SUPPORTING INFORMATION

α,γ-Cyclic Peptide Ensembles with a Functionalized Cavity

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1. General Methods, Instruments Details and Materials

General: Commercially available *N*-Boc-(*D*)-Leu-OH, 1-hydroxybenzotriazole (HOBt), O-(7-azabenzotriazol-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (HATU), 2-(1*H*-benzotriazol-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (HBTU), O-(benzotriazol-1-yl)-N,N,N,´N´-tetramethyluronium terafluoroborate (TBTU) were all used as obtained from GL Biochem (Shanghai), *N*-(3-Dimethylaminopropyl)-*N´*-ethylcarbodiimide hydrochloride (EDC·HCl), *N*-Boc-(*D*)-Tyr(Me)-OH was obtained from Aldrich. *D*- (+)- Xylose 98+% was acquired from Lancaster. All others reagents obtained from commercial suppliers were used without further purification unless otherwise noted. Dichloromethane (DCM) and piperidine were dried and distilled over calcium hydride.[1,2] Tetrahydrofuran (THF) was dried and distilled over sodium/benzophenone.[1, 2] *N,N*-Diisopropylethylamine (DIEA) was dried and distilled over calcium hydride, and the redistilled over ninhydrin.[1,2] Analytical thin-layer chromatography was performed on E. Merck silica gel 60 F_{254} plates. Compound that were not UV-active were visualized by dipping the plates in a ninhydrin or cerium ammonium molybdate solution and heating. Silica gel Flash chromatography was performed using E. Merck silica gel (type 60SDS, 230-400 mesh). Solvent mixture for chromatography is reported as v/v ratios. High Performance Liquid Chromatography (HPLC) purification was carried out on PHENOMENEX CUROSIL B 5u (250 mm x 4.6 mm x 5 μm) column and KROMASIL 100 SI (250 mm x 4.6 mm x 5 μm) column. Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded on Bruker WM-250 MHz, Varian Mercury-300 MHz or Bruker AMX-500 MHz spectrometers. Chemical shifts were reported in parts per million (ppm, δ) relative to tetramethylsilane (δ 0.00), or deuterium chloroform (δ 7.26). ^{1}H NMR splitting patterns are designated as singlet (s), doublet (d), triplet (t), quadruplet (q) or pentuplet (p). All first-order splitting patterns were assigned on the basis of the appearance of the multiplet. Splitting patterns that could not be easily interpreted are designated as multiplet (m) or broad (br). Carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded on a Bruker WM-250 MHz spectrometer, Varian Mercury-300 MHz or Bruker AMX-500 MHz spectrometers. Carbon resonances were assigned using distortion less enhancement by polarization transfer (DEPT) spectra obtained with phase angles of 135. Chemical Ionization (CI) mass spectra were recorded on a Finnigan Trace mass spectrometer. Fast Atom Bombardement (FAB) mass spectra were recorded on a MS Micromass Autospec mass spectrometer. Electrospray (ESI-TOF) mass spectra were recorded on a Bruker BIOTOF II mass spectrometer.

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[1] Brown, H. C. *"Organic Síntesis via Boranes"*, Ed. John Wiley & Sons, **1975**
[2] Perrin, D. D.; Armarego, W. I. F. *"Purification of Laboratory Chemical"*, Ed. Pergamon Press, **1988**

^{1}H NMR Assignments of Cyclic Peptide. The signal of the ^{1}H NMR spectra of the peptide in $CDCl_3$ were identified from the corresponding double-quantum-filled 2D COSY (2QF-COSY), TOCSY and or NOESY and ROESY spectra acquired at the indicated concentrations and temperatures. Mixing times (~250 ms or 400 ms) were not optimized. Spectra were also obtained on a Bruker AMX-500 MHz spectrometer.

2. Synthesis of 4-amine-3-hydroxycyclofurane-2-carboxilic acid (γ-Ahf-OH).

(2*R*,3*R*,4*S*)-4-azido-3-(benzyloxy)-2-(dimethoxymethyl)tetrahydrofuran (7): A solution of compound (2*R*,3*R*,4*S*)-4-azido-2-dimethoxymethyl-3-hydroxytetrahydrofuran **(5)**[3] (1.20 g, 5.91 mmol) in dry THF (60 mL), was treated with NaH (60% dispersion in mineral oil, 244 mg, 6.1 mmol). After stirring for 10 minutes, tetrabutylammonium iodide (1.13 g, 3.0 mmol) and benzyl bromide (0.76 mL, 6.3 mmol) were added and the mixture was stirred under Argon atmosphere for 3 h. After quenching with water, the THF was removed and the resulting aqueous solution was washed with Et_2O, and CH_2Cl_2. The combined organic layers were dried over Na_2SO_4 anhydrous, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography (30% Ethyl acetate/hexanes), to give compound **7** as a beige oil. [1.30 g, 75%, R_f = 58% (30% Ethyl acetate/hexanes)]}ç. **^{1}H NMR** (250.13 MHz, $CDCl_3$) δ: 7.43 – 7.27 (m, 5H), 4.60 (d, *J* = 4.8 Hz, 1.6H), 4.35 (d, *J* = 6.2 Hz, 1H), 4.07 – 3.87 (m, 5H), 3.44 (d, *J* = 3.9 Hz, 6H). **MS (Cl$^+$) [m/z(%)]:** 234 (27), 204 (8), 128 (39), 107 (89). **HRMS [MH]$^+$ calculated** for $C_{12}H_{16}N_3O_2$ 234.12425, found 234.12471. **IR (Film):** 2935, 2833, 2104, 1099 cm^{-1}.

(2*R*,3*R*,4*S*)-4-azido-3-(benzyloxy)tetrahydrofuran-2-carbaldehyde: A solution of acetal **7** (10.71 g, 36.55 mmol) in a TFA-water mixture (9:1, 49 mL) was stirred at rt for 3 h. Water (100 mL) and dichloromethane (100 mL) were added, the organic phase was separated, and washed with $NaHCO_3$ (sat.) and brine. The organic layers were dried over Na_2SO_4 anhydrous, filtered and concentrated under reduced pressure to give the wished aldehyde that was used without further purification. [9.02 g, 100%, R_f = 39% (30% Ethyl acetate/hexanes)]. **^{1}H NMR** (250.13 MHz, $CDCl_3$) δ: 9.62 (d, *J* = 0.9 Hz, 1H), 7.52 – 7.17 (m, 8H), 4.75 – 4.40 (m, 3H), 4.35 (s, 1H), 4.27 – 3.80 (m, 7H). **MS (Cl$^+$) [m/z(%)]:** 248 (7), 220 (46), 133 (22), 107 (100). **HRMS [MH]$^+$ calculated** for $C_{12}H_{14}N_3O_3$ 248.10352, found 248.10408.

(2*R*,3*R*,4*S*)-methyl 4-azido-3-(benzyloxy)tetrahydrofuran-2-carboxylate (8): A solution of (2*R*,3*R*,4*S*)-4-azido-3-(benzyloxy)tetrahydrofuran-2-carbaldehyde (9.0 mg, 36.43 mmol) in acetonitrile (100 mL) was treated with *N*-bromosuccinimide (32.0 g, 182.1 mmol), K_2CO_3 (25.0 g,

[3] Moravková, J.; Capková, J.; Stanek, J. *Carbohydr. Res.* **1994**, 263, 61; Talekar, R. R.; Wightman, R. H. *Tetrahedron* **1997**, 53, 3831.

182.1 mmol) and MeOH (40 mL). The mixture was stirred in the dark for 24 h and then the yellow solution was treated with $Na_2S_2O_5$. The acid **8** was extracted with a hexane/ether mixture (1:1) and the combined organic layers were washed with brine, dried over Na_2SO_4 anhydrous, filtered and concentrated under reduced pressure to provide compound **8** after purification by flash chromatography (10% Ethyl acetate/hexanes) as a light beige oil. [9.10 g, 91%, R_f = 37% (10% ethyl acetate/hexane)]. **^{1}H NMR** (250.13 MHz, $CDCl_3$) δ: 7.45 – 7.27 (m, 5H), 4.66 (q, *J* = 11.8 Hz, 2H), 4.53 (d, *J* = 2.5 Hz, 1H), 4.28 – 4.11 (m, 2H), 4.10 – 4.00 (m, 2H), 3.79 (s, 3H). **MS (FAB$^+$) [m/z(%)]:** 300 (MNa^+), (25), 278 (MH^+), (31), 154 (97), 137. **HRMS [MH]$^+$ calculated** for $C_{13}H_{16}N_3O_4$ is 278.11408, found 278.11329.

(2*R*,3*R*,4*S*)-4-azido-3-(benzyloxy)tetrahydrofuran-2-carboxylic acid (9): A solution of ester **8** (79.0 mg, 0.28 mmol) in a methanol/water mixture (3:1, 8 mL) was treated with $LiOH·H_2O$ (60.0 mg, 1.43 mmol) at 0ºC. The solution was stirred at this temperature for 10 min and then at rt for 5 h. After removal of the solvent, the residue was diluted with water, washed with CH_2Cl_2, and the aqueous solution was acidified to pH 3. The residue was extracted with CH_2Cl_2 and the combined organic layers were dried over Na_2SO_4 anhydrous and concentrated under reduced pressure, to gave the acid **9** as a light yellow oil. [73 mg, 100%, R_f = 10% (30% Ethyl acetate/hexanes)]. **^{1}H NMR** (250.13 MHz, $CDCl_3$) δ: 7.38 – 7.25 (m, 5H), 4.67 (d, *J* = 11.9 Hz, 1H), 4.57 (d, *J* = 11.9 Hz, 1H), 4.47 (d, *J* = 2.0 Hz, 1H), 4.12 (dd, *J* = 4.7 Hz, 9.0, 1H), 3.96 (s, 1H), 3.84 (dd, *J* = 2.5 Hz, 9.0, 1H), 3.76 (s, 3H), 3.49 (s, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 172.11(CO), 137.51 (C), 128.61 (CH), 128.06 (CH), 127.88 (CH), 89.86 (CH), 81.94 (CH), 75.59 (CH_2), 71.86 (CH_2), 57.31 (CH), 52.46 (CH_3). **MS (ESI-TOF$^+$) [m/z(%)]:** 286.18 (MNa^+), 69.23 (MH^+). **HRMS [MH]$^+$ calculated** for $C_{12}H_{13}N_3O_4$ 286.0796, found 286.0798. **IR (Film):** 2924, 2106, 1626, 1412, 1263, 1092 cm^{-1}.

(2*R*,3*R*,4*S*)-methyl 4-amino-3-(benzyloxy)tetrahydrofuran-2-carboxylate: A solution of methyl ester **8** (5.08 g, 18.33 mmol) in dry THF (50 mL) was treated with triphenylphosphine (6.70 g, 25.67 mmol) and the resulting mixture was stirred during 3 h. After the addition of water (5.6 mL) the resulting mixture was refluxed for 1h. The solvent was concentrated under reduced pressure and the residue was purified by flash chromatography (4% MeOH/CH_2Cl_2) to give 1.88 g of the wished amine. [1.88 g, 41%, R_f = 29% (4% MeOH/CH_2Cl_2)]. **^{1}H NMR** (500 MHz, $CDCl_3$) δ: 7.38 – 7.25 (m, 5H), 4.67 (d, *J* = 11.9 Hz, 1H), 4.57 (d, *J* = 11.9 Hz, 1H), 4.47 (d, *J* = 2.0 Hz, 1H), 4.12 (dd, *J* = 4.7 Hz, 9.0 Hz, 1H), 3.96 (s, 1H), 3.84 (dd, *J* = 2.5 Hz, 9.0 Hz, 1H), 3.76 (s, 3H), 3.49 (s, 1H). **MS (ESI-TOF$^+$) [m/z(%)]:** 374 (MNa^+), 355 (MH^+). **HRMS [MH]$^+$ calculated** for $C_{13}H_{18}N_1Na_1O_4$ 374.1586, found 374.1574. **IR (Film):** 3367, 2945, 2833, 1670, 1541, 1456, 1271, 1219, 1095, 1028 cm^{-1}.

(2*R*,3*R*,4*S*)-methyl-3-(benzyloxy)-4-(tert-butoxycarbonylamino)tetrahydrofuran-2-carboxylate (4): To a solution of (2*R*,3*R*,4*S*)-methyl-4-amino-3-(benzyloxy)tetrahydrofuran-2-carboxylate (0.337 mg, 1.34 mmol) in dry dioxane (50 mL) was added DIEA (0.26 mL, 1.5 mmol),

under argon. After 20 minutes, a solution of Boc_2O (0.33 mg, 1.5 mmol) in dry dioxane (10 mL) was added drop wise to the stirred solution. After completing the addition of Boc_2O, the solution was stirred for 2 h and the solvent concentrated under reduced pressure. The resulting residue was dissolved in dichloromethane and the solution washed with water and brine, dried over Na_2SO_4 anhydrous, filtered and concentrated under reduced pressure to give a residue that was purified by flash chromatography (60% Ethyl acetate/hexanes) to provide 320 mg of the compound **4** as a white foam. [320 mg, 68%, R_f = 77% (60% Ethyl acetate/hexanes)]. **^{1}H NMR** (250,13 MHz, $CDCl_3$) δ: 7.61 (d, *J* = 8.7 Hz, 1H), 7.47 – 7.17 (m, 13H), 5.25 (br, 1H), 4.94 – 4.54 (m, 7H), 4.53 – 3.91 (m, 12H), 3.78 (d, *J* = 12.3 Hz, 3H), 1.53 – 1.19 (m, 13H). **MS (ESI-TOF$^+$) [m/z(%)]:** 374 (MNa^+), 352 (MH^+). **HRMS [MH]$^+$ calculated** for $C_{18}H_{25}N_1Na_1O_6$ 351.1586, found 374.1574. **IR (Film):** 3390, 2956, 2925, 2854, 1716, 1674, 1520, 1456, 1367, 1265, 1095 cm^{-1}.

(2*R*,3*R*,4*S*)-3-(benzyloxy)-4-(*tert*-butoxycarbonylamino)tetrahydrofuran-2-carboxylic acid: A solution of **4** (320.0 mg, 0.91 mmol) in a methanol/water mixture (3:1, 8 mL) was treated with $LiOH·H_2O$ (191.0 mg, 4.56 mmol) at 0ºC. The solution was stirred 10 min at this temperature and then at rt 5 h. After removal of the solvent, the residue was diluted with water, washed with CH_2Cl_2 and the resulting aqueous solution was acidified to pH 3. The acid was extracted with CH_2Cl_2 and the combined organic layers were dried over Na_2SO_4 anhydrous and concentrated under reduced pressure, to give wished acid as a light yellow oil. [211 mg, 71%, R_f = 60% (4% MeOH/CH_2Cl_2)]. **^{1}H NMR** (250.13 MHz, $CDCl_3$) δ: 7.56 – 7.19 (m, 5H), 7.10 (d, *J* = 5.3 Hz, 0.5 H), 6.30 (d, J = 6.6 Hz, 0.5 H), 4.86 – 4.55 (m, 2H), 4.32 (t, *J* = 8.3 Hz, 2H), 4.08 (m, 2H), 1.48 (s, 4H). **MS (FAB$^+$) [m/z(%)]:** 337 (MH^+). **HRMS [MH]$^+$ calculated** for $C_{17}H_{23}N_1Na_1O_6$ is 360.1424, found 360.1418.

3. Cyclic Peptide Synthesis.

Boc-*D*-Leu-*L*-γ-Ahf(Bn)-OMe (10a): A 0ºC cooled solution of Boc-*D*-Leu-OH (321.0 mg, 1.39 mmol) in dry THF (5 mL) was treated with HOBt (58.0 mg, 0.43 mmol) and DIC (0.068 mL, 0.43 mmol). After 10 min., a solution of the azide **9** (100.0 mg, 0.36 mmol) in dry THF (5mL) was added dropwise to the resulting stirred solution. The solution was cooled at -78ºC, stirred for 10 minutes at this temperature and then PBu_3 (0.090 mL, 0.36 mmol) was added. After stirring at this temperature for 5 h, the solution was concentrated under reduced pressure, and the residue dissolved with CH_2Cl_2, poured into a separation funnel and washed with HCl (5%). The organic layer was dried over Na_2SO_4 anhydrous, filtered and concentrated under reduced pressure. The resulting yellow oil was purified by flash chromatography (6% MeOH/CH_2Cl_2) to give 164 mg of compound **10a**. [164 mg, 98%, R_f = 53% (4% MeOH/CH_2Cl_2)]. **^{1}H NMR** (250.13 MHz, $CDCl_3$) δ: 7.31 (m, 5H), 6.81 (d, *J* = 6.9 Hz, 0.5H), 4.90 (d, *J* = 7.0 Hz, 0.5H), 4.78 (d, *J* = 11.8 Hz, 1H), 4.68 (d, *J* = 11.8 Hz, 1H), 4.48 (s, 2H), 4.26 – 3.91 (m, 3H), 3.77 (s, 2H), 1.80 – 1.06 (m, 13H), 0.91 (d,

J = 0.93 Hz, 6H). **MS (ESI-TOF$^+$) [m/z(%)]:** 487 (MNa^+), 465 (MH^+), 409, 338. **HRMS [MH]$^+$ calculated** for $C_{24}H_{37}N_2O_7$ 465.2595, found 465.2595.

Boc-*D*-Leu-*L*-γ-Ahf(Bn)-OH (10b): A 0ºC cooled solution of Boc-*D*-Leu-*L*-γ-Ahf(Bn)-OMe (**10a**) (250 mg, 0.583 mmol) in MeOH:H_2O (3:1) (8 mL) was treated with LiOH (115 mg, 2.74 mmol) and the solution was stirred at rt for 5 h. After the removal of the solvent, the residue was dissolved in water, the solution was washed with CH_2Cl_2 and then the aqueous solution was acidified to pH 3 with HCl (5%), and extracted with CH_2Cl_2. The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure to give compound **10b** as white foam that was not further purified. [200.0 mg, 83%, R_f = 49% (20% MeOH/CH_2Cl_2)]. **^{1}H NMR** (250.13 MHz, $CDCl_3$) δ: 7.25 (m, 5H), 5.40-3.40 (m, 6H), 2.56 (m, 1H), 1.70-1.00 (m, 12H), 0.86 (m, 6H). **MS (ESI-TOF$^+$) [m/z(%)]:** 473 (MNa^+), 452 (MH^+), 395, 351. **HRMS [MH]$^+$ calculated** for $C_{23}H_{35}N_2O_7$ 452.2425, found 452.2439. **IR (Film):** 3388, 2945, 2835, 1653, 1456, 1415, 1267, 1217, 1024 cm^{-1}.

Boc-*D*-Leu-*L*-γ-Ahf(Bn)-OMe (10a): A solution of compound **4** (321.0 mg, 1.28 mmol) in TFA/CH_2Cl_2 (1:1, 30 mL) was stirred at rt for 15 min. After removal the solvent, the residue was dried under high vacuum for 3 h. The result TFA salt was dissolved in dry CH_2Cl_2 (30 mL) was successively treated with Boc-*D*-Leu-OH (323.0 mg, 1.40 mmol), HATU (0.53 g, 1.4 mmol) and DIEA (0.9 mL, 5.11 mmol). After 2 h stirring at rt, the solution was poured into a separation funnel and washed with HCl (5%) and $NaHCO_3$ (sat. sol.). The organic layers were dried over Na_2SO_4, filtered and concentrated under reduced pressure, to provide a yellow oil that was purified by flash chromatography (2-4% MeOH/CH_2Cl_2) to give 534 mg of compound **10a** as a white foam. [534.0 mg, 90%, R_f = 79% (4% MeOH/CH_2Cl_2)]. **^{1}H NMR** (250.13 MHz, $CDCl_3$) δ: 7.31 (m, 5H), 6.81 (d, *J* = 6.9 Hz, 0.5H), 4.90 (d, *J* = 7.0 Hz, 0.5H), 4.78 (d, *J* = 11.8 Hz, 1H), 4.68 (d, *J* = 11.8 Hz, 1H), 4.48 (s, 2H), 4.26 – 3.91 (m, 3H), 3.77 (s, 2H), 1.80 – 1.06 (m, 13H), 0.91 (d, *J* = 0.93 Hz, 6H). **MS (ESI-TOF$^+$) [m/z(%)]:** 487 (MNa^+), 465 (MH^+), 409, 338. **HRMS [MH]$^+$ calculated** for $C_{24}H_{37}N_2O_7$ 465.2595, found 465.2595.

Boc-*D*-Tyr(Me)-*L*-γ-^{Me}*N*-Acp-OFm (11): A solution of (1*R*,3*S*)-(9*H*-fluoren-9-yl)methyl-3-(*tert*-butoxycarbonyl(methyl)aminocyclopentanecarboxylate [**γ-Boc-*L*-^{Me}*N*-Acp-OH**][4] (355 g, 0.82 mmol) in a TFA/CH_2Cl_2 mixture (1:1, 20 mL) was stirred at rt for 15 min. After removal the solvent, the residue was dried under high vacuum for 3 h. The resulting TFA salt was dissolved in dry CH_2Cl_2 (30 mL), and Boc-*D*-Tyr(Me)-OH (260.0 mg, 0.90 mmol), HATU (0.34 g, 1.1 mmol) and DIEA (0.6 mL, 3.26 mmol) were successively added. After 2 h stirring at rt, the solution was poured into a separation funnel and washed with HCl (5%) and $NaHCO_3$ (sat.). The organic

[4] For *D*-Boc-γ-^{Me}N-Acp-OH synthesis, see: a) Brea, R. J.; Amorín, M.; Castedo, L.; Granja, J. R. *Angew. Chem. Int. Ed.* **2005**, *44*, 5710-5713. b) Reiriz, C.; Castedo, L.; Granja, J. R. *J. Pept. Sci.* **2008**, *14*, 241-249.

layers were dried over Na_2SO_4, filtered and concentrated under reduced pressure, to provide yellow oil that was purified by flash chromatography (2-4% MeOH/CH_2Cl_2) to give 132 mg of compound **11** as a white foam. [132.0 mg, 28%, R_f = 74% (4% MeOH/CH_2Cl_2)]. **^{1}H NMR** (250.13 MHz, $CDCl_3$) δ: 7.86 – 7.49 (m, 4H), 7.49 – 7.22 (m, 6H), 7.08 (t, *J* = 7.5 Hz, 2H), 6.80 (d, *J* = 8.5 Hz, 2H), 5.37 (t, *J* = 8.7 Hz, 8.7 Hz, 1H), 5.10 – 4.59 (m, 1H), 4.59 – 4.32 (m, 2H), 4.28 – 3.90 (m, 2H), 3.85 – 3.59 (m, 3H), 3.11 – 2.28 (m, 5H), 2.23 – 0.62 (m, 23H). **MS (ESI-TOF$^+$) [m/z(%)]:** 1219, 917, 621 (MNa^+), 599 (MH^+), 543, 291. **HRMS [MH]$^+$ calculated** for $C_{36}H_{43}N_2O_6$ 599.3115, found 599.3116. **IR (Film):** 3421, 3053, 2956, 2927, 2850, 1732, 1712, 1637, 1512, 1450, 1265, 1171 cm^{-1}.

Boc-*D*-Leu-*L*-γ-Ahf(Bn)-*D*-Tyr(Me)-*L*-γ-^{Me}*N*-Acp-OFm (13): A solution of the dipeptide **11** (133 mg, 0.22 mmol) in of TFA/ CH_2Cl_2 (1:1, 30 mL) was stirred at rt for 15 min. After removal the solvent, the residue was dried under high vacuum for 3 h. The resulting TFA salt was dissolved in dry CH_2Cl_2 (25 mL), and dipeptide **10b** (98.0 mg, 0.22 mmol), HATU (91 mg, 0.24 mmol) and DIEA (0.33 mL, 1.95 mmol) were successively added. After 5 h stirring at rt, the solution was poured into a separation funnel and washed with HCl (5%) and $NaHCO_3$ (sat.). The organic layers were dried over Na_2SO_4, filtered and concentrated under reduced pressure, to provide a yellow oil that was purified by flash chromatography (1-2% MeOH/CH_2Cl_2) to give 187 mg of tetrapeptide **13** as a white foam. [187.0 mg, 93%, R_f = 56% (4% MeOH/CH_2Cl_2)]. **^{1}H NMR** (250.13 MHz, $CDCl_3$) δ: 7.76 (t, *J* = 6.0 Hz, 2H), 7.56 (d, *J* = 7.1 Hz, 3H), 7.48 – 7.20 (m, 16H), 7.09 (t, *J* = 8.4 Hz, 2H), 6.88 – 6.71 (m, 3H), 5.22 – 4.58 (m, 8H), 4.57 – 4.36 (m, 4H), 4.30 (dd, *J* = 2.5 Hz, 6.7 Hz, 2H), 4.25 – 3.57 (m, 13H), 3.20 – 2.09 (m, 12H), 2.09 – 0.53 (m, 49H). **MS (ESI-TOF$^+$) [m/z(%)]:** 953 (MNa^+), 931 (MH^+), 734, 435. **HRMS [MH]$^+$ calculated** for $C_{54}H_{67}N_4O_{10}$ 931.4848, found 931.4852. **IR (Film):** 3570, 3496, 2937, 2856, 2796, 1730, 1448, 1367, 1244, 1209, 1113 cm^{-1}.

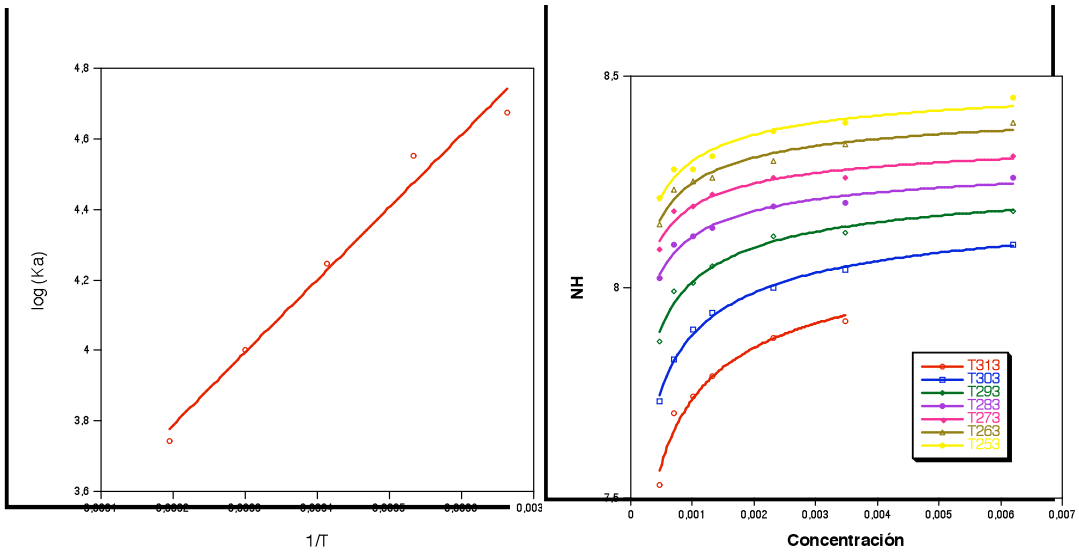
cyclo[*D*-Leu-*L*-γ-Ahf(Bn)-*D*-Tyr(Me)-*L*-γ-^{Me}*N*-Acp-] (15): A solution of Boc-*D*-Leu-γ-Ahf(Bn)-*D*-Tyr(Me)-γ-*L*-^{Me}*N*-Acp-OFm (**13**) (12.0 mg, 0.013 mmol) and piperidine (1mL) in CH_2Cl_2 (4 mL) was stirred at rt for 20 min. After removal of the solvent, the residue was dissolved in CH_2Cl_2 and the solution was washed with HCl (5%), dried over Na_2SO_4, filtered and concentrated. The resulting residue was dissolved in a TFA/CH_2Cl_2 mixture (1:1, 4 mL) and stirred at rt for 20 min. After removal of the solvent, the residue was dried under high vacuum for 3 h and used without further purification. The linear peptide was dissolved in CH_2Cl_2 (8.5 mL) and treated with TBTU (6.26 mg, 0.019 mmol) and DIEA (13 μL, 0.078 mmol). The resulting mixture was stirred at rt staring material was not detected on ht MS. The mixture was diluted with CH_2Cl_2, poured into a separation funnel and washed with HCl (5%) and $NaHCO_3$ (sat. sol.). The organic layers were dried over Na_2SO_4, filtered and concentrated under reduced pressure, and the crude was purified by HPLC (1-4% MeOH/CH_2Cl_2, 30 min, silica gel) to give 8 mg of cyclic peptide **15** as a white

solid. [6.7 mg, 81%, R_f = 14% (1% MeOH/CH_2Cl_2)]. **^{1}H NMR** (500 MHz, $CDCl_3$) δ: 7.54 – 7.09 (m, 13H), 7.00 (d, *J* = 7.8 Hz, 2H), 6.74 (d, *J* = 7.9 Hz, 2H), 6.05 (d, *J* = 7.2 Hz, 1H), 5.74 (d, *J* = 8.6 Hz, 1H), 5.28 (s, 1H), 5.05 (s, 1H), 4.90 (m, 1H), 4.80 (d, *J* = 11.5 Hz, 1H), 4.57 (d, *J* = 11.5 Hz, 1H), 4.46 (s, 1H), 4.32 (d, *J* = 7.5 Hz, 1H), 4.28 – 4.07 (m, 4H), 3.96 (d, *J* = 9.1 Hz, 1H), 3.73 (d, *J* = 13.0 Hz, 5H), 2.91 (t, *J* = 29.7 Hz, 1H), 2.84 – 2.67 (m, 4H), 2.61 (s, 1H), 2.36 – 2.07 (m, 3H), 2.05 – 1.81 (m, 6H), 1.81 – 1.35 (m, 26H), 1.34 – 1.06 (m, 21H), 0.94 – 0.71 (m, 14H). **MS (ESI-TOF$^+$) [m/z(%)]:** 657 (MNa^+), 635 (MH^+), 323 ($M2H^{+2}$), **HRMS [MH]$^+$ calculated** for $C_{35}H_{47}N_4O_7$ 635.3435, found 635.3439. **IR (Film):** 3466, 3386, 3293, 2955, 1651, 1624, 1535, 1513, 1248, 1106 cm^{-1}.

cyclo[*D*-Leu-*L*-γ-Ahf-*D*-Tyr(Me)-*L*-γ-^{Me}N-Acp-] (16): A solution of cyclic peptide **15** (50 mg, 0.079 mmol) in MeOH (20 mL) was treated with $Pd(OH)_2$ (20% Pd/C) (200 mg), under H_2(g) atmosphere and the resulting suspension was stirred for 2 days. The mixture was filtered through a celite path, and the organic layers were concentrated under reduced pressure. The resulting crude was purified on reverse phase HPLC (10-30% ACN/H_2O, 0.1% TFA) to provide 28.2 mg of cyclic peptide **16** (66%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ: 8.02 (s, 1H), 7.42 (s, 1H), 7.03 (d, *J* = 8.4 Hz, 2H), 6.73 (d, *J* = 8.5 Hz, 2H), 6.53 (brs, 1H), 4.98 (d, *J* = 7.9 Hz, 1H), 4.32 (d, *J* = 14.9 Hz, 2H), 4.15 (m, 3H), 4.03 (m, 2H), 3.68 (s, 3H), 2.90 (dd, *J* = 22.5 and 7.7 Hz, 1H), 2.80 (dd, *J* = 13.2 and 7.7 Hz, 1H), 2.72 (s, 1H), 2.69 (s, 3H), 2.29 (m, 1H), 2.16 (m, 1H), 0.81 (overlapped d, *J* = 6.0 Hz, 6H). **MS (ESI-TOF$^+$) [m/z(%)]:** 1111 ($2MNa^+$), 1089 ($2MH^+$), 567 (MNa^+), 567 (MH^+), 457. **HRMS [MH]$^+$ calculated** for $C_{28}H_{41}N_4O_7$ 545.2967, found 545.2970. **IR (Film):** 3409, 3288, 3052, 1651, 1539, 1265 cm^{-1}.

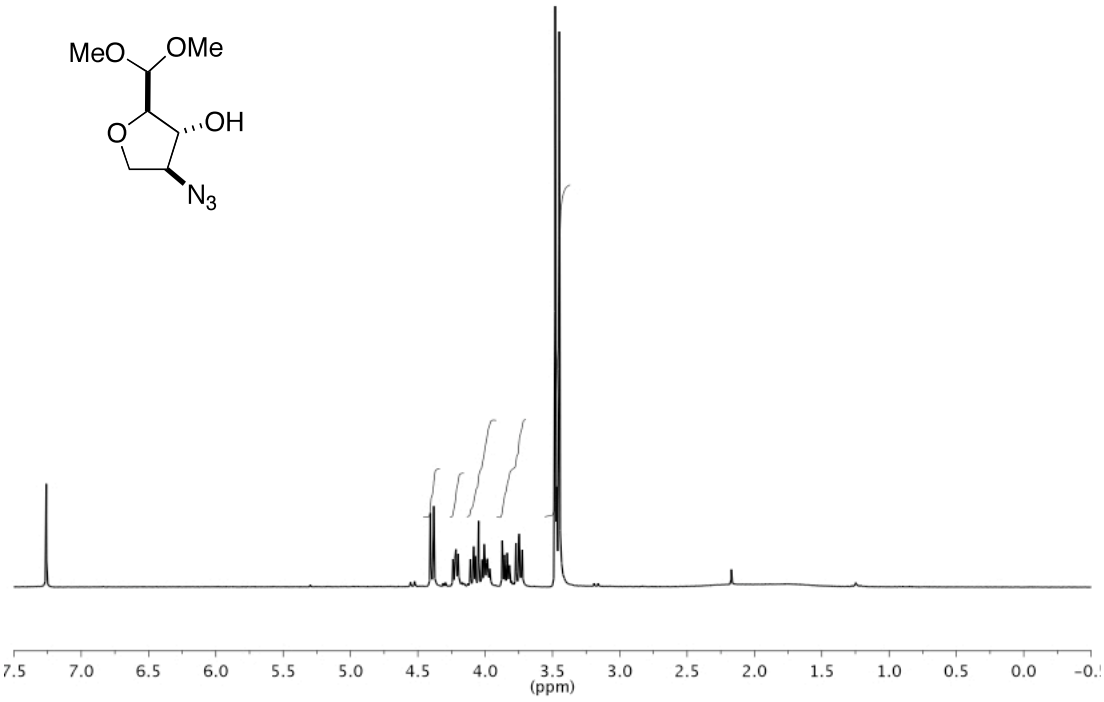
3. Van´t Hoff Analysis of Dimerization.

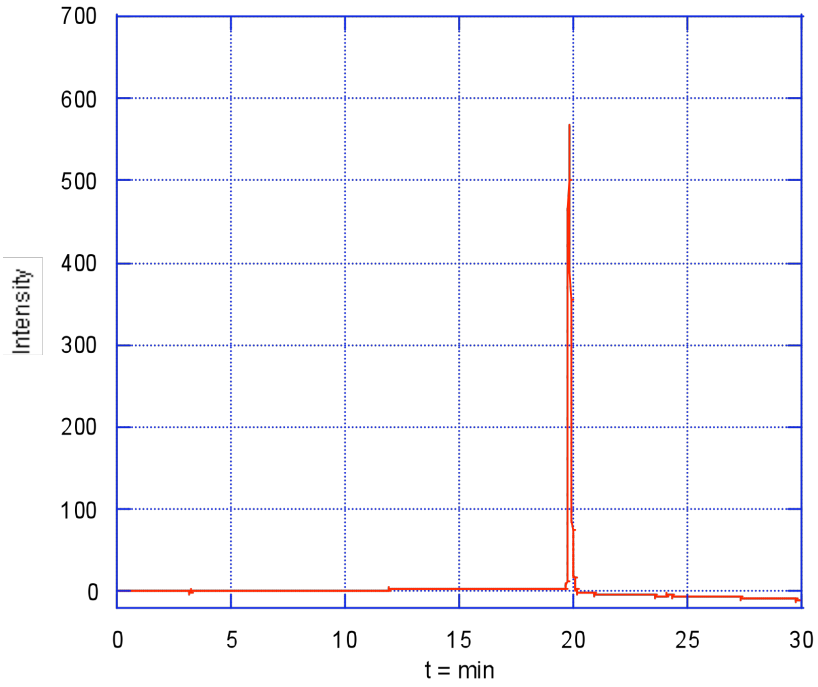
The HPLC-purified cyclic peptide **16** was dissolved in dry $CDCl_3$ at concentration of 6.204, 3.490, 2.320, 1.320, 1.01, 0.700, 0.47 mM. ^{1}H-NMR spectra of the resulting samples were acquired at intervals of 10 K in the temperature range of 313-253 K. Single point determinations of Ka were estimated at each temperature as described previously.[5] Analysis of a plot of *1/T* (K) *vs* ln K_a afforded the values ΔH^o_{298}= 39.03 KJ mol^{-1} and ΔS^o_{298}= -53.38 JK^{-1} mol^{-1}.



[5] Sanchez-Quesada J, Kim HS, Ghadiri MR. *Angew. Chem. Int. Ed.* 2001; **40**: 2503-2506.

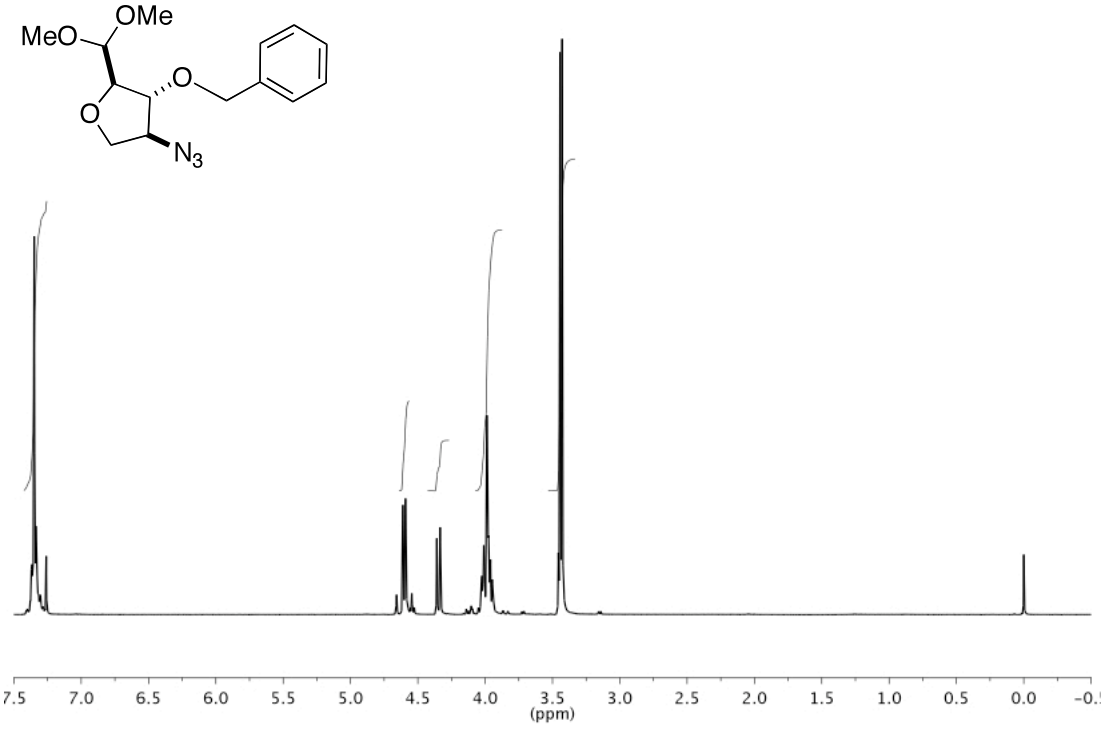
(5)

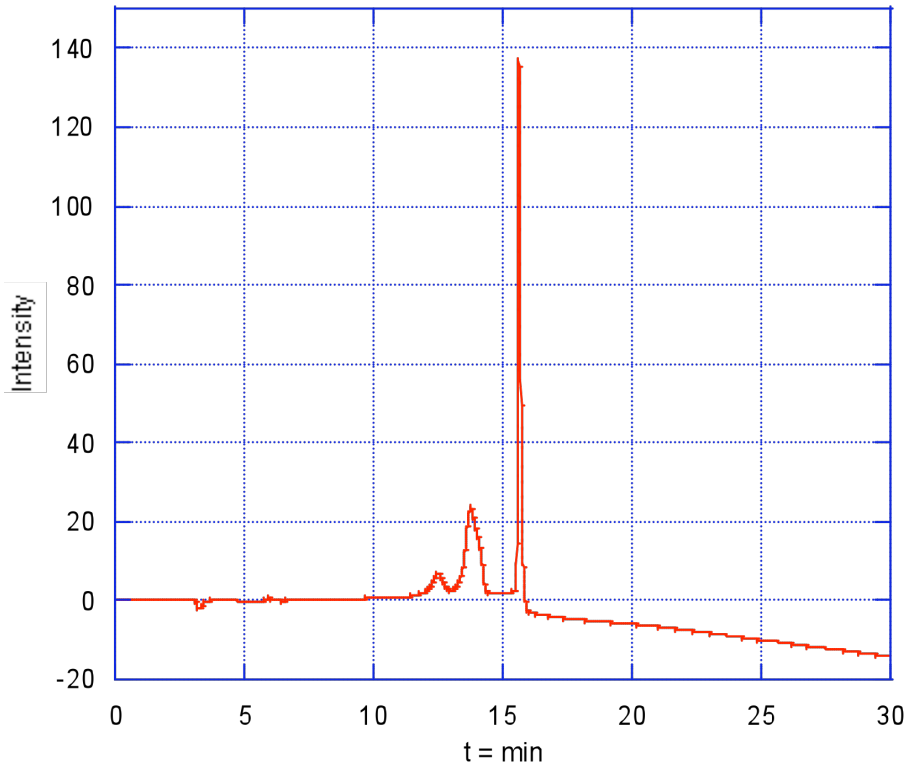




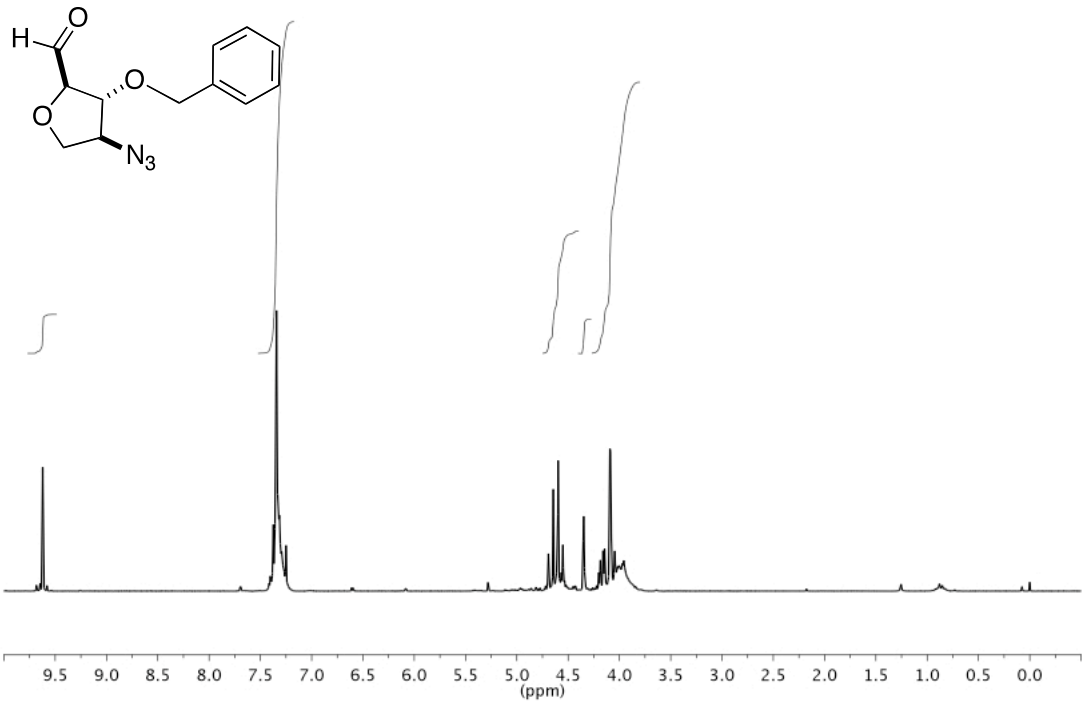
PHENOMENEX CUROSIL B 5u (250 mm x 4.6 mm, micron) column. Gradient: 0% to 5% MeOH/CH_2Cl_2 in 30 min, 1.0 mL/min.

(7)

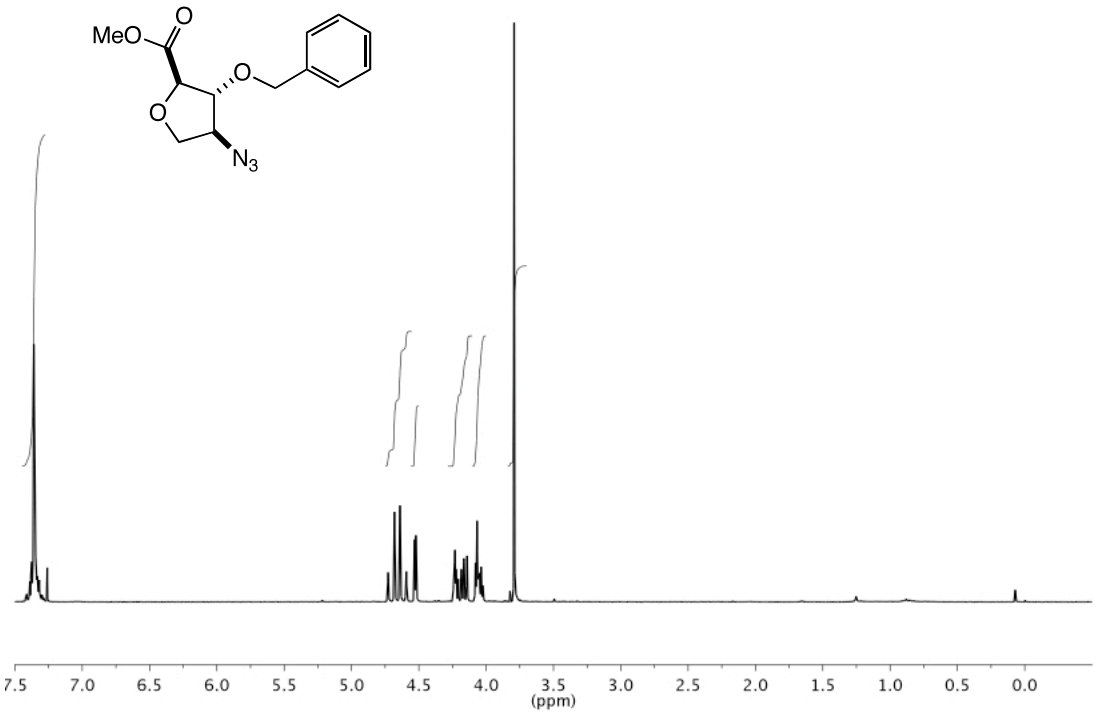




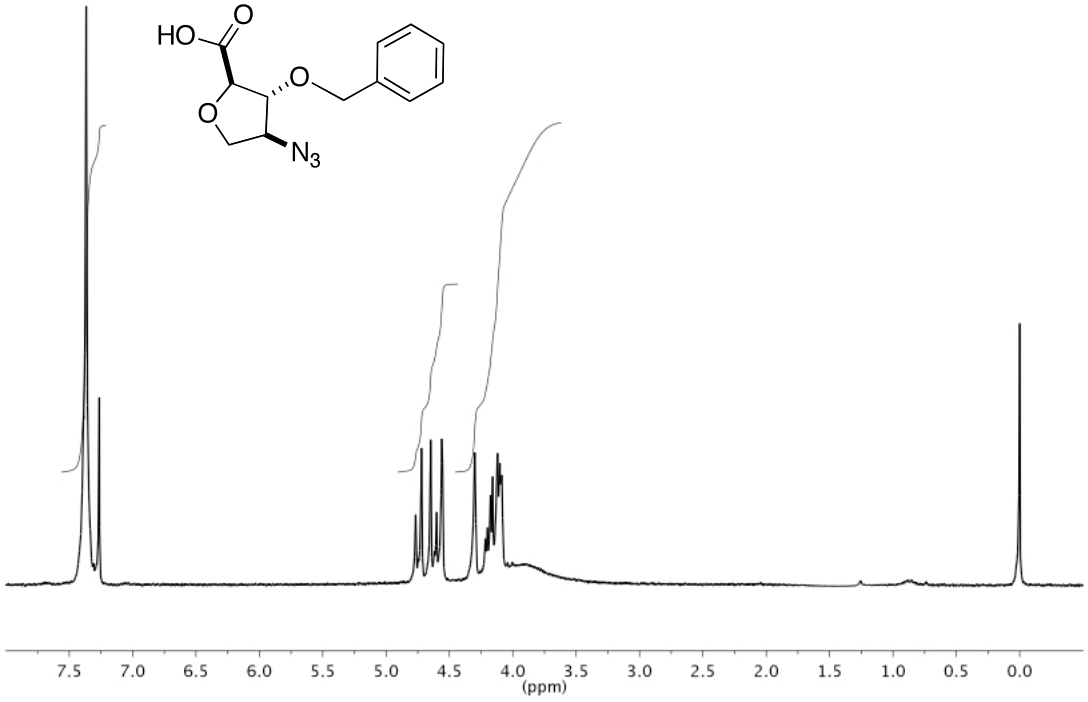
PHENOMENEX CUROSIL B 5u (250 mm x 4.6 mm, micron) column. Gradient: 0% to 5% MeOH/CH_2Cl_2 in 30 min, 1.0 mL/min.

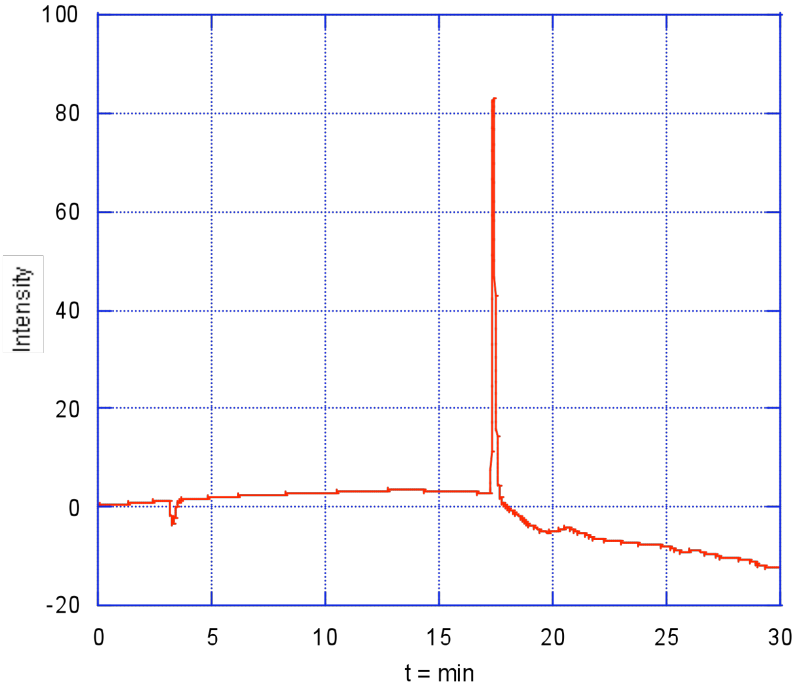

H
O
O
O
N3
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
(ppm)

(8)

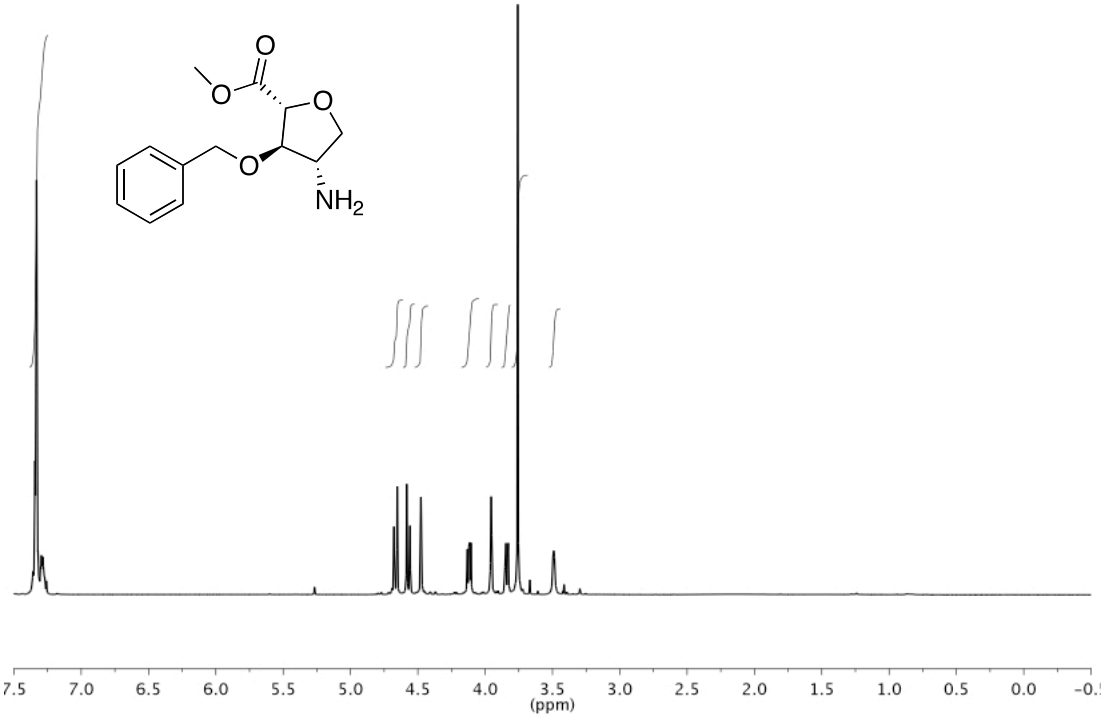

MeO
O
O
O
N3
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
(ppm)

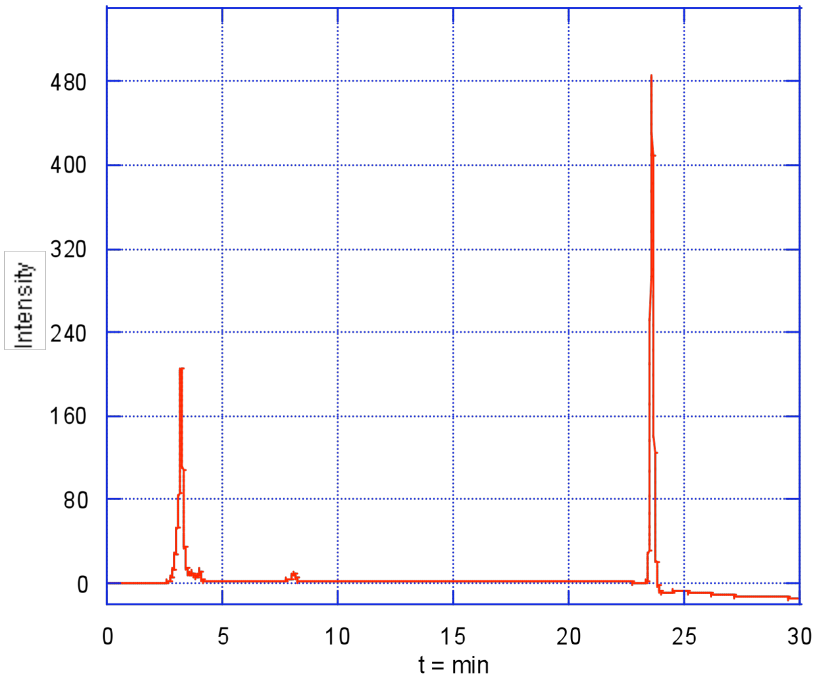
(9)





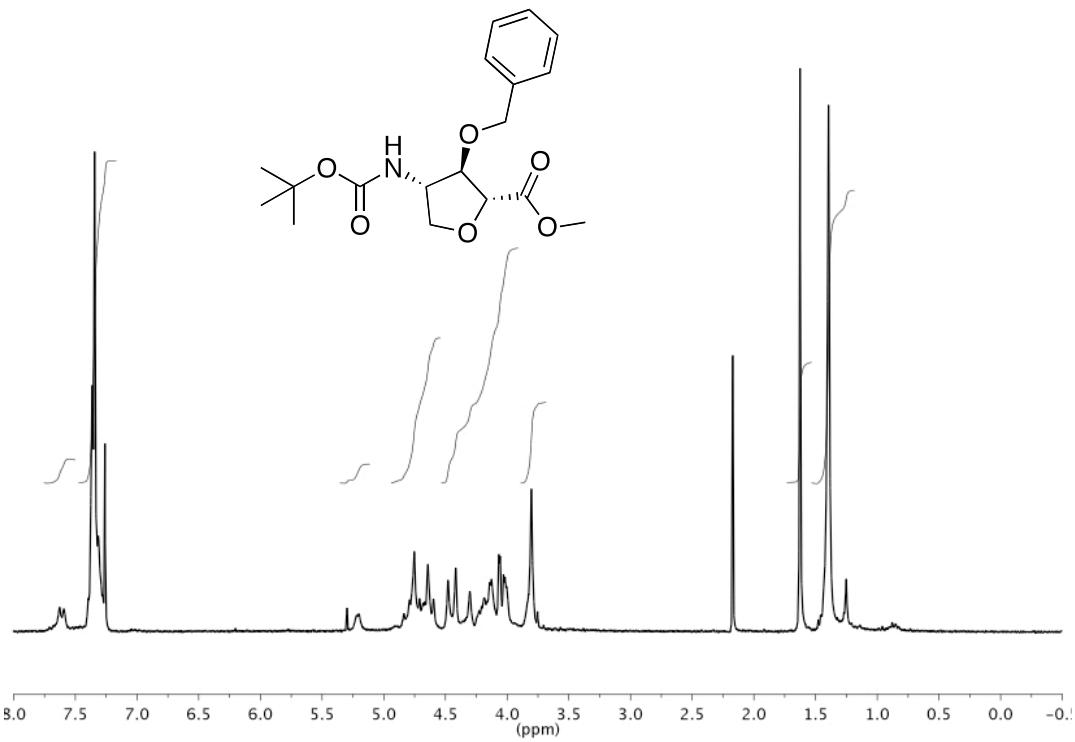
PHENOMENEX CUROSIL B 5u (250 mm x 4.6 mm, micron) column. Gradient: 0% to 5% MeOH/CH_2Cl_2 in 30 min, 1.0 mL/min.

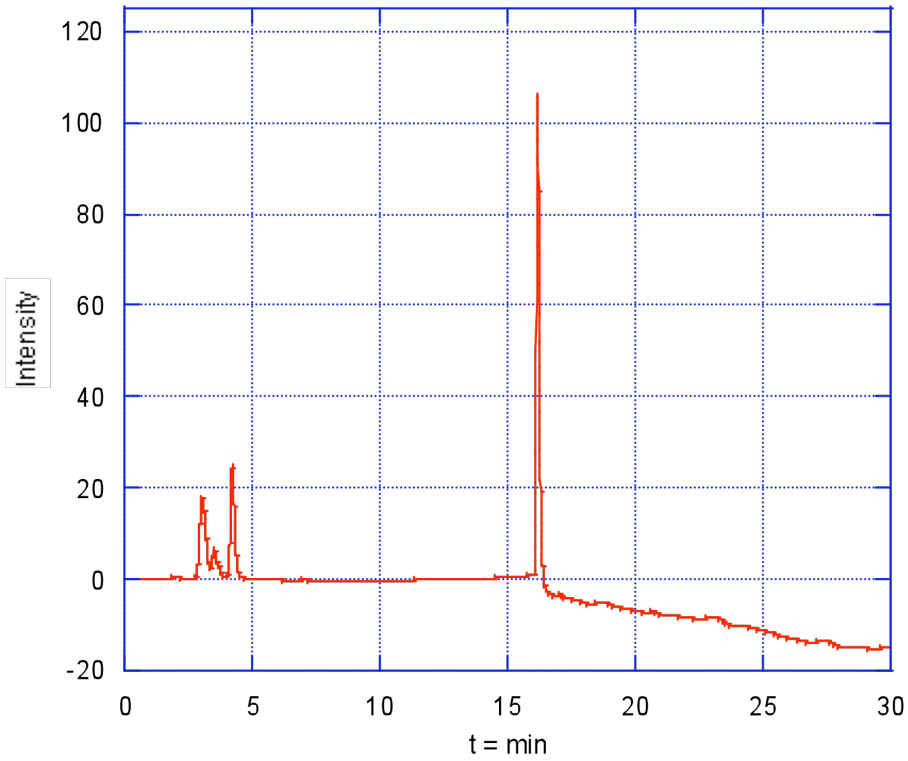




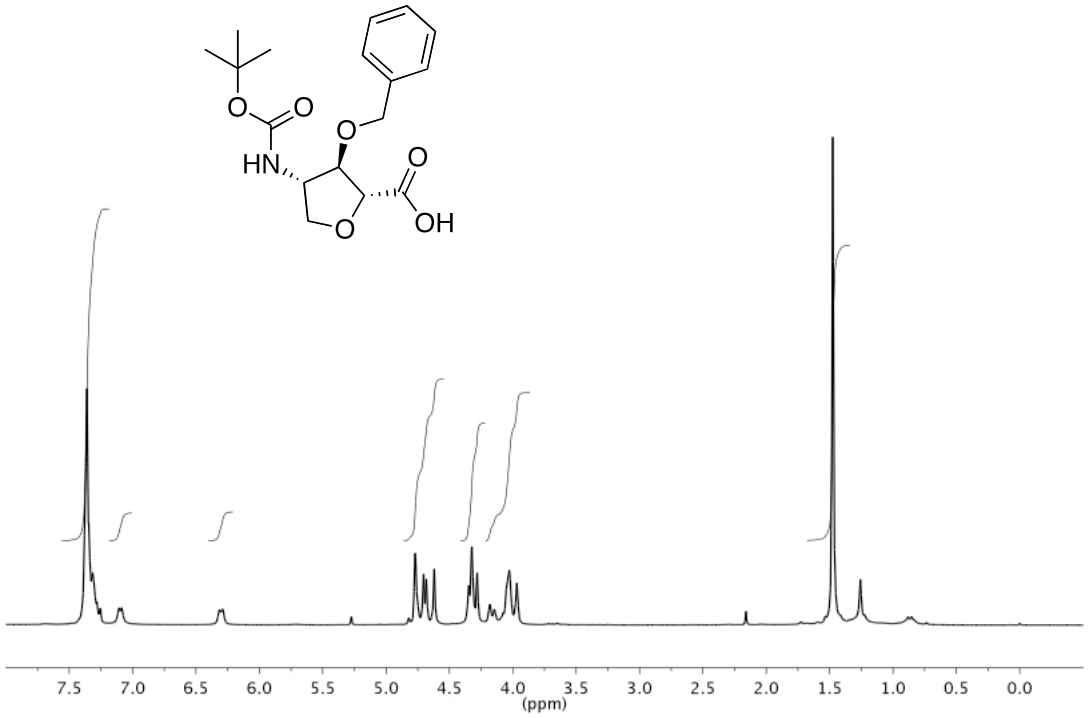
PHENOMENEX CUROSIL B 5u (250 mm x 4.6 mm, micron) column. Gradient: 0% to 5% MeOH/CH_2Cl_2 in 30 min, 1.0 mL/min.

(8)

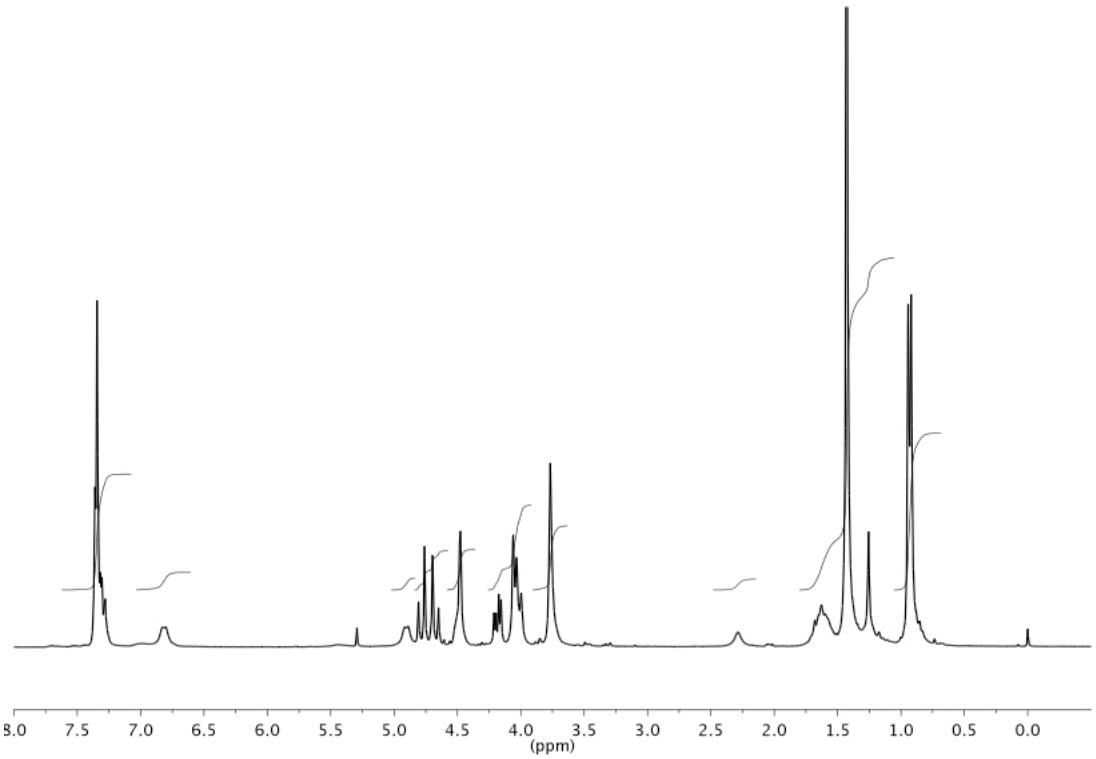

H
N
O
O
O
O
O
O
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
(ppm)


Intensity
120
100
80
60
40
20
0
-20
0
5
10
15
20
25
30
t = min

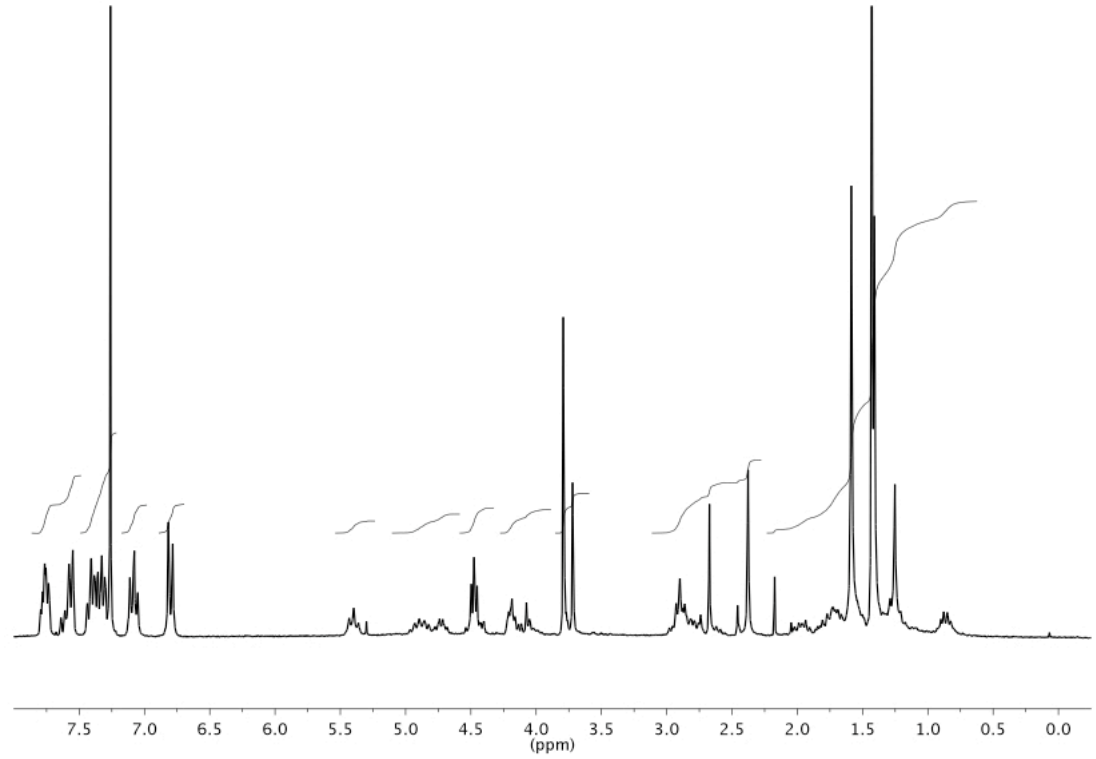
PHENOMENEX CUROSIL B 5u (250 mm x 4.6 mm, micron) column. Gradient: 0% to 5% MeOH/CH_2Cl_2 in 30 min, 1.0 mL/min.

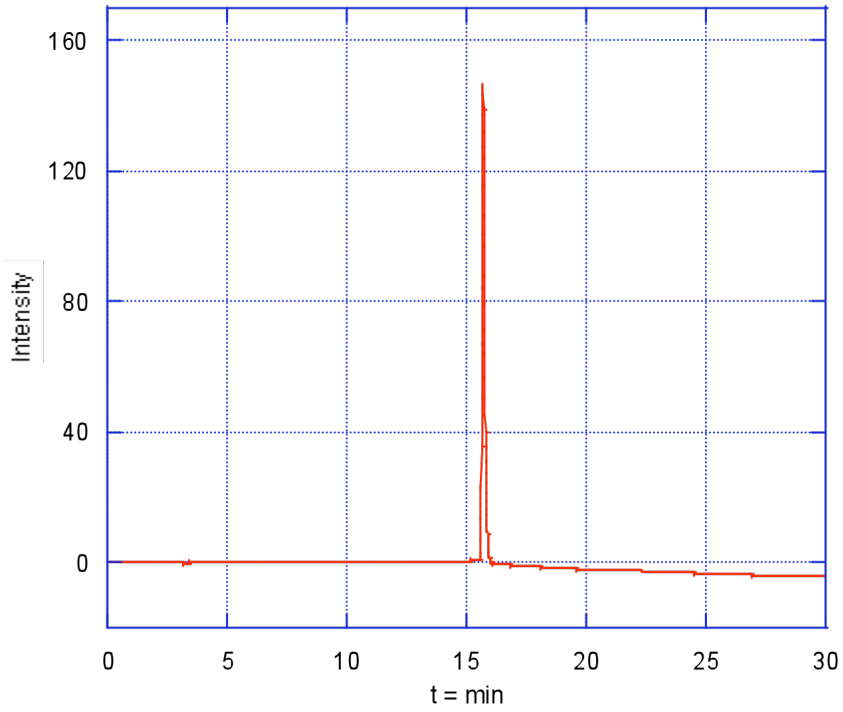


Boc-*D*-Leu-γ-Ahf(Bn)-OMe (10a)



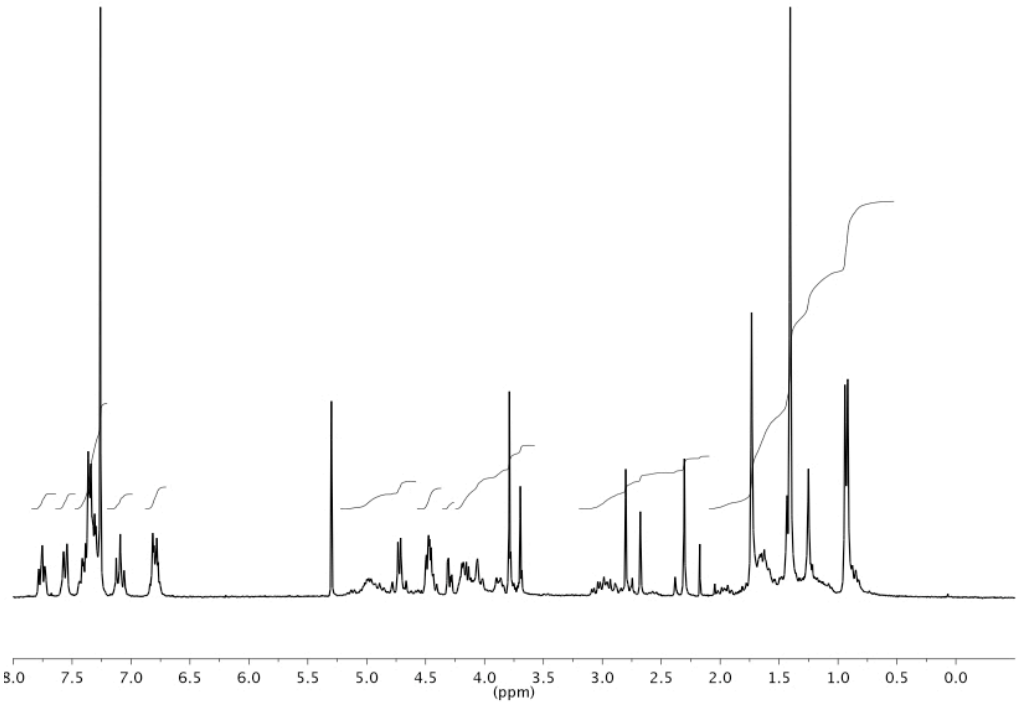
Boc-*D*-Tyr(Me)-γ-*L*-^{Me}N-Acp-OFm (11)

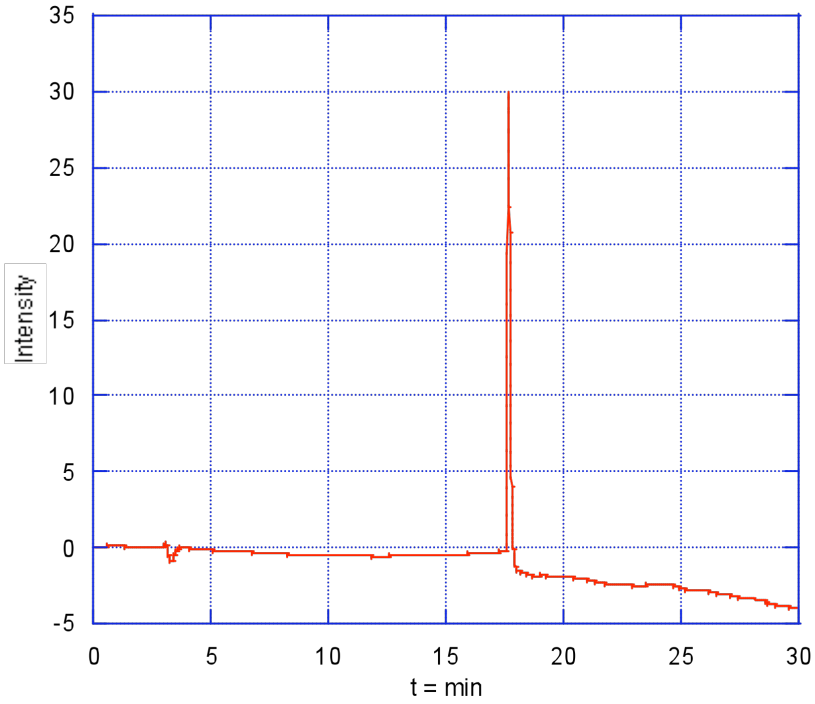




PHENOMENEX CUROSIL B 5u (250 mm x 4.6 mm, micron) column. Gradient: 0% to 5% MeOH/CH_2Cl_2 in 30 min, 1.0 mL/min.

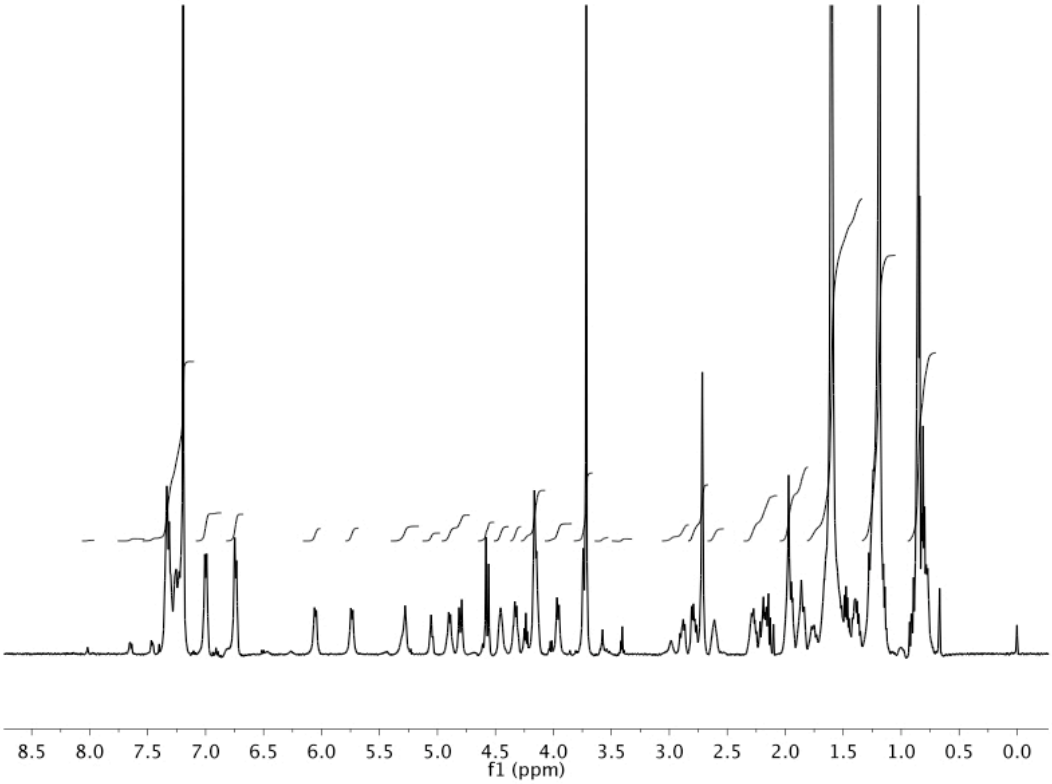
Boc-*D*-Leu-γ-Ahf(Bn)-*D*-Tyr(Me)-γ(*L*-^{Me}N-Acp-OFm (13)



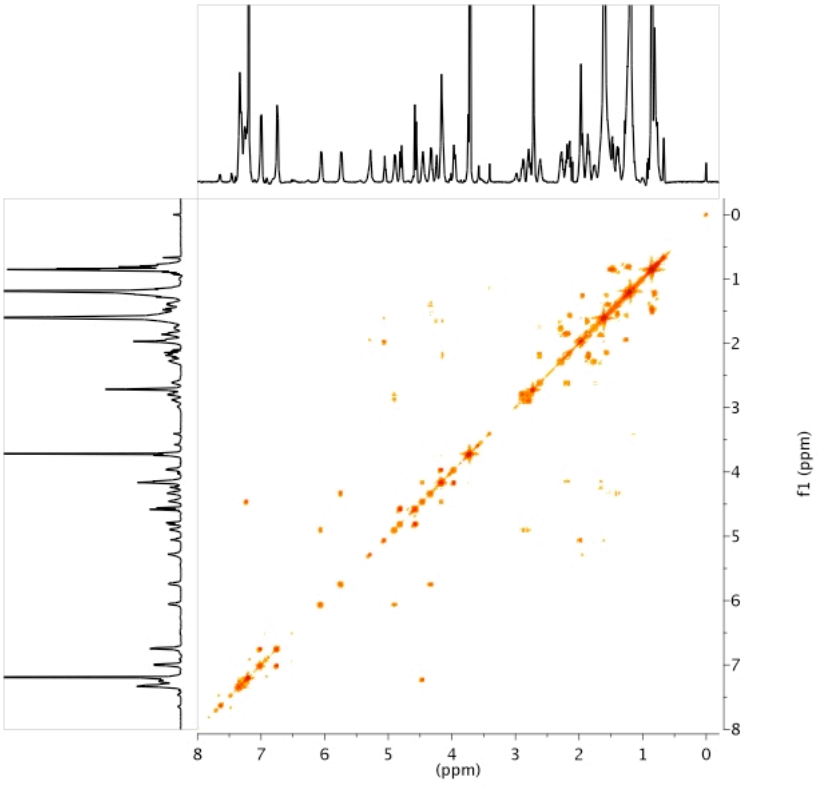


PHENOMENEX CUROSIL B 5u (250 mm x 4.6 mm, micron) column. Gradient: 0% to 5% MeOH/CH_2Cl_2 in 30 min, 1.0 mL/min.

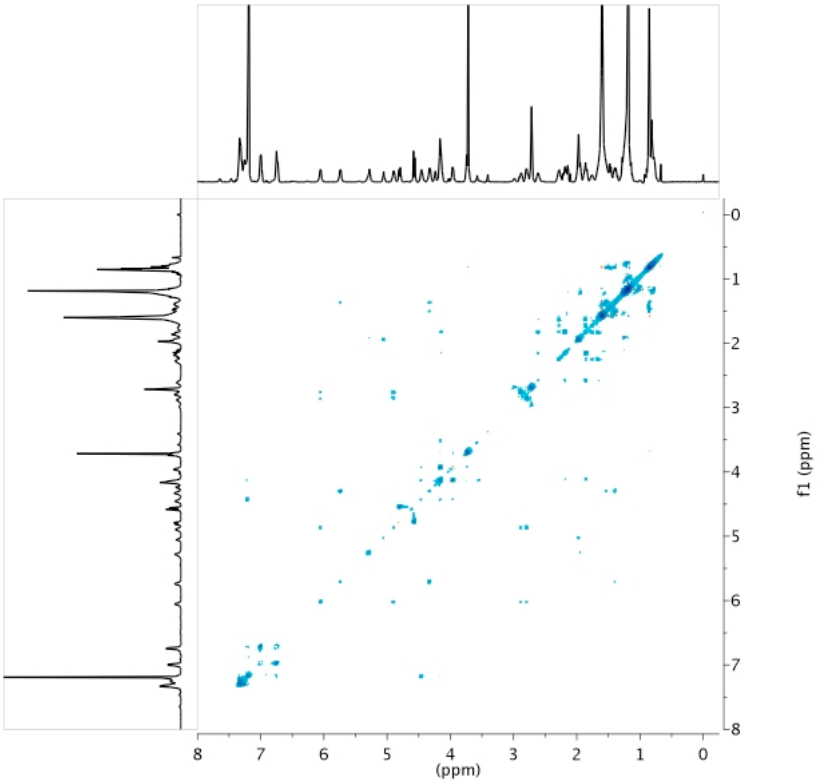
cyclo[*D*-Leu-γ-Ahf(Bn)-*D*-Tyr(Me)-γ-*L*-^{Me}N-Acp-] (15)



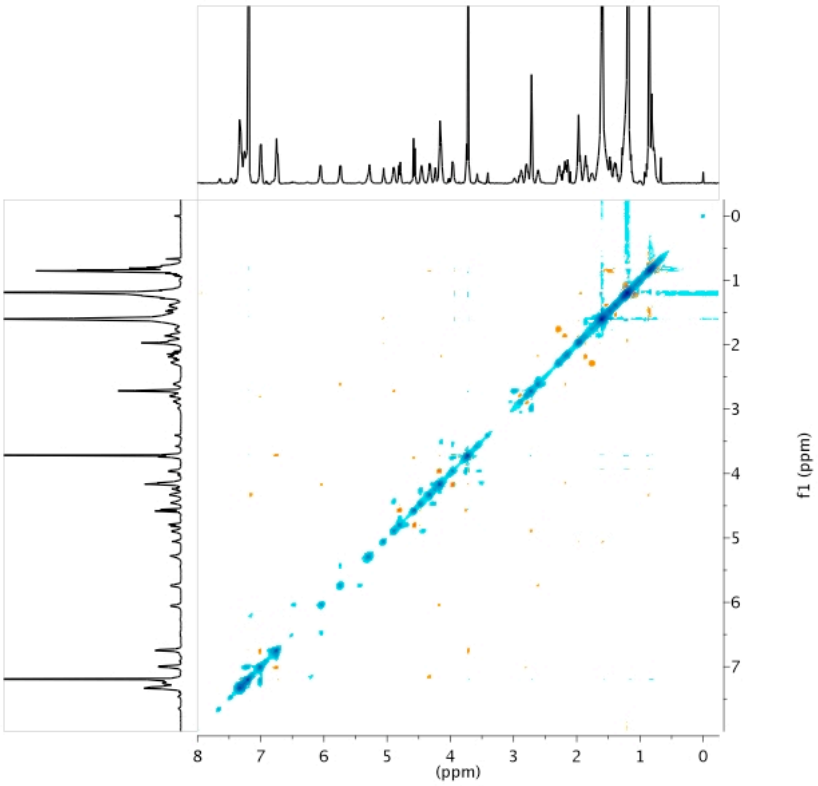
COSY (CDCl3, 500 MHz):



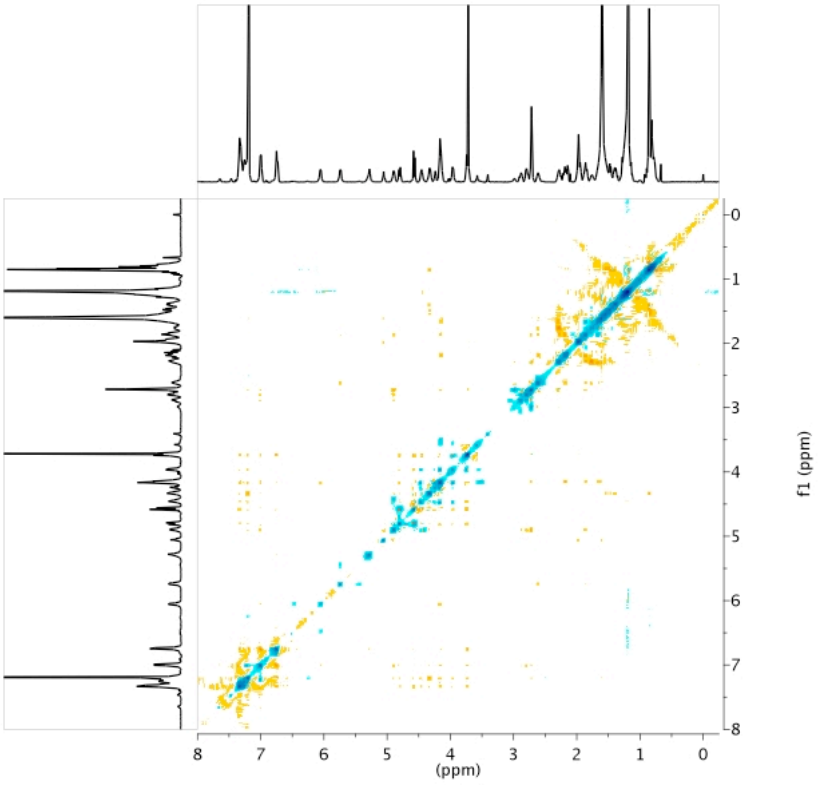
TOCSY (CDCl3, 500 MHz):

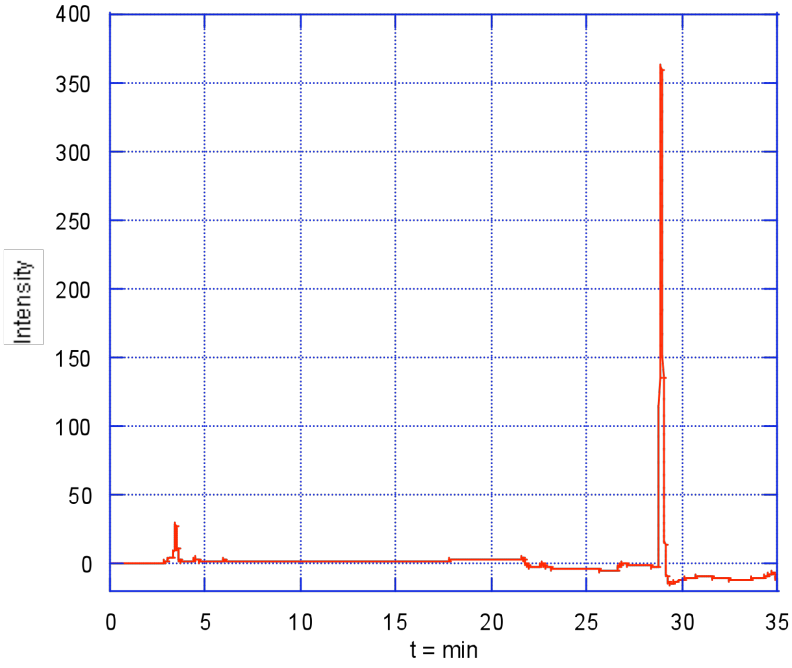


NOESY (CDCl3, 500 MHz):



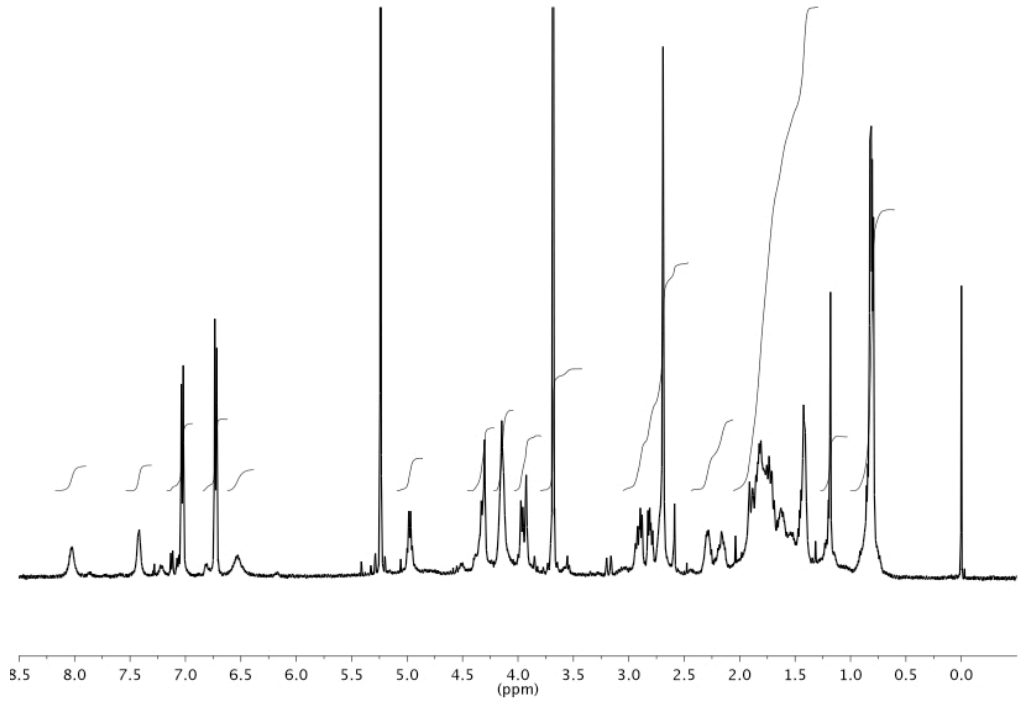
ROESY (CDCl3, 500 MHz):

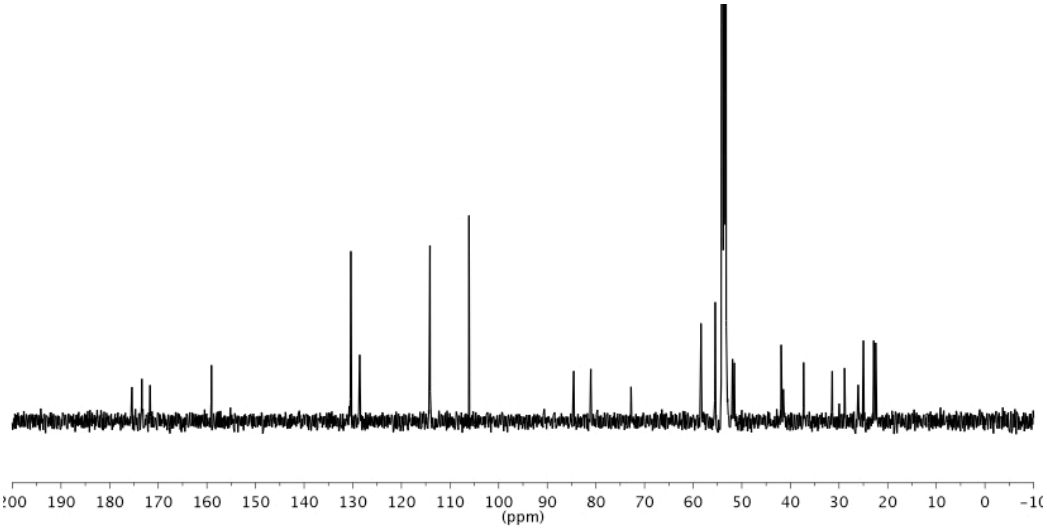


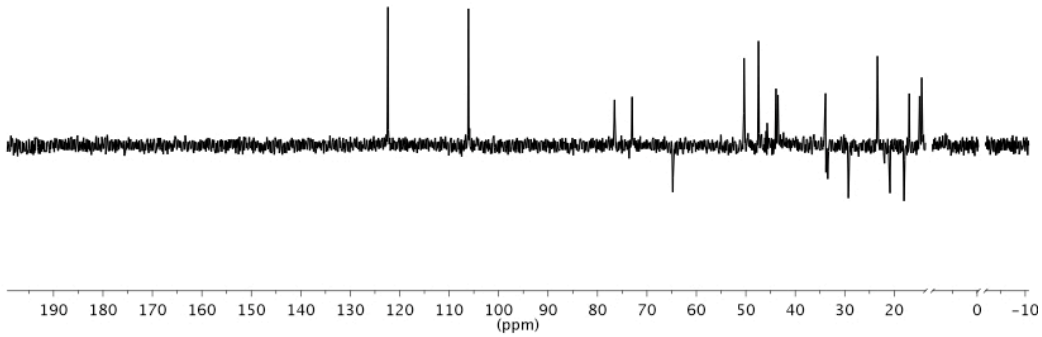


KROMASIL 100 SI (250 mm x 4.6 mm x 5 μm) column. Gradient: 1% to 3% in 10 min, 3% to 5% in 10 min and 5% to 7% MeOH/CH_2Cl_2 in 10 min, 1.0 mL/min.

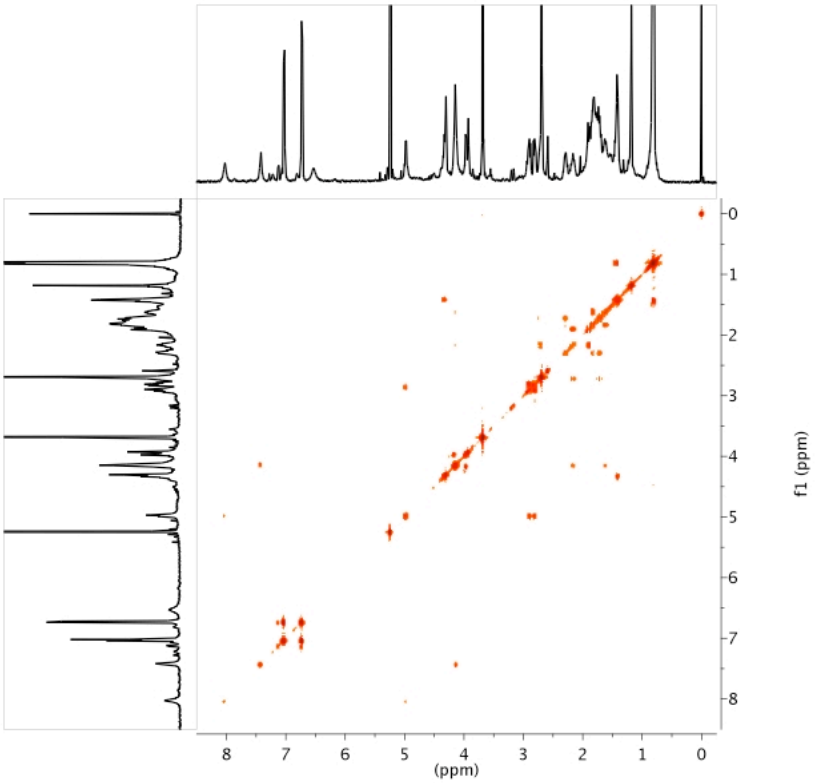
cyclo[*D*-Leu-γ-Ahf-*D*-Tyr(Me)-γ-*L*-^{Me}*N*-Acp-] (16)



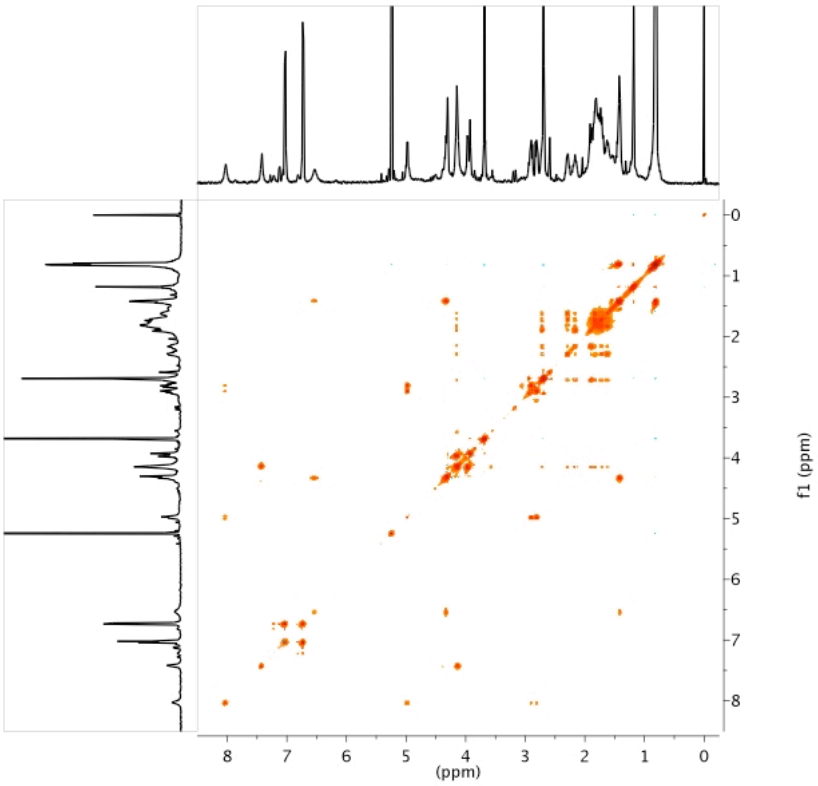




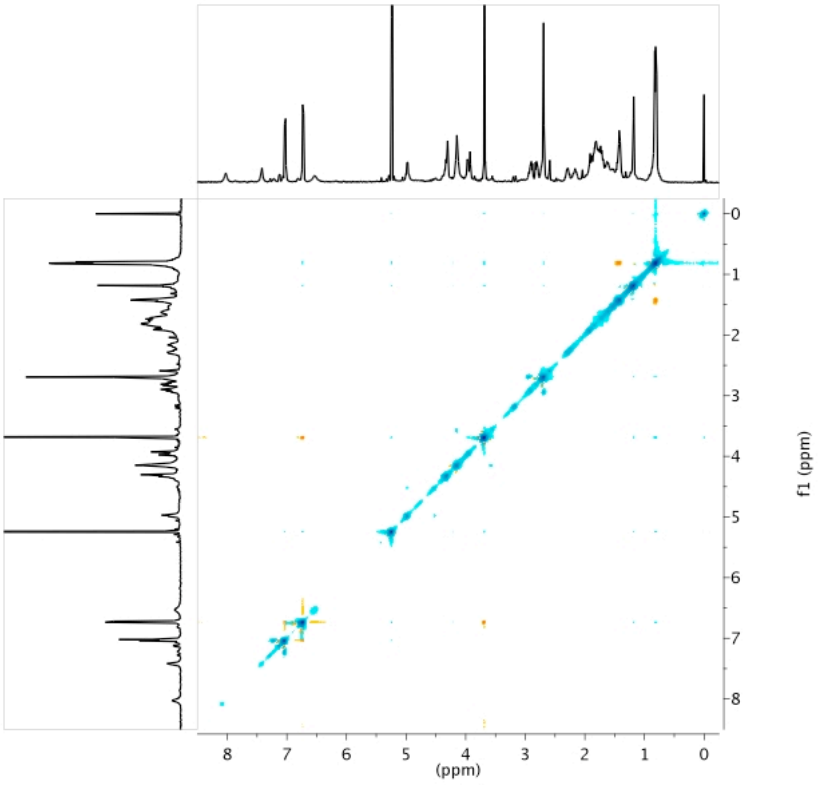
COSY (CH_2Cl_2, 500 MHz):



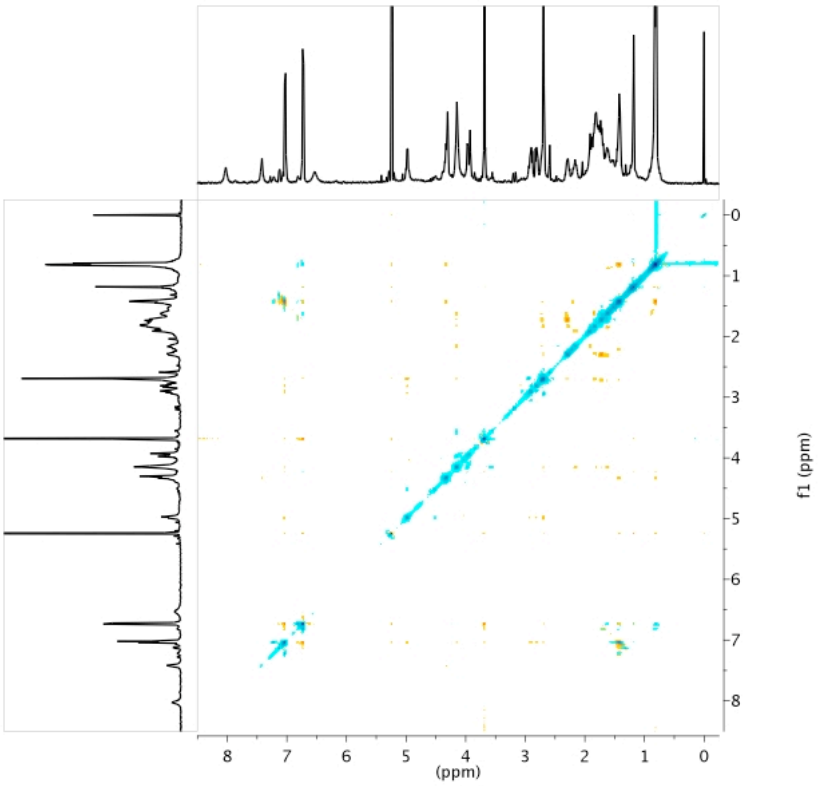
TOCSY (CH_2Cl_2, 500 MHz):

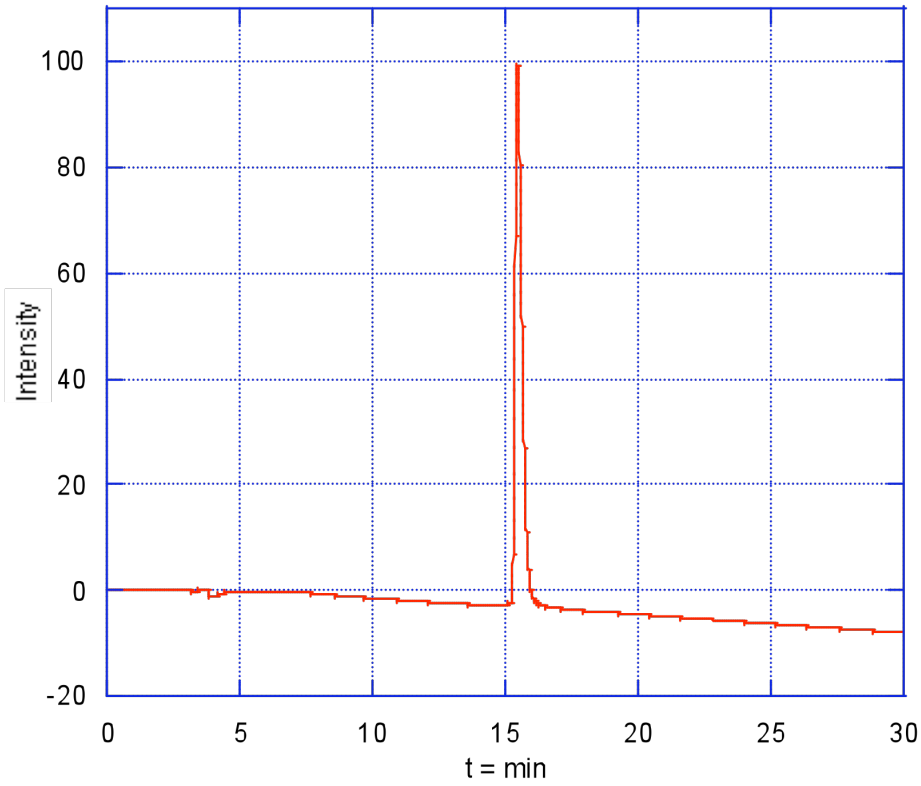


NOESY (CH_2Cl_2, 500 MHz):



ROESY (CH_2Cl_2, 500 MHz):





PHENOMENEX CUROSIL B 5u (250 mm x 4.6 mm, micron) column. Gradient: 1% to 10% MeOH/CH_2Cl_2 in 30 min, 1.0 mL/min.

Atomic Cartesian coordinates for the stationary points calculated with basis set [B3LYP/6-31G(d)]

$D_{c\text{-}16}$

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	7	0	-4.066598	-1.239830	-0.967769
2	6	0	-4.619480	-1.745055	0.296386
3	6	0	-5.120096	-3.183374	0.163789
4	6	0	-3.488963	-1.621469	1.343594
5	8	0	-2.493135	-2.349201	1.208834
6	7	0	-3.570393	-0.653251	2.298614
7	6	0	-4.749808	0.218479	2.426314
8	6	0	-2.276191	-0.219063	2.881423
9	6	0	-1.571209	0.761913	1.903151
10	6	0	-1.028776	1.941586	2.750699
11	6	0	-2.025938	2.012497	3.922225
12	6	0	-2.336913	0.535179	4.237313
13	6	0	-1.025086	3.163029	1.841525
14	8	0	-2.079353	3.742509	1.547013
15	7	0	0.165089	3.483735	1.269337
16	6	0	0.190984	4.383458	0.109501
17	6	0	1.520698	5.113146	-0.028496
18	6	0	-0.138950	3.545169	-1.151780
19	8	0	0.736185	3.107360	-1.898428
20	7	0	-1.471022	3.311156	-1.324674
21	6	0	-2.005677	2.481938	-2.392239
22	6	0	-2.002157	0.947119	-2.145854
23	6	0	-3.430726	0.498078	-2.582952
24	8	0	-4.021747	1.604712	-3.238777
25	6	0	-3.487479	2.795173	-2.668613
26	6	0	-4.263001	0.057780	-1.363815
27	8	0	-5.019575	0.832604	-0.786802
28	8	0	-0.984497	0.360046	-2.943772
29	1	0	-3.295069	-1.762342	-1.376026
30	1	0	-5.456516	-1.088034	0.520887
31	1	0	-4.299570	-3.872918	-0.049207
32	1	0	-5.859171	-3.249230	-0.639995
33	1	0	-5.592959	-3.506386	1.098232
34	1	0	-5.643152	-0.381980	2.621815
35	1	0	-4.610276	0.874523	3.283471
36	1	0	-4.916592	0.829871	1.534987
37	1	0	-1.701586	-1.137494	2.990787

38	1	0	-0.800477	0.281692	1.296853
39	1	0	-2.328708	1.160923	1.220501
40	1	0	-0.014970	1.722149	3.104821
41	1	0	-1.628481	2.552268	4.788117
42	1	0	-2.919172	2.546148	3.578725
43	1	0	-3.275698	0.387972	4.780007
44	1	0	-1.547538	0.127646	4.880535
45	1	0	0.984054	2.902515	1.456034
46	1	0	-0.613548	5.104517	0.274281
47	1	0	2.328250	4.426696	-0.292127
48	1	0	1.769267	5.623231	0.907201
49	1	0	1.456183	5.859454	-0.826584
50	1	0	-2.083990	3.589509	-0.559951
51	1	0	-1.396473	2.647805	-3.284265
52	1	0	-1.822552	0.728695	-1.085102
53	1	0	-3.364257	-0.321125	-3.306988
54	1	0	-4.018133	3.049769	-1.740673
55	1	0	-3.627602	3.601304	-3.392875
56	1	0	-1.020268	-0.618759	-2.815541
57	7	0	0.028471	-3.699129	0.338800
58	6	0	-0.193797	-4.189391	-1.026702
59	6	0	-1.549798	-4.872082	-1.146196
60	6	0	-0.041793	-3.003373	-2.003072
61	8	0	-1.019700	-2.332927	-2.372181
62	7	0	1.242460	-2.782588	-2.372036
63	6	0	1.718851	-1.537503	-2.952697
64	6	0	2.125146	-0.518422	-1.868506
65	6	0	3.112501	0.406184	-2.637681
66	8	0	3.564430	-0.330078	-3.765959
67	6	0	3.039285	-1.657677	-3.725700
68	6	0	4.232433	0.740131	-1.652299
69	8	0	5.296359	0.134483	-1.617578
70	7	0	3.846045	1.667800	-0.715545
71	6	0	4.464266	1.694499	0.613511
72	6	0	4.779586	3.115115	1.085083
73	6	0	3.482890	1.004982	1.591481
74	8	0	2.510163	1.657984	2.005751
75	7	0	3.675546	-0.293501	1.961706
76	6	0	4.664434	-1.201635	1.370935
77	6	0	2.668755	-0.849553	2.897811
78	6	0	1.382162	-1.342674	2.180170
79	6	0	1.365591	-2.909790	2.231345
80	6	0	2.656417	-3.327598	2.978872
81	6	0	3.132417	-2.067449	3.727390
82	6	0	1.282228	-3.498208	0.823931
83	8	0	2.295036	-3.749985	0.153177

84	8	0	1.098175	0.136617	-1.177539
85	1	0	-0.776084	-3.298110	0.821063
86	1	0	0.605704	-4.907557	-1.231022
87	1	0	-1.708743	-5.227736	-2.168668
88	1	0	-2.350681	-4.175249	-0.894732
89	1	0	-1.599303	-5.726563	-0.464549
90	1	0	1.921851	-3.287182	-1.798844
91	1	0	0.943480	-1.126044	-3.601504
92	1	0	2.681983	-1.078799	-1.107751
93	1	0	2.593881	1.312931	-2.973917
94	1	0	3.734279	-2.337743	-3.207710
95	1	0	2.914561	-2.003793	-4.755049
96	1	0	2.888198	2.005311	-0.779308
97	1	0	5.400621	1.149622	0.512787
98	1	0	3.867529	3.698120	1.226401
99	1	0	5.415569	3.612105	0.346804
100	1	0	5.311572	3.087510	2.042915
101	1	0	5.397810	-1.522919	2.118921
102	1	0	4.160209	-2.086138	0.970315
103	1	0	5.189960	-0.734848	0.540936
104	1	0	2.419095	-0.017406	3.555860
105	1	0	0.510503	-0.958906	2.713998
106	1	0	1.323688	-0.948658	1.162023
107	1	0	0.481043	-3.235727	2.789221
108	1	0	3.397014	-3.662743	2.248713
109	1	0	2.475928	-4.164826	3.661147
110	1	0	4.205247	-2.070014	3.941974
111	1	0	2.623203	-2.003442	4.697046
112	1	0	0.488135	0.529844	-1.843001

$D_{t\text{-}16}$

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	7	0	2.539527	2.836760	0.470591
2	6	0	2.529128	2.856785	1.930665
3	6	0	2.196139	4.240116	2.487894
4	6	0	1.567219	1.793996	2.512548
5	8	0	0.377132	2.032790	2.740755
6	7	0	2.163135	0.605836	2.792955
7	6	0	1.527271	-0.469216	3.545401
8	6	0	0.713482	-1.493733	2.711718
9	6	0	1.609406	-2.758940	2.744036
10	8	0	2.315490	-2.694595	3.963489

11	6	0	2.597236	-1.331745	4.265850
12	6	0	2.541929	-2.827234	1.529730
13	8	0	3.730998	-2.526438	1.582301
14	7	0	1.916557	-3.239667	0.385878
15	6	0	2.600409	-3.297373	-0.902053
16	6	0	2.065083	-4.462964	-1.741292
17	6	0	2.392717	-1.973940	-1.668971
18	8	0	1.245017	-1.743126	-2.112577
19	7	0	3.423614	-1.127622	-1.877835
20	6	0	4.749445	-1.303395	-1.262256
21	6	0	3.177492	-0.014021	-2.838272
22	6	0	2.370701	1.168793	-2.261778
23	6	0	3.392090	2.213717	-1.729240
24	6	0	4.730722	1.888334	-2.444101
25	6	0	4.452593	0.675674	-3.368656
26	6	0	3.495154	2.135144	-0.202686
27	8	0	4.366161	1.482595	0.381794
28	8	0	-0.502376	-1.750783	3.383167
29	1	0	1.748491	3.224695	-0.045128
30	1	0	3.547274	2.589310	2.222050
31	1	0	1.150927	4.500439	2.309210
32	1	0	2.841283	4.995265	2.028939
33	1	0	2.355076	4.257466	3.571367
34	1	0	0.828415	-0.003854	4.243452
35	1	0	0.534841	-1.120133	1.695949
36	1	0	0.984876	-3.658122	2.769865
37	1	0	3.605781	-1.068455	3.920389
38	1	0	2.560739	-1.222617	5.353459
39	1	0	0.906554	-3.337735	0.393364
40	1	0	3.650732	-3.470939	-0.677803
41	1	0	1.005665	-4.322666	-1.974641
42	1	0	2.193568	-5.401509	-1.193964
43	1	0	2.608464	-4.535467	-2.689364
44	1	0	5.432778	-1.845303	-1.927611
45	1	0	5.160921	-0.324618	-1.025492
46	1	0	4.655669	-1.825248	-0.311151
47	1	0	2.613829	-0.470313	-3.656150
48	1	0	1.812087	1.620658	-3.088241
49	1	0	1.637527	0.881240	-1.510518
50	1	0	3.033032	3.214828	-1.984144
51	1	0	5.492821	1.657643	-1.695468
52	1	0	5.093410	2.745273	-3.020088
53	1	0	5.308690	0.002974	-3.469813
54	1	0	4.216218	1.029342	-4.379094
55	1	0	-1.059799	-2.230714	2.733256
56	1	0	3.105701	0.463095	2.443419

57	7	0	-2.046200	3.319563	1.062348
58	6	0	-1.765679	4.245542	-0.044175
59	6	0	-0.990825	5.473162	0.416630
60	6	0	-1.036824	3.476560	-1.171378
61	8	0	0.189680	3.494040	-1.305914
62	7	0	-1.891920	2.775493	-1.964158
63	6	0	-1.473290	1.666284	-2.802119
64	6	0	-1.605157	0.310536	-2.077904
65	6	0	-1.723868	-0.691822	-3.256425
66	8	0	-2.184700	0.048673	-4.374653
67	6	0	-2.382676	1.419860	-4.014965
68	6	0	-2.693857	-1.787441	-2.805477
69	8	0	-3.877073	-1.815227	-3.114381
70	7	0	-2.115361	-2.641493	-1.896308
71	6	0	-2.903697	-3.370233	-0.899067
72	6	0	-2.431123	-4.818801	-0.764104
73	6	0	-2.764562	-2.621544	0.453108
74	8	0	-1.762928	-2.886027	1.148810
75	7	0	-3.687144	-1.698827	0.828795
76	6	0	-4.772644	-1.204213	-0.024681
77	6	0	-3.434246	-0.976818	2.105111
78	6	0	-2.474471	0.232351	1.927103
79	6	0	-3.296568	1.539155	2.191357
80	6	0	-4.762297	1.094868	2.405640
81	6	0	-4.686513	-0.391905	2.798308
82	6	0	-3.140045	2.506729	1.024020
83	8	0	-3.940774	2.534267	0.076653
84	8	0	-0.636438	-0.004329	-1.109795
85	1	0	-1.290706	3.092887	1.710312
86	1	0	-2.745244	4.554092	-0.419726
87	1	0	-0.916467	6.195709	-0.402364
88	1	0	0.026529	5.215772	0.717255
89	1	0	-1.503945	5.950397	1.256941
90	1	0	-2.845846	2.726298	-1.600234
91	1	0	-0.440561	1.840318	-3.109254
92	1	0	-2.562034	0.342660	-1.540907
93	1	0	-0.740359	-1.122613	-3.486979
94	1	0	-3.436560	1.600029	-3.752013
95	1	0	-2.132530	2.037743	-4.881725
96	1	0	-1.146779	-2.458325	-1.649541
97	1	0	-3.929160	-3.366632	-1.265152
98	1	0	-1.392241	-4.863959	-0.427027
99	1	0	-2.516380	-5.320247	-1.732454
100	1	0	-3.041684	-5.358431	-0.032262
101	1	0	-5.747442	-1.428979	0.420756
102	1	0	-4.684278	-0.118825	-0.135745

103	1	0	-4.734970	-1.633808	-1.022780
104	1	0	-2.982850	-1.717595	2.760908
105	1	0	-1.656292	0.161368	2.642922
106	1	0	-2.017065	0.218323	0.934115
107	1	0	-2.906064	2.019861	3.094561
108	1	0	-5.316919	1.236471	1.474677
109	1	0	-5.262749	1.695943	3.172198
110	1	0	-5.606043	-0.946527	2.587395
111	1	0	-4.514954	-0.476988	3.878068
112	1	0	0.121817	-0.458091	-1.538144

D$_{c\text{-}16}$ (dehydroxylated)

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	7	0	-3.414985	-2.050150	-0.836020
2	6	0	-3.890547	-2.354118	0.518374
3	6	0	-3.911654	-3.856270	0.802726
4	6	0	-2.955260	-1.619175	1.505585
5	8	0	-1.782388	-2.021620	1.613243
6	7	0	-3.400992	-0.518247	2.165386
7	6	0	-4.774862	-0.005429	2.037774
8	6	0	-2.369389	0.270270	2.890159
9	6	0	-1.562204	1.150824	1.891201
10	6	0	-1.619447	2.617890	2.403931
11	6	0	-2.863285	2.661347	3.306333
12	6	0	-2.904866	1.262988	3.954283
13	6	0	-1.690394	3.517609	1.176472
14	8	0	-2.766622	3.843066	0.664265
15	7	0	-0.486962	3.837787	0.615507
16	6	0	-0.455766	4.404197	-0.737544
17	6	0	0.748385	5.309705	-0.967986
18	6	0	-0.505173	3.237388	-1.750888
19	8	0	0.517980	2.726772	-2.219688
20	7	0	-1.762762	2.814703	-2.038910
21	6	0	-2.059141	1.672884	-2.896076
22	6	0	-1.845048	0.277965	-2.255838
23	6	0	-3.066951	-0.555018	-2.737586
24	8	0	-3.800188	0.275725	-3.626977
25	6	0	-3.550171	1.630290	-3.283850
26	6	0	-3.911696	-0.974501	-1.525585
27	8	0	-4.910442	-0.349801	-1.180250
28	1	0	-2.501540	-2.408375	-1.113220
29	1	0	-4.907930	-1.972693	0.560994

30	1	0	-2.901481	-4.270701	0.829524
31	1	0	-4.492120	-4.374100	0.033433
32	1	0	-4.376496	-4.048488	1.776357
33	1	0	-5.468405	-0.561003	2.681166
34	1	0	-4.794560	1.038161	2.345292
35	1	0	-5.116242	-0.042086	1.002420
36	1	0	-1.719133	-0.470512	3.356031
37	1	0	-0.529522	0.828251	1.767282
38	1	0	-2.047144	1.087408	0.912332
39	1	0	-0.711796	2.835697	2.978313
40	1	0	-2.819534	3.464721	4.049288
41	1	0	-3.740501	2.848226	2.677238
42	1	0	-3.886695	0.990673	4.353094
43	1	0	-2.210535	1.238322	4.803138
44	1	0	0.348092	3.352012	0.949477
45	1	0	-1.373916	4.988379	-0.829620
46	1	0	1.682828	4.744869	-0.978067
47	1	0	0.798602	6.073177	-0.185755
48	1	0	0.659830	5.809904	-1.937989
49	1	0	-2.507442	3.188896	-1.454298
50	1	0	-1.438820	1.764657	-3.791546
51	1	0	-1.811208	0.363388	-1.166059
52	1	0	-2.752412	-1.440918	-3.297181
53	1	0	-4.180164	1.940599	-2.436388
54	1	0	-3.793695	2.245853	-4.153870
55	1	0	0.944275	0.189457	-2.668815
56	7	0	0.486351	-3.826145	0.632520
57	6	0	0.466975	-4.399367	-0.717548
58	6	0	-0.734826	-5.306928	-0.952693
59	6	0	0.524361	-3.239489	-1.738471
60	8	0	-0.495315	-2.735045	-2.221518
61	7	0	1.783320	-2.815955	-2.017842
62	6	0	2.086003	-1.691688	-2.896000
63	6	0	1.849762	-0.281758	-2.295402
64	6	0	3.094387	0.537938	-2.740245
65	8	0	3.839853	-0.300027	-3.611868
66	6	0	3.583696	-1.651163	-3.259456
67	6	0	3.915760	0.948524	-1.508706
68	8	0	4.903758	0.316669	-1.145292
69	7	0	3.416425	2.029311	-0.829837
70	6	0	3.885268	2.342392	0.524653
71	6	0	3.914738	3.846881	0.795740
72	6	0	2.940789	1.622145	1.513293
73	8	0	1.767570	2.027024	1.606896
74	7	0	3.380797	0.529840	2.190643
75	6	0	4.757281	0.019456	2.080060

76	6	0	2.341133	-0.249851	2.913570
77	6	0	1.535859	-1.133025	1.914983
78	6	0	1.600216	-2.600470	2.427408
79	6	0	2.837389	-2.637324	3.339088
80	6	0	2.864860	-1.238537	3.986307
81	6	0	1.684454	-3.500785	1.201630
82	8	0	2.765486	-3.823848	0.698173
83	1	0	-0.352940	-3.343455	0.960021
84	1	0	1.386094	-4.983730	-0.798573
85	1	0	-0.638856	-5.811624	-1.919610
86	1	0	-1.669797	-4.743140	-0.972286
87	1	0	-0.790090	-6.066726	-0.167215
88	1	0	2.524591	-3.184569	-1.425497
89	1	0	1.480813	-1.809305	-3.798771
90	1	0	1.760969	-0.339067	-1.206821
91	1	0	2.806361	1.428598	-3.306491
92	1	0	4.199796	-1.952567	-2.398900
93	1	0	3.841656	-2.274963	-4.119375
94	1	0	2.509023	2.393848	-1.119129
95	1	0	4.899671	1.954170	0.576456
96	1	0	2.907121	4.267897	0.814608
97	1	0	4.501702	4.354436	0.024517
98	1	0	4.376686	4.044744	1.769633
99	1	0	5.448811	0.604773	2.698648
100	1	0	4.783779	-1.009864	2.430704
101	1	0	5.096505	0.017344	1.043034
102	1	0	1.691368	0.496810	3.370801
103	1	0	0.501036	-0.815759	1.795808
104	1	0	2.016295	-1.065192	0.934017
105	1	0	0.690017	-2.823919	2.995579
106	1	0	3.720503	-2.819429	2.716909
107	1	0	2.792054	-3.440655	4.081995
108	1	0	3.838953	-0.961489	4.400620
109	1	0	2.156893	-1.215906	4.823957
110	1	0	-0.921042	-0.199136	-2.571371

$\mathbf{D}_{t\text{-}16}$ (dehydroxylated)

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	7	0	-2.280505	3.297119	0.518332
2	6	0	-2.339103	3.875664	-0.829303
3	6	0	-1.759794	5.283949	-0.883543
4	6	0	-1.630869	2.917334	-1.813506

5	8	0	-0.424067	2.995203	-2.068857
6	7	0	-2.463760	1.977669	-2.330977
7	6	0	-1.991141	0.810632	-3.060370
8	6	0	-1.532347	-0.342372	-2.147415
9	6	0	-1.883122	-1.619296	-2.957086
10	8	0	-2.615954	-1.193645	-4.101045
11	6	0	-3.100510	0.122665	-3.876691
12	6	0	-2.705275	-2.519672	-2.029404
13	8	0	-3.931958	-2.529688	-2.039093
14	7	0	-1.940668	-3.181184	-1.105303
15	6	0	-2.517771	-3.632679	0.162102
16	6	0	-1.971131	-4.996812	0.588844
17	6	0	-2.190693	-2.565750	1.235833
18	8	0	-1.033964	-2.535022	1.692846
19	7	0	-3.139781	-1.676876	1.644489
20	6	0	-4.454011	-1.503908	1.011896
21	6	0	-2.732902	-0.730923	2.715170
22	6	0	-1.996508	0.525920	2.179238
23	6	0	-2.970749	1.747337	2.281589
24	6	0	-4.270290	1.206499	2.927005
25	6	0	-3.892870	-0.150842	3.555520
26	6	0	-3.191717	2.357108	0.900347
27	8	0	-4.112590	1.997056	0.154414
28	1	0	-1.420454	3.399475	1.058885
29	1	0	-3.400905	3.911156	-1.085404
30	1	0	-0.675401	5.273116	-0.761816
31	1	0	-2.205840	5.908666	-0.103830
32	1	0	-1.974942	5.736737	-1.856963
33	1	0	-3.356303	1.885771	-1.846156
34	1	0	-1.182384	1.134058	-3.719999
35	1	0	-2.115713	-0.296859	-1.221117
36	1	0	-0.984519	-2.138082	-3.303947
37	1	0	-4.043808	0.103815	-3.308284
38	1	0	-3.282542	0.585787	-4.850277
39	1	0	-0.929090	-3.044622	-1.141278
40	1	0	-3.587287	-3.725754	-0.012768
41	1	0	-0.897599	-4.951039	0.786167
42	1	0	-2.160950	-5.729855	-0.200718
43	1	0	-2.464965	-5.335882	1.506337
44	1	0	-5.260744	-1.812791	1.686343
45	1	0	-4.595044	-0.452564	0.747427
46	1	0	-4.524476	-2.068596	0.084970
47	1	0	-2.055632	-1.305655	3.347100
48	1	0	-1.116698	0.733342	2.790143
49	1	0	-1.637553	0.361176	1.159578
50	1	0	-2.508200	2.506057	2.920480

51	1	0	-5.033689	1.092237	2.153830
52	1	0	-4.669861	1.901472	3.672814
53	1	0	-4.742578	-0.832208	3.658548
54	1	0	-3.500165	0.010911	4.566834
55	1	0	-0.478792	-0.310167	-1.881036
56	7	0	2.281161	3.296800	-0.518410
57	6	0	2.339842	3.875380	0.829206
58	6	0	1.760893	5.283814	0.883376
59	6	0	1.631328	2.917254	1.813399
60	8	0	0.424516	2.995371	2.068627
61	7	0	2.463990	1.977455	2.331004
62	6	0	1.991034	0.810467	3.060258
63	6	0	1.532394	-0.342451	2.147131
64	6	0	1.882581	-1.619422	2.956966
65	8	0	2.615271	-1.193917	4.101079
66	6	0	3.100068	0.122338	3.876893
67	6	0	2.704691	-2.520037	2.029496
68	8	0	3.931374	-2.530170	2.039272
69	7	0	1.940080	-3.181563	1.105410
70	6	0	2.517210	-3.633075	-0.161976
71	6	0	1.970401	-4.997109	-0.588817
72	6	0	2.190332	-2.566059	-1.235678
73	8	0	1.033611	-2.535101	-1.692694
74	7	0	3.139581	-1.677338	-1.644276
75	6	0	4.454012	-1.504990	-1.011930
76	6	0	2.732968	-0.731405	-2.715081
77	6	0	1.996672	0.525587	-2.179374
78	6	0	2.971106	1.746853	-2.281631
79	6	0	4.270593	1.205852	-2.927026
80	6	0	3.893125	-0.151570	-3.555349
81	6	0	3.192155	2.356544	-0.900365
82	8	0	4.112899	1.996266	-0.154390
83	1	0	1.421151	3.399311	-1.058987
84	1	0	3.401643	3.910613	1.085348
85	1	0	1.976088	5.736562	1.856811
86	1	0	0.676505	5.273267	0.761569
87	1	0	2.207163	5.908404	0.103689
88	1	0	3.356541	1.885338	1.846228
89	1	0	1.182123	1.133985	3.719652
90	1	0	2.116184	-0.297052	1.221093
91	1	0	0.983726	-2.137912	3.303614
92	1	0	4.043537	0.103382	3.308774
93	1	0	3.281866	0.585420	4.850543
94	1	0	0.928516	-3.044851	1.141312
95	1	0	3.586702	-3.726298	0.012961
96	1	0	0.896861	-4.951200	-0.786070

97	1	0	2.160185	-5.730251	0.200662
98	1	0	2.464138	-5.336141	-1.506370
99	1	0	5.260471	-1.815080	-1.686162
100	1	0	4.595910	-0.453565	-0.748302
101	1	0	4.524036	-2.068981	-0.084539
102	1	0	2.055685	-1.306089	-3.347048
103	1	0	1.117025	0.733106	-2.790485
104	1	0	1.637468	0.360971	-1.159783
105	1	0	2.508699	2.505680	-2.920496
106	1	0	5.034026	1.091684	-2.153870
107	1	0	4.670157	1.900703	-3.672953
108	1	0	4.742790	-0.833028	-3.658109
109	1	0	3.500607	0.010031	-4.566758
110	1	0	0.478952	-0.310040	1.880298

Computed energies (atomic units) for the stationary points calculated with basis set [B3LYP or M05-2X/6-31G+(d, p)] at the B3LYP/6-31G(d) optimized geometries.

	B3LYP	M05-2X
$D_{c\text{-}16}$	-2746.5612213	-2746.2017122
$D_{t\text{-}16}$	-2746.5587887	-2746.1986349
$D_{c\text{-}16}$ (dehydroxylated)	-2596.1142363	-2595.8374995
$D_{t\text{-}16}$ (dehydroxylated)	-2596.1167672	-2595.8426094

Interaction energies (in kcal/mol) for dimers $D_{c\text{-}16}$ and $D_{t\text{-}16}$ and the analogous dehydroxylated.[a]

$D_{c\text{-}16}$	**$D_{t\text{-}16}$**	**$D_{c\text{-}16}$** (dehydroxylated)	**$D_{t\text{-}16}$** (dehydroxylated)
-43.0 (3.6)	-43.9 (3.5)	-31.5 (2.6)	-33.2 (2.7)

[a]Single point calculations with the M05-2X/6-31+G(d,p) basis set at the B3LYP/6-31G(d) optimized geometries. The energies were corrected for BSSE (values in parenthesis).