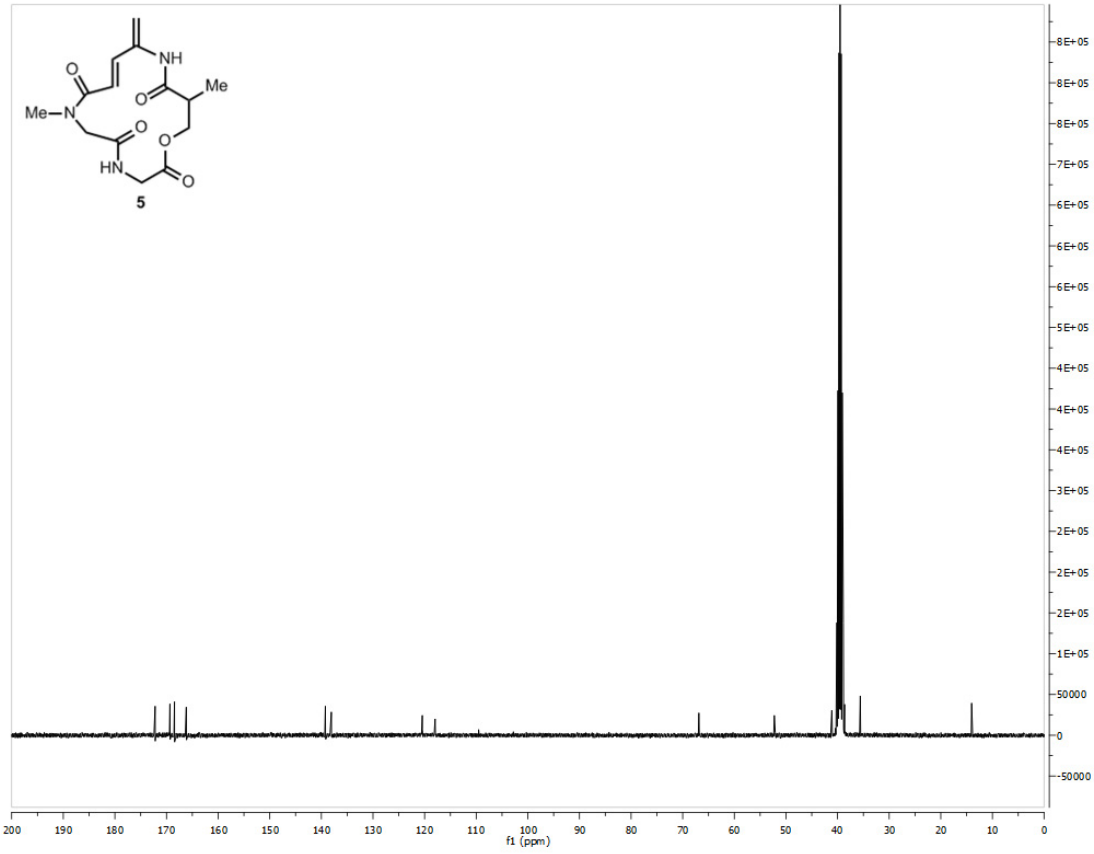

NH
O
Me
O
Me–N
O
OTBDPS
O
HN
O
OMe
15
4000
3500
3000
2500
2000
1500
1000
500
0
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

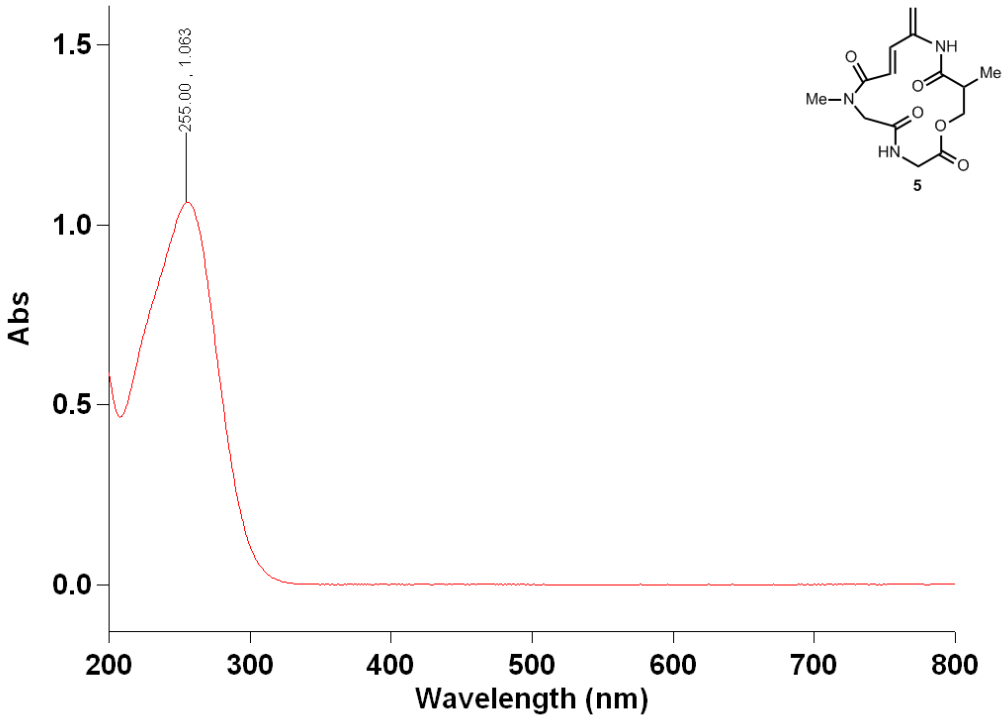

NH
O
Me
O
Me–N
O
OTBDPS
O
HN
O
OMe
15
1E+05
1E+05
1E+05
1E+05
90000
80000
70000
60000
50000
40000
30000
20000
10000
0
-10000
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

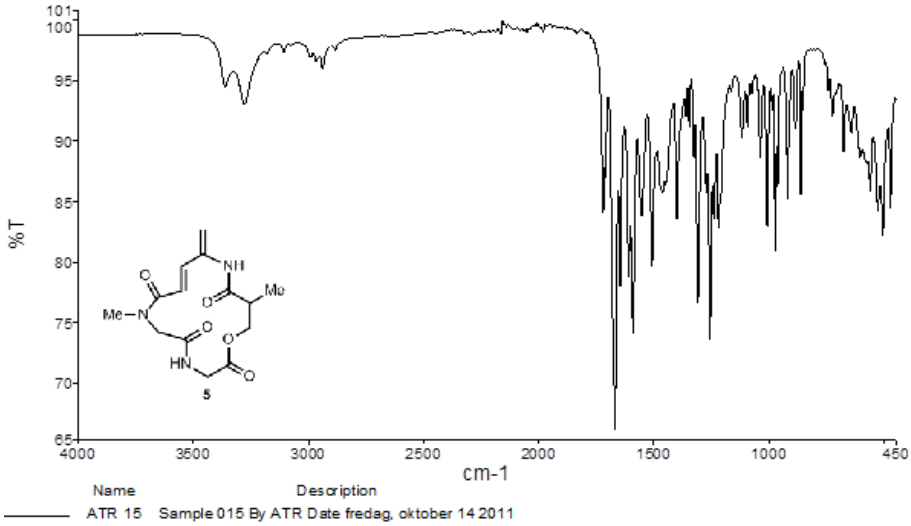

NH
O
Me
Me–N
O
OH
O
HN
O
OMe
16
f1 (ppm)


NH
O
Me
Me–N
O
OH
O
HN
O
OMe
16
f1 (ppm)


NH
O
Me
Me–N
O
O
O
HN
O
5
f1 (ppm)


NH
O
Me
Me–N
O
O
O
HN
O
5
f1 (ppm)


255.00 , 1.063
1.5
1.0
0.5
0.0
Abs
200
300
400
500
600
700
800
Wavelength (nm)
NH
Me
Me–N
O
HN
5


101
100
95
90
85
80
75
70
65
%T
4000
3500
3000
2500
2000
1500
1000
450
cm-1
NH
Me
Me–N
HN
5
Name
Description
ATR 15
Sample 015 By ATR Date fredag, oktober 14 2011

NOE-experiments with rakicidin macrocycle (5)