An aerobic Cu-catalyzed practical approach to aromatic nitriles using cyanide anions as the nitrogen source

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Supporting Information

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(A) Materials and equipment

Reagents were obtained commercially and used as received. Solvents were purified and dried by standard methods. ^{1}H NMR spectra were recorded on a Bruker-400 NMR spectrometer using TMS as an internal standard. Chemical shift values (δ) are given in ppm. Coupling constants (J) were measured in Hz. GC-MS analyses were performed on a SHIMADZU QP2010. High Resolution mass spectrometer (HRMS) spectra were recorded on a Bruker micrOTOF-Q II analyzer. 200-300 mesh silica gel was used for column chromatography.

(B) Isotope incorporation experiment of the nitrogenation

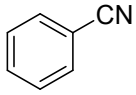
(1) Synthesis of ^{13}C-labeled 1-(1-Methyl-1H-indol-3-yl)ethanone 1n

A sealable tube with a magnetic stir bar was charged with (Phen)$Pd(OAc)_2$ (20.2 mg, 0.05 mmol), N-methyl-indole (0.5 mmol), ^{13}C-labeled $CH_3{}^{13}CN$ (1.5 mmol), H_2O (200 μL), CH_3COOH (300 μL) and 1,4-dioxane (1.0 mL) under air. The resulting solution was heated at 140 °C for 36 h and then cooled to ambient temperature. The mixture was diluted with 30 mL of CH_2Cl_2, filtered through a celite pad, and then washed with 10 mL of CH_2Cl_2. The combined organic phases were concentrated and the resulting residue was purified by column chromatography on silica gel to give ^{13}C-labeled **1n**.

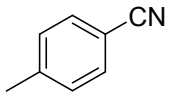
(2) ^{13}C-labeling experiments

CuCN (0.35 mmol), DMSO (1.5 mL), and ^{13}C-labeled **1n** (0.2 mmol) at 150 ˚C in O_2 for 16 h. After the reaction was finished, the reaction mixture was then cooled to ambient temperature, diluted with 8 mL EtOAc, filtered through a Celite pad, and washed with 10 mL of EtOAc. The organic portion was washed with a saturated solution of brine (8 mL), dried (Na_2SO_4) and concentrated in vacuum, and the resulting residue was purified by silica gel column chromatography (hexane/ethyl acetate) to provide ^{13}C-labeled **2n**. HRMS *m/z* (ESI) calcd for $C_9{}^{13}CH_9N_2$ $(M+H)^+$ 157.0761, found 157.0766, (98% ^{13}C-incorporation).

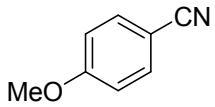
(C) Analytical data



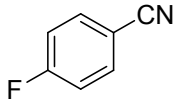
Benzonitrile 2a. ^{1}H NMR (400 MHz, $CDCl_3$, TMS, ppm): δ 7.65 (d, J = 5.2 Hz, 2H), 7.60 (t, J = 5.2 Hz, 1H), 7.60 (t, J = 5.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 132.6, 132.0, 129.0, 118.5, 112.4; LRMS (EI 70 ev): *m/z* (%): 103 (M^+, 100); HRMS *m/z* (ESI) calcd for C_7H_6N $(M+H)^+$ 104.0523, found 104.0520.



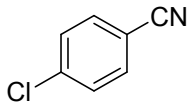
4-Methylbenzonitrile 2b. ^{1}H NMR (400 MHz, $CDCl_3$, TMS, ppm): δ 7.56 (d, J = 8.4 Hz, 2H), 7.28 (d, J = 8.4 Hz, 2H), 2.44 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 143.2, 131.6, 129.6, 119.0, 109.5, 21.6; LRMS (EI 70 ev) *m/z* (%): 117 (M^+, 100); HRMS *m/z* (ESI) calcd for C_8H_8N $(M+H)^+$ 118.0679, found 118.0686.



4-Methoxybenzonitrile 2c. ^{1}H NMR (400 MHz, $CDCl_3$, TMS, ppm): δ 7.60 (d, J = 9.2 Hz, 2H), 6.95 (d, J = 8.8 Hz, 2H); 3.85 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 162.7, 133.9, 119.2, 114.6, 103.8, 55.5; LRMS (EI 70 ev) *m/z* (%): 133 (M^+, 100); HRMS *m/z* (ESI) calcd for C_8H_8NO $(M+H)^+$ 134.0629, found 134.0621.

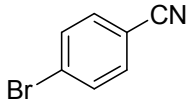


4-Fluorobenzonitrile 2d. ^{1}H NMR (400 MHz, $CDCl_3$, TMS, ppm): δ 7.71-7.68 (m, 2H), 7.21 (t, J = 5.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 164.8 (d, J = 253.4 Hz), 134.4 (d, J = 9.5 Hz), 118.1, 117.0 (d, J = 21.4 Hz), 108.5 (d, J = 4.7 Hz), LRMS (EI 70 ev) *m/z* (%): 121 (M^+, 100); HRMS *m/z* (ESI) calcd for C_7H_5FN $(M+H)^+$ 122.0429, found 122.0422.

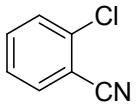


4-Chlorobenzonitrile 2e. ^{1}H NMR (400 MHz, $CDCl_3$, TMS, ppm): δ 7.63 (d, J = 8.0 Hz, 2H), 7.47 (d, J = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 139.5, 133.5,

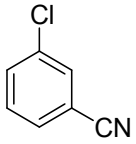
130.0, 118.2, 110.6; LRMS (EI 70 ev) *m/z* (%): 137 (M^+, 100); HRMS *m/z* (ESI) calcd for C_7H_5ClN $(M+H)^+$ 138.0133, found 138.0141.



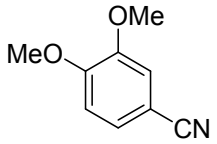
4-Bromobenzonitrile 2f. ^1H NMR (400 MHz, $CDCl_3$, TMS, ppm): δ 7.65-7.62 (m, 2H), 7.54-7.51 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 133.3, 132.6, 128.0, 118.0, 111.1; LRMS (EI 70 ev) *m/z* (%): 183 $[M+1]^+$ (45), 181 (53); HRMS *m/z* (ESI) calcd for C_7H_5BrN $(M+H)^+$ 181.9629, found 181.9644.



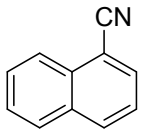
2-Chlorobenzonitrile 2g. ^1H NMR (400 MHz, $CDCl_3$, TMS, ppm): δ 7.69-7.66 (m, 1H), 7.57-7.50 (m, 2H), 7.40-7.36 (m, 1H), ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 136.8, 133.9, 133.8, 130.0, 127.1, 115.9, 113.3; LRMS (EI 70 ev) *m/z* (%): 137 (M^+, 100); HRMS *m/z* (ESI) calcd for C_7H_5ClN $(M+H)^+$ 138.0133, found 138.0139.



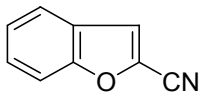
3-Chlorobenzonitrile 2h. ^1H NMR (400 MHz, $CDCl_3$, TMS, ppm): δ 7.54 (s, 1H), 7.50-7.46 (m, 2H), 7.35 (t, J = 5.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 135.6, 133.0, 131.5, 130.0, 129.8, 117.5, 114.1; LRMS (EI 70 ev) *m/z* (%): 137 (M^+, 100); HRMS *m/z* (ESI) calcd for C_7H_5ClN $(M+H)^+$ 138.0133, found 138.0143.



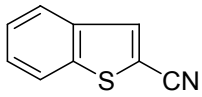
3,4-Dimethoxybenzonitrile 2i. ^1H NMR (400 MHz, $CDCl_3$, TMS, ppm): δ 7.30 (dd, J = 2.0 Hz, J = 8.0 Hz, 1H), 7.09 (d, J = 1.6 Hz, 1H), 6.92 (d, J = 8.8 Hz, 1H), 3.93 (s, 3H), 3.90 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 152.8, 149.3, 126.3, 119.3, 113.9, 111.2, 103.6, 56.1, 56.0; LRMS (EI 70 ev) *m/z* (%): 163 (M^+, 100); HRMS *m/z* (ESI) calcd for $C_9H_{10}NO_2$ $(M+H)^+$ 164.0717, found 164.0722.



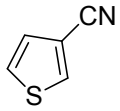
1-Naphthonitrile 2j. ^{1}H NMR (400 MHz, $CDCl_3$, TMS, ppm): δ 8.21 (d, J = 8.0 Hz, 1H), 8.05 (d, J = 8.0 Hz, 1H), 7.91-7.88 (m, 2H), 7.69-7.65 (m, 1H), 7.62-7.58 (m, 1H), 7.52 (dd, J = 3.6 Hz, J = 4.4 Hz,1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 133.3, 132.8, 132.4, 132.3, 128.5, 128.4, 127.5, 124.9, 124.6, 117.5, 110.0; LRMS (EI 70 ev) *m/z* (%): 153 (M^+, 100); HRMS *m/z* (ESI) calcd for $C_{11}H_8N$ $(M+H)^+$ 154.0680, found 154.0684.



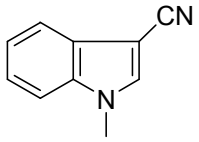
Benzofuran-2-carbonitrile 2k. ^{1}H NMR (400 MHz, $CDCl_3$, TMS, ppm): δ 7.69 (d, J = 8.0 Hz, 1H), 7.56-7.48 (m, 2H), 7.45 (s, 1H), 7.38-7.34 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 155.6, 128.4, 127.2, 125.4, 124.5, 122.5, 118.4, 112.0, 111.7; LRMS (EI 70 ev) *m/z* (%): 143 (M^+, 100); HRMS *m/z* (ESI) calcd for C_9H_6NO $(M+H)^+$ 144.0454, found 144.0461.



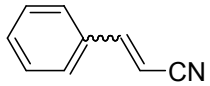
Benzo[b]thiophene-2-carbonitrile 2l. ^{1}H NMR (400 MHz, $CDCl_3$, TMS, ppm): δ 7.89-7.85 (m, 2H), 7.55-7.45 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 141.2, 137.4, 134.9, 127.8, 125.7, 125.2, 122.3, 114.4, 109.6; LRMS (EI 70 ev) *m/z* (%): 159 (M^+, 100); HRMS *m/z* (ESI) calcd for C_9H_6NS $(M+H)^+$ 160.0225, found 160.0229.



Thiophene-3-carbonitrile 2m. ^{1}H NMR (400 MHz, $CDCl_3$, TMS, ppm): δ 7.93-7.92 (m, 1H), 7.42-7.39 (m, 1H), 7.27-7.25 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 135.2, 128.3, 127.1, 114.9, 110.1; LRMS (EI 70 ev) *m/z* (%): 109 (M^+, 100); HRMS *m/z* (ESI) calcd for C_5H_4NS $(M+H)^+$ 110.0086, found 110.0082.

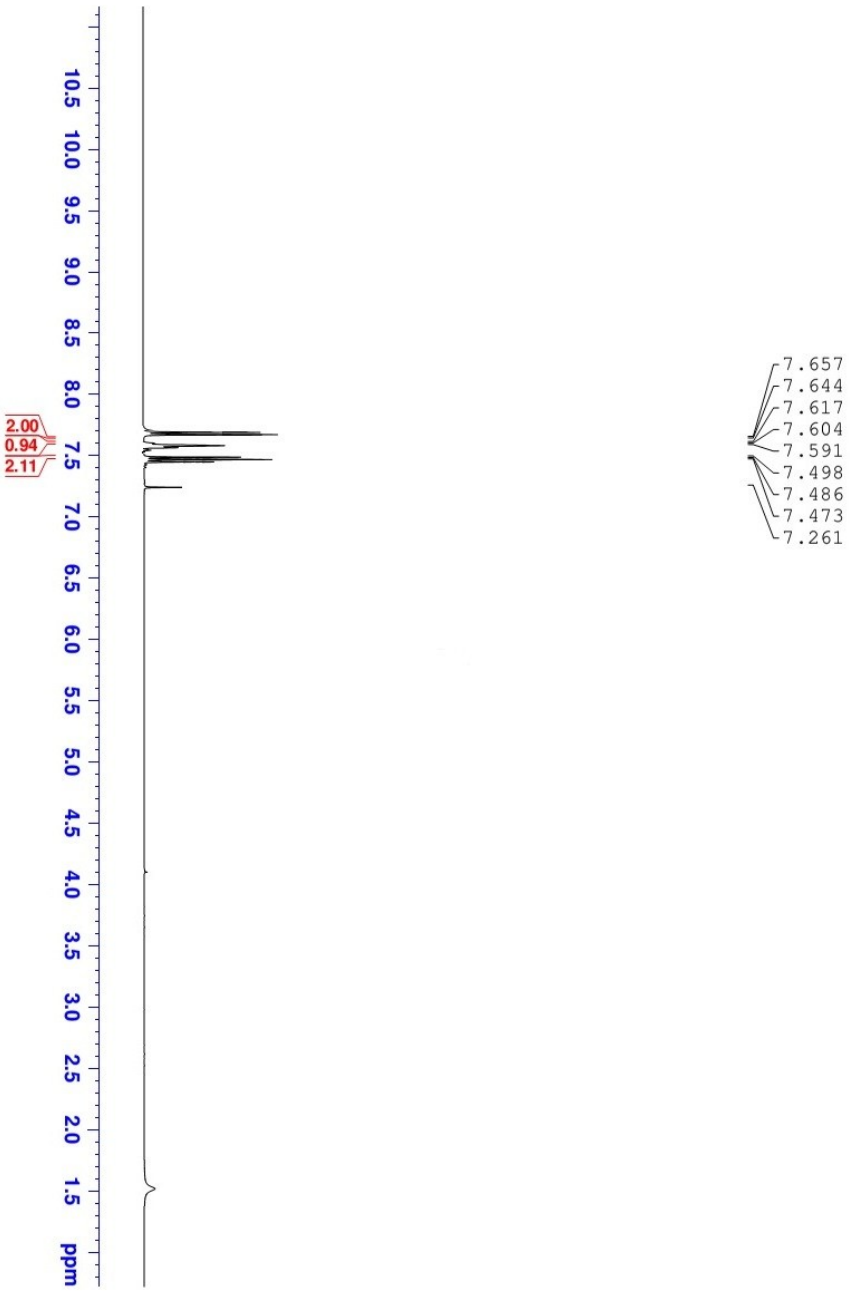


1-Methyl-1H-indole-3-carbonitrile 2n. ^{1}H NMR (400 MHz, $CDCl_3$, TMS, ppm): δ 7.73 (d, J = 7.2 Hz, 1H), 7.52 (s, 1H), 7.39-7.27 (m, 3H), 3.82 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 136.2, 135.4, 127.8, 123.9, 122.1, 120.0, 115.8, 110.2, 85.4, 33.5; LRMS (EI 70 ev) *m/z* (%): 156 (M^+, 100); HRMS *m/z* (ESI) calcd for $C_{10}H_9N_2$ $(M+H)^+$ 157.0761, found 157.0757.

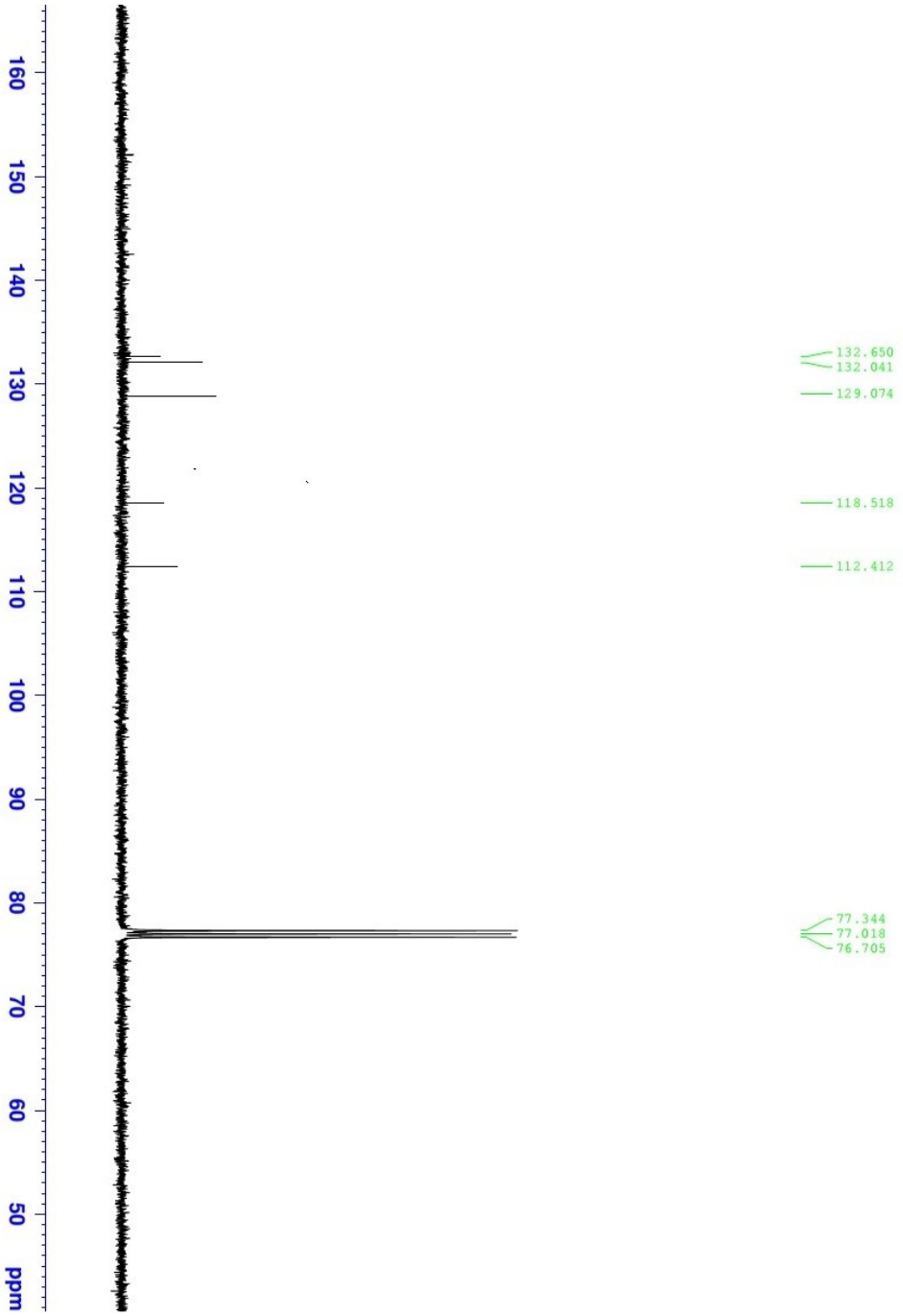


Cinnamonitrile 2o. ^{1}H NMR (400 MHz, $CDCl_3$, TMS, ppm): δ 7.47-7.39 (m, 6H), 5.91 (d, J = 16.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 150.6, 133.3, 131.3, 129.2, 127.3, 118.1, 96.3; LRMS (EI 70 ev) *m/z* (%): 129 (M^+, 100); HRMS *m/z* (ESI) calcd for C_9H_8N $(M+H)^+$ 130.0662, found 130.0670.

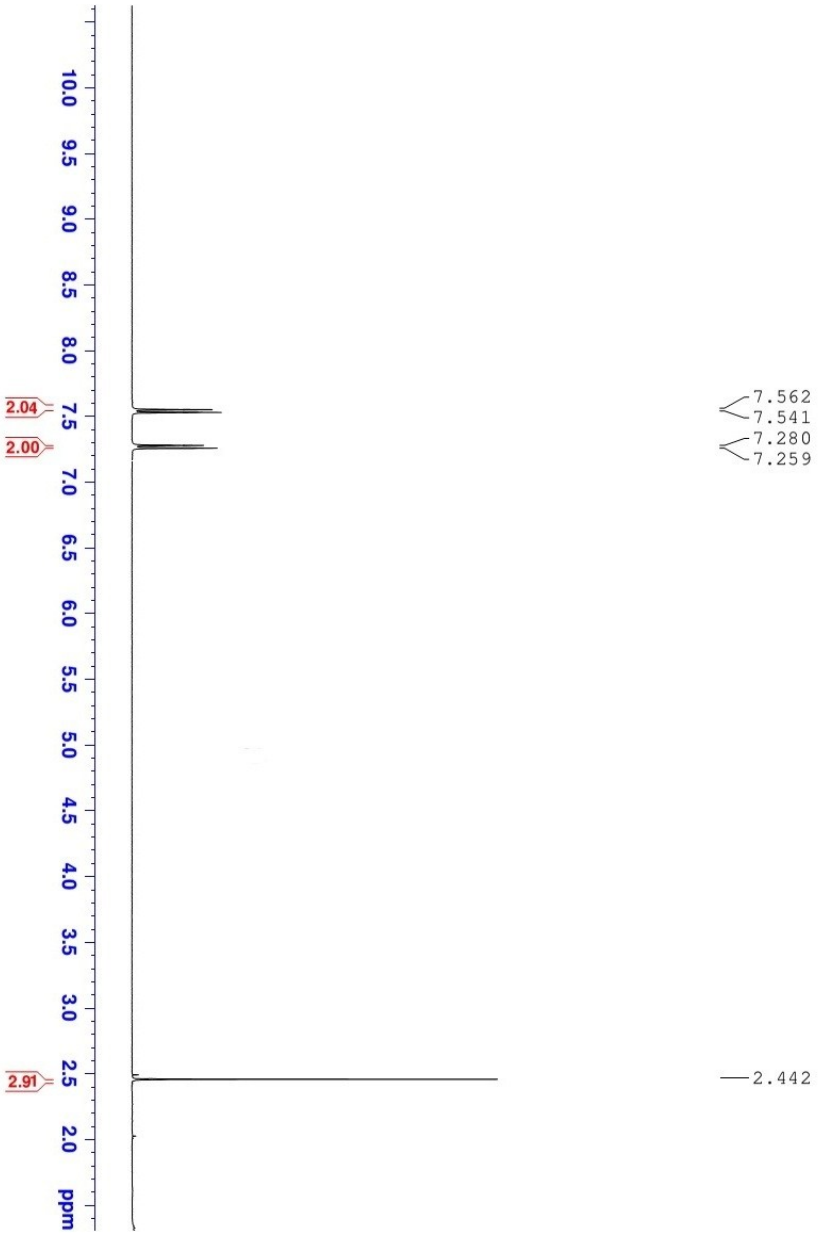
(E) Spectra



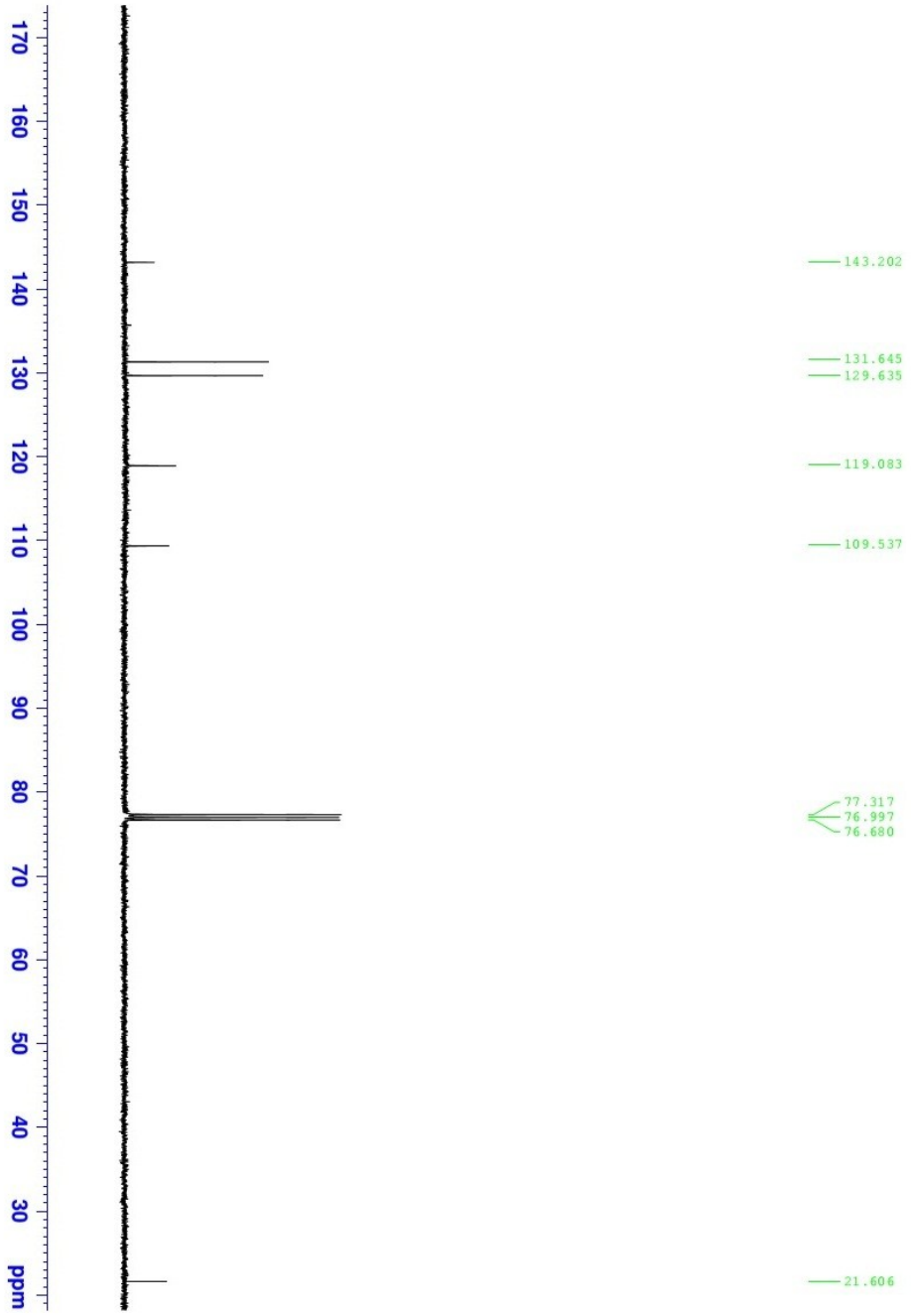
^{1}H NMR of Compound 2a



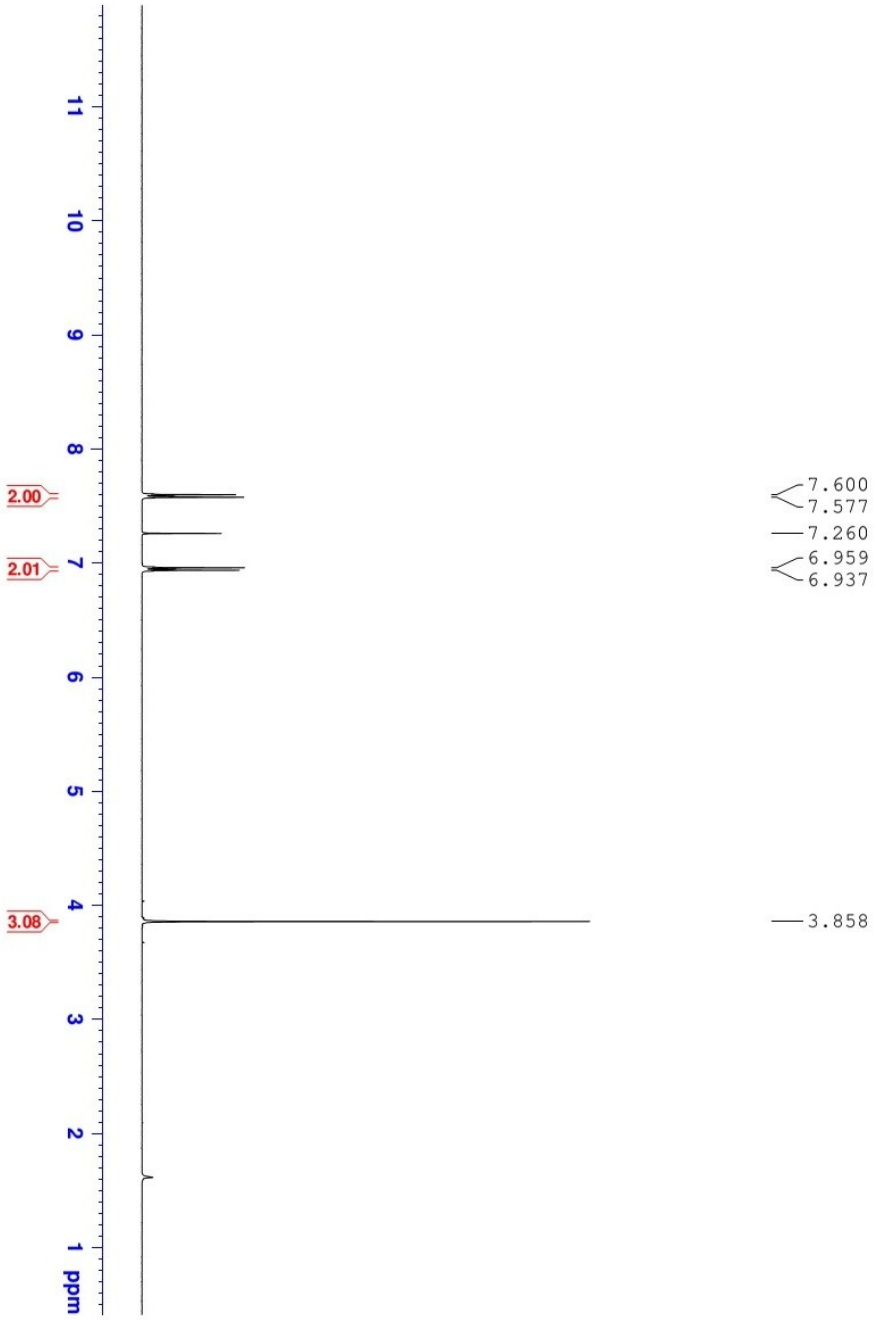
^{13}C NMR of Compound 2a



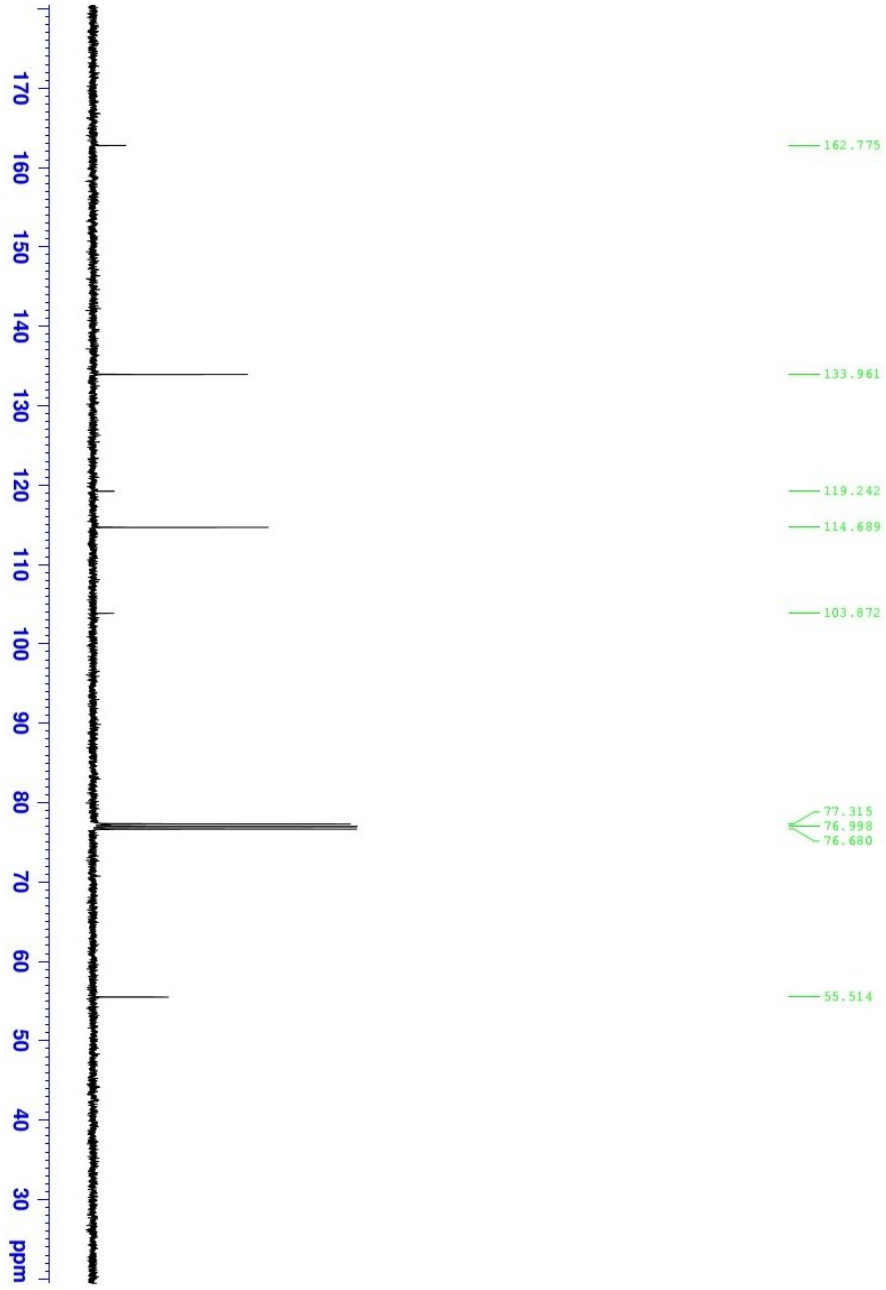
^{1}H NMR of Compound 2b



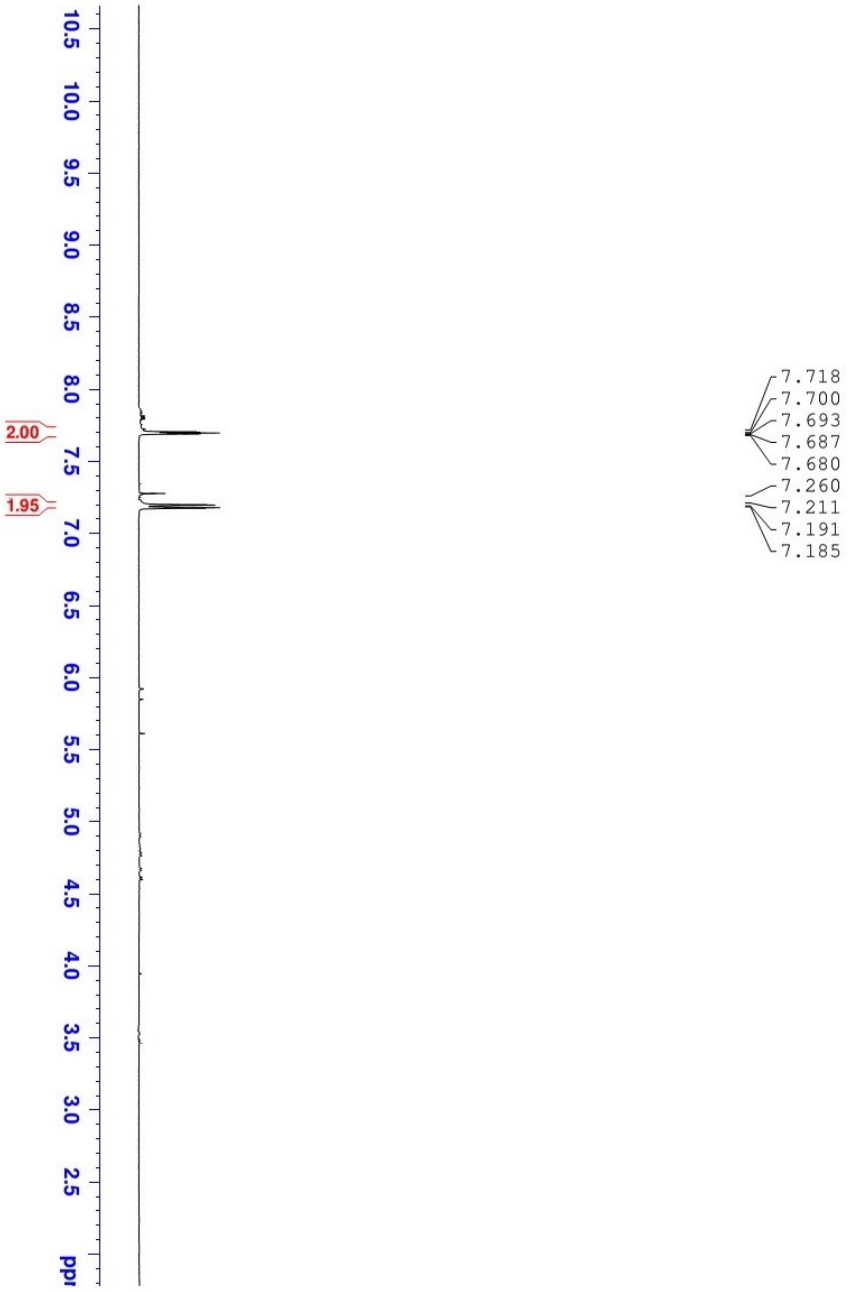
^{13}C NMR of Compound 2b



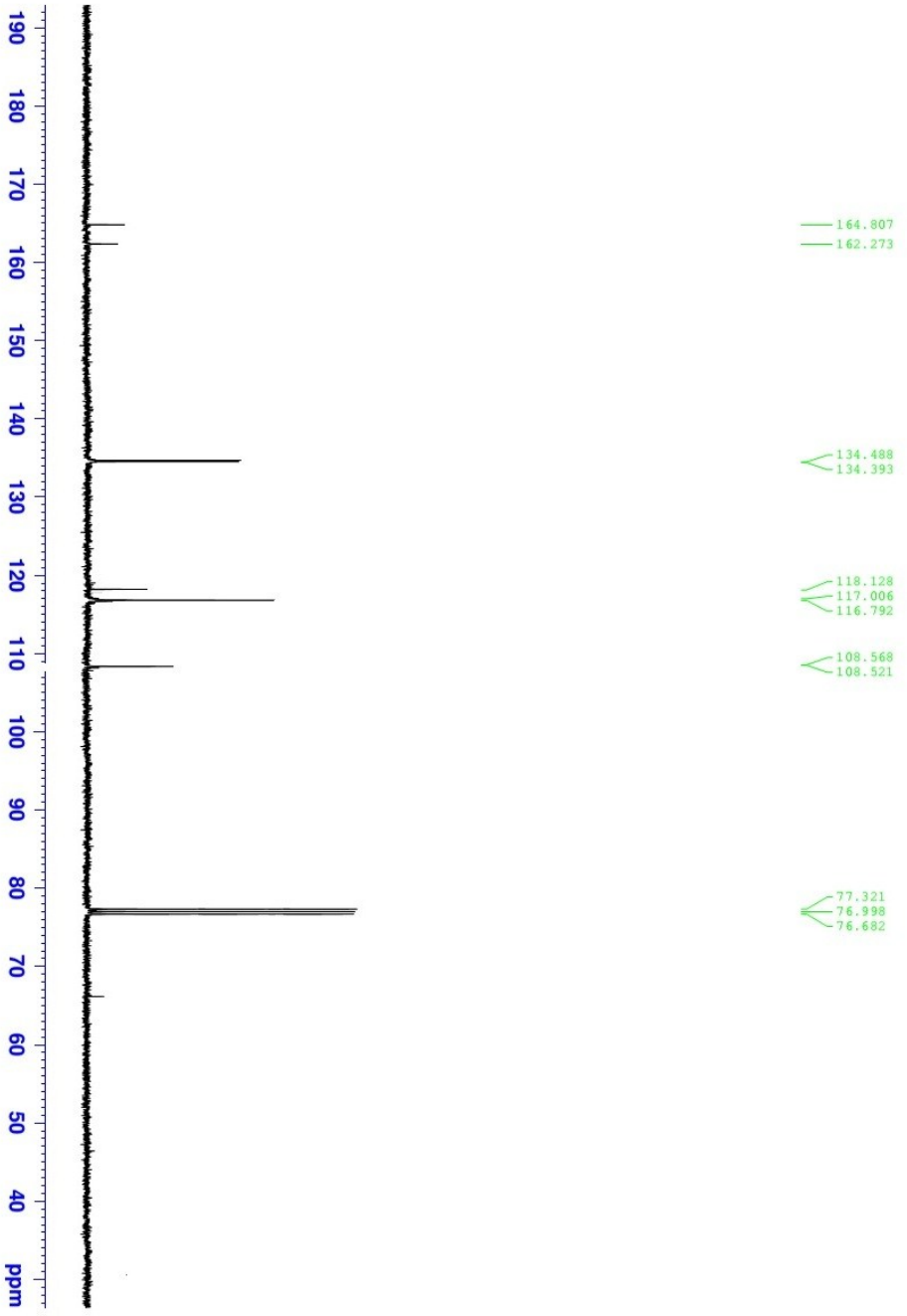
^{1}H NMR of Compound 2c



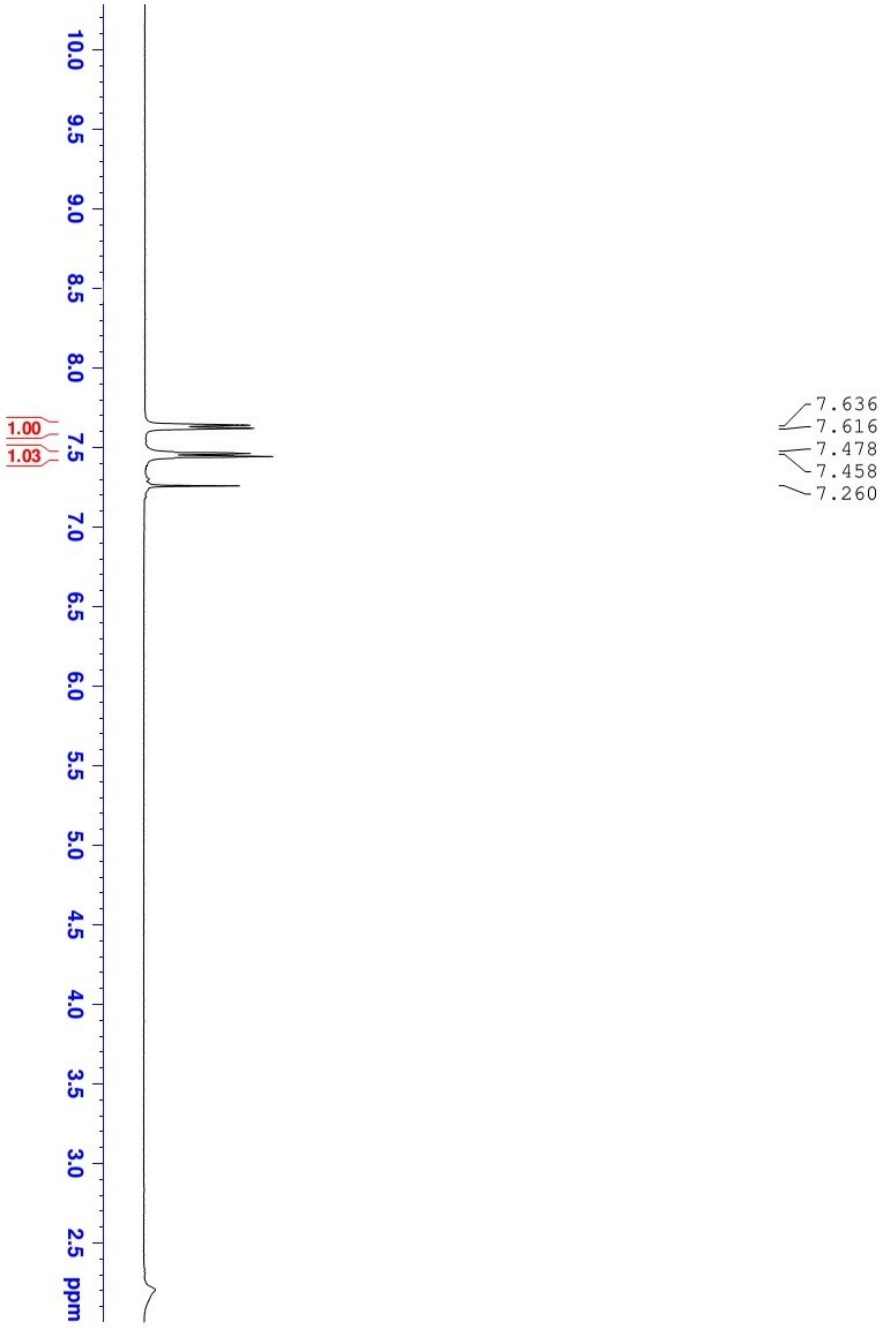
^{13}C NMR of Compound 2c



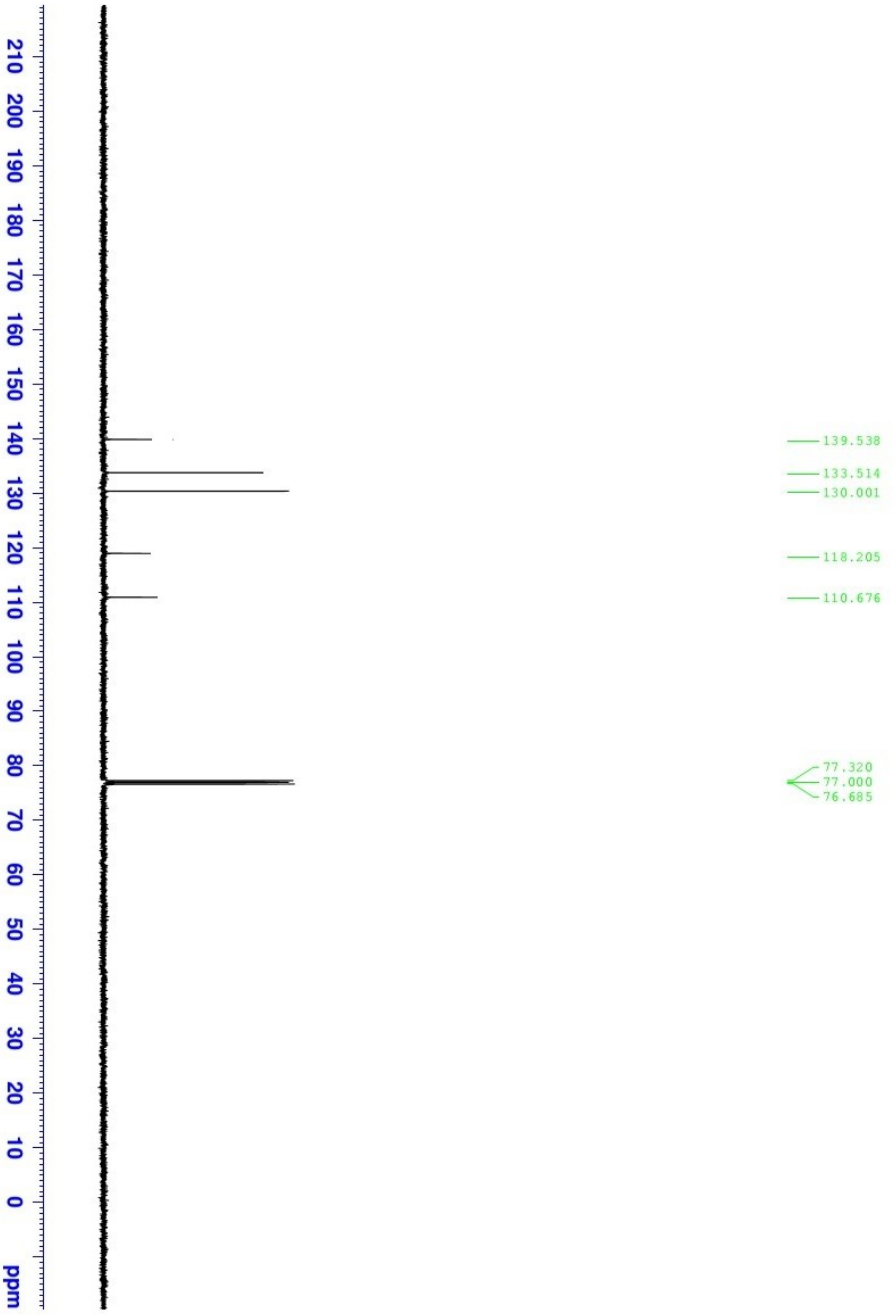
^{1}H NMR of Compound 2d



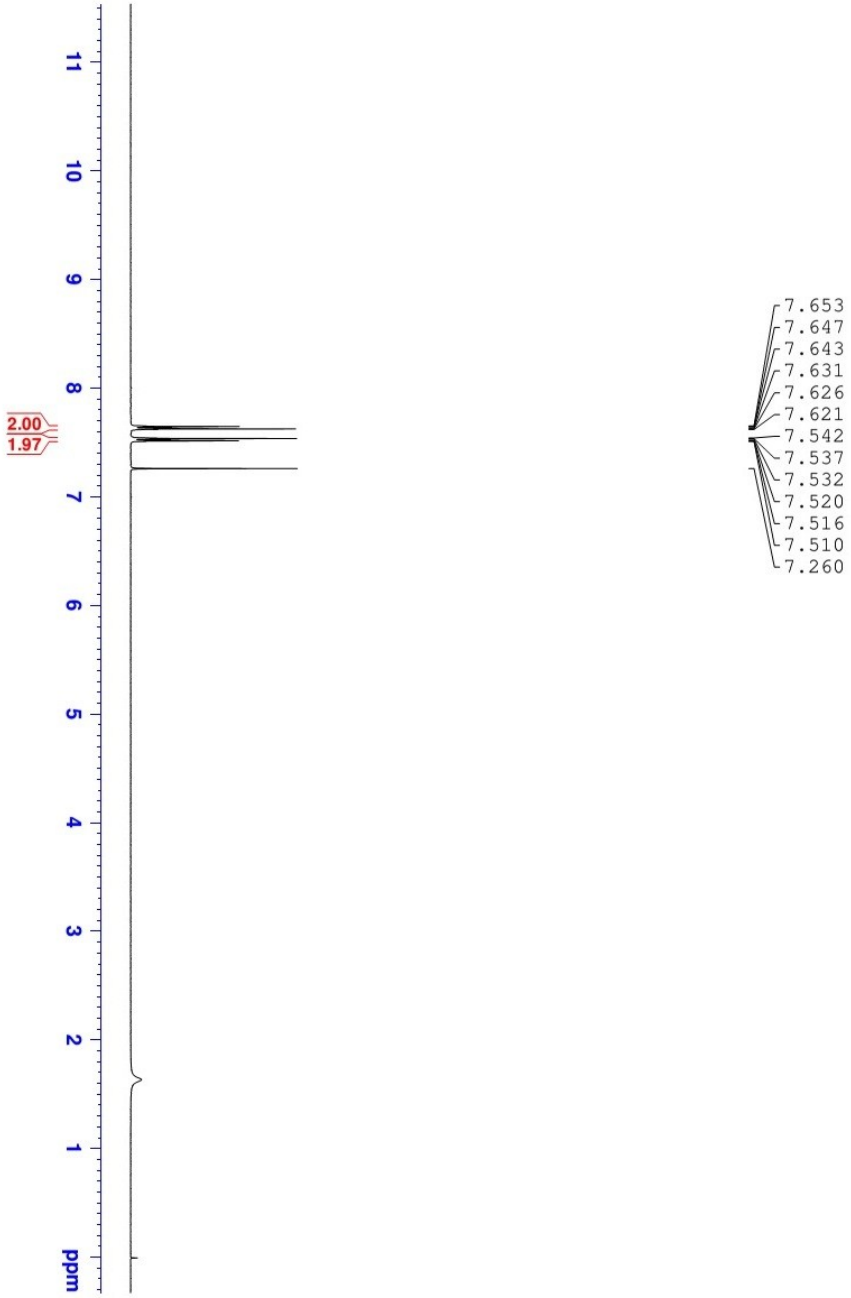
^{13}C NMR of Compound 2d



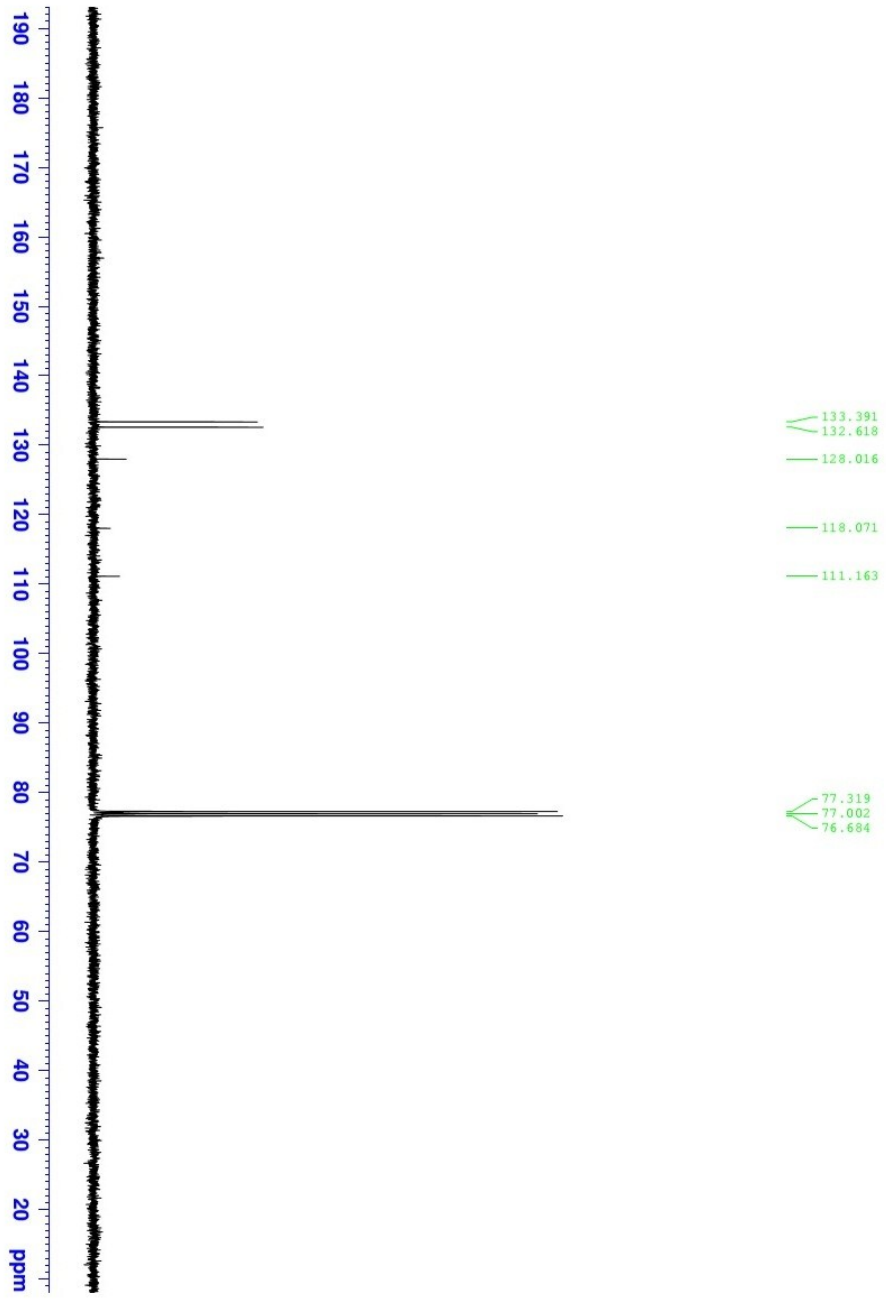
^{1}H NMR of Compound 2e



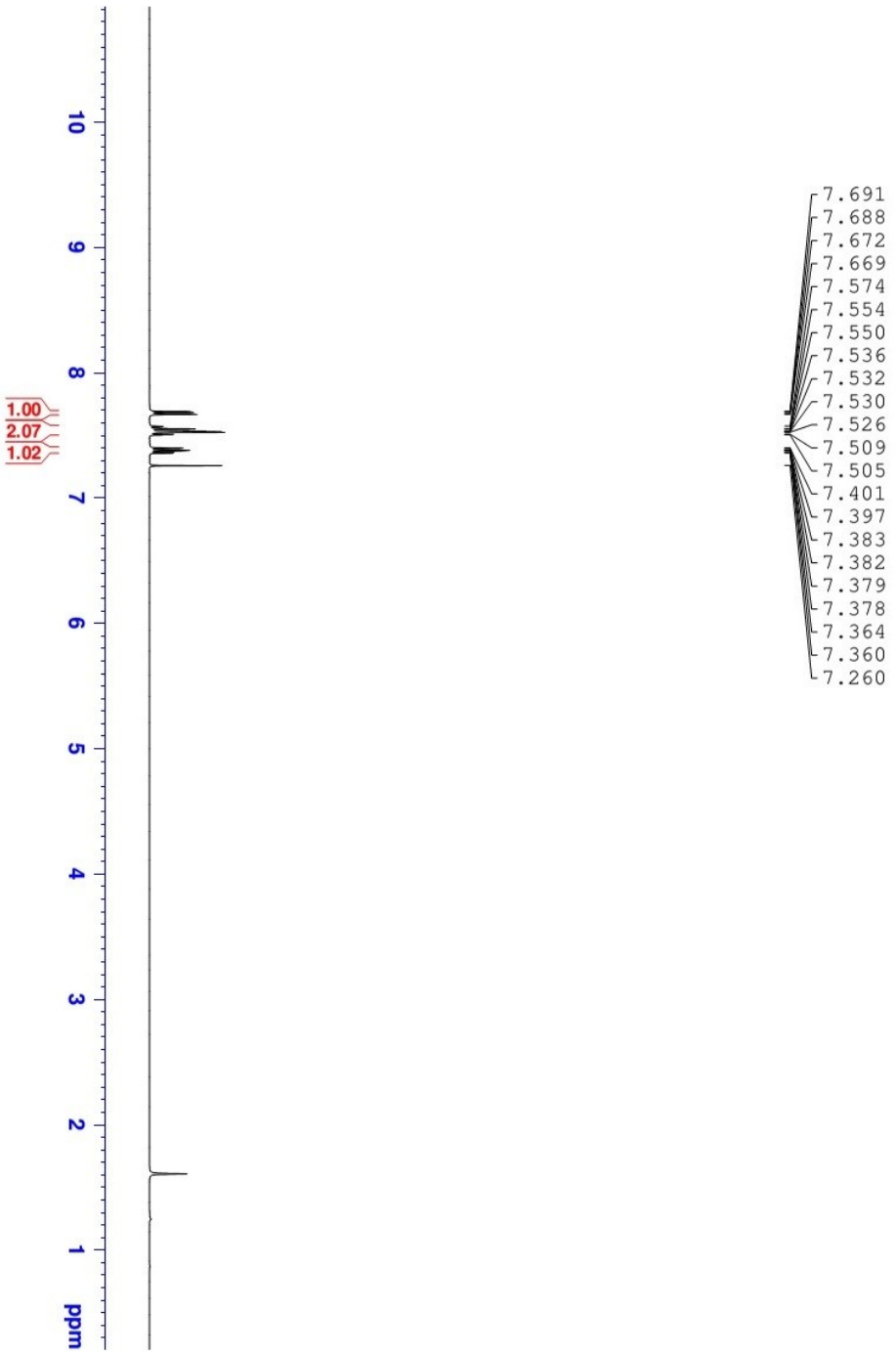
^{13}C NMR of Compound 2e



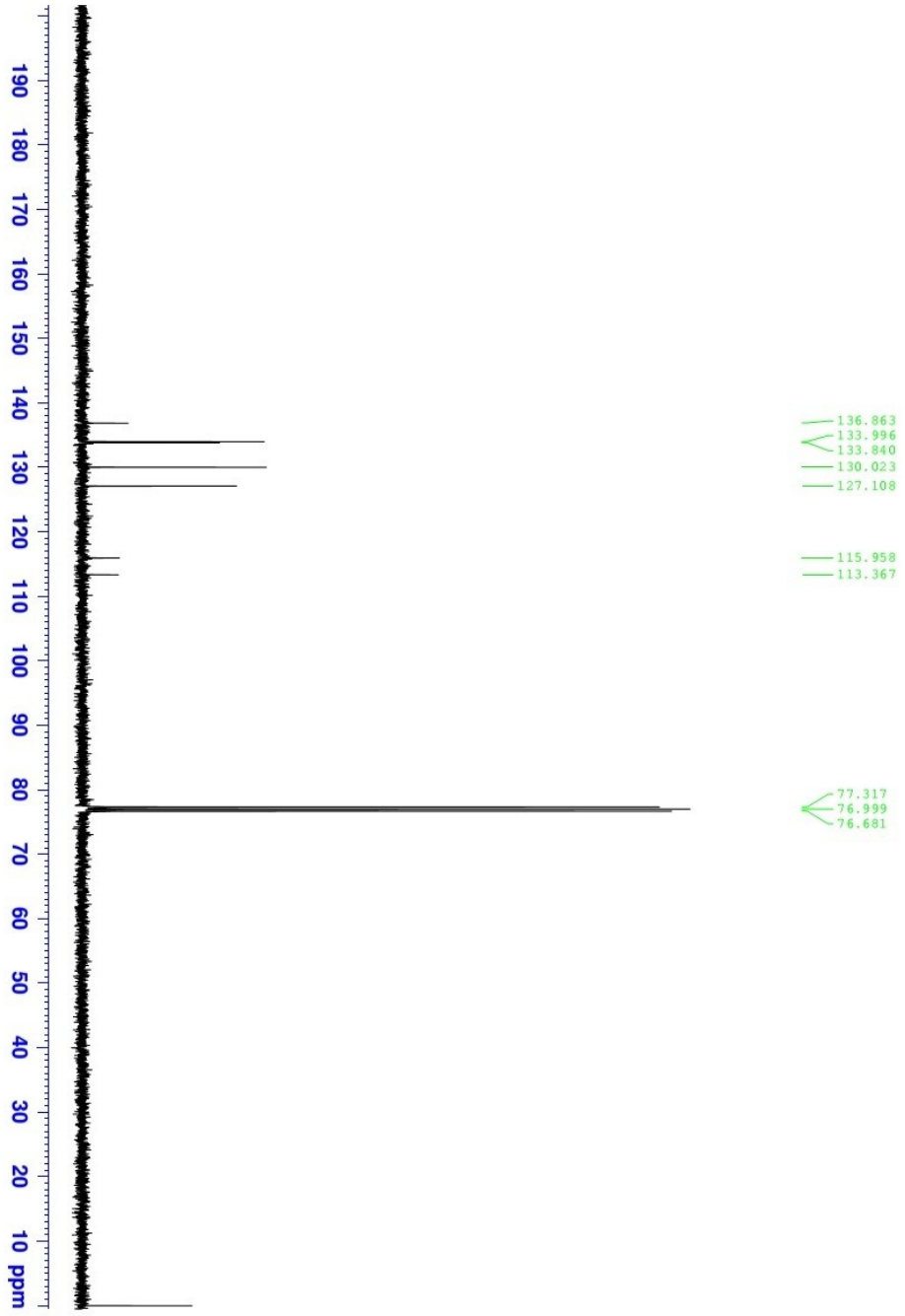
^{1}H NMR of Compound 2f



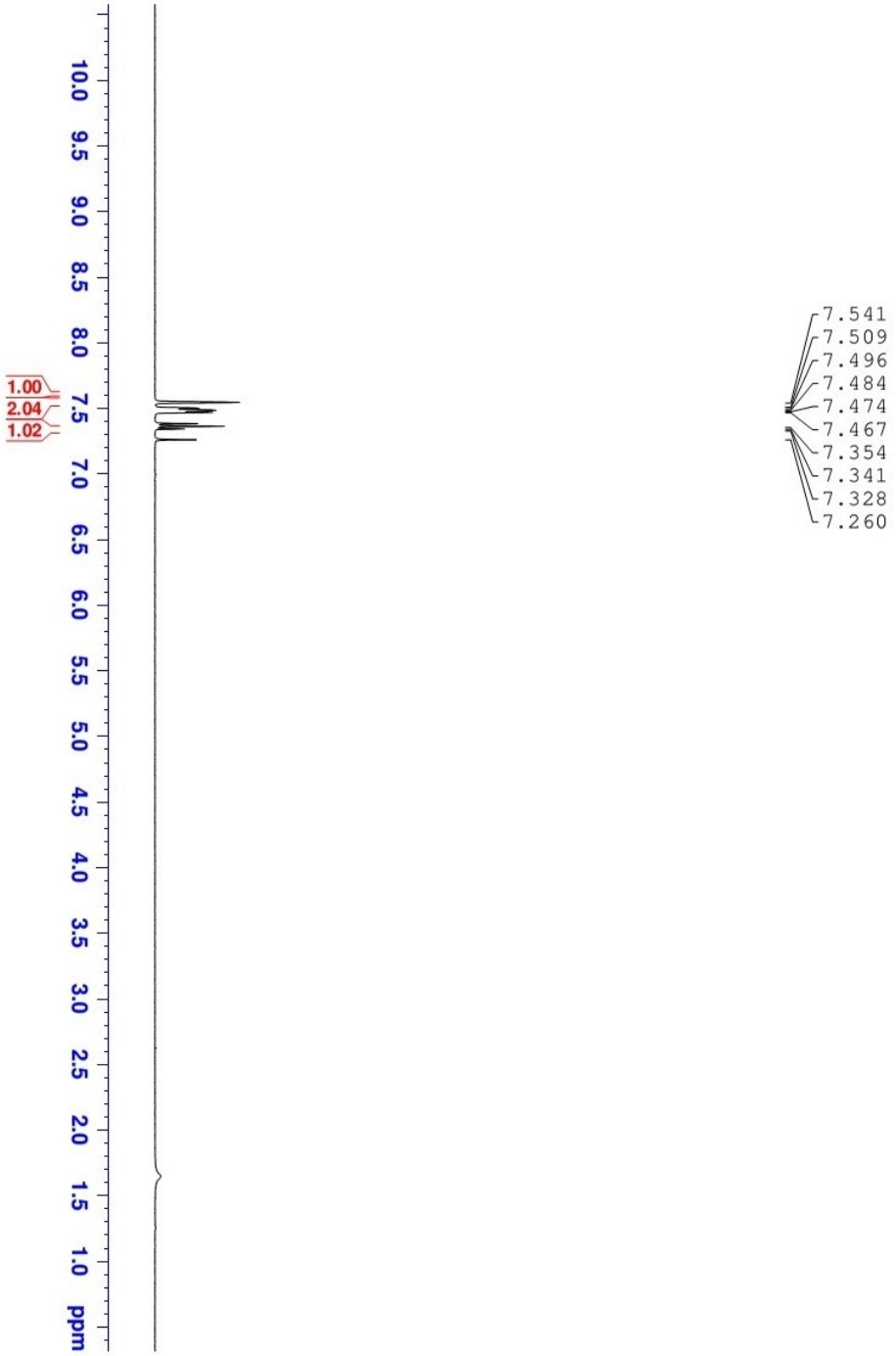
^{13}C NMR of Compound 2f



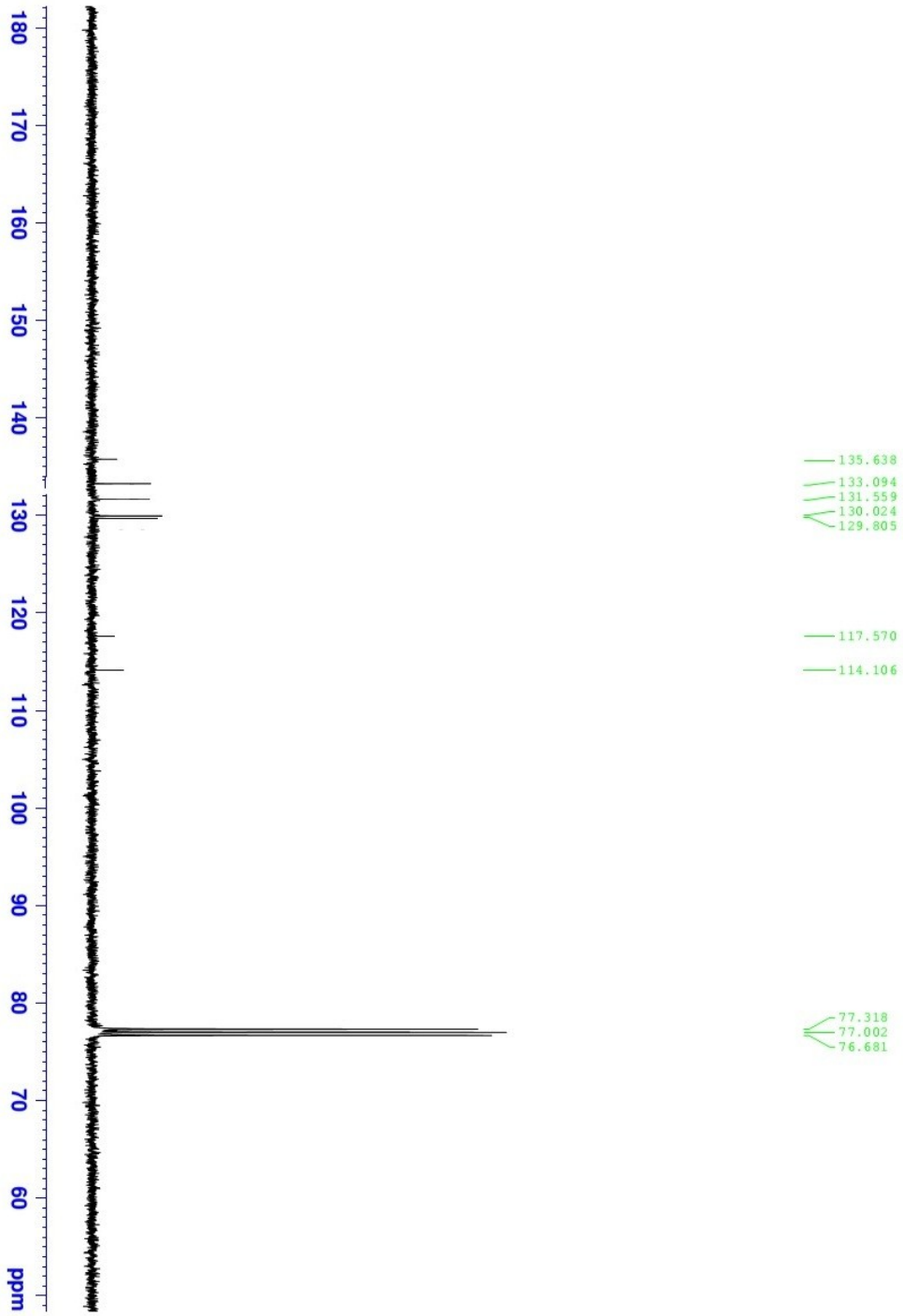
^{1}H NMR of Compound 2g



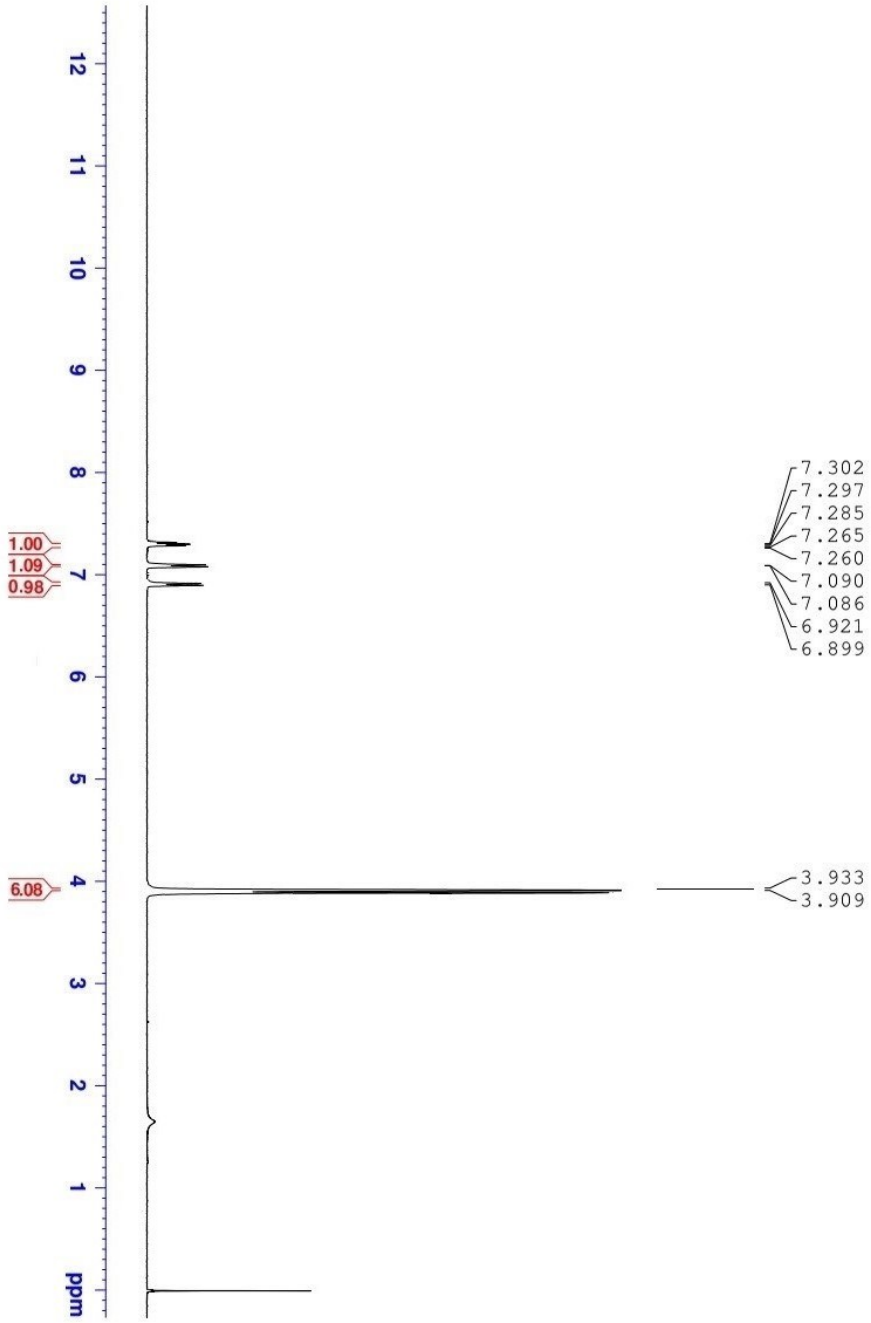
^{13}C NMR of Compound 2g



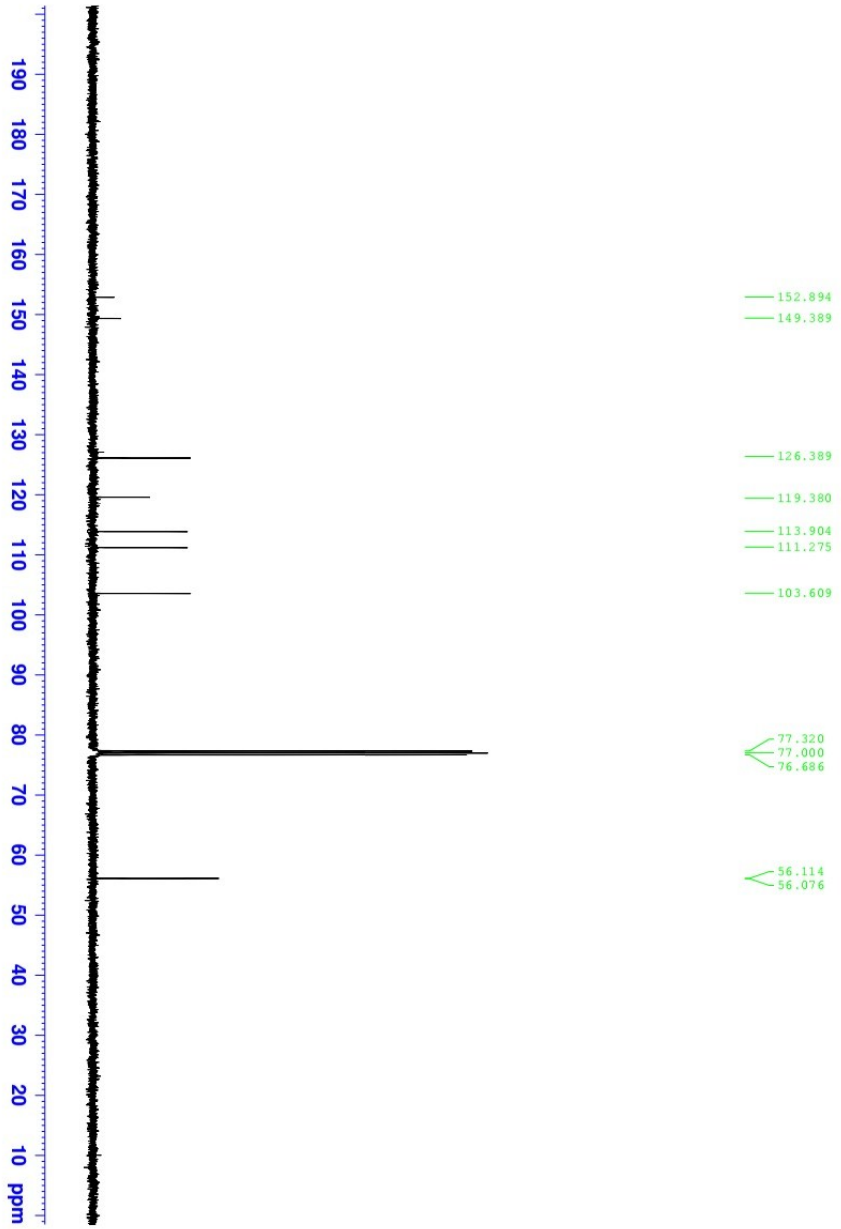
^{1}H NMR of Compound 2h



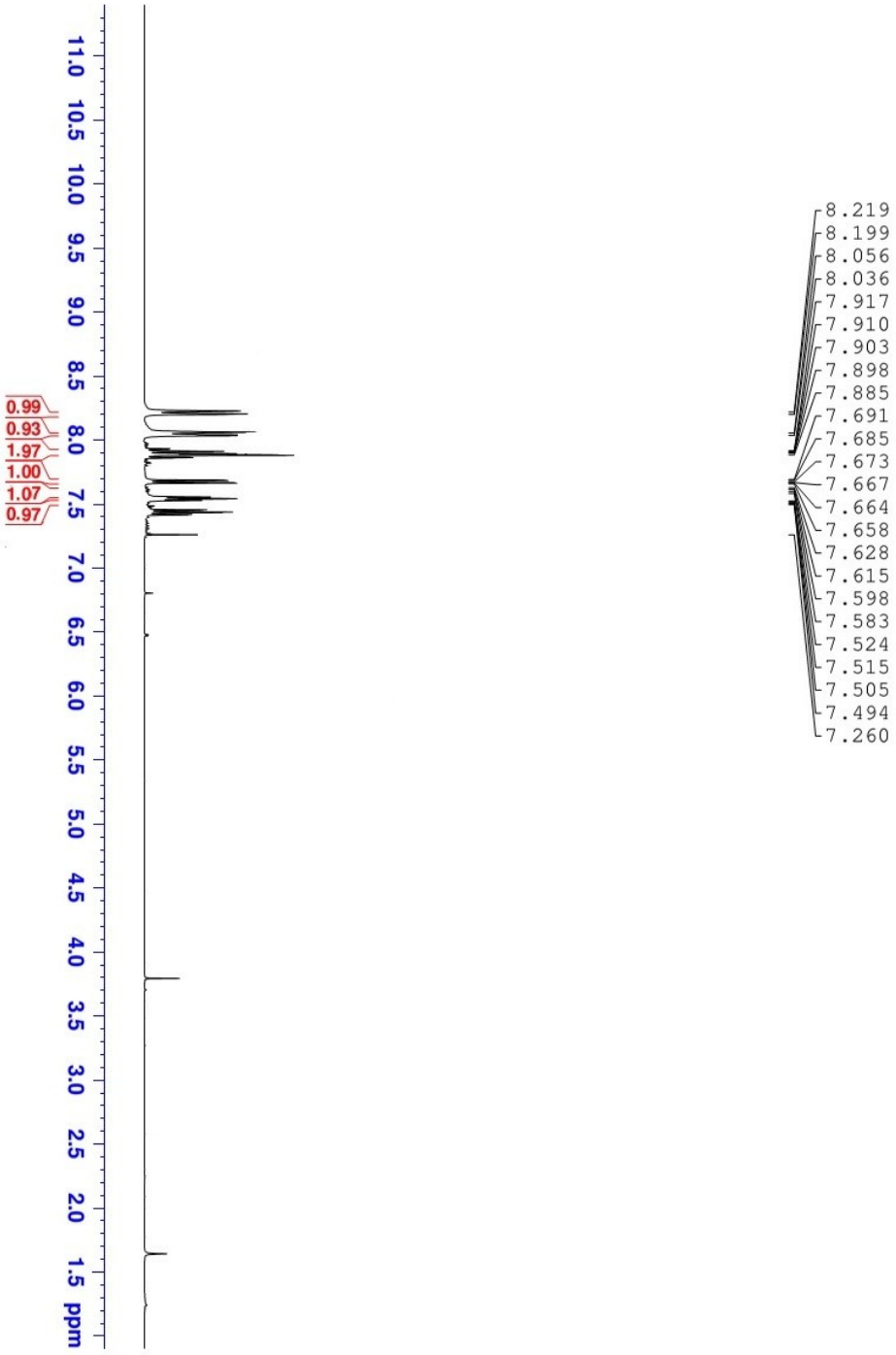
^{13}C NMR of Compound 2h



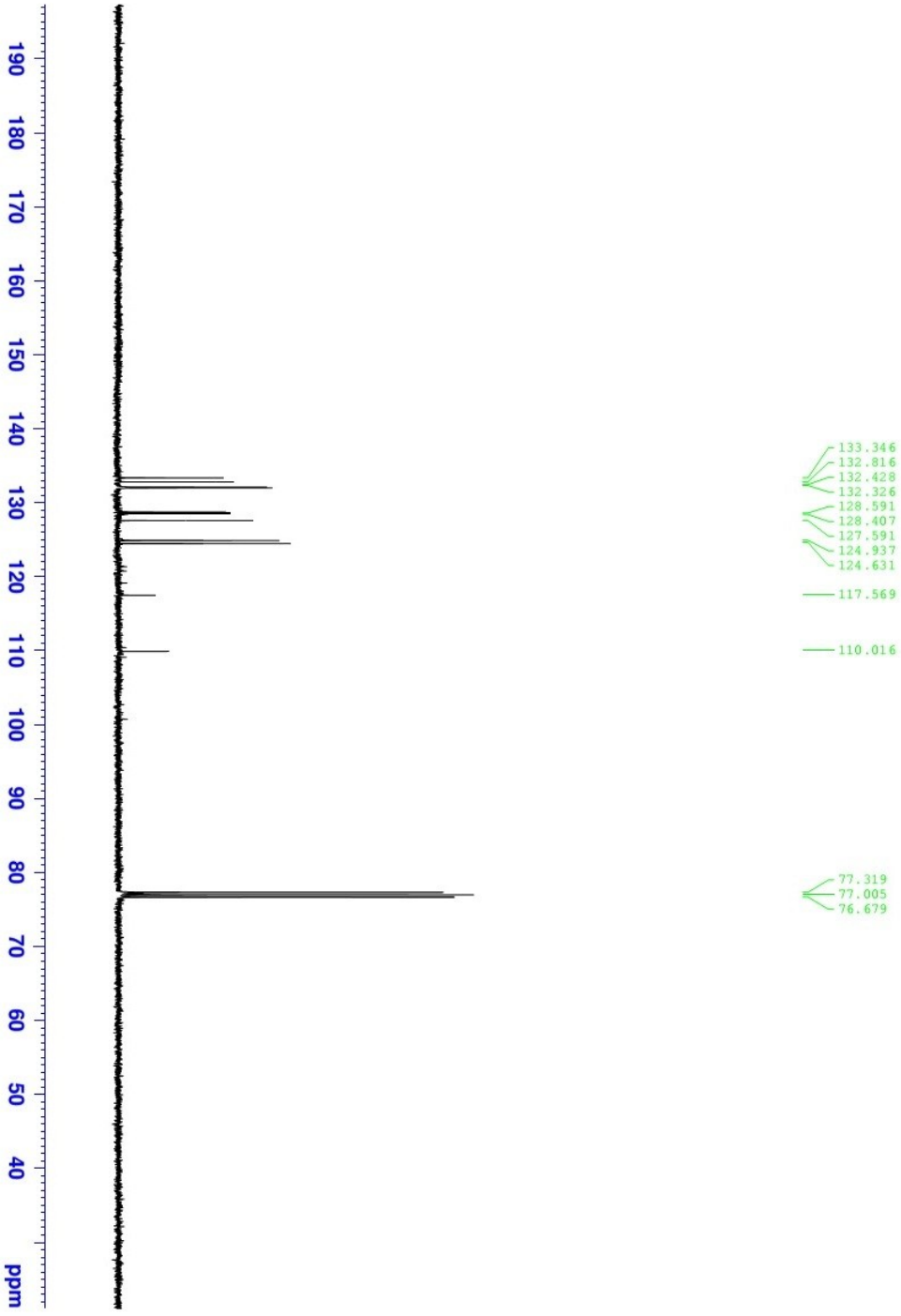
^{1}H NMR of Compound 2i



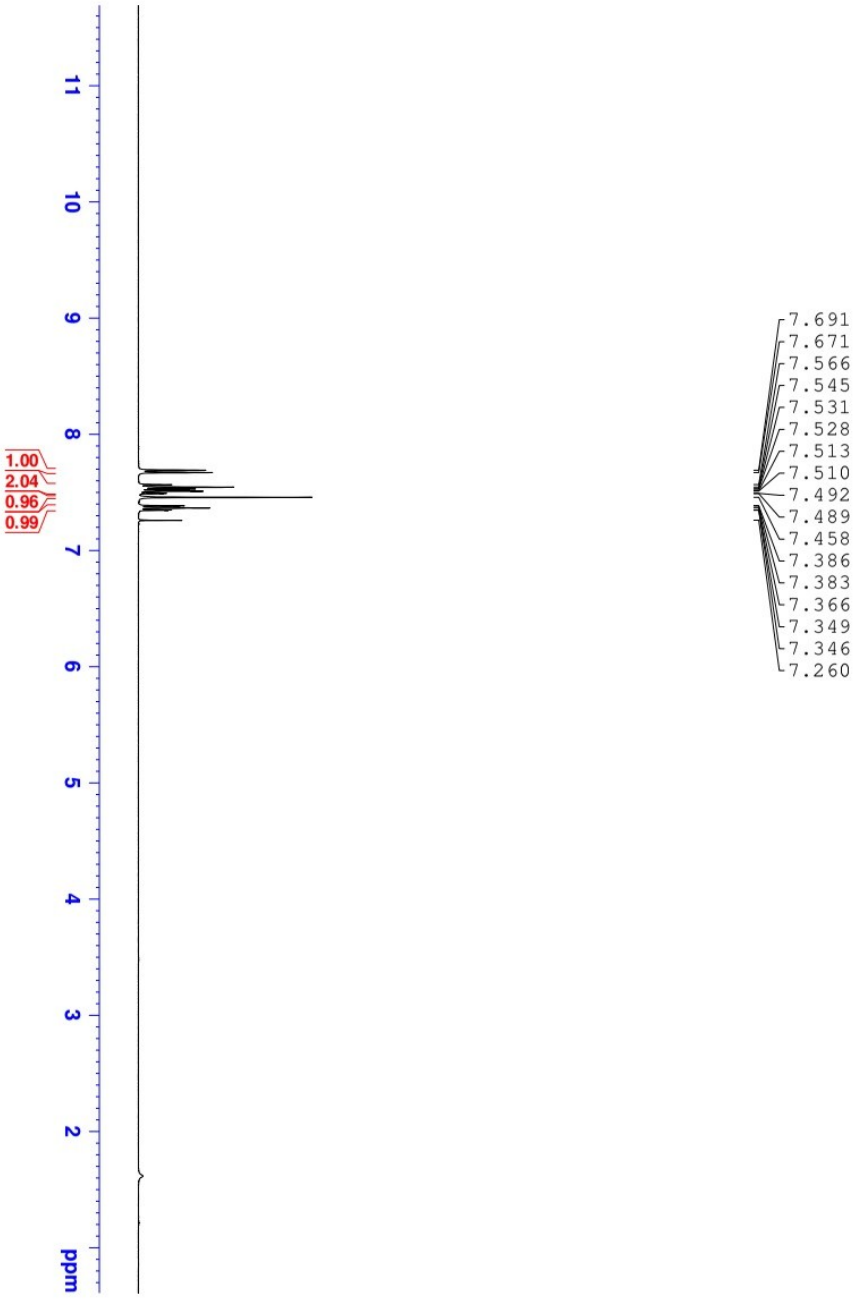
^{13}C NMR of Compound 2i



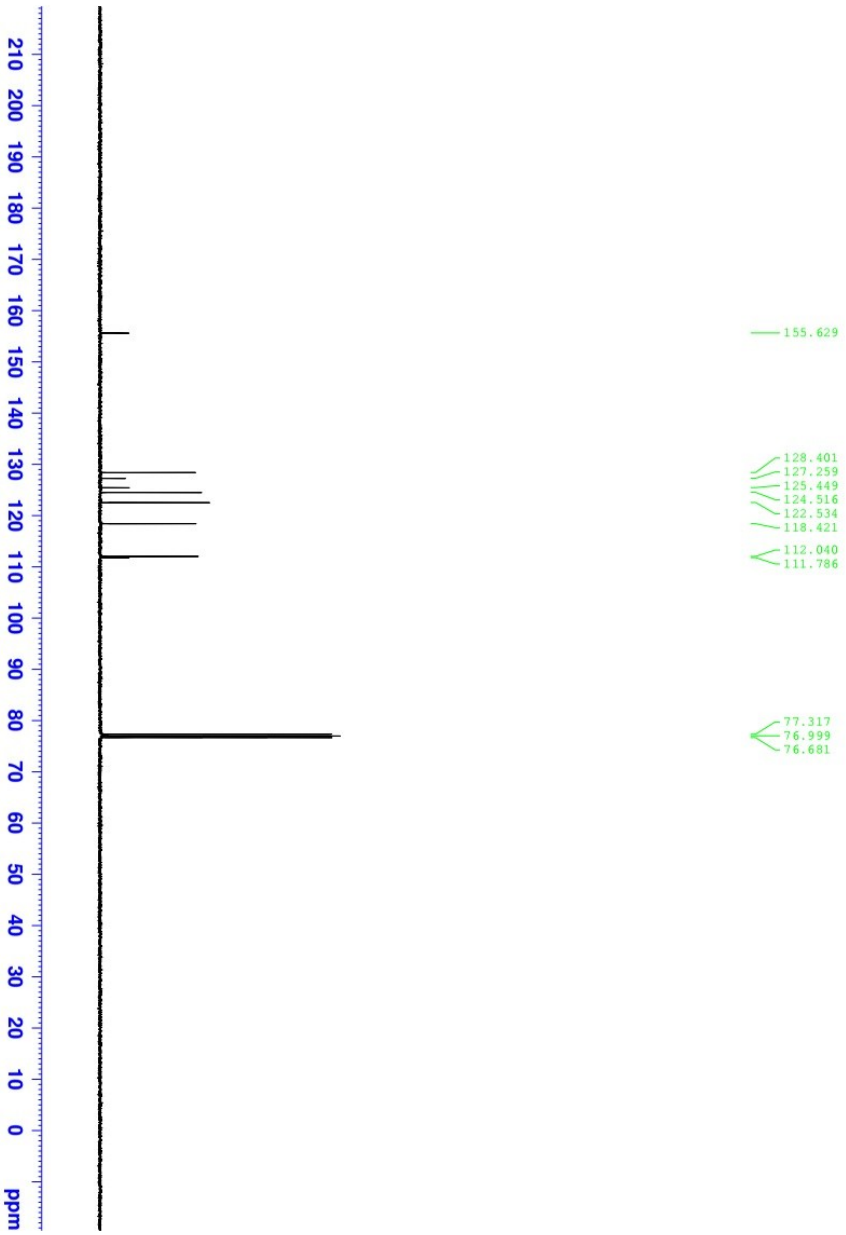
^{1}H NMR of Compound 2j



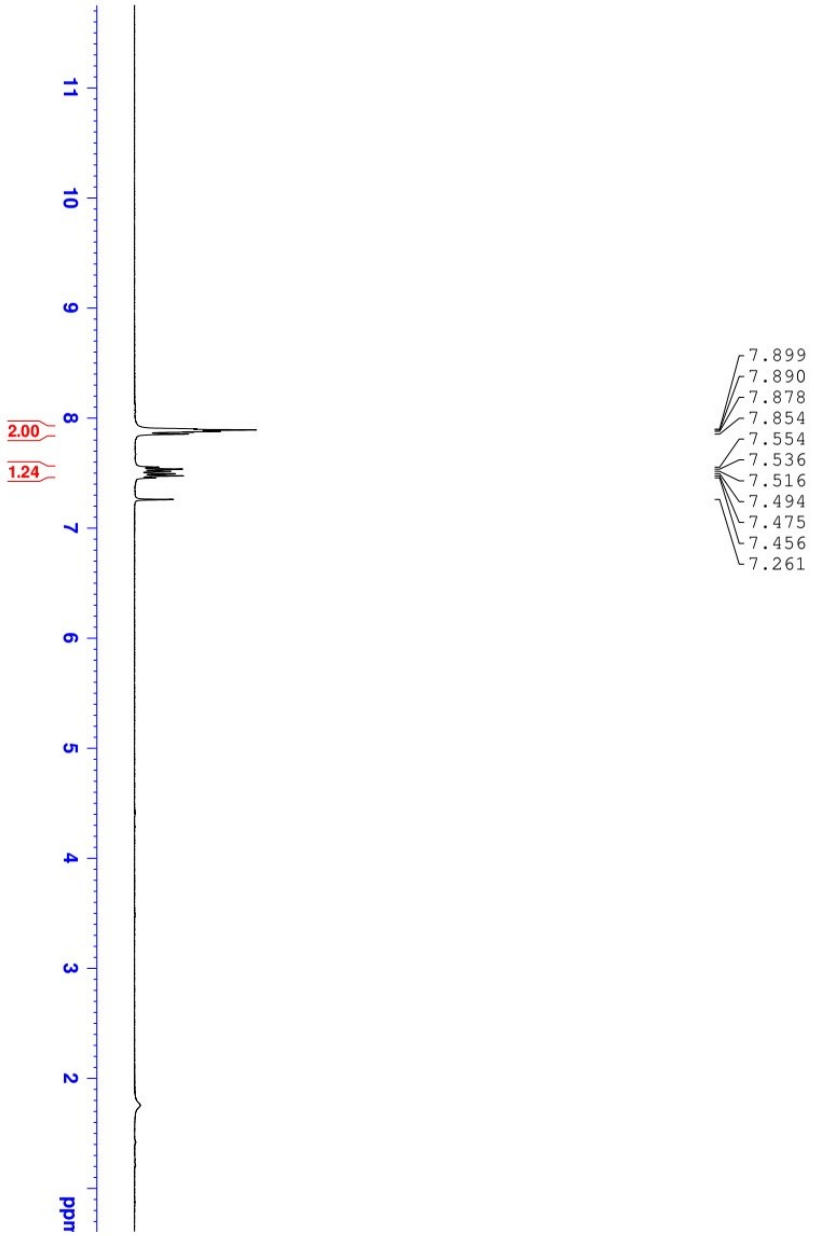
^{13}C NMR of Compound 2j



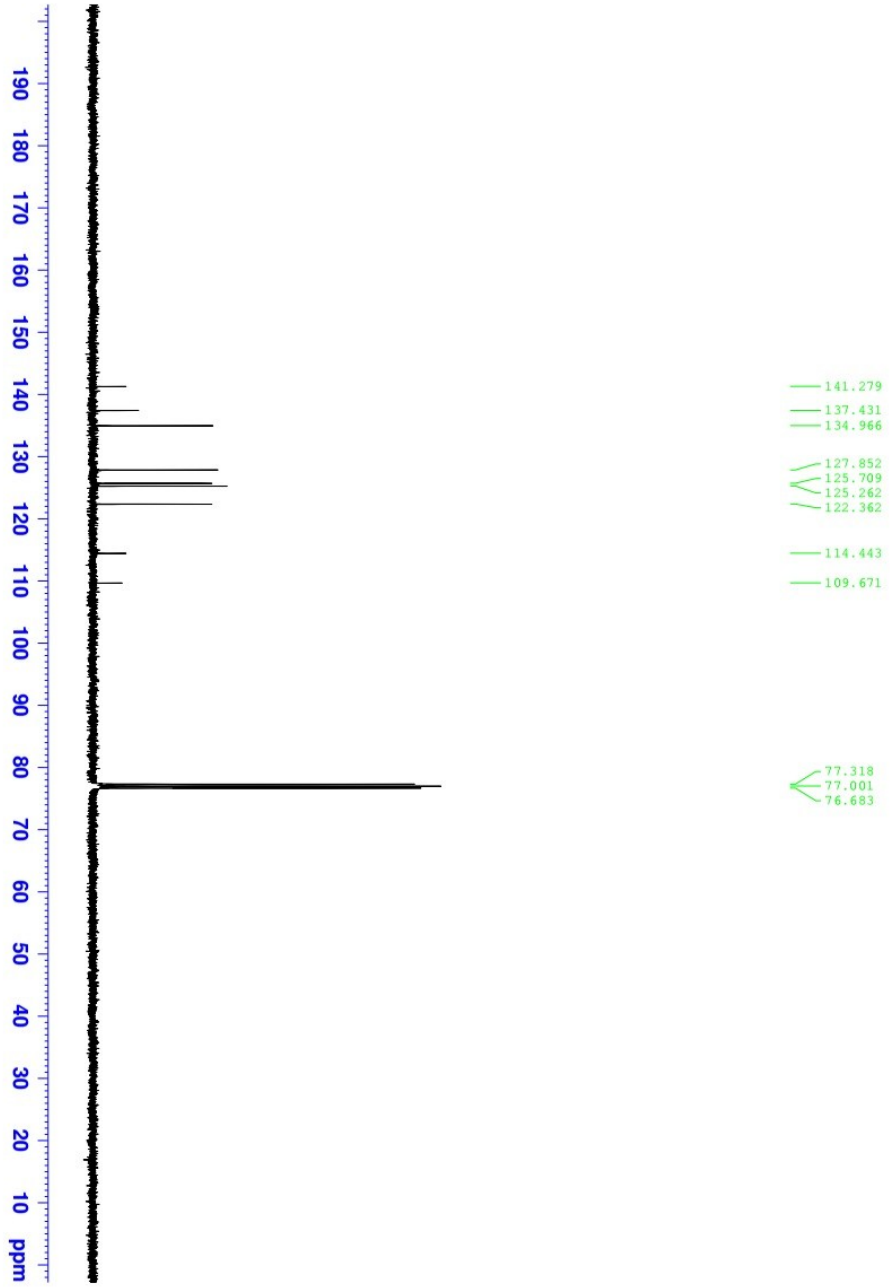
^{1}H NMR of Compound 2k



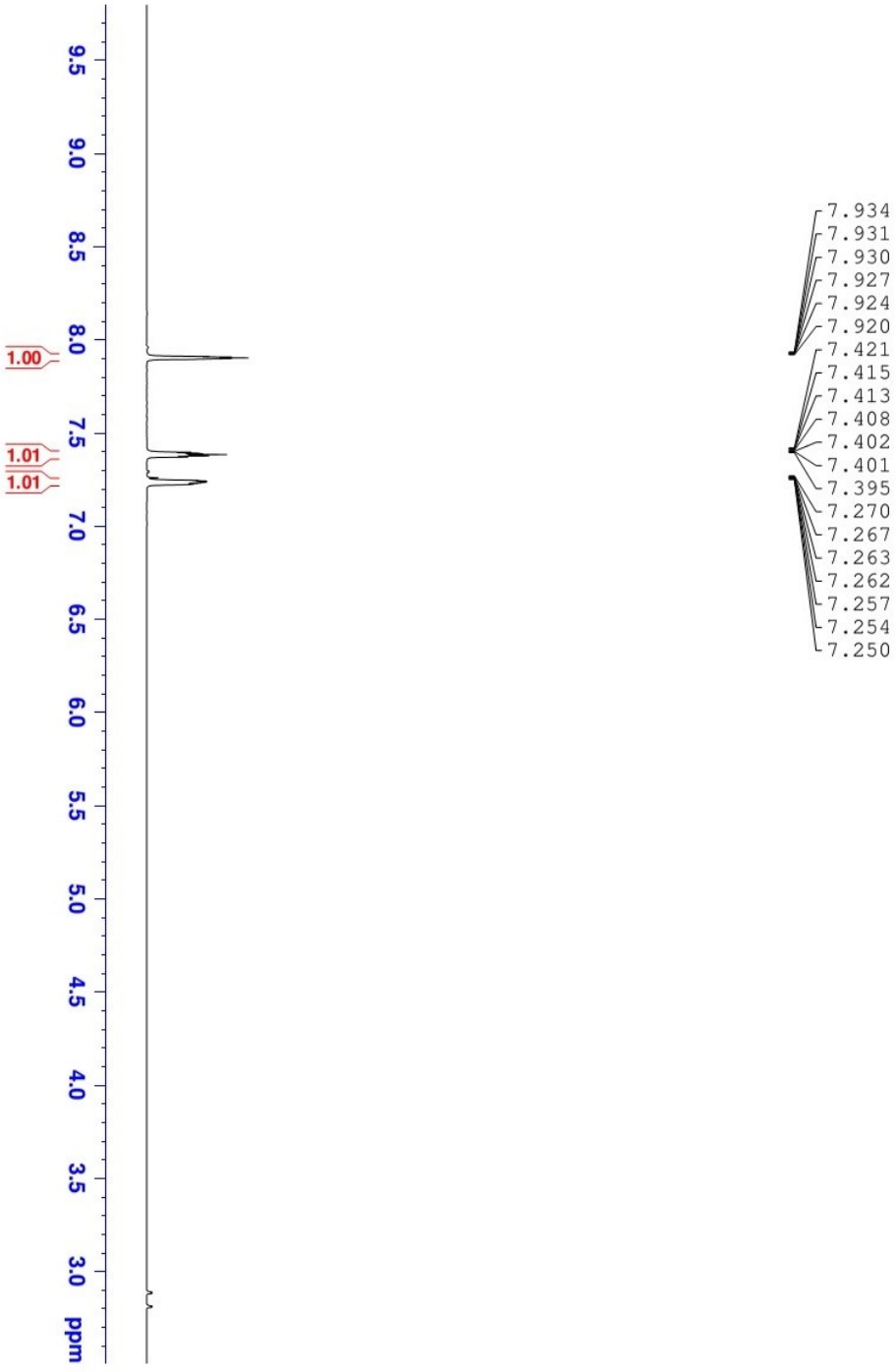
^{13}C NMR of Compound 2k



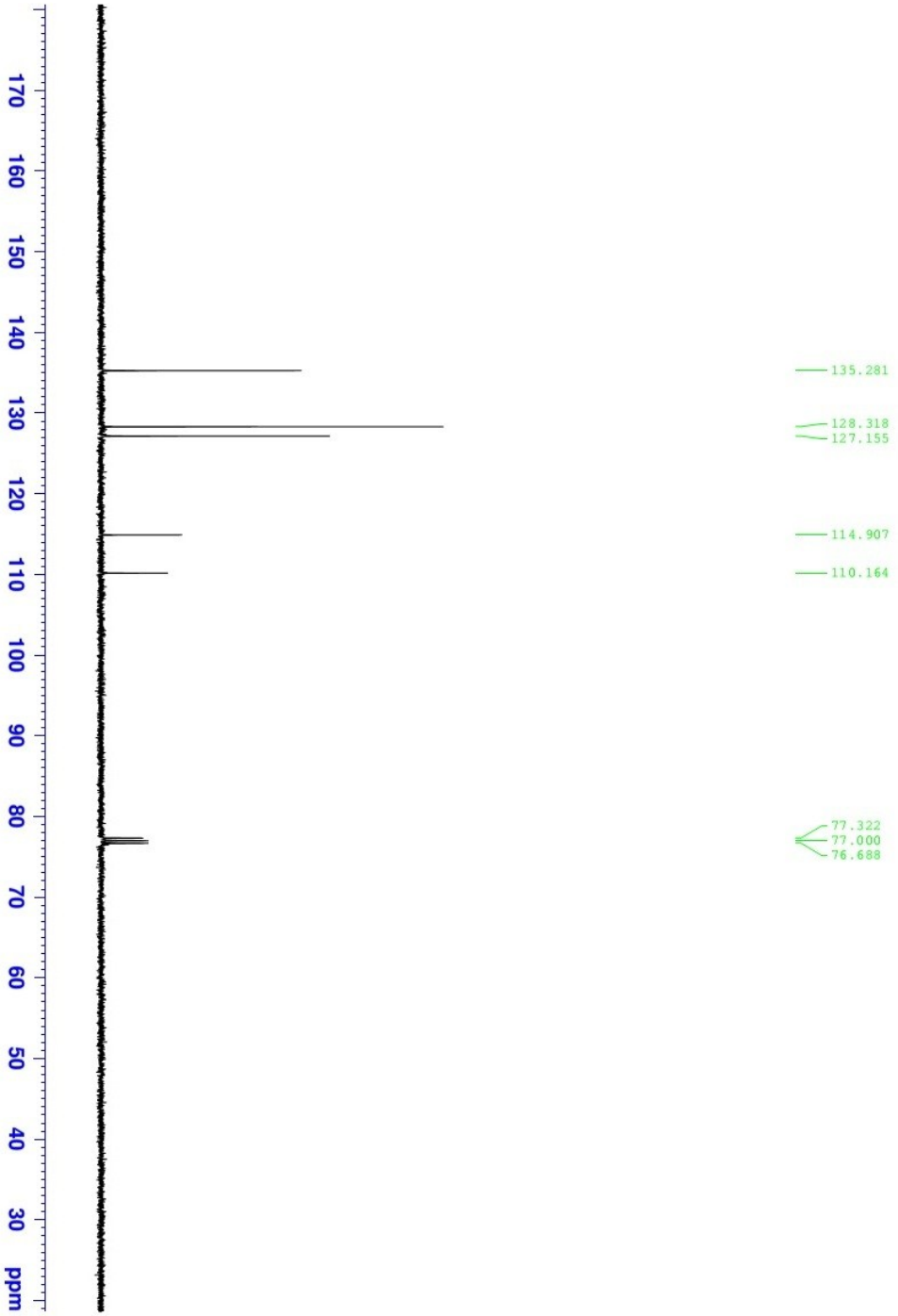
^{1}H NMR of Compound 2l



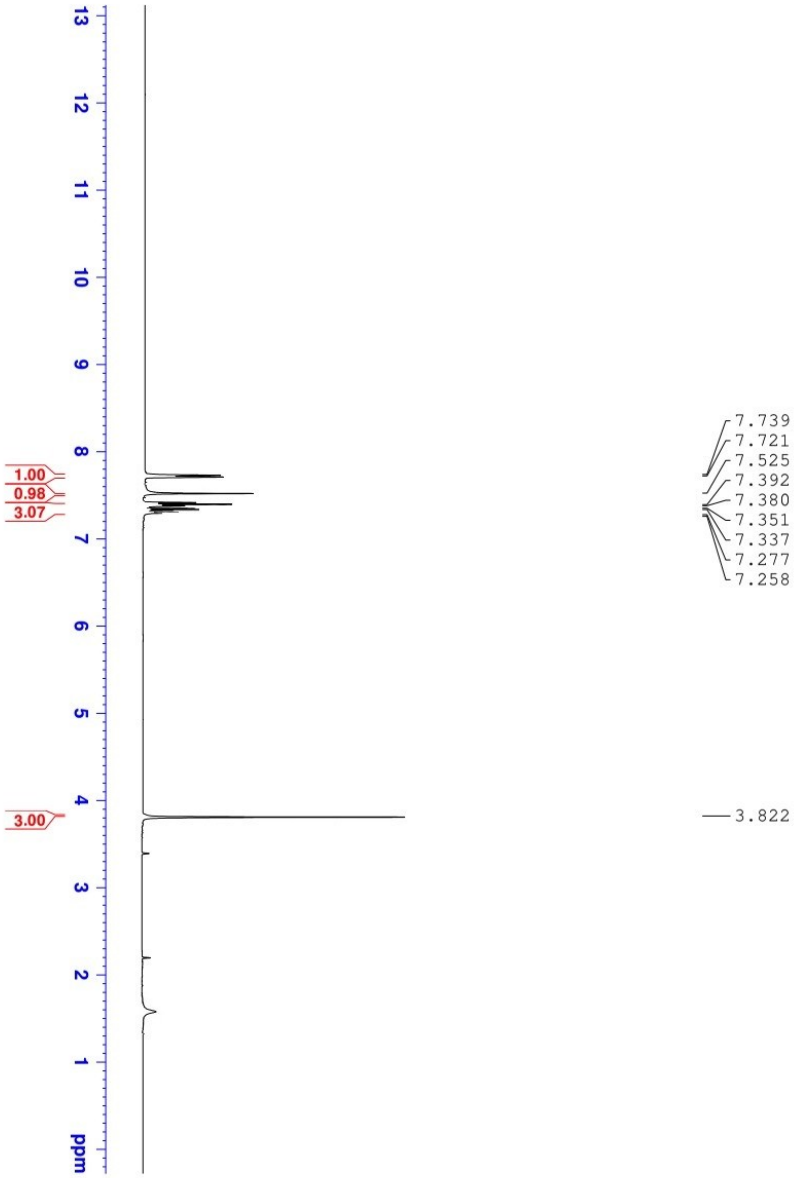
^{13}C NMR of Compound 2l



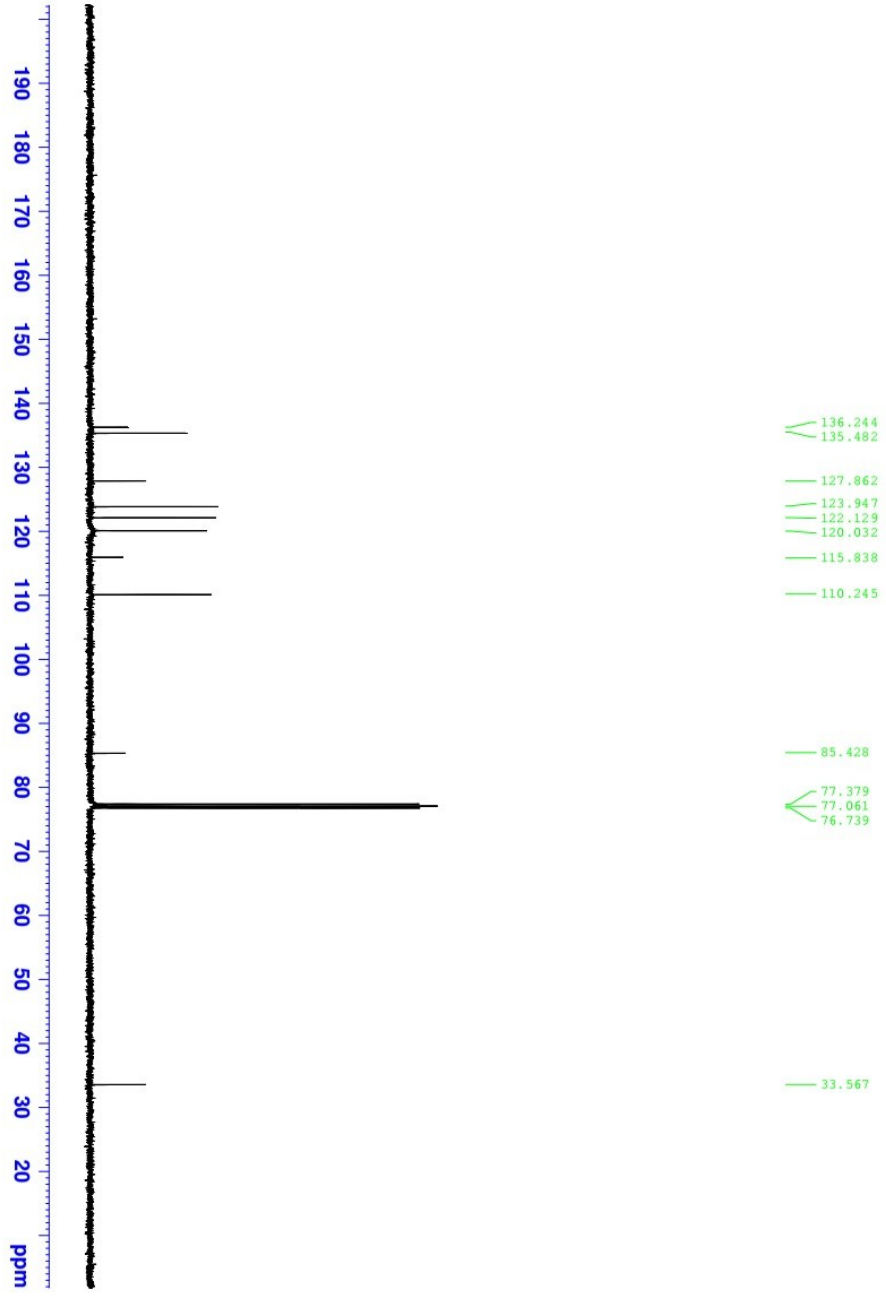
^{1}H NMR of Compound 2m



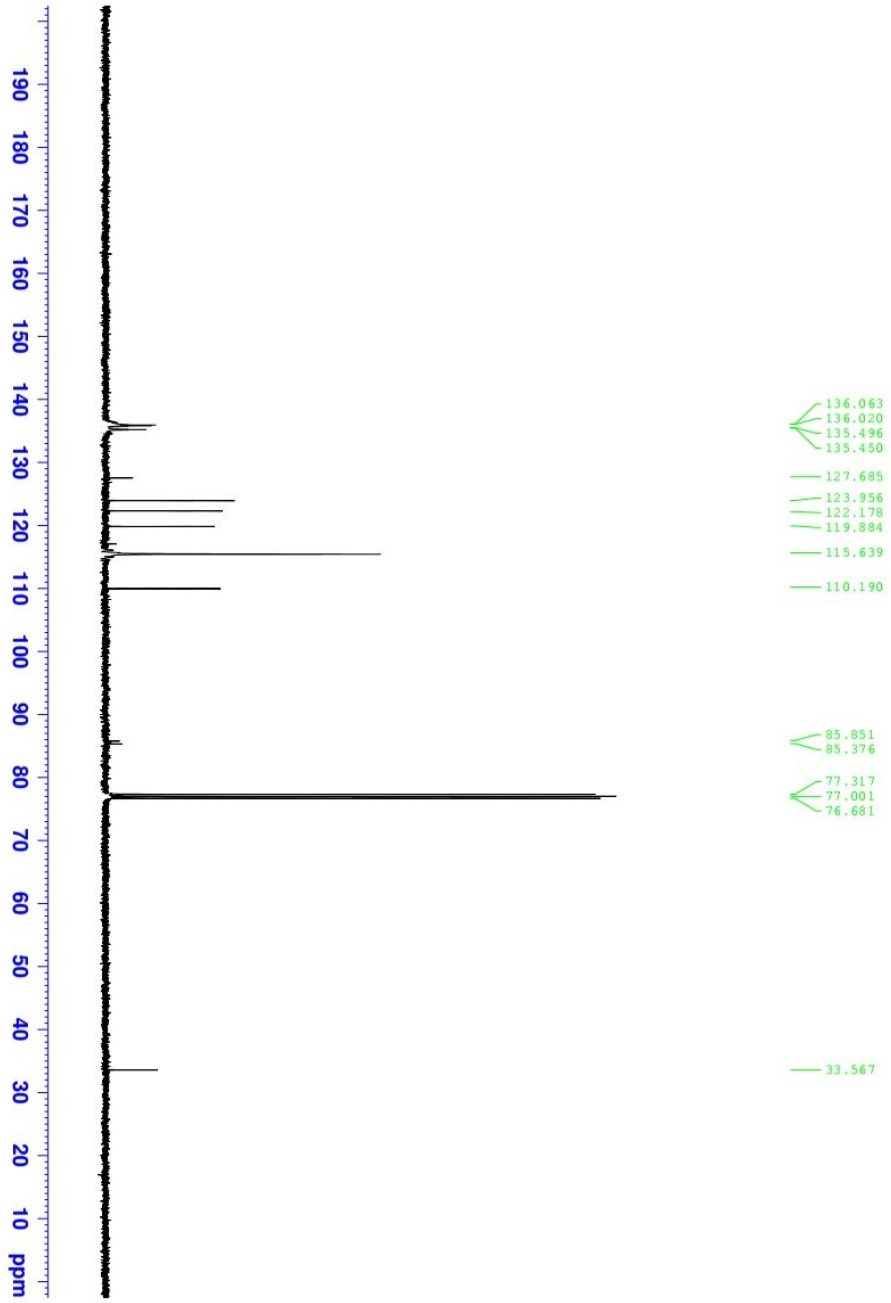
^{13}C NMR of Compound 2m



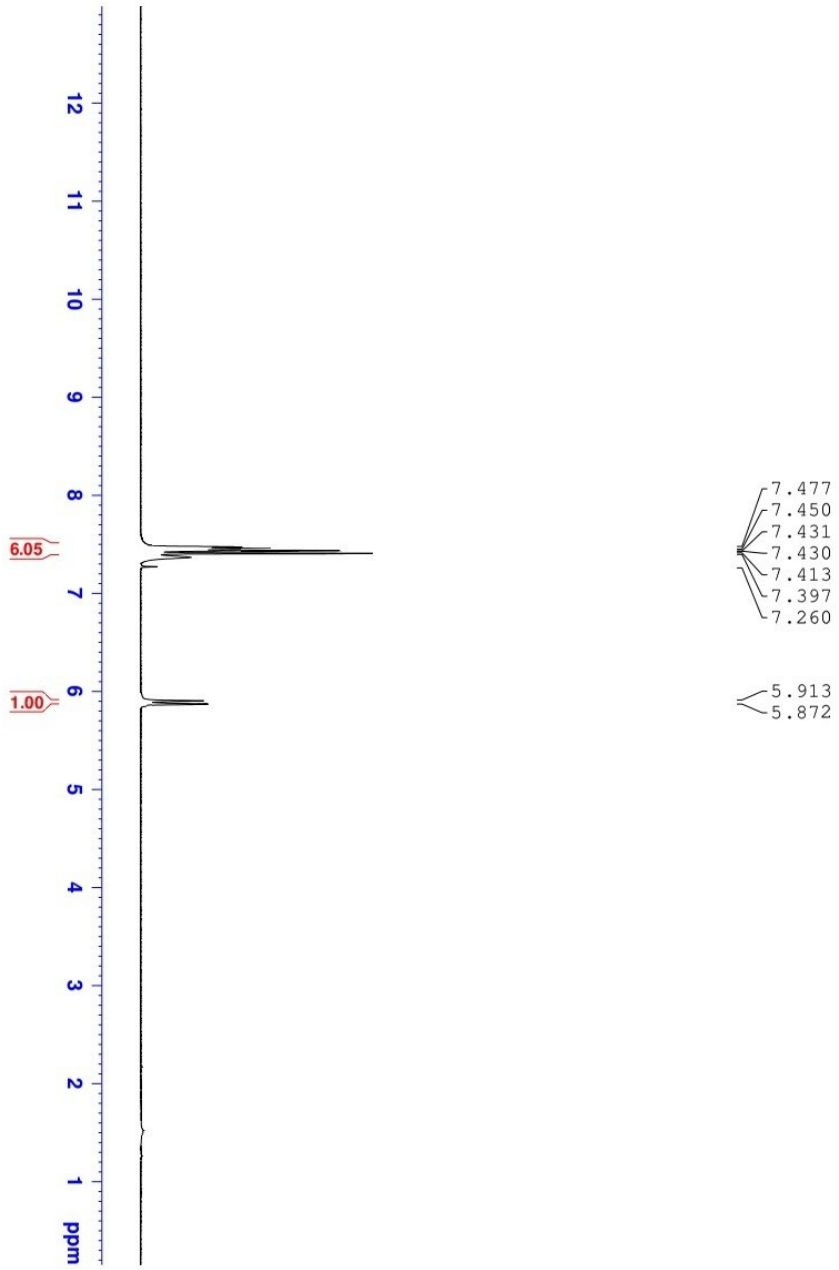
^{1}H NMR of Compound 2n



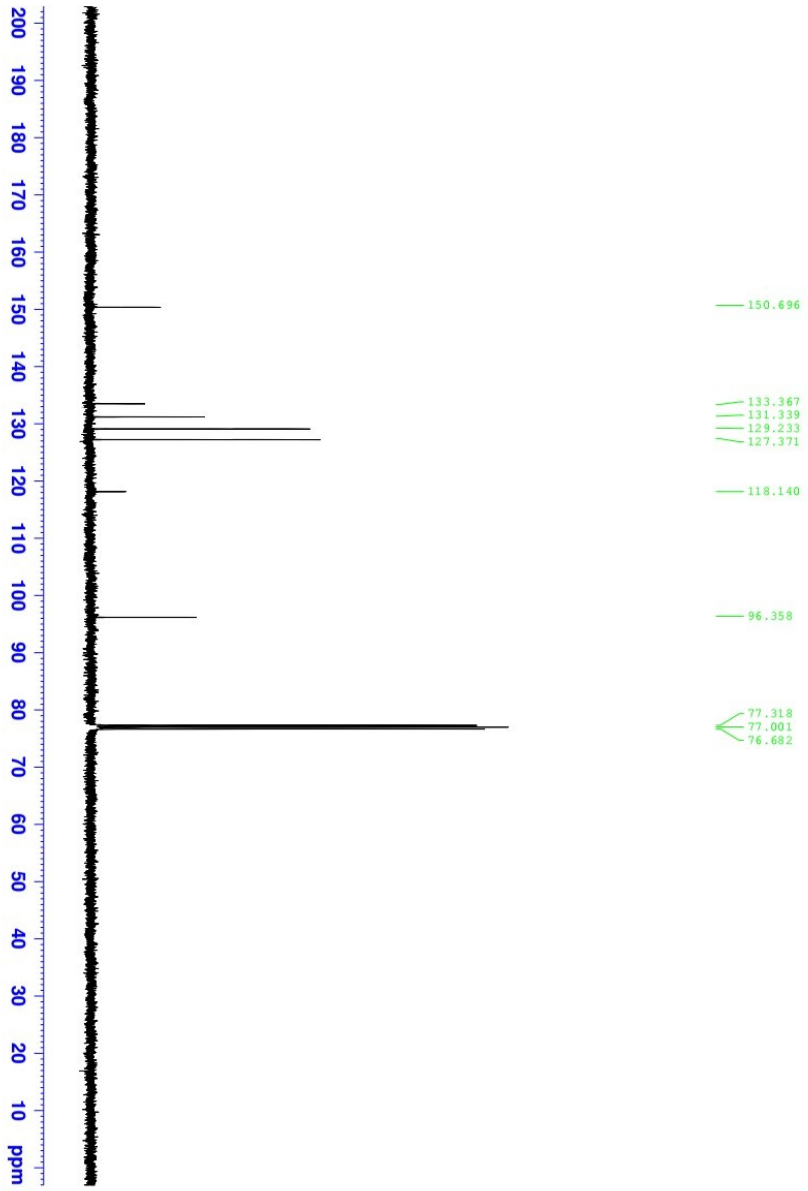
^{13}C NMR of Compound 2n



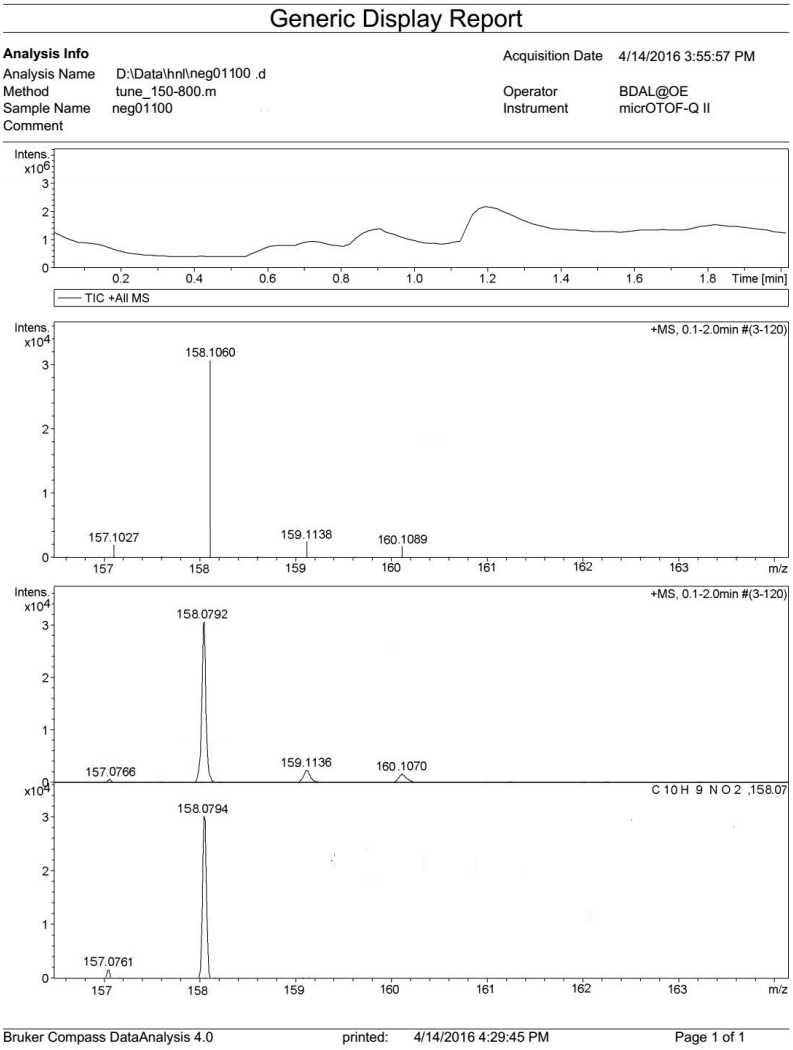
^{13}C NMR of ^{13}C-labeled 2n



^{1}H NMR of Compound 2o



^{13}C NMR of Compound 2o



HRMS **of ^{13}C-labeled 2n**