

Enantioselective Total Synthesis of Plectosphaeroic Acid B

Salman Y. Jabri and Larry E. Overman*

Department of Chemistry, 1102 Natural Sciences II, University of California, Irvine, California 92697-2025

leoverma@uci.edu

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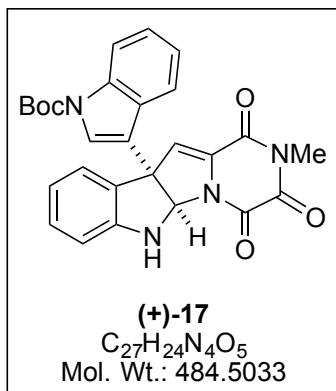
Complete reference 6c: Kung, A. L.; Zabłudoff, S. D.; France, D. S.; Freedman, S. J.; Tanner, E. A.; Vieira, A.; Cornell–Kennon, S.; Lee, J.; Wang, B.; Wang, J.; Memmert, K.; Naegeli, H. U.; Petersen, F.; Eck, M. J.; Bair, K. W.; Wood, A. W.; Livingston, D. M. *Cancer Cell* **2004**, *6*, 33–43.

Materials and Methods. Reactions were performed in oven-dried or flame-dried glassware under a positive pressure of nitrogen or argon, except where noted. Tetrahydrofuran (THF), toluene (PhMe), dichloromethane, methanol (MeOH), acetonitrile (MeCN), pyridine and triethylamine were dried by passage through activated alumina or molecular sieves.¹ Boron trifluoride diethyl etherate (BF₃·OEt₂) was distilled over CaH₂. 1,4-Benzoquinone was recrystallized from petroleum ether. The di-(*tert*-butoxycarbonyl) derivative **16** of gliocladin C² and 2-amino-6-bromo-3-hydroxybenzoic acid (**S9**)³ were prepared according to literature procedures. All other commercial reagents were used as received from the manufacturer. Analytical thin layer chromatography (TLC) was conducted on EMD 250 µm silica gel 60 F₂₅₄ glass-backed plates; for preparatory applications on EMD 500 µm silica gel 60 F₂₅₄ glass-backed plates, or for reverse-phase applications on EMD 250 µm silica gel 60 RP-18 F₂₅₄ glass-backed plates. Eluted plates were visualized by UV light (254 nm) or stained with iodine (on silica), potassium permanganate, or ceric ammonium molybdate (CAM) stains. Flash chromatography was performed using forced flow of the indicated solvent system on EMD Geduran® Silica Gel 60 or on a Biotage® Isolera™ Spektra One flash purification system using SNAP Ultra prep-packed silica cartridges. Reverse-phase HPLC was performed on an Agilent 1100 using a Phenomenex Luna® 5 µm C18(2) 100Å 250 x 10 mm column. NMR spectra were obtained at 298 K unless otherwise indicated, with Bruker FT-NMR spectrometers at indicated frequencies. Chemical shifts (δ) were reported in parts per million relative to the residual solvent signals (CDCl₃, DMSO-*d*₆, acetone-*d*₆). ¹H NMR coupling constants are reported in Hertz. Splitting patterns are abbreviated as follows: singlet (s), doublet (d), triplet (t), quartet (q), multiplet (m), broad (br), apparent (app). Carbon multiplicity was determined by a combination of DEPT-135 and HMQC experiments. Infrared (IR) spectra were obtained using a Varian 800 FT-IR spectrometer as thin films from CH₂Cl₂ or MeCN or KBr pellets. Optical rotations were obtained using a Jasco J-1010 polarimeter with 50 mm length cells. CD spectra were obtained using a Jasco J-810 spectrometer with 1 mm quartz cells. High-resolution mass spectra (HRMS) were obtained from the UC Irvine Mass Spectrometry Facility. Melting points were determined on a melting point apparatus (Thomas Hoover, Uni-melt) and are uncorrected. Abbreviations used can be found on the Internet at http://pubs.acs.org/paragonplus/submission/joceah/joceah_abbreviations.pdf.

¹ Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometallics* **1996**, *15*, 1518–1520.

² DeLorbe, J. D.; Jabri, S. Y.; Mennen, S. M.; Overman, L. E.; Zhang, F.-L. *J. Am. Chem. Soc.* **2011**, *133*, 6549–6522.

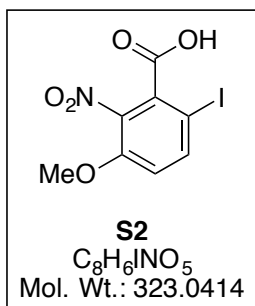
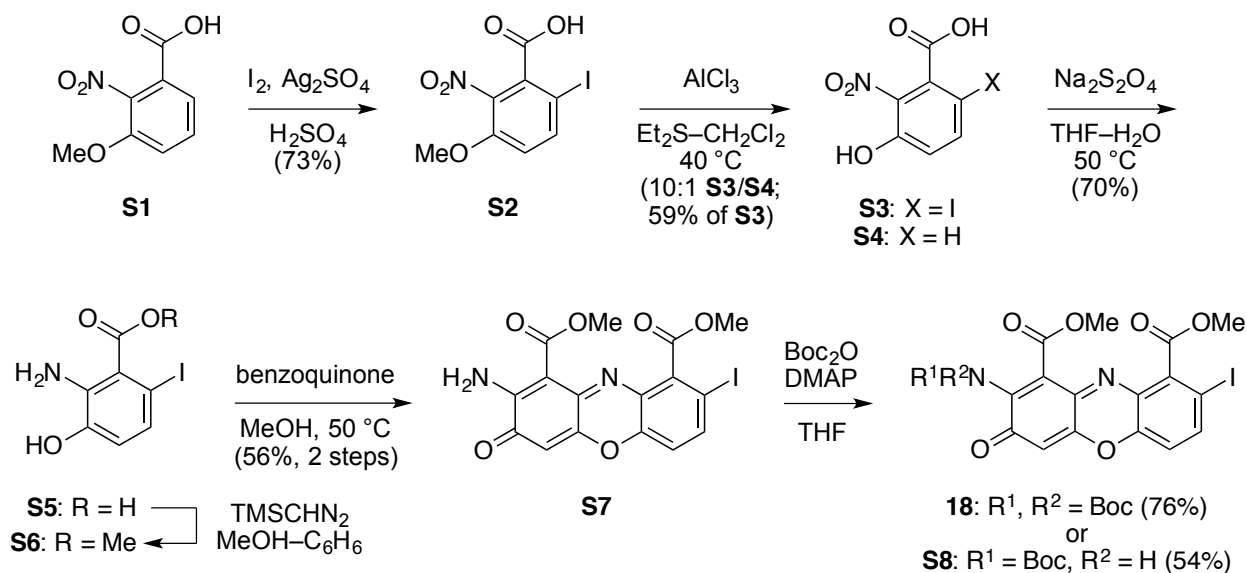
³ The preparation of **S9** was previously reported in three steps from commercially available 3-methoxy-2-nitrobenzoic acid **S1** [4920-80-3], see (a) Fairfax, D. K.; Yang, Z. Benzoxazole Carboxamides for Treating CINV and IBS-D. US Patent 2006/183769 A1, 08/17/2006. (b) Manthey, M. K.; Pyne, S. G.; Truscott, R. J. W. *J. Org. Chem.* **1990**, *55*, 4581–4585.


mono-(*tert*-Butoxycarbonyl) derivative of gliocladin C (+)-17;

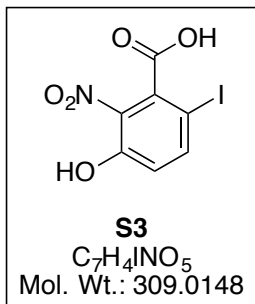
Method A: A solution of scandium triflate ($Sc(OTf)_3$) (1.6 mg, 3.3 μ mol) and MeCN (50 μ L) was added dropwise to a solution of the di-(*tert*-butoxycarbonyl) derivative **16** of gliocladin C (19 mg, 33 μ mol) and MeCN (0.33 mL) cooled to 0 °C. The reaction mixture was allowed to warm to rt. After 3 h, the reaction mixture was poured into a mixture of ethyl acetate (EtOAc) (10 mL) and saturated aqueous $NaHCO_3$ (5 mL). The layers were separated and the aqueous layer was further extracted with EtOAc (2 x 5 mL). The combined organic layers were washed sequentially with H_2O (10 mL) and brine (10 mL), dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by silica

gel chromatography (1:9 EtOAc/hexanes $\rightarrow$ 3:7 EtOAc/hexanes) to afford the title compound **17** as a yellow solid (12 mg, 76%).

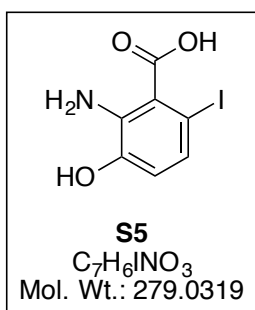
Method B: The di-(*tert*-butoxycarbonyl) derivative **16** of gliocladin C (150 mg, 260 μ mol, concentrated in vacuo from a THF solution into a vial) was heated (neat) under a slight vacuum (160 mmHg) at 180 °C (preheated oil bath) for 20 min (reaction times may vary slightly; removal of both Boc groups of **16** were monitored by TLC). The reaction mixture was allowed to cool to rt, then THF (4 mL), di-*tert*-butyl dicarbonate (Boc_2O) (56 mg, 260 μ mol) and *N,N*-dimethyl-4-aminopyridine (DMAP) (6.0 mg, 4.9 μ mol) were added to the vial sequentially (under a N_2 atmosphere). After 1 h (in some cases, additional Boc_2O was added to drive the reaction to completion), the reaction mixture was poured into a mixture of EtOAc (20 mL) and saturated aqueous NH_4Cl (10 mL). The layers were separated and the aqueous layer was extracted with EtOAc (2 x 10 mL). The combined organic layers were washed with brine (10 mL), dried over Na_2SO_4 and concentrated under reduced pressure. The crude residue was purified by silica gel chromatography (1:3 EtOAc/hexanes) to afford the title compound **17** (118 mg, 95% as a tan foam: $[\alpha]_D^{24} +148$, $[\alpha]_D^{577} +144$, $[\alpha]_D^{546} +139$ ($c = 0.2$, CH_2Cl_2); 1H NMR (500 MHz, acetone- d_6) δ 8.15 (d, $J = 8.3$ Hz, 1H), 7.60 (s, 1H), 7.33 (d, $J = 6.9$ Hz, 1H), 7.30 (dt, $J = 8.3, 1.0$ Hz, 1H), 7.19 (d, $J = 7.2$ Hz, 1H), 7.15 (dt, $J = 7.7, 1.2$ Hz, 1H), 7.09 (dt, $J = 8.0, 0.9$ Hz, 1H), 7.01 (s, 1H), 6.88 (d, $J = 7.9$ Hz, 1H), 6.75–6.70 (comp, 2H), 6.28 (d, $J = 2.6$ Hz, 1H), 3.25 (s, 3H), 1.67 (s, 9H); ^{13}C NMR (125 MHz, acetone- d_6) δ 158.6 (C), 158.0 (C), 150.7 (C), 150.3 (C), 150.1 (C), 137.9 (C), 133.9 (C), 130.2 (CH), 130.1 (C), 129.0 (C), 125.7 (CH), 125.4 (CH), 125.3 (CH), 124.3 (CH), 123.7 (CH), 122.0 (C), 120.9 (CH), 120.0 (CH), 116.3 (CH), 110.9 (CH), 85.0 (C), 84.0 (CH), 60.6 (C), 28.3 (CH_3), 27.2 (CH_3); IR (film) 3365, 3102, 3064, 2979, 1736, 1686, 1606, 1452; TLC R_f 0.32 (1:1 EtOAc/hexanes), 0.41 (2:98 MeOH/ CH_2Cl_2 , plate was eluted twice); HRMS (ESI) m/z calcd for $C_{27}H_{24}N_4O_5Na$ ($M+Na$) $^+$ 507.1644, found 507.1643.

Scheme 1. Preparation of Phenoxazinone Iodides **18 and **S8****

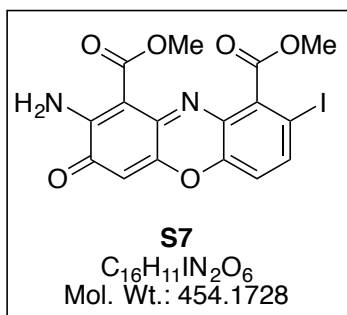
6-Iodo-3-methoxy-2-nitrobenzoic acid (S2): To a suspension of commercially available 2-methoxy-3-nitrobenzoic acid (**S1**) [4920-80-3] (10.0 g, 50.7 mmol) in concentrated H_2SO_4 (150 mL) was added Ag_2SO_4 (20.6 g, 65.9 mmol) and iodine (13.5 g, 53.5 mmol). The heterogeneous mixture was shielded from light (by covering the reaction vessel with aluminum foil) and stirred vigorously at rt for 48 h. At which point, the reaction mixture was cooled in an ice-water bath, then water (200 mL, ice-water mixture) was slowly added to the reaction mixture. *Caution: exotherm or rapid increase in temperature observed over the course of the addition.* The resulting precipitate was separated from the mother liquor by filtration, and then dissolved in acetone (200–300 mL). The insoluble material was removed by filtration, and the mother liquor was dried over Na_2SO_4 and concentrated under reduced pressure to afford the title compound **S2** (12 g, 73%) in sufficient purity to use in the next step: ^1H NMR (500 MHz, $\text{DMSO}-d_6$) δ 8.07 (d, J = 8.9 Hz, 1H), 7.24 (d, J = 9.0 Hz, 1H), 3.91 (s, 3H); ^{13}C NMR (125 MHz, $\text{DMSO}-d_6$) δ 165.8 (C), 150.6 (C), 143.0 (CH), 138.7 (C), 134.1 (C), 117.1 (CH), 81.6 (C), 57.2 (CH_3); IR (film) 3074, ~3000 (broad), 2947, 1713; HRMS (ESI) m/z calcd for $\text{C}_8\text{H}_6\text{INO}_5\text{Na}$ ($\text{M}+\text{Na}$)⁺ 345.9189, found 345.9188; mp: 178–181 °C.



3-Hydroxy-6-iodo-2-nitrobenzoic acid (S3): To a solution of arylmethyl ether **S2** (14.5 g, 44.9 mmol), Et_2S (40 mL) and CH_2Cl_2 (400 mL) was added $AlCl_3$ (21.0 g, 157 mmol) in a portion-wise fashion. The reaction mixture was stirred at 40 °C for 48 h (the reaction progress was monitored by 1H NMR of aliquots sampled during the course of the reaction), then allowed to cool to rt and concentrated under reduced pressure (to approximately 1/3 volume). The crude residue was poured into a mixture of EtOAc (600 mL) and aqueous solution of HCl (0.125 M, 450 mL). The layers were separated and the aqueous layer was extracted with EtOAc (2 x 200 mL). The combined organic layers were washed with brine (200 mL), dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was crystallized (in some cases, precipitated) from CH_2Cl_2 (100 mL) in order to remove minor amounts of the hydrodehalogenated by-product, 3-hydroxy-2-nitrobenzoic acid (**S4**) [602-00-6] (1:10, **S4/S3** by NMR). After removal of the mother liquor by filtration, the product was redissolved in Et_2O to remove residual, purple-colored insoluble material, which was filtered away. The filtrate was concentrated under reduced pressure to afford the title compound **S3** (6.10 g, second crop: 2.10 g; combined 59%) as a tan solid: 1H NMR (500 MHz, CD_3OD) δ 7.89 (d, $J = 8.8$ Hz, 1H), 6.90 (d, $J = 8.8$ Hz, 1H); ^{13}C NMR (125 MHz, CD_3OD) δ 168.7 (C), 152.5 (C), 145.0 (CH), 138.6 (C), 137.2 (C), 122.4 (CH), 79.7 (C); IR (KBr) 3411, 3088, ~3000 (broad), 2898, 2654, 2590, 2526, 1701, 1600, 1442; HRMS (ESI) m/z calcd for $C_7H_3INO_5$ (M-H) $^-$ 307.9056, found 307.9051; mp: 174–176 °C (dec.).



2-Amino-3-hydroxy-6-iodobenzoic acid (S5): To a solution of nitroarene **S3** (7.3 g, 24 mmol) and THF (200 mL) was added a solution of $Na_2S_2O_4$ (41 g, 240 mmol) and water (100 mL). The reaction mixture was stirred vigorously at 50 °C for 3–4 h, then allowed to cool to rt and EtOAc (300 mL) was added. The layers were separated and the aqueous layer was extracted with EtOAc (2 x 200 mL). The combined organic layers were washed with brine (50 mL), dried over Na_2SO_4 and concentrated under reduced pressure to afford the title compound **S5** (4.6 g, 70%) in sufficient purity to use in the next step: 1H NMR (500 MHz, $DMSO-d_6$) δ 9.82 (s, 1H), 7.80 (bs, 2H), 6.93 (d, $J = 8.2$ Hz, 1H), 6.48 (d, $J = 8.2$ Hz, 1H); ^{13}C NMR (125 MHz, $DMSO-d_6$) δ 169.0 (C), 144.8 (C), 137.5 (C), 126.8 (CH), 121.4 (C), 116.4 (CH), 80.7 (C); IR (KBr) 3423, 3221, 2921, 1603; HRMS (ESI) m/z calcd for $C_7H_7INO_3$ (M+H) $^+$ 279.9471, found 279.9479; mp: 180–182 °C (dec.).

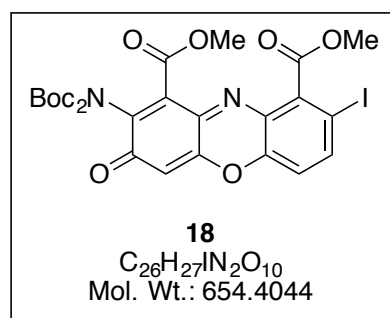


Dimethyl 2-amino-9-iodophenoxazin-3-one 1,10-dicarboxylate

(S7): To a suspension of 2-amino-3-hydroxy-4-iodobenzoic acid (**S5**) (4.4 g, 16 mmol) in a co-solvent mixture of PhMe and MeOH (160, 50 mL, respectively) was slowly added trimethylsilyl diazomethane (TMSCHN₂) (8.8 mL, 18 mmol, 2.0 M solution in hexane) while stirring. *Caution: evolution of N₂(g) over the course of the addition.* After 30 min, the resulting solution was poured into a mixture of EtOAc (50 mL) and water (25 mL). The layers were separated and the aqueous layer was extracted with EtOAc (2 x 20 mL). The combined organic layers were washed with

brine (10 mL), dried over Na₂SO₄ and concentrated under reduced pressure to afford methyl 2-amino-3-hydroxy-4-iodobenzoate (**S6**), which was used immediately in the following transformation: TLC R_f 0.45 (3:7 EtOAc/hexanes).

To a solution of o-aminophenol **S6** (16 mmol) in MeOH (160 mL) was added 1,4-benzoquinone (3.0 g, 27 mmol, freshly recrystallized from petroleum ether).⁴ The reaction mixture was maintained at 50 °C for 3 h (the reaction was shielded from light by covering the reaction vessel with aluminum foil), followed by placement in a freezer (−20 °C) for 12h. The resulting suspension was concentrated under reduced pressure (to approximately 1/2 volume), then filtered to separate the mother liquor from the precipitate, which was subsequently washed with EtOAc/hexane (100 mL, 1:1) to afford the title compound **S7** (2.0 g, 56%) as an orange-red solid in sufficient purity to use in the next step: ¹H NMR (500 MHz, DMSO-*d*₆) δ 8.00 (bs, 2H), 7.87 (d, *J* = 7.4 Hz, 1H), 7.39 (d, *J* = 7.4 Hz, 1H), 6.49 (s, 1H), 3.92 (s, 3H), 3.80 (s, 3H); ¹³C NMR (125 MHz, DMSO-*d*₆) δ 178.4 (C), 167.2 (C), 167.1 (C), 148.9 (C), 148.4 (C), 146.2 (C), 141.3 (C), 138.6 (C), 138.0 (CH), 131.6 (C), 118.4 (CH), 104.3 (CH), 99.0 (C), 86.6 (C), 52.7 (CH₃), 51.6 (CH₃); IR (film) 3446, 3326, 3075, 2948, 2922, 2854, 1730, 1672, 1641, 1575; TLC R_f 0.36 (3:7 EtOAc/hexanes), 0.52 (3:7 EtOAc/hexanes, plate was eluted twice); HRMS (ESI) *m/z* calcd for C₁₆H₁₁IN₂O₆Na (M+Na)⁺ 476.9560, found 476.9573; mp: 233–235 °C.



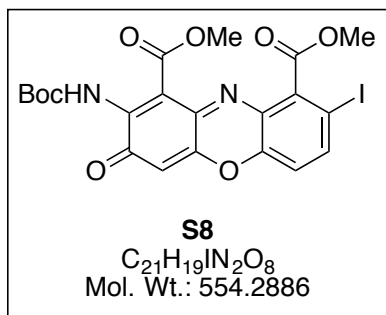
Dimethyl 2-(di(*tert*-butoxycarbonyl)amino)-9-iodophenoxazin-3-one-1,10-dicarboxylate

(18): To a solution of 2-aminophenoxazinone **S7** (2.0 g, 4.4 mmol) in THF (88 mL) were sequentially added Boc₂O (2.3 g, 11 mmol) and DMAP (50 mg, 0.10 mmol). After 2 h (in some cases, additional Boc₂O was added to drive the reaction to completion), the reaction mixture was poured into a mixture of EtOAc (300 mL) and saturated aqueous NH₄Cl (200 mL). The layers were separated and the aqueous layer was extracted with EtOAc (2 x 100 mL).

The combined organic layers were washed with brine (100 mL), dried over Na₂SO₄ and concentrated under reduced pressure. The crude residue was purified by silica gel chromatography (1:3 EtOAc/hexanes) to afford the title compound **18** (2.2 g, 76%) as a

⁴ 1,4-Benzoquinone has been used as the oxidant in dimerizations of this type to prepare cinnabaric acid and questiomycin, respectively, see (a) Christen, S.; Southwell-Keely, P. T.; Stocker, R. *Biochemistry* **1992**, *31*, 8090–8097. (b) Osman, A.; Bassioumi, I. *J. Am. Chem. Soc.* **1960**, *82*, 1607–1609.

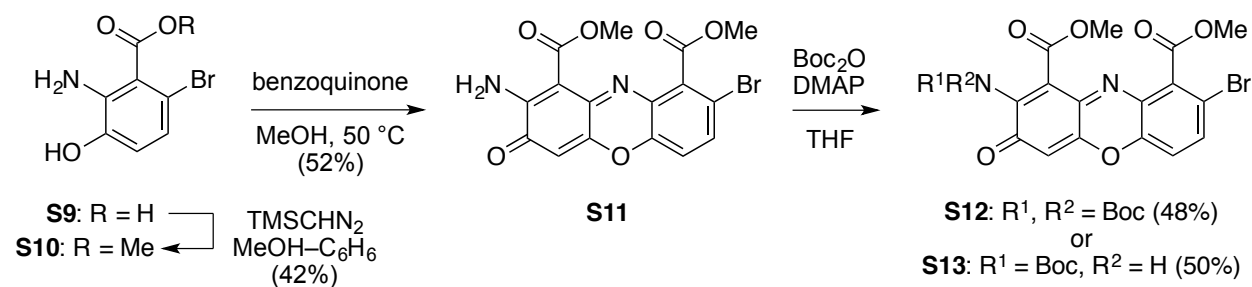
red solid: ^1H NMR (500 MHz, CDCl_3) δ 8.01 (s, 1H), 7.92 (d, $J = 8.7$ Hz, 1H), 7.15 (d, $J = 8.7$ Hz, 1H), 6.42 (s, 1H), 3.99 (s, 3H), 3.91 (s, 3H), 1.41 (s, 18H); ^{13}C NMR (125 MHz, CDCl_3) δ 179.9 (C), 166.5 (C), 162.6 (C), 149.2 (C), 148.2 (C), 147.5 (C), 143.5 (C), 142.8 (CH), 141.4 (C), 138.5 (C), 133.8 (C), 131.3 (C), 118.7 (CH), 107.2 (CH), 86.2 (C), 84.2 (C), 53.3 (CH_3), 53.0 (CH_3), 27.9 (CH_3); IR (film) 2980, 2953, 1801, 1745, 1640; TLC R_f 0.48 (3:7 EtOAc/hexanes, plate was eluted twice); HRMS (ESI) m/z calcd for $\text{C}_{26}\text{H}_{27}\text{IN}_2\text{O}_{10}\text{Na}$ ($\text{M}+\text{Na}$) $^+$ 677.0608, found 677.0611.

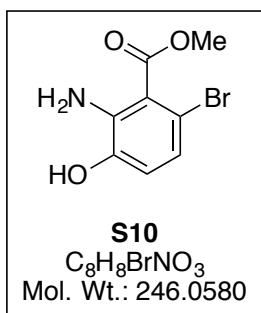


Dimethyl 2-(di-(*tert*-butoxycarbonyl)amino)-9-iodophenoxazin-3-one-1,10-dicarboxylate (S8): To a solution of 2-aminophenoxazinone **S7** (300 mg, 0.66 mmol) in THF (13 mL) were added sequentially Boc_2O (170 mg, 0.79 mmol) and DMAP (16 mg, 0.13 mmol). After 2 h, the reaction mixture was poured into a mixture of EtOAc (60 mL) and saturated aqueous NH_4Cl (30 mL). The layers were separated and the aqueous layer was extracted with EtOAc (2 x 30 mL). The combined organic layers were washed with brine (30 mL), dried over Na_2SO_4 and concentrated under reduced pressure.

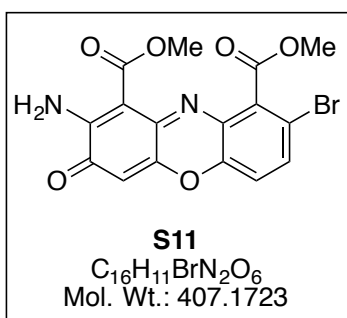
The crude residue was purified by silica gel chromatography (1:3 EtOAc/hexanes) to afford the title compound **S8** (200 mg, 54%; the remainder of mass balance consisted of a co-polar mixture of starting material **S7** and the di-*tert*-butoxycarbonyl derivative **18**) as an orange/red solid: ^1H NMR (500 MHz, CDCl_3) δ 8.01 (s, 1H), 7.88 (d, $J = 8.7$ Hz, 1H), 7.18 (d, $J = 8.7$ Hz, 1H), 6.48 (s, 1H), 4.03 (s, 3H), 3.92 (s, 3H), 1.50 (s, 9H); ^{13}C NMR (125 MHz, CDCl_3) δ 179.0 (C), 166.8 (C), 164.4 (C), 151.1 (C), 148.1 (C), 147.4 (C), 142.6 (C), 141.3 (CH), 141.0 (C), 135.0 (C), 131.9 (C), 118.4 (CH), 116.9 (C), 105.2 (CH), 86.4 (C), 83.0 (C), 53.3 (CH_3), 52.5 (CH_3), 28.2 (CH_3); IR (film) 3330, 2980, 2950, 2917, 2849, 1737, 1631, 1509, 1492; TLC R_f 0.64 (3:7 EtOAc/hexanes); HRMS (ESI) m/z calcd for $\text{C}_{21}\text{H}_{19}\text{IN}_2\text{O}_8\text{Na}$ ($\text{M}+\text{Na}$) $^+$ 577.0084, found 577.0086.

Scheme 2. Preparation of Phenoxazinone Bromide **S12** and **S13**



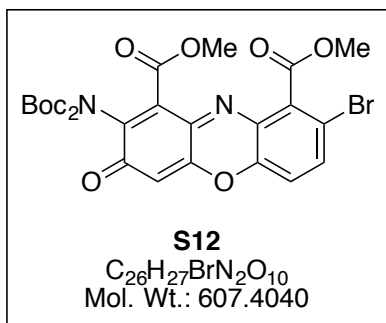


Methyl 2-amino-6-bromo-3-hydroxybenzoate (S10): To a suspension of 2-amino-6-bromo-3-hydroxybenzoic acid (**S9**) (0.95 g, 4.1 mmol) in a co-solvent mixture of PhMe and MeOH (14, 3.5 mL, respectively) was slowly added TMSCHN₂ (2.2 mL, 4.3 mol, 2.0 M solution in hexane) while stirring. *Caution: evolution of N₂(g) over the course of the addition.* After 30 min, the resulting solution was poured into a mixture of EtOAc (50 mL) and water (25 mL). The layers were separated and the aqueous layer was extracted with EtOAc (2 x 20 mL). The combined organic layers were washed with brine (10 mL), dried over Na₂SO₄ and concentrated under reduced pressure. The crude residue was purified by silica gel chromatography (0% → 40% EtOAc/hexanes)⁵ to afford the title compound **S10** (400 mg, 42%): ¹H NMR (500 MHz, CDCl₃) δ 6.80 (d, *J* = 8.4 Hz, 1H), 6.58 (d, *J* = 8.4 Hz, 1H), 5.10 (bs, 3H), 3.93 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 168.3 (C), 143.0 (C), 138.3 (C), 122.2 (CH), 117.7 (C), 117.4 (CH), 112.2 (C), 52.5 (CH₃); IR (film) 3499, 3387, 3350, 3288, 2953, 1681; HRMS (ESI) *m/z* calcd for C₈H₉BrNO₃ (M+H)⁺ 245.9766 and 247.9746, found 245.9763 and 247.9743; mp: 97–99 °C.



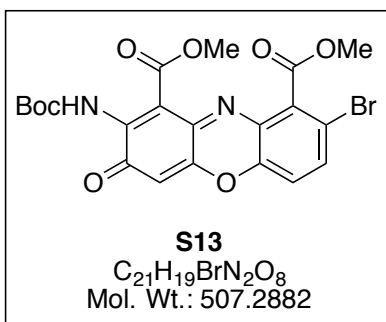
Dimethyl 2-amino-9-bromophenoxazin-3-one-1,10-dicarboxylate (S11): To a solution of o-aminophenol **S10** (210 mg, 0.87 mmol) in EtOH (20 mL) was added 1,4-benzoquinone (160 mg, 1.5 mmol, freshly recrystallized from petroleum ether).⁴ The reaction mixture was maintained at 45 °C for 24 h (the reaction was shielded from light by covering the reaction vessel with aluminum foil), then allowed to cool to rt and concentrated under reduced pressure. The crude residue was suspended in ethyl acetate/hexanes (1:1, 20 mL), and the solids were filtered away from the mother liquor to afford the title compound **S11** (90 mg, 52%) as an orange-red solid in sufficient purity to use in the following transformations: ¹H NMR (500 MHz, DMSO-*d*₆) δ 7.72 (d, *J* = 7.4 Hz, 1H), 7.55 (d, *J* = 7.4 Hz, 1H), 6.50 (s, 1H), 3.92 (s, 3H), 3.80 (s, 3H); TLC R_f 0.17 (3:7 EtOAc/hexanes).

⁵ The poor conversion in this transformation is attributed to the instability of the product **S10** toward purification by silica gel chromatography. In a more efficient protocol, **S10** would be used as a crude residue in the subsequent transformation. See the preparation of **S7** for a corresponding procedure.

**Dimethyl****9-bromo-2-(di(*tert*-butoxycarbonyl)amino)phenoxazin-3-one-1,10-dicarboxylate (S12):**

To a suspension of 2-aminophenoxazinone **S11** (50 mg, 0.12 mmol), Boc₂O (67 mg, 0.31 mmol) and THF (1.3 mL) was added DMAP (1.5 mg, 0.012 mmol). The reaction mixture was stirred for 1 h at rt, then poured into a mixture of EtOAc (20 mL) and water (10 mL). The layers were separated and the aqueous layer was extracted with EtOAc (2 x 20 mL). The combined organic layers were washed with brine (10 mL), dried over Na₂SO₄ and

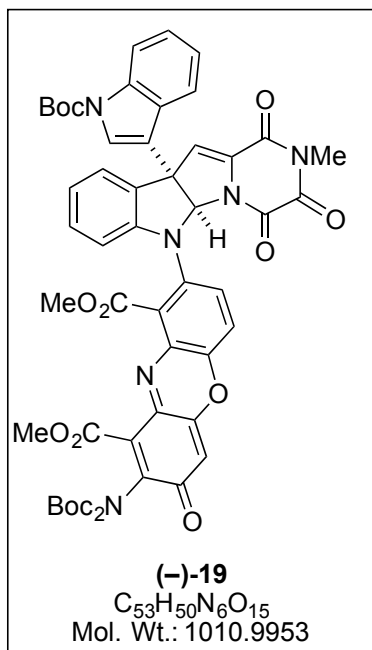
concentrated under reduced pressure. The crude residue was purified by silica gel chromatography (3/7 EtOAc/hexanes) to afford the title compound **S12** (30 mg, 48%) as a deep red solid: ¹H NMR (500 MHz, CDCl₃) δ 7.72 (d, *J* = 11.1 Hz, 1H), 7.28 (d, *J* = 11.1 Hz, 1H), 6.42 (s, 1H), 3.99 (s, 3H), 3.91 (s, 3H), 1.41 (s, 9H); ¹³C NMR (125 MHz, CDCl₃) δ 179.9 (C), 165.3 (C), 162.5 (C), 149.2 (C), 148.3 (C), 147.7 (C), 142.7 (C), 138.6 (C), 136.8 (CH), 136.7 (C), 133.8 (C), 131.3 (C), 118.5 (CH), 115.0 (C), 107.1 (CH), 84.2 (C), 53.3 (C), 53.0 (C), 27.9 (CH₃); IR (film) 3077, 2980, 2952, 2930, 1803, 1745, 1640; TLC *R*_f 0.17 (3:7 EtOAc/hexanes); HRMS (ESI) *m/z* calcd for C₂₆H₂₇BrN₂O₁₀Na (M+Na)⁺ 629.0746 and 631.0731 found 629.0740 and 631.0753.

**Dimethyl****9-bromo-2-(*tert*-butoxycarbonylamino)phenoxazin-3-one-1,10-dicarboxylate (S13):**

To a suspension of 2-aminophenoxazinone **S11** (80 mg, 0.20 mmol), Boc₂O (45 mg, 0.21 mmol) and a co-solvent mixture of CH₂Cl₂ and THF (2.0, 1.0 mL respectively) was added DMAP (2.4 mg, 0.020 mmol). The reaction mixture was stirred for 2 h at rt, then poured into a mixture of EtOAc (20 mL) and water (10 mL). The layers were separated and the aqueous layer was extracted with EtOAc (2 x 20 mL). The combined organic layers were washed

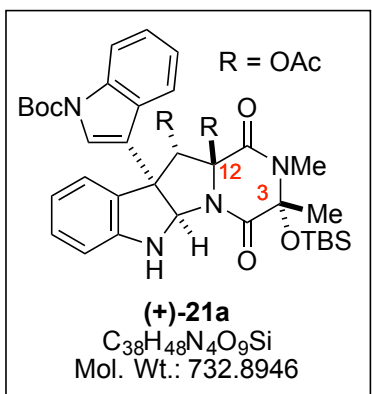
with brine (10 mL), dried over Na₂SO₄ and concentrated under reduced pressure. The crude residue was purified by silica gel chromatography (3/7 EtOAc/hexanes) to afford the title compound **S13** (50 mg, 50%; the remainder of mass balance consisted of a co-polar mixture⁶ of starting material **S11** and the di-*tert*-butoxycarbonyl derivative **S12**) as an orange solid: ¹H NMR (500 MHz, CDCl₃) δ 8.02 (s, 1H), 7.67 (d, *J* = 8.9 Hz, 1H), 7.31 (d, *J* = 8.9 Hz, 1H), 6.48 (s, 1H), 4.03 (s, 3H), 3.92 (s, 3H), 1.50 (s, 9H); ¹³C NMR (125 MHz, CDCl₃) δ 179.0 (C), 165.6 (C), 164.4 (C), 151.1 (C), 148.1 (C), 147.6 (C), 141.8 (C), 136.3 (C), 135.2 (CH), 135.1 (C), 131.9 (C), 118.2 (CH), 116.9 (C), 115.0 (C), 105.1 (CH), 83.0 (C), 53.2 (C), 52.5 (C), 28.2 (CH₃); IR (film) 3329, 2980, 2951, 1743, 1633, 1509, 1491; TLC *R*_f 0.25 (3:7 EtOAc/hexanes); HRMS (ESI) *m/z* calcd for C₂₁H₁₉BrN₂O₈Na (M+Na)⁺ 529.0222 and 531.0206 found 529.0217 and 531.0224.

⁶ This mixture of **S11** and **S12** was treated with Boc₂O (ca. 4 equiv), DMAP (2.0 mg) and THF (1 mL), which furnished **S12** as a single compound after purification (30 mg, 25% yield from the initial lot of **S11**).



Cross-coupled product (-)-19: The components of this reaction were combined in a screw-top vial inside a N_2 -filled glovebox. The reaction vial was sealed with a Teflon-lined cap, then brought outside the glovebox and heated in an aluminum block for the period of time indicated. The reaction vessel was charged with pyrrolinoindoline **17** (10 mg, 21 μ mol), phenoxazinone iodide **18** (30 mg, 46 μ mol), copper(I) thiophene-2-carboxylate (CuTC)⁷ (12 mg, 62 μ mol) and K_2CO_3 (11 mg, 83 μ mol), then PhMe (200 μ L) was added by syringe. The reaction mixture was heated at 90 °C for 36 h. After being allowed to cool to rt, the reaction mixture was passed directly through a short plug of silica gel (eluting with EtOAc) to remove the metal salts, then concentrated under reduced pressure. The crude residue was purified by chromatography on silica gel (1:19 EtOAc/hexanes $\rightarrow$ 1:3 EtOAc/hexanes) to afford the title compound **(-)-19** (14 mg, 67%) as a red solid: $[\alpha]_D^{24} -68.7$, $[\alpha]_D^{577} -72.2$ ($c = 0.075$, CH_2Cl_2); 1H NMR (500 MHz, $CDCl_3$) δ 8.18 (d, $J = 7.0$ Hz, 1H), 7.68 (d, $J = 7.3$ Hz, 1H), 7.6–7.5 (comp, 2H), 7.35 (t, $J = 7.6$ Hz, 1H), 7.15 (t, $J = 7.6$ Hz, 1H), 7.12 (t, $J = 7.3$ Hz, 1H),

7.05 (d, $J = 4.1$ Hz, 1H), 6.96 (d, $J = 7.6$, 1H), 6.83 (s, 1H), 6.78 (m, 1H), 6.75 (s, 1H), 6.45 (s, 1H), 6.37 (d, $J = 7.0$ Hz, 1H), 3.84 (s, 3H), 3.63 (s, 3H), 3.41 (s, 3H), 1.70 (s, 9H), 1.43 (s, 18H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 180.1 (C), 165.2 (C), 162.6 (C), 157.2 (C), 157.0 (C), 150.4 (C), 149.6 (C), 149.1 (C), 148.7 (C), 148.5 (CH), 147.3 (C), 143.0 (CH), 138.3 (C), 136.5 (C), 136.3 (C), 135.8 (C), 133.8 (C), 133.5 (CH), 131.6 (C), 131.0 (C), 129.8 (CH), 127.8 (C), 126.9 (C), 126.3 (CH), 125.4 (CH), 124.9 (CH), 124.1 (CH), 123.4 (CH), 120.8 (CH), 119.5 (2 x CH), 119.1 (C), 116.2 (CH), 108.2 (CH), 106.9 (CH), 88.0 (CH), 85.0 (C), 84.2 (C), 59.3 (C), 52.9 (2 x CH_3), 28.4 (CH_3), 27.9 (CH_3), 27.7 (CH_3); IR (film) 3056, 2980, 2952, 2933, 1804, 1741, 1714, 1692, 1642; TLC R_f 0.41 (4:6 EtOAc/hexanes); HRMS (ESI) m/z calcd for $C_{53}H_{50}N_6O_{15}Na$ ($M+Na$)⁺ 1033.3232, found 1033.3240.



Indoline (+)-21a (C3 α -OTBS epimer): In multiple, sealed vials, intermediate **20a** (5 x 40 mg, 0.048 mmol) was maintained (neat) at 175 °C in a pre-heated oil bath for 40–50 min. The reaction vessels were allowed to cool to rt, then THF (0.48 mL), DMAP (1 mg) and Boc_2O (10 mg, 0.048 mmol, 0.1 mL of a pre-made 0.5 M THF solution) were added sequentially to the reaction mixtures. After 1 h, the reaction mixtures were combined and poured into a mixture of EtOAc (20 mL) and saturated aqueous NH_4Cl (10 mL). The layers were separated and the aqueous layer was further extracted with EtOAc (10 mL). The combined organic layers were washed successively

with H_2O (10 mL) and brine (10 mL), dried over Na_2SO_4 and concentrated under reduced

⁷ Copper(I) thiophene-2-carboxylate (CuTC) [68986-76-5] was purchased from Sigma Aldrich Co.

pressure. The crude product was purified by silica gel chromatography (1:9 EtOAc/hexanes $\rightarrow$ 1:3 EtOAc/hexanes) to afford the title compound **(+)-21a** (125 mg, 71%; in some of these reactions the di-*tert*-butoxycarbonyl derivative **(-)-S14a** was also isolated as a minor by-product)⁸ as a colorless foam: $[\alpha]_{24}^D +93.8$, $[\alpha]_{24}^{577} +95.0$, $[\alpha]_{24}^{546} +100$, $[\alpha]_{24}^{435} +178$ (c 0.14, CH_2Cl_2); ^1H NMR (500 MHz, CDCl_3) δ 8.10 (br d, $J = 5.5$ Hz, 1H), 7.61 (d, $J = 7.5$ Hz, 1H), 7.59 (d, $J = 8.0$ Hz, 1H), 7.40 (s, 1H), 7.27 (t, $J = 7.8$ Hz, 1H), 7.19 (t, $J = 7.8$ Hz, 1H), 7.13 (t, $J = 7.7$ Hz, 1H), 6.92 (t, $J = 7.4$ Hz, 1H), 6.64 (d, $J = 7.8$ Hz, 1H), 6.52 (s, 1H), 6.26 (s, 1H), 4.86 (s, 1H), 3.02 (s, 3H), 1.90 (s, 3H), 1.61 (s, 9H), 1.45 (s, 3H), 1.37 (s, 3H), 0.98 (s, 9H), 0.37 (s, 3H), 0.33 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 169.3 (C), 168.13 (C), 168.08 (C), 159.1 (C), 149.5 (C), 147.2 (C), 136.4 (C), 129.5 (C), 129.3 (CH), 128.4 (C), 126.7 (CH), 125.6 (CH), 124.6 (CH), 122.6 (CH), 121.4 (CH), 119.9 (CH), 117.4 (C), 115.6 (CH), 109.7 (CH), 90.6 (C), 87.2 (C), 84.3 (C), 82.4 (CH), 80.9 (CH), 58.5 (C), 28.3 (CH_3), 28.0 (CH_3), 25.9 (CH_3), 24.0 (CH_3), 20.5 (CH_3), 20.4 (CH_3), 18.8 (C), -2.4 (CH_3), -3.1 (CH_3); IR (film) 3372, 2954, 2930, 2856, 1741, 1682, 1609, 1370, 1216; TLC R_f 0.28 (1:3 EtOAc/hexanes); HRMS (ESI) m/z calcd for $\text{C}_{38}\text{H}_{48}\text{N}_4\text{O}_9\text{SiNa}$ ($\text{M}+\text{Na}$)⁺ 755.3088, found 755.3083. The relative and absolute configuration of **(+)-21a** was confirmed by single crystal X-ray diffraction in isopropanol (X-ray quality crystals were formed by slow evaporation of the title compound in isopropanol) (see Figure 1).⁹

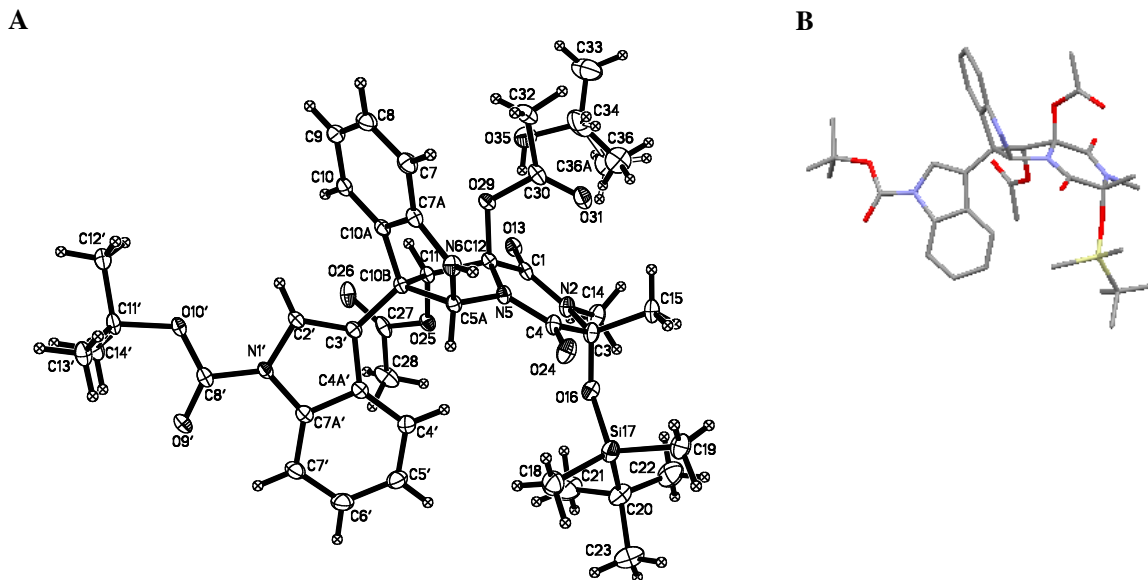
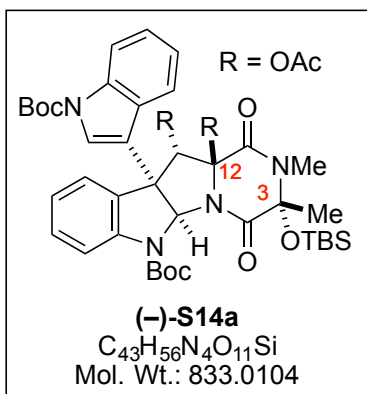


Figure 1. (A) X-ray structure of **(+)-21a** (CCDC 922842). The thermal ellipsoid plot is shown at 50% probability level. (B) Rendering of **(+)-21a** (with isopropanol molecule removed) using Mercury.¹⁰

⁸ The two-step sequence ranged from 60–80% yields on various scales (5 mg–100 mg of **20a**).

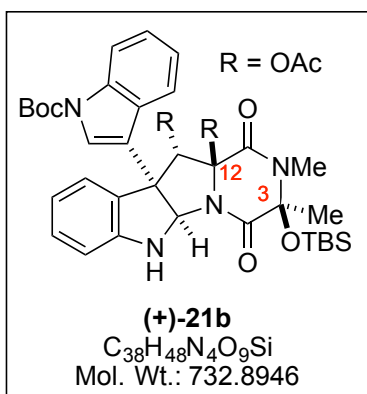
⁹ These data have been deposited at The Cambridge Crystallographic Data Centre as entry CCDC 922842 and can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif.

¹⁰ Mercury is a crystal structure visualization software available free of charge via <http://www.ccdc.cam.ac.uk/products/mercury>.



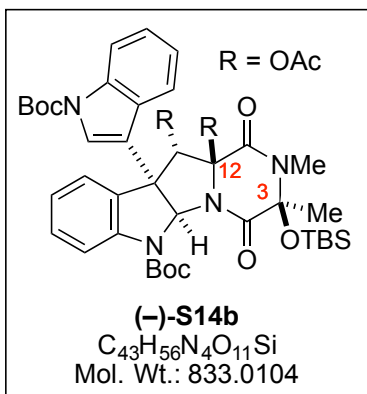
Data for di-*tert*-Butoxycarbonyl derivative (-)-S14a: $[\alpha]_D^{24} -3.2$, $[\alpha]_D^{577} -3.5$, $[\alpha]_D^{546} -2.8$, $[\alpha]_D^{435} -16.0$ (*c* 0.16, CH_2Cl_2); 1H NMR (500 MHz, $CDCl_3$) δ 8.11 (br d, *J* = 6.6 Hz, 1H), 7.89 (d, *J* = 7.9 Hz, 1H), 7.70 (d, *J* = 7.4 Hz, 1H), 7.57 (d, *J* = 7.9 Hz, 1H), 7.40 (s, 1H), 7.34 (s, 1H), 7.32–7.28 (comp, 3H), 7.25 (t, *J* = 7.6 Hz, 1H), 7.19 (t, *J* = 7.4 Hz, 1H), 6.11 (s, 1H), 3.03 (s, 3H), 1.90 (s, 3H), 1.61 (s, 9H), 1.49 (s, 9H), 1.43 (2 x s, 6H), 0.98 (s, 9H), 0.43 (s, 3H), 0.40 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.3 (C), 168.0 (C), 166.9 (C), 158.9 (C), 151.9 (C), 149.4 (C), 141.9 (C), 136.4 (C), 131.7 (C), 129.3 (CH), 128.0 (C), 127.5 (CH), 125.6 (CH), 124.7 (CH), 123.4 (CH), 122.9 (CH), 121.5 (CH), 116.8 (C), 115.8 (CH), 115.5 (CH), 92.0 (C),

87.1 (C), 84.4 (C), 83.4 (CH), 82.8 (C), 80.1 (CH), 56.9 (C), 28.5 (CH₃), 28.2 (CH₃), 27.9 (CH₃), 26.1 (CH₃), 24.8 (CH₃), 20.5 (CH₃), 20.3 (CH₃), 18.9 (C), -2.38 (CH₃), -2.42 (CH₃); IR (film) 2953, 2929, 2853, 1766, 1740, 1714, 1682, 1484, 1455, 1371; TLC *R_f* 0.35 (1:3 EtOAc/hexanes); HRMS (ESI) *m/z* calcd for $C_{43}H_{56}N_4O_{11}SiNa$ (*M*+*Na*)⁺ 855.3613, found 855.3622.



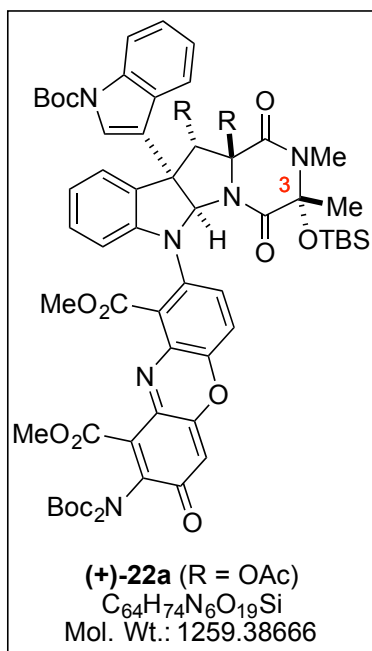
Indoline (+)-21b (C3 β -OTBS epimer): Following a similar procedure as described for formation of (+)-21a, intermediate 20b (200 mg, 0.26 mmol) was converted to the title compound (+)-21b (110 mg, 63%; in some of these reactions the di-*tert*-butoxycarbonyl derivative (-)-S14b was also isolated as a minor by-product), which was isolated as a colorless foam: $[\alpha]_D^{24} +50.7$, $[\alpha]_D^{577} +52.4$, $[\alpha]_D^{546} +60.5$, $[\alpha]_D^{435} +112$, $[\alpha]_D^{405} +144$ (*c* 0.10, CH_2Cl_2); 1H NMR (500 MHz, acetone-*d*₆) δ 8.16 (d, *J* = 8.3 Hz, 1H), 7.56 (d, *J* = 7.4 Hz, 1H), 7.52 (d, *J* = 8.0 Hz, 1H), 7.48 (s, 1H), 7.34 (t, *J* = 7.8 Hz, 1H), 7.26 (t, *J* = 7.6 Hz, 1H), 7.18 (t, *J* = 7.6 Hz, 1H), 6.93 (t, *J* = 7.4 Hz, 1H), 6.77 (d, *J* = 7.8 Hz, 1H), 6.52 (s, 1H), 6.49 (d, *J* = 2.8 Hz, 1H), 6.11 (s, 1H),

3.03 (s, 3H), 1.97 (s, 3H), 1.63 (s, 9H), 1.44 (s, 3H), 1.41 (s, 3H), 0.93 (s, 9H), 0.34 (s, 3H), 0.16 (s, 3H); ^{13}C NMR (125 MHz, acetone-*d*₆) δ 168.7 (C), 168.5 (C), 167.7 (C), 160.2 (C), 150.0 (C), 149.9 (C), 137.1 (C), 130.2 (C), 130.0 (CH), 129.2 (C), 126.8 (CH), 125.7 (CH), 125.4 (CH), 123.3 (CH), 121.9 (CH), 119.6 (CH), 119.2 (C), 116.4 (CH), 110.6 (CH), 91.2 (C), 86.9 (C), 85.0 (C), 84.1 (CH), 82.2 (CH), 59.6 (C), 29.4 (CH₃), 28.2 (CH₃), 28.0 (CH₃), 26.3 (CH₃), 20.5 (CH₃), 20.2 (CH₃), 19.2 (C), -2.9 (CH₃), -3.6 (CH₃); IR (film) 3376, 2954, 2917, 2850, 1766, 1740, 1682, 1609, 1371, 1215; TLC *R_f* 0.25 (3:7 EtOAc/hexanes); HRMS (ESI) *m/z* calcd for $C_{38}H_{48}N_4O_9SiNa$ (*M*+*Na*)⁺ 755.3088, found 755.3098.



Data for di-*tert*-Butoxycarbonyl derivative (-)-S14b: $[\alpha]_D^{24} -20.5$, $[\alpha]_D^{577} -31.4$, $[\alpha]_D^{546} -37.8$, $[\alpha]_D^{435} -82.9$ (c 0.18, CH_2Cl_2); 1H NMR (500 MHz, $CDCl_3$) δ 8.12 (br d, $J = 6.4$ Hz, 1H), 7.72 (br d, 1H), 7.71 (d, $J = 7.6$ Hz, 1H), 7.40 (s, 1H), 7.36 (d, $J = 8.0$ Hz, 1H), 7.32 (t, $J = 8.0$ Hz, 1H), 7.29 (t, $J = 7.5$ Hz, 1H), 7.27 (s, 1H), 7.22–7.18 (comp, 2H), 6.11 (s, 1H), 3.04 (s, 3H), 1.94 (s, 3H), 1.61 (s, 9H), 1.55 (s, 9H), 1.45 (s, 3H), 1.33 (s, 3H), 0.92 (s, 9H), 0.33 (s, 3H), 0.14 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.8 (C), 167.3 (C), 165.4 (C), 159.6 (C), 152.0 (C), 149.4 (C), 142.1 (C), 136.3 (C), 132.0 (C), 129.3 (CH), 128.0 (C), 127.1 (CH), 125.7 (CH), 124.7 (CH), 123.7 (CH), 122.7 (CH), 120.9 (CH), 116.7 (C), 116.4 (CH), 115.7

(CH), 91.1 (C), 85.9 (C), 84.5 (C), 83.9 (CH), 83.1 (C), 81.8 (CH), 56.9 (C), 28.5 (CH₃), 28.4 (CH₃), 28.3 (CH₃), 28.1 (CH₃), 25.9 (CH₃), 20.5 (CH₃), 20.3 (CH₃), 18.6 (C), -3.2 (CH₃), -4.1 (CH₃); IR (film) 2954, 2917, 2850, 1768, 1737, 1716, 1685, 1476, 1455, 1370; TLC R_f 0.35 (1:3 EtOAc/hexanes); HRMS (ESI) m/z calcd for $C_{43}H_{56}N_4O_{11}SiNa$ ($M+Na$)⁺ 855.3613, found 855.3600.

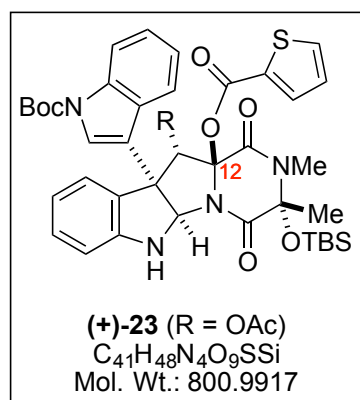


Cross-coupled product (+)-22a: The components of this reaction were combined in a screw-top vial inside a N_2 -filled glovebox. The reaction vial was sealed with a Teflon-lined cap, then brought outside the glovebox and heated in an aluminum block for the period of time indicated. The reaction vessel was charged with pyrrolidinoindoline **21a** (10 mg, 14 μ mol), phenoxazinone iodide **18** (27 mg, 42 μ mol), copper(I) acetate ($CuOAc$)¹¹ (10 mg, 82 μ mol) and KOAc (3.0 mg, 31 μ mol), then toluene (200 μ L) was added by syringe. The reaction mixture was maintained at 90 °C for 8 h. After being allowed to cool to rt, the reaction mixture was passed directly through a short plug of silica gel (eluting with EtOAc) to remove the metal salts, then concentrated under reduced pressure. The crude residue was purified by chromatography on silica gel (1:19 EtOAc/hexanes $\rightarrow$ 1:3 EtOAc/hexanes) to afford the title compound **(+)-22a** (10 mg, 58%) as a red solid: $[\alpha]_D^{24} +43.9$ (c 0.063, MeOH); **(+)-22a** was observed as a 3:1 mixture of atropisomers by NMR at 298 K; 1H NMR (500 MHz, acetone- d_6) δ 8.21 (d, $J = 8.3$ Hz, 1.33H), 7.76 (d, $J = 7.5$ Hz, 1.33H),

7.67 (d, $J = 8.8$ Hz, 1H), 7.62 (d, $J = 8.0$ Hz, 1H), 7.56 (s, 1H), 7.53 (s, 0.33H), 7.51 (d, $J = 8.1$ Hz, 0.33H), 7.41–7.38 (comp, 1.66H), 7.31 (d, $J = 8.8$ Hz, 1H), 7.30–7.19 (comp, 3H), 7.08 (t, $J = 7.4$ Hz, 1H), 6.92 (d, $J = 8.8$ Hz, 0.33H), 6.89 (s, 1H), 6.72 (s, 0.33H), 6.69 (d, $J = 8.0$ Hz, 0.33H), 6.48 (s, 1H), 6.44 (s, 0.33H), 6.31 (d, $J = 7.9$ Hz, 1H), 6.20 (s, 1H), 6.11 (s, 0.33H), 3.94 (s, 1H), 3.89 (s, 1H), 3.79 (s, 3H), 3.04 (s, 1H), 3.02 (s, 3H), 2.88 (s, 3H), 2.00 (s, 1H), 1.89 (s, 3H), 1.65 (s, 12H), 1.52 (s, 4H), 1.39 (s, 3H), 1.39 (s, 6H), 1.37 (2 x s, 19H), 1.01 (s, 1H), 0.98

¹¹ Copper(I) acetate ($CuOAc$) [598-54-9] was purchased from Strem Chemicals Inc.

(s, 9H), 0.40 (s, 1H), 0.35 (s, 1H), 0.32 (s, 3H), 0.30 (s, 3H); ^{13}C NMR (125 MHz, acetone- d_6) δ 180.6 (C, major), 170.0 (C, major), 169.6 (C, minor), 168.5 (C, major), 168.3 (C, minor), 168.2 (C, major), 167.4 (C, minor), 166.4 (C, minor), 165.4 (C, major), 163.73 (C, minor), 163.65 (C, major), 159.3 (C, minor), 159.2 (C, major), 151.0 (C, minor), 150.3 (C, minor), 150.2 (C, major), 150.0 (C, major), 149.8 (C, major), 148.8 (C, major), 148.4 (C, minor), 148.2 (C, major), 144.2 (C, major), 144.0 (C, minor), 140.3 (C, minor), 139.0 (C, major), 137.9 (C, minor), 137.33 (C, minor), 137.27 (C, major), 137.0 (C, major), 136.1 (CH, major), 134.83 (CH, minor), 134.75 (C, major), 134.71 (C, major), 131.84 (C, major), 131.79 (C, minor), 131.3 (C, minor), 130.22 (C, major), 130.19 (CH, minor), 130.1 (CH, major), 129.1 (C, major), 128.8 (C, minor), 128.6 (CH, minor), 128.1 (CH, major), 126.1 (CH, major), 125.8 (CH, minor), 125.6 (C, minor), 125.5 (CH, major), 123.6 (CH, major), 123.5 (CH, minor), 122.5 (CH, minor), 122.3 (CH, major), 122.1 (CH, minor), 120.5 (CH, major), 120.4 (CH, minor), 119.4 (CH, major), 118.5 (C, minor), 118.1 (C, major), 116.5 (CH, minor), 116.4 (CH, major), 114.3 (CH, minor), 108.8 (CH, major), 106.8 (CH, major), 106.7 (CH, minor), 92.0 (C, major), 91.5 (C, minor), 88.5 (CH, minor), 88.2 (C, minor), 87.9 (C, major), 86.7 (CH, major), 85.34 (C, minor), 85.25 (C, major), 83.74 (CH, minor), 83.70 (C, major), 83.4 (CH, major), 59.6 (C, minor), 58.5 (C, major), 53.3 (CH₃, minor), 53.2 (CH₃, minor), 53.1 (CH₃, major), 51.8 (CH₃, major), 28.3 (CH₃, major), 28.2 (CH₃, major), 27.93 (CH₃, minor), 27.92 (CH₃, major), 26.35 (CH₃, minor), 26.32 (CH₃, major), 24.83 (CH₃, minor), 24.80 (CH₃, major), 20.5 (CH₃, major), 20.3 (CH₃, major), 20.1 (CH₃, minor), 19.30 (C, minor), 19.28 (C, major), -2.0 (CH₃, minor), -2.3 (CH₃, major), -2.4 (CH₃, minor), -2.7 (CH₃, major);¹² IR (film) 2954, 2918, 2850, 1807, 1744, 1683, 1643, 1578, 1369; TLC R_f 0.10 (3:7 EtOAc/hexanes); HRMS (ESI) m/z calcd for C₆₄H₇₄N₆O₁₉SiNa (M+Na)⁺ 1281.4675, found 1281.4697.

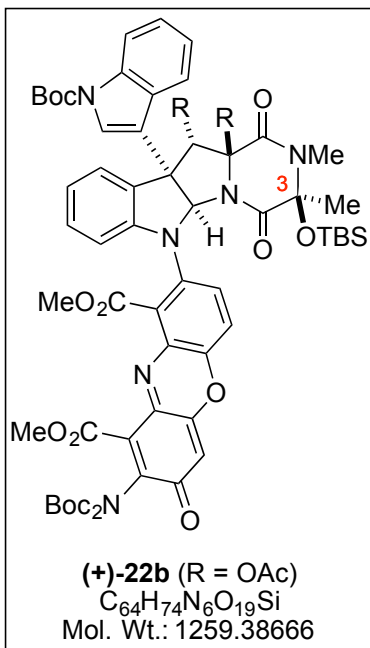


Thiophene-2-carboxylate adduct (+)-23:¹³ $[\alpha]_D^{24} +29.8$, $[\alpha]_D^{577} +38.3$, $[\alpha]_D^{546} +44.0$, $[\alpha]_D^{435} +93.8$ (c 0.10, CH₂Cl₂); ^1H NMR (500 MHz, acetone- d_6) δ 8.16 (d, $J = 7.8$ Hz, 1H), 7.81 (d, $J = 4.8$ Hz, 1H), 7.72 (d, $J = 8.1$ Hz, 1H), 7.71 (d, $J = 6.8$ Hz, 1H), 7.49 (s, 1H), 7.36 (t, $J = 7.8$ Hz, 1H), 7.28 (t, $J = 7.6$ Hz, 1H), 7.06 (t, $J = 7.6$ Hz, 1H), 7.01 (t, $J = 7.3$ Hz, 1H), 6.98 (t, $J = 4.3$ Hz, 1H), 6.62 (d, $J = 1.5$ Hz, 1H), 6.56 (s, 1H), 6.49 (s, 1H), 6.48 (d, $J = 7.8$ Hz, 1H), 6.37 (s, 1H), 3.05 (s, 3H), 1.99 (s, 3H), 1.64 (s, 9H), 1.50 (s, 3H), 1.01 (s, 9H), 0.42 (s, 3H), 0.32 (s, 3H); ^{13}C NMR (125 MHz, acetone- d_6) δ 167.9 (C), 167.8 (C), 160.3 (C), 159.0 (C), 149.3 (C), 149.0 (C), 136.5 (C), 135.4 (CH), 135.0 (CH), 131.8 (C), 129.7 (CH), 129.6 (C), 128.5 (C), 128.2 (CH), 126.0 (CH), 125.1 (CH), 124.8 (CH), 122.8 (CH), 121.6 (CH), 119.03 (C), 119.00 (CH), 115.7 (CH), 110.3 (CH), 91.8 (C), 87.3 (C), 84.4 (C), 82.9 (CH), 81.6 (CH), 59.0 (C), 27.65 (CH₃), 27.57 (CH₃), 25.7 (CH₃), 23.9 (CH₃), 19.8 (CH₃), 18.7 (C), -2.9 (CH₃), -3.4 (CH₃); IR (film) 3376, 2954, 2918, 2851, 1765, 1736, 1710, 1683, 1608, 1371, 1218; TLC R_f 0.56 (3:7 EtOAc/hexanes, plate

¹² In the ^{13}C NMR spectrum for **22a**, multiple carbons of the minor atropisomer were not detected or coincided with other carbon resonances.

¹³ During preliminary cross-coupling experiments, allowing **21a** to react with varying amounts of **18**, CuTC, and K₂CO₃ in PhMe at 90 °C resulted in the formation of **23** in minor quantities.

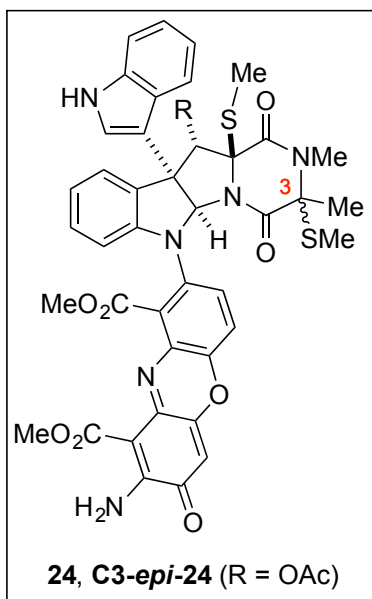
was eluted twice); HRMS (ESI) m/z calcd for $C_{41}H_{48}N_4O_9SSiNa$ ($M+Na$)⁺ 823.2809, found 823.2798.



Cross-coupled product (+)-22b: Following a similar procedure as described for formation of (+)-22a, intermediate **21b** (17 mg, 23 μ mol) was converted to the title compound (+)-22b (15 mg, 51%), which was isolated as a red solid: $[\alpha]_D^{24} +28.0$ (c 0.053, MeOH); 1H NMR (500 MHz, acetone- d_6) δ 8.22 (d, J = 8.3 Hz, 1H), 7.74 (d, J = 7.5 Hz, 1H), 7.59 (d, J = 8.8 Hz, 1H), 7.56 (s, 1H), 7.41–7.38 (comp, 3H), 7.29 (t, J = 7.6 Hz, 1H), 7.23 (t, J = 7.7 Hz, 1H), 7.09 (t, J = 7.7 Hz, 1H), 6.79 (s, 1H), 6.48 (s, 1H), 6.34 (d, J = 7.6 Hz, 1H), 6.11 (s, 1H), 3.78 (s, 3H), 3.04 (s, 3H), 2.84 (s, 3H), 1.96 (s, 3H), 1.65 (s, 9H), 1.59 (s, 3H), 1.40 (2 x s, 21H), 0.98 (s, 9H), 0.24 (s, 3H), 0.09 (s, 3H); ^{13}C NMR (125 MHz, acetone- d_6) δ 180.6 (C), 169.4 (C), 168.3 (C), 167.8 (C), 165.3 (C), 163.6 (C), 159.8 (C), 150.1 (C), 150.0 (C), 149.7 (C), 149.0 (C), 148.1 (C), 144.2 (C), 139.0 (C), 137.22 (C), 137.17 (CH), 136.7 (CH), 134.79 (C), 134.76 (C), 131.9 (C), 130.1 (CH), 129.8 (C), 129.1 (C), 127.9 (CH), 126.1 (CH), 125.6 (CH), 123.3 (CH), 121.8 (CH), 120.6 (CH), 119.4 (CH), 118.3 (C), 116.5 (CH), 108.9 (CH), 106.9 (CH), 91.6 (C), 88.0 (CH), 87.1 (C), 85.3 (C), 84.3 (CH), 83.4 (C), 59.0 (C), 53.1 (CH₃),

51.7 (CH₃), 29.4 (CH₃),¹⁴ 28.2 (CH₃), 28.1 (CH₃), 27.9 (CH₃), 26.2 (CH₃), 20.6 (CH₃), 20.1 (CH₃), 19.2 (C), -2.8 (CH₃), -3.1 (CH₃); IR (film) 2979, 2952, 2929, 2851, 1807, 1768, 1747, 1687, 1577, 1370; TLC R_f 0.24 (4:6 EtOAc/hexanes); HRMS (ESI) m/z calcd for $C_{64}H_{74}N_6O_{19}SiNa$ ($M+Na$)⁺ 1281.4675, found 1281.4680.

¹⁴ In the ^{13}C NMR spectrum of **22b**, this carbon coincided with the acetone- d_6 (solvent) peaks and was assigned by DEPT and HMQC experiments.

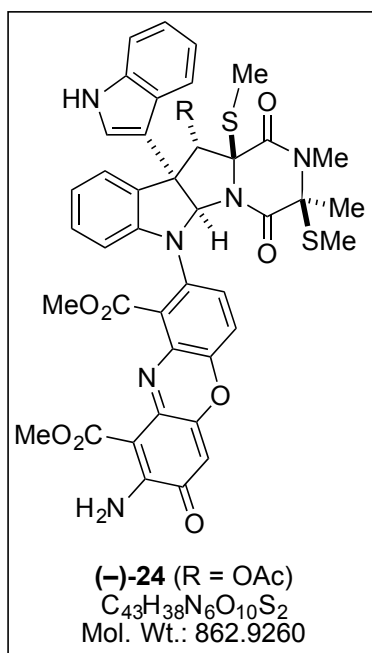


Incorporation of the methyl sulfides; Method A: Hydrogen sulfide (bp $-60\text{ }^{\circ}\text{C}$, ca. $200\text{ }\mu\text{L}$) was condensed at $-78\text{ }^{\circ}\text{C}$ in a thick-walled, glass pressure tube fitted with a rubber septum. A solution of **22a** (5.0 mg , $4.0\text{ }\mu\text{mol}$) in CH_2Cl_2 ($400\text{ }\mu\text{L}$) and $\text{BF}_3\cdot\text{OEt}_2$ ($10\text{ }\mu\text{L}$, $80\text{ }\mu\text{mol}$) were injected sequentially into the reaction vessel maintained at $-78\text{ }^{\circ}\text{C}$. The rubber septum was replaced by the corresponding Teflon screw cap, which was used to seal the vessel. The cold bath was removed and the reaction mixture was allowed to warm to rt *behind a blast shield*. After 1 h, the reaction mixture was cooled to $-78\text{ }^{\circ}\text{C}$, the Teflon cap was replaced by the rubber septum, which was equipped with a needle vented to base (KOH/isopropanol) and bleach traps (attached in series). The cooling bath was removed and the resulting brown suspension was allowed to warm up to rt. Upon evolution of the majority of hydrogen sulfide gas, an argon-filled balloon was attached (by needle) to fully purge the reaction mixture, which was subsequently poured into a mixture

of EtOAc (2 mL) and saturated aqueous NH_4Cl (2 mL). The layers were separated and the aqueous layer was extracted with EtOAc (2 mL). The combined organic layers were washed with brine (4 mL), dried over Na_2SO_4 and filtered. To the resulting solution was immediately added MeI ($20\text{ }\mu\text{L}$, $200\text{ }\mu\text{mol}$) and K_2CO_3 (14 mg , $100\text{ }\mu\text{mol}$). *Performing the S-alkylation step prior to any further manipulations prevented competitive oxidation of the dithiol intermediate to the undesired epidisulfide congener.* The reaction mixture was stirred for 12 h at rt, then poured into a mixture of EtOAc (10 mL) and saturated aqueous NH_4Cl (10 mL). The layers were separated and the aqueous layer was extracted with EtOAc ($2 \times 5\text{ mL}$). The combined organic layers were washed with brine (10 mL), dried over Na_2SO_4 and concentrated under reduced pressure. The crude residue was purified by preparatory thin layer chromatography (6/4 EtOAc/hexanes) to afford the title compound (–)-**24** (3.0 mg , 88%) as a single diastereomer (by ^1H NMR analysis). In corresponding experiments with **22b** (10 mg , $8.0\text{ }\mu\text{mol}$), the title compound (–)-**24** (5.5 mg , 80%) was obtained in similar efficiency and diastereoselectivity as a red solid.

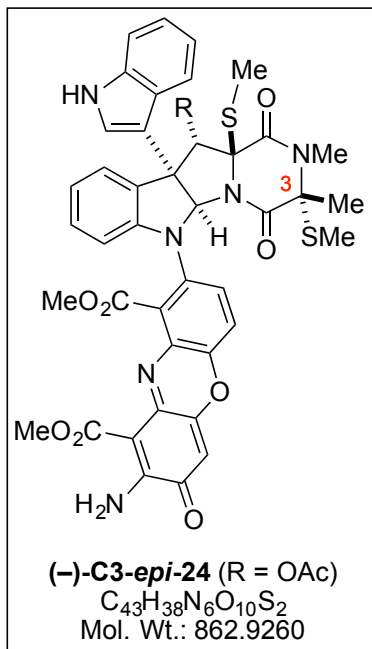
Method B: Methanethiol (bp $6\text{ }^{\circ}\text{C}$, ca. $200\text{ }\mu\text{L}$) was condensed at $-78\text{ }^{\circ}\text{C}$ in a thick-walled, glass pressure tube fitted with a rubber septum. A solution of **22a** (23 mg , $18\text{ }\mu\text{mol}$) in CH_2Cl_2 ($400\text{ }\mu\text{L}$) and $\text{BF}_3\cdot\text{OEt}_2$ ($30\text{ }\mu\text{L}$, $240\text{ }\mu\text{mol}$) were injected sequentially into the reaction vessel maintained at $-78\text{ }^{\circ}\text{C}$. The rubber septum was replaced by the corresponding Teflon screw cap, which was used to seal the vessel. The cold bath was removed and the reaction mixture was allowed to warm to rt *behind a blast shield*. After 1 hour, the reaction mixture was cooled back down to $-78\text{ }^{\circ}\text{C}$, the Teflon cap was replaced by the rubber septum, which was equipped with a needle vented to base (KOH/isopropanol) and bleach traps (attached in series). The cooling bath was removed and the resulting brown suspension was allowed to warm up to rt. Upon evolution of the majority of methanethiol gas, an argon-filled balloon was attached (by needle) to fully purge the reaction mixture, which was subsequently poured into a mixture of EtOAc (10 mL) and saturated aqueous NaHCO_3 (10 mL). The layers were separated and the aqueous layer was extracted with EtOAc ($2 \times 10\text{ mL}$). The combined organic layers were washed with brine (10 mL), dried over Na_2SO_4 , and then concentrated under reduced pressure. This reaction was conducted three times consecutively, and then the crude residues were combined for purification by preparatory thin layer chromatography (6/4 EtOAc/hexanes) to afford the title compound (–)-

24 (21 mg, 45%) and **(-)-C3-*epi*-24** (16 mg, 34%) as red solids. In corresponding experiments with **22b** (30 mg, 24 μ mol), the title compound **(-)-24** and **(-)-C3-*epi*-24** was obtained in similar efficiency (19 mg, 92% overall) and diastereoselectivity (1.3:1 dr, respectively) as a red solid.



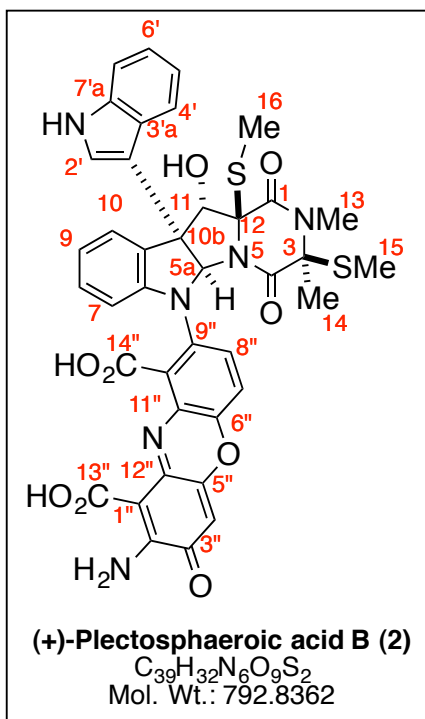
Data for *cis*-di(thiomethyl)ether **24:** $[\alpha]_D^{24} -142$, $[\alpha]_D^{577} -168$, $[\alpha]_D^{546} -217$ (*c* 0.050, CH_2Cl_2); 1H NMR (500 MHz, $CDCl_3$) δ 8.21 (s, 1H), 7.71–7.67 (comp, 2H), 7.45 (d, $J = 8.0$ Hz, 1H), 7.36 (d, $J = 8.8$ Hz, 1H), 7.31 (d, $J = 8.2$ Hz, 1H), 7.26 (s, 1H), 7.16–7.13 (comp, 1H), 7.10 (s, 1H), 7.15 (t, $J = 7.6$ Hz, 1H), 7.02 (d, $J = 2.5$ Hz, 1H), 6.89 (t, $J = 7.4$ Hz, 1H), 6.45 (s, 1H), 6.29 (s, 1H), 6.22 (d, $J = 7.8$ Hz, 1H), 3.75 (s, 3H), 3.10 (s, 3H), 2.65 (s, 3H), 2.16 (s, 3H), 2.00 (s, 3H), 1.87 (s, 3H), 1.32 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.5 (C), 169.1 (C), 168.9 (C), 166.1 (C), 163.8 (C), 163.5 (C), 150.8 (C), 150.2 (C), 149.4 (C), 145.9 (C), 141.1 (C), 137.3 (C), 135.6 (C), 134.7 (C), 132.0 (C), 131.4 (CH), 129.7 (C), 129.6 (CH), 126.1 (C), 126.0 (CH), 124.2 (CH), 122.3 (CH), 121.1 (CH), 120.1 (CH), 118.8 (CH), 117.4 (CH), 112.9 (C), 111.8 (CH), 107.7 (CH), 105.0 (CH), 98.2 (C), 86.1 (CH), 81.2 (CH), 72.6 (C), 67.2 (C), 57.5 (C), 51.6 (CH₃), 51.3 (CH₃), 29.2 (CH₃), 23.7 (CH₃), 20.5 (CH₃), 16.4 (CH₃), 14.6 (CH₃); IR (film) 3412, 3308, 2947, 2918, 2849, 1745, 1668, 1581, 1374; TLC R_f 0.38 (1:1 EtOAc/hexanes, plate was eluted twice); HRMS (ESI) m/z calcd

for $C_{43}H_{38}N_6O_{10}S_2Na$ ($M+Na$)⁺ 885.1989, found 885.1968. Note, for comparison, the 1H NMR of **(-)-24** was also obtained in acetone- d_6 : 1H NMR (500 MHz, acetone- d_6) δ 10.37 (s, 1H), 7.73 (d, $J = 7.3$ Hz, 1H), 7.67 (d, $J = 8.7$ Hz, 1H), 7.62 (d, $J = 8.7$ Hz, 1H), 7.54 (d, $J = 8.0$ Hz, 1H), 7.45 (d, $J = 8.2$ Hz, 1H), 7.2–7.1 (comp, 3H), 7.07 (s, 1H), 7.04 (t, $J = 7.5$ Hz, 1H), 6.90 (t, $J = 7.4$ Hz, 1H), 6.44 (s, 1H), 6.30 (s, 1H), 6.16 (d, $J = 7.8$ Hz, 1H), 3.73 (s, 3H), 3.08 (s, 3H), 2.69 (s, 3H), 2.13 (s, 3H), 2.05 (s, 3H), 1.85 (s, 3H), 1.29 (s, 3H).



Data for *trans*-di(thiomethyl)ether (-)-C3-epi-24: $[\alpha]_D^{24} -103$, $[\alpha]^{577}_{24} -110$, $[\alpha]^{546}_{24} -136$ (c 0.11, CH_2Cl_2); (-)-C3-epi-24 was observed as a 4:1 mixture of atropisomers by NMR at 298 K (subsequent data is provided for the major isomer only); 1H NMR (500 MHz, $acetone-d_6$) δ 10.39 (s, 1H), 7.73 (d, $J = 7.3$ Hz, 1H), 7.61 (d, $J = 8.0$ Hz, 1H), 7.60 (d, $J = 8.6$ Hz, 1H), 7.53 (d, $J = 8.8$ Hz, 1H), 7.46 (d, $J = 8.1$ Hz, 1H), 7.2–7.1 (comp, 3H), 7.05 (t, $J = 7.8$ Hz, 1H), 7.04 (s, 1H), 6.92 (t, $J = 7.5$ Hz, 1H), 6.45 (s, 1H), 6.23 (s, 1H), 6.19 (d, $J = 7.9$ Hz, 1H), 3.73 (s, 3H), 3.11 (s, 3H), 2.62 (s, 3H), 2.16 (s, 3H), 2.12 (s, 3H), 1.74 (s, 3H), 1.29 (s, 3H); ^{13}C NMR (125 MHz, $acetone-d_6$) δ 179.0 (C), 169.3 (C), 168.6 (C), 166.2 (C), 165.1 (C), 163.6 (C), 151.3 (C), 151.2 (C), 150.4 (C), 146.8 (C), 142.1 (C), 138.7 (C), 136.4 (C), 135.1 (C), 132.6 (C), 132.1 (CH), 130.9 (C), 130.1 (CH), 127.2 (CH), 127.1 (C), 125.1 (CH), 122.5 (CH), 121.9 (CH), 119.8 (CH), 119.3 (CH), 118.2 (CH), 112.98 (CH), 112.96 (C), 108.1 (CH), 105.3 (CH), 87.3 (CH), 81.6 (CH), 74.5 (C), 73.8 (C), 58.6 (C), 51.7 (CH₃), 51.2 (CH₃), 30.2 (CH₃), 25.2 (CH₃), 20.3 (CH₃), 16.1 (CH₃), 13.2 (CH₃);¹⁵ IR (film) 3389, 3307, 2947, 2917, 2849, 1747, 1667, 1581, 1377; TLC R_f 0.28 (1:1 EtOAc/hexanes, plate was eluted twice); HRMS (ESI) m/z calcd for $C_{43}H_{38}N_6O_{10}S_2Na$ (M+Na)⁺ 885.1989, found 885.1960.

¹⁵ In the ^{13}C NMR spectrum of C3-epi-24, a quaternary carbon was not detected or coincided with another carbon resonance.



(+)-Plectosphaeroic acid B (2):¹⁶ To a solution of *cis*-di(thiomethyl)ether **24** (8 mg, 9.3 μ mol) in MeOH (100 mL) was added lanthanum(III) trifluoromethanesulfonate ($La(OTf)_3$) (56 mg, 93 μ mol) and DMAP (1.4 mg, 11 μ mol). The reaction mixture was maintained at 45 °C. After 5 h (the consumption of the starting material was monitored by TLC, heating times varied in some instances), the reaction mixture was allowed to cool to rt, then poured into a mixture of EtOAc (10 mL) and saturated aqueous NH_4Cl (10 mL). The layers were separated and the aqueous layer was extracted with EtOAc (2 x 10 mL). The combined organic layers were washed with brine (10 mL), dried over Na_2SO_4 and concentrated under reduced pressure. The crude residue was purified by preparatory thin layer chromatography (7:3 EtOAc/hexanes) to afford the de-acetylated, C11-secondary alcohol intermediate (6 mg, contaminated with a closely eluting by-product arising from the in-situ hydrolysis of a methyl ester group) as a red solid. The product mixture from the first step was dissolved in pyridine (100 mL) and LiI (50 mg, 370 μ mol) was added to

the solution. The reaction mixture was stirred for 12 h at 90 °C (formation of product was observed by RP-18 TLC) then allowed to cool to rt and poured into a mixture of EtOAc (5 mL) and 1N HCl (2 mL). The layers were separated, the organic layers was washed with 1N HCl (2 x 2 mL). The combined aqueous layers were extracted with EtOAc (4 mL), and then the combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The crude residue was purified by reverse-phase HPLC (step-gradient eluting 20%, 40%, 60%, 65%, 70%, 75%, 90% MeOH/ H_2O + 0.1% TFA) to afford plectosphaeroic acid B (**2**) (4.8 mg, 65% over two steps, eluting at 75% MeOH/ H_2O + 0.1% TFA) as a red solid: $[\alpha]_D^{24} +228$ (*c* 0.08, MeOH), compare with reported value $[\alpha]_D^{24} +69.8$ (*c* 0.27, MeOH) of the natural sample;¹⁶ RP-18 TLC R_f 0.57 (4:1 MeOH/ H_2O); HRMS (ESI) m/z calcd for $C_{39}H_{32}N_6O_9S_2Na$ ($M-H$)⁻ 791.1594, found 791.1610; See Table 1 for NMR data, as well as Figure 2 for CD spectrum of synthetic **2**.

¹⁶ For the isolation and structure elucidation of (+)-plectosphaeroic acid B (**2**), see ref 1 of the communication: Carr, G.; Tay, W.; Bottriell, H.; Andersen, S. K.; Mauk, A. G.; Andersen, R. J. *Org. Lett.* **2009**, *11*, 2996–2999.

Table 1. NMR Data for Plectosphaeroic Acid B (**2**)

Pos.	Literature (600 MHz, DMSO- <i>d</i> ₆) ^a		Synthetic (500 MHz, DMSO- <i>d</i> ₆)	
	δH (multiplicity, <i>J</i> /Hz)	δC	δH (multiplicity, <i>J</i> /Hz)	δC
1		163.5 (C)		163.5 (C)
2				
3		66.2 (C)		66.3 (C)
4		163.6 (C)		163.6 (C)
5				
5a	6.74 (s)	86.1 (CH)	6.74 (s)	86.1 (C)
6				
6a		149.1 (C)		149.1 (C)
7	5.98 (d, 7.9)	106.7 (CH)	5.98 (d, 7.9)	106.7 (CH)
8	6.90 (t, 7.6)	127.9 (CH)	6.90 (t, 7.6)	127.9 (CH)
9	6.56 (t, 7.3)	118.0 (CH)	6.56 (t, 7.4)	118.0 (CH)
10	7.60 (d, 7.6)	122.4 (CH)	7.57 (d, 7.6)	122.4 (CH)
10a		133.3 (C)		133.3 (C)
10b		58.6 (C)		58.6 (C)
11	5.44 (br s)	78.5 (CH)	5.44 (br s)	78.6 (CH)
11-OH	5.74 (br s)		5.73 (br s)	
12		74.1 (C)		74.1 (C)
13	2.93 (s)	28.5 (CH ₃)	2.93 (s)	28.5 (CH ₃)
14	1.59 (s)	22.6 (CH ₃)	1.59 (s)	22.6 (CH ₃)
15	1.88 (s)	13.6 (CH ₃)	1.88 (s)	13.9 (CH ₃)
16	2.14 (s)	15.4 (CH ₃)	2.14 (s)	15.7 (CH ₃)
1'				
2'	7.34 (s)	122.5 (CH)	7.36 (s)	122.5 (CH)
3'		115.9 (C)		115.9 (C)
3'a		125.3 (C)		125.3 (C)
4'	8.04 (d, 7.6)	121.5 (CH)	8.06 (d, 7.6)	121.5 (CH)
5'	7.06 (m)	118.6 (CH)	7.06 (m)	118.6 (CH)
6'	7.09 (m)	120.9 (CH)	7.09 (m)	120.9 (CH)
7'	7.36 (m)	111.4 (CH)	7.36 (m)	111.4 (CH)
7'a		137.1 (C)		137.1 (C)
1''	10.86 (br s)	92.4 (C)	10.85 (s)	92.4 (C)
2''		152.6		152.6 (C)
2''-NH ₂	9.72 (br s)		9.72 (br s)	
	8.91 (br s)		8.91 (br s)	
3''		178.1 (C)		178.1 (C)
4''	6.68 (s)	105.5 (CH)	6.68 (s)	105.5 (CH)
5''		151.0		151.0 (C)
6''		141.2 (C)		141.2 (C)
7''	7.72 (d, 8.9)	117.8 (CH)	7.72 (d, 8.8)	117.8 (CH)
8''	7.69 (d, 8.9)	130.7 (CH)	7.69 (d, 8.8)	130.7 (CH)
9''		135.0 (C)		135.0 (C)
10''		133.3 (C)		133.3 (C)
11''		127.3 (C)		127.4 (C)
12''		147.6 (C)		147.6 (C)
13''		168.9 (C)		168.9 (C)
14''		167.2 (C)		167.2 (C)

^a See ref 16

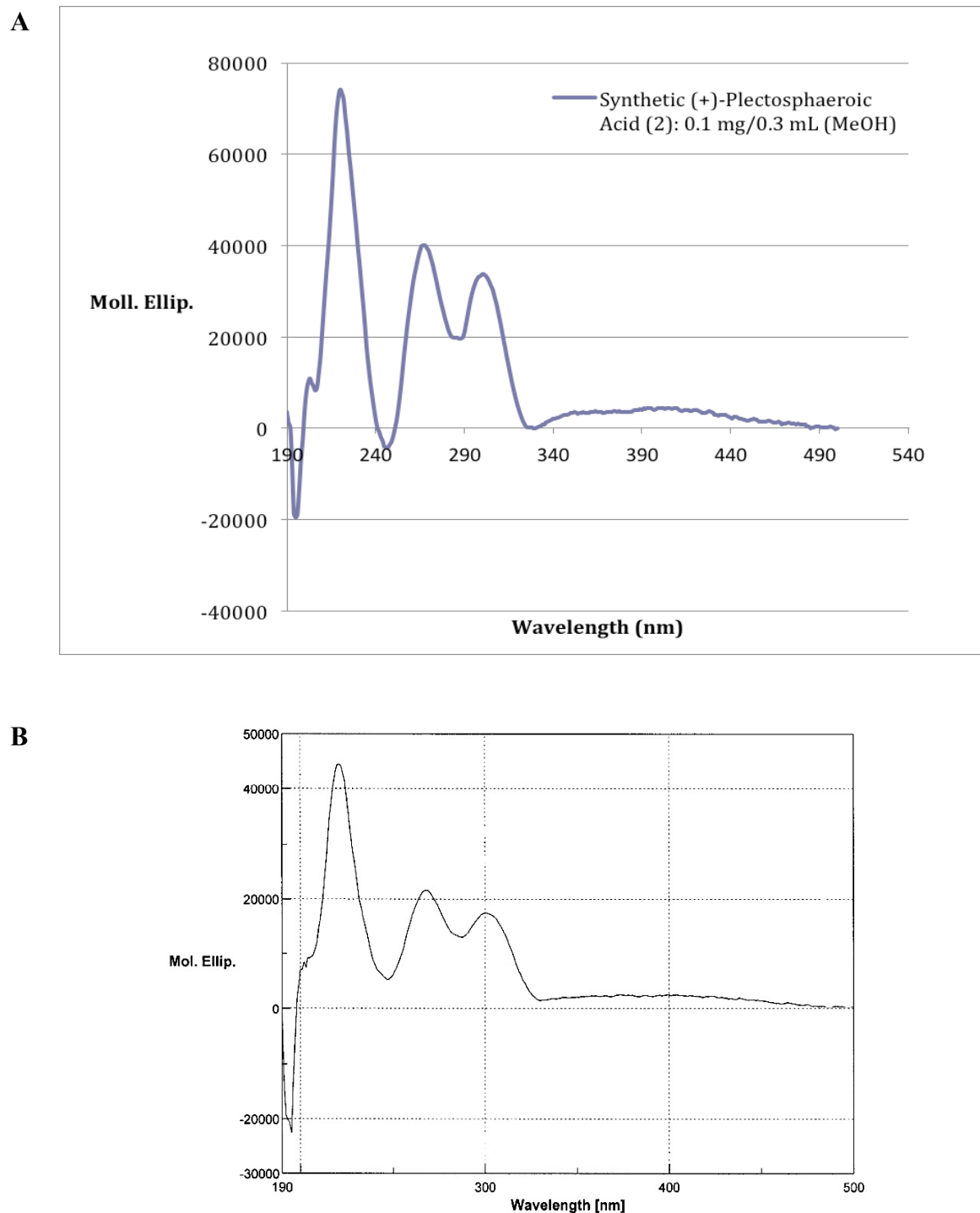
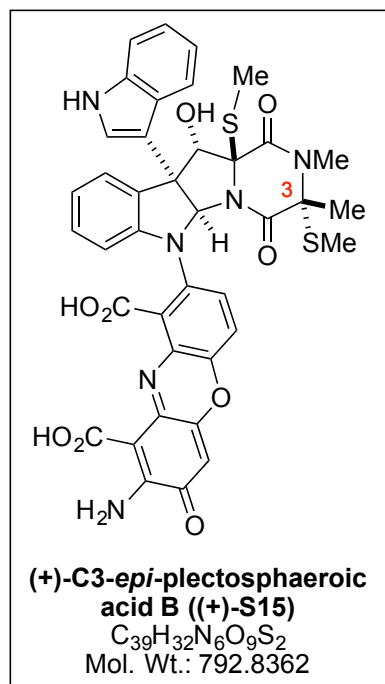


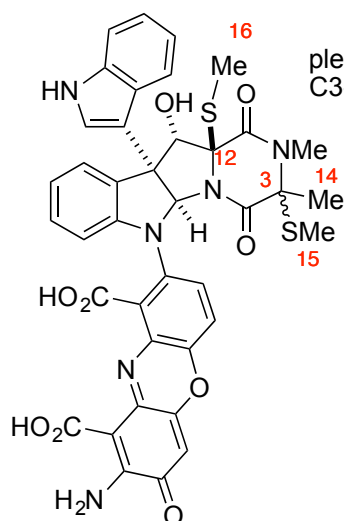
Figure 2. (A) The CD spectrum obtained for synthetic (+)-plectosphaeroic acid B (2). (B) Reproduction of the CD spectrum of natural (+)-plectosphaeroic acid B (2) from Carr, G.; Tay, W.; Bottriell, H.; Andersen, S. K.; Mauk, A. G.; Andersen, R. J. *Org. Lett.* **2009**, *11*, 2996–2999 (measurements of sample reported as 0.1 mg/0.3 mL, MeOH) for comparison.



(+)-C3-epi-plectosphaeroic acid B ((+)-S15): Following a similar procedure as described for formation of plectosphaeroic acid B (**2**), **(-)-C3-epi-24** (18 mg, 19 μ mol) was converted to the title compound **S15** (8.0 mg, 48%), which was isolated as a red solid: $[\alpha]_D^{24} +236$ (*c* 0.062, MeOH); **(+)-S15** was observed as an 8:1 mixture of atropisomers by NMR at 298 K (subsequent data is provided for the major isomer only); 1H NMR (500 MHz, DMSO- d_6) δ 10.87 (s, 1H), 9.72 (s, 1H), 8.91 (s, 1H), 8.00 (d, *J* = 7.7 Hz, 1H), 7.72 (d, *J* = 8.8 Hz, 1H), 7.6–7.5 (comp, 2H), 7.35 (d, *J* = 8.1 Hz, 1H), 7.31 (s, 1H), 7.1–7.0 (comp, 2H), 6.93 (t, *J* = 7.7 Hz, 1H), 6.69 (s, 1H), 6.68 (s, 1H), 6.60 (t, *J* = 7.3 Hz, 1H), 6.10 (bs, 1H), 6.01 (d, *J* = 7.9 Hz, 1H), 5.41 (s, 1H), 2.97 (s, 3H), 2.10 (s, 3H), 1.71 (s, 3H), 1.53 (s, 3H); ^{13}C NMR (125 MHz, DMSO- d_6) δ 178.1 (C), 168.9 (C), 167.1 (C), 164.7 (C), 162.8 (C), 152.6 (C), 150.9 (C), 149.3 (C), 147.55 (C), 141.2 (C), 137.1 (C), 135.2 (C), 133.2 (2 x C), 130.6 (CH), 128.7 (CH), 127.6 (C), 125.3 (C), 122.9 (CH), 122.4 (CH), 121.4 (CH), 120.9 (CH), 118.6 (CH), 118.3 (CH), 117.7 (CH), 115.8 (C), 111.4 (CH), 106.9 (CH), 105.5 (CH),

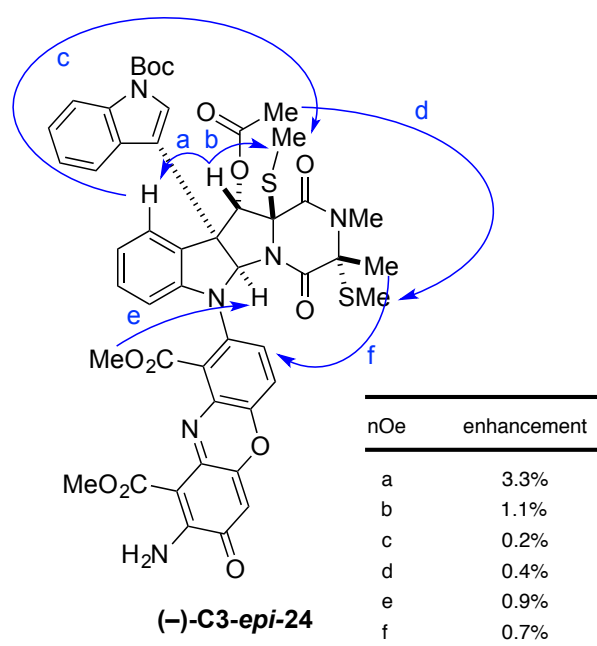
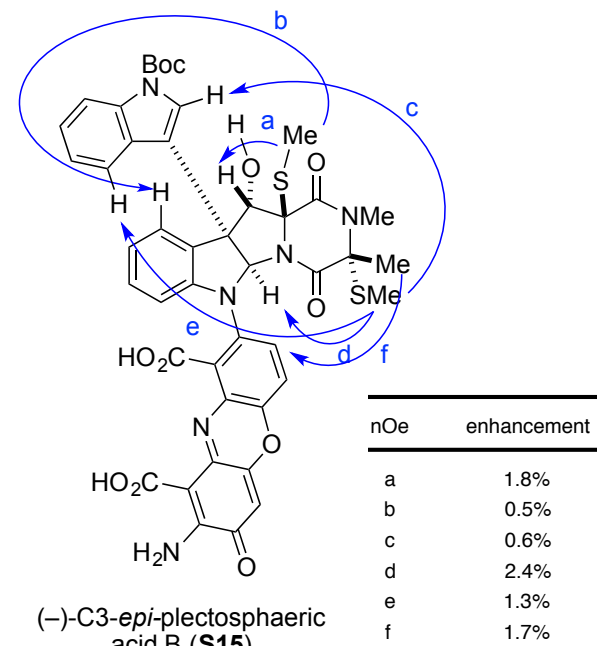
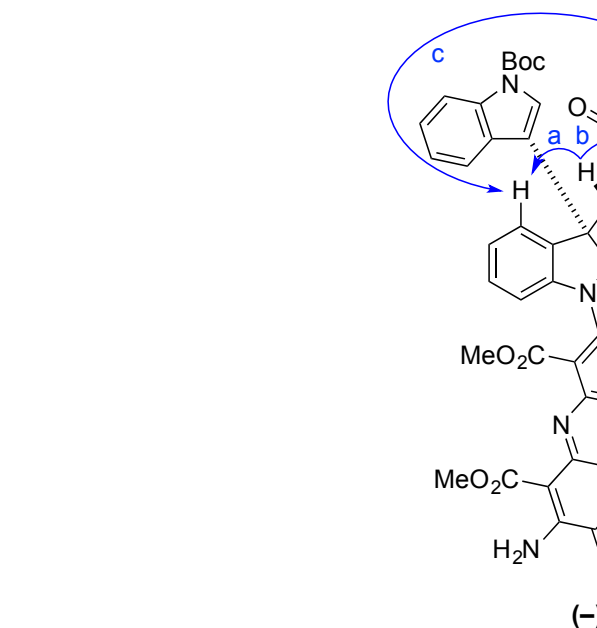
92.4 (C), 86.7 (CH), 78.7 (CH), 75.4 (C), 73.3 (C), 58.7 (C), 29.4 (CH₃), 25.1 (CH₃), 15.3 (CH₃), 12.3 (CH₃); IR (film) 3374, 3270, 3062, 2919, 2850, 1681, 1588, 1487, 1385; RP-18 TLC *R_f* 0.53 (4:1 MeOH/H₂O); HRMS (ESI) *m/z* calcd for $C_{39}H_{32}N_6O_9S_2Na$ (M-H)⁻ 791.1594, found 791.1595.

Table 2. Diagnostic NMR Chemical Shifts of Plectosphaeroic Acid B (**2**) and C3-epi-Plectosphaeroic Acid B (**S15**)



Pos.	2 (500 MHz, DMSO- d_6)		S15 (500 MHz, DMSO- d_6)	
	δ H (multiplicity)	δ C	δ H (multiplicity)	δ C
3		66.3 (C)		73.3 (C)
12		74.1 (C)		75.4 (C)
14	1.59 (s)	22.6 (CH ₃)	1.53 (s)	25.1 (CH ₃)
15	1.88 (s)	13.9 (CH ₃)	1.71 (s)	12.3 (CH ₃)
16	2.14 (s)	15.7 (CH ₃)	2.10 (s)	15.3 (CH ₃)

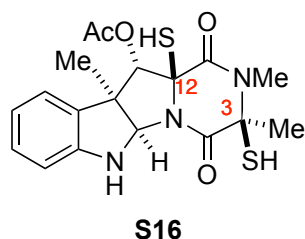
Table 3. Diagnostic 1-D NOE Signals¹⁷ Used to Assign Relative Stereochemistry of Sulfur Incorporation

 (-)-C3-<i>epi</i>-24 <table border="1"> <thead> <tr> <th>nOe</th> <th>enhancement</th> </tr> </thead> <tbody> <tr><td>a</td><td>3.3%</td></tr> <tr><td>b</td><td>1.1%</td></tr> <tr><td>c</td><td>0.2%</td></tr> <tr><td>d</td><td>0.4%</td></tr> <tr><td>e</td><td>0.9%</td></tr> <tr><td>f</td><td>0.7%</td></tr> </tbody> </table>	nOe	enhancement	a	3.3%	b	1.1%	c	0.2%	d	0.4%	e	0.9%	f	0.7%	 (-)-C3-<i>epi</i>-plectosphaeric acid B (S15) <table border="1"> <thead> <tr> <th>nOe</th> <th>enhancement</th> </tr> </thead> <tbody> <tr><td>a</td><td>1.8%</td></tr> <tr><td>b</td><td>0.5%</td></tr> <tr><td>c</td><td>0.6%</td></tr> <tr><td>d</td><td>2.4%</td></tr> <tr><td>e</td><td>1.3%</td></tr> <tr><td>f</td><td>1.7%</td></tr> </tbody> </table>	nOe	enhancement	a	1.8%	b	0.5%	c	0.6%	d	2.4%	e	1.3%	f	1.7%
nOe	enhancement																												
a	3.3%																												
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 (-)-24 <table border="1"> <thead> <tr> <th>nOe</th> <th>enhancement</th> </tr> </thead> <tbody> <tr><td>a</td><td>1.8%</td></tr> <tr><td>b</td><td>0.7%</td></tr> <tr><td>c</td><td>0.6%</td></tr> </tbody> </table>	nOe	enhancement	a	1.8%	b	0.7%	c	0.6%																					
nOe	enhancement																												
a	1.8%																												
b	0.7%																												
c	0.6%																												

¹⁷ The double pulsed-field-gradient spin-echo (DPFGSE) sequence developed by the Shaka group at the University of California, Irvine was used. See Stott, K.; Keeler, J.; Van, Q. N.; Shaka, A. J. *J. Magn. Reson.* **1997**, *125*, 302–324.

Computational details: The TURBOMOLE V6.3¹⁸ quantum chemistry program was used. All calculations were performed with the B3-LYP¹⁹ hybrid functional and all atoms were represented by the triple ξ def2-TZVP basis set.²⁰ Full geometry optimization in gas-phase was conducted on all structures and all energies are reported as electronic energies.

Computational Data for **S16**:



SCF Energy = -1959.837120 hartree

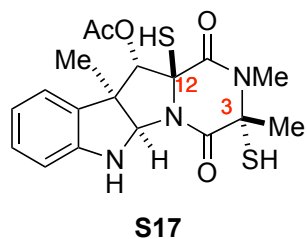
H	-1.255816	4.038508	-2.894832
C	-1.372016	2.969628	-3.026435
C	-1.686811	0.194225	-3.374633
C	-1.410535	2.111327	-1.934179
C	-1.488660	2.415745	-4.300239
C	-1.648774	1.045084	-4.480987
C	-1.554012	0.731108	-2.108251
H	-1.455806	3.068556	-5.163981
H	-1.740618	0.637746	-5.479312
H	-1.805816	-0.874263	-3.514916
C	-1.605938	0.057556	-0.743830
C	-1.188419	1.226538	0.199883
H	-1.747723	1.279573	1.132052
N	-1.379008	2.425119	-0.578185
H	-0.979605	3.285414	-0.238547
C	-3.022382	-0.455251	-0.454180
H	-3.739143	0.353565	-0.601181
H	-3.115934	-0.819751	0.568828
H	-3.283221	-1.264588	-1.137119

¹⁸ TURBOMOLE v6.3, Turbomole GmbH: Karlsruhe, Germany 2011; <http://www.turbomole.com>. (b) Treutler, O.; Ahlrichs, R. *J. Chem. Phys.* **1995**, *102*, 346–354.

¹⁹ (a) Slater, J. C. *Quantum Theory of Molecules and Solids, Vol. 4: The Self-Consistent Field for Molecules and Solids*; McGraw-Hill: New York, **1974**. (b) Vosko, S. H.; Wilk, L.; Nusair, M. *Can. J. Phys.* **1980**, *58*, 1200–1211. (c) Becke, A. D. *Phys. Rev. A* **1988**, *38*, 3098–3100. (d) Lee, C. T.; Yang, W. T.; Parr, R. G. *Phys. Rev. B* **1988**, *37*, 785–789. (e) Miehlich, B.; Savin, A.; Stoll, H.; Preuss, H. *Chem. Phys. Lett.* **1989**, *157*, 200–206. (f) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648–5652. (g) Stephens, P. J.; Devlin, F. J.; Chabalowski, C. F.; Frisch, M. J. *J. Phys. Chem.* **1994**, *98*, 11623–11627.

²⁰ (a) Eichkorn, K.; Weigend, F.; Treutler, O.; Ahlrichs, R. *Theor. Chem. Acc.* **1997**, *97*, 119–124. (b) Schäfer, A.; Huber, C.; Ahlrichs, R. *J. Chem. Phys.* **1994**, *100*, 5829–5835. (c) Weigend, F.; Furche, F.; Ahlrichs, R. *J. Chem. Phys.* **2003**, *119*, 12753–12762.

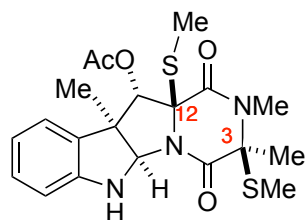
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H	-0.349859	-1.632996	-1.419983
C	0.755854	-0.228719	-0.127560
N	0.217791	0.917350	0.553075
C	1.745735	-1.042670	0.701091
N	2.318586	-0.421994	1.774214
C	0.803875	1.553301	1.599266
C	2.156517	0.999551	2.082261
O	-0.845634	-1.869145	0.569174
C	-1.127471	-3.174598	0.301226
O	-1.262275	-3.612905	-0.808529
C	-1.230804	-3.964246	1.574667
H	-1.758561	-3.401370	2.343896
H	-0.219541	-4.161673	1.937784
H	-1.730968	-4.909297	1.378753
O	2.006392	-2.185197	0.363255
O	0.271512	2.501928	2.145984
S	1.734981	0.320116	-1.644333
H	2.307090	-0.881001	-1.842492
S	3.512786	2.043558	1.311504
H	3.277230	1.657404	0.041538
C	3.384264	-1.145915	2.471793
H	3.564107	-2.074037	1.939361
H	3.094540	-1.372722	3.498001
H	4.294099	-0.544297	2.473880
C	2.256845	1.255215	3.588198
H	1.530058	0.637507	4.118457
H	2.027378	2.298328	3.785307
H	3.254391	1.031724	3.960283

Computational Data for **S17**:

SCF Energy = -1959.833100 hartree

H	1.161117	2.894410	-4.024460
C	1.258209	3.048754	-2.956696
C	1.519005	3.456759	-0.184029
C	1.342506	1.974130	-2.080057
C	1.300894	4.335789	-2.422390
C	1.433184	4.546577	-1.053416
C	1.462329	2.177019	-0.701812
H	1.231601	5.186052	-3.089925
H	1.467265	5.554631	-0.661367
H	1.616427	3.619602	0.883439

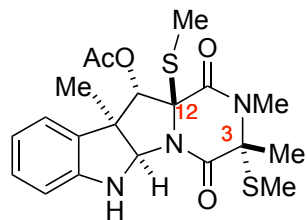
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C	1.259527	-0.165792	-1.165662
H	1.917758	-1.033027	-1.203260
N	1.374315	0.614942	-2.371067
H	1.019301	0.233947	-3.232683
C	2.971560	0.631186	0.582978
H	3.716065	0.801550	-0.195693
H	3.103162	-0.377684	0.974682
H	3.157402	1.343645	1.387504
C	0.432580	0.595045	1.037481
H	0.171719	1.498033	1.579241
C	-0.746480	0.026744	0.220033
N	-0.093036	-0.678202	-0.848528
C	-1.723140	-0.820332	1.021505
N	-2.195960	-1.953570	0.436664
C	-0.602491	-1.741465	-1.507014
C	-1.806658	-2.463892	-0.875667
O	0.806928	-0.422852	1.979845
C	1.022496	-0.041312	3.268962
O	1.064058	1.104778	3.626275
C	1.185943	-1.243309	4.154417
H	1.618125	-0.940304	5.104554
H	1.803160	-2.002145	3.674323
H	0.199345	-1.678216	4.329749
O	-2.114395	-0.433761	2.110349
O	-0.111296	-2.155723	-2.545027
S	-1.816269	1.393156	-0.513677
S	-1.192949	-4.216878	-0.580341
H	-2.402205	1.712818	0.653490
H	-0.747659	-4.384416	-1.836089
C	-3.271215	-2.638149	1.164849
H	-4.189097	-2.047642	1.141245
H	-2.980352	-2.769118	2.204810
H	-3.448994	-3.610002	0.714551
C	-2.974328	-2.446830	-1.865945
H	-2.640287	-2.829455	-2.828333
H	-3.329375	-1.421466	-1.997620
H	-3.796641	-3.064693	-1.510192

Computational Data for **S18**:**S18**

SCF Energy = -2038.430310 hartree

H	1.915715	3.121635	-3.551572
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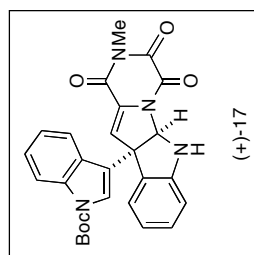
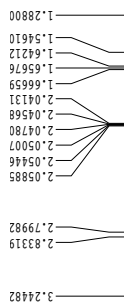
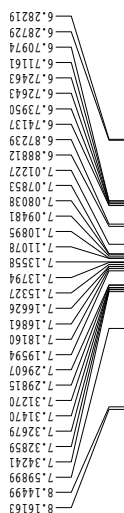
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C	1.712713	3.538356	0.318206
C	1.828912	2.128042	-1.637530
C	1.802932	4.501285	-1.894217
C	1.734810	4.660902	-0.513879
C	1.746996	2.279121	-0.249450
H	1.818378	5.375962	-2.533091
H	1.700605	5.653686	-0.084207
H	1.662755	3.660738	1.394571
C	1.777463	0.907648	0.407970
C	1.640335	-0.044374	-0.821775
H	2.304843	-0.906693	-0.800032
N	1.922717	0.782371	-1.971102
H	1.676210	0.439703	-2.885095
C	3.097237	0.702799	1.163139
H	3.934190	0.918923	0.498159
H	3.196627	-0.320166	1.526283
H	3.160734	1.380897	2.015370
C	0.524307	0.617085	1.275038
H	0.194781	1.489418	1.827822
C	-0.535924	0.081409	0.287873
N	0.260972	-0.567136	-0.724592
C	-1.577101	-0.825329	0.922236
N	-1.977396	-1.921755	0.209027
C	-0.093086	-1.674731	-1.416185
C	-1.444512	-2.317836	-1.090602
O	0.795613	-0.438376	2.213730
C	0.771064	-0.126831	3.537393
O	0.703565	0.996672	3.958448
C	0.829993	-1.373173	4.373650
H	1.559923	-2.077385	3.974859
H	-0.150837	-1.852967	4.341057
H	1.069999	-1.113323	5.401437
O	-2.055348	-0.532339	2.007188
O	0.637660	-2.157497	-2.270015
S	-1.523187	1.451652	-0.538688
S	-2.653281	-1.669843	-2.388618
C	-2.167036	2.420669	0.853686
H	-2.629877	1.774096	1.596327
H	-2.924407	3.072258	0.417064
H	-1.393706	3.038029	1.309103
C	-2.155268	-2.534404	-3.906464
H	-1.092532	-2.399130	-4.099263
H	-2.727795	-2.058849	-4.703235
H	-2.405293	-3.593653	-3.877844
C	-3.115706	-2.679352	0.735837
H	-3.609760	-2.068578	1.484345
H	-2.790690	-3.610830	1.203279
H	-3.809051	-2.901599	-0.074156
C	-1.290608	-3.836944	-1.173827
H	-0.676309	-4.186381	-0.340381
H	-0.783866	-4.104501	-2.095733
H	-2.256795	-4.334613	-1.135617

Computational Data for **S19**:**S19**

SCF Energy = -2038.428900 hartree

H	1.051385	3.292704	-3.874204
C	1.328597	3.330211	-2.827863
C	2.054241	3.434597	-0.110648
C	1.415058	2.171521	-2.066280
C	1.603418	4.547557	-2.205616
C	1.965393	4.608858	-0.863652
C	1.768770	2.224679	-0.714099
H	1.536125	5.461652	-2.783197
H	2.179352	5.564553	-0.403067
H	2.337466	3.479753	0.935110
C	1.818663	0.813493	-0.148780
C	1.227951	-0.030065	-1.326248
H	1.783832	-0.941734	-1.546405
N	1.234989	0.854492	-2.466526
H	0.686308	0.603421	-3.272527
C	3.259876	0.413624	0.189651
H	3.897365	0.580597	-0.679489
H	3.326772	-0.636340	0.474096
H	3.644915	1.021035	1.010062
C	0.831820	0.601687	1.034750
H	0.756727	1.480326	1.665888
C	-0.504122	0.208332	0.377366
N	-0.095719	-0.455998	-0.830913
C	-1.440183	-0.606221	1.250094
N	-2.146496	-1.609376	0.648230
C	-0.831365	-1.377738	-1.492702
C	-1.925831	-2.110472	-0.705790
O	1.239463	-0.510222	1.848791
C	1.633393	-0.249290	3.124149
O	1.802520	0.858825	3.557915
C	1.810891	-1.527858	3.891789
H	2.322114	-2.277214	3.288139
H	0.822052	-1.919291	4.140977
H	2.361595	-1.330837	4.807941
O	-1.609318	-0.287118	2.416971
O	-0.590821	-1.685664	-2.651338
S	-1.534671	1.694750	-0.154101
C	-1.785609	2.649379	1.368070
H	-0.871532	3.154572	1.677051
H	-2.162516	2.015805	2.167803
H	-2.532221	3.400884	1.109732

S	-1.188746	-3.830574	-0.426948
C	-1.255343	-4.650726	-2.043769
H	-2.280042	-4.821300	-2.369862
H	-0.772606	-5.616056	-1.885955
H	-0.704176	-4.082477	-2.788717
C	-3.219328	-2.222404	1.438209
H	-2.961075	-2.149267	2.490193
H	-3.321453	-3.267633	1.159541
H	-4.166424	-1.701633	1.276469
C	-3.214957	-2.144874	-1.522745
H	-2.996618	-2.456323	-2.541357
H	-3.646087	-1.141389	-1.556989
H	-3.943791	-2.827210	-1.089195

¹H spectrum

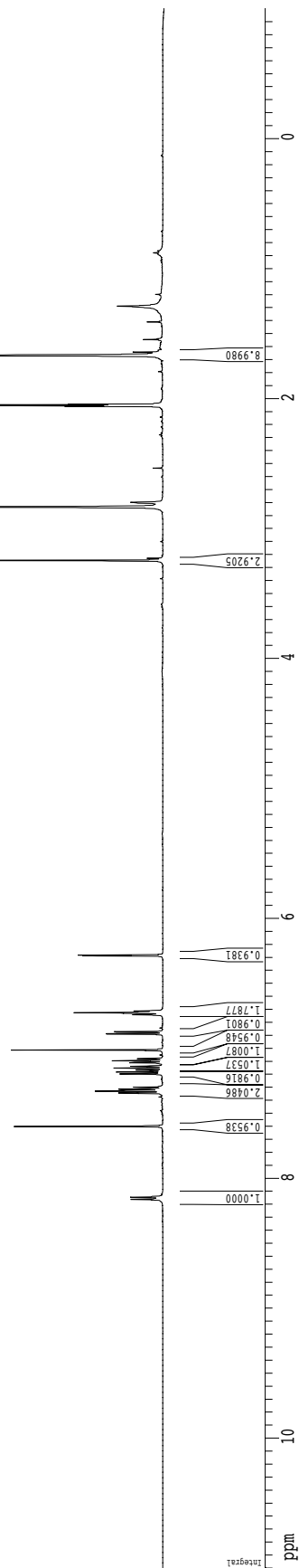
Current Data Parameters
 USER s\jabri
 NAME sy7-2-170
 EXPNO 11
 PROCNO 1

F2 - Acquisition Parameters
 Date_ 20101011
 Time 10.41
 INSTRUM cryo500
 PROHD 5 mm CPTCI 1H-
 PULPROG zg30
 TD 81728
 SOLVENT acetone
 NS 8
 DS 2
 SWH 8012.820 Hz
 FIDRES 0.098043 Hz
 AQ 5.0998774 sec
 RG 63
 RW 62.00 usec
 DE 6.00 usec
 TE 298.0 K
 D1 0.10000000 sec
 MCREST 0.00000000 sec
 MCWRR 0.01500000 sec

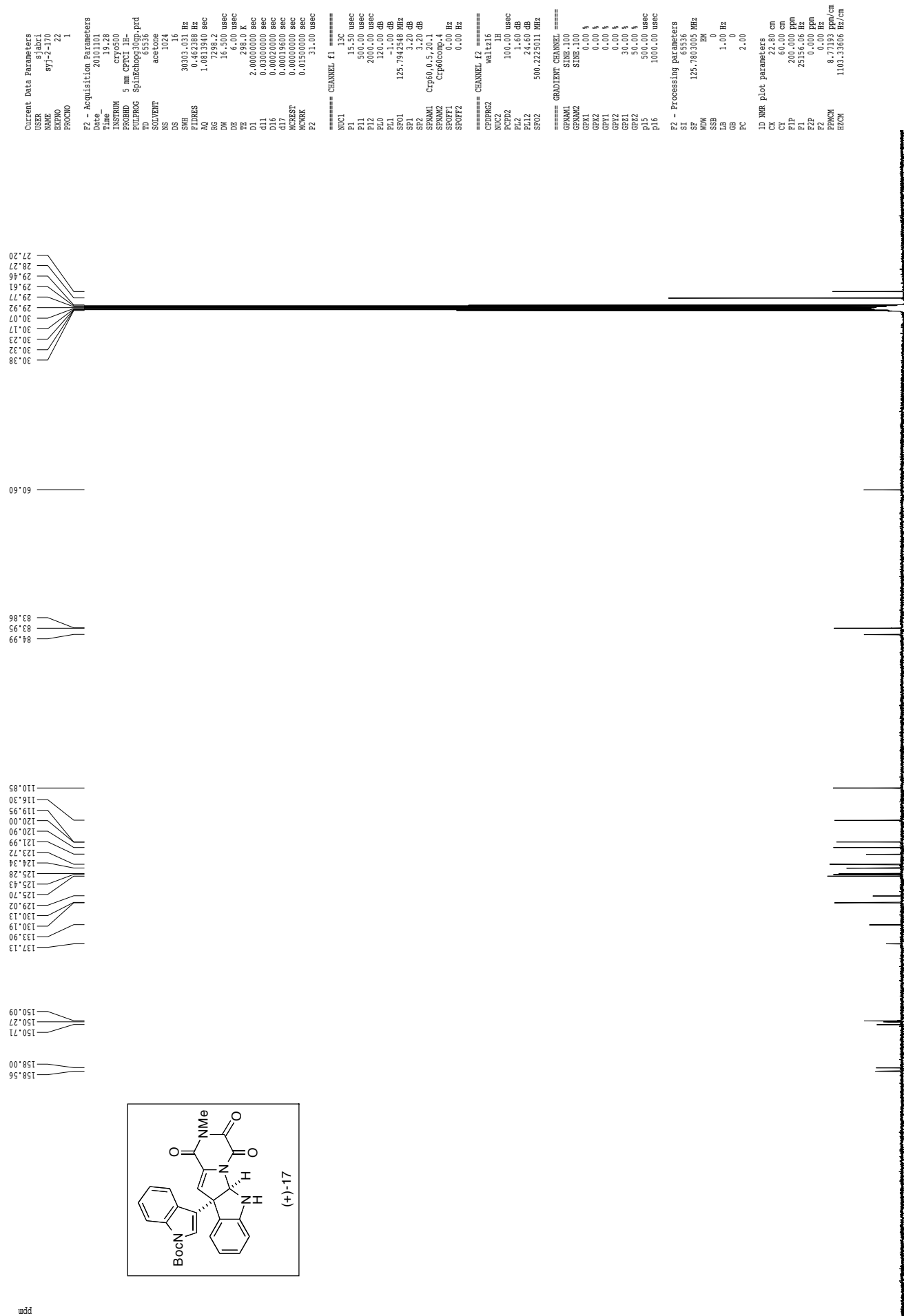
===== CHANNEL f1 =====
 NUC1 1H
 P1 7.50 usec
 PL1 1.60 dB
 SFO1 500.2235015 MHz

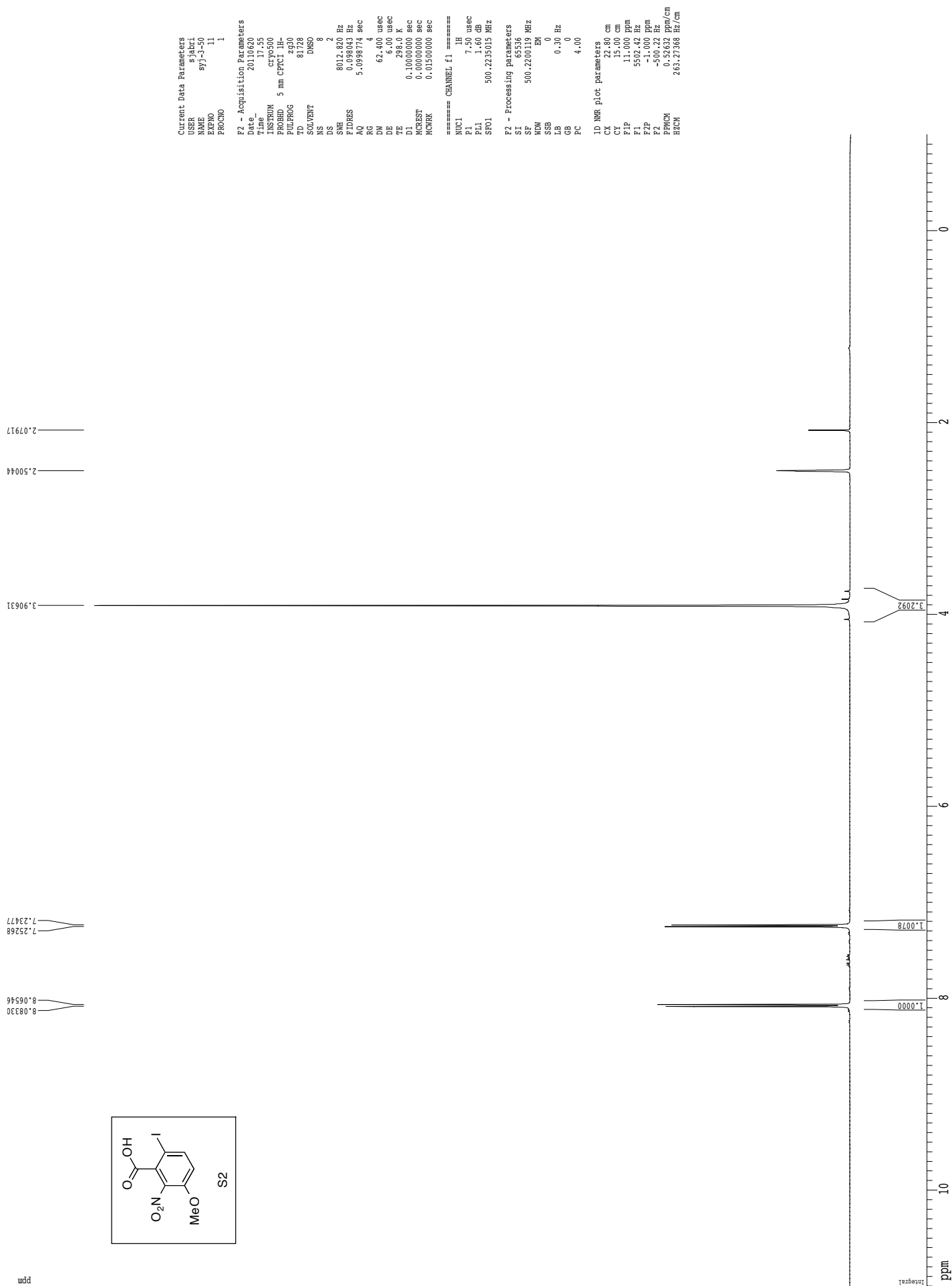
F2 - Processing parameters
 SI 32768
 SF 500.220182 MHz
 WDW EM
 SSB 0
 LB 0.30 Hz
 GB 0
 PC 4.00

1D NMR plot parameters
 CX 22.80 cm
 CY 15.00 cm
 FIP 11.000 ppm
 FI 5502.42 Hz
 F2 11.000 ppm
 F2 -500.92 ppm
 PRGM 0.56432 ppm/cm
 HZCN 263.27371 Hz/cm

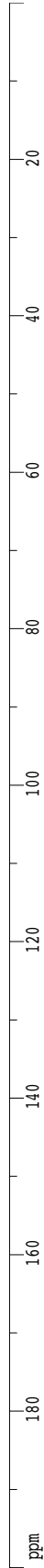
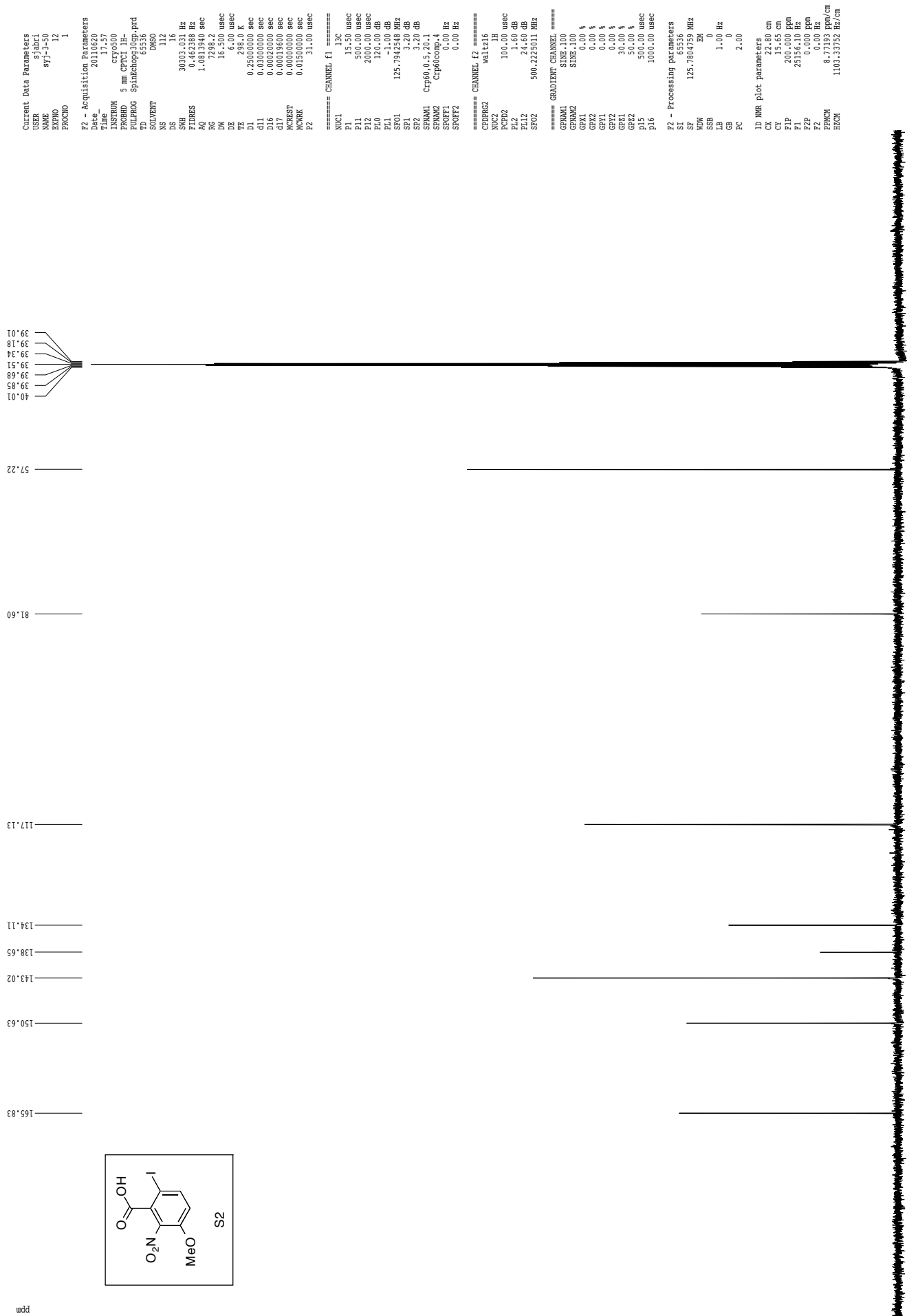


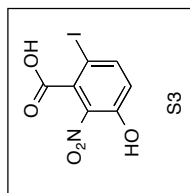
Z-restored spin-echo 13C spectrum with 1H decoupling



¹H spectrum

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



¹H spectrum

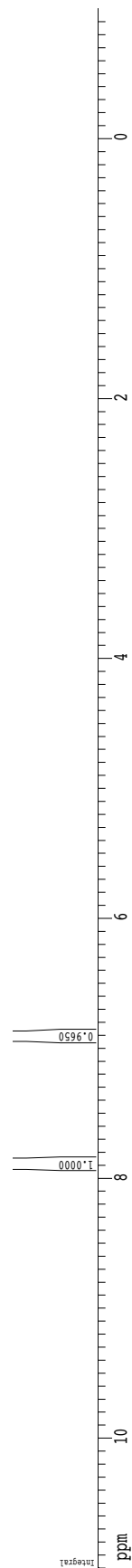
Current Data Parameters
 USER sJabri
 NAME syj-342
 EXPNO 73
 PROCNO 1

F2 - Acquisition Parameters
 Date_ 20110718
 Time 19.09
 INSTRUM cryo500
 PROBD 5 mm CPYC1 IH-
 PULPROG zg30
 TD 81728
 SOLVENT CD3OD
 NS 8
 DS 2
 SWH 8012.820 Hz
 FIDRES 0.098043 Hz
 AQ 5.0998774 sec
 RG 62.400 usec
 DE 6.00 usec
 TE 298.0 K
 D1 0.10000000 sec
 MCREST 0.00000000 sec
 MCWRR 0.01500000 sec

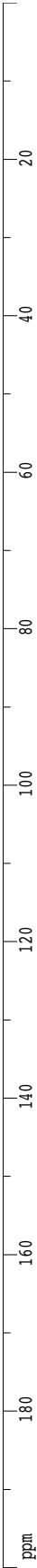
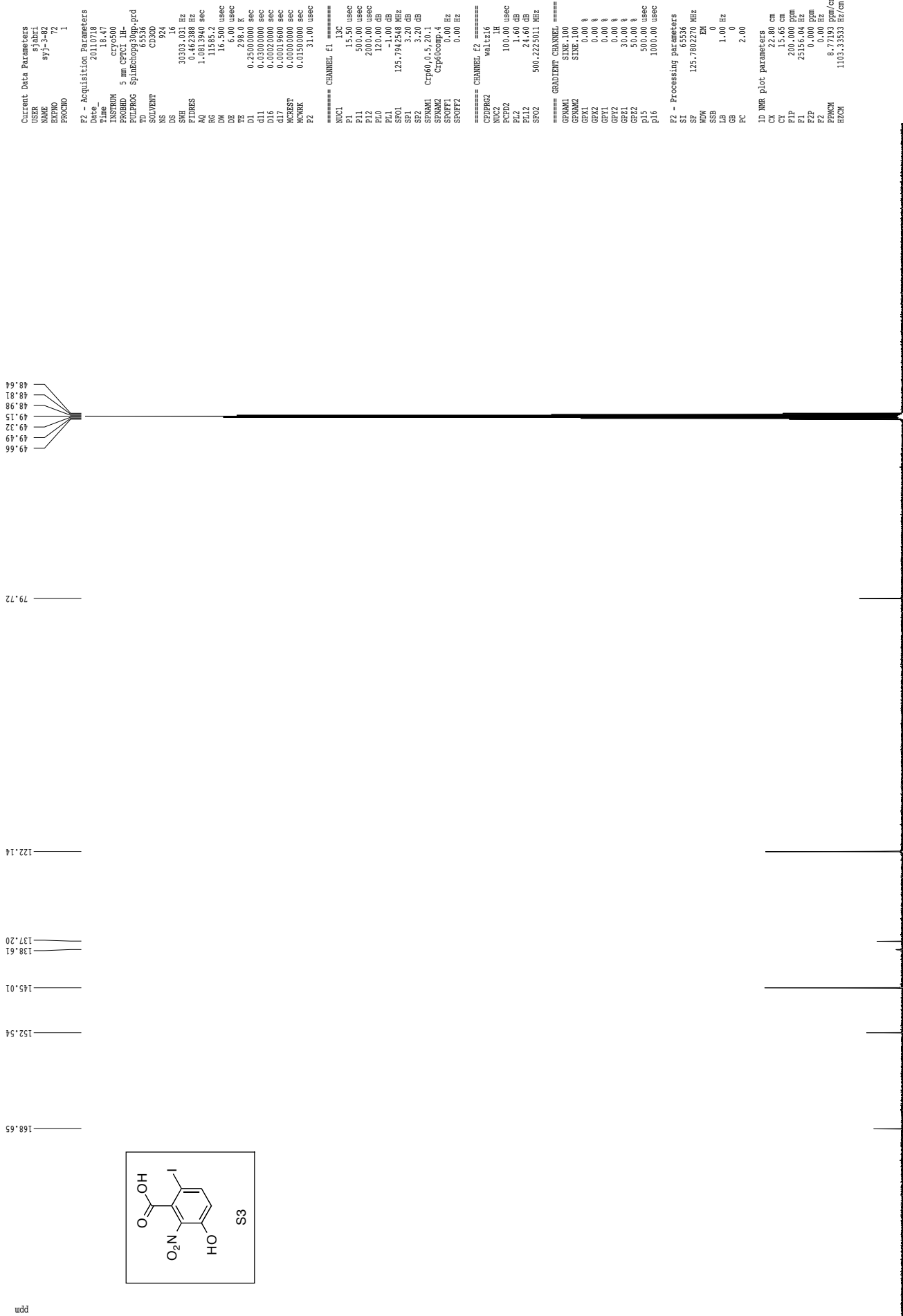
===== CHANNEL f1 =====
 NUC1 1H
 P1 7.50 usec
 PL1 1.60 dB
 SFO1 500.2235015 MHz

F2 - Processing parameters
 SI 65536
 SF 500.220133 MHz
 WDW EM
 SSB 0
 LB 0.30 Hz
 GB 0
 PC 4.00

1D NMR plot parameters
 CX 22.80 cm
 CY 15.00 cm
 FIP 11.000 ppm
 F1 5502.42 Hz
 F2 11.000 ppm
 F3 -500.92 ppm
 PPMCM 0.55452 ppm/cm
 HZCM 263.27368 Hz/cm



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



20

40

60

80

100

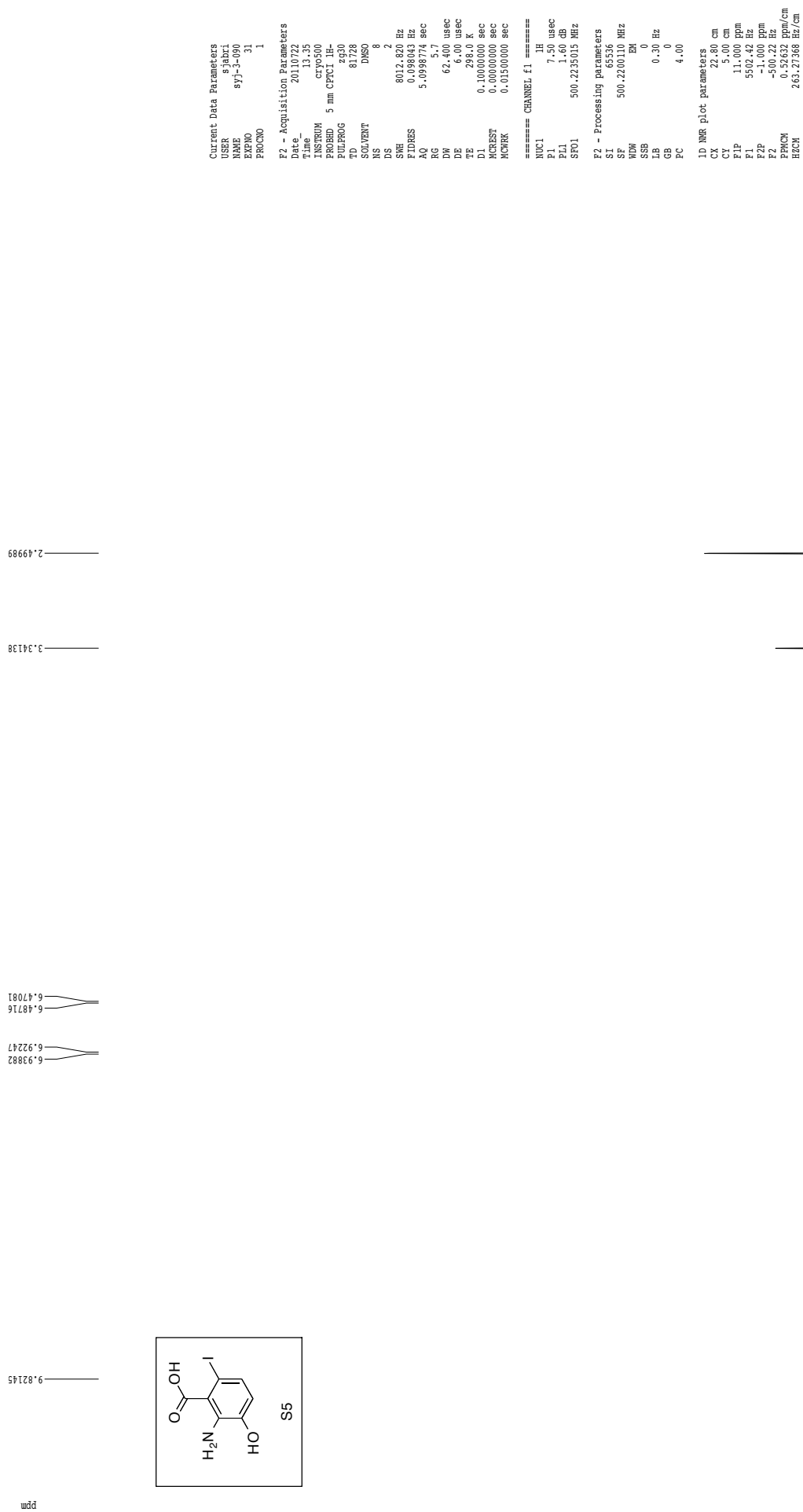
120

140

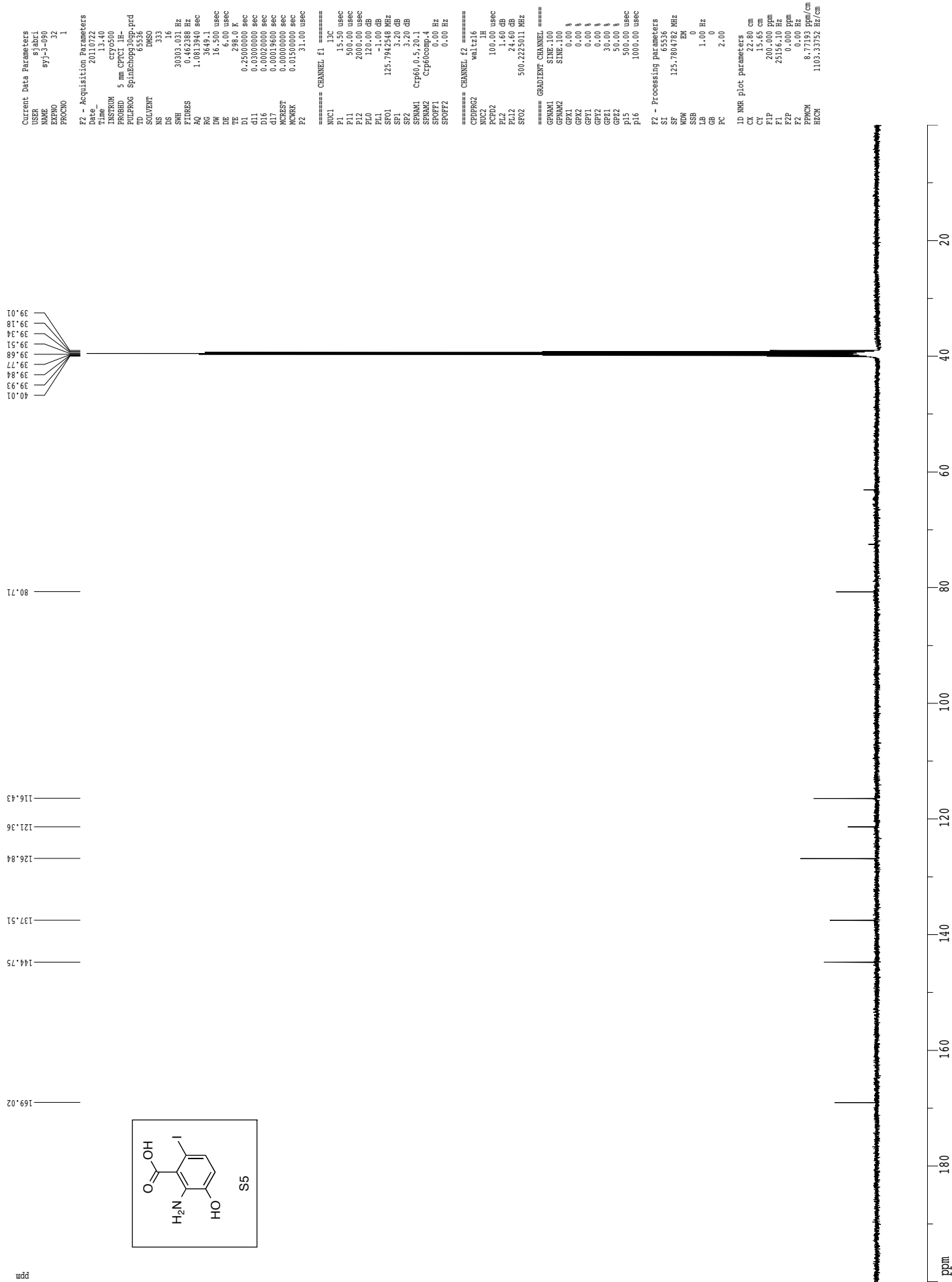
160

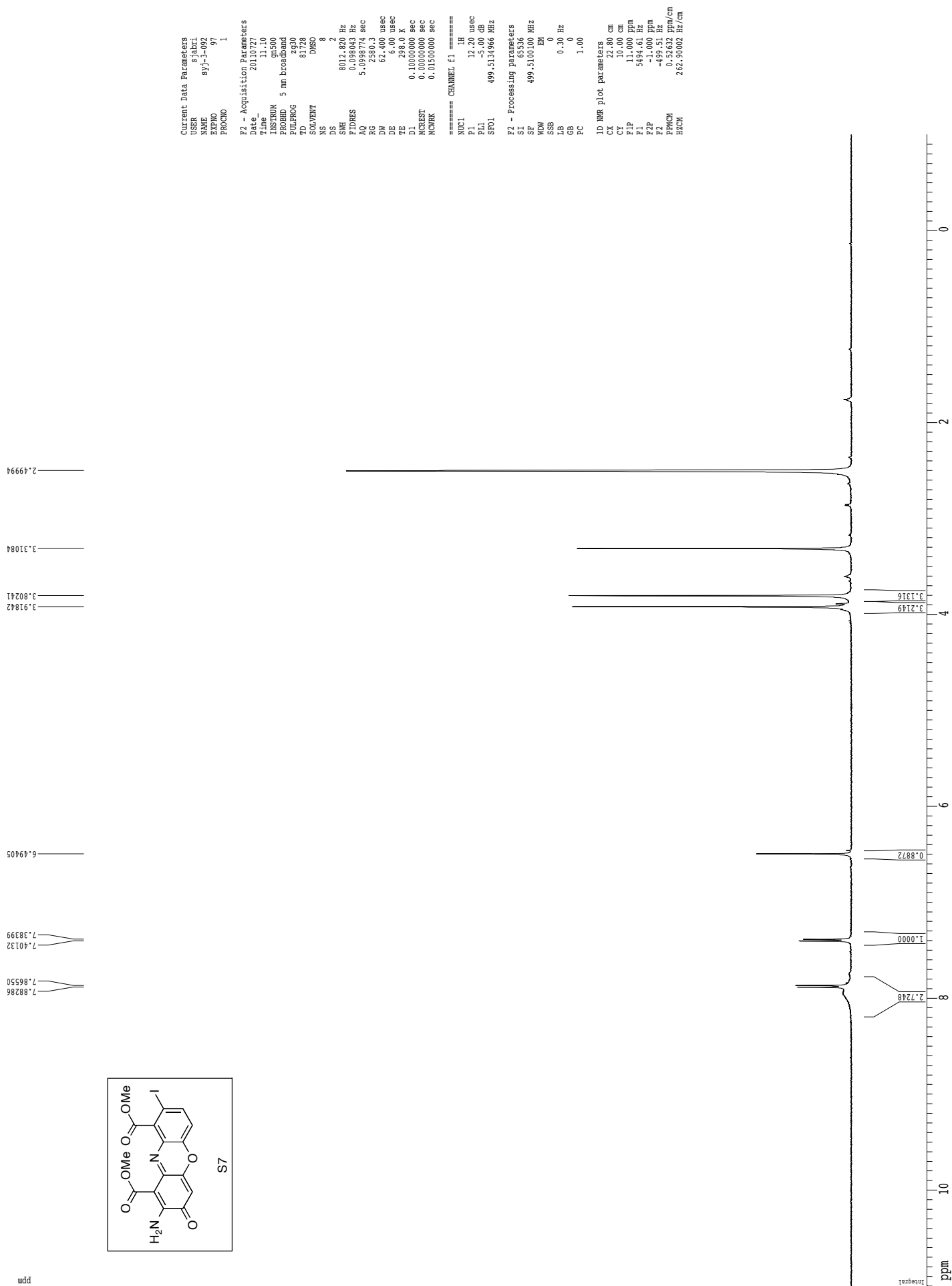
180

ppm

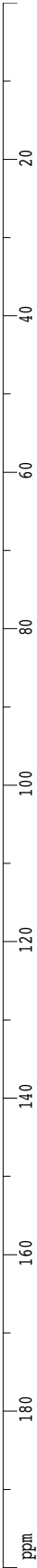
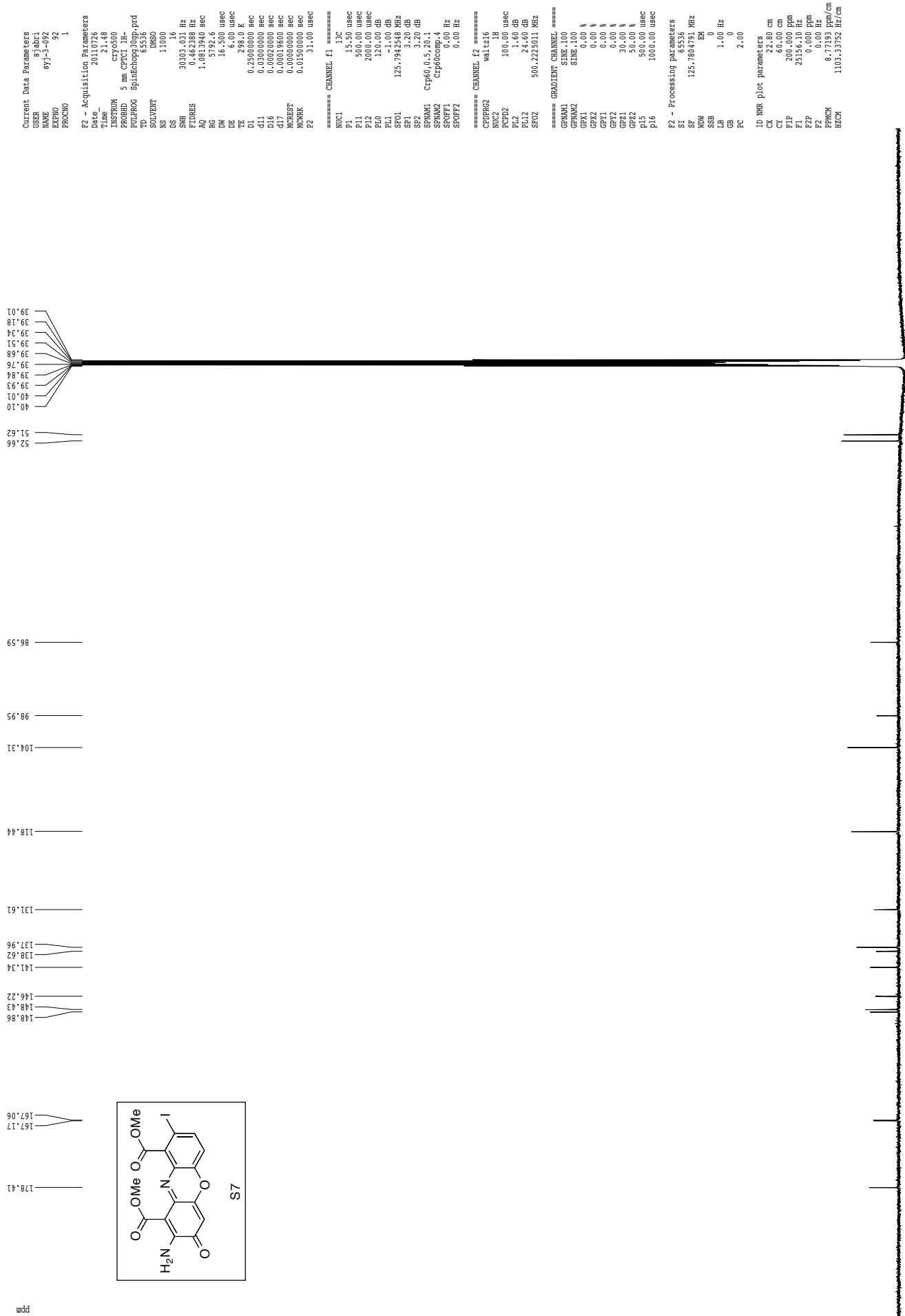
¹H spectrum

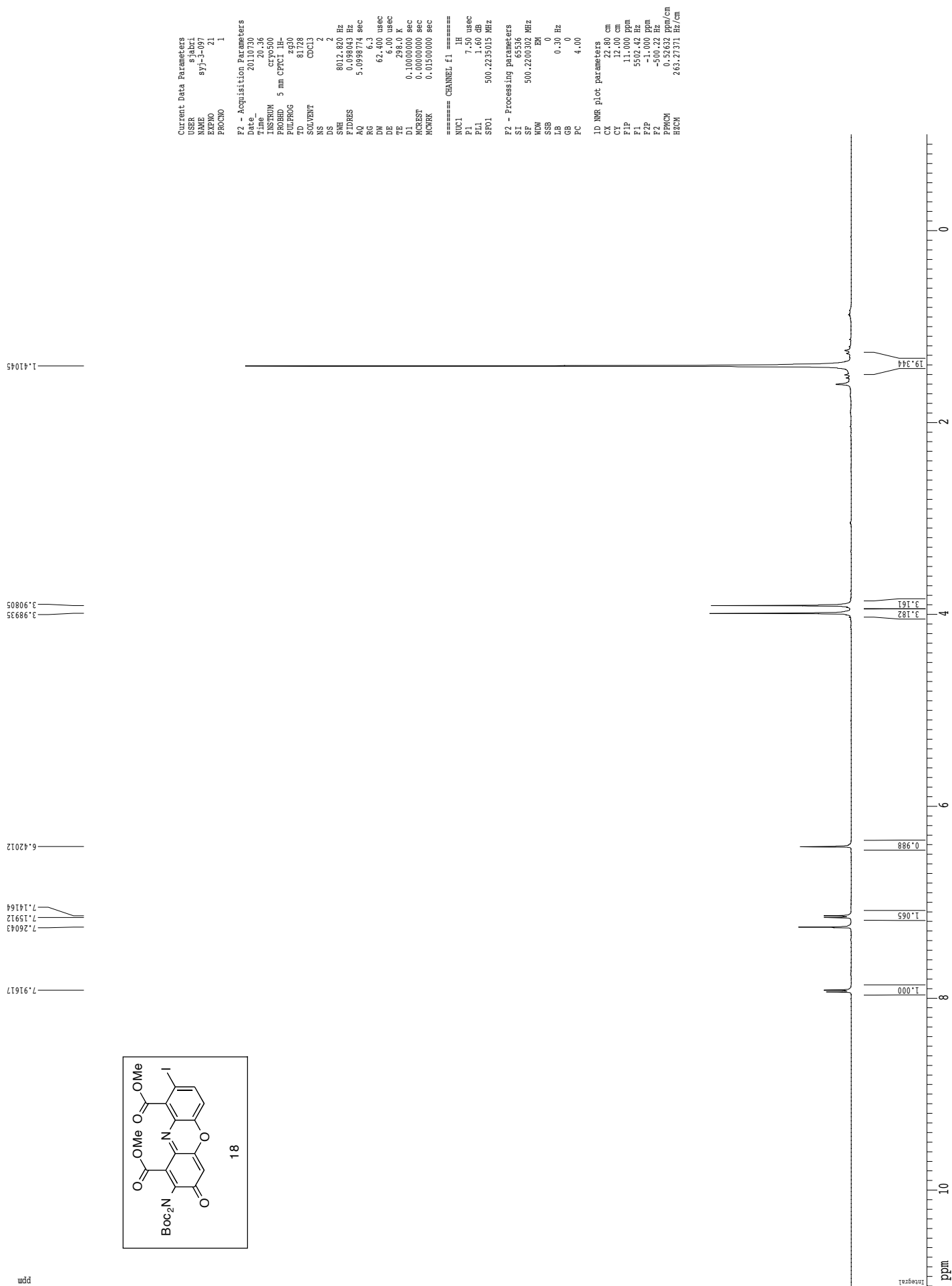
Z-restored spin-echo 13C spectrum with 1H decoupling

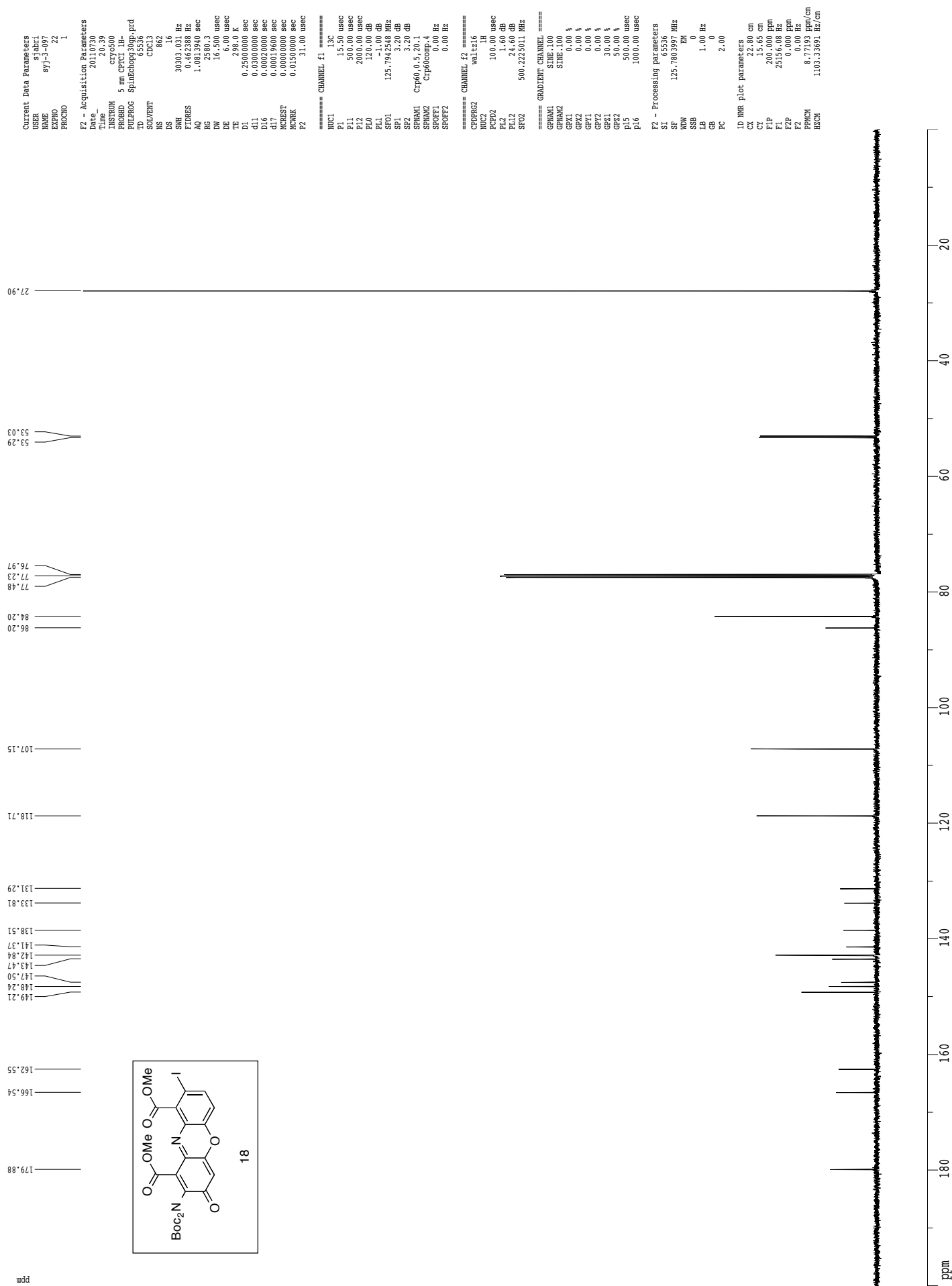


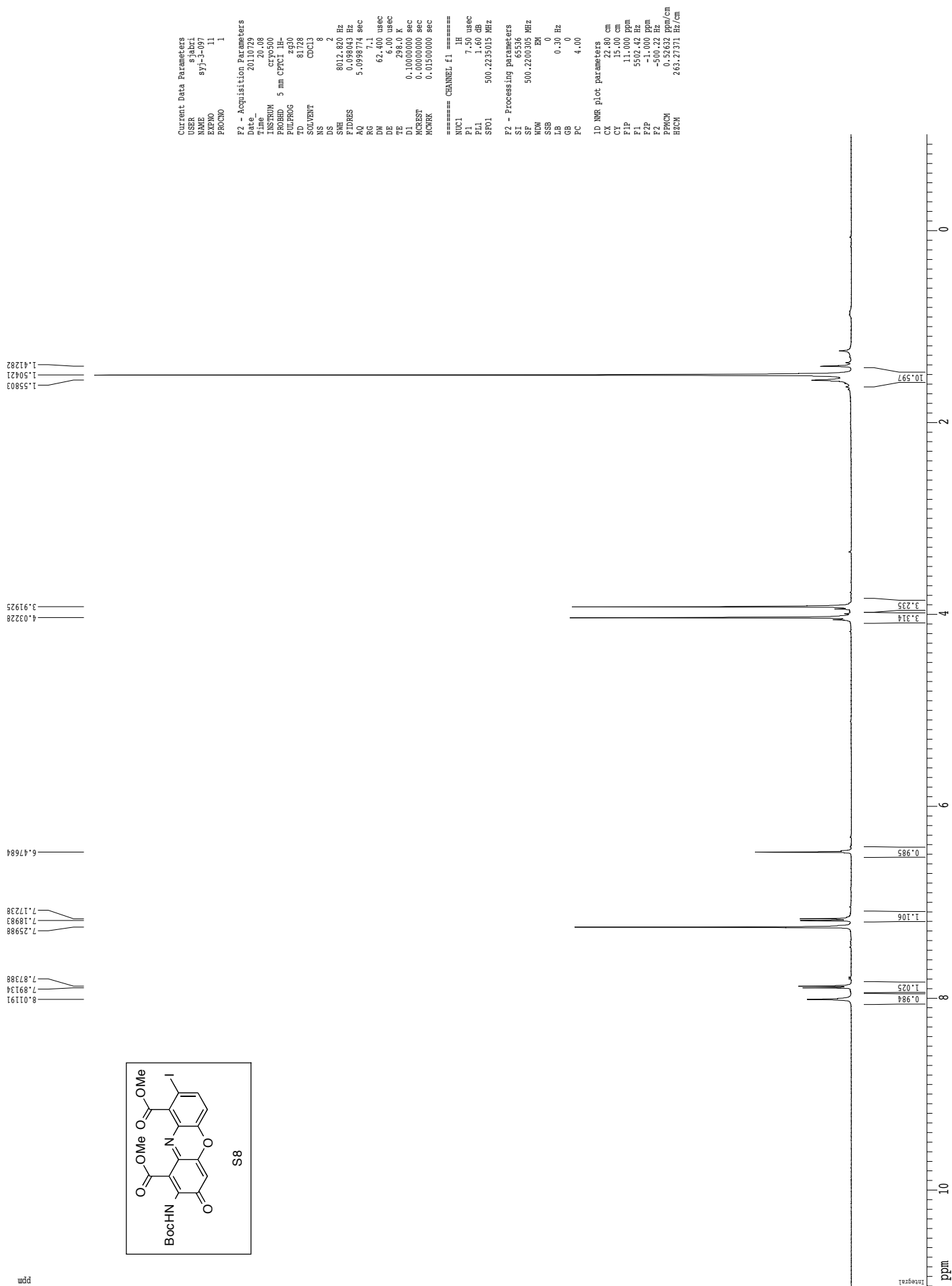
¹H spectrum

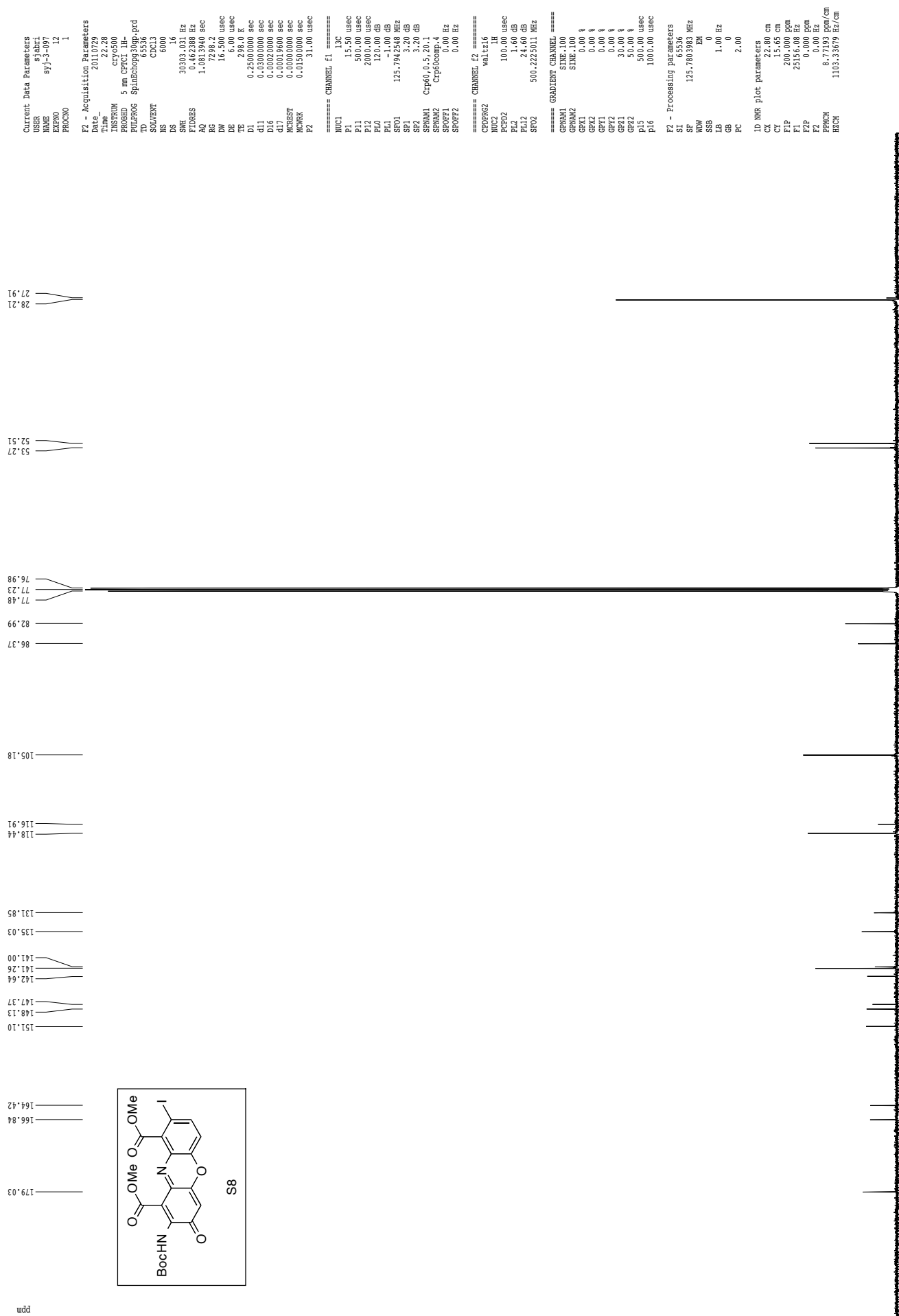
Z-restored spin-echo 13C spectrum with 1H decoupling

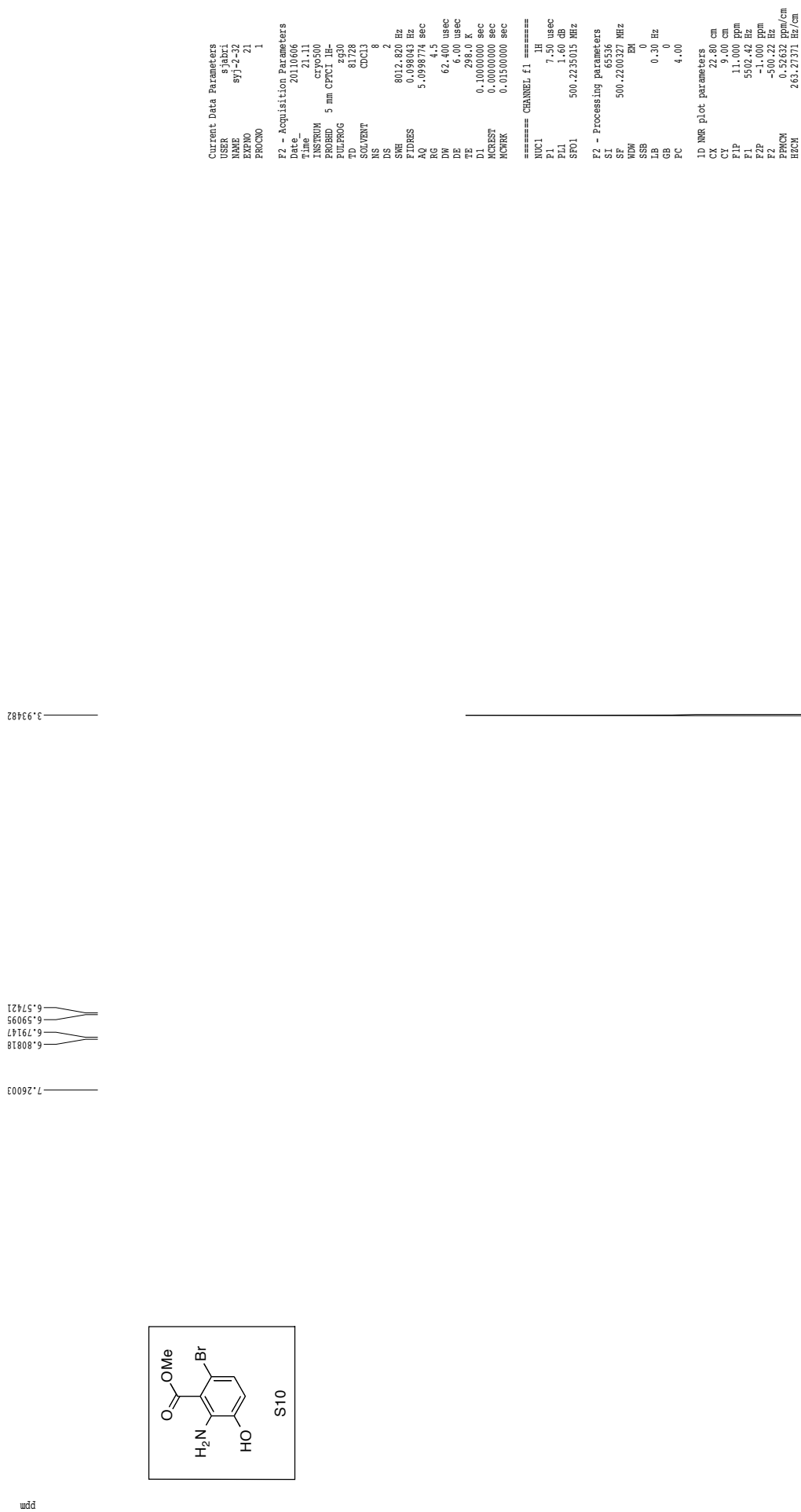


¹H spectrum

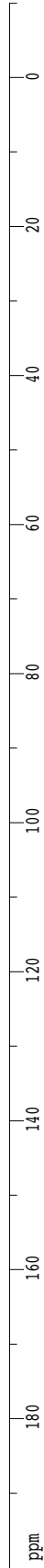
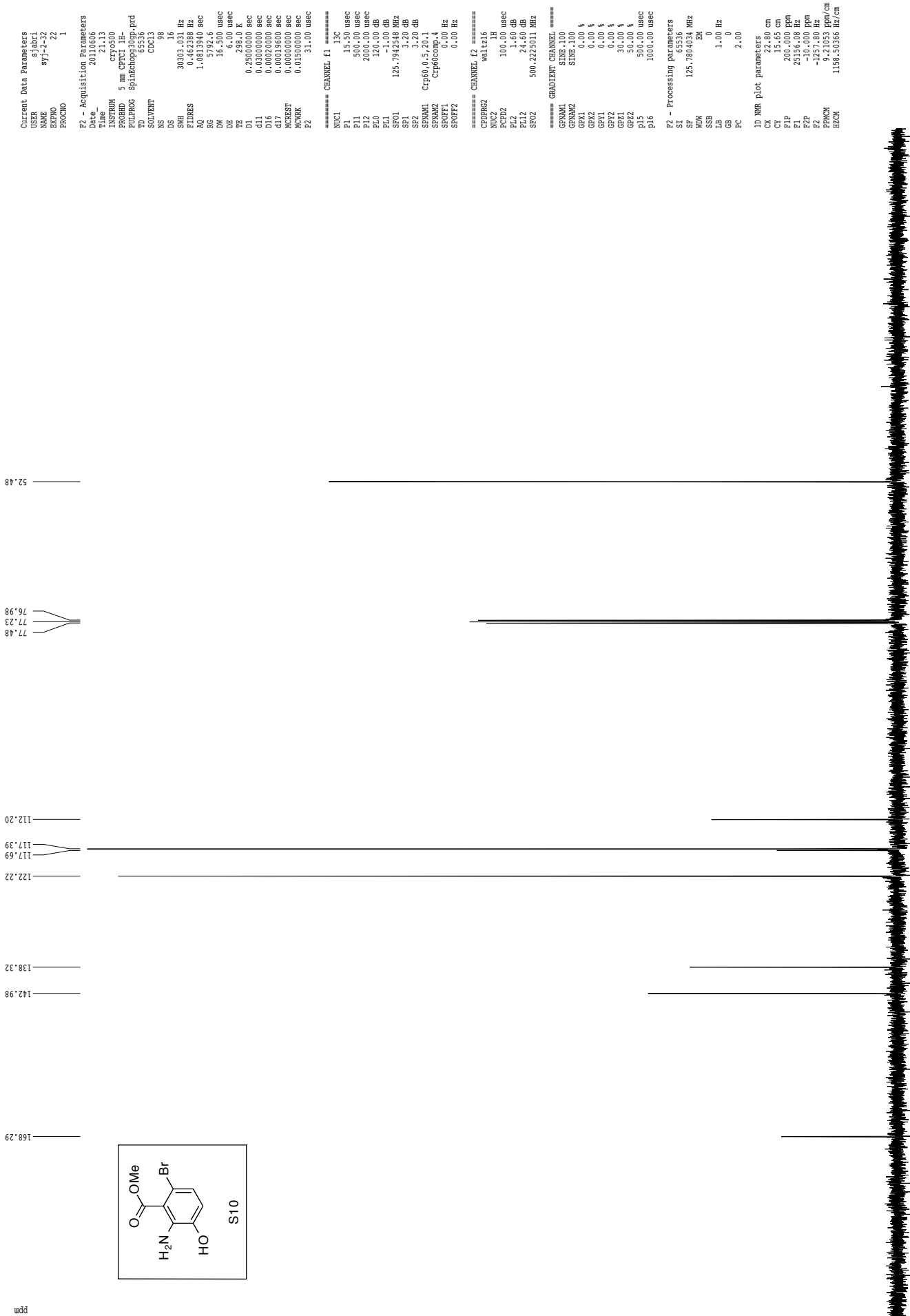
Z-restored spin-echo ¹³C spectrum with ¹H decoupling

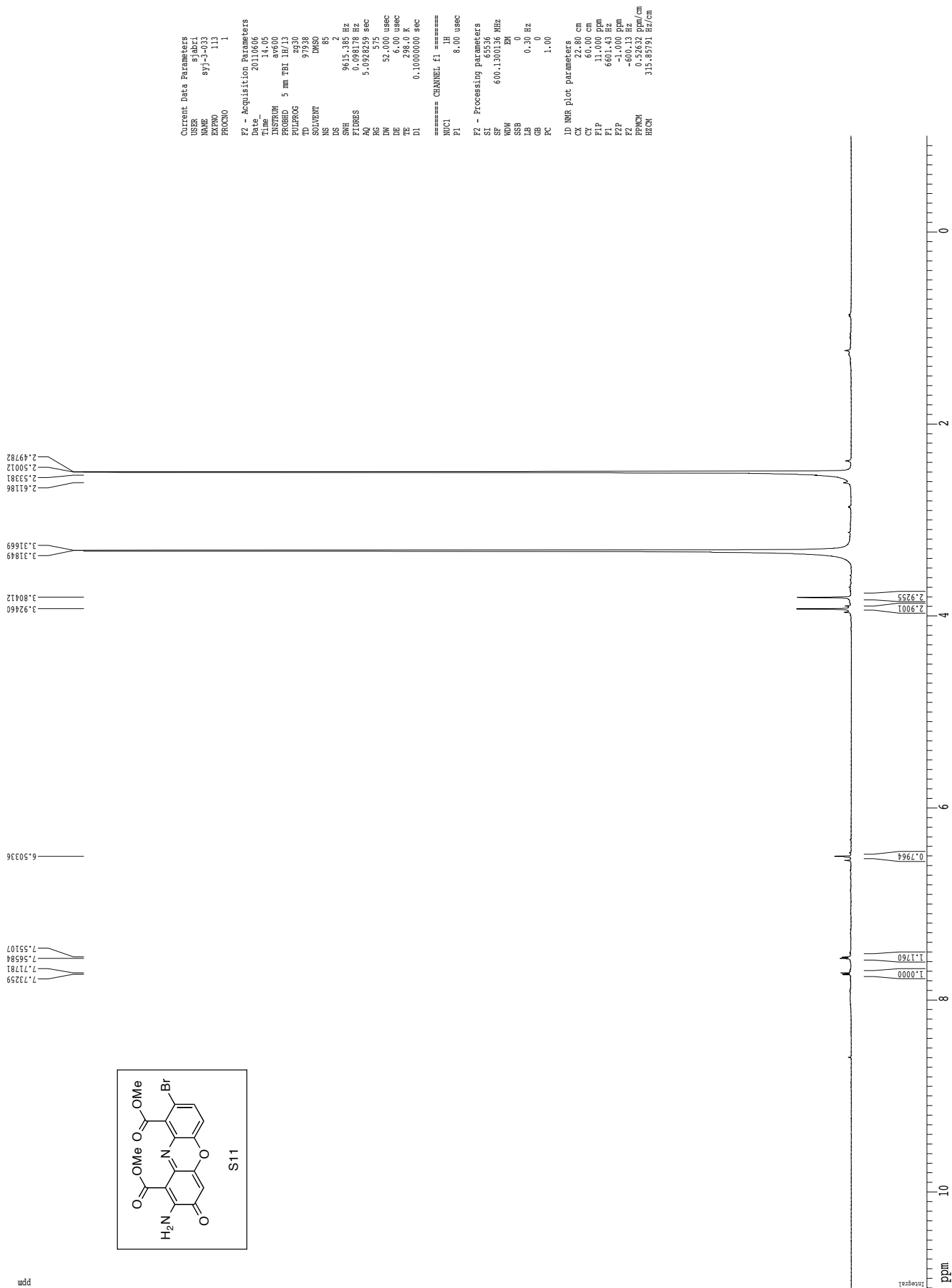
¹H spectrum

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

¹H spectrum

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



¹H spectrum

¹H spectrum

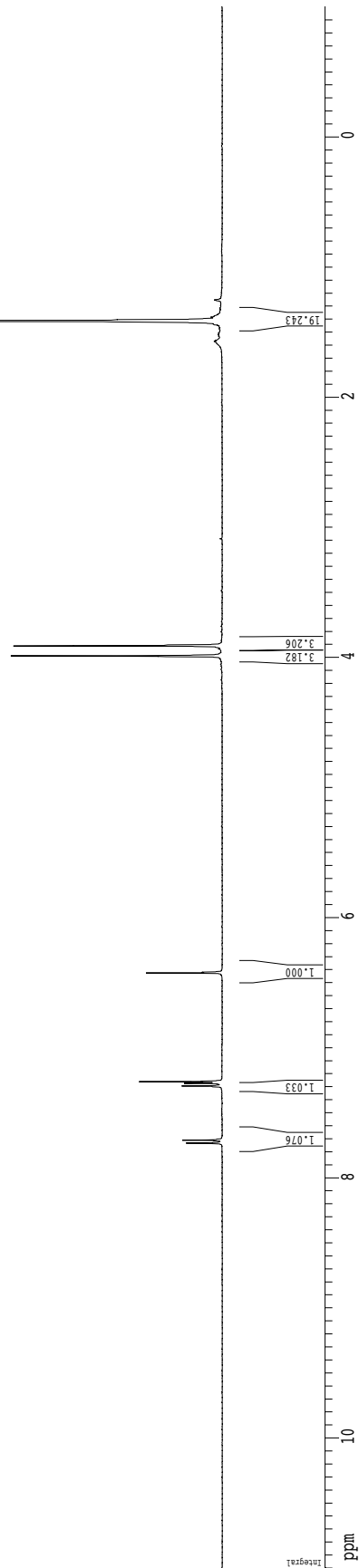
Current Data Parameters
 USER sjabri
 NAME syj-38
 EXPNO 32
 PROCNO 1

F2 - Acquisition Parameters
 Date_ 20110616
 Time 15.44
 INSTRUM spect
 PULPROG zgpg30
 PRGNAME 5 mm QNP H¹g
 FIDRES 0.097813 Hz
 AQ 5.1118579 sec
 RG 362
 DW 78.000 usec
 DE 4.50 usec
 TE 297.3 K
 T1 0.10000000 sec
 T2 0.00000000 sec
 T2RHO 0.00000000 sec
 MCHCK 0.01500000 sec

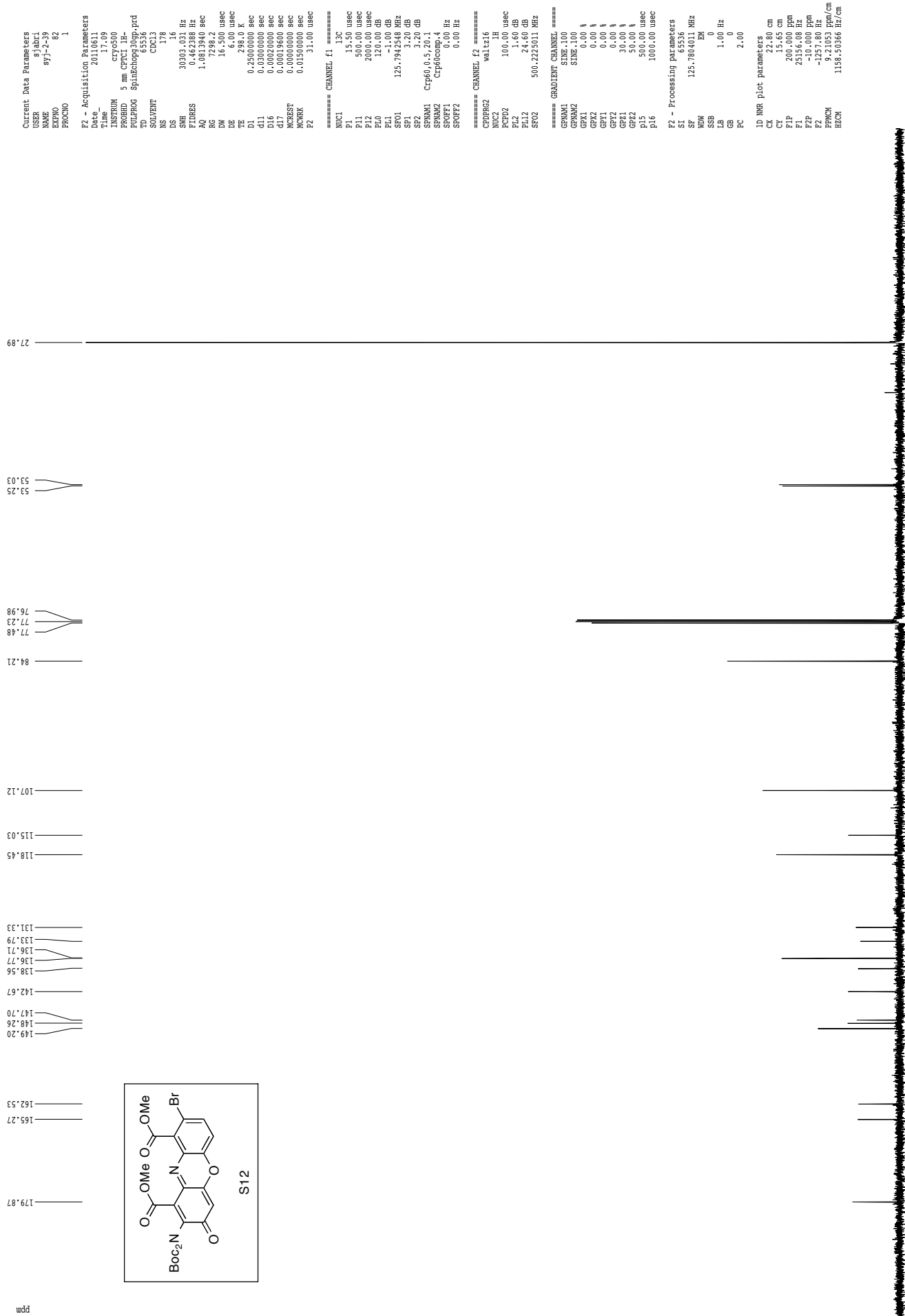
==== CHANNEL f1 =====
 NUC1 1H
 P1 12.00 usec
 PL1 -0.60 dB
 SFO1 400.1328009 MHz

F2 - Processing parameters
 SI 65536
 SF 400.1300211 MHz
 WDW EM
 SS BR
 LB 0.30 Hz
 GB 0
 PC 2.00

1D NMR plot parameters
 CX 22.80 cm
 CY 15.00 cm
 F1 11.000 ppm
 F1 4401.43 Hz
 F2 -1.000 ppm
 F2 -400.13 Hz
 PRCH 0.52632 ppm/cm
 HZCM 210.59476 Hz/cm



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



Current Data Parameters
USER sybcl
EXPNO 82
PROCNO 1

F2 - Acquisition Parameters
Date_ 20110611
Time 17.09
INSTRUM cryo500
PROBHD 5 mm CPXI 1H
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 178
DS 16
SWH 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.081940 sec
RG 327.8
RG2 327.8
RG3 327.8
DE 6.00 usec
TE 298.0 K
D1 0.25000000 sec
d11 0.03000000 sec
D16 0.00020000 sec
d17 0.00019600 sec
WCREST 0.00000000 sec
PCWRR 0.01500000 sec
F2 31.00 usec

===== CHANNEL f1 =====
NUC1 ¹³C
P1 15.50 usec
PL1 500.00 usec
PL2 2000.00 usec
PL0 120.00 dB
PL1 120.00 dB
PL2 24.60 dB
SP1 125.779454 MHz
SP2 31.20 dB
SPNAM1 Ctp60.0.5.20.1
SPNAM2 Ctp60comp.4
SFOFF1 0.00 Hz
SFOFF2 0.00 Hz

===== CHANNEL f2 =====
CPR6G2 waltz16
NUC2 ¹H
PCPD2 100.00 usec
PL2 1.60 dB
PL12 24.60 dB
SFO2 500.2225011 MHz

===== GRADIENT CHANNEL =====
GPM1 SINE-10
GPM2 SINE-10
GFX1 0.00 %
GFX2 0.00 %
GFI1 0.00 %
GFI2 0.00 %
GZ1 30.00 %
GZ2 50.00 %
p15 500.00 usec
p16 1000.00 usec

F2 - Processing parameters
SI 65536
SF 125.7804011 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
FC 2.00

1D NMR plot parameters
CX 22.80 cm
CY 15.65 cm
FIP 200.000 ppm
F1 25156.08 Hz
F2 -10.000 ppm
F2 -1257.80 Hz
PCWRR 0.01500000 sec
HECN 1158.3036 Hz/cm



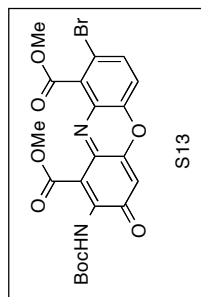
¹H spectrum

1.55301
1.50473
1.41550

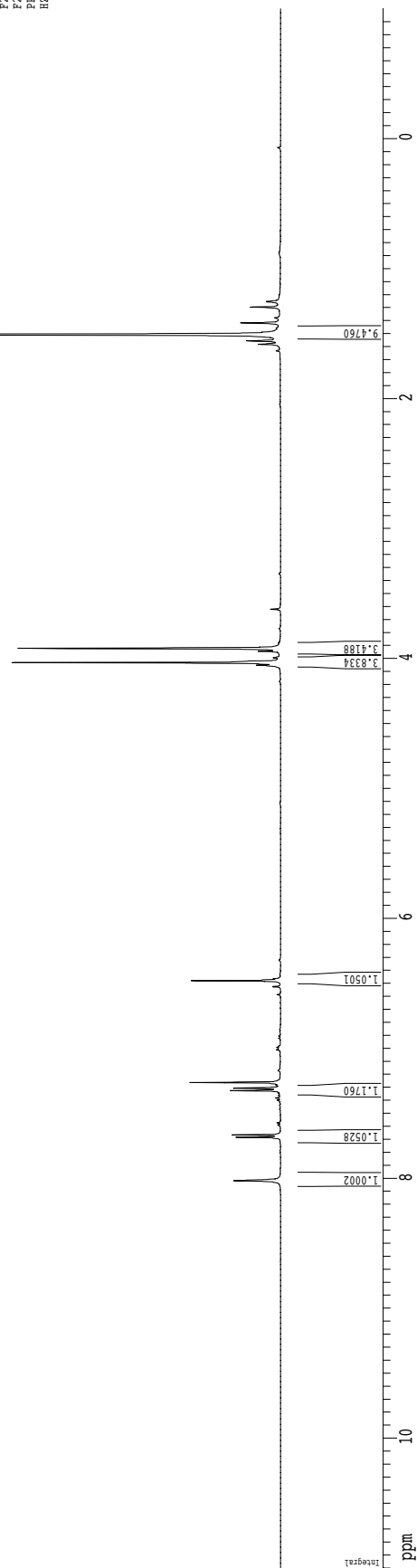
4.02956
3.91932

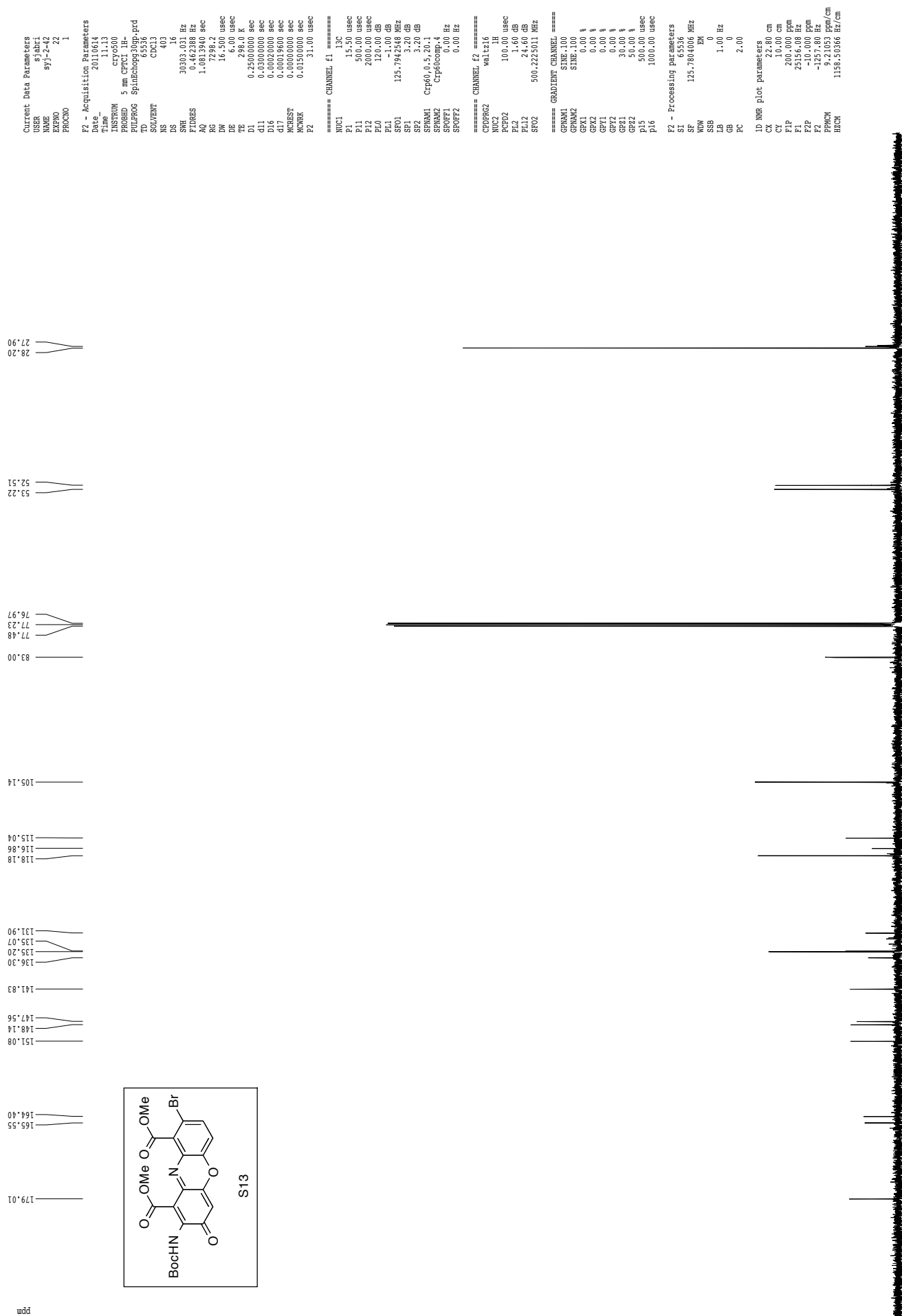
6.47662

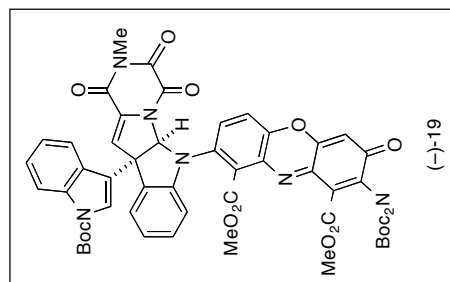
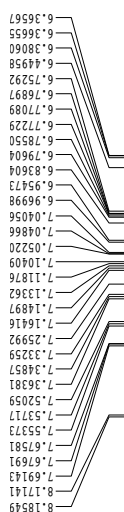
8.01564
7.68237
7.66465
7.32203
7.30429
7.26011



Current Data Parameters
 USER s\jabri
 NAME syj-42
 EXPNO 21
 PROCNO 1
 F2 - Acquisition Parameters
 Date_ 20110614
 Time 11.10
 INSTRUM cryo500
 PROBD 5 mm CPTCI 1H-
 PULPROG zg30
 TD 81728
 SOLVENT CDCl3
 NS 8
 DS 2
 SWH 8012.820 Hz
 FIDRES 0.098043 Hz
 AQ 5.0998774 sec
 RG 62.400
 DE 6.00 usec
 TE 298.0 K
 D1 0.10000000 sec
 MCREST 0.00000000 sec
 MCWRR 0.01500000 sec
 ===== CHANNEL f1 =====
 NUC1 1H
 P1 7.50 usec
 PL1 1.60 dB
 SFO1 500.2235015 MHz
 F2 - Processing parameters
 SI 32768
 SF 500.220322 MHz
 WDW EM
 SSB 0
 LB 0.30 Hz
 GB 0
 PC 4.00
 ID NMR plot parameters
 CX 22.80 cm
 CY 10.00 cm
 FIP 11.000 ppm
 F1 5502.42 Hz
 F2 11.000 ppm
 F3 -500.92 ppm
 PRMCM 0.55632 ppm/cm
 HZCM 263.27371 Hz/cm



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

¹H spectrum

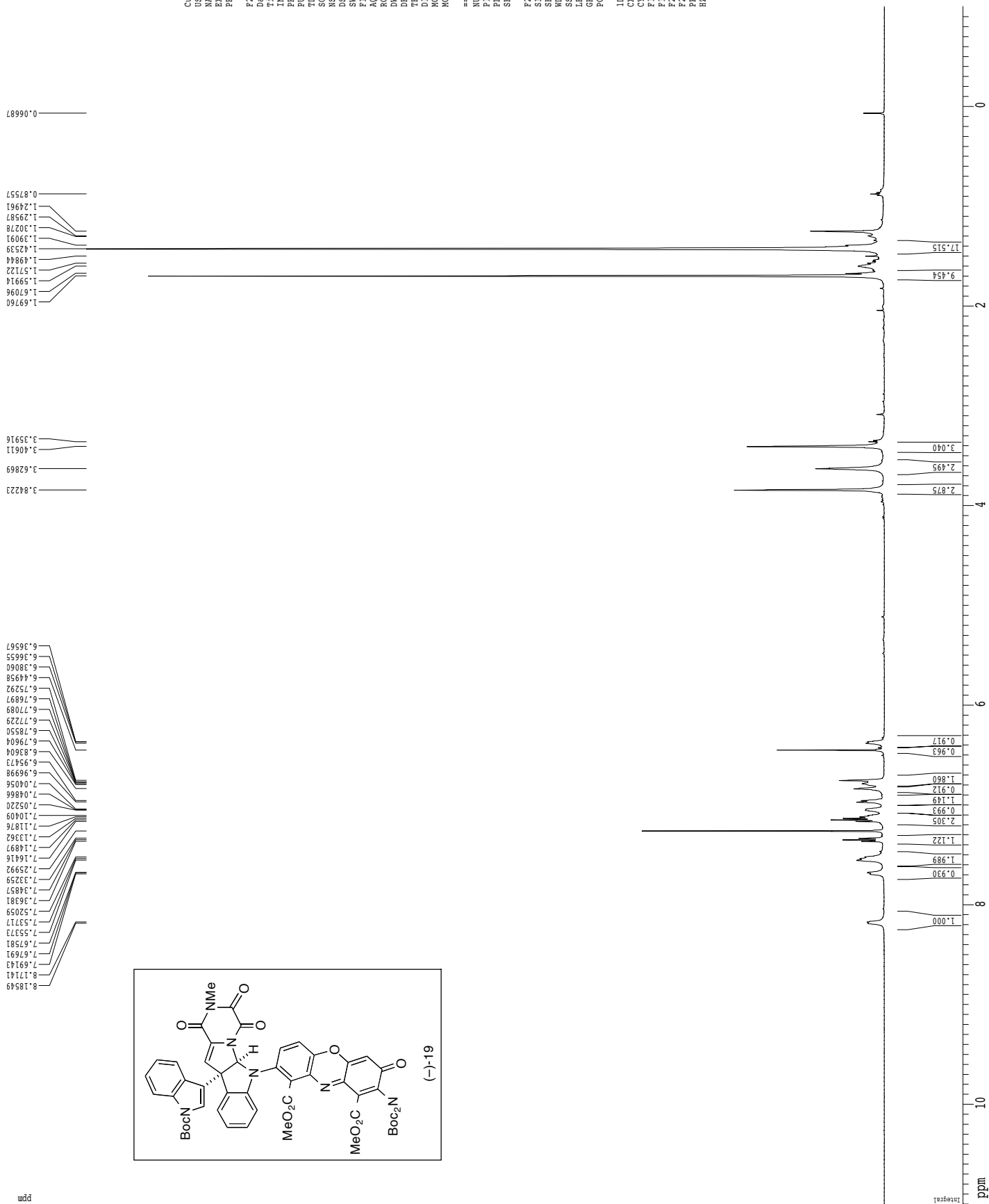
Current Data Parameters
 USER sjlabri
 NAME sy7-3-125
 EXPNO 11
 PROCNO 1

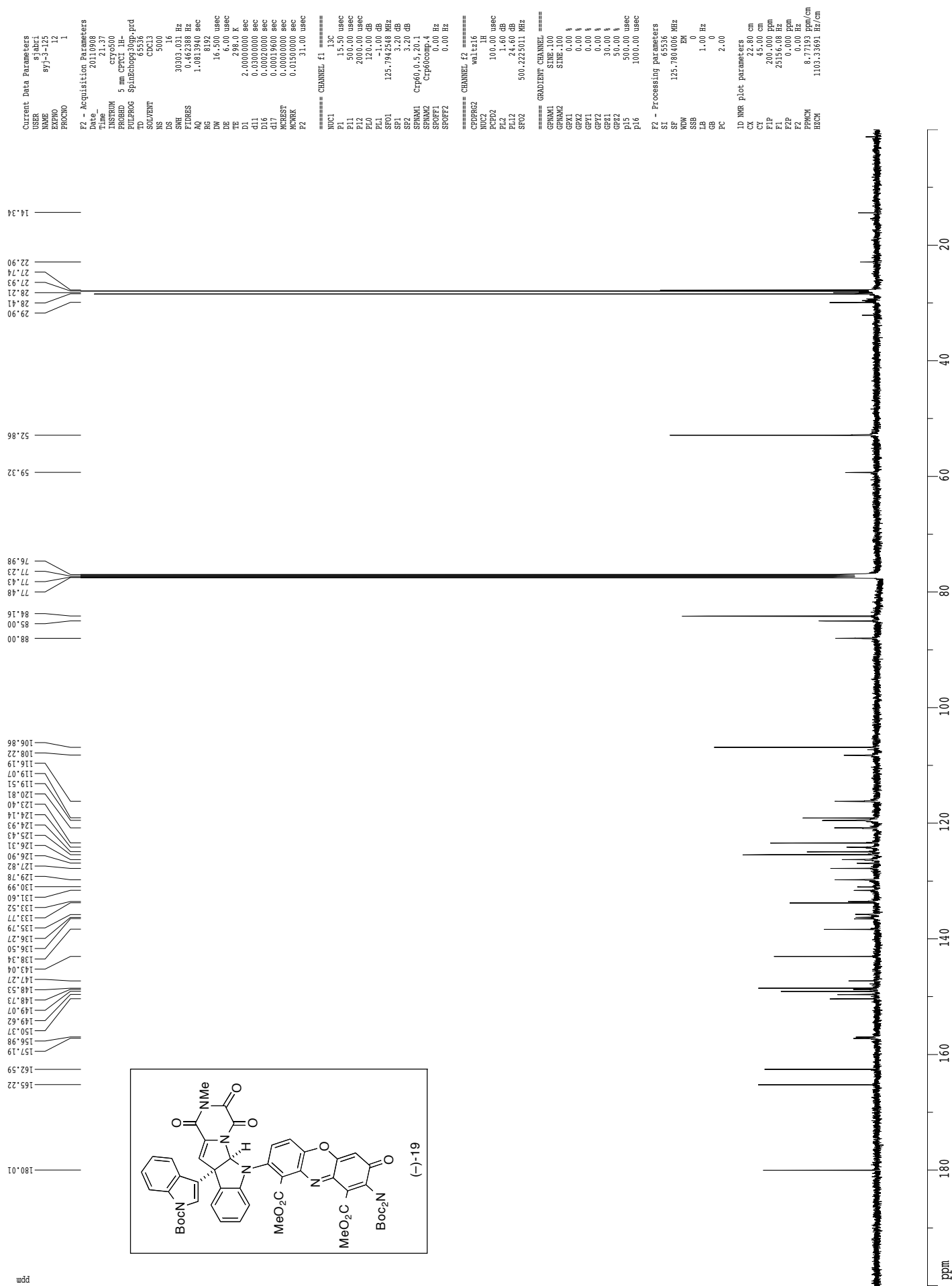
F2 - Acquisition Parameters
 Date_ 20110908
 Time_ 21.28
 INSTRUM cryo500
 PROBD 5 mm CPYC1 1H-
 PULPROG zg30
 TD 81728
 SOLVENT CDCl3
 NS 8
 DS 2
 SWH 8012.820 Hz
 FIDRES 0.098043 Hz
 AQ 5.099774 sec
 RG 371
 CW 62.00 usec
 DE 6.00 usec
 TE 298.0 K
 D1 0.10000000 sec
 MCREST 0.00000000 sec
 MCWRR 0.01500000 sec

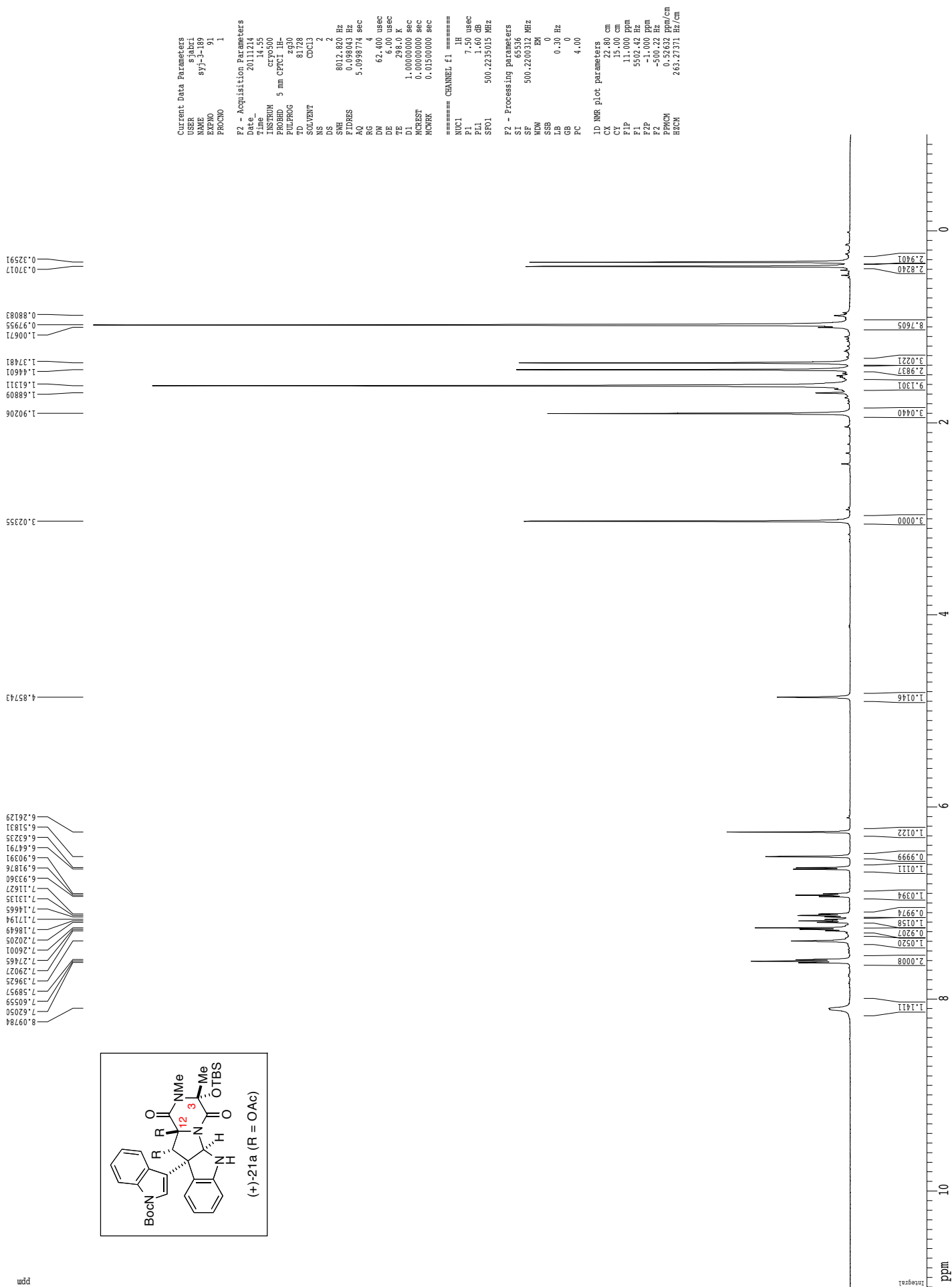
===== CHANNEL f1 =====
 NUC1 1H
 P1 7.50 usec
 PL1 1.60 dB
 SFO1 500.2235015 MHz

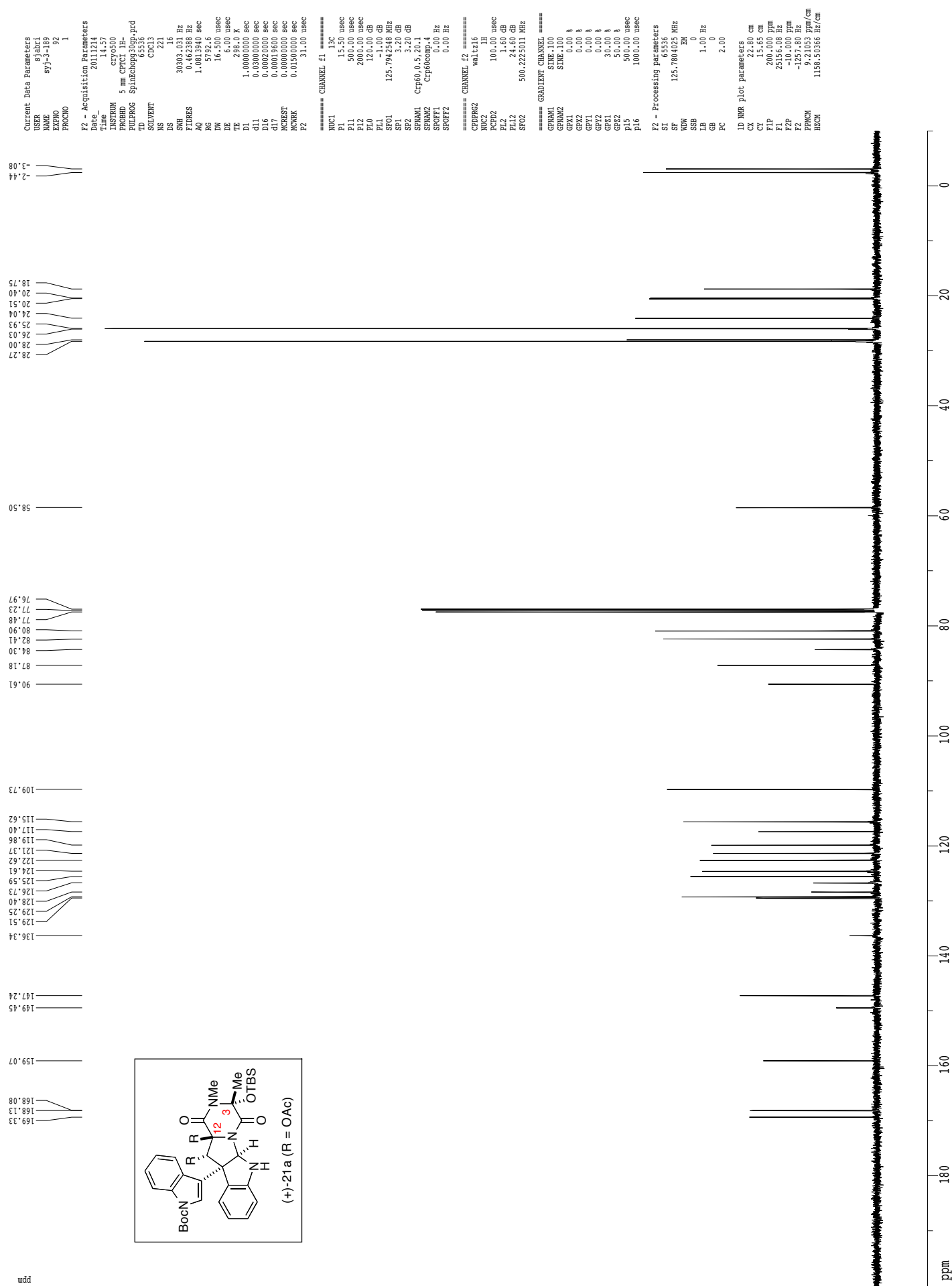
F2 - Processing parameters
 SI 32768
 SF 500.220319 MHz
 WDW EM
 SSB 0
 LB 0.30 Hz
 GB 0
 PC 0.20

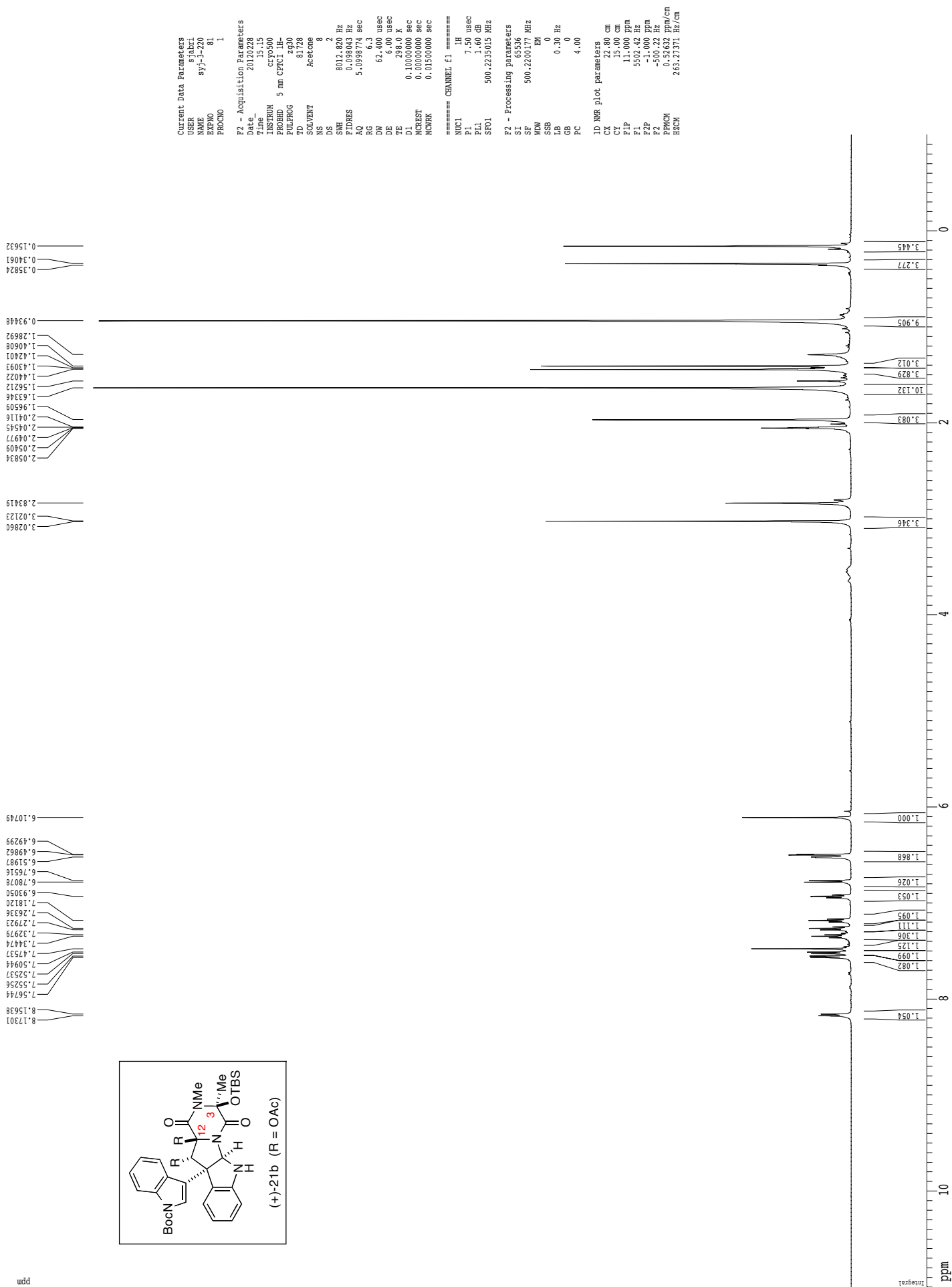
1D NMR plot parameters
 CX 22.80 cm
 CY 20.00 cm
 FIP 11.000 ppm
 F1 5502.42 Hz
 F2 11.000 ppm
 F3 -500.92 ppm
 PPMCM 0.55432 ppm/cm
 HZCM 263.27371 Hz/cm



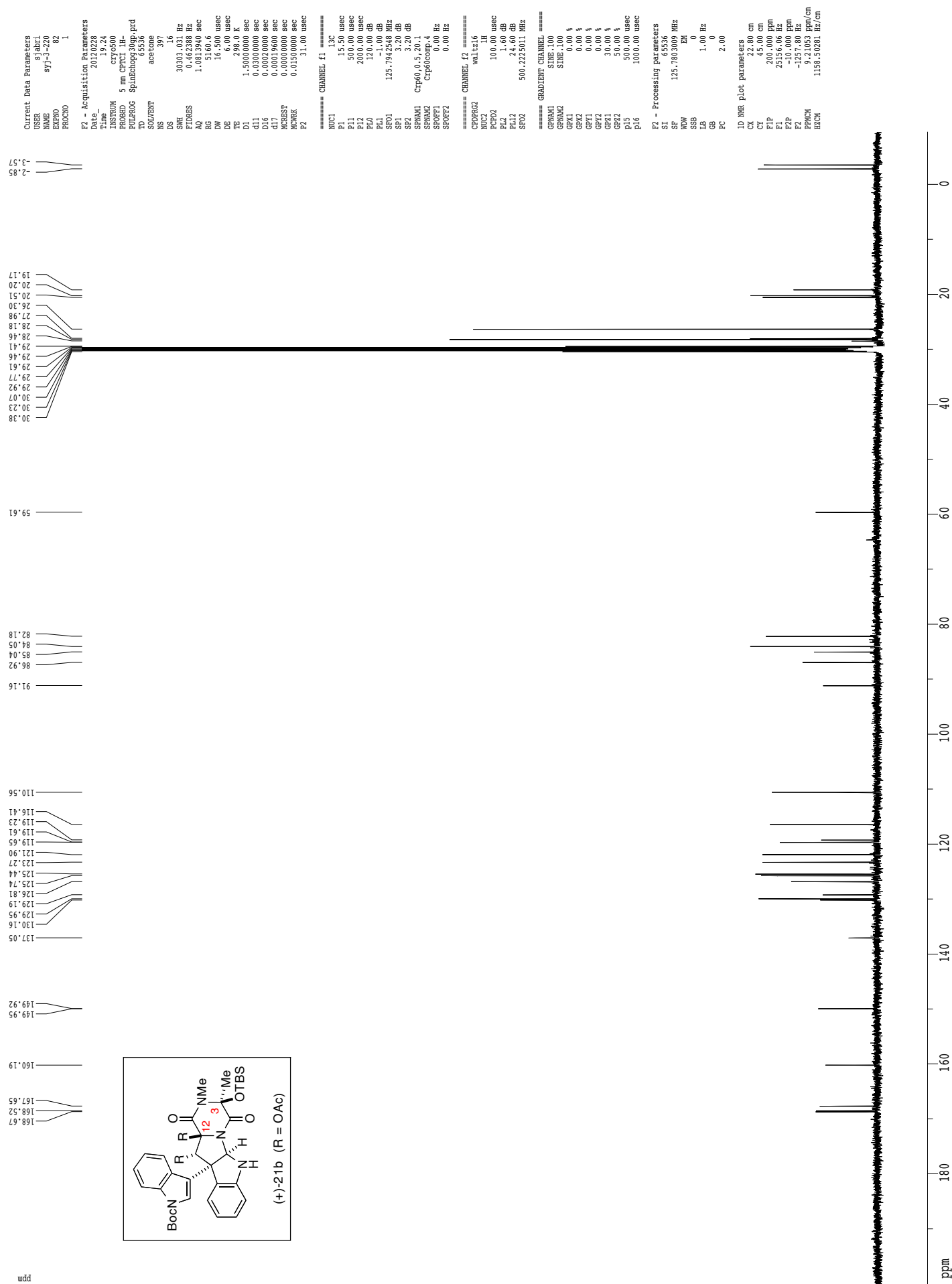
Z-restored spin-echo ^{13}C spectrum with ^1H decoupling

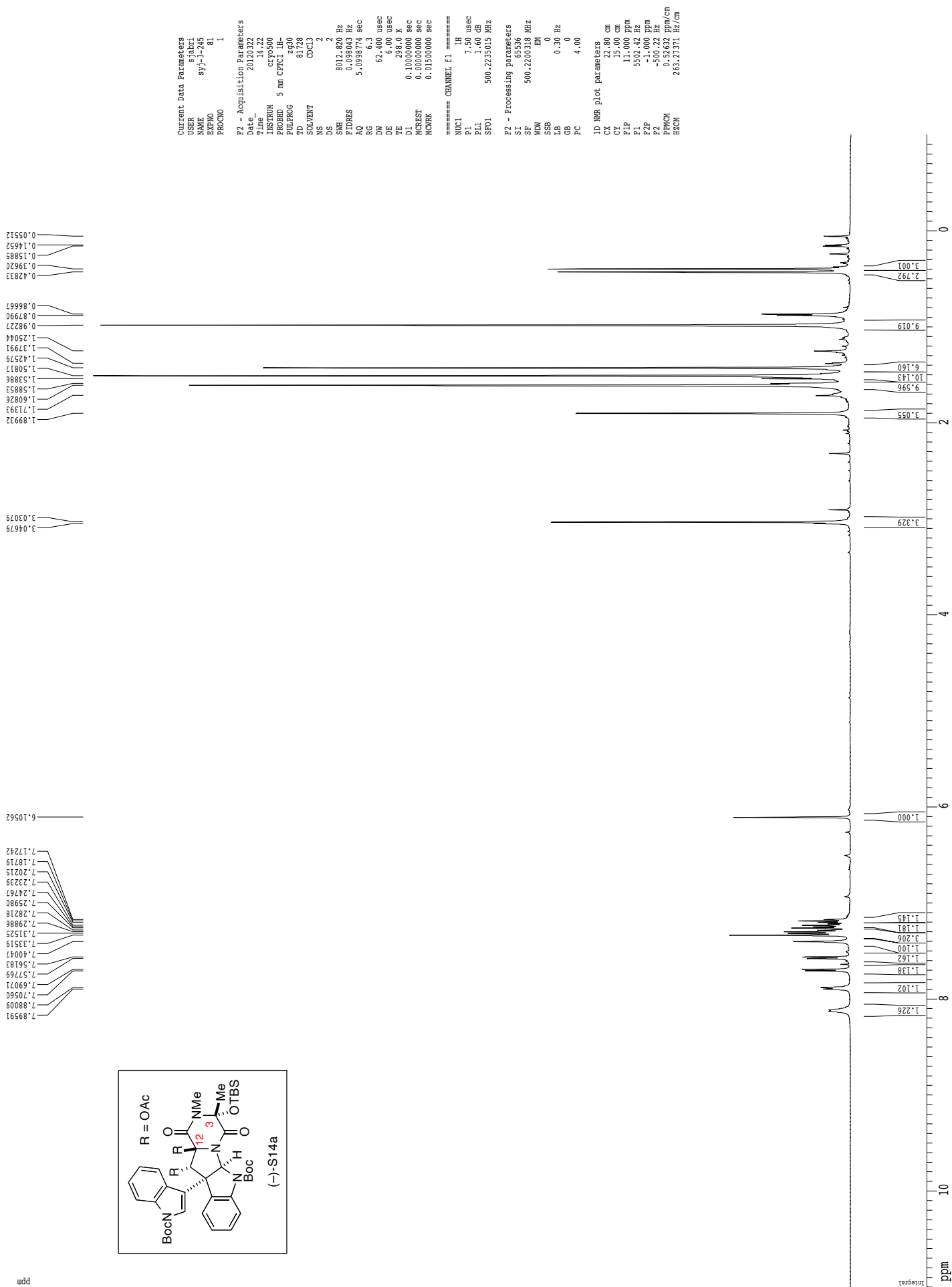
¹H spectrum

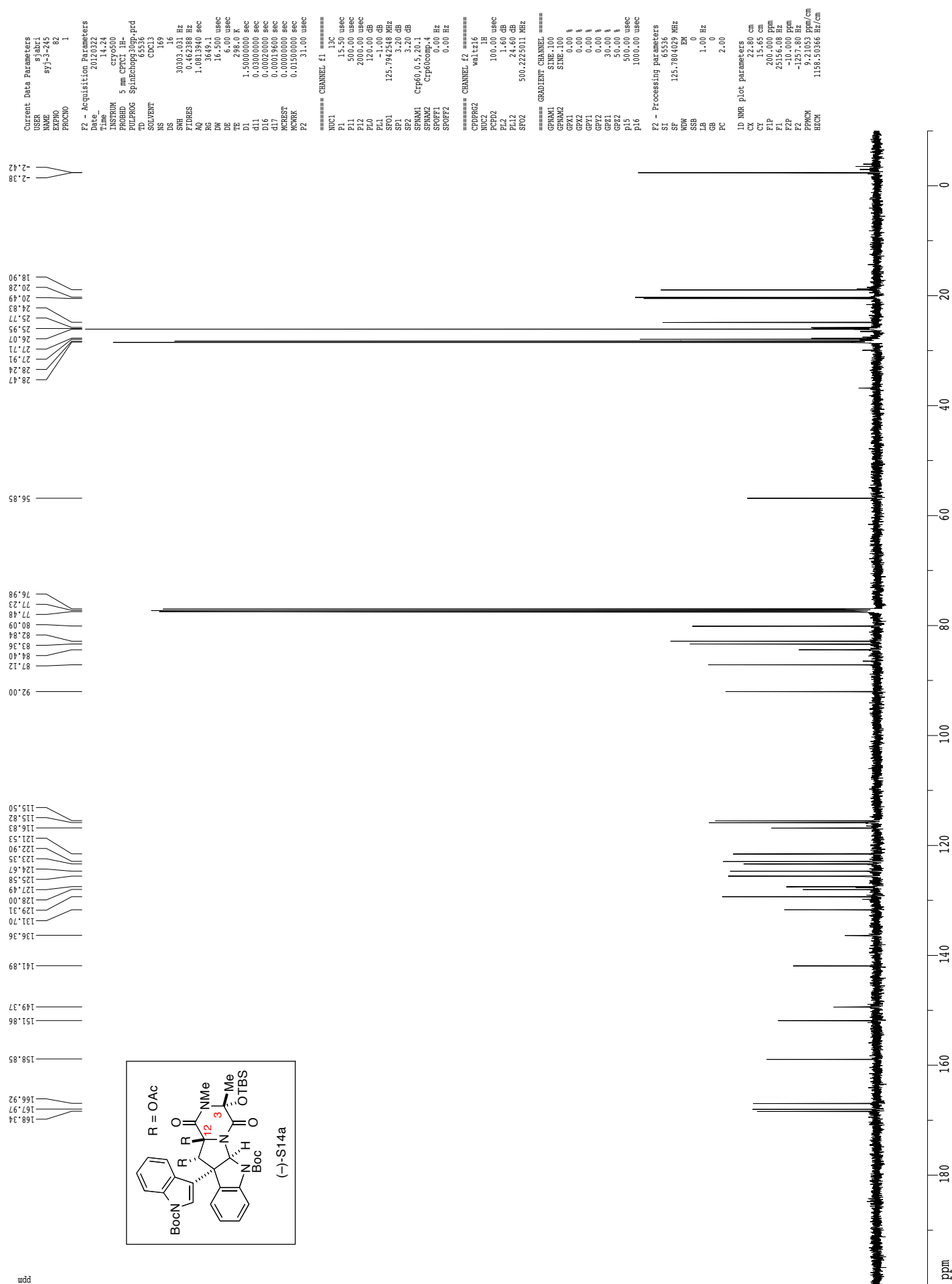
Z-restored spin-echo ^{13}C spectrum with ^1H decoupling

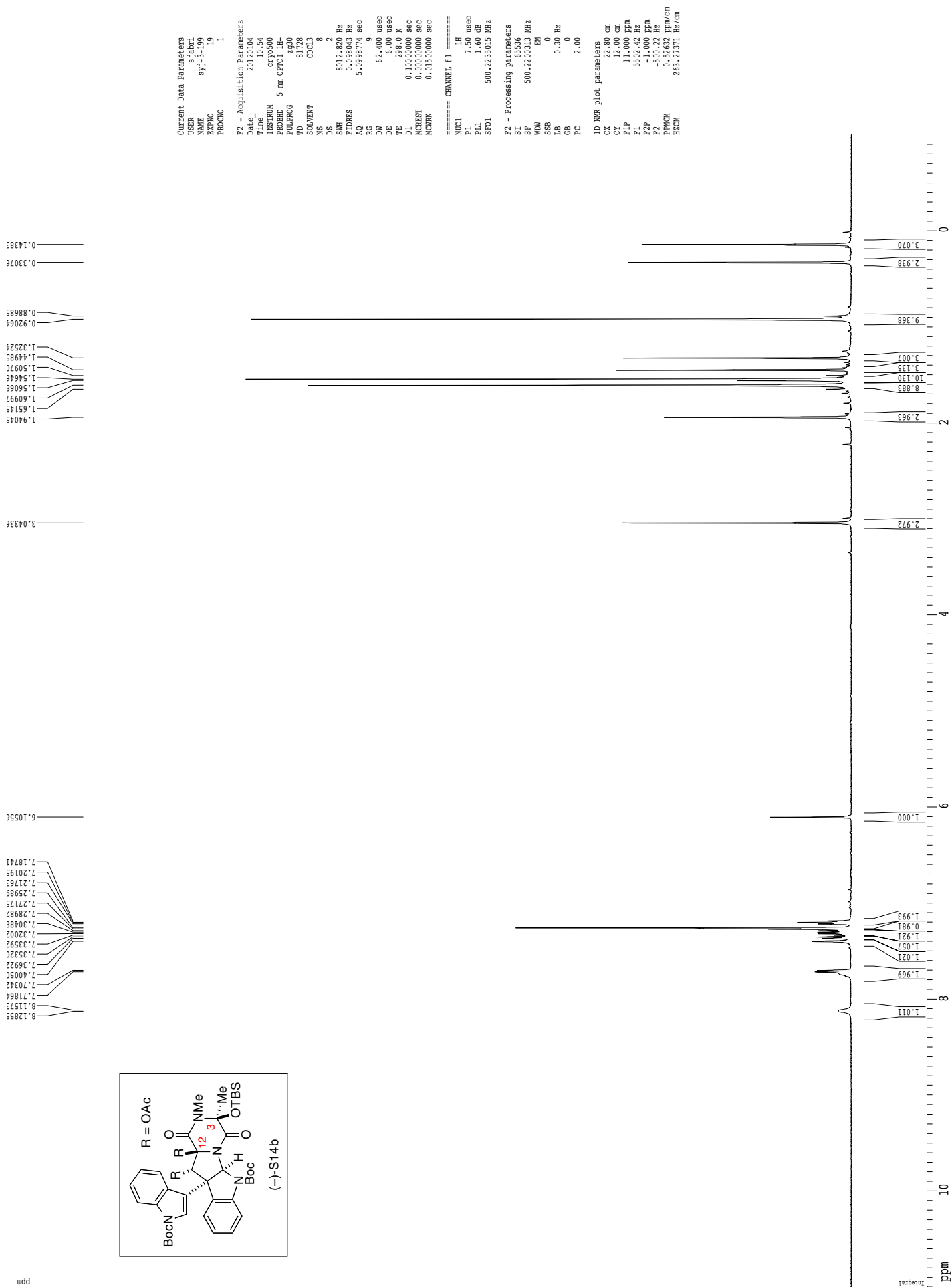
¹H spectrum

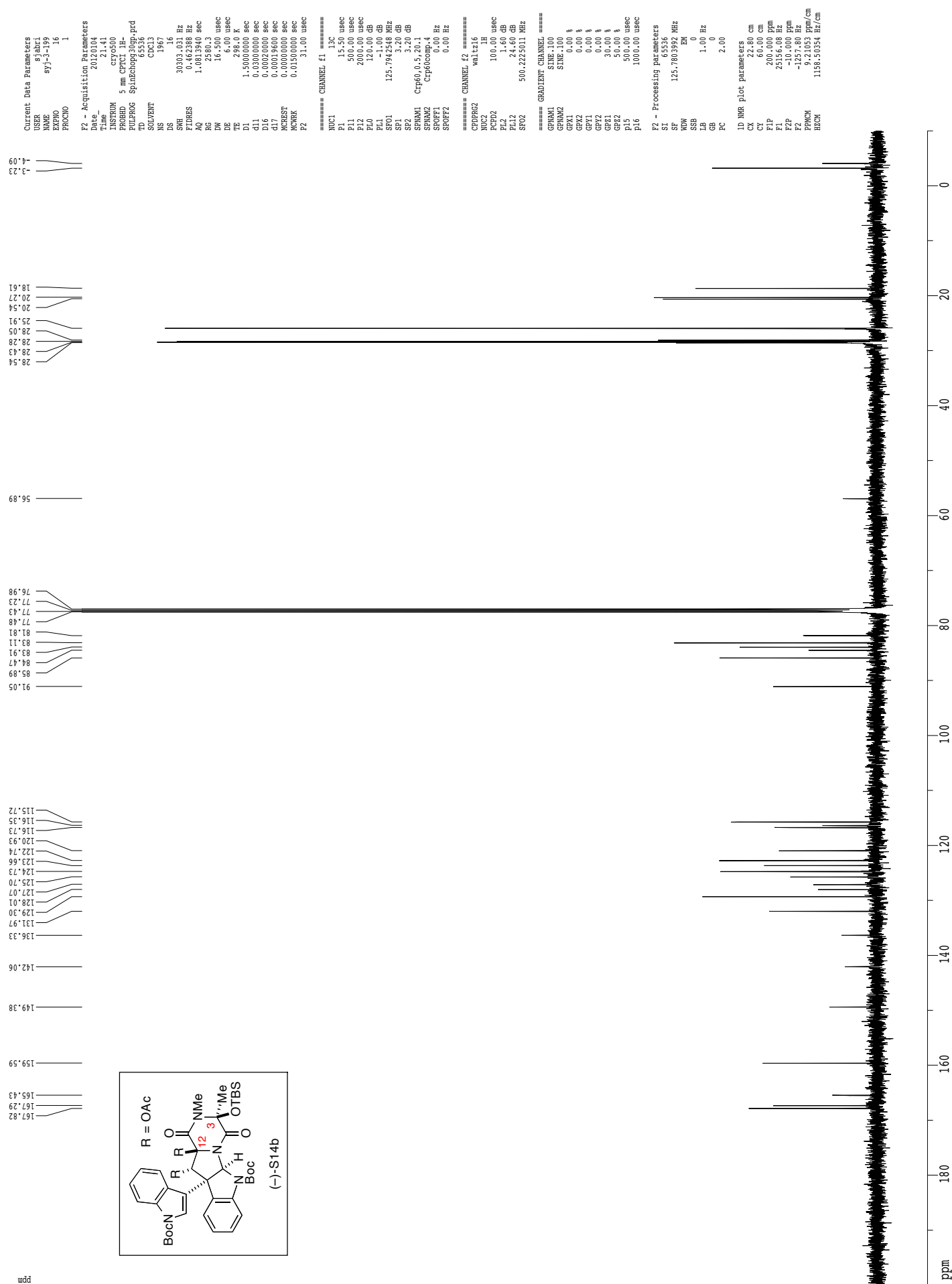
Z-restored spin-echo 13C spectrum with 1H decoupling

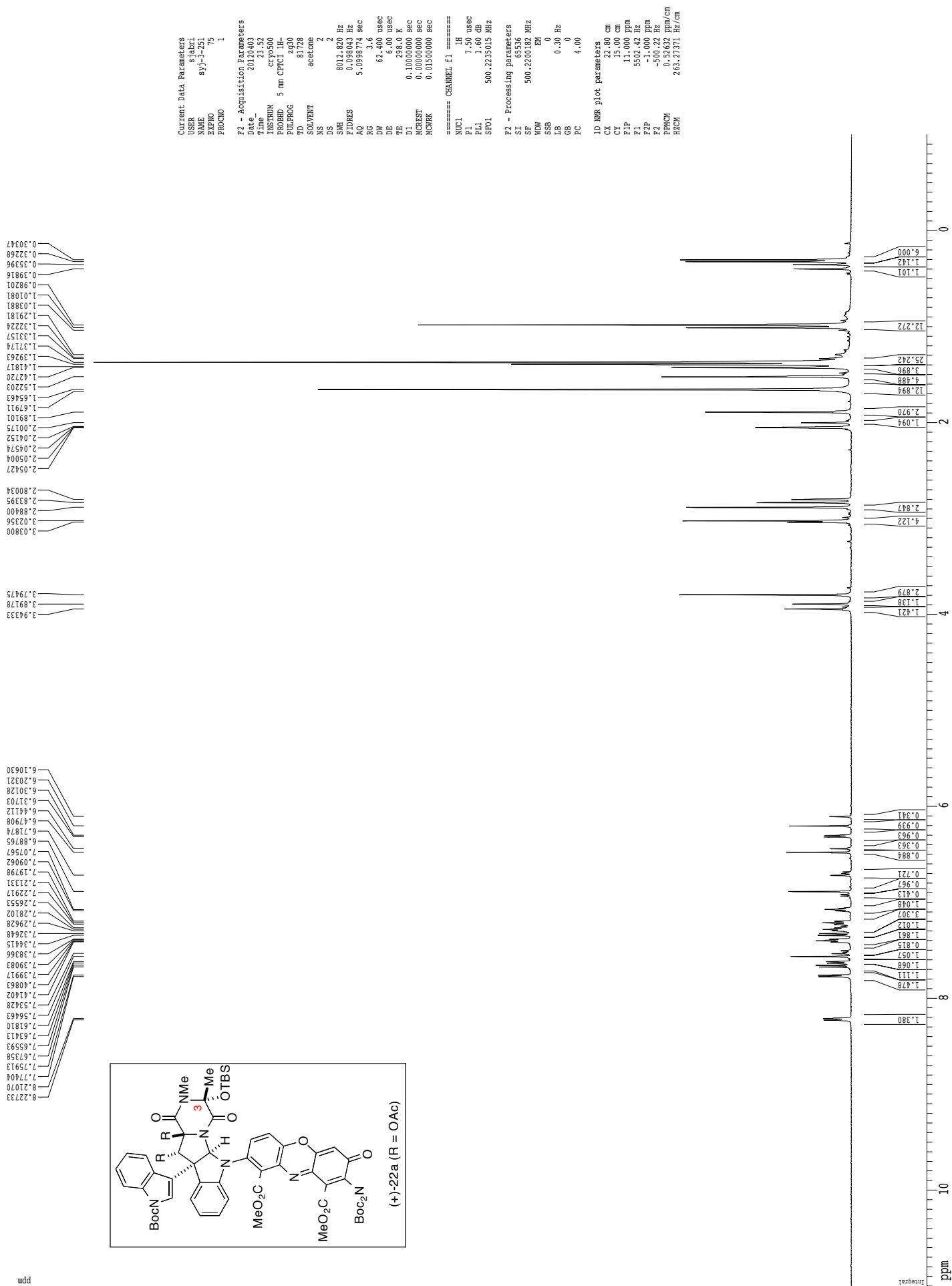


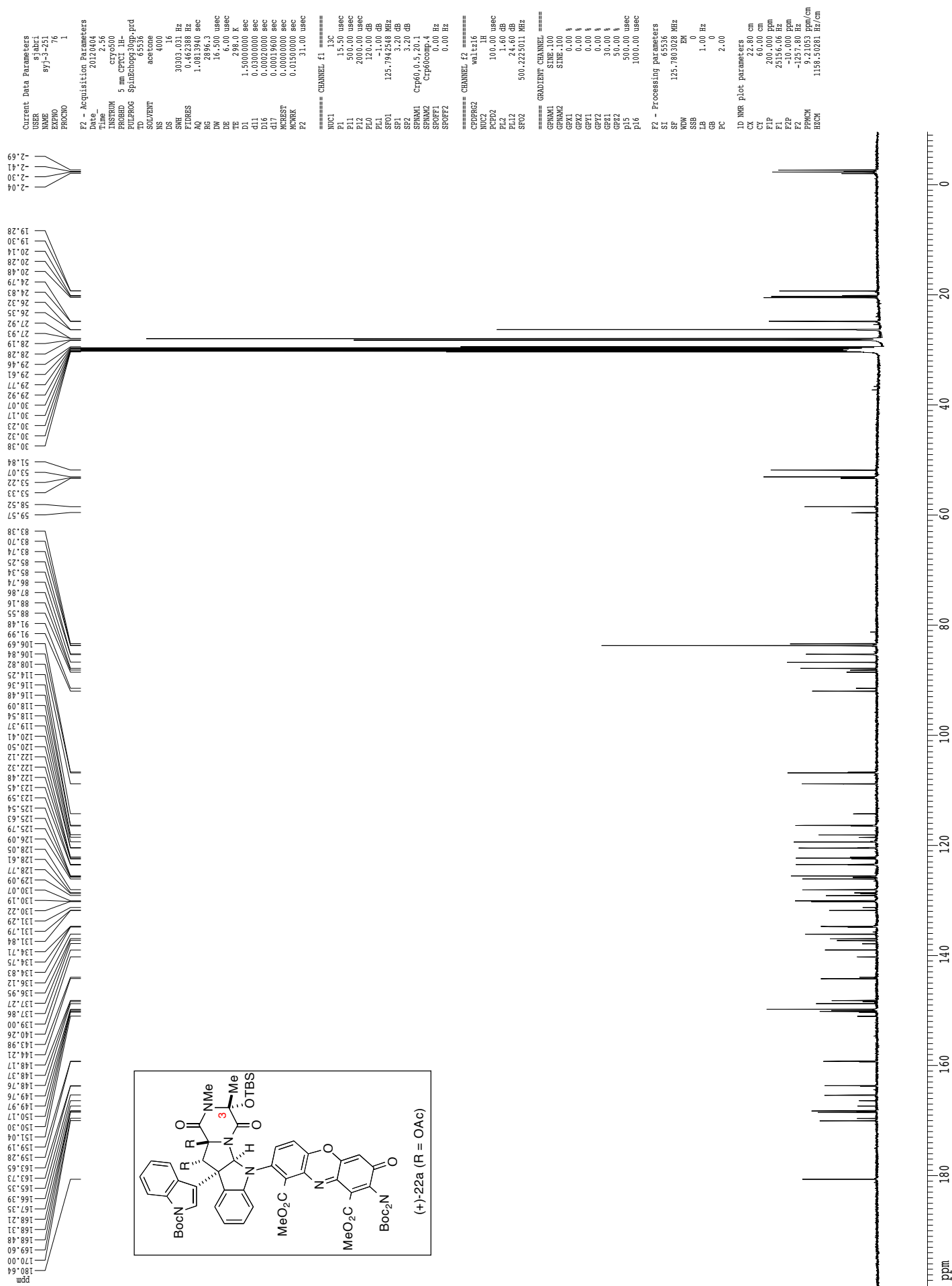
¹H spectrum

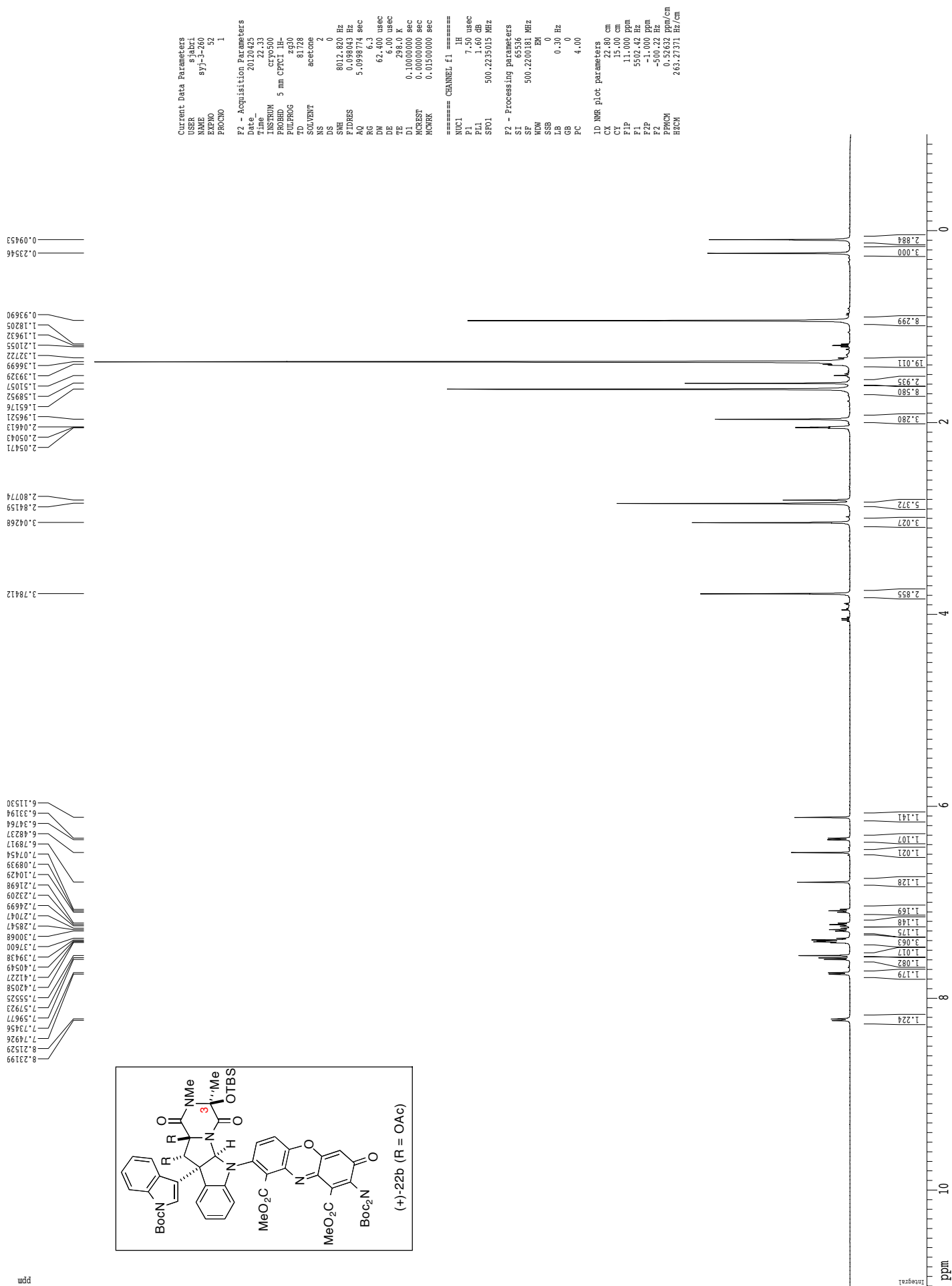
Z-restored spin-echo ^{13}C spectrum with ^1H decoupling

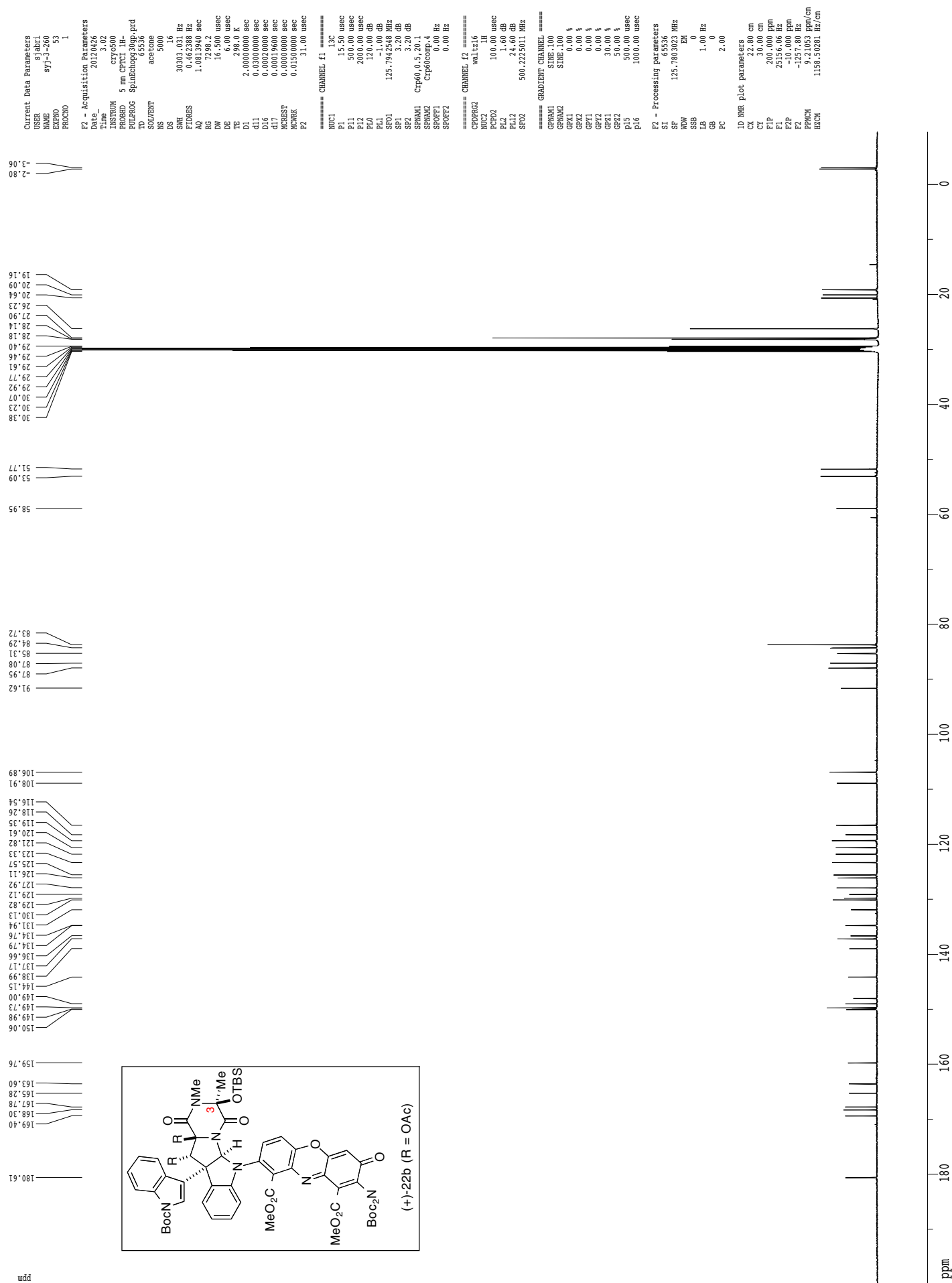
¹H spectrum

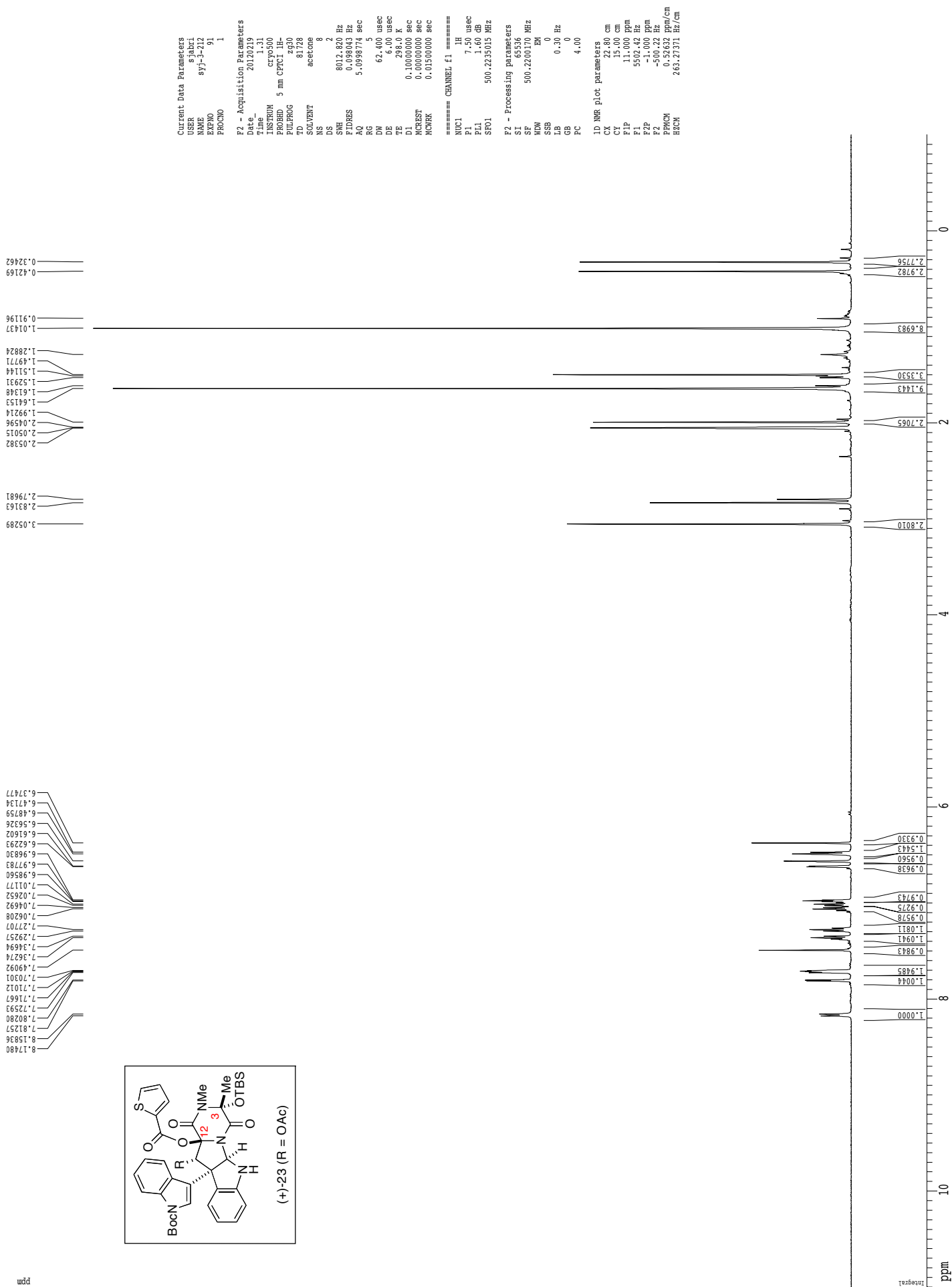
Z-restored spin-echo ^{13}C spectrum with ^1H decoupling

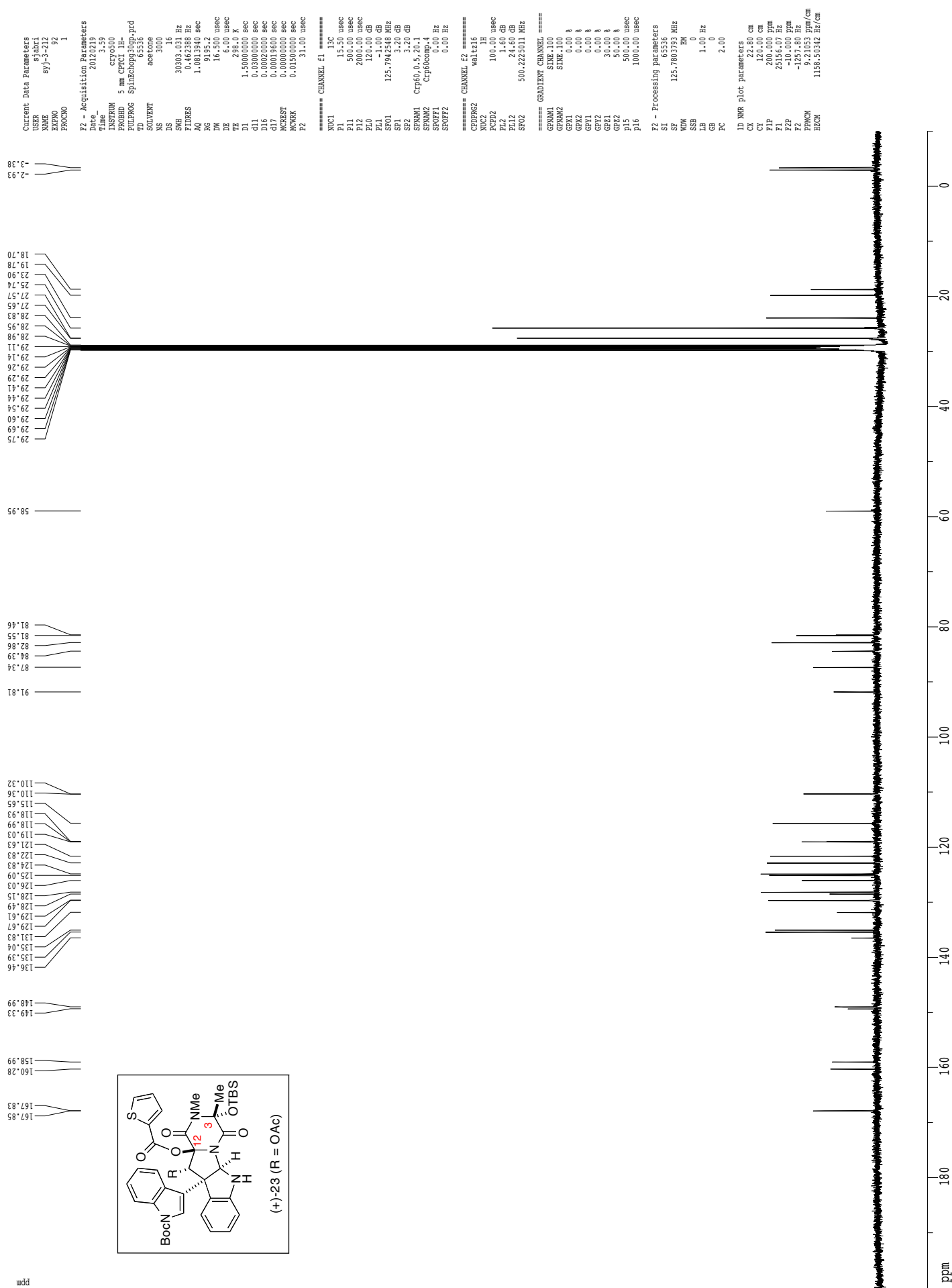
¹H spectrum

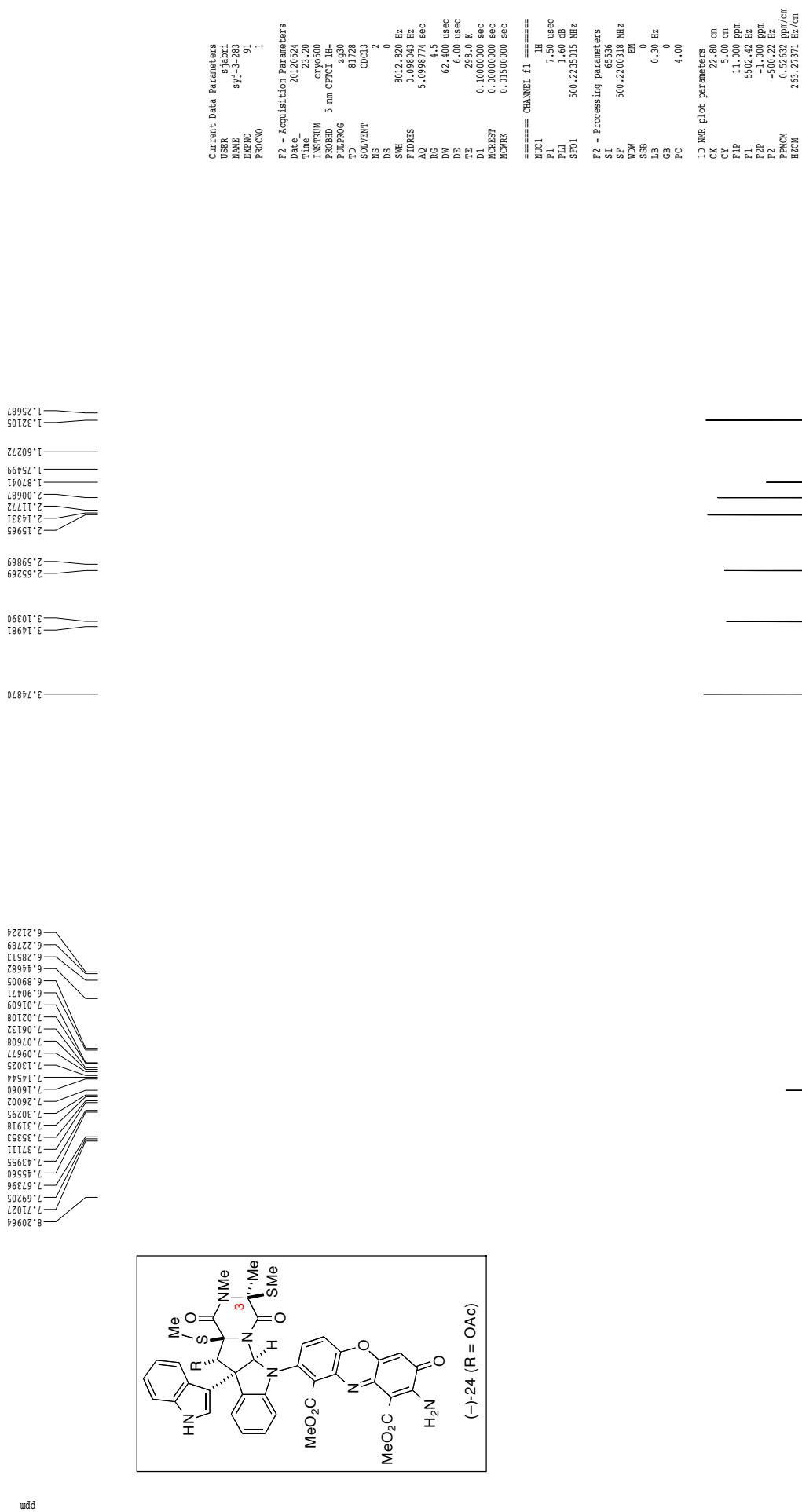
Z-restored spin-echo ¹³C spectrum with ¹H decoupling

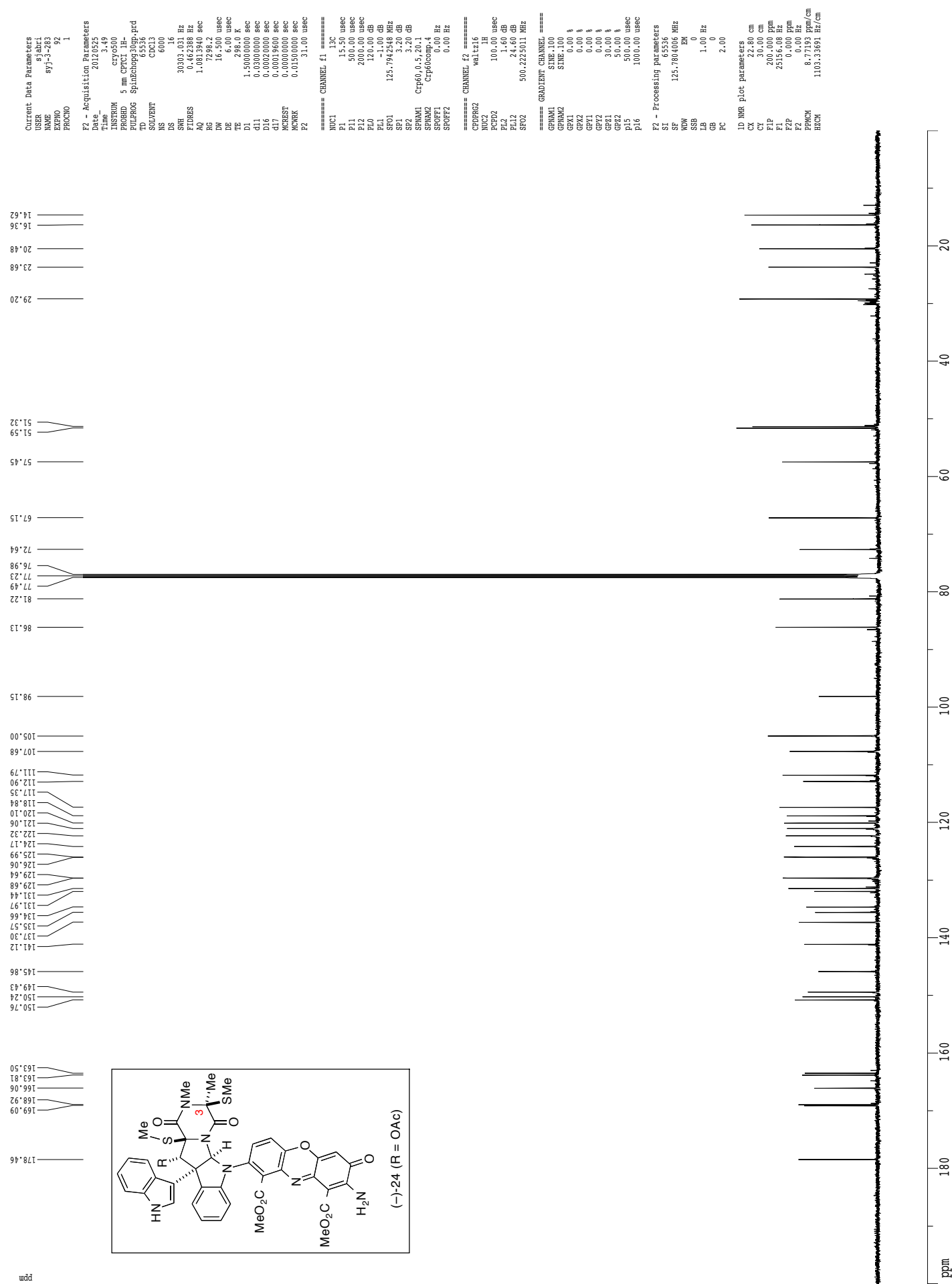
¹H spectrum

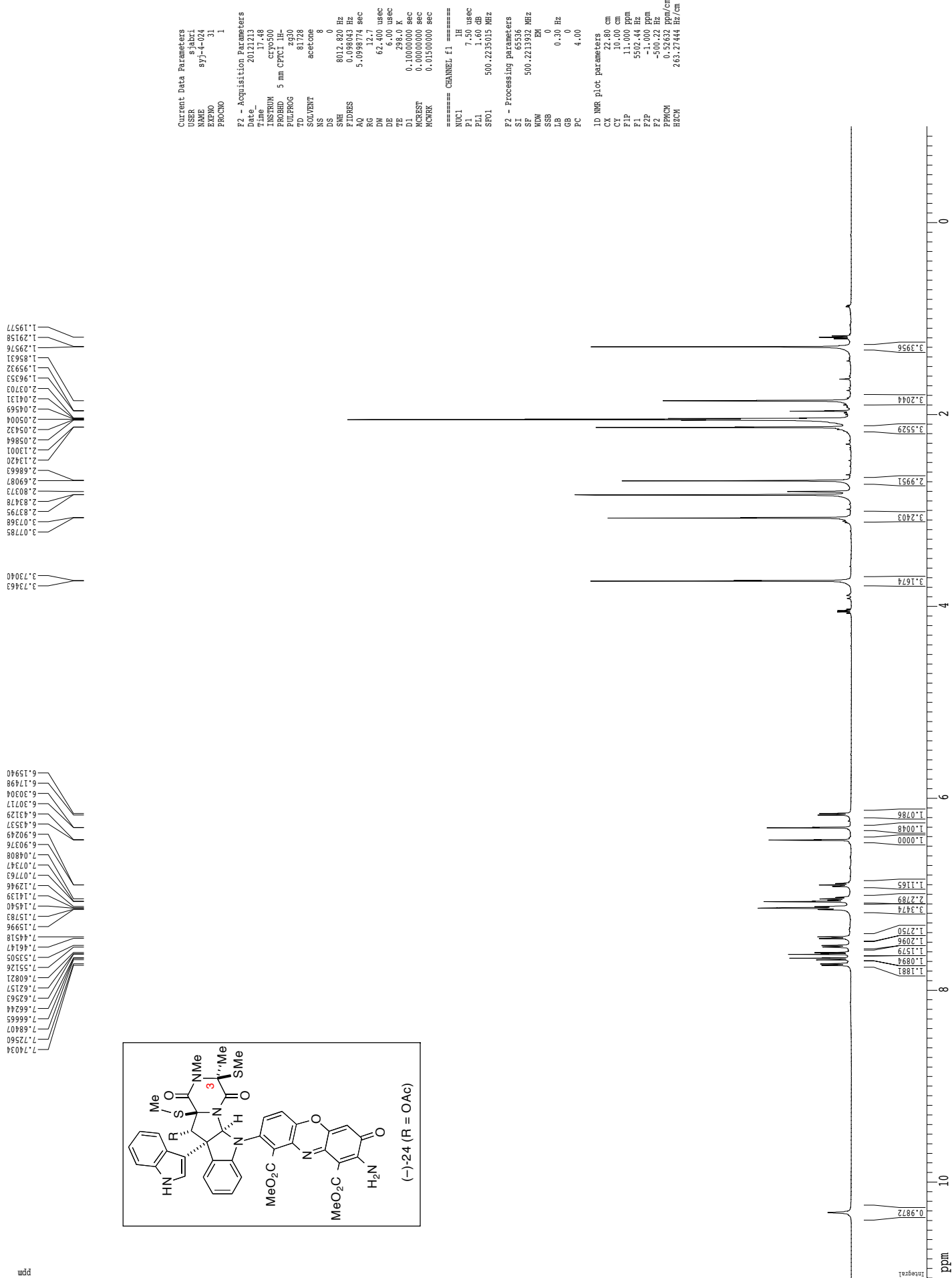
Z-restored spin-echo ^{13}C spectrum with ^1H decoupling

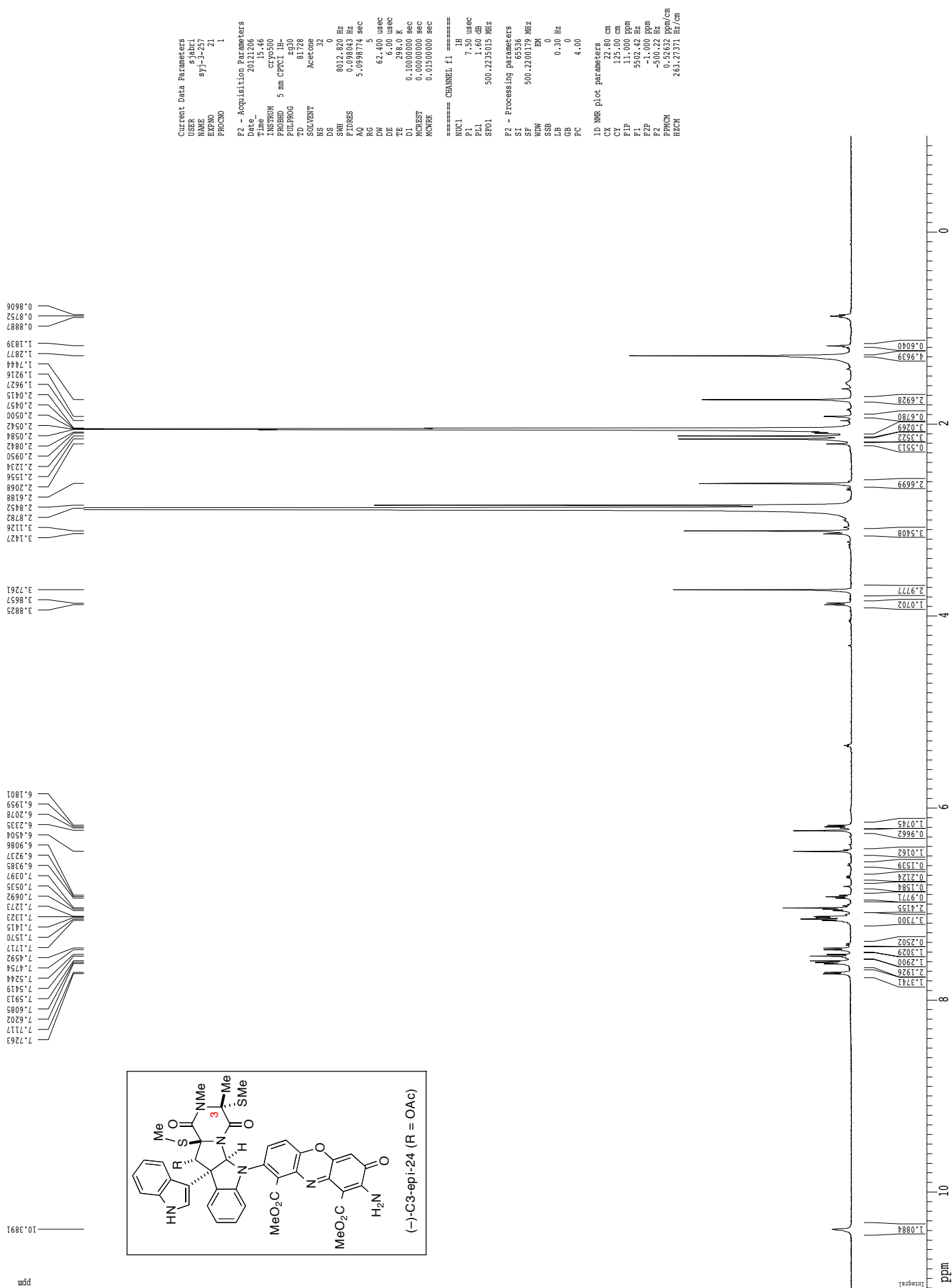
¹H spectrum

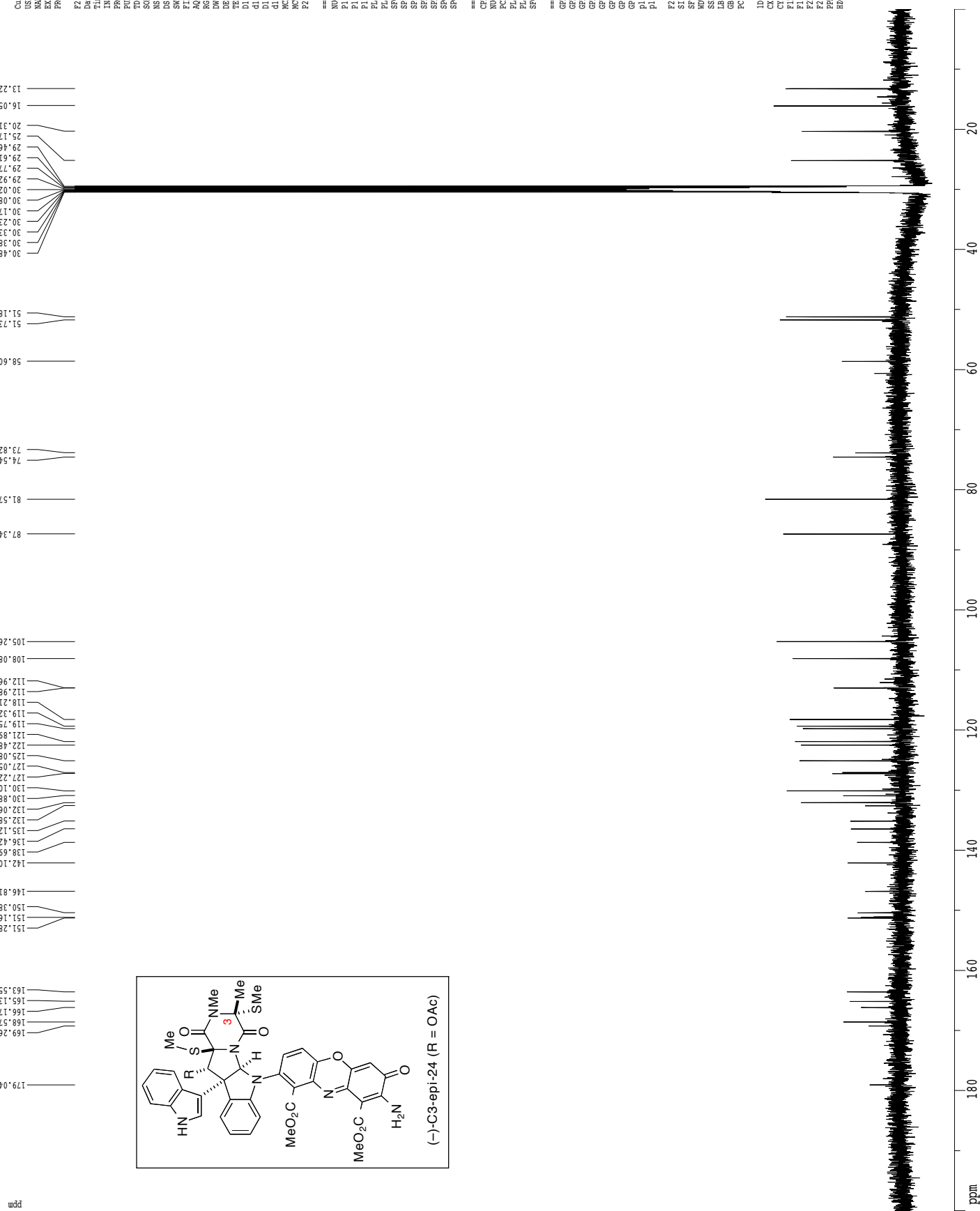
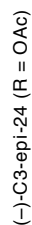
Z-restored spin-echo ^{13}C spectrum with ^1H decoupling

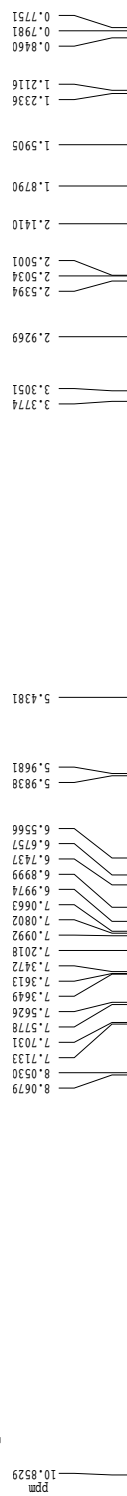
¹H spectrum

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

¹H spectrum

¹H spectrum



¹H spectrum

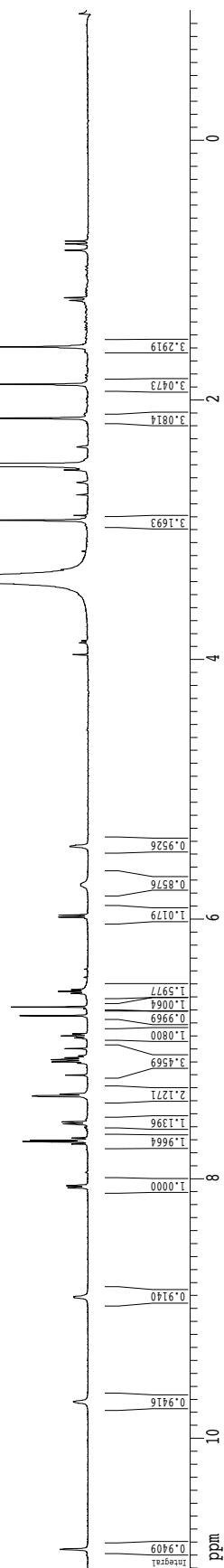
Current Data Parameters
 USER sjlabri
 NAME sy7-3-277
 EXPNO 11
 PROCNO 1

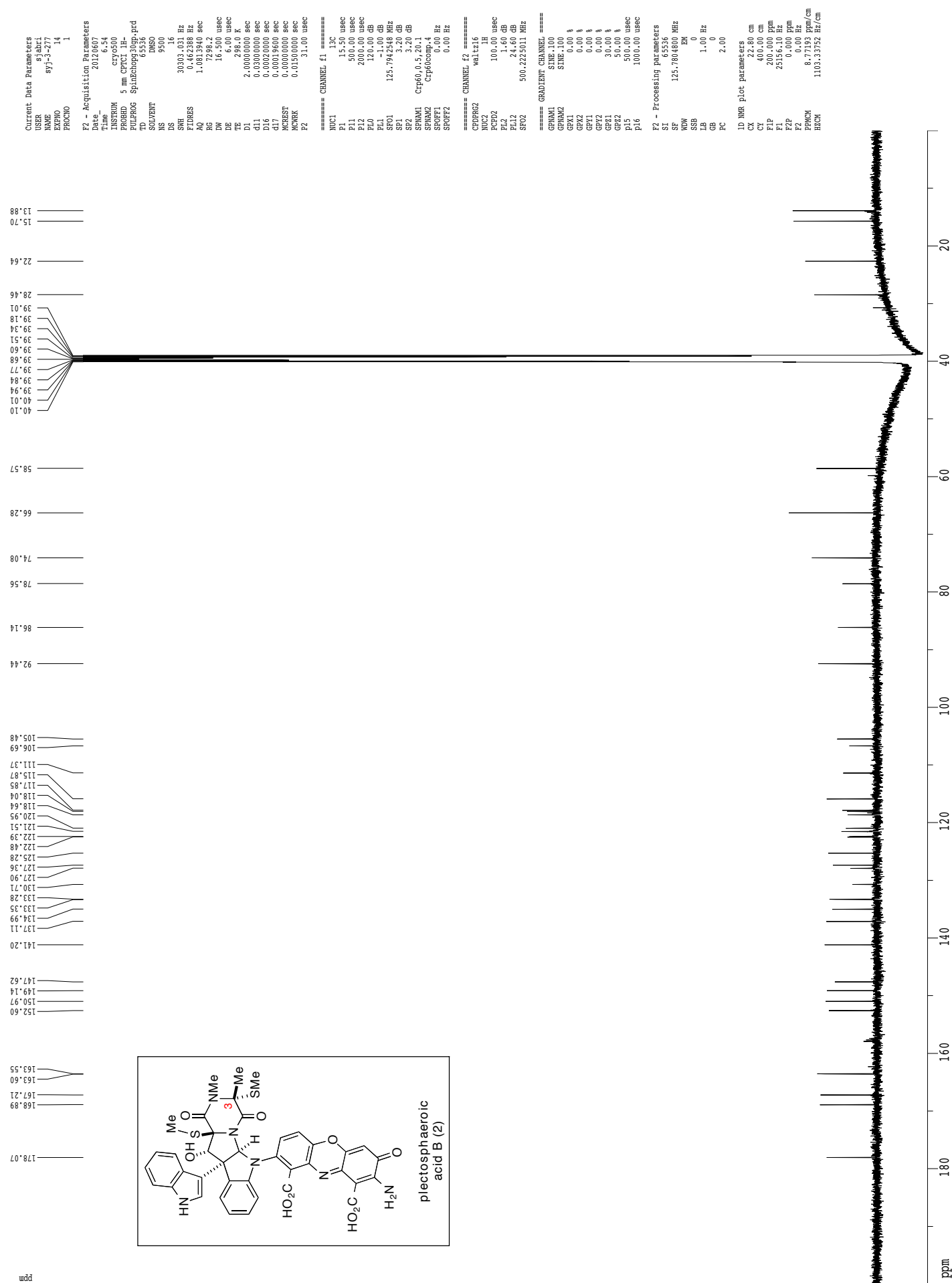
F2 - Acquisition Parameters
 Date_ 20120518
 Time 10.57
 INSTRUM cryo500
 PROBRD 5 mm CPYC1 1H-
 PULPROG zg30
 TD 81728
 SOLVENT DMSO
 NS 54
 DS 2
 SWH 8012.820 Hz
 FIDRES 0.098043 Hz
 AQ 5.0998774 sec
 RG 8
 NI 62.400 usec
 DE 6.00 usec
 TE 298.0 K
 D1 0.10000000 sec
 MCREST 0.00000000 sec
 MCWRR 0.01500000 sec

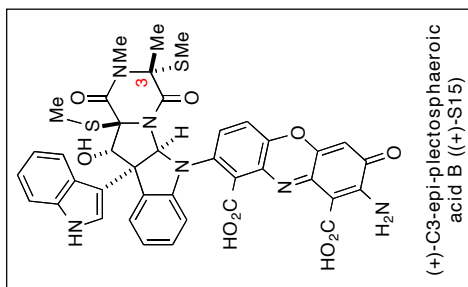
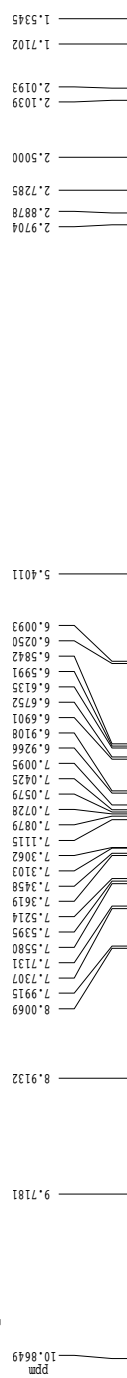
===== CHANNEL f1 =====
 NUC1 1H
 P1 7.50 usec
 PL1 1.60 dB
 SFO1 500.2235015 MHz

F2 - Processing parameters
 SI 32768
 SF 500.2235015 MHz
 WDW EM
 SSB 0
 LB 0.30 Hz
 GB 0
 PC 4.00

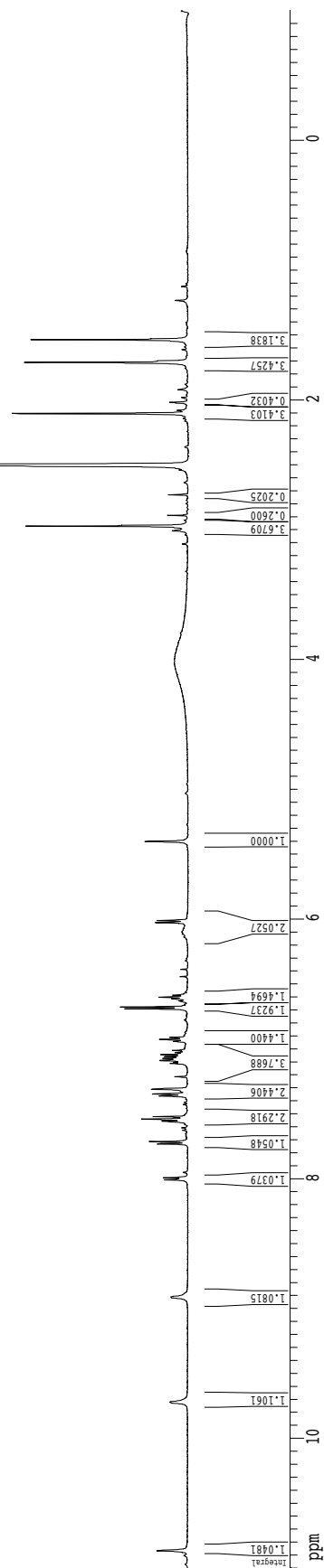
1D NMR plot parameters
 CX 22.80 cm
 CY 30.00 cm
 FIP 11.000 ppm
 FI 5502.42 Hz
 F2 11.000 ppm
 F2 -500.922 ppm
 PPMCM 0.55432 ppm/cm
 HZCM 263.27368 Hz/cm



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

¹H spectrum

Current Data Parameters
 USER sjlabri
 NAME sy7-3-283
 EXPNO 21
 PROCNO 1
 F2 - Acquisition Parameters
 Date_ 20120607
 Time_ 22.22
 INSTRUM cryo500
 PROBED 5 mm CPYC1 1H-
 PULPROG zg30
 TD 81728
 SOLVENT DMSO
 NS 8
 DS 2
 SWH 8012.820 Hz
 FIDRES 0.098043 Hz
 AQ 5.0998774 sec
 RG 327.5
 DE 62.400 usec
 TE 298.0 K
 D1 0.10000000 sec
 MCREST 0.00000000 sec
 MCWRR 0.01500000 sec
 ===== CHANNEL f1 =====
 NUC1 1H
 P1 7.50 usec
 PL1 1.60 dB
 SFO1 500.2235015 MHz
 F2 - Processing parameters
 SI 32768
 SF 500.220139 MHz
 WDW EM
 SSB 0
 LB 0.30 Hz
 GB 0
 PC 2.00
 ID NMR plot parameters
 CX 22.80 cm
 CY 10.00 cm
 FIP 11.000 ppm
 F1 5502.42 Hz
 F2 11.000 ppm
 F3 -500.92 ppm
 PPMCM 0.55632 ppm/cm
 HZCM 263.27368 Hz/cm



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

