Supporting Information

Direct Copper-Catalyzed Amination of sp^2 C-H Bonds

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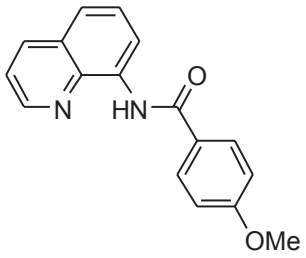
GENERAL CONSIDERATIONS. Reactions were performed without special precautions to exclude air or moisture in 1-dram screw-cap vials equipped with Teflon® liners and a stir bar or using a 10 ml Kontes flask. Column chromatography was performed on 60 Å silica gel (Dynamic Adsorbents Inc). Purification by preparative HPLC was performed on a Shimadzu Prominence LC (LC-20AB) equipped with a SPD-20A UV-Vis detector and a Varian Dynamax (250 mm × 21.4 mm) column. ^{1}H, ^{13}C and ^{19}F NMR spectra were recorded on JEOL ECX-400 and JEOL ECX-500 spectrometers using TMS or residual solvent peak as a standard. Compounds for HRMS were analyzed by positive mode electrospray ionization (ESI) using Agilent 6530 QTOF mass spectrometer at the Mass Spectrometry Facility (MSF) of the Department of Chemistry & Biochemistry, University of Texas at Austin. IR-spectra were obtained using a Perkin Elmer Spectrum 100 FT-IR spectrometer. Preparative thin layer chromatography was performed on Analtech TLC plates (20 cm × 20 cm, 20 microns).

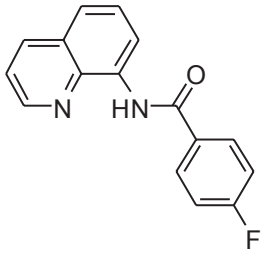
MATERIALS. The following starting materials were obtained from commercial sources and were used without further purification: 8-aminoquinoline, 4-fluorobenzoyl chloride, 4-methoxybenzoyl chloride, 4-*t*-butylbenzoyl chloride, monomethyl terephthalate, 3-methoxybenzoic acid, 2-trifluoromethylbenzoyl chloride, 2-naphthalenecarboxylic acid, 2-methylbenzoyl chloride, 2-methylnicotinic acid, 2-methyl-3-furancarboxylic acid, piconilic acid, ethyl chloroformate, cumylamine, 1-(4-fluorophenyl)-1-methylethylamine, pyrrolidine, cyclohexylamine, cyclooctylamine, N-methyl benzylamine, N-methyl propylamine, ethyl isonipecotate, 4-cyanopiperidine, 4-piperidone ethylene ketal, tert-butyl piperidin-4-ylcarbamate.

SYNTHESIS OF AMIDES

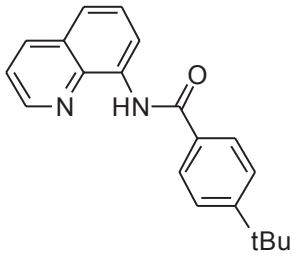


***N*-(4-Methoxybenzoyl)-8-aminoquinoline**: 8-Aminoquinoline (2.17 g, 15 mmol) and triethylamine (2.8 mL, 20 mmol) were dissolved in anhydrous CH_2Cl_2 (40 mL) in a 100 ml round-bottom flask followed by dropwise addition of 4-methoxybenzoyl chloride (3.4 g, 20 mmol) through syringe. The reaction mixture was stirred overnight. After completion, the reaction was diluted with CH_2Cl_2 (50 mL), washed by aqueous HCl (15 mL, 1N), $NaHCO_3$ (15 mL of saturated aqueous solution), brine (25 mL), and dried over Na_2SO_4. The organic solvent was removed by evaporation. Purification by column chromatography in

toluene/ethyl acetate (30:1) afforded 3.86 g of pure amide (92%) as a white solid. This compound is known.[1] ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 10.69 (*s*, 1H) 8.93 (*dd*, *J* = 7.4 Hz, *J* = 1.1 Hz, 1H) 8.85 (*dd*, *J* = 4.0 Hz, *J* = 1.7 Hz, 1H) 8.18 (*dd*, *J* = 8.6 Hz, *J* = 1.7 Hz, 1H) 8.09–8.04 (*m*, 2H) 7.59 (*t*, *J* = 8.0, 1H) 7.55–7.51 (*m*, 1H) 7.47 (*dd*, *J* = 4.6 Hz, *J* = 8.6 Hz, 1H) 7.07–7.01 (*m*, 2H) 3.89 (*s*, 3H).

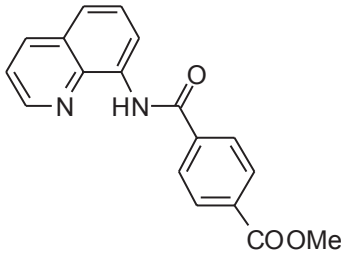


***N*-(4-Fluorobenzoyl)-8-aminoquinoline**: 8-Aminoquinoline (1.44 g, 10 mmol) and triethylamine (1.8 mL, 13 mmol) were dissolved in anhydrous CH_2Cl_2 (30 mL) in a 50 ml round-bottom flask followed by dropwise addition of 4-fluorobenzoyl chloride (2.06 g, 13.2 mmol) through syringe. The reaction mixture was stirred overnight. After completion, the reaction was diluted with CH_2Cl_2 (25 mL), washed by aqueous HCl (15 mL, 1N), $NaHCO_3$ (15 mL of saturated aqueous solution), brine (25 mL), and dried over Na_2SO_4. The organic solvent was removed by evaporation. Purification by column chromatography in toluene/ethyl acetate (20:1) afforded 2.56 g of pure amide (96%) as a light yellow solid. This compound is known.[1] ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 10.86 (*s*, 1H) 8.87 (*d*, *J* = 8.0 Hz, 1H) 8.86 – 8.81 (*m*, 1H) 8.20–8.14 (*m*, 1H) 8.12–8.05 (*m*, 2H) 7.61–7.55 (*m*, 1H) 7.55–7.50 (*m*, 1H) 7.49–7.43 (*m*, 1H) 7.24–7.18 (*m*, 2H).

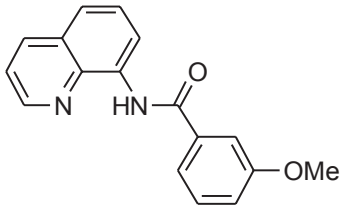


***N*-(4-*t*-Butylbenzoyl)-8-aminoquinoline**: 8-Aminoquinoline (1.44 g, 10 mmol) and triethylamine (1.8 mL, 13 mmol) were dissolved in anhydrous CH_2Cl_2 (30 mL) in a 50 ml round-bottom flask followed by dropwise addition of 4-*t*-butylbenzoyl chloride (2.56 g, 13 mmol) through syringe. The reaction mixture was stirred overnight. After completion, the reaction was diluted with CH_2Cl_2 (25 mL), washed by aqueous HCl (15 mL, 1N), $NaHCO_3$ (15 mL of saturated aqueous solution), brine (25 mL), and dried over Na_2SO_4. The organic solvent was removed by evaporation. Purification by column chromatography in toluene/ethyl acetate (50:1 to 40:1) afforded 3.01 g of pure amide (99%) as a white solid. This compound

is known.[1] ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 10.73 (*s*, 1H) 8.94 (*dd*, *J* = 7.8 Hz, *J* = 1.4 Hz, 1H) 8.85–8.81 (*m*, 1H) 8.19–8.13 (*m*, 1H) 8.06–8.00 (*m*, 2H) 7.61–7.49 (*m*, 4H) 7.48–7.43 (*m*, 1H) 1.38 (*s*, 9H).

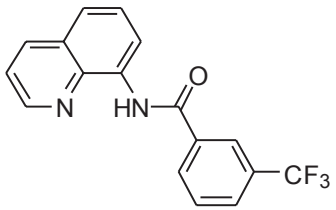


Methyl 4-(quinolin-8-ylcarbamoyl)benzoate: 8-Aminoquinoline (1.44 g, 10 mmol) and triethylamine (1.8 mL, 13 mmol) were dissolved in anhydrous CH_2Cl_2 (30 mL) in a 50 ml round-bottom flask followed by dropwise addition of the acid chloride solution in CH_2Cl_2 (10 mL) through cannula. The acid chloride was prepared from monomethyl terephthalate (2.34 g, 13 mmol).[2] The reaction mixture was stirred overnight. After completion, the reaction was diluted with CH_2Cl_2 (25 mL), washed by aqueous HCl (15 mL, 1N), $NaHCO_3$ (15 mL of saturated aqueous solution), brine (25 mL), and dried over Na_2SO_4. The organic solvent was removed by evaporation. Purification by column chromatography in toluene/ethyl acetate (30:1) afforded 2.56 g of pure amide (84%) as a light yellow solid. This compound is known.[1] ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 10.78 (*s*, 1H) 8.92 (*dd*, *J* = 6.9 Hz, *J* = 1.4 Hz, 1H) 8.85 (*dd*, *J* = 4.0 Hz, *J* = 1.8 Hz, 1H) 8.24–8.10 (*m*, 5H) 7.64–7.53 (*m*, 2H) 7.48 (*dd*, *J* = 4.1 Hz, *J* = 8.3 Hz, 1H) 3.97 (*s*, 3H).

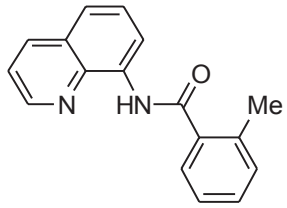


***N*-(3-Methoxybenzoyl)-8-aminoquinoline**: 8-Aminoquinoline (2.17 g, 15 mmol) and triethyl amine (2.8 mL, 20 mmol) were dissolved in anhydrous CH_2Cl_2 (30 mL) in a 100 ml round-bottom flask followed by dropwise addition of 3-methoxybezoyl chloride solution in CH_2Cl_2 (10 mL) through cannula. The acid chloride was prepared from 3-methoxybenzoic acid (3.04 g, 20 mmol).[2] The reaction mixture was stirred overnight. After completion, the reaction was diluted with CH_2Cl_2 (25 mL), washed by aqueous HCl (15 mL, 1N), $NaHCO_3$ (15 mL of saturated aqueous solution), brine (25 mL), and dried over Na_2SO_4. The organic solvent was removed by evaporation. Purification by column chromatography in toluene/ethyl acetate (30:1) afforded 3.86 g of pure amide (92%) as a white solid. This compound is known.[1] ^{1}H NMR (MHz, $CDCl_3$, ppm) δ 10.74 (*s*, 1H) 8.93 (*dd*, *J* = 7.5 Hz, *J* = 1.2 Hz, 1H) 8.85 (*dd*, *J* = 4.0 Hz, *J* = 1.7 Hz,

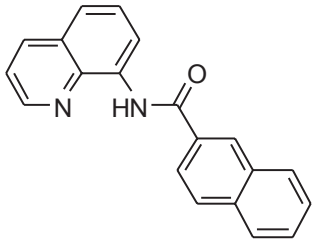
1H) 8.19 (*dd*, *J* = 1.7 Hz, *J* = 8.0 Hz, 1H) 7.68–7.52 (*m*, 4H) 7.51–7.42 (*m*, 2H) 7.15-7.10 (*m*, 1H) 3.92 (*s*, 3H).



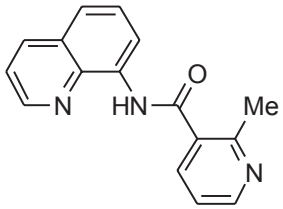
***N*-(3-Trifluoromethylbenzoyl)-8-aminoquinoline**: 8-Aminoquinoline (1.44 g, 10 mmol) and triethyl amine (1.8 mL, 13 mmol) were dissolved in anhydrous CH_2Cl_2 (30 mL) in a 50 ml round-bottom flask followed by dropwise addition of 2-trifluoromethylbenzoyl chloride (2.68 g, 12.8 mmol) through syringe. The reaction mixture was stirred overnight. After completion, the reaction was diluted with CH_2Cl_2 (25 mL), washed by aqueous HCl (15 mL, 1N), $NaHCO_3$ (15 mL of saturated aqueous solution), brine (25 mL), and dried over Na_2SO_4. The organic solvent was removed by evaporation. Purification by column chromatography in toluene/ethyl acetate (20:1) afforded 3.05 g of pure amide (96%) as a white solid. This compound is known.[3] ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 10.83 (*s*, 1H) 8.95–8.87 (*m*, 2H) 8.37 (*s*, 1H) 8.33–8.25 (*m*, 2H) 7.87–7.81 (*m*, 1H) 7.73–7.67 (*m*, 1H) 7.67–7.60 (*m*, 2H) 7.56 (*dd*, *J* = 8.1 Hz, *J* = 4.1 Hz, 1H).



***N*-(2-Methylbenzoyl)-8-aminoquinoline**: 8-Aminoquinoline (1.44 g, 10 mmol) and triethyl amine (1.8 mL, 13 mmol) were dissolved in anhydrous CH_2Cl_2 (30 mL) in a 50 ml round-bottom flask followed by dropwise addition of 2-methylbenzoyl chloride (2.04 g, 13.2 mmol) through syringe. The reaction mixture was stirred overnight. After completion, the reaction was diluted with CH_2Cl_2 (25 mL), washed by aqueous HCl (15 mL, 1N), $NaHCO_3$ (15 mL of saturated aqueous solution), brine (25 mL), and dried over Na_2SO_4. The organic solvent was removed by evaporation. Purification by column chromatography in toluene/ethyl acetate (40:1) afforded 2.78 g of pure amide (87%) as a white solid. This compound is known.[1] ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 10.21 (*s*, 1H) 8.99–8.91 (*m*, 1H) 8.78 (*dd*, *J* = 4.1 Hz, *J* = 1.8 Hz, 1H) 8.19 (*dd*, *J* = 8.2 Hz, *J* = 1.4 Hz, 1H) 7.66–7.72 (*m*, 1H) 7.53–7.64 (*m*, 2H) 7.46 (*dd*, *J* = 8.2 Hz, *J* = 4.1 Hz, 1H) 7.44–7.37 (*m*, 1H) 7.36–7.29 (*m*, 2H) 2.61 (*s*, 3H).

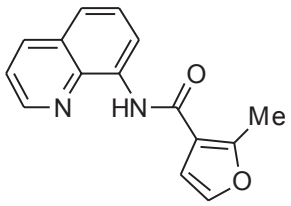


***N*-(2-Naphthalenecarbonyl)-8-aminoquinoline**: 8-Aminoquinoline (1.44 g, 10 mmol) and triethylamine (1.8 mL, 13 mmol) were dissolved in anhydrous CH_2Cl_2 (30 mL) in a 50 ml round-bottom flask followed by dropwise addition of the acid chloride solution in CH_2Cl_2 (10 mL) through cannula. The acid chloride was prepared from 2-naphthalenecarboxylic acid (2.24 g, 13 mmol).[2] The reaction mixture was stirred overnight. After completion, the reaction was diluted with CH_2Cl_2 (25 mL), washed by aqueous HCl (15 mL, 1N), $NaHCO_3$ (15 mL of saturated aqueous solution), brine (25 mL), and dried over Na_2SO_4. The organic solvent was removed by evaporation. Purification by column chromatography in toluene/ethyl acetate (30:1) afforded 2.14 g of pure amide (72%) as a light yellow solid. This compound is known.[3] ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ10.95–10.85 (*s*, 1H) 9.00 (*dd*, *J* = 7.4 Hz, *J* = 1.2 Hz, 1H) 8.89 (*dd*, *J* = 4.0 Hz, *J* = 1.7 Hz, 1H) 8.61 (*s*, 1H), 8.21 (*dd*, *J* = 8.0 Hz, *J* = 1.7 Hz, 1H) 8.14 (*dd*, *J* = 8.6 Hz, *J* = 1.7 Hz, 1H) 8.07–8.04 (*m*, 1H) 8.00 (*d*, *J* = 8.6 Hz, 1H) 7.95–7.91 (*m*, 1H) 7.65–7.55 (*m*, 4H) 7.50 (*dd*, *J* = 4.0 Hz, *J* = 8.0 Hz, 1H).

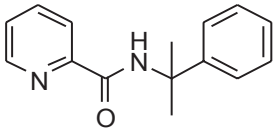


***N*-(2-methylnicotinoyl)-8-aminoquinoline**: 8-Aminoquinoline (1.44 g, 10 mmol), 2-methylnicotinic acid (2.74 g, 20 mmol), EDC (2.10 g, 11 mmol), and DMAP (2.44 g, 20 mmol) were placed in a 100 mL round bottom flask. Anhydrous CH_2Cl_2 (30 mL) was added at room temperature. Reaction mixture was allowed to stir for 48 hours. Reaction mixture was dry-sorbed on the silica gel and purified using column chromatography using hexanes/ethyl acetate (1:1 to 1:5) affording product as a tan solid (656 mg, 25%). R_f = 0.54 (SiO_2, toluene/EtOAc, 1:3), mp 138–140 °C (from hexanes/EtOAc). ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 10.31–10.199 (*s*, 1H) 8.95–8.90 (*m*, 1H) 8.79 (*dd*, *J* = 4.0 Hz, *J* = 1.7 Hz, 1H) 8.65 (*dd*, *J* = 4.6 Hz, *J* = 1.7 Hz, 1H) 8.21 (*dd*, *J* = 8.6 Hz, *J* = 1.7 Hz, 1H) 7.98 (*dd*, *J* = 7.6 Hz, *J* = 1.7 Hz, 1H) 7.64–7.57 (*m*, 2H) 7.48 (*dd*, *J* = 8.6 Hz, *J* = 4.6 Hz, 1H) 7.29 (*dd*, *J* = 7.5 Hz, *J* = 4.6 Hz, 1H) 2.85 (*s*, 3H) . ^{13}C NMR (125 MHz, $CDCl_3$, ppm) δ 166.9, 157.0, 150.9, 148.7, 138.8, 136.8, 135.5, 134.6, 132.3,

128.3, 127.7, 122.5, 122.1, 121.3, 117.0, 23.8. FT-IR (neat, cm^{-1}) υ 3352, 1678, 1533, 1490, 1430. HRMS (ESI+): Calculated for $C_{16}H_{13}N_3O$ $[M]^+$ 263.1059 Found 263.1061.

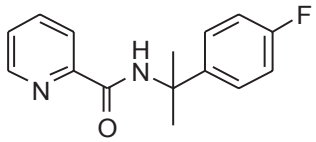


***N*-(2-Methyl-3-furanoyl)-8-aminoquinoline**: 8-Aminoquinoline (1.44 g, 10 mmol), 2-methyl-3-furancarboxylic acid (2.52 g, 20 mmol), EDC (2.10 g, 11 mmol), and DMAP (2.44 g, 20 mmol) were placed in a 100 mL round bottom flask. Anhydrous CH_2Cl_2 (30 mL) was added at room temperature. Reaction mixture was allowed to stir for 48 hours. Reaction mixture was dry-sorbed on the silica gel and purified using column chromatography using toluene/ethyl acetate (30:1) affording product as a white solid (1.46 g, 58%). R_f = 0.54 (SiO_2, hexanes/EtOAc, 3:1), mp 92–94 °C (from hexanes/EtOAc). ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 10.36–10.21 (*s*, 1H) 8.86 (*dd*, *J* = 7.4 Hz, *J* = 1.1 Hz, 1H) 8.82 (*dd*, *J* = 4.0 Hz, *J* = 1.7 Hz, 1H) 8.16 (*dd*, *J* = 8.6 Hz, *J* = 1.7 Hz, 1H) 7.59–7.53 (*m*, 1H) 7.53–7.48 (*m*, 1H) 7.45 (*dd*, *J* = 8.0 Hz, *J* = 4.0 Hz, 1H) 7.35 (*d*, *J* = 2.3 Hz, 1H) 6.82 (*d*, *J* = 2.3 Hz, 1H) 2.74 (*s*, 3H). ^{13}C NMR (125 MHz, $CDCl_3$, ppm) δ 162.4, 157.9, 148.5, 140.8, 138.9, 136.7, 135.0, 128.3, 127.8, 122.0, 121.7, 117.0, 116.5, 109.2, 14.1. FT-IR (neat, cm^{-1}) υ 3352, 1661, 1534, 1520, 1492. HRMS (ESI+): Calculated for $C_{15}H_{12}N_2O_2$ $[M]^+$ 252.0899, Found 252.0901.



***N*-(1-Methyl-1-phenylethyl)picolinamide**: Picolinic acid (2.15 g, 17.5 mmol) and triethylamine (5 mL, 35 mmol) were dissolved in CH_2Cl_2 (40 mL) in a 100 mL round-bottom flask. The resulting mixture was cooled to 0 °C followed by dropwise addition of ethyl chloroformate (1.7 mL, 17.5 mmol). The solution was stirred for 30 minutes followed by dropwise addition of cumylamine (1.36 g, 10 mmol) via syringe. The suspension was stirred for 1 hour. The reaction was warmed up to room temperature and stirred for another 24 hours. After completion, water (50 ml) was added to the reaction mixture and the layers were separated. The aqueous layer was extracted by CH_2Cl_2 (2 x 25 mL). The combined organic layers were dried over $MgSO_4$ and concentrated to remove the solvent. Purification by column choromatography in hexanes/ethyl acetate (2:1) gave 2.11 g of the desired amide (88%) as a colorless oil. This compound is known.[1] ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.58–8.53(*m*, 1H) 8.42–8.53 (*m*, 1H) 8.14 (*d*, *J* = 7.8 Hz,

1H) 7.83 (*td*, J_t = 7.8 Hz, J_d = 1.8 Hz, 1H) 7.50–7.45 (*m*, 2H) 7.44–7.39 (*m*, 1H) 7.37–7.30 (*m*, 2H) 7.27–7.21 (*m*, 1H) 1.85 (*s*, 6H).



***N*-(1-Methyl-1-(4-fluorophenyl)ethyl)picolinamide:** Picolinic acid (1.23 g, 10 mmol) and triethylamine (3 mL, 20 mmol) were placed in a 50 mL flask, followed addition of dry CH_2Cl_2 (30 mL). The resulting mixture was cooled to 0 °C followed by dropwise addition of ethyl chloroformate (1.14 g, 10 mmol). The solution was stirred for 30 minutes at 0 °C. After that, 1-(4-fluorophenyl)-1-methylethylamine (1.0 g, 6.5 mmol) was added in one portion via syringe and the suspension was allowed to warm up to the room temperature and stirred overnight. Reaction mixture was dry-absorbed on the silica gel and subjected to the column chromatography first eluting with pure CH_2Cl_2 and then with mixture of hexanes/EtOAc (9:1) affording 1.66 g (98%) of the product as a yellowish thick oil. This compound is known.[1] ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 8.57 – 8.52 (*m*, 1H), 8.46 (*br s*, 1H), 8.12 (*d*, *J* = 8.0 Hz, 1H), 8.85 – 7.78 (*m*, 1H), 7.46 – 7.36 (*m*, 3H), 7.03 – 6.96 (*m*, 2H), 1.82 (*s*, 6H).

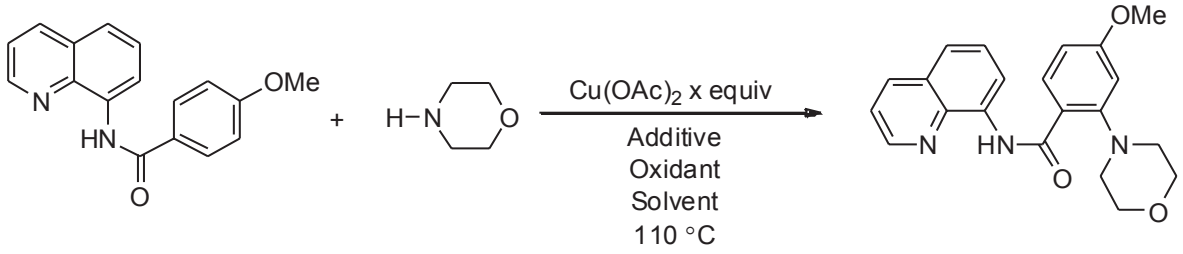
OPTIMIZATION OF REACTION CONDITIONS

General procedure for reactions without additives **(entries 1,2 table S1)**: a 1-dram vial equipped with a stir bar was charged with *N*-(4-methoxybenzoyl)-8-aminoquinoline (70 mg, 0.25 mmol, 1 equiv), $Cu(OAc)_2$, NMP (1 mL) and morpholine (0.05 mL, 0.57 mmol, 2.3 equiv). For entry 2, the vial was filled with O_2. The resulting mixture was heated with stirring at 110 °C for 12h. After completion, the reaction mixture was cooled down to room temperature and diluted with ethyl acetate (5 mL). The solution was filtered through a pad of silicagel and washed with ethyl acetate (2 × 25 mL). The yield of reaction was determined by ^{1}H NMR using trimethoxybenzene as an internal standard.

General procedure for reactions using NMO oxidant **(entries 3-6, table S1)**: a 1 dram vial equipped with a stir bar was charged with *N*-(4-methoxybenzoyl)-8-aminoquinoline (70 mg, 0.25 mmol, 1 equiv), Cu(OAc), and K_2CO_3 (34 mg, 0.25 mmol, 1equiv, for entry 3) or Ag_2CO_3 (for entries 4-6). Inside the glove box, NMO (*N*-methylmorpholine *N*-oxide) (59 mg, 0.5 mmol, 2 equiv) was added to the vial. Outside the glove box, NMP (1 mL) and morpholine (0.05 mL, 0.57 mmol, 2 equiv) were added to the resulting mixture. The vial was wrapped with aluminum foil (entries 4-6) and stirred at 110 °C for 14h 30 min (entries 4, 5) or 12h (entries 3, 6). For entries 4, 5: after completion, the reaction mixture was dry absorbed on the silica gel followed by purification by column chromatography in hexanes/ethyl acetate

(3:1 to 2:1). For entries 3, 6: after completion, the reaction mixture was cooled down to room temperature, diluted by ethyl acetate (5 mL). The solution was filtered through a pad of silicagel, and washed with ethyl acetate (2 × 25 mL). The yield of reaction was determined by ^{1}H NMR using trimethoxybenzene as an internal standard.

Table S1. Optimization of reaction conditions

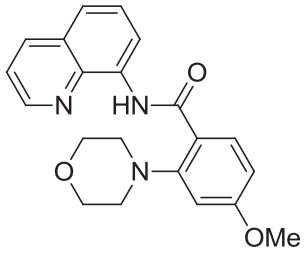


Entry	x equiv.	Oxidant	Additive	Solvent	% yield
1	1	-		NMP	39%*
2	0.5	O_2		NMP	51%*
3	0.25	NMO	K_2CO_3	NMP	44%*
4	0.25	NMO	Ag_2CO_3 (0.25 equiv)	NMP	74%
5	0.1	NMO	Ag_2CO_3 (0.13 equiv)	NMP	87%
6	0.05	NMO	Ag_2CO_3 (0.075 equiv)	NMP	80%*

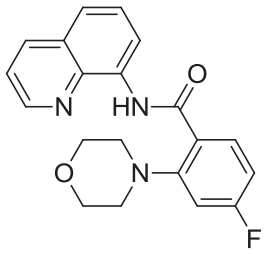
*^{1}H NMR yield

AMINATION OF BENZOIC ACID DERIVATIES

General procedure: To a 1-dram vial equipped with a stir bar was added amide (0.5 mmol, 1 equiv), $Cu(OAc)_2$ (0.1–0.25 equiv) and Ag_2CO_3 (0.125–0.25 equiv). Inside the glove box, NMO (2 equiv) was added to the vial. Outside the glove box NMP (2 mL) and morpholine (2 equiv) were added to the resulting mixture. The vial was wrapped with aluminum foil and stirred at 110 °C for indicated time. After completion, the reaction mixture was cooled down to room temperature and dry absorbed on silica gel. Purification by column chromatography provided the desired product.

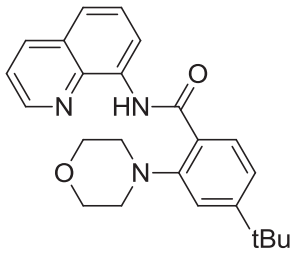


***N*-(2-Morpholino-4-methoxybenzoyl)-8-aminoquinoline (Table 2, entry 1)**: To a 1-dram vial equipped with stir bar was added *N*-4-methoxybenzoyl-8-aminoquinoline (139 mg, 0.5 mmol), $Cu(OAc)_2$ (9 mg, 0.05 mmol), and Ag_2CO_3 (17 mg, 0.06 mmol). Inside the glove box, NMO (118 mg, 1.0 mmol) was added to the vial. Outside the glove box NMP (*N*-methylpyrrolidone, 2 mL) and morpholine (0.09 mL, 1.03 mmol) were added to the resulting mixture. The vial was wrapped by aluminum foil and stirred at 110 °C for 13 h 30 min. After completion, the reaction mixture was cooled down to room temperature and dry absorbed on silica gel. Purification by column chromatography in hexanes/ethyl acetate (3:1 to 2:1) gave 158 mg (87%) of product as a white solid. R_f = 0.16 (SiO_2, hexanes/EtOAc, 3:1), mp 175-176 °C (from hexanes/CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 12.68–12.58 (*s*, 1H) 9.12 (*dd*, *J* = 7.3 Hz, *J* = 1.4 Hz, 1H) 8.88 (*dd*, *J* = 4.6 Hz, *J* = 1.8 Hz, 1H) 8.21–8.16 (*m*, 2H) 7.63–7.56 (*m*, 1H) 7.56–7.51 (*m*, 1H) 7.48 (*dd*, *J* = 8.2 Hz, *J* = 4.1 Hz,1H) 6.80–6.75 (*m*, 2H) 4.03–3.95 (*m*, 4H) 3.89 (*s*, 3H) 3.18–3.11 (*m*, 4H) . ^{13}C NMR (100 MHz, $CDCl_3$, ppm) 165.7, 163.1, 153.3, 148.4, 139.1, 136.7, 136.1, 134.4, 128.6, 127.9, 122.0, 121.8, 121.8, 117.9, 108.6, 106.4, 66.4, 55.8, 54.2 δ. FT-IR (neat, cm^{-1}) υ 2973, 2934, 2846, 1652, 1518, 1485, 1109, 1033. HRMS (ESI+): Calculated for $C_{21}H_{21}N_3O_3$ $[M+H]^+$ 364.1661, Found 364.1661.



***N*-(2-Morpholino-4-fluorobenzoyl)-8-aminoquinoline (Table 2, entry 2)**: To a 1-dram vial equipped with stir bar was added *N*-4-fluorobenzoyl-8-aminoquinoline (133 mg, 0.5 mmol), $Cu(OAc)_2$ (18 mg, 0.10 mmol), and Ag_2CO_3 (28 mg, 0.10 mmol). Inside the glove box, NMO (117 mg, 1.0 mmol) was added to the vial. Outside the glove box NMP (2 mL) and morpholine (0.09 mL, 1.03 mmol) were added to the resulting mixture. The vial was wrapped by aluminum foil and stirred at 110 °C for 14 h. After completion, the reaction mixture was cooled down to room temperature and dry absorbed on silica gel.

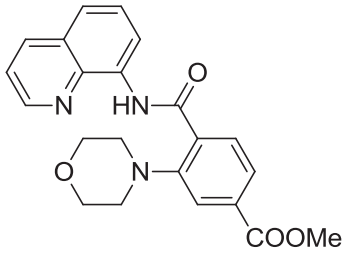
Purification by column chromatography in hexanes/ethyl acetate (4:1) gave 123 mg (70%) of product. R_f = 0.32 (SiO_2, hexanes/EtOAc, 3:1), mp 178-180 °C (from hexanes/EtOAc). ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 12.51–21.44 (*s*, 1H) 9.10 (*dd*, *J* = 7.4 Hz, *J* = 1.7 Hz, 1H) 8.88 (*dd*, *J* = 4.0 Hz, *J* = 1.7 Hz, 1H) 8.23–8.15 (*m*, 2H) 7.63–7.53 (*m*, 2H) 7.50 (*dd*, *J* = 8.0 Hz, *J* = 4.0 Hz, 1H) 6.97–6.91 (*m*, 2H) 3.99–3.93 (*m*, 4H) 3.17–3.11 (*m*, 4H). ^{13}C NMR (125 MHz, $CDCl_3$, ppm) δ 165.4 (*d*, J_{C-F} = 252.8 Hz), 165.1, 153.6 (*d*, J_{C-F} = 8.2 Hz), 148.5, 139.0, 136.8, 135.7, 134.7 (*d*, J_{C-F} = 10.0 Hz), 128.7, 127.9, 125.3 (*d*, J_{C-F} = 2.7 Hz), 122.1, 122.0, 118.0, 111.3 (*d*, J_{C-F} = 21.0 Hz) 107.0 (*d*, J_{C-F} = 22.8 Hz), 66.3, 54.1. ^{19}F NMR (470 MHz, $CDCl_3$, ppm) δ -106.3 – -106.4 (m, 1F). FT-IR (neat, cm^{-1}) υ 1646, 1520, 1484, 1110. HRMS (ESI+): Calculated for $C_{20}H_{18}FN_3O_2$ $[M+H]^+$ 352.1461, Found 352.1460.



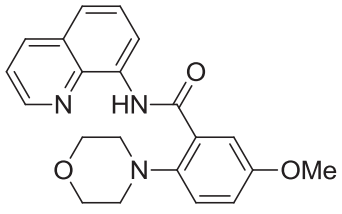
***N*-(2-Morpholino-4-*t*-butylbenzoyl)-8-aminoquinoline (Table 2, entry 3)**: To a 1-dram vial equipped with stir bar was added *N*-4-*t*-butylbenzoyl-8-aminoquinoline (152 mg, 0.5 mmol), $Cu(OAc)_2$ (11 mg, 0.06 mmol), and Ag_2CO_3 (17 mg, 0.06 mmol). Inside the glove box, NMO (117 mg, 1.0 mmol) was added to the vial. Outside the glove box NMP (2 mL) and morpholine (0.09 mL, 1.03 mmol) were added to the resulting mixture. The vial was wrapped with aluminum foil and stirred at 110 °C for 11 h 15 min. After completion, the reaction mixture was cooled down to room temperature and dry absorbed on silica gel. Purification by column chromatography in hexanes/ethyl acetate (4:1) gave 158 mg (81%) of product as a tan solid. R_f = 0.40 (SiO_2, hexanes/EtOAc, 3:1), mp 142-144 °C (from hexanes/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 12.75–12.67 (*s*, 1H) 9.13 (*dd*, *J* = 7.8 Hz, *J* = 1.4 Hz, 1H) 8.87 (*dd*, *J* = 4.1 Hz, *J* = 1.8 Hz, 1H) 8.19 (*dd*, *J* = 8.2 Hz, *J* = 1.4 Hz, 1H) 8.13 (*d*, *J* = 8.2 Hz, 1H) 7.63–7.51 (*m*, 2H) 7.48 (*dd*, *J* = 8.2 Hz, *J* = 4.1 Hz, 1H) 7.31–7.26 (*m*, 2H) 4.03–3.93 (*m*, 4H) 3.21–3.15 (*m*, 4H) 1.37 (*s*, 9H) . ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 166.0, 156.3, 151.2, 148.4, 139.2, 136.7, 136.1, 132.3, 128.7, 127.9, 126.3, 121.9, 121.8, 118.0, 116.4, 66.5, 54.3, 35.6, 31.3. Signal for one carbon could not be located. FT-IR (neat, cm^{-1}) υ 2961, 1660, 1526, 1486, 1112. HRMS (ESI+): Calculated for $C_{24}H_{27}N_3O_2$ $[M+H]^+$ 390.2182, Found 390.2184.

Large scale synthesis: To a 6-dram vial equipped with stir bar was added *N*-4-*t*-butylbenzoyl-8-aminoquinoline (1.52 g, 5.0 mmol), $Cu(OAc)_2$ (181 mg, 1.0 mmol), and Ag_2CO_3 (275 mg, 1.0 mmol). Inside the glove box, NMO (11.7 g, 10 mmol) was added to the vial. Outside the glove box NMP (10 mL)

and morpholine (0.87 mL, 10 mmol) were added to the resulting mixture. The vial was wrapped with aluminum foil and stirred at 110 °C for 39 h. After completion, the reaction mixture was cooled down to room temperature and dry absorbed on silica gel. Purification by column chromatography in hexanes/ethyl acetate (4:1) gave 1.55 g (80%) of product.

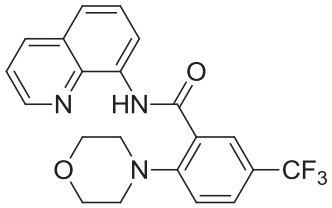


Methyl 3-morpholino-4-(quinolin-8-ylcarbamoyl)benzoate (Table 2, entry 4): To a 1-dram vial equipped with stir bar was added methyl 4-(quinolin-8-ylcarbamoyl)benzoate (153 mg, 0.5 mmol), $Cu(OAc)_2$ (18 mg, 0.10 mmol), and Ag_2CO_3 (28 mg, 0.10 mmol). Inside the glove box NMO (120 mg, 1.0 mmol) was added to the vial. Outside the glove box NMP (2 mL) and morpholine (0.09 mL, 1.03 mmol) were added to the resulting mixture. The vial was wrapped with aluminum foil and stirred at 110 °C for 14 h 30 min. After completion, the reaction mixture was cooled down to room temperature and dry absorbed on silica gel. Purification by column chromatography in hexanes/ethyl acetate (2:1) gave 133 mg (68%) of product as a yellow solid. R_f = 0.16 (SiO_2, hexanes/EtOAc, 3:1), mp 183-184 °C (from hexanes/EtOAc). ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 12.63–12.56 (*s*, 1H) 9.11 (*dd*, *J* = 7.4 Hz, *J* = 1.7 Hz, 1H) 8.88 (*dd*, *J* = 4.6 Hz, *J* = 1.7 Hz, 1H) 8.24–8.19 (*m*, 2H) 7.93–7.87 (*m*, 2H) 7.64–7.55 (*m*, 2H) 7.50 (*dd*, *J* = 8.6 Hz, *J* = 4.6 Hz, 1H) 4.00–3.93 (*m*, 7H) 3.22–3.16 (*m*, 4H) . ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 166.7, 165.2, 151.3, 148.6, 139.1, 136.8, 135.5, 133.7, 133.1, 132.6, 128.6, 127.9, 125.4, 122.5, 122.1, 120.7, 118.1, 66.4, 54.1, 52.8. FT-IR (neat, cm^{-1}) υ 2824, 1722, 1653, 1523, 1491, 1430, 1279, 1112. HRMS (ESI+): Calculated for $C_{22}H_{21}N_3O_4$ $[M+H]^+$ 392.1610, Found 392.1612.

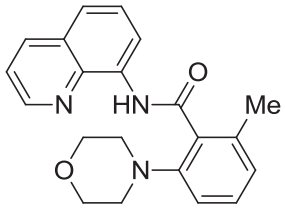


***N*-(2-Morpholino-5-methoxybenzoyl)-8-aminoquinoline (Table 2, entry 5)**: To a 1-dram vial equipped with stir bar was added *N*-(3-methoxybenzoyl)-8-aminoquinoline (139 mg, 0.50 mmol), $Cu(OAc)_2$ (11 mg, 0.06 mmol), and Ag_2CO_3 (18 mg, 0.06 mmol). Inside the glove box NMO (117 mg, 1.0 mmol) was added to the vial. Outside the glove box NMP (2 mL) and morpholine (0.09 mL, 1.03 mmol) were added

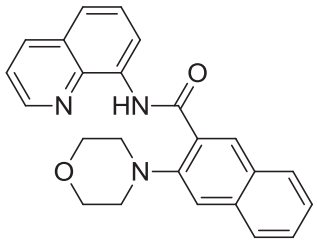
to the resulting mixture. The vial was wrapped by aluminum foil and stirred at 110 °C for 14 h 30 min. After completion, the reaction mixture was cooled down to room temperature and dry absorbed on silica gel. Purification by column chromatography in hexanes/ethyl acetate (2:1) gave 149 mg (82%) of product as a tan solid. R_f = 0.19 (SiO_2, hexanes/EtOAc, 3:1), mp 148-151 °C (from hexanes/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 13.16–13.07 (*s*, 1H) 9.14 (*dd*, *J* = 7.3 Hz, *J* = 1.4 Hz, 1H) 8.90 (*dd*, *J* = 4.1 Hz, *J* = 1.4 Hz, 1H) 8.20 (*dd*, *J* = 8.2 Hz, *J* = 1.4 Hz, 1H) 7.83 (*d*, *J* = 3.2 Hz, 1H) 7.64–7.53 (*m*, 2H) 7.50 (*dd*, *J* = 8.2 Hz, *J* = 4.6 Hz, 1H) 7.29–7.25 (*m*, 1H) 7.07 (*dd*, *J* = 8.7 Hz, *J* = 3.2 Hz, 1H) 4.06–3.99 (*m*, 4H), 3.88 (*s*, 3H) 3.14–3.08 (*m*, 4H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 165.5, 156.9, 148.4, 145.0, 139.3, 136.8, 136.1, 130.2, 128.7, 127.9, 122.2, 122.0, 121.7, 119.4, 118.5, 115.9, 66.6, 56.0, 54.6. FT-IR (neat, cm^{-1}) υ 2843, 1651, 1528, 1488, 1282, 1262, 1114. HRMS (ESI+): Calculated for $C_{21}H_{21}N_3O_3$ $[M+H]^+$ 364.1661, Found 364.1663.



***N*-(2-Morpholino 5-trifluoromethylbenzoyl)-8-aminoquinoline (Table 2, entry 6)**: To a 1-dram vial equipped with stir bar was added *N*-(3-trifluoromethylbenzoyl)-8-aminoquinoline (159 mg, 0.50 mmol), $Cu(OAc)_2$ (18 mg, 0.10 mmol), and Ag_2CO_3 (28 mg, 0.10 mmol). Inside the glove box, NMO (117 mg, 1.0 mmol) was added to the vial. Outside the glove box NMP (2 mL) and morpholine (0.09 mL, 1.03 mmol) were added to the resulting mixture. The vial was wrapped by aluminum foil and stirred at 110 °C for 24 h. After completion, the reaction mixture was cooled down to room temperature and dry absorbed on silica gel. Purification by column chromatography in hexanes/ethyl acetate (3:1 to 2:1) gave 135 mg (67%) of an oil. R_f = 0.19 (SiO_2, hexanes/EtOAc, 3:1). ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 12.41–12.31 (*s*, 1H) 9.12–9.07 (*m*, 1H) 8.90–8.84 (*m*, 1H) 8.41 (*s*, 1H) 8.24–8.18 (*m*, 1H) 8.24–7.70 (*m*, 1H) 7.65–7.55 (*m*, 2H) 7.51 (*dd*, *J* = 8.2 Hz, *J* = 4.1 Hz, 1H) 7.31 (*d*, *J* = 8.70 Hz, 1H) 3.98–3.92 (*m*, 4H) 3.24–3.17 (*m*, 4H). ^{13}C NMR (125 MHz, $CDCl_3$, ppm) δ 164.8, 153.9, 148.6, 138.9, 136.9, 135.3, 129.9, 129.5, 129.3, 128.6, 127.9, 126.3 (*q*, $J_{C\text{-}F}$ = 33.6 Hz), 124.2 (*q*, $J_{C\text{-}F}$ = 271.0 Hz), 122.5, 122.1, 119.5, 118.0, 66.3, 53.9. ^{19}F NMR (470 MHz, $CDCl_3$, ppm) δ -62.1 (s, 1F). FT-IR (neat, cm^{-1}) υ 3243, 2973, 1669, 1529, 1330, 1256, 1272, 1114, 1106, 1081. HRMS (ESI+): Calculated for $C_{21}H_{18}F_3N_3O_2$ $[M+H]^+$ 402.1429, Found 402.1431.

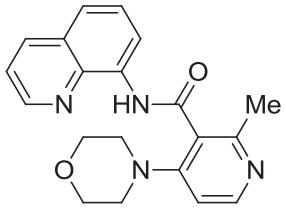


***N*-(2-Morpholino-6-methylbenzoyl)-8-aminoquinoline (Table 2, entry 7)**: To a 1-dram vial equipped with stir bar was added *N*-(2-methylbenzoyl)-8-aminoquinoline (131 mg, 0.50 mmol), $Cu(OAc)_2$ (18 mg, 0.1 mmol), and Ag_2CO_3 (28 mg, 0.10 mmol). Inside the glove box NMO (117 mg, 1.0 mmol) was added to the vial. Outside the glove box NMP (2 mL) and morpholine (0.09 mL, 1.03 mmol) were added to the resulting mixture. The vial was wrapped by aluminum foil and stirred at 110 °C for 14 h. After completion, the reaction mixture was cooled down to room temperature and dry absorbed on silica gel. Purification by column chromatography in hexanes/ethyl acetate (3:1) gave 122 mg (70%) of brown oil. R_f = 0.33 (SiO_2, hexanes/EtOAc, 3:1). ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ.10.68–10.58 (*s*, 1H) 9.00 (*dd*, *J* = 7.4 Hz, *J* = 1.1 Hz, 1H) 8.77 (*dd*, *J* = 4.0 Hz, *J* = 1.7 Hz, 1H) 8.19 (*dd*, *J* = 8.0 Hz, *J* = 1.7 Hz, 1H) 7.64–7.53 (*m*, 2H) 7.45 (*dd*, *J* = 8.0 Hz, *J* = 4.0 Hz, 1H) 7.31 (*t*, *J* = 8.0 Hz, 1H) 7.03–6.95 (*m*, 2H) 3.59–3.53 (*m*, 4H) 3.11–3.06 (*m*, 4H) 2.50 (*s*, 3H) .^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 168.2, 150.3, 148.5, 138.8, 138.6, 136.7, 135.3, 132.1, 130.4, 128.5, 127.8, 126.2, 122.0, 122.0, 116.8, 116.7, 67.2, 53.3, 20.7. FT-IR (neat, cm^{-1}) υ 3349, 2858, 2836, 1661, 1522, 1484, 1325, 1113. HRMS (ESI+): Calculated for $C_{21}H_{21}N_3O_2$ $[M+H]^+$ 348.1712, Found 348.1713.

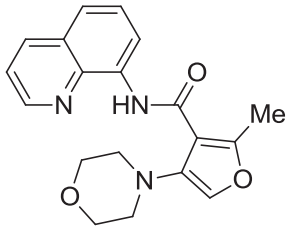


***N*-(1-Morpholino-2-napthalenecarbonyl)-8-aminoquinoline (Table 2, entry 8)**: To a 1-dram vial equipped with stir bar was added *N*-(2-naphthalenecarbonyl)-8-aminoquinoline (149 mg, 0.5 mmol), $Cu(OAc)_2$ (18 mg, 0.1 mmol), and Ag_2CO_3 (28 mg, 0.1 mmol). Inside the glove box NMO (117 mg, 1.0 mmol) was added to the vial. Outside the glove box NMP (2 mL) and morpholine (0.09 mL, 1.03 mmol) were added to the resulting mixture. The vial was wrapped by aluminum foil and stirred at 110 °C for 24 h. After completion, the reaction mixture was cooled down to room temperature and dry absorbed on silica gel. Purification by column chromatography in toluene/ethyl acetate (20:1) gave 126 mg (66%) of product as a light brown solid. R_f = 0.22 (SiO_2, hexanes/EtOAc, 3:1), mp 214-216 °C (from

hexanes/EtOAc). ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 12.74–12.64 (*s*, 1H), 9.18 (*dd*, *J* = 8.0 Hz, *J* = 1.1 Hz, 1H) 8.89 (*dd*, *J* = 4.0 Hz, *J* = 1.1 Hz, 1H) 8.71 (*s*, 1H) 8.21 (*dd*, *J* = 8.6 Hz, *J* = 1.7 Hz, 1H) 7.93 (*d*, *J* = 8.0 Hz, 1H) 7.82 (*d*, *J* = 8.0 Hz, 1H) 7.63 (*t*, *J* = 7.7 Hz, 1H) 7.59–7.52 (*m*, 3H) 7.52–7.44 (*m*, 2H) 4.03–3.96 (*m*, 4H) 3.31–31.21 (*m*, 4H) .^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 166.0, 148.5, 148.2, 139.1, 136.7, 135.9, 135.6, 134.0, 130.2, 129.3, 128.8, 128.7, 128.4, 127.9, 127.1, 125.8, 122.2, 122.0, 118.1, 116.3, 66.5, 54.4. FT-IR (neat, cm^{-1}) υ 2927, 2858, 1667, 1523, 1485, 1326, 1114. HRMS (ESI+): Calculated for $C_{24}H_{21}N_3O_2$ $[M+H]^+$ 384.1712, Found 384.1714.

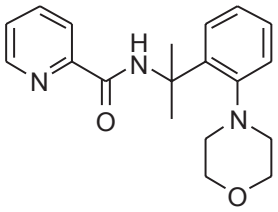


***N*-(2-Methyl-6-morpholinonicotinoyl)-8-aminoquinoline (Table 2, entry 9)**: To a 1-dram vial equipped with stir bar was added *N*-(2-methylnicotinoyl)-8-aminoquinoline (132 mg, 0.50 mmol), $Cu(OAc)_2$ (22 mg, 0.12 mmol), and Ag_2CO_3 (34 mg, 0.12 mmol). Inside the glove box NMO (117 mg, 1.0 mmol) was added to the vial. Outside the glove box NMP (2 mL) and morpholine (0.09 mL, 1.03 mmol) were added to the resulting mixture. The vial was wrapped by aluminum foil and stirred at 110 °C for 25 h. After completion, the reaction mixture was cooled down to room temperature, diluted with ethyl acetate (30 mL), extracted with H_2O (3 × 10 ml), and dried over Mg_2SO_4. The organic solvent was removed by evaporation. Purification by column chromatography in the eluent system of toluene/ethyl acetate (1:3) with triethyl amine (1.6%) followed by drying under high vacuum to remove trace amounts of NMP gave 98 mg (56%) of a yellow oil. R_f = 0.20 (SiO_2, toluene/EtOAc, 3:1). ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 10.58–10.47 (*s*, 1H), 8.96 (*dd*, *J* = 6.9 Hz, *J* = 1.7 Hz, 1H) 8.80 (*dd*, *J* = 4.0 Hz, *J* = 1.7 Hz, 1H) 8.41 (*d*, *J* = 5.7 Hz, 1H) 8.22 (*dd*, *J* = 8.0 Hz, *J* = 1.7 Hz, 1H) 7.67–7.56 (*m*, 2H) 7.49 (*dd*, *J* = 8.0 Hz, *J* = 4.0 Hz, 1H) 6.78 (*d*, *J* = 5.7 Hz, 1H) 3.61–3.55 (*m*, 4H) 3.24–3.19 (*m*, 4H) 2.69 (*s*, 3H).^{13}C NMR (125 MHz, $CDCl_3$, ppm) δ 167.1, 158.4, 156.1, 150.9, 148.7, 138.6, 136.8, 134.7, 128.5, 127.8, 124.2, 122.5, 122.2, 117.0, 110.5, 66.6, 51.5, 23.7. FT-IR (neat, cm^{-1}) υ 1670, 1574, 1523, 1484, 1452, 1327, 1116. HRMS (ESI+): Calculated for $C_{20}H_{20}N_4O_2$ $[M+H]^+$ 349.1665, Found 349.1667.



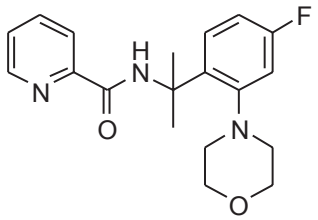
***N*-(2-Methyl-4-morpholino-3-furanoyl)-8-aminoquinoline (Table 2, entry 10)**: To a 1-dram vial equipped with stir bar was added *N*-(2-methyl-3-furanoyl)-8-aminoquinoline (126 mg, 0.5 mmol), $Cu(OAc)_2$ (18 mg, 0.10 mmol), and Ag_2CO_3 (28 mg, 0.10 mmol). Inside the glove box NMO (117 mg, 1.0 mmol) was added to the vial. Outside the glove box NMP (2 mL) and morpholine (0.09 mL, 1.03 mmol) were added to the resulting mixture. The vial was stirred at 110 °C for 22 h. After completion, the reaction mixture was cooled down to room temperature and dry absorbed on silica gel. Purification by column chromatography in toluene/ethyl acetate (30:1 to 20:1) gave 96 mg (57%) of product as a tan solid. R_f = 0.30 (SiO_2, hexanes/EtOAc, 3:1), mp 184–185 °C (from hexanes/EtOAc). ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 11.87–11.77 (*s*, 1H) 9.04 (*dd*, *J* = 7.4 Hz, *J* = 1.1 Hz, 1H) 8.91 (*dd*, *J* = 4.6 Hz, *J* = 1.7 Hz, 1H) 8.18 (*dd*, *J* = 8.0 Hz, *J* = 1.1 Hz, 1H) 7.60–7.51 (*m*, 2H) 7.49 (*dd*, *J* = 8.6 Hz, *J* = 4.6 Hz, 1H) 7.17 (*s*, 1H) 4.02–3.94 (*m*, 4H) 3.07–3.00 (*m*, 4H) 2.66 (*s*, 3H). ^{13}C NMR (125 MHz, $CDCl_3$, ppm) δ 162.7, 159.5, 148.4, 139.3, 139.3, 136.7, 136.1, 130.0, 128.5, 127.8, 121.9, 121.8, 117.7, 112.4, 66.8, 54.6, 14.7. FT-IR (neat, cm^{-1}) υ 3137, 2922, 1667, 1602, 1526, 1323, 1263, 1113. HRMS (ESI+): Calculated for $C_{19}H_{19}N_3O_3$ $[M+H]^+$ 338.1505, Found 338.1507.

AMINATION OF BENZYLAMINE DERIVATIES



***N*-(1-Methyl-1(-2-morpholinophenyl)ethyl)picolinamide** (**Scheme 1**) To a 10 mL pressure-vessel equipped with stir bar was added *N*-(1-methyl-1-phenylethyl)picolinamide (120 mg, 0.5 mmol), $Cu(OAc)_2$ (23 mg, 0.12 mmol), and Ag_2CO_3 (34 mg, 0.12 mmol). Inside the glove box, K_3PO_4 (212 mg, 1.0 mmol) and NMO (117 mg, 1.0 mmol) were added to the vial. Outside the glove box DMSO (dimethyl sulfoxide, 2 mL) and morpholine (0.09 mL, 1.03 mmol) were added to the resulting mixture. The vial was stirred at 130 °C for 36 h 30min. After completion, the reaction mixture was cooled down to room temperature and dry absorbed on silica gel. Purification by column chromatography in toluene/ethyl

acetate (10:1 to 5:1) gave 70 mg (43%) of a yellow oil. R_f = 0.17 (SiO_2, hexanes/EtOAc, 3:1). ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 8.92–8.85 (*s*, 1H) 8.57–8.53 (*m*, 1H) 8.08 (*d*, *J* = 7.4 Hz, 1H) 7.79 (*td*, J_t = 7.4 Hz, J_d = 1.7 Hz, 1H) 7.58 (*dd*, *J* = 8.0 Hz, *J* = 1.7 Hz, 1H) 7.39 (*ddd*, *J* = 7.4 Hz, *J* = 4.6 Hz, *J* = 1.1 Hz, 1H) 7.33 (*dd*, *J* = 8.0 Hz, *J* = 1.1 Hz, 1H) 7.31–7.26 (*m*, 1H) 7.25–7.19 (*m*, 1H) 3.86–3.76 (*m*, 2H) 3.76–3.68 (*m*, 2H) 2.94 (*td*, J_t = 11.5 Hz, J_d = 2.9 Hz, 2H) 2.53 (*d*, *J* = 12.0 Hz, 2H) 1.99 (*s*, 6H). ^{13}C NMR (125 MHz, $CDCl_3$, ppm) δ 162.8, 151.7, 151.0, 148.0, 143.1, 137.7, 128.5, 127.7, 126.5, 126.2, 125.8, 122.2, 67.7, 53.4, 54.5, 29.2. FT-IR (neat, cm^{-1}) υ 2955, 2934, 2858, 1676, 1510, 1454, 1431, 1112. HRMS (ESI+): Calculated for $C_{19}H_{23}N_3O_2$ $[M+H]^+$ 326.1869, Found 326.1866.

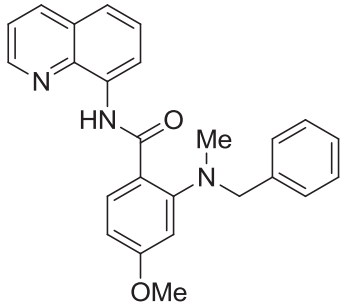


***N*-(1-Methyl-1-(4-fluoro-2-morpholinophenyl)ethyl)picolinamide (Scheme 1)**: To a 10 mL pressure-vessel equipped with stir bar was added *N*-(1-methyl-1-(4-fluorophenyl)ethyl)picolinamide (127 mg, 0.49 mmol), $Cu(OAc)_2$ (23 mg, 0.12 mmol), and Ag_2CO_3 (34 mg, 0.12 mmol). Inside the glove box, K_3PO_4 (212 mg, 1.0 mmol) and NMO (117 mg, 1.0 mmol) were added to the vial. Outside the glove box DMSO (2 mL) and morpholine (0.09 mL, 1.03 mmol) were added to the resulting mixture. The vial was stirred at 130 °C for 38 h 40min. After completion, the reaction mixture was cooled down to room temperature and dry absorbed on silica gel. Purification by column chromatography in hexanes/ethyl acetate (2:1) gave 67 mg (40%) of a yellow oil. R_f = 0.14 (SiO_2, hexanes/EtOAc, 3:1). ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 8.85–8.78 (*s*, 1H) 8.57–8.53 (*m*, 1H) 8.10 (*d*, *J* = 8.0 Hz, 1H) 7.79 (*td*, J_t = 7.4 Hz, J_d = 1.1 Hz, 1H) 7.55 (*dd*, *J* = 8.6 Hz, *J* = 6.9 Hz, 1H) 7.40 (*dd*, *J* = 6.9 Hz, *J* = 5.1 Hz, 1H) 7.03 (*dd*, *J* = 2.9 Hz, *J* = 10.3 Hz, 1H) 6.94–6.87 (*m*, 1H) 3.84–3.75 (*m*, 2H) 3.75–3.68 (*m*, 2H) 2.90–2.78 (*m*, 2H) 2.58–2.46 (*m*, 2H) 1.96 (*s*, 6H). ^{13}C NMR (125 MHz, $CDCl_3$, ppm) δ 162.6 (*d*, $J_{C\text{-}F}$ = 248.2 Hz), 162.8, 153.4 (*d*, $J_{C\text{-}F}$ = 6.4 Hz), 150.8, 148.0, 139.1 (*d*, $J_{C\text{-}F}$ = 3.6 Hz), 137.7, 129.1 (*d*, $J_{C\text{-}F}$ = 9.1 Hz), 126.3, 122.2, 113.3 (*d*, $J_{C\text{-}F}$ = 21.0 Hz), 112.9 (*d*, $J_{C\text{-}F}$ = 19.2 Hz), 67.5, 54.9, 54.5, 29.2. FT-IR (neat, cm^{-1}) υ 3374, 2964, 2928, 2852, 2822, 1673, 1587, 1612, 1498, 1261, 1157, 1113. HRMS (ESI+): Calculated for $C_{19}H_{22}FN_3O_2$ $[M+H]^+$ 344.1774, Found 344.1769

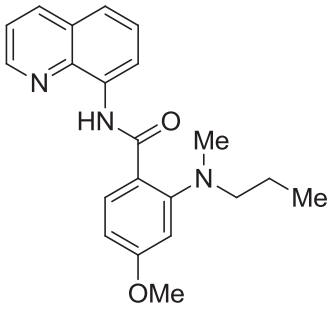
AMINATION OF PRIMARY AND SECONDARY AMINES

General procedure: To a 1-dram vial equipped with stir bar was added amide (0.5 mmol), $Cu(OAc)_2$ (0.126–0.25 equiv), and Ag_2CO_3 (0.126–0.25 equiv). Inside the glove box, NMO (*N*-methylmorpholine-

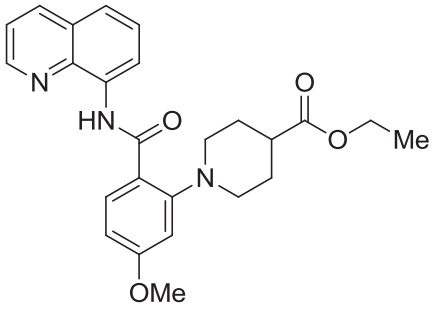
N-oxide) (2.0 equiv.) was added to the vial. Outside the glove box NMP (2 mL) and amine (2 equiv) were added to the resulting mixture. The vial was stirred at room temperature for 5 minutes followed by heating to 110 ºC and stirring for 12 h. After completion, the reaction mixture was cooled down to room temperature and dry absorbed on silica gel. Purification by column chromatography gave the desired product.



***N*-(2-*N*-Methylbenzylamino-4-methoxybenzoyl)-8-aminoquinoline (Table 3, entry 1)**: To a 1-dram vial equipped with stir bar was added *N*-4-methoxybenzoyl-8-aminoquinoline (139 mg, 0.5 mmol), $Cu(OAc)_2$ (23 mg, 0.125 mmol), and Ag_2CO_3 (34 mg, 0.125 mmol). Inside the glove box, NMO (118 mg, 1.0 mmol) was added to the vial. Outside the glove box NMP (2 mL) and *N*-methylbenzylamine (121 mg, 1.00 mmol) were added to the resulting mixture. The vial was stirred at room temperature for 5 minutes followed by heating at 110 ºC for 12 h. After completion, the reaction mixture was cooled down to room temperature and dry absorbed on silica gel. Purification by column chromatography in hexanes/ethyl acetate (3:1) gave 164 mg (82%) of product as a tan oil. R_f = 0.43 (SiO_2, hexanes/EtOAc, 3:1). ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 13.78 (*s*, 1H) 9.09 (*dd*, *J* = 7.8 Hz, *J* = 0.9 Hz, 1H) 8.75 (*dd*, *J* = 1.8 Hz, *J* = 1.8 Hz, 1H) 8.27 (*s*, *J* = 8.7 Hz, 1H) 8.16 (*dd*, *J* = 8.7 Hz, *J* = 1.8 Hz, 1H) 7.60 (*t*, *J* = 8.2 Hz, 1H) 7.51 (*dd*, *J* = 8.2 Hz, *J* = 0.9 Hz, 1H) 7.42 (*dd*, *J* = 8.2 Hz, *J* = 4.1Hz, 1H) 7.29–7.26 (*m*, 2H) 7.13–7.11 (*m*, 3H) 6.74 (*dd*, *J* = 8.7 Hz, *J* = 2.7 Hz, 1H) 6.67 (*d*, *J* = 2.3 Hz, 1H) 4.33 (*s*, 2H) 3.79 (*s*, 3H) 3.93 (*s*, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ165.0, 162.4, 152.4, 148.2, 139.6, 136.4, 136.2, 133.6, 129.7, 128.3, 128.1, 127.7, 127.4, 121.9, 121.4, 121.2, 117.5, 109.1, 108.6, 61.2, 55.4, 43.7. Signal for one carbon could not be located. FT-IR (neat, cm-1) υ 3022, 1653, 1599, 1526, 1487, 1324, 1246. HRMS (ESI+): Calculated for $C_{25}H_{23}N_3O_2$ $[M+H]^+$ 398.1869, Found 398.1870.

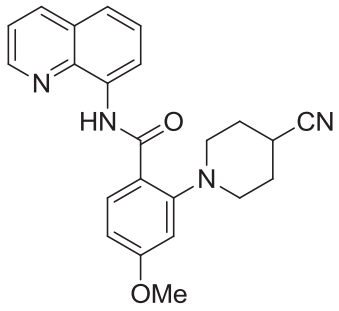


***N*-(2-*N*-Methylpropylamino-4-methoxybenzoyl)-8-aminoquinoline (Table 3, entry 2)**: To a 1-dram vial equipped with stir bar was added *N*-4-methoxybenzoyl-8-aminoquinoline (139 mg, 0.5 mmol), $Cu(OAc)_2$ (23 mg, 0.125 mmol), and Ag_2CO_3 (34 mg, 0.125 mmol). Inside the glove box NMO (118 mg, 1.0 mmol) was added to the vial. Outside the glove box NMP (2 mL) and *N*-methylpropylamine (73 mg, 1.0 mmol) were added to the resulting mixture. The vial was stirred at room temperature for 5 minutes followed by heating at 110 ºC for 12 h. After completion, the reaction mixture was cooled down to room temperature and dry absorbed on silica gel. Purification by column chromatography in hexanes/ethyl acetate (3:1) gave 129 mg (74%) of product as a clear oil. R_f = 0.51 (SiO_2, hexanes/EtOAc, 3:1). ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 14.11 (*s*, 1H) 9.08 (*dd*, *J* = 7.8 Hz, *J* = 1.4 Hz, 1H) 8.82 (*dd*, *J* = 4.1 Hz, *J* = 1.8 Hz, 1H) 8.34 (*d*, *J* = 8.7 Hz, 1H) 8.13 (*dd*, *J* = 8.2 Hz, *J* = 1.8 Hz, 1H) 7.57 (*t*, *J*= 7.8 Hz, 1H) 7.48 (*dd*, *J*= 7.8 Hz, *J* = 0.9 Hz, 1H) 7.42 (*dd*, *J*= 8.2 Hz, *J* = 4.1 Hz, 1H) 6.85 (*d*, *J*= 2.3 Hz, 1H) 6.81 (*dd*, *J* = 8.7 Hz, *J* = 2.3 Hz, 1H) 3.87 (*s*, 3H) 3.12–3.08 (*m*, 2H) 2.88 (*s*, 3H) 1.63 (*sextet*, *J* = 7.8 Hz, 2H) 0.82 (*t*, *J*= 7.8 Hz, 3H).^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 164.9, 162.7, 153.5, 148.0, 139.8, 136.6, 136.1, 133.6, 128.3, 127.6, 122.4, 121.4, 121.1, 117.6, 109.2, 108.5, 59.1, 55.5, 44.6 20.2, 12.0. FT-IR (neat, cm-1) υ 2970.3, 1651.3, 1599.1, 1526.2, 1487.1, 1251.3, 1219.3. HRMS (ESI+): Calculated for $C_{21}H_{23}N_3O_2$ $[M+H]^+$ 350.1869, Found 350.1867.



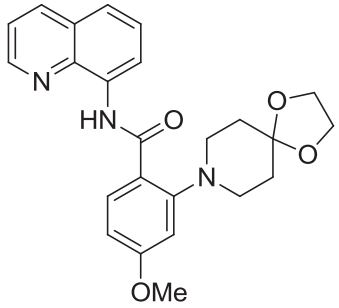
***N*-(2-Ethyl isonipecotato-4-methoxybenzoyl)-8-aminoquinoline (Table 3, entry 3)**: To a 1-dram vial equipped with stir bar was added *N*-4-methoxybenzoyl-8-aminoquinoline (139 mg, 0.5 mmol), $Cu(OAc)_2$ (12 mg, 0.063 mmol), and Ag_2CO_3 (17 mg, 0.063 mmol). Inside the glove box, NMO (118 mg, 1.0 mmol)

was added to the vial. Outside the glove box NMP (2 mL) and ethyl isonipecotate (157 mg, 1.00 mmol) were added to the resulting mixture. The vial was stirred at room temperature for 5 minutes followed by heating at 110 ºC for 12 h. After completion, the reaction mixture was cooled down to room temperature, diluted with dichloromethane (2 mL), and dry absorbed on silica gel. Purification by column chromatography in hexanes/ethyl acetate (3:1) gave 149 mg (69%) of product as white solid. R_f = 0.34 (SiO_2, hexanes/EtOAc, 3:1), mp 185−188 ºC (from hexanes/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 12.72 (*s*, 1H) 9.15 (*dd*, *J* = 7.8 Hz, *J* = 1.4 Hz, 1H) 8.89 (*dd*, *J* = 4.1 Hz, *J* = 1.8 Hz, 1H) 8.20 (*d*, *J* = 8.7 Hz, 1H) 8.15 (*dd*, *J* = 8.2 Hz, *J* = 1.4 Hz, 1H) 7.58 (*t*, *J* = 7.8 Hz, 1H) 7.51 (*dd*, *J* = 7.6 Hz, *J* = 1.4 Hz, 1H) 7.45 (*dd*, *J* = 8.2Hz, *J* = 4.1 Hz, 1H) 6.76–6.73 (*m*, 2H) 4.04 (*q*, *J* = 7.3 Hz, 1H) 3.87 (*s*, 3H) 3.41 (*d*, *J* = 11.9 Hz, 2H) 2.84 (*td*, J_t = 11.9 Hz, J_d =2.3 Hz, 2H) 2.40 (*tt*, *J* = 11.00 Hz, *J* = 3.7 Hz, 2H) 2.28 (*qd*, J_q = 11.0 Hz, J_d = 3.7 Hz, 2H) 2.00 (*dd*, *J* = 12.8 Hz, *J* = 2.7 Hz, 2H) 1.15 (*t*, *J* = 7.3 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 174.8, 165.6, 162.8, 153.9, 148.3, 139.0, 136.4, 136.2, 134.0, 128.4, 127.6, 121.6, 121.5, 121.4, 117.8 108.2, 106.5, 60.4, 55.6, 54.0, 41.0, 27.7, 14.3. FT-IR (neat, cm-1) υ 3186, 2967, 2925, 1734, 1655, 1596, 1520, 1256, 1164, 1047. HRMS (ESI+): Calculated for $C_{25}H_{27}N_3O_4$ $[M+H]^+$ 434.2080, Found 434.2079.

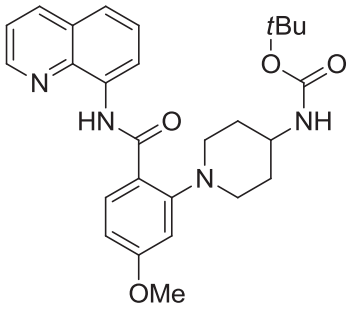


***N*-(2-4-Cyanopiperidino 4-methoxybenzoyl)-8-aminoquinoline (Table 3, entry 4)**: To a 1-dram vial equipped with stir bar was added *N*-4-methoxybenzoyl-8-aminoquinoline (139 mg, 0.5 mmol), $Cu(OAc)_2$ (12 mg, 0.063 mmol), and Ag_2CO_3 (17 mg, 0.063 mmol). Inside the glove box NMO (118 mg, 1.0 mmol) was added to the vial. Outside the glove box NMP (2 mL) and 4-cyanopiperidine (110 mg, 1.00 mmol) were added to the resulting mixture. The vial was stirred at room temperature for 5 minutes followed by heating at 110 ºC for 12 h. After completion, the reaction mixture was cooled down to room temperature and dry absorbed on silica gel. Purification by column chromatography in hexanes/ethyl acetate (3:1) gave 137 mg (71%) of product as a light yellow solid. R_f = 0.21 (SiO_2, hexanes/EtOAc, 3:1), mp 155−156 ºC (from hexanes/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 12.56 (*s*, 1H) 9.16 (*dd*, *J* = 7.8 Hz, *J* = 1.8 Hz, 1H) 8.88 (*dd*, *J* = 4.1 Hz, *J* = 1.8 Hz, 1H) 8.21 (*d*, *J* = 8.7, 1H) 8.20 (*dd*, *J*= 8.2 Hz, *J* = 1.8 Hz, 1H) 7.60 (*t*, *J*= 7.8 Hz, 1H) 7.54 (*dd*, *J* = 7.8 Hz, *J* = 1.4 Hz, 1H) 7.50 (*dd*, *J*= 8.2 Hz, *J* = 4.1 Hz, 1H) 6.77–

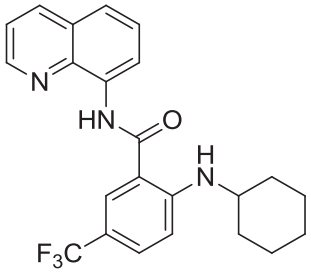
6.75 (*m*, 2H) 3.88 (*s*, 3H) 3.35–3.32 (*m*, 2H) 3.01 (*s*, 2H) 2.73 (*s*, 1H) 2.30 (*s*, 2H) 2.24 (*s*, 2H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 165.4, 162.9, 153.2, 147.9, 138.9, 136.7, 135.9, 134.2, 128.5, 127.7, 121.8, 121.6, 121.5, 118.0, 108.8, 106.6, 55.6, 52.5, 28.1, 26.1 Signal for one carbon could not be located. FT-IR (neat, cm-1) υ 3180, 2825, 1660, 1597, 1519, 1489, 1270, 1254. HRMS (ESI+): Calculated for $C_{23}H_{22}N_4O_2$ $[M+H]^+$ 387.1821, Found 387.1822.



***N*-(4-Piperidone etheyleneketalato-4-methoxybenzoyl)-8-aminoquinoline (Table 3, entry 5)**: To a 1-dram vial equipped with stir bar was added *N*-4-methoxybenzoyl-8-aminoquinoline (139 mg, 0.5 mmol), $Cu(OAc)_2$ (12 mg, 0.063 mmol), and Ag_2CO_3 (17 mg, 0.063 mmol). Inside the glove box NMO (118 mg, 1.0 mmol) was added to the vial. Outside the glove box NMP (2 mL) and 4-piperidone ethylene ketal (143 mg, 1.00 mmol) were added to the resulting mixture. The vial was stirred at room temperature for 5 minutes followed by heating at 110 ºC for 12 h. After completion, the reaction mixture was cooled down to room temperature and dry absorbed on silica gel. Purification by column chromatography in hexanes/ethyl acetate (3:1) gave 171 mg (82%) of product as a light yellow solid. R_f = 0.22 (SiO_2, hexanes/EtOAc, 3:1), mp 186–189 ºC (from hexanes/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 12.94 (*s*, 1H) 9.16 (*dd*, *J* = 7.8 Hz, *J* = 1.4 Hz, 1H) 8.93 (*dd*, *J* = 4.6 Hz, *J* = 1.8 Hz, 1H) 8.24 (*d*, *J*= 8.7 Hz, 1H) 8.16 (*dd*, *J*= 8.2 Hz, *J* = 1.8 Hz, 1H) 7.57 (*t*, *J* = 8.2 Hz, 1H) 7.51 (*dd*, *J* = 8.2 Hz, *J* = 1.4 Hz, 1H) 7.47 (*dd*, *J* = 8.2 Hz, *J* = 4.1 Hz, 1H) 6.84 (*d*, *J* = 2.3 Hz, 1H) 6.77 (*dd*, *J* = 8.7 Hz, *J* = 2.3 Hz, 1H) 3.96 (*s*, 4H) 3.87 (*s*, 3H) 3.21 (*t*, *J* = 5.5 Hz, 4H) 2.12 (*s*, 4H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 165.6, 162.9, 153.8, 148.1, 139.2, 136.4, 136.3, 134.0, 128.4, 127.6, 121.7, 121.6, 121.5, 118.0, 109.0, 107.2, 106.7, 64.4, 55.6, 52.6, 34.6. FT-IR (neat, cm-1) υ 2934, 2837, 1650, 1600, 1521, 1487, 1257, 1143, 1096. HRMS (ESI+): Calculated for $C_{24}H_{25}N_3O_4$ $[M+H]^+$ 420.1923, Found 420.1923.

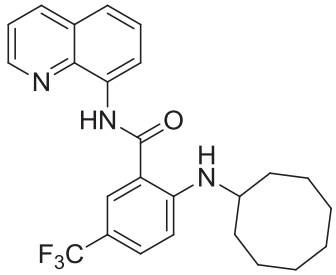


N-(tert-Butylpiperidin-4-ylcarbamate-4-methoxybenzoyl)-8-aminoquinoline (Table 3, entry 6): To a 1-dram vial equipped with stir bar was added *N*-4-methoxybenzoyl-8-aminoquinoline (139 mg, 0.5 mmol), $Cu(OAc)_2$ (23 mg, 0.125 mmol), and Ag_2CO_3 (34 mg, 0.125 mmol). Inside the glove box, NMO (118 mg, 1.0 mmol) was added to the vial. Outside the glove box NMP (2 mL) and tert-butylpiperidin-4-ylcarbamate (200 mg, 1.00 mmol) were added to the resulting mixture. The vial was stirred at room temperature for 5 minutes followed by heating at 110 ºC for 12 h. After completion, the reaction mixture was cooled down to room temperature and dry absorbed on silica gel. Purification by column chromatography in tolene/ethyl acetate (10:1 to 10:3) gave 196 mg (83%) of product as a light green solid. R_f = 0.24 (SiO_2, hexanes/EtOAc, 3:1), mp 175−177 ºC (from hexanes/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 12.62 (*s*, 1H) 9.13 (*dd*, *J* = 7.8 Hz, *J* = 1.4, 1H) 8.84 (*dd*, *J* = 4.1 Hz, *J* = 1.4 Hz, 1H) 8.19 (*dd*, *J*= 8.2 Hz, *J* = 1.8 Hz, 1H) 8.15 (*d*, *J* = 8.7 Hz, 1H) 7.59 (*t*, *J* = 8.2 Hz, 1H) 7.53 (*dd*, *J* = 8.2 Hz, *J* = 1.4 Hz, 1H) 7.49 (*dd*, *J*= 8.2 Hz, *J* = 4.6 Hz, 1H) 6.75-6.72 (*m*, 2H) 4.24 (*d*, *J* = 5.9 Hz, 1H) 3.87 (*s*, 3H) 3.61 (*s*, 1H) 3.36 (*d*, *J*= 11.9 Hz, 2H) 2.91 (*t*, *J* = 10.5 Hz, 2H) 2.03 (*d*, *J*= 11.0 Hz, 2H) 1.88 (*qd*, J_a = 11.0 Hz, J_d = 3.7 Hz, 2H) 1.41 (*s*, 9H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 165.7, 162.8, 155.2, 153.6, 147.7 139.0, 136.6, 136.1, 134.0, 129.1, 128.5, 128.3, 127.8, 121.6, 121.5, 118.0, 108.1, 106.3, 79.5, 55.6, 53.1, 31.9. 28.5. FT-IR (neat, cm-1) υ 3416, 2979, 2822, 1708, 1658, 1601, 1520, 1488, 1256, 1236, 1174, 1029. HRMS (ESI+): Calculated for $C_{27}H_{32}N_4O_4$ $[M]^+$ 477.2502, Found 477.2498.



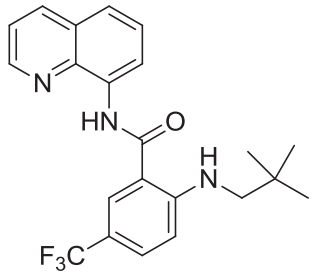
***N*-(2-Cyclohexylamino-5-trifluoromethylbenzoyl)-8-aminoquinoline (Table 3, entry 7)**: To a 1-dram vial equipped with stir bar was added *N*-3-trifluoromethylbenzoyl-8-aminoquinoline (158 mg, 0.5 mmol), $Cu(OAc)_2$ (23 mg, 0.125 mmol), and Ag_2CO_3 (34 mg, 0.125 mmol). Inside the glove box, NMO (118 mg,

1.0 mmol) was added to the vial. Outside the glove box NMP (2 mL) and cyclohexylamine (99 mg, 1.00 mmol) were added to the resulting mixture. The vial was stirred at room temperature for 5 minutes followed by heating at 110 ºC for 12 h. After completion, the reaction mixture was cooled down to room temperature and dry absorbed on silica gel. Purification by column chromatography in hexanes/ethyl acetate (10:1) gave 83 mg (40%) of product as a light yellow solid. R_f = 0.32 (SiO_2, hexanes/EtOAc, 10:1), mp 162–164 ºC (from hexanes). ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 10.59 (*s*, 1H) 8.86 (*dd*, *J* = 6.0 Hz, *J* = 1.4 Hz, 1H) 8.77 (*dd*, *J* = 6.9 Hz, *J* = 1.8 Hz, 1H) 8.19 (*dd*, *J* = 8.2 Hz, *J* =1.4 Hz, 1H) 8.16 (*s*, 1H) 7.99 (*d*, *J* = 1.4 Hz, 1H) 7.61–7.48 (*m*, 4H) 6.80 (*d*, *J* = 8.7 Hz, 1H) 3.48–3.40 (*m*, 2H) 2.07-2.04 (*m*, 1H) 1.82-1.79 (*m*, 2H) 1.67–1.64 (*m*, 1H) 1.46–1.25 (*m*, 5H).^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 167.5, 151.4, 148.6, 138.9, 136.5, 134.5, 129.8, 128.1, 127.4, 125.8, 124.9 (*q*, J_{C-F} = 269.9 Hz) 121.9, 116.6, 115.7 (*q*, J_{C-F} = 32.4 Hz) 114.3, 112.0, 50.9, 32.7, 35.9, 24.8. Signal for one carbon could not be located. ^{19}F NMR (470 MHz, $CDCl_3$, ppm) δ 57.7. FT-IR (neat, cm-1) υ 3349, 2928, 2858, 1653, 1536, 1324, 1107, 1085. HRMS (ESI+): Calculated for $C_{23}H_{22}F_3N_3O$ $[M+H]^+$ 414.1793, Found 414.1788.



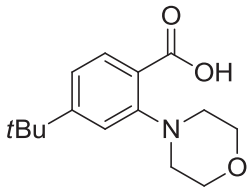
***N*-(2-Cyclooctylamino-5-trifluoromethylbenzoyl)-8-aminoquinoline (Table 3, entry 8)**: To a 1-dram vial equipped with stir bar was added *N*-3-trifluoromethylbenzoyl-8-aminoquinoline (158 mg, 0.5 mmol), $Cu(OAc)_2$ (23 mg, 0.125 mmol), and Ag_2CO_3 (34 mg, 0.125 mmol). Inside the glove box, NMO (118 mg, 1.0 mmol) was added to the vial. Outside the glove box NMP (2 mL) and cyclooctylamine (0.127 g, 1.00 mmol) were added to the resulting mixture. The vial was stirred at room temperature for 5 minutes followed by heating at 110 ºC for 12 h. After completion, the reaction mixture was cooled down to room temperature and dry absorbed on silica gel. Purification by column chromatography in hexanes/ethyl acetate (3:1) gave 114 mg (52%) of product as a light orange solid. R_f = 0.38 (SiO_2, hexanes/EtOAc, 10:1), mp 118–120 ºC (from hexanes). ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 10.59 (*s*, 1H) 8.87 (*dd*, *J* = 4.1 Hz, *J* = 1.8 Hz, 1H) 8.77 (*dd*, *J* = 6.9 Hz, *J* = 1.4 Hz, 1H) 8.19 (*dd*, *J* = 8.2 Hz, *J* = 1.4 Hz, 1H) 7.99 (*d*, *J* = 0.9 Hz, 1H) 7.61–7.53 (*m*, 3H) 7.49 (*dd*, *J* = 8.2 Hz, *J* = 4.1 Hz, 1H) 6.72 (*d*, *J* = 9.2 Hz, 1H) 3.68–3.60 (*m*, 1H) 1.98–1.91 (*m*, 2H) 1.82–1.55 (*m*, 13H).^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 167.5, 151.2, 148.6, 138.9, 136.5, 134.6, 129.9, 128.1, 127.4, 125.8, 124.9 (*q*, J_{C-F} = 269.9 Hz), 121.9, 116.6,

115.6 (*q*, J_{C-F} = 33.6 Hz), 114.4, 112.2, 52.2, 32.2, 27.2, 25.8, 24.0. Signal for one carbon could not be located. ^{19}F NMR (470 MHz, $CDCl_3$, ppm) δ 57.7. FT-IR (neat, cm-1) υ 3355, 2931, 2855, 1651, 1531, 1488, 1324, 1273, 1109, 1082. HRMS (ESI+): Calculated for $C_{25}H_{26}F_3N_3O$ $[M+H]^+$ 442.2106, Found 442.2101.



***N*-(2-Neopentylamino-5-trifluoromethylbenzoyl)-8-aminoquinoline (Table 3, entry 9)**: To a 1-dram vial equipped with stir bar was added *N*-3-trifluoromethylbenzoyl-8-aminoquinoline (158 mg, 0.5 mmol), $Cu(OAc)_2$ (23 mg, 0.125 mmol), and Ag_2CO_3 (34 mg, 0.125 mmol). Inside the glove box NMO (118 mg, 1.0 mmol) was added to the vial. Outside the glove box NMP (2 mL) and neopentylamine (87 mg, 1.00 mmol) were added to the resulting mixture. The vial was stirred at room temperature for 5 minutes followed by heating at 110 ºC for 12 h. After completion, the reaction mixture was cooled down to room temperature and dry absorbed on silica gel. Purification by column chromatography in hexanes/ethyl acetate (10:1) gave 65 mg (32%) of product as a light yellow solid. R_f = 0.77 (SiO_2, hexanes/EtOAc, 3:1), mp 148–150 ºC (from hexanes). ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 10.62 (*s*, 1H) 8.86 (*dd*, *J* = 4.1 Hz, *J* = 1.2 Hz, 1H) 8.80 (*dd*, *J* = 7.3 Hz, *J* = 1.4 Hz, 1H) 8.49–8.38 (*m*, 1H) 8.18 (*dd*, *J* = 8.2 Hz, *J* = 1.4 Hz, 1H) 8.00 (*s*, 1H) 7.61–7.51 (*m*, 3H) 7.48 (*dd*, *J* = 8.4 Hz, *J* = 4.6 Hz, 1H) 6.80 (*d*, *J* = 8.7 Hz, 1H) 3.02 (*d*, *J* = 5.0 Hz, 2H) 1.07 (*s*, 9H) . ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 167.7, 153.2, 148.8, 139.1, 136.7, 134.8, 130.2, 128.3, 127.6, 125.7 (*q*, J_{C-F} = 3.6 Hz), 125.1 (*q*, J_{C-F} = 270.4 Hz), 122.1, 122.0, 116.8, 116.0 (*q*, J_{C-F} = 32.9 Hz) 114.3, 111.8, 55.2, 32.3, 28.1. ^{19}F NMR (470 MHz, $CDCl_3$, ppm) δ -60.82. FT-IR (neat, cm-1) υ 3346, 2961, 1654, 1533, 1430, 1324, 1103, 1084. HRMS (ESI+): Calculated for $C_{22}H_{22}F_3N_3O$ $[M+H]^+$, Found.

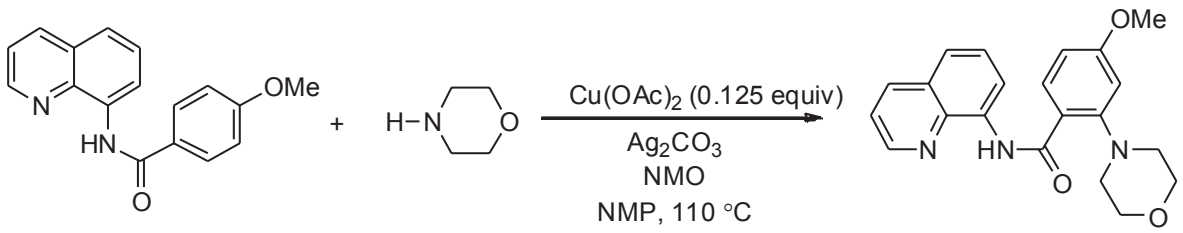
AUXILIARY CLEAVAGE



2-Morpholino-4-*t*-butylbenzoic acid: A 10 mL Kontes flask equipped with a stir bar was charged with *N*-(2-morpholino-4-*t*-butylbenzoyl)-8-aminoquinoline (97 mg, 0.25 mmol), NaOH (150 mg, 3.75 mmol) and EtOH (1 mL). The resulting mixture was stirred at 130 °C for 3 days. After completion, the reaction mixture was cooled down to room temperature, diluted by 50 mL ethyl acetate and washed by HCl (4 × 20 mL of 0.5N aqueous solution). The aqueous layers were combined and extracted with ethyl acetate (3 × 15 mL).Combined organic layers were dried over $MgSO_4$. Evaporation to remove organic solvent gave 60 mg (91%) of pure acid as a light brown solid. This compound is known.[4] ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 8.22 (*d*, *J* = 8.0 Hz, 1H) 7.45 (*d*, *J* = 8.6 Hz, 1H) 7.43 (*s*, 1H) 3.97 (*brs*, 4H) 3.10 (*brs*, 4H) 1.35 (*s*, 9H).

CONTROL EXPERIMENTS

General procedure: To a 1-dram vial equipped with stir bar was added *N*-4-methoxybenzoyl-8-aminoquinoline (70 mg, 0.5 mmol), $Cu(OAc)_2$ (6 mg, 0.03 mmol), and Ag_2CO_3 (9 mg, 0.03 mmol). Inside the glove box, NMO (59 mg, 0.50 mmol) was added to the vial. Outside the glove box NMP (1 mL) and morpholine (0.05 mL, 0.57 mmol) were added to the resulting mixture. The vial was wrapped by aluminum foil and stirred at 110 °C for 15 h. After completion, the reaction mixture was cooled to room temperature and diluted with ethyl acetate (5 mL). The solution was filtered through a pad of silicagel and washed with ethyl acetate (2 × 25 mL). The yield of reaction was determined by ^{1}H NMR using trimethoxybenzene as an internal standard.



$Cu(OAc)_2$ (purity)	% yield
98% (reagent grade)	78%
99.999% (ultra-pure)	85%
No $Cu(OAc)_2$	< 2%

DIAMINATION: To a 1-dram vial equipped with stir bar was added *N*-(4-piperidone-etheyleneketalato 4-methoxybenzoyl)-8-aminoquinoline (43 mg, 0.10 mmol), $Cu(OAc)_2$ (5 mg, 0.03 mmol), and Ag_2CO_3 (7 mg, 0.03 mmol). Inside the glove box, NMO (23 mg, 0.20 mmol) was added to the vial. Outside the glove box NMP (0.5 mL) and morpholine (0.02 mL, 0.23 mmol) were added to the resulting mixture. The vial was wrapped by aluminum foil and stirred at 110 °C for 14 h. After completion, the reaction mixture was cooled down to room temperature, diluted by ethyl acetate (5 mL), filtered through silica gel and washed by ethyl acetate (25 mL × 2 times). The solvent was evaporated under reduced pressure and analysis by ^{1}H NMR showed no diaminated product.

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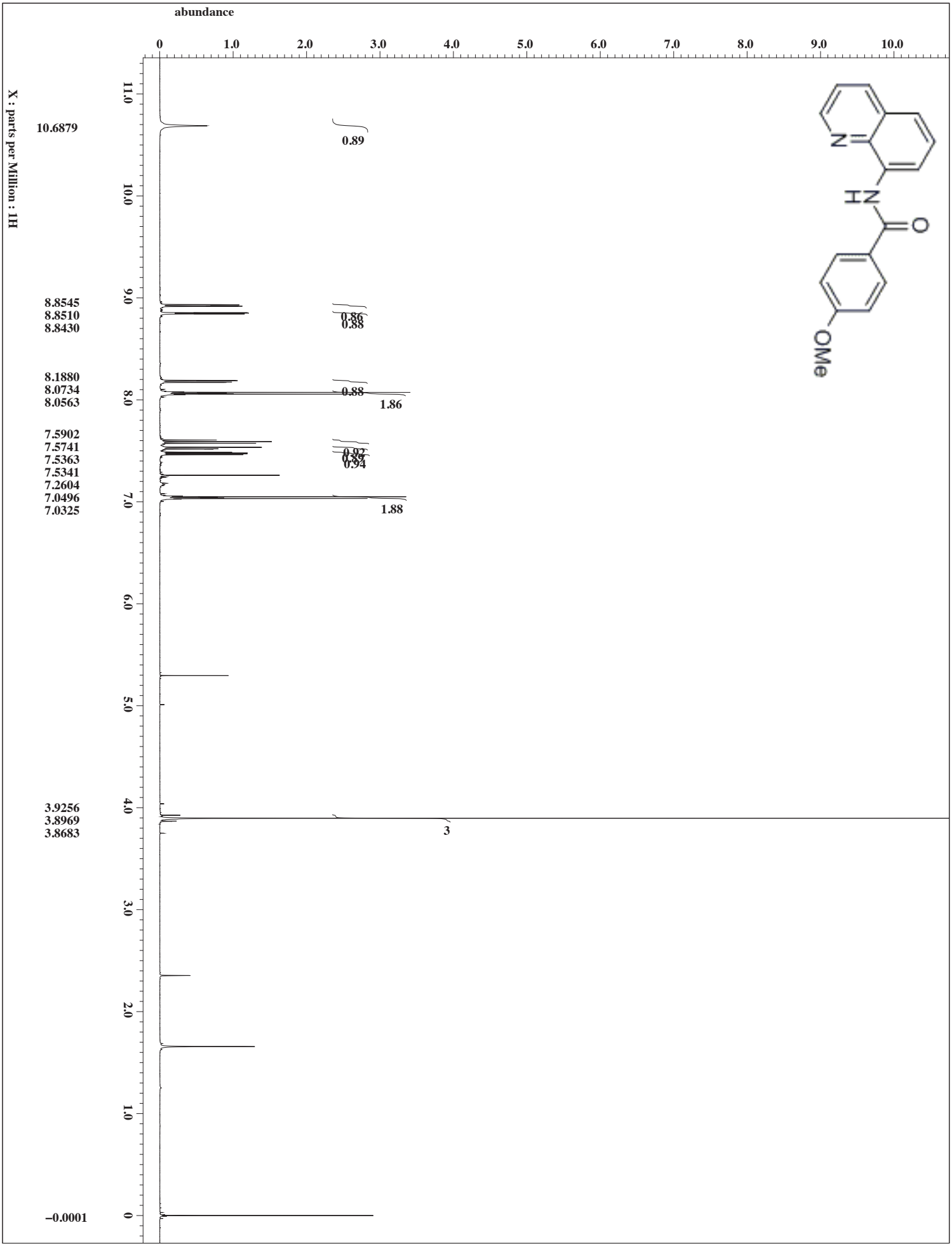
1. Tran, L. D.; Popov, I.; Daugulis, O. *J. Am. Chem. Soc*. **2012**, *134*, 18237.
2. Tran, L. D.; Daugulis, O. *Angew. Chem. Int. Ed.* **2012**, *51*, 5188.
3. Ano, Y.; Tobisu, M.; Chatani, N. *Org. Lett.* **2012**, *14*, 354.
4. Yoo, E. J.; Ma, S.; Mei, T.-S.; Chan, K. S. L.; Yu, J.-Q. *J. Am. Chem. Soc.* **2011**, *133*, 7652.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8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
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8.8510
8.8430
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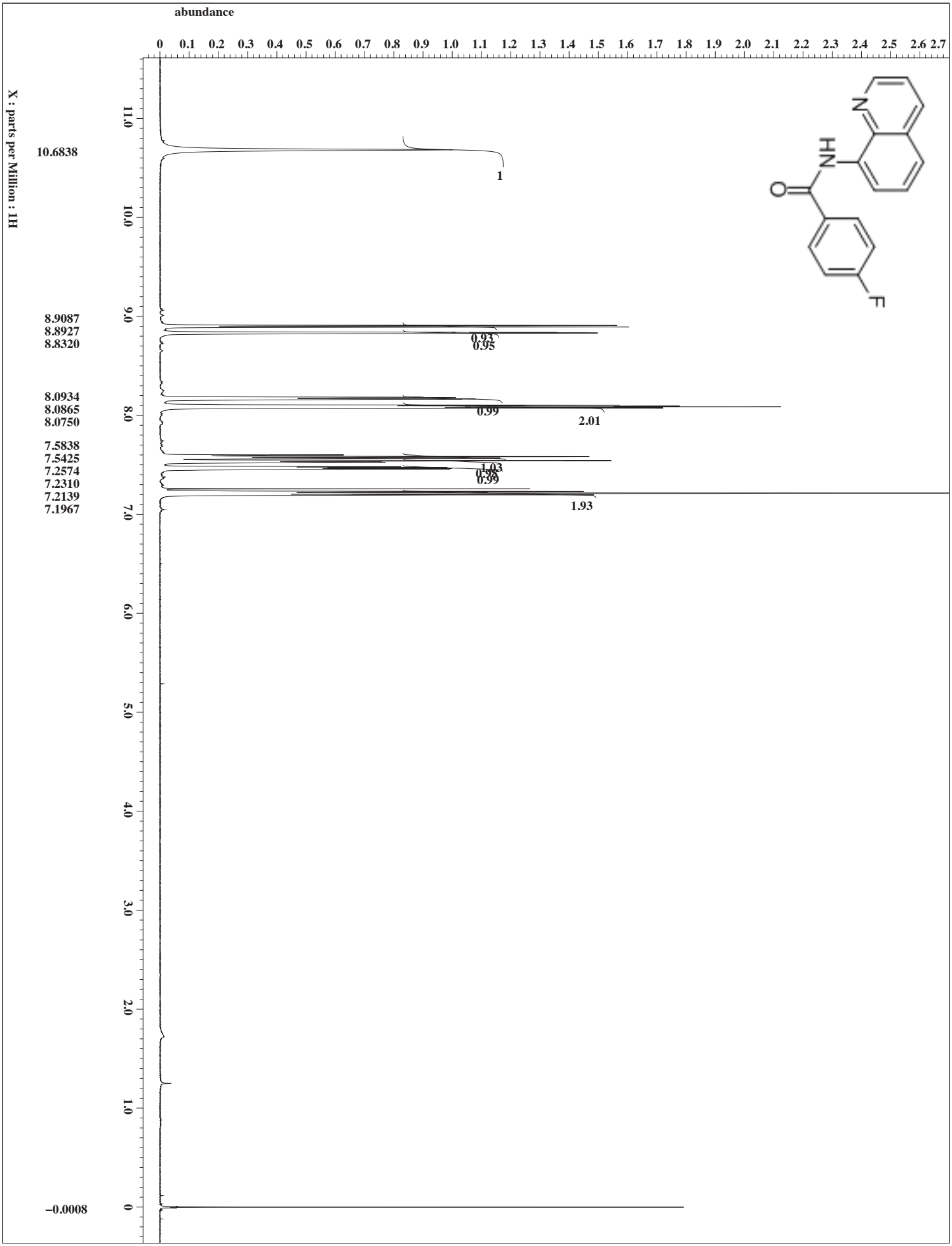
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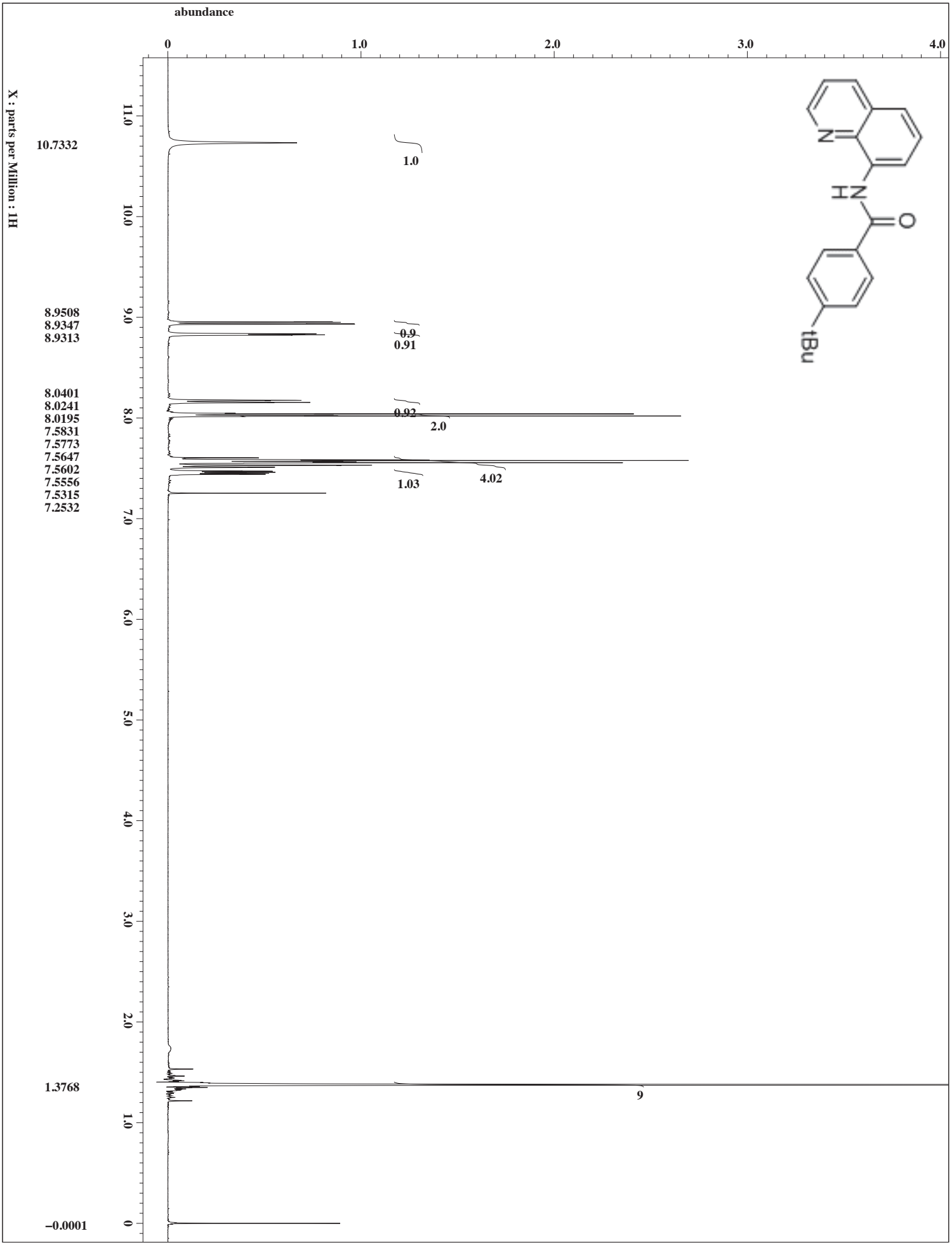
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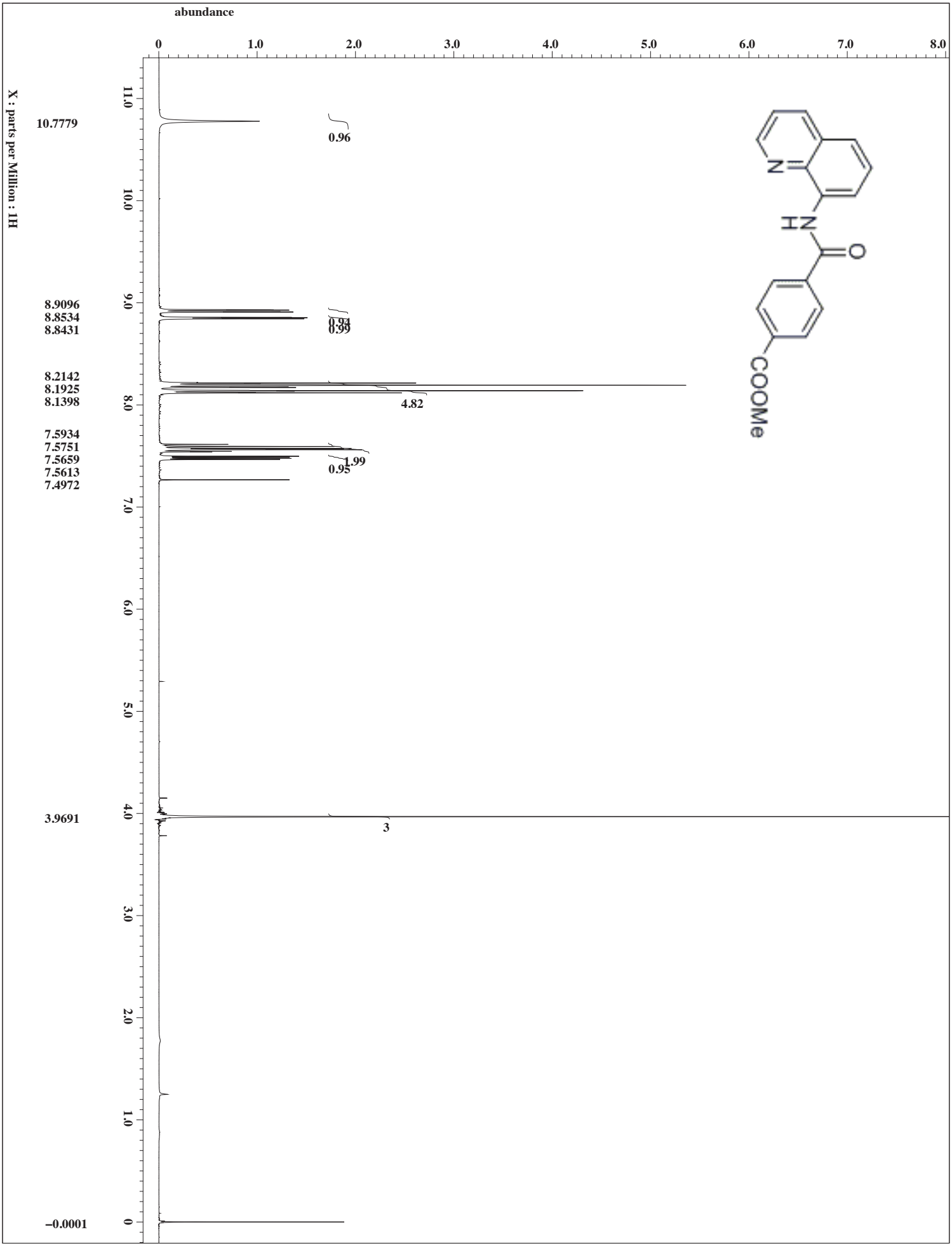
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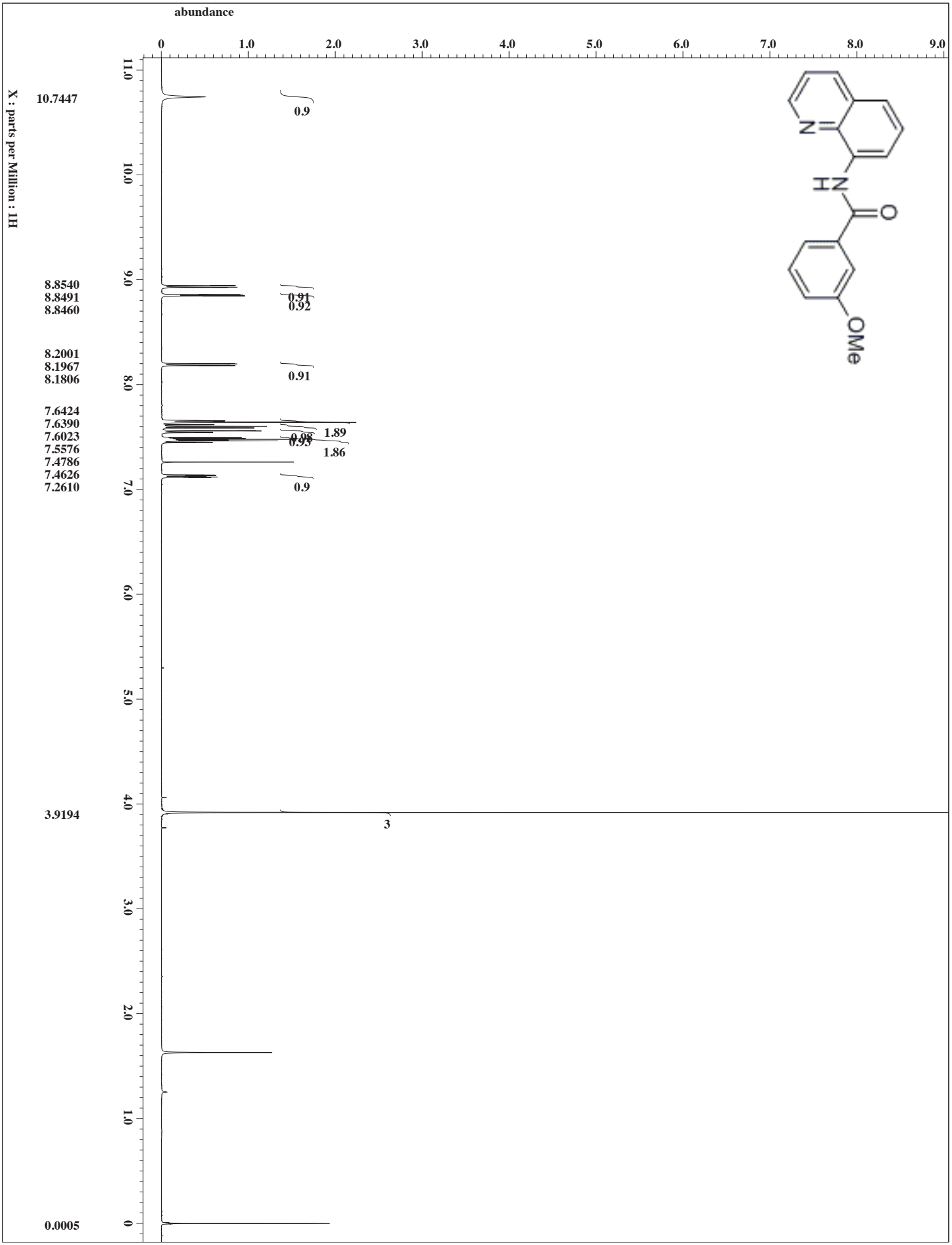
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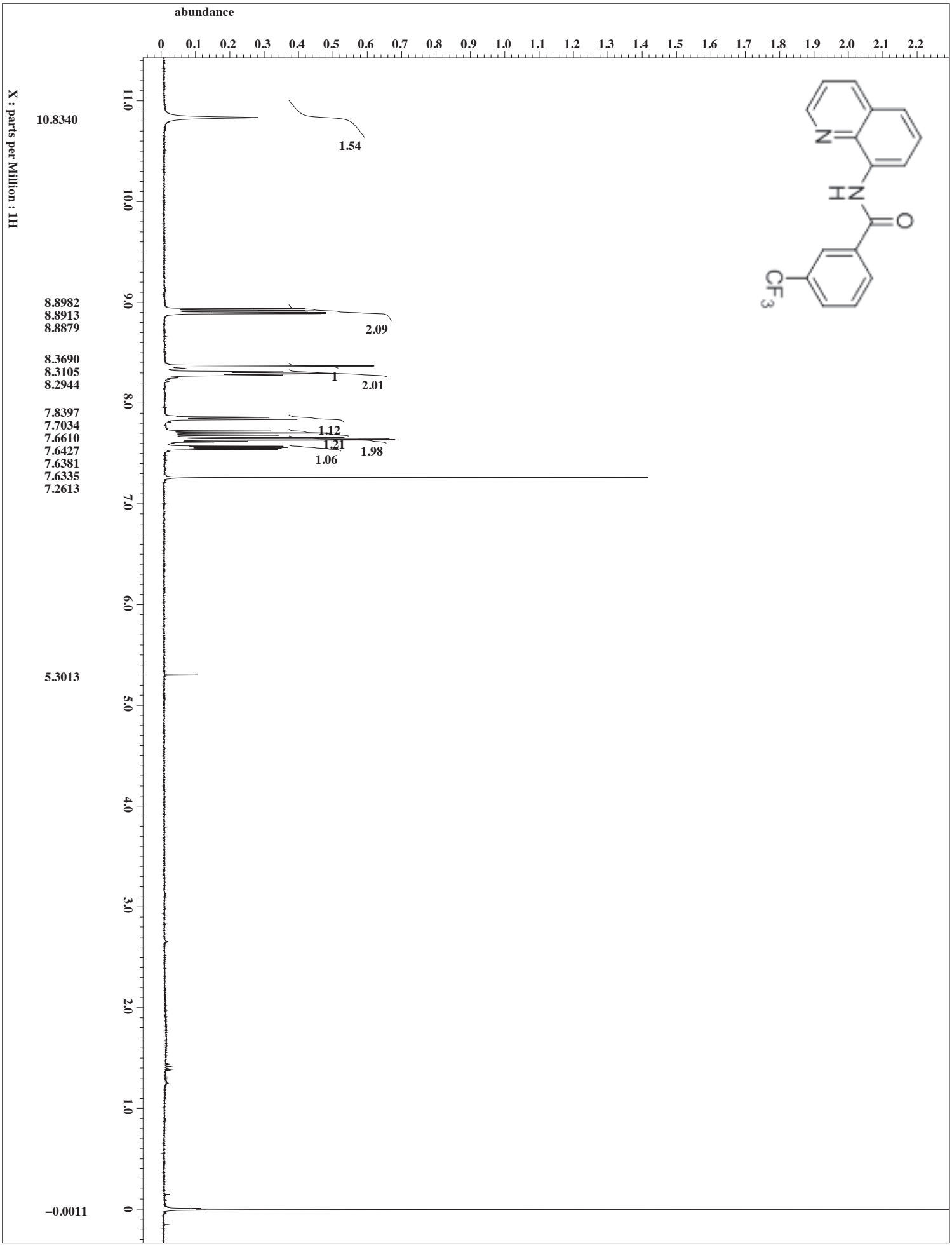
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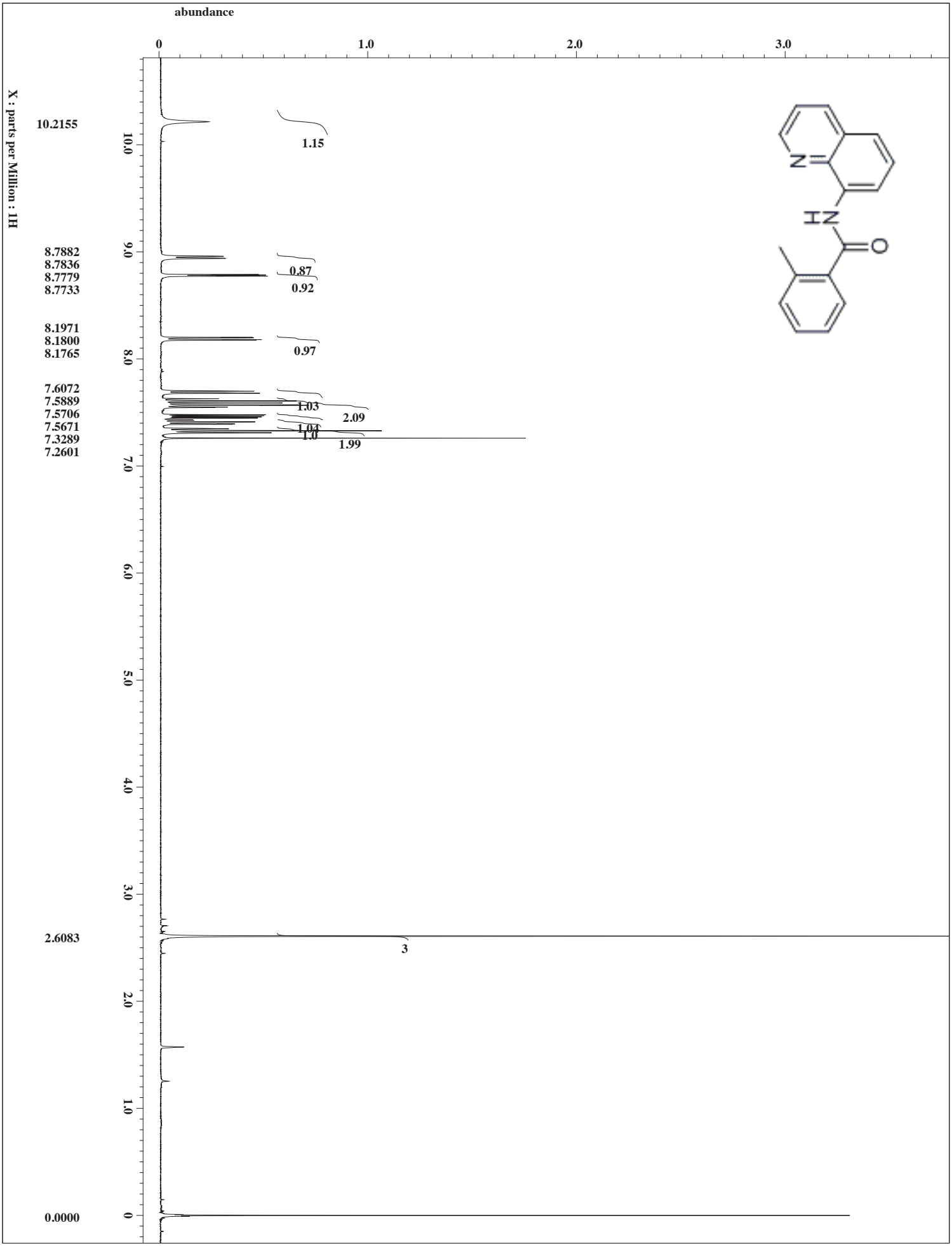
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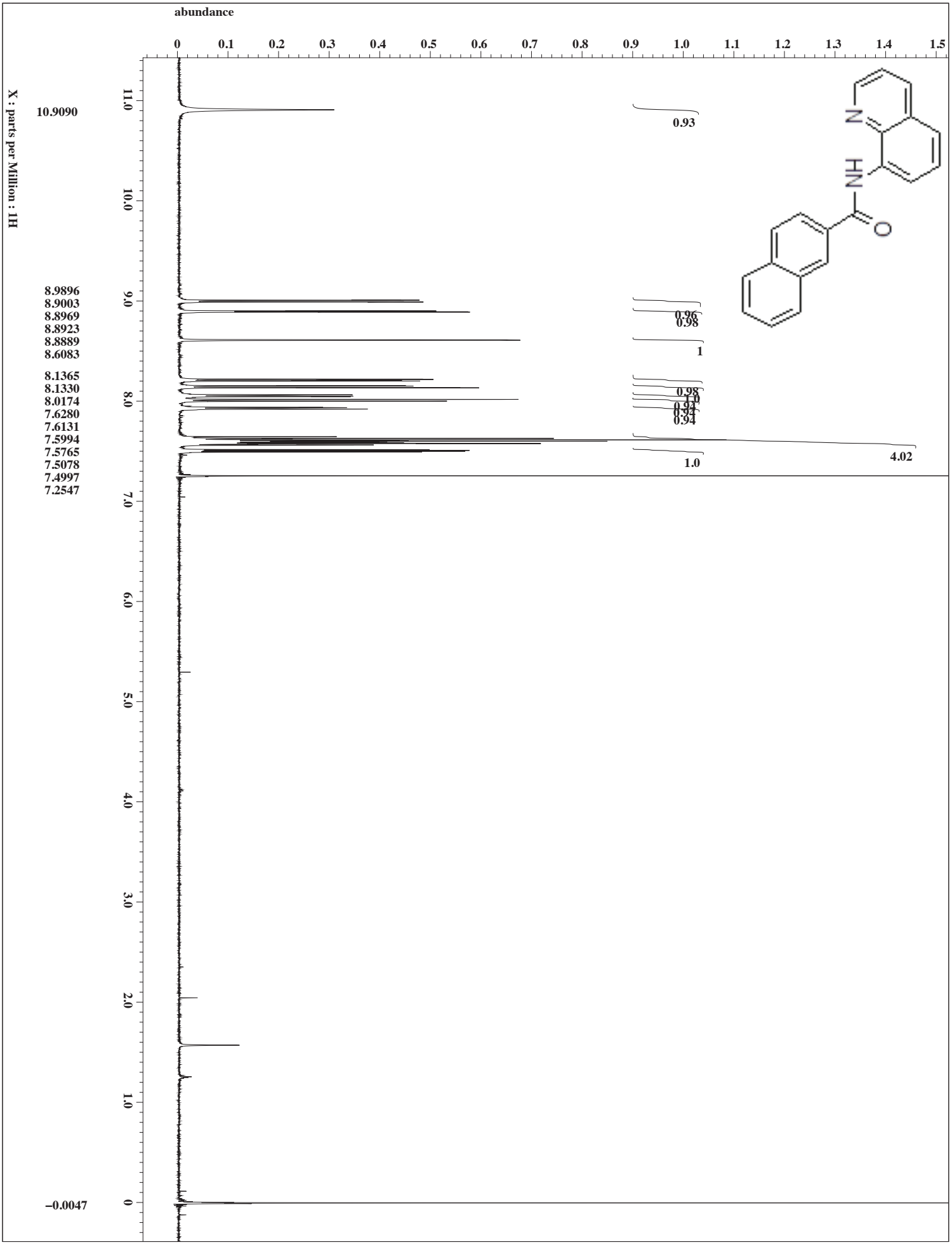
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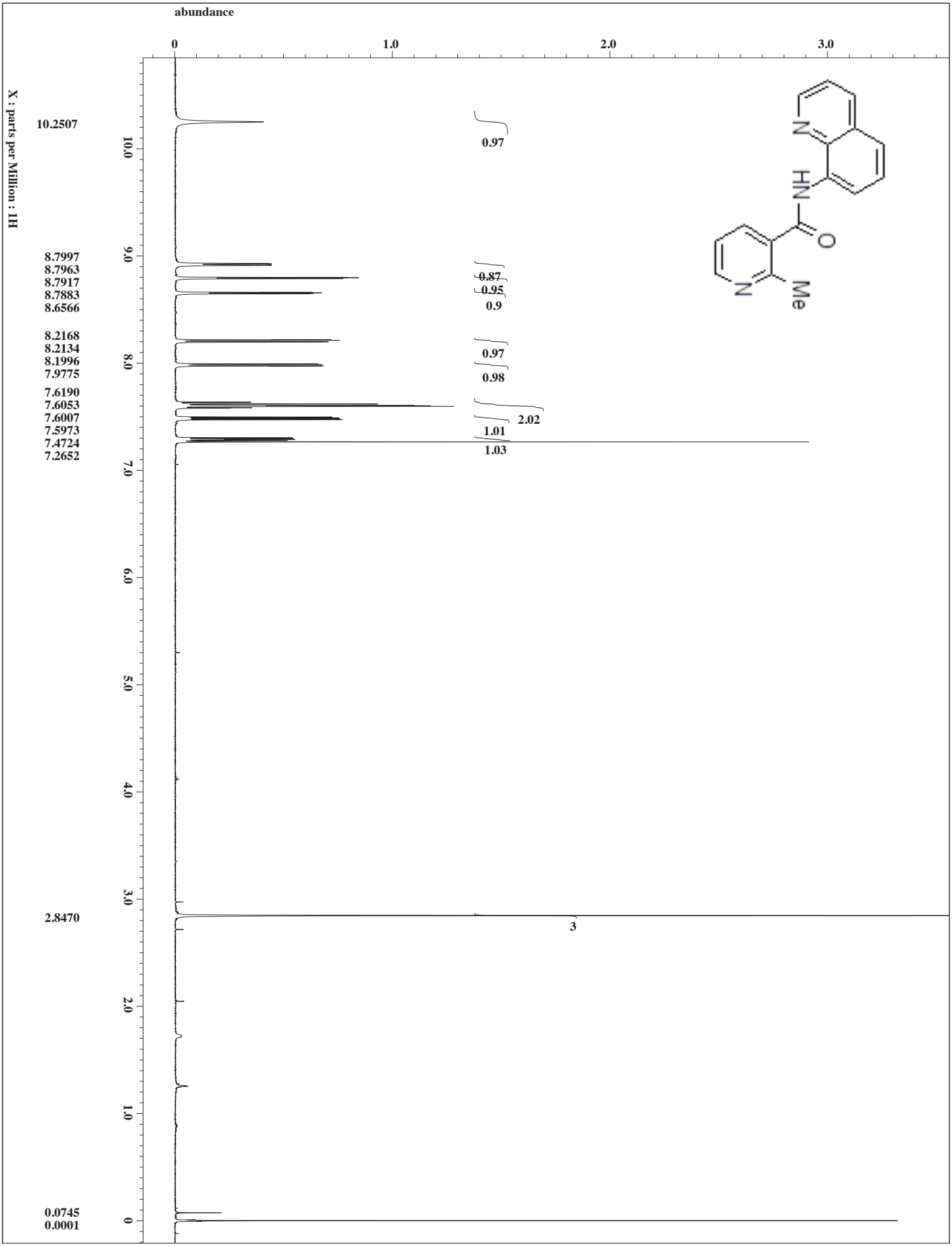
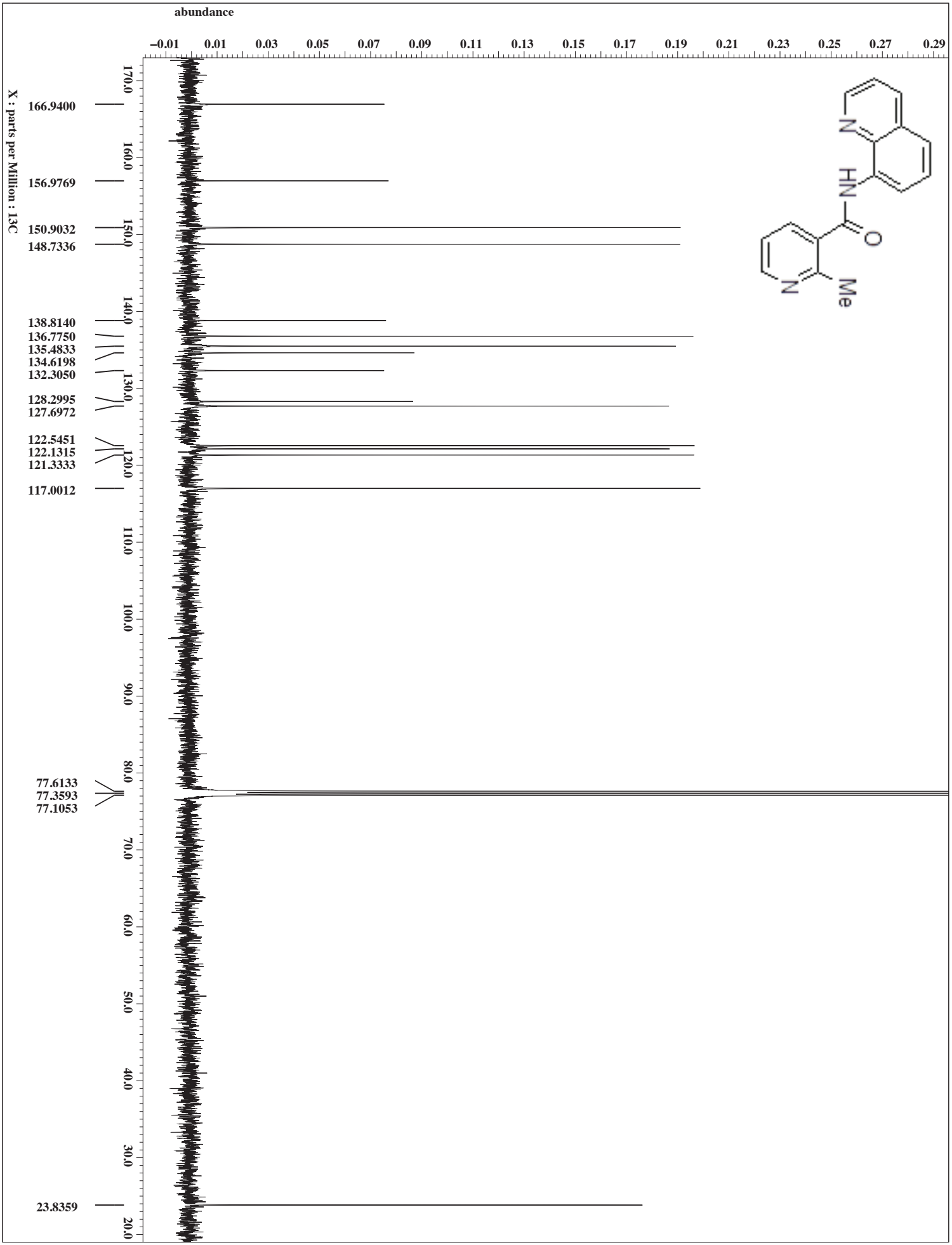
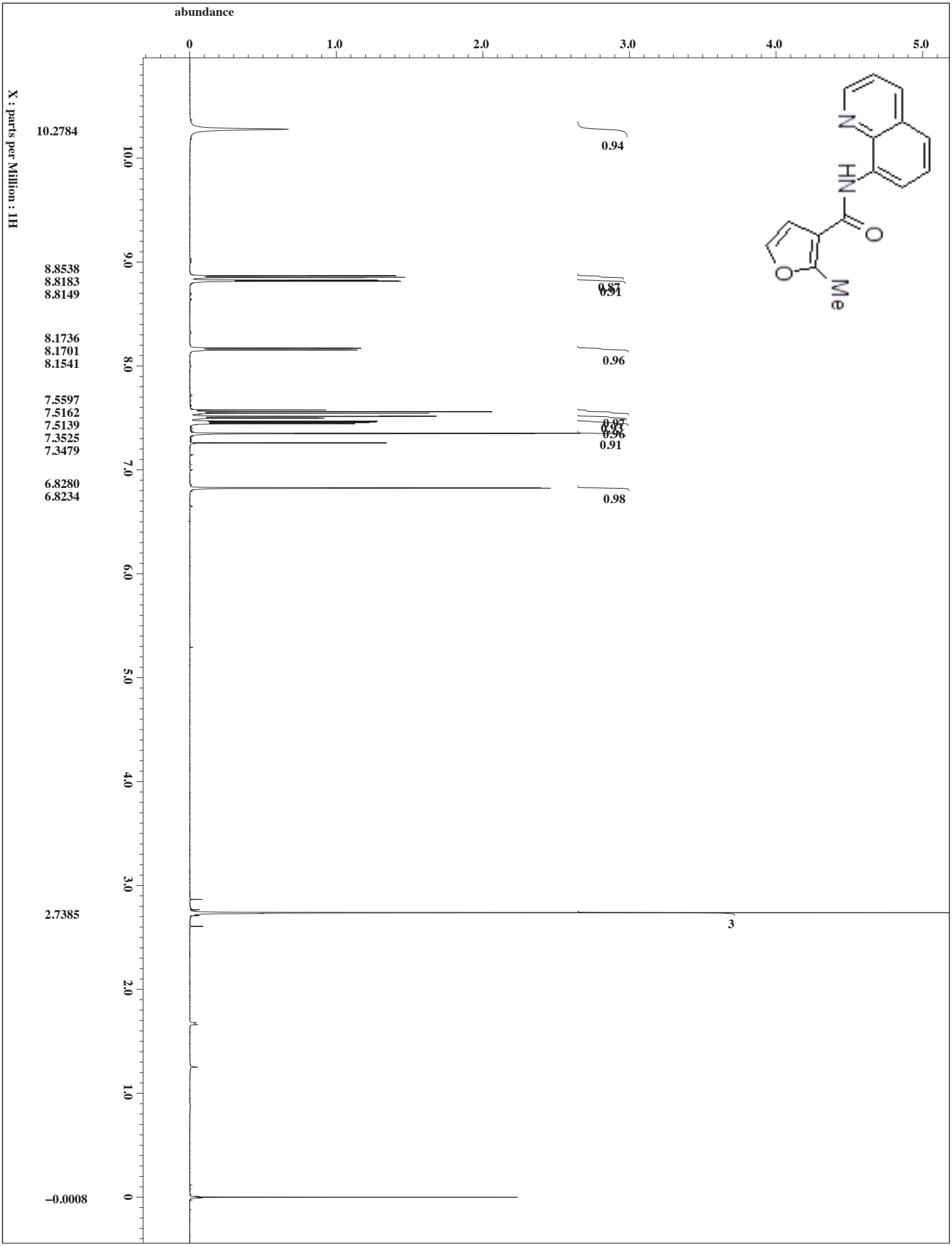
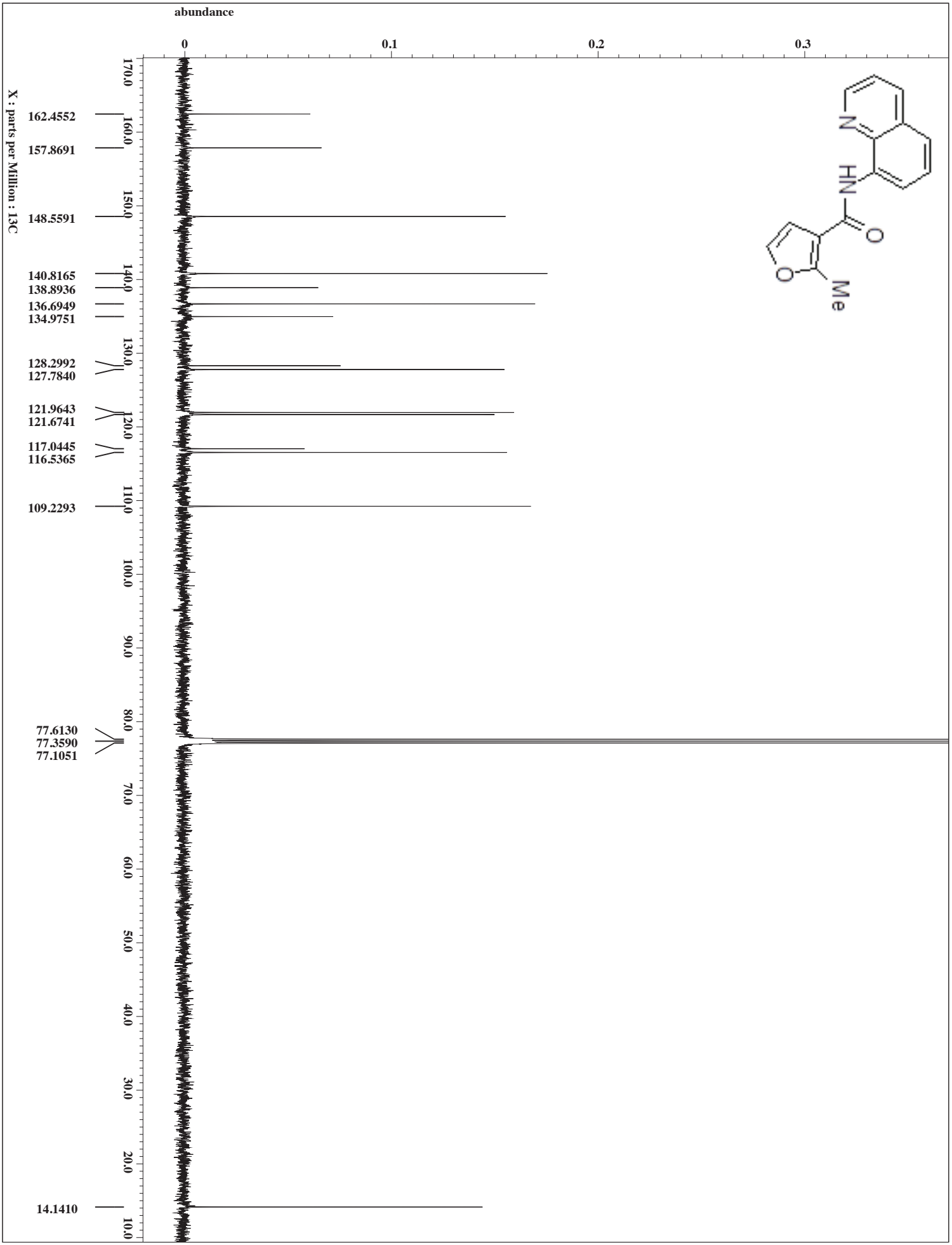
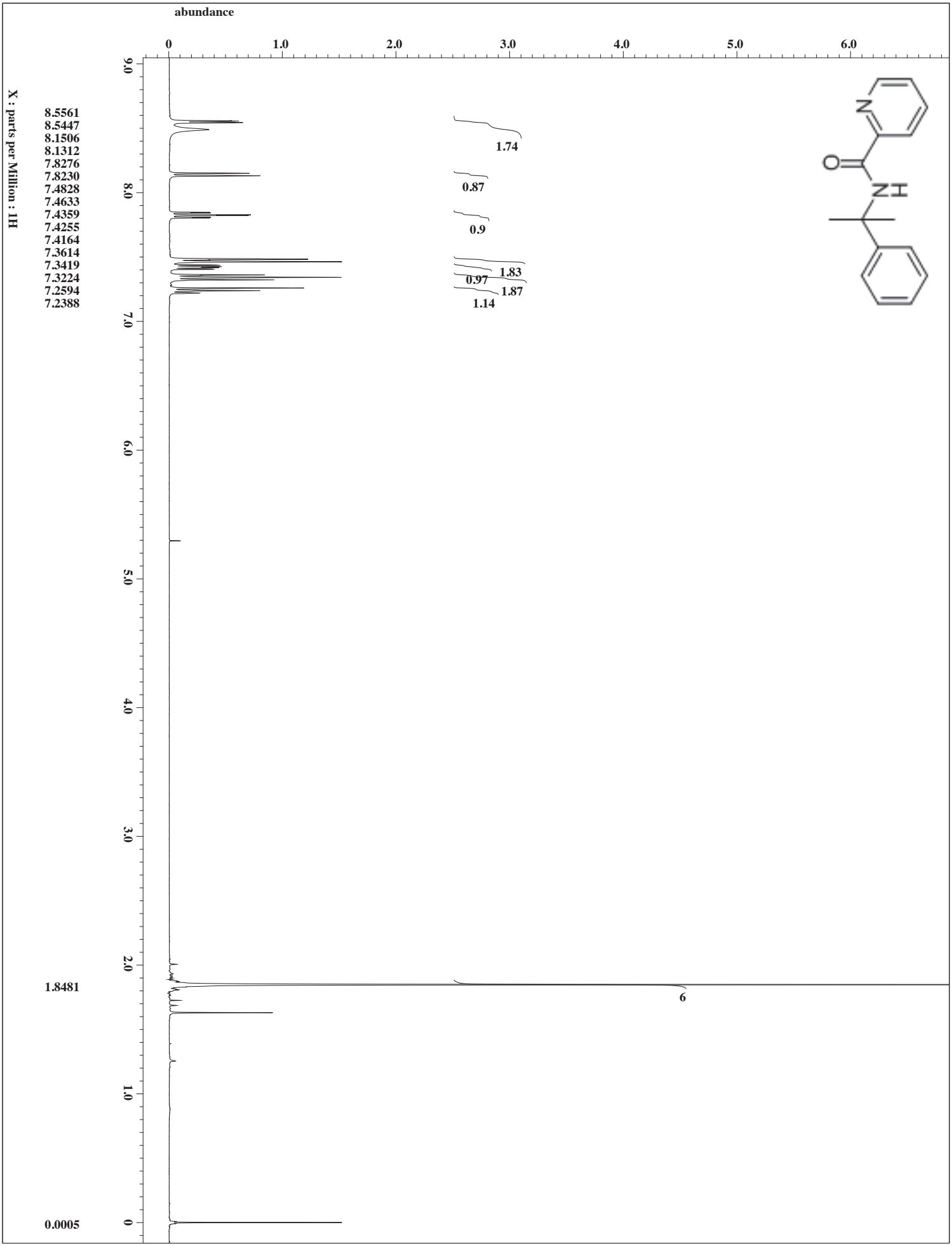
0.6
0.7
0.8
0.9
1.0
1.1
1.2
1.3
1.4
1.5
X : parts per Million : 1H
10.9090
8.9896
8.9003
8.8969
8.8923
8.8889
8.6083
8.1365
8.1330
8.0174
7.6280
7.6131
7.5994
7.5765
7.5078
7.4997
7.2547
−0.0047
0.93
0.96
0.98
1
0.98
1.0
0.91
0.94
0.94
1.0
4.02
N
NH
O

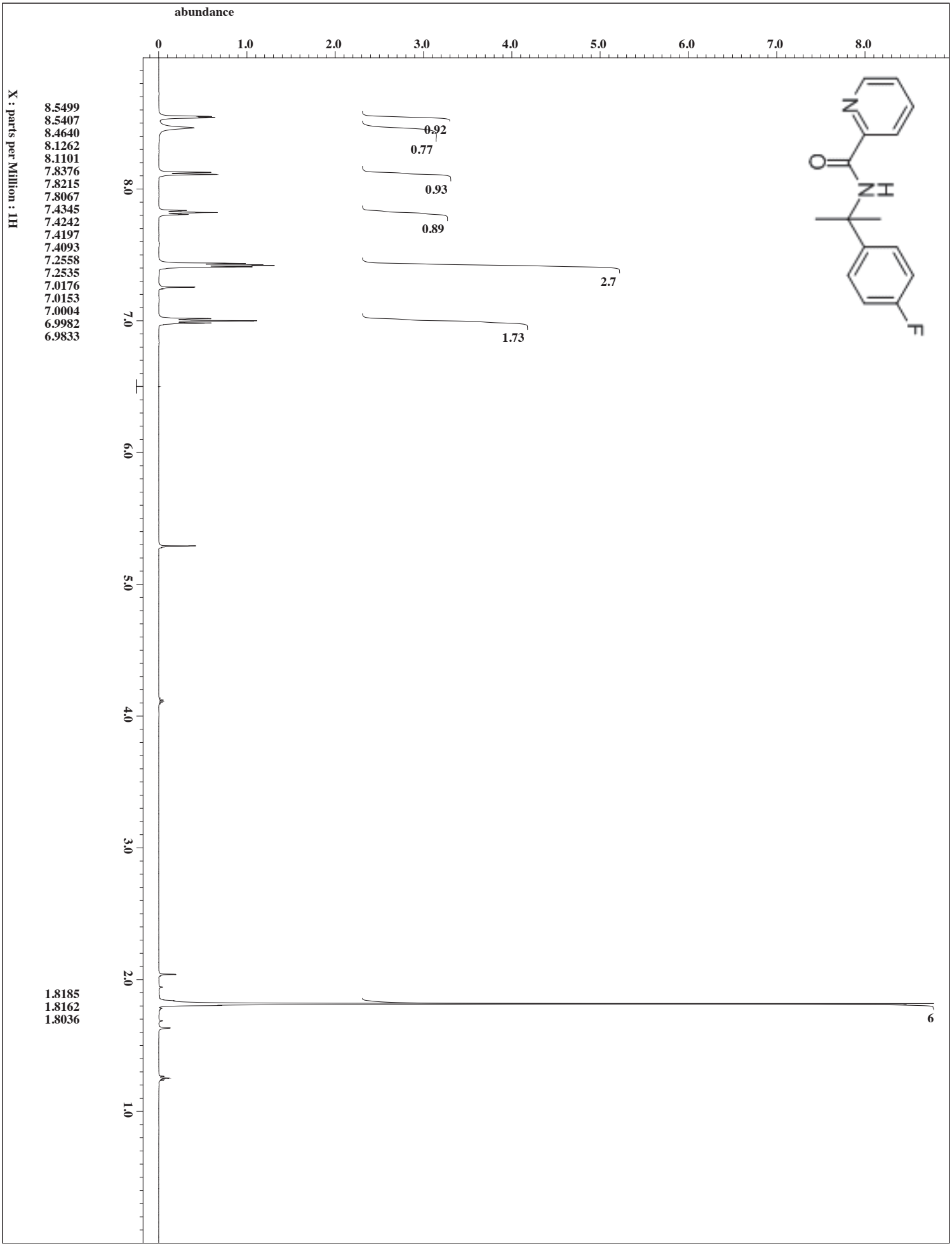

abundance
0
1.0
2.0
3.0
X : parts per Million : 1H
10.2507
8.7997
8.7963
8.7917
8.7883
8.6566
8.2168
8.2134
8.1996
7.9775
7.6190
7.6053
7.6007
7.5973
7.4724
7.2652
2.8470
0.0745
0.0001
0.97
0.87
0.95
0.9
0.97
0.98
2.02
1.01
1.03
3
HN
O
N
Me

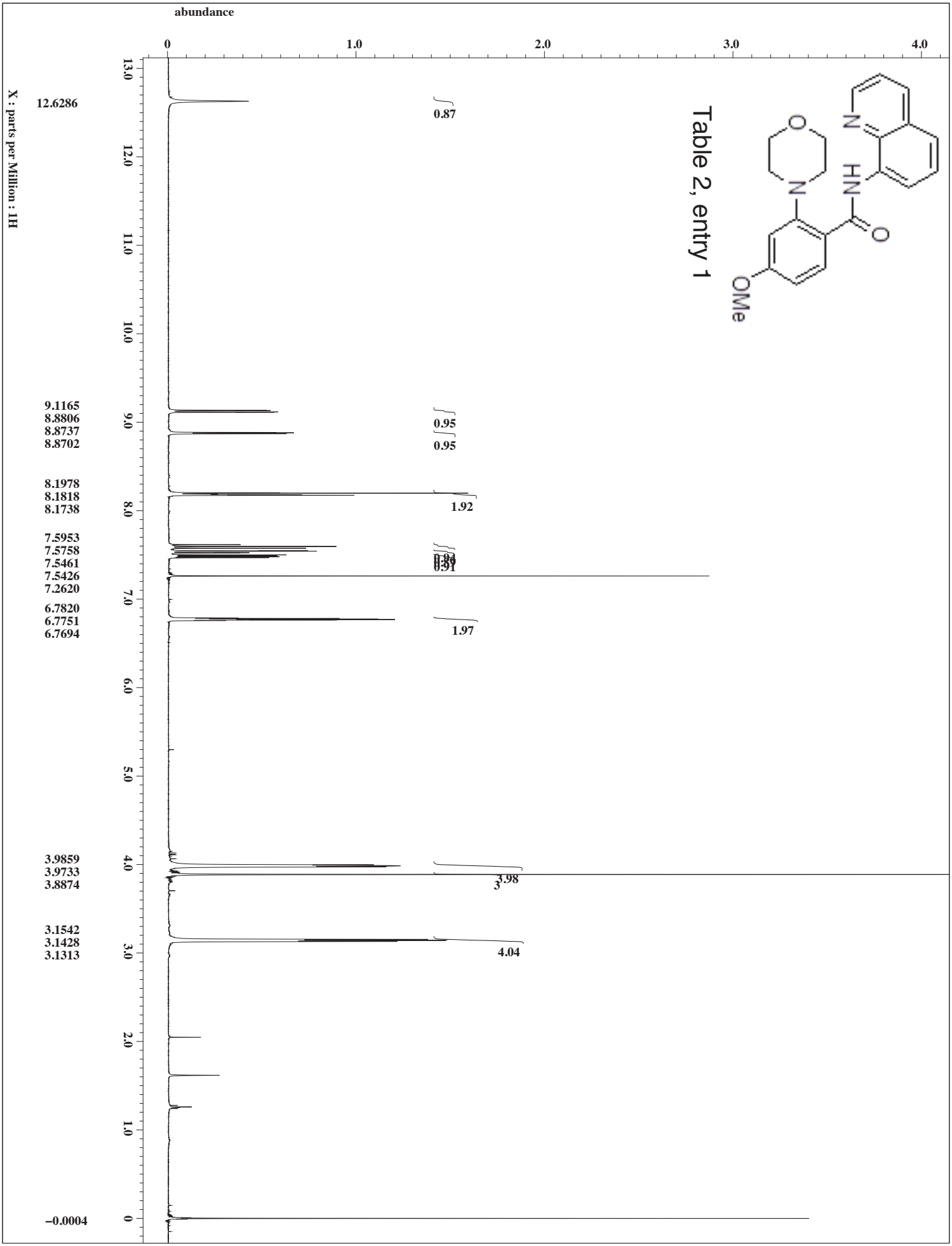

abundance
−0.01 0.01 0.03 0.05 0.07 0.09 0.11 0.13 0.15 0.17 0.19 0.21 0.23 0.25 0.27 0.29
X : parts per Million : 13C
166.9400
156.9769
150.9032
148.7336
138.8140
136.7750
135.4833
134.6198
132.3050
128.2995
127.6972
122.5451
122.1315
121.3333
117.0012
77.6133
77.3593
77.1053
23.8359
170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0
N
HN
O
N
Me

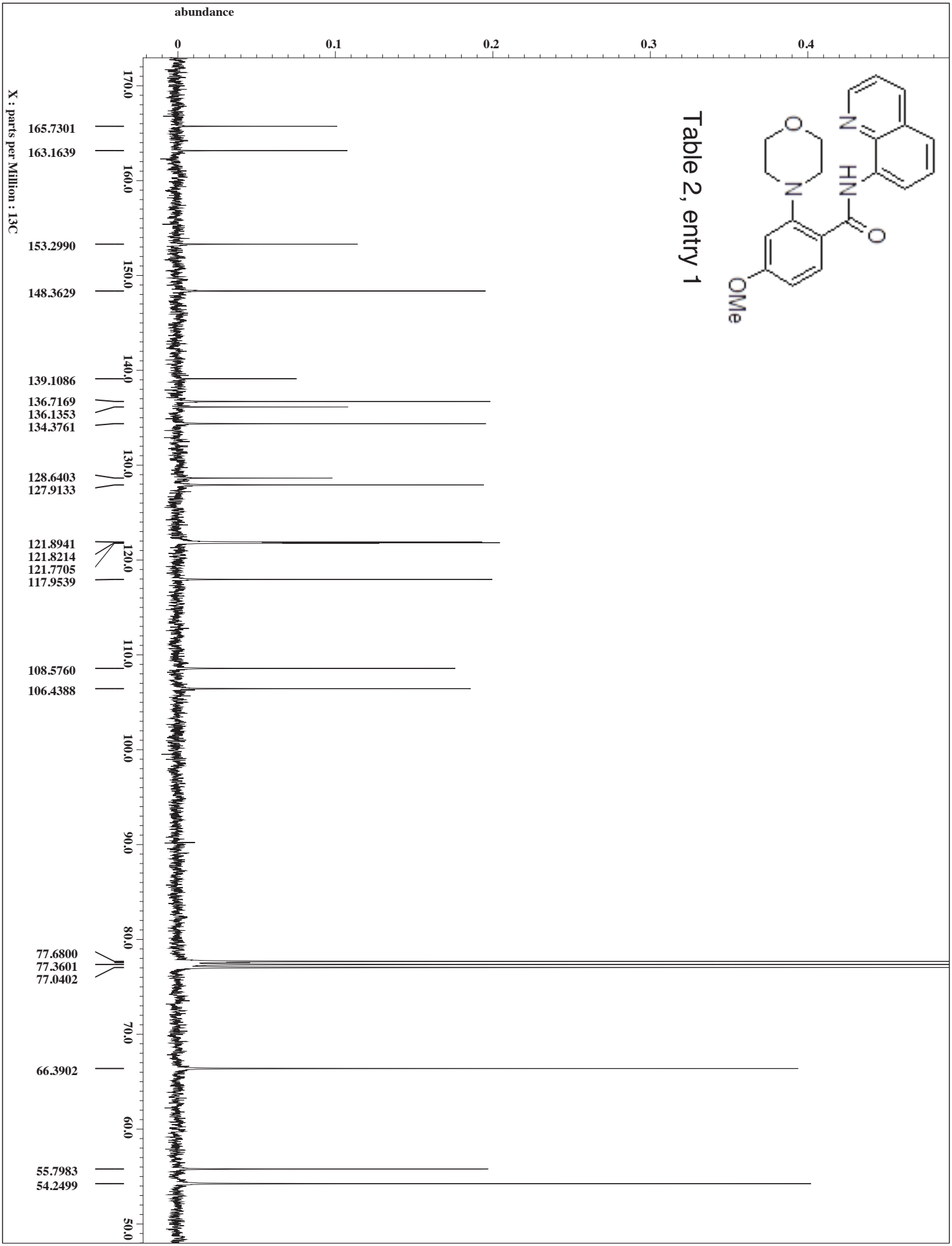

abundance
0
1.0
2.0
3.0
4.0
5.0
X : parts per Million : 1H
10.2784
8.8538
8.8183
8.8149
8.1736
8.1701
8.1541
7.5597
7.5162
7.5139
7.3525
7.3479
6.8280
6.8234
2.7385
−0.0008
0.94
0.91
0.96
0.91
0.98
3
HN
O
O
N
Me

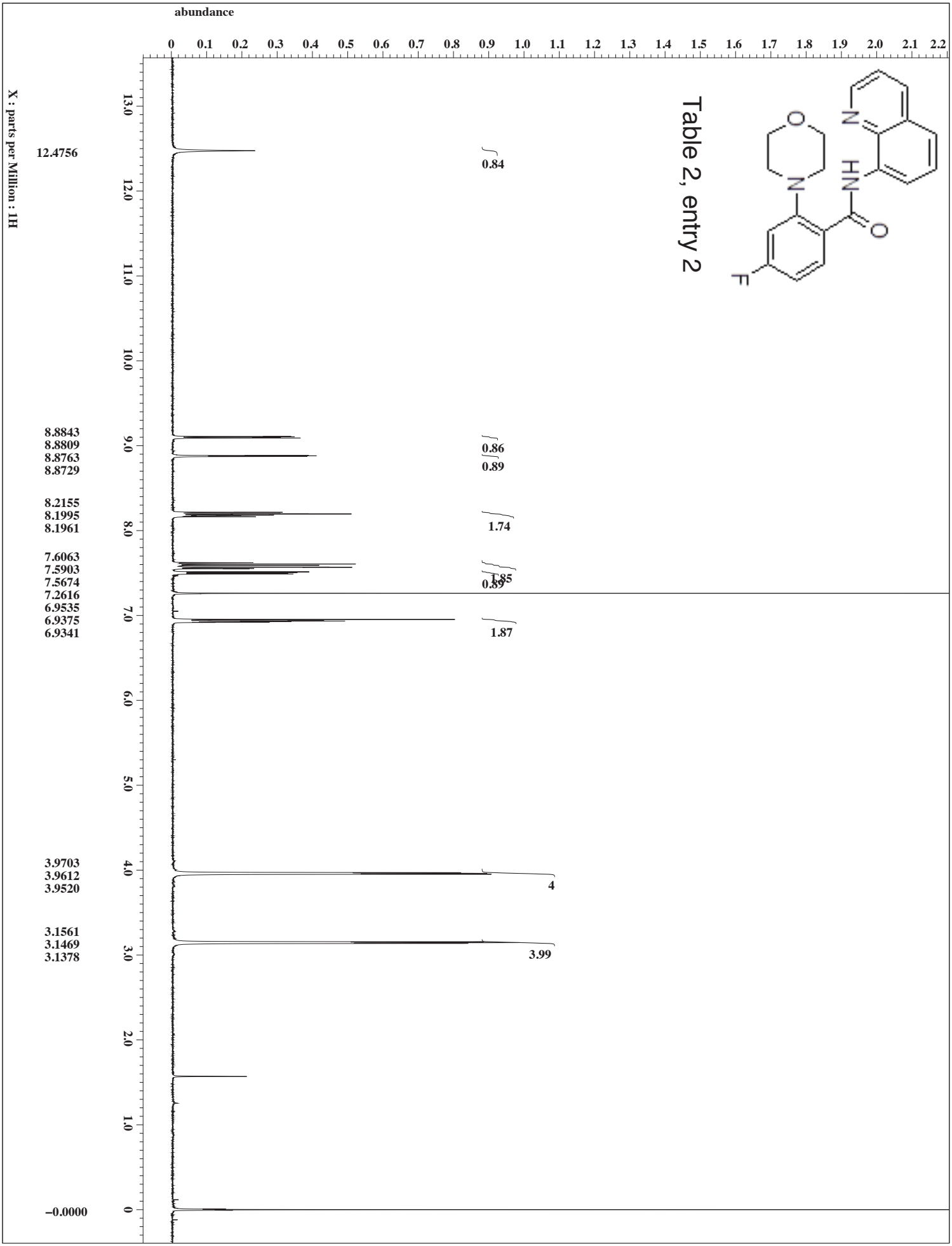

abundance
0
0.1
0.2
0.3
X : parts per Million : 13C
162.4552
157.8691
148.5591
140.8165
138.8936
136.6949
134.9751
128.2992
127.7840
121.9643
121.6741
117.0445
116.5365
109.2293
77.6130
77.3590
77.1051
14.1410
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
N
HN
O
O
Me

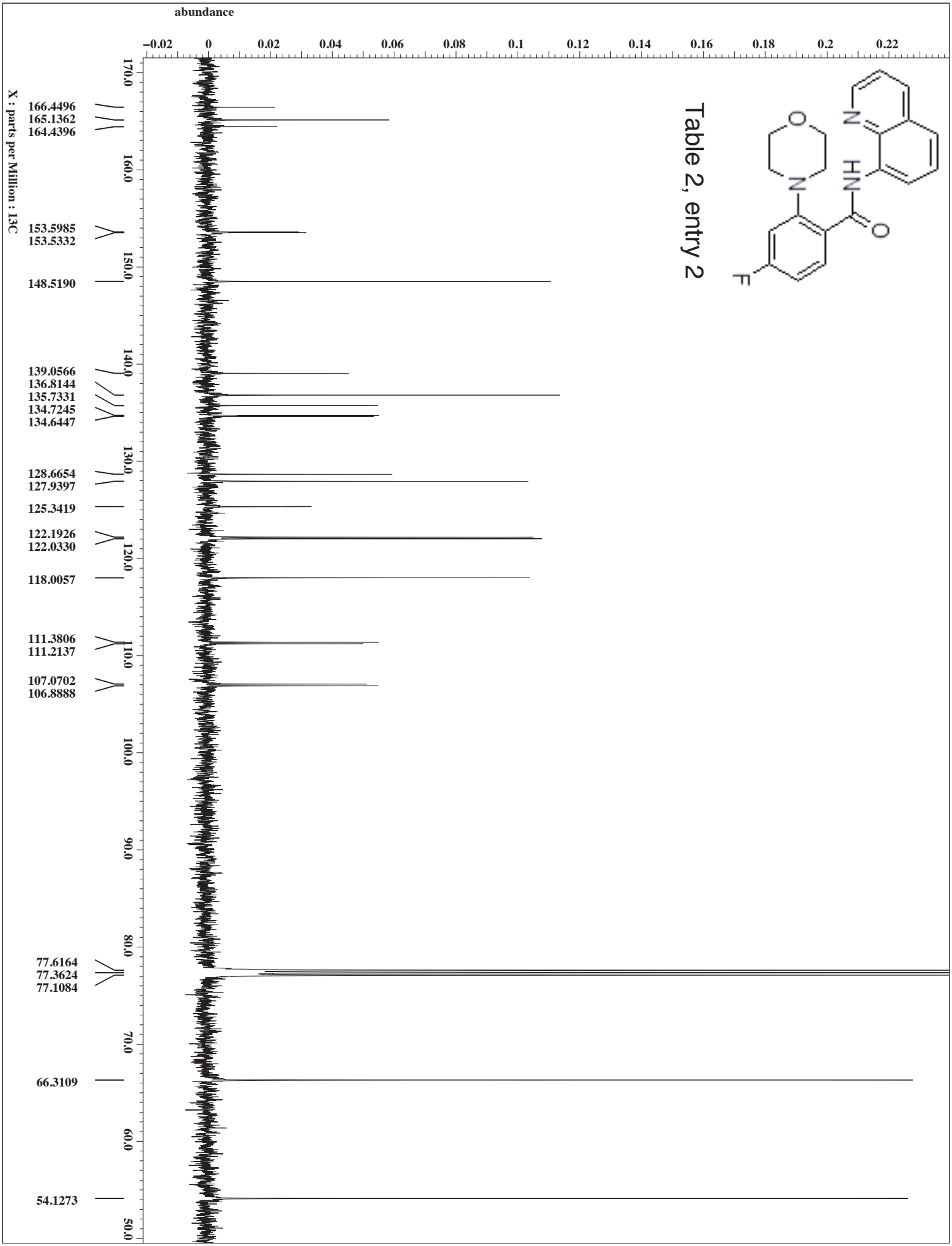

abundance
0
1.0
2.0
3.0
4.0
5.0
6.0
X : parts per Million : 1H
8.5561
8.5447
8.1506
8.1312
7.8276
7.8230
7.4828
7.4633
7.4359
7.4255
7.4164
7.3614
7.3419
7.3224
7.2594
7.2388
1.74
0.87
0.9
1.83
0.97
1.87
1.14
1.8481
6
0.0005
N
O
NH

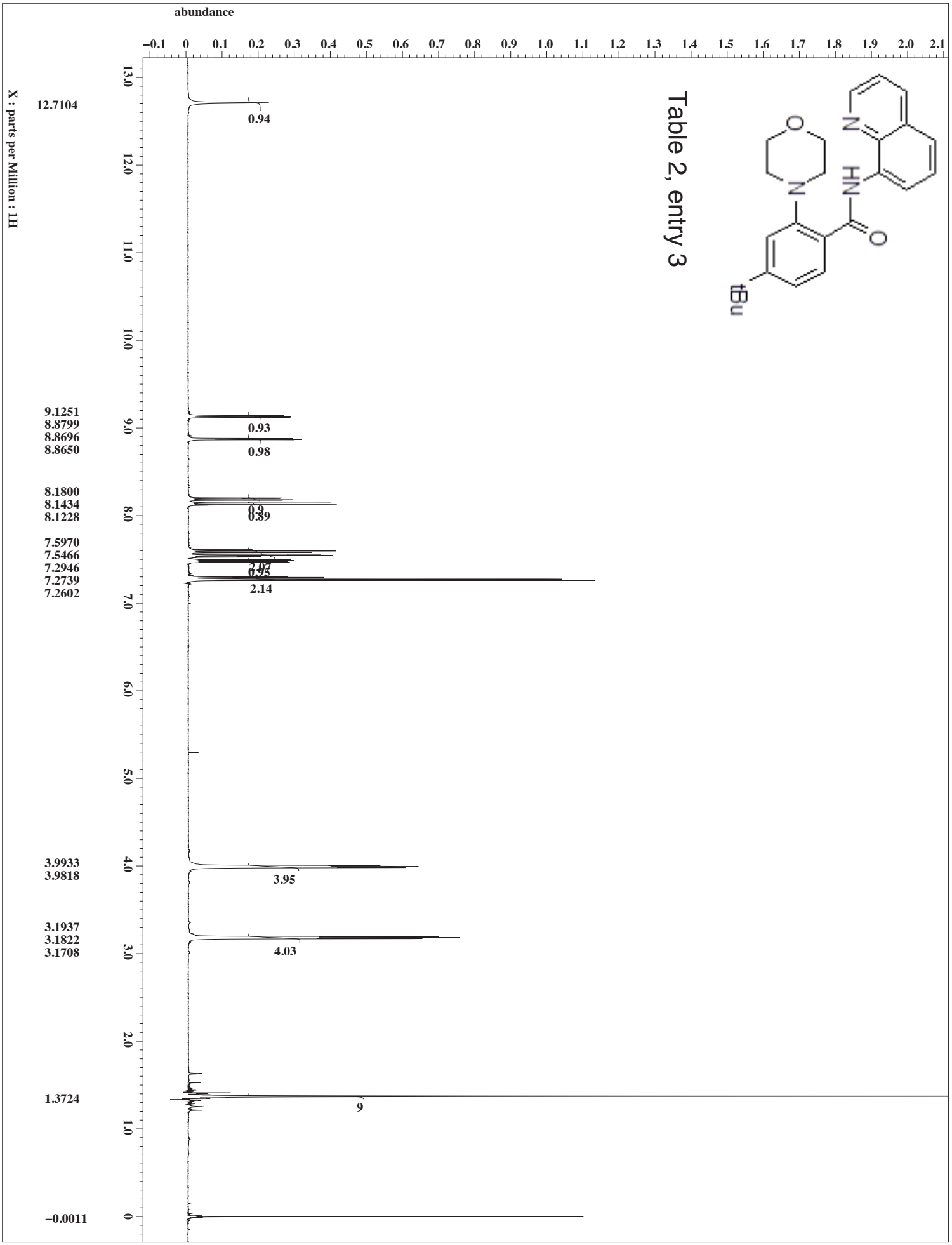

abundance
0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
X : parts per Million : 1H
8.5499
8.5407
8.4640
8.1262
8.1101
7.8376
7.8215
7.8067
7.4345
7.4242
7.4197
7.4093
7.2558
7.2535
7.0176
7.0153
7.0004
6.9982
6.9833
1.8185
1.8162
1.8036
0.92
0.77
0.93
0.89
2.7
1.73
6
N
O
NH
F

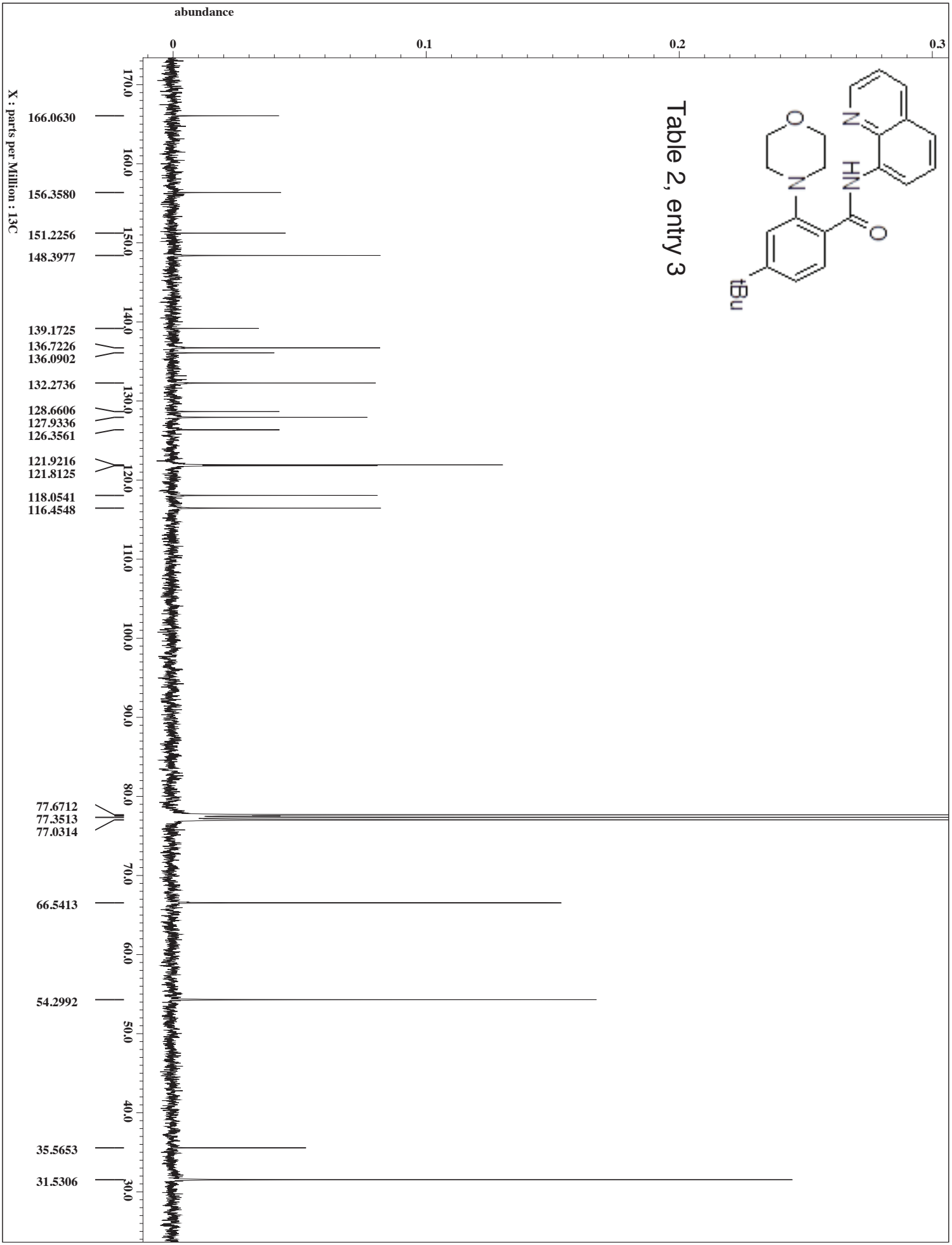

abundance
X : parts per Million : 1H
Table 2, entry 1
OMe
12.6286
9.1165
8.8806
8.8737
8.8702
8.1978
8.1818
8.1738
7.5953
7.5758
7.5461
7.5426
7.2620
6.7820
6.7751
6.7694
3.9859
3.9733
3.8874
3.1542
3.1428
3.1313
−0.0004
0.87
0.95
0.95
1.92
0.91
1.97
3.98
4.04

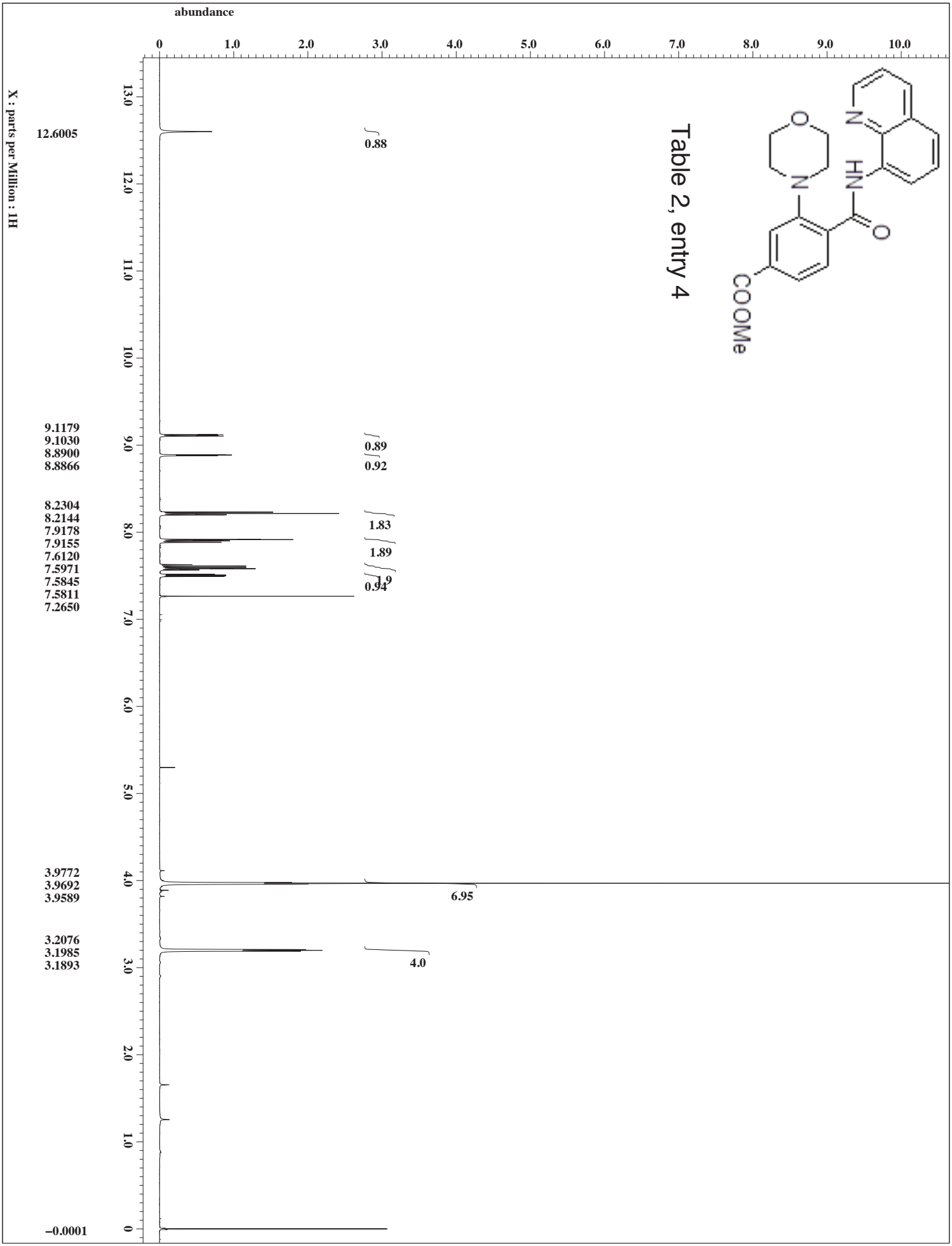

abundance
0
0.1
0.2
0.3
0.4
X : parts per Million : 13C
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
165.7301
163.1639
153.2990
148.3629
139.1086
136.7169
136.1353
134.3761
128.6403
127.9133
121.8941
121.8214
121.7705
117.9539
108.5760
106.4388
77.6800
77.3601
77.0402
66.3902
55.7983
54.2499
Table 2, entry 1
N
O
HN
O
N
OMe

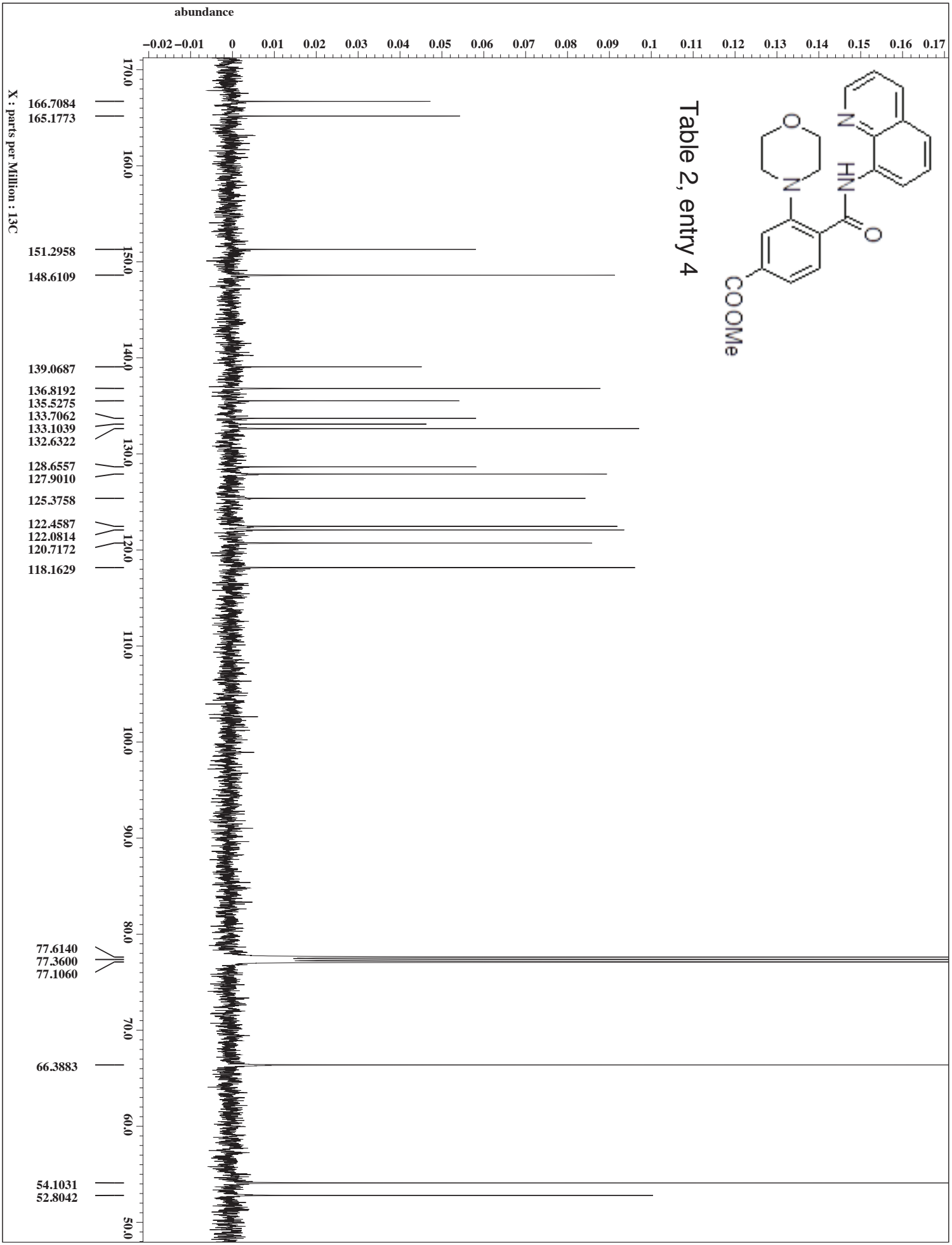

abundance
X : parts per Million : 1H
Table 2, entry 2
12.4756
8.8843
8.8809
8.8763
8.8729
8.2155
8.1995
8.1961
7.6063
7.5903
7.5674
7.2616
6.9535
6.9375
6.9341
3.9703
3.9612
3.9520
3.1561
3.1469
3.1378
−0.0000
0.84
0.86
0.89
1.74
1.85
0.89
1.87
4
3.99
HN
O
N
F

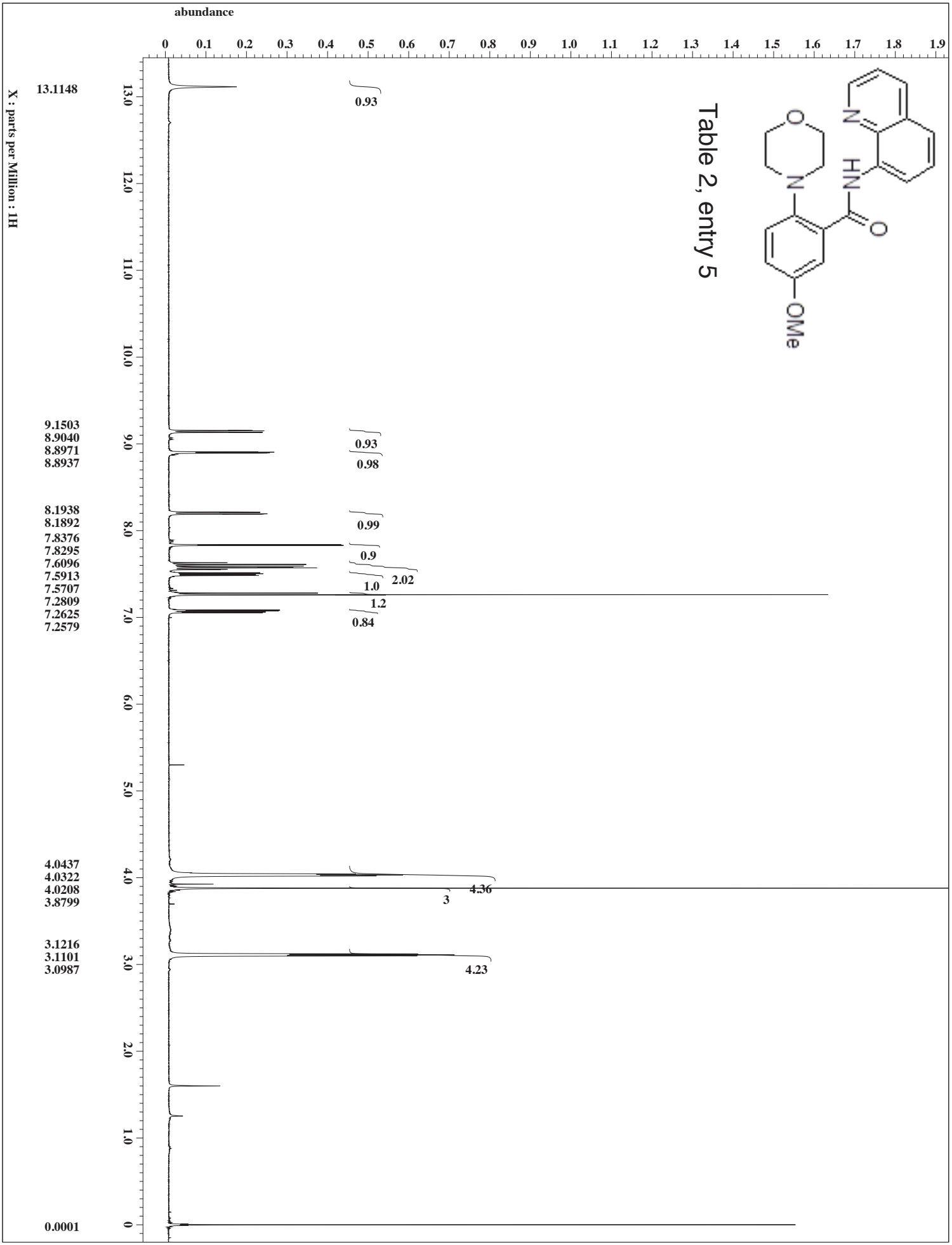

abundance
−0.02
0
0.02
0.04
0.06
0.08
0.1
0.12
0.14
0.16
0.18
0.2
0.22
X : parts per Million : 13C
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
166.4496
165.1362
164.4396
153.5985
153.5332
148.5190
139.0566
136.8144
135.7331
134.7245
134.6447
128.6654
127.9397
125.3419
122.1926
122.0330
118.0057
111.3806
111.2137
107.0702
106.8888
77.6164
77.3624
77.1084
66.3109
54.1273
Table 2, entry 2
O
N
HN
O
N
F

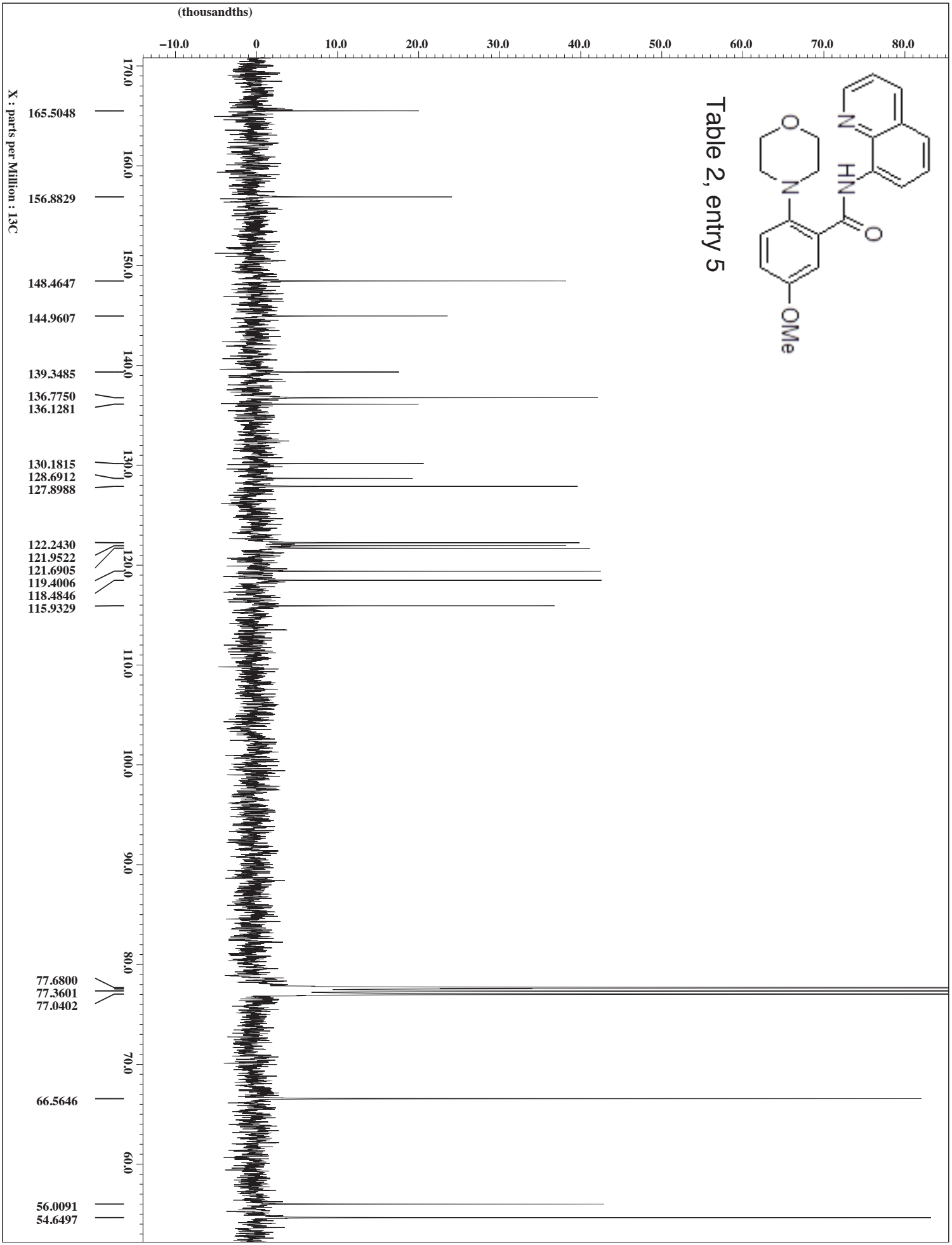

abundance
X : parts per Million : 1H
Table 2, entry 3
12.7104
9.1251
8.8799
8.8696
8.8650
8.1800
8.1434
8.1228
7.5970
7.5466
7.2946
7.2739
7.2602
3.9933
3.9818
3.1937
3.1822
3.1708
1.3724
−0.0011
0.94
0.93
0.98
0.9
0.89
2.14
3.95
4.03
9
tBu
HN
O
N

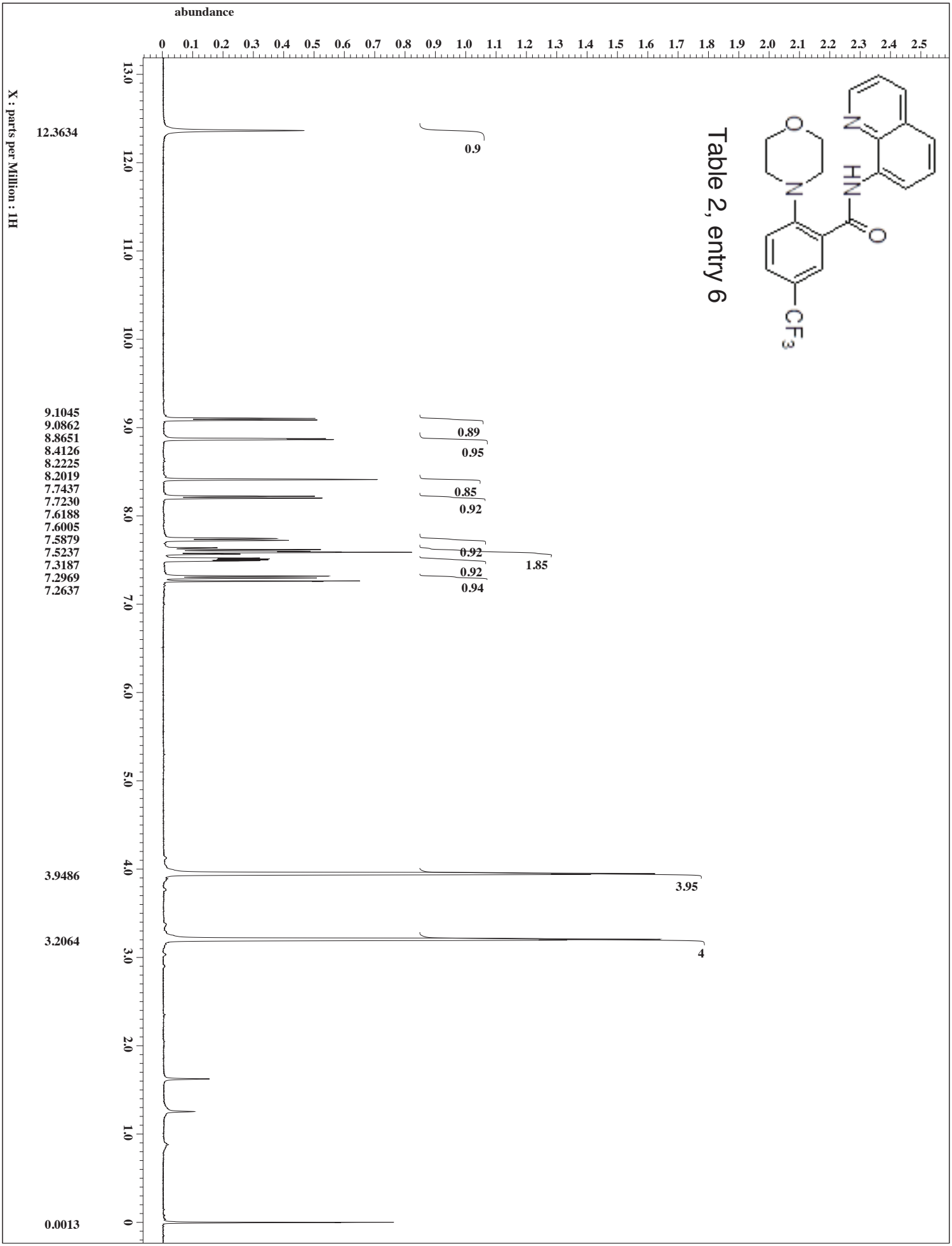

abundance
0
0.1
0.2
0.3
X : parts per Million : 13C
166.0630
156.3580
151.2256
148.3977
139.1725
136.7226
136.0902
132.2736
128.6606
127.9336
126.3561
121.9216
121.8125
118.0541
116.4548
77.6712
77.3513
77.0314
66.5413
54.2992
35.5653
31.5306
Table 2, entry 3
O
N
HN
O
tBu

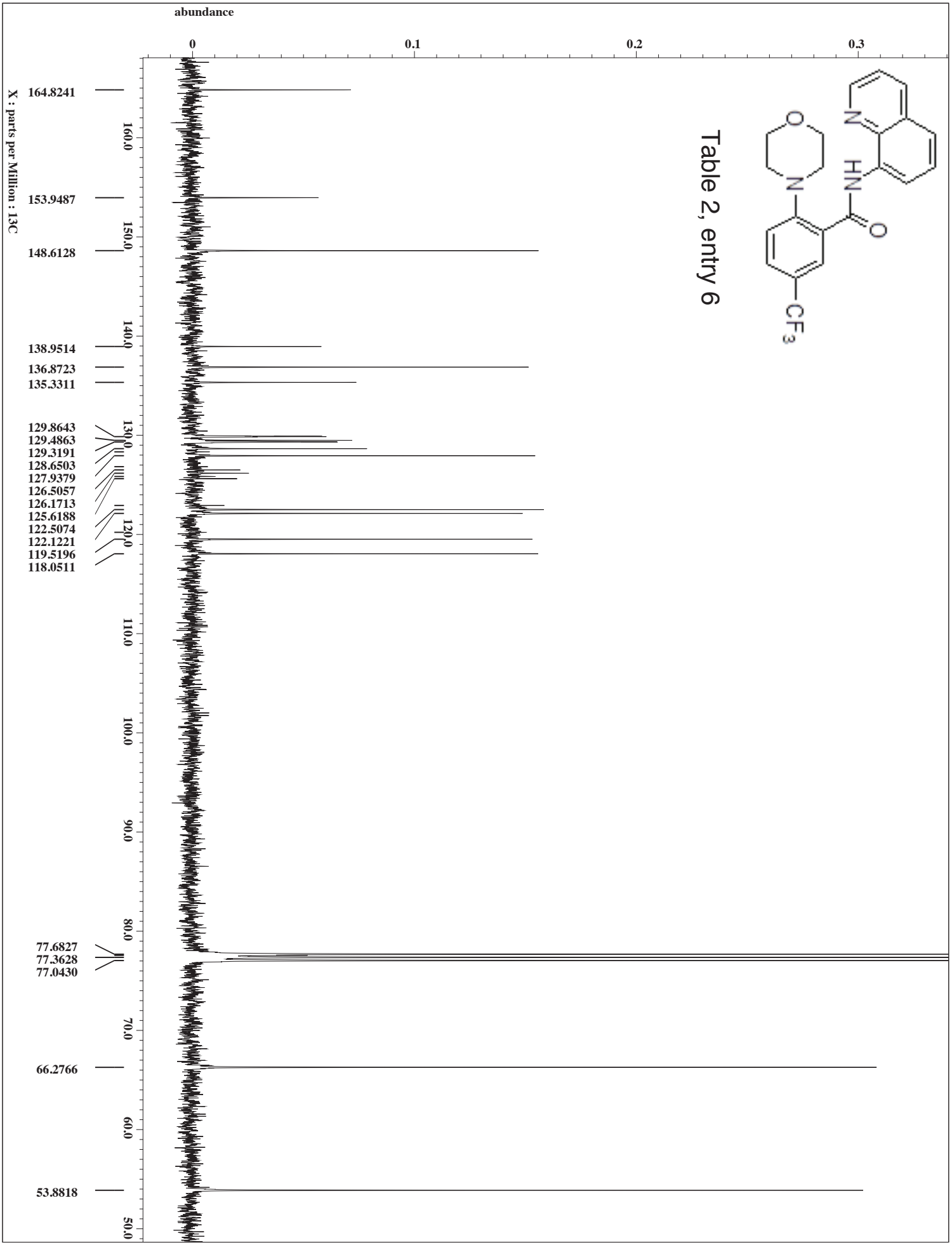

abundance
X : parts per Million : 1H
Table 2, entry 4
COOMe
12.6005
9.1179
9.1030
8.8900
8.8866
8.2304
8.2144
7.9178
7.9155
7.6120
7.5971
7.5845
7.5811
7.2650
3.9772
3.9692
3.9589
3.2076
3.1985
3.1893
−0.0001
0.88
0.89
0.92
1.83
1.89
1.9
0.94
6.95
4.0

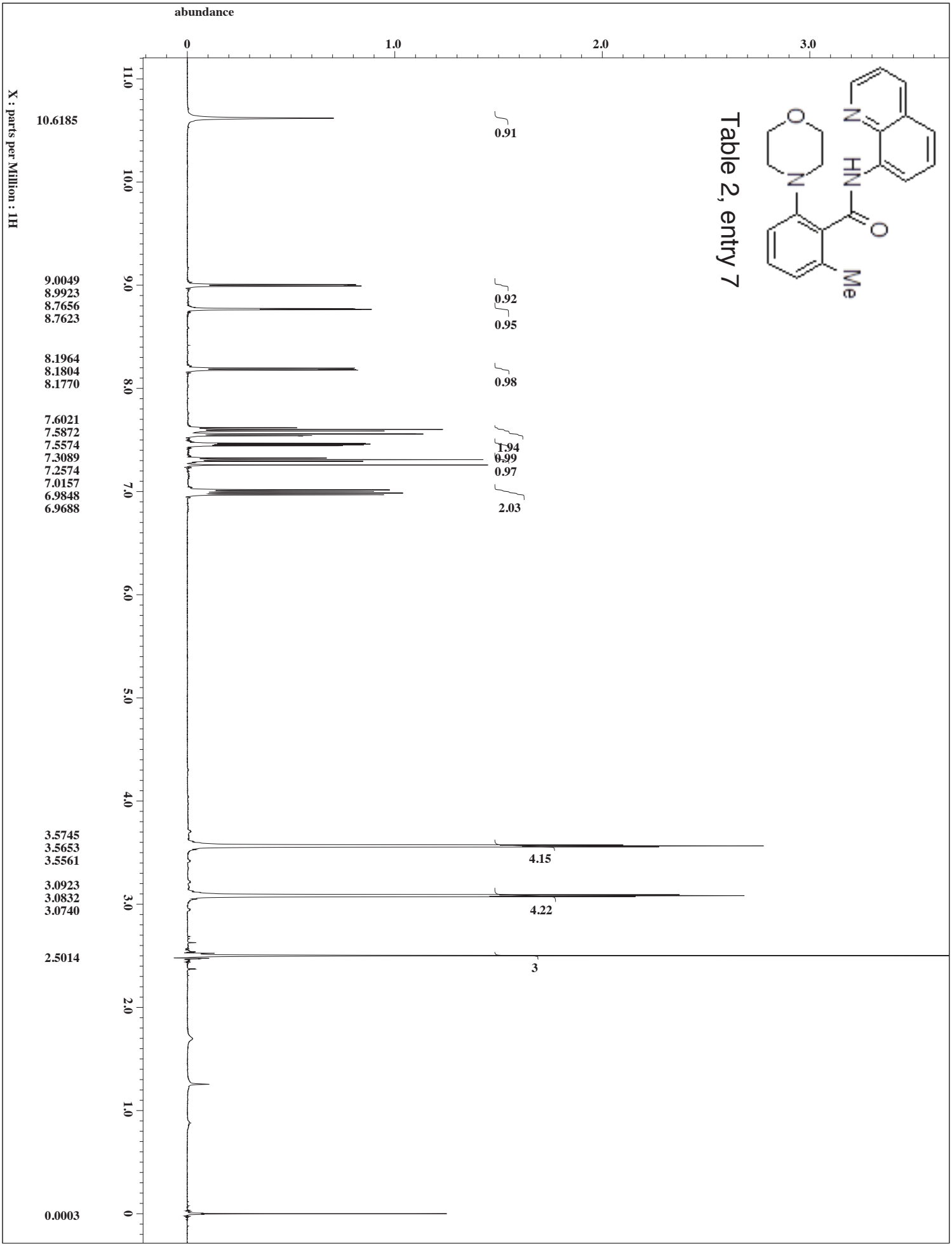

abundance
−0.02 −0.01 0 0.01 0.02 0.03 0.04 0.05 0.06 0.07 0.08 0.09 0.1 0.11 0.12 0.13 0.14 0.15 0.16 0.17
X : parts per Million : 13C
170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0
166.7084
165.1773
151.2958
148.6109
139.0687
136.8192
135.5275
133.7062
133.1039
132.6322
128.6557
127.9010
125.3758
122.4587
122.0814
120.7172
118.1629
77.6140
77.3600
77.1060
66.3883
54.1031
52.8042
Table 2, entry 4
O
N
HN
N
O
O
COOMe

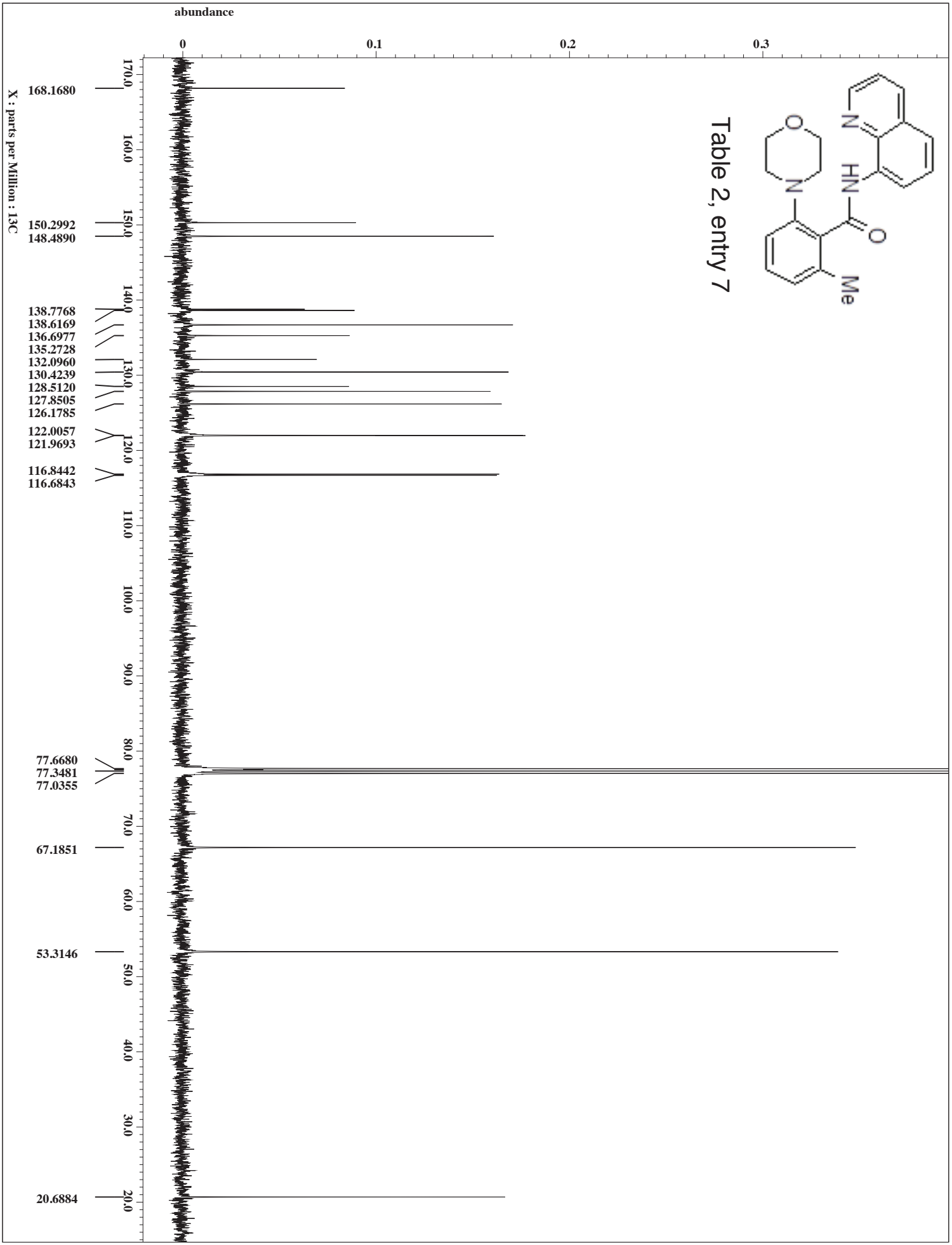

abundance
X : parts per Million : 1H
Table 2, entry 5
13.1148
9.1503
8.9040
8.8971
8.8937
8.1938
8.1892
7.8376
7.8295
7.6096
7.5913
7.5707
7.2809
7.2625
7.2579
4.0437
4.0322
4.0208
3.8799
3.1216
3.1101
3.0987
0.0001
0.93
0.93
0.98
0.99
0.9
2.02
1.0
1.2
0.84
4.36
3
4.23
HN
O
N
O
N
OMe

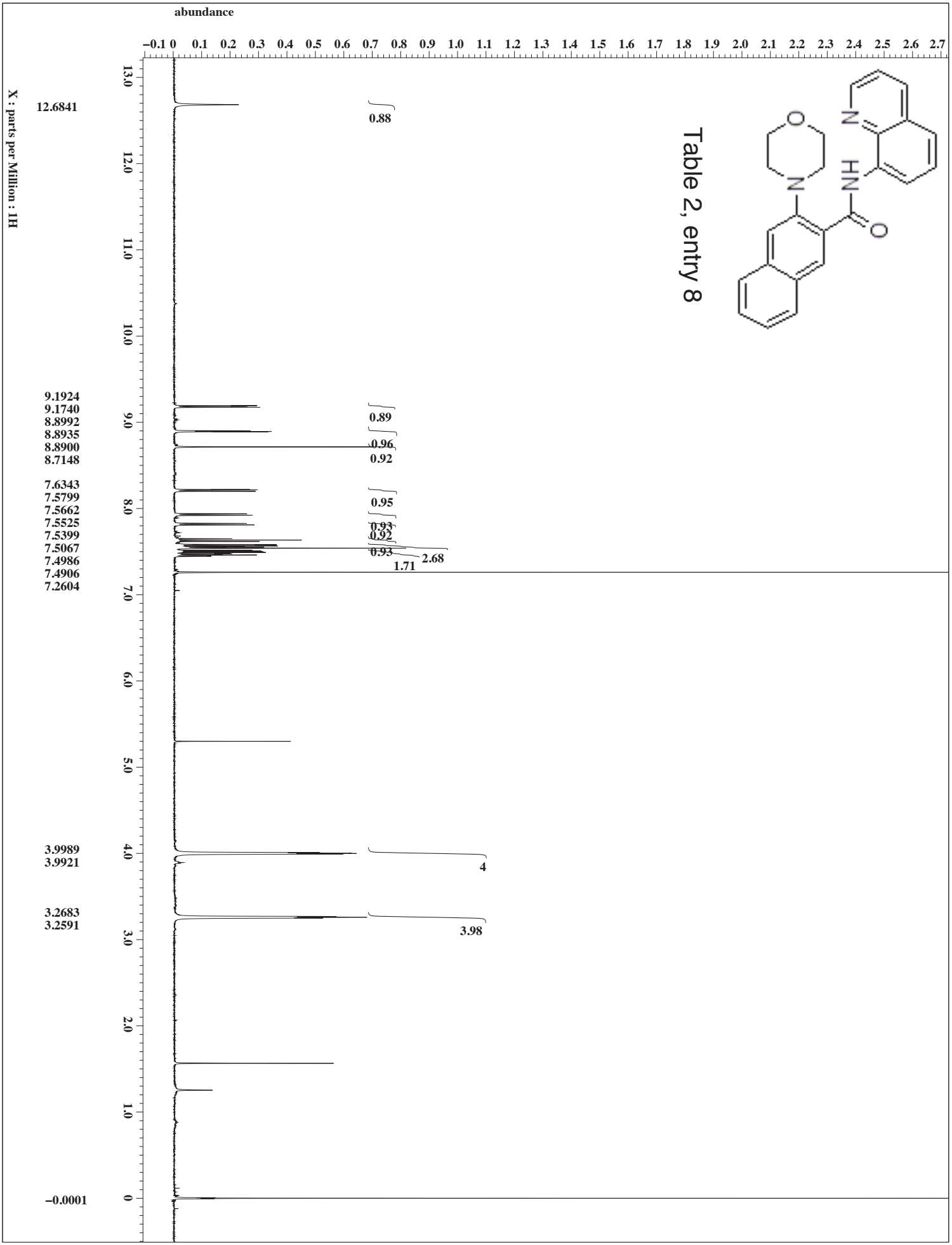

(thousandths)
−10.0
0
10.0
20.0
30.0
40.0
50.0
60.0
70.0
80.0
X : parts per Million : 13C
165.5048
156.8829
148.4647
144.9607
139.3485
136.7750
136.1281
130.1815
128.6912
127.8988
122.2430
121.9522
121.6905
119.4006
118.4846
115.9329
77.6800
77.3601
77.0402
66.5646
56.0091
54.6497
Table 2, entry 5
O
N
HN
O
N
OMe

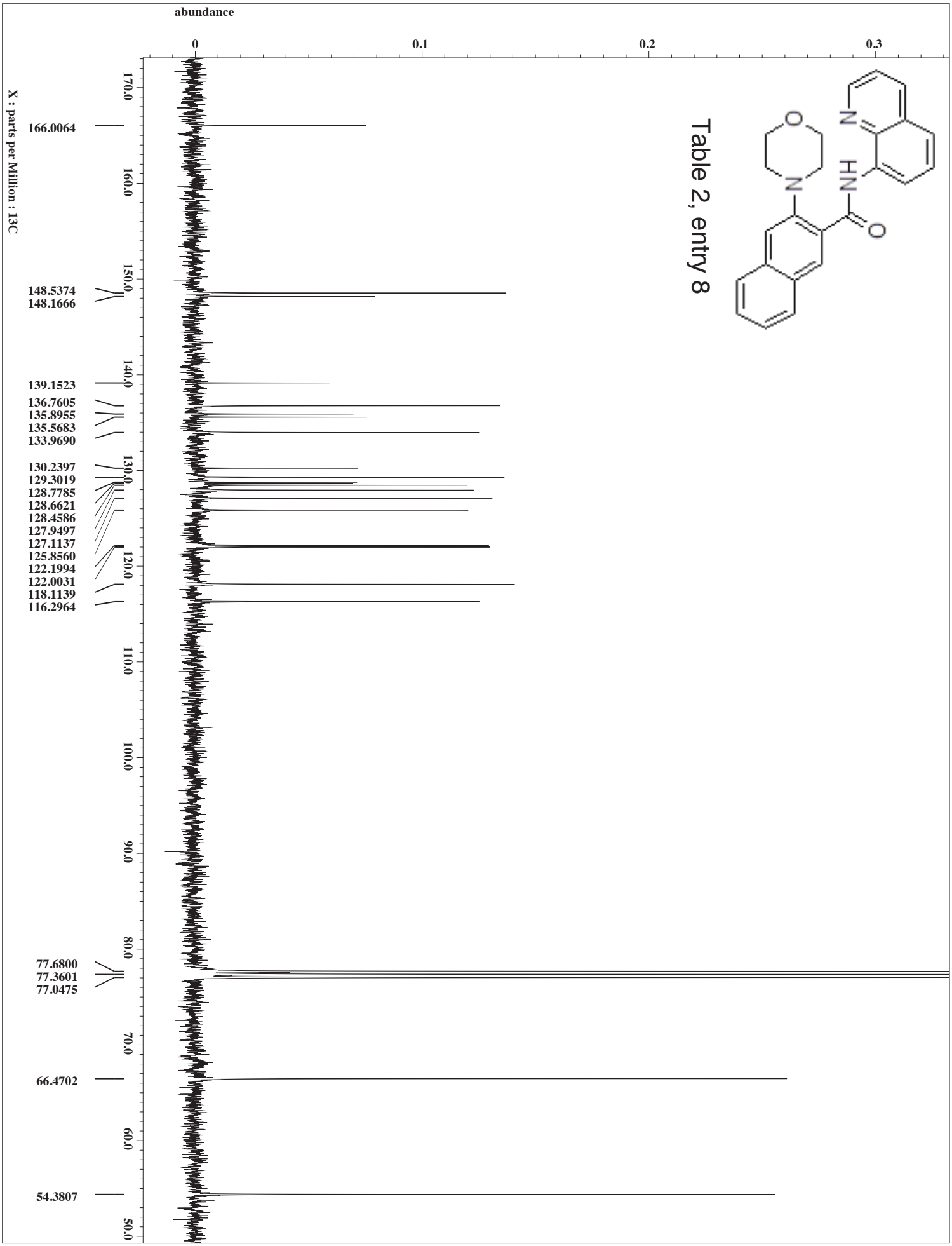

abundance
X : parts per Million : 1H
Table 2, entry 6
12.3634
9.1045
9.0862
8.8651
8.4126
8.2225
8.2019
7.7437
7.7230
7.6188
7.6005
7.5879
7.5237
7.3187
7.2969
7.2637
3.9486
3.2064
0.0013
0.9
0.89
0.95
0.85
0.92
0.92
1.85
0.92
0.94
3.95
4
HN
O
N
O
CF3

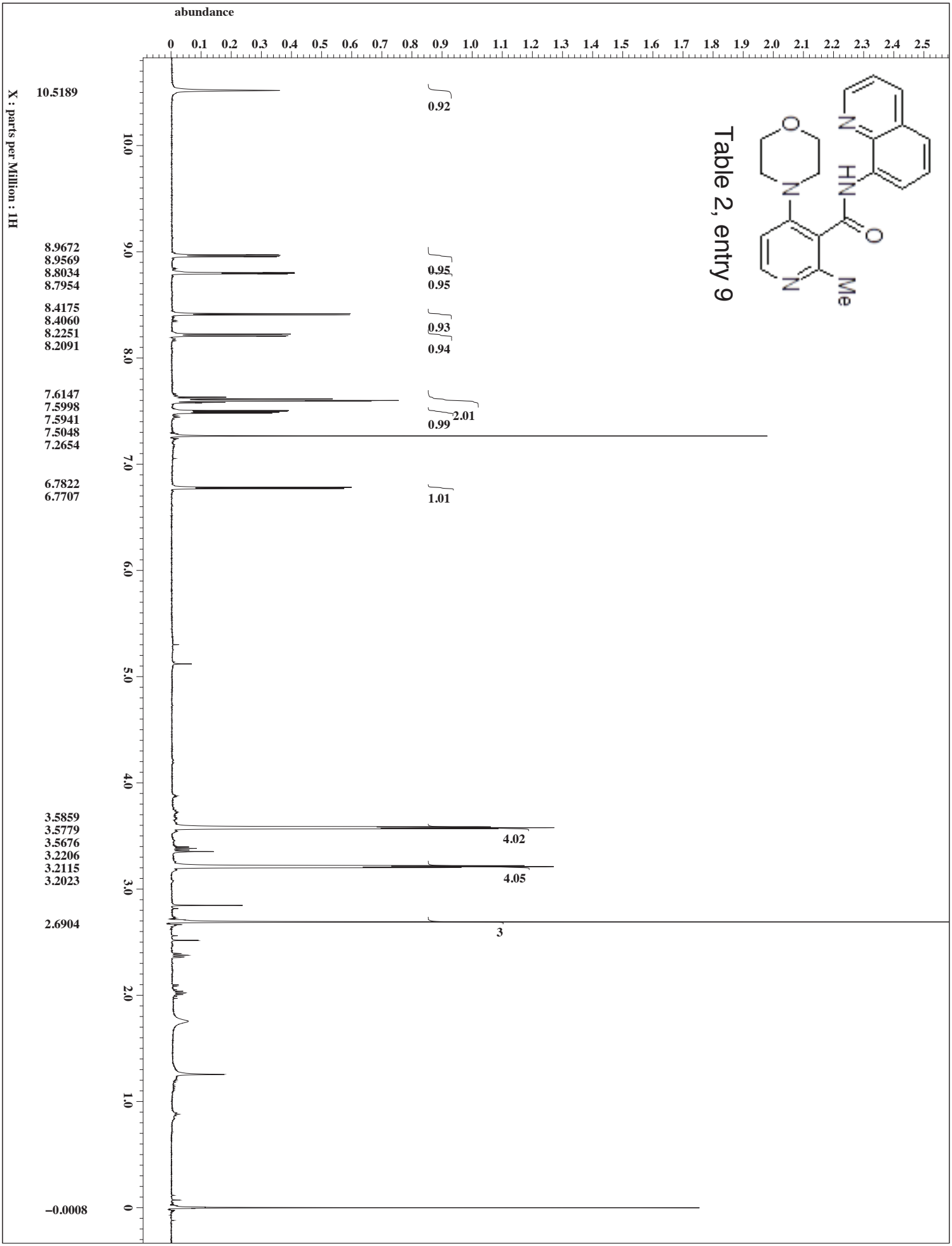

abundance
0
0.1
0.2
0.3
X : parts per Million : 13C
164.8241
153.9487
148.6128
138.9514
136.8723
135.3311
129.8643
129.4863
129.3191
128.6503
127.9379
126.5057
126.1713
125.6188
122.5074
122.1221
119.5196
118.0511
77.6827
77.3628
77.0430
66.2766
53.8818
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
Table 2, entry 6
HN
O
N
O
N
CF3

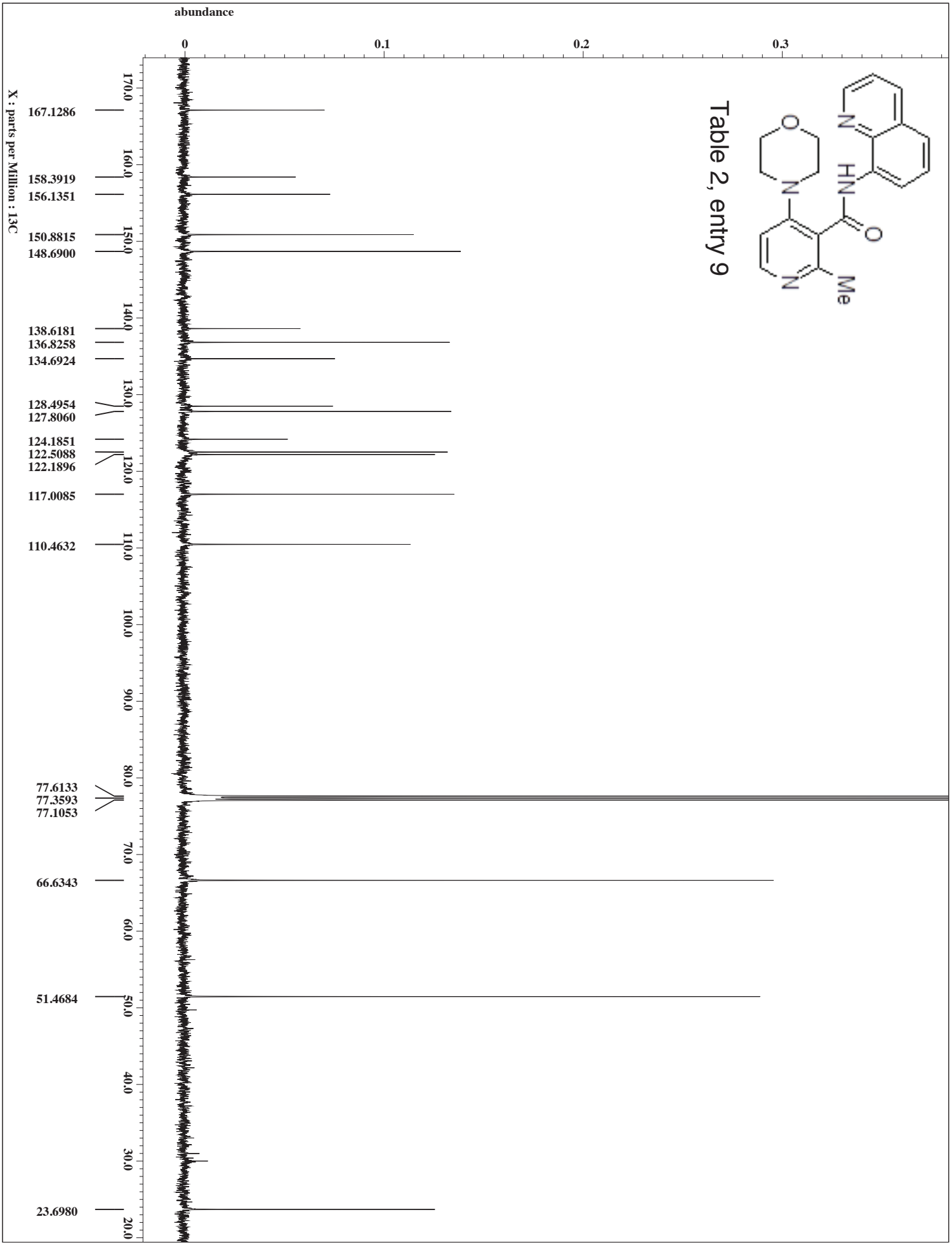

abundance
0
1.0
2.0
3.0
X : parts per Million : 1H
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
10.6185
9.0049
8.9923
8.7656
8.7623
8.1964
8.1804
8.1770
7.6021
7.5872
7.5574
7.3089
7.2574
7.0157
6.9848
6.9688
3.5745
3.5653
3.5561
3.0923
3.0832
3.0740
2.5014
0.0003
0.91
0.92
0.95
0.98
1.94
0.99
0.97
2.03
4.15
4.22
3
Table 2, entry 7
N
HN
O
O
N
Me

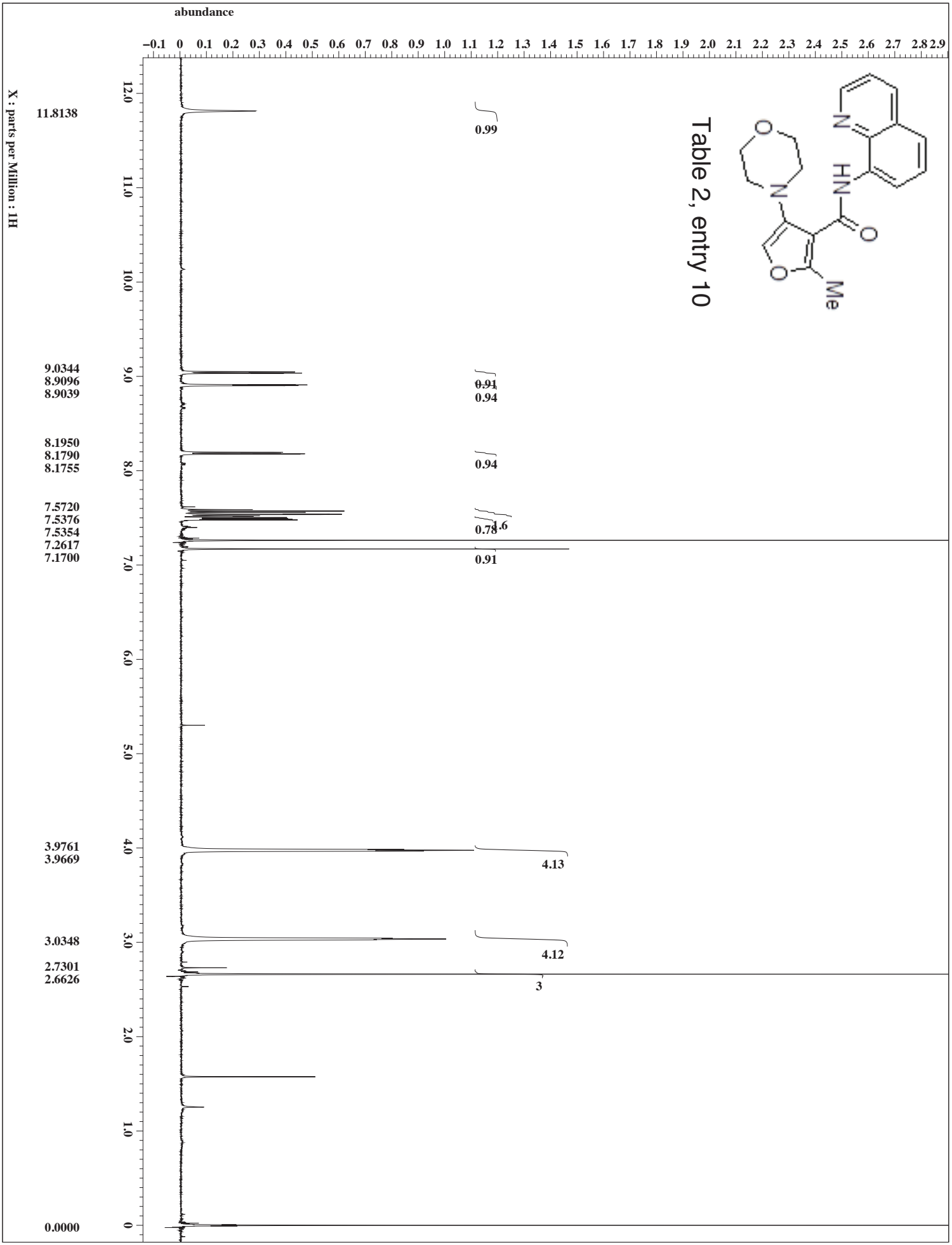

abundance
0
0.1
0.2
0.3
X : parts per Million : 13C
168.1680
150.2992
148.4890
138.7768
138.6169
136.6977
135.2728
132.0960
130.4239
128.5120
127.8505
126.1785
122.0057
121.9693
116.8442
116.6843
77.6680
77.3481
77.0355
67.1851
53.3146
20.6884
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
Table 2, entry 7
O
N
HN
N
O
Me

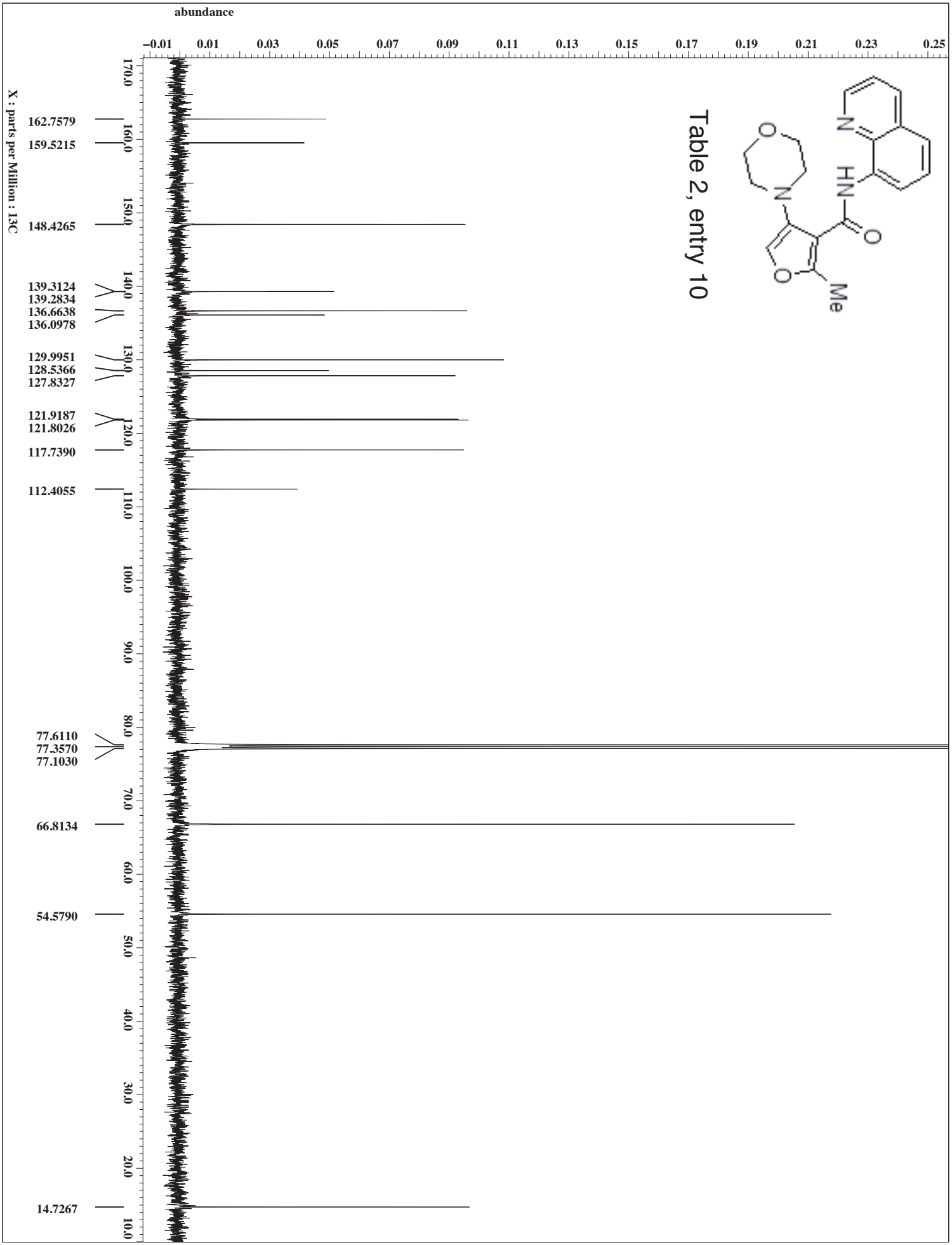

abundance
X : parts per Million : 1H
Table 2, entry 8
12.6841
9.1924
9.1740
8.8992
8.8935
8.8900
8.7148
7.6343
7.5799
7.5662
7.5525
7.5399
7.5067
7.4986
7.4906
7.2604
3.9989
3.9921
3.2683
3.2591
−0.0001
0.88
0.89
0.96
0.92
0.95
0.93
0.92
0.93
1.71
2.68
4
3.98

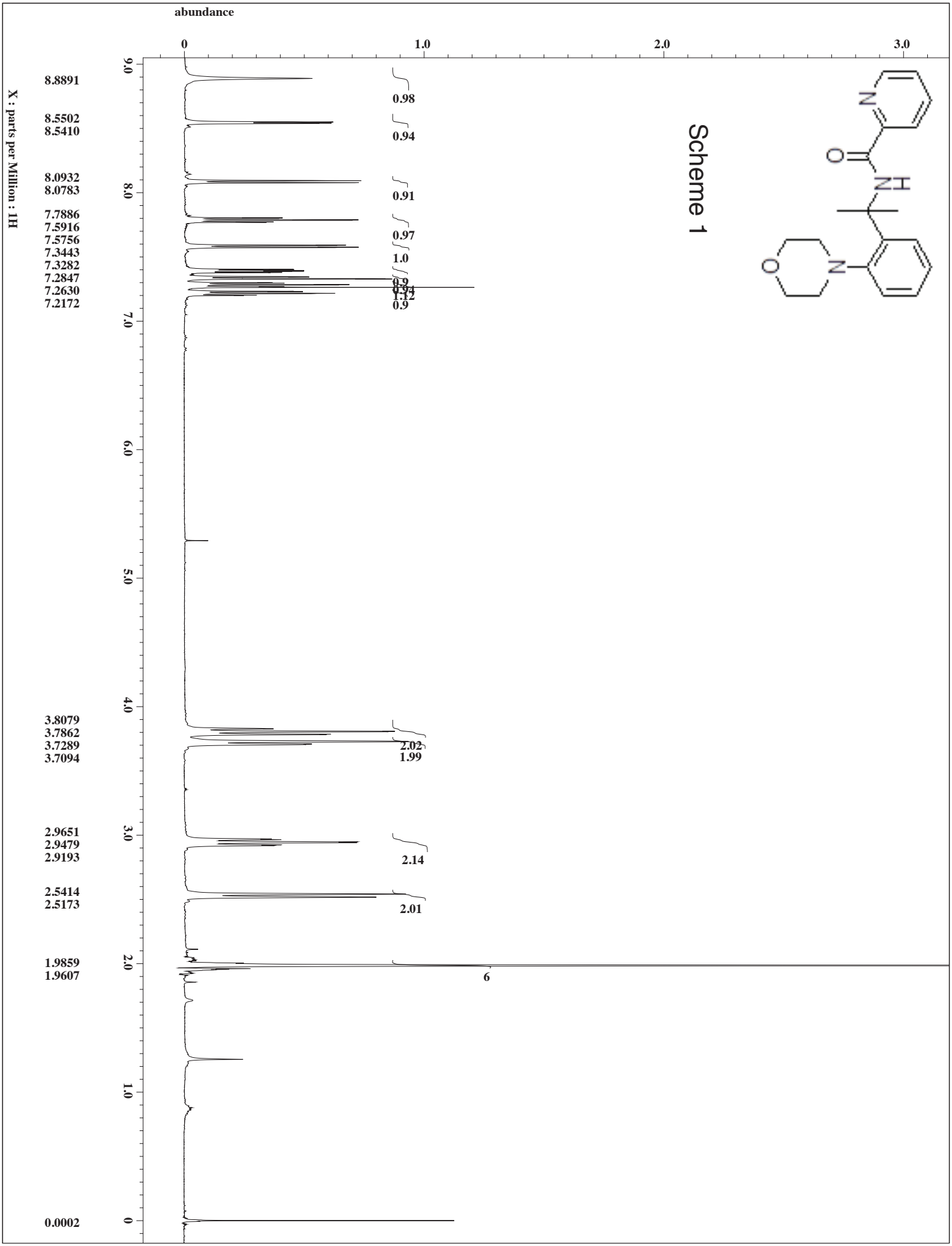

abundance
0
0.1
0.2
0.3
X : parts per Million : 13C
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
166.0064
148.5374
148.1666
139.1523
136.7605
135.8955
135.5683
133.9690
130.2397
129.3019
128.7785
128.6621
128.4586
127.9497
127.1137
125.8560
122.1994
122.0031
118.1139
116.2964
77.6800
77.3601
77.0475
66.4702
54.3807
Table 2, entry 8
N
O
N
HN
O

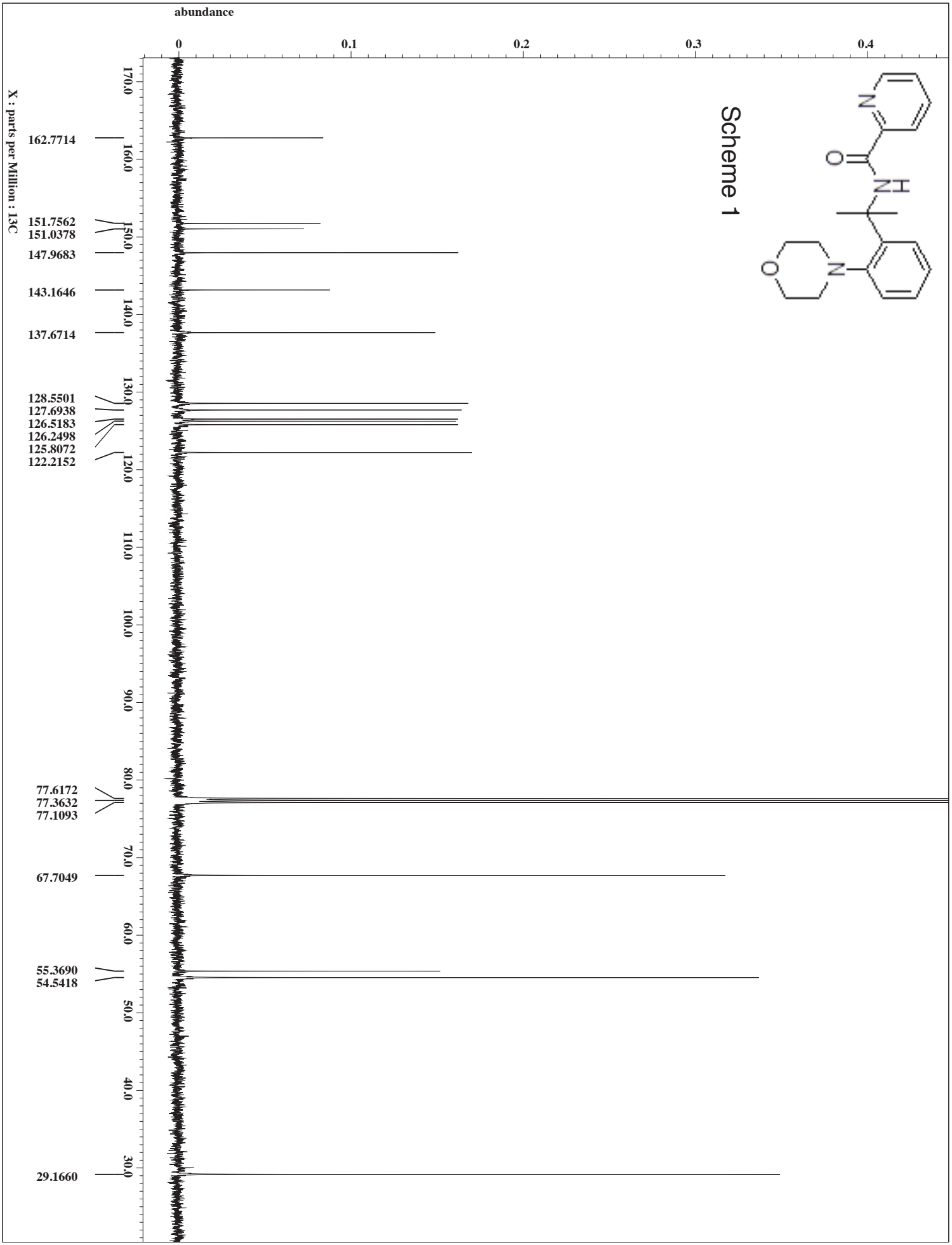

abundance
0 0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.9 1.0 1.1 1.2 1.3 1.4 1.5 1.6 1.7 1.8 1.9 2.0 2.1 2.2 2.3 2.4 2.5
X : parts per Million : 1H
10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0
10.5189
8.9672
8.9569
8.8034
8.7954
8.4175
8.4060
8.2251
8.2091
7.6147
7.5998
7.5941
7.5048
7.2654
6.7822
6.7707
3.5859
3.5779
3.5676
3.2206
3.2115
3.2023
2.6904
−0.0008
0.92
0.95
0.95
0.93
0.94
2.01
0.99
1.01
4.02
4.05
3
Table 2, entry 9
O
N
HN
O
N
N
Me

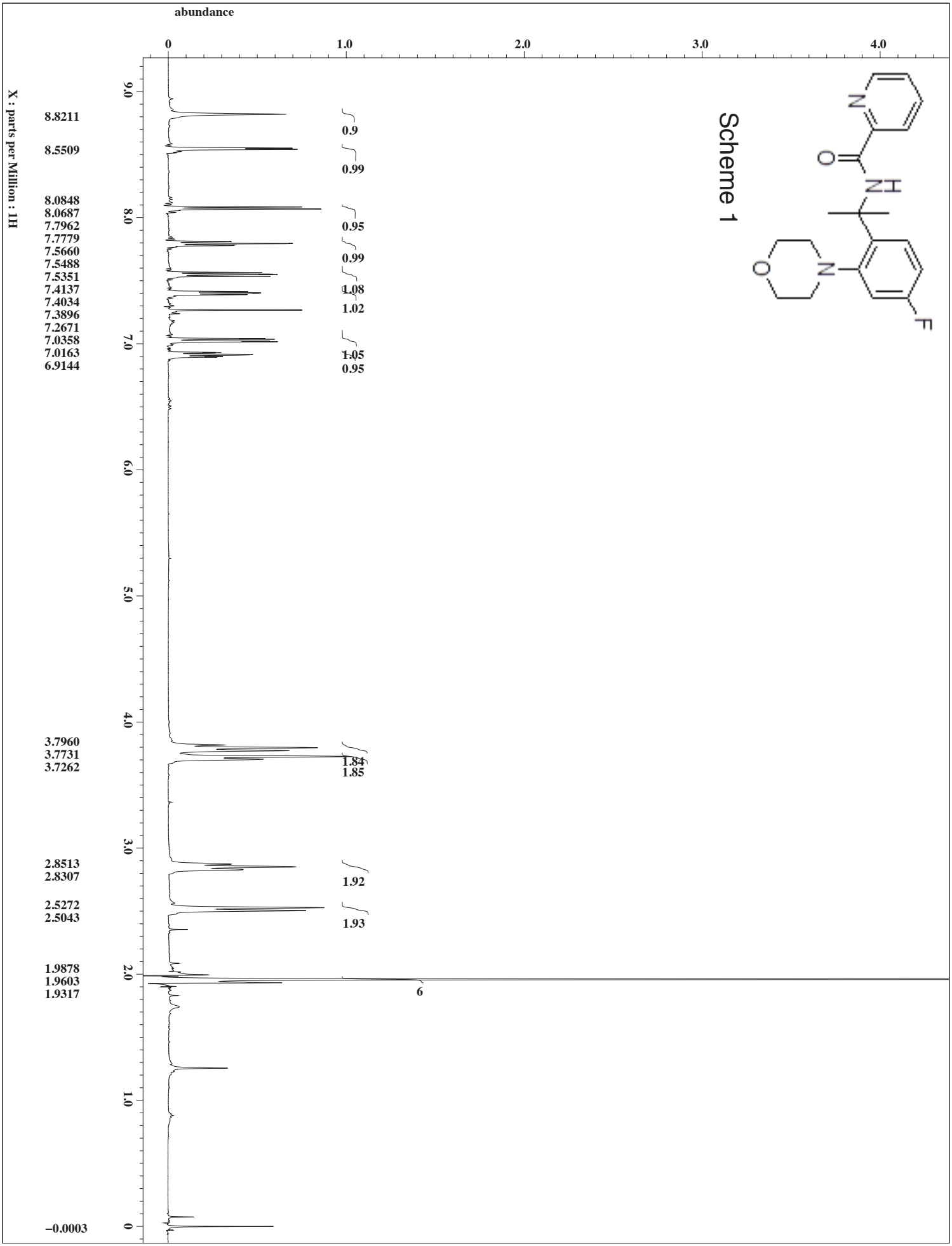

abundance
0
0.1
0.2
0.3
X : parts per Million : 13C
167.1286
158.3919
156.1351
150.8815
148.6900
138.6181
136.8258
134.6924
128.4954
127.8060
124.1851
122.5088
122.1896
117.0085
110.4632
77.6133
77.3593
77.1053
66.6343
51.4684
23.6980
Table 2, entry 9
O
N
HN
O
N
Me
N

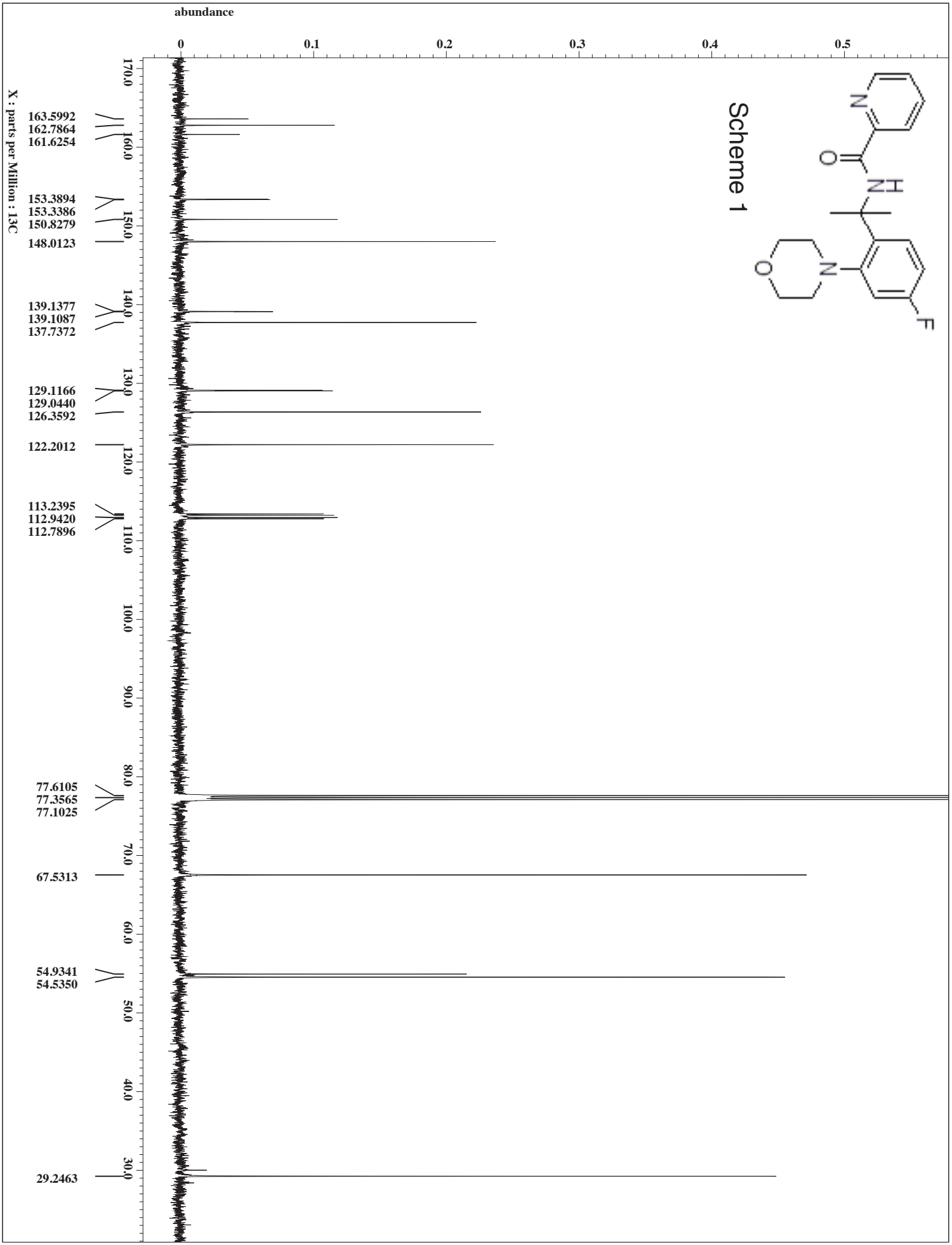

abundance
X : parts per Million : 1H
Table 2, entry 10
11.8138
9.0344
8.9096
8.9039
8.1950
8.1790
8.1755
7.5720
7.5376
7.5354
7.2617
7.1700
3.9761
3.9669
3.0348
2.7301
2.6626
0.0000
0.99
0.91
0.94
0.94
1.6
0.78
0.91
4.13
4.12
3
HN
O
N
O
O
Me

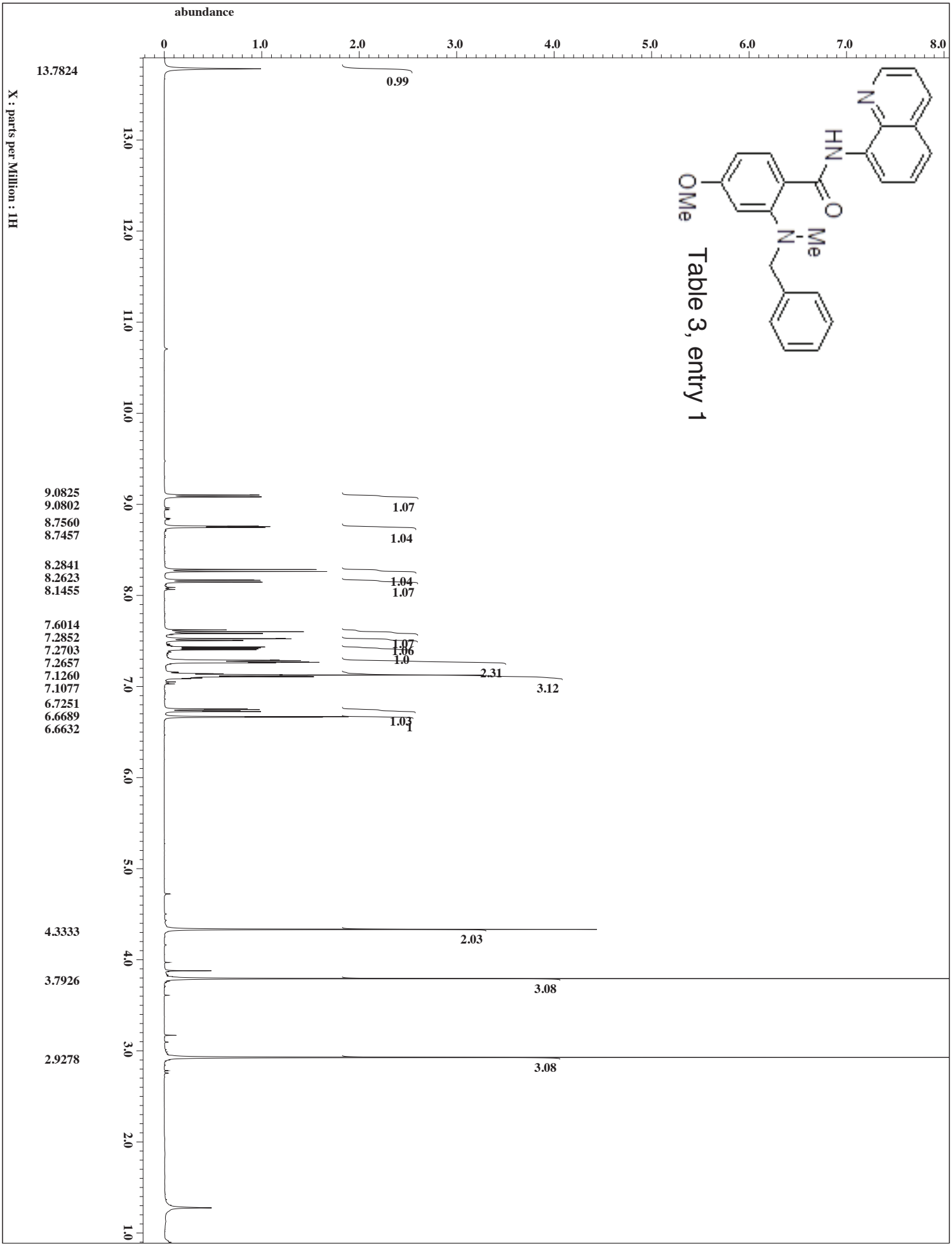

abundance
−0.01 0.01 0.03 0.05 0.07 0.09 0.11 0.13 0.15 0.17 0.19 0.21 0.23 0.25
X : parts per Million : 13C
170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0
162.7579
159.5215
148.4265
139.3124
139.2834
136.6638
136.0978
129.9951
128.5366
127.8327
121.9187
121.8026
117.7390
112.4055
77.6110
77.3570
77.1030
66.8134
54.5790
14.7267
Table 2, entry 10
N
HN
O
O
N
O
O
Me

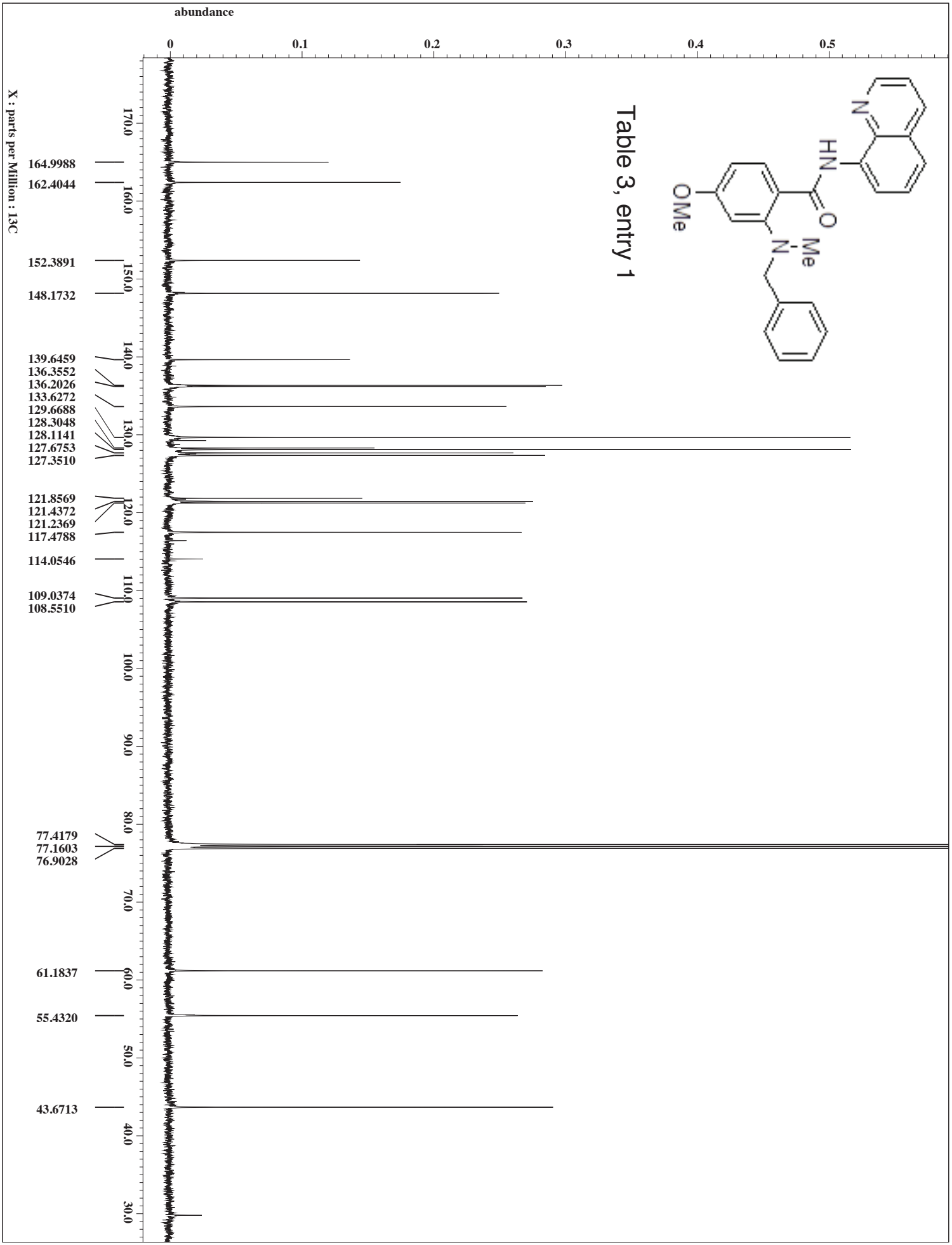

abundance
0
1.0
2.0
3.0
X : parts per Million : 1H
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
8.8891
8.5502
8.5410
8.0932
8.0783
7.7886
7.5916
7.5756
7.3443
7.3282
7.2847
7.2630
7.2172
3.8079
3.7862
3.7289
3.7094
2.9651
2.9479
2.9193
2.5414
2.5173
1.9859
1.9607
0.0002
0.98
0.94
0.91
0.97
1.0
0.9
0.94
1.12
0.9
2.02
1.99
2.14
2.01
6
Scheme 1
N
O
NH
O
N

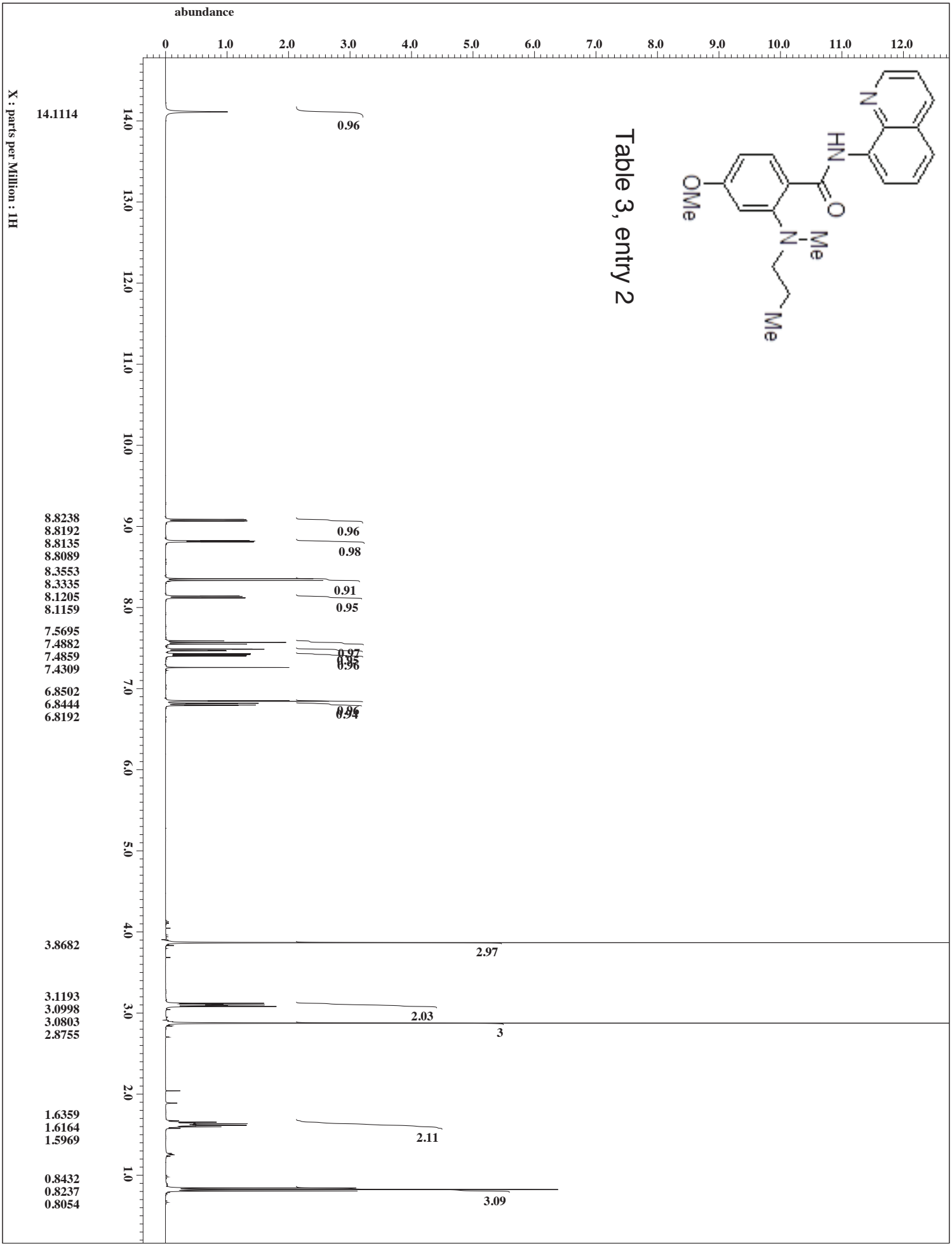

abundance
0
0.1
0.2
0.3
0.4
X : parts per Million : 13C
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
162.7714
151.7562
151.0378
147.9683
143.1646
137.6714
128.5501
127.6938
126.5183
126.2498
125.8072
122.2152
77.6172
77.3632
77.1093
67.7049
55.3690
54.5418
29.1660
Scheme 1
N
O
N
H
O
N


abundance
X : parts per Million : 1H
Scheme 1
8.8211
8.5509
8.0848
8.0687
7.7962
7.7779
7.5660
7.5488
7.5351
7.4137
7.4034
7.3896
7.2671
7.0358
7.0163
6.9144
3.7960
3.7731
3.7262
2.8513
2.8307
2.5272
2.5043
1.9878
1.9603
1.9317
−0.0003
0.9
0.99
0.95
0.99
1.08
1.02
1.05
0.95
1.84
1.85
1.92
1.93
6
N
O
H
N
O
N
F


abundance
0
0.1
0.2
0.3
0.4
0.5
X : parts per Million : 13C
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
163.5992
162.7864
161.6254
153.3894
153.3386
150.8279
148.0123
139.1377
139.1087
137.7372
129.1166
129.0440
126.3592
122.2012
113.2395
112.9420
112.7896
77.6105
77.3565
77.1025
67.5313
54.9341
54.5350
29.2463
Scheme 1
N
O
H
N
O
N
F


abundance
X : parts per Million : 1H
13.7824
9.0825
9.0802
8.7560
8.7457
8.2841
8.2623
8.1455
7.6014
7.2852
7.2703
7.2657
7.1260
7.1077
6.7251
6.6689
6.6632
4.3333
3.7926
2.9278
0.99
1.07
1.04
1.04
1.07
1.07
1.06
1.0
2.31
3.12
1.03
1
2.03
3.08
3.08
HN
O
Me
N
OMe
Table 3, entry 1


abundance
0
0.1
0.2
0.3
0.4
0.5
X : parts per Million : 13C
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
164.9988
162.4044
152.3891
148.1732
139.6459
136.3552
136.2026
133.6272
129.6688
128.3048
128.1141
127.6753
127.3510
121.8569
121.4372
121.2369
117.4788
114.0546
109.0374
108.5510
77.4179
77.1603
76.9028
61.1837
55.4320
43.6713
Table 3, entry 1
HN
O
N
Me
N
OMe


abundance
X : parts per Million : 1H
14.1114
8.8238
8.8192
8.8135
8.8089
8.3553
8.3335
8.1205
8.1159
7.5695
7.4882
7.4859
7.4309
6.8502
6.8444
6.8192
3.8682
3.1193
3.0998
3.0803
2.8755
1.6359
1.6164
1.5969
0.8432
0.8237
0.8054
0.96
0.96
0.98
0.91
0.95
2.97
2.03
3
2.11
3.09
Table 3, entry 2
OMe
HN
O
N
Me
N
Me

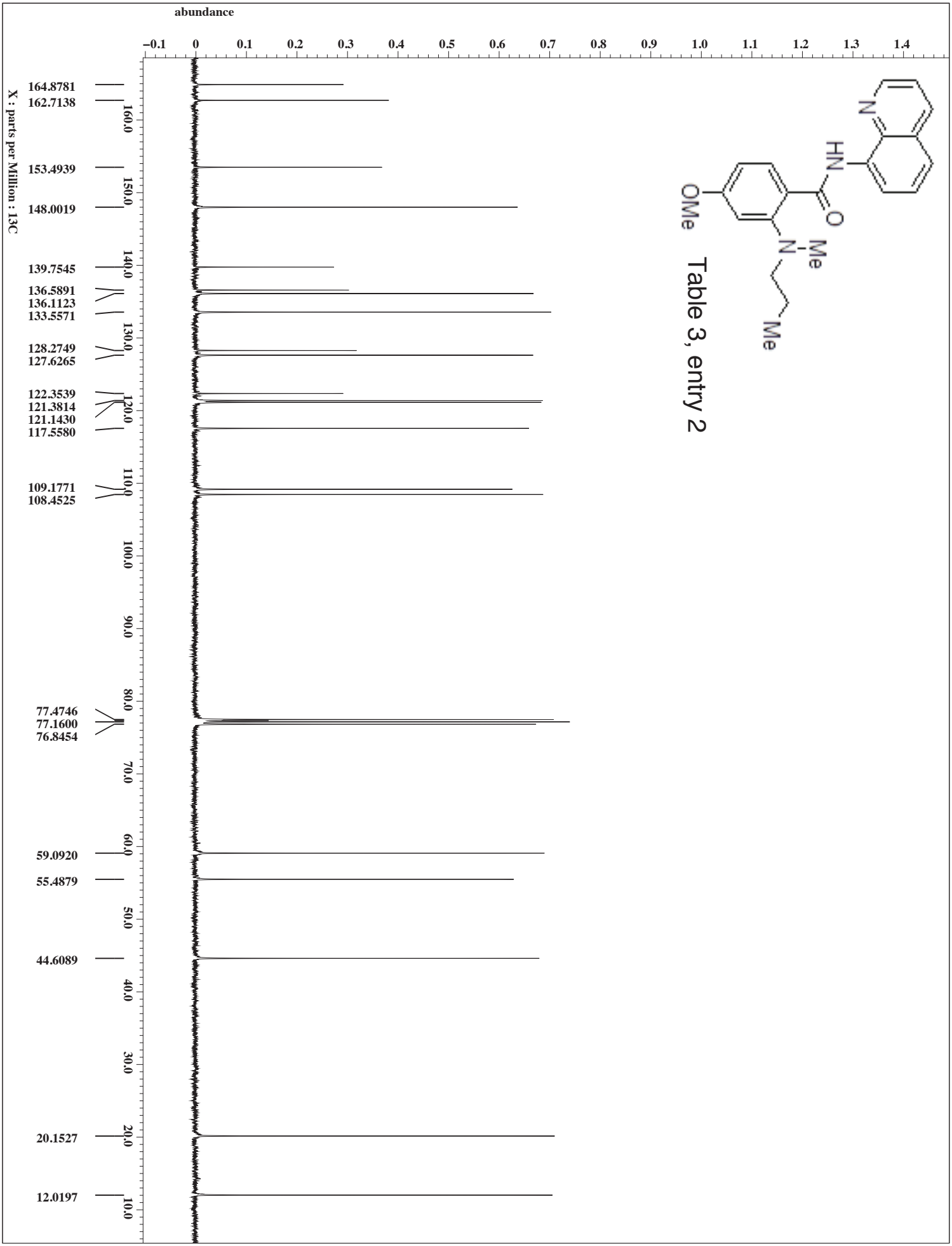


Table 3, entry 2

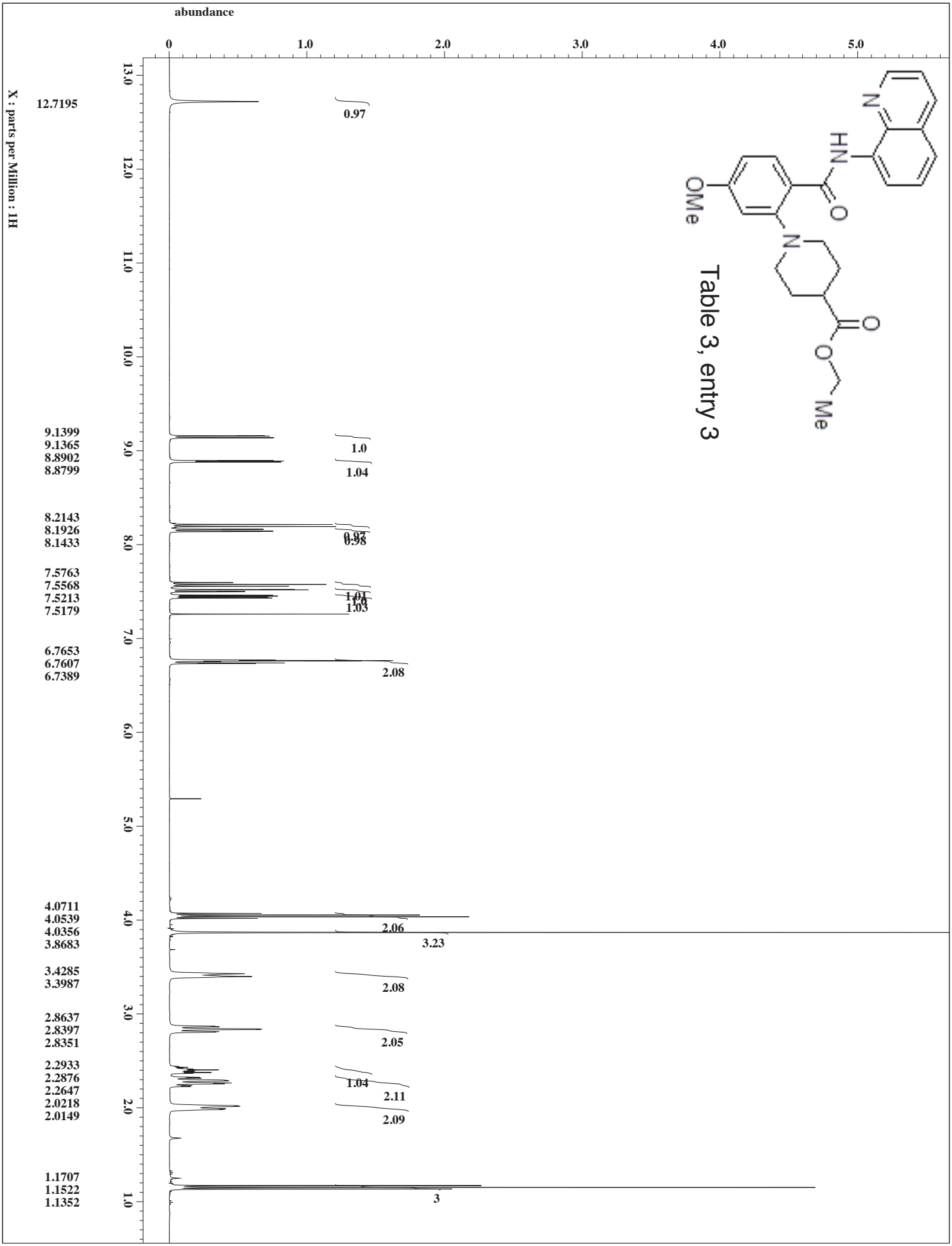
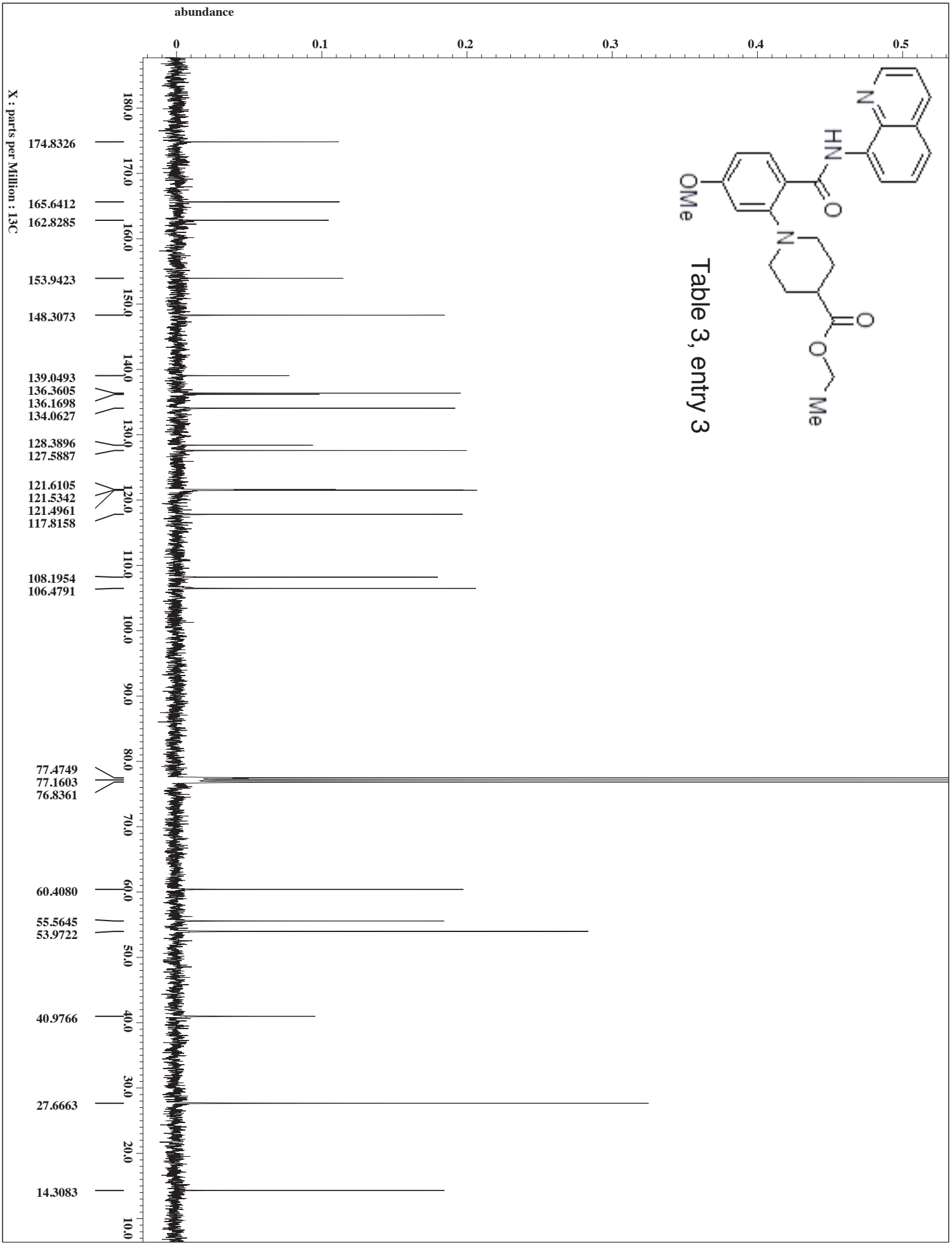
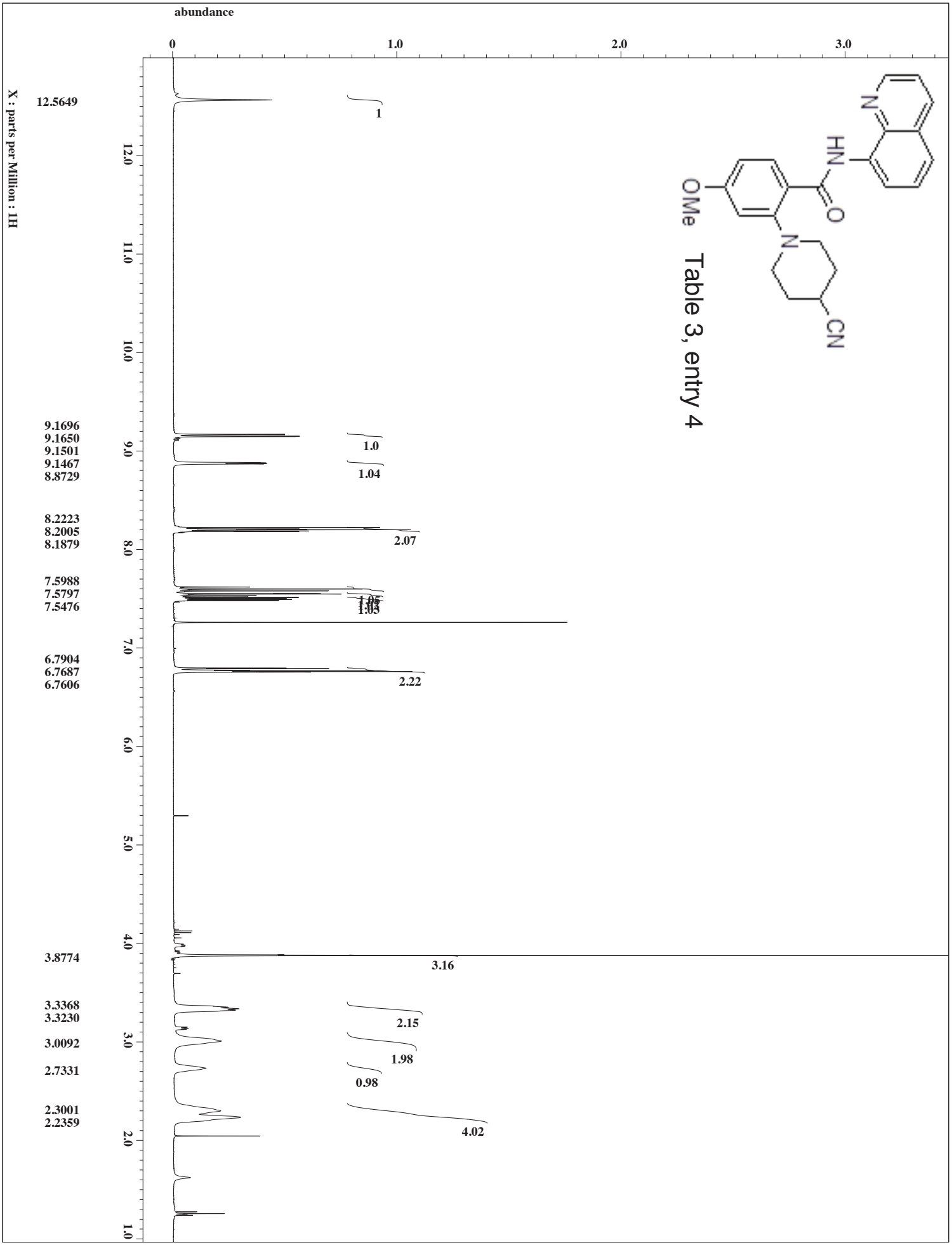
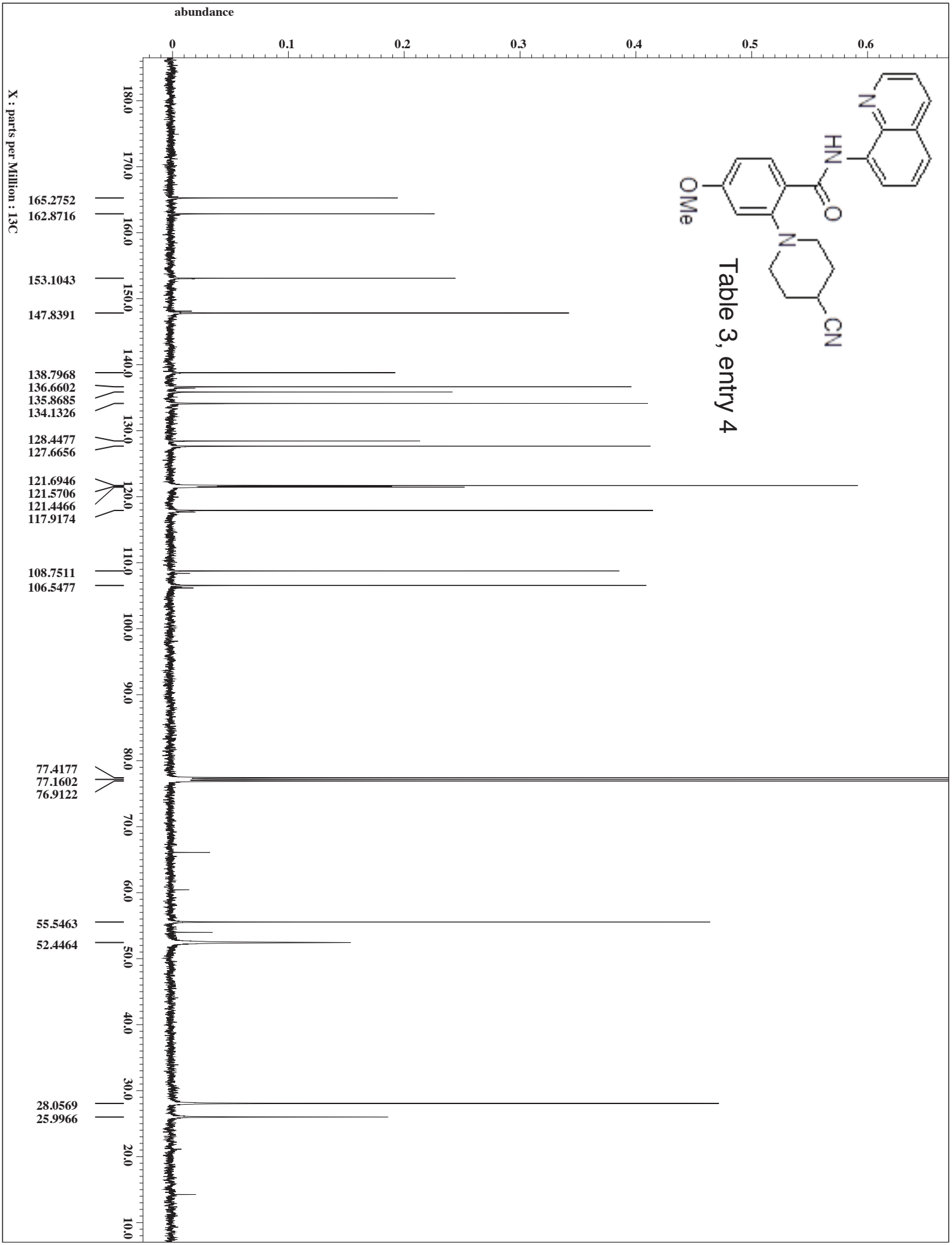
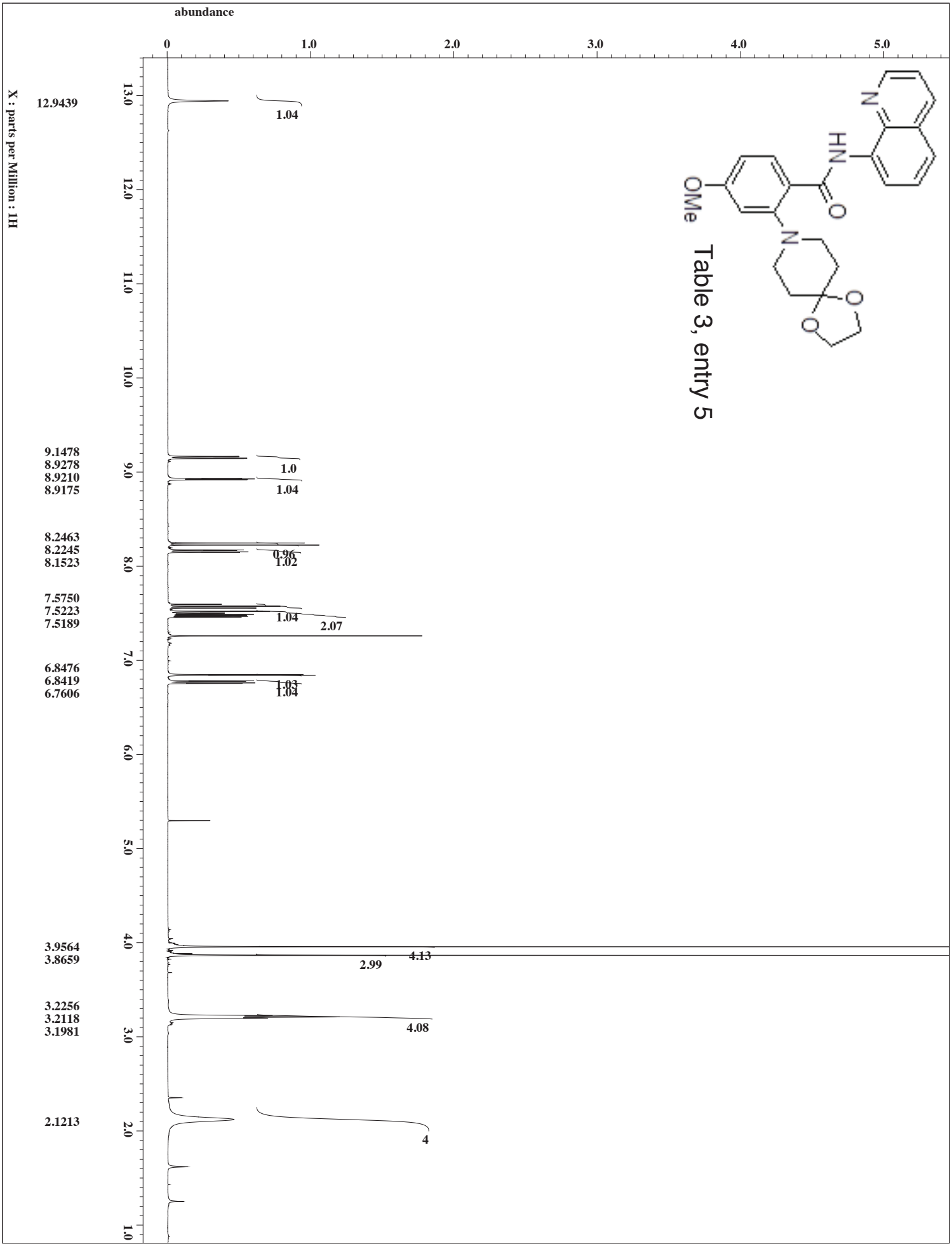


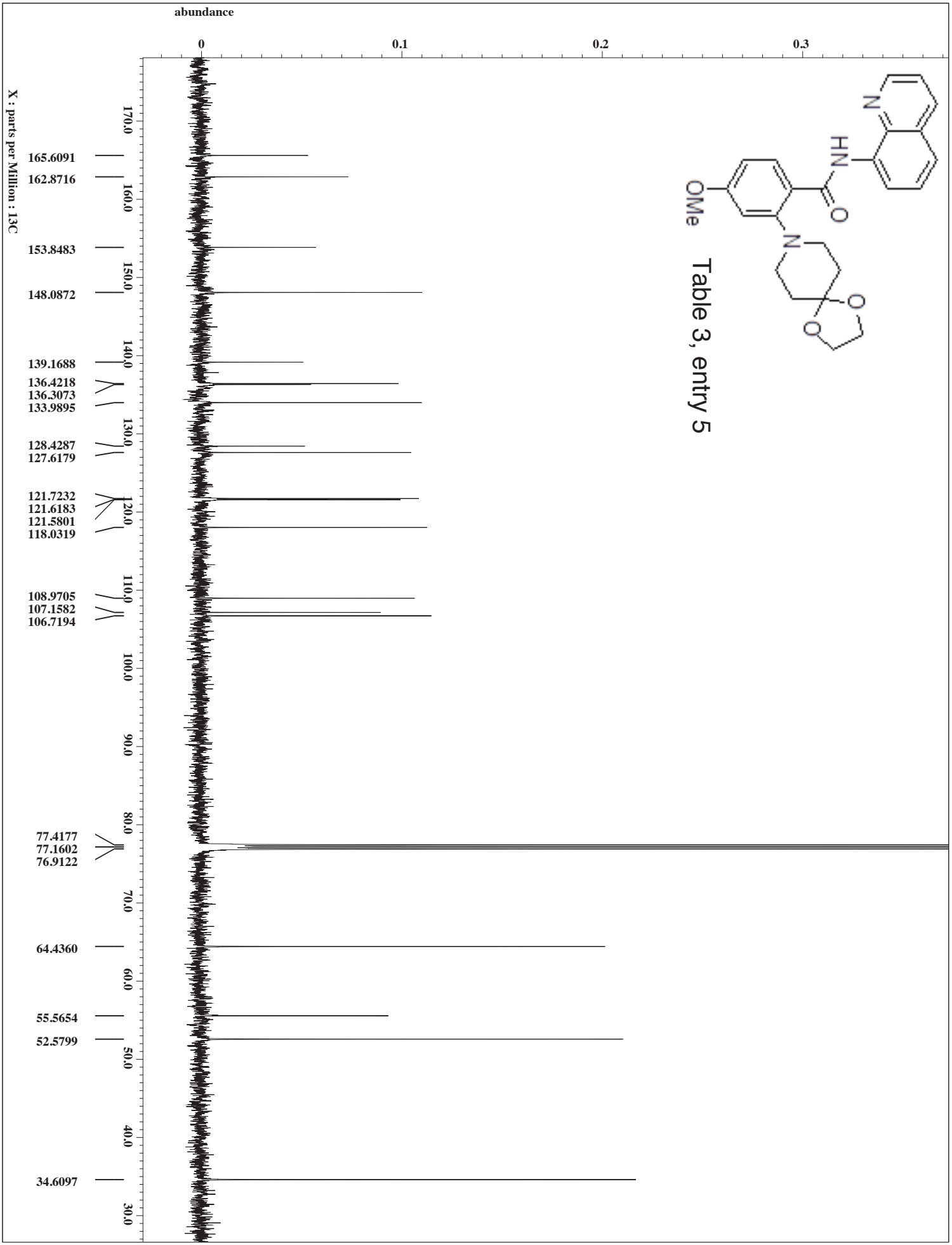
Table 3, entry 3

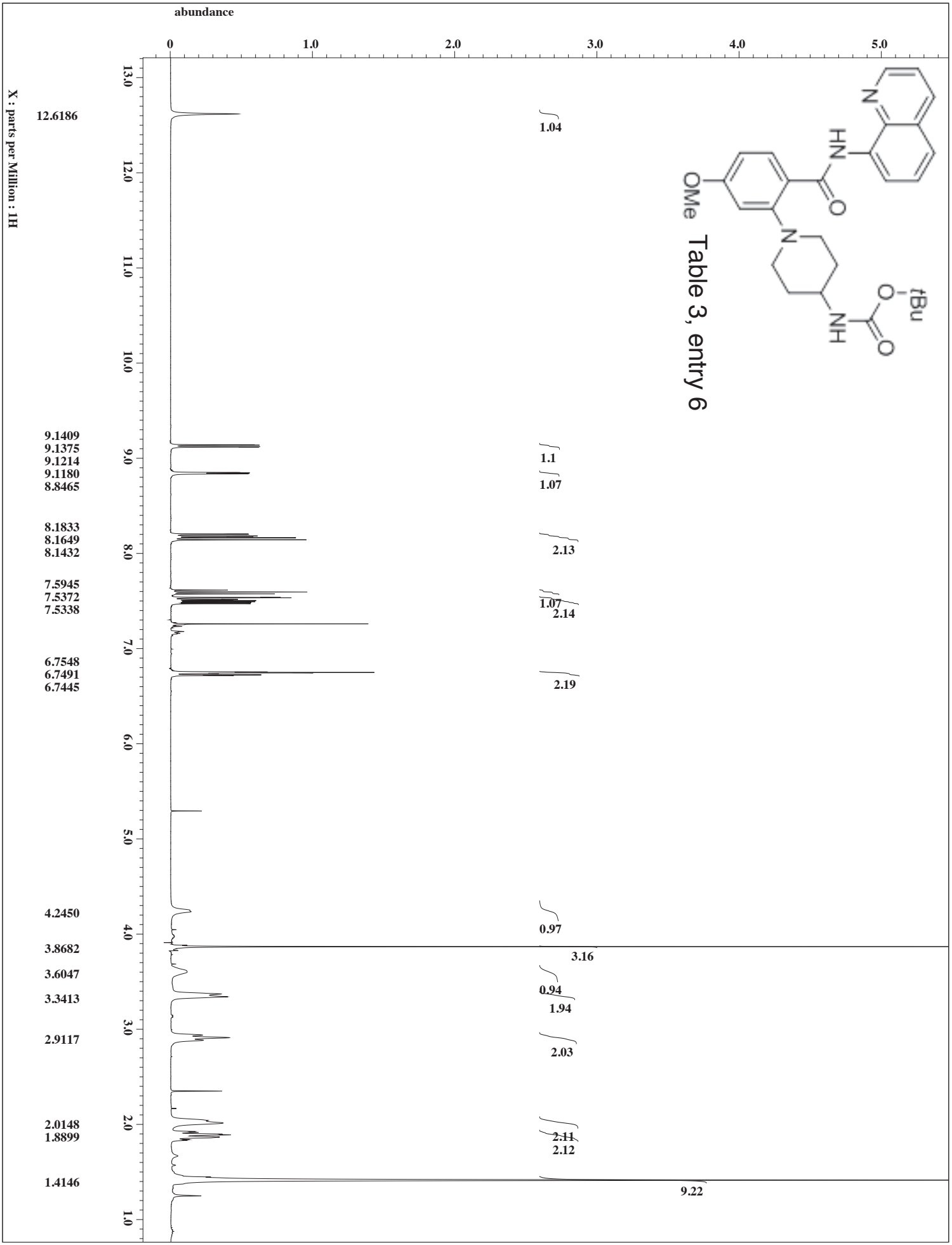

abundance
0
0.1
0.2
0.3
0.4
0.5
X : parts per Million : 13C
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
174.8326
165.6412
162.8285
153.9423
148.3073
139.0493
136.3605
136.1698
134.0627
128.3896
127.5887
121.6105
121.5342
121.4961
117.8158
108.1954
106.4791
77.4749
77.1603
76.8361
60.4080
55.5645
53.9722
40.9766
27.6663
14.3083
HN
O
OMe
N
O
O
Me
Table 3, entry 3

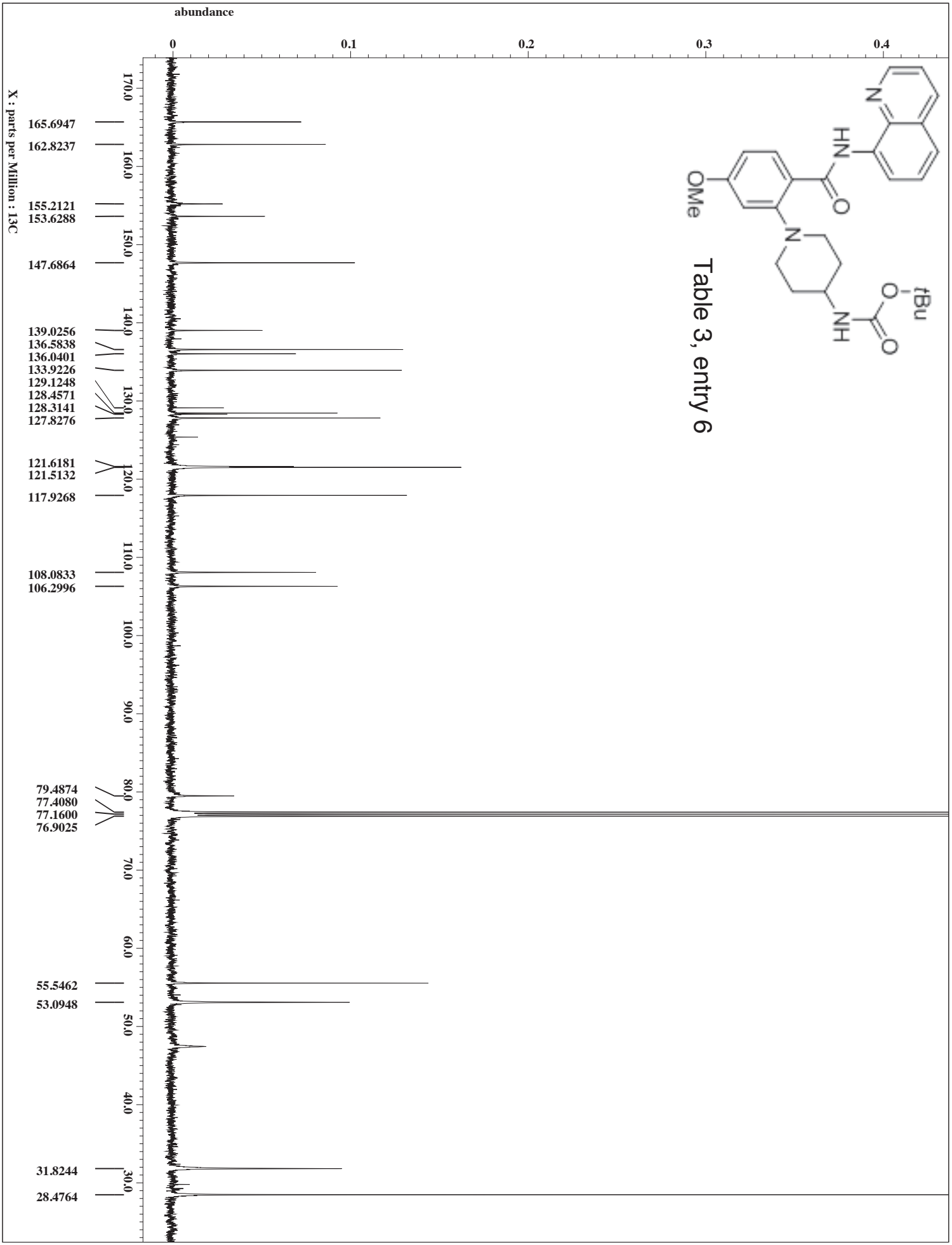

abundance
0
1.0
2.0
3.0
X : parts per Million : 1H
12.5649
9.1696
9.1650
9.1501
9.1467
8.8729
8.2223
8.2005
8.1879
7.5988
7.5797
7.5476
6.7904
6.7687
6.7606
3.8774
3.3368
3.3230
3.0092
2.7331
2.3001
2.2359
1
1.0
1.04
2.07
1.05
1.03
2.22
3.16
2.15
1.98
0.98
4.02
HN
O
N
CN
OMe
Table 3, entry 4

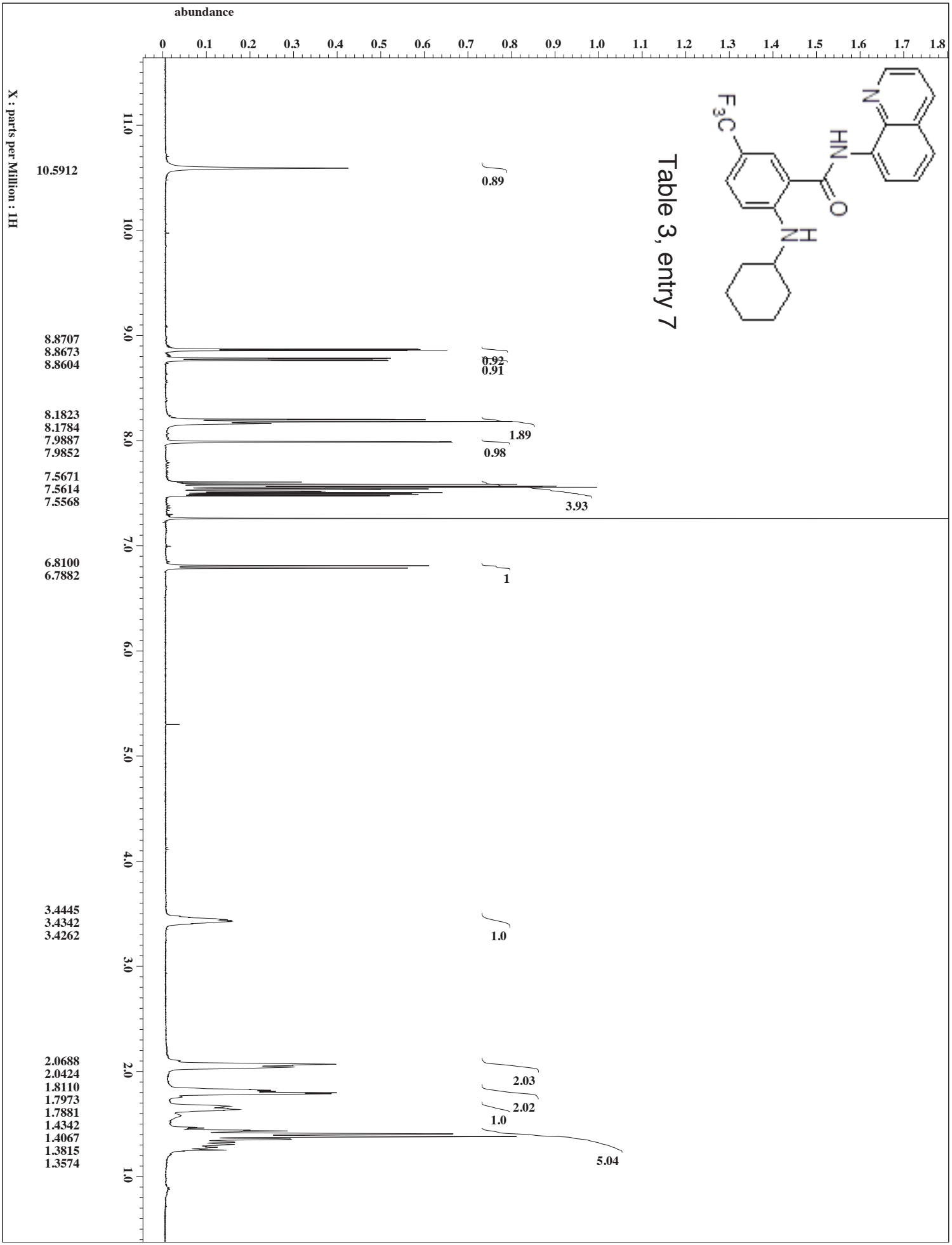

abundance
0
0.1
0.2
0.3
0.4
0.5
0.6
X : parts per Million : 13C
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
165.2752
162.8716
153.1043
147.8391
138.7968
136.6602
135.8685
134.1326
128.4477
127.6656
121.6946
121.5706
121.4466
117.9174
108.7511
106.5477
77.4177
77.1602
76.9122
55.5463
52.4464
28.0569
25.9966
HN
O
N
OMe
N
CN
Table 3, entry 4

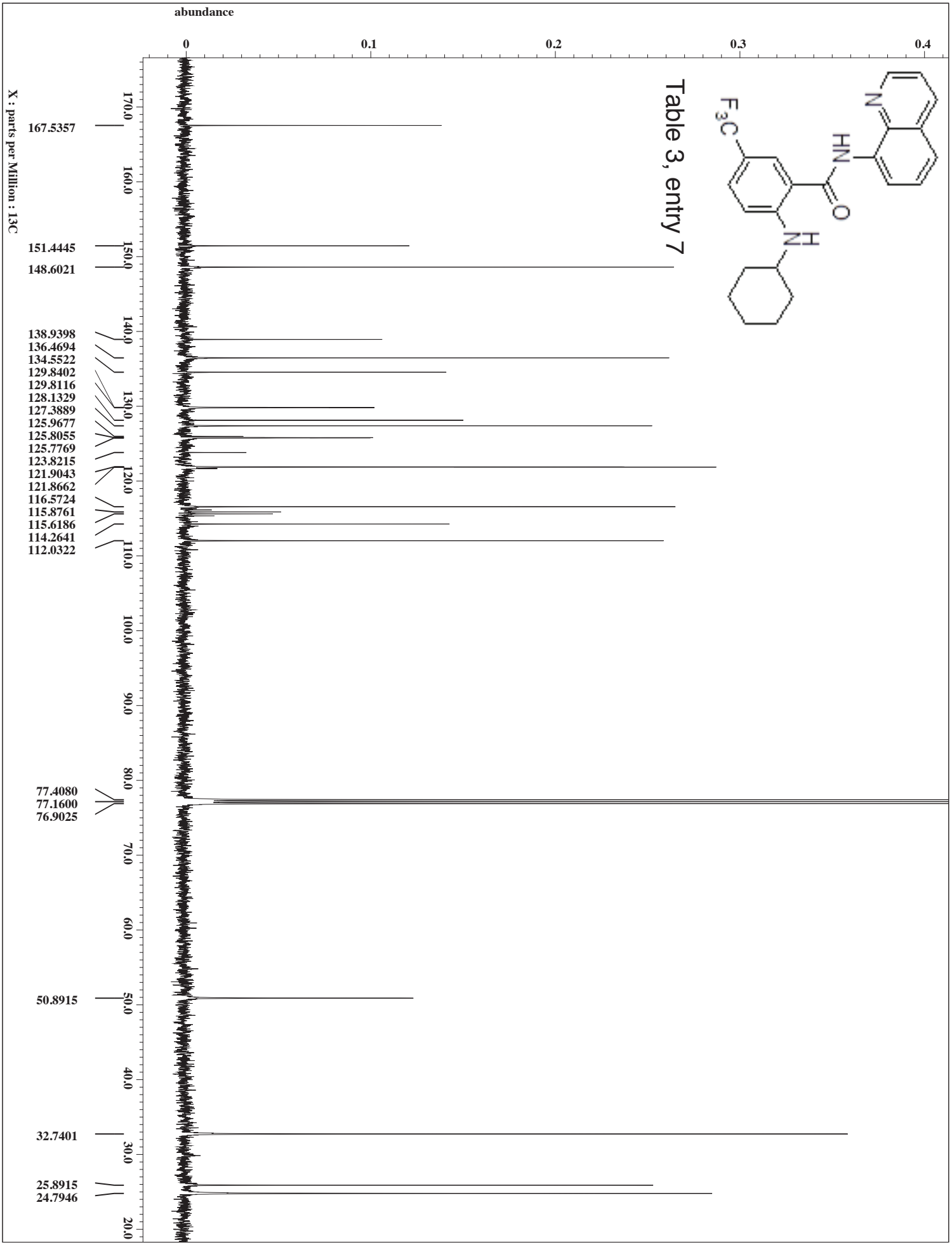

abundance
X : parts per Million : 1H
Table 3, entry 5
OMe
HN
N
O
12.9439
1.04
9.1478
8.9278
8.9210
8.9175
1.0
1.04
8.2463
8.2245
8.1523
0.96
1.02
7.5750
7.5223
7.5189
1.04
2.07
6.8476
6.8419
6.7606
1.03
1.04
3.9564
3.8659
2.99
4.13
3.2256
3.2118
3.1981
4.08
2.1213
4

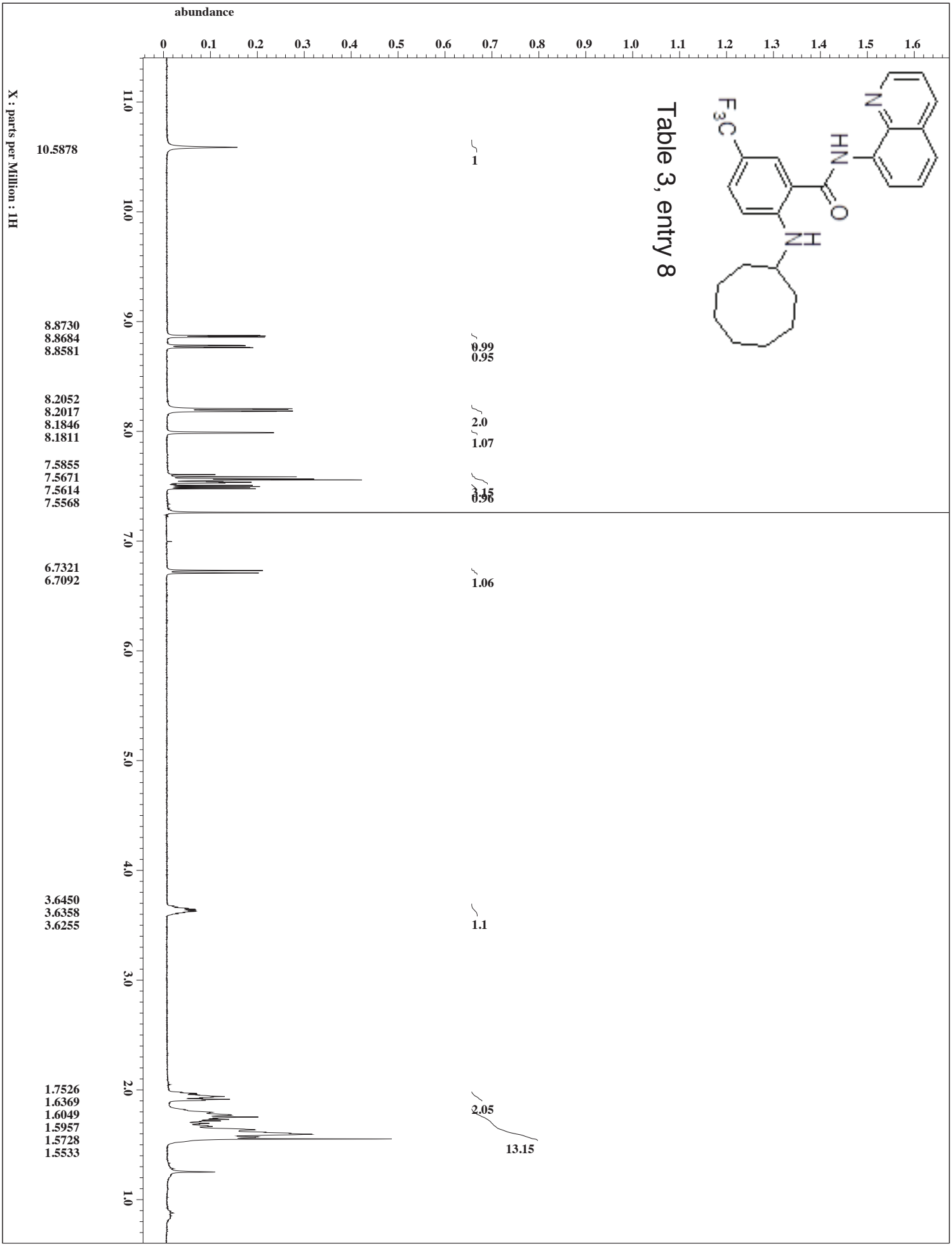

abundance
0
0.1
0.2
0.3
X : parts per Million : 13C
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
165.6091
162.8716
153.8483
148.0872
139.1688
136.4218
136.3073
133.9895
128.4287
127.6179
121.7232
121.6183
121.5801
118.0319
108.9705
107.1582
106.7194
77.4177
77.1602
76.9122
64.4360
55.5654
52.5799
34.6097
OMe
HN
O
N
O
O
Table 3, entry 5

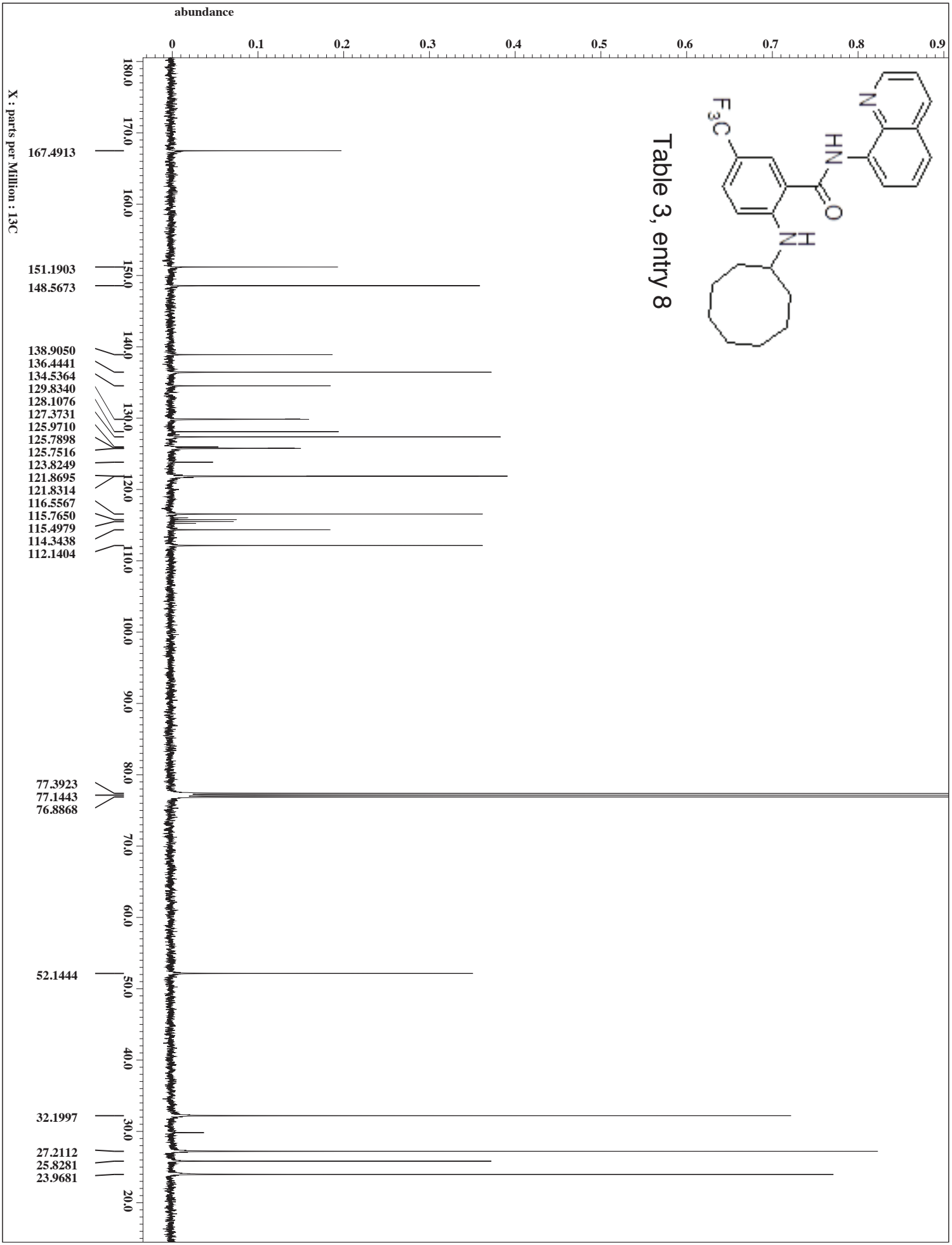

abundance
X : parts per Million : 1H
Table 3, entry 6
OMe
HN
N
O
N
NH
O
O
tBu
12.6186
9.1409
9.1375
9.1214
9.1180
8.8465
8.1833
8.1649
8.1432
7.5945
7.5372
7.5338
6.7548
6.7491
6.7445
4.2450
3.8682
3.6047
3.3413
2.9117
2.0148
1.8899
1.4146
1.04
1.1
1.07
2.13
1.07
2.14
2.19
0.97
3.16
0.94
1.94
2.03
2.11
2.12
9.22

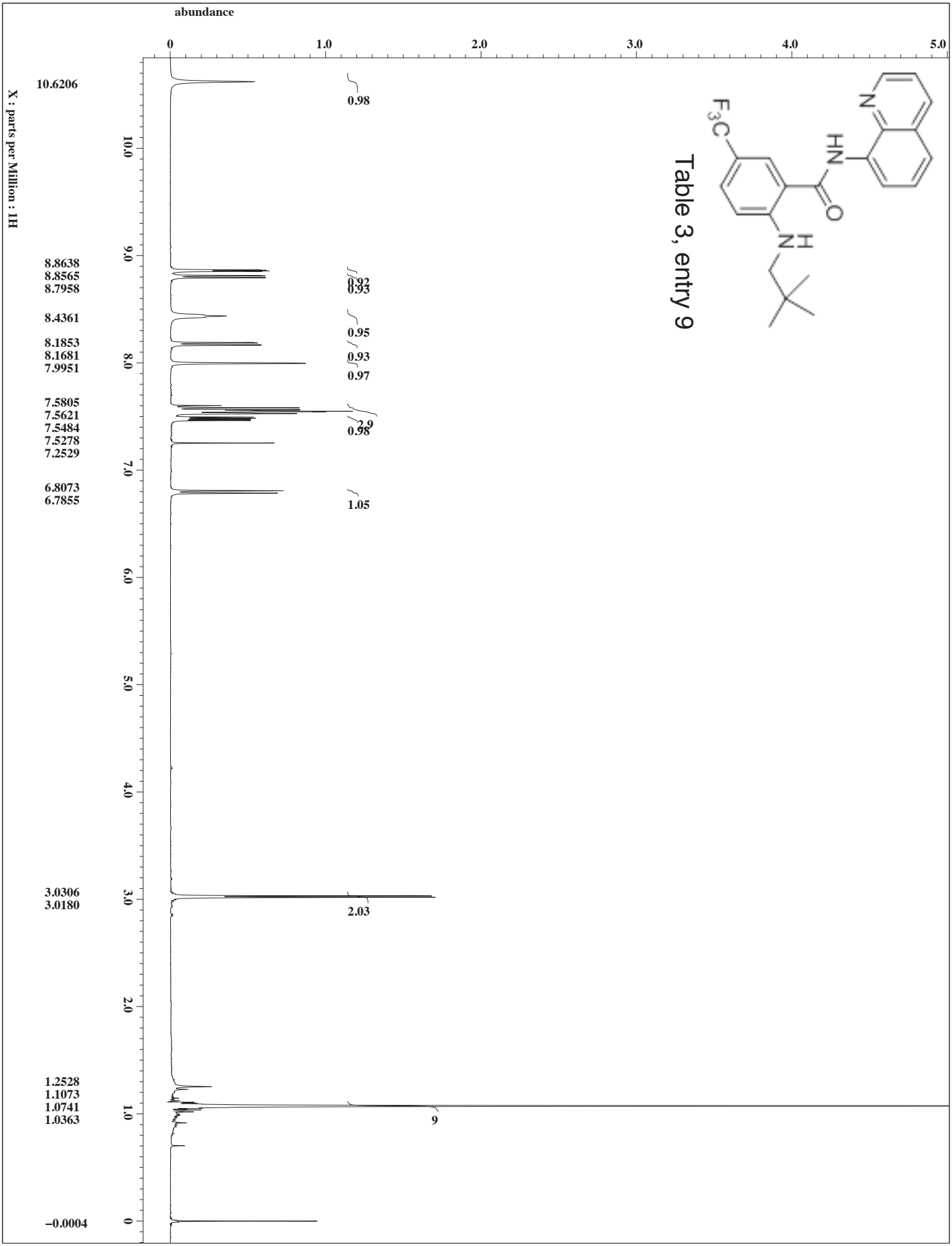

abundance
0
0.1
0.2
0.3
0.4
X : parts per Million : 13C
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
165.6947
162.8237
155.2121
153.6288
147.6864
139.0256
136.5838
136.0401
133.9226
129.1248
128.4571
128.3141
127.8276
121.6181
121.5132
117.9268
108.0833
106.2996
79.4874
77.4080
77.1600
76.9025
55.5462
53.0948
31.8244
28.4764
HN
O
N
OMe
N
NH
O
O
tBu
Table 3, entry 6

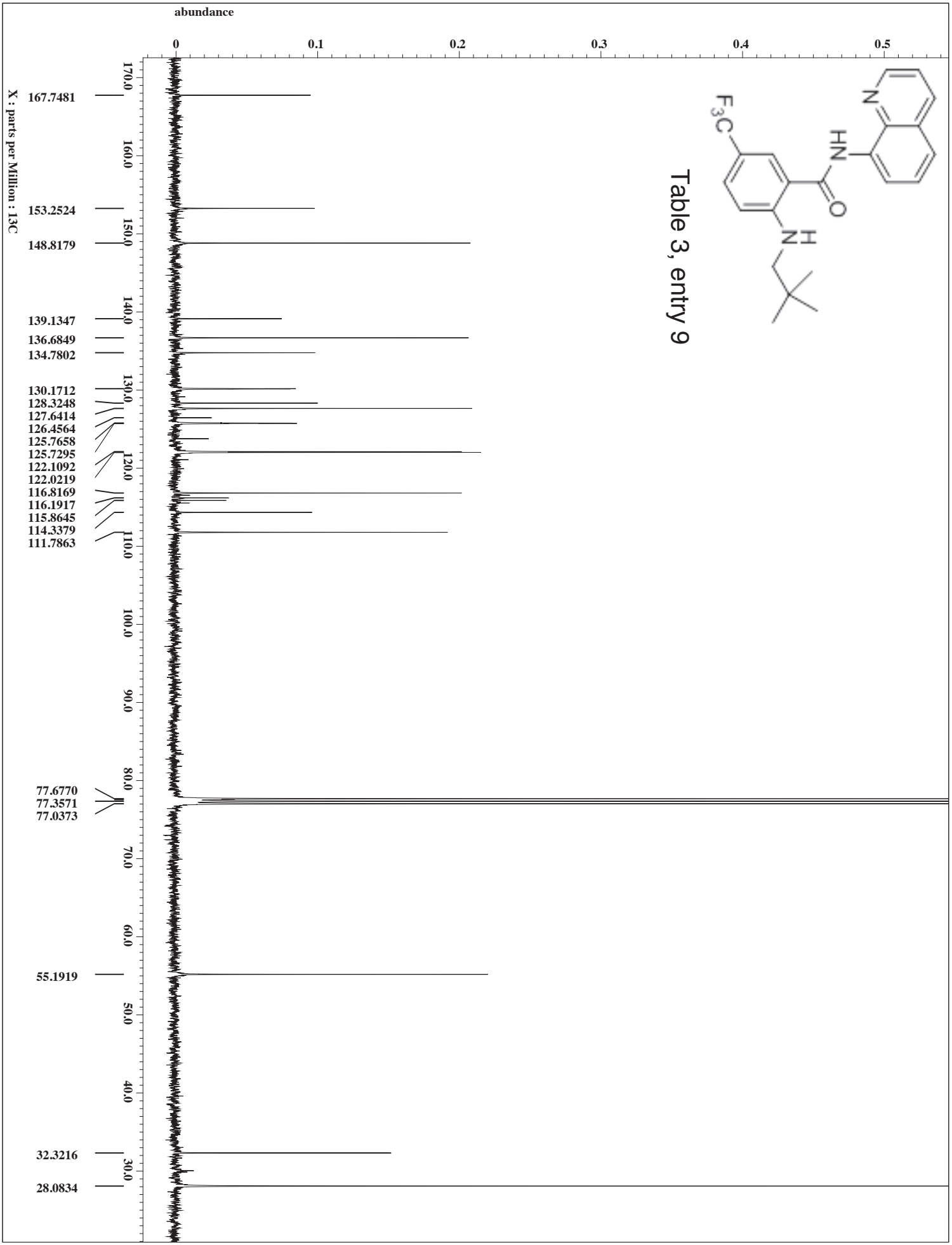

abundance
X : parts per Million : 1H
Table 3, entry 7
10.5912
8.8707
8.8673
8.8604
8.1823
8.1784
7.9887
7.9852
7.5671
7.5614
7.5568
6.8100
6.7882
3.4445
3.4342
3.4262
2.0688
2.0424
1.8110
1.7973
1.7881
1.4342
1.4067
1.3815
1.3574
0.89
0.92
0.91
1.89
0.98
3.93
1
1.0
2.03
2.02
1.0
5.04

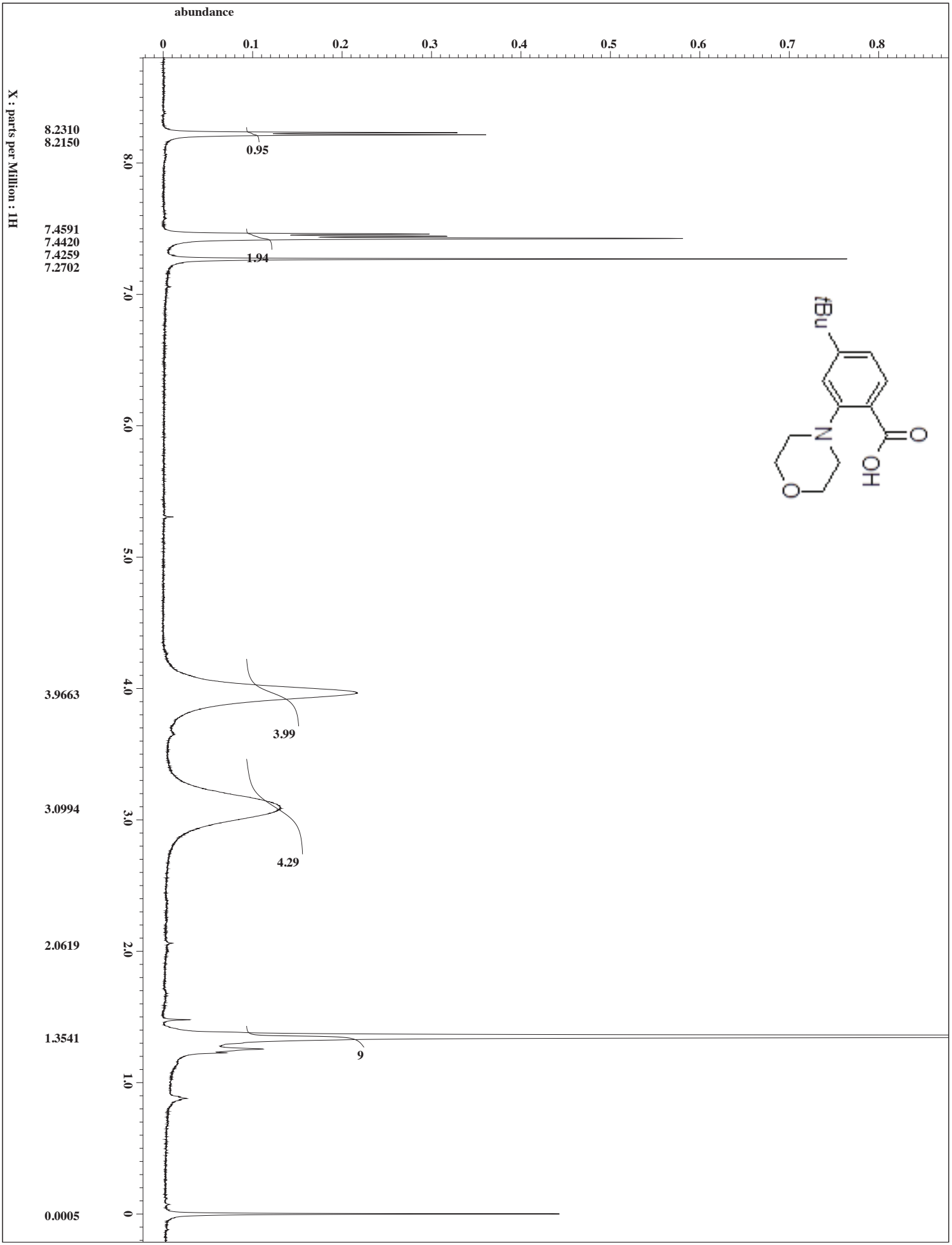

abundance
0
0.1
0.2
0.3
0.4
X : parts per Million : 13C
167.5357
151.4445
148.6021
138.9398
136.4694
134.5522
129.8402
129.8116
128.1329
127.3889
125.9677
125.8055
125.7769
123.8215
121.9043
121.8662
116.5724
115.8761
115.6186
114.2641
112.0322
77.4080
77.1600
76.9025
50.8915
32.7401
25.8915
24.7946
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
Table 3, entry 7
F3C
HN
O
N
H
N


abundance
X : parts per Million : 1H
Table 3, entry 8
10.5878
8.8730
8.8684
8.8581
8.2052
8.2017
8.1846
8.1811
7.5855
7.5671
7.5614
7.5568
6.7321
6.7092
3.6450
3.6358
3.6255
1.7526
1.6369
1.6049
1.5957
1.5728
1.5533
1
0.99
0.95
2.0
1.07
3.15
0.96
1.06
1.1
2.05
13.15


abundance
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
X : parts per Million : 13C
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
167.4913
151.1903
148.5673
138.9050
136.4441
134.5364
129.8340
128.1076
127.3731
125.9710
125.7898
125.7516
123.8249
121.8695
121.8314
116.5567
115.7650
115.4979
114.3438
112.1404
77.3923
77.1443
76.8868
52.1444
32.1997
27.2112
25.8281
23.9681
Table 3, entry 8
F3C
HN
O
N
H
N


abundance
0
1.0
2.0
3.0
4.0
5.0
X : parts per Million : 1H
10.6206
8.8638
8.8565
8.7958
8.4361
8.1853
8.1681
7.9951
7.5805
7.5621
7.5484
7.5278
7.2529
6.8073
6.7855
3.0306
3.0180
1.2528
1.1073
1.0741
1.0363
−0.0004
0.98
0.92
0.93
0.95
0.93
0.97
2.9
0.98
1.05
2.03
9
Table 3, entry 9


abundance
0
0.1
0.2
0.3
0.4
0.5
X : parts per Million : 13C
167.7481
153.2524
148.8179
139.1347
136.6849
134.7802
130.1712
128.3248
127.6414
126.4564
125.7658
125.7295
122.1092
122.0219
116.8169
116.1917
115.8645
114.3379
111.7863
77.6770
77.3571
77.0373
55.1919
32.3216
28.0834
Table 3, entry 9


abundance
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
X : parts per Million : 1H
8.2310
8.2150
0.95
7.4591
7.4420
7.4259
7.2702
1.94
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
tBu
N
O
O
OH
3.9663
3.99
3.0994
4.29
2.0619
1.3541
9
0.0005