

Amphipathic α -Helix Mimetics Based on a 1,2- Diphenylacetylene Scaffold

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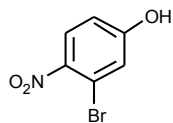
Supplementary Information

Chemistry

Experimental Section

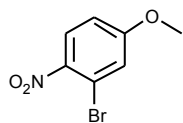
Unless otherwise stated, all reactions were performed under an inert (N₂) atmosphere. Reagents and solvents were reagent grade and purchased from Sigma-Aldrich, Alfa Aesar, Oakwood and TCI America. ¹H and ¹³C NMR spectra were recorded on a Varian INOVA 400 MHz NMR spectrometer at 25 °C. Chemical shifts are reported in parts per million (ppm). Data for ¹H NMR are reported as follows: chemical shift (δ ppm) (integration, multiplicity, coupling constant (Hz)). Multiplicities are reported as follows: s = singlet, d = doublet, t = triplet, q = quartet, sep = septet, dd = doublet of doublets, m = multiplet. Data for ¹³C are reported in terms of chemical shifts (δ ppm). The residual solvent peak was used as an internal reference. The mass spectra were obtained on an Electrospray TOF (ESI-TOF) mass spectrometer (BrukeramaZon X). Microwave assisted reactions were performed in a Biotage Initiator 2.5 microwave reactor.

3-Bromo-4-nitrophenol (**4**)



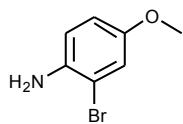
Sulfuric acid (98%, 10.0 mL, 187.4 mmol) was added dropwise to a solution of NaNO₃ (13.5 g, 159.6 mmol) in H₂O (30 mL), keeping the temperature between 20 and 30 °C. A solution of 3-bromophenol (12.0 g, 69.4 mmol) dissolved in EtOH (25 mL) was then added dropwise at this temperature. The reaction mixture was stirred at room temperature overnight, then poured into ice-water (300 mL), and extracted with dichloromethane (3 x 100 mL). The combined organic layer was dried over anhydrous Na₂SO₄, filtered, concentrated and purified by silica column chromatography (30 % EtOAc in hexanes) to afford compound **4** in 37.1 % (5.59 g) yield as a yellow solid. ¹H-NMR (DMSO-d₆, 400 MHz) δ 11.2 (1H, s, OH), 7.98 (1H, d, *J*=8.4 Hz, *Ar*), 7.16 (1H, d, *J*=1.6 Hz, *Ar*), 6.90 (1H, dd, *J*=8.4 Hz, 1.6 Hz, *Ar*); ¹³C-NMR (CDCl₃, 100 MHz) δ 162.5, 141.0, 129.0, 121.4, 116.2, 115.7; MS (ESI) *m/z* Calcd for C₆H₄BrNO₃ (M⁺): 216.9, Found: 217.9 (M+H⁺).

2-Bromo-4-methoxy-1-nitrobenzene (**5**)



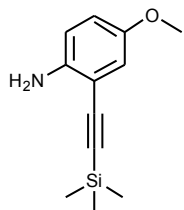
Compound **4** (2.0 g, 9.22 mmol) was dissolved in DMF (40 mL), and K₂CO₃ (2.5 g, 18.44 mmol) was added. The reaction mixture was stirred at room temperature for 20 min. After cooling to 0 °C, a solution of iodomethane (861 μL, 13.83 mmol) in DMF (5 mL) was added dropwise, and the resulting mixture was stirred at room temperature for 2 h. The reaction was quenched by adding H₂O (100 mL) and partitioned with Et₂O (200 mL). The organic layer was washed with H₂O (3 x 50 mL) and brine (50 mL). The organic layer was collected, dried over anhydrous Na₂SO₄, filtered, concentrated, and purified by silica column chromatography (20 % EtOAc in hexanes) to afford compound **5** in 85.0 % (1.81 g) yield as a yellow solid. ¹H-NMR (CDCl₃, 400 MHz) δ 7.89 (1H, d, *J*=9.2 Hz, *Ar*), 7.22 (1H, s, *Ar*), 6.91 (1H, d, *J*=9.2 Hz, *Ar*), 3.89 (3H, s, OCH₃); MS (ESI) *m/z* Calcd for C₇H₆BrNO₃ (M⁺): 231.0, Found: 232.1 (M+H⁺).

2-Bromo-4-methoxyaniline (**6**)



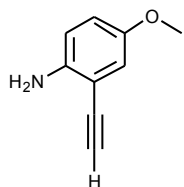
Compound **5** (2.0 g, 8.75 mmol) was dissolved in EtOAc (87 mL). SnCl₂·2H₂O (9.9 g, 43.75 mmol) was added, then the reaction mixture was stirred at 50 °C overnight. The reaction mixture was diluted with EtOAc (400 mL), and partitioned with sat'd NaHCO₃(aq). The organic layer was collected, dried over anhydrous Na₂SO₄, filtered, concentrated, and purified by silica column chromatography (33 % EtOAc in hexanes) to afford compound **6** in 80.7 % (1.42 g) yield as a brown oil. ¹H-NMR (CDCl₃, 400 MHz) δ 7.00 (1H, s, *Ar*), 6.72 (2H, m, *Ar*), 3.82 (2H, m, NH₂), 3.73 (3H, s, OCH₃); ¹³C-NMR (CDCl₃, 100 MHz) δ 152.6, 137.9, 117.5, 116.6, 115.0, 109.6, 55.9; MS (ESI) *m/z* Calcd for C₇H₈BrNO (M⁺): 201.0, Found: 202.0 (M+H⁺).

4-Methoxy-2-((trimethylsilyl)ethynyl)aniline (7)



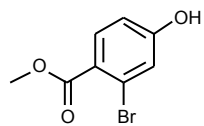
Compound **6** (1.40 g, 6.97 mmol), triphenylphosphine (55 mg, 3 mol %) and copper (I) iodide (13 mg, 1 mol %) were added to an oven-dried reaction flask containing toluene (27 mL) and Et₃N (7 mL). The reaction mixture was stirred at room temperature for 5 min with N₂ (g) bubbling. Bis(triphenylphosphine)palladium (II) dichloride (48 mg, 1 mol %) and a solution of trimethylsilylacetylene (1.49 mL, 10.46 mmol) in Et₃N (3 mL) were added. The reaction mixture was stirred at 100 °C for 24 h. The reaction was cooled to room temperature, then diluted with EtOAc (300 mL) and washed with brine (3 x 70 mL). The organic layer was collected, dried over anhydrous Na₂SO₄, filtered, concentrated and purified by silica column chromatography (8 % EtOAc in hexanes) to afford compound **7** in 70.0 % (1.07 g) yield as a brown oil. ¹H-NMR (CDCl₃, 400 MHz) δ 6.81 (1H, s, *Ar*), 6.74 (1H, d, *J*=8.8 Hz, *Ar*), 6.63 (1H, d, *J*=8.8 Hz, *Ar*), 3.70 (3H, s, OCH₃), 3.50 (2H, bs, NH₂), 0.24 (9H, s, Si(CH₃)₃); ¹³C-NMR (CDCl₃, 100 MHz) δ 151.7, 142.4, 117.7, 115.8, 115.6, 108.3, 101.7, 99.7, 55.7, 0.08; MS (ESI) *m/z* Calcd for C₁₂H₁₇NOSi (M⁺): 219.1, Found: 220.1 (M+H⁺).

2-Ethynyl-4-methoxyaniline (8)



Compound **7** (1.07 g, 4.88 mmol) was dissolved in MeOH (40 mL). K₂CO₃ (1.35 g, 9.77 mmol) was added, and then the reaction mixture was stirred at room temperature for 30 min. After evaporation of most of the solvent, the crude material was diluted in EtOAc (200 mL), and washed with H₂O (2 x 50 mL) and brine (50 mL). The organic layer was collected, dried over anhydrous Na₂SO₄, filtered, concentrated and purified by silica column chromatography (20 % EtOAc in hexanes) to afford compound **8** in 93.0 % (667 mg) yield as a dark brown oil. ¹H-NMR (CDCl₃, 400 MHz) δ 6.87 (1H, d, *J*=2.4 Hz, *Ar*), 6.79 (1H, dd, *J*=8.4 Hz, 2.4 Hz, *Ar*), 6.64 (1H, d, *J*=8.4 Hz, *Ar*), 3.97 (2H, bs, NH₂), 3.73 (3H, s, OCH₃), 3.38 (1H, s, CH); ¹³C-NMR (CDCl₃, 100 MHz) δ 151.7, 142.7, 117.8, 116.2, 115.9, 107.2, 82.3, 80.6, 55.7; MS (ESI) *m/z* Calcd for C₉H₉NO (M⁺): 147.1, Found: 148.0 (M+H⁺).

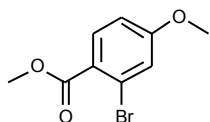
Methyl 2-bromo-4-hydroxybenzoate (10)



2-Bromo-4-nitrobenzoic acid (6.2 g, 25.3 mmol) was dissolved in MeOH (120 mL), and SOCl₂ (5.5 mL, 75.9 mmol) was added dropwise at 0 °C. The reaction mixture was refluxed for 6 h. The reaction solvent was concentrated to dryness. Residual SOCl₂ was removed by co-evaporation with CH₂Cl₂ (x3). The solid was dried under vacuum to afford methyl 2-bromo-4-nitrobenzoate in 99.5 % (6.52 g) yield as a light yellow solid. ¹H-NMR (CDCl₃, 400 MHz) δ 8.50 (1H, s, *Ar*), 8.21 (1H, d, *J*=8.4 Hz, *Ar*), 7.91 (1H, d, *J*=8.4 Hz, *Ar*), 3.97 (3H, s, OCH₃); ¹³C-NMR (CDCl₃, 100 MHz) δ 165.2, 149.2,

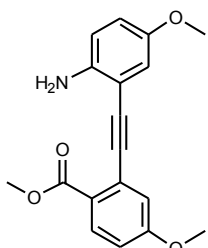
137.9, 131.7, 129.1, 122.1, 122.0, 53.1; MS (ESI) m/z Calcd for $C_8H_6BrNO_4$ (M^+): 259.0, Found: 260.1 ($M+H^+$). Next, the nitro group of methyl 2-bromo-4-nitrobenzoate (6.38 g, 24.6 mmol) was chemoselectively reduced with $SnCl_2 \cdot 2H_2O$ (27.8 g, 123.2 mmol) in a manner similar to that described for compound **6** to deliver methyl 4-amino-2-bromobenzoate in 96.0 % (5.41 g) yield as a yellow solid. 1H -NMR ($CDCl_3$, 400 MHz) δ 7.74 (1H, d, $J=8.8$ Hz, *Ar*), 6.90 (1H, d, $J=1.6$ Hz, *Ar*), 6.55 (1H, dd, $J=8.8$ Hz, 1.6 Hz, *Ar*), 4.06 (2H, s, NH_2), 3.83 (3H, s, OCH_3); ^{13}C -NMR ($CDCl_3$, 100 MHz) δ 165.9, 150.4, 133.6, 124.1, 119.7, 119.6, 112.7, 51.8; MS (ESI) m/z Calcd for $C_8H_8BrNO_2$ (M^+): 229.0, Found: 230.1 ($M+H^+$). Finally, a solution of sulfuric acid (98 %, 6 mL) in H_2O (75 mL) was added to methyl 4-amino-2-bromobenzoate (1.23 g, 5.38 mmol) and the resulting suspension was heated to 90 °C, then stirred for 5 h at this temperature. The reaction mixture was cooled to 0 °C and a solution of $NaNO_2$ (384 mg, 5.57 mmol) in H_2O (5 mL) was added dropwise, then the reaction was allowed to warm to ambient temperature. The reaction mixture was then added to a solution of sulfuric acid (98 %, 6 mL) in H_2O (75 mL) that had been preheated to 90 °C. The reaction mixture was stirred at 90 °C for 1 h, and then allowed to cool. The reaction mixture was partitioned between EtOAc (200 mL) and aqueous solution. The organic layer was collected, dried over anhydrous Na_2SO_4 , filtered, concentrated and purified by silica column chromatography (35 % EtOAc in hexanes) to afford compound **10** in 41.1 % (508 mg) yield as a light brown solid. 1H -NMR ($CDCl_3$, 400 MHz) δ 7.76 (1H, d, $J=8.8$ Hz, *Ar*), 7.09 (1H, s, *Ar*), 6.75 (1H, d, $J=8.8$ Hz, *Ar*), 3.84 (3H, s, OCH_3); ^{13}C -NMR ($CDCl_3$, 100 MHz) δ 166.2, 160.3, 133.5, 123.4, 122.1, 121.4, 114.3, 52.1; MS (ESI) m/z Calcd for $C_8H_7BrO_3$ (M^+): 230.0, Found: 231.0 ($M+H^+$).

Methyl 2-bromo-4-methoxybenzoate (**11**)



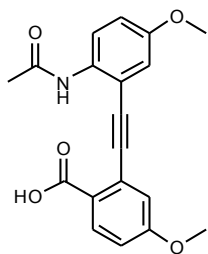
Compound **10** (815 mg, 3.54 mmol) was dissolved in DMF (20 mL). K_2CO_3 (1.17 g, 8.50 mmol) was added, then the reaction mixture was stirred at room temperature for 20 min. The reaction mixture was cooled to 0 °C, a solution of iodomethane (265 μ L, 4.25 mmol) in DMF (1 mL) was added dropwise, and then the reaction was stirred at room temperature for 2 h. The reaction was quenched by adding H_2O (50 mL), then partitioned with Et_2O (200 mL). The Et_2O layer was washed with H_2O (3 x 40 mL) and brine (40 mL). The organic layer was collected, dried over anhydrous Na_2SO_4 , filtered, concentrated, and purified by silica column chromatography (15 % EtOAc in hexanes) to afford compound **11** in 95.9 % (849 mg) yield as a brown liquid. 1H -NMR ($CDCl_3$, 400 MHz) δ 7.87 (1H, d, $J=8.4$ Hz, *Ar*), 7.19 (1H, s, *Ar*), 6.88 (1H, d, $J=8.4$ Hz, *Ar*), 3.90 (3H, s, OCH_3), 3.84 (3H, s, OCH_3); ^{13}C -NMR ($CDCl_3$, 100 MHz) δ 165.8, 162.2, 133.1, 123.5, 123.3, 119.7, 113.0, 55.6, 52.1; MS (ESI) m/z Calcd for $C_9H_9BrO_3$ (M^+): 244.0, Found: 244.1 (M^+).

Methyl 2-((2-amino-5-methoxyphenyl)ethynyl)-4-methoxybenzoate (**12**)



Compound **11** (106 mg, 0.43 mmol) and copper (I) iodide (1.6 mg, 2 mol %) were added to an oven-dried reaction flask containing toluene (2 mL) and Et₃N (2 mL). The reaction mixture was stirred at room temperature for 5 min with N₂ (g) bubbling. Bis(triphenylphosphine)palladium(II) dichloride (3 mg, 1 mol %) and a solution of compound **8** (63 mg, 0.43 mmol) in Et₃N (1 mL) were added. The reaction mixture was stirred at 100 °C for 24 h. The reaction was cooled to room temperature, then diluted with EtOAc (50 mL) and washed with brine (3 x 20 mL). The organic layer was collected, dried over anhydrous Na₂SO₄, filtered, concentrated and purified by silica column chromatography (20 % EtOAc in hexanes) to afford compound **12** in 62.8 % (84 mg) yield as a brown solid. ¹H-NMR (CDCl₃, 400 MHz) δ 8.00 (1H, d, *J*=8.4 Hz, *Ar*), 7.14 (1H, s, *Ar*), 6.93 (1H, d, *J*=1.6 Hz, *Ar*), 6.88 (1H, dd, *J*=8.4 Hz, 1.6 Hz, *Ar*), 6.81 (1H, dd, *J*=8.4 Hz, 1.6 Hz, *Ar*), 6.68 (1H, d, *J*=8.4 Hz, *Ar*), 4.79 (2H, s, NH₂), 3.89 (6H, s, 2 x OCH₃), 3.76 (3H, s, OCH₃); ¹³C-NMR (CDCl₃, 100 MHz) δ 165.9, 162.3, 151.4, 144.5, 132.8, 126.6, 122.9, 118.5, 117.9, 115.8, 115.6, 114.4, 107.6, 93.9, 92.6, 56.0, 55.7, 52.2; MS (ESI) *m/z* Calcd for C₁₈H₁₇NO₄ (M⁺): 311.1, Found: 312.0 (M+H⁺).

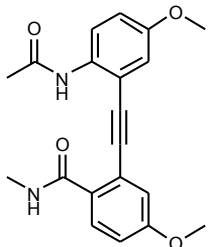
2-((2-Acetamido-5-methoxyphenyl)ethynyl)-4-methoxybenzoic acid (**13**)



Compound **12** (84 mg, 0.27 mmol) was dissolved in MeOH (4 mL), and then acetic anhydride (28 μL, 0.30 mmol) was added. The reaction mixture was refluxed for 30 min. The reaction solvent was removed by evaporation, and then the residue was dissolved in CH₂Cl₂ (30 mL), and washed with H₂O (3 x 10 mL). The organic layer was collected, dried over Na₂SO₄, filtered, concentrated and purified by silica column chromatography (40 % EtOAc in hexanes) to afford methyl 2-((2-acetamido-5-methoxyphenyl)ethynyl)-4-methoxybenzoate in 81.8 % (78 mg) yield as a yellow solid. ¹H-NMR (CDCl₃, 400 MHz) δ 9.30 (1H, s, NH), 8.51 (1H, d, *J*=9.6 Hz, *Ar*), 8.03 (1H, d, *J*=8.8 Hz, *Ar*), 7.14 (1H, s, *Ar*), 7.01 (1H, s, *Ar*), 6.93 (1H, d, *J*=9.6 Hz, *Ar*), 6.89 (1H, d, *J*=8.8 Hz, *Ar*), 3.88 (6H, s, 2 x OCH₃), 3.79 (3H, s, OCH₃), 2.39 (3H, s, CH₃); ¹³C-NMR (CDCl₃, 100 MHz) δ 169.8, 166.0, 162.7, 154.9, 135.3, 132.8, 126.2, 122.5, 121.2, 118.2, 116.7, 116.2, 114.9, 112.4, 94.6, 91.0, 55.8, 55.7, 52.3, 24.6; MS (ESI) *m/z* Calcd for C₂₀H₁₉NO₅ (M⁺): 353.1, Found: 352.0 (M-H⁺). LiOH·H₂O (25 mg, 0.60 mmol) was added to a solution of methyl 2-((2-acetamido-5-methoxyphenyl)ethynyl)-4-methoxybenzoate (41 mg, 0.12 mmol) in THF/MeOH/H₂O (ratio=3:1:1, 2 mL). The reaction mixture was stirred at room temperature overnight. The reaction mixture was neutralized by adding 1M HCl (aq) and partitioned between EtOAc and sat'd NaH₂PO₄ (aq). The organic layer was collected, dried over Na₂SO₄, filtered, concentrated and dried under vacuum to afford compound **13** in 99.5 % (40 mg) yield as a brown solid. ¹H-NMR (DMSO-d₆, 400 MHz) δ 9.69 (1H, s, NH), 8.27 (1H, d, *J*=8.4 Hz, *Ar*), 8.01 (1H, d, *J*=8.0 Hz, *Ar*), 7.19 (1H, s, *Ar*), 7.08 (1H, s, *Ar*), 7.06 (1H,

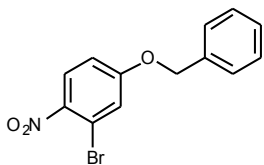
d, $J=8.0$ Hz, *Ar*), 6.99 (1H, d, $J=8.4$ Hz, *Ar*), 3.87 (3H, s, OCH₃), 3.77 (3H, s, OCH₃), 2.26 (3H, s, CH₃); ¹³C-NMR (DMSO-d₆, 100 MHz) δ 169.5, 167.6, 161.4, 154.8, 135.0, 133.1, 124.3, 121.6, 117.5, 116.6, 115.6, 115.2, 113.2, 96.1, 89.8, 56.0, 55.7, 24.5; MS (ESI) m/z Calcd for C₁₉H₁₇NO₅ (M⁺): 339.1, Found: 338.1 (M-H⁺).

2-((2-Acetamido-5-methoxyphenyl)ethynyl)-4-methoxy-N-methylbenzamide (2)



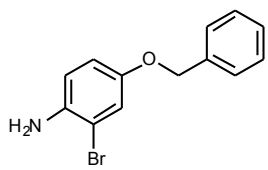
To a solution of compound **13** (40 mg, 0.12 mmol), HBTU (68 mg, 0.18 mmol) and CH₃NH₂·HCl (12 mg, 0.18 mmol) in DMF (2 mL) was added DIPEA (84 μ L, 0.48 mmol). The reaction mixture was stirred at room temperature overnight, then diluted with EtOAc (40 mL), and washed with H₂O (4 x 10 mL). The organic layer was collected, dried over Na₂SO₄, filtered, concentrated and purified by silica column chromatography (30 % EtOAc in CH₂Cl₂) to afford compound **2** in 80.5 % (34 mg) yield as a white solid. ¹H-NMR (CDCl₃, 400 MHz) δ 9.15 (1H, s, NH), 8.47 (1H, d, $J=8.8$ Hz, *Ar*), 7.50 (1H, d, $J=8.8$ Hz, *Ar*), 7.13 (1H, s, *Ar*), 6.98 (1H, s, *Ar*), 6.92-6.87 (2H, m, *Ar*), 6.15 (1H, s, NH), 3.87 (3H, s, OCH₃), 3.79 (3H, s, OCH₃), 2.98 (3H, d, $J=3.2$ Hz, CH₃NH), 2.45 (3H, s, CH₃); ¹³C-NMR (CDCl₃+CD₃OD, 100 MHz) δ 170.5, 168.2, 160.8, 154.8, 134.4, 129.0, 128.6, 123.2, 121.5, 117.7, 116.0, 115.9, 114.6, 112.9, 93.8, 89.5, 55.4, 26.7, 24.0; MS (ESI) m/z Calcd for C₂₀H₂₀N₂O₄ (M⁺): 352.1, Found: 352.1 (M⁺).

4-(Benzyloxy)-2-bromo-1-nitrobenzene (15)



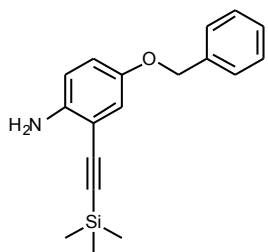
Compound **4** (930 mg, 4.29 mmol) was dissolved in DMF (40 mL), then K₂CO₃ (890 mg, 6.44 mmol) was added. The reaction mixture was stirred at room temperature for 20 min, at which point benzyl bromide (407 μ L, 3.43 mmol) was added. After stirring overnight at room temperature, the reaction was quenched by adding H₂O (100 mL), and partitioned with Et₂O (200 mL). The organic layer was washed with H₂O (3 x 50 mL) and brine (50 mL). The organic layer was collected, dried over anhydrous Na₂SO₄, filtered, concentrated, and purified by silica column chromatography (15 % EtOAc in hexanes) to afford compound **15** in 99.5 % (1.05 g) yield as a brown solid. ¹H-NMR (CDCl₃, 400 MHz) δ 7.99 (1H, d, $J=8.4$ Hz, *Ar*), 7.41 (5H, m, *Ar*), 7.31 (1H, s, *Ar*), 6.99 (1H, d, $J=8.4$ Hz, *Ar*), 5.13 (2H, s, OCH₂); ¹³C-NMR (CDCl₃, 100 MHz) δ 161.7, 142.5, 134.9, 128.8, 128.6, 127.9, 127.5, 121.0, 116.8, 114.1, 70.9; MS (ESI) m/z Calcd for C₁₃H₁₀BrNO₃ (M⁺): 307.0, Found: 308.1 (M+H⁺).

4-(Benzyloxy)-2-bromoaniline (16)



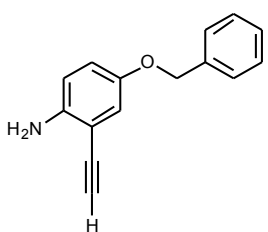
The title compound **16** was prepared from compound **15** (1.06 g, 3.46 mmol) and $\text{SnCl}_2 \cdot 2\text{H}_2\text{O}$ (3.90 g, 17.28 mmol) in a manner similar to that described for compound **6** in 72.2 % (692 mg) yield as a brown solid. $^1\text{H-NMR}$ (CDCl_3 , 400 MHz) δ 7.40-7.33 (5H, m, *Ar*), 7.10 (1H, s, *Ar*), 6.81 (1H, d, $J=8.0$ Hz, *Ar*), 6.73 (1H, d, $J=8.0$ Hz, *Ar*), 4.97 (2H, s, OCH_2), 3.79 (2H, bs, NH_2); $^1\text{H-NMR}$ (CDCl_3 , 400 MHz) δ 151.8, 138.1, 136.9, 128.5, 127.9, 127.5, 118.9, 116.5, 116.0, 109.6, 70.9; MS (ESI) m/z Calcd for $\text{C}_{13}\text{H}_{12}\text{BrNO}$ (M^+): 227.0, Found: 228.1 ($\text{M}+\text{H}^+$).

4-(Benzyloxy)-2-((trimethylsilyl)ethynyl)aniline (17)



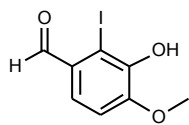
Compound **16** (388 mg, 1.40 mmol), triphenylphosphine (37 mg, 10 mol %) and copper (I) iodide (53 mg, 10 mol %) were added to a 20 mL oven-dried microwave vial containing toluene (3.0 mL) and Et_3N (3.0 mL). The reaction mixture was stirred at room temperature for 5 min with N_2 (g) bubbling. Bis(triphenylphosphine)palladium(II) dichloride (98 mg, 10 mol %) and a solution of trimethylsilylacetylene (300 μL , 2.10 mmol) in Et_3N (1.0 mL) were added successively. The reaction was placed in the microwave reactor and heated to 110 $^\circ\text{C}$ for 1 h. The reaction was cooled to room temperature and diluted with EtOAc (60 mL), and washed with brine (3 x 30 mL). The organic layer was collected, dried over anhydrous Na_2SO_4 , filtered, concentrated and purified by silica column chromatography (30 % EtOAc in hexanes) to afford compound **17** in 85.2 % (352 mg) yield as a yellow oil. $^1\text{H-NMR}$ (CDCl_3 , 400 MHz) δ 7.38-7.29 (5H, m, *Ar*), 6.92 (1H, s, *Ar*), 6.81 (1H, d, $J=8.8$ Hz, *Ar*), 6.63 (1H, d, $J=8.8$ Hz, *Ar*), 4.95 (3H, s, OCH_3), 4.00 (2H, bs, NH_2), 0.24 (9H, s, $\text{Si}(\text{CH}_3)_3$); $^{13}\text{C-NMR}$ (CDCl_3 , 100 MHz) δ 150.8, 142.7, 137.2, 128.4, 127.8, 127.4, 118.7, 117.2, 115.7, 108.3, 101.6, 99.8, 70.8, 0.09; MS (ESI) m/z Calcd for $\text{C}_{18}\text{H}_{21}\text{NOSi}$ (M^+): 295.1, Found: 296.1 ($\text{M}+\text{H}^+$).

4-(Benzyloxy)-2-ethynylaniline (18).



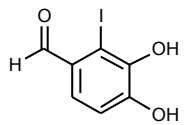
The title compound **18** was prepared from compound **17** (177 mg, 0.60 mmol) and K_2CO_3 (166 mg, 1.20 mmol) in a manner similar to that described for compound **8** in 99.5 % (133 mg) yield as a dark brown solid. $^1\text{H-NMR}$ (CDCl_3 , 400 MHz) δ 7.40-7.32 (5H, m, *Ar*), 6.96 (1H, s, *Ar*), 6.86 (1H, d, $J=8.8$ Hz, *Ar*), 6.66 (1H, d, $J=8.8$ Hz, *Ar*), 4.97 (2H, s, OCH_2), 3.99 (2H, s, NH_2), 3.37 (1H, s, $\equiv\text{CH}$); $^{13}\text{C-NMR}$ (CDCl_3 , 100 MHz) δ 150.8, 143.0, 137.1, 128.5, 127.8, 127.4, 118.8, 117.7, 115.8, 107.2, 82.4, 80.5, 70.5; MS (ESI) m/z Calcd for $\text{C}_{15}\text{H}_{13}\text{NO}$ (M^+): 223.1, Found: 224.0 ($\text{M}+\text{H}^+$).

3-Hydroxy-2-iodo-4-methoxybenzaldehyde (**20**)



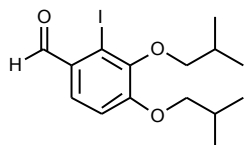
A mixture of 3-hydroxy-4-methoxybenzaldehyde (4.56 g, 30.0 mmol), pyridine (4.44 mL, 56.0 mmol) and iodine (3.82 g, 15.0 mmol) in H₂O (200 mL) was maintained at 30 °C. H₂O₂ (30 %, 4.38 mL) was added over 1 h. Upon addition of all of the H₂O₂, the reaction mixture was stirred for a further 2 h, and then 10 % aqueous Na₂SO₃ (45 mL) was added, maintaining the reaction temperature at 40 °C for 30 min. After another 1 h at room temperature, a yellow precipitate was detected, which was collected by filtration. The precipitate was washed with H₂O (3 x 60 mL), and dried in vacuum oven at 70 °C to afford compound **20** in 45.6 % (3.80 g) yield as a yellow solid. ¹H-NMR (DMSO-d₆, 400 MHz) δ 9.95 (1H, s, OH), 9.87 (1H, s, CHO), 7.35 (1H, d, *J*=8.4 Hz, *Ar*), 7.11 (1H, d, *J*=8.4 Hz, *Ar*), 3.88 (3H, s, OCH₃); ¹³C-NMR (DMSO-d₆, 100 MHz) δ 195.1, 152.5, 146.8, 128.7, 123.3, 111.4, 91.5, 56.8; MS (ESI) *m/z* Calcd for C₈H₇IO₃ (M⁺): 277.9, Found: 278.9 (M+H⁺).

3,4-Dihydroxybenzaldehyde (**21**)



To a stirred suspension of compound **20** (1.20 g, 4.32 mmol) in CH₂Cl₂ (40 mL) was added AlCl₃ (691 mg, 5.18 mmol) gradually over a period of 5 min. Pyridine (1.53 mL, 19.01 mmol) was then added dropwise to the vigorously stirred mixture. The reaction mixture was refluxed for 20 h, then cooled to 0 °C, and acidified to pH ~1 with 6 N aqueous HCl. TLC analysis revealed the precipitate was mostly the product, which was then dissolved in a minimum volume of acetone. The aqueous layer of the filtrate was separated and extracted with Et₂O (3 x 80 mL). The Et₂O extracts were combined with the acetone solution of the precipitate and the resulting mixture was diluted with Et₂O (300 mL), and washed with 0.1 N aqueous HCl (3 x 30 mL). The organic layer was collected, dried over anhydrous Na₂SO₄, filtered, concentrated and dried under vacuum to afford compound **21** in 96.1 % (1.10 g) yield as a yellow solid. ¹H-NMR (DMSO-d₆, 400 MHz) δ 10.99 (1H, s, OH), 9.81 (1H, s, CHO), 9.63 (1H, s, OH), 7.24 (1H, d, *J*=8.4 Hz, *Ar*), 6.87 (1H, d, *J*=8.4 Hz, *Ar*); ¹³C-NMR (DMSO-d₆, 100 MHz) δ 194.9, 151.4, 146.1, 127.6, 123.6, 115.0, 92.7; MS (ESI) *m/z* Calcd for C₇H₅IO₃ (M⁺): 263.9, Found: 264.9 (M+H⁺).

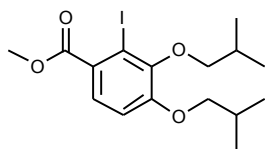
2-Iodo-3,4-diisobutoxybenzaldehyde (**22**)



K₂CO₃ (1.92 g, 13.92 mmol) was added to a solution of compound **21** (918 mg, 3.48 mmol) in DMF (20 mL), which was then stirred at room temperature for 30 min. Isobutyl iodide (1.20 mL, 10.43 mmol) was added to the reaction mixture, and stirring was continued at 50 °C for 3 days. The reaction was diluted with Et₂O (200 mL) and washed with H₂O (3 x 50 mL), and brine. The organic layer was collected, dried over anhydrous Na₂SO₄, filtered, concentrated, and purified by

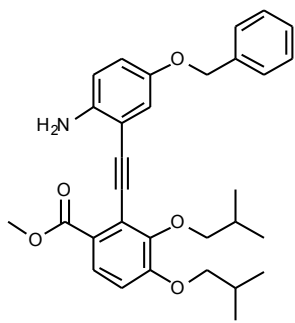
silica column chromatography (8 % EtOAc in hexanes) to afford compound **22** in 73.1 % (955 mg) yield as a colorless oil. $^1\text{H-NMR}$ (CDCl_3 , 400 MHz) δ 10.01 (1H, s, CHO), 7.68 (1H, d, $J=8.4$ Hz, *Ar*), 6.93 (1H, d, $J=8.4$ Hz, *Ar*), 3.84 (2H, d, $J=5.6$ Hz, OCH_2), 3.78 (2H, d, $J=5.6$ Hz, OCH_2), 2.23-2.14 (2H, m, 2 x $\text{CH}(\text{CH}_3)_2$), 1.11 (6H, d, $J=6.4$ Hz, $\text{CH}(\text{CH}_3)_2$), 1.08 (6H, d, $J=6.4$ Hz, $\text{CH}(\text{CH}_3)_2$); $^{13}\text{C-NMR}$ (CDCl_3 , 100 MHz) δ 195.2, 157.3, 147.9, 128.6, 127.0, 112.3, 100.7, 79.1, 75.3, 29.2, 28.2, 19.4, 19.2; MS (ESI) m/z Calcd for $\text{C}_{15}\text{H}_{21}\text{IO}_3$ (M^+): 376.1, Found: 377.0 ($\text{M}+\text{H}^+$).

Methyl 2-iodo-3,4-diisobutoxybenzoate (**23**)



To a solution of compound **22** (300 mg, 0.80 mmol) in acetone (8 mL) and H_2O (4 mL) was added KMnO_4 (441 mg, 2.79 mmol) in portions over 12 h. The reaction mixture was stirred at room temperature for 24 h and then filtered over a pad of Celite, washed with H_2O (50 mL) and acetone (50 mL). The organic solvent was removed by evaporation, and the aqueous layer was basified by adding 1 N aqueous NaOH (4.5 mL), and then washed with Et_2O (3 x 20 mL). The aqueous layer was cooled to 0 $^\circ\text{C}$, acidified to pH \sim 2 with 3 N aqueous HCl , then extracted with EtOAc (4 x 30 mL). The combined organic layers were dried over anhydrous Na_2SO_4 , filtered, concentrated, and dried under vacuum to afford 2-iodo-3,4-diisobutoxybenzoic acid in 82.3 % (258 mg) yield as a brown solid. $^1\text{H-NMR}$ (DMSO-d_6 , 400 MHz) δ 12.86 (1H, s, CO_2H), 7.46 (1H, d, $J=8.4$ Hz, *Ar*), 7.06 (1H, d, $J=8.4$ Hz, *Ar*), 3.80 (2H, d, $J=5.6$ Hz, OCH_2), 3.65 (2H, d, $J=5.6$ Hz, OCH_2), 2.07-2.00 (2H, m, 2 x $\text{CH}(\text{CH}_3)_2$), 1.01 (6H, d, $J=6.8$ Hz, $\text{CH}(\text{CH}_3)_2$), 0.98 (6H, d, $J=6.8$ Hz, $\text{CH}(\text{CH}_3)_2$); $^{13}\text{C-NMR}$ (DMSO-d_6 , 100 MHz) δ 168.0, 154.1, 148.2, 129.4, 127.2, 113.0, 94.7, 78.5, 74.9, 29.1, 28.2, 19.7, 19.4; MS (ESI) m/z Calcd for $\text{C}_{15}\text{H}_{21}\text{IO}_4$ (M^+): 392.5, Found: 391.5 ($\text{M}-\text{H}^+$). The title compound **23** was prepared from 2-iodo-3,4-diisobutoxybenzoic acid (220 mg, 0.56 mmol), K_2CO_3 (116 mg, 0.84) and iodomethane (38 μL , 0.62 mmol) in a manner similar to that described for compound **11** in 99.5 % (226 mg) yield as a colorless oil. $^1\text{H-NMR}$ (CDCl_3 , 400 MHz) δ 7.55 (1H, d, $J=8.8$ Hz, *Ar*), 6.83 (1H, d, $J=8.8$ Hz, *Ar*), 3.87 (3H, s, OCH_3), 3.77 (2H, d, $J=6.0$ Hz, OCH_2), 3.73 (2H, d, $J=6.0$ Hz, OCH_2), 2.20-2.11 (2H, m, 2 x $\text{CH}(\text{CH}_3)_2$), 1.08 (6H, d, $J=5.6$ Hz, $\text{CH}(\text{CH}_3)_2$), 1.05 (6H, d, $J=5.6$ Hz, $\text{CH}(\text{CH}_3)_2$); $^{13}\text{C-NMR}$ (CDCl_3 , 100 MHz) δ 166.7, 154.7, 148.8, 127.5, 127.4, 111.8, 94.8, 78.8, 75.1, 52.2, 29.1, 28.3, 19.4, 19.2; MS (ESI) m/z Calcd for $\text{C}_{16}\text{H}_{23}\text{IO}_4$ (M^+): 406.1, Found: 407.1 ($\text{M}+\text{H}^+$).

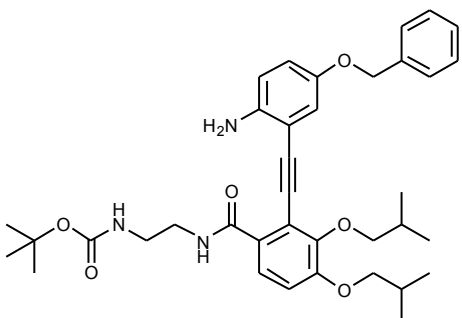
Methyl 2-((2-amino-5-(benzyloxy)phenyl)ethynyl)-3,4-diisobutoxybenzoate (24)



The title compound **24** was prepared from compound **18** (177 mg, 0.60 mmol), compound **23** (188 mg, 0.46 mmol), copper (I) iodide (9 mg, 10 mol %), bis(triphenylphosphine)palladium(II) dichloride (32 mg, 10 mol %) and Et₃N (3 mL) in a manner similar to that described for compound **17** in 50.0 % (147 mg) yield as a dark brown oil. ¹H-NMR (CDCl₃, 400 MHz) δ 7.75 (1H, d, *J*=8.8 Hz, *Ar*), 7.42-7.28 (5H, m, *Ar*), 6.99 (1H, s, *Ar*), 6.85-6.80 (2H, m, *Ar*), 6.65 (1H, d, *J*=9.6 Hz, *Ar*), 4.97 (2H, s, OCH₂), 4.80 (2H, s, NH₂), 3.87 (5H, s, OCH₂+OCH₃), 3.79 (2H, d, *J*=5.6 Hz,

OCH₂), 2.19-2.13 (2H, m, 2 x CH(CH₃)₂), 1.11 (6H, d, *J*=5.6 Hz, CH(CH₃)₂), 1.06 (6H, d, *J*=5.6 Hz, CH(CH₃)₂); ¹³C-NMR (CDCl₃, 100 MHz) δ 165.8, 155.8, 150.3, 149.8, 144.4, 137.3, 134.7, 128.4, 127.8, 127.4, 127.2, 122.9, 119.9, 119.0, 116.7, 115.4, 111.4, 108.1, 96.3, 89.4, 79.9, 75.0, 70.8, 51.9, 29.4, 28.3, 19.4, 19.2; MS (ESI) *m/z* Calcd for C₃₁H₃₅NO₅ (M⁺): 501.2, Found: 501.1 (M⁺).

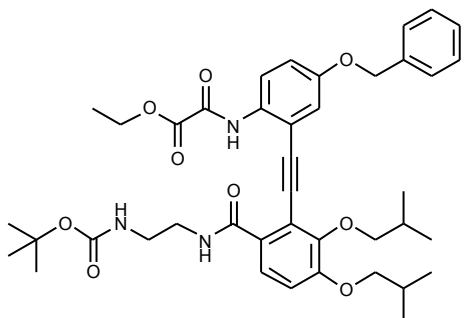
tert-Butyl 2-((2-((2-amino-5-(benzyloxy)phenyl)ethynyl)-3,4-diisobutoxybenzamido)ethyl)carbamate (25)



To a solution of **24** (100 mg, 0.20 mmol) in THF/MeOH/H₂O (ratio=3:1:1, 3 mL) was added LiOH·H₂O (42 mg, 1.00 mmol). The reaction mixture was stirred at room temperature overnight. The reaction mixture was neutralized by adding 1M HCl (aq) and partitioned between EtOAc and sat'd NaH₂PO₄ (aq). The organic layer was collected, dried over Na₂SO₄, filtered, concentrated and dried under vacuum to afford 2-((2-Amino-5-(benzyloxy)phenyl)ethynyl)-3,4-diisobutoxybenzoic acid in 82.0 % (80 mg) yield as a dark brown solid. ¹H-NMR (DMSO-d₆, 400 MHz) δ 7.59-7.52 (5H, m, *Ar*), 7.35 (2H, m, NH₂), 7.28 (1H, m, *Ar*), 6.94 (1H, d, *J*=8.0 Hz, *Ar*), 6.77 (1H, d, *J*=6.8 Hz, *Ar*), 6.68 (1H, s, *Ar*), 6.59 (1H, d, *J*=8.0 Hz, *Ar*), 4.92 (2H, s, OCH₂), 3.75-3.74 (4H, m, 2 x OCH₂), 2.03-2.01 (2H, m, 2 x CH(CH₃)₂), 1.02 (6H, d, *J*=5.2 Hz, CH(CH₃)₂), 0.99 (6H, d, *J*=6.0 Hz, CH(CH₃)₂); ¹³C-NMR (DMSO-d₆, 100 MHz) δ 148.8, 148.5, 146.7, 138.1, 133.6, 132.6, 132.5, 132.0, 131.9, 129.4, 129.3, 128.7, 128.5, 128.3, 127.6, 127.0, 119.1, 116.4, 114.8, 112.3, 106.3, 79.8, 75.1, 70.4, 29.4, 28.3, 19.8, 19.6; MS (ESI) *m/z* Calcd for C₃₀H₃₃NO₅ (M⁺): 487.2, Found: 486.2 (M-H⁺). The title compound **25** was prepared from 2-((2-amino-5-(benzyloxy)phenyl)ethynyl)-3,4-diisobutoxybenzoic acid (56 mg, 0.11 mmol), *N*-Boc-ethylenediamine (73 mg, 0.46 mmol), HBTU (63 mg, 0.17 mmol) and DIPEA (77 μL, 0.44 mmol) in a manner similar to that described for compound **2** in 87.0 % (60 mg) yield as a yellow oil. ¹H-NMR (CDCl₃, 400 MHz) δ 7.69-7.64 (3H, m, *Ar*), 7.54-7.50 (2H, m, *Ar*), 7.46 (2H, m, NH₂), 7.41-7.36 (3H, m, *Ar*), 7.33 (1H, d, *J*=7.2 Hz, *Ar*), 6.94 (1H, s, *Ar*), 6.87 (1H, d, *J*=8.8 Hz, *Ar*), 6.69 (1H, d, *J*=8.8 Hz, *Ar*), 4.99 (2H, s, OCH₂), 3.87 (2H, d, *J*=5.6 Hz, OCH₂), 3.78

(2H, d, $J=5.6$ Hz, OCH₂), 3.53 (2H, m, NHCH₂CH₂), 3.34 (2H, m, NHCH₂CH₂), 2.15-2.13 (2H, m, 2 x CH(CH₃)₂), 1.36 (9H, s, C(CH₃)₃), 1.07 (12H, d, $J=5.6$ Hz, 2 x CH(CH₃)₂); ¹³C-NMR (CDCl₃, 100 MHz) δ 167.7, 156.6, 154.2, 150.9, 149.7, 143.1, 137.2, 133.0, 132.1, 132.0, 131.9, 128.7, 128.5, 128.4, 127.8, 127.4, 124.7, 119.0, 116.6, 116.2, 116.0, 112.5, 112.2, 108.0, 95.8, 89.2, 40.6, 40.5, 29.6, 29.3, 28.3, 28.2, 19.4, 19.2; MS (ESI) m/z Calcd for C₃₇H₄₇N₃O₆ (M⁺): 629.3, Found: 629.4 (M⁺).

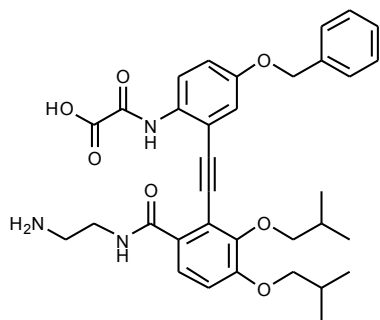
Ethyl 2-((4-(benzyloxy)-2-(((6-((2-((tert-butoxycarbonyl)amino)ethyl)carbamoyl)-2,3-diisobutoxyphenyl)ethynyl)phenyl)amino)-2-oxoacetate (26).



To an ice-cooled solution of compound **25** (60 mg, 0.10 mmol) and Et₃N (21 μL, 0.15 mmol) in CH₂Cl₂ (2 mL) was added dropwise a solution of ethyl chlorooxoacetate (14 μL, 0.12 mmol) in CH₂Cl₂ (1 mL). The reaction mixture was stirred at room temperature for 1 h and then partitioned between CH₂Cl₂ and H₂O. The organic layer was washed with brine, dried over anhydrous Na₂SO₄, filtered, concentrated and purified by silica gel column chromatography (30 % EtOAc in hexanes) to afford compound **26** in 81.0 % (59 mg) yield as a yellow solid.

¹H-NMR (CDCl₃, 400 MHz) δ 9.69 (1H, s, NH), 8.38 (1H, d, $J=9.2$ Hz, *Ar*), 7.49 (1H, d, $J=8.0$ Hz, *Ar*), 7.42-7.32 (6H, m, *Ar* + NH), 7.12 (1H, d, $J=2.4$ Hz, *Ar*), 7.07 (1H, t, $J=4.8$ Hz, NH), 7.03 (1H, dd, $J=2.4$ Hz, 9.2 Hz, *Ar*), 6.90 (1H, d, $J=9.2$ Hz, *Ar*), 5.06 (2H, s, OCH₂), 4.35 (2H, q, $J=7.2$ Hz, OCH₂CH₃), 3.87 (2H, d, $J=6.4$ Hz, OCH₂), 3.77 (2H, d, $J=6.4$ Hz, OCH₂), 3.47 (2H, m, NHCH₂CH₂), 3.28 (2H, m, NHCH₂CH₂), 2.13 (1H, sep, $J=6.4$ Hz, CH(CH₃)₂), 2.04 (1H, sep, $J=6.4$ Hz, CH(CH₃)₂), 1.35 (9H, s, C(CH₃)₃), 1.32 (3H, t, $J=7.2$ Hz, OCH₂CH₃), 1.06 (6H, d, $J=6.4$ Hz, CH(CH₃)₂), 1.00 (6H, d, $J=6.4$ Hz, CH(CH₃)₂); ¹³C-NMR (CDCl₃, 100 MHz) δ 167.2, 160.7, 156.6, 155.3, 154.8, 154.2, 150.3, 136.4, 131.7, 129.4, 128.6, 128.0, 127.4, 124.6, 121.4, 117.1, 115.1, 114.2, 113.2, 92.5, 91.1, 80.0, 79.4, 75.1, 70.3, 63.2, 40.8, 40.4, 29.2, 28.3, 28.2, 19.2, 13.8; MS (ESI) m/z Calcd for C₄₁H₅₁N₃O₉ (M⁺): 729.4, Found: 730.3 (M+H⁺).

2-((2-((6-((2-Aminoethyl)carbamoyl)-2,3-diisobutoxyphenyl)ethynyl)phenyl)amino)-2-oxoacetic acid (14**).**



Compound

2-((4-(benzyloxy)-2-((6-((2-((tert-

butoxycarbonyl)amino)ethyl)carbamoyl)-2,3-

diisobutoxyphenyl)ethynyl)phenyl)amino)-2-oxoacetic acid (Boc-protected **14**)

was prepared from compound **26** (38 mg, 0.052 mmol) and LiOH·H₂O (2.0 mg,

0.052 mmol) in a manner similar to that described for compound **13** in 99.5 %

(36 mg) yield as a light yellow solid. ¹H-NMR (DMSO-d₆, 400 MHz) δ 9.96

(1H, s, NH), 8.22 (1H, s, NH), 8.09 (1H, d, *J*=8.0 Hz, *Ar*), 7.40-7.30 (6H, m,

Ar +NH), 7.12-7.06 (3H, m, *Ar*), 6.77-6.73 (1H, m, *Ar*), 5.09 (2H, s, OCH₂), 3.80 (4H, m, 2 x OCH₂), 3.20 (2H,

m, NHCH₂CH₂), 3.02 (2H, m, NHCH₂CH₂), 2.03-2.01 (1H, m, CH(CH₃)₂), 1.95-1.94 (1H, m, CH(CH₃)₂), 1.30

(9H, s, C(CH₃)₃), 0.99 (6H, d, *J*=5.2 Hz, CH(CH₃)₂), 0.92 (6H, d, *J*=6.4 Hz, CH(CH₃)₂); ¹³C-NMR (CDCl₃, 100

MHz) δ 167.8, 167.5, 163.0, 161.4, 158.3, 157.0, 156.4, 155.6, 154.2, 153.9, 150.2, 136.4, 131.2, 128.9, 128.6,

128.1, 127.4, 124.5, 121.6, 117.2, 117.0, 115.3, 115.1, 113.1, 92.4, 91.2, 81.9, 80.0, 75.0, 70.3, 40.7, 40.1, 29.2,

28.3, 28.2, 19.3, 19.2; MS (ESI) *m/z* Calcd for C₃₉H₄₇N₃O₉ (M⁺): 701.3, Found: 701.2 (M⁺). To a solution of 2-

((4-(benzyloxy)-2-((6-((2-((tert-butoxycarbonyl)amino)ethyl)carbamoyl)-2,3-

diisobutoxyphenyl)ethynyl)phenyl)amino)-2-oxoacetic acid (Boc-protected **14**; 32 mg, 0.046 mmol) in CH₂Cl₂

(1 mL) was added 20 % TFA in CH₂Cl₂ (1 mL) and the reaction solution was stirred at room temperature for 30

min. The reaction solvent and TFA were removed by evaporation. Residual TFA was removed by co-evaporation

with toluene (x3). The product was purified by prep-TLC using CH₂Cl₂/MeOH/H₂O (ratio=62:25:4) to afford

compound **14** in 75.1 % (21 mg) yield as a white solid. ¹H-NMR (DMSO-d₆, 400 MHz) δ 9.94 (1H, s, NH), 8.34

(3H, bs, NH₂ + NH), 8.25 (1H, d, *J*=8.8 Hz, *Ar*), 7.39-7.36 (5H, m, *Ar*), 7.31 (1H, d, *J*=6.0 Hz, *Ar*), 7.15 (1H, d,

J=8.8 Hz, *Ar*), 7.07 (1H, d, *J*=8.8 Hz, *Ar*), 6.97 (1H, s, *Ar*), 5.07 (2H, s, OCH₂), 3.82 (2H, d, *J*=4.8 Hz, OCH₂),

3.79 (2H, d, *J*=4.8 Hz, OCH₂), 3.50 (2H, m, NHCH₂CH₂), 2.93 (2H, m, NHCH₂CH₂), 2.03-2.01(2H, m, 2 x

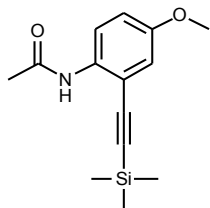
CH(CH₃)₂), 0.98 (12H, d, *J*=3.2 Hz, 2 x CH(CH₃)₂); ¹³C-NMR (DMSO-d₆, 100 MHz) δ 166.6, 165.2, 154.1,

154.0, 149.9, 137.2, 134.2, 129.4, 128.9, 128.3, 127.9, 124.6, 121.0, 117.3, 116.8, 116.3, 113.8, 113.6, 93.0, 91.1,

79.7, 74.9, 69.9, 38.7, 37.6, 29.4, 29.3, 28.2, 19.6, 19.4; MS (ESI) *m/z* Calcd for C₃₄H₃₉N₃O₇ (M⁺): 601.3, Found:

624.2 (M+Na⁺).

N-(4-methoxy-2-((trimethylsilyl)ethynyl)phenyl)acetamide



Compound 7 (10 mg, 0.046 mmol) was dissolved in MeOH (2 mL) and acetic anhydride (6 μ L, 0.059 mmol) was added then the reaction mixture was stirred at reflux condition for 1 h. The reaction solvent was removed by evaporation and the residue was dissolved in EtOAc (20 mL), and washed with water (2 x 10 mL). The organic layer was collected, dried over anhydrous Na₂SO₄, filtered, concentrated and purified by silica column chromatography (15

% EtOAc in hexanes) to afford product in 99.9 % (12 mg) yield as a light-yellow oil. ¹H-NMR (CDCl₃, 400 MHz) δ 8.24 (1H, d, J =8.8 Hz, *Ar*), 7.78 (1H, s, NH), 6.90-6.85 (2H, m, *Ar*), 3.75 (3H, s, OCH₃), 2.16 (3H, s, CH₃CO), 0.27 (9H, s, Si(CH₃)₃); ¹³C-NMR (CDCl₃, 100 MHz) δ 167.7, 155.0, 133.2, 120.6, 116.2, 115.6, 112.7, 102.0, 100.2, 55.5, 24.6, 0.08.

Computational Details

A CHARMM-compatible force field for compounds **2** and **14** was constructed in the framework of the CHARMM General Force Fields (CGenFF) version 2b7.¹ Atom types, charges and parameters were initially assigned using the CGenFF program^{2,3} and manually refined to improve analogy with existing CGenFF model compounds and standard CHARMM force field charge assignment rules. The critical rotational barrier around the triple bond was fit to its CCSD(T)/cc-pVTZ//MP2/cc-pVTZ value of 0.49 kcal/mol. We defined the phenylacetylenyl monomer as a polymerizable CHARMM residue and the various side chains as patches,^{*} thus providing basic building block for convenient generation of a variety of derivatives for present and future research. Solution phase calculations of compounds **2** and **14** were performed by placing a minimized conformation of the solute in a pre-equilibrated cubic cell containing 2025 TIP3P water molecules and removing all water molecules with atoms within 2 Å from any solute atom. In the presence of periodic boundary conditions,⁴ the system was then partially minimized for 200 steepest decent steps in order to alleviate any bad contacts or other strong interactions. Finally, the system was gradually heated to 298.15K during a 20ps MD simulation and then equilibrated for 100 ps; the edge length of the box after equilibration was about 39 Å in both cases. This equilibration was followed by a 200ns production simulation during which snapshots were taken at 2ps intervals, yielding 100000 snapshots on which analysis was performed. The particle mesh Ewald method⁵ was used for the treatment of the Coulomb interactions with a real space cutoff of 12 Å, a 6th order cubic spline and a kappa value of 0.32. For the LJ interactions, a force-switching function⁶ was applied over the range of 10-12 Å, and a long-range correction was used to account for LJ interactions beyond the cutoff distance.⁴ A timestep of 2 fs was used in conjunction with the “Leap-frog” algorithm⁷ to integrate the equations of motion. The SHAKE algorithm⁸ was applied to constrain the length of covalent bonds to hydrogen atoms to their equilibrium values. The Nosé-Hoover thermostat^{9,10} and the Langevin piston barostat¹¹ were used to generate the isothermal-isobaric ensemble (NPT) with continuous dynamics. Free energy profiles were derived from probability distributions using the relation $\Delta G = -RT \ln P$, where P represents the normalized probability.

* Keyword “PRES” in the CHARMM Residue Topology File (rtf) format specification.

Figures

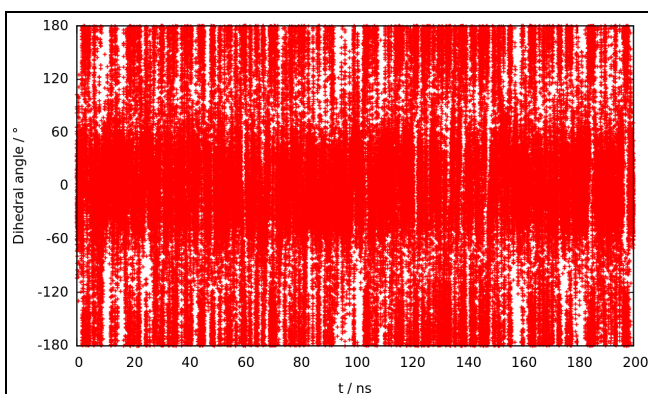


Figure A: Time series for inter-phenyl twist dihedral angle in **2** from a 200 ns MD simulation.

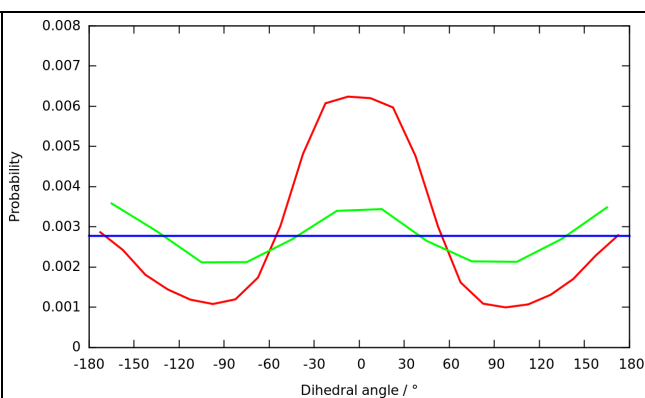


Figure B: Probability distribution (red curve) for inter-phenyl twist dihedral angle in **2**. The blue line represents an ideal free rotor and the green curve results from a 50ns MD simulation of a derivative of **2** that only has the i and $i+7$ substituents and not the $i+2$ and $i+5$ amides. Note that the green curve is not significantly different from biphenylacetylene without any substituents.

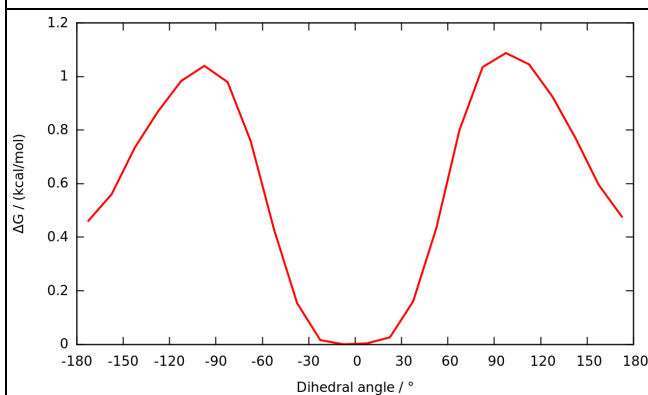


Figure C: Free energy profile as a function of the inter-phenyl twist dihedral angle in **2**.

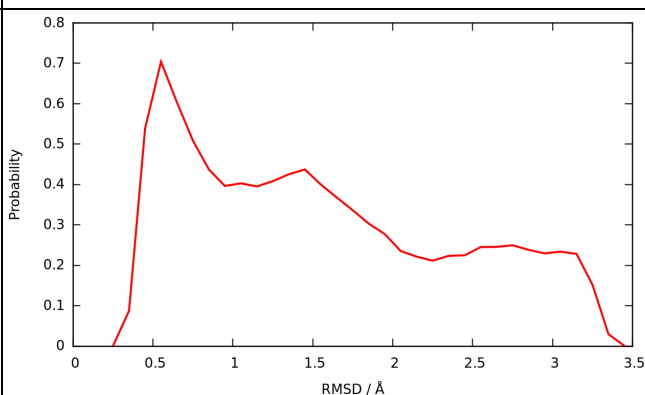


Figure D: RMSD probability distribution for the superpositions of 4 atoms in **2** with an idealized polyaniline α -helix for the 100000 MD snapshots.

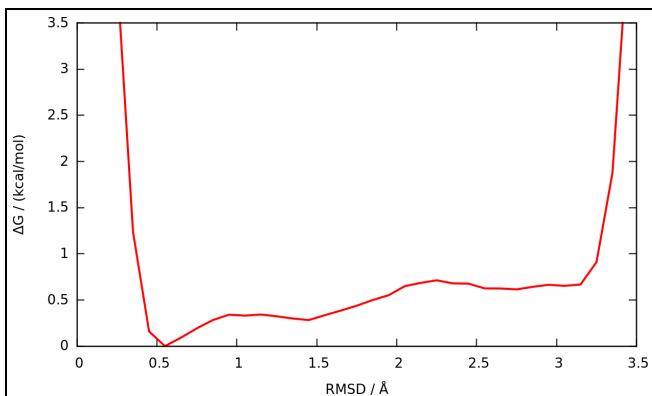


Figure E: Free energy profile as a function of the RMSD as defined in the caption of Figure D. This can be interpreted as the free energy difference between virtual ensembles of conformations that share the same RMSD and is a measure for **2**'s propensity to assume a conformation with a given RMSD.

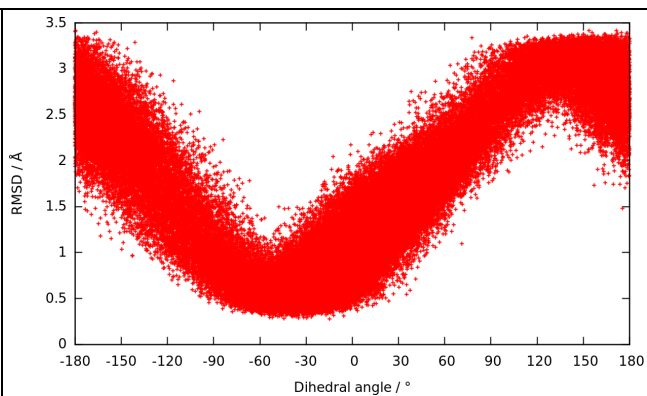


Figure F: scatter plot of RMSD in function of twist angle for the 100000 MD snapshots of **2**.

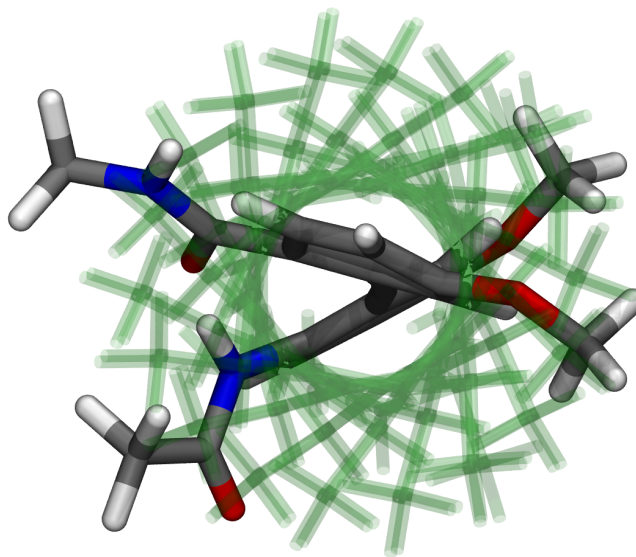


Figure G: Low-RMSD conformation (RMSD = 0.29 Å) of **2** superimposed on a poly-alanine α -helix (green), viewed along the helical axis.

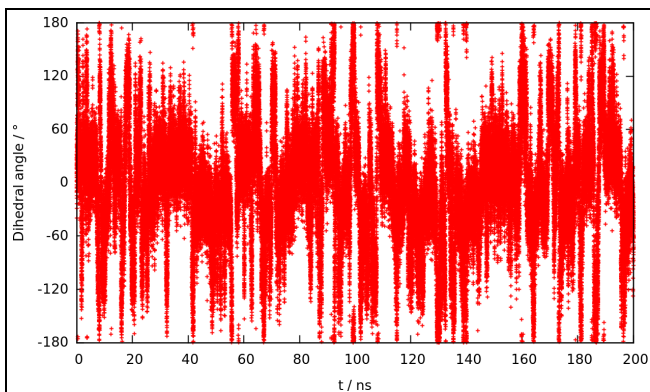


Figure H: Time series for inter-phenyl twist dihedral angle in **14** from a 200 ns MD simulation.

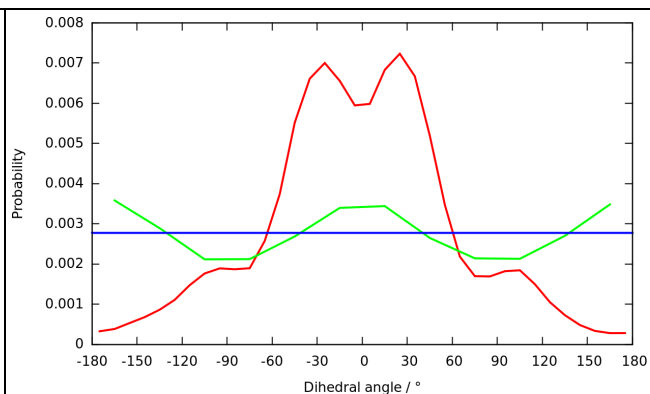


Figure I: Probability distribution (red curve) for inter-phenyl twist dihedral angle in **14**. The blue and green curves are the same as in Figure B.

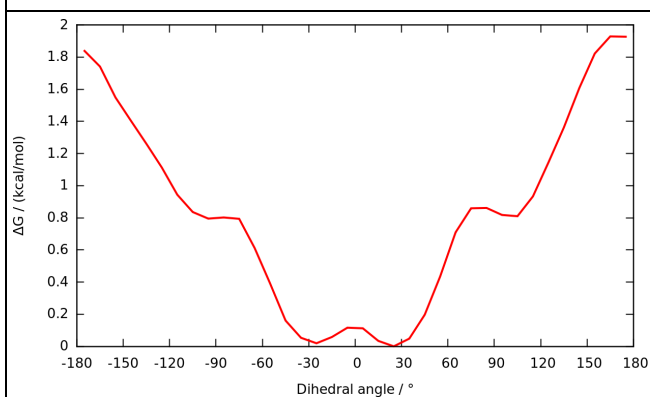


Figure J: Free energy profile as a function of the inter-phenyl twist dihedral angle in **14**.

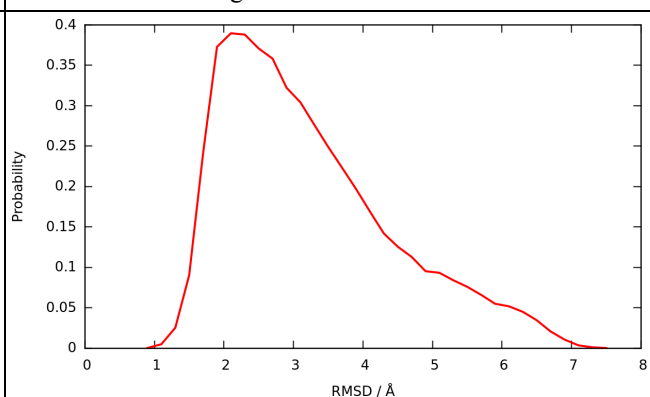


Figure K: RMSD probability distribution for the superpositions of 10 atoms in **14** with the Bim BH3 helix in complex with Mcl-1¹² for the 100000 MD snapshots.

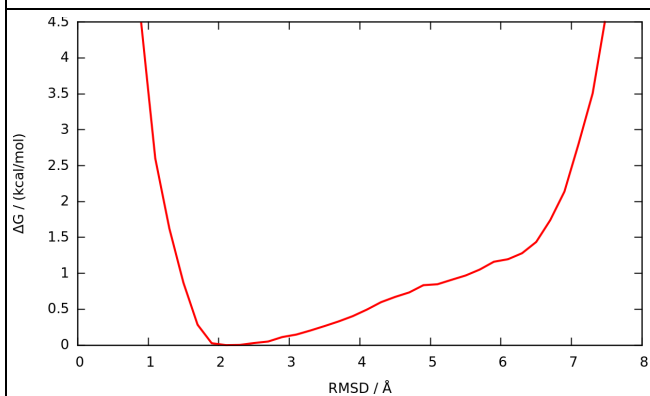


Figure L: Free energy profile as a function of the RMSD as defined in the caption of Figure K. This can be interpreted as the free energy difference between virtual ensembles of conformations that share the same RMSD and is a measure for **14**'s propensity to assume a conformation with a given RMSD.

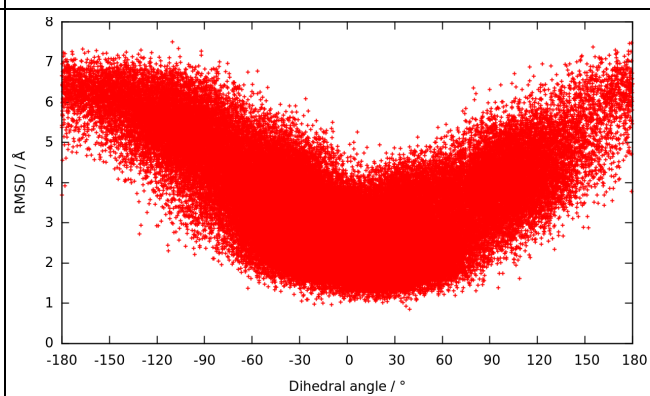


Figure M: scatter plot of RMSD in function of twist angle for the 100000 MD snapshots of **14**.

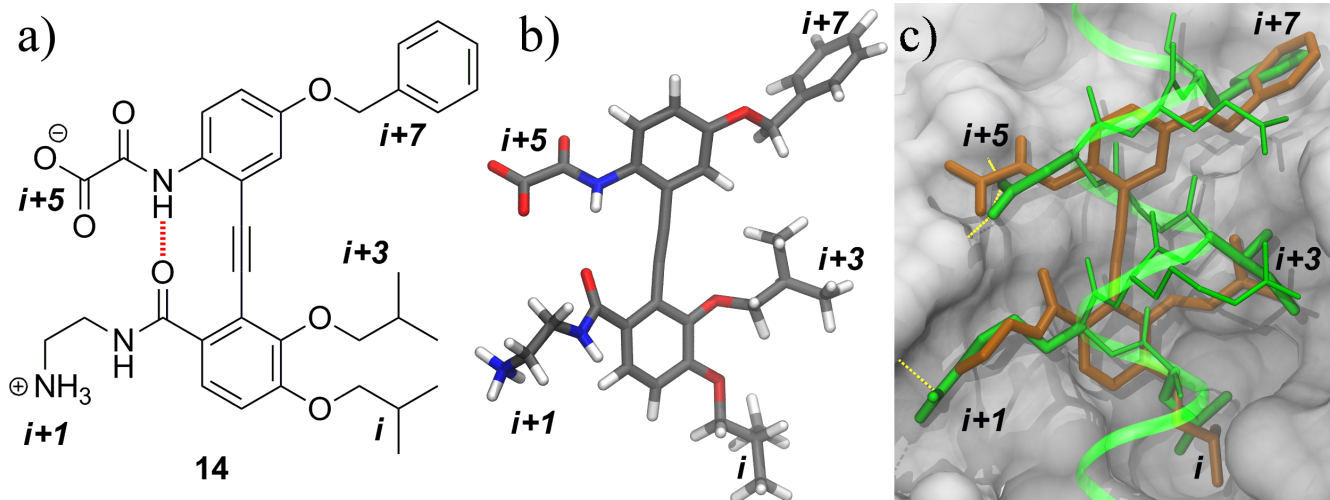


Figure N: Larger version of Figure 4 in the article.

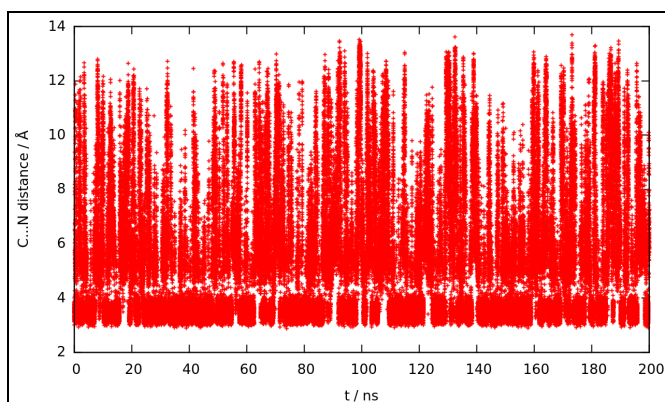


Figure O: Time series for ionic interaction distance in **14**, defined as the distance between the $.i+1$ anine N and the $.i+5$ carboxylate C atoms.

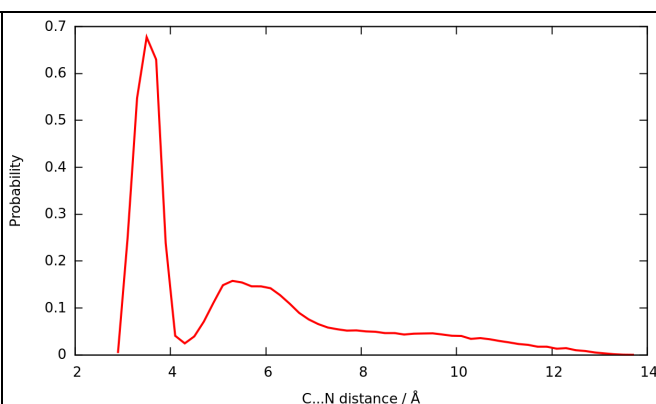


Figure P: Probability distribution for the ionic interaction distance in **14**, defined as in Figure O. The peaks around 3.5 and 5.5 Å respectively indicate a salt bridge and a water-mediated ionic interaction.

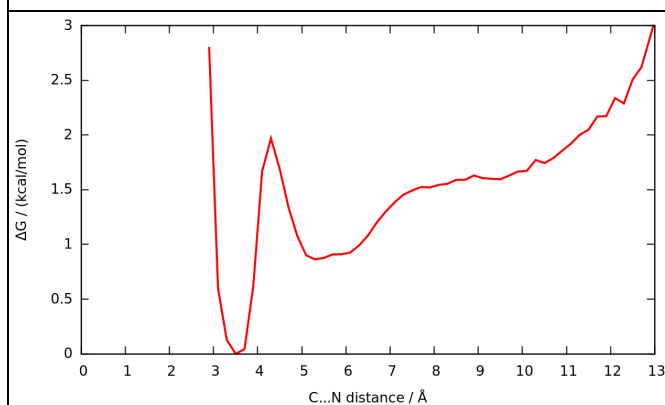


Figure Q: Free energy profile as a function of the ionic interaction distance in **14**.

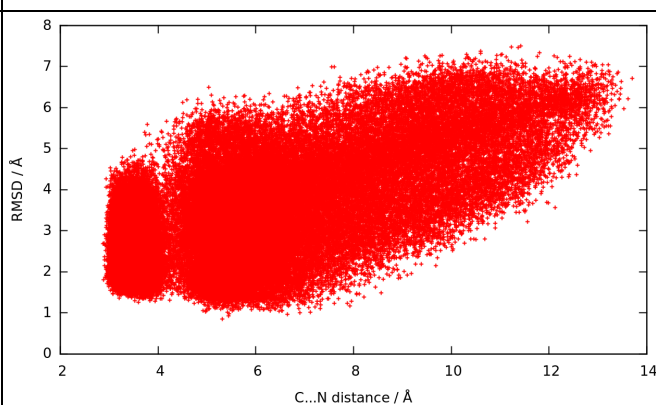


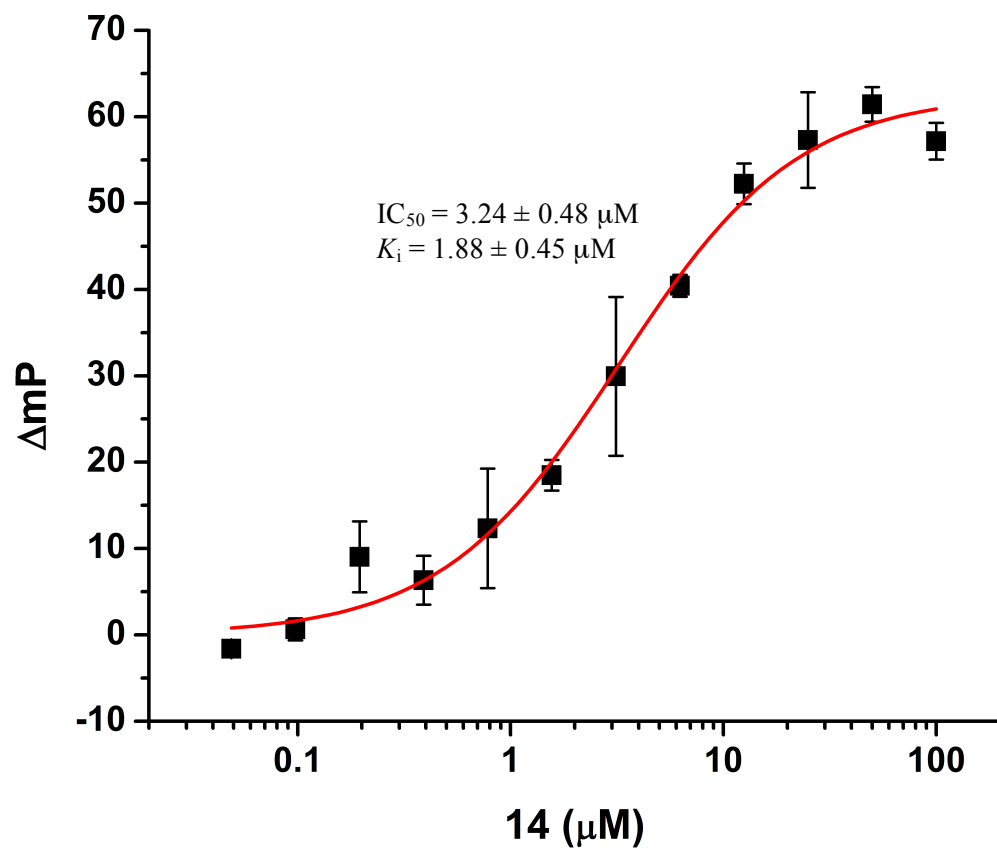
Figure R: scatter plot of RMSD in function of ionic interaction distance for the 100000 MD snapshots of **14**.

Fluorescence Polarization Assays

Fluorescence polarization experiments were conducted using a BMG PHERAstar FS multimode microplate reader equipped with two PMTs for simultaneous measurements of the perpendicular and parallel fluorescence emission with a 485 nm excitation and 520 nm emission filters. Human Mcl-1 was purchased from Genscript (as the His₆-Trx tag), and was stored in 1x PBS, pH 7.4 at -78 °C. A 6-aminohexanoic acid linker was conjugated to the N-terminus of the Bak BH3 peptide GQVGRQLAIIGDDINR which was then capped with fluorescein (on the amino group of the linker) and the peptide was amidated on the C-terminus to give FITC-Ahx-GQVGRQLAIIGDDINR-CONH₂, hereafter referred to as “FITC-Bak” (synthesized by Neo BioScience in >95% purity). To determine the K_d of the FITC-Bak peptide, the assay was performed in black polypropylene 384-well microplate (Costar) with a final volume of 20 μ L containing varying concentrations of Mcl-1 in the presence of 15 nM FITC-Bak peptide in PBS (pH 7.4) at room temperature. The fluorescence polarization competition assays (FPCA) were performed using 40 nM Mcl-1 in the same buffer (thus, 15 nM FITC-Bak) with varying concentrations of compound **14**. Regression analysis was carried out using Origin (OriginLab, Northampton, MA) to fit the data to the Hill equation (1) to determine the binding affinity (K_d) of Bcl-x_L for the binding of the FITC-Bak peptide and to determine the IC₅₀ in the FPCA. The Cheng-Prusoff equation (1) was then used to determine the K_i for compound **14**.

$$\text{Equation (1): } K_i = \text{IC}_{50} / (1 + [\text{L}_T^{\text{FITC-Bak}}] / K_d^{\text{FITC-Bak}})$$

(IC₅₀ = determined using Hill equation, $[\text{L}_T^{\text{FITC-Bak}}]$ = total ligand (15 nM FITC-Bak), $K_d^{\text{FITC-Bak}} = 20.81 \pm 0.70$ nM the affinity of Mcl-1 for FITC-Bak peptide under the assay conditions.)



JKY-4-034B

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Data Collected on:

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Archive directory:

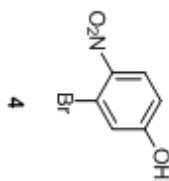
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Filename: PROTON

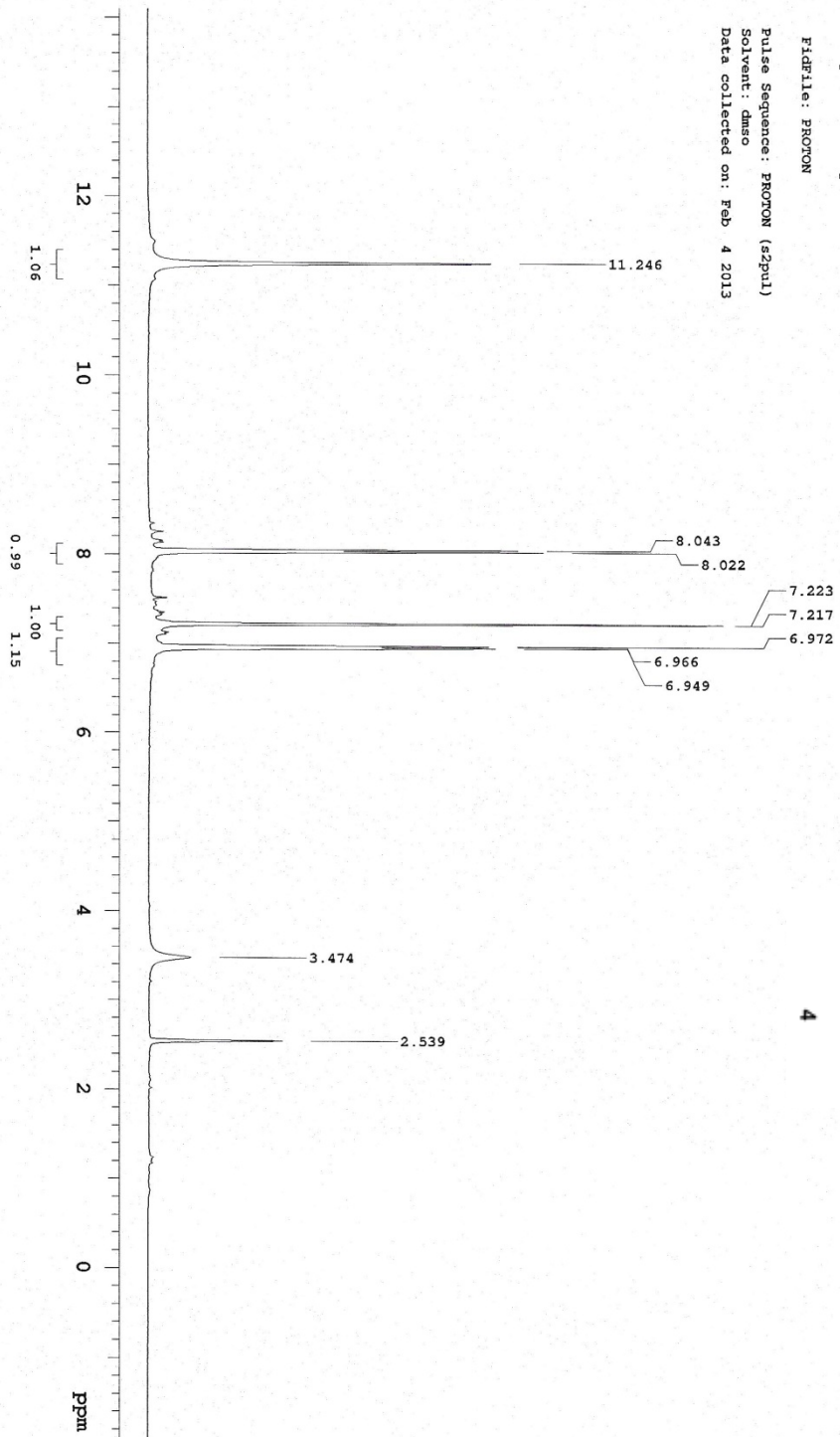
Pulse Sequence: PROTON (s2pu1)

Solvent: dmsc

Data collected on: Feb 4 2013



VARIAN



13C NMR of JKY-4-034B

Sample Name:

Data Collected on:

400mr-vmrz400

Archive directory:

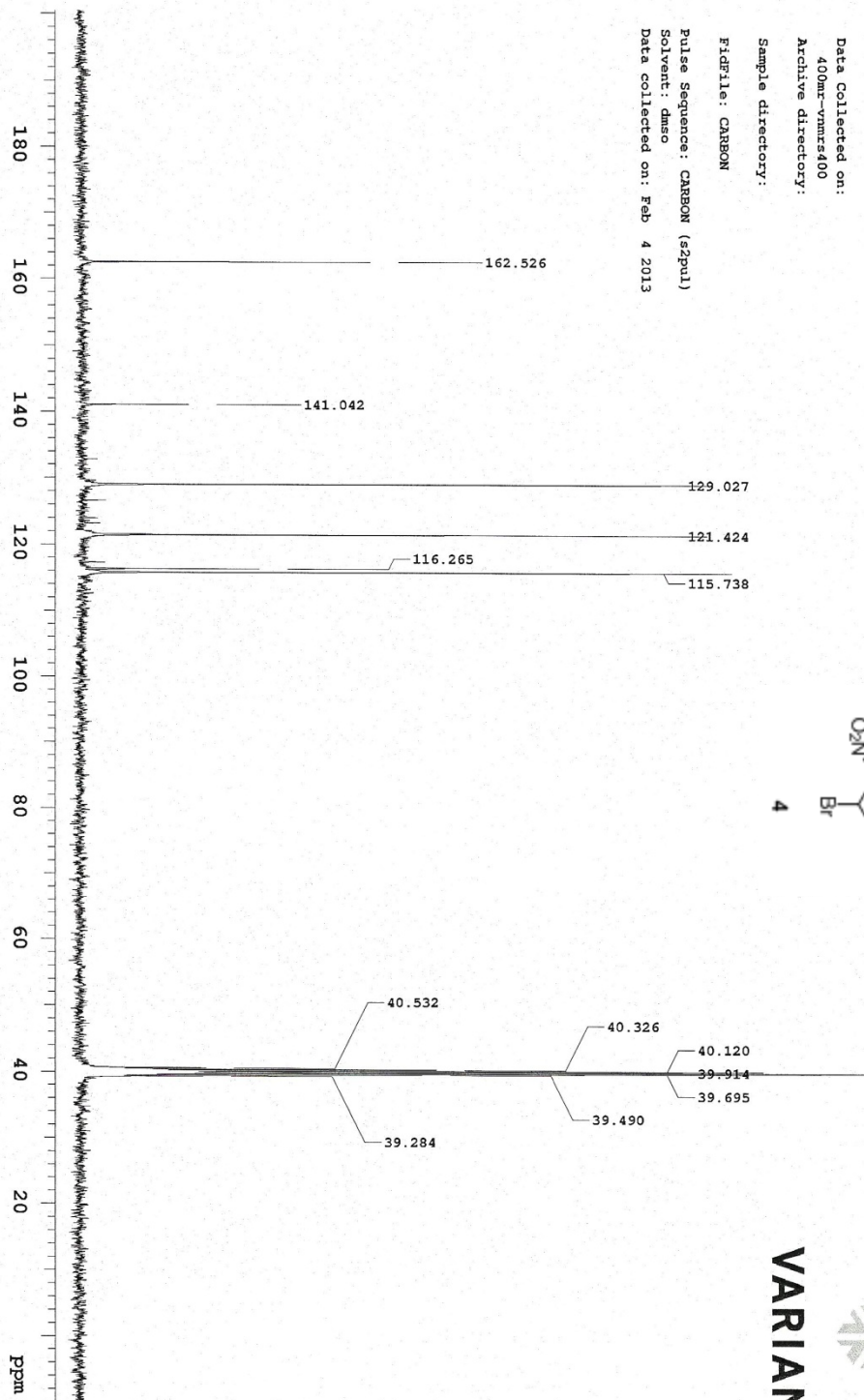
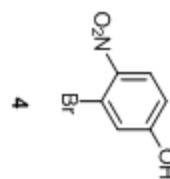
Sample directory:

File: CARBON

Pulse Sequence: CARBON (s2pu1)

Solvent: dmsc

Data collected on: Feb 4 2013



VARIAN

CG-1-002

Sample Name:

Data Collected on:

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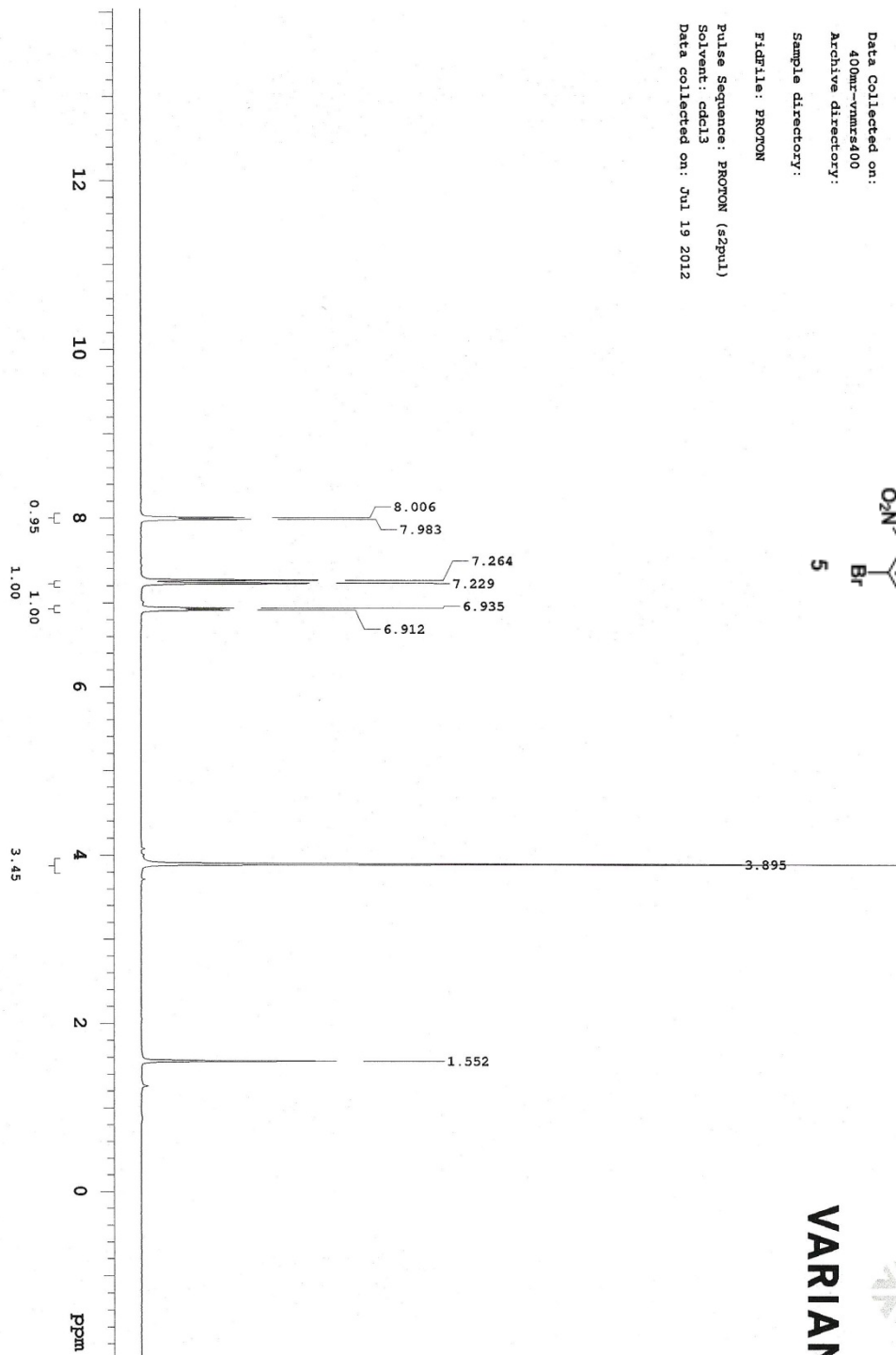
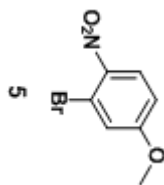
Sample directory:

FIDFile: PROTON

Pulse Sequence: PROTON (s2pu1)

Solvent: cdcl3

Data collected on: Jul 19 2012



VARIAN

CG-1-005

Sample Name:

Data Collected on:

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Archive directory:

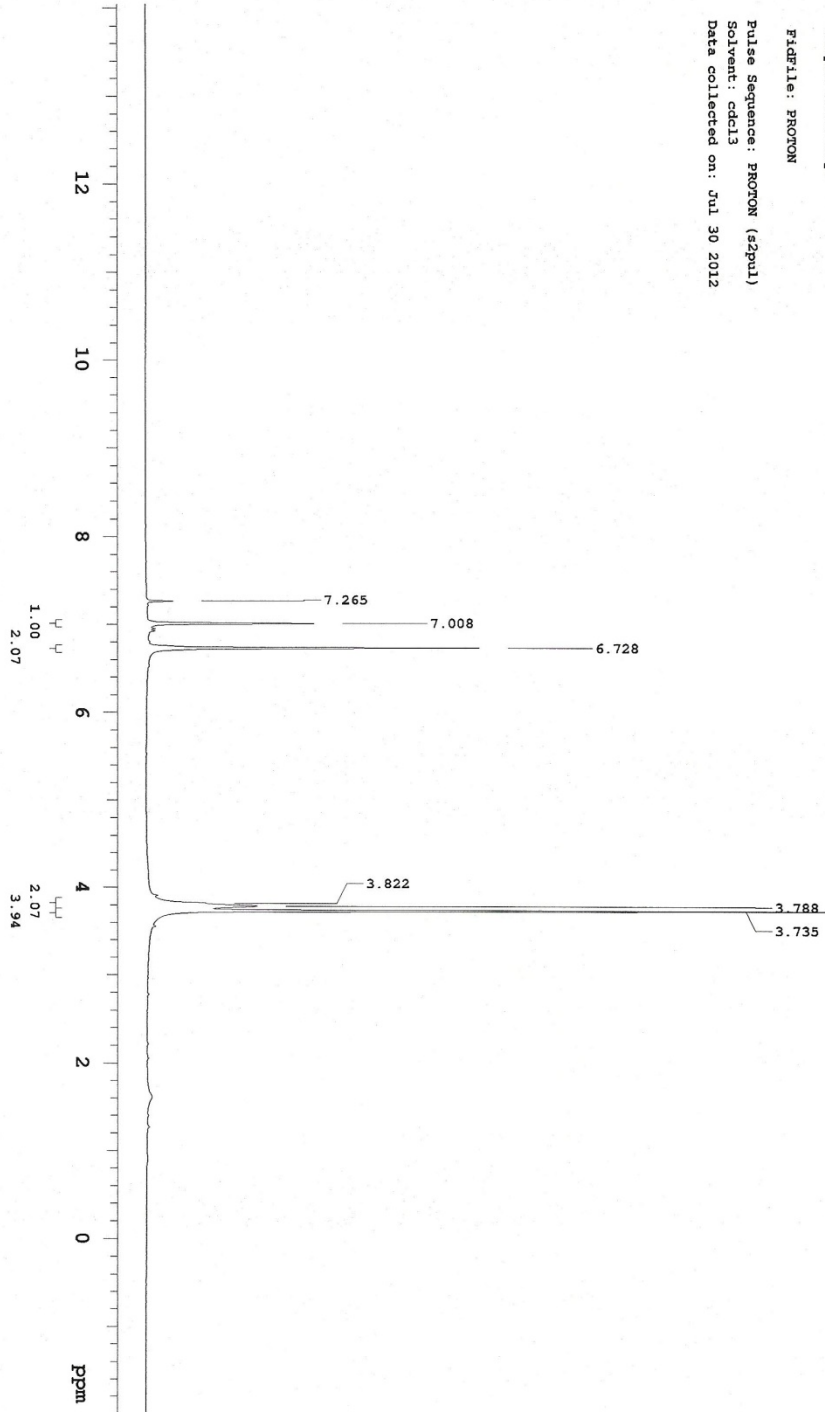
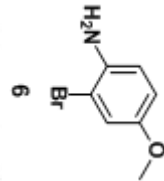
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Pulse Sequence: PROTON (a2pu1)

Solvent: cdcl3

Data collected on: Jul 30 2012



¹³C NMR of CG-1-005

Sample Name:

Data Collected on:
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Archive directory:

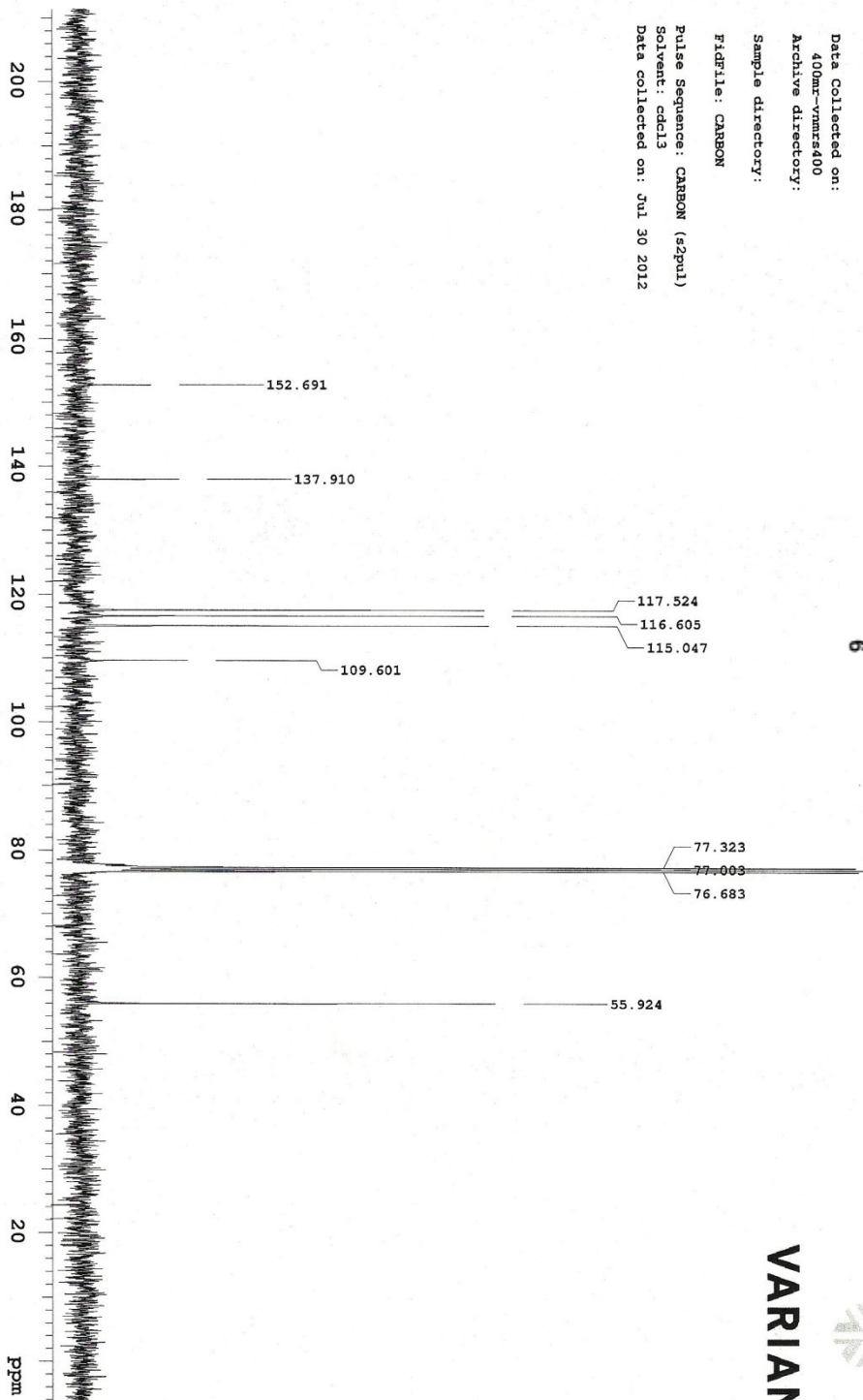
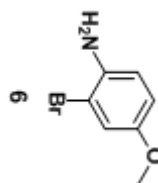
Sample directory:

File: CARBON

Pulse Sequence: CARBON (s2pu1)

Solvent: cdcl3

Data collected on: Jul 30 2012



VARIAN

CG-1-006

Sample Name:

Data Collected on:

400mr-vnmr400

Archive directory:

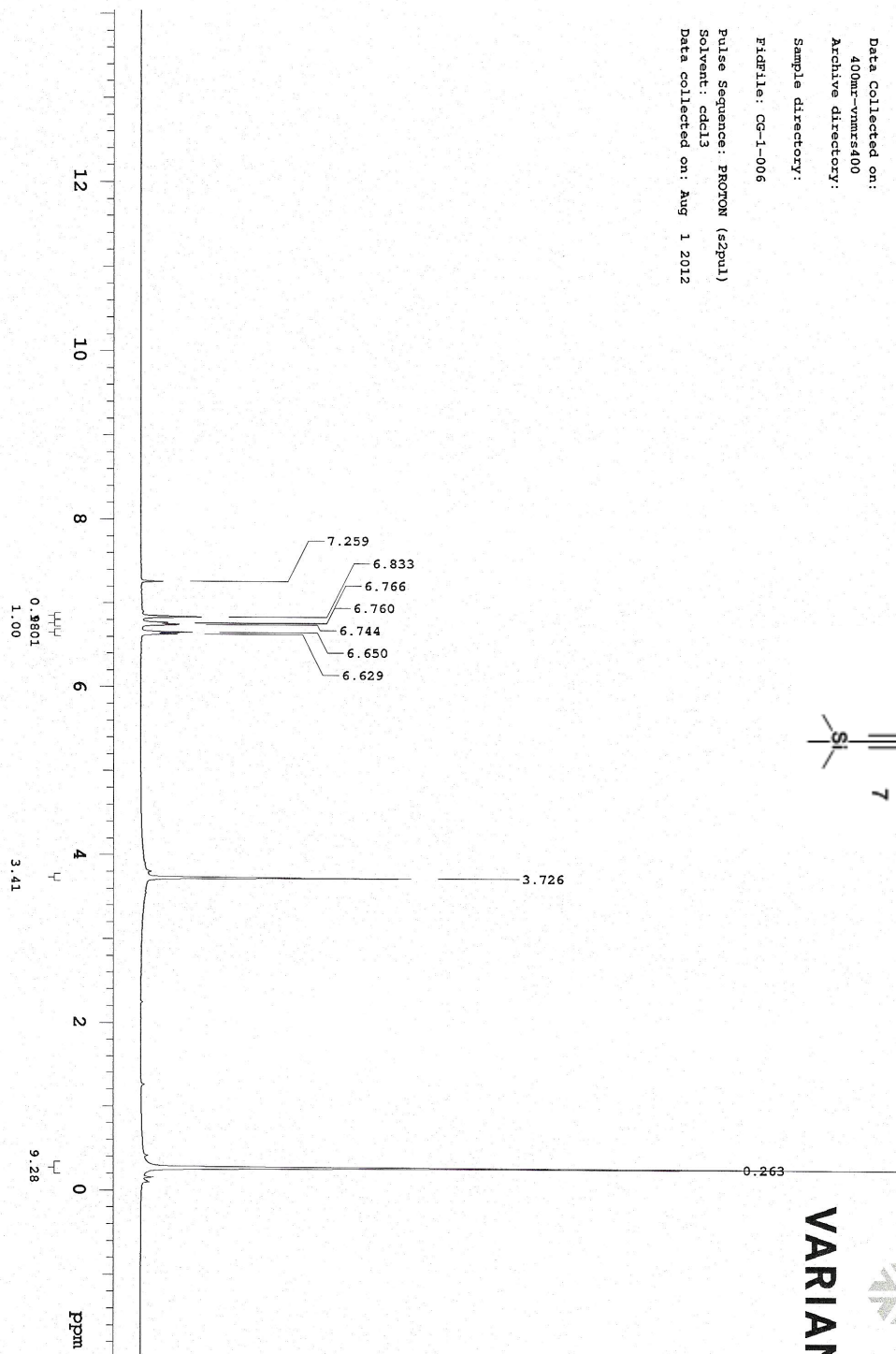
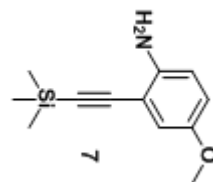
Sample directory:

File: CG-1-006

Pulse Sequence: PROTON (s2pu1)

Solvent: cdcl3

Data collected on: Aug 1 2012




VARIAN

¹³C NMR of CG-1-006

Sample Name:

Data Collected on:

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Archive directory:

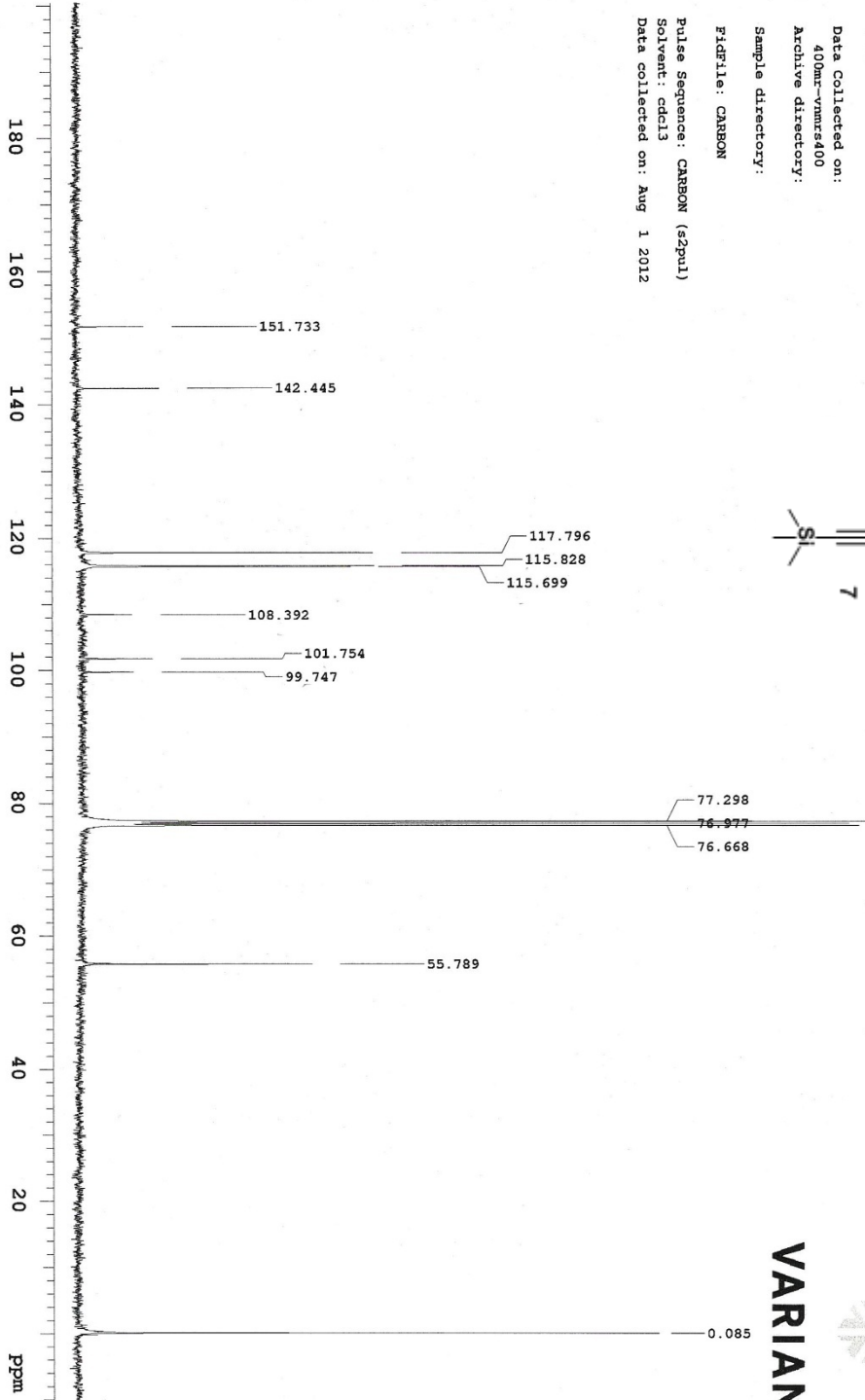
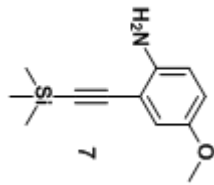
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Pulse Sequence: CARBON (szpul)

Solvent: cdcl3

Data collected on: Aug 1 2012



VARIAN

CG-1-008

Sample Name:

Data Collected on:

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Archive directory:

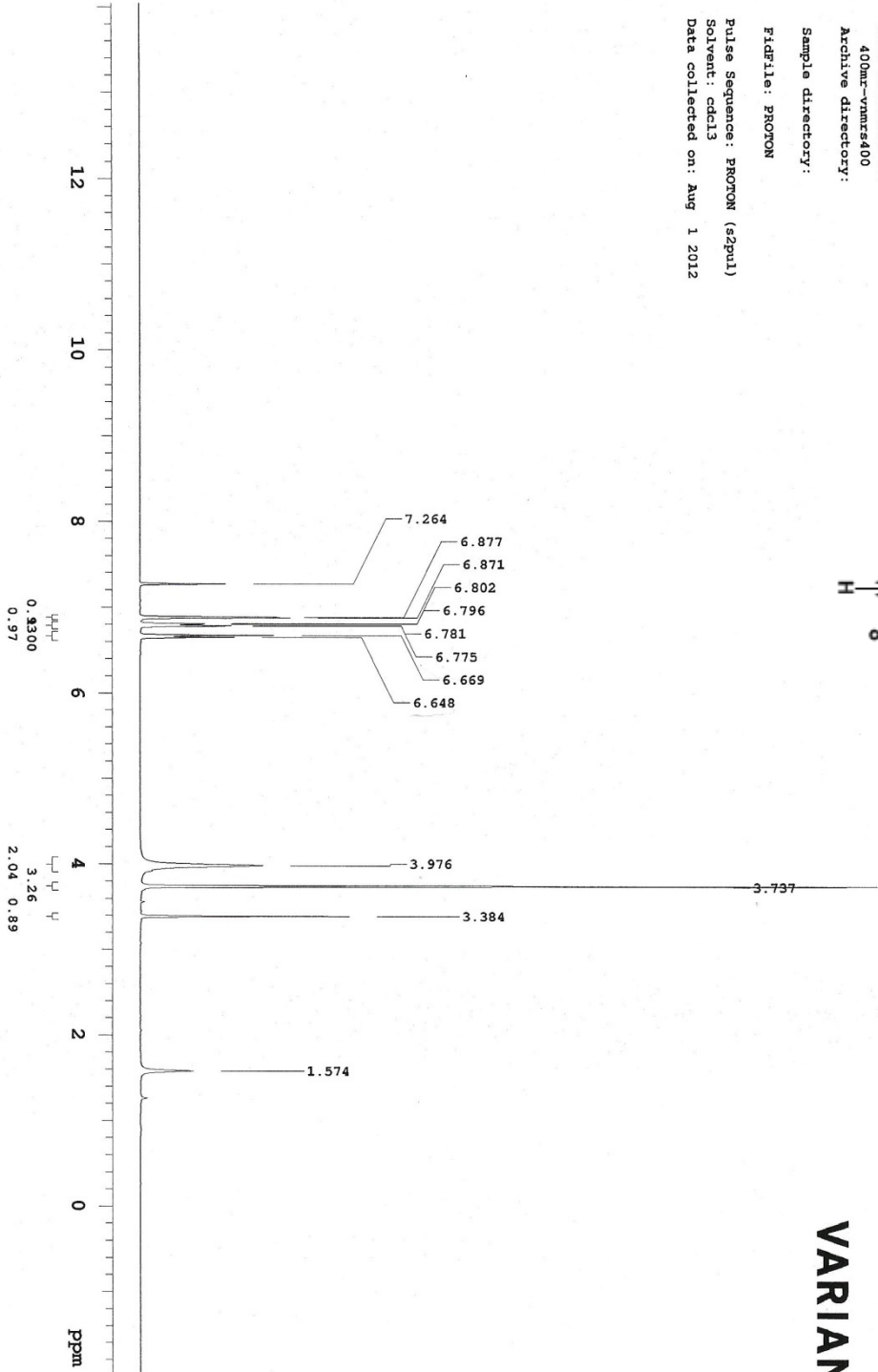
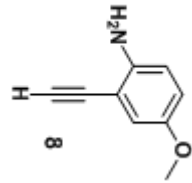
Sample directory:

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Pulse Sequence: PROTON (s2pu1)

Solvent: cdcl3

Data collected on: Aug 1 2012



VARIAN

¹³C NMR of CG-1-008

Sample Name:

Data Collected on:

400mm-vnmr400

Archive directory:

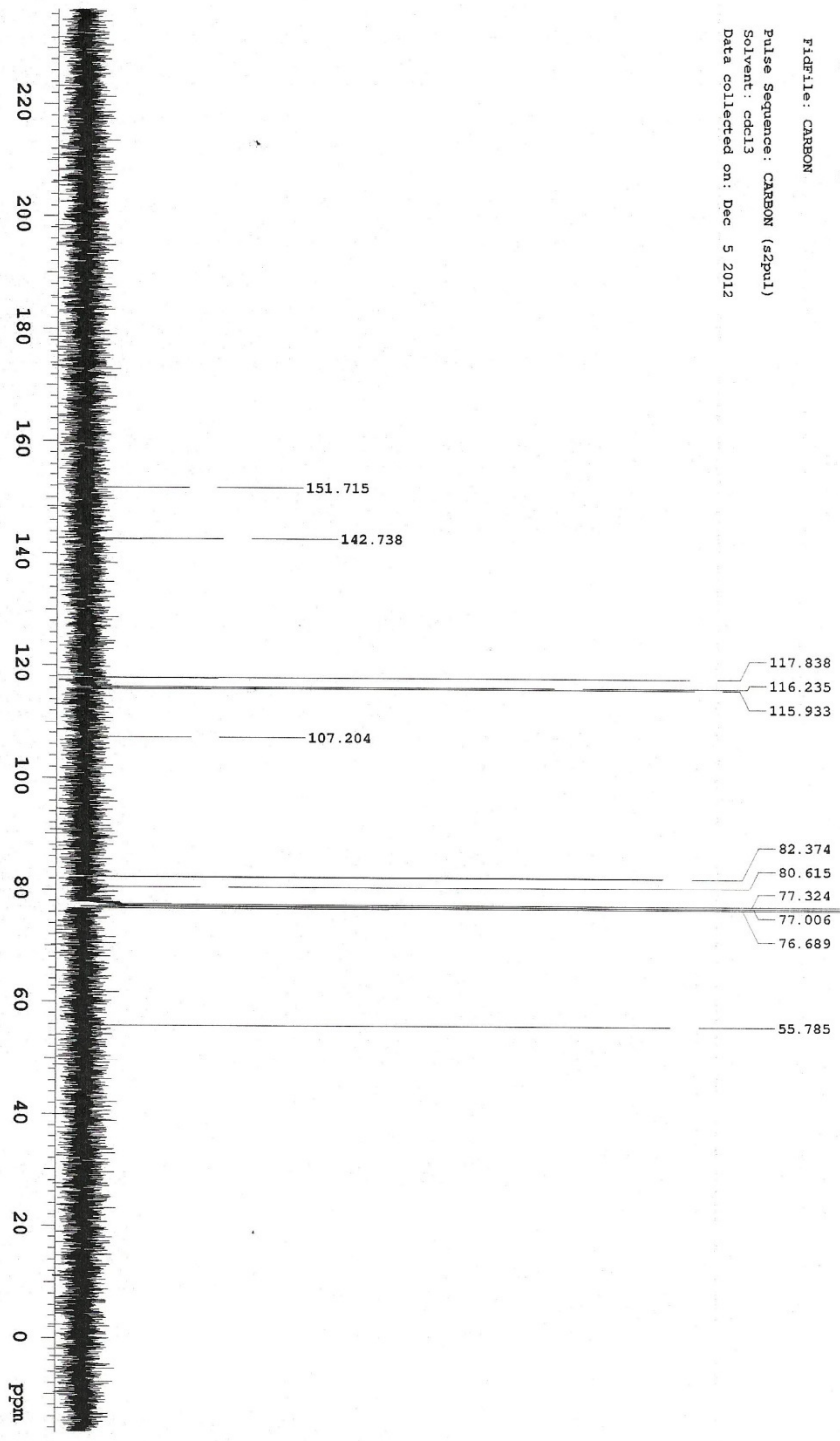
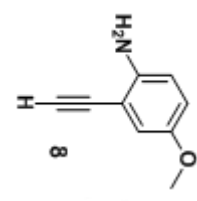
Sample directory:

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Pulse Sequence: CARBON (zgpg1)

Solvent: cdcl3

Data collected on: Dec 5 2012



JKY-4-036

Sample Name:

Data Collected on:

400mz-vnmz400

Archive directory:

Sample directory:

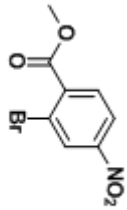
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Pulse Sequence: PROTON (s2pu1)

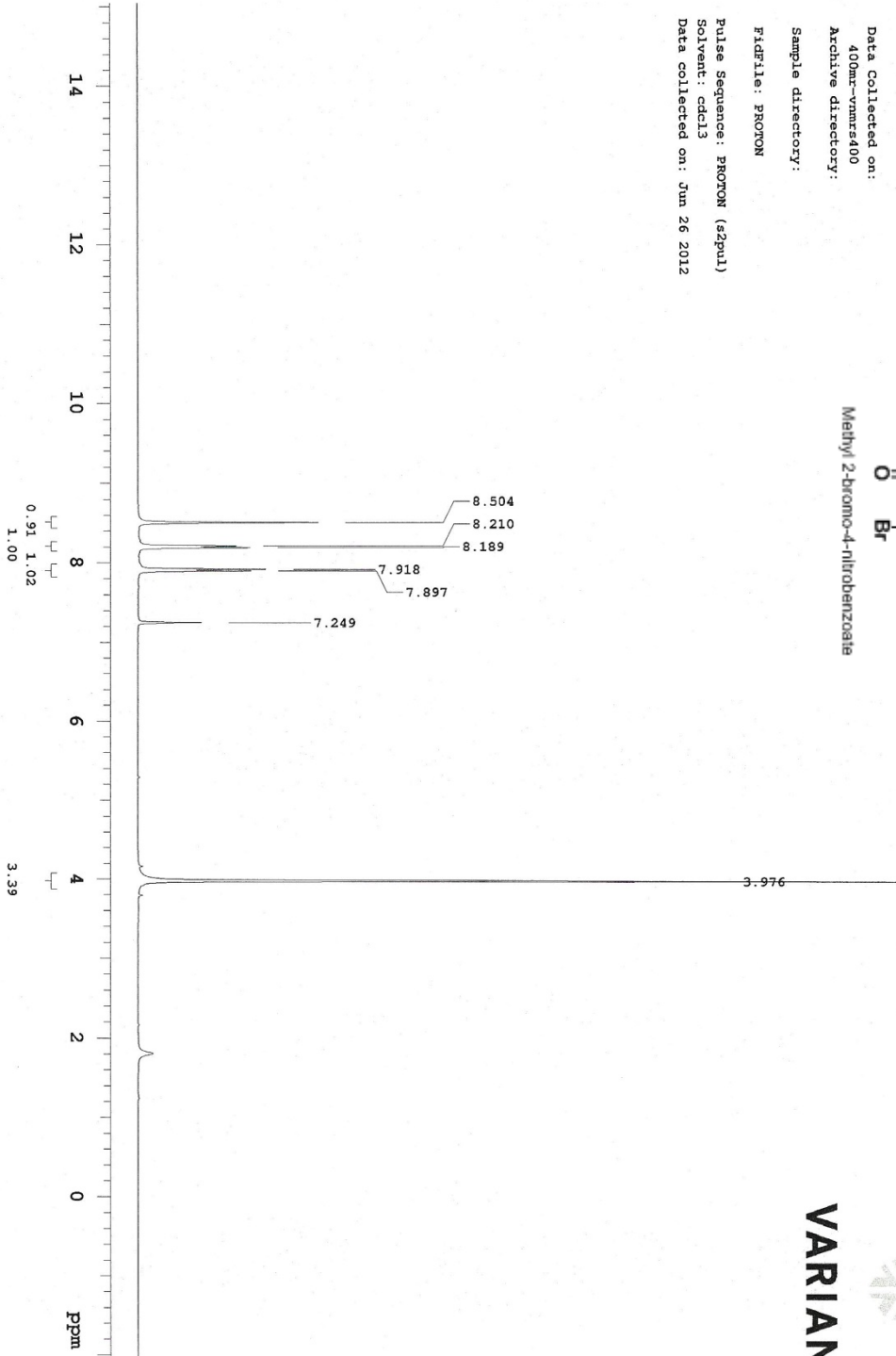
Solvent: cdcl3

Data collected on: Jun 26 2012

Methyl 2-bromo-4-nitrobenzoate



VARIAN



13C NMR of JKY-4-036

Sample Name:

Data Collected on:

400mz-vnmrs400

Archive directory:

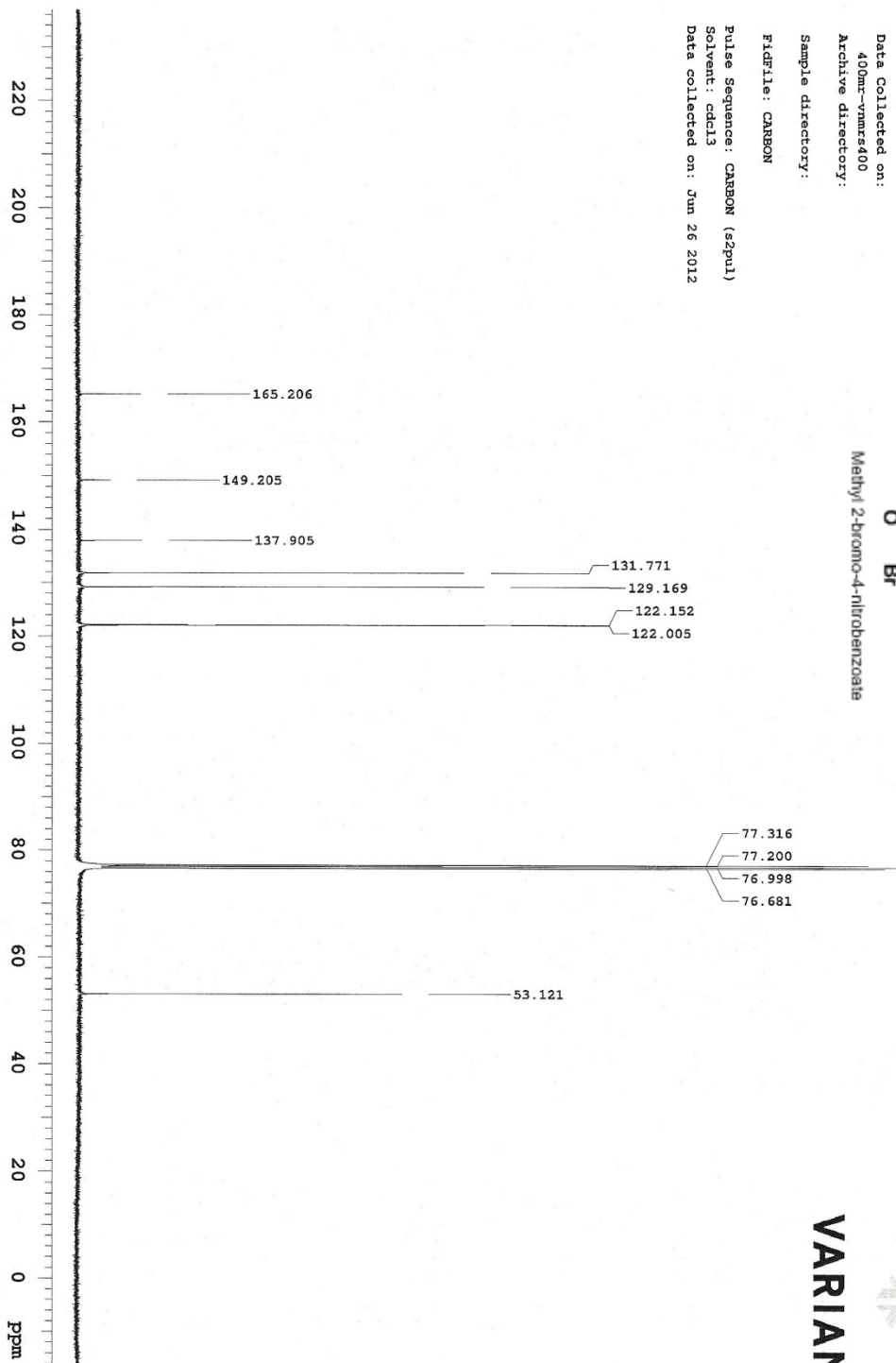
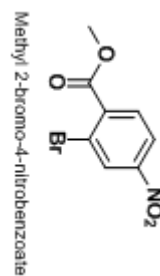
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Solvent: cdcl3

Data collected on: Jun 26 2012

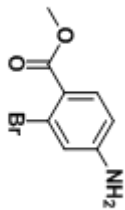


VARIAN

JKY-4-038

Sample Name:

Methyl 4-amino-2-bromobenzoate



Data Collected on:
400mr-vmrz400

Archive directory:

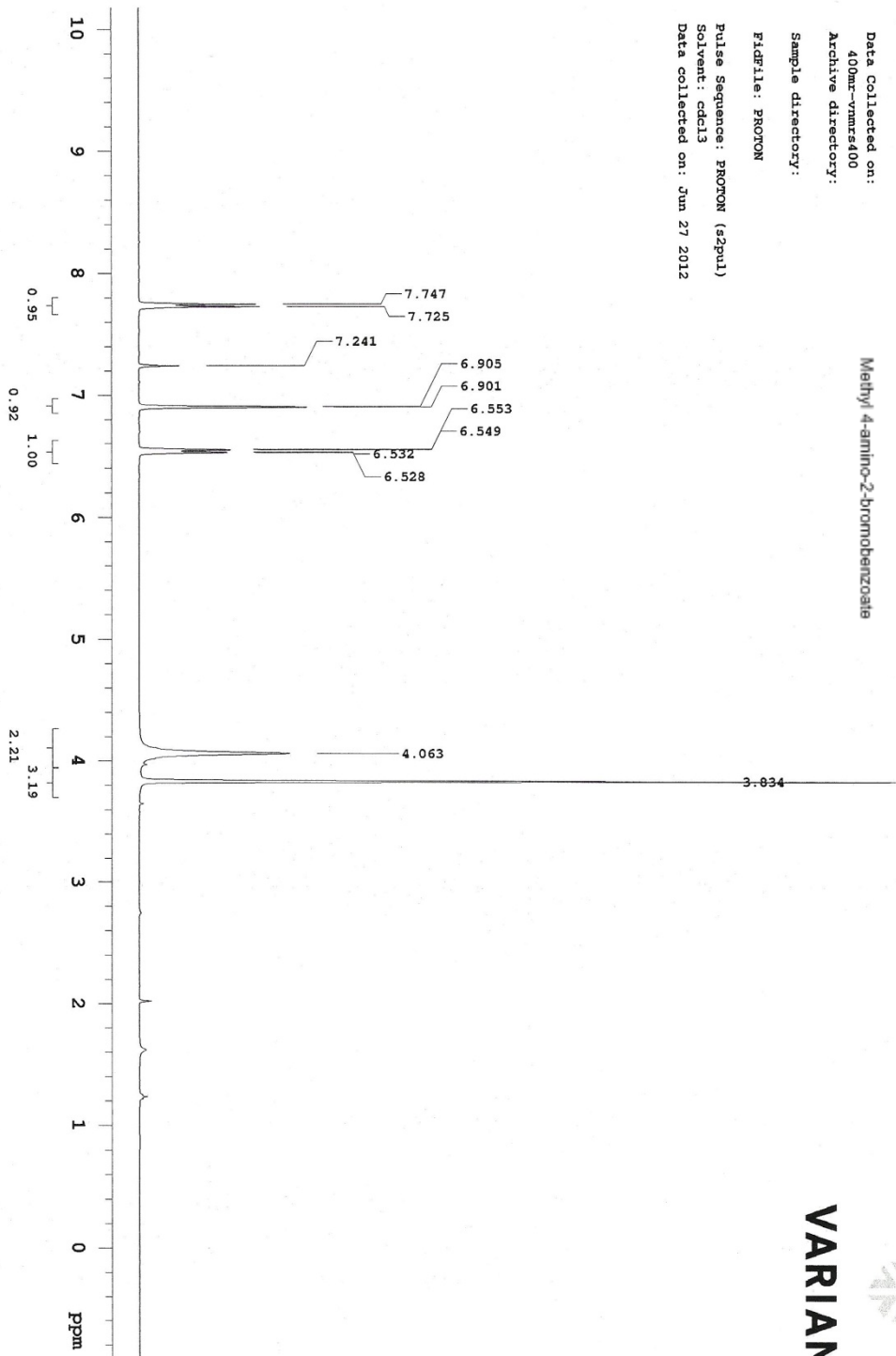
Sample directory:

File: PROTON

Pulse Sequence: PROTON (s2pu1)

Solvent: cdcl3

Data collected on: Jun 27 2012

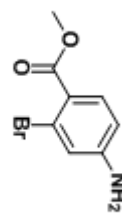


VARIAN

¹³C NMR of JKY-4-038

Sample Name:

Methyl 4-amino-2-bromobenzoate



Data Collected on:

400mr-vmrz400

Archive directory:

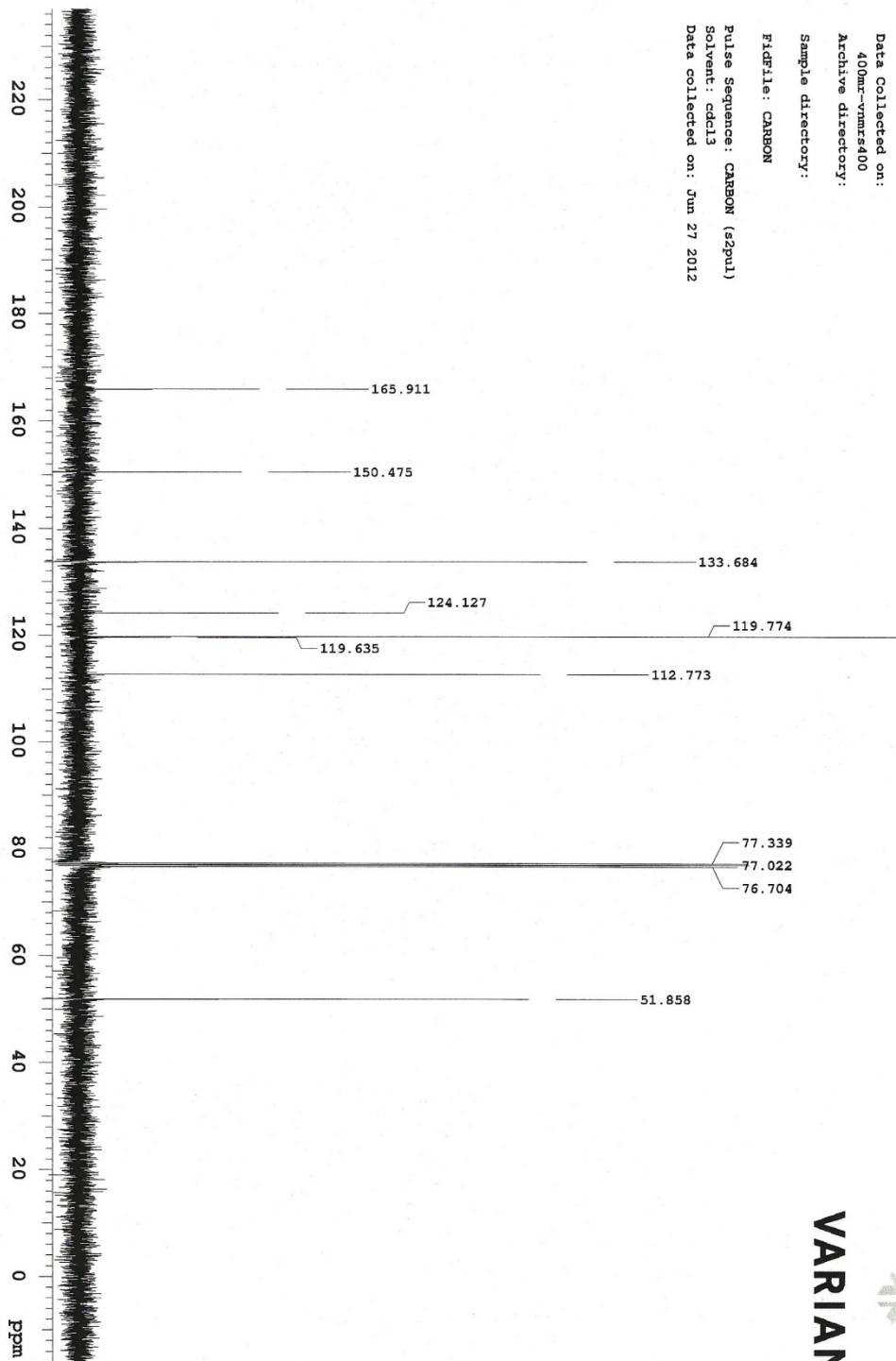
Sample directory:

File: CARBON

Pulse Sequence: CARBON (s2pu1)

Solvent: cdcl3

Data collected on: Jun 27 2012



VARIAN

JKY-4-055

Sample Name:

Data Collected on:

400mr-vnmrs400

Archive directory:

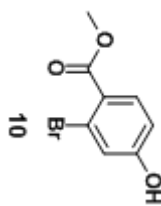
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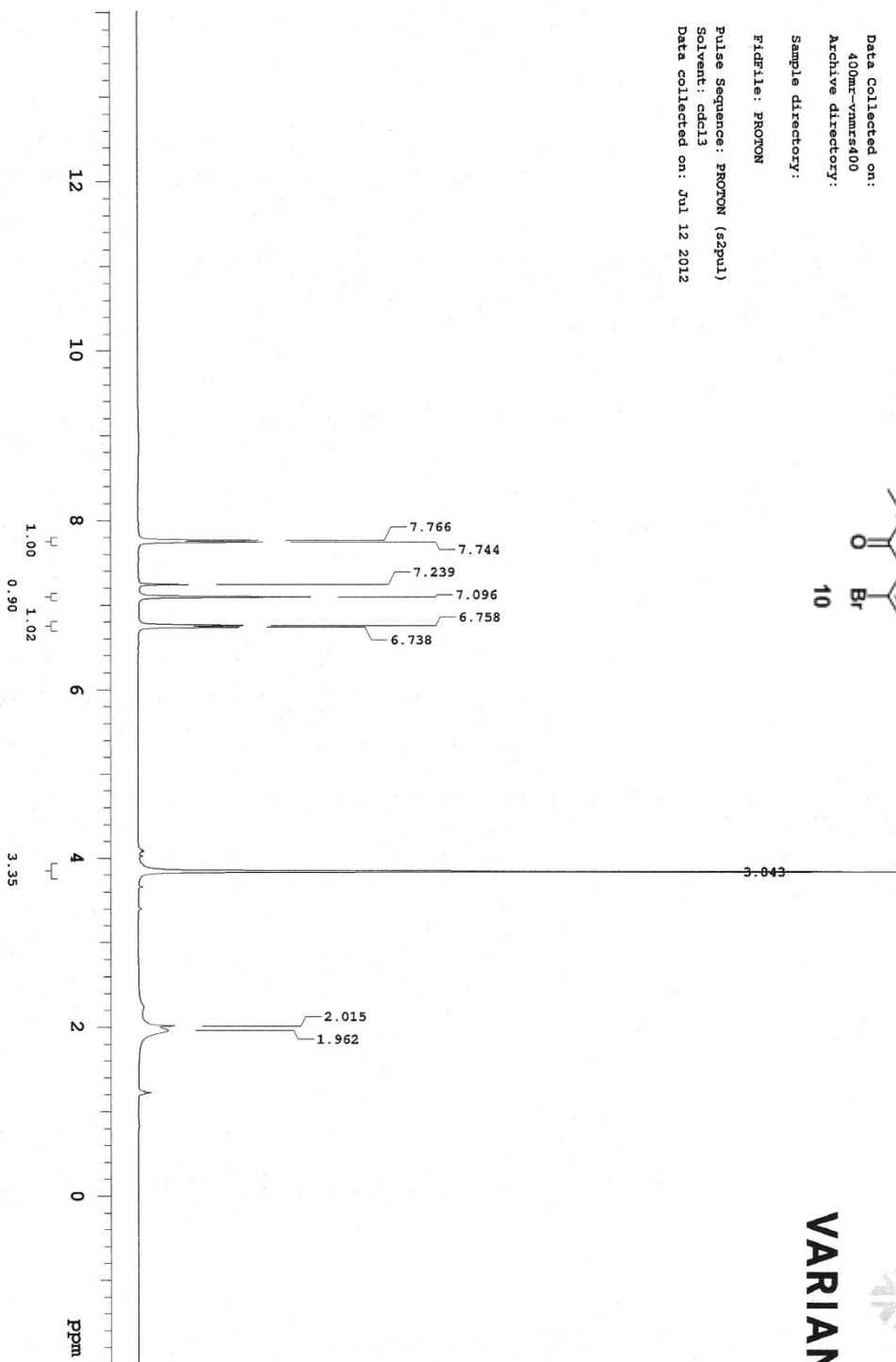
Pulse Sequence: PROTON (s2pu1)

Solvent: cdcl3

Data collected on: Jul 12 2012



VARIAN



¹³C NMR of JKY-4-055

Sample Name:

Data Collected on:

400mr-rmrs400

Archive directory:

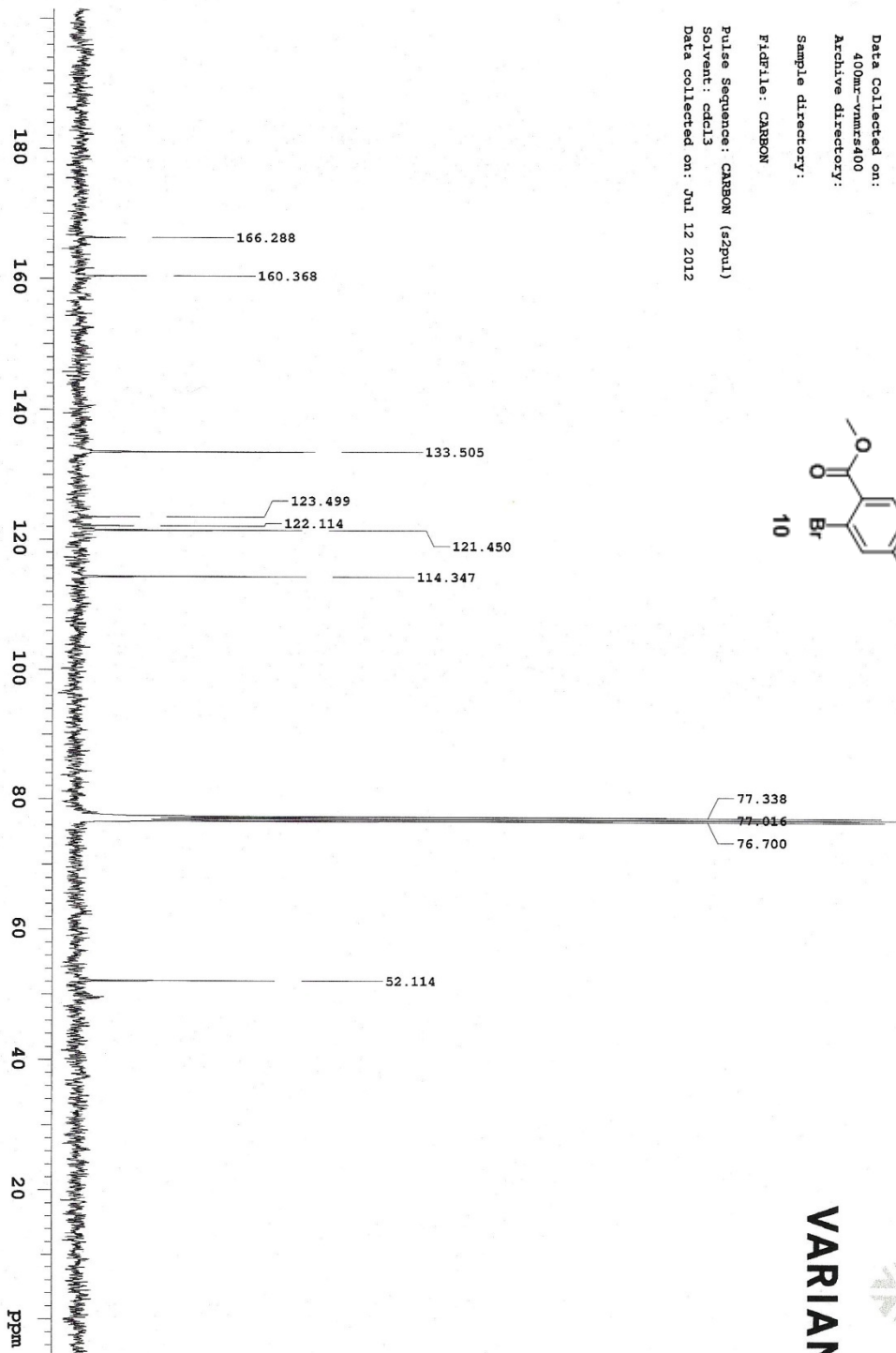
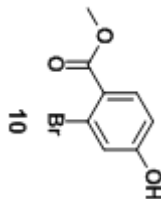
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File: CARBON

Pulse Sequence: CARBON (s2pul)

Solvent: cdcl3

Data collected on: Jul 12 2012




VARIAN

CG-1-004

Sample Name:

Data Collected on:

400mz-vnmr3400

Archive directory:

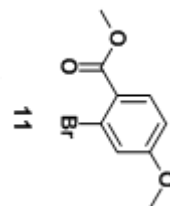
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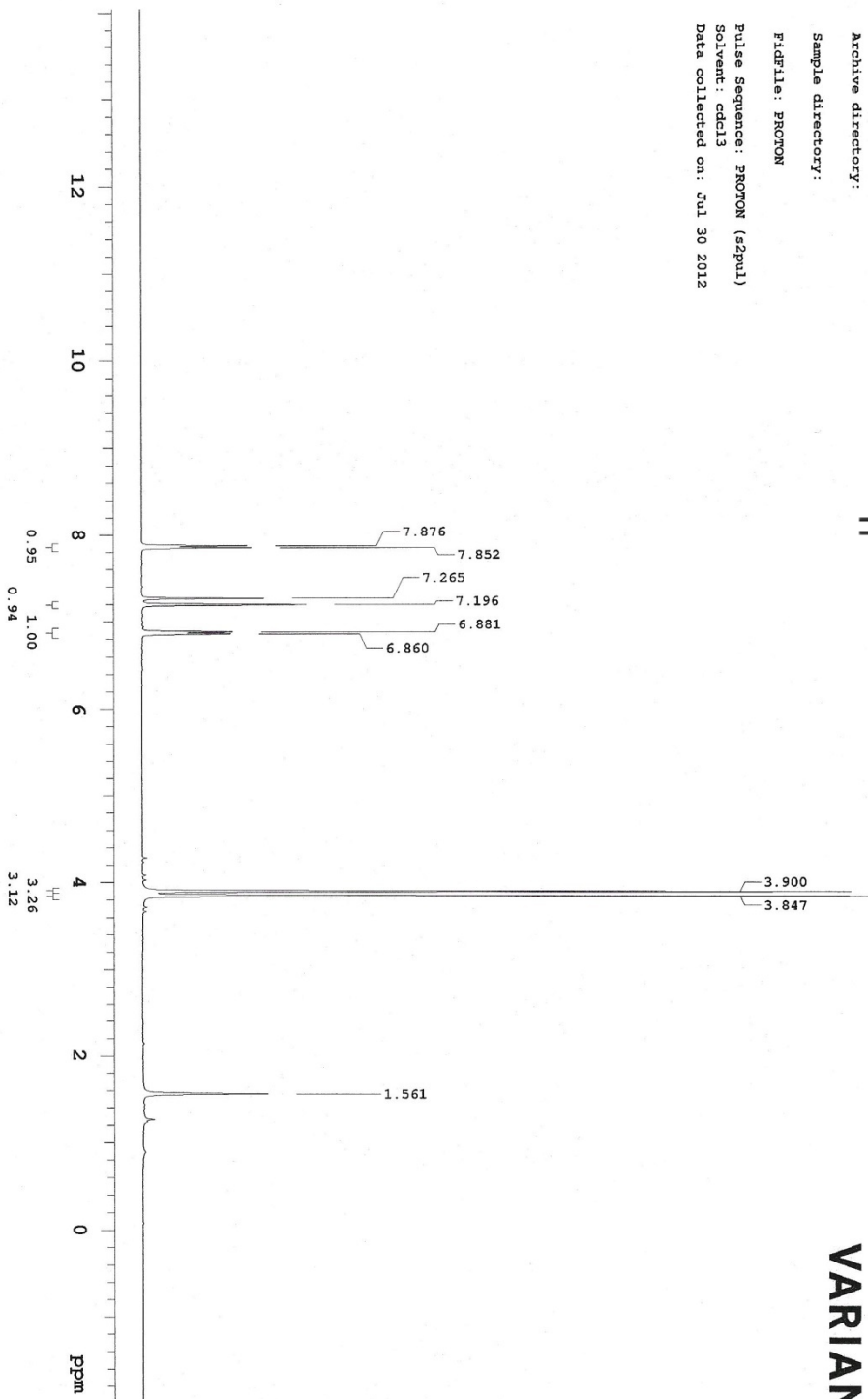
Pulse Sequence: PROTON (szpu1)

Solvent: cdcl3

Data collected on: Jul 30 2012



VARIAN



13C NMR of CG-1-004

Sample Name:

Data Collected on:

400mr-vmr400

Archive directory:

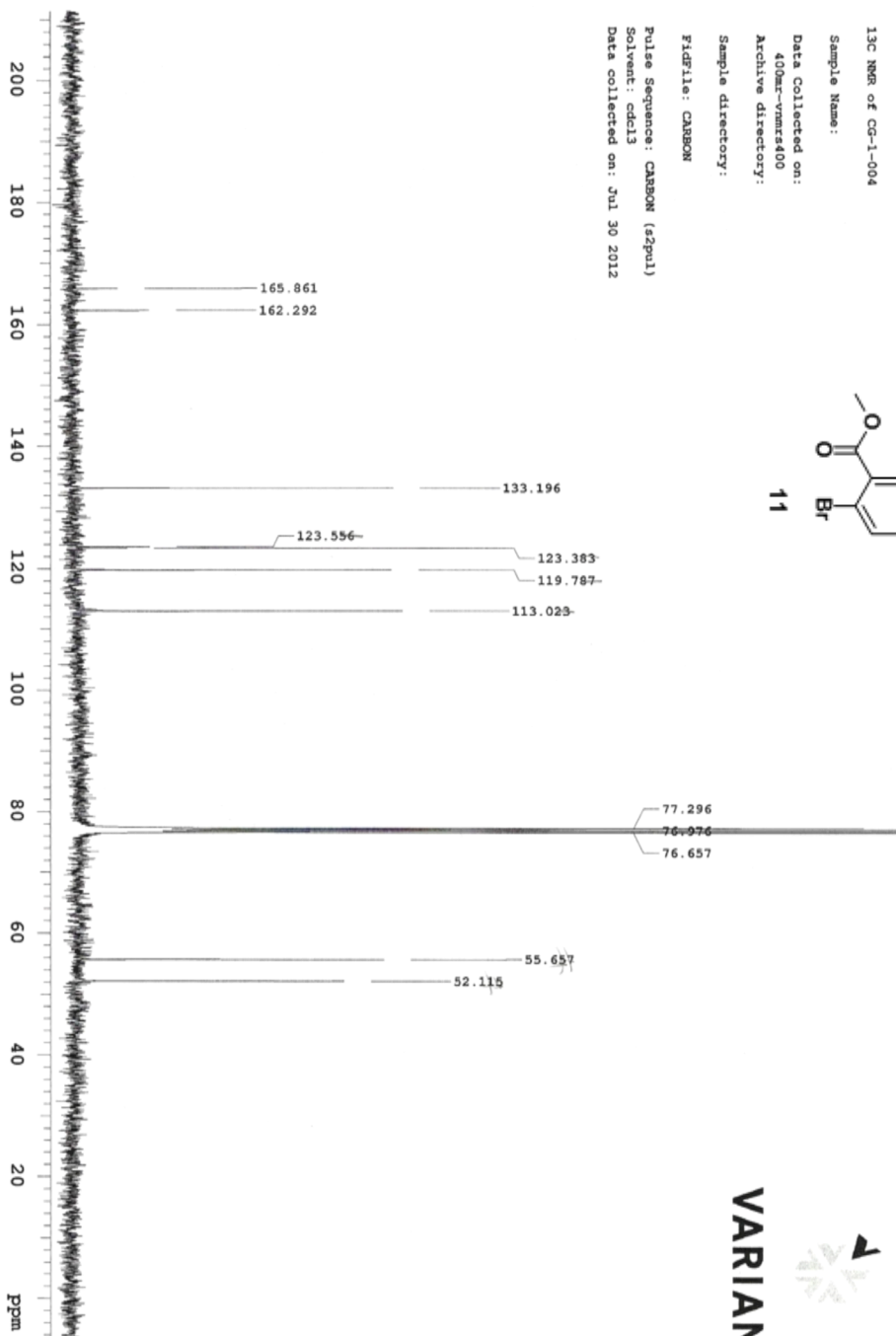
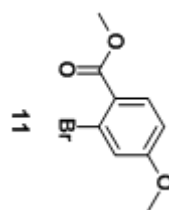
Sample directory:

F1: FILE: CARBON

Pulse Sequence: CARBON (zgpg1)

Solvent: cdcl3

Data collected on: Jul 30 2012



VARIAN

CG-1-0099

Sample Name:

Data Collected on:

400mr-vmrz400

Archive directory:

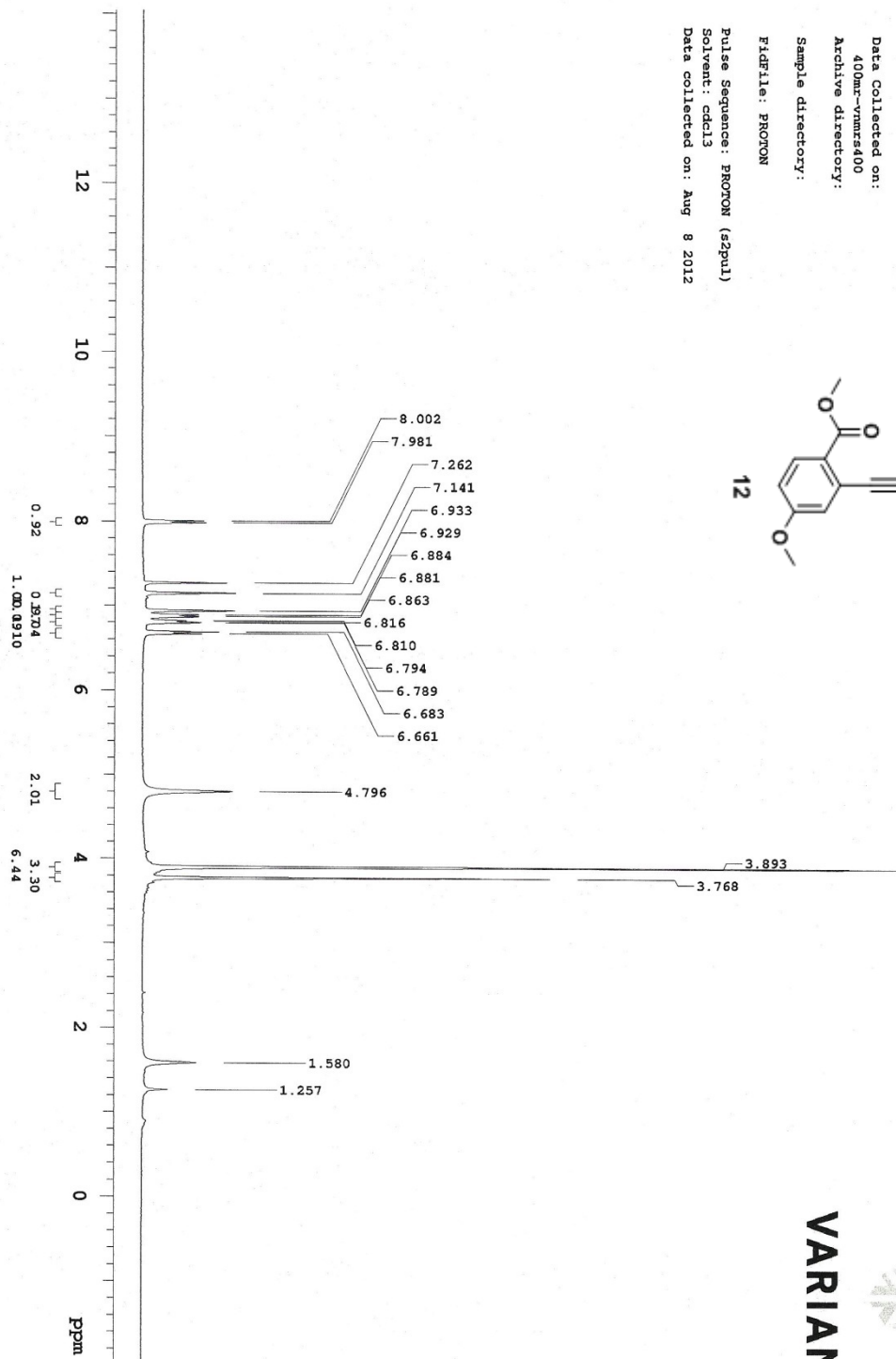
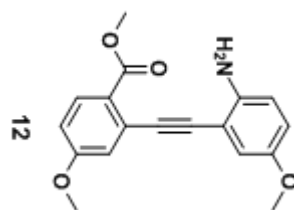
Sample directory:

FIDFile: PROTON

Pulse Sequence: PROTON (s2pu1)

Solvent: cdcl3

Data collected on: Aug 8 2012




VARIAN

¹³C NMR of CG-1-0098

Sample Name:

Data Collected on:

400mr-vmr3400

Archive directory:

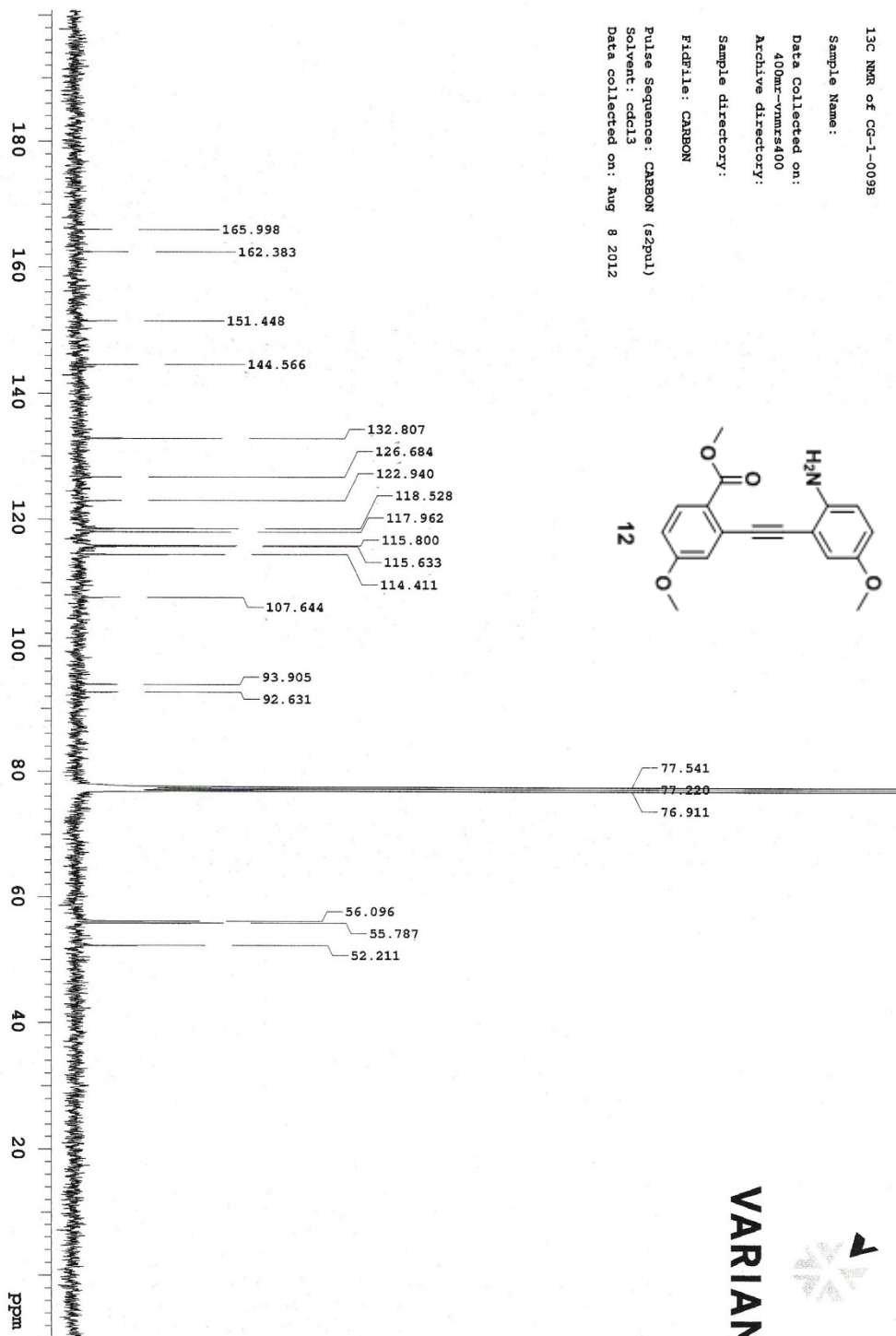
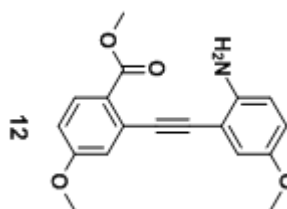
Sample directory:

Filefile: CARBON

Pulse Sequence: CARBON (szpu1)

Solvent: cdcl3

Data collected on: Aug 8 2012



VARIAN

CG-1-011

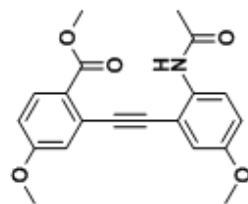
Sample Name:

Data Collected on:
400mr-vmr400

Archive directory:

Sample directory:

Methyl 2-((2-acetamido-5-methoxyphenyl)ethynyl)-4-methoxybenzoate

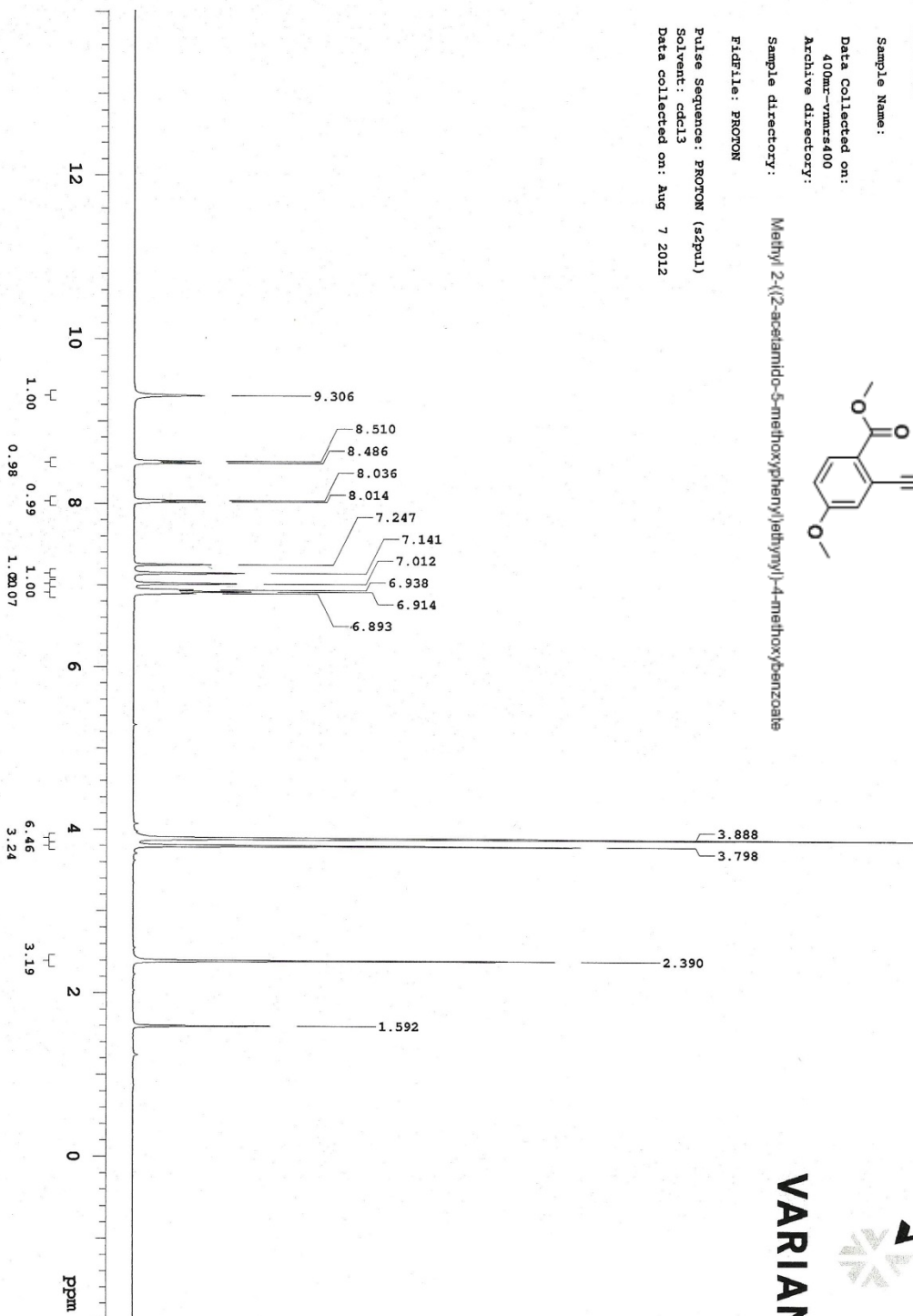


F1: PROTON

Pulse Sequence: PROTON (s2pu1)

Solvent: cdcl3

Data collected on: Aug 7 2012



13C NMR of CG-1-011

Sample Name:

Data Collected on:

40mm-vnmr400

Archive directory:

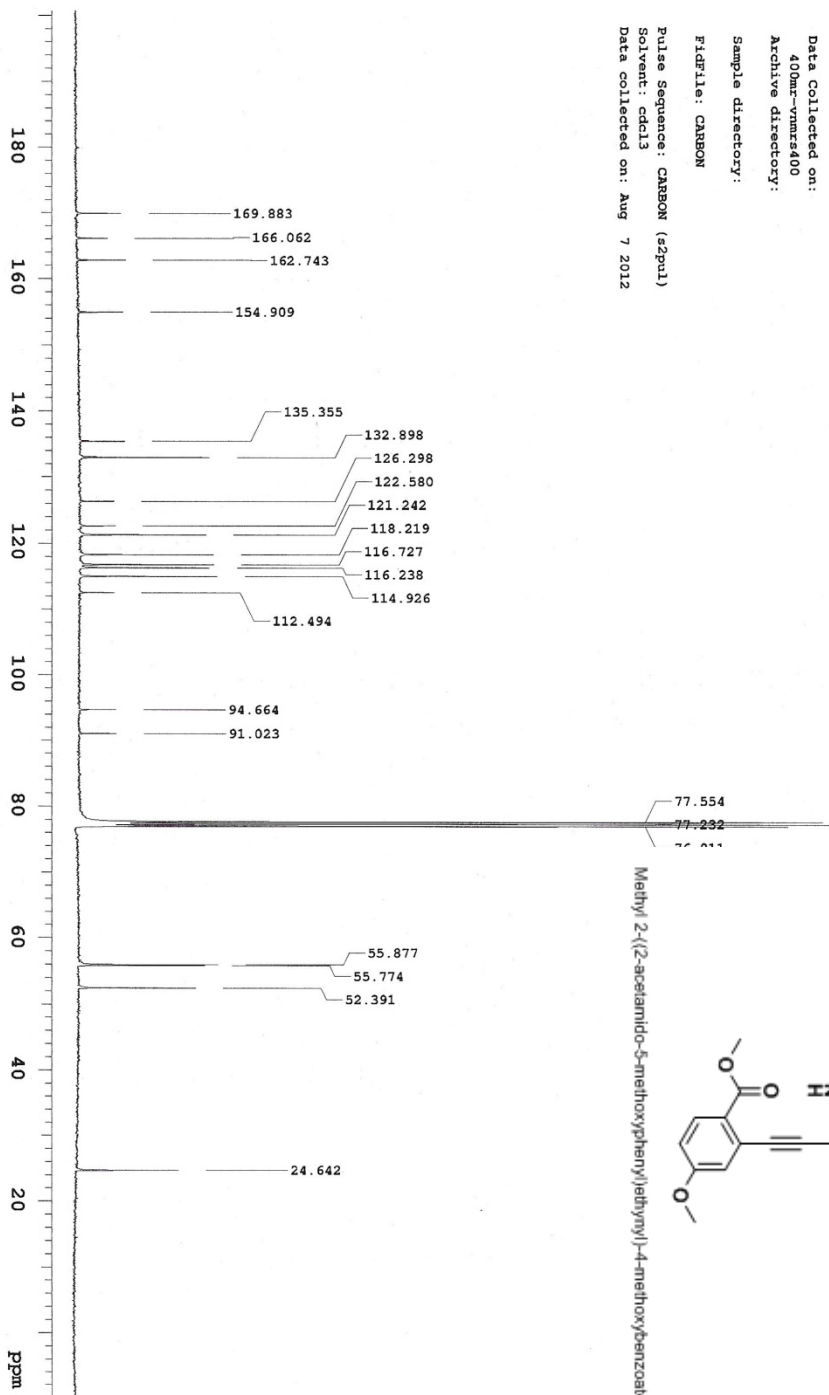
Sample directory:

File(s): CARBON

Pulse Sequence: CARBON (zgpg)

Solvent: cdcl3

Data collected on: Aug 7 2012



JKY-4-279

Sample Name:

Data Collected on:

400MHz-nmrs400

Archive directory:

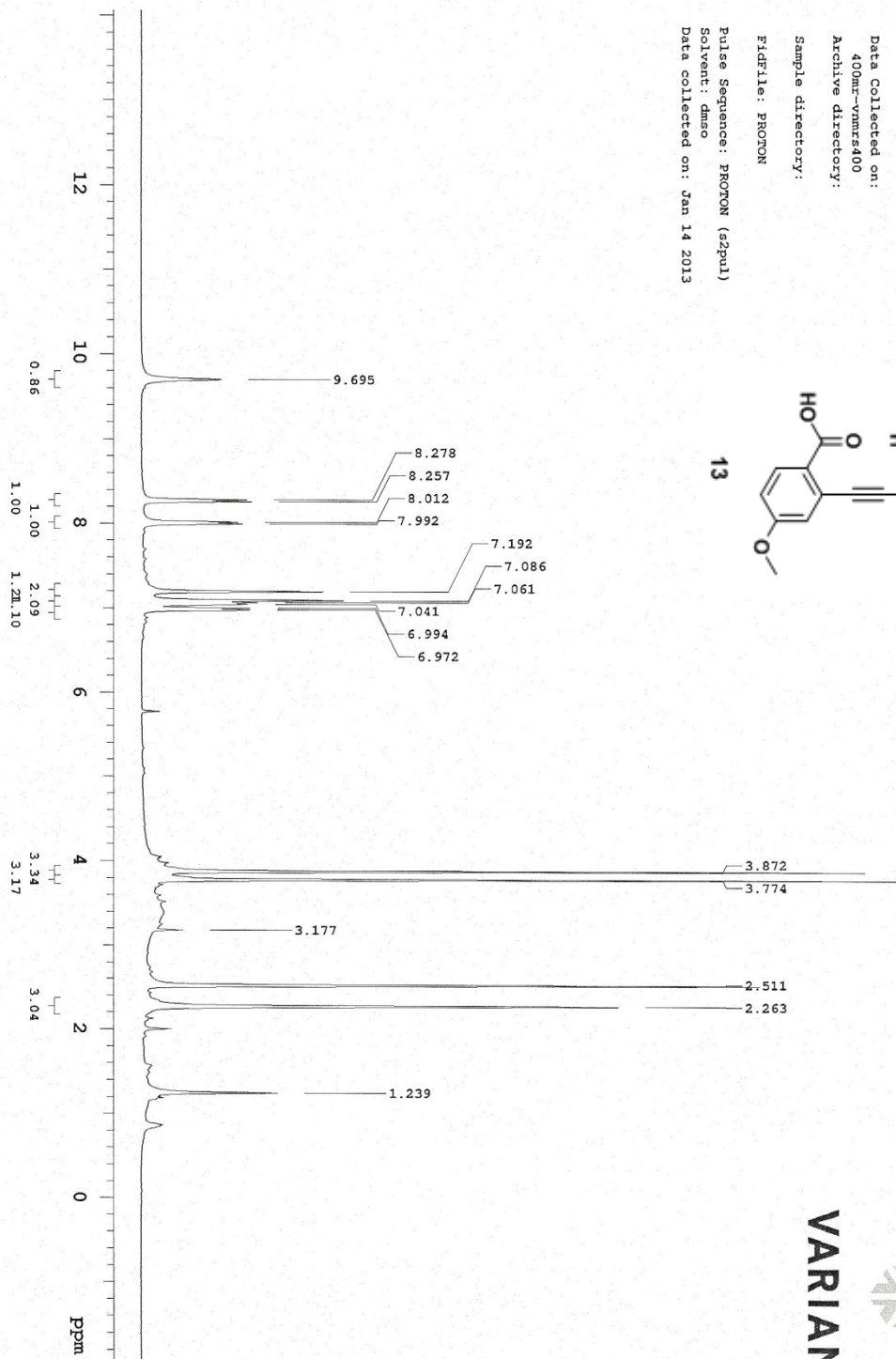
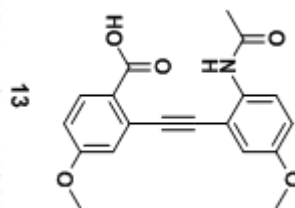
Sample directory:

F1F1File: PROTON

Pulse Sequence: PROTON (szpul)

Solvent: dmso

Data collected on: Jan 14 2013




VARIAN

¹³C NMR of JKY-4-279dmsc

Sample Name:

Data Collected on:

400ms-vnmr400

Archive directory:

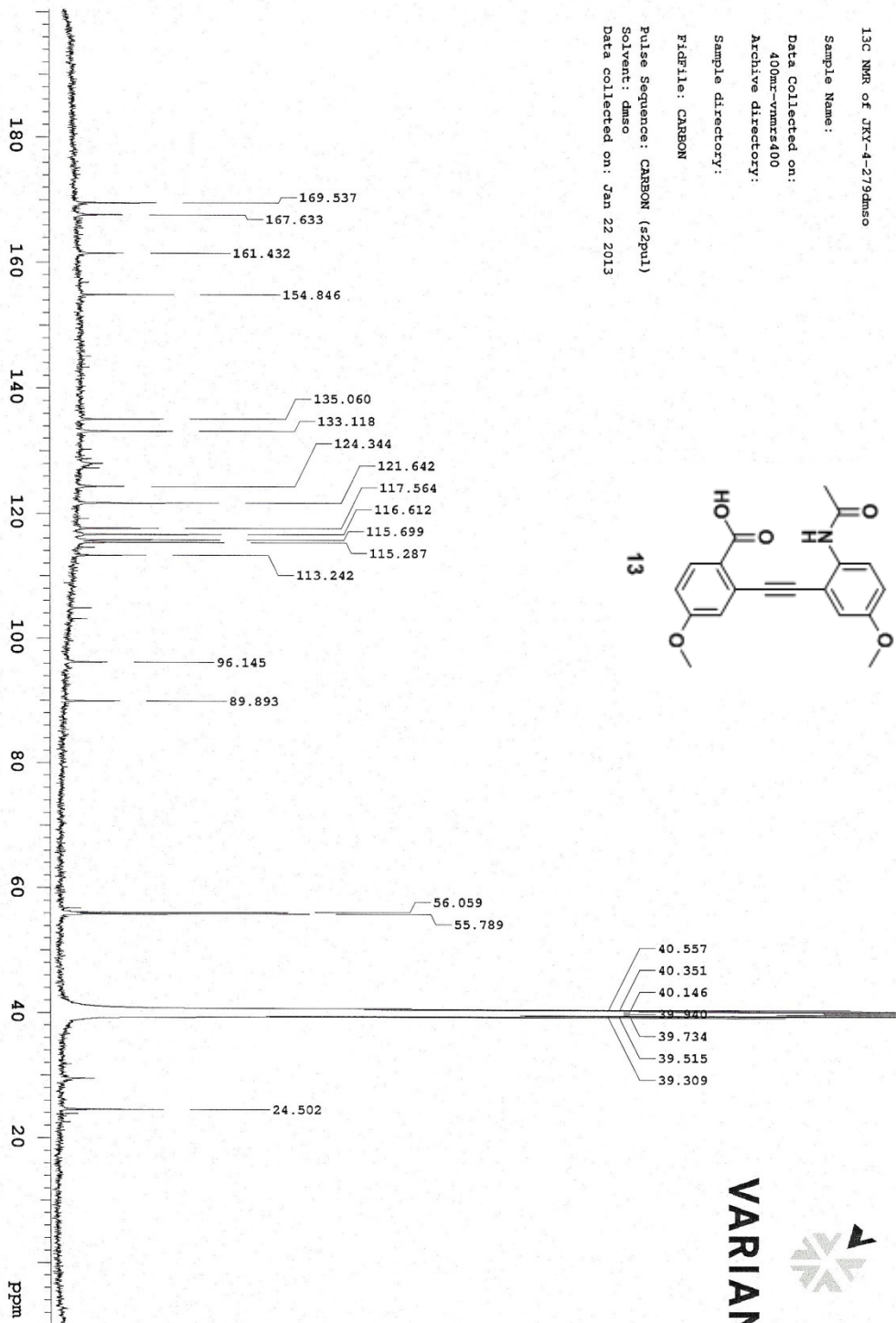
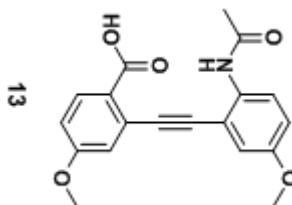
Sample directory:

File: CARBON

Pulse Sequence: CARBON (s2pu1)

Solvent: dmsc

Data collected on: Jan 22 2013



VARIAN

JKY-4-289

Sample Name:

Data Collected on:

400mc-vnmr400

Archive directory:

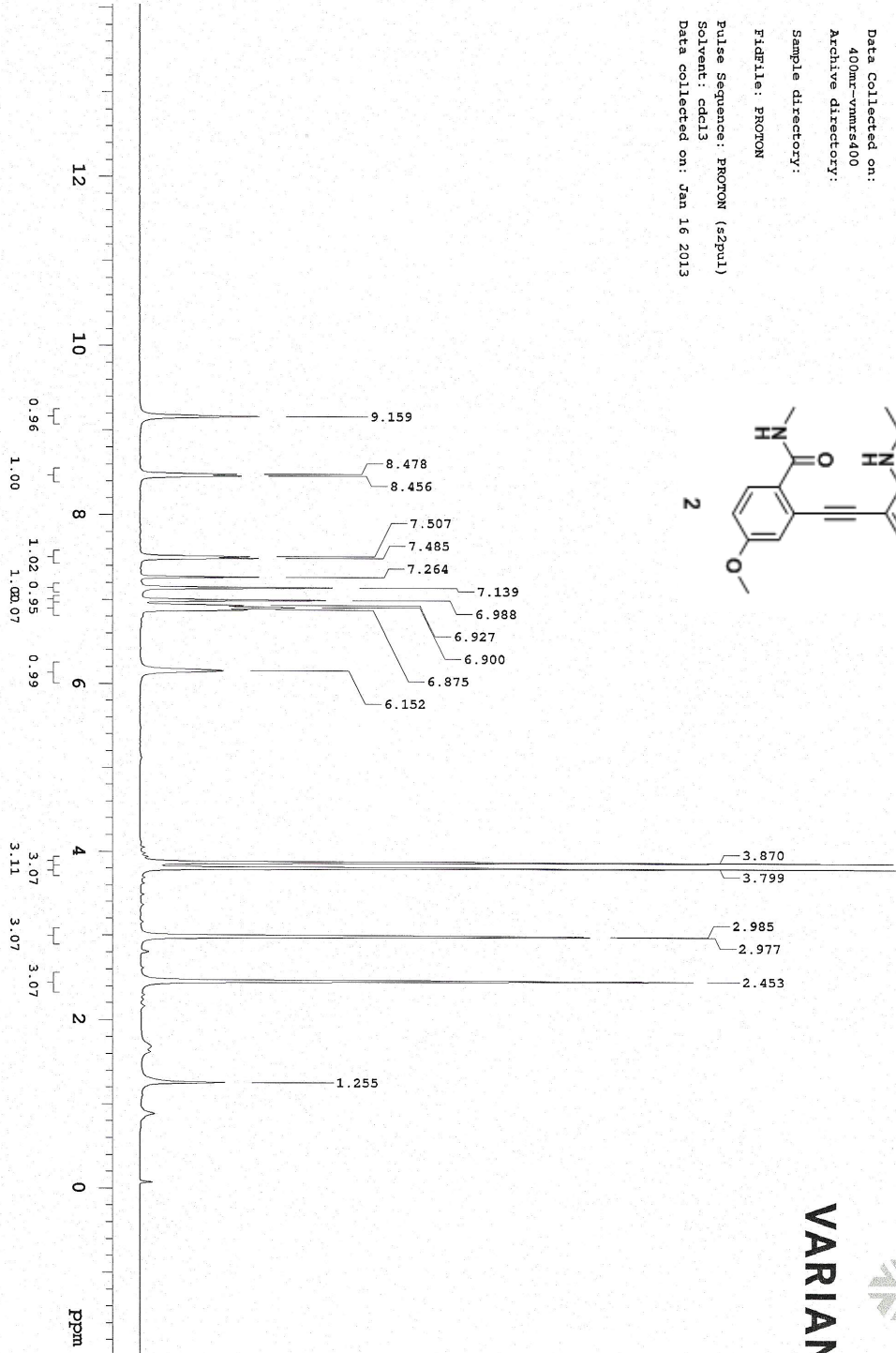
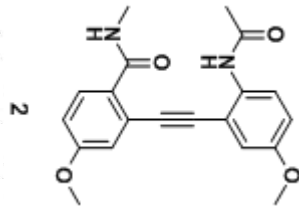
Sample directory:

F1dFile: PROTON

Pulse Sequence: PROTON (szpul)

Solvent: cdcl3

Data collected on: Jan 16 2013



VARIAN

¹³C NMR of JKY-4-289

Sample Name:

Data Collected on:

400mz-vnmrs400

Archive directory:

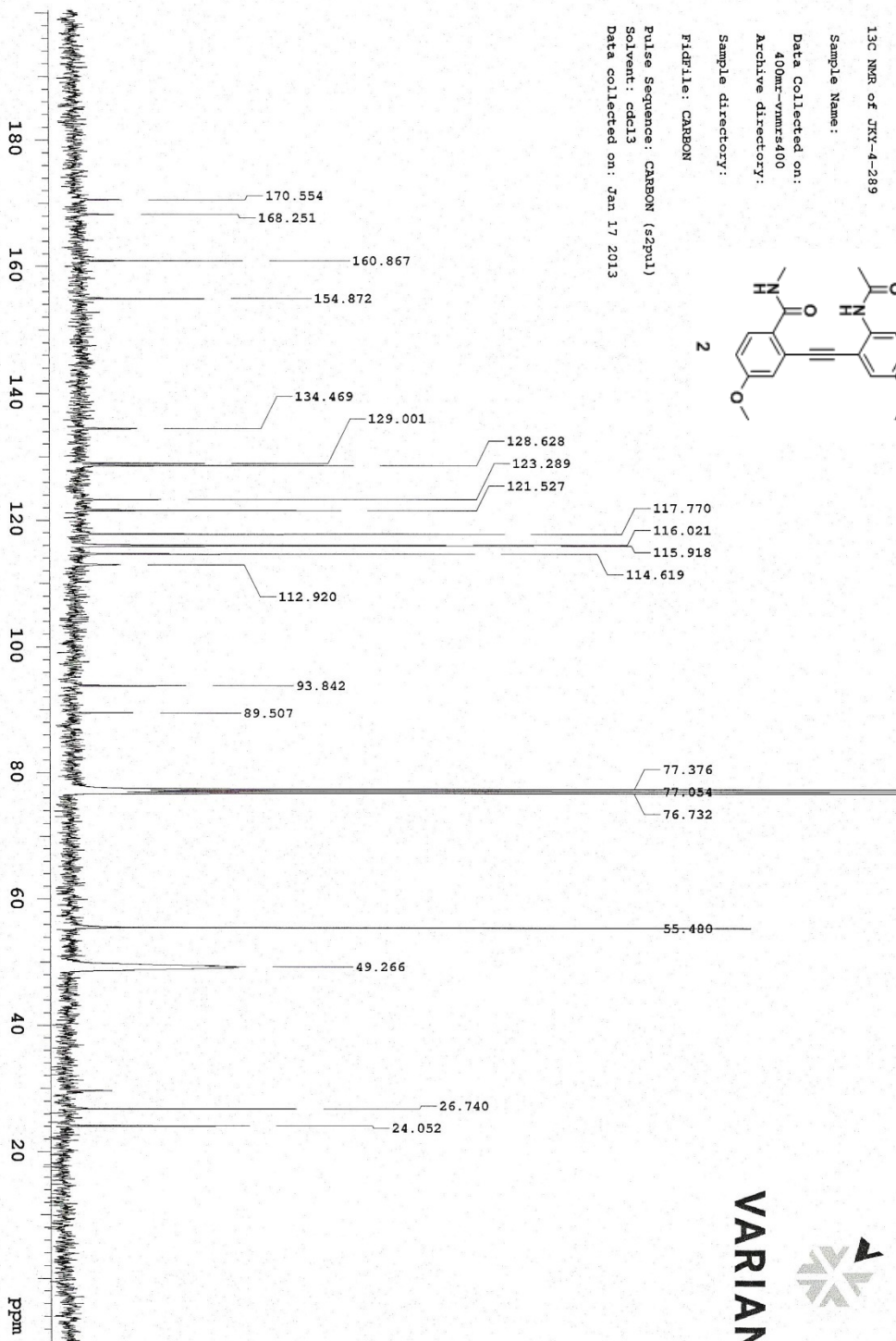
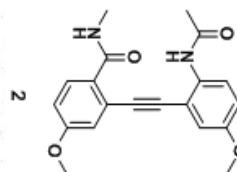
Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (szpu1)

Solvent: cdcl3

Data collected on: Jan 17 2013



VARIAN



JKY-4-304

Sample Name:

Data Collected on:

40mm-vnmr400

Archive directory:

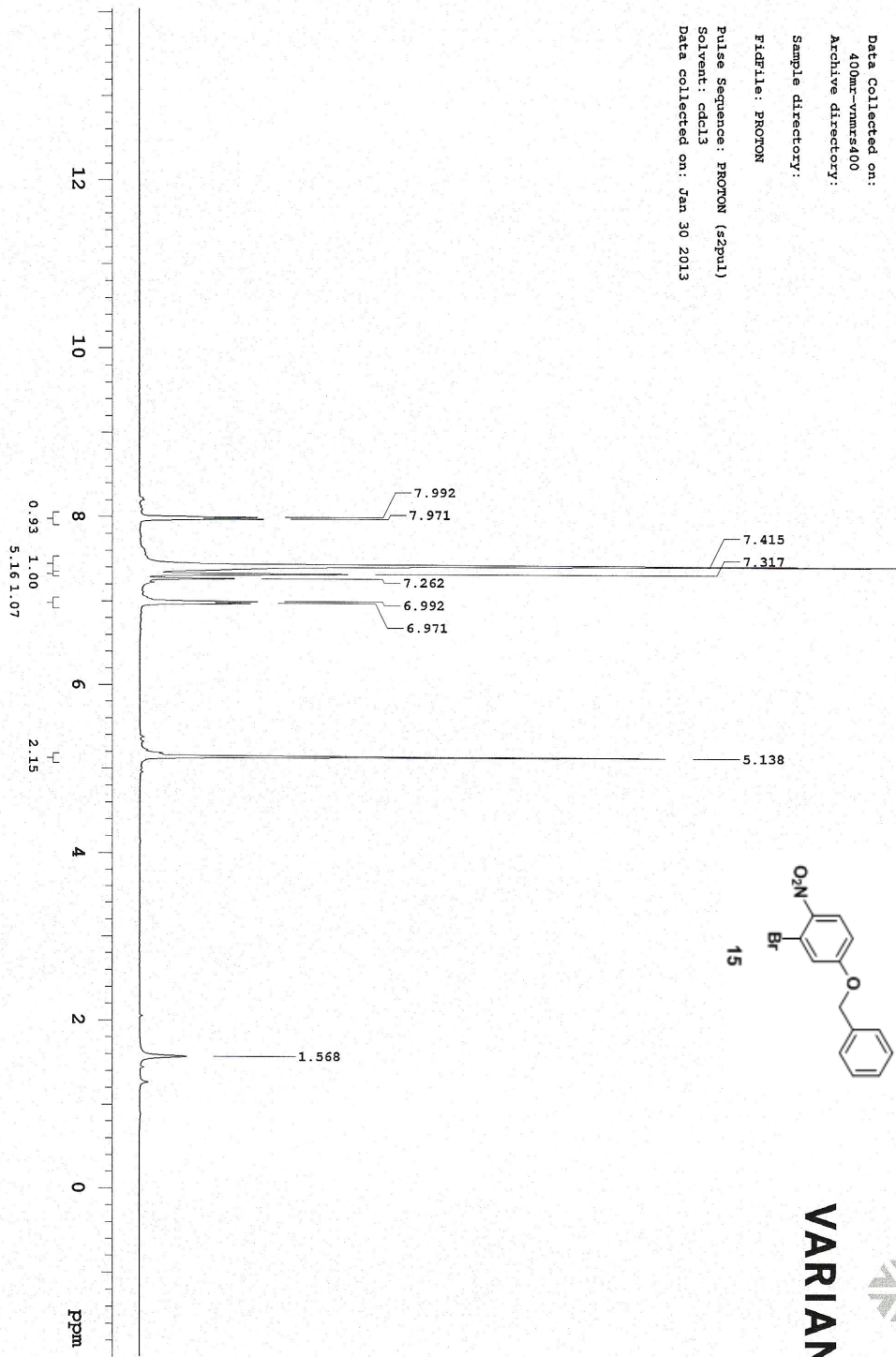
Sample directory:

File: PROMON

Pulse Sequence: PROMON (z2pu1)

Solvent: cdcl3

Data collected on: Jan 30 2013



VARIAN

¹³C NMR of JKY-4-304

Sample Name:

Data Collected on:

400mr-vnmr400

Archive directory:

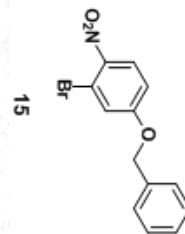
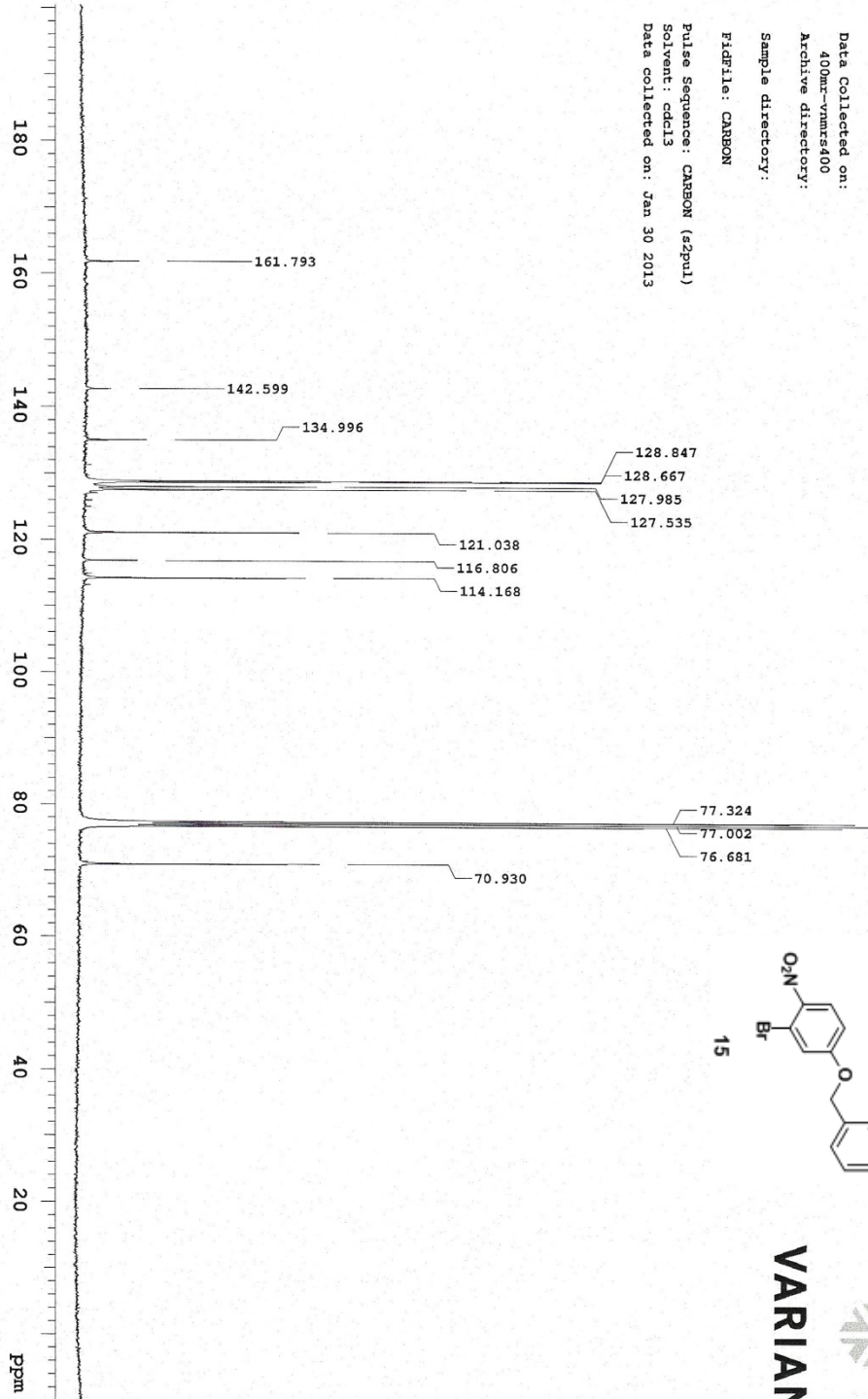
Sample directory:

FIDFile: CARBON

Pulse Sequence: CARBON (2pul)

Solvent: cdcl3

Data collected on: Jan 30 2013



VARIAN



JRY-4-305

Sample Name:

Data Collected on:

40nmr-vmrz400

Archive directory:

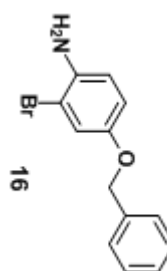
Sample directory:

File: PROTON

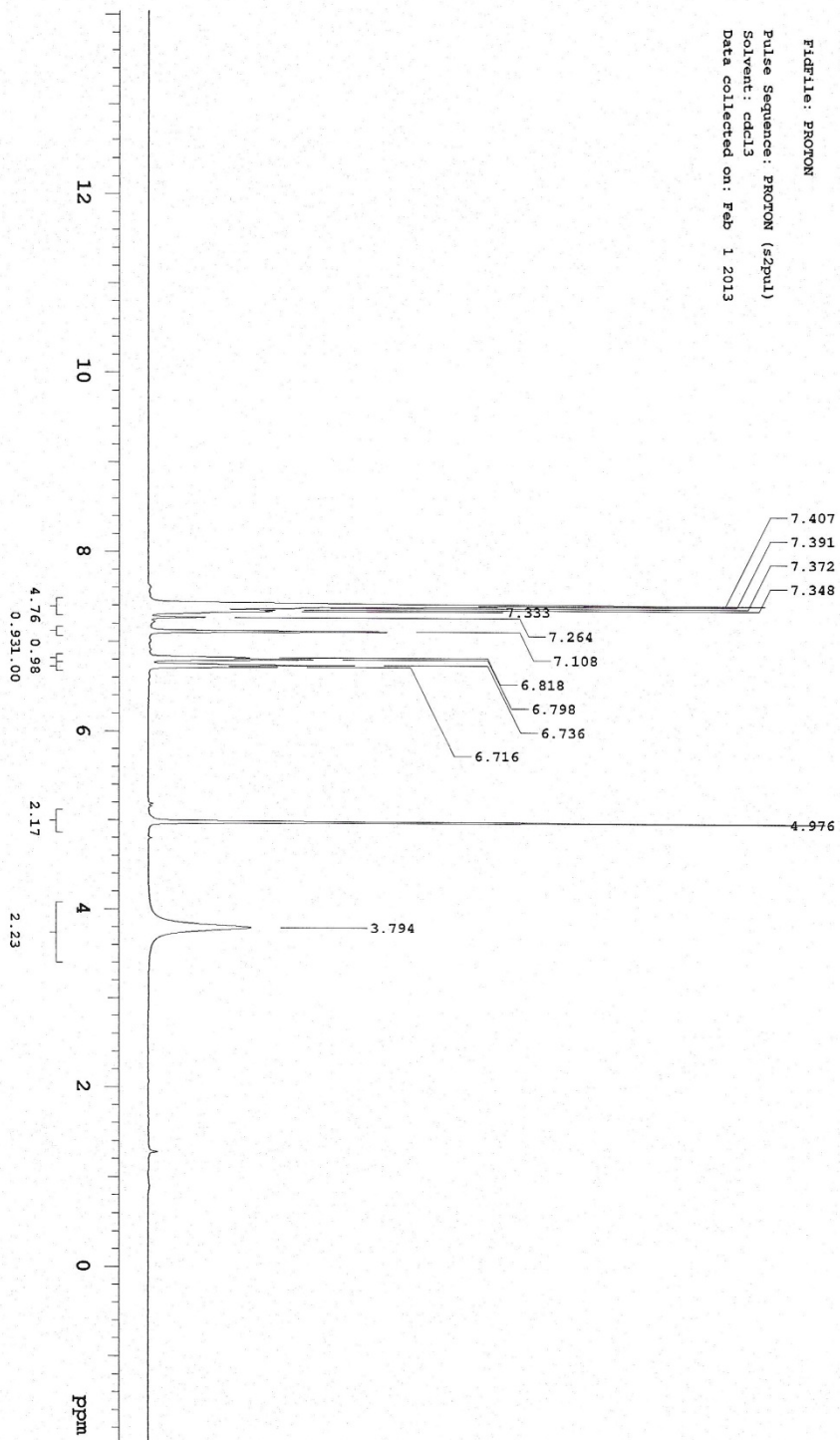
Pulse Sequence: PROTON (szpu1)

Solvent: cdcl3

Data collected on: Feb 1 2013



VARIAN



¹³C NMR of JKY-4-305

Sample Name:

Data Collected on:

400mr-vmr400

Archive directory:

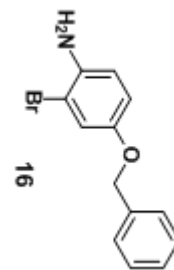
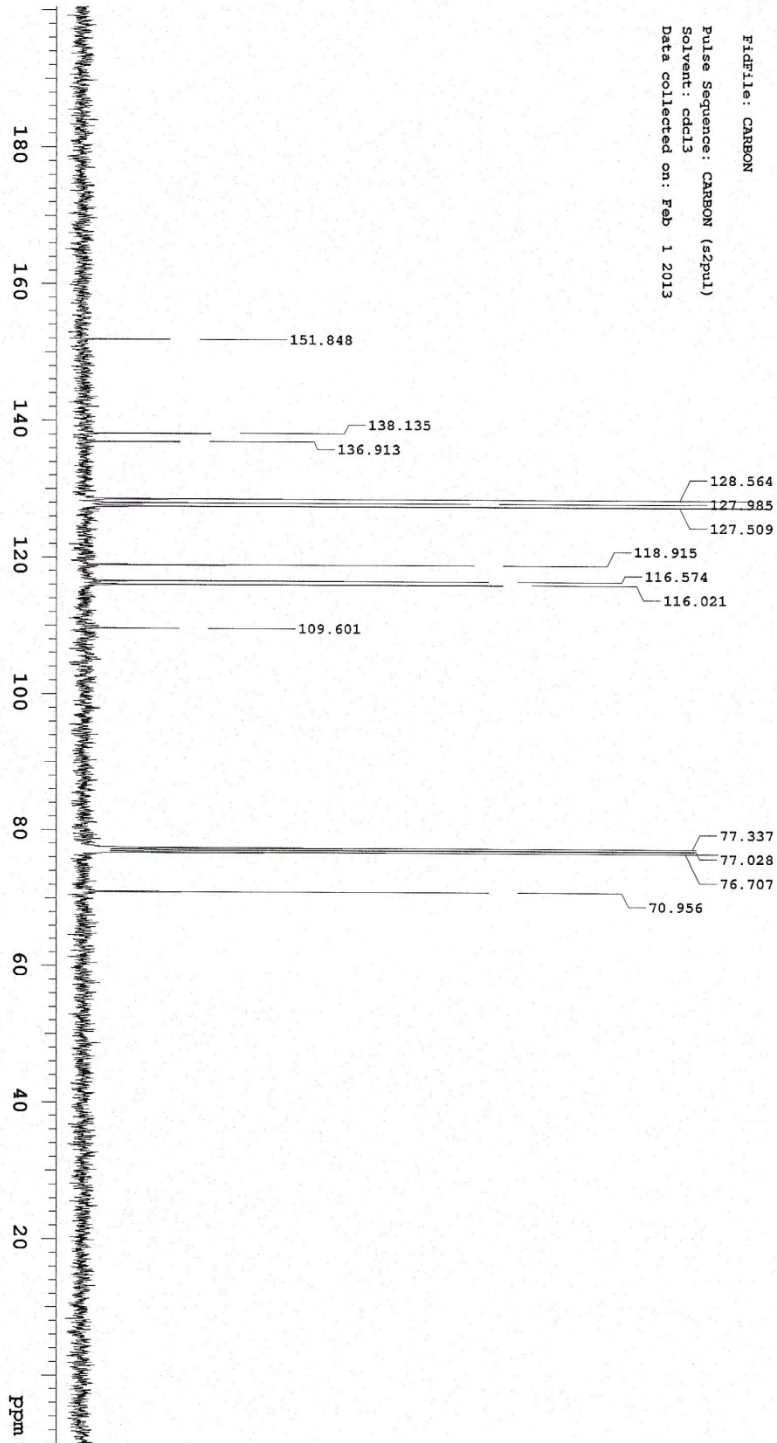
Sample directory:

File: CARBON

Pulse Sequence: CARBON (z2pu1)

Solvent: cdcl3

Data collected on: Feb 1 2013




VARIAN

JKY-4-256

Sample Name:

Data Collected on:

400MHz-nmrms400

Archive directory:

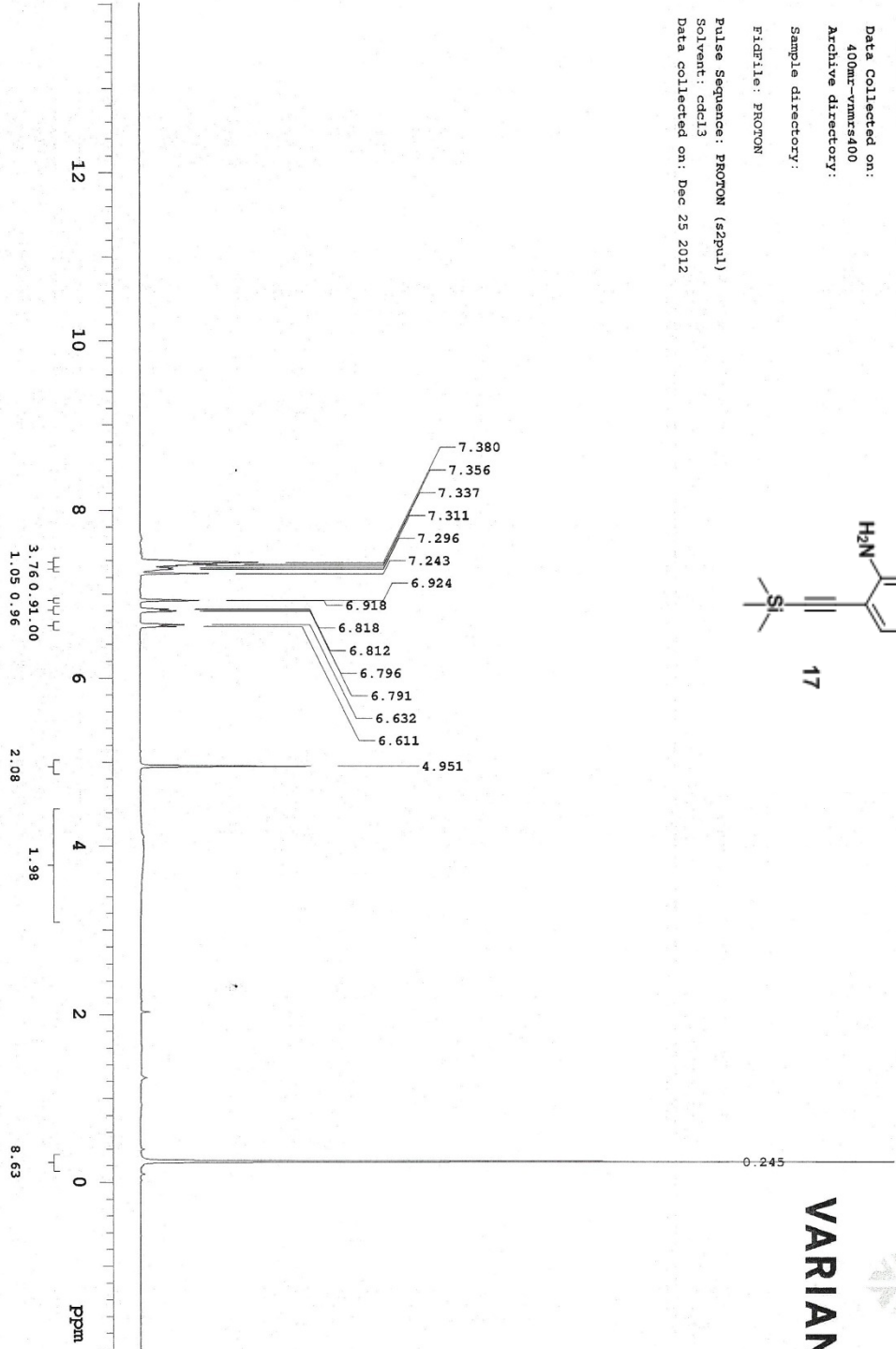
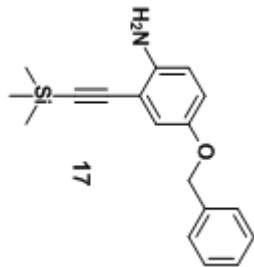
Sample directory:

F1F1File: PROTON

Pulse Sequence: PROTON (s2pul)

Solvent: cdcl3

Data collected on: Dec 25 2012



VARIAN

13C NMR of JKY-4-256

Sample Name:

Data Collected on:

400m-vnmr400

Archive directory:

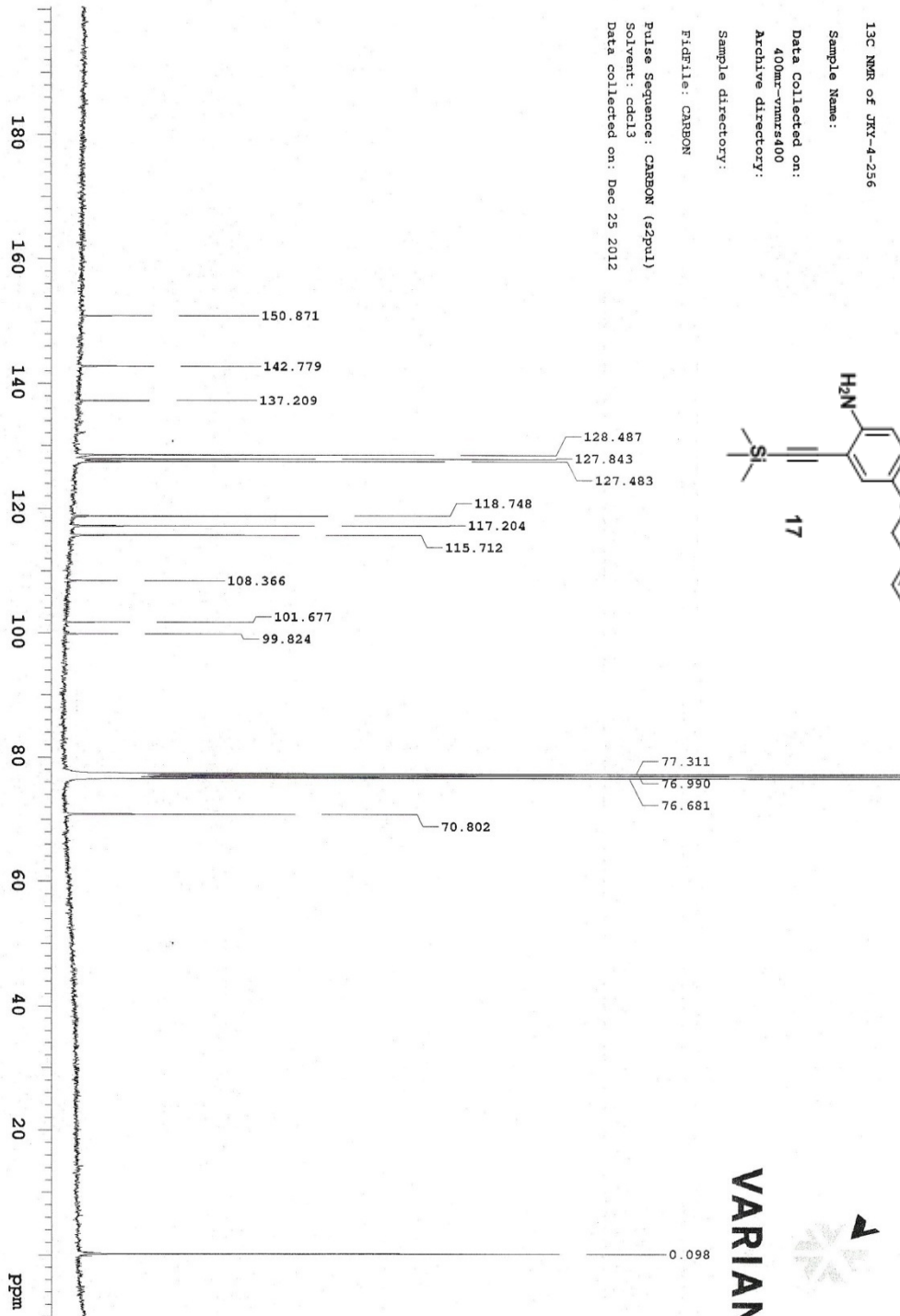
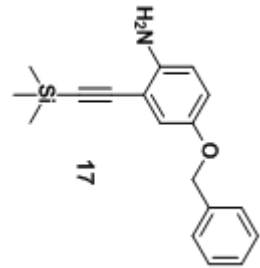
Sample directory:

FIDFile: CARBON

Pulse Sequence: CARBON (szpul)

Solvent: cdcl3

Data collected on: Dec 25 2012



VARIAN



JKY-4-311

Sample Name:

Data Collected on:

40mm-vnmr400

Archive directory:

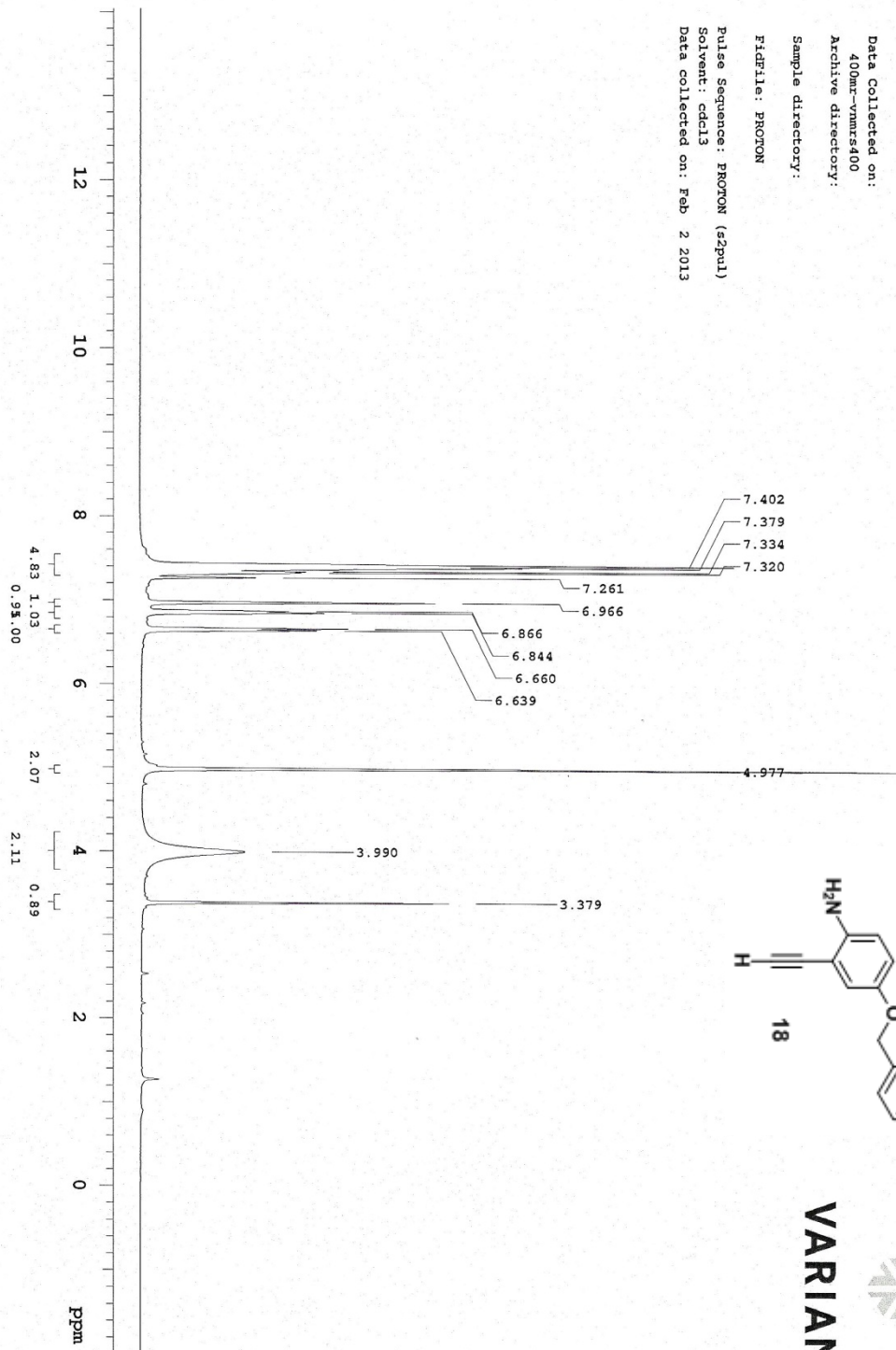
Sample directory:

File: PROTON

Pulse Sequence: PROTON (zgpg3)

Solvent: cdcl3

Data collected on: Feb 2 2013



¹³C NMR of JKY-4-311

Sample Name:

Data Collected on:

400mr-vmrz400

Archive directory:

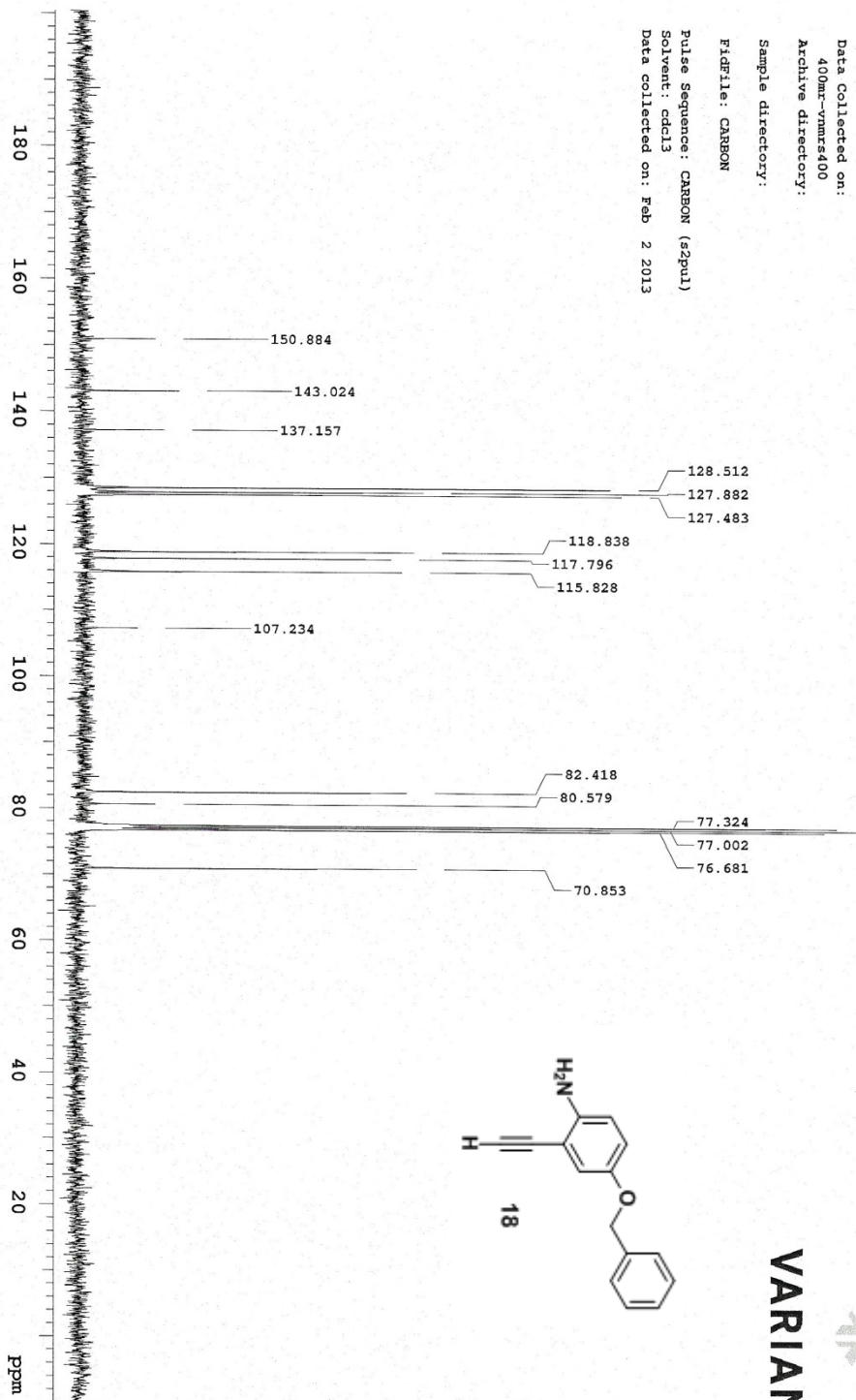
Sample directory:

File: CARBON

Pulse Sequence: CARBON (s2pul)

Solvent: cdcl3

Data collected on: Feb 2 2013



VARIAN

JKY-4-236

Sample Name:

Data Collected on:

400mc-vnmz400

Archive directory:

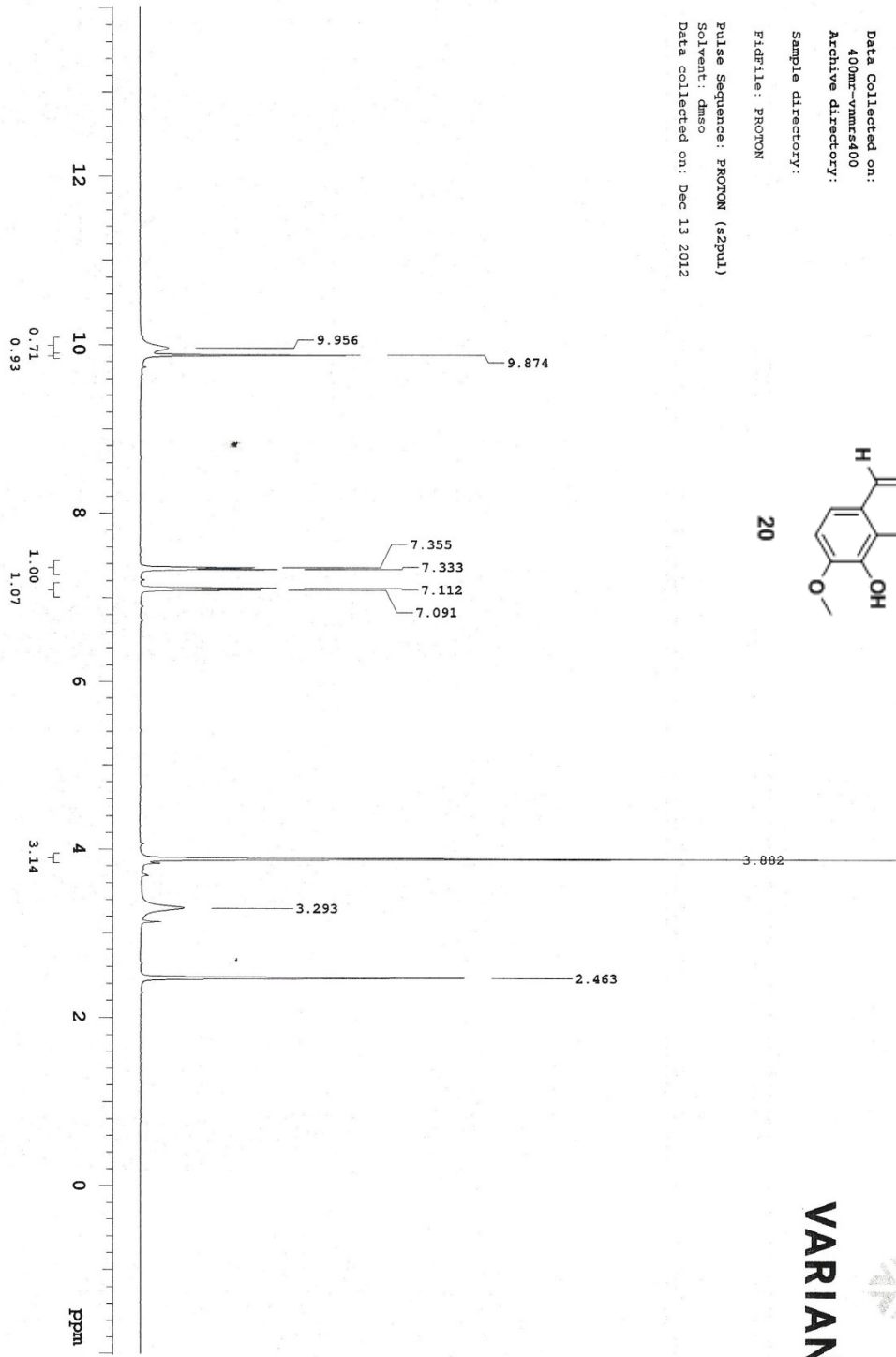
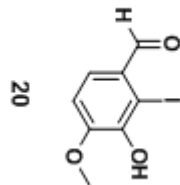
Sample directory:

F1: PROTON

Pulse Sequence: PROTON (s2pu1)

Solvent: dmso

Data collected on: Dec 13 2012



VARIAN

13C NMR of JKY-4-236

Sample Name:

Data Collected on:
400MHz-vnmr400

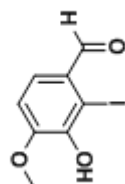
Archive directory:

Sample directory:

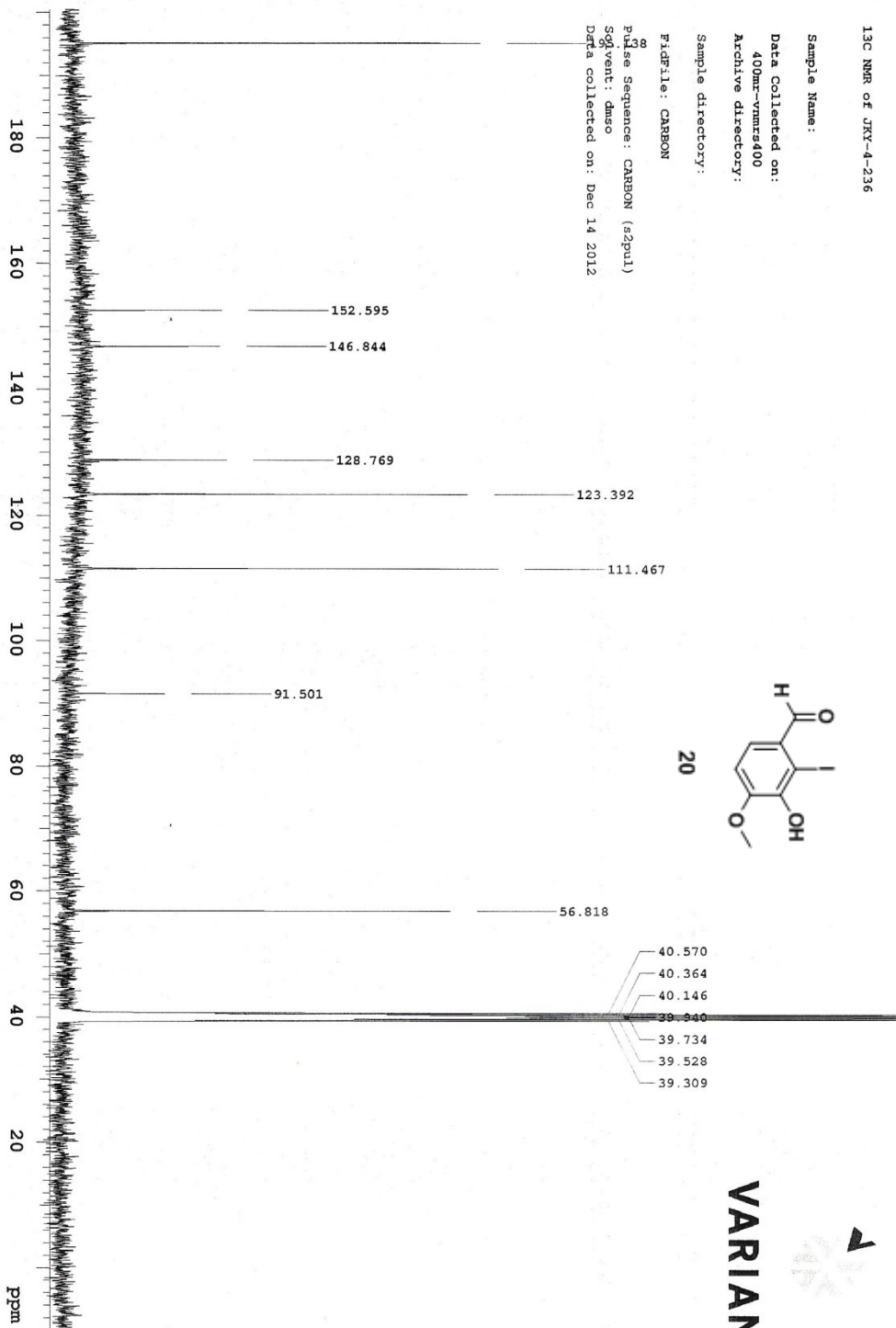
Filefile: CARBON

Pulse Sequence: CARBON (s2pul)

Solvent: dms0
Data collected on: Dec 14 2012



20



JKY-4-237

Sample Name:

Data Collected on:

400mz-vnmz400

Archive directory:

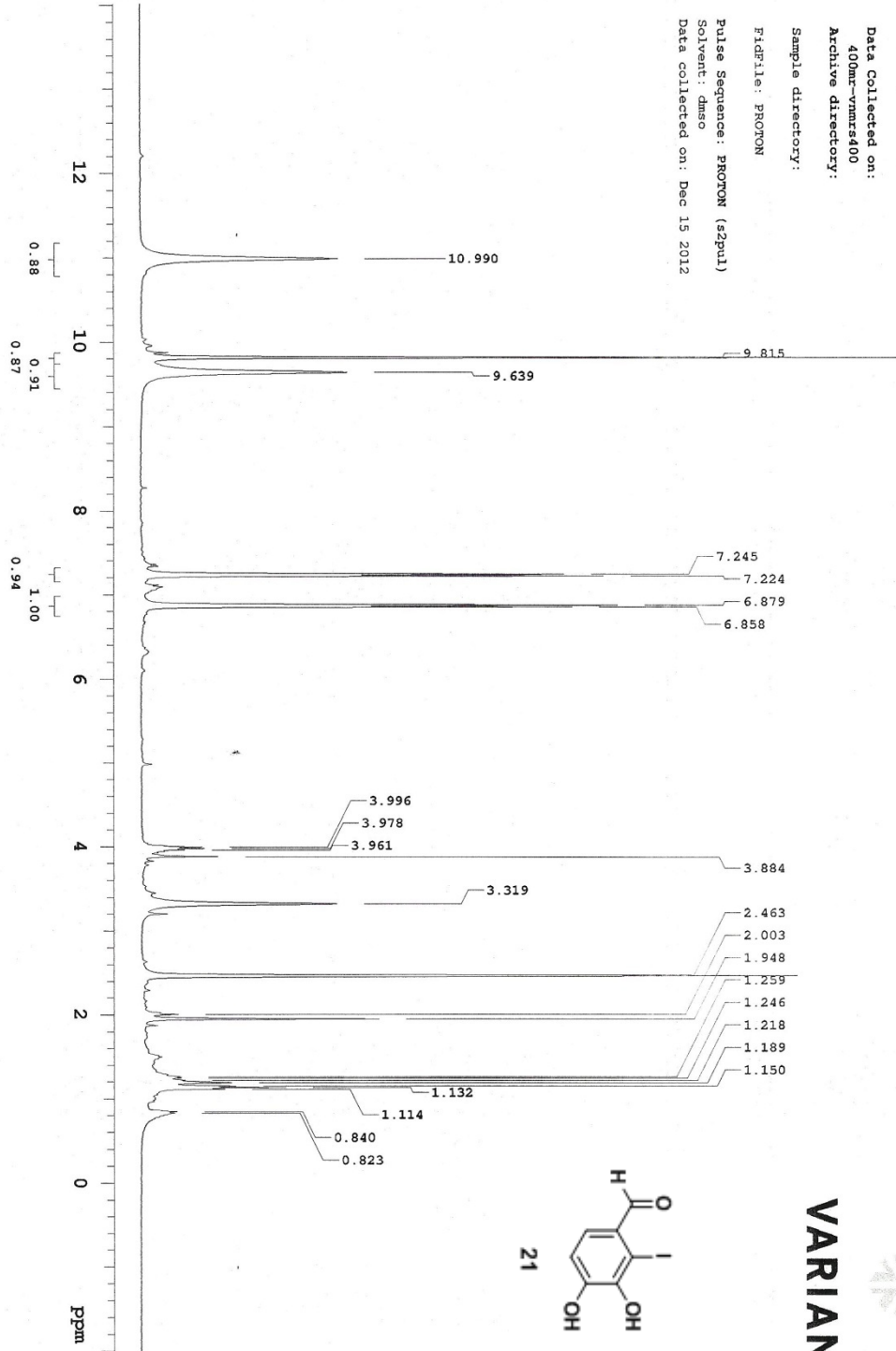
Sample directory:

F1: File: PROTON

Pulse Sequence: PROTON (s2pu1)

Solvent: dmsc

Data collected on: Dec 15 2012



VARIAN

¹³C NMR of JKY-4-237

Sample Name:

Data Collected on:
400mr-vnmr400

Archive directory:

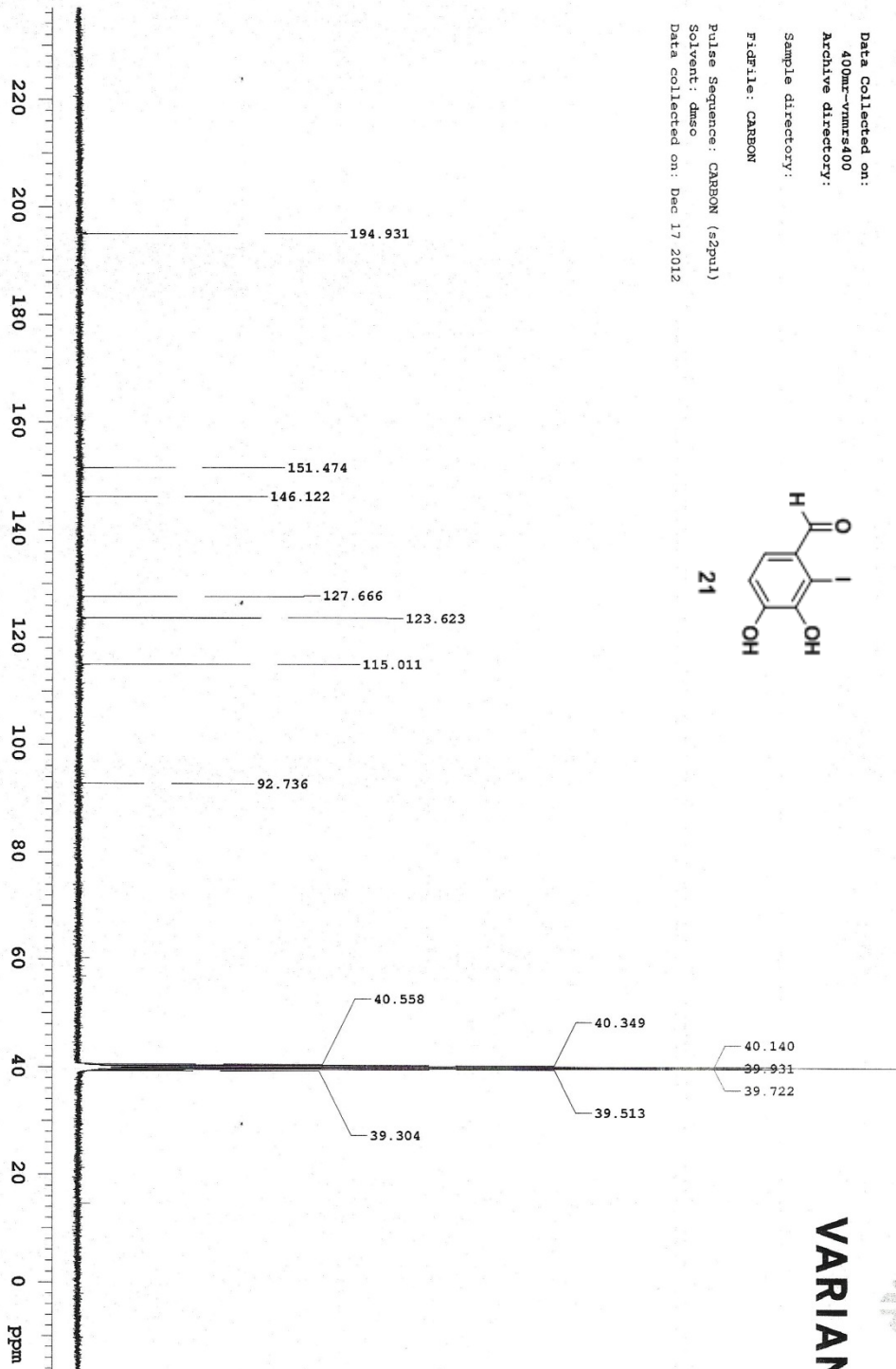
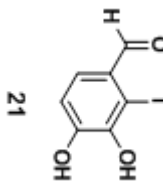
Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)

Solvent: dmsc

Data collected on: Dec 17 2012



JKY-4-254A

Sample Name:

Data Collected on:

400MHz-nmms400

Archive directory:

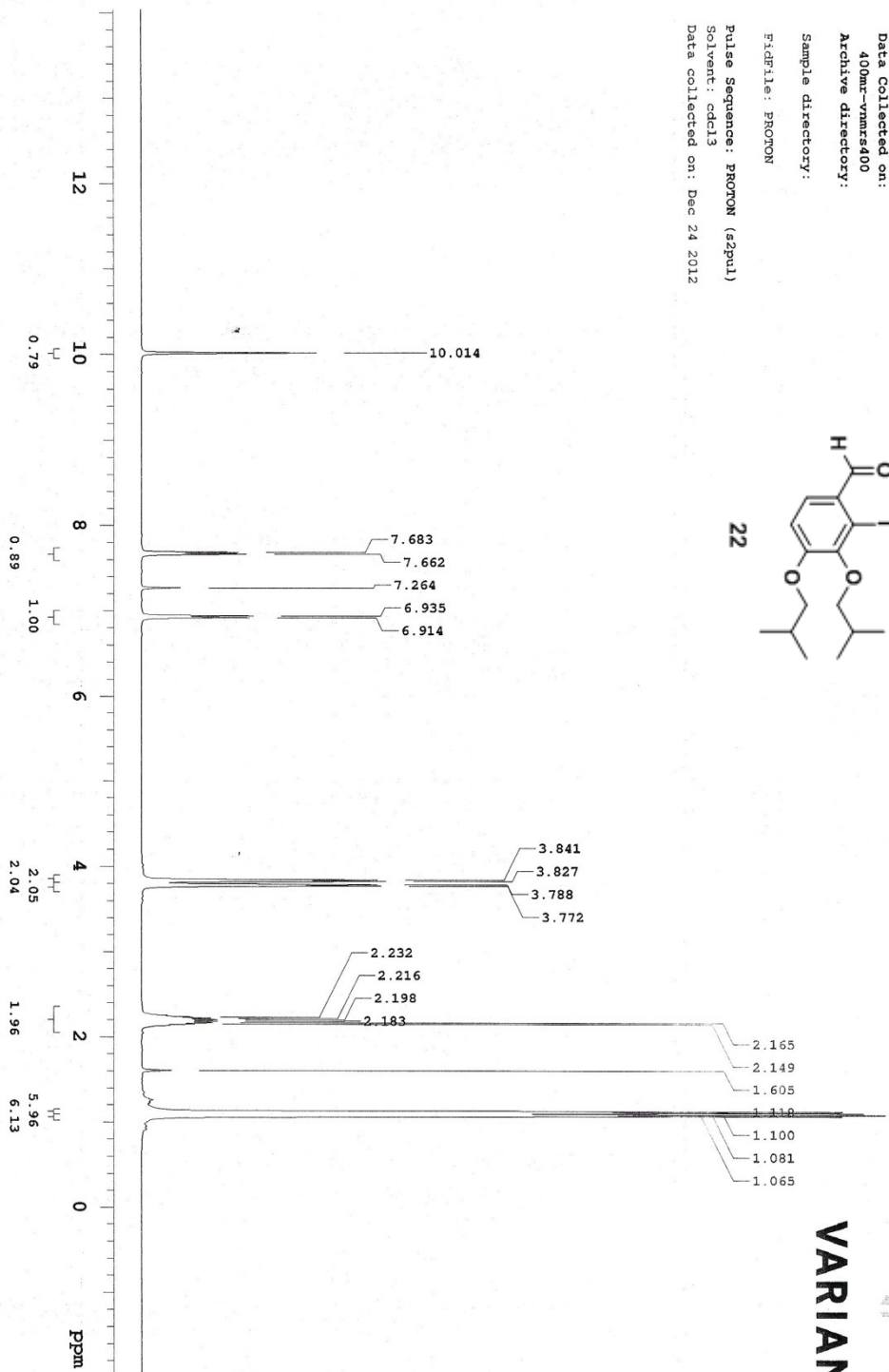
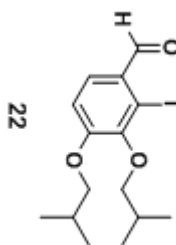
Sample directory:

Filefile: PROTON

Pulse Sequence: PROTON (s2pu1)

Solvent: cdcl3

Data collected on: Dec 24 2012



VARIAN

¹³C NMR of JKY-4-254A

Sample Name:

Data Collected on:

400m-vnmr400

Archive directory:

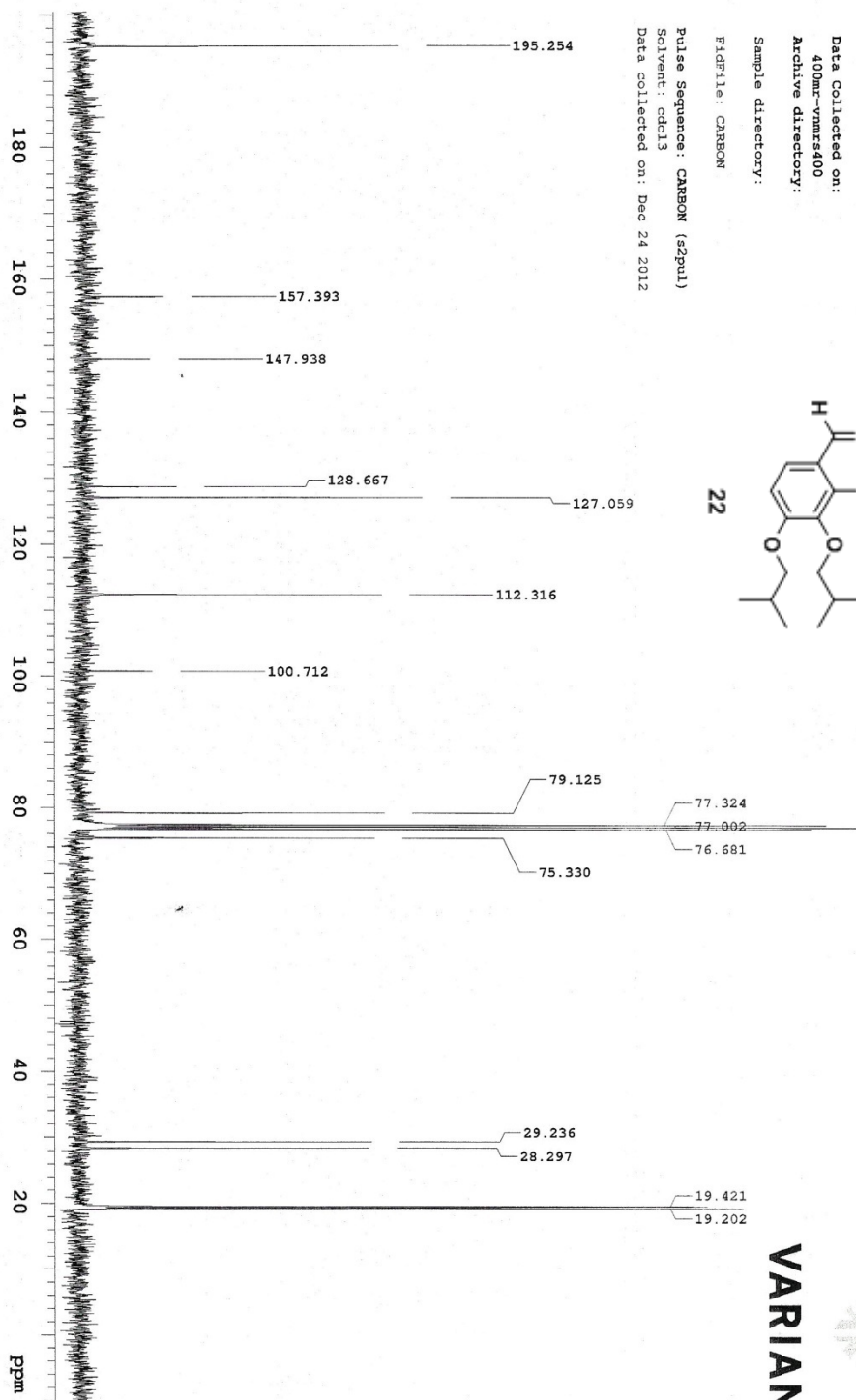
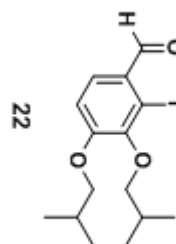
Sample directory:

Expfile: CARBON

Pulse Sequence: CARBON (s2pul)

Solvent: cdcl3

Data collected on: Dec 24 2012



JKY-4-255

Sample Name:

Data Collected on:

400mc-vnmr400

Archive directory:

Sample directory:

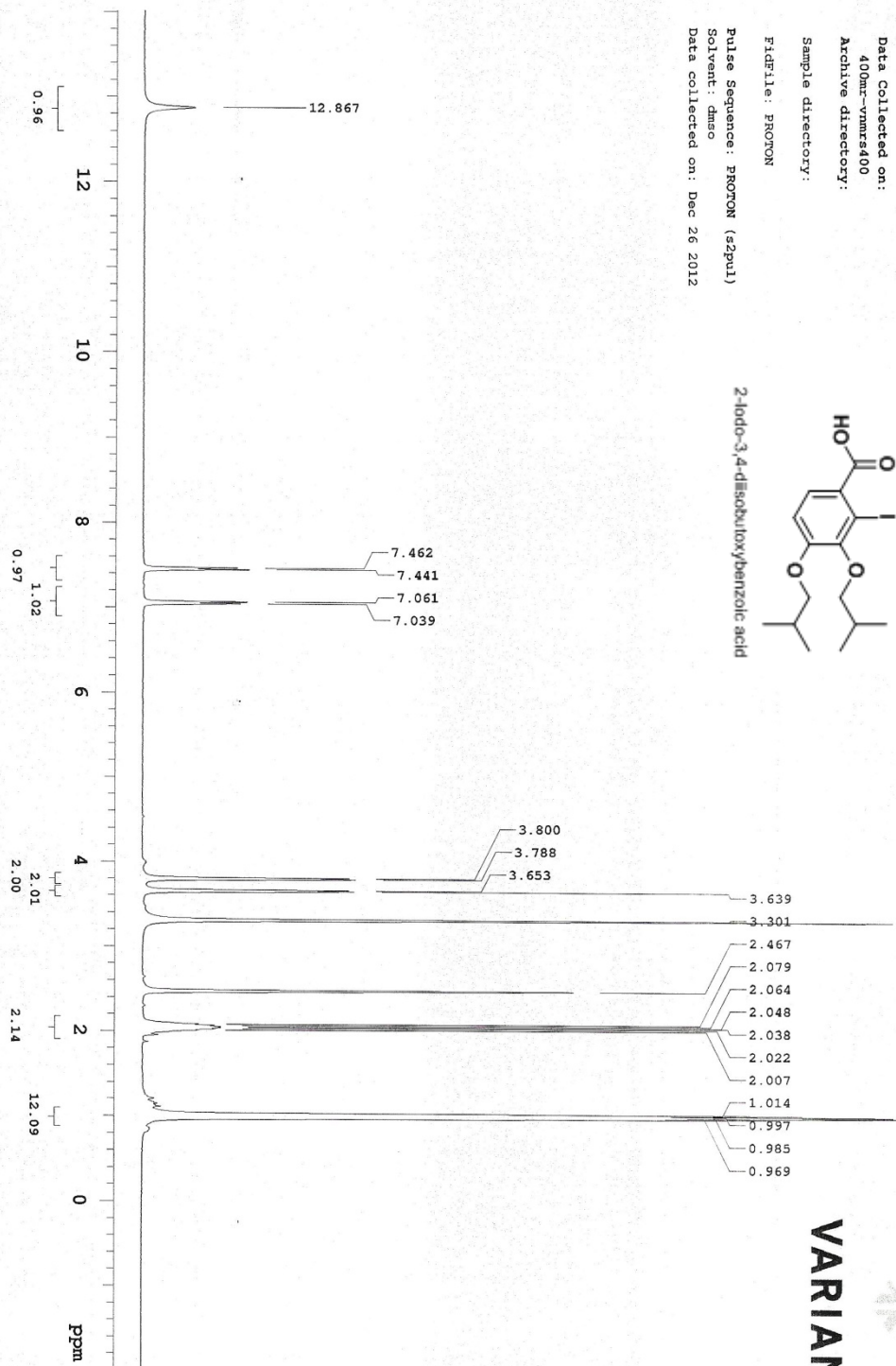
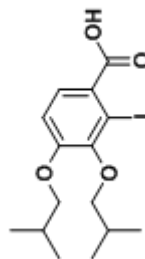
F1File: PROTON

Pulse Sequence: PROTON (s2pu1)

Solvent: dmsc

Data collected on: Dec 26 2012

2-Iodo-3,4-diisobutoxybenzoic acid



VARIAN

¹³C NMR of JKY-4-255

Sample Name:

Data Collected on:

400MHz-nmr400

Archive directory:

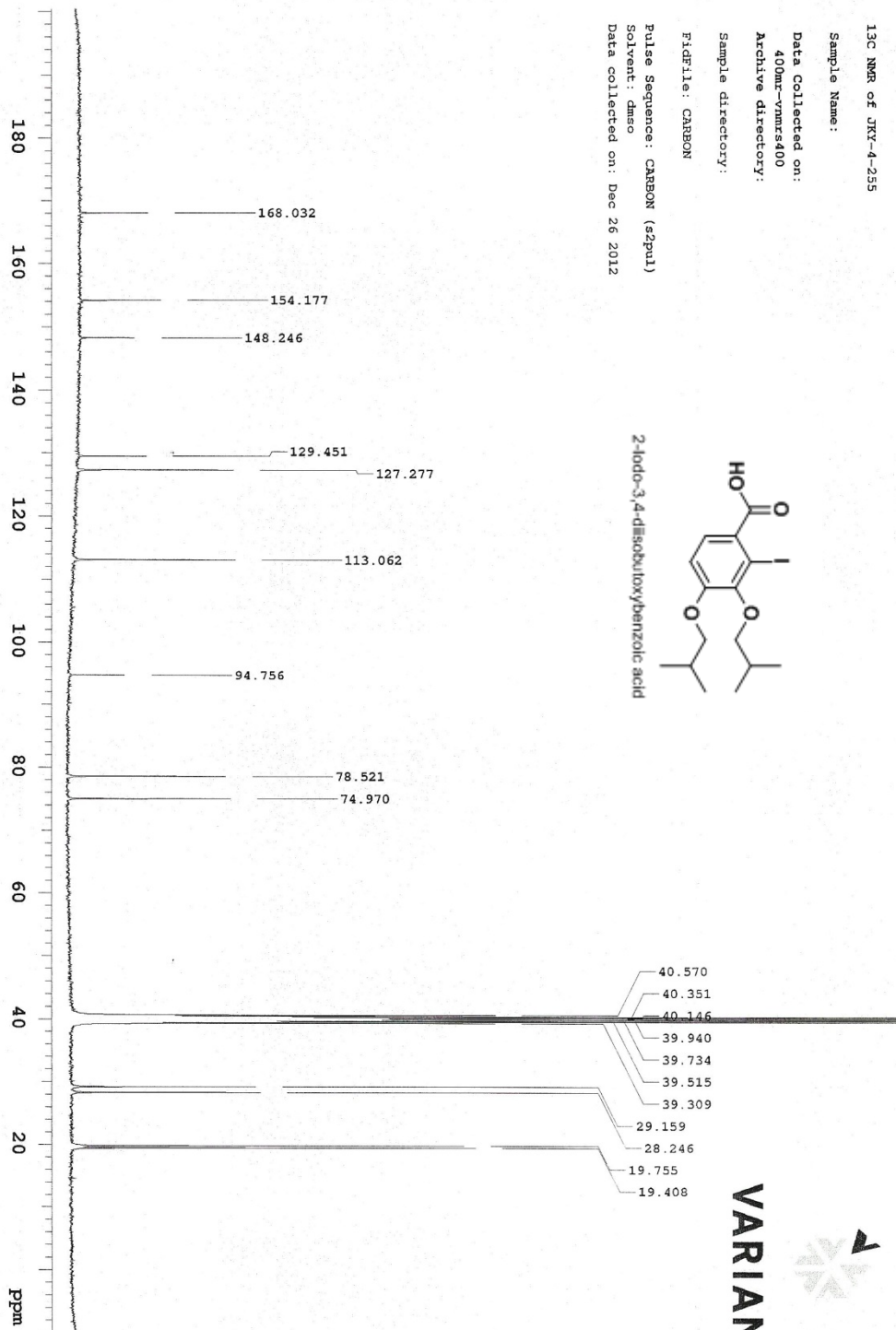
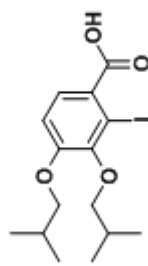
Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (zgpg3)

Solvent: dmso

Data collected on: Dec 26 2012



JKY-4-257

Sample Name:

Data Collected on:

40mm-vnmr400

Archive directory:

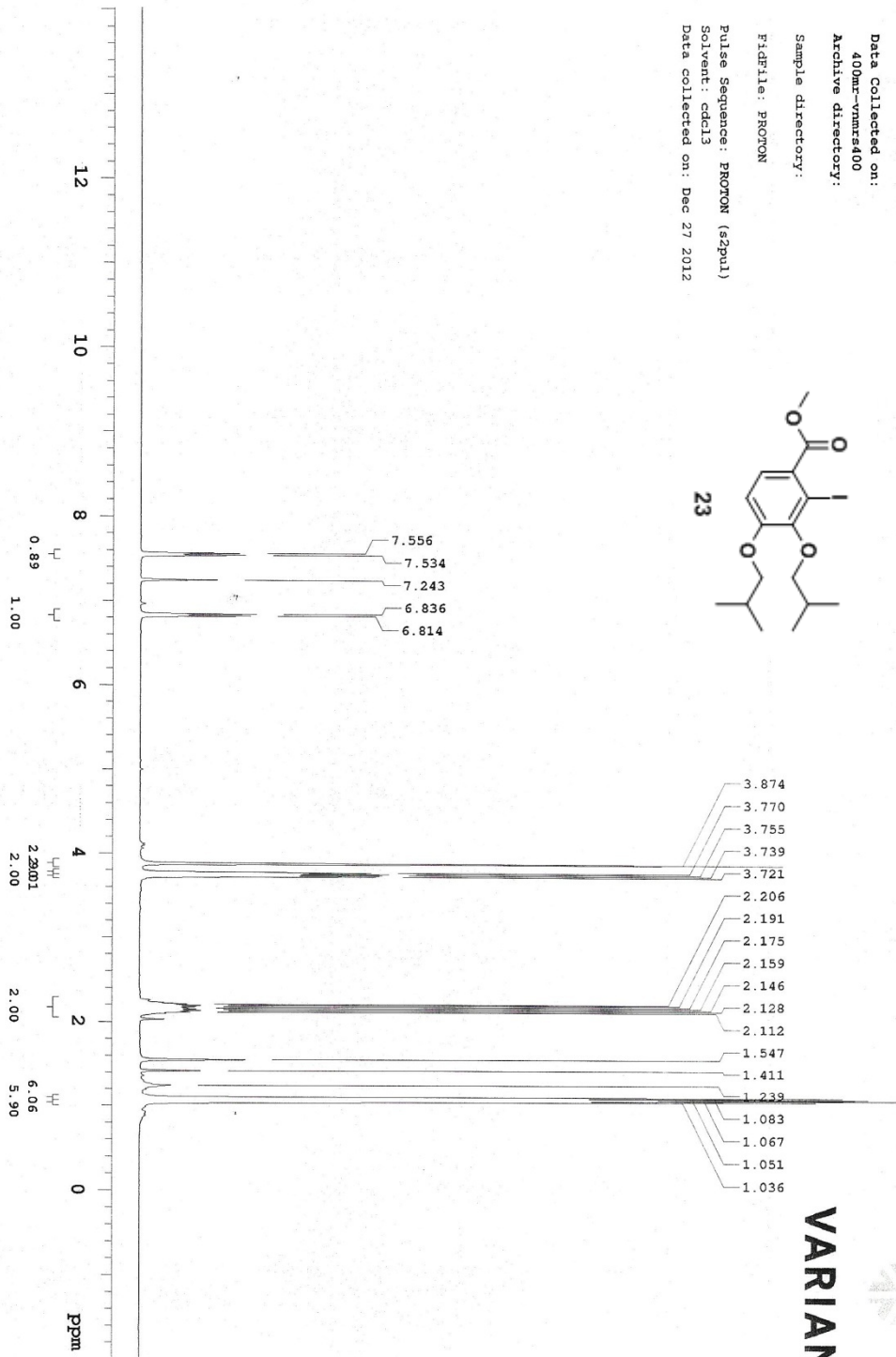
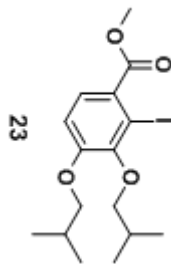
Sample directory:

FIDFILE: PROTON

Pulse Sequence: PROTON (s2pu1)

Solvent: cdcl3

Data collected on: Dec 27 2012



VARIAN



¹³C NMR of JKY-4-257

Sample Name:

Data collected on:

400m-ymms400

Archive directory:

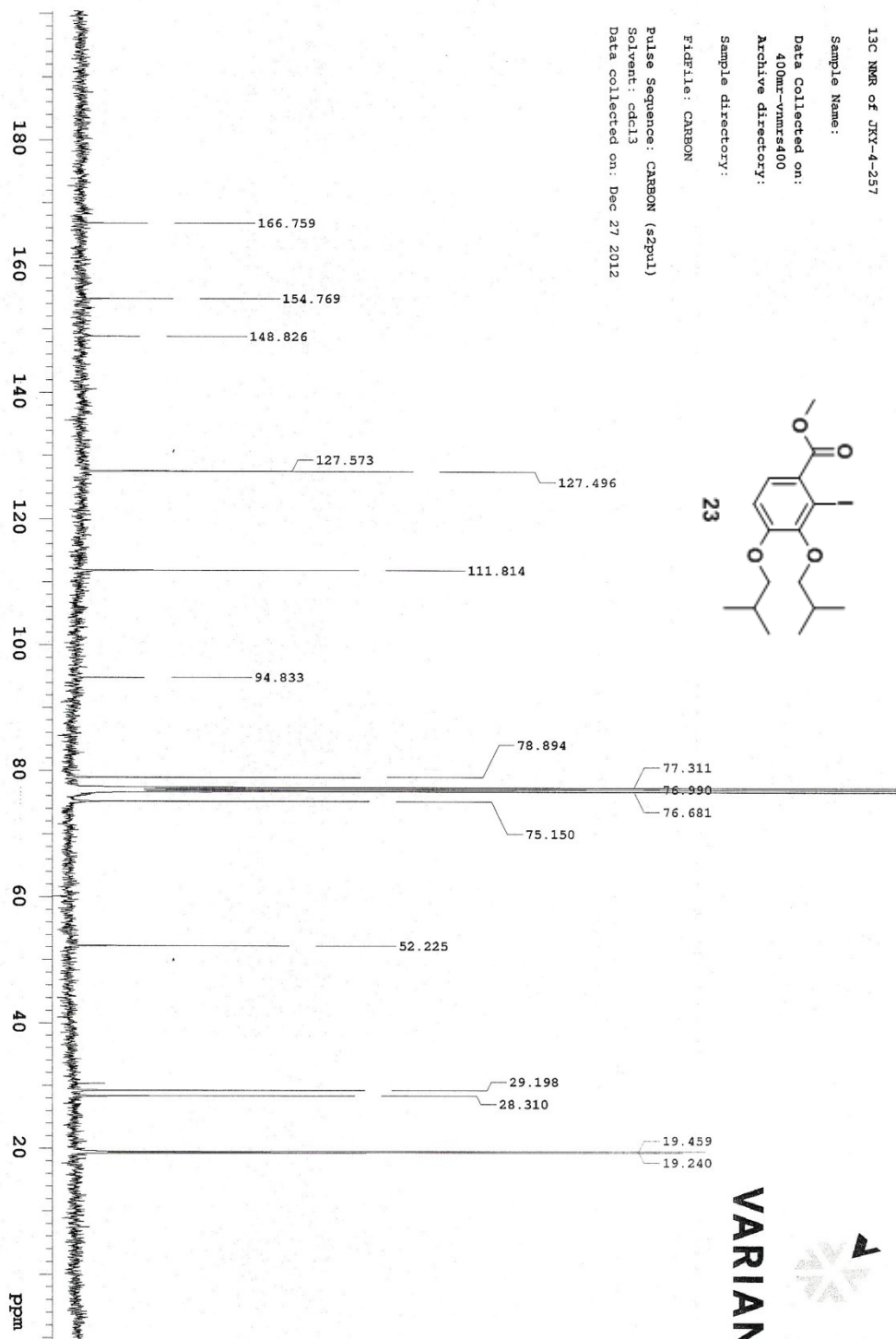
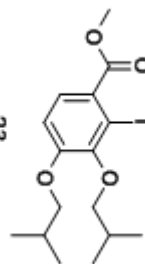
Sample directory:

Fidfile: CARBON

Pulse Sequence: CARBON (szpu)

Solvent: cdcl3

Data collected on: Dec 27 2012



JKV-4-259

Sample Name:

Data Collected on:

400MHz-Vnmr400

Archive directory:

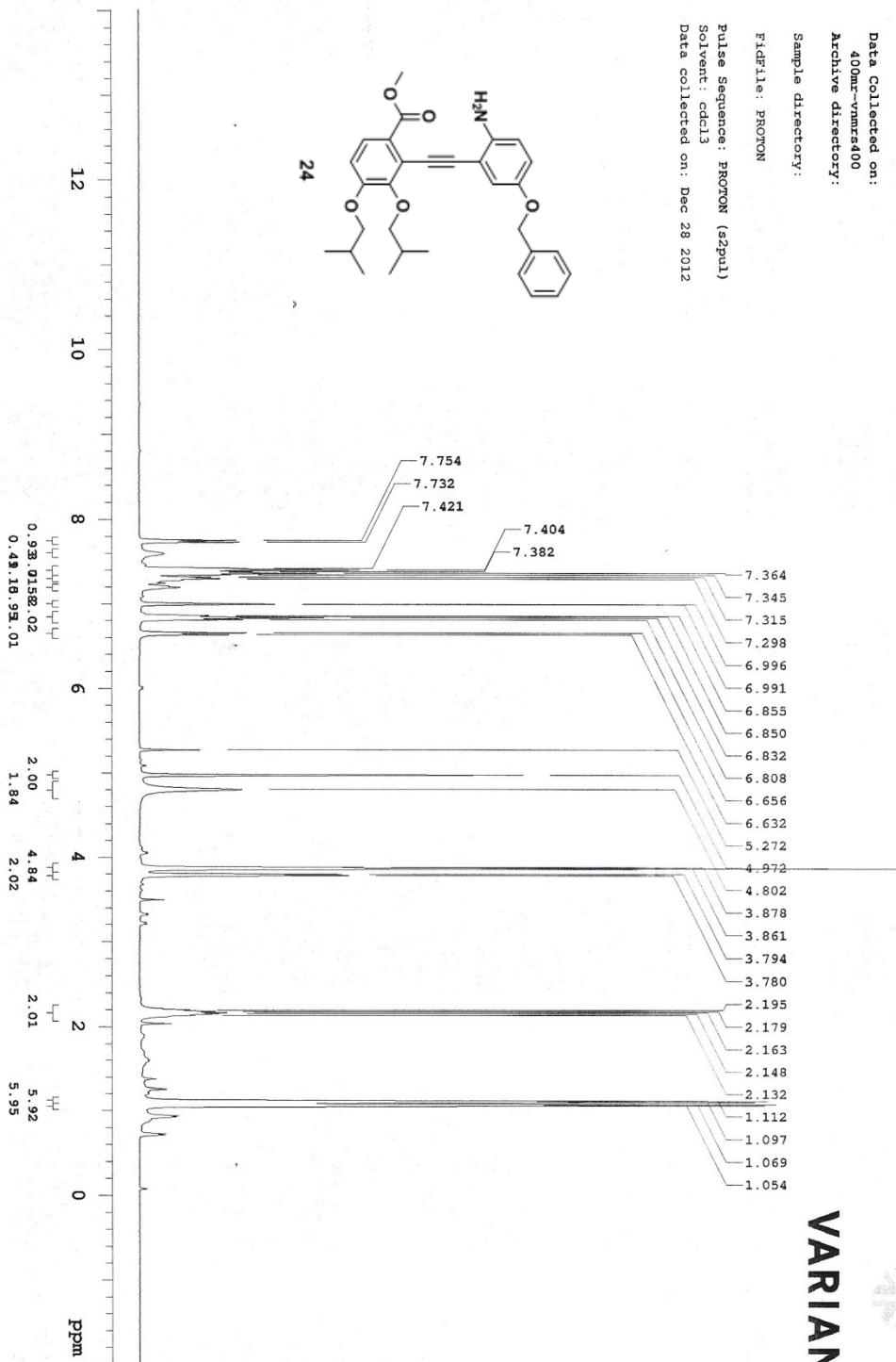
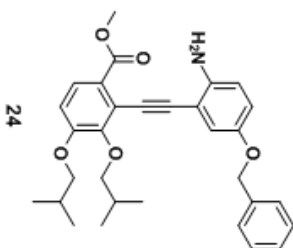
Sample directory:

FidFile: PROTON

Pulse Sequence: PROTON (s2pu1)

Solvent: cdcl3

Data collected on: Dec 28 2012



¹³C NMR of JKY-4-259

Sample Name:

Data Collected on:

400m-vmr400

Archive directory:

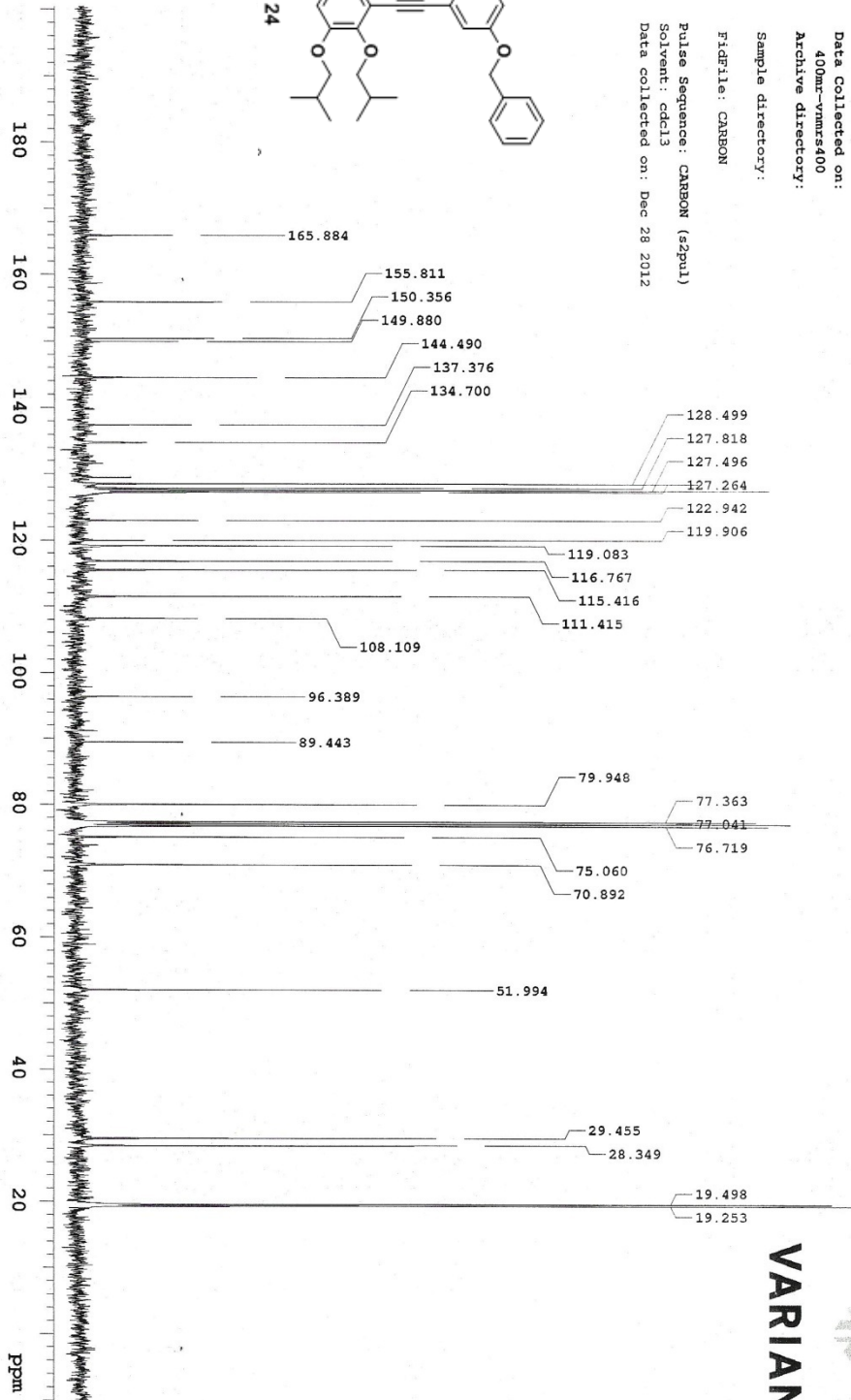
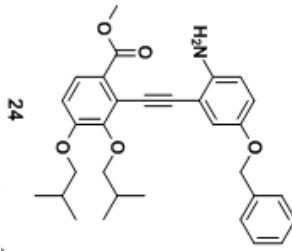
Sample directory:

File: CARBON

Pulse Sequence: CARBON (szpu1)

Solvent: cdcl3

Data collected on: Dec 28 2012



VARIAN



JKX-4-230

Sample Name:

Data Collected on:

400mz-vrms400

Archive directory:

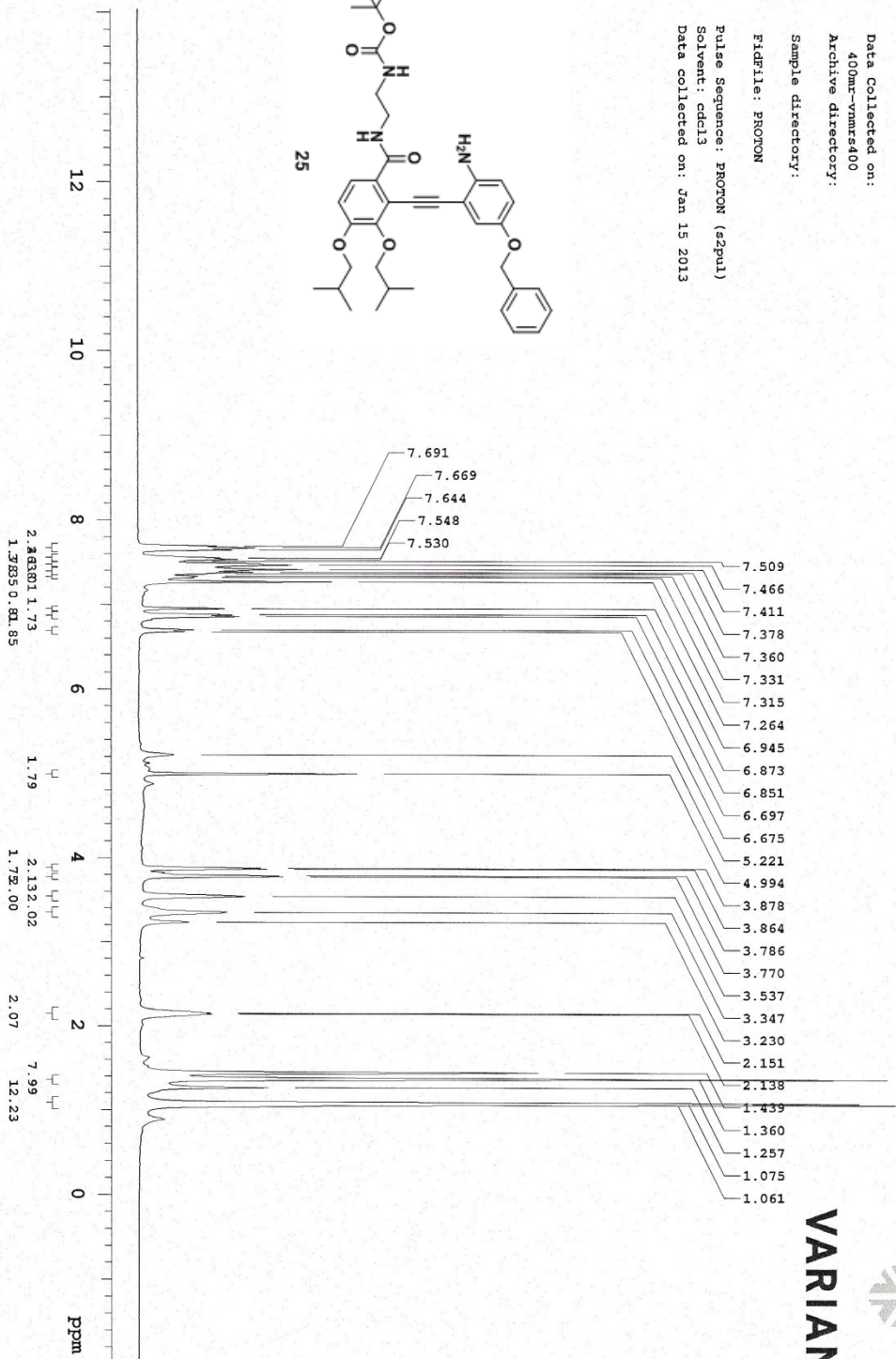
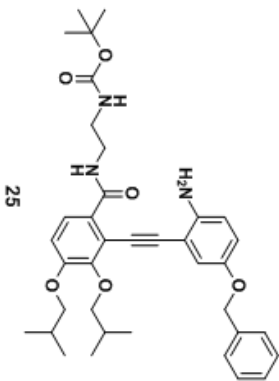
Sample directory:

FIDFile: PROTON

Pulse Sequence: PROTON (s2pu1)

Solvent: cdcl3

Data collected on: Jan 15 2013



VARIAN

¹³C NMR of JKY-4-290

Sample Name:

Data Collected on:

400MHz-nmr400

Archive directory:

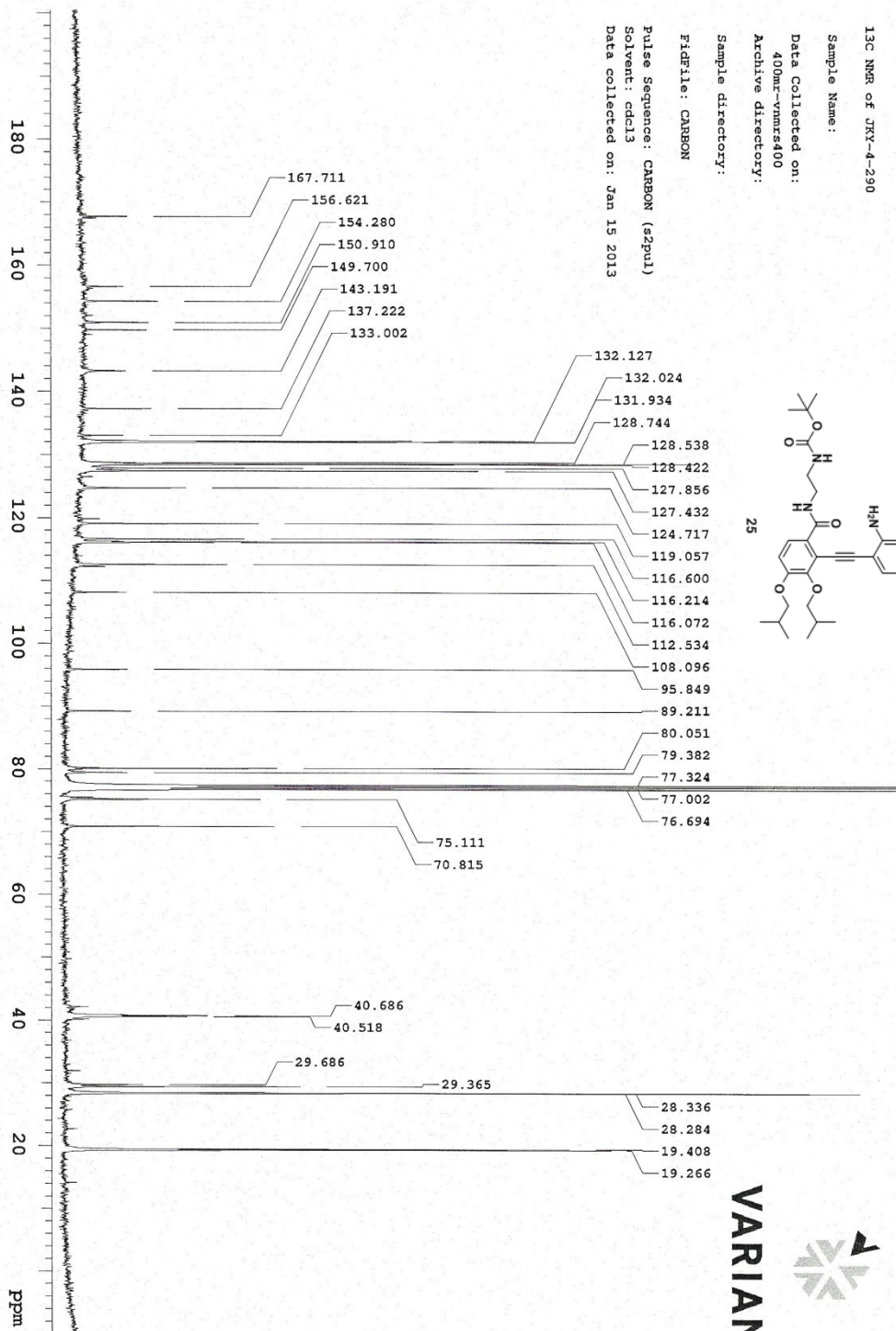
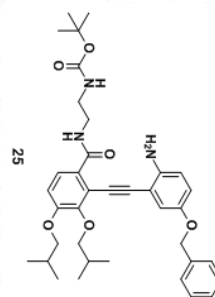
Sample directory:

F1F1File: CARBON

Pulse Sequence: CARBON (szpu1)

Solvent: cdcl3

Data collected on: Jan 15 2013



VARIAN



JKY-4-292

Sample Name:

Data Collected on:

400MHz-nmr400

Archive directory:

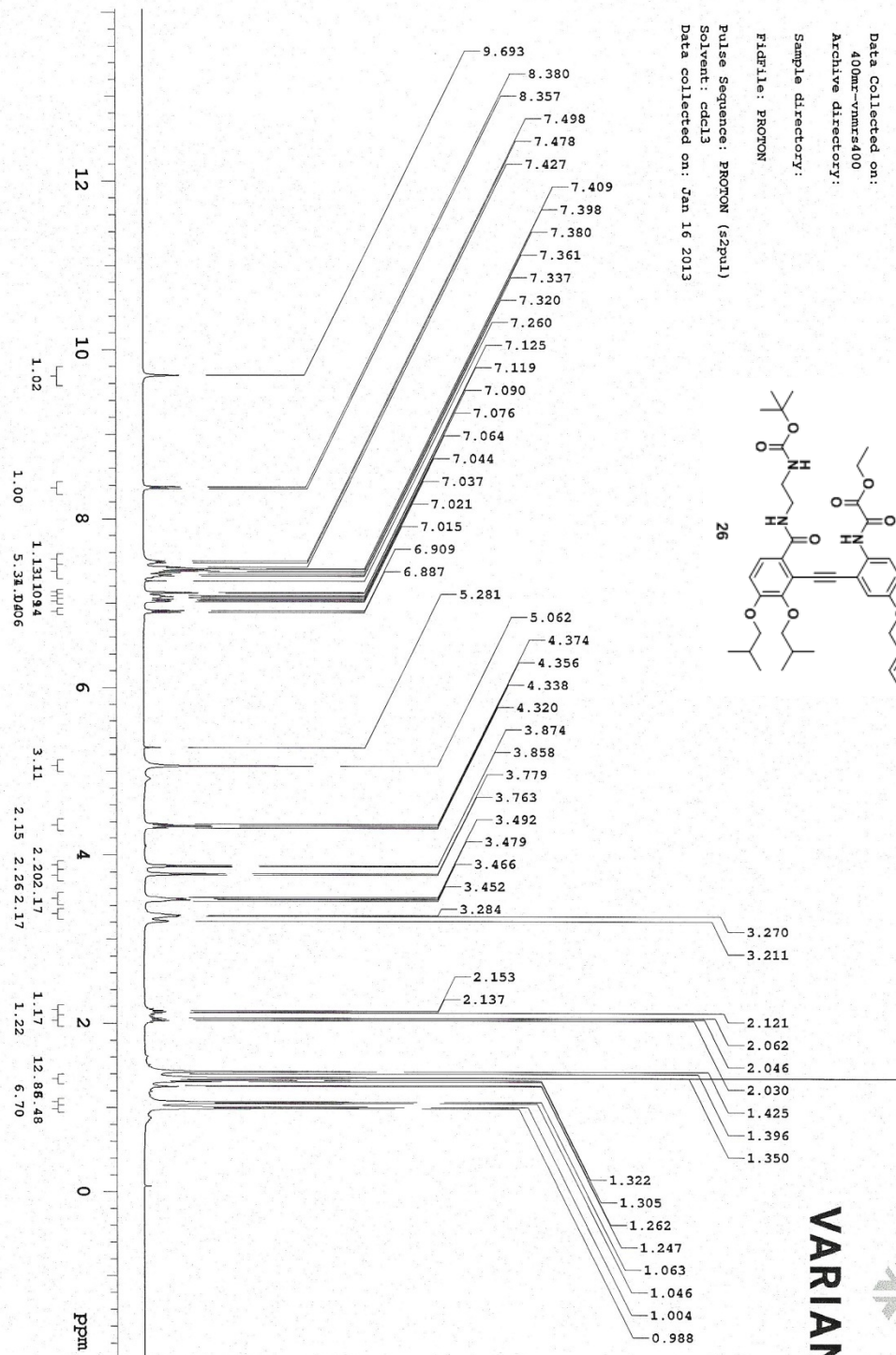
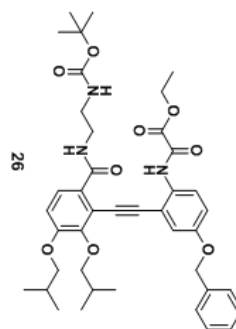
Sample directory:

FidFile: PROTON

Pulse Sequence: PROTON (s2pu1)

Solvent: cdcl3

Data collected on: Jan 16 2013



¹³C NMR of JKY-4-292

Sample Name:

Data Collected on:

400mr-vmr400

Archive directory:

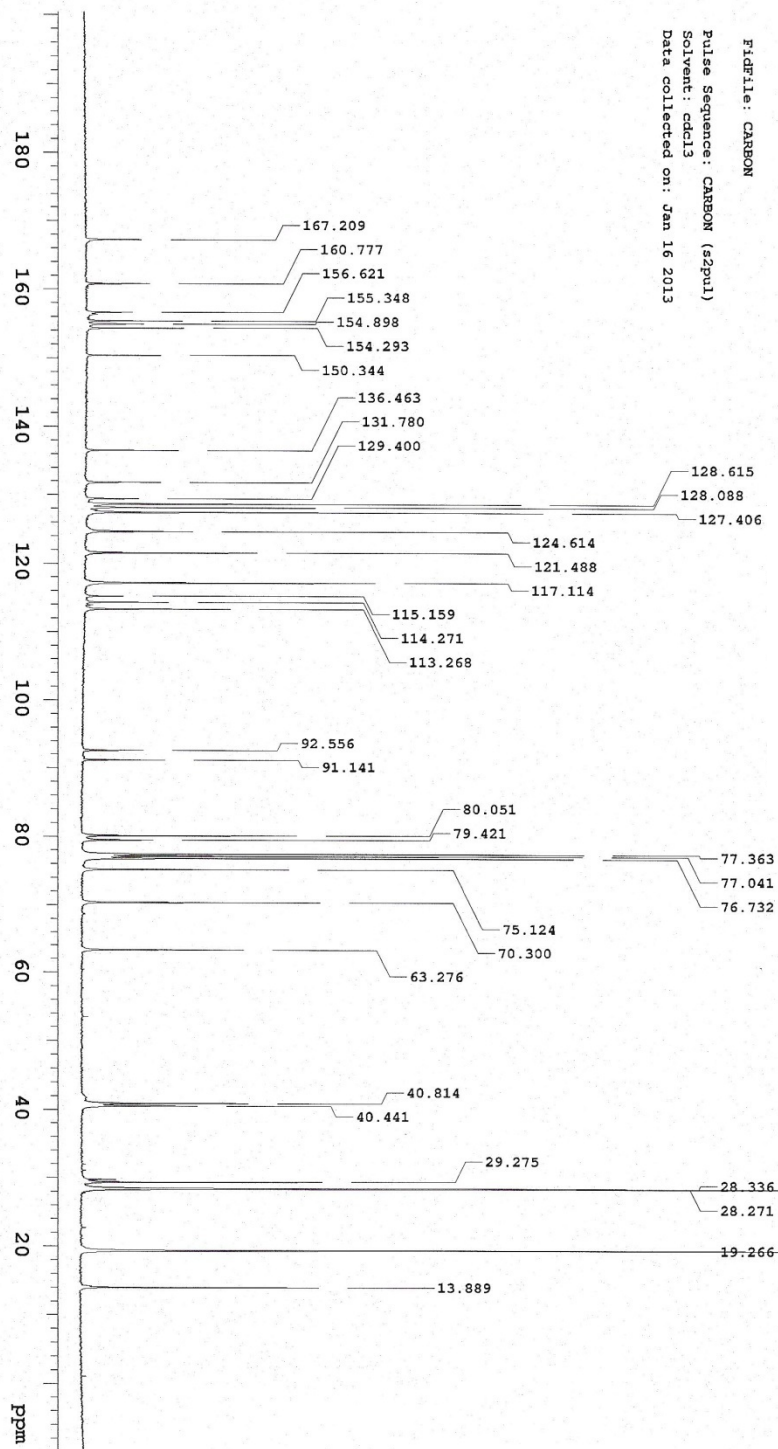
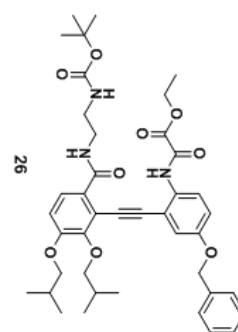
Sample directory:

F1: CARBON

Pulse Sequence: CARBON (s2pu1)

Solvent: cdcl3

Data collected on: Jan 16 2013



JKY-4-295 low concentration

Sample Name:

Data Collected on:

400mr-vmrz400

Archive directory:

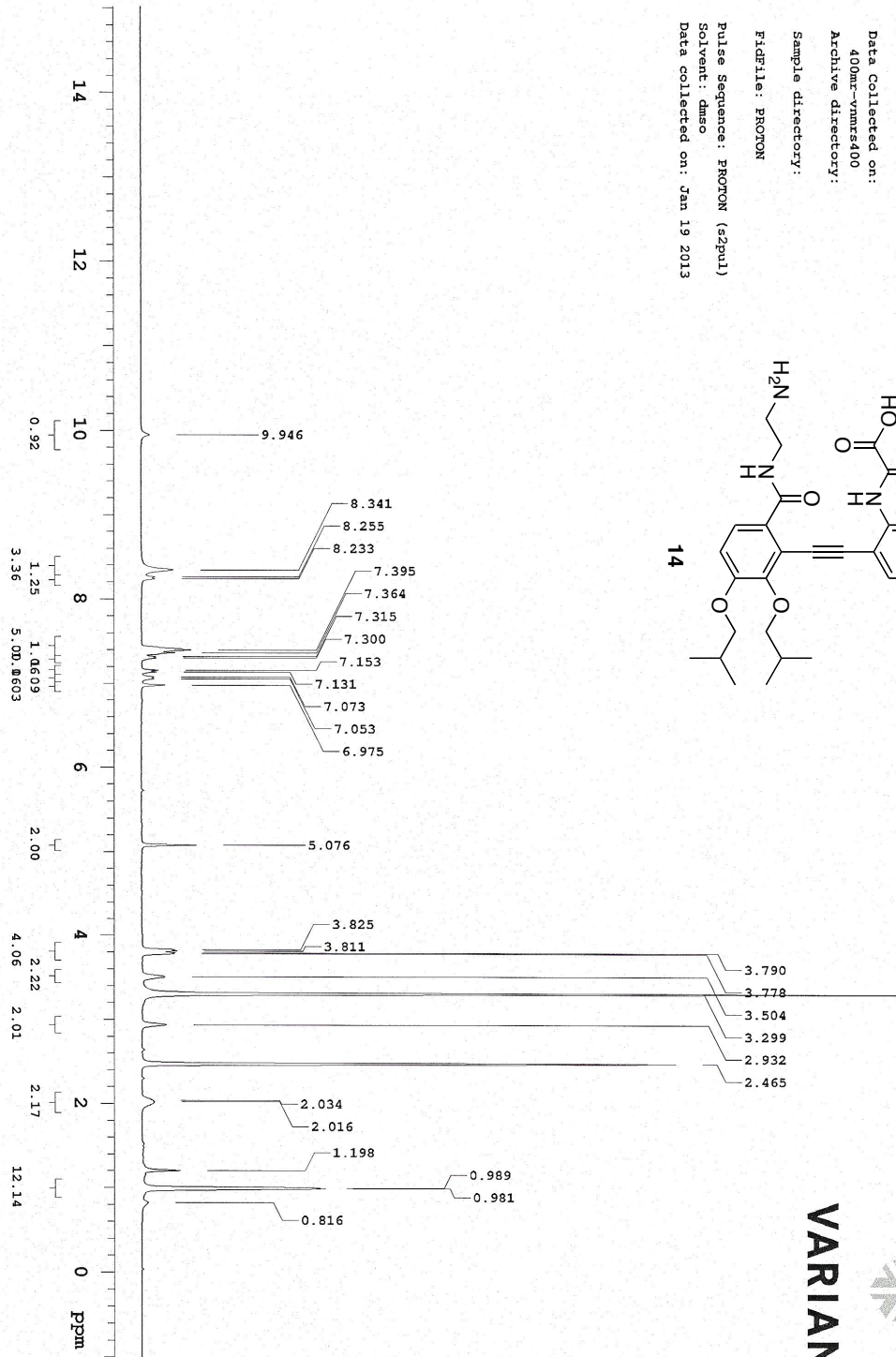
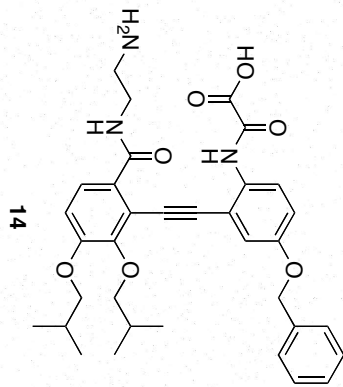
Sample directory:

File: PROTON

Pulse Sequence: PROTON (s2pul)

Solvent: dmsc

Data collected on: Jan 19 2013



VARIAN

¹³C NMR of JKY-4-295

Sample Name:

Data Collected on:

400mc-vnmr400

Archive directory:

Sample directory:

F1dFile: CARBON

Pulse Sequence: CARBON (szpul)

Solvent: dmsc

Data collected on: Jan 21 2013

Temp: 26.0 C / 299.1 K

Operator: work

Relax. delay 1.000 sec

Pulse 45.0 degrees

Acq. time 0.813 sec

Width 21186.4 Hz

29848 repetitions

OBSERVE C13, 100.5180202 MHz

DECOUPLE H1, 399.751914 MHz

Power 39 dB

continuously on

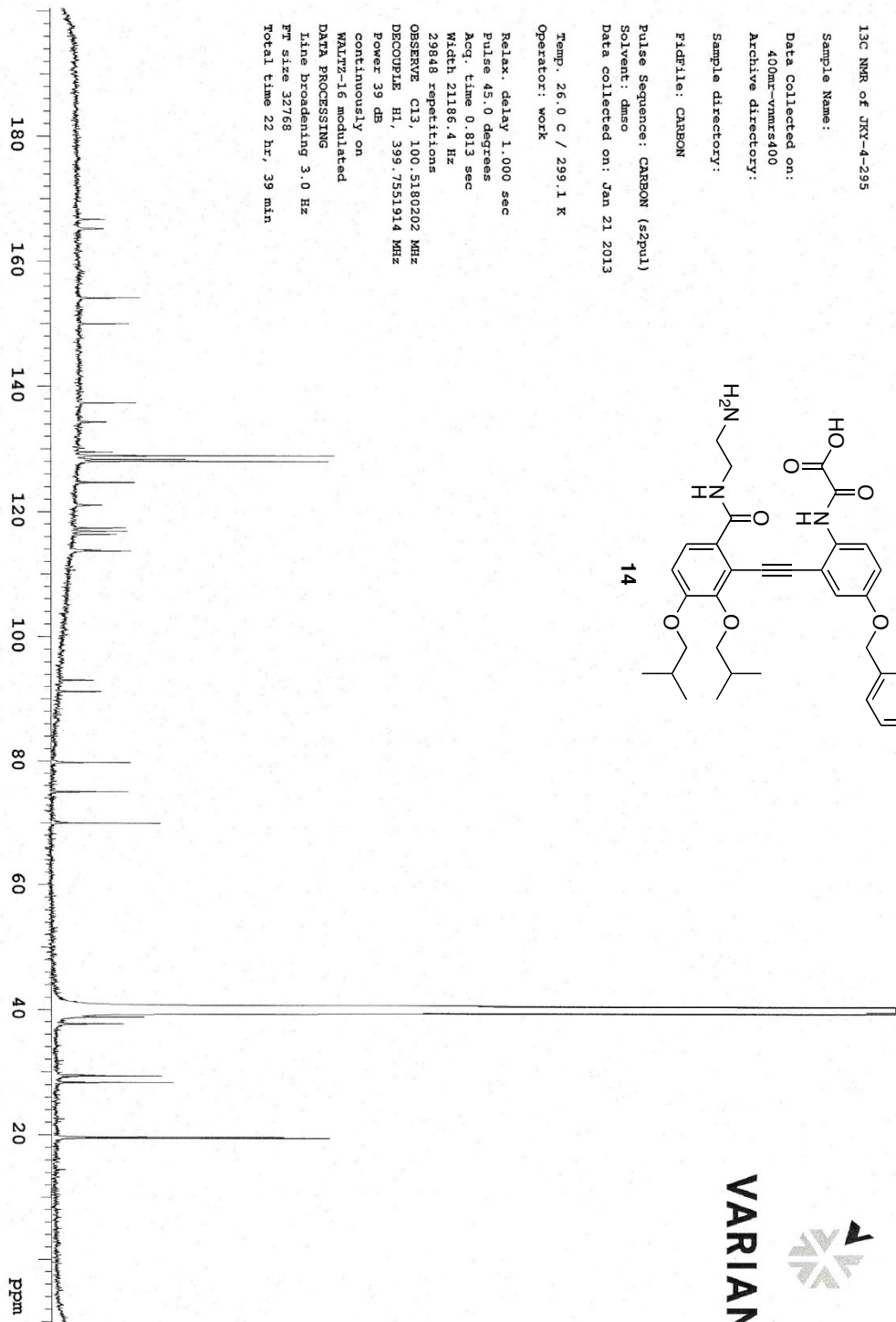
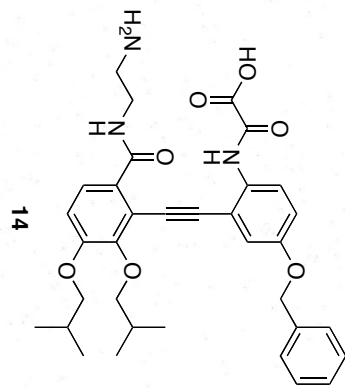
WALTZ-16 modulated

DATA PROCESSING

Line broadening 3.0 Hz

FT size 32768

Total time 22 hr, 39 min



VARIAN

JKY-4-361

Sample Name:

Data Collected on:

400MHz-nmr4100

Archive directory:

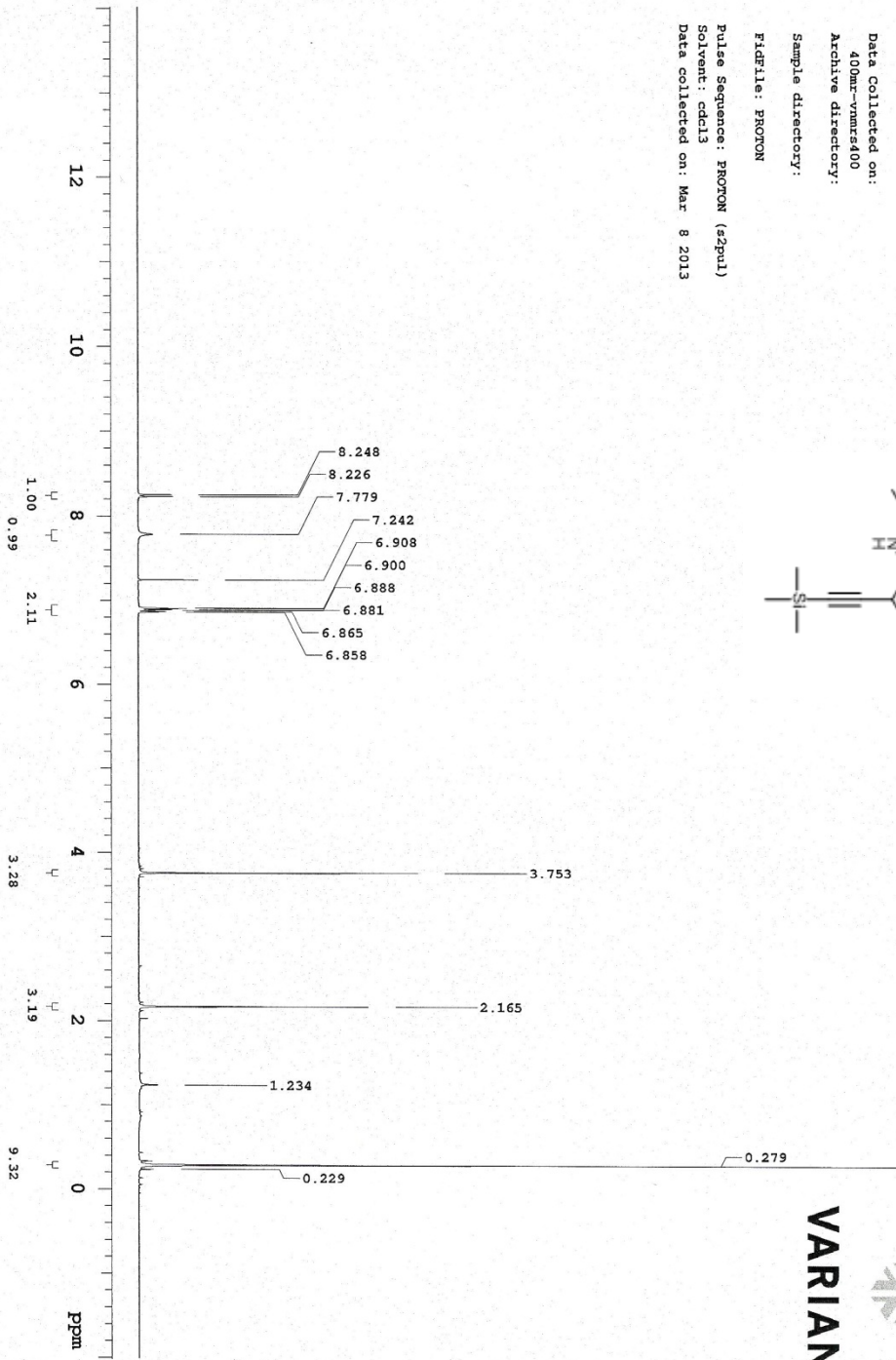
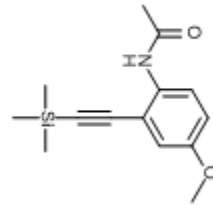
Sample directory:

FID:File: PROTON

Pulse Sequence: PROTON (s2pu1)

Solvent: cdcl3

Data collected on: Mar 8 2013



¹³C NMR of JKY-4-361

Sample Name:

Data Collected on:

400mr-vmmr400

Archive directory:

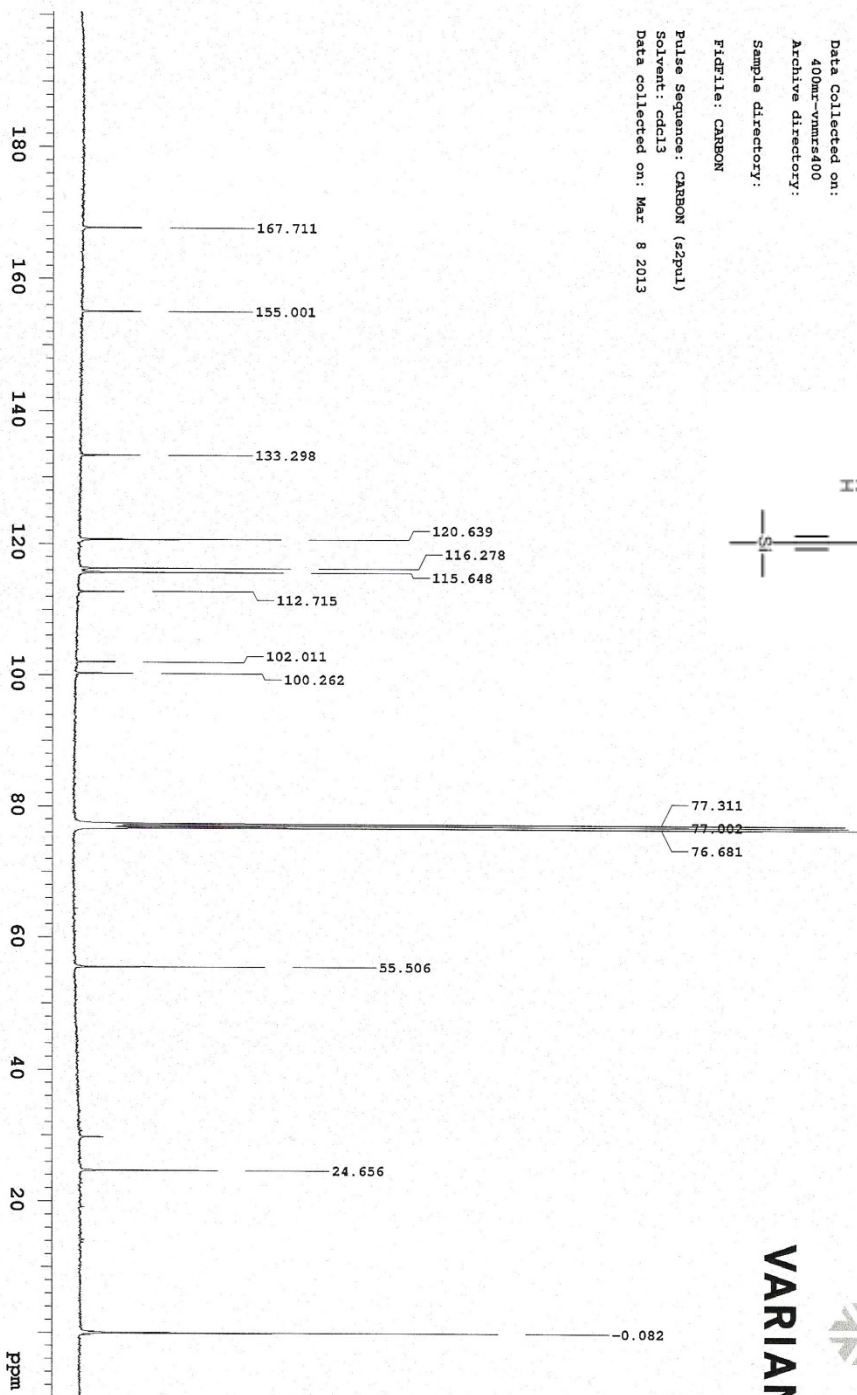
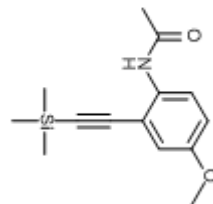
Sample directory:

FIDFile: CARBON

Pulse Sequence: CARBON (z2pul)

Solvent: cdcl3

Data collected on: Mar 8 2013



VARIAN



References

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