Tricyclic Analogues of Epidithiodioxopiperazine Alkaloids with Promising *In Vitro* and *In Vivo* Antitumor Activity

Marcus Baumann, André P. Dieskau, Brad M. Loertscher, Mary C. Walton, Sangkil Nam, Jun Xie, David Horne,* and Larry E. Overman*

Electronic Supplementary Information

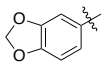
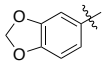
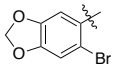
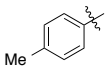
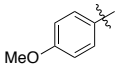
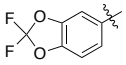
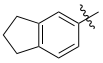
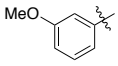
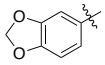
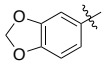
1. Materials and Methods

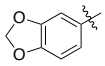
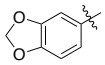
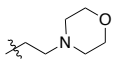
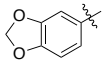
Reactions were performed in oven- or flame-dried glassware under a positive pressure of nitrogen (N_2) or argon (Ar), unless otherwise noted. Tetrahydrofuran (THF), toluene (PhMe), methylene chloride (CH_2Cl_2), methanol (MeOH), acetonitrile (MeCN), *N*,*N*-diisopropylethylamine (*i*-Pr_2NEt), and triethylamine (Et_3N) were dried by passage through activated alumina columns prior to use. Benzaldehyde was distilled prior to use. Precipitated sulfur was recrystallized from benzene prior to use. All other commercial reagents were used as received from the manufacturer unless otherwise stated. Reaction temperatures were controlled using an IKAmag temperature module. Analytical thin-layer chromatography (TLC) and preparative thin-layer chromatography (PTLC) were conducted with E. Merck silica gel 60 F_{254} glass-backed plates (250 μm and 500 μm, respectively). Eluted plates were visualized by UV light (254 nm) or by staining with potassium permanganate or ceric ammonium molybdate. Flash chromatography was performed using forced flow of the indicated solvent system on EMD Geduran® Silica Gel 60. NMR spectra were obtained at 298 K, unless otherwise noted. ^{1}H NMR spectra were obtained using Bruker FT NMR spectrometers (at 500 or 600 MHz) and a Varian FT NMR spectrometer (at 400 MHz). Chemical shifts (δ) are reported in parts per million (ppm) relative to residual $CHCl_3$ signals (δ = 7.26). Data for ^{1}H NMR spectra are reported as follows: chemical shift (δ), multiplicity, coupling constant (Hz), and integration. Splitting patterns are abbreviated as follows: singlet (s), doublet (d), triplet (t), quartet (q), quintet (quint), multiplet (m), broad (br), apparent (app). ^{13}C NMR spectra were recorded on Bruker FT NMR spectrometers (at 125 MHz) and a Varian FT NMR spectrometer (at 100 MHz). Chemical shifts (δ) are reported in parts per million (ppm) relative to residual $CDCl_3$ signals (δ = 77.16). Infrared (IR) spectra were obtained using a Varian 640-IR FT-IR spectrometer as thin films from CH_2Cl_2 on KBr plates and are reported in terms of frequency of absorption (cm^{-1}). High-resolution mass spectra (HRMS) were obtained from the UC Irvine Mass Spectrometry Facility using electrospray ionization (ESI) or chemical ionization (CI).

2. Experimental Procedures

2-1. Table Summary of Yields

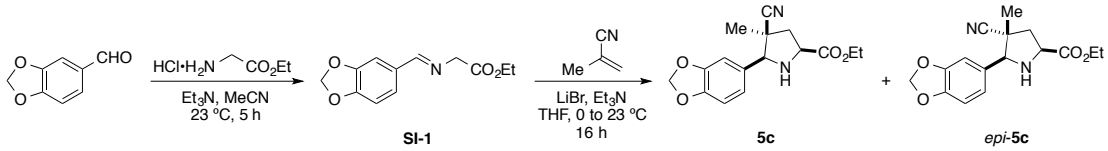
Table 1 Examples and yields for each step of the synthesis

Compound	EWG	R^1	R^2	R^3	Yield[a] **5**	Yield[a] **8**	Yield[a] **3**
a	CO_2Me		Me	Me	87% (endo)	40% (2 steps)	6%
b	CO_2Me		Me	Me	78% (endo)	59% (2 steps)	8%
c	CN		Me	Me	48% (endo) 14% (exo)[b]	80% (2 steps) 4:1 dr	**3c** 46% **13** 3%
d	CN		Me	Me	46% (endo)[c]	59% (2 steps) 2.8:1 dr	**3d** 13% **SI-2** 3%
e	CN		Me	Me	50% (endo) 7% (exo)[d]	44% (2 steps) 5:1 dr	**3e** 20% **12** 3%
f	CN		Me	Me	62% (endo)	61% (2 steps) 10:1 dr	22%
g	CN		Me	Me	48% (endo) 11% (exo)[f]	75% (2 steps)	30%
h	CN		Me	Me	48% (endo)[g]	55% (2 steps) 8:1 dr	27%
i	CN		Me	Me	–[h]	53% (3 steps)	37%
j	CN		Me	Me	13%	41% (2 steps)	28%
k	CN		Me	Me	67%[i]	70% (2 steps)	13%
l	CN		Me	Et	see **5c**	73% (2 steps)	24%
m	CN		Me	*n*-Bu	see **5c**	72% (2 steps)	31%

n	CN		Me		see **5c**	17% (2 steps)	13%
o	CN		Me		see **5c**	70% (2 steps)	27%
p	CN		Bn	Me	see **5c**	63% (3 steps)[j]	12%

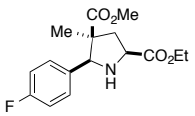
[a]Yield of isolated product. [b]2.4:1 ratio of endo:exo products by ^{1}H NMR analysis of the crude cycloadduct. [c]12:1 ratio of endo:exo products by ^{1}H NMR analysis of the crude cycloadduct. [d]3.0:1 ratio of endo:exo products by ^{1}H NMR analysis of the crude cycloadduct. [e]3.1:1 ratio of endo:exo products by ^{1}H NMR analysis of the crude cycloadduct. [f]2.6:1 ratio of endo:exo products by ^{1}H NMR analysis of the crude cycloadduct. [g]3.5:1 ratio of endo:exo products by ^{1}H NMR analysis of the crude cycloadduct. [h]13:1 ratio of endo:exo products by ^{1}H NMR analysis of the crude cycloadduct. Crude cycloadduct **5i** was carried forward without purification. [i]2.0:1 ratio of endo:exo products by ^{1}H NMR analysis of the crude cycloadduct. [j]Average of yields for both diastereomers, see procedure of **8p** for details.

2-2. General Procedure 1: Preparation of Pyrrolidines



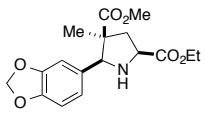
Imine **SI-1** was prepared using an adaptation of the procedure of Zhang and coworkers.[1] A 250 mL round-bottom flask was charged with piperonal (2.3 g, 15 mmol, 1.0 equiv), glycine ethyl ester hydrochloride (3.2 g, 23 mmol, 1.5 equiv), and a magnetic stir bar. MeCN (25 mL) was added, followed by Et_3N (3.1 mL, 23 mmol, 1.5 equiv). The heterogeneous reaction mixture was stirred vigorously at 23 °C for 5 h. The crude reaction mixture was concentrated under reduced pressure and the resulting solid was transferred to a separatory funnel with CH_2Cl_2 (25 mL) and H_2O (40 mL). The layers of the resulting biphasic mixture were partitioned, and the aqueous layer was extracted with CH_2Cl_2 (2 x 25 mL). The combined organic layers were dried over Na_2SO_4. Upon concentrating under reduced pressure, imine **SI-1** (3.5 g, quantitative yield) was isolated as a light yellow oil and carried forward without further purification. A 100 mL round-bottom flask was charged with a solution of imine **SI-1** (3.5 g, 15 mmol, 1.0 equiv) in THF (25 mL) and a magnetic stir bar. Solid LiBr (1.6 g, 18 mmol, 1.2 equiv) was added followed by Et_3N (2.5 mL, 18 mmol, 1.2 equiv). The reaction mixture was cooled to 0 °C and methacrylonitrile (1.9 mL, 23 mmol, 1.5 equiv) was added dropwise. The homogenous solution was allowed to warm to 23 °C. After 16 h, the reaction mixture was concentrated under reduced pressure and

the resulting oil was transferred to a separatory funnel with CH_2Cl_2 (25 mL) and H_2O (40 mL). The layers of the resulting biphasic mixture were partitioned and the aqueous layer was extracted with CH_2Cl_2 (2 x 25 mL). The combined organic layers were washed with brine (40 mL), dried over Na_2SO_4, and concentrated under reduced pressure. ^{1}H NMR analysis of the crude material indicated a 2.4:1 mixture of **5c**:*epi*-**5c**. The crude product was purified by flash chromatography (4:1 to 1:1 EtOAc/hexanes, gradient elution) to afford pyrrolidines **5c** (2.15 g, 48% yield) and *epi*-**5c** (650 mg, 14% yield) as yellow oils. The spectral data were consistent with those previously reported.[2] **Ethyl *rac*-(2*S*,4*S*,5*S*)-5-(benzo[*d*][1,3]dioxol-5-yl)-4-cyano-4-methylpyrrolidine-2-carboxylate (5c).** ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.08 (s, 1H), 6.94 (d, *J* = 8.5 Hz, 1H), 6.80 (d, *J* = 8.5 Hz, 1H), 5.96 (s, 2H), 4.28 (q, *J* = 7.0 Hz, 2H), 3.95 (dd, *J* = 9.5, 4.5 Hz, 1H), 3.85 (s, 1H), 2.80 (dd, *J* = 13.5, 4.0 Hz, 1H), 2.69 (br s, 1H), 2.25 (dd, *J* = 13.5, 9.5 Hz, 1H), 1.40 (s, 3H), 1.33 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 173.0 (C), 148.1 (C), 147.9 (C), 130.6 (C), 122.1 (C), 121.2 (CH), 108.2 (CH), 107.9 (CH), 101.3 (CH_2), 72.2 (CH), 61.7 (CH_2), 57.1 (CH), 43.9 (C), 42.2 (CH_2), 22.2 (CH_3), 14.3 (CH_3); IR (thin film): 3361, 2984, 2900, 2254, 1734, 1490, 1447, 1265, 1041, 909 cm^{-1}; HRMS-ESI (*m/z*) $[M + Na]^+$ calculated for $C_{16}H_{18}N_2O_4Na$, 325.1164; found, 325.1161. **Ethyl *rac*-(2*S*,4*R*,5*S*)-5-(benzo[*d*][1,3]dioxol-5-yl)-4-cyano-4-methylpyrrolidine-2-carboxylate (*epi*-5c).** ^{1}H NMR (600 MHz, $CDCl_3$): δ 6.98 (app d, *J* = 1.4 Hz, 1H), 6.93 (app dd, *J* = 8.1, 1.4 Hz, 1H), 6.80 (app d, *J* = 8.1 Hz, 1H), 5.96 (s, 2H), 4.50 (s, 1H), 4.24 (q, *J* = 7.1 Hz, 2H), 4.05–4.02 (m, 1H), 2.72 (dd, *J* = 13.2, 9.9 Hz, 1H), 2.63 (br s, 1H), 2.21 (dd, *J* = 13.2, 6.0 Hz, 1H), 1.31 (t, *J* = 7.1 Hz, 3H), 1.00 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 173.1 (C), 147.9 (C), 147.7 (C), 130.5 (C), 124.1 (C), 120.7 (CH), 108.4 (CH), 107.7 (CH), 101.3 (CH_2), 69.3 (CH), 61.7 (CH_2), 57.2 (CH), 41.5 (CH_2), 40.2 (C), 20.6 (CH_3), 14.3 (CH_3); IR (thin film): 3348, 2982, 2901, 2234, 1735, 1489, 1445 cm^{-1}; HRMS-ESI (*m/z*) $[M + Na]^+$ calculated for $C_{16}H_{18}N_2O_4Na$, 325.1164; found, 325.1156.



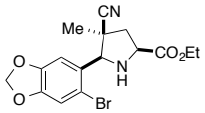
5a

2-Ethyl 4-methyl *rac*-(2*S*,4*S*,5*S*)-5-(4-fluorophenyl)-4-methylpyrrolidine-2,4-dicarboxylate (5a). Prepared according to **General Procedure 1** from 4-fluorobenzaldehyde (110 μL, 1.0 mmol) and methyl methacrylate (160 μL, 1.5 mmol) affording **5a** (270 mg, 0.87 mmol, 87% yield) as a clear oil. The spectral data were consistent with those previously reported.[2] ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.26 (dd, *J* = 8.5, 5.5 Hz, 2H), 6.98 (app t, *J* = 8.6 Hz, 2H), 4.30–4.24 (m, 2H), 4.04 (s, 1H), 4.00 (dd, *J* = 8.7, 7.4 Hz, 1H), 3.25 (s, 3H), 2.70 (dd, *J* = 13.4, 7.4 Hz, 1H), 2.61 (br s, 1H), 2.09 (dd, *J* = 13.4, 8.7 Hz, 1H) 1.39 (s, 3H), 1.32 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 174.6 (C), 173.8 (C), 162.4 (d, $J_{C–F}$ = 245.0 Hz, C), 134.8 (d, $J_{C–F}$ = 3.1 Hz, C), 128.4 (d, $J_{C–F}$ = 8.0 Hz, 2CH), 115.0 (d, $J_{C–F}$ = 21.2 Hz, 2CH), 73.2 (CH), 61.2 (CH_2), 59.0 (CH), 54.7 (CH), 51.5 (CH_3), 41.2 (CH_2), 22.7 (CH_3), 14.3 (CH_3); IR (thin film): 3373, 2982, 2951, 1733, 1605, 1511, 1448, 1378, 1225, 1160, 1112, 1034, 839 cm^{-1}; HRMS-ESI (*m/z*) [M + Na]$^+$ calculated for $C_{16}H_{20}FNO_4Na$, 332.1274; found, 332.1264.



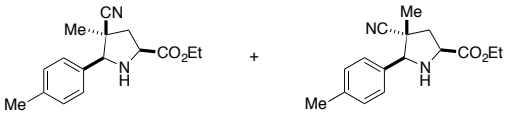
5b

2-Ethyl 4-methyl *rac*-(2*S*,4*S*,5*S*)-5-(benzo[*d*][1,3]dioxol-5-yl)-4-methylpyrrolidine-2,4-dicarboxylate (5b). Prepared according to **General Procedure 1** from piperonal (630 mg, 4.2 mmol) and methyl methacrylate (680 μL, 6.4 mmol) affording **5b** (1.1 g, 3.3 mmol, 78% yield) as a clear oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.77 (s, 1H), 6.72 (d, *J* = 9.8 Hz, 1H), 6.70 (d, *J* = 9.8 Hz, 1H), 5.90 (d, *J* = 8.0 Hz, 1H), 4.29–4.22 (m, 2H), 3.96 (dd, *J* = 10.7, 8.4 Hz, 1H), 3.95 (s, 1H), 3.32 (s, 3H), 2.72 (br s, 1H), 2.67 (dd, *J* = 16.0, 8.4 Hz, 1H), 2.06 (dd, *J* = 16.0, 10.8 Hz, 1H), 1.35 (s, 3H), 1.30 (t, *J* = 8.6 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 174.8 (C), 173.8 (C), 147.6 (C), 147.2 (C), 132.7 (C), 120.2 (CH), 108.0 (CH), 107.3 (CH), 101.1 (CH_2), 73.7 (CH), 61.2 (CH_2), 58.9 (CH), 54.5 (C), 51.6 (CH_3), 41.2 (CH_2), 22.6 (CH_3), 14.3 (CH_3); IR (thin film): 3367, 2982, 2950, 2901, 2780, 1731, 1489, 1446, 1381, 1342, 1247, 1137, 1107, 1038, 933, 808 cm^{-1}; HRMS-ESI (*m/z*) [M + Na]$^+$ calculated for $C_{17}H_{21}NO_6Na$, 358.1266; found, 358.1262.



5d

Ethyl *rac*-(2*S*,4*S*,5*R*)-5-(6-bromobenzo[*d*][1,3]dioxol-5-yl)-4-cyano-4-methylpyrrolidine-2-carboxylate (5d). Prepared according to **General Procedure 1** from 6-bromopiperonal (370 mg, 1.6 mmol) and methacrylonitrile (210 μL, 2.5 mmol) affording **5d** (280 mg, 0.73 mmol, 46% yield) as a colorless solid (mp = 97–99 ºC). The spectral data were consistent with those previously reported.[2] ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.50 (s, 1H), 7.01 (s, 1H), 6.01 (d, *J* = 1.0 Hz, 1H), 5.98 (d, *J* = 1.0 Hz, 1H), 4.63 (s, 1H), 4.33–4.24 (m, 2H), 4.04 (dd, *J* = 8.8, 6.0 Hz, 1H), 2.74 (dd, *J* = 13.4, 6.0 Hz, 1H), 2.59 (br s, 1H), 2.31 (dd, *J* = 13.4, 8.8 Hz, 1H), 1.57 (s, 3H), 1.27 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 172.8 (C), 148.6 (C), 147.8 (C), 130.6 (C), 122.0 (C), 114.7 (C), 112.6 (CH), 109.5 (CH), 102.1 (CH_2), 68.7 (CH), 61.7 (CH_2), 57.3 (CH), 44.4 (C), 41.7 (CH_2), 23.5 (CH_3), 14.3 (CH_3); IR (thin film): 3370, 2982, 2904, 2237, 1736, 1504, 1476, 1408, 1241, 1206, 1116, 1037, 931, 844 cm^{-1}; HRMS-ESI (*m/z*) [M + Na]$^+$ calculated for $C_{16}H_{17}BrN_2O_4Na$, 403.0269; found, 403.0256.



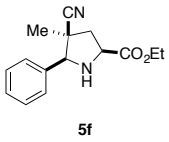
5e *epi*-**5e**

Ethyl *rac*-(2*S*,4*S*,5*S*)-4-cyano-4-methyl-5-(*p*-tolyl)pyrrolidine-2-carboxylate (5e) and **ethyl *rac*-(2*S*,4*R*,5*S*)-4-cyano-4-methyl-5-(*p*-tolyl)pyrrolidine-2-carboxylate (*epi*-5e).** Prepared according to **General Procedure 1** from *p*-tolualdehyde (2.0 g, 17.0 mmol). The cycloaddition step was performed on a smaller scale using the resulting crude imine (310 mg, 1.5 mmol) and methacrylonitrile (190 μL, 2.3 mmol) affording **5e** (210 mg, 0.76 mmol, 50% yield) as a yellow oil and *epi*-**5e** (29 mg, 0.11 mmol, 7% yield) as a clear oil. **5e**: ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.41 (app d, *J* = 8.2 Hz, 2H), 7.21 (app d, *J* = 8.2 Hz, 2H), 4.35–4.24 (m, 2H), 3.97 (dd, *J* = 9.6, 4.1 Hz, 1H), 3.90 (s, 1H), 2.82 (dd, *J* = 13.6, 4.1 Hz, 1H),

2.70 (br s, 1H), 2.36 (s, 3H), 2.29 (dd, *J* = 13.6, 9.6 Hz, 1H), 1.41 (s, 3H), 1.34 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 173.1 (C), 138.8 (C), 133.5 (C), 129.4 (2CH), 127.4 (2CH), 122.1 (C), 72.4 (CH), 61.8 (CH_2), 57.4 (CH), 44.1 (C), 42.6 (CH_2), 22.0 (CH_3), 21.3 (CH_3), 14.3 (CH_3); IR (thin film): 3349, 2980, 2875, 2234, 1735, 1515, 1450, 1208 cm^{-1}; HRMS-ESI (*m/z*) $[M + Na]^+$ calculated for $C_{16}H_{20}N_2O_2Na$, 295.1422; found, 295.1412. *epi*-**5e**: ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.35 (app d, *J* = 8.1 Hz, 2H), 7.18 (app d, *J* = 8.1 Hz, 2H), 4.55 (s, 1H), 4.26 (q, *J* = 7.2 Hz, 2H), 4.05 (dd, *J* = 9.7, 6.1 Hz, 1H), 2.76 (dd, *J* = 13.5, 9.7 Hz, 1H), 2.35 (s, 3H), 2.22 (dd, *J* = 13.5, 6.1 Hz, 1H), 1.32 (t, *J* = 7.2 Hz, 3H), 0.97 (s, 3H), missing NH signal; ^{13}C NMR (125 MHz, $CDCl_3$): δ 173.3 (C), 138.3 (C), 133.5 (C), 129.3 (2CH), 127.1 (2CH), 124.2 (C), 69.5 (CH), 61.7 (CH_2), 57.4 (CH), 42.0 (CH_2), 40.1 (C), 21.3 (CH_3), 20.5 (CH_3), 14.3 (CH_3); IR (thin film): 3344, 2982, 2875, 2234, 1736, 1514, 1452, 1200 cm^{-1}; HRMS-CI (*m/z*) $[M + H]^+$ calculated for $C_{16}H_{21}N_2O_2$, 273.1603; found, 273.1594.

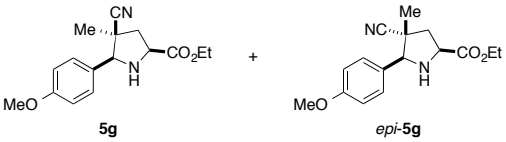
Relative stereochemistry of both **5e** and *epi*-**5e** was confirmed by 2D NOESY ^{1}H NMR. Figure 1 shows the diagnostic NOE correlations for each diastereomer.

Figure 1. Diagnostic NOE correlations of **5e** and *epi*-**5e**.



Ethyl *rac*-(2*S*,4*S*,5*S*)-4-cyano-4-methyl-5-phenylpyrrolidine-2-carboxylate (5f). Prepared according to **General Procedure 1** from benzaldehyde (1.52 mL, 15.0 mmol) and methacrylonitrile (1.90 mL, 22.5 mmol) affording **5f** (2.4 g, 9.4 mmol, 62% yield) as a clear oil. The spectral data were consistent with those previously reported.[2] ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.52 (app d, *J* = 7.1 Hz, 2H), 7.41–7.34 (m, 3H), 4.34–4.24 (m, 2H), 3.98 (dd, *J* = 9.6, 4.2 Hz, 1H), 3.93 (s, 1H), 2.90 (br s, 1H), 2.82 (dd, *J* = 13.6, 4.2 Hz, 1H), 2.29 (dd, *J* = 13.6, 9.6 Hz, 1H), 1.42 (s, 3H), 1.34 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz,

$CDCl_3$): δ 173.0 (C), 136.5 (C), 128.9 (CH), 128.6 (2CH), 127.6 (2CH), 121.9 (C), 72.4 (CH), 61.7 (CH_2), 57.3 (CH), 44.1 (C), 42.4 (CH_2), 22.0 (CH_3), 14.2 (CH_3); IR (thin film): 3348, 2980, 2234, 1734, 1454 cm^{-1}; HRMS-ESI (*m/z*) $[M + Na]^+$ calculated for $C_{15}H_{18}N_2O_2Na$, 281.1266; found, 281.1263.

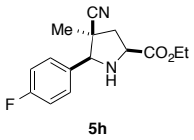


5g *epi*-**5g**

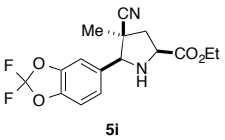
Ethyl *rac*-(2*S*,4*S*,5*S*)-4-cyano-5-(4-methoxyphenyl)-4-methylpyrrolidine-2-carboxylate (5g) and **ethyl *rac*-(2*S*,4*R*,5*S*)-4-cyano-5-(4-methoxyphenyl)-4-methylpyrrolidine-2-carboxylate (*epi*-5g).** Prepared according to **General Procedure 1** from *p*-methoxybenzaldehyde (1.46 mL, 12.0 mmol). The cycloaddition step was performed on a smaller scale using the resulting crude imine (220 mg, 1.0 mmol) and methacrylonitrile (130 μL, 1.5 mmol) affording **5g** (140 mg, 0.48 mmol, 48% yield) as a clear oil and *epi*-**5g** (30 mg, 0.11 mmol, 11% yield) as a yellow oil. **5g**: ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.46 (app d, *J* = 8.6 Hz, 2H), 6.93 (app d, *J* = 8.6 Hz, 2H), 4.35–4.25 (m, 2H), 3.98 (dd, *J* = 9.6, 4.1 Hz, 1H), 3.90 (s, 1H), 3.82 (s, 3H), 2.82 (dd, *J* = 13.5, 4.1 Hz, 1H), 2.29 (dd, *J* = 13.5, 9.6 Hz, 1H), 2.25 (br s, 1H), 1.41 (s, 3H), 1.35 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 173.2 (C), 160.1 (C), 128.8 (2CH), 128.5 (C), 122.2 (C), 114.1 (2CH), 72.2 (CH), 61.8 (CH_2), 57.4 (CH), 55.4 (CH_3), 44.1 (C), 42.5 (CH_2), 22.0 (CH_3), 14.3 (CH_3); IR (thin film): 3350, 2979, 2838, 2234, 1735, 1514, 1249 cm^{-1}; HRMS-ESI (*m/z*) $[M + Na]^+$ calculated for $C_{16}H_{20}N_2O_3Na$, 311.1372; found, 311.1362. *epi*-**5g**: ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.38 (app d, *J* = 8.6 Hz, 2H), 6.90 (app d, *J* = 8.6 Hz, 2H), 4.53 (s, 1H), 4.25 (q, *J* = 7.1 Hz, 2H), 4.04 (dd, *J* = 9.7, 6.2 Hz, 1H), 3.81 (s, 3H), 2.74 (dd, *J* = 13.4, 9.7 Hz, 1H), 2.53 (br s, 1H), 2.21 (dd, *J* = 13.4, 6.2 Hz, 1H), 1.31 (t, *J* = 7.1 Hz, 3H), 0.97 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 173.3 (C), 159.7 (C), 128.6 (C), 128.4 (2CH), 124.2 (C), 114.0 (2CH), 69.2 (CH), 61.6 (CH_2), 57.3 (CH), 55.4 (CH_3), 41.8 (CH_2), 40.2 (C), 20.5 (CH_3), 14.3 (CH_3); IR (thin film): 3346, 2982, 2838, 2234, 1736, 1514, 1249 cm^{-1}; HRMS-ESI (*m/z*) $[M + Na]^+$ calculated for $C_{16}H_{20}N_2O_3Na$, 311.1372; found, 311.1371.

Relative stereochemistry of both **5g** and *epi*-**5g** was confirmed by 2D NOESY ^{1}H NMR. Figure 2 shows diagnostic NOE correlations for each diastereomer.

Figure 2. Diagnostic NOE correlations of **5g** and *epi*-**5g**.

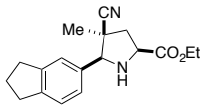


Ethyl *rac*-(2*S*,4*S*,5*S*)-4-cyano-5-(4-fluorophenyl)-4-methyl-pyrrolidine-2-carboxylate (5h). Prepared according to **General Procedure 1** from *p*-fluorobenzaldehyde (1.6 mL, 15 mmol) and methacrylonitrile (1.90 mL, 22.5 mmol) affording **5h** (2.5 g, 9.2 mmol, 61% yield) as a clear oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.52 (app dd, J = 8.7, 5.4 Hz, 2H), 7.09 (app t, J = 8.7 Hz, 2H), 4.34–4.24 (m, 2H), 3.99 (dd, J = 9.6, 4.2 Hz, 1H), 3.95 (s, 1H), 2.83 (dd, J = 13.7, 4.2 Hz, 1H), 2.82 (br s, 1H), 2.29 (dd, J = 13.7, 9.6 Hz, 1H), 1.41 (s, 3H), 1.34 (t, J = 7.1, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 172.9 (C), 163.2 (d, $J_{C–F}$ = 246.1 Hz, C), 132.4 (C), 129.4 (d, $J_{C–F}$ = 8.3 Hz, 2CH), 121.8 (C), 115.7 (d, $J_{C–F}$ = 21.3 Hz, 2CH), 71.7 (CH), 61.9 (CH_2), 57.3 (CH), 44.0 (C), 42.2 (CH_2), 22.0 (CH_3), 14.3 (CH_3); IR (thin film): 3348, 2982, 2235, 1736, 1605, 1510 cm^{-1}; HRMS-ESI (*m/z*) $[M + Na]^+$ calculated for $C_{15}H_{17}FN_2O_2Na$, 299.1172; found, 299.1177.



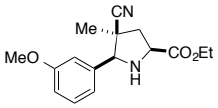
Ethyl *rac*-(2*S*,4*S*,5*S*)-4-cyano-5-(2,2-difluorobenzo[*d*][1,3]dioxol-5-yl)-4-methylpyrrolidine-2-carboxylate (5i). Prepared according to **General Procedure 1** from 2,2-difluorobenzo[*d*][1,3]dioxole-5-carbaldehyde (560 mg, 3.0 mmol) and methacrylonitrile (340 μL, 4.0 mmol) affording crude **5i** (840 mg,

2.5 mmol, 83% yield) as a white solid. The spectral data were consistent with those previously reported.[2] ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.38 (d, *J* = 1.3 Hz, 1H), 7.22 (dd, *J* = 8.3, 1.3 Hz, 1H), 7.07 (d, *J* = 8.3 Hz, 1H), 4.34–4.25 (m, 2H), 4.00 (dd, *J* = 9.5, 4.4 Hz, 1H), 3.97 (s, 1H), 2.85 (dd, *J* = 13.7, 4.4 Hz, 1H), 2.29 (dd, *J* = 13.7, 9.6 Hz, 1H), 1.44 (s, 3H), 1.35 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 172.8 (C), 144.2 (d, *J* = 5.7 Hz, C), 133.3 (C), 132.4, 131.8 (t, $J_{C–F}$ = 255.7 Hz, C), 123.2 (CH), 121.7 (C), 109.4 (CH), 109.1 (CH), 71.9 (CH), 61.8 (CH), 57.1 (CH), 44.0 (C), 41.9 (CH_2), 22.1 (CH_3), 14.3 (CH_3); IR (thin film): 3351, 3078, 2983, 2236, 1738, 1497, 1448, 1382, 1239, 1148, 1034, 818, 703 cm^{-1}; HRMS-ESI (*m/z*) [M + Na]$^+$ calculated for $C_{16}H_{16}F_2N_2O_4Na$, 361.0976; found, 361.0980.



5j

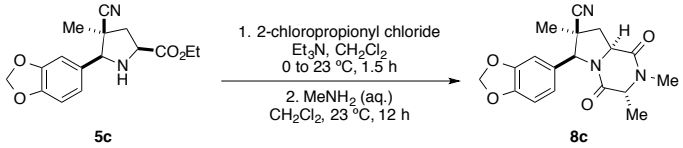
Ethyl *rac*-(2*S*,4*S*,5*S*)-4-cyano-5-(2,3-dihydro-1*H*-inden-5-yl)-4-methylpyrrolidine-2-carboxylate (5j). Prepared according to **General Procedure 1** from a 7.2:1 mixture of 2,3-dihydro-1*H*-indene-5-carbaldehyde and 2,3-dihydro-1*H*-indene-4-carbaldehyde[3] (2.9 g, 20.0 mmol). The cycloaddition step was performed on a smaller scale using the resulting crude imine (2.3 g, 10 mmol) and methacrylonitrile (1.3 mL, 1.6 mmol) affording **5j** (390 mg, 1.3 mmol, 13% yield) as a yellow oil. The spectral data were consistent with those previously reported.[2] ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.40 (s, 1H), 7.27–7.23 (m, 2H), 4.34–4.26 (m, 2H), 3.98 (dd, *J* = 9.6, 3.9 Hz, 1H), 3.90 (s, 1H), 2.97–2.89 (m, 4H), 2.83 (dd, *J* = 13.8, 4.2 Hz, 1H), 2.30 (dd, *J* = 13.8, 9.7 Hz, 1H), 2.09 (app quint, *J* = 7.4 Hz, 2H), 1.62 (br s, 1H), 1.42 (s, 3H), 1.35 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 173.2 (C), 145.3 (C), 144.8 (C), 134.3 (C), 125.6 (CH), 124.5 (CH), 123.4 (CH), 122.2 (C), 72.8 (CH), 61.8 (CH_2), 57.5 (CH), 44.2 (C), 42.8 (CH_2), 33.0 (CH_2), 32.8 (CH_2), 25.6 (CH_2), 22.1 (CH_3), 14.4 (CH_3); IR (thin film) 2940, 2234, 1735, 1447, 1378, 1209, 1139, 1097, 1032, 826 cm^{-1}; HRMS-ESI (*m/z*) [M + Na]$^+$ calculated for $C_{18}H_{22}N_2O_2Na$, 321.1579; found 321.1577.



5k

Ethyl *rac*-(2*S*,4*S*,5*S*)-4-cyano-5-(3-methoxyphenyl)-4-methylpyrrolidine-2-carboxylate (5k). Prepared according to **General Procedure 1** from 3-methoxybenzaldehyde (2.9 mL, 24 mmol) and methacrylonitrile (3.5 mL, 42 mmol) affording **5k** (4.5 g, 16 mmol, 67% yield) as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.31 (app t, *J* = 7.8 Hz, 1H), 7.13 (app t, *J* = 2.0 Hz, 1H), 7.09 (app d, *J* = 7.6 Hz, 1H), 6.92–6.89 (m, 1H), 4.37–4.24 (m, 2H), 4.00 (dd, *J* = 9.6, 4.2 Hz, 1H), 3.93 (s, 1H), 3.84 (s, 3H), 2.84 (dd, *J* = 13.6, 4.2 Hz, 1H), 2.45 (br s, 1H), 2.30 (dd, *J* = 13.6, 9.6 Hz, 1H), 1.44 (s, 3H), 1.35 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 173.0 (C), 159.9 (C), 138.2 (C), 129.7 (CH), 122.0 (C), 119.9 (CH), 114.6 (CH), 113.2 (CH), 72.5 (CH), 61.9 (CH_2), 57.5 (CH_3), 55.4 (CH), 44.1 (C), 42.6 (CH_2), 22.2 (CH_3), 14.3 (CH_3); IR (thin film): 3346, 2979, 2938, 2905, 1876, 2837, 2234, 1734, 1602, 1586, 1490, 1455, 1379, 1316, 1273, 1206, 1142, 1095, 1043, 859, 785 cm^{-1}; HRMS-ESI (*m/z*) $[M + Na]^+$ calculated for $C_{16}H_{20}N_2O_3Na$, 311.1372; found, 311.1379.

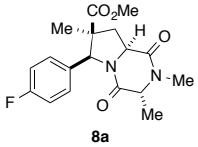
2-3. General Procedure 2: Preparation of Dioxopiperazines



5c **8c**

***Rac*-(3*R*,7*S*)-6-(benzo[*d*][1,3]dioxol-5-yl)-2,3,7-trimethyl-1,4-dioxooctahydropyrrolo[1,2-*a*]pyrazine-7-carbonitrile (8c).** A 50 mL round-bottom flask was charged with **5c** (410 mg, 1.4 mmol, 1.0 equiv) and a magnetic stir bar. The solution was cooled to 0 °C. Et_3N was added (240 µL, 1.7 mmol, 1.2 equiv) followed by dropwise addition of 2-chloropropionyl chloride (160 µL, 1.7 mmol, 1.2 equiv). The reaction was maintained at 0 °C for 30 min, then at 23 °C for 1 h. The reaction was quenched with H_2O (10 mL).

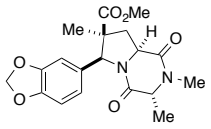
The phases were partitioned in a separatory funnel and the aqueous layer was extracted with CH_2Cl_2 (2 x 20 mL). Combined extracts were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The resulting orange foam was dissolved in CH_2Cl_2 (20 mL) and a solution of $MeNH_2$ (20 mL, 40% in H_2O) was added. The biphasic mixture was stirred vigorously at 23 ºC for 12 h. The phases were partitioned in a separatory funnel and the aqueous layer was extracted with CH_2Cl_2 (2 x 20 mL). Combined extracts were dried over Na_2SO_4, filtered, and concentrated *in vacuo.* ^{1}H NMR analysis of the crude material indicated a 4:1 mixture of methyl epimers. The pale yellow foam was dissolved in CH_2Cl_2 (10 mL) and MeOH (10 mL) was added. The solution was stirred under a stream of air until it became a thick slurry (*ca.* 3 mL). Filtration afforded dioxopiperazine **8c** (330 mg, 1.0 mmol, 69% yield) as a colorless powder. The filtrate was concentrated *in vacuo* and the trituration procedure was repeated to afford additional **8c** (54 mg, 0.16 mmol, 11% yield) as a colorless powder. mp = 226–229 ºC; ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.78 (d, *J* = 9.0 Hz, 1H), 6.62 (d, *J* = 9.0 Hz, 1H), 6.56 (s, 1H), 5.95 (s, 2H), 4.81 (s, 1H), 4.35 (dd, *J* = 11.0, 6.5 Hz, 1H), 3.89 (q, *J* = 7.0 Hz, 1H), 3.03 (s, 3H), 2.75 (app t, *J* = 7.0 Hz, 1H), 2.44 (dd, *J* = 13.5, 6.5 Hz, 1H), 1.65 (s, 3H), 1.46 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 166.7 (C), 166.1 (C), 148.3 (C), 148.2 (C), 130.9 (C), 120.0 (CH), 119.9 (C), 108.8 (CH), 106.3 (CH), 101.5 (CH_2), 69.7 (CH), 60.9 (CH), 56.2 (CH), 42.7 (C), 36.8 (CH_2), 32.1 (CH_3), 25.3 (CH_3), 15.4 (CH_3); IR (thin film): 2982, 2917, 2244, 1671, 1491, 1447, 1246, 1037, 925, 721 cm^{-1}; HRMS-ESI (*m/z*) $[M + Na]^+$ calculated for $C_{18}H_{19}N_3O_4Na$, 364.1273; found, 364.1273.



8a

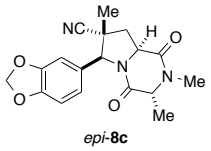
Methyl *rac*-(3*R*,6*S*,7*S*,8a*S*)-6-(4-fluorophenyl)-2,3,7-trimethyl-1,4-dioxooctahydropyrrolo[1,2-*a*]pyrazine-7-carboxylate (8a). Prepared according to **General Procedure 2** from pyrrolidine **5a** (210 mg, 0.68 mmol), 2-chloropropionyl chloride (70 μL, 0.72 mmol) and $MeNH_2$ (5 mL, 40% in H_2O) affording **8a** (95 mg, 0.27 mmol, 40% yield) as a colorless powder. The spectral data were consistent with

those previously reported.[2] mp = 184–187 ºC; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.00–7.10 (m, 2H), 6.91 (t, *J* = 8.5 Hz, 2H), 4.81 (s, 1H), 4.36 (dd, *J* = 11.5, 6.5 Hz, 1H), 3.81 (q, *J* = 9.0 Hz, 1H), 3.22 (s, 3H), 2.94 (s, 3H), 2.90–2.95 (m, 1H), 2.16 (dd, *J* = 14.0, 6.5 Hz, 1H), 1.53 (s, 3H), 1.44 (d, *J* = 9.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 172.1 (C), 167.2 (C), 166.8 (C), 162.3 (d, $J_{C–F}$ = 247.4 Hz, C), 133.6 (d, $J_{C–F}$ = 3.2 Hz, C), 128.3 (d, $J_{C–F}$ = 7.6 Hz, 2CH), 115.2 (d, $J_{C–F}$ = 21.7 Hz, 2CH), 69.4 (CH), 60.9 (CH), 56.9 (CH), 53.3 (C), 51.8 (CH_3), 34.3 (CH_2), 32.0 (CH_3), 24.2 (CH_3), 15.2 (CH_3); IR (thin film): 2975, 2929, 1736, 1677, 1605, 1509, 1433, 1401, 1299, 1248, 1225, 1126, 1158, 849 cm^{-1}; HRMS-ESI [M + H]$^{+}$ calculated for $C_{18}H_{22}FN_2O_4$, 349.1583; found, 349.1570.



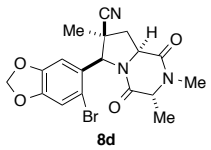
8b

Methyl *rac*-(3*R*,6*S*,7*S*,8a*S*)-6-(benzo[*d*][1,3]dioxol-5-yl)-2,3,7-trimethyl-1,4-dioxooctahydropyrrolo[1,2-*a*]pyrazine-7-carboxylate (8b). Prepared according to **General Procedure 2** from pyrrolidine **5b** (170 mg, 0.51 mmol), 2-chloropropionyl chloride (60 μL, 0.62 mmol), and $MeNH_2$ (5 mL, 40% in H_2O) affording **8b** (130 mg, 0.30 mmol, 59% yield) as a colorless powder (mp = 178–181 ºC). The spectral data were consistent with those previously reported.[2] ^{1}H NMR (*ca.* 10:1 mixture of diastereomers, 500 MHz, $CDCl_3$): δ 6.67 (d, *J* = 8.0 Hz, 1H), 6.53 (d, *J* = 8.0 Hz, 1H), 6.50 (s, 1H), 5.89 (s, 2H), 4.77 (s, 1H), 4.35 (dd, *J* = 11.5, 6.5 Hz, 1H), 3.84 (t, *J* = 7.0 Hz, 1H), 3.31 (s, 3H), 3.02 (s, 3H), 3.02–2.93 (m, 1H), 2.15 (dd, *J* = 8.5, 8.5 Hz, 1H), 1.52 (s, 3H), 1.46 (d, *J* = 7.1 Hz, 3H); ^{13}C NMR (*ca.* 10:1 mixture of diastereomers, 125 MHz, $CDCl_3$): δ 172.2 (C), 167.3 (C), 166.9 (C), 147.6 (C), 147.4 (C), 131.5 (C), 120.4 (CH), 108.1 (CH), 107.0 (CH), 101.2 (CH_2), 69.9 (CH), 60.9 (CH), 56.9 (CH_3), 53.3 (C), 52.0 (CH), 34.3 (CH_2), 32.0 (CH_3), 24.2 (CH_3), 15.3 (CH_3); IR (thin film): 2953, 2949, 1735, 1672, 1490, 1432, 1294, 1245, 1122, 1037 cm^{-1}; HRMS-ESI (*m/z*) [M + Na]$^{+}$ calculated for $C_{19}H_{22}N_2O_6Na$, 397.1376; found, 397.1367.



epi-**8c**

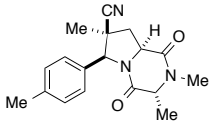
***Rac*-(3*R*,6*S*,7*R*,8a*S*)-6-(benzo[*d*][1,3]dioxol-5-yl)-2,3,7-trimethyl-1,4-dioxooctahydropyrrolo[1,2-*a*]pyrazine-7-carbonitrile (*epi*-8c).** Prepared in analogous fashion from pyrrolidine *epi*-**5c** (2.9 g, 9.6 mmol), 2-chloropropionyl chloride (1.1 mL, 11.4 mmol), and $MeNH_2$ (20 mL, 40% in H_2O). The crude material was purified by flash chromatography (SiO_2, 0 to 10% EtOAc in CH_2Cl_2, gradient elution) to afford *epi*-**8c** (*ca.* 2.5:1 mixture of diastereomers, 2.9 g, 9.6 mmol, 35% yield) as a yellow solid (mp = 233–239 ºC). ^{1}H NMR (*ca.* 2.5:1 mixture of diastereomers, 600 MHz, $CDCl_3$): δ 6.76 (d, *J* = 7.8 Hz, 1H), 6.46 (app br s, 2H), 5.95, (app d, *J* = 1.8 Hz, 2H), 5.24 (s, 1H), 4.62–4.55 (m, 1H), 4.20 (q, *J* = 7.1 Hz, 1H), 3.07 (s, 3H), 2.65 (dd, *J* = 13.5, 6.3 Hz, 1H), 2.33 (dd, *J* = 13.5, 11.3 Hz, 1H), 1.54 (d, *J* = 7.3 Hz, 3H), 1.06 (s, 3H); ^{13}C NMR (*ca.* 2.5:1 mixture of diastereomers, 125 MHz, $(CD_3)_2SO$, 348 K): δ 168.0, 166.1, 147.1, 146.8, 129.6, 123.2, 119.7, 107.7, 106.8, 100.8, 66.3, 57.0, 55.0, 40.4, 36.0, 28.6, 19.3, 13.1; IR (thin film): 3056, 2990, 2937, 2899, 2235, 1673, 1490, 1448, 1422, 1390, 1244, 1097, 1038, 929 cm^{-1}; HRMS-ESI (*m/z*) $[M + Na]^+$ calculated for $C_{18}H_{19}N_3O_4Na$, 364.1273; found, 364.1267.



8d

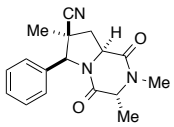
***Rac*-(3*R*,6*R*,7*S*,8a*S*)-6-(6-bromobenzo[*d*][1,3]dioxol-5-yl)-2,3,7-trimethyl-1,4-dioxooctahydropyrrolo[1,2-*a*]pyrazine-7-carbonitrile (8d).** Prepared according to **General Procedure 2** from pyrrolidine **5d** (120 mg, 0.31 mmol) 2-chloropropionyl chloride (40 μL, 0.41 mmol), and $MeNH_2$ (5 mL, 40% in H_2O) affording **8d** (78 mg, 0.19 mmol, 59% yield) as a colorless crystalline solid after recrystallization from MeOH. The spectral data were consistent with those previously reported.[2] ^{1}H NMR (*ca.* 2.8:1 mixture of diastereomers, 500 MHz, $CDCl_3$): δ 7.07 (s, 1H), 6.34 (s, 1H), 5.98 (s, 2H), 5.34 (s, 1H), 4.36 (dd, *J* = 12.0, 6.5 Hz, 1H), 3.92 (q, *J* = 7.0 Hz, 1H), 3.04 (s, 3H), 2.66 (app t, *J* = 13.0 Hz, 1H),

2.48 (dd, *J* = 13.0, 6.5 Hz, 1H), 1.74 (s, 3H), 1.47 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (*ca*. 2.8:1 mixture of diastereomers, 125 MHz, $CDCl_3$): δ 166.5 (C), 166.0 (C), 148.8 (C), 148.1 (C), 129.1 (C), 119.7 (C), 115.0 (C), 113.5 (CH), 105.0 (CH), 102.3 (CH_2), 68.3 (CH), 60.8 (CH), 56.4 (CH), 42.2 (C), 37.4 (CH_2), 32.2, 25.0 (CH_3), 15.5 (CH_3); IR (thin film): 2982, 2246, 1675, 1503, 1478, 1429, 1402, 1307, 1248, 1120, 1036, 928 cm^{-1}; HRMS-ESI (*m/z*) $[M + Na]^+$ calculated for $C_{18}H_{18}BrN_3O_4Na$, 442.0378; found, 442.0385.



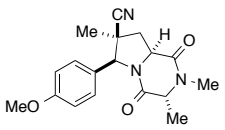
8e

***Rac*-(3*R*,6*S*,7*S*,8a*S*)-2,3,7-trimethyl-1,4-dioxo-6-(*p*-tolyl)octahydropyrrolo[1,2-*a*]pyrazine-7-carbonitrile (8e).** Prepared according to **General Procedure 2** from pyrrolidine **5e** (200 mg, 0.74 mmol), 2-chloropropionyl chloride (86 μL, 0.88 mmol), and methylamine (2 mL, 40% in H_2O) affording **8e** (100 mg, 0.32 mmol, 44% yield) as a colorless powder. The spectral data were consistent with those previously reported.[2] mp = 204–209 ºC; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.17 (app d, *J* = 7.5 Hz, 2H), 7.01 (app d, *J* = 7.5 Hz, 2H), 4.88 (s, 1H), 4.38 (dd, *J* = 11.0, 6.5 Hz, 1H), 3.89 (q, *J* = 7.0 Hz, 1H), 3.04 (s, 3H), 2.79 (dd, *J* = 12.5, 11.0 Hz, 1H), 2.44 (dd, *J* = 12.5, 6.5 Hz, 1H), 2.32 (s, 3H), 1.67 (s, 3H), 1.47 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 166.7 (C), 166.2 (C), 138.9 (C), 134.0 (C), 129.8 (2CH), 125.9 (2CH), 120.0 (C), 69.6 (CH), 60.9 (CH), 56.2 (CH), 42.6 (C), 36.7 (CH_2), 32.2 (CH_3), 25.2 (CH_3), 21.3 (CH_3), 15.4 (CH_3); IR (thin film): 3054, 2982, 2935, 2877, 2243, 1681, 1515, 1452, 1430, 1402, 1306, 1246, 1230, 1063, 804, 734 cm^{-1}; HRMS-ESI (*m/z*) $[M + Na]^+$ calculated for $C_{18}H_{21}N_3O_2Na$, 334.1531; found, 334.1536. Structure was confirmed by single-crystal X-ray analysis (CCDC 1061870).[4]



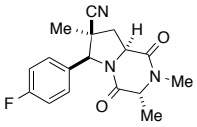
8f

***Rac*-(3*R*,6*S*,7*S*,8a*S*)-2,3,7-trimethyl-1,4-dioxo-6-phenyloctahydropyrrolo[1,2-*a*]pyrazine-7-carbonitrile (8f).** Prepared according to **General Procedure 2** from pyrrolidine **5f** (2.4 g, 9.3 mmol), 2-chloropropionyl chloride (1.1 mL, 11 mmol), and methylamine (19 mL, 40% in H_2O) affording **8f** (1.7 g, 5.7 mmol, 61% yield) as a colorless powder. The spectral data were consistent with those previously reported.[2] mp = 258–262 ºC; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.39–7.33 (m, 3H), 7.12 (app d, *J* = 7.2 Hz, 2H), 4.91 (s, 1H), 4.40 (dd, *J* = 11.2, 6.6 Hz, 1H), 3.91 (q, *J* = 7.2 Hz, 1H), 3.05 (s, 3H), 2.79 (dd, *J* = 13.0, 11.2 Hz, 1H), 2.46 (dd, *J* = 13.0, 6.6 Hz, 1H), 1.69 (s, 3H), 1.48 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 166.7 (C), 166.2 (C), 136.9 (C), 129.2 (2CH), 129.1 (2CH), 126.1 (CH), 119.9 (C), 69.8 (CH), 60.9 (CH), 56.3 (CH), 42.6 (C), 36.7 (CH_2), 32.2 (CH_3), 25.3 (CH_3), 15.4 (CH_3); IR (thin film): 2981, 2937, 2244, 1673 cm^{-1}; HRMS-ESI (*m/z*) $[M + Na]^+$ calculated for $C_{17}H_{19}N_3O_2Na$, 320.1375; found, 320.1380. Structure was confirmed by single-crystal X-ray analysis (CCDC 1061869).[4]



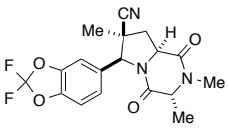
8g

***Rac*-(3*R*,6*S*,7*S*,8a*S*)-6-(4-methoxyphenyl)-2,3,7-trimethyl-1,4-dioxooctahydropyrrolo[1,2-*a*]pyrazine-7-carbonitrile (8g).** Prepared according to **General Procedure 2** from pyrrolidine **5g** (55 mg, 0.2 mmol) affording **8g** (46 mg, 0.14 mmol, 70% yield) as a colorless powder. The spectral data were consistent with those previously reported.[2] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.06 (d, *J* = 8.7 Hz, 2H), 6.89 (d, *J* = 8.7 Hz, 2H), 4.88 (s, 1H), 4.38 (dd, *J* = 11.3, 6.6 Hz, 1H), 3.90 (q, *J* = 7.3 Hz, 1H), 3.78 (s, 3H), 3.06 (s, 3H), 2.80 (dd, *J* = 13.0, 11.6 Hz, 1H), 2.46 (dd, *J* = 13.3, 6.6 Hz, 1H), 1.69 (s, 3H), 1.49 (d, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.8 (C), 166.0 (C), 139.2 (C), 132.5 (2CH), 130.7 (2CH), 123.3 (C), 119.6 (C), 69.3 (CH), 60.9 (CH), 56.4 (CH), 42.5 (C), 37.0 (CH_2), 32.3 (CH_3), 25.4 (CH_3), 15.5 (CH_3); IR (thin film): 2981, 2919, 2852, 2246, 1673, 1490, 1303, 1235, 1093, 756 cm^{-1}; HRMS-ESI (*m/z*) $[M + Na]^+$ calculated for $C_{18}H_{21}N_3O_3Na$, 350.1481; found, 350.1465.



8h

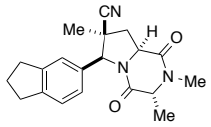
***Rac*-(3*R*,6*S*,7*S*,8a*S*)-6-(4-fluorophenyl)-2,3,7-trimethyl-1,4-dioxo-octahydropyrrolo-[1,2-*a*]pyrazine-7-carbonitrile (8h).** Prepared according to **General Procedure 2** from pyrrolidine **5h** (2.5 g, 9.2 mmol), 2-chloropropionyl chloride (1.1 mL, 11 mmol), and methylamine (18 mL, 40% in H_2O) affording **8h** (1.6 g, 5.1 mmol, 55% yield, *ca*. 8:1 mixture of diastereomers) as a colorless powder. The spectral data were consistent with those previously reported.[2] mp = 235–237 ºC; ^{1}H NMR (*ca*. 8:1 mixture of diastereomers, 500 MHz, $CDCl_3$): δ 7.13–7.05 (m, 4H), 4.90 (s, 1H), 4.39 (dd, *J* = 11.3, 6.6 Hz, 1H), 3.91 (q, *J* = 7.1 Hz, 1H), 3.06 (s, 3H), 2.76 (app t, *J* = 12.6 Hz, 1H), 2.47 (dd, *J* = 13.4, 6.6 Hz, 1H), 1.69 (s, 3H), 1.49 (d, *J* = 7.1 Hz, 3H); ^{13}C NMR (*ca*. 8:1 mixture of diastereomers, 125 MHz, $CDCl_3$): δ 166.8 (C), 166.1 (C), 163.0 (d, $J_{C–F}$ = 245.5 Hz, C), 132.8 (d, $J_{C–F}$ = 3.1 Hz, C), 127.9 (d, $J_{C–F}$ = 8.4 Hz, 2CH), 119.8 (C), 116.2 (d, $J_{C–F}$ = 21.8 Hz, 2CH), 69.2 (CH), 60.9 (CH), 56.3 (CH), 42.6 (C), 36.8 (CH_2), 32.2 (CH_3), 25.3 (CH_3), 15.4 (CH_3); IR (thin film): 2989, 2940, 2241, 1681 cm^{-1}; HRMS-ESI (*m/z*) $[M + Na]^+$ calculated for $C_{17}H_{18}FN_3O_2Na$, 338.1281; found, 338.1283.



8i

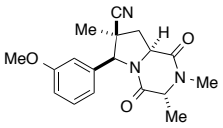
***Rac*-(3*R*,6*S*,7*S*,8a*S*)-6-(2,2-difluorobenzo[*d*][1,3]dioxol-5-yl)-2,3,7-trimethyl-1,4-dioxooctahydropyrrolo[1,2-*a*]pyrazine-7-carbonitrile (8i).** Prepared according to **General Procedure 2** from pyrrolidine **5i** (840 mg, 2.5 mmol), 2-chloropropionyl chloride (390 μL, 4.0 mmol) and $MeNH_2$ (5 mL, 40% in H_2O) affording **8i** (600 mg, 1.6 mmol, 64% yield) as a colorless powder. The spectral data were consistent with those previously reported.[2] mp = 246–249 ºC; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.07 (d, *J* = 8.0 Hz, 1H), 6.90 (d, *J* = 8.0 Hz, 1H), 6.83 (s, 1H), 4.88 (s, 1H), 4.39 (dd, *J* = 11.5, 6.5 Hz, 1H), 3.92

(q, J = 7.0 Hz, 1H), 3.07 (s, 3H), 2.75 (app t, *J* = 12.5 Hz, 1H), 2.51 (dd, *J* = 13.5, 6.5 Hz, 1H), 1.71 (s, 3H), 1.50 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 166.9 (C), 165.9 (C), 144.3 (C), 144.2 (C), 133.3 (C), 131.8 (t, $J_{C–F}$ = 256.3 Hz, C), 121.9 (CH), 119.7 (C), 110.1 (CH), 107.5 (CH), 69.5 (CH), 60.9 (CH), 56.3 (CH), 42.6 (C), 36.9 (CH_2), 32.3 (CH_3), 25.4 (CH_3), 15.5 (CH_3); IR (thin film): 2984, 2939, 2246, 1674, 1500, 1452, 1429, 1403, 1241, 1150, 912, 732 cm^{-1}; HRMS-ESI (*m/z*) $[M + Na]^+$ calculated for $C_{18}H_{17}F_2N_3O_4Na$, 400.1085; found, 400.1092.



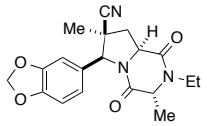
8j

(3*R*,6*S*,7*S*)-6-(2,3-dihydro-1*H*-inden-5-yl)-2,3,7-trimethyl-1,4-dioxooctahydropyrrolo[1,2-*a*]pyrazine-7-carbonitrile (8j). Prepared according to **General Procedure 2** from pyrrolidine **5j** (390 mg, 1.3 mmol) affording **8j** (180 mg, 0.53 mmol, 41% yield) as a colorless powder. The spectral data were consistent with those previously reported.[2] mp = 190–195 ºC; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.19 (d, *J* = 7.7 Hz, 1H), 6.96 (s, 1H), 6.93 (d, *J* = 7.7 Hz, 1H), 4.89 (s, 1H), 4.38 (dd, *J* = 11.6, 6.7 Hz, 1H), 3.91 (q, *J* = 7.3 Hz, 1H), 3.07 (s, 3H), 2.90–2.80 (m, 5H), 2.45 (dd, *J* = 13.3, 6.6 Hz, 1H), 2.05 (app quint, *J* = 7.5 Hz, 2H), 1.69 (s, 3H), 1.49 (d, *J* = 7.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 166.8 (C), 166.3 (C), 145.5 (C), 145.2 (C), 134.8 (C), 125.0 (CH), 123.9 (CH), 122.1 (CH), 120.1 (C), 70.1 (CH), 61.0 (CH), 56.3 (CH), 42.8 (C), 36.8 (CH_2), 33.0 (CH_2), 32.8 (CH_2), 32.2 (CH_3), 25.4 (CH_3), 25.4 (CH_2), 15.5 (CH_2); IR (thin film) 1940, 1673, 1431, 1402, 1306, 1239, 1062, 814, 733 cm^{-1}; HRMS-ESI (*m/z*) $[M + Na]^+$ calculated for $C_{20}H_{23}N_3O_2Na$, 360.1688; found 360.1684.



8k

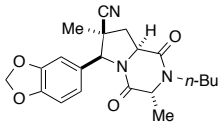
***Rac*-(3*R*,6*S*,7*S*)-6-(3-methoxyphenyl)-2,3,7-trimethyl-1,4-dioxooctahydropyrrolo[1,2-*a*]pyrazine-7-carbonitrile (8k).** Prepared according to **General Procedure 2** from pyrrolidine **5k** (4.5 g, 16 mmol), 2-chloropropionyl chloride (1.7 mL, 17.5 mmol), and $MeNH_2$ (30 mL, 40% in H_2O) affording **8k** (3.6 g, 11 mmol, 70% yield) as a colorless powder (mp = 245–248 ºC). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.29 (app t, *J* = 7.9 Hz, 1H), 6.87 (dd, *J* = 8.0, 2.2 Hz, 1H), 6.70 (d, *J* = 7.7 Hz, 1H), 6.65 (app t, *J* = 2.0 Hz, 1H), 4.88 (s, 1H), 4.39 (dd, *J* = 11.6, 6.5 Hz, 1H), 3.92 (q, *J* = 7.3 Hz, 1H), 3.79 (s, 3H), 3.06 (s, 3H), 2.80 (dd, *J* = 13.2, 11.6 Hz, 1H), 2.46 (dd, *J* = 13.2, 6.6 Hz, 1H), 1.69 (s, 3H), 1.49 (d, *J* = 7.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 166.8 (C), 166.2 (C), 160.0 (C), 138.5 (C), 130.3 (CH), 119.9 (C), 118.2 (CH), 114.1 (CH), 112.5 (CH), 69.8 (CH), 61.0 (CH), 56.3 (CH_3), 55.3 (CH), 42.6 (C), 36.9 (CH_2), 32.2 (CH_3), 25.4 (CH_3), 15.5 (CH_3); IR (thin film): 3056, 2983, 2939, 2881, 2839, 2244, 1673, 1603, 1492, 1492, 1453, 1430, 1308, 1285, 1262, 1166, 1227, 1048, 785, 734, 697 cm^{-1}; HRMS-ESI (*m/z*) $[M + Na]^+$ calculated for $C_{18}H_{21}N_3O_3Na$, 350.1481; found 350.1475.



8l

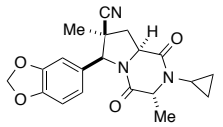
***Rac*-(3*R*,6*S*,7*S*,8a*S*)-6-(benzo[*d*][1,3]dioxol-5-yl)-2-ethyl-3,7-dimethyl-1,4-dioxooctahydropyrrolo[1,2-*a*]pyrazine-7-carbonitrile (8l).** Prepared according to **General Procedure 2** from pyrrolidine **5c** (300 mg, 1.0 mmol), 2-chloropropionyl chloride (120 μL, 1.2 mmol), and ethylamine (10 mL, 70% solution in H_2O) affording **8l** (260 mg, 0.73 mmol, 73% yield) as a colorless powder. mp = 220–224 ºC; ^{1}H NMR (600 MHz, $CDCl_3$): δ 6.78 (d, *J* = 8.0 Hz, 1H), 6.60 (d, *J* = 8.0 Hz, 1H), 6.53 (s, 1H), 5.95 (s, 2H), 4.84 (s, 1H), 4.38 (dd, *J* = 11.2, 6.7 Hz, 1H), 3.95 (q, *J* = 7.3 Hz, 1H), 3.84 (dq, *J* = 14.0, 7.1 Hz, 1H), 3.13 (dq, *J* = 14.0, 7.1 Hz, 1H), 2.79 (app t, *J* = 12.3 Hz, 1H), 2.44 (*J* = 13.3, 6.7 Hz, 1H), 1.67 (s, 3H), 1.49 (d, *J* = 7.3 Hz, 3H), 1.22 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 167.2 (C), 165.8 (C), 148.4 (C), 148.3 (C), 130.9 (C), 120.0 (C), 119.9 (CH), 108.8 (CH), 108.8 (CH), 106.2 (CH), 101.6 (CH_2), 69.6 (CH), 58.8 (CH), 56.3 (CH), 42.8 (C), 40.3 (CH_2), 36.7 (CH_2), 25.3 (CH_3),

16.4 (CH_3), 13.3 (CH_3); IR (thin film): 2982, 2936, 2244, 1669, 1504, 1491, 1448, 1427, 1245, 1038, 927, 734 cm^{-1}; HRMS-ESI (*m/z*) $[M + Na]^+$ calculated for $C_{19}H_{21}N_3O_4Na$, 378.1430; found 378.1426.



8m

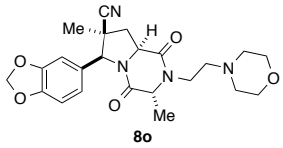
***Rac*-(3*R*,6*S*,7*S*,8a*S*)-6-(benzo[*d*][1,3]dioxol-5-yl)-2-butyl-3,7-dimethyl-1,4-dioxooctahydropyrrolo[1,2-*a*]pyrazine-7-carbonitrile (8m)**. Prepared according to **General Procedure 2** from pyrrolidine **5c** (58 mg, 0.2 mmol) and *n*-butylamine (0.2 mL, 146 mg, 2 mmol) affording **8m** (54 mg, 0.14 mmol, 72% yield) as a colorless powder. The spectral data were consistent with those previously reported.[2] ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.78 (d, *J* = 8.0 Hz, 1H), 6.61 (dd, *J* = 8.0, 1.7 Hz, 1H), 6.54 (d, *J* = 1.7 Hz, 1H), 5.96 (s, 2H), 4.84 (s, 1H), 4.38 (dd, *J* = 11.2, 6.7 Hz, 1H), 3.97–3.86 (m, 2H), 3.00–2.94 (m, 1H), 2.81 (dd, *J* = 13.3, 11.5 Hz, 1H), 2.45 (dd, *J* = 13.3, 6.7 Hz, 1H), 1.66–1.56 (m, 2H), 1.55 (s, 3H), 1.49 (d, *J* = 7.2 Hz, 3H) 1.41–1.30 (m, 2H), 0.96 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.2 (C), 166.3 (C), 148.6 (C), 148.4 (C), 131.1 (C), 120.0 (CH), 119.9 (C), 108.8 (CH), 106.4 (CH), 101.7 (CH_2), 69.7 (CH), 59.0 (CH), 56.5 (CH), 44.8 (C), 42.9 (CH_2), 36.9 (CH_2), 30.0 (CH_2), 25.4 (CH_3), 20.2 (CH_2), 16.2 (CH_3). 13.9 (CH_3); IR (thin film): 2982, 2917, 2244, 1671, 1491, 1447, 1246, 1037, 925, 721 cm^{-1}; HRMS-ESI (*m/z*) $[M + Na]^+$ calculated for $C_{21}H_{25}N_3O_4Na$, 406.1743; found, 406.1730.



8n

***Rac*-(3*R*,6*S*,7*S*,8a*S*)-6-(benzo[*d*][1,3]dioxol-5-yl)-2-cyclopropyl-3,7-dimethyl-1,4-dioxooctahydropyrrolo[1,2-*a*]pyrazine-7-carbonitrile (8n).** Pyrrolidine **5c** (450 mg, 1.5 mmol) was acylated with 2-chloropropionyl chloride (200 μL, 2.1 mmol) as described in **General Procedure 2**. The resulting crude amide was dissolved in THF (14 mL) and H_2O (9 mL) and cyclopropylamine (360 μL, 5.2

mmol) was added. The biphasic mixture was stirred at 80 ºC for 12 h, then at 100 ºC for 2 days. The biphasic mixture was extracted with CH_2Cl_2 (3 x 20 mL). Combined extracts were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude material was purified by trituration as described in **General Procedure 2** to afford **8n** (96 mg, 0.26 mmol, 17% yield) as a colorless powder. The spectral data were consistent with those previously reported.[2] mp = 220–223 ºC; ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.76 (d, *J* = 8.0 Hz, 1H), 6.56 (d, *J* = 8.0 Hz, 1H), 6.47 (s, 1H), 5.95 (s, 2H), 4.80 (s, 1H), 4.38 (dd, *J* = 11.3, 6.7 Hz, 1H), 3.98 (q, *J* = 7.3 Hz, 1H), 2.74–2.69 (m, 2H), 2.45 (dd, *J* = 13.3, 6.7 Hz, 1H), 1.65 (s, 3H), 1.49 (d, *J* = 7.3 Hz, 3H), 1.09 (dq, *J* = 9.5, 6.6 Hz, 1H), 0.88–0.83 (m, 1H), 0.79 (dq, *J* = 9.5, 6.5 Hz, 1H), 0.58 (dq, *J* = 10.4, 5.2 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 168.2 (C), 167.2 (C), 148.3 (C), 148.2 (C), 130.9 (C), 119.9 (CH), 119.8 (CH), 108.7 (CH), 106.1 (CH), 101.5 (CH_2), 69.4 (CH), 59.8 (CH), 56.7 (CH), 42.7 (C), 36.7 (CH_2), 28.0 (CH), 25.2 (CH_3), 16.2 (CH_3), 8.7 (CH_2), 5.7 (CH_2); IR (thin film): 2984, 1675, 1490, 1424, 1376, 1245, 1189, 1036, 932, 733 cm^{-1}; HRMS-ESI (*m/z*) [M + Na]$^+$ calculated for $C_{20}H_{21}N_3O_4Na^+$, 390.1430; found, 390.1433.

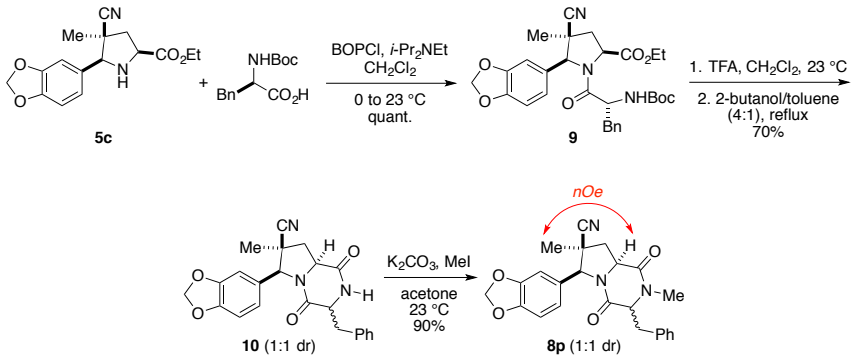


8o

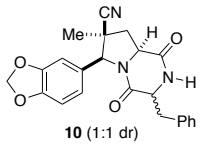
***Rac*-(3*R*,6*S*,7*S*,8a*S*)-6-(benzo[*d*][1,3]dioxol-5-yl)-3,7-dimethyl-2-(2-morpholinoethyl)-1,4-dioxooctahydropyrrolo[1,2-*a*]pyrazine-7-carbonitrile (8o).** Pyrrolidine **5c** (180 mg, 0.60 mmol) was acylated with 2-chloropropionyl chloride (70 μL, 0.72 mmol) as described in **General Procedure 2**. The resulting crude amide was dissolved in CH_2Cl_2 (5 mL) and 2-morpholinoethylamine (5.0 mL, 38 mmol) was added. The solution was maintained at 23 ºC for 12 h, then diluted with H_2O (20 mL). The biphasic mixture was extracted with CH_2Cl_2 (3 x 10 mL). Combined extracts were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. Flash chromatography (SiO_2, 5 to 10% MeOH in CH_2Cl_2, gradient elution) afforded **8o** (180 mg, 0.41 mmol, 69% yield) as a colorless solid. The spectral data were consistent with those previously reported.[2] mp = 160–165 ºC; ^{1}H NMR (500 MHz, 1:1 $CD_3OD/CDCl_3$): δ 6.61 (d, *J* = 9.5

Hz, 1H), 6.49 (d, *J* = 9.5 Hz, 1H), 6.36 (s, 1H), 5.77 (s, 2H), 4.67 (s, 1H), 4.31 (dd, *J* = 11.0, 6.5 Hz 1H), 3.88 (q, *J* = 9.0 Hz, 1H), 3.84–3.76 (m, 1H), 3.44–3.50 (m, 4H), 2.88–2.95 (m, 1H), 2.55 (app t, *J* = 6.5 Hz, 1H), 2.20–2.45 (m, 7H), 1.49 (s, 3H), 1.31 (d, *J* = 9.0 Hz, 3H); ^{13}C NMR (125 MHz, 1:1 $CD_3OD/CDCl_3$): δ 167.1 (C), 166.2 (C), 147.9 (C), 147.8 (C), 130.7 (C), 119.9 (CH), 119.7 (C), 108.2 (CH), 105.5 (CH), 101.2 (CH_2), 69.1 (CH), 66.6 ($2CH_2$), 59.4 (CH), 56.1 (C), 55.8 (CH_2), 53.4 ($2CH_2$), 42.5 (C), 41.3 (CH_2), 36.2 (CH_2), 24.5 (CH_3), 15.3 (CH_3); IR (thin film): 2955, 2858, 2813, 2244, 1672, 1491, 1448, 1427, 1296, 1246, 1115, 1037, 922 cm^{-1}; HRMS-ESI (*m/z*) $[M + Na]^+$ calculated for $C_{23}H_{28}N_4O_5Na$, 463.1957; found, 463.1946.

2-4. Synthesis of Dioxopiperazine 8p

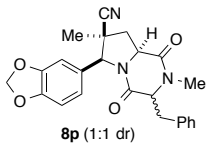


To a solution of *N*-Boc-phenylalanine (260 mg, 1.0 mmol, 1.5 equiv) in CH_2Cl_2 (2 mL) at 0 °C was added *i*-Pr_2NEt (0.12 mL, 0.66 mmol, 1.0 equiv) and BOPCl (250 mg, 1.0 mmol, 1.5 equiv) and the reaction was allowed to warm to 23 °C over 1 h. After recooling to 0 °C additional *i*-Pr_2NEt (0.23 mL, 1.3 mmol, 2.0 equiv) was added, followed by the dropwise addition of a solution of **5c** (200 mg, 0.66 mmol, 1.0 equiv) in CH_2Cl_2 (1.3 mL). The reaction was allowed to warm to 23 °C overnight, after which time TLC analysis showed full consumption of the starting material. After an extractive work up (CH_2Cl_2/H_2O), the crude product was filtered through a silica gel plug using hexanes/EtOAc (1:1) as the eluent and the volatile components were removed *in vacuo* to afford crude acylated pyrrolidine **9** (370 mg, 0.66 mmol, 100% yield), which was used directly without further purification.



10 (1:1 dr)

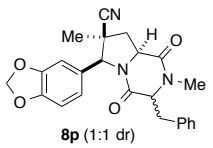
Crude amide **9** (370 mg, 0.66 mmol) was dissolved in CH_2Cl_2 (2.1 mL) and cooled to 0 °C. Trifluoroacetic acid (TFA, 0.8 mL) was added, the reaction allowed to warm to room temperature over 3 h, and the volatile components were removed under reduced pressure. The resulting residue was dissolved in a 4:1 mixture *i*-BuOH/PhMe (18 mL) containing *i*-Pr_2NEt (0.46 mL, 2.7 mmol, 4.0 equiv) and transferred to a scintillation vial. The vial was sealed with a Teflon cap and heated to 100 °C overnight. After an extractive work up (CH_2Cl_2/H_2O) and concentration, two diastereomeric dioxopiperazines were separated by flash chromatography (SiO_2, 3:1 EtOAc:hexanes). NMR data for **10** diastereomer A: ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.38–7.35 (m, 3H), 7.26–7.25 (m, 2H), 7.00 (d, *J* = 3.7 Hz, 1H), 6.78 (d, *J* = 8.0 Hz, 1H), 6.63 (d, *J* = 7.2 Hz, 1H), 6.55 (s, 1H), 5.92 (s, 2H), 4.71 (s, 1H), 4.29 (app q, *J* = 4.2 Hz, 1H), 3.31 (dd, *J* = 13.9, 4.6 Hz, 1H), 2.95 (dd, *J* = 13.9, 4.4 Hz, 1H), 2.64 (dd, *J* = 11.9, 6.2 Hz, 1H), 2.44 (app t, *J* = 12.5 Hz, 1H), 2.05 (dd, *J* = 13.0, 6.3 Hz, 1H), 1.32 (s, 3H). NMR data for **10** diastereomer B: ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.37–7.34 (m, 2H), 7.32–7.29 (m, 1H), 7.22–7.19 (m, 2H), 6.81 (d, *J* = 8.0 Hz, 1H), 6.64 (dd, *J* = 8.8, 1.7 Hz, 1H), 6.60 (d, *J* = 1.8 Hz, 1H), 6.00 (d, *J* = 1.5 Hz, 1H), 5.99 (d, *J* = 1.5 Hz, 1H), 5.69 (br s, 1H), 4.91 (s, 1H), 4.40 (dd, *J* = 11.3, 6.9 Hz, 1H), 4.32 (dd, *J* = 10.2, 4.2 Hz, 1H), 3.51 (dd, *J* = 14.7, 3.9 Hz, 1H), 2.79 (dd, *J* = 11.5, 4.1 Hz, 1H), 2.77 (dd, *J* = 10.3, 4.4 Hz, 1H), 2.40 (dd, *J* = 13.4, 6.8 Hz, 1H), 1.68 (s, 3H).



8p (1:1 dr)

***Rac*-(6*S*,7*S*,8a*S*)-6-(benzo[*d*][1,3]dioxol-5-yl)-3-benzyl-2,7-dimethyl-1,4-dioxooctahydropyrrolo[1,2-*a*]pyrazine-7-carbonitrile (8p** diastereomer A).[5] To dioxopiperazine **10**, diastereomer A (91 mg, 0.23 mmol) in acetone (2.8 mL) was added K_2CO_3 (620 mg, 4.5 mmol) and MeI (1.4 mL, 23 mmol) and the

reaction was maintained for 2 d at 23 ºC with the exclusion of light. The reaction was diluted with H_2O and extracted with CH_2Cl_2. Combined extracts were dried over Na_2SO_4, filtered, and concentrate *in vacuo* to afford **8p** diastereomer A (77 mg, 0.18 mmol, 80% yield) as a colorless amorphous solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.34–7.31 (m, 3H), 7.18–7.13 (m, 2H), 6.77 (d, *J* = 7.8 Hz, 1H), 6.59 (d, *J* = 7.8 Hz, 1H), 6.51 (s, 1H), 5.95 (s, 2H), 4.65 (s, 1H), 4.18 (t, *J* = 4.1 Hz, 1H), 3.28 (dd, *J* = 14.1, 3.9 Hz, 1H), 3.14–3.10 (m, 4H), 2.40–2.39 (m, 2H), 2.04–2.01 (m, 1H), 1.26 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 166.5 (C), 165.5 (C), 148.3 (C), 148.2 (C), 135.4 (C), 131.1 (C), 129.9 (2CH), 129.2 (2CH), 128.1 (CH), 120.0 (C), 119.9 (CH), 108.8 (CH), 106.1 (CH), 101.5 (CH_2), 69.5 (CH), 66.4 (CH), 55.4 (CH), 42.3 (C), 36.8 (CH_2), 36.4 (CH_2), 32.4 (CH_3), 24.8 (CH_3); IR (thin film): 2934, 2247, 1673, 1505, 1491, 1446, 1403, 1304, 1247, 1102, 1053 cm^{-1}; HRMS-ESI (*m/z*) $[M + Na]^+$ calculated for $C_{24}H_{23}N_3O_4Na$, 440.1586; found, 440.1580.



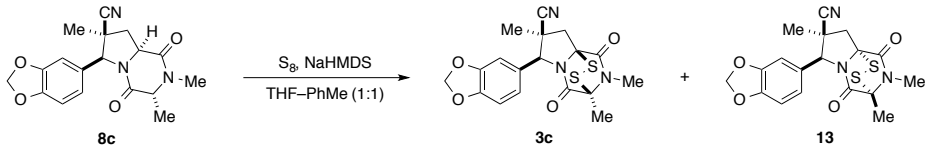
8p (1:1 dr)

***Rac*-(,6*S*,7*S*,8a*S*)-6-(benzo[*d*][1,3]dioxol-5-yl)-3-benzyl-2,7-dimethyl-1,4-dioxooctahydropyrrolo[1,2-*a*]pyrazine-7-carbonitrile** (**8p** diastereomer B). Prepared by same procedure as **8p** diastereomer A from **10** diastereomer B (91 mg, 0.23 mmol), affording **8p** diastereomer B (96 mg, 0.23 mmol, 100%) as a colorless amorphous solid.[5] ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.26–7.19 (m, 3H), 7.14–7.11 (m, 2H), 6.76 (d, *J* = 8.0 Hz, 1H), 6.55 (d, *J* = 8.4 Hz, 1H), 6.52 (s, 1H), 5.99–5.96 (m, 2H), 4.82 (s, 1H), 4.43 (t, *J* = 5.2 Hz, 1H), 4.37 (dd, *J* = 11.3, 6.8 Hz, 1H), 3.48 (dd, *J* = 16.0, 5.6 Hz, 1H), 3.42 (dd, *J* = 16.0, 5.5 Hz, 1H), 3.04 (s, 3H), 2.81 (dd, *J* = 13.1, 11.5 Hz, 1H), 2.46 (dd, *J* = 13.4, 6.6 Hz, 1H), 1.66 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 168.1 (C), 165.8 (C), 148.3 (C), 136.5 (C), 130.8 (C), 129.0 (2CH), 128.8 (2CH), 127.1 (CH), 120.1 (C), 120.07 (C), 120.4 (CH), 108.8 (CH), 106.7 (CH), 101.2 (CH_2), 69.8 (CH), 61.3 (CH), 57.4 (CH), 42.8 (C), 37.0 (CH_2), 33.5 (CH_2), 30.9 (CH_3), 25.6 (CH_3); IR (thin film): 1675, 1504,

1491, 1448, 1390, 1306, 1244, 1039, 912, 733, 700 cm^{-1}; HRMS-ESI (*m/z*) $[M + Na]^+$ calculated for $C_{24}H_{23}N_3O_4Na$, 440.1586; found, 440.1577.

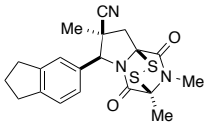
2-5. Synthesis of Epidithiodioxopiperazines

Two variations on the procedure for ETP formation were used (**General Procedures 3** and **4**) as our studies evolved and the procedure used to prepare each compound is indicated. However, these procedures were not optimized and which procedure was best for the formation of a particular product was rarely ascertained. Yields are not directly related to reaction efficiency but reflect the efficiency of chromatographic purification of pure (>95%) ETPs **3**.



General Procedure 3: *Rac*-(3*S*,6*S*,7*S*,8a*S*)-6-(benzo[*d*][1,3]dioxol-5-yl)-2,3,7-trimethyl-1,4-dioxohexahydro-6*H*-3,8a-epidithiopyrrolo[1,2-*a*]pyrazine-7-carbonitrile (3c) and ***rac*-(3*R*,6*S*,7*S*,8a*R*)-6-(benzo[*d*][1,3]dioxol-5-yl)-2,3,7-trimethyl-1,4-dioxohexahydro-6*H*-3,8a-epidithiopyrrolo[1,2-*a*]pyrazine-7-carbonitrile (13).** Dioxopiperazine **8c** (370 mg, 1.1 mmol, 1.0 equiv) and S_8 (290 mg, 1.1 mmol, 1.0 equiv) were added to a 50 mL round-bottom flask and azeotropically dried with dry PhMe (3 x 10 mL). The solids were suspended in THF (11 mL) and the heterogeneous mixture was sparged with Ar for 10 min. The suspension was cooled to 0 ºC for 5 min, then NaHMDS (0.6 M in PhMe, 11 mL, 6.6 mmol, 6.0 equiv) was added over *ca.* 2 min with vigorous stirring. The reaction was maintained at 0 ºC for 3 h, then quenched with sat. aq. NH_4Cl (20 mL) and extracted with EtOAc (3 x 20 mL). Combined extracts were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was dissolved in MeCN (40 mL) and washed with hexanes (3 x 20 mL) to remove HMDS-related byproducts. The MeCN layer was concentrated *in vacuo*. Flash chromatography (SiO_2, 3% EtOAc in CH_2Cl_2) afforded **3c** (200 mg, 0.50 mmol, 45% yield) and **13** (14 mg, 0.035 mmol, 3% yield) as colorless solids.

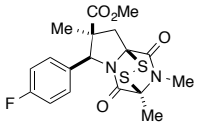
The spectral data for **3c** and **13** were consistent with those previously reported.[2] **3c**: mp = 196–200 ºC (decomp.); ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.96 (s, 1H), 6.91 (s, 2H), 6.06 (s, 2H), 4.89 (s, 1H), 3.36 (d, *J* = 14.5 Hz, 1H), 3.14 (s, 3H), 3.06 (d, *J* = 14.5 Hz, 1H), 2.00 (s, 3H), 1.73 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 165.6 (C), 162.1 (C), 148.5 (C), 148.3 (C), 127.5 (C), 120.7 (CH), 120.3 (C), 108.6 (CH), 107.2 (CH), 101.5 (CH_2), 73.4 (C), 73.3 (C), 72.4 (CH), 44.4 (C), 42.8 (CH_2), 27.8 (CH_3), 24.8 (CH_3), 18.1 (CH_3); IR (thin film): 2984, 2902, 2250, 1688, 1491, 1446, 1358, 1250, 1038, 731 cm^{-1}; HRMS-ESI (*m/z*) $[M + Na]^+$ calculated for $C_{18}H_{17}N_3O_4S_2Na$, 426.0558; found, 426.0555. Structure was confirmed by single-crystal X-ray analysis (CCDC 1061873).[4] **13**: ^{1}H NMR (600 MHz, $CDCl_3$): δ 6.80 (d, *J* = 8.0 Hz, 1H), 6.60 (d, *J* = 8.0 Hz, 1H), 6.55 (s, 1H), 5.98 (app d, *J* = 1.6 Hz, 2H), 5.03 (s, 1H), 3.81 (d, *J* = 15.5 Hz, 1H), 3.12 (s, 3H), 2.51 (d, *J* = 15.5 Hz, 1H), 2.00 (s, 3H), 1.94 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 165.4 (C), 162.5 (C), 148.7 (C), 148.6 (C), 129.5 (C), 120.1 (CH), 119.7 (C), 109.0 (CH), 106.4 (C), 101.7 (CH), 73.9 (C), 73.8 (C), 71.7 (CH), 43.9 (C), 42.4 (CH_2), 27.9 (CH_3), 27.3 (CH_3), 18.4 (CH_3); IR (thin film): 2988, 2940, 2900, 2249, 1694, 1504, 1448, 1355, 1248, 1111, 1038, 912, 731 cm^{-1}; HRMS-ESI (*m/z*) $[M + Na]^+$ calculated for $C_{18}H_{17}N_3O_4S_2Na$, 426.0558; found, 426.0553.



3j

General Procedure 4: *Rac*-(3*S*,6*S*,7*S*,8a*S*)-6-(2,3-dihydro-1*H*-inden-5-yl)-2,3,7-trimethyl-1,4-dioxohexahydro-6*H*-3,8a-epidithiopyrrolo[1,2-*a*]pyrazine-7-carbonitrile (3j). To a suspension of S_8 (74 mg, 0.29 mmol, 1.1 equiv) in dry THF (1.5 mL) was added a solution of NaHMDS (0.6 M in PhMe, 1.4 mL, 0.84 mmol, 3.3 equiv) at 23 ºC over 1 min. After 1 min of vigorous stirring, a solution of dioxopiperazine **8j** (85 mg, 0.25 mmol) in THF (2.3 mL) was added dropwise, followed by additional NaHMDS solution (0.6 M in PhMe, 0.9 mL, 0.54 mmol, 2.2 equiv) over 1 min. The resulting orange-yellow solution was stirred for 50 min at 23 ºC and quenched by the sat. aq. NH_4Cl (5 mL). The resultant mixture was extracted with CH_2Cl_2 (3 x 10 mL). Combined extracts were dried over Na_2SO_4, filtered, and

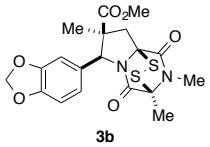
concentrated *in vacuo* to obtain a yellow-brown amorphous residue. This residue was evaporated onto 2.2 g SiO_2 and placed on top of a filter frit containing 12 g SiO_2. The silica plug was washed with hexanes (150 mL) then with MeCN (150 mL). The MeCN filtrate was concentrated *in vacuo* and the resulting crude material was purified by preparative TLC (3% EtOAc/CH_2Cl_2) to afford **3j** (28 mg, 0.070 mmol, 28% yield) as an off-white solid. mp = 195–197 ºC; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.26 (d, *J* = 7.2 Hz, 1H), 7.20 (s, 1H), 7.15 (d, *J* = 7.2 Hz, 1H), 4.87 (s, 1H), 3.30 (d, *J* = 14.9 Hz, 1H), 3.07 (s, 3H), 3.00 (d, *J* = 14.9 Hz, 1H), 2.94–2.89 (m, 4H), 2.08 (app quint, *J* = 7.5 Hz, 2H), 1.93 (s, 3H), 1.67 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 165.8 (C), 162.2 (C), 145.8 (C), 145.0 (C), 131.5 (C), 124.9 (CH), 124.8 (CH), 122.9 (CH), 120.5 (C), 73.6 (C), 73.4 (C), 72.8 (CH), 44.6 (C), 43.0 (CH_2), 33.0 (CH_2), 32.8 (CH_2), 27.9 (CH_3), 25.4 (CH_2), 24.8 (CH_3), 18.2 (CH_3); IR (thin film) 2941, 2251, 1696, 1440, 1359, 1254, 1202, 1145, 1112, 1067, 1030, 911, 731 cm^{-1}; HRMS-ESI (*m/z*) $[M + Na]^+$ calculated for $C_{20}H_{21}N_3O_2S_2Na$, 422.0973; found 422.0965.



3a

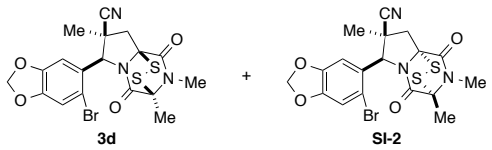
Methyl *rac*-(3*S*,6*S*,7*S*,8a*S*)-6-(4-fluorophenyl)-2,3,7-trimethyl-1,4-dioxohexahydro-6*H*-3,8a-epidithiopyrrolo[1,2-*a*]pyrazine-7-carboxylate (3a). Prepared according to **General Procedure 3** from **8a** (44 mg, 0.13 mmol) affording **3a** (3 mg, 0.008 mmol, 6% yield) as a pale yellow solid. The spectral data were consistent with those previously reported.[2] mp = 148–151 ºC (decomp.); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.42–7.38 (m, 2H), 7.03 (t, *J* = 9.0 Hz, 2H), 5.09 (s, 1H), 3.36 (s, 3H), 3.34 (d, *J* = 14.5 Hz, 1H), 3.25 (d, *J* = 14.5 Hz, 1H), 3.11 (s, 3H), 1.97 (s, 3H), 1.55 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 171.6 (C), 166.4 (C), 163.2 (C), 162.7 (d, $J_{C–F}$ = 246.5 Hz, C), 131.9 (C), 129.5 (d, $J_{C–F}$ = 8.3 Hz, 2CH), 115.6 (d, $J_{C–F}$ = 21.7 Hz, 2CH), 74.7 (C), 73.5 (C), 72.5 (CH), 55.1 (C), 52.4 (CH_3), 39.0 (CH_2), 27.9

(CH_3), 25.6 (CH_3), 18.4 (CH_3); IR (thin film): 2951, 1736, 1692, 1606, 1511, 1255, 1228, 1161, 1129, 848, 733 cm^{-1}; HRMS-ESI (*m/z*) $[M+Na]^+$ calculated for $C_{18}HF_{19}N_2O_4S_2Na$, 433.0668; found, 433.0660.



3b

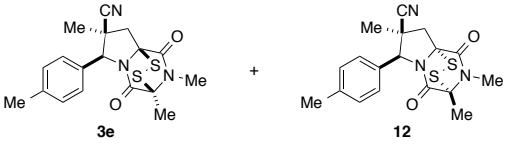
Methyl *rac*-(3*S*,6*S*,7*S*,8a*S*)-6-(benzo[*d*][1,3]dioxol-5-yl)-2,3,7-trimethyl-1,4-dioxohexahydro-6*H*-3,8a-epidithiopyrrolo[1,2-*a*]pyrazine-7-carboxylate (3b). Prepared according to **General Procedure 3** from **8b** (46 mg, 0.12 mmol) affording **3b** (*ca.* 5:1 mixture of diastereomers, 5 mg, 0.01 mmol, 8% yield) as a pale yellow solid. The spectral data were consistent with those previously reported.[2] mp = 167–171 ºC; ^{1}H NMR (*ca.* 5:1 mixture of diastereomers, 500 MHz, $CDCl_3$): δ 6.98 (s, 1H), 6.87 (d, *J* = 8.0 Hz, 1H), 6.76 (d, *J* = 8.0 Hz, 1H), 5.96 (s, 2H), 5.03 (s, 1H), 3.42 (s, 3H), 3.34 (d, *J* = 14.0 Hz, 1H), 3.22 (d, *J* = 14.0 Hz, 1H), 3.10 (s, 3H), 1.96 (s, 3H), 1.52 (s, 3H); ^{13}C NMR (*ca.* 5:1 mixture of diastereomers, 500 MHz, $CDCl_3$125 MHz, $CDCl_3$): δ 171.6 (C), 166.3 (C), 163.1 (C), 147.9 (C), 147.6 (C), 129.7 (C), 121.3 (CH), 108.2 (CH), 108.0 (CH), 101.3 (CH_2), 74.6 (C), 73.4 (C), 72.9 (CH), 55.1 (C), 52.3 (CH_3), 38.8 (CH_2), 27.8 (CH_3), 25.4 (CH_3), 18.4 (CH_3); IR (thin film): 2953, 1736, 1692, 1490, 1447, 1356, 1250, 1038 cm^{-1}; HRMS-ESI (*m/z*) $[M + Na]^+$ calculated for $C_{19}H_{20}N_2O_6S_2Na$, 459.0660; found, 459.0652.



3d **SI-2**

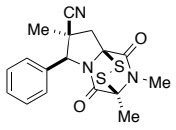
***Rac*-(3*S*,6*R*,7*S*,8a*S*)-6-(6-bromobenzo[*d*][1,3]dioxol-5-yl)-2,3,7-trimethyl-1,4-dioxohexahydro-6*H*-3,8a-epidithiopyrrolo[1,2-*a*]pyrazine-7-carbonitrile (3d).** Prepared according to **General Procedure 3** from **8d** (78 mg, 0.19 mmol) affording **3d** (12 mg, 0.025 mmol, 13% yield) as a colorless solid and **SI-2** (3 mg, 0.06 mmol, 3% yield) as a pale yellow solid. The spectral data were consistent with those previously reported.[2] **3d**: mp = 142–146 ºC (decomp.); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.13 (d, *J* = 8.5 Hz,

1H), 6.69 (d, *J* = 8.5 Hz, 1H), 5.90 (s, 1H), 5.80 (s, 1H), 5.65 (s, 1H), 3.88 (d, *J* = 15.5 Hz, 1H), 3.06 (s, 3H), 2.57 (d, *J* = 15.5 Hz, 1H), 2.12 (s, 3H), 1.95 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 165.6 (C), 162.3 (C), 149.2 (C), 148.3 (C), 126.9 (CH), 120.1 (C), 114.5 (C), 113.3 (C), 108.1 (CH), 102.4 (CH_2), 73.7 (C), 73.4 (C), 71.1 (CH), 44.3 (CH_2), 42.9 (C), 27.9 (CH_3), 25.6 (CH_3), 18.2 (CH_3); IR (thin film): 2986, 2880, 2250, 1695, 1457, 1357, 1242, 1059, 1035, 932, 731 cm^{-1}; HRMS-ESI (*m/z*) $[M + Na]^+$ calculated for $C_{18}H_{16}BrN_3O_4S_2Na$, 503.9663; found, 503.9655. **SI-2:** ^{1}H NMR (500 MHz, CDCl3): δ 7.13 (d, *J* = 8.5 Hz, 1H), 6.69 (d, *J* = 8.5 Hz, 1H), 5.90 (s, 1H), 5.80 (s, 1H), 5.65 (s, 1H), 3.88 (d, *J* = 15.5 Hz, 1H), 3.06 (s, 3H), 2.57 (d, *J* = 15.5 Hz, 1H), 2.12 (s, 3H), 1.95 (s, 3H); ^{13}C NMR (125 MHz, CDCl3): δ 165.5 (C), 161.7 (C), 147.7 (C), 145.2 (C), 126.5 (CH), 119.7 (C), 117.8 (C), 115.0 (C), 110.5 (CH), 102.2 (CH2), 74.7 (C), 73.7 (C), 68.6 (CH), 44.4 (CH2), 43.1 (C), 27.7 (CH3), 27.6 (CH3), 18.4 (CH3). IR (film): ν/cm-1 2986, 2880, 2250, 1695, 1457, 1357, 1242, 1059, 1035, 932, 731. HRMS-ESI (*m/z*) $[M + Na]^+$ calculated for $C_{18}H_{16}N_3O_4BrS_2Na$, 503.9663; found, 503.9655. Structure was confirmed by single-crystal X-ray analysis (CCDC 1061872).[4]



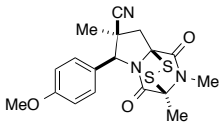
***Rac*-(3*S*,6*S*,7*S*,8a*S*)-2,3,7-trimethyl-1,4-dioxo-6-(*p*-tolyl)hexahydro-6*H*-3,8a-epidithiopyrrolo[1,2-*a*]pyrazine-7-carbonitrile (3e)** and ***Rac*-(3*R*,6*S*,7*S*,8a*R*)-2,3,7-trimethyl-1,4-dioxo-6-(*p*-tolyl)hexahydro-6*H*-3,8a-epidithiopyrrolo[1,2-*a*]pyrazine-7-carbonitrile (12).** Prepared according to **General Procedure 3** from **8e** (98 mg, 0.31 mmol) affording **3e** (24 mg, 0.064 mmol, 21% yield) as a colorless solid and **12** (4 mg, 0.01 mmol, 3%) as a pale yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.28–7.35 (m, 4H), 4.94 (s, 1H), 3.37 (d, *J* = 15.0 Hz, 1H), 3.14 (s, 3H), 3.06 (d, *J* = 15.0 Hz, 1H), 2.43 (s, 3H), 2.00 (s, 3H), 1.74 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 165.8 (C), 162.2 (C), 139.4 (C), 130.7 (C), 129.8 (2CH), 126.8 (2CH), 120.4 (C), 73.6 (C), 73.4 (C), 72.4 (CH), 44.5 (C), 43.0 (CH_2), 27.9 (CH_3), 24.8 (CH_3), 21.4 (CH_3), 18.2 (CH_3); IR (thin film): 2990, 2921, 2245, 1685, 1516, 1358, 1253, 816 cm^{-1};

HRMS-ESI (*m/z*) $[M + Na]^+$ calculated for $C_{18}H_{19}N_3O_2S_2Na$, 396.0816; found, 396.0800. Structure was confirmed by single-crystal X-ray analysis (CCDC 1061871).[4] **12**: ^1H NMR (600 MHz, $CDCl_3$): δ 7.19 (d, *J* = 7.8 Hz, 2H), 6.99 (d, *J* = 7.8 Hz, 2H) 5.09 (s, 1H), 3.83 (d, *J* = 15.4 Hz, 1H), 3.12 (s, 3H), 2.52 (d, *J* = 15.4 Hz, 1H), 2.33 (s, 3H), 2.01 (s, 3H), 1.93 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 165.3 (C), 162.3 (C), 139.4 (C), 132.5 (C), 129.9 (2CH), 125.9 (2CH), 119.6 (C), 73.72 (C), 73.67 (C), 71.4 (CH), 43.6 (C), 42.2 (CH_2), 27.7 (CH_3), 27.0 (CH_3), 21.2 (CH_3), 18.2 (CH_3); IR (thin film): 2923, 2246, 1692, 1515, 1355, 912 cm^{-1}; HRMS-ESI (*m/z*) $[M + Na]^+$ calculated for $C_{18}H_{19}N_3O_2S_2Na$, 396.0816; found, 396.0831.



3f

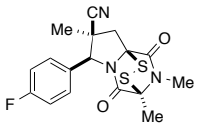
***Rac*-(3*S*,6*S*,7*S*,8a*S*)-2,3,7-trimethyl-1,4-dioxo-6-phenylhexahydro-6*H*-3,8a-epidithiopyrrolo[1,2-*a*]pyrazine-7-carbonitrile (3f).** Prepared according to **General Procedure 3** from dioxopiperazine **8f** (100 mg, 0.34 mmol) affording **3f** (27 mg, 0.08 mmol, 22% yield) as a colorless powder. The spectral data were consistent with those previously reported.[2] mp = 243–246 ºC; ^1H NMR (500 MHz, $CDCl_3$): δ 7.46–7.38 (m, 5H), 4.91 (s, 1H), 3.32 (d, *J* = 15.0 Hz, 1H), 3.09 (s, 3H), 3.00 (d, *J* = 15.0 Hz, 1H), 1.94 (s, 3H), 1.69 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 165.7 (C), 162.2 (C), 133.8 (C), 129.6 (CH), 129.1 (2CH), 126.9 (2CH), 120.2 (C), 73.4 (C), 72.5 (CH), 44.5 (C), 43.0 (CH_2), 29.8 (C), 27.9 (CH_3), 24.9 (CH_3), 18.2 (CH_3); IR (thin film): 2917, 2849, 1705, 1680 cm^{-1}; HRMS-ESI (*m/z*) $[M + Na]^+$ calculated for $C_{17}H_{17}N_3O_2S_2Na$, 382.0660; found, 382.0671.



3g

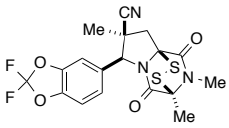
***Rac*-(3*S*,6*S*,7*S*,8a*S*)-6-(4-methoxyphenyl)-2,3,7-trimethyl-1,4-dioxohexahydro-6*H*-3,8a-epidithiopyrrolo[1,2-*a*]pyrazine-7-carbonitrile (3g).** Prepared according to **General Procedure 3** from

8g (33 mg, 0.1 mmol) affording **3g** (12 mg, 0.03 mmol, 30% yield) as a colorless solid. The spectral data were consistent with those previously reported.[2] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32 (d, *J* = 8.7 Hz, 2H), 6.95 (d, *J* = 8.7 Hz, 2H), 4.87 (s, 1H), 3.81 (s, 3H), 3.29 (d, *J* = 14.9 Hz, 1H), 3.08 (s, 3H), 2.99 (d, *J* = 14.9 Hz, 1H), 1.94 (s, 3H), 1.67 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.7 (C), 162.2 (C), 160.4 (C), 128.2 (2CH), 125.7 (C), 120.4 (C), 114.4 (2CH), 73.55 (C), 73.45 (C), 72.2 (CH), 55.4 (CH_3), 44.6 (C), 42.8 (CH_2), 27.9 (CH_3), 24.8 (CH_3), 18.2 (CH_3); IR (thin film): 2988, 2940, 2246, 1690, 1493, 1359, 1255, 1093, 756 cm^{-1}; HRMS-ESI (*m/z*) $[M + Na]^+$ calculated for $C_{18}H_{19}N_3O_3S_2Na$, 412.0760; found, 412.0753.



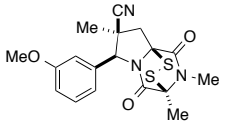
3h

***Rac*-(3*S*,6*S*,7*S*,8a*S*)-6-(4-fluorophenyl)-2,3,7-trimethyl-1,4-dioxohexahydro-6*H*-3,8a-epidithiopyrrolo[1,2-*a*]pyrazine-7-carbonitrile (3h).** Prepared according to **General Procedure 3** from dioxopiperazine **8h** (110 mg, 0.34 mmol) affording **3h** (35 mg, 0.09 mmol, 27% yield) as a colorless powder. The spectral data were consistent with those previously reported.[2] mp = 221–223 ºC; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.37 (app dd, *J* = 8.6, 5.2 Hz, 2H), 7.13 (app t, *J* = 8.5 Hz, 2H), 4.89 (s, 1H), 3.31 (d, *J* = 15.0 Hz, 1H), 3.08 (s, 3H), 2.99 (d, *J* = 15.0 Hz, 1H), 1.94 (s, 3H), 1.68 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 165.6 (C), 163.4 (d, $J_{C–F}$ = 248.2 Hz, C), 162.2 (C), 129.6 (d, $J_{C–F}$ = 3.1 Hz, C), 128.8 (d, $J_{C–F}$ = 8.5 Hz, 2CH), 120.2 (C), 116.2 (d, $J_{C–F}$ = 22.1 Hz, 2CH), 73.52 (C), 73.46 (C), 71.9 (CH), 44.5 (C), 42.9 (CH_2), 27.9 (CH_3), 24.7 (CH_3), 18.2 (CH_3); IR (thin film): 2988, 2926, 1687, 1511 cm^{-1}; HRMS-ESI (*m/z*) $[M + Na]^+$ calculated for $C_{17}H_{16}FN_3O_2S_2Na$, 400.0566; found, 400.0559.



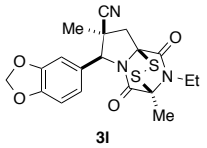
3i

***Rac*-(3*S*,6*S*,7*S*,8a*S*)-6-(2,2-difluorobenzo[*d*][1,3]dioxol-5-yl)-2,3,7-trimethyl-1,4-dioxohexahydro-6*H*-3,8a-epidithiopyrrolo[1,2-*a*]pyrazine-7-carbonitrile (3i).** Prepared according to **General Procedure 3** from **8i** (100 mg, 0.27 mmol) affording **3i** (44 mg, 0.10 mmol, 37% yield) as an off-white solid. The spectral data were consistent with those previously reported.[2] mp = 199–201 ºC; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.09–7.15 (m, 3H), 4.89 (s, 1H), 3.33 (d, *J* = 14.5 Hz, 1H), 3.08 (s, 3H), 3.00 (d, *J* = 14.5 Hz, 1H), 1.95 (s, 3H), 1.69 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 165.5 (C), 162.1 (C), 144.5 (C), 144.3 (C), 131.8 (t, $J_{C–F}$ = 256.8 Hz, C), 130.1 (C), 122.7 (CH), 120.0 (C), 109.9 (CH), 108.4 (CH), 73.5 (C), 73.4 (C), 72.1 (CH), 44.5 (C), 43.0 (CH_2), 27.9 (CH_3), 24.9 (CH_3), 18.1 (CH_3); IR (thin film): 2986, 2942, 2253, 1697, 1501, 1450, 1358, 1240, 1154, 1034, 903, 731 cm^{-1}; HRMS-ESI (*m/z*) [M + Na]$^{+}$ calculated for $C_{18}H_{15}F_2N_3O_4S_2Na$, 462.0370; found, 462.0377.



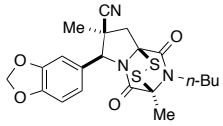
3k

***Rac*-(3*S*,6*S*,7*S*,8a*S*)-6-(3-methoxyphenyl)-2,3,7-trimethyl-1,4-dioxohexahydro-6*H*-3,8a-epidithiopyrrolo[1,2-*a*]pyrazine-7-carbonitrile (3k).** Prepared according to **General Procedure 3** from **8k** (130 mg, 0.40 mmol) affording **3k** (20 mg, 0.05 mmol, 13% yield) as a colorless solid. mp = 189–195 ºC, decomp.); ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.34 (app t, *J* = 7.9 Hz, 1H), 6.99–6.90 (m, 3H), 4.91 (s, 1H), 3.81 (s, 3H), 3.32 (d, *J* = 14.8 Hz, 1H), 3.08 (s, 3H), 2.99 (d, *J* = 14.8 Hz, 1H), 1.94 (s, 3H), 1.67 (s, 3H); ^{13}C NMR (125 MHz, CDCl3): δ 165.6 (C), 162.1 (C), 160.0 (C), 135.3 (C), 130.0 (CH), 120.2 (C), 119.2 (CH), 115.3 (CH), 112.1 (CH), 73.8 (C), 73.5 (C), 72.3 (CH_3), 55.4 (CH), 44.4 (C), 42.8 (CH_2), 27.9 (CH_3), 25.0 (CH_3), 18.2 (CH_3); IR (thin film): 3056, 2984, 2939, 2836, 2240, 1696, 1604, 1438, 1492, 1456, 1361, 1288, 1263, 1161, 1112, 1049, 735 cm^{-1}; HRMS-ESI (*m/z*) [M + Na]$^{+}$ calculated for $C_{18}H_{19}N_3O_3S_2Na$, 412.0766; found, 412.0757.



3l

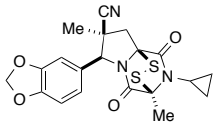
***Rac*-(3*S*,6*S*,7*S*,8a*S*)-6-(benzo[*d*][1,3]dioxol-5-yl)-2-ethyl-3,7-dimethyl-1,4-dioxohexahydro-6*H*-3,8a-epidithiopyrrolo[1,2-*a*]pyrazine-7-carbonitrile (3l).** Prepared according to **General Procedure 4** from **8l** (32 mg, 0.12 mmol) affording **3l** (12 mg, 0.029 mmol, 24% yield) as a colorless solid. mp = 218–220 ºC (decomp.); ^{1}H NMR (600 MHz, $CDCl_3$): δ 6.88 (s, 1H), 6.84 (app s, 2H), 5.99 (app s, 2H), 4.81 (s, 1H), 3.86 (dq, *J* = 14.4, 7.2 Hz, 1H), 3.41 (dq, *J* = 14.4, 7.2 Hz, 1H), 3.29 (d, *J* = 14.9 Hz, 1H), 3.00 (d, *J* = 14.9 Hz, 1H), 2.00 (s, 3H), 1.67 (s, 3H), 1.27 (app t, *J* = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 164.8 (C), 162.2 (C), 148.6 (C), 148.3 (C), 127.6 (C), 120.7 (CH), 120.4 (C), 108.7 (CH), 107.2 (CH), 101.6 (CH_2), 73.8 (C), 72.8 (C), 72.4 (CH), 44.5 (C), 42.9 (CH_2), 38.3 (CH_2), 24.8 (CH_3), 17.6 (CH_3), 12.5 (CH_3); IR (thin film): 2978, 2903, 1687, 1491, 1446, 1362, 1313, 1248, 1038, 927, 736 cm^{-1}; HRMS-ESI (*m/z*) $[M + Na]^+$ calculated for $C_{19}H_{19}N_3O_4S_2Na$, 440.0715; found 440.0707.



3m

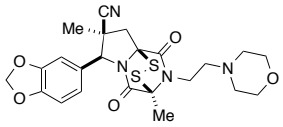
***Rac*-(3*S*,6*S*,7*S*,8a*S*)-6-(benzo[*d*][1,3]dioxol-5-yl)-2-butyl-3,7-dimethyl-1,4-dioxohexahydro-6*H*-3,8a-epidithiopyrrolo[1,2-*a*]pyrazine-7-carbonitrile (3m).** Prepared according to **General Procedure 3** from **8m** (37 mg, 0.1 mmol) affording **3m** (13 mg, 0.03 mmol, 33% yield) as a colorless solid. The spectral data were consistent with those previously reported.[2] ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.88 (s, 1H), 6.84 (app s, 2H), 5.99 (s, 2H), 4.81 (s, 1H), 3.83–3.74, (m, 1H), 3.29 (d, *J* = 14.9 Hz, 1H), 2.99 (d, *J* = 14.9 Hz, 1H), 1.99 (s, 3H), 1.66 (s, 3H), 1.66–1.58 (m, 2H), 1.42–1.32 (m, 2H), 0.96 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.2 (C), 162.3 (C), 148.6 (C), 148.4 (C), 127.7 (C), 120.7 (CH), 120.4 (C), 108.7 (CH), 107.3 (CH), 101.6 (CH_2), 73.8 (C), 72.9 (C), 72.4 (CH), 44.5 (C), 43.2 (CH_2), 42.9 (CH_2), 29.8 (CH_2), 24.9 (CH_3), 20.4 (CH_2), 17.7 (CH_3), 13.9 (CH_3); IR (thin film): 2984, 2902, 2250, 1688, 1491,

1446, 1358, 1250, 1038, 731 cm^{-1}; HRMS-ESI (*m/z*) $[M + Na]^+$ calculated for $C_{21}H_{23}N_3O_4S_2Na$, 468.1022; found, 468.1018.



3n

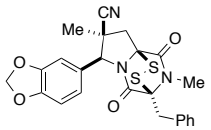
***Rac*-(3*S*,6*S*,7*S*,8a*S*)-6-(benzo[*d*][1,3]dioxol-5-yl)-2-cyclopropyl-3,7-dimethyl-1,4-dioxohexahydro-6*H*-3,8a-epidithiopyrrolo[1,2-*a*]pyrazine-7-carbonitrile (3n).** Prepared according to **General Procedure 4** from **8n** (120 mg, 0.33 mmol) affording **3n** (19 mg, 0.044 mmol, 13% yield) as an off-white solid. The spectral data were consistent with those previously reported.[2] mp = 220–222 ºC; ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.87 (s, 1H), 6.83 (app s, 2H), 5.99 (s, 2H), 4.80 (s, 1H), 3.27 (d, *J* = 14.9 Hz, 1H), 2.93 (d, *J* = 14.9 Hz, 1H), 2.57–2.53 (m, 1H), 2.12 (s, 3H), 1.66 (s, 3H), 1.29–1.24 (m, 1H), 1.06–0.97 (m, 2H), 0.96–0.90 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 165.7 (C), 162.3 (C), 148.6 (C), 148.3 (C), 127.6 (C), 120.7 (CH), 120.4 (C), 108.6 (CH), 107.2 (CH), 101.6 (CH_2), 74.4 (C), 74.1 (C), 72.4 (CH), 44.5 (C), 42.9 (CH_2), 25.8 (CH), 24.8 (CH_3), 17.8 (CH_3), 8.2 (CH_2), 7.7 (CH_2); IR (thin film): 1696, 1491, 1446, 1348, 1248, 1189, 1037, 930, 735 cm^{-1}; HRMS-ESI (*m/z*) $[M + Na]^+$ calculated for $C_{20}H_{19}N_3O_4S_2Na$, 452.0715; found, 452.0702.



3o

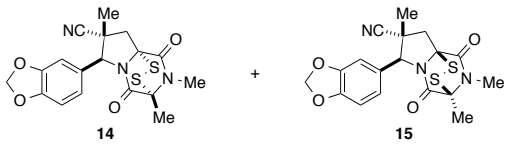
***Rac*-(3*S*,6*S*,7*S*,8a*S*)-6-(benzo[*d*][1,3]dioxol-5-yl)-3,7-dimethyl-2-(2-morpholinoethyl)-1,4-dioxohexahydro-6*H*-3,8a-epidithiopyrrolo[1,2-*a*]pyrazine-7-carbonitrile (3o).** Prepared according to **General Procedure 4** from **8o** (60 mg, 0.14 mmol) affording **3o** (19 mg, 0.038 mmol, 27% yield) as a colorless solid. The spectral data were consistent with those previously reported.[2] ^{1}H NMR (600 MHz, $CDCl_3$): δ 6.88 (s, 1H), 6.84 (s, 2H), 6.0 (s, 2H), 4.82 (s, 1H), 3.92 (app dt, *J* = 14.2, 7.1 Hz, 1H), 3.70,

(app s, 4H), 3.41 (s, 1H), 3.28 (d, *J* = 14.9 Hz, 1H), 2.99 (d, *J* = 14.9 Hz, 1H), 2.67–2.44 (m, 6H), 2.02 (s, 3H), 1.66 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 165.0 (C), 162.1 (C), 148.5 (C), 148.2 (C), 127.4 (C), 120.6 (CH), 120.2 (C), 108.5 (CH), 107.1 (CH), 101.5 (CH_2), 73.4 (C), 72.8 (C), 72.2 (CH), 66.8 (CH_2), 55.5 (CH_2), 53.8 ($2CH_2$), 44.4 (CH_2), 42.7 ($2CH_2$) 40.4 (C), 24.7 (CH_3), 17.7 (CH_3); IR (thin film): 3055, 2958, 2921, 2856, 2814, 2241, 1690, 1504, 1492, 1447, 1383, 1314, 1249, 1116, 1038, 930, 735 cm^{-1}; HRMS-ESI (*m/z*) $[M + Na]^+$ calculated for $C_{23}H_{26}N_4O_5S_2Na$, 525.1242; found, 525.1257.



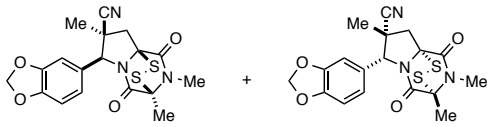
3p

***Rac*-(3*S*,6*S*,7*S*,8a*S*)-6-(benzo[*d*][1,3]dioxol-5-yl)-3-benzyl-2,7-dimethyl-1,4-dioxohexahydro-6*H*-3,8a-epidithiopyrrolo[1,2-*a*]pyrazine-7-carbonitrile (3p).** Prepared according to **General Procedure 4** from dioxopiperazine **8p** (diastereomer B, 75 mg, 0.18 mmol) affording **3p** (10 mg, 0.021 mmol, 12% yield) as a colorless solid. The spectral data were consistent with those previously reported.[2] mp = 182–184 ºC; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.33–7.31 (m, 2H), 7.29–7.24 (m, 3H), 6.86 (s, 1H), 6.82–6.81 (m, 2H), 5.99–5.98 (m, 2H), 4.90 (s, 1H), 3.82 (d, *J* = 15.3 Hz, 1H), 3.75 (d, *J* = 15.3 Hz, 1H), 3.32 (d, *J* = 14.9 Hz, 1H), 3.07 (s, 3H), 3.02 (d, *J* = 14.9 Hz, 1H), 1.70 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 166.4 (C), 161.4 (C), 148.6 (C), 148.3 (C), 133.6 (C), 129.9 (2CH), 128.7 (2CH), 127.8 (CH), 127.4 (C), 120.8 (CH), 120.3 (C), 108.7 (CH), 107.4 (CH), 101.6 (CH_2), 77.8 (C), 73.5 (C), 72.7 (CH), 44.5 (C), 42.9 (CH_2), 36.6 (CH_2), 29.4 (CH_3), 25.0 (CH_3); IR (thin film): 2917, 1695, 1491, 1447, 1357, 1249, 1190, 1037, 931, 817 cm^{-1}; HRMS-ESI (*m/z*) $[M + Na]^+$ calculated for $C_{24}H_{21}N_3O_4S_2Na$, 502.0871; found, 502.0867.



***Rac*-(3*R*,6*S*,7*R*,8a*R*)-6-(benzo[*d*][1,3]dioxol-5-yl)-2,3,7-trimethyl-1,4-dioxohexahydro-6*H*-3,8a-epidithiopyrrolo[1,2-*a*]pyrazine-7-carbonitrile (14)** and ***rac*-(3*S*,6*S*,7*R*,8a*S*)-6-(benzo[*d*][1,3]dioxol-5-yl)-2,3,7-trimethyl-1,4-dioxohexahydro-6*H*-3,8a-epidithiopyrrolo[1,2-*a*]pyrazine-7-carbonitrile (15).** Prepared according to **General Procedure 3** from *epi*-**8c** (60 mg, 0.18 mmol) affording **14** (8 mg, 0.02 mmol, 11% yield) and **15** (8 mg, 0.02 mmol, 11% yield) as colorless solids. **14**: ^{1}H NMR (600 MHz, $CDCl_3$): δ 6.78 (d, *J* = 6.5 Hz, 1H), 6.48 (app br s, 2H), 5.98 (s, 2H), 5.49 (s, 1H), 3.18 (d, *J* = 15.6 Hz, 1H), 3.12 (s, 3H), 2.79 (d, *J* = 15.6 Hz, 1H), 1.95 (s, 3H), 1.16 (s, 3H); ^{13}C NMR (125 MHz, $(CD_3)_2SO$, 348 K): δ 164.7, 161.4, 147.3, 147.2, 128.1, 123.0, 119.8, 108.0, 106.8, 101.0, 7.3.4, 73.2, 68.2, 41.0, 40.1, 27.0, 20.6, 17.3; IR (thin film): 2922, 2852, 1689, 1504, 1490, 1447, 1355, 1246, 1100, 1036, 9288, 732 cm^{-1}; HRMS-ESI (*m/z*) $[M + Na]^+$ calculated for $C_{18}H_{19}N_3O_4S_2Na$ 426.0558; found 426.0555. **15** (mp, 194–195 ºC, decomp.): ^{1}H NMR (600 MHz, $CDCl_3$): 6.88 (s, 1H), 6.87–6.82 (m, 2H), 5.99 (s, 2H), 5.46 (s, 1H), 3.78 (d, *J* = 14.5 Hz, 1H), 3.11 (s, 3H), 2.50 (d, *J* = 14.5 Hz, 1H), 1.97 (s, 3H), 1.25 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 165.2 (C), 162.6 (C), 148.5 (C), 148.4 (C), 126.9 (C), 122.4 (C), 121.3 (CH), 108.9 (CH), 107.7 (CH), 101.7 (CH_2), 73.75 (C), 73.73 (C), 71.0 (CH), 42.1 (C), 41.9 (CH_2), 28.0 (CH_3), 21.9 (CH_3), 18.3 (CH_3); IR (thin film): 2993, 2942, 2900, 1696, 1504, 1491, 1357, 1251, 1109, 1038, 911, 731 cm^{-1}; HRMS-ESI (*m/z*) $[M + Na]^+$ calculated for $C_{18}H_{17}N_3O_4S_2Na$ 426.0558; found, 426.0554.

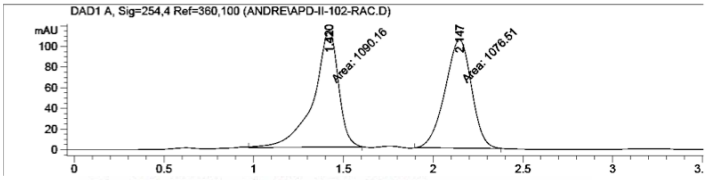
2-6. Resolution of 3c enantiomers



(+)-(*S,S,S,S*)-**3c** (–)-(*R,R,R,R*)-**3c**

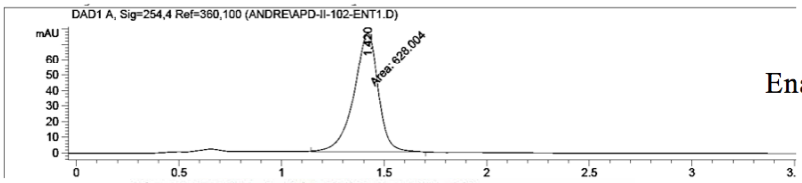
The two enantiomers were resolved by preparative chiral HPLC (stationary phase: CHIRALPAK IA (250 x 50 mm i.d., 5 micron), mobile phase: reagent alcohol 100%), flow rate 2.5 mL/min). The enantiomeric excess was determined by means of analytical chiral HPLC (stationary phase CHIRALPAK IA-3 (50 x 4.6 mm i.d., 3 micron), mobile phase: reagent alcohol 100%, flow rate 1 mL/min, 254 nm):

(3*S*,6*S*,7*S*,8a*S*)-enantiomer*:* t_{ret} = 1.40 min; (3*R*,6*R*,7*R*,8a*R*)-enantiomer: t_{ret} = 2.11 min. Enantiomer 1: (+)-(*S*,*S*,*S*,*S*)-**3c**: t_{ret} = 1.40 min; Enantiomer 2: (–)-(*R*,*R*,*R*,*R*)-**3c**: t_{ret} = 2.11 min.



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

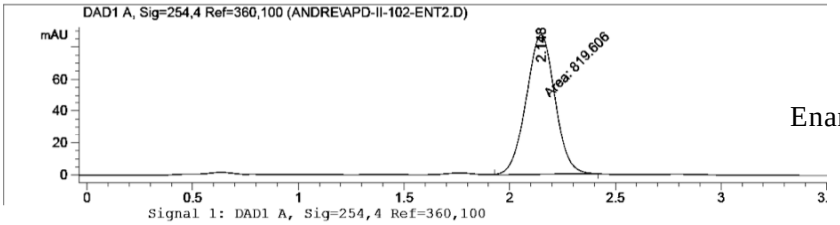
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.420	MM	0.1599	1090.15759	113.59747	50.3148
2	2.147	MM	0.1706	1076.51428	105.14082	49.6852
Totals :				2166.67187	218.73829	



Enantiomer 1: (+)-(*S*,*S*,*S*,*S*)-**3c**

Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.420	MM	0.1369	628.00409	76.42750	100.0000
Totals :				628.00409	76.42750	

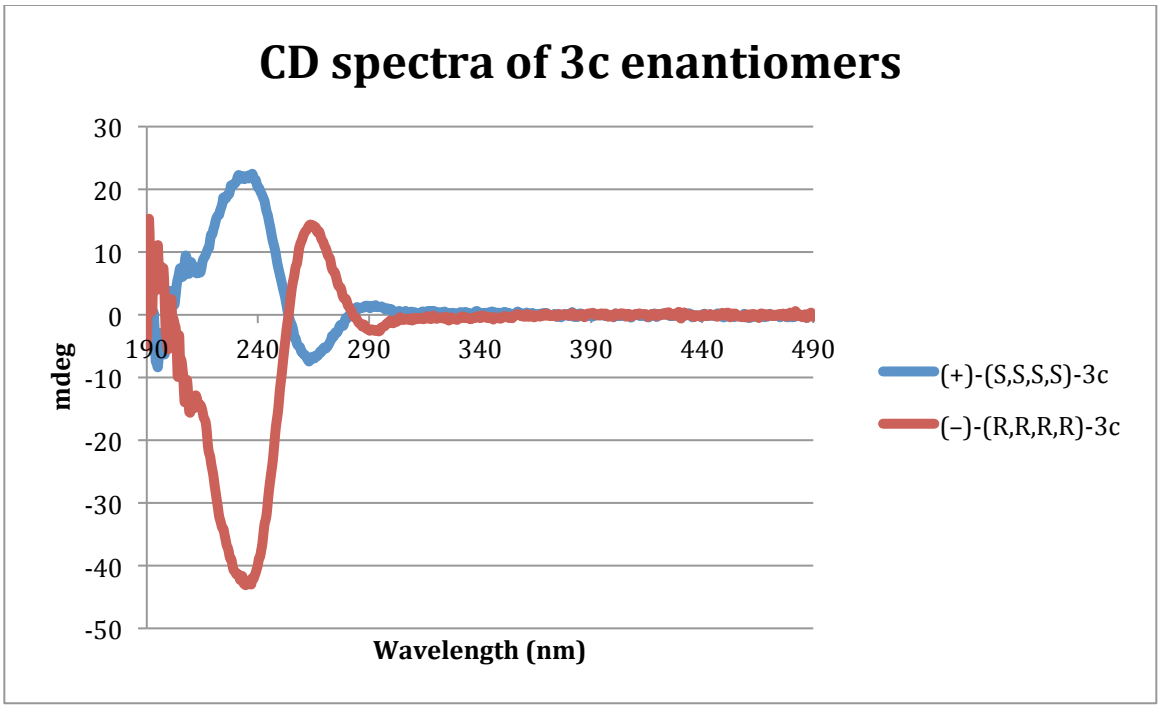


Enantiomer 2: (–)-(*R*,*R*,*R*,*R*)-**3c**

Signal 1: DAD1 A, Sig=254,4 Ref=360,100

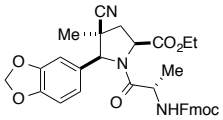
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.148	MM	0.1568	819.60620	87.12536	100.0000
Totals :				819.60620	87.12536	

b) Circular Dichroism Data: Obtained using solutions EtOH ($c \approx 1 \times 10^{-4}$ M)



Absolute configuration was assigned on the basis of CD data and existing precedent.[7] Absolute configuration was also confirmed by X-ray analysis.[4]

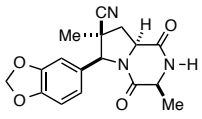
2-7. Enantioselective Synthesis of ETP 3c



16

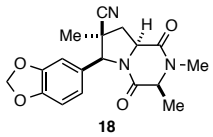
Ethyl (2*S*,4*S*,5*S*)-1-((((9*H*-fluoren-9-yl)methoxy)carbonyl)-*L*-alanyl)-5-(benzo[*d*][1,3]dioxol-5-yl)-4-isocyano-4-methylpyrrolidine-2-carboxylate (16). To a stirred solution of racemic **5c** (2.1 g, 6.9 mmol) in CH_2Cl_2 (14 mL) were added Et_3N (1.9 mL, 1.4 g, 14 mmol) and Fmoc-L-alanyl chloride[8] (3.3 g, 10 mmol) in CH_2Cl_2 (14 mL) at 0 ºC. The reaction was stirred overnight. The reaction was quenched with sat. aq. $NaHCO_3$ (20 mL) and extracted with CH_2Cl_2 (3 x 30 mL) . The combined organic layer was dried over $MgSO_4$ and concentrated to dryness. The crude product was purified by flash chromatography (SiO_2, 33% EtOAc in hexanes) to afford **16** (1.9 g, 3.2 mmol, 46% yield) as a colorless solid and the (2*R*,4*R*,5*R*)-*L*-alanyl diastereomer (1.7 g, 2.8 mmol, 42% yield) as a colorless solid. ^{1}H NMR (400 MHz, $CDCl_3$): 7.76

(d, *J* = 7.5 Hz, 2H), 7.55 (d, *J* = 7.4 Hz, 2H), 7.40 (t, *J* = 7.4 Hz, 2H), 7.30 (t, *J* = 7.4 Hz, 3H), 7.20 (dd, *J* = 8.1, 1.4 Hz, 1H), 6.87 (d, *J* = 8.0 Hz, 1H), 6.01 (d, *J* = 6.6 Hz, 2H), 5.22 (s, 1H), 5.19 (d, *J* = 7.8 Hz, 2H), 4.61 (dd, *J* = 9.8, 7.2 Hz, 1H), 4.40–4.23 (m, 4H), 4.22–4.14 (m, 2H), 2.59 (dd, *J* = 12.8, 9.8 Hz, 1H), 2.35 (dd, *J* = 12.8, 7.2 Hz, 1H), 1.61 (s, 3H), 1.35 (t, *J* = 7.2 Hz, 3H), 0.99 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 174.4, 170.4, 156.2, 148.49, 148.45, 143.9, 143.8, 141.5, 132.0, 127.94, 127.91, 127.2, 125.3, 125.2, 121.5, 120.18, 120.16, 108.7, 108.0, 101.6, 70.5, 67.4, 62.1, 58.4, 48.0, 47.2, 44.7, 37.5, 24.5, 17.6, 14.2; IR (thin film): 2988, 2920, 2245, 1671, 1491, 1447, 1246, 1039, 928, 782, 721 cm^{-1}; HRMS-ESI (*m/z*) $[M + Na]^+$ calculated for $C_{34}H_{33}N_3O_7Na$, 618.2211; found, 618.2205; $[\alpha]_D^{20}$= +63.4 (c=0.72, $CHCl_3$).



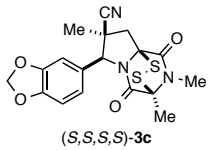
17

(3*S*,6*S*,7*S*,8a*S*)-6-(benzo[*d*][1,3]dioxol-5-yl)-7-isocyano-3,7-dimethylhexahydropyrrolo[1,2-*a*]pyrazine-1,4-dione (17). To a stirred solution of intermediate **16** (2.8 g, 4.7 mmol) in CH_2Cl_2 (18 mL) was added piperidine (4.0 g, 47 mmol). After 30 min, the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (SiO_2, 3% MeOH/CH_2Cl_2) to afford dioxopiperazine **17** (1.4 g, 4.3 mmol, 91% yield) as colorless solid. ^{1}H NMR (400 MHz, $CDCl_3$): 6.79 (d, *J* = 8.0 Hz, 1H), 6.62 (dd, *J* = 8.0, 1.8 Hz, 1H), 6.58 (d, *J* = 1.8 Hz, 2H), 5.96 (s, 2H), 5.91 (br s, 1H), 4.87 (s, 1H), 4.43 (dd, *J* = 11.0, 6.9 Hz, 1H), 4.17 (q, *J* = 6.8 Hz, 1H), 2.82 (dd, *J* = 13.4, 11.2, Hz, 1H), 2.35 (dd, *J* = 13.4, 6.9 Hz, 1H), 1.68 (s, 3H), 1.44 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 169.1, 167.1, 148.5, 148.4, 131.0, 119.9, 108.9, 106.4, 101.6, 69.5, 57.7, 51.8, 43.0, 36.0, 25.5, 15.6; IR (thin film): 2983, 2915, 2244, 1671, 1490, 1447, 1248, 1037, 921, 725 cm^{-1}; HRMS-ESI (*m/z*) $[M + Na]^+$ calculated for $C_{17}H_{17}N_3O_4Na$, 350.1111; found, 350.1123. $[\alpha]_D^{20}$= –38.2 (c=0.43, $CHCl_3$).



18

(3*S*,6*S*,7*S*,8a*S*)-6-(benzo[*d*][1,3]dioxol-5-yl)-7-isocyano-2,3,7-trimethylhexahydropyrrolo[1,2-*a*]pyrazine-1,4-dione (18). To a stirred solution of compound **17** (1.4 g, 4.3 mmol) in THF (43 mL) was added NaH (60 wt% in mineral oil, 260 mg, 6.5 mmol) at 0 ºC. After 20 min at 23 ºC, MeI (1.85 g, 13 mmol) was added at 0 ºC. After 2 h at 23 ºC, the reaction was quenched with sat. aq. NH_4Cl (20 mL). The solvent was removed under reduced pressure and the resulting residue was extracted with CH_2Cl_2 (3 x 50 mL). The combined organic layers were dried over $MgSO_4$ and evaporated to dryness. The crude product was purified by flash chromatography (SiO_2, 25% EtOAc/hexanes) to afford dioxopiperazine **18** (1.25 g, 3.7 mmol, 86% yield) as a colorless solid. ^{1}H NMR (400 MHz, $CDCl_3$): 6.83 (d, *J* = 8.2 Hz, 2H), 6.73 (d, *J* = 1.7 Hz, 1H), 6.71 (s, 1H), 5.98 (s, 2H), 4.74 (dd, *J* = 10.6, 6.2 Hz, 1H), 3.88 (q, *J* = 7.1 Hz, 1H), 3.01 (s, 3H), 2.93 (dd, *J* = 13.2, 6.2 Hz, 1H), 2.26 (dd, *J* = 13.2, 10.4 Hz, 1H), 1.60 (s, 3H), 1.56 (d, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 166.1, 165.4, 148.4, 148.3, 129.5, 120.5, 119.6, 108.7, 106.3, 101.6, 70.4, 60.8, 58.6, 44.3, 41.8, 32.3, 22.9, 16.9; IR (thin film): 2982, 2917, 2244, 1671, 1491, 1447, 1246, 1037, 925, 721 cm^{-1}; HRMS-ESI (*m/z*) $[M + Na]^+$ calculated for $C_{18}H_{19}N_3O_4Na$, 364.1268; found, 364.1272. $[\alpha]_D^{20}$= +129.0 (c=0.57, $CHCl_3$);



(*S*,*S*,*S*,*S*)-**3c**

(3*S*,6*S*,7*S*,8a*S*)-6-(benzo[*d*][1,3]dioxol-5-yl)-7-isocyano-2,3,7-trimethyltetrahydro-6*H*-3,8a-epidithiopyrrolo[1,2-*a*]pyrazine-1,4-dione ((*S*,*S*,*S*,*S*)-**3c).** Prepared according to **General Procedure 4** from dioxopiperazine **18** (340 mg, 1.0 mmol) affording (*S*,*S*,*S*,*S*)-**3c** (130 mg, 0.32 mmol, 32% yield) as a colorless solid. ^{1}H NMR, ^{13}C NMR, IR, and HRMS data were identical with racemic **3c**. HPLC analysis

as described above indicated 99% *ee*. $[\alpha]_D^{20}$= +210.0 (c=0.18, $CHCl_3$); (*S*,*S*,*S*,*S*)-**3c** was recrystallized from CH_2Cl_2–EtOAc (1:4) and the absolute streochemistry was confirmed by single-crystal X-ray analysis.[4]

3. Biology Experimental Procedures

Cell viability assays. Cell viability was determined using a MTS metabolic activity assay as described by the supplier (Promega).[6] Briefly, cells (2500/well and 5000/well for solid and blood tumor cell lines, respectively) were seeded in 96-well plates, incubated overnight at 37 ºC in 5% (v/v) CO_2 and exposed to ETPs in a dose-dependent manner for 48 h. DMSO was used as the vehicle control. Cell viability was determined by tetrazolium conversion to its formazan dye and absorbance was measured at 490 nm using an automated ELISA plate reader. Each experiment was performed in quadruplicate and mean values are reported in Tables 2 and 3.

Mouse xenograft models. A2058 human melanoma cells (3×10^6) were resuspended in serum-free RPMI1640 medium and subcutaneously injected into the flanks of 5–6 weeks old Athymic female nude mice (NCI). When palpable tumor sizes reached at approximately 100 mm^3, mice were divided into two groups (vehicle = 5, treatment = 5). Then, ETP **3c** was administered by IP injection at 20 mg/kg with vehicle (10% DMSO + 0.5% TWEEN® 20 + 89.5% saline) once daily for 13 days. For xenograft model of human lung cancer, A549 human non-small lung cancer cells (5×10^6) were resuspended in serum-free DMEM medium and Matrigel (ratio of 1:1) and subcutaneously injected into the flanks of 5–6 weeks old female NOD/SCID/ IL-2rg(ko)(NSG) mice. When palpable tumor sizes reached at approximately 50 mm^3, mice were divided into two groups (vehicle = 10, treatment = 10). Then, ETP **3c** was administered orally at 10 mg/kg with vehicle (10% DMSO + 30% Solutol + 60% saline) once daily for 31 days. Tumor volumes were calculated by the formula $\frac{1}{2} a \times b^2$, where a is the long diameter, and b is the short diameter. Tumors were weighed at end points. The statistical

significance of group differences was analyzed using a Student's t-test with the two-tailed distribution. *P* values less than 0.05 were considered statistically significant.

4. References

1. J. M. Longmire, B. Wang, X. Zhang, *J. Am. Chem. Soc.* 2002, **124**, 13400.

2. L. E. Overman, M. Baumann, S. Nam, D. Horne, R. Jove, L. J. Xie, C. Kwolik, "Preparation of Epipolythiodioxopiperazine ETP Derivatives for Treatment of Cancer" *PCT Int. Appl*. 2014, WO 2014066435 A1.

3. Prepared according to procedure from A. S. Kumar, *et al*. "Novel Protein Tyrosine Phosphatase-IB Inhibitors" WO2009109999, 2009.

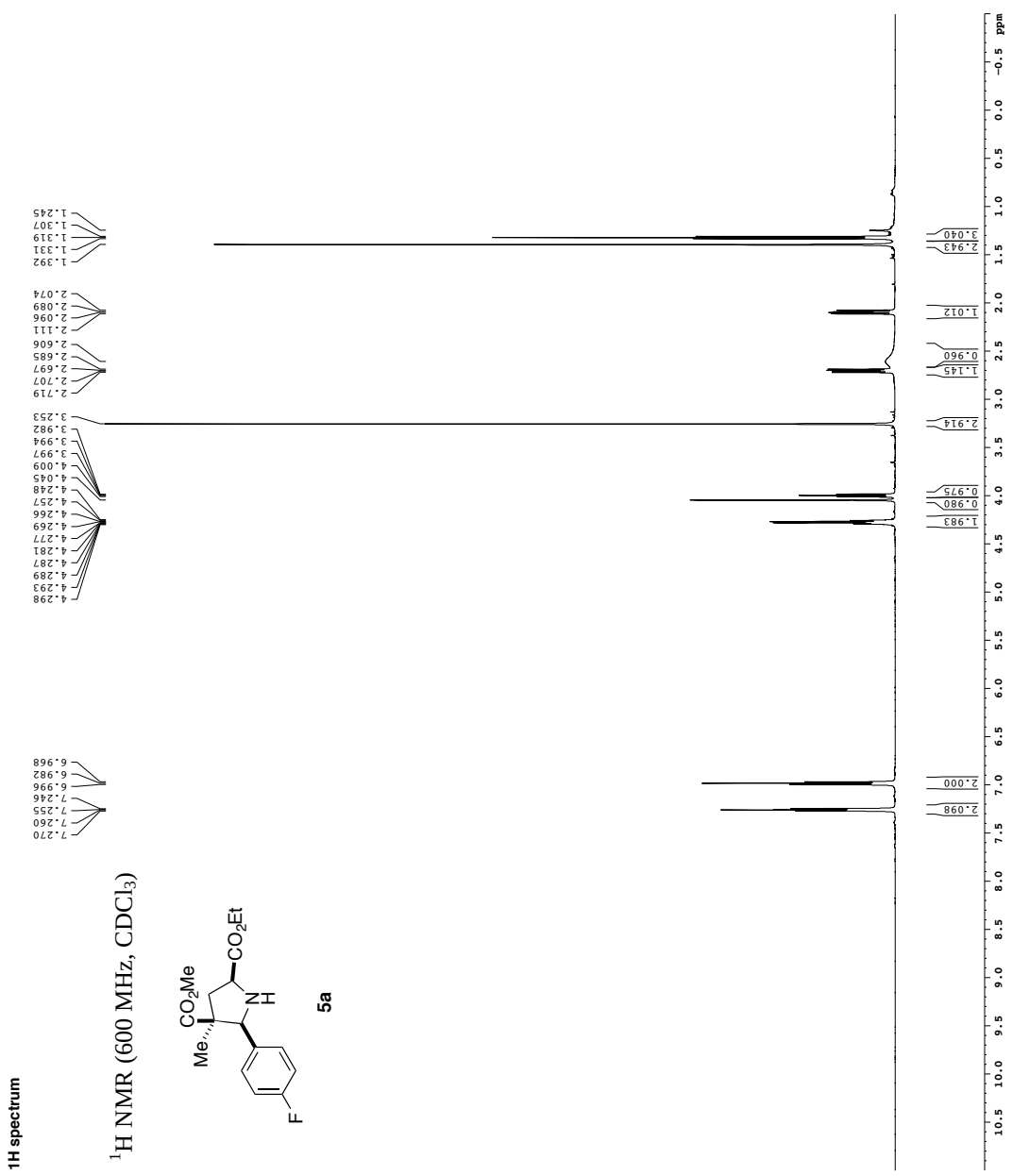
4. X-ray coordinates deposited with CSD.

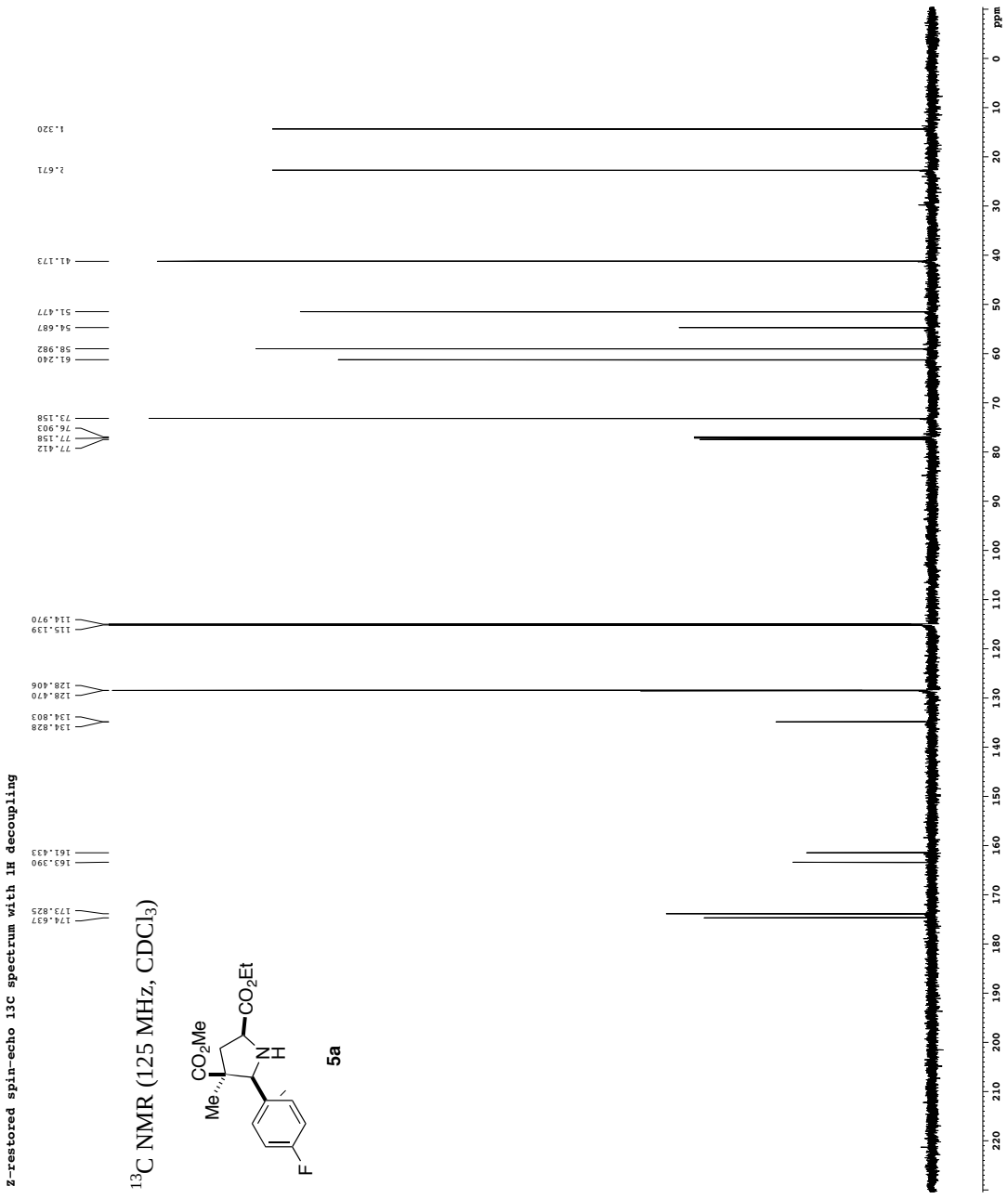
5. Although diastereomers of compound **11** were isolated, the configuration at C3 of the dioxopiperazine ring was not assigned.

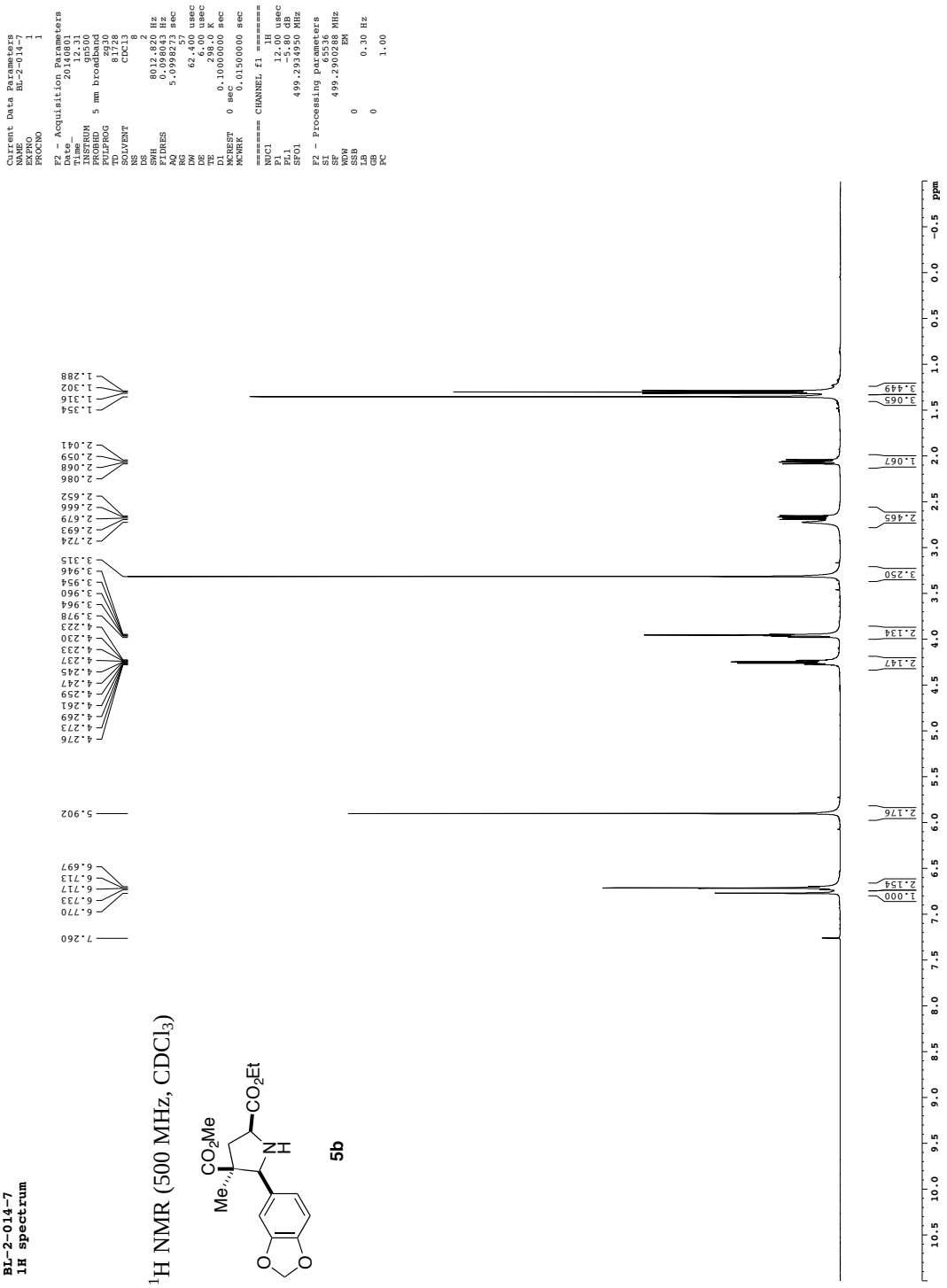
6. S. Nam, A. Williams, A. Vultur, A. List, K. Bhalla, D. Smith, F. Y. Lee, R. Jove, *Mol. Cancer Ther.* 2007, **6**, 1400.

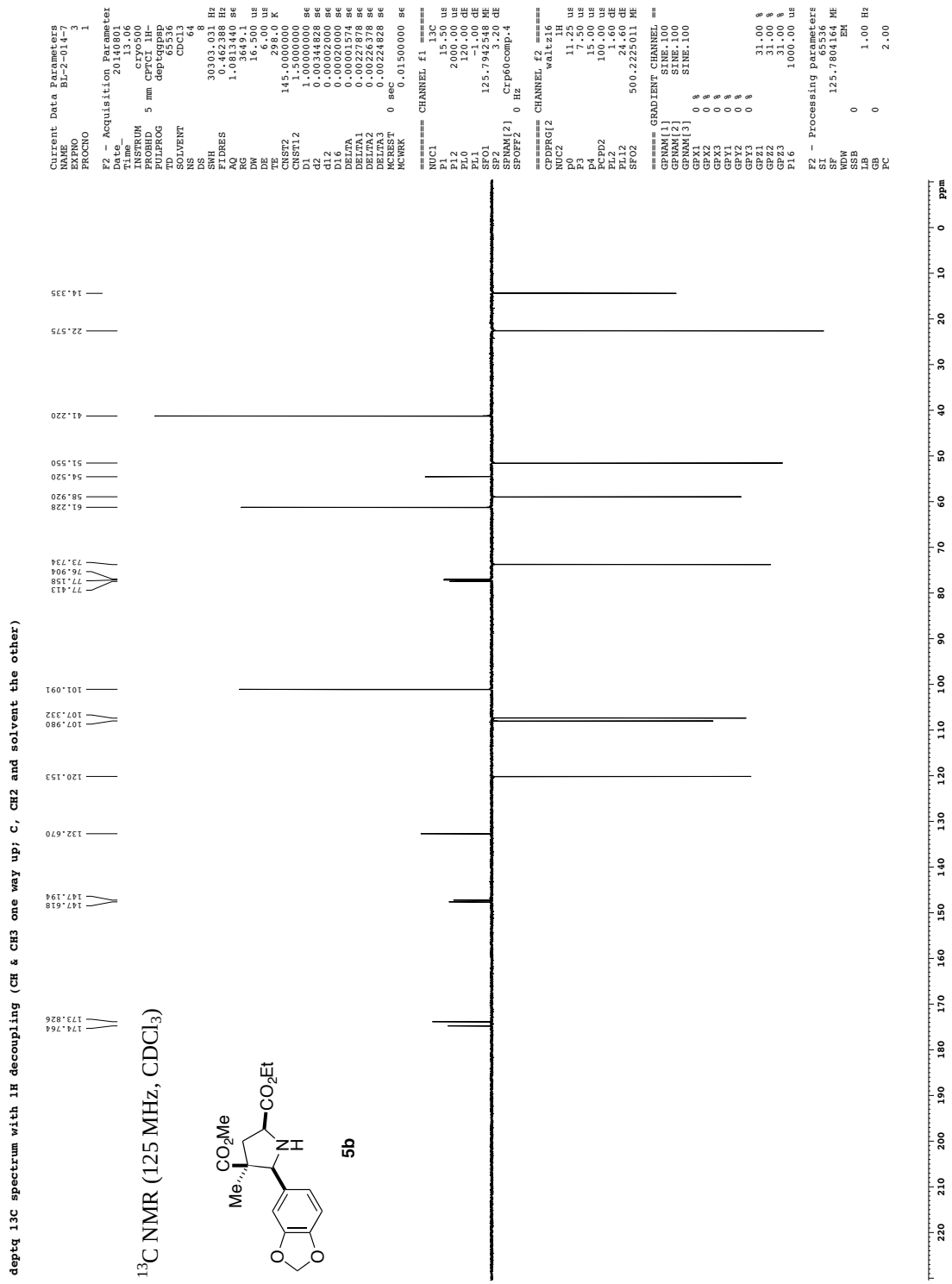
7. M. Carmack, L. A. Neubert, *J. Am. Chem. Soc.* 1967, **89**, 7134. D. Hauser, H. P. Weber, H. P. Sigg, *Helv. Chim. Acta* 1970, **53**, 1061. H. Minato, M. Matsumoto, T. Katayama, *J. Chem. Soc. D.* 1971, 44. R. Nagarajan, R. W. Woody, *J. Am. Chem. Soc.* 1973, **95**, 7212. R. W. Woody, *Tetrahedron* 1973, **29**, 1273.

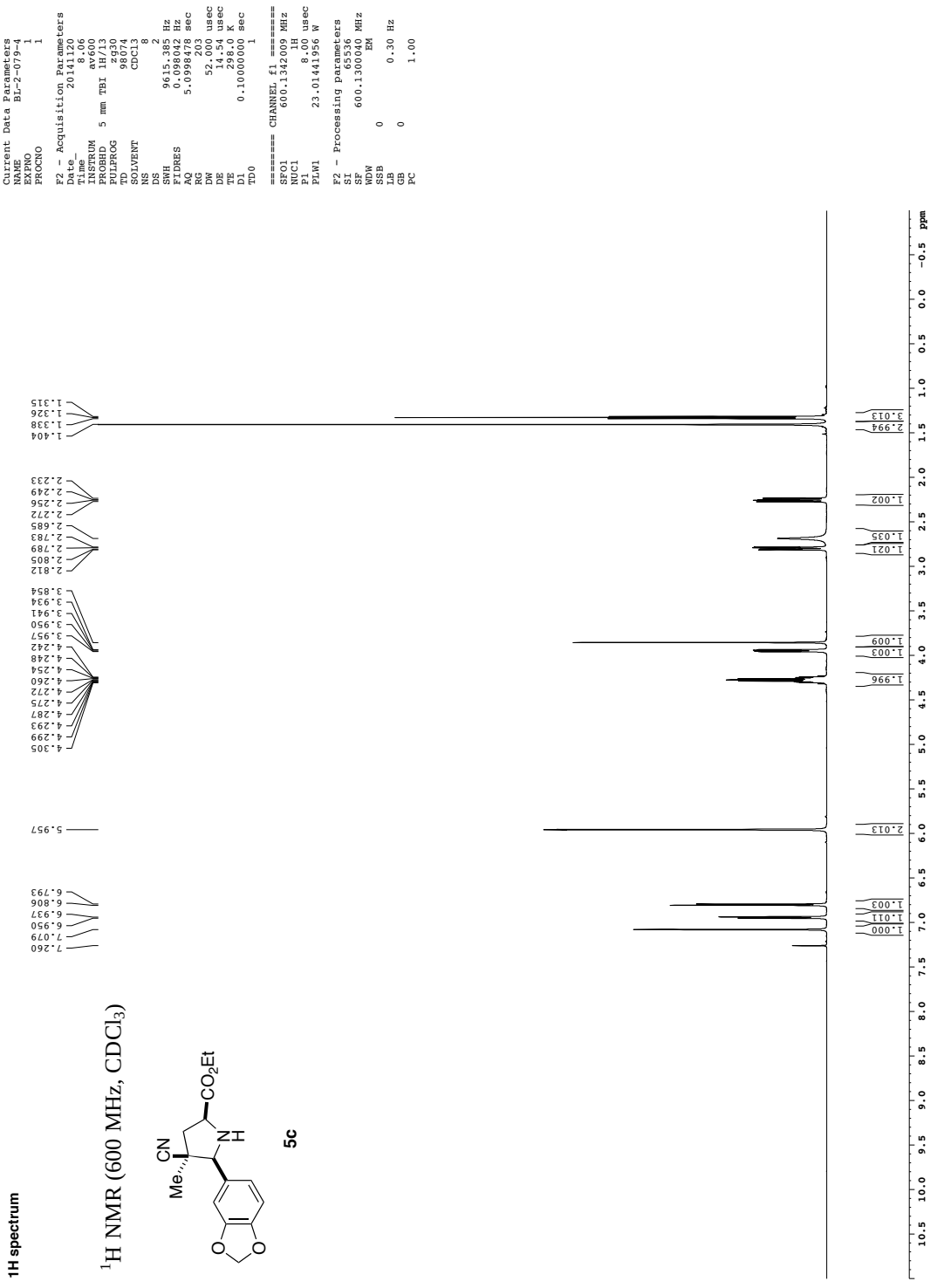
8. Prepared according to a procedure by L. A. Carpino, B. J. Cohen, K. E. Stephens, S. Y. Sadat-Aalaee, J. Tien, D. C. Langridge, *J. Org. Chem.* 1986, **51**, 3732.

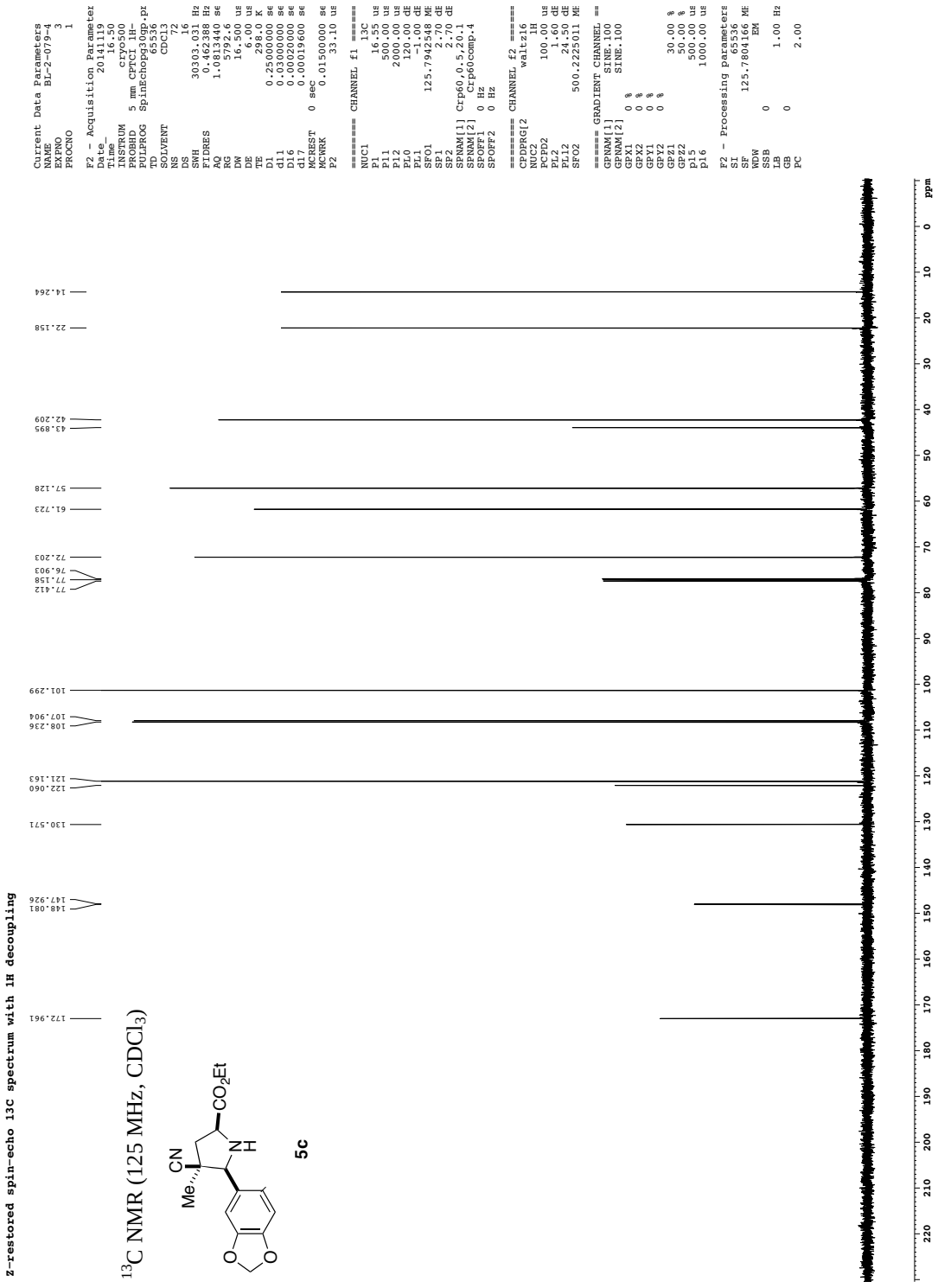

1H spectrum
^{1}H NMR (600 MHz, CDCl$_3$)
CO2Me
Me
CO2Et
N
H
F
5a
Current Data Parameters
NAME BL-2-022-4
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20140813
Time 8.26
INSTRUM av600
PROBHD 5 mm TBI 1H/13
PULPROG zg30
TD 98074
SOLVENT CDCl3
NS 8
DS 2
SWH 9615.385 Hz
FIDRES 0.098042 Hz
AQ 5.0998478 sec
RG 287
DW 52.000 usec
DE 14.54 usec
TE 298.1 K
D1 0.10000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 600.1342009 MHz
NUC1 1H
P1 8.00 usec
PLW1 23.01441956 W
F2 - Processing parameters
SI 65536
SF 600.1300341 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
7.270
7.260
7.255
7.246
6.996
6.982
6.968
4.298
4.293
4.289
4.287
4.281
4.277
4.269
4.266
4.257
4.248
4.045
4.009
3.997
3.994
3.982
3.253
2.719
2.707
2.697
2.685
2.606
2.111
2.096
2.089
2.074
1.392
1.331
1.319
1.307
1.245
2.000
2.098
1.983
0.980
0.975
2.914
1.145
0.960
1.012
2.943
3.040
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
−0.5
ppm

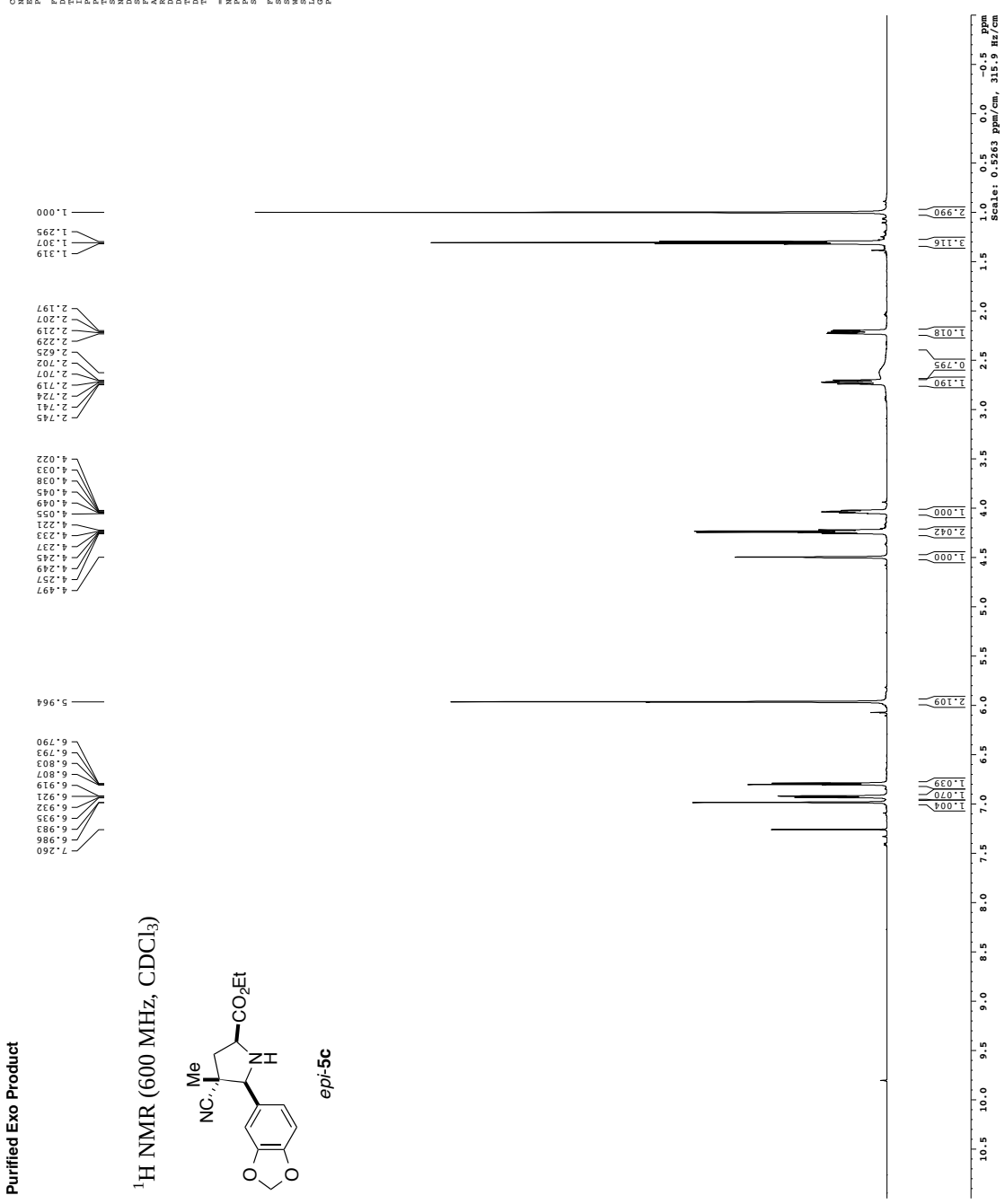

Z-restored spin-echo 13C spectrum with 1H decoupling
13C NMR (125 MHz, CDCl3)
5a
Current Data Parameters
NAME BL-2-022-4
EXPNO 3
PROCNO 1
F2 - Acquisition Parameter
Date_ 20140813
Time 8.44
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG SpinEchoPg3gp.pr
TD 65536
SOLVENT CDCl3
NS 56
DS 16
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0813440 sec
RG 164.1
DW 16.500 us
DE 6.00 us
TE 298.0 K
D1 0.25000000 sec
d11 0.03000000 sec
D16 0.00020000 sec
d17 0.00019600 sec
MCREST 0 sec 0.01500000 sec
MCWRK 31.00 us
P2
======== CHANNEL f1 ======
NUC1 13C
P1 15.50 us
P11 500.00 us
P12 2000.00 us
PL2 120.00 dB
PL1 -1.00 dB
SFO1 125.7942548 MHz
SP1 3.20 dB
SP2 3.20 dB
SPNAM[1] Crp60,0.5,20.1
SPNAM[2] Crp60comp.4
SPOAL1 0 Hz
SPOFF2 0 Hz
========= CHANNEL f2 ======
CPDPRG[2 waltz16
NUC2 1H
PCPD2 100.00 us
PL2 1.60 dB
PL12 24.60 dB
SFO2 500.2225011 MHz
====== GRADIENT CHANNEL ==
GPNAM[1] SINE.100
GPNAM[2] SINE.100
GPX1 0 %
GPX2 0 %
GPY1 0 %
GPY2 0 %
GPZ1 30.00 %
GPZ2 50.00 %
p15 500.00 us
p16 1000.00 us
F2 - Processing parameters
SI 65536
SF 125.7804165 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00
174.637
173.825
163.390
161.633
134.828
134.803
128.470
128.406
115.139
114.970
77.412
77.158
76.903
73.158
61.240
58.982
54.687
51.477
41.173
2.671
1.320
ppm

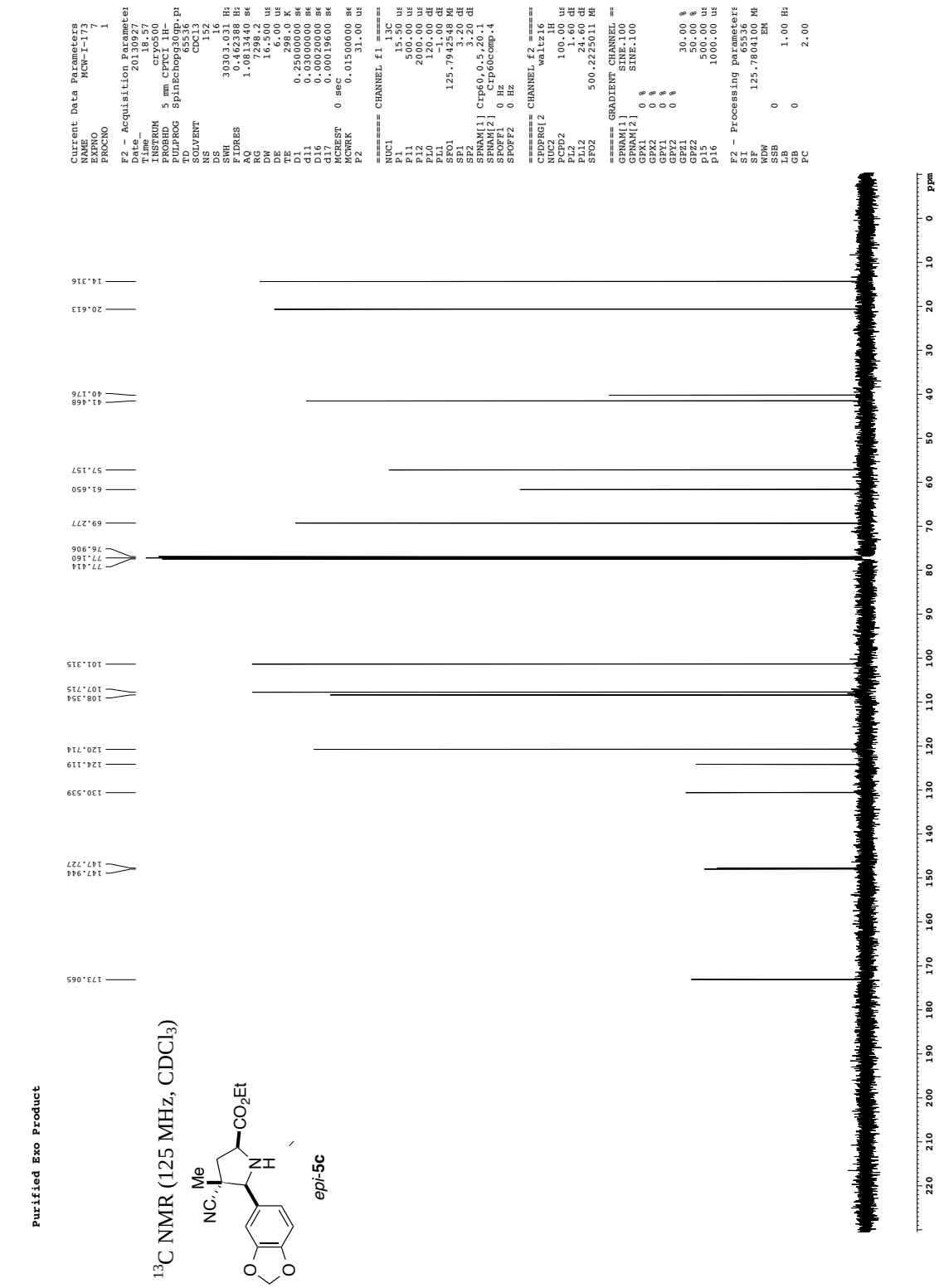

BL-2-014-7
1H spectrum
Current Data Parameters
NAME BL-2-014-7
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20140801
Time 12.31
INSTRUM av500
PROBHD 5 mm broadband
PULPROG zg30
TD 81728
SOLVENT CDCl3
NS 8
DS 2
SWH 8012.820 Hz
FIDRES 0.098043 Hz
AQ 5.099827 sec
RG 57
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 12.00 usec
PL1 -5.80 dB
SFO1 499.2934950 MHz
F2 - Processing parameters
SI 65536
SF 499.2900288 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
1H NMR (500 MHz, CDCl3)
5b
7.260
6.770
6.733
6.717
6.713
6.697
5.902
4.276
4.273
4.269
4.261
4.259
4.247
4.245
4.237
4.233
4.230
4.223
3.978
3.964
3.960
3.954
3.946
3.315
2.724
2.693
2.679
2.666
2.652
2.086
2.068
2.059
2.041
1.354
1.316
1.302
1.288
1.000
2.154
2.176
1.147
2.134
3.250
2.465
1.067
3.065
3.449
ppm

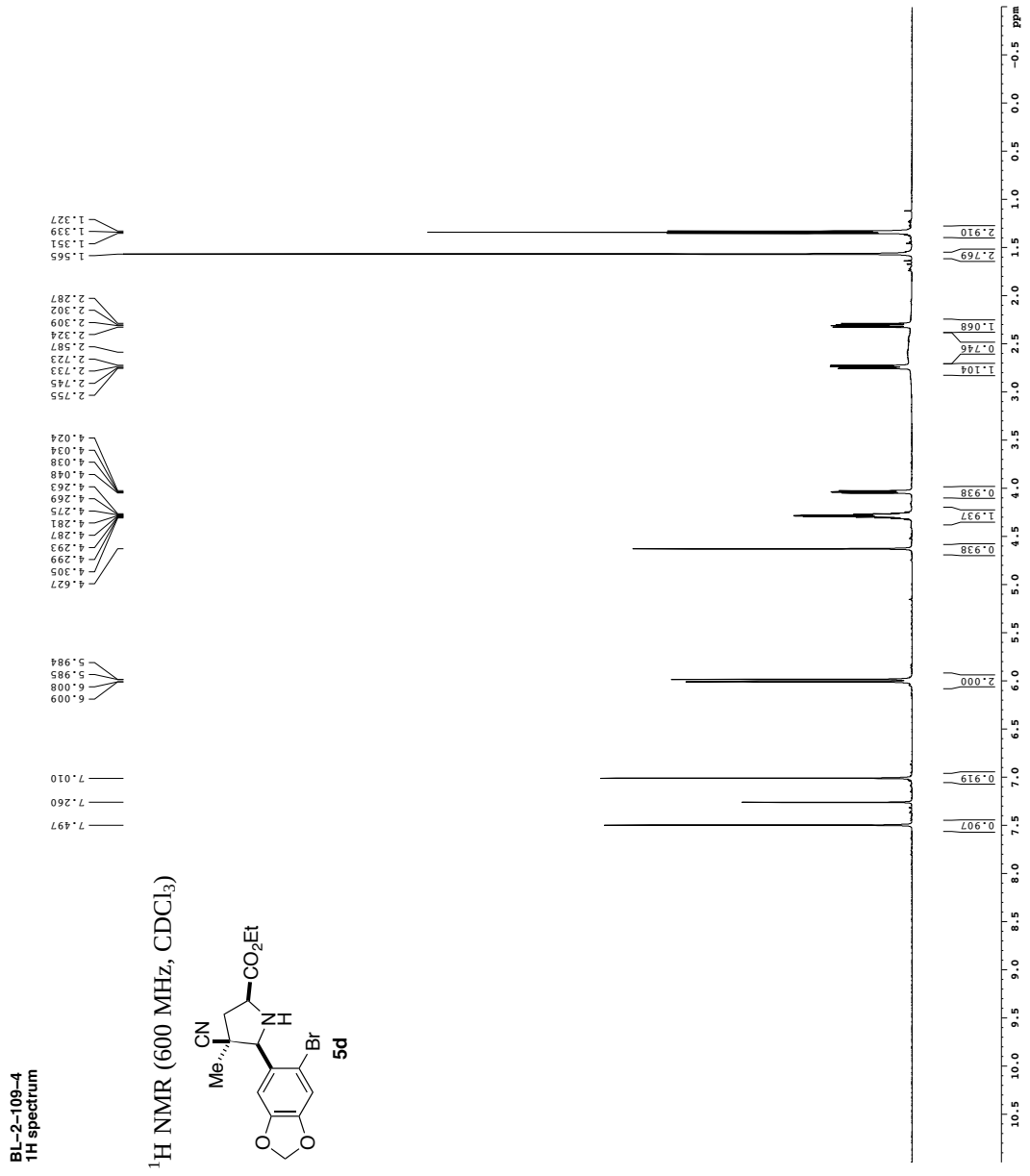

deptq 13C spectrum with 1H decoupling (CH & CH3 one way up; C, CH2 and solvent the other)
13C NMR (125 MHz, CDCl3)
5b
Current Data Parameters
NAME BL-2-014-7
EXPNO 3
PROCNO 1
F2 - Acquisition Parameter
Date_ 20140801
Time 13.06
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG deptqgpsp
TD 65536
SOLVENT CDCl3
NS 64
DS 8
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0813440 sec
RG 364.1
DW 16.500 us
DE 6.00 us
TE 298.0 K
CNST2 145.0000000
CNST12 1.5000000
D1 1.00000000 sec
d2 0.00344828 sec
d12 0.00020000 sec
D16 0.00020000 sec
DELTA 0.00001574 sec
DELTA1 0.00227878 sec
DELTA2 0.00226378 sec
DELTA3 0.00224828 sec
MCREST 0 sec 0.01500000 sec
MCWRK
======== CHANNEL f1 ======
NUC1 13C
P1 15.50 us
P12 2000.00 us
PL0 120.00 dB
PL1 1.00 dB
SFO1 125.7904548 MHz
SPNAM[2] Crp60comp.4
SPOFF2 0 Hz
======== CHANNEL f2 ======
CPDPRG[2 waltz16
NUC2 1H
P0 11.25 us
P3 7.50 us
P4 15.00 us
PCPD2 100.00 us
PL2 1.60 dB
PL12 24.60 dB
SFO2 500.2225011 MHz
====== GRADIENT CHANNEL ==
GPNAM[1] SINE.100
GPNAM[2] SINE.100
GPNAM[3] SINE.100
GPX1 0 %
GPX2 0 %
GPX3 0 %
GPY1 0 %
GPY2 0 %
GPY3 0 %
GPZ1 31.00 %
GPZ2 31.00 %
GPZ3 31.00 %
P16 1000.00 us
F2 - Processing parameters
SI 65536
SF 125.7804164 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00
174.764
173.826
147.618
147.194
132.670
120.153
107.980
107.332
101.091
77.413
77.158
76.904
73.734
61.228
58.920
54.520
51.550
41.220
22.575
14.335
ppm

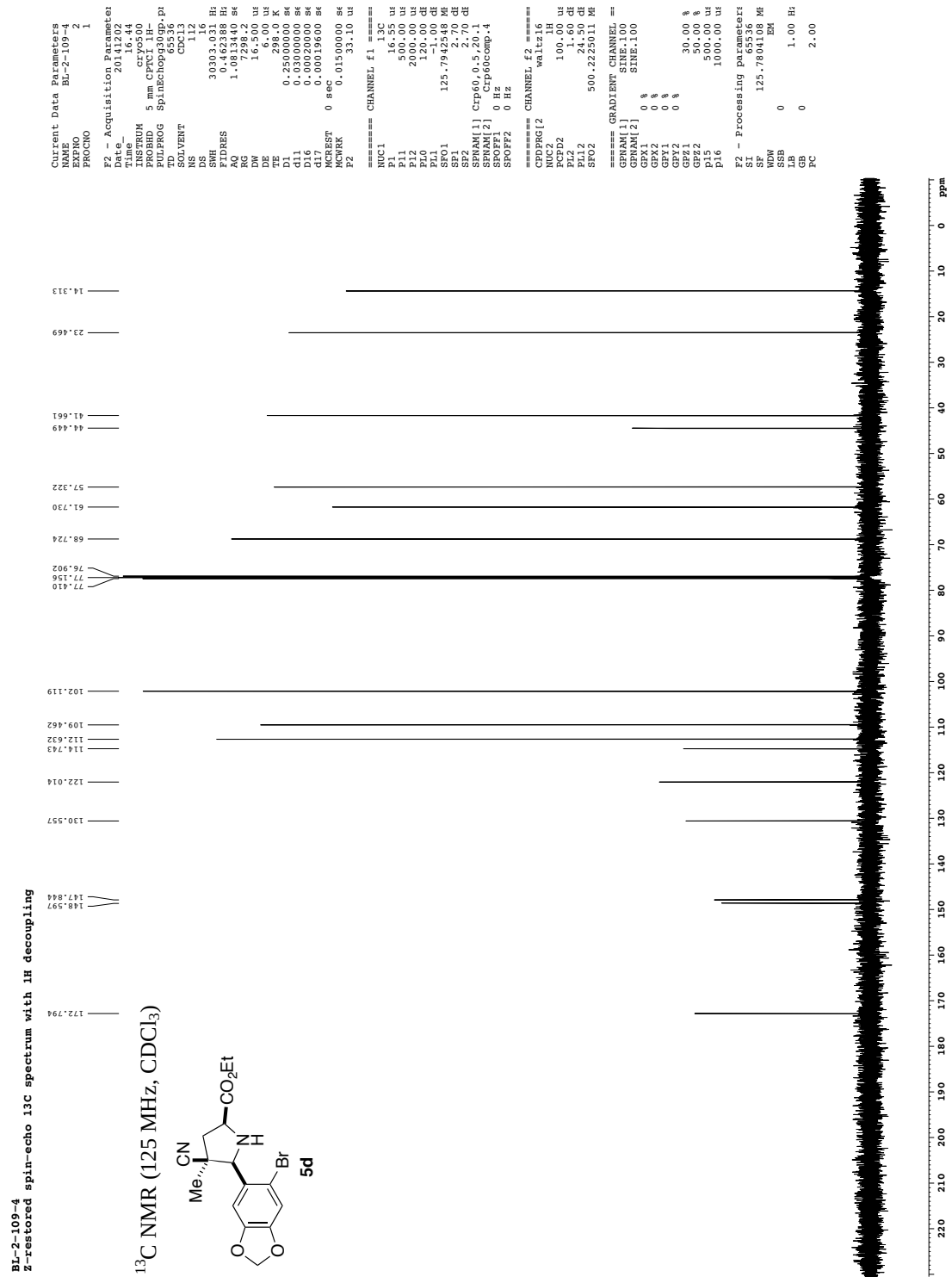

1H spectrum
Current Data Parameters
NAME BL-2-079-4
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20141120
Time_ 8.06
INSTRUM av600
PROBHD 5 mm TBI 1H/13
PULPROG zg30
TD 98074
SOLVENT CDCl3
NS 8
DS 2
SWH 9615.385 Hz
FIDRES 0.098042 Hz
AQ 5.0998478 sec
RG 203
DW 52.000 usec
DE 14.54 usec
TE 298.0 K
D1 0.10000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 600.1342009 MHz
NUC1 1H
P1 8.00 usec
PLW1 23.01441956 W
F2 - Processing parameters
SI 65536
SF 600.1300040 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
1H NMR (600 MHz, CDCl3)
5c
CN
Me
CO2Et
N
H
O
O
7.260
7.079
6.950
6.937
6.806
6.793
5.957
4.305
4.299
4.293
4.287
4.275
4.272
4.260
4.254
4.248
4.242
3.957
3.950
3.941
3.934
3.854
2.812
2.805
2.789
2.783
2.685
2.272
2.256
2.249
2.233
1.404
1.338
1.326
1.315
1.000
1.011
1.003
2.013
1.996
1.009
1.003
1.035
1.021
1.002
2.994
3.013
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
−0.5
ppm


Z-restored spin-echo 13C spectrum with 1H decoupling
13C NMR (125 MHz, CDCl3)
5c
CN
Me
CO2Et
N
H
O
O
Current Data Parameters
NAME BL-2-079-4
EXPNO 3
PROCNO 1
F2 - Acquisition Parameter
Date_ 20141119
Time 16.50
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG SpinEchoPg3gp.pr
TD 65536
SOLVENT CDCl3
NS 72
DS 16
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0813440 sec
RG 799.6
DW 16.500 us
DE 6.00 us
TE 298.0 K
D1 0.25000000 sec
d11 0.03000000 sec
D16 0.00020000 sec
d12 0.00019600 sec
MCREST 0 sec
MCWRK 0.01500000 sec
P2 33.10 us
======== CHANNEL f1 ======
NUC1 13C
P1 16.55 us
P11 500.00 us
PL2 200.00 dB
PL2 120.00 dB
PL1 -1.00 dB
SFO1 125.7942548 MHz
SP1 2.70 dB
SP2 2.70 dB
SPNAM[1] Crp60,0.5,20.1
SPNAM[2] Crp60comp.4
SPOFF1 0 Hz
SPOFF2 0 Hz
========= CHANNEL f2 ======
CPDPRG[2 waltz16
NUC2 1H
PCPD2 100.00 us
PL2 1.60 dB
PL12 24.50 dB
SFO2 500.2225011 MHz
====== GRADIENT CHANNEL ==
GPNAM[1] SINE.100
GPNAM[2] SINE.100
GPX1 0 %
GPX2 0 %
GPY1 0 %
GPY2 0 %
GPZ1 30.00 %
GPZ2 50.00 %
p15 500.00 us
p16 1000.00 us
F2 - Processing parameter
SI 65536
SF 125.7804166 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00
14.264
22.158
42.209
43.895
57.128
61.723
72.203
76.903
77.158
77.412
101.299
107.904
108.236
121.163
122.060
130.571
147.926
148.081
172.961
ppm


Purified Exo Product
^{1}H NMR (600 MHz, CDCl$_3$)
epi-5c
Me
NC
CO$_2$Et
N
H
O
O
Current Data Parameters
NAME MCM-I-173
EXPNO 4
PROCNO 1
F2 - Acquisition Parameters
Date_ 20130927
TIME 18.25
INSTRUM spect
PROBHD 5 mm TBI 1H/13
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 12
DS 0
SWH 9615.385 Hz
FIDRES 0.098042 Hz
AQ 5.0998528 sec
RG 128
DW 52.000 usec
DE 14.44 usec
TE 294.5 K
D1 0.10000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 8.00 usec
PL1 23.01441956 W
SFO1 600.1342809 MHz
F2 - Processing parameters
SI 65536
SF 600.1300351 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
7.260
6.986
6.983
6.935
6.932
6.921
6.919
6.807
6.803
6.793
6.790
5.964
4.497
4.257
4.249
4.245
4.237
4.233
4.221
4.055
4.049
4.045
4.038
4.033
4.022
2.745
2.741
2.724
2.719
2.707
2.702
2.625
2.229
2.219
2.207
2.197
1.319
1.307
1.295
1.000
2.990
3.116
1.018
0.795
1.190
1.000
2.042
1.000
2.109
1.039
1.070
1.004
ppm
Scale: 0.5263 ppm/cm, 315.9 Hz/cm


Purified Exo Product
^{13}C NMR (125 MHz, CDCl$_3$)
epi-5c
Current Data Parameters
NAME MCW-I-173
EXPNO 7
PROCNO 1
F2 - Acquisition Parameters
Date_ 20130927
Time 18.57
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 152
DS 16
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0813440 sec
RG 7298.2
DW 16.500 usec
DE 6.00 usec
TE 298.0 K
D1 0.25000000 sec
d11 0.03000000 sec
D16 0.00020000 sec
D17 0.00019600 sec
MCREST 0 sec
MCWRK 0.01500000 sec
P2 31.00 usec
======== CHANNEL f1 ========
NUC1 13C
P1 15.50 usec
P11 500.00 usec
P12 2000.00 usec
PL0 120.00 dB
PL1 -1.00 dB
SFO1 125.7942548 MHz
SP1 3.20 dB
SP2 3.20 dB
SPNAM[1] Crp60,0.5,20.1
SPNAM[2] Crp60comp.4
SPOFF1 0 Hz
SPOFF2 0 Hz
======== CHANNEL f2 ========
CPDPRG[2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 1.60 dB
PL12 24.60 dB
SFO2 500.2225011 MHz
====== GRADIENT CHANNEL ==
GPNAM[1] SINE.100
GPNAM[2] SINE.100
GPX1 0 %
GPX2 0 %
GPY1 0 %
GPY2 0 %
GPZ1 30.00 %
GPZ2 50.00 %
p15 500.00 usec
p16 1000.00 usec
F2 - Processing parameters
SI 65536
SF 125.7804100 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00
173.065
147.944
147.727
130.539
124.119
120.714
108.354
107.715
101.315
77.414
77.160
76.906
69.277
61.650
57.157
41.468
40.176
20.613
14.316
ppm

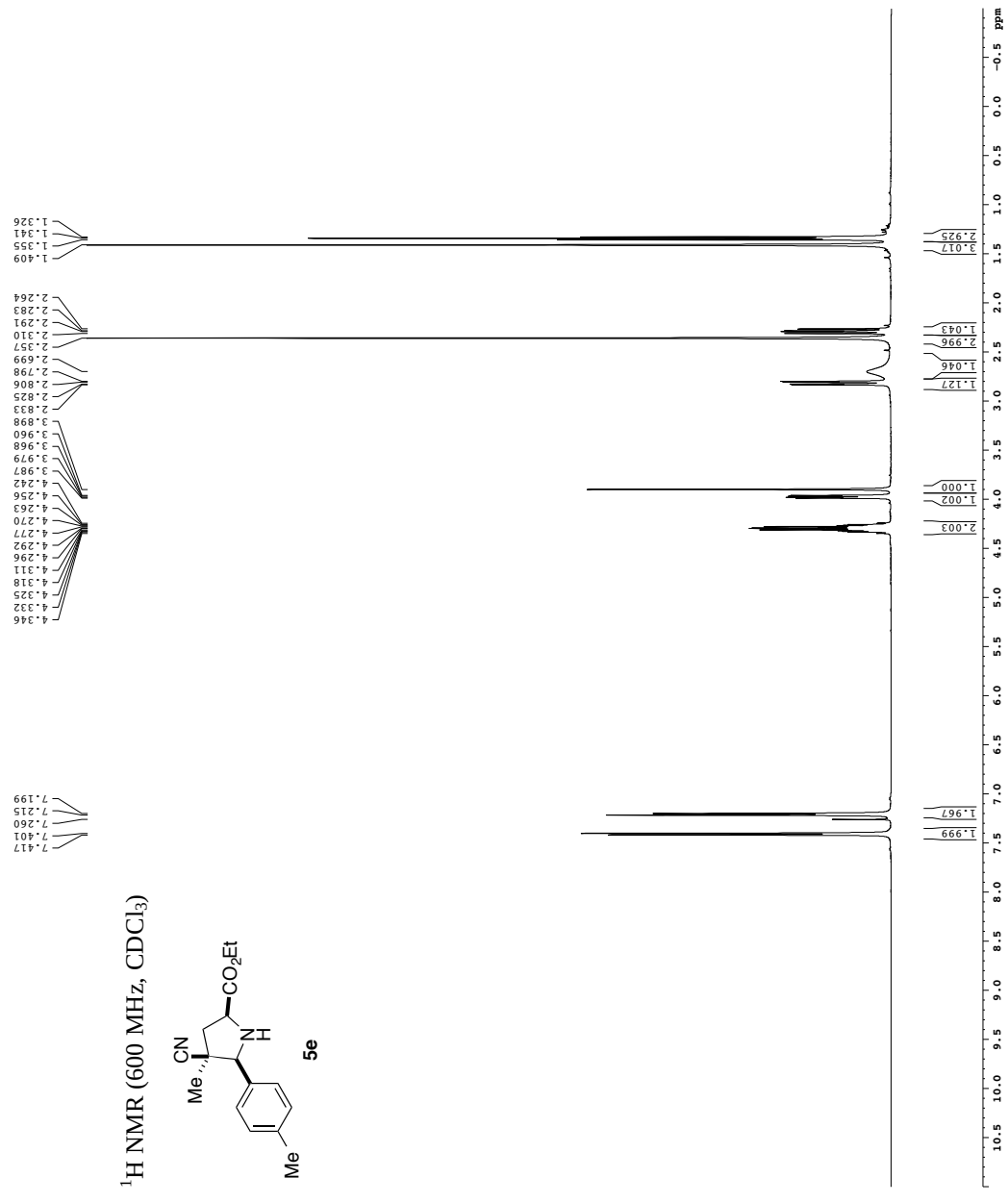

BL-2-109-4
1H spectrum
Current Data Parameters
NAME BL-2-109-4
EXPNO 5
PROCNO 1
F2 - Acquisition Parameters
Date_ 20141205
Time 12.23
INSTRUM av600
PROBHD 5 mm TBI 1H/13
PULPROG zg30
TD 98074
SOLVENT CDCl3
NS 8
DS 2
SWH 9615.385 Hz
FIDRES 0.098042 Hz
AQ 5.0998478 sec
RG 228
DW 52.000 usec
DE 14.54 usec
TE 298.0 K
D1 0.10000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 600.1342009 MHz
NUC1 1H
P1 8.00 usec
PLW1 23.01441956 W
F2 - Processing parameters
SI 65536
SF 600.1300345 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
1H NMR (600 MHz, CDCl3)
CN
Me
CO2Et
N
H
Br
O
O
5d
7.497
7.260
7.010
6.009
6.008
5.985
5.984
4.627
4.305
4.299
4.293
4.287
4.281
4.275
4.269
4.263
4.048
4.038
4.034
4.024
2.755
2.745
2.733
2.723
2.587
2.324
2.309
2.302
2.287
1.565
1.351
1.339
1.327
0.907
0.919
2.000
0.938
1.937
0.938
1.104
0.746
1.068
2.769
2.910
ppm

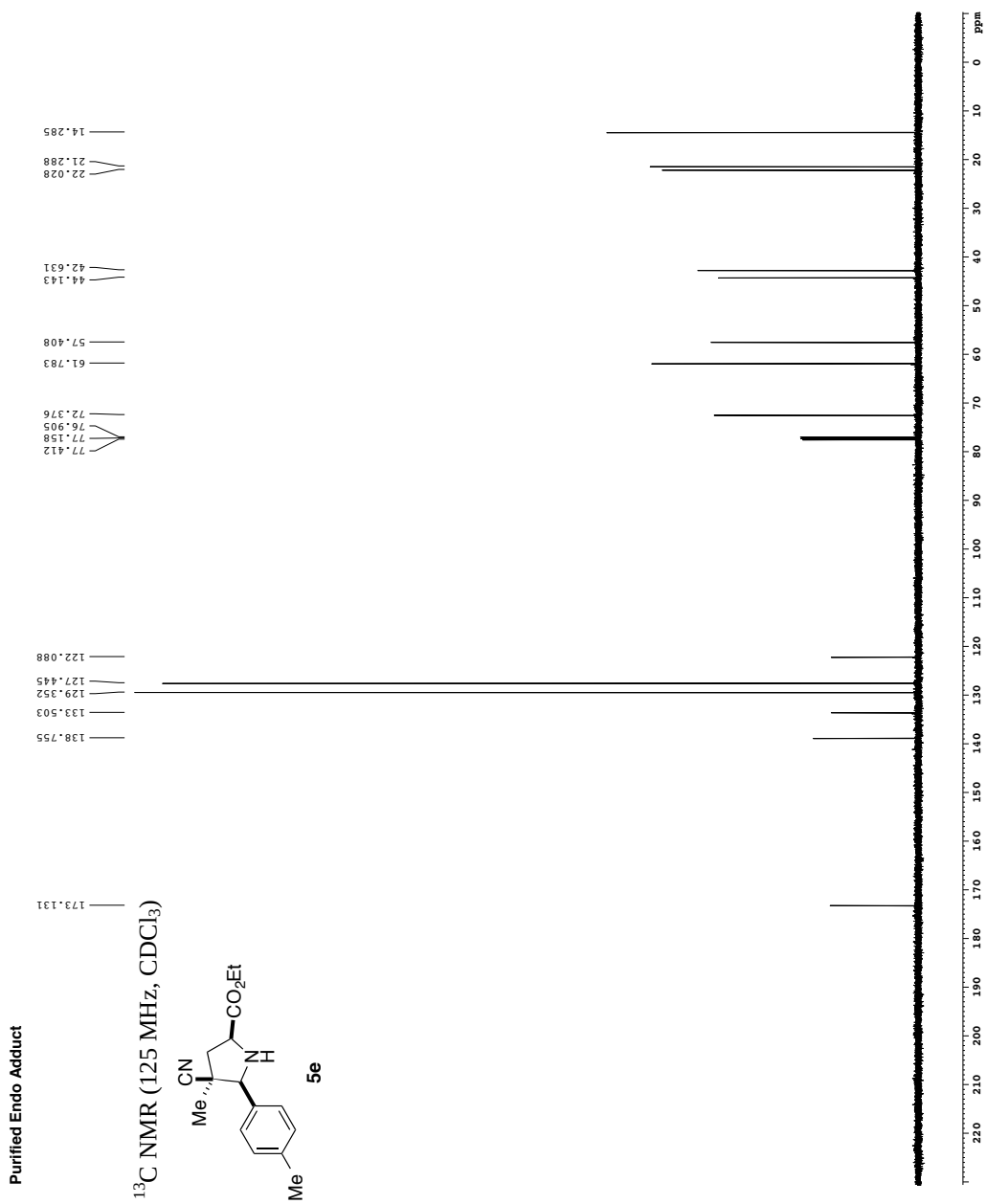

BL-2-109-4
Z-restored spin-echo 13C spectrum with 1H decoupling
13C NMR (125 MHz, CDCl3)
5d
Current Data Parameters
NAME BL-2-109-4
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20141202
Time 16.44
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG SpinEchopg.zgpr
TD 65536
SOLVENT CDCl3
NS 112
DS 16
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0813440 sec
RG 71298.2
DW 16.500 usec
DE 6.00 usec
TE 298.0 K
D1 0.25000000 sec
d11 0.03000000 sec
D16 0.00020000 sec
d12 0.00019600 sec
MCWREST 0 sec.01500000 sec
MCWRK 33.10 usec
P2
======== CHANNEL f1 ======
NUC1 13C
P1 16.55 usec
P11 500.00 usec
P12 2000.00 usec
PL0 120.00 dB
PL1 -1.00 dB
SFO1 125.7942548 MHz
SP1 2.70 dB
SP2 2.70 dB
SPNAM[1] Crp60,0.5,20.1
SPNAM[2] Crp60comp.4
SPOFF1 0 Hz
SPOFF2 0 Hz
======== CHANNEL f2 ======
CPDPRG[2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 1.60 dB
PL12 24.50 dB
SFO2 500.2225011 MHz
====== GRADIENT CHANNEL ==
GPNAM[1] SINE.100
GPNAM[2] SINE.100
GPX1 0 %
GPX2 0 %
GPY1 0 %
GPY2 0 %
GPZ1 30.00 %
GPZ2 50.00 %
p15 500.00 usec
p16 1000.00 usec
F2 - Processing parameters
SI 65536
SF 125.7804108 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00
14.313
23.469
41.661
44.449
57.322
61.730
68.724
76.902
77.156
77.410
102.119
109.462
112.632
114.743
122.014
130.557
147.844
148.597
ppm
CN
Me
CO2Et
NH
Br
O
O

Purified Endo Adduct

^{1}H NMR (600 MHz, $CDCl_3$)

5e

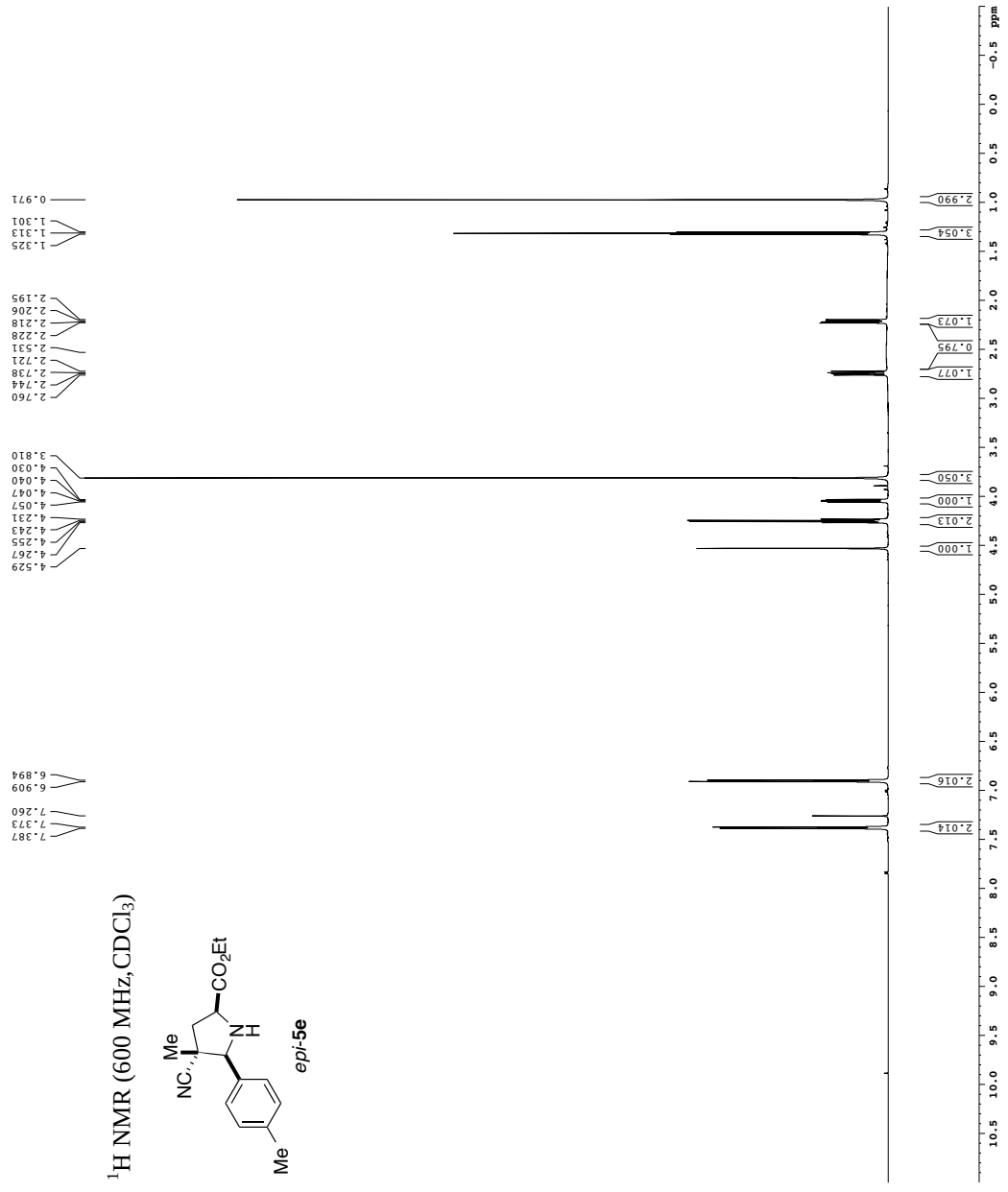


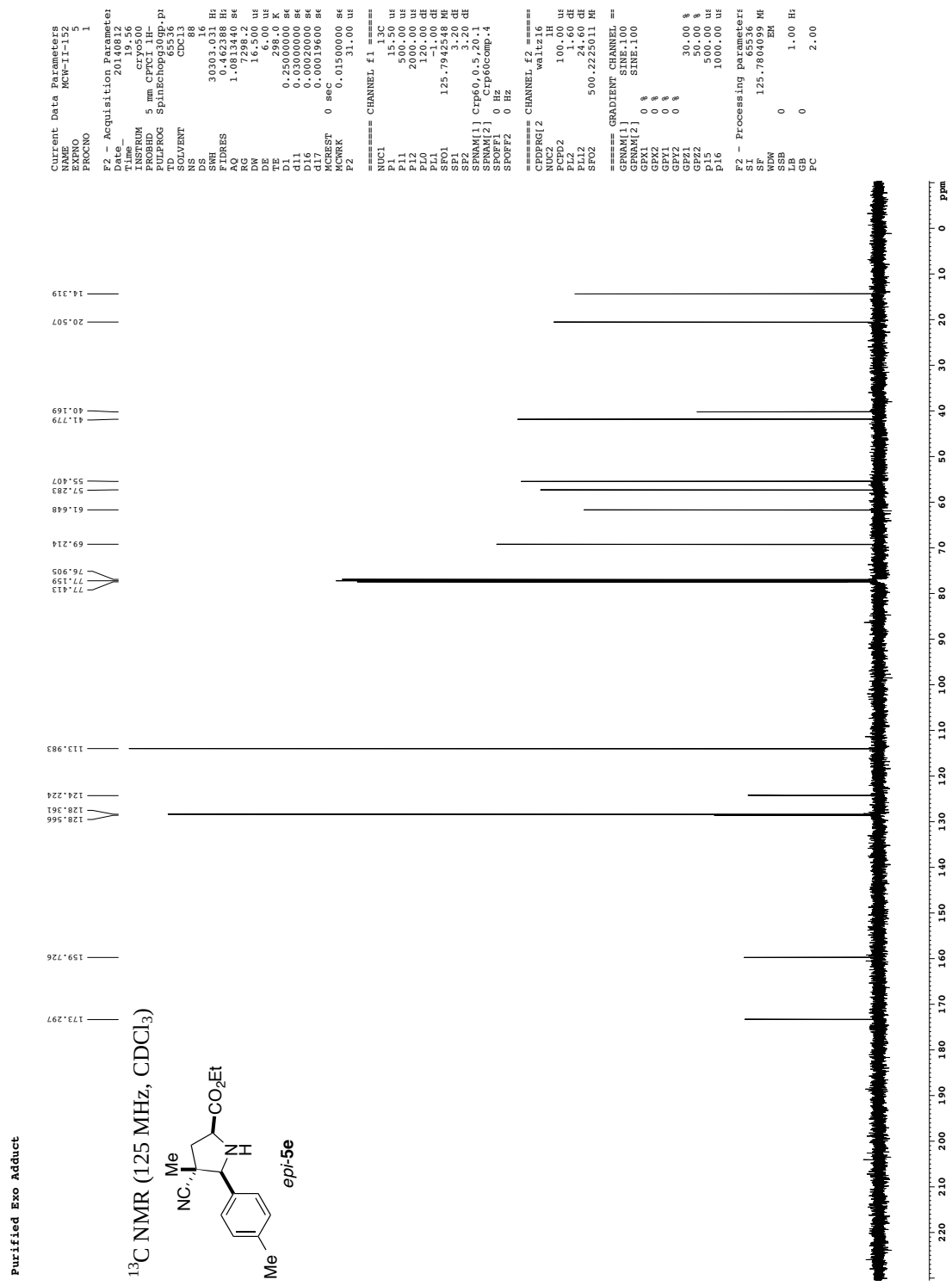

Purified Endo Adduct
^{13}C NMR (125 MHz, $CDCl_3$)
5e
Current Data Parameters
NAME MCW-II-144
EXPNO 7
PROCNO 1
F2 - Acquisition Parameters
Date_ 20140729
Time 8.43
INSTRUM czyo500
PROBHD 5 mm CPTCI 1H-
PULPROG spinechopg.3gp.prd
TD 65536
SOLVENT CDCl3
NS 104
DS 16
SWH 30303.031 Hz
FIDRES 0.4623388 Hz
AQ 1.0813440 sec
RG 65.50
DW 16.500 usec
DE 6.00 usec
TE 298.0 K
D1 0.25000000 sec
d11 0.03000000 sec
D16 0.00020000 sec
d12 0.00019600 sec
MPFREQST 0 sec
MCWRK 0.01500000 sec
P2 31.00 usec
======== CHANNEL f1 ========
NUC1 13C
P1 15.50 usec
P11 500.00 usec
P12 2000.00 usec
PL0 120.00 dB
PL1 -1.00 dB
SFO1 125.79425548 MHz
SP1 3.20 dB
SP2 3.20 dB
SPNAM[1] Crp60,0.5,20.1
SPNAM[2] Crp60comp.4
SPOFFS1 0 Hz
SPOFF2 0 Hz
======== CHANNEL f2 ========
CPDPRG[2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 1.60 dB
PL12 24.60 dB
SFO2 500.22250011 MHz
====== GRADIENT CHANNEL =====
GPNAM[1] SINE.100
GPNAM[2] SINE.100
GPX1 0 %
GPX2 0 %
GPY1 0 %
GPY2 0 %
GPZ1 30.00 %
GPZ2 50.00 %
p15 500.00 usec
p16 1000.00 usec
F2 - Processing parameters
SI 65536
SF 125.7804001 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 2.00
173.131
138.755
133.503
129.352
127.445
122.088
77.412
77.158
76.905
72.376
61.783
57.408
44.143
42.631
22.028
21.288
14.285
ppm

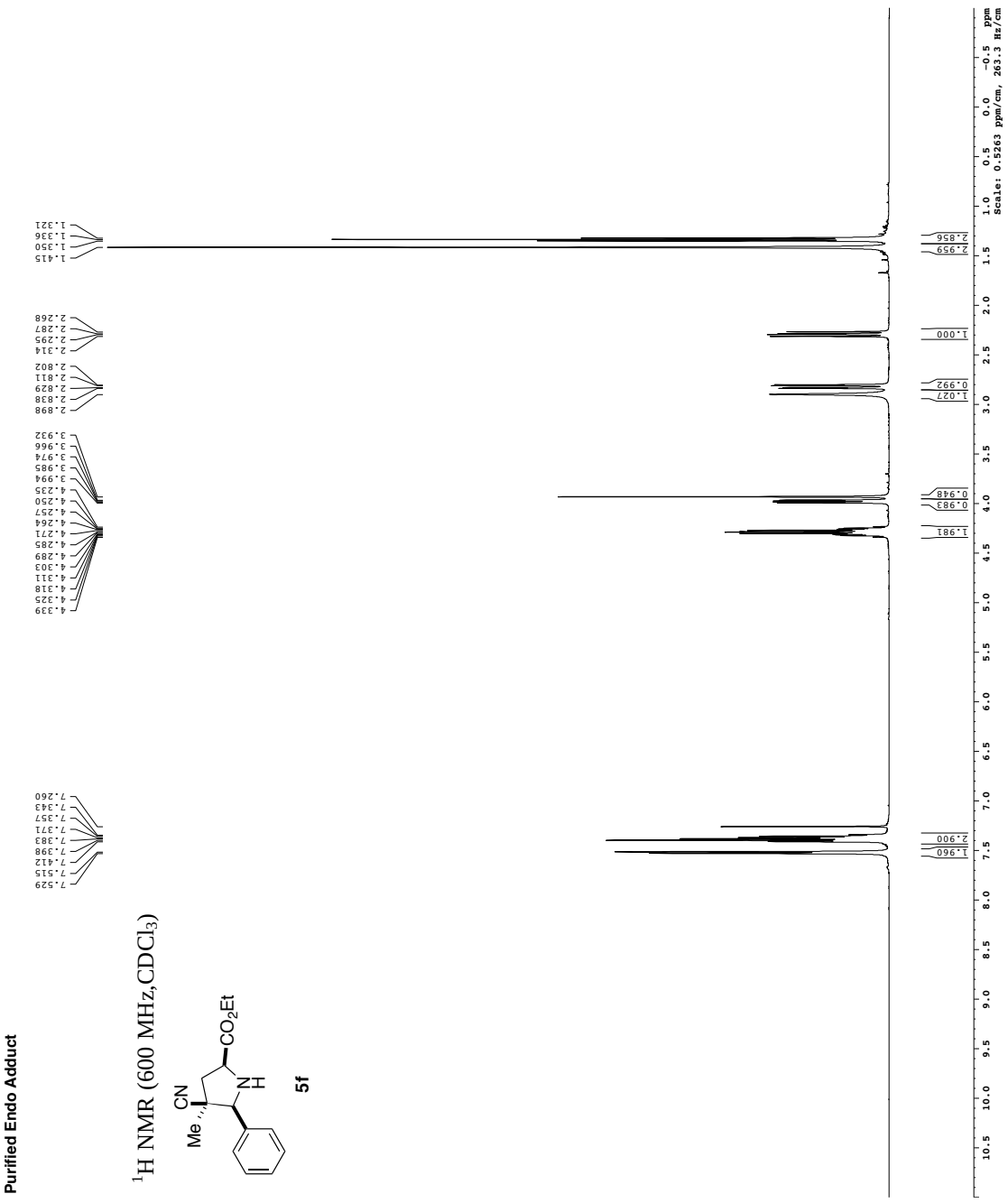
Purified Exo Adduct

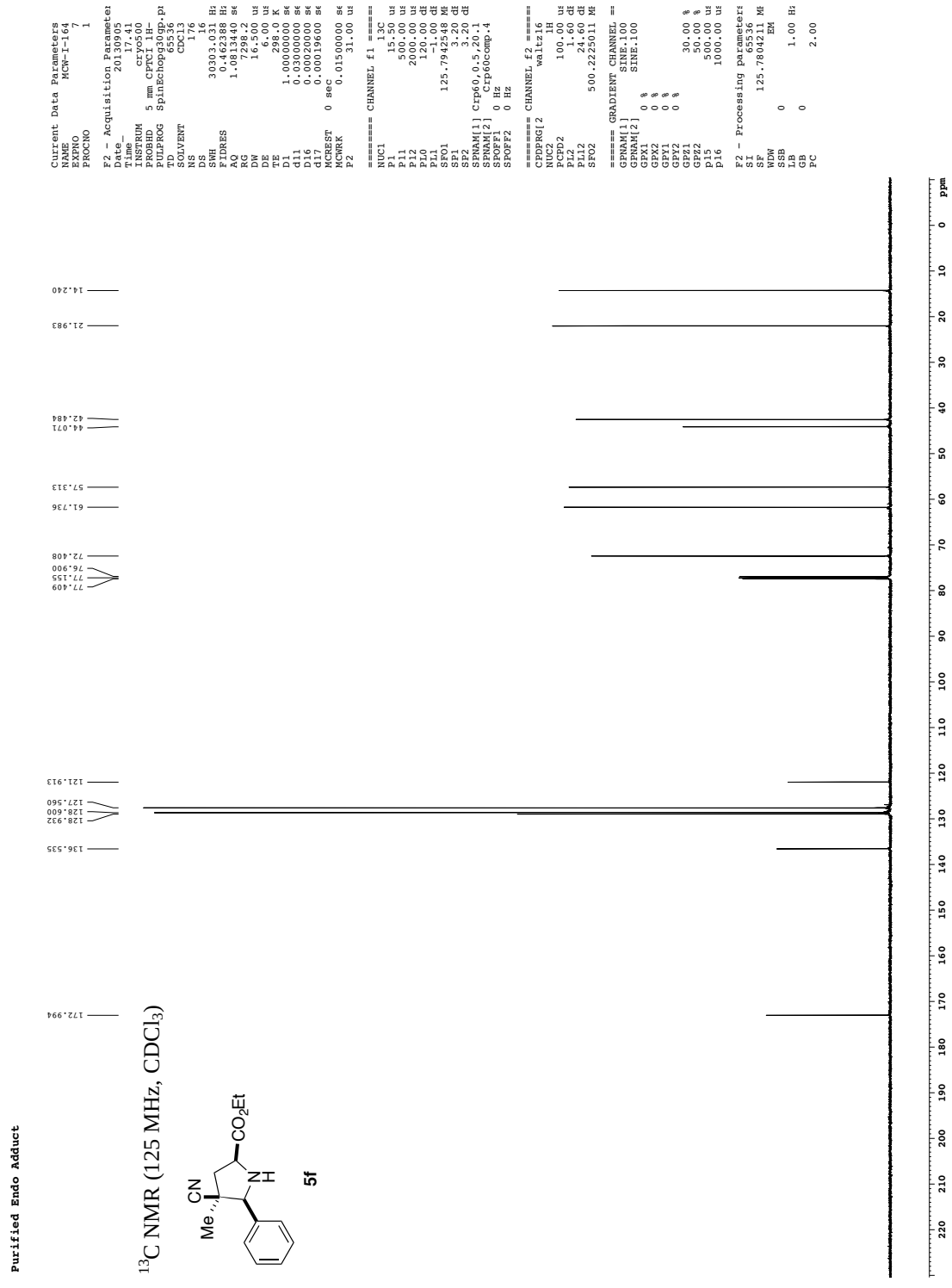
^{1}H NMR (600 MHz,$CDCl_3$)

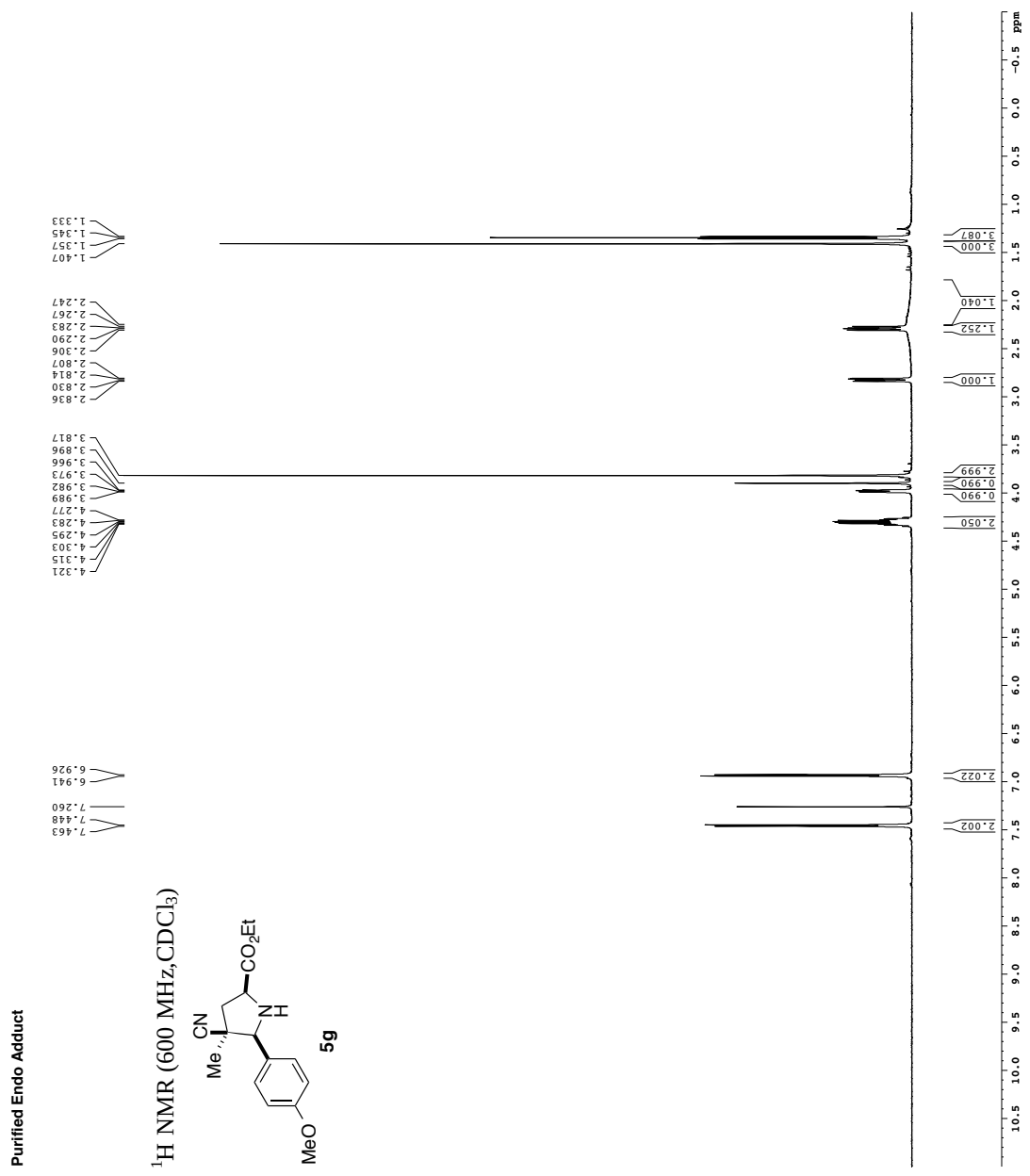
epi-**5e**

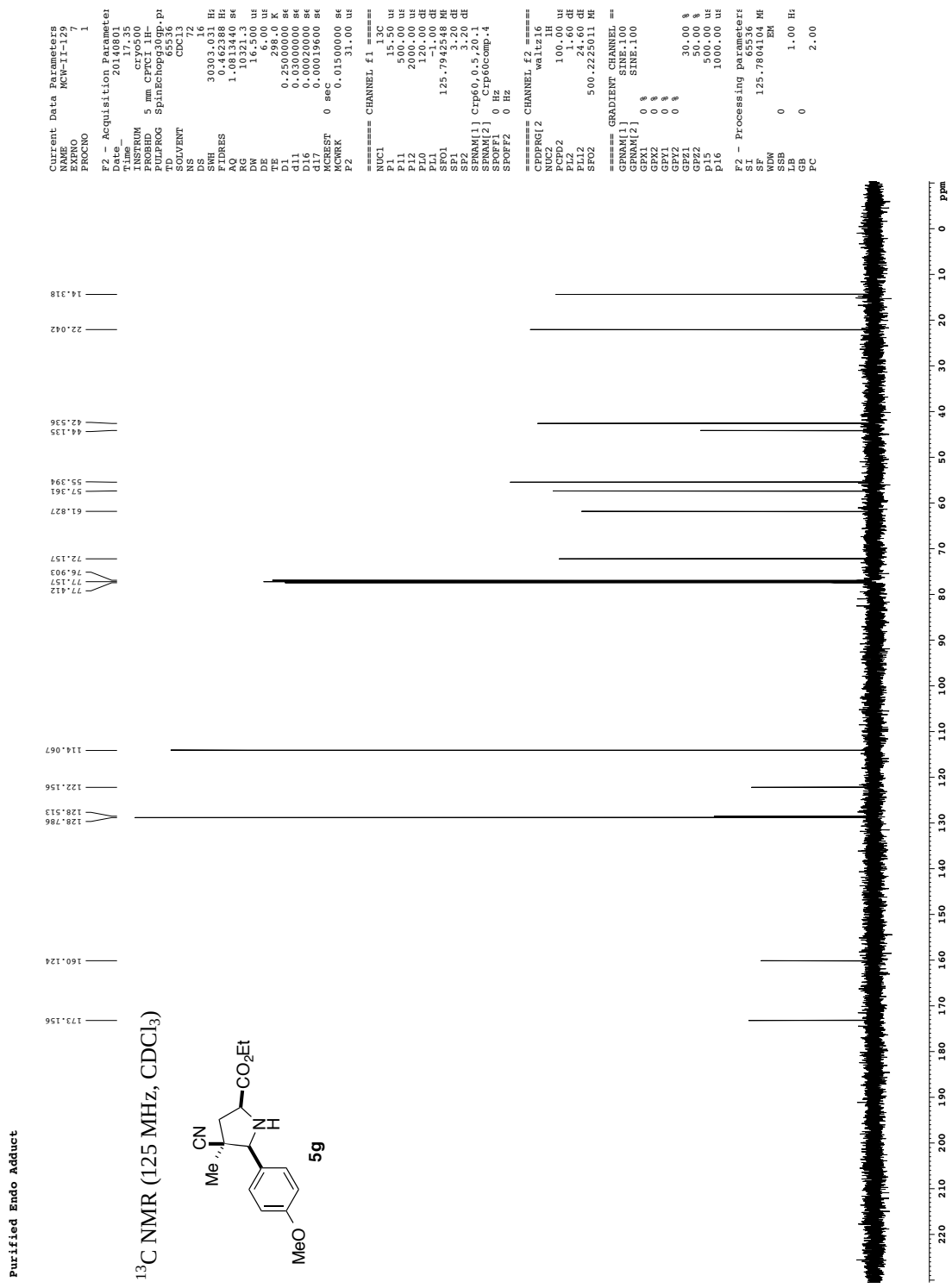



Purified Exo Adduct
^{13}C NMR (125 MHz, $CDCl_3$)
epi-5e
Me
NC
CO_2Et
N
H
Me
Current Data Parameters
NAME MCW-II-152
EXPNO 5
PROCNO 1
F2 - Acquisition Parameters
Date_ 20140812
Time 19.56
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zgpg30.pr
TD 65536
SOLVENT CDCl3
NS 88
DS 16
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0813440 sec
RG 71298.2
DW 16.500 usec
DE 6.00 usec
TE 298.0 K
D1 0.25000000 sec
d11 0.03000000 sec
D16 0.00020000 sec
MCREST 0.00019600 sec
MCWRK 0.01500000 sec
P2 31.00 usec
======== CHANNEL f1 ========
NUC1 13C
P1 15.50 usec
P11 500.00 usec
P12 2000.00 usec
PL0 120.00 dB
PL1 -1.00 dB
SFO1 125.7942548 MHz
SP1 3.20 dB
SP2 3.20 dB
SPNAM[1] Crp60,0.5,20.1
SPNAM[2] Crp60comp.4
SPOFF1 0 Hz
SPOFF2 0 Hz
======== CHANNEL f2 ========
CPDPRG[2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 1.60 dB
PL12 24.60 dB
SFO2 500.2225011 MHz
====== GRADIENT CHANNEL ==
GPNAM[1] SINE.100
GPNAM[2] SINE.100
GPX1 0 %
GPX2 0 %
GPY1 0 %
GPY2 0 %
GPZ1 30.00 %
GPZ2 50.00 %
p15 500.00 usec
p16 1000.00 usec
F2 - Processing parameters
SI 65536
SF 125.7804099 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00
173.297
159.726
128.566
128.361
124.224
113.983
77.413
77.159
76.905
69.214
61.648
57.283
55.407
41.779
40.169
20.507
14.319
ppm


Purified Endo Adduct
^{1}H NMR (600 MHz,$CDCl_3$)
5f
Current Data Parameters
NAME MCW-I-164
EXPNO 6
PROCNO 1
F2 - Acquisition Parameters
Date_ 20130905
TIME 17:32
INSTRUM spect
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 81928
SOLVENT CDCl3
NS 8
DS 2
SWH 8012.820 Hz
FIDRES 0.098043 Hz
AQ 5.0998273 sec
RG 4
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCWREST 0 sec
MCWPRK 0.01500000 sec
===== CHANNEL f1 =====
NUC1 1H
P1 7.50 usec
PL1 1.60 dB
SFO1 500.2235015 MHz
F2 - Processing parameters
SI 65536
SF 500.2200310 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00
7.529
7.515
7.412
7.398
7.383
7.371
7.357
7.343
7.260
4.339
4.325
4.318
4.311
4.303
4.289
4.285
4.271
4.264
4.257
4.250
4.235
3.994
3.985
3.974
3.966
3.932
2.898
2.858
2.829
2.811
2.802
2.314
2.295
2.287
2.268
1.415
1.350
1.336
1.321
1.960
2.900
0.948
0.983
1.981
1.027
0.992
1.000
2.959
2.856
ppm
Scale: 0.5263 ppm/cm, 263.3 Hz/cm


Purified Endo Adduct
^{13}C NMR (125 MHz, CDCl$_3$)
5f
Current Data Parameters
NAME MCW-I-164
EXPNO 7
PROCNO 1
F2 - Acquisition Parameters
Date_ 20130905
Time 17.41
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG spinechopc90.pp
TD 65536
SOLVENT CDCl3
NS 176
DS 16
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0813440 sec
RG 72028.2
DW 16.500 usec
DE 6.00 usec
TE 298.0 K
D1 1.00000000 sec
d11 0.03000000 sec
D16 0.00020000 sec
MCREST 0.00019600 sec
MCWRK 0.01500000 sec
P2 31.00 usec
======== CHANNEL f1 ========
NUC1 13C
P1 15.50 usec
P11 500.00 usec
PL2 20000.00 dB
PL0 120.00 dB
PL1 -1.00 dB
SFO1 125.7942548 MHz
SP1 3.20 dB
SP2 3.20 dB
SPNAM[1] Crp60,0.5,20.1
SPNAM[2] Crp60comp.4
SPOFF1 0 Hz
SPOFF2 0 Hz
======== CHANNEL f2 ========
CPDPRG[2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 1.60 dB
PL12 24.60 dB
SFO2 500.2225011 MHz
====== GRADIENT CHANNEL ==
GPNAM[1] SINE.100
GPNAM[2] SINE.100
GPX1 0 %
GPX2 0 %
GPY1 0 %
GPY2 0 %
GPZ1 30.00 %
GPZ2 50.00 %
p15 500.00 usec
p16 1000.00 usec
F2 - Processing parameters
SI 65536
SF 125.7804211 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00
172.994
136.535
128.932
128.600
127.560
121.913
77.409
76.900
72.408
61.736
57.313
44.071
42.484
21.983
14.240
ppm

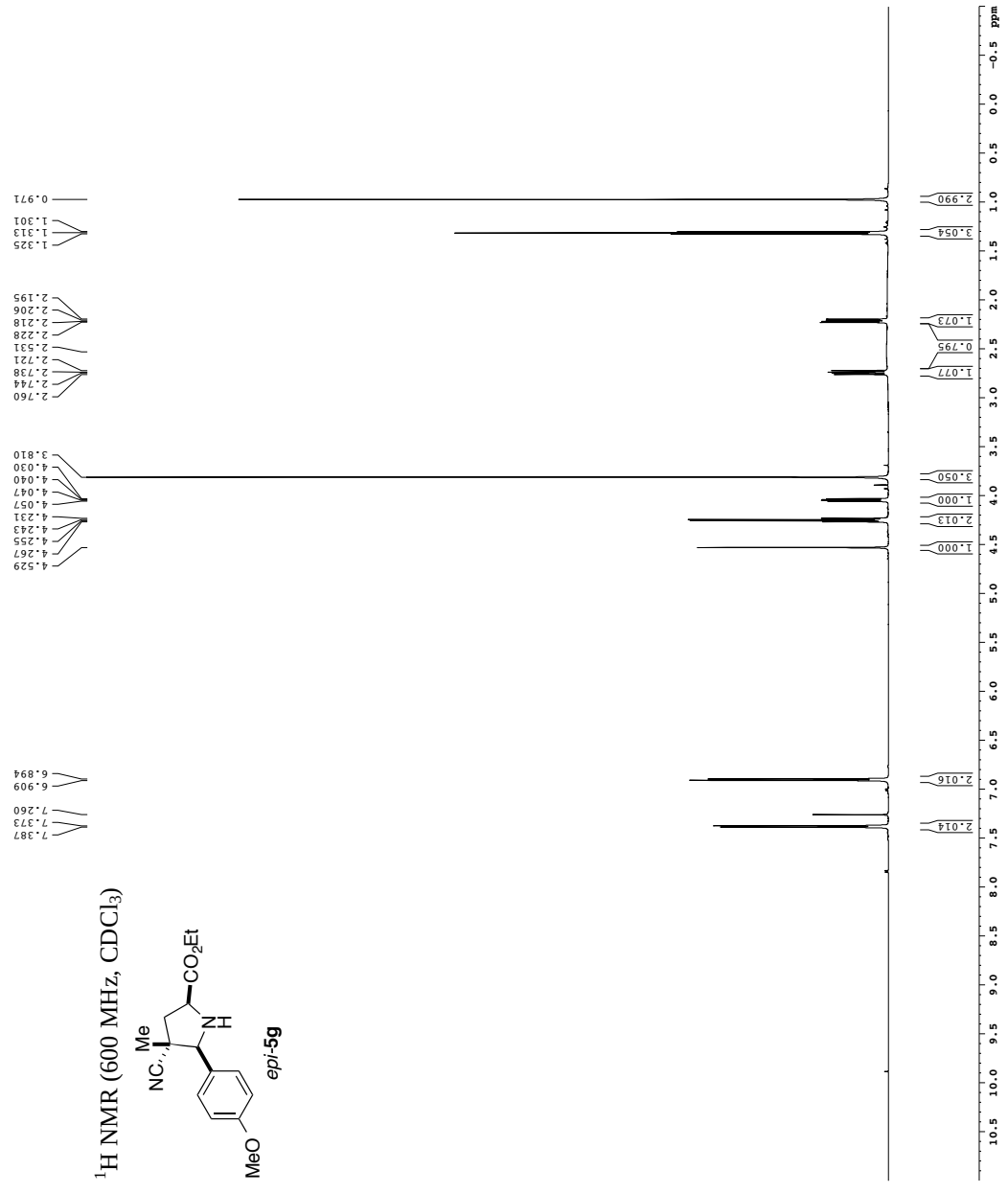

Purified Endo Adduct
^{1}H NMR (600 MHz, $CDCl_3$)
5g
Current Data Parameters
NAME MCW-II-129
EXPNO 13
PROCNO 1
F2 - Acquisition Parameters
Date_ 20140804
Time 10.36
INSTRUM av600
PROBHD 5 mm TBI 1H/13
PULPROG zg30
TD 98074
SOLVENT CDCl3
NS 14
DS 0
SWH 9615.385 Hz
FIDRES 0.098042 Hz
AQ 5.09984478 sec
RG 1.70
DW 52.000 usec
DE 14.54 usec
TE 298.1 K
D1 0.10000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 600.1342009 MHz
NUC1 1H
P1 8.00 usec
PLW1 23.01441956 W
F2 - Processing parameters
SI 65536
SF 600.1300343 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
7.463
7.448
7.260
6.941
6.926
4.321
4.315
4.303
4.295
4.283
4.277
3.989
3.982
3.973
3.966
3.896
3.817
2.836
2.830
2.814
2.807
2.306
2.290
2.283
2.267
2.247
1.407
1.357
1.345
1.333
2.002
2.022
2.050
0.990
0.999
2.999
1.000
1.252
1.040
3.000
3.087
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5 ppm

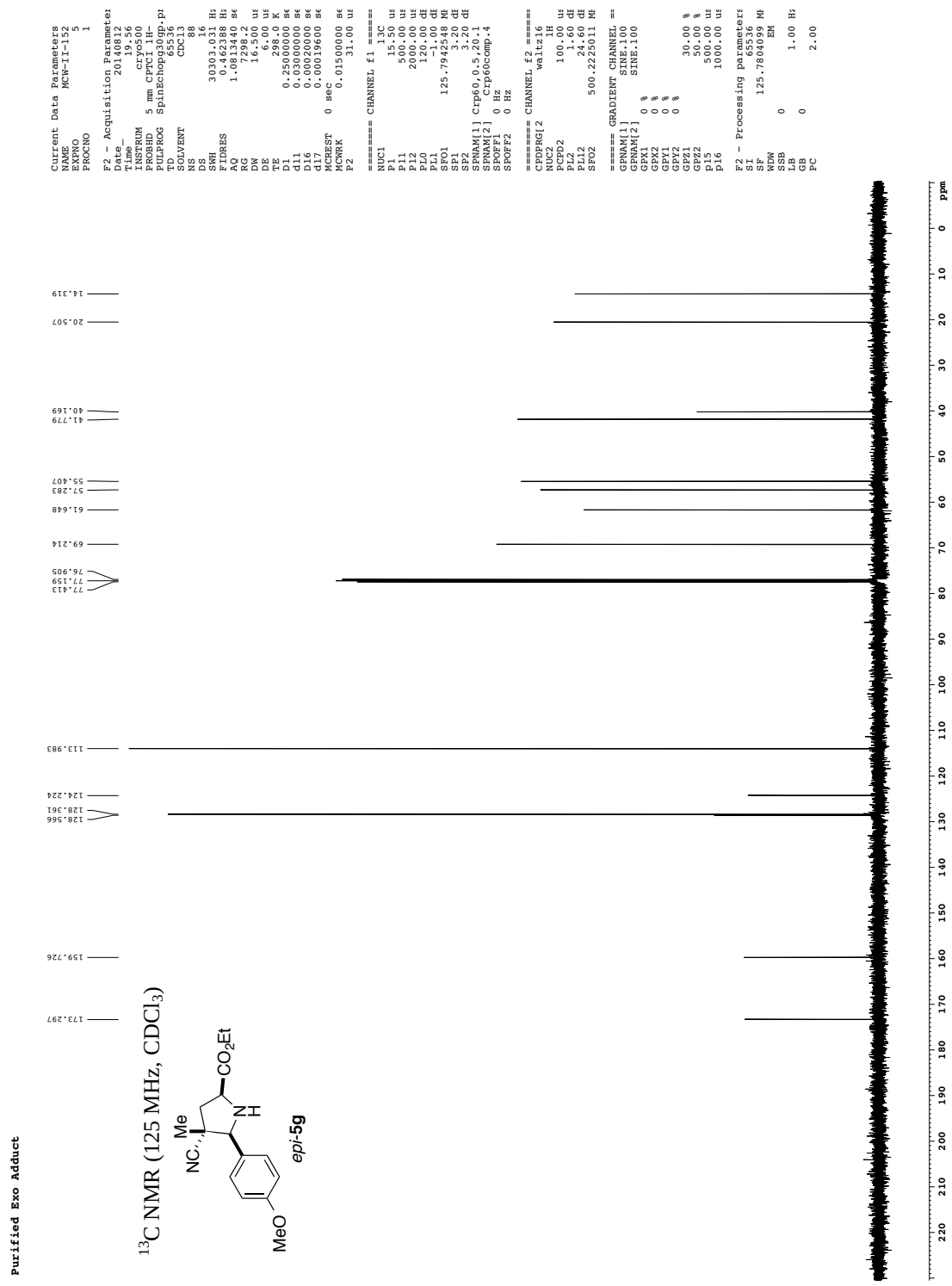

Purified Endo Adduct
^{13}C NMR (125 MHz, CDCl$_3$)
5g
MeO
CN
Me
CO$_2$Et
H
N
Current Data Parameters
NAME MCW-II-129
EXPNO 7
PROCNO 1
F2 - Acquisition Parameters
Date_ 20140801
Time 17.35
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zgpg30.pr
TD 65536
SOLVENT CDCl3
NS 72
DS 16
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0813440 sec
RG 102.3
DW 16.500 usec
DE 6.00 usec
TE 298.0 K
D1 0.25000000 sec
d11 0.03000000 sec
D16 0.00020000 sec
MCREST 0.00019600 sec
MCWRK 0.01500000 sec
P2 31.00 usec
======== CHANNEL f1 ========
NUC1 13C
P1 15.50 usec
P11 500.00 usec
P12 2000.00 usec
PL0 120.00 dB
PL1 -1.00 dB
SFO1 125.7942548 MHz
SP1 3.20 dB
SP2 3.20 dB
SPNAM[1] Crp60,0.5,20.1
SPNAM[2] Crp60comp.4
SPOFF1 0 Hz
SPOFF2 0 Hz
======== CHANNEL f2 ========
CPDPRG[2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 1.60 dB
PL12 24.60 dB
SFO2 500.2225011 MHz
====== GRADIENT CHANNEL ==
GPNAM[1] SINE.100
GPNAM[2] SINE.100
GPX1 0 %
GPX2 0 %
GPY1 0 %
GPY2 0 %
GPZ1 30.00 %
GPZ2 50.00 %
p15 500.00 usec
p16 1000.00 usec
F2 - Processing parameters
SI 65536
SF 125.7804104 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00
14.318
22.042
42.536
44.135
55.394
57.361
61.827
72.157
76.903
77.157
77.412
114.067
122.156
128.513
128.786
160.124
173.156
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

Purified Exo Adduct

^{1}H NMR (600 MHz, $CDCl_3$)

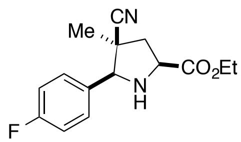
epi-**5g**



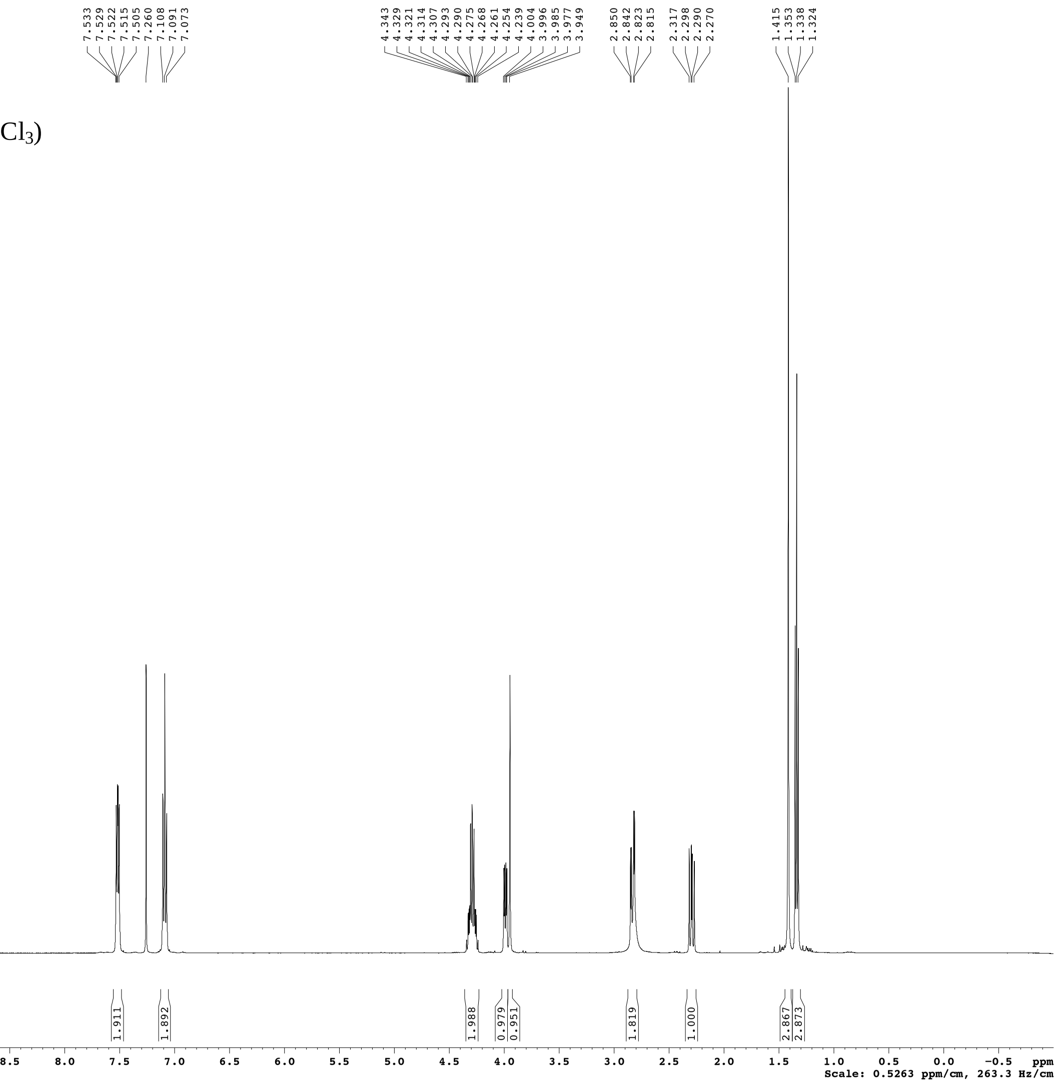

Purified Exo Adduct
^{13}C NMR (125 MHz, CDCl$_3$)
Me
NC
CO$_2$Et
N
H
MeO
epi-5g
173.297
159.726
128.566
128.361
124.224
113.983
77.413
77.159
76.905
69.214
61.648
57.283
55.407
41.779
40.169
20.507
14.319
ppm

Purified Endo Adduct

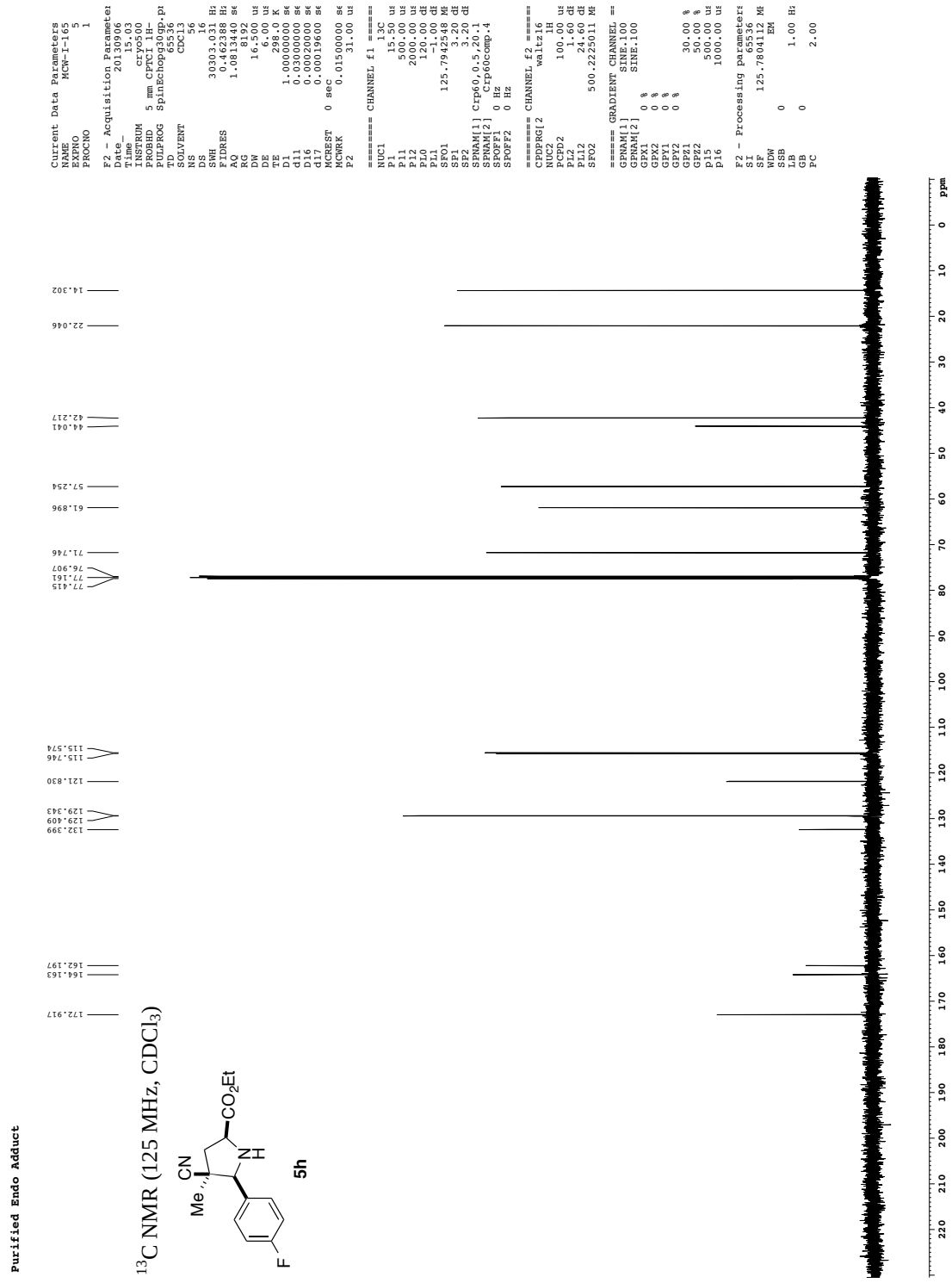
^{1}H NMR (500 MHz, $CDCl_3$)

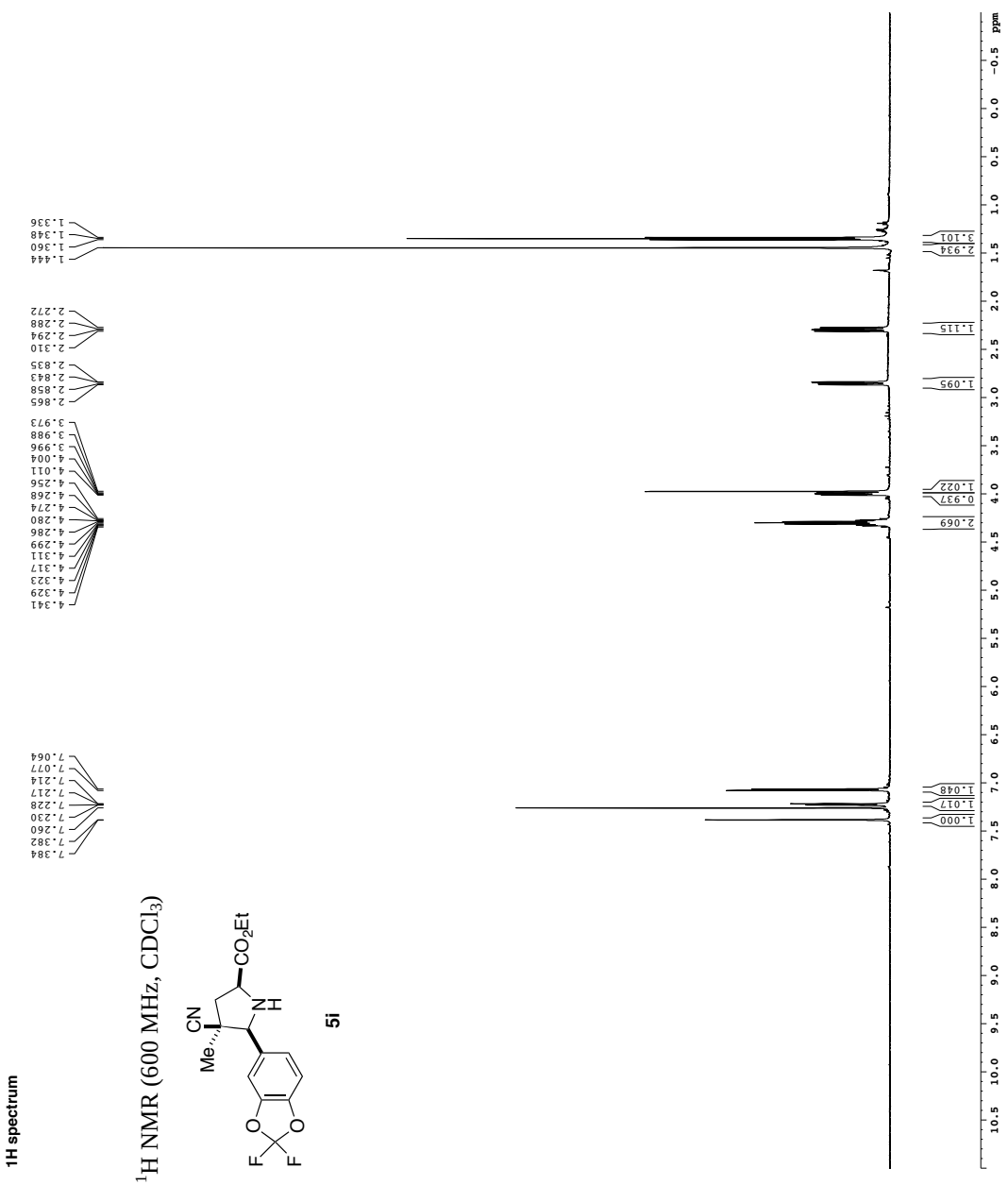


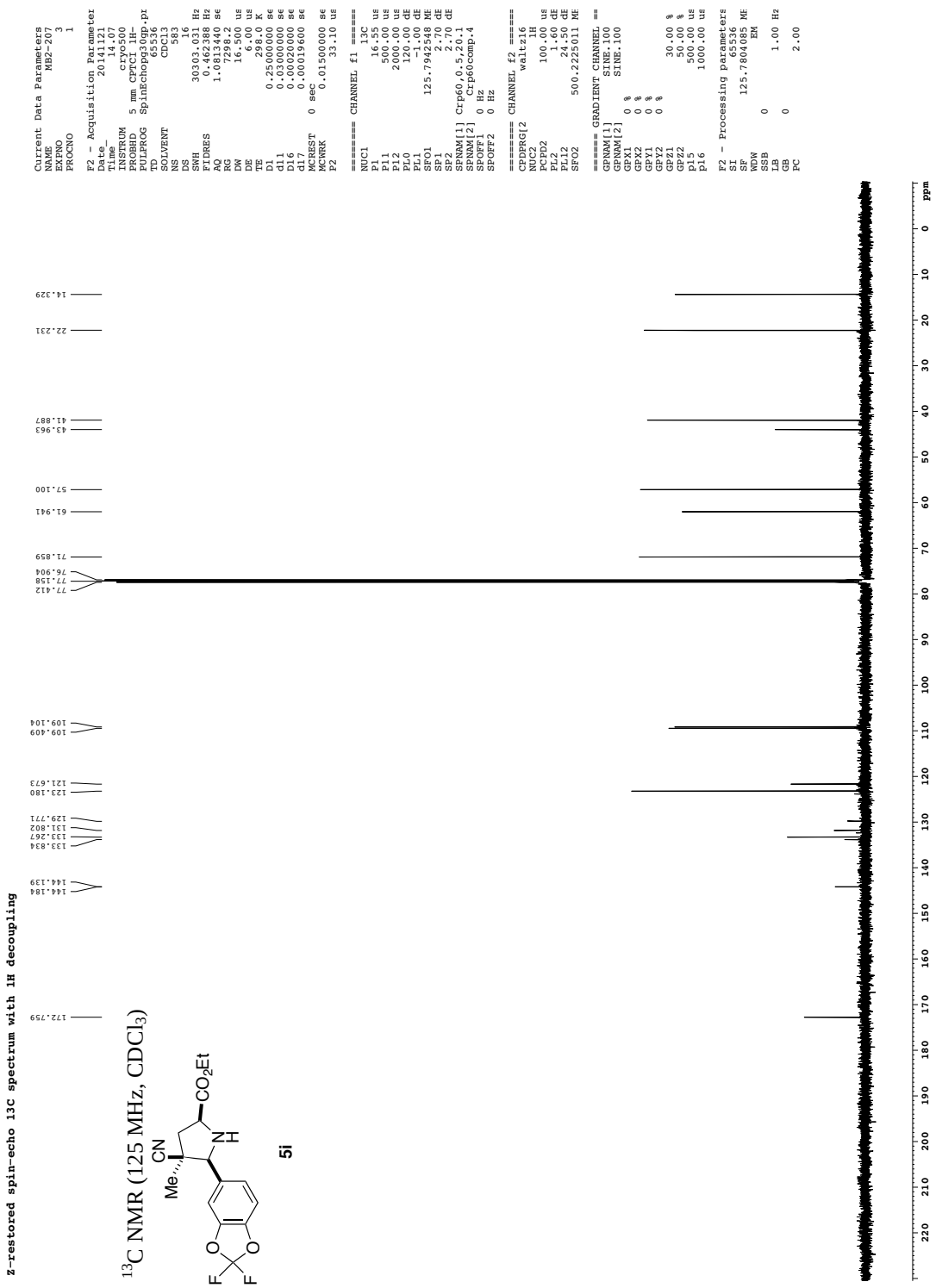
5h

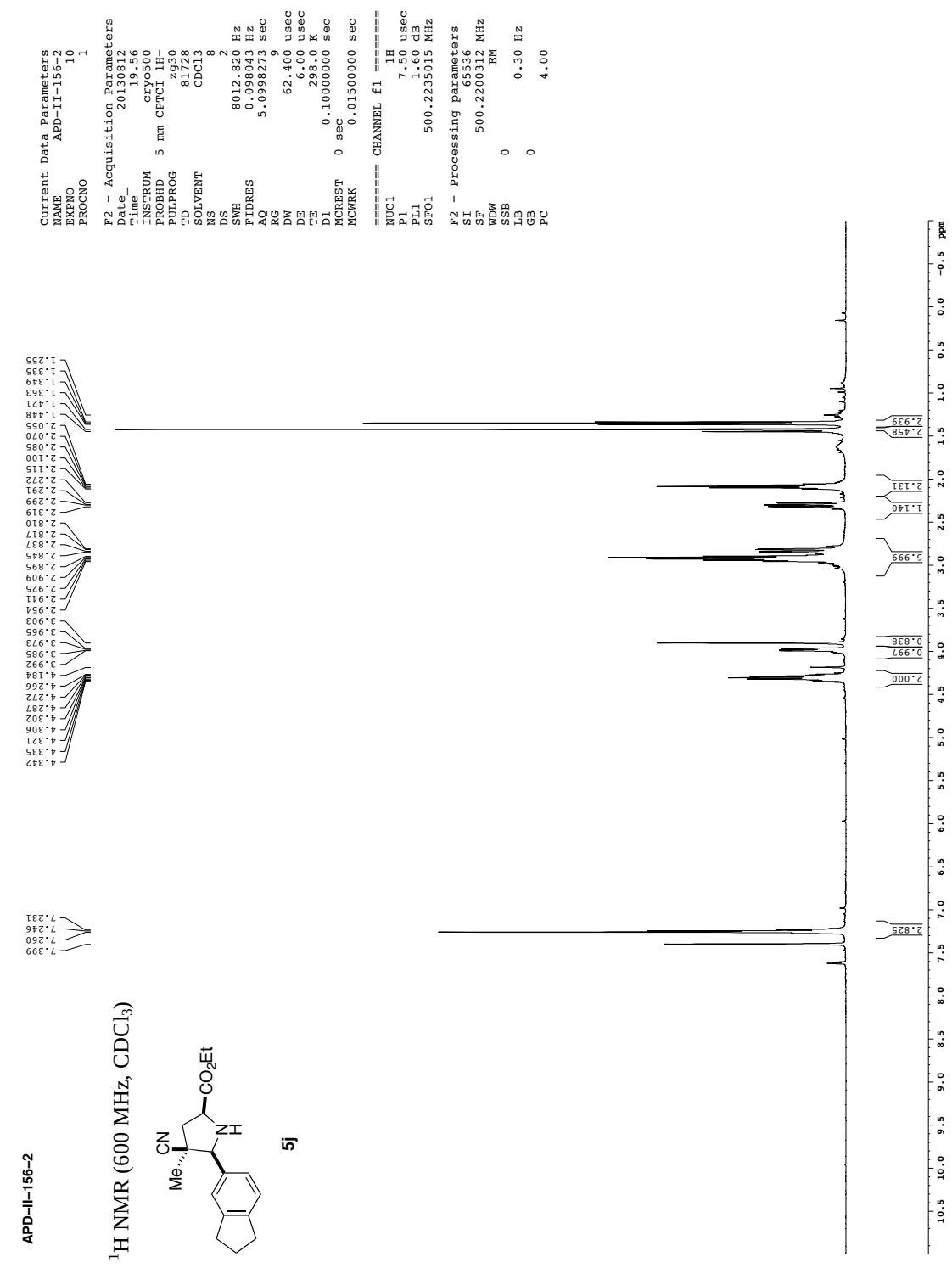


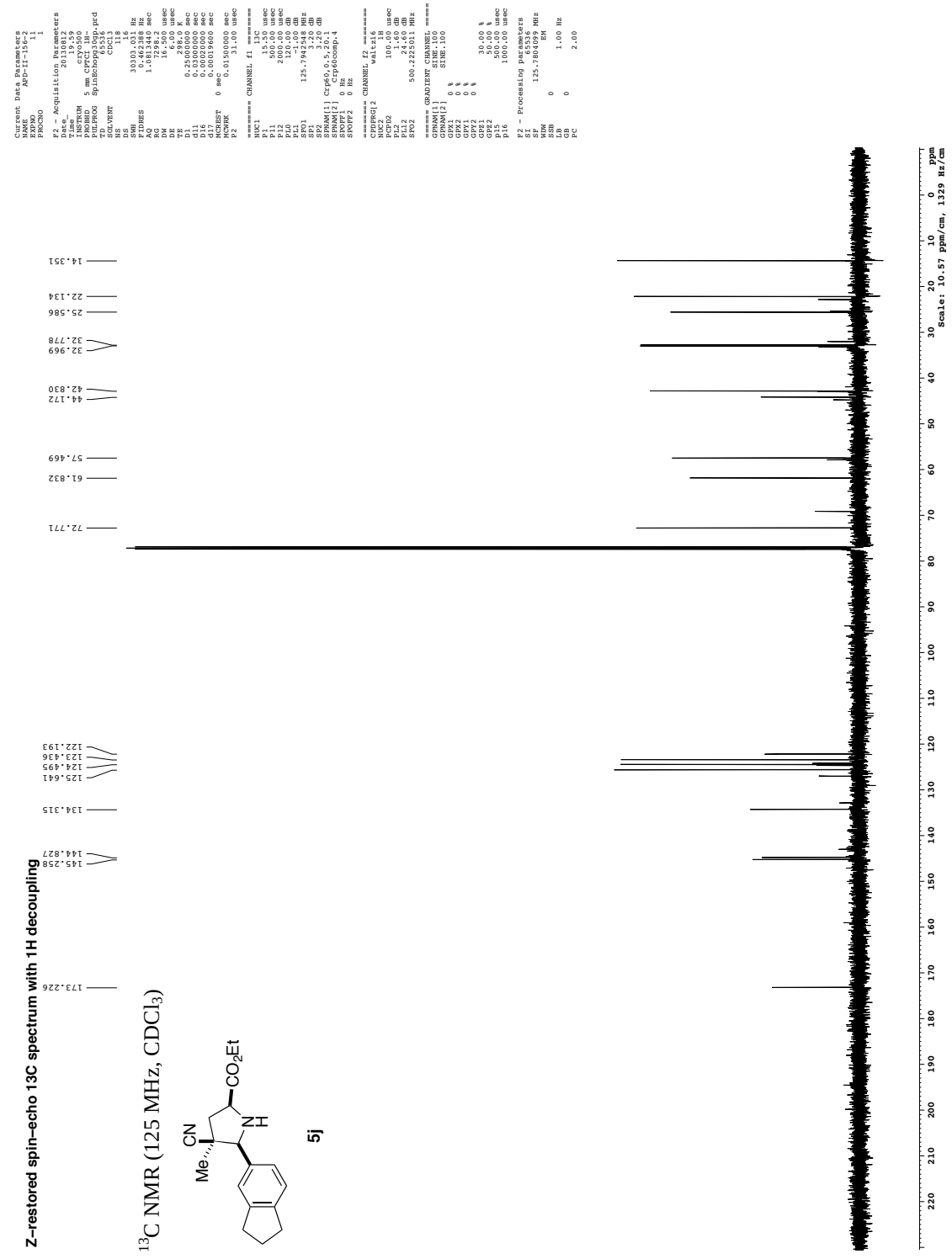

```
Current Data Parameters
NAME            MCW-I-165
EXPNO                   4
PROCNO                  1

F2 - Acquisition Parameters
Date_            20130906
Time                15.01
INSTRUM           cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG              zg30
TD                  81728
SOLVENT             CDCl3
NS                      8
DS                      2
SWH              8012.820 Hz
FIDRES           0.098043 Hz
AQ              5.0998273 sec
RG                    4.5
DW                 62.400 usec
DE                   6.00 usec
TE                  298.0 K
D1             0.10000000 sec
MCREST   0 sec
MCWRK          0.01500000 sec

======== CHANNEL f1 ========
NUC1                   1H
P1                   7.50 usec
PL1                  1.60 dB
SFO1         500.2235015 MHz

F2 - Processing parameters
SI                  65536
SF            500.2200309 MHz
WDW                    EM
SSB      0
LB                   0.30 Hz
GB       0
PC                   4.00
```

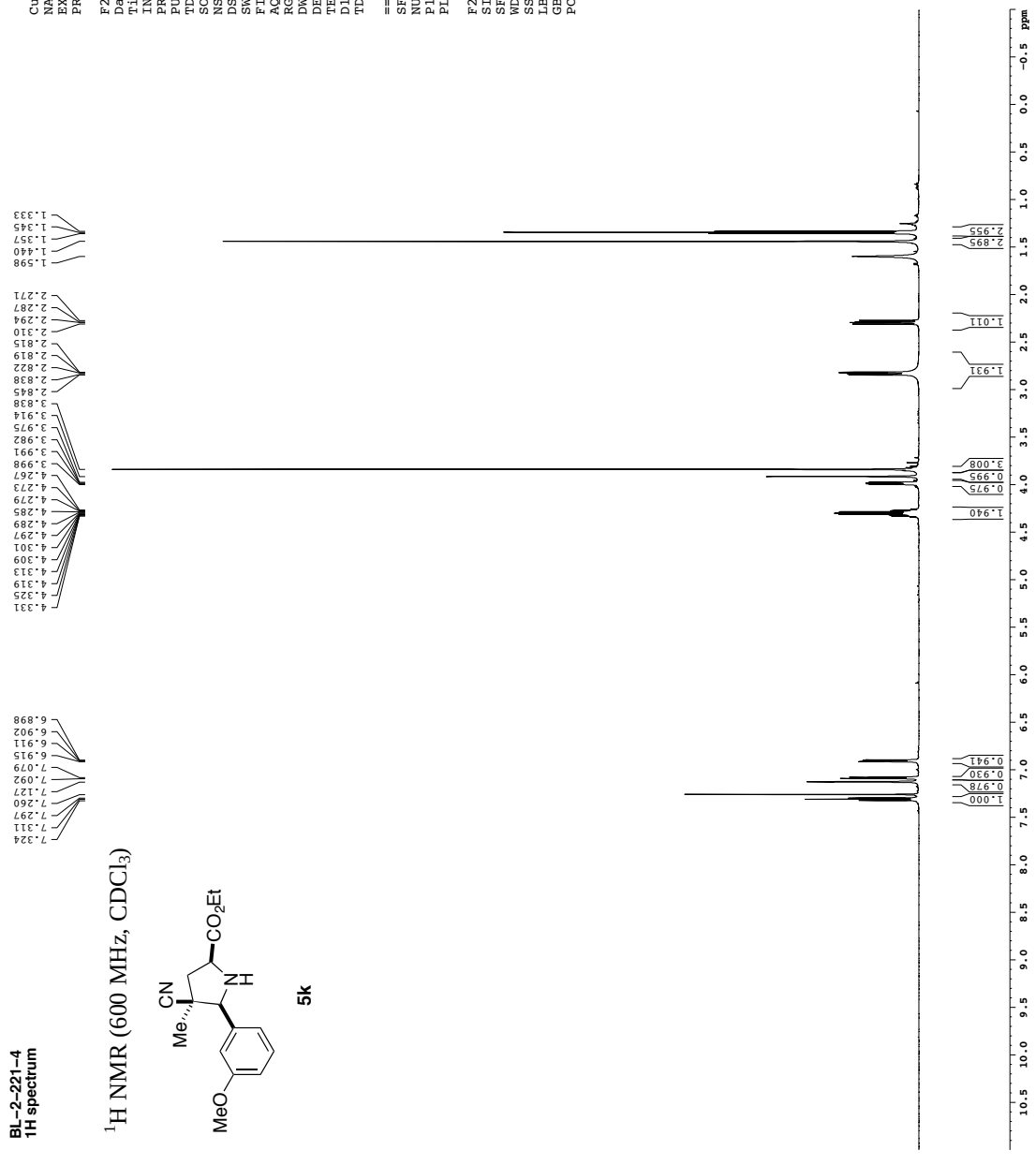

Purified Endo Adduct
^{13}C NMR (125 MHz, CDCl$_3$)
5h
Current Data Parameters
NAME MCW-I-165
EXPNO 5
PROCNO 1
F2 - Acquisition Parameters
Date_ 20130906
Time 15.03
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 56
DS 16
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0813440 sec
RG 8192
DW 16.500 usec
DE 6.00 usec
TE 298.0 K
D1 1.00000000 sec
d11 0.03000000 sec
D16 0.00020000 sec
MCREST 0.00019600 sec
MCWRK 0.01500000 sec
P2 31.00 usec
======== CHANNEL f1 ========
NUC1 13C
P1 15.50 usec
P11 500.00 usec
P12 20000.00 usec
PL0 120.00 dB
PL1 -1.00 dB
SFO1 125.7942548 MHz
SP1 3.20 dB
SP2 3.20 dB
SPNAM[1] Crp60,0.5,20.1
SPNAM[2] Crp60comp.4
SPOFF1 0 Hz
SPOFF2 0 Hz
======== CHANNEL f2 ========
CPDPRG[2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 1.60 dB
PL12 24.60 dB
SFO2 500.2225011 MHz
====== GRADIENT CHANNEL ==
GPNAM[1] SINE.100
GPNAM[2] SINE.100
GPX1 0 %
GPX2 0 %
GPY1 0 %
GPY2 0 %
GPZ1 30.00 %
GPZ2 50.00 %
p15 500.00 usec
p16 1000.00 usec
F2 - Processing parameters
SI 65536
SF 125.7804112 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00
172.917
164.163
162.197
132.399
129.409
129.343
121.830
115.746
115.574
77.415
77.161
76.907
71.746
61.896
57.254
44.041
42.217
22.046
14.302
ppm


1H spectrum
^{1}H NMR (600 MHz, CDCl$_3$)
5i
Current Data Parameters
NAME MB2-207
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20141120
Time_ 7.52
INSTRUM av600
PROBHD 5 mm TBI 1H/13
PULPROG zg30
TD 98074
SOLVENT CDCl3
NS 8
DS 2
SWH 9615.385 Hz
FIDRES 0.098042 Hz
AQ 5.0998478 sec
RG 1.60
DW 52.000 usec
DE 14.54 usec
TE 298.0 K
D1 0.10000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 600.1342009 MHz
NUC1 1H
P1 8.00 usec
PLW1 23.01441956 W
F2 - Processing parameters
SI 65536
SF 600.1300346 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
7.384
7.382
7.260
7.230
7.228
7.217
7.214
7.077
7.064
4.341
4.329
4.323
4.317
4.311
4.299
4.286
4.280
4.274
4.268
4.256
4.011
4.004
3.996
3.988
3.973
2.865
2.858
2.843
2.835
2.310
2.294
2.288
2.272
1.444
1.360
1.348
1.336
1.000
1.017
1.048
2.069
0.937
1.022
1.095
1.115
2.934
3.101
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
−0.5
ppm


Z-restored spin-echo 13C spectrum with 1H decoupling
13C NMR (125 MHz, CDCl3)
5i
Current Data Parameters
NAME MB2-207
EXPNO 3
PROCNO 1
F2 - Acquisition Parameter
Date_ 20141121
Time 14.07
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG SpinEchoPg3gp.pr
TD 65536
SOLVENT CDCl3
NS 583
DS 16
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0813440 sec
RG 79.2
DW 16.500 us
DE 6.00 us
TE 298.0 K
D1 0.25000000 sec
d11 0.03000000 sec
D16 0.00020000 sec
d12 0.00019600 sec
MCREST 0 sec 0.01500000 sec
MCWRK 33.10 us
P2
======== CHANNEL f1 ======
NUC1 13C
P1 16.55 us
P11 500.00 us
P12 2000.00 us
PL2 120.00 dB
PL1 -1.00 dB
SFO1 125.7942548 MH
SP1 2.70 dB
SP2 2.70 dB
SPNAM[1] Crp60,0.5,20.1
SPNAM[2] Crp60comp.4
SPOFF1 0 Hz
SPOFF2 0 Hz
======== CHANNEL f2 ======
CPDPRG[2 waltz16
NUC2 1H
PCPD2 100.00 us
PL2 1.60 dB
PL12 24.50 dB
SFO2 500.2225011 MH
====== GRADIENT CHANNEL ==
GPNAM[1] SINE.100
GPNAM[2] SINE.100
GPX1 0 %
GPX2 0 %
GPY1 0 %
GPY2 0 %
GPZ1 30.00 %
GPZ2 50.00 %
p15 500.00 us
p16 1000.00 us
F2 - Processing parameter
SI 65536
SF 125.7804085 MH
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00
172.759
144.184
144.139
133.834
133.267
131.802
129.771
123.180
121.673
109.409
109.104
77.412
77.158
76.904
71.859
61.941
57.100
43.963
41.887
22.231
14.329
ppm

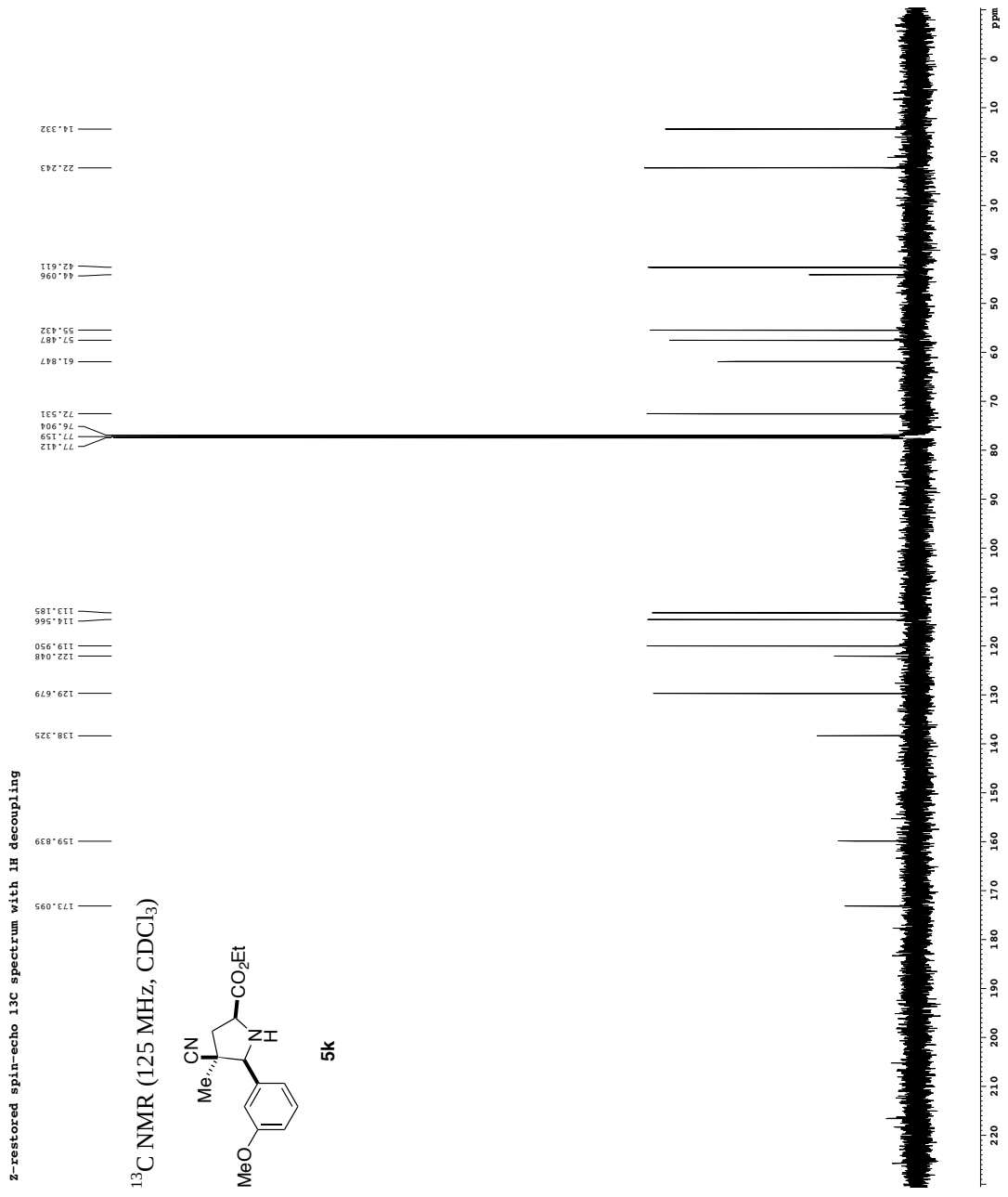

APD-II-156-2
^{1}H NMR (600 MHz, $CDCl_3$)
5j
Current Data Parameters
NAME APD-II-156-2
EXPNO 10
PROCNO 1
F2 - Acquisition Parameters
Date_ 20130812
Time_ 19.56
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 81728
SOLVENT CDCl3
NS 8
DS 2
SWH 8012.820 Hz
FIDRES 0.098043 Hz
AQ 5.0998273 sec
RG 9
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0 sec 0.01500000 sec
MCWRK
======== CHANNEL f1 ========
NUC1 1H
P1 7.50 usec
PL1 1.60 dB
SFO1 500.2235015 MHz
F2 - Processing parameters
SI 65536
SF 500.2200312 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00
7.399
7.260
7.246
7.231
4.342
4.335
4.321
4.306
4.302
4.287
4.272
4.266
4.184
3.992
3.985
3.973
3.965
3.903
2.954
2.941
2.925
2.909
2.895
2.845
2.837
2.817
2.810
2.319
2.299
2.291
2.272
2.115
2.100
2.085
2.070
2.055
1.448
1.421
1.363
1.349
1.335
1.255
2.825
2.000
0.997
0.838
5.999
1.140
2.131
2.458
2.939
ppm


Z-restored spin-echo 13C spectrum with 1H decoupling
13C NMR (125 MHz, CDCl3)
5j
CN
Me
CO2Et
N
H
173.226
145.258
144.827
134.315
125.641
124.495
123.436
122.193
72.771
61.832
57.469
44.172
42.830
32.969
32.778
25.586
22.134
14.351
ppm
Scale: 10.57 ppm/cm, 1329 Hz/cm

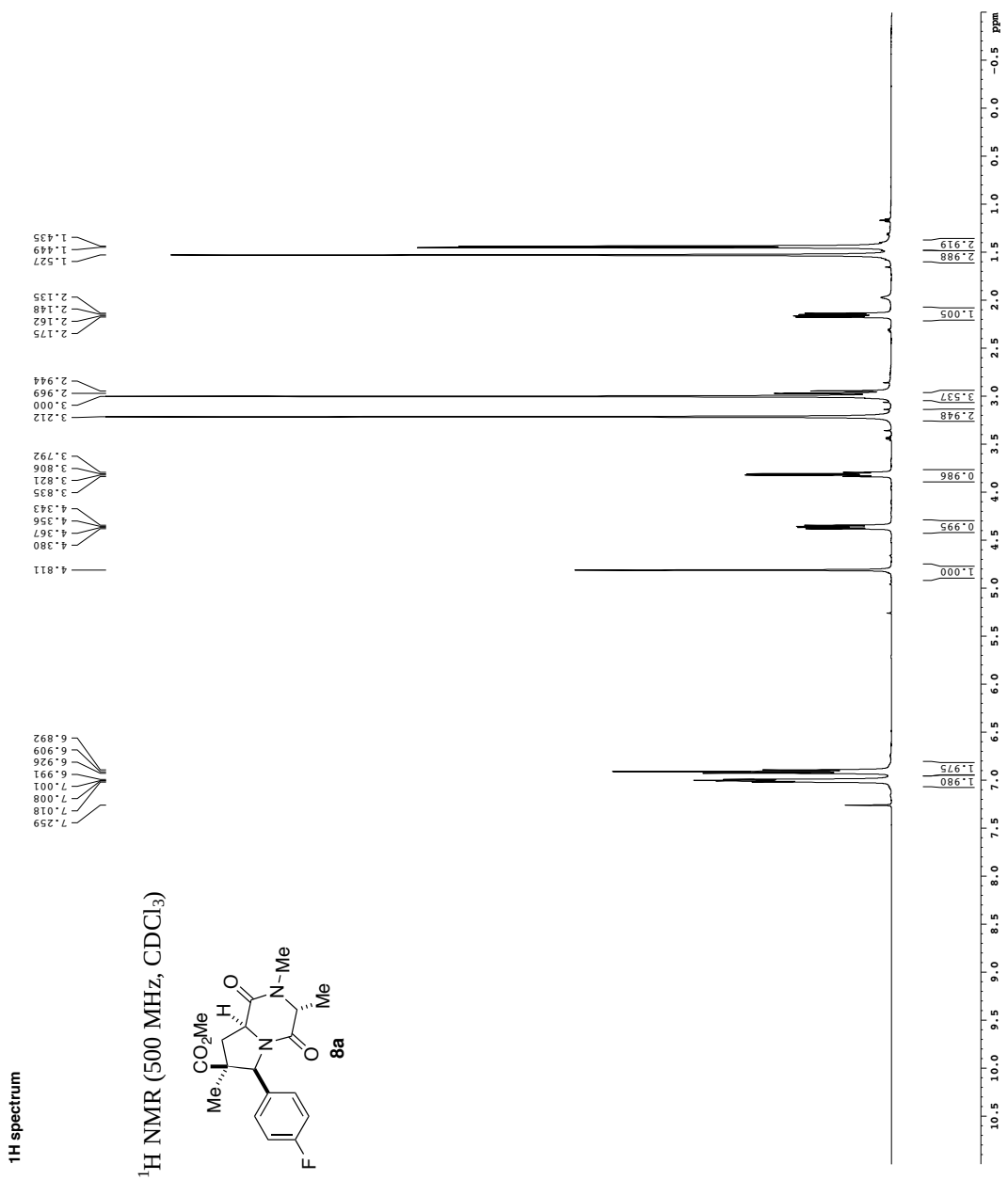


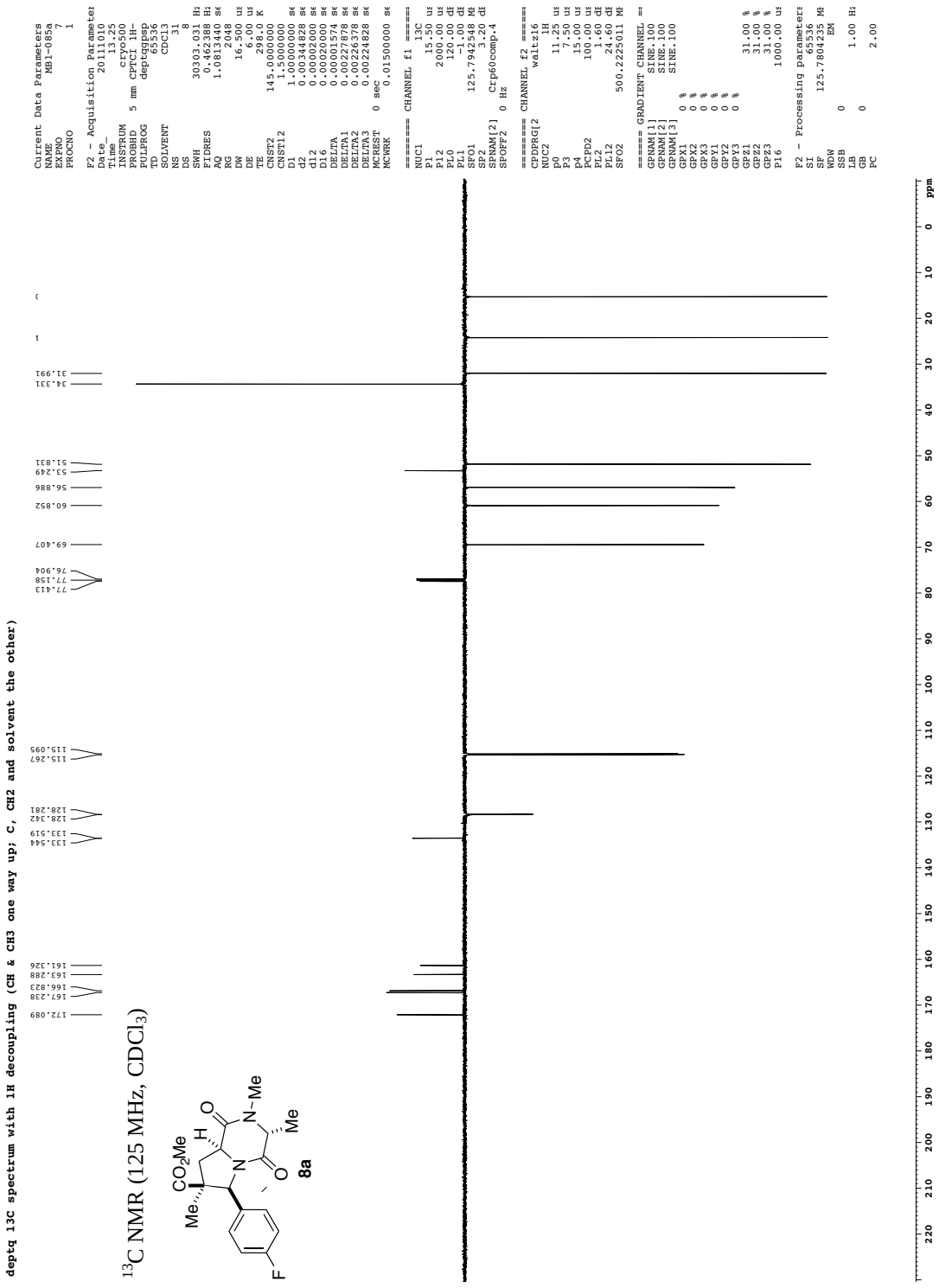
^{1}H NMR (600 MHz, $CDCl_3$)

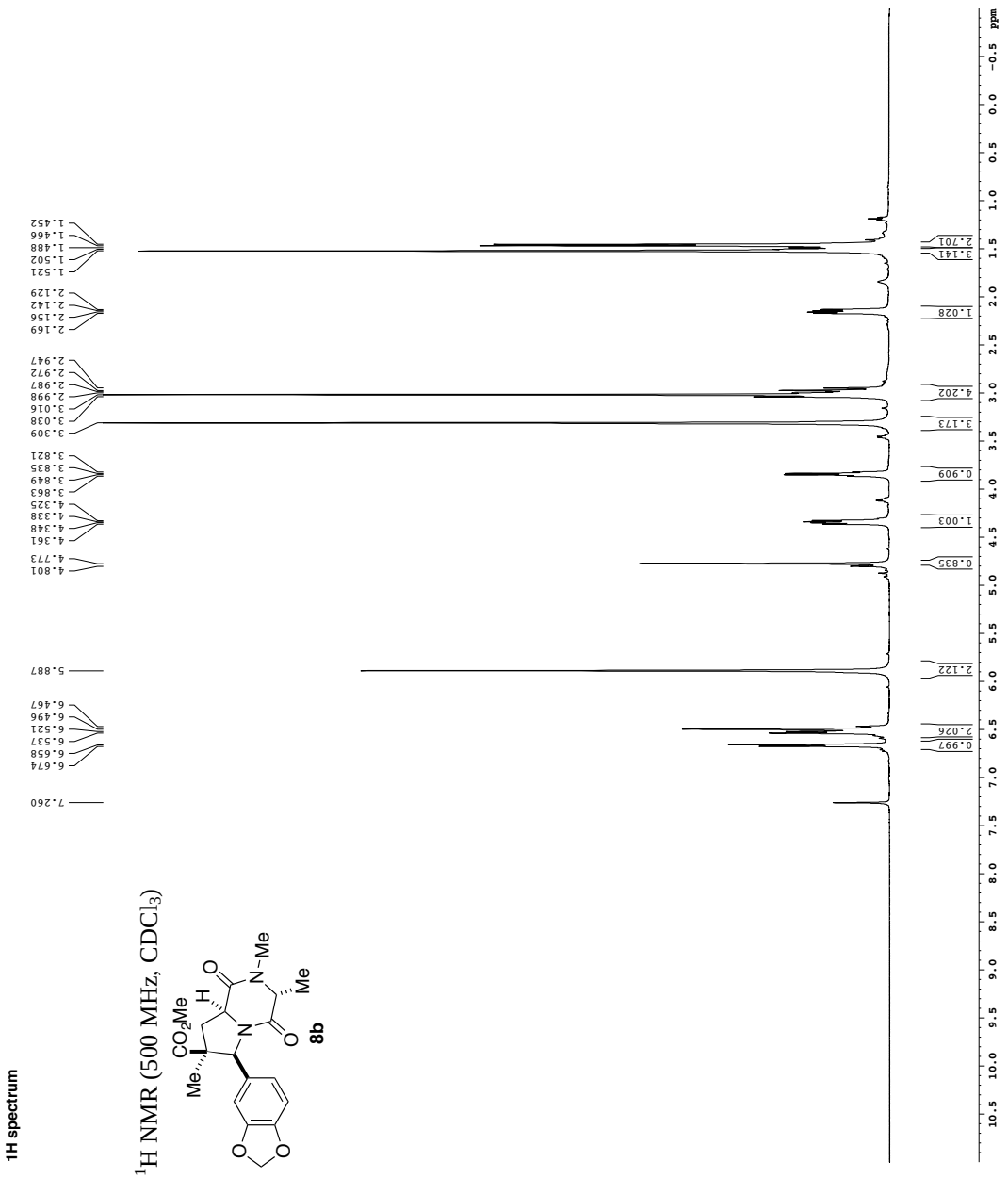
5k


Z-restored spin-echo 13C spectrum with 1H decoupling
13C NMR (125 MHz, CDCl3)
5k
MeO
CN
Me
CO2Et
N
H
Current Data Parameters
NAME BL-2-221-4
EXPNO 3
PROCNO 1
F2 - Acquisition Parameter
Date_ 20150309
Time_ 13.43
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG SpinEchopg30gp.pr
TD 65536
SOLVENT CDCl3
NS 200
DS 16
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.081344 sec
RG 4096
DW 16.550 us
DE 6.00 us
TE 298.0 K
D1 0.25000000 sec
d11 0.03000000 sec
D16 0.00020000 sec
d17 0.00019600 sec
MCREST 0 sec 0.01500000 sec
MCWRK 0.01500000 sec
P2 33.10 us
======== CHANNEL f1 ======
NUC1 13C
P1 16.55 us
P11 500.00 us
P12 2000.00 us
PL0 120.00 dB
PL1 -1.00 dB
SFO1 125.7942548 MHz
SP1 2.70 dB
SP2 2.70 dB
SPNAM[1] Crp60,0.5,20.1
SPNAM[2] Crp60comp.4
SPOFF1 0 Hz
SPOFF2 0 Hz
======== CHANNEL f2 ======
CPDPRG[2 waltz16
NUC2 1H
PCPD2 100.00 us
PL2 1.60 dB
PL12 24.50 dB
SFO2 500.2225011 MHz
====== GRADIENT CHANNEL ==
GPNAM[1] SINE.100
GPNAM[2] SINE.100
GPX1 0 %
GPX2 0 %
GPY1 0 %
GPY2 0 %
GPZ1 30.00 %
GPZ2 50.00 %
p15 500.00 us
p16 1000.00 us
F2 - Processing parameters
SI 65536
SF 125.7804094 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00
14.332
22.243
42.611
44.096
55.432
57.487
61.847
72.531
76.904
77.159
77.412
113.185
114.566
119.950
122.048
129.679
138.325
159.839
173.095
ppm

MB1-085a H NMR

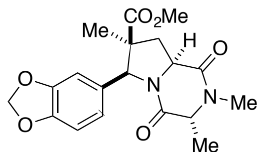



deptq 13C spectrum with 1H decoupling (CH & CH3 one way up; C, CH2 and solvent the other)
13C NMR (125 MHz, CDCl3)
8a
Current Data Parameters
NAME MB1-085a
EXPNO 7
PROCNO 1
F2 - Acquisition Parameters
Date_ 20111010
Time 13.25
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG deptqgsap
TD 65536
SOLVENT CDCl3
NS 31
DS 8
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0813440 sec
RG 2048
DW 16.500 usec
DE 6.00 usec
TE 298.0 K
CNST2 145.0000000
CNST12 1.5000000
D1 1.00000000 sec
d2 0.00344828 sec
d12 0.00020000 sec
d16 0.00020000 sec
DELTA 0.00001574 sec
DELTA1 0.00227878 sec
DELTA2 0.00226378 sec
DELTA3 0.00224828 sec
MCREST 0 sec 0.01500000 sec
MCWRK
======== CHANNEL f1 ======
NUC1 13C
P1 15.50 usec
P12 2000.00 usec
PL0 120.00 dB
PL1 -1.00 dB
SFO1 125.7942548 MHz
SP2 120.00 dB
SPNAM[2] Crp60comp.4
SPOFF2 0 Hz
======== CHANNEL f2 ======
CPDPRG[2 waltz16
NUC2 1H
P0 11.25 usec
P3 7.50 usec
P4 15.00 usec
PCPD2 100.00 usec
PL2 1.60 dB
PL12 24.60 dB
SFO2 500.2225011 MHz
====== GRADIENT CHANNEL ==
GPNAM[1] SINE.100
GPNAM[2] SINE.100
GPNAM[3] SINE.100
GPX1 0 %
GPX2 0 %
GPX3 0 %
GPY1 0 %
GPY2 0 %
GPY3 0 %
GPZ1 31.00 %
GPZ2 31.00 %
GPZ3 31.00 %
P16 1000.00 usec
F2 - Processing parameters
SI 65536
SF 125.7804235 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00
172.089
166.823
163.288
161.326
133.544
133.519
128.342
128.281
115.267
115.095
77.413
77.158
76.904
69.407
60.852
56.886
53.249
51.831
34.331
31.991
ppm

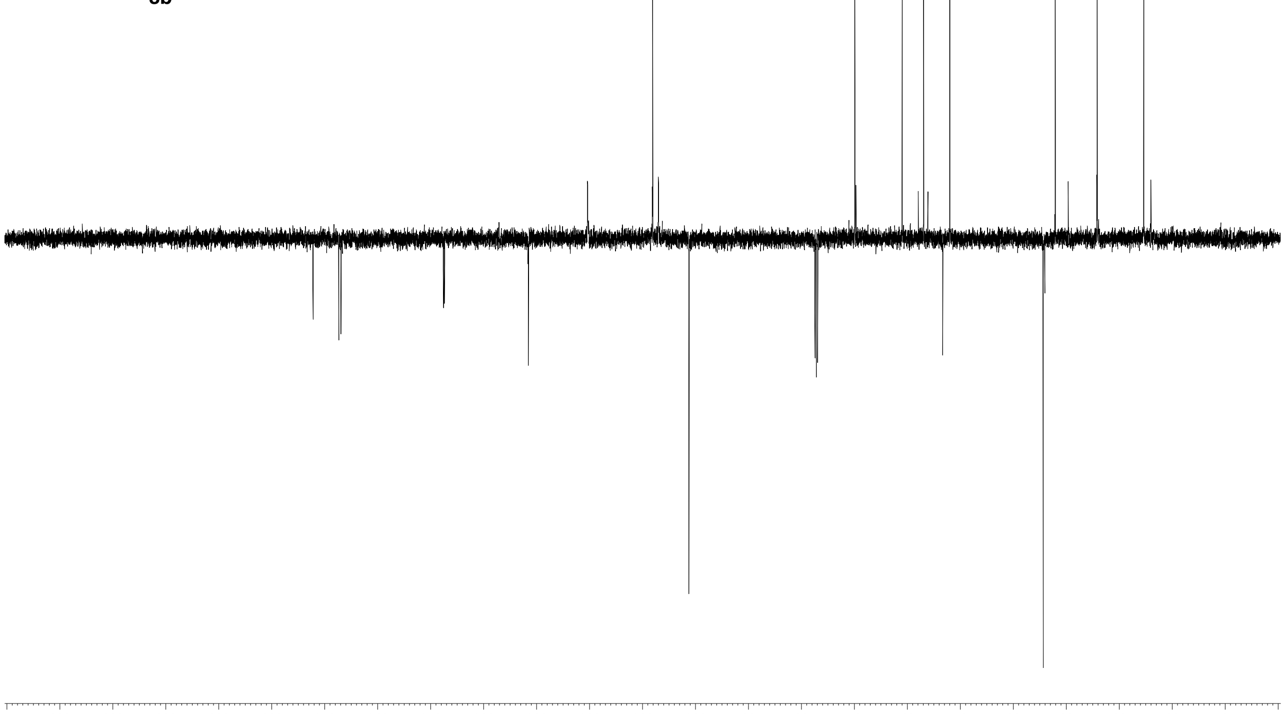

1H spectrum
Current Data Parameters
NAME MB1-112
EXPNO 3
PROCNO 1
F2 - Acquisition Parameters
Date_ 20111219
Time_ 13.29
INSTRUM gn500
PROBHD 5 mm broadband
PULPROG z30
TD 81728
SOLVENT CDCl3
NS 8
DS 2
SWH 8012.820 Hz
FIDRES 0.098043 Hz
AQ 5.0998273 sec
RG 71.8
DW 62.400 usec
DE 6.00 usec
TE 292.3 K
D1 0.10000000 sec
MCREST 0 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 12.20 usec
PL1 -5.00 dB
SFO1 499.5134966 MHz
F2 - Processing parameters
SI 65536
SF 499.5100276 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
1H NMR (500 MHz, CDCl3)
8b
ppm

DEPTQ: 13C spectrum with 1H decoupling (CH & CH3 one way up; C, CH2 and solvent the other)

^{13}C NMR (125 MHz, $CDCl_3$)



8b



Current Data Parameters
NAME MB1-112
EXPNO 4
PROCNO 1

F2 - Acquisition Parameter
Date_ 20111219
Time 13.32
INSTRUM gn500
PROBHD 5 mm broadband
PULPROG deptqgpsp
TD 65536
SOLVENT CDCl3
NS 100
DS 8
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0813440 se
RG 26008
DW 16.500 us
DE 6.00 us
TE 292.6 K
CNST2 145.0000000
CNST12 1.5000000
D1 1.00000000 se
d2 0.00344828 se
d12 0.00002000 se
D16 0.00020000 se
DELTA 0.00000580 se
DELTA1 0.00227998 se
DELTA2 0.00225598 se
DELTA3 0.00224828 se
MCREST 0 sec
MCWRK 0.01500000 se

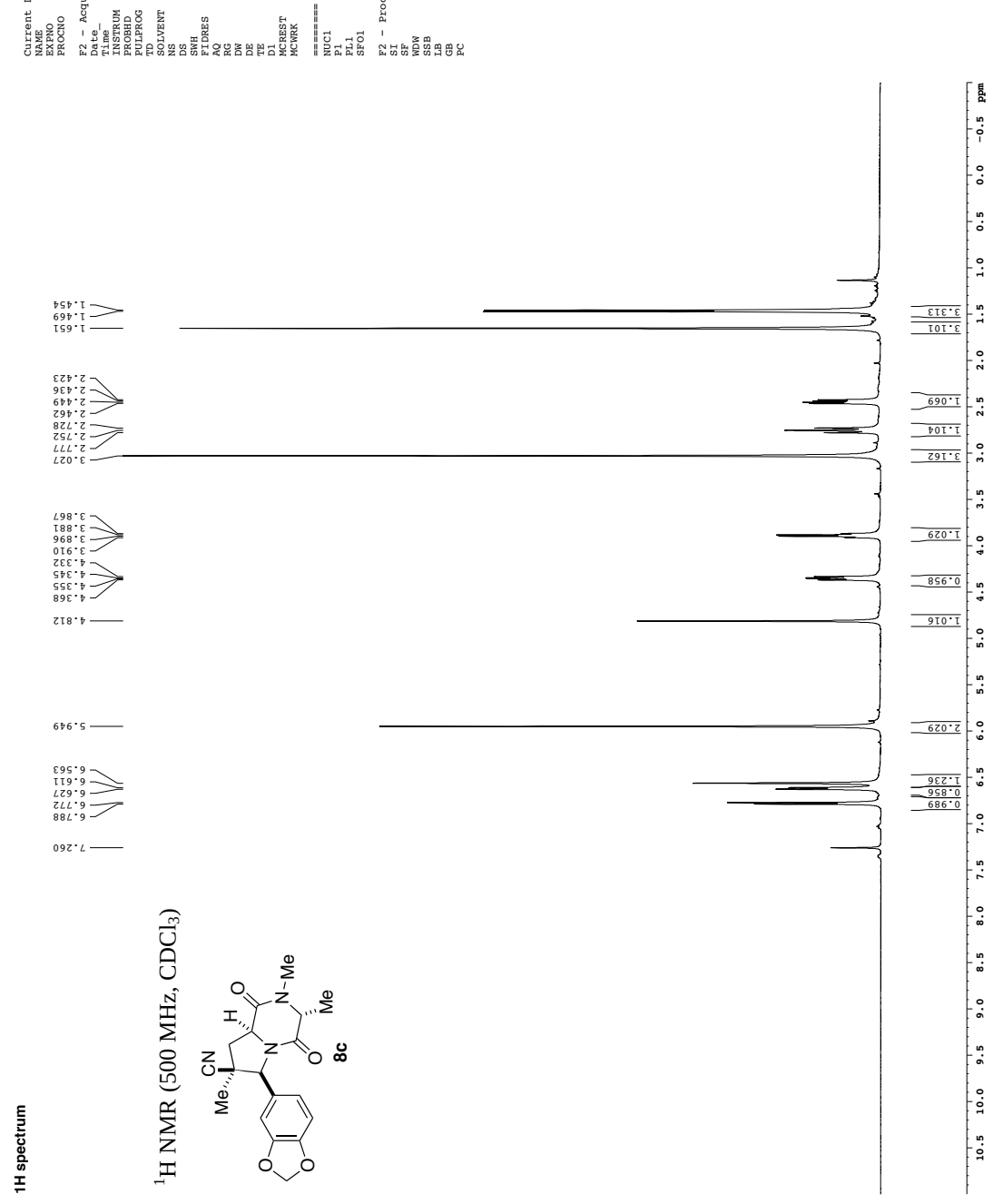
======== CHANNEL f1 =====
NUC1 13C
P1 7.70 us
P12 2000.00 us
PL0 120.00 dB
PL1 0 dB
SFO1 125.6157052 MH
SP2 11.20 dB
SPNAM[2] Crp60comp.4
SPOFF2 0 Hz

======== CHANNEL f2 =====
CPDPRG[2 waltz16
NUC2 1H
p0 18.00 us
P3 12.00 us
p4 24.00 us
PCPD2 80.00 us
PL2 -5.00 dB
PL12 13.20 dB
SFO2 499.5124975 MH

====== GRADIENT CHANNEL ==
GPNAM[1] SINE.100
GPNAM[2] SINE.100
GPNAM[3] SINE.100
GPX1 0 %
GPX2 0 %
GPX3 0 %
GPY1 0 %
GPY2 0 %
GPY3 0 %
GPZ1 31.00 %
GPZ2 31.00 %
GPZ3 31.00 %
P16 1000.00 us

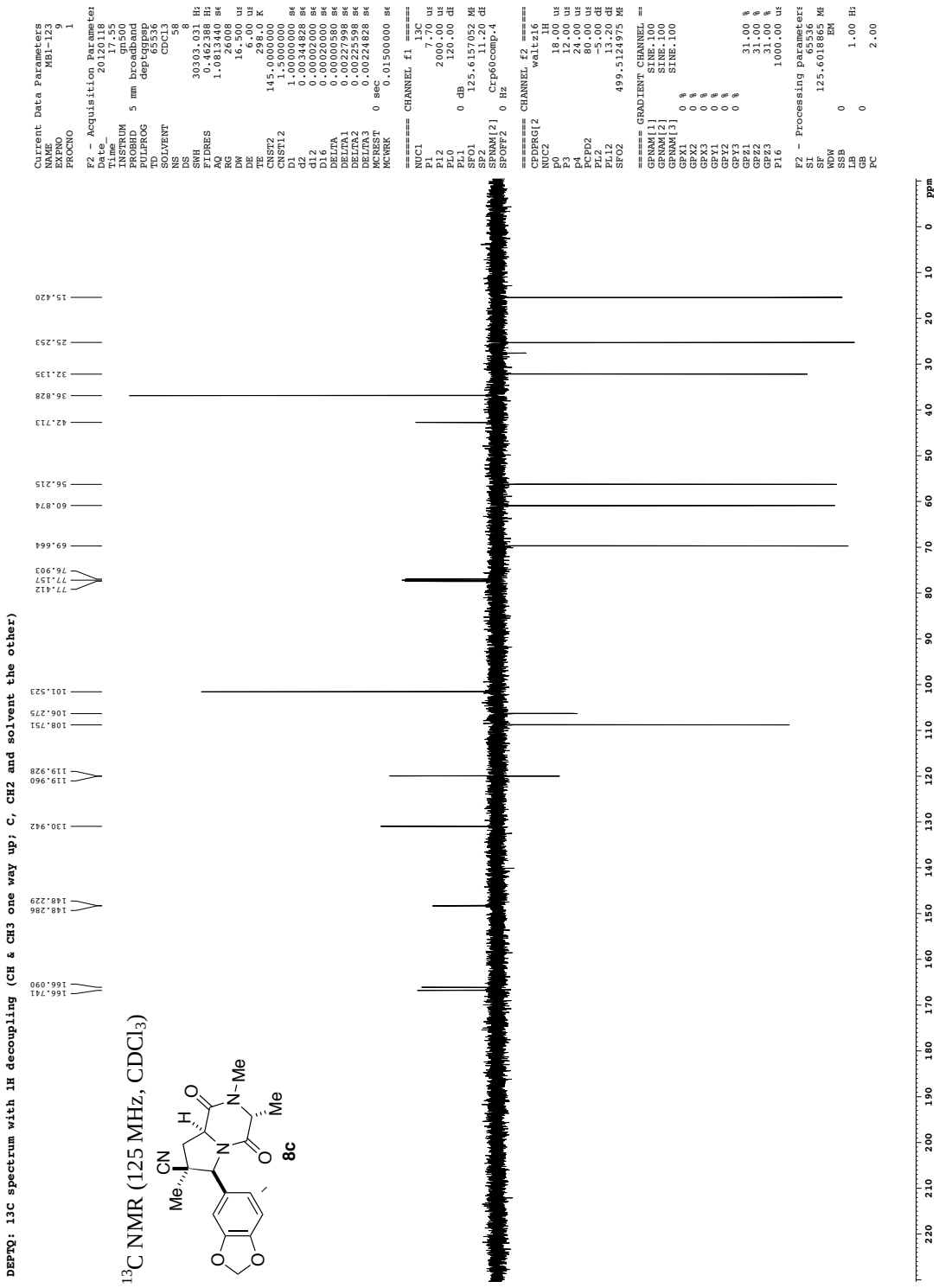
F2 - Processing parameters
SI 65536
SF 125.6018874 MH
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00

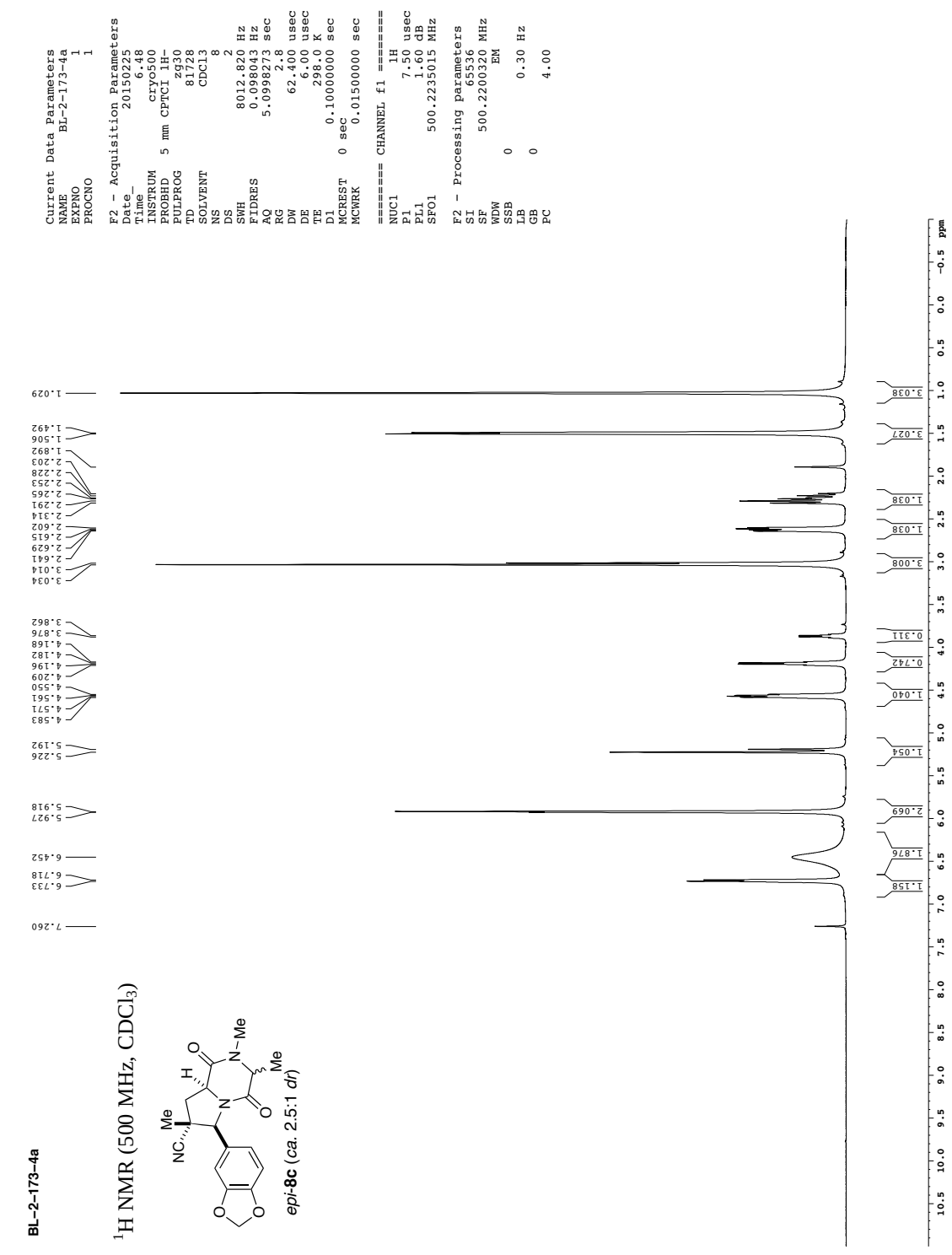
1H spectrum

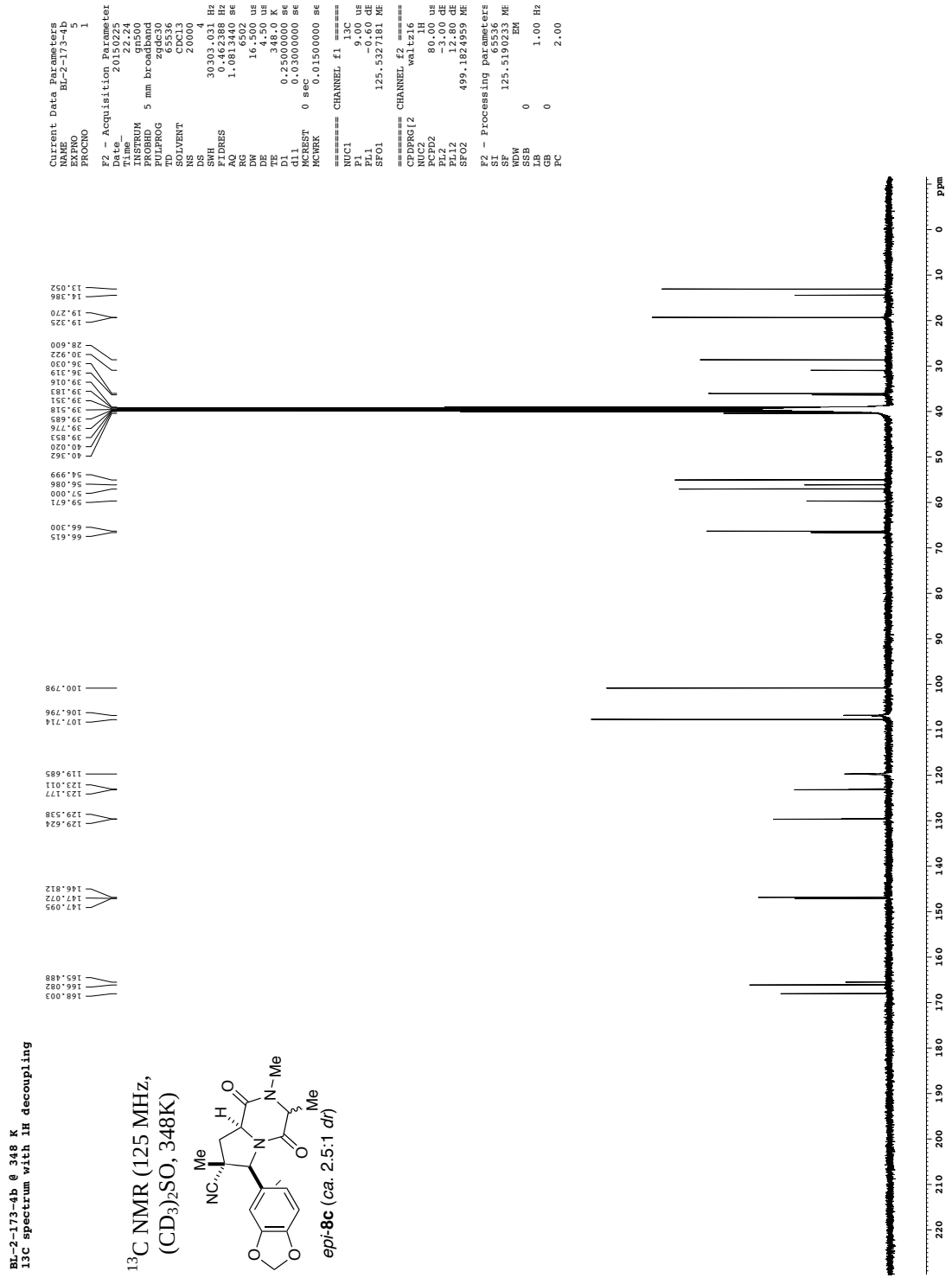


^{1}H NMR (500 MHz, $CDCl_3$)

8c


DEPTQ: 13C spectrum with 1H decoupling (CH & CH3 one way up; C, CH2 and solvent the other)
13C NMR (125 MHz, CDCl3)
8c
Current Data Parameters
NAME MB1-123
EXPNO 9
PROCNO 1
F2 - Acquisition Parameters
Date_ 20120118
Time 17.55
INSTRUM qn500
PROBHD 5 mm broadband
PULPROG deptqtgsp
TD 65536
SOLVENT CDCl3
NS 58
DS 8
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0813440 sec
RG 16000
DW 16.500 usec
DE 6.00 usec
TE 298.0 K
CNST2 145.0000000
CNST12 1.5000000
D1 1.00000000 sec
d2 0.00344828 sec
d12 0.00000000 sec
D16 0.00020000 sec
DELTA 0.00000580 sec
DELTA1 0.00227998 sec
DELTA2 0.00225598 sec
DELTA3 0.00224828 sec
MCREST 0 sec 0.01500000 sec
MCWRK
======== CHANNEL f1 ======
NUC1 13C
P1 7.70 usec
P12 2000.00 usec
PL0 120.00 dB
PL1 0 dB 125.6157052 MHz
SFO1 SPNAM[2] Crp60comp.4
SPOFF2 0 Hz
======== CHANNEL f2 ======
CPDPRG[2 waltz16
NUC2 1H
P0 18.00 usec
P3 12.00 usec
P4 24.00 usec
PCPD2 80.00 usec
PL2 -5.00 dB
PL12 13.20 dB
SFO2 499.5124975 MHz
====== GRADIENT CHANNEL ==
GPNAM[1] SINE.100
GPNAM[2] SINE.100
GPNAM[3] SINE.100
GPX1 0 %
GPX2 0 %
GPX3 0 %
GPY1 0 %
GPY2 0 %
GPY3 0 %
GPZ1 31.00 %
GPZ2 31.00 %
GPZ3 31.00 %
P16 1000.00 usec
F2 - Processing parameters
SI 65536
SF 125.6018865 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00
15.420
25.253
32.135
36.828
42.713
56.215
60.874
69.664
76.903
77.157
77.412
101.523
106.275
108.751
119.928
119.960
130.942
148.229
148.286
166.090
166.741
ppm

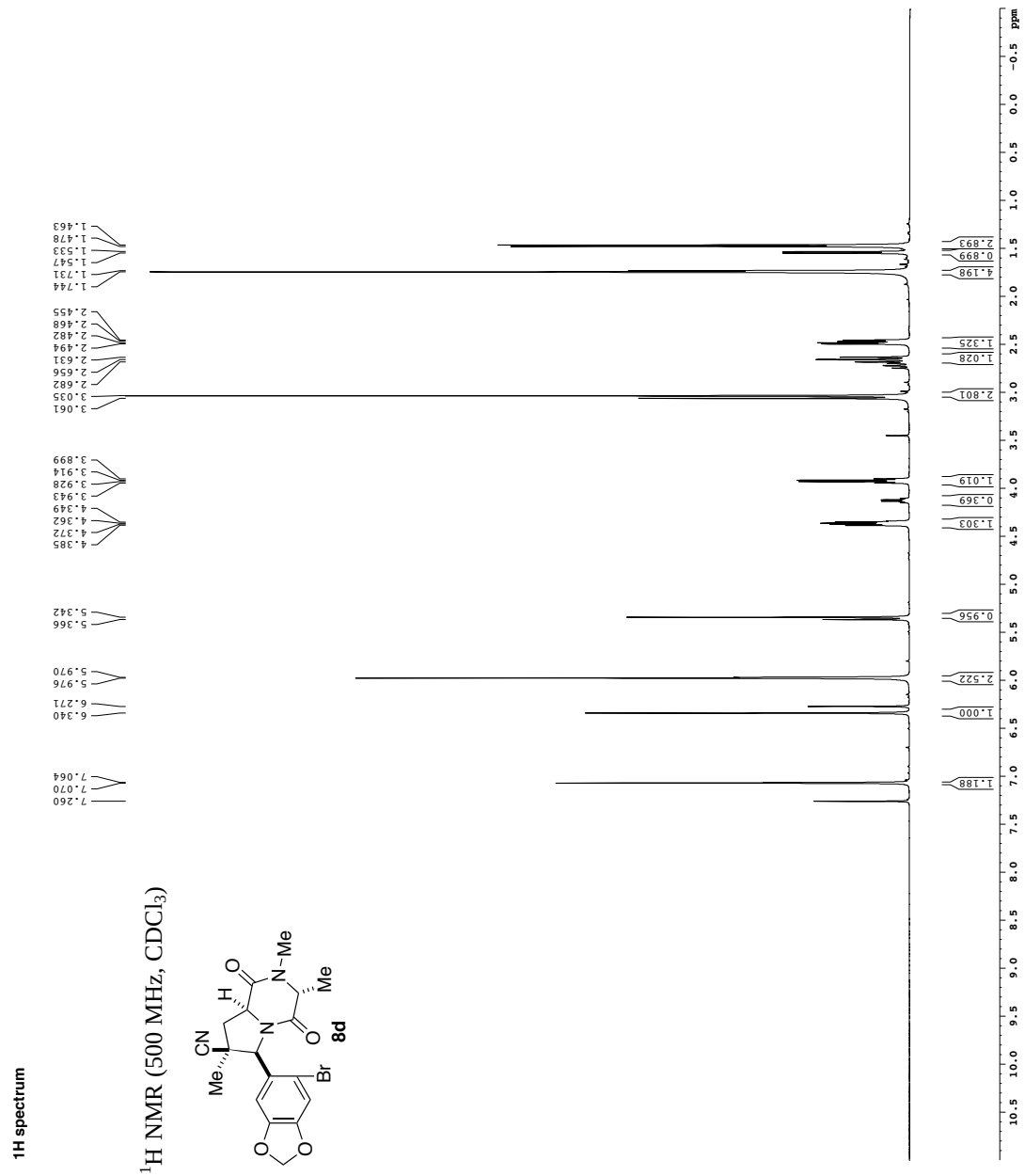

BL-2-173-4a
Current Data Parameters
NAME BL-2-173-4a
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20150225
Time_ 6.48
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 81728
SOLVENT CDCl3
NS 8
DS 2
SWH 8012.820 Hz
FIDRES 0.098043 Hz
AQ 5.0998273 sec
RG 2.8
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0 sec 0.01500000 sec
MCWRK
======== CHANNEL f1 ========
NUC1 1H
P1 7.50 usec
PL1 1.60 dB
SFO1 500.2235015 MHz
F2 - Processing parameters
SI 65536
SF 500.2200320 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00
1H NMR (500 MHz, CDCl3)
epi-8c (ca. 2.5:1 dr)
Me
NC
H
O
N
Me
N
O
Me
O
O
7.260
6.733
6.718
6.452
5.927
5.918
5.226
5.192
4.583
4.571
4.561
4.550
4.209
4.196
4.182
4.168
3.876
3.862
3.034
3.014
2.641
2.629
2.615
2.602
2.314
2.291
2.265
2.253
2.228
2.203
1.892
1.506
1.492
1.029
1.158
1.876
2.069
1.054
1.040
0.742
0.311
3.008
1.038
1.038
1.038
3.027
3.038
ppm


BL-2-173-4b @ 348 K
13C spectrum with 1H decoupling
13C NMR (125 MHz, (CD3)2SO, 348K)
epi-8c (ca. 2.5:1 dr)
Me
NC
H
O
N
Me
O
N
O
Me
O
O
Current Data Parameters
NAME BL-2-173-4b
EXPNO 5
PROCNO 1
F2 - Acquisition Parameter
Date_ 20150225
Time 22.24
INSTRUM gn500
PROBHD 5 mm broadband
PULPROG zgdc30
TD 65536
SOLVENT CDCl3
NS 20000
DS 4
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0813440 sec
RG 6502
DW 16.500 us
DE 4.50 us
TE 348.0 K
D1 0.25000000 sec
D11 0.03000000 sec
MCREST 0 sec
MCWRK 0.01500000 sec
CHANNEL f1
NUC1 13C
P1 9.00 us
PL1 -0.60 dB
SFO1 125.5327181 MHz
CHANNEL f2
CPDPRG[2 waltz16
NUC2 1H
PCPD2 80.00 us
PL2 -3.00 dB
PL12 12.80 dB
SFO2 499.1824959 MHz
F2 - Processing parameters
SI 65536
SF 125.5190233 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00
168.003
166.082
165.488
147.095
147.073
146.812
129.624
129.538
123.177
123.011
119.685
107.714
106.796
100.798
66.615
66.300
59.671
57.000
56.086
54.999
40.362
40.020
39.853
39.776
39.685
39.518
39.351
39.183
39.016
36.319
36.030
30.922
28.600
19.325
19.270
14.386
13.052
ppm

1H spectrum

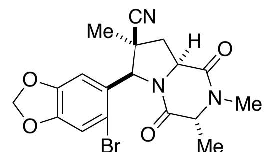
^{1}H NMR (500 MHz, $CDCl_3$)

8d

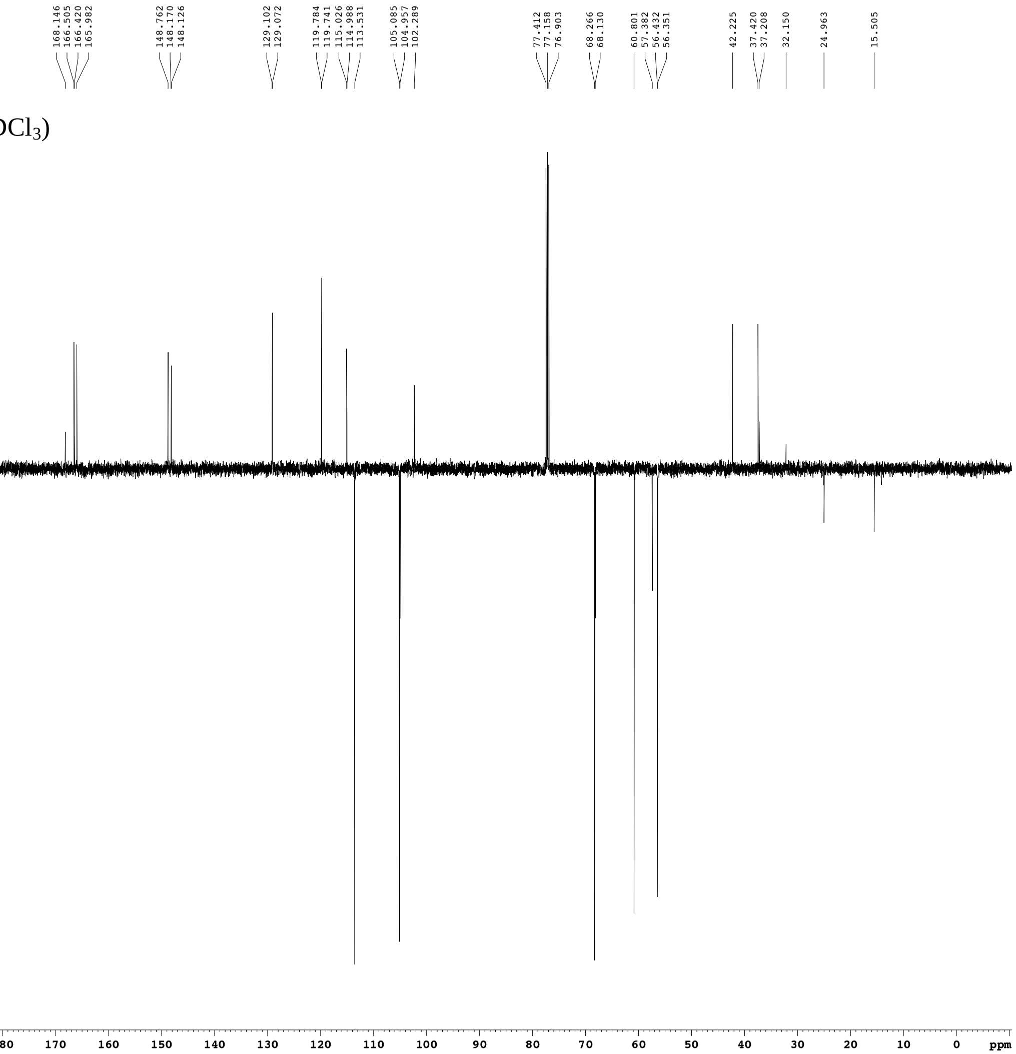


deptq 13C spectrum with 1H decoupling (CH & CH3 one way up; C, CH2 and solvent the other)

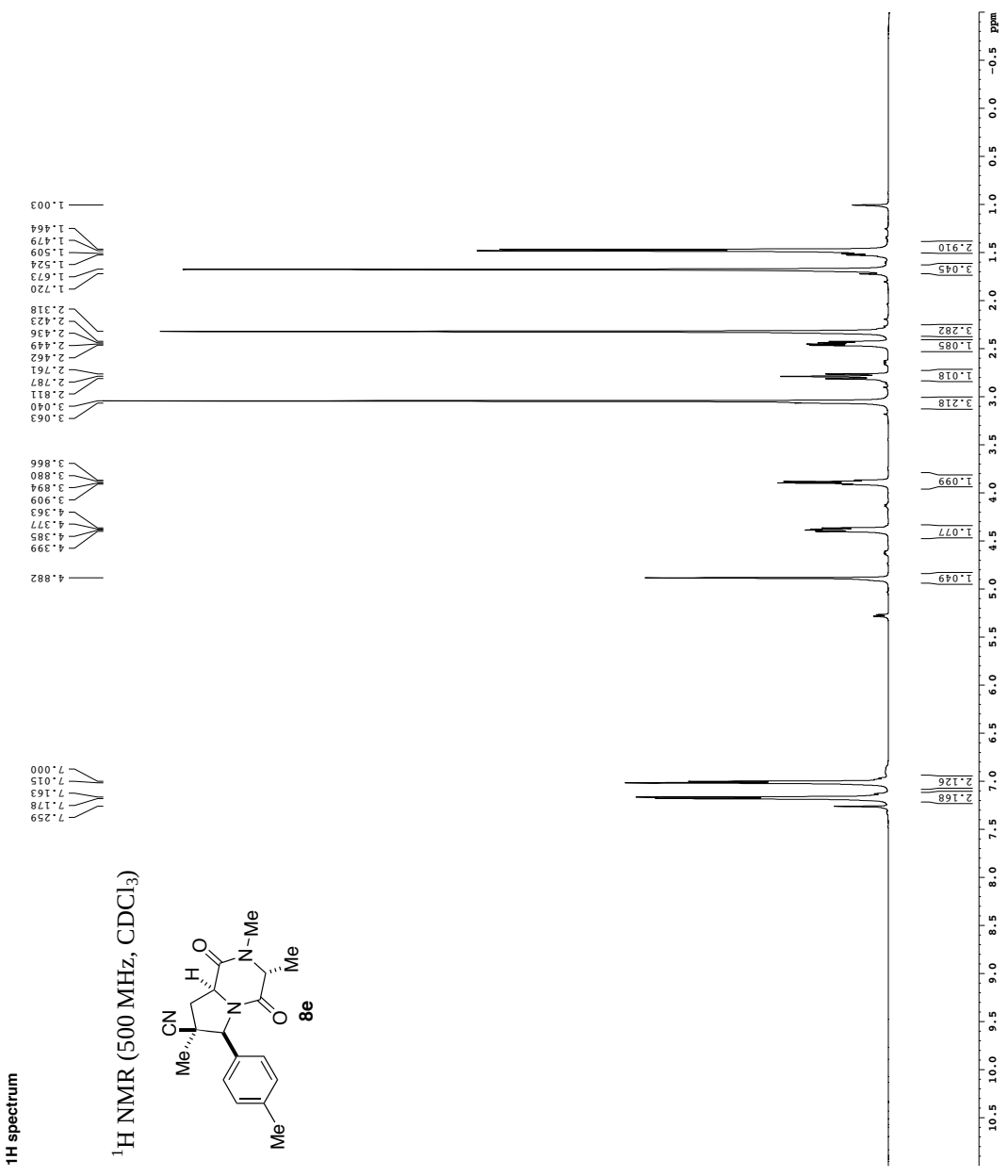
^{13}C NMR (125 MHz, $CDCl_3$)



8d

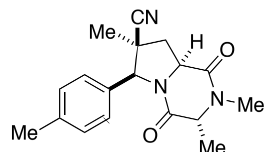



```
Current Data Parameters
NAME          MB2-59a
EXPNO               4
PROCNO              1

F2 - Acquisition Parameter
Date_        20120809
Time            10.47
INSTRUM       cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG      deptqgpsp
TD              65536
SOLVENT         CDCl3
NS                 50
DS                  0
SWH         30303.031 Hz
FIDRES       0.462388 Hz
AQ          1.0813440 sec
RG               2048
DW             16.500 us
DE               6.00 us
TE              298.0 K
CNST2     145.0000000
CNST12      1.5000000
D1         1.00000000 sec
d2         0.00344828 sec
d12        0.00002000 sec
D16        0.00020000 sec
DELTA      0.00001574 sec
DELTA1     0.00227878 sec
DELTA2     0.00226378 sec
DELTA3     0.00224828 sec
MCREST   0 sec
MCWRK      0.01500000 sec

======== CHANNEL f1 ======
NUC1              13C
P1              15.50 us
P12           2000.00 us
PL0            120.00 dB
PL1             -1.00 dB
SFO1      125.7942548 MHz
SP2              3.20 dB
SPNAM[2]   Crp60comp.4
SPOFF2   0 Hz

======== CHANNEL f2 ======
CPDPRG[2       waltz16
NUC2                1H
p0              11.25 us
P3               7.50 us
p4              15.00 us
PCPD2          100.00 us
PL2              1.60 dB
PL12            24.60 dB
SFO2      500.2225011 MHz

====== GRADIENT CHANNEL ==
GPNAM[1]      SINE.100
GPNAM[2]      SINE.100
GPNAM[3]      SINE.100
GPX1      0 %
GPX2      0 %
GPX3      0 %
GPY1      0 %
GPY2      0 %
GPY3      0 %
GPZ1            31.00 %
GPZ2            31.00 %
GPZ3            31.00 %
P16           1000.00 us

F2 - Processing parameters
SI              65536
SF        125.7804163 MHz
WDW                EM
SSB      0
LB               1.00 Hz
GB       0
PC               2.00
```

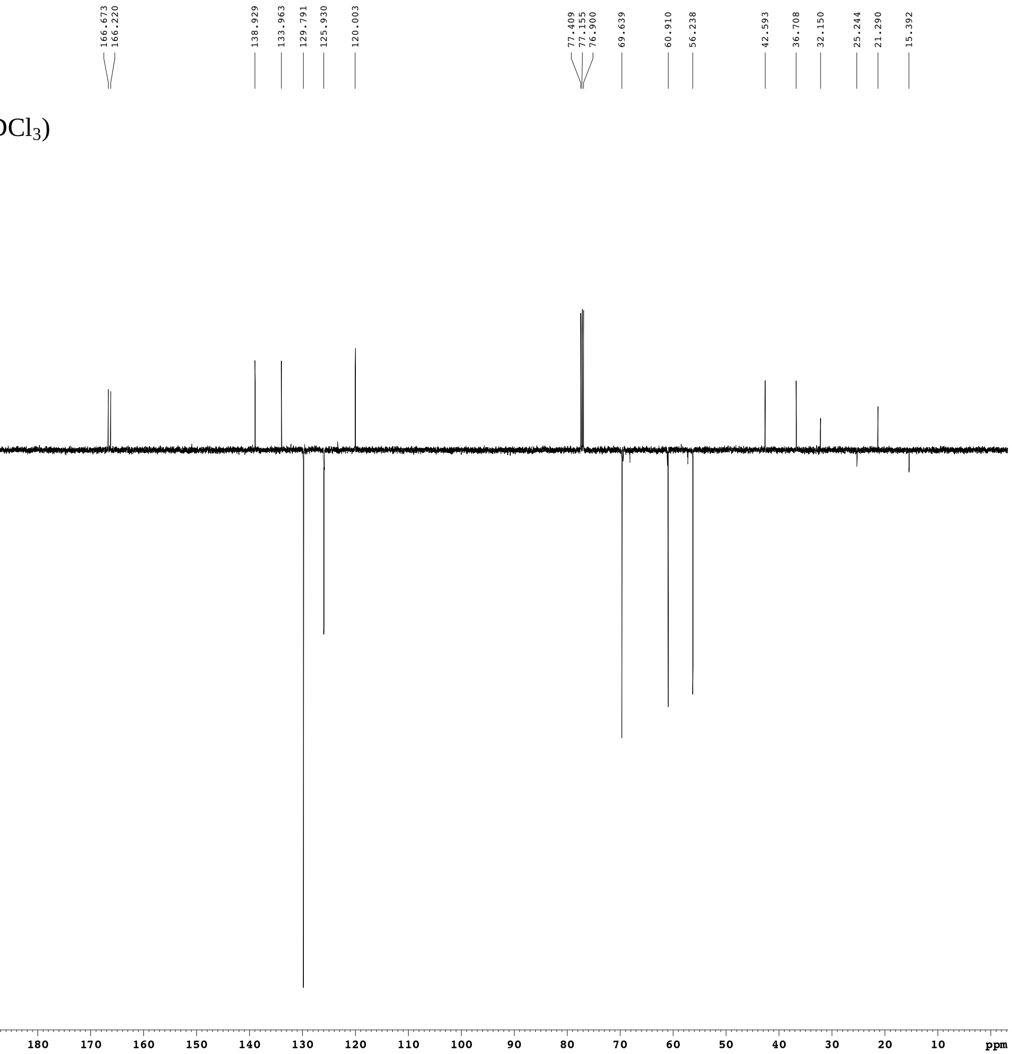

1H spectrum
^{1}H NMR (500 MHz, CDCl$_3$)
8e
Current Data Parameters
NAME MB2-240a
EXPNO 4
PROCNO 1
F2 - Acquisition Parameters
Date_ 20130123
Time_ 17.00
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 81728
SOLVENT CDCl3
NS 8
DS 0
SWH 8012.820 Hz
FIDRES 0.098043 Hz
AQ 5.0998273 sec
RG 8
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 7.50 usec
PL1 1.60 dB
SFO1 500.2235015 MHz
F2 - Processing parameters
SI 65536
SF 500.2200306 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00
7.259
7.178
7.163
7.015
7.000
4.882
4.399
4.385
4.377
4.363
3.909
3.894
3.880
3.866
3.063
3.040
2.811
2.787
2.761
2.462
2.449
2.436
2.423
2.318
1.720
1.673
1.524
1.509
1.479
1.464
1.003
2.168
2.126
1.049
1.077
1.099
3.218
1.018
1.085
3.282
2.910
3.045
ppm

deptq 13C spectrum with 1H decoupling (CH & CH3 one way up; C, CH2 and solvent the other)

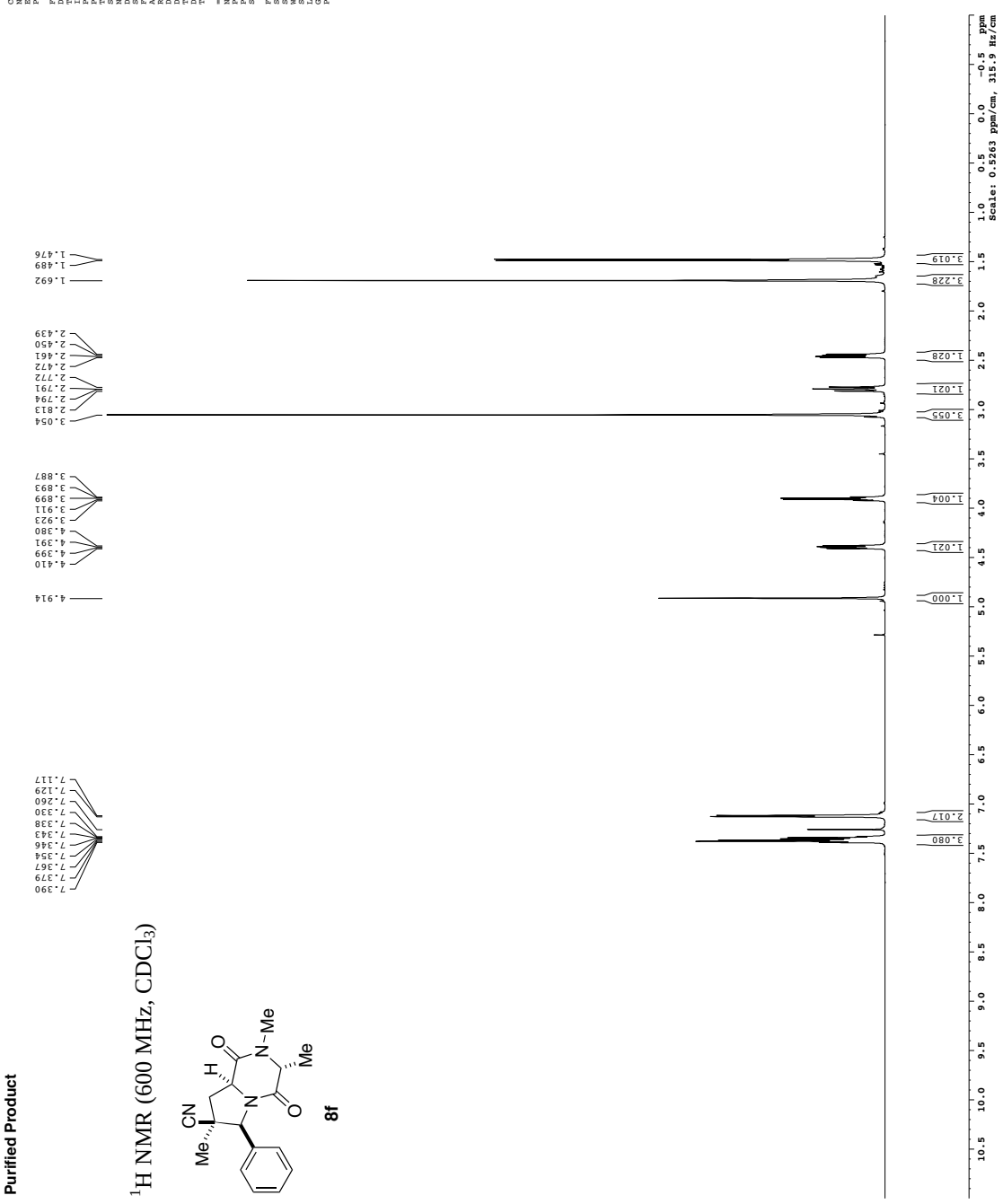
^{13}C NMR (125 MHz, $CDCl_3$)

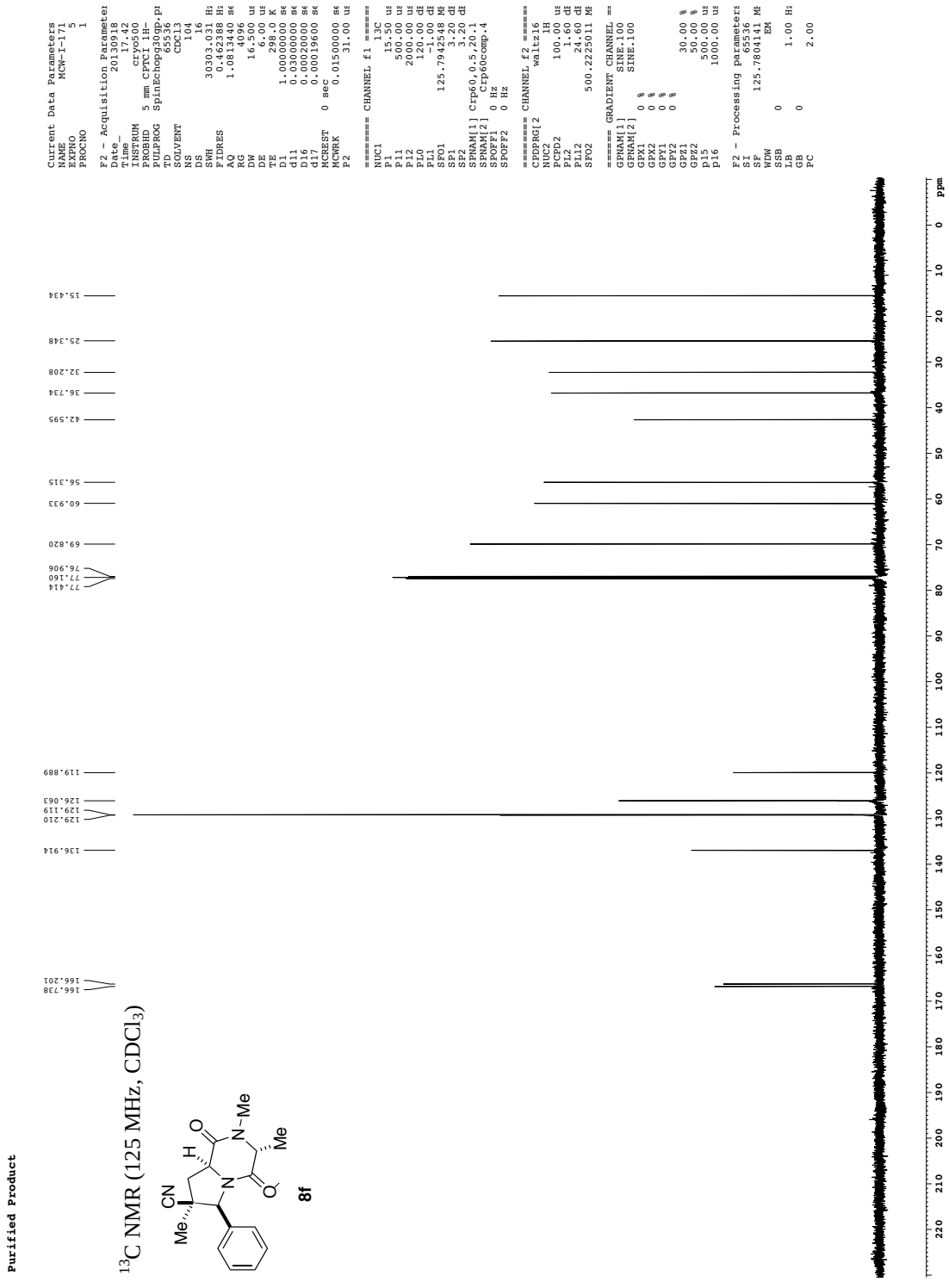


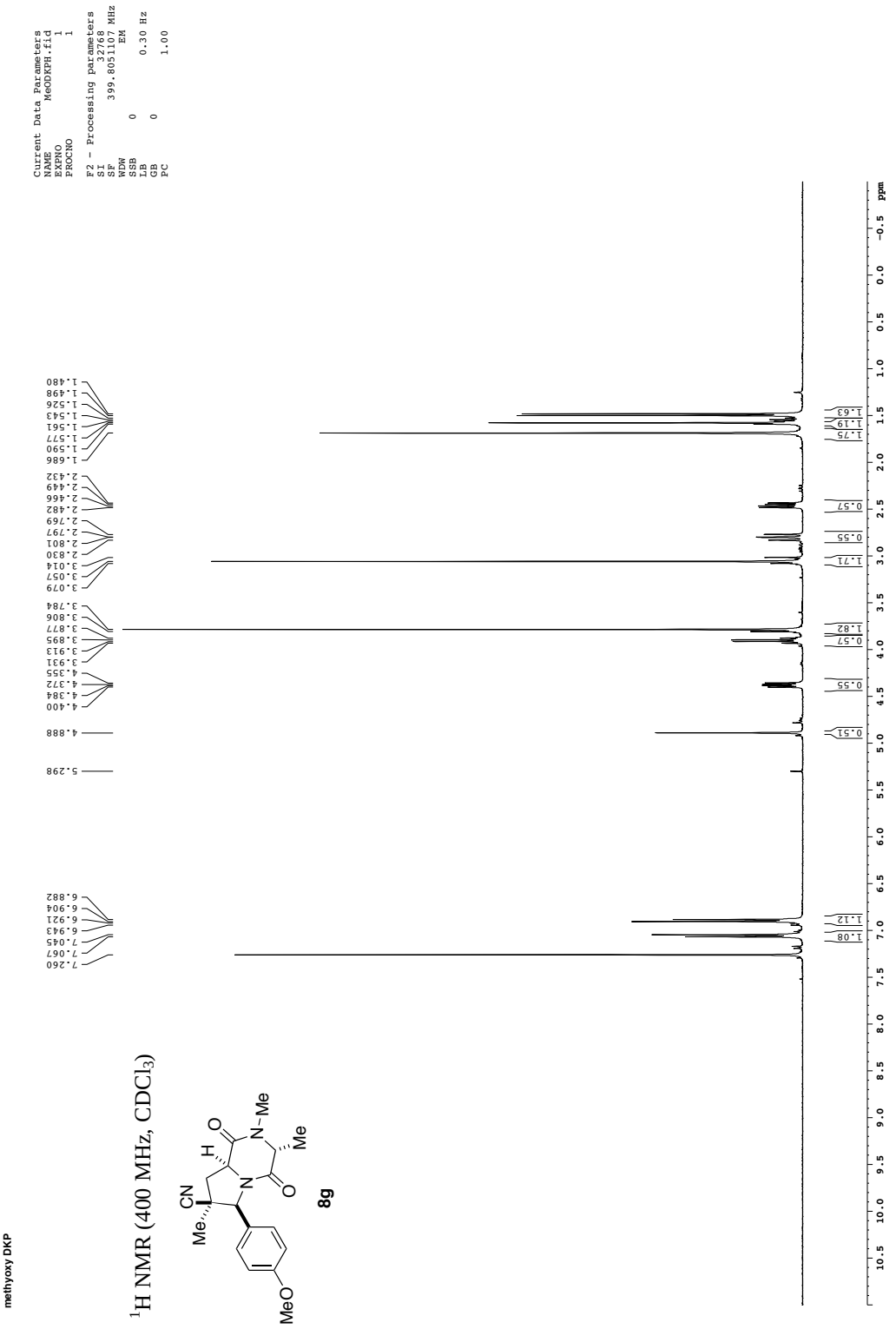
8e




```
Current Data Parameters
NAME            MB2-240a
EXPNO                  5
PROCNO                 1

F2 - Acquisition Parameter
Date_           20130123
Time               17.01
INSTRUM          cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG        deptqgpsp
TD                 65536
SOLVENT            CDCl3
NS                    64
DS                     0
SWH            30303.031 Hz
FIDRES          0.462388 Hz
AQ             1.0813440 se
RG                  2048
DW                16.500 us
DE                  6.00 us
TE                 298.0 K
CNST2        145.0000000
CNST12         1.5000000
D1            1.00000000 se
d2            0.00344828 se
d12           0.00002000 se
D16           0.00020000 se
DELTA         0.00001574 se
DELTA1        0.00227878 se
DELTA2        0.00226378 se
DELTA3        0.00224828 se
MCREST   0 sec
MCWRK         0.01500000 se

======== CHANNEL f1 ======
NUC1                 13C
P1                 15.50 us
P12              2000.00 us
PL0               120.00 dE
PL1                -1.00 dE
SFO1         125.7942548 MH
SP2                 3.20 dE
SPNAM[2]    Crp60comp.4
SPOFF2   0 Hz

======== CHANNEL f2 ======
CPDPRG[2         waltz16
NUC2                  1H
p0                 11.25 us
P3                  7.50 us
p4                 15.00 us
PCPD2             100.00 us
PL2                 1.60 dE
PL12               24.60 dE
SFO2         500.2225011 MH

====== GRADIENT CHANNEL ==
GPNAM[1]        SINE.100
GPNAM[2]        SINE.100
GPNAM[3]        SINE.100
GPX1     0 %
GPX2     0 %
GPX3     0 %
GPY1     0 %
GPY2     0 %
GPY3     0 %
GPZ1               31.00 %
GPZ2               31.00 %
GPZ3               31.00 %
P16              1000.00 us

F2 - Processing parameters
SI                 65536
SF           125.7804182 MH
WDW                   EM
SSB      0
LB                  1.00 Hz
GB       0
PC                  2.00
```

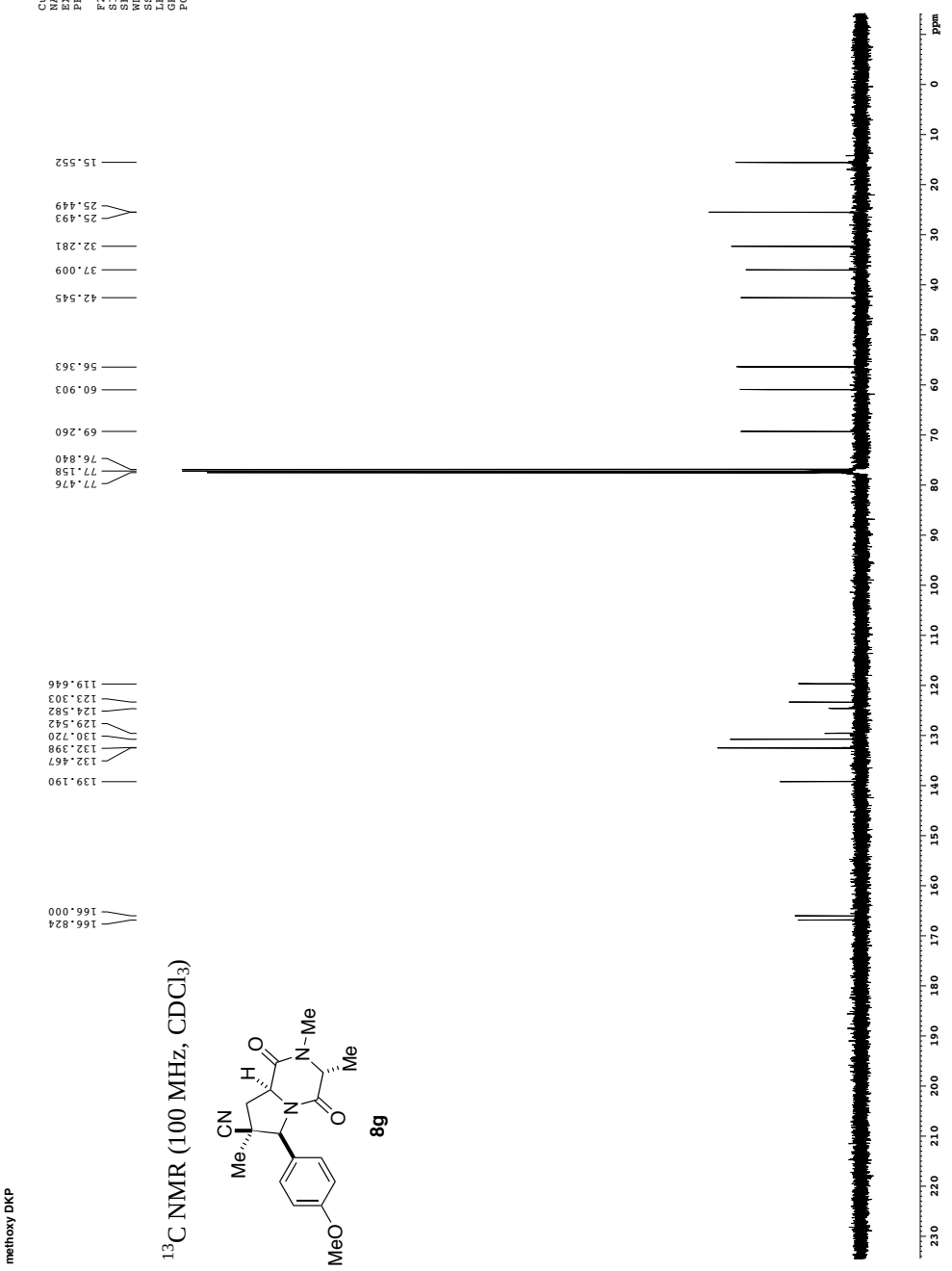

Purified Product
^{1}H NMR (600 MHz, CDCl$_3$)
8f
Current Data Parameters
NAME MCM-I-171
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20130918
Time 17.10
INSTRUM spect
PROBHD 5 mm TBI 1H/13
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 12
DS 0
SWH 9615.385 Hz
FIDRES 0.098042 Hz
AQ 5.099968 sec
RG 101
DW 52.000 usec
DE 14.44 usec
TE 296.2 K
D1 0.10000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 8.00 usec
PL1 W
SFO1 600.1342809 MHz
F2 - Processing parameters
SI 65536
SF 600.1300346 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB
PC 1.00
7.390
7.379
7.367
7.354
7.343
7.346
7.338
7.330
7.260
7.129
7.117
4.914
4.410
4.399
4.391
4.380
3.923
3.911
3.899
3.893
3.887
3.054
2.813
2.794
2.791
2.772
2.472
2.461
2.450
2.439
1.692
1.489
1.476
1.000
1.021
1.004
1.021
3.055
1.028
1.021
3.228
3.019
2.017
3.080
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
−0.5
ppm
Scale: 0.5263 ppm/cm, 315.9 Hz/cm


Purified Product
^{13}C NMR (125 MHz, CDCl$_3$)
8f
Current Data Parameters
NAME MCW-I-171
EXPNO 5
PROCNO 1
F2 - Acquisition Parameters
Date_ 20130918
Time 17.42
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zgpg30.pr
TD 65536
SOLVENT CDCl3
NS 104
DS 16
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0813440 sec
RG 4096
DW 16.500 usec
DE 6.00 usec
TE 298.0 K
D1 1.00000000 sec
d11 0.03000000 sec
D16 0.00020000 sec
MCREST 0.00019600 sec
MCWRK 0.01500000 sec
P2 31.00 usec
======== CHANNEL f1 ========
NUC1 13C
P1 15.50 usec
P11 500.00 usec
P12 2000.00 usec
PL0 120.00 dB
PL1 -1.00 dB
SFO1 125.7942548 MHz
SP1 3.20 dB
SPNAM[1] Crp60,0.5,20.1
SPNAM[2] Crp60comp.4
SPOFF1 0 Hz
SPOFF2 0 Hz
======== CHANNEL f2 ========
CPDPRG[2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 1.60 dB
PL12 24.60 dB
SFO2 500.2225011 MHz
====== GRADIENT CHANNEL ====
GPNAM[1] SINE.100
GPNAM[2] SINE.100
GPX1 0 %
GPX2 0 %
GPY1 0 %
GPY2 0 %
GPZ1 30.00 %
GPZ2 50.00 %
p15 500.00 usec
p16 1000.00 usec
F2 - Processing parameters
SI 65536
SF 125.7804141 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00
166.738
166.201
136.914
129.210
129.119
126.063
119.889
77.414
77.160
76.906
69.820
60.933
56.315
42.595
36.734
32.208
25.348
15.434
ppm



^{1}H NMR (400 MHz, $CDCl_3$)

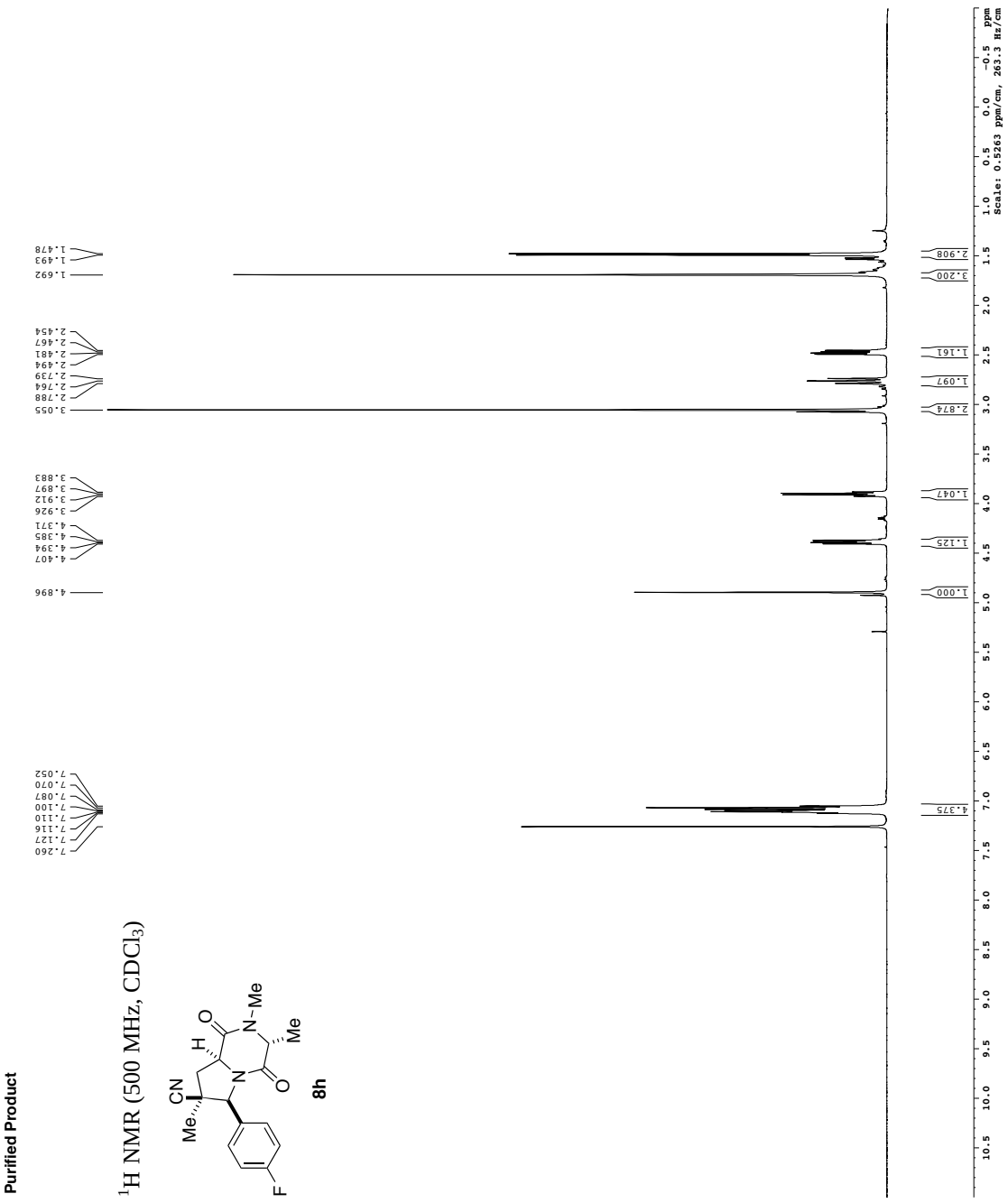
8g


methoxy DKP
Current Data Parameters
NAME MeODKPC.fid
EXPNO 1
PROCNO 1
F2 - Processing parameters
SI 65536
SF 100.5324918 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
15.552
25.449
25.493
32.281
37.009
42.545
56.363
60.903
69.260
76.840
77.158
77.476
119.646
123.303
124.582
129.542
130.720
132.398
132.467
139.190
166.000
166.824
ppm
^{13}C NMR (100 MHz, CDCl$_3$)
8g

Purified Product

^{1}H NMR (500 MHz, $CDCl_3$)

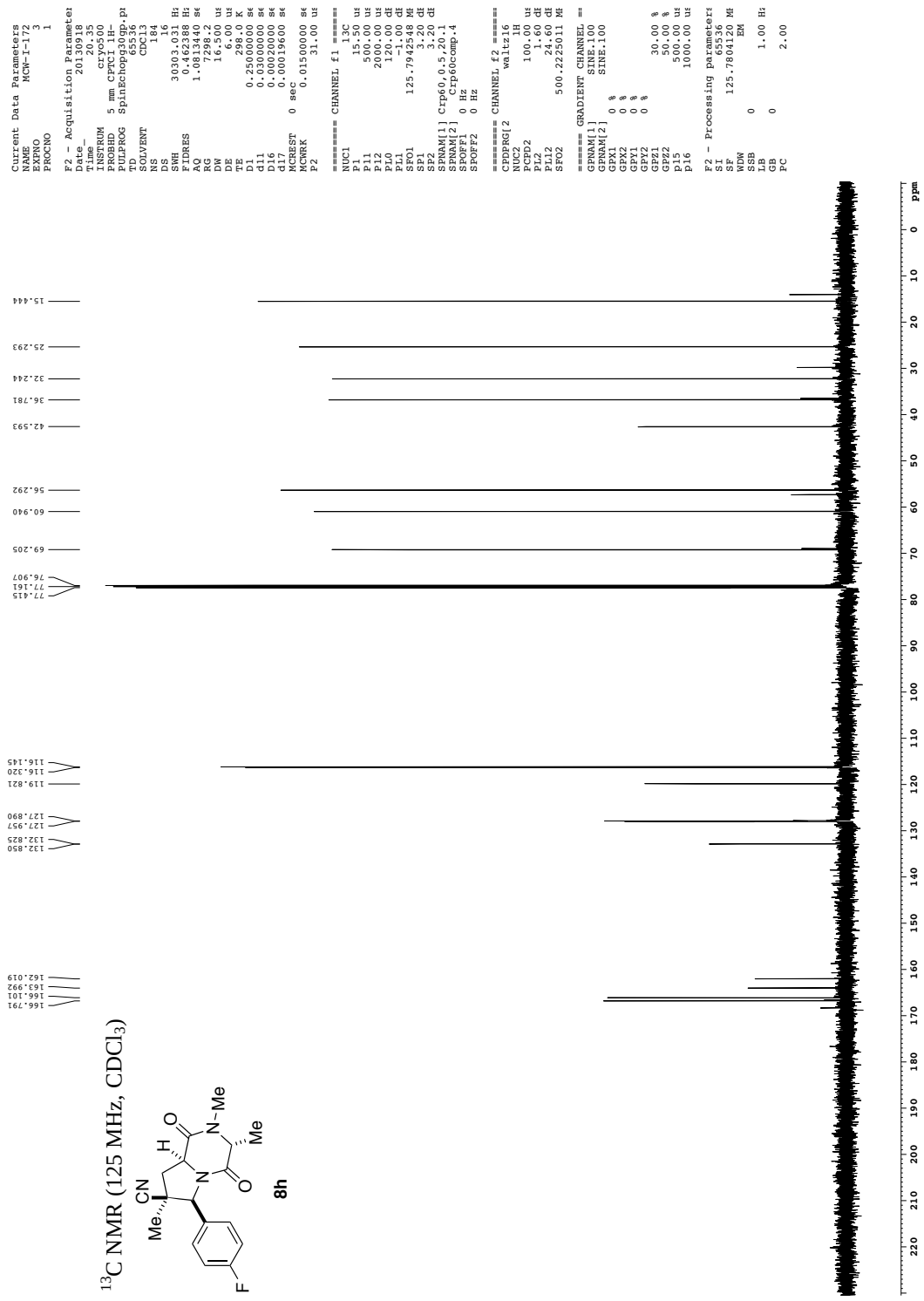
8h

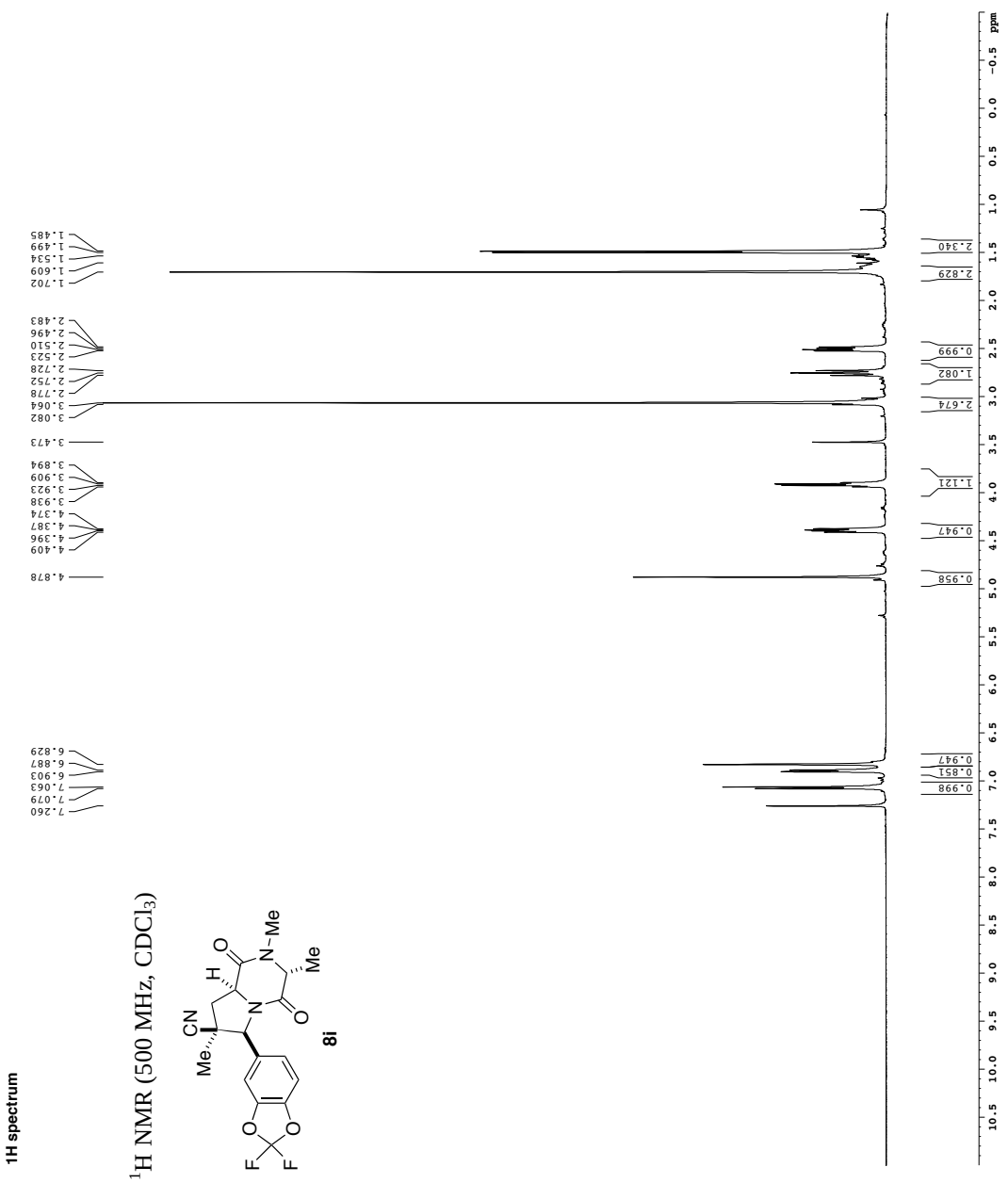


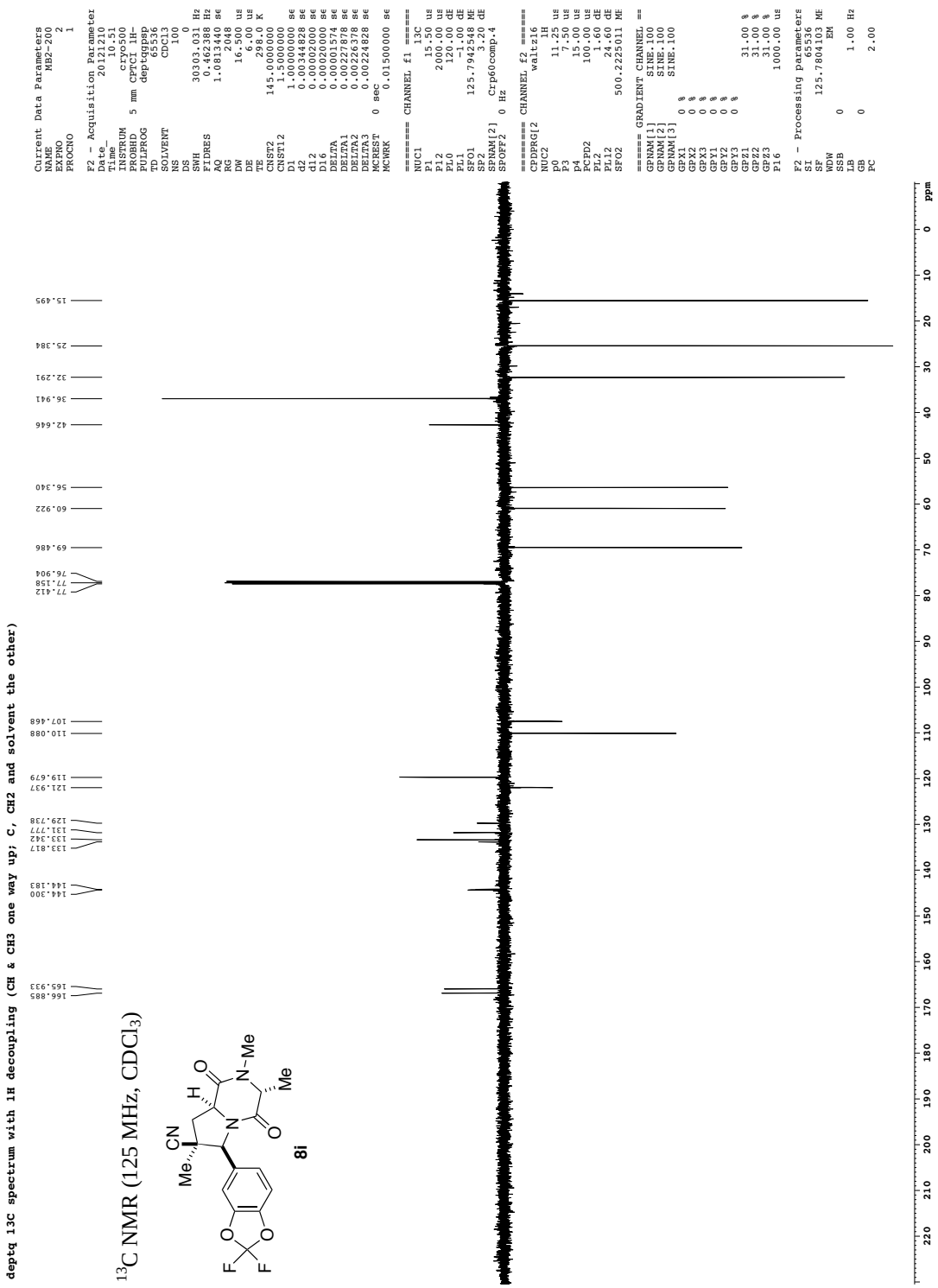
Purified Product

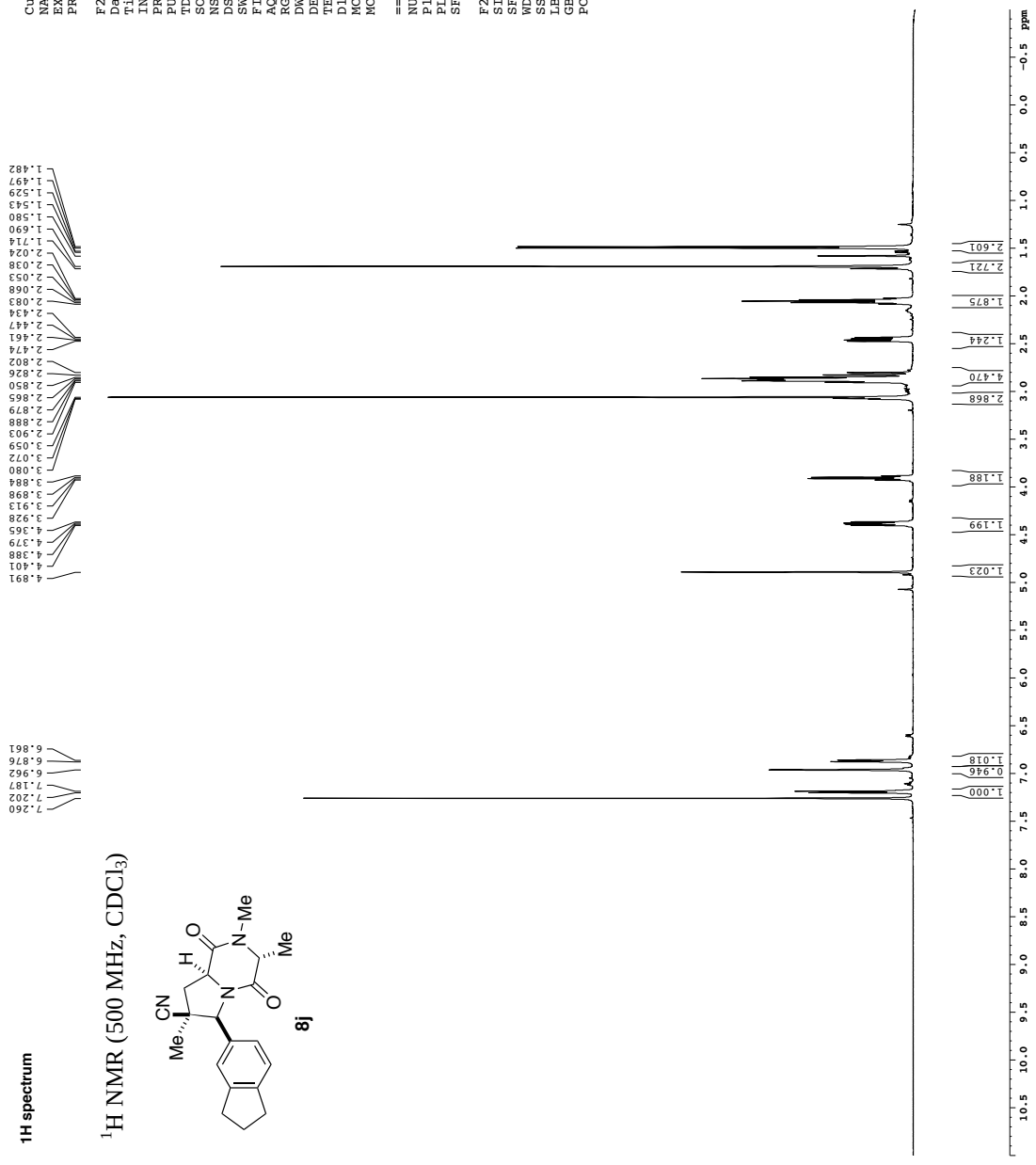
^{13}C NMR (125 MHz, $CDCl_3$)

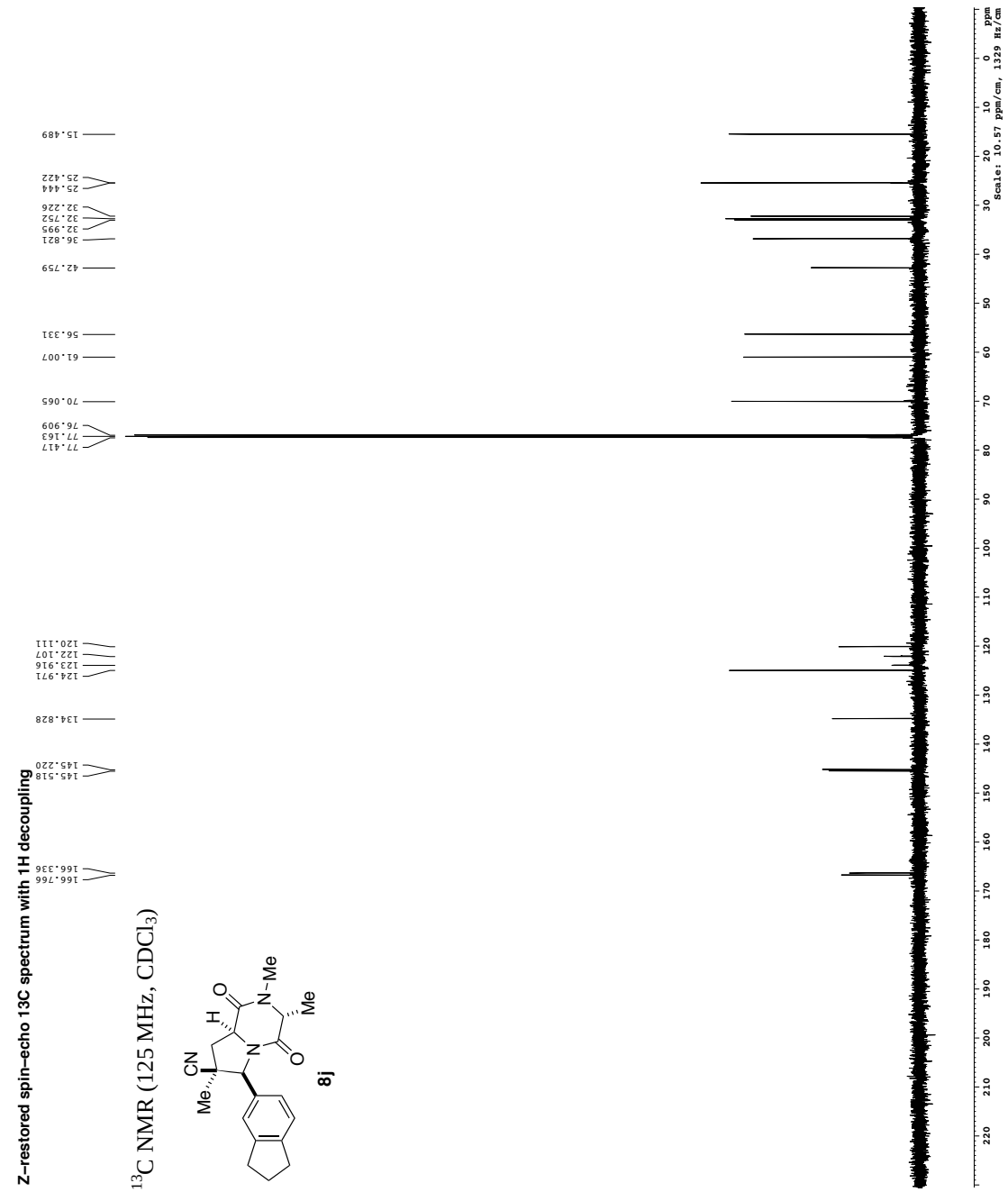
8h

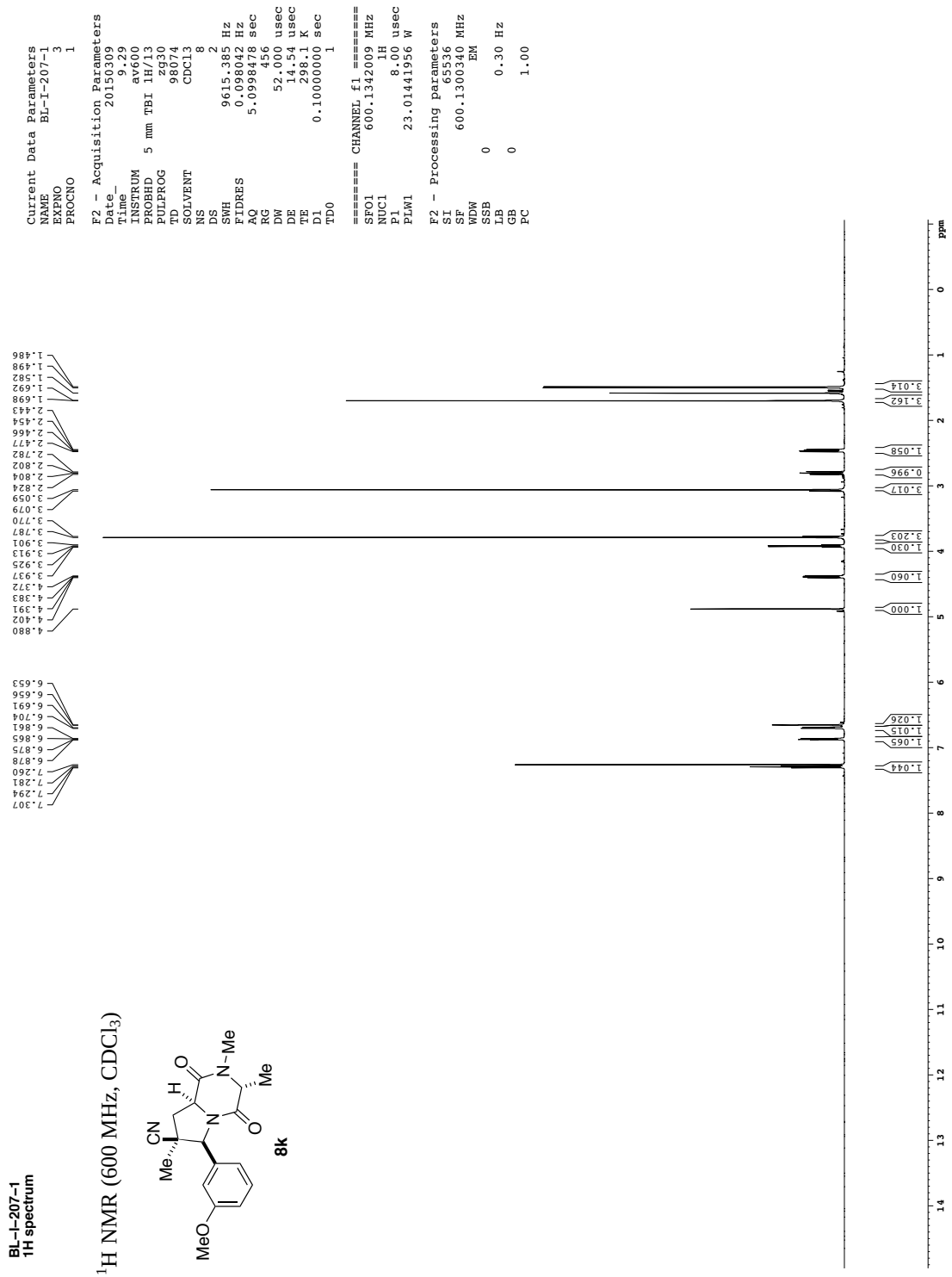



1H spectrum
^{1}H NMR (500 MHz, CDCl$_3$)
8i
Current Data Parameters
NAME MB2-200
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20121210
Time_ 10.49
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 81728
SOLVENT CDCl3
NS 8
DS 2
SWH 8012.820 Hz
FIDRES 0.098043 Hz
AQ 5.0998273 sec
RG 5
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 7.50 usec
PL1 1.60 dB
SFO1 500.2235015 MHz
F2 - Processing parameters
SI 65536
SF 500.2200317 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00
7.260
7.079
7.063
6.903
6.887
6.829
4.878
4.409
4.396
4.387
4.374
3.938
3.923
3.909
3.894
3.473
3.082
3.064
2.778
2.752
2.728
2.523
2.510
2.496
2.483
1.702
1.609
1.534
1.499
1.485
0.998
0.851
0.947
0.958
1.121
2.674
1.082
0.999
2.829
2.340
ppm


deptq 13C spectrum with 1H decoupling (CH & CH3 one way up; C, CH2 and solvent the other)
13C NMR (125 MHz, CDCl3)
8i
Current Data Parameters
NAME MB2-200
EXPNO 2
PROCNO 1
F2 - Acquisition Parameter
Date_ 20121210
Time 10.51
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG deptqgpsp
TD 65536
SOLVENT CDCl3
NS 100
DS 0
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0813440 sec
RG 2048
DW 16.500 usec
DE 6.00 usec
TE 298.0 K
CNST2 145.0000000
CNST12 1.5000000
D1 1.00000000 sec
d2 0.00344828 sec
d12 0.00020000 sec
d16 0.00020000 sec
DELTA 0.00001574 sec
DELTA1 0.00227878 sec
DELTA2 0.00226378 sec
DELTA3 0.00224828 sec
MCREST 0 sec 0.01500000 sec
MCWRK
======== CHANNEL f1 ======
NUC1 13C
P1 15.50 usec
P12 2000.00 usec
PL0 120.00 dB
PL1 -1.00 dB
SFO1 125.7942548 MHz
SP1 120.00 dB
SPNAM[2] Crp60comp.4
SPOFF2 0 Hz
======== CHANNEL f2 ======
CPDPRG[2 waltz16
NUC2 1H
P0 11.25 usec
P3 7.50 usec
P4 15.00 usec
PCPD2 100.00 usec
PL2 1.60 dB
PL12 24.60 dB
SFO2 500.2225011 MHz
====== GRADIENT CHANNEL ==
GPNAM[1] SINE.100
GPNAM[2] SINE.100
GPNAM[3] SINE.100
GPX1 0 %
GPX2 0 %
GPX3 0 %
GPY1 0 %
GPY2 0 %
GPY3 0 %
GPZ1 31.00 %
GPZ2 31.00 %
GPZ3 31.00 %
P16 1000.00 usec
F2 - Processing parameters
SI 65536
SF 125.7804103 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00
15.495
25.384
32.291
36.941
42.646
56.340
60.922
69.486
76.904
77.158
77.412
107.468
110.088
119.679
121.937
129.738
131.777
133.342
133.817
144.183
144.300
165.933
166.885
ppm


1H spectrum
^{1}H NMR (500 MHz, CDCl$_3$)
8j
Current Data Parameters
NAME APD-II-158-1
EXPNO 10
PROCNO 1
F2 - Acquisition Parameters
Date_ 20130812
Time_ 20.31
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 81728
SOLVENT CDCl3
NS 8
DS 2
SWH 8012.820 Hz
FIDRES 0.098043 Hz
AQ 5.0998273 sec
RG 11.3
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0 sec 0.01500000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 7.50 usec
PL1 1.60 dB
SFO1 500.2235015 MHz
F2 - Processing parameters
SI 65536
SF 500.2200314 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00
7.260
7.202
7.187
6.962
6.876
6.861
4.891
4.401
4.388
4.379
4.365
3.928
3.913
3.898
3.884
3.080
3.072
3.059
2.903
2.888
2.879
2.865
2.850
2.826
2.802
2.474
2.461
2.447
2.434
2.083
2.068
2.053
2.038
2.024
1.714
1.690
1.580
1.543
1.529
1.497
1.482
1.000
0.946
1.018
1.023
1.199
1.188
2.868
4.470
1.244
1.875
2.721
2.601
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5 ppm


Z–restored spin–echo 13C spectrum with 1H decoupling
^{13}C NMR (125 MHz, CDCl$_3$)
8j
Scale: 10.57 ppm/cm, 1329 Hz/cm

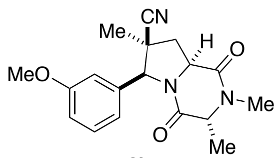


^{1}H NMR (600 MHz, $CDCl_3$)

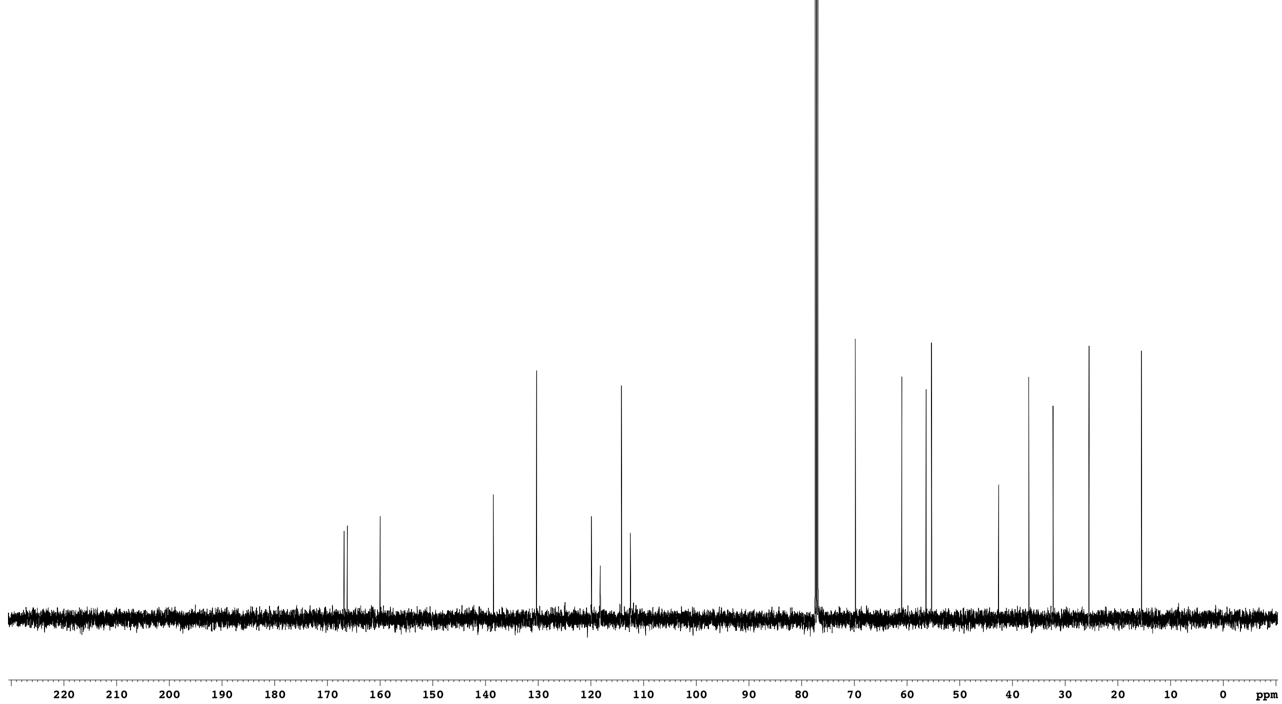
8k

Z-restored spin-echo 13C spectrum with 1H decoupling

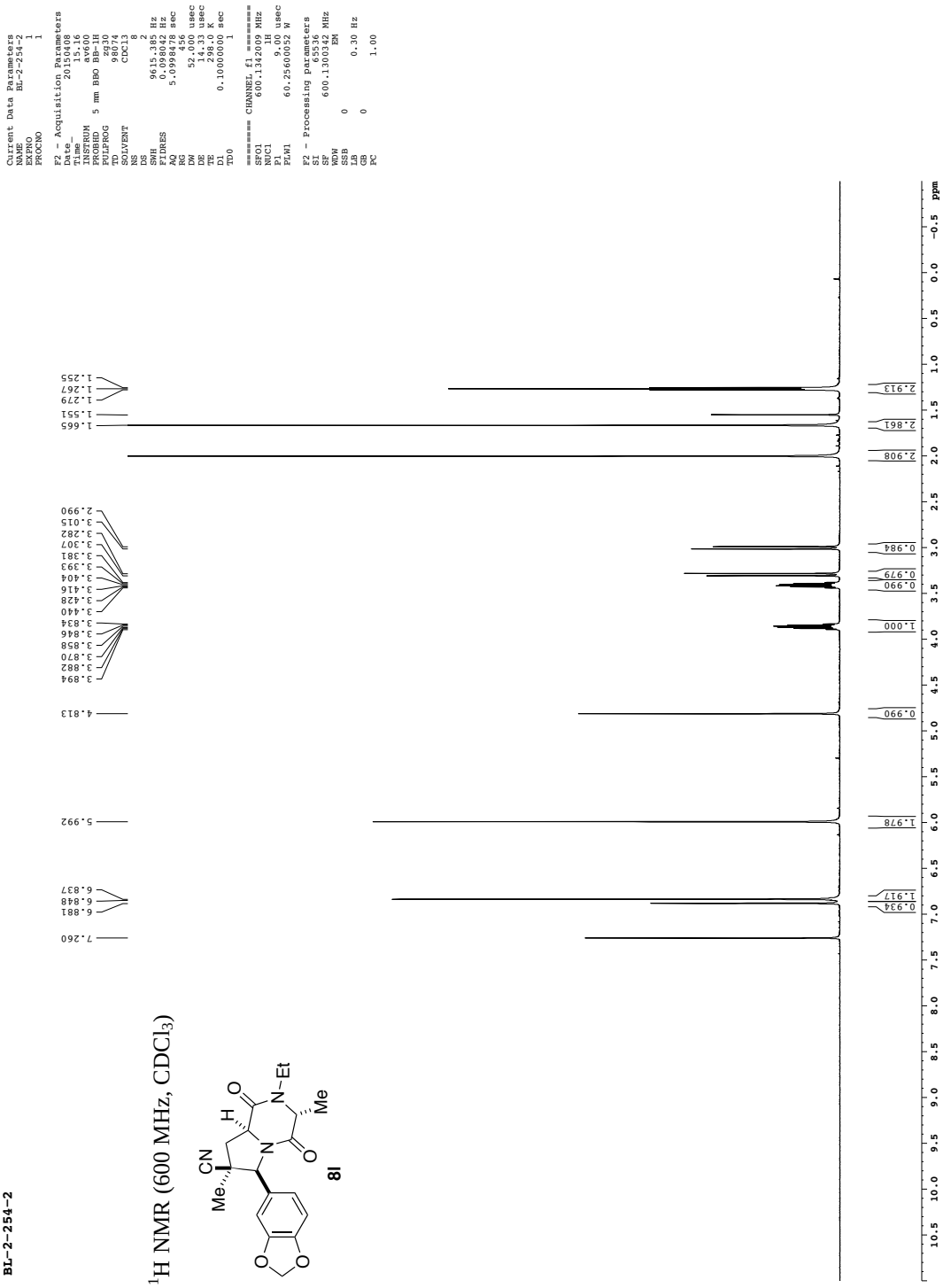
^{13}C NMR (125 MHz, $CDCl_3$)



8k

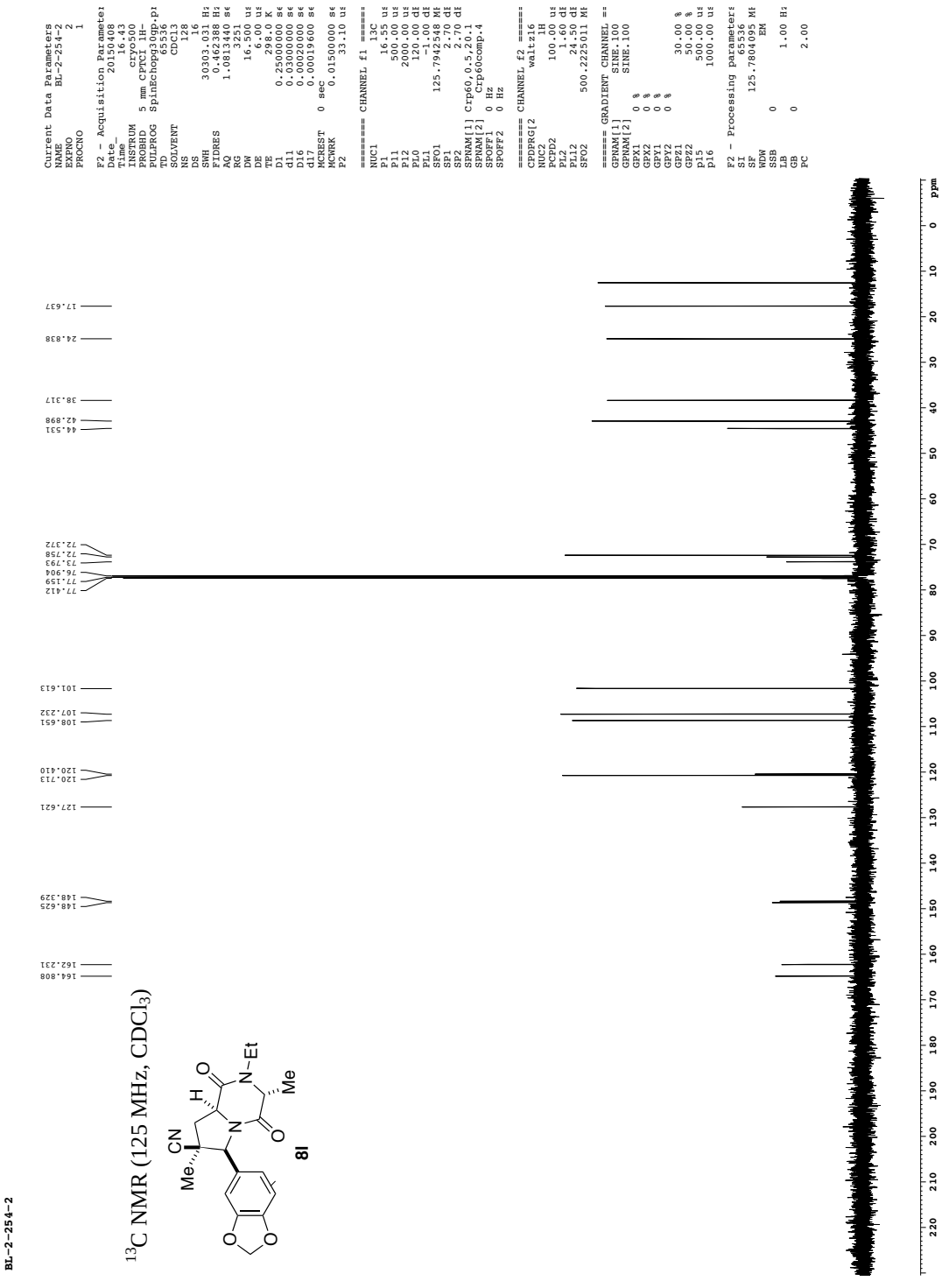


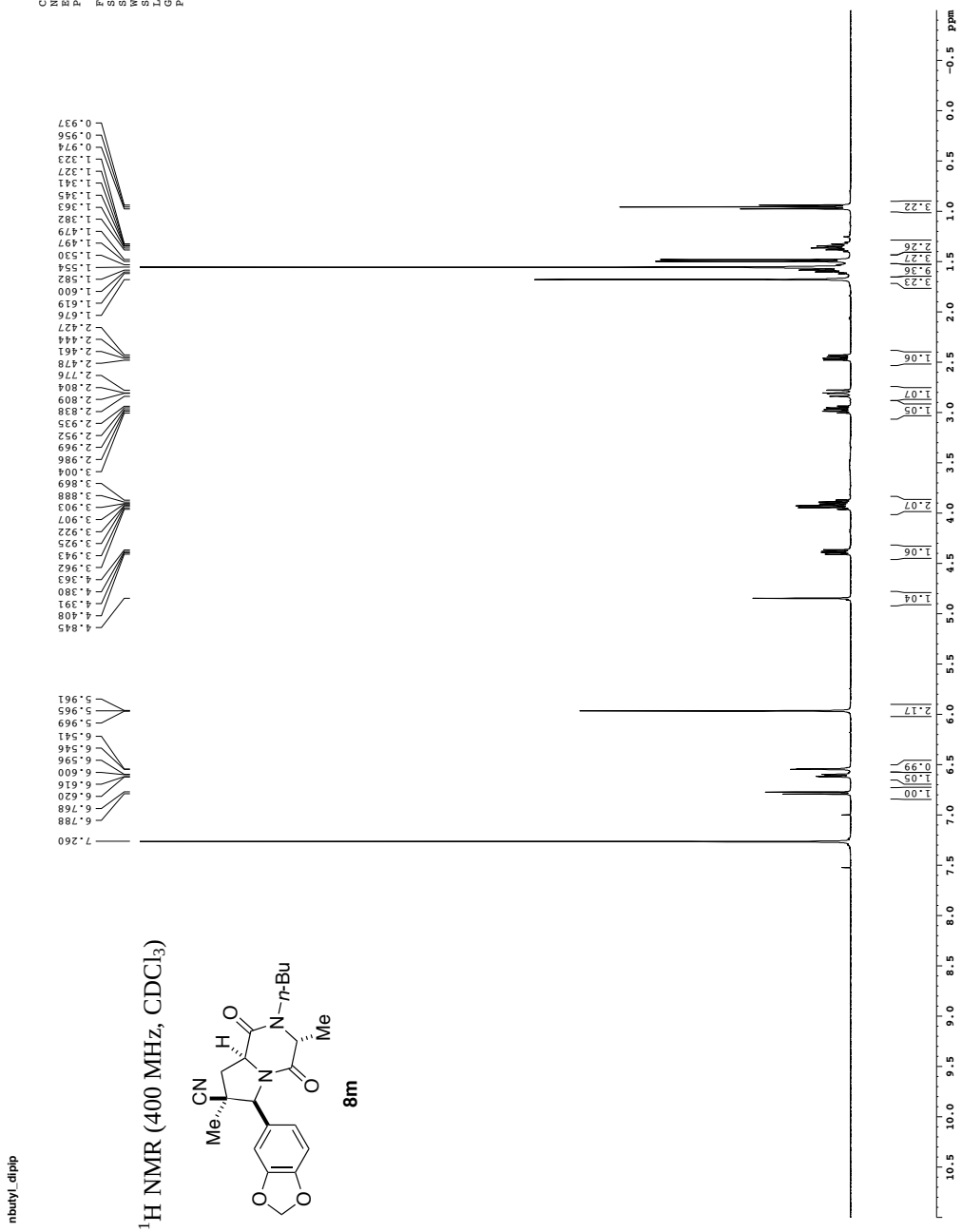

```
Current Data Parameters
NAME          BL-I-207-1
EXPNO                 10
PROCNO                 1

F2 - Acquisition Parameter
Date_           20150309
Time               14.01
INSTRUM          cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.pr
TD                 65536
SOLVENT            CDCl3
NS                   304
DS                    16
SWH            30303.031 Hz
FIDRES          0.462388 Hz
AQ             1.0813440 se
RG                4597.6
DW                16.500 us
DE                  6.00 us
TE                 298.0 K
D1            0.25000000 se
d11           0.03000000 se
D16           0.00020000 se
d17           0.00019600 se
MCREST   0 sec
MCWRK         0.01500000 se
P2                 33.10 us

======== CHANNEL f1 ======
NUC1                 13C
P1                 16.55 us
P11               500.00 us
P12              2000.00 us
PL0               120.00 dB
PL1                -1.00 dB
SFO1         125.7942548 MH
SP1                 2.70 dB
SP2                 2.70 dB
SPNAM[1] Crp60,0.5,20.1
SPNAM[2]    Crp60comp.4
SPOFF1   0 Hz
SPOFF2   0 Hz

======== CHANNEL f2 ======
CPDPRG[2         waltz16
NUC2                  1H
PCPD2             100.00 us
PL2                 1.60 dB
PL12               24.50 dB
SFO2         500.2225011 MH

====== GRADIENT CHANNEL ==
GPNAM[1]        SINE.100
GPNAM[2]        SINE.100
GPX1      0 %
GPX2      0 %
GPY1      0 %
GPY2      0 %
GPZ1               30.00 %
GPZ2               50.00 %
p15               500.00 us
p16              1000.00 us

F2 - Processing parameters
SI                 65536
SF           125.7804092 MH
WDW                   EM
SSB       0
LB                  1.00 Hz
GB        0
PC                  2.00
```

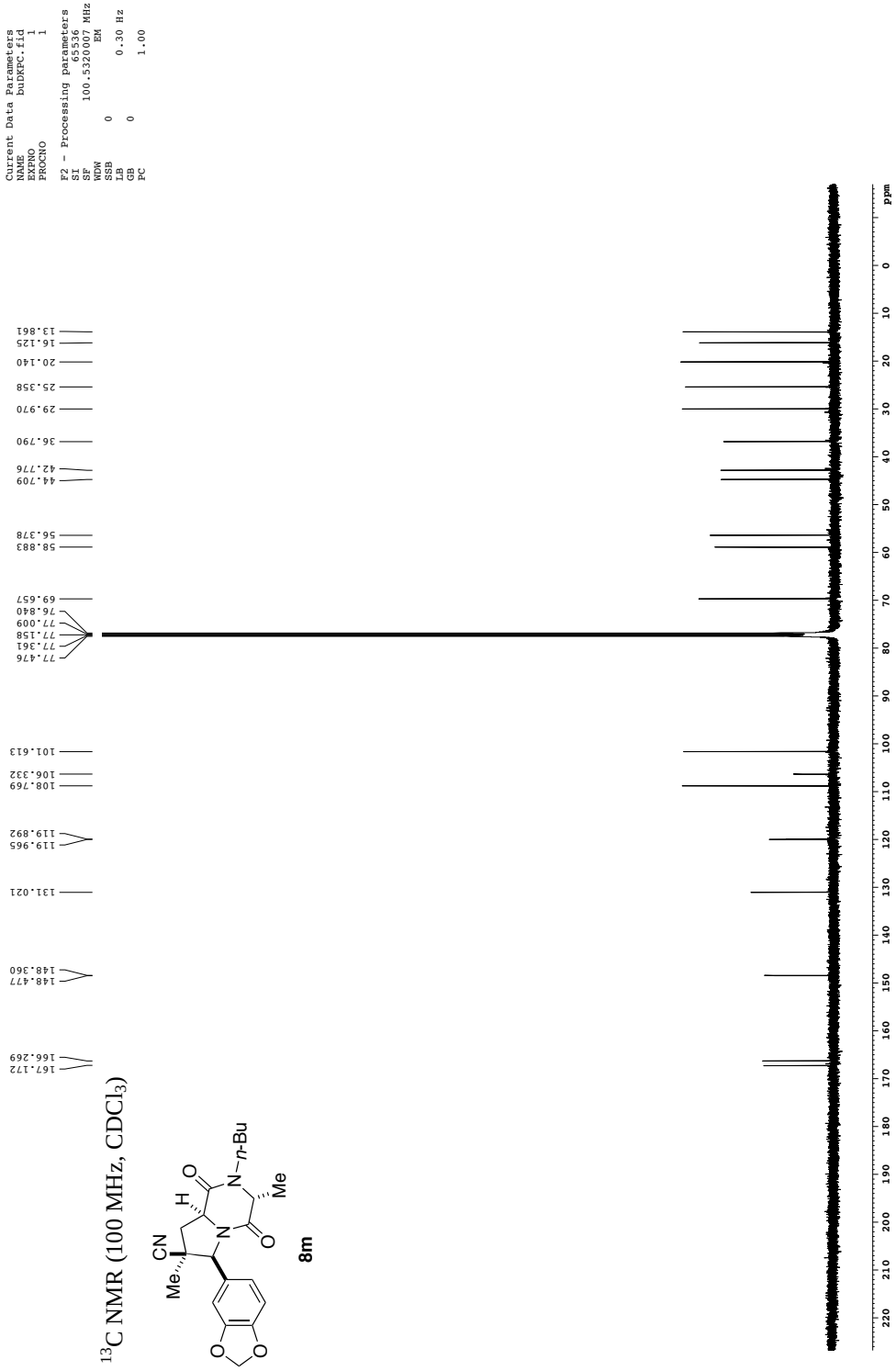


^{1}H NMR (600 MHz, $CDCl_3$)

8l

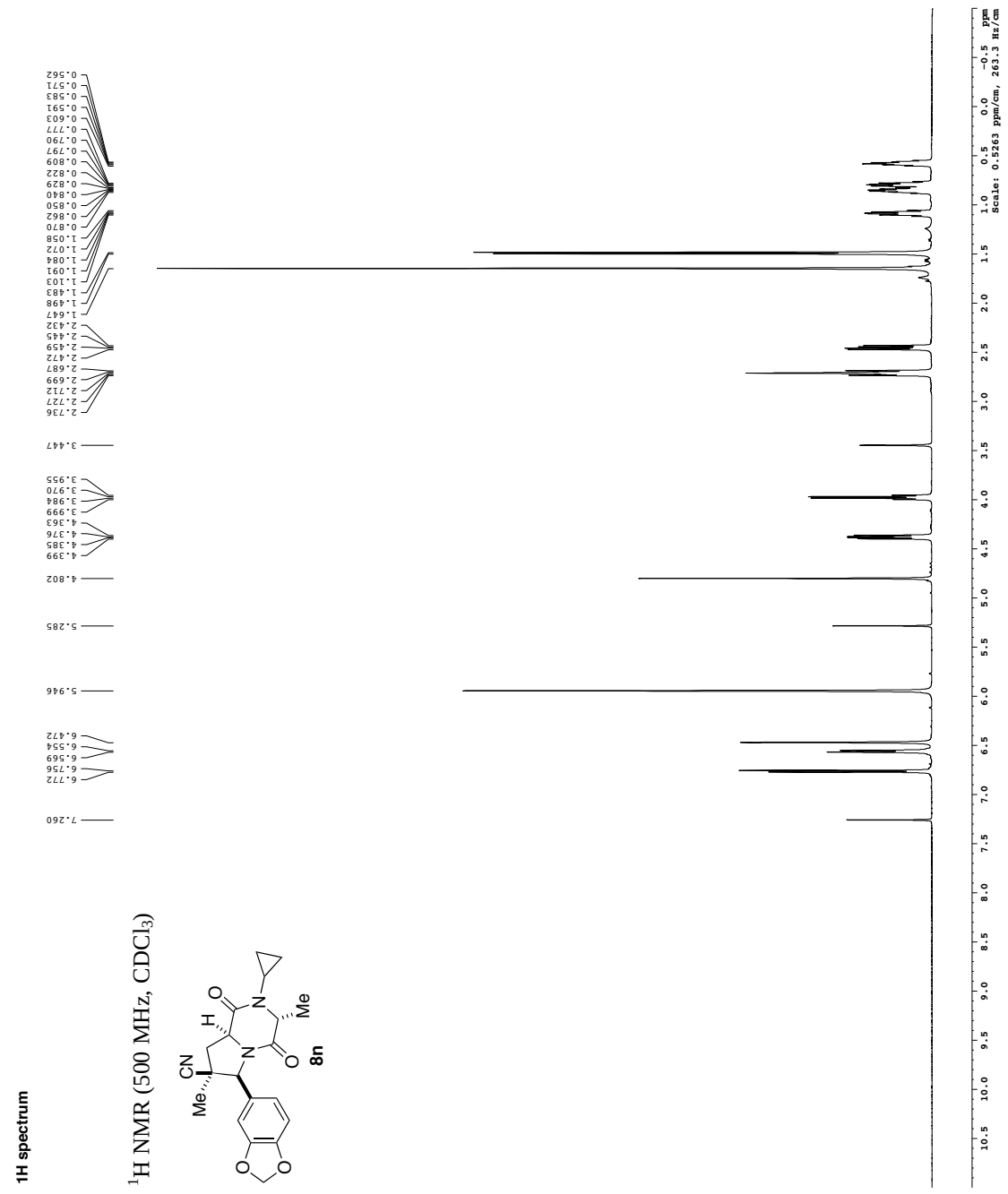

BL-2-254-2
^{13}C NMR (125 MHz, CDCl$_3$)
8l
Current Data Parameters
NAME BL-2-254-2
EXPNO 2
PROCNO 1
CHANNEL f1
NUC1 13C
CHANNEL f2
NUC2 1H
SINE.100
ppm

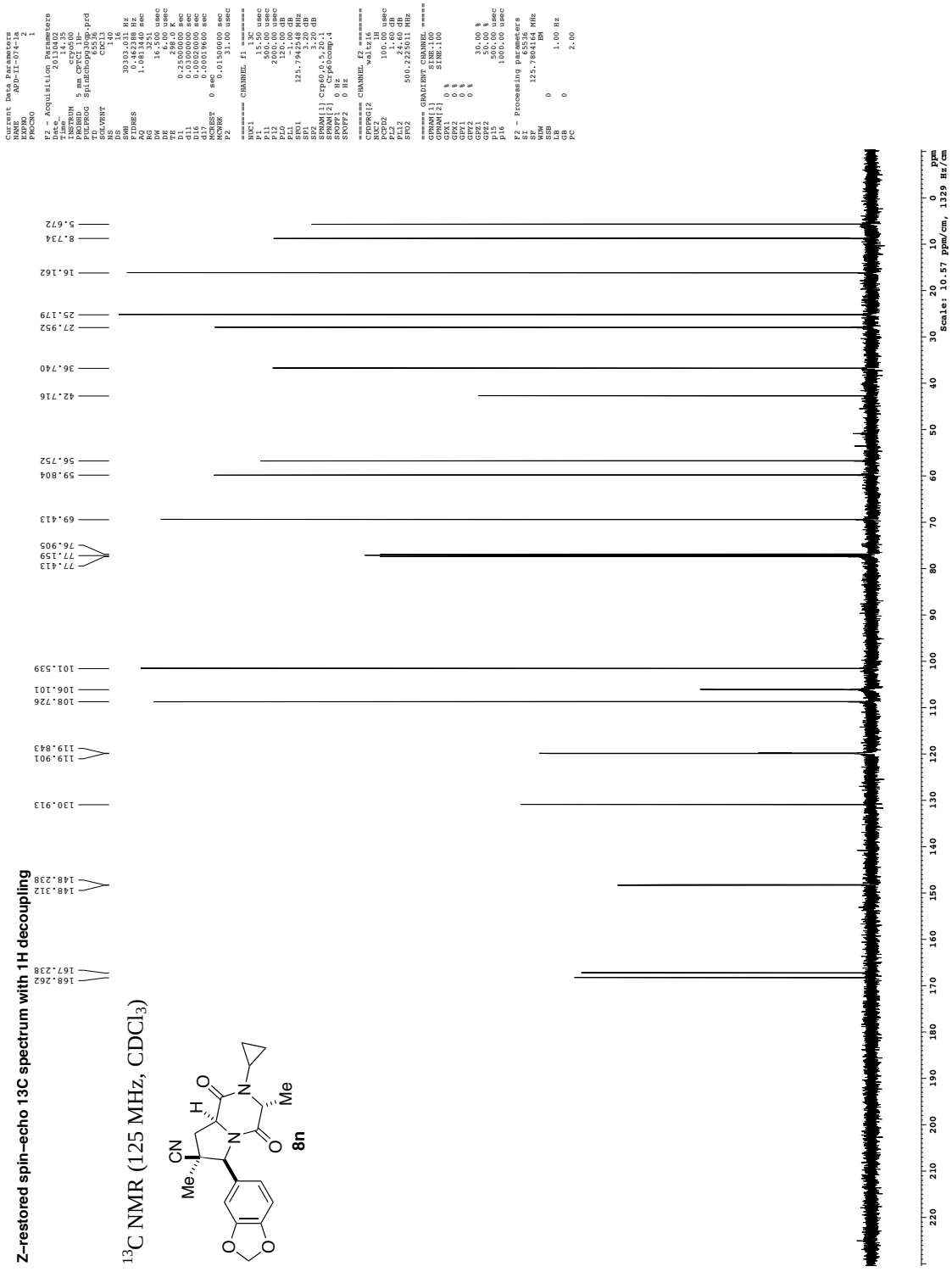

nbutyl_dipip
Current Data Parameters
NAME JX-buDKP
EXPNO 1
PROCNO 1
F2 - Processing parameters
SI 27648
SF 399.8051109 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
^{1}H NMR (400 MHz, CDCl$_3$)
8m

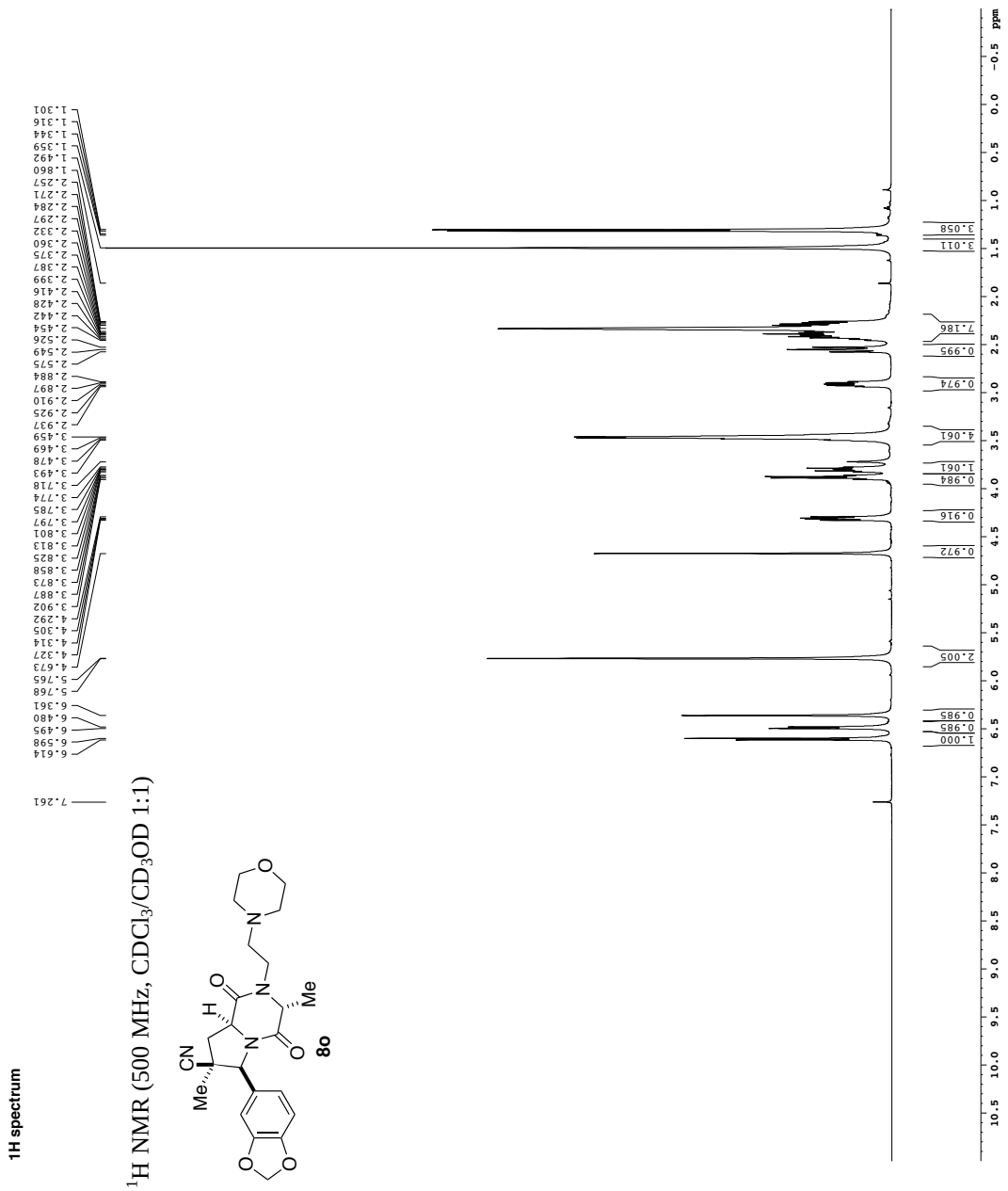


^{13}C NMR (100 MHz, $CDCl_3$)

8m


1H spectrum
^{1}H NMR (500 MHz, CDCl$_3$)
8n
Me
CN
Me
H
O
N
N
O
O
O
O
Current Data Parameters
NAME APD-II-074-1a
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20150402
Time 14.32
INSTRUM spect
PROBHD 5 mm CPCI 1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 8
DS 2
SWH 8012.820 Hz
FIDRES 0.098043 Hz
AQ 5.0998273 sec
RG 64
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 7.50 usec
PL1 1.60 dB
SFO1 500.2235015 MHz
F2 - Processing parameters
SI 65536
SF 500.2200311 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00
7.260
6.772
6.756
6.569
6.554
6.472
5.946
5.285
4.802
4.399
4.385
4.376
4.363
3.999
3.984
3.970
3.955
3.447
2.736
2.727
2.712
2.699
2.687
2.472
2.459
2.445
2.432
1.647
1.498
1.483
1.103
1.091
1.084
1.072
1.058
0.870
0.862
0.850
0.840
0.822
0.809
0.797
0.790
0.777
0.603
0.591
0.583
0.571
0.562
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
−0.5
ppm
Scale: 0.5263 ppm/cm, 263.3 Hz/cm


Z–restored spin–echo 13C spectrum with 1H decoupling
13C NMR (125 MHz, CDCl3)
8n
Me
CN
Me
H
O
N
N
O
O
O
O
168.262
167.238
148.312
148.238
130.913
119.901
119.843
108.726
106.101
101.539
76.905
77.159
77.413
69.413
59.804
56.752
42.716
36.740
27.952
25.179
16.162
8.734
5.672
Scale: 10.57 ppm/cm, 1329 Hz/cm
ppm

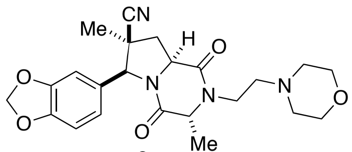


^{1}H NMR (500 MHz, $CDCl_3$/CD_3OD 1:1)

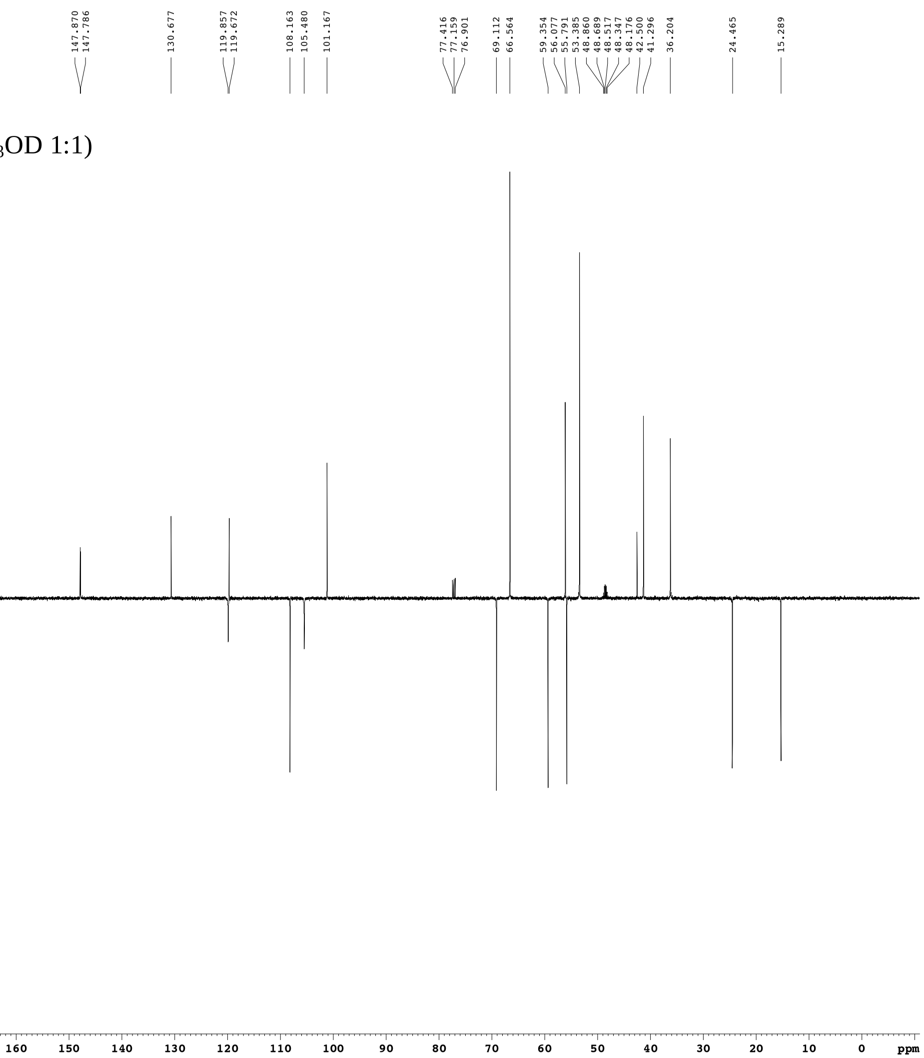
8o

DEPTQ: 13C spectrum with 1H decoupling (CH & CH3 one way up; C, CH2 and solvent the other)

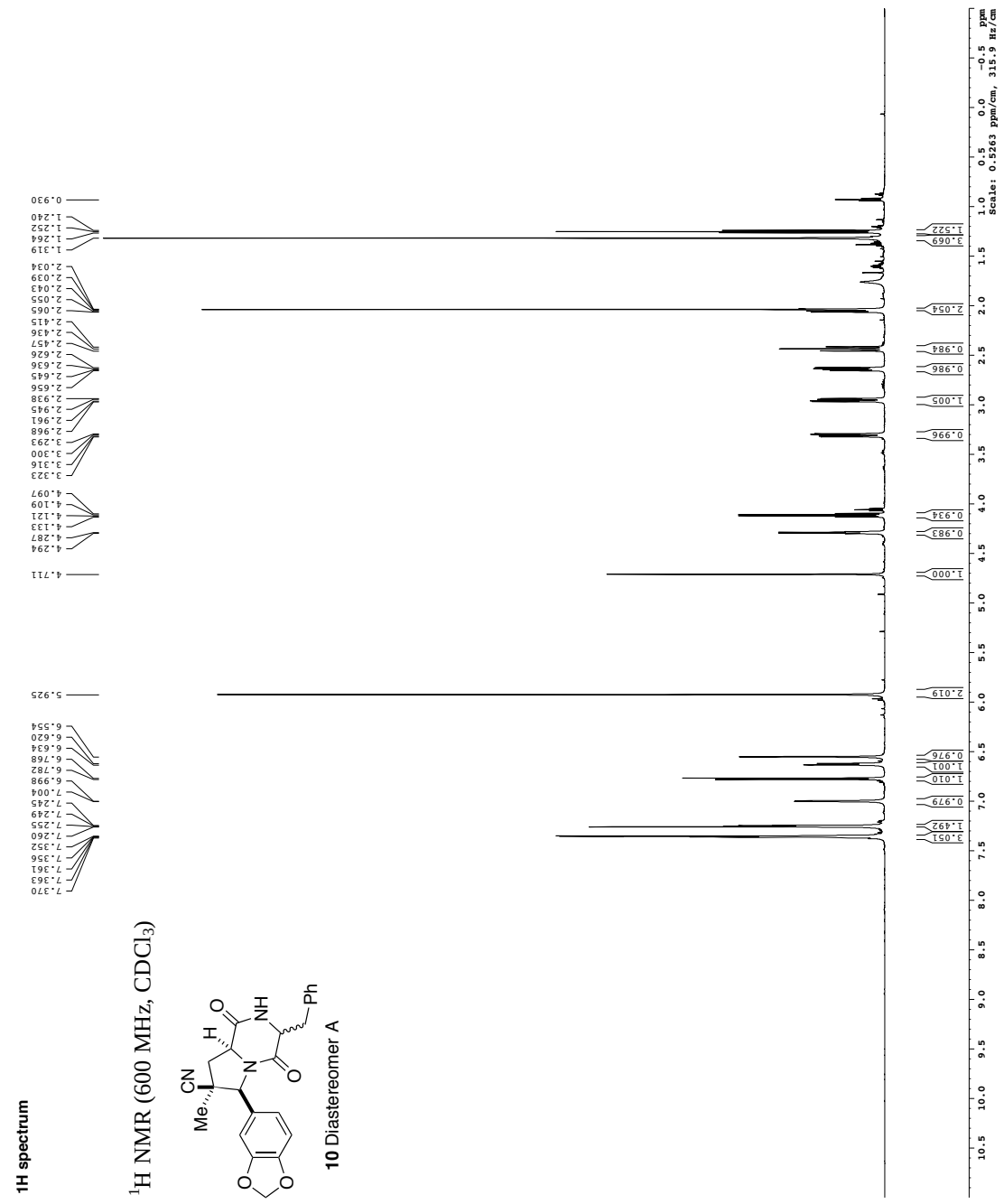
^{13}C NMR (125 MHz, $CDCl_3/CD_3OD$ 1:1)

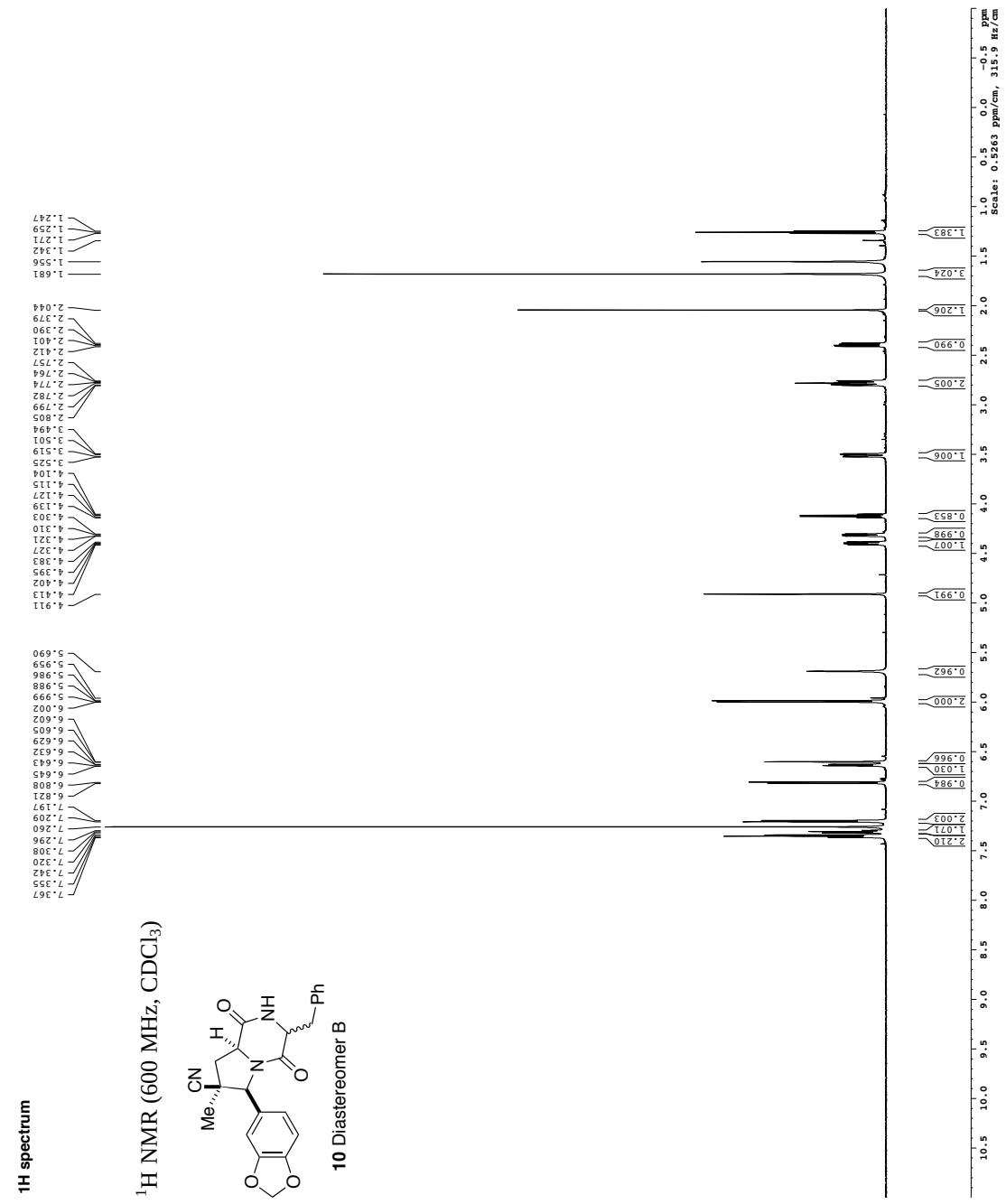


8o



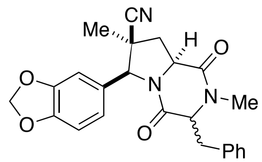

```
Current Data Parameters
NAME              MB1-271
EXPNO                   4
PROCNO                  1

F2 - Acquisition Parameter
Date_            20120712
Time                10.23
INSTRUM             gn500
PROBHD   5 mm broadband
PULPROG        deptqgpsp
TD                  65536
SOLVENT             CDCl3
NS                    104
DS                      0
SWH             30303.031 Hz
FIDRES           0.462388 Hz
AQ              1.0813440 se
RG                  26008
DW                 16.500 us
DE                   6.00 us
TE                  298.0 K
CNST2         145.0000000
CNST12          1.5000000
D1             1.00000000 se
d2             0.00344828 se
d12            0.00002000 se
D16            0.00020000 se
DELTA          0.00000580 se
DELTA1         0.00227998 se
DELTA2         0.00225598 se
DELTA3         0.00224828 se
MCREST   0 sec
MCWRK          0.01500000 se

======== CHANNEL f1 =====
NUC1                  13C
P1                   7.70 us
P12               2000.00 us
PL0                120.00 dB
PL1      0 dB
SFO1          125.5880432 MH
SP2                 11.20 dB
SPNAM[2]     Crp60comp.4
SPOFF2   0 Hz

======== CHANNEL f2 =====
CPDPRG[2          waltz16
NUC2                   1H
p0                  18.00 us
P3                  12.00 us
p4                  24.00 us
PCPD2               80.00 us
PL2                 -5.00 dB
PL12                13.20 dB
SFO2          499.4024970 MH

====== GRADIENT CHANNEL ==
GPNAM[1]         SINE.100
GPNAM[2]         SINE.100
GPNAM[3]         SINE.100
GPX1     0 %
GPX2     0 %
GPX3     0 %
GPY1     0 %
GPY2     0 %
GPY3     0 %
GPZ1                31.00 %
GPZ2                31.00 %
GPZ3                31.00 %
P16               1000.00 us

F2 - Processing parameters
SI                  65536
SF          125.5742698 MH
WDW                    EM
SSB      0
LB                   1.00 Hz
GB       0
PC                   2.00
```


1H spectrum
^{1}H NMR (600 MHz, CDCl$_3$)
10 Diastereomer A
Current Data Parameters
NAME APD-II-130-1
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20150814
Time 19.33
INSTRUM spect
PROBHD 5 mm TBI 1H/D
PULPROG zg30
TD 80874
SOLVENT CDCl3
NS 8
DS 2
SWH 9615.385 Hz
FIDRES 0.098042 Hz
AQ 5.0998336 sec
RG 287
DW 52.000 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 8.00 usec
PLW1 23.01441956 W
SFO1 600.1342099 MHz
F2 - Processing parameters
SI 65536
SF 600.1300352 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
0.930
1.240
1.252
1.264
1.319
2.034
2.039
2.043
2.055
2.065
2.415
2.436
2.457
2.626
2.636
2.645
2.656
2.938
2.945
2.961
2.968
3.293
3.300
3.316
3.323
4.097
4.109
4.121
4.133
4.287
4.294
4.711
5.925
6.554
6.620
6.634
6.768
6.782
6.998
7.004
7.245
7.249
7.255
7.260
7.352
7.356
7.361
7.363
7.370
3.051
1.492
0.979
1.010
1.001
0.976
7.019
1.000
0.983
0.934
0.996
1.005
0.986
0.984
2.054
3.069
1.522
Scale: 0.5263 ppm/cm, 315.9 Hz/cm
ppm

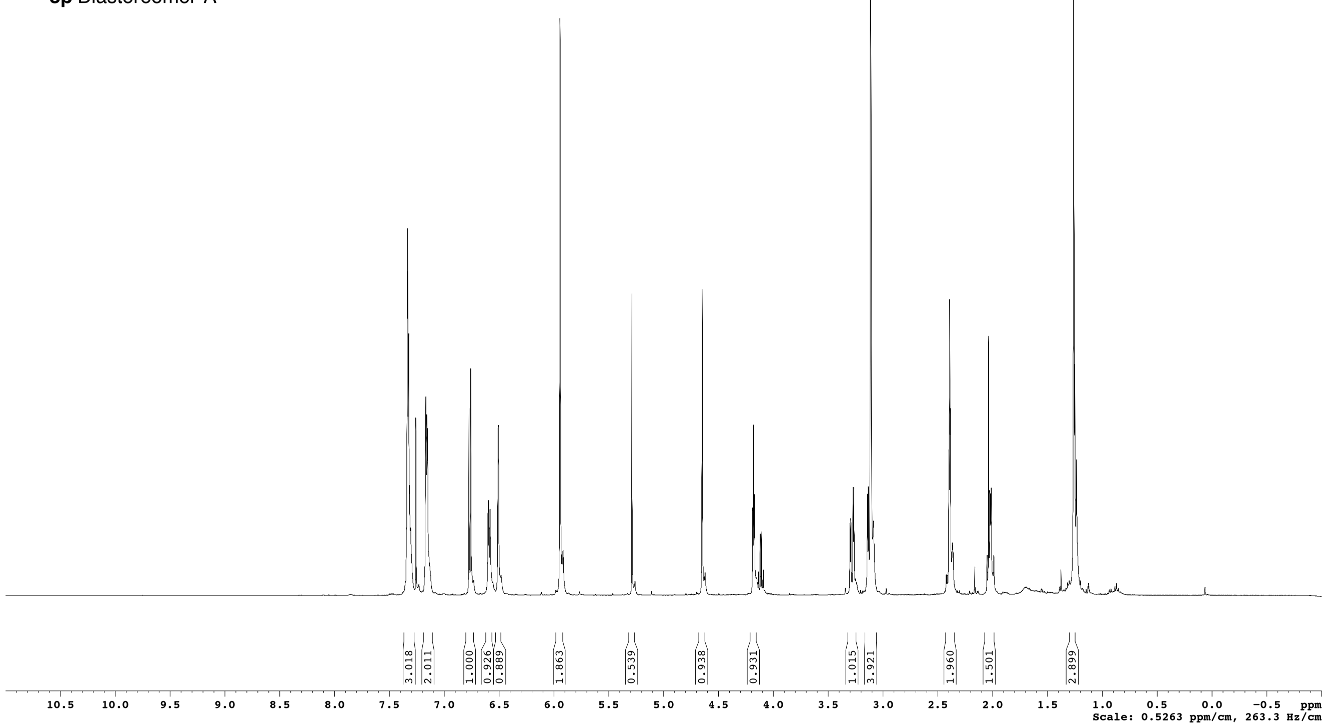

1H spectrum
^{1}H NMR (600 MHz, CDCl$_3$)
10 Diastereomer B
Scale: 0.5263 ppm/cm, 315.9 Hz/cm

1H spectrum

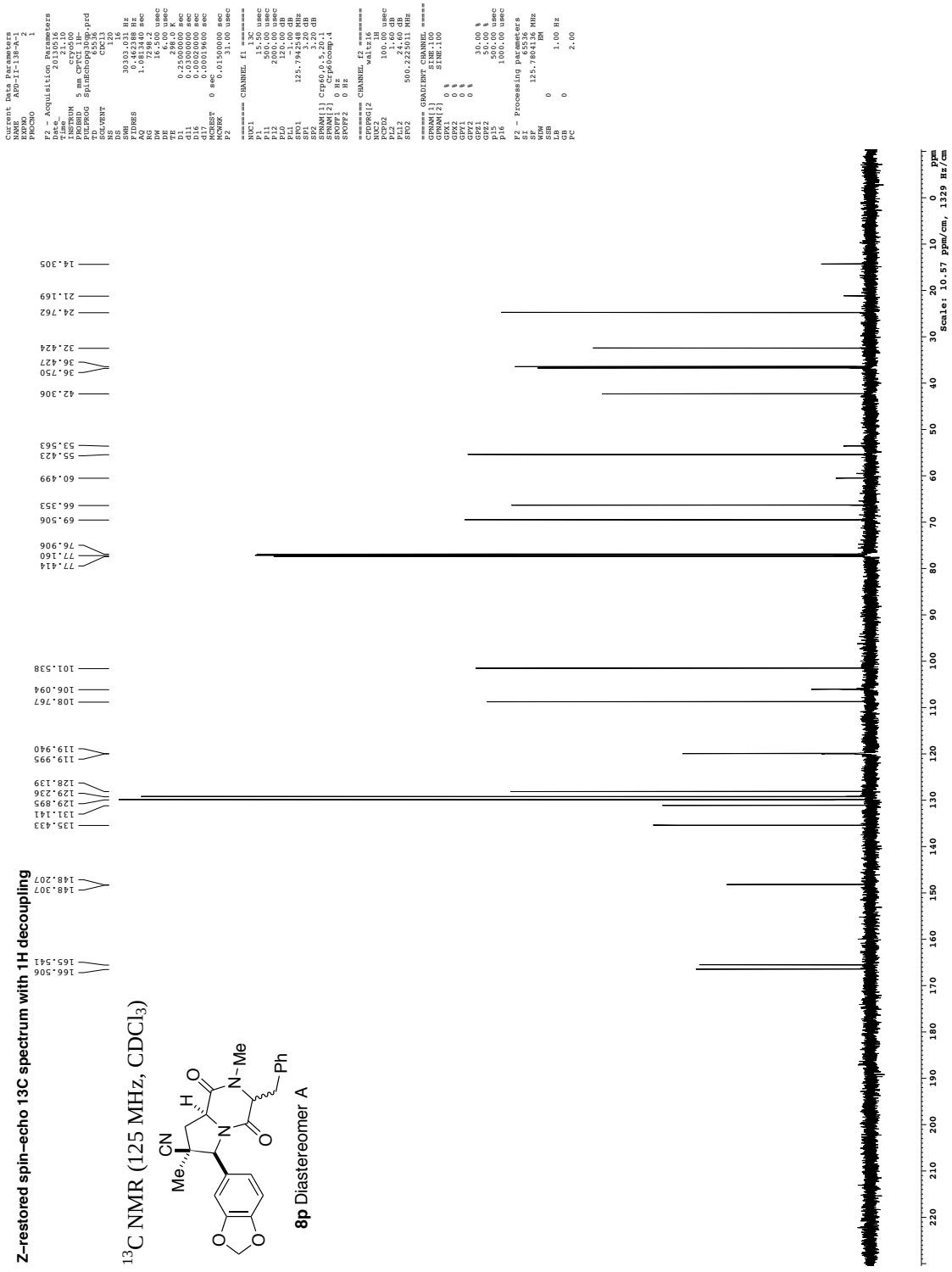
^{1}H NMR (500 MHz, $CDCl_3$)



8p Diastereomer A

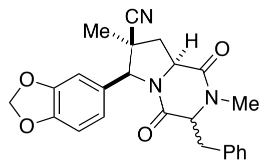



```
Current Data Parameters
NAME     APD-II-138-A-1
EXPNO                 1
PROCNO                1

F2 - Acquisition Parameters
Date_          20130516
Time              21.07
INSTRUM         cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG            zg30
TD                81728
SOLVENT           CDCl3
NS                    8
DS                    2
SWH            8012.820 Hz
FIDRES         0.098043 Hz
AQ            5.0998273 sec
RG                  3.6
DW               62.400 usec
DE                 6.00 usec
TE                298.0 K
D1           0.10000000 sec
MCREST   0 sec
MCWRK        0.01500000 sec

======== CHANNEL f1 ========
NUC1                 1H
P1                 7.50 usec
PL1                1.60 dB
SFO1        500.2235015 MHz

F2 - Processing parameters
SI                65536
SF          500.2200317 MHz
WDW                  EM
SSB      0
LB                 0.30 Hz
GB       0
PC                 4.00
```

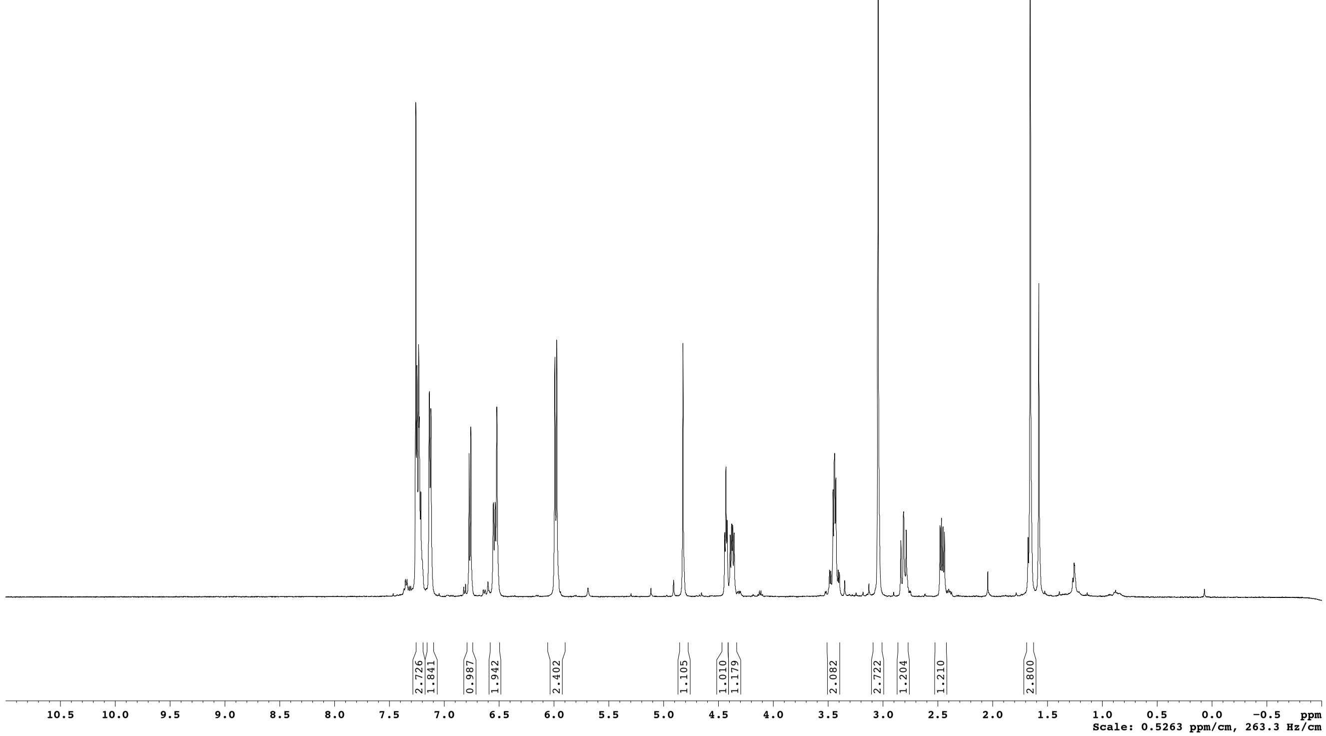

Z–restored spin–echo 13C spectrum with 1H decoupling
13C NMR (125 MHz, CDCl3)
8p Diastereomer A
Scale: 10.57 ppm/cm, 1329 Hz/cm
ppm

1H spectrum

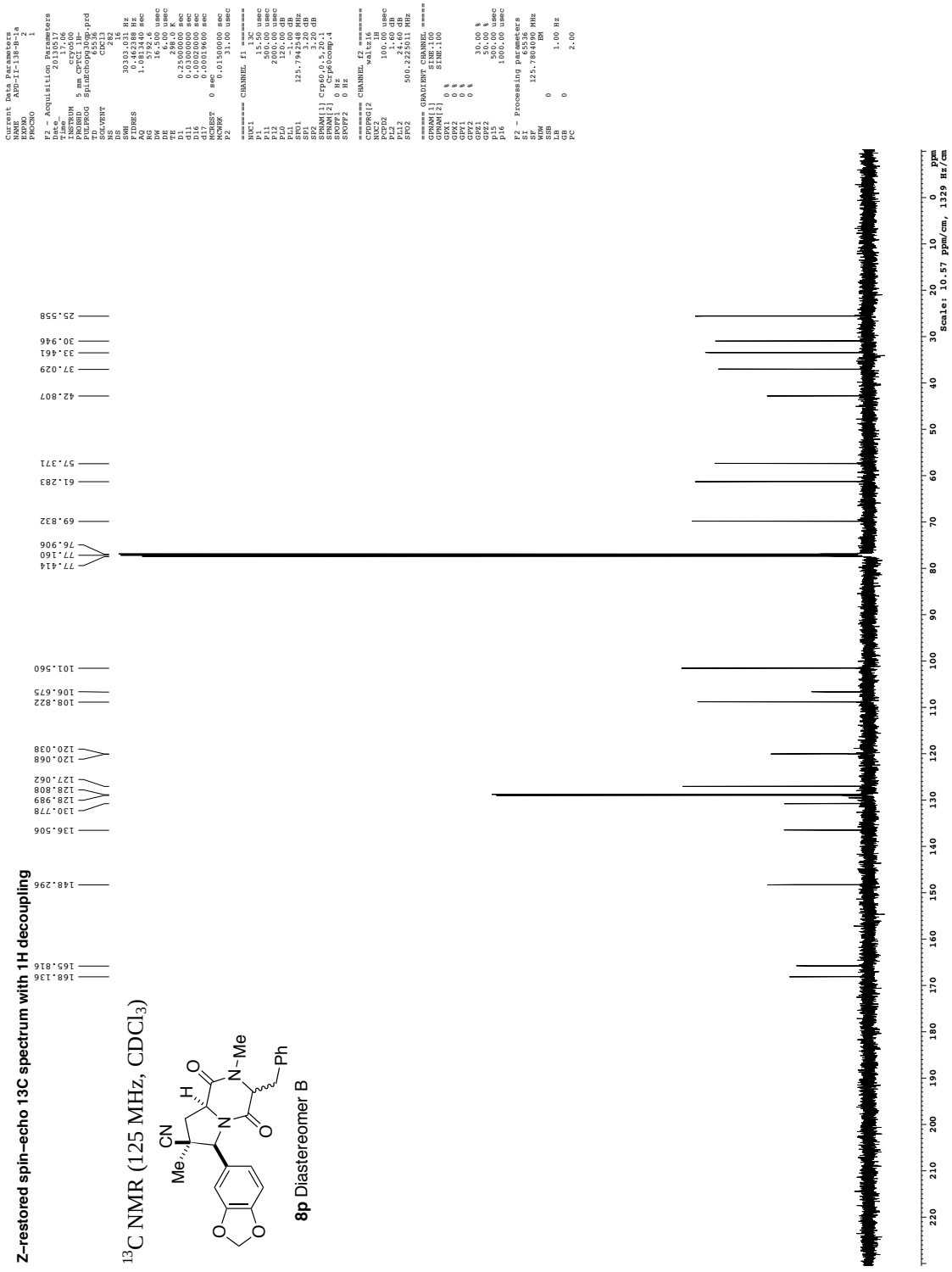
^{1}H NMR (500 MHz, $CDCl_3$)

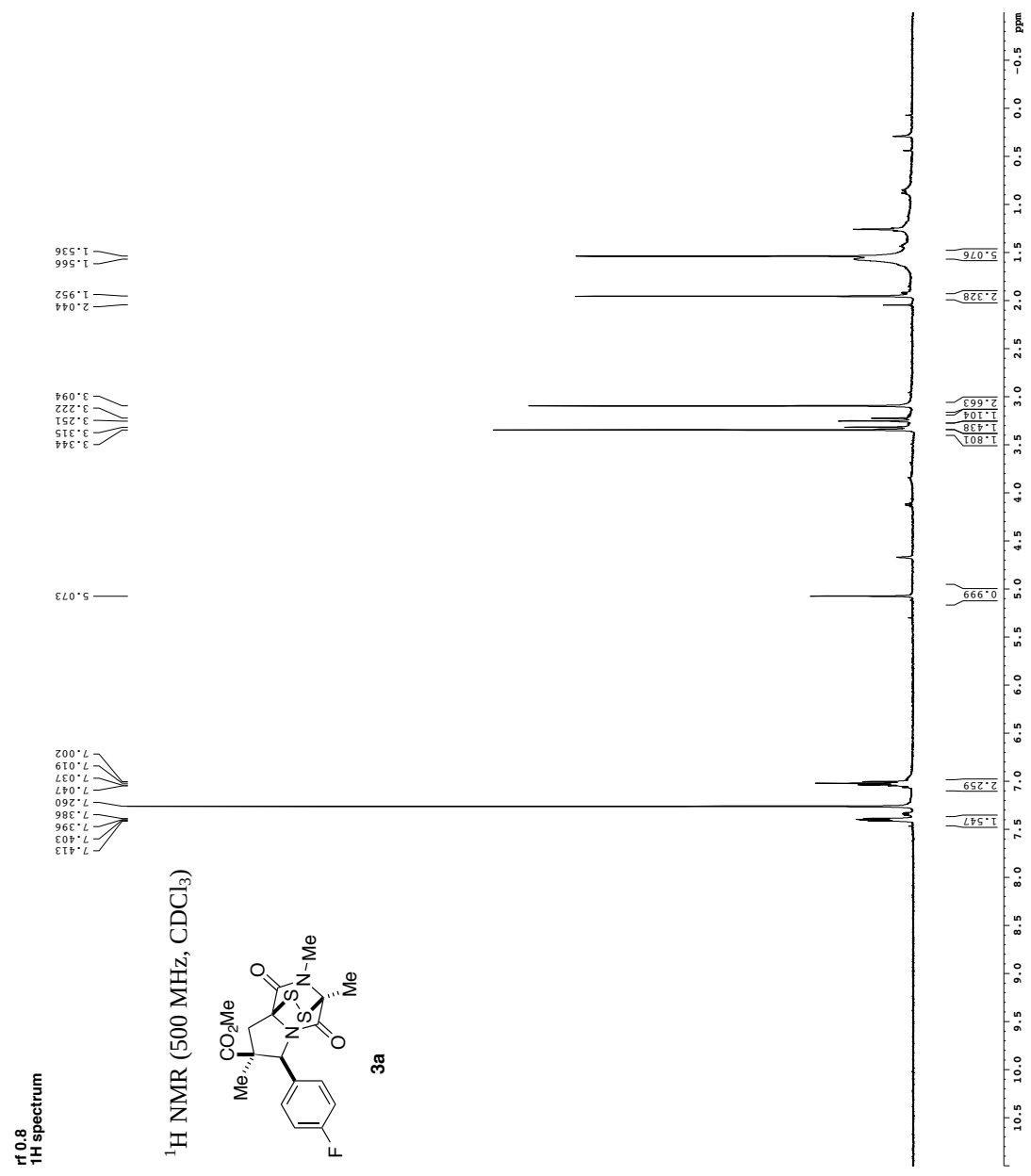


8p Diastereomer B



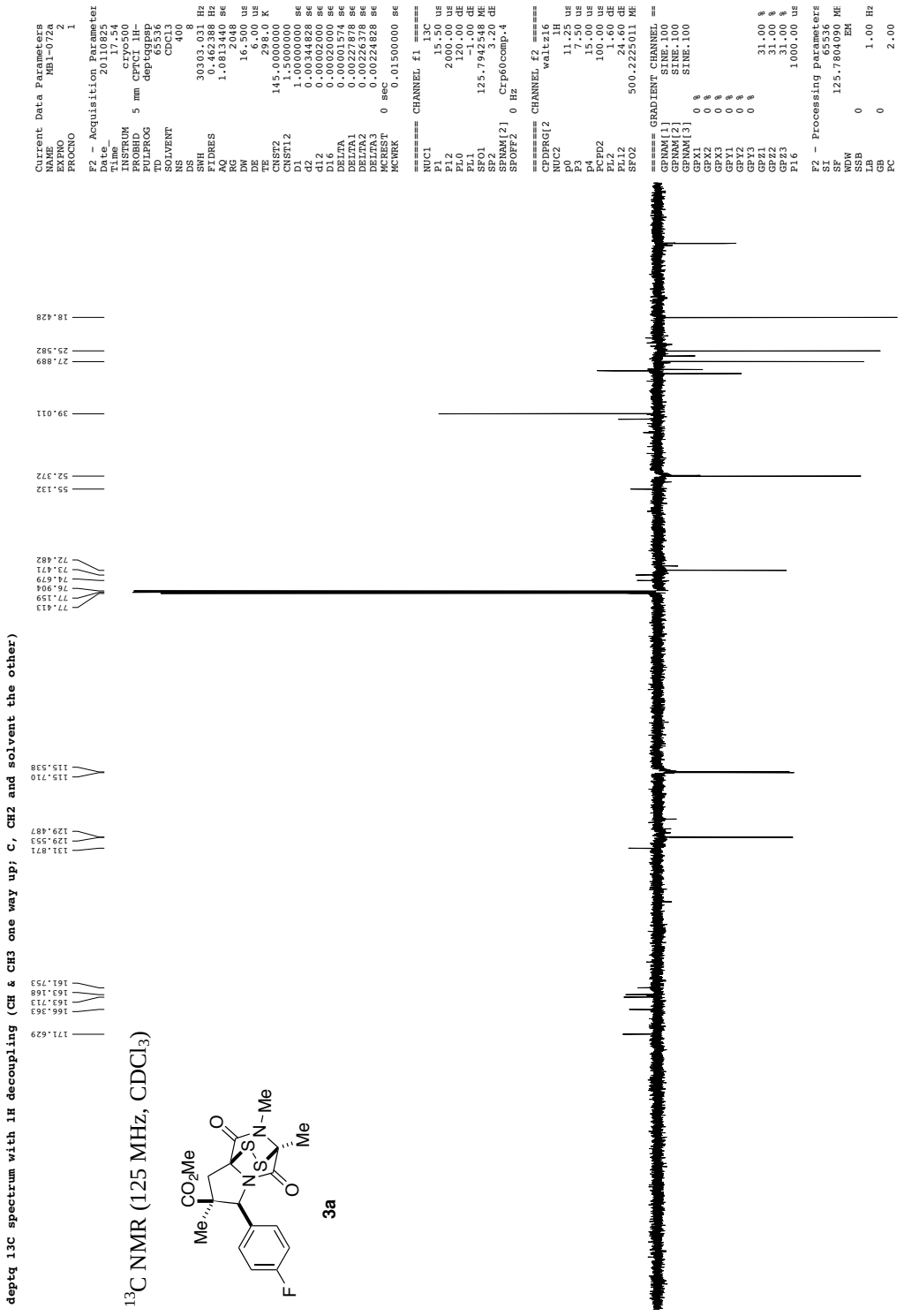

```
Current Data Parameters
NAME      APD-II-138-B-1a
EXPNO                   1
PROCNO                  1

F2 - Acquisition Parameters
Date_            20130517
Time                17.04
INSTRUM           cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG              zg30
TD                  81728
SOLVENT             CDCl3
NS                      8
DS                      2
SWH             8012.820 Hz
FIDRES          0.098043 Hz
AQ             5.0998273 sec
RG                    7.1
DW                 62.400 usec
DE                   6.00 usec
TE                  298.0 K
D1             0.10000000 sec
MCREST   0 sec
MCWRK          0.01500000 sec

======== CHANNEL f1 ========
NUC1                   1H
P1                   7.50 usec
PL1                  1.60 dB
SFO1          500.2235015 MHz

F2 - Processing parameters
SI                  65536
SF            500.2200313 MHz
WDW                    EM
SSB      0
LB                   0.30 Hz
GB       0
PC                   4.00
```


Z–restored spin–echo 13C spectrum with 1H decoupling
^{13}C NMR (125 MHz, CDCl$_3$)
8p Diastereomer B
Me
CN
H
O
N
Me
Ph
O
O
O
N
Scale: 10.57 ppm/cm, 1329 Hz/cm
ppm



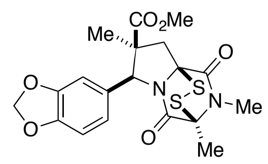
^{1}H NMR (500 MHz, $CDCl_3$)

3a

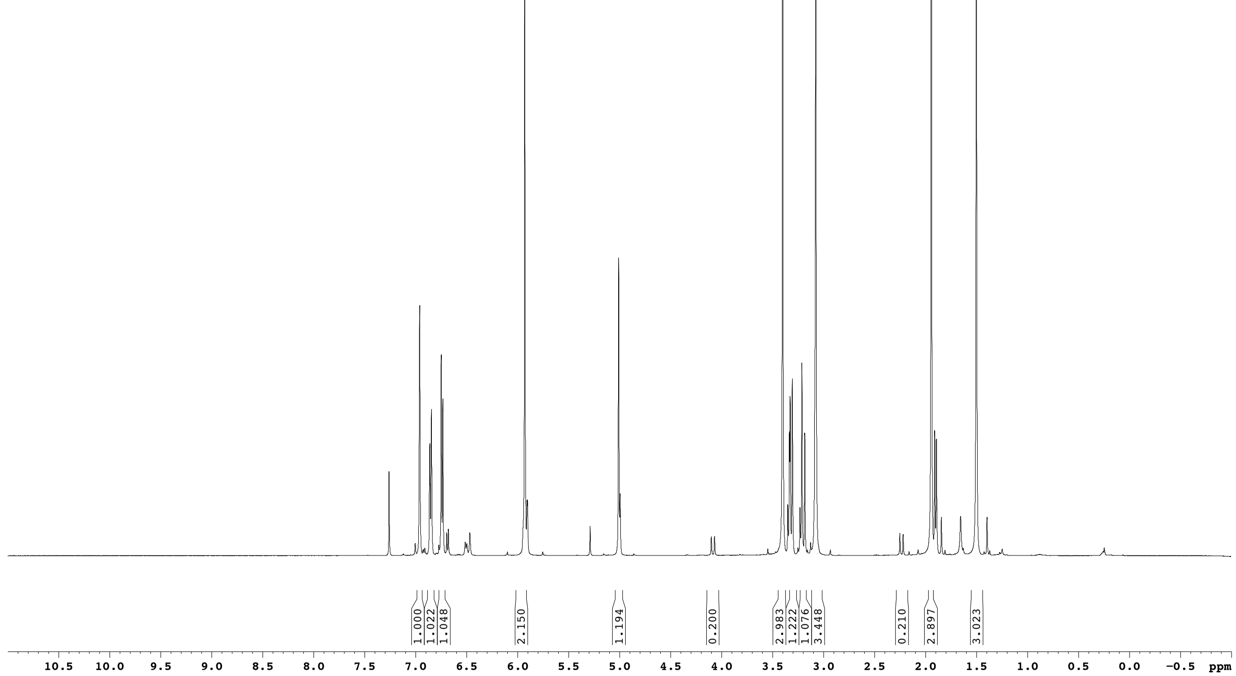

deptq 13C spectrum with 1H decoupling (CH & CH3 one way up; C, CH2 and solvent the other)
13C NMR (125 MHz, CDCl3)
3a
Current Data Parameters
F2 - Acquisition Parameter
F2 - Processing parameters
ppm

1H spectrum

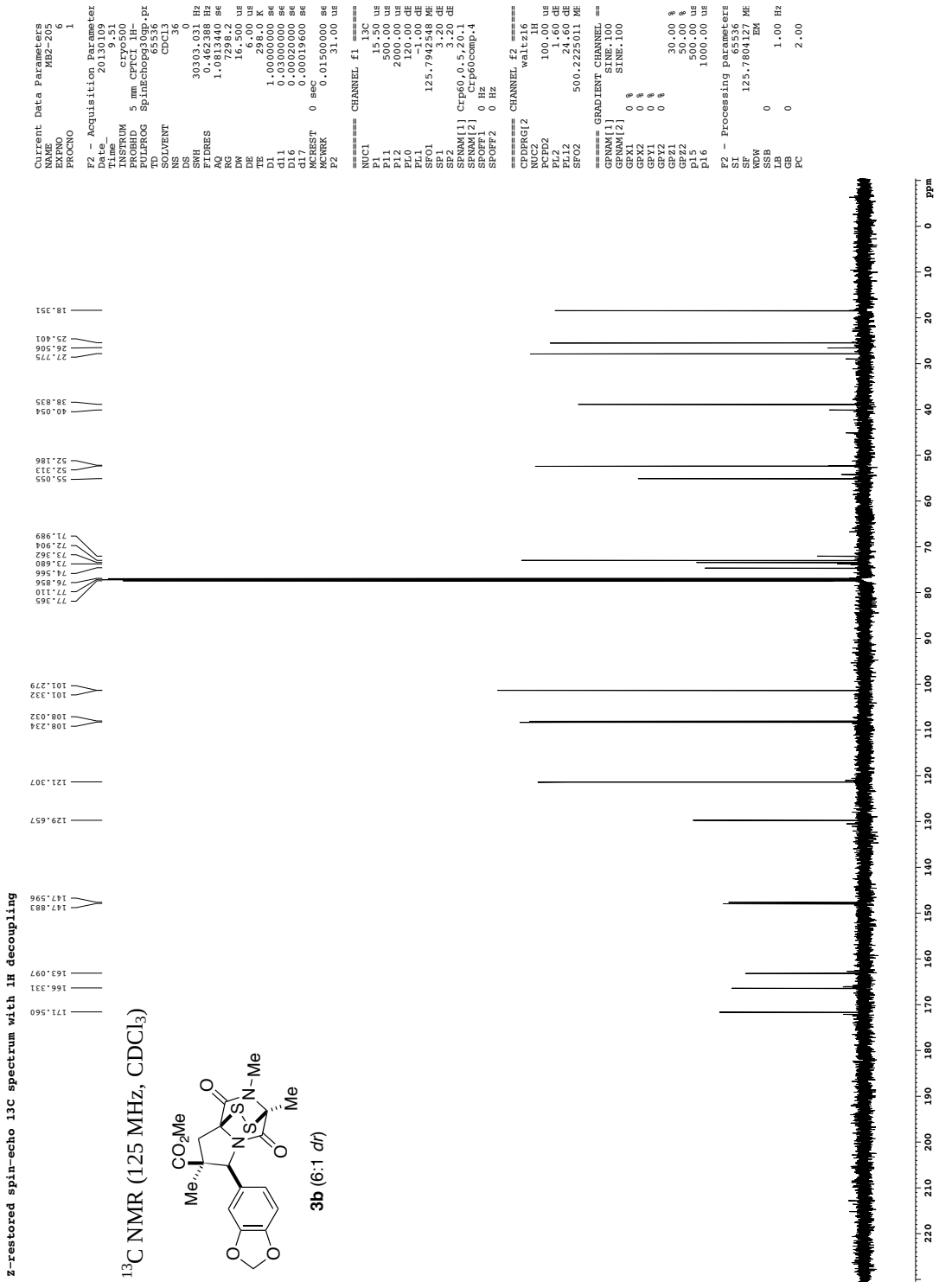
^{1}H NMR (500 MHz, $CDCl_3$)

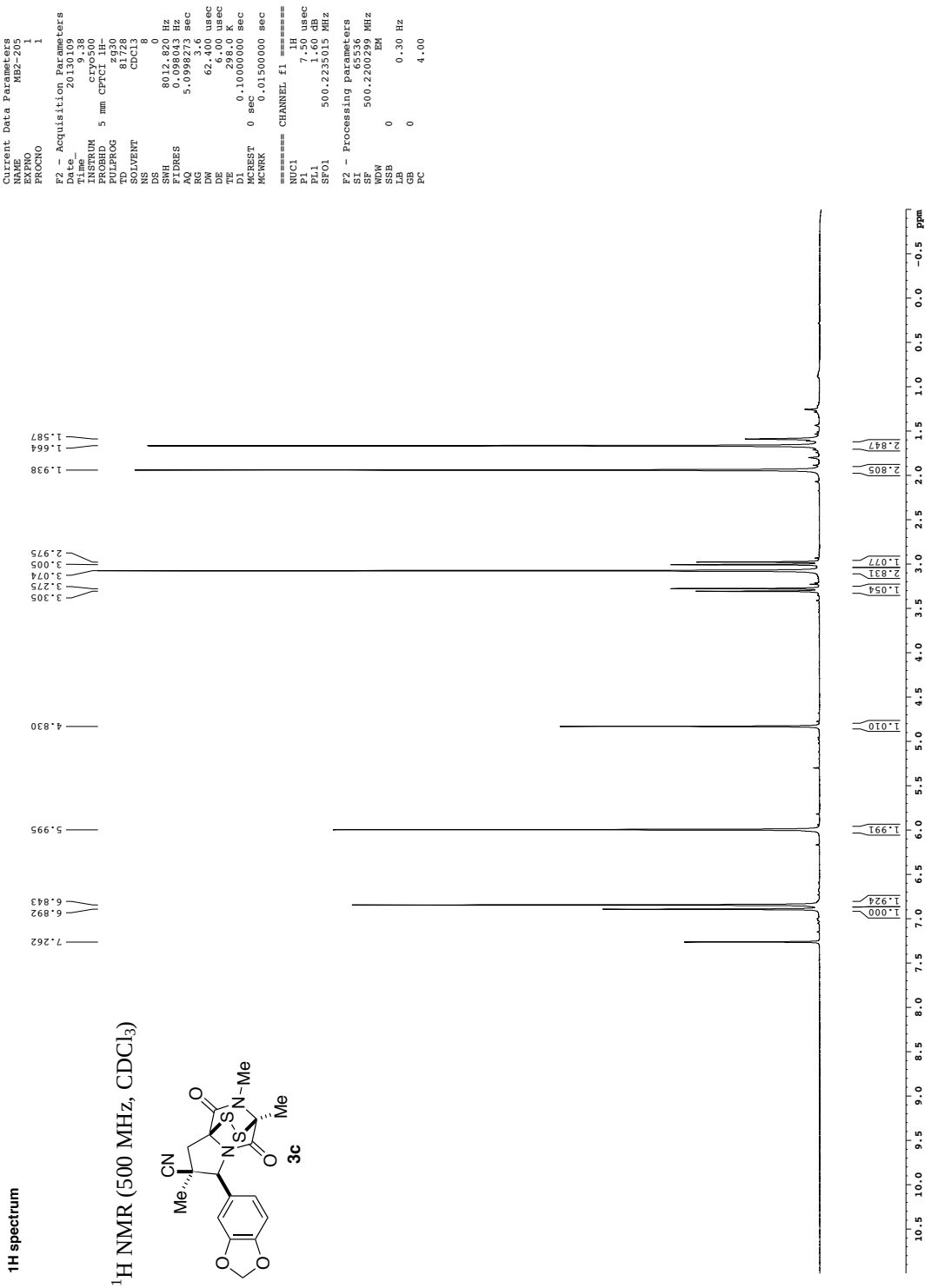


3b (6:1 *dr*)



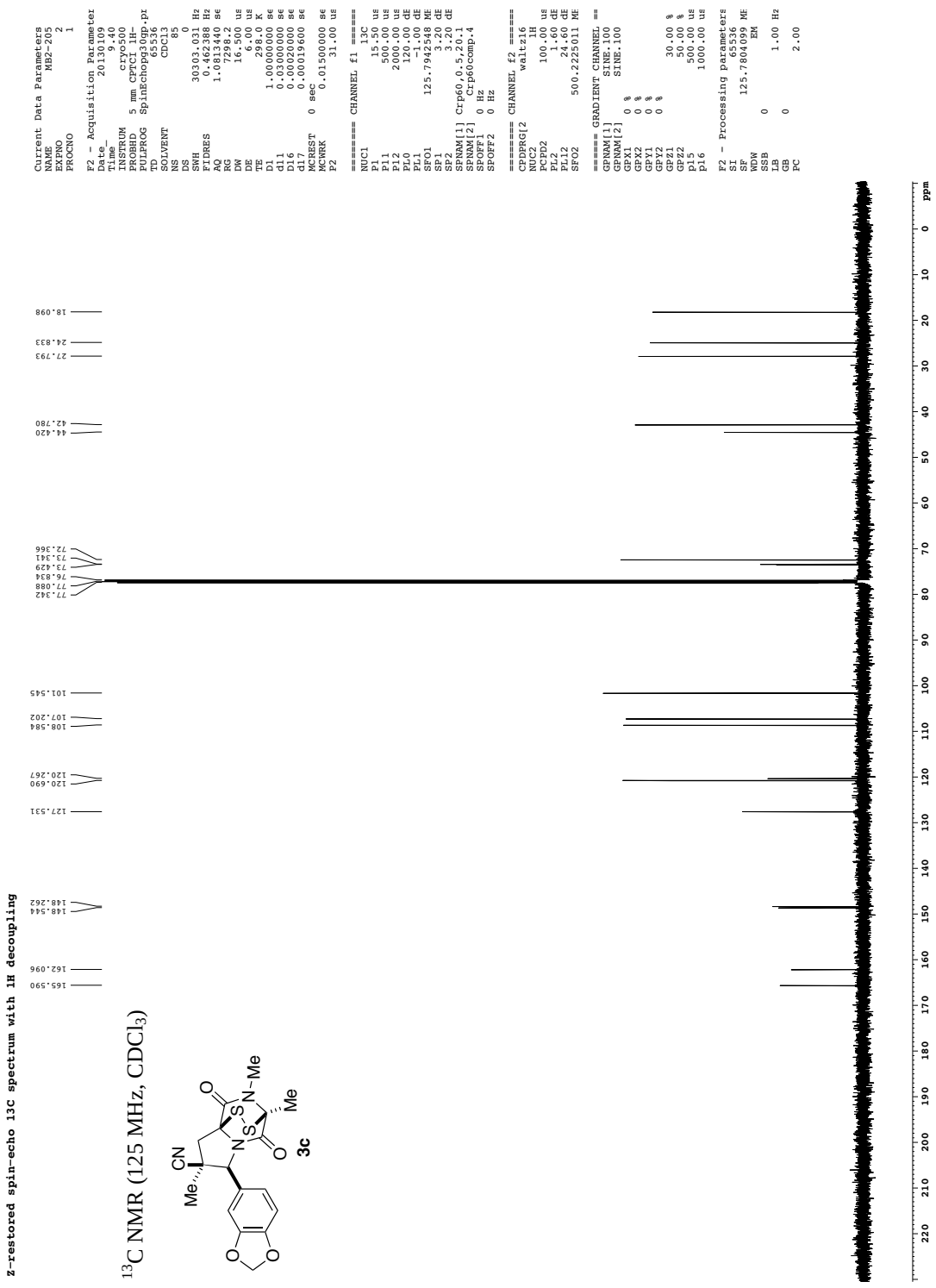

```
Current Data Parameters
NAME              MB2-205
EXPNO                   5
PROCNO                  1

F2 - Acquisition Parameters
Date_            20130109
Time                 9.49
INSTRUM           cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG              zg30
TD                  81728
SOLVENT             CDCl3
NS                      8
DS                      0
SWH             8012.820 Hz
FIDRES          0.098043 Hz
AQ             5.0998273 sec
RG                      5
DW                 62.400 usec
DE                   6.00 usec
TE                  298.0 K
D1             0.10000000 sec
MCREST   0 sec
MCWRK          0.01500000 sec

======== CHANNEL f1 ========
NUC1                   1H
P1                   7.50 usec
PL1                  1.60 dB
SFO1         500.2235015 MHz

F2 - Processing parameters
SI                  65536
SF            500.2200296 MHz
WDW                    EM
SSB      0
LB                   0.30 Hz
GB       0
PC                   4.00
```

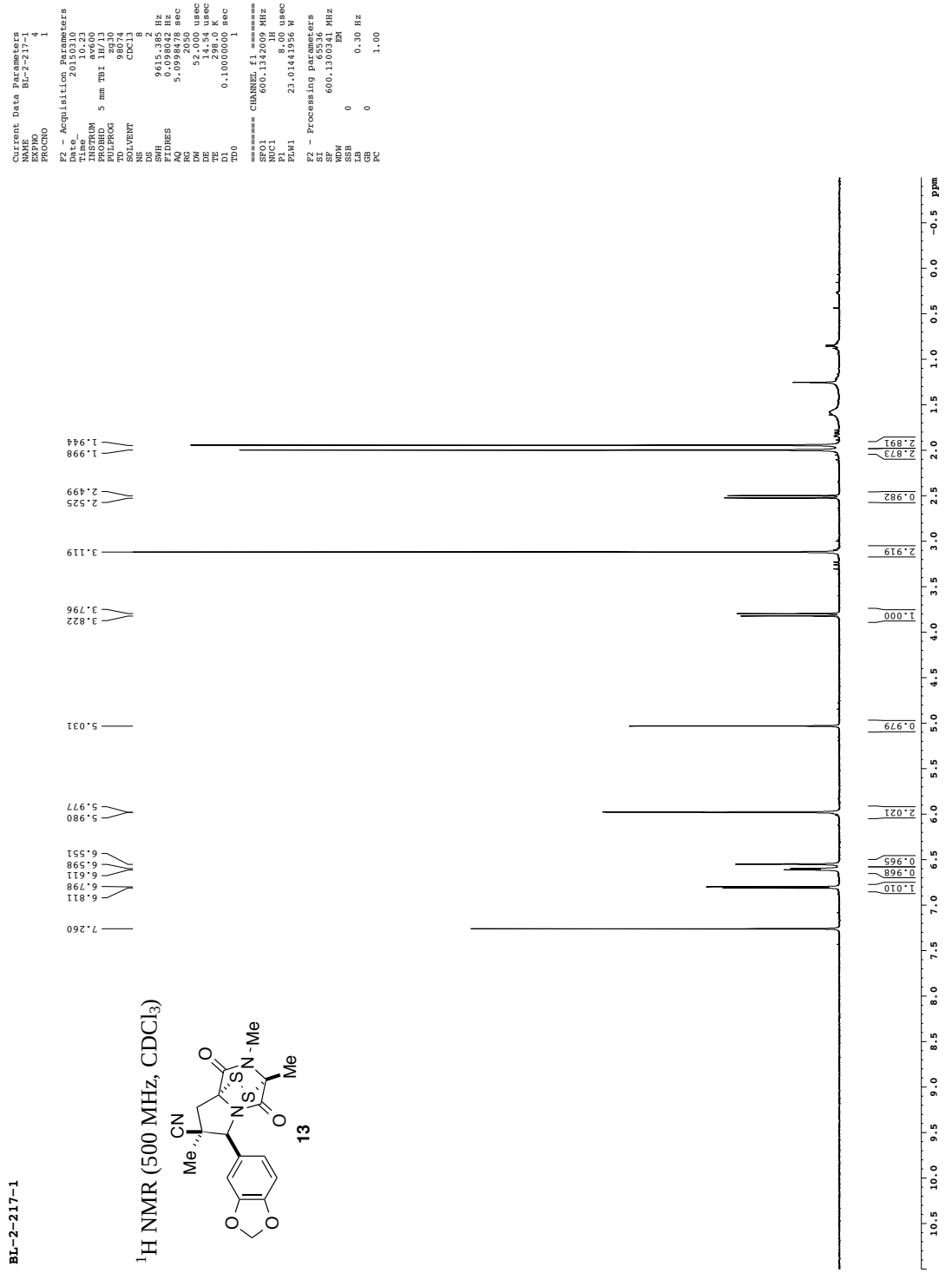

Z-restored spin-echo 13C spectrum with 1H decoupling
13C NMR (125 MHz, CDCl3)
3b (6:1 dr)
Me
CO2Me
N-Me
Current Data Parameters
NAME MB2-205
EXPNO 6
PROCNO 1
F2 - Acquisition Parameter
Date_ 20130109
Time 9.51
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG SpinEchoPg3gp.pr
TD 65536
SOLVENT CDCl3
NS 36
DS 0
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0813440 sec
RG 79.2
DW 16.500 us
DE 6.00 us
TE 298.0 K
D1 1.00000000 sec
d11 0.03000000 sec
D16 0.00020000 sec
d12 0.00019600 sec
MC2REST 0 sec
MCWRK 0.01500000 sec
P2 31.00 us
======== CHANNEL f1 ======
NUC1 13C
P1 15.50 us
P11 500.00 us
P12 2000.00 us
PL2 120.00 dB
PL1 -1.00 dB
SFO1 125.7942548 MHz
SP1 3.20 dB
SP2 3.20 dB
SPNAM[1] Crp60,0.5,20.1
SPNAM[2] Crp60comp.4
SPOFF1 0 Hz
SPOFF2 0 Hz
======== CHANNEL f2 ======
CPDPRG[2 waltz16
NUC2 1H
PCPD2 100.00 us
PL2 1.60 dB
PL12 24.60 dB
SFO2 500.2225011 MHz
====== GRADIENT CHANNEL ==
GPNAM[1] SINE.100
GPNAM[2] SINE.100
GPX1 0 %
GPX2 0 %
GPY1 0 %
GPY2 0 %
GPZ1 30.00 %
GPZ2 50.00 %
p15 500.00 us
p16 1000.00 us
F2 - Processing parameters
SI 65536
SF 125.7804127 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00
171.560
166.331
163.097
147.883
147.596
129.657
121.307
108.234
108.032
101.332
101.279
77.365
77.110
74.856
74.566
73.680
73.362
72.904
71.989
55.055
52.313
52.186
40.054
38.835
27.775
26.506
25.401
18.351
ppm

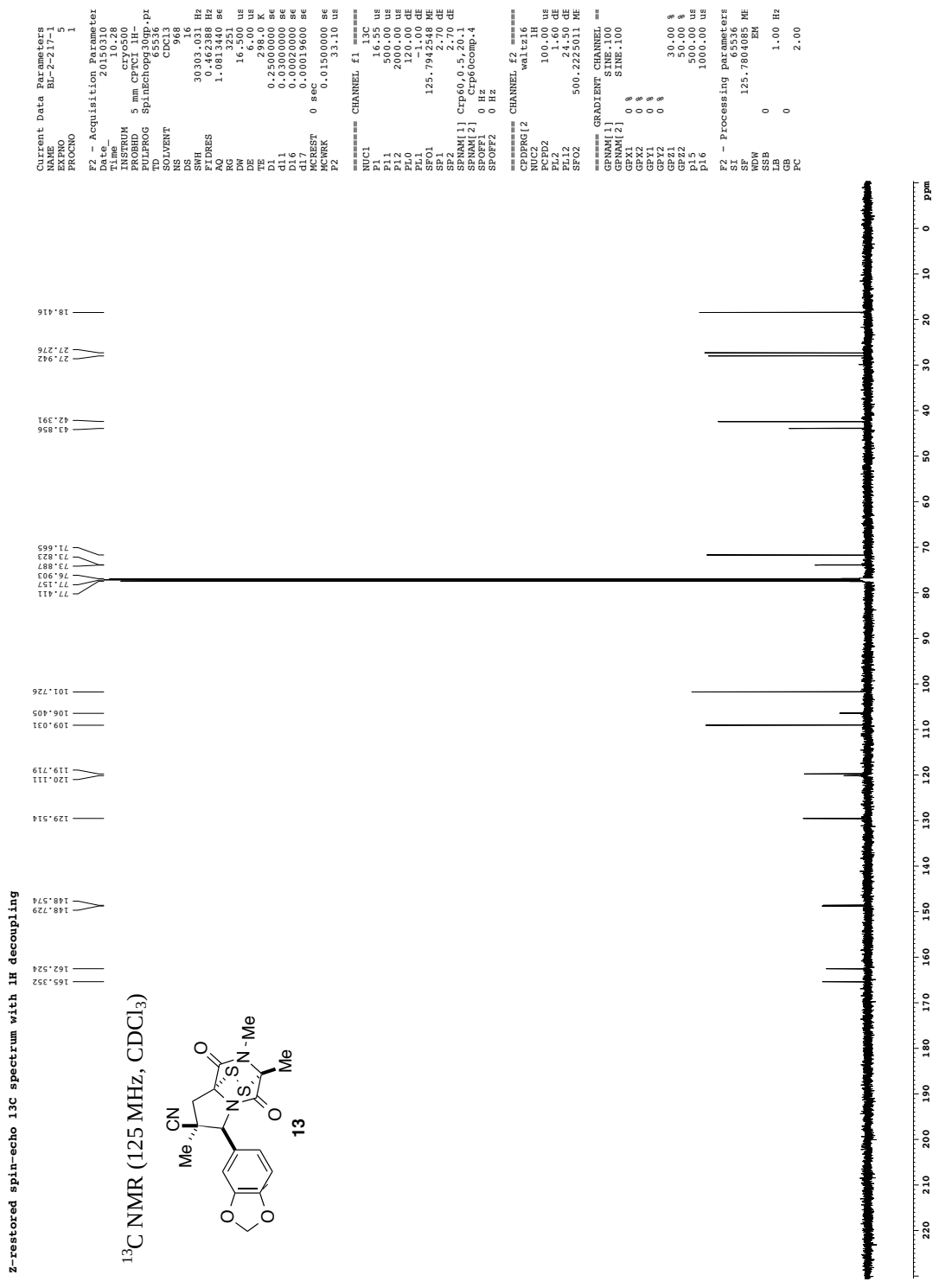


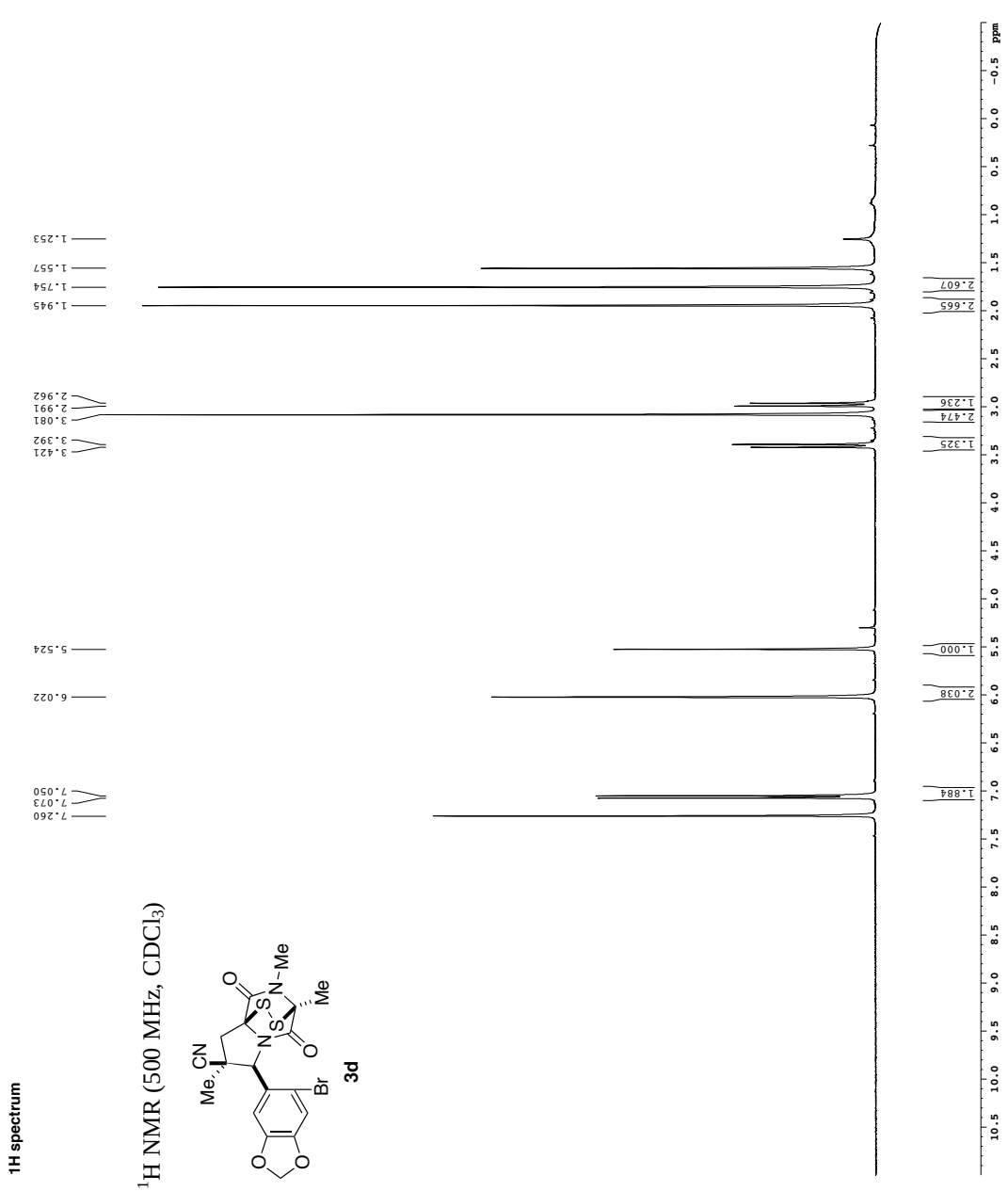
^{1}H NMR (500 MHz, $CDCl_3$)

3c


Z-restored spin-echo 13C spectrum with 1H decoupling
13C NMR (125 MHz, CDCl3)
3c
Current Data Parameters
NAME MB2-205
EXPNO 2
PROCNO 1
F2 - Acquisition Parameter
Date_ 20130109
Time 9.40
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG SpinEchoPg3gp.pr
TD 65536
SOLVENT CDCl3
NS 85
DS 0
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0813440 sec
RG 79.2
DW 16.500 us
DE 6.00 us
TE 298.0 K
D1 1.00000000 sec
d11 0.03000000 sec
D16 0.00020000 sec
d12 0.00019600 sec
MCREST 0 sec 0.01500000 sec
MCWRK 31.00 us
P2
======== CHANNEL f1 ======
NUC1 13C
P1 15.50 us
P11 500.00 us
P12 2000.00 us
PL2 120.00 dB
PL1 -1.00 dB
SFO1 125.7942548 MH
SP1 3.20 dB
SP2 3.20 dB
SPNAM[1] Crp60,0.5,20.1
SPNAM[2] Crp60comp.4
SPOFF1 0 Hz
SPOFF2 0 Hz
======== CHANNEL f2 ======
CPDPRG[2 waltz16
NUC2 1H
PCPD2 100.00 us
PL2 1.60 dB
PL12 24.60 dB
SFO2 500.2225011 MH
====== GRADIENT CHANNEL ==
GPNAM[1] SINE.100
GPNAM[2] SINE.100
GPX1 0 %
GPX2 0 %
GPY1 0 %
GPY2 0 %
GPZ1 30.00 %
GPZ2 50.00 %
p15 500.00 us
p16 1000.00 us
F2 - Processing parameter
SI 65536
SF 125.7804099 MH
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00
18.098
24.833
27.793
42.780
44.420
72.366
73.341
73.429
76.834
77.088
77.342
101.545
107.202
108.584
120.267
120.690
127.531
148.262
148.544
162.096
165.590
ppm

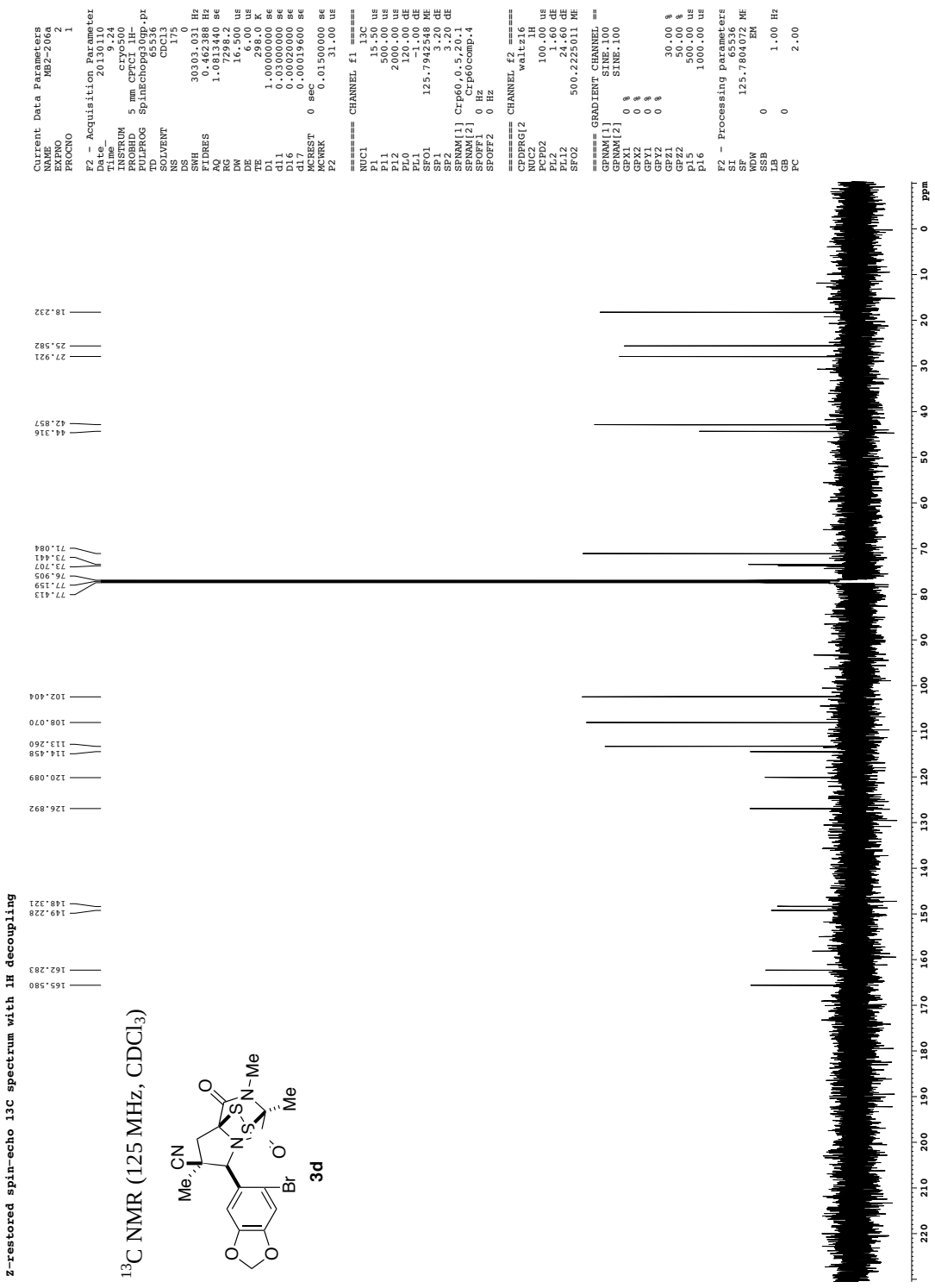

BL-2-217-1
^{1}H NMR (500 MHz, CDCl$_3$)
13
Current Data Parameters
NAME BL-2-217-1
EXPNO 4
PROCNO 1
F2 - Acquisition Parameters
Date_ 20150710
Time 10.23
INSTRUM av600
PROBHD 5 mm TBI 1H/13
PULPROG zg30
TD 98304
SOLVENT CDCl3
NS 8
DS 2
SWH 9615.385 Hz
FIDRES 0.039242 Hz
AQ 5.09998478 sec
RG 2050
DW 52.000 usec
DE 14.54 usec
TE 298.0 K
D1 0.10000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 600.1342009 MHz
NUC1 1H
P1 8.00 usec
PLW1 23.01441956 W
F2 - Processing parameters
SI 65536
SF 600.1300341 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
7.260
6.811
6.798
6.611
6.598
6.551
5.980
5.977
5.031
3.822
3.796
3.119
2.525
2.499
1.998
1.944
1.010
0.968
0.965
2.021
0.979
1.000
2.919
0.982
2.873
2.891
ppm

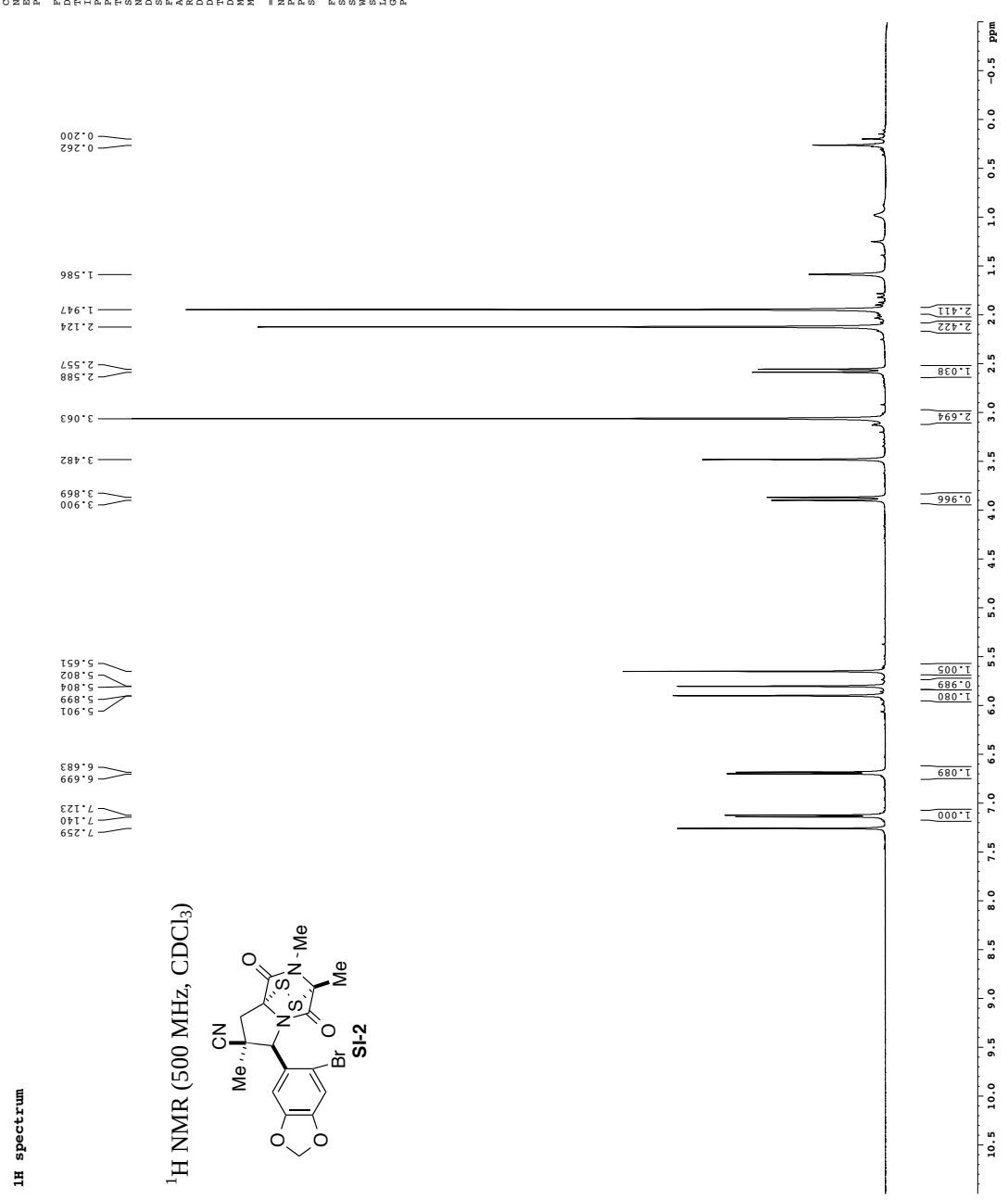

Z-restored spin-echo 13C spectrum with 1H decoupling
Current Data Parameters
NAME BL-2-217-1
EXPNO 5
PROCNO 1
F2 - Acquisition Parameter
Date_ 20150310
Time 10.28
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG SpinEchopg3Ugp.pr
TD 65536
SOLVENT CDCl3
NS 968
DS 16
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0813440 sec
RG 3251
DW 16.550 usec
DE 6.00 usec
TE 298.0 K
D1 0.25000000 sec
d11 0.03000000 sec
D16 0.00020000 sec
d17 0.00019600 sec
MCREST 0 sec 0.01500000 sec
MCWRK 0.01500000 sec
P2 33.10 usec
======== CHANNEL f1 ======
NUC1 13C
P1 16.55 usec
P11 500.00 usec
P12 2000.00 usec
PL0 120.00 dB
PL1 -1.00 dB
SFO1 125.7942548 MHz
SP1 2.70 dB
SP2 2.70 dB
SPNAM[1] Crp60,0.5,20.1
SPNAM[2] Crp60comp.4
SPOFF1 0 Hz
SPOFF2 0 Hz
======== CHANNEL f2 ======
CPDPRG[2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 1.60 dB
PL12 24.50 dB
SFO2 500.2225011 MHz
====== GRADIENT CHANNEL ==
GPNAM[1] SINE.100
GPNAM[2] SINE.100
GPX1 0 %
GPX2 0 %
GPY1 0 %
GPY2 0 %
GPZ1 30.00 %
GPZ2 50.00 %
p15 500.00 usec
p16 1000.00 usec
F2 - Processing parameters
SI 65536
SF 125.7804085 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00
18.416
27.942
27.276
43.856
42.391
71.665
73.823
73.887
76.903
77.157
77.411
101.726
106.405
109.031
119.719
120.111
129.514
148.729
148.574
162.524
165.352
ppm
^{13}C NMR (125 MHz, CDCl$_3$)
13

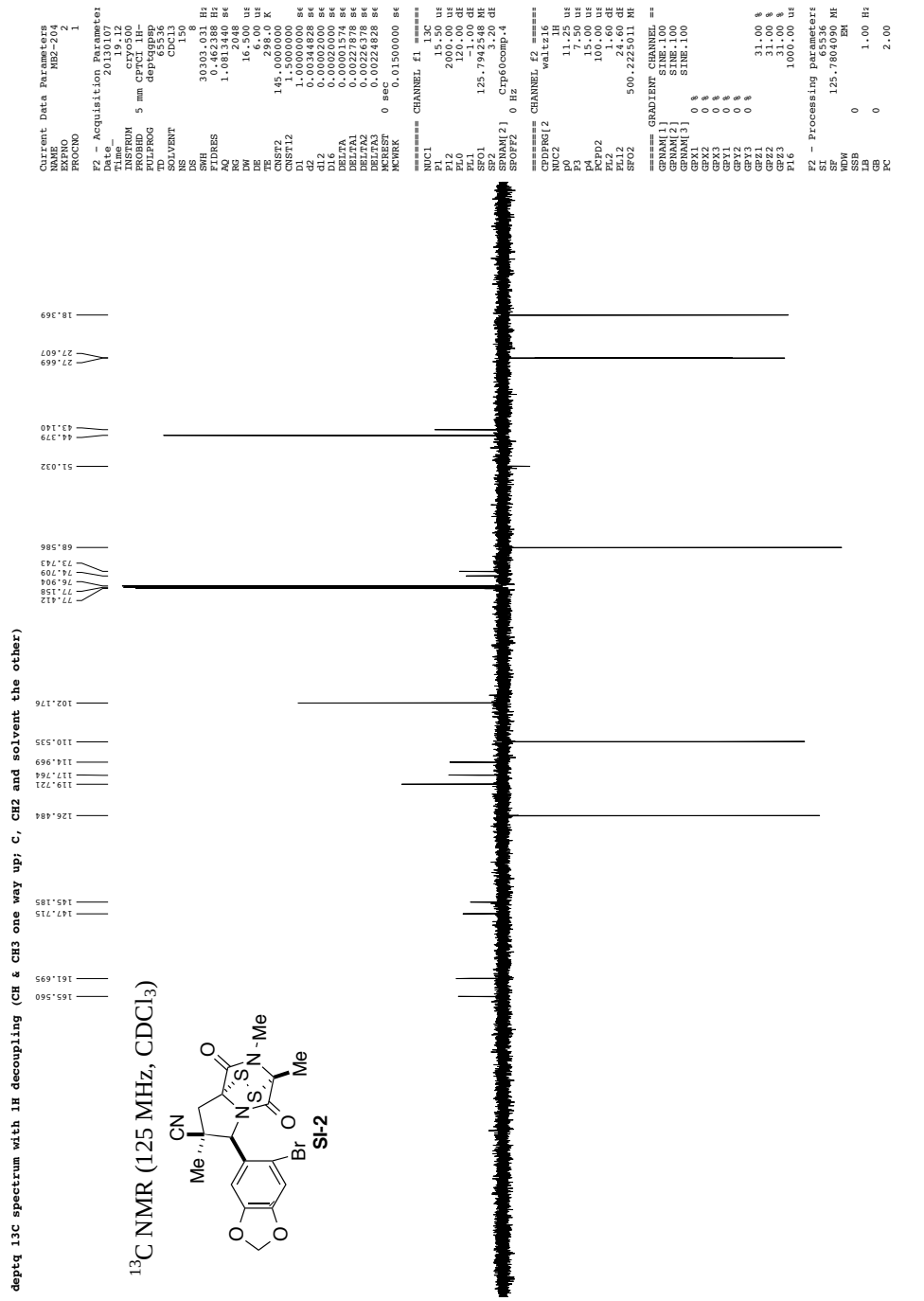


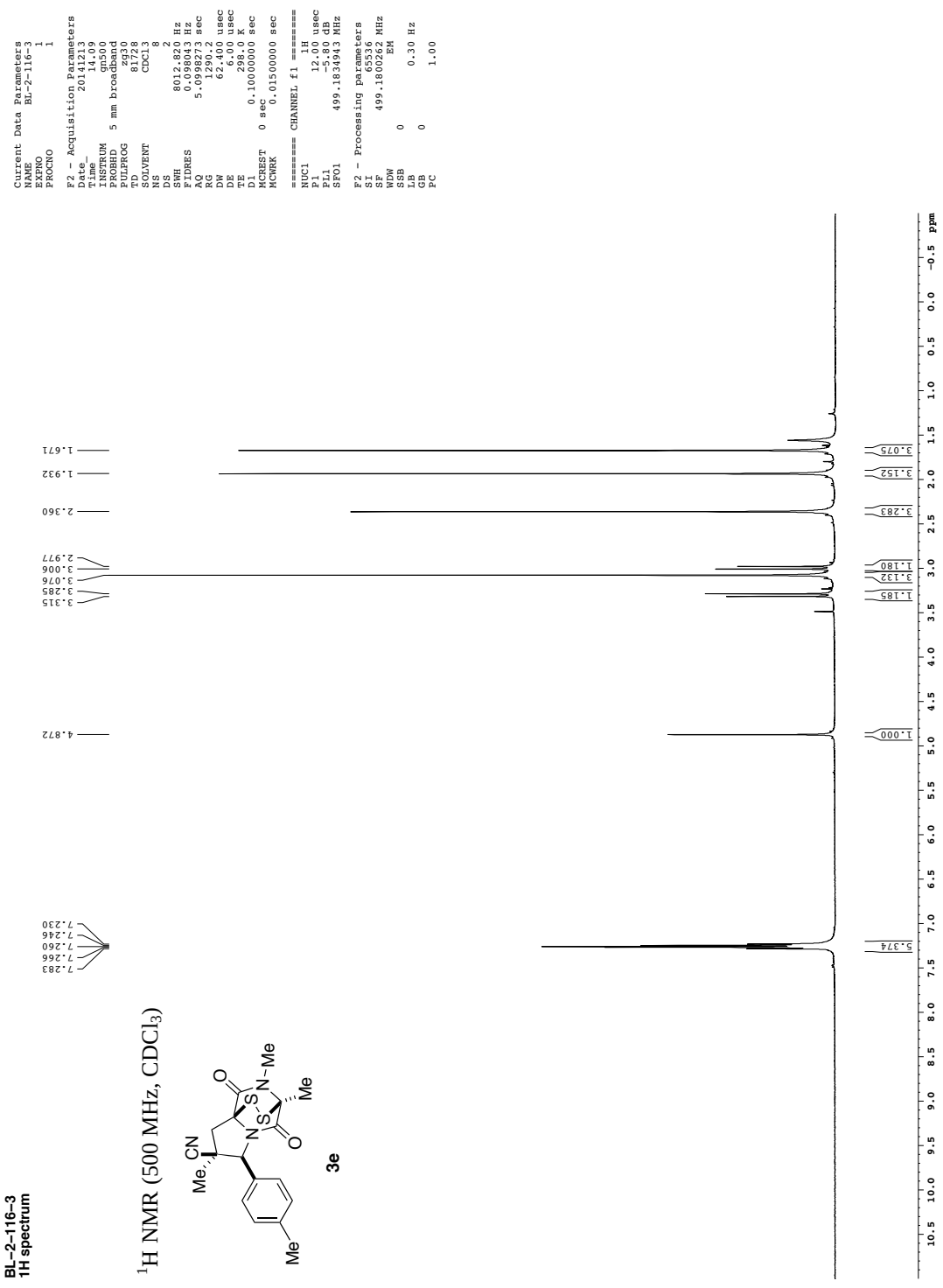
^{1}H NMR (500 MHz, $CDCl_3$)

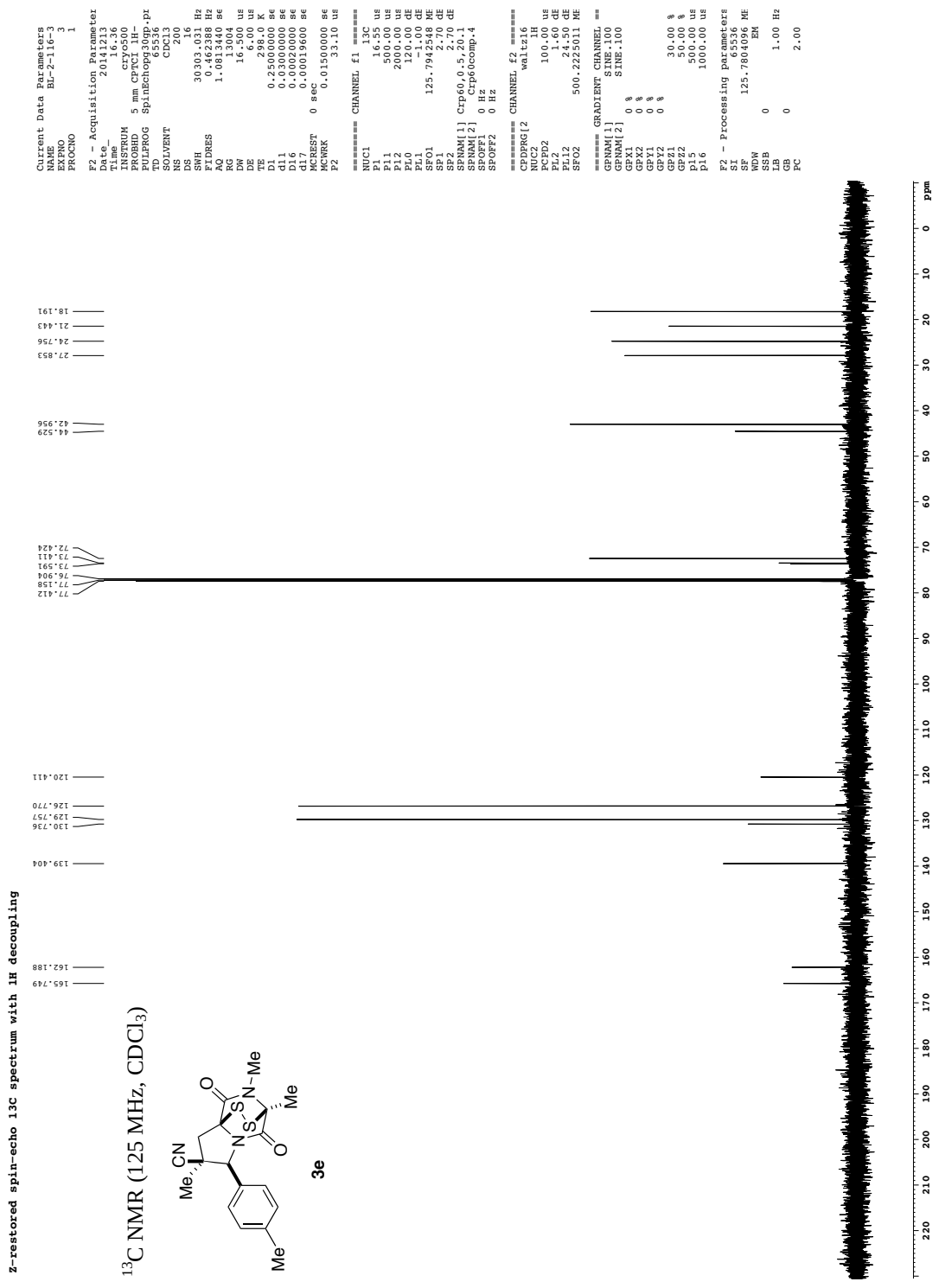
3d

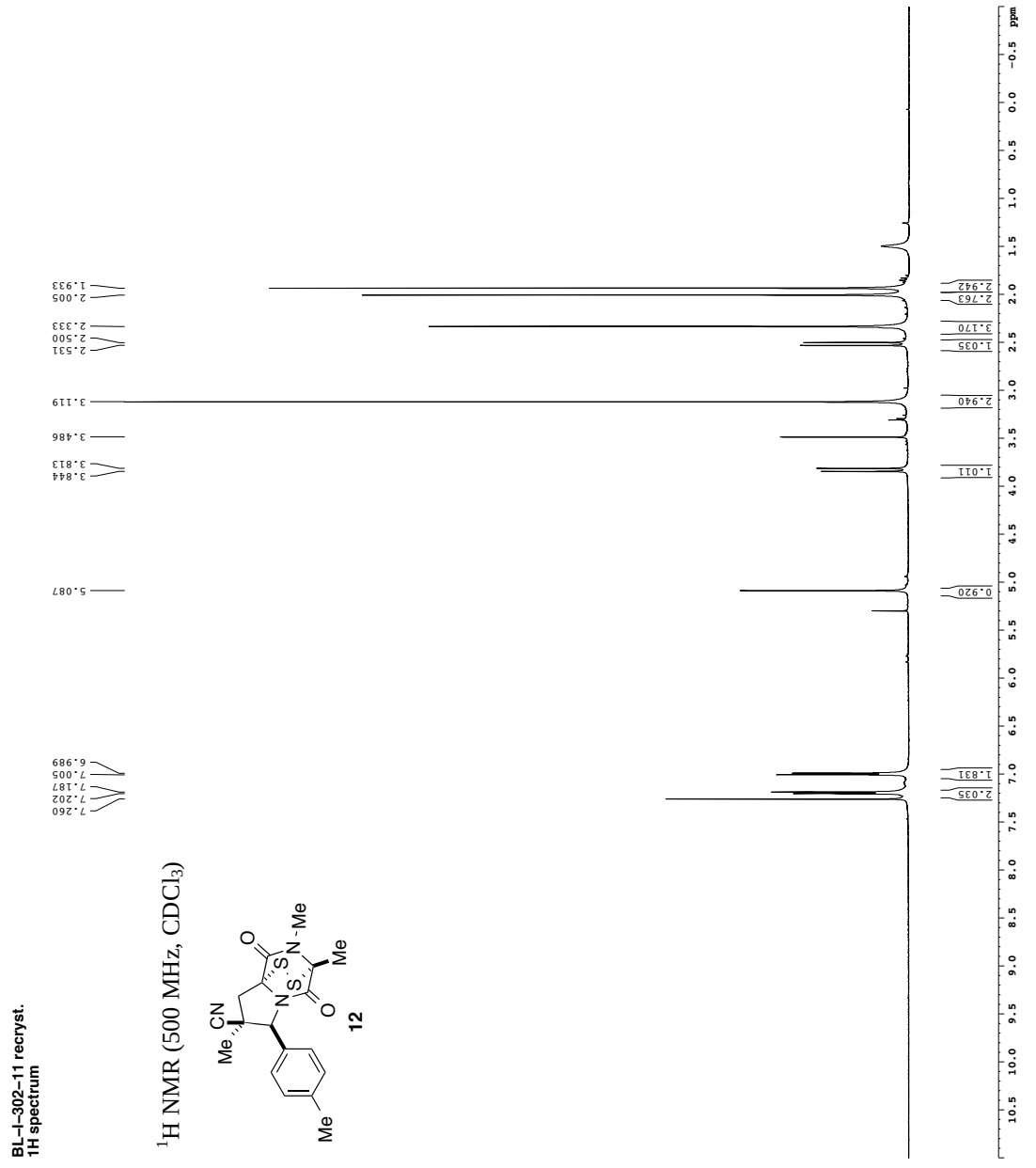

Z-restored spin-echo 13C spectrum with 1H decoupling
13C NMR (125 MHz, CDCl3)
3d
Current Data Parameters
NAME MB2-206a
EXPNO 2
PROCNO 1
F2 - Acquisition Parameter
Date_ 20130110
Time 9.24
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG SpinEchoPg3gp.pr
TD 65536
SOLVENT CDCl3
NS 175
DS 0
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0813440 sec
RG 79842.7
DW 16.500 us
DE 6.00 us
TE 298.0 K
D1 1.00000000 sec
d11 0.03000000 sec
D16 0.00020000 sec
d12 0.00019600 sec
MCREST 0 sec 0.01500000 sec
MCWRK 0.01500000 sec
P2 31.00 us
======== CHANNEL f1 ======
NUC1 13C
P1 15.50 us
P11 500.00 us
P12 2000.00 us
PL2 120.00 dB
PL1 -1.00 dB
SFO1 125.7942548 MHz
SP1 3.20 dB
SP2 3.20 dB
SPNAM[1] Crp60,0.5,20.1
SPNAM[2] Crp60comp.4
SPOFF1 0 Hz
SPOFF2 0 Hz
======== CHANNEL f2 ======
CPDPRG[2 waltz16
NUC2 1H
PCPD2 100.00 us
PL2 1.60 dB
PL12 24.60 dB
SFO2 500.2225011 MHz
====== GRADIENT CHANNEL ==
GPNAM[1] SINE.100
GPNAM[2] SINE.100
GPX1 0 %
GPX2 0 %
GPY1 0 %
GPY2 0 %
GPZ1 30.00 %
GPZ2 50.00 %
p15 500.00 us
p16 1000.00 us
F2 - Processing parameters
SI 65536
SF 125.7804072 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00
165.580
162.283
149.228
148.321
126.892
120.089
114.458
113.260
108.070
102.404
77.413
77.159
76.905
73.707
73.441
71.084
44.316
42.857
27.921
25.582
18.232
ppm


1H spectrum
^{1}H NMR (500 MHz, CDCl$_3$)
SI-2
Me
CN
Br
O
N
S
Me
7.259
7.140
7.123
6.699
6.683
5.901
5.899
5.804
5.802
5.651
3.900
3.869
3.482
3.063
2.588
2.557
2.124
1.947
1.586
0.262
0.200
1.000
1.089
1.080
0.989
1.005
0.966
2.694
1.038
2.422
2.411
ppm

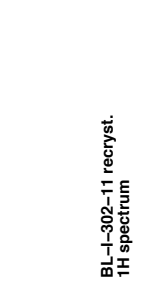

deptq 13C spectrum with 1H decoupling (CH & CH3 one way up; C, CH2 and solvent the other)
13C NMR (125 MHz, CDCl3)
SI-2
Me
CN
Br
N-Me
Current Data Parameters
NAME MB2-204
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20130107
Time_ 19.12
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG deptqgpsp
TD 65536
SOLVENT CDCl3
NS 150
DS 8
SWH 30303.031 Hz
FIDRES 0.462398 Hz
AQ 1.0813440 sec
RG 2048
DW 16.500 us
DE 6.00 us
TE 298.0 K
CNST2 145.0000000
CNST12 1.5000000
D1 1.00000000 sec
D2 0.00344828 sec
d12 0.00002000 sec
D16 0.00020000 sec
DELTA 0.00001574 sec
DELTA1 0.00227878 sec
DELTA2 0.00226378 sec
DELTA3 0.00224828 sec
MCREST 0 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ======
NUC1 13C
P1 15.50 us
P12 2000.00 us
PL0 120.00 dB
PL1 -1.00 dB
SFO1 125.7943276 MHz
SP2 3.20 dB
SPNAM[2] Crp60comp.4
SPOFF2 0 Hz
======== CHANNEL f2 ======
CPDPRG[2 waltz16
NUC2 1H
p0 11.25 us
P3 7.50 us
P4 15.00 us
PCPD2 100.00 us
PL2 1.60 dB
PL12 24.60 dB
SFO2 500.2225011 MHz
====== GRADIENT CHANNEL ==
GPNAM[1] SINE.100
GPNAM[2] SINE.100
GPNAM[3] SINE.100
GPX1 0 %
GPX2 0 %
GPX3 0 %
GPY1 0 %
GPY2 0 %
GPY3 0 %
GPZ1 31.00 %
GPZ2 31.00 %
GPZ3 31.00 %
P16 1000.00 us
F2 - Processing parameters
SI 65536
SF 125.7804090 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00
165.560
161.695
147.715
145.185
126.484
119.721
117.744
114.969
110.535
102.176
77.412
77.158
76.904
74.709
73.743
68.586
51.032
44.379
43.140
27.669
27.607
18.369
ppm


BL–2–116–3
1H spectrum
Current Data Parameters
NAME BL-2-116-3
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20141213
Time_ 14.09
INSTRUM qn500
PROBHD 5 mm broadband
PULPROG zg30
TD 81728
SOLVENT CDCl3
NS 8
DS 2
SWH 8012.820 Hz
FIDRES 0.098043 Hz
AQ 5.0998273 sec
RG 1290.2
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 12.00 usec
PL1 -5.80 dB
SFO1 499.1834943 MHz
F2 - Processing parameters
SI 65536
SF 499.1800262 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
1H NMR (500 MHz, CDCl3)
3e
7.283
7.266
7.260
7.246
7.230
4.872
3.315
3.285
3.076
3.006
2.977
2.360
1.932
1.671
5.374
1.000
1.185
3.132
1.180
3.283
3.152
3.075
ppm


Z-restored spin-echo 13C spectrum with 1H decoupling
13C NMR (125 MHz, CDCl3)
3e
Current Data Parameters
NAME BL-2-116-3
EXPNO 3
PROCNO 1
F2 - Acquisition Parameter
Date_ 20141213
Time 16.36
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG SpinEchopg30gp.pr
TD 65536
SOLVENT CDCl3
NS 200
DS 16
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0813440 sec
RG 13004
DW 16.500 us
DE 6.00 us
TE 298.0 K
D1 0.25000000 sec
d11 0.03000000 sec
D16 0.00020000 sec
d17 0.00019600 sec
MCREST 0 sec
MCWRK 0.01500000 sec
P2 33.10 us
======== CHANNEL f1 ======
NUC1 13C
P1 16.55 us
P11 500.00 us
P12 2000.00 us
PL0 120.00 dB
PL1 -1.00 dB
SFO1 125.7942548 MHz
SP1 2.70 dB
SP2 2.70 dB
SPNAM[1] Crp60,0.5,20.1
SPNAM[2] Crp60comp.4
SPOFF1 0 Hz
SPOFF2 0 Hz
======== CHANNEL f2 ======
CPDPRG[2 waltz16
NUC2 1H
PCPD2 100.00 us
PL2 1.60 dB
PL12 24.50 dB
SFO2 500.2225011 MHz
====== GRADIENT CHANNEL ==
GPNAM[1] SINE.100
GPNAM[2] SINE.100
GPX1 0 %
GPX2 0 %
GPY1 0 %
GPY2 0 %
GPZ1 30.00 %
GPZ2 50.00 %
p15 500.00 us
p16 1000.00 us
F2 - Processing parameters
SI 65536
SF 125.7804096 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00
18.191
21.443
24.756
27.853
42.956
44.529
72.424
73.411
73.591
76.904
77.158
77.412
120.411
126.770
129.757
130.736
139.404
162.188
165.749
ppm



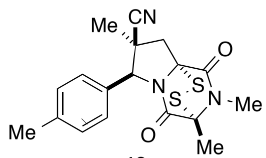
^{1}H NMR (500 MHz, $CDCl_3$)



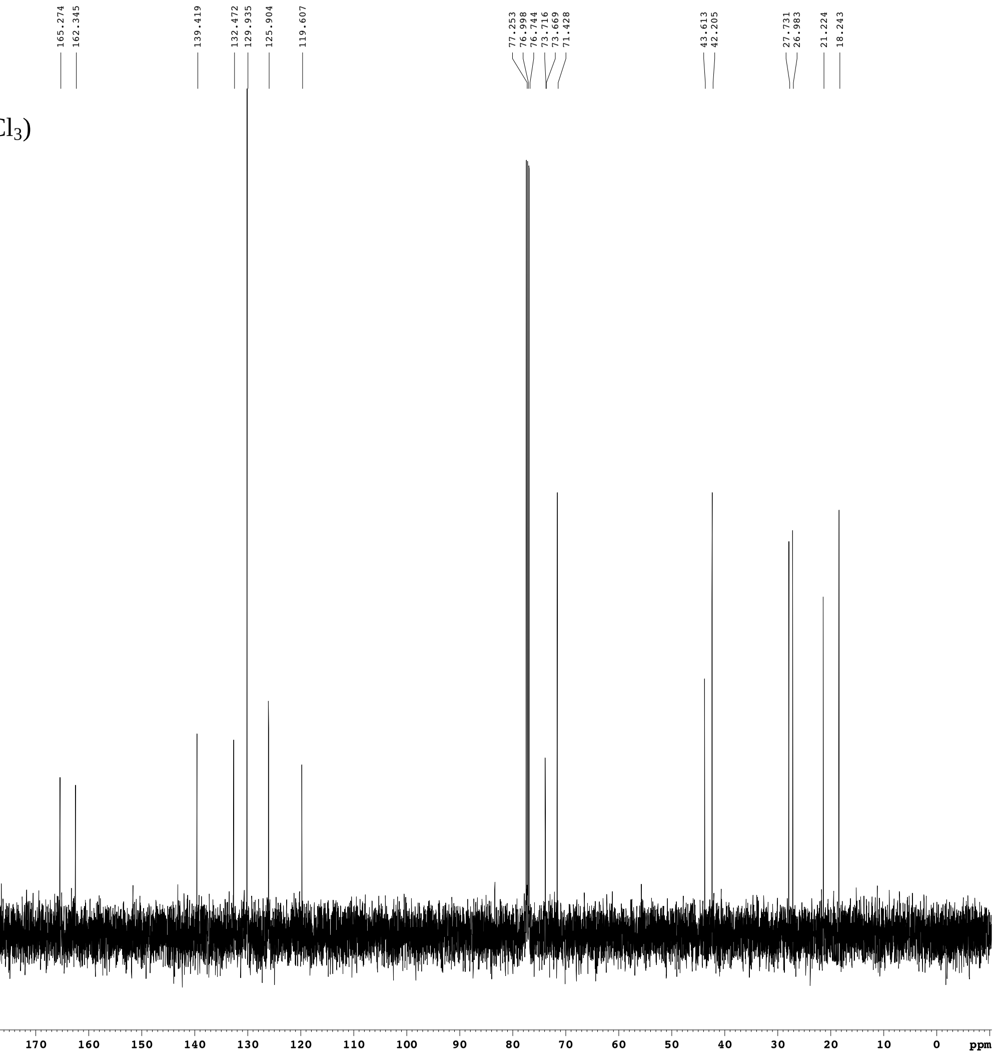
12

Z-restored spin-echo 13C spectrum with 1H decoupling

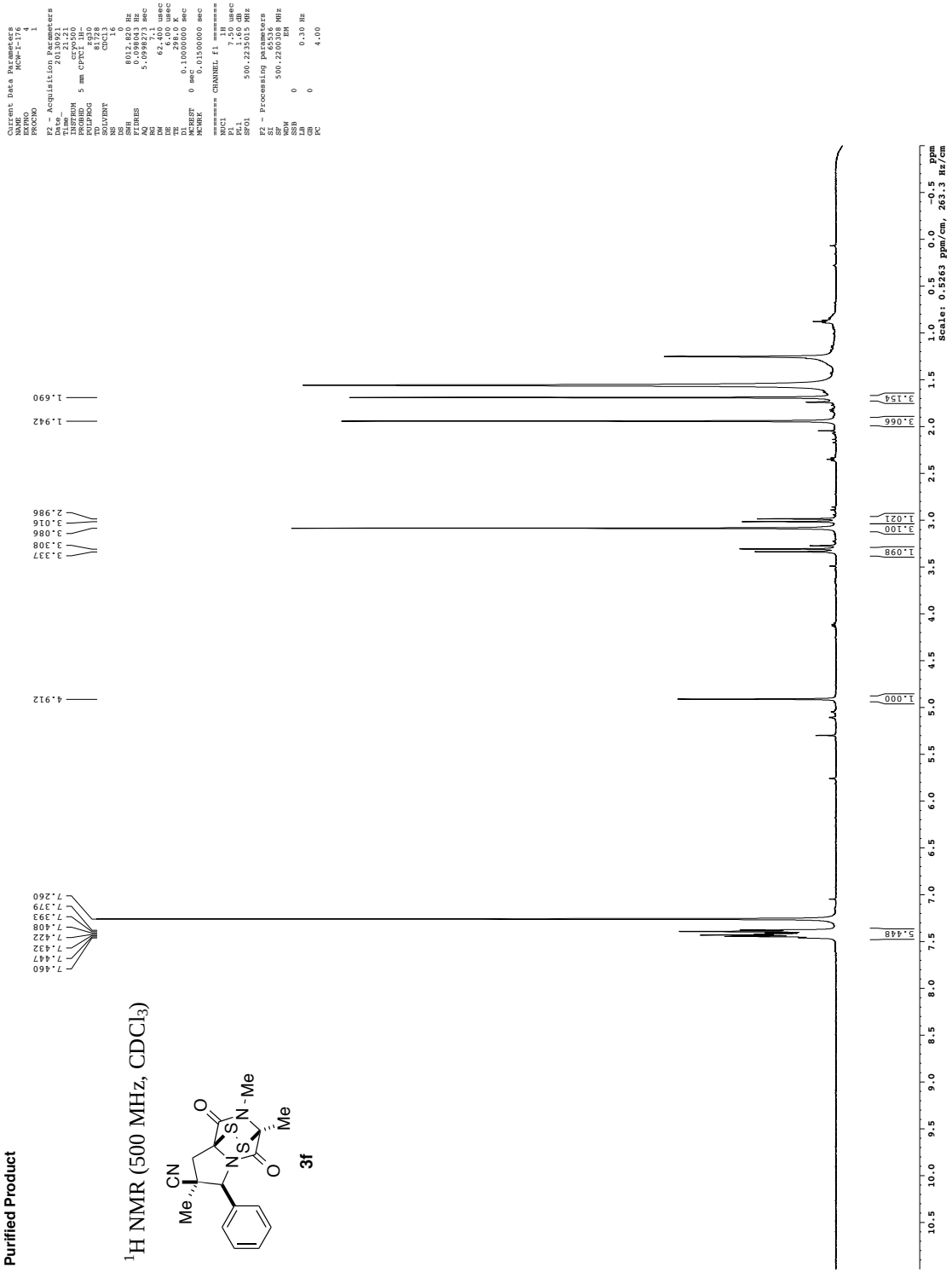
^{13}C NMR (125 MHz, $CDCl_3$)



12



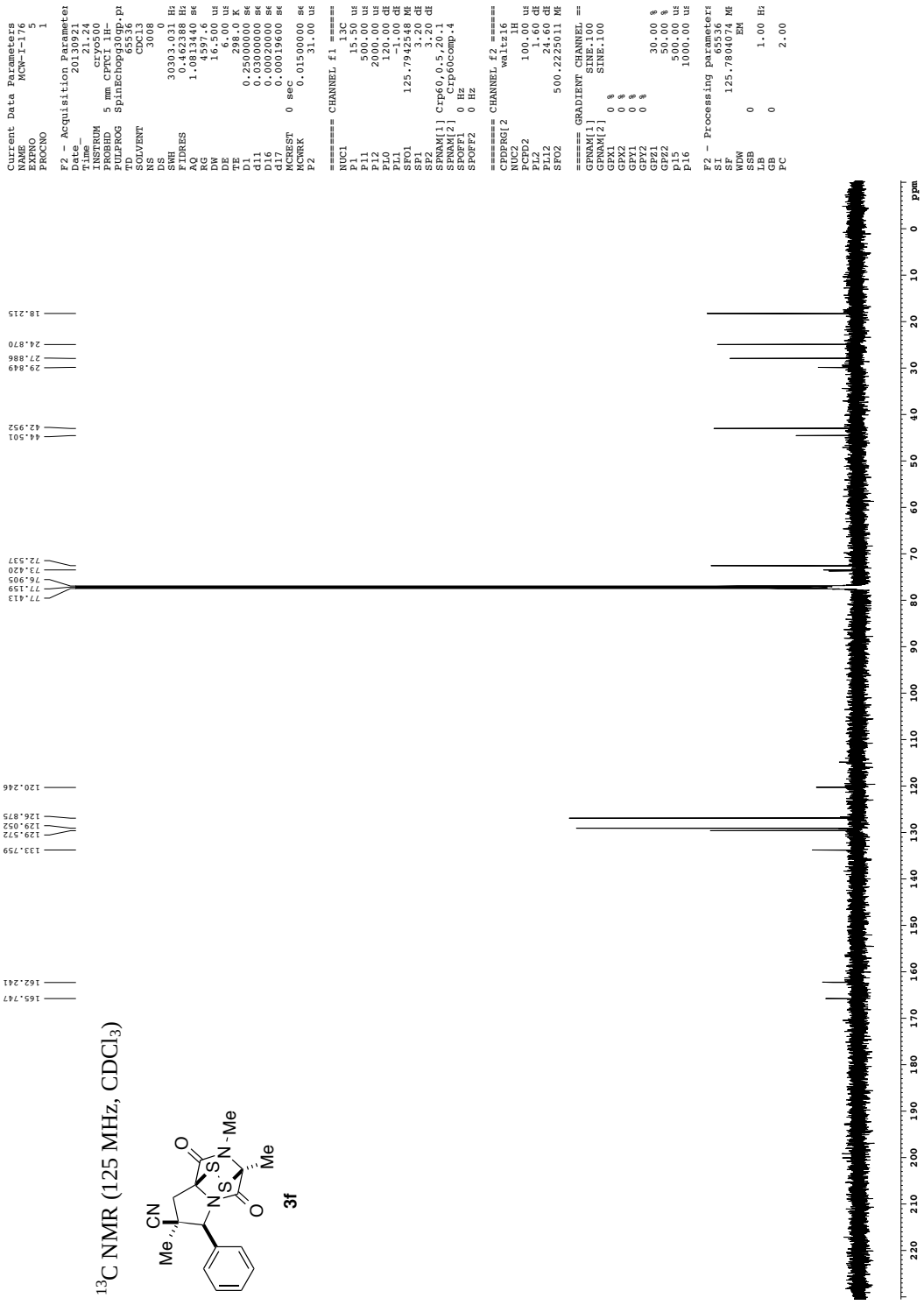

```
Current Data Parameters
NAME        BL-I-302-11
EXPNO                 7
PROCNO                1

F2 - Acquisition Parameter
Date_          20140808
Time               9.05
INSTRUM         cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.pr
TD                65536
SOLVENT           CDCl3
NS                  144
DS                   16
SWH           30303.031 Hz
FIDRES         0.462388 Hz
AQ            1.0813440 se
RG               7298.2
DW               16.500 us
DE                 6.00 us
TE                298.0 K
D1           0.25000000 se
d11          0.03000000 se
D16          0.00020000 se
d17          0.00019600 se
MCREST   0 sec
MCWRK        0.01500000 se
P2                31.00 us

======== CHANNEL f1 ======
NUC1                13C
P1                15.50 us
P11              500.00 us
P12             2000.00 us
PL0              120.00 dB
PL1               -1.00 dB
SFO1        125.7942548 MH
SP1                3.20 dB
SP2                3.20 dB
SPNAM[1] Crp60,0.5,20.1
SPNAM[2]    Crp60comp.4
SPOFF1   0 Hz
SPOFF2   0 Hz

======== CHANNEL f2 ======
CPDPRG[2        waltz16
NUC2                 1H
PCPD2            100.00 us
PL2                1.60 dB
PL12              24.60 dB
SFO2        500.2225011 MH

====== GRADIENT CHANNEL ==
GPNAM[1]       SINE.100
GPNAM[2]       SINE.100
GPX1     0 %
GPX2     0 %
GPY1     0 %
GPY2     0 %
GPZ1              30.00 %
GPZ2              50.00 %
p15              500.00 us
p16             1000.00 us

F2 - Processing parameters
SI                65536
SF          125.7804116 MH
WDW                  EM
SSB      0
LB                 1.00 Hz
GB       0
PC                 2.00
```

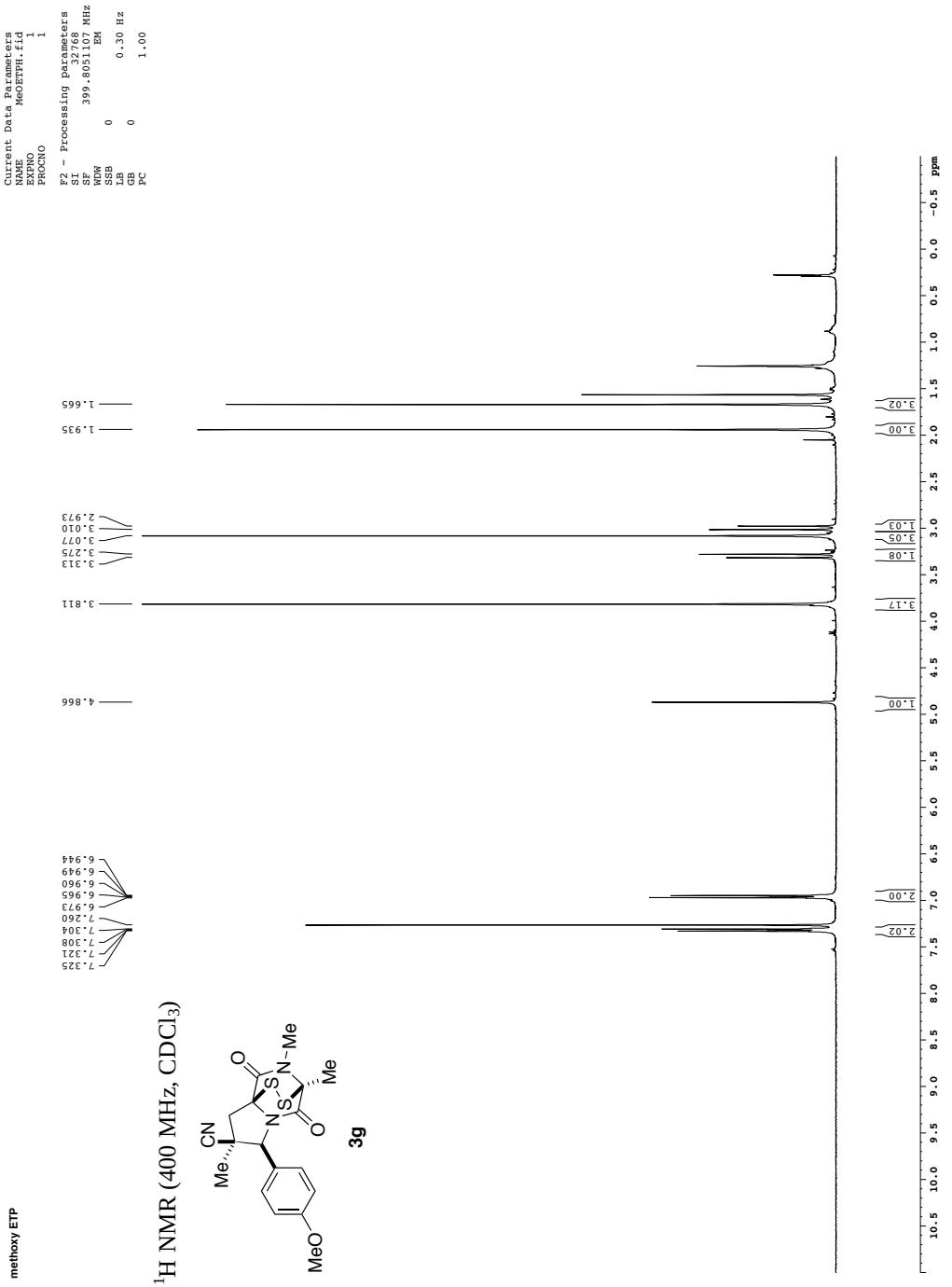

Purified Product
^{1}H NMR (500 MHz, CDCl$_3$)
3f
Current Data Parameters
NAME MCW-I-176
EXPNO 4
PROCNO 1
F2 - Acquisition Parameters
Date_ 20130921
Time 21:21
INSTRUM cryo600
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 81920
SOLVENT CDCl3
NS 16
DS 0
SWH 8012.820 Hz
FIDRES 0.098043 Hz
AQ 5.099873 sec
RG 71.1
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
WURSTEST 0 sec
MCWREK 0.01500000 sec
mmmmmm CHANNEL f1 mmmmmm
NUC1 1H
P1 7.50 usec
PL1 1.60 dB
SFO1 500.2235015 MHz
F2 - Processing parameters
SI 65536
SF 500.2200308 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00
7.460
7.447
7.432
7.422
7.408
7.393
7.379
7.260
4.912
3.337
3.308
3.086
3.016
2.986
1.942
1.690
5.448
1.000
1.098
3.100
1.021
3.066
3.154
ppm
Scale: 0.5263 ppm/cm, 263.3 Hz/cm

Purified Product

^{13}C NMR (125 MHz, $CDCl_3$)

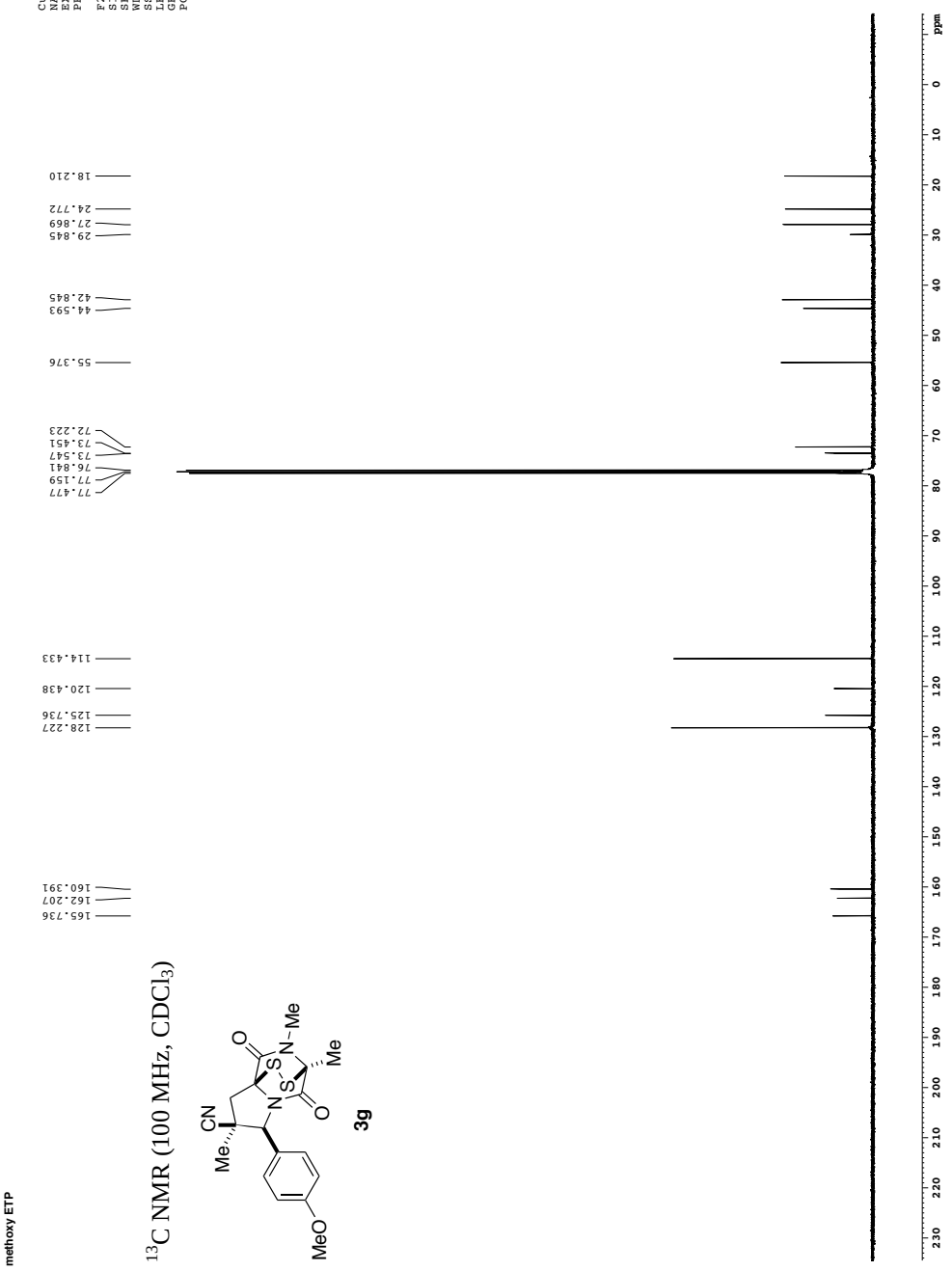
3f

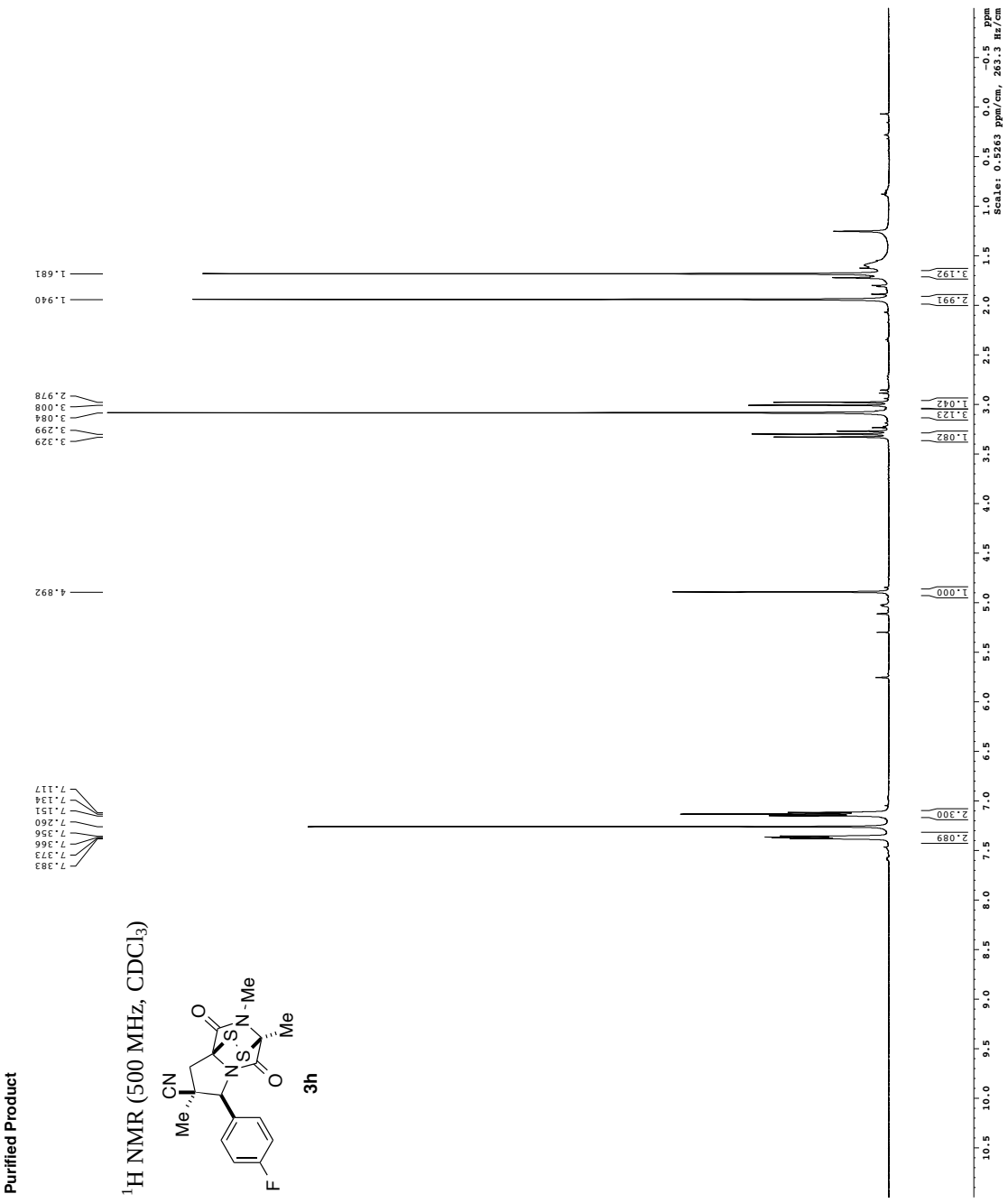


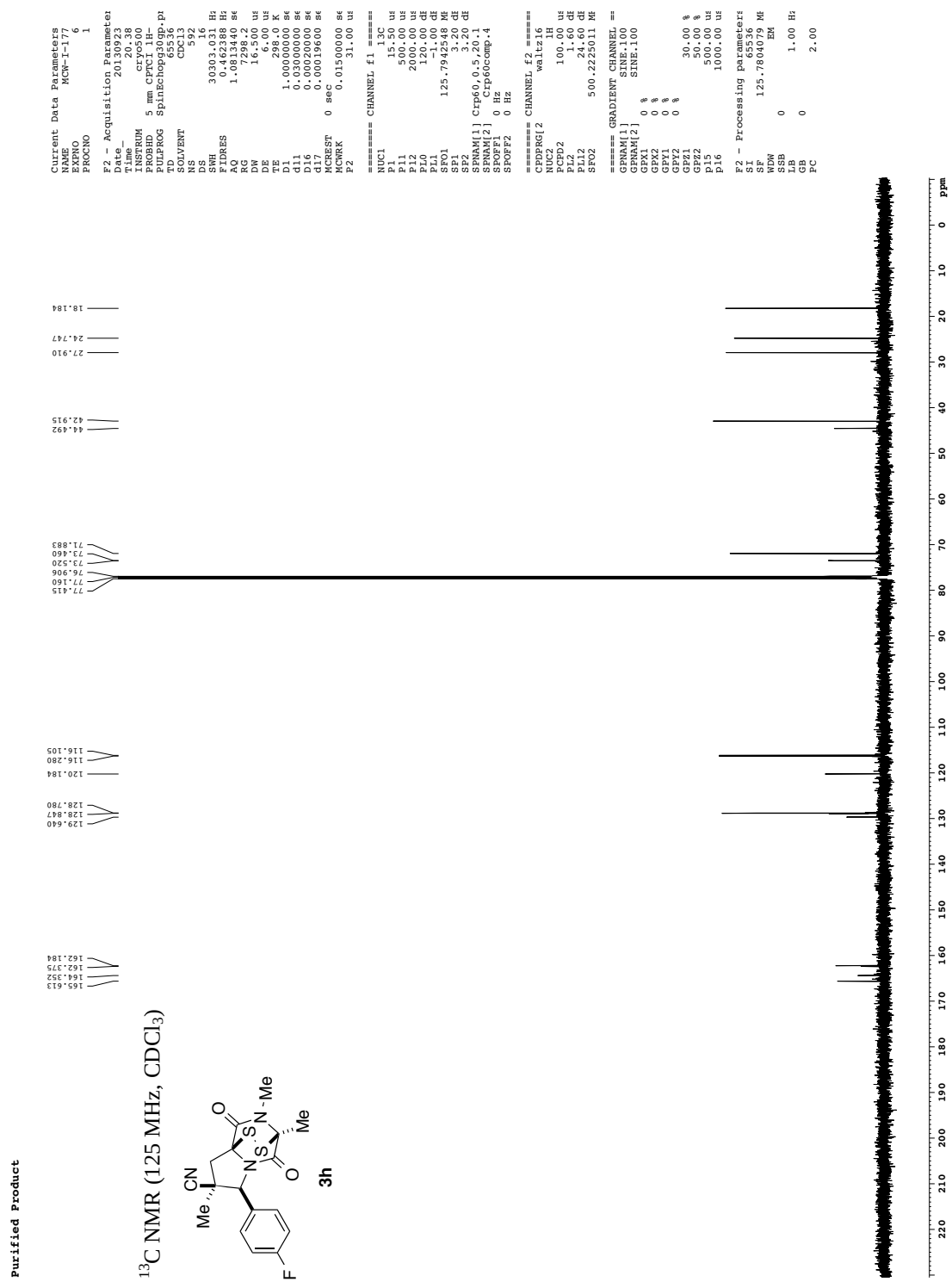


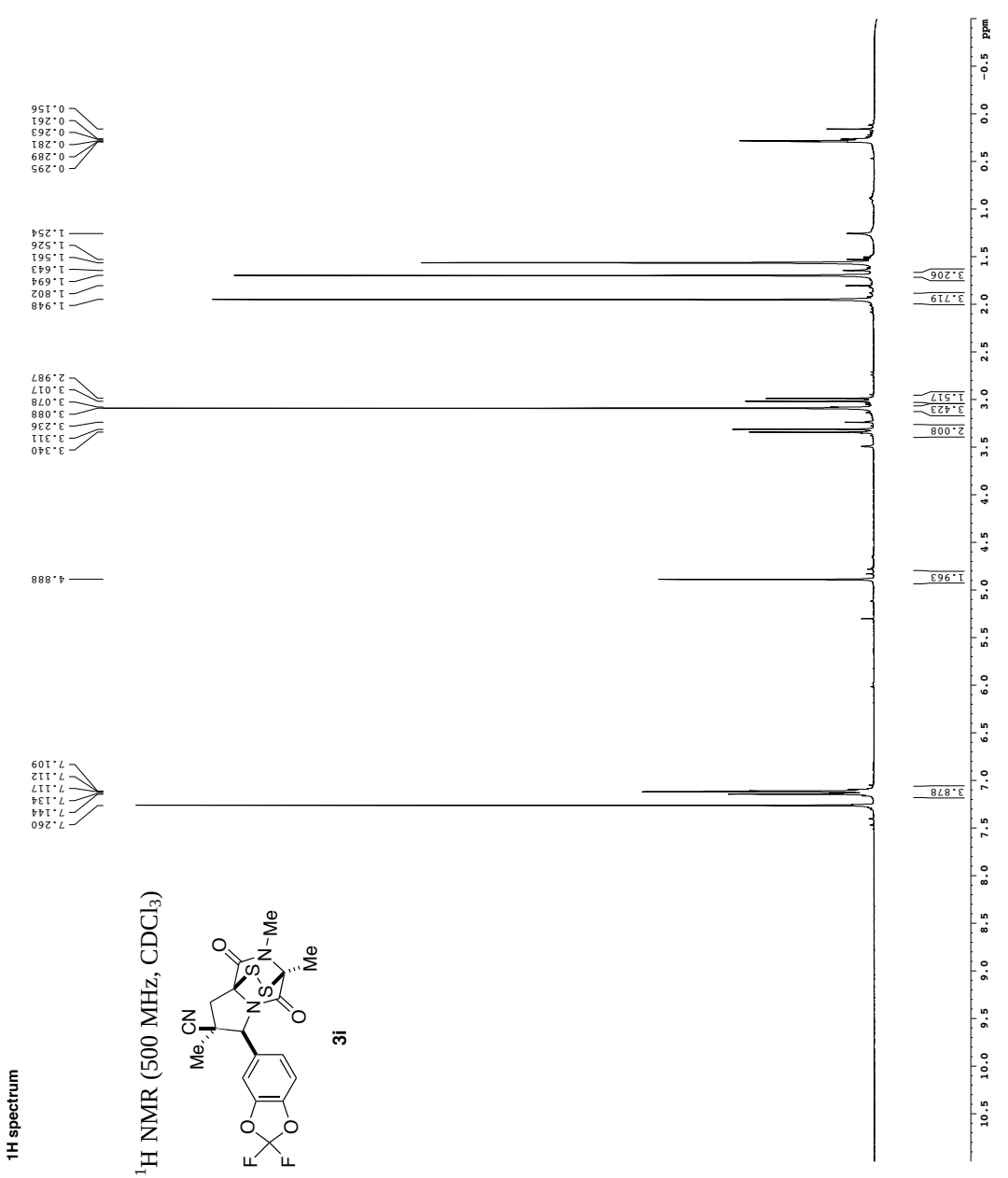
^{1}H NMR (400 MHz, $CDCl_3$)

3g


methoxy ETP
Current Data Parameters
NAME MeOETPC.fid
EXPNO 1
PROCNO 1
F2 - Processing parameters
SI 65536
SF 100.5324904 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
18.210
24.772
27.869
29.845
42.845
44.593
55.376
72.223
73.451
73.547
76.841
77.159
77.477
114.433
120.438
125.736
128.227
160.391
162.207
165.736
ppm
^{13}C NMR (100 MHz, CDCl$_3$)
3g

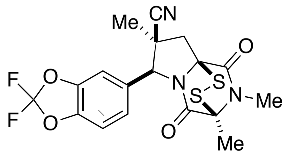

Purified Product
^{1}H NMR (500 MHz, $CDCl_3$)
3h
Current Data Parameters
NAME MCW-I-177
EXPNO 5
PROCNO 1
F2 - Acquisition Parameters
Date_ 20130923
Time 20.34
INSTRUM spect
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 81928
SOLVENT CDCl3
NS 8
DS 2
SWH 8012.820 Hz
FIDRES 0.098043 Hz
AQ 5.099827 sec
RG 2
DW 62.400 usec
DE 6.00 usec
TE 296.0 K
D1 0.10000000 sec
MCWREST 0 sec
MCWPRK 0.01500000 sec
mmmmmm CHANNEL f1 mmmmmm
NUC1 1H
P1 7.50 usec
PL1 1.60 dB
SFO1 500.2235015 MHz
F2 - Processing parameters
SI 65536
SF 500.2200307 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00
7.383
7.373
7.366
7.356
7.260
7.151
7.134
7.117
4.892
3.329
3.299
3.084
3.008
2.978
1.940
1.681
1.000
2.089
2.300
1.082
1.042
1.123
2.991
1.192
Scale: 0.5263 ppm/cm, 263.3 Hz/cm
ppm


Purified Product
^{13}C NMR (125 MHz, CDCl$_3$)
3h
Current Data Parameters
NAME MCW-I-177
EXPNO 6
PROCNO 1
F2 - Acquisition Parameters
Date_ 20130923
Time 20.38
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zgpg30.pr
TD 65536
SOLVENT CDCl3
NS 592
DS 16
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0813440 sec
RG 71208.2
DW 16.500 usec
DE 6.00 usec
TE 298.0 K
D1 1.00000000 sec
d11 0.03000000 sec
D16 0.00020000 sec
D17 0.00019600 sec
MCREST 0 sec
MCWRK 0.01500000 sec
P2 31.00 usec
CHANNEL f1
NUC1 13C
P1 15.50 usec
P11 500.00 usec
P12 2000.00 usec
PL0 120.00 dB
PL1 -1.00 dB
SFO1 125.7942548 MHz
SP1 3.20 dB
SPNAM[1] Crp60,0.5,20.1
SPNAM[2] Crp60comp.4
SPOFF1 0 Hz
SPOFF2 0 Hz
CHANNEL f2
CPDPRG[2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 1.60 dB
PL12 24.60 dB
SFO2 500.2225011 MHz
GRADIENT CHANNEL
GPNAM[1] SINE.100
GPNAM[2] SINE.100
GPX1 0 %
GPX2 0 %
GPY1 0 %
GPY2 0 %
GPZ1 30.00 %
GPZ2 50.00 %
p15 500.00 usec
p16 1000.00 usec
F2 - Processing parameters
SI 65536
SF 125.7804079 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00
18.184
24.747
27.910
42.915
44.492
71.883
73.460
73.520
76.906
77.160
77.415
116.105
116.280
120.184
128.780
128.847
129.640
162.184
162.375
164.352
165.613
ppm

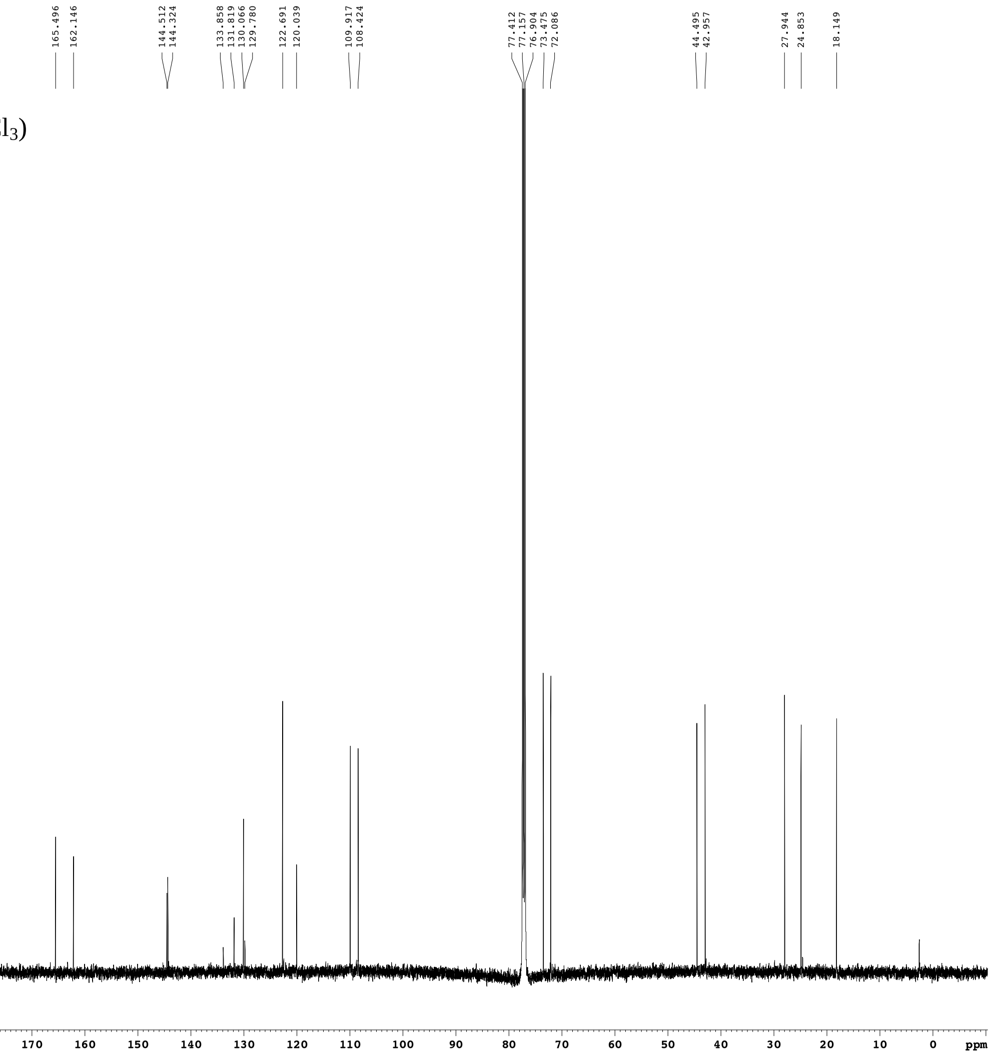

1H spectrum
^{1}H NMR (500 MHz, CDCl$_3$)
3i
Current Data Parameters
NAME MB2-251a
EXPNO 8
PROCNO 1
F2 - Acquisition Parameters
Date_ 20130124
Time_ 21.58
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 81728
SOLVENT CDCl3
NS 8
DS 2
SWH 8012.820 Hz
FIDRES 0.098043 Hz
AQ 5.0998273 sec
RG 71
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0 sec 0.01500000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 7.50 usec
PL1 1.60 dB
SFO1 500.2235015 MHz
F2 - Processing parameters
SI 65536
SF 500.2200311 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00
7.260
7.144
7.134
7.117
7.112
7.109
4.888
3.340
3.311
3.236
3.088
3.078
3.017
2.987
1.948
1.802
1.694
1.643
1.561
1.526
1.254
0.295
0.289
0.281
0.263
0.261
0.156
3.878
1.963
2.008
3.423
1.517
3.719
3.206
ppm

Z-restored spin-echo 13C spectrum with 1H decoupling

^{13}C NMR (125 MHz, $CDCl_3$)



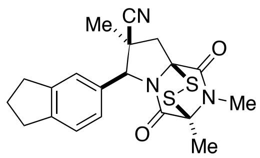
3i



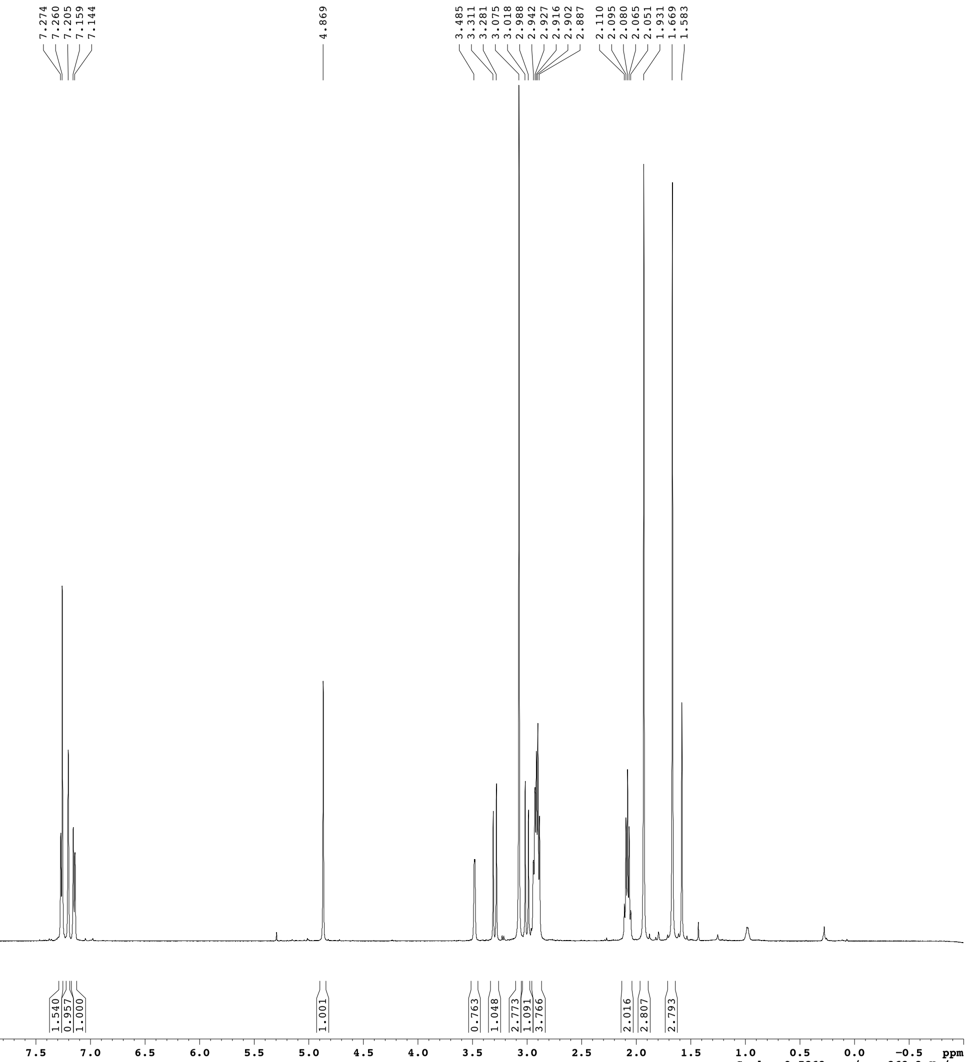

```
Current Data Parameters
NAME          MB2-251a
EXPNO                9
PROCNO               1

F2 - Acquisition Parameter
Date_         20130124
Time             22.03
INSTRUM        cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG  SpinEchopg30gp.pr
TD               65536
SOLVENT          CDCl3
NS                3500
DS                  16
SWH          30303.031 Hz
FIDRES        0.462388 Hz
AQ           1.0813440 se
RG              7298.2
DW              16.500 us
DE                6.00 us
TE               298.0 K
D1          3.00000000 se
d11         0.03000000 se
D16         0.00020000 se
d17         0.00019600 se
MCREST   0 sec
MCWRK       0.01500000 se
P2               31.00 us

======== CHANNEL f1 ======
NUC1               13C
P1               15.50 us
P11             500.00 us
P12            2000.00 us
PL0             120.00 dB
PL1              -1.00 dB
SFO1       125.7942548 MH
SP1               3.20 dB
SP2               3.20 dB
SPNAM[1] Crp60,0.5,20.1
SPNAM[2]    Crp60comp.4
SPOFF1   0 Hz
SPOFF2   0 Hz

======== CHANNEL f2 ======
CPDPRG[2         waltz16
NUC2                  1H
PCPD2             100.00 us
PL2                 1.60 dB
PL12               24.60 dB
SFO2         500.2225011 MH

====== GRADIENT CHANNEL ==
GPNAM[1]        SINE.100
GPNAM[2]        SINE.100
GPX1      0 %
GPX2      0 %
GPY1      0 %
GPY2      0 %
GPZ1               30.00 %
GPZ2               50.00 %
p15               500.00 us
p16              1000.00 us

F2 - Processing parameters
SI                 65536
SF           125.7804080 MH
WDW                   EM
SSB      0
LB                  1.00 Hz
GB       0
PC                  2.00
```

1H spectrum

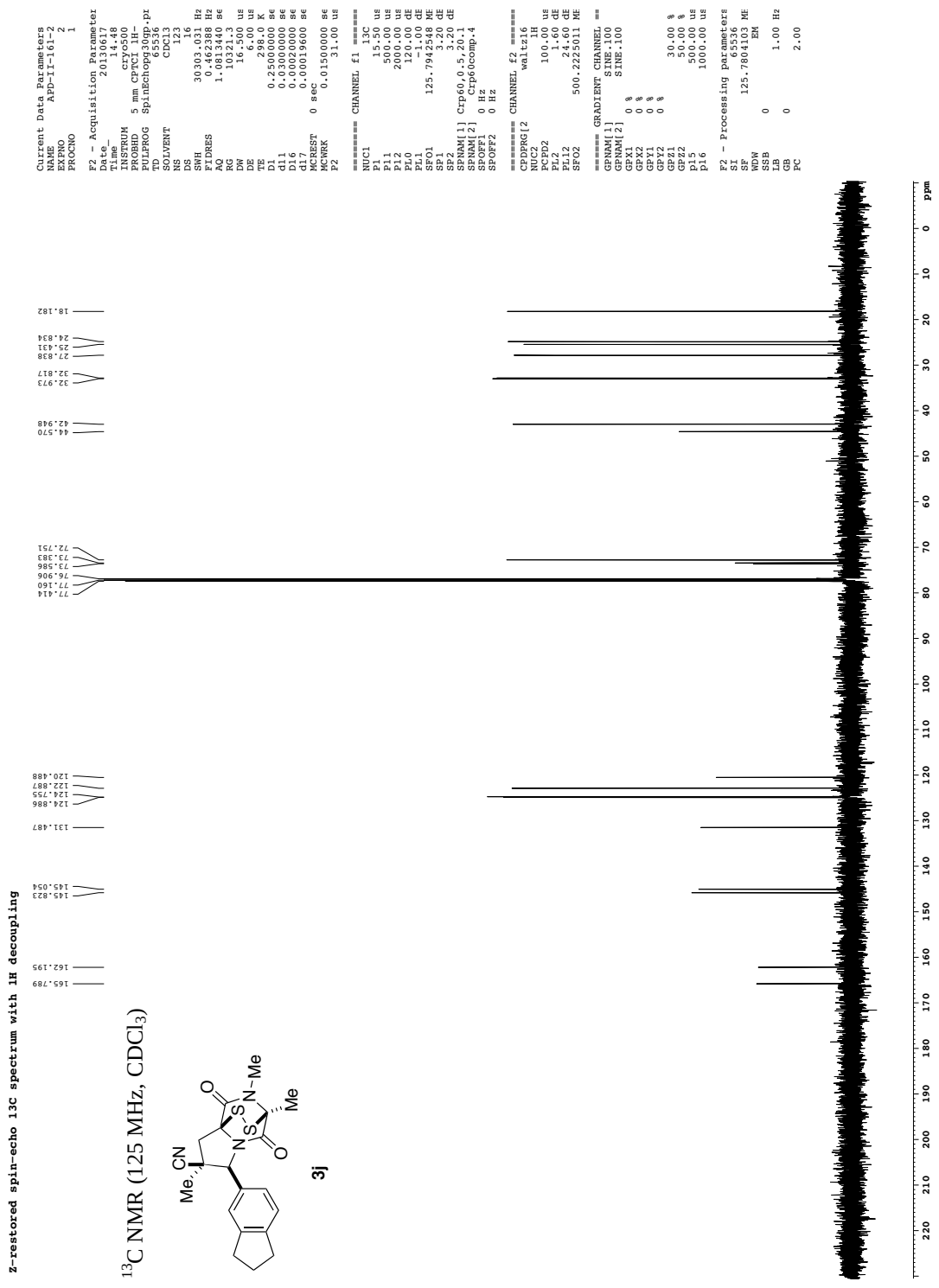
^{1}H NMR (500 MHz, $CDCl_3$)

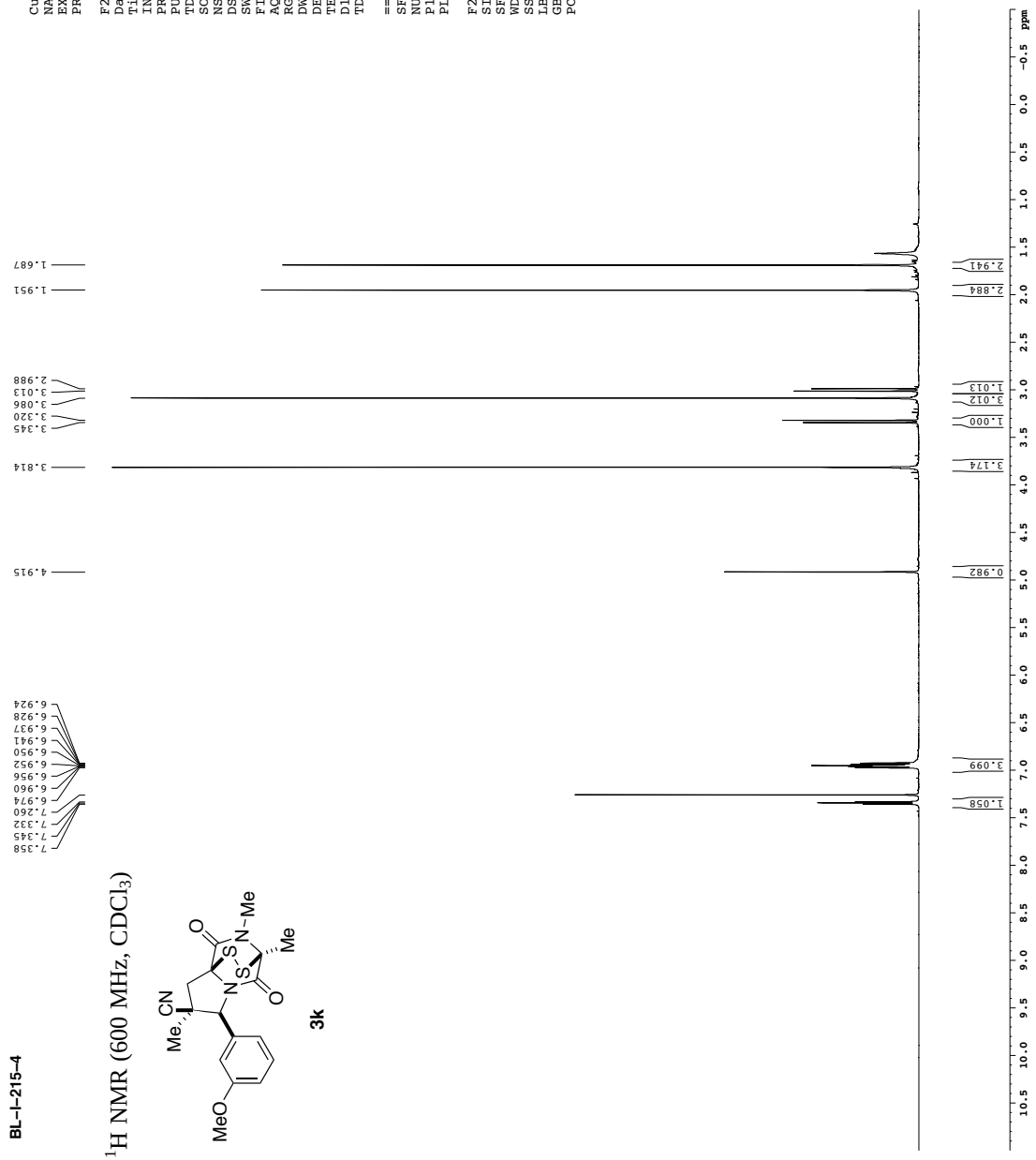


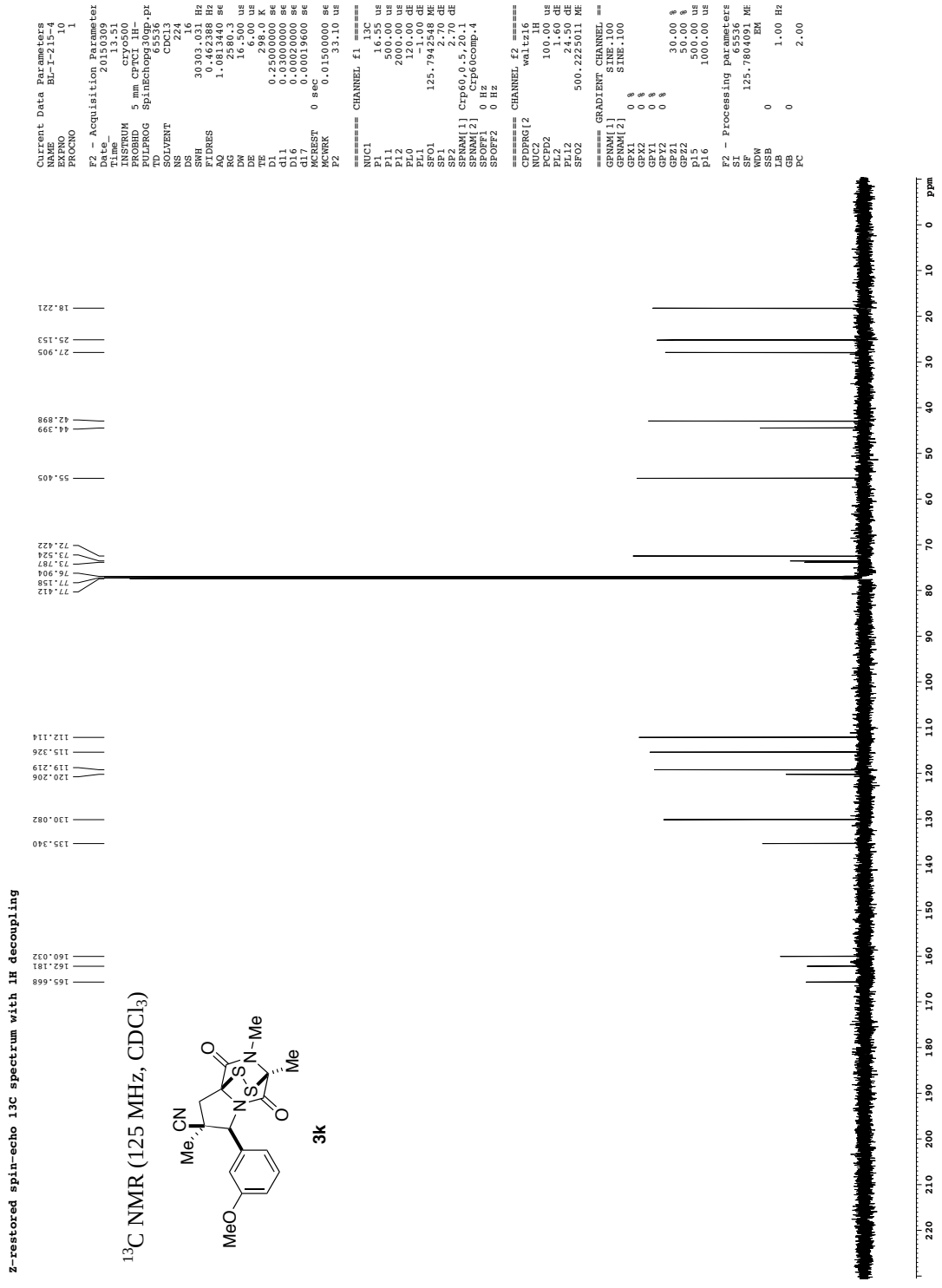
3j

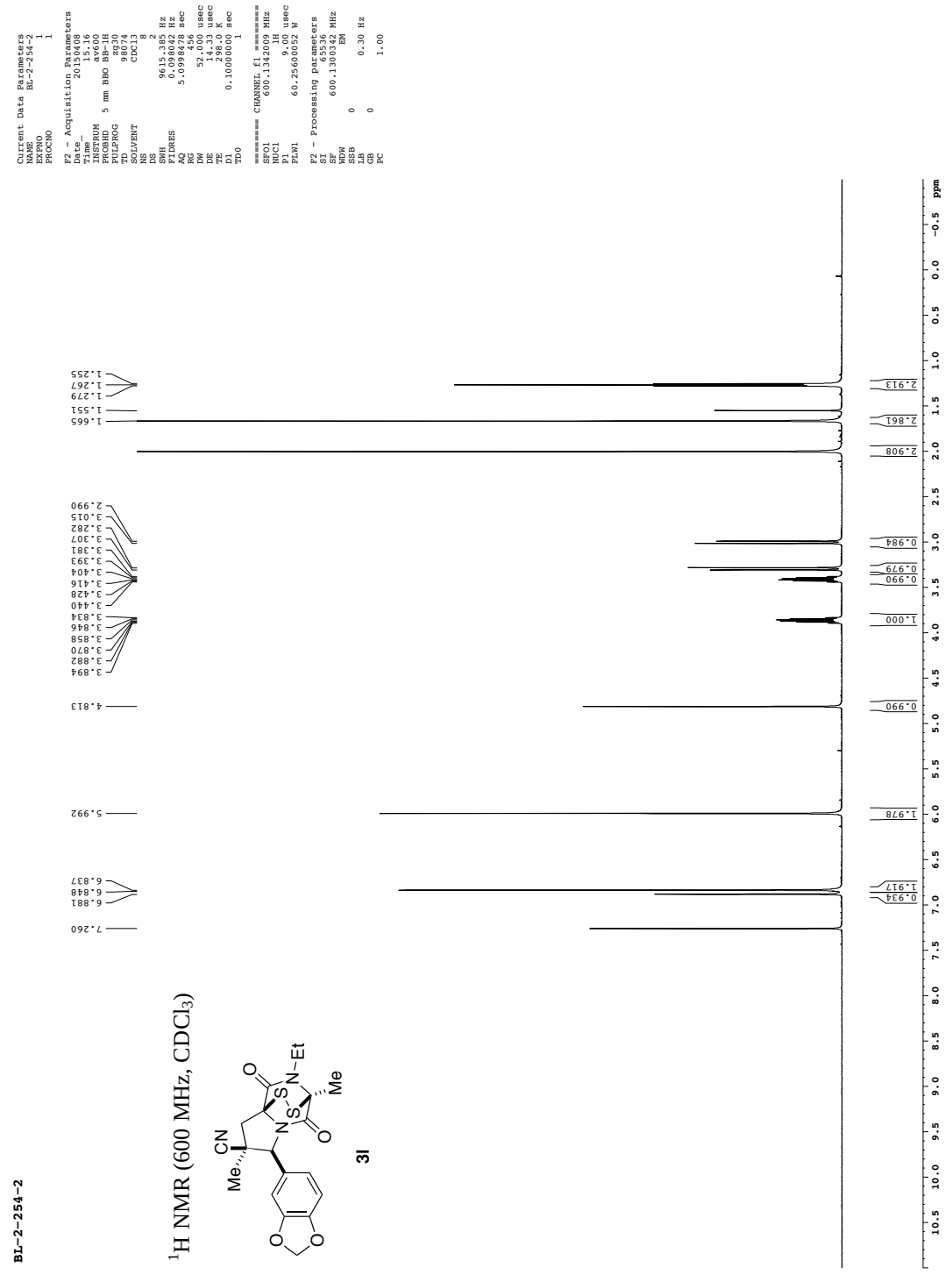


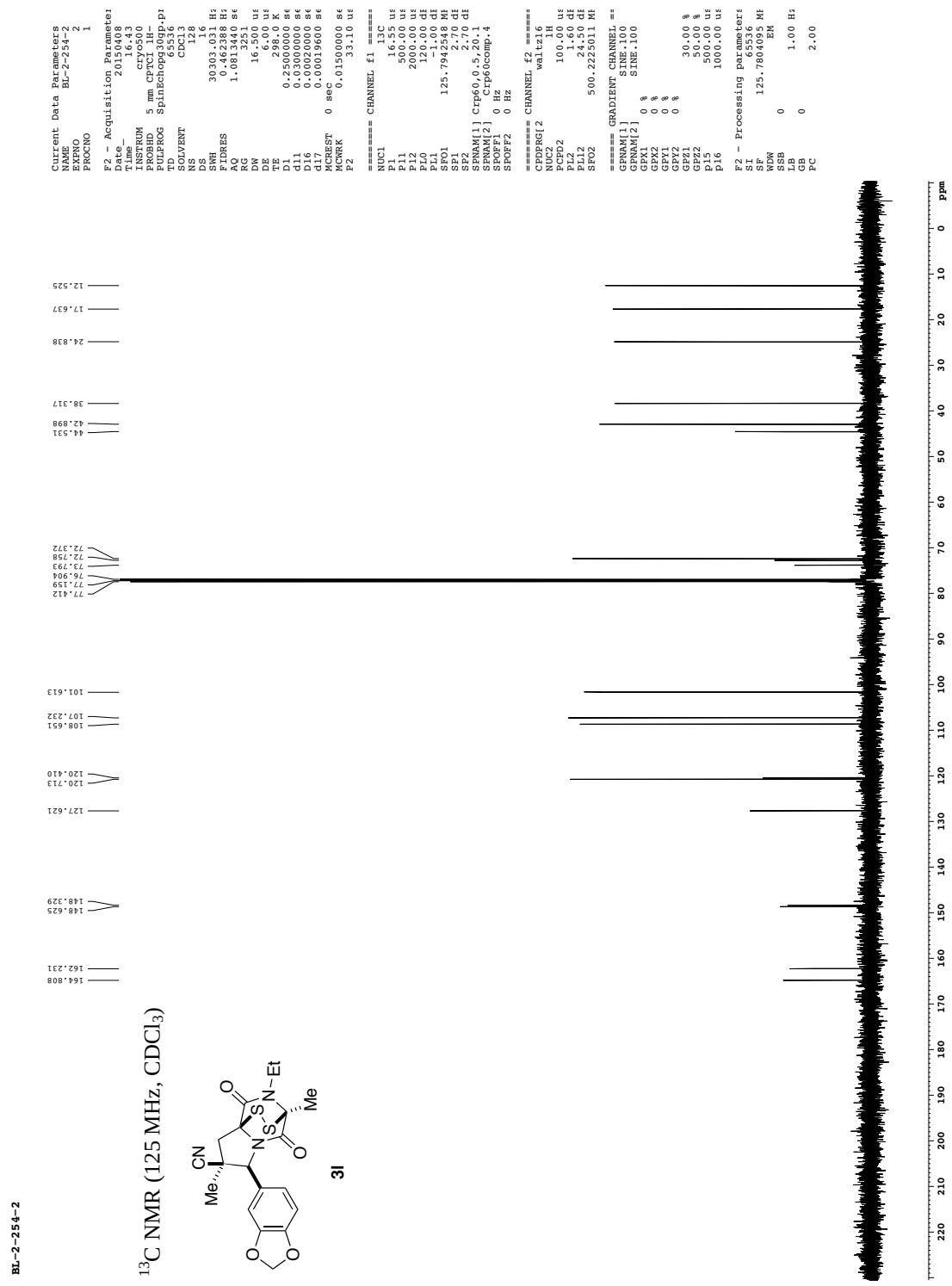

```
Current Data Parameters
NAME        APD-II-161-2
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20130617
Time               14.46
INSTRUM         cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG             zg30
TD                 81728
SOLVENT            CDCl3
NS                     8
DS                     2
SWH             8012.820 Hz
FIDRES          0.098043 Hz
AQ             5.0998273 sec
RG                   6.3
DW                62.400 usec
DE                  6.00 usec
TE                 298.0 K
D1            0.10000000 sec
MCREST   0 sec
MCWRK         0.01500000 sec

======== CHANNEL f1 ========
NUC1                  1H
P1                  7.50 usec
PL1                 1.60 dB
SFO1         500.2235015 MHz

F2 - Processing parameters
SI                 65536
SF           500.2200313 MHz
WDW                   EM
SSB      0
LB                  0.30 Hz
GB       0
PC                  4.00
```

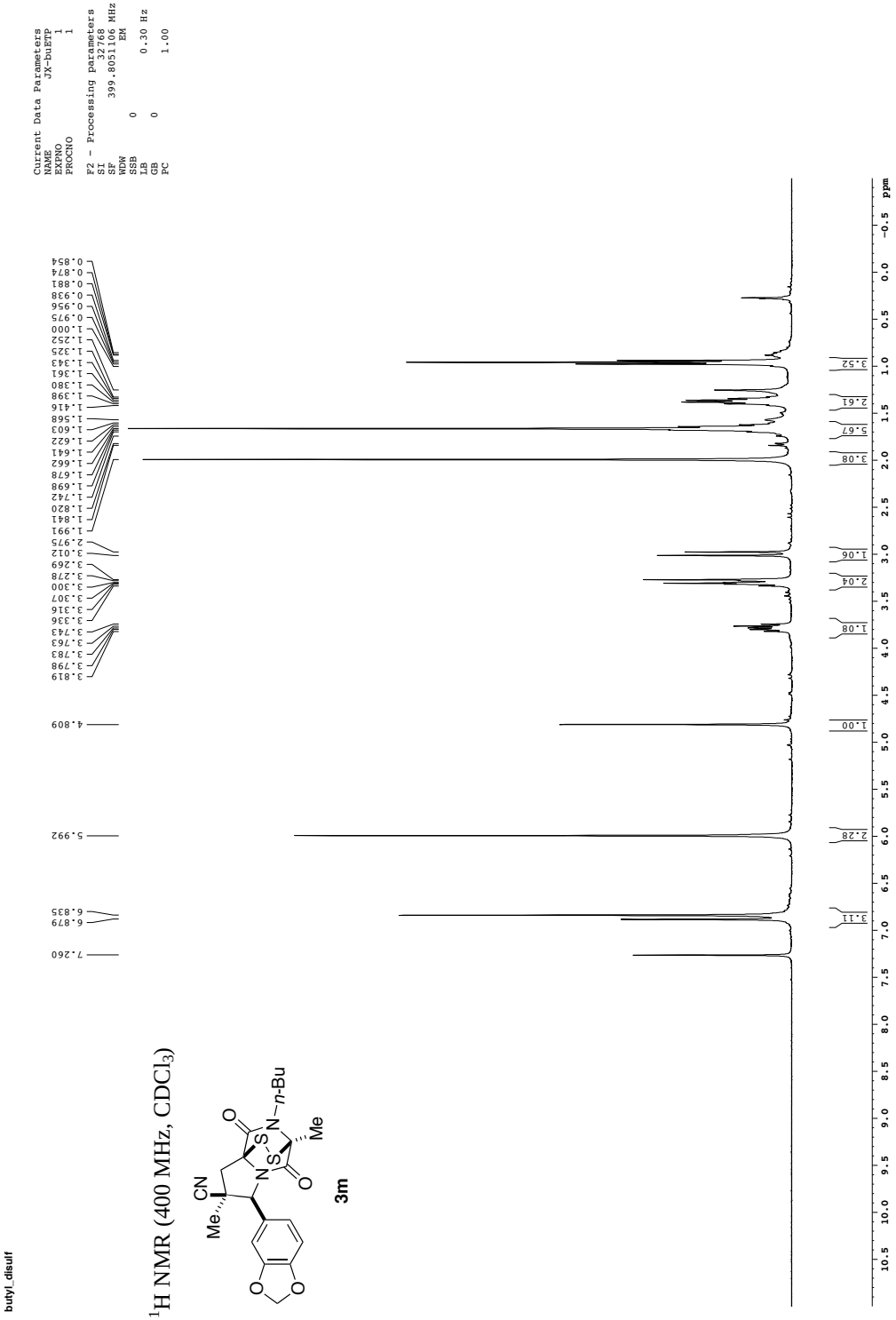

Z-restored spin-echo 13C spectrum with 1H decoupling
13C NMR (125 MHz, CDCl3)
3j
Current Data Parameters
NAME APD-II-161-2
EXPNO 2
PROCNO 1
F2 - Acquisition Parameter
Date_ 20130617
Time 14.48
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG SpinEchopg30gp.pr
TD 65536
SOLVENT CDCl3
NS 16
DS 16
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0813440 sec
RG 10321.3
DW 16.500 us
DE 6.00 us
TE 298.0 K
D1 0.25000000 sec
d11 0.03000000 sec
D16 0.00020000 sec
d17 0.00019600 sec
MCREST 0 sec
MCWRK 0.01500000 sec
P2 31.00 us
======== CHANNEL f1 ======
NUC1 13C
P1 15.50 us
P11 500.00 us
P12 2000.00 us
PL0 120.00 dB
PL1 -1.00 dB
SFO1 125.7942548 MHz
SP1 3.20 dB
SP2 3.20 dB
SPNAM[1] Crp60,0.5,20.1
SPNAM[2] Crp60comp.4
SPOFF1 0 Hz
SPOFF2 0 Hz
======== CHANNEL f2 ======
CPDPRG[2 waltz16
NUC2 1H
PCPD2 100.00 us
PL2 1.60 dB
PL12 24.60 dB
SFO2 500.2225011 MHz
====== GRADIENT CHANNEL ==
GPNAM[1] SINE.100
GPNAM[2] SINE.100
GPX1 0 %
GPX2 0 %
GPY1 0 %
GPY2 0 %
GPZ1 30.00 %
GPZ2 50.00 %
p15 500.00 us
p16 1000.00 us
F2 - Processing parameters
SI 65536
SF 125.7804103 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00
18.182
24.834
25.431
27.838
32.817
32.973
42.948
44.570
72.751
73.383
73.586
76.906
77.160
77.414
120.488
122.887
124.755
124.886
131.487
145.054
145.823
162.195
165.789
ppm

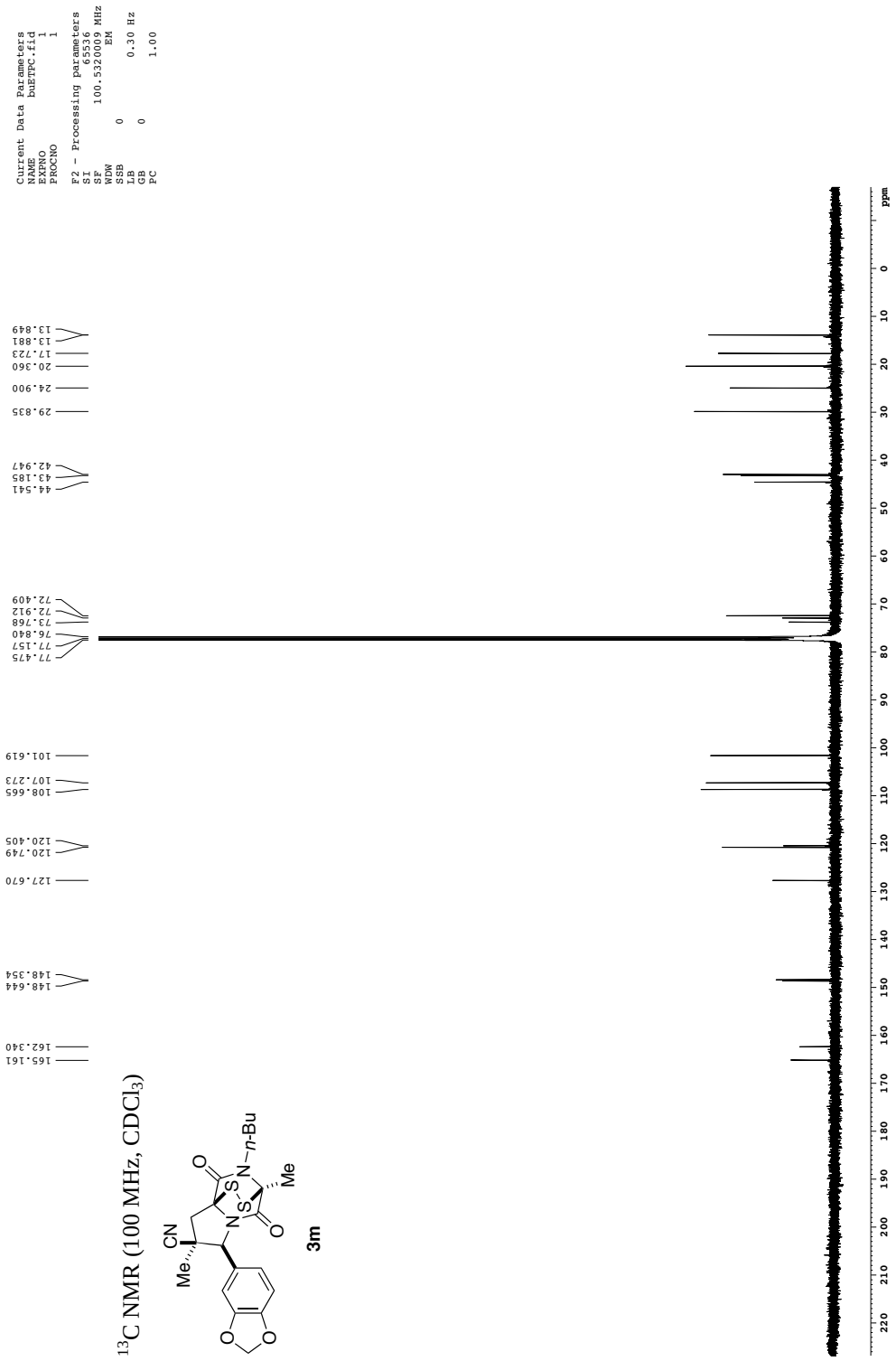

BL-I-215-4
^{1}H NMR (600 MHz, CDCl$_3$)
3k
Current Data Parameters
NAME BL-I-215-4
EXPNO 6
PROCNO 1
F2 - Acquisition Parameters
Date_ 20150309
Time_ 9.32
INSTRUM av600
PROBHD 5 mm TBI 1H/13
PULPROG zg30
TD 98074
SOLVENT CDCl3
NS 8
DS 2
SWH 9615.385 Hz
FIDRES 0.098042 Hz
AQ 5.0998478 sec
RG 512
DW 52.000 usec
DE 14.54 usec
TE 298.1 K
D1 0.10000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 600.1342009 MHz
NUC1 1H
P1 8.00 usec
PLW1 23.01441956 W
F2 - Processing parameters
SI 65536
SF 600.1300338 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
7.358
7.345
7.332
7.260
6.974
6.960
6.956
6.950
6.952
6.941
6.937
6.928
6.924
4.915
3.814
3.345
3.320
3.086
3.013
2.988
1.951
1.687
1.058
3.099
0.982
3.174
1.000
3.012
1.013
2.884
2.941
ppm


Z-restored spin-echo 13C spectrum with 1H decoupling
13C NMR (125 MHz, CDCl3)
3k
Current Data Parameters
NAME BL-I-215-4
EXPNO 10
PROCNO 1
F2 - Acquisition Parameter
Date_ 20150309
Time 13.51
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG SpinEchopg3Ugp.pr
TD 65536
SOLVENT CDCl3
NS 224
DS 16
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0813440 sec
RG 2580.3
DW 16.500 us
DE 6.00 us
TE 298.0 K
D1 0.25000000 sec
d11 0.03000000 sec
D16 0.00020000 sec
d17 0.00019600 sec
MCREST 0 sec 0.01500000 sec
MCWRK 0.01500000 sec
P2 33.10 us
======== CHANNEL f1 ======
NUC1 13C
P1 16.55 us
P11 500.00 us
P12 2000.00 us
PL0 120.00 dB
PL1 -1.00 dB
SFO1 125.7942548 MHz
SP1 2.70 dB
SP2 2.70 dB
SPNAM[1] Crp60,0.5,20.1
SPNAM[2] Crp60comp.4
SPOFF1 0 Hz
SPOFF2 0 Hz
======== CHANNEL f2 ======
CPDPRG[2 waltz16
NUC2 1H
PCPD2 100.00 us
PL2 1.60 dB
PL12 24.50 dB
SFO2 500.2225011 MHz
====== GRADIENT CHANNEL ==
GPNAM[1] SINE.100
GPNAM[2] SINE.100
GPX1 0 %
GPX2 0 %
GPY1 0 %
GPY2 0 %
GPZ1 30.00 %
GPZ2 50.00 %
p15 500.00 us
p16 1000.00 us
F2 - Processing parameters
SI 65536
SF 125.7804091 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00
18.221
25.153
27.905
42.898
44.399
55.405
72.422
73.524
73.787
76.904
77.158
77.412
112.114
115.326
119.219
120.206
130.082
135.340
160.032
162.181
165.668
ppm


BL-2-254-2
^{1}H NMR (600 MHz, CDCl$_3$)
3l
Current Data Parameters
NAME BL-2-254-2
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20150408
Time 15.16
INSTRUM 400-UH
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 98074
SOLVENT CDCl3
NS 8
DS 2
SWH 9615.385 Hz
FIDRES 0.098042 Hz
AQ 5.099648 sec
RG 456
DW 52.000 usec
DE 14.33 usec
TE 298.0 K
D1 0.10000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 600.1342009 MHz
NUC1 1H
P1 9.00 usec
PLW1 60.25600052 W
F2 - Processing parameters
SI 65536
SF 600.1300342 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
7.260
6.881
6.848
6.837
5.992
4.813
3.894
3.882
3.870
3.858
3.846
3.834
3.440
3.428
3.416
3.404
3.393
3.381
3.307
3.282
3.015
2.990
1.665
1.551
1.279
1.267
1.255
2.913
2.861
2.908
0.984
0.979
0.990
1.000
0.990
1.978
0.934
1.917
ppm


BL-2-254-2
^{13}C NMR (125 MHz, CDCl$_3$)
3l
Current Data Parameters
NAME BL-2-254-2
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20150408
Time 16.43
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG spinEchopg3gp.p1
TD 65536
SOLVENT CDCl3
NS 128
DS 16
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0813440 sec
RG 203.1
DW 16.500 us
DE 6.00 us
TE 298.0 K
D1 0.25000000 sec
d11 0.03000000 sec
D16 0.00020000 sec
d12 0.00019600 sec
MCREST 0 sec 0.01500000 sec
MCWRK 0.01500000 sec
P2 33.10 us
======== CHANNEL f1 ========
NUC1 13C
P1 16.55 us
P11 500.00 us
P12 2000.00 us
PL0 120.00 dB
PL1 -1.00 dB
SFO1 125.7942548 MHz
SP1 2.70 dB
SP2 2.70 dB
SPNAM[1] Crp60,0.5,20.1
SPNAM[2] Crp60comp.4
SPOFF1 0 Hz
SPOFF2 0 Hz
======== CHANNEL f2 ========
CPDPRG[2 waltz16
NUC2 1H
PCPD2 100.00 us
PL2 1.60 dB
PL12 24.50 dB
SFO2 500.2225011 MHz
====== GRADIENT CHANNEL ==
GPNAM[1] SINE.100
GPNAM[2] SINE.100
GPX1 0 %
GPX2 0 %
GPY1 0 %
GPY2 0 %
GPZ1 30.00 %
GPZ2 50.00 %
p15 500.00 us
p16 1000.00 us
F2 - Processing parameters
SI 65536
SF 125.7804095 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00
164.808
162.231
148.625
148.329
127.621
120.713
120.410
108.651
107.232
101.613
77.412
77.159
76.904
73.793
72.758
72.372
44.531
42.898
38.317
24.838
17.637
12.525
ppm


butyl_disulf
Current Data Parameters
NAME JX-buETP
EXPNO 1
PROCNO 1
F2 - Processing parameters
SI 27648
SF 399.8051106 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
^{1}H NMR (400 MHz, CDCl$_3$)
3m
n-Bu
Me
CN
Me
7.260
6.879
6.835
5.992
4.809
3.819
3.798
3.783
3.763
3.743
3.336
3.316
3.307
3.300
3.278
3.269
3.012
2.975
1.991
1.841
1.820
1.742
1.698
1.678
1.662
1.641
1.603
1.622
1.568
1.416
1.398
1.380
1.361
1.343
1.325
1.252
1.000
0.975
0.956
0.938
0.881
0.874
0.854
3.11
2.28
1.00
1.08
2.04
1.06
3.08
5.67
2.61
3.52
ppm

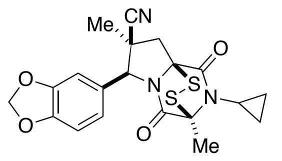


^{13}C NMR (100 MHz, $CDCl_3$)

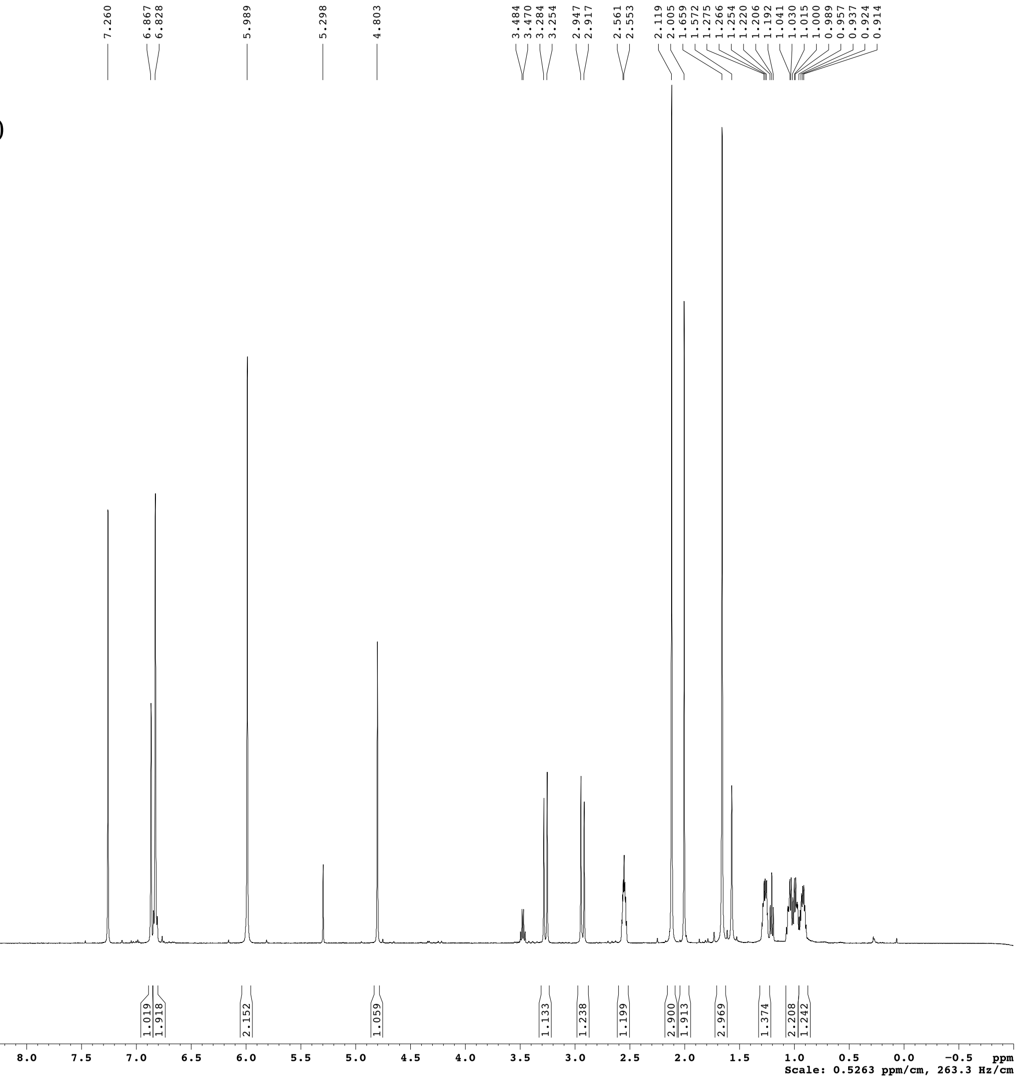
3m

1H spectrum

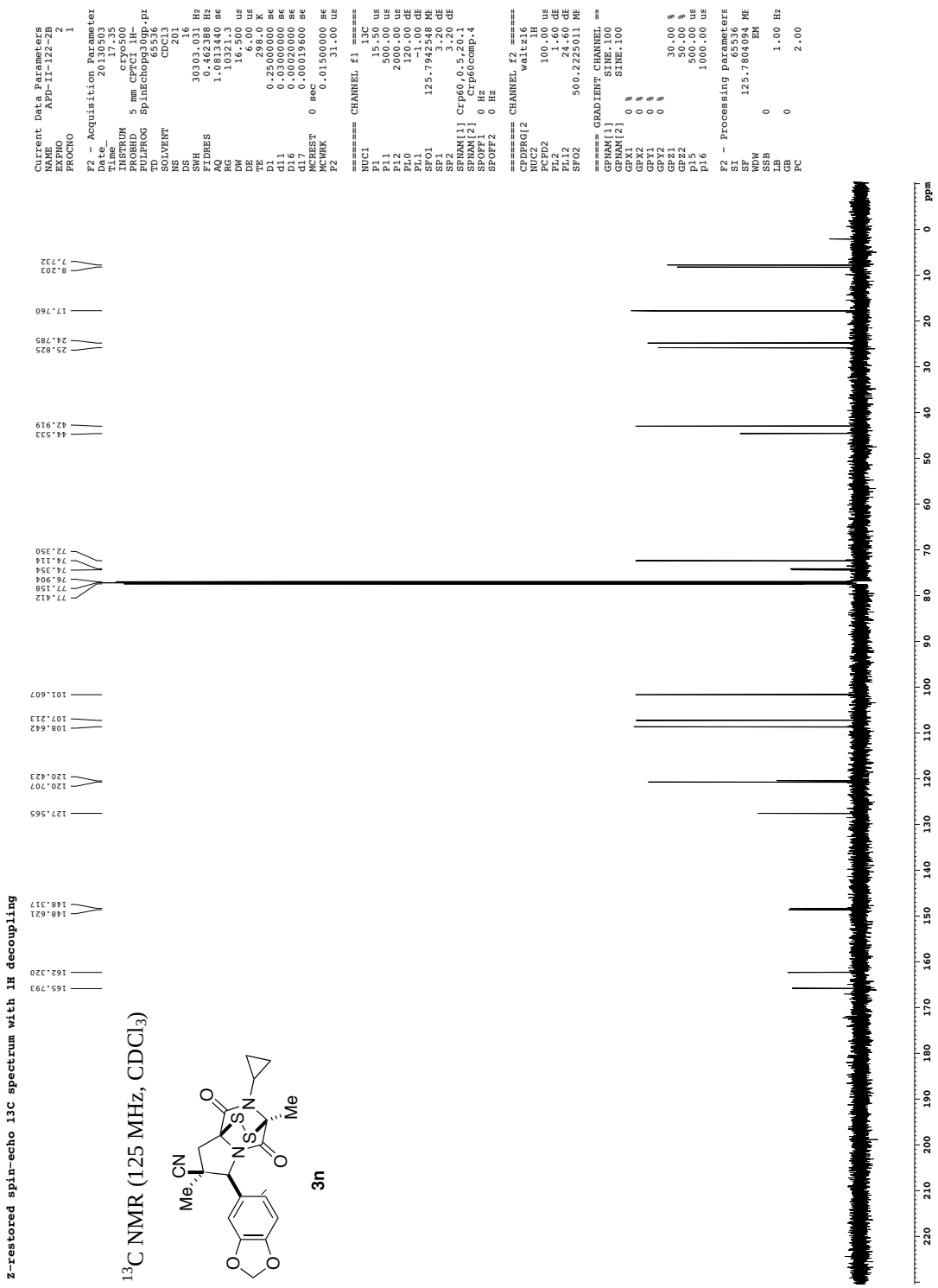
^{1}H NMR (500 MHz, $CDCl_3$)

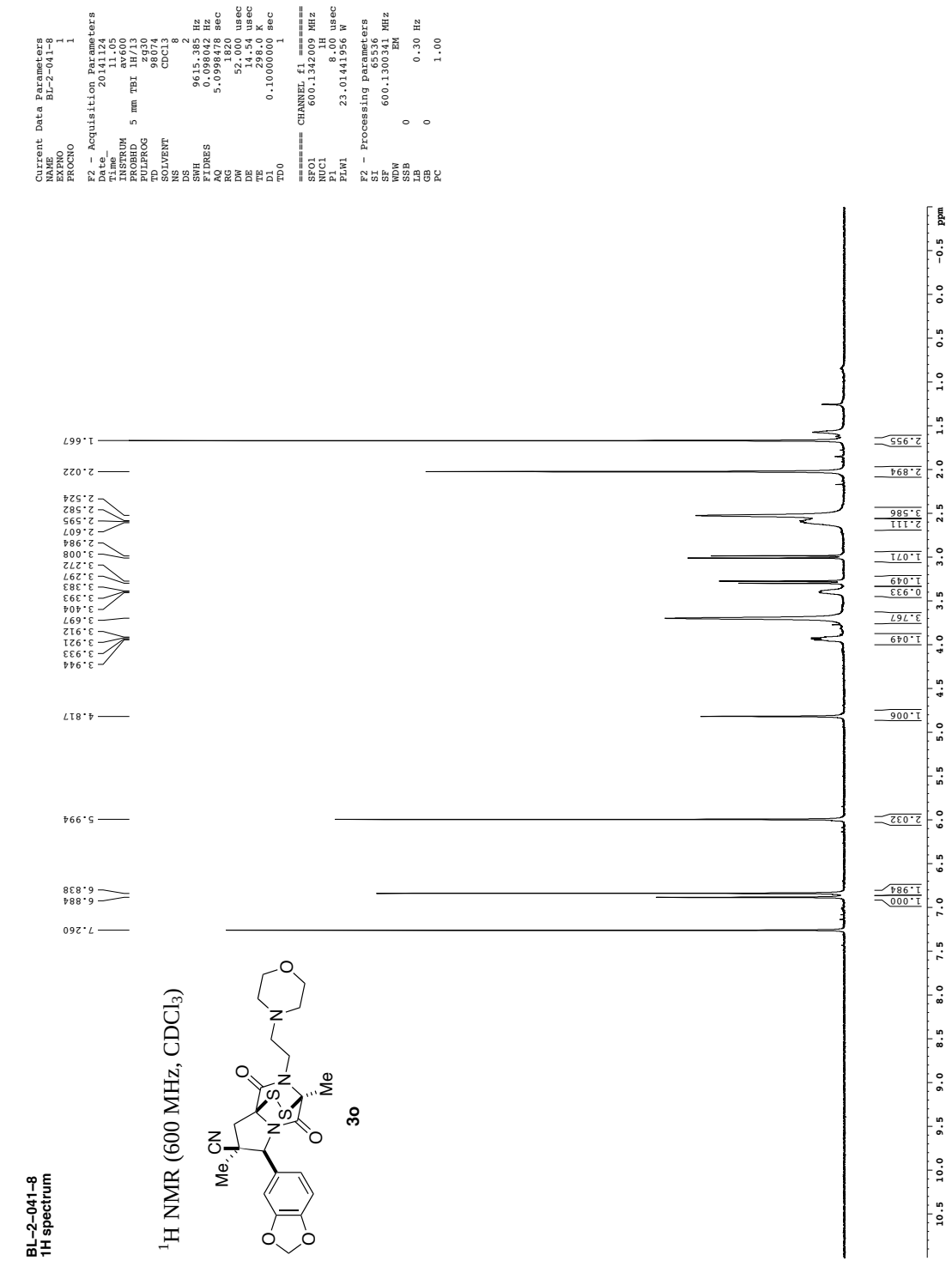


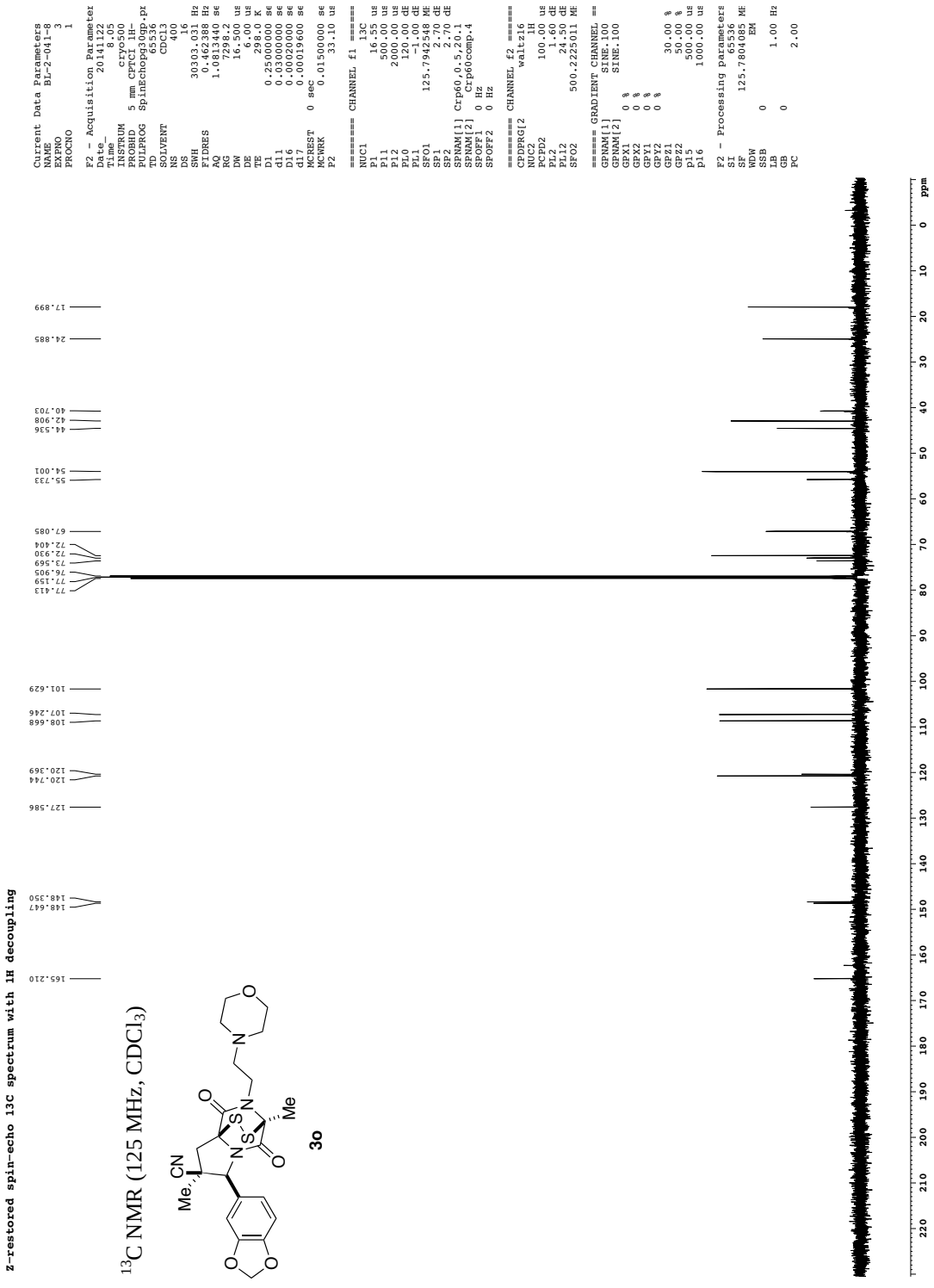
3n




```
Current Data Parameters
NAME       APD-II-122-2B
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20130503
Time               17.29
INSTRUM          cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG             zg30
TD                 81728
SOLVENT            CDCl3
NS                     8
DS                     2
SWH             8012.820 Hz
FIDRES          0.098043 Hz
AQ             5.0998273 sec
RG                   6.3
DW                62.400 usec
DE                  6.00 usec
TE                 298.0 K
D1            0.10000000 sec
MCREST   0 sec
MCWRK         0.01500000 sec

======== CHANNEL f1 ========
NUC1                  1H
P1                  7.50 usec
PL1                 1.60 dB
SFO1         500.2235015 MHz

F2 - Processing parameters
SI                 65536
SF           500.2200313 MHz
WDW                   EM
SSB      0
LB                  0.30 Hz
GB       0
PC                  4.00
```

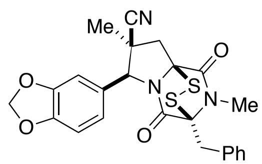

Z-restored spin-echo 13C spectrum with 1H decoupling
13C NMR (125 MHz, CDCl3)
3n
Me
CN
Me
Current Data Parameters
NAME APD-II-122-2B
EXPNO 2
PROCNO 1
F2 - Acquisition Parameter
Date_ 20130503
Time 17.35
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG SpinEchoPg3gp.pr
TD 65536
SOLVENT CDCl3
NS 16
DS 201
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0813440 sec
RG 102.3
DW 16.500 usec
DE 6.00 usec
TE 298.0 K
D1 0.25000000 sec
d11 0.03000000 sec
D16 0.00020000 sec
d12 0.00019600 sec
MC2REST 0 sec
MCWRK 0.01500000 sec
P2 31.00 usec
======== CHANNEL f1 ======
NUC1 13C
P1 15.50 usec
P11 500.00 usec
P12 2000.00 usec
PL2 120.00 dB
PL1 -1.00 dB
SFO1 125.7942548 MHz
SP1 3.20 dB
SP2 3.20 dB
SPNAM[1] Crp60,0.5,20.1
SPNAM[2] Crp60comp.4
SPOFF1 0 Hz
SPOFF2 0 Hz
======== CHANNEL f2 ======
CPDPRG[2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 1.60 dB
PL12 24.60 dB
SFO2 500.2225011 MHz
====== GRADIENT CHANNEL ==
GPNAM[1] SINE.100
GPNAM[2] SINE.100
GPX1 0 %
GPX2 0 %
GPY1 0 %
GPY2 0 %
GPZ1 30.00 %
GPZ2 50.00 %
p15 500.00 usec
p16 1000.00 usec
F2 - Processing parameters
SI 65536
SF 125.7804094 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00
165.793
162.320
148.621
148.317
127.565
120.707
120.423
108.642
107.213
101.607
77.412
77.158
76.904
74.354
74.114
72.350
44.533
42.919
25.825
24.785
17.760
8.203
7.732
ppm


BL-2-041-8
1H spectrum
^{1}H NMR (600 MHz, CDCl$_3$)
3o
Me
CN
Current Data Parameters
NAME BL-2-041-8
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20141124
Time_ 11.05
INSTRUM av600
PROBHD 5 mm TBI 1H/13
PULPROG zg30
TD 98074
SOLVENT CDCl3
NS 8
DS 2
SWH 9615.385 Hz
FIDRES 0.098042 Hz
AQ 5.0998478 sec
RG 1820
DW 52.000 usec
DE 14.54 usec
TE 298.0 K
D1 0.10000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 600.1342009 MHz
NUC1 1H
P1 8.00 usec
PLW1 23.01441956 W
F2 - Processing parameters
SI 65536
SF 600.1300341 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
7.260
6.884
6.838
5.994
4.817
3.944
3.933
3.921
3.912
3.697
3.404
3.393
3.383
3.297
3.272
3.008
2.984
2.607
2.595
2.582
2.524
2.022
1.667
1.000
1.984
2.032
1.049
3.767
0.933
1.049
1.071
2.111
3.586
2.894
2.955
ppm

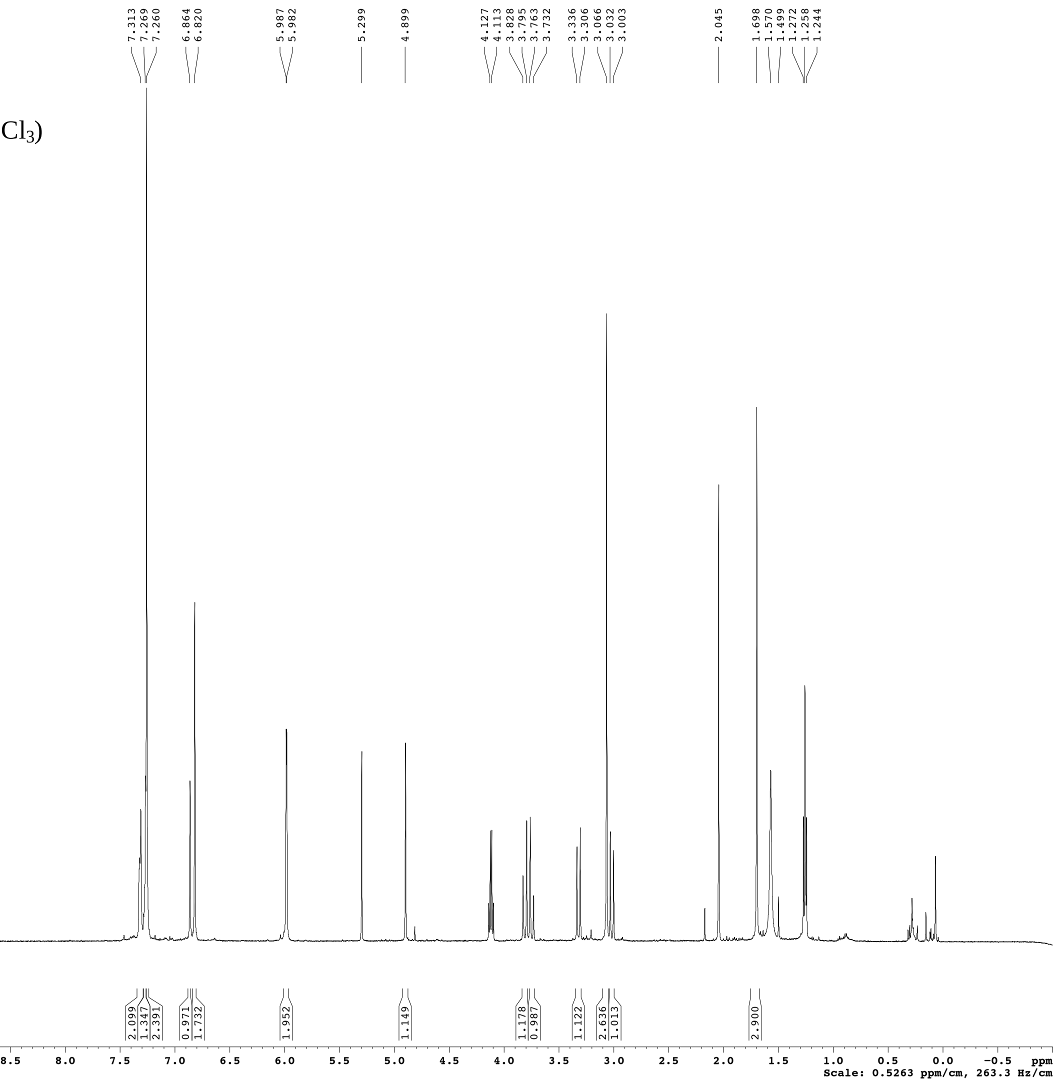

Z-restored spin-echo 13C spectrum with 1H decoupling
13C NMR (125 MHz, CDCl3)
3o
Me
CN
Current Data Parameters
NAME BL-2-041-8
EXPNO 3
PROCNO 1
F2 - Acquisition Parameters
Date_ 20141122
Time 8.05
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG SpinEchoPg3gp.pr
TD 65536
SOLVENT CDCl3
NS 400
DS 16
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0813440 sec
RG 29.70
DW 16.500 usec
DE 6.00 usec
TE 298.0 K
D1 0.25000000 sec
d11 0.03000000 sec
D16 0.00020000 sec
d12 0.00019600 sec
MCREST 0 sec 0.01500000 sec
MCWRK 33.10 usec
P2
======== CHANNEL f1 ======
NUC1 13C
P1 16.55 usec
P11 500.00 usec
P12 2000.00 usec
PL2 120.00 dB
PL1 -1.00 dB
SFO1 125.7942548 MHz
SP1 2.70 dB
SP2 2.70 dB
SPNAM[1] Crp60,0.5,20.1
SPNAM[2] Crp60comp.4
SPOAL2 0 Hz
SPOFF2 0 Hz
======== CHANNEL f2 ======
CPDPRG[2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 1.60 dB
PL12 24.50 dB
SFO2 500.2225011 MHz
====== GRADIENT CHANNEL ==
GPNAM[1] SINE.100
GPNAM[2] SINE.100
GPX1 0 %
GPX2 0 %
GPY1 0 %
GPY2 0 %
GPZ1 30.00 %
GPZ2 50.00 %
p15 500.00 usec
p16 1000.00 usec
F2 - Processing parameters
SI 65536
SF 125.7804085 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00
ppm

1H spectrum

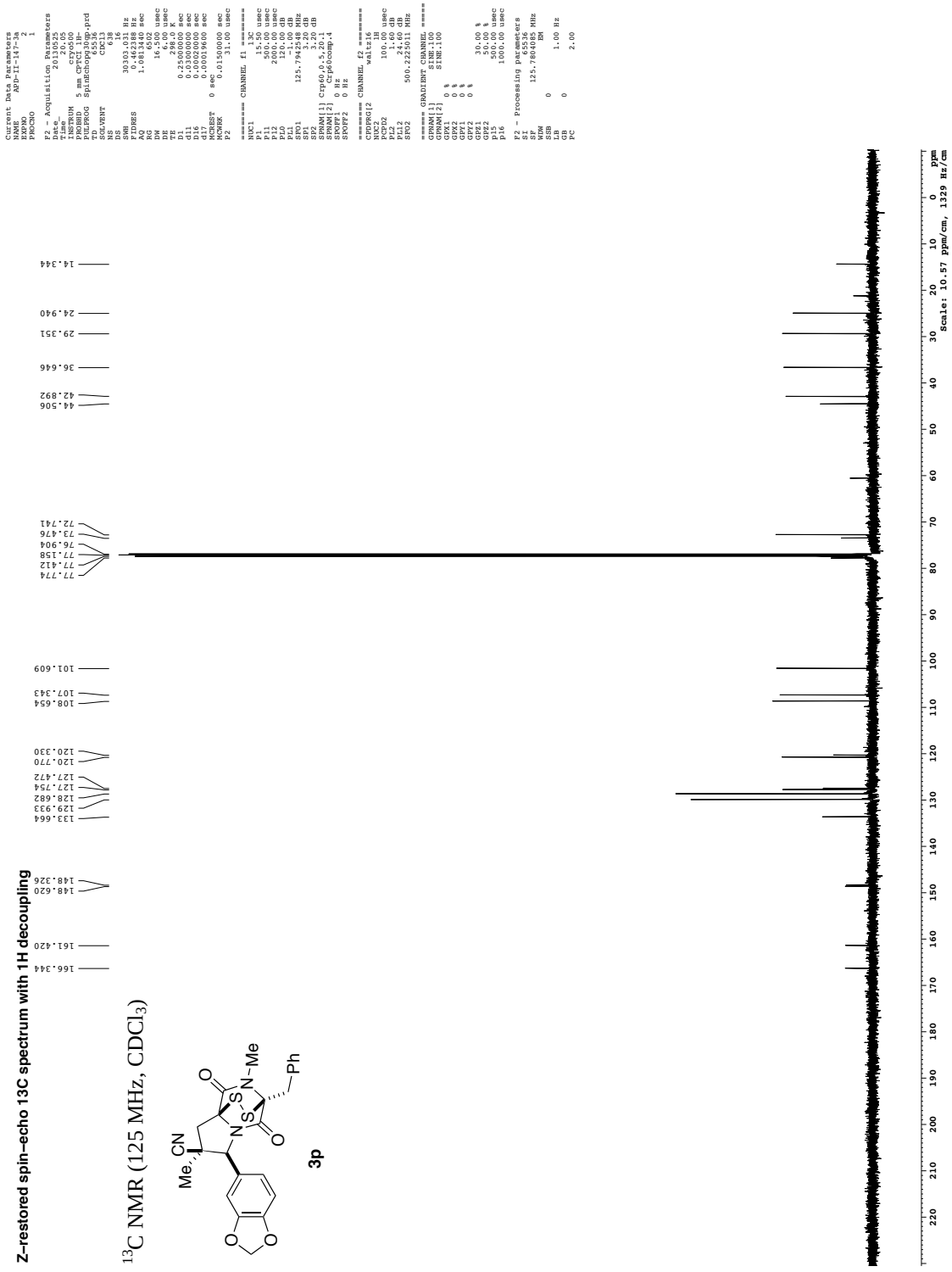
^1H NMR (500 MHz, $CDCl_3$)

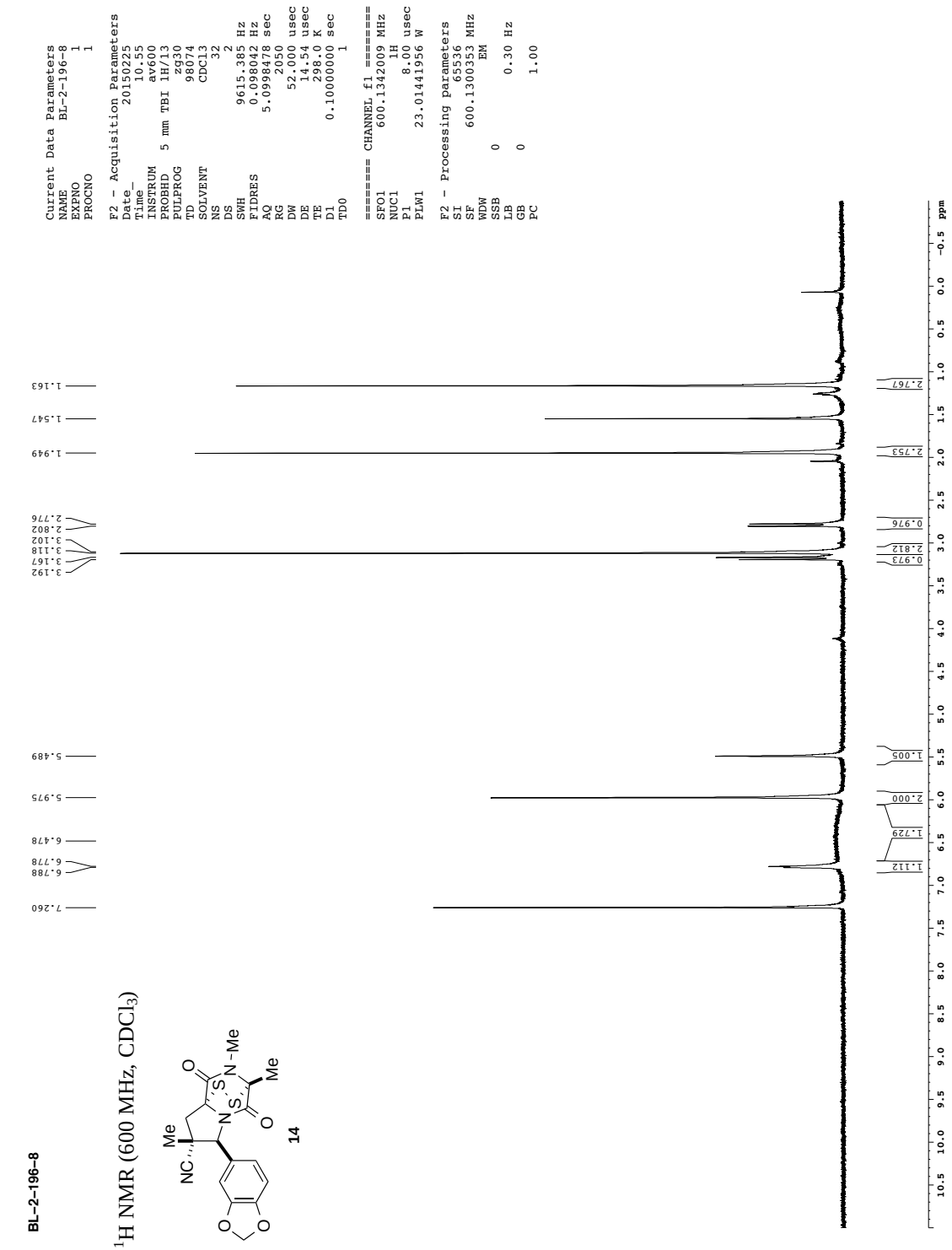


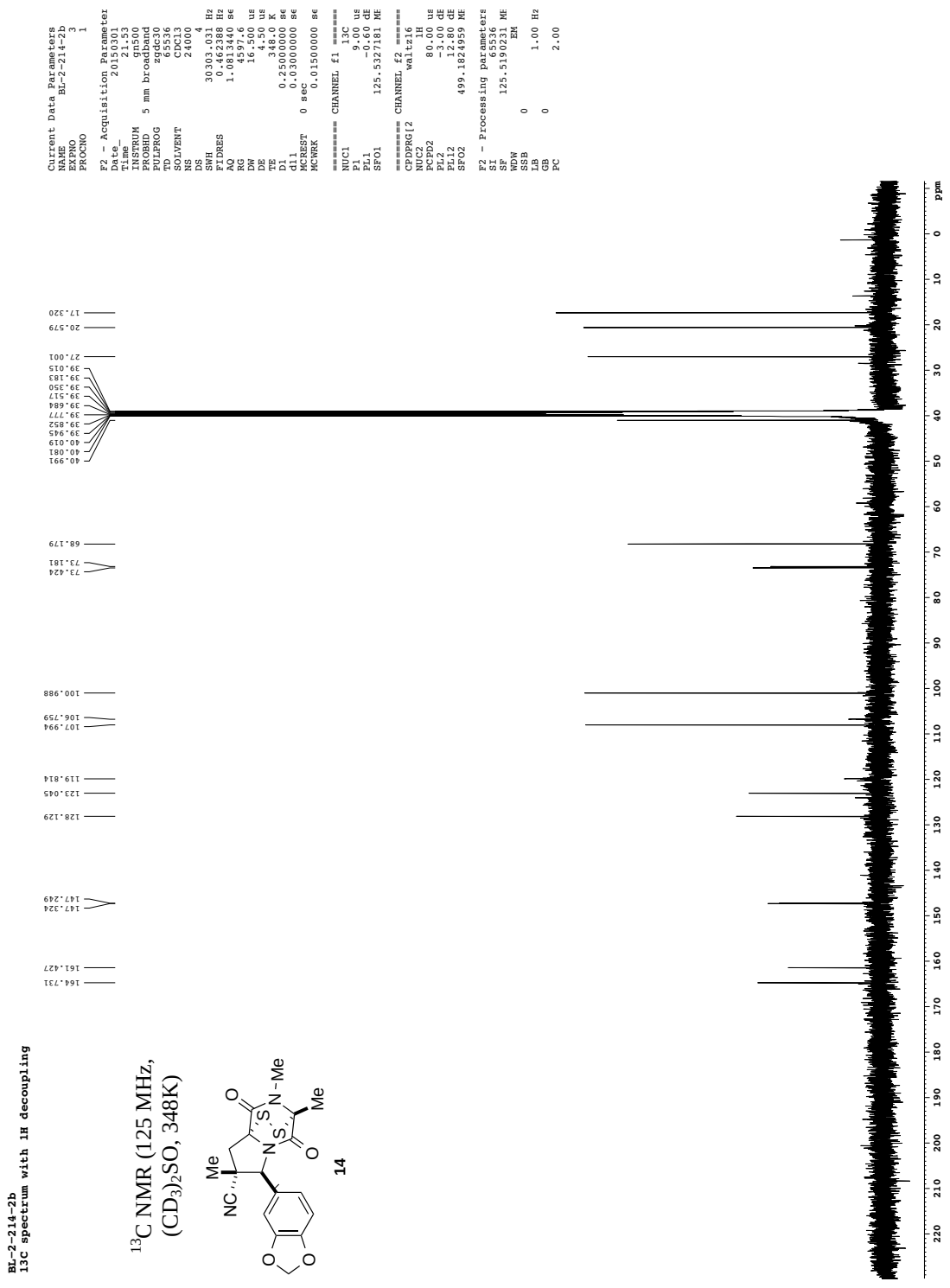
3p

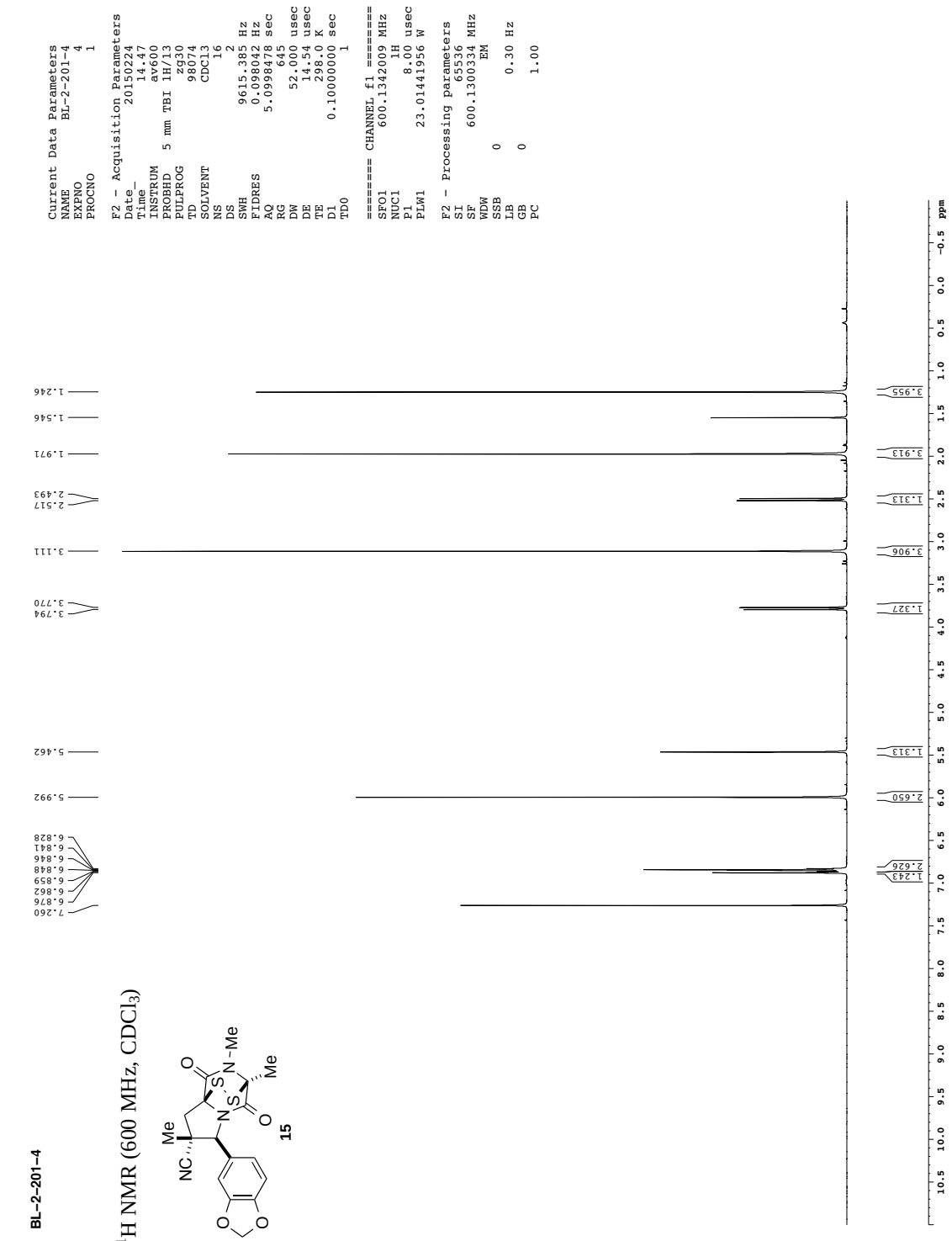


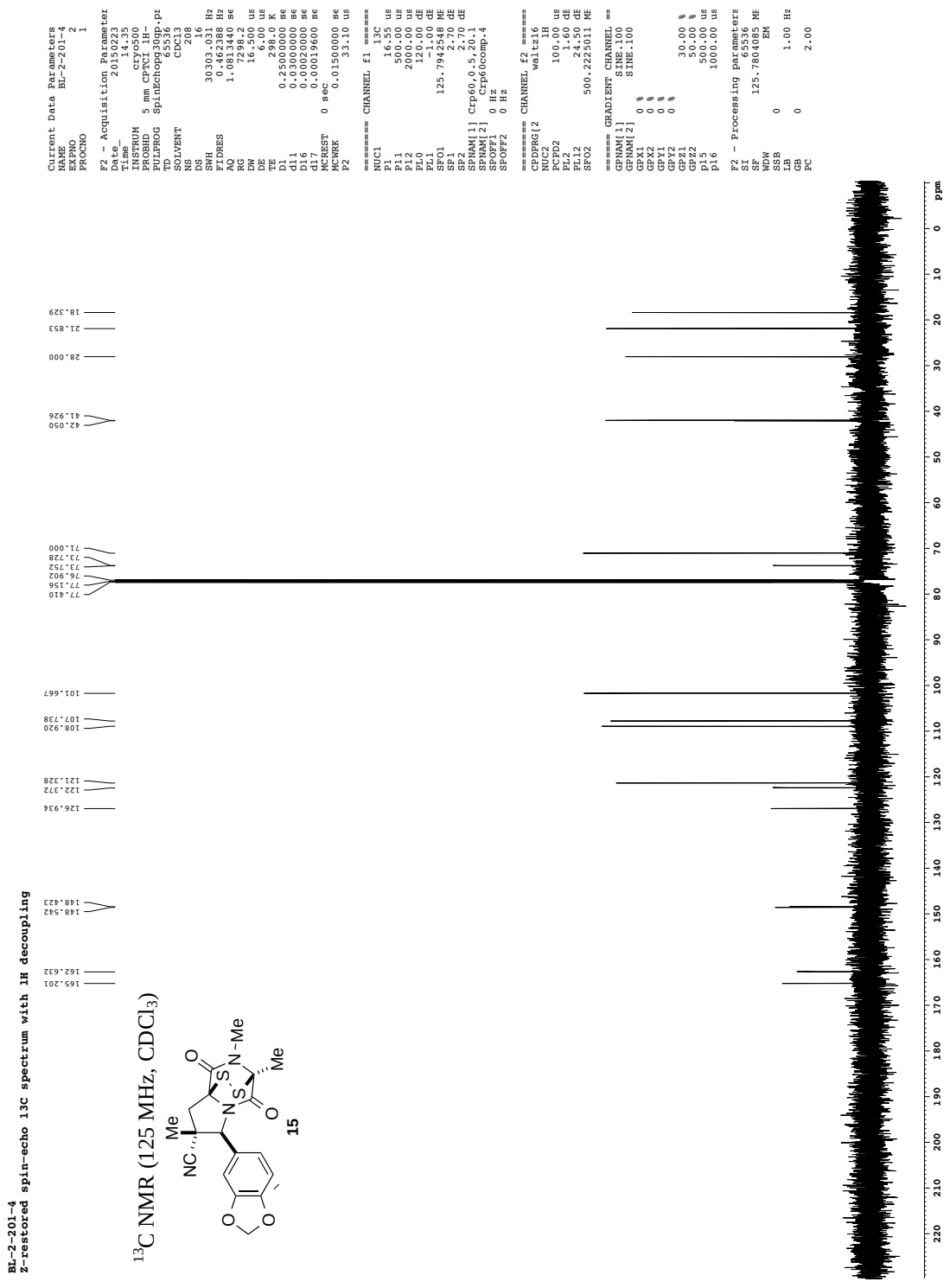

```
Current Data Parameters
NAME        APD-II-147-3a
EXPNO                   1
PROCNO                  1

F2 - Acquisition Parameters
Date_            20130525
Time                19.59
INSTRUM           cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG              zg30
TD                  81728
SOLVENT             CDCl3
NS                      8
DS                      2
SWH              8012.820 Hz
FIDRES           0.098043 Hz
AQ              5.0998273 sec
RG                    6.3
DW                 62.400 usec
DE                   6.00 usec
TE                  298.0 K
D1             0.10000000 sec
MCREST   0 sec
MCWRK          0.01500000 sec

======== CHANNEL f1 ========
NUC1                   1H
P1                   7.50 usec
PL1                  1.60 dB
SFO1          500.2235015 MHz

F2 - Processing parameters
SI                  65536
SF            500.2200316 MHz
WDW                    EM
SSB      0
LB                   0.30 Hz
GB       0
PC                   4.00
```

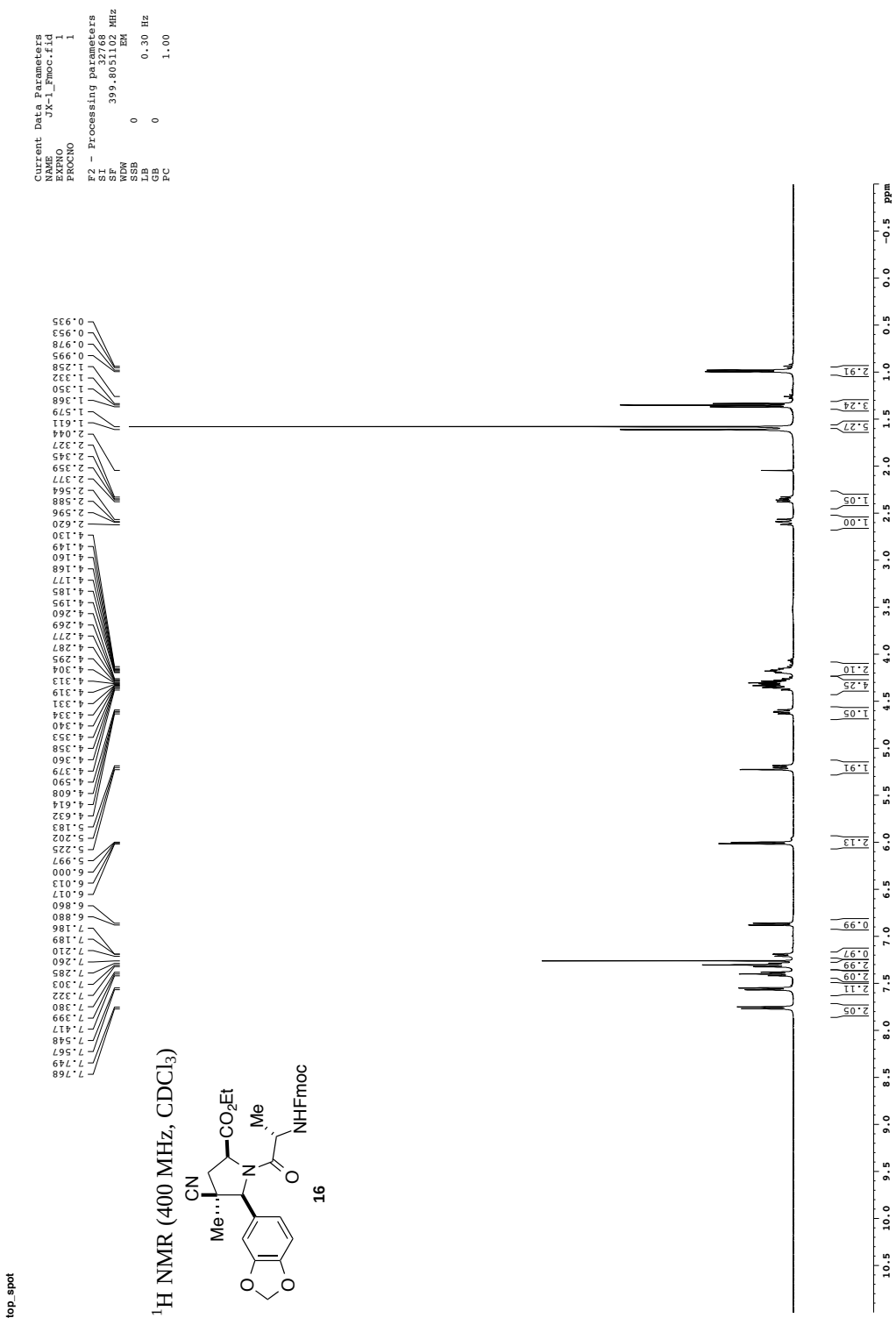

Z–restored spin–echo 13C spectrum with 1H decoupling
13C NMR (125 MHz, CDCl3)
3p
Me
CN
Ph
Scale: 10.57 ppm/cm, 1329 Hz/cm
ppm

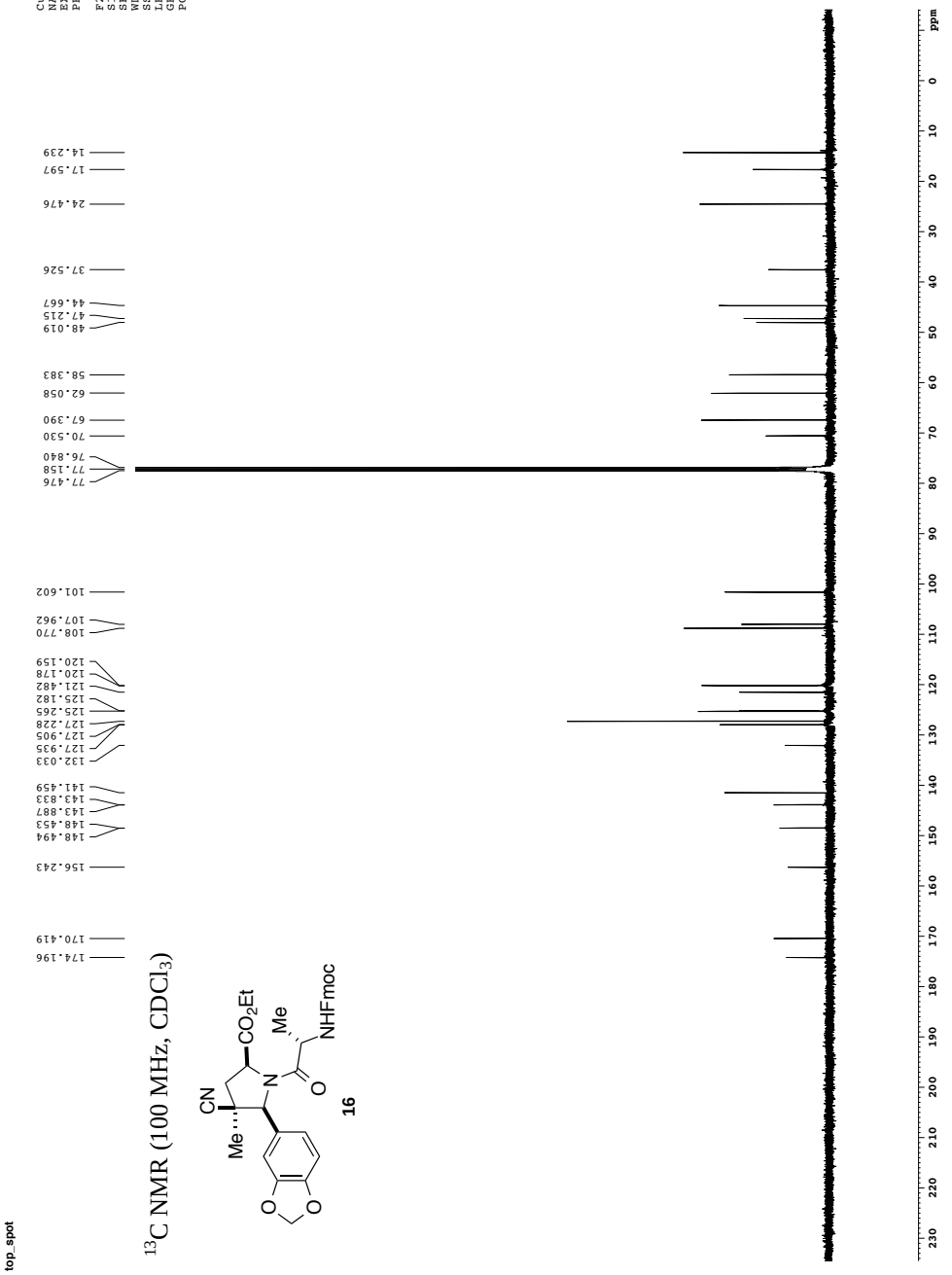

BL-2-196-8
^{1}H NMR (600 MHz, CDCl$_3$)
14
Current Data Parameters
NAME BL-2-196-8
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20150225
Time_ 10.55
INSTRUM av600
PROBHD 5 mm TBI 1H/13
PULPROG zg30
TD 98074
SOLVENT CDCl3
NS 32
DS 2
SWH 9615.385 Hz
FIDRES 0.098042 Hz
AQ 5.0998478 sec
RG 2050
DW 52.000 usec
DE 14.54 usec
TE 298.0 K
D1 0.10000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 600.1342009 MHz
NUC1 1H
P1 8.00 usec
PLW1 23.01441956 W
F2 - Processing parameters
SI 65536
SF 600.1300353 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
7.260
6.788
6.778
6.478
5.975
5.489
3.192
3.167
3.118
3.102
2.802
2.776
1.949
1.547
1.163
1.112
1.729
2.000
1.005
0.973
2.812
0.976
2.753
2.767
ppm

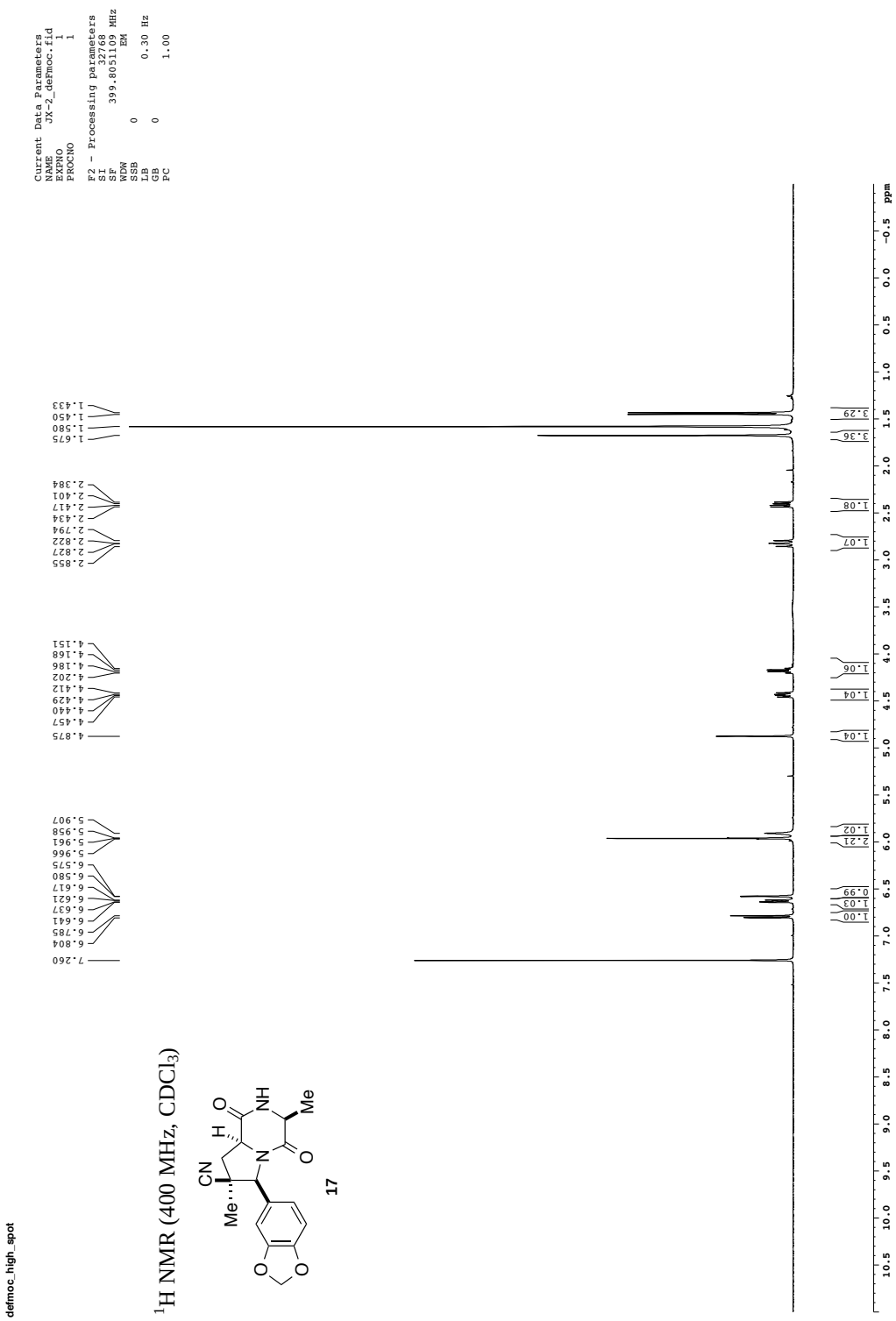

BL-2-214-2b
13C spectrum with 1H decoupling
^{13}C NMR (125 MHz, $(CD_3)_2SO$, 348K)
14
Current Data Parameters
NAME BL-2-214-2b
EXPNO 3
PROCNO 1
F2 - Acquisition Parameter
Date_ 20150301
Time 21.53
INSTRUM gn500
PROBHD 5 mm broadband
PULPROG zgdc30
TD 65536
SOLVENT CDCl3
NS 24000
DS 4
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0813440 sec
RG 4597.6
DW 16.500 us
DE 4.50 us
TE 348.0 K
D1 0.25000000 sec
D11 0.03000000 sec
MCREST 0 sec
MCWRK 0.01500000 sec
CHANNEL f1
NUC1 13C
P1 9.00 us
PL1 -0.60 dB
SFO1 125.5327181 MHz
CHANNEL f2
CPDPRG[2 waltz16
NUC2 1H
PCPD2 80.00 us
PL2 -3.00 dB
PL12 12.80 dB
SFO2 499.1824959 MHz
F2 - Processing parameters
SI 65536
SF 125.5190231 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00
17.320
20.579
27.001
39.015
39.183
39.350
39.517
39.684
39.777
39.852
39.945
40.019
40.081
40.991
68.179
73.181
73.424
100.988
106.759
107.994
119.814
123.045
128.129
147.249
147.324
161.427
164.731
ppm

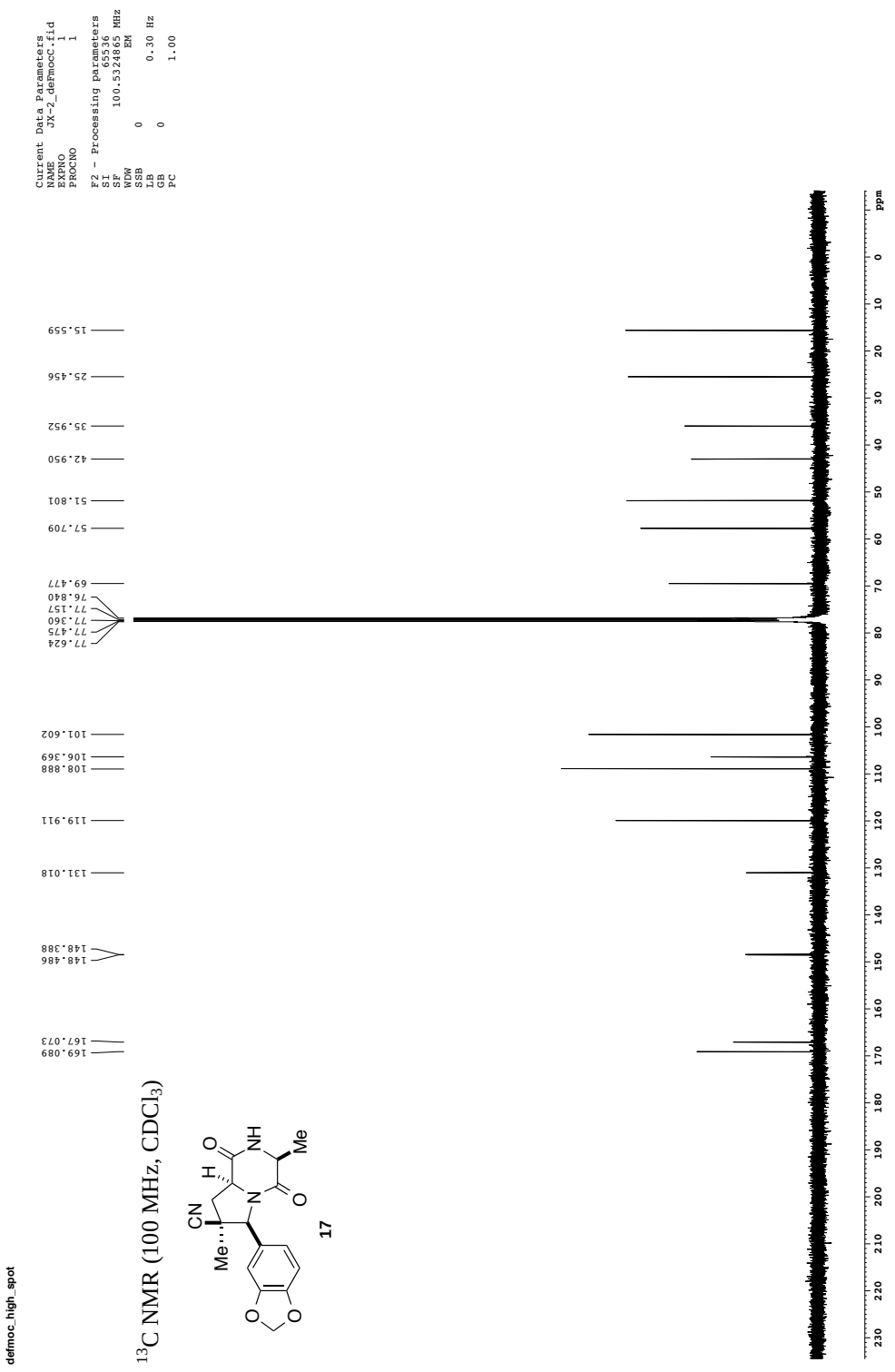

BL-2-201-4
^{1}H NMR (600 MHz, CDCl$_3$)
15
Current Data Parameters
NAME BL-2-201-4
EXPNO 4
PROCNO 1
F2 - Acquisition Parameters
Date_ 20150224
Time_ 14.47
INSTRUM av600
PROBHD 5 mm TBI 1H/13
PULPROG zg30
TD 98074
SOLVENT CDCl3
NS 16
DS 2
SWH 9615.385 Hz
FIDRES 0.098042 Hz
AQ 5.0998478 sec
RG 645
DW 52.000 usec
DE 14.54 usec
TE 298.0 K
D1 0.10000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 600.1342009 MHz
NUC1 1H
P1 8.00 usec
PLW1 23.01441956 W
F2 - Processing parameters
SI 65536
SF 600.1300334 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
7.260
6.876
6.862
6.859
6.848
6.846
6.841
6.828
5.992
5.462
3.794
3.770
3.111
2.517
2.493
1.971
1.546
1.246
3.955
3.913
1.313
3.906
1.327
1.313
2.650
2.626
1.243
ppm

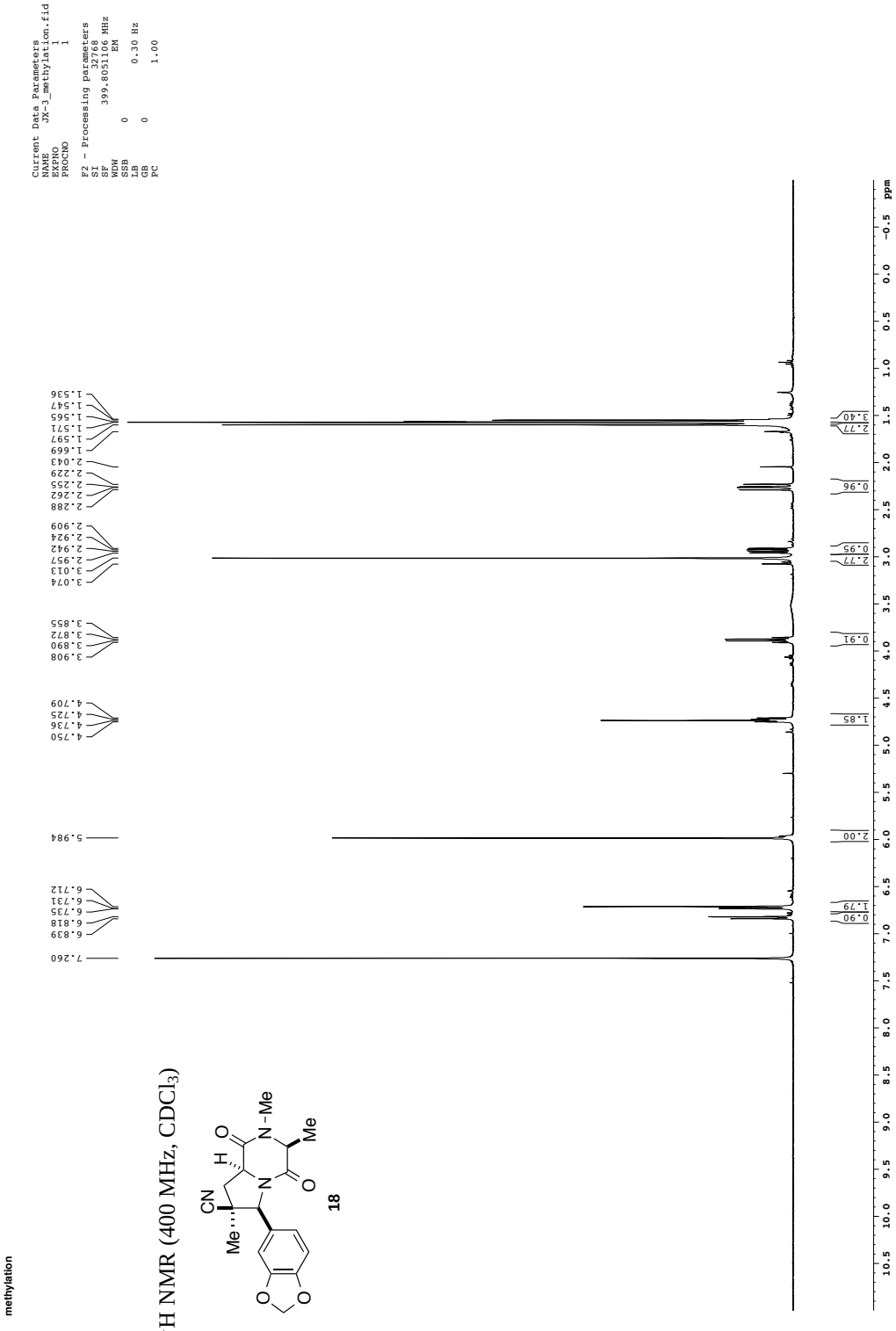

BL-2-201-4
Z-restored spin-echo 13C spectrum with 1H decoupling
^{13}C NMR (125 MHz, CDCl$_3$)
15
Current Data Parameters
NAME BL-2-201-4
EXPNO 2
PROCNO 1
F2 - Acquisition Parameter
Date_ 20150223
Time_ 14.35
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG SpinEchopg30gp.pr
TD 65536
SOLVENT CDCl3
NS 208
DS 16
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0813440 sec
RG 7298.2
DW 16.500 us
DE 6.00 us
TE 298.0 K
D1 0.25000000 sec
d11 0.03000000 sec
D16 0.00020000 sec
d17 0.00019600 sec
MCREST 0 sec 0.01500000 sec
MCWRK 0.01500000 sec
P2 33.10 us
======== CHANNEL f1 ======
NUC1 13C
P1 16.55 us
P11 500.00 us
P12 2000.00 us
PL0 120.00 dB
PL1 -1.00 dB
SFO1 125.7942548 MHz
SP1 2.70 dB
SP2 2.70 dB
SPNAM[1] Crp60,0.5,20.1
SPNAM[2] Crp60comp.4
SPOFF1 0 Hz
SPOFF2 0 Hz
======== CHANNEL f2 ======
CPDPRG[2 waltz16
NUC2 1H
PCPD2 100.00 us
PL2 1.60 dB
PL12 24.50 dB
SFO2 500.2225011 MHz
====== GRADIENT CHANNEL ==
GPNAM[1] SINE.100
GPNAM[2] SINE.100
GPX1 0 %
GPX2 0 %
GPY1 0 %
GPY2 0 %
GPZ1 30.00 %
GPZ2 50.00 %
p15 500.00 us
p16 1000.00 us
F2 - Processing parameters
SI 65536
SF 125.7804085 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00
18.329
21.853
28.000
41.926
42.050
71.000
73.728
73.752
76.902
77.156
77.410
101.667
107.738
108.920
121.328
122.372
126.934
148.423
148.542
162.632
165.201
ppm

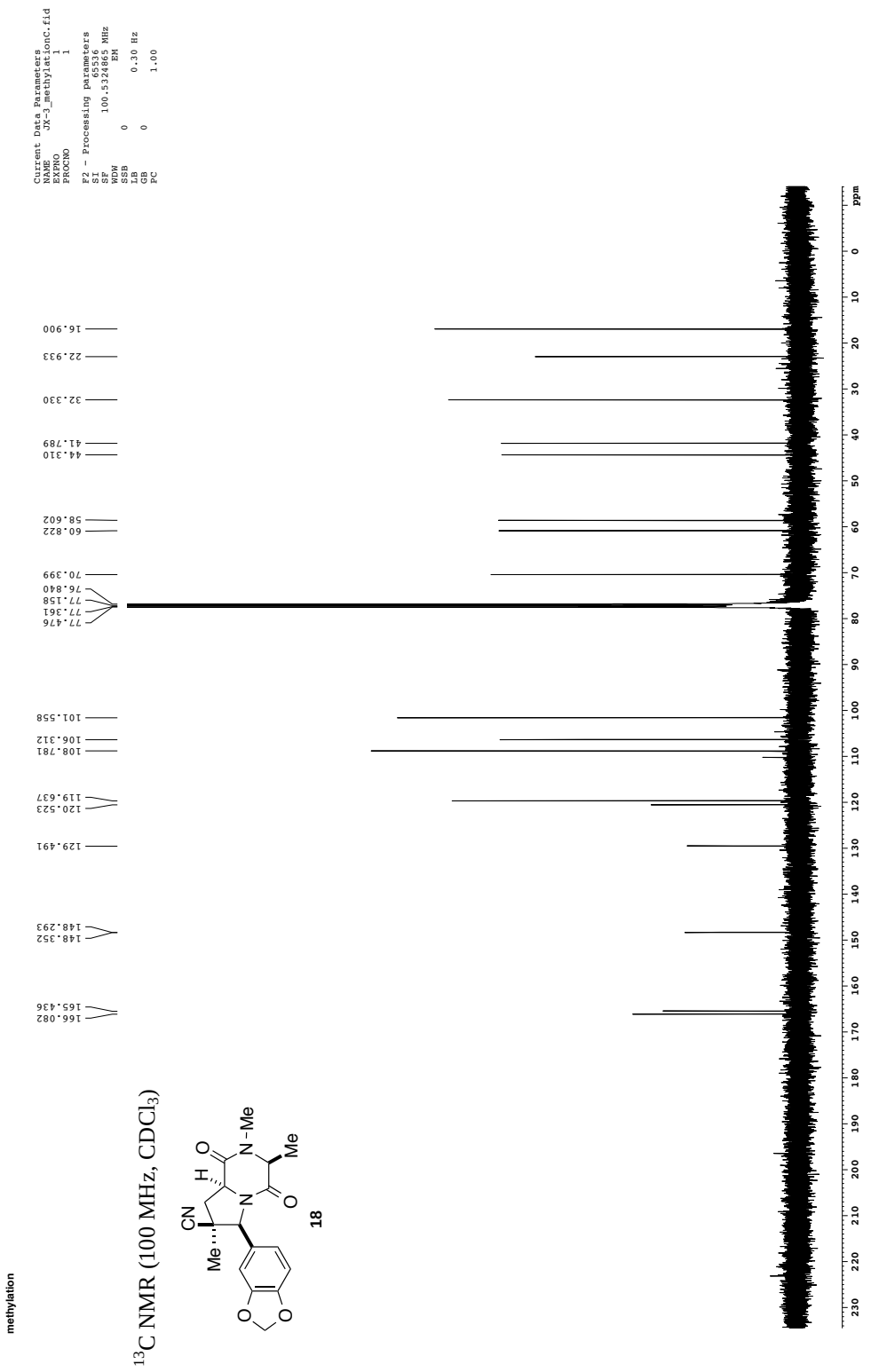

top_spot
Current Data Parameters
NAME JX-1_Fmoc.fid
EXPNO 1
PROCNO 1
F2 - Processing parameters
SI 32768
SF 399.8051102 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
^{1}H NMR (400 MHz, CDCl$_3$)
CN
Me
CO$_2$Et
N
Me
O
NHFmoc
O
O
16
ppm

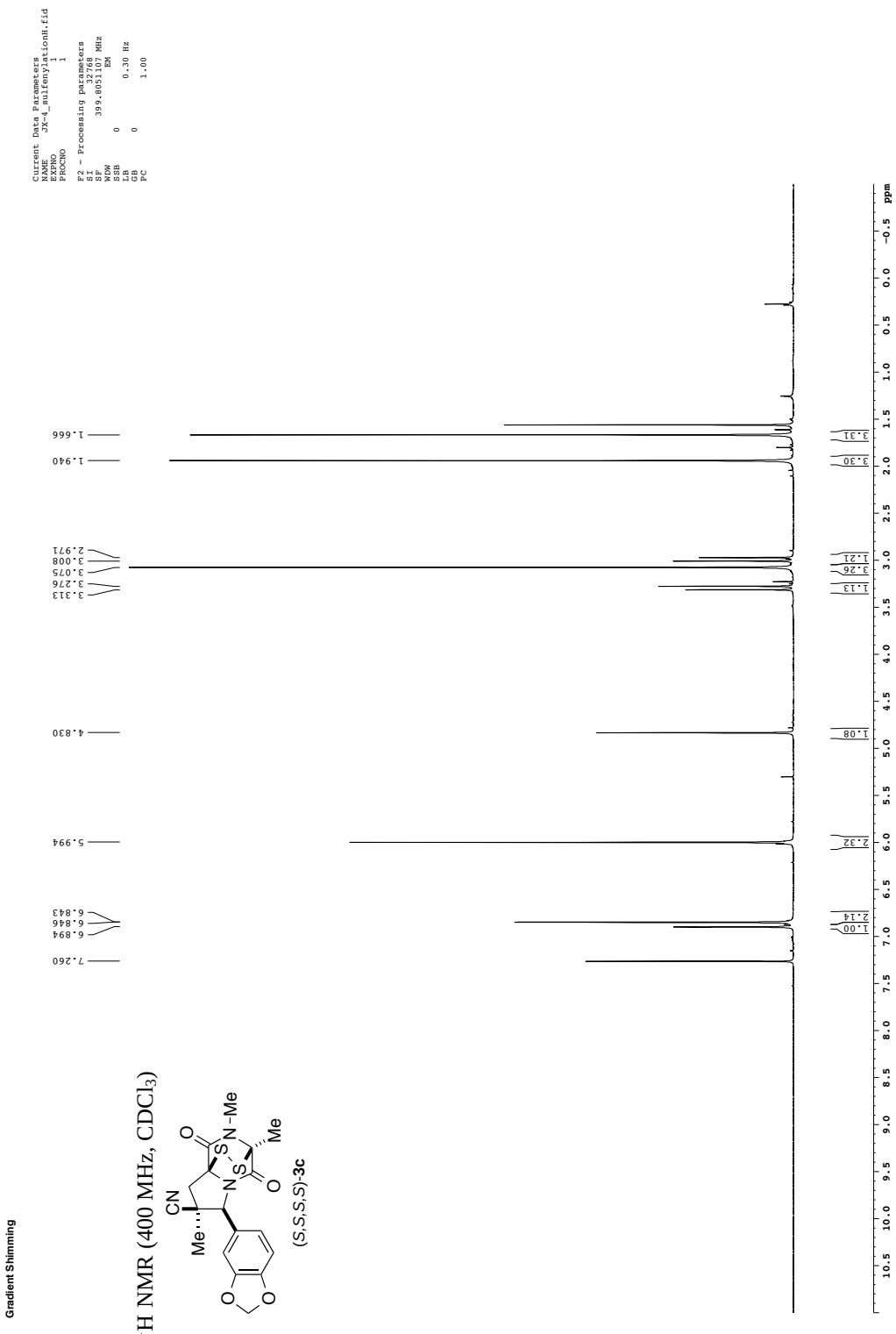

top_spot
^{13}C NMR (100 MHz, $CDCl_3$)
16
Current Data Parameters
NAME JX-1_FmocC.fid
EXPNO 1
PROCNO 1
F2 - Processing parameters
SI 65536
SF 100.5324865 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
174.196
170.419
156.243
148.494
148.453
143.887
143.833
141.459
132.033
127.935
127.905
127.228
125.265
125.182
121.482
120.178
120.159
108.770
107.962
101.602
77.476
77.158
76.840
70.530
67.390
62.058
58.383
48.019
47.215
44.667
37.526
24.476
17.597
14.239
ppm

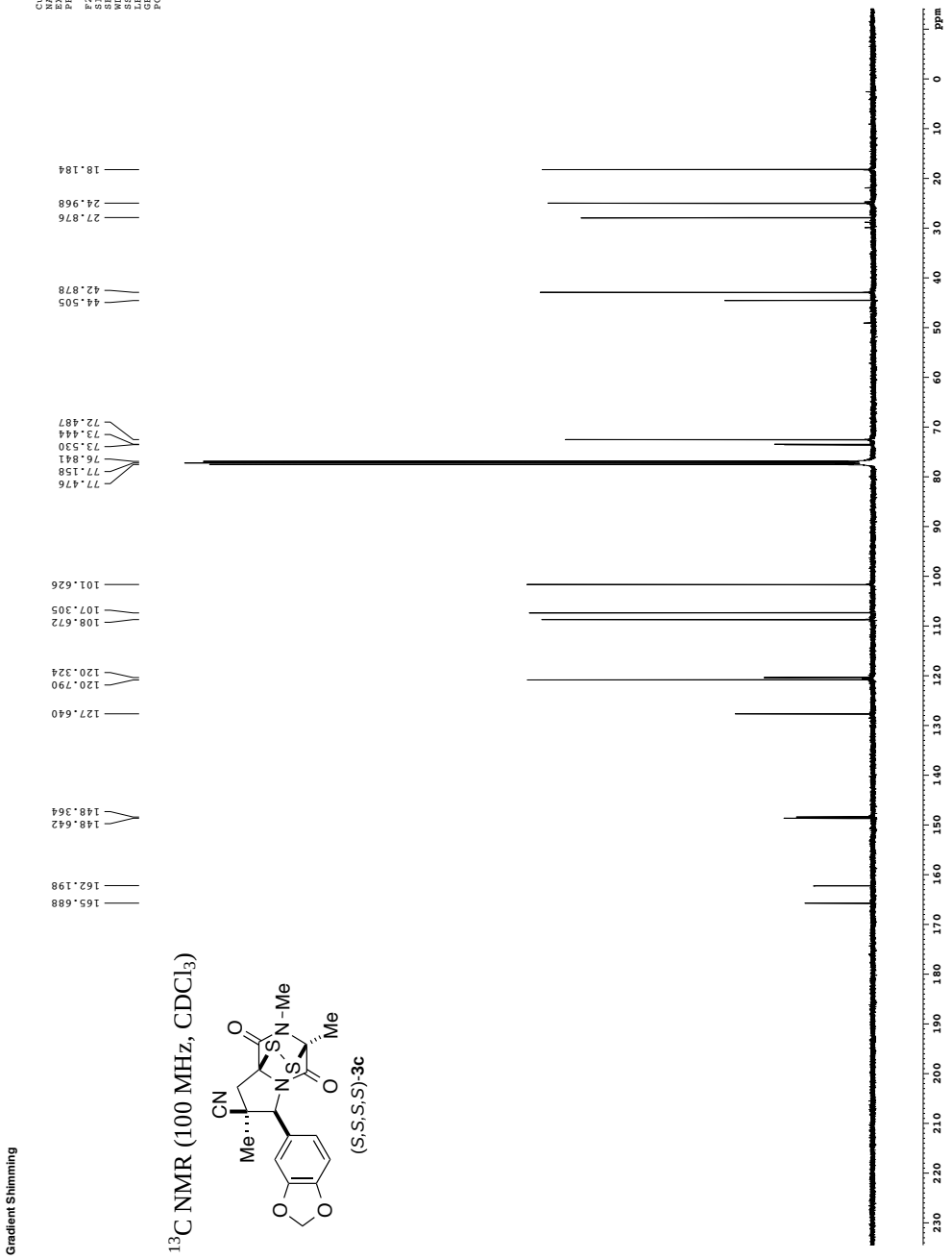

defmoc_high_spot
Current Data Parameters
NAME JX-2_defmoc.fid
EXPNO 1
PROCNO 1
F2 - Processing parameters
SI 32768
SF 399.8051109 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
1H NMR (400 MHz, CDCl3)
17
7.260
6.804
6.785
6.641
6.637
6.621
6.617
6.580
6.575
5.966
5.961
5.958
5.907
4.875
4.457
4.440
4.429
4.412
4.202
4.186
4.168
4.151
2.855
2.827
2.822
2.794
2.434
2.417
2.401
2.384
1.675
1.580
1.450
1.433
1.00
1.03
0.99
2.21
1.02
1.04
1.06
1.04
1.07
1.08
3.36
3.29
ppm


defmoc_high_spot
^{13}C NMR (100 MHz, CDCl$_3$)
17
Current Data Parameters
NAME JX-2_defmocC.fid
EXPNO 1
PROCNO 1
F2 - Processing parameters
SI 65536
SF 100.5324865 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
15.559
25.456
35.952
42.950
51.801
57.709
69.477
76.840
77.157
77.360
77.475
77.624
101.602
106.369
108.888
119.911
131.018
148.388
148.486
167.073
169.089
ppm


methylation
Current Data Parameters
NAME JX-3_methylation.fid
EXPNO 1
PROCNO 1
F2 - Processing parameters
SI 32768
SF 399.8051106 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
1H NMR (400 MHz, CDCl3)
18
7.260
6.839
6.818
6.735
6.731
6.712
5.984
4.750
4.736
4.725
4.709
3.908
3.890
3.872
3.855
3.074
3.013
2.957
2.942
2.924
2.909
2.288
2.262
2.255
2.229
2.043
1.669
1.597
1.571
1.565
1.547
1.536
0.90
1.79
2.00
1.85
0.91
2.77
0.95
0.96
2.77
3.40
ppm


methylation
^{13}C NMR (100 MHz, CDCl$_3$)
18
Current Data Parameters
NAME JX-J_methylationC.fid
EXPNO 1
PROCNO 1
F2 - Processing parameters
SI 65536
SF 100.5324865 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
166.082
165.436
148.352
148.293
129.491
120.523
119.637
108.781
106.312
101.558
77.476
77.361
77.158
76.840
70.399
60.822
58.602
44.310
41.789
32.330
22.933
16.900
ppm


Current Data Parameters
NAME 3Xr4_sulfenylationH.fid
EXPNO 1
PROCNO 1
F2 - Processing parameters
SI 32768
SF 399.8051107 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
1.666
1.940
2.971
3.008
3.075
3.276
3.313
4.830
5.994
6.843
6.846
6.894
7.260
3.31
3.30
1.21
3.26
1.13
1.08
2.32
1.00
2.14
ppm
Gradient Shimming
^{1}H NMR (400 MHz, CDCl$_3$)
(S,S,S,S)-3c



^{13}C NMR (100 MHz, $CDCl_3$)

(*S,S,S,S*)-**3c**