

***n*→*π** Interactions Modulate the Disulfide Reduction Potential of Epidithiodiketopiperazines**

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Table S1. PDB-derived $\angle C-S-S-C$ Values (Resolution <3.0 Å)^a

$\angle C-S-S-C$ (°)	Bin Count ^b
-170	21
-160	24
-150	24
-140	33
-130	51
-120	134
-110	482
-100	1736
-90	3171
-80	1446
-70	277
-60	59
-50	14
-40	6
-30	6
-20	4
-10	4
0	4
10	10
20	11
30	18
40	28
50	84
60	331
70	882
80	1242
90	1923
100	1318
110	364
120	85
130	31
140	29
150	26
160	16
170	34
180	24

^aData were used to generate Figure 1C.

^bThe bin width was 10°.

Table S2. Calculated $E - E_0$ Values^a

$\angle \text{C}-\text{S}-\text{S}-\text{C}$ (°)	$E - E_0$ (kcal/mol)
-170	5.32
-160	5.04
-150	4.57
-140	3.89
-130	3.05
-120	2.12
-110	1.22
-100	0.47
-90	0.02
-80	0.00
-70	0.47
-60	1.42
-50	2.79
-40	4.51
-30	6.43
-20	8.25
-10	9.61
0	10.18
10	9.62
20	8.25
30	6.43
40	4.51
50	2.78
60	1.42
70	0.47
80	0.00
90	0.02
100	0.47
110	1.22
120	2.12
130	3.05
140	3.89
150	4.57
160	5.04
170	5.32
180	5.41

^aData were used to generate Figure 1C.

Table S3. Epidithiodiketopiperazine Natural Product Structures

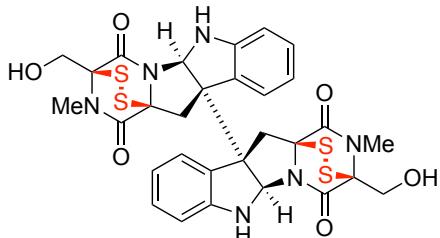
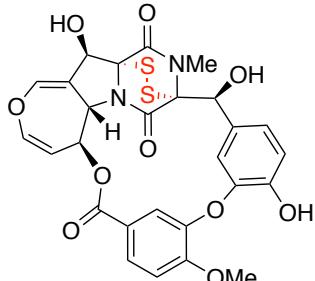
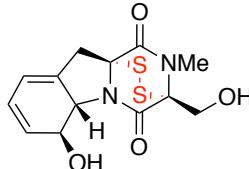
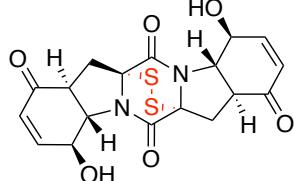
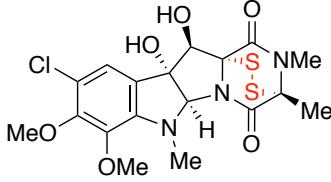
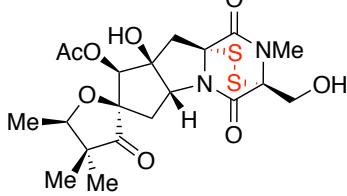
Compound	Structure	CCDC Deposition Number
Chaetocin A		1118990
Emestrin		1133525
Gliotoxin		1169258
Epicorazine A		1870981
Sporidesmin A		1263199
Sirodesmin		1259864

Table S4. Data Used to Compose Plots in Figure 2

Compound	$E_{n \rightarrow \pi^*}$ (1) (kcal/mol)	$E_{n \rightarrow \pi^*}$ (2) (kcal/mol)	r_{S-S} (Å)	$d_{S-C=O}$ (1) (Å)	$d_{S-C=O}$ (2) (Å)	$\angle S \cdots C=O$ (1) (°)	$\angle S \cdots C=O$ (2) (°)	$\angle C-S-S-C$ (°)
Epicorazine	4.56	3.32	2.097	2.670	2.719	121.20	127.38	-14.59
Soridesmin	4.93	5.01	2.063	2.640	2.650	120.14	118.90	-17.02
Sporidesmin	4.55	3.36	2.090	2.635	2.709	120.87	122.18	-9.26
Gliotoxin	3.93	4.67	2.083	2.668	2.641	122.35	121.25	8.70
Emestrin	4.55	3.67	2.074	2.656	2.700	121.39	128.02	-17.98
Chaetocin	3.68	4.69	2.074	2.700	2.648	125.70	119.60	12.80
	3.47	4.22	2.078	2.706	2.667	123.00	120.70	8.20

Table S5. Data Used to Compose Plots in Figure 5

Compound	$E_{n \rightarrow \pi^*}$ (1) (kcal/mol)	$E_{n \rightarrow \pi^*}$ (2) (kcal/mol)	r_{S-S} (Å)	$d_{S-C=O}$ (1) (Å)	$d_{S-C=O}$ (2) (Å)	$\angle S \cdots C=O$ (1) (°)	$\angle S \cdots C=O$ (2) (°)	$\angle C-S-S-C$ (°)
cis-4-F	4.17	3.83	2.085	2.678	2.694	123.95	123.73	11.95
trans-4-F	3.30	3.29	2.094	2.708	2.710	125.29	127.21	8.93
cis-4-OH	3.76	4.88	2.086	2.695	2.646	125.00	121.54	-13.13
trans-4-OH	2.85	3.03	2.093	2.718	2.704	123.97	121.42	4.20

Table S6. Data used to Compose Plots in Figure 7

Compound	M06		PBE0		$\lambda_{\max}^{\text{exp}}$ (nm)
	$\lambda_{\max}^{\text{comp}}$ (nm)	Oscillator Strength, f (a.u.)	$\lambda_{\max}^{\text{comp}}$ (nm)	Oscillator Strength, f (a.u.)	
cis-C4-F	368.66	0.0001	362.24	0	346.5
cis-C4-OH	371.30	0.0001	365.15	0.0001	345.0
trans-C4-OH	372.38	0.0001	366.34	0	346.5
C4-H	366.82	0.0001	360.86	0	342.5
cis-C4-OAc	369.75	0.0001	363.02	0.0001	345.0
trans-C4-OAc	363.34	0	357.96	0	340.0
trans-C4-F	372.30	0	366.64	0.0001	349.8

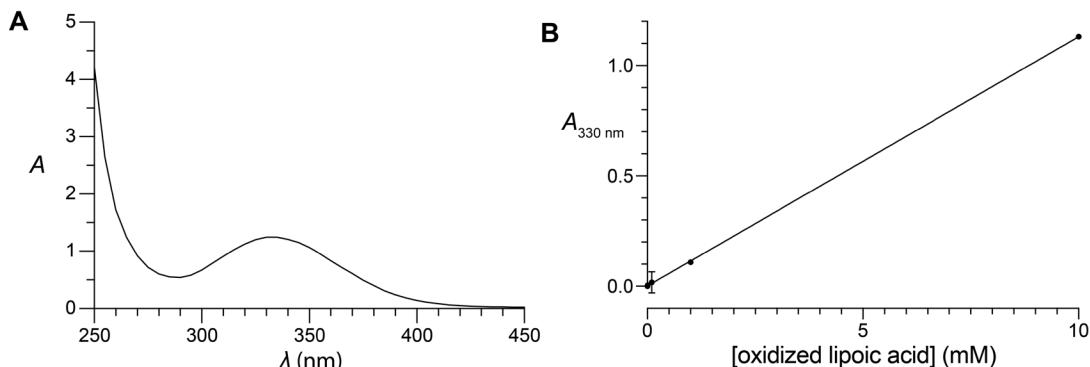


Figure S1. UV-vis spectroscopy of oxidized lipoic acid. (A) Spectrum of 10 mM oxidized lipoic acid.¹ (B) Graph of the absorbance at 330 nm of solutions of oxidized lipoic acid (1 μ M–10 mM) in 20 mM BIS-TRIS buffer, pH 7.5. Values are the mean \pm SD of four replicates. Data were fitted to the equation: $A_{330 \text{ nm}} = 112.9 \times [\text{oxidized lipoic acid}] - 0.0014$ with $R^2 = 0.99$.

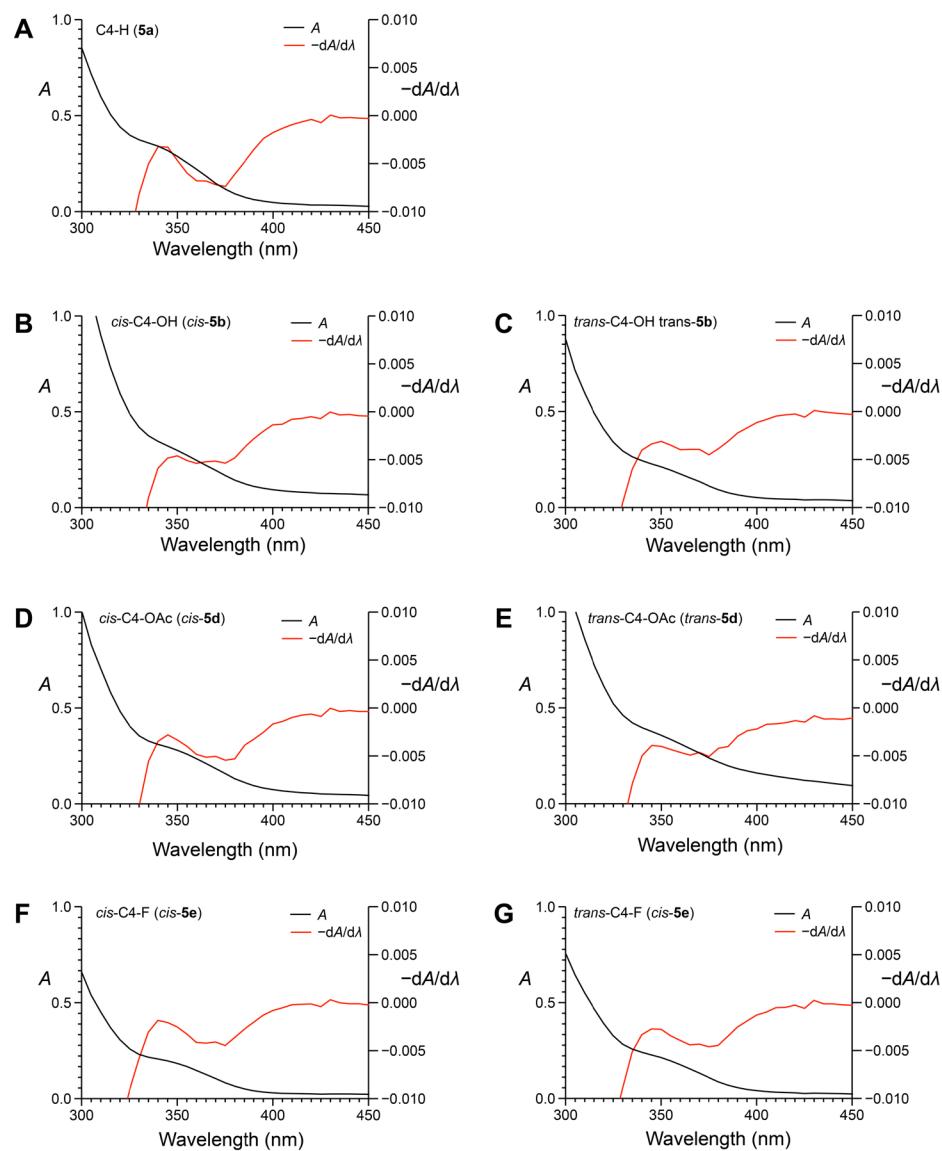


Figure S2. UV-vis absorption spectra (—) and first-derivative spectra (—) of synthetic ETPs.

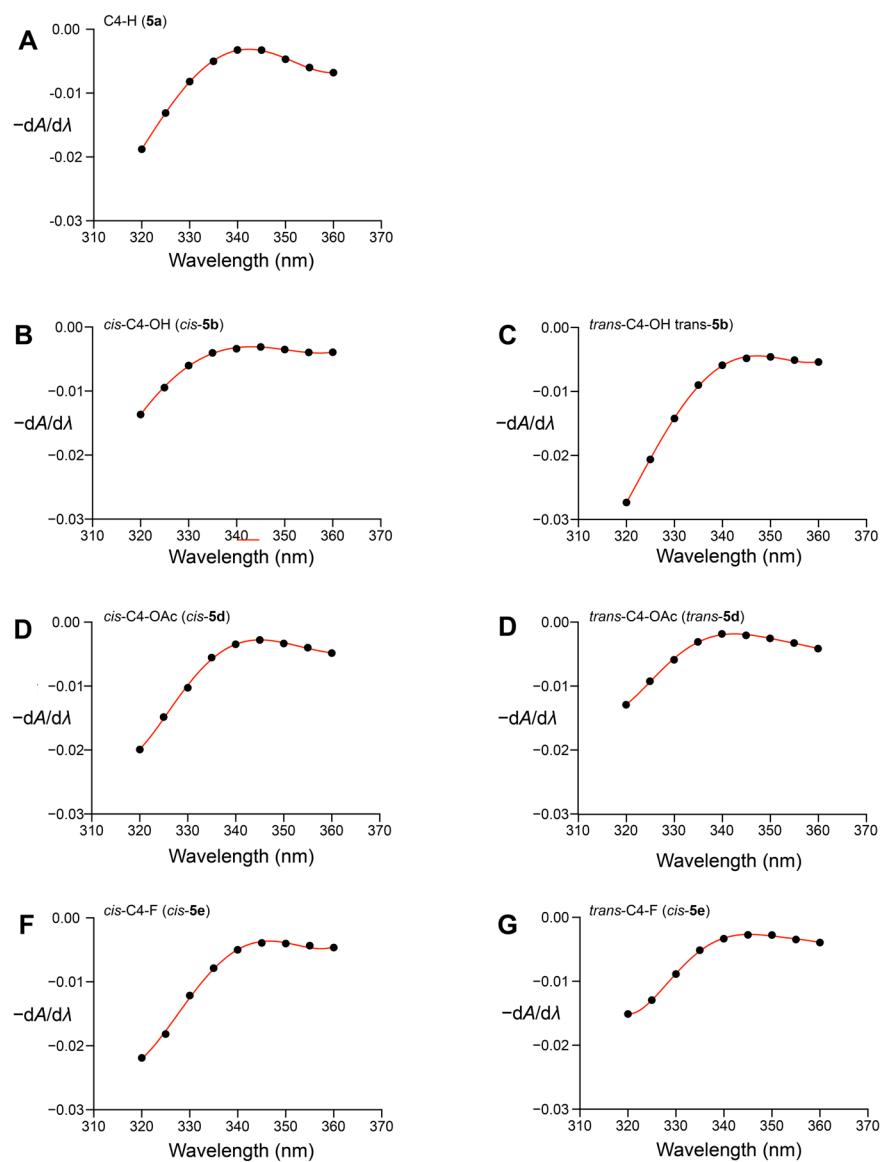


Figure S3. UV-vis absorption first-derivative spectral data of synthetic ETPs (●) fitted with 5th-order polynomials (—).

Quantum Mechanical Calculations. Quantum mechanical calculations were performed with Gaussian 16, revision C.01 at the M06-2X/6-311+G(d,p) level of theory.² Optimization was performed in the gas phase, and ground-state geometries were found to possess no imaginary frequencies. Energies were calculated by second-order perturbation theory analysis of optimized structures as implemented with NBO 6.0.³ Natural bond orbitals were rendered with the program NBOView 1.1.⁴ Single-point calculations on X-ray crystal structures of ETPs were performed by considering one molecule of the unit cell. Conformational scans were executed by holding constant the C–S–S–C dihedral angle, θ , and optimizing dimethyl disulfide about the geometry. From these conformationally constrained calculations, $E - E_0$ was evaluated by subtracting the energy of dimethyl disulfide in the unconstrained conformation (E_0) from the conformationally constrained energy, E . The resulting values of $E - E_0$ are listed in Table S2 and plotted in Figure 1C. The value of $E - E_0$ for hydrogen disulfide in its eclipsed conformation was calculated similarly.

Excited State Calculations. Model ETP structures were fully optimized at the M06-2X/6-311+G(d,p) in water as implemented through the integral equation formalism of the polarizable continuum model (IEFPCM), and found to possess no imaginary frequencies. The first twenty excited states of the model ETPs were then calculated using time-dependent density functional theory, employing either the M06-2X/6-311+G(d,p) or the PBE0/6-311+G(d,p) functional in water (IEFPCM). Natural transition orbitals describing the $S_0 \rightarrow S_1$ excitation were visualized and found to correspond to excitation of electron density from the disulfide *p*-type lone pair of the S_0 state to the sulfur–sulfur antibonding orbital of the S_1 state.

Analysis of Absorption Spectra. Solutions of model ETPs were prepared at 5 mM in 20 mM BIS-TRIS buffer, pH 7.5, and their spectra were recorded with an Agilent Cary 60 UV-vis spectrophotometer. Derivatives of recorded spectra were generated by using the approximation:

$$\frac{dA}{d\lambda} \approx A(\lambda + h) - A(\lambda)/h \quad (\text{S1})$$

where A is the absorbance at wavelength λ , and h is the difference between individual points data points. Disulfide chromophore absorbance maxima, $\lambda_{\max}^{\text{exp}}$, of model ETPs were estimated by interpolation from a 5th-order polynomial fit of $dA/d\lambda$ over the range 320–360 nm.

Measurement of ETP Reduction Potentials. Absorbance was measured with a Cary 60 UV-vis spectrophotometer from Agilent operating in kinetic mode at room temperature. ETPs were dissolved in dimethylsulfoxide (DMSO) at a concentration of 10 mM. To 980 μL of 20 mM of BIS-TRIS buffer, pH 7.5 in a glass cuvette was added 10 μL of a 10 mM solution of an ETP in DMSO. This solution was mixed thoroughly, then blanked in the spectrophotometer. To this solution was added 10 μL of a solution of reduced lipoic acid (Sigma–Aldrich) in BIS-TRIS buffer, pH 7.5. The resulting solution was mixed, and its absorbance was recorded at 330 nm. The concentration of oxidized lipoic acid was calculated by using the equation: $A_{330 \text{ nm}} = 112.9 \times [\text{oxidized lipoic acid}] - 0.0014$ (Figure S1). The value of E°' for the ETP was calculated by using an equation that describes the thiol–disulfide exchange equilibrium (Eq S2) and the Nernst equation (Eq S3), with $E^\circ'_{\text{ref}} = -288$ mV for oxidized lipoic acid.⁵ Values of E°' are listed in Table 1.

$$K_{\text{eq}} = \frac{[\text{reduced ETP}][\text{oxidized lipoic acid}]}{[\text{oxidized ETP}][\text{reduced lipoic acid}]} = \frac{[\text{oxidized lipoic acid}]^2}{[\text{reduced lipoic acid}]^2} \quad (\text{S2})$$

$$E^{\circ'}_{\text{ETP}} = E^{\circ'}_{\text{ref}} - \frac{RT}{n_e F} \ln \frac{[\text{oxidized lipoic acid}]}{[\text{reduced lipoic acid}]} \quad (\text{S3})$$

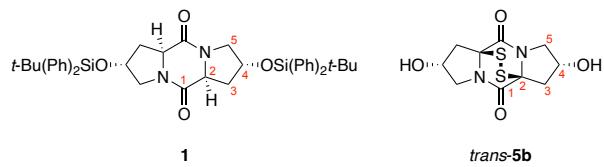
General Synthetic Procedures. All reactions were performed in oven-dried or flame-dried round-bottom flasks or modified Schlenk (Kjeldahl shape) flasks. The flasks were fitted with rubber septa, and reactions were conducted under a positive pressure of argon. Cannulae or gas-tight syringes with stainless steel needles were used to transfer air- or moisture-sensitive liquids. Flash column chromatography was performed as described by Still et al.⁶ using granular silica gel (60-Å pore size, 40–63 µm, 4–6% H₂O content, Zeochem®). Analytical thin layer chromatography (TLC) was performed using glass plates pre-coated with 0.25 mm 230–400 mesh silica gel impregnated with a fluorescent indicator (254 nm). Thin layer chromatography plates were visualized by exposure to short wave ultraviolet light (254 nm) and irreversibly stained by treatment with an aqueous solution of ceric ammonium molybdate (CAM), an ethanolic solution of phosphomolybdic acid (PMA), an aqueous solution of silver nitrate (AgNO₃),⁷ a solution of Ellman's reagent (DTNB, 5,5'-dithiobis-(2-nitrobenzoic acid)) in dimethylformamide,⁷ or an aqueous solution of potassium permanganate (KMnO₄), followed by heating (~1 min) on a hot plate (~250 °C). Organic solutions were concentrated at 29–30 °C on rotary evaporators capable of achieving a minimum pressure of ~2 Torr.

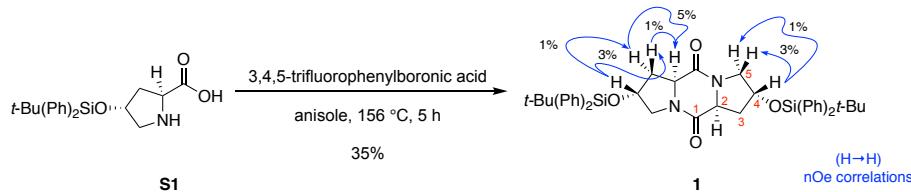
Materials. Commercial reagents and solvents were used as received with the following exceptions: dichloromethane, acetonitrile, tetrahydrofuran, pyridine, and methanol were purchased from J. T. Baker (Cycletainer™) or Sigma–Aldrich and were purified by the method of Grubbs et al.⁸ under positive argon pressure. Benzene was dried by distillation over calcium hydride under an inert nitrogen atmosphere. Diazabicyclo[5.4.0]undec-7-ene (DBU) and triethylamine trihydrofluoride were purchased from Matrix Scientific. *p*-Methoxybenzyl thiol and carbon disulfide were purchased from Alfa Aesar. *Tert*-butyldiphenylchlorosilane and *N*-[(Dimethylamino)-1*H*-1,2,3-triazolo-[4,5-*b*]pyridin-1-ylmethylene]-*N*-methylmethan-aminium hexafluorophosphate *N*-oxide (HATU) were purchased from Oakwood chemicals. 3,4,5-Trifluorophenylboronic acid was purchased from Combi-Blocks. Elemental sulfur was purchased from Mallinckrodt. *N*-Boc-*trans*-4-fluoro-L-proline was purchased from OmegaChem. All other solvents and chemicals were purchased from Sigma–Aldrich.

Instrumentation. Proton nuclear magnetic resonance (¹H NMR) spectra were recorded with a Bruker AVANCE 600 spectrometer, a Bruker AVANCE NEO 500 spectrometer, a Varian inverse probe 500 INOVA spectrometer, or a Bruker AVANCE III 400 spectrometer. Chemical shifts are recorded in parts per million on the δ scale and are referenced from the residual protium in the NMR solvent (CHCl₃: δ 7.26, CD₂HCN: 1.94, CD₂HOD: 3.31, CD₃SOCD₂H: 2.50, CD₃COCD₂H: 2.05, HOD: 4.79).⁹ Data are reported as follows: chemical shift [multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, app= apparent), coupling constant(s) in Hertz, integration, assignment]. Carbon-13 nuclear magnetic resonance (¹³C NMR) spectra were recorded with a Bruker AVANCE 600 spectrometer, a Bruker AVANCE NEO 500 spectrometer, a Varian inverse probe 500 INOVA spectrometer, or a Bruker AVANCE III 400 spectrometer. Chemical shifts are recorded in parts per million on the δ scale and are referenced from the carbon resonances of the solvent (CDCl₃: δ 77.16, CD₃CN: 118.26, CD₃OD: 49.00, CD₃SOCD₃: 39.52, CD₃COCD₃: 29.84). Fluorine-19 nuclear magnetic resonance (¹⁹F NMR) spectra were recorded with a Bruker AVANCE 600 spectrometer. Chemical shifts are recorded in parts per million on the δ scale and are referenced from the fluorine resonance of fluorobenzene (C₆H₅F δ –113.15). For fluorinated derivatives the ¹H & ¹³C NMR spectra were collected with ¹⁹F decoupling and the ¹⁹F NMR spectra were collected with ¹H decoupling. Infrared data were obtained with a Bruker Alpha II Platinum

ATR and are reported as follows: [frequency of absorption (cm^{-1}), intensity of absorption (s = strong, m = medium, w = weak, br = broad). We thank Dr. Mohanraja Kumar and Dr. Liam Kelly at the Massachusetts Institute of Technology Department of Chemistry instrumentation facility for assistance in obtaining mass spectroscopic data. High resolution mass spectra (HRMS) were recorded on a JEOL AccuTOF LC-plus 4G or an Agilent 6545 Q-TOF LC/MS using direct analysis in real time (DART) or electrospray (ESI) (m/z) ionization source. The crystal structures of *cis*-**5b**, *trans*-**5b**, *cis*-**5e**, and *trans*-**5e** were obtained with the assistance of Dr. Peter Müller at the X-ray diffraction facility of the Department of Chemistry, Massachusetts Institute of Technology.

Positional Numbering System. In assigning the ^1H , ^{13}C , and ^{19}F NMR data of all intermediates en route to our epidisulfide synthetic analogues, we employed the uniform numbering scheme as shown below.





Silyloxydiketopiperazine 1:

Silyloxyproline **S1**¹⁰ (8.90 g, 24.1 mmol, 1 equiv) and 3,4,5-trifluorophenylboronic acid (230 mg, 1.3 mmol, 0.050 equiv) were suspended in anisole (80 mL).¹¹ The reaction flask was equipped with a Dean–Stark trap containing activated powdered 4 Å-molecular sieves (7.3 g) and with a spiral-coil reflux condenser attached at the top. The reaction mixture was heated to reflux for 5 h as the heterogeneous mixture became clear and colorless. Upon cooling to 23 °C, the resulting solution was directly purified by flash column chromatography (silica gel: 269 g, 14 × 7.5 cm, 0 → 65% ethyl acetate in hexanes) to afford silyloxydiketopiperazine **1** (3.0 g, 35%) as a white solid.¹² Structural assignments were made with additional information from gCOSY, gHSQC, gHMBC, and nOe experiments.

¹H NMR (500 MHz, CDCl₃, 25 °C):

δ 7.67–7.59 (m, 8H, SiPh-*ortho*-H), 7.48–7.42 (m, 4H, SiPh-*para*-H), 7.42–7.35 (m, 8H, SiPh-*meta*-H), 4.70 (dd, J = 10.9, 6.3 Hz, 2H, C2H), 4.48 (t, J = 4.2 Hz, 2H, C4H), 3.57 (d, J = 12.7 Hz, 2H, C5H_a), 3.49 (dd, J = 12.7, 4.2 Hz, 2H, C5H_b), 2.33 (dd, J = 13.4, 6.3 Hz, 2H, C3H_a), 1.96 (ddd, J = 13.3, 11.0, 4.1 Hz, 2H, C3H_b), 1.07 (s, 18H, C(CH₃)₃).

¹³C NMR (125 MHz, CDCl₃, 25 °C):

δ 166.6 (**C1**), 135.8 (SiPh-*ortho*-C_{a/b}), 135.8 (SiPh-*ortho*-C_{a/b}), 133.2 (2C, SiPh-*ipso*-C), 130.2 (SiPh-*para*-C_{a/b}), 130.2 (SiPh-*para*-C_{a/b}), 128.1 (SiPh-*meta*-C_{a/b}), 128.1 (SiPh-*meta*-C_{a/b}), 70.7 (**C4**), 59.3 (**C2**), 54.5 (**C5**), 37.7 (**C3**), 27.0 (C(CH₃)₃), 19.2 (**C(CH₃)₃**).

FTIR (thin film) cm⁻¹:

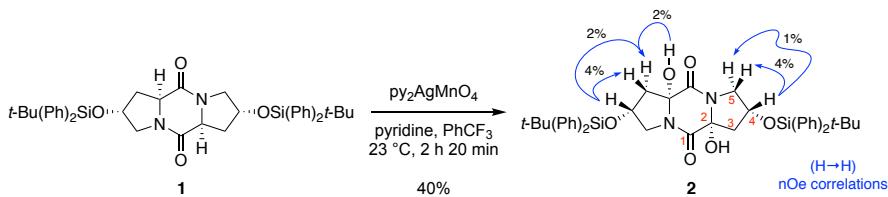
2959 (w), 2930 (w), 2856 (w), 1667 (s), 1426 (m), 1105 (m), 1019 (m), 819 (w), 704 (s), 510 (m).

HRMS (DART-TOF) (*m/z*):

calc'd for C₄₂H₅₁N₂O₄Si₂ [M+H]⁺: 703.3382, found: 703.3379.

TLC (40% ethyl acetate in hexanes), R_f:

1, 0.38 (CAM, UV),
epi-**1**, 0.14 (CAM, UV).



Diol 2:

Bis(pyridine)silver(I) permanganate (7.73 g, 20.1 mmol, 5.14 equiv) was added as a solid in one portion to a solution of silyloxydiketopiperazine **1** (2.83 g, 4.03 mmol, 1 equiv) in anhydrous pyridine (40 mL) and anhydrous α,α,α -trifluorotoluene (40 mL), resulting in a dark purple solution. After 2 h 20 min, the reaction mixture was diluted with ethyl acetate–hexanes (9:1, 100 mL) and poured into a saturated aqueous sodium bisulfite solution (100 mL). The layers were separated, and the aqueous layer was extracted with ethyl acetate–hexanes (9:1, 100 mL). The combined organic layers were washed with a saturated aqueous copper sulfate solution (3×100 mL), deionized water (1×75 mL), a saturated aqueous ammonium chloride solution (2×75 mL), and a saturated aqueous sodium chloride solution (1×50 mL). The aqueous layers were extracted sequentially with ethyl acetate–hexanes (9:1, 100 mL). The combined organic layers were dried over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure. The resulting light blue foam (3.2 g) was dissolved in dichloromethane (25 mL) and adsorbed onto silica gel (9.2 g) by concentration under reduced pressure until a free-flowing powder was obtained. The silica-adsorbed crude mixture was purified by flash column chromatography (silica gel: 200 g, 17×5.7 cm, 1→5% diethyl ether in dichloromethane) to afford diol **2** (1.18 g, 40.0%) as a white foam. Structural assignments were made with additional information from gCOSY, gHSQC, gHMBC, and nOe experiments.

^1H NMR (500 MHz, CDCl_3 , 25 °C):

δ 7.70–7.61 (m, 8H, SiPh-*ortho*-H), 7.51–7.44 (m, 4H, SiPh-*para*-H), 7.44–7.38 (m, 8H, SiPh-*meta*-H), 5.09 (s, 2H, C2OH), 4.61–4.36 (m, 2H, C4H), 3.75 (d, $J = 12.7$ Hz, 2H, C5H $_{\alpha}$), 3.53 (dd, $J = 12.7, 4.7$ Hz, 2H, C5H $_{\beta}$), 2.48 (d, $J = 14.3$ Hz, 2H, C3H $_{\alpha}$), 2.32 (dd, $J = 14.4, 4.8$ Hz, 2H, C3H $_{\beta}$), 1.09 (s, 18H, C(CH₃)₃).

^{13}C NMR (125 MHz, CDCl_3 , 25 °C):

δ 165.4 (C1), 135.8 (SiPh-*ortho*-C $_{\alpha/\beta}$), 135.8 (SiPh-*ortho*-C $_{\alpha/\beta}$), 132.5 (SiPh-*ipso*-C $_{\alpha/\beta}$), 132.4 (SiPh-*ipso*-C $_{\alpha/\beta}$), 130.4 (2C, SiPh-*para*-C), 128.2 (2C, SiPh-*meta*-C), 90.2 (C2), 70.5 (C4), 54.2 (C5), 43.6 (C3), 27.0 (C(CH₃)₃), 19.1 (C(CH₃)₃).

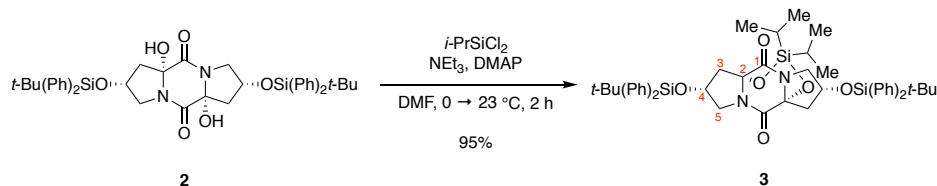
FTIR (thin film) cm^{-1} :

2931 (w), 2857 (w), 1692 (m), 1407 (m), 1105 (s), 966 (w), 821 (w), 701 (s), 506 (s).

HRMS (ESI) (m/z):

calc'd for $\text{C}_{42}\text{H}_{50}\text{N}_2\text{NaO}_6\text{Si}_2$ [M+Na]⁺: 757.3100, found: 757.3095.

TLC (5% diethyl ether in dichloromethane), R_f : 0.51 (CAM, UV).



Dioxasilane 3:

Diol **2** (666 mg, 0.906 mmol, 1 equiv) and 4-(dimethylamino)pyridine (9.6 mg, 95 μ mol, 0.10 equiv) were dried azeotropically by concentration from anhydrous benzene (2×10 mL) under reduced pressure. The resulting foam was dissolved in dimethylformamide (55 mL) via cannula and was cooled to 0 °C. Triethylamine (0.50 mL, 3.6 mmol, 4.0 equiv) was added via syringe, followed by the dropwise addition of dichlorodiisopropylsilane (0.200 mL, 1.11 mmol, 1.23 equiv) via syringe over 30 seconds. The ice-bath was removed, and the suspension was allowed to stir and warm to 23 °C. After 2 h, the reaction mixture was diluted with ethyl acetate–hexanes (5:1, 250 mL) and was washed with an aqueous ammonium chloride solution (66% saturated, 150 mL). The layers were separated, and the aqueous layer was extracted with ethyl acetate–hexanes (5:1, 250 mL). The combined organic layers were washed with deionized water (3×200 mL), were washed with a saturated aqueous sodium chloride solution (100 mL), were dried over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure. The resulting residue (890 mg) was purified by flash column chromatography (silica gel: 72 g, 15 × 4 cm, 50% hexanes in dichloromethane → 100% dichloromethane) to afford dioxasilane **3** (732 mg, 95.4%) as a white solid.

^1H NMR (600 MHz, CDCl_3 , 25 °C):

δ 7.68 (dd, $J = 8.0, 1.3$ Hz, 4H, SiPh-*ortho*-**H_{a/b}**), 7.62 (dd, $J = 8.0, 1.3$ Hz, 4H, SiPh-*ortho*-**H_{a/b}**), 7.47–7.39 (m, 4H, SiPh-*para*-**H**), 7.39–7.37 (m, 8H, SiPh-*meta*-**H**), 4.33 (tt, $J = 5.9, 2.9$ Hz, 2H, C4**H**), 3.73 (dd, $J = 12.3, 2.5$ Hz, 2H, C5**H_a**), 3.65 (dd, $J = 12.3, 5.8$ Hz, 2H, C5**H_b**), 2.60 (dd, $J = 14.7, 6.2$ Hz, 2H, C3**H_a**), 2.34 (dd, $J = 14.7, 2.8$ Hz, 2H, C3**H_b**), 1.13–1.05 (m, 32H, C(CH₃)₃, SiCH(CH₃)₂, SiCH(CH₃)₂).

^{13}C NMR (150 MHz, CDCl_3 , 25 °C):

δ 166.6 (**C1**), 135.9 (SiPh-*ortho*-**C_{a/b}**), 135.8 (SiPh-*ortho*-**C_{a/b}**), 133.5 (SiPh-*ipso*-**C_{a/b}**), 133.2 (SiPh-*ipso*-**C_{a/b}**), 130.1 (SiPh-*para*-**C_{a/b}**), 130.1 (SiPh-*para*-**C_{a/b}**), 128.0 (SiPh-*meta*-**C_{a/b}**), 127.9 (SiPh-*meta*-**C_{a/b}**), 91.1 (**C2**), 70.0 (**C4**), 54.2 (**C5**), 44.0 (**C3**), 27.0 (C(CH₃)₃), 19.2 (C(CH₃)₃), 16.3 (SiCH(C_aH₃)₂), 16.0 (SiCH(C_bH₃)₂), 13.4 (SiC_aH(CH₃)₂, SiC_bH(CH₃)₂).

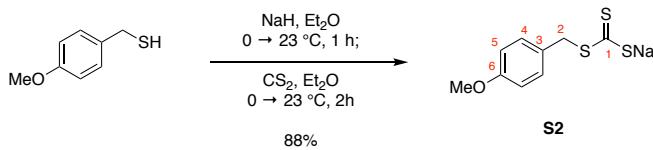
FTIR (thin film) cm^{-1} :

2950 (m), 2859 (m), 1698 (s), 1400 (m), 1114 (s), 1001 (m), 823 (w), 702 (m), 611 (w), 512 (m).

HRMS (ESI) (*m/z*):

calc'd for $\text{C}_{48}\text{H}_{62}\text{N}_2\text{NaO}_6\text{Si}_3$ [M+Na]⁺: 869.3808, found: 869.3812.

TLC (90% dichloromethane in hexanes), R_f : 0.27 (UV, CAM).



Sodium 4-methoxybenzyl trithiocarbonate S2:

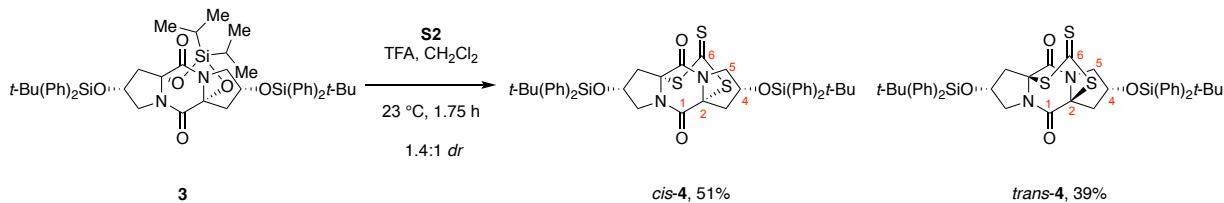
A suspension of sodium hydride (60% dispersion, 1.03 g, 25.8 mmol, 1 equiv) in diethyl ether (125 mL) at 0 °C was sparged with argon for 20 min by discharge of a balloon equipped with a needle extending into the reaction mixture. *p*-Methoxybenzyl thiol (4.5 mL, 33 mmol, 1.3 equiv) was added dropwise via syringe over 2 min, the solution was stirred for 5 min, then the ice–water bath was removed and the reaction mixture was allowed to stir and warm to 23 °C. After 1 h, the light-gray suspension was cooled to 0 °C, and carbon disulfide (2.0 mL, 33 mmol, 1.3 equiv) was added dropwise via syringe over 3.5 min. The ice–water bath was removed and the reaction mixture was allowed to stir and warm to 23 °C. After 2 h, the yellow suspension was filtered through a 350-mL medium-porosity fritted-glass funnel. The resulting yellow precipitate was washed with hexanes (2 × 50 mL) and was dried under reduced pressure to give sodium 4-methoxybenzyl trithiocarbonate **S2** (5.76 g, 88.4%) as a bright yellow solid. Structural assignments were made with additional information from gCOSY, gHSQC, and gHMBC experiments.

¹H NMR (500 MHz, DMSO-d₆, 25 °C): δ 7.20 (d, *J* = 8.6 Hz, 2H, C4H), 6.81 (d, *J* = 8.6 Hz, 2H, C5H), 4.29 (s, 2H, C2H), 3.70 (s, 3H, OCH₃).

¹³C NMR (125 MHz, DMSO-d₆, 25 °C): δ 239.0 (**C1**), 157.8 (**C6**), 130.9 (**C3**), 129.8 (**C4**), 113.6 (**C5**), 55.0 (OCH₃), 44.6 (**C2**).

FTIR (thin film) cm⁻¹: 1507 (w), 1248 (w), 1229 (w), 1177 (w), 1003 (s), 833 (m), 539 (m).

HRMS (DART-TOF) (*m/z*): calc'd for C₉H₉OS₃ [M–Na]⁺: 228.9821, found: 228.9813.



Dithiepanethiones *cis*-**4** and *trans*-**4**.¹³

Trifluoroacetic acid (TFA, 12 mL) was added via syringe over 1 min to a yellow suspension of dioxasilane **3** (712 mg, 0.840 mmol, 1 equiv) and sodium 4-methoxybenzyl trithiocarbonate **S2** (862 mg, 3.42 mmol, 4.07 equiv) in dichloromethane (48 mL). After 1.75 h, the yellow solution was diluted with ethyl acetate–hexanes (9:1, 200 mL) and poured into a saturated aqueous sodium bicarbonate solution (200 mL). The biphasic mixture was vigorously stirred for 30 min, resulting in a colorless aqueous layer. The layers were separated, and the organic layer was washed with deionized water (2×100 mL), was washed with a saturated aqueous sodium chloride solution (50 mL), was dried over anhydrous sodium sulfate, was filtered, and was concentrated under reduced pressure. The resulting residue (1.4 g) was purified by flash column chromatography (silica gel: 108 g, 14×4.8 cm, 50% toluene in hexanes \rightarrow 100% toluene) to afford dithiepanethione *trans*-**4** as a yellow foam. Further elution (0 \rightarrow 10% acetone in toluene) provided dithiepanethione *cis*-**4** as a yellow foam. Dithiepanethione *trans*-**4** (300 mg) was subjected to a second flash column chromatographic purification (silica gel: 21.6 g, 13×2.4 cm, 0 \rightarrow 5% ethyl acetate in hexanes) to afford dithiepanethione *trans*-**4** (267 mg, 39.3%) as a yellow-orange solid. Dithiepanethione *cis*-**4** (451 mg) was dissolved in ethyl acetate (100 mL) and adsorbed onto Celite (1.8 g) by concentration under reduced pressure until a free-flowing powder was obtained. The Celite-adsorbed mixture of *cis*-**4** was subjected to a second flash column chromatographic purification (silica gel: 35 g, 15×2.8 cm, 10% ethyl acetate in hexanes \rightarrow 100% ethyl acetate) to afford dithiepanethione *cis*-**4** (348 mg, 51.1%) as a yellow solid.

cis-**4**:

^1H NMR (500 MHz, CDCl_3 , 25 °C):

δ 7.66 (d, $J = 7.1$ Hz, 4H, SiPh-*ortho*- $\text{H}_{\text{a/b}}$), 7.61 (d, $J = 7.2$ Hz, 4H, SiPh-*ortho*- $\text{H}_{\text{a/b}}$), 7.51–7.35 (m, 12H, SiPh-*para*- H , SiPh-*meta*- H), 4.55–4.48 (m, 2H, C4H), 3.74–3.64 (m, 4H, C5H_a, C5H_b), 2.85 (dd, $J = 15.3$, 5.8 Hz, 2H, C3H_a), 2.43 (d, $J = 15.3$, 2H, C3H_b), 1.10 (s, 18H, C(CH₃)₃).

^{13}C NMR (100 MHz, CDCl_3 , 25 °C):

δ 216.5 (**C6**), 162.6 (**C1**), 135.9 (SiPh-*ortho*- $\text{C}_{\text{a/b}}$), 135.7 (SiPh-*ortho*- $\text{C}_{\text{a/b}}$), 132.8 (SiPh-*ipso*- $\text{C}_{\text{a/b}}$), 132.6 SiPh-*ipso*- $\text{C}_{\text{a/b}}$), 130.4 (SiPh-*para*- $\text{C}_{\text{a/b}}$), 130.3 (SiPh-*para*- $\text{C}_{\text{a/b}}$), 128.2 (SiPh-*meta*- $\text{C}_{\text{a/b}}$), 128.2 (SiPh-*meta*- $\text{C}_{\text{a/b}}$), 75.4 (**C2**), 69.2 (**C4**), 55.2 (**C5**), 43.4 (**C3**), 26.9 (C(CH₃)₃), 19.2 (**C(CH₃)₃**).

FTIR (thin film) cm^{-1} :

2930 (w), 2858 (w), 1695 (s), 1391 (m), 1105 (s), 1016 (m), 702 (m), 507 (w).

HRMS (ESI) (m/z):

calc'd for $C_{43}H_{49}N_2O_4S_3Si_2$ [M+H]⁺: 809.2387,
found: 809.2390.

TLC (5% acetone in toluene), R_f:

0.35 (UV, I₂, CAM, AgNO₃, DTNB).

TLC (30% ethyl acetate in hexanes), R_f:

0.33 (UV, I₂, CAM, AgNO₃, DTNB).

trans-4:

¹H NMR (500 MHz, CDCl₃, 25 °C):

δ 7.65 (d, $J = 7.8$ Hz, 4H, SiPh-*ortho*-H_{a/b}), 7.61 (d, $J = 6.7$ Hz, 4H, SiPh-*ortho*-H_{a/b}), 7.52–7.39 (m, 12H, SiPh-*para*-H, SiPh-*meta*-H), 4.61 (app-p, $J = 5.7$ Hz, 2H, C4H), 3.76 (dd, $J = 12.0, 4.6$ Hz, 2H, C5H_a), 3.67 (dd, $J = 12.0, 5.9$ Hz, 2H, C5H_b), 3.09 (dd, $J = 14.5, 6.1$ Hz, 2H, C3H_a), 2.32 (dd, $J = 14.5, 5.6$ Hz, 2H, C3H_b), 1.06 (s, 18H, C(CH₃)₃).

¹³C NMR (150 MHz, CDCl₃, 25 °C):

δ 216.9 (C6), 162.6 (C1), 135.7 (SiPh-*ortho*-C_{a/b}), 135.7 (SiPh-*ortho*-C_{a/b}), 132.6 (2C, SiPh-*ipso*-C), 130.5 (SiPh-*para*-C), 128.2 (SiPh-*meta*-C), 75.3 (C2), 69.3 (C4), 53.8 (C5), 42.8 (C3), 26.9 (C(CH₃)₃), 19.2 (C(CH₃)₃).

FTIR (thin film) cm⁻¹:

3070 (w), 2931 (w), 2857 (w), 1693 (s), 1394 (m), 1111 (s), 822 (w), 701 (s), 612 (w), 506 (m).

HRMS (ESI) (m/z):

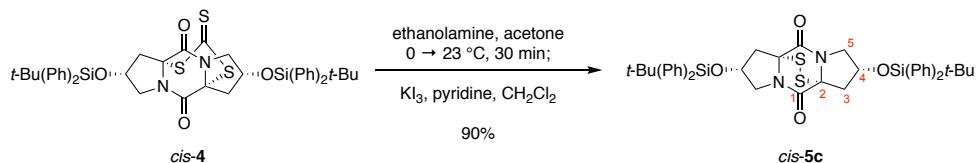
calc'd for $C_{43}H_{48}N_2NaO_4S_3Si_2$ [M+Na]⁺: 831.2207,
found: 831.2197.

TLC (80% toluene in hexanes), R_f:

0.28 (UV, I₂, CAM, AgNO₃, DTNB).

TLC (5% ethyl acetate in hexanes), R_f:

0.28 (UV, I₂, CAM, AgNO₃, DTNB).



Bis(silyloxy)epidisulfide *cis*-5c:

A suspension of dithiepanethione *cis*-4 (429 mg, 0.531 mmol, 1 equiv) in acetone (20 mL) at 0 °C was sparged with argon for 15 min by discharge of a balloon equipped with a needle extending into the reaction mixture. Ethanolamine (10 mL) was injected dropwise via syringe over 45 seconds. The ice–water bath was removed and the yellow suspension was allowed to stir and warm to 23 °C, gradually becoming clear and colorless. After 30 min, the reaction mixture was diluted with dichloromethane (100 mL) and poured into an aqueous hydrogen chloride solution (1 N, 175 mL). The aqueous layer was extracted with dichloromethane (2 × 50 mL). A stock solution of potassium triiodide in pyridine¹⁴ was added dropwise to the combined organic layers until the solution maintained a faint yellow color. The resulting mixture was washed with an aqueous hydrogen chloride solution (1 N, 2 × 40 mL), was washed with a mixture of deionized water, saturated aqueous sodium thiosulfate solution, and saturated aqueous bicarbonate solution (2:1:1, 80 mL), and was washed with a saturated aqueous sodium chloride solution (100 mL). The organic layer was dried over anhydrous sodium sulfate, was filtered, and was concentrated under reduced pressure. The resulting residue (549 mg) was purified by flash column chromatography (silica gel: 49 g, 21.0 × 2.8 cm, 40→100% dichloromethane in hexanes) to afford bis(silyloxy)epidisulfide *cis*-5c (365 mg, 89.9%) as a white foam. Structural assignments were made with additional information from gCOSY, gHSQC, and gHMBC experiments.

¹H NMR (400 MHz, CDCl₃, 25 °C):

δ 7.69–7.60 (m, 8H, SiPh-*ortho*-H), 7.50–7.35 (m, 12H, SiPh-*para*-H, SiPh-*meta*-H), 4.53 (tt, *J* = 6.0, 3.2 Hz, 2H, C4H), 3.73 (dd, *J* = 12.1, 3.3 Hz, 2H, C5H_a), 3.55 (dd, *J* = 12.1, 5.5 Hz, 2H, C5H_b), 3.06 (dd, *J* = 15.0, 5.9 Hz, 2H, C3H_a), 2.37 (dd, *J* = 15.0, 3.1 Hz, 2H, C3H_b), 1.09 (s, 18H, C(CH₃)₃).

¹³C NMR (100 MHz, CDCl₃, 25 °C):

δ 163.4 (**C1**), 135.8 (SiPh-*ortho*-C_{a/b}), 135.8 (SiPh-*ortho*-C_{a/b}), 133.0 (SiPh-*ipso*-C_{a/b}), 132.8 (SiPh-*ipso*-C_{a/b}), 130.3 (SiPh-*para*-C_{a/b}), 130.2 (SiPh-*para*-C_{a/b}), 128.1 (SiPh-*meta*-C_{a/b}), 128.1 (SiPh-*meta*-C_{a/b}), 75.1 (**C2**), 70.5 (**C4**), 53.6 (**C5**), 41.0 (**C3**), 26.9 (C(CH₃)₃), 19.2 (C(CH₃)₃).

FTIR (thin film) cm⁻¹:

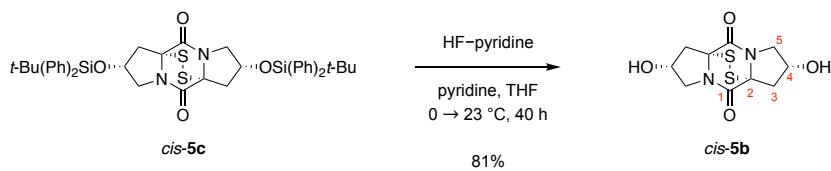
2930 (w), 2856 (w), 1696 (s), 1379 (m), 1103 (s), 1012 (m), 821 (w), 701 (s), 611 (m), 506 (s).

HRMS (ESI) (*m/z*):

calc'd for C₄₂H₄₈N₂NaO₄S₂Si₂ [M+Na]⁺: 787.2486, found: 787.2485.

TLC (10% hexanes in dichloromethane),

R_f: 0.28 (CAM, AgNO₃, UV).



Bis(hydroxy)epidisulfide *cis*-5b:

A freshly prepared solution of hydrogen fluoride–pyridine (70% HF, 0.25 mL), pyridine (0.5 mL), and tetrahydrofuran (2.0 mL) at 0 °C was added via plastic syringe to a solution of bis(silyloxy)epidisulfide *cis*-5c (103 mg, 0.135 mmol, 1 equiv) in tetrahydrofuran (2.5 mL) at 0 °C in a 45-mL polypropylene Falcon tube. After 5 min, the ice–water bath was removed and the reaction mixture was allowed to stir and warm to 23 °C. After 40 h, the reaction mixture was cooled to 0 °C, and was slowly diluted with a saturated aqueous sodium bicarbonate solution (15 mL) in portions (0.5 mL) over 5 min. The reaction mixture was allowed to warm to 23 °C, was washed with dichloromethane (3 \times 5 mL), and the combined organic layers were extracted with deionized water (4 \times 10 mL). The combined aqueous extracts were frozen in a 250-mL round-bottom flask by immersion in a liquid nitrogen bath and were subjected to lyophilization under reduced pressure. The resulting solids were suspended in dichloromethane–methanol (9:1, 200 mL) and sonicated for 10 min, and were filtered through a pad of silica gel (10 g, 3 \times 3 cm) covered with a pad of Celite (0.5 cm). The filter cake was washed with dichloromethane–methanol (9:1, 100 mL) and the filtrate was concentrated under reduced pressure. The resulting residue (92 mg) was purified by flash column chromatography (silica gel: 7.7 g, 3.5 \times 2.8 cm, 25–50% acetone in dichloromethane) to afford epidisulfide *cis*-5b (31.6 mg, 81.2%) as a white solid. Structural assignments were made with additional information from gCOSY, gHSQC, and gHMBC experiments. Crystals suitable for X-ray diffraction were obtained by slow evaporation of epidisulfide *cis*-5b from dichloromethane–methanol (10:1). The thermal ellipsoid representation of epidisulfide *cis*-5b is shown later in this document.

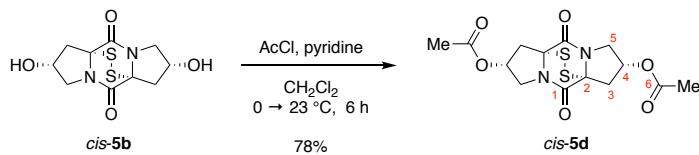
¹H NMR (500 MHz, D₂O–CD₃CN (1:1), 25 °C): δ 5.21 (tt, *J* = 5.3, 1.8 Hz, 2H, C4H), 4.29 (dd, *J* = 12.5, 5.2 Hz, 2H, C5H_a), 4.19 (d, *J* = 12.5 Hz, 2H, C5H_b), 3.64 (dd, *J* = 15.5, 5.5 Hz, 2H, C3H_a), 2.91 (d, *J* = 15.4 Hz, 2H, C3H_b).

¹³C NMR (150 MHz, D₂O–CD₃CN (1:1), 25 °C): δ 164.0 (C1), 74.9 (C2), 68.2 (C4), 53.7 (C5), 39.6 (C3).

FTIR (thin film) cm⁻¹: 3372 (br), 2945 (w), 1662 (s), 1394 (m), 1330 (w), 1208 (w), 1091 (m), 641 (m), 411 (m).

HRMS (ESI) (*m/z*): calc'd for C₁₀H₁₂N₂NaO₄S₂ [M+Na]⁺: 311.0131, found: 311.0127.

TLC (10% methanol in dichloromethane), R_f: 0.27 (UV, PMA, CAM, AgNO₃).



Bis(acetoxy)epidisulfide *cis*-5d:

Pyridine (0.10 mL, 1.2 mmol, 16 equiv) and acetyl chloride (32 μ L, 0.45 mmol, 6.0 equiv) were added dropwise via syringe to a suspension of bis(hydroxy)-epidisulfide *cis*-5b (21.7 mg, 75.3 μ mol, 1 equiv) in dichloromethane (1.5 mL) at 0 °C. The ice–water bath was removed, and the reaction mixture was allowed to stir and warm to 23 °C. After 6 h, the reaction mixture was diluted with dichloromethane (15 mL) and was washed with a saturated aqueous sodium bicarbonate solution (15 mL). The aqueous layer was extracted with dichloromethane (10 mL), and the combined organic layers were washed with a saturated aqueous sodium chloride solution (10 mL). The layers were separated and the aqueous layer was extracted with dichloromethane (10 mL). The combined organic layers were dried over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure. The resulting residue (33 mg) was purified by flash column chromatography (silica gel: 2.3 g, 8 \times 1.2 cm, 0→40% acetone in dichloromethane) to afford bis(acetoxy)epidisulfide *cis*-5d (21.7 mg, 77.5%) as a white solid. Structural assignments were made with additional information from gCOSY, gHSQC, and gHMBC experiments.

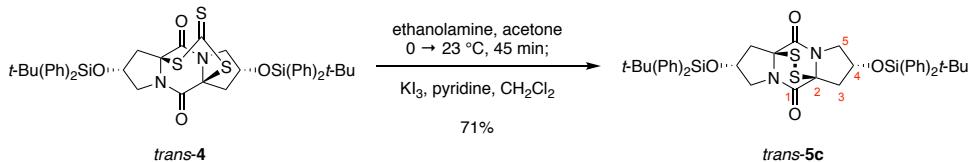
¹H NMR (500 MHz, CDCl₃, 25 °C): δ 5.49–5.44 (m, 2H, C4H), 3.92 (d, J = 3.8 Hz, 4H, C5H_a, C5H_b), 3.31 (dd, J = 16.2, 6.1 Hz, 2H, C3H_a), 2.51 (d, J = 16.2, 2H, C3H_b), 2.13 (s, 6H, CH₃).

¹³C NMR (125 MHz, CDCl₃, 25 °C): δ 170.4 (C6), 162.9 (C1), 75.4 (C2), 71.0 (C4), 52.0 (C5), 38.3 (C3), 21.2 (CH₃).

FTIR (thin film) cm⁻¹: 2989 (w), 2948 (w), 1732 (s), 1700 (s), 1431 (w), 1374 (m), 1224 (s), 1071 (m), 1012 (m), 625 (w).

HRMS (ESI) (*m/z*): calc'd for C₁₄H₁₆N₂NaO₆S₂ [M+Na]⁺: 395.0342, found: 395.0343.

TLC (20% acetone in dichloromethane), R_f: 0.43 (UV, CAM, AgNO₃).



Bis(silyloxy)epidisulfide *trans*-5c:

A yellow solution of dithiepanethione *trans*-4 (350 mg, 0.433 mmol, 1 equiv) in acetone (15 mL) at 0 °C was sparged with argon for 15 min by discharge of a balloon equipped with a needle extending into the reaction mixture. Ethanolamine (7.5 mL) was injected dropwise via syringe over 2.5 min, resulting in a clear and colorless solution. After 15 min, the ice–water bath was removed and the reaction mixture was allowed to stir and warm to 23 °C. After 30 min, the reaction mixture was diluted with dichloromethane (100 mL) and poured into an aqueous hydrogen chloride solution (1 N, 130 mL). The aqueous layer was extracted with dichloromethane (50 mL). A stock solution of potassium triiodide in pyridine¹⁴ was added dropwise to the combined organic layers containing crude bisthiol until a persistent yellow color was observed. The resulting mixture was washed with an aqueous hydrogen chloride solution (1 N, 2 × 50 mL), was washed with a mixture of deionized water, saturated aqueous sodium thiosulfate solution, and saturated aqueous bicarbonate solution (2:1:1, 80 mL), and was washed with a saturated aqueous sodium chloride solution (75 mL). The aqueous layers were separately extracted with a single portion of dichloromethane (50 mL). The combined organic extracts were dried over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure. The resulting residue (437 mg) was purified by flash column chromatography (silica gel: 42 g, 13 × 3.4 cm, 0→20% ethyl acetate in hexanes) to afford bis(silyloxy)epidisulfide *trans*-5c (47.8 mg, 87.4%) as a white foam. Structural assignments were made with additional information from gCOSY, gHSQC, and gHMBC experiments.

¹H NMR (400 MHz, CDCl₃, 25 °C):

δ 7.70–7.66 (m, 4H, SiPh-*ortho*-H_{a/b}), 7.65–7.60 (m, 4H, SiPh-*ortho*-H_{a/b}), 7.50–7.38 (m, 12H, SiPh-*para*-H, SiPh-*meta*-H), 4.68 (app-p, *J* = 6.0 Hz, 2H, C4H), 3.79 (dd, *J* = 11.6, 5.9 Hz, 2H, C5H_a), 3.62 (dd, *J* = 11.6, 4.7 Hz, 2H, C5H_b), 3.13 (dd, *J* = 14.6, 6.0 Hz, 2H, C3H_a), 2.29 (dd, *J* = 14.6, 6.0 Hz, 2H, C3H_b), 1.05 (s, 18H, C(CH₃)₃).

¹³C NMR (100 MHz, CDCl₃, 25 °C):

δ 163.3 (**C1**), 135.8 (SiPh-*ortho*-C_{a/b}), 135.7 (SiPh-*ortho*-C_{a/b}), 132.9 (2C, SiPh-*ipso*-C), 130.3 (SiPh-*para*-C_{a/b}), 130.3 (SiPh-*para*-C_{a/b}), 128.1 (SiPh-*meta*-C_{a/b}), 128.1 (SiPh-*meta*-C_{a/b}), 75.7 (**C2**), 70.9 (**C4**), 53.0 (**C5**), 40.8 (**C3**), 26.9 (C(CH₃)₃), 19.1 (C(CH₃)₃).

FTIR (thin film) cm⁻¹:

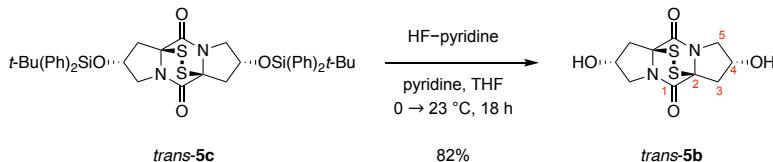
3071 (w), 2931 (w), 2857 (w), 1700 (s), 1385 (m), 1111 (w), 822 (w), 702 (s), 506 (m).

HRMS (ESI) (*m/z*):

calc'd for C₄₂H₄₈N₂NaO₄S₂Si₂ [M+Na]⁺: 787.2486, found: 787.2511.

TLC (20% ethyl acetate in hexanes), R_f:

0.46 (UV, CAM, AgNO₃).



Bis(hydroxy)epidisulfide *trans*-5b:

A freshly prepared solution of hydrogen fluoride–pyridine (70% HF, 0.15 mL), pyridine (0.3 mL), and tetrahydrofuran (1.2 mL) at 0 °C was added via plastic syringe to a solution of bis(silyloxy)epidisulfide *trans*-5c (59.2 mg, 77.4 µmol, 1 equiv) in tetrahydrofuran (1.5 mL) at 0 °C in a 45-mL polypropylene Falcon tube. After 5 min, the ice–water bath was removed and the reaction mixture was allowed to stir and warm to 23 °C. After 18 h, the reaction mixture was cooled to 0 °C, and was slowly diluted with a saturated aqueous sodium bicarbonate solution (11 mL) was added in portions (0.5 mL) over 5 min. The reaction mixture was allowed to warm to 23 °C, was washed with dichloromethane (3 × 5 mL), and the combined organic layers were extracted with deionized water (4 × 10 mL). The combined aqueous extracts were frozen in a 250-mL round-bottom flask by immersion in a liquid nitrogen bath and were subjected to lyophilization under reduced pressure. The resulting solids were suspended in dichloromethane–methanol (9:1, 200 mL) and sonicated for 10 min, and were filtered through a pad of silica gel (10 g, 3 × 3 cm) covered with a pad of Celite (0.5 cm). The filter cake was washed with dichloromethane–methanol (9:1, 100 mL) and the filtrate was concentrated under reduced pressure. The resulting residue (22 mg) was purified by flash column chromatography (silica gel: 2.5 g, 11 × 1 cm, 20–50% acetone in dichloromethane) to afford epidisulfide *trans*-5b (18.0 mg, 81.6%) as a white solid. Structural assignments were made with additional information from gCOSY, gHSQC, and gHMBC experiments. Crystals suitable for X-ray diffraction were obtained by slow evaporation of epidisulfide *trans*-5b from dichloromethane–methanol (10:1). The thermal ellipsoid representation of epidisulfide *trans*-5b is shown later in this document.

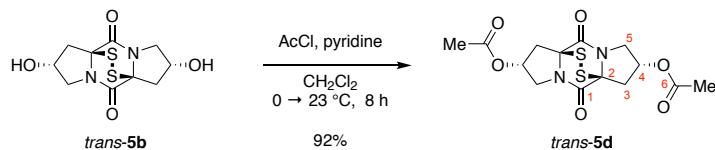
¹H NMR (500 MHz, D₂O–CD₃CN (1:1), 25 °C): δ 5.23 (tt, *J* = 5.1, 3.6 Hz, 2H, C4H), 4.35 (dd, *J* = 12.1, 4.9 Hz, 2H, C5H_a), 4.10 (ddd, *J* = 12.1, 3.3, 1.3 Hz, 2H, C5H_b), 3.51 (ddd, *J* = 14.8, 4.2, 1.4 Hz, 2H, C3H_a), 3.11 (dd, *J* = 14.8, 5.6 Hz, 2H, C3H_b).

¹³C NMR (150 MHz, D₂O–CD₃CN (1:1), 25 °C): δ 164.1 (**C1**), 75.3 (**C2**), 68.8 (**C4**), 52.0 (**C5**), 39.3 (**C3**).

FTIR (thin film) cm⁻¹: 3490 (br-m), 3401 (br-m), 2945 (br-w), 1697 (s), 1678 (s), 1383 (m), 1327 (w), 1182 (w) 1067 (m), 660 (w).

HRMS (ESI) (*m/z*): calc'd for C₁₀H₁₃N₂O₄S₂ [M+H]⁺: 289.0311, found: 289.0309.

TLC (10% methanol in dichloromethane), R_f: 0.38 (UV, PMA, CAM, AgNO₃).



Bis(acetoxy)epidisulfide *trans*-5d:

Pyridine (50 μ L, 620 μ mol, 12 equiv) and acetyl chloride (30 μ L, 400 μ mol, 8 equiv) were added dropwise via syringe to a suspension of bis(hydroxy)-epidisulfide *trans*-5b (14.5 mg, 50.3 μ mol, 1 equiv) in dichloromethane (1 mL) at 0 $^{\circ}$ C. The ice–water bath was removed, and the reaction mixture was allowed to stir and warm to 23 $^{\circ}$ C. After 8 h, the reaction mixture was diluted with dichloromethane (10 mL) and was washed with a saturated aqueous sodium bicarbonate solution (15 mL). The aqueous layer was extracted with dichloromethane (2×10 mL), and the combined organic layers were dried over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure. The resulting residue (39 mg) was purified by flash column chromatography (silica gel: 4.7 g, 8.5 \times 1.5 cm, 10 \rightarrow 60% acetone in hexanes) to afford bis(acetoxy)epidisulfide *trans*-5d (17.3 mg, 92.4%) as a white solid. Structural assignments were made with additional information from gCOSY, gHSQC, and gHMBC experiments.

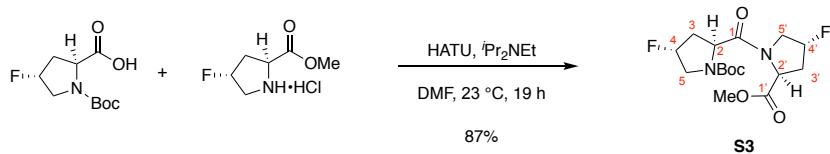
1 H NMR (500 MHz, CDCl₃, 25 $^{\circ}$ C): δ 5.50 (tt, *J* = 6.3, 3.5 Hz, 2H, C4H), 4.03 (dd, *J* = 12.8, 5.6 Hz, 2H, C5H_a), 3.82 (ddd, *J* = 12.8, 3.1, 1.2 Hz, 2H, C5H_b), 3.26 (ddd, *J* = 15.4, 4.3, 1.2 Hz, 2H, C3H_a), 2.67 (dd, *J* = 15.4, 6.4 Hz, 2H, C3H_b), 2.07 (s, 6H, CH₃).

13 C NMR (125 MHz, CDCl₃, 25 $^{\circ}$ C): δ 170.3 (C6), 163.0 (C1), 75.8 (C2), 71.4 (C4), 50.6 (C5), 38.2 (C3), 21.0 (CH₃).

FTIR (thin film) cm⁻¹: 3610 (br-w), 2918 (w), 1739 (s), 1693 (s), 1374 (m), 1047 (m), 898 (w), 649 (w), 438 (w).

HRMS (ESI) (*m/z*): calc'd for C₁₄H₁₆N₂NaO₆S₂ [M+Na]⁺: 395.0342, found: 395.0339.

TLC (3% acetone in dichloromethane), R_f: 0.23 (UV, CAM, AgNO₃).



Dipeptide S3:

N,N-Diisopropylethylamine (12.5 mL, 71.8 mmol, 4.99 equiv) was added by syringe to a solution of *N*-Boc-*trans*-4-fluoro-L-proline (3.36 g, 14.4 mmol, 1 equiv), *trans*-4-fluoro-L-proline-OMe hydrochloride¹⁵ (4.00 g, 21.8 mmol, 1.51 equiv), and *N*-[(Dimethylamino)-1*H*-1,2,3-triazolo-[4,5-*b*]pyridin-1-ylmethylene]-*N*-methyl-methanaminium hexafluorophosphate *N*-oxide (HATU, 8.22 g, 21.6 mmol, 1.50 equiv) in *N,N*-dimethylformamide (30 mL). After 19 h, the dark red reaction mixture was cooled to 0 °C and was diluted with ethyl acetate (50 mL) and an aqueous hydrogen chloride solution (1 N, 100 mL). The ice–water bath was removed and the reaction mixture was allowed to stir and warm to 23 °C. After 30 min, the layers were separated and the aqueous layer was extracted with ethyl acetate–hexanes (9:1, 6 × 40 mL). The combined organic layers were washed with deionized water (3 × 75 mL), and were washed with a saturated aqueous sodium chloride solution (1 × 50 mL). The combined aqueous layers were extracted with ethyl acetate–hexanes (9:1, 2 × 50 mL), and the organic extracts were washed separately with deionized water (2 × 25 mL) and with a saturated aqueous sodium chloride solution (1 × 50 mL). The combined organic layers were dried over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure. The resulting residue (8.7 g) was dissolved in methanol–dichloromethane (1:20, 100 mL) and was adsorbed onto silica gel (35 g) by concentration under reduced pressure until a free-flowing powder was obtained. The silica-adsorbed crude mixture was purified by flash column chromatography (silica gel: 260 g, 14 × 8.0 cm, 40→45% acetone in hexanes) to afford dipeptide S3 (4.50 g, 86.2%) as a white foam. Structural assignments were made using additional information from gCOSY, gHSQC, and gHMBC experiments.

¹H {¹⁹F} NMR (600 MHz, CDCl₃, 25 °C, 1.4:1 mixture of atropisomers, *denotes minor atropisomer): δ 5.35–5.32 (m, 1H, C_{4/4'}H), 5.32–5.28 (m, 1H, C_{4/4'}H*), 5.25–5.20 (m, 2H, C_{4/4'}H, C_{4/4'}H*), 4.69–4.61 (m, 3H, C_{2/2'}H, C_{2/2'}H*, C_{2/2'}H*), 4.58 (t, J = 8.1 Hz, 1H, C_{2/2'}H), 4.32 (d, J = 11.7 Hz, 1H, C_{5/5'}H_a*), 4.06 (d, J = 11.8 Hz, 1H, C_{5/5'}H_a), 3.90 (d, J = 12.2 Hz, 1H, C_{5/5'}H_a), 3.82 (d, J = 12.8 Hz, 1H, C_{5/5'}H_a*), 3.79–3.74 (m, 2H, C_{5/5'}H_b, C_{5/5'}H_b*), 3.74 (s, 3H, OCH₃), 3.72 (s, 3H, OCH₃*), 3.66 (dd, J = 13.0, 3.2 Hz, 1H, C_{5/5'}H_b), 3.62 (dd, J = 12.9, 3.5 Hz, 1H, C_{5/5'}H_b*), 2.65–2.55 (m, 2H, C_{3/3'}H_a, C_{3/3'}H_a*), 2.65–2.55 (m, 2H, C_{3/3'}H_a, C_{3/3'}H_a*), 2.20 (ddd, J = 14.2, 7.3, 4.6 Hz, 1H, C_{3/3'}H_b*), 2.13 (ddd, J = 13.8, 8.6, 4.1 Hz, 1H, C_{3/3'}H_b), 2.07 (ddd, J = 13.9, 9.5, 3.9 Hz, 2H, C_{3/3'}H_b, C_{3/3'}H_b*), 1.44 (s, 9H, C(CH₃)₃*), 1.40 (s, 9H, C(CH₃)₃).

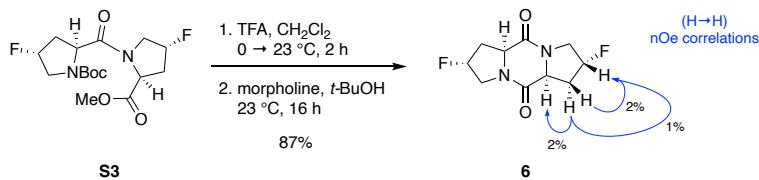
¹³C {¹⁹F} NMR (150 MHz, CDCl₃, 25 °C, 1.4:1 mixture of atropisomers, *denotes minor atropisomer): δ 172.4 (**C_{1'}***), 172.2 (**C_{1'}**), 171.4 (NC(O) OC(CH₃)₃), 171.2 (NC(O)OC(CH₃)₃*), 154.4 (**C_{1'}***), 153.6 (**C_{1'}**), 92.5 (**C_{4/4'}***), 92.0 (**C_{4/4'}**), 91.7 (**C_{4/4'}**), 91.6 (**C_{4/4'}***), 80.8 (C(CH₃)₃), 80.4 (C(CH₃)₃*), 57.9 (**C_{2/2'}**), 57.9 (**C_{2/2'}***), 56.3 (**C_{2/2'}**), 56.2 (**C_{2/2'}***), 53.6 (**C_{5/5'}***), 53.4 (**C_{5/5'}**), 53.3 (**C_{5/5'}**), 53.1 (**C_{5/5'}***), 52.6 (OCH₃), 52.5 (OCH₃*), 37.2 (**C_{3/3'}**), 36.3 (**C_{3/3'}***), 35.7 (**C_{3/3'}**, **C_{3/3'}***), 28.5 (NC(O)OC(CH₃)₃*), 28.4 (NC(O)OC(CH₃)₃).

¹⁹F{¹H} NMR (565 MHz, CDCl₃, 25 °C): δ -175.7 (C_{4/4'}F*), -176.4 (C_{4/4'}F), -176.5 (C_{4/4'}F), -177.3 (C_{4/4'}F*).

FTIR (thin film) cm⁻¹: 2978 (w), 1749 (m), 1700 (s), 1665 (s), 1437 (m), 1403 (s), 1366 (m), 1203 (m), 1162 (s), 1125 (w), 1066 (w), 773 (w).

HRMS (ESI) (*m/z*): calc'd for C₁₆H₂₅F₂N₂O₅ [M+H]⁺: 363.1726, found: 363.1740.

TLC (40% acetone in hexanes), R_f: 0.31 (UV, CAM)



Bis(fluoro)diketopiperazine 6:

Trifluoroacetic acid (25 mL) was added to a stirring solution of dipeptide **S3** (4.50 g, 12.4 mmol, 1 equiv) in dichloromethane (125 mL) at 0 °C. The ice–water bath was removed and the solution was allowed to stir and warm to 23 °C. After 2 h, the reaction mixture was concentrated under reduced pressure, and the resulting viscous brown residue was dissolved in *tert*-butanol (125 mL). The reaction mixture was stirred vigorously at 23 °C as morpholine (25 mL) was added. After 16 h, the reaction mixture was concentrated under reduced pressure down to approximately 15 mL, was diluted with dichloromethane (50 mL) and toluene (50 mL), and was concentrated under reduced pressure. The resulting residue was dissolved in dichloromethane–isopropanol (20:1, 50 mL) and adsorbed onto silica gel (30 g) by concentration under reduced pressure until a free-flowing powder was obtained. The silica-adsorbed crude mixture was purified by flash column chromatography (silica gel: 240 g, 14 × 7.5 cm, 5→10% isopropanol in dichloromethane) to afford bis(fluoro)diketopiperazine **6** (2.5 g, 87%) as a white solid. Structural assignments were made using additional information from nOe, gCOSY, gHSQC, and gHMBC experiments.

¹H {¹⁹F} NMR (600 MHz, CDCl₃, 25 °C): δ 5.33 (t, *J* = 3.3 Hz, 2H, C4H), 4.56 (dd, *J* = 10.8, 6.4 Hz, 2H, C2H), 3.84 (d, *J* = 14.3 Hz, 2H, C5H_α), 3.72 (dd, *J* = 14.2, 3.6 Hz, 2H, C5H_β), 2.67 (dd, *J* = 14.5, 6.1 Hz, 2H, C3H_α), 2.21 (ddd, *J* = 14.6, 11.5, 3.4 Hz, 2H, C3H_β).

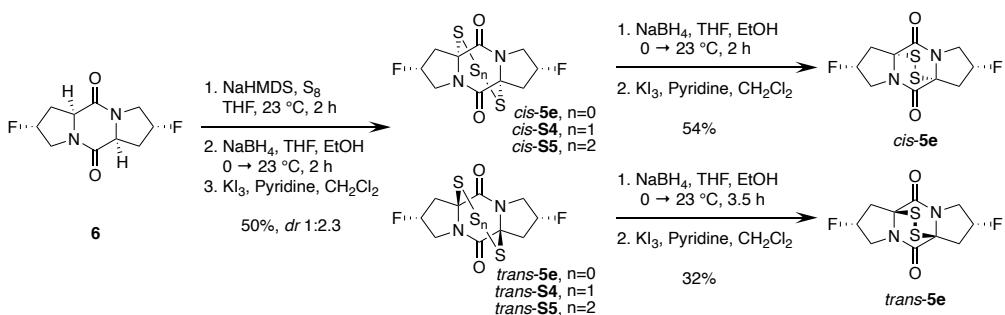
¹³C {¹⁹F} NMR (150 MHz, CDCl₃, 25 °C): δ 165.8 (**C1**), 90.8 (**C4**), 58.9 (**C2**), 52.3 (**C5**), 35.4 (**C3**).

¹⁹F {¹H} NMR (565 MHz, CDCl₃, 25 °C): δ -174.3 (s, C4F).

FTIR (thin film) cm⁻¹: 1665 (s), 1433 (m), 1209 (w), 1088 (w), 1057 (w), 975 (w), 959 (w), 852 (w), 625 (w), 443 (w).

HRMS (ESI) (*m/z*): calc'd for C₁₀H₁₃F₂N₂O₂ [M+H]⁺: 231.0940, found: 231.0938.

TLC (5% isopropanol in dichloromethane), R_f: 0.4 (UV, KMnO₄)



Bis(fluoro)epidisulfides *cis*-5e and *trans*-5e:

A solution of sodium bis(trimethylsilyl)amide (NaHMDS, 1.0 M, 3.0 mL, 3.0 mmol, 3.0 equiv) in tetrahydrofuran was added dropwise via syringe over 5 min to a vigorously stirring suspension of sulfur (257 mg, 8.02 mmol, 8.08 equiv) in tetrahydrofuran (5 mL), resulting in the suspension becoming dark brown and then light yellow. After 1 min, a solution of diketopiperazine **6** (229 mg, 0.993 mmol, 1 equiv) in tetrahydrofuran (5 mL) was added dropwise via cannula over 5 min. After 1 min, a solution of sodium bis(trimethylsilyl)amide (NaHMDS, 1.0 M, 2.0 mL, 2.0 mmol, 2.0 equiv) in tetrahydrofuran was added dropwise via syringe over 2 min, during which the reaction mixture changed from yellow-orange to yellow-green. After 2 h, the reaction mixture was diluted with dichloromethane (25 mL) and was poured into a saturated aqueous solution of ammonium chloride (25 mL). The layers were separated, and the aqueous layer was extracted with dichloromethane (4 × 25 mL). The combined organic layers were dried over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure. The resulting crude residue was dissolved in tetrahydrofuran (10 mL) and anhydrous ethanol (10 mL), and was sparged with argon for 20 min at 0 °C by discharge of a balloon equipped with a needle extending into the reaction mixture. Sodium borohydride (943 mg, 24.9 mmol, 25.1 equiv) was added as a solid in portions over 15 min. After 5 min, the ice–water bath was removed and the reaction mixture was allowed to stir and warm to 23 °C. After 2 h, the reaction mixture was cooled to 0 °C, was diluted with cold (0 °C) dichloromethane (20 mL), and was poured into an aqueous hydrogen chloride solution (1 N, 300 mL) at 10 °C. The layers were separated, and the aqueous layer was extracted with dichloromethane (3 × 50 mL). A stock solution of potassium triiodide in pyridine¹⁴ was added dropwise into the combined organic layers until the solution maintained a yellow color. The organic layer was washed sequentially with an aqueous hydrogen chloride solution (1 N, 2 × 75 mL), an aqueous sodium thiosulfate solution (50% saturated, 50 mL), and a saturated aqueous sodium chloride solution (100 mL). The aqueous layers were separately extracted with a single portion of dichloromethane (50 mL), and the combined organic extracts were dried over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure. The resulting residue (470 mg) was dissolved in dichloromethane (50 mL) and adsorbed onto silica gel (2.0 g) by concentration under reduced pressure until a free-flowing powder was obtained. The silica-adsorbed crude mixture was purified by flash column chromatography (silica gel: 43 g, 13 × 3.0 cm, 20→60% acetone in hexanes) to afford a mixture of bis(fluoro)epithiodiketopiperazines¹⁶ *trans*-5e, *trans*-S4, and *trans*-S5 (46 mg, 15%) and a mixture of bis(fluoro)epithiodiketopiperazines¹⁷ *cis*-5e, *cis*-S4, and *cis*-S5 (112 mg, 35%).

A solution of bis(fluoro)epithiodiketopiperazines *cis*-5e, *cis*-S4, and *cis*-S5 (112 mg, 336 µmol, 1 equiv) in tetrahydrofuran (3 mL) and anhydrous ethanol (2 mL) at 0 °C was sparged with argon for 20 min by discharge of a balloon equipped with a needle extending into the reaction mixture. Sodium borohydride (308 mg, 8.14 mmol, 24.2 equiv) was added as a solid in portions

over 3 min, then the ice–water bath was removed and the reaction mixture was allowed to stir and warm to 23 °C. After 45 min, the reaction mixture was cooled to 0 °C, and additional sodium borohydride (78.3 mg, 2.07 mmol, 6.16 equiv) was added as a solid in portions over 2 min, then the ice–water bath was removed and the reaction mixture was allowed to stir and warm to 23 °C. After 2 h, the reaction mixture was diluted with dichloromethane (25 mL), and was poured into an aqueous hydrogen chloride solution (1 N, 100 mL). The layers were separated, and the aqueous layer was extracted with dichloromethane (3 × 25 mL). A stock solution of potassium triiodide in pyridine¹⁴ was added dropwise into the combined organic layers until the solution maintained a yellow color. The organic layer was washed with an aqueous hydrogen chloride solution (1 N, 2 × 35 mL), an aqueous sodium thiosulfate solution (50% saturated, 40 mL), and a saturated aqueous sodium chloride solution (40 mL). The aqueous layers were separately extracted with a single portion of dichloromethane (50 mL), and the combined organic extracts were dried over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure. The resulting residue (117 mg) was purified by flash column chromatography (silica gel: 11.5 g, 18 × 1.5 cm, 30→65% ethyl acetate in hexanes) to afford epidisulfide *cis*-5e (53 mg, 54%) as a white solid. Structural assignments were made using additional information from nOe, gCOSY, gHSQC, and gHMBC experiments. Crystals suitable for X-ray diffraction were obtained by recrystallization of epidisulfide *cis*-5e from acetone–hexanes (3:1). The thermal ellipsoid representation of epidisulfide *cis*-5e is shown later in this document.

Similarly, a solution of bis(fluoro)epithiodiketopiperazines *trans*-5e, *trans*-S4, and *trans*-S5 (45.5 mg, 137 µmol, 1 equiv) in tetrahydrofuran (1.5 mL) and anhydrous ethanol (1.5 mL) at 0 °C was sparged with argon for 20 min by discharge of a balloon equipped with a needle extending into the reaction mixture. Sodium borohydride (98.3 mg, 2.60 mmol, 19.0 equiv) was added as a solid in portions over 1 min, then the ice–water bath was removed and the reaction mixture was allowed to stir and warm to 23 °C. After 1.5 h, the reaction mixture was cooled to 0 °C and additional sodium borohydride (60.6 mg, 1.60 mmol, 11.7 equiv) was added as a solid in portions over 1 min, then the ice–water bath was removed and the reaction mixture was allowed to stir and warm to 23 °C. After 3.5 h, the reaction mixture was diluted with dichloromethane (15 mL), and poured into an aqueous hydrogen chloride solution (1 N, 50 mL). The layers were separated, and the aqueous layer was extracted with dichloromethane (4 × 15 mL). A stock solution of potassium triiodide in pyridine¹⁴ was added dropwise into the combined organic layers until the solution maintained a yellow color. The organic layer was washed with an aqueous hydrogen chloride solution (1 N, 2 × 25 mL), an aqueous sodium thiosulfate solution (50% saturated, 25 mL), and a saturated aqueous sodium chloride solution (25 mL). The aqueous layers were separately extracted with a single portion of dichloromethane (25 mL), and the combined organic layers were dried over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure. The resulting residue (51 mg) was purified by flash column chromatography (silica gel: 5.0 g, 16 × 1.2 cm, 10→50% ethyl acetate in hexanes) to afford epidisulfide *trans*-5e (12.8 mg, 32.0%) as a white solid. Structural assignments were made using additional information from nOe, gCOSY, gHSQC, and gHMBC experiments. Crystals suitable for X-ray diffraction were obtained by slow evaporation of a saturated solution of epidisulfide *trans*-5e in acetone–hexanes (1:7) at 23 °C. The thermal ellipsoid representation of epidisulfide *trans*-5e is shown later in this document.

cis-5e:¹⁸

^1H { ^{19}F } NMR (600 MHz, DMSO- d_6 , 25 °C): δ 5.54 (app-t, J = 4.2 Hz, 2H, C4H), 3.91 (d, J = 13.7 Hz, 2H, C5H $_{\alpha}$), 3.85 (dd, J = 13.6, 4.2 Hz, 2H, C5H $_{\beta}$), 3.17 (dd, J = 16.4, 4.4 Hz, 2H, C3H $_{\beta}$), 2.74 (d, J = 16.4 Hz, 2H, C3H $_{\alpha}$).

^{13}C { ^{19}F } NMR (150 MHz, DMSO- d_6 , 25 °C): δ 162.2 (**C1**), 91.1 (**C4**), 75.3 (**C2**), 52.5 (**C5**), 38.6 (**C3**).

^{19}F { ^1H } NMR (565 MHz, DMSO- d_6 , 25 °C): δ -168.3 (s, C4F).

FTIR (thin film) cm $^{-1}$: 1691 (s), 1428 (w), 1390 (m), 1073 (m), 1042 (w), 950 (w), 786 (w), 652 (w), 441 (w).

HRMS (ESI) (m/z): calc'd for $\text{C}_{10}\text{H}_{10}\text{F}_2\text{N}_2\text{NaO}_2\text{S}_2$ [M+Na] $^+$: 315.0044, found: 315.0058.

TLC (40% acetone in hexanes), Rf: 0.23 (UV, CAM, AgNO₃).

trans-5e:¹⁹

^1H { ^{19}F } NMR (600 MHz, CDCl₃, 25 °C): δ 5.44 (app-tq, J = 3.8, 1.4 Hz, 2H, C4H), 4.14 (dt, J = 13.4, 1.6 Hz, 2H, C5H $_{\alpha}$), 3.89 (dd, J = 13.4, 3.9 Hz, 2H, C5H $_{\beta}$), 3.57 (dt, J = 15.9, 1.8 Hz, 2H, C3H $_{\alpha}$), 2.58 (dd, J = 15.9, 5.3 Hz, 2H, C3H $_{\beta}$).

^{13}C { ^{19}F } NMR (150 MHz, CDCl₃, 25 °C): δ 162.9 (**C1**), 90.6 (**C4**), 76.2 (**C2**), 51.5 (**C5**), 39.3 (**C3**).

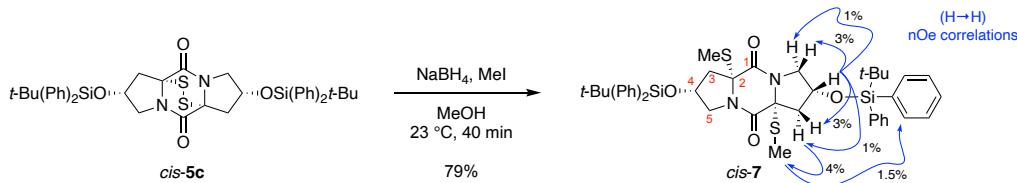
^{19}F { ^1H } NMR (565 MHz, CDCl₃, 25 °C): δ -175.3 (s, C4F).

FTIR (thin film) cm $^{-1}$: 1697 (s), 1424 (w), 1388 (m), 1187 (w), 1061 (w), 1036 (w), 952 (w), 794 (w), 439 (w).

HRMS (ESI) (m/z): calc'd for $\text{C}_{10}\text{H}_{10}\text{F}_2\text{N}_2\text{NaO}_2\text{S}_2$ [M+Na] $^+$: 315.0044, found: 315.0039.

TLC (40% acetone in hexanes), Rf: 0.53 (UV, CAM, AgNO₃).

TLC (50% ethyl acetate in hexanes), Rf: 0.33 (UV, CAM, AgNO₃).



Bis(methylthioether)diketopiperazine *cis*-7:

Sodium borohydride (4.4 mg, 0.12 mmol, 12 equiv) was added as a solid in one portion to a solution of epidithiodiketopiperazine *cis*-5c (7.3 mg, 9.5 μ mol, 1 equiv) in anhydrous methanol (0.5 mL) and methyl iodide (0.5 mL). After 40 min, the reaction mixture was diluted with ethyl acetate–hexanes (9:1, 10 mL), and washed with saturated aqueous sodium bicarbonate solution (10 mL). The aqueous layer was extracted with ethyl acetate–hexanes (9:1, 10 mL). The combined organic layers were washed with deionized water (15 mL) and a saturated aqueous sodium chloride solution (10 mL). The combined aqueous layers were extracted with ethyl acetate–hexanes (9:1, 10 mL), and the combined organic layers were dried over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure. The resulting residue (9.2 mg) was purified by flash column chromatography (silica gel: 1.1 g, 4.5 \times 0.9 cm, 0–25% ethyl acetate in hexanes) to afford bis(methylthioether)diketopiperazine *cis*-7 (6.0 mg, 79%) as a white solid. Structural assignments were made with additional information from gCOSY, gHSQC, gHMBC, and nOe experiments.

^1H NMR (500 MHz, CDCl_3 , 25 °C):

δ 7.63 (t, $J = 6.8$ Hz, 8H, SiPh-*ortho*-H), 7.43 (t, $J = 7.5$ Hz, 4H, SiPh-*para*-H), 7.37 (t, $J = 7.0$ Hz, 8H, SiPh-*meta*-H), 4.39 (tdd, $J = 7.4, 3.5, 1.7$ Hz, 2H, C4H), 4.02 (dd, $J = 12.9, 7.1$ Hz, 2H, C5H_b), 3.53 (dd, $J = 12.9, 3.5$ Hz, 2H, C5H_a), 2.61 (d, $J = 14.8$ Hz, 2H, C3H_a), 2.35 (s, 6H, SCH₃), 2.27 (dd, $J = 14.9, 7.3$ Hz, 2H, C3H_b), 1.08 (s, 18H, C(CH₃)₃).

^{13}C NMR (150 MHz, CDCl_3 , 25 °C):

δ 164.4 (C1), 135.8 (SiPh-*ortho*-C_{a/b}), 135.8 (SiPh-*ortho*-C_{a/b}), 133.4 (SiPh-*ipso*-C_{a/b}), 133.3 (SiPh-*ipso*-C_{a/b}), 130.2 (SiPh-*para*-C_{a/b}), 130.1 (SiPh-*para*-C_{a/b}), 128.0 (SiPh-*meta*-C_{a/b}), 128.0 (SiPh-*meta*-C_{a/b}), 69.7 (C2), 68.7 (C4), 54.2 (C5), 43.8 (C3), 26.9 (C(CH₃)₃), 19.2 (C(CH₃)₃), 15.5 (SCH₃).

FTIR (thin film) cm^{-1} :

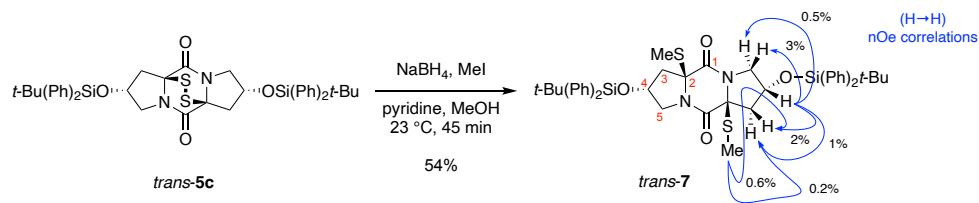
2956 (w), 2857 (w), 1666 (s), 1402 (m), 1105 (s), 1020 (w), 702 (s), 507 (m).

HRMS (ESI) (m/z):

calc'd for $\text{C}_{44}\text{H}_{54}\text{N}_2\text{NaO}_4\text{S}_2\text{Si}_2$ [M+Na]⁺: 817.2956, found: 817.2939.

TLC (30% ethyl acetate in hexanes), R_f :

0.30 (UV, KMnO₄).



Bis(methylthioether)diketopiperazine *trans*-7:

Sodium borohydride (5.3 mg, 0.14 mmol, 12 equiv) was added as a solid in one portion to a solution of epidithiodiketopiperazine *trans*-5c (10.1 mg, 13.2 μ mol, 1 equiv) in anhydrous methanol (0.65 mL) and methyl iodide (0.65 mL). After 45 min, the reaction mixture was diluted with ethyl acetate–hexanes (9:1, 15 mL), and washed with a saturated aqueous sodium bicarbonate solution (10 mL). The aqueous layer was extracted with ethyl acetate–hexanes (9:1, 10 mL). The combined organic layers were washed with deionized water (15 mL), and were washed with saturated aqueous sodium chloride solution (15 mL). The aqueous layers were extracted with ethyl acetate–hexanes (9:1, 10 mL), and the combined organic layers were dried over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure. The resulting residue (11.9 mg) was purified by flash column chromatography (silica gel: 1.4 g, 5.0 \times 0.9 cm, 50 \rightarrow 95% dichloromethane in hexanes) to afford bis(methylthioether)diketopiperazine *trans*-7 (5.7 mg, 54%) as a white solid. Structural assignments were made with additional information from gCOSY, gHSQC, gHMBC, and nOe experiments.

¹H NMR (500 MHz, CDCl₃, 25 °C):

δ 7.71–7.60 (m, 8H, SiPh-ortho-H), 7.49–7.38 (m, 12H, SiPh-para-H, SiPh-meta-H), 4.67 (app-p, J = 6.1 Hz, 2H, C4H), 3.80 (dd, J = 12.0, 5.1 Hz, 2H, C5H_a), 3.62 (dd, J = 12.0, 6.8 Hz, 2H, C5H_b), 2.52 (dd, J = 13.6, 5.8 Hz, 2H, C3H_b), 2.44 (dd, J = 13.5, 7.3 Hz, 2H, C3H_a), 1.96 (s, 6H, SCH₃), 1.05 (d, J = 1.5 Hz, 18H, C(CH₃)₃).

¹³C NMR (125 MHz, CDCl₃, 25 °C):

δ 164.6 (C1), 135.8 (SiPh-ortho-C_{a/b}), 135.7 (SiPh-ortho-C_{a/b}), 133.2 (SiPh-ipso-C_{a/b}), 133.1 (SiPh-ipso-C_{a/b}), 130.2 (2C, SiPh-para-C), 128.1 (SiPh-meta-C_{a/b}), 128.0 (SiPh-meta-C_{a/b}), 69.7 (C2), 69.2 (C4), 53.1 (C5), 43.5 (C3), 26.9 (C(CH₃)₃), 19.1 (C(CH₃)₃), 14.4 (SCH₃).

FTIR (thin film) cm⁻¹:

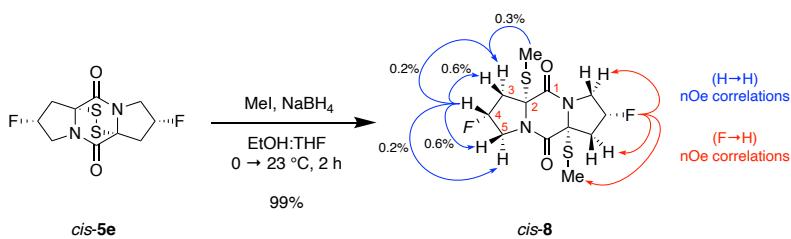
2930 (w), 2857 (w), 1667 (s), 1400 (s), 1111 (s), 1068 (m), 822 (m), 702 (s), 613 (w), 506 (m).

HRMS (ESI) (*m/z*):

calc'd for C₄₄H₅₄N₂NaO₄S₂Si₂ [M+Na]⁺: 817.2956, found: 817.2953.

TLC (100% dichloromethane), R_f:

0.46 (UV, KMnO₄).



Bis(methylthioether)diketopiperazine *cis*-8:

A solution of epidisulfide *cis*-5e (6.7 mg, 23 μ mol, 1 equiv) in tetrahydrofuran (1.5 mL) and anhydrous ethanol (1.5 mL) at 0 °C was sparged with argon for 10 min by discharge of a balloon equipped with a needle extending into the reaction mixture. Methyl iodide (0.30 mL, 4.8 mmol, 210 equiv) was added via syringe, the solution was sparged for 2 min with argon, and sodium borohydride (12.0 mg, 0.318 mmol, 13.8 equiv) was added as a solid in one portion. The ice–water bath was removed, and the reaction mixture was allowed to stir and warm to 23 °C. After 2 h, the reaction mixture was diluted with ethyl acetate–hexanes (9:1, 10 mL) and was washed with a saturated aqueous sodium bicarbonate solution (15 mL). The layers were separated, and the aqueous layer was extracted with ethyl acetate–hexanes (9:1, 2 \times 10 mL). The combined organic layers were washed with deionized water (10 mL), were washed with a saturated aqueous sodium chloride solution (10 mL), and the aqueous layers were separately extracted with a single portion of ethyl acetate–hexanes (9:1, 10 mL). The combined organic layers were dried over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure. The resulting residue (13.2 mg) was purified by flash column chromatography (silica gel: 1.3 g, 5 \times 0.9 cm, 10–20% acetone in dichloromethane) to afford bis(methylthioether)diketopiperazine *cis*-8 (7.3 mg, 99%) as a white solid. Structural assignments were made using additional information from nOe, gCOSY, gHSQC, and gHMBC experiments.

¹H {¹⁹F} NMR (600 MHz, acetone-*d*₆, 25 °C): δ 5.38 (t, J = 5.8 Hz, 2H, C4H), 4.26 (dd, J = 14.3, 6.1 Hz, 2H, C5H_β), 3.64 (d, J = 14.3 Hz, 2H, C5H_α), 2.85 (d, J = 15.7 Hz, 2H, C3H_α), 2.54 (dd, J = 15.7, 5.6 Hz, 2H, C3H_β), 2.26 (s, 6H, SCH₃).

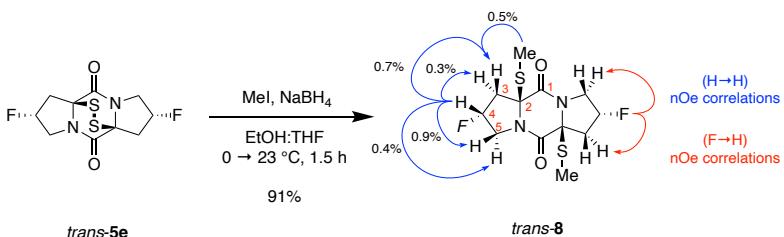
¹³C {¹⁹F} NMR (150 MHz, acetone-*d*₆, 25 °C): δ 165.2 (C1), 90.3 (C4), 70.6 (C2), 53.9 (C5), 41.9 (C3), 15.0 (SCH₃).

¹⁹F {¹H} NMR (565 MHz, acetone-*d*₆, 25 °C): δ -169.2 (s, C4F).

FTIR (thin film) cm⁻¹: 2924 (w), 1668 (s), 1403 (m), 1074 (m), 841 (w), 662 (w).

HRMS (ESI) (*m/z*): calc'd for C₁₂H₁₆F₂N₂NaO₂S₂ [M+Na]⁺: 345.0513, found: 345.0511.

TLC (15% acetone in dichloromethane), R_f: 0.23 (UV, KMnO₄)



Bis(methylthioether)diketopiperazine *trans*-8:

A solution of epidisulfide *trans*-5e (6.0 mg, 21 μ mol, 1 equiv) in tetrahydrofuran (1.5 mL) and anhydrous ethanol (1.5 mL) at 0 °C was sparged with argon for 10 min by discharge of a balloon equipped with a needle extending into the reaction mixture. Methyl iodide (0.30 mL, 4.8 mmol, 230 equiv) was added via syringe, the solution was sparged for 2 min with argon, and sodium borohydride (12.0 mg, 0.318 mmol, 13.8 equiv) was added as a solid in one portion. The ice–water bath was removed, and the reaction mixture was allowed to stir and warm to 23 °C. After 1.5 h, the reaction mixture was diluted with ethyl acetate–hexanes (9:1, 10 mL) and was washed with a saturated aqueous sodium bicarbonate solution (15 mL). The layers were separated, and the aqueous layer was extracted with ethyl acetate–hexanes (9:1, 2 \times 10 mL). The combined organic layers were washed with deionized water (15 mL), were washed with a saturated aqueous sodium chloride solution (15 mL), and the aqueous layers were separately extracted with a single portion of ethyl acetate–hexanes (9:1, 10 mL). The combined organic layers were dried over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure. The resulting residue (13.6 mg) was purified by flash column chromatography (silica gel: 1.0 g, 3.8 \times 0.9 cm, 2% acetone in dichloromethane) to afford bis(methylthioether) *trans*-8 (6.0 mg, 91%) as a white solid. Structural assignments were made using additional information from nOe, gCOSY, gHSQC, and gHMBC experiments.

^1H { ^{19}F } NMR (600 MHz, acetone- d_6 , 25 °C): δ 5.50–5.44 (br-m, 2H, C4H), 4.27 (d, J = 13.6 Hz, 2H, C5H $_{\alpha}$), 3.71 (dd, J = 13.6, 4.7 Hz, 2H, C5H $_{\beta}$), 3.05 (dd, J = 15.3, 5.8 Hz, 2H, C3H $_{\beta}$), 2.84 (ddd, J = 15.3, 3.1, 1.8 Hz, 2H, C3H $_{\alpha}$), 2.25 (s, 6H, SCH $_3$).

^{13}C { ^{19}F } NMR (150 MHz, acetone- d_6 , 25 °C): δ 164.6 (C1), 90.8 (C4), 70.2 (C2), 52.2 (C5), 44.2 (C3), 14.1 (SCH $_3$).

^{19}F { ^1H } NMR (565 MHz, acetone- d_6 , 25 °C): δ –177.5 (s, C4F).

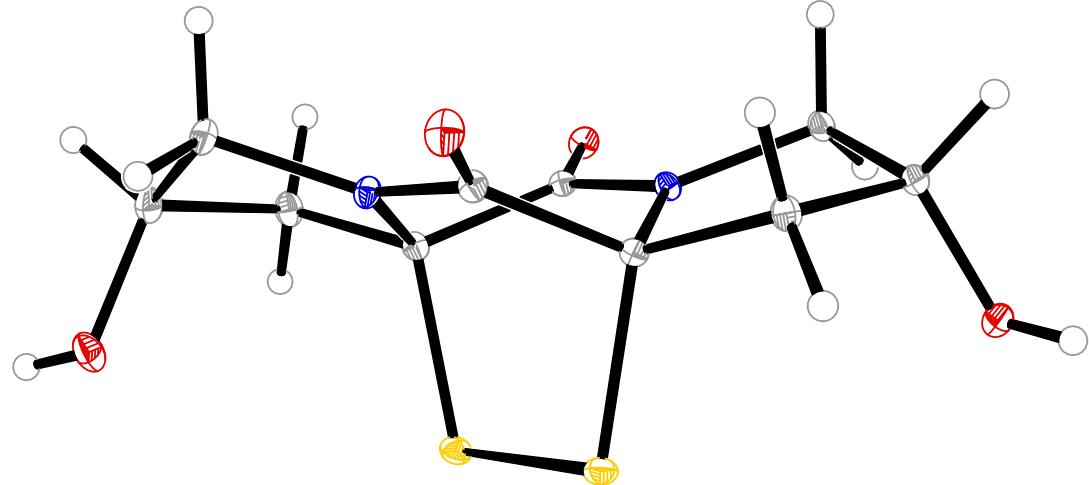
FTIR (thin film) cm^{-1} : 2924 (w), 1669 (s), 1406 (m), 1062 (w), 1038 (w), 960 (w), 792 (w).

HRMS (ESI) (m/z): calc'd for C₁₂H₁₆F₂N₂NaO₂S₂ [M+Na]⁺: 345.0513, found: 345.0506.

TLC (2% acetone in dichloromethane), R f : 0.34 (UV, KMnO₄)

Crystal Structure of Bis(hydroxy)epidisulfide *cis*-5b

View 1:



View 2:

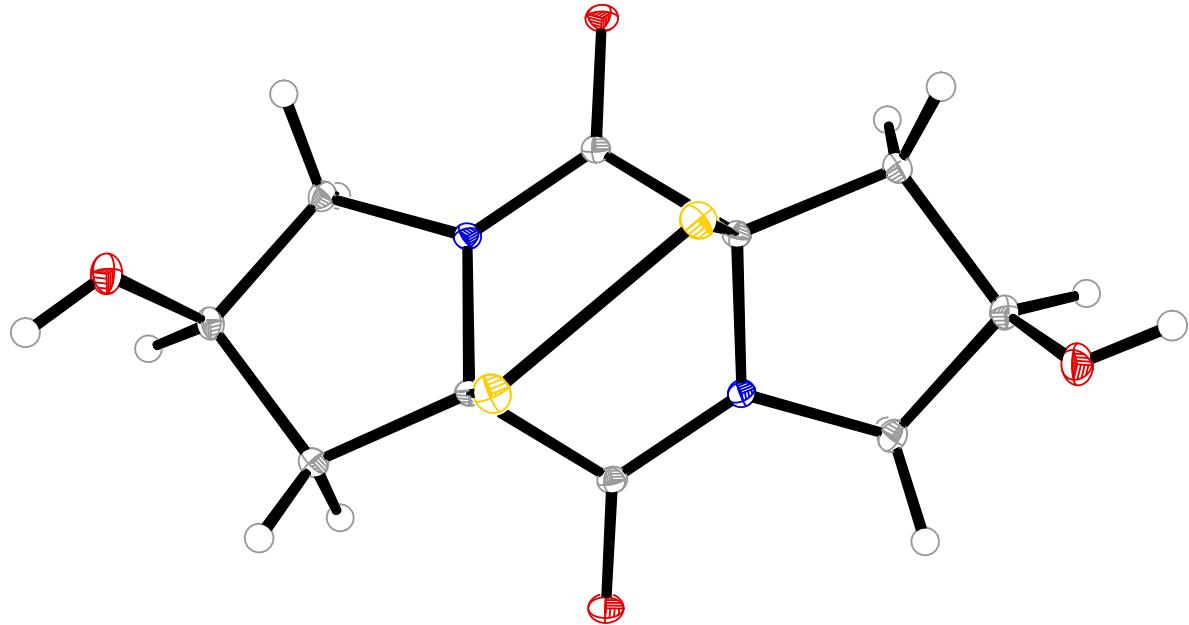


Table S7. Crystal data and structure refinement for bis(hydroxy)epidisulfide *cis*-**5b**.

Identification code	CCDC 1965015
Empirical formula	C10 H12 N2 O4 S2
Formula weight	288.34
Temperature	100(2) K
Wavelength	0.71073 Å
Crystal system	Orthorhombic
Space group	P2(1)2(1)2(1)
Unit cell dimensions	$a = 9.3427(3)$ Å $\alpha = 90^\circ$ $b = 10.4271(3)$ Å $\beta = 90^\circ$ $c = 11.7539(4)$ Å $\gamma = 90^\circ$
Volume	1145.03(6) Å ³
Z	4
Density (calculated)	1.673 Mg/m ³
Absorption coefficient	0.474 mm ⁻¹
F(000)	600
Crystal size	0.280 × 0.220 × 0.168 mm ³
Theta range for data collection	2.611 to 42.927°
Index ranges	$-17 \leq h \leq 17, -19 \leq k \leq 19, -22 \leq l \leq 22$
Reflections collected	79094
Independent reflections	8316 [R(int) = 0.0539]
Completeness to theta = 25.242°	100.0%
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7484 and 0.7106
Refinement method	Full-matrix least-squares on F ²
Data / restraints / parameters	8316 / 1 / 173
Goodness-of-fit on F ²	1.021
Final R indices [I>2sigma(I)]	R1 = 0.0328, wR2 = 0.0710
R indices (all data)	R1 = 0.0453, wR2 = 0.0771
Absolute structure parameter	0.008(15)
Extinction coefficient	n/a
Largest diff. peak and hole	0.474 and -0.352 e·Å ⁻³

Table S8. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for bis(hydroxy)epidisulfide *cis*-**5b**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	<i>x</i>	<i>y</i>	<i>z</i>	U(eq)
S(1)	525(1)	2158(1)	7918(1)	13(1)
S(2)	876(1)	635(1)	6802(1)	13(1)
O(1)	4556(1)	380(1)	6989(1)	13(1)
O(2)	1982(1)	4710(1)	6296(1)	17(1)
O(3)	536(1)	1166(1)	3964(1)	18(1)
O(4)	2826(1)	2689(1)	10343(1)	15(1)
C(1)	3624(1)	1219(1)	6971(1)	10(1)
C(2)	2481(1)	1320(1)	6051(1)	10(1)
C(3)	2788(1)	618(1)	4936(1)	14(1)
C(4)	2031(1)	1438(1)	4028(1)	15(1)
C(5)	2224(1)	2803(1)	4470(1)	14(1)
N(6)	2251(1)	2634(1)	5711(1)	11(1)
C(7)	2156(1)	3564(1)	6497(1)	11(1)
C(8)	2269(1)	3007(1)	7696(1)	10(1)
C(9)	2557(1)	3994(1)	8627(1)	12(1)
C(10)	3586(1)	3339(1)	9462(1)	12(1)
C(11)	4400(1)	2356(1)	8748(1)	12(1)
N(12)	3454(1)	2120(1)	7773(1)	10(1)

Table S9. Bond lengths [\AA] and angles [$^\circ$] for bis(hydroxy)epidisulfide *cis*-**5b**.

S(1)-C(8)	1.8723(11)	C(4)-C(5)	1.5267(18)
S(1)-S(2)	2.0862(4)	C(4)-H(4)	1.0000
S(2)-C(2)	1.8803(12)	C(5)-N(6)	1.4691(15)
O(1)-C(1)	1.2347(14)	C(5)-H(5A)	0.9900
O(2)-C(7)	1.2292(14)	C(5)-H(5B)	0.9900
O(3)-C(4)	1.4266(17)	N(6)-C(7)	1.3424(15)
O(3)-H(13)	0.811(18)	C(7)-C(8)	1.5282(15)
O(4)-C(10)	1.4267(15)	C(8)-N(12)	1.4457(14)
O(4)-H(14)	0.813(18)	C(8)-C(9)	1.5263(16)
C(1)-N(12)	1.3406(14)	C(9)-C(10)	1.5340(16)
C(1)-C(2)	1.5225(15)	C(9)-H(9A)	0.97(2)
C(2)-N(6)	1.4439(14)	C(9)-H(9B)	0.99(2)
C(2)-C(3)	1.5285(16)	C(10)-C(11)	1.5268(16)
C(3)-C(4)	1.5395(17)	C(10)-H(10)	1.0000
C(3)-H(3A)	0.9900	C(11)-N(12)	1.4675(14)
C(3)-H(3B)	0.9900	C(11)-H(11A)	0.9900

C(11)-H(11B)	0.9900	C(2)-N(6)-C(5)	113.07(9)
C(8)-S(1)-S(2)	97.79(4)	O(2)-C(7)-N(6)	125.35(11)
C(2)-S(2)-S(1)	97.55(4)	O(2)-C(7)-C(8)	123.78(10)
C(4)-O(3)-H(13)	109.5	N(6)-C(7)-C(8)	110.85(9)
C(10)-O(4)-H(14)	109.5	N(12)-C(8)-C(9)	104.58(9)
O(1)-C(1)-N(12)	124.58(10)	N(12)-C(8)-C(7)	110.72(9)
O(1)-C(1)-C(2)	123.77(10)	C(9)-C(8)-C(7)	114.67(9)
N(12)-C(1)-C(2)	111.60(9)	N(12)-C(8)-S(1)	110.77(7)
N(6)-C(2)-C(1)	111.49(9)	C(9)-C(8)-S(1)	111.87(8)
N(6)-C(2)-C(3)	104.17(9)	C(7)-C(8)-S(1)	104.38(7)
C(1)-C(2)-C(3)	116.37(9)	C(8)-C(9)-C(10)	105.57(9)
N(6)-C(2)-S(2)	111.83(8)	C(8)-C(9)-H(9A)	105.9(12)
C(1)-C(2)-S(2)	101.54(7)	C(10)-C(9)-H(9A)	111.9(13)
C(3)-C(2)-S(2)	111.70(8)	C(8)-C(9)-H(9B)	113.6(13)
C(2)-C(3)-C(4)	104.03(9)	C(10)-C(9)-H(9B)	111.1(12)
C(2)-C(3)-H(3A)	110.9	H(9A)-C(9)-H(9B)	108.7(18)
C(4)-C(3)-H(3A)	110.9	O(4)-C(10)-C(11)	109.14(10)
C(2)-C(3)-H(3B)	110.9	O(4)-C(10)-C(9)	111.32(10)
C(4)-C(3)-H(3B)	110.9	C(11)-C(10)-C(9)	105.05(9)
H(3A)-C(3)-H(3B)	109.0	O(4)-C(10)-H(10)	110.4
O(3)-C(4)-C(5)	108.58(10)	C(11)-C(10)-H(10)	110.4
O(3)-C(4)-C(3)	112.09(11)	C(9)-C(10)-H(10)	110.4
C(5)-C(4)-C(3)	103.17(9)	N(12)-C(11)-C(10)	104.00(9)
O(3)-C(4)-H(4)	110.9	N(12)-C(11)-H(11A)	111.0
C(5)-C(4)-H(4)	110.9	C(10)-C(11)-H(11A)	111.0
C(3)-C(4)-H(4)	110.9	N(12)-C(11)-H(11B)	111.0
N(6)-C(5)-C(4)	103.17(9)	C(10)-C(11)-H(11B)	111.0
N(6)-C(5)-H(5A)	111.1	H(11A)-C(11)-H(11B)	109.0
C(4)-C(5)-H(5A)	111.1	C(1)-N(12)-C(8)	119.68(9)
N(6)-C(5)-H(5B)	111.1	C(1)-N(12)-C(11)	126.55(9)
C(4)-C(5)-H(5B)	111.1	C(8)-N(12)-C(11)	113.73(9)
H(5A)-C(5)-H(5B)	109.1		
C(7)-N(6)-C(2)	120.31(9)		
C(7)-N(6)-C(5)	126.54(10)		

Symmetry transformations used to generate equivalent atoms:

Table S10. Anisotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for bis(hydroxy)epidisulfide *cis*-**5b**. The anisotropic displacement factor exponent takes the form: $-2\pi^2 [h^2 a^* U^{11} + \dots + 2 h k a^* b^* U^{12}]$

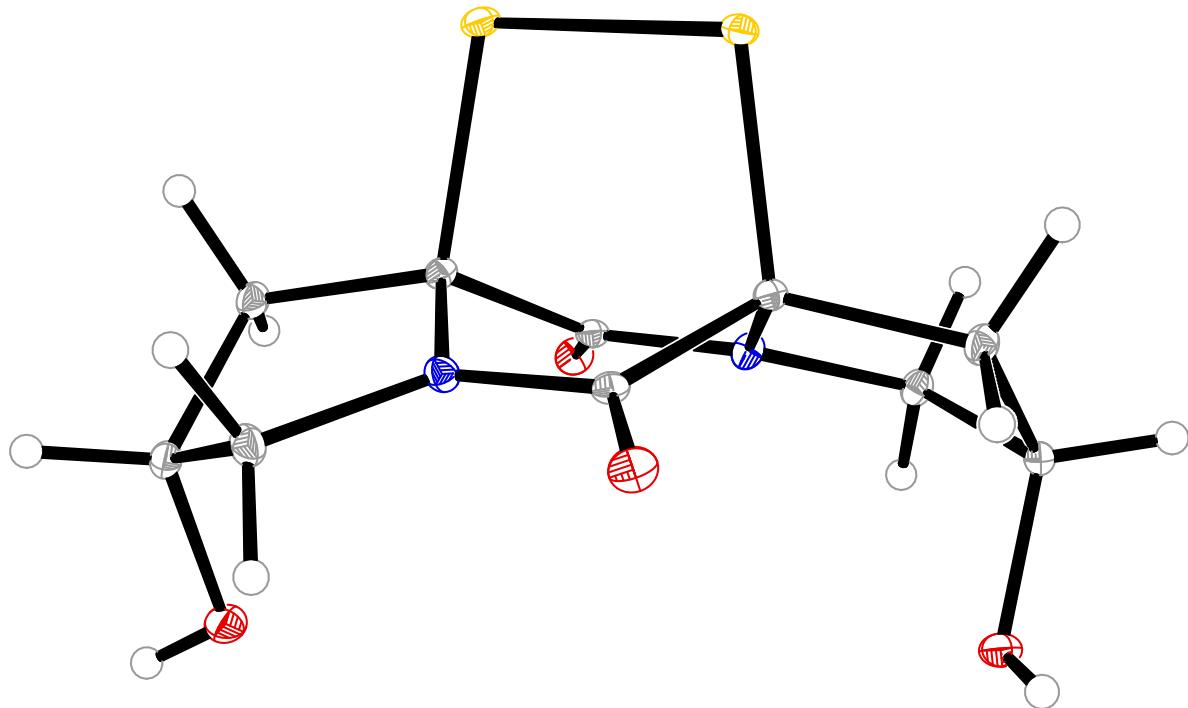
	U ¹¹	U ²²	U ³³	U ²³	U ¹³	U ¹²
S(1)	10(1)	16(1)	15(1)	-1(1)	2(1)	-1(1)
S(2)	12(1)	12(1)	15(1)	0(1)	-1(1)	-3(1)
O(1)	13(1)	13(1)	14(1)	1(1)	1(1)	4(1)
O(2)	25(1)	9(1)	17(1)	2(1)	-2(1)	2(1)
O(3)	16(1)	22(1)	17(1)	-6(1)	-4(1)	2(1)
O(4)	17(1)	18(1)	12(1)	0(1)	2(1)	-3(1)
C(1)	10(1)	10(1)	10(1)	0(1)	1(1)	0(1)
C(2)	11(1)	9(1)	11(1)	0(1)	-2(1)	0(1)
C(3)	16(1)	13(1)	12(1)	-3(1)	-2(1)	3(1)
C(4)	17(1)	16(1)	11(1)	-2(1)	-1(1)	2(1)
C(5)	18(1)	14(1)	10(1)	2(1)	-1(1)	1(1)
N(6)	14(1)	9(1)	10(1)	1(1)	-1(1)	0(1)
C(7)	12(1)	9(1)	12(1)	1(1)	-1(1)	1(1)
C(8)	9(1)	9(1)	10(1)	0(1)	0(1)	1(1)
C(9)	14(1)	11(1)	12(1)	-2(1)	-1(1)	1(1)
C(10)	12(1)	12(1)	11(1)	-1(1)	-1(1)	-2(1)
C(11)	11(1)	13(1)	11(1)	-1(1)	-2(1)	0(1)
N(12)	9(1)	10(1)	11(1)	-1(1)	-1(1)	1(1)

Table S11. Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for bis(hydroxy)epidisulfide *cis*-**5b**.

	x	y	z	U(eq)
H(13)	391(5)	650(20)	3457(18)	27
H(14)	2590(20)	3202(12)	10829(14)	23
H(3A)	2393	-263	4953	17
H(3B)	3830	571	4789	17
H(4)	2497	1330	3268	18
H(5A)	3131	3182	4192	17
H(5B)	1417	3358	4235	17
H(9A)	3000(20)	4720(19)	8250(18)	15
H(9B)	1680(20)	4290(20)	9022(18)	15
H(10)	4264	3980	9794	14
H(11A)	5333	2704	8495	14
H(11B)	4566	1558	9184	14

Crystal Structure of Bis(hydroxy)epidsulfide *trans*-5b

View 1:



View 2:

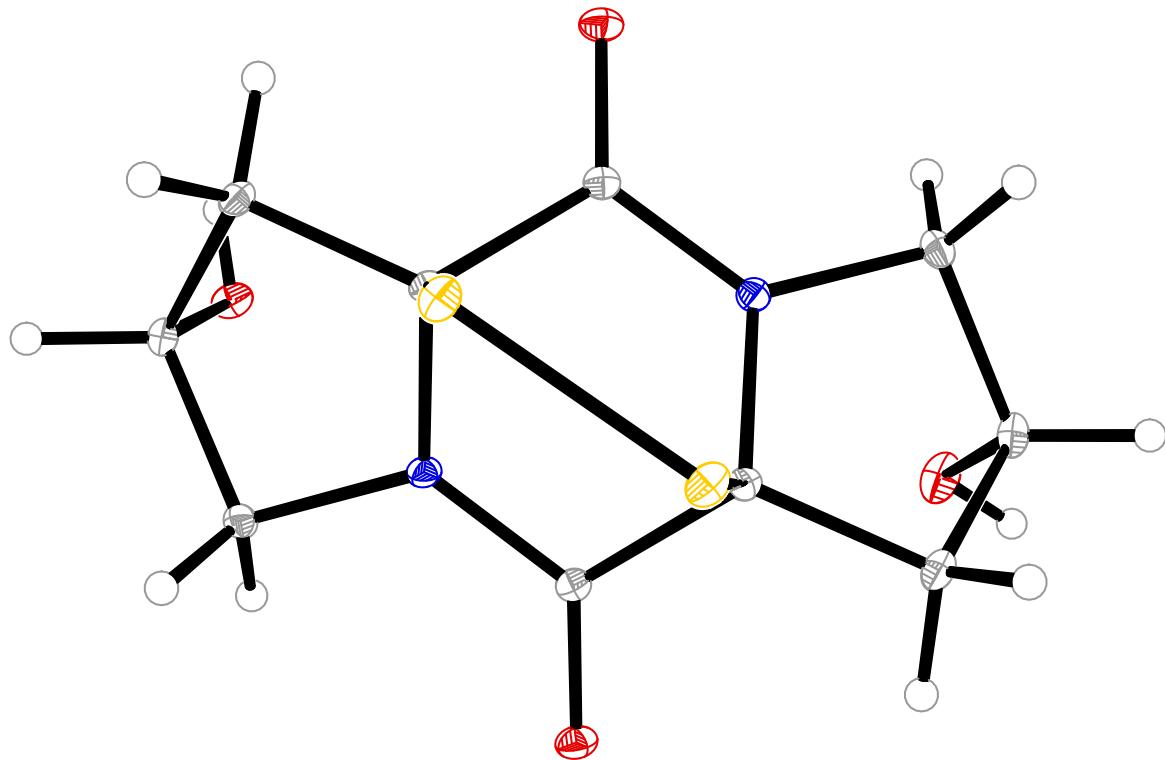


Table S12. Crystal data and structure refinement for bis(hydroxy)epidisulfide *trans*-**5b**.

Identification code	CCDC 1965016
Empirical formula	C10 H12 N2 O4 S2
Formula weight	288.34
Temperature	100(2) K
Wavelength	0.71073 Å
Crystal system	Orthorhombic
Space group	P2(1)2(1)2(1)
Unit cell dimensions	$a = 8.9033(5)$ Å $\alpha = 90^\circ$ $b = 12.0026(7)$ Å $\beta = 90^\circ$ $c = 21.7070(14)$ Å $\gamma = 90^\circ$
Volume	2319.7(2) Å ³
Z	8
Density (calculated)	1.651 Mg/m ³
Absorption coefficient	0.468 mm ⁻¹
F(000)	1200
Crystal size	0.104 × 0.098 × 0.066 mm ³
Theta range for data collection	1.876 to 33.142°
Index ranges	$-13 \leq h \leq 13, -18 \leq k \leq 18, -33 \leq l \leq 33$
Reflections collected	113254
Independent reflections	8813 [R(int) = 0.0388]
Completeness to theta = 25.242°	100.0 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7467 and 0.7207
Refinement method	Full-matrix least-squares on F ²
Data / restraints / parameters	8813 / 0 / 333
Goodness-of-fit on F ²	1.010
Final R indices [I>2sigma(I)]	R1 = 0.0231, wR2 = 0.0570
R indices (all data)	R1 = 0.0256, wR2 = 0.0583
Absolute structure parameter	0.004(9)
Extinction coefficient	n/a
Largest diff. peak and hole	0.327 and -0.210 e·Å ⁻³

Table S13. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for bis(hydroxy)epidisulfide *trans*-**5b**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	<i>x</i>	<i>y</i>	<i>z</i>	U(eq)
S(1A)	11974(1)	2084(1)	6090(1)	12(1)
S(2A)	10263(1)	1090(1)	6457(1)	12(1)
O(1A)	8952(1)	3099(1)	7539(1)	15(1)
O(2A)	9623(1)	3743(1)	5167(1)	14(1)
O(3A)	5513(1)	3092(1)	6401(1)	14(1)
O(4A)	10636(1)	5985(1)	6324(1)	19(1)
C(1A)	9388(2)	3032(1)	7006(1)	10(1)
C(2A)	8791(2)	2193(1)	6534(1)	9(1)
C(3A)	7291(2)	1626(1)	6688(1)	12(1)
C(4A)	6181(2)	2078(1)	6204(1)	11(1)
C(5A)	7163(2)	2354(1)	5649(1)	12(1)
N(6A)	8553(1)	2734(1)	5945(1)	11(1)
C(7A)	9656(2)	3348(1)	5685(1)	10(1)
C(8A)	10988(2)	3458(1)	6130(1)	10(1)
C(9A)	12122(2)	4389(1)	5993(1)	13(1)
C(10A)	11833(2)	5268(1)	6498(1)	14(1)
C(11A)	11321(2)	4572(1)	7048(1)	14(1)
N(12A)	10470(1)	3679(1)	6751(1)	11(1)
S(3B)	1740(1)	3467(1)	8689(1)	12(1)
S(4B)	3026(1)	4023(1)	9435(1)	13(1)
O(1B)	4691(1)	3466(1)	7616(1)	13(1)
O(2B)	4794(1)	1431(1)	9748(1)	15(1)
O(3B)	4513(1)	609(1)	7703(1)	17(1)
O(4B)	8303(1)	3008(1)	9175(1)	17(1)
C(1B)	4460(2)	3191(1)	8157(1)	9(1)
C(2B)	3138(2)	2479(1)	8362(1)	9(1)
C(3B)	2391(2)	1776(1)	7859(1)	11(1)
C(4B)	3047(2)	615(1)	7969(1)	13(1)
C(5B)	3141(2)	541(1)	8673(1)	13(1)
N(6B)	3608(1)	1682(1)	8826(1)	10(1)
C(7B)	4418(2)	2020(1)	9312(1)	10(1)
C(8B)	4789(2)	3262(1)	9261(1)	9(1)
C(9B)	6035(2)	3701(1)	9684(1)	12(1)
C(10B)	7361(2)	3955(1)	9249(1)	11(1)
C(11B)	6643(2)	4214(1)	8627(1)	11(1)
N(12B)	5296(1)	3510(1)	8638(1)	10(1)

Table S14. Bond lengths [Å] and angles [°] for bis(hydroxy)epidisulfide *trans*-**5b**.

S(1A)-C(8A)	1.8709(14)	C(2B)-N(6B)	1.4506(18)
S(1A)-S(2A)	2.0922(5)	C(2B)-C(3B)	1.5316(19)
S(2A)-C(2A)	1.8698(14)	C(3B)-C(4B)	1.530(2)
O(1A)-C(1A)	1.2226(17)	C(3B)-H(3C)	0.9900
O(2A)-C(7A)	1.2217(17)	C(3B)-H(3D)	0.9900
O(3A)-C(4A)	1.4198(17)	C(4B)-C(5B)	1.533(2)
O(3A)-H(13A)	0.74(3)	C(4B)-H(4C)	1.0000
O(4A)-C(10A)	1.4216(18)	C(5B)-N(6B)	1.4694(18)
O(4A)-H(14A)	0.80(3)	C(5B)-H(5C)	0.9900
C(1A)-N(12A)	1.3548(19)	C(5B)-H(5D)	0.9900
C(1A)-C(2A)	1.533(2)	N(6B)-C(7B)	1.3413(18)
C(2A)-N(6A)	1.4499(18)	C(7B)-C(8B)	1.531(2)
C(2A)-C(3A)	1.536(2)	C(8B)-N(12B)	1.4562(18)
C(3A)-C(4A)	1.542(2)	C(8B)-C(9B)	1.534(2)
C(3A)-H(3A)	0.9900	C(9B)-C(10B)	1.542(2)
C(3A)-H(3B)	0.9900	C(9B)-H(9C)	0.9900
C(4A)-C(5A)	1.525(2)	C(9B)-H(9D)	0.9900
C(4A)-H(4A)	1.0000	C(10B)-C(11B)	1.525(2)
C(5A)-N(6A)	1.4669(19)	C(10B)-H(10C)	1.0000
C(5A)-H(5B)	0.9900	C(11B)-N(12B)	1.4673(18)
C(5A)-H(5A)	0.9900	C(11B)-H(11C)	0.9900
N(6A)-C(7A)	1.3509(18)	C(11B)-H(11D)	0.9900
C(7A)-C(8A)	1.535(2)		
C(8A)-N(12A)	1.4489(18)	C(8A)-S(1A)-S(2A)	98.26(5)
C(8A)-C(9A)	1.535(2)	C(2A)-S(2A)-S(1A)	98.08(5)
C(9A)-C(10A)	1.543(2)	C(4A)-O(3A)-H(13A)	109.5
C(9A)-H(9A)	0.9900	C(10A)-O(4A)-H(14A)	109.5
C(9A)-H(9B)	0.9900	O(1A)-C(1A)-N(12A)	125.10(14)
C(10A)-C(11A)	1.527(2)	O(1A)-C(1A)-C(2A)	124.44(13)
C(10A)-H(10A)	1.0000	N(12A)-C(1A)-C(2A)	110.46(12)
C(11A)-N(12A)	1.4632(19)	N(6A)-C(2A)-C(1A)	110.23(11)
C(11A)-H(11A)	0.9900	N(6A)-C(2A)-C(3A)	105.29(11)
C(11A)-H(11B)	0.9900	C(1A)-C(2A)-C(3A)	116.54(12)
S(3B)-C(2B)	1.8597(14)	N(6A)-C(2A)-S(2A)	109.96(9)
S(3B)-S(4B)	2.0926(5)	C(1A)-C(2A)-S(2A)	106.40(9)
S(4B)-C(8B)	1.8556(15)	C(3A)-C(2A)-S(2A)	108.37(9)
O(1B)-C(1B)	1.2361(17)	C(2A)-C(3A)-C(4A)	104.64(11)
O(2B)-C(7B)	1.2282(17)	C(2A)-C(3A)-H(3A)	110.8
O(3B)-C(4B)	1.4274(19)	C(4A)-C(3A)-H(3A)	110.8
O(3B)-H(13C)	0.85(3)	C(2A)-C(3A)-H(3B)	110.8
O(4B)-C(10B)	1.4217(18)	C(4A)-C(3A)-H(3B)	110.8
O(4B)-H(14C)	0.83(3)	H(3A)-C(3A)-H(3B)	108.9
C(1B)-N(12B)	1.3380(17)	O(3A)-C(4A)-C(5A)	106.99(12)
C(1B)-C(2B)	1.522(2)	O(3A)-C(4A)-C(3A)	111.42(12)

C(5A)-C(4A)-C(3A)	104.31(11)	C(10B)-O(4B)-H(14C)	109.5
O(3A)-C(4A)-H(4A)	111.3	O(1B)-C(1B)-N(12B)	124.91(13)
C(5A)-C(4A)-H(4A)	111.3	O(1B)-C(1B)-C(2B)	123.80(13)
C(3A)-C(4A)-H(4A)	111.3	N(12B)-C(1B)-C(2B)	111.24(12)
N(6A)-C(5A)-C(4A)	101.84(11)	N(6B)-C(2B)-C(1B)	110.52(12)
N(6A)-C(5A)-H(5B)	111.4	N(6B)-C(2B)-C(3B)	104.91(11)
C(4A)-C(5A)-H(5B)	111.4	C(1B)-C(2B)-C(3B)	115.87(11)
N(6A)-C(5A)-H(5A)	111.4	N(6B)-C(2B)-S(3B)	110.40(9)
C(4A)-C(5A)-H(5A)	111.4	C(1B)-C(2B)-S(3B)	105.75(9)
H(5B)-C(5A)-H(5A)	109.3	C(3B)-C(2B)-S(3B)	109.42(10)
C(7A)-N(6A)-C(2A)	120.37(12)	C(2B)-C(3B)-C(4B)	102.96(11)
C(7A)-N(6A)-C(5A)	126.91(12)	C(2B)-C(3B)-H(3C)	111.2
C(2A)-N(6A)-C(5A)	111.72(11)	C(4B)-C(3B)-H(3C)	111.2
O(2A)-C(7A)-N(6A)	125.34(14)	C(2B)-C(3B)-H(3D)	111.2
O(2A)-C(7A)-C(8A)	124.36(13)	C(4B)-C(3B)-H(3D)	111.2
N(6A)-C(7A)-C(8A)	110.28(11)	H(3C)-C(3B)-H(3D)	109.1
N(12A)-C(8A)-C(7A)	110.76(11)	O(3B)-C(4B)-C(5B)	110.68(13)
N(12A)-C(8A)-C(9A)	104.88(11)	O(3B)-C(4B)-C(3B)	106.88(12)
C(7A)-C(8A)-C(9A)	116.69(11)	C(5B)-C(4B)-C(3B)	103.26(11)
N(12A)-C(8A)-S(1A)	110.69(9)	O(3B)-C(4B)-H(4C)	111.9
C(7A)-C(8A)-S(1A)	104.92(9)	C(5B)-C(4B)-H(4C)	111.9
C(9A)-C(8A)-S(1A)	108.94(9)	C(3B)-C(4B)-H(4C)	111.9
C(8A)-C(9A)-C(10A)	104.50(11)	N(6B)-C(5B)-C(4B)	100.77(11)
C(8A)-C(9A)-H(9A)	110.9	N(6B)-C(5B)-H(5C)	111.6
C(10A)-C(9A)-H(9A)	110.9	C(4B)-C(5B)-H(5C)	111.6
C(8A)-C(9A)-H(9B)	110.9	N(6B)-C(5B)-H(5D)	111.6
C(10A)-C(9A)-H(9B)	110.9	C(4B)-C(5B)-H(5D)	111.6
H(9A)-C(9A)-H(9B)	108.9	H(5C)-C(5B)-H(5D)	109.4
O(4A)-C(10A)-C(11A)	108.39(12)	C(7B)-N(6B)-C(2B)	120.13(12)
O(4A)-C(10A)-C(9A)	110.46(13)	C(7B)-N(6B)-C(5B)	127.74(12)
C(11A)-C(10A)-C(9A)	103.41(11)	C(2B)-N(6B)-C(5B)	112.09(11)
O(4A)-C(10A)-H(10A)	111.4	O(2B)-C(7B)-N(6B)	125.39(13)
C(11A)-C(10A)-H(10A)	111.4	O(2B)-C(7B)-C(8B)	123.91(13)
C(9A)-C(10A)-H(10A)	111.4	N(6B)-C(7B)-C(8B)	110.68(12)
N(12A)-C(11A)-C(10A)	102.14(12)	N(12B)-C(8B)-C(7B)	109.53(11)
N(12A)-C(11A)-H(11A)	111.3	N(12B)-C(8B)-C(9B)	105.17(11)
C(10A)-C(11A)-H(11A)	111.3	C(7B)-C(8B)-C(9B)	116.57(12)
N(12A)-C(11A)-H(11B)	111.3	N(12B)-C(8B)-S(4B)	110.52(9)
C(10A)-C(11A)-H(11B)	111.3	C(7B)-C(8B)-S(4B)	106.36(9)
H(11A)-C(11A)-H(11B)	109.2	C(9B)-C(8B)-S(4B)	108.69(9)
C(1A)-N(12A)-C(8A)	120.14(12)	C(8B)-C(9B)-C(10B)	104.76(11)
C(1A)-N(12A)-C(11A)	127.39(12)	C(8B)-C(9B)-H(9C)	110.8
C(8A)-N(12A)-C(11A)	112.29(12)	C(10B)-C(9B)-H(9C)	110.8
C(2B)-S(3B)-S(4B)	97.61(5)	C(8B)-C(9B)-H(9D)	110.8
C(8B)-S(4B)-S(3B)	98.52(5)	C(10B)-C(9B)-H(9D)	110.8
C(4B)-O(3B)-H(13C)	109.5	H(9C)-C(9B)-H(9D)	108.9

O(4B)-C(10B)-C(11B)	108.11(11)	C(10B)-C(11B)-H(11D)	111.3
O(4B)-C(10B)-C(9B)	111.24(12)	H(11C)-C(11B)-H(11D)	109.2
C(11B)-C(10B)-C(9B)	105.15(11)	C(1B)-N(12B)-C(8B)	119.60(12)
O(4B)-C(10B)-H(10C)	110.7	C(1B)-N(12B)-C(11B)	127.39(12)
C(11B)-C(10B)-H(10C)	110.7	C(8B)-N(12B)-C(11B)	112.67(11)
C(9B)-C(10B)-H(10C)	110.7		
N(12B)-C(11B)-C(10B)	102.21(11)	Symmetry transformations used to generate equivalent atoms:	
N(12B)-C(11B)-H(11C)	111.3		
C(10B)-C(11B)-H(11C)	111.3		
N(12B)-C(11B)-H(11D)	111.3		

Table S15. Anisotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for bis(hydroxy)epidisulfide *trans*-5b. The anisotropic displacement factor exponent takes the form: $-2\pi^2 [h^2 a^{*2} U^{11} + \dots + 2 h k a^* b^* U^{12}]$

	U11	U22	U33	U23	U13	U12
S(1A)	10(1)	12(1)	16(1)	2(1)	3(1)	3(1)
S(2A)	12(1)	9(1)	16(1)	1(1)	2(1)	2(1)
O(1A)	16(1)	18(1)	10(1)	0(1)	3(1)	1(1)
O(2A)	15(1)	16(1)	11(1)	4(1)	1(1)	1(1)
O(3A)	16(1)	12(1)	15(1)	1(1)	4(1)	3(1)
O(4A)	15(1)	12(1)	30(1)	5(1)	0(1)	2(1)
C(1A)	10(1)	10(1)	10(1)	1(1)	0(1)	2(1)
C(2A)	9(1)	9(1)	9(1)	2(1)	1(1)	1(1)
C(3A)	10(1)	13(1)	13(1)	3(1)	1(1)	-1(1)
C(4A)	9(1)	10(1)	14(1)	0(1)	0(1)	-1(1)
C(5A)	10(1)	15(1)	11(1)	-1(1)	-1(1)	-1(1)
N(6A)	10(1)	14(1)	9(1)	3(1)	-1(1)	0(1)
C(7A)	10(1)	9(1)	11(1)	0(1)	1(1)	2(1)
C(8A)	9(1)	10(1)	10(1)	1(1)	0(1)	1(1)
C(9A)	10(1)	12(1)	17(1)	3(1)	1(1)	-2(1)
C(10A)	10(1)	12(1)	20(1)	1(1)	-2(1)	-1(1)
C(11A)	14(1)	13(1)	14(1)	-2(1)	-3(1)	-2(1)
N(12A)	12(1)	11(1)	10(1)	-1(1)	1(1)	-1(1)
S(3B)	9(1)	12(1)	16(1)	-2(1)	0(1)	2(1)
S(4B)	12(1)	14(1)	14(1)	-5(1)	1(1)	3(1)
O(1B)	14(1)	14(1)	9(1)	2(1)	1(1)	-2(1)
O(2B)	16(1)	17(1)	12(1)	4(1)	-1(1)	1(1)
O(3B)	16(1)	15(1)	21(1)	-4(1)	6(1)	2(1)
O(4B)	16(1)	21(1)	15(1)	-2(1)	-1(1)	8(1)
C(1B)	9(1)	9(1)	10(1)	0(1)	0(1)	0(1)
C(2B)	9(1)	8(1)	10(1)	0(1)	0(1)	1(1)

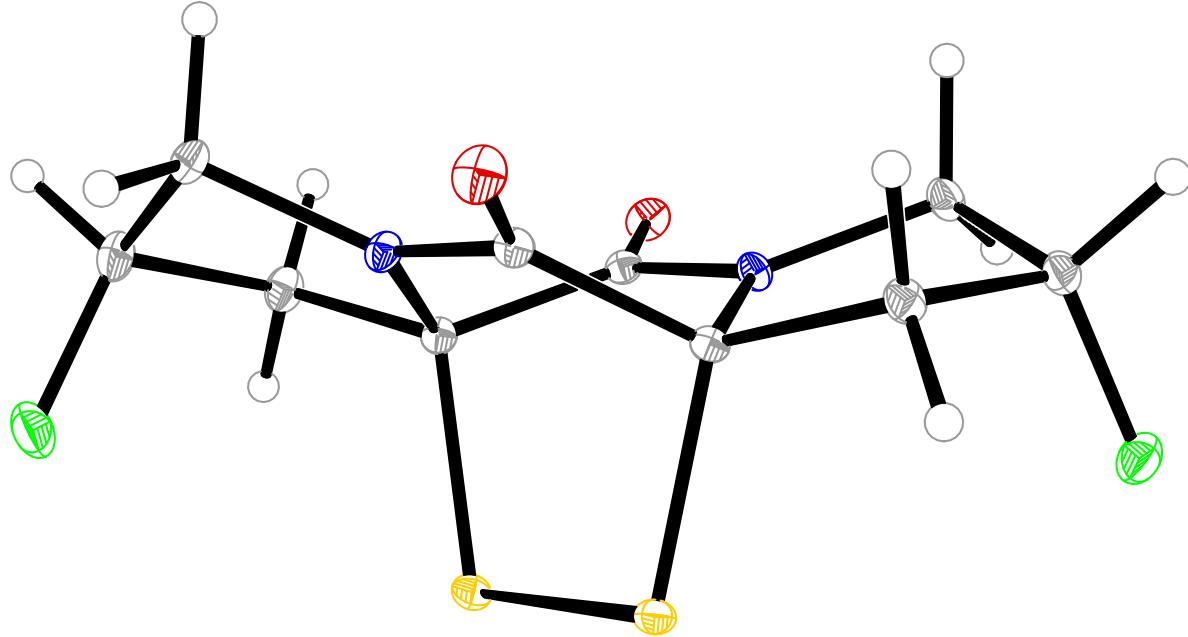
C(3B)	11(1)	12(1)	12(1)	-1(1)	-2(1)	-2(1)
C(4B)	12(1)	10(1)	15(1)	-3(1)	1(1)	-2(1)
C(5B)	16(1)	7(1)	15(1)	0(1)	1(1)	-1(1)
N(6B)	12(1)	7(1)	10(1)	0(1)	-1(1)	-1(1)
C(7B)	10(1)	11(1)	10(1)	0(1)	2(1)	0(1)
C(8B)	9(1)	11(1)	9(1)	-1(1)	1(1)	-1(1)
C(9B)	11(1)	15(1)	10(1)	-3(1)	0(1)	-1(1)
C(10B)	10(1)	12(1)	12(1)	-1(1)	-1(1)	0(1)
C(11B)	10(1)	12(1)	13(1)	1(1)	-1(1)	-3(1)
N(12B)	9(1)	11(1)	8(1)	0(1)	1(1)	-3(1)

Table S16. Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for bis(hydroxy)epidisulfide *trans*-5b.

	x	y	z	U(eq)
H(13A)	5200(30)	3019(6)	6715(12)	21
H(14A)	10970(11)	6580(20)	6221(11)	28
H(3A)	6960	1822	7110	15
H(3B)	7381	806	6657	15
H(4A)	5401	1511	6098	13
H(5B)	7341	1688	5390	14
H(5A)	6709	2948	5394	14
H(9A)	11950	4708	5578	16
H(9B)	13164	4105	6016	16
H(10A)	12765	5698	6595	17
H(11A)	12188	4274	7281	16
H(11B)	10678	5012	7330	16
H(13C)	4792(15)	-60(20)	7645(11)	26
H(14C)	8940(30)	3000(12)	9451(11)	26
H(3C)	2652	2056	7443	14
H(3D)	1285	1774	7905	14
H(4C)	2395	17	7792	15
H(5C)	2155	356	8857	15
H(5D)	3896	-14	8807	15
H(9C)	6321	3133	9993	14
H(9D)	5705	4384	9901	14
H(10C)	7951	4608	9402	14
H(11C)	6377	5013	8593	14
H(11D)	7317	4009	8283	14

Crystal Structure of Bis(fluoro)epidisulfide *cis*-5e

View 1:



View 2:

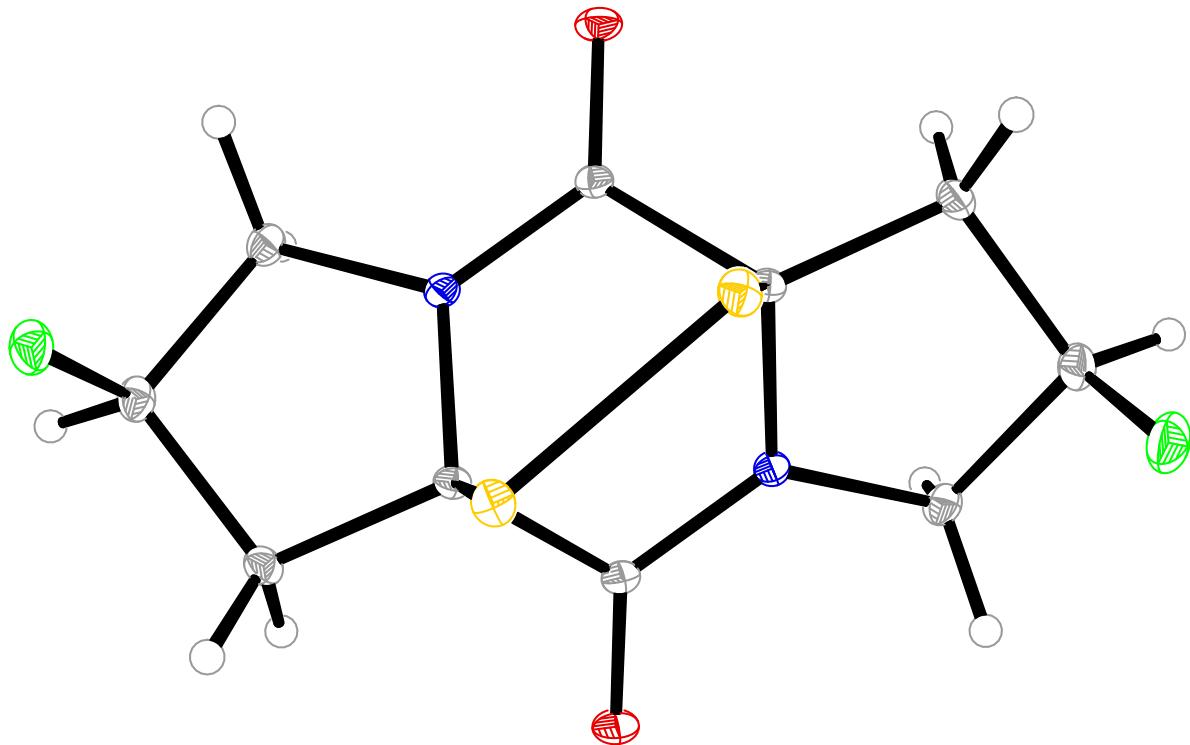


Table S17. Crystal data and structure refinement for bis(fluoro)epidisulfide *cis*-**5e**.

Identification code	CCDC 1965017
Empirical formula	C10 H10 F2 N2 O2 S2
Formula weight	292.32
Temperature	100(2) K
Wavelength	0.71073 Å
Crystal system	Orthorhombic
Space group	P2(1)2(1)2(1)
Unit cell dimensions	$a = 9.0873(2)$ Å $\alpha = 90^\circ$ $b = 10.5429(2)$ Å $\beta = 90^\circ$ $c = 11.8323(3)$ Å $\gamma = 90^\circ$
Volume	1133.61(4) Å ³
Z	4
Density (calculated)	1.713 Mg/m ³
Absorption coefficient	0.491 mm ⁻¹
F(000)	600
Crystal size	0.140 × 0.135 × 0.060 mm ³
Theta range for data collection	2.588 to 36.369°
Index ranges	$-15 \leq h \leq 14, -17 \leq k \leq 17, -19 \leq l \leq 19$
Reflections collected	60688
Independent reflections	5511 [R(int) = 0.0322]
Completeness to theta = 25.242°	100.0 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7471 and 0.7030
Refinement method	Full-matrix least-squares on F ²
Data / restraints / parameters	5511 / 0 / 173
Goodness-of-fit on F ²	1.075
Final R indices [I>2sigma(I)]	R1 = 0.0190, wR2 = 0.0526
R indices (all data)	R1 = 0.0199, wR2 = 0.0533
Absolute structure parameter	0.005(10)
Extinction coefficient	n/a
Largest diff. peak and hole	0.433 and -0.224 e·Å ⁻³

Table S18. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for bis(fluoro)epidisulfide *cis*-5e. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	<i>x</i>	<i>y</i>	<i>z</i>	U(eq)
S(1)	992(1)	9497(1)	3324(1)	14(1)
S(2)	518(1)	8116(1)	2116(1)	13(1)
F(1)	697(1)	8738(1)	6066(1)	25(1)
F(2)	2813(1)	7702(1)	-222(1)	21(1)
O(1)	4851(1)	9488(1)	3170(1)	16(1)
O(2)	1738(1)	5402(1)	3580(1)	18(1)
C(1)	3800(1)	8765(1)	3112(1)	12(1)
C(2)	2595(1)	8680(1)	4006(1)	12(1)
C(3)	2954(1)	9282(1)	5153(1)	17(1)
C(4)	2198(1)	8416(1)	6002(1)	19(1)
C(5)	2326(1)	7104(1)	5492(1)	16(1)
N(6)	2279(1)	7371(1)	4276(1)	12(1)
C(7)	2060(1)	6518(1)	3441(1)	12(1)
C(8)	2232(1)	7154(1)	2287(1)	11(1)
C(9)	2433(1)	6243(1)	1295(1)	14(1)
C(10)	3557(1)	6881(1)	529(1)	16(1)
C(11)	4518(1)	7672(1)	1309(1)	16(1)
N(12)	3536(1)	7942(1)	2261(1)	12(1)

Table S19. Bond lengths [\AA] and angles [$^\circ$] for bis(fluoro)epidisulfide *cis*-5e.

S(1)-C(2)	1.8750(10)	C(5)-N(6)	1.4677(12)
S(1)-S(2)	2.0848(3)	C(5)-H(5A)	0.9900
S(2)-C(8)	1.8698(9)	C(5)-H(5B)	0.9900
F(1)-C(4)	1.4078(15)	N(6)-C(7)	1.3506(12)
F(2)-C(10)	1.4117(12)	C(7)-C(8)	1.5295(13)
O(1)-C(1)	1.2234(11)	C(8)-N(12)	1.4475(12)
O(2)-C(7)	1.2232(11)	C(8)-C(9)	1.5278(13)
C(1)-N(12)	1.3499(12)	C(9)-C(10)	1.5226(14)
C(1)-C(2)	1.5256(13)	C(9)-H(9A)	0.9900
C(2)-N(6)	1.4448(12)	C(9)-H(9B)	0.9900
C(2)-C(3)	1.5329(13)	C(10)-C(11)	1.5199(15)
C(3)-C(4)	1.5215(15)	C(10)-H(10)	1.0000
C(3)-H(3A)	0.9900	C(11)-N(12)	1.4650(13)
C(3)-H(3B)	0.9900	C(11)-H(11A)	0.9900
C(4)-C(5)	1.5137(15)	C(11)-H(11B)	0.9900
C(4)-H(4)	1.0000		

C(2)-S(1)-S(2)	97.74(3)	O(2)-C(7)-C(8)	124.51(9)
C(8)-S(2)-S(1)	97.62(3)	N(6)-C(7)-C(8)	110.19(7)
O(1)-C(1)-N(12)	125.51(9)	N(12)-C(8)-C(9)	104.32(7)
O(1)-C(1)-C(2)	123.90(8)	N(12)-C(8)-C(7)	110.77(7)
N(12)-C(1)-C(2)	110.59(8)	C(9)-C(8)-C(7)	114.95(7)
N(6)-C(2)-C(1)	110.60(7)	N(12)-C(8)-S(2)	111.62(6)
N(6)-C(2)-C(3)	104.02(7)	C(9)-C(8)-S(2)	110.94(6)
C(1)-C(2)-C(3)	115.91(8)	C(7)-C(8)-S(2)	104.42(6)
N(6)-C(2)-S(1)	112.28(7)	C(10)-C(9)-C(8)	105.02(8)
C(1)-C(2)-S(1)	103.43(6)	C(10)-C(9)-H(9A)	110.7
C(3)-C(2)-S(1)	110.86(7)	C(8)-C(9)-H(9A)	110.7
C(4)-C(3)-C(2)	103.89(8)	C(10)-C(9)-H(9B)	110.7
C(4)-C(3)-H(3A)	111.0	C(8)-C(9)-H(9B)	110.7
C(2)-C(3)-H(3A)	111.0	H(9A)-C(9)-H(9B)	108.8
C(4)-C(3)-H(3B)	111.0	F(2)-C(10)-C(11)	108.72(8)
C(2)-C(3)-H(3B)	111.0	F(2)-C(10)-C(9)	108.95(8)
H(3A)-C(3)-H(3B)	109.0	C(11)-C(10)-C(9)	105.45(8)
F(1)-C(4)-C(5)	108.44(9)	F(2)-C(10)-H(10)	111.2
F(1)-C(4)-C(3)	109.16(9)	C(11)-C(10)-H(10)	111.2
C(5)-C(4)-C(3)	104.51(8)	C(9)-C(10)-H(10)	111.2
F(1)-C(4)-H(4)	111.5	N(12)-C(11)-C(10)	102.93(8)
C(5)-C(4)-H(4)	111.5	N(12)-C(11)-H(11A)	111.2
C(3)-C(4)-H(4)	111.5	C(10)-C(11)-H(11A)	111.2
N(6)-C(5)-C(4)	102.29(8)	N(12)-C(11)-H(11B)	111.2
N(6)-C(5)-H(5A)	111.3	C(10)-C(11)-H(11B)	111.2
C(4)-C(5)-H(5A)	111.3	H(11A)-C(11)-H(11B)	109.1
N(6)-C(5)-H(5B)	111.3	C(1)-N(12)-C(8)	119.90(7)
C(4)-C(5)-H(5B)	111.3	C(1)-N(12)-C(11)	126.17(8)
H(5A)-C(5)-H(5B)	109.2	C(8)-N(12)-C(11)	113.76(8)
C(7)-N(6)-C(2)	120.28(8)		
C(7)-N(6)-C(5)	126.38(8)		
C(2)-N(6)-C(5)	113.22(8)		
O(2)-C(7)-N(6)	125.28(9)		

Symmetry transformations used to generate equivalent atoms:

Table S20. Anisotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for bis(fluoro)epidisulfide *cis*-**5b**. The anisotropic displacement factor exponent takes the form: $-2\pi^2 [h^2 a^{*2} U^{11} + \dots + 2 h k a^* b^* U^{12}]$

	U11	U22	U33	U23	U13	U12
S(1)	15(1)	11(1)	15(1)	0(1)	1(1)	4(1)
S(2)	11(1)	15(1)	14(1)	-1(1)	-2(1)	2(1)
F(1)	25(1)	28(1)	23(1)	-2(1)	9(1)	4(1)
F(2)	29(1)	19(1)	15(1)	2(1)	-2(1)	3(1)

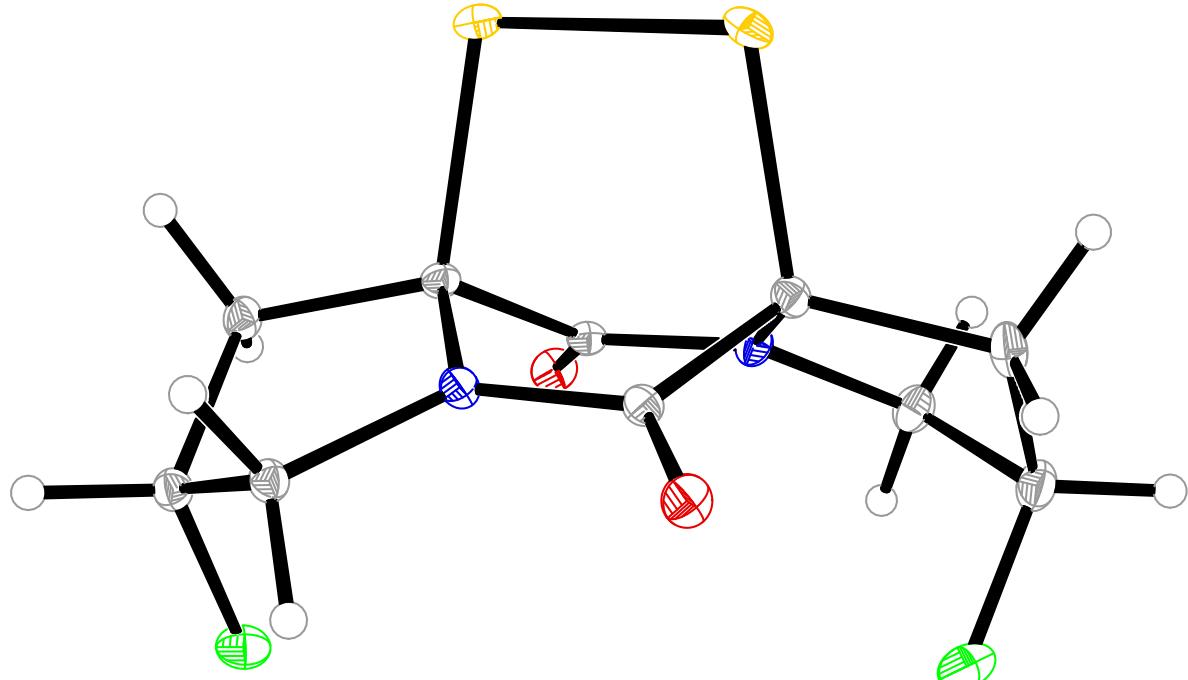
O(1)	15(1)	16(1)	19(1)	2(1)	-2(1)	-6(1)
O(2)	24(1)	10(1)	20(1)	2(1)	1(1)	-5(1)
C(1)	12(1)	11(1)	12(1)	1(1)	-1(1)	-1(1)
C(2)	13(1)	10(1)	12(1)	0(1)	0(1)	0(1)
C(3)	23(1)	14(1)	13(1)	-3(1)	-1(1)	-2(1)
C(4)	24(1)	20(1)	12(1)	-1(1)	1(1)	-1(1)
C(5)	18(1)	16(1)	12(1)	3(1)	0(1)	0(1)
N(6)	16(1)	10(1)	11(1)	1(1)	0(1)	-1(1)
C(7)	12(1)	11(1)	14(1)	1(1)	1(1)	-1(1)
C(8)	10(1)	9(1)	13(1)	0(1)	0(1)	0(1)
C(9)	16(1)	12(1)	15(1)	-3(1)	0(1)	0(1)
C(10)	18(1)	15(1)	14(1)	-1(1)	2(1)	3(1)
C(11)	13(1)	18(1)	15(1)	-1(1)	4(1)	0(1)
N(12)	10(1)	12(1)	13(1)	-1(1)	2(1)	-1(1)

Table S21. Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for bis(fluoro)epidisulfide *cis*-5b.

	<i>x</i>	<i>y</i>	<i>z</i>	U(eq)
H(3A)	4030	9305	5283	22(4)
H(3B)	2560	10156	5200	35(5)
H(4)	2681	8460	6760	28(5)
H(5A)	3264	6692	5709	28(5)
H(5B)	1495	6556	5725	30(5)
H(9A)	2801	5411	1561	27(5)
H(9B)	1490	6113	892	26(5)
H(10)	4154	6240	108	27(5)
H(11A)	5394	7189	1558	27(5)
H(11B)	4842	8464	934	23(5)

Crystal Structure of Bis(fluoro)epidisulfide *trans*-5e

View 1:



View 2:

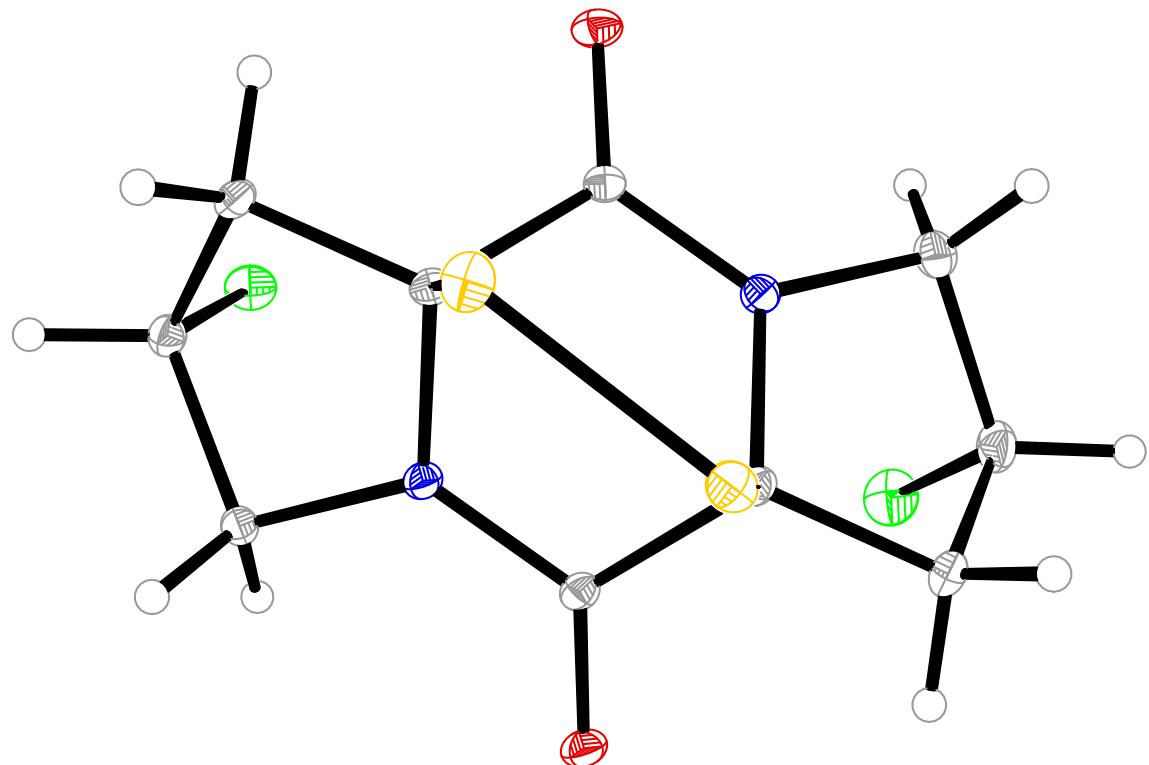


Table S22. Crystal data and structure refinement for bis(fluoro)epidisulfide *trans*-**5e**.

Identification code	CCDC 1965018
Empirical formula	C10 H10 F2 N2 O2 S2
Formula weight	292.32
Temperature	100(2) K
Wavelength	0.71073 Å
Crystal system	Orthorhombic
Space group	P2(1)2(1)2(1)
Unit cell dimensions	$a = 8.5479(4)$ Å $\alpha = 90^\circ$ $b = 11.7072(6)$ Å $\beta = 90^\circ$ $c = 23.5380(13)$ Å $\gamma = 90^\circ$
Volume	2355.5(2) Å ³
Z	8
Density (calculated)	1.649 g/m ³
Absorption coefficient	0.473 mm ⁻¹
F(000)	1200
Crystal size	0.350 × 0.140 × 0.025 mm ³
Theta range for data collection	1.730 to 33.176°
Index ranges	$-13 \leq h \leq 13, -18 \leq k \leq 18, -36 \leq l \leq 36$
Reflections collected	124821
Independent reflections	9008 [R(int) = 0.0622]
Completeness to theta = 25.242°	100.0%
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7465 and 0.6380
Refinement method	Full-matrix least-squares on F ²
Data / restraints / parameters	9008 / 0 / 325
Goodness-of-fit on F ²	1.044
Final R indices [I>2sigma(I)]	R1 = 0.0252, wR2 = 0.0595
R indices (all data)	R1 = 0.0282, wR2 = 0.0614
Absolute structure parameter	-0.008(14)
Extinction coefficient	n/a
Largest diff. peak and hole	0.352 and -0.232 e·Å ⁻³

Table S23. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for bis(fluoro)epidisulfide *trans*-**5e**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
S(1A)	7273(1)	8575(1)	3689(1)	19(1)
S(2A)	5472(1)	9772(1)	3602(1)	19(1)
F(1A)	5307(1)	4750(1)	3349(1)	27(1)
F(2A)	659(1)	7857(1)	4054(1)	25(1)
O(1A)	5262(1)	6569(1)	4582(1)	18(1)
O(2A)	2938(1)	8089(1)	2730(1)	19(1)
C(1A)	5074(2)	7232(1)	4187(1)	13(1)
C(2A)	6066(2)	7249(1)	3647(1)	13(1)
C(3A)	7142(2)	6217(1)	3559(1)	20(1)
C(4A)	6356(2)	5518(1)	3093(1)	21(1)
C(5A)	5424(2)	6365(1)	2740(1)	19(1)
N(6A)	5052(2)	7257(1)	3155(1)	14(1)
C(7A)	3859(2)	8006(1)	3127(1)	13(1)
C(8A)	3798(2)	8754(1)	3661(1)	13(1)
C(9A)	2260(2)	9404(1)	3749(1)	18(1)
C(10A)	1498(2)	8809(1)	4253(1)	17(1)
C(11A)	2843(2)	8371(1)	4608(1)	15(1)
N(12A)	3972(2)	8057(1)	4165(1)	13(1)
S(1B)	1442(1)	5567(1)	3532(1)	17(1)
S(2B)	1187(1)	4410(1)	2860(1)	19(1)
F(1B)	1864(1)	3339(1)	5213(1)	27(1)
F(2B)	-749(1)	878(1)	3638(1)	21(1)
O(1B)	-1298(1)	4326(1)	4483(1)	18(1)
O(2B)	3109(1)	2042(1)	3496(1)	18(1)
C(1B)	-307(2)	4061(1)	4134(1)	13(1)
C(2B)	1377(2)	4514(1)	4130(1)	14(1)
C(3B)	1907(2)	5067(1)	4688(1)	19(1)
C(4B)	2887(2)	4136(2)	4965(1)	21(1)
C(5B)	3708(2)	3548(2)	4473(1)	20(1)
N(6B)	2478(1)	3594(1)	4037(1)	14(1)
C(7B)	2245(2)	2840(1)	3614(1)	13(1)
C(8B)	726(2)	3118(1)	3293(1)	13(1)
C(9B)	103(2)	2155(1)	2912(1)	16(1)
C(10B)	-1298(2)	1686(1)	3238(1)	15(1)
C(11B)	-1961(2)	2693(1)	3562(1)	14(1)
N(12B)	-533(1)	3342(1)	3691(1)	13(1)

Table S24. Bond lengths [\AA] and angles [$^\circ$] for bis(fluoro)epidisulfide *trans*-**5e**.

S(1A)-C(2A)	1.8660(15)	C(3B)-H(3C)	0.9900
S(1A)-S(2A)	2.0927(6)	C(3B)-H(3D)	0.9900
S(2A)-C(8A)	1.8673(15)	C(4B)-C(5B)	1.519(2)
F(1A)-C(4A)	1.405(2)	C(4B)-H(4B)	1.0000
F(2A)-C(10A)	1.4063(19)	C(5B)-N(6B)	1.4690(19)
O(1A)-C(1A)	1.2210(17)	C(5B)-H(5C)	0.9900
O(2A)-C(7A)	1.2249(17)	C(5B)-H(5D)	0.9900
C(1A)-N(12A)	1.3508(19)	N(6B)-C(7B)	1.3468(18)
C(1A)-C(2A)	1.528(2)	C(7B)-C(8B)	1.536(2)
C(2A)-N(6A)	1.4477(18)	C(8B)-N(12B)	1.4500(18)
C(2A)-C(3A)	1.532(2)	C(8B)-C(9B)	1.536(2)
C(3A)-C(4A)	1.525(2)	C(9B)-C(10B)	1.525(2)
C(3A)-H(3A)	0.9900	C(9B)-H(9C)	0.9900
C(3A)-H(3B)	0.9900	C(9B)-H(9D)	0.9900
C(4A)-C(5A)	1.518(2)	C(10B)-C(11B)	1.514(2)
C(4A)-H(4A)	1.0000	C(10B)-H(10B)	1.0000
C(5A)-N(6A)	1.4641(19)	C(11B)-N(12B)	1.4691(18)
C(5A)-H(5A)	0.9900	C(11B)-H(11C)	0.9900
C(5A)-H(5B)	0.9900	C(11B)-H(11D)	0.9900
N(6A)-C(7A)	1.3462(19)		
C(7A)-C(8A)	1.533(2)	C(2A)-S(1A)-S(2A)	98.37(5)
C(8A)-N(12A)	1.4469(18)	C(8A)-S(2A)-S(1A)	97.37(5)
C(8A)-C(9A)	1.533(2)	O(1A)-C(1A)-N(12A)	125.16(14)
C(9A)-C(10A)	1.523(2)	O(1A)-C(1A)-C(2A)	124.60(13)
C(9A)-H(9A)	0.9900	N(12A)-C(1A)-C(2A)	110.24(12)
C(9A)-H(9B)	0.9900	N(6A)-C(2A)-C(1A)	109.49(11)
C(10A)-C(11A)	1.512(2)	N(6A)-C(2A)-C(3A)	104.83(12)
C(10A)-H(10A)	1.0000	C(1A)-C(2A)-C(3A)	115.79(12)
C(11A)-N(12A)	1.4675(19)	N(6A)-C(2A)-S(1A)	111.57(10)
C(11A)-H(11A)	0.9900	C(1A)-C(2A)-S(1A)	105.91(10)
C(11A)-H(11B)	0.9900	C(3A)-C(2A)-S(1A)	109.35(10)
S(1B)-C(2B)	1.8714(15)	C(4A)-C(3A)-C(2A)	104.86(12)
S(1B)-S(2B)	2.0938(6)	C(4A)-C(3A)-H(3A)	110.8
S(2B)-C(8B)	1.8659(15)	C(2A)-C(3A)-H(3A)	110.8
F(1B)-C(4B)	1.407(2)	C(4A)-C(3A)-H(3B)	110.8
F(2B)-C(10B)	1.4139(18)	C(2A)-C(3A)-H(3B)	110.8
O(1B)-C(1B)	1.2204(17)	H(3A)-C(3A)-H(3B)	108.9
O(2B)-C(7B)	1.2224(17)	F(1A)-C(4A)-C(5A)	108.49(13)
C(1B)-N(12B)	1.3540(18)	F(1A)-C(4A)-C(3A)	108.39(13)
C(1B)-C(2B)	1.533(2)	C(5A)-C(4A)-C(3A)	105.88(13)
C(2B)-N(6B)	1.4472(19)	F(1A)-C(4A)-H(4A)	111.3
C(2B)-C(3B)	1.534(2)	C(5A)-C(4A)-H(4A)	111.3
C(3B)-C(4B)	1.521(2)	C(3A)-C(4A)-H(4A)	111.3

N(6A)-C(5A)-C(4A)	102.50(12)	C(1B)-C(2B)-C(3B)	114.74(12)
N(6A)-C(5A)-H(5A)	111.3	N(6B)-C(2B)-S(1B)	110.94(10)
C(4A)-C(5A)-H(5A)	111.3	C(1B)-C(2B)-S(1B)	105.07(10)
N(6A)-C(5A)-H(5B)	111.3	C(3B)-C(2B)-S(1B)	110.93(10)
C(4A)-C(5A)-H(5B)	111.3	C(4B)-C(3B)-C(2B)	103.06(13)
H(5A)-C(5A)-H(5B)	109.2	C(4B)-C(3B)-H(3C)	111.2
C(7A)-N(6A)-C(2A)	119.78(12)	C(2B)-C(3B)-H(3C)	111.2
C(7A)-N(6A)-C(5A)	126.67(13)	C(4B)-C(3B)-H(3D)	111.2
C(2A)-N(6A)-C(5A)	113.47(12)	C(2B)-C(3B)-H(3D)	111.2
O(2A)-C(7A)-N(6A)	125.13(14)	H(3C)-C(3B)-H(3D)	109.1
O(2A)-C(7A)-C(8A)	123.91(13)	F(1B)-C(4B)-C(5B)	107.70(14)
N(6A)-C(7A)-C(8A)	110.96(12)	F(1B)-C(4B)-C(3B)	108.14(13)
N(12A)-C(8A)-C(9A)	104.91(11)	C(5B)-C(4B)-C(3B)	104.69(13)
N(12A)-C(8A)-C(7A)	110.31(11)	F(1B)-C(4B)-H(4B)	112.0
C(9A)-C(8A)-C(7A)	115.02(12)	C(5B)-C(4B)-H(4B)	112.0
N(12A)-C(8A)-S(2A)	110.05(10)	C(3B)-C(4B)-H(4B)	112.0
C(9A)-C(8A)-S(2A)	110.47(10)	N(6B)-C(5B)-C(4B)	100.62(12)
C(7A)-C(8A)-S(2A)	106.10(9)	N(6B)-C(5B)-H(5C)	111.6
C(10A)-C(9A)-C(8A)	104.17(12)	C(4B)-C(5B)-H(5C)	111.6
C(10A)-C(9A)-H(9A)	110.9	N(6B)-C(5B)-H(5D)	111.6
C(8A)-C(9A)-H(9A)	110.9	C(4B)-C(5B)-H(5D)	111.6
C(10A)-C(9A)-H(9B)	110.9	H(5C)-C(5B)-H(5D)	109.4
C(8A)-C(9A)-H(9B)	110.9	C(7B)-N(6B)-C(2B)	120.19(12)
H(9A)-C(9A)-H(9B)	108.9	C(7B)-N(6B)-C(5B)	126.79(13)
F(2A)-C(10A)-C(11A)	107.67(12)	C(2B)-N(6B)-C(5B)	112.80(12)
F(2A)-C(10A)-C(9A)	108.67(13)	O(2B)-C(7B)-N(6B)	125.39(14)
C(11A)-C(10A)-C(9A)	105.11(12)	O(2B)-C(7B)-C(8B)	124.13(13)
F(2A)-C(10A)-H(10A)	111.7	N(6B)-C(7B)-C(8B)	110.47(12)
C(11A)-C(10A)-H(10A)	111.7	N(12B)-C(8B)-C(7B)	110.49(11)
C(9A)-C(10A)-H(10A)	111.7	N(12B)-C(8B)-C(9B)	104.60(11)
N(12A)-C(11A)-C(10A)	101.05(11)	C(7B)-C(8B)-C(9B)	115.13(12)
N(12A)-C(11A)-H(11A)	111.6	N(12B)-C(8B)-S(2B)	111.22(10)
C(10A)-C(11A)-H(11A)	111.6	C(7B)-C(8B)-S(2B)	105.13(9)
N(12A)-C(11A)-H(11B)	111.6	C(9B)-C(8B)-S(2B)	110.41(10)
C(10A)-C(11A)-H(11B)	111.6	C(10B)-C(9B)-C(8B)	104.02(11)
H(11A)-C(11A)-H(11B)	109.4	C(10B)-C(9B)-H(9C)	111.0
C(1A)-N(12A)-C(8A)	120.40(12)	C(8B)-C(9B)-H(9C)	111.0
C(1A)-N(12A)-C(11A)	127.60(12)	C(10B)-C(9B)-H(9D)	111.0
C(8A)-N(12A)-C(11A)	112.00(11)	C(8B)-C(9B)-H(9D)	111.0
C(2B)-S(1B)-S(2B)	97.97(5)	H(9C)-C(9B)-H(9D)	109.0
C(8B)-S(2B)-S(1B)	97.68(5)	F(2B)-C(10B)-C(11B)	108.09(12)
O(1B)-C(1B)-N(12B)	125.26(14)	F(2B)-C(10B)-C(9B)	108.33(12)
O(1B)-C(1B)-C(2B)	124.57(13)	C(11B)-C(10B)-C(9B)	105.51(12)
N(12B)-C(1B)-C(2B)	110.16(12)	F(2B)-C(10B)-H(10B)	111.5
N(6B)-C(2B)-C(1B)	110.75(11)	C(11B)-C(10B)-H(10B)	111.5
N(6B)-C(2B)-C(3B)	104.55(12)	C(9B)-C(10B)-H(10B)	111.5

N(12B)-C(11B)-C(10B)	101.26(11)	C(1B)-N(12B)-C(8B)	120.21(12)
N(12B)-C(11B)-H(11C)	111.5	C(1B)-N(12B)-C(11B)	126.76(12)
C(10B)-C(11B)-H(11C)	111.5	C(8B)-N(12B)-C(11B)	113.00(11)
N(12B)-C(11B)-H(11D)	111.5		
C(10B)-C(11B)-H(11D)	111.5	Symmetry transformations used to generate equivalent atoms:	
H(11C)-C(11B)-H(11D)	109.3		

Table S25. Anisotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for bis(fluoro)epidisulfide *trans*-**5e**. The anisotropic displacement factor exponent takes the form: $-2p^2 [h^2 a^{*2}U^{11} + \dots + 2 h k a^* b^* U^{12}]$.

	U ¹¹	U ²²	U ³³	U ²³	U ¹³	U ¹²
S(1A)	12(1)	23(1)	22(1)	4(1)	-1(1)	-4(1)
S(2A)	20(1)	14(1)	22(1)	3(1)	0(1)	-3(1)
F(1A)	26(1)	20(1)	34(1)	6(1)	6(1)	2(1)
F(2A)	18(1)	21(1)	35(1)	-2(1)	-5(1)	-1(1)
O(1A)	17(1)	21(1)	15(1)	6(1)	-3(1)	2(1)
O(2A)	18(1)	24(1)	14(1)	2(1)	-5(1)	4(1)
C(1A)	12(1)	15(1)	12(1)	0(1)	-2(1)	0(1)
C(2A)	10(1)	16(1)	13(1)	3(1)	-1(1)	2(1)
C(3A)	14(1)	22(1)	22(1)	4(1)	2(1)	8(1)
C(4A)	20(1)	19(1)	22(1)	2(1)	8(1)	6(1)
C(5A)	24(1)	20(1)	14(1)	-2(1)	3(1)	5(1)
N(6A)	14(1)	16(1)	11(1)	0(1)	-1(1)	3(1)
C(7A)	13(1)	15(1)	12(1)	2(1)	0(1)	1(1)
C(8A)	14(1)	13(1)	12(1)	2(1)	0(1)	1(1)
C(9A)	19(1)	16(1)	19(1)	2(1)	3(1)	7(1)
C(10A)	16(1)	15(1)	20(1)	-2(1)	3(1)	2(1)
C(11A)	18(1)	15(1)	12(1)	-2(1)	4(1)	1(1)
N(12A)	14(1)	15(1)	10(1)	2(1)	1(1)	2(1)
S(1B)	17(1)	11(1)	23(1)	3(1)	0(1)	-1(1)
S(2B)	24(1)	18(1)	15(1)	5(1)	-1(1)	-2(1)
F(1B)	33(1)	32(1)	17(1)	5(1)	1(1)	-2(1)
F(2B)	25(1)	14(1)	24(1)	4(1)	1(1)	3(1)
O(1B)	18(1)	18(1)	17(1)	-4(1)	4(1)	1(1)
O(2B)	19(1)	16(1)	19(1)	-1(1)	2(1)	6(1)
C(1B)	15(1)	10(1)	14(1)	-1(1)	0(1)	1(1)
C(2B)	15(1)	11(1)	15(1)	-1(1)	0(1)	1(1)
C(3B)	20(1)	19(1)	20(1)	-7(1)	-1(1)	-3(1)
C(4B)	21(1)	27(1)	16(1)	-2(1)	-4(1)	-3(1)
C(5B)	17(1)	24(1)	18(1)	0(1)	-5(1)	2(1)
N(6B)	14(1)	14(1)	14(1)	-1(1)	-2(1)	3(1)

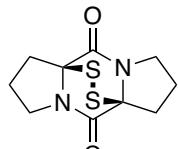
C(7B)	14(1)	13(1)	12(1)	1(1)	2(1)	1(1)
C(8B)	14(1)	12(1)	12(1)	1(1)	2(1)	1(1)
C(9B)	17(1)	17(1)	13(1)	-4(1)	1(1)	0(1)
C(10B)	16(1)	14(1)	15(1)	-1(1)	-1(1)	-1(1)
C(11B)	13(1)	14(1)	15(1)	0(1)	-1(1)	0(1)
N(12B)	13(1)	14(1)	14(1)	-2(1)	2(1)	-1(1)

Table S26. Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for bis(fluoro)epidisulfide *trans*-5e.

	x	y	z	U(eq)
H(3A)	8199	6465	3439	23
H(3B)	7234	5766	3913	23
H(4A)	7146	5107	2855	25
H(5A)	6057	6671	2423	23
H(5B)	4462	6011	2586	23
H(9A)	2461	10219	3834	22
H(9B)	1589	9352	3407	22
H(10A)	814	9342	4474	20
H(11A)	3264	8972	4862	18
H(11B)	2532	7701	4839	18
H(3C)	2539	5761	4616	23
H(3D)	999	5272	4929	23
H(4B)	3646	4454	5246	25
H(5C)	4656	3971	4353	23
H(5D)	3995	2752	4568	23
H(9C)	-221	2455	2537	19
H(9D)	906	1556	2856	19
H(10B)	-2093	1345	2977	18
H(11C)	-2695	3142	3326	17
H(11D)	-2500	2446	3914	17

Atomic Coordinates of Optimized ETP Structures

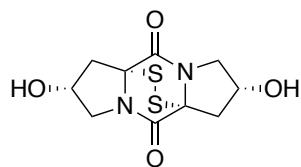
Table S27. C4-H (5a)



5a

N	-1.12818200	0.75345600	-0.57484900
C	-1.16987200	-0.58092300	-0.04626300
C	0.04273700	1.43705300	-0.61334700
C	1.16979500	0.58126100	-0.04601200
N	1.12776200	-0.75197700	-0.57744500
C	-0.04301800	-1.43585200	-0.61530000
O	-0.17977600	-2.56747300	-1.02041500
O	0.17939900	2.56887500	-1.01789400
S	-0.85587400	-0.61367900	1.81157400
S	0.85669000	0.61066100	1.81203800
C	-2.44552900	1.29831700	-0.89894800
H	-2.55806200	2.28936800	-0.46074000
C	2.44524200	-1.29701300	-0.90101400
H	2.55690600	-2.28865200	-0.46394000
C	2.58468500	1.05402000	-0.33797300
H	2.92874400	1.80556400	0.37050600
C	-2.58469500	-1.05348700	-0.33907500
H	-2.92876100	-1.80583400	0.36854600
H	2.58004700	1.50953900	-1.33086200
H	2.54915500	-1.38514500	-1.98475300
H	-2.57974200	-1.50799000	-1.33241200
H	-2.54860500	1.38781100	-1.98266400
C	-3.39609900	0.24898700	-0.30863100
C	3.39579400	-0.24866400	-0.30884700
H	4.32484700	-0.17314000	-0.87022300
H	3.63664600	-0.51074700	0.72191600
H	-4.32491400	0.17400500	-0.87049700
H	-3.63760200	0.50974200	0.72233800

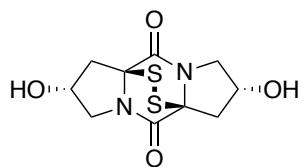
Table S28. *cis*-C4-OH (*cis*-5b)



cis-5b

N	-1.17594000	0.67125800	-0.63667400
C	-1.12969000	-0.66197200	-0.09626300
C	-0.05560400	1.43314500	-0.67553500
C	1.12968700	0.66213700	-0.09582800
N	1.17584900	-0.67064700	-0.63737400
C	0.05545300	-1.43239000	-0.67700900
O	-0.00344000	-2.56211000	-1.10729500
O	0.00347800	2.56282500	-1.10590000
S	-0.82427100	-0.65903600	1.75073600
S	0.82464600	0.65754600	1.75119000
C	-2.50582100	1.09383400	-1.05325500
H	-2.74834500	2.06940800	-0.62823600
C	2.50573000	-1.09298000	-1.05420000
H	2.74816600	-2.06892300	-0.62996800
C	2.49604700	1.24438800	-0.43333200
H	2.85368100	1.96111700	0.30330700
C	-2.49607100	-1.24399900	-0.43405000
H	-2.85364600	-1.96125600	0.30210500
H	2.41279100	1.75194800	-1.39608900
H	2.55210400	-1.16910900	-2.14345100
H	-2.41282900	-1.75088700	-1.39716100
H	-2.55212900	1.17081900	-2.14244900
C	-3.41455000	-0.02441100	-0.52321800
C	3.41447300	0.02481000	-0.52326700
H	4.25085100	0.20600700	-1.20363400
H	-4.25084000	-0.20518500	-1.20380200
O	3.88387200	-0.23558500	0.78372300
H	4.36974100	-1.06519600	0.79340800
O	-3.88412000	0.23505300	0.78389900
H	-4.37115700	1.06398200	0.79382200

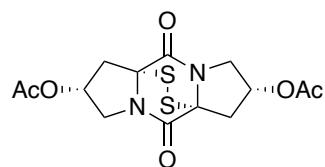
Table S29. *trans*-C4-OH (*trans*-5b)



trans-5b

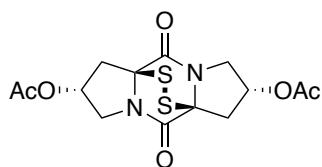
	1.01869800	-0.16821300	0.87891700
N	1.23882200	0.38052900	-0.43559700
C	-0.22002000	-0.18181900	1.43408400
C	-1.23881700	0.38060500	0.43554800
N	-1.01874100	-0.16808800	-0.87898900
C	0.21998400	-0.18180000	-1.43414300
O	0.48269500	-0.55504100	-2.55263800
O	-0.48275200	-0.55505400	2.55257900
S	0.97185500	2.23443400	-0.42939700
S	-0.97171000	2.23448900	0.42945700
C	2.25326400	-0.59455800	1.51407400
H	2.05247400	-1.42418100	2.19320900
C	-2.25328800	-0.59455500	-1.51410500
H	-2.05246000	-1.42428700	-2.19308800
H	-2.70763200	0.22721900	-2.07886400
C	-2.70548000	0.06539900	0.75606900
H	-3.32286800	0.95961000	0.65817900
H	-2.79571800	-0.33487600	1.76526100
C	2.70547300	0.06525200	-0.75612100
H	3.32290100	0.95945000	-0.65836200
H	2.70758600	0.22730500	2.07872300
C	3.10354300	-0.97469300	0.29846800
H	4.17427600	-0.94060900	0.52005600
H	2.79566000	-0.33513700	-1.76527400
C	-3.10355200	-0.97461500	-0.29844400
H	-4.17428500	-0.94056500	-0.52002800
O	2.72990400	-2.23540300	-0.22120500
O	-2.72982900	-2.23528000	0.22127200
H	-2.84643700	-2.90749900	-0.45535900
H	2.84476300	-2.90731500	0.45602800

Table S30. *cis*-C4-OAc (*cis*-5d)



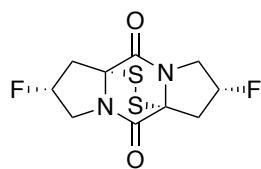
<i>cis</i> -5d			
N	-1.21491600	-0.59883400	-1.16630900
C	-0.07972300	-1.30291900	-0.62736000
C	-1.21491600	0.75815600	-1.23695400
C	0.07972300	1.30291900	-0.62736000
N	1.21491600	0.59883400	-1.16630900
C	1.21491600	-0.75815600	-1.23695400
O	2.09044700	-1.44083000	-1.71408500
O	-2.09044700	1.44083000	-1.71408500
S	0.15750600	-1.04001000	1.22415200
S	-0.15750600	1.04001000	1.22415200
C	-2.29399900	-1.47807700	-1.60464300
H	-3.26077300	-1.07578700	-1.32139200
C	2.29399900	1.47807700	-1.60464300
H	3.26077300	1.07578700	-1.32139200
C	0.38670400	2.76653400	-0.91636500
H	-0.03308400	3.45230000	-0.18219100
C	-0.38670400	-2.76653400	-0.91636500
H	0.03308400	-3.45230000	-0.18219100
H	-0.02979500	3.01188900	-1.89682800
H	2.25164800	1.60226400	-2.69163300
H	0.02979500	-3.01188900	-1.89682800
H	-2.25164800	-1.60226400	-2.69163300
C	-1.92078200	-2.81360700	-0.95240700
C	1.92078200	2.81360700	-0.95240700
H	2.28212700	3.65104800	-1.54709000
H	-2.28212700	-3.65104800	-1.54709000
O	2.41271100	3.08091700	0.37002700
O	-2.41271100	-3.08091700	0.37002700
C	-2.93623800	-2.16292500	1.22101700
C	2.93623800	2.16292500	1.22101700
O	-3.20719000	-1.03242000	0.93817100
O	3.20719000	1.03242000	0.93817100
C	3.12051300	2.78557400	2.57592300
H	3.72508500	2.12639100	3.19328700
H	3.58046000	3.76922400	2.48753500
H	2.13409000	2.91117700	3.02786800
C	-3.12051300	-2.78557400	2.57592300
H	-2.13409000	-2.91117700	3.02786800
H	-3.72508500	-2.12639100	3.19328700
H	-3.58046000	-3.76922400	2.48753500

Table S31. *trans*-C4-OAc (*trans*-5d)



	<i>trans</i> -5d		
N	-0.73447600	1.13330600	-0.56592900
C	0.59679000	1.16733100	-1.09894100
C	-1.44727700	-0.01832200	-0.54530000
C	-0.59679000	-1.16733100	-1.09894100
N	0.73447600	-1.13330600	-0.56592900
C	1.44727700	0.01832200	-0.54530000
O	2.59845300	0.12205700	-0.19063300
O	-2.59845300	-0.12205700	-0.19063300
S	0.56684500	0.89573100	-2.96251200
S	-0.56684500	-0.89573100	-2.96251200
C	-1.23114100	2.41789700	-0.11256800
H	-1.95022100	2.82479400	-0.82920100
C	1.23114100	-2.41789700	-0.11256800
H	1.95022100	-2.82479400	-0.82920100
C	-1.13718500	-2.56575200	-0.80161000
H	-1.37435800	-3.10053600	-1.72156200
C	1.13718500	2.56575200	-0.80161000
H	1.37435800	3.10053600	-1.72156200
H	-2.05247700	-2.47780800	-0.21616200
H	1.72797000	-2.30458500	0.85178800
H	2.05247700	2.47780800	-0.21616200
H	-1.72797000	2.30458500	0.85178800
C	0.02289000	3.30495300	-0.02786800
C	-0.02289000	-3.30495300	-0.02786800
H	0.17267200	-4.27867500	-0.46983200
H	-0.17267200	4.27867500	-0.46983200
O	0.39345300	3.64953800	1.31492200
O	-0.39345300	-3.64953800	1.31492200
C	0.73395200	2.65195300	2.16066800
C	-0.73395200	-2.65195300	2.16066800
C	-1.10394500	-3.19547300	3.51048000
H	-1.33999000	-2.36892600	4.17499100
H	-1.96535300	-3.85738800	3.41077600
H	-0.27692400	-3.78314300	3.91034700
C	1.10394500	3.19547300	3.51048000
H	1.33999000	2.36892600	4.17499100
H	1.96535300	3.85738800	3.41077600
H	0.27692400	3.78314300	3.91034700
O	-0.73395200	-1.49618100	1.84338400
O	0.73395200	1.49618100	1.84338400

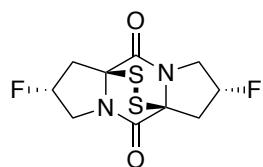
Table S32. *cis*-C4-F (*cis*-5e)



cis-5e

N	-1.17338500	0.67738400	-0.65296200
C	-1.12999300	-0.65490000	-0.11047000
C	-0.04937700	1.43593100	-0.68594100
C	1.12980100	0.65518400	-0.10993900
N	1.17297700	-0.67623800	-0.65477000
C	0.04901500	-1.43490000	-0.68783700
O	-0.01722300	-2.56742100	-1.10589300
O	0.01684000	2.56877300	-1.10314100
S	-0.83003200	-0.65176900	1.73812800
S	0.83079100	0.64909000	1.73869400
C	-2.51414600	1.12852400	-1.00776500
H	-2.75669800	2.07084800	-0.51666300
C	2.51393000	-1.12758400	-1.00871500
H	2.75594700	-2.07004900	-0.51759600
C	2.50083800	1.23018800	-0.43508200
H	2.85557600	1.95436000	0.29576000
C	-2.50108800	-1.22953900	-0.43606000
H	-2.85583800	-1.95430500	0.29420000
H	2.43683000	1.72609400	-1.40597800
H	2.59635700	-1.25846100	-2.08956400
H	-2.43722900	-1.72462800	-1.40737600
H	-2.59585500	1.25948000	-2.08866500
C	-3.40512600	-0.00392100	-0.50538700
C	3.40489800	0.00462800	-0.50565600
H	4.28582700	0.15716400	-1.12798000
H	-4.28627100	-0.15587400	-1.12752300
F	-3.85127000	0.30160300	0.76956700
F	3.85156100	-0.30185400	0.76884800

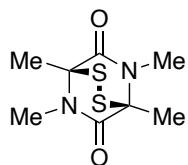
Table S33. *trans*-C4-F (*trans*-5e)



trans-5e

N	-1.10742200	-0.76499900	-0.19316300
C	0.10706800	-1.30691800	0.36359300
C	-1.33098300	0.57486900	-0.20153500
C	-0.10706800	1.30691800	0.36359300
N	1.10742200	0.76499900	-0.19316300
C	1.33098300	-0.57486900	-0.20153500
O	2.34319100	-1.11611900	-0.57529700
O	-2.34319100	1.11611900	-0.57529700
S	0.16805700	-1.04852600	2.21630900
S	-0.16805700	1.04852600	2.21630900
C	-2.04703500	-1.79712500	-0.60253100
H	-2.62685500	-1.46293900	-1.46167700
C	2.04703500	1.79712500	-0.60253100
H	2.62685500	1.46293900	-1.46167700
H	2.72204900	2.06138200	0.21846800
C	-0.05166000	2.80783500	0.05273000
H	0.15650300	3.38594400	0.95459000
H	-0.99364300	3.14294400	-0.38108700
C	0.05166000	-2.80783500	0.05273000
H	-0.15650300	-3.38594400	0.95459000
H	-2.72204900	-2.06138200	0.21846800
C	-1.10742200	-2.94682200	-0.93600500
H	-1.58740600	-3.92473200	-0.90590000
H	0.99364300	-3.14294400	-0.38108700
F	-0.62183000	-2.75730700	-2.22092600
C	1.10742200	2.94682200	-0.93600500
H	1.58740600	3.92473200	-0.90590000
F	0.62183000	2.75730700	-2.22092600

Table S34. *N,N'*-Dimethyl-bisalanyl-ETP



	1.00642600	-0.95202400	-0.67721500
N	1.27468900	0.34815700	-0.12411900
C	-0.29126100	-1.38682900	-0.66783900
C	-1.27466100	-0.34812700	-0.12449000
N	-1.00627700	0.95220600	-0.67716800
C	0.29140800	1.38700500	-0.66740200
O	0.64396000	2.49222900	-1.00738100
O	-0.64374000	-2.49195900	-1.00819600
S	0.97614800	0.39121000	1.73729800
S	-0.97653200	-0.39168400	1.73698100
C	2.07042300	-1.94272400	-0.77359200
H	2.51978700	-2.10874700	0.20896900
H	2.83468200	-1.61717900	-1.47664500
H	1.62347900	-2.86745400	-1.12596600
C	-2.07024700	1.94294400	-0.77346600
H	-2.83439700	1.61758800	-1.47672500
H	-1.62323200	2.86775700	-1.12553300
H	-2.51976500	2.10872400	0.20906500
C	-2.69916200	-0.81703500	-0.33616000
H	-3.40890400	-0.14697000	0.14531500
H	-2.90454500	-0.86515500	-1.40645700
H	-2.80629400	-1.82047800	0.06885400
C	2.69923500	0.81712800	-0.33535000
H	3.40887700	0.14692100	0.14607600
H	2.90484300	0.86556400	-1.40559000
H	2.80628500	1.82045200	0.06997800

Table S35. C4-H (5a)
M06-2X/6-311+G(d,p) / IEFPCM=Water

N	1.12947300	-0.75513900	-0.57221300
C	1.17226000	0.58510200	-0.05025900
C	-0.03567400	-1.43710800	-0.60885700
C	-1.17218700	-0.58551700	-0.04980300
N	-1.12907800	0.75330800	-0.57516600
C	0.03589600	1.43559500	-0.61132900
O	0.16834600	2.58080000	-1.00140300
O	-0.16814900	-2.58256900	-0.99816700
S	0.86426800	0.61013000	1.81246400
S	-0.86488200	-0.60619600	1.81327800
C	2.45362700	-1.29384400	-0.90806500
H	2.57294200	-2.28586600	-0.47315700
C	-2.45340100	1.29201700	-0.91066700
H	-2.57187100	2.28486200	-0.47741000
C	-2.58942300	-1.05718500	-0.34540000
H	-2.93672100	-1.81120300	0.35978700
C	2.58941100	1.05647400	-0.34710000
H	2.93683700	1.81160000	0.35682800
H	-2.58687500	-1.49983000	-1.34453900
H	-2.54907500	1.36486100	-1.99618400
H	2.58641700	1.49762100	-1.34688600
H	2.54834300	-1.36856400	-1.99355100
C	3.40181700	-0.24535600	-0.31325000
C	-3.40157700	0.24487900	-0.31338200
H	-4.32888000	0.16551900	-0.87721300
H	-3.64351200	0.50808000	0.71729100
H	4.32882600	-0.16678300	-0.87768300
H	3.64456200	-0.50662200	0.71773800

Table S36. *cis*-C4-OH (*cis*-5b)
M06-2X/6-311+G(d,p) / IEFPCM=Water

C	0.06156200	-1.43241700	-0.67686000
O	0.00329500	-2.57379200	-1.09307700
S	0.81448400	0.67539800	1.75113000
C	-1.13117000	-0.66374800	-0.10369500
O	-0.00300500	2.57229300	-1.09598800
S	-0.81478300	-0.67263700	1.75195100
C	-2.50351800	-1.24249800	-0.42907000
O	-3.87481100	0.41865800	0.74850300
C	-3.42007600	-0.01294300	-0.52296700
O	3.87463600	-0.41791600	0.74913800
C	-2.51410100	1.08716900	-1.07426800
N	-1.17877100	0.67377900	-0.63443500
C	-0.06129400	1.43128200	-0.67876900
C	1.13131700	0.66340500	-0.10423300
C	2.50361600	1.24180500	-0.43065900
C	3.42016300	0.01222200	-0.52296200
C	2.51425700	-1.08853800	-1.07299700
N	1.17915000	-0.67508100	-0.63262500
H	-4.26477200	-0.20105200	-1.18840100
H	4.26499400	0.19947600	-1.18846900
H	-4.41875500	-0.27458400	1.13614500
H	4.41486700	0.27753100	1.13804500
H	-2.84796900	-1.97288800	0.30312300
H	-2.43615200	-1.74005900	-1.39929600
H	-2.54636300	1.13054300	-2.16451700
H	-2.77260900	2.06211900	-0.66198500
H	2.43609000	1.73809600	-1.40146800
H	2.84810900	1.97323600	0.30050500
H	2.54593300	-1.13278500	-2.16323300
H	2.77329100	-2.06308300	-0.66005800

Table S37. *trans*-C4-OH (*trans*-**5b**)
M06-2X/6-311+G(d,p) / IEFPCM=Water

C	-0.25988000	-0.13420800	-1.42708100
O	-0.57259100	-0.51335100	-2.53897000
C	-1.24667100	0.41968000	-0.39043000
O	0.58686700	-0.61282800	2.50026300
C	-2.72348300	0.10867700	-0.66145600
O	-2.61115400	-2.22701400	-0.28591000
S	-0.97965700	2.26903300	-0.36083400
C	-3.04539700	-1.02134200	0.32038300
O	2.52421000	-2.28732200	0.10892700
S	0.98894300	2.25296000	0.43902000
C	-2.18905700	-0.67901300	1.54167500
N	-0.98175200	-0.15715200	0.90862800
C	0.27267600	-0.19083300	1.40389700
C	1.25798800	0.40571500	0.39069500
C	2.73251800	0.08260100	0.64969600
C	3.03027300	-1.04498500	-0.35059400
C	2.19436900	-0.66087500	-1.56570100
N	0.99469100	-0.11881800	-0.93081700
H	-2.87346400	-0.19353200	-1.69599800
H	-3.34475500	0.97747500	-0.44158100
H	-4.10859800	-1.06148900	0.56340600
H	-2.66590500	0.08632800	2.16064500
H	-1.94325400	-1.54366100	2.15717200
H	2.88981100	-0.21449600	1.68571400
H	3.35997900	0.94686400	0.42590000
H	4.09401900	-1.11278100	-0.58527100
H	2.69303200	0.09951700	-2.17142400
H	1.93418200	-1.51778500	-2.18472100
H	-2.79008400	-2.96056500	0.31142600
H	2.95718900	-2.51434200	0.93807700

Table S38. *cis*-C4-OAc (*cis*-5d)
M06-2X/6-311+G(d,p) / IEFPCM=Water

N	-1.28723300	-0.91763000	-0.42801000
C	-0.97740400	-0.38346400	0.87261600
C	-0.34277800	-0.95329500	-1.39412200
C	0.97758200	-0.38446800	-0.87234600
N	1.28743400	-0.91702100	0.42894900
C	0.34298100	-0.95157400	1.39509800
O	0.51346500	-1.35330600	2.52930700
O	-0.51334500	-1.35607800	-2.52794100
S	-0.67981700	1.47300500	0.80995200
S	0.67993000	1.47203100	-0.81199700
C	-2.68614000	-1.32081800	-0.58744900
H	-3.11635400	-0.88007800	-1.48613600
C	2.68629900	-1.32017800	0.58883700
H	3.11663100	-0.87839700	1.48696200
C	2.20859500	-0.71029000	-1.71090800
H	2.40923500	0.02066800	-2.49241800
C	-2.20845700	-0.70813000	1.71157900
H	-2.40909500	0.02397100	2.49202700
H	2.04837700	-1.68329700	-2.17930100
H	2.75638500	-2.40753000	0.65670800
H	-2.04831300	-1.68045000	2.18140200
H	-2.75630500	-2.40824200	-0.65407300
C	-3.34426800	-0.80193600	0.69514000
C	3.34440500	-0.80278000	-0.69435900
H	4.15246900	-1.45074500	-1.02659800
H	-4.15221200	-1.44963400	1.02821300
O	3.85495300	0.52503800	-0.50884800
O	-3.85501400	0.52559900	0.50828000
C	-5.00750600	0.63589800	-0.17790500
C	5.00727200	0.63621100	0.17747900
O	-5.58350700	-0.31899300	-0.63543900
O	5.58321300	-0.31809000	0.63627700
C	5.44464300	2.06530200	0.28105600
H	6.37106000	2.12417000	0.84548500
H	5.58585400	2.47509700	-0.71977500
H	4.66456400	2.64706700	0.77390900
C	-5.44519500	2.06477200	-0.28276900
H	-4.66390400	2.64723100	-0.77281400
H	-6.36992800	2.12319800	-0.84999300
H	-5.58997200	2.47410400	0.71777200

Table S39. *trans*-C4-OAc (*trans*-**5d**)
M06-2X/6-311+G(d,p) / IEFPCM=Water

N	-1.22840900	0.57119000	-0.18916700
C	-1.06625900	-0.75219900	0.34869200
C	-0.18458000	1.42837200	-0.19938300
C	1.06629700	0.75295600	0.34724200
N	1.22849500	-0.57153600	-0.18788000
C	0.18466500	-1.42873600	-0.19643700
O	0.23266800	-2.58841200	-0.55359000
O	-0.23255700	2.58732100	-0.55889300
S	-0.77477200	-0.71206600	2.20961600
S	0.77465000	0.71664100	2.20821900
C	-2.61970200	0.93090200	-0.45562500
H	-2.88291600	1.85113600	0.06091100
C	2.61980900	-0.93179600	-0.45348200
H	2.88299300	-1.85094400	0.06500100
C	2.38364500	1.44159600	0.04832300
H	2.62371100	2.23780400	0.74937000
C	-2.38358800	-1.44144400	0.05109600
H	-2.62369800	-2.23621600	0.75375400
H	2.32522900	1.86685100	-0.95577100
H	2.78144200	-1.06311200	-1.52524500
H	-2.32511500	-1.86875800	-0.95212000
H	-2.78126200	1.05997100	-1.52767300
C	-3.39167600	-0.29277300	0.06410600
C	3.39174600	0.29296700	0.06373400
H	3.76840000	0.10472300	1.06858600
H	-3.76833900	-0.10244400	1.06856300
O	-4.48340500	-0.65652400	-0.77632200
O	4.48348600	0.65500500	-0.77742100
C	-5.52464800	0.19627600	-0.78929300
C	5.52473200	-0.19781400	-0.78864100
C	6.63384100	0.29892800	-1.66166500
H	7.43977700	-0.42784000	-1.67568900
H	6.25599700	0.46574800	-2.67005100
H	6.99398700	1.25353100	-1.27789900
C	-6.63404600	-0.30258200	-1.66074200
H	-7.44023700	0.42388300	-1.67578200
H	-6.25665300	-0.47125300	-2.66898700
H	-6.99367800	-1.25655200	-1.27492500
O	5.52267500	-1.22494800	-0.16047500
O	-5.52283200	1.22440300	-0.16275200

Table S40. *cis*-C4-F (*cis*-**5e**)
M06-2X/6-311+G(d,p) / IEFPCM=Water

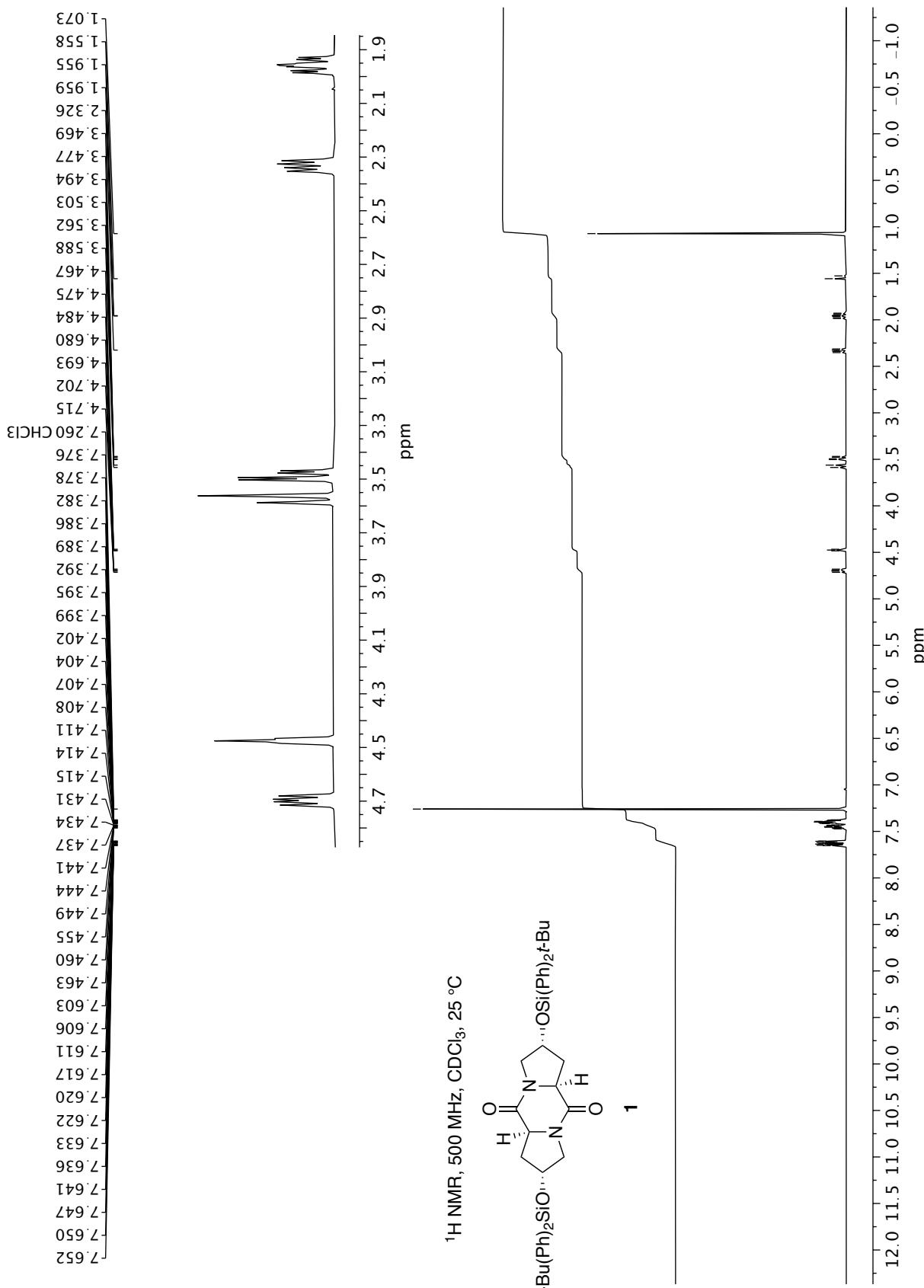
C	-0.05891000	1.43540300	-0.67960500
O	-0.00021600	2.57930800	-1.08422700
S	0.82708200	0.66052500	1.74664600
C	1.13044700	0.66163000	-0.10907100
O	0.00019300	-2.57972400	-1.08360900
S	-0.82706400	-0.65996600	1.74677300
C	2.50490700	1.23870400	-0.43145000
C	3.40739000	0.01361400	-0.51909900
C	2.51714300	-1.10587800	-1.04452500
N	1.17645900	-0.67628100	-0.64180100
C	0.05880800	-1.43573100	-0.67923700
C	-1.13052600	-0.66179200	-0.10898200
C	-2.50513500	-1.23881900	-0.43072800
C	-3.40748400	-0.01368000	-0.51874300
C	-2.51722000	1.10511100	-1.04546200
N	-1.17648800	0.67587800	-0.64237900
F	3.84351000	-0.32247600	0.76440800
F	-3.84299900	0.32347100	0.76464200
H	4.29433300	0.17402900	-1.12791900
H	-4.29473800	-0.17436300	-1.12704800
H	2.44810000	1.73075900	-1.40478200
H	2.86049000	1.96165500	0.30110500
H	2.57563600	-1.18270300	-2.13178100
H	2.77333000	-2.06642200	-0.59750200
H	-2.44871500	-1.73104300	-1.40408300
H	-2.86044300	-1.96166800	0.30199500
H	-2.57592500	1.18026700	-2.13286000
H	-2.77309100	2.06636900	-0.59990800

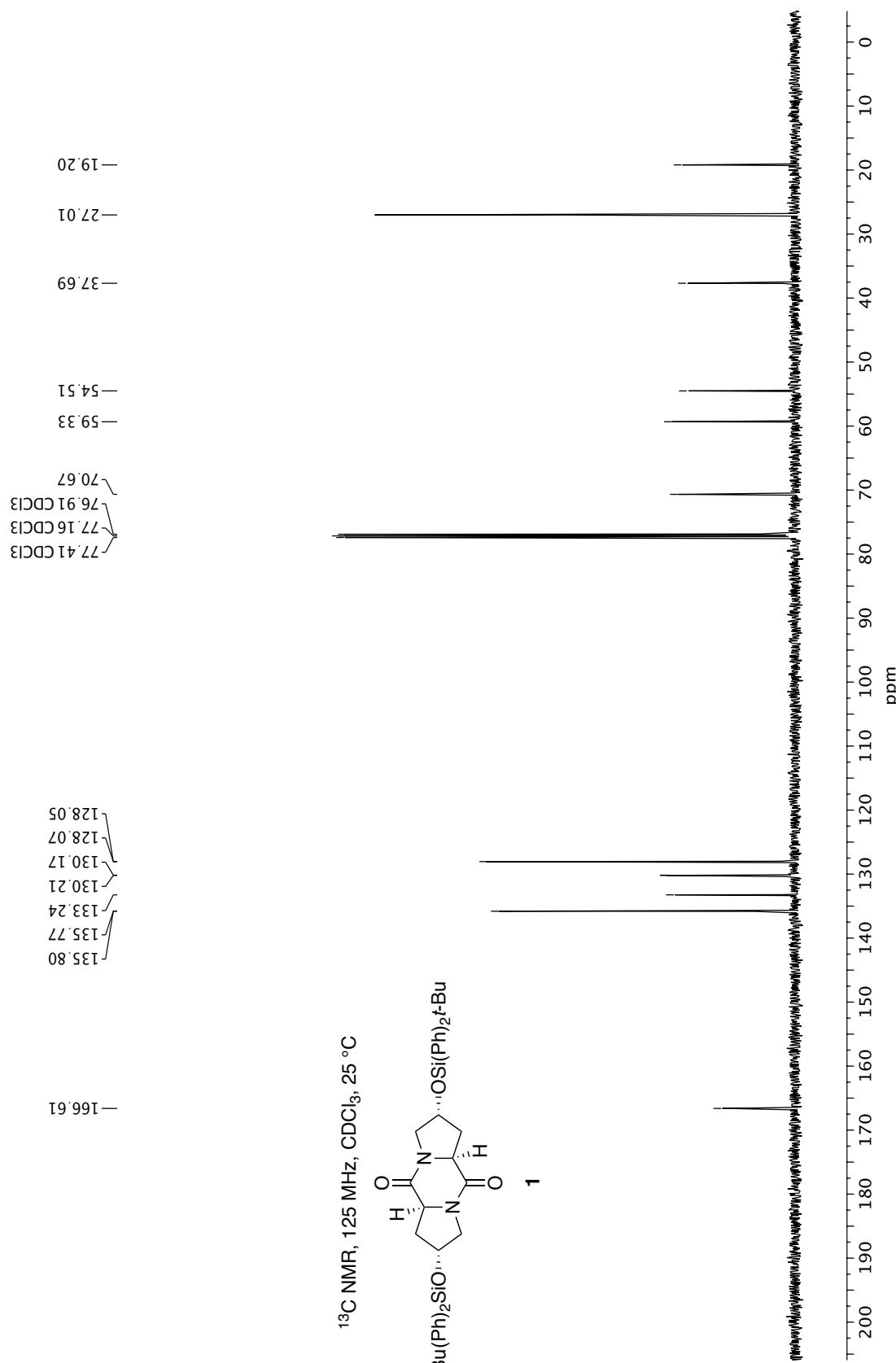
Table S41. *trans*-C4-F (*trans*-**5e**)
M06-2X/6-311+G(d,p) / IEFPCM=Water

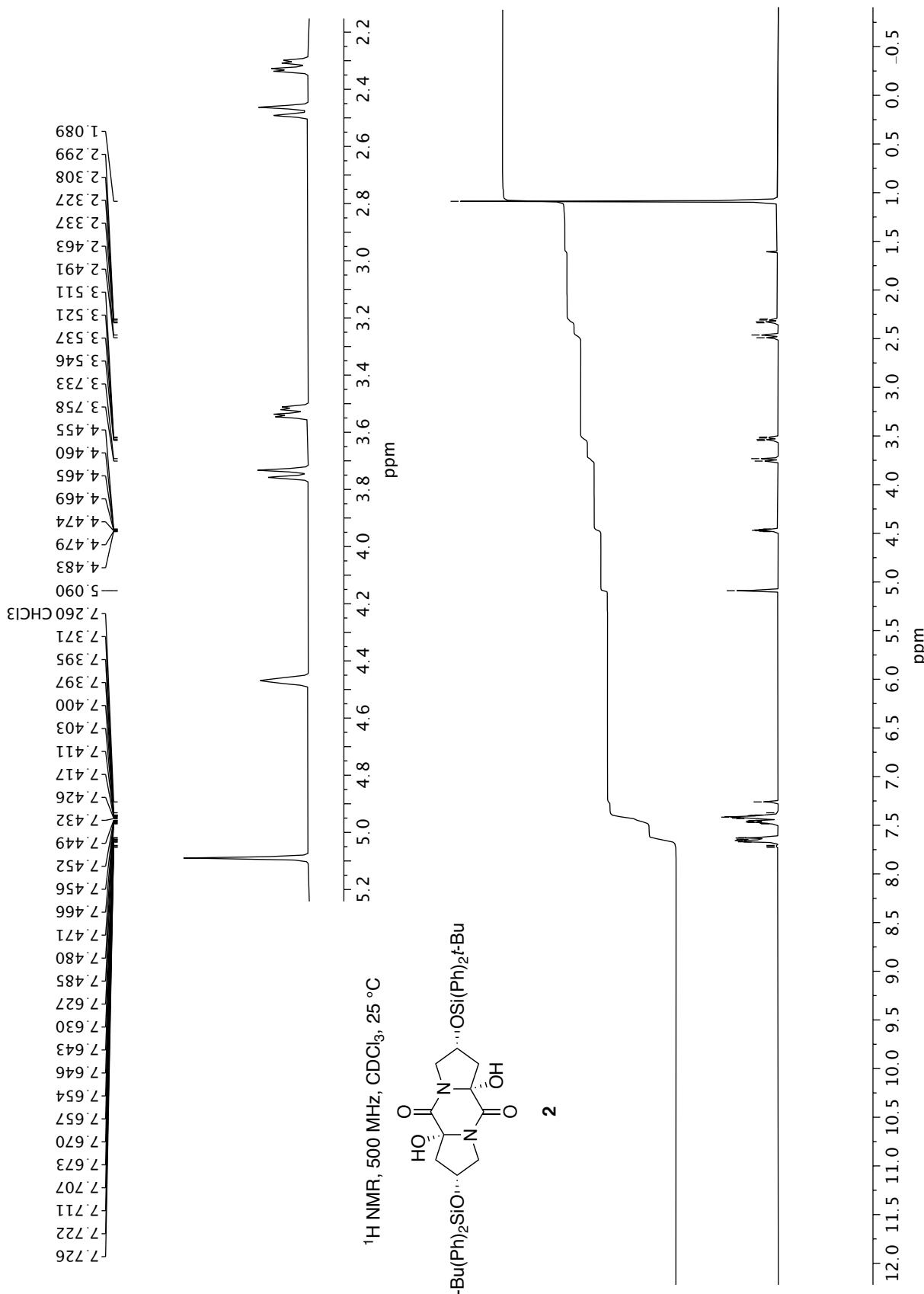
C	-0.24448000	-0.18175200	-1.42017700
O	-0.54042700	-0.58318300	-2.52732700
S	-0.97776700	2.24251300	-0.41540900
C	-1.24608200	0.39531800	-0.41068100
O	0.54007200	-0.58443600	2.52734600
S	0.97767200	2.24229300	0.41583300
C	-2.71804700	0.07886900	-0.70328700
C	-3.07154600	-0.99443300	0.32143100
C	-2.21935600	-0.66374100	1.53476100
N	-1.00307400	-0.16053400	0.90241500
C	0.24410900	-0.18223100	1.42048800
C	1.24572500	0.39512000	0.41119100
C	2.71772700	0.07864200	0.70374400
C	3.07186600	-0.99344600	-0.32203300
C	2.21914800	-0.66245200	-1.53490000
N	1.00261100	-0.16082100	-0.90188100
F	-2.65484200	-2.23197100	-0.17690800
F	2.65644100	-2.23183200	0.17530600
H	-3.34501900	0.95598700	-0.53827600
H	-2.84973000	-0.27056800	-1.72570100
H	-4.13567800	-1.06468400	0.53478700
H	-2.69335600	0.10779700	2.14718800
H	-1.99669300	-1.53668600	2.14597400
H	3.34460200	0.95609900	0.54007900
H	2.84915200	-0.27200900	1.72576700
H	4.13600700	-1.06254700	-0.53571500
H	2.69238600	0.11004600	-2.14674700
H	1.99714200	-1.53503500	-2.14685000

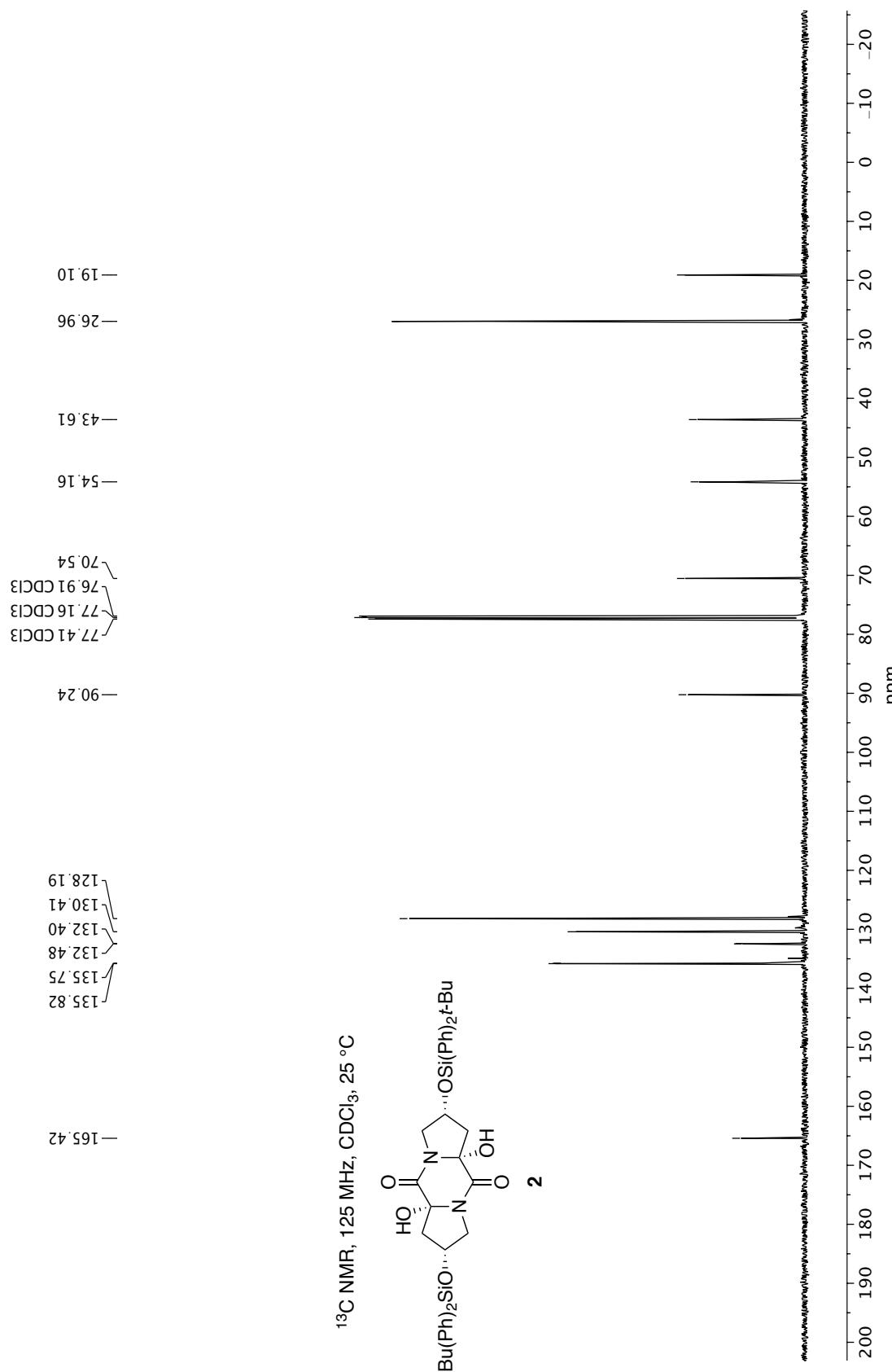
References

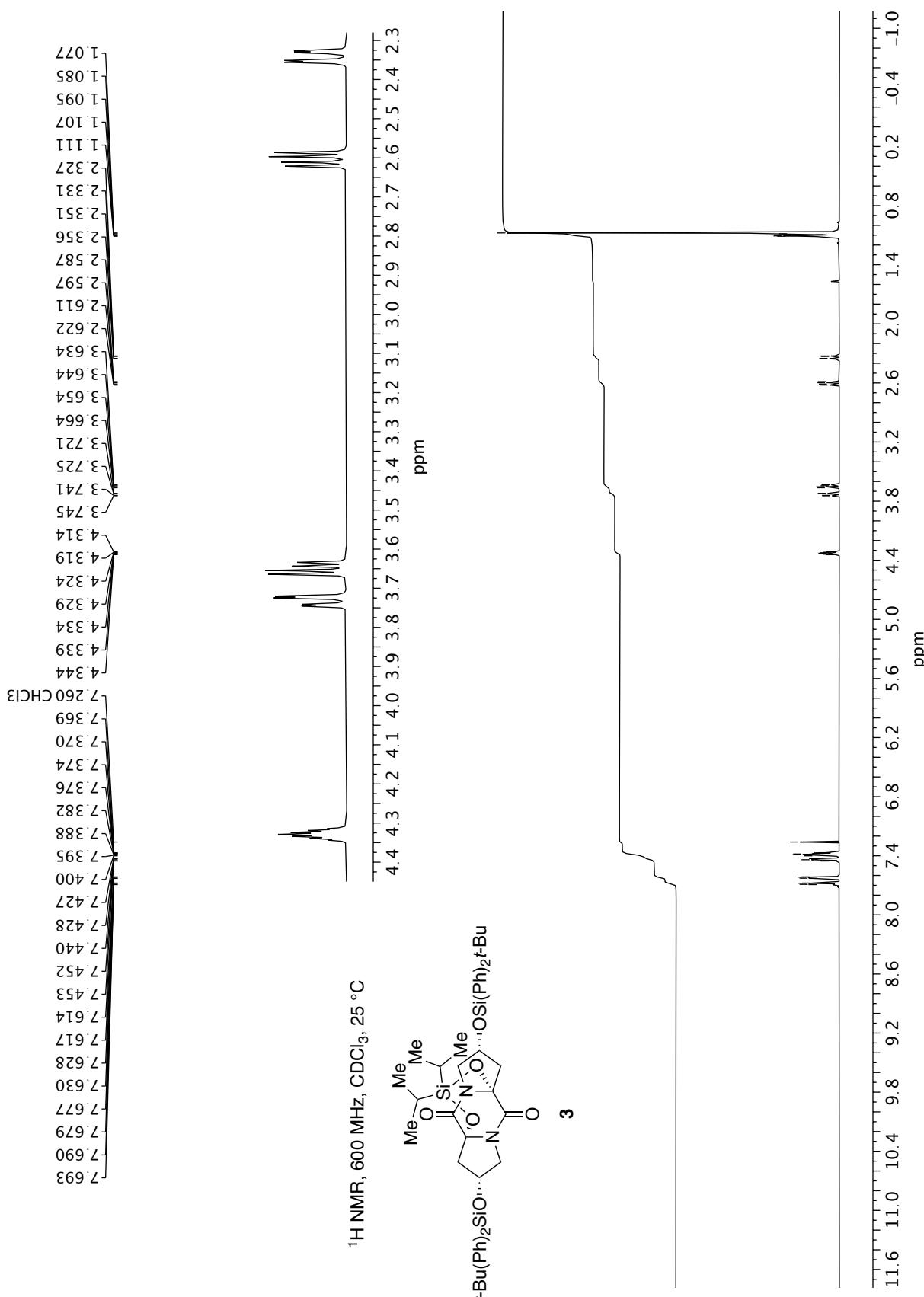
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- (11) For a related procedure, see Ishihara, K.; Ohara, S.; Yamamoto, H. 3,4,5-Trifluorobenzenboronic acid as an extremely active amidation catalyst. *J. Org. Chem.* **1996**, *61*, 4196–4197.
- (12) Another portion of silyloxydiketopiperazine **1** (1.7 g, 20%) was obtained that contained the C_2 -epimerization side product, *epi*-silyloxydiketopiperazine *epi*-**1** ($1:epi\text{-}1 = 1.8:1$).
- (13) The stereochemistry of dithiepanethiones *cis*-**4** and *trans*-**4** have been established by X-ray crystal structure analysis of the corresponding epidisulfides *cis*-**5b** and *trans*-**5b**, respectively.
- (14) Prepared by stirring potassium iodide (0.200 g, 1.20 mmol) and iodine (305 mg, 1.20 mmol) in pyridine (5 mL) for 30 min.
- (15) *Trans*-4-fluoro-L-proline methyl ester hydrogen chloride was prepared in quantitative yield using thionyl chloride and methanol, see: Loscher, S.; Schobert, R. Total synthesis and absolute configuration of epicoccamide D, a naturally occurring mannosylated 3-acyltetrameric acid. *Chem. Eur. J.* **2013**, *19*, 10619–10624.
- (16) The desired disulfide *trans*-**5e** was present as a minor component based on ^{19}F NMR analysis in combination with LCMS (disulfide:trisulfide:tetralsulfide = 1:2:2).
- (17) The desired disulfide *cis*-**5e** was present as a minor component based on ^{19}F NMR analysis in combination with LCMS (disulfide:trisulfide:tetralsulfide = 1:3:3).
- (18) The stereochemistry of epidisulfide *cis*-**5e** has been established by the X-ray crystal structure, and by key nOe correlations observed for the corresponding bis(methylthioether)diketopiperazine *cis*-**8**.
- (19) The stereochemistry of epidisulfide *trans*-**5e** has been established by the X-ray crystal structure, and by key nOe correlations observed for the corresponding bis(methylthioether)diketopiperazine *trans*-**8**.

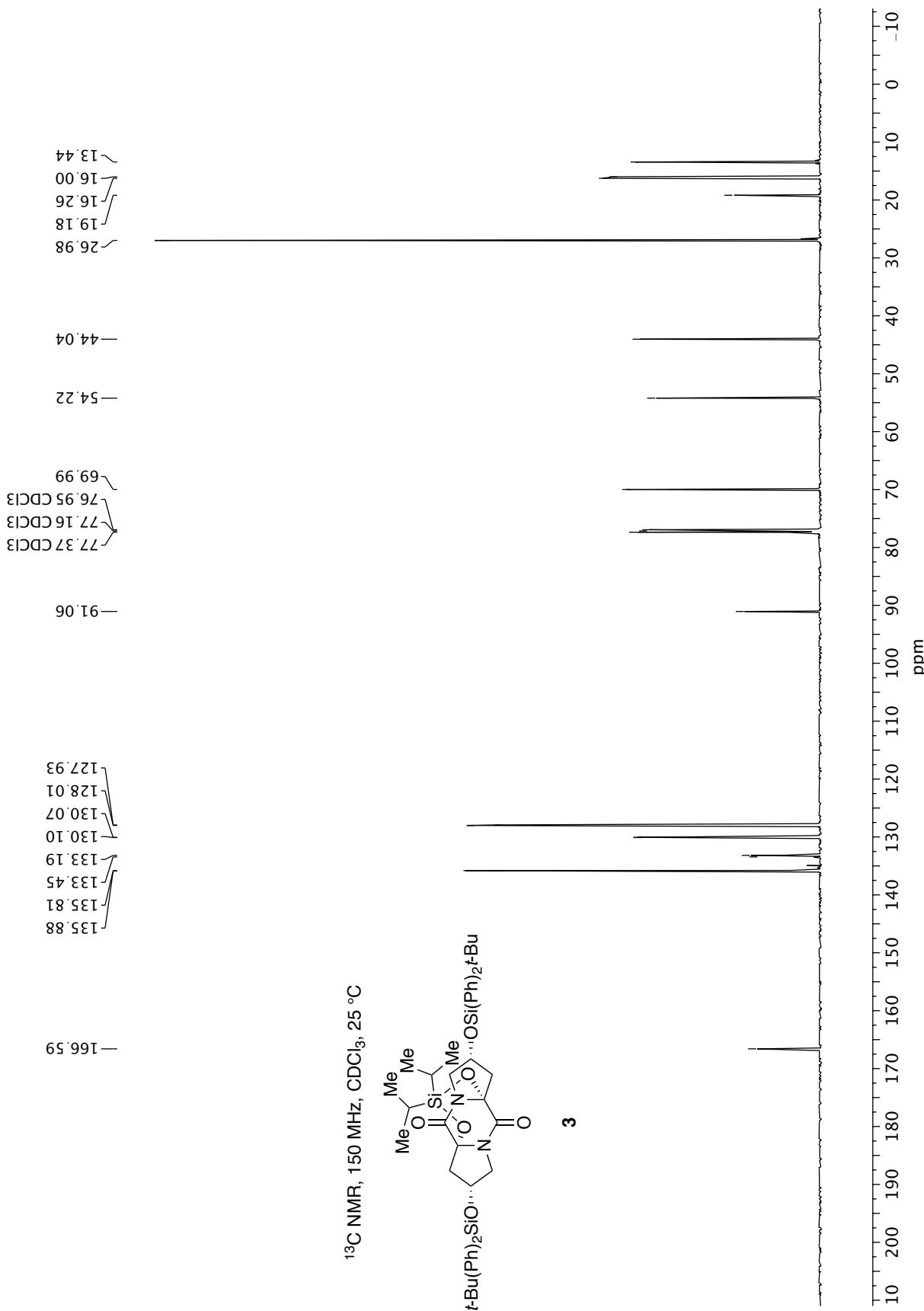




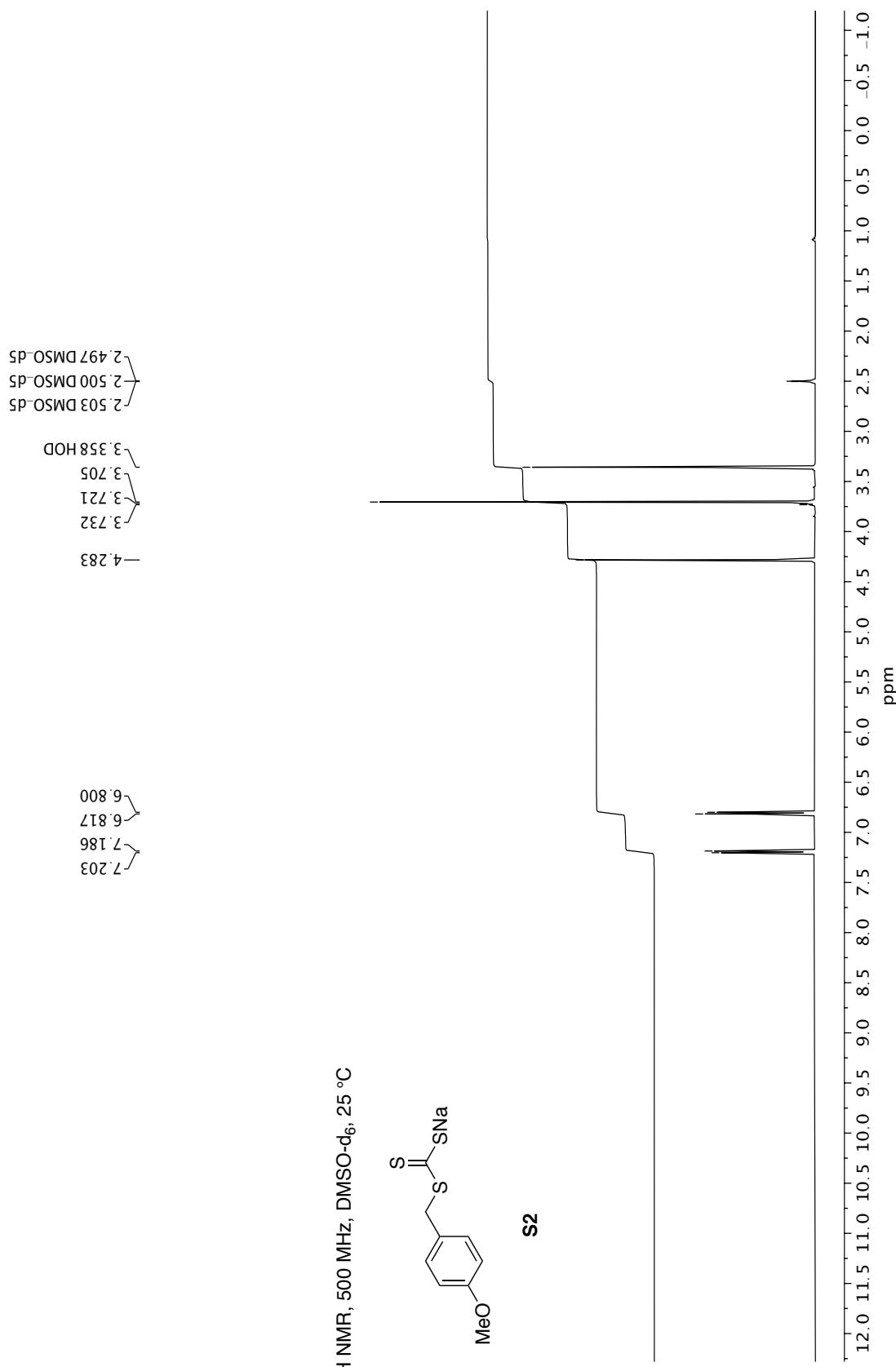
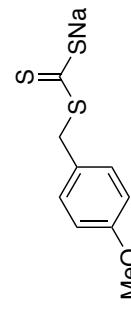


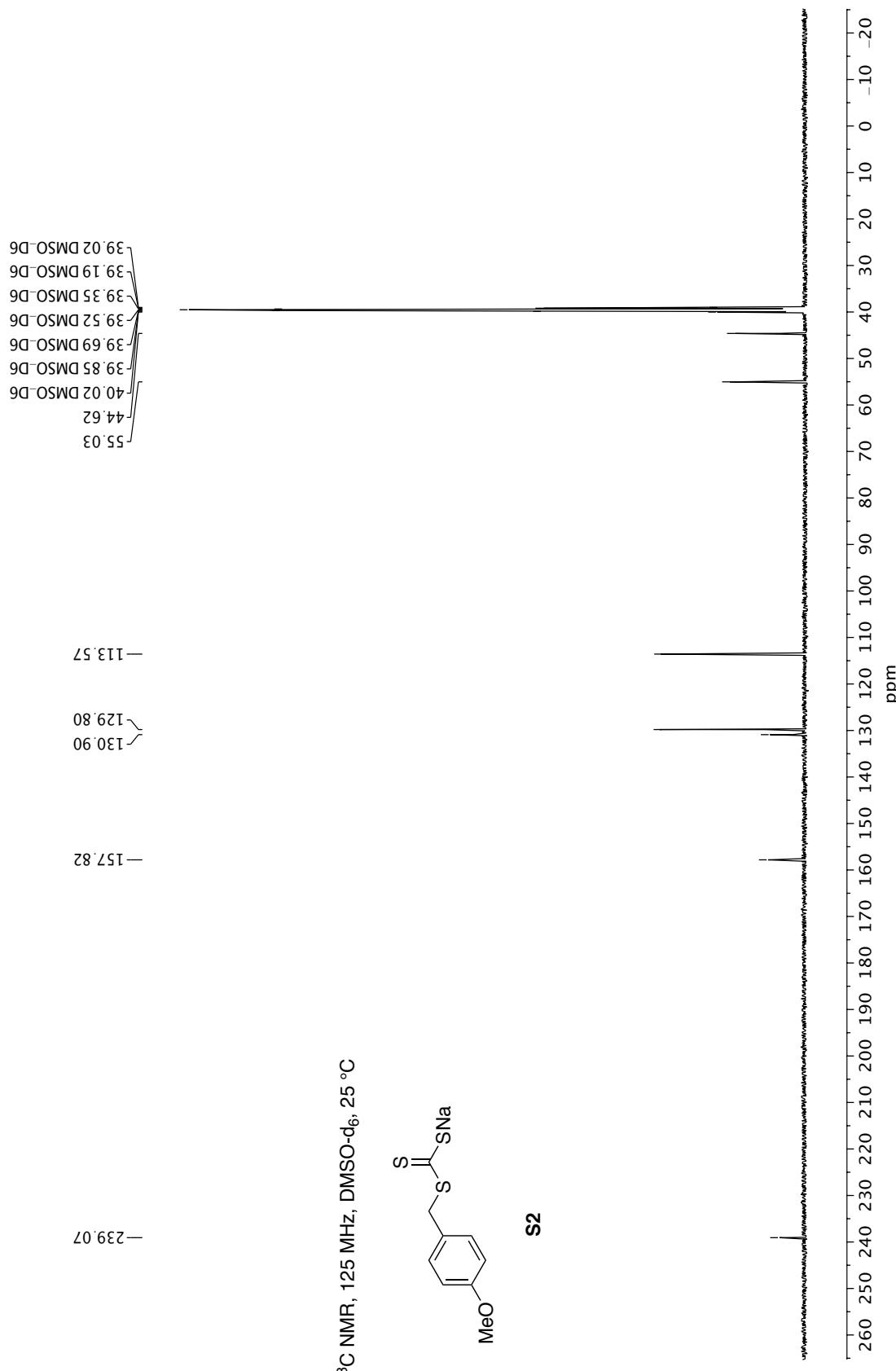


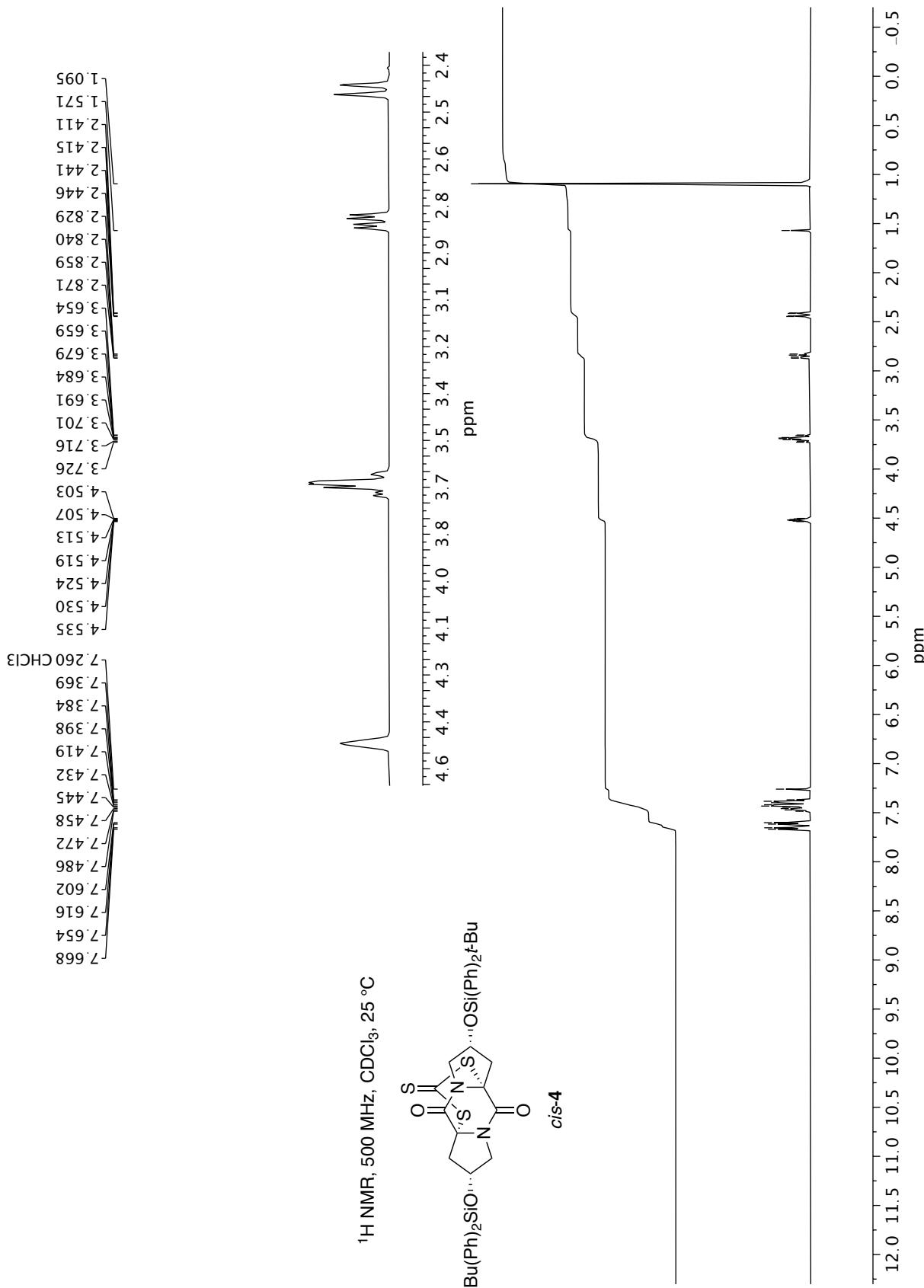


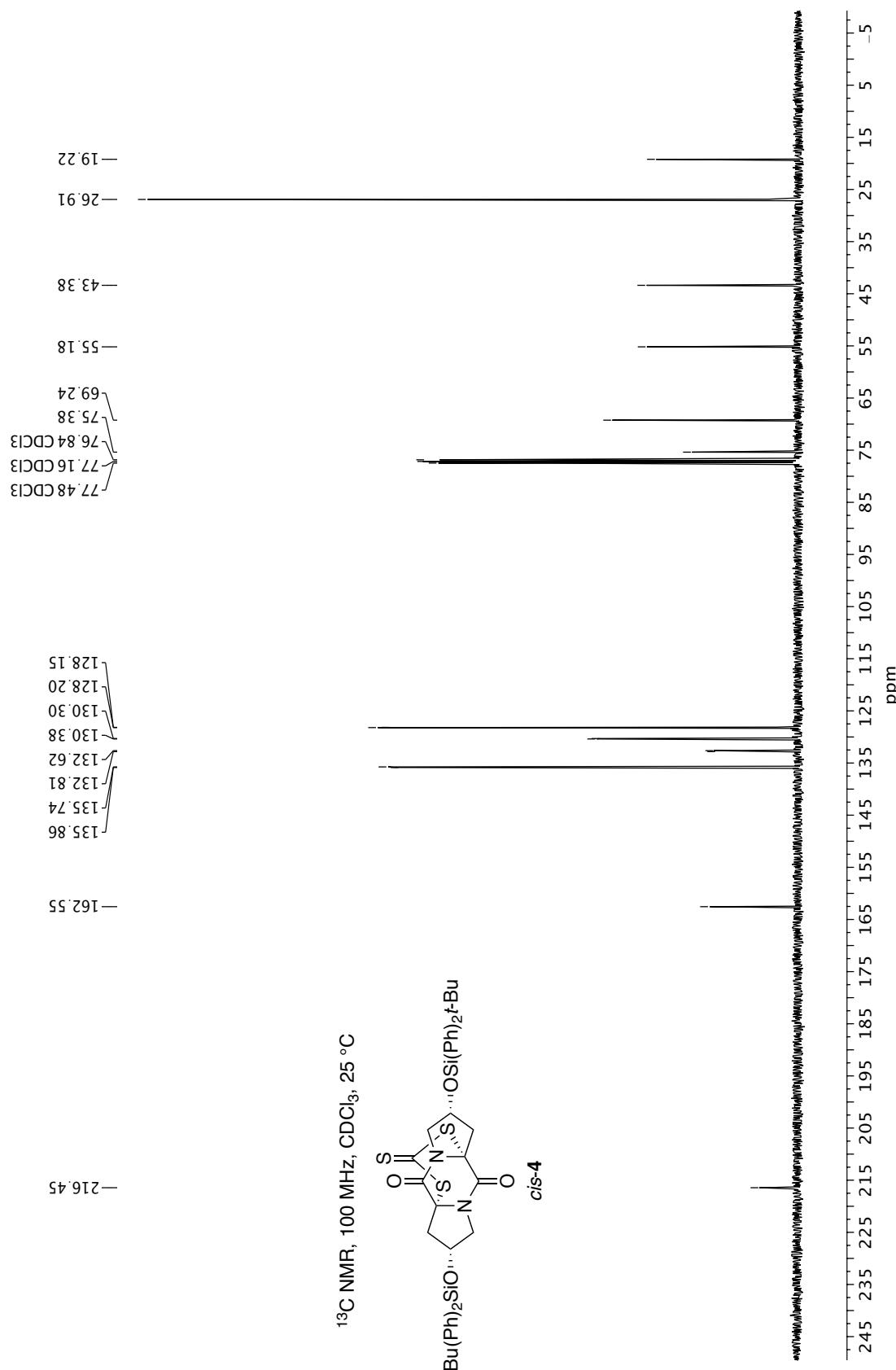


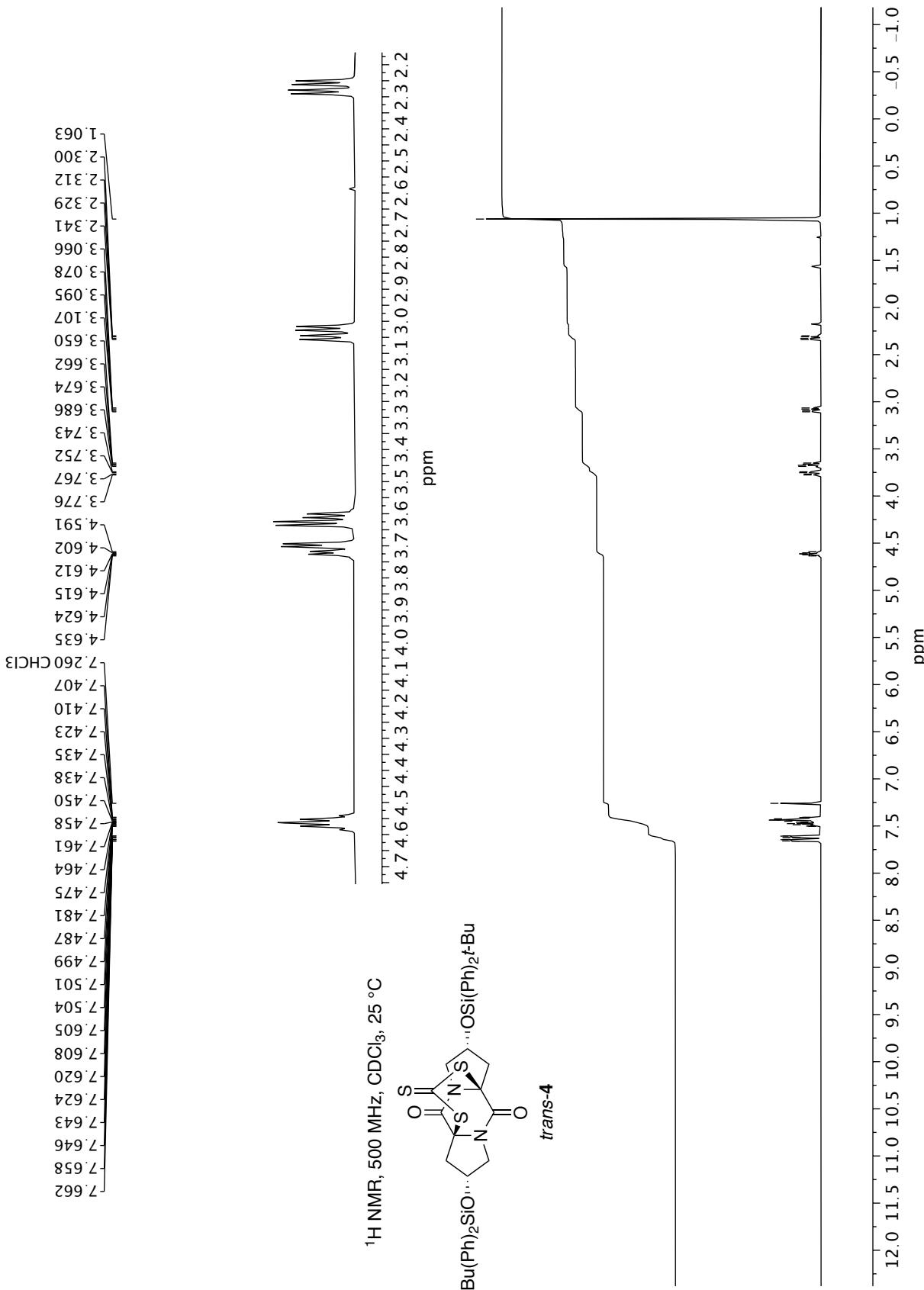
¹H NMR, 500 MHz, DMSO-d₆, 25 °C

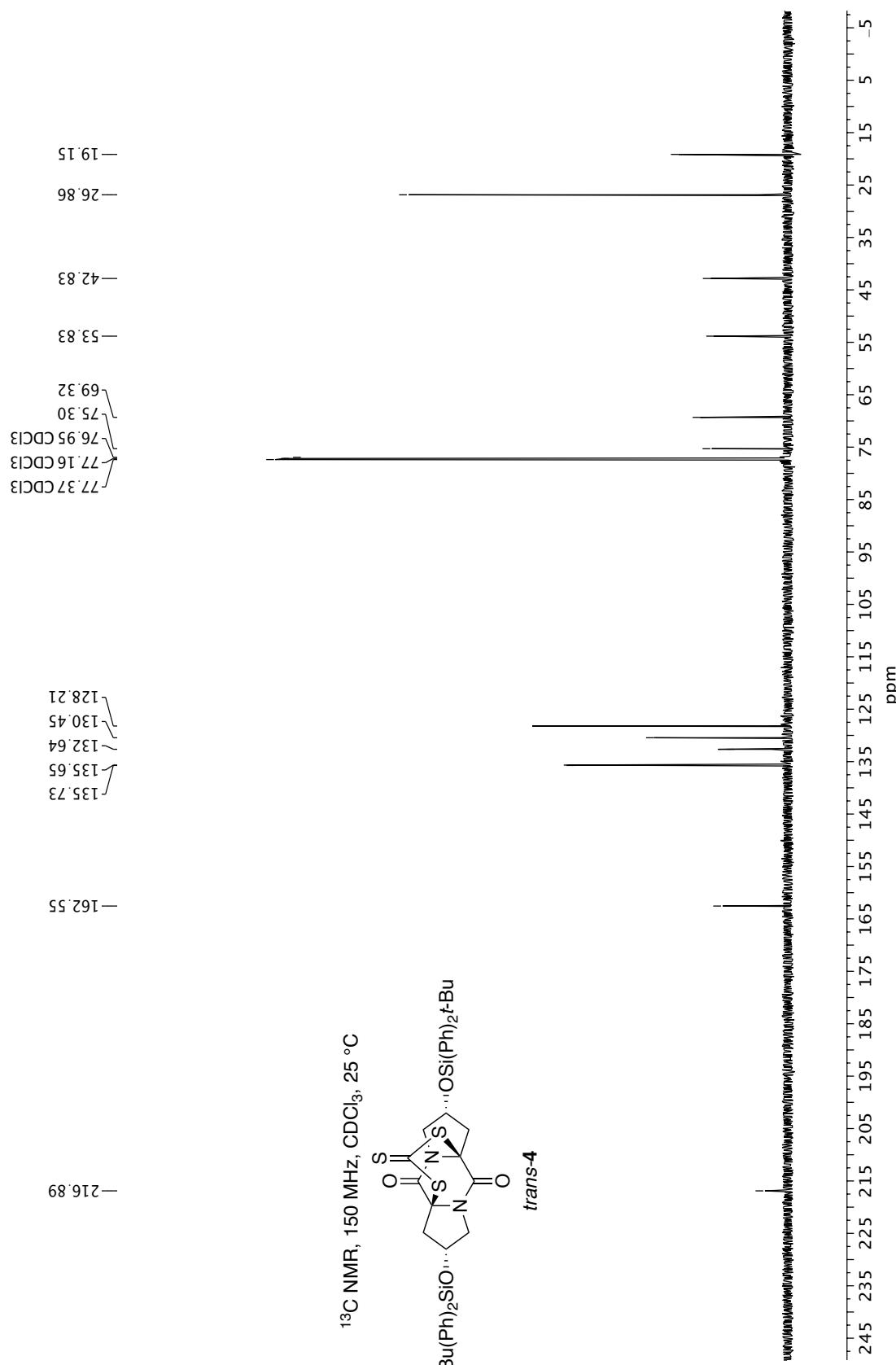


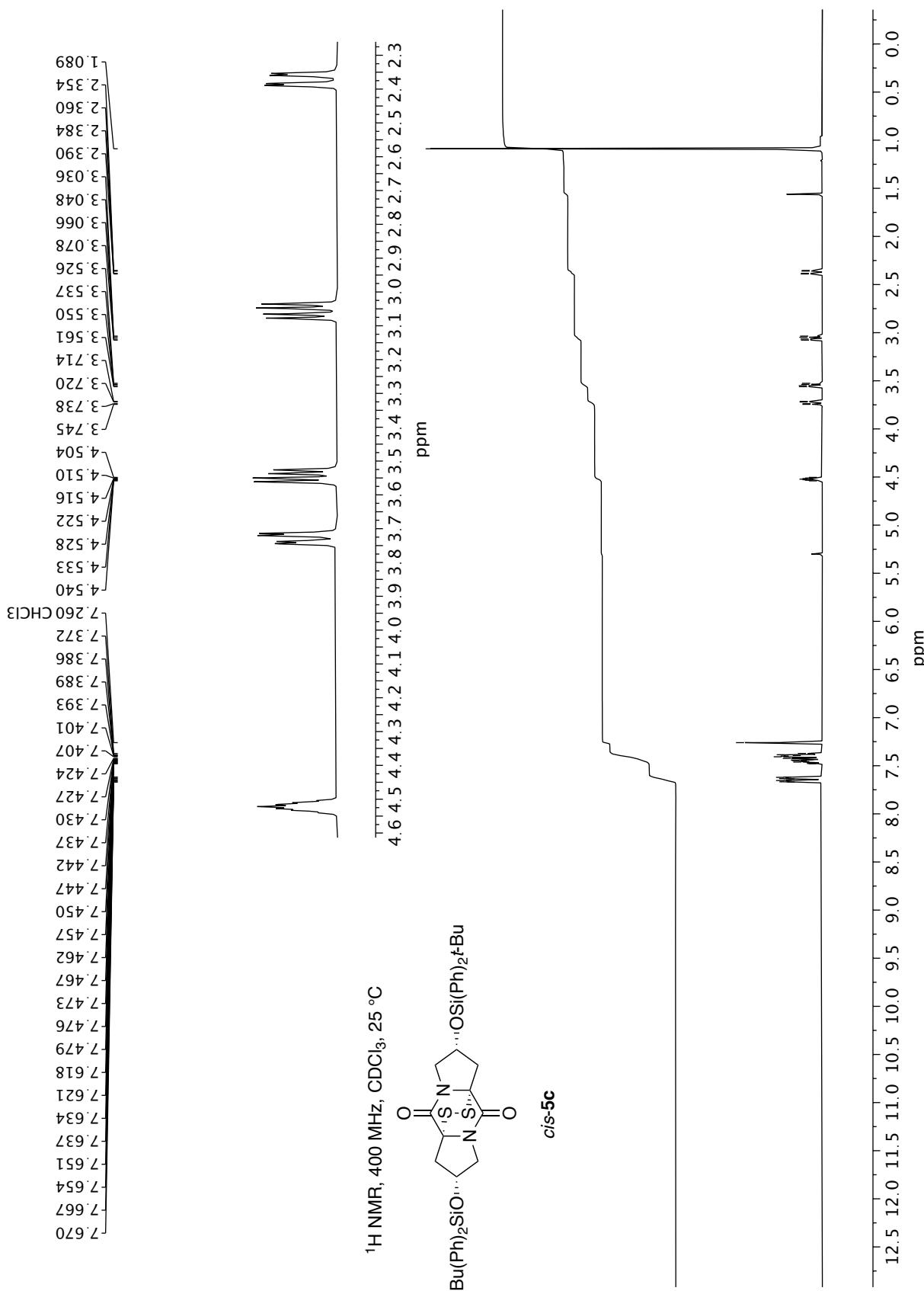


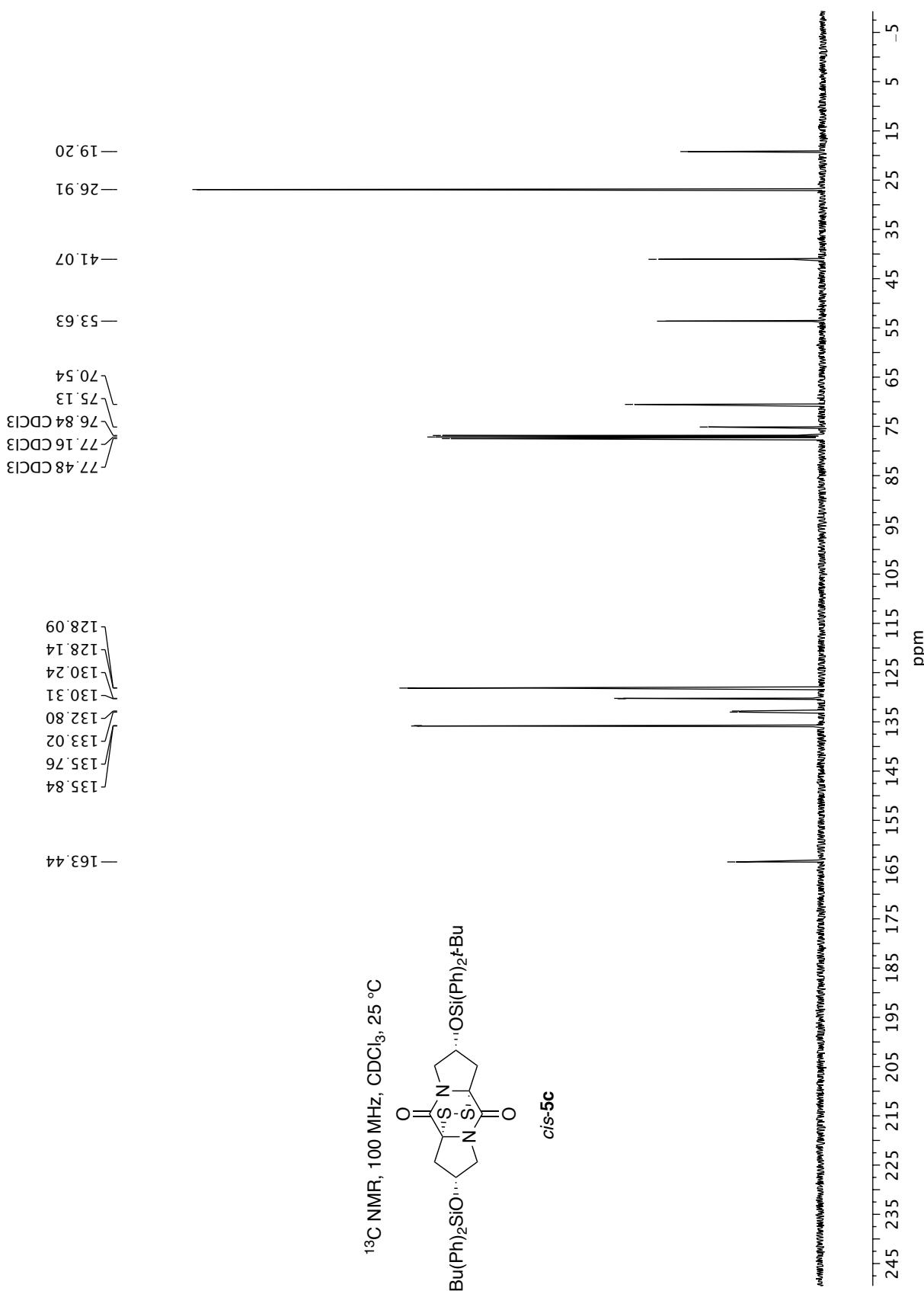


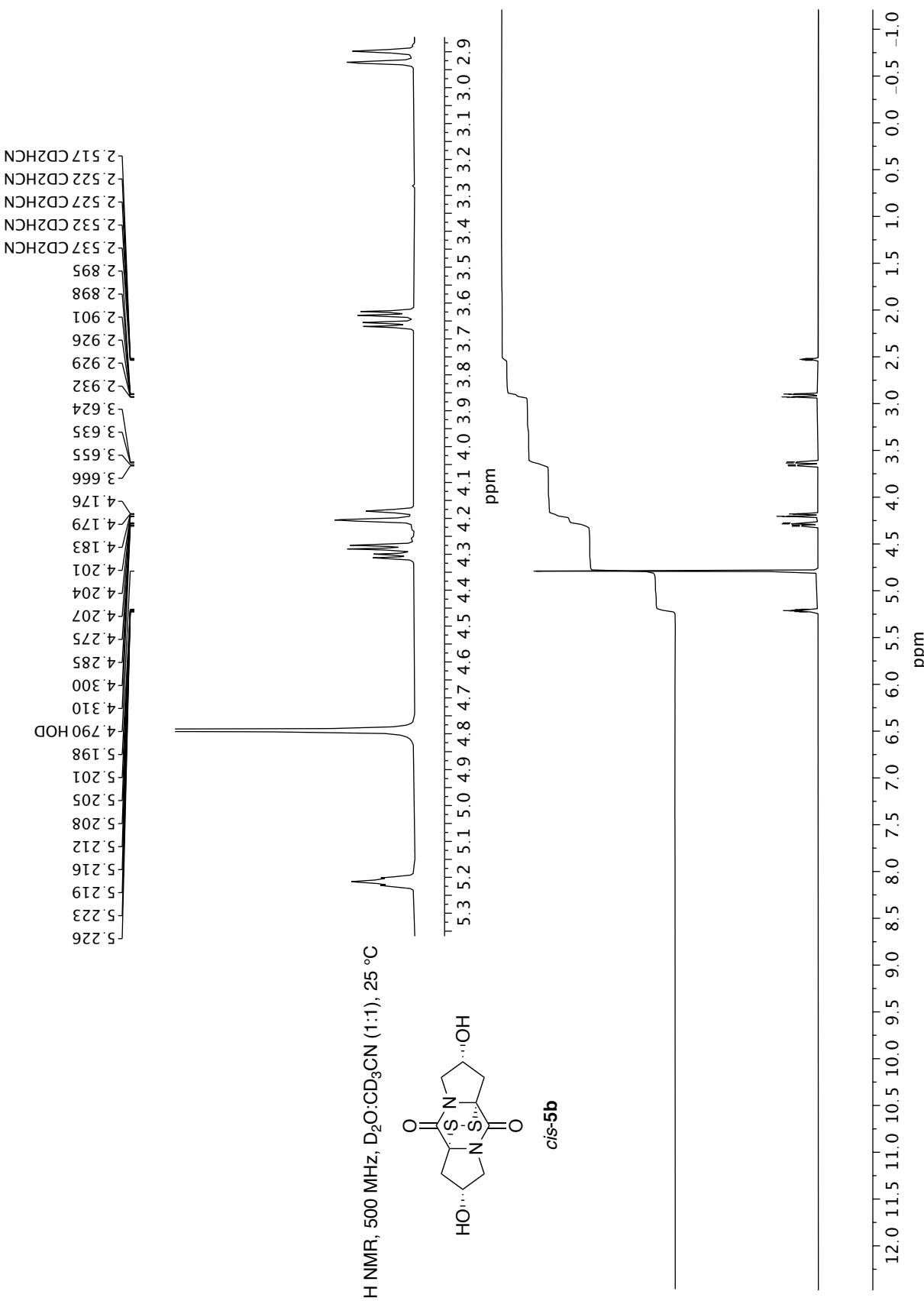


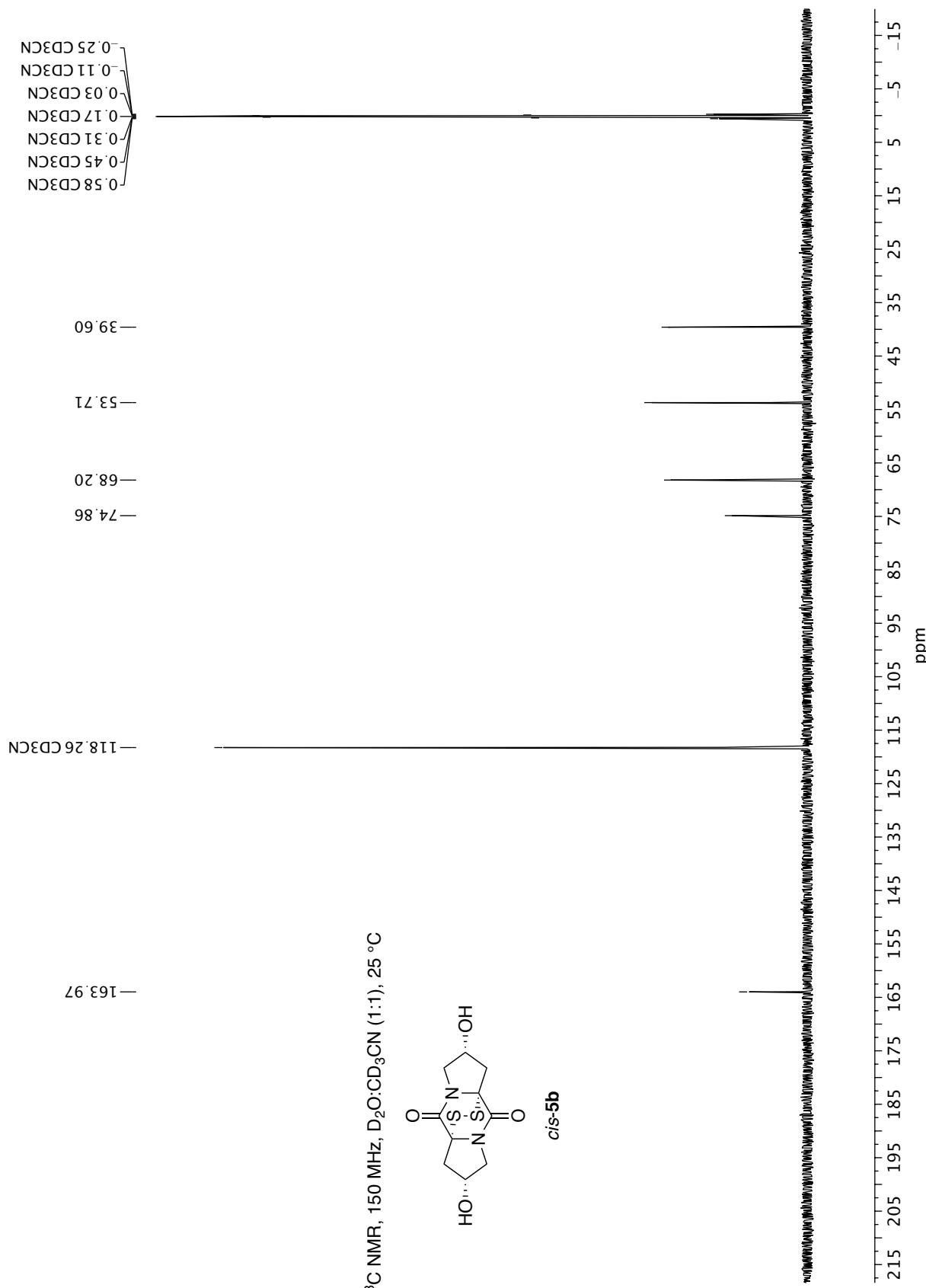


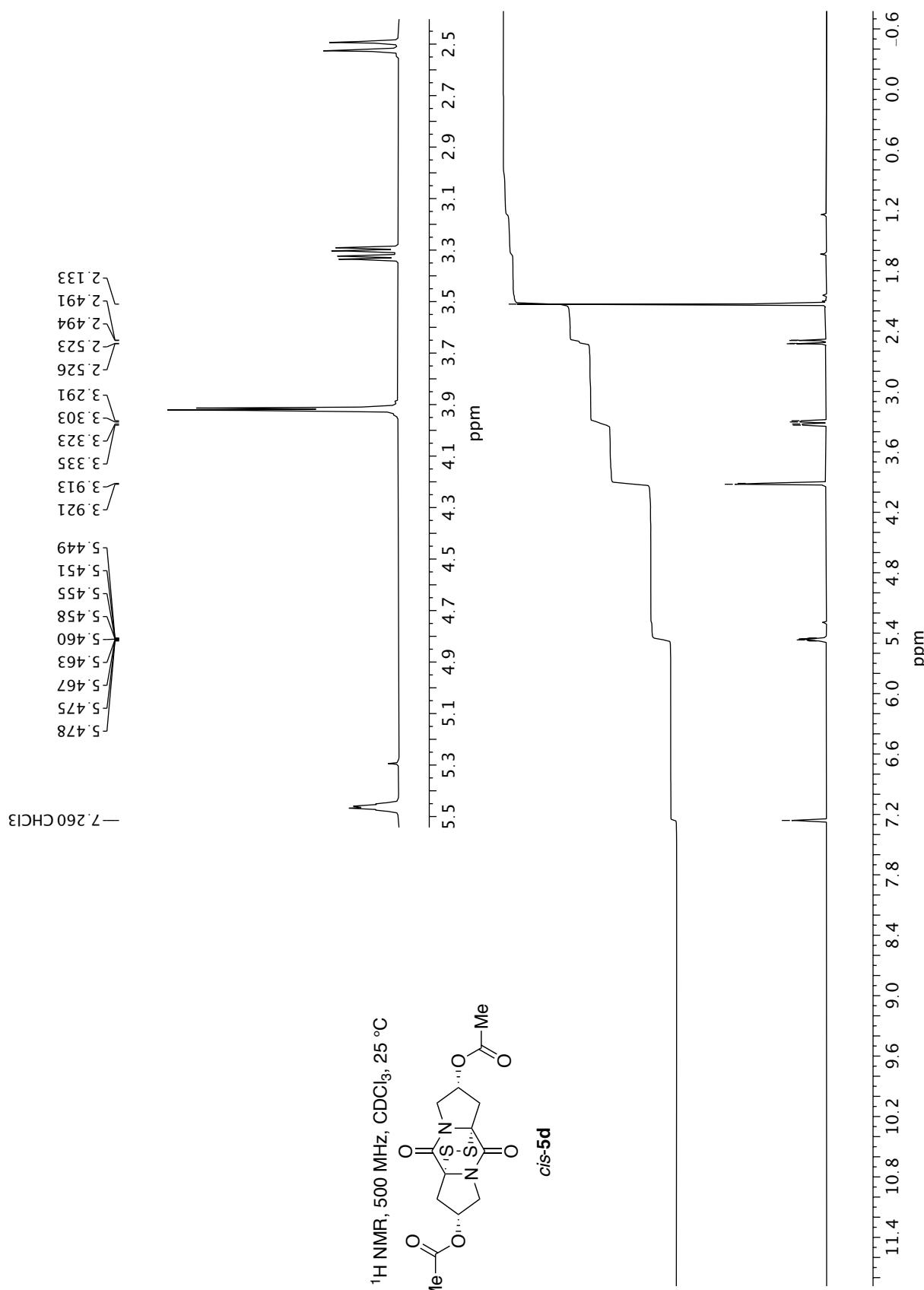


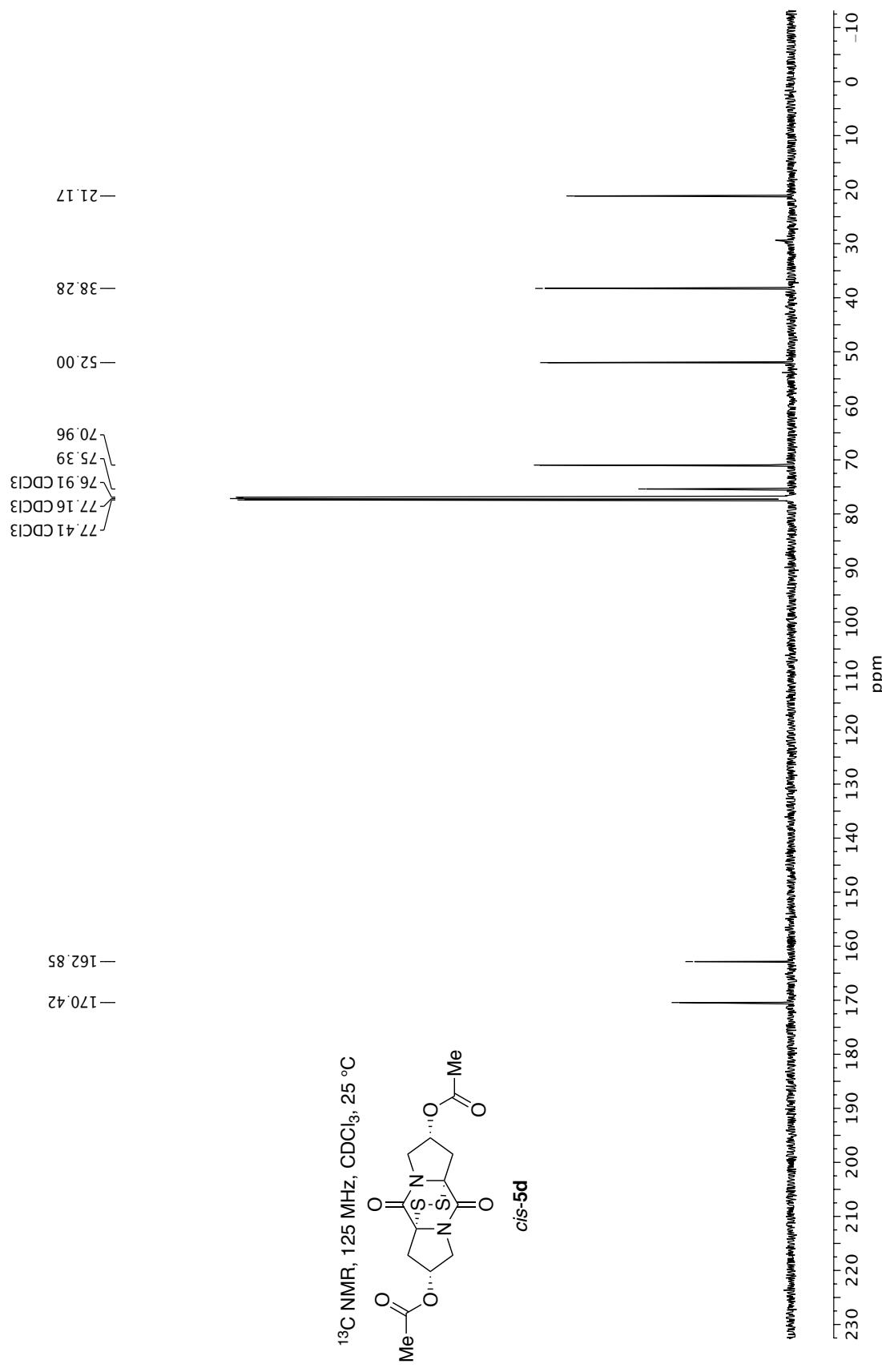


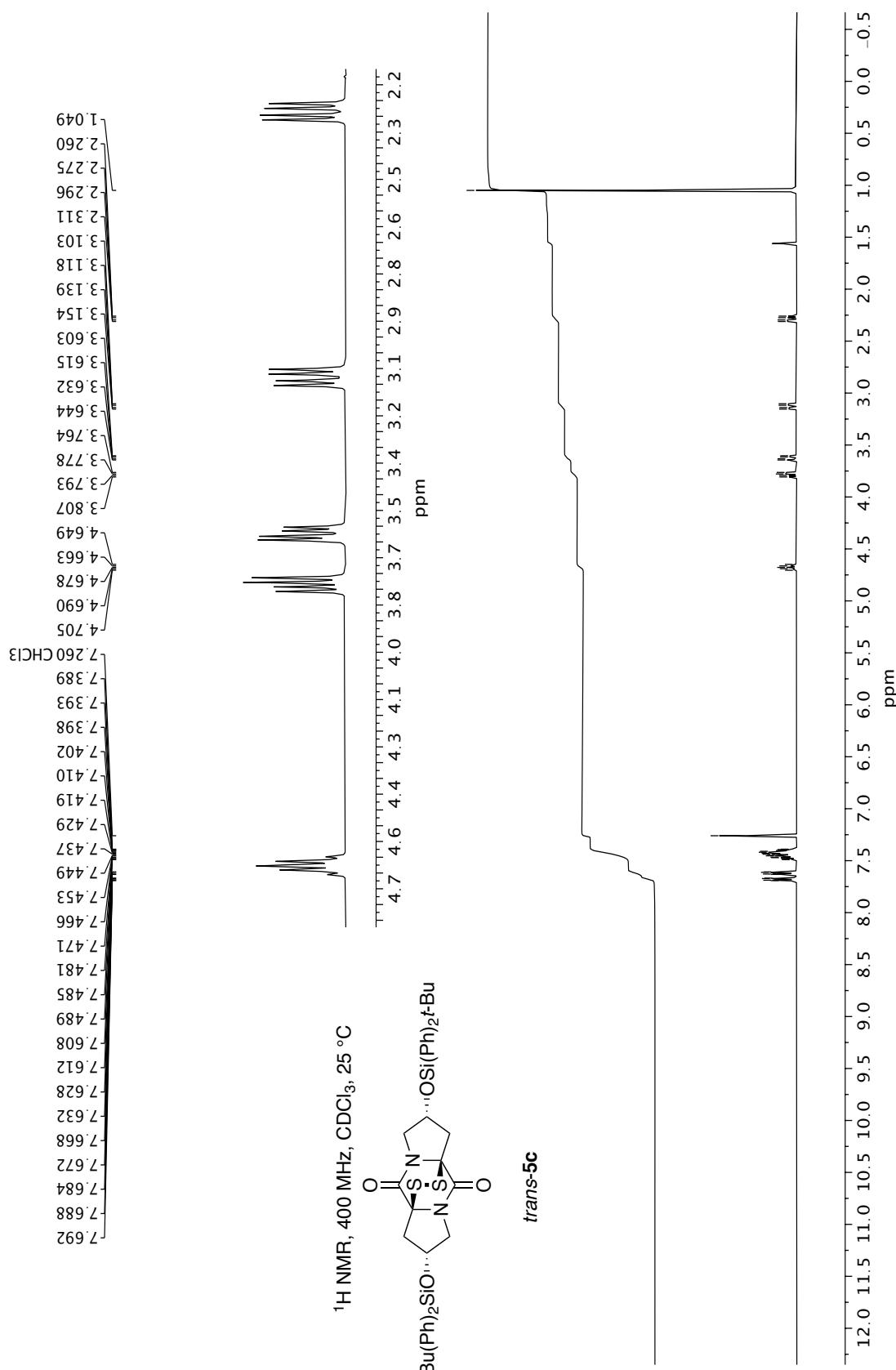


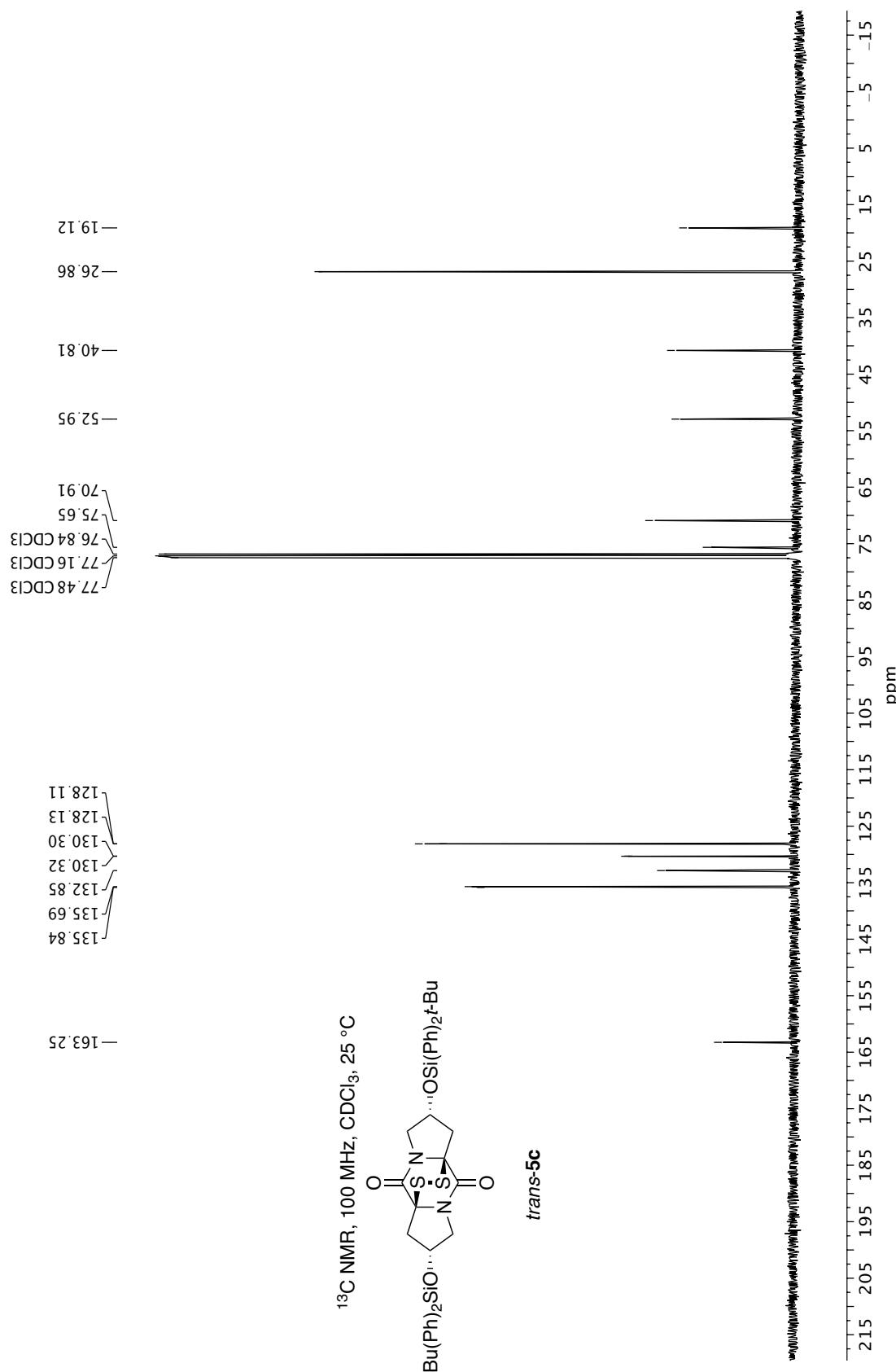


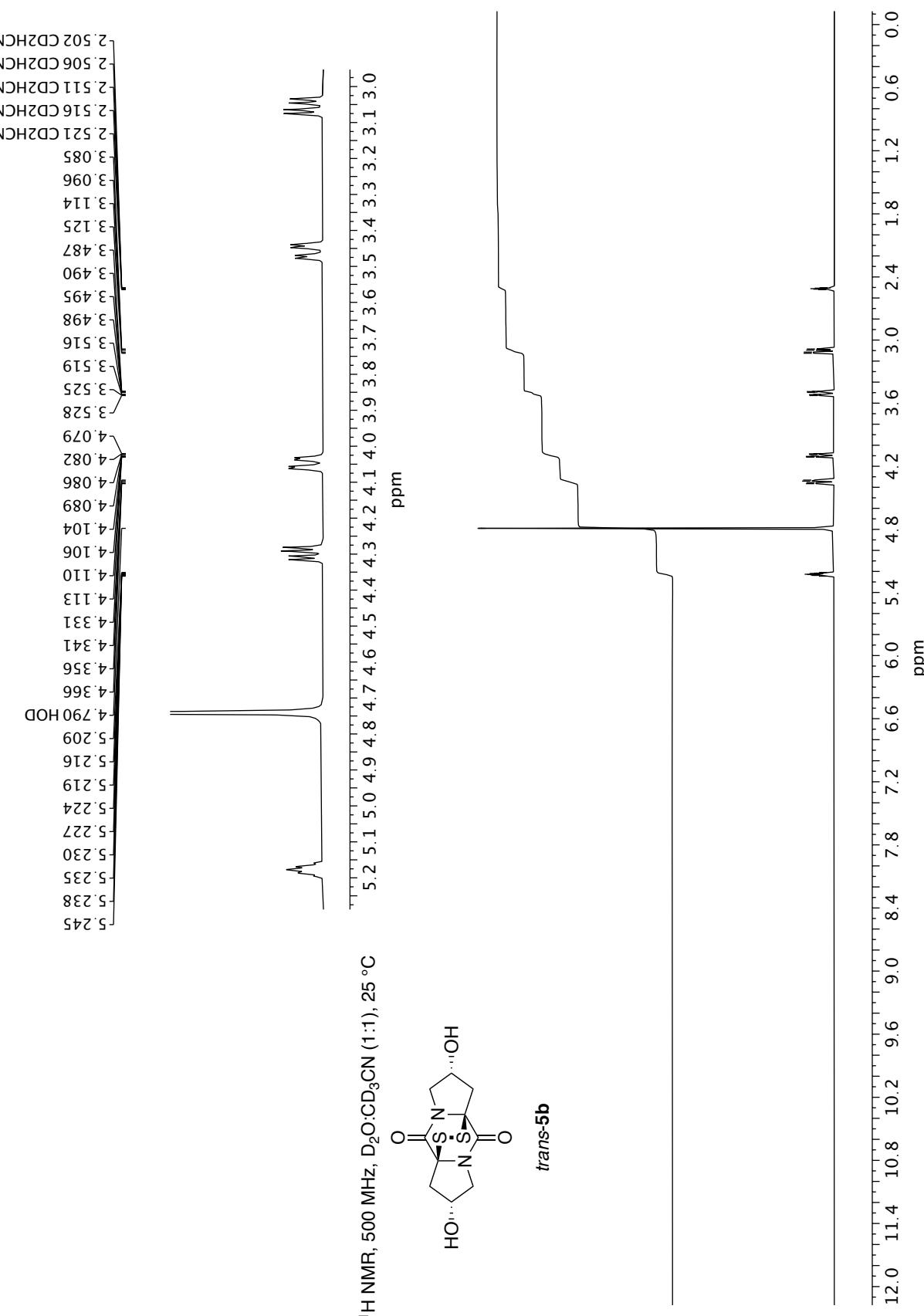


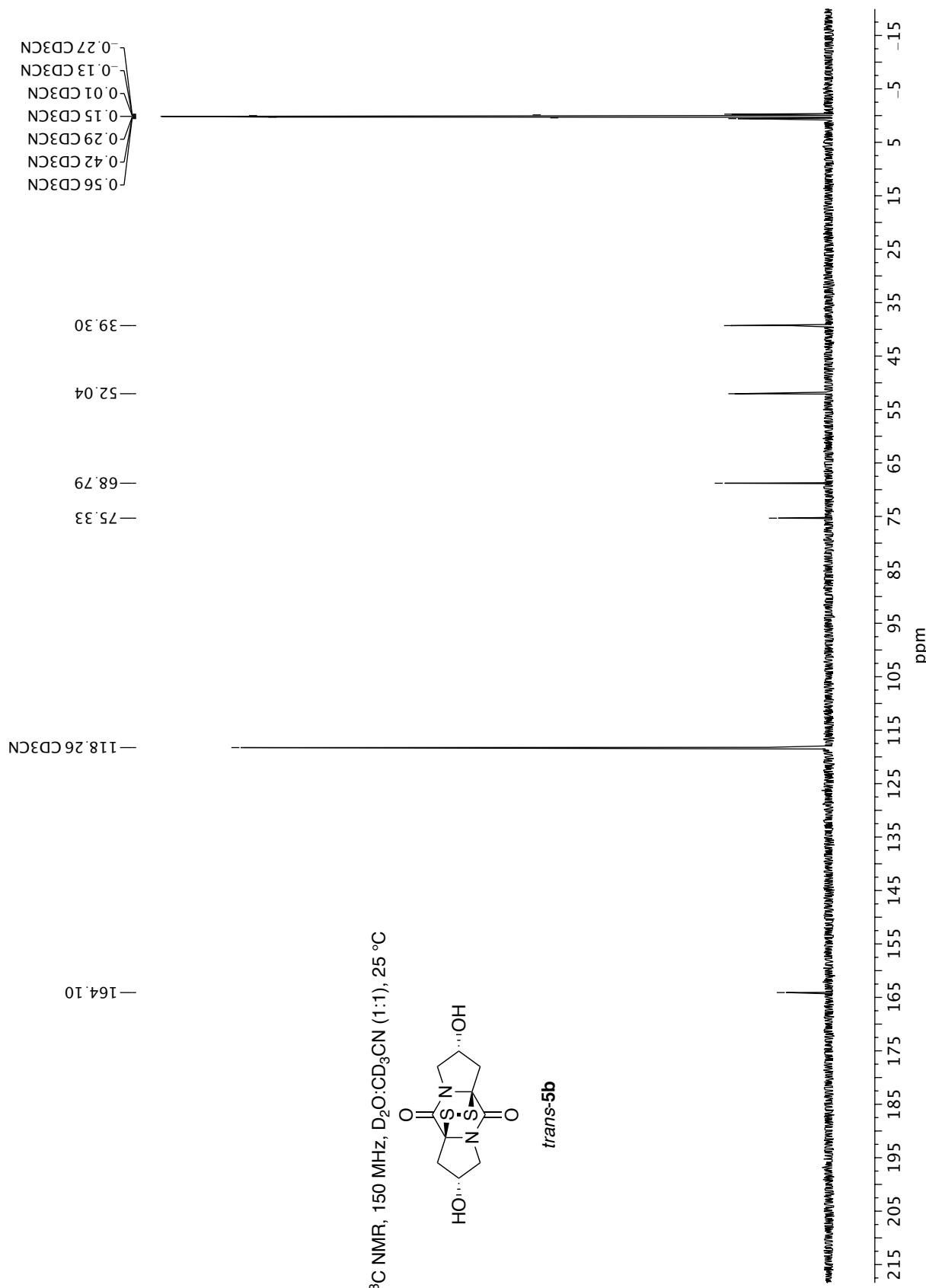


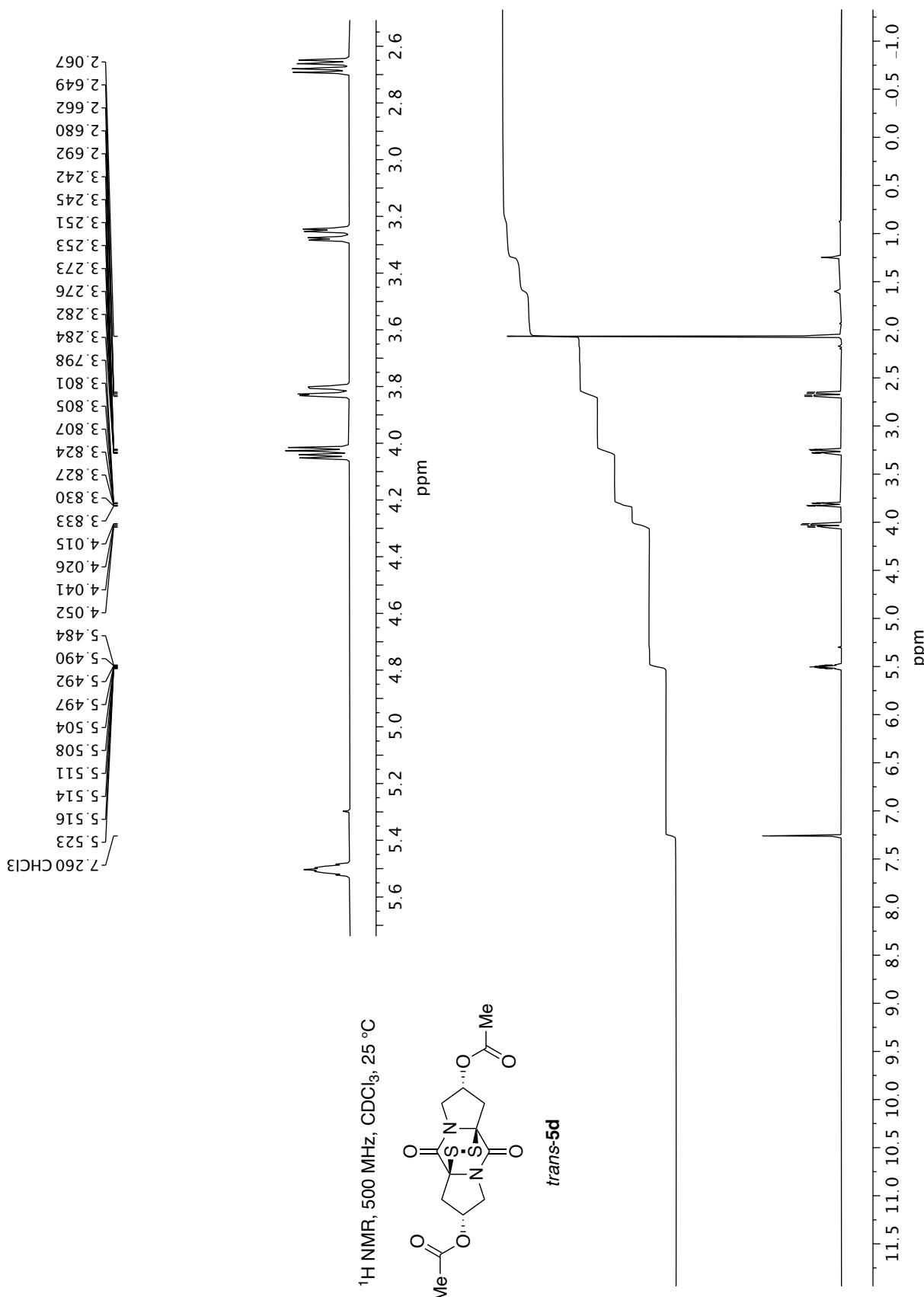


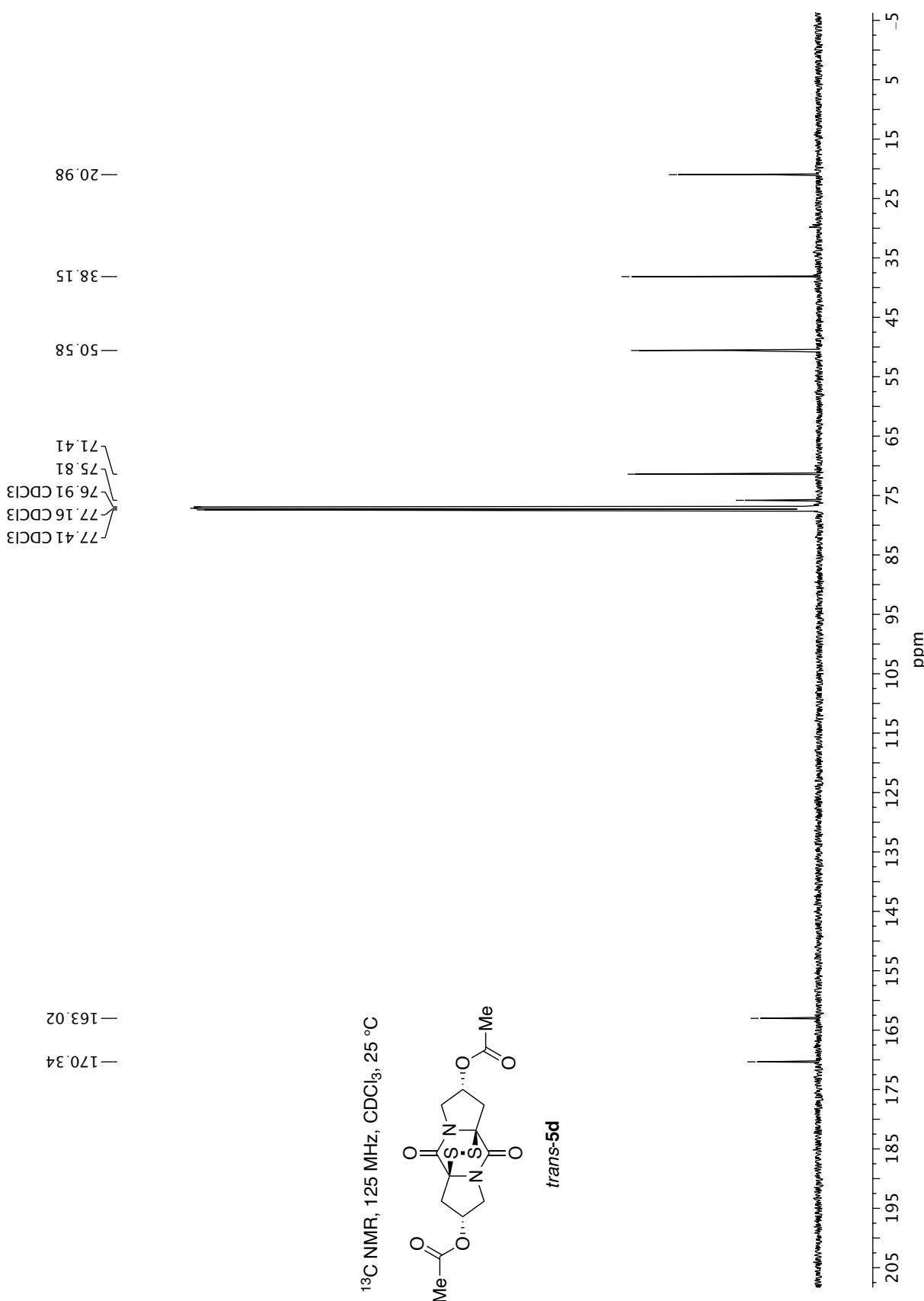


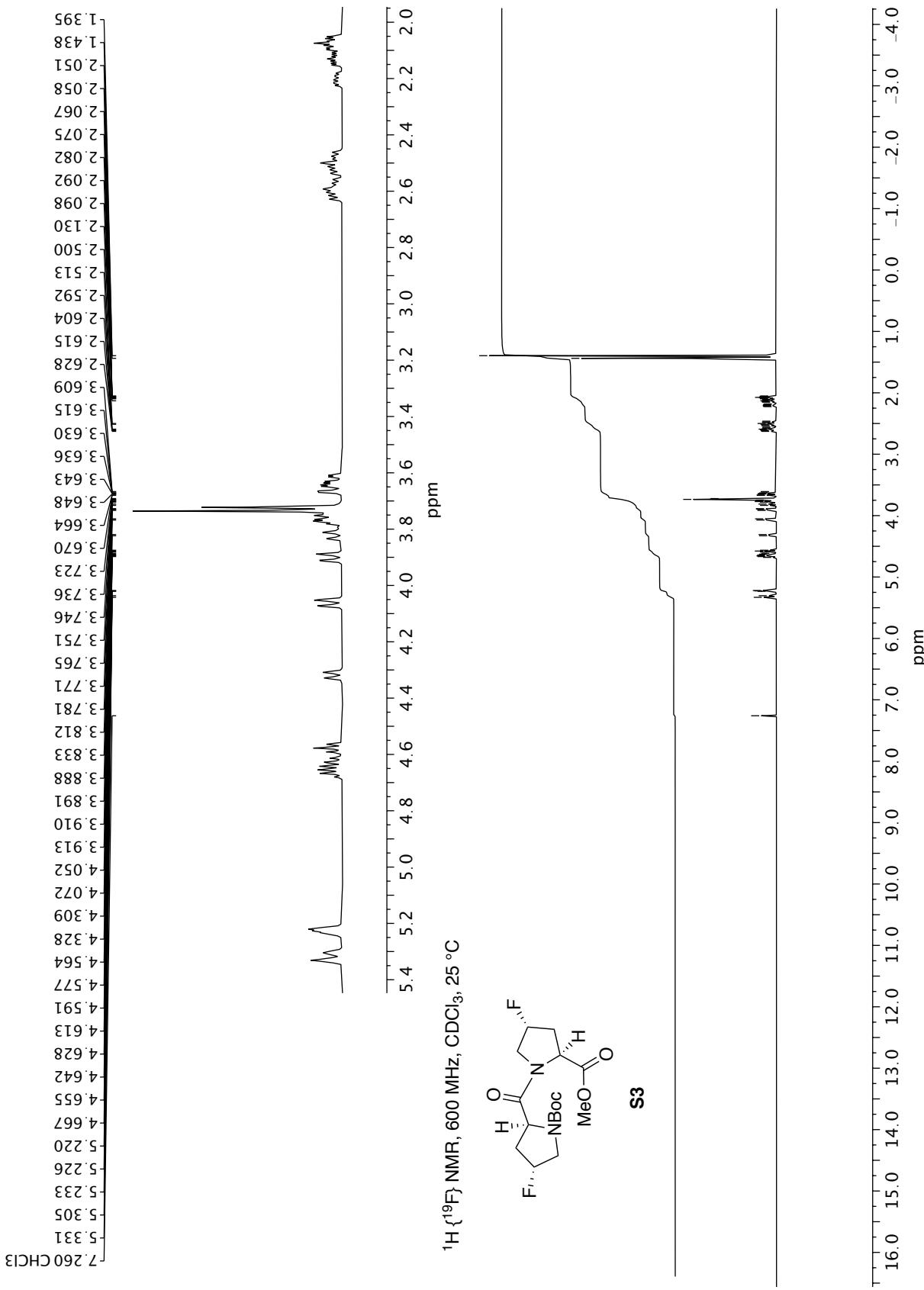


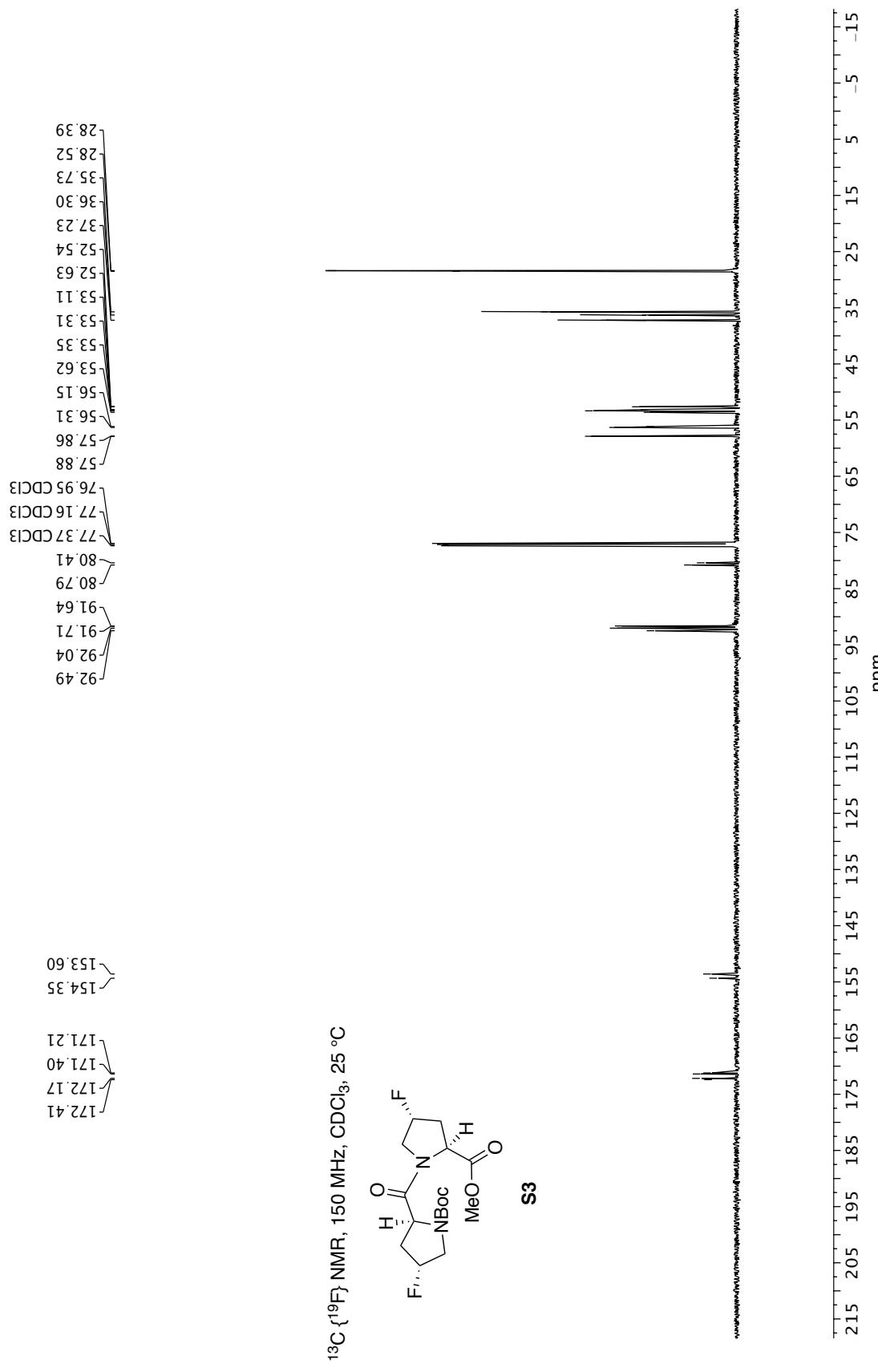


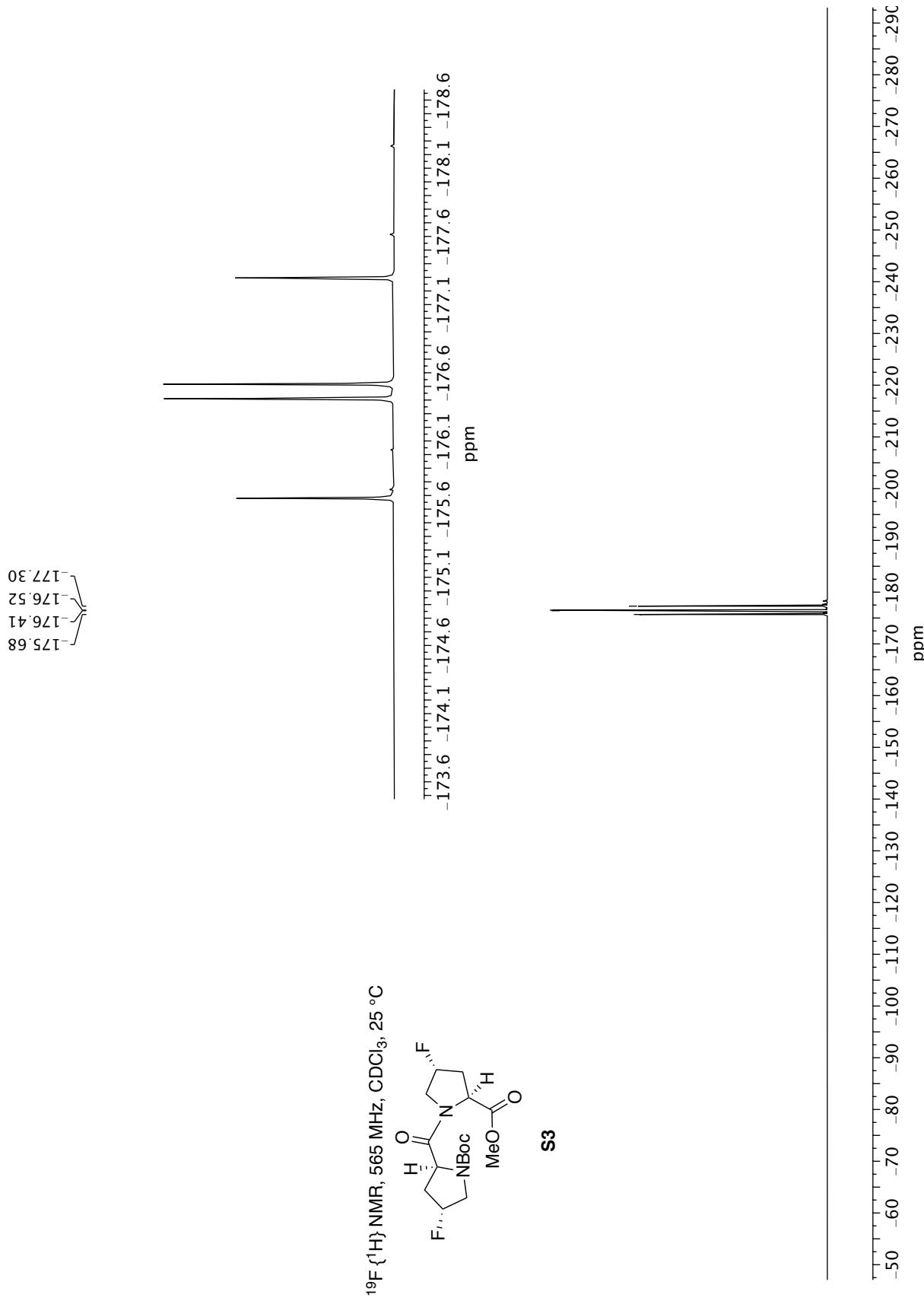


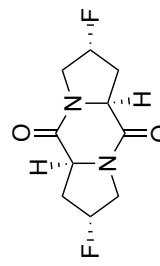
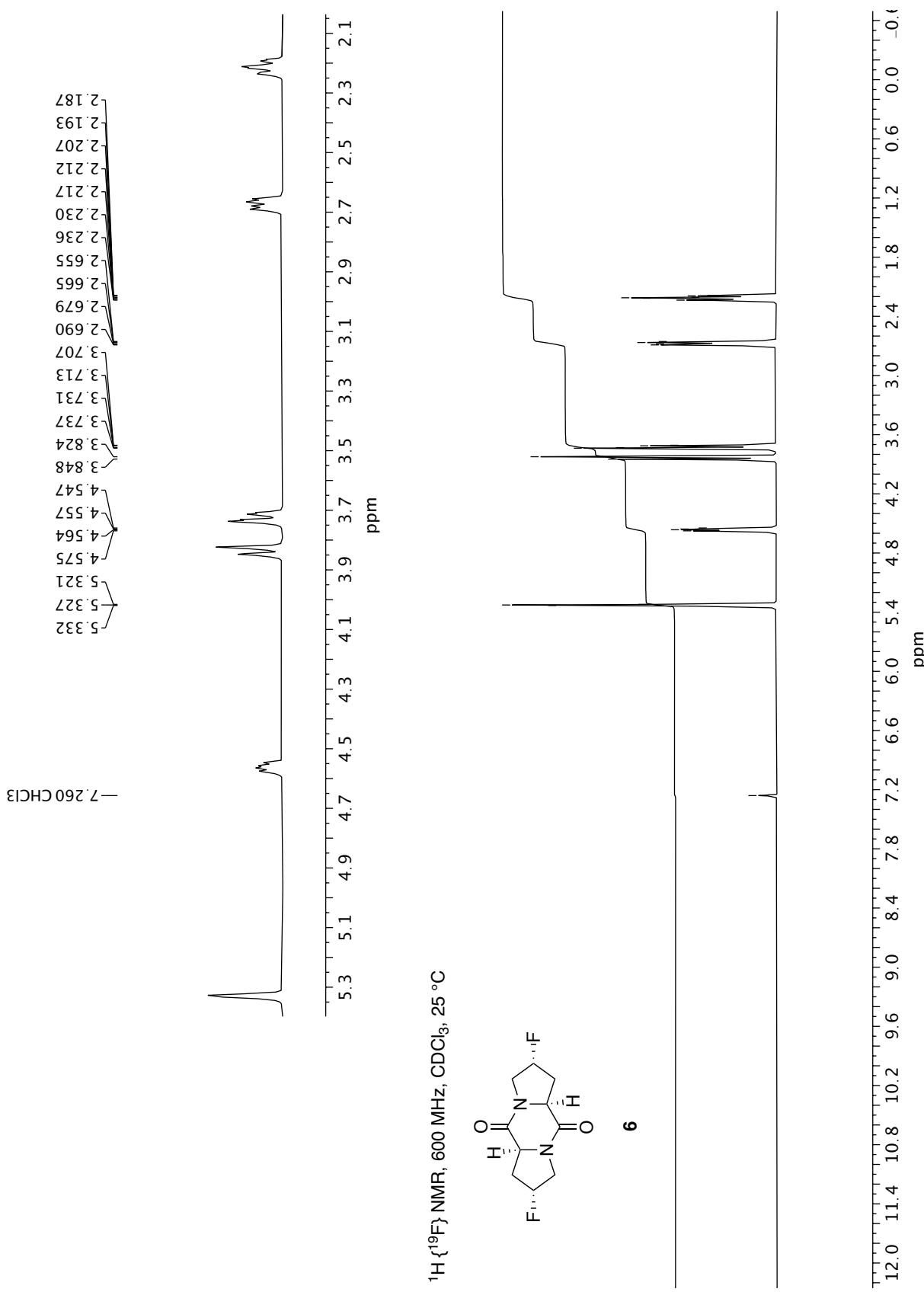


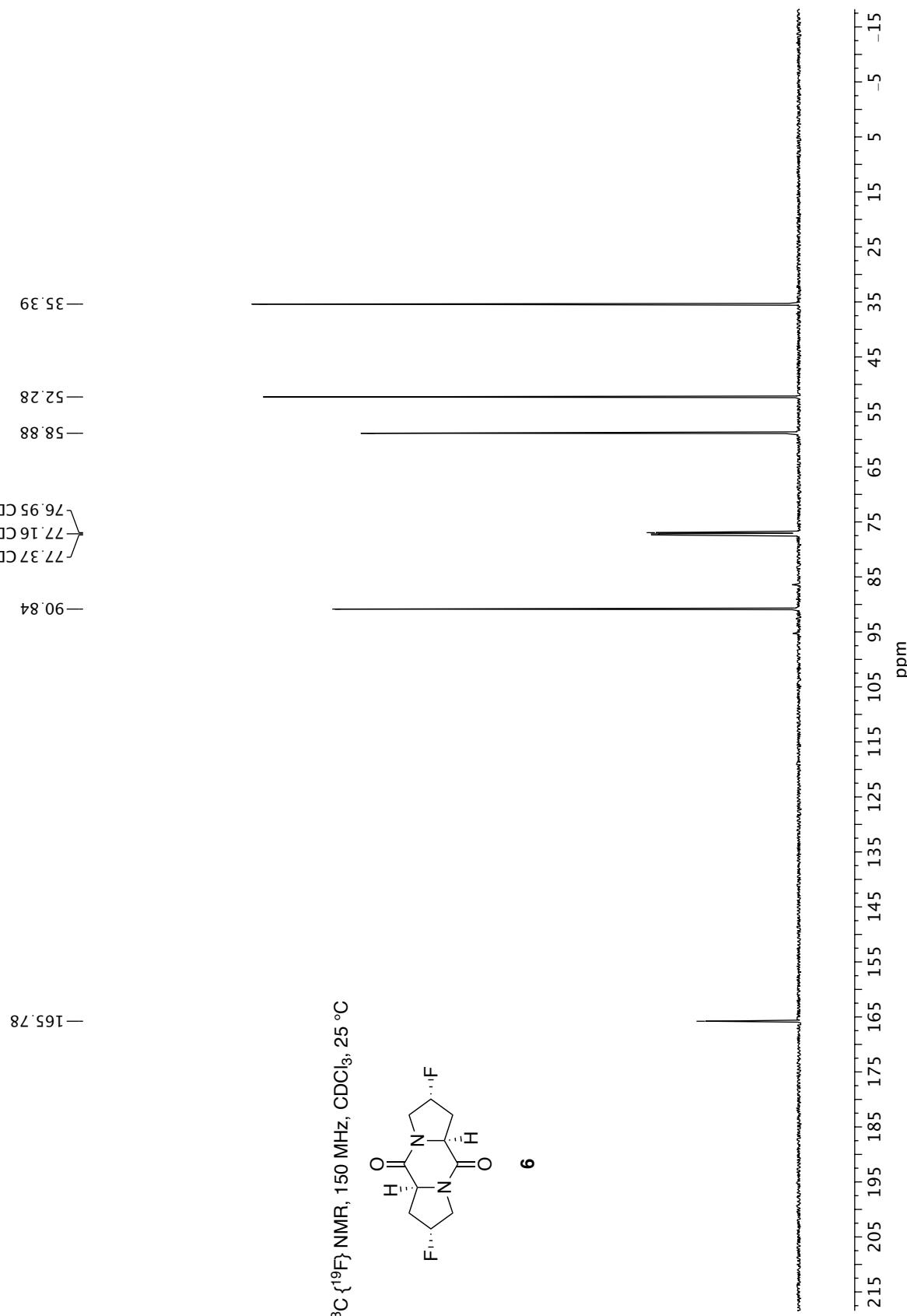






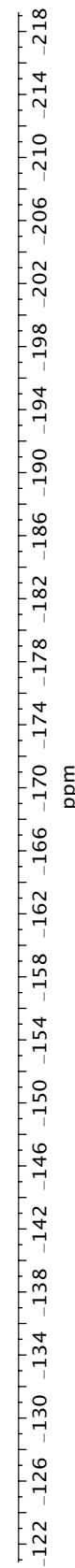
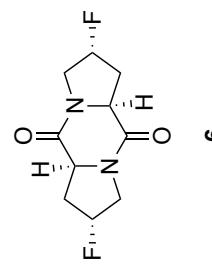


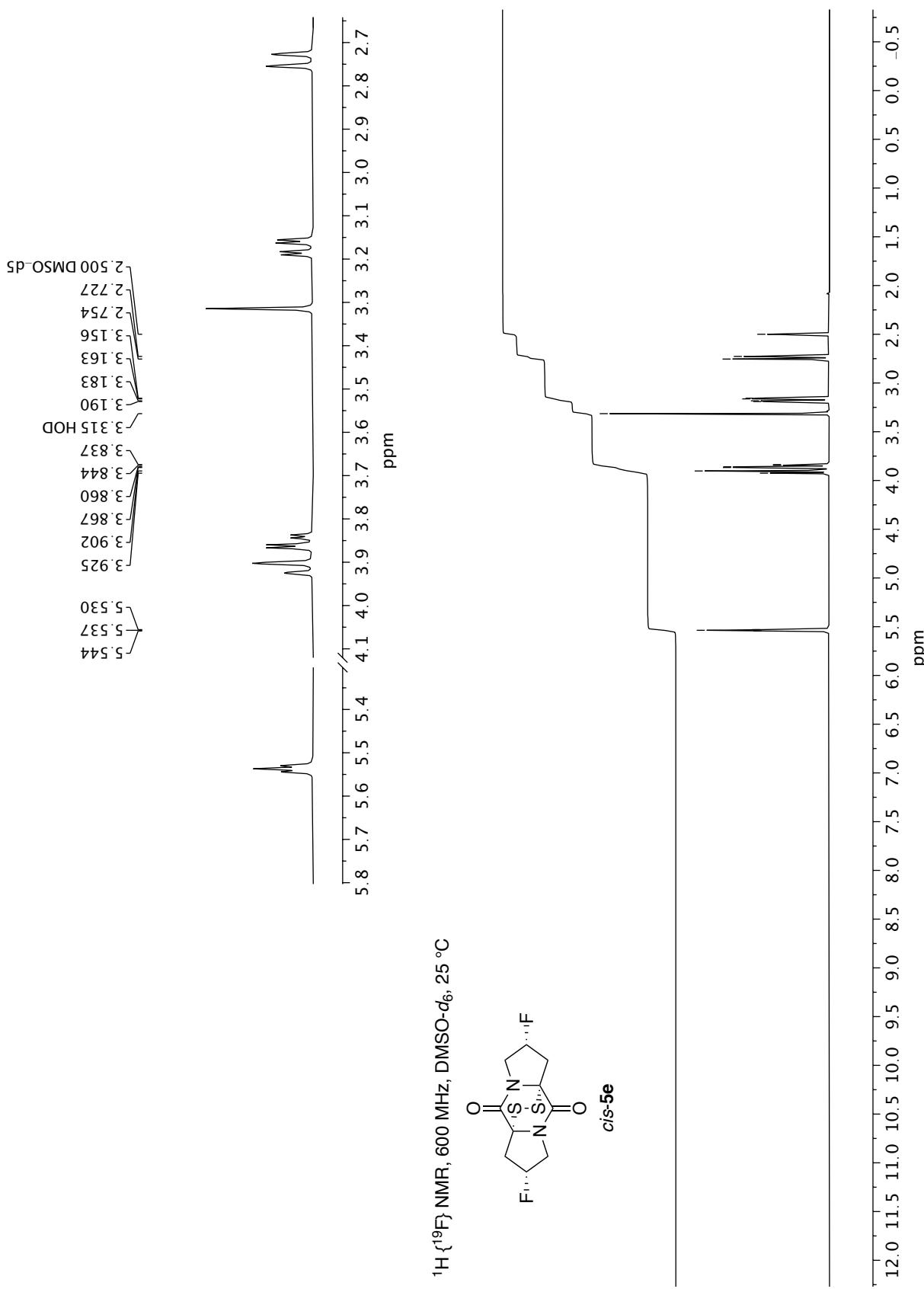


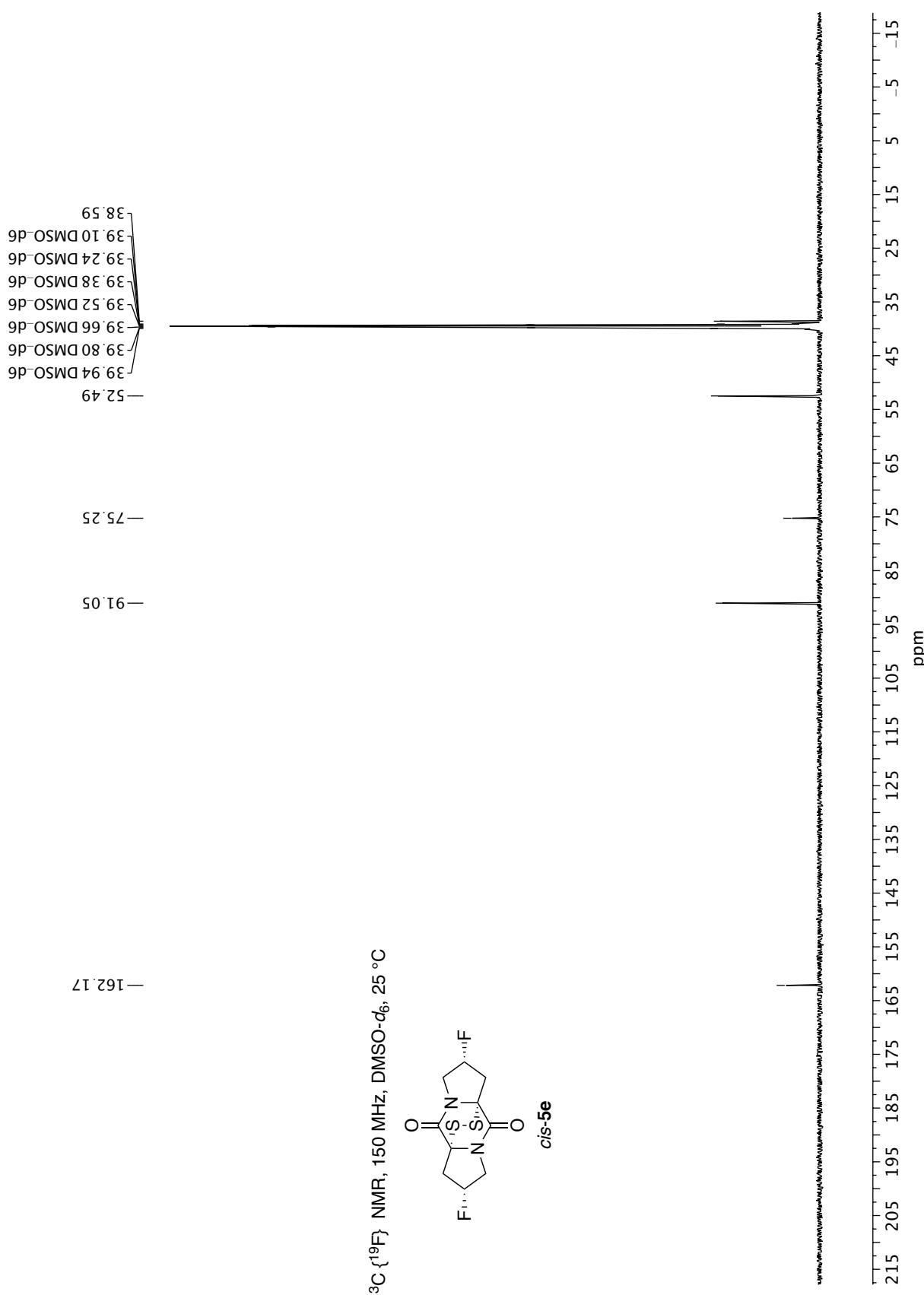


—^{174.33}

¹⁹F-{¹H} NMR, 565 MHz, CDCl₃, 25 °C

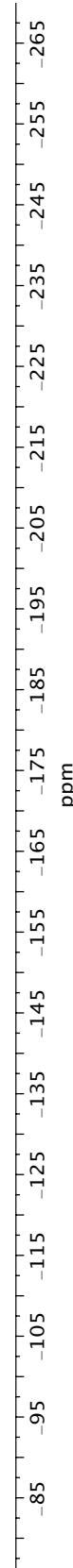
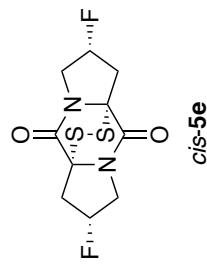


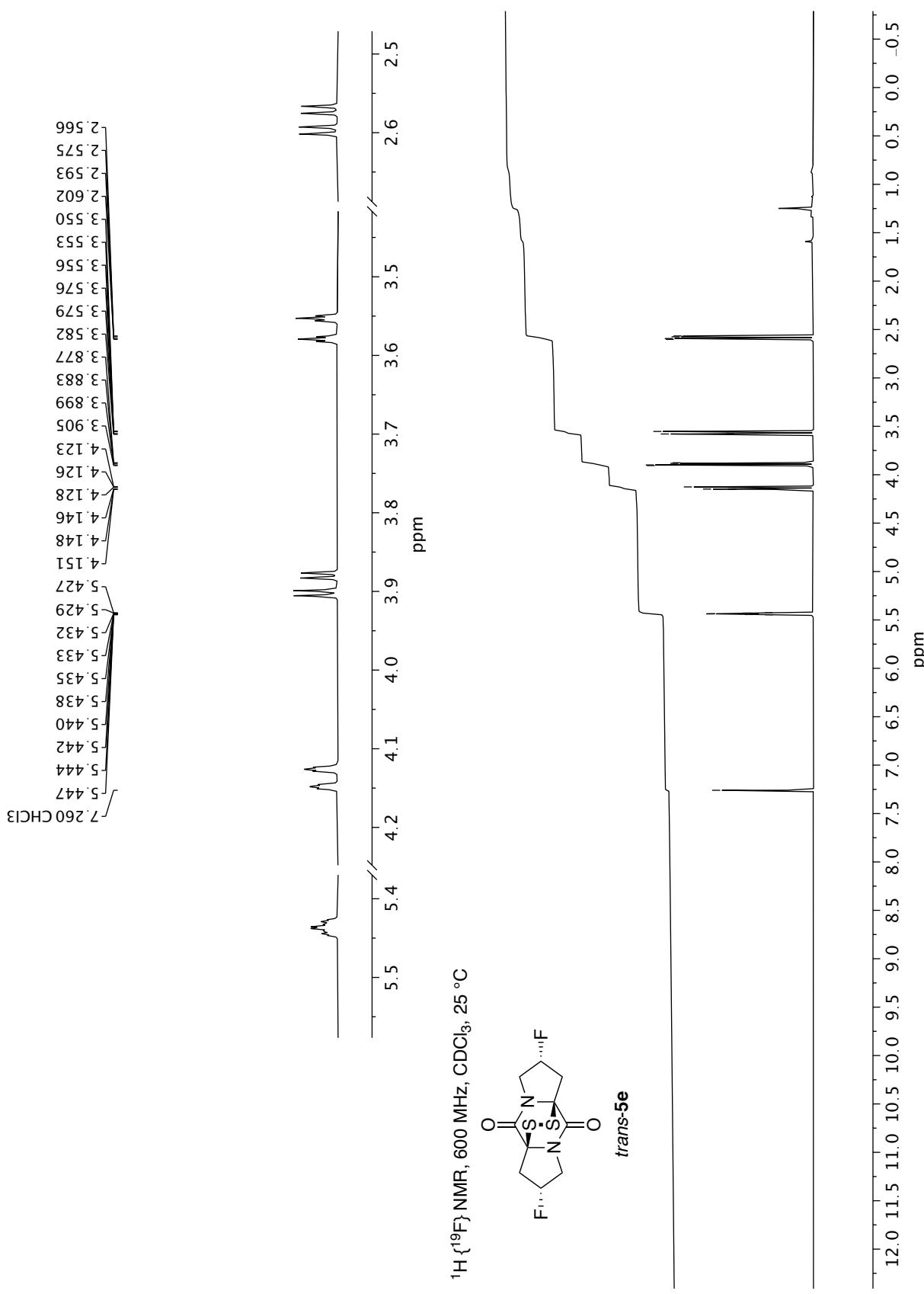


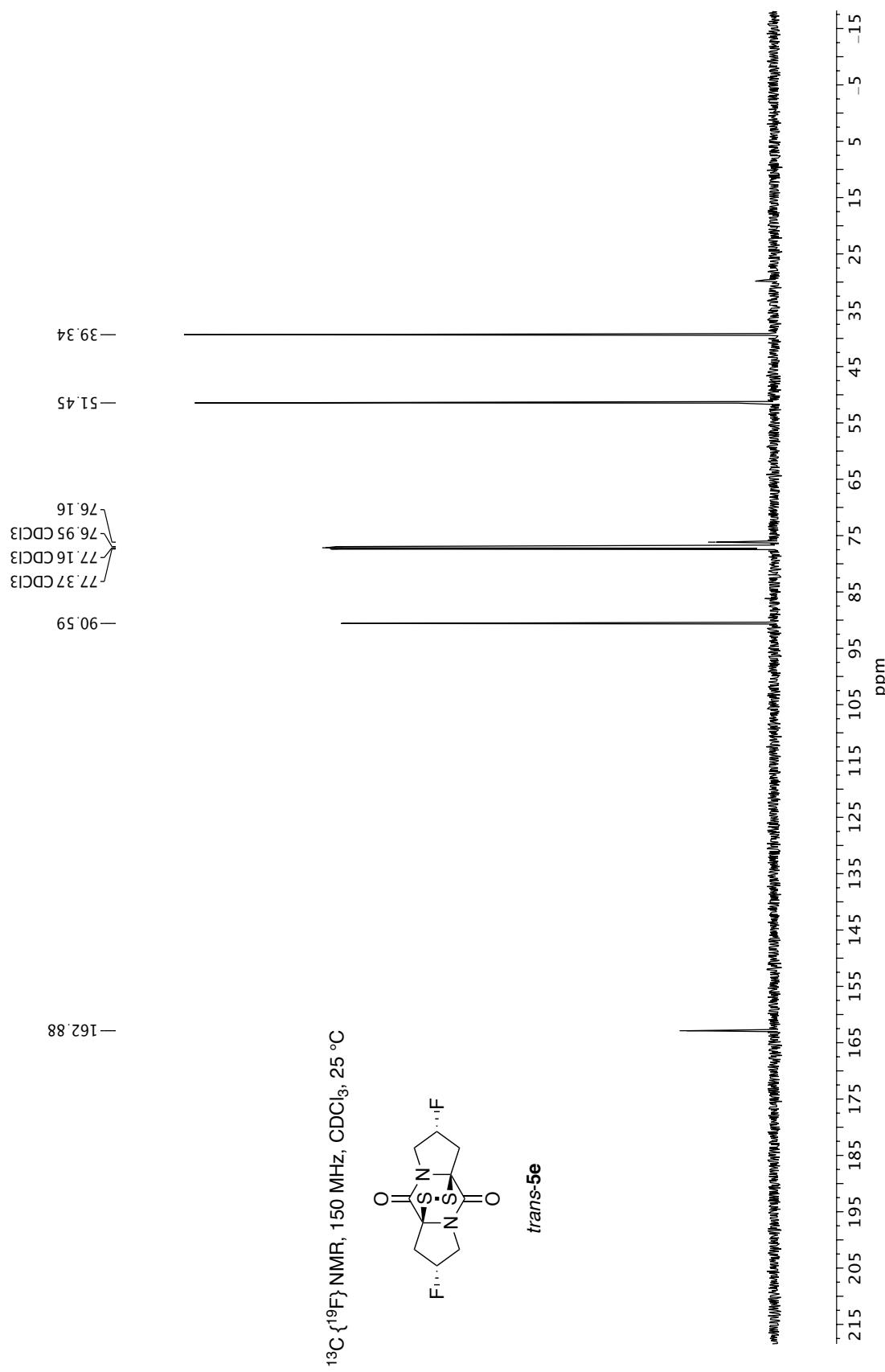


—¹⁹F-1H NMR, 565 MHz, DMSO-d₆, 25 °C

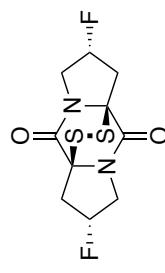
¹⁹F-{¹H} NMR, 565 MHz, DMSO-d₆, 25 °C





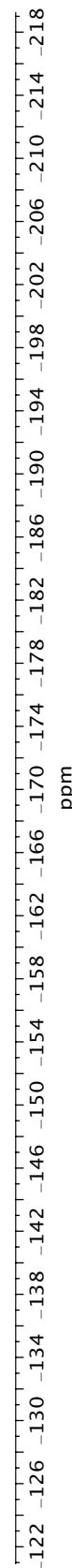


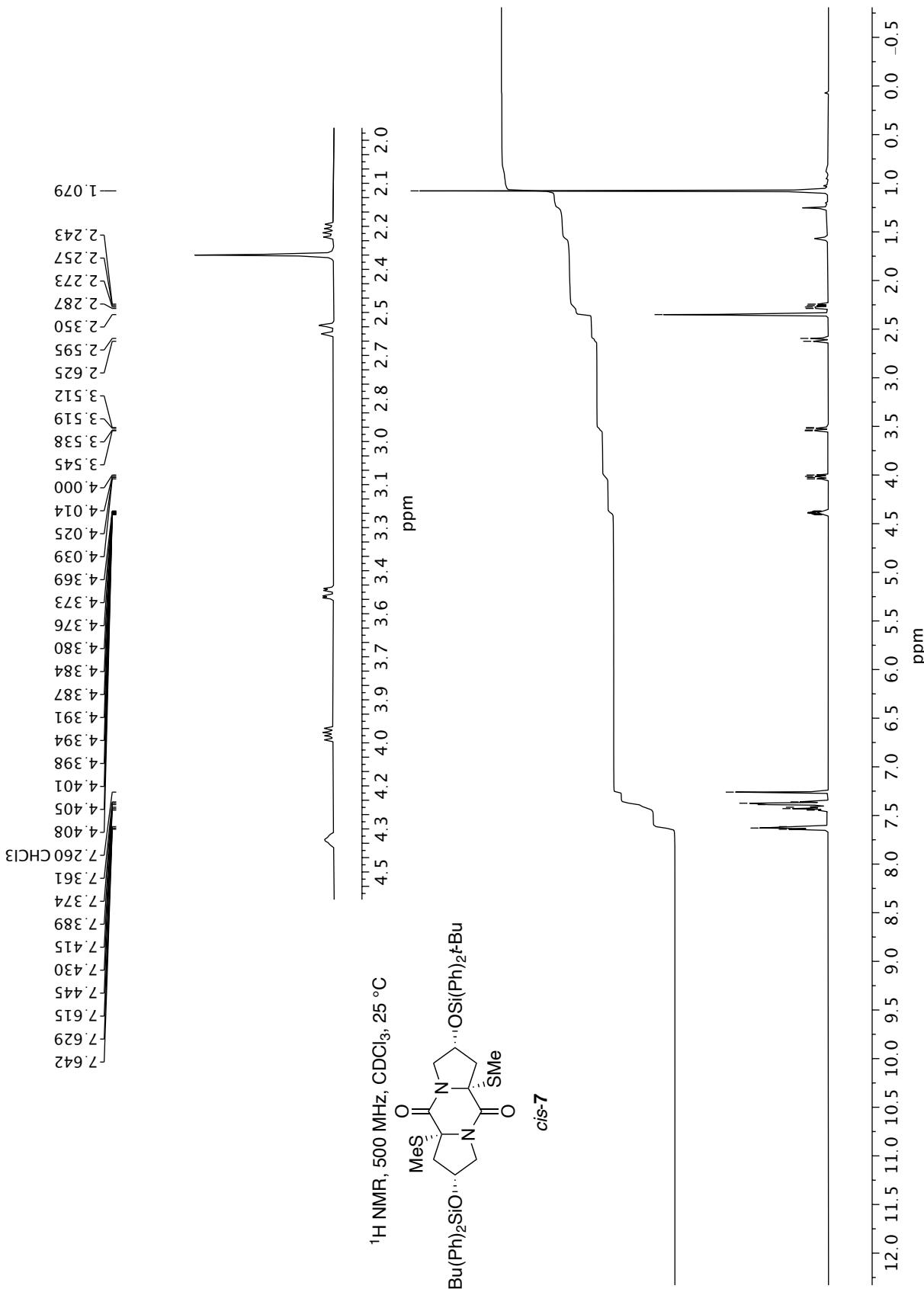
$^{19}\text{F}\{\text{H}\}$ NMR, 565 MHz, CDCl_3 , 25 °C

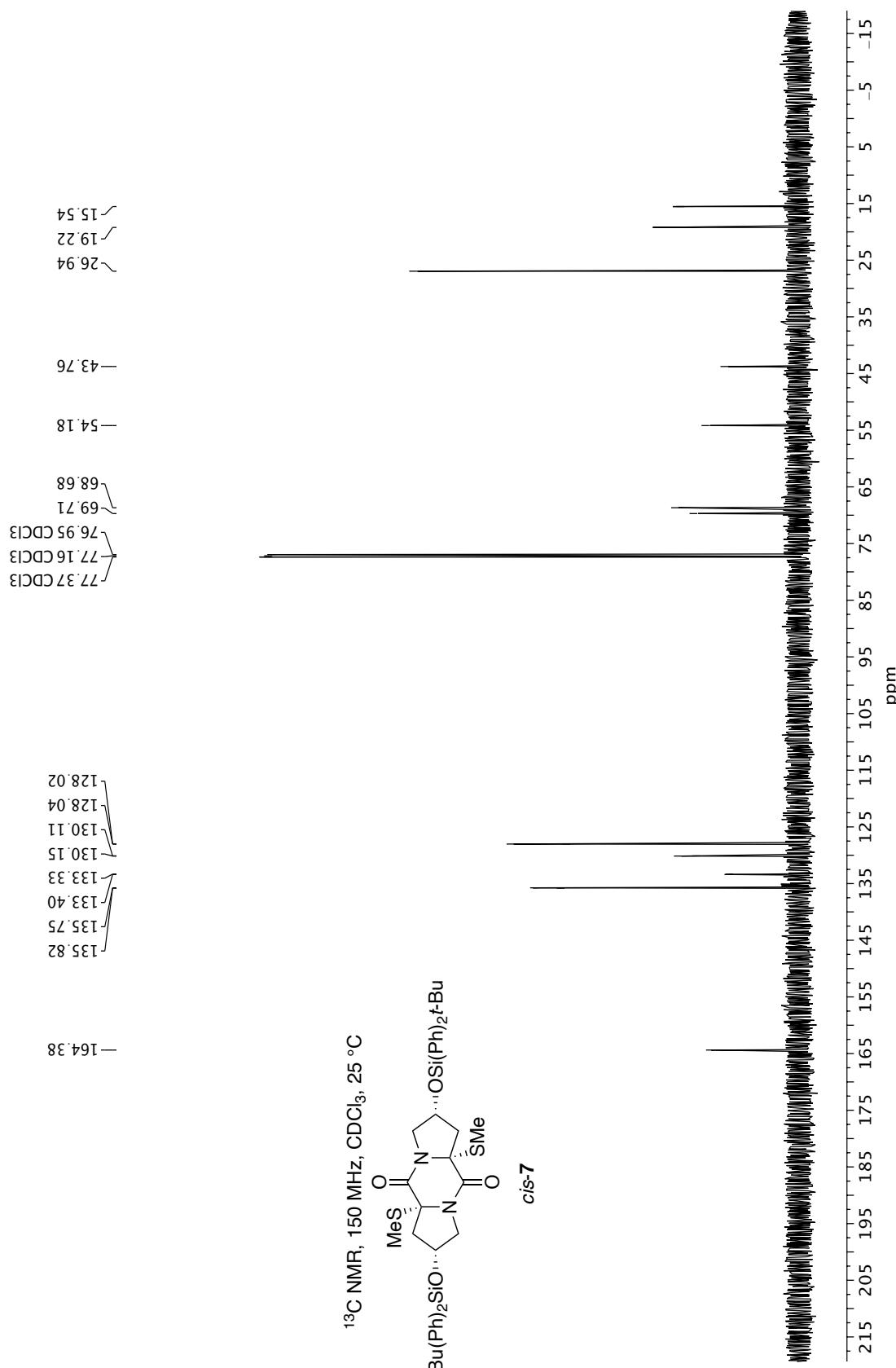


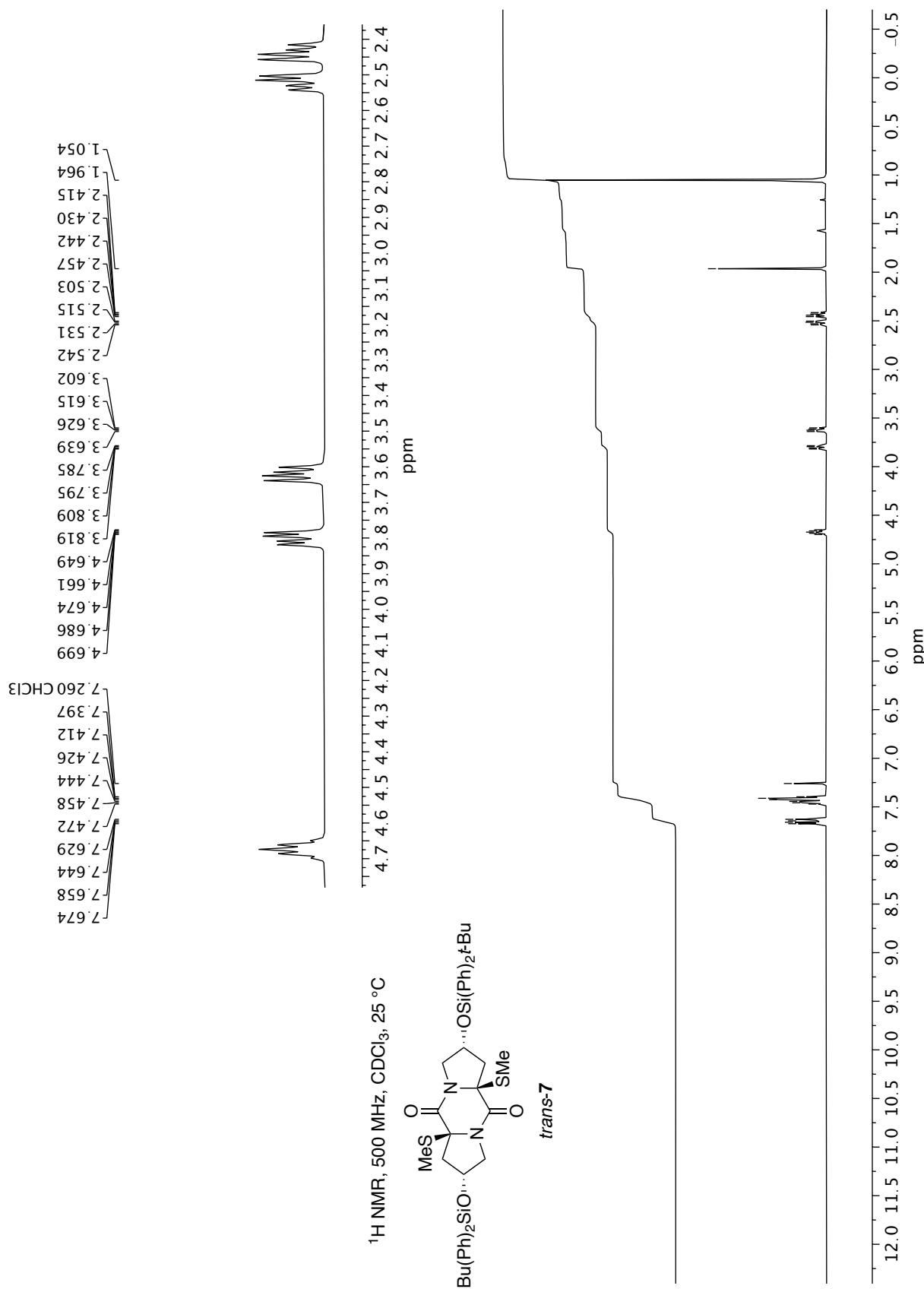
trans-5e

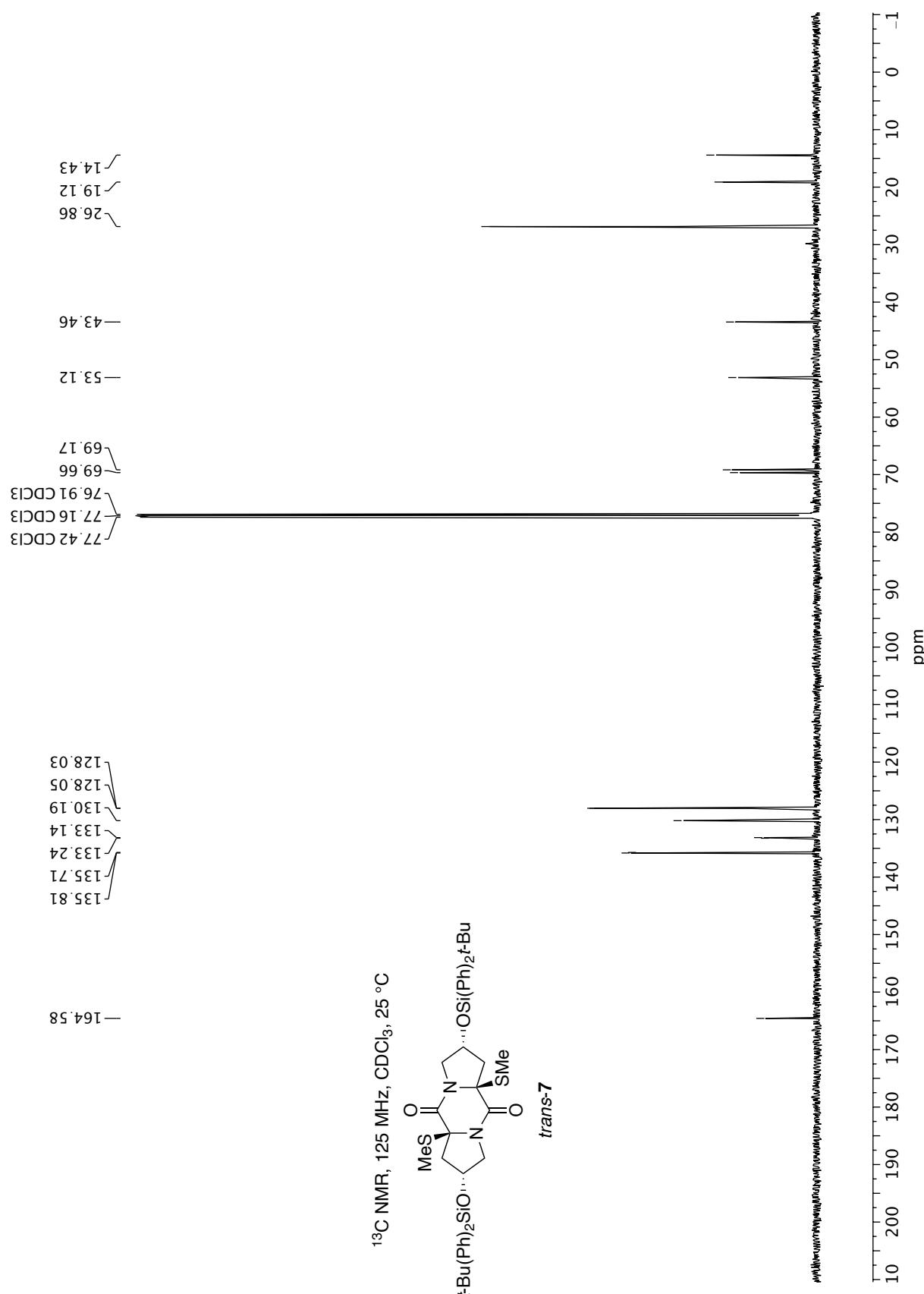
—175.31

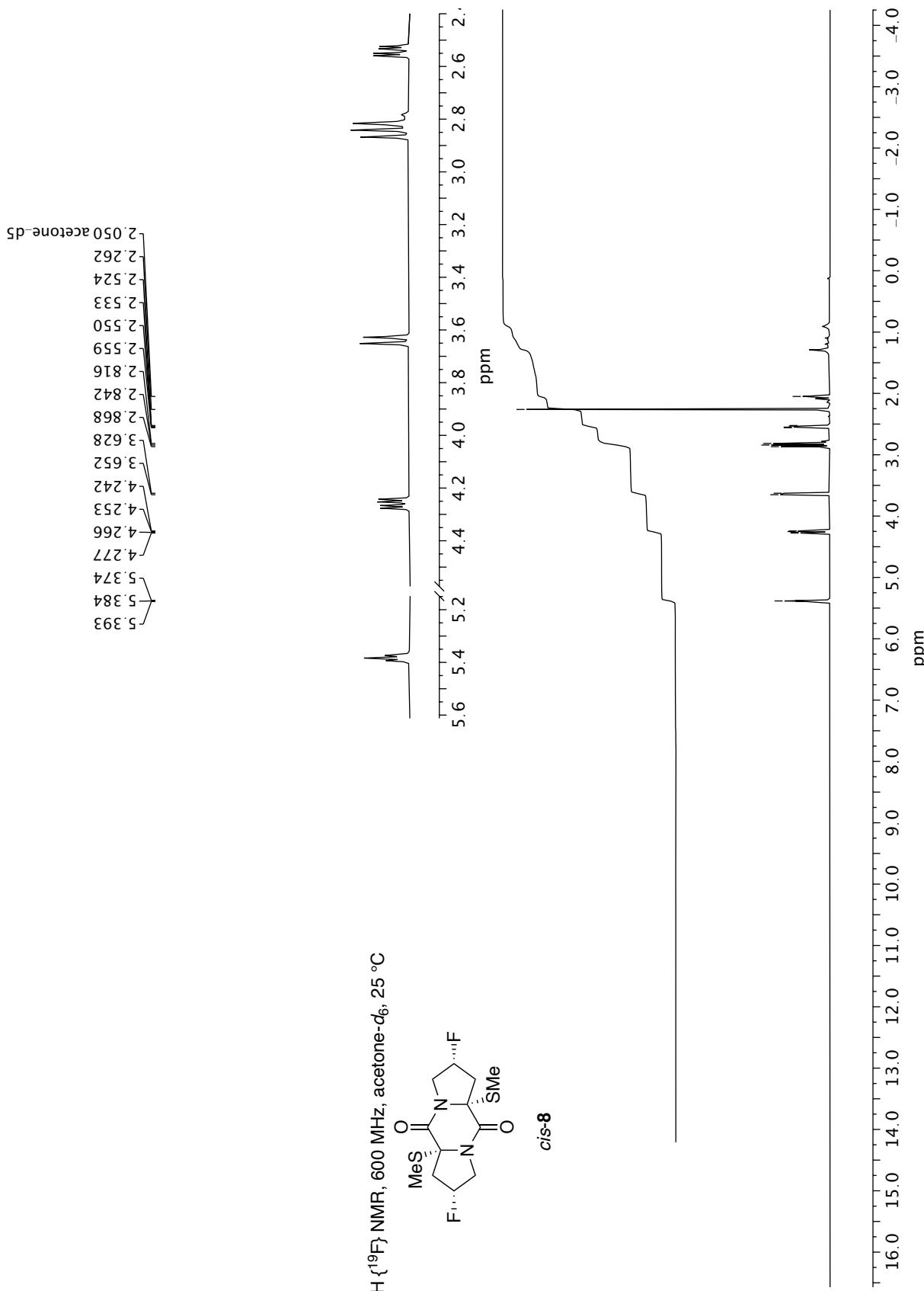


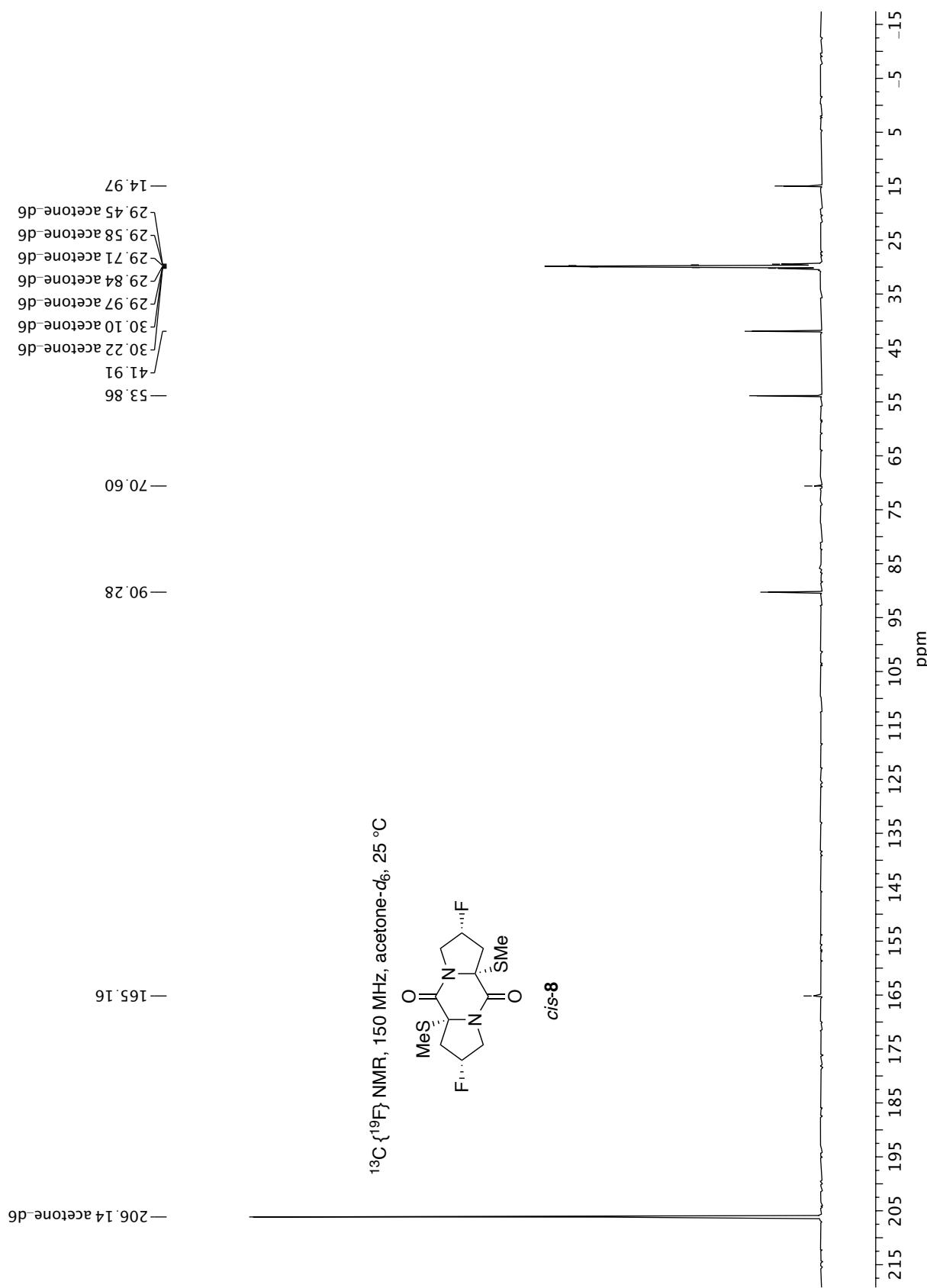




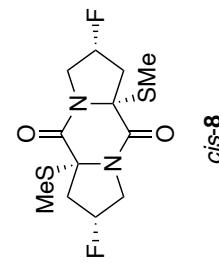




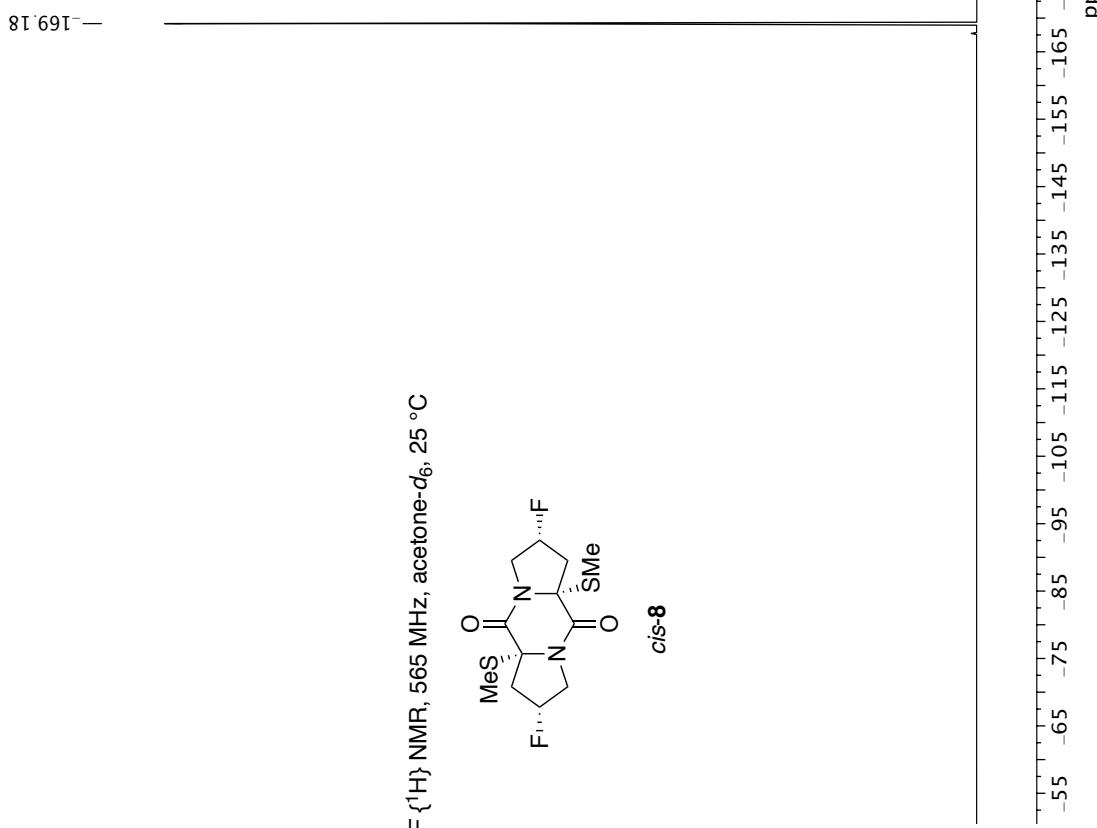


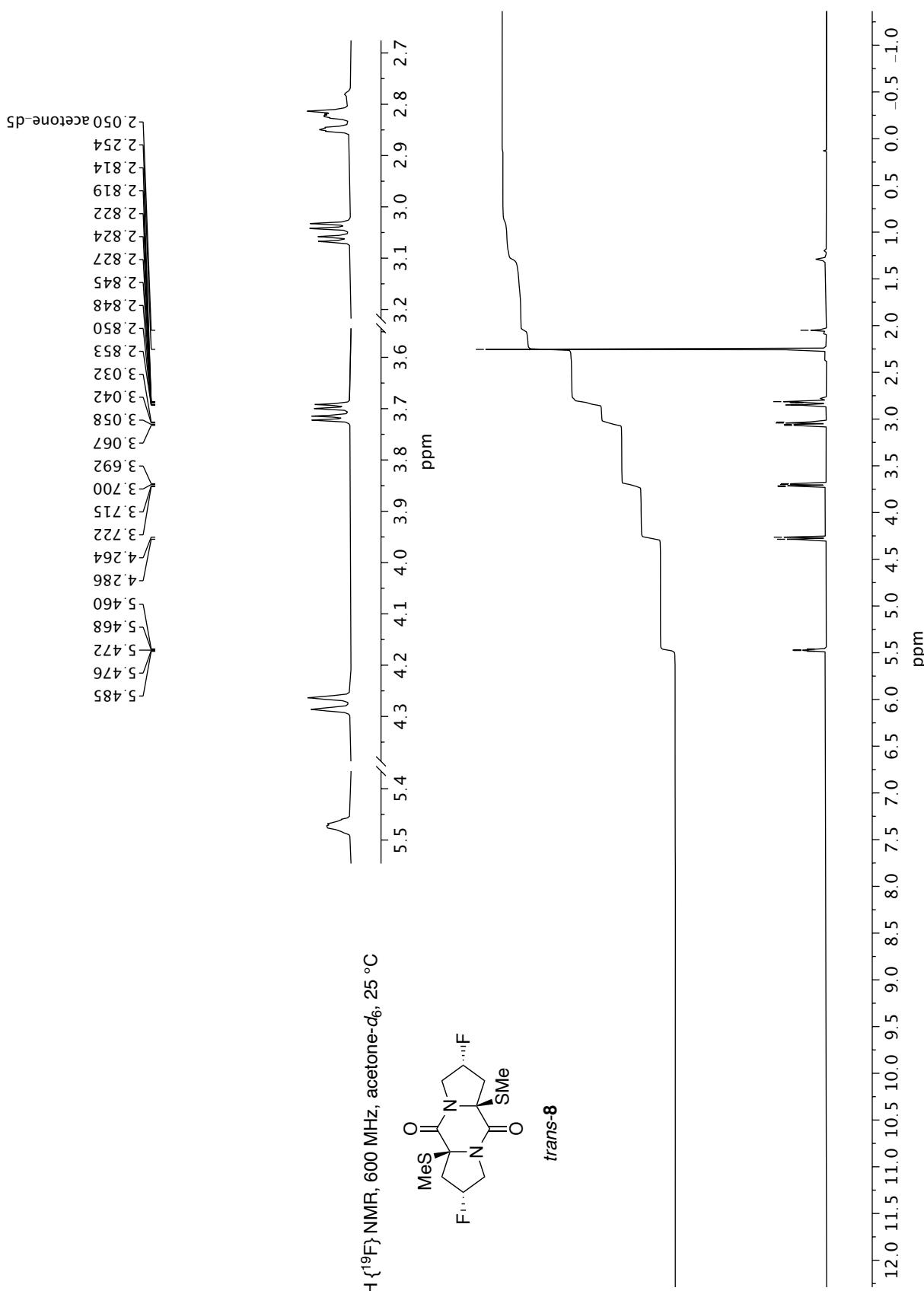


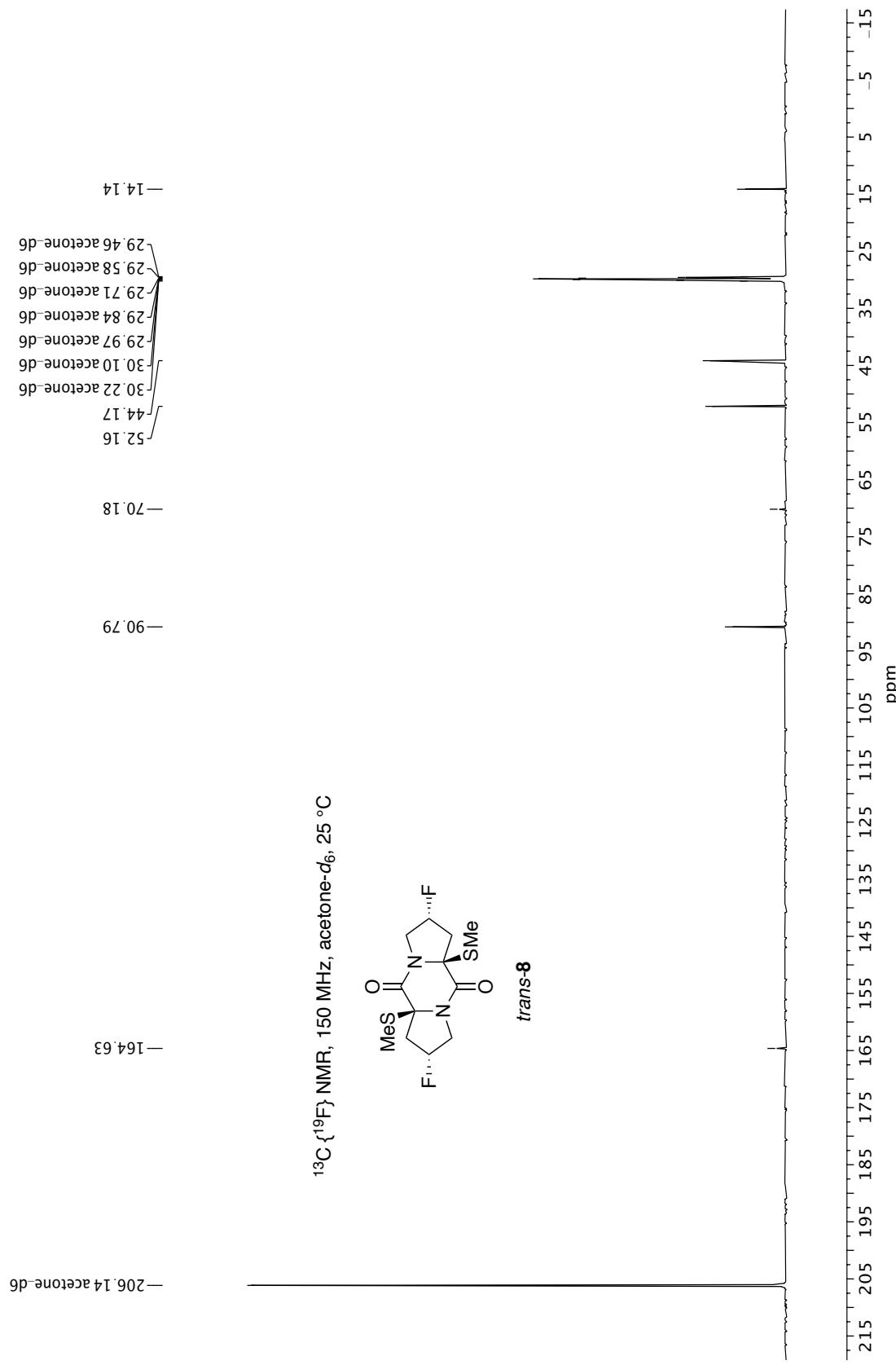
$^{19}\text{F}\{\text{H}\}$ NMR, 565 MHz, acetone- d_6 , 25 °C



cis-8

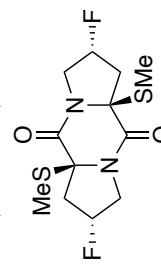






—177.50

$^{19}\text{F}\{\text{'H}\}$ NMR, 565 MHz, acetone- d_6 , 25 °C



trans-8

