Introducing sequential aza-amino acids induces repeated β-turns and helical conformations in peptides

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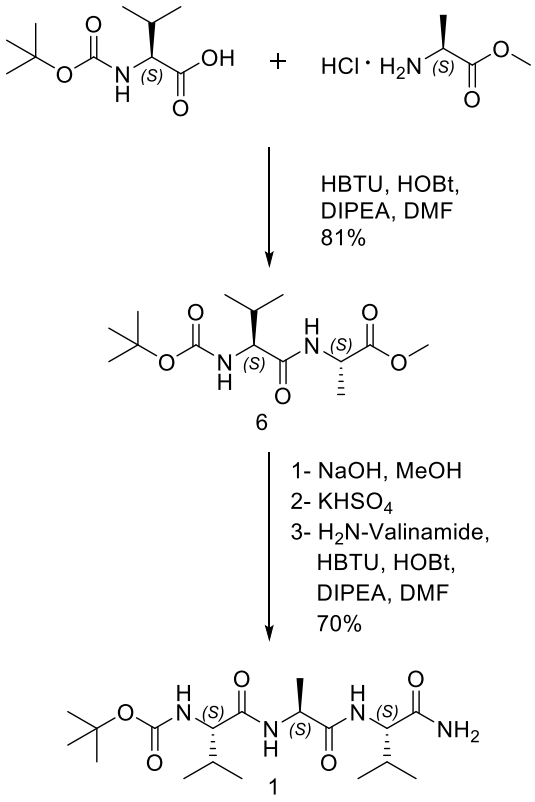
General Experimental Methods

Usual dry solvents were purchased from commercial sources. 4-nitrophenyl chloroformate, *N,N,N′,N′*-Tetramethyl-*O*-(1*H*-benzotriazol-1-yl)uronium hexafluorophosphate (HBTU), 4-(4,6-dimethoxy-1,3,5-triazin-2-yl)-4-methylmorpholinium chloride (DMTMM(Cl^-)), 1-hydroxybenzotriazole (HOBt), 1-[Bis(dimethylamino)methylene]-1*H*-1,2,3-triazolo[4,5-*b*]pyridinium 3-oxid hexafluorophosphate (HATU), 1-Hydroxy-7-azabenzotriazole (HOAt), Boc-NH-Val-OH, *L*-Ala-OCH_3, *L*-Val-NH_2 and *L*-Val-OBn were purchased from commercial sources. Boc-aVal-aAla-Val-NH_2 **2** and Boc-aGly-aGly-Val-NH_2 **4** were prepared according to our published methods (F. Bizet, N. Tonali, J.-L. Soulier, A. Oliva, J. Kaffy, B. Crousse, S. Ongeri, *N. J. Chem*. **2018**, *42*, 17062-17072; L. Dufau, A. S. Marques Ressurreição, R. Fanelli, N. Kihal, A. Vidu, T.Milcent, J.-L. Soulier, J. Rodrigo, A. Desvergne, K. Leblanc, G. Bernadat, B. Crousse, M. Reboud-Ravaux,S. Ongeri, *J. Med. Chem.* **2012**, *55*, 6762–6775). Pure products were obtained after liquid chromatography using Merck silica gel 60 (40−63 µm). TLC analyses were performed on silica gel 60F-250 (0.26 mm thickness) plates. The plates were visualized with UV light (λ = 254 nm) or revealed with a 5% solution of phosphomolybdic acid in EtOH or with a solution of ninhydrin in EtOH. Melting points were determined on a Kofler melting point apparatus. Element analyses (C, H, and N) were performed on a PerkinElmer C, H, N Analyzer 2400 at the Microanalyses Service of the Faculty of Pharmacy at Châtenay-Malabry (BioCIS, France). NMR spectra were recorded on an Ultrafield Bruker AVANCE 300 (^{1}H, 300 MHz, ^{13}C, 75 MHz) or on a Bruker Avance 400 (^{1}H, 400 MHz, ^{13}C, 100 MHz), or on a Bruker NMR spectrometer operating at a ^{1}H frequency of 500.3 MHz and equipped with either a room temperature TXI probe or a cryogenic TCI probe. Chemical shifts δ are in ppm, and the following abbreviations are used: singlet (s), broad singlet (bs), doublet (d), doublet of triplet (dt), triplet (t), multiplet (m). IR spectra were recorded on a Bruker Vector 22 FT-IR spectrometer. HRMS were obtained using a TOF LCT Premier apparatus (Waters), with an electrospray ionization source. The purity of compounds was determined by HPLC using the 2695 Alliance system (Waters) and a XBridge Select (C_{18}, 3.5 µm, 150 mm × 2.1 mm); mobile phase, MeCN/H_2O + 0.1% formic acid from 5 to 100% in 20 min; detection at 220 nm or 245 nm; flow rate 0.25 mL/min.

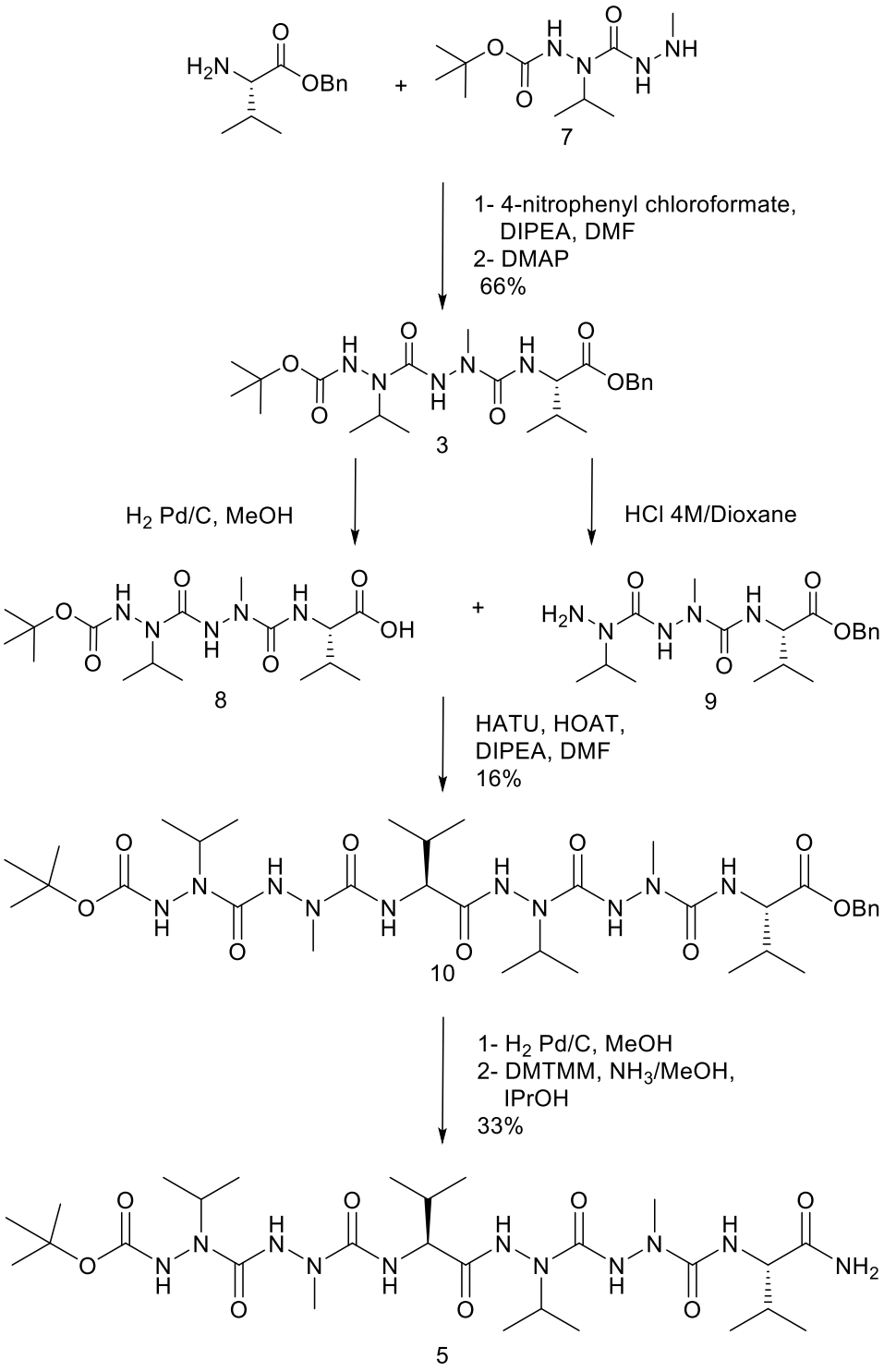


Scheme S1

Methyl (2S)-2-[[(2S)-2-(*tert*-butoxycarbonylamino)-3-methyl-butanoyl]amino]propanoate (6): Boc-NH-Val-OH (500 mg, 2.3 mmol, 1.0 eq.) was dissolved in DMF (10.0 mL) under a nitrogen atmosphere and the solution was cooled at 0°C. At this moment, HOBt (387 mg, 2.5 mmol, 1.1 eq.) and HBTU (960 mg, 2.5 mmol, 1.1 eq.) were added. The solution was stirred at 0°C for 30 min and the solution of $HCl{\cdot}NH_2$-Ala-OCH_3 (321 mg, 2.3 mmol, 1.0 eq.) and DIPEA (1.2 mL, 6.9 mmol, 3.0 eq.) in DMF (10.0 mL) was added. The reaction was stirred at room temperature overnight. After evaporation of the volatiles under vacuum, the oily residue was taken up with EtOAc. The organic layer was successively washed with 10% aqueous citric solution, water, 10% aqueous K_2CO_3 solution, brine, and then dried over Na_2SO_4, filtered and concentrated under reduced pressure. Purification by column chromatography on silica gel using Cyclohexane/EtOAc 7:3 as eluent afforded compound **6** (564 mg, 1.87 mmol, 81%) as a white solid. R_f = 0.35 (Cyclohexane /EtOAc 7:3); ^{1}H NMR (DMSO-d_6, 300 MHz): 8.29 (1H, d, *J* = 6.5 Hz); 6.61 (1H, d, *J* = 9.0 Hz); 4.25 (1H, m); 3.78 (1H, m); 3.60 (3H, s); 1.92 (1H, m); 1.37 (9H, s); 1.27 (3H, d, *J* = 7.3 Hz); 0.86 (3H, d, *J* = 6.7 Hz);0.81 (3H, d, *J* = 6.7 Hz) ^{13}C NMR (DMSO-d_6, 75 MHz): 172.9; 171.3; 155.4; 78.0; 59.1; 51.8; 47.5; 30.6; 28.2; 19.1, 18.0; 16.9; mp = 142-144 °C; IR: 3310 cm^{-1}; 2976 cm^{-1}; 1751, 1682, 1649 cm^{-1}; 1557, 1524 cm^{-1}; 1160 cm^{-1}. HRMS (TOF ESI, ion polarity positive): m/z 325.1739 calc. for $[C_{14}H_{26}N_2O_5 + Na]^+$, found 325.1746.

***tert*-butyl N-[(1S)-1-[[(1S)-2-[[(1S)-1-carbamoyl-2-methyl-propyl]amino]-1-methyl-2-oxo-ethyl]carbamoyl]-2-methyl-propyl]carbamate (1):** Compound **6** (495 mg, 1.64 mmol, 1.0 eq.) was dissolved in MeOH (20.0 mL) and an aqueous solution of NaOH 2 M (4.1 mL, 8.19 mmol, 5.0 eq.) was added dropwise to the solution. The reaction was stirred at 60° C for 1 h. The volatiles were evaporated and the solid obtained was solubilized in water. The mixture was acidified with 10% aqueous $KHSO_4$ solution until pH = 2-3. The product was extracted from the water phase with DCM. The organic phase was dried over Na_2SO_4 and concentrated under vacuum to afford the free carboxylic acid (417 mg, 1.45 mmol, 89%) that was used without any further purification and dissolved in anhydrous DMF (10mL). The solution was cooled at 0°C and HOBt (245 mg, 1.6 mmol, 1.1 eq.) and HBTU (607 mg, 1.6 mmol, 1.1 eq.) were added. The reaction mixture was stirred at 0°C for 30 min and the solution of $HCl{\cdot}NH_2$-Val-NH_2 (221 mg, 1.45 mmol, 1.0 eq.) and DIPEA (0.74 mL, 4.35 mmol, 3.0 eq.) in DMF (10.0 mL) were added. The reaction was carried at room temperature overnight. After evaporation of the volatiles under vacuum, the oily residue was taken up with EtOAc. After few minutes a white solid precipitated which after filtration afforded compound **1** (440 mg, 1.14 mmol,79% so 70% for two steps from compound **6**) as a white solid. ^{1}H NMR (DMSO-d_6, 400 MHz): 7.92 (1H, d, *J* = 7.2 Hz); 7.69 (1H, d, *J* = 8.9 Hz); 7.36 (1H, s); 7.01 (1H, s); 6.71 (1H, d, *J* = 8.9 Hz); 4.38 (1H, m); 4.09 (1H, dd, *J* = 8.8, 6.5 Hz); 3.80 (1H, m); 1.94 (2H, m); 1.37 (9H, s); 1.19 (3H, d, *J* = 6.9 Hz); 0.82 (12H, m); ^{13}C NMR (DMSO-d_6, 400 MHz): 172.7; 171.8; 170.9; 155.4; 78.0; 59.5; 57.2; 48.0; 30.5, 30.3; 28.2;

19.2; 18.1; 17.9; 17.8;; mp = 266-270 °C; IR: 3293 cm^{-1}; 2960 cm^{-1}; 1671, 1626 cm^{-1}; 1529 cm^{-1}. HRMS (TOF ESI, ion polarity positive): m/z 387.2607 calc. for $[C_{18}H_{35}N_4O_5+ H]^+$ and 409.2427 calc. for $[C_{18}H_{35}N_4O_5+ Na]^+$, found 387.2602 and 409.2427; Elemental analysis: $C_{18}H_{34}N_4O_5$ + 1.5 H_2O calcd C 52.28, H 9.04, N 13.55; found C 52.37, H 8.24, N 13.60. HPLC purity (XBridge Select C18, 3.5 µm, H_2O + 0.1% form. ac./ACN – grd 5-100% in 20 min, detection at 245 nm): TR = 11.83 min, 100%.



Scheme S2

Benzyl (2S)-2-[[[[(*tert*-butoxycarbonylamino)-isopropyl-carbamoyl]amino]-methyl-carbamoyl]amino]-3-methyl-butanoate (3): To a solution of H-L-Val-OBn hydrochloride (110 mg, 0.45 mmol; 1.1 eq.) in dry DMF (5 mL), were added under argon atmosphere DIPEA (0.16 mL, 0.90 mmol, 2.2 eq.) and p-nitrophenyl chloroformate (90.7 mg, 0.45 mmol, 1.1 eq.). The clear solution obtained was stirred at room temperature and monitored by TLC. After formation of the activated intermediate, a solution of compound **7** (100 mg, 0.41 mmol) and DMAP (20.1 mg, 0.41 mmol, 1.0eq.) in DMF (1mL) was added to the reaction mixture and the reaction was stirred overnight at room temperature. After evaporation of the volatiles under vacuum, the oily residue was purified by chromatography on silica gel using EtOAc 100% to afford compound **3** (130 mg, 0.27 mmol, 66%) as a white solid. R_f= 0.55 (EtOAc 100%) ^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.33 (5H, m); 7.18 (1H, bp); 6.35 (1H, bp); 6.19 (1H, bp); 5.16 (2H, m); 4.66 (1H, m); 4.42 (1H, m); 3.14 (3H, s); 2.09 (1H, m); 1.49 (9H, s); 1.12 (6H, m).0.93 (6H, m); ^{13}C NMR (100 MHz, DMSO-d_6): 173.0; 158.6; 151.9; 144.5; 135.9; 128.6, 128.3; 82.9; 66.5; 58.7; 48.9; 36.2; 31.1; 28.1; 19.2; 18.9; mp = 174 – 176 °C; IR: 3391, 3296 cm^{-1} (N-H stretch); 2975 cm^{-1} (C-H stretch); 1740, 1725, 1673, 1643 cm^{-1} (C=O stretch); 1536, 1494 cm^{-1} (N-H bend); 1272, 1243 cm^{-1} (C-N stretch); 1179 cm^{-1} (C-C(O)-C stretch); HRMS (TOF ESI, ion polarity positive): m/z 480.2822 calc. for $[C_{23}H_{38}N_5O_6+ H]^+$, found 480.2823; HPLC purity (XBridge Select C18, 3.5 µm, H_2O + 0.1% form. ac./ACN – grd 5-100% in 20 min): TR = 17.63 min, 97%

(2S)-2-[[[[(*tert*-butoxycarbonylamino)-isopropyl-carbamoyl]amino]-methyl-carbamoyl]amino]-3-methyl-butanoic acid (8): 3 (100 mg, 0.21 mmol, 1.0 eq) was dissolved in methanol (3 mL) and then Pd/C 10% was added (10 mg). The reaction mixture was stirred at room temperature under hydrogen atmosphere. After complete disappearance of the starting material, the mixture was filtered through a celite pad and after evaporation of the volatiles the desired product **8** was obtained (82 mg, 0.21 mmol, 100 %) and used without any further purification. HRMS (TOF ESI, ion polarity positive): m/z 390.2308 calc. for $[C_{16}H_{31}N_5O_6+ H]^+$ and 412.2172 calc. for $[C_{16}H_{31}N_5O_6+ Na]^+$, found 390.2345 and 412.2177.

Benzyl (2S)-2-[[[[amino(isopropyl)carbamoyl]amino]-methyl-carbamoyl]amino]-3-methyl-butanoate (9):
To a solution of **3** (100.0 mg, 0.21 mmol, 1.0 eq) in dioxane (3 mL), a 4 N solution of HCl in dioxane (1.7 mL, 40.0 eq.) was added at 0°C. The mixture was stirred at room temperature until complete disappearance of the starting material (monitored by TLC). The desired product **9** (79.7 mg, 0.21 mmol, 100 %) was isolated as its hydrochloride salt by precipitation in diethyl ether and used for the next step without any further purification. HRMS (TOF ESI, ion polarity positive): m/z 380.2253 calc. for $[C_{17}H_{28}N_4O_6+ H]^+$ and 402.2117 calc. for $[C_{17}H_{28}N_4O_6+ Na]^+$, found 380.2292 and 402.2139.

Benzyl (2S)-2-[[[[[[(2S)-2-[[[[(tert-butoxycarbonylamino)-isopropyl-carbamoyl]amino]-methyl-carbamoyl]amino]-3-methyl-butanoyl]amino]-isopropyl-carbamoyl]amino]-methyl-carbamoyl]amino]-3-methyl-butanoate (10): 8 (79.7 mg, 0.21 mmol) was dissolved in DMF (2 mL) under hydrogen atmosphere and cooled at 0°C. At these time HOAt (32 mg, 0.23 mmol, 1.1 eq) and HATU (88mg, 0.23 mmol, 1.1 eq) were added and the mixture was stirred for 1 hour. Then **9** (81.8 mg, 0.21mmol) and DIPEA (146 µL, 0.84 mmol, 4.0 eq) were added and the mixture was stirred at room temperature overnight. The volatiles were evaporated under reduced pressure, the residue was taken up with AcOEt and washed with citric acid (10% in water), saturated $NaHCO_3$ and brine, dried over Na_2SO_4 filtered and concentrated under vacuum. The crude was purified by column chromatography on a silica gel using AcOEt/MeOH 95:5 as eluent to afford **10** (24 mg, 0.031 mmol, 16 %) R_f= 0.2 (AcOEt/MeOH 95/5) ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.78 (1H, bs); 8.18 (1H, bs); 8.11 (1H, bs); 7.96 (1H, bs); 7.28 (5H, m); 6.61 (1H, bs); 6.10 (1H, bs); 5.14 (2H, m); 4.62 (2H, m); 4.37 (2H, m); 3.20 (6H, s); 2.90 (2H, m); 1.39 (9H, s); 1.20- 0.90 (24H, m); ^{13}C NMR (75 MHz, $CDCl_3$): 174.0; 157.5; 152.1; 142.1; 136.0; 128.7, 127.0; 82.9; 66.5; 59.1; 48.9; 48.8; 36.4; 31.1; 30.9; 28.3; 20.0; 19.6; 18.2; HRMS (TOF ESI, ion polarity positive): m/z 751.4466 calc. for $[C_{34}H_{58}N_{10}O_9+ H]^+$ and 773.4286 calc. for $[C_{34}H_{58}N_{10}O_9+ Na]^+$, found 751.4482 and 773.4291;

***tert*-butyl N-[[[(1S)-1-[[[[(1S)-1-carbamoyl-2-methyl-propyl]carbamoyl-methyl-amino]carbamoyl-isopropyl-amino]carbamoyl]-2-methyl-propyl]carbamoyl-methyl-amino]carbamoyl-isopropyl-amino]carbamate (5):** To a solution of **10** (24.0 mg, 0.031 mmol,1.0 eq) in methanol (1 mL) was added Pd/C 10% (10.0 mg, 0.009 mmol, 0.3 eq). The reaction mixture was stirred at room temperature under hydrogen atmosphere. After complete disappearance of the starting material, the mixture was filtered through a celite pad. After evaporation of the volatiles under reduced pressure the white solid was dissolved in isopropanol (1 mL) and DMTMM·HCl (12.5 mg, 0.045mmol, 1.5 eq) was added. At the resulting suspension, a solution of NH_3 in methanol (13 µL, 0.087 mmol, 3 eq) was slowly dropped. The mixture was stirred at room temperature for 3h. The volatiles were removed under vacuum, the residue was taken with

AcOEt and the organic layer was washed with saturated aqueous $NaHCO_3$, dried over Na_2SO_4, filtered and concentrated under vacuum. Purification by column chromatography on silica gel AcOEt/MeOH 95/5 and then 80/20 afforded compound **5** (6.3 mg, 9.6 µmol, 33%) as a white solid. R_f= 0.1 (AcOEt/MeOH 95/5). For ^{1}H and ^{13}C NMR, see Tables S13-S14. HRMS (TOF ESI, ion polarity positive): m/z 660.4157 calc. for $[C_{27}H_{53}N_{11}O_8+ H]^+$ and 682.3976 calc. for $[C_{27}H_{53}N_{11}O_8+ Na]^+$ found 660.4157 and 682.3978; HPLC purity (XBridge Select C18, 3.5 µm, H_2O + 0.1% form. ac./ACN – grd 5-100% in 20 min): TR = 15.12 min.

HRMS and HPLC-MS spectra of compound 1

Elemental Composition Report

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Monoisotopic Mass, Even Electron Ions
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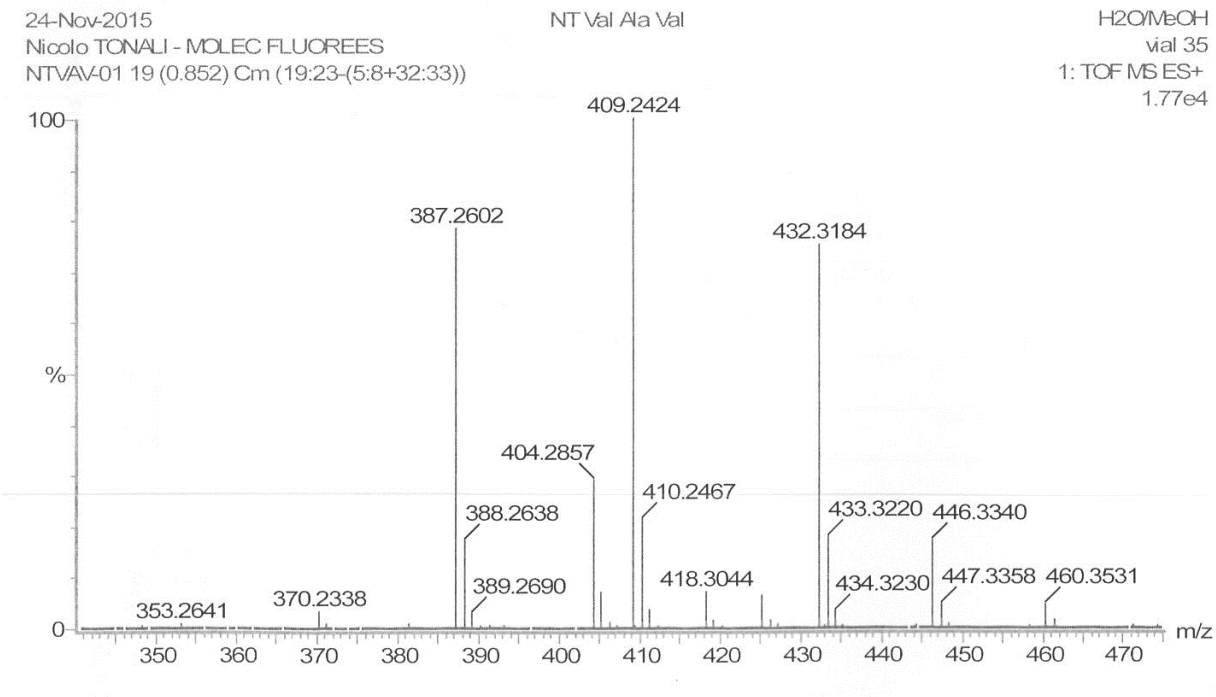

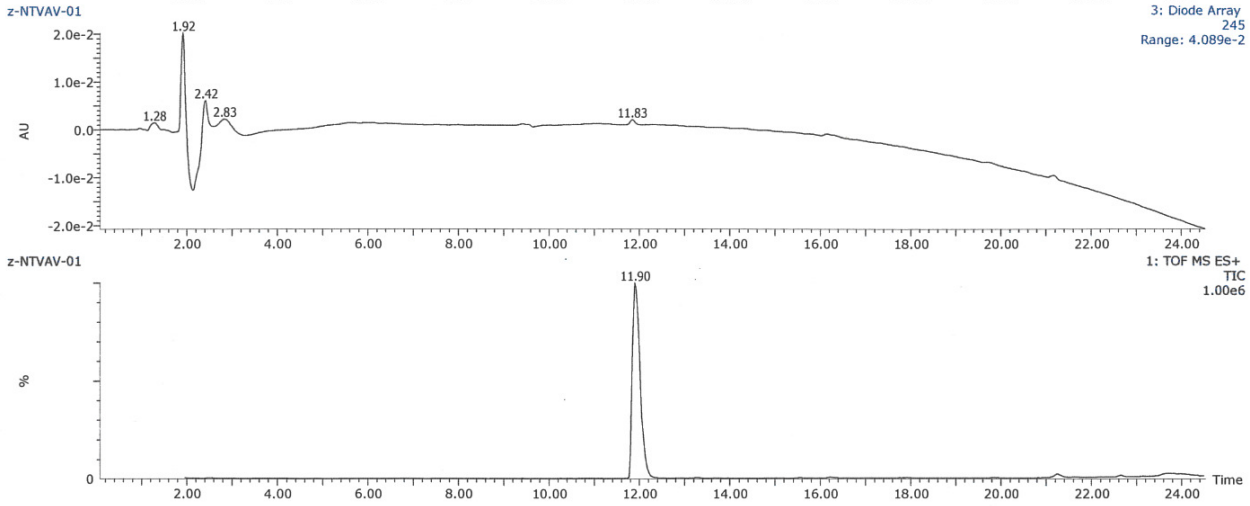
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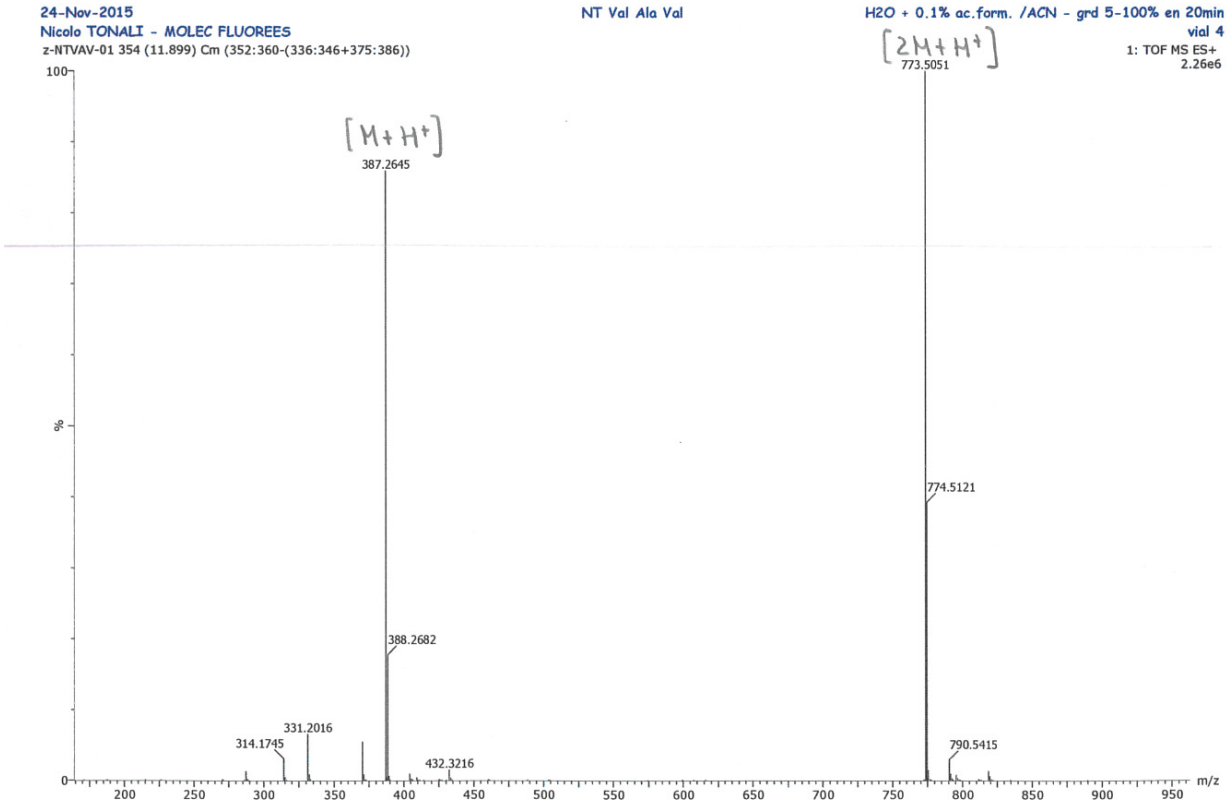
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HRMS and HPLC-MS spectra of compound 3

Elemental Composition Report

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Selected filters: None

Monoisotopic Mass, Even Electron Ions
2266 formula(e) evaluated with 9 results within limits (up to 3 best isotopic matches for each mass)
Elements Used:
C: 0-70 H: 1-130 N: 0-6 O: 0-7 Na: 0-1 F: 0-3

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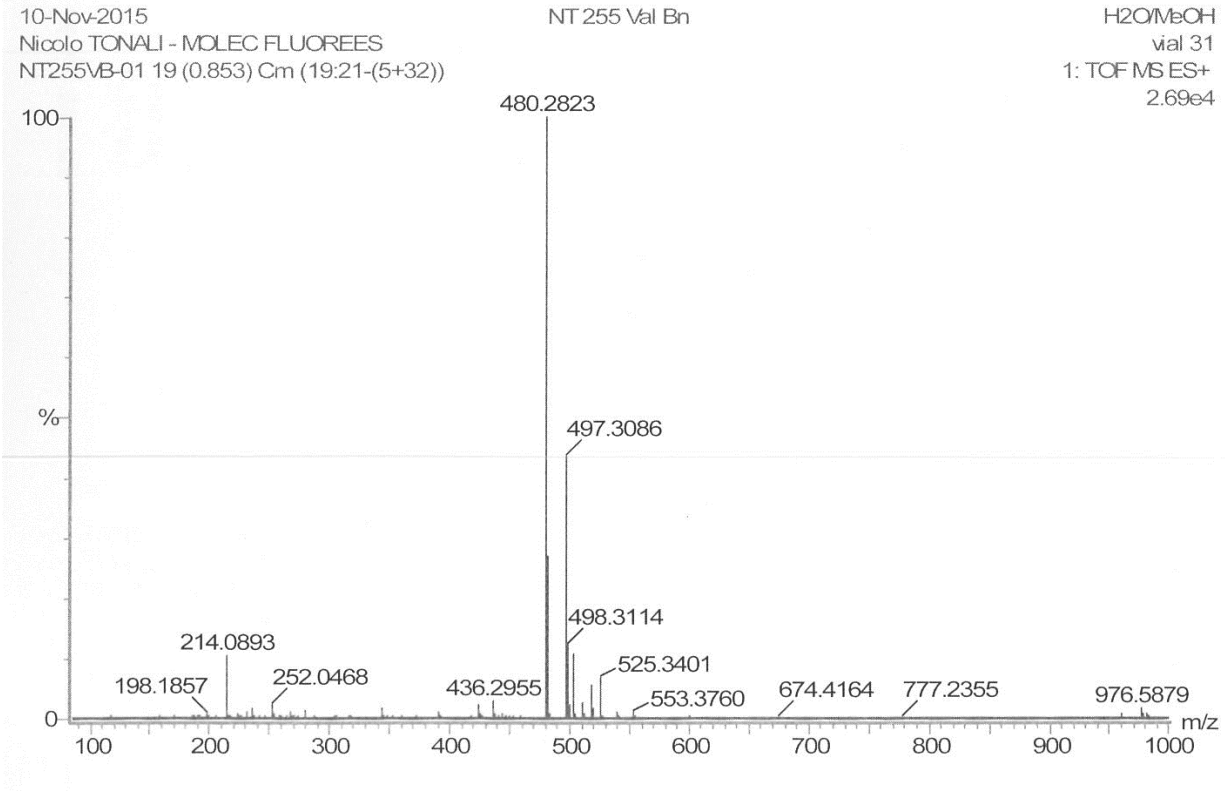

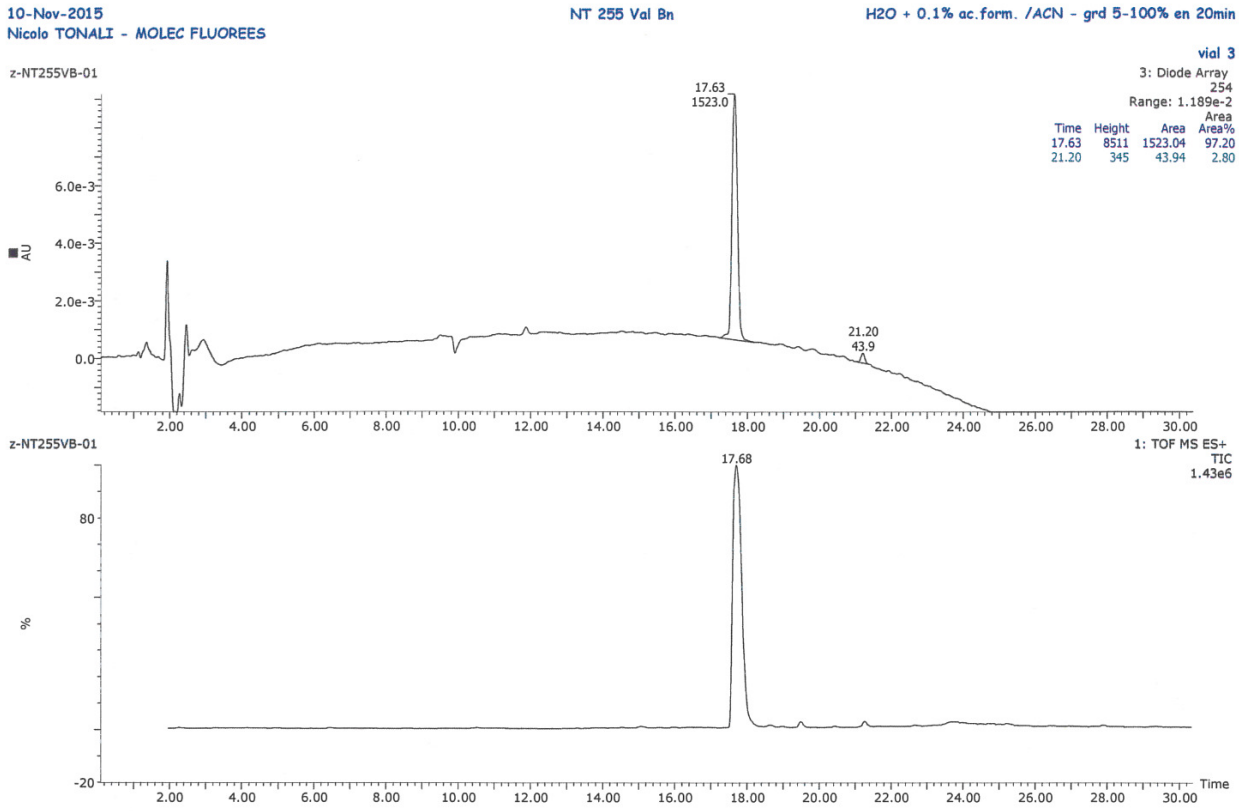
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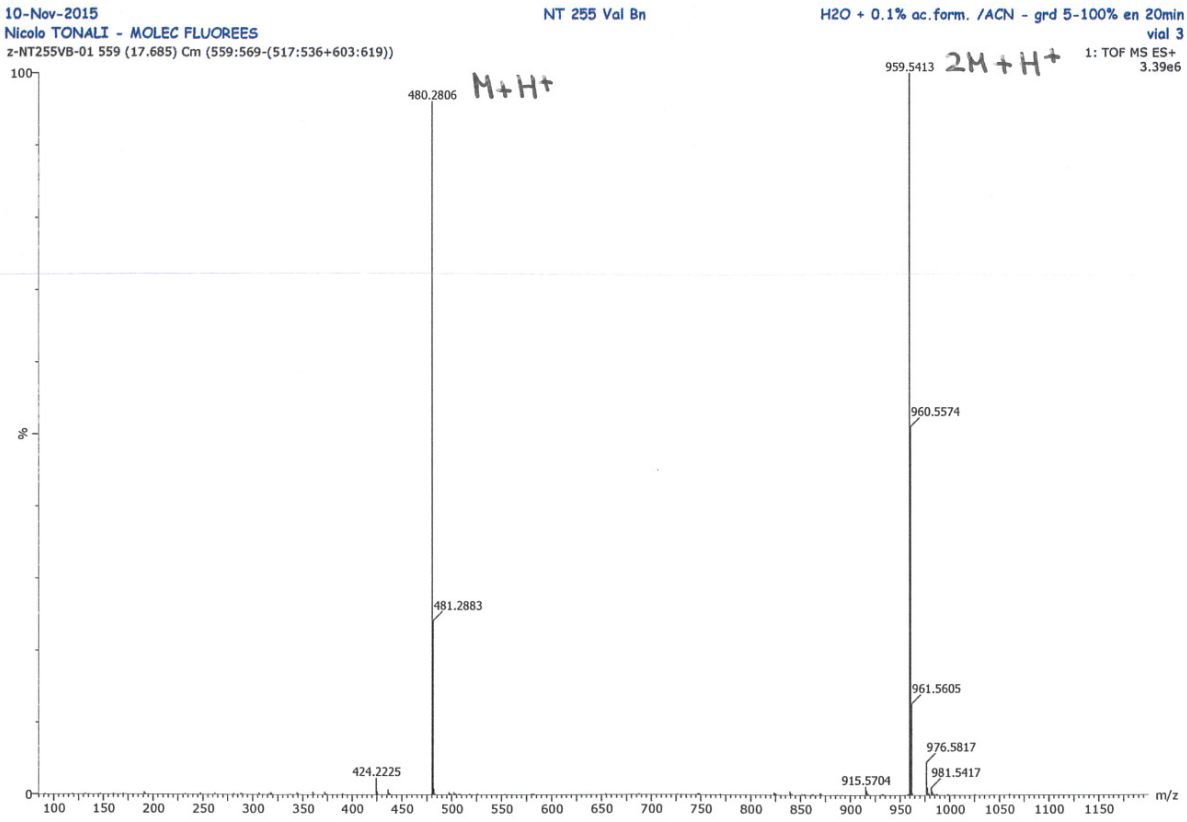
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HRMS and HPLC-MS spectra of compound 5

Elemental Composition Report

Multiple Mass Analysis: 3 mass(es) processed
Tolerance = 5.0 PPM / DBE: min = -2.0, max = 100.0
Selected filters: None

Monoisotopic Mass, Even Electron Ions
4804 formula(e) evaluated with 23 results within limits (up to 3 best isotopic matches for each mass)

Elements Used:
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682.3978	**29**	**682.3976**	**0.2**	**0.3**	**6.5**	**1.48E+04**	**C27 H53 N11 O8 Na**
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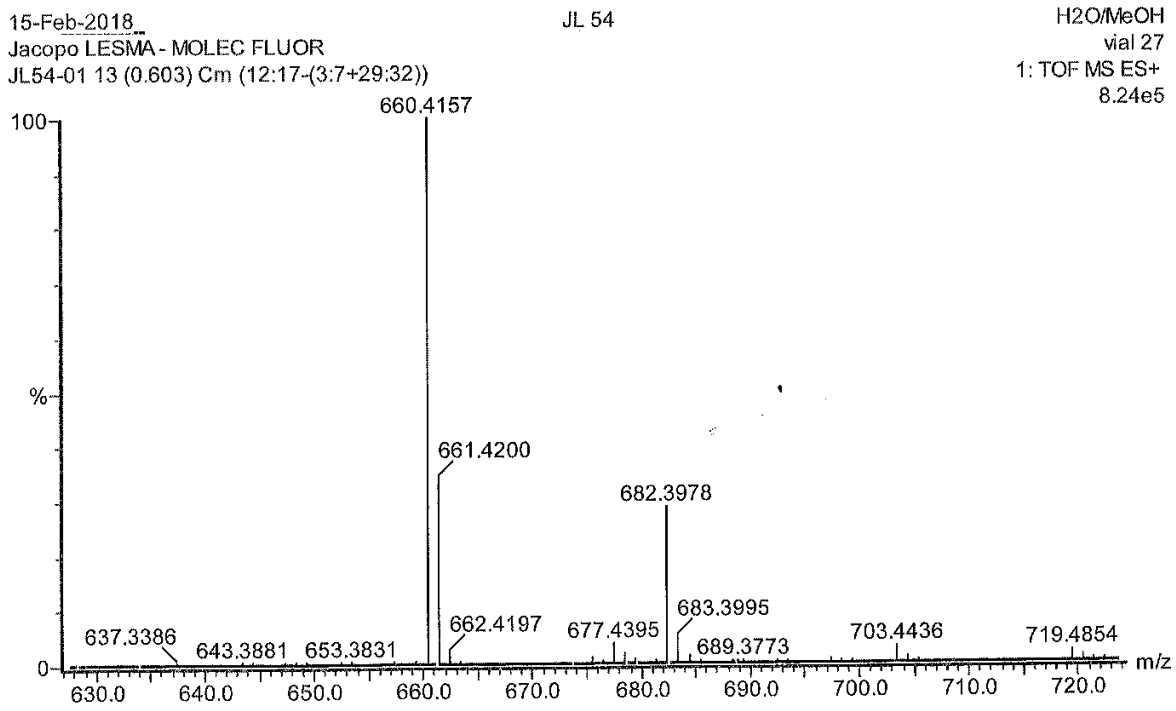

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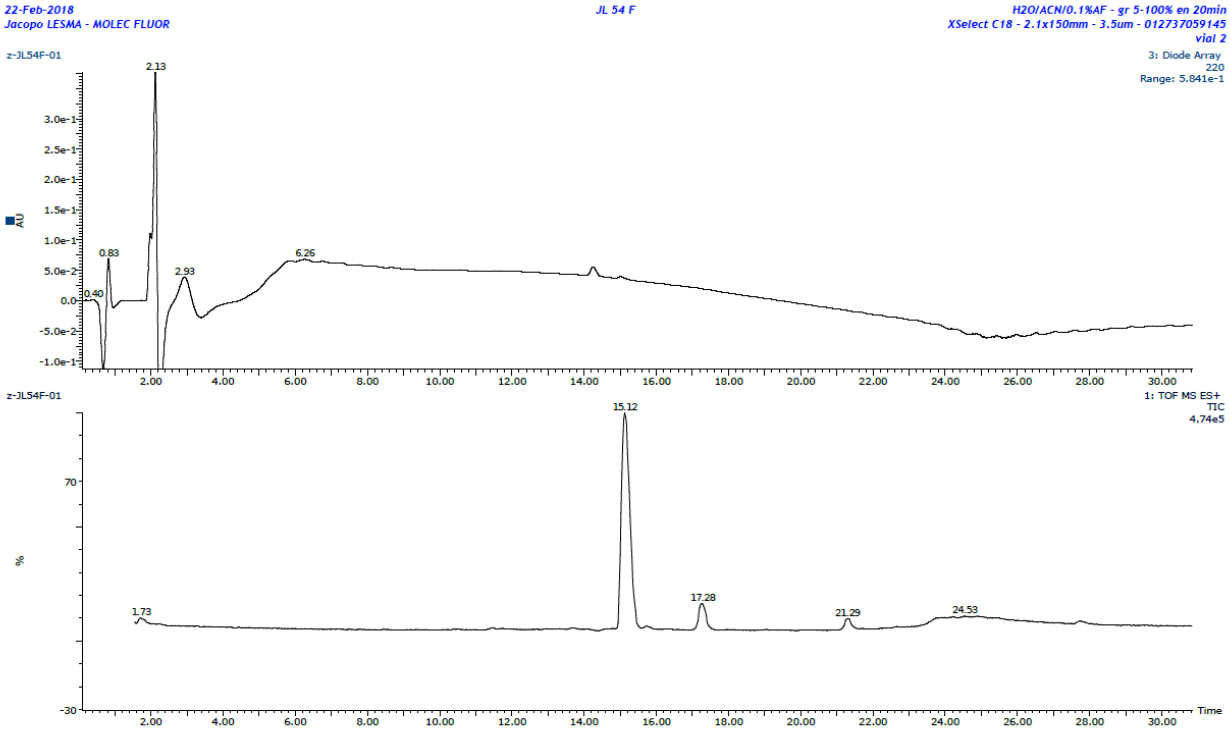
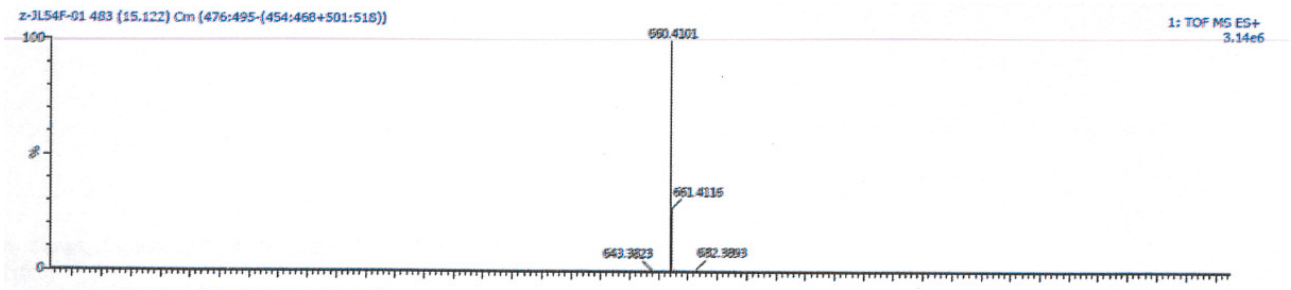
JL 54 F





NMR data of compounds 1-5

NMR data for peptide 1 (Boc-Val-Ala-Val-NH_2)

Table S1. ^{1}H NMR chemical shifts of peptide **1** (4 mM) in CD_3OH at 293 K

Residue	δ HN (ppm), ^{3}J (Hz)	δ H^{α} (ppm), ^{3}J (Hz)	δ H^{β} (ppm)	δ Other protons (ppm)
Boc				CH_3 1.44
Val[1]	6.62 (d, *J* = 8.7)	3.87 (dd, *J* = 8.7, 7.0)	2.03	γ CH_3 0.95, γ' CH_3 0.91
Ala[2]	8.18 (d, *J* = 6.6)	4.41 (q, *J* = 6.9)	1.36	
Val[3]	7.86 (d, *J* = 8.6)	4.17 (dd, *J* = 8.6, 6.8)	2.07	γ CH_3 0.96, γ' CH_3 0.95
$NH_{2\ Z,\ E}$	7.04 (s), 7.60 (s)			

Table S2. ^{13}C NMR chemical shifts of peptide **1** (4 mM) in CD_3OH at 293 K

Residue	δ CO (ppm)	δ C^{α} (ppm)	δ C^{β} (ppm)	δ Other carbons (ppm)
Boc	158.0			Cq 80.5, CH_3 28.6
Val[1]	174.3	61.4	32.0	γ CH_3 19.74, γ' CH_3 18.2
Ala[2]	174.7	50.4	17.9	
Val[3]	176.1	59.8	31.8	γ CH_3 19.69, γ' CH_3 18.3

Table S3. NMR conformational parameters for peptide **1** in CD_3OH at 293 K

Residue	ΔδHN/ΔT (ppb/K)	$^{3}J_{HN\text{-}H\alpha}$ (Hz)	$^{3}J_{H\alpha\text{-}H\beta}$ (Hz)
Val[1]	-8.5	8.7	7.0
Ala[2]	-7.7	6.6	6.9
Val[3]	-8.4	8.6	6.8
$NH_{2\ Z,\ E}$	-7.1, -8.3		

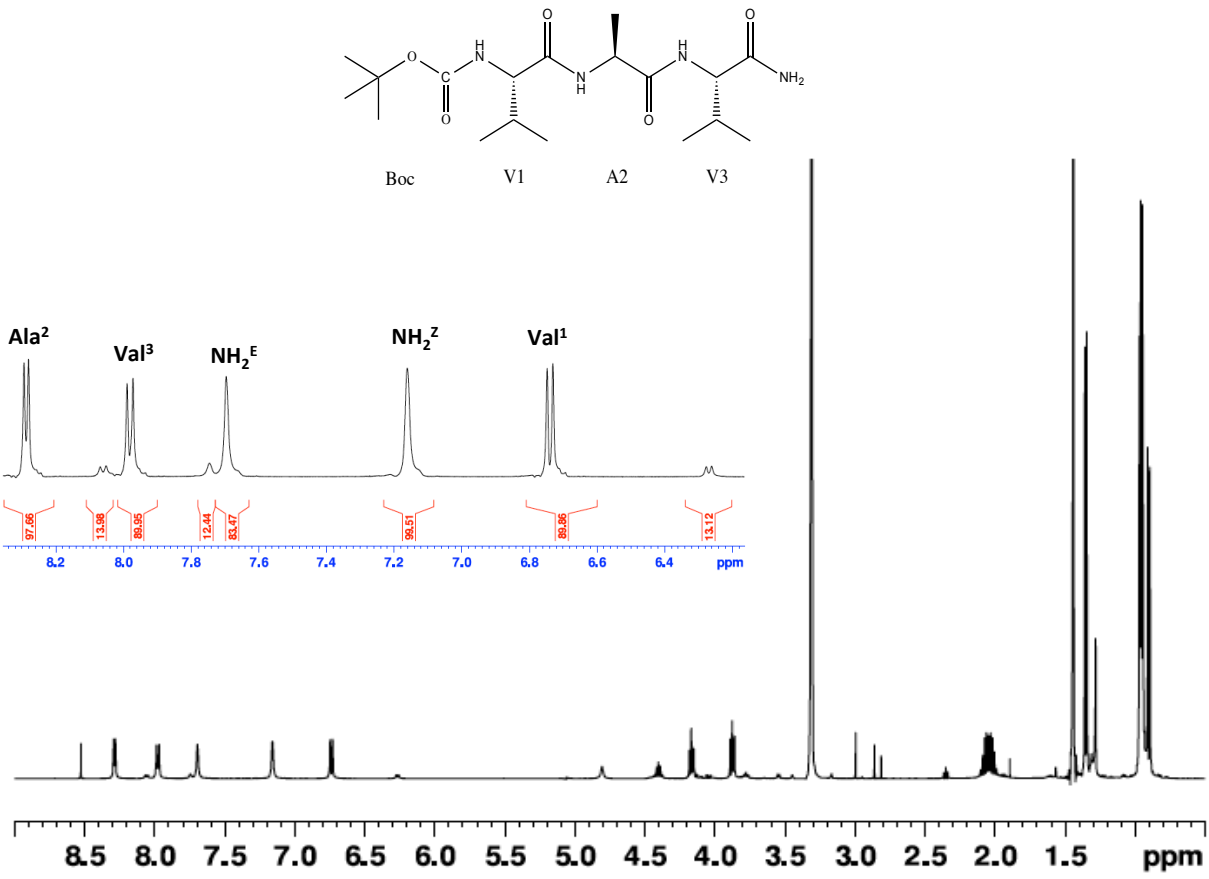


Figure S1: 1D ^{1}H NMR spectrum of peptide **1** (4 mM) in methanol at 278.4 K (500.3 MHz)

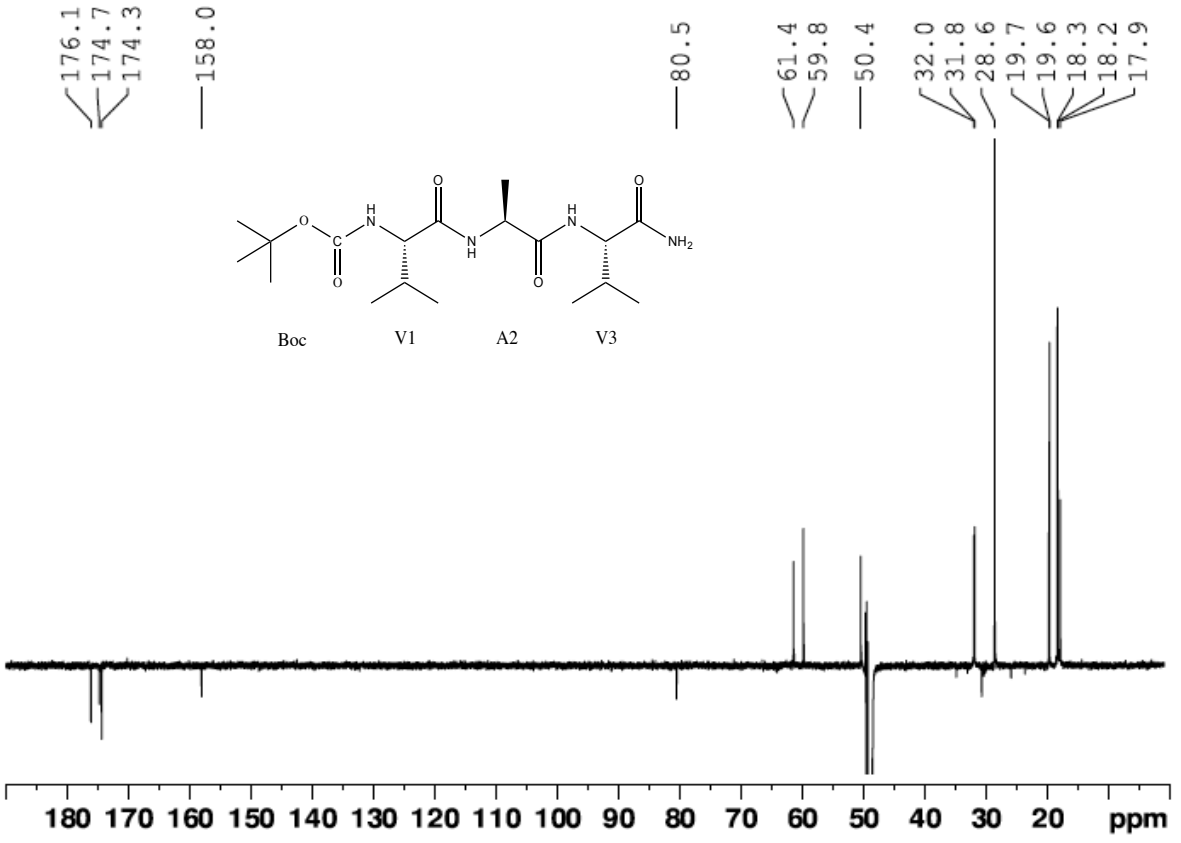


Figure S2: 1D ^{13}C DEPTQ NMR spectrum of peptide **1** (4 mM) in methanol at 278.4 K (125.8 MHz)

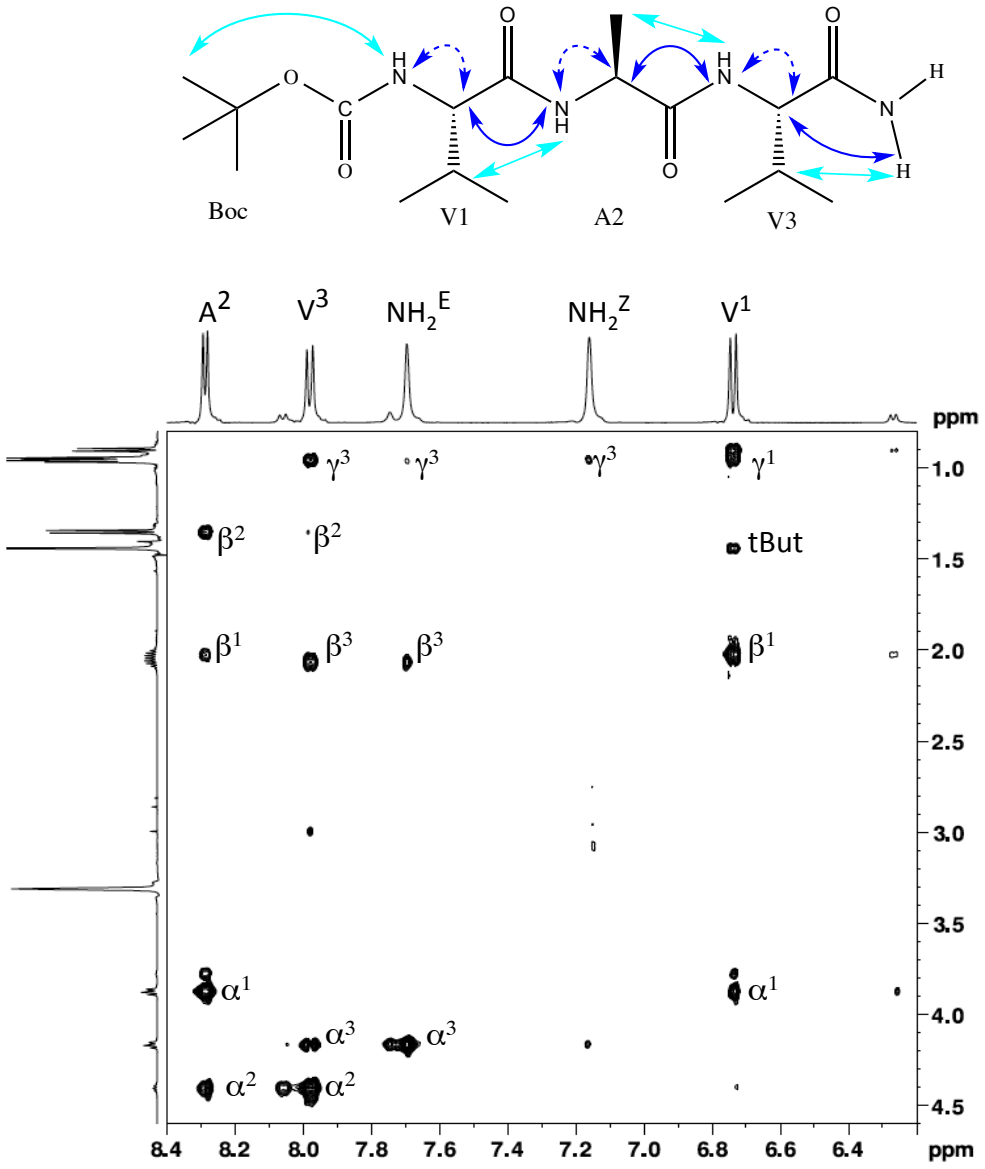


Figure S3: Expansion of the 2D ^{1}H-^{1}H ROESY spectrum of pseudopeptide **1** (4 mM) in methanol at 278.4 K (500.3 MHz, ROE mixing time of 800 ms), showing the sequential and intra-residue correlation peaks (plain and dash blue arrows correspond to strong/medium intensity respectively, cyan arrows correspond to weaker intensity).

NMR data for compound 2 (Boc-aVal-aAla-Val-NH_2)

Table S4. ^{1}H NMR chemical shifts for the two conformers (A, B) of pseudotripeptide **2** (28.6 mM) in CD_3OH at 273 K

Residue	δ HN (ppm), ^{3}J (Hz)	δ H^α (ppm)	δ H^β (ppm)	δ Other protons (ppm)
Boc				CH_3 1.52 (A)
				CH_3 1.51 (B)
aVal[1]	9.26 (A)		4.55 (A)	γ CH_3 1.12, γ' CH_3 1.08 (A)
	9.16 (B)		4.54 (B)	γ CH_3 1.11, γ' CH_3 1.04 (B)
aAla[2]	9.65 (A)		3.07 (A)	
	9.35 (B)		3.08 (B)	
Val[3]	6.55 (A) (d, ^3J = 9.0)	4.08 (A)	2.33 (A)	γ CH_3 0.987, γ' CH_3 0.98 (A)
	6.52 (B) (d, ^3J = 8.4)	3.98 (B)	2.17 (B)	γ CH_3 0.990, γ' CH_3 0.98 (B)
$NH_{2\ Z,\ E}$	7.35, 7.39 (A)			
	7.19, 7.54 (B)			

Table S5. ^{13}C NMR chemical shifts for the two conformers (A, B) of pseudotripeptide **2** (28.6 mM) in CD_3OH at 273 K

Residue	δ CO (ppm)	δ C^α (ppm)	δ C^β (ppm)	δ Other carbons (ppm)
Boc	157.7 (A)			Cq 82.4, CH_3 28.4 (A)
	157.8 (B)			Cq 82.3, CH_3 28.5 (B)
aVal[1]	158.6 (A)		50.3 (A)	γ CH_3 19.8, γ' CH_3 19.1 (A)
	158.0 (B)		50.0 (B)	γ CH_3 20.1, γ' CH_3 19.1 (B)
aAla[2]	161.0 (A)		36.8 (A)	
	160.6 (B)		36.5 (B)	
Val[3]	178.2 (A)	61.3 (A)	30.5 (A)	γ CH_3 17.3, γ' CH_3 19.8 (A)
	177.8 (B)	61.5 (B)	31.1 (B)	γ CH_3 18.3, γ' CH_3 19.9 (B)

Table S6. NMR conformational parameters for **2** in CD_3OH

Residue	$\Delta\delta HN/\Delta T$ (ppb/K)	$^3J_{HN\text{-}H\alpha}$ (Hz)*
aVal[1]	-7.3 (A)	
	-7.1 (B)	
aAla[2]	-6.55 (A)	
	-6.8 (B)	
Val[3]	-2.6 (A)	9.0 (A)
	-2.3 (B)	8.4 (B)
$NH_{2\ Z,\ E}$	-8.4, -3.3 (A)	
	-7.3, -6.2 (B)	

* measured at 247.5 K

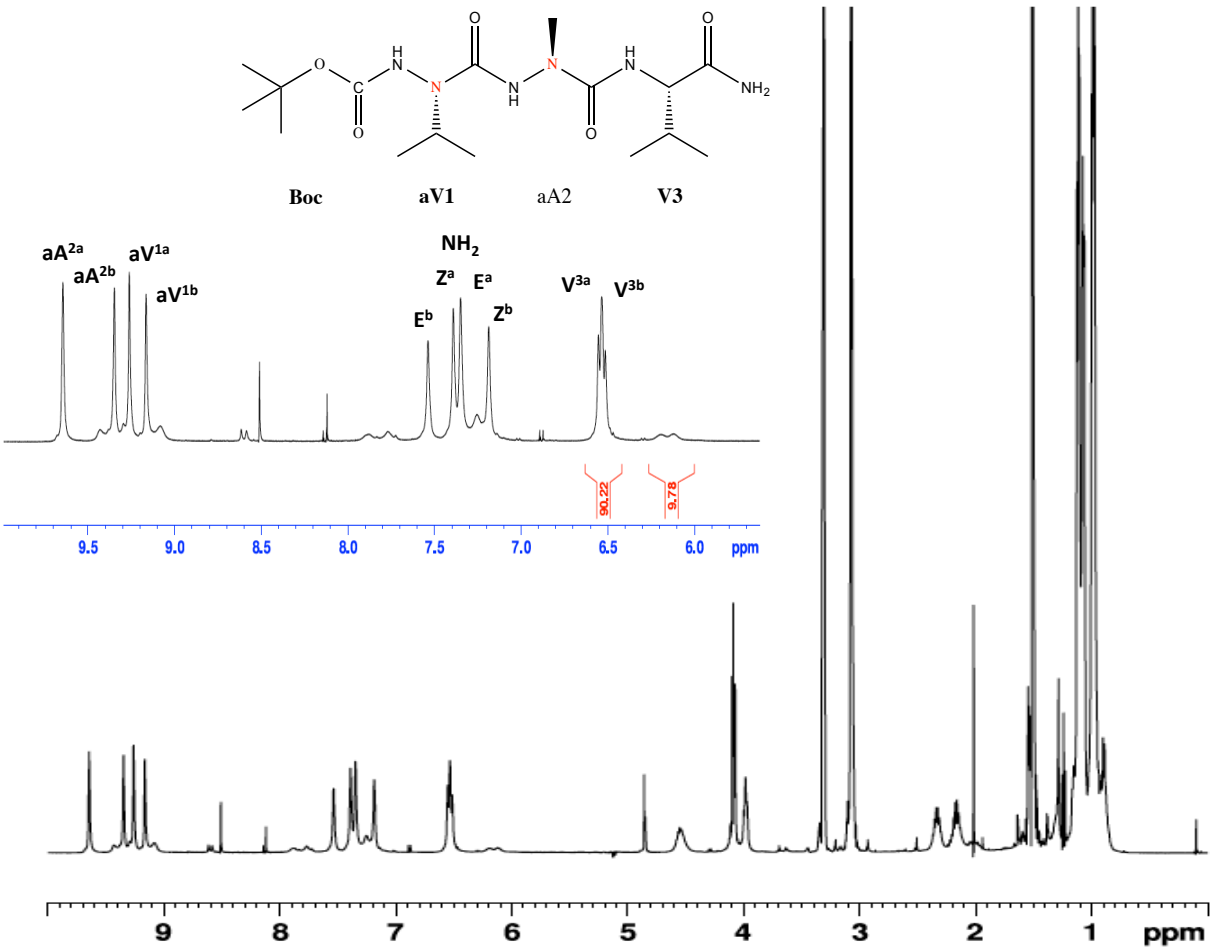


Figure S4: 1D ^{1}H NMR spectrum of pseudopeptide **2** (28.6 mM) in methanol at 273 K (500.3 MHz)

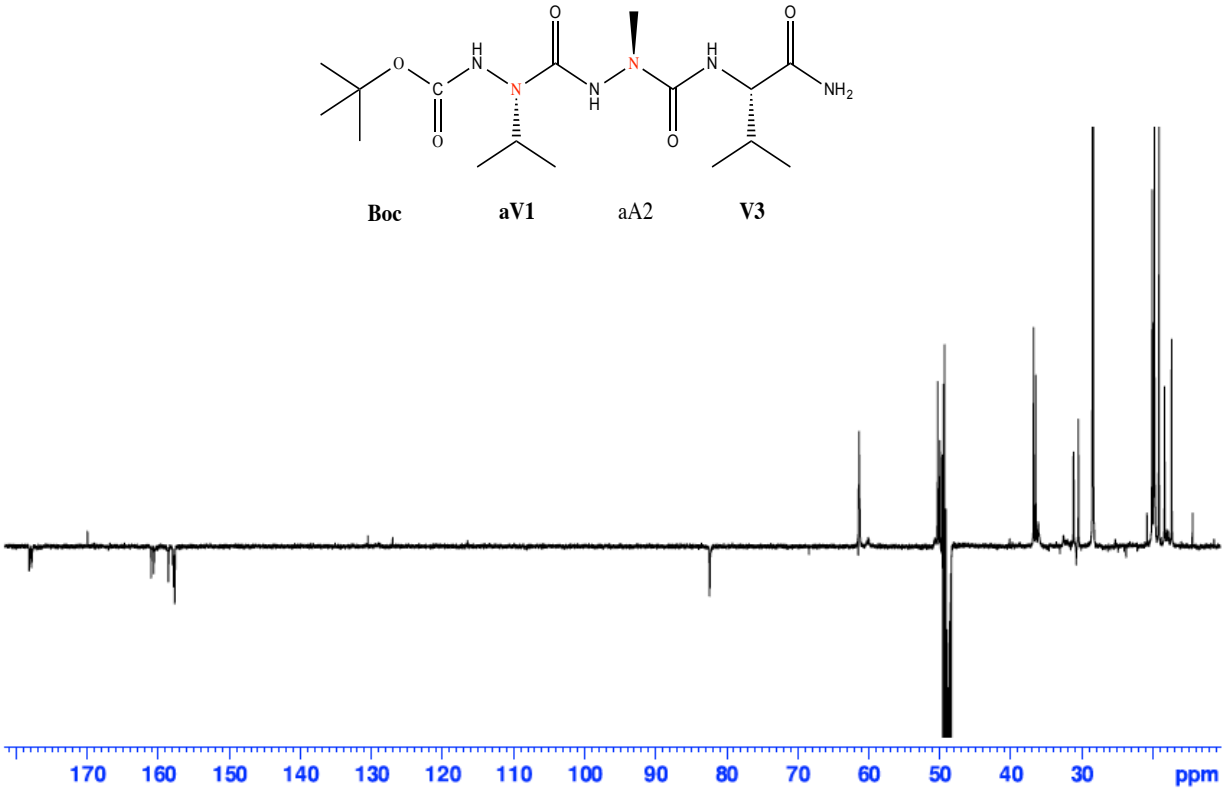


Figure S5: 1D ^{13}C DEPTQ NMR spectrum of pseudopeptide **2** (28.6 mM) in methanol at 273 K (125.8 MHz)

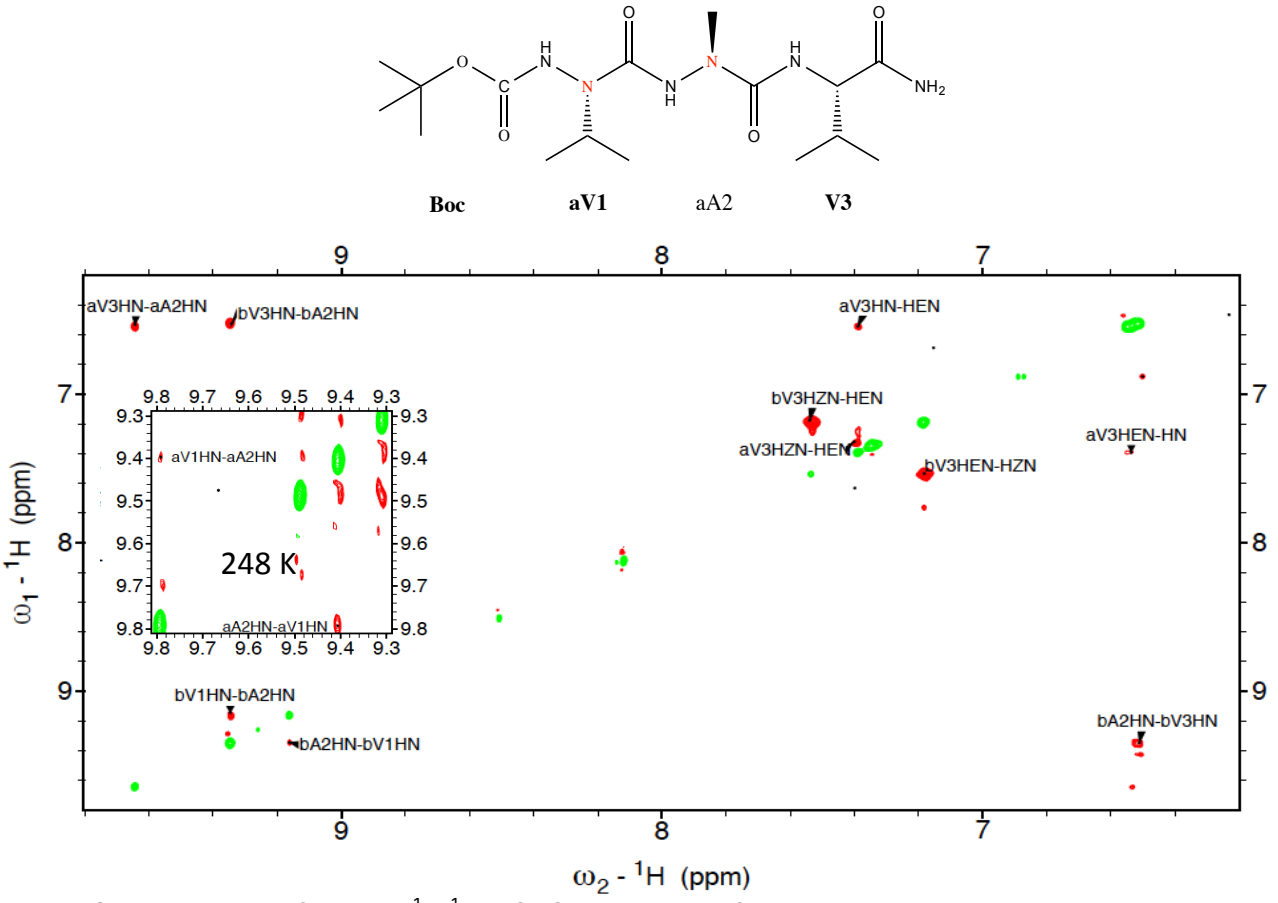


Figure S6: Expansion of the 2D ^{1}H-^{1}H ROESY spectrum of pseudopeptide **2** (28.6 mM) in methanol at 273 K (500.3 MHz, mixing time of 800 ms), showing the sequential correlation peaks NHi-NHi+1 (in red) for conformers A and B. The insert shows the sequential ROE observed for aV1 and aV2 residues of conformer A at 248 K (which is not observed at 273 K).

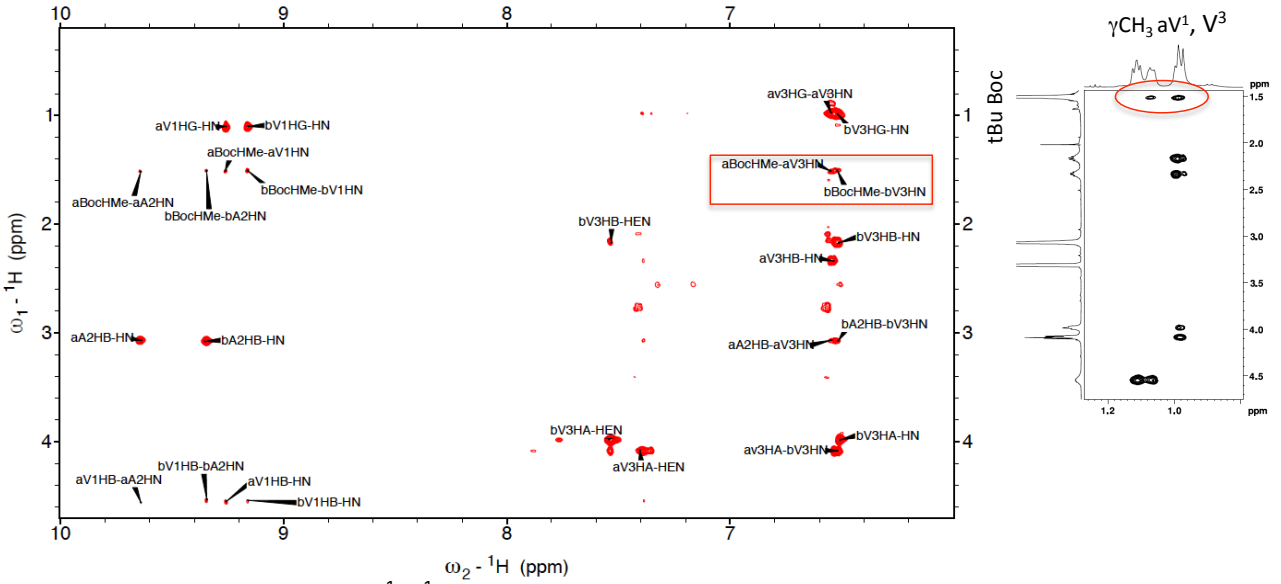


Figure S7: Expansion of the 2D ^{1}H-^{1}H ROESY spectrum of pseudopeptide **2** (28.6 mM) in methanol at 273 K (500.3 MHz, mixing time of 800 ms), showing the correlation peaks between NH and side chain protons for conformers A and B. The insert shows additional long-distance ROEs indicating the folding of conformers A and B.

NMR data for compound 3 (Boc-aVal-aAla-Val-OBn)

Table S7. ^{1}H NMR chemical shifts for the two conformers of pseudotripeptide **3** (28.6 mM) in CD_3OH at 273 K

Residue	δ HN (ppm), ^{3}J (Hz)	δH$^{\alpha}$(ppm)	δ H$^{\beta}$(ppm)	δ Other protons (ppm)
Boc				CH_3 1.49 (A)
				CH_3 1.50 (B)
aVal[1]	9.13 (A)		4.53 (A, B)	γ CH_3 1.11, γ' CH_3 1.06 (A, B)
	9.08 (B)			
aAla[2]	9.43 (A)		3.08 (A)	
	9.38 (B)		3.07 (B)	
Val[3]	6.71 (A, B) (d, *J* = 8.8)	4.12 (A, B)	2.18 (A)	γ CH_3 0.96, γ' CH_3 0.93 (A)
			2.11 (B)	γ CH_3 0.93, γ' CH_3 0.89 (B)
OBz				CH_2 (5.17, 5.10), Ph 7.4 (A, B)

Table S8. ^{13}C NMR chemical shifts for the two conformers of pseudotripeptide **3** (28.6 mM) in CD_3OH at 273 K

Residue	δ CO(ppm)	δ C$^{\alpha}$(ppm)	δ C$^{\beta}$ (ppm)	δ Other carbons (ppm)
Boc	157.6 (A)			Cq 82.2, CH_3 28.5 (A)
	157.7 (B)			Cq 82.0, CH_3 28.4 (B)
aVal[1]	158.02 (A)		49.9 (A, B)	γ CH_3 20.1, γ' CH_3 19.06 (A, B)
	157.97 (B)			
aAla[2]	160.7 (A)		36.3 (A, B)	
	160.6 (B)			
Val[3]	174.0 (A, B)	60.9 (A)	31.4 (A)	γ CH_3 18.6, γ' CH_3 19.6 (A)
		60.8 (B)	31.9 (B)	γ CH_3 19.13, γ' CH_3 19.4 (B)
OBz				CH_2 67.4, Ph (137.2, 129.36, 129.40, 129.2)

Table S9. NMR conformational parameters for **3** in CD_3OH

Residue	ΔδHN/ΔT (ppb/K)	^{3}JHN-Hα (Hz) *
aVal[1]	-7.0 (A) -6.92 (B)	
aAla[2]	-7.75 (A) -7.69 (B)	
Val[3]	-3.9 (A, B)	8.8 (A, B)

* measured at 251 K

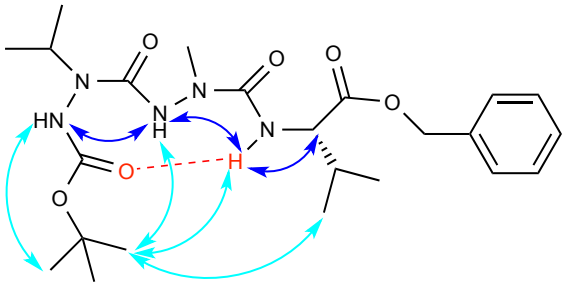


Figure S8. Schematic representation of NMR parameters obtained for Boc-aVal-aAla-Val-OBn **3**. ROEs are indicated by blue arrows and hydrogen bond by red line. Similar ROEs are observed for the two major conformers.

NMR data for compound 4 (Boc-aGly-aGly-Val-NH_2)

Table S10. ^{1}H NMR chemical shifts of pseudotripeptide **4** (15 mM) in CD_3OH at 293 K

Residue	δ HN (ppm)	δH^{α} (ppm)	δ H^{β} (ppm)	δ Other protons (ppm)
Boc				CH_3 1.47
aGly^1	8.56 (br)			
aGly^2	7.91 (br)			
Val^3	6.47 (br)	4.11 (dd, ^3J = 8.7, 6.1 Hz)	2.16 (m)	γ CH_3 0.99 (d, ^3J = 7.0 Hz)
				γ' CH_3 0.95 (d, ^3J = 7.2 Hz)
$NH_{2\ Z,\ E}$	7.09 (s), 7.62 (br)			

br: broad

Table S11. ^{13}C NMR chemical shifts of pseudotripeptide **4** (15 mM) in CD_3OH at 293 K

Residue	δ CO (ppm)	δ C^{α} (ppm)	δ C^{β} (ppm)	δ Other carbons (ppm)
Boc	158.3			Cq 81.9, CH_3 28.4
aGly^1	161.3			
aGly^2	160.9			
Val^3	177.3	60.3	31.6	γ CH_3 19.7, γ' CH_3 17.9

Table S12. Temperature coefficients ($\Delta\delta/\Delta T$) of the amide protons chemical shifts of pseudotripeptide **4** in methanol solution.

Residue	$\Delta\delta HN/\Delta T$ (ppb/K)
aGly^1	-9.4
aGly^2	-6.3
Val^3	-4.2
$NH_{2\ Z,\ E}$	-6.1, -8.6

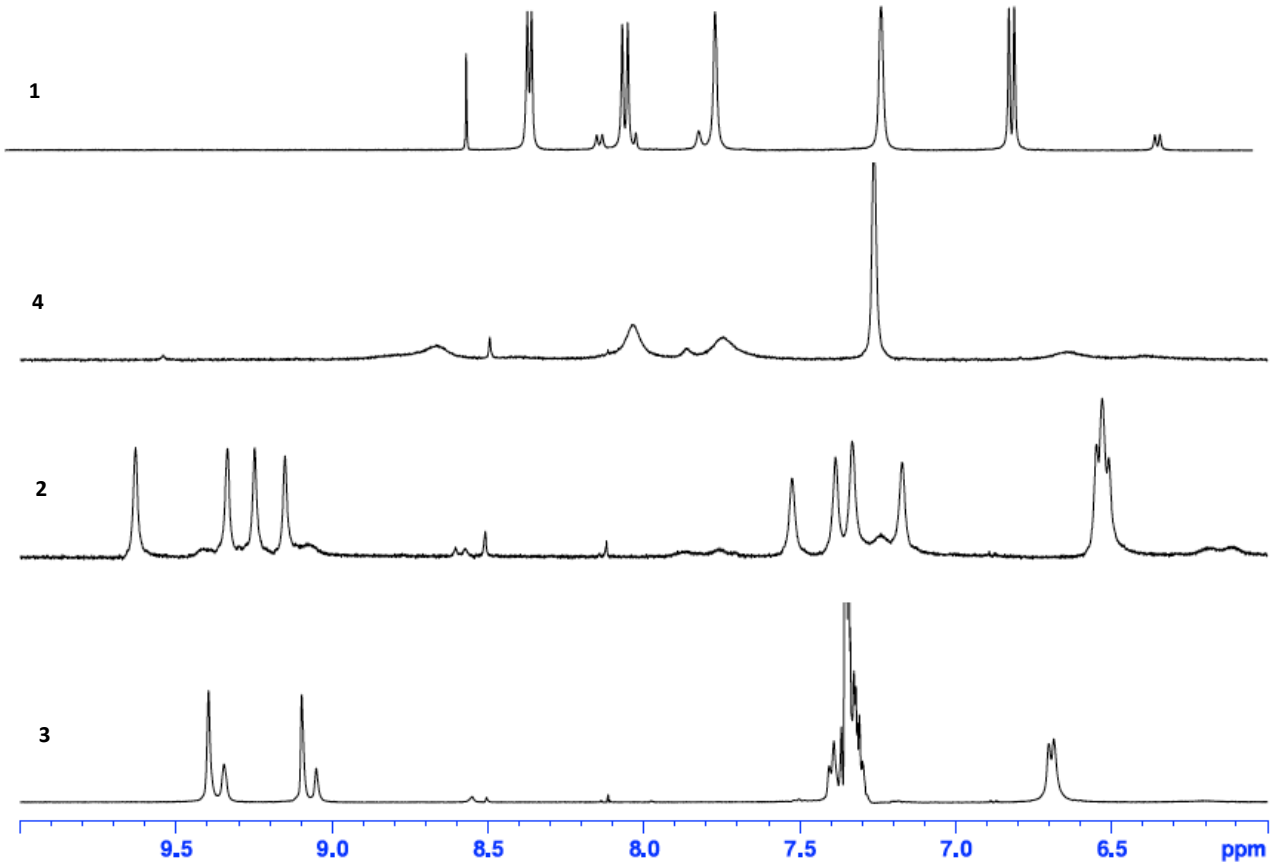


Figure S9: Comparison of peptide **1** amide region with that of pseudopeptides **2**, **3** and **4**, in methanol at 273 K (500.3 MHz)

NMR data for compound 5 (Boc-aVal-aAla-Val-aVal-aAla-Val-NH_2)

Table S13. ^{1}H NMR chemical shifts for the two major conformers of pseudopeptide **5** (15 mM) in CD_3OH at 273 K

Residue	δ HN (ppm), ^{3}J (Hz)	δH^{α} (ppm)	δH^{β} (ppm)	δ Other protons (ppm)
Boc				CH_3 1.50 (A)
				CH_3 1.53 (B)
aVal[1]	9.10 (A)		4.56 (A)	γ CH_3 1.10, γ' CH_3 1.08 (A)
	9.40 (B)		4.61 (B)	γ CH_3 1.12, γ' CH_3 1.12 (B)
aAla[2]	9.62 (A)		2.88 (A)	
	9.87 (B)		3.09 (B)	
Val[3]	6.78 (A) (d, ^{3}J = 6.5)	3.62 (A)	2.10 (A)	γ CH_3 1.12, γ' CH_3 1.05 (A)
	6.86 (B) (d, ^{3}J = 5.2)	3.96 (B)	2.27 (B)	γ CH_3 1.116, γ' CH_3 1.116 (B)
aVal[4]	10.54 (A)		4.52 (A)	γ CH_3 1.14, γ' CH_3 1.06 (A)
	9.71 (B)		4.60 (B)	γ CH_3 1.17, γ' CH_3 1.11 (B)
aAla[5]	9.18 (A)		3.10 (A)	
	9.05 (B)		3.09 (B)	
Val[6]	6.39 (A) (d, ^{3}J = 9.3)	3.85 (A)	2.30 (A)	γ CH_3 0.95, γ' CH_3 0.94 (A)
	6.43 (B) (d, ^{3}J = 8.2)	4.07 (B)	2.33 (B)	γ CH_3 1.00, γ' CH_3 1.00 (B)
$NH_{2\ Z,\ E}$	6.83, 7.60 (A)			
	7.35, 7.43 (B)			

Table S14. ^{13}C NMR chemical shifts for the two major conformers of pseudopeptide **5** (15 mM) in CD_3OH at 273 K

Residue	δ CO (ppm)	δC^{α} (ppm)	δC^{β} (ppm)	δ Other carbons (ppm)
Boc	157.9 (A)			Cq 82.4, CH_3 28.8 (A)
	158.0 (B)			Cq 82.2, CH_3 28.5 (B)
aVal[1]	158.4 (A)		49.8 (A)	γ CH_3 20.1, γ' CH_3 19.2 (A)
	159.1 (B)		50.1 (B)	γ CH_3 20.1, γ' CH_3 20.1(B)
aAla[2]	161.9 (A)		36.5 (A)	
	162.6 (B)		37.0 (B)	
Val[3]	176.8 (A)	62.6 (A)	30.1 (A)	γ CH_3 20.1, γ' CH_3 20.3 (A)
	174.8 (B)	63.7 (B)	30.7 (B)	γ CH_3 19.3, γ' CH_3 19.3 (B)
aVal[4]	157.2 (A)		49.7 (A)	γ CH_3 20.1, γ' CH_3 20.3 (A)
	157.7 (B)		50.2 (B)	γ CH_3 20.2, γ' CH_3 20.2 (B)
aAla[5]	160.3 (A)		37.0 (A)	
	160.6 (B)		37.0 (B)	
Val[6]	176.5 (A)	61.4 (A)	31.0 (A)	γ CH_3 20.14, γ' CH_3 19.18 (A)
	178.2 (B)	61.6 (B)	30.8 (B)	γ CH_3 17.6, γ' CH_3 19.8 (B)

Table S15. Comparison of experimental distances inferred from ROE intensities and calculated distances in DFT-minimized NMR conformers (Å)				
Distance	**Conformer 5A**		**Conformer 5B**	
	Experimental (ROE)	**Calculated**	**Experimental (ROE)**	**Calculated**
Intraresidual				
aVal1 HN - Hβ	3.8	3.8	3.5	3.7
aAla2 HN - Hβ	3.5	3.3	3.6	3.3
Val3 HN - Hα	**2.7**	2.9	**2.7**	2.9
Val3 HN - Hβ	**2.3**	2.4	**2.7**	2.3
aVal4 HN - Hβ	4.1	3.8	3.5	3.7
aAla5 HN - Hβ	**2.9**	3.3	**3.3**	3.3
Val6 HN - Hα	**2.6**	2.9	**3.1**	3.0
Sequential				
Boc Me - aVal1 HN	4.3	4.5	4.0	4.9
aVal1 HN - aAla2 HN	**2.8**	2.8	**3.3**	2.9
aVal1 Hβ - aAla2 HN	4.0	4.4	4.9	4.4
aAla2 HN - Val3 HN	**2.7**	2.5	**3.0**	2.6
aAla2 Hβ - Val3 HN	4.5	4.5	4.4	4.5
Val3 HN - aVal4 HN	n.d.	4.5	**3.1**	2.7
Val3 Hα - aVal4 HN	2.3	2.2	3.5	3.6
Val3 Hβ - aVal4 HN	n.d.	4.3	4.6	3.1
aVal4 HN - aAla5 HN	**2.8**	2.6	**2.9**	2.7
aVal4 Hβ - aAla5 HN	4.2	4.4	4.4	4.4
aAla5 HN - Val6 HN	**2.7**	2.5	**2.9**	2.5
aAla5 Hβ - Val6 HN	4.5	4.5	4.1	4.5
Val6 HN - NH_2 H_E	4.1	3.8	**3.3**	2.1
Val6 Hα - NH_2 H_E	**2.4**	4.5	3.4	3.6
Medium-range				
Boc Me - aAla2 HN	4.7	4.2	4.9	4.0
Boc Me - Val3 HN	3.8	3.6	4.1	3.8
Boc Me - Val3 Hβ	**2.4**	2.8	4.4	4.1
aAla2 Hβ - aVal4 HN	n.d.	5.9	5.2	4.2
aAla2 Hβ - aAla5HN	4.0	3.7	ambiguous	3.5
aAla2 HN - Val6 HN	4.3	4.0	n.d.	7.4
aAla2 Hβ - Val6 HN	4.4	4.5	n.d.	5.8
aAla2 Hβ - Val6 Hα	4.5	5.3	n.d.	8.1
Val3 HN - aAla5 HN	4.3	4.2	n.d.	4.1
Val3 Hα - aAla5 HN	**3.3**	3.4	3.4	3.6
Val3 Hα - Val6 HN	4.6	4.5	4.0	3.7
Long-range				
Boc Me - NH_2 H_Z	4.4	5.7	n.d.	11
aVal1 HN - NH_2 H_Z	3.9	4.4	n.d.	11.6
aAla2 HN - NH_2 H_Z	**3.2**	2.8	n.d.	10.1
aAla2 Hβ - NH_2 H_Z	4.4	3.0	n.d.	9.3
Strong ROEs corresponding to distances lower than 3.3 Å are indicated in bold; n.d, not detected.				

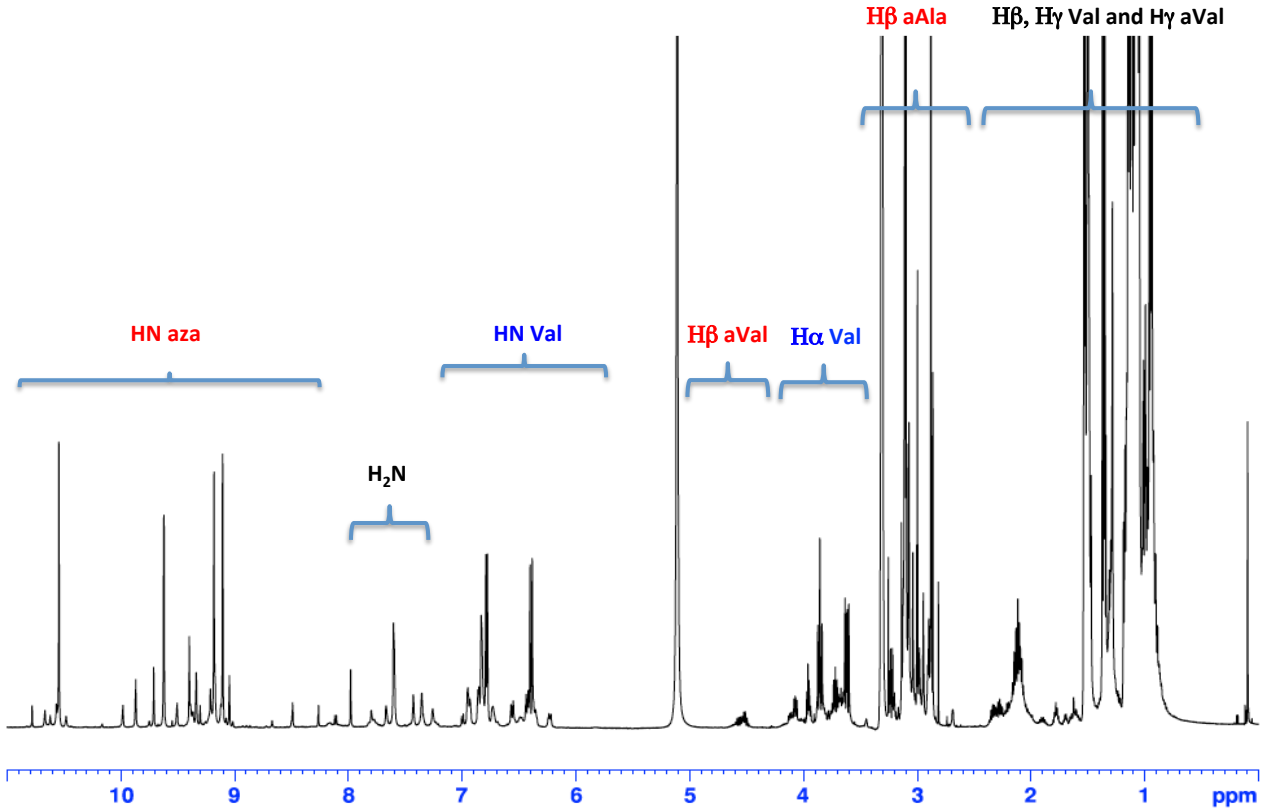


Figure S10: 1D ^{1}H NMR spectrum of compound **5** (15 mM) in methanol at 273 K (500.3 MHz)

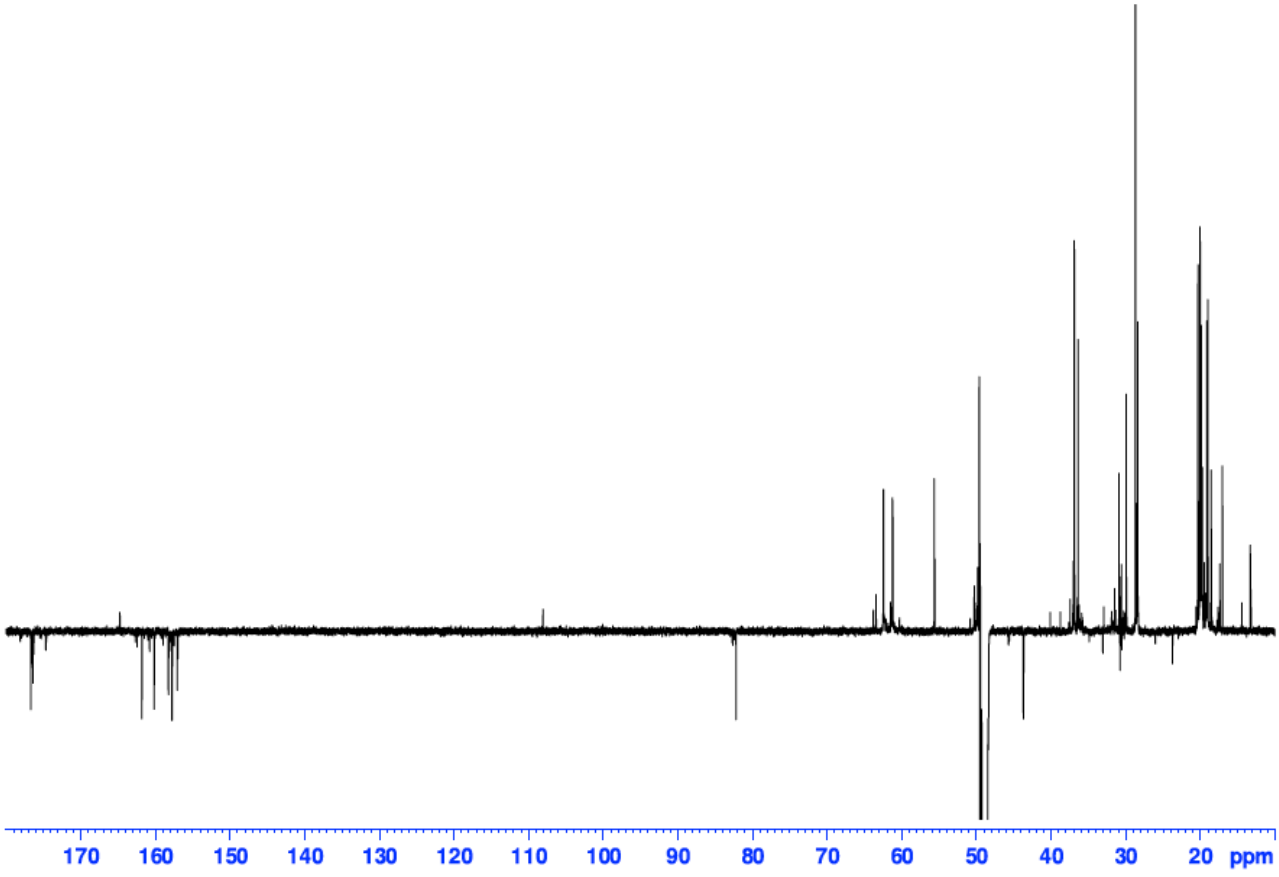


Figure S11: 1D ^{13}C DEPTQ spectrum of compound **5** (15 mM) in methanol at 273 K (125.8 MHz)

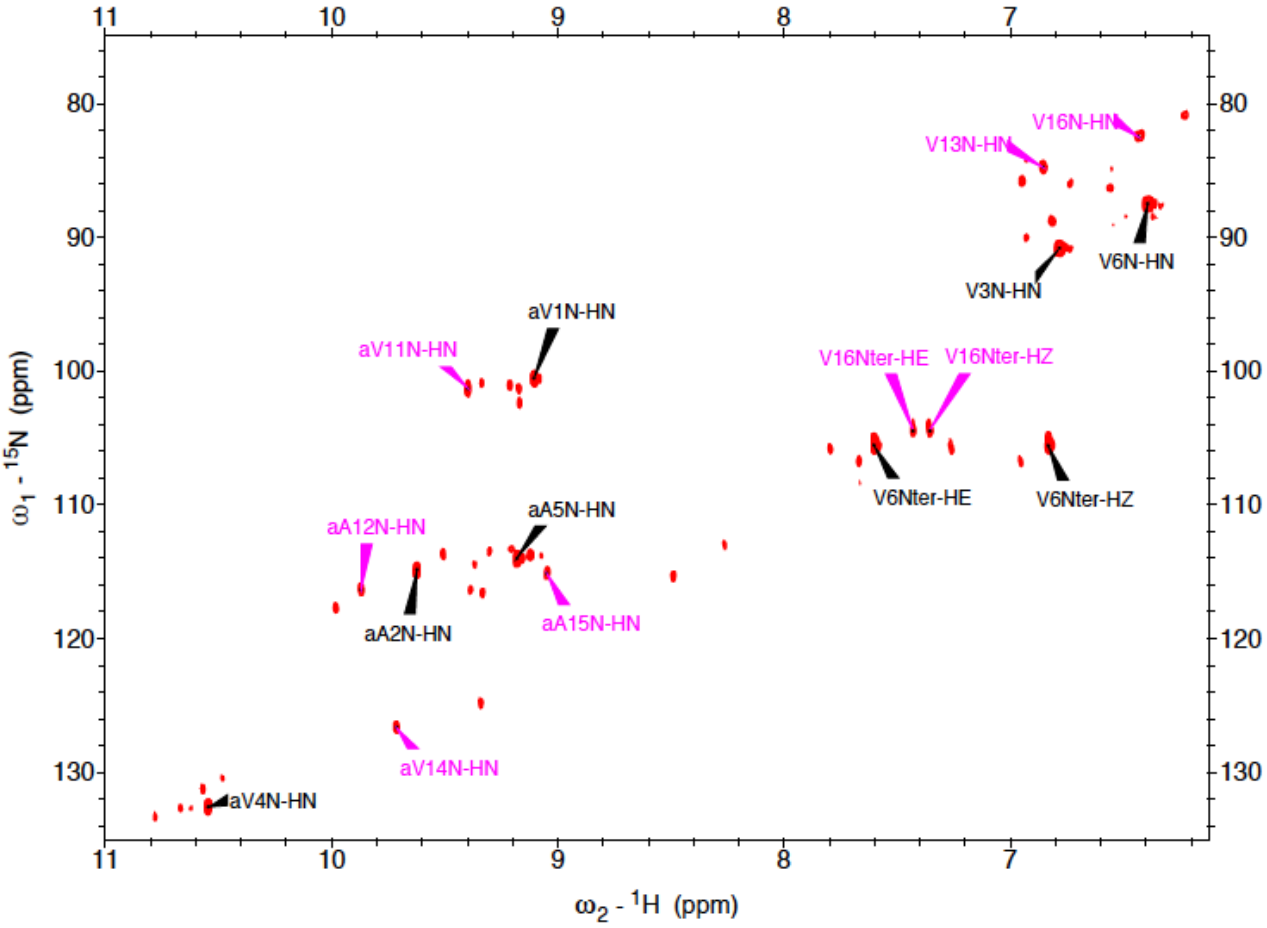


Figure S12: 2D ^{15}N-^{1}H HSQC spectrum of compound **5** (15 mM) in methanol at 273 K (500.3 MHz). The assignments of the two most-populated conformers are shown in black and magenta (numbered 1-6 and 11-16, respectively).

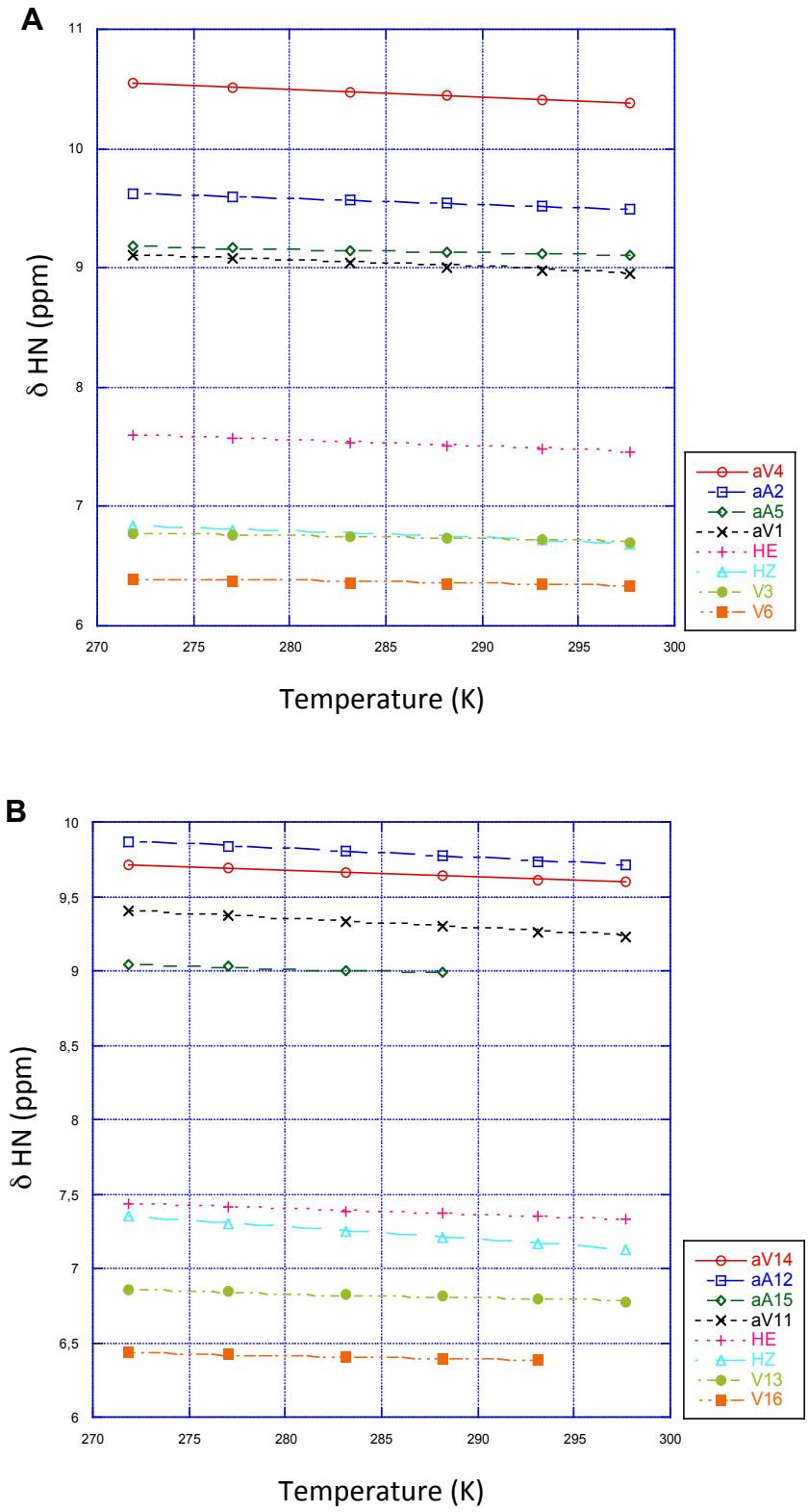


Figure S13: Diagrams of the amide proton temperature coefficients for the two most-populated conformers of compound **5** in methanol (**5A** and **5B**).

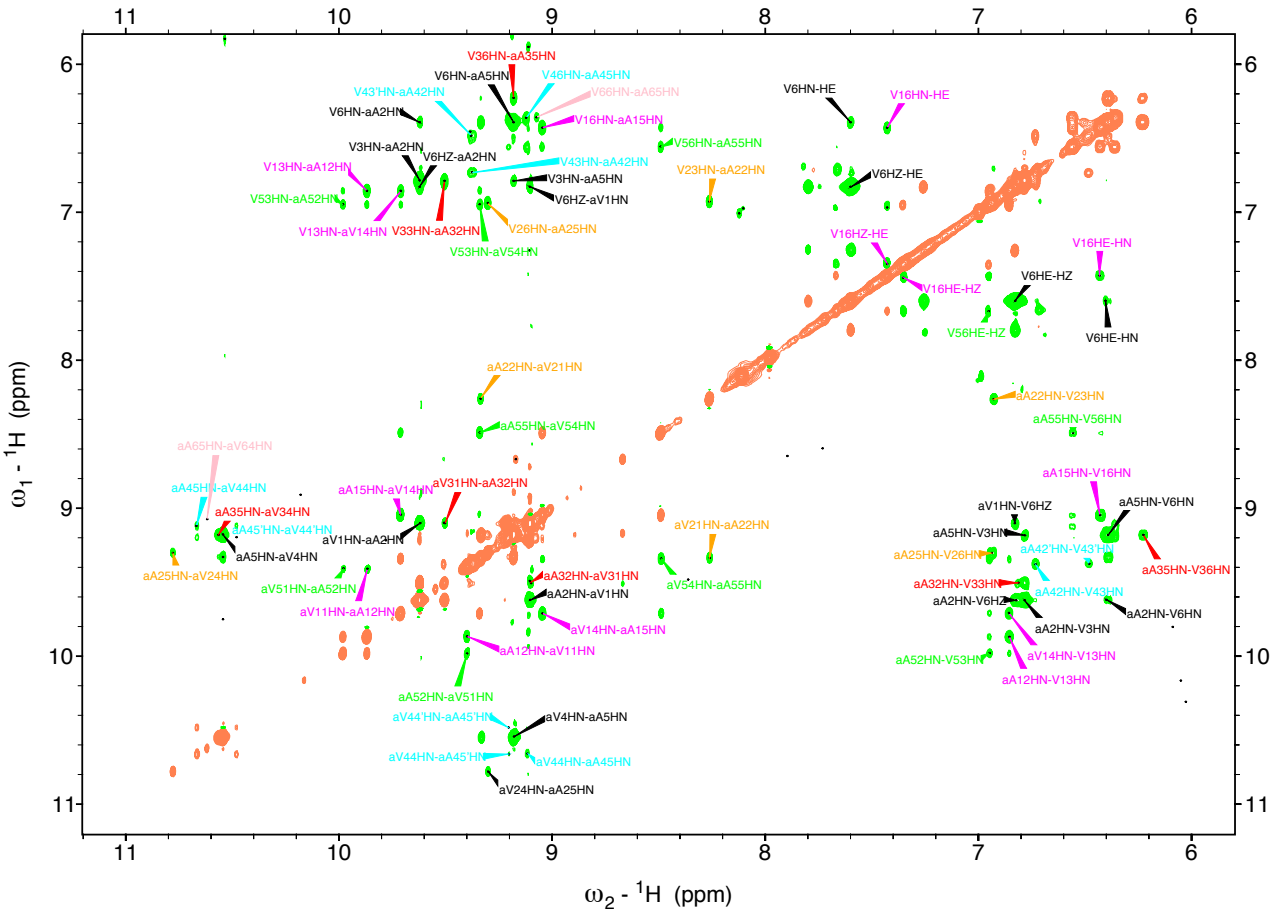


Figure S14: Expansion of the 2D ^{1}H-^{1}H ROESY spectrum of compound **5** (15 mM) in methanol at 273 K (500.3 MHz, mixing time of 500 ms), showing the dipolar correlation peaks NHi-NHi+1 for the 8 detected species. The diagonal and exchange peaks are in orange.

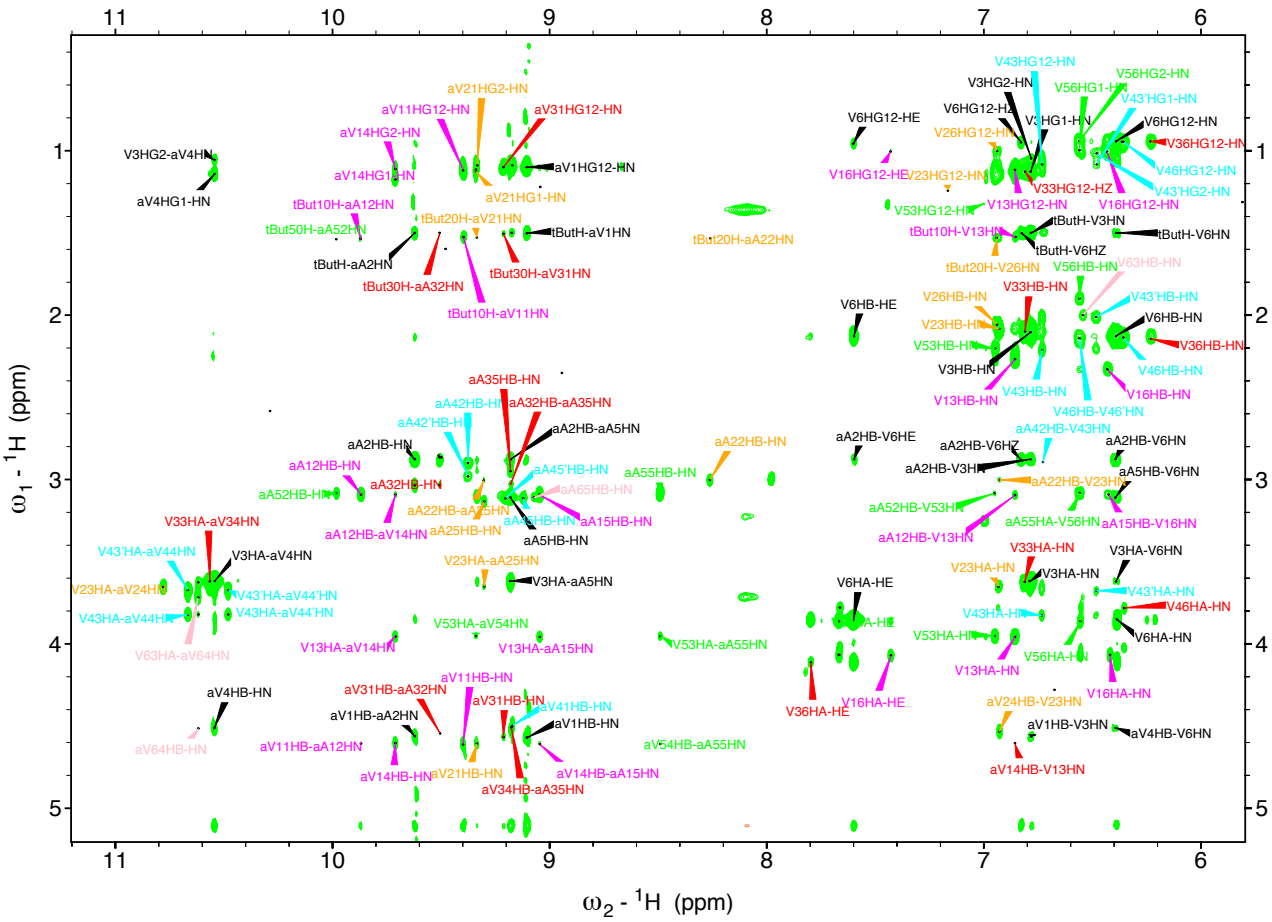


Figure S15: Expansion of the 2D ^{1}H-^{1}H NMR ROESY spectrum of compound **5** (15 mM) in methanol at 273 K (500.3 MHz, mixing time of 500 ms), showing the long-distance dipolar correlation peaks between NH and Aliphatic protons for the 8 species.

X-ray crystallography

Crystallographic data for Boc-aVal-aAla-Val-NH_2 2

The crystal structure has been deposited within CCDC with deposition number 1949709.

Formula: C_{16} H_{32} N_6 O_5

Space group: P 2_1

Cell Lengths: **a** 10.4497(3) **b** 14.6303(4) **c** 15.2786(5)

Cell Angles: α 90 β 108.211(2) γ 90

Cell volume : 2218.83

Z, Z' : **Z** : 4 **Z' :** 0

R-Factor (%) : 4

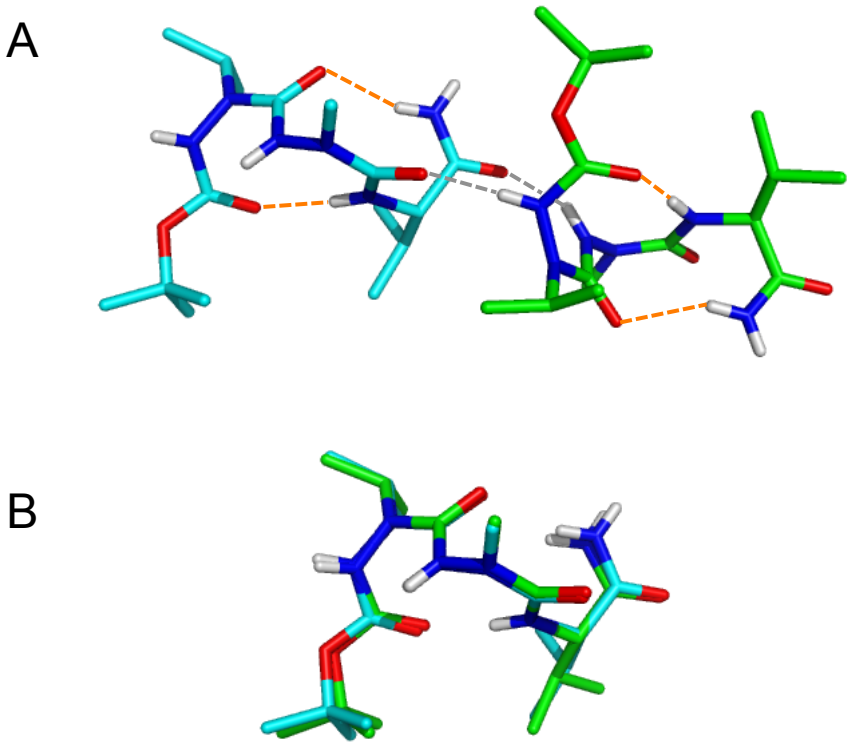


Figure S16: X-ray structure of compound Boc-aVal-aAla-Val-NH_2 **2**. A) View of the two molecules within the asymmetric unit. Intramolecular hydrogen bonds are displayed in orange and intermolecular hydrogen bonds between the two molecules are displayed in grey. The carbon atoms of the two molecules are shown with different colours, in cyan and green. B) Superimposition of the two molecules of the asymmetric unit. The two chains differ mainly by the rotation of Val3 side chain, with *trans* (χ1 +171°) and *gauche* rotamers (χ1 –59°). The rms deviation of backbone atoms positions is 0.2 Å.

NMR structures

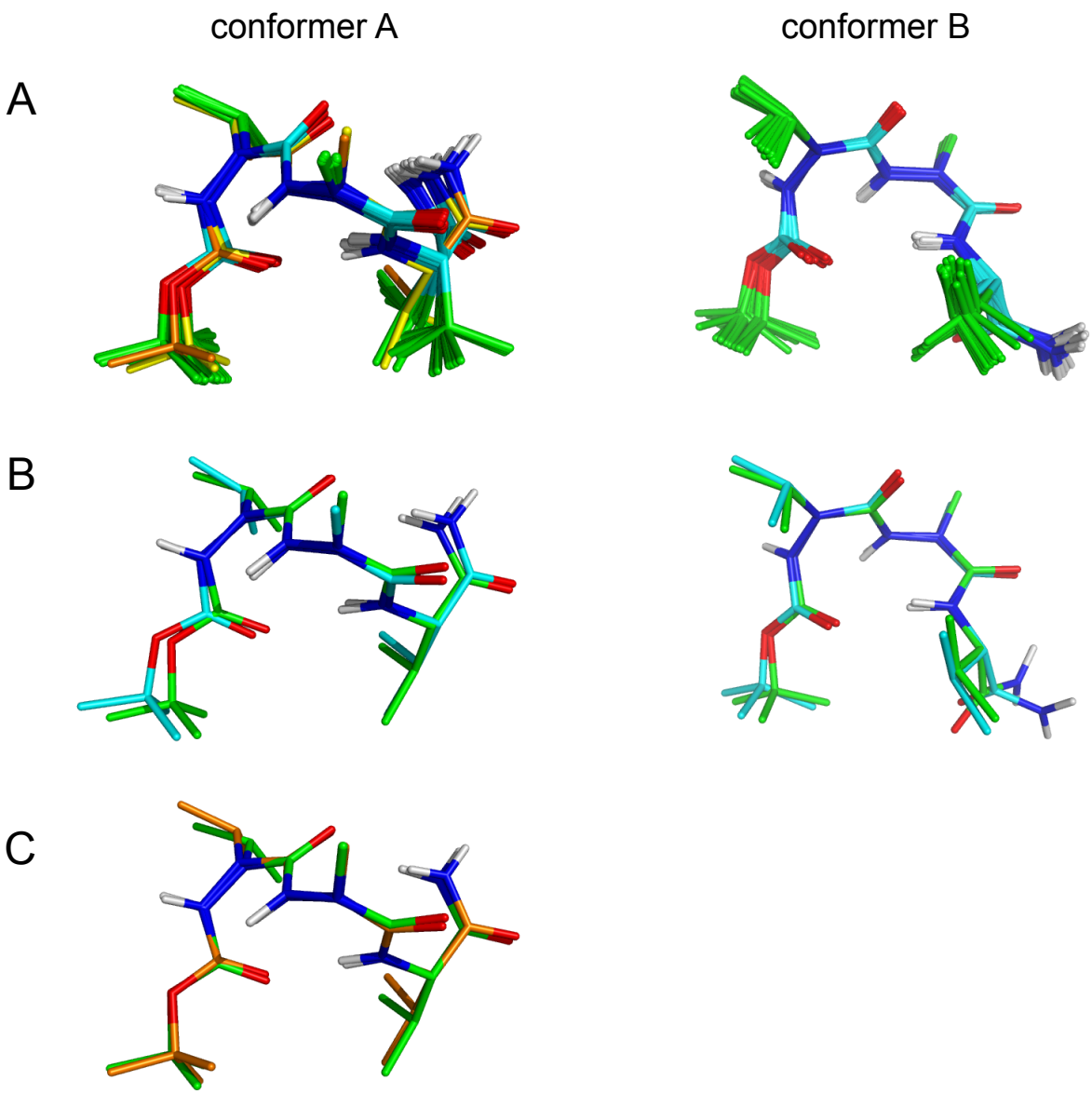
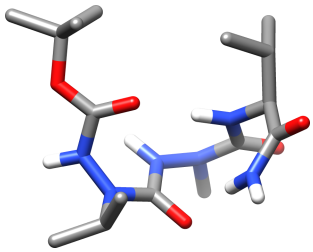
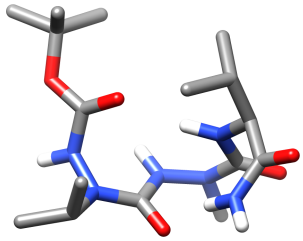
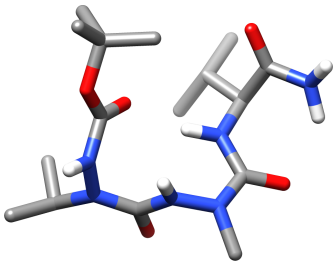


Figure S17: Comparison of the X-ray and NMR structures of compound Boc-aVal-aAla-Val-NH_2 **2**. A) View of the two NMR structure ensembles corresponding to conformational isomers A and B observed in solution. In conformer A family, the two X-ray structures of the asymmetric unit are superimposed (carbon atoms coloured in orange and yellow). The carbon atoms of NMR structures are shown in cyan and green colours, corresponding to backbone and side chain atoms, respectively. B) Superimposition of a selected NMR conformer before (cyan carbon atoms) and after DFT refinement (green carbon atoms). C) Superimposition of DFT-refined NMR conformer (green carbon atoms) with the closest X-ray structure (orange carbon atoms). The rms deviation of backbone atoms positions is 0.14 Å.

Table S16. DFT calculations for selected NMR conformers of compound 2. Conformers 2A-2 and 2B correspond to the two conformers shown in figures 4B and S17.

Conformer	Energy statistics	Structure
2A-1	Electronic energy (B3LYP): −1334.26191331 Ha. Lowest frequency: 21.3604 cm^{-1}. Free energy: −1333.820938 Ha.	
2A-2	Electronic energy (B3LYP): −1334.26179403 Ha. Lowest frequency: 19.7783 cm^{-1}. Free energy: −1333.820796 Ha.	
2B	Electronic energy (B3LYP): −1334.25905892 Ha. Lowest frequency: 16.2206 cm^{-1}. Free energy: −1333.820185 Ha.	

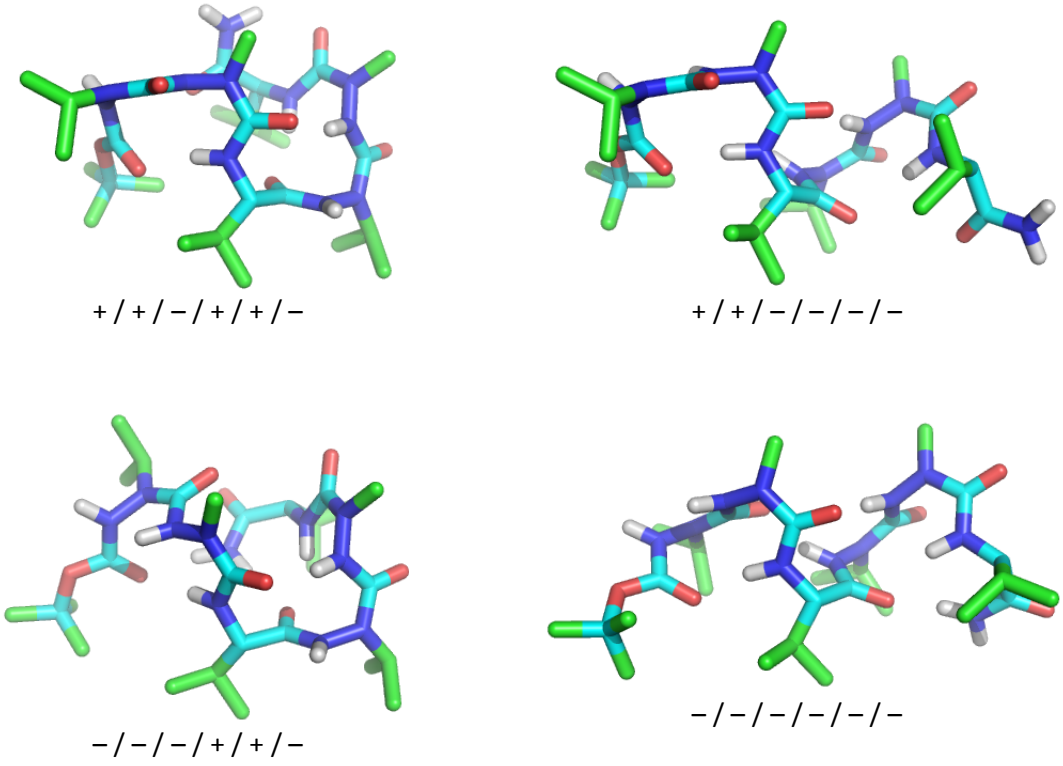


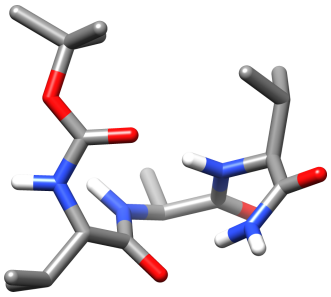
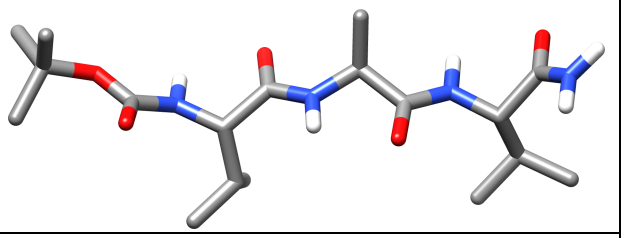
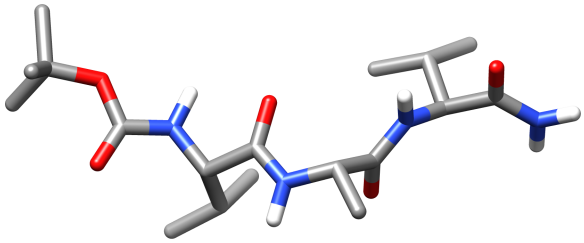
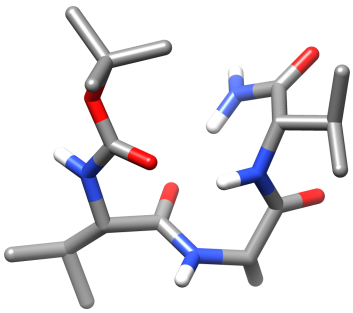
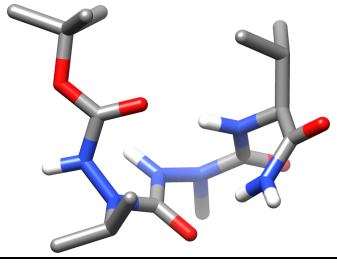
Figure S18. Modelled conformations of Boc-aVal-aAla-Val-aVal-aAla-Val-NH_2 **5** showing repeated β-turns or helical conformations. Structures were calculated using AMBER and refined by DFT at the B3LYP-D3/cc-pVTZ level with methanol PCM solvation model (see Table S18). The conformers differ by the sign of ϕ dihedral angles within each diazapeptide unit (either +/+ or –/–).

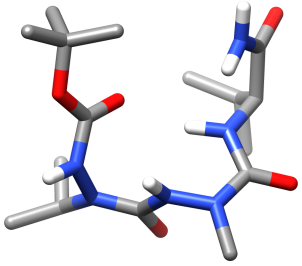
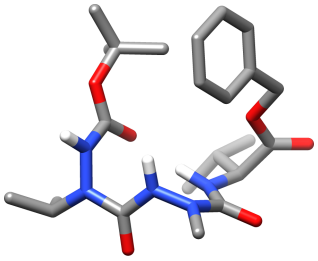
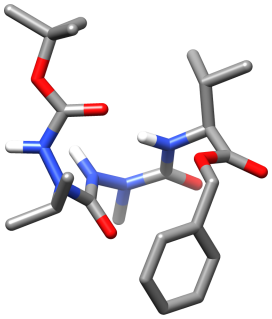
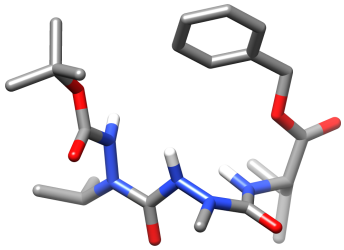
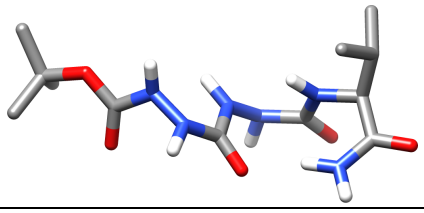
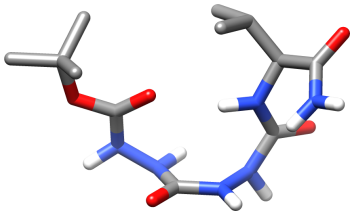
Ab initio conformational search: molecular mechanics studies and DFT calculations

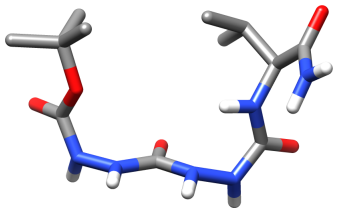
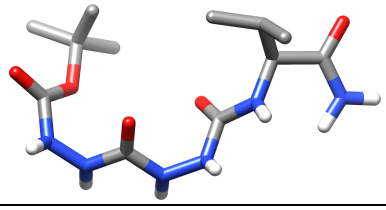
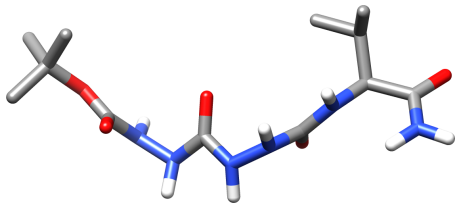
Table S17. Conformational descriptors and energies of DFT-minimized conformers obtained from *ab initio* conformational search

Cpd. / conf.	Peptide bond			Urea geometry		φ angle (°)			ψ angle (°)			ΔG (kcal mol^{-1})
	1	2	3	1	2	1	2	3	1	2	3	
1 (a)	*trans*	*trans*	*trans*	n/a	n/a	-66.8	-58.6	-110.1	-17.3	-23.8	13.8	0.00
1 (b)	*trans*	*trans*	*trans*	n/a	n/a	-131.0	-152.7	-131.8	163.2	157.0	134.4	3.86
1 (c)	*trans*	*trans*	*trans*	n/a	n/a	-131.7	-64.2	-134.4	162.1	139.3	131.9	3.87
1 (d)	*trans*	*trans*	*trans*	n/a	n/a	-60.1	58.4	59.9	129.2	24.6	35.1	4.90
2 (a)	*trans*	*trans*	*trans*	*E, Z*	*E, Z*	−70.7	−67.3	−105.4	−13.2	−17.2	11.8	0.00
2 (b)	*trans*	*trans*	*trans*	*E, Z*	*E, Z*	72.6	80.0	−124.7	12.2	12.3	9.8	0.70
3 (a)	*trans*	*trans*	*trans*	*E, Z*	*E, Z*	72.4	80.3	−59.2	12.9	2.7	−38.9	0.00
3 (b)	*trans*	*trans*	*trans*	*E, Z*	*E, Z*	−80.8	−73.4	−94.1	-6.5	−14.2	−56.2	2.03
3 (c)	*trans*	*trans*	*trans*	*E, Z*	*E, Z*	−101,7	91.4	−94.9	0.8	2.7	0.4	2.40
4 (a)	*trans*	*trans*	*trans*	*E, Z*	*E, Z*	89.9	−70.9	−80.2	18.0	−20.2	−7.4	0.00
4 (b)	*trans*	*cis*	*trans*	*Z, E*	*E, Z*	54.5	107.2	−86.7	−149.3	−29.3	−13.1	1.81
4 (c)	*cis*	*trans*	*trans*	*Z, Z*	*E, Z*	−82.0	85.7	−120.0	−180.0	20.9	6.0	2.71
4 (d)	*cis*	*trans*	*trans*	*Z, Z*	*Z, Z*	61.1	-65.0	−125.1	−172.3	163.9	9.7	3.95
4 (e)	*trans*	*trans*	*trans*	*Z, Z*	*Z, Z*	−62.7	−63.3	−122.6	164.3	165.9	7.8	4.18

Table S18. DFT statistics for selected conformers of compounds 1-4 calculated from *ab initio* conformational search

Conformer	Energy statistics	Structure
1a	Electronic energy (B3LYP): –1302.22855290 Ha. Lowest frequency: 16.2871 cm^{-1}. Free energy: –1301.763619 Ha.	
1b	Electronic energy (B3LYP): –1302.21580581 Ha. Lowest frequency: 9.9099 cm^{-1}.Free energy: –1301.75747 Ha.	
1c	Electronic energy (B3LYP): –1302.21686165 Ha. Lowest frequency: 9.8326 cm^{-1}. Free energy: –1301.757458 Ha.	
1d	Electronic energy (B3LYP): –1302.22029291 Ha. Lowest frequency: 14.2234 cm^{-1}. Free energy: –1301.755818 Ha.	
2a	Electronic energy (B3LYP): −1334.26277825 Ha. Lowest frequency: 19.9132 cm^{-1}. Free energy: −1333.822029 Ha.	

2b	Electronic energy (B3LYP): −1334.26046535 Ha. Lowest frequency: 24.5349 cm^{-1}. Free energy: −1333.820911 Ha.	
3a	Electronic energy (B3LYP): −1624.59308144 Ha. Lowest frequency: 17.4456 cm^{-1}. Free energy: −1624.064872 Ha.	
3b	Electronic energy (B3LYP): –1624.59053947 Ha. Lowest frequency: 14.2055 cm^{-1}. Free energy: –1624.061572 Ha.	
3c	Electronic energy (B3LYP): −1624.58678978 Ha. Lowest frequency: 12.9646 cm^{-1}. Free energy: −1624.061055 Ha.	
4a	Electronic energy (B3LYP): −1176.94113258 Ha. Lowest frequency: 13.7268 cm^{-1}. Free energy: −1176.608668 Ha.	
4b	Electronic energy (B3LYP): −1176.94083349 Ha. Lowest frequency: 19.3529 cm^{-1}. Free energy: −1176.605776 Ha.	

4c	Electronic energy (B3LYP): −1176.93661645 Ha. Lowest frequency: 12.4244 cm^{-1}. Free energy: −1176.604347 Ha.	
4d	Electronic energy (B3LYP): −1176.93453150 Ha. Lowest frequency: 8.8321 cm^{-1}. Free energy: −1176.602374 Ha.	
4e	Electronic energy (B3LYP): −1176.93232000 Ha. Lowest frequency: 10.2437 cm^{-1}. Free energy: −1176.60201 Ha.	

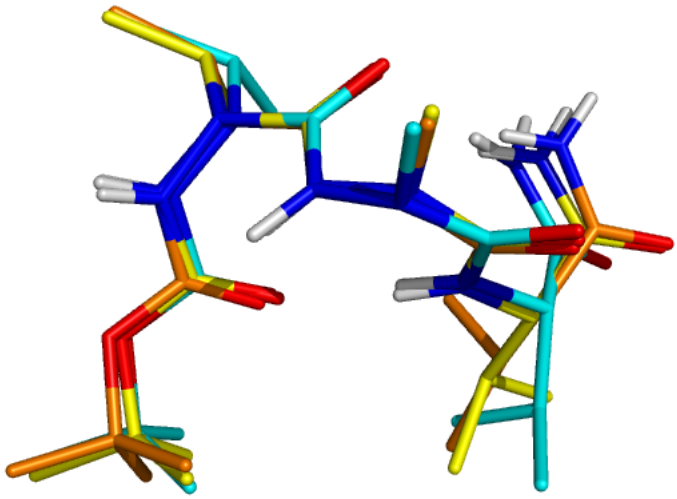


Figure S19: Comparison of conformer **2a** calculated from *ab initio* conformational search with the X-ray structure of compound Boc-aVal-aAla-Val-NH_2 **2**. Carbon atoms of conformer **2a** are shown in cyan while carbon atoms of the two crystallographic structures within the asymmetric unit are shown in orange and yellow. The rms deviation of backbone atoms positions between **2a** and the closest X-ray conformer is 0.27 Å.

Atomic coordinates of molecular models

Compound **1**, conformation **a** (from *ab initio* conformational search)

1	C	-1.773474	3.355175	-0.187459
2	O	-2.432826	2.048733	0.044483
3	C	-2.939759	4.237741	-0.615079
4	C	-0.758977	3.210707	-1.317593
5	C	-1.151973	3.869844	1.106894
6	C	-1.737192	0.958117	0.384448
7	N	-2.502506	-0.157851	0.258629
8	O	-0.567186	0.925519	0.742192
9	C	-2.032105	-1.448456	0.729058
10	C	-0.837161	-1.976733	-0.069791
11	C	-3.163400	-2.498552	0.768465
12	N	-0.599477	-1.422193	-1.268394
13	O	-0.122866	-2.859245	0.409205
14	C	0.565672	-1.754216	-2.069715
15	C	1.904217	-1.481747	-1.364622
16	C	0.516158	-0.994659	-3.394068
17	N	1.914542	-0.562773	-0.375885
18	O	2.901047	-2.085912	-1.748985
19	C	3.114755	-0.272231	0.391416
20	C	3.032711	-0.763477	1.846585
21	C	3.552530	1.205480	0.305476
22	N	2.041225	-1.621249	2.148174
23	O	3.870308	-0.399059	2.667787
24	C	-4.233224	-2.120972	1.795973
25	C	-3.773689	-2.772244	-0.609799
26	C	3.801811	1.604558	-1.149854
27	C	2.566109	2.157038	0.983816
28	H	-3.685797	4.294967	0.177063
29	H	-2.580544	5.244021	-0.827333
30	H	-3.412352	3.840066	-1.512660
31	H	0.061298	2.557265	-1.036189
32	H	-1.242022	2.806489	-2.207249
33	H	-0.350506	4.190623	-1.563396
34	H	-0.315898	3.252869	1.419493
35	H	-0.798730	4.889450	0.951638
36	H	-1.898615	3.883942	1.901064
37	H	-3.463874	-0.036979	-0.010574
38	H	-1.640105	-1.335509	1.741824
39	H	-2.674727	-3.412657	1.109977
40	H	-1.226061	-0.704551	-1.594269
41	H	0.571492	-2.827277	-2.259495
42	H	1.386760	-1.247636	-3.994446
43	H	-0.381071	-1.262739	-3.950907
44	H	0.514005	0.082388	-3.220898
45	H	1.052446	-0.097999	-0.116880
46	H	3.903373	-0.875803	-0.059916
47	H	4.497904	1.254519	0.846772
48	H	1.389338	-1.985140	1.467124
49	H	2.017865	-2.003143	3.079152
50	H	-4.966628	-2.922662	1.884065
51	H	-3.793948	-1.951571	2.779769
52	H	-4.772417	-1.216609	1.508087
53	H	-4.505166	-3.576820	-0.536911
54	H	-4.293291	-1.898267	-1.007537
55	H	-3.017595	-3.070950	-1.336195
56	H	4.190742	2.621960	-1.203105
57	H	4.522514	0.939437	-1.628363
58	H	2.877648	1.569586	-1.729294
59	H	2.430877	1.906582	2.036255
60	H	2.931663	3.183103	0.927036
61	H	1.589057	2.124985	0.506274

Compound **1**, conformation **b** (from *ab initio* conformational search)

1	C	6.599092	-0.727395	-0.049562
2	O	5.242545	-0.416415	-0.534189
3	C	6.549470	-1.892873	0.934694
4	C	7.237265	0.520237	0.555290
5	C	7.320647	-1.134198	-1.330047
6	C	4.269903	0.011373	0.297461
7	N	3.147492	0.277953	-0.416782
8	O	4.375099	0.155460	1.504453
9	C	1.878720	0.587435	0.206136
10	C	0.795471	-0.284573	-0.441144
11	C	1.505882	2.092535	0.099445
12	N	-0.350673	-0.372114	0.253742
13	O	0.961682	-0.819515	-1.536110
14	C	-1.533569	-1.045293	-0.248330
15	C	-2.752087	-0.393890	0.412975
16	C	-1.508811	-2.550887	0.051105
17	N	-3.904654	-0.538222	-0.262722
18	O	-2.656677	0.179050	1.496048
19	C	-5.203290	-0.111044	0.235909
20	C	-6.163962	-1.286457	0.023763
21	C	-5.717564	1.151117	-0.499703
22	N	-6.965994	-1.599373	1.054973
23	O	-6.183531	-1.880643	-1.050015
24	C	2.522823	2.951450	0.852031
25	C	1.364565	2.547481	-1.354409
26	C	-7.105152	1.562107	-0.000363
27	C	-4.726499	2.307171	-0.352379
28	H	7.565924	-2.203551	1.177547
29	H	6.039794	-1.610733	1.851270
30	H	6.030367	-2.740558	0.486558
31	H	7.195691	1.345569	-0.156011
32	H	6.731420	0.816093	1.469703
33	H	8.283940	0.316114	0.782056
34	H	8.354713	-1.394153	-1.106113
35	H	6.835421	-1.997992	-1.783981
36	H	7.315622	-0.314447	-2.048113
37	H	3.112820	-0.036336	-1.373655
38	H	1.957999	0.331800	1.262545
39	H	0.535988	2.205004	0.590683
40	H	-0.449945	0.080477	1.150319
41	H	-1.572677	-0.894893	-1.326915
42	H	-2.393571	-3.041327	-0.353510
43	H	-1.474443	-2.720523	1.127266
44	H	-0.624920	-2.994000	-0.403874
45	H	-3.911446	-1.032568	-1.141993
46	H	-5.083706	0.114156	1.294276
47	H	-5.791930	0.885213	-1.558134
48	H	-7.646540	-2.333647	0.945859
49	H	-6.935514	-1.102634	1.927622
50	H	2.229055	4.001279	0.818085
51	H	2.603752	2.650496	1.896687
52	H	3.511930	2.864291	0.400220
53	H	1.084454	3.600337	-1.394665
54	H	2.310436	2.433106	-1.886918
55	H	0.604834	1.976685	-1.889209
56	H	-7.439088	2.459189	-0.521781
57	H	-7.851520	0.785315	-0.163225
58	H	-7.080185	1.788139	1.068323
59	H	-5.077433	3.174139	-0.912949
60	H	-4.626678	2.599438	0.694778
61	H	-3.738142	2.043524	-0.725948

Compound **1**, conformation **c** (from *ab initio* conformational search)

1	C	-5.823278	1.235036	0.664272
2	O	-4.394478	1.061069	0.347199
3	C	-6.157864	0.535685	1.979024
4	C	-6.680316	0.736453	-0.496092
5	C	-5.945546	2.747852	0.813070
6	C	-3.859271	-0.156003	0.117943
7	N	-2.548920	-0.021359	-0.206997
8	O	-4.453761	-1.219875	0.176121
9	C	-1.656304	-1.151467	-0.344988
10	C	-0.378994	-0.855865	0.445198
11	C	-1.309221	-1.470244	-1.827604
12	N	0.387765	-1.925202	0.736466
13	O	-0.055841	0.288827	0.753327
14	C	1.732943	-1.769298	1.263199
15	C	2.624291	-1.076189	0.216121
16	C	2.318837	-3.133895	1.616108
17	N	3.470190	-0.155963	0.713485
18	O	2.568338	-1.388760	-0.968356
19	C	4.428169	0.587893	-0.088284
20	C	5.757808	0.561236	0.671449
21	C	3.969117	2.047167	-0.329036
22	N	6.847689	0.230595	-0.041862
23	O	5.793986	0.844067	1.865184
24	C	-2.573000	-1.845771	-2.601935
25	C	-0.558392	-0.320763	-2.503181
26	C	5.016476	2.836467	-1.118893
27	C	2.613535	2.081973	-1.038066
28	H	-5.482690	0.872983	2.765940
29	H	-7.177485	0.787345	2.271795
30	H	-6.076316	-0.542883	1.881609
31	H	-6.599711	-0.340734	-0.609146
32	H	-6.369358	1.214852	-1.425227
33	H	-7.723305	0.994029	-0.310605
34	H	-6.974333	3.014557	1.052762
35	H	-5.297907	3.106434	1.612850
36	H	-5.663596	3.246907	-0.113788
37	H	-2.117829	0.878734	-0.067650
38	H	-2.153994	-2.021758	0.082192
39	H	-0.650418	-2.342145	-1.809061
40	H	0.116993	-2.830900	0.390645
41	H	1.674792	-1.147120	2.156241
42	H	3.315940	-3.017354	2.036972
43	H	1.689890	-3.636787	2.349827
44	H	2.391839	-3.758097	0.724913
45	H	3.444111	0.067953	1.695883
46	H	4.511481	0.075772	-1.045392
47	H	3.860804	2.504324	0.658931
48	H	6.796768	-0.002552	-1.017623
49	H	7.751313	0.239261	0.402532
50	H	-2.318457	-2.125833	-3.624799
51	H	-3.093869	-2.682128	-2.135448
52	H	-3.264038	-1.002856	-2.646402
53	H	-0.352731	-0.569137	-3.544961
54	H	-1.157133	0.591957	-2.491280
55	H	0.392892	-0.117364	-2.013052
56	H	5.191209	2.377842	-2.095093
57	H	4.667707	3.855298	-1.288407
58	H	5.972145	2.894308	-0.598367
59	H	2.280881	3.114359	-1.154253
60	H	2.688849	1.639585	-2.033559
61	H	1.848594	1.540423	-0.484259

Compound **1**, conformation **d** (from *ab initio* conformational search)

1	C	0.539766	3.805571	-0.055281
2	O	1.456418	2.718258	0.346440
3	C	0.879379	4.903463	0.945799
4	C	-0.913548	3.367928	0.094628
5	C	0.869658	4.238440	-1.479714
6	C	1.486667	1.534513	-0.282186
7	N	2.537380	0.798490	0.153451
8	O	0.696391	1.147782	-1.135332
9	C	2.750656	-0.565286	-0.293235
10	C	1.539384	-1.419693	0.098853
11	C	4.045642	-1.135158	0.320490
12	N	0.997238	-2.155945	-0.887086
13	O	1.096538	-1.403224	1.246672
14	C	-0.161309	-3.026258	-0.702331
15	C	-1.399130	-2.263446	-0.191692
16	C	0.154657	-4.238683	0.171214
17	N	-1.450332	-0.946060	-0.463298
18	O	-2.301878	-2.856980	0.389924
19	C	-2.541053	-0.096208	-0.004521
20	C	-2.642632	-0.097860	1.539269
21	C	-3.903808	-0.347488	-0.694354
22	N	-1.467388	-0.177537	2.198666
23	O	-3.712741	0.047412	2.119522
24	C	4.223726	-2.613302	-0.036424
25	C	5.266875	-0.325808	-0.126058
26	C	-4.757497	0.925351	-0.646394
27	C	-3.730063	-0.804323	-2.144182
28	H	1.933845	5.169251	0.878216
29	H	0.282272	5.790361	0.737256
30	H	0.666965	4.572177	1.962076
31	H	-1.193691	2.675264	-0.692101
32	H	-1.068145	2.890451	1.062125
33	H	-1.560396	4.243073	0.034641
34	H	0.663061	3.438882	-2.186845
35	H	0.261705	5.103383	-1.745109
36	H	1.920018	4.519491	-1.556470
37	H	3.045257	1.139350	0.952017
38	H	2.850426	-0.559808	-1.380784
39	H	3.940936	-1.056101	1.406711
40	H	1.392155	-2.085213	-1.809540
41	H	-0.432106	-3.373386	-1.700685
42	H	-0.722942	-4.874199	0.254229
43	H	0.966606	-4.809151	-0.277011
44	H	0.452259	-3.920330	1.167740
45	H	-0.664325	-0.487647	-0.901063
46	H	-2.226636	0.914920	-0.263346
47	H	-4.415529	-1.134051	-0.140468
48	H	-1.508909	-0.214030	3.203869
49	H	-0.612106	-0.488499	1.756979
50	H	5.154118	-2.987603	0.389859
51	H	3.411832	-3.231328	0.345519
52	H	4.273962	-2.750170	-1.118808
53	H	6.168096	-0.718592	0.345017
54	H	5.394886	-0.395750	-1.208427
55	H	5.188131	0.728933	0.134181
56	H	-5.746981	0.736128	-1.065395
57	H	-4.879475	1.282892	0.372948
58	H	-4.292028	1.718287	-1.238335
59	H	-4.706570	-0.896568	-2.621643
60	H	-3.145659	-0.080148	-2.716766
61	H	-3.231364	-1.769416	-2.213815

Compound **2**, conformation **a** (from *ab initio* conformational search)

1	C	4.798779	2.188230	0.971713
2	C	3.380788	2.014958	0.444221
3	O	3.218437	0.535871	0.455016
4	C	2.078077	-0.041514	0.090733
5	N	2.108325	-1.374674	0.435580
6	N	1.138486	-2.247505	-0.011877
7	C	1.366133	-2.952027	-1.297322
8	C	1.273070	-2.002747	-2.490181
9	C	2.694961	-3.698699	-1.251892
10	C	-0.131115	-2.137655	0.504542
11	N	-0.256636	-1.352513	1.624561
12	N	-1.498339	-1.117161	2.175472
13	C	-1.992607	-2.138164	3.096219
14	C	-2.412998	-0.354598	1.450072
15	N	-1.899600	0.393524	0.433306
16	C	-2.766487	1.129932	-0.466783
17	C	-2.417622	2.631058	-0.566616
18	C	-2.487151	3.288730	0.812115
19	C	-1.067567	2.888137	-1.238938
20	C	-2.889859	0.483139	-1.857907
21	N	-2.408430	-0.766249	-1.998017
22	O	-3.437583	1.090115	-2.774883
23	O	-3.604223	-0.363776	1.750489
24	O	-1.104097	-2.680166	-0.015369
25	O	1.111784	0.486730	-0.425355
26	C	2.361975	2.636625	1.392571
27	C	3.259514	2.540022	-0.981936
28	H	5.514253	1.695335	0.314220
29	H	5.044227	3.248365	1.019949
30	H	4.890799	1.763673	1.970839
31	H	2.931866	-1.765773	0.863986
32	H	0.555816	-3.673572	-1.352796
33	H	1.381125	-2.568650	-3.415797
34	H	0.314945	-1.486878	-2.504667
35	H	2.066019	-1.255162	-2.458892
36	H	2.804616	-4.296891	-2.155631
37	H	3.538296	-3.007994	-1.209180
38	H	2.743293	-4.364332	-0.390062
39	H	0.537948	-0.940307	2.081725
40	H	-2.878052	-1.762459	3.596562
41	H	-2.238267	-3.061130	2.566921
42	H	-1.217917	-2.337314	3.833094
43	H	-0.906069	0.385370	0.249142
44	H	-3.767903	1.055564	-0.041824
45	H	-3.195784	3.062463	-1.197154
46	H	-2.326407	4.364259	0.728935
47	H	-3.457898	3.125647	1.283469
48	H	-1.720320	2.885998	1.475952
49	H	-0.892711	3.960829	-1.332582
50	H	-0.245616	2.466445	-0.663543
51	H	-1.032124	2.455309	-2.239259
52	H	-2.546886	-1.227098	-2.882068
53	H	-2.020258	-1.304070	-1.235548
54	H	1.346537	2.499982	1.031911
55	H	2.449286	2.192993	2.384316
56	H	2.557797	3.705372	1.476238
57	H	2.246922	2.435743	-1.359218
58	H	3.532185	3.595291	-0.994762
59	H	3.941757	2.002284	-1.640298

Compound **2**, conformation **b** (from *ab initio* conformational search)

1	C	4.543138	2.437900	-1.228690
2	C	3.225446	2.169942	-0.513621
3	O	3.090471	0.695326	-0.643174
4	C	2.027081	0.046403	-0.175935
5	N	2.113499	-1.281623	-0.533634
6	N	1.267794	-2.229303	0.004677
7	C	1.685973	-2.923074	1.245077
8	C	3.063456	-3.550192	1.055213
9	C	1.630998	-1.999275	2.459655
10	C	-0.050947	-2.248179	-0.395712
11	N	-0.336049	-1.473451	-1.500308
12	N	-1.626427	-1.380788	-1.966609
13	C	-2.121174	-2.495484	-2.766778
14	C	-2.509413	-0.519881	-1.328780
15	N	-1.949330	0.361707	-0.446164
16	C	-2.783416	1.207380	0.389214
17	C	-2.802523	0.777775	1.874906
18	C	-3.309187	-0.659370	2.009663
19	C	-1.444373	0.950906	2.558074
20	C	-2.462548	2.700831	0.239591
21	N	-1.628562	3.038034	-0.762380
22	O	-2.972008	3.527842	0.989435
23	O	-3.708550	-0.539220	-1.595804
24	O	-0.914004	-2.884660	0.192907
25	O	1.083759	0.513842	0.432172
26	C	3.314551	2.541054	0.962255
27	C	2.065640	2.858953	-1.223285
28	H	4.482612	2.128638	-2.271723
29	H	4.768687	3.502989	-1.194157
30	H	5.356417	1.894306	-0.748919
31	H	2.925701	-1.609643	-1.031319
32	H	0.951242	-3.714180	1.367615
33	H	3.312898	-4.148581	1.930654
34	H	3.083399	-4.197996	0.178695
35	H	3.836681	-2.788365	0.945615
36	H	1.899979	-2.556296	3.357508
37	H	2.331555	-1.170453	2.354894
38	H	0.631325	-1.589811	2.589734
39	H	0.391040	-1.066042	-2.063368
40	H	-2.218413	-3.396697	-2.159125
41	H	-3.088071	-2.228810	-3.178333
42	H	-1.420284	-2.679673	-3.578841
43	H	-0.977519	0.252355	-0.191352
44	H	-3.797534	1.101978	0.002638
45	H	-3.514271	1.448131	2.358362
46	H	-3.392814	-0.932741	3.062410
47	H	-4.290321	-0.780735	1.548042
48	H	-2.623408	-1.362328	1.533653
49	H	-1.519132	0.684651	3.613285
50	H	-0.685415	0.313711	2.106894
51	H	-1.094220	1.982120	2.497688
52	H	-1.436988	4.009649	-0.938708
53	H	-1.268804	2.342899	-1.392106
54	H	2.378087	2.341366	1.475334
55	H	4.112825	1.977977	1.445747
56	H	3.542420	3.603329	1.049866
57	H	1.128946	2.701052	-0.697918
58	H	2.262537	3.930026	-1.267991
59	H	1.970813	2.485950	-2.243225

Compound **2**, conformation A-1 (from NMR parameters-restrained molecular dynamics)

1	O	-3.219905	-0.528572	0.461053
2	C	-3.387348	-2.007192	0.447535
3	C	-4.806740	-2.176420	0.972554
4	C	-3.265566	-2.530071	-0.979376
5	C	-2.372145	-2.634100	1.396350
6	C	-2.077262	0.045167	0.097889
7	O	-1.111445	-0.486460	-0.415099
8	H	-5.519489	-1.679826	0.314899
9	H	-5.056069	-3.235753	1.018500
10	H	-4.898916	-1.753401	1.972328
11	H	-2.252237	-2.427976	-1.355263
12	H	-3.541169	-3.584547	-0.994494
13	H	-3.945455	-1.989335	-1.637714
14	H	-2.571756	-3.702311	1.477829
15	H	-1.355667	-2.500450	1.037462
16	H	-2.459587	-2.192202	2.388888
17	N	-2.104063	1.379117	0.441455
18	H	-2.930061	1.773627	0.861901
19	N	-1.134588	2.249922	-0.011541
20	C	-1.363333	2.947400	-1.300709
21	H	-0.552988	3.668578	-1.360483
22	C	-1.271197	1.992078	-2.488811
23	H	-0.313908	1.474667	-2.500435
24	H	-2.065124	1.245665	-2.454369
25	H	-1.378211	2.553598	-3.417227
26	C	-2.692082	3.694433	-1.258203
27	H	-3.535650	3.004135	-1.212562
28	H	-2.740220	4.364008	-0.399391
29	H	-2.801985	4.288670	-2.164513
30	C	0.136772	2.140083	0.501687
31	O	1.108403	2.680266	-0.022355
32	N	0.264336	1.358647	1.624148
33	H	-0.529475	0.945745	2.081864
34	N	1.507121	1.121593	2.172081
35	C	2.007528	2.145929	3.085872
36	H	2.250703	3.066414	2.551184
37	H	1.237571	2.348612	3.826822
38	H	2.895904	1.771497	3.581916
39	C	2.418357	0.354267	1.446197
40	O	3.609660	0.359929	1.744848
41	N	1.900511	-0.394390	0.431973
42	H	0.907013	-0.382378	0.248170
43	C	2.763813	-1.134732	-0.468584
44	H	3.766645	-1.059341	-0.047114
45	C	2.413670	-2.635883	-0.562040
46	H	3.189298	-3.069850	-1.193919
47	C	2.487479	-3.288895	0.818686
48	H	1.722751	-2.883756	1.483550
49	H	3.459572	-3.124211	1.286639
50	H	2.326330	-4.364706	0.739775
51	C	1.061208	-2.894430	-1.228914
52	H	1.022917	-2.465070	-2.230558
53	H	0.241429	-2.470090	-0.652309
54	H	0.885303	-3.967346	-1.318226
55	C	2.882931	-0.492709	-1.862336
56	O	3.422537	-1.104749	-2.780409
57	N	2.406901	0.758925	-2.003176
58	H	2.025891	1.300803	-1.240079
59	H	2.544613	1.216973	-2.888747

Compound **2**, conformation A-2 (from NMR parameters-restrained molecular dynamics)

1	O	-3.399170	-0.023265	0.362070
2	C	-3.864526	-1.428682	0.519678
3	C	-3.698990	-2.177627	-0.797895
4	C	-3.107531	-2.082636	1.669349
5	C	-5.336094	-1.244104	0.864593
6	C	-2.133096	0.263223	0.080689
7	O	-1.244471	-0.516795	-0.203994
8	H	-4.175064	-1.625233	-1.607997
9	H	-2.651269	-2.328909	-1.039517
10	H	-4.184601	-3.149975	-0.715293
11	H	-2.054555	-2.204562	1.432125
12	H	-3.202091	-1.482989	2.574598
13	H	-3.534781	-3.066198	1.863486
14	H	-5.801680	-2.217396	1.013882
15	H	-5.856814	-0.729738	0.057497
16	H	-5.445297	-0.662050	1.779068
17	N	-1.927734	1.619563	0.218071
18	H	-2.706846	2.213968	0.451889
19	N	-0.795008	2.232305	-0.279538
20	C	-0.812151	2.721917	-1.681339
21	H	0.062430	3.362748	-1.751299
22	C	-0.670591	1.574645	-2.679445
23	H	-0.633150	1.972345	-3.693948
24	H	0.241464	1.010486	-2.493695
25	H	-1.517288	0.891103	-2.615321
26	C	-2.060506	3.560836	-1.928651
27	H	-2.151956	4.359572	-1.192268
28	H	-1.998740	4.012522	-2.917813
29	H	-2.965011	2.951882	-1.900368
30	C	0.405029	2.033264	0.361393
31	O	1.476407	2.372983	-0.135848
32	N	0.338327	1.406990	1.581605
33	H	-0.534918	1.104672	1.975929
34	N	1.491265	1.025410	2.235000
35	C	2.096688	2.037077	3.097535
36	H	2.518405	2.854993	2.509438
37	H	2.881202	1.574691	3.685913
38	H	1.327707	2.425708	3.761068
39	C	2.308113	0.062579	1.641503
40	O	3.462965	-0.099843	2.027323
41	N	1.755370	-0.677734	0.640988
42	H	0.790918	-0.547413	0.371448
43	C	2.585722	-1.612887	-0.097145
44	H	3.219350	-2.135649	0.618533
45	C	1.761593	-2.678709	-0.856612
46	H	2.510839	-3.375882	-1.235145
47	C	0.835600	-3.440864	0.093900
48	H	0.377855	-4.284274	-0.424544
49	H	0.031129	-2.802947	0.458489
50	H	1.382298	-3.827482	0.955557
51	C	0.995713	-2.118947	-2.060352
52	H	0.248854	-1.387689	-1.759486
53	H	1.667116	-1.648518	-2.778928
54	H	0.474909	-2.928455	-2.573863
55	C	3.570309	-0.938926	-1.066657
56	O	4.481123	-1.603102	-1.556823
57	N	3.358802	0.353703	-1.368835
58	H	2.658063	0.923657	-0.913621
59	H	4.007834	0.804576	-1.991944

Compound **2**, conformation B (from NMR parameters-restrained molecular dynamics)

1	O	2.420343	1.747985	-0.853621
2	C	1.823499	3.110746	-0.791818
3	C	1.847255	3.613064	0.647107
4	C	2.772516	3.915717	-1.669879
5	C	0.418240	3.081650	-1.382874
6	C	1.844274	0.711761	-0.253500
7	O	0.880637	0.732284	0.489825
8	H	1.534875	4.657268	0.663985
9	H	2.857122	3.550940	1.052744
10	H	1.175218	3.037283	1.276574
11	H	3.786586	3.877255	-1.273129
12	H	2.779319	3.524035	-2.686621
13	H	2.450383	4.955819	-1.699968
14	H	0.063659	4.105715	-1.500520
15	H	0.433831	2.612756	-2.367154
16	H	-0.282899	2.550924	-0.745536
17	N	2.474634	-0.450802	-0.635218
18	H	3.266655	-0.411187	-1.256483
19	N	2.189080	-1.655469	-0.026542
20	C	2.998546	-2.053720	1.147815
21	H	2.675038	-3.068680	1.361794
22	C	4.478383	-2.070510	0.777591
23	H	4.845872	-1.065712	0.563643
24	H	5.058204	-2.462309	1.612583
25	H	4.658348	-2.701250	-0.093082
26	C	2.715276	-1.173021	2.362724
27	H	1.657208	-1.187456	2.615307
28	H	3.285873	-1.534595	3.218533
29	H	3.009155	-0.139955	2.175043
30	C	0.964310	-2.247742	-0.265248
31	O	0.513663	-3.143464	0.433261
32	N	0.279720	-1.748408	-1.353133
33	H	0.700369	-1.094372	-1.991200
34	N	-1.004692	-2.158721	-1.621183
35	C	-1.166295	-3.420638	-2.331445
36	H	-0.599675	-3.380744	-3.260449
37	H	-0.808936	-4.253334	-1.723691
38	H	-2.218059	-3.559505	-2.555620
39	C	-2.054830	-1.585925	-0.918036
40	O	-3.210437	-2.002275	-1.053268
41	N	-1.734944	-0.543271	-0.114112
42	H	-0.784437	-0.204648	-0.050790
43	C	-2.743812	0.159858	0.668676
44	H	-3.542733	-0.551022	0.882726
45	C	-2.166745	0.675554	1.992310
46	H	-1.399220	1.413167	1.751129
47	C	-3.260186	1.357397	2.819803
48	H	-3.698764	2.201286	2.290335
49	H	-4.057387	0.650164	3.062635
50	H	-2.848012	1.726706	3.759571
51	C	-1.523460	-0.462824	2.789246
52	H	-0.715620	-0.941211	2.239827
53	H	-1.113987	-0.080592	3.725156
54	H	-2.263921	-1.228063	3.035751
55	C	-3.311330	1.281759	-0.225310
56	O	-2.929275	2.444499	-0.160616
57	N	-4.235935	0.852240	-1.112365
58	H	-4.361570	-0.140572	-1.251621
59	H	-4.530822	1.481903	-1.841222

Compound **3**, conformation **a**

1	C	0.642845	-2.676130	-3.053414
2	C	0.122790	-3.010713	-1.660302
3	O	1.168813	-2.701353	-0.646856
4	C	1.587262	-1.457536	-0.436930
5	N	2.368895	-1.423639	0.696367
6	N	3.108811	-0.308580	1.031875
7	C	4.492673	-0.202712	0.514283
8	C	5.287678	-1.449554	0.887756
9	C	4.517492	0.074163	-0.987632
10	C	2.452661	0.812182	1.499027
11	N	1.133839	0.611684	1.845907
12	N	0.332447	1.672211	2.193167
13	C	0.383144	2.116531	3.579471
14	C	-0.228713	2.458055	1.197060
15	N	0.019222	2.073507	-0.085531
16	C	-0.808286	2.604172	-1.153836
17	C	-0.300093	2.094031	-2.521580
18	C	-1.196858	2.567069	-3.667495
19	C	1.147898	2.536738	-2.750247
20	C	-2.280329	2.247577	-0.937098
21	O	-2.400089	1.005213	-0.458464
22	O	-3.211968	2.979279	-1.176400
23	O	-0.926442	3.433756	1.473137
24	O	2.992686	1.904716	1.592579
25	O	1.314358	-0.465999	-1.087492
26	C	-1.155100	-2.262344	-1.307530
27	C	-0.057944	-4.512918	-1.486914
28	C	-3.710491	0.548583	-0.044909
29	C	-3.499920	-0.683967	0.786576
30	C	-2.571482	-0.670125	1.829830
31	C	-2.338683	-1.815439	2.578493
32	C	-3.042093	-2.986324	2.301952
33	C	-3.978931	-3.001078	1.275775
34	C	-4.202094	-1.854479	0.518083
35	H	1.600720	-3.166268	-3.228083
36	H	-0.068719	-3.041008	-3.794219
37	H	0.763729	-1.604645	-3.182548
38	H	2.558612	-2.278413	1.194789
39	H	4.908569	0.652771	1.039403
40	H	6.329402	-1.315946	0.598447
41	H	5.249149	-1.633214	1.961614
42	H	4.911287	-2.331979	0.368289
43	H	5.547236	0.209326	-1.319533
44	H	4.089473	-0.757842	-1.547200
45	H	3.952136	0.973440	-1.225078
46	H	0.717498	-0.304200	1.848623
47	H	-0.346599	2.906885	3.715438
48	H	0.137293	1.280674	4.232901
49	H	1.378530	2.489286	3.825298
50	H	0.451673	1.175577	-0.257712
51	H	-0.766287	3.692698	-1.139716
52	H	-0.323517	1.002346	-2.487733
53	H	-0.801087	2.209415	-4.618140
54	H	-2.218569	2.201216	-3.572478
55	H	-1.234145	3.657750	-3.707756
56	H	1.508903	2.153127	-3.705114
57	H	1.215233	3.626805	-2.777498
58	H	1.811811	2.171861	-1.969603
59	H	-1.448845	-2.473683	-0.280775
60	H	-1.041512	-1.188719	-1.422458
61	H	-1.957869	-2.596514	-1.964465
62	H	-0.385727	-4.743659	-0.473768
63	H	-0.811114	-4.873950	-2.186180
64	H	0.877147	-5.037396	-1.681406
65	H	-4.186240	1.349918	0.521540
66	H	-4.316475	0.345355	-0.926671
67	H	-2.017374	0.235065	2.039574
68	H	-1.608858	-1.796697	3.376891
69	H	-2.857848	-3.880083	2.882568
70	H	-4.525637	-3.907333	1.052758
71	H	-4.913885	-1.877825	-0.297048

Compound **3**, conformation **b**

1	C	4.564980	0.810850	-0.176187
2	C	4.557349	-0.558613	-0.844663
3	O	3.626638	-1.463604	-0.117907
4	C	2.334245	-1.181059	0.005604
5	N	1.741288	-2.100089	0.847071
6	N	0.367846	-2.211106	0.903674
7	C	-0.303862	-3.165124	-0.006419
8	C	0.117444	-2.938416	-1.455485
9	C	-0.056612	-4.600921	0.451032
10	C	-0.350009	-1.317303	1.665242
11	N	0.407654	-0.454156	2.430070
12	N	-0.188674	0.631825	3.032346
13	C	-0.849107	0.387262	4.309357
14	C	-0.567653	1.714307	2.242254
15	N	-0.049043	1.737682	0.984544
16	C	-0.334966	2.818250	0.062797
17	C	0.916617	3.180111	-0.766551
18	C	0.584648	4.199047	-1.858727
19	C	2.019685	3.706194	0.153575
20	C	-1.520341	2.466616	-0.835363
21	O	-1.307127	1.322313	-1.496543
22	O	-2.512689	3.150154	-0.943849
23	O	-1.286779	2.603689	2.693870
24	O	-1.572172	-1.271056	1.661574
25	O	1.731787	-0.244805	-0.484439
26	C	4.156566	-0.494278	-2.313989
27	C	5.896105	-1.262894	-0.670385
28	C	-2.331894	0.854642	-2.425088
29	C	-3.234274	-0.151402	-1.769704
30	C	-3.105792	-1.508064	-2.059967
31	C	-3.922223	-2.446399	-1.437032
32	C	-4.877369	-2.032674	-0.515452
33	C	-5.016309	-0.677884	-0.223747
34	C	-4.201060	0.257546	-0.847867
35	H	4.767746	0.710732	0.890156
36	H	5.354036	1.418432	-0.618917
37	H	3.617545	1.322608	-0.310206
38	H	2.286791	-2.876495	1.187908
39	H	-1.360248	-2.932690	0.093653
40	H	-0.463863	-3.591198	-2.105672
41	H	-0.050651	-1.906152	-1.753565
42	H	1.171734	-3.176176	-1.604676
43	H	-0.602649	-5.294238	-0.188815
44	H	1.002355	-4.859584	0.389173
45	H	-0.389601	-4.743875	1.478755
46	H	1.411027	-0.508563	2.457385
47	H	-1.732199	-0.240666	4.179482
48	H	-0.145233	-0.110468	4.973243
49	H	-1.140978	1.338623	4.740285
50	H	0.496786	0.965235	0.628431
51	H	-0.650751	3.682263	0.642361
52	H	1.263790	2.259721	-1.241843
53	H	1.486609	4.464618	-2.410209
54	H	-0.138729	3.812122	-2.577347
55	H	0.173865	5.113747	-1.425865
56	H	2.928996	3.899707	-0.416065
57	H	1.711329	4.642007	0.625362
58	H	2.260298	2.993519	0.941148
59	H	4.089263	-1.498954	-2.731264
60	H	3.201465	0.007271	-2.440354
61	H	4.917660	0.056265	-2.866807
62	H	5.862278	-2.262329	-1.102920
63	H	6.677213	-0.693030	-1.172079
64	H	6.150230	-1.346549	0.385798
65	H	-2.885269	1.716886	-2.789351
66	H	-1.772577	0.408426	-3.242572
67	H	-2.361591	-1.833336	-2.774168
68	H	-3.808571	-3.496838	-1.668828
69	H	-5.511607	-2.760329	-0.027261
70	H	-5.760614	-0.351577	0.490216
71	H	-4.303667	1.309472	-0.619573

Compound **3**, conformation **c**

1	C	5.987946	-0.270168	0.020222
2	C	4.878062	0.772661	0.089748
3	O	3.629261	0.133844	0.578223
4	C	3.019705	-0.832173	-0.114016
5	N	1.838321	-1.158527	0.532524
6	N	1.177510	-2.321502	0.196645
7	C	1.477224	-3.557107	0.956595
8	C	2.977434	-3.823207	0.999041
9	C	0.854840	-3.491439	2.351610
10	C	0.074113	-2.253149	-0.621247
11	N	-0.262804	-0.978041	-1.053380
12	N	-1.165605	-0.840164	-2.089274
13	C	-0.699791	-1.184843	-3.425782
14	C	-2.514145	-0.713585	-1.799978
15	N	-2.819735	-0.679970	-0.469303
16	C	-4.075531	-0.143173	0.003004
17	C	-4.669899	-0.978511	1.161255
18	C	-5.029051	-2.382597	0.676297
19	C	-3.733856	-1.029343	2.372538
20	C	-3.973106	1.329028	0.413207
21	O	-2.741594	1.814408	0.240228
22	O	-4.901201	1.969101	0.850373
23	O	-3.356020	-0.639365	-2.691709
24	O	-0.585364	-3.234196	-0.931345
25	O	3.378421	-1.336897	-1.153512
26	C	5.166990	1.802347	1.174857
27	C	4.619074	1.447399	-1.252809
28	C	-2.486599	3.179658	0.650544
29	C	-1.023089	3.446407	0.441259
30	C	-0.599203	4.645351	-0.126515
31	C	0.757802	4.904650	-0.297750
32	C	1.701386	3.958692	0.085230
33	C	1.284099	2.754042	0.646017
34	C	-0.069317	2.503178	0.829061
35	H	5.785966	-1.009802	-0.749001
36	H	6.930282	0.226930	-0.209856
37	H	6.091907	-0.774845	0.980740
38	H	1.679309	-0.781778	1.455708
39	H	0.992752	-4.346832	0.389398
40	H	3.157106	-4.779432	1.488964
41	H	3.398560	-3.856318	-0.003686
42	H	3.502853	-3.056191	1.569937
43	H	1.021549	-4.429689	2.880773
44	H	1.301901	-2.692821	2.946979
45	H	-0.219428	-3.318247	2.287660
46	H	0.385830	-0.217284	-0.928328
47	H	-1.492189	-0.970936	-4.134060
48	H	0.175116	-0.582672	-3.667698
49	H	-0.437645	-2.242790	-3.479294
50	H	-2.033532	-0.606031	0.153591
51	H	-4.772708	-0.169689	-0.833918
52	H	-5.585496	-0.463599	1.456317
53	H	-5.484832	-2.958225	1.482582
54	H	-5.733803	-2.346636	-0.155902
55	H	-4.137680	-2.915339	0.342154
56	H	-4.214229	-1.555025	3.197791
57	H	-2.811775	-1.565511	2.138880
58	H	-3.468046	-0.031154	2.725423
59	H	4.358512	2.528395	1.247869
60	H	5.285848	1.315318	2.142099
61	H	6.087168	2.334603	0.937721
62	H	3.764548	2.119439	-1.181440
63	H	5.494198	2.034580	-1.530586
64	H	4.427909	0.715685	-2.032387
65	H	-3.109755	3.853333	0.064530
66	H	-2.772587	3.278162	1.698978
67	H	-1.330757	5.378742	-0.440942
68	H	1.074352	5.839838	-0.739556
69	H	2.755277	4.157866	-0.055361
70	H	2.010834	2.008886	0.936412
71	H	-0.389675	1.566645	1.264621

Compound **4**, conformation **a**

1	C	6.273152	-0.490975	-0.776041
2	C	5.549755	0.492662	0.136741
3	O	4.187617	0.754881	-0.395471
4	C	3.273979	-0.208229	-0.489081
5	N	2.080225	0.350803	-0.929100
6	N	1.067610	-0.486562	-1.347222
7	C	0.126413	-0.953981	-0.460810
8	N	0.028933	-0.255069	0.716990
9	N	-0.785606	-0.711443	1.735252
10	C	-2.175021	-0.651000	1.599019
11	N	-2.635768	0.223680	0.673905
12	C	-4.041062	0.319473	0.335645
13	C	-4.401094	1.722421	-0.201163
14	C	-4.191722	2.791337	0.872401
15	C	-3.655253	2.071172	-1.493747
16	C	-4.528917	-0.764831	-0.642107
17	O	-5.729255	-0.848195	-0.891406
18	O	-2.888424	-1.343077	2.314699
19	O	-0.621450	-1.879868	-0.751469
20	O	3.392901	-1.382966	-0.220691
21	C	5.449322	-0.002446	1.575092
22	C	6.193961	1.871490	0.076117
23	N	-3.605255	-1.570630	-1.191338
24	H	6.259915	-0.130628	-1.804683
25	H	7.311722	-0.576097	-0.456348
26	H	5.814554	-1.475017	-0.738722
27	H	2.112788	1.256952	-1.370650
28	H	1.264606	-1.108963	-2.119116
29	H	0.716554	0.439636	0.957787
30	H	-0.481462	-1.567852	2.178771
31	H	-1.964448	0.736738	0.129146
32	H	-4.611117	0.146756	1.247913
33	H	-5.465245	1.667111	-0.432321
34	H	-4.518666	3.765124	0.506320
35	H	-4.758570	2.560126	1.775460
36	H	-3.139231	2.875130	1.148148
37	H	-4.023217	3.016721	-1.892107
38	H	-2.582181	2.194079	-1.328287
39	H	-3.792240	1.307931	-2.260446
40	H	4.866646	0.696496	2.175213
41	H	4.986565	-0.984060	1.624080
42	H	6.450848	-0.066649	2.000209
43	H	5.640157	2.580235	0.691011
44	H	7.216791	1.814548	0.446477
45	H	6.215278	2.239384	-0.949223
46	H	-3.921519	-2.292872	-1.817084
47	H	-2.621704	-1.539023	-0.958634

Compound **4**, conformation **b**

1	C	5.370854	-1.085657	0.009176
2	C	3.854721	-1.106579	0.152378
3	O	3.476884	0.260875	-0.290837
4	C	2.207983	0.654934	-0.324031
5	N	2.125596	1.940045	-0.817232
6	N	0.914714	2.595290	-0.693579
7	C	0.379268	2.673179	0.586977
8	N	-0.988708	2.694370	0.636106
9	N	-1.793429	2.548984	-0.476998
10	C	-2.518629	1.367664	-0.701977
11	N	-1.977280	0.226870	-0.204257
12	C	-2.647643	-1.048776	-0.424568
13	C	-1.666215	-2.234474	-0.556033
14	C	-0.763522	-2.067046	-1.780448
15	C	-0.860382	-2.496616	0.721188
16	C	-3.713706	-1.370499	0.633943
17	O	-4.500488	-2.292389	0.442313
18	O	-3.559710	1.418743	-1.343151
19	O	1.058322	2.731499	1.597164
20	O	1.227084	0.006825	-0.009115
21	C	3.229732	-2.140489	-0.777862
22	C	3.443864	-1.303312	1.607540
23	N	-3.715998	-0.616654	1.746577
24	H	5.804326	-0.309946	0.639715
25	H	5.780967	-2.048608	0.310830
26	H	5.654891	-0.895149	-1.025346
27	H	2.950556	2.517502	-0.792071
28	H	0.260887	2.385661	-1.433443
29	H	-1.414513	2.816383	1.543661
30	H	-2.314807	3.375050	-0.736034
31	H	-1.015780	0.233620	0.107755
32	H	-3.203509	-0.971916	-1.358221
33	H	-2.312831	-3.096958	-0.725495
34	H	-0.143363	-2.954517	-1.912885
35	H	-1.355103	-1.929456	-2.687069
36	H	-0.097388	-1.213092	-1.669128
37	H	-0.250192	-3.391572	0.594241
38	H	-0.182234	-1.676187	0.949521
39	H	-1.512181	-2.657341	1.580672
40	H	2.149511	-2.167448	-0.672515
41	H	3.480739	-1.916743	-1.814781
42	H	3.629675	-3.124634	-0.533652
43	H	2.363139	-1.325928	1.713256
44	H	3.850347	-2.248674	1.966897
45	H	3.845758	-0.500185	2.225235
46	H	-4.387556	-0.805032	2.471342
47	H	-3.050282	0.124447	1.874497

Compound **4**, conformation **c**

1	C	-2.882225	-2.026128	1.098646
2	C	-3.312278	-1.599956	-0.300245
3	O	-2.904372	-0.190434	-0.523658
4	C	-3.431094	0.805707	0.180855
5	N	-2.943314	2.036066	-0.233662
6	N	-1.748943	2.159460	-0.902903
7	C	-0.572214	2.180954	-0.202938
8	N	0.559845	2.311038	-1.003081
9	N	1.744473	2.701712	-0.398466
10	C	2.578336	1.752360	0.189740
11	N	2.403093	0.475849	-0.241257
12	C	3.071272	-0.648481	0.389163
13	C	2.084840	-1.591584	1.114152
14	C	1.381438	-0.862628	2.260178
15	C	1.072310	-2.214519	0.151055
16	C	3.981899	-1.430303	-0.570100
17	O	4.534666	-2.459186	-0.194322
18	O	3.436144	2.109853	0.987312
19	O	-0.509139	2.069835	1.008462
20	O	-4.278096	0.733704	1.047994
21	C	-2.526329	-2.342938	-1.373319
22	C	-4.811609	-1.760246	-0.531166
23	N	4.141762	-0.917633	-1.803062
24	H	-3.441080	-1.488126	1.859730
25	H	-3.061955	-3.094067	1.221411
26	H	-1.818617	-1.838345	1.239831
27	H	-3.165776	2.791508	0.398179
28	H	-1.797440	2.313778	-1.896266
29	H	0.458439	2.637092	-1.952203
30	H	1.702032	3.560018	0.134928
31	H	1.587966	0.299337	-0.806340
32	H	3.745599	-0.223372	1.132823
33	H	2.700386	-2.391126	1.526818
34	H	0.726715	-1.548737	2.798996
35	H	2.101928	-0.454127	2.970597
36	H	0.769282	-0.039230	1.888042
37	H	0.447100	-2.938344	0.673482
38	H	0.403559	-1.457507	-0.262759
39	H	1.559253	-2.729630	-0.677948
40	H	-2.818791	-2.000518	-2.365550
41	H	-1.457547	-2.183190	-1.250566
42	H	-2.727119	-3.411110	-1.300914
43	H	-5.088484	-1.353767	-1.504144
44	H	-5.057063	-2.822299	-0.523009
45	H	-5.390385	-1.260764	0.239308
46	H	4.770130	-1.369441	-2.445757
47	H	3.713762	-0.047069	-2.064099

Compound **4**, conformation **d**

1	C	-2.163026	2.301254	0.582829
2	C	-2.906088	1.761227	-0.633959
3	O	-3.088372	0.297946	-0.483229
4	C	-3.759243	-0.226088	0.537389
5	N	-3.693328	-1.610767	0.517621
6	N	-2.689565	-2.284527	-0.146838
7	C	-1.378541	-2.085276	0.243988
8	N	-0.457091	-2.678286	-0.598934
9	N	0.880614	-2.399121	-0.420616
10	C	1.314253	-1.090558	-0.637315
11	N	2.547227	-0.828403	-0.112470
12	C	3.115290	0.510231	-0.118445
13	C	3.126922	1.162158	1.282501
14	C	1.699746	1.379588	1.786433
15	C	3.961838	0.365240	2.288521
16	C	4.501046	0.573641	-0.780277
17	O	5.168180	1.601341	-0.721823
18	O	0.664191	-0.296149	-1.298699
19	O	-1.068951	-1.513913	1.273539
20	O	-4.412061	0.361355	1.376680
21	C	-4.257099	2.434000	-0.848921
22	C	-2.041289	1.854976	-1.884951
23	N	4.908952	-0.530400	-1.431650
24	H	-1.244597	1.737176	0.738546
25	H	-1.901794	3.345123	0.409706
26	H	-2.773883	2.238559	1.479369
27	H	-4.011799	-2.048039	1.368443
28	H	-2.900386	-2.525708	-1.102141
29	H	-0.716472	-2.923827	-1.540968
30	H	1.305527	-2.926338	0.327097
31	H	2.931802	-1.487438	0.544950
32	H	2.468587	1.106049	-0.763002
33	H	3.601303	2.133769	1.143564
34	H	1.710592	1.859955	2.765408
35	H	1.133934	2.014620	1.104061
36	H	1.164667	0.433216	1.884368
37	H	4.029043	0.905889	3.232766
38	H	3.509935	-0.604772	2.508654
39	H	4.977300	0.195986	1.927539
40	H	-4.781925	1.967364	-1.682834
41	H	-4.876875	2.369260	0.040462
42	H	-4.096483	3.484713	-1.091242
43	H	-2.562228	1.422985	-2.739606
44	H	-1.828200	2.901072	-2.103460
45	H	-1.102570	1.323475	-1.740278
46	H	5.781904	-0.510251	-1.931295
47	H	4.318220	-1.339308	-1.508411

Compound **4**, conformation **e**

1	C	-6.511705	-0.021578	0.709475
2	C	-5.524355	0.967049	0.098503
3	O	-4.506346	0.235942	-0.691708
4	C	-3.682165	-0.650413	-0.127304
5	N	-2.889650	-1.211681	-1.113286
6	N	-1.765660	-1.917471	-0.744128
7	C	-0.752792	-1.249758	-0.076337
8	N	0.148121	-2.101037	0.539593
9	N	1.360747	-1.590401	0.955293
10	C	2.230893	-1.093061	-0.015524
11	N	3.252742	-0.343680	0.494687
12	C	4.179740	0.374681	-0.364779
13	C	3.992439	1.907289	-0.298288
14	C	2.602452	2.302941	-0.798256
15	C	4.264459	2.468240	1.100269
16	C	5.647532	-0.019619	-0.137361
17	O	6.546177	0.593280	-0.704665
18	O	2.107120	-1.375711	-1.196994
19	O	-0.667226	-0.037530	-0.030939
20	O	-3.628364	-0.973152	1.039641
21	C	-6.201877	1.830685	-0.958204
22	C	-4.832772	1.831483	1.147692
23	N	5.872490	-1.063277	0.680682
24	H	-6.034513	-0.640077	1.464208
25	H	-7.328892	0.530376	1.173887
26	H	-6.929644	-0.664372	-0.065477
27	H	-2.825078	-0.723621	-1.992636
28	H	-1.934587	-2.889525	-0.535837
29	H	0.181876	-3.068344	0.257752
30	H	1.312931	-1.120629	1.846286
31	H	3.193640	-0.048733	1.455946
32	H	3.956518	0.050527	-1.381308
33	H	4.739709	2.317364	-0.977939
34	H	2.493196	3.387931	-0.795994
35	H	2.429436	1.945989	-1.814482
36	H	1.820374	1.887673	-0.160305
37	H	4.208910	3.556915	1.085582
38	H	3.524431	2.121885	1.825654
39	H	5.254758	2.189163	1.462359
40	H	-5.480278	2.500436	-1.425108
41	H	-6.651607	1.207711	-1.730837
42	H	-6.984746	2.430737	-0.495797
43	H	-4.085935	2.470162	0.675860
44	H	-5.573229	2.468897	1.631024
45	H	-4.348765	1.220817	1.904496
46	H	6.814835	-1.390640	0.810731
47	H	5.113153	-1.578073	1.090040

Compound **5**, conformation **5A +/+/–/+/+/–** (from NMR parameters-restrained molecular dynamics)

1	O	3.776497	0.116395	-1.982659
2	C	3.253150	1.050987	-3.013496
3	C	1.730593	1.034945	-2.998453
4	C	3.789384	0.440602	-4.301898
5	C	3.835307	2.439127	-2.775380
6	C	3.472005	0.255554	-0.696738
7	O	2.823153	1.150390	-0.185476
8	H	1.358799	1.550592	-3.883871
9	H	1.373995	0.008756	-3.011638
10	H	1.332493	1.525313	-2.115651
11	H	3.490814	1.054854	-5.150467
12	H	3.391114	-0.563830	-4.442577
13	H	4.877382	0.386331	-4.277116
14	H	3.547508	3.092313	-3.599314
15	H	4.923808	2.393765	-2.737552
16	H	3.464642	2.864943	-1.847117
17	N	3.984295	-0.804075	0.013730
18	H	4.486714	-1.528213	-0.473243
19	N	4.067693	-0.781835	1.389887
20	C	5.291312	-0.217081	2.003888
21	H	5.199345	-0.463700	3.058031
22	C	6.527948	-0.908627	1.438952
23	H	7.412731	-0.563749	1.972880
24	H	6.458611	-1.990863	1.550910
25	H	6.667812	-0.674856	0.382566
26	C	5.355728	1.301703	1.852924
27	H	6.233846	1.686706	2.372277
28	H	4.467391	1.769587	2.273291
29	H	5.431592	1.589687	0.804134
30	C	2.914045	-0.912294	2.137575
31	O	2.876001	-0.659024	3.334452
32	N	1.814402	-1.358146	1.442024
33	H	1.812974	-1.568683	0.445911
34	N	0.585666	-1.359962	2.064208
35	C	0.232245	-2.535905	2.845946
36	H	-0.784652	-2.422831	3.204514
37	H	0.911107	-2.647983	3.691992
38	H	0.291390	-3.417465	2.210713
39	C	-0.132912	-0.192737	2.150177
40	O	-1.207153	-0.144543	2.771824
41	N	0.367409	0.892362	1.508131
42	H	1.178526	0.808147	0.908222
43	C	-0.465369	2.073437	1.353755
44	H	-0.796112	2.398577	2.341684
45	C	0.323213	3.219353	0.694584
46	H	0.696643	2.846094	-0.261223
47	C	-0.587278	4.420568	0.429310
48	H	-1.395937	4.181111	-0.261159
49	H	-0.012176	5.236194	-0.008293
50	H	-1.033030	4.785597	1.357353
51	C	1.517527	3.622494	1.562882
52	H	2.194556	2.788784	1.732166
53	H	1.178535	3.997858	2.531185
54	H	2.082197	4.416680	1.073410
55	C	-1.688187	1.682041	0.513202
56	O	-1.576876	1.120574	-0.567149
57	N	-2.893082	1.946680	1.087098
58	H	-2.929480	2.289434	2.034446
59	N	-4.087543	1.515408	0.537348
60	C	-4.856517	2.476676	-0.281711
61	H	-5.818199	1.992461	-0.429870
62	C	-5.066920	3.772284	0.495189
63	H	-5.536586	3.579306	1.459899
64	H	-4.122736	4.290824	0.665547
65	H	-5.713952	4.437216	-0.075840

66	C	-4.205075	2.711662	-1.643123
67	H	-4.822654	3.386115	-2.237205
68	H	-4.091716	1.773790	-2.183333
69	H	-3.218841	3.161643	-1.531983
70	C	-4.337496	0.154933	0.448947
71	O	-5.232495	-0.298780	-0.250395
72	N	-3.516925	-0.637267	1.218353
73	H	-2.783453	-0.283524	1.829724
74	N	-3.568956	-2.006857	1.088999
75	C	-4.491830	-2.724576	1.952082
76	H	-4.388965	-3.787132	1.761446
77	H	-5.516729	-2.414788	1.744613
78	H	-4.258029	-2.519313	2.997136
79	C	-2.824873	-2.635817	0.112904
80	O	-2.843910	-3.865117	-0.022296
81	N	-2.074067	-1.824802	-0.676976
82	H	-2.026590	-0.828732	-0.515462
83	C	-1.278314	-2.353917	-1.773815
84	H	-1.757595	-3.272467	-2.112869
85	C	-1.209618	-1.362404	-2.940510
86	H	-0.715796	-0.462698	-2.573047
87	C	-0.387021	-1.946355	-4.091898
88	H	0.627418	-2.193220	-3.782561
89	H	-0.320930	-1.229504	-4.910751
90	H	-0.857629	-2.853025	-4.479881
91	C	-2.614251	-0.985877	-3.420048
92	H	-2.549549	-0.272371	-4.242352
93	H	-3.149046	-1.867272	-3.782591
94	H	-3.208915	-0.533495	-2.628808
95	C	0.102026	-2.707283	-1.192953
96	O	1.060190	-1.933072	-1.235689
97	N	0.154773	-3.907747	-0.589909
98	H	-0.701425	-4.415126	-0.416663
99	H	0.986928	-4.169701	-0.086526

Compound **5**, conformation **5B –/–/–/–/–** (from NMR parameters-restrained molecular dynamics)

1	O	-6.110056	0.717578	-0.399788
2	C	-6.383647	2.180840	-0.326396
3	C	-7.879942	2.243002	-0.600254
4	C	-5.592599	2.889529	-1.418726
5	C	-6.059244	2.698446	1.070204
6	C	-4.889521	0.227837	-0.231916
7	O	-3.893027	0.827478	0.127505
8	H	-8.431260	1.688999	0.158798
9	H	-8.211325	3.280428	-0.582525
10	H	-8.108955	1.821018	-1.578165
11	H	-5.814510	2.451835	-2.391864
12	H	-4.523596	2.827777	-1.236510
13	H	-5.878729	3.940725	-1.441607
14	H	-6.414007	3.725459	1.156154
15	H	-6.568225	2.096535	1.822957
16	H	-4.991023	2.679666	1.263064
17	N	-4.873337	-1.106253	-0.585974
18	H	-5.733843	-1.557676	-0.852693
19	N	-3.822072	-1.920627	-0.213362
20	C	-3.885919	-2.593869	1.108162
21	H	-3.020804	-3.250512	1.114239
22	C	-3.762990	-1.594347	2.255988
23	H	-3.716352	-2.131508	3.203125
24	H	-4.623555	-0.925905	2.291407
25	H	-2.863705	-0.991473	2.152075
26	C	-5.152598	-3.437185	1.203852
27	H	-6.047890	-2.813707	1.210024
28	H	-5.220300	-4.140879	0.374369
29	H	-5.140633	-4.002485	2.134872
30	C	-2.623287	-1.784001	-0.863818
31	O	-1.580640	-2.276543	-0.432914
32	N	-2.640638	-1.039063	-2.019288
33	H	-3.482237	-0.614638	-2.369000
34	N	-1.451330	-0.692956	-2.629448
35	C	-0.919530	-1.656812	-3.592600
36	H	-0.102369	-1.196831	-4.136967
37	H	-0.559941	-2.555147	-3.087636
38	H	-1.715483	-1.918818	-4.284611
39	C	-0.567138	0.106093	-1.921024
40	O	0.627444	0.161738	-2.235216
41	N	-1.066832	0.799863	-0.869113
42	H	-2.046262	0.738616	-0.619550
43	C	-0.167590	1.484929	0.045636
44	H	0.413230	2.234062	-0.494346
45	C	-0.992627	2.193003	1.147950
46	H	-1.691811	1.454988	1.549725
47	C	-0.121579	2.706629	2.295731
48	H	-0.742744	3.252200	3.006121
49	H	0.650853	3.384152	1.929212
50	H	0.371653	1.899747	2.834665
51	C	-1.797120	3.343737	0.535323
52	H	-2.449623	3.787208	1.287560
53	H	-1.124840	4.121839	0.167663
54	H	-2.423401	3.012782	-0.289356
55	C	0.894096	0.545121	0.628387
56	O	2.006009	0.973513	0.922463
57	N	0.535249	-0.750830	0.780089
58	H	-0.342300	-1.114398	0.415266
59	N	1.428589	-1.709854	1.225801
60	C	1.369786	-2.100529	2.650365
61	H	1.911420	-3.042007	2.694922
62	C	2.073956	-1.080681	3.542976
63	H	2.045156	-1.410249	4.582126
64	H	3.114220	-0.965870	3.243788
65	H	1.586126	-0.108093	3.479357

66	C	-0.077266	-2.338864	3.068411
67	H	-0.098777	-2.760005	4.072763
68	H	-0.575569	-3.030723	2.389773
69	H	-0.642344	-1.407290	3.084827
70	C	2.517658	-2.049106	0.449953
71	O	3.446634	-2.713380	0.892322
72	N	2.488272	-1.603219	-0.853149
73	H	1.730881	-1.067586	-1.263657
74	N	3.601365	-1.786382	-1.650501
75	C	3.753669	-3.103580	-2.256192
76	H	3.978378	-3.860788	-1.502617
77	H	4.559012	-3.066443	-2.981827
78	H	2.823512	-3.358425	-2.759920
79	C	4.721876	-0.991238	-1.426501
80	O	5.817202	-1.295685	-1.894838
81	N	4.496307	0.140603	-0.703465
82	H	3.554859	0.354233	-0.416422
83	C	5.564396	1.062633	-0.367882
84	H	6.478206	0.628706	-0.763990
85	C	5.364742	2.444787	-1.050375
86	H	5.189185	2.198474	-2.101249
87	C	4.141232	3.202509	-0.529640
88	H	4.277517	3.496941	0.512752
89	H	3.229681	2.609326	-0.587314
90	H	3.988368	4.110403	-1.114416
91	C	6.622631	3.311627	-0.971372
92	H	6.481215	4.227337	-1.547321
93	H	7.492279	2.788769	-1.372022
94	H	6.846223	3.588225	0.058684
95	C	5.807099	1.189336	1.143580
96	O	6.931281	1.463344	1.558992
97	N	4.755774	1.013617	1.966695
98	H	3.808319	0.866257	1.647290
99	H	4.906657	1.147052	2.952866

Compound **5**, conformation **5C +/+/–/–/–/–** (from NMR parameters-restrained molecular dynamics)

1	O	5.238902	1.304696	-0.566744
2	C	4.897541	2.663588	-0.065107
3	C	5.842927	3.549473	-0.865170
4	C	3.442387	2.982158	-0.389927
5	C	5.196788	2.744043	1.427259
6	C	4.584806	0.225845	-0.150198
7	O	3.724109	0.172094	0.709375
8	H	5.648287	3.451751	-1.932709
9	H	5.699105	4.590540	-0.579055
10	H	6.879397	3.275434	-0.671437
11	H	3.240236	2.807286	-1.446593
12	H	3.252122	4.033283	-0.176037
13	H	2.761720	2.381976	0.206001
14	H	6.226085	2.443703	1.622797
15	H	5.071139	3.774342	1.759964
16	H	4.526479	2.108223	1.998495
17	N	4.985955	-0.867624	-0.882419
18	H	5.698171	-0.765275	-1.587631
19	N	4.588704	-2.144941	-0.544740
20	C	5.457026	-2.930627	0.362431
21	H	5.003556	-3.917960	0.374875
22	C	6.862115	-3.035065	-0.222042
23	H	7.464635	-3.699344	0.396421
24	H	6.837262	-3.435988	-1.235377
25	H	7.357841	-2.063391	-0.241945
26	C	5.459155	-2.363872	1.780308
27	H	4.449491	-2.319556	2.183341
28	H	5.881763	-1.358935	1.800711
29	H	6.066807	-2.997099	2.427071
30	C	3.270387	-2.503965	-0.737141
31	O	2.769176	-3.496718	-0.232538
32	N	2.547721	-1.640376	-1.535704
33	H	2.988512	-0.900441	-2.055740
34	N	1.197932	-1.819784	-1.709399
35	C	0.766334	-2.746457	-2.747885
36	H	1.106976	-3.755779	-2.515622
37	H	-0.316478	-2.729231	-2.799894
38	H	1.181115	-2.433842	-3.705209
39	C	0.328732	-1.323620	-0.764820
40	O	-0.893579	-1.501483	-0.858491
41	N	0.867956	-0.591000	0.244349
42	H	1.868370	-0.457504	0.314884
43	C	0.023229	-0.113075	1.328695
44	H	-0.567685	-0.941205	1.723346
45	C	0.904944	0.448754	2.469250
46	H	1.609906	1.152645	2.020063
47	C	0.086959	1.193252	3.525763
48	H	0.744615	1.517731	4.332308
49	H	-0.681130	0.547048	3.953371
50	H	-0.407913	2.074526	3.121939
51	C	1.700894	-0.688625	3.118591
52	H	2.294780	-1.241673	2.394997
53	H	1.024225	-1.386922	3.615857
54	H	2.383395	-0.287316	3.868033
55	C	-1.027571	0.889253	0.841469
56	O	-2.122802	0.981623	1.369508
57	N	-0.654716	1.645892	-0.229179
58	H	0.226442	1.466460	-0.684012
59	N	-1.517441	2.522166	-0.860825
60	C	-1.451814	3.948195	-0.475217
61	H	-2.042083	4.457947	-1.231972
62	C	-2.079540	4.194591	0.894964
63	H	-2.084395	5.262874	1.114530
64	H	-1.515149	3.687483	1.677049
65	H	-3.103020	3.825080	0.920006

66	C	-0.011177	4.442149	-0.549998
67	H	0.421605	4.250802	-1.532177
68	H	0.611991	3.958544	0.202246
69	H	0.015830	5.515479	-0.365125
70	C	-2.634590	2.023638	-1.510668
71	O	-3.532506	2.754356	-1.906780
72	N	-2.642386	0.662559	-1.701068
73	H	-1.890912	0.038734	-1.420337
74	N	-3.704457	0.078085	-2.351853
75	C	-3.616272	-0.012342	-3.800262
76	H	-2.797552	-0.669783	-4.104172
77	H	-4.551268	-0.405174	-4.184037
78	H	-3.447452	0.983667	-4.206254
79	C	-4.627204	-0.660480	-1.631765
80	O	-5.476583	-1.342449	-2.208882
81	N	-4.527715	-0.574362	-0.277790
82	H	-3.861330	0.052452	0.145852
83	C	-5.400467	-1.330077	0.589007
84	H	-6.153914	-1.784121	-0.052636
85	C	-4.661464	-2.476650	1.337698
86	H	-5.433303	-3.048244	1.859870
87	C	-3.973567	-3.408249	0.337279
88	H	-4.673941	-3.772528	-0.415258
89	H	-3.160371	-2.892935	-0.175185
90	H	-3.550310	-4.269450	0.856101
91	C	-3.667176	-1.953191	2.375607
92	H	-3.156239	-2.785707	2.860882
93	H	-2.913715	-1.318080	1.911380
94	H	-4.160753	-1.365956	3.151035
95	C	-6.106730	-0.390589	1.574476
96	O	-5.709375	0.744963	1.803112
97	N	-7.177297	-0.925380	2.200094
98	H	-7.531151	-1.838120	1.975198
99	H	-7.670236	-0.378067	2.885454

Compound **5**, conformation **5D –/–/–/–/–** (from NMR parameters-restrained molecular dynamics)

1	O	5.240668	0.922583	0.074672
2	C	5.596914	2.082732	-0.785062
3	C	5.660453	1.628935	-2.238872
4	C	4.601051	3.213801	-0.564928
5	C	6.978219	2.457943	-0.265241
6	C	4.086632	0.276384	-0.056389
7	O	3.174670	0.543720	-0.815598
8	H	6.331725	0.776227	-2.339912
9	H	4.677343	1.352531	-2.609536
10	H	6.047333	2.444403	-2.849761
11	H	3.618794	2.956750	-0.948132
12	H	4.517558	3.444063	0.496815
13	H	4.955459	4.105875	-1.081260
14	H	7.363273	3.306372	-0.829426
15	H	7.669329	1.623155	-0.376971
16	H	6.929297	2.733794	0.787709
17	N	4.040091	-0.754260	0.861300
18	H	4.883275	-0.976651	1.369944
19	N	3.103139	-1.755986	0.717581
20	C	3.484856	-2.999990	0.007465
21	H	2.539471	-3.461484	-0.259714
22	C	4.241878	-2.680159	-1.275145
23	H	5.197871	-2.195342	-1.071830
24	H	3.643597	-2.046028	-1.924273
25	H	4.448777	-3.610502	-1.802832
26	C	4.269834	-3.921969	0.939528
27	H	3.689436	-4.152528	1.832706
28	H	5.212757	-3.464318	1.246637
29	H	4.505612	-4.857391	0.431673
30	C	1.902349	-1.651607	1.374971
31	O	1.025319	-2.494462	1.298753
32	N	1.748596	-0.469625	2.096479
33	H	2.570138	-0.011751	2.463834
34	N	0.569551	-0.271416	2.780605
35	C	0.303645	-1.065287	3.972984
36	H	-0.676307	-0.797992	4.351889
37	H	0.320869	-2.121676	3.715470
38	H	1.057314	-0.858835	4.734687
39	C	-0.271933	0.722519	2.352968
40	O	-1.361717	0.937031	2.903139
41	N	0.155723	1.470524	1.300178
42	H	1.000004	1.204403	0.819824
43	C	-0.667447	2.543984	0.768856
44	H	-1.013880	3.155380	1.603270
45	C	0.139414	3.432121	-0.192780
46	H	0.553521	2.780752	-0.967641
47	C	-0.769407	4.463173	-0.866447
48	H	-1.538972	3.993321	-1.478608
49	H	-1.261995	5.092634	-0.122385
50	H	-0.181858	5.110978	-1.516238
51	C	1.285000	4.122554	0.550802
52	H	1.876119	4.720615	-0.141964
53	H	1.955308	3.411122	1.029616
54	H	0.891514	4.788721	1.321589
55	C	-1.872300	1.913163	0.064821
56	O	-1.738759	1.173428	-0.902948
57	N	-3.073677	2.179170	0.633419
58	H	-3.099526	2.670066	1.514127
59	N	-4.236223	1.531594	0.251740
60	C	-5.149851	2.245560	-0.665816
61	H	-6.048478	1.634365	-0.676042
62	C	-5.487803	3.620408	-0.098877
63	H	-6.230791	4.102613	-0.733079
64	H	-4.607064	4.263142	-0.068778
65	H	-5.894722	3.539782	0.909239

66	C	-4.582785	2.320833	-2.081466
67	H	-5.299516	2.808918	-2.742486
68	H	-4.374601	1.324534	-2.466405
69	H	-3.657164	2.896189	-2.099856
70	C	-4.315381	0.155265	0.402433
71	O	-5.169457	-0.514082	-0.160894
72	N	-3.352539	-0.391385	1.220043
73	H	-2.762404	0.160755	1.836167
74	N	-3.268025	-1.757671	1.370546
75	C	-4.172690	-2.373722	2.329553
76	H	-3.947018	-3.432424	2.388485
77	H	-4.025276	-1.918340	3.308413
78	H	-5.210505	-2.237626	2.020370
79	C	-2.578101	-2.513475	0.430049
80	O	-2.534868	-3.739830	0.522291
81	N	-1.957751	-1.807058	-0.553844
82	H	-2.113646	-0.813692	-0.612651
83	C	-1.209650	-2.465411	-1.607496
84	H	-1.125216	-3.507900	-1.314441
85	C	-1.931900	-2.418572	-2.981036
86	H	-1.288002	-2.974196	-3.667216
87	C	-3.283476	-3.130438	-2.897486
88	H	-3.759897	-3.158280	-3.878438
89	H	-3.953294	-2.605982	-2.214057
90	H	-3.173518	-4.154827	-2.540335
91	C	-2.097924	-0.994722	-3.518472
92	H	-1.139157	-0.491230	-3.641202
93	H	-2.706208	-0.388240	-2.846695
94	H	-2.594728	-1.015210	-4.489182
95	C	0.239845	-1.983775	-1.751222
96	O	1.075883	-2.756170	-2.221774
97	N	0.530637	-0.722372	-1.400554
98	H	-0.173731	-0.074226	-1.081130
99	H	1.494568	-0.414610	-1.399738