Electronic Supplementary Information (ESI) for *RSC Advances*

Supplementary Information for

An unprecedented approach to the Gabriel amine synthesis utilizing tosylhydrazones as alkylating agents

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General information: All commercially available reagents were purchased from commercial suppliers and used without further purification. Solvents were purified by the usual methods and stored over molecular sieves. All reactions were performed using oven-dried glass ware heated on oil bath under a nitrogen atmosphere. Organic solutions were concentrated using a Buchi rotary evaporator. Column chromatography was carried out over silica gel (Merck 100–200 mesh) and TLC was performed using silica gel GF254 (Merck) plates. Melting points were determined by open glass capillary method and are uncorrected. IR spectra in KBr/neat were recorded on a Perkin-Elmer 993 IR spectrophotometer. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded on a Bruker AVII spectrometer in $CDCl_3$, TMS as internal reference with chemical shift value being reported in ppm. All coupling constants (*J*) are reported in Hertz (Hz). MS (EI) spectra were recorded on double focusing mass spectrometer.

General procedure for synthesis of *N*-(1-phenylethyl)phthalimide (2a): A mixture of tosylhydrazone **1a'** (1.0 mmol), phthalimide (1.0 mmol), Cs_2CO_3 (3.0 equiv.), CuI (10 mol%) and dioxane (4 mL) was stirred at 110 ^{o}C for 2 h under a nitrogen atmosphere. After completion of the reaction (as monitored by TLC), the mixture was allowed to reach at r.t. It was quenched with water (10 mL) and extracted with ethyl acetate (3 × 10 mL). The organic phase was dried over anhydrous magnesium sulfate and concentrated in vacuo. The crude product was purified by silica gel column chromatography (EtOAc-Hexane) to give the desired compound **2a**.

General procedure for hydrazinolysis[1] of *N*-alkylphthalimides 2 to 3: A mixture of *N*-alkylphthalimide (1.0 mmol) and $H_2NNH_2.H_2O$ (80%, 1.5 mmol) in methanol (2 mL) was refluxed for 1-2 h. Then, 2 mL of acidified water was added and the precipitated solid (phthalazine) was removed by filteration. The filtrate was made alkaline with 40% excess of NaOH solution and extracted with 4 mL diethyl ether (2 × 4 mL). The combined ether extracts were dried over anhydrous magnesium sulfate. The resulting solution was concentrated in a rotary evaporator and purified by silica gel column chromatography give pure primary amines **3**.

General procedure for one-pot reductive hydroamination of carbonyl compounds 1 to 3: A mixture of carbonyl compound **1** (1.0 mmol) and $TsNHNH_2$ (1.0 mmol) in dioxane (4 mL) was stirred at 60 ^{o}C for 30 min. Then, phthalimide (1.0 mmol), Cs_2CO_3 (3.0 equiv.) and CuI (10 mol%) were added and the content stirred at 110 ^{o}C for 2-4 h under a nitrogen atmosphere. After the completion of the reaction (as monitor by TLC), $H_2NNH_2.H_2O$ (80%, 1.5 mmol) was added and the mixture was stirred at same temperature for 1-2 h. The reaction mixture was allowed to cool to r.t. It was quenched with acidified water (10 mL) followed by filtration. The filtrate was made alkaline with 40% excess of NaOH solution and extracted with diethyl ether (3 × 10 mL). The organic phase was dried over anhydrous magnesium sulfate and concentrated in vacuo. The crude product was purified by silica gel column chromatography (EtOAc-Hexane) to give an analytically pure sample of **3a-3p**. The charecterisation data of all the products are given below with relevant references.[2]

***N*-(1-phenylethyl)phthalimide (2a)**[2c]: White solid (mp 125-126 °C, lit (126 °C), IR (KBr): 2981, 2832, 1774, 1720, 756, 721, 698 cm^{-1}, ^1H NMR (400 MHz, $CDCl_3$): δ = 7.42 (d, *J* = 8.4 Hz, 2H), 7.30-7.29 (d, *J* = 8.4 Hz, 2H), 7.28-7.13 (m, 4H), 4.24 (q, *J* = 7.2 Hz, 1H), 1.76 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.1, 140.3, 133.6, 131.7, 128.6, 127.4, 127.2, 123.2, 49.4, 17.5. HRMS (EI): calcd for $C_{16}H_{13}NO_2$ 252.1025, found 252.1021.

1-Phenylethanamine (3a)[2a,d,e]: Yellowish oil, IR (neet): 3359, 3062, 3028, 2968, 2640, 1605, 1572, 1451, 1362, 1083, 1028, 841, 770, 703, 521 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.36-7.16 (m, 5H), 4.16 (q, *J* = 6.6 Hz, 1H), 1.40 (d, *J* = 6.6 Hz, 3H), 1.34 (br s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.6, 134.1, 131.6, 130.1, 43.4, 21.2. HRMS (EI): calcd for $C_8H_{11}N$ 121.0891, found 121.0890.

1-(4-Methoxyphenyl)ethanamine (3b)[2d]: Yellowish oil, IR (neet): 3387, 3238, 3042, 2998, 2934, 2834, 1611, 1541, 1463, 1246, 1175, 1034, 822, 753, 637 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.29–7.24 (m, 2H), 6.85–6.35 (m, 2H), 4.12 (q, *J* = 6.6 Hz, 1H), 3.80 (s, 3H), 1.35 (d, *J* = 6.5 Hz, 3H), 1.29 (br s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.3, 136.6, 130.1, 113.6, 56.4, 43.6, 23.4; HRMS (EI): calcd for $C_9H_{13}NO$ 151.0997, found 151.0995.

Diphenylmethanamine (3c) [2d,e]: Yellowish oil, IR (neet): 3369, 3243, 3060, 3026, 1600, 1492, 1452, 1277, 1190, 1027, 903, 742, 699, 552 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.39–7.25 (m, 10H), 5.25 (s, 1H), 1.53 (br s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.5, 129.7, 127.1, 123.5, 58.4; HRMS (EI): calcd for $C_{13}H_{13}N$ 183.1048, found 183.1045.

Cyclohexanamine (3d): Yellowish oil, IR (neet): 3406, 3367, 3028, 2950, 1260, 1117, 1025, 653 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 2.75 (d, *J* = 4.8 Hz, 1H), 1.73-1.53 (m, 4H), 1.33-1.17 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 42.4, 32.3, 28.0, 22.6. HRMS (EI): calcd for $C_6H_{13}N$ 99.1048, found 99.1046.

1-(Pyridin-2-yl)ethanamine (3e): Yellowish oil, IR (neet): 3376, 3257, 3028, 2954, 2794, 1604, 1587, 1453, 1332, 1090, 1003, 817, 741, 694 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.59 (t, *J* = 6.4, 1H), 7.73-7.67 (m, 1H), 7.47 (m, 1H), 7.23-7.19 (m, 1H), 4.28 (q, *J* = 8.2 Hz, 1H), 1.37 (d, *J* = 8.2 Hz, 3H), 1.32 (br s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 147.5, 141.6, 135.6, 109.2, 108.7, 41.7, 22.3. HRMS (EI): calcd for $C_7H_{10}N_2$ 122.0844, found 122.0840.

1-(4-Bromophenyl)ethanamine (3f): Yellowish oil, IR (neat): 3361, 3326, 1617, 1512, 1437, 1203, 1151, 1082, 1035, 850, 741, 687, 553 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.36 (d, *J* = 8.4 Hz, 2H), 7.16 (d, *J* = 8.4 Hz, 2H), 4.15 (q, 5.6 Hz, 1H), 1.41 (d, *J* = 5.6 Hz, 3H), 1.33 (br s,

2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 139.6, 131.7, 128.4, 121.9, 47.0, 22.1. HRMS (EI): calcd for $C_8H_{10}BrN$ 198.9997, found 199.0007.

Phenylmethanamine (**3g**)[2a,b]: Yellowish oil, IR (neat): 3400, 3313, 3080, 3040, 2980, 2815, 1610, 1595, 1421, 1247, 1181, 1040, 817, 705, 681 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.34-7.22 (m, 5H), 3.85 (s, 2H), 1.36 (br s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.5, 129.0, 127.2, 123.6, 49.4; HRMS (EI): calcd for C_7H_9N 107.0735, found 107.0732.

***p*-Tolylmethanamine** (**3h**)[2a]: Colorless oil, IR (neat): 3395, 3290, 2971, 2857, 1610, 1513, 1208, 114t, 800, 747, 702 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.20 (d, *J* = 6.4 Hz, 2H), 7.15 (d, *J* = 6.4 Hz, 2H), 3.72 (s, 2H), 2.34 (s, 3H), 1.34 (br s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 139.8, 136.2, 129.2, 127.2, 45.7, 21.6; HRMS (EI): calcd for 122.0981, found 122.0980.

(4-Methoxyphenyl)methanamine (**3i**)[2a]: Yellowish oil; IR (neat): 3397, 3287, 1611, 1519, 1437, 1256, 1132, 1119, 813, 746 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.28 (d, *J* = 5.8 Hz, 2H), 6.99 (d, *J* = 6.0 Hz, 2H), 3.97 (s, 5H), 1.85 (br s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.2, 132.5, 129.2, 114.2, 55.4, 45.4; HRMS (EI): calcd for $C_8H_{11}NO$, 137.0840, found 137.0842.

(4-Fluorophenyl)methanamine (**3j**)[2a,b]: Yellowish oil, IR (neat): 3381, 3337, 2973, 2846, 1606, 1503, 1357, 1253, 1141, 1080, 1035, 912, 803, 757, 693, 501 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.25 (m, 2H), 7.03 (m, 2H), 3.77 (s, 2H), 1.37 (br s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.0, 137.6, 127.2, 115.6, 49.4; HRMS (EI): calcd for C_7H_8FN 125.0640, found 125.0636.

(4-Chlorophenyl)methanamine (3k): Yellowish oil, IR (neat): 3369, 3307, 2953, 2836, 1641, 1547, 1432, 1241, 1103, 807, 775, 712, 681 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7. 64 (d, *J* = 8.5 Hz, 2H), 7.56 (d, *J* = 8.5 Hz, 2H), 3.51 (s, 2H), 1.54 (br s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 138.6, 131.7, 128.4, 121.9, 53.0; HRMS (EI): calcd for C_7H_8ClN 141.0345, found 141.0341.

4-(Aminomethyl)-*N*, *N*-dimethylbenzenamine (**3l**)[2a]: Yellowish oil, IR (neet): 3387, 3313, 3037, 3007, 2971, 2821, 1612, 1522, 1345, 1186, 947, 806, 752, 693 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.54 (d, *J* = 8.5 Hz, 2H), 6.74 (d, *J* = 8.5 Hz, 2H), 3.74 (s, 2H), 2.95 (s, 6H), 1.81 (br s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 147.4, 129.5, 122.6, 112.3, 51.6, 40.3; HRMS (EI): calcd for $C_9H_{14}N_2$ 150.1157, found 150.1154.

2-Phenylethanamine (**3m**)[2a,b]: Yellowish oil, IR: 3400, 3257, 2966, 2854, 1605, 1509, 1457, 1376, 1222, 1158, 811, 765, 551, 503 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.31-7.19 (m, 5H),

2.96 (t, *J* = 5.6 Hz, 2H), 2.87 (t, *J* = 5.6 Hz, 2H), 1.06 (br s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 139.0, 131.5, 129.6, 127.2, 43.1, 39.0; HRMS (EI): calcd for $C_8H_{11}N$, 121.0891, found 121.0891.

Hexan-1-amine (**3n**)[2b]: Yellowish oil, IR (neet): 3407, 3373, 2938, 2875, 1263, 1137, 1061, 817, 623 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.69 (t, *J* = 5.6 Hz, 2H), 1.45-1.22 (m, 10H), 0.90 (t, *J* = 5.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 41.1, 32.3, 30.5, 22.8, 21.3, 14.4. HRMS (EI): calcd for $C_6H_{15}N$ 101.1204, found 101.1203.

(Furan-2-yl)methanamine (**3o**)[2b]: Yellowish oil, IR (neet): 3387, 3341, 2937, 2875, 1604, 1546, 1445, 1263, 1137, 1061, 817, 784, 686 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.35 (d, *J* = 1.2, 1H), 6.31 (q, *J* = 1.2 Hz, 1H), 6.13 (d, *J* = 1.2 Hz, 1H), 3.82 (s, 2H), 1.42 (br s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 146.2, 141.7, 109.2, 104.7, 42.1. HRMS (EI): calcd for C_5H_7NO 97.0527, found 97.0525.

(4-Nitrophenyl)methanamine (3p): Yellowish oil, IR (neat): 3381, 3337, 3108, 2952, 2832, 1608, 1595, 1507, 1352, 1253, 1141, 1080, 1035, 923, 851, 753, 682 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.24 (d, *J* = 9.0 Hz, 2H), 7.60 (d, *J* = 9.0 Hz, 2H), 3.84 (s, 2H), 1.57 (br s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 148.3, 145.4, 127.0, 119.7, 52.6; HRMS (EI): calcd for $C_7H_8N_2O_2$ 152.0586, found 152.0581.

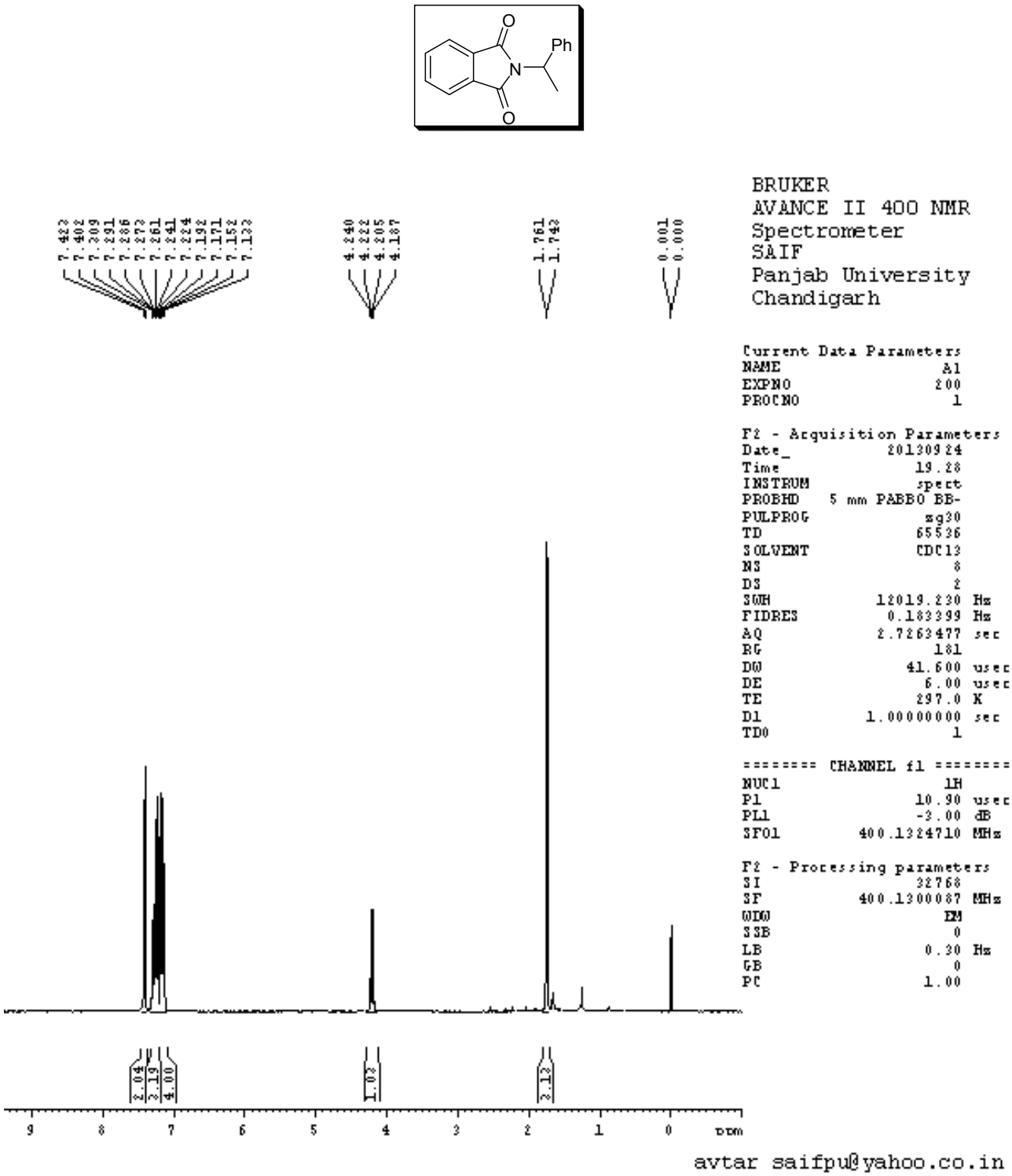
References:

1 W. G. Nigh, *J. Chem. Edu.,* 1975, **52**, 2348.

2 (*a*) D. Haddenham, L. Pasumansky, J. DeSoto, S. Eagon and B. Singaram, *J. Org. Chem*., 2009, **74**, 1964; (*b*) C. Gunanathan and D. Milstein, *Angew. Chem. Int. Ed*. 2008, **47**, 8661; (*c*) J. Fraga-Dubreuil, G. Comak, A. W. Taylora and M. Poliakoff, *Green Chem.*, 2007, **9**, 1067; (*d*) B. Miriyala, S. Bhattacharyya and J. S. Williumson, *Tetrahedron*, 2004, **60**, 1463; (*e*) Franz J. Weiberth, Stan S. Hall, *J. Org. Chem.,* 1986, **51**, 5339.

Copies of ^{1}H and ^{13}C NMR spectra of all the products.

Compound 2a. ^{1}H NMR Spectrum ($CDCl_3$).



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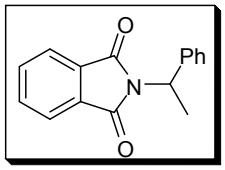

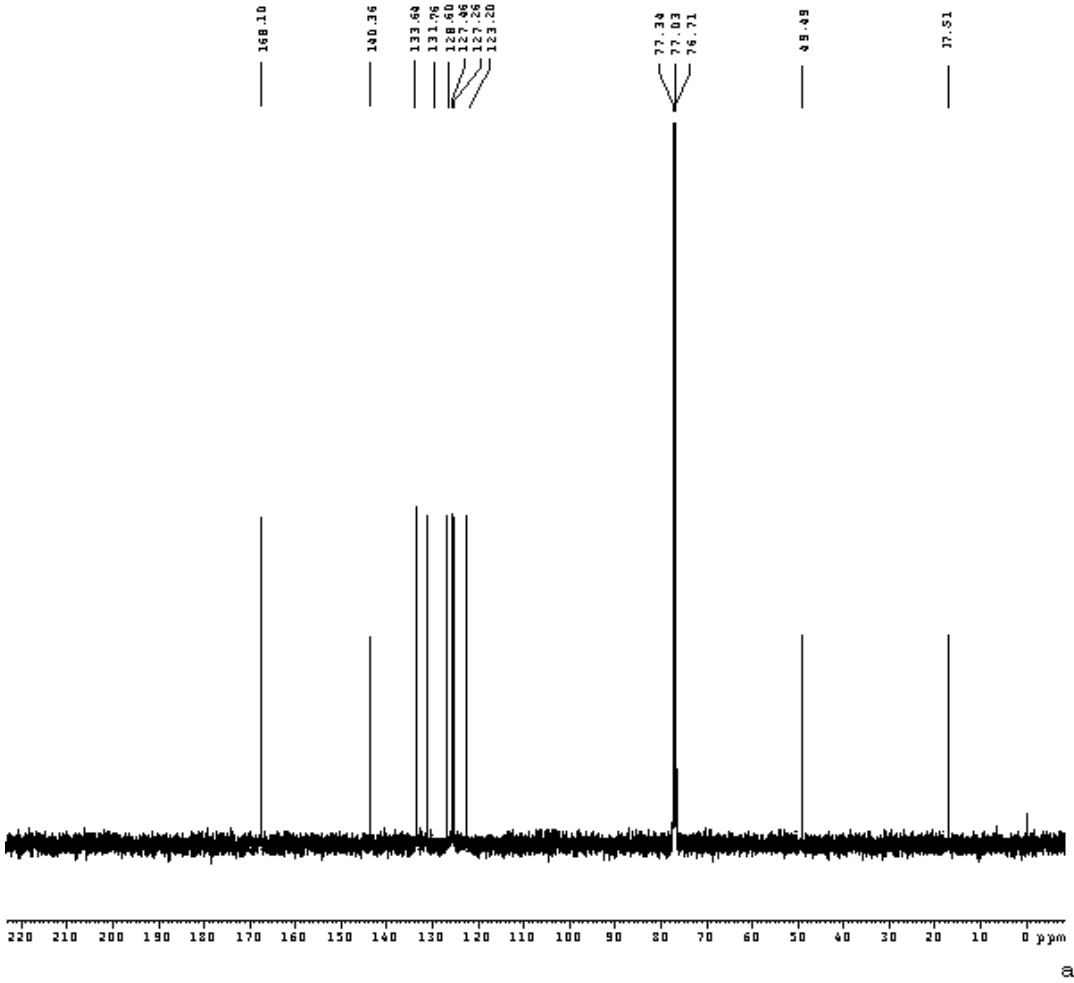

BRUKER
AVANCE II 400 NMR
Spectrometer
SAIF
Panjab University
Chandigarh

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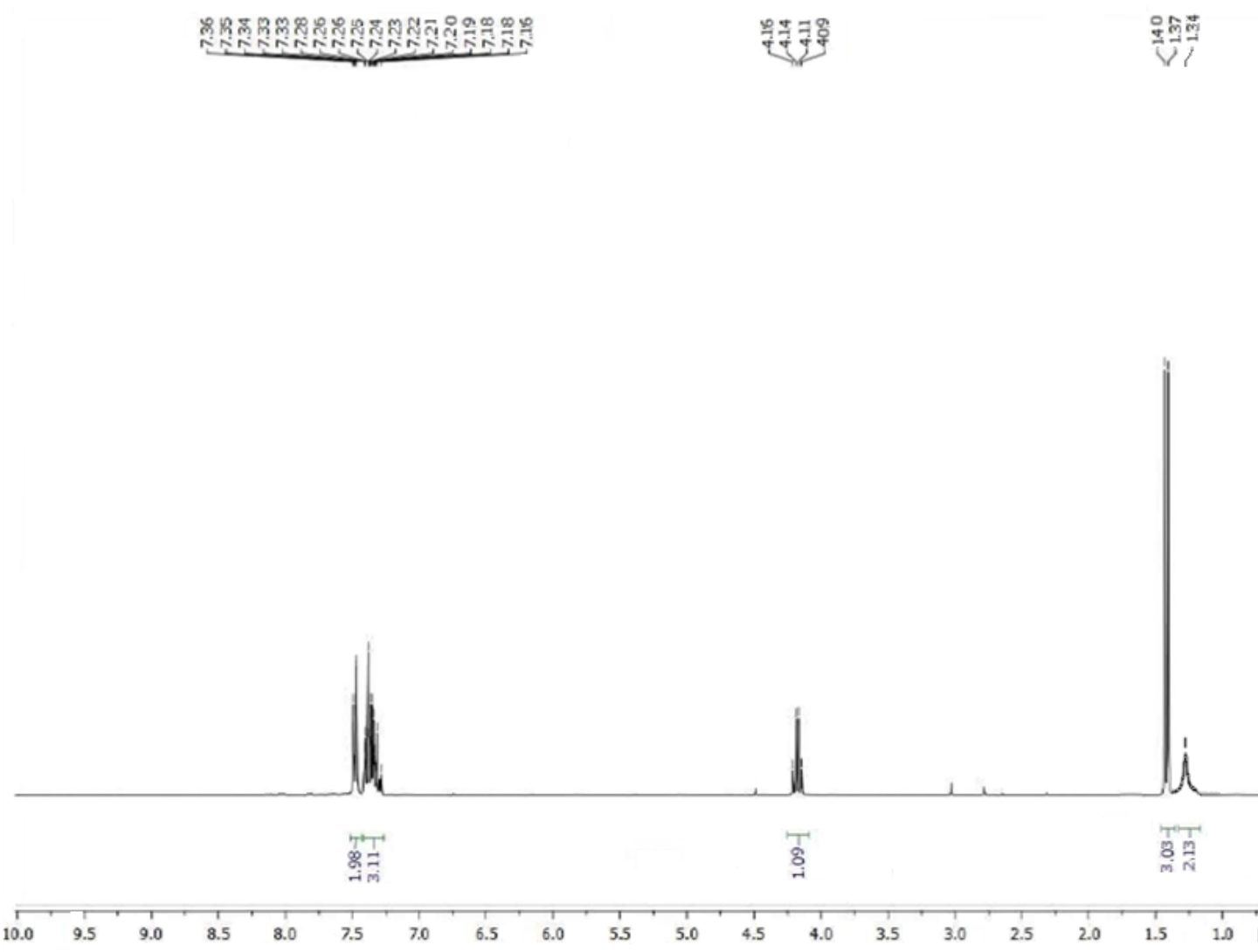
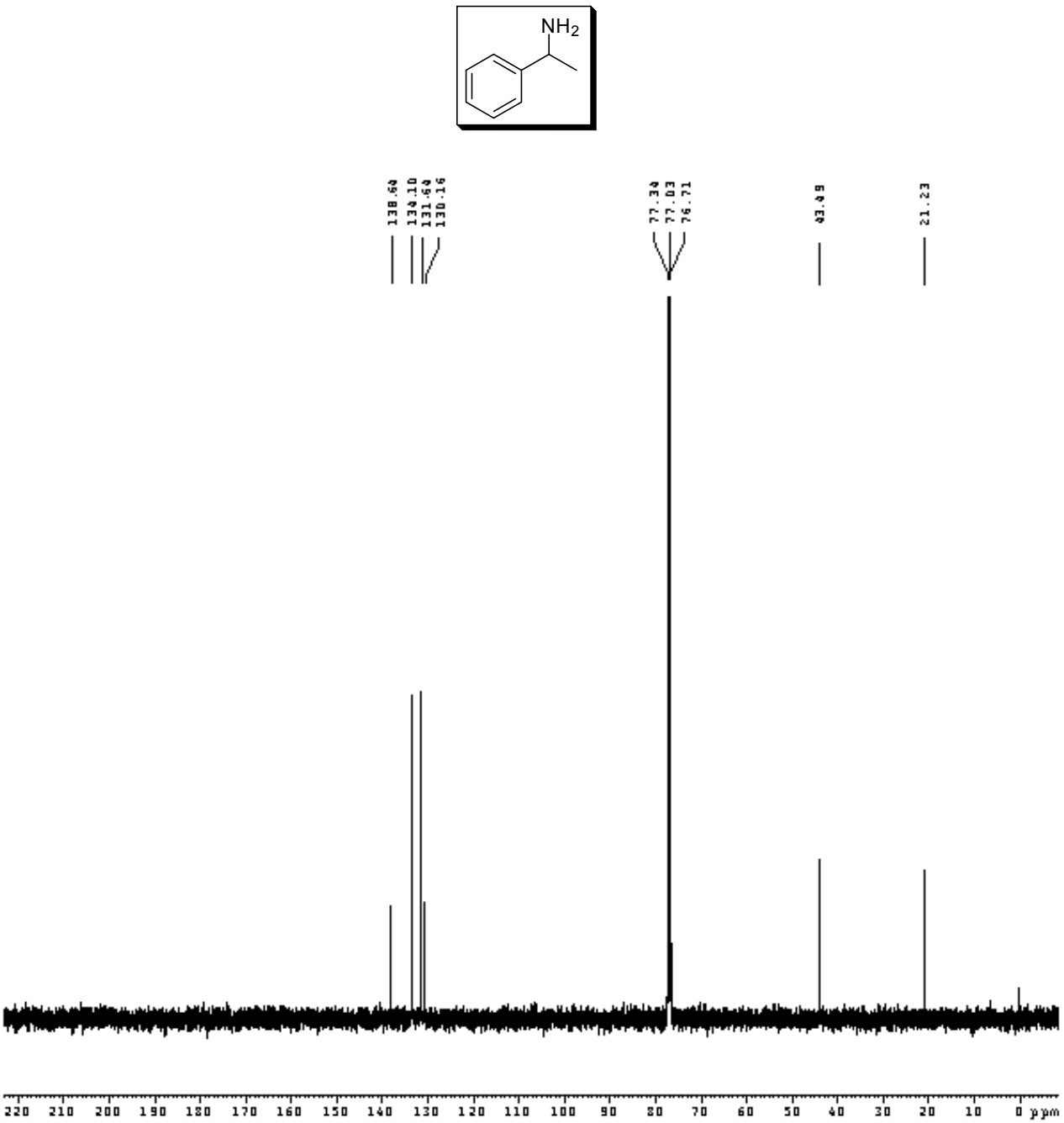
avtar saifpu@yahoo.co.in

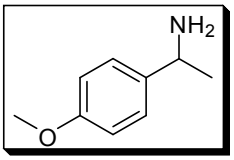
Compound 3a. ^{1}H NMR Spectrum ($CDCl_3$).

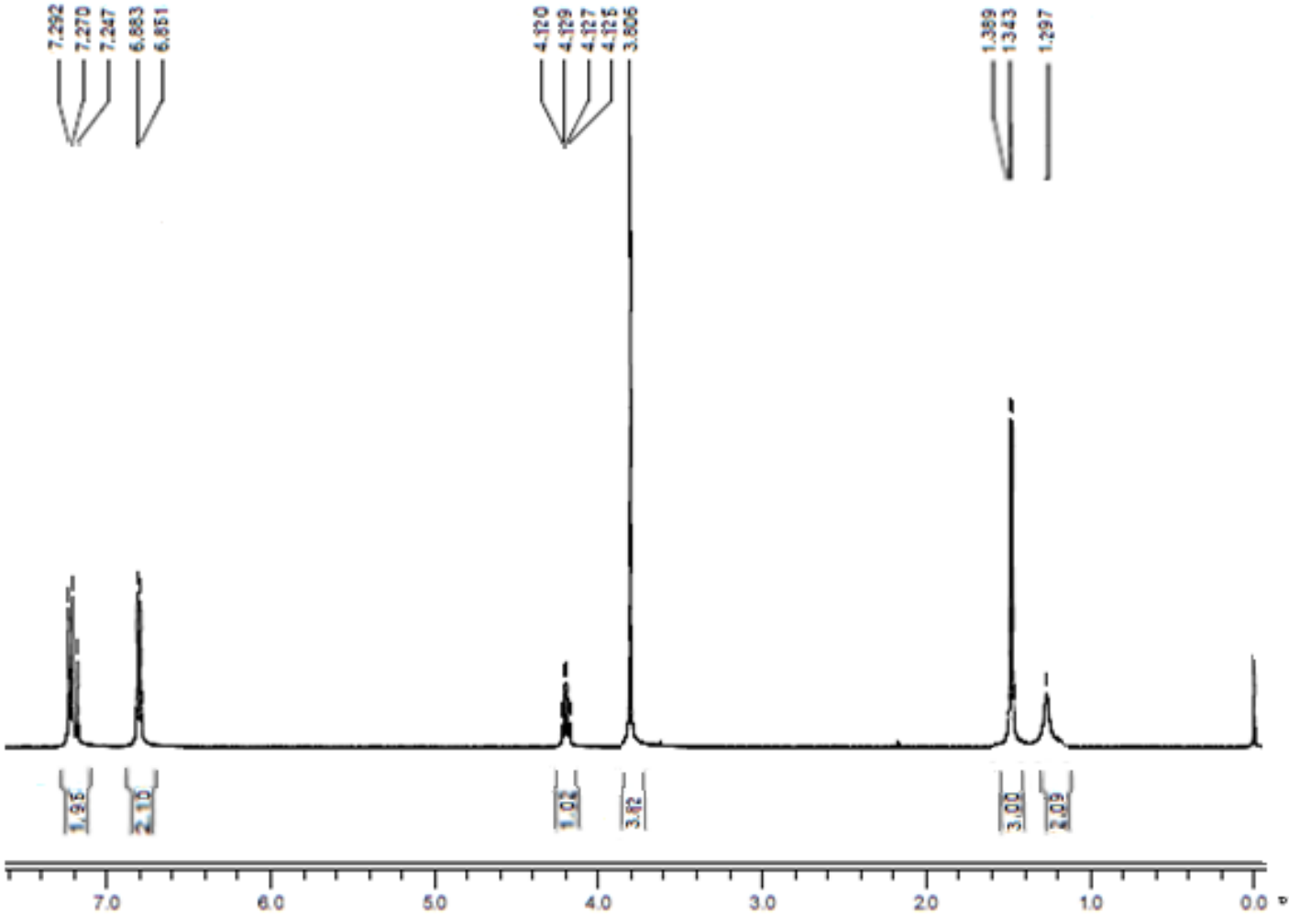


Compound 3a. ^{13}C NMR Spectrum ($CDCl_3$).

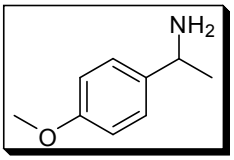


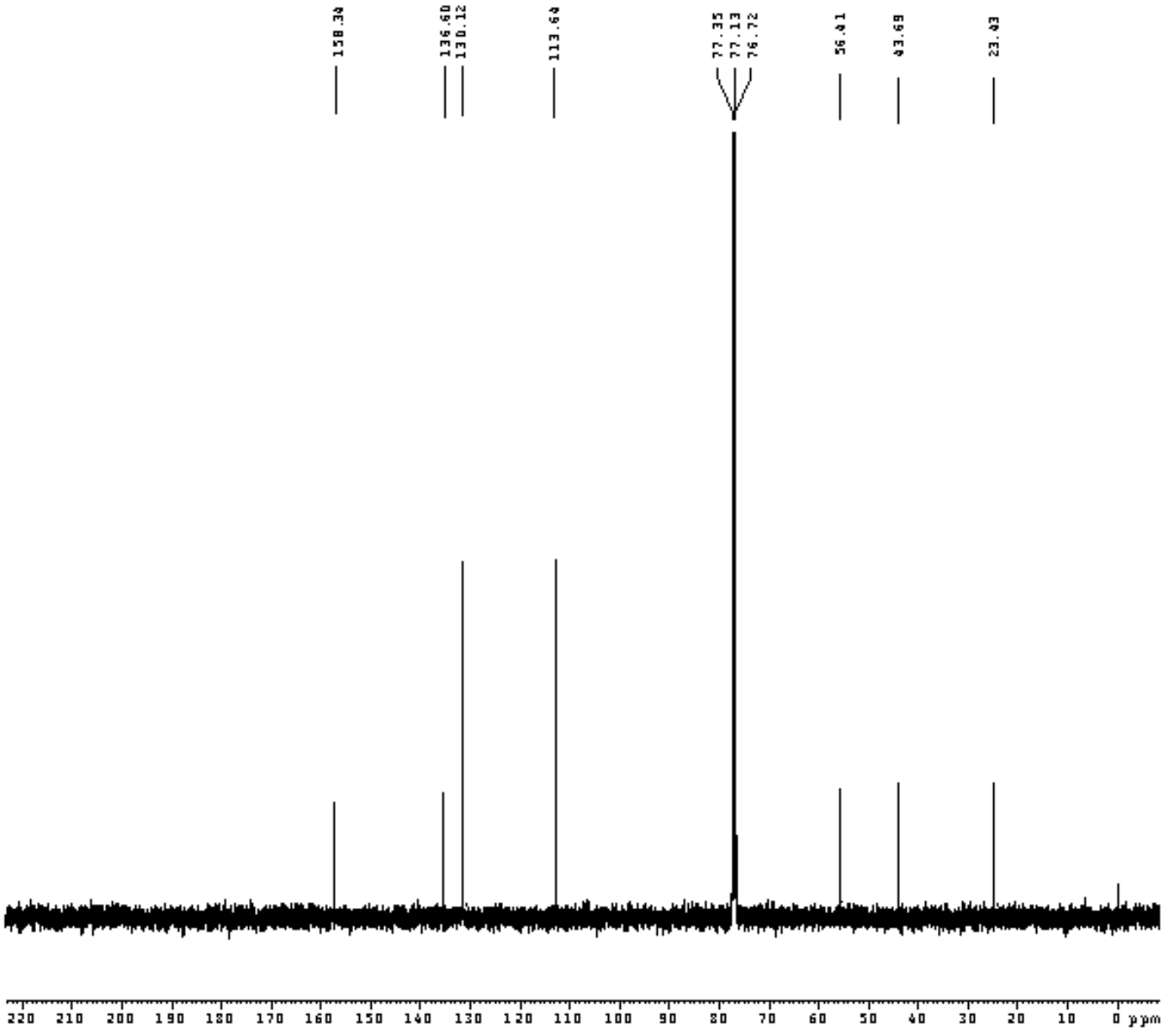
Compound 3b. ^{1}H NMR Spectrum ($CDCl_3$).



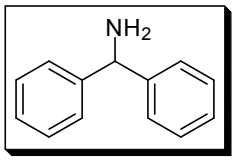


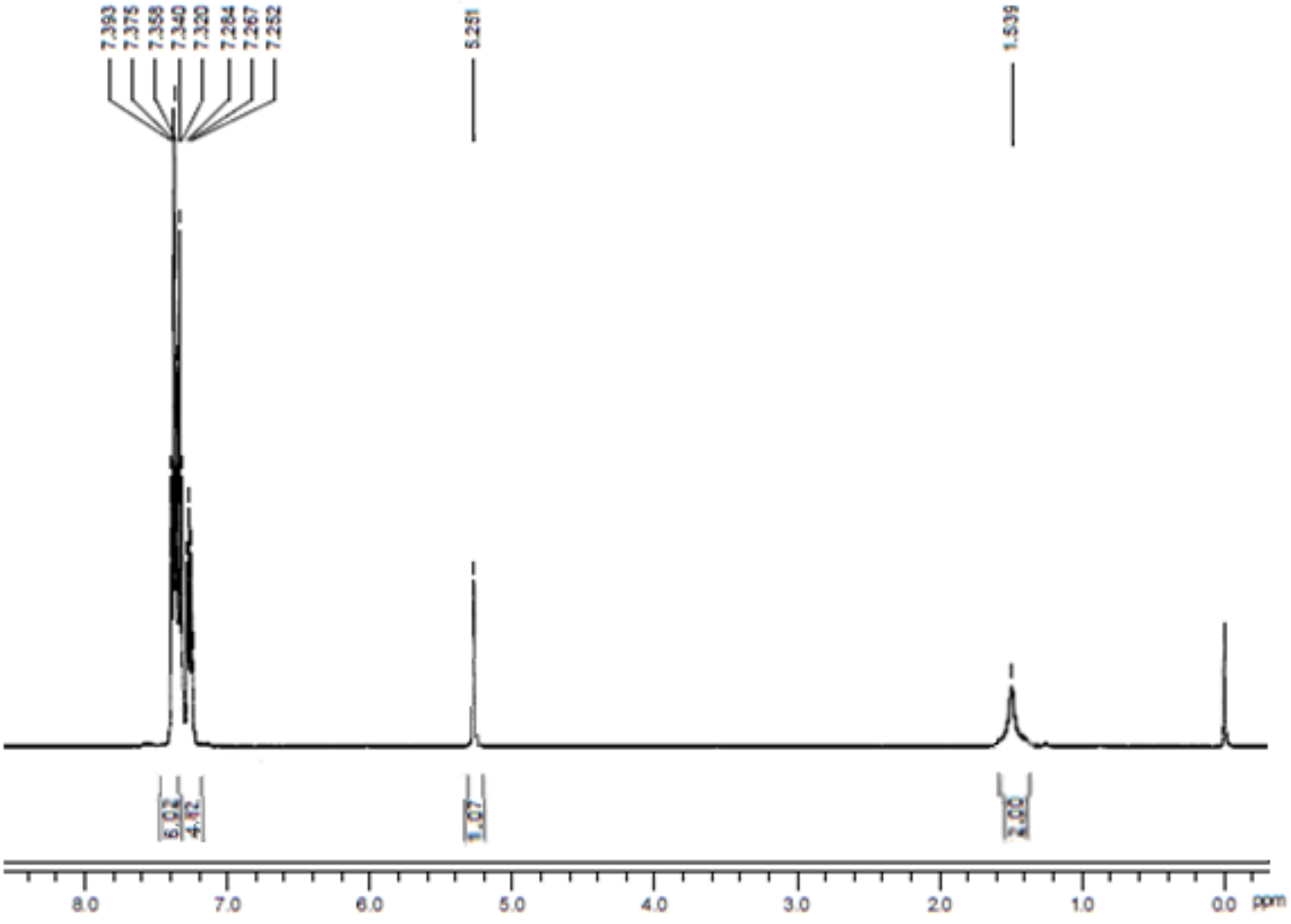
Compound 3b. ^{13}C NMR Spectrum ($CDCl_3$).



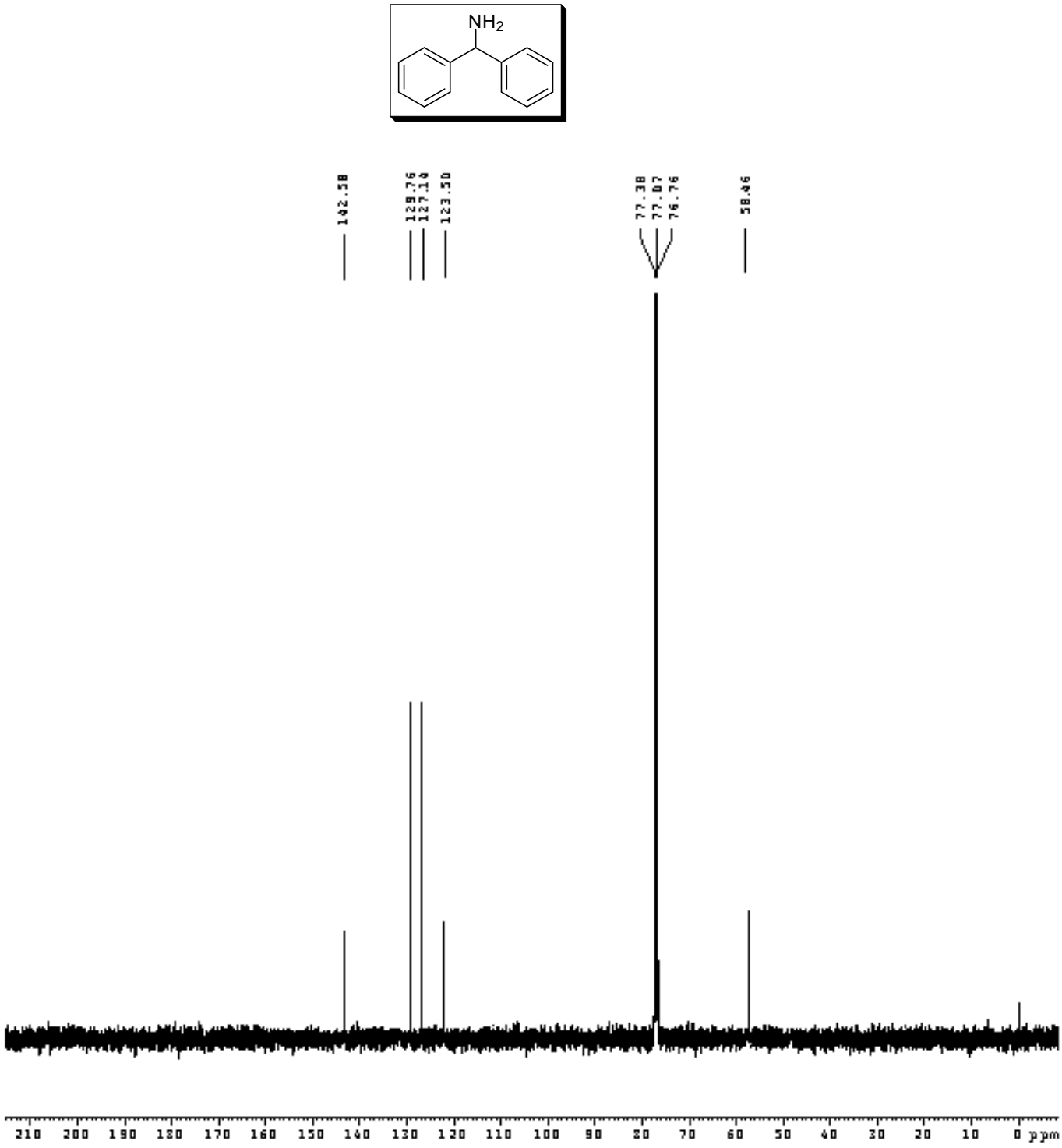


Compound 3c. ^{1}H NMR Spectrum ($CDCl_3$).

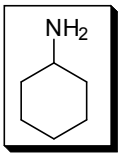


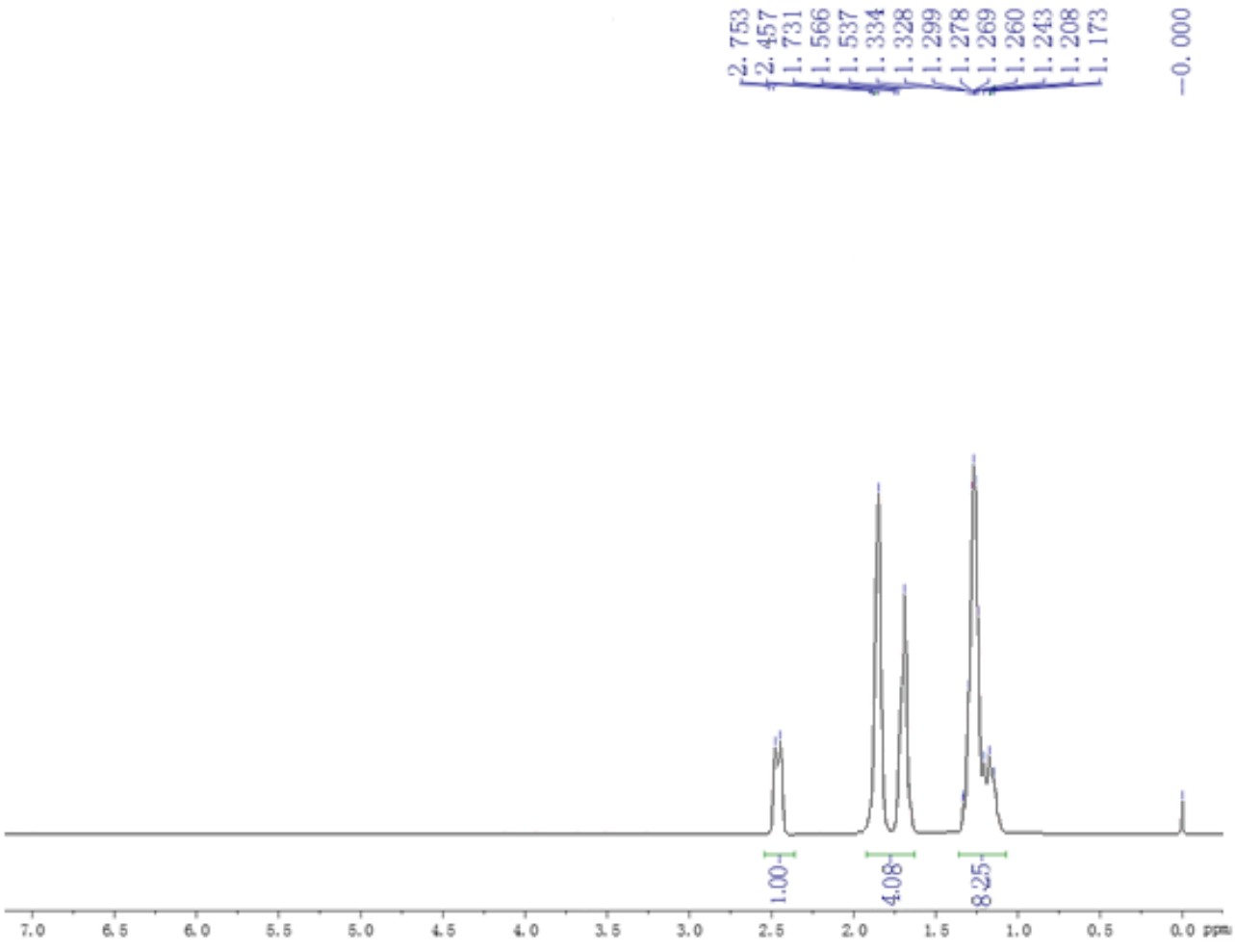


Compound 3c. ^{13}C NMR Spectrum ($CDCl_3$).

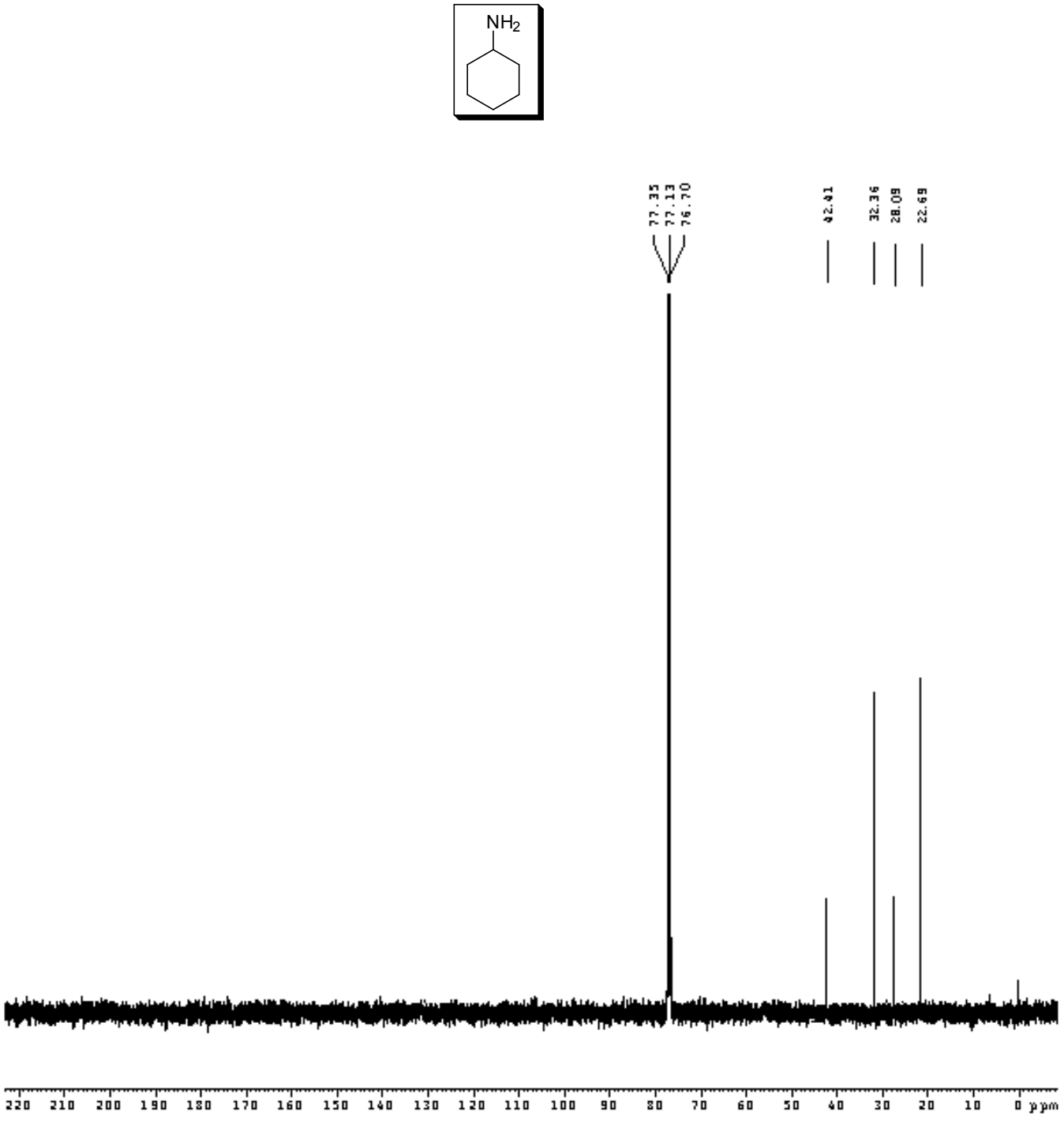


Compound 3d. ^{1}H NMR Spectrum ($CDCl_3$).

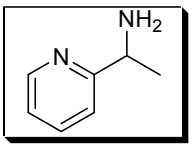


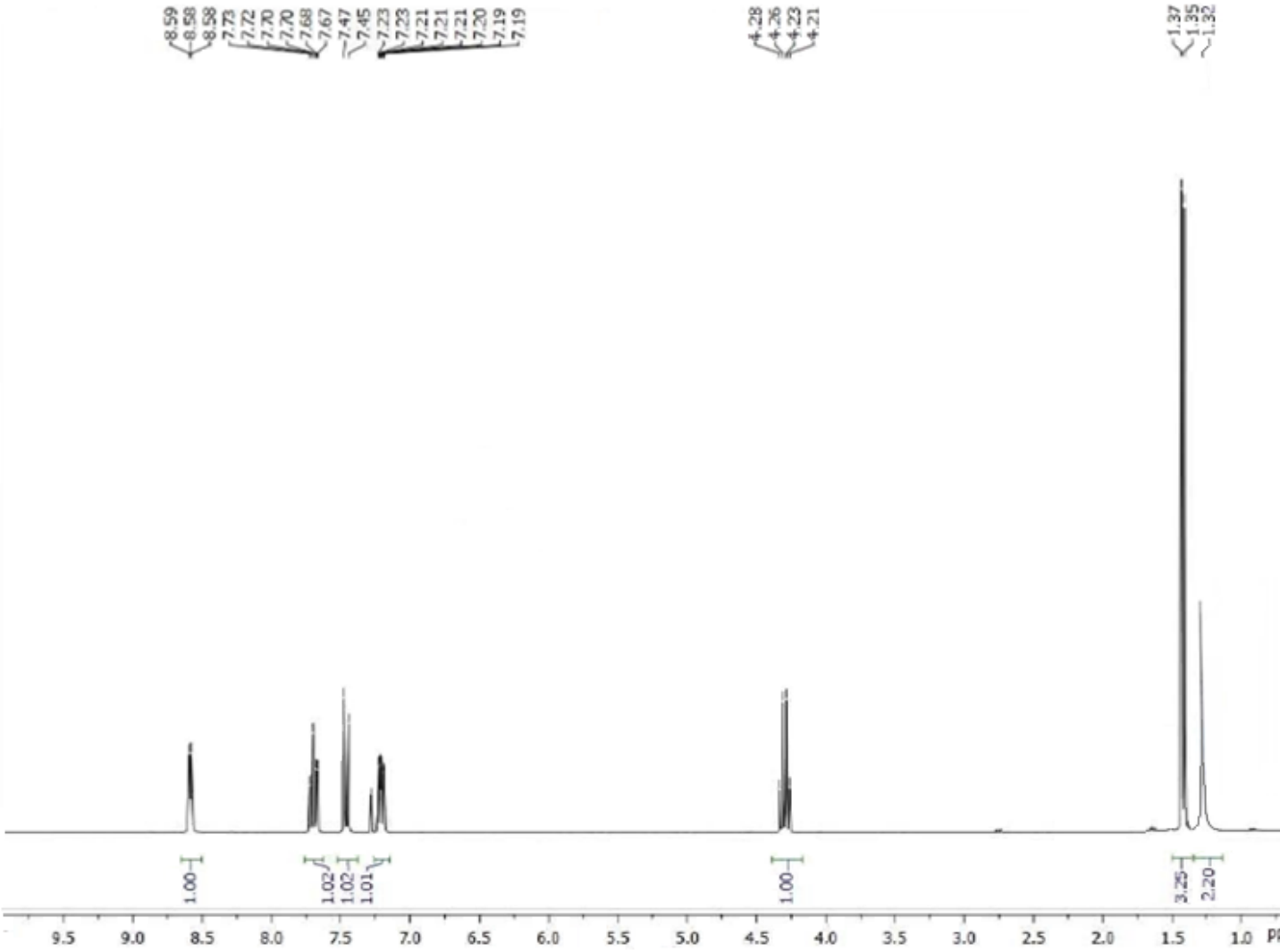


Compound 3d. ^{13}C NMR Spectrum ($CDCl_3$).

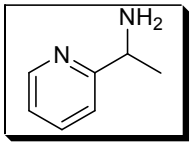


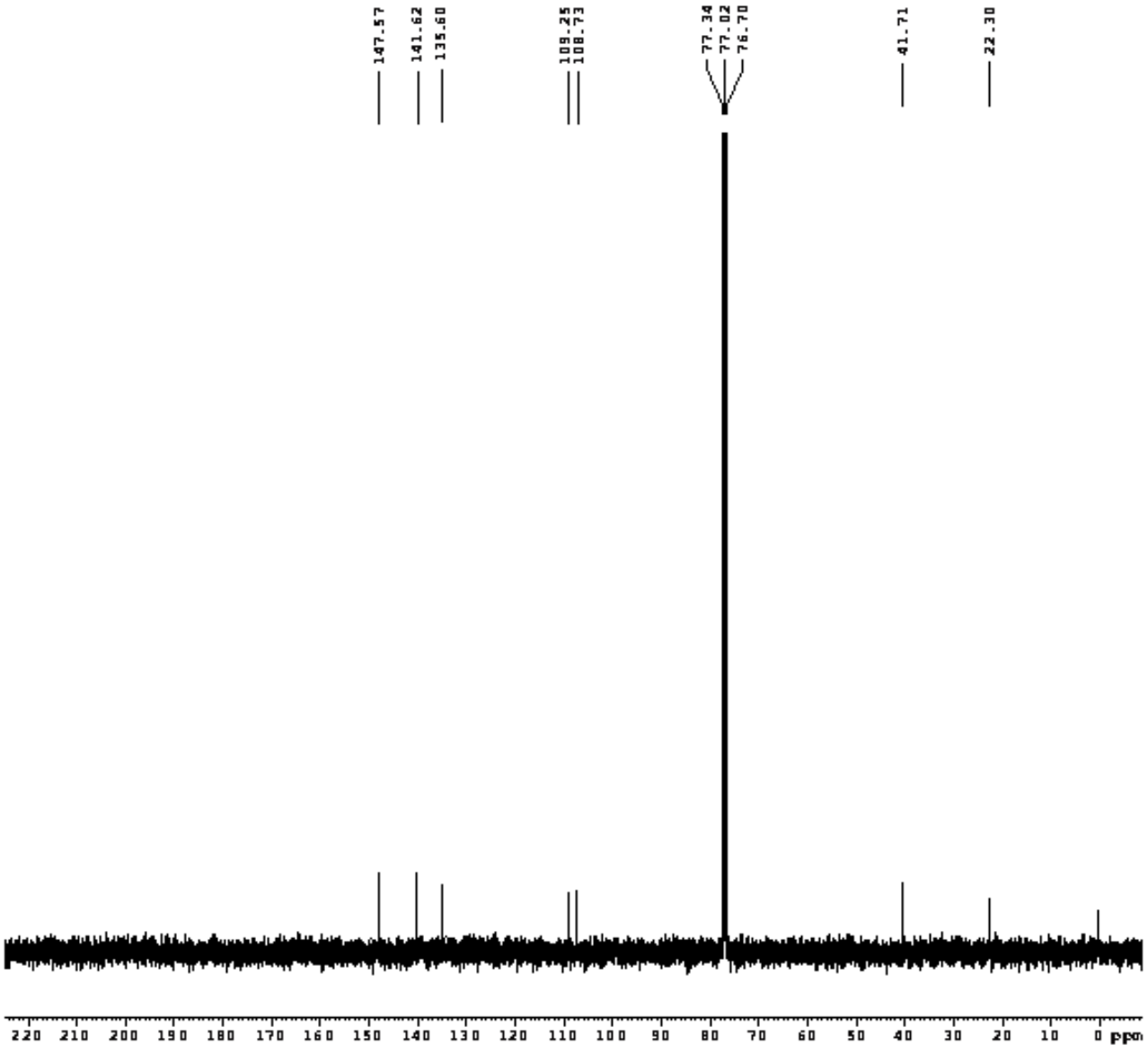
Compound 3e. ^{1}H NMR Spectrum ($CDCl_3$).



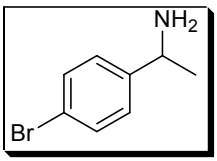


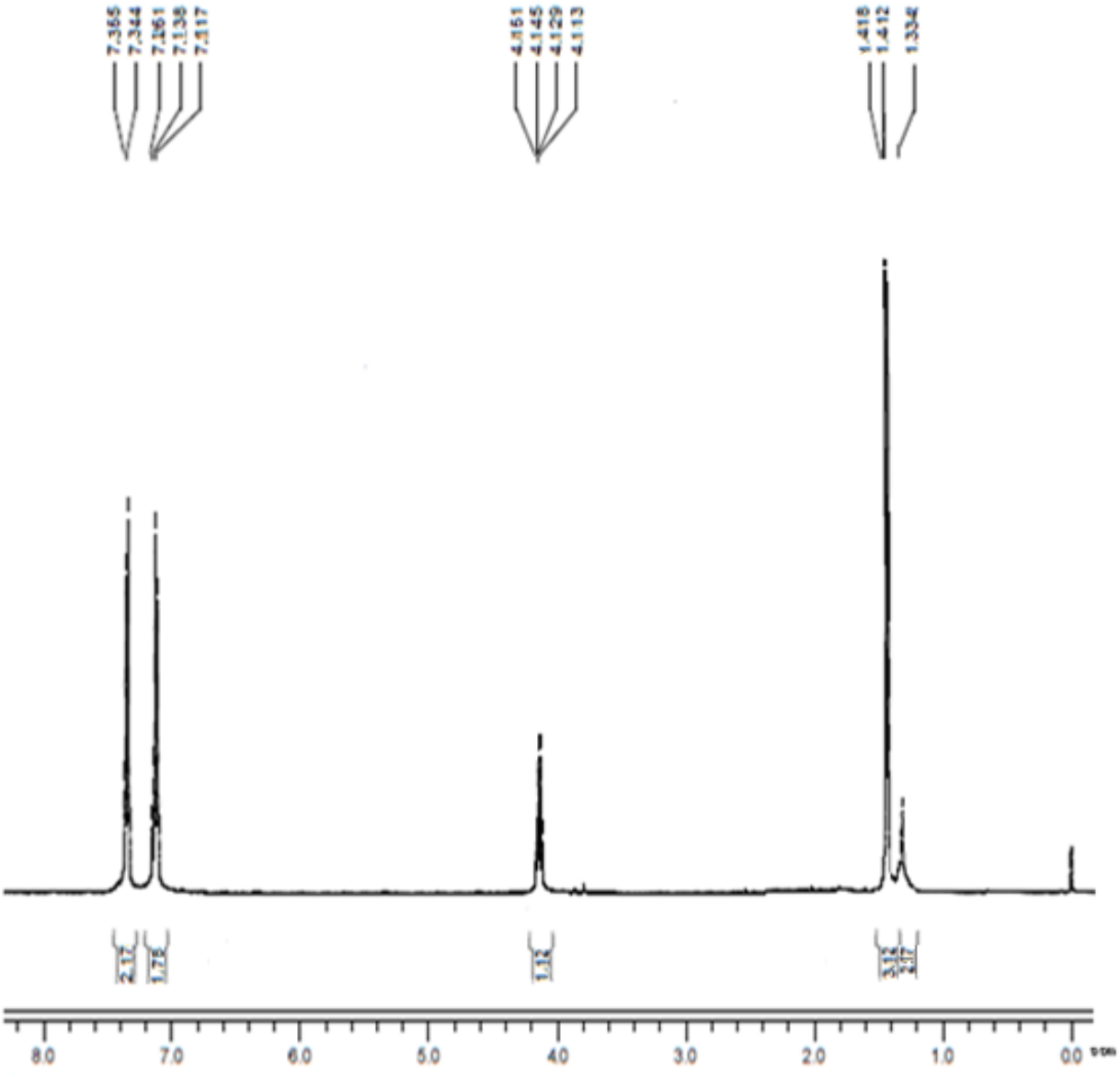
Compound 3e. ^{13}C NMR Spectrum ($CDCl_3$).



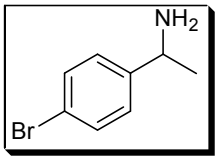


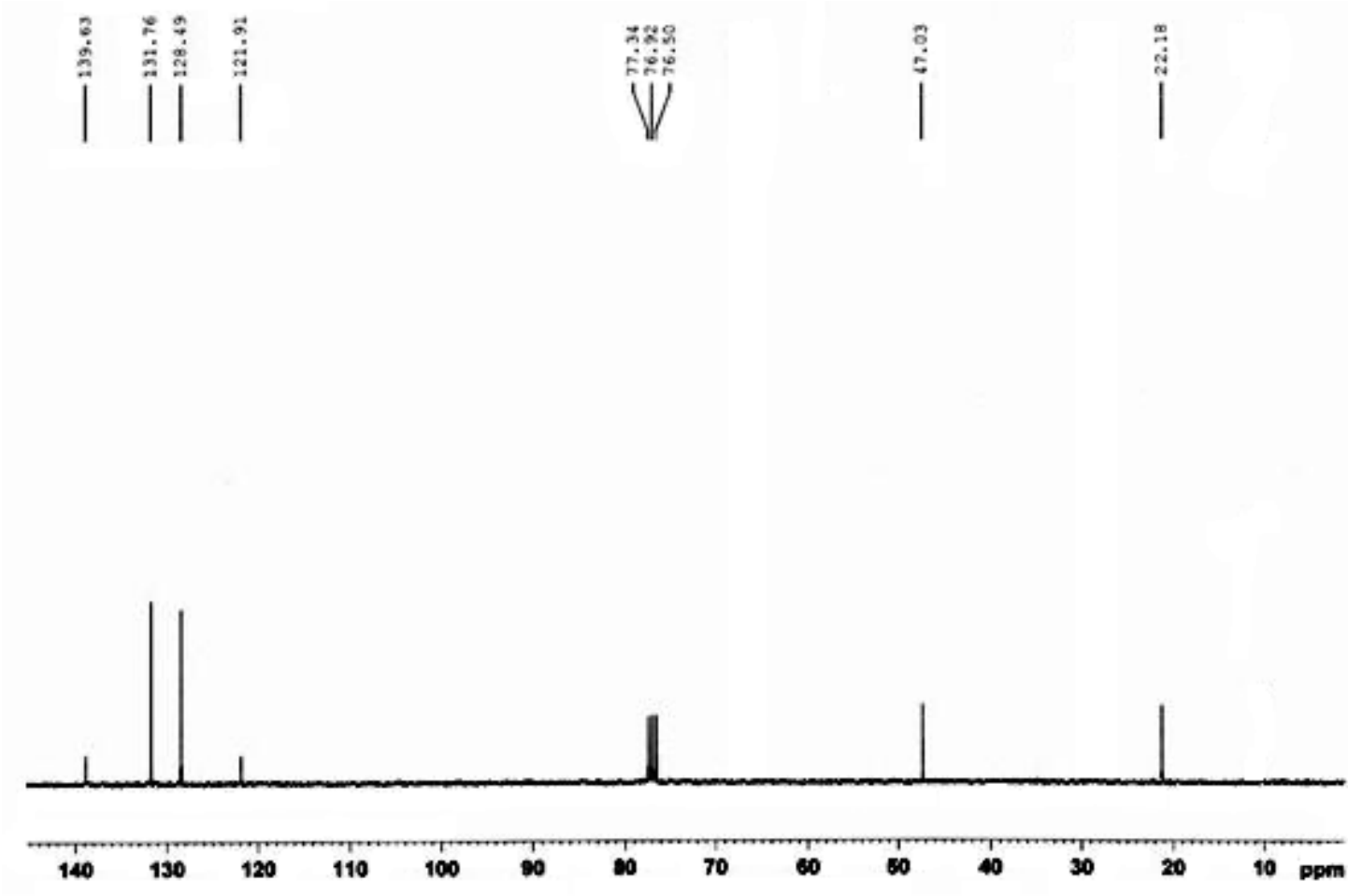
Compound 3f. ^{1}H NMR Spectrum ($CDCl_3$).



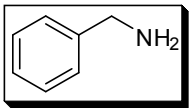


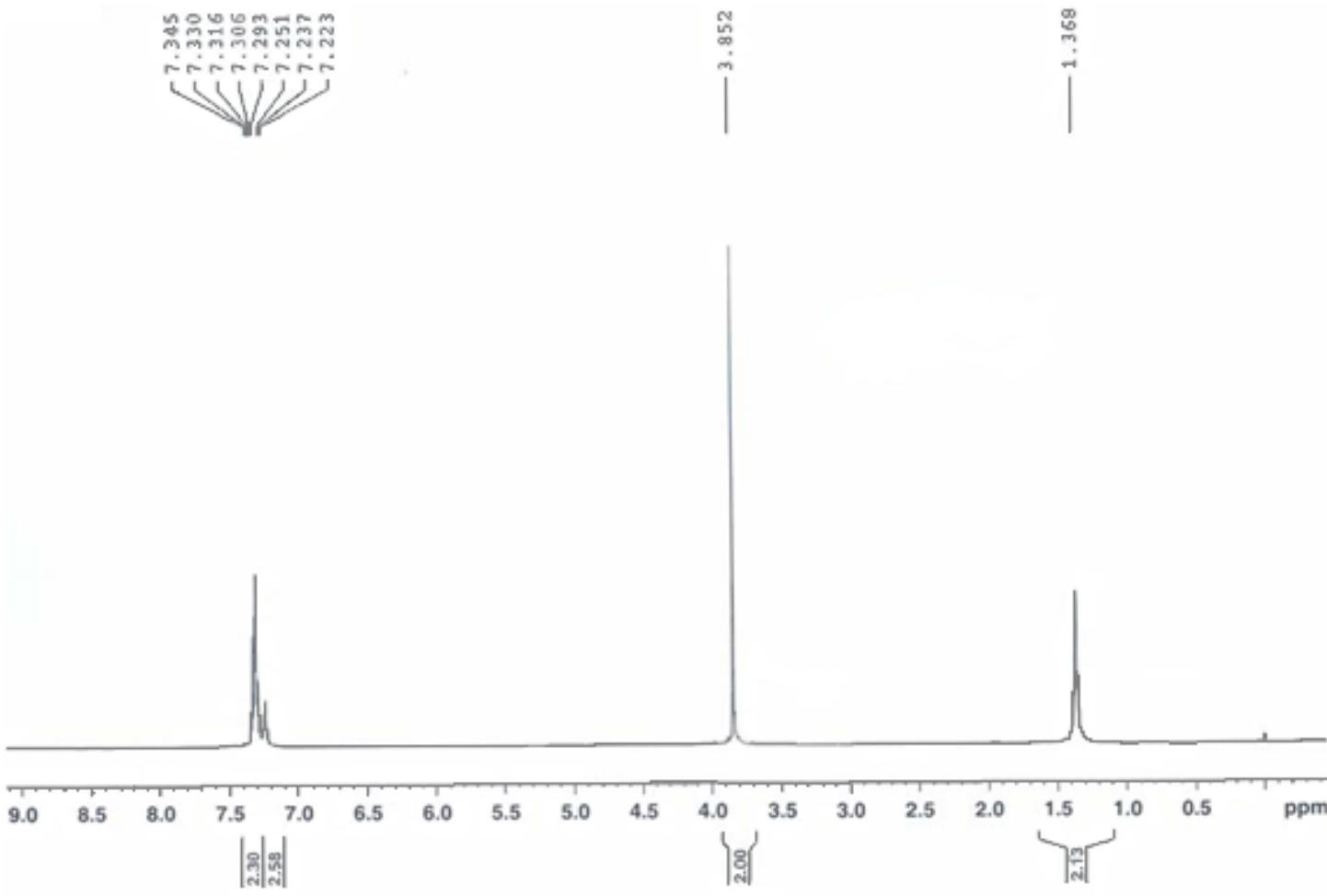
Compound 3f. ^{13}C NMR Spectrum ($CDCl_3$).



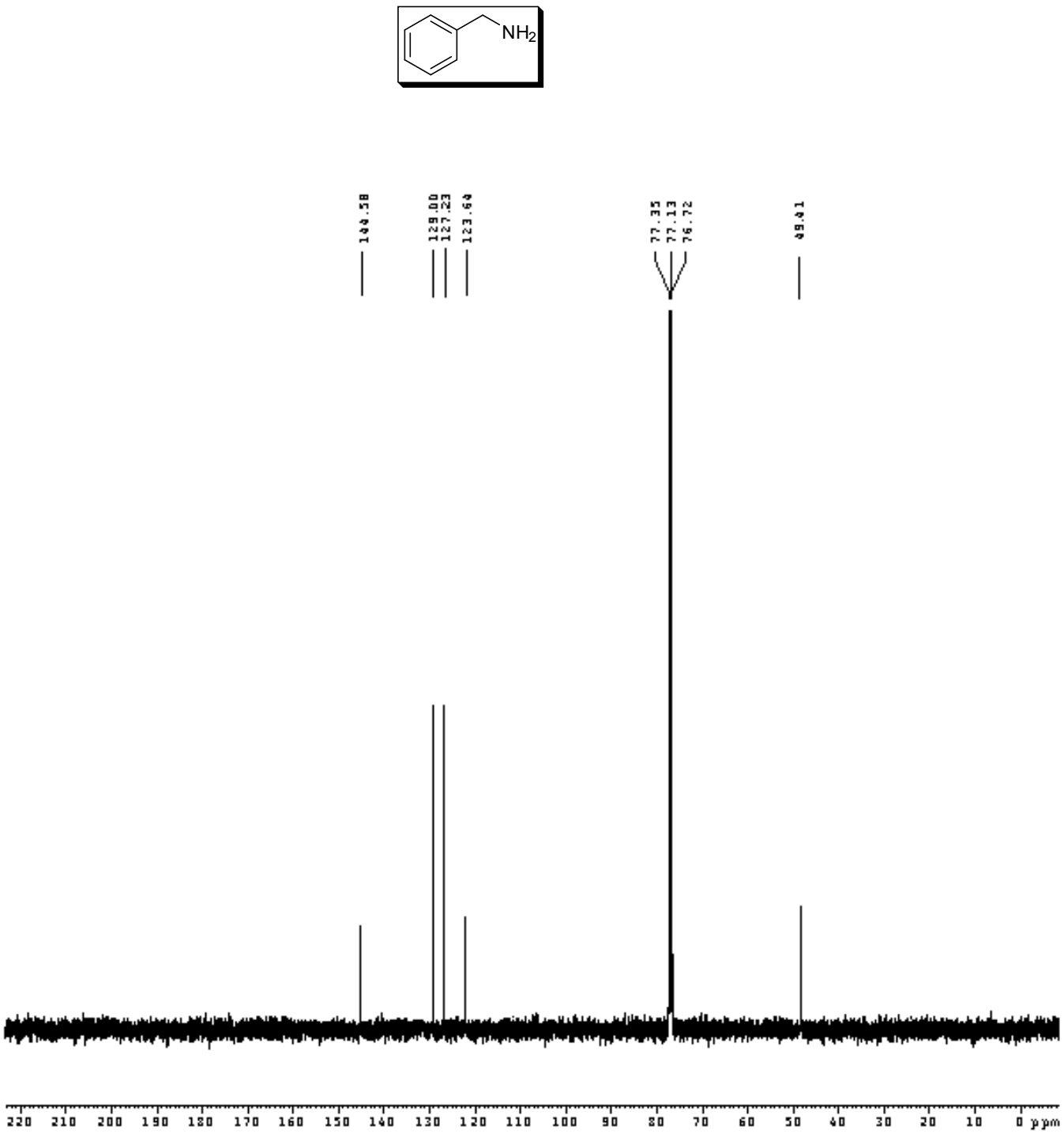


Compound 3g. ^{1}H NMR Spectrum ($CDCl_3$).

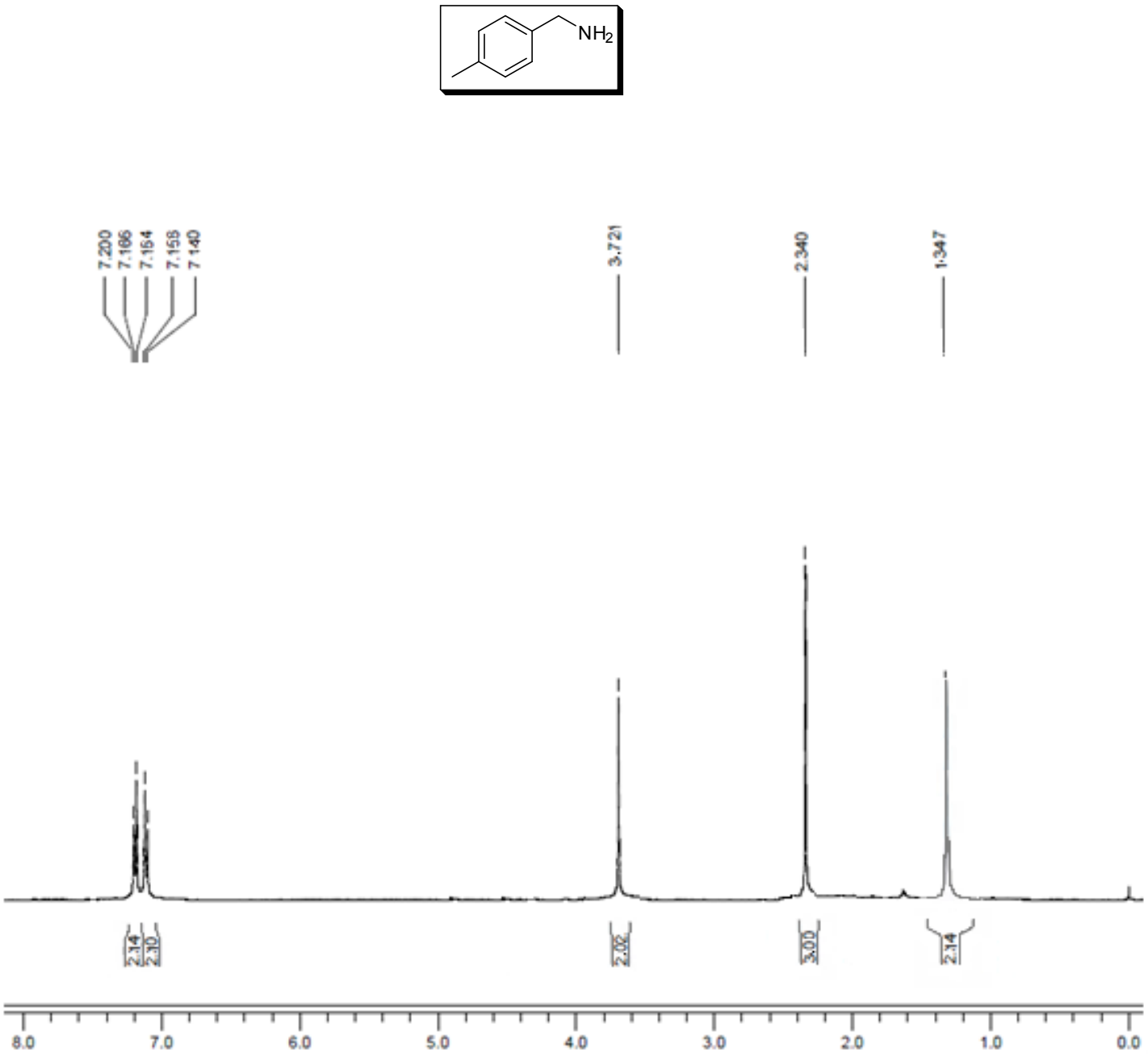




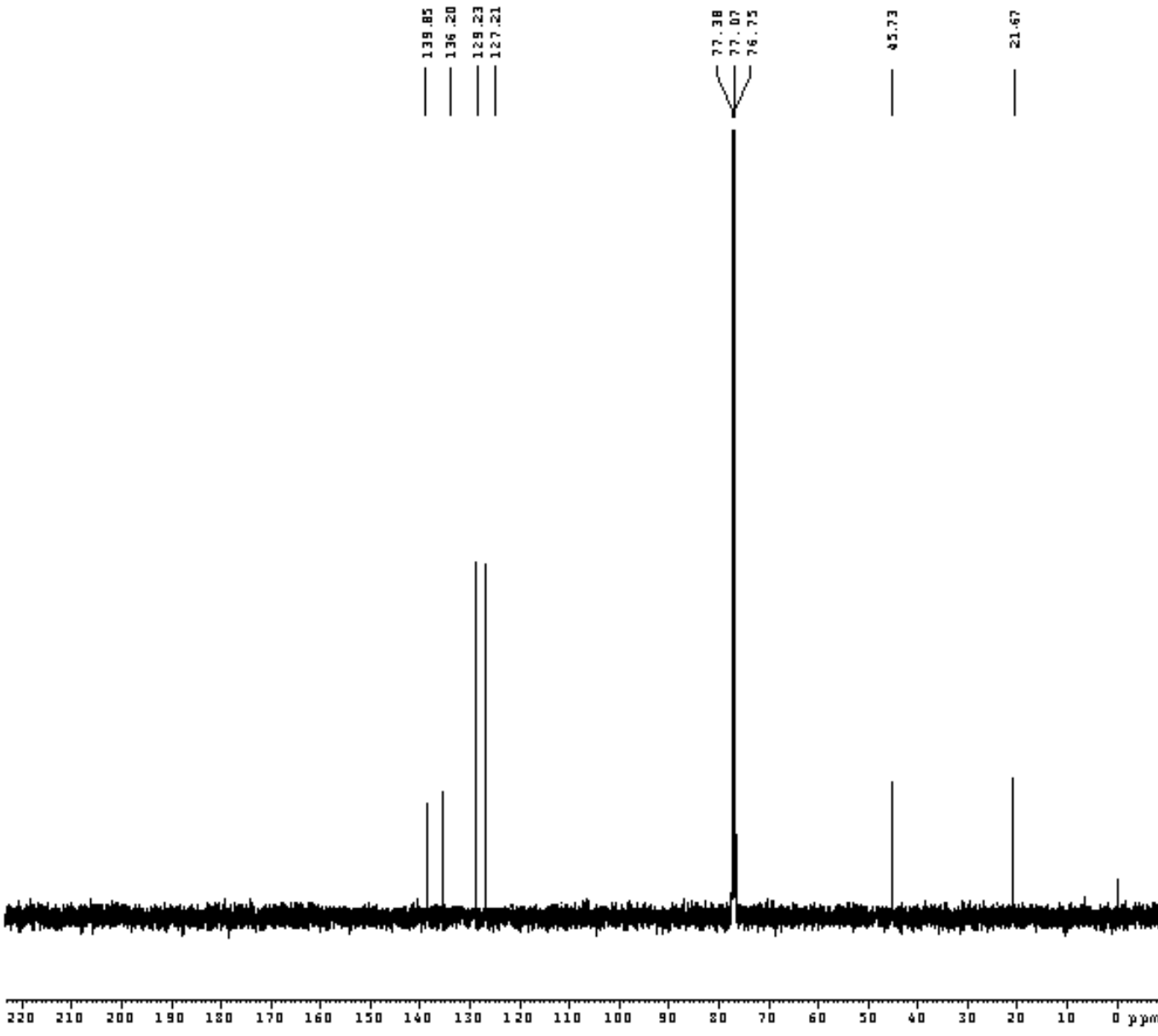
Compound 3g. ^{13}C NMR Spectrum ($CDCl_3$).



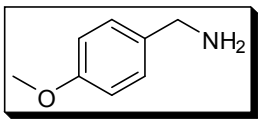
Compound 3h. ^{1}H NMR Spectrum ($CDCl_3$).

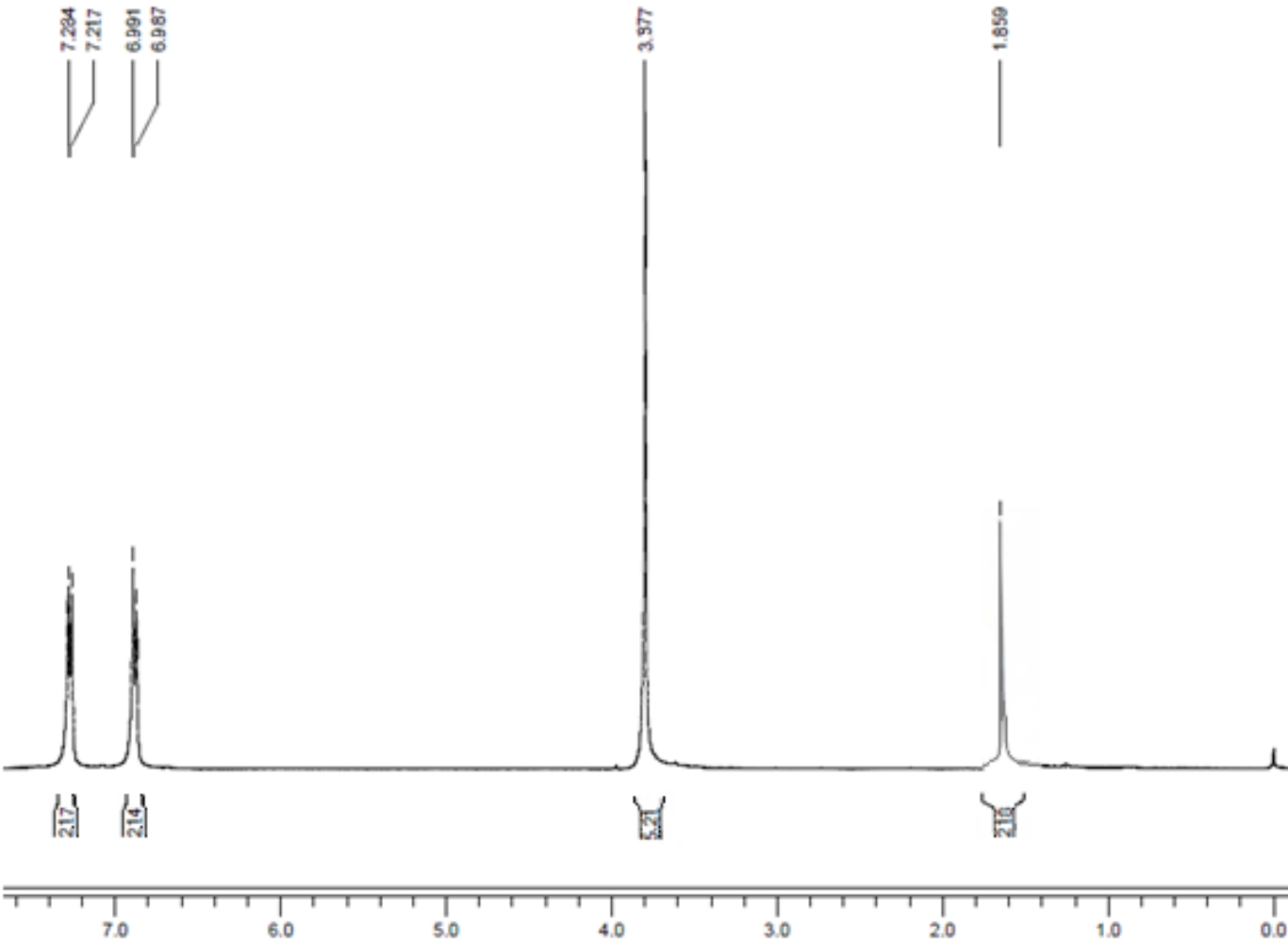


Compound 3h. ^{13}C NMR Spectrum ($CDCl_3$).

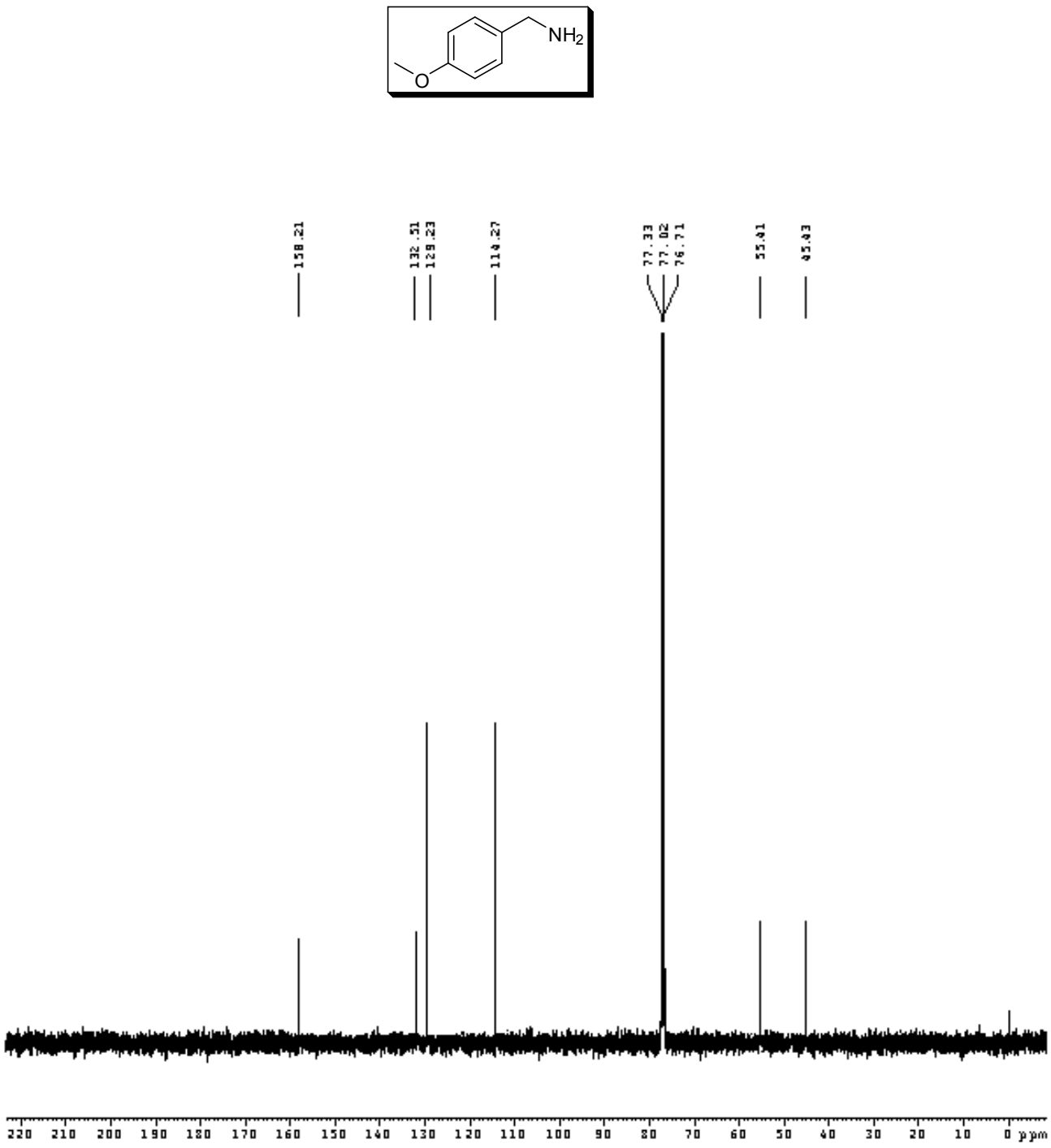


Compound 3i. ^{1}H NMR Spectrum ($CDCl_3$).

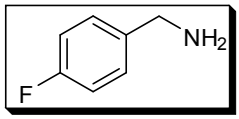


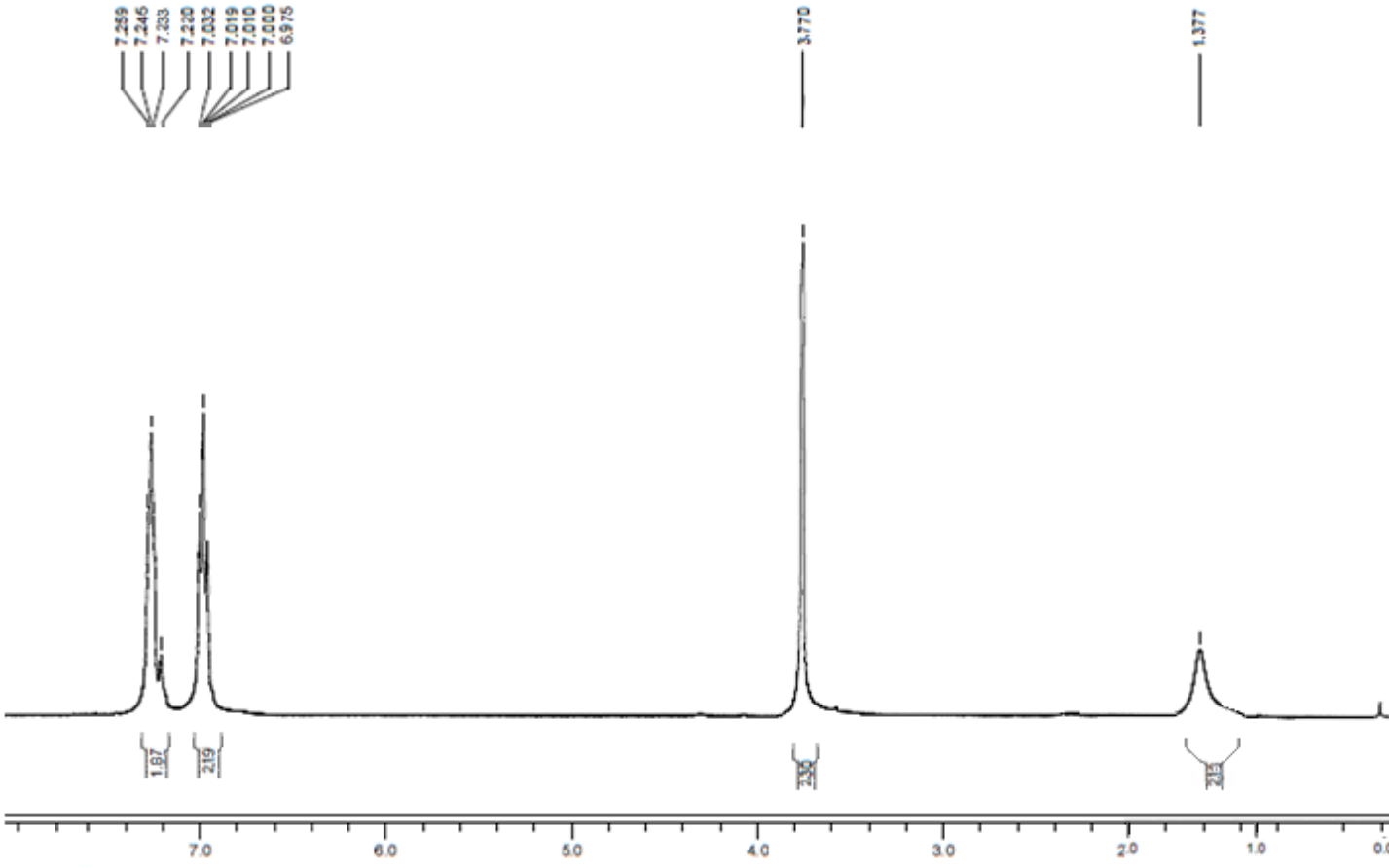


Compound 3i. ^{13}C NMR Spectrum ($CDCl_3$).

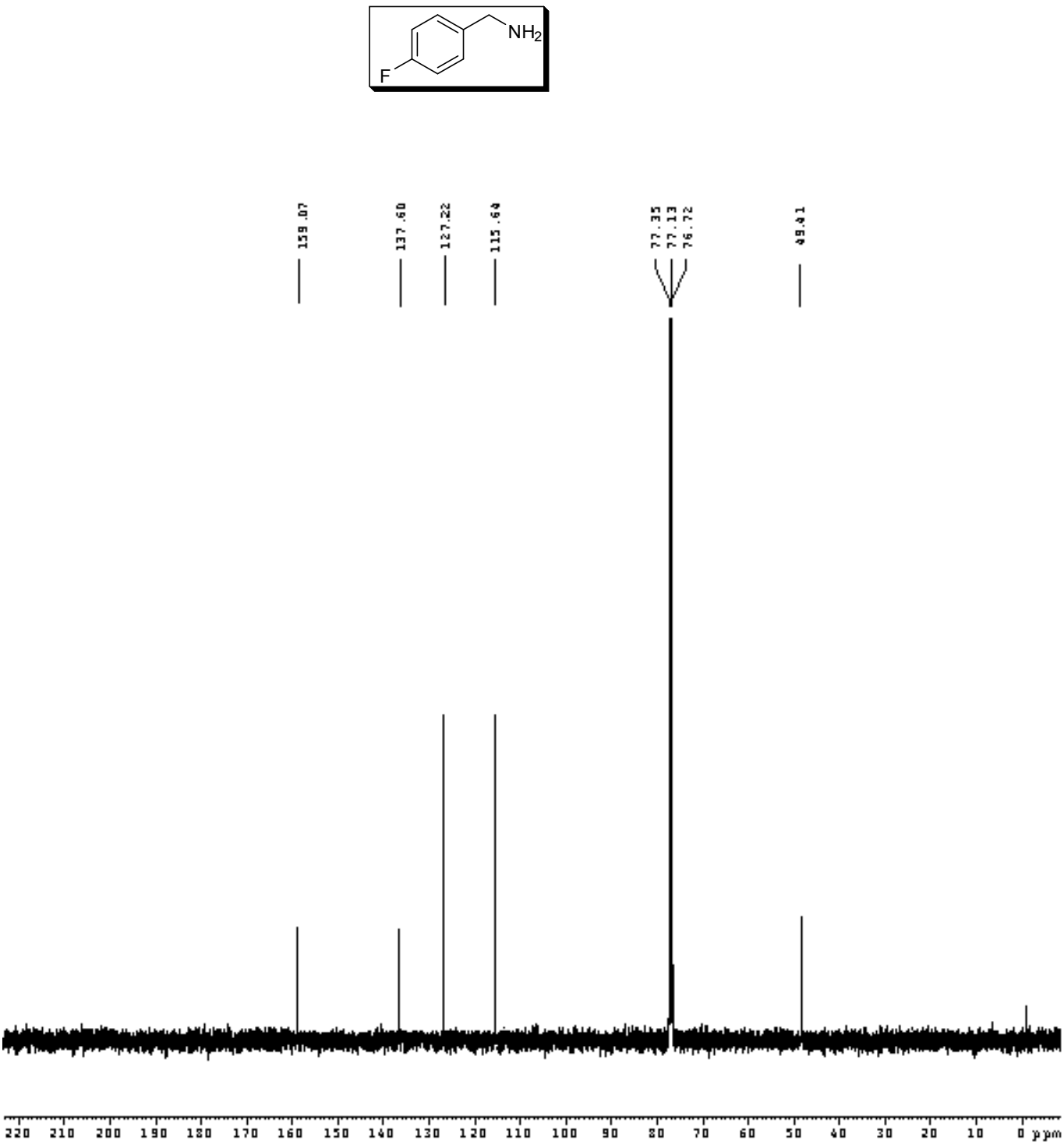


Compound 3j. ^{1}H NMR Spectrum ($CDCl_3$).

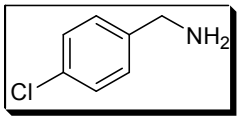


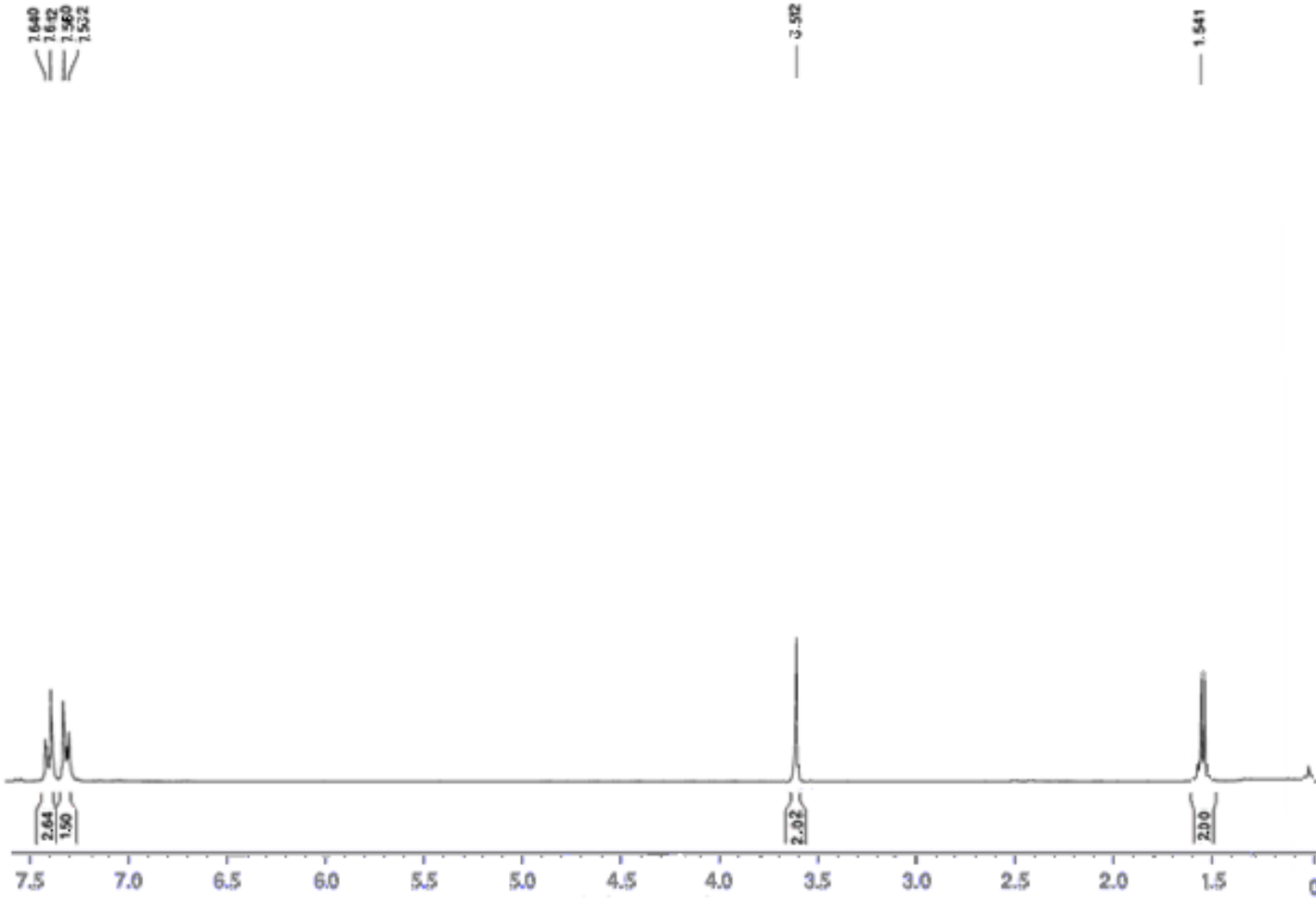


Compound 3j. ^{13}C NMR Spectrum ($CDCl_3$).

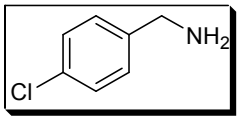


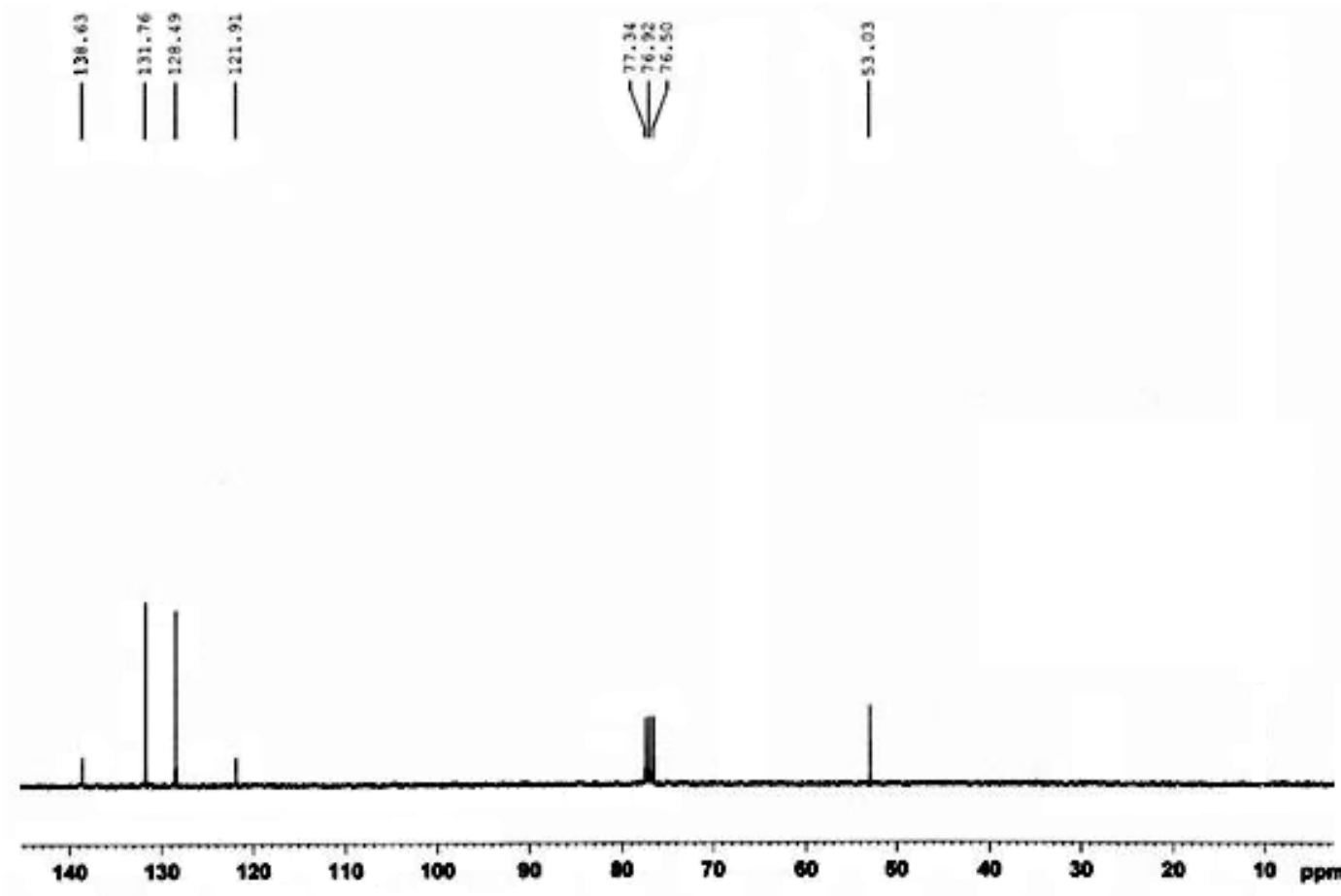
Compound 3k. ^{1}H NMR Spectrum ($CDCl_3$).



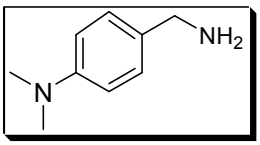


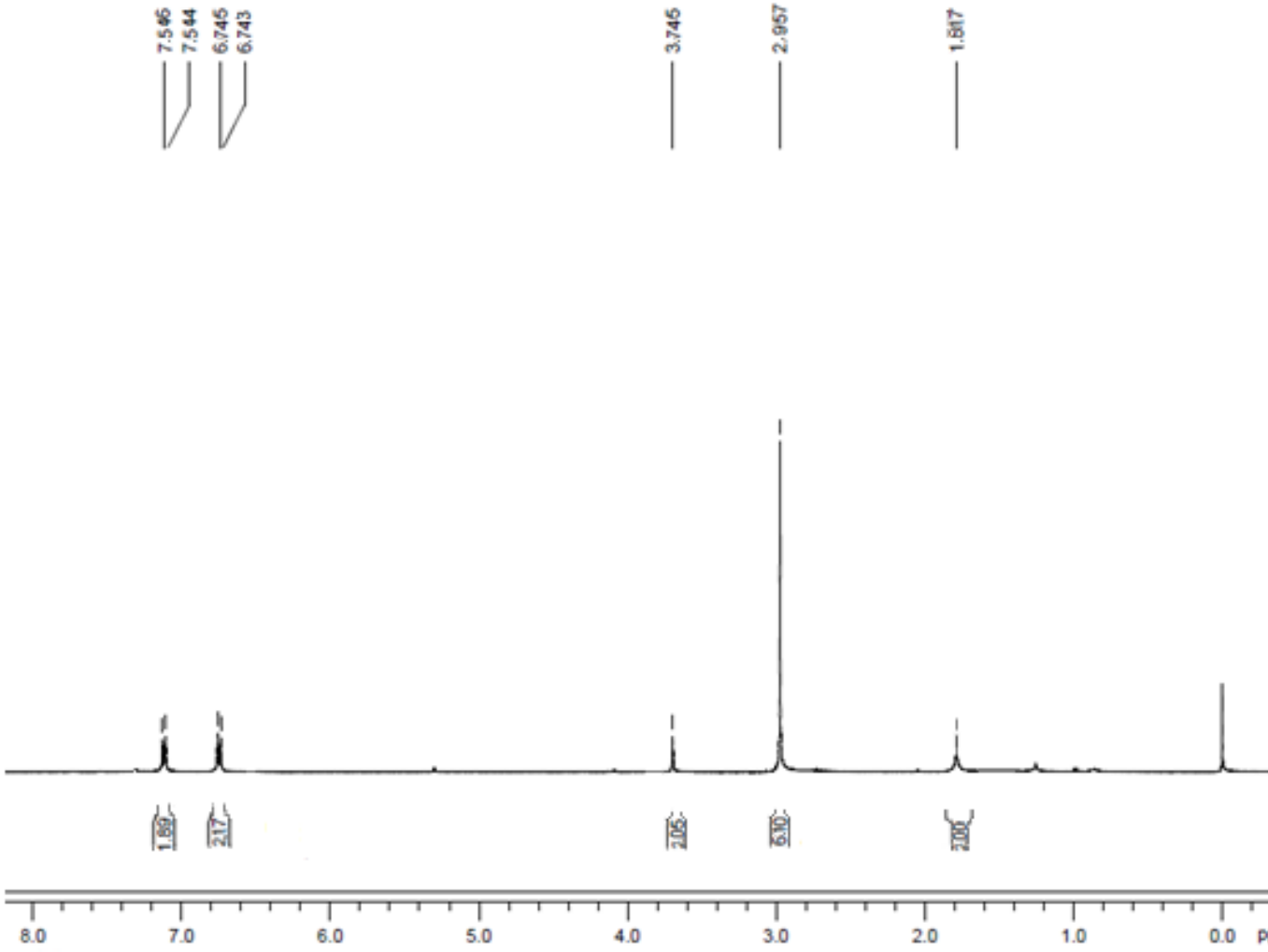
Compound 3k. ^{13}C NMR Spectrum ($CDCl_3$).



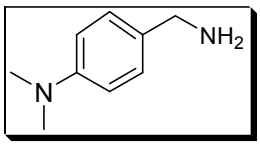


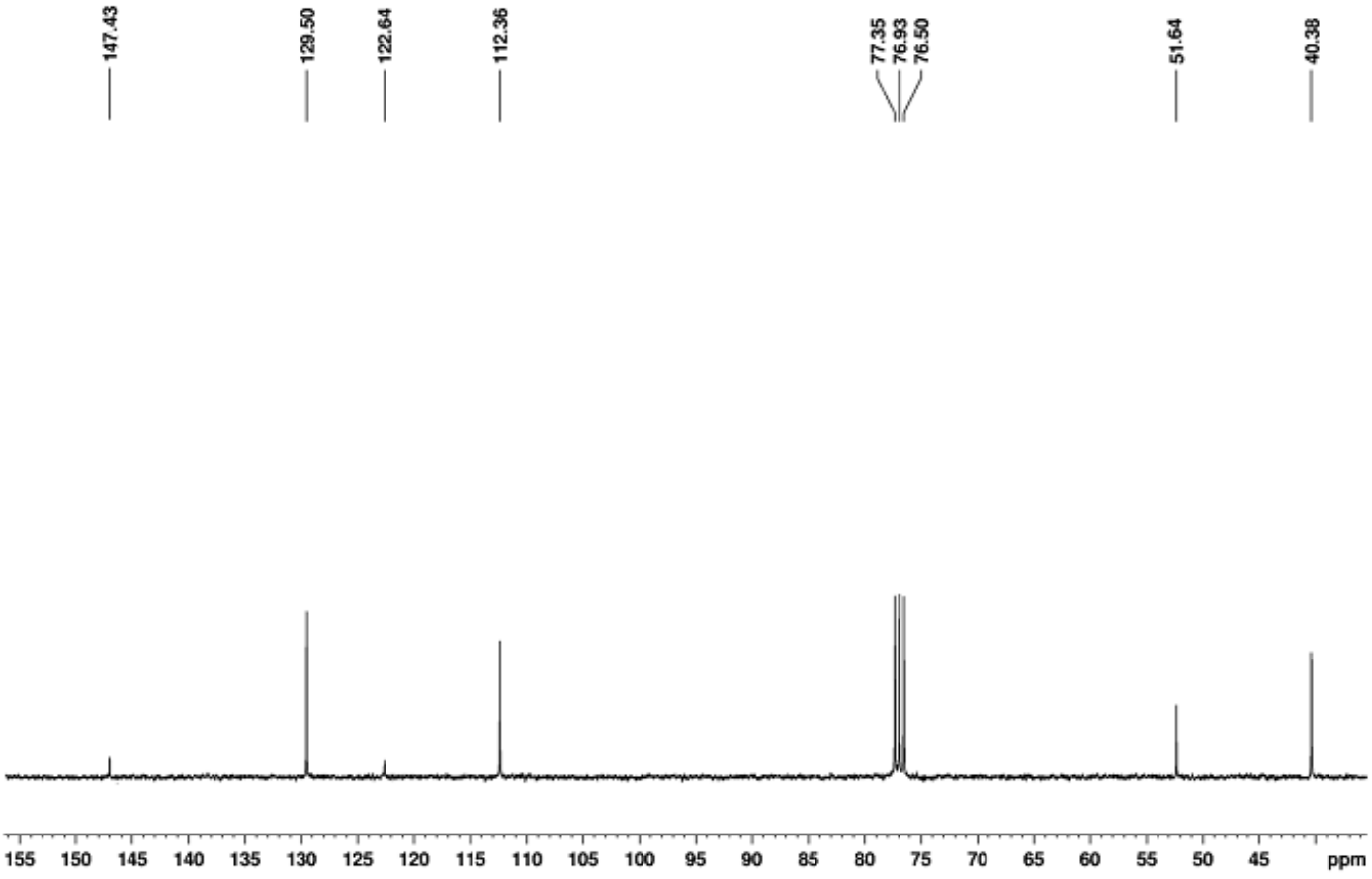
Compound 3l. ^{1}H NMR Spectrum ($CDCl_3$).



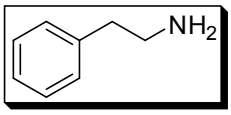


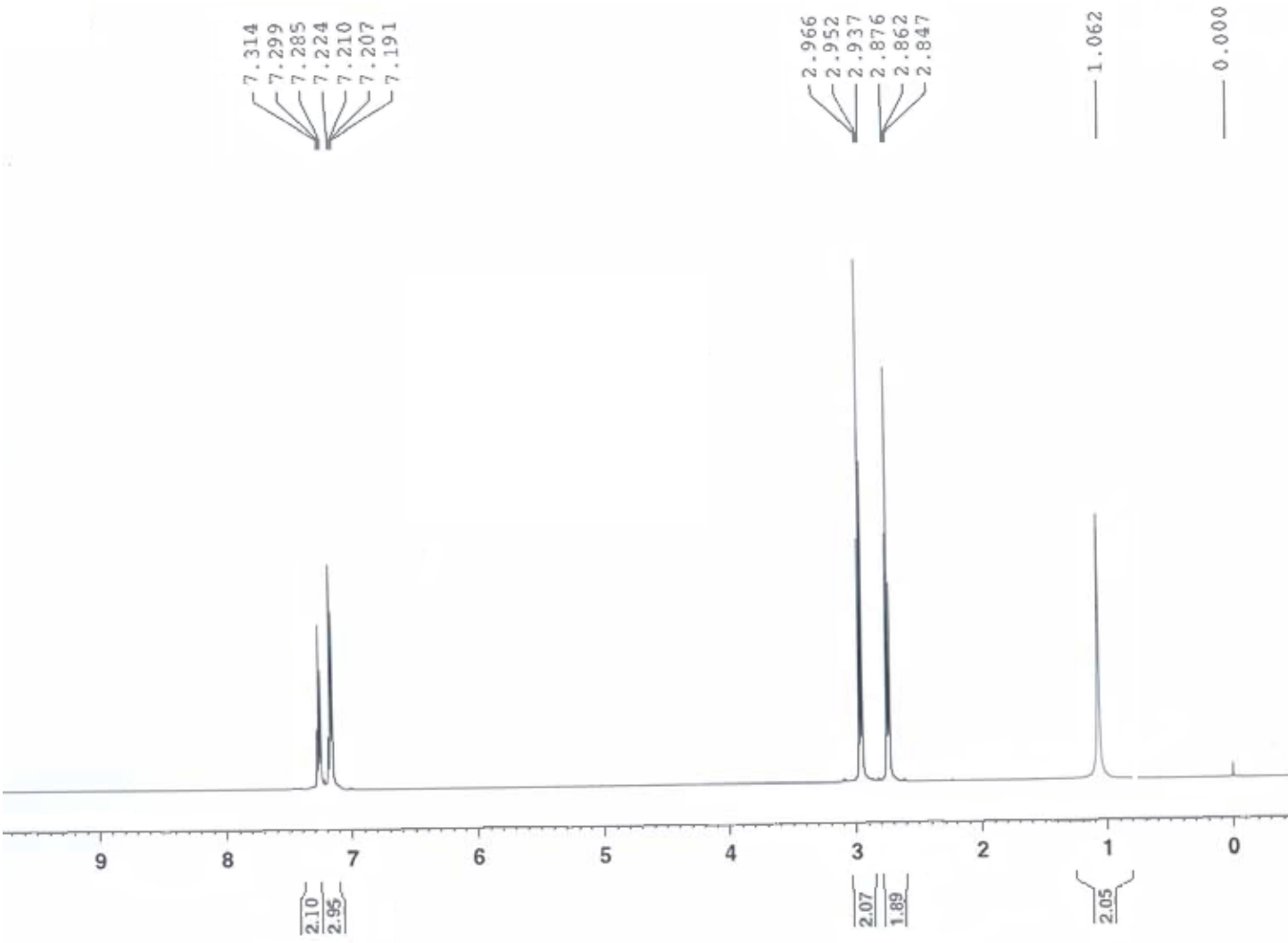
Compound 3l. ^{13}C NMR Spectrum ($CDCl_3$).



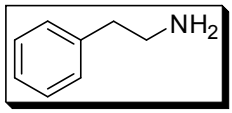


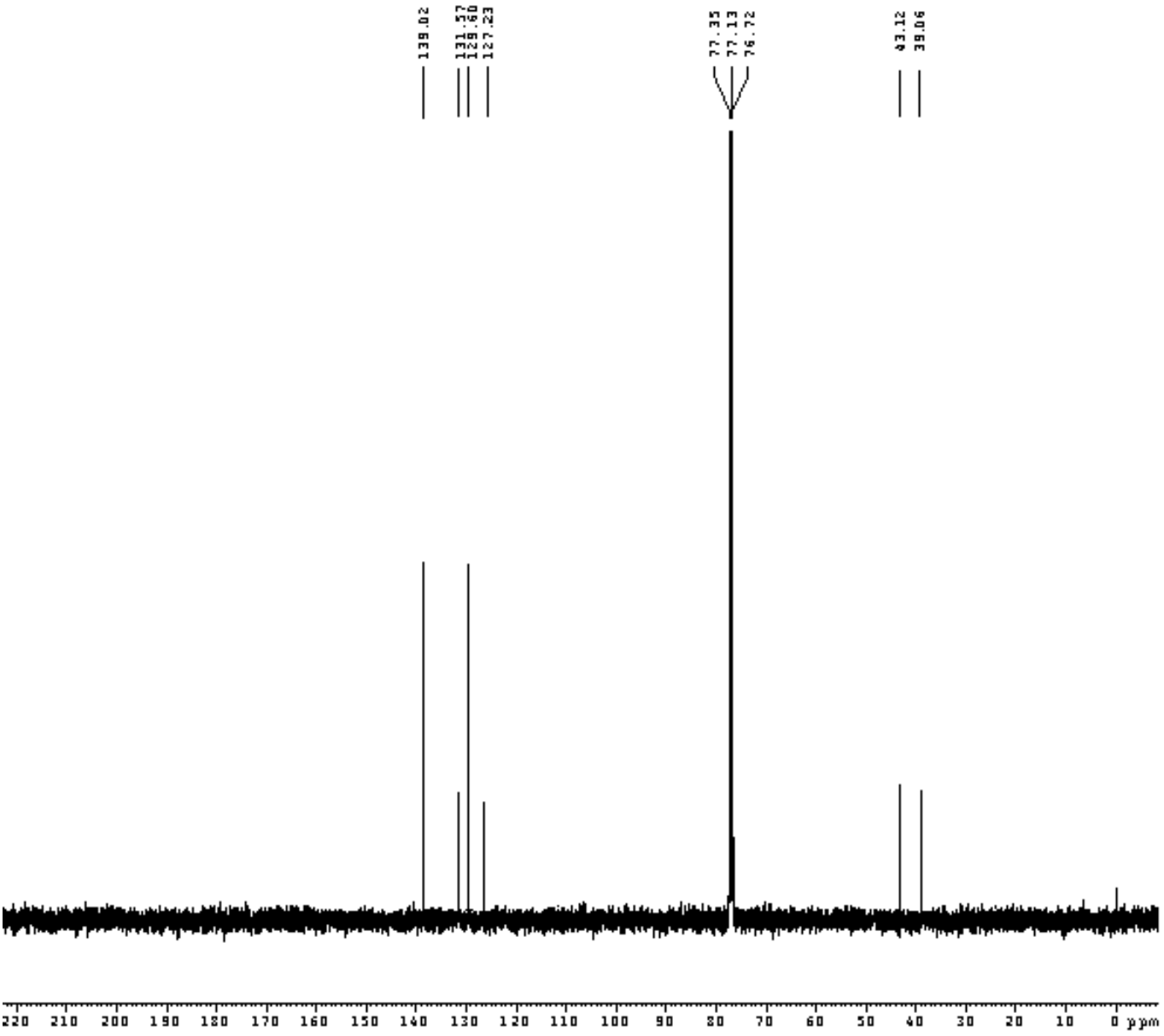
Compound 3m. ^{1}H NMR Spectrum ($CDCl_3$).



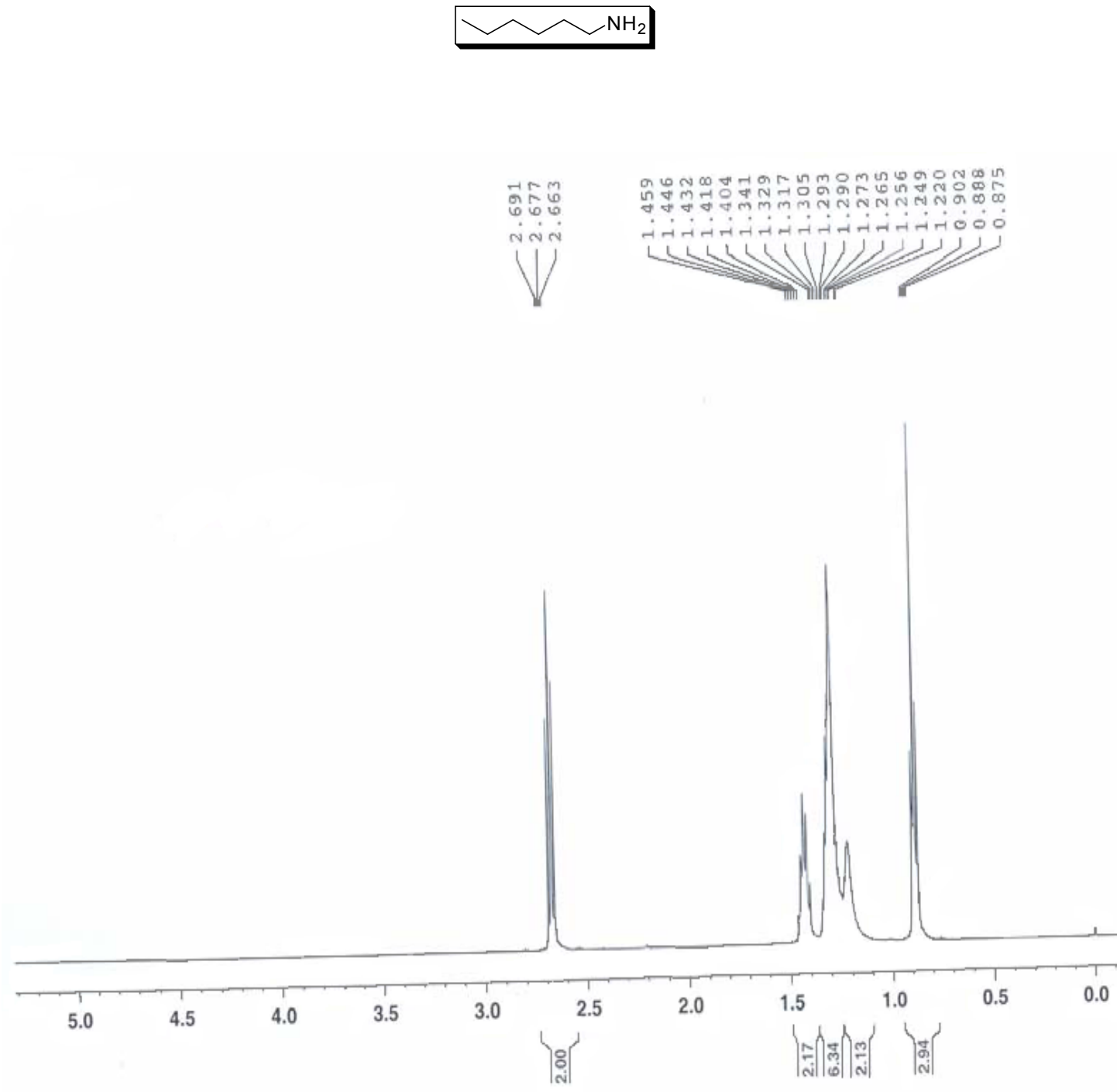


Compound 3m. ^{13}C NMR Spectrum ($CDCl_3$).

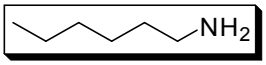


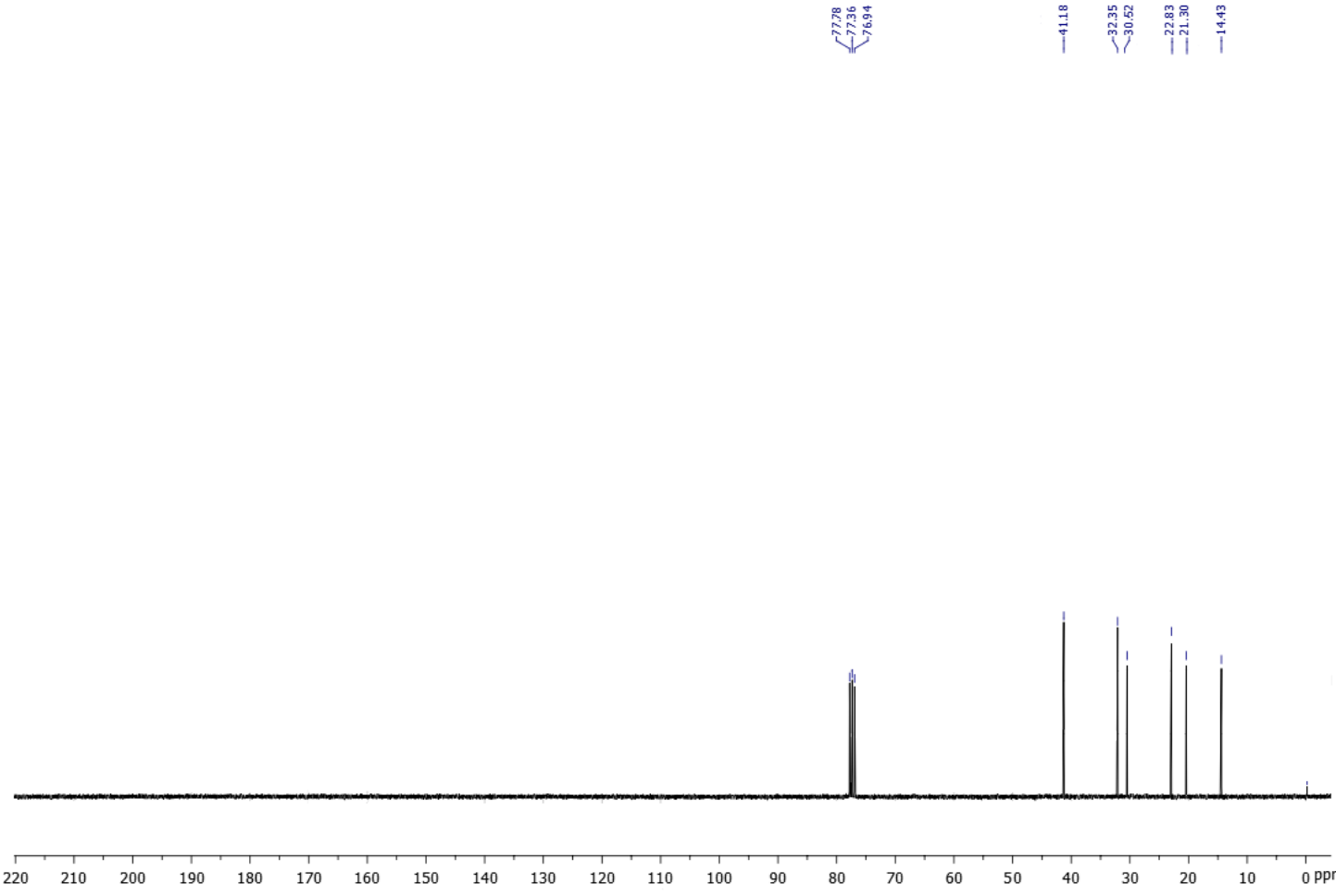


Compound 3n. ^{1}H NMR Spectrum ($CDCl_3$).

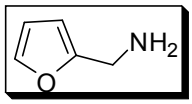


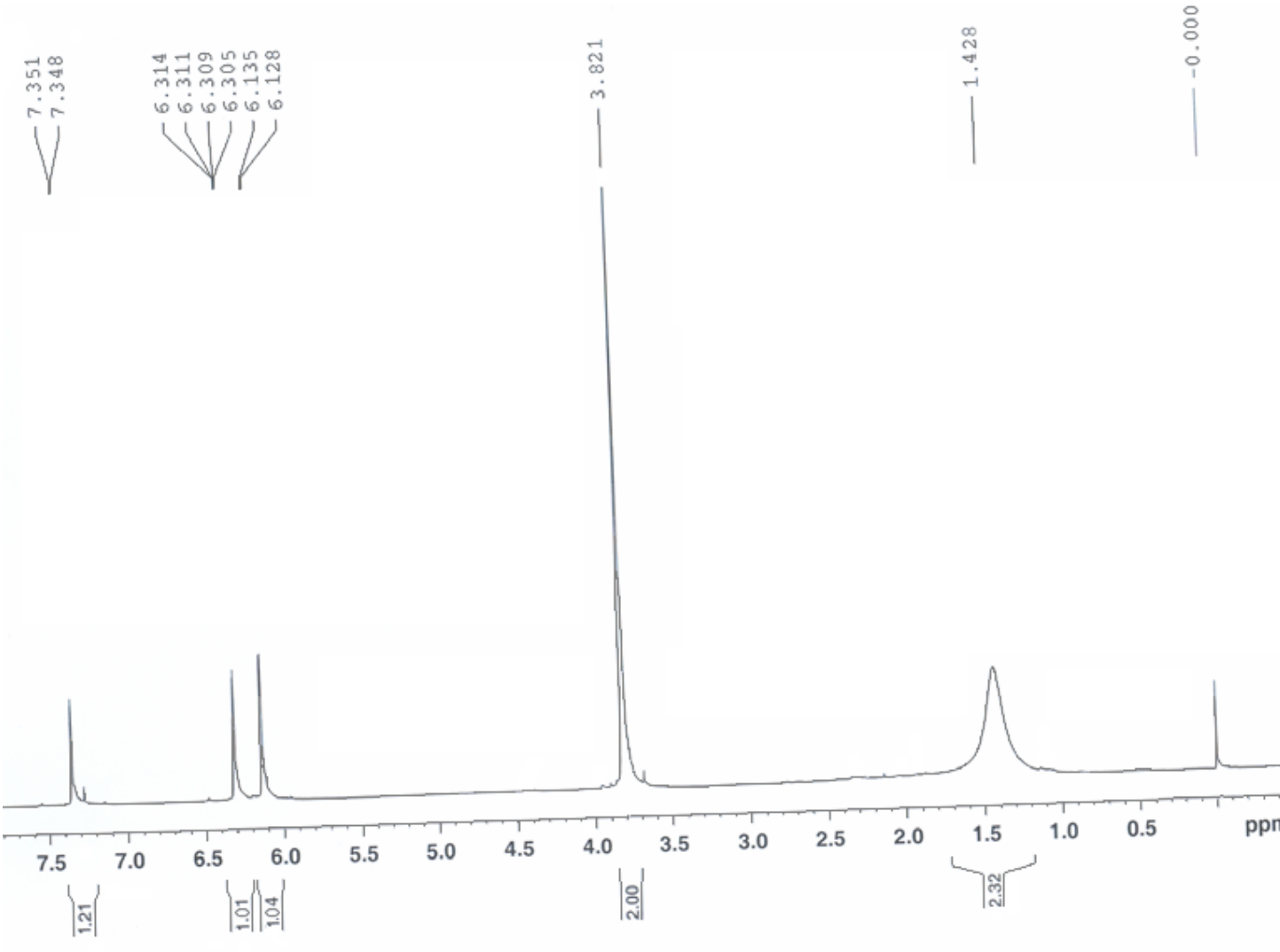
Compound 3n. ^{13}C NMR Spectrum ($CDCl_3$).



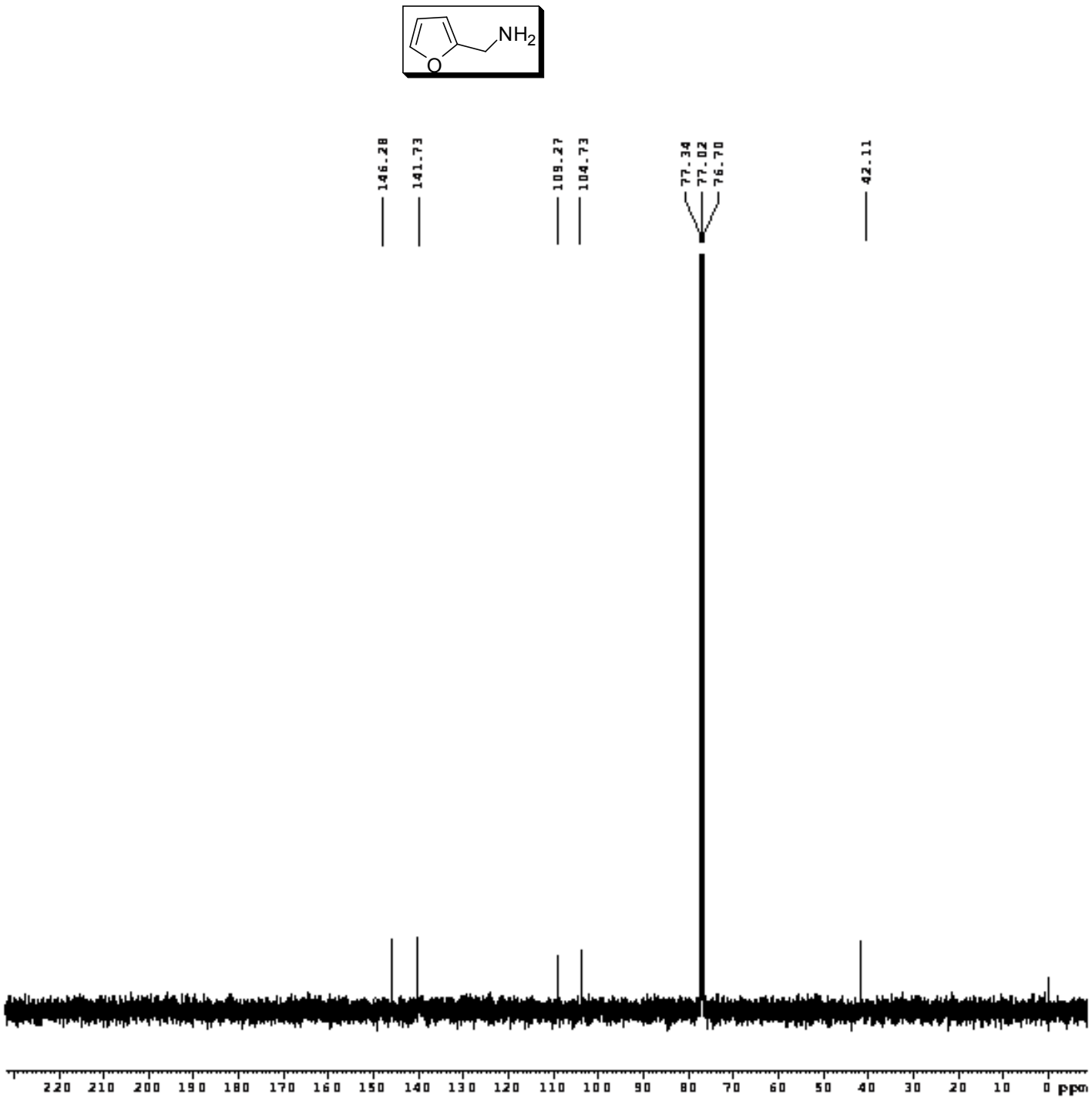


Compound 3o. ^{1}H NMR Spectrum ($CDCl_3$).

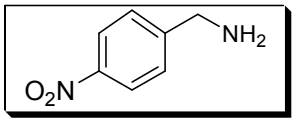


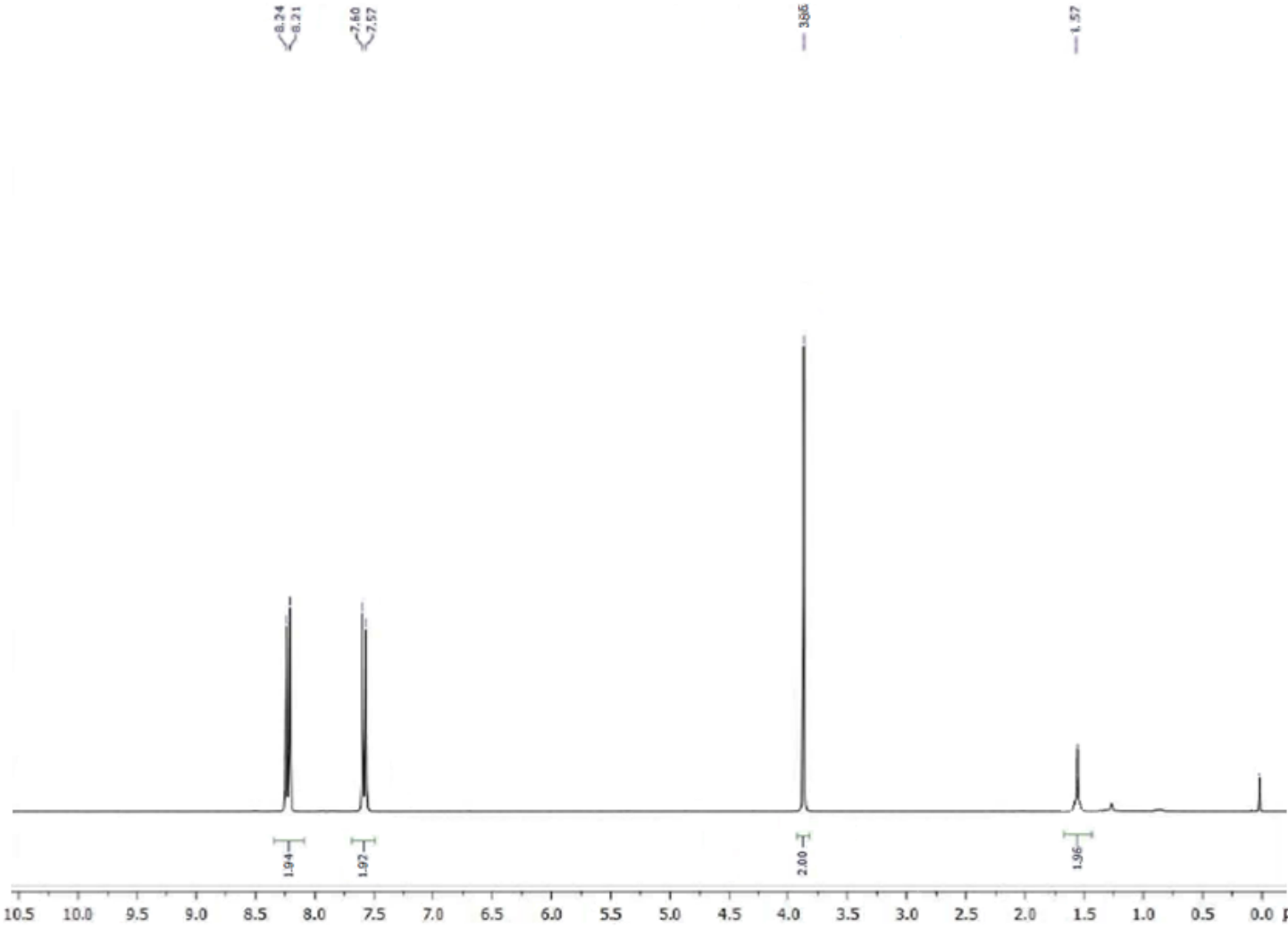


Compound 3o. ^{13}C NMR Spectrum ($CDCl_3$).



Compound 3p. ^{1}H NMR Spectrum ($CDCl_3$).





Compound 3p. ^{13}C NMR Spectrum ($CDCl_3$).