Nature of Amide Carbonyl–Carbonyl Interactions in Proteins

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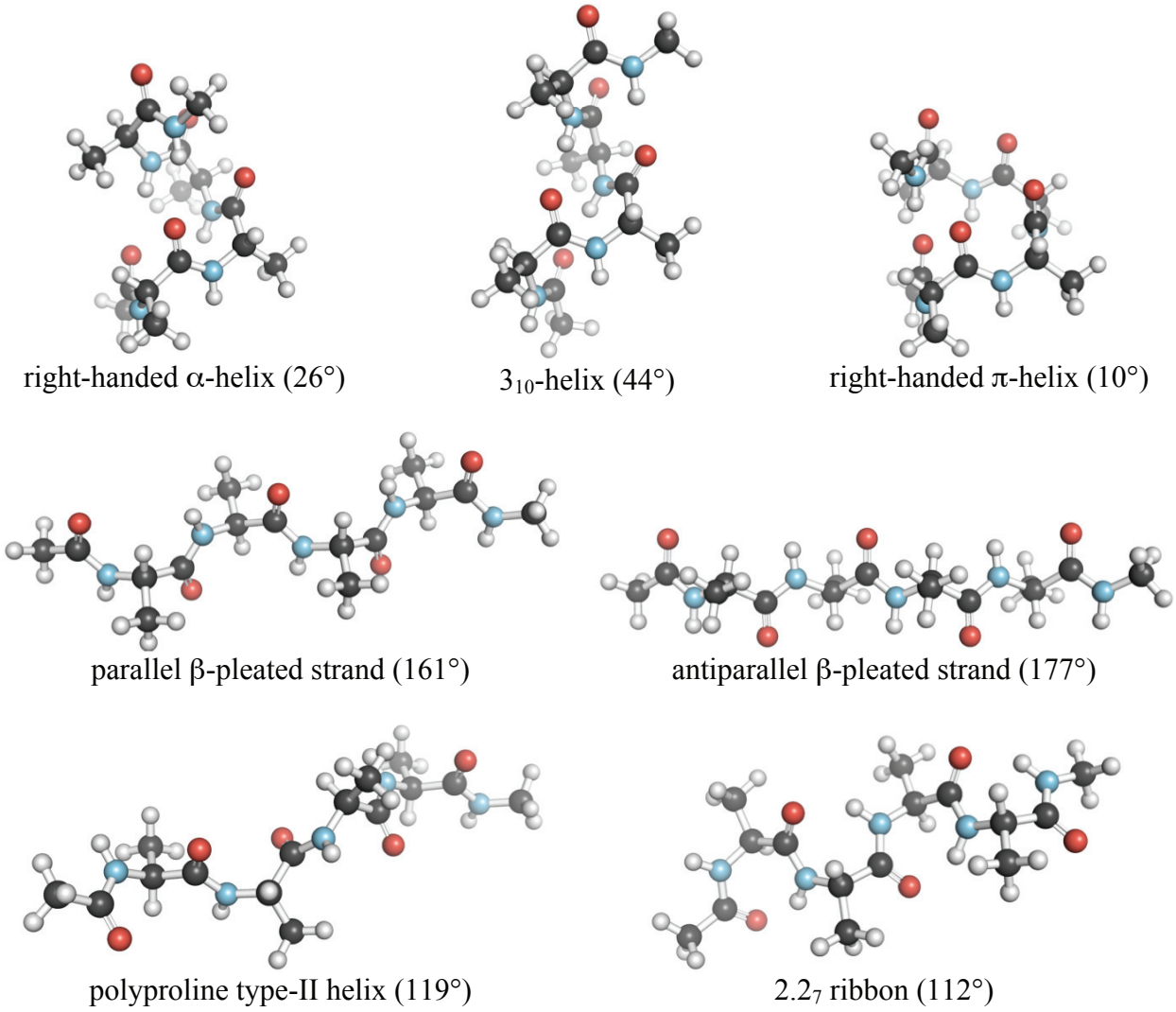


Figure S1. Orientation of carbonyl groups in common secondary structures, depicted with Ac–Ala_4–NHMe. Values in parentheses refer to the angles between the dipole moments of C'_{i-1}=O_{i-1} and C'_i=O_i.

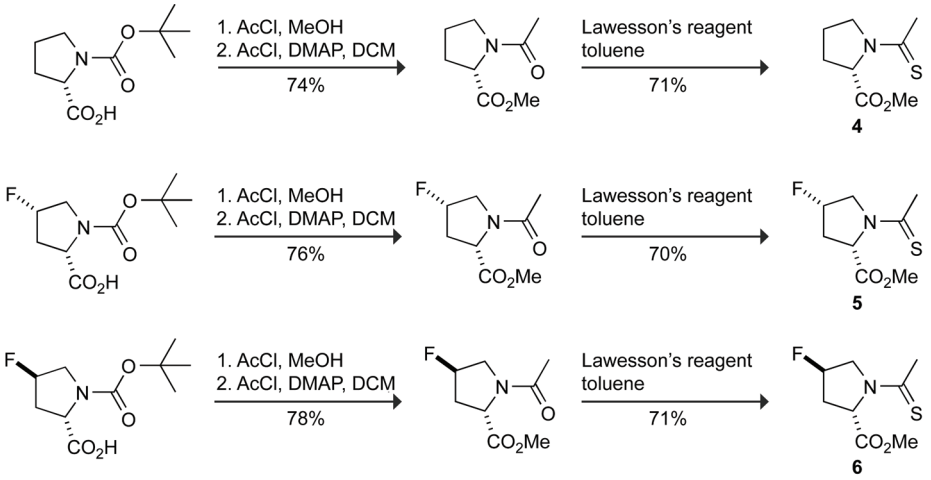
General Experimental. Commercial chemicals were of reagent grade or better, and were used without further purification. Anhydrous THF, DMF, and CH_2Cl_2 were obtained from CYCLE-TAINER® solvent delivery systems (J. T. Baker, Phillipsburg, NJ). Other anhydrous solvents were obtained in septum-sealed bottles. Reactions were monitored by thin-layer chromatography with visualization by UV light or staining with $KMnO_4$, or I_2. In all reactions involving anhydrous solvents, glassware was either oven- or flame-dried. Flash chromatography was performed with columns of silica gel 60, 230–400 mesh (Silicycle, Québec City, Canada). The removal of solvents and other volatile materials "under reduced pressure" refers to the use of a rotary evaporator at water-aspirator pressure (<20 torr) and a water bath of <45 °C. All reported yields are unoptimized.

Instrumentation. NMR spectra were acquired at ambient temperature with a Bruker DMX-400 Avance spectrometer (^{1}H, 400 MHz; ^{13}C, 100.6 MHz) in the National Magnetic Resonance Facility at Madison (NMRFAM). Carbon-13 spectra were proton-decoupled. Mass Spectrometry was performed with a Micromass LCT (electrospray ionization, ESI) instrument in the Mass Spectrometry Facility of the Department of Chemistry at the University of Wisconsin–Madison. X-Ray data were collected in the Molecular Structure Laboratory of the Department of Chemistry at the University of Wisconsin–Madison.

***N*-Acetyl–(2*S*)-proline methyl ester (1), *N*-acetyl–(2*S*,4*R*)-4-fluoroproline methyl ester (2), and *N*-acetyl–(2*S*,4*S*)-4-fluoroproline methyl ester (3).** Amides **1**–**3** were synthesized by using the methods of Nudleman et al.[S1]

***N*-Thioacetyl–(2*S*)-proline methyl ester (4), *N*-thioacetyl–(2*S*,4*R*)-4-fluoroproline methyl ester (5), and *N*-acetyl–(2*S*,4*S*)-4-fluoroproline methyl ester (6).** Thioamides **4**–**6** were synthesized by the routes shown in Scheme S1 and described below.

Scheme S1



***N*-Thioacetyl–(2*S*)-proline methyl ester (4).** A solution of *N*-Acetyl-(2*S*)-proline methyl ester (0.50 g, 2.9 mmol) and the Lawesson's reagent (0.74 g, 1.83 mmol) in anhydrous toluene (20 mL) was heated at reflux for 30 min. The reaction mixture was filtered, evaporated, and chromatographed using hexane/EtOAc to afford **4** as a white solid (0.39 g, 71%). ^{1}H NMR ($CDCl_3$, 400 MHz, 5.2:1 mixture of two rotamers): δ 5.10–4.96 (dd, J = 8.0, 2.9 Hz, 0.84H), 4.68–4.60 (dd, J = 8.0, 2.0 Hz, 0.16H), 4.10–3.60 (m, 5H), 2.69–2.58 (s, 2.52H), 2.58–2.50 (s, 0.48H), 2.50–1.98 (m, 4H); ^{13}C NMR ($CDCl_3$, 100.6 MHz, 5.2:1 mixture of two rotamers): δ

198.5, 171.0, 170.7, 65.2, 63.2, 54.1, 52.9, 52.4, 51.6, 32.8, 31.8, 29.6, 25.0, 22.9; ESI–MS: $[M + Na]^+$ calcd 210.0565; found 210.0557 (3.8 ppm).

***N*-Thioacetyl–(2*S*,4*S*)-4-fluoroproline methyl ester (5).** *N*-Acetyl–(2*S*,4*R*)-4-fluoroproline methyl ester (0.3 g, 1.58 mmol) and the Lawesson's reagent (0.28 g, 0.69 mmol) were heated at reflux in anhydrous toluene (15 mL) for 30 min. The reaction mixture was filtered, evaporated under reduced pressure, and chromatographed using hexane/EtOAc to afford **5** as a white solid (0.23 g, 71%). ^{1}H NMR ($CDCl_3$, 400MHz, 1.6:1 mixture of two rotamers): δ 5.52–5.18 (m, 1.61H), 4.82–4.72 (m, 0.32H), 4.32–3.84 (m, 2H), 3.80 and 3.76 (s, 3H), 2.90–2.38 (m, 5H); ^{13}C NMR ($CDCl_3$, 100.6 MHz, 1.6:1 mixture of two rotamers): δ 199.8, 169.7, 169.5, 93.0, 91.3, 89.5, 63.4, 61.5, 60.3, 60.1, 57.6, 57.3, 53.2, 52.6, 38.6, 38.4, 36.3, 36.1, 32.9, 32.7; ESI–MS: $[M + Na]^+$ calcd 228.0470; found 228.0472 (<1 ppm).

***N*-Thioacetyl–(2*S*,4*R*)-4-fluoroproline methyl ester (6).** *N*-Acetyl–(2*S*,4*R*)-4-fluoroproline methyl ester (0.35 g, 1.85 mmol) and the Lawesson's reagent (0.32 g, 0.79 mmol) were heated at reflux in anhydrous toluene (20 mL) for 30 min. The reaction mixture was filtered, evaporated, and chromatographed using hexane/EtOAc to afford **6** as a white solid (0.27 g, 70%). ^{1}H NMR ($CDCl_3$, 400 MHz, 6.2:1 mixture of two rotamers): δ 5.50–5.20 (m, 1H), 5.10–4.68 (m, 1H), 4.25–3.65 (m, 5H), 2.95–2.15 (m, 5H); ^{13}C NMR ($CDCl_3$, 100.6 MHz, 6.2:1 mixture of two rotamers): δ 199.4, 170.7, 92.2, 90.4, 63.3, 61.1, 60.1, 57.7, 57.5, 53.2, 52.6, 36.4, 36.1, 33.0, 32.2; ESI–MS: $[M + Na]^+$ calcd 228.0470; found 228.0477 (3.1 ppm).

Measurement of $K_{trans/cis}$ values for thioamides 4–6. Each compound (5–10 mg) was dissolved in D_2O with enough CD_3OD added to solubilize the compound (less than 20% of total volume) and equilibrated for a day. ^{1}H spectra were acquired and worked up using the software package NUTS.[S2] Values of $K_{trans/cis}$ were determined from the relative areas of the trans and cis peaks. NOEDIFF experiments were carried out to confirm the proton assignments. In addition, compounds **4–6** with ^{13}C at the C-2 acetyl carbon were synthesized and the $K_{trans/cis}$ was determined from the ^{1}H and ^{13}C spectra (acquired using an inverse-gated decoupled pulse program). The $K_{trans/cis}$ of **5** and **6** were verified further by using inverse-gated decoupled ^{19}F NMR spectroscopy.

Crystal structure determination of thioamides 4–6. The desired compounds were dissolved in hexane with minimal amount of EtOAc. Slow evaporation afforded crystals suitable for X-ray diffraction analysis after ~4 d. X-ray intensity data were collected on a Bruker CCD-1000 diffractometer with Mo K_α (λ = 0.71073 Å) radiation at 105(2) K with the diffractometer to crystal distance of 4.9 cm. Preliminary indexing was carried out for the determination of cell constants. This indexing consisted of three series of ω scans at different initial angles with each series consisting of 20 frames at intervals of 0.3° with the exposure time of 10 s per frame. The reflections were indexed by an automated indexing routine built in the SMART program. Data were collected by using the full sphere data collection routine to a resolution of 0.80 Å. The intensity data was then corrected for absorption and Lorentz and polarization effects. Structure solution and refinement was carried out using SHELXTL V.6.10.[S3] Figures S2–S4 display **4**, **5**, and **6** with 50% probability thermal ellipsoids.

Computational methodology. The conformational preferences of **4–6** were examined by hybrid density functional theory as implemented in Gaussian 03.[S4] Geometry optimizations and frequency calculations at the B3LYP/6-311+G (2d,p) level of theory were performed on the C^γ-endo and C^γ-exo conformers[S5] in both trans and cis geometries. Frequency calculations of the optimized structures yielded no imaginary frequencies, indicating a true stationary point on the potential energy surface. The resulting self-consistent field (SCF) energies were corrected by the

zero-point vibrational energy (ZPVE) determined in the frequency calculations, and are listed in Table S1. Optimized geometries were analyzed by NBO 5.0 at the B3LYP/6-311+G(2d,p) level of theory.

References

(S1) Nudelman, A.; Bechor, Y.; Falb, E.; Fischer, B.; Wexler, B. A.; Nudelman, A., *Synth. Commun.* **1998,** *28*, 471–474.

(S2) NUTS–NMR Utility Transform Software, Acorn NMR, Inc., 7670 Las Positas Road, Livermore, CA 94551.

(S3) Bruker-AXS. (2000–2003) SADABS V.2.05, SAINT V.6.22, SHELXTL V.6.10 & SMART 5.622 Software Reference Manuals. Bruker-AXS, Madison, Wisconsin, USA.

(S4) Gaussian 03, Revision C.02, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, J. A. Montgomery, Jr., T. Vreven, K. N. Kudin, J. C. Burant, J. M. Millam, S. S. Iyengar, J. Tomasi, V. Barone, B. Mennucci, M. Cossi, G. Scalmani, N. Rega, G. A. Petersson, H. Nakatsuji, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, M. Klene, X. Li, J. E. Knox, H. P. Hratchian, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, P. Y. Ayala, K. Morokuma, G. A. Voth, P. Salvador, J. J. Dannenberg, V. G. Zakrzewski, S. Dapprich, A. D. Daniels, M. C. Strain, O. Farkas, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. V. Ortiz, Q. Cui, A. G. Baboul, S. Clifford, J. Cioslowski, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, M. Challacombe, P. M. W. Gill, B. Johnson, W. Chen, M. W. Wong, C. Gonzalez, and J. A. Pople, Gaussian, Inc., Wallingford CT, 2004.

(S5) The pyrrolidine ring of proline actually prefers two distinct twist, rather than envelope, conformations. As C^{γ} experiences a large out-of-plane displacement in these twisted rings, we refer to pyrrolidine ring conformations simply as "C^{γ}-exo" and "C^{γ}-endo". Giacovazzo, C.; Monaco, H. L.; Artioli, G.; Viterbo, D.; Ferraris, G.; Gilli, G.; Zanotti, G.; Catti, M. Fundamentals of Crystallography, 2nd edn.; Oxford University Press: Oxford, UK, 2002.

Table S1. SCF energies (atomic units; au) of **4**–**6** calculated at the B3LYP/6-311+G(2d,p) level of theory.

Compound; conformer	Energy	ZPE correction	Energy (corrected)
4; trans, endo	–916.2706849	0.207310	–916.0633749
4, trans, exo	–916.2695113	0.207265	–916.0622463
4; cis, endo	–916.2686456	0.207061	–916.0615846
4; cis, exo	–916.2670958	0.207159	–916.0599368
5; trans, endo	–1015.539073	0.199029	–1015.340044
5; trans, exo	–1015.538317	0.199311	–1015.339006
5; cis, endo	–1015.539221	0.199078	–1015.340143
5; cis, exo	–1015.535290	0.199044	–1015.336246
6; trans, endo	–1015.539898	0.199131	–1015.340767
6; trans, exo	–1015.540908	0.199137	–1015.341771
6; cis, endo	–1015.537276	0.199002	–1015.338274
6; cis exo	–1015.538736	0.198991	–1015.339745

Table S2. Natural charge on X_{i-1} of **1**–**6** calculated at the B3LYP/6-311+G(2d,p) level of theory.

Compound; conformer	Natural charge on X_{i-1}
1; trans, endo	–0.64507
1, trans, exo	–0.64337
2; trans, endo	–0.63779
2; trans, exo	—
3; trans, endo	—
3; trans, exo	–0.63692
4; trans, endo	–0.17817
4; trans, exo	–0.17098
5; trans, endo	–0.16172
5; trans, exo	–0.15628
6; trans, endo	–0.16570
6; trans, exo	–0.15441

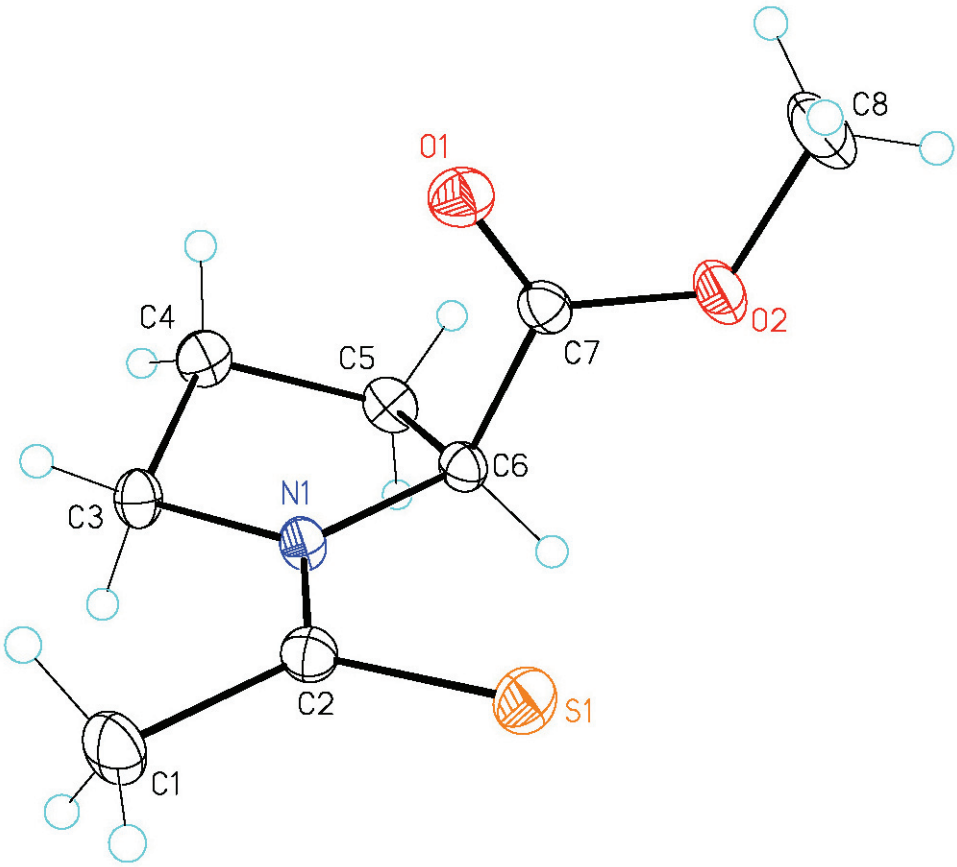


Figure S2. Molecular drawing of **4** drawn at 50% probability ellipsoids.

Table S3. Crystal data and structure refinement for **4**.

Identification code	raines10	
Empirical formula	$C_8H_{13}NO_2S$	
Formula weight	187.25	
Temperature	105(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	$P2_12_12_1$	
Unit cell dimensions	a = 8.0208(4) Å	α = 90°
	b = 9.2791(5) Å	β = 90°
	c = 13.0486(7) Å	γ = 90°
Volume	971.15(9) Å^3	
Z	4	
Density (calculated)	1.281 Mg/m^3	
Absorption coefficient	0.295 mm^{-1}	
F(000)	400	
Crystal size	0.47 × 0.46 × 0.46 mm^3	
Theta range for data collection	2.69 to 29.13°	
Index ranges	$-10 \leq h \leq 10$, $-12 \leq k \leq 12$, $-17 \leq l \leq 17$	
Reflections collected	17074	
Independent reflections	2595 [R(int) = 0.0213]	
Completeness to theta = 29.13°	99.9%	
Absorption correction	Empirical with SADABS	
Max. and min. transmission	0.8762 and 0.8737	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2595 / 0 / 162	
Goodness-of-fit on F^2	0.973	
Final R indices [$I > 2\sigma$(I)]	$R1$ = 0.0222, $wR2$ = 0.0584	
R indices (all data)	$R1$ = 0.0227, $wR2$ = 0.0589	
Absolute structure parameter	0.00(4)	
Largest diff. peak and hole	0.294 and –0.139 e.Å^{-3}	

Table S4. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($Å^2 \times 10^3$) for **4**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
S(1)	8287(1)	-337(1)	6347(1)	21(1)
O(2)	4060(1)	1541(1)	6428(1)	23(1)
O(1)	6193(1)	3107(1)	6598(1)	20(1)
N(1)	7670(1)	1169(1)	8012(1)	14(1)
C(6)	5882(1)	1112(1)	7790(1)	14(1)
C(2)	8802(1)	516(1)	7434(1)	16(1)
C(3)	8034(1)	1992(1)	8959(1)	16(1)
C(7)	5457(1)	2040(1)	6864(1)	16(1)
C(5)	5077(1)	1720(1)	8770(1)	18(1)
C(8)	3424(2)	2383(1)	5579(1)	34(1)
C(1)	10580(1)	577(1)	7805(1)	24(1)
C(4)	6397(1)	2764(1)	9179(1)	19(1)

Table S5. Bond lengths [Å] and angles [°] for **4**.

S(1)-C(2)	1.6752(9)
O(2)-C(7)	1.3394(11)
O(2)-C(8)	1.4479(12)
O(1)-C(7)	1.2039(11)
N(1)-C(2)	1.3277(12)
N(1)-C(6)	1.4636(11)
N(1)-C(3)	1.4815(11)
C(6)-C(7)	1.5222(12)
C(6)-C(5)	1.5400(12)
C(6)-H(10)	0.933(13)
C(2)-C(1)	1.5074(13)
C(3)-C(4)	1.5229(12)
C(3)-H(5)	1.000(14)
C(3)-H(4)	0.960(14)
C(5)-C(4)	1.5313(13)
C(5)-H(9)	0.963(13)
C(5)-H(8)	0.943(16)
C(8)-H(13)	0.98(2)
C(8)-H(11)	0.95(2)
C(8)-H(12)	0.88(2)
C(1)-H(2)	0.962(16)
C(1)-H(1)	0.945(17)
C(1)-H(14)	0.934(17)
C(4)-H(7)	0.978(14)
C(4)-H(6)	0.945(14)
C(7)-O(2)-C(8)	115.70(8)
C(2)-N(1)-C(6)	122.73(8)
C(2)-N(1)-C(3)	125.07(7)
C(6)-N(1)-C(3)	112.18(7)
N(1)-C(6)-C(7)	110.89(7)
N(1)-C(6)-C(5)	103.46(7)
C(7)-C(6)-C(5)	110.94(7)
N(1)-C(6)-H(10)	111.0(8)
C(7)-C(6)-H(10)	107.4(7)
C(5)-C(6)-H(10)	113.2(8)
N(1)-C(2)-C(1)	116.57(8)
N(1)-C(2)-S(1)	121.90(7)
C(1)-C(2)-S(1)	121.53(7)
N(1)-C(3)-C(4)	103.28(7)
N(1)-C(3)-H(5)	109.1(8)
C(4)-C(3)-H(5)	110.8(8)
N(1)-C(3)-H(4)	111.1(8)
C(4)-C(3)-H(4)	113.5(8)
H(5)-C(3)-H(4)	108.9(11)
O(1)-C(7)-O(2)	124.87(8)
O(1)-C(7)-C(6)	125.74(8)
O(2)-C(7)-C(6)	109.24(7)
C(4)-C(5)-C(6)	103.39(7)
C(4)-C(5)-H(9)	113.4(8)
C(6)-C(5)-H(9)	114.0(8)
C(4)-C(5)-H(8)	111.5(9)
C(6)-C(5)-H(8)	107.5(9)
H(9)-C(5)-H(8)	107.0(12)

O(2)-C(8)-H(13)	110.6(13)
O(2)-C(8)-H(11)	111.2(12)
H(13)-C(8)-H(11)	109.9(18)
O(2)-C(8)-H(12)	105.5(13)
H(13)-C(8)-H(12)	108.5(18)
H(11)-C(8)-H(12)	111.0(19)
C(2)-C(1)-H(2)	110.2(10)
C(2)-C(1)-H(1)	108.3(10)
H(2)-C(1)-H(1)	106.7(13)
C(2)-C(1)-H(14)	111.0(10)
H(2)-C(1)-H(14)	109.7(13)
H(1)-C(1)-H(14)	110.7(14)
C(3)-C(4)-C(5)	103.48(7)
C(3)-C(4)-H(7)	111.3(8)
C(5)-C(4)-H(7)	111.5(8)
C(3)-C(4)-H(6)	111.9(9)
C(5)-C(4)-H(6)	107.5(9)
H(7)-C(4)-H(6)	110.8(12)

Table S6. Anisotropic displacement parameters ($Å^2 \times 10^3$) for **4**. The anisotropic displacement factor exponent takes the form: $-2p^2[h^2\ a^{*2}U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
S(1)	22(1)	22(1)	18(1)	-6(1)	0(1)	3(1)
O(2)	19(1)	26(1)	22(1)	3(1)	-9(1)	-2(1)
O(1)	22(1)	19(1)	20(1)	3(1)	1(1)	-1(1)
N(1)	12(1)	17(1)	14(1)	-1(1)	-1(1)	0(1)
C(6)	12(1)	15(1)	16(1)	1(1)	-1(1)	-1(1)
C(2)	15(1)	16(1)	17(1)	-1(1)	0(1)	1(1)
C(3)	15(1)	20(1)	13(1)	-3(1)	0(1)	-1(1)
C(7)	15(1)	18(1)	14(1)	-1(1)	0(1)	3(1)
C(5)	14(1)	23(1)	16(1)	1(1)	3(1)	1(1)
C(8)	33(1)	41(1)	28(1)	7(1)	-15(1)	3(1)
C(1)	14(1)	31(1)	28(1)	-8(1)	-1(1)	4(1)
C(4)	19(1)	21(1)	16(1)	-3(1)	2(1)	2(1)

Table S7. Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($Å^2 \times 10^3$) for **4**.

	x	*y*	*z*	*U*(eq)
H(10)	5545(16)	172(14)	7641(9)	14(3)
H(5)	8315(19)	1303(14)	9522(10)	22(3)
H(7)	6255(17)	2939(15)	9913(10)	21(3)
H(9)	4008(16)	2166(14)	8660(11)	19(3)
H(6)	6301(18)	3632(15)	8804(11)	26(3)
H(4)	8958(17)	2635(15)	8859(10)	21(3)
H(2)	10650(20)	221(16)	8496(13)	35(4)
H(8)	4905(19)	942(17)	9222(12)	26(3)
H(1)	10920(20)	1553(18)	7823(12)	33(4)
H(13)	4280(30)	2500(20)	5051(15)	53(5)
H(11)	3040(30)	3300(20)	5802(15)	54(5)
H(12)	2600(30)	1870(20)	5318(15)	54(5)
H(14)	11280(20)	40(18)	7379(13)	38(4)

Table S8. Torsion angles [°] for **4**.

C(2)-N(1)-C(6)-C(7)	-72.79(10)
C(3)-N(1)-C(6)-C(7)	108.85(8)
C(2)-N(1)-C(6)-C(5)	168.21(8)
C(3)-N(1)-C(6)-C(5)	-10.15(10)
C(6)-N(1)-C(2)-C(1)	-175.46(8)
C(3)-N(1)-C(2)-C(1)	2.68(13)
C(6)-N(1)-C(2)-S(1)	4.42(12)
C(3)-N(1)-C(2)-S(1)	-177.44(7)
C(2)-N(1)-C(3)-C(4)	168.27(8)
C(6)-N(1)-C(3)-C(4)	-13.42(9)
C(8)-O(2)-C(7)-O(1)	-0.28(14)
C(8)-O(2)-C(7)-C(6)	175.52(8)
N(1)-C(6)-C(7)-O(1)	-29.34(12)
C(5)-C(6)-C(7)-O(1)	85.04(10)
N(1)-C(6)-C(7)-O(2)	154.91(7)
C(5)-C(6)-C(7)-O(2)	-90.71(9)
N(1)-C(6)-C(5)-C(4)	29.49(9)
C(7)-C(6)-C(5)-C(4)	-89.47(8)
N(1)-C(3)-C(4)-C(5)	31.47(8)
C(6)-C(5)-C(4)-C(3)	-38.05(8)

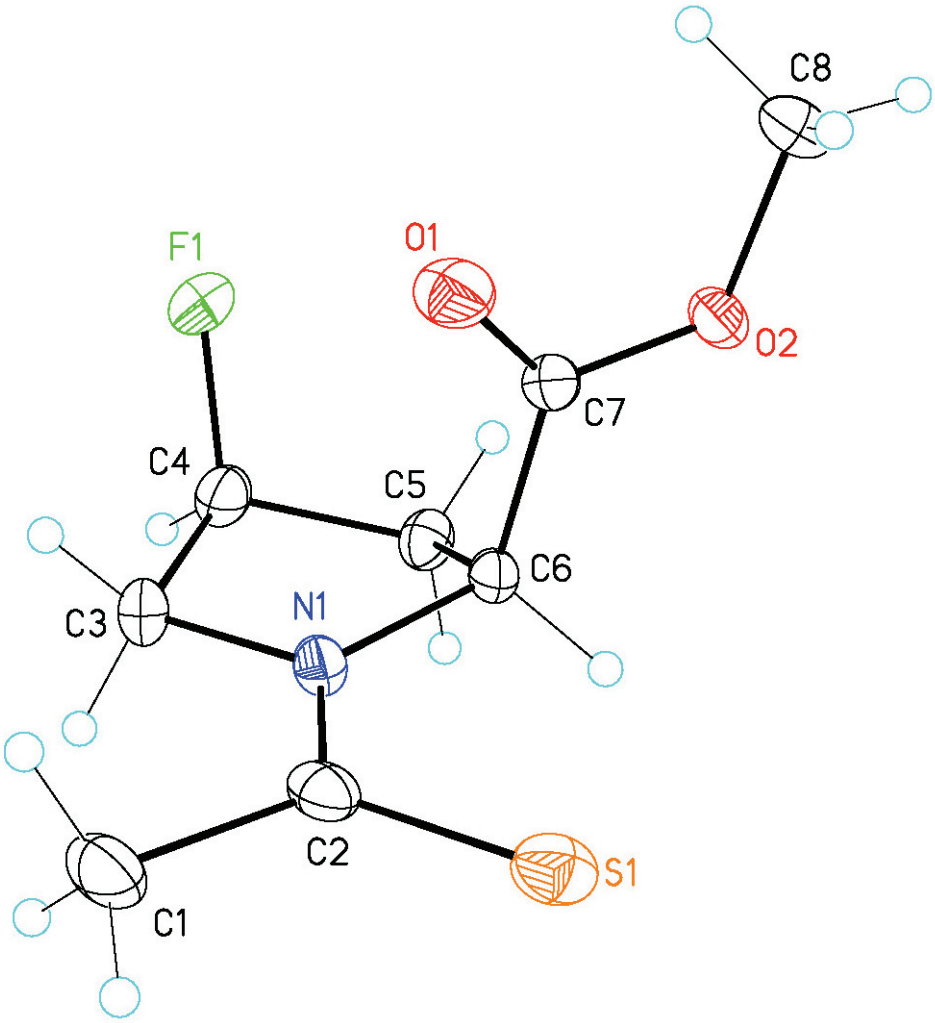


Figure S3. Molecular drawing of **5** drawn at 50% probability ellipsoids.

Table S9. Crystal data and structure refinement for **5**.

Identification code	raines13	
Empirical formula	$C_8H_{12}FNO_2S$	
Formula weight	205.25	
Temperature	105(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	$P2_12_12_1$	
Unit cell dimensions	a = 8.1337(5) Å	α = 90°
	b = 10.5589(6) Å	β = 90°
	c = 11.2694(7) Å	γ = 90°
Volume	967.85(10) Å^3	
Z	4	
Density (calculated)	1.409 Mg/m^3	
Absorption coefficient	0.317 mm^{-1}	
F(000)	432	
Crystal size	0.50 × 0.50 × 0.40 mm^3	
Theta range for data collection	2.64 to 29.12°	
Index ranges	$-11 \le h \le 11$, $-13 \le k \le 14$, $-15 \le l \le 15$	
Reflections collected	13218	
Independent reflections	2592 [R(int) = 0.0250]	
Completeness to theta = 29.12°	99.9%	
Absorption correction	Empirical with SADABS	
Max. and min. transmission	0.8836 and 0.8575	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2592 / 0 / 121	
Goodness-of-fit on F^2	1.077	
Final R indices [$I > 2\sigma$(I)]	$R1$ = 0.0228, $wR2$ = 0.0649	
R indices (all data)	$R1$ = 0.0230, $wR2$ = 0.0651	
Absolute structure parameter	0.00(5)	
Largest diff. peak and hole	0.281 and –0.155 e.Å^{-3}	

Table S10. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($Å^2 \times 10^3$) for **5**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
S(1)	10525(1)	2987(1)	6618(1)	25(1)
N(1)	7824(1)	1591(1)	6622(1)	18(1)
O(2)	6581(1)	3392(1)	9188(1)	21(1)
O(1)	7965(1)	1555(1)	9062(1)	26(1)
F(1)	4841(1)	318(1)	7923(1)	29(1)
C(2)	9403(1)	1692(1)	6332(1)	20(1)
C(5)	5128(1)	2302(1)	6942(1)	19(1)
C(7)	7245(1)	2418(1)	8604(1)	16(1)
C(6)	6925(1)	2565(1)	7273(1)	15(1)
C(3)	6752(1)	501(1)	6327(1)	23(1)
C(4)	5069(1)	875(1)	6796(1)	22(1)
C(8)	6792(2)	3367(1)	10466(1)	26(1)
C(1)	10136(2)	552(1)	5724(1)	29(1)

Table S11. Bond lengths [Å] and angles [°] for **5**.

S(1)-C(2)	1.6752(11)
N(1)-C(2)	1.3295(13)
N(1)-C(6)	1.4589(11)
N(1)-C(3)	1.4824(12)
O(2)-C(7)	1.3353(11)
O(2)-C(8)	1.4502(12)
O(1)-C(7)	1.1995(12)
F(1)-C(4)	1.4123(12)
C(2)-C(1)	1.5087(14)
C(5)-C(4)	1.5157(13)
C(5)-C(6)	1.5342(12)
C(5)-H(5A)	0.9900
C(5)-H(5B)	0.9900
C(7)-C(6)	1.5303(12)
C(6)-H(6)	1.0000
C(3)-C(4)	1.5195(15)
C(3)-H(3A)	0.9900
C(3)-H(3B)	0.9900
C(4)-H(4)	1.0000
C(8)-H(8A)	0.9800
C(8)-H(8B)	0.9800
C(8)-H(8C)	0.9800
C(1)-H(1A)	0.9800
C(1)-H(1B)	0.9800
C(1)-H(1C)	0.9800
C(2)-N(1)-C(6)	123.43(8)
C(2)-N(1)-C(3)	125.11(9)
C(6)-N(1)-C(3)	111.46(8)
C(7)-O(2)-C(8)	115.32(8)
N(1)-C(2)-C(1)	115.45(10)
N(1)-C(2)-S(1)	122.97(8)
C(1)-C(2)-S(1)	121.57(8)
C(4)-C(5)-C(6)	103.69(8)
C(4)-C(5)-H(5A)	111.0
C(6)-C(5)-H(5A)	111.0
C(4)-C(5)-H(5B)	111.0
C(6)-C(5)-H(5B)	111.0
H(5A)-C(5)-H(5B)	109.0
O(1)-C(7)-O(2)	124.74(9)
O(1)-C(7)-C(6)	125.59(9)
O(2)-C(7)-C(6)	109.66(7)
N(1)-C(6)-C(7)	109.62(7)
N(1)-C(6)-C(5)	103.15(7)
C(7)-C(6)-C(5)	112.43(7)
N(1)-C(6)-H(6)	110.5
C(7)-C(6)-H(6)	110.5
C(5)-C(6)-H(6)	110.5
N(1)-C(3)-C(4)	104.44(8)
N(1)-C(3)-H(3A)	110.9
C(4)-C(3)-H(3A)	110.9
N(1)-C(3)-H(3B)	110.9
C(4)-C(3)-H(3B)	110.9
H(3A)-C(3)-H(3B)	108.9

F(1)-C(4)-C(5)	108.68(8)
F(1)-C(4)-C(3)	108.82(8)
C(5)-C(4)-C(3)	105.56(8)
F(1)-C(4)-H(4)	111.2
C(5)-C(4)-H(4)	111.2
C(3)-C(4)-H(4)	111.2
O(2)-C(8)-H(8A)	109.5
O(2)-C(8)-H(8B)	109.5
H(8A)-C(8)-H(8B)	109.5
O(2)-C(8)-H(8C)	109.5
H(8A)-C(8)-H(8C)	109.5
H(8B)-C(8)-H(8C)	109.5
C(2)-C(1)-H(1A)	109.5
C(2)-C(1)-H(1B)	109.5
H(1A)-C(1)-H(1B)	109.5
C(2)-C(1)-H(1C)	109.5
H(1A)-C(1)-H(1C)	109.5
H(1B)-C(1)-H(1C)	109.5

Table S12. Anisotropic displacement parameters (Å^2 × 10^3) for **5**. The anisotropic displacement factor exponent takes the form: $-2p^2[h^2\ a^{*2}U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
S(1)	21(1)	33(1)	21(1)	-1(1)	2(1)	-3(1)
N(1)	24(1)	14(1)	16(1)	-2(1)	1(1)	2(1)
O(2)	30(1)	18(1)	14(1)	-2(1)	-1(1)	4(1)
O(1)	32(1)	26(1)	21(1)	4(1)	1(1)	10(1)
F(1)	39(1)	20(1)	27(1)	4(1)	7(1)	-4(1)
C(2)	25(1)	23(1)	13(1)	2(1)	1(1)	5(1)
C(5)	19(1)	16(1)	20(1)	1(1)	-3(1)	-1(1)
C(7)	17(1)	16(1)	15(1)	0(1)	0(1)	-1(1)
C(6)	20(1)	12(1)	14(1)	0(1)	0(1)	1(1)
C(3)	33(1)	14(1)	22(1)	-4(1)	2(1)	-2(1)
C(4)	29(1)	17(1)	21(1)	0(1)	-1(1)	-5(1)
C(8)	34(1)	29(1)	14(1)	-3(1)	0(1)	0(1)
C(1)	36(1)	28(1)	23(1)	0(1)	8(1)	12(1)

Table S13. Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($Å^2 \times 10^3$) for **5**.

	x	*y*	*z*	*U*(eq)
H(5A)	4375	2584	7580	22
H(5B)	4826	2735	6194	22
H(6)	7260	3428	6998	19
H(3A)	7149	-281	6718	28
H(3B)	6716	360	5459	28
H(4)	4178	618	6234	27
H(8A)	6302	2591	10787	38
H(8B)	6251	4106	10817	38
H(8C)	7968	3386	10657	38
H(1A)	10254	-140	6298	43
H(1B)	11218	772	5403	43
H(1C)	9412	281	5076	43

Table S14. Torsion angles [°] for **5**.

C(6)-N(1)-C(2)-C(1)	176.49(8)
C(3)-N(1)-C(2)-C(1)	-4.02(13)
C(6)-N(1)-C(2)-S(1)	-3.33(13)
C(3)-N(1)-C(2)-S(1)	176.16(7)
C(8)-O(2)-C(7)-O(1)	0.58(14)
C(8)-O(2)-C(7)-C(6)	179.81(8)
C(2)-N(1)-C(6)-C(7)	-82.68(10)
C(3)-N(1)-C(6)-C(7)	97.77(9)
C(2)-N(1)-C(6)-C(5)	157.37(8)
C(3)-N(1)-C(6)-C(5)	-22.18(10)
O(1)-C(7)-C(6)-N(1)	-7.90(13)
O(2)-C(7)-C(6)-N(1)	172.88(7)
O(1)-C(7)-C(6)-C(5)	106.20(11)
O(2)-C(7)-C(6)-C(5)	-73.01(10)
C(4)-C(5)-C(6)-N(1)	33.05(9)
C(4)-C(5)-C(6)-C(7)	-84.95(9)
C(2)-N(1)-C(3)-C(4)	-177.27(9)
C(6)-N(1)-C(3)-C(4)	2.27(11)
C(6)-C(5)-C(4)-F(1)	84.19(9)
C(6)-C(5)-C(4)-C(3)	-32.41(10)
N(1)-C(3)-C(4)-F(1)	-97.44(9)
N(1)-C(3)-C(4)-C(5)	19.06(10)

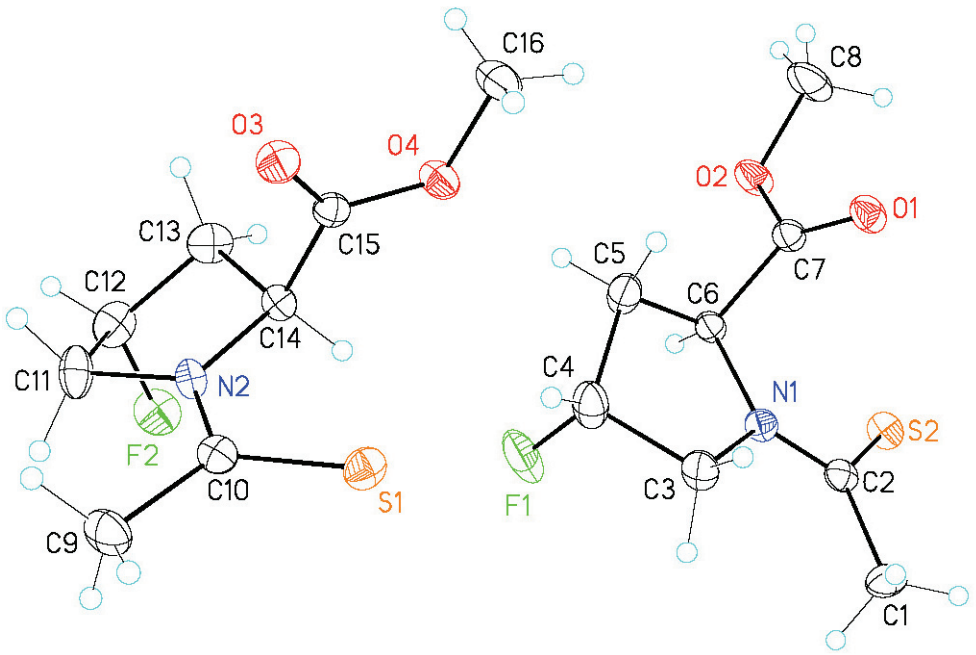


Figure S4. Molecular drawing of **6** drawn at 50% probability ellipsoids.

Table S15. Crystal data and structure refinement for **6**.

Identification code	raines15	
Empirical formula	$C_8H_{12}FNO_2S$	
Formula weight	205.25	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	C2	
Unit cell dimensions	a = 24.5661(16) Å	α = 90°
	b = 6.8549(4) Å	β = 124.5610(10)°
	c = 14.3019(9) Å	γ = 90°
Volume	1983.4(2) Å^3	
Z	8	
Density (calculated)	1.375 Mg/m^3	
Absorption coefficient	0.310 mm^{-1}	
F(000)	864	
Crystal size	0.51 × 0.25 × 0.16 mm^3	
Theta range for data collection	1.73 to 30.03°	
Index ranges	$-34 \leq h \leq 33$, $-9 \leq k \leq 9$, $-20 \leq l \leq 19$	
Reflections collected	14950	
Independent reflections	5510 [R(int) = 0.0200]	
Completeness to theta = 30.03°	97.6%	
Absorption correction	Empirical with SADABS	
Max. and min. transmission	0.9521 and 0.8581	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	5510 / 1 / 251	
Goodness-of-fit on F^2	0.634	
Final R indices [$I > 2\sigma$(I)]	$R1$ = 0.0268, $wR2$ = 0.0730	
R indices (all data)	$R1$ = 0.0282, $wR2$ = 0.0778	
Absolute structure parameter	0.00(4)	
Largest diff. peak and hole	0.412 and –0.151 e.Å^{-3}	

Table S16. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($Å^2 \times 10^3$) for **6**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
S(1)	1719(1)	2231(1)	3399(1)	20(1)
S(2)	6071(1)	2194(1)	8718(1)	21(1)
O(3)	1681(1)	6257(1)	1959(1)	22(1)
N(2)	1729(1)	2239(2)	1568(1)	16(1)
O(4)	2764(1)	6102(1)	3389(1)	21(1)
F(2)	2588(1)	274(1)	1083(1)	29(1)
N(1)	4790(1)	2533(1)	7191(1)	17(1)
O(1)	5250(1)	6515(1)	7735(1)	22(1)
F(1)	3919(1)	1013(2)	4866(1)	40(1)
O(2)	5631(1)	6123(1)	6633(1)	25(1)
C(7)	5293(1)	5583(2)	7065(1)	18(1)
C(15)	2200(1)	5404(2)	2483(1)	16(1)
C(3)	4082(1)	2018(2)	6597(1)	22(1)
C(10)	1426(1)	1681(2)	2051(1)	18(1)
C(2)	5276(1)	1803(2)	8190(1)	17(1)
C(6)	4910(1)	3732(2)	6479(1)	16(1)
C(14)	2328(1)	3430(2)	2158(1)	16(1)
C(9)	805(1)	511(2)	1315(1)	26(1)
C(11)	1547(1)	1645(2)	430(1)	24(1)
C(1)	5070(1)	568(2)	8810(1)	23(1)
C(4)	3799(1)	2559(2)	5379(1)	27(1)
C(5)	4207(1)	4287(2)	5467(1)	23(1)
C(13)	2498(1)	3685(2)	1280(1)	23(1)
C(12)	2186(1)	1914(2)	525(1)	25(1)
C(8)	5942(1)	8026(2)	6985(2)	37(1)
C(16)	2711(1)	8049(2)	3724(1)	26(1)

Table S17. Bond lengths [Å] and angles [°] for **6**.

S(1)-C(10)	1.6731(12)
S(2)-C(2)	1.6683(12)
O(3)-C(15)	1.2023(14)
N(2)-C(10)	1.3289(15)
N(2)-C(14)	1.4603(14)
N(2)-C(11)	1.4786(14)
O(4)-C(15)	1.3381(13)
O(4)-C(16)	1.4480(16)
F(2)-C(12)	1.4080(15)
N(1)-C(2)	1.3344(15)
N(1)-C(6)	1.4644(14)
N(1)-C(3)	1.4809(13)
O(1)-C(7)	1.2061(15)
F(1)-C(4)	1.4109(17)
O(2)-C(7)	1.3383(14)
O(2)-C(8)	1.4496(16)
C(7)-C(6)	1.5164(16)
C(15)-C(14)	1.5202(16)
C(3)-C(4)	1.5112(17)
C(3)-H(3A)	0.9900
C(3)-H(3B)	0.9900
C(10)-C(9)	1.5016(16)
C(2)-C(1)	1.5057(16)
C(6)-C(5)	1.5453(16)
C(6)-H(6)	1.0000
C(14)-C(13)	1.5436(16)
C(14)-H(14)	1.0000
C(9)-H(9A)	0.9800
C(9)-H(9B)	0.9800
C(9)-H(9C)	0.9800
C(11)-C(12)	1.5087(18)
C(11)-H(11A)	0.9900
C(11)-H(11B)	0.9900
C(1)-H(1A)	0.9800
C(1)-H(1B)	0.9800
C(1)-H(1C)	0.9800
C(4)-C(5)	1.5100(18)
C(4)-H(4)	1.0000
C(5)-H(5A)	0.9900
C(5)-H(5B)	0.9900
C(13)-C(12)	1.5131(19)
C(13)-H(13A)	0.9900
C(13)-H(13B)	0.9900
C(12)-H(12)	1.0000
C(8)-H(8A)	0.9800
C(8)-H(8B)	0.9800
C(8)-H(8C)	0.9800
C(16)-H(3)	1.007(18)
C(16)-H(2)	0.84(2)
C(16)-H(1)	1.01(2)
C(10)-N(2)-C(14)	122.53(9)
C(10)-N(2)-C(11)	125.75(10)
C(14)-N(2)-C(11)	111.57(9)

C(15)-O(4)-C(16)	114.34(10)
C(2)-N(1)-C(6)	122.91(9)
C(2)-N(1)-C(3)	124.85(10)
C(6)-N(1)-C(3)	111.71(9)
C(7)-O(2)-C(8)	115.55(10)
O(1)-C(7)-O(2)	125.25(11)
O(1)-C(7)-C(6)	125.21(11)
O(2)-C(7)-C(6)	109.21(9)
O(3)-C(15)-O(4)	125.34(11)
O(3)-C(15)-C(14)	124.93(11)
O(4)-C(15)-C(14)	109.56(9)
N(1)-C(3)-C(4)	103.01(9)
N(1)-C(3)-H(3A)	111.2
C(4)-C(3)-H(3A)	111.2
N(1)-C(3)-H(3B)	111.2
C(4)-C(3)-H(3B)	111.2
H(3A)-C(3)-H(3B)	109.1
N(2)-C(10)-C(9)	115.76(10)
N(2)-C(10)-S(1)	122.15(8)
C(9)-C(10)-S(1)	122.08(9)
N(1)-C(2)-C(1)	116.46(10)
N(1)-C(2)-S(2)	122.12(9)
C(1)-C(2)-S(2)	121.41(9)
N(1)-C(6)-C(7)	113.08(9)
N(1)-C(6)-C(5)	103.29(9)
C(7)-C(6)-C(5)	108.94(10)
N(1)-C(6)-H(6)	110.4
C(7)-C(6)-H(6)	110.4
C(5)-C(6)-H(6)	110.4
N(2)-C(14)-C(15)	111.09(9)
N(2)-C(14)-C(13)	104.00(9)
C(15)-C(14)-C(13)	110.27(9)
N(2)-C(14)-H(14)	110.4
C(15)-C(14)-H(14)	110.4
C(13)-C(14)-H(14)	110.4
C(10)-C(9)-H(9A)	109.5
C(10)-C(9)-H(9B)	109.5
H(9A)-C(9)-H(9B)	109.5
C(10)-C(9)-H(9C)	109.5
H(9A)-C(9)-H(9C)	109.5
H(9B)-C(9)-H(9C)	109.5
N(2)-C(11)-C(12)	102.55(9)
N(2)-C(11)-H(11A)	111.3
C(12)-C(11)-H(11A)	111.3
N(2)-C(11)-H(11B)	111.3
C(12)-C(11)-H(11B)	111.3
H(11A)-C(11)-H(11B)	109.2
C(2)-C(1)-H(1A)	109.5
C(2)-C(1)-H(1B)	109.5
H(1A)-C(1)-H(1B)	109.5
C(2)-C(1)-H(1C)	109.5
H(1A)-C(1)-H(1C)	109.5
H(1B)-C(1)-H(1C)	109.5
F(1)-C(4)-C(3)	108.65(12)
F(1)-C(4)-C(5)	107.97(11)
C(3)-C(4)-C(5)	104.31(10)

F(1)-C(4)-H(4)	111.8
C(3)-C(4)-H(4)	111.9
C(5)-C(4)-H(4)	111.9
C(4)-C(5)-C(6)	102.80(10)
C(4)-C(5)-H(5A)	111.2
C(6)-C(5)-H(5A)	111.2
C(4)-C(5)-H(5B)	111.2
C(6)-C(5)-H(5B)	111.2
H(5A)-C(5)-H(5B)	109.1
C(12)-C(13)-C(14)	103.17(10)
C(12)-C(13)-H(13A)	111.1
C(14)-C(13)-H(13A)	111.1
C(12)-C(13)-H(13B)	111.1
C(14)-C(13)-H(13B)	111.1
H(13A)-C(13)-H(13B)	109.1
F(2)-C(12)-C(13)	109.08(10)
F(2)-C(12)-C(11)	108.25(11)
C(13)-C(12)-C(11)	104.07(10)
F(2)-C(12)-H(12)	111.7
C(13)-C(12)-H(12)	111.7
C(11)-C(12)-H(12)	111.7
O(2)-C(8)-H(8A)	109.5
O(2)-C(8)-H(8B)	109.5
H(8A)-C(8)-H(8B)	109.5
O(2)-C(8)-H(8C)	109.5
H(8A)-C(8)-H(8C)	109.5
H(8B)-C(8)-H(8C)	109.5
O(4)-C(16)-H(3)	108.9(12)
O(4)-C(16)-H(2)	107.1(14)
H(3)-C(16)-H(2)	113.6(17)
O(4)-C(16)-H(1)	101.0(12)
H(3)-C(16)-H(1)	116.0(15)
H(2)-C(16)-H(1)	109.3(18)

Table S18. Anisotropic displacement parameters (Å^2 × 10^3) for **6**. The anisotropic 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}
S(1)	24(1)	23(1)	20(1)	1(1)	16(1)	2(1)
S(2)	17(1)	23(1)	24(1)	-2(1)	11(1)	0(1)
O(3)	20(1)	21(1)	24(1)	1(1)	12(1)	4(1)
N(2)	14(1)	19(1)	14(1)	-4(1)	7(1)	-1(1)
O(4)	17(1)	18(1)	24(1)	-3(1)	9(1)	-2(1)
F(2)	27(1)	26(1)	36(1)	-3(1)	20(1)	6(1)
N(1)	17(1)	19(1)	18(1)	-2(1)	12(1)	-4(1)
O(1)	27(1)	20(1)	25(1)	-6(1)	18(1)	-4(1)
F(1)	47(1)	45(1)	36(1)	-25(1)	29(1)	-27(1)
O(2)	36(1)	22(1)	31(1)	-9(1)	27(1)	-12(1)
C(7)	18(1)	18(1)	19(1)	-1(1)	12(1)	-3(1)
C(15)	17(1)	16(1)	18(1)	0(1)	11(1)	0(1)
C(3)	17(1)	29(1)	21(1)	-3(1)	12(1)	-8(1)
C(10)	16(1)	17(1)	21(1)	0(1)	10(1)	2(1)
C(2)	21(1)	15(1)	21(1)	-3(1)	15(1)	-1(1)
C(6)	19(1)	17(1)	17(1)	-3(1)	13(1)	-4(1)
C(14)	14(1)	17(1)	18(1)	-1(1)	9(1)	0(1)
C(9)	17(1)	25(1)	31(1)	-1(1)	11(1)	-4(1)
C(11)	21(1)	34(1)	16(1)	-7(1)	9(1)	4(1)
C(1)	31(1)	19(1)	28(1)	4(1)	22(1)	3(1)
C(4)	22(1)	38(1)	21(1)	-6(1)	12(1)	-10(1)
C(5)	20(1)	30(1)	17(1)	1(1)	10(1)	-4(1)
C(13)	28(1)	24(1)	29(1)	1(1)	22(1)	2(1)
C(12)	30(1)	29(1)	24(1)	0(1)	19(1)	7(1)
C(8)	56(1)	27(1)	45(1)	-14(1)	39(1)	-23(1)
C(16)	27(1)	17(1)	30(1)	-5(1)	14(1)	-2(1)

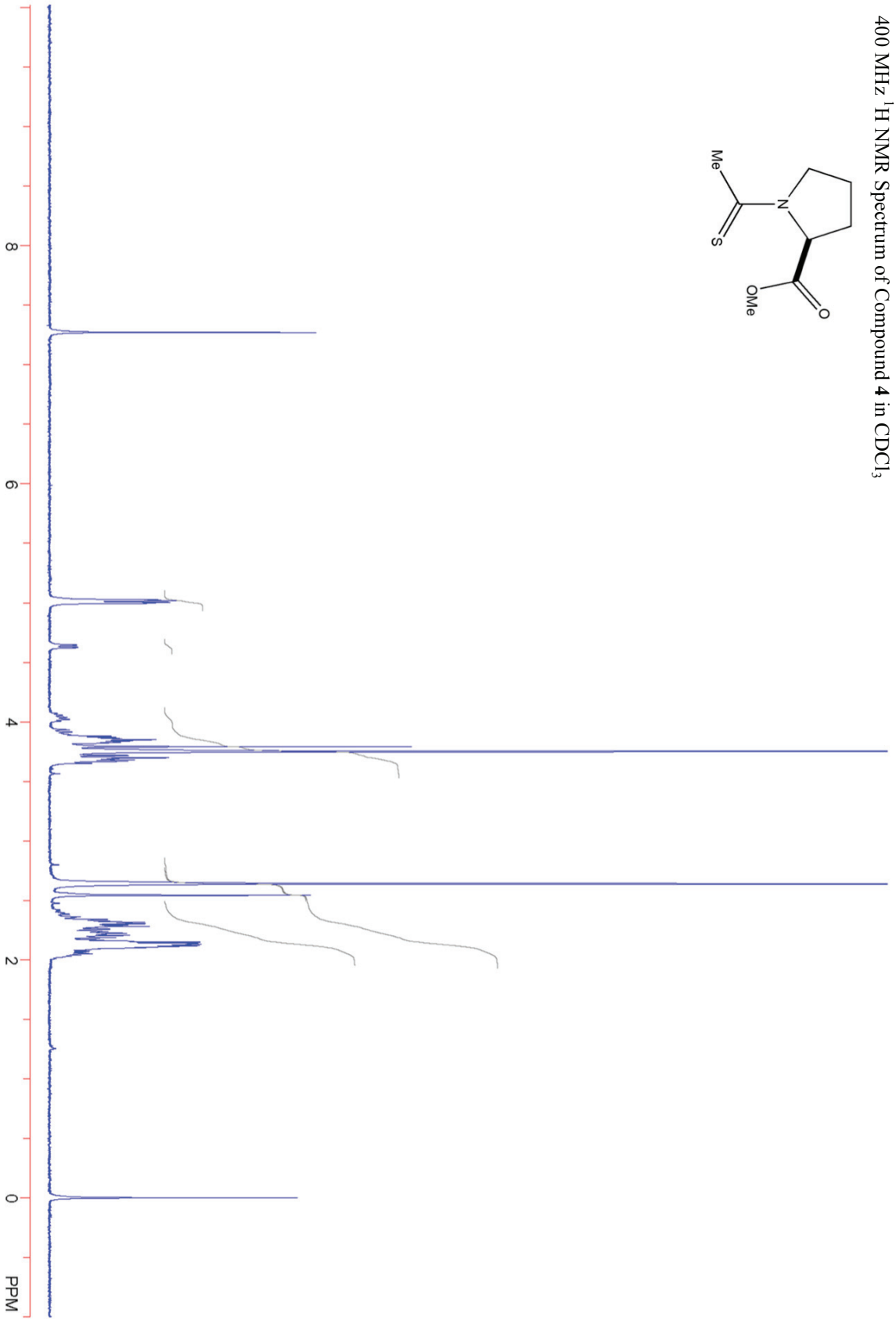
Table S19. Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($Å^2 \times 10^3$) for **6**.

	x	*y*	*z*	*U*(eq)
H(3A)	3870	2777	6898	26
H(3B)	4025	609	6670	26
H(6)	5142	2954	6212	20
H(14)	2693	2734	2847	19
H(9A)	537	1100	558	39
H(9B)	553	496	1654	39
H(9C)	921	-829	1252	39
H(11A)	1193	2488	-170	29
H(11B)	1399	269	267	29
H(1A)	4685	1158	8738	34
H(1B)	5436	487	9614	34
H(1C)	4957	-745	8481	34
H(4)	3318	2887	4950	32
H(5A)	4054	5504	5622	28
H(5B)	4190	4453	4763	28
H(13A)	2307	4907	842	28
H(13B)	2983	3699	1653	28
H(12)	2107	2120	-236	30
H(8A)	5602	9028	6746	55
H(8B)	6180	8282	6634	55
H(8C)	6252	8055	7813	55
H(3)	2370(9)	8040(30)	3905(15)	26(4)
H(2)	2617(9)	8800(30)	3189(17)	28(5)
H(1)	3182(10)	8290(30)	4385(16)	32(5)

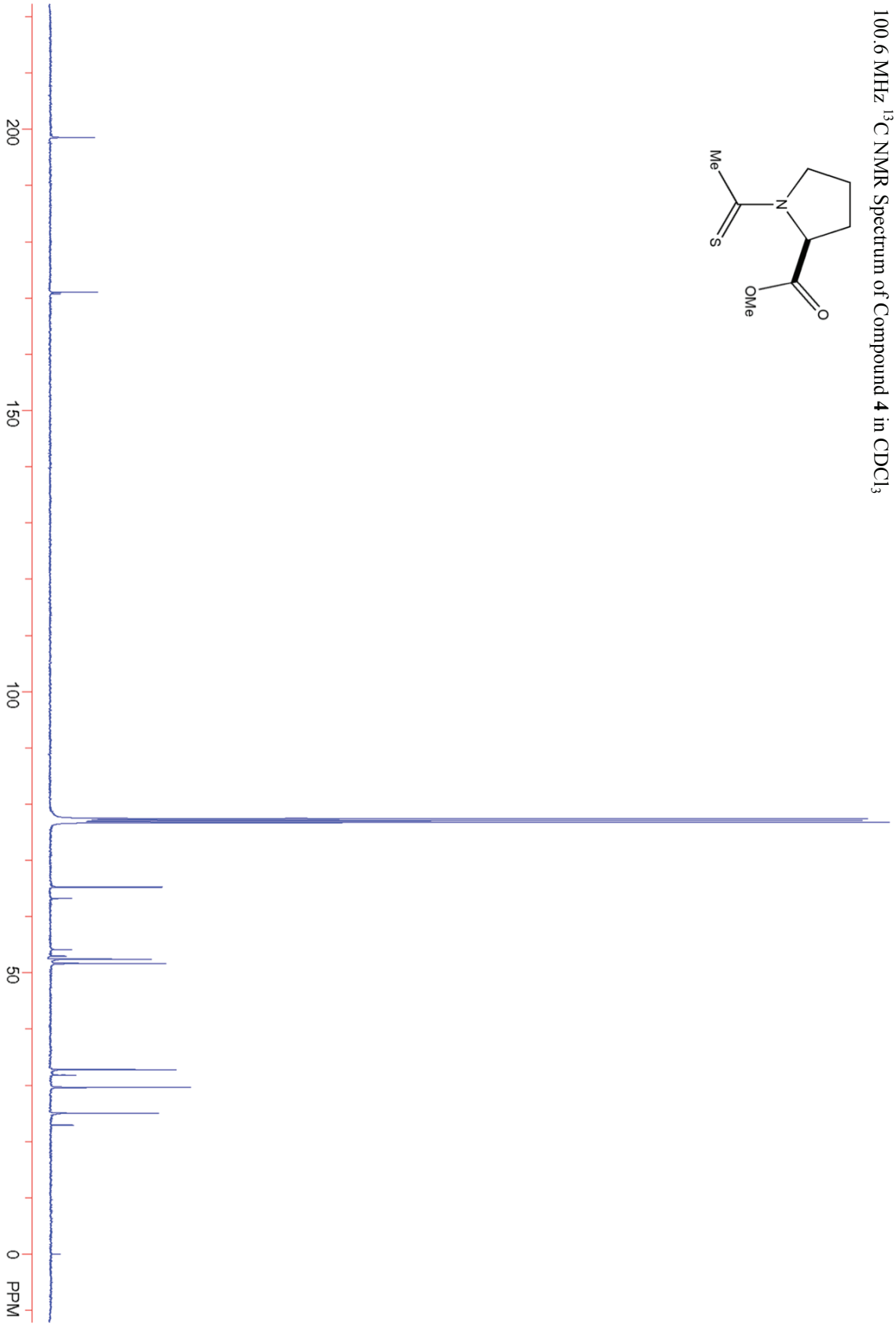
Table S20. Torsion angles [°] for **6**.

C(8)-O(2)-C(7)-O(1)	-2.63(19)
C(8)-O(2)-C(7)-C(6)	171.03(12)
C(16)-O(4)-C(15)-O(3)	0.13(17)
C(16)-O(4)-C(15)-C(14)	175.61(10)
C(2)-N(1)-C(3)-C(4)	-158.56(11)
C(6)-N(1)-C(3)-C(4)	13.25(13)
C(14)-N(2)-C(10)-C(9)	178.27(10)
C(11)-N(2)-C(10)-C(9)	-6.44(17)
C(14)-N(2)-C(10)-S(1)	-2.24(16)
C(11)-N(2)-C(10)-S(1)	173.05(9)
C(6)-N(1)-C(2)-C(1)	-178.93(10)
C(3)-N(1)-C(2)-C(1)	-8.00(16)
C(6)-N(1)-C(2)-S(2)	-0.14(15)
C(3)-N(1)-C(2)-S(2)	170.80(9)
C(2)-N(1)-C(6)-C(7)	-59.80(14)
C(3)-N(1)-C(6)-C(7)	128.20(10)
C(2)-N(1)-C(6)-C(5)	-177.39(10)
C(3)-N(1)-C(6)-C(5)	10.61(12)
O(1)-C(7)-C(6)-N(1)	-33.76(16)
O(2)-C(7)-C(6)-N(1)	152.58(10)
O(1)-C(7)-C(6)-C(5)	80.47(14)
O(2)-C(7)-C(6)-C(5)	-93.19(11)
C(10)-N(2)-C(14)-C(15)	-61.87(14)
C(11)-N(2)-C(14)-C(15)	122.24(10)
C(10)-N(2)-C(14)-C(13)	179.52(10)
C(11)-N(2)-C(14)-C(13)	3.63(13)
O(3)-C(15)-C(14)-N(2)	-30.66(15)
O(4)-C(15)-C(14)-N(2)	153.83(9)
O(3)-C(15)-C(14)-C(13)	84.10(14)
O(4)-C(15)-C(14)-C(13)	-91.41(11)
C(10)-N(2)-C(11)-C(12)	-156.12(11)
C(14)-N(2)-C(11)-C(12)	19.61(13)
N(1)-C(3)-C(4)-F(1)	82.65(12)
N(1)-C(3)-C(4)-C(5)	-32.32(13)
F(1)-C(4)-C(5)-C(6)	-76.39(12)
C(3)-C(4)-C(5)-C(6)	39.06(13)
N(1)-C(6)-C(5)-C(4)	-30.21(12)
C(7)-C(6)-C(5)-C(4)	-150.66(10)
N(2)-C(14)-C(13)-C(12)	-25.40(12)
C(15)-C(14)-C(13)-C(12)	-144.57(10)
C(14)-C(13)-C(12)-F(2)	-77.51(12)
C(14)-C(13)-C(12)-C(11)	37.84(12)
N(2)-C(11)-C(12)-F(2)	80.74(12)
N(2)-C(11)-C(12)-C(13)	-35.21(13)

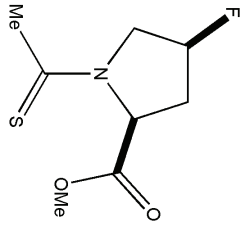
400 MHz ^{1}H NMR Spectrum of Compound **4** in $CDCl_3$

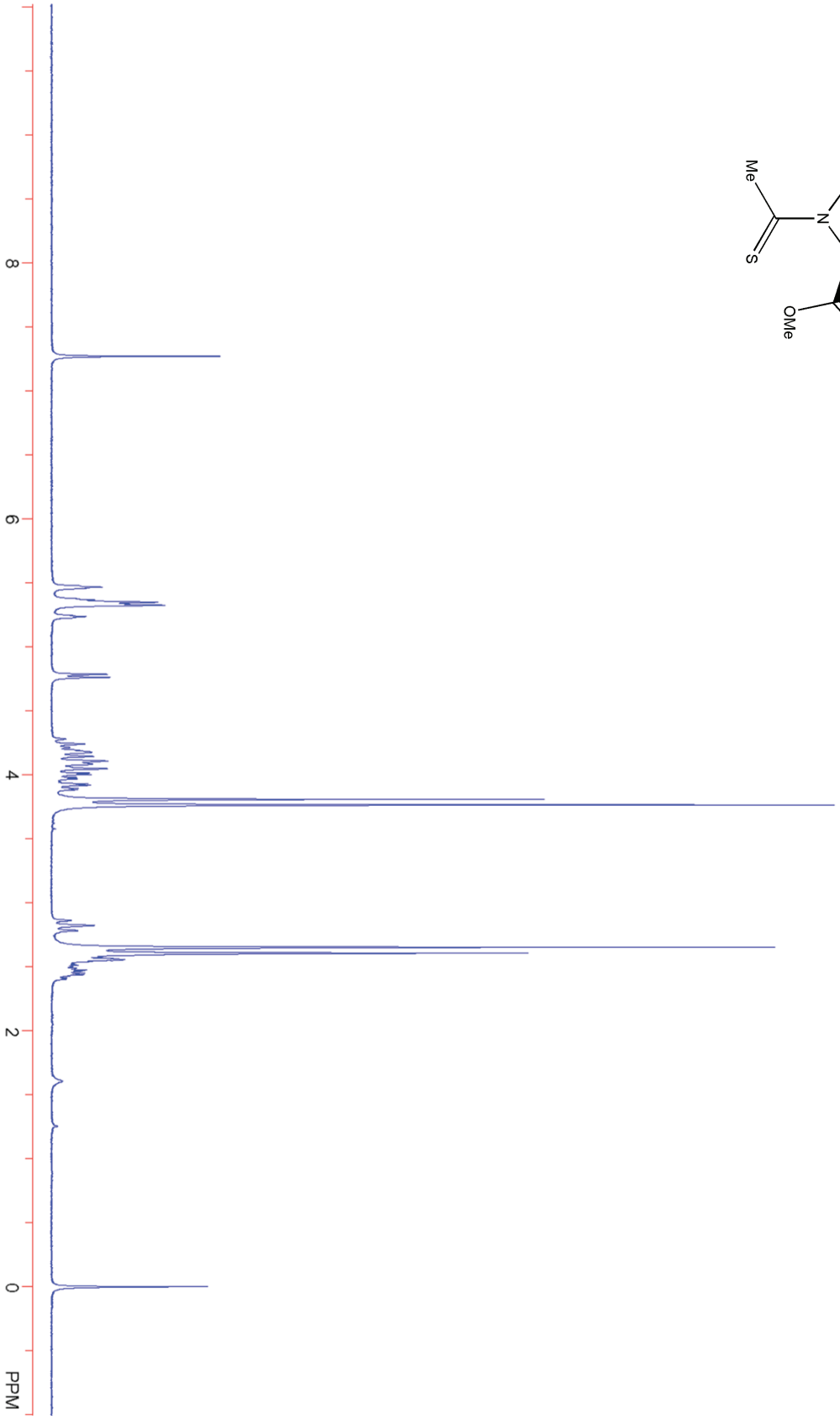


100.6 MHz ^{13}C NMR Spectrum of Compound **4** in $CDCl_3$

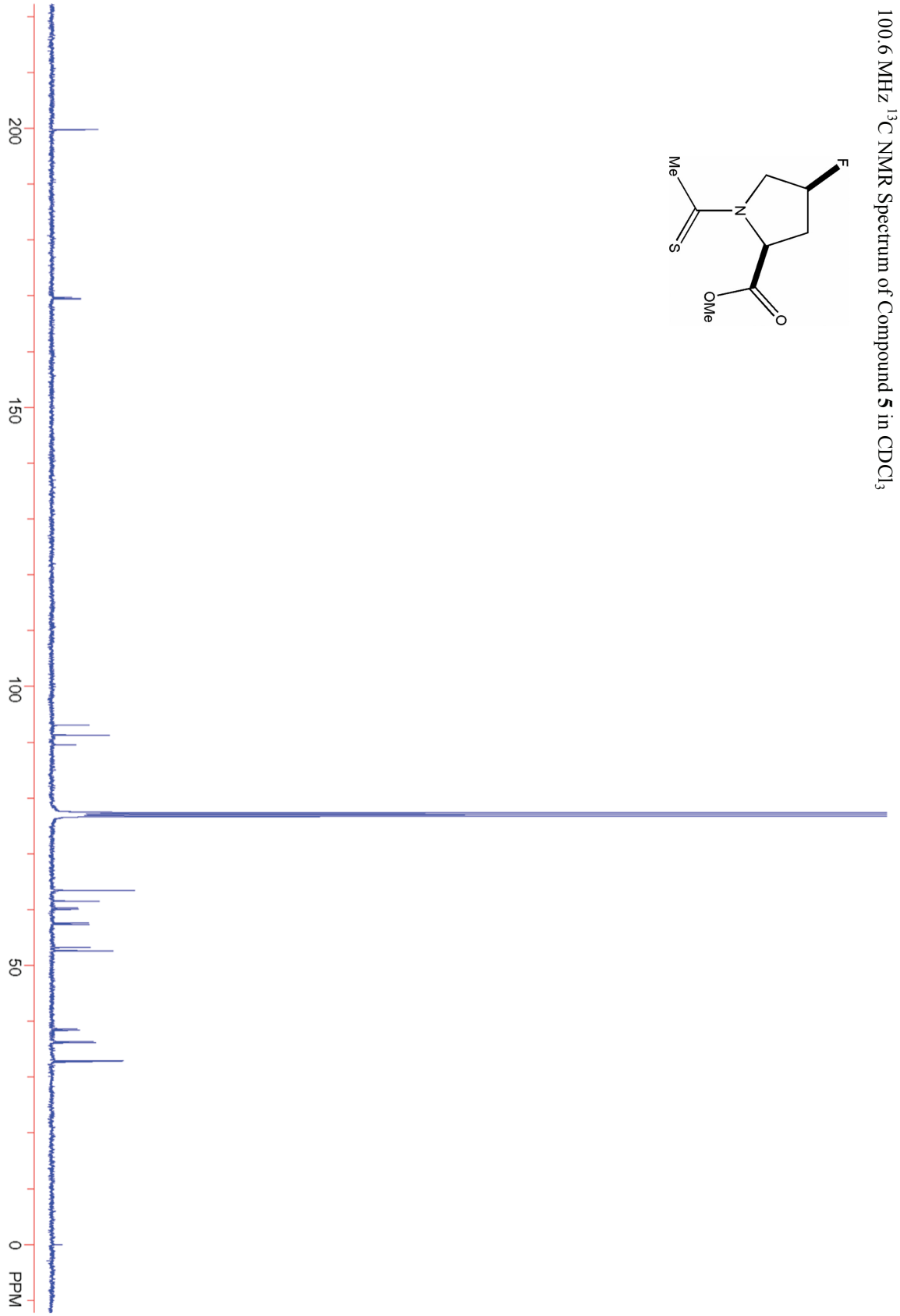


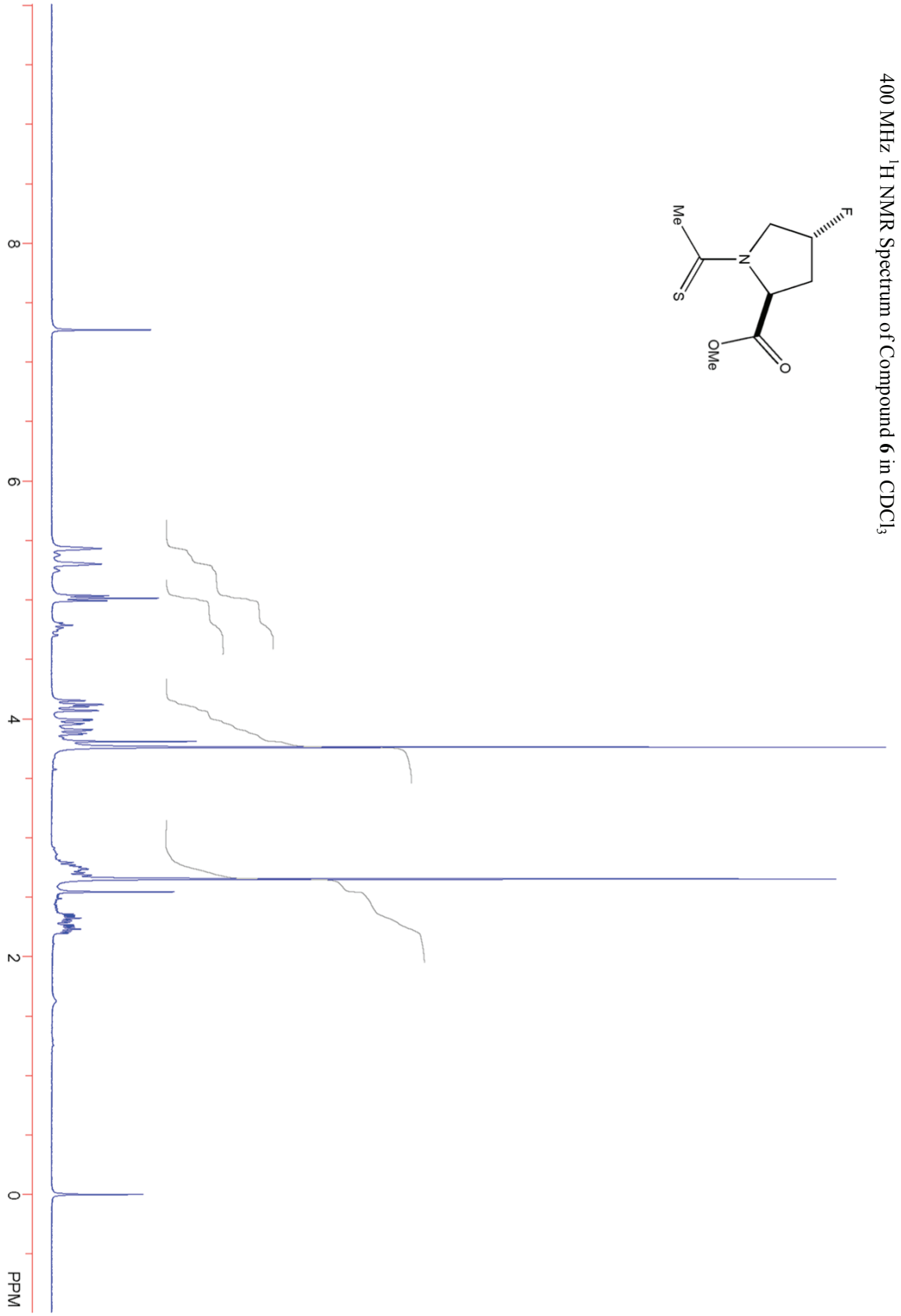
400 MHz ^{1}H NMR Spectrum of Compound **5** in $CDCl_3$





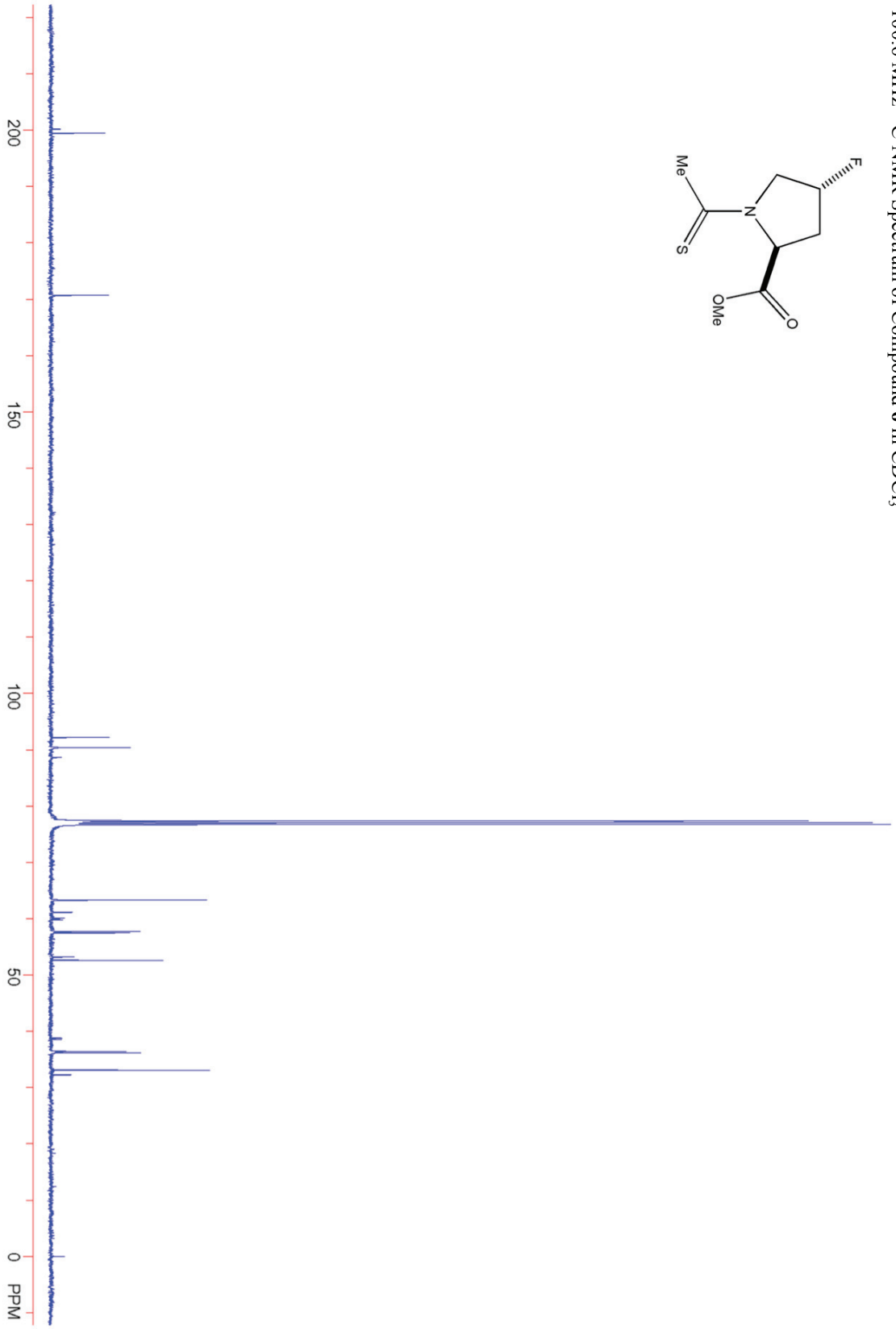
100.6 MHz ^{13}C NMR Spectrum of Compound **5** in $CDCl_3$

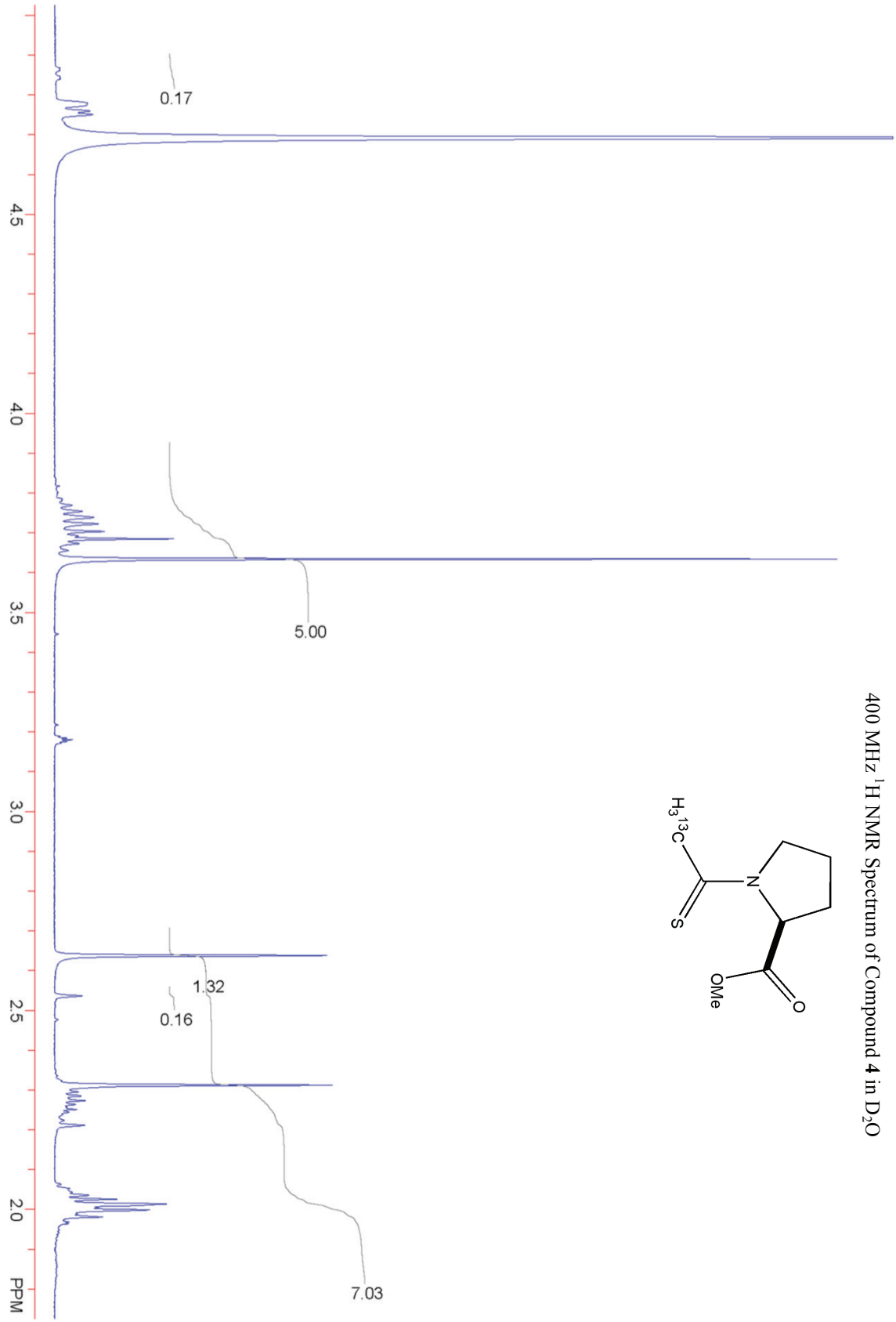




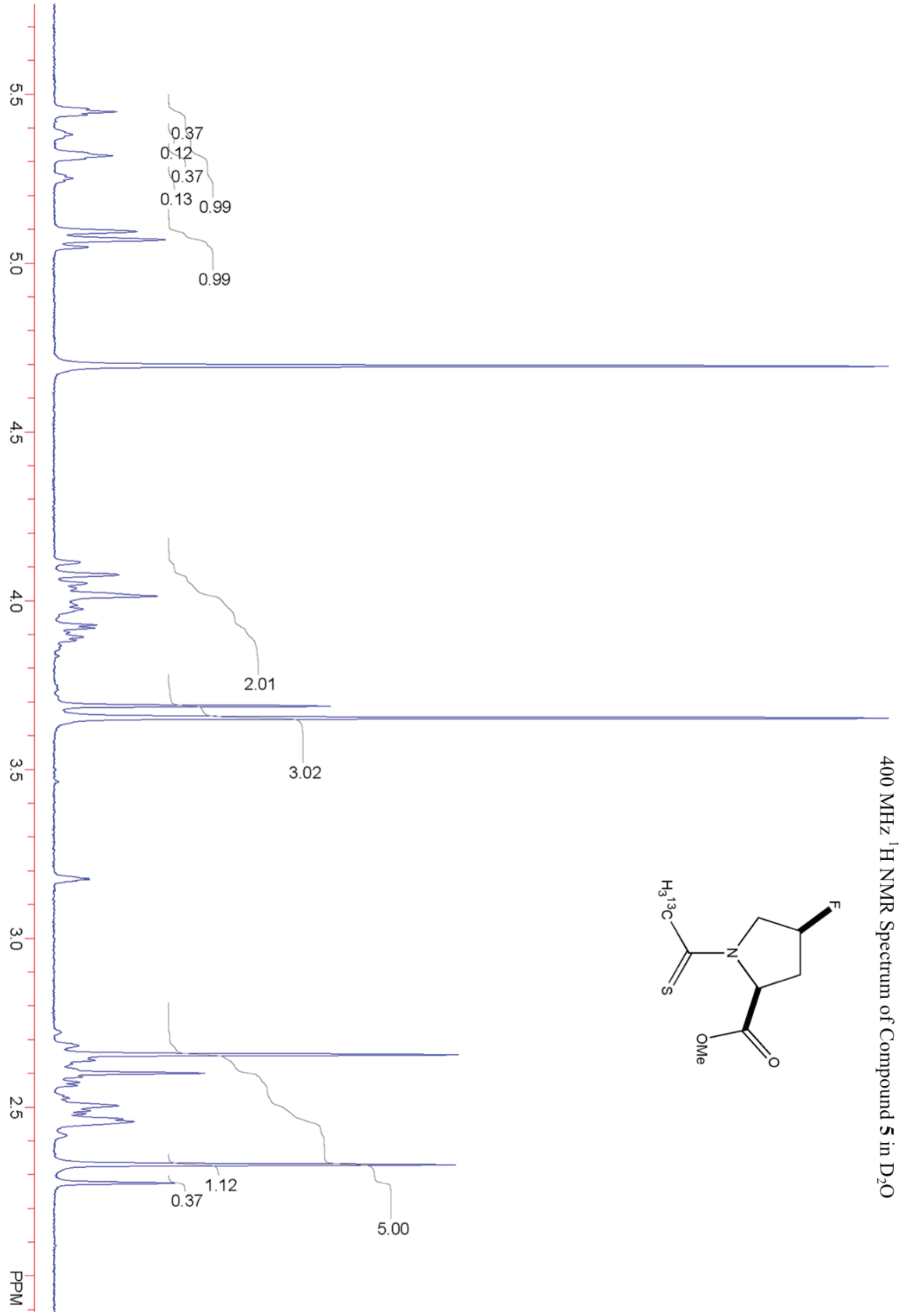
400 MHz ^{1}H NMR Spectrum of Compound **6** in $CDCl_3$

100.6 MHz ^{13}C NMR Spectrum of Compound **6** in $CDCl_3$

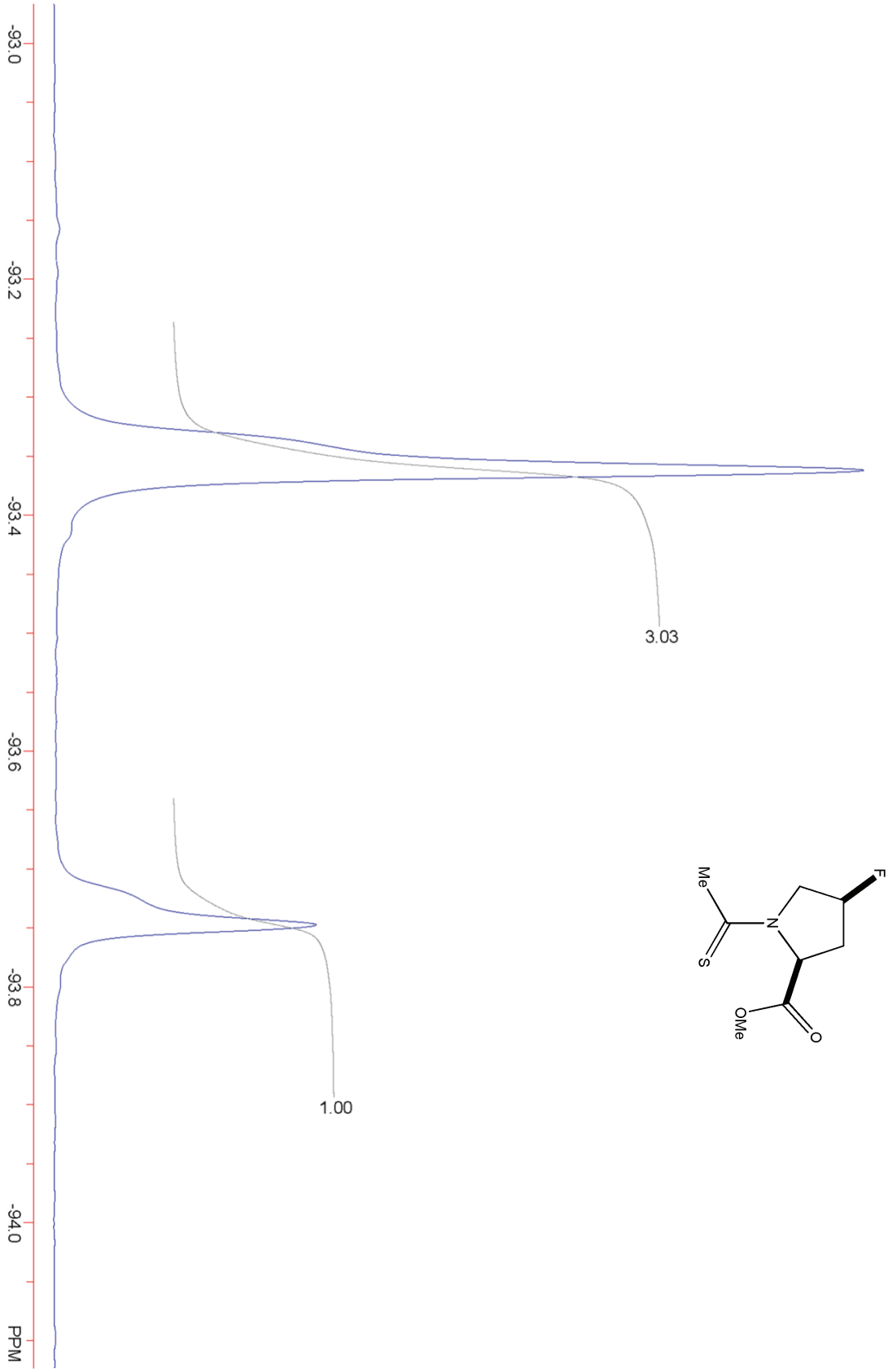




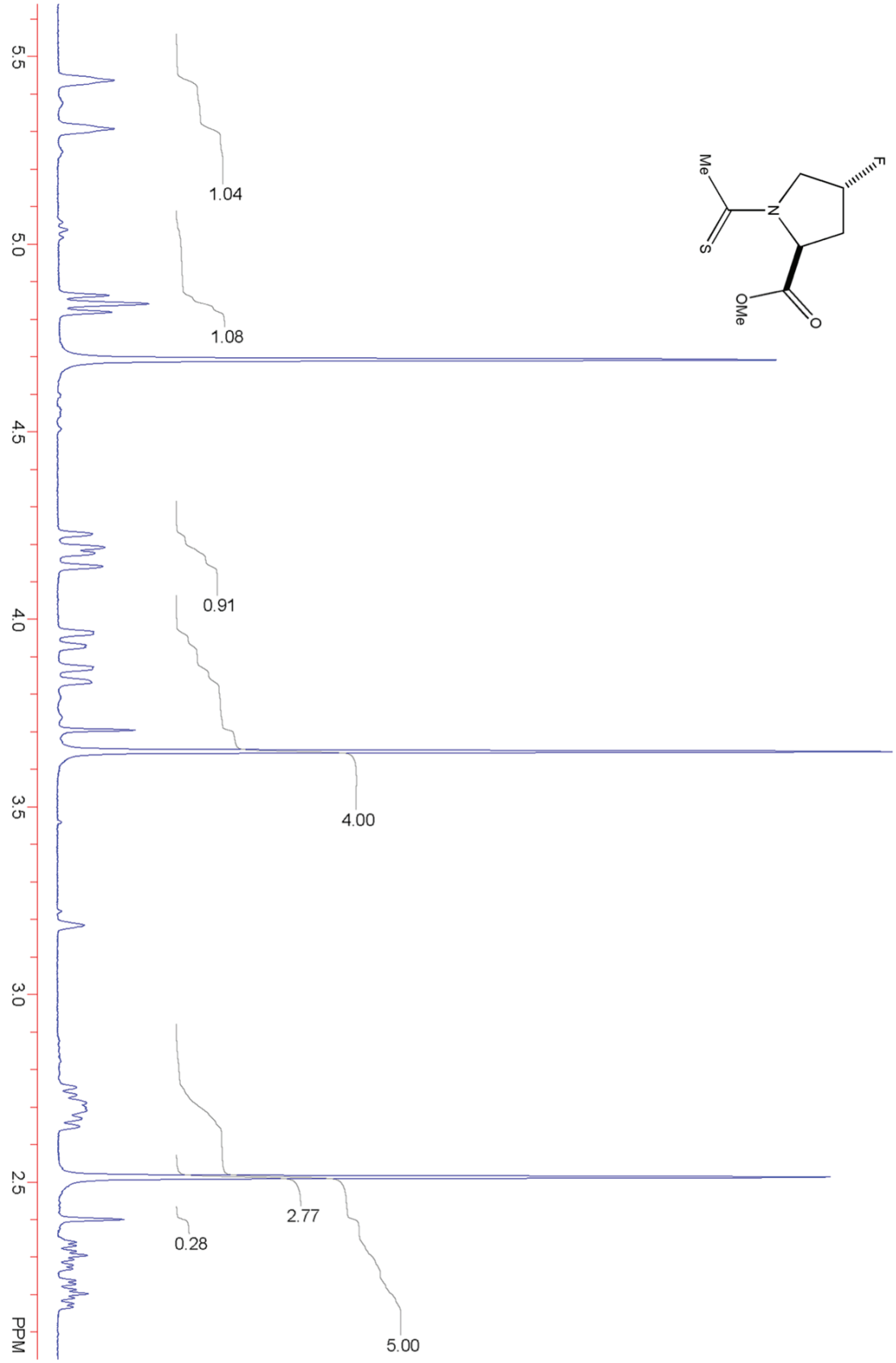
400 MHz ^{1}H NMR Spectrum of Compound **4** in D_2O



400 MHz ^{1}H NMR Spectrum of Compound **5** in D_2O



Inverse gated decoupled ^{19}F NMR Spectrum of Compound **5** in D_2O



400 MHz ^{1}H NMR Spectrum of Compound **6** in D_2O

Inverse gated decoupled ^{19}F NMR Spectrum of Compound **6** in D_2O