

## Structure-Based Design of 3-Carboxy-Substituted 1,2,3,4-Tetrahydroquinolines as Inhibitors of Myeloid Cell Leukemia-1 (Mcl-1)

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## Chemistry

All reactions were performed in oven-dried glassware under an inert ( $N_2$ ) atmosphere, unless otherwise stated. Anhydrous solvents were used as supplied without further purification.  $^1H$  and  $^{13}C$  NMR spectra were recorded on a Varian 400 MHz NMR spectrometer at 25 °C. Chemical shifts are reported in parts per million (ppm) and are referenced to residual non-deuterated solvent peak ( $CHCl_3$ :  $\delta_H$  7.26,  $\delta_C$  77.2; DMSO:  $\delta_H$  2.50,  $\delta_C$  39.5). Mass spectra were recorded on a Bruker AmaZon X mass spectrometer using atmospheric pressure chemical ionization (APCI). All final molecules were confirmed to be >90% pure by HPLC prior to biological testing using a Waters 1525 analytical/preparative HPLC equipped with a Atlantis T3 C18 reversed phase column according to one of the following gradients: (I) 100% solvent (A) to 100% solvent (B) over 10min at 1 ml  $min^{-1}$ ; (II) 50% solvent (A) to 100% solvent (B) over 22 min at 1 ml  $min^{-1}$ ; or (III) 100% solvent (B) isocratic over 22min at 1 ml  $min^{-1}$ , where solvent (A) is  $H_2O$  with 0.1% TFA and solvent (B) is  $CH_3CN-H_2O$ , 9:1 with 0.1% TFA.

**General procedure A: Sulfonamide synthesis.** Compound  $\pm-5$  was dissolved in anhydrous chloroform (0.1 M), followed by adding corresponding sulfonyl chloride (2 eq), DIPEA (2.5 eq), DMAP (0.1 eq). Reaction was refluxed overnight under  $N_2$  atmosphere. TLC indicated the reaction was complete. The volatiles were evaporated and the residual was reconstituted in EtOAc and washed with 1M HCl. The organic layer was collected and dried over  $Na_2SO_4$ , filtered, concentrated and purified by flash column chromatography over silica gel using an eluent of Hex/EtOAc 3:1 to give compounds  $\pm-7a-e$ .

**General procedure B: Ester hydrolysis.** Compound  $\pm-7a-e$ ,  $\pm-5$ ,  $\pm-9$  or  $\pm-10$  was dissolved in a mixed solvent of THF/MeOH/ $H_2O$  3:1:1 (0.1 M).  $LiOH \cdot H_2O$  (5 eq) was added to the reaction, which was then stirred overnight at room temperature. TLC indicated the reaction was complete. The volatiles were evaporated, and the residue was partitioned between  $Et_2O$  and 1M NaOH. The aqueous layer was collected and acidified with 1M HCl, then partitioned with  $CH_2Cl_2$ . The  $CH_2Cl_2$  layer was collected, dried over  $Na_2SO_4$ , filtered, and concentrated to yield products  $\pm-8a-e$ ,  $\pm-6$ ,  $\pm-2$  or  $\pm-11$ .

*Methyl quinoline-3-carboxylate*<sup>1</sup> (**4**). Quinoline-3-carboxylic acid **3** (2.50 g, 14.4 mmol, 1 eq) was suspended in MeOH (72 mL), and  $SOCl_2$  (2.09 mL, 28.8 mmol, 2 eq) was added slowly at 0 °C. The reaction was then heated at a gentle reflux overnight. TLC indicated the reaction was complete. The volatiles were evaporated and the residue was partitioned between DCM and saturated  $NaHCO_3$  solution. The organic layer was collected and dried over  $Na_2SO_4$ , filtered and concentrated to yield compound **4** as a yellow solid (2.64 g, 98%):  $^1H$  NMR ( $CDCl_3$ , 400 MHz)  $\delta$  9.46 (1H, s, Ar), 8.88 (1H, s, Ar), 8.20 (1H, d,  $J = 8.8Hz$ , Ar), 7.95 (1H, d,  $J = 8.8Hz$ , Ar), 7.85 (1H, t,  $J = 8.0Hz$ , Ar), 7.64 (1H, t,  $J = 7.2Hz$ , Ar), 4.02 (3H, s,  $CH_3$ );  $^{13}C$  NMR ( $CDCl_3$ , 100 MHz)  $\delta$  160.9, 145.2, 144.9, 133.9, 127.0, 124.6, 124.3, 122.6, 121.9, 118.1, 47.7.

$\pm$ -*Methyl 1,2,3,4-tetrahydroquinoline-3-carboxylate*<sup>2</sup> ( $\pm-5$ ). Borane-pyridine complex (8M; 3.50 mL, 27.6 mmol, 2 eq) was added to a solution of **4** (2.58 g, 13.8 mmol, 1 eq) in glacial acetic acid (100 mL), and the reaction was stirred at room temperature overnight. TLC indicated the reaction was complete. The reaction mixture was concentrated to dryness, and then partitioned between EtOAc and saturated  $NaHCO_3$  solution. The organic layer was collected and dried over  $Na_2SO_4$ , filtered, concentrated and

purified by flash column chromatography over silica gel using an eluent of Hex:EtOAc 1:1 to give compound  $\pm$ -**5** as a pale solid (2.32 g, 88%):  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  7.02-6.98 (2H, m, Ar), 6.66 (1H, t,  $J = 7.2\text{Hz}$ , Ar), 6.53 (1H, d,  $J = 8.0\text{Hz}$ , Ar), 3.97 (1H, s, NH), 3.74 (3H, s,  $\text{CH}_3$ ), 3.58-3.54 (1H, m,  $\text{CH}_a\text{CH}_b\text{N}$ ), 3.39-3.34 (1H, m,  $\text{CH}_a\text{CH}_b\text{N}$ ), 3.03-3.01 (2H, m, CH and  $\text{CH}_a\text{CH}_b\text{CH}$ ), 2.96-2.92 (1H, m,  $\text{CH}_a\text{CH}_b\text{CH}$ );  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  169.5, 139.1, 124.8, 122.4, 114.7, 112.7, 109.6, 47.2, 38.8, 33.6, 24.9.

$\pm$ -1,2,3,4-Tetrahydroquinoline-3-carboxylic acid<sup>3</sup> ( $\pm$ -**6**). Compound  $\pm$ -**5** was saponified on a scale of 0.32 mmol according to general procedure B to yield compound  $\pm$ -**6** as a light brown solid (25 mg, 43%):  $^1\text{H}$  NMR ( $\text{DMSO}-d_6$ , 400 MHz)  $\delta$  12.36 (1H, s, COOH), 6.85-6.78 (2H, m, Ar), 6.41-6.37 (2H, m, Ar), 5.69 (1H, s, NH), 3.35-3.32 (1H, m,  $\text{CH}_a\text{CH}_b\text{NH}$ ), 3.12 (1H, m,  $\text{CH}_a\text{CH}_b\text{NH}$ ), 2.78-2.66 (3H, m, CH and  $\text{CH}_2\text{CHCH}_2\text{NH}$ );  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  143.7, 129.8, 127.4, 119.7, 118.2, 114.8, 43.5, 38.4, 29.5;  $t_R = 1.3$  min (96.3%, l).

$\pm$ -Methyl 1-(phenylsulfonyl)-1,2,3,4-tetrahydroquinoline-3-carboxylate ( $\pm$ -**7a**). Compound  $\pm$ -**5** was coupled to benzenesulfonyl chloride according general procedure A on a scale of 0.79 mmol to yield compound  $\pm$ -**7a** as a light yellow solid (242 mg, 93%):  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  7.76 (1H, d,  $J = 8.0\text{Hz}$ , Ar), 7.62 (2H, d,  $J = 7.6\text{Hz}$ , Ar), 7.54 (1H, t,  $J = 7.2\text{Hz}$ , Ar), 7.42 (2H, t,  $J = 7.6\text{Hz}$ , Ar), 7.21 (1H, t,  $J = 7.6\text{Hz}$ , Ar), 7.10 (1H, t,  $J = 6.8\text{Hz}$ , Ar), 7.04 (1H, d,  $J = 7.2\text{Hz}$ , Ar), 4.47-4.42 (1H, m,  $\text{CH}_a\text{CH}_b\text{N}$ ), 3.69 (3H, s,  $\text{CH}_3$ ), 3.52-3.45 (1H, m,  $\text{CH}_a\text{CH}_b\text{N}$ ), 2.68 (2H, m, CH and  $\text{CH}_a\text{CH}_b\text{CH}$ ), 2.56-2.51 (1H, m,  $\text{CH}_a\text{CH}_b\text{CH}$ );  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  167.9, 134.5, 131.2, 128.3, 124.5, 124.4, 123.8, 122.2, 122.1, 120.7, 120.0, 47.5, 42.6, 32.9, 24.4.

$\pm$ -Methyl 1-((4-bromophenyl)sulfonyl)-1,2,3,4-tetrahydroquinoline-3-carboxylate ( $\pm$ -**7b**). Compound  $\pm$ -**5** was coupled to 4-bromobenzenesulfonyl chloride according to general procedure A on a scale of 0.53 mmol to yield compound  $\pm$ -**7b** as a light brown solid (195 mg, 90%):  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  7.75 (1H, d,  $J = 7.6\text{Hz}$ , Ar), 7.56 (2H, d,  $J = 8.8\text{Hz}$ , Ar), 7.48 (2H, d,  $J = 8.4\text{Hz}$ , Ar), 7.22 (1H, t,  $J = 7.2\text{Hz}$ , Ar), 7.13 (1H, t,  $J = 6.8\text{Hz}$ , Ar), 7.07 (1H, d,  $J = 7.6\text{Hz}$ , Ar), 4.45-4.41 (1H, m,  $\text{CH}_a\text{CH}_b\text{N}$ ), 3.71 (3H, s,  $\text{CH}_3$ ), 3.54-3.48 (1H, m,  $\text{CH}_a\text{CH}_b\text{N}$ ), 2.77-2.69 (2H, m, CH and  $\text{CH}_a\text{CH}_b\text{CH}$ ), 2.63-2.56 (1H, m,  $\text{CH}_a\text{CH}_b\text{CH}$ );  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  167.8, 133.6, 130.9, 127.7, 124.6, 123.9, 123.8, 123.4, 122.3, 121.0, 119.9, 47.5, 42.7, 33.2, 24.4.

$\pm$ -Methyl 1-((4-fluorophenyl)sulfonyl)-1,2,3,4-tetrahydroquinoline-3-carboxylate ( $\pm$ -**7c**). Compound  $\pm$ -**5** was coupled to 4-fluorobenzenesulfonyl chloride according to general procedure A on a scale of 1.05 mmol to yield compound  $\pm$ -**7c** as a light yellow solid (307 mg, 84%):  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  7.76 (1H, d,  $J = 7.6\text{Hz}$ , Ar), 7.65-7.62 (2H, m, Ar), 7.23 (1H, t,  $J = 7.2\text{Hz}$ , Ar), 7.14-7.06 (4H, m, Ar), 4.45-4.41 (1H, m,  $\text{CH}_a\text{CH}_b\text{N}$ ), 3.71 (3H, s,  $\text{CH}_3$ ), 3.54-3.47 (1H, m,  $\text{CH}_a\text{CH}_b\text{N}$ ), 2.75-2.64 (2H, m, CH and  $\text{CH}_a\text{CH}_b\text{CH}$ ), 2.60-2.53 (1H, m,  $\text{CH}_a\text{CH}_b\text{CH}$ );  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  167.8, 161.8, 159.2, 131.0, 130.6, 125.0, 124.9, 124.5, 123.9, 122.3, 120.9, 120.1, 111.8, 111.6, 47.5, 42.6, 33.1, 24.4.

$\pm$ -Methyl 1-([1,1'-biphenyl]-4-ylsulfonyl)-1,2,3,4-tetrahydroquinoline-3-carboxylate ( $\pm$ -**7d**). Compound  $\pm$ -**5** was coupled to 4-biphenylsulfonyl chloride according to general procedure A on a scale of 0.52 mmol to yield compound  $\pm$ -**7d** as a pale solid (203 mg, 96%):  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  7.82 (1H, d,  $J = 8.0\text{Hz}$ , Ar), 7.70 (2H, d,  $J = 8.4\text{Hz}$ , Ar), 7.64 (2H, d,  $J = 8.8\text{Hz}$ , Ar), 7.58 (2H, d,  $J = 7.2\text{Hz}$ , Ar), 7.48-7.39 (3H, m, Ar), 7.24 (1H, t,  $J = 7.6\text{Hz}$ , Ar), 7.13 (1H, t,  $J = 8.0\text{Hz}$ , Ar), 7.07 (1H, d,  $J = 7.6\text{Hz}$ , Ar), 4.53-4.48 (1H, m,  $\text{CH}_a\text{CH}_b\text{N}$ ), 3.72 (3H, s,  $\text{CH}_3$ ), 3.56-3.49 (1H, m,  $\text{CH}_a\text{CH}_b\text{N}$ ), 2.75 (2H, d,  $J = 8.4\text{Hz}$ ,  $\text{CH}_2\text{CH}$ ), 2.67-2.62 (1H, m,

CH);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  167.9, 141.1, 134.2, 133.1, 131.3, 124.5, 124.3, 123.8, 122.9, 122.8, 122.5, 122.2, 120.8, 120.0, 47.5, 42.6, 33.1, 24.5.

$\pm$ -Methyl 1-(naphthalen-2-ylsulfonyl)-1,2,3,4-tetrahydroquinoline-3-carboxylate ( $\pm$ -7e). Compound  $\pm$ -5 was coupled to 2-naphthylsulfonyl chloride according to general procedure A on a scale of 0.54 mmol to yield compound  $\pm$ -7e as an off-white solid (197 mg, 95%):  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400MHz)  $\delta$  8.29 (1H, s, Ar), 7.90-7.83 (4H, m, Ar), 7.65-7.53 (3H, m, Ar), 7.24 (1H, t,  $J = 8.4\text{Hz}$ , Ar), 7.12 (1H, t,  $J = 7.2\text{Hz}$ , Ar), 7.03 (1H, d,  $J = 8.0\text{Hz}$ , Ar), 4.47-4.42 (1H, m,  $\text{CH}_a\text{CH}_b\text{N}$ ), 3.58 (3H, s,  $\text{CH}_3$ ), 3.48-3.42 (1H, m,  $\text{CH}_a\text{CH}_b\text{N}$ ), 2.59 (2H, d,  $J = 8.0\text{Hz}$ ,  $\text{CH}_2\text{CH}$ ), 2.53-2.48 (1H, m, CH);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100MHz)  $\delta$  167.9, 131.6, 131.3, 130.1, 127.3, 124.7, 124.5, 124.2, 123.8, 123.2, 122.9, 122.2, 120.7, 119.9, 117.4, 47.4, 42.7, 33.1, 24.4.

$\pm$ -1-(Phenylsulfonyl)-1,2,3,4-tetrahydroquinoline-3-carboxylic acid ( $\pm$ -8a). Compound  $\pm$ -7a was saponified according to general procedure B on a scale of 0.35 mmol to yield compound  $\pm$ -8a as a pale solid (108 mg, 98%):  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400MHz)  $\delta$  7.79 (1H, d,  $J = 8.8\text{Hz}$ , Ar), 7.64 (2H, d,  $J = 7.2\text{Hz}$ , Ar), 7.57 (1H, t,  $J = 7.6\text{Hz}$ , Ar), 7.44 (2H, t,  $J = 8.0\text{Hz}$ , Ar), 7.24 (1H, t,  $J = 8.0\text{Hz}$ , Ar), 7.13 (1H, t,  $J = 7.2\text{Hz}$ , Ar), 7.06 (1H, d,  $J = 6.8\text{Hz}$ , Ar), 4.48-4.43 (1H, m,  $\text{CH}_a\text{CH}_b\text{N}$ ), 3.56-3.50 (1H, m,  $\text{CH}_a\text{CH}_b\text{N}$ ), 2.75-2.69 (2H, m, CH and  $\text{CH}_a\text{CH}_b\text{CH}$ ), 2.60-2.54 (1H, m,  $\text{CH}_a\text{CH}_b\text{CH}$ );  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100MHz)  $\delta$  173.4, 134.4, 131.2, 128.4, 124.5, 123.5, 122.4, 122.3, 120.9, 120.2, 42.2, 32.9, 24.1; MS (APCI+)  $m/z$  Calcd ( $\text{M}^+$ ): 317.0, Found: 317.0 ( $\text{M}^+$ );  $t_R = 11.7$  min (100%, II).

$\pm$ -1-((4-Bromophenyl)sulfonyl)-1,2,3,4-tetrahydroquinoline-3-carboxylic acid ( $\pm$ -8b). Compound  $\pm$ -7b was saponified according to general procedure B on a scale of 0.26 mmol to yield compound  $\pm$ -8b as a pale solid (97 mg, 95%):  $^1\text{H}$  NMR ( $\text{DMSO}-d_6$ , 400MHz)  $\delta$  12.76 (1H, s, COOH), 7.74 (2H, d,  $J = 8.4\text{Hz}$ , Ar), 7.54-7.50 (3H, m, Ar), 7.19-7.05 (3H, m, Ar), 4.20-4.16 (1H, m,  $\text{CH}_a\text{CH}_b\text{N}$ ), 3.64-3.58 (1H, m,  $\text{CH}_a\text{CH}_b\text{N}$ ), 2.67-2.53 (3H, m, CH and  $\text{CH}_2\text{CH}$ );  $^{13}\text{C}$  NMR ( $\text{DMSO}-d_6$ , 100MHz)  $\delta$  173.7, 138.3, 135.9, 133.1, 130.0, 129.5, 129.1, 127.9, 127.1, 125.6, 123.6, 47.5, 38.1, 29.1; MS (APCI+)  $m/z$  Calcd ( $\text{M}^+$ ): 396.9, Found: 396.9 ( $\text{M}^+$ );  $t_R = 15.1$  min (100%, II).

$\pm$ -1-((4-Fluorophenyl)sulfonyl)-1,2,3,4-tetrahydroquinoline-3-carboxylic acid ( $\pm$ -8c). Compound  $\pm$ -7c was saponified according to general procedure B on a scale of 0.26 mmol to yield compound  $\pm$ -8c as a pale solid (84 mg, 97%):  $^1\text{H}$  NMR ( $\text{DMSO}-d_6$ , 400MHz)  $\delta$  12.75 (1H, s, COOH), 7.73-7.69 (2H, m, Ar), 7.57 (1H, d,  $J = 7.6\text{Hz}$ , Ar), 7.42 (2H, t,  $J = 8.4\text{Hz}$ , Ar), 7.24-7.09 (3H, m, Ar), 4.20-4.16 (1H, m,  $\text{CH}_a\text{CH}_b\text{N}$ ), 3.63-3.57 (1H, m,  $\text{CH}_a\text{CH}_b\text{N}$ ), 2.69-2.55 (3H, m, CH and  $\text{CH}_2\text{CH}$ );  $^{13}\text{C}$  NMR ( $\text{DMSO}-d_6$ , 100MHz)  $\delta$  173.7, 166.4, 163.9, 135.9, 130.3, 130.2, 129.9, 129.5, 127.1, 125.6, 123.7, 117.4, 117.2, 47.5, 38.0, 29.1; MS (APCI+)  $m/z$  Calcd ( $\text{M}^+$ ): 335.0, Found: 336.0 ( $\text{M}+\text{H}^+$ );  $t_R = 12.8$  min (100%, II).

$\pm$ -1-([1,1'-Biphenyl]-4-ylsulfonyl)-1,2,3,4-tetrahydroquinoline-3-carboxylic acid ( $\pm$ -8d). Compound  $\pm$ -7d was saponified according to general procedure B on a scale of 0.33 mmol to yield compound  $\pm$ -8d as a pale solid (123 mg, 95%):  $^1\text{H}$  NMR ( $\text{DMSO}-d_6$ , 400 MHz)  $\delta$  12.75 (1H, s, COOH), 7.88 (2H, d,  $J = 8.8\text{Hz}$ , Ar), 7.43 (4H, d,  $J = 7.2\text{Hz}$ , Ar), 7.62 (1H, d,  $J = 8.4\text{Hz}$ , Ar), 7.52-7.42 (3H, m, Ar), 7.24-7.09 (3H, m, Ar), 4.26-4.21 (1H, m,  $\text{CH}_a\text{CH}_b\text{N}$ ), 3.65-3.59 (1H, m,  $\text{CH}_a\text{CH}_b\text{N}$ ), 2.70-2.59 (3H, m, CH and  $\text{CH}_2\text{CH}$ );  $^{13}\text{C}$  NMR ( $\text{DMSO}-d_6$ , 100 MHz)  $\delta$  173.7, 145.2, 138.4, 137.9, 136.2, 130.0, 129.6, 129.3, 129.2, 128.0, 127.8, 127.5, 127.1,

125.4, 123.5, 47.5, 38.0, 29.2; MS (APCI+)  $m/z$  Calcd ( $M^+$ ): 393.1, Found: 394.0 ( $M+H^+$ );  $t_R$  = 17.7 min (98.4%, II).

$\pm$ -1-(Naphthalen-2-ylsulfonyl)-1,2,3,4-tetrahydroquinoline-3-carboxylic acid ( $\pm$ -8e). Compound  $\pm$ -7e was saponified according to general procedure B on a scale of 0.31 mmol to yield compound  $\pm$ -8e as a pale solid (113 mg, 98%):  $^1H$  NMR (DMSO- $d_6$ , 400 MHz)  $\delta$  12.73 (1H, s, COOH), 8.48 (1H, s, Ar), 8.15 (1H, d, J = 8.4Hz, Ar), 8.08-8.02 (2H, m, Ar), 7.74-7.62 (3H, m, Ar), 7.56 (1H, d, J = 8.4Hz, Ar), 7.21 (1H, t, J = 7.2Hz, Ar), 7.14-7.07 (2H, m, Ar), 4.34-4.30 (1H, m,  $CH_aCH_bN$ ), 3.74-3.68 (1H, m,  $CH_aCH_bN$ ), 2.67-2.59 (3H, m, CH and  $CH_2CH$ );  $^{13}C$  NMR (DMSO- $d_6$ , 100 MHz)  $\delta$  137.7, 136.2, 134.8, 132.1, 130.1, 129.9, 129.8, 129.7, 129.3, 128.7, 128.3, 127.1, 125.3, 123.4, 122.2, 47.6, 38.1, 29.2; MS (APCI+)  $m/z$  Calcd ( $M^+$ ): 367.0, Found: 368.0 ( $M+H^+$ );  $t_R$  = 15.5 min (100%, II).

$\pm$ -Methyl 1-((4-(4-chloro-3,5-dimethylphenoxy)phenyl)sulfonyl)-1,2,3,4-tetrahydroquinoline-3-carboxylate ( $\pm$ -9).  $\pm$ -7c (170 mg, 0.49 mmol, 1 eq) was dissolved in 4 mL DMSO (0.1 M), followed by the addition of 4-chloro-3,5-dimethylphenol (92 mg, 0.59 mmol, 1.2 eq) and  $K_2CO_3$  (101 mg, 0.74 mmol, 1.5 eq). The reaction was stirred at 100 °C for 48 h. TLC indicated the reaction was complete. The reaction mixture was cooled and then partitioned between EtOAc (80 mL) and  $H_2O$  (40 mL). The organic layer was collected, washed repeatedly with  $H_2O$  (5 x 40 mL), dried over  $Na_2SO_4$ , filtered, concentrated and purified by flash column chromatography over silica gel using an eluent of Hex/EtOAc 6:1 to give compound  $\pm$ -9 as a light brown oil (170 mg, 73%):  $^1H$  NMR ( $CDCl_3$ , 400 MHz)  $\delta$  7.77 (1H, d, J = 8.0Hz, Ar), 7.57 (2H, d, J = 8.4Hz, Ar), 7.21 (1H, t, J = 6.4Hz, Ar), 7.12-7.05 (2H, m, Ar), 6.93 (2H, d, J = 8.4Hz, Ar), 6.77 (2H, s, Ar), 4.47-4.42 (1H, m,  $CH_aCH_bN$ ), 3.71 (3H, s,  $CH_3$ ), 3.51-3.45 (1H, m,  $CH_aCH_bN$ ), 2.78-2.69 (2H, d, J = 8.0Hz,  $CH_2CH$ ), 2.65-2.60 (1H, m, CH), 2.36 (6H, s,  $2 \times CH_3$ );  $^{13}C$  NMR ( $CDCl_3$ , 100 MHz)  $\delta$  167.9, 156.9, 147.8, 133.5, 131.3, 128.2, 125.9, 124.5, 123.7, 122.2, 120.7, 119.9, 115.3, 112.8, 47.5, 42.6, 33.0, 24.5, 16.1; MS (APCI+)  $m/z$  Calcd ( $M^+$ ): 485.1, Found: 486.0 ( $M+H^+$ );  $t_R$  = 11.9 min (97.3%, III).

$\pm$ -1-((4-(4-Chloro-3,5-dimethylphenoxy)phenyl)sulfonyl)-1,2,3,4-tetrahydroquinoline-3-carboxylic acid ( $\pm$ -2). Compound  $\pm$ -9 was saponified according to general procedure B on a scale of 0.30 mmol to yield compound  $\pm$ -2 as an off-white solid (140 mg, 99%):  $^1H$  NMR (DMSO- $d_6$ , 400 MHz)  $\delta$  12.74 (1H, s, COOH), 7.64 (2H, d, J = 8.8Hz, Ar), 7.57 (1H, d, J = 8.4Hz, Ar), 7.22-7.16 (2H, m, Ar), 7.12-7.07 (3H, m, Ar), 7.00 (2H, s, Ar), 4.23-4.19 (1H, m,  $CH_aCH_bN$ ), 3.64-3.58 (1H, m,  $CH_aCH_bN$ ), 2.75-2.59 (3H, m, CH and  $CH_2CH$ ), 2.33 (6H, s,  $2 \times CH_3$ );  $^{13}C$  NMR (DMSO- $d_6$ , 100 MHz)  $\delta$  173.8, 161.5, 152.9, 138.3, 136.2, 133.1, 129.9, 129.8, 129.3, 127.0, 125.4, 124.7, 123.6, 120.7, 118.3, 47.4, 37.9, 29.2, 20.7; MS (APCI+)  $m/z$  Calcd ( $M^+$ ): 471.1, Found: 472.0 ( $M+H^+$ );  $t_R$  = 9.7 min (96.5%, III).

$\pm$ -Methyl 1-(3-(4-chloro-3,5-dimethylphenoxy)propyl)-1,2,3,4-tetrahydroquinoline-3-carboxylate ( $\pm$ -10). Compound  $\pm$ -6 (153 mg, 0.80 mmol, 1 eq) was dissolved in 8 mL 1,2-dichloroethane (0.1 M), followed by 3-(4-chloro-3,5-dimethylphenoxy)propanal (170 mg, 0.80 mmol, 1 eq), and  $NaBH(OAc)_3$  (340 mg, 1.60 mmol, 2 eq). The reaction was stirred at 35 °C overnight. TLC indicated the reaction was complete. Saturated  $NaHCO_3$  solution was added to the mixture to quench the reaction. Then the reaction mixture was partitioned between DCM and  $H_2O$ , and organic layer was collected, dried over  $Na_2SO_4$ , filtered, concentrated and purified by flash column chromatography over silica gel using an eluent of Hex/EtOAc 7:3 to yield compound  $\pm$ -10 as a light yellow solid (135 mg, 44%):  $^1H$  NMR ( $CDCl_3$ , 400 MHz)  $\delta$  7.08-6.99

(2H, m, Ar), 6.66-6.59 (4H, m, Ar), 3.98 (2H, t, J = 5.6Hz, O-CH<sub>2</sub>), 3.71 (3H, s, CH<sub>3</sub>), 3.54-3.38 (4H, m, CH<sub>2</sub>N and NCH<sub>2</sub>CH<sub>2</sub>), 3.01 (2H, d, J = 6.8Hz, CH<sub>2</sub>CH), 2.94-2.93 (1H, m, CH), 2.35 (6H, s, 2xCH<sub>3</sub>), 2.06-2.03 (2H, m, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>, 100 MHz) δ 173.9, 156.6, 144.4, 137.1, 129.4, 127.5, 120.4, 116.2, 114.5, 110.9, 65.5, 51.9, 50.7, 48.2, 38.2, 30.6, 29.7, 26.4, 20.9.

**±-1-(3-(4-Chloro-3,5-dimethylphenoxy)propyl)-1,2,3,4-tetrahydroquinoline-3-carboxylic acid (±-11).** Compound (±-10) was saponified according to general procedure B on a scale of 0.13 mmol to give compound ±-11 as a pale brown solid (43 mg, 90%): <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz) δ 7.07-7.00 (2H, m, Ar), 6.71-6.65 (4H, m, Ar), 3.98 (2H, t, J = 5.6Hz, O-CH<sub>2</sub>), 3.54-3.45 (4H, m, CH<sub>2</sub>N and NCH<sub>2</sub>CH<sub>2</sub>), 3.05-2.98 (3H, m, CH<sub>2</sub>CH and CH), 2.34 (6H, s, 2xCH<sub>3</sub>), 2.08-2.05 (2H, m, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz) δ 179.1, 156.6, 144.4, 137.1, 129.5, 127.5, 120.1, 116.4, 114.5, 111.0, 65.5, 50.5, 48.3, 38.2, 30.3, 26.3, 20.9; MS (APCI+) m/z Calcd (M<sup>+</sup>): 373.1, Found: 372.3 (M+H<sup>+</sup>); t<sub>R</sub> = 8.6 min (97.6%, III).

**±-Acetoxymethyl 1-((4-(4-chloro-3,5-dimethylphenoxy)phenyl)sulfonyl)-1,2,3,4-tetrahydroquinoline-3-carboxylate (±-12).** Compound ±-2 (100 mg, 0.20 mmol, 1 eq) was dissolved in DMF (2 mL), followed by bromomethyl acetate (20 μL, 0.20 mmol, 1 eq) and K<sub>2</sub>CO<sub>3</sub> (59 mg, 0.40 mmol, 2 eq). The reaction mixture was stirred at room temperature overnight. TLC indicated the reaction was complete, which was then partitioned between EtOAc (50 mL) and H<sub>2</sub>O (50 mL). The organic layer was collected, washed repeatedly with H<sub>2</sub>O (4 x 20 mL), then dried over Na<sub>2</sub>SO<sub>4</sub>, filtered, concentrated and purified by flash column chromatography over silica gel using an eluent of Hex/EtOAc 1:1 to give compound ±-12 as a white powder (103 mg, 95%): <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz) δ 7.74 (1H, d, J = 8.0Hz, Ar), 7.57 (2H, d, J = 8.4Hz, Ar), 7.22 (1H, t, J = 8.0Hz, Ar), 7.13-7.06 (2H, m, Ar), 6.93 (2H, d, J = 8.4Hz, Ar), 6.78 (2H, s, Ar), 5.75 (2H, s, OCH<sub>2</sub>O), 4.42-4.37 (1H, m, CH<sub>a</sub>CH<sub>b</sub>N), 3.57-3.51 (1H, m, CH<sub>a</sub>CH<sub>b</sub>N), 2.78-2.66 (3H, m, CH<sub>2</sub>CHCH<sub>2</sub>N), 2.63 (6H, s, 2xCH<sub>3</sub>), 2.12 (3H, s, CH<sub>3</sub>); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz) δ 171.1, 169.4, 161.8, 152.5, 138.3, 136.0, 132.8, 130.8, 129.3, 129.1, 128.1, 127.1, 125.5, 124.8, 120.1, 117.5, 46.9, 37.9, 28.9, 20.9, 20.7; MS (APCI+) m/z Calcd (M<sup>+</sup>): 543.1, Found: 544.0 (M+H<sup>+</sup>); t<sub>R</sub> = 10.7 min (100%, III).

## Biology

**General.** All chemical reagents were ACS grade or higher unless otherwise indicated. All buffers were passed through Chelex-100 (Bio-Rad, Hercules, CA) to remove trace metals. The D<sub>2</sub>O, DMSO-*d*<sub>6</sub>, <sup>15</sup>NH<sub>4</sub>Cl, and <sup>13</sup>C-labeled glucose were purchased from Cambridge Isotope Laboratories, Inc. (Andover, MA).

**Protein Production.** A His6-MBP tagged recombinant human Mcl-1 residues 172 to 327 was produced in *E. coli* in either LB or minimal media supplemented with <sup>15</sup>NH<sub>4</sub>Cl to produce unlabeled or <sup>15</sup>N-labeled Mcl-1. The tagged protein was initially purified from the crude cell lysate by IMAC chromatography (GE Healthcare Life Sciences), and after dialysis to remove the imidazole the affinity tag was cleaved using PreScission Protease (GE Healthcare Life Sciences). A Sephacryl S-200 size exclusion column was used as a final purification step before the protein was concentrated with a 10,000 MWCO centrifugal filter concentrator (Millipore). The protein purity was shown to be >98% by Coomassie Brilliant Blue (Bio-Rad) stained SDS-PAGE gel and the final concentration was determined using the Bradford protein assay (Bio-Rad) with BSA standards (Pierce).

**FITC-Bak BH3 Peptide.** A 6-aminohexanoic acid linker was conjugated to the *N*-terminus of the Bak-BH3 peptide (GQVGRQLAIIGDDINR), capped with fluorescein (on the amino group of the linker), and the peptide was amidated on the C-terminus to give FITC-Ahx-GQVGRQLAIIGDDINR-CONH<sub>2</sub>, hereafter referred to as “FITC-Bak” (synthesized by Neo BioScience in >95% purity).

**Fluorescence Polarization Competition Assay.** 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. The assays were performed in black polypropylene 384-well microplate (Costar) with a final volume of 20 μL. Initially the affinity (*K<sub>d</sub>*) of the FITC-Bak peptide was determined by titrating Mcl-1<sup>172-327</sup> into 10 nM FITC-Bak peptide in 20 mM HEPES, pH 6.8, 50 mM NaCl, 3 mM DTT, 0.01% Triton X-100 and 5% DMSO at room temperature while monitoring the perpendicular and parallel fluorescence emission with a 485 nm excitation and 520 nm emission filters. The fluorescence polarization competition assay (FPCA) was performed using 100 nM Mcl-1<sup>172-327</sup> in the same buffer (thus, 15 nM FITC-Bak) with varying concentrations of either unlabeled peptide or THQ-based Mcl-1 inhibitor. Regression analysis was carried out using Origin (OriginLab, Northampton, MA) to fit the data to the Hill equation (1) to determine the initial binding affinity (*K<sub>d</sub>*) and the IC<sub>50</sub> in the FPCA. For the fluorescence polarization competition titrations, an equation derived by Nikolovska-Coleska *et al.* was used to calculate the *K<sub>i</sub>* from the IC<sub>50</sub> data.<sup>4</sup> The affinity of FITC-Bak for Mcl-1<sup>172-327</sup> was determined to be 33.8 ± 0.50 nM in the assay conditions used.

**<sup>15</sup>N-Mcl-1 Nuclear Magnetic Resonance Spectroscopy.** NMR spectra was collected at 25 °C with a Bruker AVANCE 800 NMR spectrometer (800.27 MHz for protons) equipped with pulsed-field gradients, four frequency channels, and triple resonance, z-axis gradient cryogenic probes. A one-second relaxation delay was used, and quadrature detection in the indirect dimensions was obtained with states-TPPI phase cycling; initial delays in the indirect dimensions were set to give zero- and first-order phase corrections of 90° and -180°, respectively.<sup>5,6</sup> Data were processed using the processing program nmrPipe on Linux workstations.<sup>7</sup> All proton chemical shifts are reported with respect to the H<sub>2</sub>O or HDO

signal, taken to be 4.658 ppm relative to external TSP (0.0 ppm) at 37 °C. The <sup>15</sup>N chemical shifts were indirectly referenced using the zero-point frequency at 37 °C of 0.10132905 for <sup>15</sup>N-<sup>1</sup>H, as previously described.<sup>8,9</sup>

Uniformly <sup>15</sup>N-labeled Mcl-1 was used to collect two-dimensional <sup>1</sup>H,<sup>15</sup>N-fast HSQC (heteronuclear single quantum coherence) spectra of Mcl-1 with and without **±-2** to detect changes in the backbone <sup>15</sup>N and <sup>1</sup>H resonances of Mcl-1 due to the direct interaction with the compound.<sup>10</sup> The NMR samples contained 131 μM <sup>15</sup>N-labeled Mcl-1, (182 μM **±-2**), 20 mM HEPES, pH 6.8, 50 mM NaCl, 3 mM DTT, 20% D<sub>2</sub>O, and 5% DMSO-*d*<sub>6</sub>.

**CellTiter-Blue® viability assay.** A375 cells were plated at 5,000 cells/well seeding density in a 96 well black walled plate (Corning). Cells were cultured in 100 μL DMEM (Gibco) plus 10% HIFBS and PenStrep overnight. Using a separate plate, serial dilutions were made of each compound in DMEM. 10 μL of each serial dilution was transferred into the experimental plate so that the final compound concentrations were 4.69, 9.38, 18.75, 37.5, 75, 150, or 300 μM and 1% DMSO solvent. Untreated control cells also received DMSO vehicle at 1% final concentration. Cells were cultured with and without test compounds for 48 h and then 20 μL of CellTiter-Blue® reagent (Promega) was added to each well and to control wells containing media only to account for background. Cells were then incubated for 2 h and fluorescence was read using Molecular Devices Spectra Max M5 (560Ex/590Em). Results were recorded as percent viability determined by dividing the experimental values by the untreated controls and subtracting the background from cell-free wells.

## References

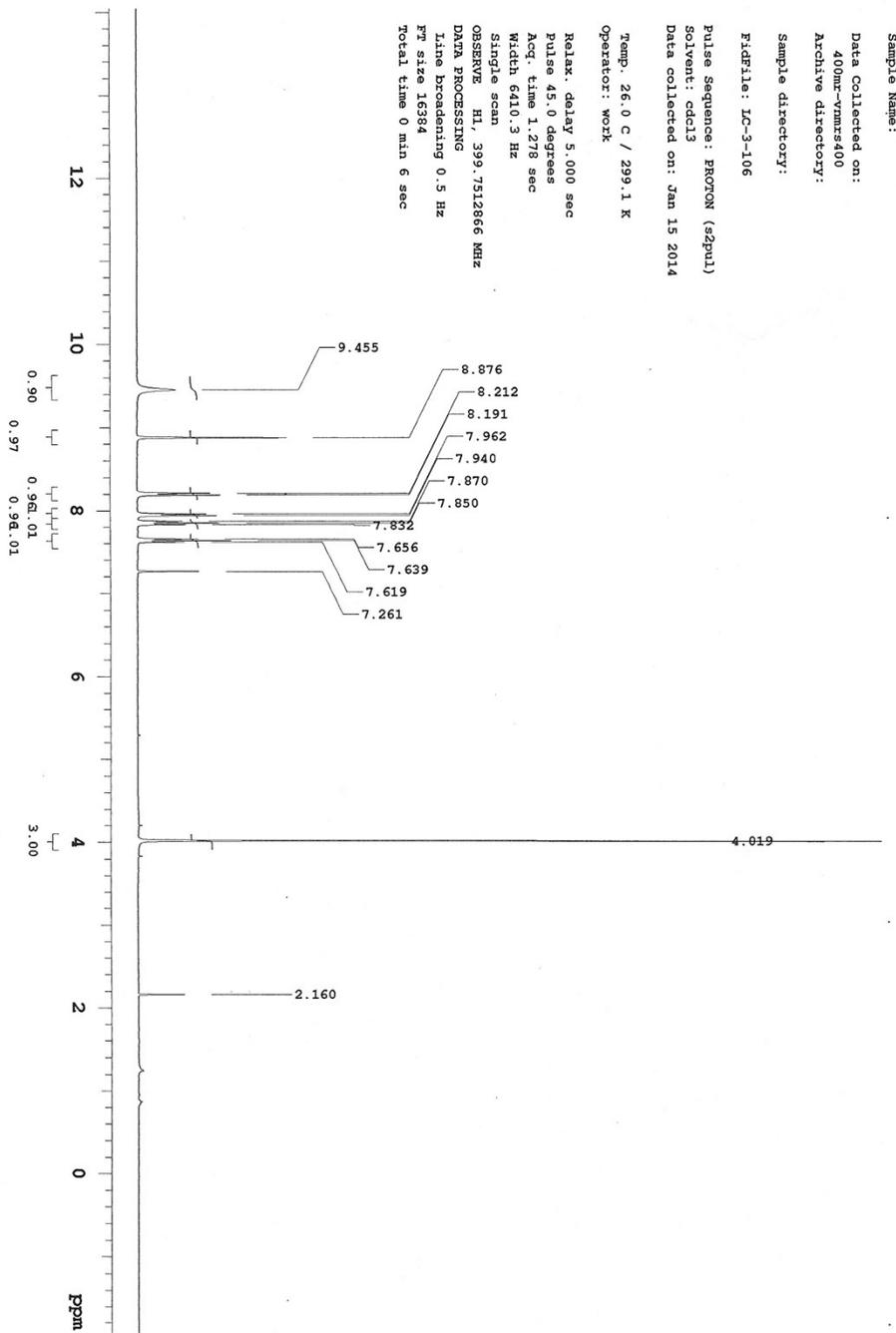
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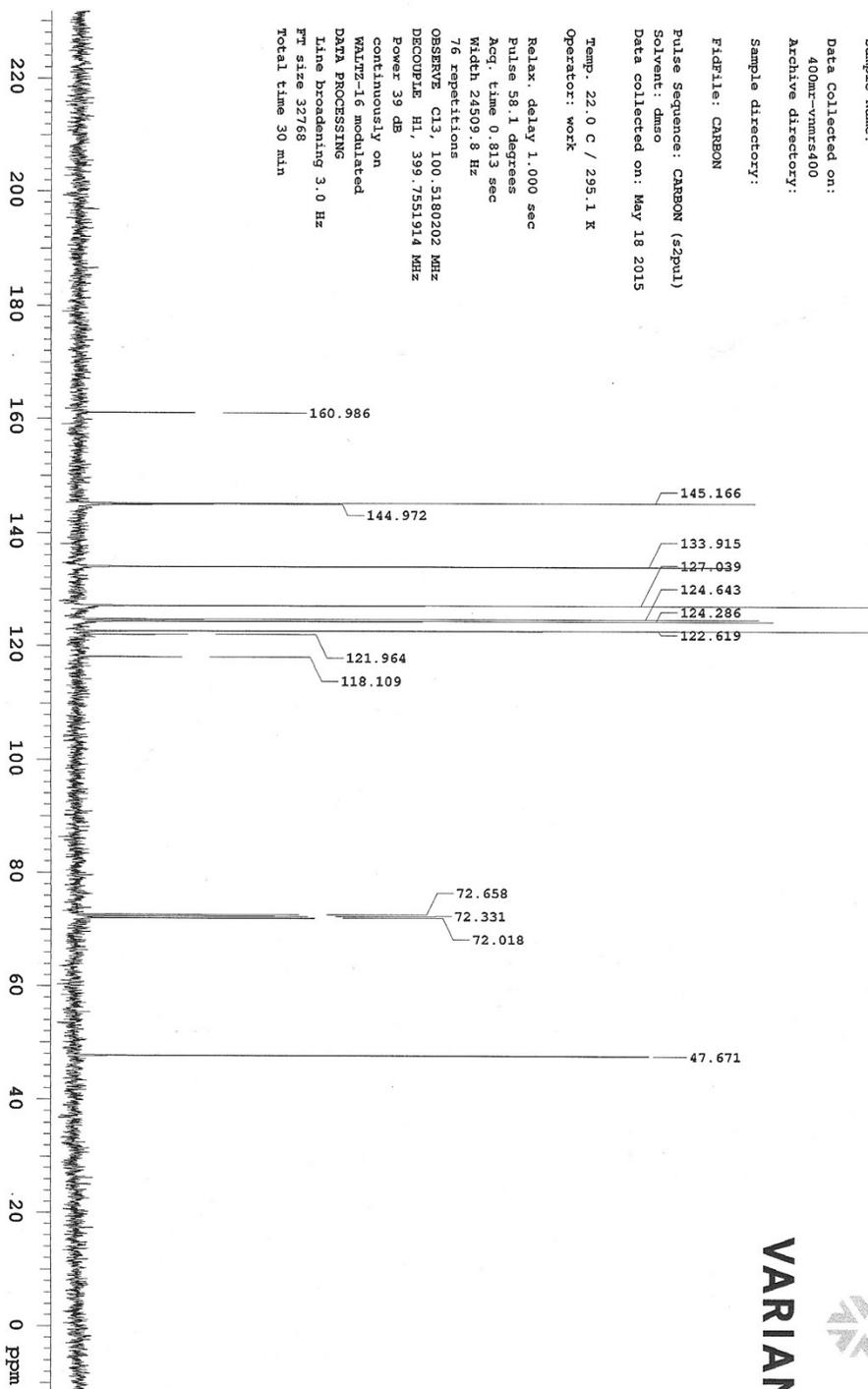
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# <sup>1</sup>H and <sup>13</sup>C NMR Spectra

## Methyl quinoline-3-carboxylate (4).



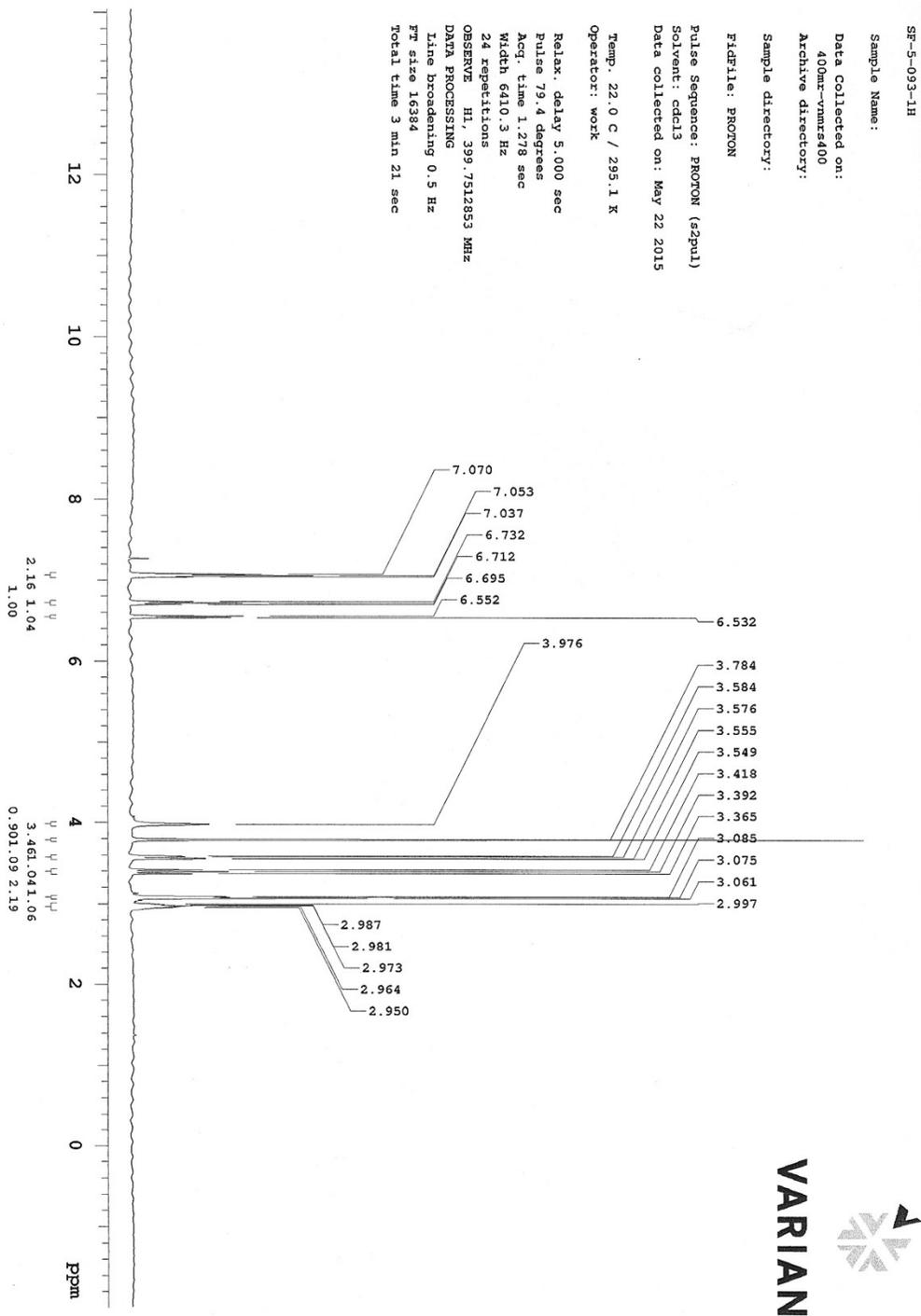
Methyl quinoline-3-carboxylate (4).



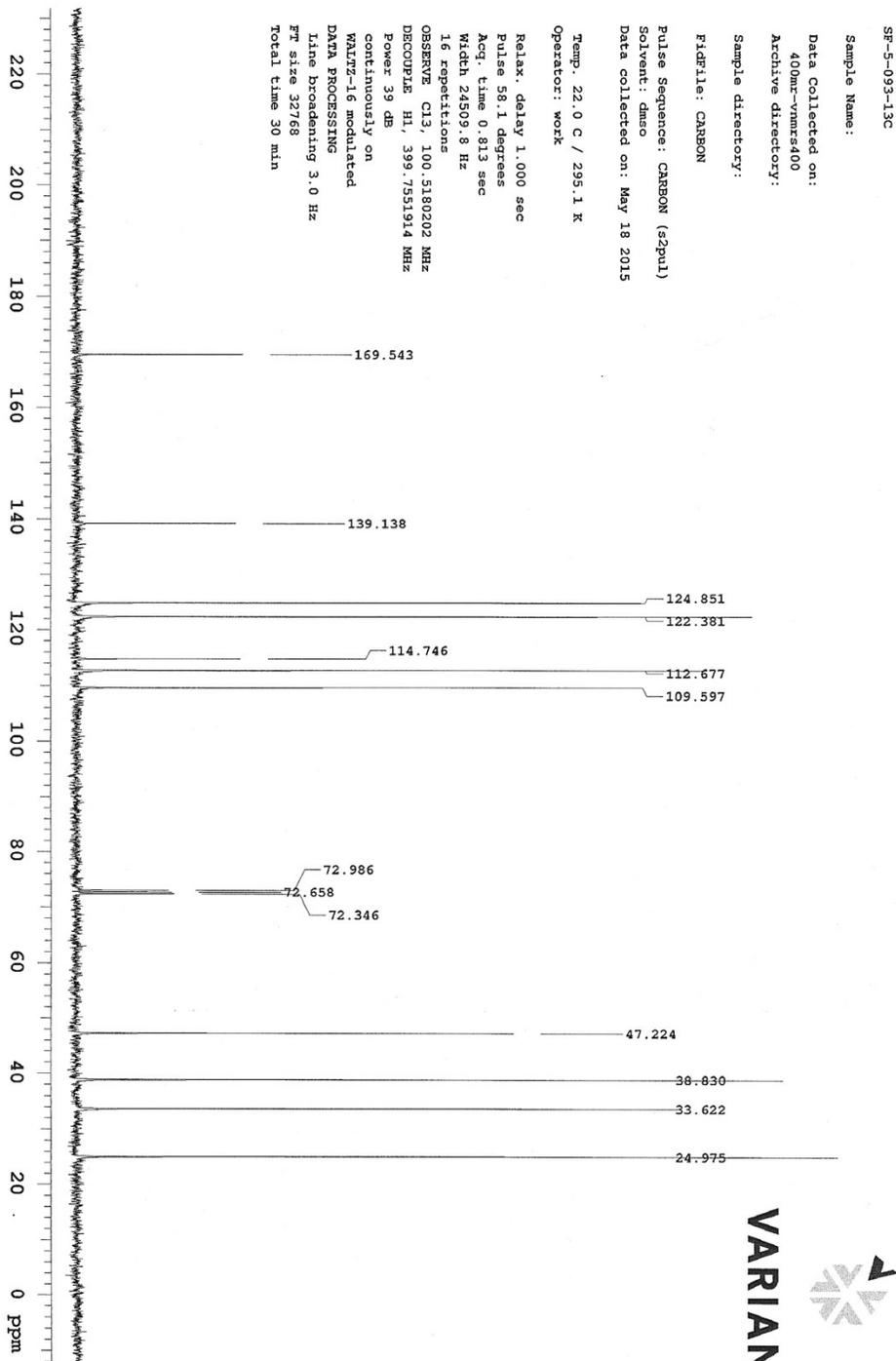
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Solvent: dmsc  
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DECOUPLE H1, 399.7551914 MHz  
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Line broadening 3.0 Hz  
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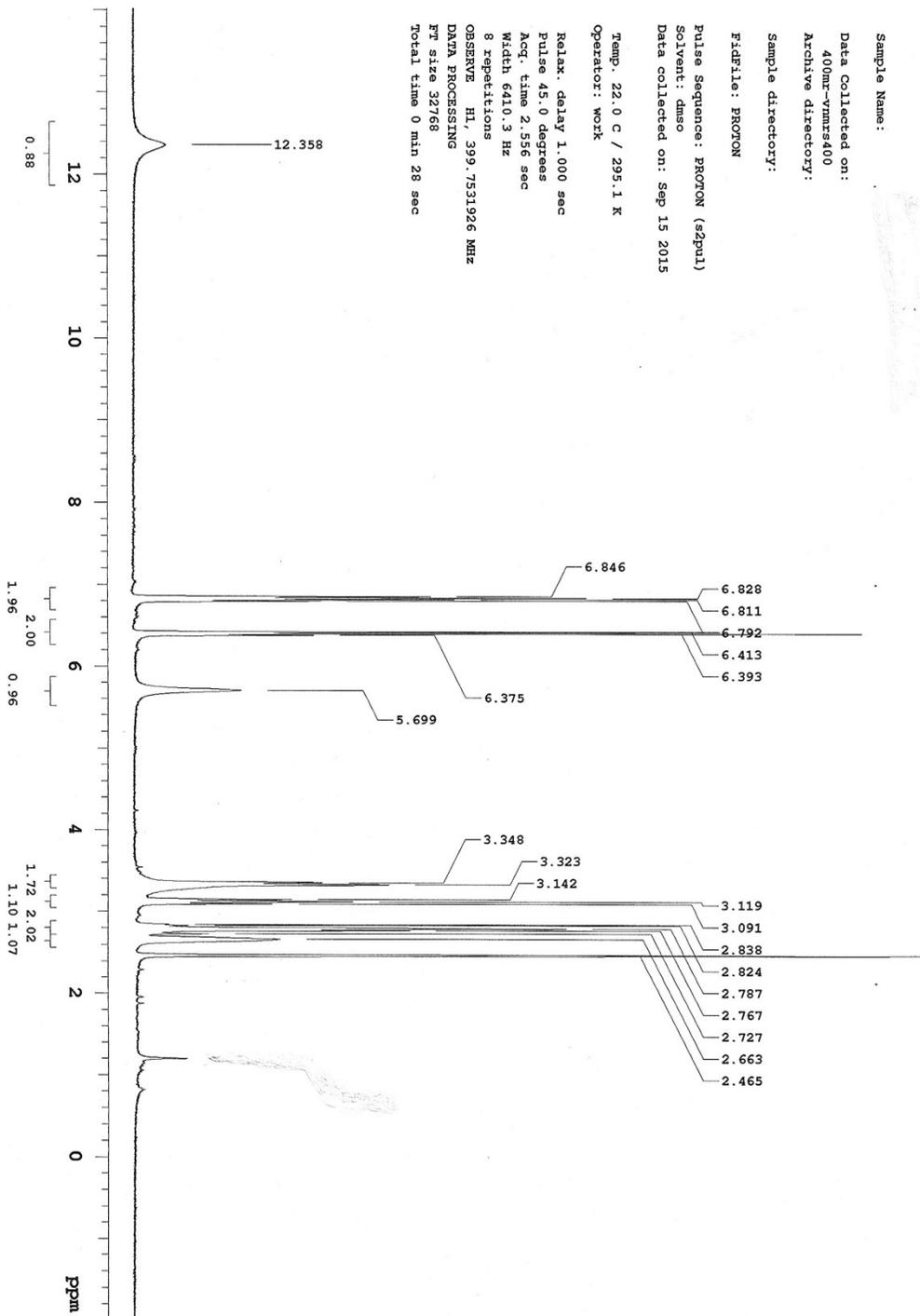
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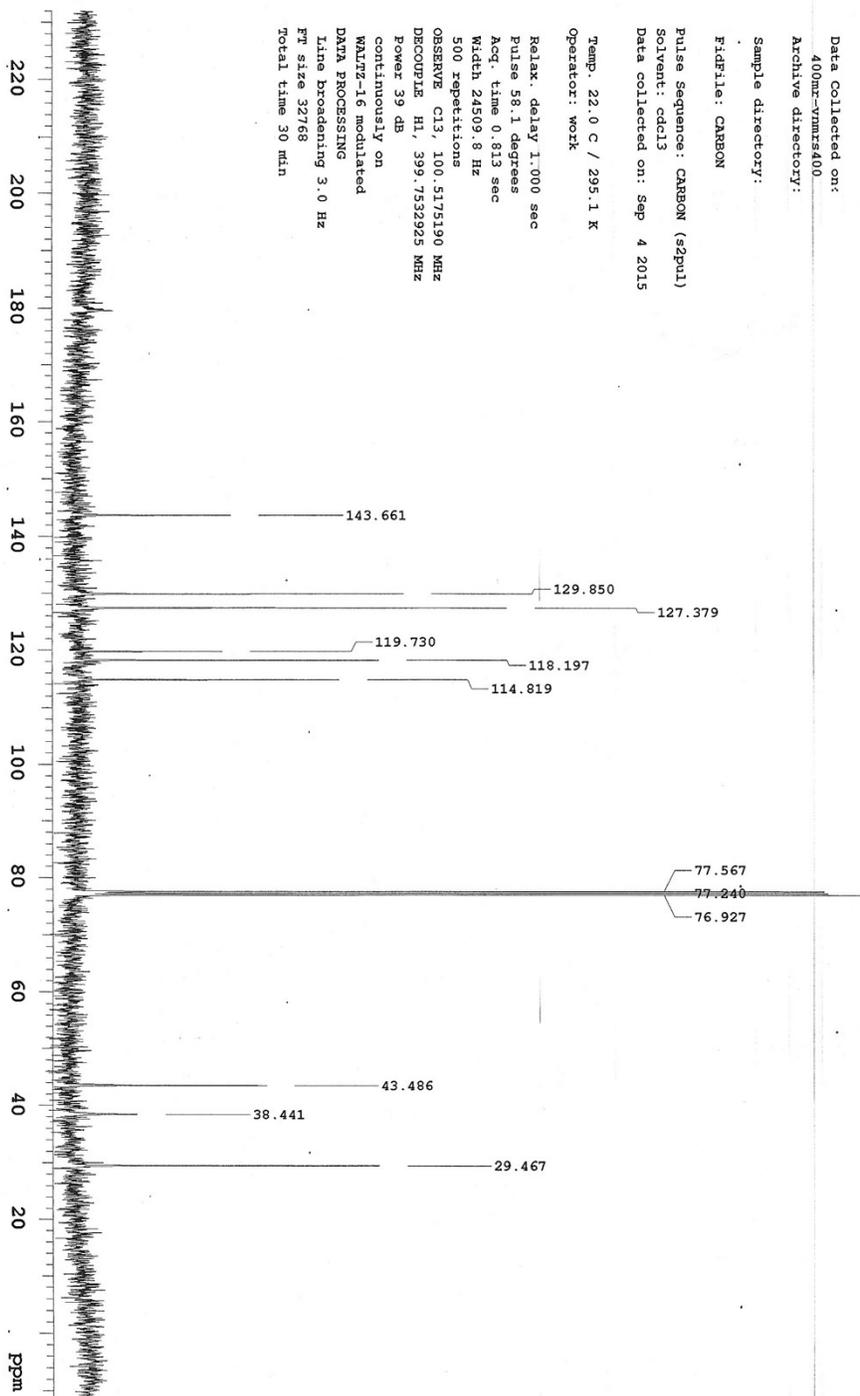
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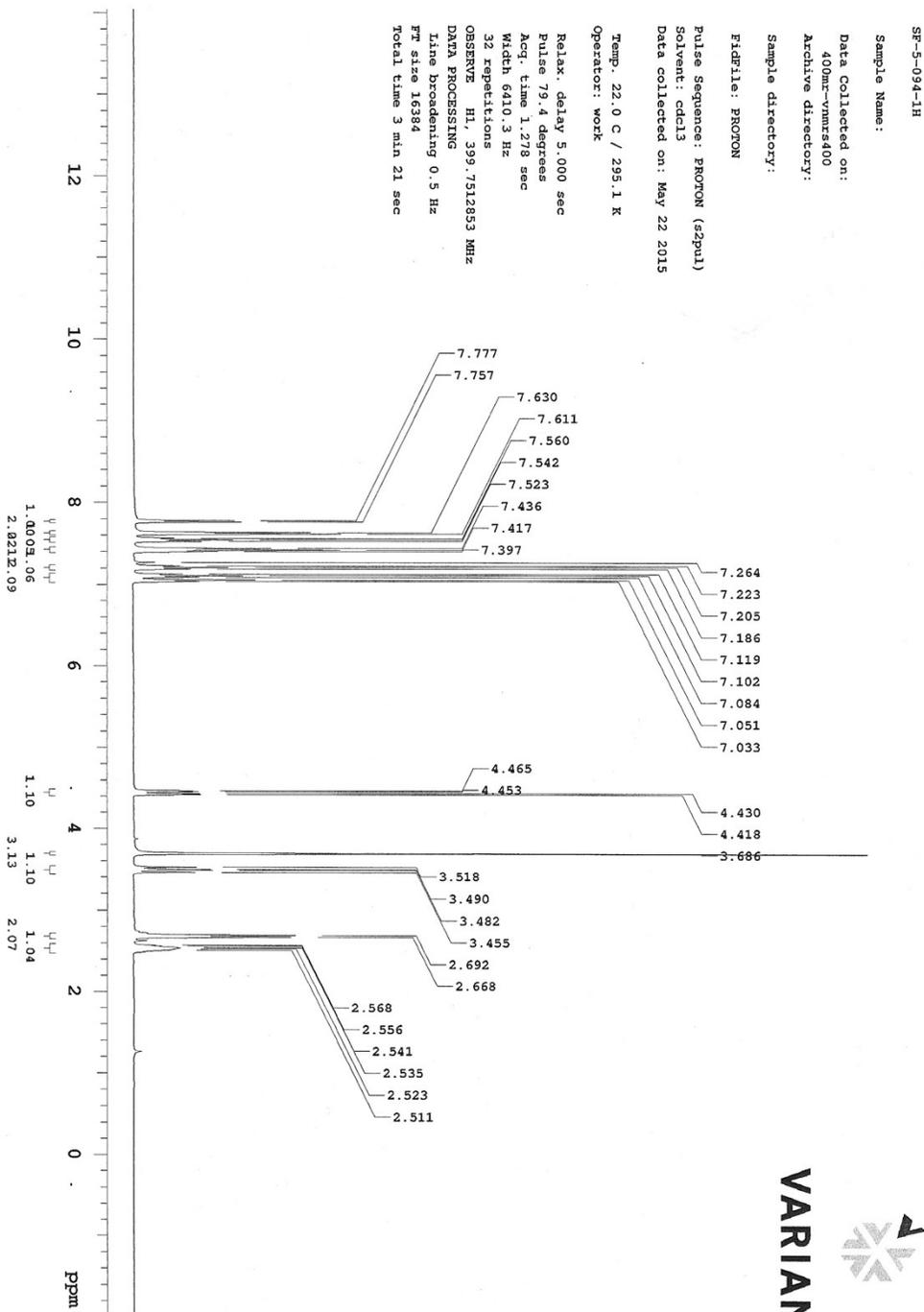
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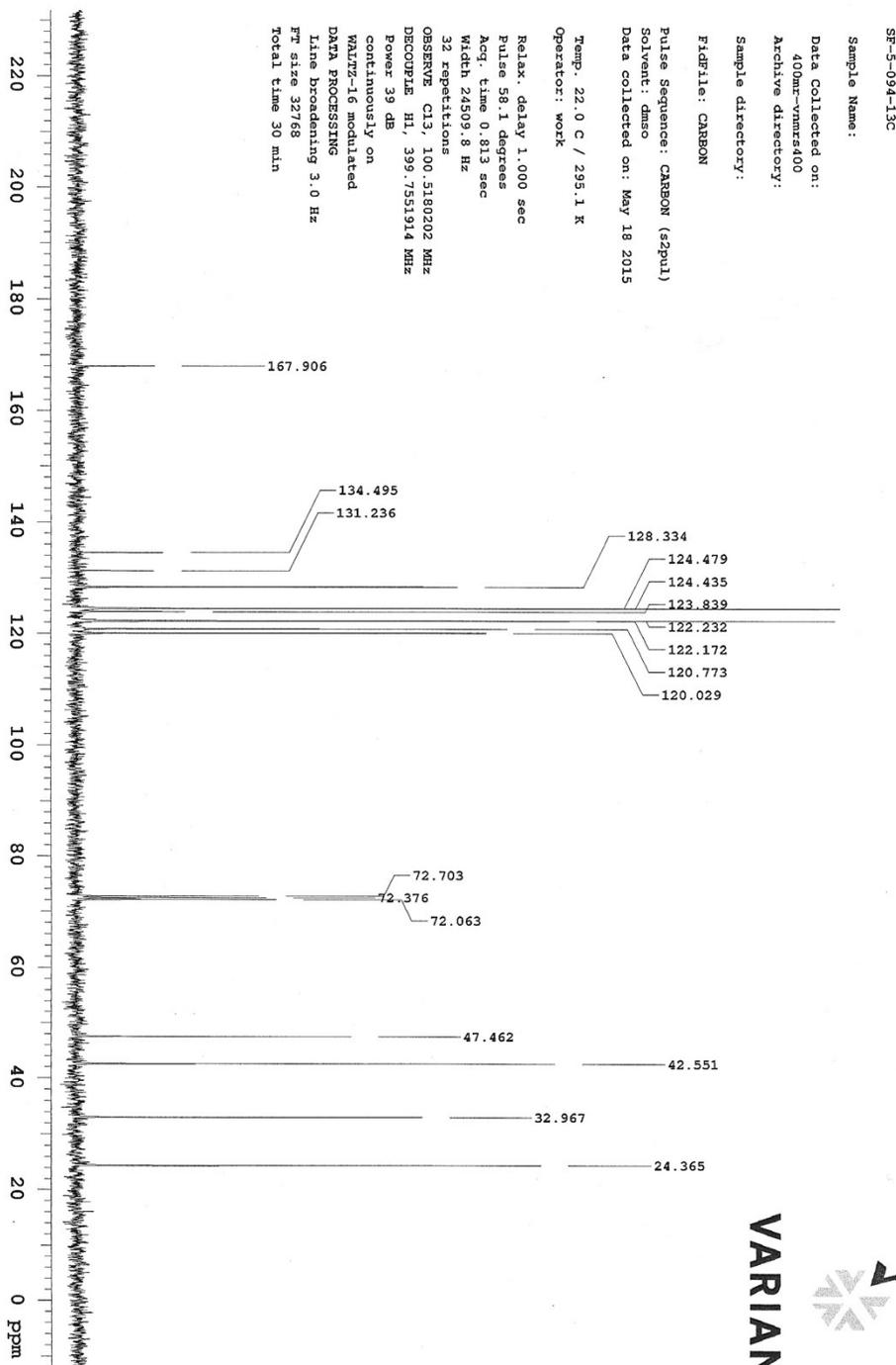
1,2,3,4-Tetrahydroquinoline-3-carboxylic acid ( $\pm$ -6).



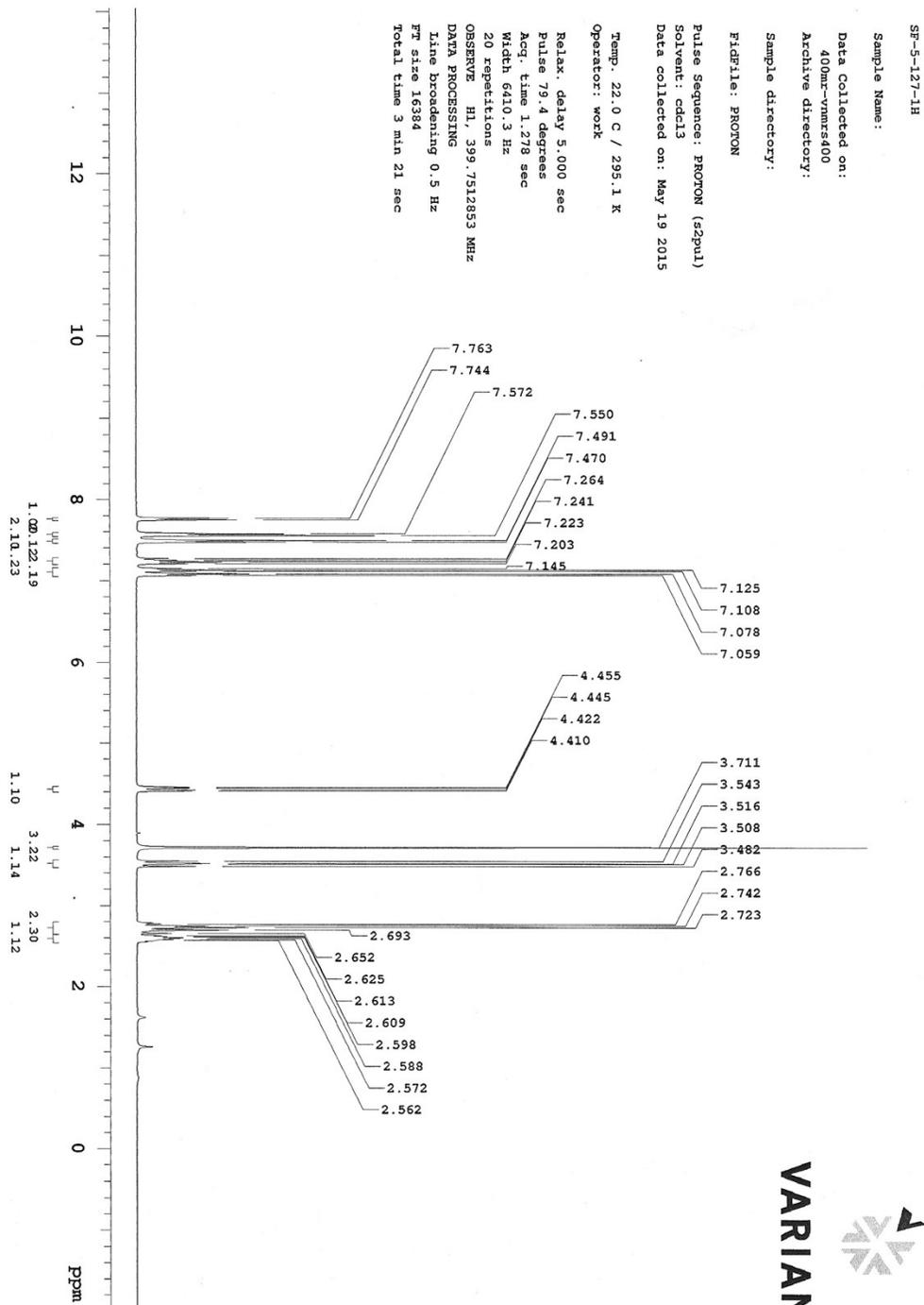
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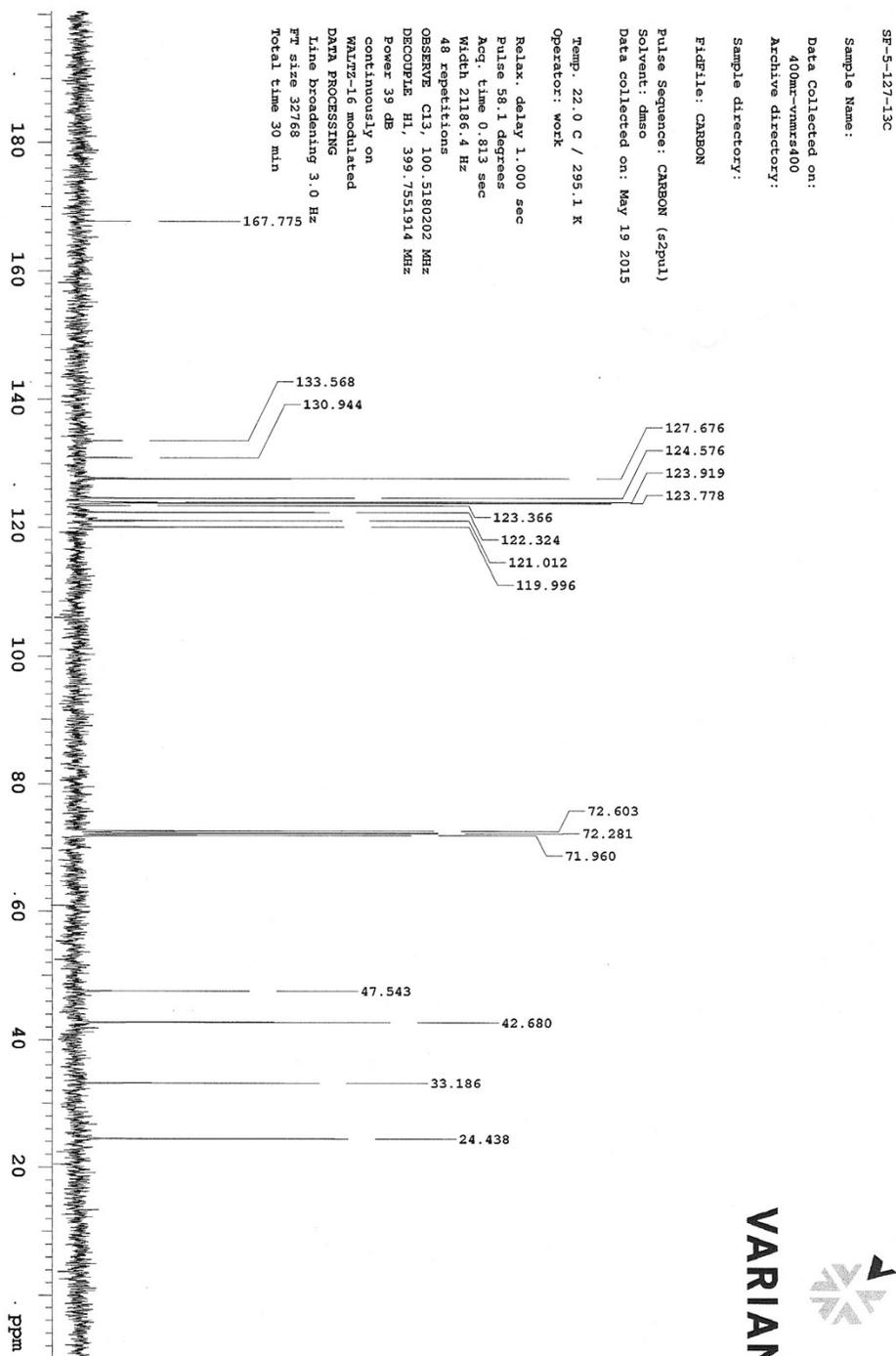
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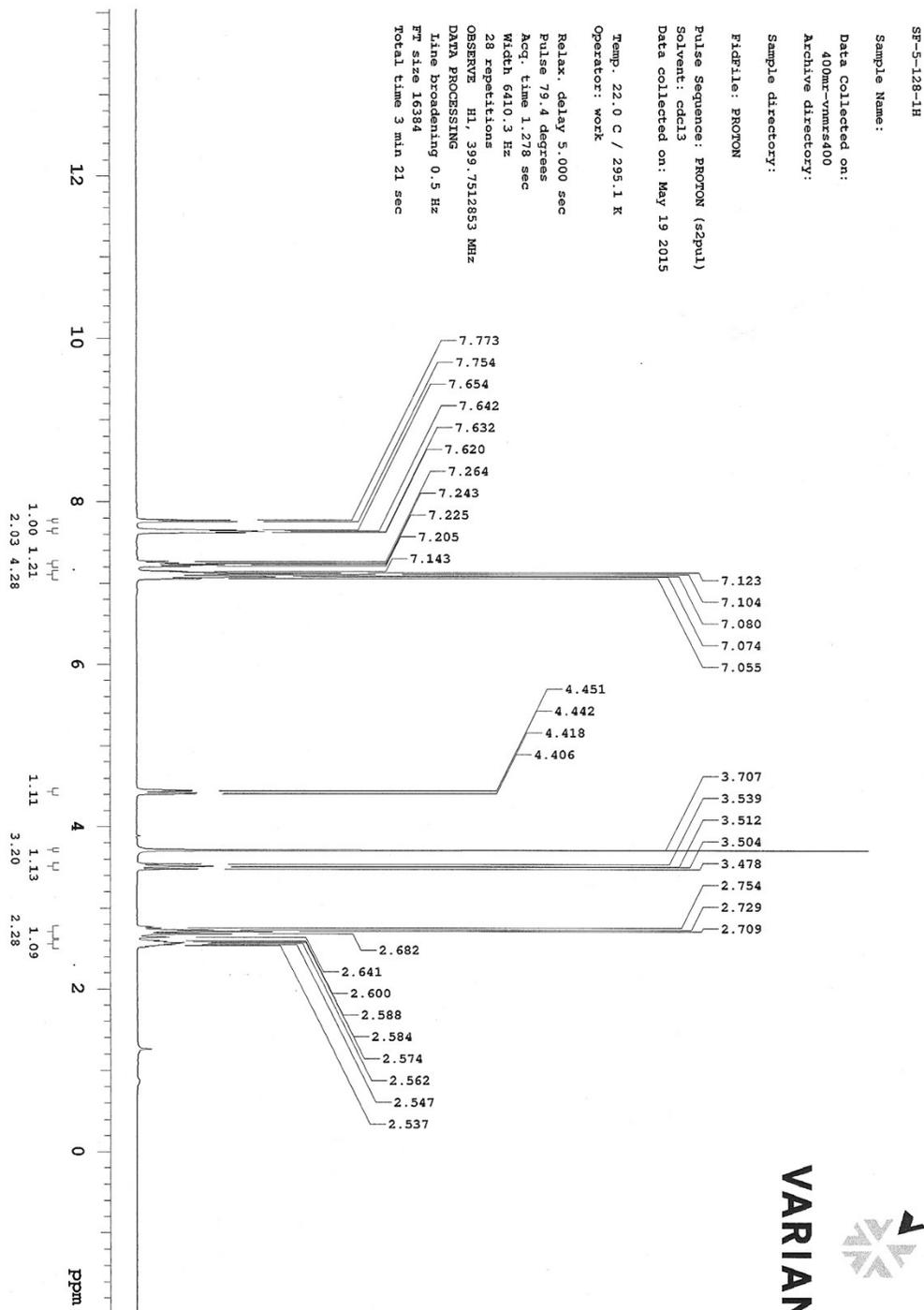
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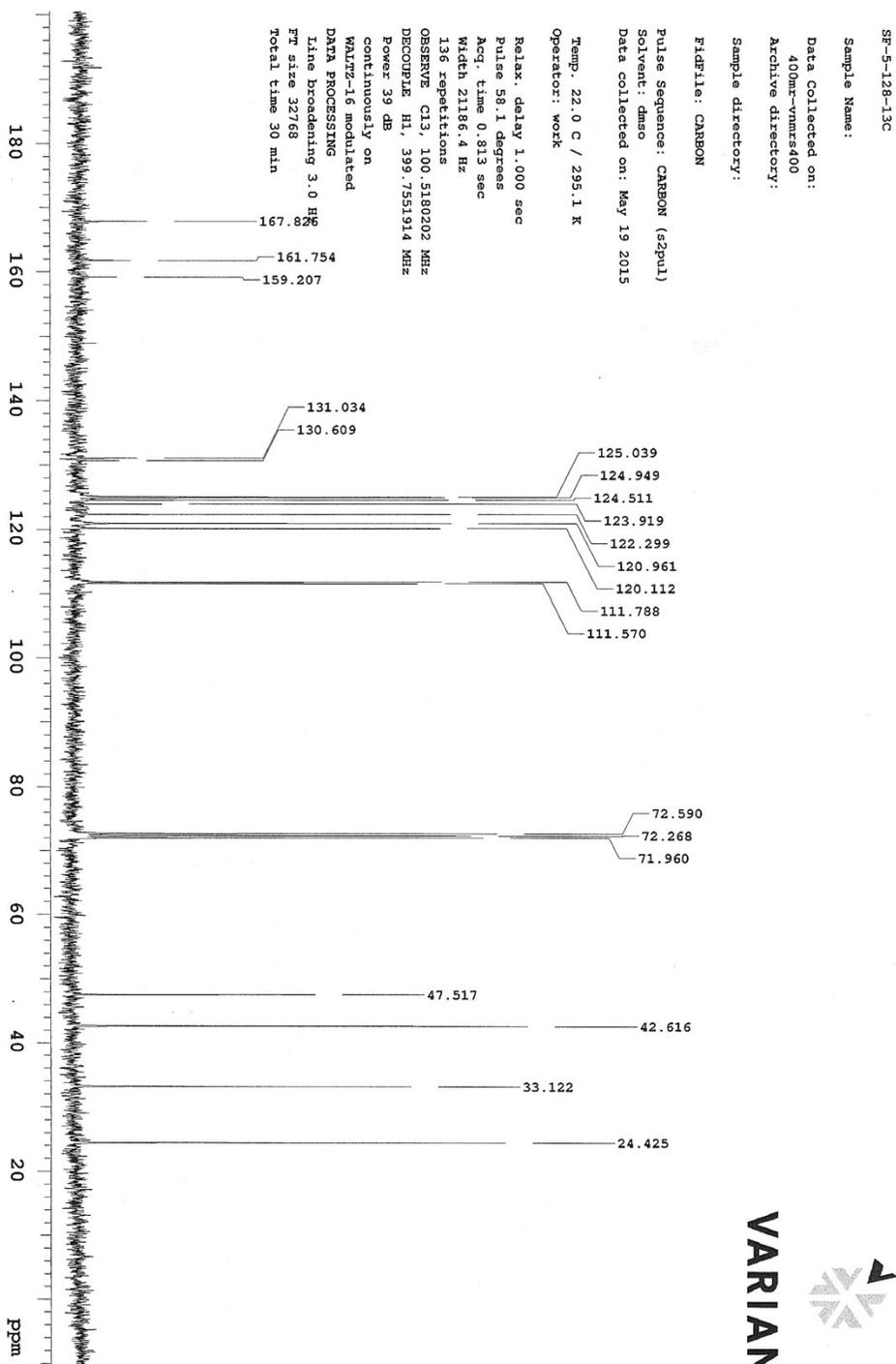
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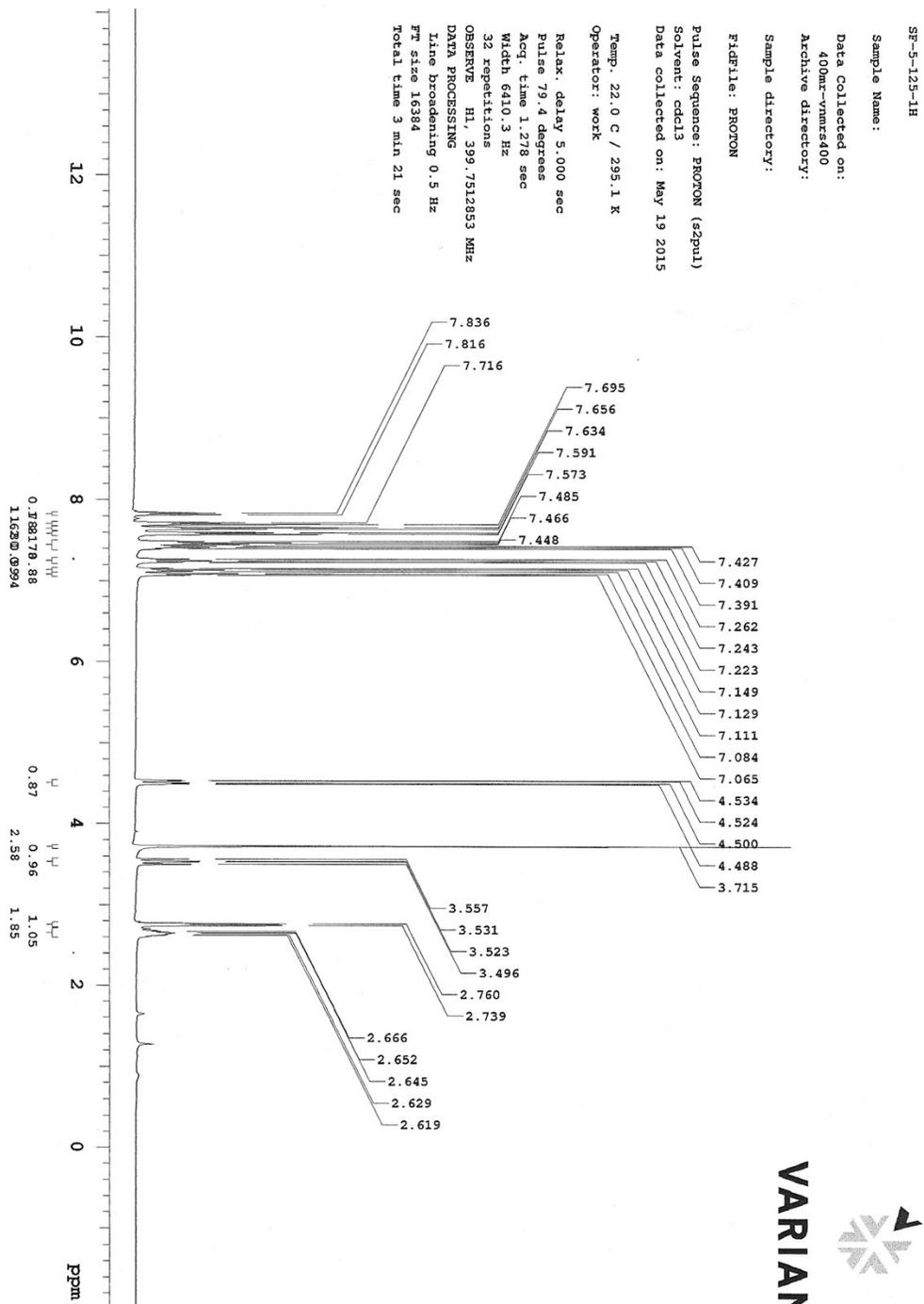
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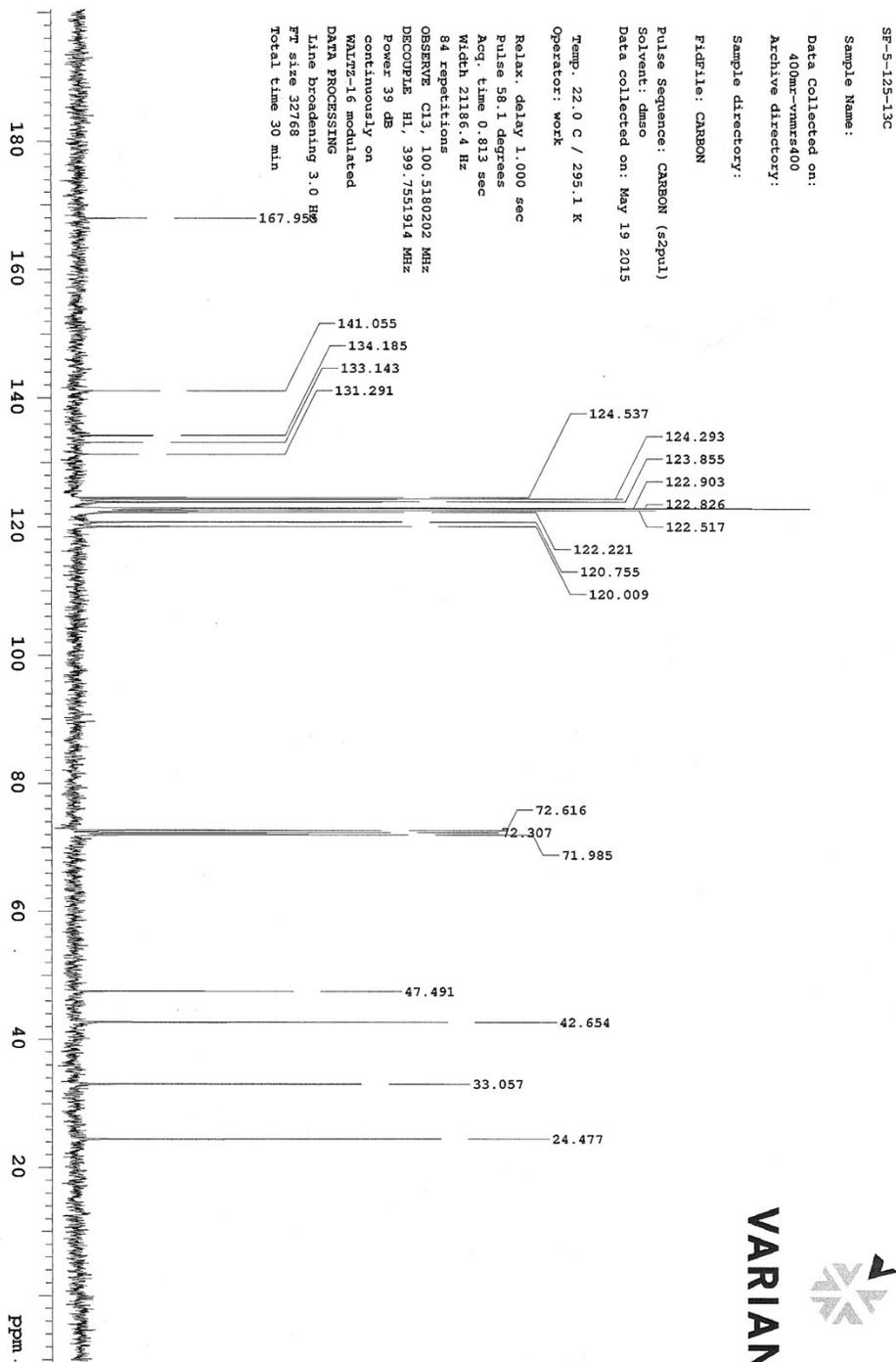
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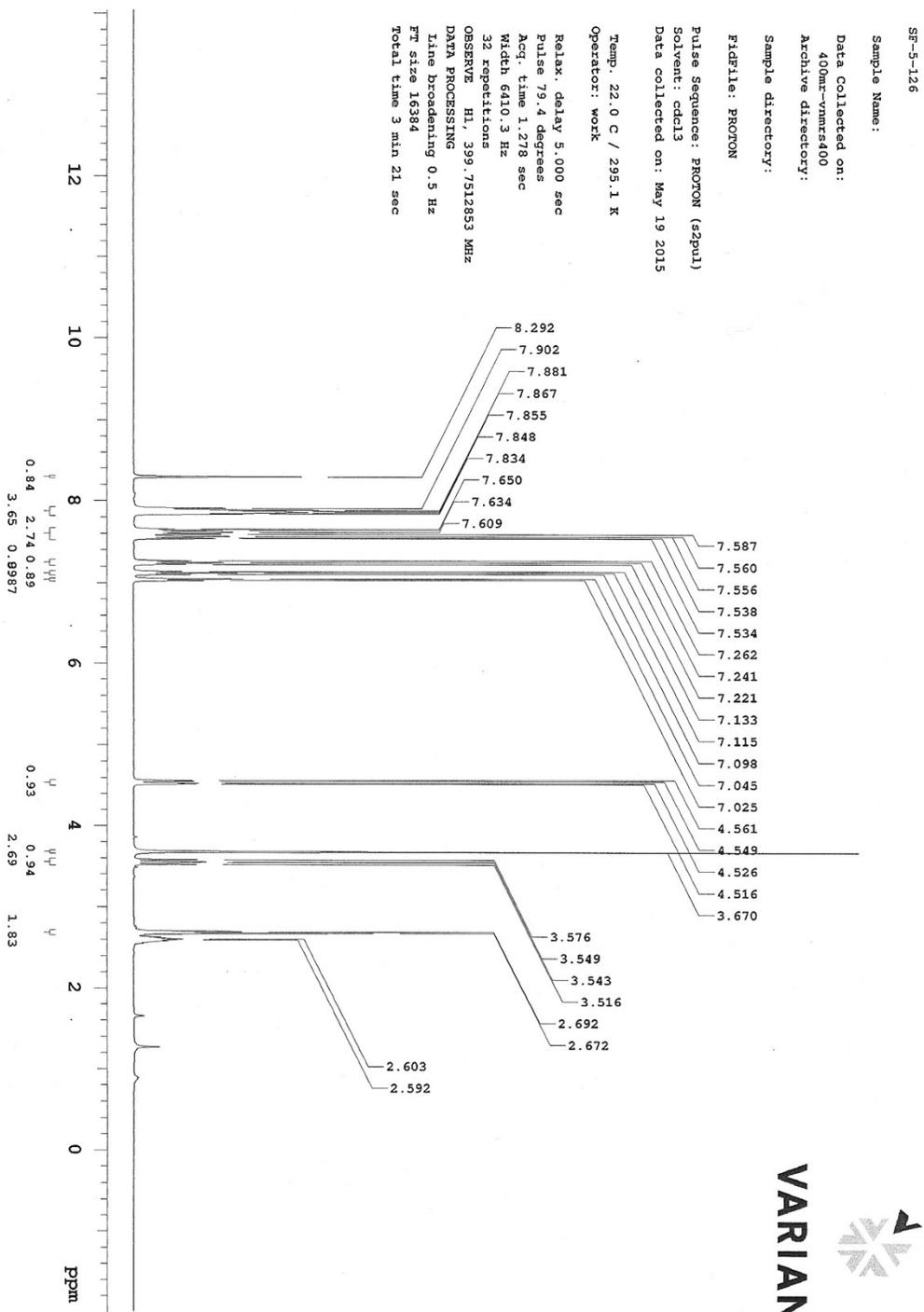
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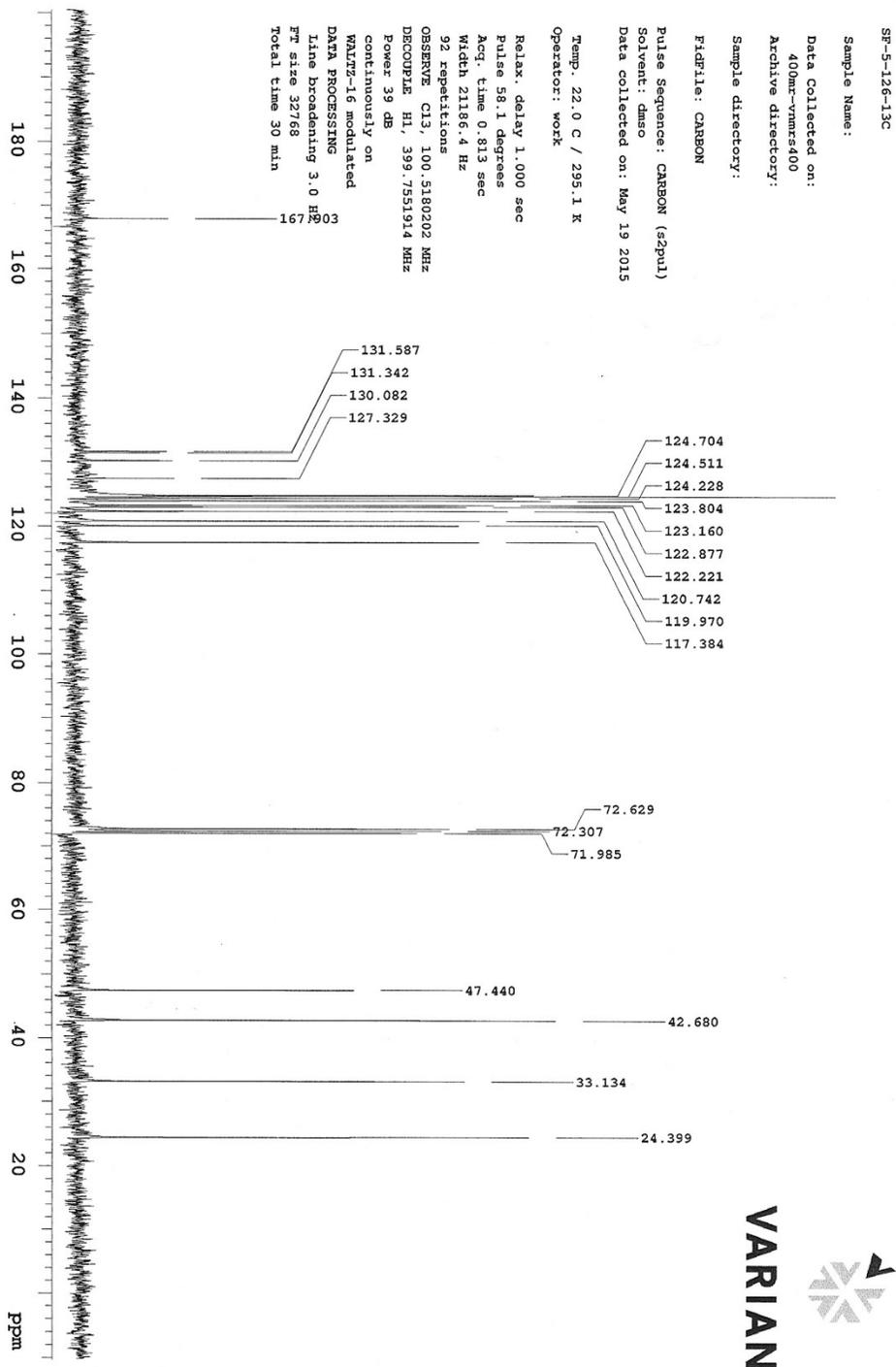
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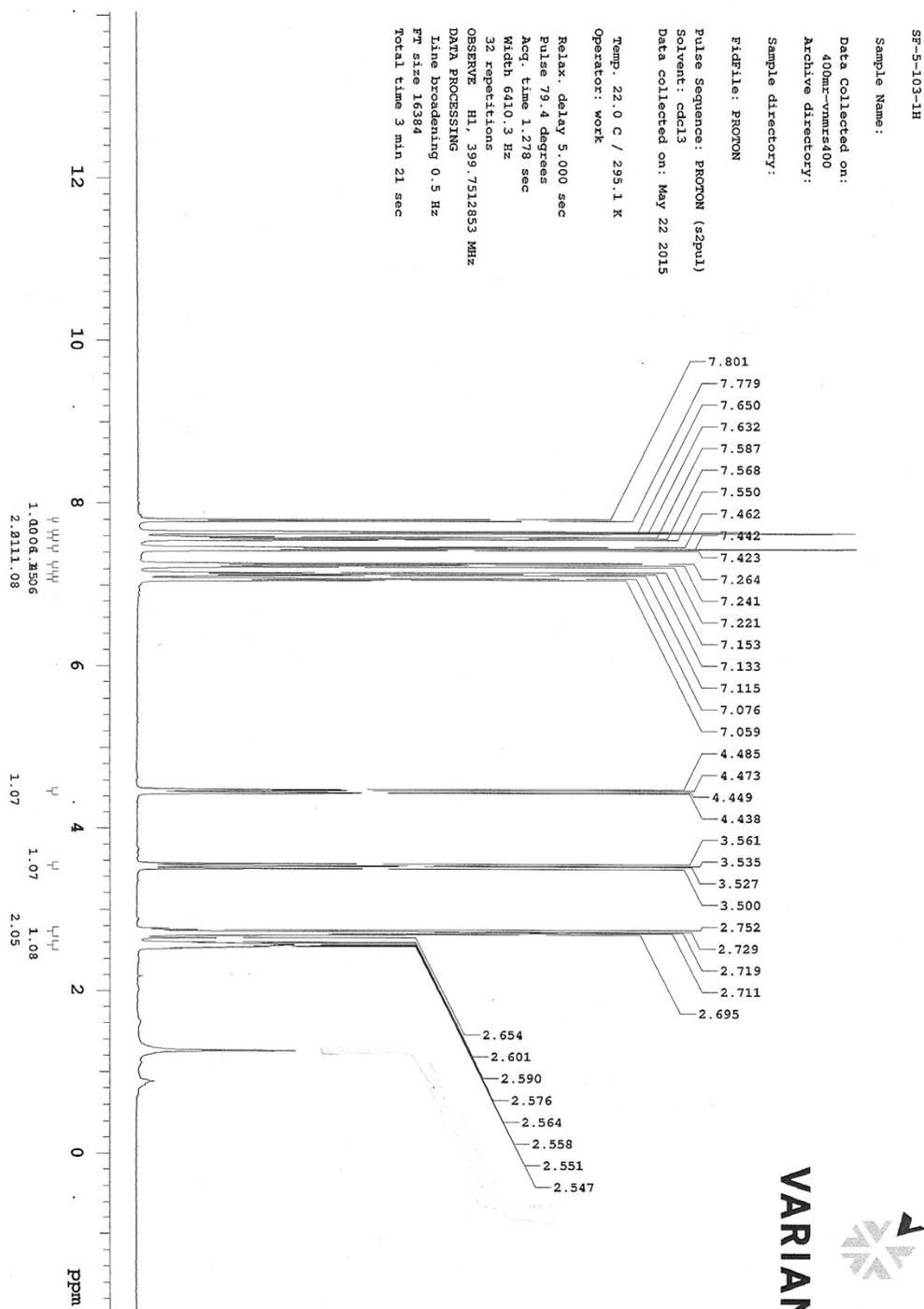
Methyl 1-(naphthalen-2-ylsulfonyl)-1,2,3,4-tetrahydroquinoline-3-carboxylate ( $\pm$ -7e).



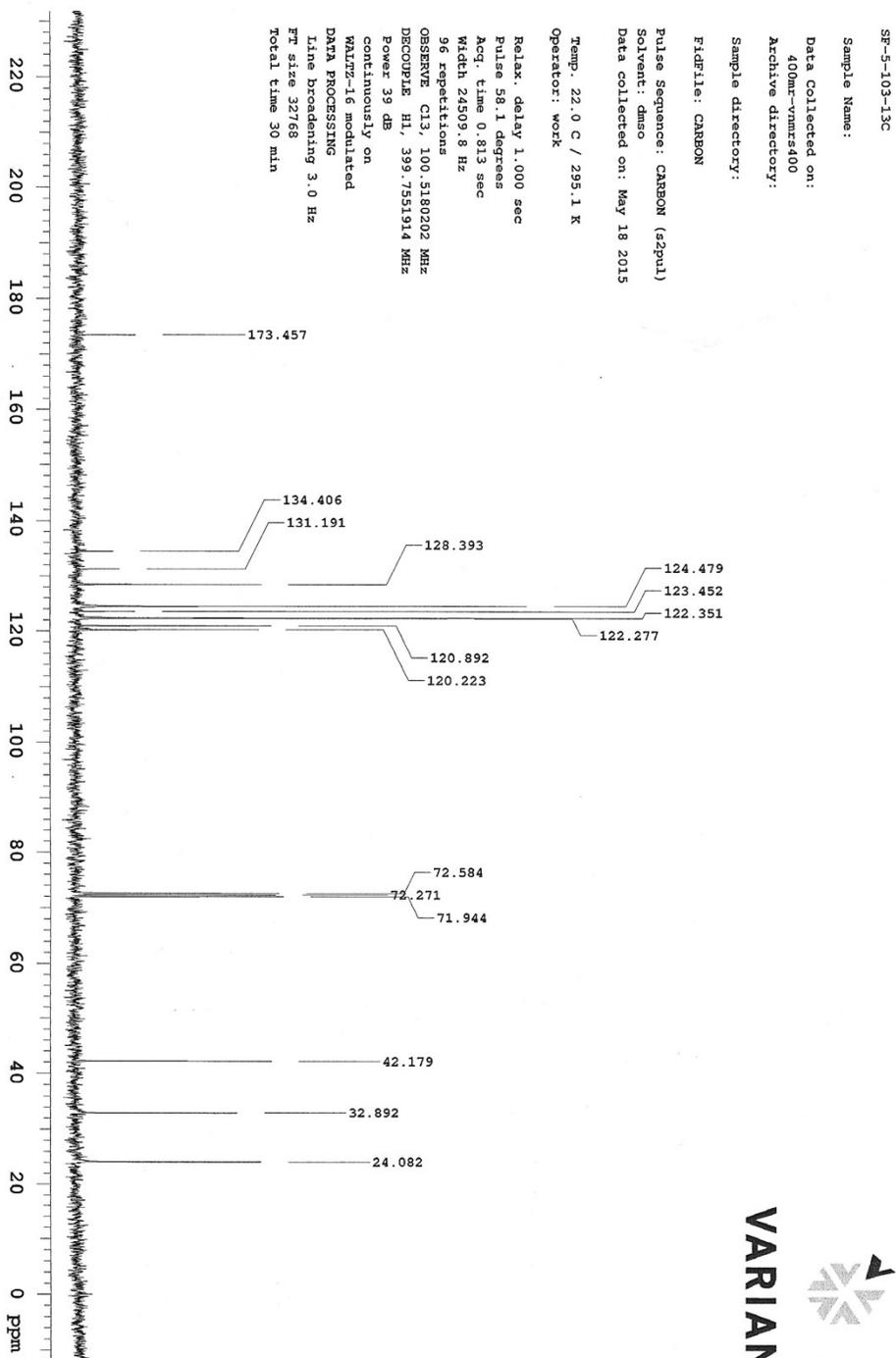
Methyl 1-(naphthalen-2-ylsulfonyl)-1,2,3,4-tetrahydroquinoline-3-carboxylate ( $\pm$ -7e).



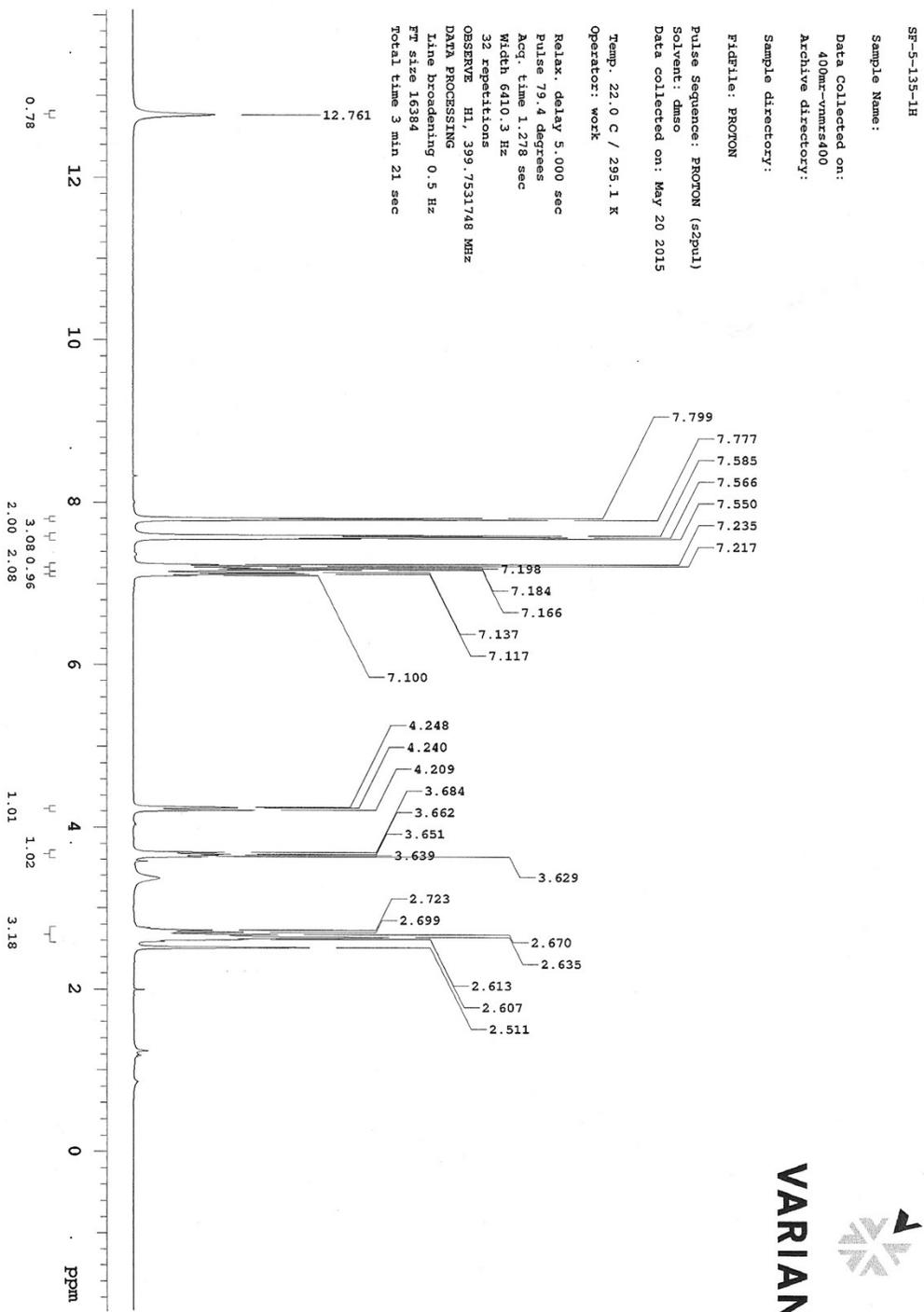
1-(Phenylsulfonyl)-1,2,3,4-tetrahydroquinoline-3-carboxylic acid( $\pm$ -8a).



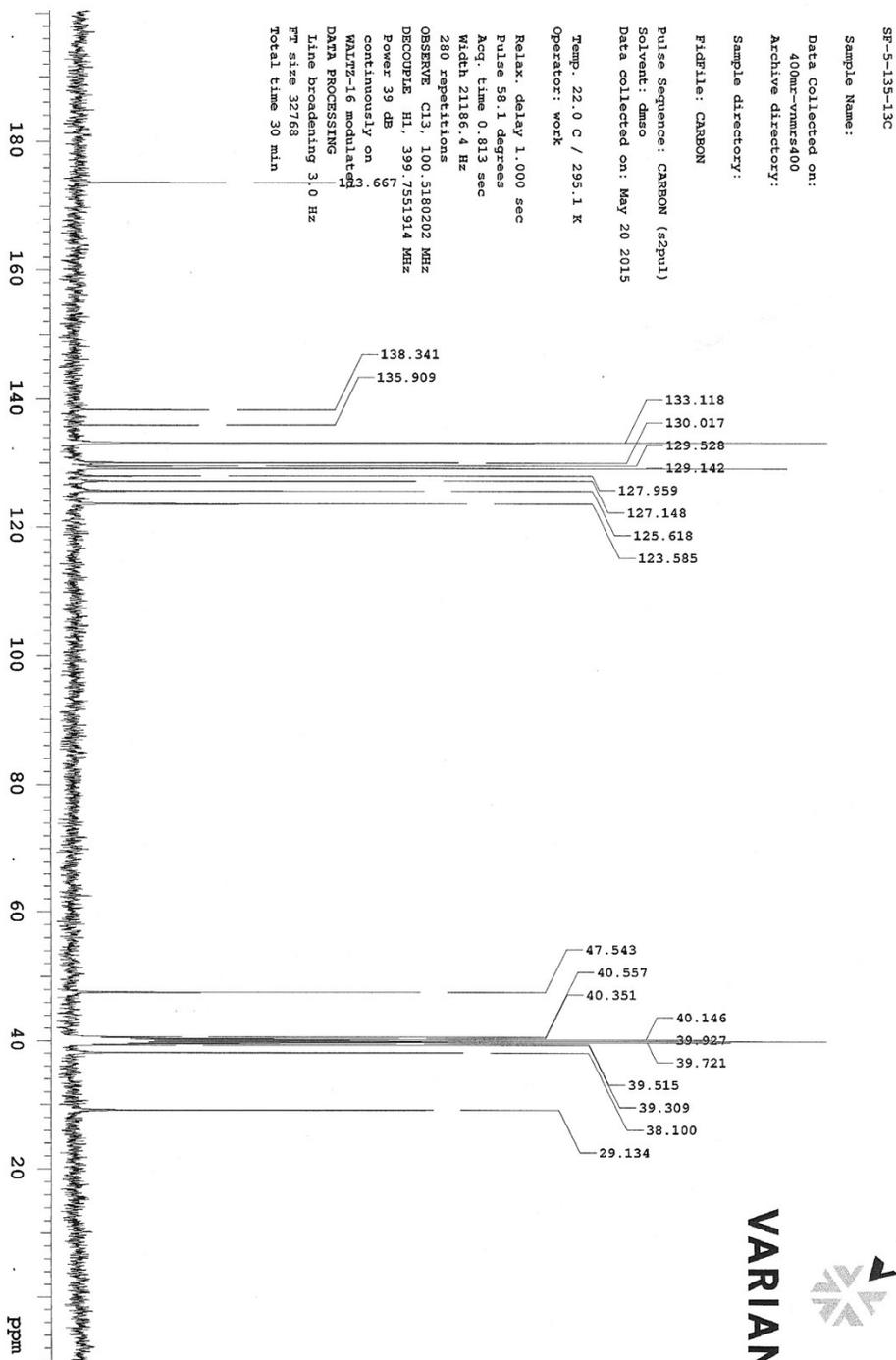
1-(Phenylsulfonyl)-1,2,3,4-tetrahydroquinoline-3-carboxylic acid( $\pm$ -8a).



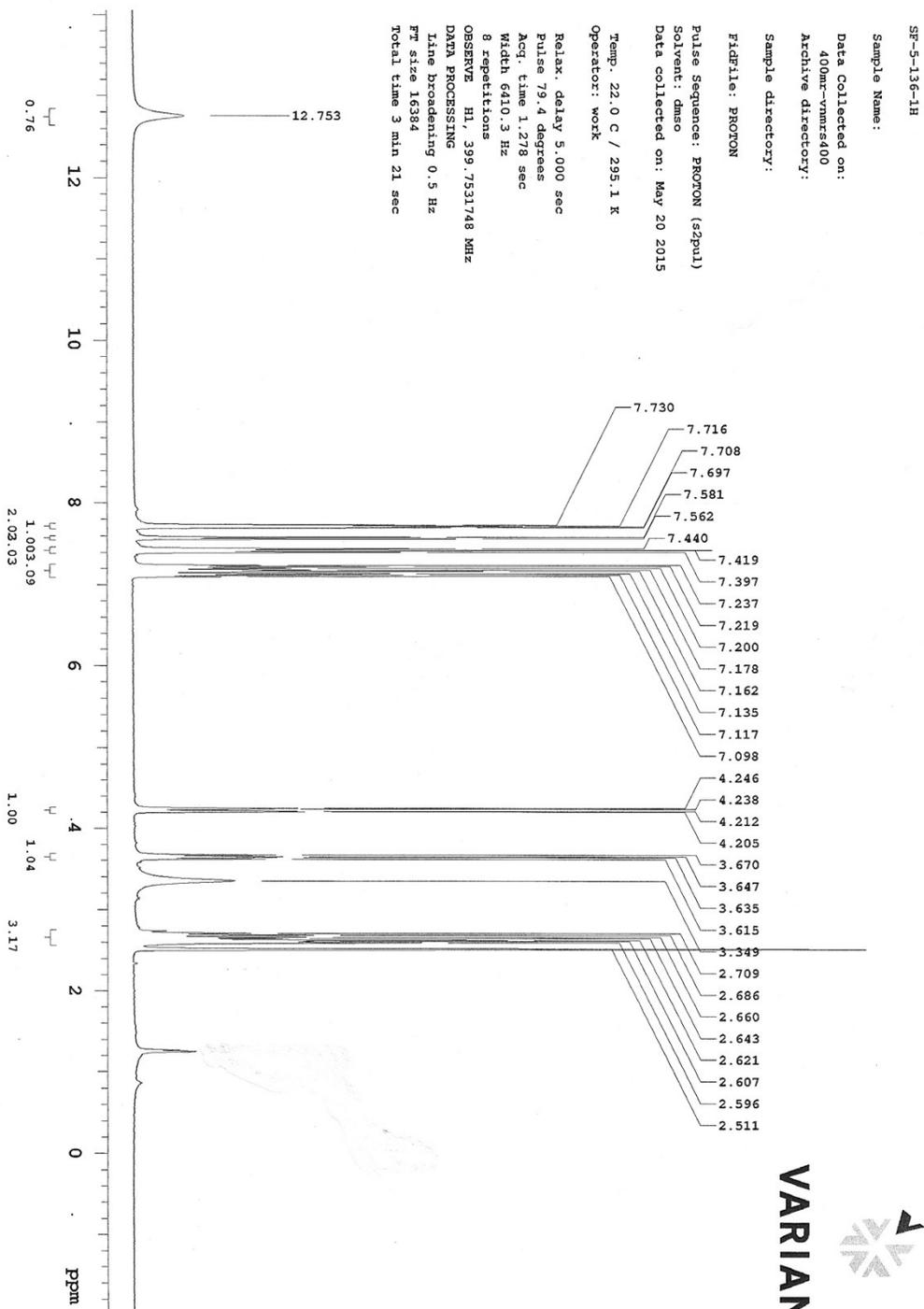
1-((4-Bromophenyl)sulfonyl)-1,2,3,4-tetrahydroquinoline-3-carboxylic acid ( $\pm$ -8b).



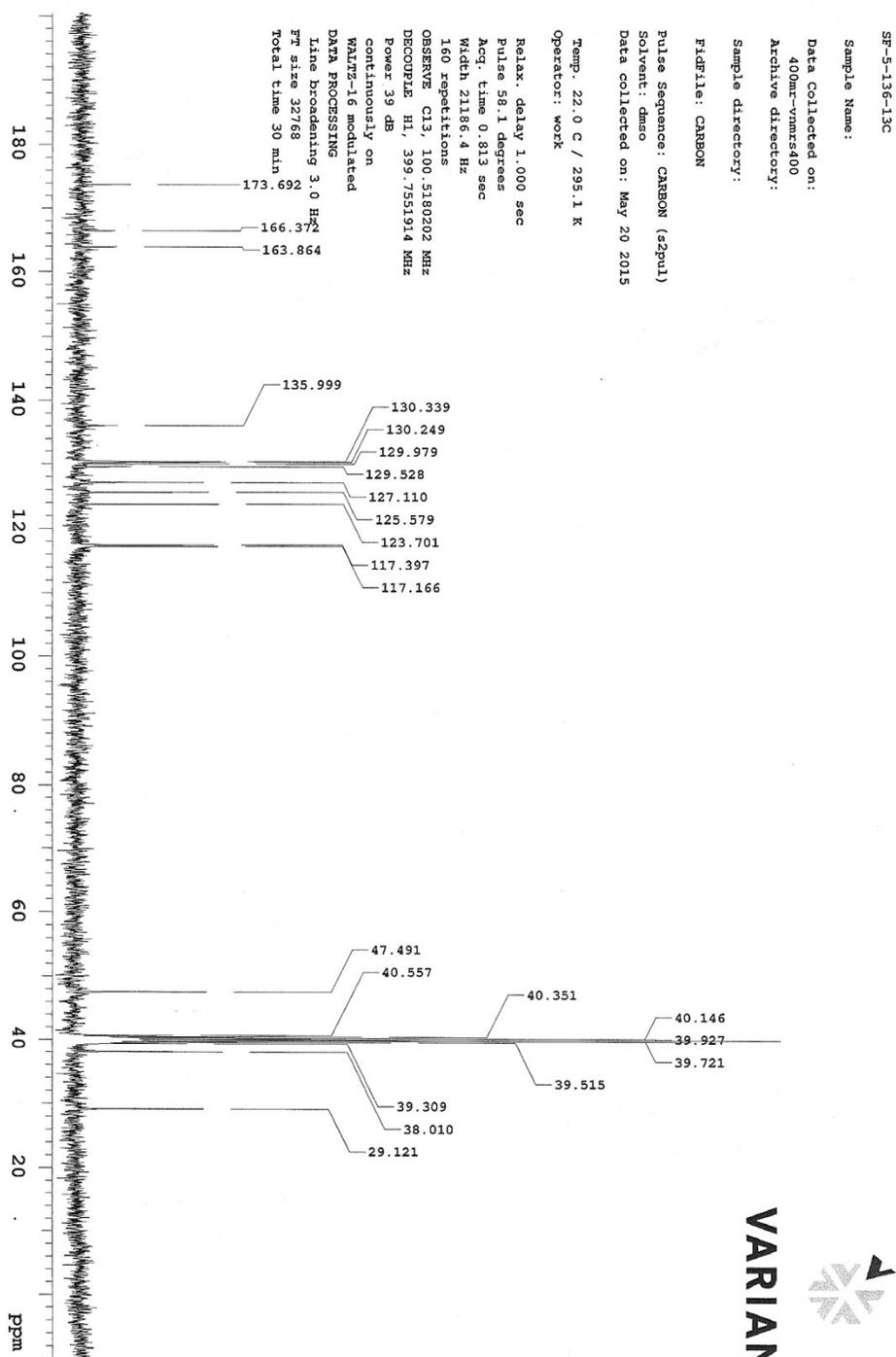
1-((4-Bromophenyl)sulfonyl)-1,2,3,4-tetrahydroquinoline-3-carboxylic acid ( $\pm$ -8b).



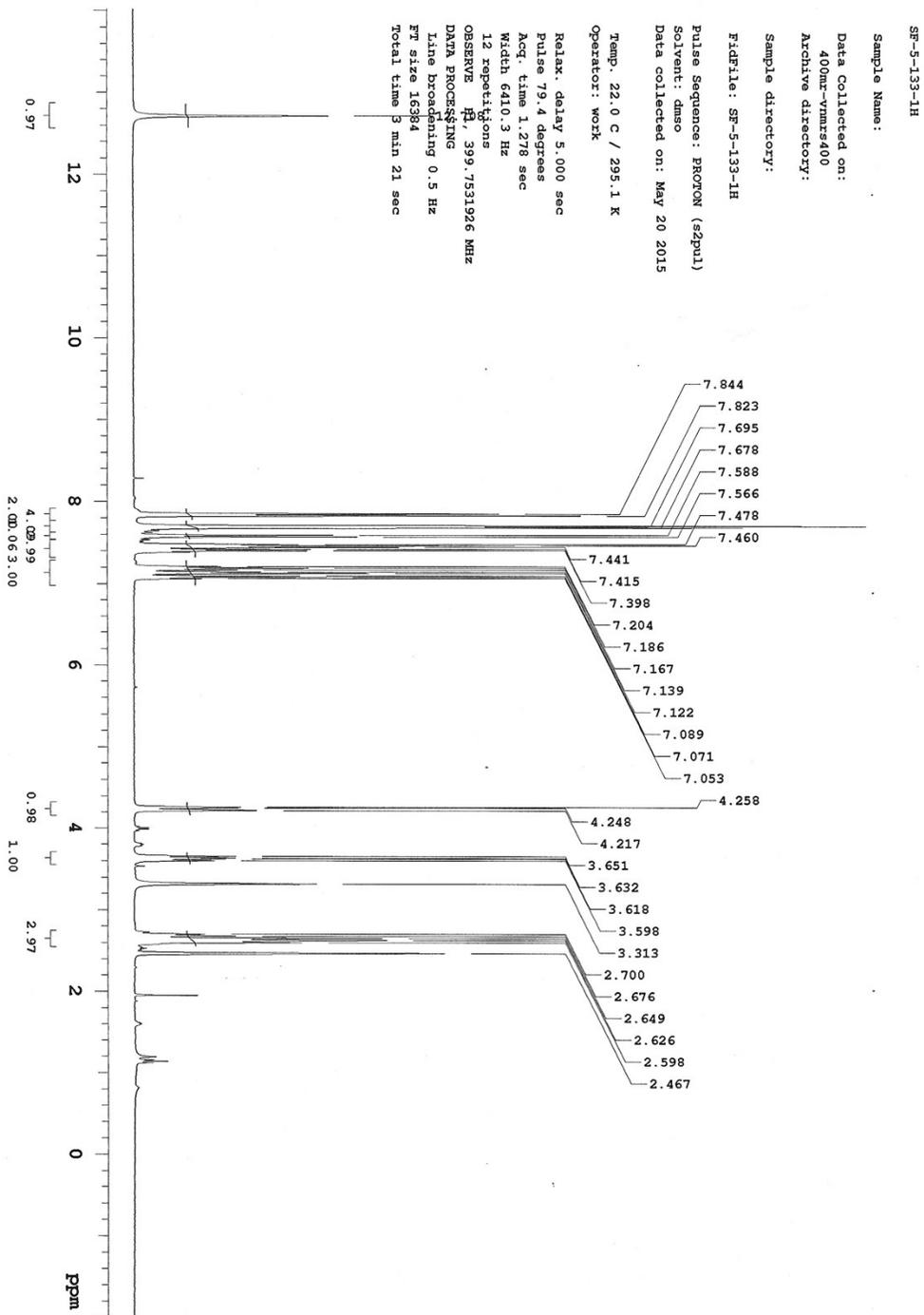
1-((4-Fluorophenyl)sulfonyl)-1,2,3,4-tetrahydroquinoline-3-carboxylic acid ( $\pm$ -8c).



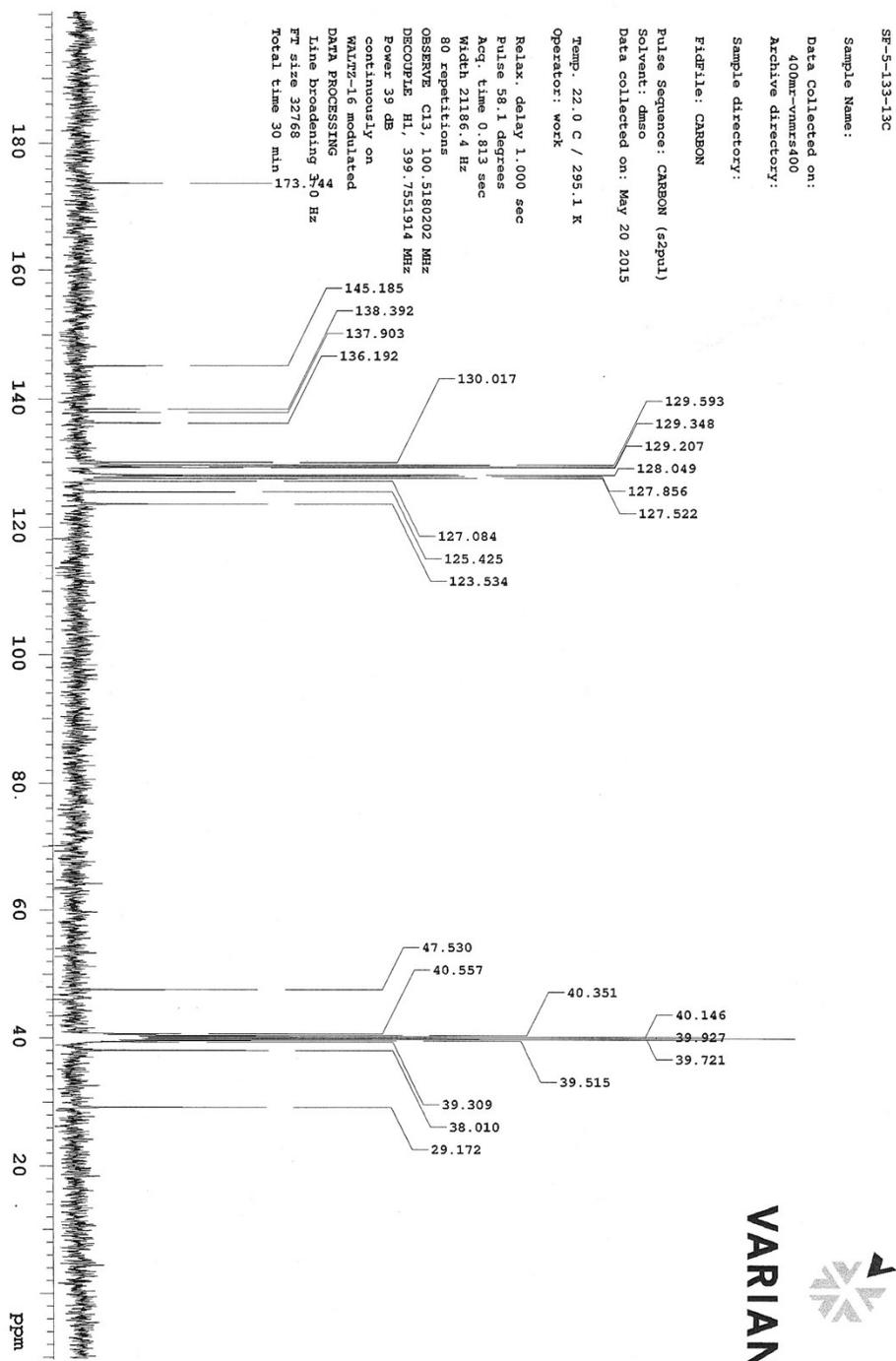
1-((4-Fluorophenyl)sulfonyl)-1,2,3,4-tetrahydroquinoline-3-carboxylic acid ( $\pm$ -8c).



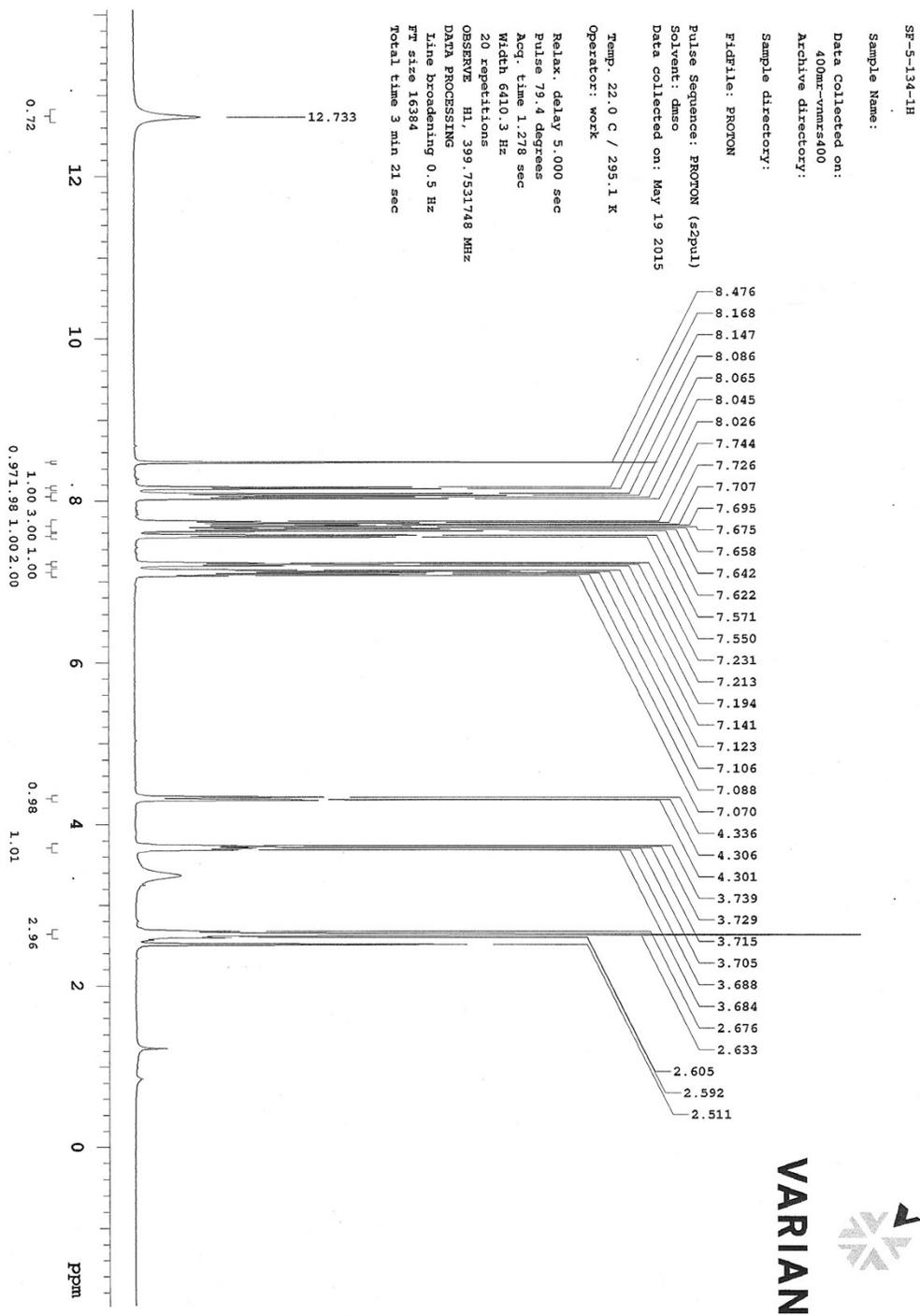
1-([1,1'-Biphenyl]-4-ylsulfonyl)-1,2,3,4-tetrahydroquinoline-3-carboxylic acid ( $\pm$  8d).



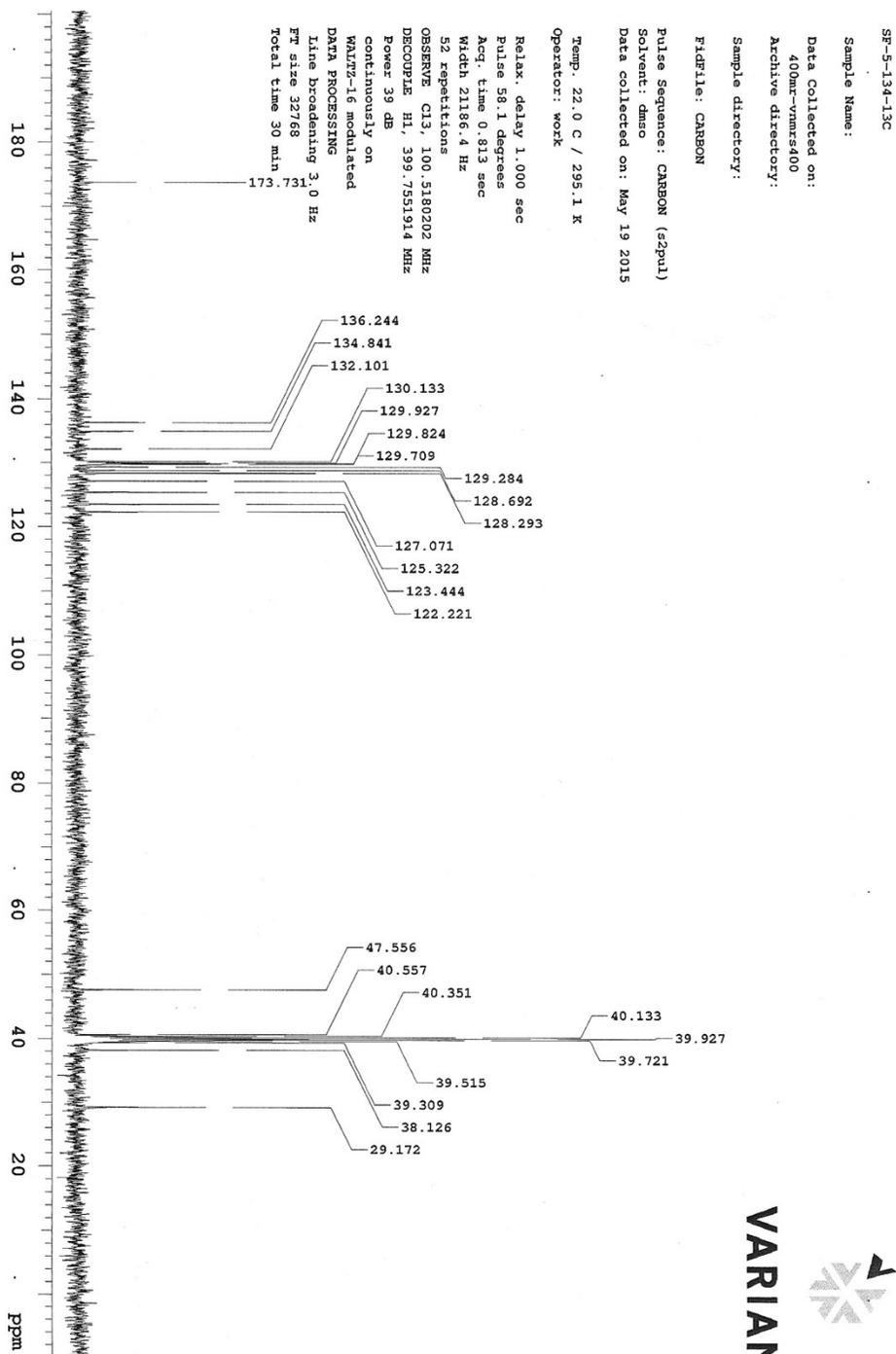
1-([1,1'-Biphenyl]-4-ylsulfonyl)-1,2,3,4-tetrahydroquinoline-3-carboxylic acid ( $\pm$  8d).



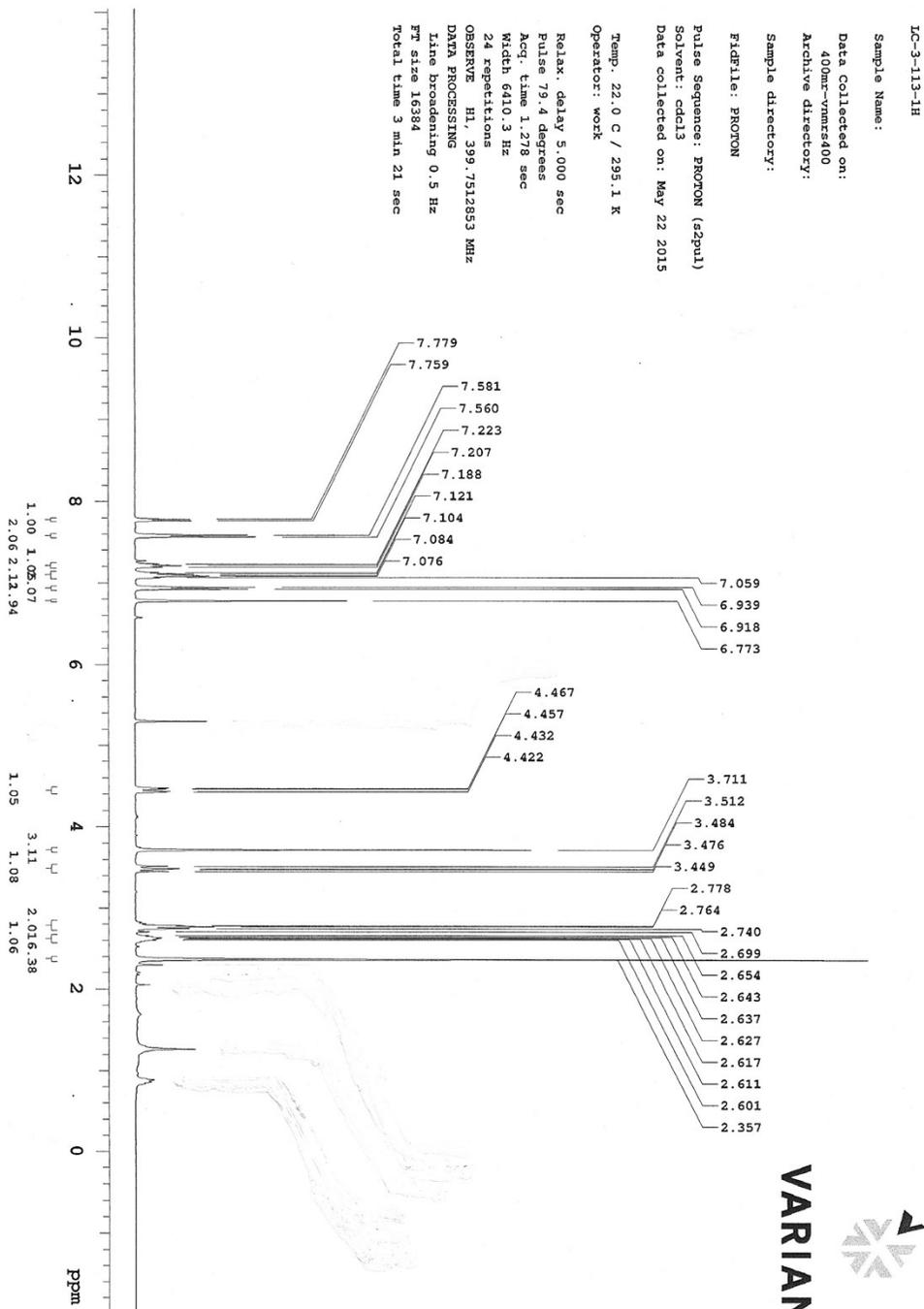
1-(Naphthalen-2-ylsulfonyl)-1,2,3,4-tetrahydroquinoline-3-carboxylic acid ( $\pm$ -8e).



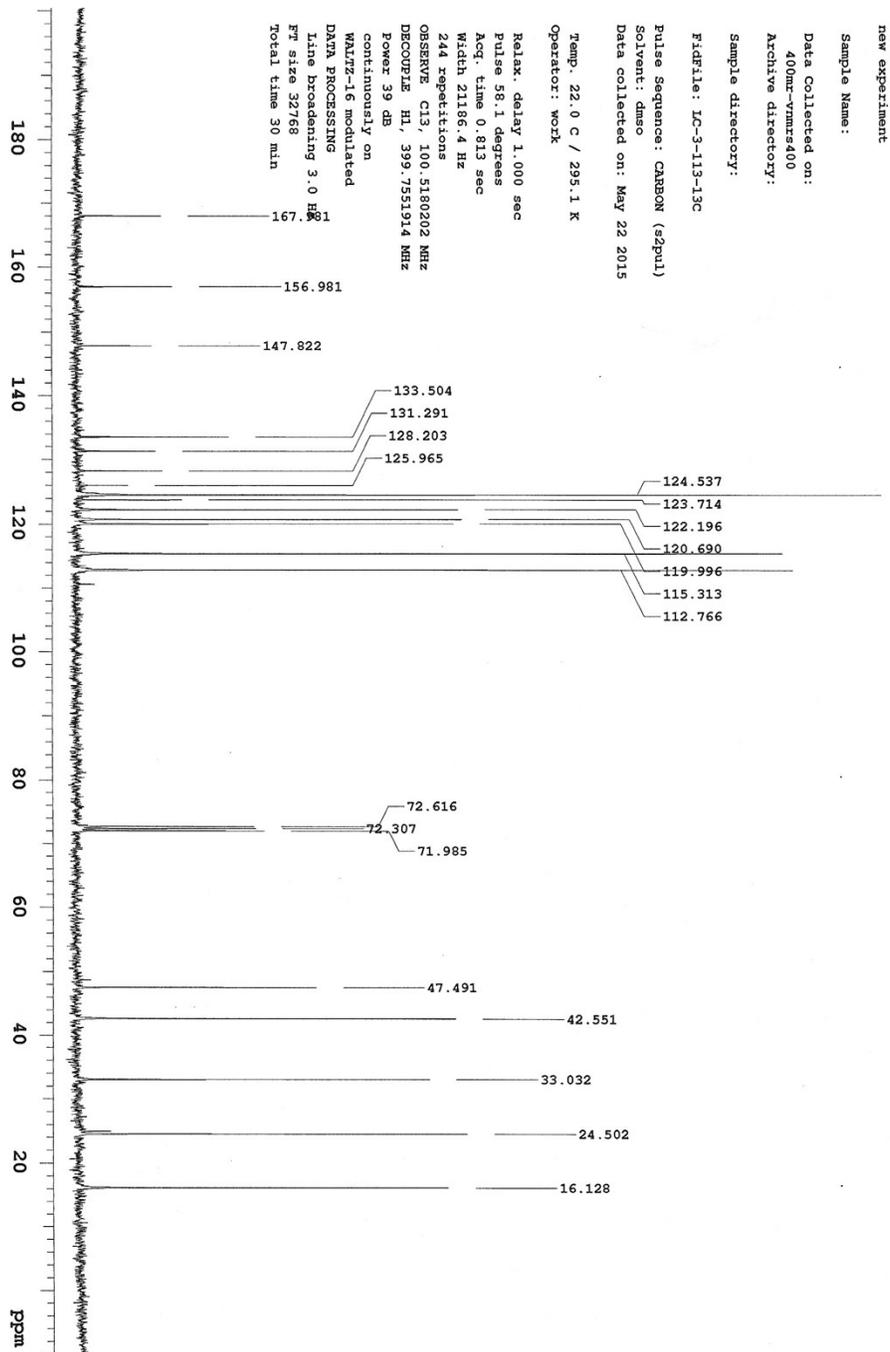
1-(Naphthalen-2-ylsulfonyl)-1,2,3,4-tetrahydroquinoline-3-carboxylic acid ( $\pm$ -8e).



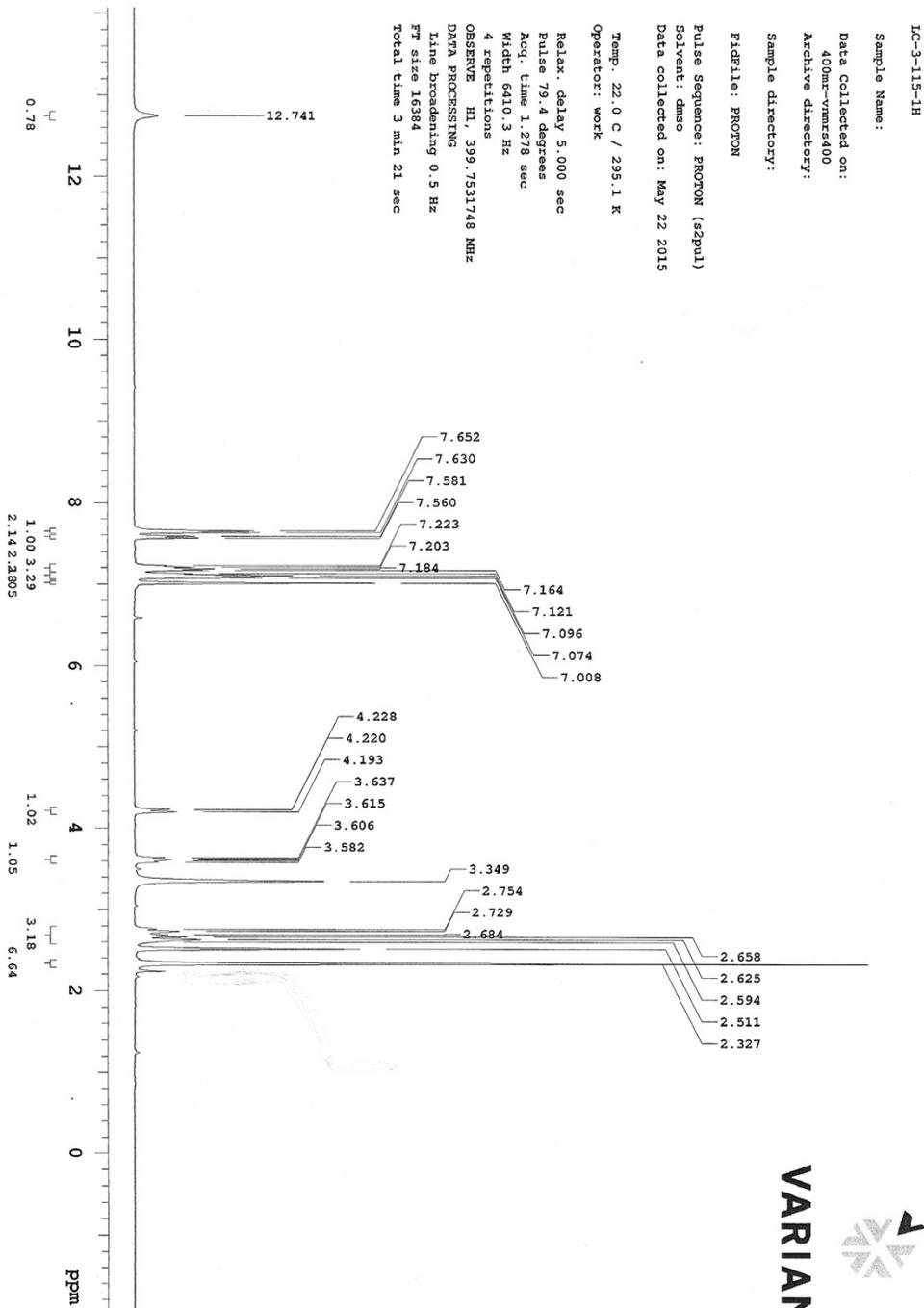
Methyl 1-((4-(4-chloro-3,5-dimethylphenoxy)phenyl)sulfonyl)-1,2,3,4-tetrahydroquinoline-3-carboxylate (±-9).



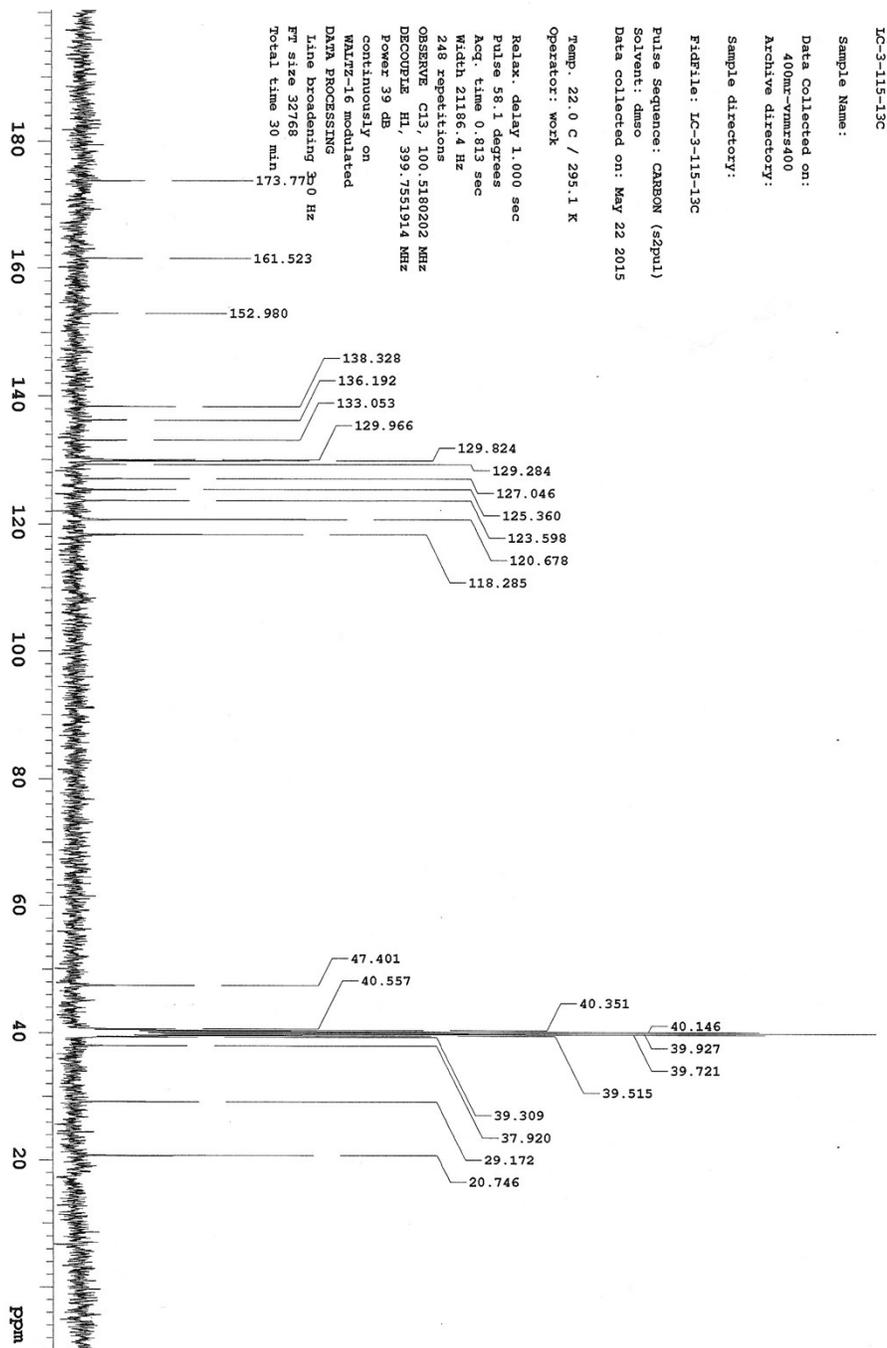
Methyl 1-((4-(4-chloro-3,5-dimethylphenoxy)phenyl)sulfonyl)-1,2,3,4-tetrahydroquinoline-3-carboxylate ( $\pm$ -9).



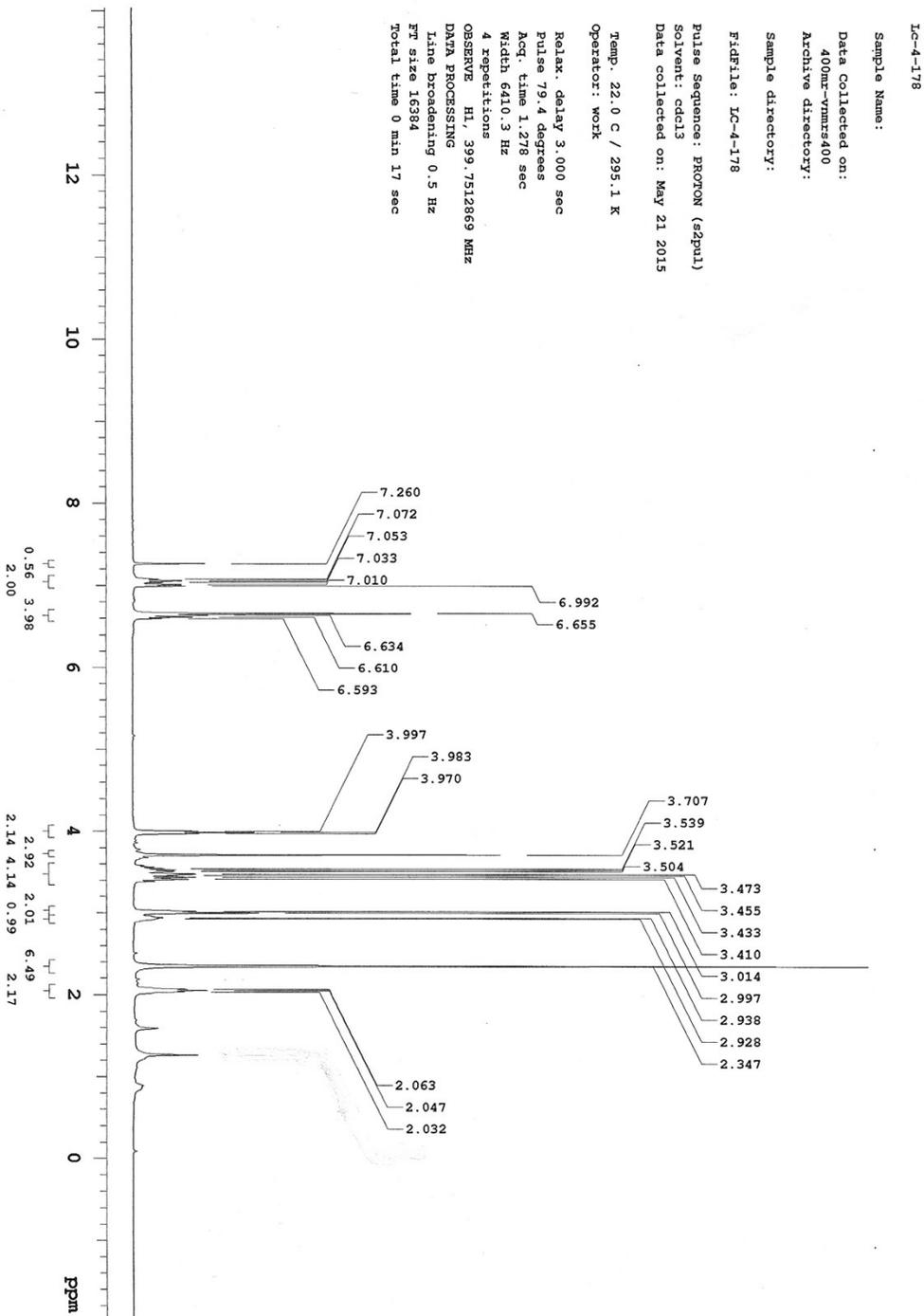
1-((4-(4-Chloro-3,5-dimethylphenoxy)phenyl)sulfonyl)-1,2,3,4-tetrahydroquinoline-3-carboxylic acid ( $\pm$  2).



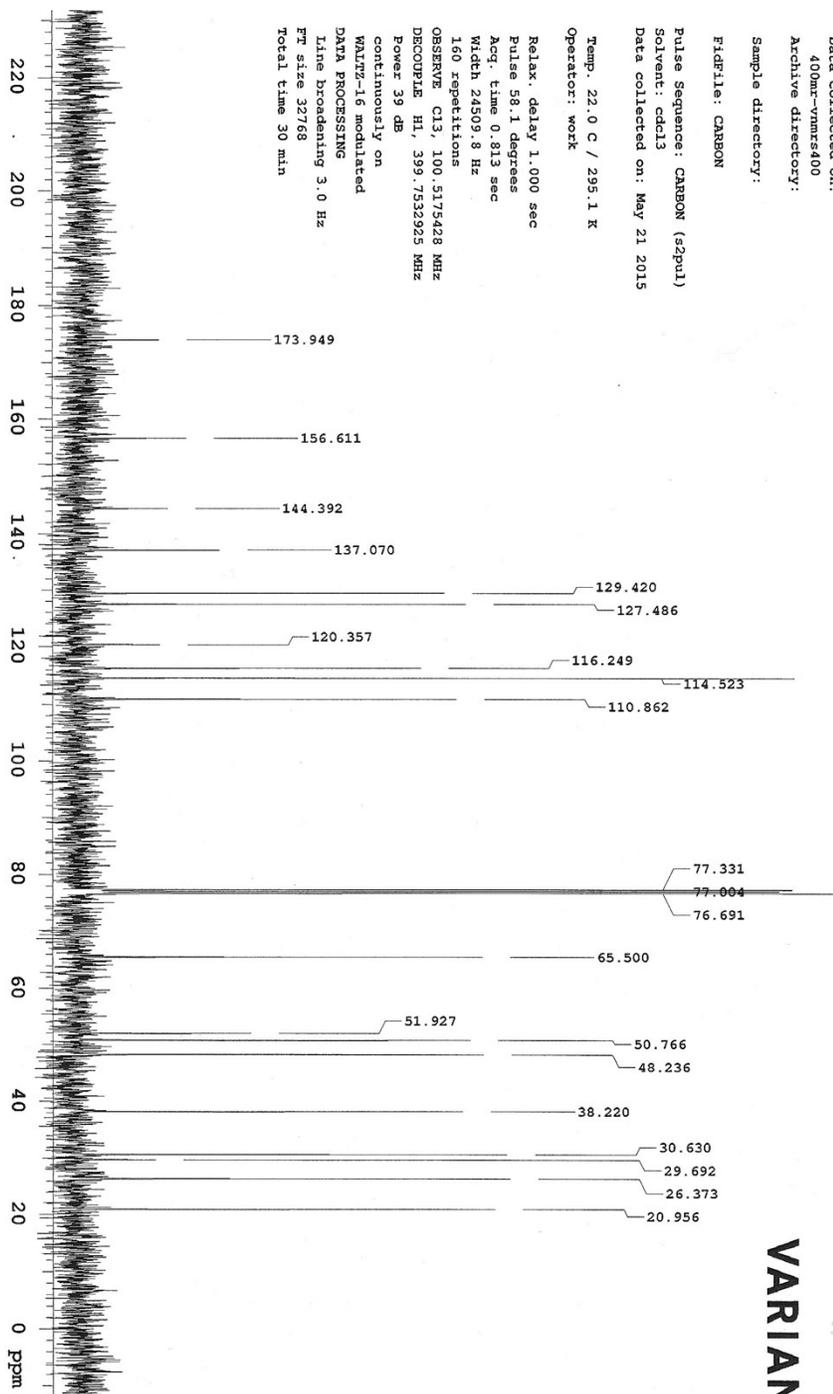
1-((4-(4-Chloro-3,5-dimethylphenoxy)phenyl)sulfonyl)-1,2,3,4-tetrahydroquinoline-3-carboxylic acid ( $\pm$  2).



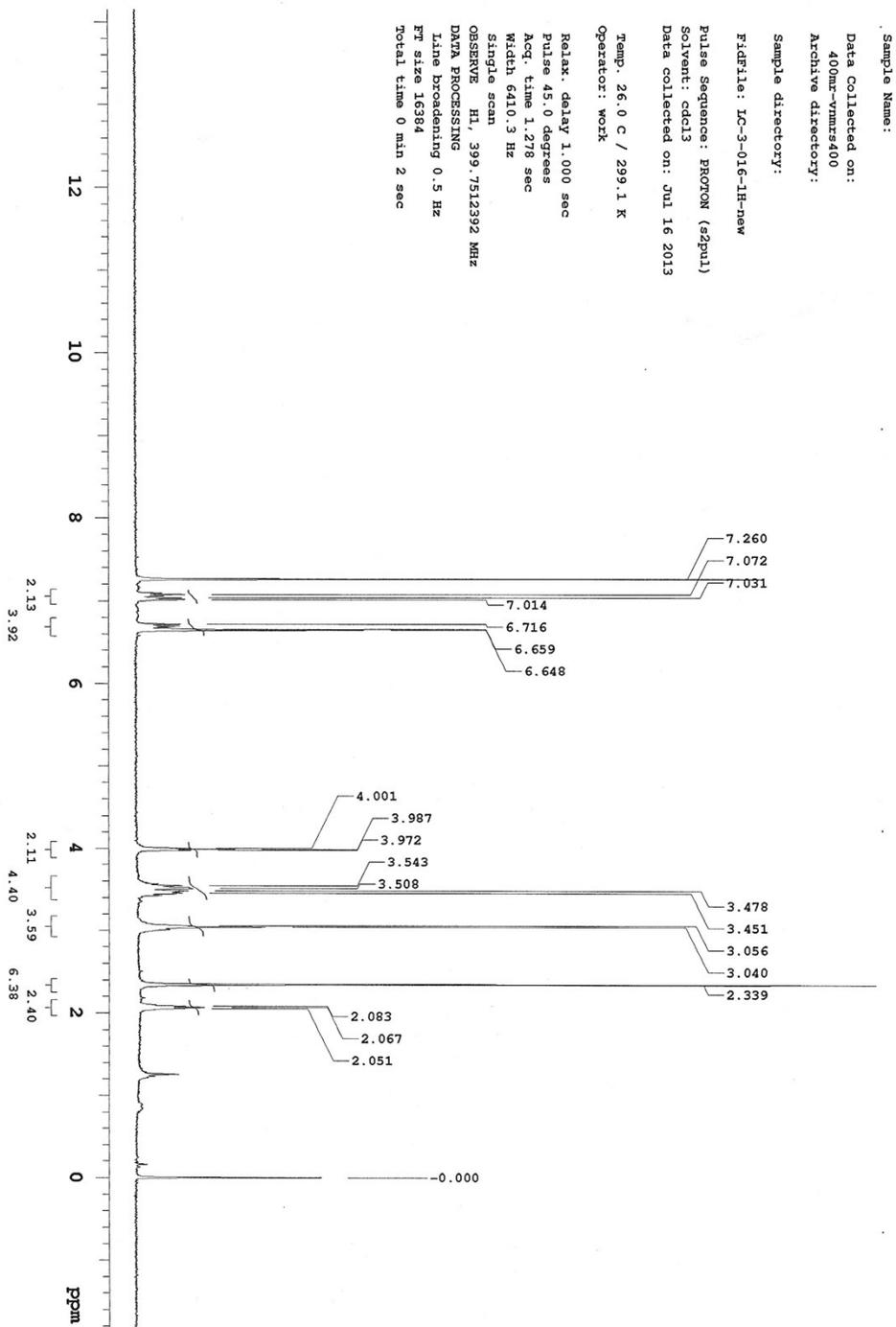
Methyl 1-(3-(4-chloro-3,5-dimethylphenoxy)propyl)-1,2,3,4-tetrahydroquinoline-3-carboxylate ( $\pm$ -10).



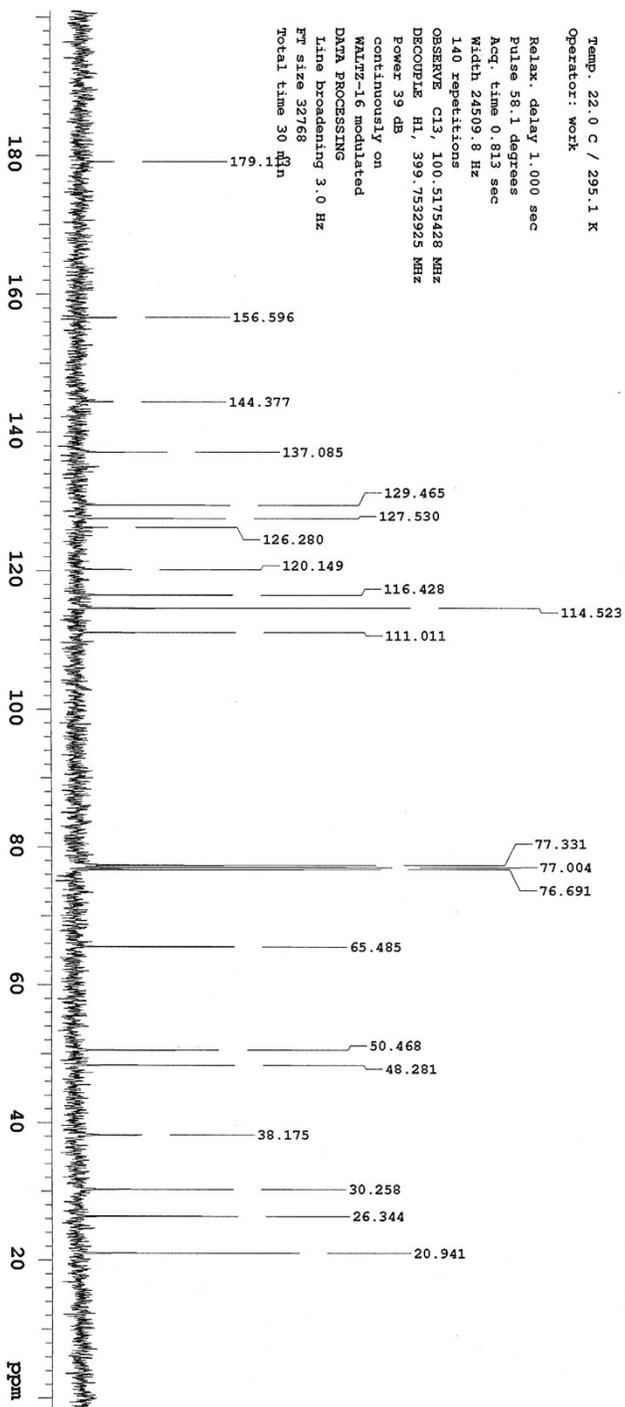
Methyl 1-(3-(4-chloro-3,5-dimethylphenoxy)propyl)-1,2,3,4-tetrahydroquinoline-3-carboxylate ( $\pm$ -10).



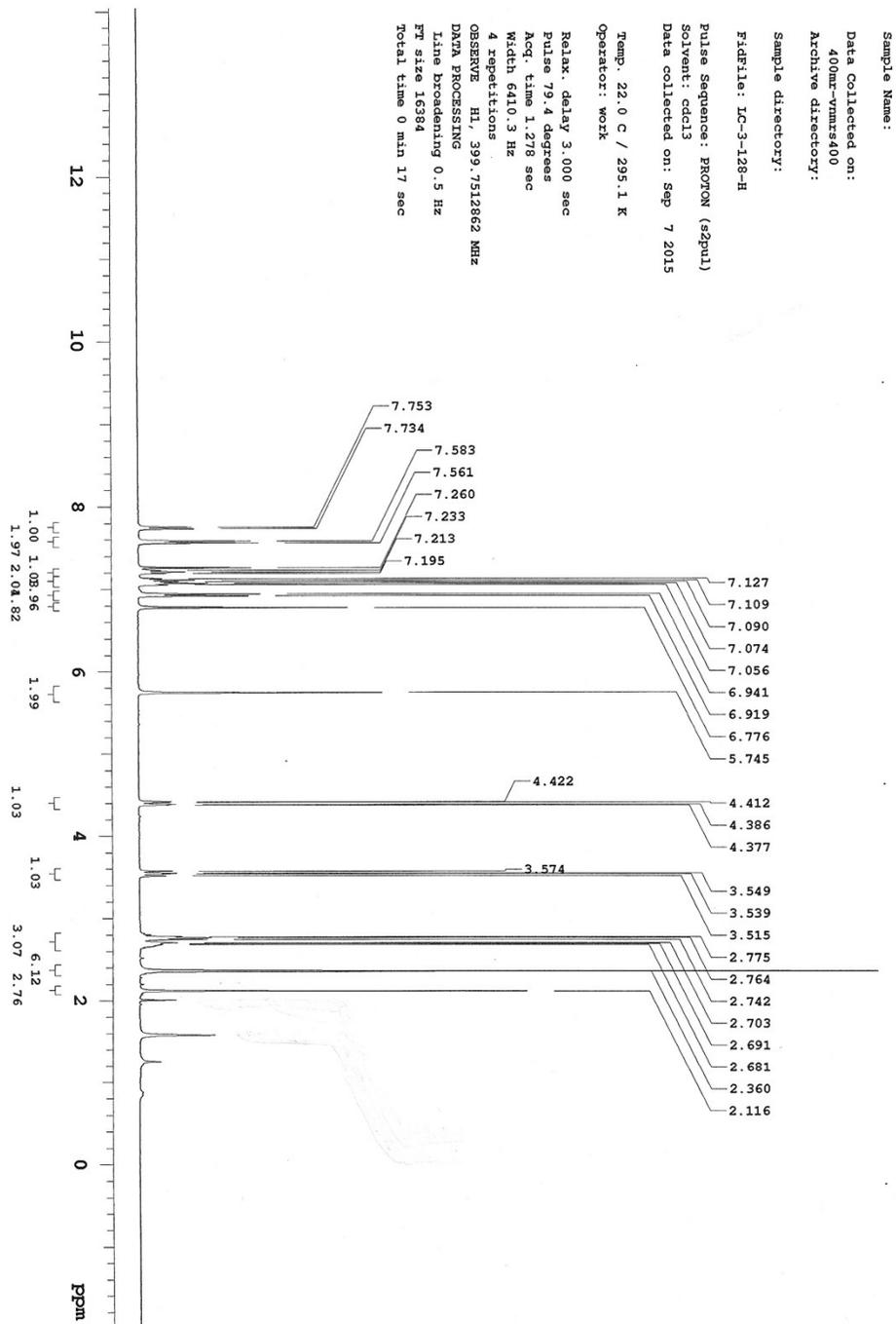
1-(3-(4-Chloro-3,5-dimethylphenoxy)propyl)-1,2,3,4-tetrahydroquinoline-3-carboxylic acid ( $\pm$ -11).



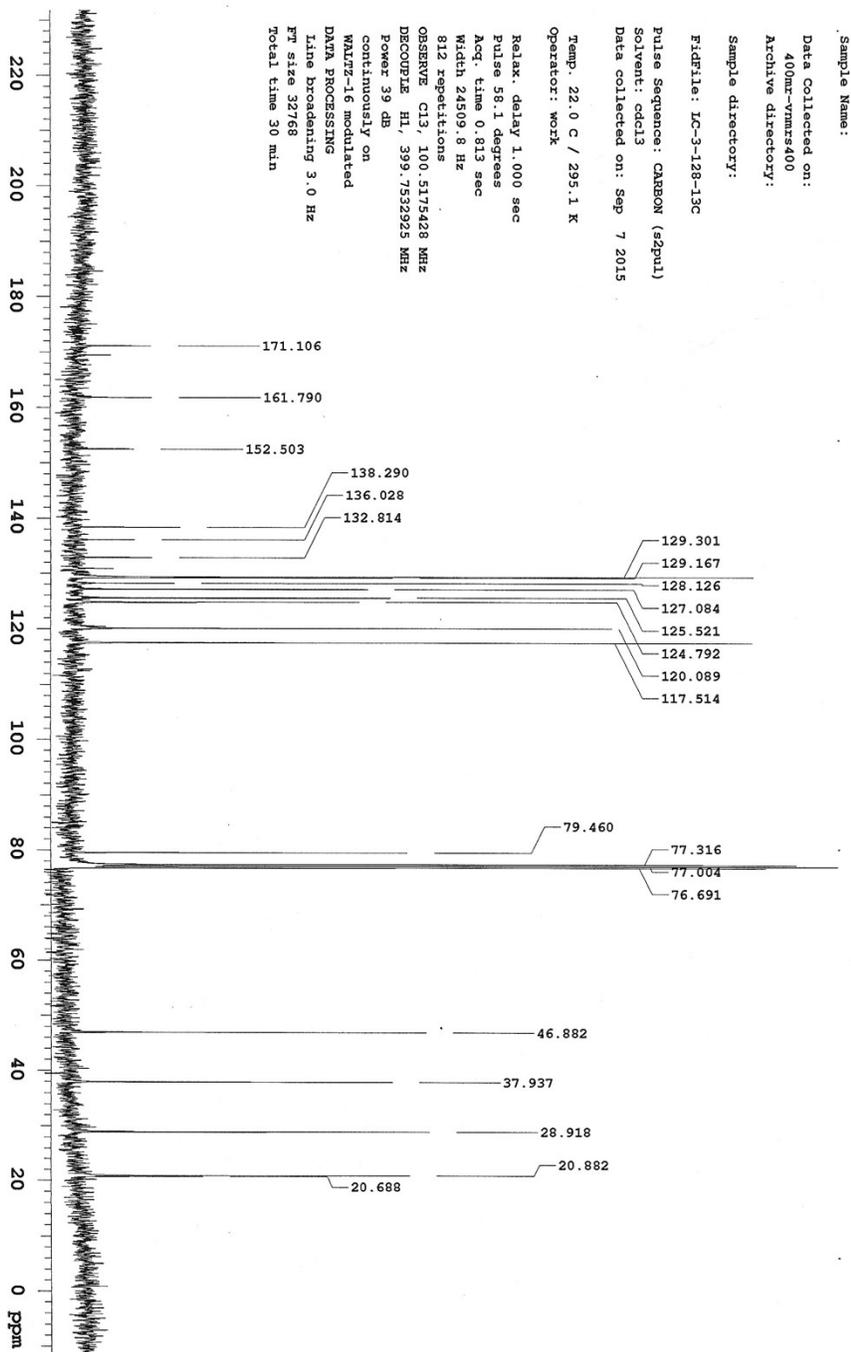
1-(3-(4-Chloro-3,5-dimethylphenoxy)propyl)-1,2,3,4-tetrahydroquinoline-3-carboxylic acid ( $\pm$ -11).



Acetoxymethyl 1-((4-(4-chloro-3,5-dimethylphenoxy)phenyl)sulfonyl)-1,2,3,4-tetrahydroquinoline-3-carboxylate ( $\pm$ -12).



Acetoxymethyl 1-((4-(4-chloro-3,5-dimethylphenoxy)phenyl)sulfonyl)-1,2,3,4-tetrahydroquinoline-3-carboxylate ( $\pm$ -12).



## HPLC Spectra

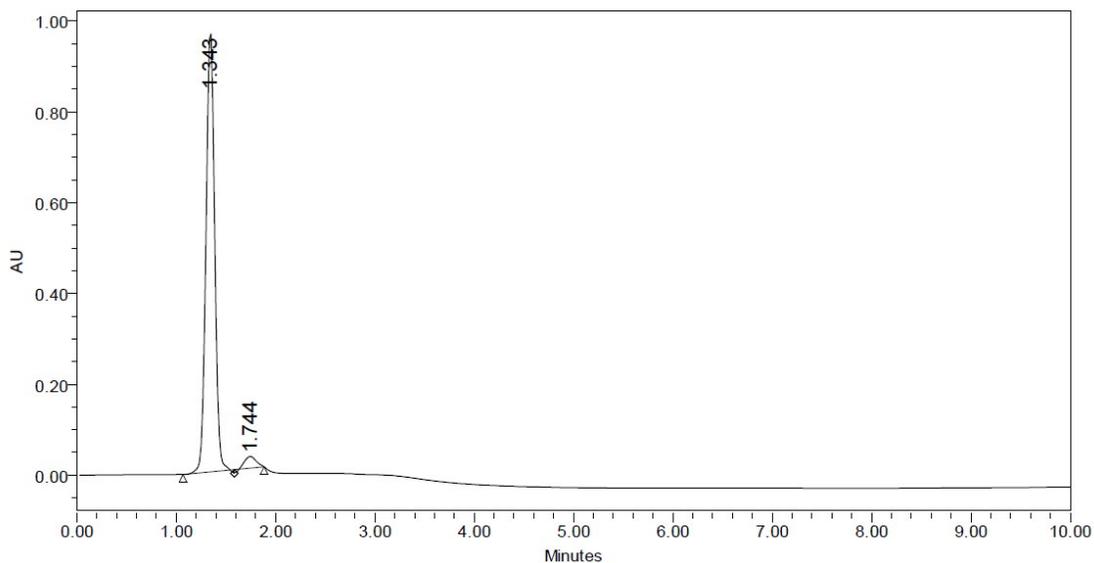
1,2,3,4-Tetrahydroquinoline-3-carboxylic acid ( $\pm$ -6).



Mcl-1

### SAMPLE INFORMATION

Sample Name:	LC-5-052	Acquired By:	System
Sample Type:	Unknown	Sample Set Name:	
Vial:	1:B,3	Acq. Method Set:	Anal_254_10min
Injection #:	1	Processing Method:	Lee_THQ_10min
Injection Volume:	25.00 ul	Channel Name:	W2489 ChA
Run Time:	10.0 Minutes	Proc. Chnl. Descr.:	W2489 ChA 254nm
Date Acquired:	9/4/2015 11:47:43 AM EDT		
Date Processed:	10/19/2015 5:56:14 PM EDT		



	RT	Area	% Area	Height
1	1.343	5915182	96.33	969569
2	1.744	225252	3.67	26026

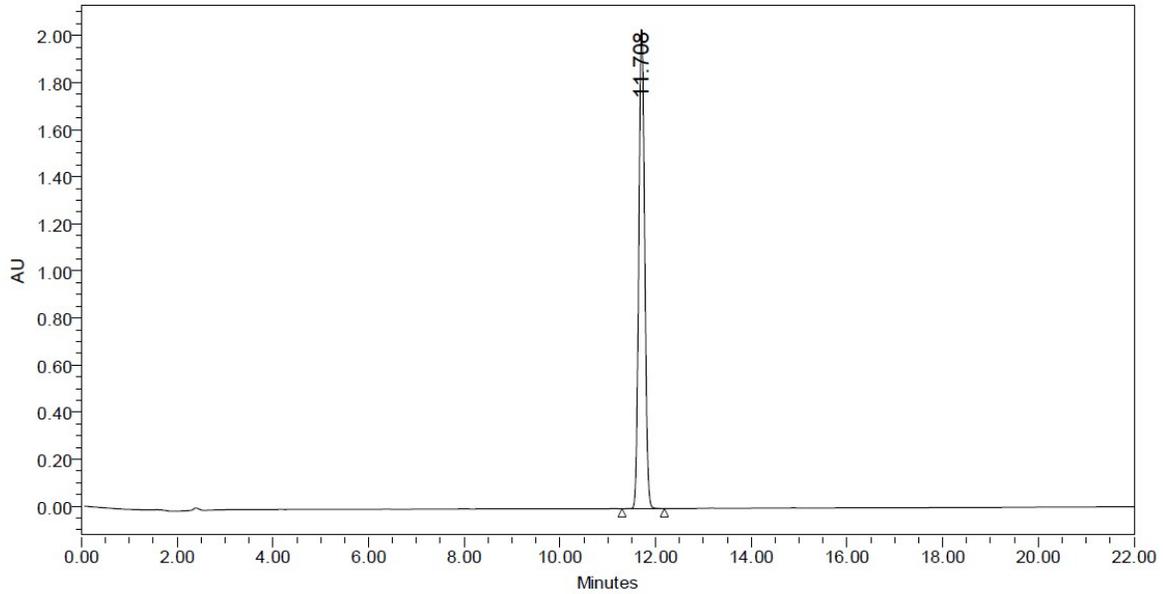
Reported by User: System  
Report Method: University of Maryland  
Report Method ID: 1270  
Page: 1 of 1

Project Name: Mcl-1  
Date Printed:  
10/19/2015  
6:05:24 PM US/Eastern

1-(Phenylsulfonyl)-1,2,3,4-tetrahydroquinoline-3-carboxylic acid( $\pm$ -8a).

SAMPLE INFORMATION

Sample Name:	SF-5-103	Acquired By:	System
Sample Type:	Unknown	Sample Set Name:	
Vial:	1:e,1	Acq. Method Set:	Anal_254_50%A_22min
Injection #:	1	Processing Method:	Lee_THQ
Injection Volume:	25.00 ul	Channel Name:	W2489 ChA
Run Time:	22.0 Minutes	Proc. Chnl. Descr.:	W2489 ChA 254nm
Date Acquired:	9/2/2015 5:39:19 PM EDT		
Date Processed:	10/19/2015 5:57:13 PM EDT		

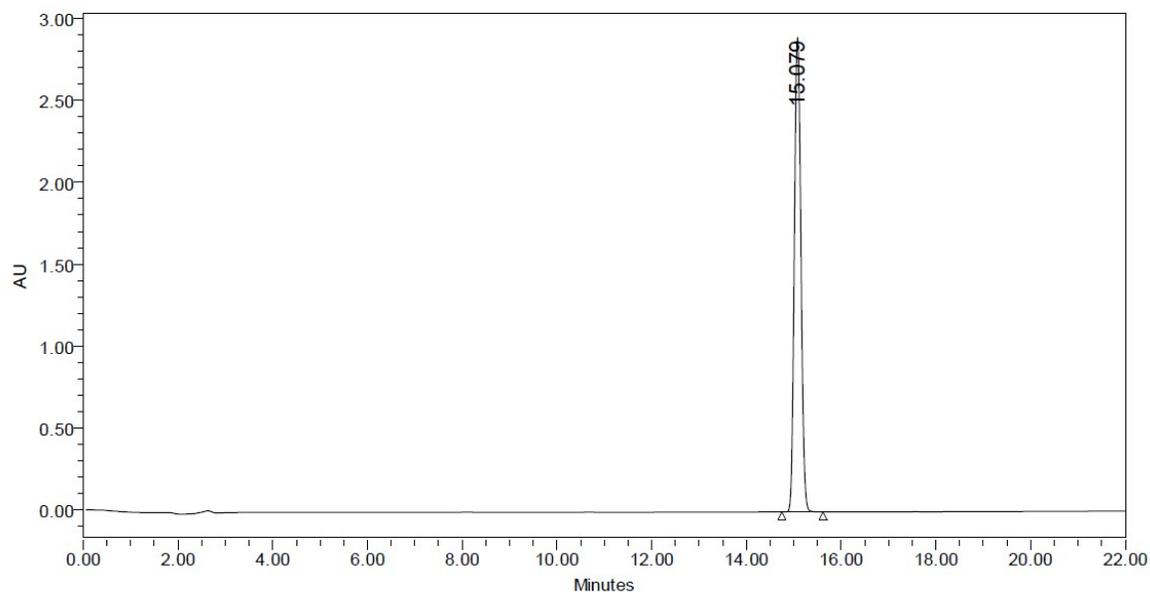


	RT	Area	% Area	Height
1	11.708	17576364	100.00	2048726

1-((4-Bromophenyl)sulfonyl)-1,2,3,4-tetrahydroquinoline-3-carboxylic acid ( $\pm$ -8b).

### SAMPLE INFORMATION

Sample Name:	SF-5-135	Acquired By:	System
Sample Type:	Unknown	Sample Set Name:	
Vial:	1:b,1	Acq. Method Set:	Anal_254_50%A_22min
Injection #:	1	Processing Method:	Lee_THQ
Injection Volume:	25.00 ul	Channel Name:	W2489 ChA
Run Time:	22.0 Minutes	Proc. Chnl. Descr.:	W2489 ChA 254nm
Date Acquired:	9/2/2015 3:08:55 PM EDT		
Date Processed:	10/19/2015 5:57:37 PM EDT		

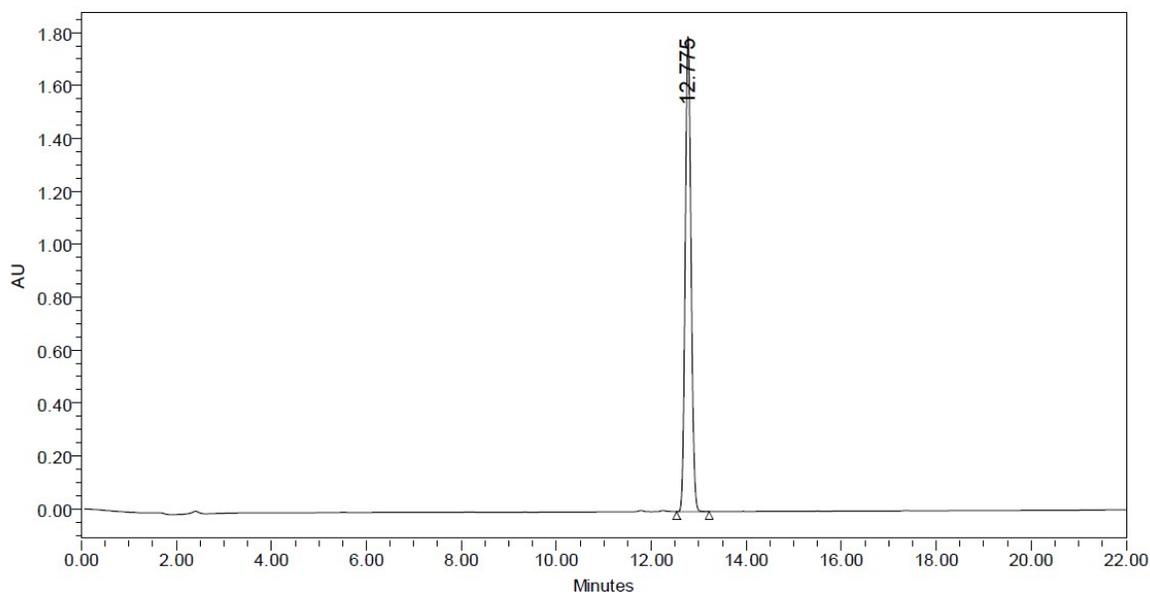


	RT	Area	% Area	Height
1	15.079	27620261	100.00	2899541

1-((4-Fluorophenyl)sulfonyl)-1,2,3,4-tetrahydroquinoline-3-carboxylic acid ( $\pm$ -8c).

### SAMPLE INFORMATION

Sample Name:	SF-5-136	Acquired By:	System
Sample Type:	Unknown	Sample Set Name:	
Vial:	1:d,1	Acq. Method Set:	Anal_254_50%A_22min
Injection #:	1	Processing Method:	Lee_THQ
Injection Volume:	25.00 ul	Channel Name:	W2489 ChA
Run Time:	22.0 Minutes	Proc. Chnl. Descr.:	W2489 ChA 254nm
Date Acquired:	9/2/2015 5:10:21 PM EDT		
Date Processed:	10/19/2015 5:54:52 PM EDT		

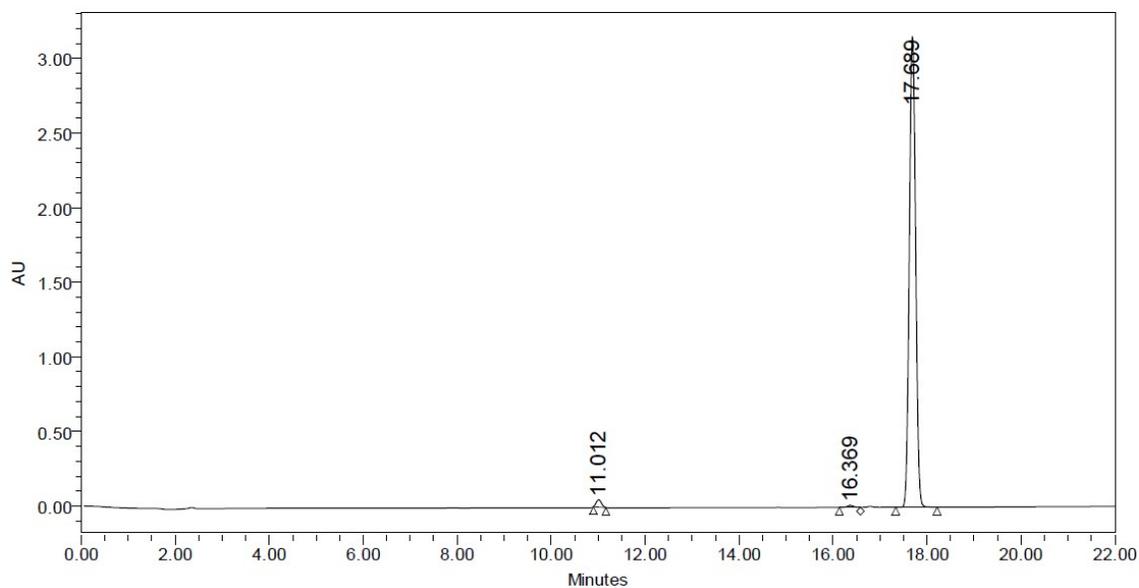


	RT	Area	% Area	Height
1	12.775	15486944	100.00	1807669

1-([1,1'-Biphenyl]-4-ylsulfonyl)-1,2,3,4-tetrahydroquinoline-3-carboxylic acid ( $\pm$ -8d).

### SAMPLE INFORMATION

Sample Name:	SF-5-133	Acquired By:	System
Sample Type:	Unknown	Sample Set Name:	
Vial:	1:f,1	Acq. Method Set:	Anal_254_50%A_22min
Injection #:	1	Processing Method:	Lee_THQ
Injection Volume:	25.00 ul	Channel Name:	W2489 ChA
Run Time:	22.0 Minutes	Proc. Chnl. Descr.:	W2489 ChA 254nm
Date Acquired:	9/2/2015 6:07:59 PM EDT		
Date Processed:	10/19/2015 5:58:39 PM EDT		

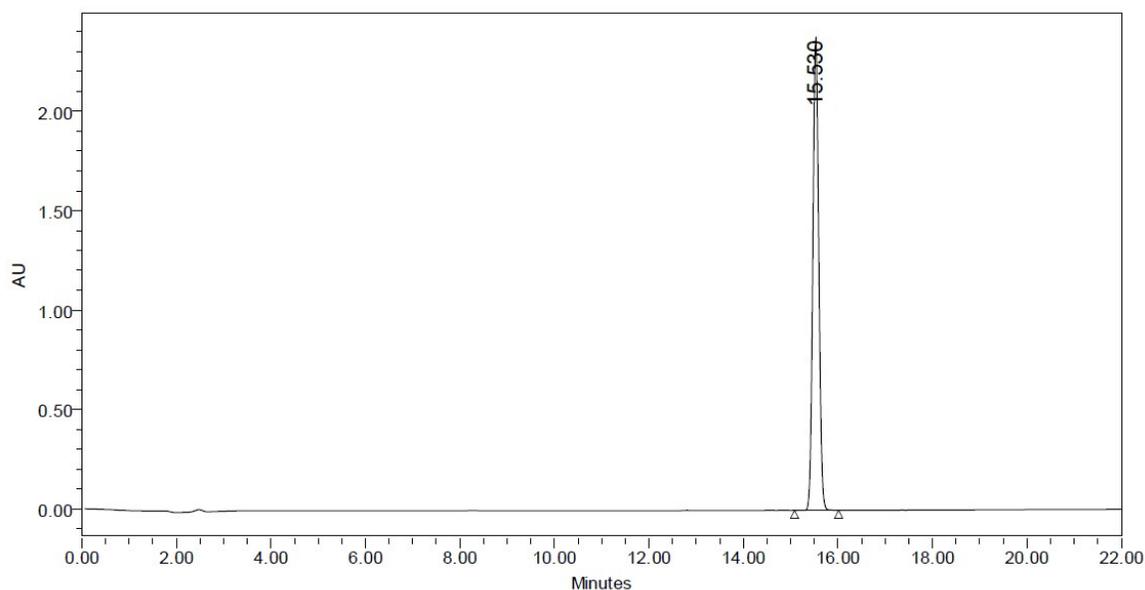


	RT	Area	% Area	Height
1	11.012	378616	1.26	49026
2	16.369	114286	0.38	12041
3	17.689	29626225	98.36	3163727

1-(Naphthalen-2-ylsulfonyl)-1,2,3,4-tetrahydroquinoline-3-carboxylic acid ( $\pm$ -8e).

### SAMPLE INFORMATION

Sample Name:	SF-5-134	Acquired By:	System
Sample Type:	Unknown	Sample Set Name:	
Vial:	1:c,1	Acq. Method Set:	Anal_254_50%A_22min
Injection #:	1	Processing Method:	Lee_THQ
Injection Volume:	25.00 ul	Channel Name:	W2489 ChA
Run Time:	22.0 Minutes	Proc. Chnl. Descr.:	W2489 ChA 254nm
Date Acquired:	9/2/2015 4:41:42 PM EDT		
Date Processed:	10/19/2015 5:59:10 PM EDT		

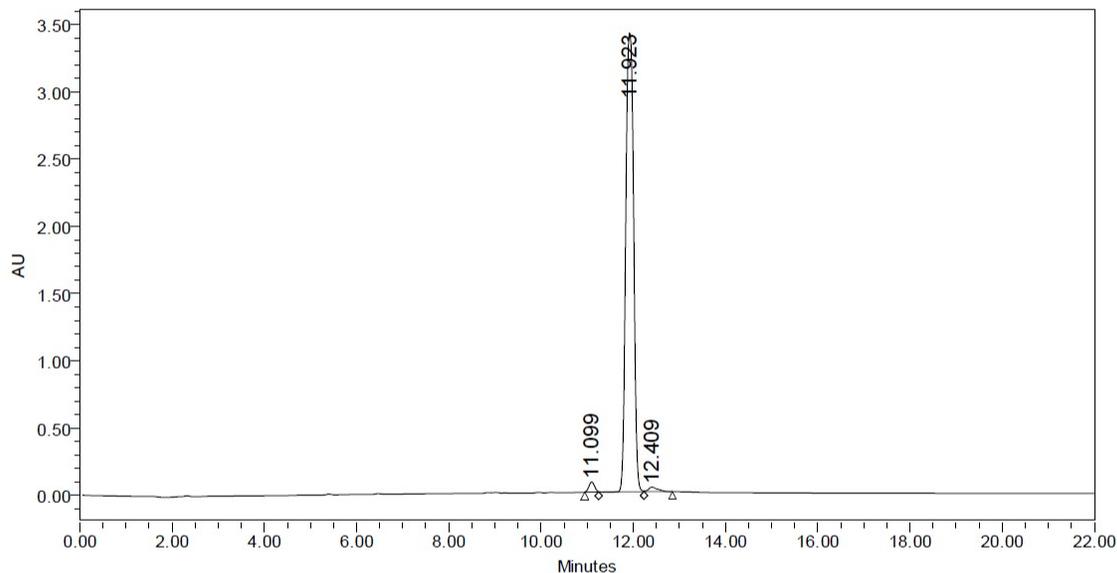


	RT	Area	% Area	Height
1	15.530	20888428	100.00	2380718

Methyl 1-((4-(4-chloro-3,5-dimethylphenoxy)phenyl)sulfonyl)-1,2,3,4-tetrahydroquinoline-3-carboxylate (±-9).

SAMPLE INFORMATION

Sample Name:	LC-3-113	Acquired By:	System
Sample Type:	Unknown	Sample Set Name:	
Vial:	1:A,2	Acq. Method Set:	Anal_254_100%B_22min
Injection #:	1	Processing Method:	Lee_THQ
Injection Volume:	25.00 ul	Channel Name:	W2489 ChA
Run Time:	22.0 Minutes	Proc. Chnl. Descr.:	W2489 ChA 254nm
Date Acquired:	9/3/2015 10:04:27 AM EDT		
Date Processed:	10/19/2015 5:59:53 PM EDT		

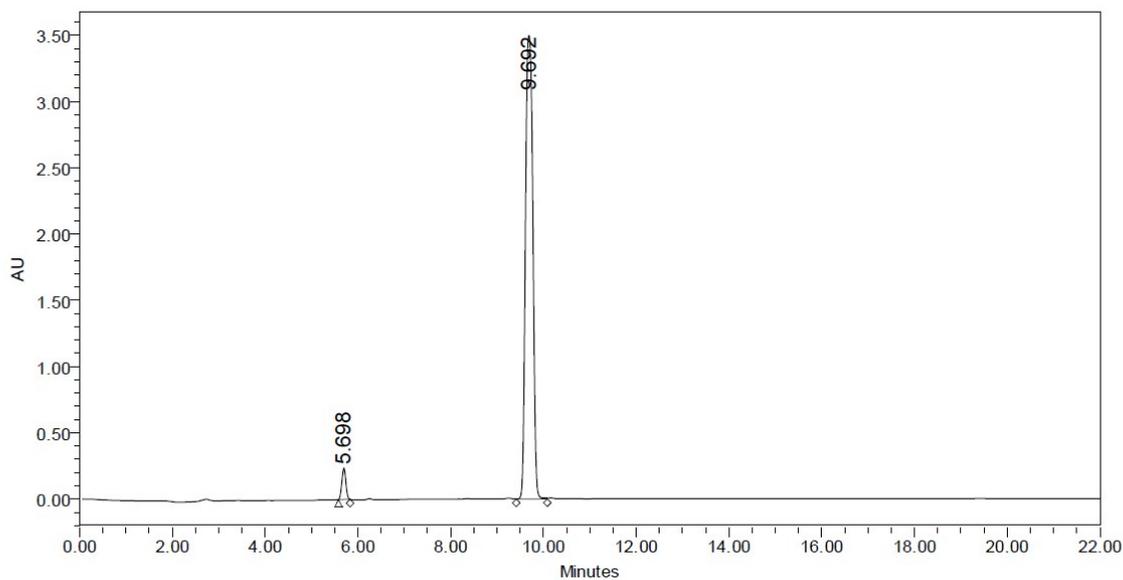


	RT	Area	% Area	Height
1	11.099	634068	1.55	74229
2	11.923	39715737	97.27	3423250
3	12.409	480640	1.18	34365

1-((4-(4-Chloro-3,5-dimethylphenoxy)phenyl)sulfonyl)-1,2,3,4-tetrahydroquinoline-3-carboxylic acid ( $\pm$ -2).

**SAMPLE INFORMATION**

Sample Name:	SF-5-141	Acquired By:	System
Sample Type:	Unknown	Sample Set Name:	
Vial:	1:a,1	Acq. Method Set:	Anal_254_100%B_22min
Injection #:	1	Processing Method:	Lee_THQ
Injection Volume:	25.00 ul	Channel Name:	W2489 ChA
Run Time:	22.0 Minutes	Proc. Chnl. Descr.:	W2489 ChA 254nm
Date Acquired:	9/2/2015 2:40:15 PM EDT		
Date Processed:	10/19/2015 6:01:21 PM EDT		

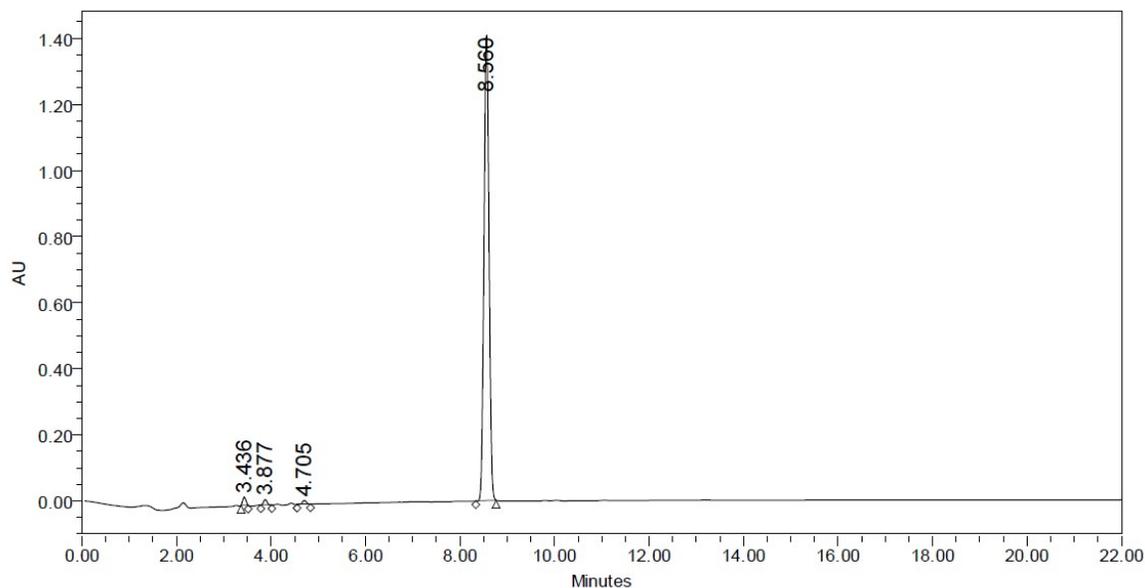


	RT	Area	% Area	Height
1	5.698	1397944	3.54	235453
2	9.692	38142368	96.46	3513657

1-(3-(4-Chloro-3,5-dimethylphenoxy)propyl)-1,2,3,4-tetrahydroquinoline-3-carboxylic acid ( $\pm$ -11).

### SAMPLE INFORMATION

Sample Name:	LC-3-016	Acquired By:	System
Sample Type:	Unknown	Sample Set Name:	
Vial:	1:B,2	Acq. Method Set:	Anal_254_100%B_22min
Injection #:	1	Processing Method:	Lee_THQ
Injection Volume:	25.00 ul	Channel Name:	W2489 ChA
Run Time:	22.0 Minutes	Proc. Chnl. Descr.:	W2489 ChA 254nm
Date Acquired:	9/3/2015 2:18:03 PM EDT		
Date Processed:	10/19/2015 6:02:22 PM EDT		

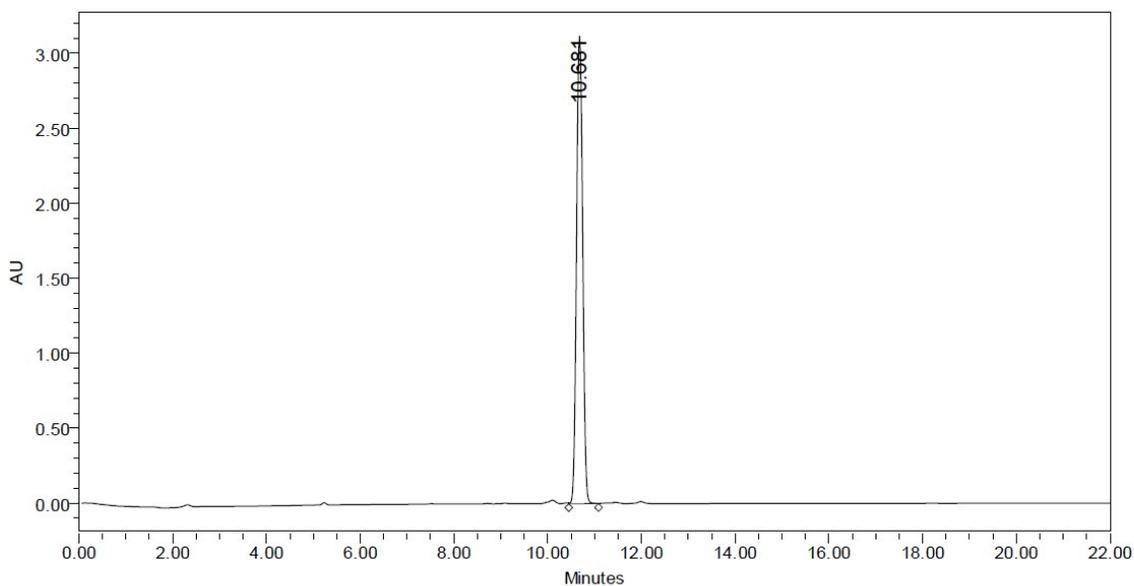


	RT	Area	% Area	Height
1	3.436	111060	1.04	23533
2	3.877	81294	0.76	15446
3	4.705	61485	0.58	10659
4	8.560	10427155	97.62	1416563

Acetoxymethyl 1-((4-(4-chloro-3,5-dimethylphenoxy)phenyl)sulfonyl)-1,2,3,4-tetrahydroquinoline-3-carboxylate ( $\pm$ -12).

### SAMPLE INFORMATION

Sample Name:	LC-3-128	Acquired By:	System
Sample Type:	Unknown	Sample Set Name:	
Vial:	1:D,2	Acq. Method Set:	Anal_254_100%B_22min
Injection #:	1	Processing Method:	Lee_THQ
Injection Volume:	25.00 ul	Channel Name:	W2489 ChA
Run Time:	22.0 Minutes	Proc. Chnl. Descr.:	W2489 ChA 254nm
Date Acquired:	9/2/2015 8:02:41 PM EDT		
Date Processed:	10/19/2015 6:03:03 PM EDT		



	RT	Area	% Area	Height
1	10.681	28190717	100.00	3118478