Supporting Information

Synthesis of crambescin B carboxylic acid, a potent inhibitor of voltage-gated sodium channels

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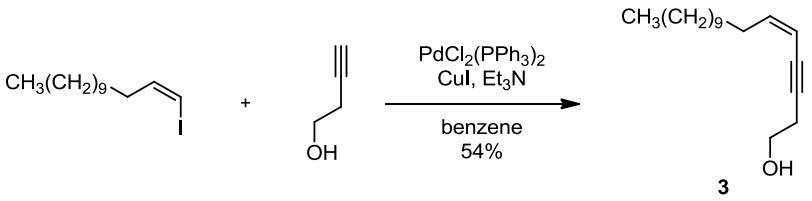
General Experimental

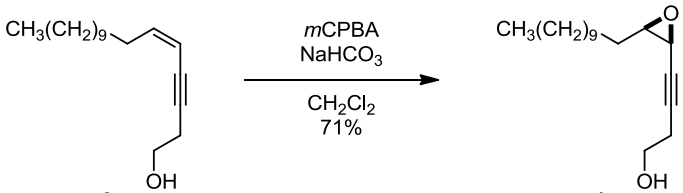
Infrared spectra (IR) were recorded on a JASCO FT/IR-8300 spectrophotometer and are reported in wave number (cm^{-1}). Proton nuclear magnetic resonance (^1H NMR) spectra were recorded on a Bruker ARX-400 (400 MHz) or a Bruker Avance-400 (400 MHz) spectrometer. Chemical shifts of all compounds are reported in ppm relative to the residual undeuterated solvent (chloroform-*d* as $\delta = 7.26$, methanol-d_4 as $\delta = 3.31$). Data were reported as follows: Chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broadened), coupling constant, and assignment. Carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded on a Bruker ARX-400 (100 MHz) or a Bruker Avance-400 (100 MHz) spectrometer. Chemical shifts of all compounds are reported in ppm relative to the solvent (chloroform-*d* as $\delta = 77.0$, methanol-d_4 as $\delta = 49.0$). All NMR were measured at 300 K. High-resolution mass spectra (HRMS) were recorded on an Applied Biosystems Mariner ESI-TOF spectrometer and reported in *m*/z.

Reactions were monitored by thin layer chromatography (TLC) on 0.25 mm silica gel coated glass plates $60F_{254}$ (Merck, #1.05715.0009). Visualization was achieved by using UV light (254 nm) and appropriate reagent (ethanolic phosphomolybdic acid, *p*-anisaldehyde solution in H_2SO_4/AcOH/EtOH, or ninhydrin solution in *n*-BuOH/H_2O/AcOH), followed by heating. Silica gel 60 (particle size 0.063-0.021 mm, Kanto, #37565-84) was used for open-column chromatography. Silica gel 60N (spherical, neutral, particle size 0.04-0.05 mm, Kanto, #37563-79) was used for flash-column chromatography. Preparative TLC separations were carried out on 0.5 mm silica gel plates $60F_{254}$ (Merck, #1.05744.0009). Dehydrated THF, Et_2O and CH_2Cl_2 were purchased from Kanto Chemical Co., Inc. MeCN, benzene, toluene, DMF, DMSO, Et_3N, $BF_3{\cdot}OEt_2$, HMPA were distilled from CaH_2. Celite® (Hyflo Super-Cel Celite®) was purchased from Nacalai tesque Co., Inc. Florisil® was purchased from Kanto Chemical Co., Inc. InI (indium(I) iodide, anhydrous, powder, 99.999%) was purchased from Sigma-Aldrich. All other commercially available reagents were as received.



3

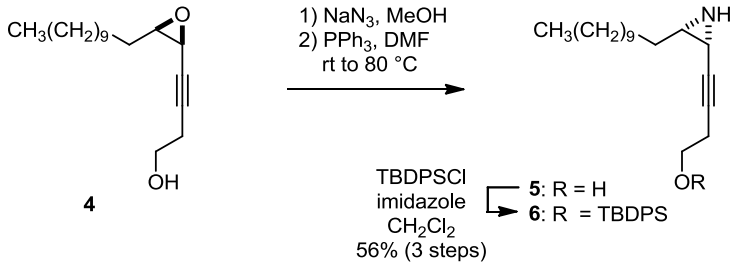
Enyne 3: To a mixture of *cis*-1-iodotridecene (906 mg, 2.94 mmol) prepared according to the literature (D. J. Hart *et al*. *Synlett*, **2004**, 1339), $PdCl_2(PPh_3)_2$ (206 mg, 0.294 mmol) and CuI (112 mg, 0.588 mmol) were added a degassed solution of benzene (33 mL), 3-butyn-1-ol (0.70 mL, 8.8 mmol) and Et_3N (1.60 mL, 11.8 mmol) at 0 °C under the argon atmosphere. After being stirred for 3 h at room temperature, the reaction mixture was diluted with Et_2O. The resulting mixture was washed with sat. NH_4Cl solution (x 2), water (x 2) and brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/Et_2O = 4/1) to afford enyne **3** (396 mg, 54%) as a yellow oil. IR (film): ν_{max} (cm^{-1}) 3338, 2917, 2851, 1468, 1055, 721. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 0.88 (3H, t, J = 6.5 Hz, -CH_2CH_3), 1.20-1.44 (18H, m, -$CH_2(CH_2)_9CH_3$), 1.76 (1H, br, -O*H*), 2.28 (2H, qd, J = 7, 1 Hz, -CH_2CH=CH-), 2.63 (2H, td, J = 6, 2 Hz, -CHC≡CCH_2-), 3.75 (2H, t, J = 6 Hz, -CH_2OH), 5.43 (1H, m, -CH_2CH=C*H*-), 5.87 (1H, dt, J = 10.5, 7.5 Hz, -CH_2C*H*=CH-). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 14.1, 22.7, 23.9, 28.8, 29.2, 29.3, 29.5, 29.57, 29.61, 29.64, 30.1, 31.9, 61.2, 79.3, 90.2, 108.7, 143.7. HRMS (ESI, positive): calcd. For $C_{17}H_{30}ONa$ $[M+Na]^+$, 273.2189 ; found, 273.2176.



3 4

Epoxide 4: To a mixture of enyne **3** (3.95 g, 15.8 mmol) and $NaHCO_3$ (1.3 g, 16 mmol) in CH_2Cl_2 (100 mL) was added *m*CPBA (10.9 g, 63.1 mmol) in 4 portions over 4 h at room temperature. After being stirred for 1 h at room temperature, the reaction was quenched with sat. $Na_2S_2O_3$ solution (100 mL). The resulting mixture was partitioned, and the aqueous layer was extracted with EtOAc (100 mL x 2). The combined organic layer was washed with sat. $NaHCO_3$ solution (300 mL x 2), water (300 mL) and brine (300 mL), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography (hexane/Et_2O

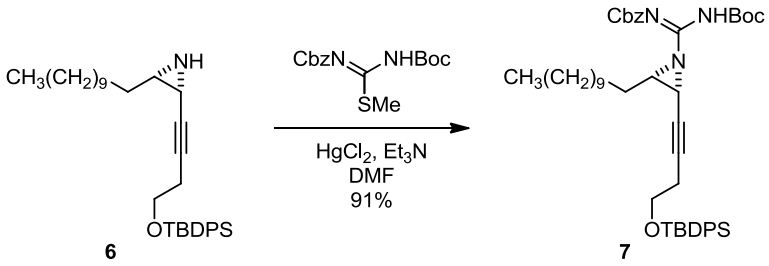
= 3/1 to 2/1) to afford epoxide **4** (2.99 g, 71%) as a colorless oil.
IR (film): ν_{max} (cm^{-1}) 3272, 2919, 2848, 1465, 1046, 879, 855. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 0.88 (3H, t, J = 6.5 Hz, -CH_2CH_3), 1.20-1.42 (16H, m, -$CH_2(CH_2)_8CH_3$), 1.42-1.56 (2H, m, -$CH_2(CH_2)_8CH_3$), 1.59-1.75 (2H, m, -$CH_2(CH_2)_9CH_3$), 1.86 (1H, br, -O*H*), 2.50 (2H, td, J = 6, 1.5 Hz, -CHC≡CCH_2-), 3.00 (1H, td, J = 6, 4 Hz, -C*H*CHC≡C-), 3.42 (1H, dt, J = 4, 1.5 Hz, -CHC*H*C≡C-), 3.73 (2H, t, J = 6 Hz, -CH_2OH). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 14.0, 22.6, 23.1, 25.9, 29.2, 29.3, 29.4, 29.47, 29.48, 29.55, 29.57, 31.8, 45.3, 58.1, 60.8, 76.9, 82.9. HRMS (ESI, positive): calcd. For $C_{17}H_{30}O_2Na$ $[M+Na]^+$, 289.2138; found, 289.2134.



Aziridine 6: To a solution of epoxide **4** (2.99 g, 11.2 mmol) in MeOH (160 mL) was added NaN_3 (2.20 g, 33.7 mmol) at room temperature. After being stirred for 21 h at room temperature, to the reaction mixture was added NaN_3 (729 mg, 11.2 mmol). After being stirred for 5 h at room temperature, to the reaction mixture were added MeOH (40 mL) and NaN_3 (729 mg, 11.2 mmol). After being stirred for 5 h at room temperature, water (200 mL) was added. The resulting mixture was extracted with EtOAc (200 mL x 3). The combined organic layer was washed with brine (600 mL), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure to provide crude aziridine **5**. The residue of **5** was dissolved in DMF (160 mL), and then PPh_3 (4.41 g, 16.8 mmol) was added to the solution. After being stirred for 5 h at room temperature, the reaction mixture was warmed to 80 °C. After being stirred for 12 h at 80 °C, the reaction mixture was concentrated under reduced pressure. The residue was dissolved in CH_2Cl_2 (80 mL), and then imidazole (1.68 g, 24.7 mmol) and TBDPSCl (3.21 mL, 12.3 mmol) were added to the solution at 0 °C. After being stirred for 1 h at room temperature, the reaction mixture was poured into sat. NH_4Cl solution (100 mL). The resulting mixture was partitioned, and the aqueous layer was extracted with EtOAc (100 mL x 2). The combined organic layer was washed with water (300 mL) and brine (300 mL), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography (hexane/EtOAc = 30/1 with 1% *i*-Pr_2NH to 20/1 with 1% *i*-Pr_2NH) to afford aziridine **6** (2.15 g, 56% in 3 steps) as a

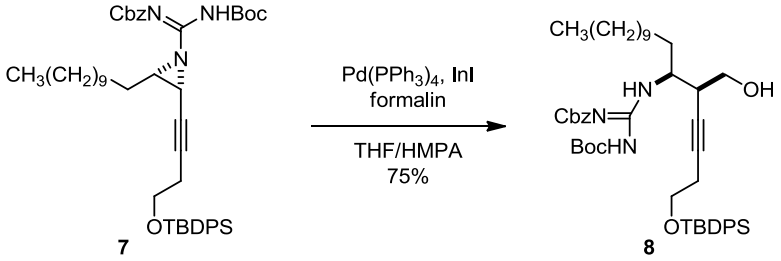
colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 0.88 (3H, t, J = 6.5 Hz, -CH_2CH_3), 1.05 (9H, s, -Si-^{t}Bu), 1.19-1.36 (16H, m, -$CH_2(CH_2)_8CH_3$), 1.39-1.49 (2H, m, -$CH_2(CH_2)_8CH_3$), 1.49-1.57 (2H, m, -$CH_2(CH_2)_9CH_3$), 1.97-2.05 (1H, m, -CHCHC≡C-), 2.40-2.48 (3H, m -CHC≡CCH_2-, -CHCHC≡C-), 3.75 (2H, t, J = 7 Hz, -CH_2OTBDPS), 7.34-7.46 (6H, m, -Si-Ph), 7.63-7.74 (4H, m, -Si-Ph). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 14.1, 19.2, 22.7, 23.0, 24.4, 26.8, 27.4, 29.3, 29.4, 29.57, 29.60, 29.63, 29.7, 30.7, 31.9, 37.0, 62.6, 78.8, 127.7, 129.6, 133.6, 135.5. HRMS (ESI, positive): calcd. For $C_{33}H_{50}NOSi$ $[M+H]^+$, 504.3656; found, 504.3671.



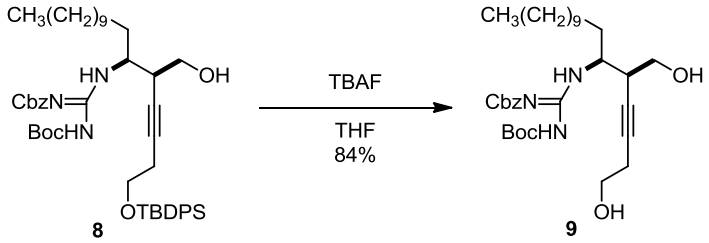
Guanidino-aziridine 7: To a solution of aziridine **6** (511 mg, 1.01 mmol), Boc,Cbz-methylisothiourea (362 mg, 1.12 mmol) and Et_3N (1.5 mL, 10 mmol) in DMF (10 mL) was added $HgCl_2$ (303 mg, 1.12 mmol) at room temperature. After being stirred for 1 h at room temperature, the reaction mixture was diluted with EtOAc (20 mL), and then filtered through a pad of Celite® (eluted with EtOAc). The filtrate was washed with water (30 mL x 3), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash column chromatography (hexane/EtOAc = 20/1 with 1% i-Pr_2NH) to afford guanidino-aziridine **7** (722 mg, 91%) as a colorless oil.

IR (film): ν_{max} (cm^{-1}) 2926, 2855, 1766, 1651, 1596, 1111. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 0.89 (3H, t, J = 6.5 Hz, -CH_2CH_3), 1.06 (9H, s, -Si-^{t}Bu), 1.18-1.64 (19H, m, -$CH_aH_b(CH_2)_9CH_3$), 1.48 (9H, s, -O-^{t}Bu), 2.06-2.17 (1H, m, -$CH_aH_b(CH_2)_9CH_3$), 2.49 (2H, td, J = 7, 1.5 Hz, -CHC≡CCH_2-), 2.70 (1H, ddd, J = 8.5, 6, 4 Hz, -CHCHC≡CCH_2-), 3.24 (1H, dt, J = 6, 1.5 Hz, -CHC≡CCH_2-), 3.78 (2H, t, J = 7 Hz, -CH_2OTBDPS), 5.16 (2H, s, -CH_2Ph), 7.28-7.45 (11H, m, -Si-Ph, -CH_2Ph), 7.64-7.70 (4H, m, -Si-Ph), 10.94 (1H, br, -NHBoc). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 14.1, 19.2, 22.7, 23.0, 26.1, 26.8, 28.0, 28.7, 29.31, 29.34, 29.50, 29.53, 29.63, 29.64, 31.9, 34.7, 46.8, 62.5, 67.7, 75.6, 81.4, 82.4, 127.7, 128.2, 128.5, 129.6, 133.6, 135.5, 148.5, 163.6. HRMS (ESI, positive): calcd. For $C_{47}H_{66}N_3O_5Si$ $[M+H]^+$, 780.4766; found, 780.4750.



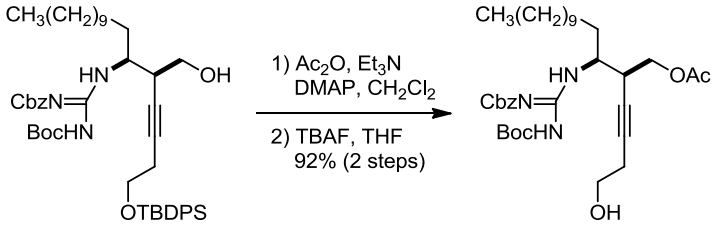
Alcohol 8: To a mixture of guanidino-aziridine **7** (781 mg, 1.00 mmol), $Pd(PPh_3)_4$ (57.9 mg, 0.0501 mmol) and InI (363 mg, 1.50 mmol) was added a degassed solution of THF/HMPA (10 mL, 4/1) and formalin (165 μL, 1.80 mmol, 30% solution) at room temperature under the argon atmosphere. After being stirred for 30 min at room temperature, the solution was passed through a short pad of flash silica gel (eluted with EtOAc with 1% *i*-Pr_2NH), and the resulting solvent was washed with water (50 mL x 3) and brine (50 mL), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash column chromatography (hexane/EtOAc = 10/1 with 1% *i*-Pr_2NH) to afford alcohol **8** (610 mg, 75%, dr = >95 : <5 determined by ^{1}H NMR analysis of diol **11**) as a colorless oil.

IR (film): ν_{max} (cm^{-1}) 3319, 2927, 2855, 1723, 1646, 1618, 1132, 1057. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 0.88 (3H, t, J = 6.5 Hz, -CH_2CH_3), 1.05 (9H, s, -Si-^{t}Bu), 1.19-1.33 (19H, m, $CH_aH_b(CH_2)_9CH_3$), 1.49 (9H, s, -O-^{t}Bu), 2.02 (1H, m, -$CH_aCH_b(CH_2)_9CH_3$), 2.36 (1H, m, -$CHCH_2OH$), 2.48 (2H, td, J = 7, 2.5 Hz, -CH_2CH_2OTBDPS), 3.55-3.66 (2H, m, -CH_2OH), 3.76 (2H, t, J = 6.5 Hz, -CH_2OTBDPS), 4.11 (1H, qd, J = 9, 2.5 Hz, -NHC*H*-), 5.07 (1H, d, J = 12 Hz, -CH_aH_bPh), 5.12 (1H, d, J = 12 Hz, -CH_aH_bPh), 7.27-7.43 (11H, m, -Si-Ph, -CH_2Ph), 7.65-7.69 (4H, m, -Si-Ph), 8.31 (1H, d, J = 9 Hz, -N*H*(=NCbz)NHBoc), 11.33 (1H, br s, -N*H*Boc). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 14.1, 19.2, 22.7, 23.0, 25.7, 26.8, 28.0, 28.1, 29.2, 29.3, 29.4, 29.4, 29.5, 29.6, 29.6, 31.9, 33.0, 33.1, 41.0, 51.2, 61.8, 62.7, 67.0, 79.7, 80.8, 83.6, 127.8, 128.4, 128.6, 128.7, 128.8, 129.6, 133.6, 135.5, 135.5, 136.5, 153.0, 157.3, 163.1. HRMS (ESI, positive): calcd. For $C_{48}H_{70}N_3O_6Si$ $[M+H]^+$, 812.5028; found, 812.5064.



8 9

Diol 9: To a solution of alcohol **8** (610 mg, 0.752 mmol) in THF (7.5 mL) was added TBAF (1.1 mL, 1.1 mmol, 1.0 M solution in THF) at room temperature. After being stirred for 1 h at room temperature, the reaction was quenched with brine (10 mL). The resulting mixture was extracted with EtOAc (10 mL x 3). The combined organic layer was dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash column chromatography (hexane/EtOAc = 3/1 with 1% *i*-Pr_2NH to 1/1 with 1% *i*-Pr_2NH) to afford diol **9** (361 mg, 84%) as a colorless oil. IR (film): ν_{max} (cm^{-1}) 3319, 2925, 2854, 1724, 1647, 1617, 1132, 1057. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 0.88 (3H, t, J = 6.5 Hz, -CH_2CH_3), 1.19-1.59 (19H, m, -$CH_aH_b(CH_2)_9CH_3$), 1.45 (1H, s, -O*H*), 1.50 (9H, s, -O-^{t}Bu), 1.94-2.05 (1H, m, -$CH_aCH_b(CH_2)_9CH_3$), 2.38-2.45 (1H, m, -C*H*CH_2OH), 2.46 (2H, td, J = 6, 2.5 Hz, -CH_2CH_2OTBDPS), 3.62 (1H, dd, J = 12.5, 2.5 Hz,-CH_aH_bOH), 3.67 (1H, dd, J = 12.5, 3 Hz,-CH_aH_bOH), 3.70 (2H, t, J = 6 Hz,-CH_2OH), 4.15 (1H, qd, J =9, 2.5 Hz,-NHC*H*-), 4.74 (1H, br, -O*H*), 5.08 (1H, d, J = 12 Hz,-CH_aH_bPh), 5.13 (1H, d, J = 12 Hz,-CH_aH_bPh), 7.26-7.40 (5H m, Ph), 8.37 (1H, d, J = 8.5 Hz, -N*H*(=NCbz)NHBoc), 11.35 (1H, br s, -N*H*Boc). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 14.1, 22.7, 23.3, 25.7, 28.0, 28.1, 29.3, 29.3, 29.4, 29.5, 29.6, 31.9, 32.8, 40.9, 51.2, 61.1, 61.9, 67.0, 80.8, 81.0, 84.0, 127.7, 127.9, 128.4, 128.6, 128.7, 128.9, 136.5, 153.0, 157.2, 163.0. HRMS (ESI, positive): calcd. For $C_{32}H_{52}N_3O_6$ $[M+H]^+$, 574.3851; found, 574.3871.

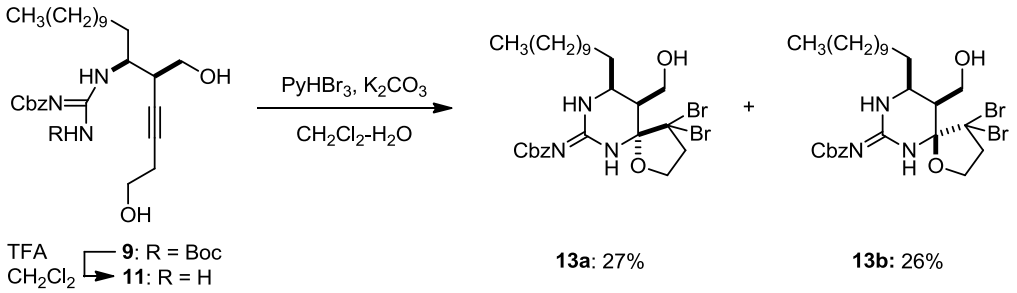


8 10

Alcohol 10: To a solution of alcohol **8** (322 mg, 0.398 mmol) in CH_2Cl_2 (30 mL) were added Et_3N (1 mL), Ac_2O (1 mL) and DMAP (4.9 mg, 0.040 mmol) at room temperature. After being stirred for 1 h at room temperature, the reaction mixture was concentrated under reduced pressure with toluene/MeOH (2/1) to provide crude acetate.

The residue of the acetate was dissolved in THF (30 mL), and then TBAF (600 μL, 0.600 mmol, 1.0 M solution in THF) was added at room temperature. After being stirred for 1 h at room temperature, the reaction was quenched with brine (30 mL). The resulting mixture was extracted with EtOAc (30 mL x 3). The combined organic layer was dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash column chromatography (hexane/EtOAc = 3/1 with 1% *i*-Pr_2NH) to afford alcohol **10** (226 mg, 92% in 2 steps) as a colorless oil.

IR (film): ν_{max} (cm^{-1}) 3319, 2925, 2854, 1724, 1640, 1619, 1250, 1056. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 0.87 (3H, t, J = 6.5 Hz, -CH_2CH_3), 1.17-1.40 (18H, m, -$CH_2(CH_2)_9CH_3$), 1.49 (9H, s, -O-^{t}Bu), 1.53-1.62 (2H, m, -$CH_2(CH_2)_9CH_3$), 2.05 (3H, s, -CO-CH_3), 2.43 (2H, td, J = 5.5, 2.5 Hz, -CH_2CH_2OH), 3.03 (1H, m, -$CHCH_2OAc$), 3.68 (2H, m, -CH_2OH), 4.03 (1H, dd, J = 11, 6.5 Hz, -CH_aH_bOAc), 4.22 (1H, dd, J = 11, 6.5 Hz, -CH_aH_bOAc), 4.40 (1H, ddd, J = 14, 9, 5 Hz, -NHC*H*-), 5.10 (1H, d, J = 12 Hz, -CH_aH_bPh), 5.14 (1H, d, J = 12 Hz, -CH_aH_bPh), 7.27-7.40 (5H, m, Ph), 8.56 (1H, d, J = 9.5 Hz, -N*H*(=NCbz)NHBoc), 11.45 (1H, br s, -N*H*Boc). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 14.1, 20.8, 20.9, 22.6, 23.3, 25.5, 28.0, 28.2, 29.3, 29.5, 29.5, 29.5, 29.6, 30.5, 31.9, 36.5, 36.5, 50.2, 61.1, 63.8, 67.0, 78.0, 79.4, 82.0, 83.7, 127.8, 127.9, 128.4, 128.6, 128.6, 128.8, 136.9, 153.2, 156.2, 163.7, 170.9. HRMS (ESI, positive): calcd. For $C_{34}H_{54}N_3O_7$ $[M+H]^+$, 616.3956; found, 616.3981.

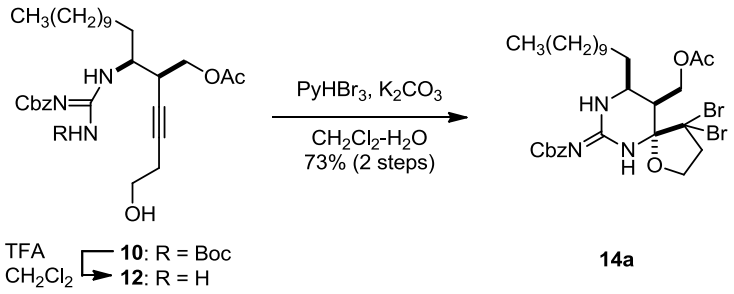


***spiro*-Hemiaminals 13a and 13b:** A solution of guanidino-alcohol **9** (818 mg, 1.43 mmol) in CH_2Cl_2 (5 mL) and TFA (0.5 mL) was stirred for 2 h at room temperature and then the reaction mixture was concentrated under reduced pressure with toluene/MeOH (2/1). The residue was dissolved in MeOH (10 mL), and then ion exchange resin (Amberlite® IRA-410, 800 mg) was added to the solution. After being stirred for 12 h at room temperature, the reaction mixture was filtered through a pad of Celite® (eluted with MeOH) to remove the resin, and concentrated under reduced pressure to afford crude **11**. The residue of **11** was dissolved in CH_2Cl_2/H_2O (28 mL, 1/1), then K_2CO_3 (3.55 g, 8.55 mmol) was added. To a vigorously stirred mixture was added $PyHBr_3$

(1.37 g, 4.28 mmol). After being stirred for 30 min at room temperature, the reaction was quenched with sat. Na_2SO_3 solution (30 mL). The resulting mixture was partitioned, and the aqueous layer was extracted with EtOAc (30 mL x 2). The combined organic layer was washed with water (100 mL) and brine (100 mL), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash column chromatography (hexane/EtOAc = 3/1 with 1% *i*-Pr_2NH) to afford *spiro*-hemiaminal **13a** (247 mg, 27%, dr = >95 : <5 determined by ^{1}H NMR analysis) as a white amorphous solid and epimer **13b** (235 mg, 26%, dr = >95 : <5 determined by ^{1}H NMR analysis) as a white amorphous solid. Relative stereochemistry of **13a** and **13b** was determined by NOESY correlations of the corresponding debromo analogues **16a** and **16b**, respectively.

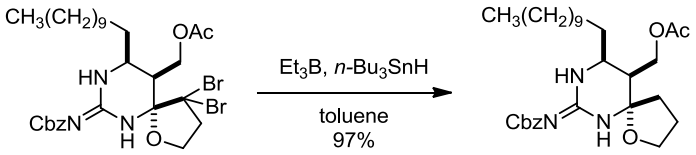
***spiro*-Hemiaminal 13a:** IR (film): ν_{max} (cm^{-1}) 3264, 2925, 2853, 1623, 1263, 1101, 1028. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 0.91 (3H, t, J = 7 Hz, -CH_2CH_3), 1.20-1.50 (18H, m, -$CH_2(CH_2)_9CH_3$), 1.69-1.86 (2H, m, -$CH_2(CH_2)_9CH_3$), 2.47 (1H, m, -$CHCH_2OH$), 3.19 (1H, ddd, J = 14.5, 7, 2 Hz, -$CH_aH_bCBr_2$-), 3.32 (1H, dt, J = 14.5, 9 Hz, -$CH_aH_bCBr_2$-), 3.91-4.10 (4H, m, -CH_aH_bOH, -OCH_2CH_2-, -NHC*H*-), 4.19 (1H, dd, J = 12.5, 2.5 Hz, -CH_aH_bOH), 5.11 (2H, s, -CH_2Ph), 7.27-7.42 (5H, m, Ph). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 14.1, 22.7, 26.1, 29.3, 29.4, 29.4, 29.5, 29.6, 31.4, 31.9, 44.4, 48.8, 50.9, 56.9, 63.0, 63.3, 66.6,, 93.3, 127.8, 127.9, 128.0, 128.3, 128.4, 136.7, 157.0, 162.8. HRMS (ESI, positive): calcd. For $C_{27}H_{42}N_3O_4Br_2$ $[M+H]^+$, 630.1537; found, 630.1521.

***spiro*-Hemiaminal 13b:** IR (film): ν_{max} (cm^{-1}) 3258, 2925, 2853, 1631, 1225, 1090, 1052. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 0.88 (3H, t, J = 6.5 Hz, -CH_2CH_3), 1.20-1.49 (18H, m, -$CH_2(CH_2)_9CH_3$), 1.58-1.75 (2H, m, -$CH_2(CH_2)_9CH_3$), 2.94 (1H, m, -$CHCH_2OH$), 3.17 (1H, ddd, J = 14, 5.5, 2.5 Hz, -$CH_aH_bCBr_2$-), 3.22 (1H, dt, J = 14, 9.5 Hz, -$CH_aH_bCBr_2$-), 3.78 (1H, t, J = 11.5 Hz, -CH_aH_bOH), 3.75 (1H, dd, J = 12.5, 11.5 Hz, -CH_aH_bOH), 4.03-4.12 (3H, m, -OCH_2CH_2-, -NHC*H*-), 5.07 (1H, d, J = 12 Hz, -CH_aH_bPh), 5.12 (1H, d, J = 12 Hz, -CH_aH_bPh), 7.27-7.39 (5H, m, Ph). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 14.1, 22.7, 25.5, 29.3, 29.3, 29.4, 29.5, 29.6, 31.2, 31.9, 42.1, 46.9, 49.3, 59.3, 65.5, 66.8, 70.2, 96.6, 128.0, 128.1, 128.4, 136.3, 155.4, 161.4. HRMS (ESI, positive): calcd. For $C_{27}H_{42}N_3O_4Br_2$ $[M+H]^+$, 630.1537; found, 630.1518.



***spiro*-Hemiaminal 14a:** A solution of guanidino-alcohol **10** (221 mg, 0.359 mmol) in CH_2Cl_2 (10 mL) and TFA (1 mL) was stirred for 2 h at room temperature and then the reaction mixture was concentrated under reduced pressure with toluene/MeOH (2/1) to afford crude **12**. The residue of **12** was dissolved in CH_2Cl_2/H_2O (40 mL, 1/1), then K_2CO_3 (298 mg, 2.15 mmol) was added. To a vigorously stirred mixture was added $PyHBr_3$ (344 mg, 1.08 mmol). After being stirred for 30 min at room temperature, the reaction was quenched with sat. Na_2SO_3 solution (40 mL). The resulting mixture was partitioned, and the aqueous layer was extracted with EtOAc (40 mL x 2). The combined organic layer was washed with water (100 mL) and brine (100 mL), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash column chromatography (hexane/EtOAc = 5/1 with 1% *i*-Pr_2NH) to afford *spiro*-hemiaminal **14a** (176 mg, 73%, dr = >95 : <5 determined by ^1H NMR analysis) as a colorless oil.

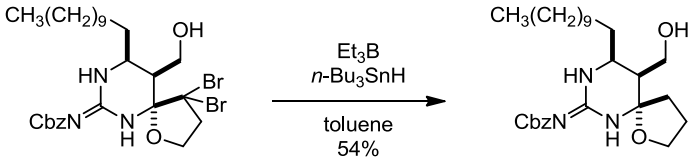
IR (film): ν_{max} (cm^{-1}) 2925, 2853, 1744, 1635, 1241, 1030. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 0.88 (3H, t, J = 6.5 Hz, -CH_2CH_3), 1.18-1.46 (18H, m, -$CH_2(CH_2)_9CH_3$), 1.53-1.72 (2H, m, -$CH_2(CH_2)_9CH_3$), 2.02 (3H, s, -CO-CH_3), 2.67 (1H, dt, J = 5.5, 3.5 Hz, -$CH$$CH_2$OAc), 3.17 (1H, ddd, J = 14.5, 7, 2 Hz, -$CH_aH_bCBr_2$-), 3.27 (1H, dt, J = 14.5, 9 Hz, -$CH_aH_bCBr_2$-), 3.92-4.00 (2H, m, -$OCH_aH_bCH_2$-, -NHCH-), 4.05 (1H, q, J = 8 Hz, -$OCH_aH_bCH_2$-), 4.32 (1H, dd, J = 12.5, 5.5 Hz, -CH_aH_bOAc), 4.54 (1H, dd, J = 12.5, 3.5 Hz, -CH_aH_bOAc), 5.10 (2H, s, -CH_2Ph), 7.25-7.39 (5H, m, Ph). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 14.1, 20.8, 22.6, 25.8, 29.3, 29.4, 29.5, 29.5, 31.3, 31.9, 41.2, 48.9, 50.5, 58.5, 62.2, 63.3, 66.4, 93.1, 127.7, 127.8, 128.3, 136.7, 157.2, 163.1, 170.4. HRMS (ESI, positive): calcd. For $C_{29}H_{44}N_3O_5Br_2$ $[M+H]^+$, 672.1642; found, 672.1633.



14a **15**

***spiro*-Hemiaminal 15:** To a solution of *spiro*-hemiaminal **14a** (147 mg, 0.218 mmol) and *n*-Bu_3SnH (293 μL, 1.09 mmol) in toluene (2.2 mL) were added Et_3B (109 μL, 0.109 mmol, 1.0 M solution in hexane) and air at room temperature. After being stirred for 4.5 h at room temperature, the solution was passed through a short pad of flash silica gel (eluted with hexane/EtOAc = 1/1 with 1% *i*-Pr_2NH) and then concentrated. The residue was purified by flash column chromatography (hexane/EtOAc = 5/1 with 1% *i*-Pr_2NH to 1/1 with 1% *i*-Pr_2NH) to afford *spiro*-hemiaminal **15** (109 mg, 97%) as a colorless oil.

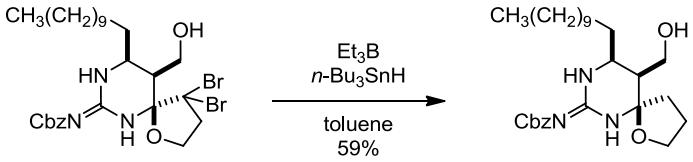
IR (film): ν_{max} (cm^{-1}) 2925, 2854, 1744, 1628, 1228. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 0.87 (3H, t, J = 6.5 Hz, -CH_2CH_3), 1.20-1.37 (18H, m, -$CH_2(CH_2)_9CH_3$), 1.54-1.62 (2H, m, -$CH_2(CH_2)_9CH_3$), 1.91-2.13 (5H, m, -$OCH_2CH_2CH_2$-, -$CHCH_2OAc$), 2.00 (3H, s, -CO-CH_3), 3.80 (1H, m, -$OCH_aH_bCH_2$-), 3.87-3.94 (2H, m, -$OCH_aH_bCH_2$-, -NHC*H*-), 3.99 (1H, dd, J = 12, 4.5 Hz, -CH_aH_bOAc), 4.08 (1H, dd, J = 12, 5.5 Hz, -CH_aH_bOAc), 5.02 (1H, d, J = 12.5 Hz, -CH_aH_bPh), 5.06 (1H, d, J = 12.5 Hz, -CH_aH_bPh), 7.21-7.37 (5H, m, Ph). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 14.0, 20.8, 22.6, 24.6, 25.7, 29.2, 29.4, 29.4, 29.5, 31.4, 31.8, 34.8, 41.8, 49.7, 60.6, 66.1, 66.4, 90.2, 127.5, 127.7, 128.0, 128.2, 137.1, 158.0, 163.7, 170.5. HRMS (ESI, positive): calcd. For $C_{29}H_{46}N_3O_5$ $[M+H]^+$, 516.3432; found, 516.3414.



13a **16a**

Alcohol 16a: To a solution of *spiro*-hemiaminal **13a** (4.7 mg, 7.4 μmol) and *n*-Bu_3SnH (10 μL, 37 μmol) in toluene (0.5 mL) were added Et_3B (4 μL, 4 μmol, 1.0 M solution in hexane) and air at room temperature. After being stirred for 4.5 h at room temperature, the reaction mixture was concentrated under reduced pressure. The residue was purified by preparative TLC (EtOAc) to afford alcohol **16a** (1.9 mg, 54%, dr = >95 : <5 determined by ^1H NMR analysis) as a colorless oil. Relative stereochemistry of **16a** was determined by NOESY correlations.

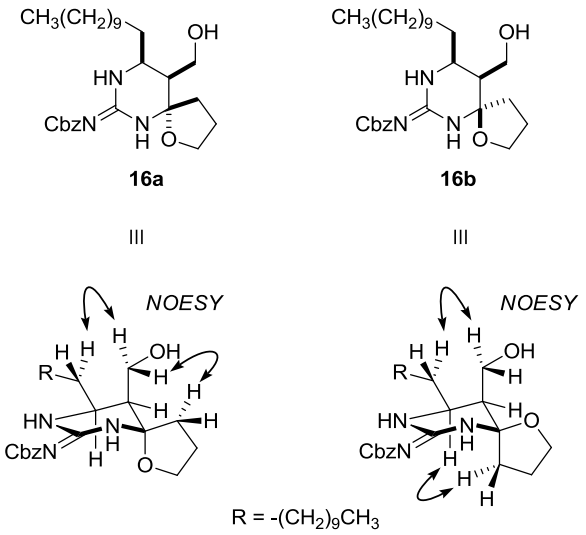
IR (film): ν_{max} (cm^{-1}) 3263, 2925, 2853, 1618, 1241, 1101, 1049. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 0.88 (3H, t, J = 6.5 Hz, -CH_2CH_3), 1.16-1.48 (18H, m, -$CH_2(CH_2)_9CH_3$), 1.53-1.70 (2H, m, -$CH_2(CH_2)_9CH_3$), 1.91 (1H, td, J = 5, 4.5 Hz, -$CHCH_2OH$), 1.96-2.20 (4H, m, -$OCH_2CH_2CH_2$-), 3.55 (1H, dd, J = 11.5, 5 Hz, -CH_aH_bOH), 3.73 (1H, dd, J = 11.5, 4.5 Hz, -CH_aH_bOH), 3.83 (1H, m, -$OCH_aH_bCH_2$-), 3.87-3.98 (2H, m, -$OCH_aH_bCH_2$-, -NHC*H*-), 5.05 (1H, d, J = 12 Hz, -CH_aH_bPh), 5.09 (1H, d, J = 12 Hz, -CH_aH_bPh), 7.24-7.36 (5H, m, Ph). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 14.1, 22.7, 24.7, 26.0, 29.3, 29.4, 29.4, 29.5, 29.6, 31.5, 31.9, 35.1, 44.8, 50.0, 58.9, 66.4, 66.4, 90.7, 127.7, 127.9, 128.3, 136.9, 157.3, 162.7. HRMS (ESI, positive): calcd. For $C_{27}H_{44}N_3O_4$ $[M+H]^+$, 474.3326; found, 474.3328.



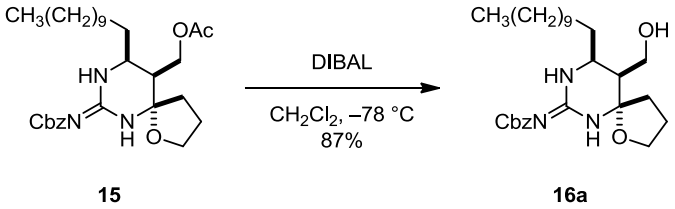
13b **16b**

Alcohol 16b: To a solution of *spiro*-hemiaminal **13b** (16.5 mg, 0.0261 mmol) and *n*-Bu_3SnH (35 μL, 0.13 mmol) in toluene (1 mL) were added Et_3B (13 μL, 0.013 mmol, 1.0 M solution in hexane) and air at room temperature. After being stirred for 4.5 h at room temperature, the reaction mixture was concentrated under reduced pressure. The residue was purified by preparative TLC (EtOAc) to afford alcohol **16b** (7.3 mg, 59%, dr = >95 : <5 determined by ^{1}H NMR analysis) as a colorless oil. Relative stereochemistry of **16b** was determined by NOESY correlations.

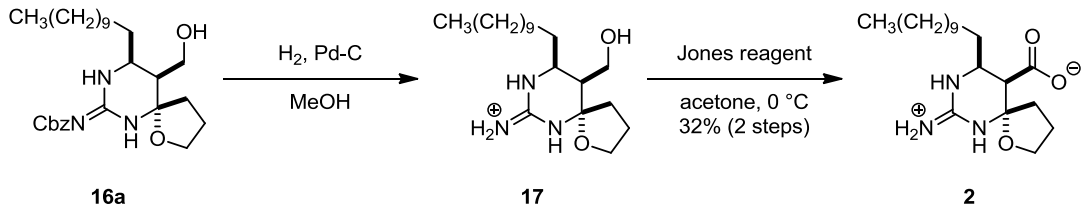
IR (film): ν_{max} (cm^{-1}) 3265, 2925, 2854, 1637, 1247, 1041, 1028. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 0.88 (3H, t, J = 6.5 Hz, -CH_2CH_3), 1.17-1.47 (18H, m, -$CH_2(CH_2)_9CH_3$), 1.53-1.69 (2H, m, -$CH_2(CH_2)_9CH_3$), 1.92-2.24 (5H, m, -$OCH_2CH_2CH_2$-, -$CHCH_2OH$), 3.53 (1H, ddd, J = 8, 6, 4 Hz, -NHC*H*-), 3.69 (1H, dd, J = 12, 4 Hz, -CH_aH_bOH), 3.87 (1H, dd, J = 12, 8 Hz, -CH_aH_bOH), 3.91 (1H, dd, J = 8, 6 Hz, -$OCH_aH_bCH_2$-), 4.10 (1H, ddd, J = 8, 7, 4 Hz, -$OCH_aH_bCH_2$-), 5.06 (1H, d, J = 12 Hz, -CH_aH_bPh), 5.10 (1H, d, J = 12 Hz, -CH_aH_bPh), 7.24-7.41 (5H, m, Ph). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 14.1, 22.7, 24.0, 26.1, 29.3, 29.4, 29.5, 29.6, 31.3, 31.9, 40.5, 44.8, 51.0, 58.8, 66.4, 68.8, 93.6, 127.7, 127.8, 128.3, 137.1, 156.7, 163.4. HRMS (ESI, positive): calcd. For $C_{27}H_{44}N_3O_4$ $[M+H]^+$, 474.3326; found, 474.3315.



NOESY correlations of **16a** and **16b**



Alcohol 16a: To a solution of acetate **15** (15.5 mg, 0.0301 mmol) in CH_2Cl_2 (1 mL) was added dropwise DIBAL (120 μL, 0.120 mmol, 1.0 M in toluene) at −78 ºC under the nitrogen atmosphere. After stirring for 30 min, the reaction mixture was quenched with acetone. The reaction mixture was allowed to warm to room temperature, and sat. potassium sodium tartrate solution (3 mL) was added to the reaction mixture. After vigorously stirring at room temperature for 1 h, the resulting mixture was extracted with EtOAc (5 mL x 3). The combined organic layer was washed with water (20 mL) and brine (20 mL), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash column chromatography (CH_2Cl_2/MeOH = 20/1 with 1% *i*-Pr_2NH) to afford alcohol **16a** (12.5 mg, 87%) as a colorless oil.



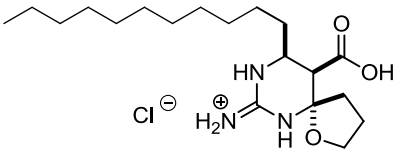
16a **17** **2**

Carboxylic acid 2: Alcohol **16a** (6.3 mg, 0.013 mmol), 10% Pd-C (6.0 mg) and MeOH (1 mL) were placed in a recovered frask (10 mL) connected to an inlet adaptor. The atmosphere of the reaction vessel was replaced by nitrogen, and then filled with hydrogen (1.0 atm). After being stirred for 5 h at room temperature, the catalyst was filtered off through a pad of Celite® (eluted with MeOH), and then the filtrate was concentrated under reduced pressure to afford guanidine **17**, which was used in the next reaction without further purification. To a solution of Jones reagent (32 μL, 0.085 mmol) in acetone (0.3 mL) was added a solution of the crude guanidine **17** (2.9 mg) in acetone (0.5 mL) at 0 ºC. After being stirred for 1 h at 0 ºC, the reaction was quenched with *i*-PrOH (2 mL). The resulting mixture was extracted with EtOAc (10 mL x 3). The combined organic layer was dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by a reverse phase preparative TLC (MeOH) to afford carboxylic acid **2** (1.5 mg, 32%).

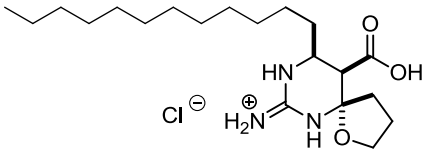
IR (film): ν_{max} (cm^{-1}) 3247, 2924, 2853, 1683, 1616, 1568, 1403, 1040. ^{1}H NMR (400 MHz, CD_3OD): δ (ppm) 0.90 (3H, t, J = 7.0 Hz, -CH_2CH_3), 1.22-1.40 (18H, m, -$CH_2(CH_2)_9CH_3$), 1.60 (1H, m, -$CH_aH_b(CH_2)_9CH_3$), 1.72 (1H, m, -$CH_aH_b(CH_2)_9CH_3$), 1.97-2.30 (4H, m, -$OCH_2CH_2CH_2$-), 2.61 (1H, d, J = 4.5 Hz, -$CHCO_2H$), 3.67 (1H, td, J = 7.0, 4.5 Hz, -NHC*H*-), 3.89 (1H, dt, J = 8.0, 6.5 Hz, -$OCH_aH_bCH_2$-), 3.97 (1H, dt, J = 8.0, 7.0 Hz, -$OCH_aH_bCH_2$-). ^{13}C NMR (100 MHz, CD_3OD): δ (ppm) 14.4, 23.7, 25.7, 26.9, 30.5, 30.6, 30.7, 30.7, 30.8, 33.1, 33.2, 36.2, 50.6, 52.8, 68.4, 90.9, 155.3, 175.3. HRMS (ESI, positive): calcd. For $C_{19}H_{36}N_3O_3$ $[M+H]^+$, 354.2751; found, 354.2741.

HCl salt of 2: IR (film): ν_{max} (cm^{-1}) 3367, 2944, 2834, 1674, 1617, 1450, 1417, 1218. ^{1}H NMR (400 MHz, CD_3OD): δ (ppm) 0.90 (3H, t, J = 7.0 Hz), 1.24-1.42 (16H, m, -$CH_2(CH_2)_8CH_3$), 1.43-1.52 (2H, m, -$CH_2(CH_2)_8CH_3$), 1.62-1.67 (2H, m, -$CH_2(CH_2)_9CH_3$), 2.04-2.21 (4H, m, -$OCH_2CH_2CH_2$-), 2.91 (1H, d, J = 4.0 Hz, -$CHCO_2H$), 3.84 (1H, td, J = 7.0, 4.5 Hz, -NHC*H*-), 3.88-3.97 (1H, m, -$OCH_aH_bCH_2$-), 3.98-4.05 (1H, m, -$OCH_aH_bCH_2$-). ^{13}C NMR (100 MHz, CD_3OD): δ (ppm) 14.4, 23.7, 25.7, 26.5, 30.4, 30.5, 30.6, 30.7, 32.8, 33.1, 36.2, 49.8, 49.9, 68.8, 90.0, 155.2, 171.4. HRMS (ESI, positive): calcd. For $C_{19}H_{36}N_3O_3$ $[M+H]^+$, 354.2751; found, 354.2767.

Comparison of ^{1}H NMR data of carboxylic acid **2** and the related carboxylic acid reported by Snider *et al.*[*]



2



this report[a]		Snider *et al.*[b]	
δ	integration, multiplicity, *J* in Hz	δ	integration, multiplicity, *J* in Hz
3.98-4.05	1H, m	4.01	1H, m
3.88-3.97	1H, m	3.91	1H, m
3.84	1H, dt, 4.5, 7.0	3.83	1H, dt, 4.3, 7.1
2.91	1H, d, 4.0	2.88	1H, d, 3.9
2.04-2.21	4H, m	2.00-2.22	4H, m
1.62-1.67	2H, m	1.63	2H, m
1.43-1.52	2H, m	1.48	2H, m
1.24-1.42	16H, m	1.20-1.42	18H, m
0.90	3H, t, 7.0	0.90	3H, t, 6.7

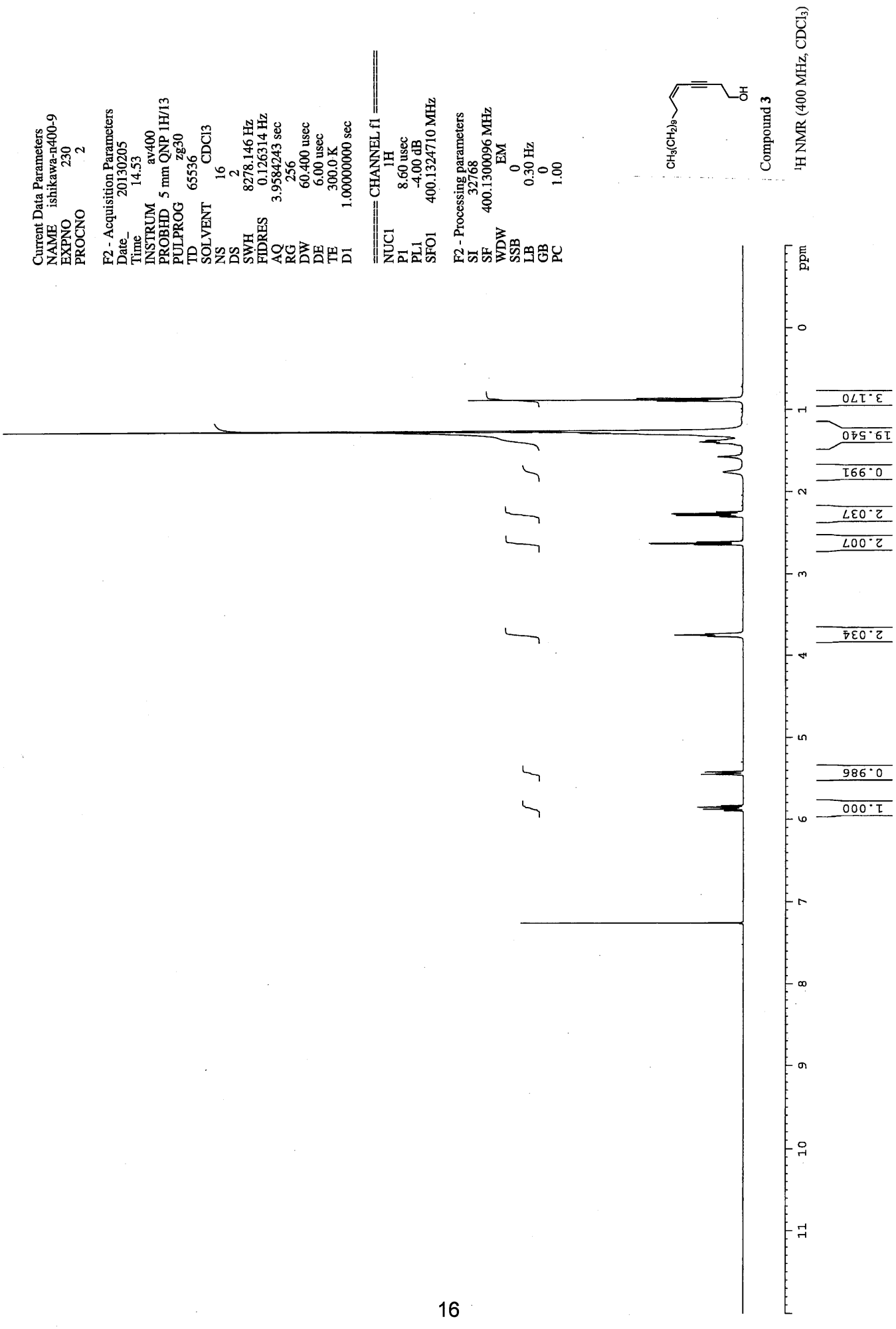
[a] 400 MHz in CD_3OD. [b] 300 MHz in CD_3OD.

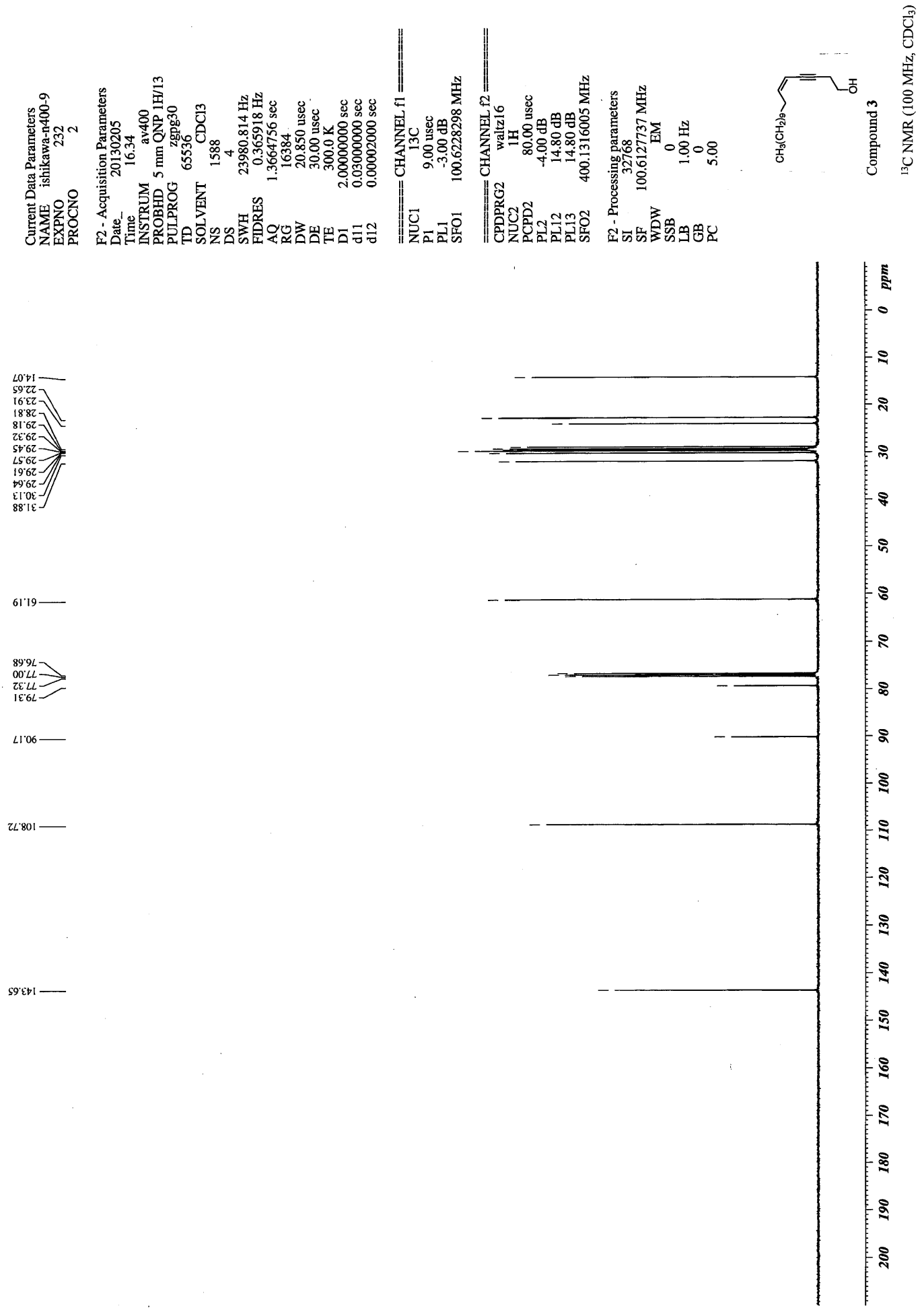
Comparison of ^{13}C NMR data of carboxylic acid **2** and the related carboxylic acid reported by Snider *et al.*[*]

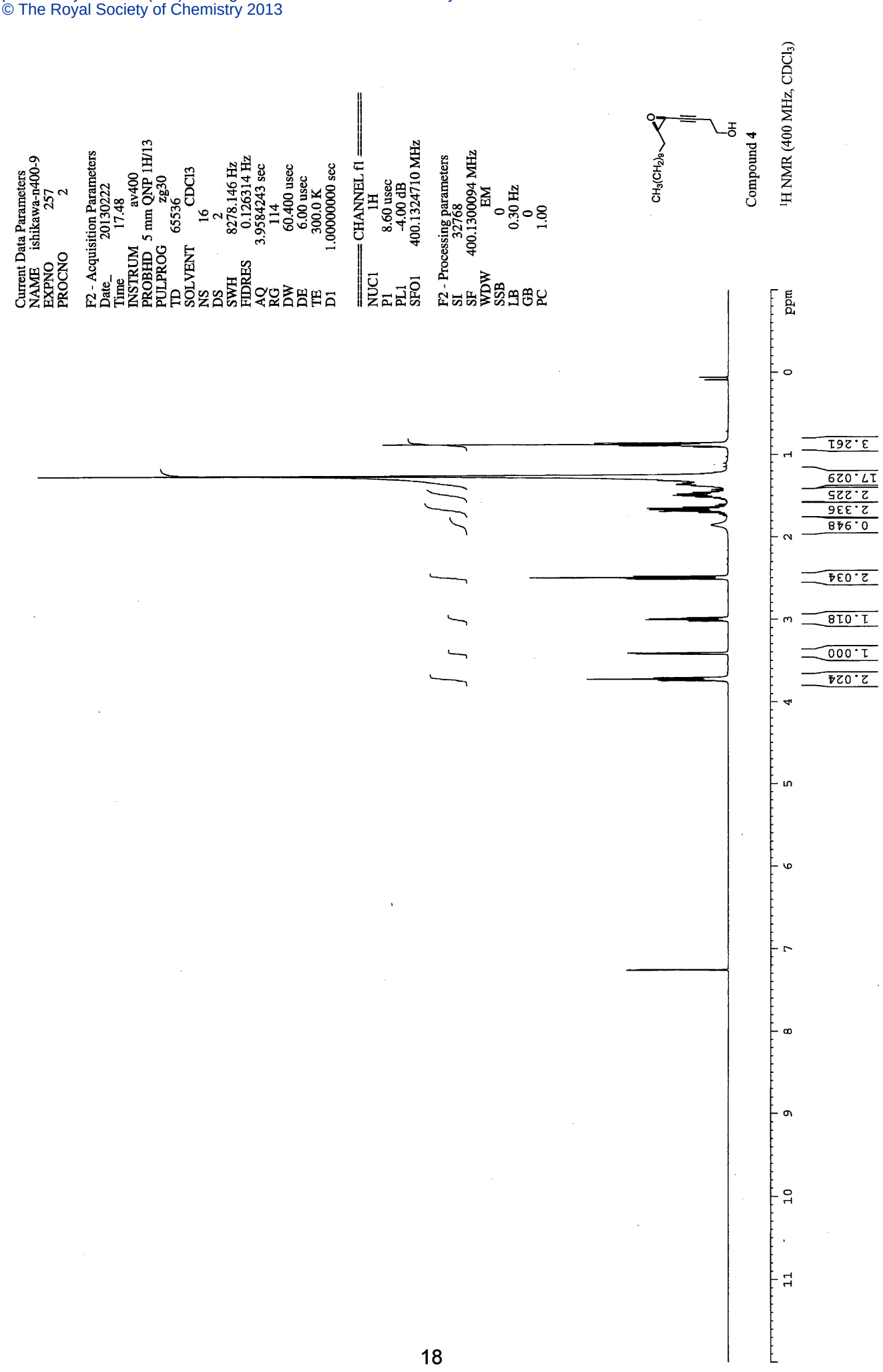
this report[a]	Snider *et al.*[b]
δ	δ
171.4	171.7
155.2	155.4
90.0	90.2
68.8	69.1
49.9	50.1
49.8	49.9
36.2	36.4
33.1	33.4
32.8	33.1
30.7	31.05
30.6	30.9
30.5	30.8
30.4	30.7
26.5	26.8
25.7	26.0
23.7	24.0
14.4	14.7

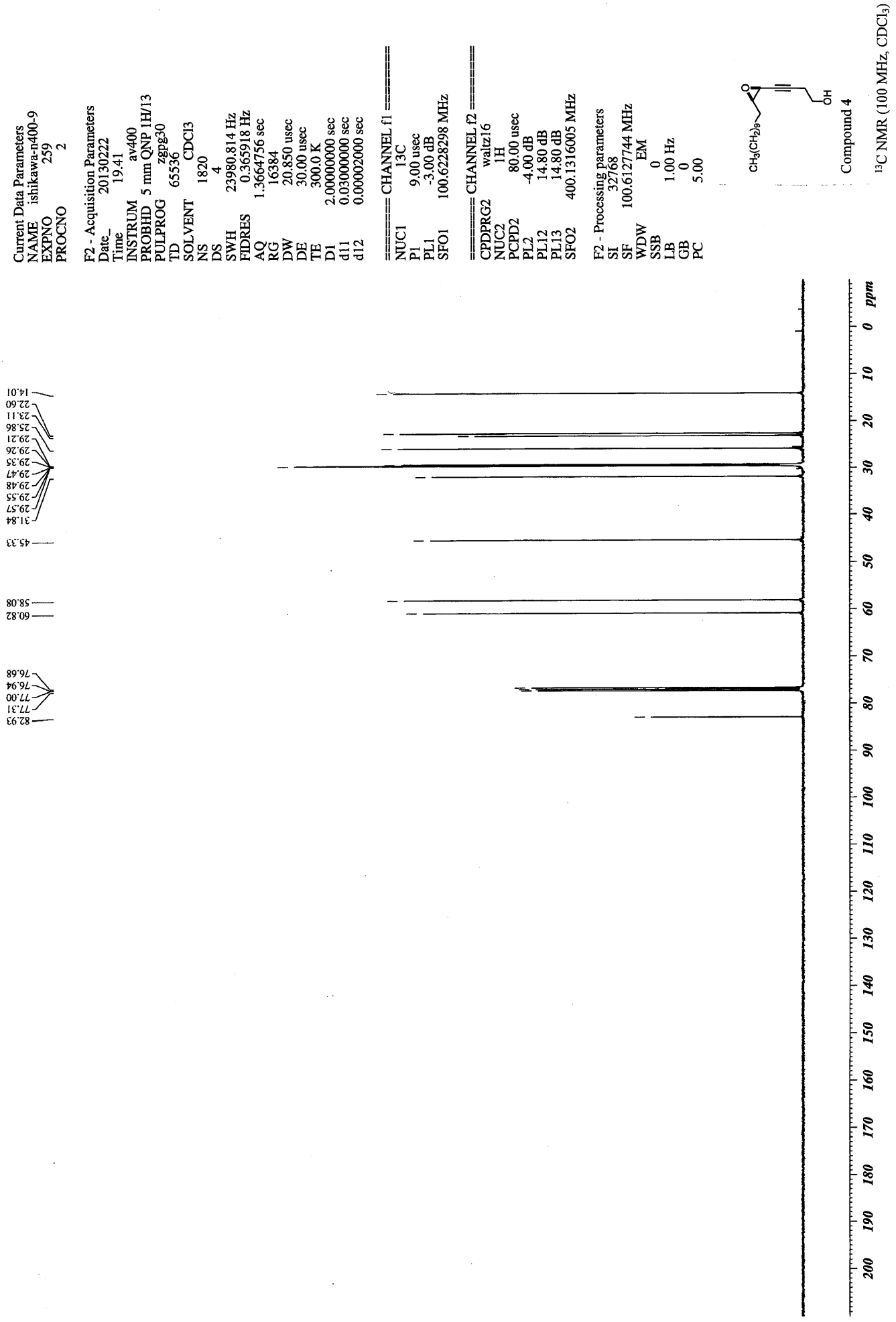
[a] 100 MHz in CD_3OD. [b] 75 MHz in CD_3OD.

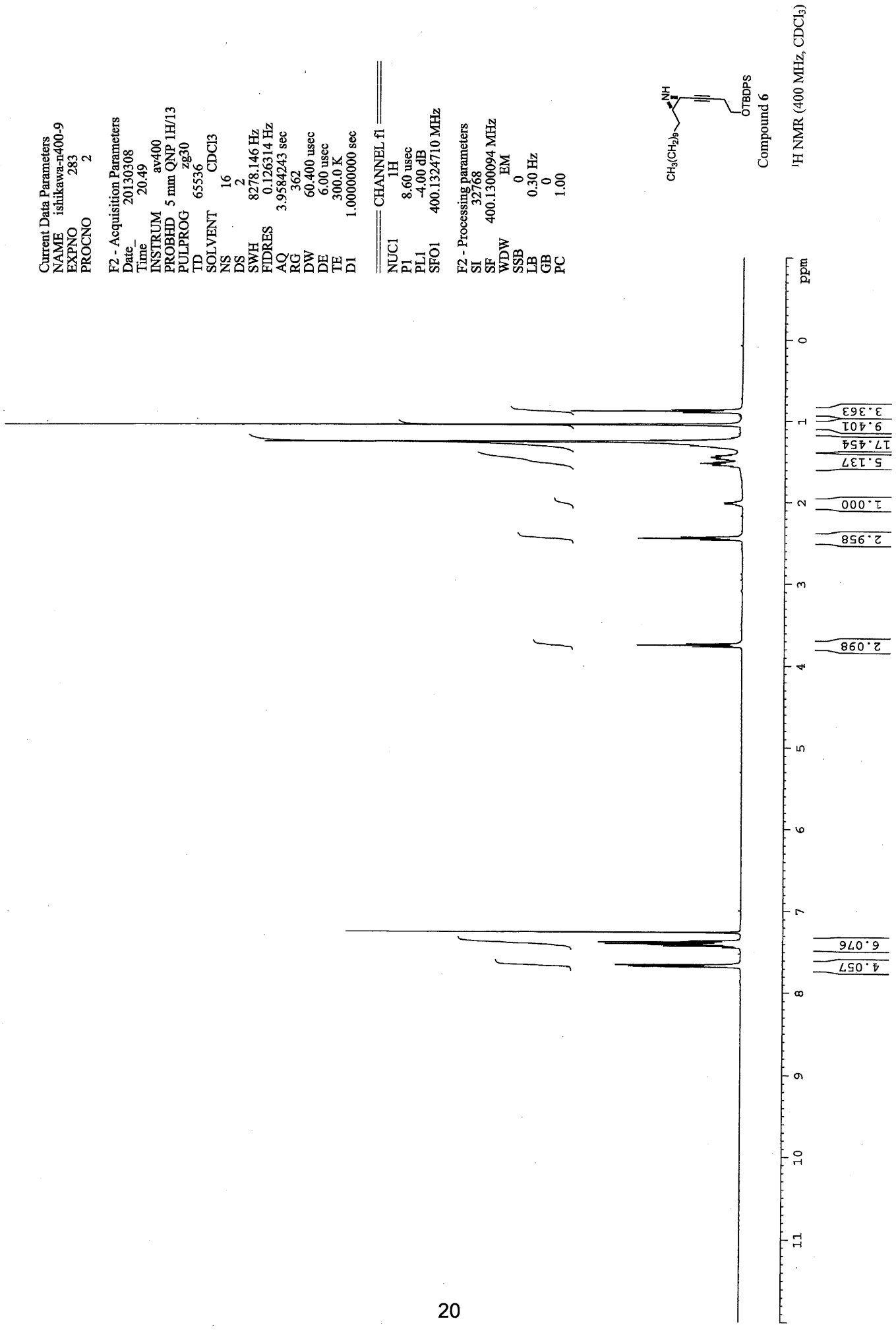
[*] B. B. Snider and Z. Shi, *J. Org. Chem.*, 1993, **58**, 3828-3839.

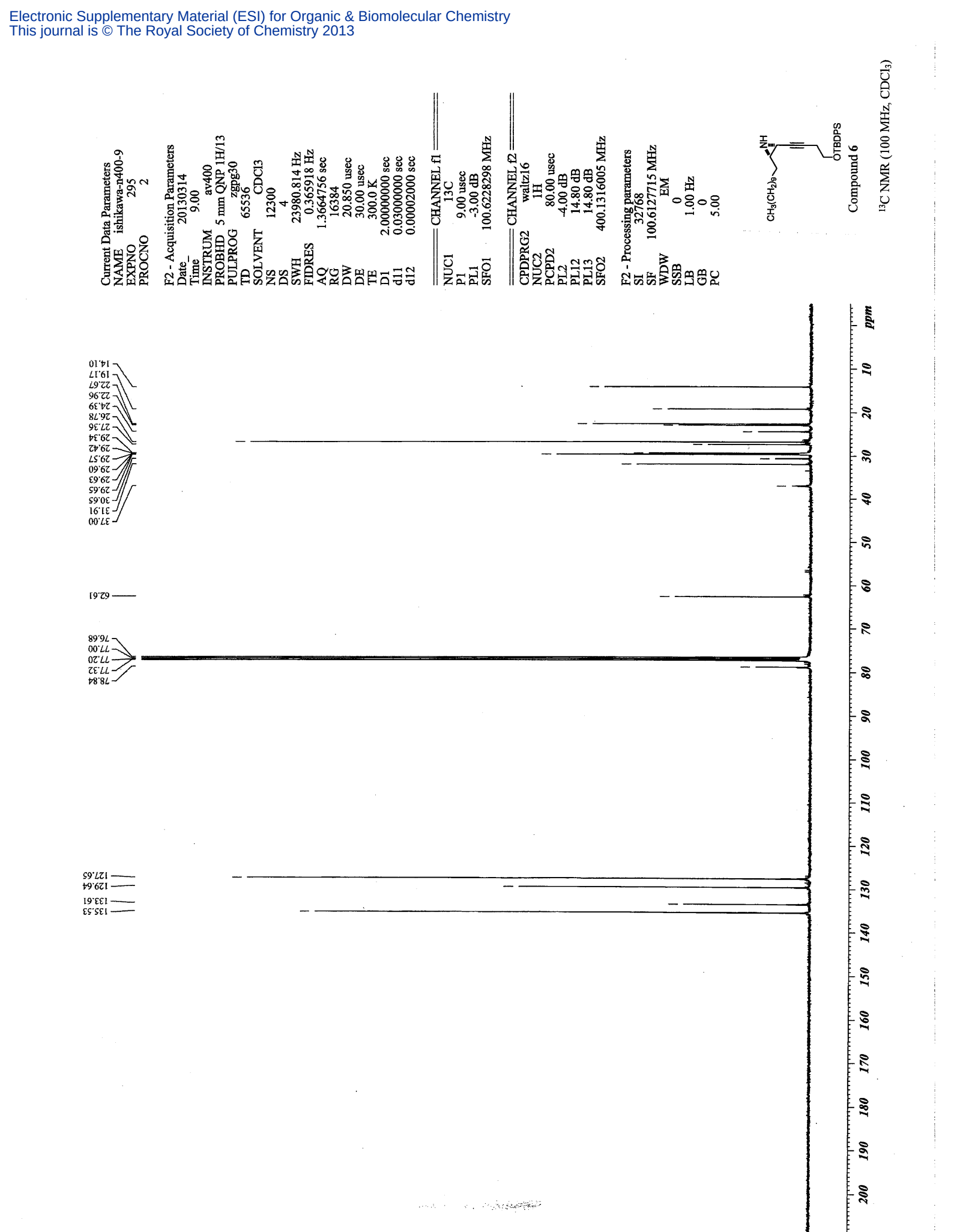


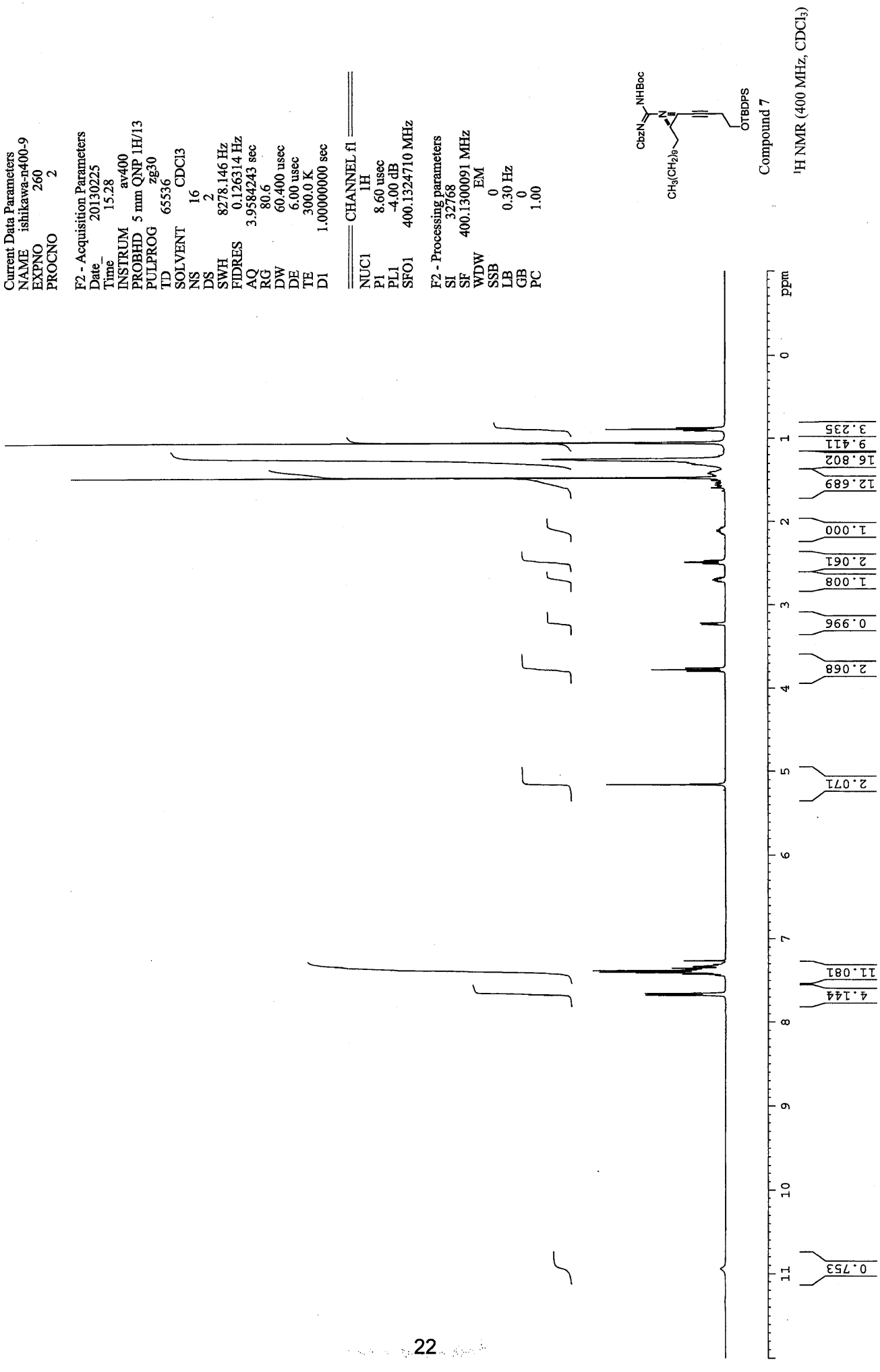


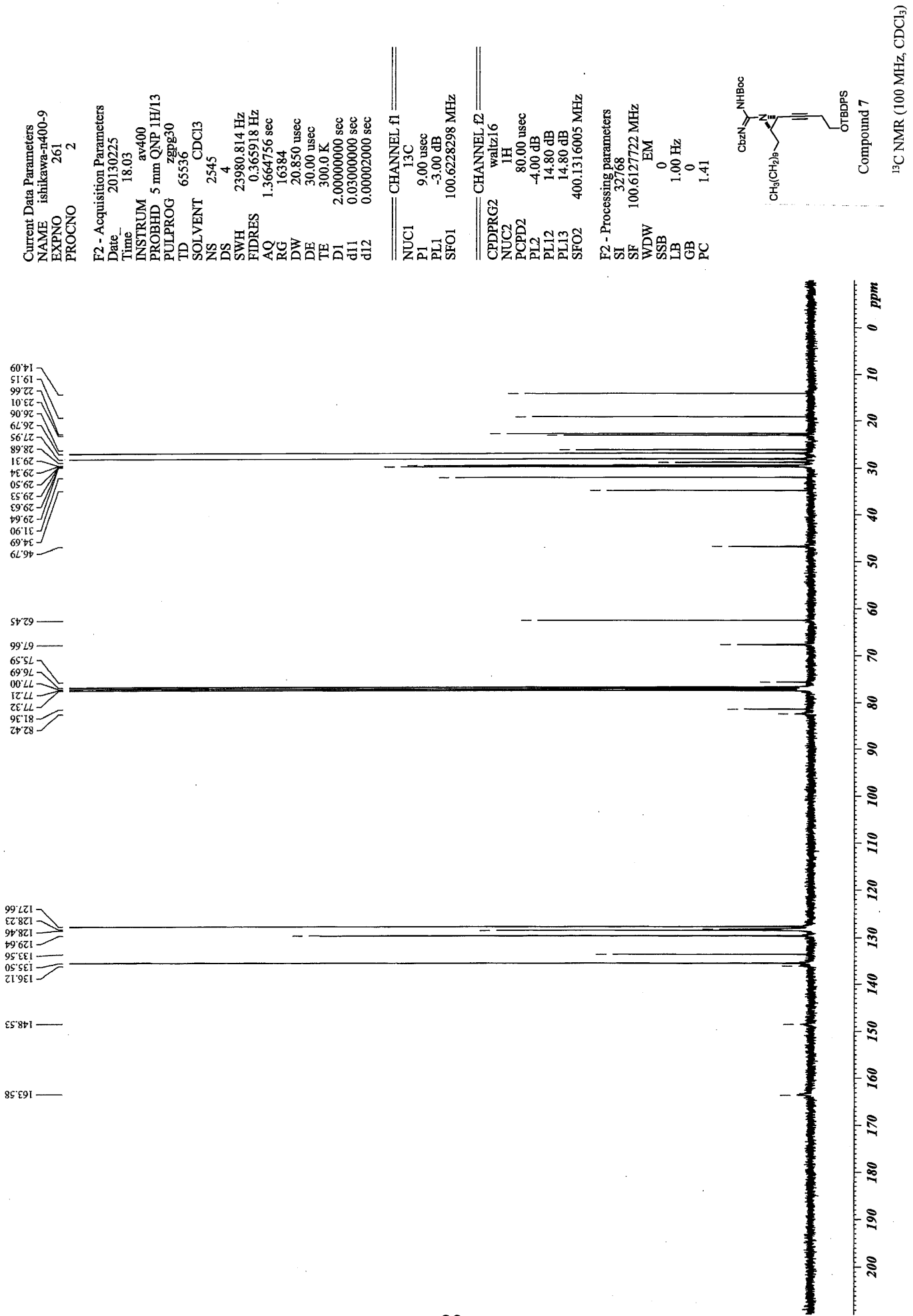


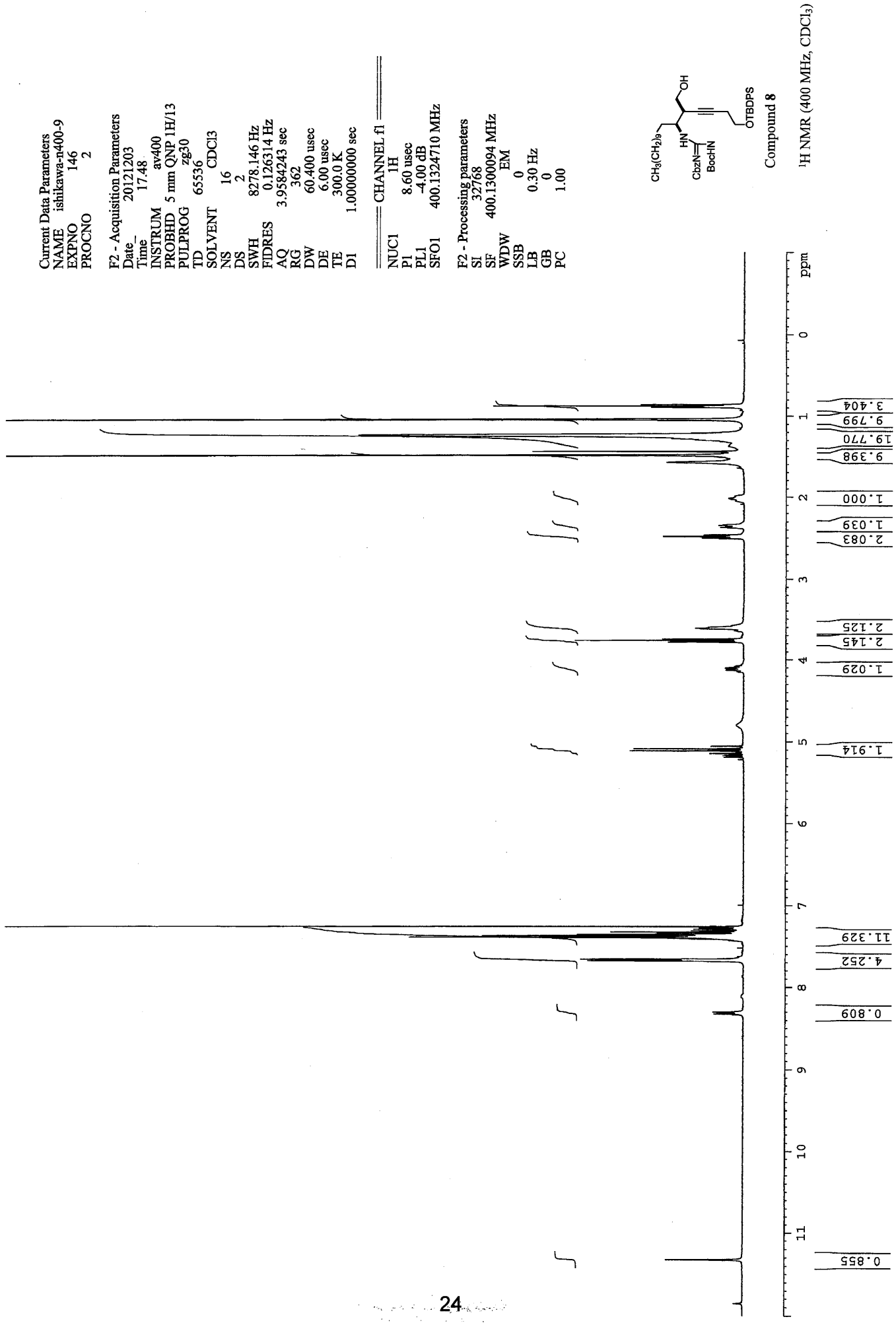

Current Data Parameters
NAME ishikawa-n400-9
EXPNO 259
PROCNO 2
F2 - Acquisition Parameters
Date_ 20130222
Time 19.41
INSTRUM av400
PROBHD 5 mm QNP 1H/13
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 1820
DS 4
SWH 23980.814 Hz
FIDRES 0.365918 Hz
AQ 1.3664756 sec
RG 16384
DW 20.850 usec
DE 30.00 usec
TE 300.0 K
D1 2.00000000 sec
d11 0.03000000 sec
d12 0.00002000 sec
======== CHANNEL f1 ========
NUC1 13C
P1 9.00 usec
PL1 -3.00 dB
SFO1 100.6228298 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 -4.00 dB
PL12 14.80 dB
PL13 14.80 dB
SFO2 400.1316005 MHz
F2 - Processing parameters
SI 32768
SF 100.6127744 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 5.00
CH3(CH2)9
OH
Compound 4
13C NMR (100 MHz, CDCl3)
14.01
22.60
23.11
25.86
29.21
29.26
29.35
29.47
29.48
29.55
29.57
31.84
45.33
58.08
60.82
76.68
76.94
77.00
77.31
82.93
ppm

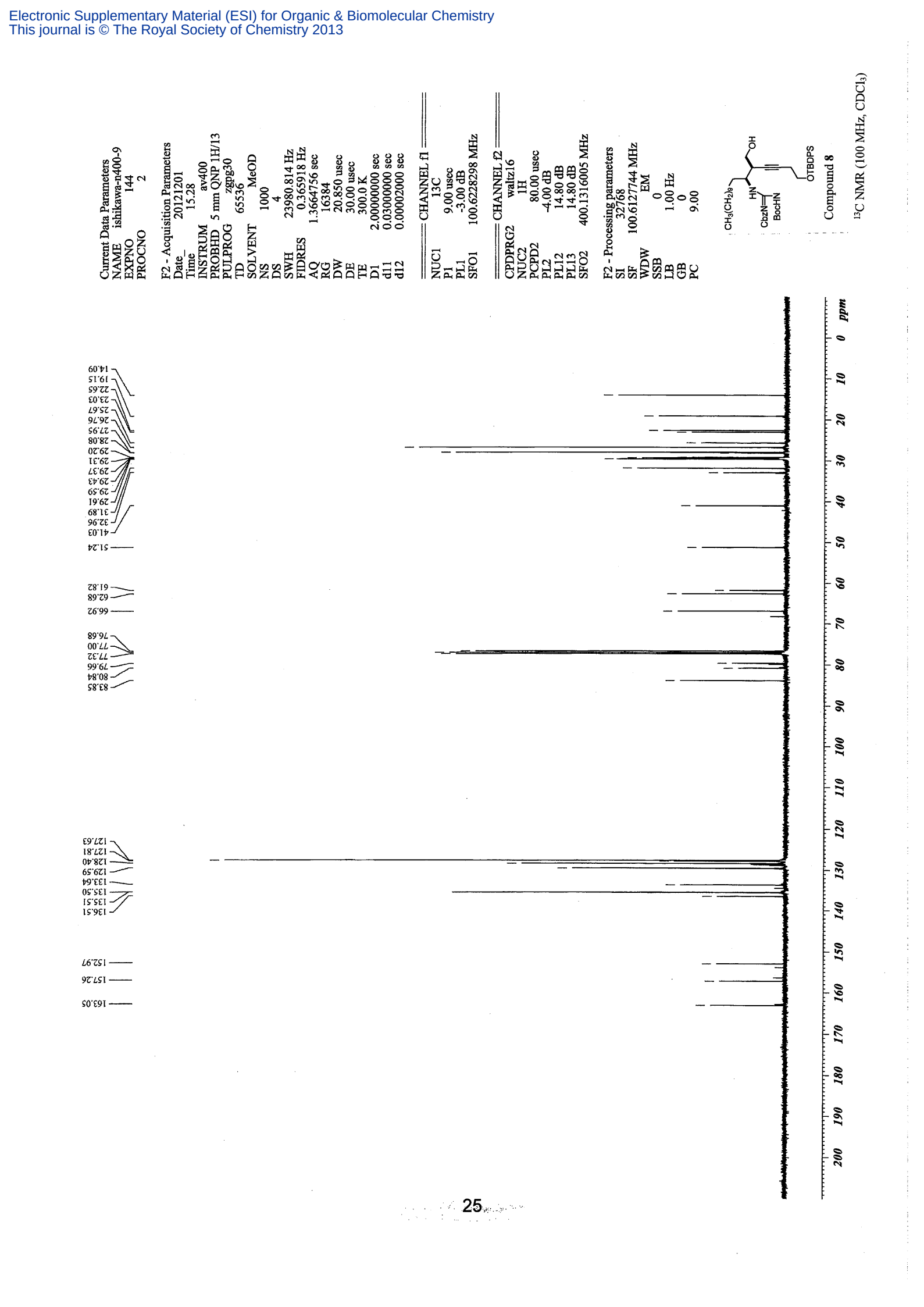

Current Data Parameters
NAME ishikawa-n400-9
EXPNO 283
PROCNO 2
F2 - Acquisition Parameters
Date_ 20130308
Time 20.49
INSTRUM av400
PROBHD 5 mm QNP 1H/13
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8278.146 Hz
FIDRES 0.126314 Hz
AQ 3.9584243 sec
RG 362
DW 60.400 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec
CHANNEL f1
NUC1 1H
P1 8.60 usec
PL1 -4.00 dB
SFO1 400.1324710 MHz
F2 - Processing parameters
SI 32768
SF 400.1300094 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
NH
CH3(CH2)9
OTBDPS
Compound 6
1H NMR (400 MHz, CDCl3)
ppm
0
1
2
3
4
5
6
7
8
9
10
11
3.363
9.401
17.454
5.137
1.000
2.958
2.098
6.076
4.057

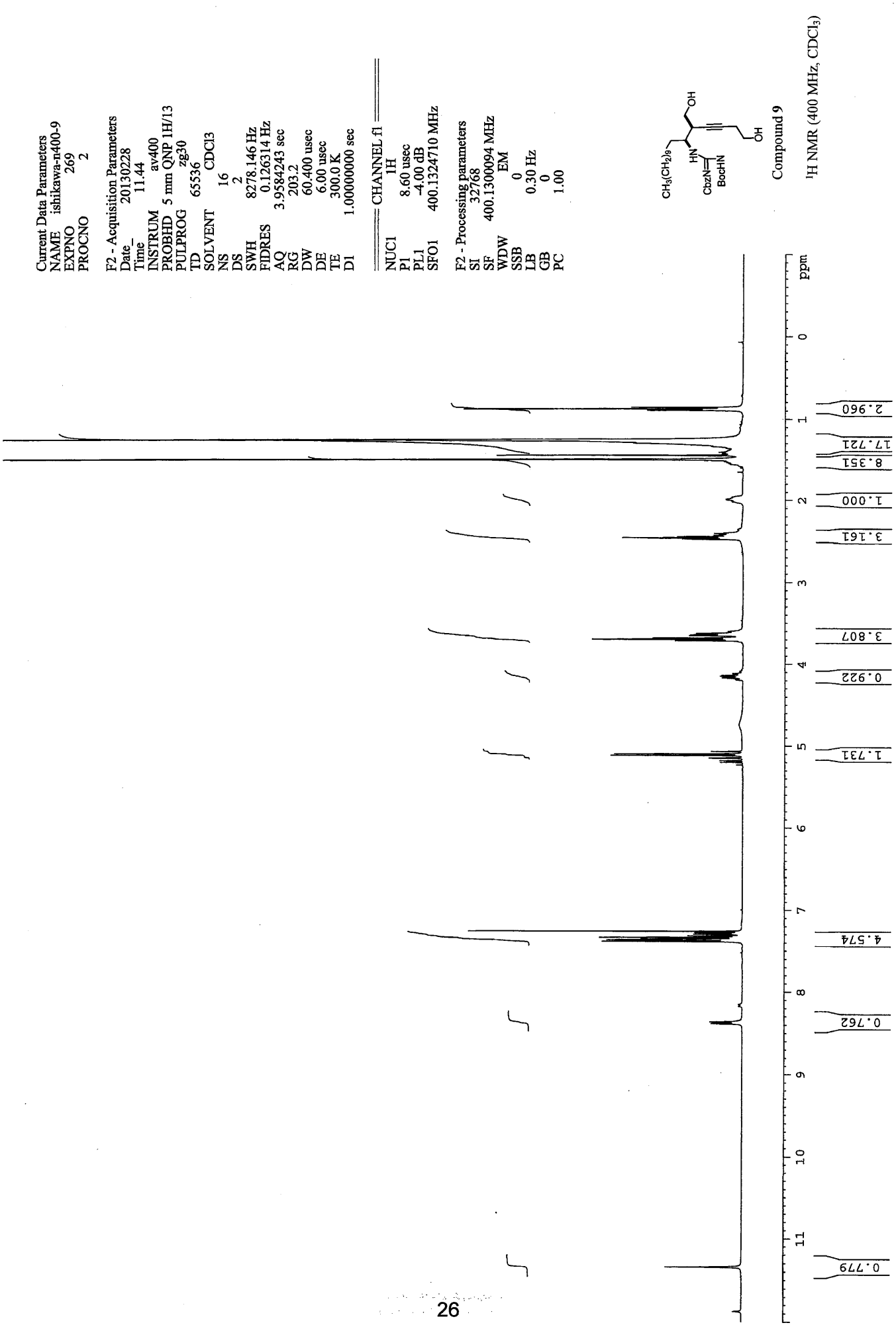


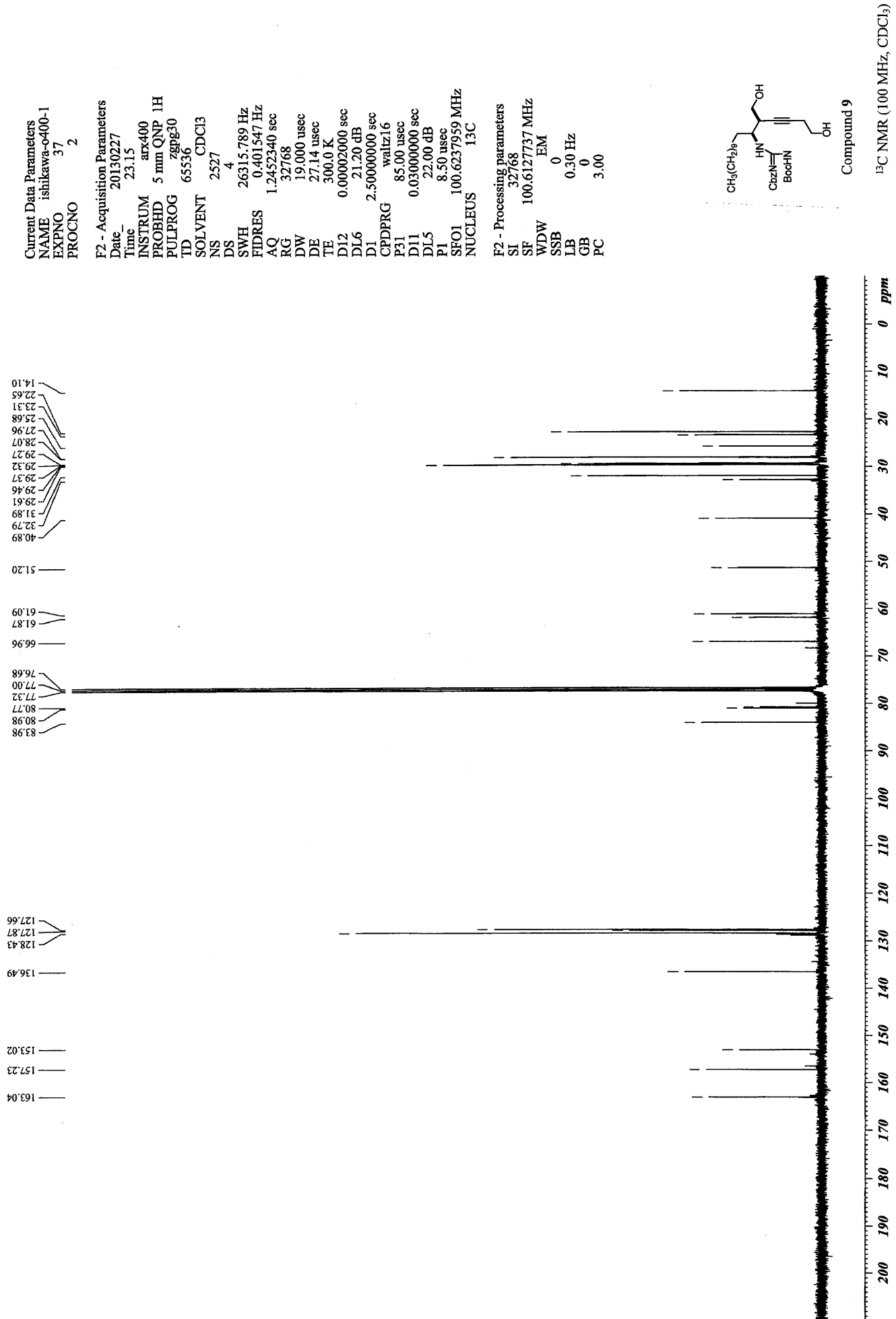

Current Data Parameters
NAME ishikawa-n400-9
EXPNO 260
PROCNO 2
F2 - Acquisition Parameters
Date_ 20130225
Time 15.28
INSTRUM av400
PROBHD 5 mm QNP 1H/13
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8278.146 Hz
FIDRES 0.126314 Hz
AQ 3.9584243 sec
RG 80.6
DW 60.400 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec
CHANNEL f1
NUC1 1H
P1 8.60 usec
PL1 -4.00 dB
SFO1 400.1324710 MHz
F2 - Processing parameters
SI 32768
SF 400.1300091 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
CbzN
NHBoc
N
CH3(CH2)9
OTBDPS
Compound 7
1H NMR (400 MHz, CDCl3)
ppm
3.235
9.411
16.802
12.689
1.000
2.061
1.008
0.996
2.068
2.071
11.081
4.144
0.753

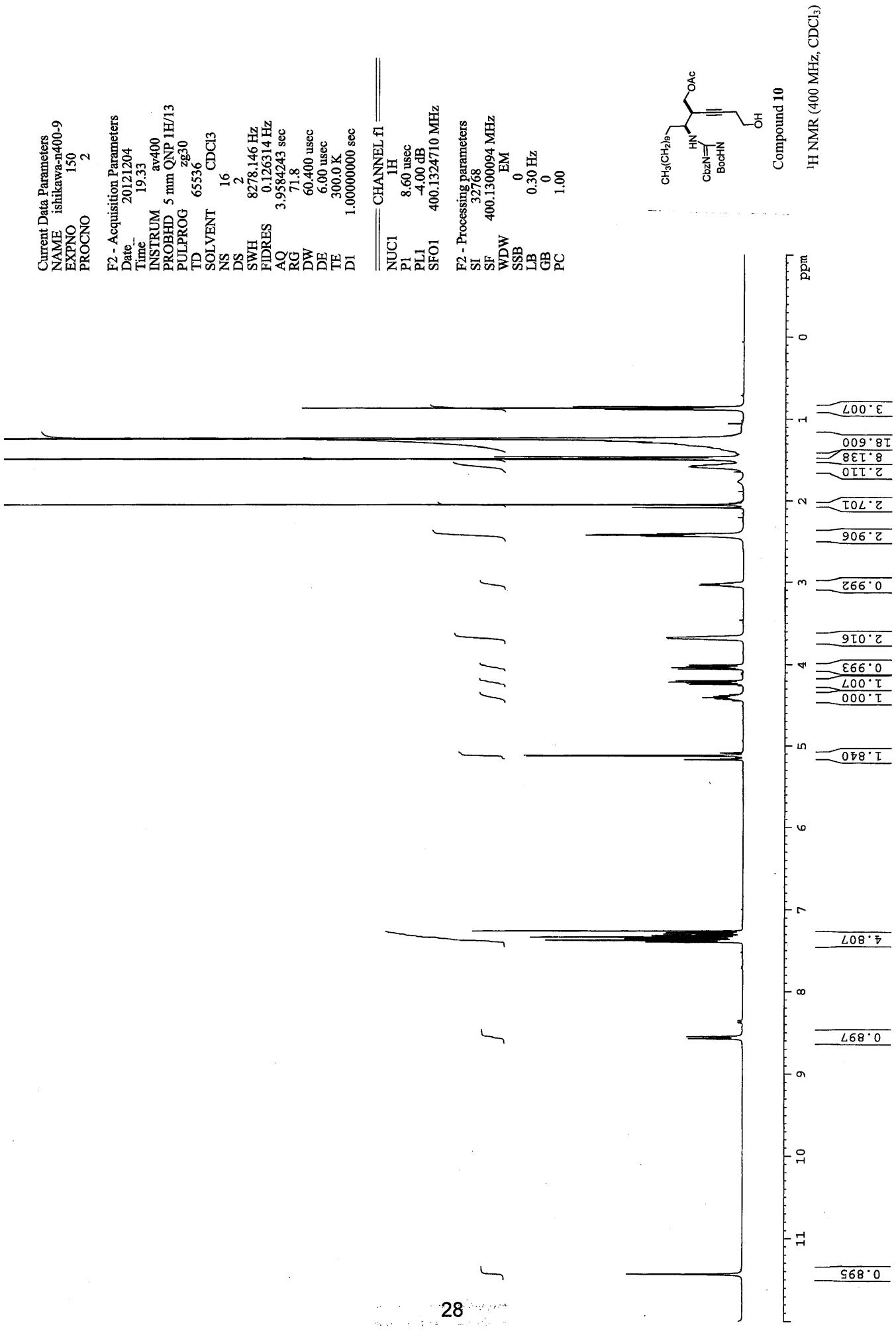

Current Data Parameters
NAME ishikawa-n400-9
EXPNO 261
PROCNO 2
F2 - Acquisition Parameters
Date_ 20130225
Time 18.03
INSTRUM av400
PROBHD 5 mm QNP 1H/13
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 2545
DS 4
SWH 23980.814 Hz
FIDRES 0.365918 Hz
AQ 1.3664756 sec
RG 16384
DW 20.850 usec
DE 30.00 usec
TE 300.0 K
D1 2.00000000 sec
d11 0.03000000 sec
d12 0.00002000 sec
CHANNEL f1
NUC1 13C
P1 9.00 usec
PL1 -3.00 dB
SFO1 100.6228298 MHz
CHANNEL f2
CPDPRG2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 -4.00 dB
PL12 14.80 dB
PL13 14.80 dB
SFO2 400.1316005 MHz
F2 - Processing parameters
SI 32768
SF 100.6127722 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.41
CbzN
NHBoc
OTBDPS
$CH_3(CH_2)_9$
Compound 7
^{13}C NMR (100 MHz, $CDCl_3$)
14.09
19.15
22.66
23.01
26.06
26.79
27.95
28.68
29.31
29.34
29.50
29.53
29.63
29.64
31.90
34.69
46.79
62.45
67.66
75.59
76.69
77.00
77.21
77.32
81.36
82.42
127.66
128.23
128.46
129.64
133.56
135.50
136.12
148.53
163.58
ppm

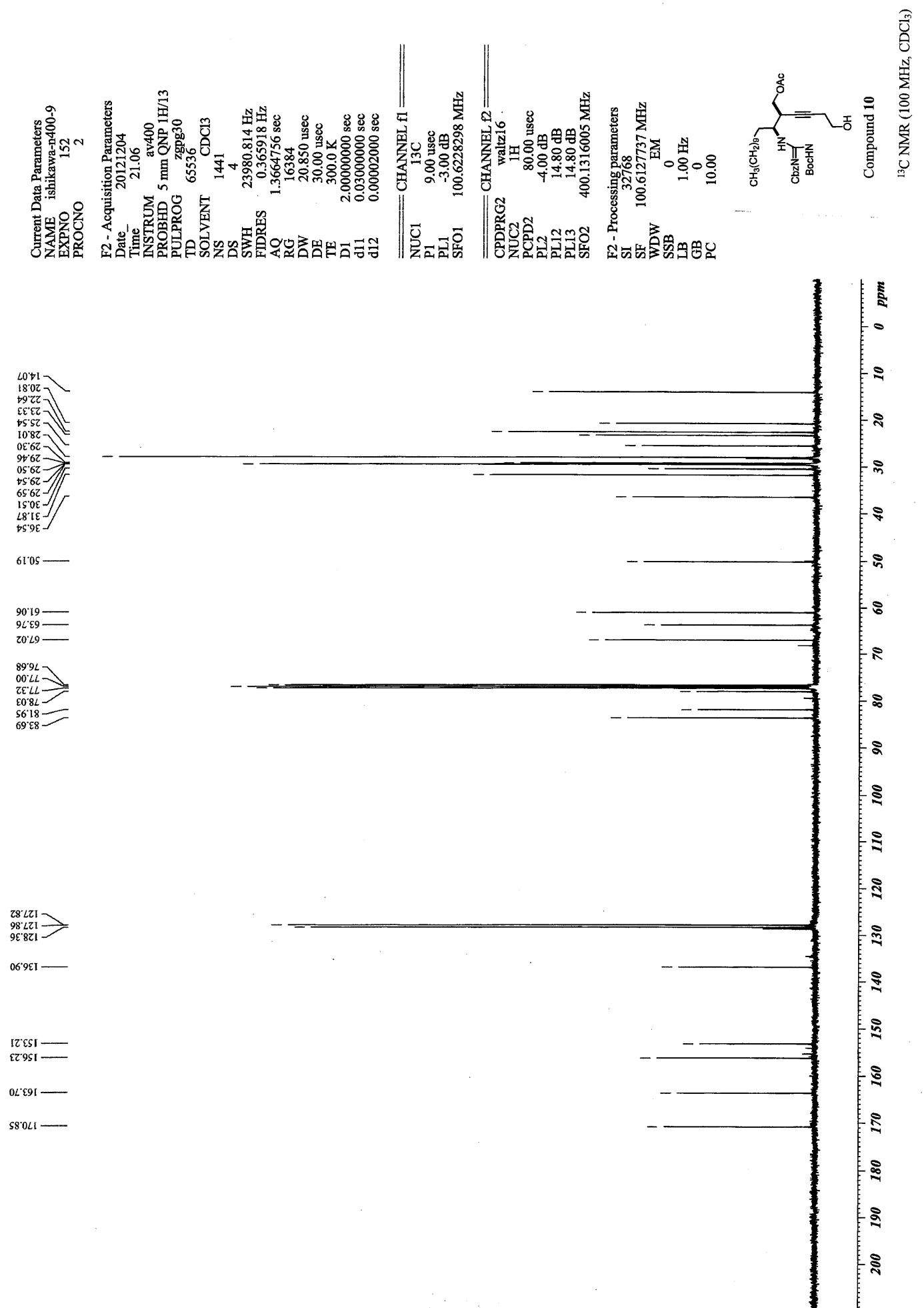

Current Data Parameters
NAME ishikawa-n400-9
EXPNO 146
PROCNO 2
F2 - Acquisition Parameters
Date_ 20121203
Time 17.48
INSTRUM av400
PROBHD 5 mm QNP 1H/13
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8278.146 Hz
FIDRES 0.126314 Hz
AQ 3.9584243 sec
RG 362
DW 60.400 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec
CHANNEL f1
NUC1 1H
P1 8.60 usec
PL1 -4.00 dB
SFO1 400.1324710 MHz
F2 - Processing parameters
SI 32768
SF 400.1300094 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
CH3(CH2)9
OH
HN
CbzN
BocHN
OTBDPS
Compound 8
1H NMR (400 MHz, CDCl3)
ppm
0
1
2
3
4
5
6
7
8
9
10
11
3.404
9.799
19.770
9.398
1.000
1.039
2.083
2.125
2.145
1.029
1.914
11.329
4.252
0.809
0.855

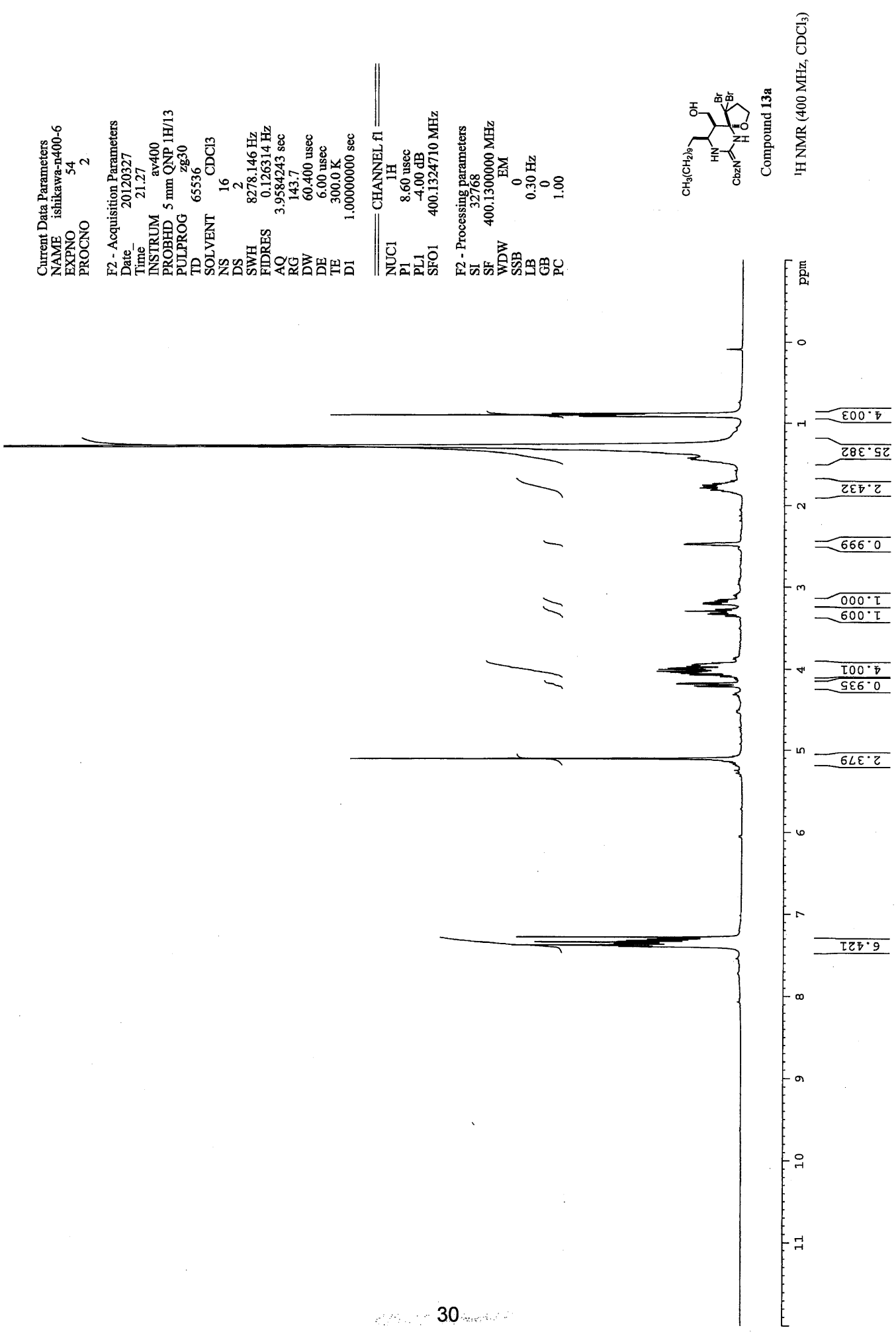


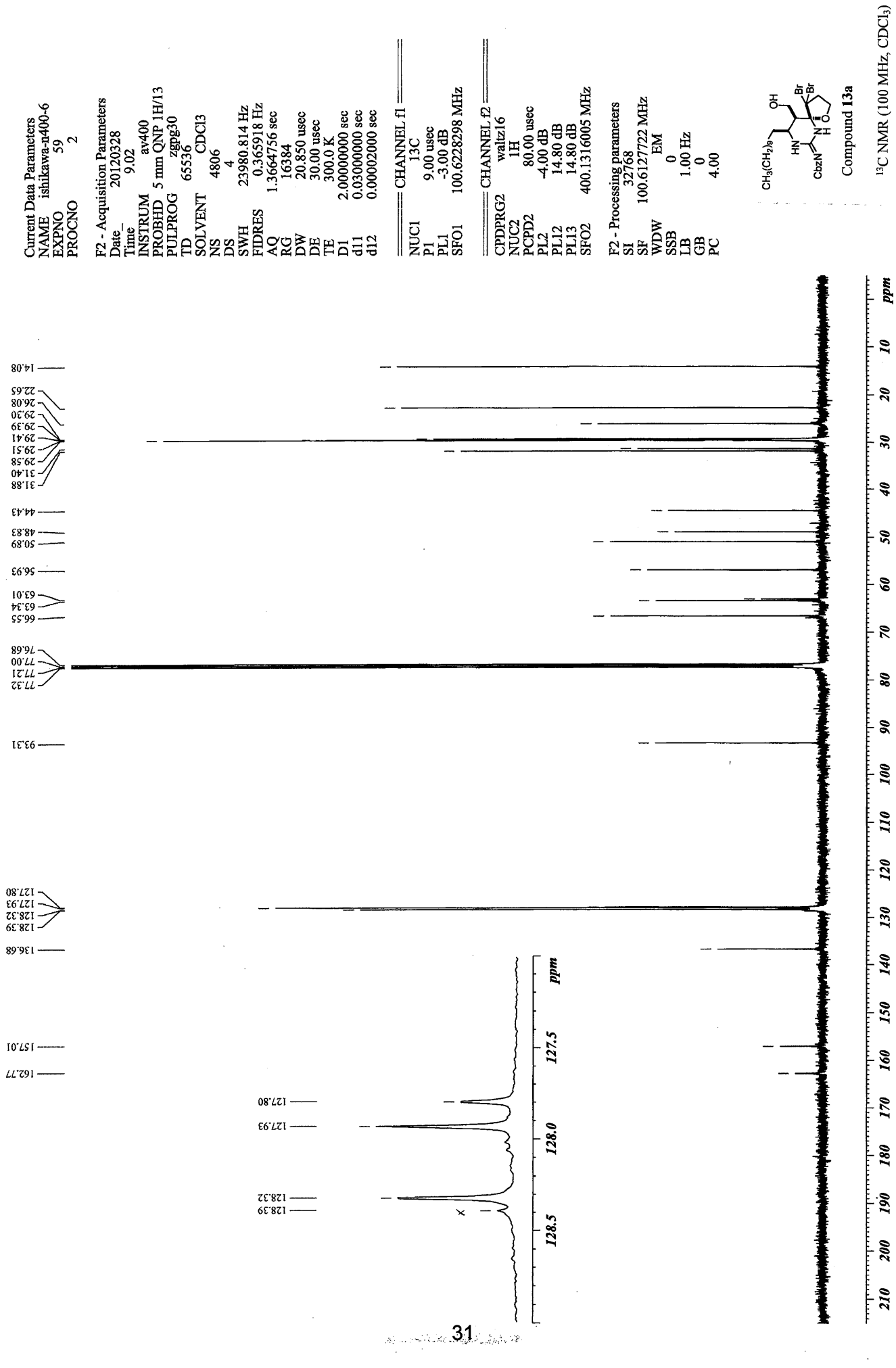

Current Data Parameters
NAME ishikawa-n400-9
EXPNO 269
PROCNO 2
F2 - Acquisition Parameters
Date_ 20130228
Time 11.44
INSTRUM av400
PROBHD 5 mm QNP 1H/13
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8278.146 Hz
FIDRES 0.126314 Hz
AQ 3.9584243 sec
RG 203.2
DW 60.400 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec
CHANNEL f1
NUC1 1H
P1 8.60 usec
PL1 -4.00 dB
SFO1 400.1324710 MHz
F2 - Processing parameters
SI 32768
SF 400.1300094 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
Compound 9
^{1}H NMR (400 MHz, $CDCl_3$)
ppm
2.960
17.721
8.351
1.000
3.161
3.807
0.922
1.731
4.574
0.762
0.779

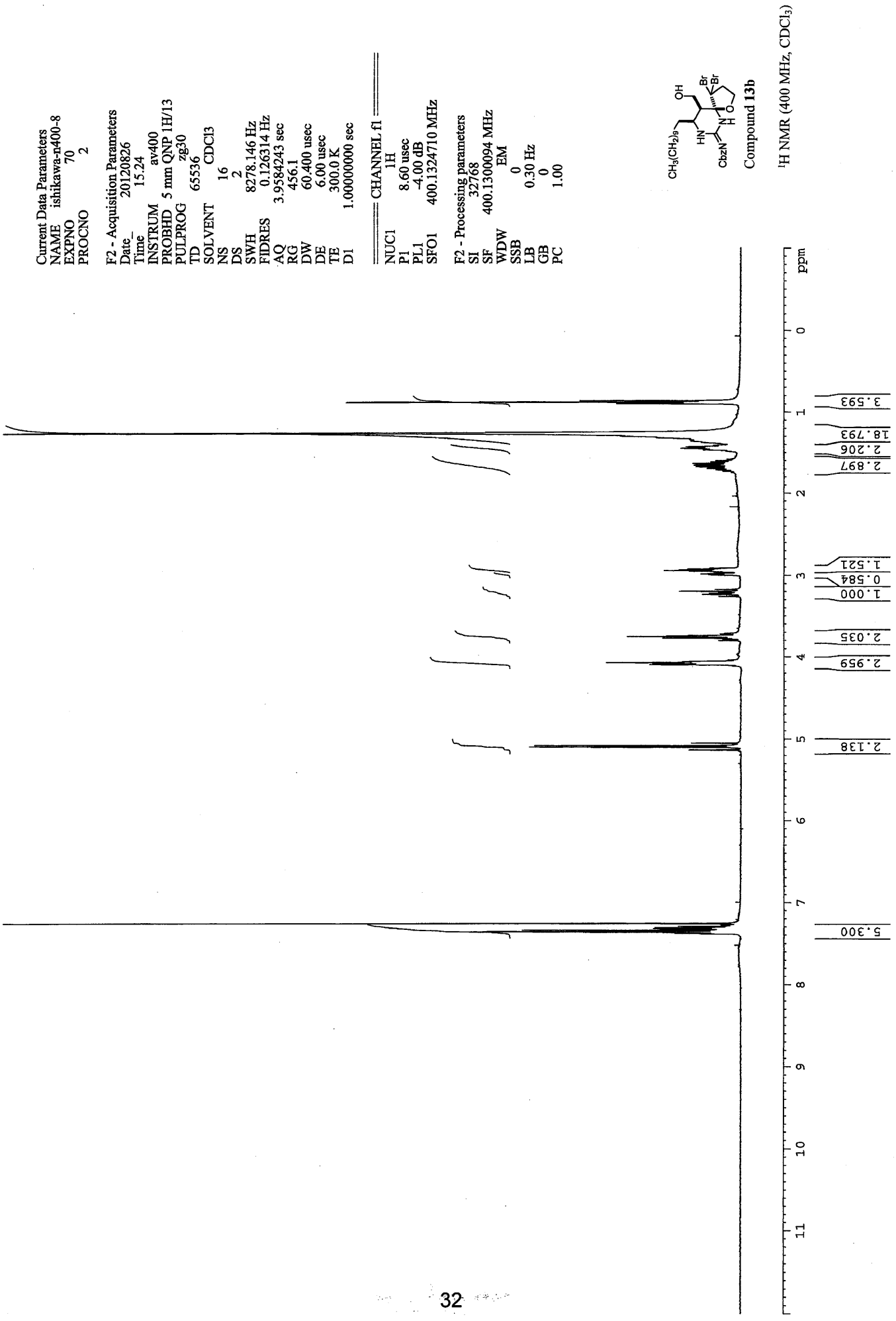

Current Data Parameters
NAME ishikawa-o400-1
EXPNO 37
PROCNO 2
F2 - Acquisition Parameters
Date_ 20130227
Time 23.15
INSTRUM arx400
PROBHD 5 mm QNP 1H
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 2527
DS 4
SWH 26315.789 Hz
FIDRES 0.401547 Hz
AQ 1.2452340 sec
RG 32768
DW 19.000 usec
DE 27.14 usec
TE 300.0 K
D12 0.00002000 sec
DL6 21.20 dB
D1 2.50000000 sec
CPDPRG waltz16
P31 85.00 usec
D11 0.03000000 sec
DL5 22.00 dB
P1 8.50 usec
SFO1 100.6237959 MHz
NUCLEUS 13C
F2 - Processing parameters
SI 32768
SF 100.6127737 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 3.00
CH3(CH2)9
HN
CbzN
BocHN
OH
OH
Compound 9
13C NMR (100 MHz, CDCl3)
14.10
22.65
23.31
25.68
27.96
28.07
29.27
29.32
29.37
29.46
29.61
31.89
32.79
40.89
51.20
61.09
61.87
66.96
76.68
77.00
77.32
80.77
80.98
83.98
127.66
127.87
128.43
136.49
153.02
157.23
163.04
ppm

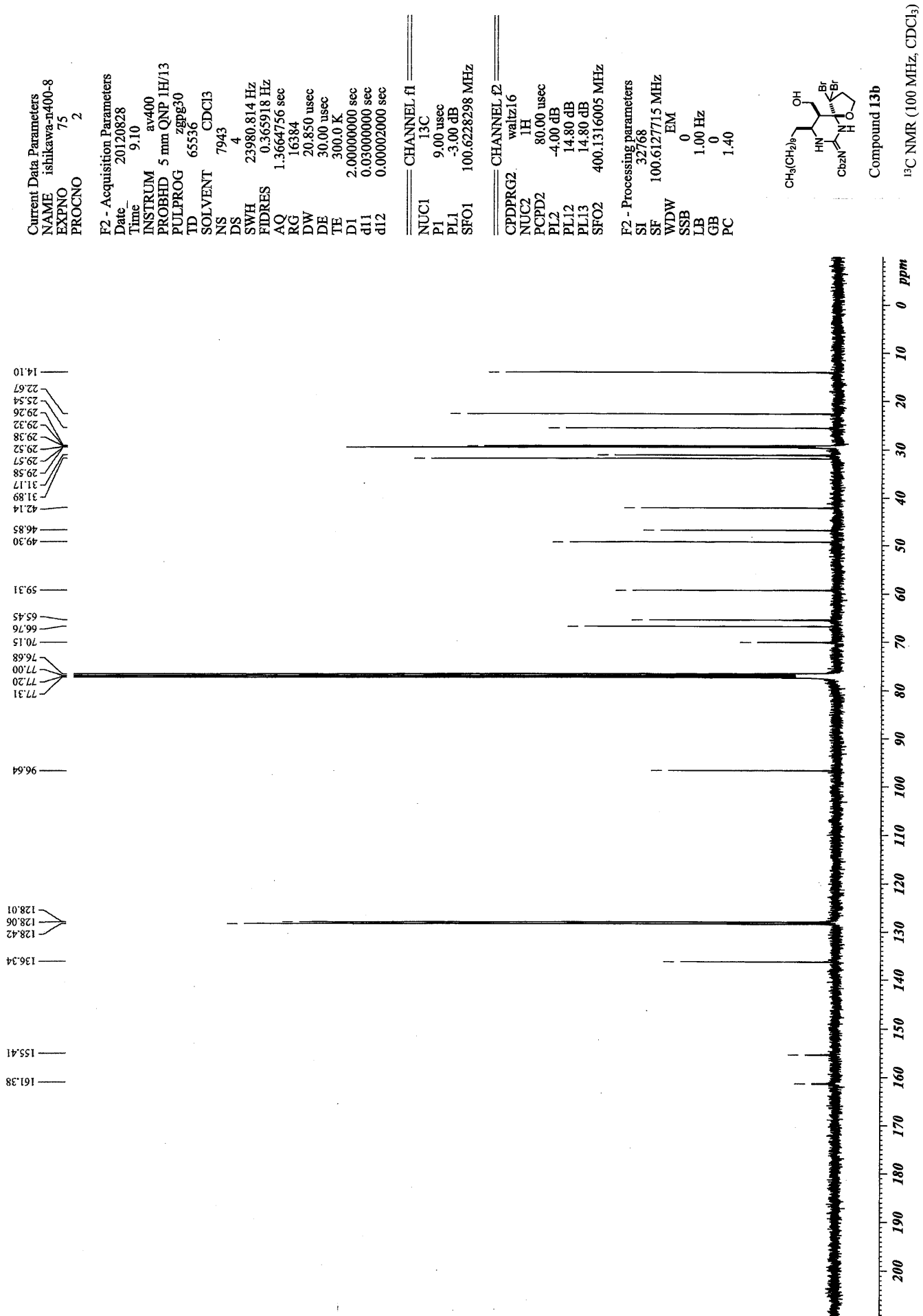


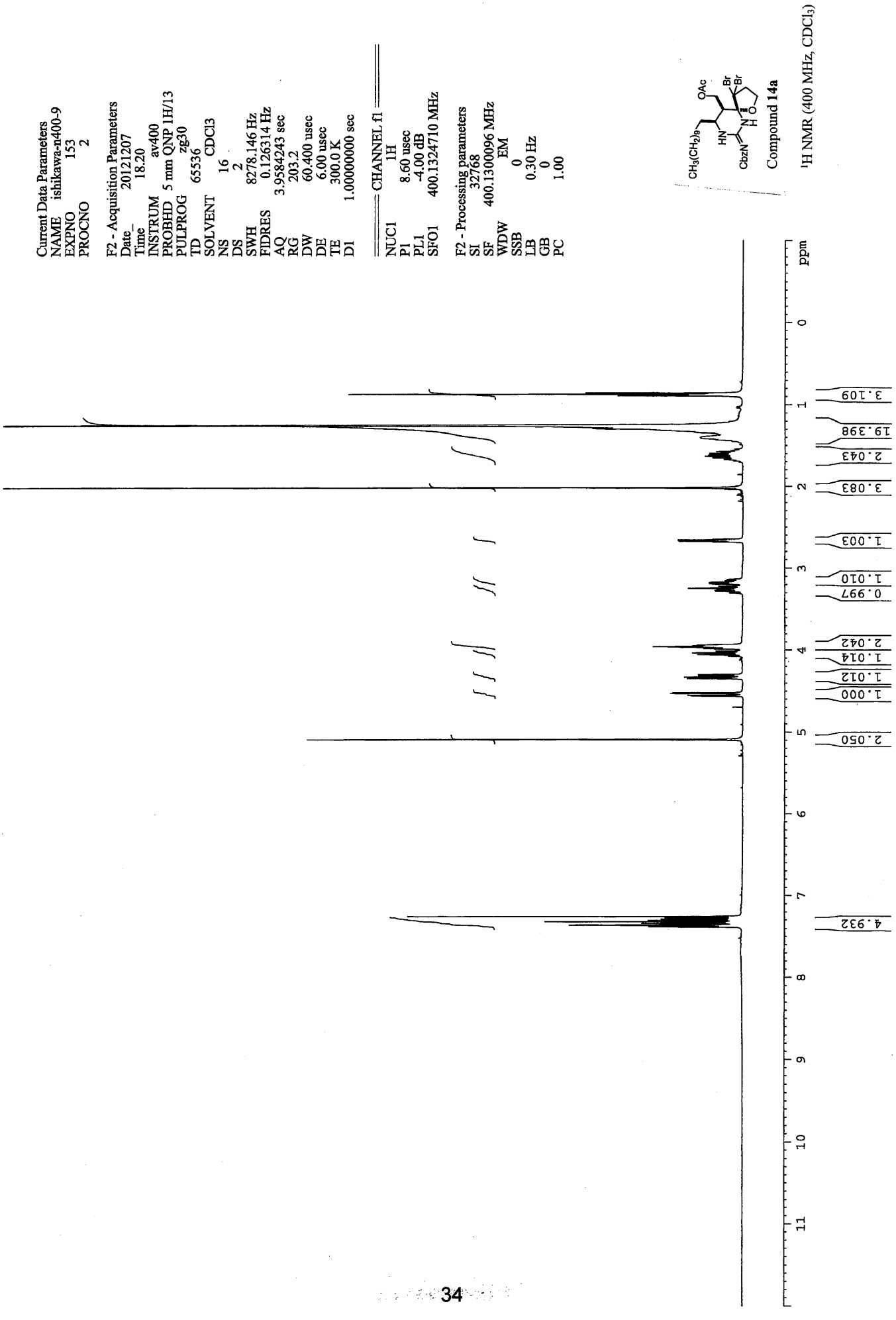

Current Data Parameters
NAME ishikawa-n400-9
EXPNO 152
PROCNO 2
F2 - Acquisition Parameters
Date_ 20121204
Time 21.06
INSTRUM av400
PROBHD 5 mm QNP 1H/13
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 1441
DS 4
SWH 23980.814 Hz
FIDRES 0.365918 Hz
AQ 1.3664756 sec
RG 16384
DW 20.850 usec
DE 30.00 usec
TE 300.0 K
D1 2.00000000 sec
d11 0.03000000 sec
d12 0.00002000 sec
CHANNEL f1
NUC1 13C
P1 9.00 usec
PL1 -3.00 dB
SFO1 100.6228298 MHz
CHANNEL f2
CPDPRG2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 -4.00 dB
PL12 14.80 dB
PL13 14.80 dB
SFO2 400.1316005 MHz
F2 - Processing parameters
SI 32768
SF 100.6127737 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 10.00
14.07
20.81
22.64
23.33
25.54
28.01
29.30
29.46
29.50
29.54
29.59
30.51
31.87
36.54
50.19
61.06
63.76
67.02
76.68
77.00
77.32
78.03
81.95
83.69
127.82
127.86
128.36
136.90
153.21
156.23
163.70
170.85
ppm
Compound 10
^{13}C NMR (100 MHz, $CDCl_3$)

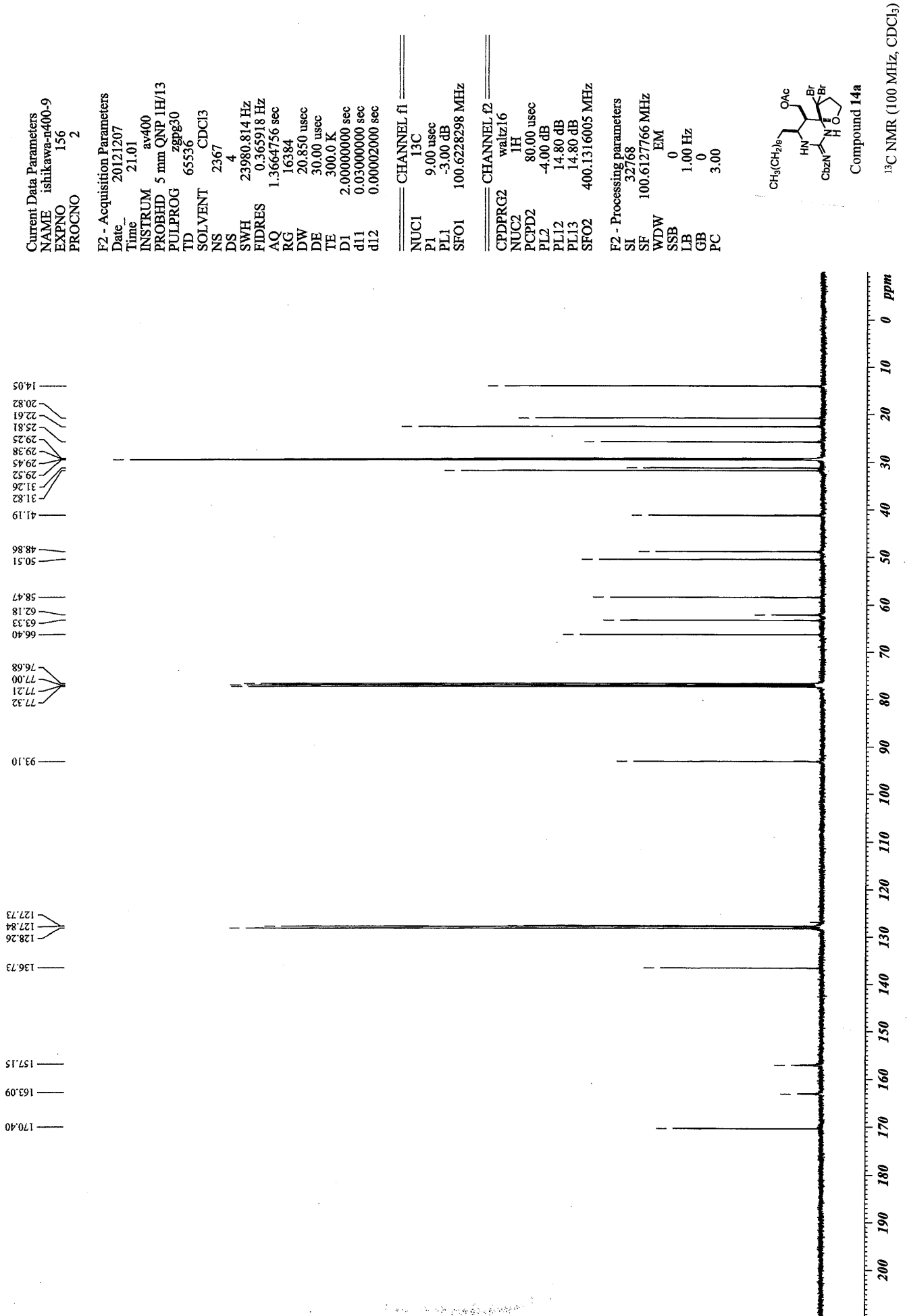

Current Data Parameters
NAME ishikawa-n400-6
EXPNO 54
PROCNO 2
F2 - Acquisition Parameters
Date_ 20120327
Time 21.27
INSTRUM av400
PROBHD 5 mm QNP 1H/13
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8278.146 Hz
FIDRES 0.126314 Hz
AQ 3.9584243 sec
RG 143.7
DW 60.400 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec
CHANNEL f1
NUC1 1H
P1 8.60 usec
PL1 -4.00 dB
SFO1 400.1324710 MHz
F2 - Processing parameters
SI 32768
SF 400.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
OH
Br
Br
HN
N
O
H
CbzN
CH3(CH2)9
Compound 13a
1H NMR (400 MHz, CDCl3)
ppm
4.003
25.382
2.432
0.999
1.000
1.009
4.001
0.935
2.379
6.421

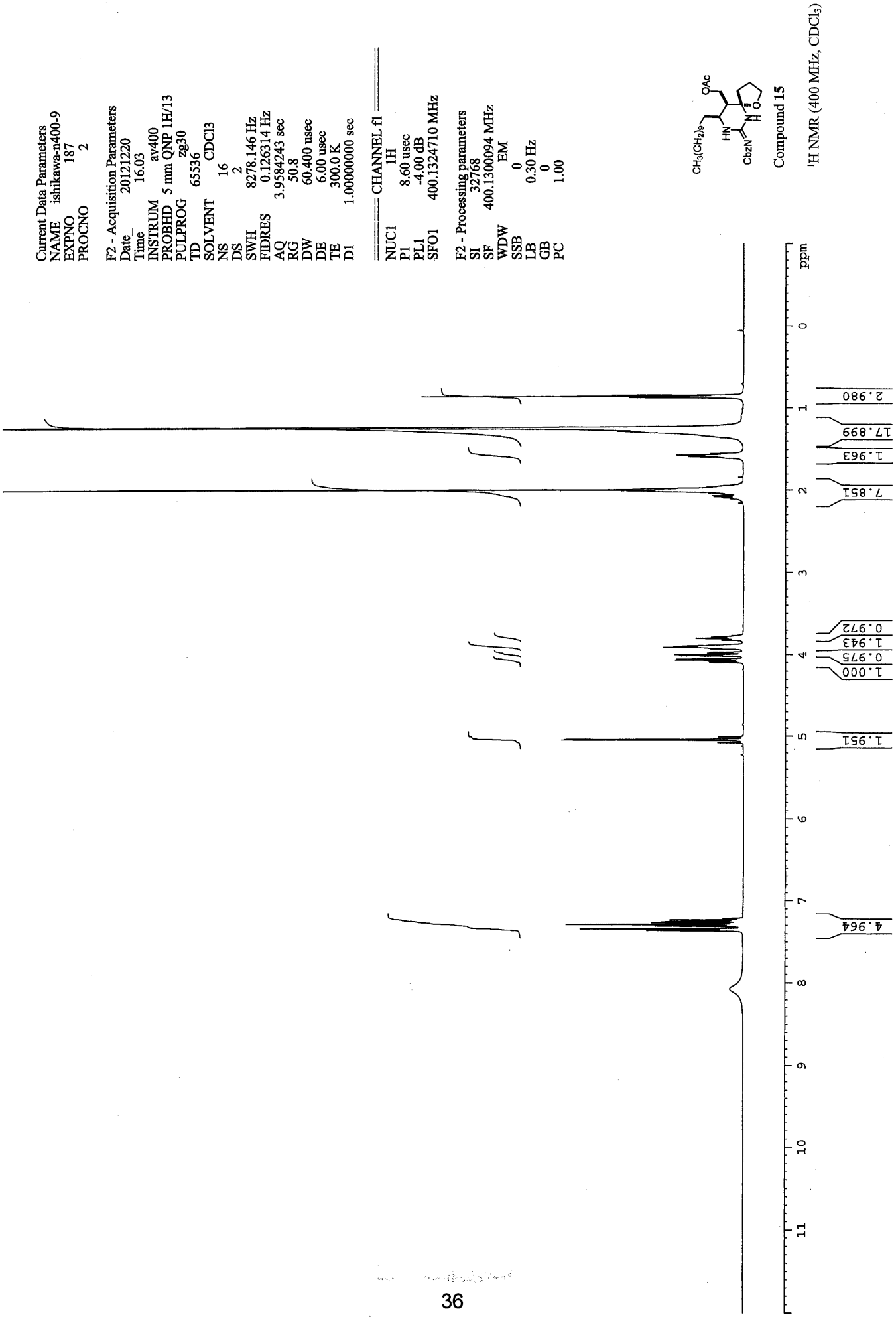

Current Data Parameters
NAME ishikawa-n400-6
EXPNO 59
PROCNO 2
F2 - Acquisition Parameters
Date_ 20120328
Time 9.02
INSTRUM av400
PROBHD 5 mm QNP 1H/13
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 4806
DS 4
SWH 23980.814 Hz
FIDRES 0.365918 Hz
AQ 1.3664756 sec
RG 16384
DW 20.850 usec
DE 30.00 usec
TE 300.0 K
D1 2.00000000 sec
d11 0.03000000 sec
d12 0.00002000 sec
CHANNEL f1
NUC1 13C
P1 9.00 usec
PL1 -3.00 dB
SFO1 100.6228298 MHz
CHANNEL f2
CPDPRG2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 -4.00 dB
PL12 14.80 dB
PL13 14.80 dB
SFO2 400.1316005 MHz
F2 - Processing parameters
SI 32768
SF 100.6127722 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 4.00
Compound 13a
13C NMR (100 MHz, CDCl3)
ppm

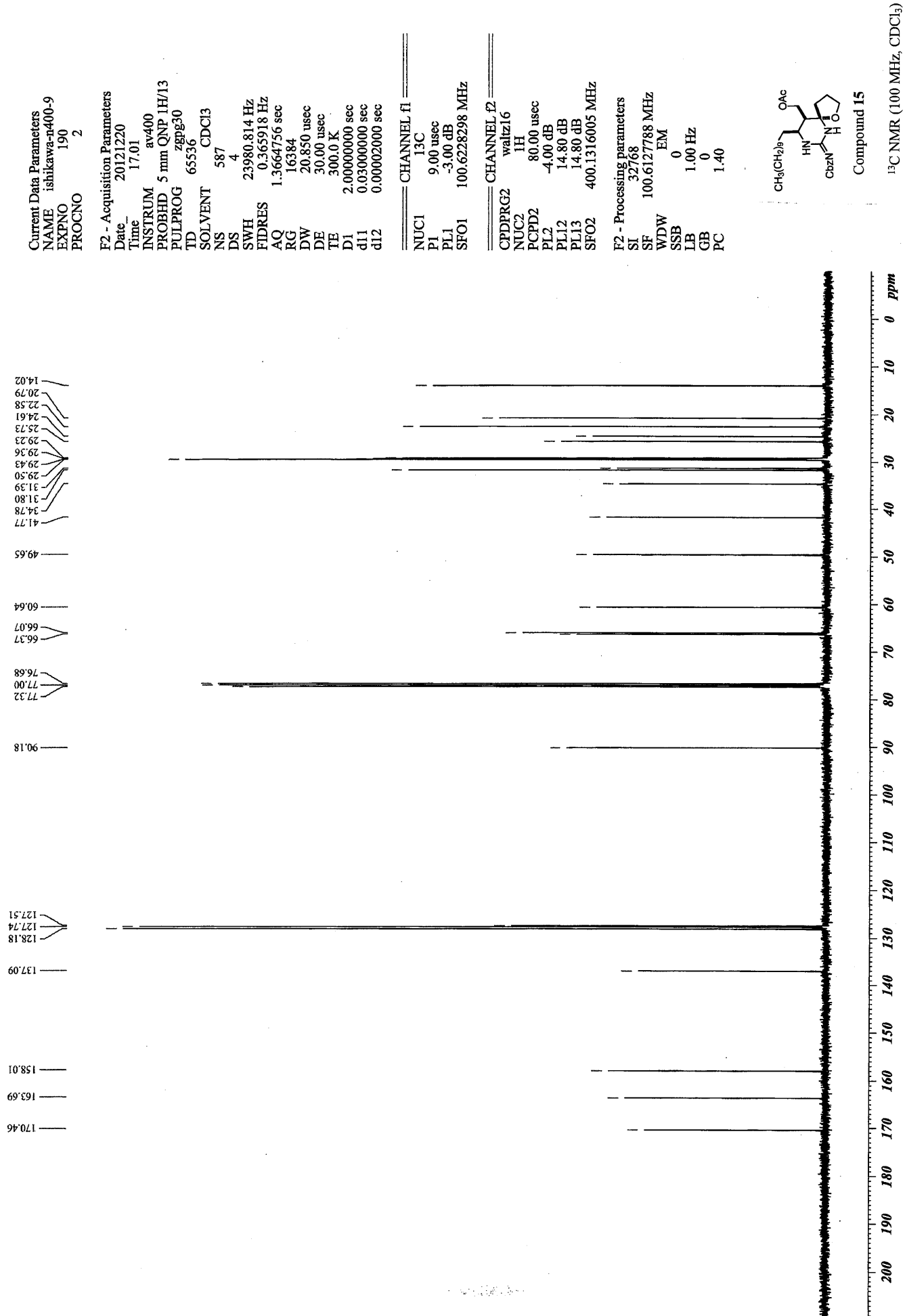


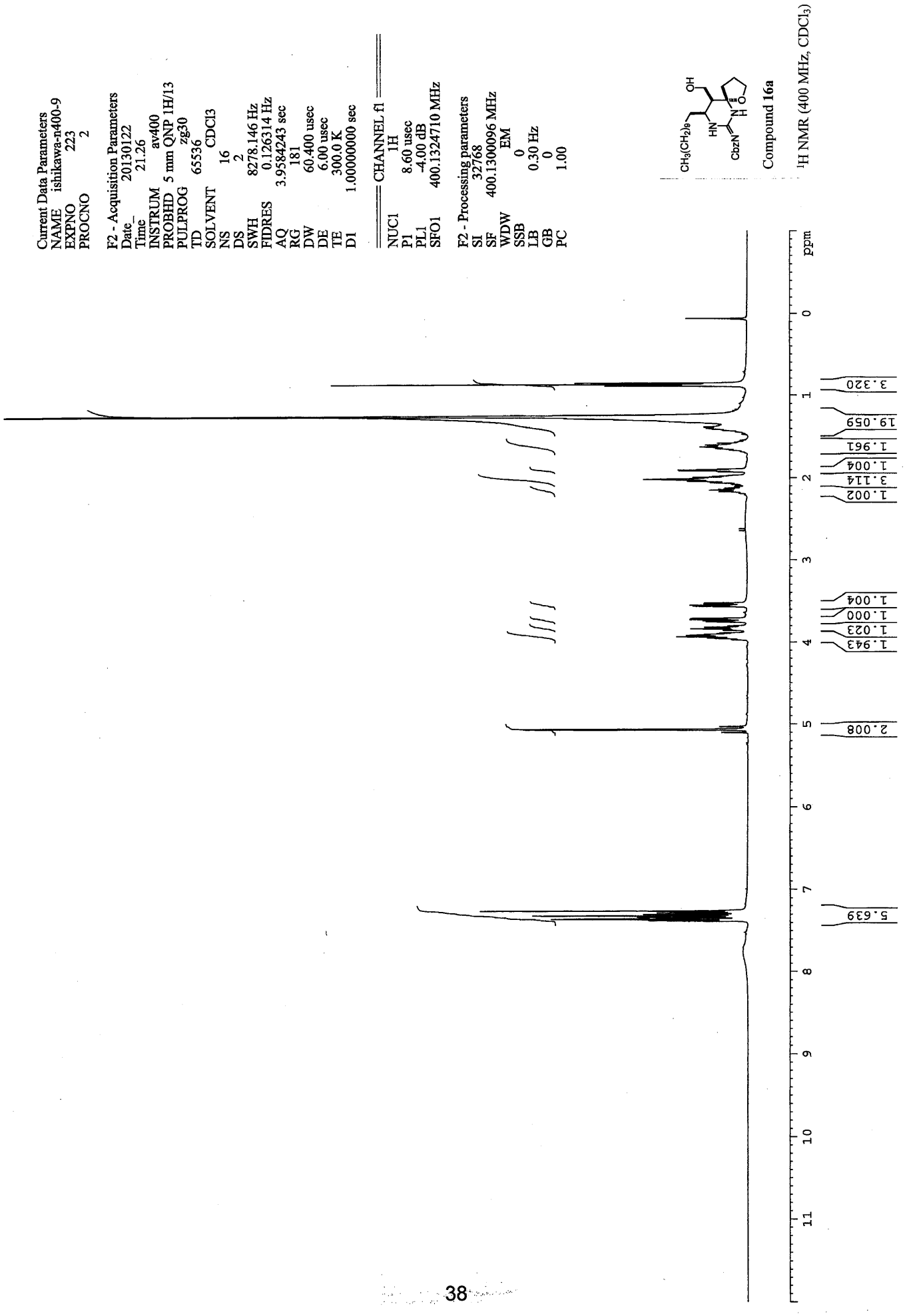

Current Data Parameters
NAME ishikawa-n400-8
EXPNO 75
PROCNO 2
F2 - Acquisition Parameters
Date_ 20120828
Time 9.10
INSTRUM av400
PROBHD 5 mm QNP 1H/13
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 7943
DS 4
SWH 23980.814 Hz
FIDRES 0.365918 Hz
AQ 1.3664756 sec
RG 16384
DW 20.850 usec
DE 30.00 usec
TE 300.0 K
D1 2.00000000 sec
d11 0.03000000 sec
d12 0.00002000 sec
CHANNEL f1
NUC1 13C
P1 9.00 usec
PL1 -3.00 dB
SFO1 100.6228298 MHz
CHANNEL f2
CPDPRG2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 -4.00 dB
PL12 14.80 dB
PL13 14.80 dB
SFO2 400.1316005 MHz
F2 - Processing parameters
SI 32768
SF 100.6127715 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
Compound 13b
13C NMR (100 MHz, CDCl3)
14.10
22.67
25.54
29.26
29.32
29.38
29.52
29.57
29.58
31.17
31.89
42.14
46.85
49.30
59.31
65.45
66.76
70.15
76.68
77.00
77.20
77.31
96.64
128.01
128.06
128.42
136.34
155.41
161.38
ppm

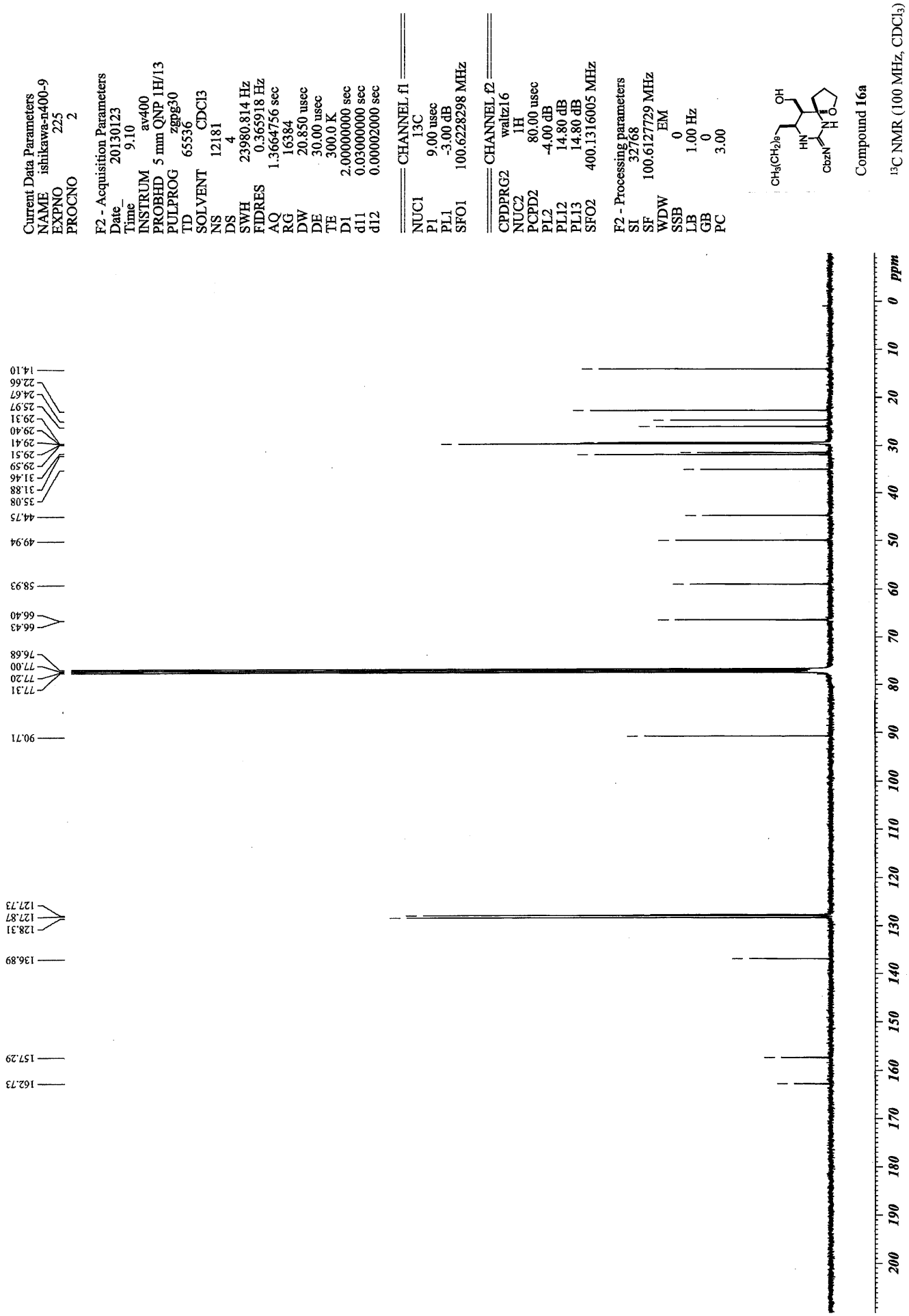


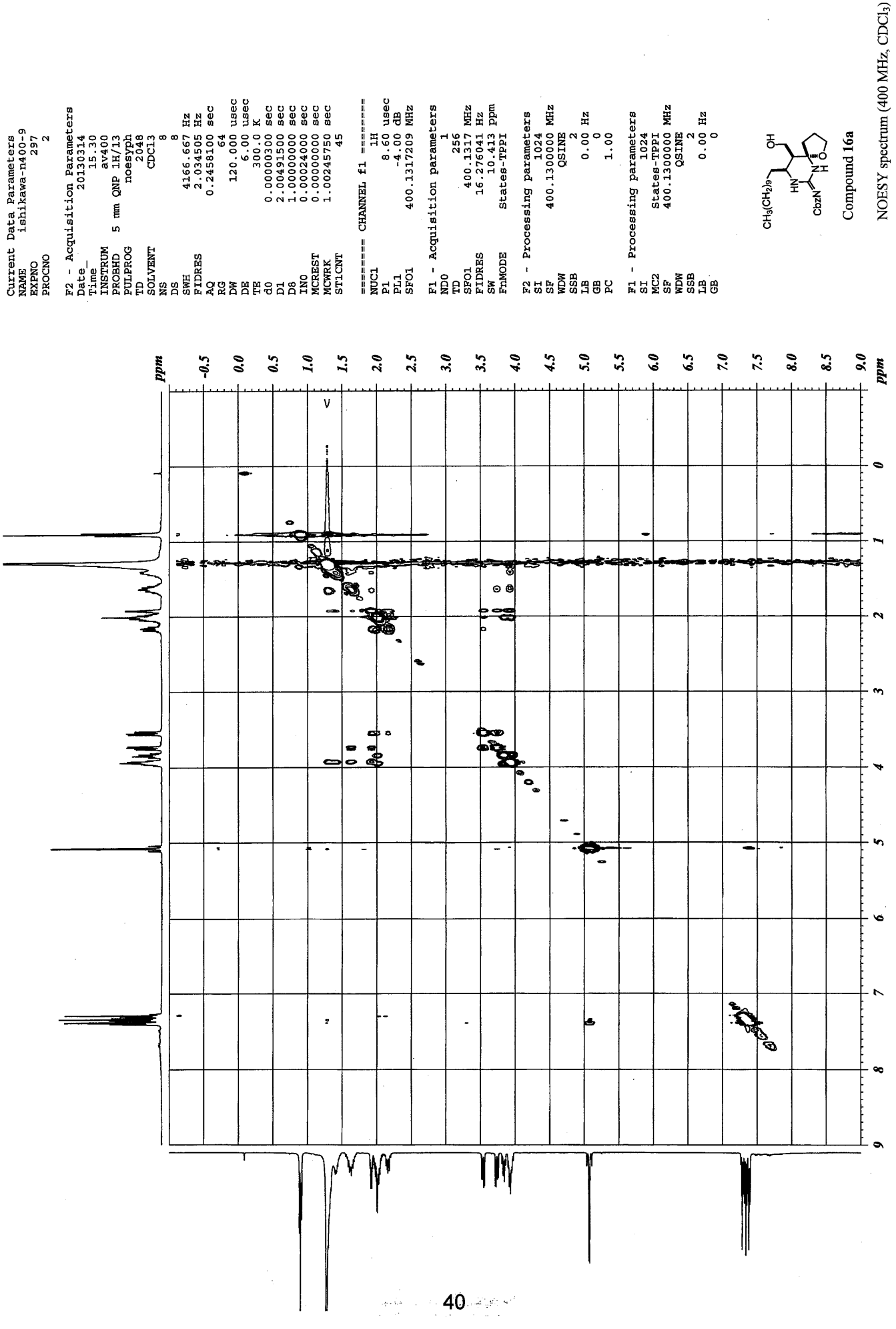

Current Data Parameters
NAME ishikawa-n400-9
EXPNO 156
PROCNO 2
F2 - Acquisition Parameters
Date_ 20121207
Time_ 21.01
INSTRUM av400
PROBHD 5 mm QNP 1H/13
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 2367
DS 4
SWH 23980.814 Hz
FIDRES 0.365918 Hz
AQ 1.3664756 sec
RG 16384
DW 20.850 usec
DE 30.00 usec
TE 300.0 K
D1 2.00000000 sec
d11 0.03000000 sec
d12 0.00002000 sec
CHANNEL f1
NUC1 13C
P1 9.00 usec
PL1 -3.00 dB
SFO1 100.6228298 MHz
CHANNEL f2
CPDPRG2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 -4.00 dB
PL12 14.80 dB
PL13 14.80 dB
SFO2 400.1316005 MHz
F2 - Processing parameters
SI 32768
SF 100.6127766 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 3.00
Compound 14a
13C NMR (100 MHz, CDCl3)
14.05
20.82
22.61
25.81
29.25
29.38
29.45
29.52
31.26
31.82
41.19
48.86
50.51
58.47
62.18
63.33
66.40
76.68
77.00
77.21
77.32
93.10
127.73
127.84
128.26
136.73
157.15
163.09
170.40
ppm

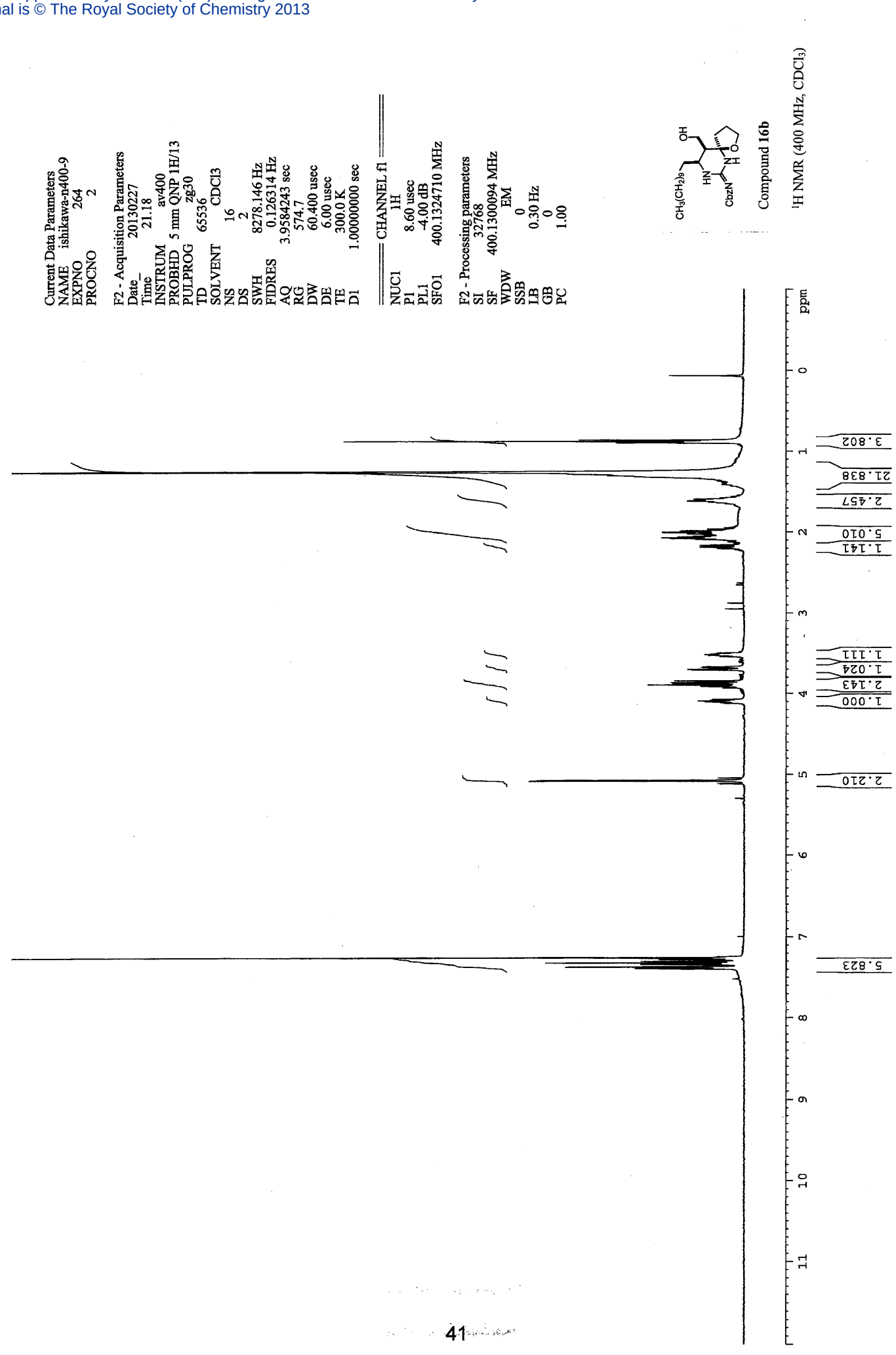


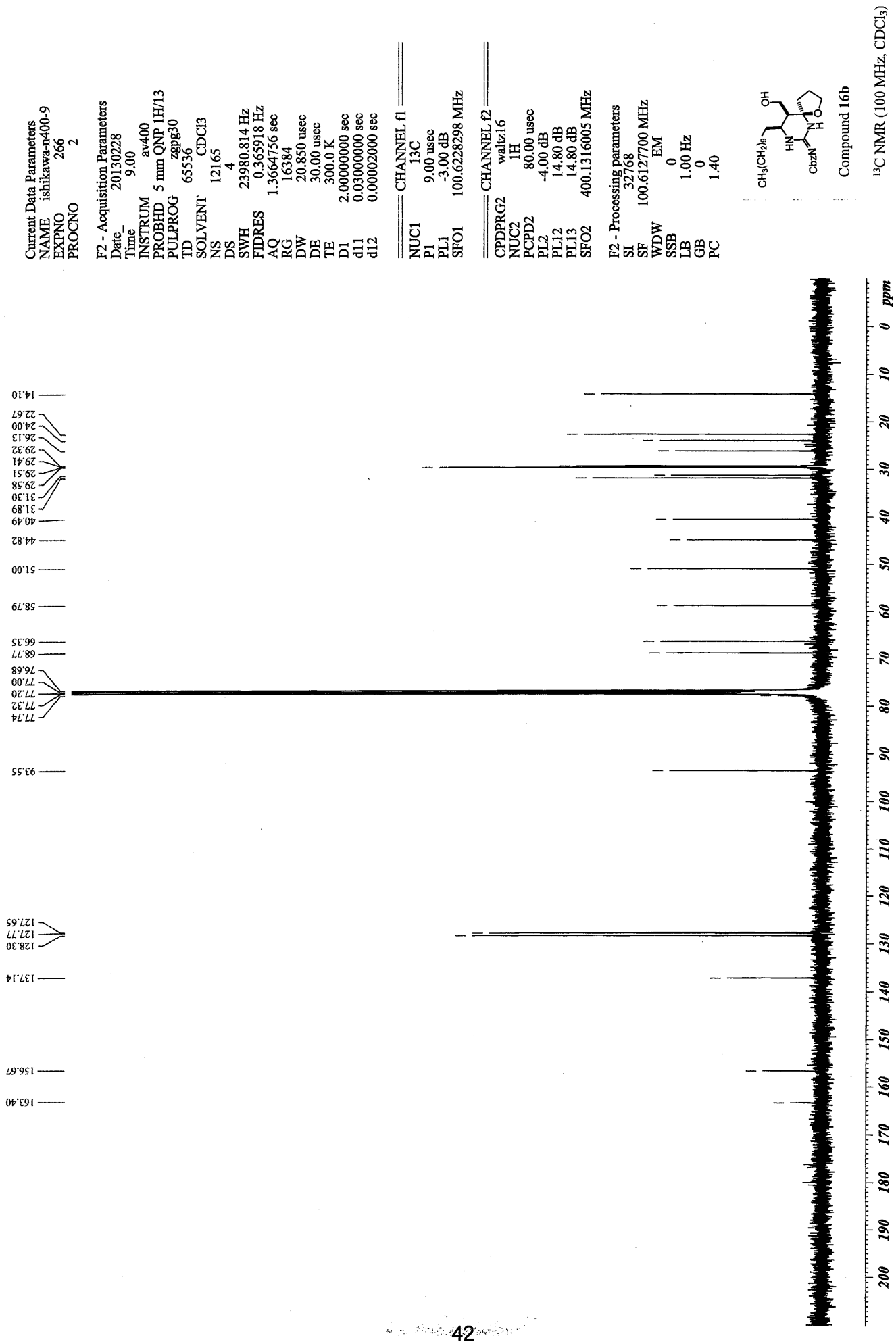

Current Data Parameters
NAME ishikawa-n400-9
EXPNO 190
PROCNO 2
F2 - Acquisition Parameters
Date_ 20121220
Time 17.01
INSTRUM av400
PROBHD 5 mm QNP 1H/13
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 587
DS 4
SWH 23980.814 Hz
FIDRES 0.365918 Hz
AQ 1.3664756 sec
RG 16384
DW 20.850 usec
DE 30.00 usec
TE 300.0 K
D1 2.00000000 sec
d11 0.03000000 sec
d12 0.00002000 sec
CHANNEL f1
NUC1 13C
P1 9.00 usec
PL1 -3.00 dB
SFO1 100.6228298 MHz
CHANNEL f2
CPDPRG2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 -4.00 dB
PL12 14.80 dB
PL13 14.80 dB
SFO2 400.1316005 MHz
F2 - Processing parameters
SI 32768
SF 100.6127788 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
CH3(CH2)9
OAc
HN
CbzN
Compound 15
13C NMR (100 MHz, CDCl3)
14.02
20.79
22.58
24.61
25.73
29.23
29.36
29.43
29.50
31.39
31.80
34.78
41.77
49.65
60.64
66.37
66.07
76.68
77.00
77.32
90.18
127.51
127.74
128.18
137.09
158.01
163.69
170.46
ppm

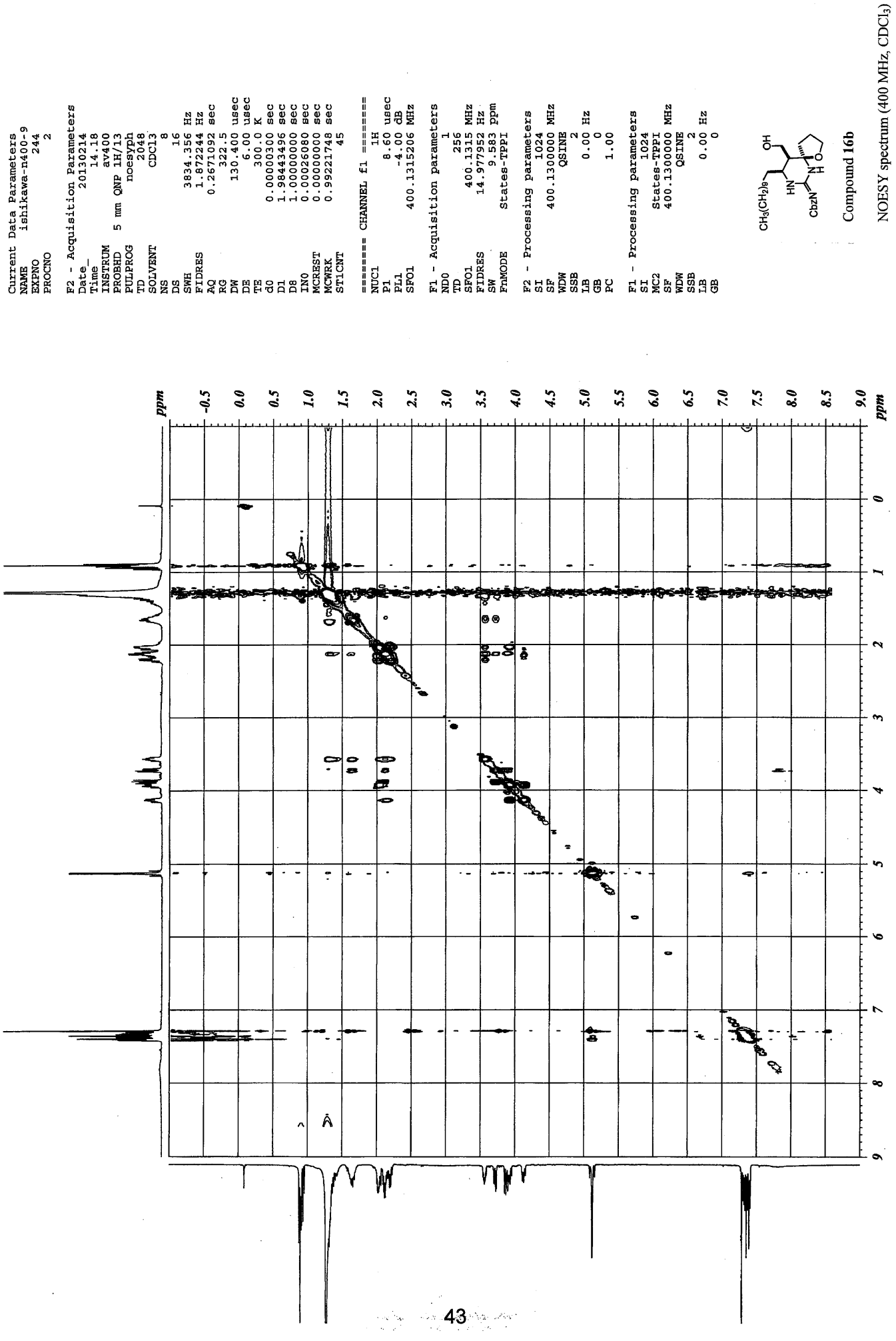


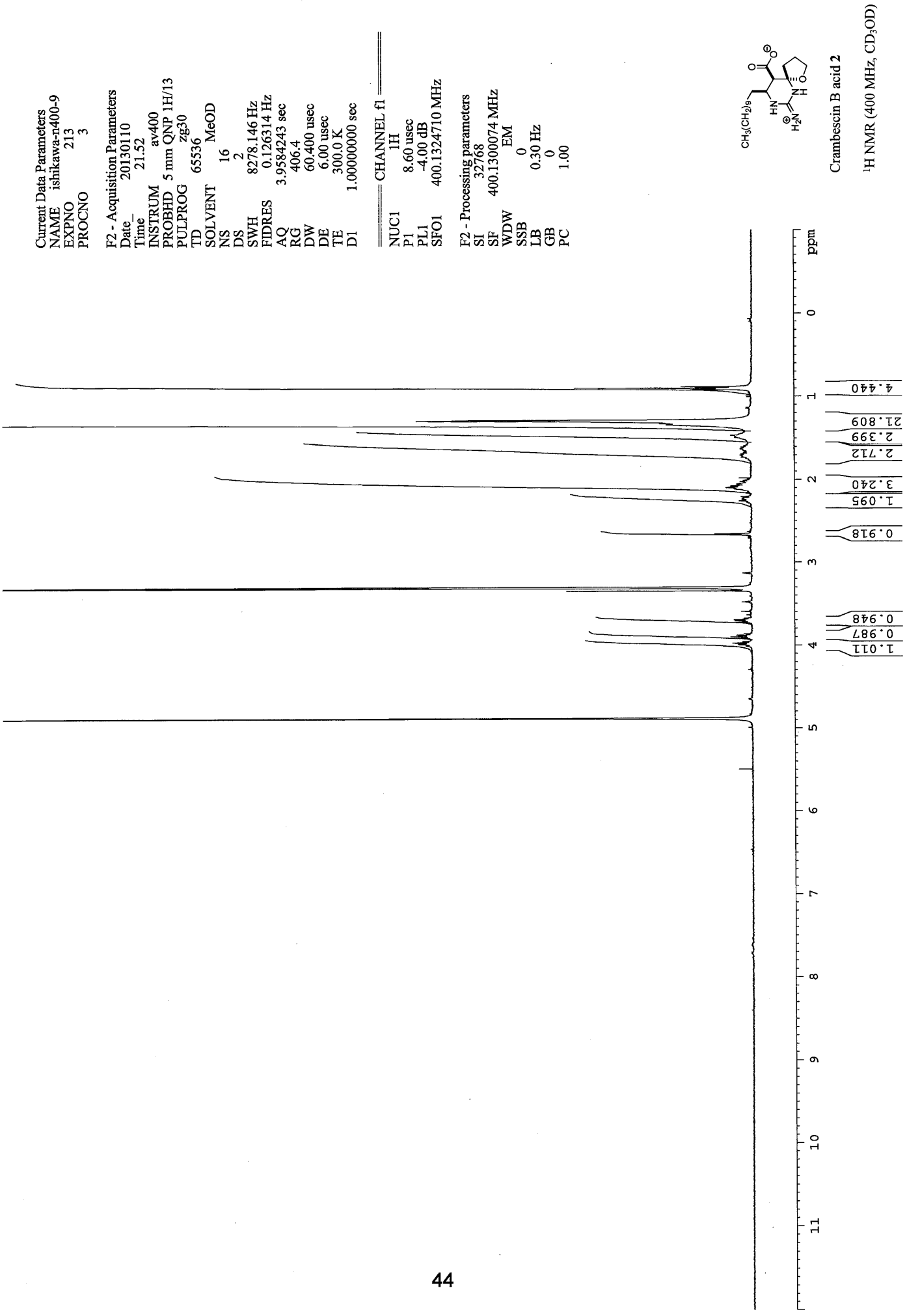

Current Data Parameters
NAME ishikawa-n400-9
EXPNO 225
PROCNO 2
F2 - Acquisition Parameters
Date_ 20130123
Time 9.10
INSTRUM av400
PROBHD 5 mm QNP 1H/13
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 12181
DS 4
SWH 23980.814 Hz
FIDRES 0.365918 Hz
AQ 1.3664756 sec
RG 16384
DW 20.850 usec
DE 30.00 usec
TE 300.0 K
D1 2.00000000 sec
d11 0.03000000 sec
d12 0.00002000 sec
CHANNEL f1
NUC1 13C
P1 9.00 usec
PL1 -3.00 dB
SFO1 100.6228298 MHz
CHANNEL f2
CPDPRG2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 -4.00 dB
PL12 14.80 dB
PL13 14.80 dB
SFO2 400.1316005 MHz
F2 - Processing parameters
SI 32768
SF 100.6127729 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 3.00
Compound 16a
13C NMR (100 MHz, CDCl3)
ppm

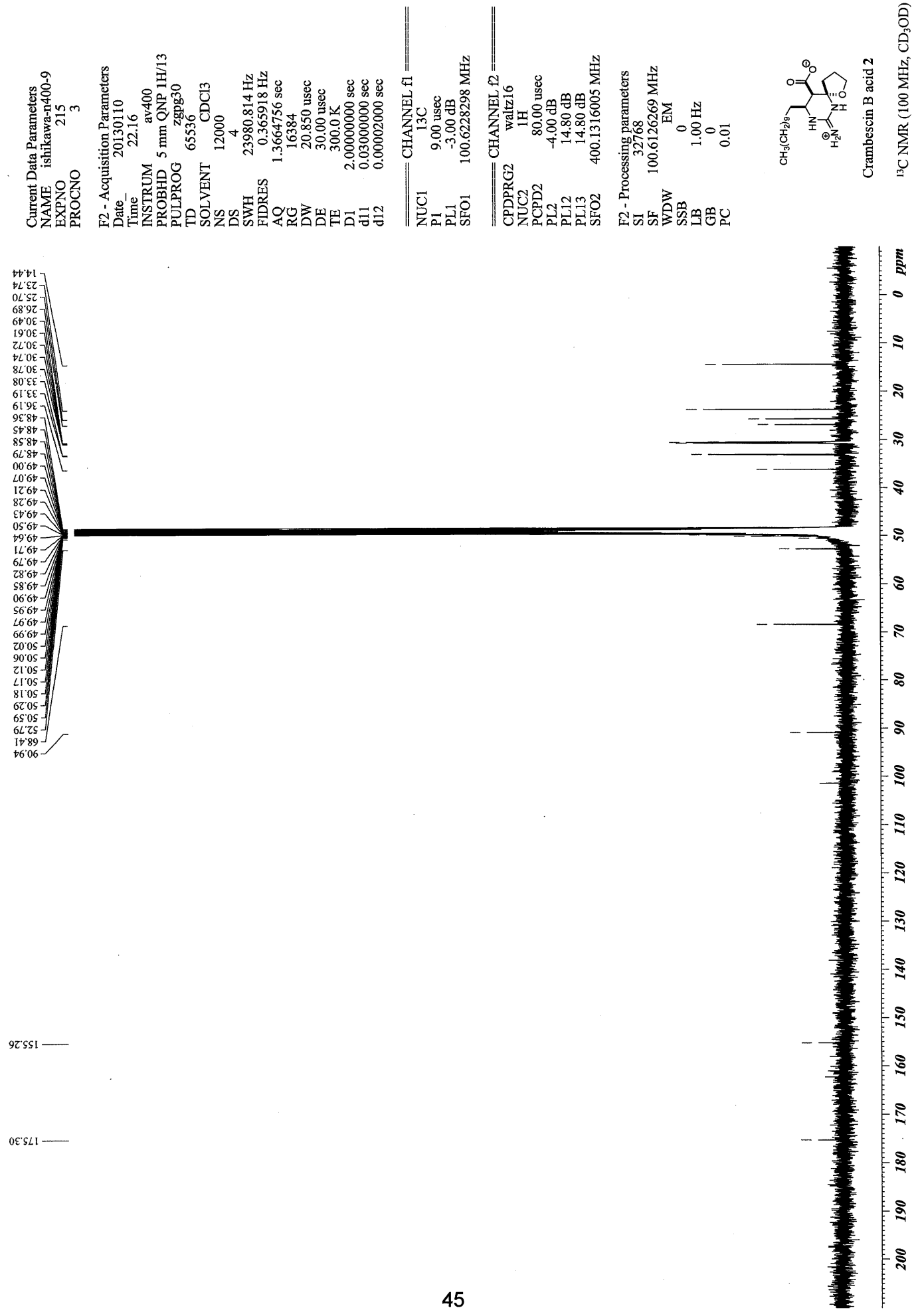

Current Data Parameters
NAME ishikawa-n400-9
EXPNO 297
PROCNO 2
F2 - Acquisition Parameters
Date_ 20130314
Time 15.30
INSTRUM av400
PROBHD 5 mm QNP 1H/13
PULPROG noesyph
TD 2048
SOLVENT CDCl3
NS 8
DS 8
SWH 4166.667 Hz
FIDRES 2.034505 Hz
AQ 0.2458100 sec
RG 64
DW 120.000 usec
DE 6.00 usec
TE 300.0 K
d0 0.00000300 sec
D1 2.00491500 sec
D8 1.00000000 sec
IN0 0.00024000 sec
MCREST 0.00000000 sec
MCWRK 1.00245750 sec
STLCNT 45
======== CHANNEL f1 ========
NUC1 1H
P1 8.60 usec
PL1 -4.00 dB
SFO1 400.1317209 MHz
F1 - Acquisition parameters
ND0 1
TD 256
SFO1 400.1317 MHz
FIDRES 16.276041 Hz
SW 10.413 ppm
FnMODE States-TPPI
F2 - Processing parameters
SI 1024
SF 400.1300000 MHz
WDW QSINE
SSB 2
LB 0.00 Hz
GB 0
PC 1.00
F1 - Processing parameters
SI 1024
MC2 States-TPPI
SF 400.1300000 MHz
WDW QSINE
SSB 2
LB 0.00 Hz
GB 0
OH
HN
CbzN
Compound 16a
NOESY spectrum (400 MHz, CDCl3)
ppm
ppm

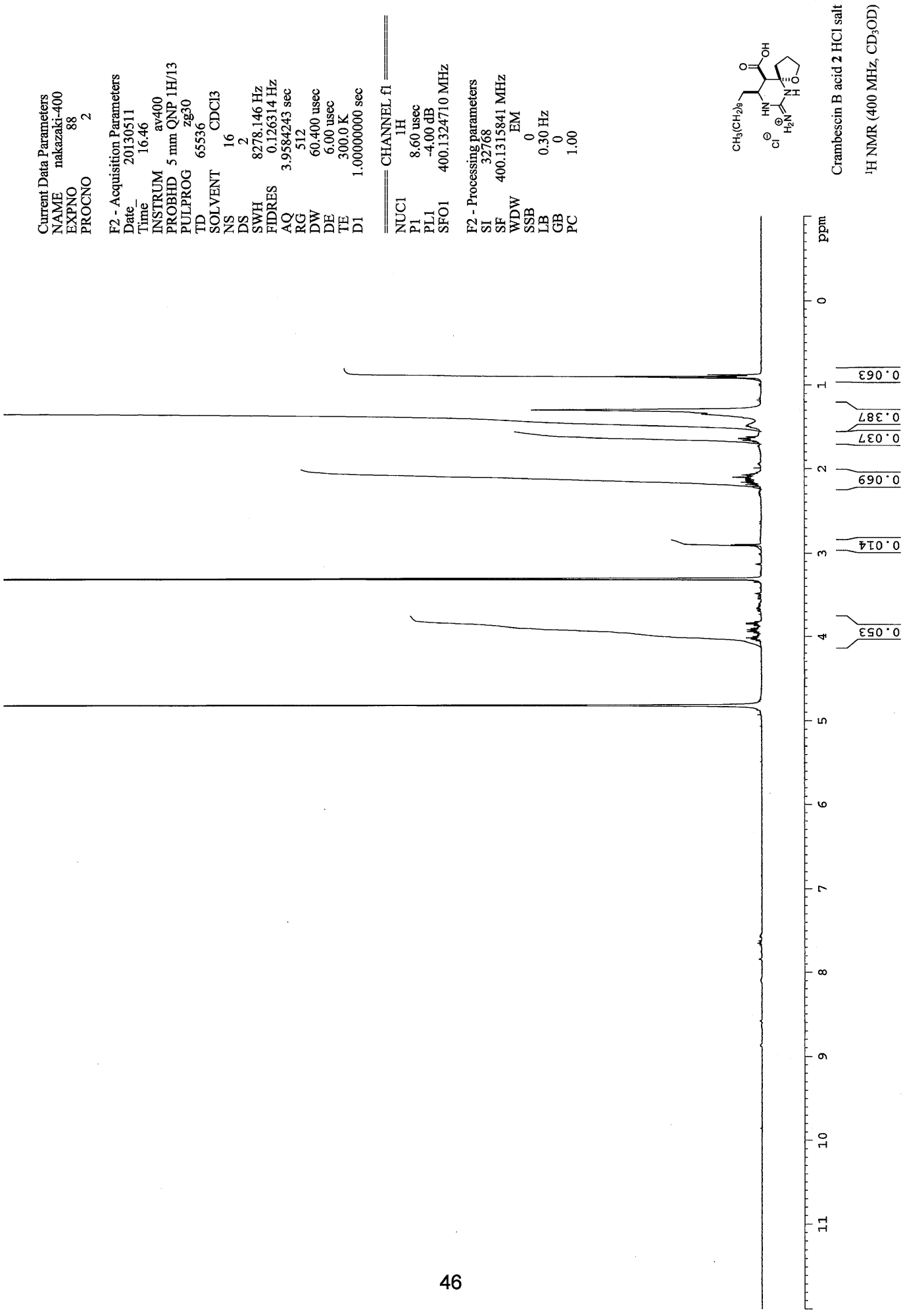

Current Data Parameters
NAME ishikawa-n400-9
EXPNO 264
PROCNO 2
F2 - Acquisition Parameters
Date_ 20130227
Time 21.18
INSTRUM av400
PROBHD 5 mm QNP 1H/13
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8278.146 Hz
FIDRES 0.126314 Hz
AQ 3.9584243 sec
RG 574.7
DW 60.400 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec
CHANNEL f1
NUC1 1H
P1 8.60 usec
PL1 -4.00 dB
SFO1 400.1324710 MHz
F2 - Processing parameters
SI 32768
SF 400.1300094 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
OH
CH3(CH2)8
HN
CbzN
O
N
H
Compound 16b
1H NMR (400 MHz, CDCl3)
ppm
0
1
2
3
4
5
6
7
8
9
10
11
3.802
21.838
2.457
5.010
1.141
1.111
1.024
2.143
1.000
2.210
5.823


Current Data Parameters
NAME ishikawa-n400-9
EXPNO 266
PROCNO 2
F2 - Acquisition Parameters
Date_ 20130228
Time 9.00
INSTRUM av400
PROBHD 5 mm QNP 1H/13
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 12165
DS 4
SWH 23980.814 Hz
FIDRES 0.365918 Hz
AQ 1.3664756 sec
RG 16384
DW 20.850 usec
DE 30.00 usec
TE 300.0 K
D1 2.00000000 sec
d11 0.03000000 sec
d12 0.00002000 sec
CHANNEL f1
NUC1 13C
P1 9.00 usec
PL1 -3.00 dB
SFO1 100.6228298 MHz
CHANNEL f2
CPDPRG2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 -4.00 dB
PL12 14.80 dB
PL13 14.80 dB
SFO2 400.1316005 MHz
F2 - Processing parameters
SI 32768
SF 100.6127700 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
Compound 16b
13C NMR (100 MHz, CDCl3)
ppm


Current Data Parameters
NAME ishikawa-n400-9
EXPNO 244
PROCNO 2
F2 - Acquisition Parameters
Date_ 20130214
Time 14.18
INSTRUM av400
PROBHD 5 mm QNP 1H/13
PULPROG noesyph
TD 2048
SOLVENT CDCl3
NS 8
DS 16
SWH 3834.356 Hz
FIDRES 1.872244 Hz
AQ 0.2671092 sec
RG 322.5
DW 130.400 usec
DE 6.00 usec
TE 300.0 K
d0 0.00000300 sec
D1 1.98443496 sec
D8 1.00000000 sec
IN0 0.00026080 sec
MCREST 0.00000000 sec
MCWRK 0.99221748 sec
ST1CNT 45
======== CHANNEL f1 ========
NUC1 1H
P1 8.60 usec
PL1 -4.00 dB
SFO1 400.1315206 MHz
F1 - Acquisition parameters
ND0 1
TD 256
SFO1 400.1315 MHz
FIDRES 14.977952 Hz
SW 9.583 ppm
FnMODE States-TPPI
F2 - Processing parameters
SI 1024
SF 400.1300000 MHz
WDW QSINE
SSB 2
LB 0.00 Hz
GB 0
PC 1.00
F1 - Processing parameters
SI 1024
MC2 States-TPPI
SF 400.1300000 MHz
WDW QSINE
SSB 2
LB 0.00 Hz
GB 0
CH3(CH2)9
OH
HN
CbzN
O
Compound 16b
NOESY spectrum (400 MHz, CDCl3)
ppm
ppm




Current Data Parameters
NAME ishikawa-n400-9
EXPNO 215
PROCNO 3
F2 - Acquisition Parameters
Date_ 20130110
Time 22.16
INSTRUM av400
PROBHD 5 mm QNP 1H/13
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 12000
DS 4
SWH 23980.814 Hz
FIDRES 0.365918 Hz
AQ 1.3664756 sec
RG 16384
DW 20.850 usec
DE 30.00 usec
TE 300.0 K
D1 2.00000000 sec
d11 0.03000000 sec
d12 0.00002000 sec
CHANNEL f1
NUC1 13C
P1 9.00 usec
PL1 -3.00 dB
SFO1 100.6228298 MHz
CHANNEL f2
CPDPRG2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 -4.00 dB
PL12 14.80 dB
PL13 14.80 dB
SFO2 400.1316005 MHz
F2 - Processing parameters
SI 32768
SF 100.6126269 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 0.01
Crambescin B acid 2
13C NMR (100 MHz, CD3OD)
ppm


Current Data Parameters
NAME nakazaki-400
EXPNO 88
PROCNO 2
F2 - Acquisition Parameters
Date_ 20130511
Time_ 16.46
INSTRUM av400
PROBHD 5 mm QNP 1H/13
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8278.146 Hz
FIDRES 0.126314 Hz
AQ 3.9584243 sec
RG 512
DW 60.400 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 8.60 usec
PL1 -4.00 dB
SFO1 400.1324710 MHz
F2 - Processing parameters
SI 32768
SF 400.1315841 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
0.063
0.387
0.037
0.069
0.014
0.053
ppm
Crambescin B acid 2 HCl salt
1H NMR (400 MHz, CD3OD)