SUPPORTING INFORMATION

Neighboring π-Amide Participation in Thioether Oxidation: Conformational Control

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EXPERIMENTAL PROCEDURES

NMR Experiments. The proline amide and diketopiperazine were analyzed by 1D and 2D NMR experiments performed on a Bruker DRX-600 NMR spectrometer operating at a ^{1}H frequency of 600.13 MHz. 1D 1H and 2D HSQC, HMBC, DQF-COSY and NOESY experiments gave unambiguous assignments for all ^{1}H and ^{13}C chemical shifts. In particular, 2D NOESY data were consistent with the X-ray crystal structures of these two compounds, indicating that the conformation in solution is not significantly different from the conformation in the crystalline state.

Methyl -6-*endo*-(methylthio)bicyclo[2.2.1]heptane-2-*endo*-carbonyl)pyrrolidine-2-carboxylate (5).

The previously reported[1] procedure for synthesis of 6-*endo*-(methylthio)bicyclo[2.2.1]heptane-2-*endo*-carboxamide was modified and used. To a solution of 6-*endo*-(methylthio)bicyclo[2.2.1] heptane-2-*endo*-carboxylic acid (200mg, 1.07 mmol) in THF (4 mL) at 0°C, was added thionyl chloride (0.117 mL, 1.61 mmol) and a drop of DMF. After the reaction was stirred for 6 h at 5-10°C, the solution was allowed to warm up to room temperature. The THF and excess thionyl chloride was evaporated off under reduced pressure. The crude acid chloride was dissolved in dry dichloromethane (5 mL) and added dropwise to the solution of $_{L}$-proline methyl ester hydrochloric acid (1.77g, 10.7 mmol) and TEA (3.00 mL, 21.4 mmol) in dry dichloromethane (30 mL) at 0°C. The resulting solution was allowed to warm up to room temperature and stirred overnight. The dichloromethane and excess TEA was evaporated under reduced pressure. The residue was dissolved in EtOAc (50 mL) and washed successively with satd. $NaHCO_3$ (50 mL), 1M HCl (50 mL), and brine (50 mL). The organic layer was dried (anhydr $MgSO_4$), filtered, and concentrated under reduced pressure. The crude product was purified by silica gel chromatography using ethyl acetate/chloroform (1:1) as eluent to give **1b** as a slightly brown oil (70% yield). ^{1}H NMR (500MHz, $CDCl_3$) δ(diastereomers +rotamers) 1.20 (m, 1.18H), 1.45-1.58 (m, 2.10H), 1.58-1.77 (m, 1.03H), 1.78-2.30 (m, 10.72H), 2.51 (dt, *J*=11.5, 4.0Hz, 0.19H), 2.75 (m, 0.45), 2.81-2.87 (m, 1.36H), 2.88-3.02 (m, 1.01H), 3.46-3.61 (m, 0.52H), 3.62-3.73 (m, 4.55H), 4.36 (dd, *J*=8.5, 2.5Hz, 0.49H), 4.55 (dd, *J*=8.0, 4.5Hz, 0.23H), 4.66 (dd, *J*=8.5, 2.0Hz, 0.17H); ^{13}C NMR (500MHz, $CDCl_3$) δ(diastereomers +rotamers) 13.87, 14.37, 16.91, 17.10, 17.27, 19.29, 21.22, 22.37, 25.30, 25.42, 29.11, 29.17, 30.82, 31.97, 32.38, 32.94, 33.37, 36.39, 36.91, 37.04, 37.17, 37.75, 42.56, 42.68, 42.87, 43.67, 43.83, 44.15, 44.43, 44.45, 45.74, 47.34, 47.38, 47.55, 48.25, 49.18, 49.33, 51.99, 52.19, 52.67, 58.94, 59.59, 59.85, 60.56, 172.37, 172.40, 172.73, 172.82, 173.26, 173.71; IR (neat) 1195, 1418, 1634, 1750, 2874, 2953, 3468 cm^{-1}; HRMS (GCT EI^{+}, *m/z*): Calcd. for $C_{15}H_{23}NO_3S$, 297.1399; Found: 297.1398.

Diastereomerically pure methyl 6-*endo*-(methylthio)bicyclo[2.2.1]heptane-2-*endo*-carbonyl)pyrrolidine-2-carboxylate (5). 6-*endo*-(methylthio)-bicyclo[2.2.1]heptane-2-*endo*-carboxylic acid (862 mg, 4.63 mmol) was dissolved in 10 mL of chloroform and the solution was heated to almost boiling. Then, (R)-(+)-methylbenzylamine was cautiously added to the

solution. The solution was allowed to cool to room temperature and stand for 2 d to crystallize. The white crystalline salt was filtered and washed with cold chloroform and then dried under vacuum. The ^{1}H NMR spectrum of this salt showed one peak for SMe (unlike the diastereomeric mixture whose ^{1}H NMR spectrum shows two peaks for SMe). The salt was partially dissolved in H_2O (20mL) and 1M HCl (20mL) to convert the amine salt into the free acid which was extracted with EtOAc (3×50 mL) and dried (anhydr $MgSO_4$). The EtOAc was removed under reduced pressure to obtain the enantiomerically pure carboxylic acid **7**. ^{1}H NMR spectroscopic analysis showed identical peaks with racemic carboxylic acid **7** and the melting point was 133-134°C. Following the procedure outlined above, the crude product was obtained and purified by silica gel chromatography using ethyl acetate/chloroform (1:1) as eluent to give diasteremerically pure **5** as a slightly brown oil (70% yield). The product was further purified by vacuum distillation (100°C) and recrystalized from ether: mp = 84-85°C; $[\alpha]_D^{25}$ = -109° (c = 1.00, MeOH) ^{1}H NMR (500MHz, $CDCl_3$) δ 1.26 (ddd, J=2.0, 6.5, 12.0Hz, 1H), 1.55 (m, 1H), 1.58 (m, 1H), 1.69 (m, 1H), 1.95-2.02 (m, 2H), 2.03 (s, 3H), 2.07-2.17 (m, 3H), 2.22-2.27 (m, 1H), 2.33 (t, J=4.5Hz, 1H), 2.86-2.92 (m, 2H), 2.99 (m, 1H), 3.67-3.78 (m, 2H), 3.72 (s, 3H), 4.41 (m, 1H); ^{13}C NMR (500MHz, $CDCl_3$) δ16.94, 25.32, 29.19, 32.97, 36.93, 37.19, 42.70, 43.68, 44.46, 47.40, 49.19, 52.21, 59.85, 172.32, 173.65; IR (neat) 1168, 1196, 1293, 1318, 1419, 1635, 1730, 1748, 2875, 2959cm^{-1}; HRMS (LCQ ESI$^+$, *m/z*): Calcd. for $C_{15}H_{24}NO_3S$ ($M+H^+$), 298.14732; Found: 298.14714.

X-ray Crystallographic Structure Study of 5. A crystal suitable for analysis by single crystal X-ray diffraction was selected and used for the structure study. The compound crystallized with one molecule per asymmetric unit, and four molecules per unit cell in the chiral space A clear colorless irregularly shaped crystal of $C_{15}H_{23}NO_3S$, with approximate dimensions 0.30 mm x 0.32 mm x 0.34 mm, was used for the X-ray crystallographic analysis. The X-ray intensity data were measured using APEX2.[2] The total exposure time was 7.14 h. The frames were integrated with the Bruker SAINT[3] package using a narrow-frame algorithm. The integration of the data using an orthorhombic unit cell yielded a total of 72366 reflections to a maximum θ angle of 33.75° (0.64 Å resolution), of which 5744 were independent (average redundancy 12.6, completeness = 97.8%, R_{int} = 3.54%, R_{sig} = 1.87%) and 5395 (93.92%) were greater than $2\sigma(F^2)$. The final cell constants of a = 6.3439(4) Å, b = 12.6464(7) Å, c = 18.5358(11) Å, volume = 1487.08(15) Å^3, are based upon the refinement of the XYZ-centroids of 9483 reflections above 20 σ(I) with 4.391° < 2θ < 65.25°. Data were corrected for absorption effects using the multi-scan method (SADABS)[3]. The ratio of minimum to maximum apparent transmission was 0.933. The calculated minimum and maximum transmission coefficients (based on crystal size) are 0.9275 and 0.9356.

The structure was solved and refined using the Bruker SHELXTL[5] Software Package, using the space group P2(1)2(1)2(1) with Z = 4 for the formula unit, $C_{15}H_{23}NO_3S$. The final anisotropic full-matrix least-squares refinement on F^2 with 183 variables converged at R1 = 2.78%, for the observed data and wR2 = 7.30% for all data. The goodness-of-fit was 1.042. The largest peak in the final difference electron density synthesis was 0.351 e$^-$/Å^3 and the largest hole was -0.185 e$^-$

/Å^3 with an RMS deviation of 0.046 e$^-$/Å^3. On the basis of the final model, the calculated density was 1.328 g/cm^3 and F(000), 640 e$^-$. group $P2_12_12_1$. The chirality about C12 has been determined to be S.

Sample Preparation for Capillary LC-MS analysis.
LC-MS analyses of the reaction mixtures were performed on a capillary Ultra Performance Liquid Chromatography (UPLC) System (Waters Corporation, Milford, MA, USA). 10 µL of each sample were injected onto a C18 Vydac column (25 cm x 0.5 mm, 3.5 µm, Grace, Deerfield, IL), and eluted with a linear gradient delivered at the rate of 35 µL min^{-1}. Mobile phases consisted of water/acetonitrile/formic acid at a ratio of 99%, 1%, 0.08% (v:v:v) for solvent A and a ratio of 1%, 99%, 0.06% (v:v:v) for solvent B. The following linear gradient was set: 1-50% of solvent B within 30 min.

Nano-Electrospray Ionization Time-of-Flight MS (ESI-TOF-MS).

ESI-MS spectra of **1b** and its oxidation products (Fig. S2 and Table S9) were acquired on a QTOF Premier (Waters Corp., Milford, MA). The QTOF Premier instrument was operated for maximum resolution with all lenses optimized on the $[M + H]^+$ ion from the Leucine-enkephalin. The capillary voltage was set to 2.5 kV. The source and desolvation temperatures were set at 110^{o}C and 250^{o}C, respectively. The cone and desolvation gas flow were set to 36 L/hr and 800 L/hr, respectively. The cone voltage was 45 V and Ar was admitted to the collision cell. The spectra were acquired using a mass range of 50-2,000 amu (amu = atomic mass unit). The data were accumulated for 0.5 sec per cycle. The peak areas of the products were used to calculate their relative ratios.

Electrochemical Studies of 1b and 5. The electrochemistry of both compounds was carried out in dry acetonitrile (Acroseal™, Acros Organics) with 0.1 M $NaClO_4$ as supporting electrolyte. A 2 mm Pt electrode served as the working electrode and as the auxiliary electrode a 3mm glassy carbon electrode (3 mm) was employed. The reference electrode was a Ag/Ag^+ (0.1M $AgNO_3$) electrode in acetonitrile. The reference electrode was routinely calibrated against a 1 mM solution of ferrocene. Each electrode was isolated in a separated compartment H-cell. The potentiostat was a CH Instruments Model 6207.

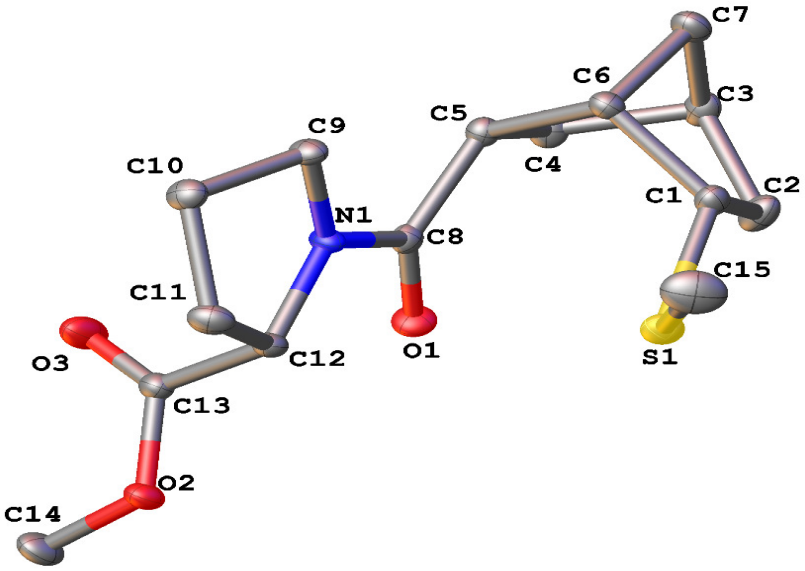


Figure S1. ORTEP[6] Drawing of **5.** Thermal ellipsoids are shown at 50% probability.

Tables of x-ray crystallographic parameters, atomic coordinates, bond lengths, bond angles, and torsion angles follow.

Table S1. Crystallographic parameters**.**

Chemical formula	$C_{15}H_{23}NO_3S$	
Formula weight	297.41	
Temperature	102(2) K	
Wavelength	0.71073 Å	
Crystal size	0.300 x 0.320 x 0.340 mm	
Crystal habit	clear colorless irregular	
Crystal system	orthorhombic	
Space group	P2(1)2(1)2(1)	
Unit cell dimensions	a = 6.3439(4) Å	α = 90°
	b = 12.6464(7) Å	β = 90°
	c = 18.5358(11) Å	γ = 90°
Volume	1487.08(15) $Å^3$	
Z	4	
Density (calculated)	1.328 g/cm^3	
Absorption coefficient	0.225 mm^{-1}	
F(000)	640	

Theta range for data collection	1.95 to 33.75°
Index ranges	-9<=h<=9, -19<=k<=19, -28<=l<=28
Reflections collected	72366
Independent reflections	5744 [R(int) = 0.0354]
Coverage of independent reflections	97.8%
Absorption correction	multi-scan
Max. and min. transmission	0.9356 and 0.9275
Structure solution technique	direct methods
Structure solution program	SHELXS-97 (Sheldrick, 2008)
Refinement method	Full-matrix least-squares on F2
Refinement program	SHELXL-97 (Sheldrick, 2008)
Function minimized	Σ w(Fo2 - Fc2)2
Data / restraints / parameters	5744 / 0 / 183
Goodness-of-fit on F2	1.042
Δ/σmax	0.002
Final R indices	5395 data; I>2σ(I) R1 = 0.0278, wR2 = 0.0710
	all data R1 = 0.0316, wR2 = 0.0730
Weighting scheme	$w=1/[\sigma^2(F_o^2)+(0.0450P)^2+0.1609P]$
Absolute structure parameter	-0.0(0)
Largest diff. peak and hole	0.351 and -0.185 eÅ^{-3}
R.M.S. deviation from mean	0.046 eÅ^{-3}

Table S2. Atomic coordinates (Å) and equivalent isotropic atomic displacement parameters ($Å^2$) for **5**.

U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x/a	**y/b**	**z/c**	**U(eq)**
S1	0.77954(4)	0.393396(17)	0.942737(12)	0.01741(5)
O2	0.79550(11)	0.70384(5)	0.73852(3)	0.01725(12)
O3	0.57791(14)	0.79771(6)	0.80944(4)	0.02612(17)
O1	0.79459(11)	0.65260(5)	0.93471(4)	0.01763(12)
N1	0.48548(11)	0.60599(6)	0.88585(4)	0.01292(12)
C15	0.6122(2)	0.28535(10)	0.91681(7)	0.0311(2)
C1	0.67025(14)	0.41918(7)	0.03147(5)	0.01522(15)
C6	0.47229(13)	0.48883(7)	0.03853(4)	0.01313(14)
C5	0.51346(13)	0.60644(7)	0.01750(4)	0.01296(13)
C8	0.61128(13)	0.62346(6)	0.94362(5)	0.01261(13)
C12	0.57935(13)	0.60518(7)	0.81443(4)	0.01348(14)
C13	0.64749(14)	0.71444(7)	0.79003(5)	0.01426(14)
C14	0.87714(18)	0.80071(8)	0.70932(6)	0.02327(19)
C2	0.82715(16)	0.47300(8)	0.08405(5)	0.02008(17)
C3	0.68615(15)	0.54974(7)	0.12694(5)	0.01737(16)
C4	0.65221(16)	0.64841(7)	0.08022(5)	0.01763(16)
C7	0.46715(15)	0.49788(8)	0.12145(5)	0.01773(16)
C11	0.40240(16)	0.56299(8)	0.76541(5)	0.01798(16)
C10	0.20159(15)	0.58772(7)	0.80766(5)	0.01679(15)
C9	0.26601(14)	0.56930(7)	0.88572(4)	0.01443(15)

Table S3. Bond lengths (Å).

S1-C15	1.7958(12)	S1-C1	1.8144(9)
O2-C13	1.3458(10)	O2-C14	1.4360(11)
O3-C13	1.1971(11)	O1-C8	1.2310(10)
N1-C8	1.3536(11)	N1-C12	1.4516(10)
N1-C9	1.4676(11)	C15-H1A	0.98
C15-H1B	0.98	C15-H1C	0.98
C1-C6	1.5396(12)	C1-C2	1.5505(13)
C1-H2	1.0	C6-C7	1.5417(12)
C6-C5	1.5596(12)	C6-H3	1.0
C5-C8	1.5188(12)	C5-C4	1.5518(12)
C5-H4	1.0	C12-C13	1.5168(12)
C12-C11	1.5397(13)	C12-H6	1.0
C14-H8A	0.98	C14-H8B	0.98
C14-H8C	0.98	C2-C3	1.5408(13)
C2-H9A	0.99	C2-H9B	0.99
C3-C4	1.5340(13)	C3-C7	1.5398(14)
C3-H10	1.0	C4-H11A	0.99
C4-H11B	0.99	C7-H12A	0.99
C7-H12B	0.99	C11-C10	1.5278(14)
C11-H13A	0.99	C11-H13B	0.99
C10-C9	1.5215(12)	C10-H14A	0.99
C10-H14B	0.99	C9-H15A	0.99
C9-H15B	0.99		

Table S4. Bond angles (°).

C15-S1-C1	98.83(5)	C13-O2-C14	115.73(7)
C8-N1-C12	118.73(7)	C8-N1-C9	127.75(7)
C12-N1-C9	112.67(7)	S1-C15-H1A	109.5
S1-C15-H1B	109.5	H1A-C15-H1B	109.5
S1-C15-H1C	109.5	H1A-C15-H1C	109.5
H1B-C15-H1C	109.5	C6-C1-C2	102.65(7)
C6-C1-S1	119.45(6)	C2-C1-S1	113.79(6)
C6-C1-H2	106.7	C2-C1-H2	106.7
S1-C1-H2	106.7	C1-C6-C7	98.31(7)
C1-C6-C5	112.82(7)	C7-C6-C5	100.49(7)
C1-C6-H3	114.4	C7-C6-H3	114.4
C5-C6-H3	114.4	C8-C5-C4	113.29(7)
C8-C5-C6	115.40(7)	C4-C5-C6	103.53(7)
C8-C5-H4	108.1	C4-C5-H4	108.1
C6-C5-H4	108.1	O1-C8-N1	119.98(8)
O1-C8-C5	123.32(8)	N1-C8-C5	116.70(7)
N1-C12-C13	112.49(7)	N1-C12-C11	103.98(7)
C13-C12-C11	110.33(7)	N1-C12-H6	110.0
C13-C12-H6	110.0	C11-C12-H6	110.0
O3-C13-O2	123.92(8)	O3-C13-C12	127.34(8)
O2-C13-C12	108.64(7)	O2-C14-H8A	109.5
O2-C14-H8B	109.5	H8A-C14-H8B	109.5
O2-C14-H8C	109.5	H8A-C14-H8C	109.5
H8B-C14-H8C	109.5	C3-C2-C1	103.19(7)
C3-C2-H9A	111.1	C1-C2-H9A	111.1
C3-C2-H9B	111.1	C1-C2-H9B	111.1
H9A-C2-H9B	109.1	C4-C3-C2	107.62(8)
C4-C3-C7	100.52(7)	C2-C3-C7	102.79(7)
C4-C3-H10	114.8	C2-C3-H10	114.8
C7-C3-H10	114.8	C3-C4-C5	102.96(7)

C3-C4-H11A	111.2	C5-C4-H11A	111.2
C3-C4-H11B	111.2	C5-C4-H11B	111.2
H11A-C4-H11B	109.1	C3-C7-C6	94.49(7)
C3-C7-H12A	112.8	C6-C7-H12A	112.8
C3-C7-H12B	112.8	C6-C7-H12B	112.8
H12A-C7-H12B	110.3	C10-C11-C12	103.56(7)
C10-C11-H13A	111.0	C12-C11-H13A	111.0
C10-C11-H13B	111.0	C12-C11-H13B	111.0
H13A-C11-H13B	109.0	C9-C10-C11	103.43(7)
C9-C10-H14A	111.1	C11-C10-H14A	111.1
C9-C10-H14B	111.1	C11-C10-H14B	111.1
H14A-C10-H14B	109.0	N1-C9-C10	102.00(7)
N1-C9-H15A	111.4	C10-C9-H15A	111.4
N1-C9-H15B	111.4	C10-C9-H15B	111.4
H15A-C9-H15B	109.2		

Table S5. Torsion angles (°).

C15-S1-C1-C6	-83.36(8)	C15-S1-C1-C2	155.05(8)
C2-C1-C6-C7	-45.44(8)	S1-C1-C6-C7	-172.42(6)
C2-C1-C6-C5	59.68(9)	S1-C1-C6-C5	-67.30(9)
C1-C6-C5-C8	53.51(9)	C7-C6-C5-C8	157.23(7)
C1-C6-C5-C4	-70.85(8)	C7-C6-C5-C4	32.88(8)
C12-N1-C8-O1	10.03(12)	C9-N1-C8-O1	178.67(8)
C12-N1-C8-C5	-170.62(7)	C9-N1-C8-C5	-1.98(12)
C4-C5-C8-O1	10.43(11)	C6-C5-C8-O1	-108.67(9)
C4-C5-C8-N1	-168.90(8)	C6-C5-C8-N1	72.00(9)
C8-N1-C12-C13	-70.94(10)	C9-N1-C12-C13	118.78(8)
C8-N1-C12-C11	169.68(8)	C9-N1-C12-C11	-0.60(9)
C14-O2-C13-O3	3.14(14)	C14-O2-C13-C12	179.90(8)
N1-C12-C13-O3	-25.41(13)	C11-C12-C13-O3	90.20(12)
N1-C12-C13-O2	157.98(7)	C11-C12-C13-O2	-86.41(9)
C6-C1-C2-C3	12.40(9)	S1-C1-C2-C3	142.91(6)
C1-C2-C3-C4	-80.26(9)	C1-C2-C3-C7	25.32(9)
C2-C3-C4-C5	68.49(9)	C7-C3-C4-C5	-38.69(8)
C8-C5-C4-C3	-122.29(8)	C6-C5-C4-C3	3.43(9)
C4-C3-C7-C6	58.39(7)	C2-C3-C7-C6	-52.58(8)
C1-C6-C7-C3	59.68(7)	C5-C6-C7-C3	-55.51(7)
N1-C12-C11-C10	23.11(9)	C13-C12-C11-C10	-97.73(8)
C12-C11-C10-C9	-36.66(9)	C8-N1-C9-C10	168.68(8)
C12-N1-C9-C10	-22.11(9)	C11-C10-C9-N1	35.58(8)

Table S6. Anisotropic atomic displacement parameters (Å^2).

The anisotropic atomic displacement factor exponent takes the form: $-2\pi^2[h^2 a^{*2} U_{11} + ... + 2 h k a^* b^* U_{12}]$

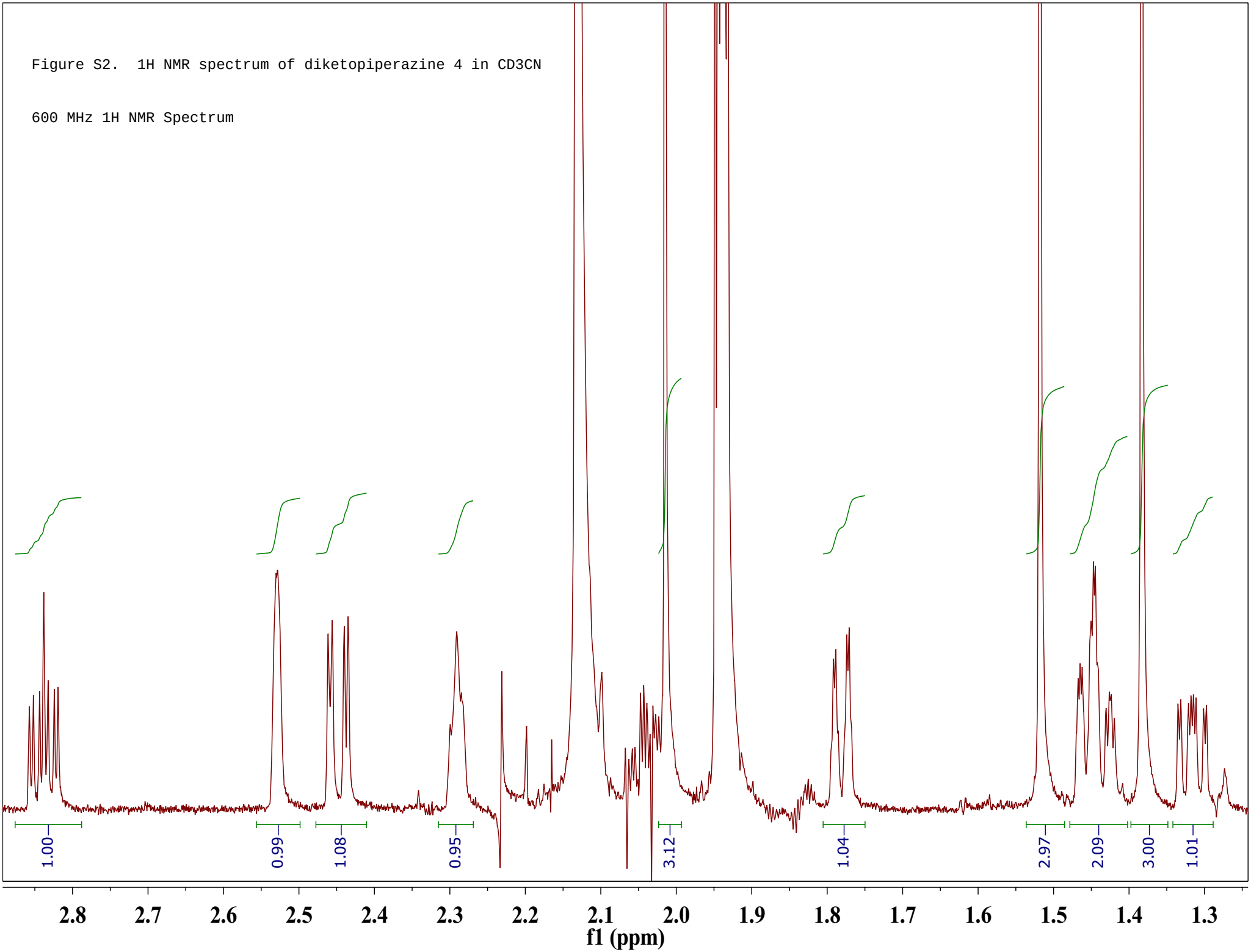
	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
S1	0.01959(10)	0.01588(9)	0.01674(9)	-0.00321(7)	0.00333(8)	0.00158(8)
O2	0.0180(3)	0.0160(3)	0.0177(3)	0.0028(2)	0.0070(2)	0.0002(2)
O3	0.0331(4)	0.0162(3)	0.0290(4)	0.0034(3)	0.0149(3)	0.0049(3)
O1	0.0119(3)	0.0187(3)	0.0223(3)	0.0002(2)	0.0001(2)	-0.0040(2)
N1	0.0098(3)	0.0172(3)	0.0117(3)	0.0017(3)	0.0011(2)	-0.0014(3)
C15	0.0346(6)	0.0289(5)	0.0297(5)	-0.0133(4)	0.0030(5)	-0.0081(5)
C1	0.0177(4)	0.0142(3)	0.0138(3)	0.0003(3)	0.0009(3)	0.0030(3)
C6	0.0137(3)	0.0138(3)	0.0119(3)	0.0003(3)	0.0010(3)	-0.0010(3)
C5	0.0137(3)	0.0123(3)	0.0129(3)	-0.0005(3)	-0.0009(3)	0.0005(3)
C8	0.0122(3)	0.0104(3)	0.0153(3)	0.0008(3)	-0.0010(3)	-0.0001(2)
C12	0.0125(3)	0.0140(3)	0.0139(3)	0.0014(3)	0.0030(3)	0.0007(3)
C13	0.0132(3)	0.0163(3)	0.0132(3)	0.0022(3)	0.0014(3)	0.0010(3)
C14	0.0266(5)	0.0191(4)	0.0240(4)	0.0051(3)	0.0091(4)	-0.0030(4)
C2	0.0188(4)	0.0237(4)	0.0177(4)	-0.0038(3)	-0.0046(3)	0.0072(3)
C3	0.0198(4)	0.0195(4)	0.0128(3)	-0.0020(3)	-0.0033(3)	0.0039(3)
C4	0.0213(4)	0.0155(3)	0.0161(3)	-0.0031(3)	-0.0044(3)	-0.0010(3)
C7	0.0215(4)	0.0197(4)	0.0119(3)	0.0003(3)	0.0025(3)	0.0016(3)
C11	0.0183(4)	0.0216(4)	0.0141(4)	-0.0036(3)	0.0023(3)	-0.0028(3)
C10	0.0137(3)	0.0217(4)	0.0149(3)	-0.0015(3)	-0.0021(3)	0.0010(3)
C9	0.0104(3)	0.0189(3)	0.0141(3)	0.0001(3)	0.0004(3)	-0.0006(3)

Table S7. Hydrogen atomic coordinates and isotropic atomic displacement parameters ($Å^2$).

	x/a	y/b	z/c	U(eq)
H1A	0.6400	0.2245	0.9481	0.047
H1B	0.6411	0.2661	0.8666	0.047
H1C	0.4643	0.3066	0.9216	0.047
H2	0.6341	0.3489	1.0529	0.018
H3	0.3421	0.4576	1.0168	0.016
H4	0.3757	0.6449	1.0189	0.016
H6	0.7024	0.5558	0.8134	0.016
H8A	0.7604	0.8440	0.6913	0.035
H8B	0.9741	0.7847	0.6696	0.035
H8C	0.9526	0.8395	0.7471	0.035
H9A	0.8941	0.4204	1.1163	0.024
H9B	0.9384	0.5116	1.0574	0.024
H10	0.7348	0.5644	1.1773	0.021
H11A	0.7879	0.6765	1.0621	0.021
H11B	0.5785	0.7046	1.1076	0.021
H12A	0.3525	0.5443	1.1391	0.021
H12B	0.4604	0.4282	1.1457	0.021
H13A	0.4026	0.5995	0.7182	0.022
H13B	0.4175	0.4860	0.7574	0.022
H14A	0.1567	0.6618	0.7999	0.02
H14B	0.0853	0.5398	0.7934	0.02
H15A	0.1780	0.6112	0.9193	0.017
H15B	0.2563	0.4936	0.8988	0.017

Figure S2. 1H NMR spectrum of diketopiperazine 4 in CD3CN

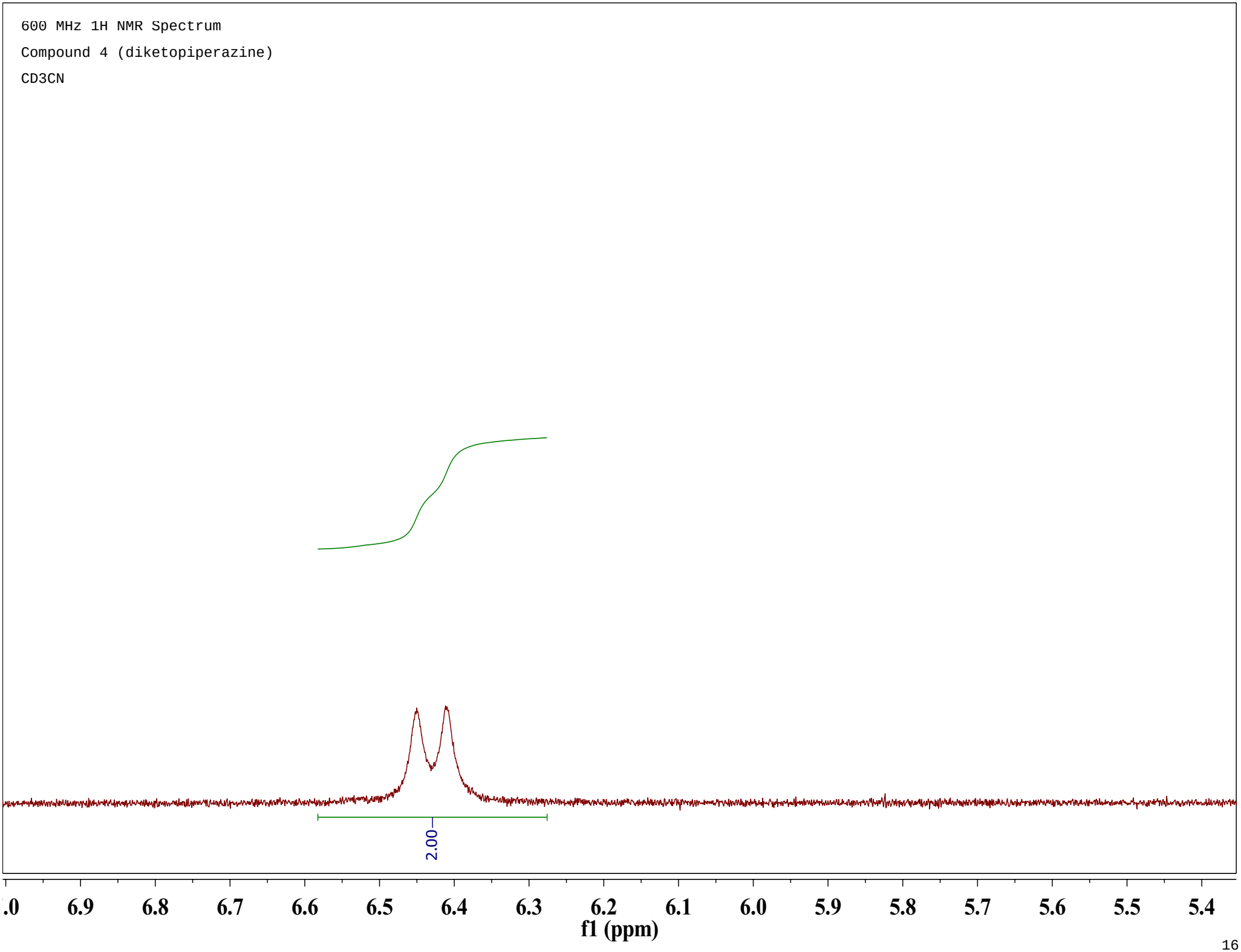
600 MHz 1H NMR Spectrum



600 MHz 1H NMR Spectrum

Compound 4 (diketopiperazine)

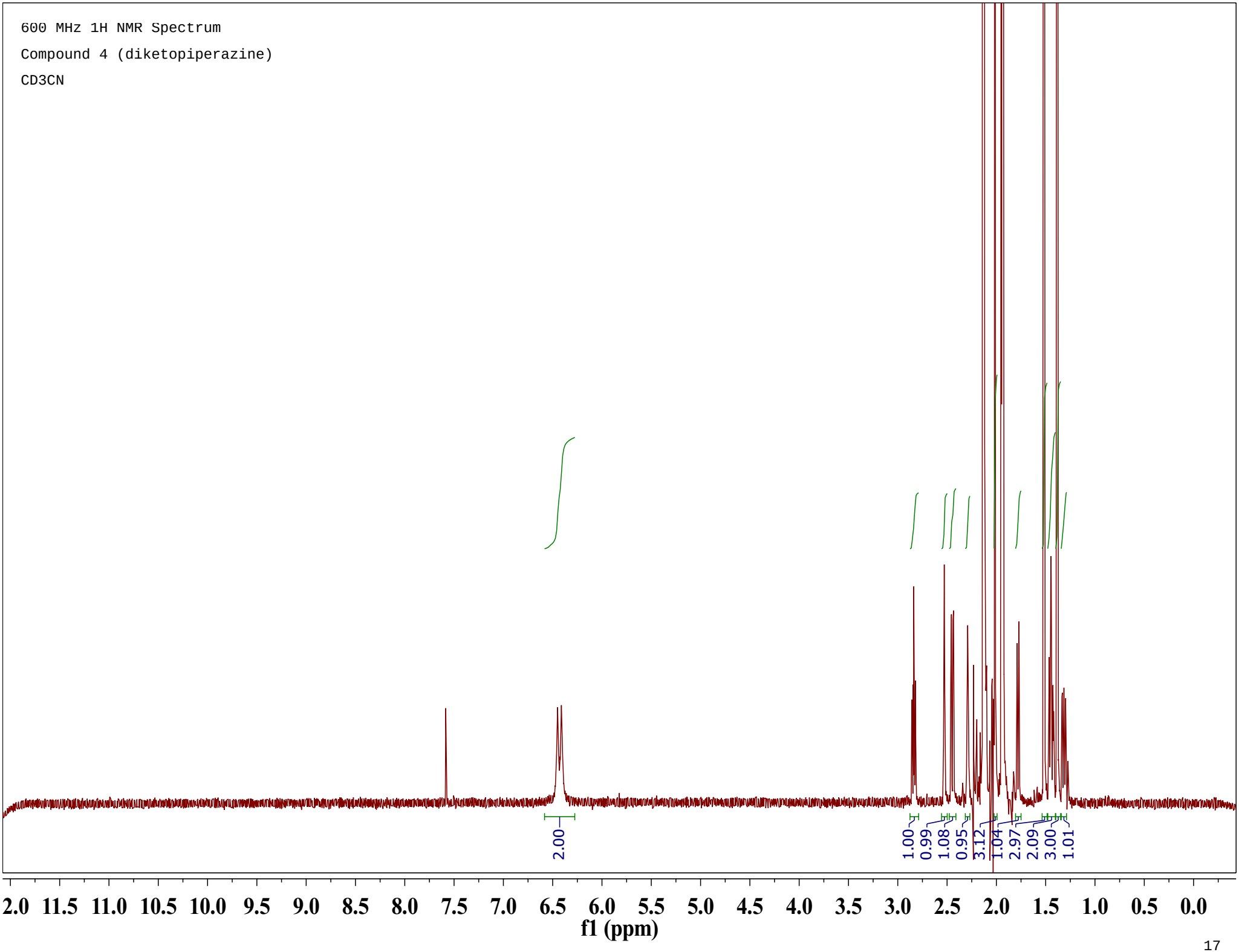
CD3CN



600 MHz 1H NMR Spectrum

Compound 4 (diketopiperazine)

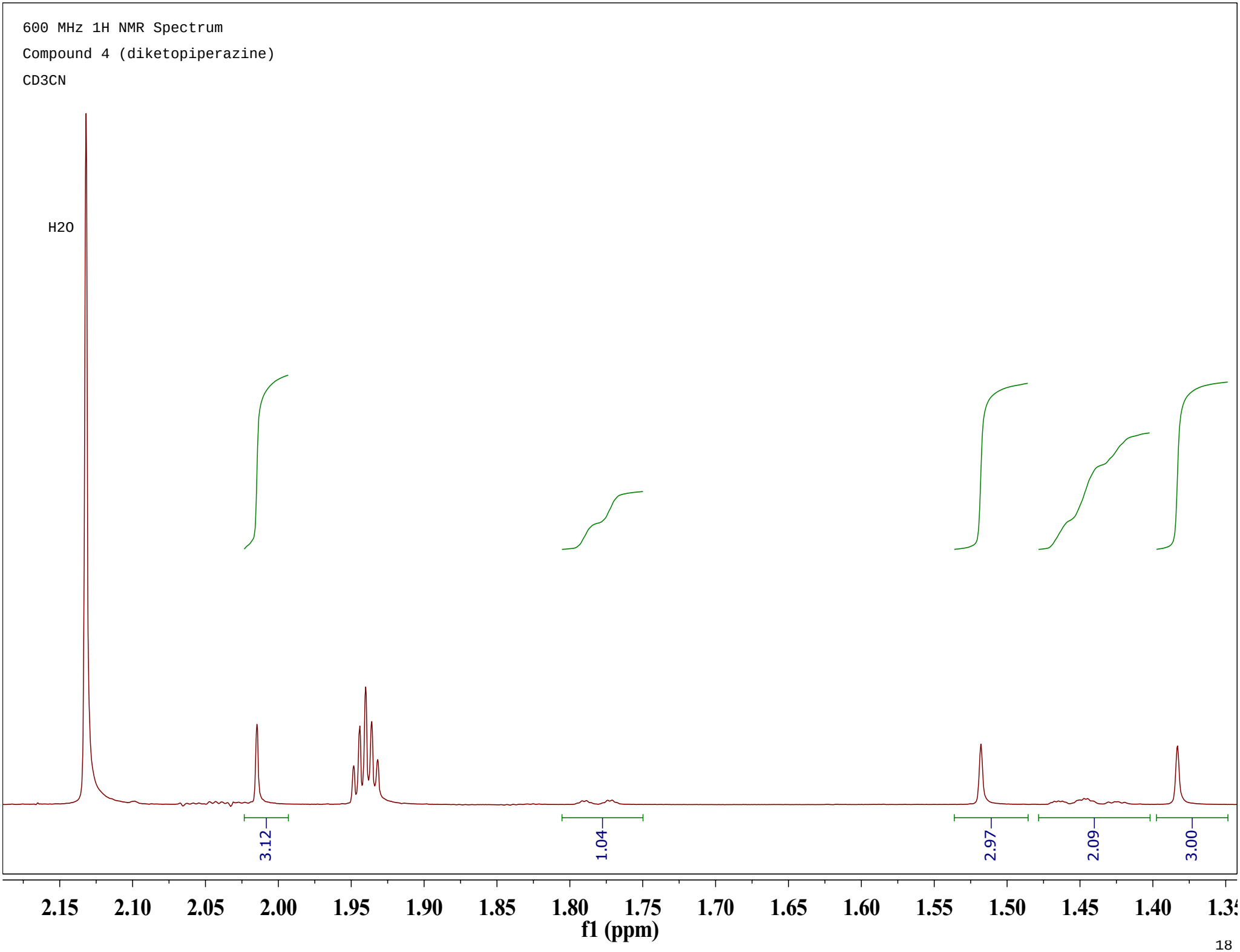
CD3CN



600 MHz 1H NMR Spectrum

Compound 4 (diketopiperazine)

CD3CN



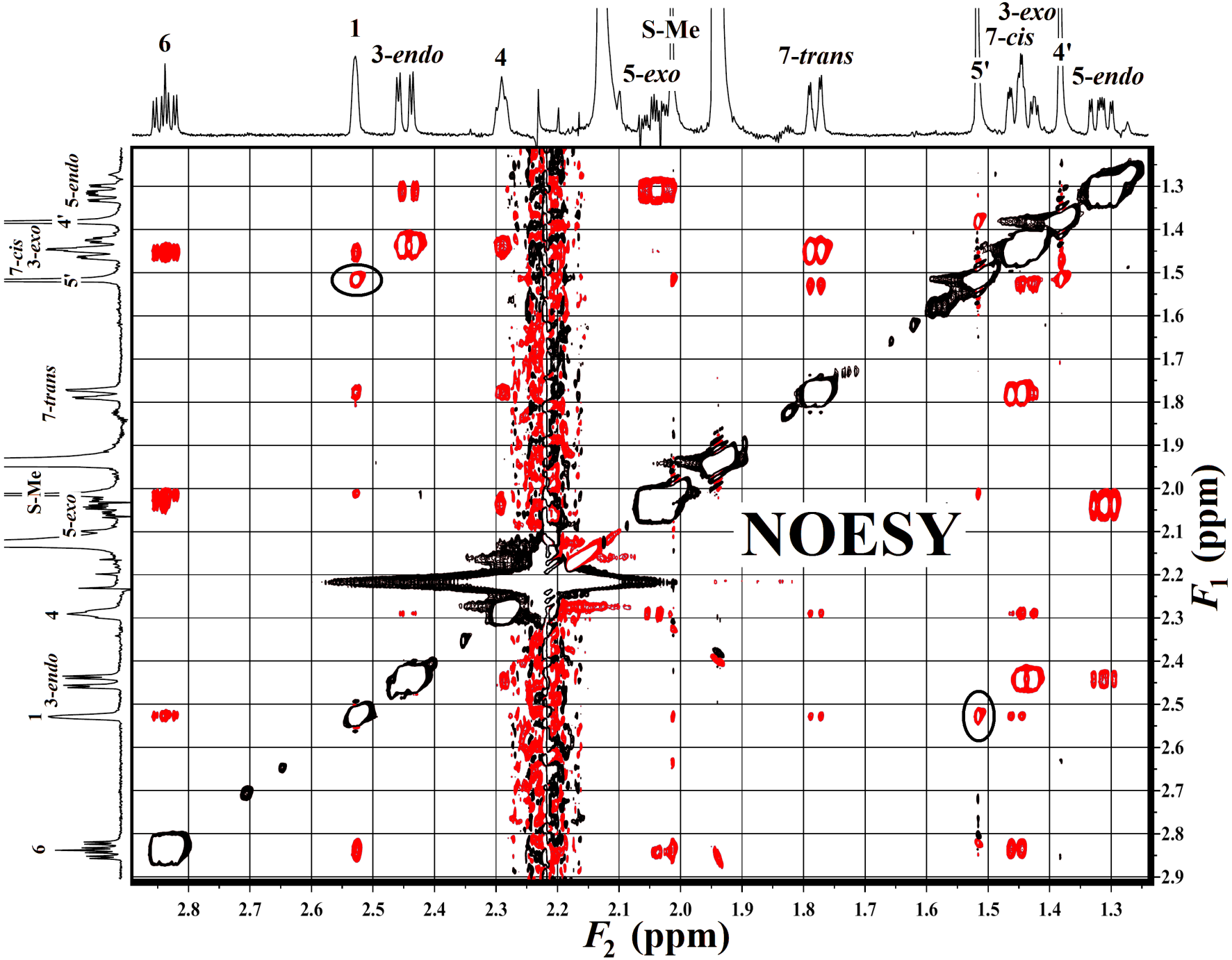


Figure S3. 600 MHz NOESY spectrum of diketopiperazine **4** in CD_3CN (τ_m = 0.9 s).

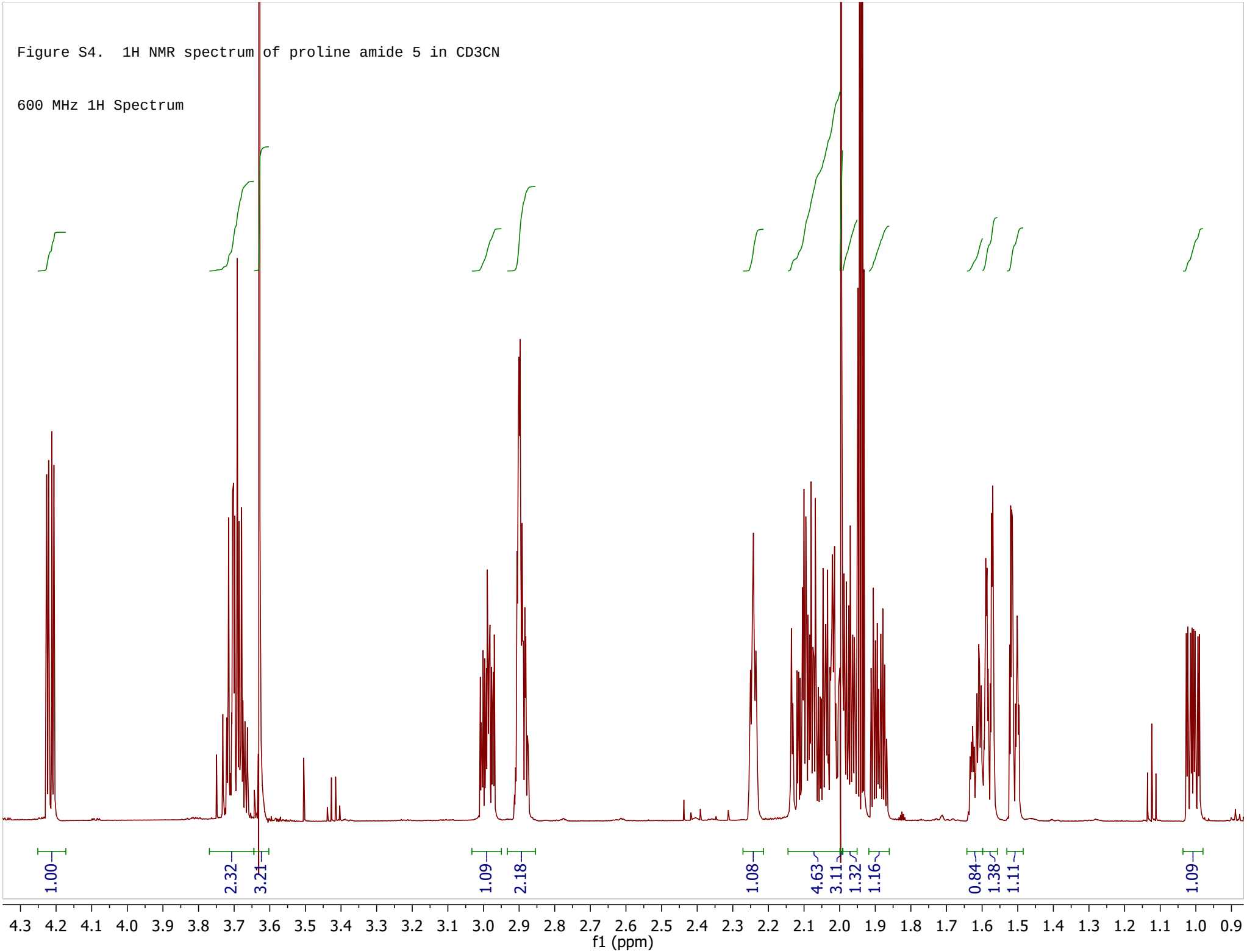
Table S8. NMR Data for diketopiperazine **4** in CD_3CN.[a]

Position	δ ^{1}H	Mult.	*J*	Int.	δ ^{13}C	Type	HMBC	COSY	NOESY[b]
1	2.528	br. s		1H	56.60	CH	C3,4,5	(4),6,7-*cis*,(7-*trans*)	3,SMe,6,7-*cis*,7-*trans*
2	----	----	----	----	64.54	C_q	----	----	----
3-exo	1.433	ddd	12.8,4.1,2.5	1H	46.15	CH_2	C2,5	3-*endo*,4,5-*exo*	3-*endo*,4
3-endo	2.450	dd	12.8,3.3	1H	"	"	C1,2,4,5,7,1′	*3-exo*,7-*cis*	3-*exo*,4,5-*endo*
4	2.289	br. t	5.1	1H	37.72	CH	----	(1,3-*exo*),5-*exo*,(7-*trans)*	3-*exo*,5-*exo*,5-*endo*,7-*trans*
5-exo	2.039	m	----	1H	34.05	CH_2	C3	3-*exo*,4,5-*endo*,6	4,5-*endo*,6
5-endo	1.313	ddd	12.2,8.2,2.2	1H	"	"	C3,4,6,7	5-*exo*,6,7-*trans*	3-*endo*,5-*exo*
6	2.837	ddd	11.4,8.2,3.2	1H	50.37	CH	C1,2,5,7	1,*5-exo*,*5-endo*	1,5-*exo*,7-*cis*,SMe
7-cis[c]	1.455	ddt	10.4,3.3,1.5	1H	40.84	CH_2	C3	3-*endo*,7-*trans*	1,6,7-*trans*
7-trans	1.781	dq	10.4,1.9	1H	"	CH_2	C5,6	(1,4),5-*endo*,7-*cis*	1,4,7-*cis*
SMe	2.016	s	----	3H	18.72	CH_3	C6	----	1,6
1'	----		----	----	170.81	C_q	----	----	----
2'	----	----	----	----	57.82	C_q	----	----	----
3'	----	----	----	----	174.08	C_q	----	----	----
4'	1.383	s	----	3H	28.73	CH_3	C2',3',5'	5'	5'
5'	1.519	s	----	3H	29.80	CH_3	C2′,3′,4′	4'	1,4'
HN	6.410	br. s	----	1H			----	----	----
HN	6.450	br. s	----	1H			----	----	----

[a] Bruker DRX-600 (^{1}H = 600.13 MHz), TXI (HCN 3-axis gradient 5 mm) probe, 25°C with reference ^{1}H = δ 1.94 ($C\underline{H}D_2CN$); ^{13}C = δ 118.69 ($CHD_2\underline{C}N$) [b] 0.9 s mixing time [c] *cis* to the SMe substitutent

Figure S4. 1H NMR spectrum of proline amide 5 in CD3CN

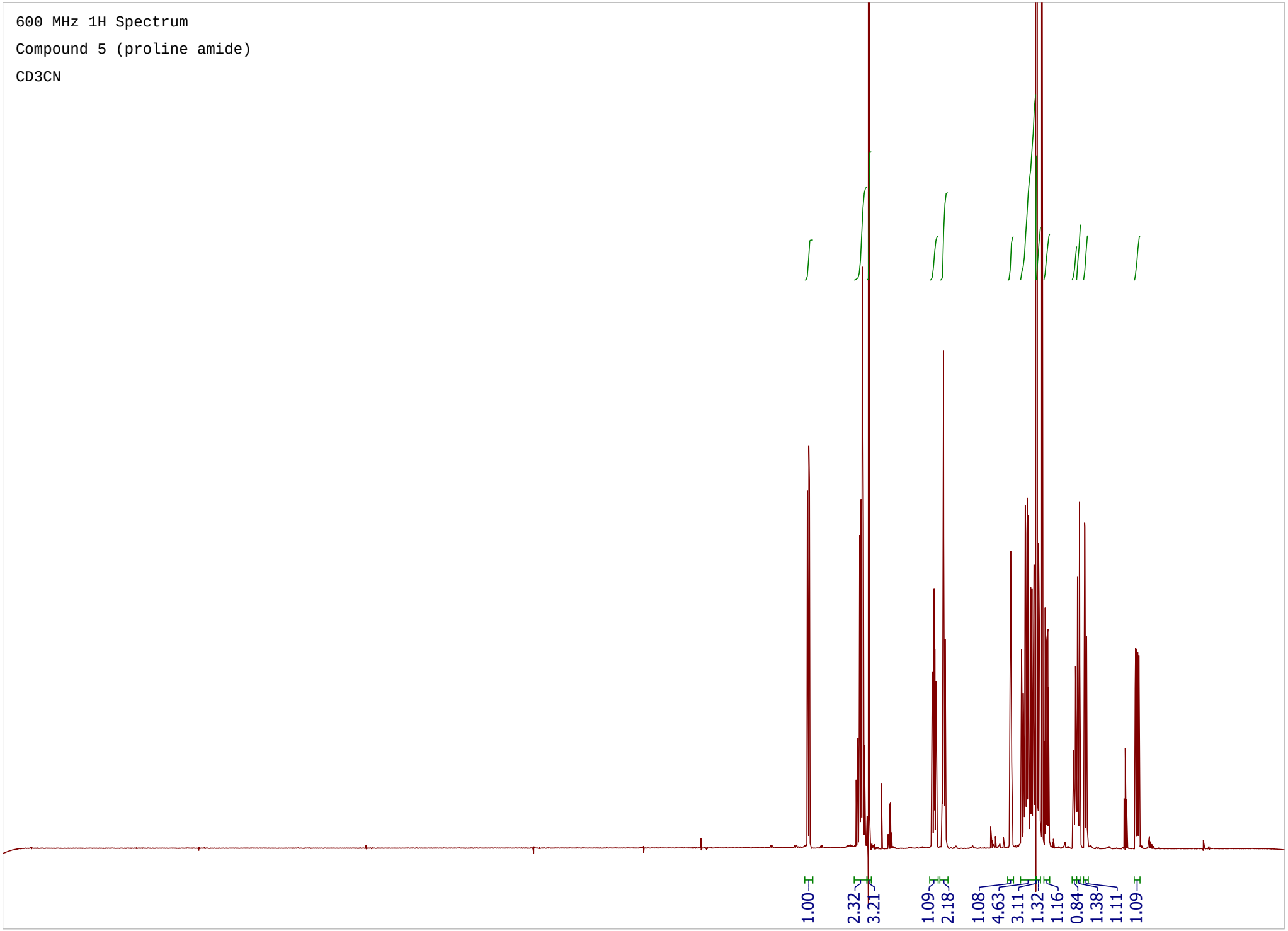
600 MHz 1H Spectrum



600 MHz 1H Spectrum

Compound 5 (proline amide)

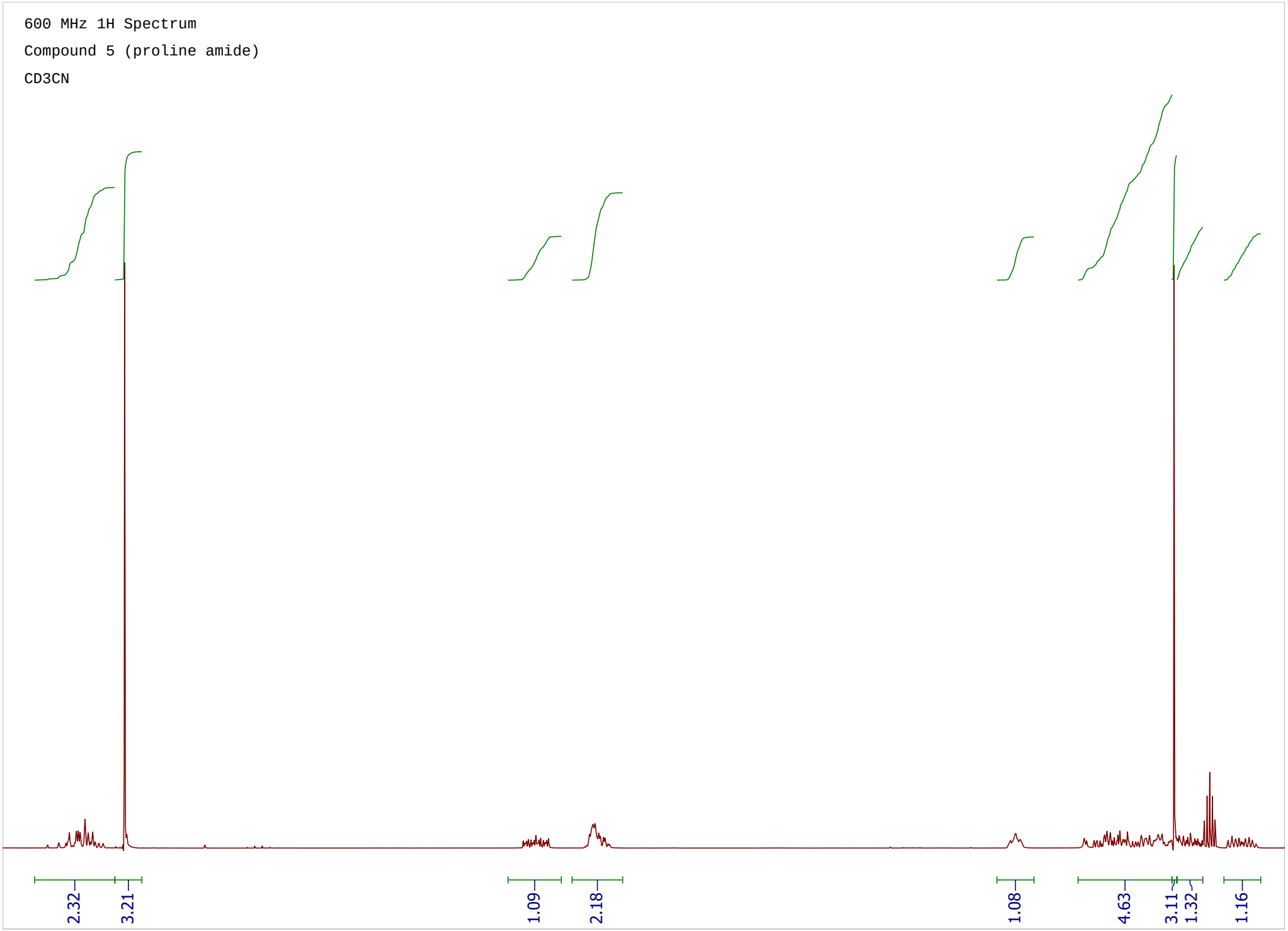
CD3CN



600 MHz 1H Spectrum

Compound 5 (proline amide)

CD3CN



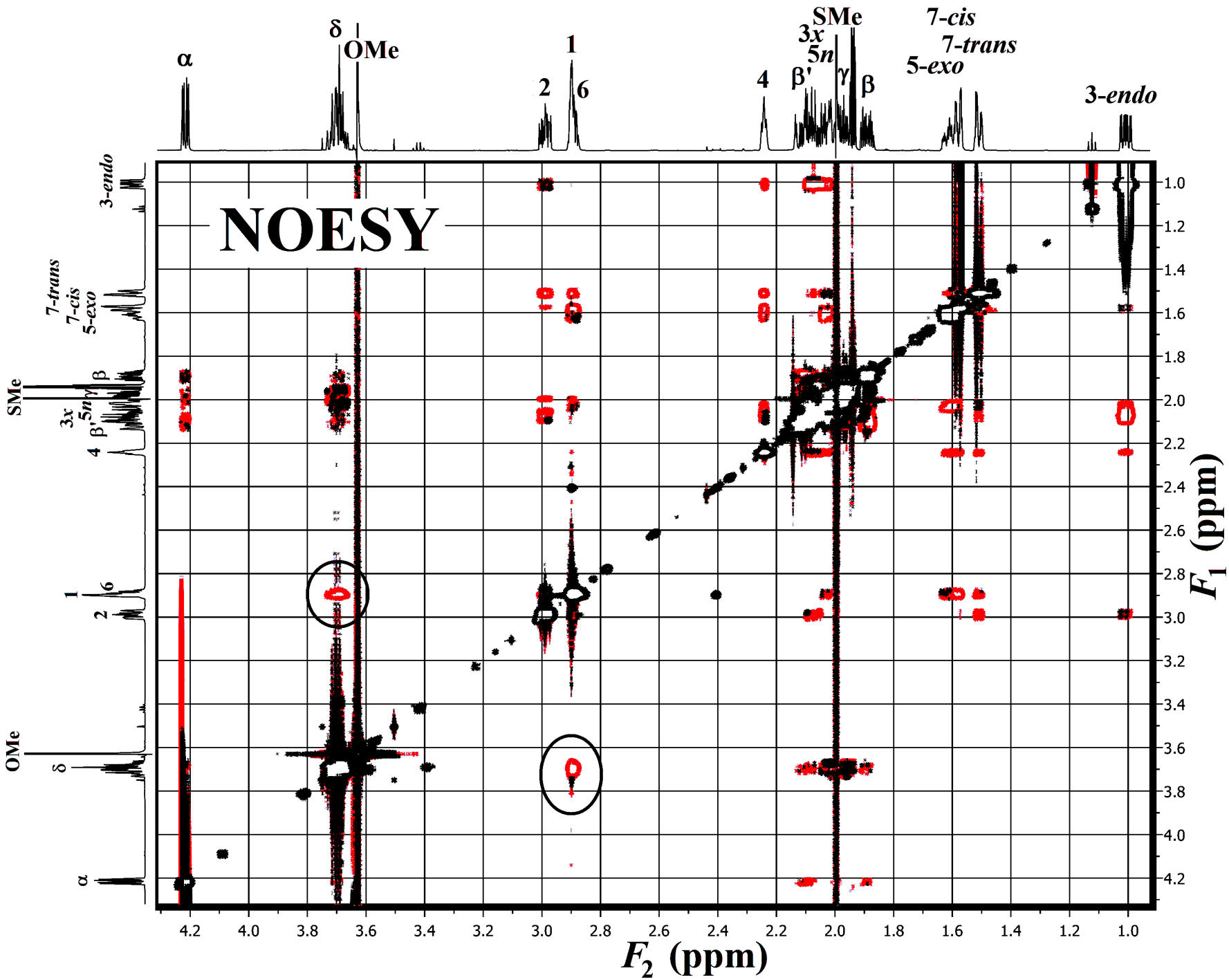


Figure S5. 600 MHz NOESY spectrum of proline amide **5** in CD_3CN (τ_m = 0.9 s).

Table S9: NMR Data for proline amide **5** in CD_3CN.[a]

Position	δ ^{1}H	Mult.	*J*	Int.	δ ^{13}C	Type	HMBC	COSY	NOESY[b]
1	2.899	m	----	1H	44.25	CH	C3, 4	2, 7-*cis*, 7-*trans*	7-*trans*, δ
2	2.989	dddd	11.6, 7.2, 3.1, 1.6	1H	50.25	CH	C1, 3, 6, (7), S-Me	1, 3-*exo*, 3-*endo*	3-*exo*, 7-*trans*, SMe,
3-*endo*	1.008	ddd	12.4, 7.2, 2.4	1H	37.32	CH_2	C2, 4, 5, 7	2, 3-*exo*, 7-*cis*	3-*exo*, 4, 5-*endo*
3-*exo*	2.074	m	----	1H	"	"	C1, 2, 4, 5	2, 3-*endo*, 4, 5-*exo*	2, 3-*endo*
4	2.242	m	----	1H	38.24	CH	C1, 2, 6	3-*exo*, 5-*exo*, 7-*cis*, 7-*trans*	3-*endo*, 5-*exo*, 7-*cis*, 7-*trans*
5-*endo*	2.030	m	----	1H	33.84	CH_2	C3, 7, 8	5-*exo*, 6, 7-*trans*	3-*endo*, 5-*exo*
5-*exo*	1.608	m	----	1H	"	"	C3, 8	3-*exo*, 4, 5-*endo*, 6	4, 5-*endo*
6	2.893	ddt	11.7[c], 1.4, 4.3	1H	45.06	CH	C1, 2, 5, 8	5-*endo*, 5-*exo*	7-*cis*, δ
7-*cis*[d]	1.579	m	----	1H	43.21	CH_2	C1, 2, 3, 4, 5, 6	1, 3-*endo*, 4, 7-*trans*	4, 6
7-*trans*	1.509	ddt	9.8, 3.1, 1.6	1H	"	"	C(1), 2, (3, 4), 5, 6, 8	1, 4, 5-*endo*, 7-*cis*	1, 2, 4
C'	----	----	----	----	174.91	C_q	----	----	----
SMe	1.996	s	----	3H	17.18	CH_3	C2	----	2
8	----	----	----	----	173.16	C_q	----	----	----
α	4.216	dd	8.9, 3.4	1H	61.09	CH	C', (8), β, γ, δ	β', β	β', β, γ
β'	1.890	ddt	12.5, 6.6, 3.8	1H	30.13	CH_2	C', (α), δ	α, β, γ	α
β	2.100	m	----	1H	"	"	C', α, δ	α, β'	α
γ'	1.968	m	----	1H	26.27	CH_2	Cα, δ	β', δ	α
γ	2.008	m	----	1H	"	"			
δ'	3.682	ddd	9.8, 7.6, 4.2	1H	48.35	CH_2	Cα, β, γ	γ	1/6
δ	3.709	ddd	9.8, 8.3, 6.6	1H	"	"			
OMe	3.629	s	----	3H	52.68	CH_3	C'	----	

[a] Bruker DRX-600 (^{1}H = 600.13 MHz), TXI (HCN 3-axis gradient 5 mm) probe, 25°C with reference: ^{1}H = 1.94 ($C\underline{H}D_2CN$); ^{13}C = 118.69 ($CHD_2\underline{C}N$). [b] 0.9 s mixing time [c] estimated from HSQC crosspeak [d] *cis* to the SMe substitutent

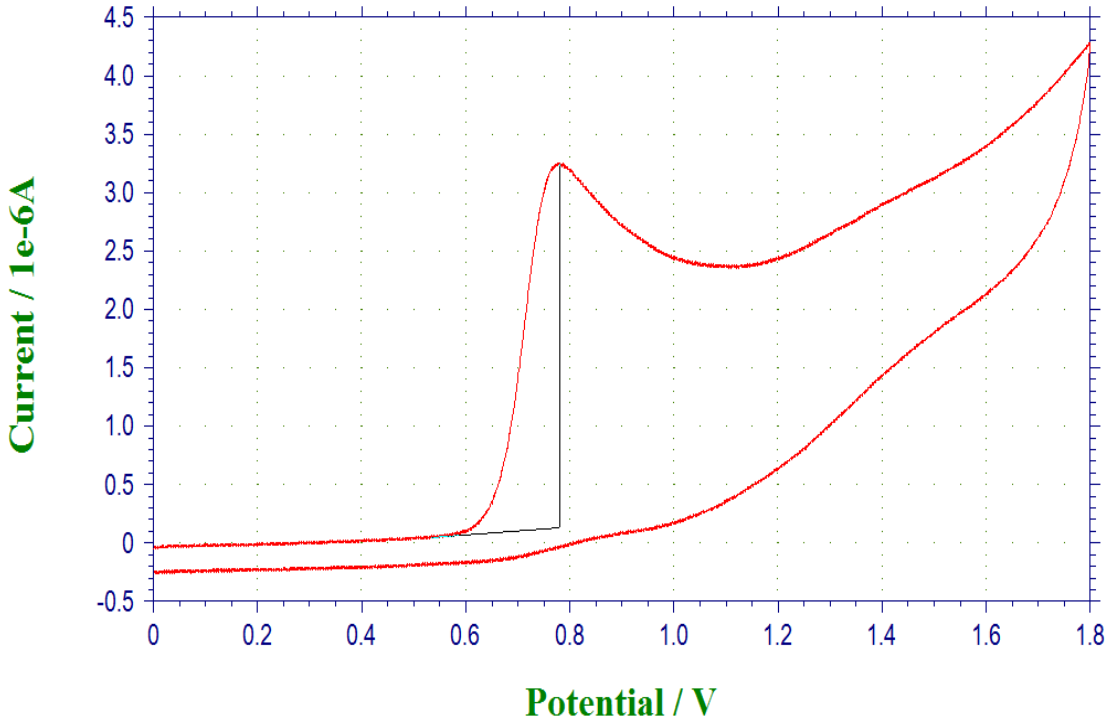


Figure S6. Cyclic Voltammetry of **5** (2.1 X 10^{-4} M), Scan rate 0.1V/s. Peak potential: 0.781 V.

Table S10. Peak Potentials for **1b** and **5** Determined by Cyclic Voltammetry (0.1 V/s)

	E_p(corr) V		E_p(corr) V
1b	0.750 ±0.003V (n=7)	**5**	0.819±0.063V (n=5)

Mean ±Standard Deviation

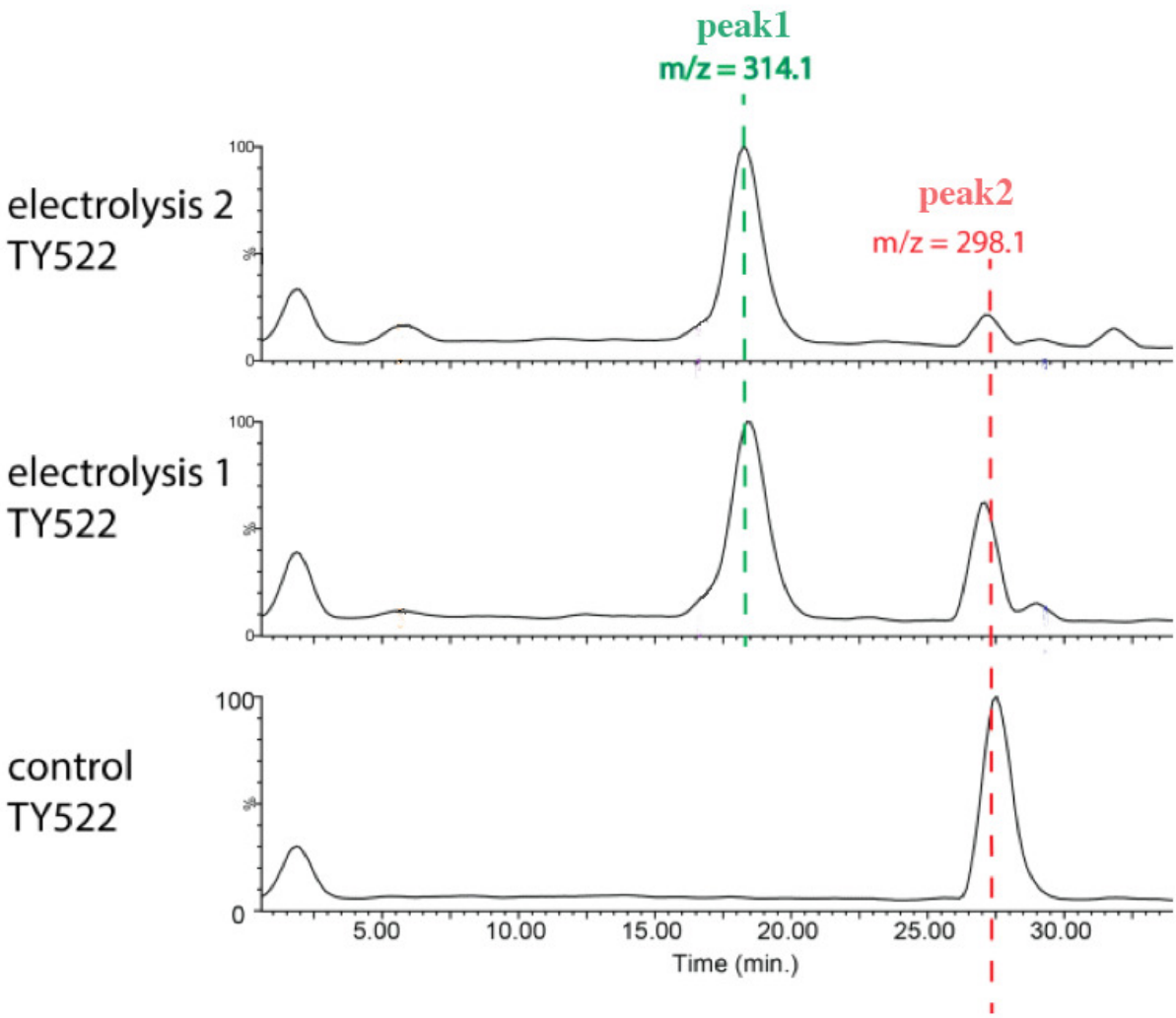
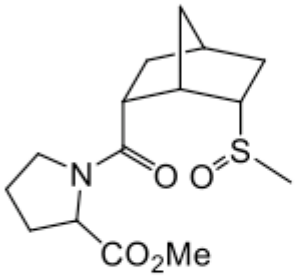
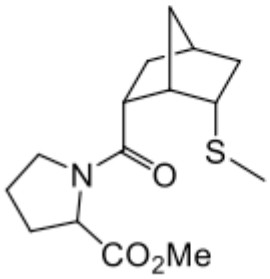


Figure S7. HPLC-MS of controlled potential electrolysis of **5**. Electrolyses 1 and 2 were carried out at 1.0V and 1.4V, respectively, using an 8 mm glassy carbon rotating disk electrode. The rotation speed was 1500 rpm.

Table S11. Relative Percentages of Compounds after Controlled Potential Electrolysis of **5** as Determined by HPLC-MS.

		Percent relative product yield of electrolysis	
		Elect. #1	**Elect. #2**
	**peak 1** ; m/z = 314.1	**58**	**80**
	**peak 2** ; m/z = 298.1 **(parent)**	**32**	**11**

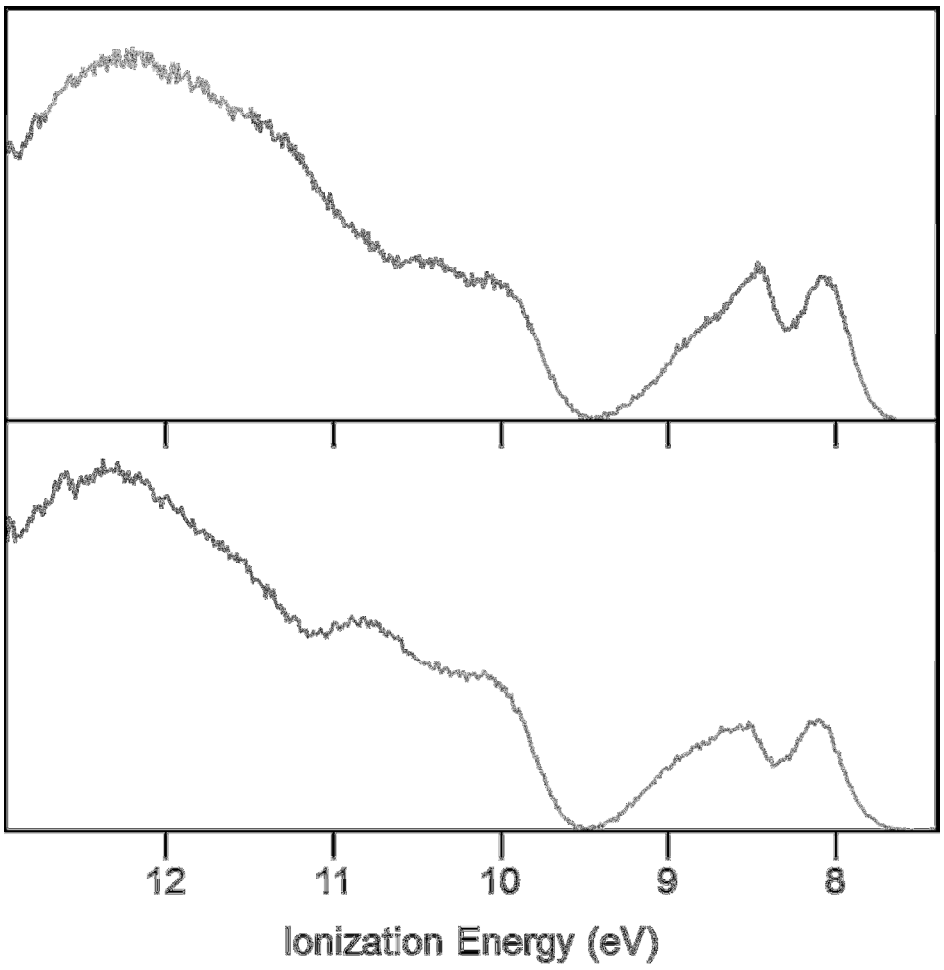


Figure S8. Photoelectron spectra of **1a** (top) and **5** (bottom).

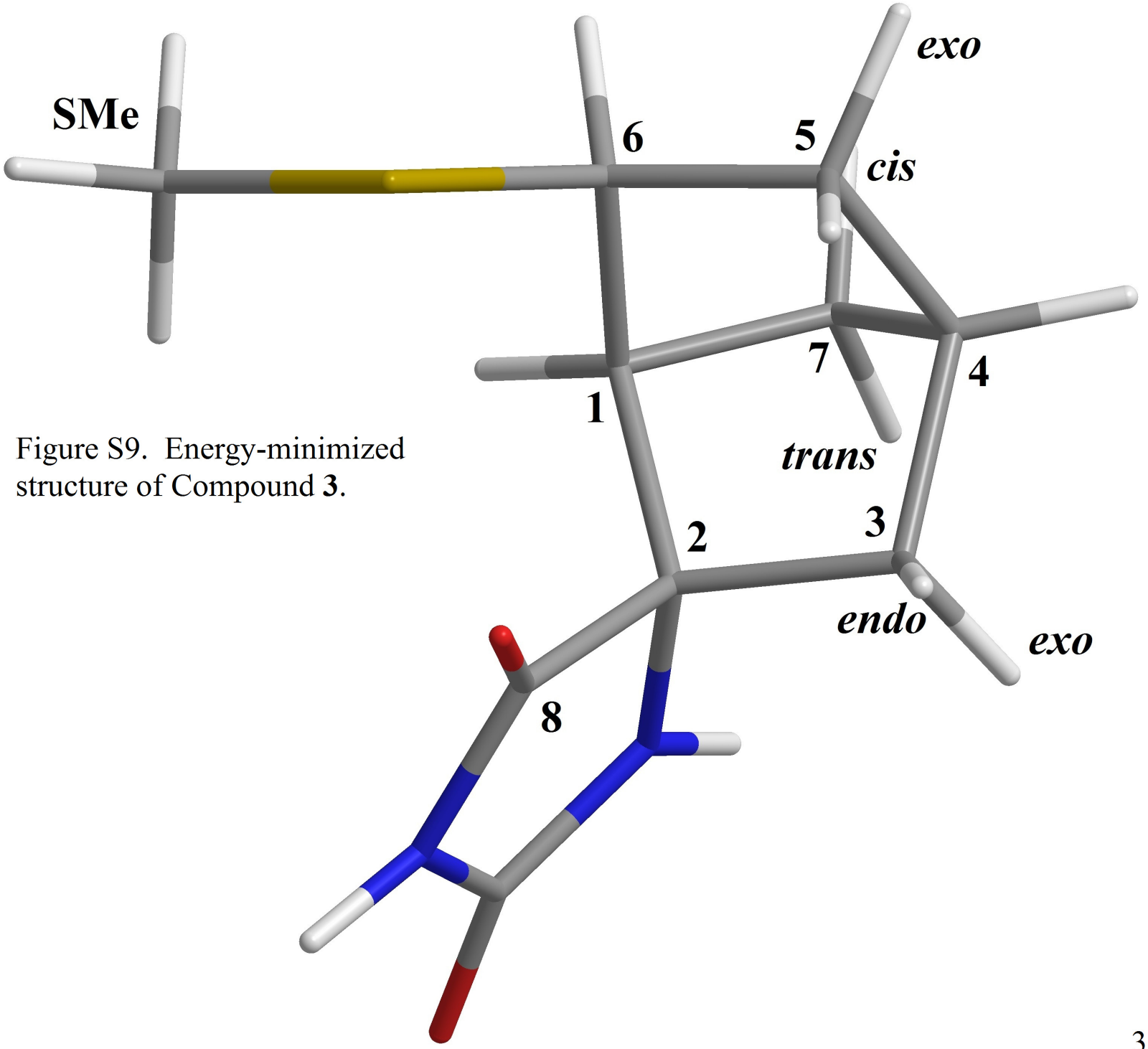


Figure S9. Energy-minimized structure of Compound **3**.

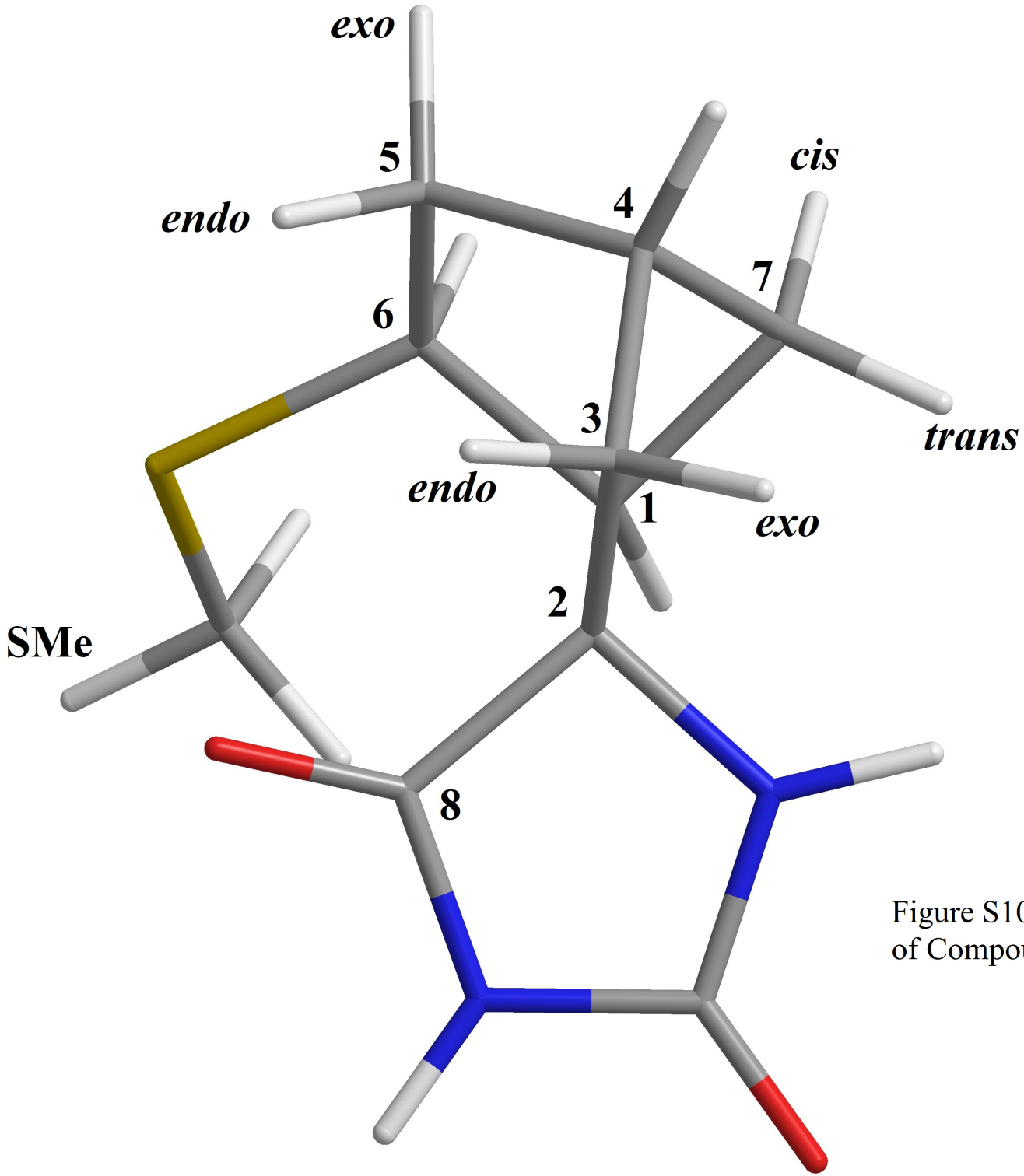


Figure S10. Energy-minimized structure of Compound **3**.

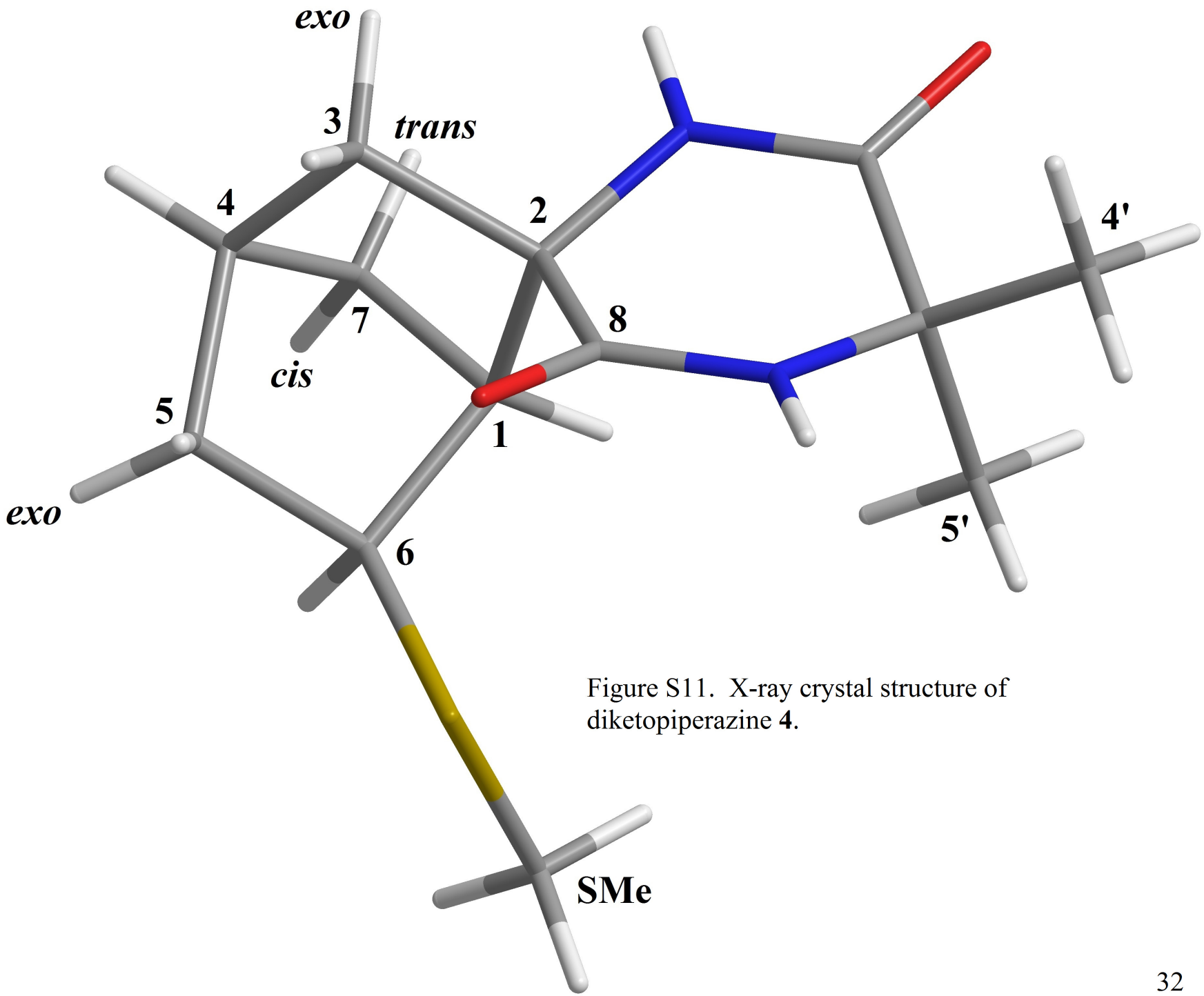
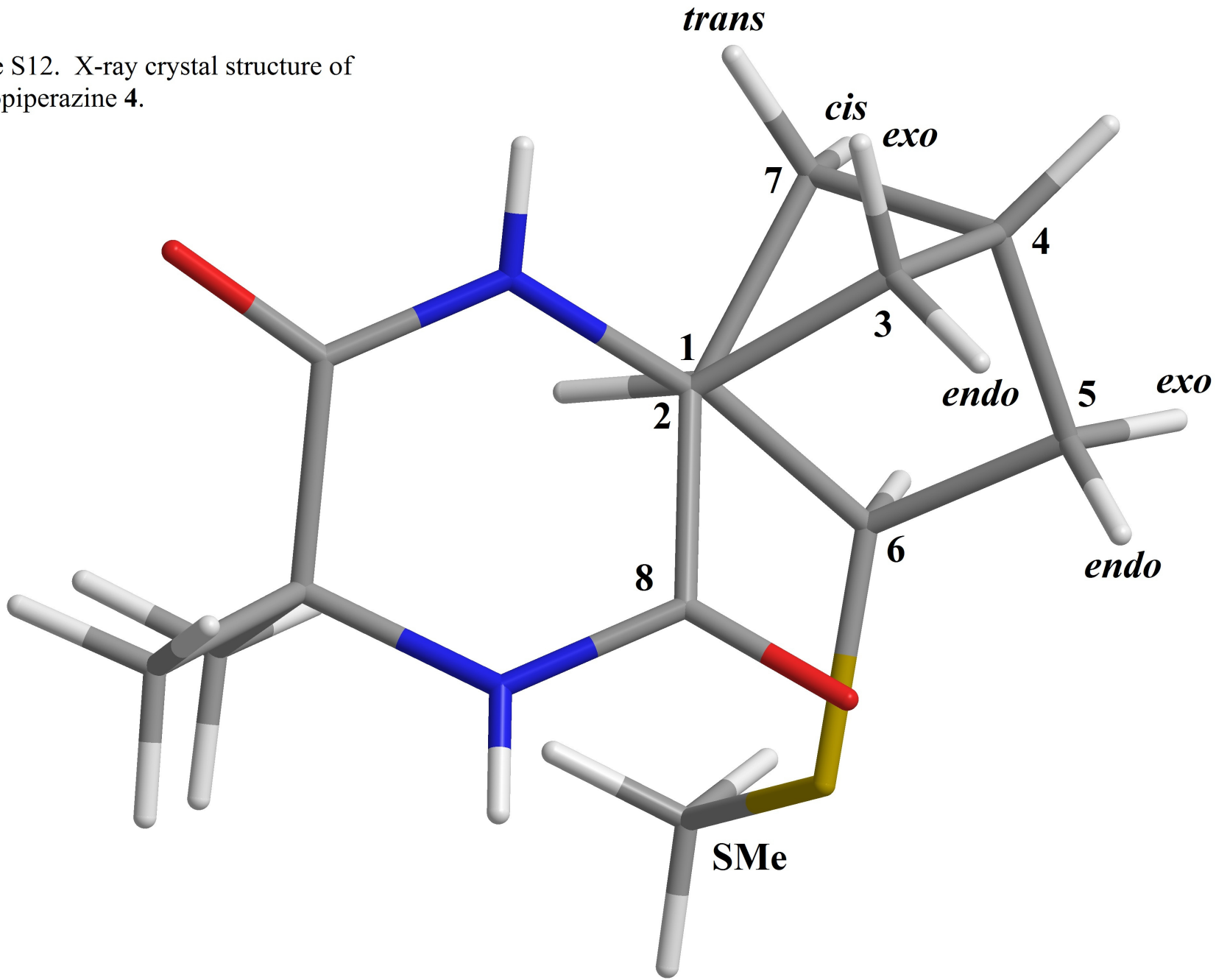


Figure S11. X-ray crystal structure of diketopiperazine **4**.

Figure S12. X-ray crystal structure of diketopiperazine **4**.



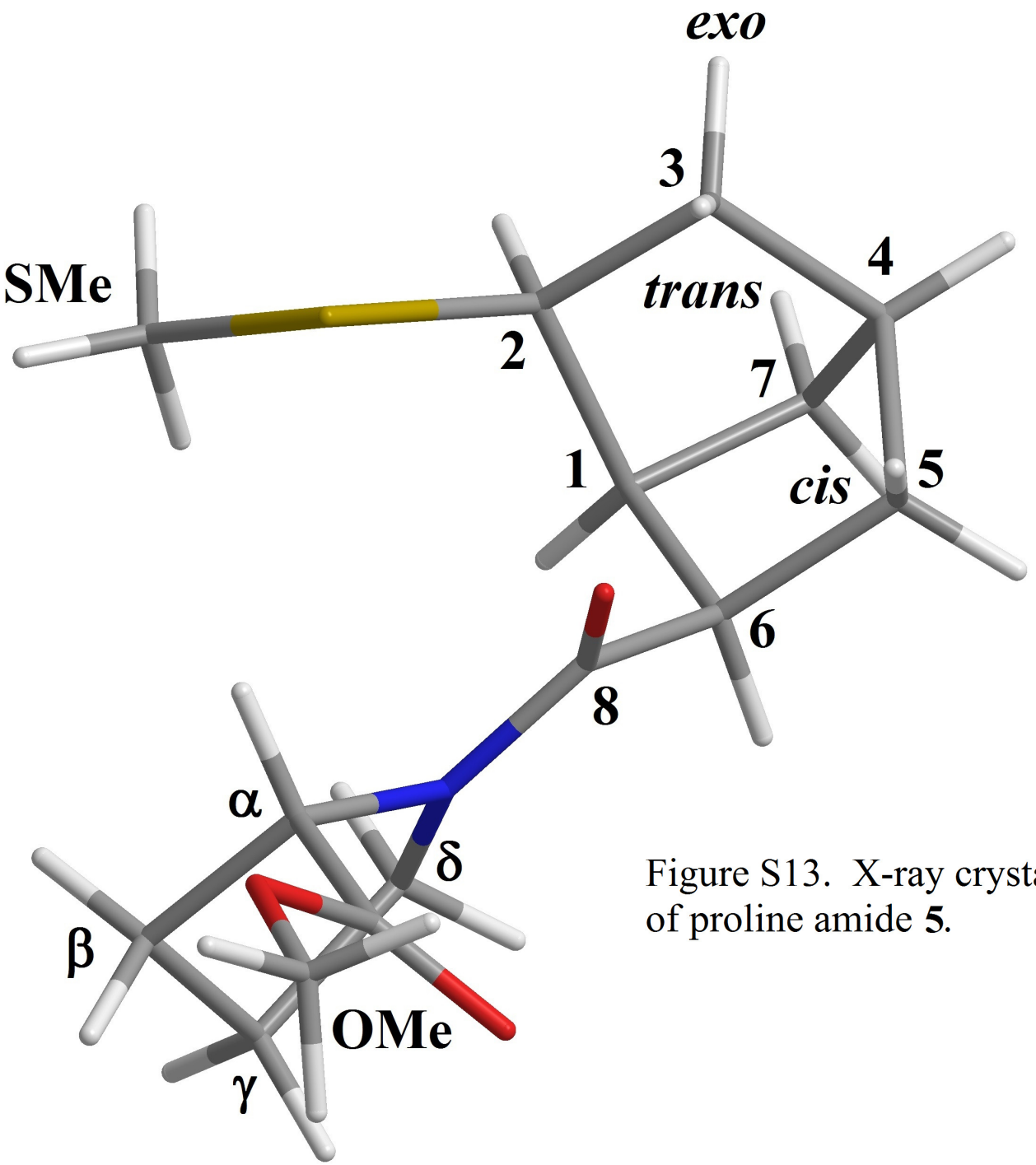


Figure S13. X-ray crystal structure of proline amide **5**.

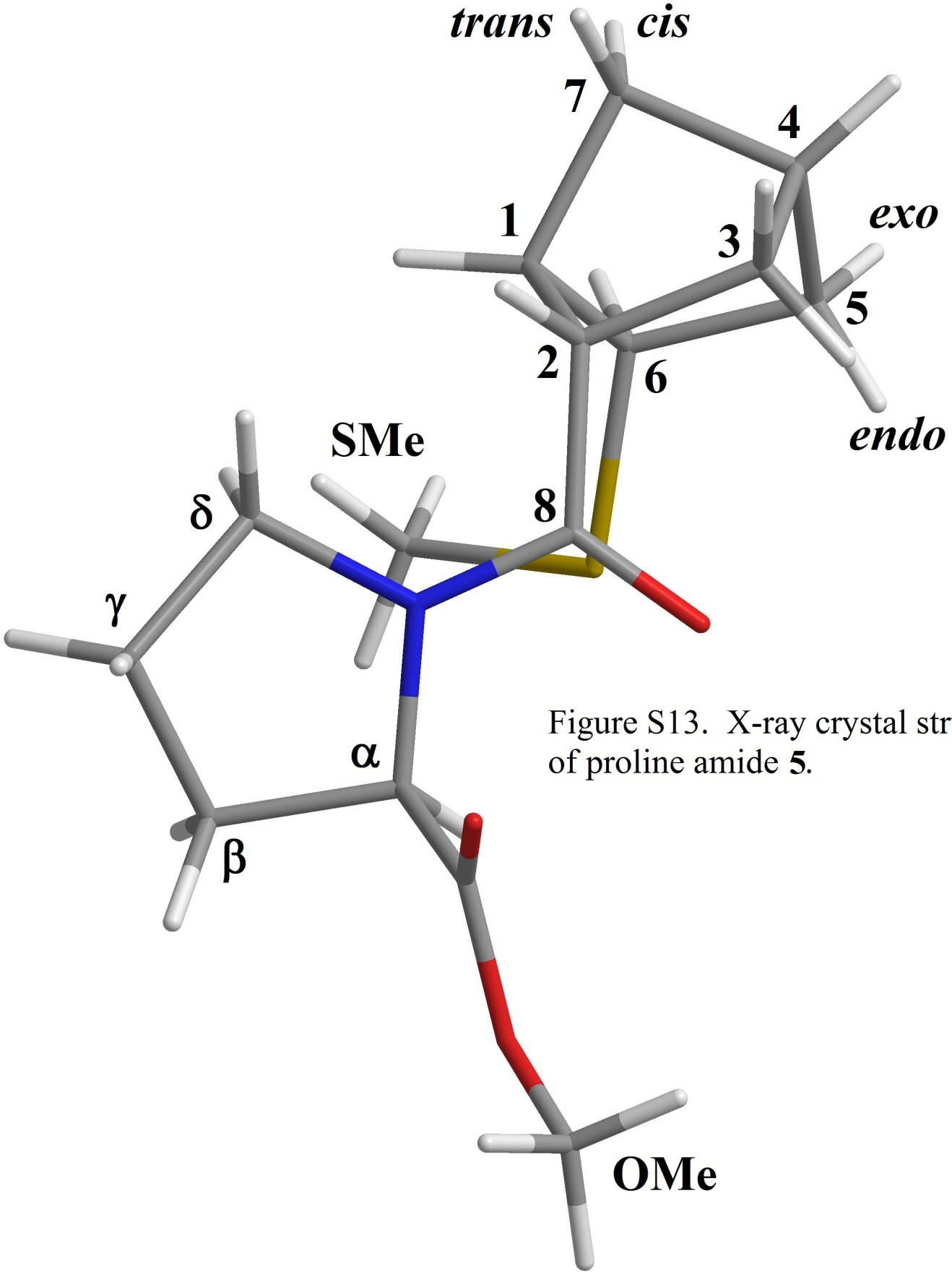


Figure S13. X-ray crystal structure of proline amide **5**.

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