Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

I_2 – Catalysed Transformation of o-Aminobenzamide to o-Ureidobenzonitrile Using Isothiocyanates

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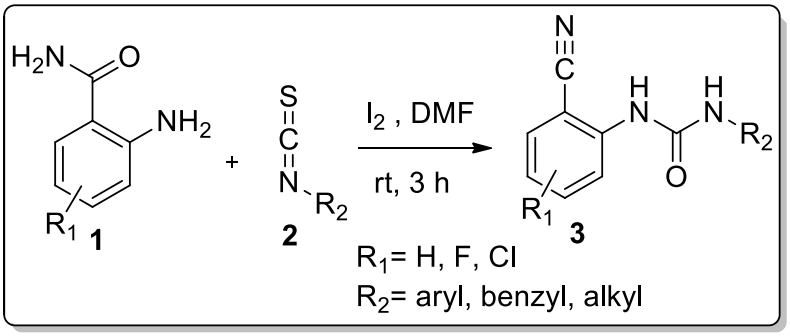
Contents

1. General Experimental Details:

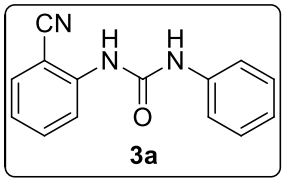
All the reagents, chemicals and solvents used were from Sigma Aldrich and Sd-fine chemicals and were used without additional purification. The instrumental techniques employed for the characterization of the newly synthesized compounds include ^{1}H and ^{13}C NMR and HRMS. ^{1}H and ^{13}C NMR spectra were recorded on Agilent 400 MHz spectrometer in DMSO-d_6 solution using tetramethylsilane (TMS) as internal standard. Chemical shifts were recorded in ppm relative to TMS. High resolution mass spectra were obtained via electrospray (ESI). Column chromatography was performed on silica gel 60 (60–120 mesh) and thin layer chromatography was performed on TLC plates (Merck, silica gel 60 F254). The mobile phases employed for column chromatography and TLC were hexane and ethyl acetate in 9:1 ratio.

2. General Procedure for the synthesis of o-ureidobenzonitriles (3a-3x).



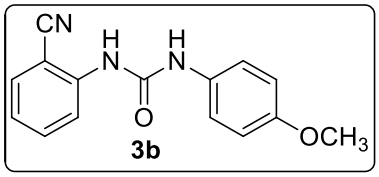
The mixture of o-aminobenzamide (1) (1 mmol) and isothiocyanates (2) (1 mmol) were allowed to stir in DMF solvent (2 ml) in presence of molecular iodine (0.3 mmol) at room temperature for 3 h. After that, the contents were poured to 30 ml, 10 % aqueous solution of sodium thiosulfate and extracted with 30 ml ethyl acetate. The ethyl acetate extract was separated and dried over anhydrous sodium sulphate then the solvent was removed under reduced pressure to afford corresponding o-ureidobenzonitrile. The crude residue thus obtained was purified by column chromatography over silica gel using ethyl acetate in hexane as eluent to get pure o-ureidobenzonitrile.

3. Characterization details of the synthesized Products



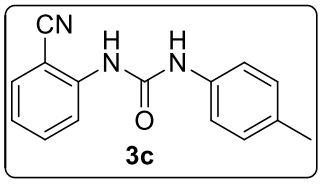
1-(2-cyanophenyl)-3-phenylurea (3a)

Yield: 192 mg, 81 %; MP. 178 °C; White solid; ^{1}H-NMR (400 MHz, DMSO-d_6): δ ppm : 6.971-7.008 (t, 1H, Ar, J = 7.6 Hz), 7.139-7.176 (t, 1H, Ar, J = 7.6 Hz), 7.269-7.307 (t, 2H, Ar, J = 8 Hz), 7.450-7.470 (d, 2H, Ar, J = 8 Hz), 7.602-7.641 (t, 1H, Ar, J = 7.6 Hz), 7.718-7.738 (d, 1H, Ar, J = 8Hz), 8.059-8.080 (d, 1H, Ar, J = 8.4 Hz), 8.747 (s, 1H, -NH-), 9.402 (s, 1H, -NH-); ^{13}C- NMR (400 MHz, DMSO-d_6): δ ppm: 102.452, 117.395, 118.826, 121.725, 122.795, 123.447, 129.343, 133.565, 134.421, 139.665, 142.389, 152.459; HRMS: m/z calculated for [$C_{14}H_{11}N_3O$+H^+] = 238.0975: found = 238.0974.



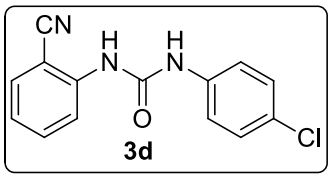
1-(2-cyanophenyl)-3-(4-methoxyphenyl)urea (3b)

Yield: 222 mg, 83 %; MP. 188 °C; White solid; ^{1}H-NMR (400 MHz, DMSO-d_6): 3.687 (s, 3H, -OCH_3,), 6.846-6.868 (d, 2H, Ar, J = 8.8 Hz), 7.103-7.141 (t, 1H, Ar, J = 7.6 Hz), 7.332-7.354 (d, 2H, Ar, J = 8.8 Hz), 7.572-7.610 (t, 1H, Ar, J = 7.6 Hz), 7.688-7.707 (d, 1H, Ar, J = 7.6 Hz), 8.047-8.068 (d, 1H, Ar, J = 8.4 Hz), 8.617 (s, 1H, -NH-), 9.183 (s, 1H, -NH-); ^{13}C- NMR (400 MHz, DMSO-d_6): 55.626, 102.121, 114.535, 117.405, 120.606, 121.491, 123.194, 132.612, 133.507, 134.373, 142.594, 152.527, 155.251; HRMS: m/z calculated for [$C_{15}H_{13}N_3O_2$ + H^+] = 268.1081: found = 268.1084.



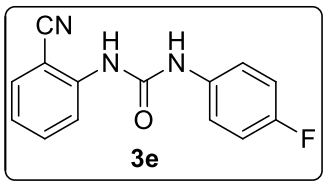
1-(2-cyanophenyl)-3-(p-tolyl)urea (3c)

Yield: 201 mg, 80 %; MP. 196 °C; White solid; ^{1}H-NMR (400 MHz, DMSO-d_6): δ ppm: 2.219 (s, 3H, -CH_3), 7.067-7.088 (d, 2H, Ar, J = 8.4 Hz), 7.116-7.155 (t, 1H, Ar, J = 7.6 Hz), 7.310-7.331 (d, 2H, Ar, J = 8.4 Hz), 7.577-7.621 (m, 1H, Ar), 7.694-7.716 (m, 1H, Ar), 8.042-8.063 (d, 1H, Ar, J = 8.4 Hz), 8.658 (s, 1H, -NH-), 9.260 (s, 1H, -NH-); ^{13}C- NMR (400 MHz, DMSO-d_6): δ ppm: 102.257, 117.395, 118.903, 121.598, 123.311, 129.712, 131.678, 133.536, 134.392, 137.048, 142.477, 152.430; HRMS: m/z calculated for [$C_{15}H_{13}N_3O$ + H^+] = 252.1137: found = 252.1142.



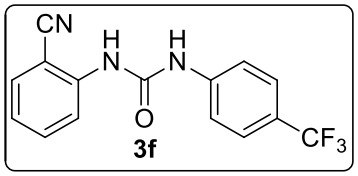
1-(4-chlorophenyl)-3-(2-cyanophenyl)urea (3d)

Yield: 223 mg, 82 %; MP. 198 °C; White solid; ^{1}H-NMR (400 MHz, DMSO-d_6): δ ppm: 7.137-7.174 (t, 1H, Ar, J = 7.2 Hz), 7.305-7.327 (d, 2H, Ar, J = 8.8 Hz), 7.458-7.480 (d, 2H, Ar, J = 8.8 Hz), 7.587-7.629 (m, 1H, Ar), 7.704-7.726 (m, 1H, Ar), 8.016-8.036 (d, 1H, Ar, J = 8 Hz), 8.725 (s, 1H, -NH-), 9.470 (s, 1H, -NH-); ^{13}C- NMR (400 MHz, DMSO-d_6): δ ppm: 102.724, 117.337, 120.353, 121.861, 123.641, 126.356, 129.177, 133.555, 134.421, 138.644, 142.166, 152.401; HRMS: m/z calculated for [$C_{14}H_{10}ClN_3O$ + H^+] = 272.0591: found = 272.0595.



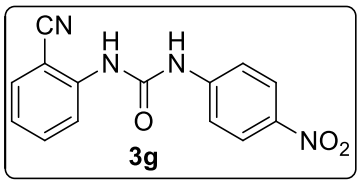
1-(2-cyanophenyl)-3-(4-fluorophenyl)urea (3e)

Yield: 200 mg, 78 %; MP. 205 °C; White solid; ^{1}H-NMR (400 MHz, DMSO-d_6): δ ppm: 7.105-7.180 (m, 3H, Ar), 7.445-7.478 (m, 2H, Ar), 7.601-7.639 (t, 1H, Ar, J = 7.6 Hz), 7.718-7.737 (d, 1H, Ar, J = 7.6 Hz), 8.034-8.055 (d, 1H, Ar, J = 8.4 Hz), 8.702 (s, 1H, -NH-), 9.388 (s, 1H, -NH-); ^{13}C- NMR (400 MHz, DMSO-d_6): δ ppm: 102.57, 115.74, 115.96, 117.36, 120.59, 120.66, 121.77, 123.50, 133.54, 134.41, 135.96, 142.32, 152.53, 156.86, 159.24; HRMS: m/z calculated for [$C_{14}H_{10}FN_3O$ + H^+] = 256.0881: found = 256.0886.



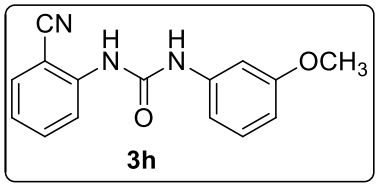
1-(2-cyanophenyl)-3-(4-(trifluoromethyl)phenyl)urea (3f)

Yield: 247 mg, 81 %; MP. 185 °C; White solid; ^{1}H-NMR (400 MHz, DMSO-d_6): δ ppm: 7.158-7.196 (t, 1H, Ar, J = 7.6 Hz), 7.303-7.321 (d, 1H, Ar, J = 7.2 Hz), 7.484-7.523 (t, 1H, Ar, J = 8 Hz), 7.552-7.573 (d, 1H, Ar, J = 8.4 Hz), 7.599-7.641 (m, 1H, Ar), 7.719-7.742 (t, 1H, Ar, J = 8.4 Hz), 7.987-8.039 (t, 2H, Ar, J = 12.4 Hz), 8.807 (s, 1H, -NH-), 9.704 (s,1H, -NH-); ^{13}C- NMR (400 MHz, DMSO-d_6): δ ppm: 103.094, 114.720, 117.308, 119.040, 122.386, 123.885, 130.471, 133.555, 134.431, 140.541, 141.961, 152.556; LCMS: m/z calculated for [$C_{15}H_{10}F_3N_3O$ + H^+] = 306.0854 : found = 306.0859.



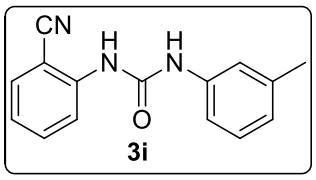
1-(2-cyanophenyl)-3-(4-nitrophenyl)urea (3g)

Yield: 226 mg, 80 %; MP. >250 °C; White solid; ^{1}H-NMR (400 MHz-DMSO-d_6): δ ppm: 7.200-7.238 (t, 1H, Ar, J = 7.6 Hz), 7.630-7.692 (m, 3H, Ar), 7.752-7.772 (d, 1H, Ar, J = 8 Hz), 7.981-8.002 (d, 1H, Ar, J = 8.4 Hz), 8.176- 8.198 (d, 2H, Ar, J = 8.8 Hz), 8.934 (s, 1H, -NH-), 10.016 (s, 1H, -NH-); ^{13}C- NMR (400 MHz, DMSO-d_6): δ ppm: 103.639, 117.220, 118.252, 122.464, 124.332, 125.607, 133.643, 134.643, 141.572, 141.913, 146.252, 152.206; HRMS: m/z calculated for [$C_{14}H_{10}N_4O_3$ + H^+] = 281.0826: found = 281.0830.



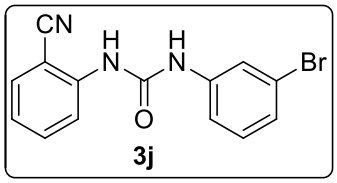
1-(2-cyanophenyl)-3-(3-methoxyphenyl)urea (3h)

Yield: 214 mg, 80 %; MP. 188 °C; White solid; ^{1}H-NMR (400 MHz, DMSO-d_6): δ ppm: 3.718 (s, 3H, -OCH_3,), 6.564-6.583 (d, 1H, Ar, J = 7.6 Hz), 6.936-6.955 (d, 1H, Ar, J = 7.6 Hz), 7.163-7.206 (t, 3H, Ar, J = 8.8 Hz), 7.604-7.643 (t, 1H, Ar, J = 8.0 Hz), 7.722-7.740 (d, 1H, Ar, J = 7.2 Hz), 8.055-8.076 (d, 1H, Ar, J = 8.4 Hz), 8.702 (s, 1H, -NH-), 9.379 (s, 1H, -NH-); ^{13}C- NMR (400 MHz, DMSO-d_6): δ ppm: 55.392, 102.384, 104.573, 108.270, 111.091, 117.376, 121.686, 123.466, 130.121, 133.555, 134.431, 140.862, 142.331, 152.381, 160.164; HRMS: m/z calculated for [$C_{15}H_{13}N_3O_2$ + H^+] = 268.1081: found = 268.1085.



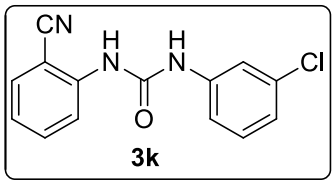
1-(2-cyanophenyl)-3-(m-tolyl)urea (3i)

Yield: 214 mg, 85 %; MP. 189 °C; White solid; ^{1}H-NMR (400 MHz, DMSO-d_6): δ ppm: 2.287 (s, 3H, -CH_3), 6.823-6.841 (d, 1H, ar, J = 7.2 Hz), 7.162-7.200 (t, 2H, Ar, J = 7.6 Hz), 7.237-7.257 (d, 1H, Ar, J = 8.0 Hz), 7.316 (s, 1H, Ar), 7.638 (s, 1H, Ar), 7.738-7.757 (d, 1H, Ar, J = 7.6 Hz), 8.080-8.101 (d, 1H, Ar, J = 8.4 Hz), 8.713 (s, 1H, -NH-), 9.316 (s, 1H, -NH-); ^{13}C- NMR (400 MHz, DMSO-d_6): δ ppm: 21.651, 102.306, 116.024, 117.396, 119.361, 121.628, 123.379, 123.544, 129.168, 133.546, 134.402, 138.527, 139.568, 142.429, 152.411; HRMS: m/z calculated for [$C_{15}H_{13}N_3O$ + H^+] = 252.1137: found = 252.1142.



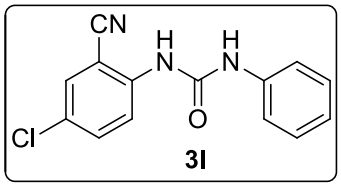
1-(3-bromophenyl)-3-(2-cyanophenyl)urea (3j)

Yield: 258 mg, 82 %; MP. 191 °C; White solid; ^{1}H-NMR (400 MHz, DMSO-d_6): δ ppm: 7.158-7.295 (m, 4H, Ar), 7.605-7.643 (t, 1H, Ar, J = 7.6 Hz), 7.724-7.743 (d, 1H, Ar, J = 7.6 Hz), 7.839 (s, 1H, Ar), 7.994-8.015 (d, 1H, Ar, J = 8.4 Hz), 8.767 (s, 1H, -NH-), 9.519 (s, 1H, -NH-); ^{13}C- NMR (400 MHz, DMSO-d_6): δ ppm: 103.016, 117.328, 117.658, 121.083, 122.056, 122.221, 123.846, 125.344, 131.269, 133.585, 134.451, 141.339, 142.020, 152.401; HRMS: m/z calculated for [$C_{14}H_{10}BrN_3O + H^+$] = 316:0080: found = 316.0085.



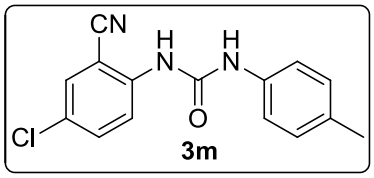
1-(3-chlorophenyl)-3-(2-cyanophenyl)urea (3k)

Yield: 228 mg, 84 %; MP. 186 °C; White solid; ^{1}H-NMR (400 MHz, DMSO-d_6): δ ppm: 7.022-7.041 (d, 1H, Ar, J = 7.6 Hz), 7.179-7.198 (d, 1H, Ar, J = 7.6 Hz), 7.232-7.252 (d, 1H, Ar, J = 8 Hz), 7.281-7.301 (d, 1H, Ar, J = 8 Hz), 7.694 (s, 1H, Ar), 7.724-7.744 (d, 1H, Ar, J = 8 Hz), 7.996-8.018 (d, 1H, Ar, J = 8.8 Hz), 8.771 (s, 1H, -NH-), 9.531 (s, 1H, -NH-); ^{13}C- NMR (400 MHz, DMSO-d_6): δ ppm: 102.996, 117.240, 117.337, 118.174, 122.046, 122.426, 123.836, 130.968, 133.595, 133.702, 134.461, 141.203, 142.010, 152.411; HRMS: m/z calculated for [$C_{14}H_{10}ClN_3O + H^+$] = 272.0591: found = 272.0595.



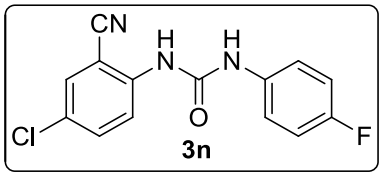
1-(4-chloro-2-cyanophenyl)-3-phenylurea (3l)

Yield: 217 mg, 80 %; MP. 204 °C; White solid; ^{1}H-NMR (400 MHz, DMSO-d_6): δ ppm: 6.968-7.004 (t, 1H, Ar, J = 7.2 Hz), 7.257-7.297 (t, 2H, Ar, J = 8.4 Hz), 7.423-7.442 (d, 1H, Ar, J = 7.6 Hz), 7.660-7.690 (m, 1H, Ar), 7.897-7.903 (d, 1H, Ar, J = 2.4 Hz), 8.085-8.108 (d, 1H, Ar, J = 9.2 Hz), 8.798 (s, 1H, -NH-), 9.406 (s, 1H, -NH); ^{13}C- NMR (400 MHz, DMSO-d_6): δ ppm: 103.726, 116.121, 118.903, 122.951, 123.126, 126.716, 129.343, 132.602, 134.470, 139.461, 141.562, 152.274; HRMS: m/z calculated for [$C_{14}H_{10}ClN_3O + H^+$] = 272.0591: found = 272.0593.



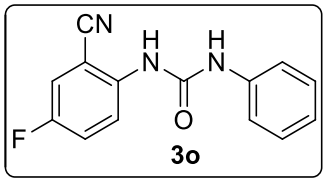
1-(4-chloro-2-cyanophenyl)-3-(p-tolyl)urea (3m)

Yield: 222 mg, 78 %; MP.195 °C; White solid; ^{1}H-NMR (400 MHz, DMSO-d_6): δ ppm: 2.220 (s, 3H, -CH_3-), 7.070-7.091 (d, 2H, Ar, J = 8.4 Hz), 7.302-7.322 (d, 2H, Ar, J = 8 Hz), 7.646-7.674 (m, 1H, Ar), 7.873-7.879 (d, 1H, Ar, J = 2.4 Hz), 8.081-8.104 (d, 1H, Ar, J = 9.2 Hz), 8.727 (s, 1H, -NH-), 9.283 (s, 1H, -NH-); ^{13}C- NMR (400 MHz, DMSO-d_6): δ ppm: 103.580, 116.131, 119.010, 123.048, 126.589, 129.722, 131.872, 132.563, 134.441, 136.863, 141.660, 152.264; HRMS: m/z calculated for [$C_{15}H_{12}ClN_3O$ + H^+] = 286.0742: found = 286.0743.



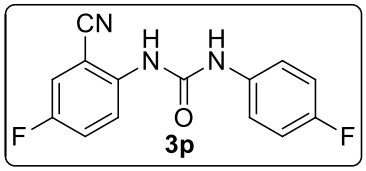
1-(4-chloro-2-cyanophenyl)-3-(4-fluorophenyl)urea (3n)

Yield: 225 mg, 78 %; MP. 196 °C; White solid; ^{1}H-NMR (400 MHz, DMSO-d_6): δ ppm: 7.094-7.139 (t, 2H, Ar, J = 9.2 Hz), 7.425-7.460 (m, 2H, Ar), 7.659-7.688 (m, 1H, Ar), 7.890-7.896 (d, 1H, Ar, J = 2.4 Hz), 8.057-8.079 (d, 1H, Ar, J = 8.8 Hz), 8.763 (s, 1H, -NH-), 9.405 (s, 1H, -NH-); ^{13}C- NMR (400 MHz, DMSO-d_6): δ ppm: 103.862, 115.771, 115.995, 116.121, 120.674, 120.752, 123.184, 126.794, 132.602, 134.461, 135.784, 141.524, 152.372, 156.945, 159.319; HRMS: m/z calculated for [$C_{14}H_9ClFN_3O$ + H^+] = 290.0496: found = 290.0507.



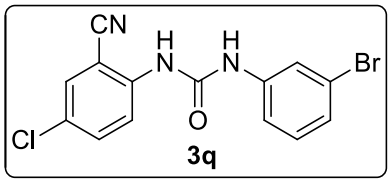
1-(2-cyano-4-fluorophenyl)-3-phenylurea (3o)

Yield: 199 mg, 78 %; MP. 191 °C; White solid; ^{1}H-NMR (400 MHz, DMSO-d_6): δ ppm: 6.963-6.999 (t, 2H, ar, J = 7.2 Hz), 7.259-7.297 (t, 2H, Ar, J = 7.6 Hz), 7.445-7.465 (d, 2H, Ar, J = 8.0 Hz), 7.518-7.560 (m, 1H, Ar), 7.735-7.755 (t, 1H, Ar, J = 2.4 Hz), 7.944-7.979 (m, 1H, Ar), 8.932 (s, 1H, -NH-), 9.452 (s, 1H, -NH-) ; ^{13}C-NMR (400 MHz, DMSO-d_6): δ ppm: 104.242, 104.339, 116.287, 118.874, 119.468, 119.731, 121.832, 122.056, 122.805, 124.478, 124.566, 129.314, 139.170, 139.637; HRMS: m/z calculated for [$C_{14}H_{10}FN_3O$ + H^+] = 256.0881: found = 256.0885.



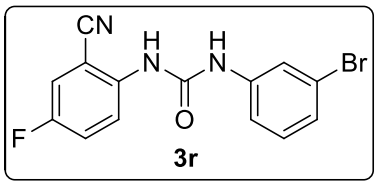
1-(2-cyano-4-fluorophenyl)-3-(4-fluorophenyl)urea (3p)

Yield: 207 mg, 76 %; MP. 208 °C; White solid; ^{1}H-NMR (400 MHz, DMSO-d_6): δ ppm: 7.124-7.168 (t, 2H, Ar, J = 8.8 Hz), 7.459-7.494 (m, 2H, Ar), 7.534-7.585 (m, 1H, Ar), 7.761-7.789 (m, 1H, Ar), 7.977-8.013 (m, 1H, Ar), 8.742 (s, 1H, -NH-), 9.345 (s, 1H, -NH-); ^{13}C- NMR (400 MHz, DMSO-d_6): δ ppm: 104.602, 104.699, 115.703, 115.917, 116.287, 119.458, 119.721, 120.538, 120.616, 121.774, 121.998, 124.683, 124.761, 136.017, 139.092, 139.072, 152.751, 156.127, 156.847, 158.531, 159.221; HRMS: m/z calculated for [$C_{14}H_9F_2N_3O$ + H^+] = 274.0786: found = 274.0786.



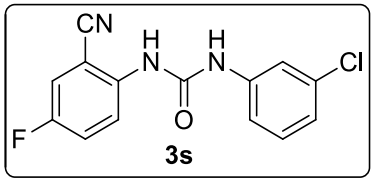
1-(3-bromophenyl)-3-(4-chloro-2-cyanophenyl)urea (3q)

Yield: 279 mg, 80 %; MP. 183 °C; White solid; ^{1}H-NMR (400 MHz, DMSO-d_6): δ ppm: 7.165-7.180 (d, 1H, Ar, J = 6.0 Hz), 7.224-7.262 (t, 1H, Ar, J = 7.6 Hz), 7.313 (s, 1H, Ar), 7.685-7.705 (d, 1H, Ar, J = 8.0 Hz), 7.844 (s, 1H, Ar), 7.919 (s, 1H, Ar), 7.987-8.008 (d, 1H, Ar, J = 8.4 Hz), 9.160 (s, 1H, -NH-), 9.808 (s, 1H, -NH-); ^{13}C-NMR (400 MHz, DMSO-d_6): δ ppm: 104.320, 116.063, 117.736, 121.180, 122.212, 123.486, 125.490, 127.154, 131.269, 132.641, 134.470, 141.174, 141.213, 152.236; HRMS: m/z calculated for [$C_{14}H_9BrClN_3O$ + H^+] = 349.9690: found = 349.9681.



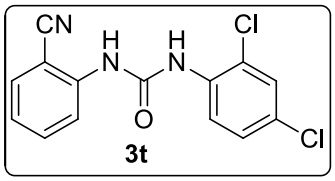
1-(3-bromophenyl)-3-(2-cyano-4-fluorophenyl)urea (3r)

Yield: 256mg, 77 %; MP. 182 °C; White solid; ^{1}H-NMR (400 MHz, DMSO-d_6): δ ppm: 7.157-7.175 (d, 1H, Ar, J = 7.2 Hz), 7.220-7.307 (m, 2H, Ar), 7.525-7.562 (t, 1H, Ar, J = 8.0 Hz), 7.756-7.770 (d, 1H, Ar, J = 5.6 Hz), 7.840 (s, 1H, Ar), 7.935-7.969 (m, 1H, Ar), 8.797 (s, 1H, -NH-), 9.475 (s, 1H, -NH-); ^{13}C- NMR (400 MHz, DMSO-d_6): δ ppm: 104.971, 105.069, 116.248, 117.688, 119.565, 119.828, 121.122, 121.842, 122.066, 122.202, 124.926, 125.004, 125.344, 131.250, 138.780, 141.359, 152.576, 156.312, 158.725; HRMS: m/z calculated for [$C_{14}H_9BrFN_3O$ + H^+] = 333.9991: found = 333.9997.



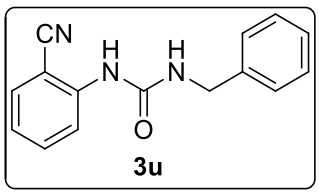
1-(3-chlorophenyl)-3-(2-cyano-4-fluorophenyl)urea (3s)

Yield: 234 mg, 81 %; MP. 198 °C; White solid; ^{1}H-NMR (400 MHz, DMSO-d_6): δ ppm: 7.050-7.069 (d, 1H, Ar, J = 7.6 Hz), 7.257-7.349 (m, 2H, Ar), 7.547-7.589 (m, 1H, Ar), 7.710 (s, 1H, Ar), 7.759-7.780 (d, 1H, Ar, J = 8.4 Hz), 7.962-7.997 (m, 1H, Ar), 8.785 (s, 1H, -NH-), 9.474 (s, 1H, -NH-); ^{13}C- NMR (400 MHz, DMSO-d_6): δ ppm: 104.95, 105.05, 116.23, 117.67, 119.55, 119.81, 121.10, 121.82, 122.04, 122.18, 124.91, 124.99, 125.32, 131.22, 138.76, 141.33, 152.55, 156.29, 158.71; HRMS: m/z calculated for [$C_{14}H_9ClFN_3O$ + H^+] = 290.0496: found = 290.0502.



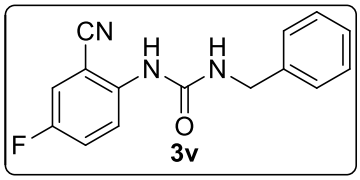
1-(2-cyanophenyl)-3-(2,4-dichlorophenyl)urea (3t)

Yield: 279 mg, 75 %; MP. 184 °C; White solid; ^{1}H-NMR (400 MHz, DMSO-d_6): δ ppm: 7.212 (s, 1H, Ar), 7.383-7.400 (d, 1H, Ar, J = 6.8 Hz), 7.631 (s, 2H, Ar), 7.759 (s, 1H, Ar), 7.986-8.002 (d, 1H, Ar, J = 6.0 Hz), 8.097-8.116 (d, 1H, Ar, J = 7.6 Hz), 9.039 (s, 1H, -NH-), 9.518 (s, 1H, -NH-); ^{13}C- NMR (400 MHz, DMSO-d_6): δ ppm:103.321, 117.554, 122.798, 123.771, 124.112, 124.229, 127.498, 128.218, 129.278, 133.880, 134.561, 135.378, 141.926, 152.541; HRMS: m/z calculated for [$C_{14}H_9Cl_2N_3O$ + H^+] = 306.0201: found = 306.0208.



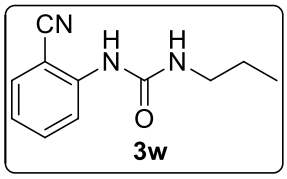
1-benzyl-3-(2-cyanophenyl)urea (3u)

Yield: 188 mg, 75 %; MP. 208 °C; White solid; ^{1}H-NMR (400 MHz, DMSO-d_6): δ ppm: 4.304-4.317 (d, 2H, -CH_2-, J = 5.6 Hz), 7.074-7.111 (t, 1H, Ar, J = 7.2 Hz), 7.111-7.360 (m, 5H, Ar), 7.412-7.426 (d, 1H, Ar, J = 5.6 Hz), 7.553-7.590 (t, 1H, Ar, J = 7.6 Hz), 7.666-7.683 (d, 1H, Ar, J = 6.8 Hz), 8.055-8.077 (d, 1H, -NH-, 8.8 Hz), 8.569 (s, 1H, -NH-); ^{13}C- NMR (400 MHz, DMSO-d_6): δ ppm: 43.286, 101.537, 117.464, 121.190, 122.717, 127.349, 127.728, 128.827, 133.429, 134.305, 140.084, 143.139, 154.979; HRMS: m/z calculated for [$C_{15}H_{13}N_3O$ + H^+] = 252.1136: found = 252.1139.



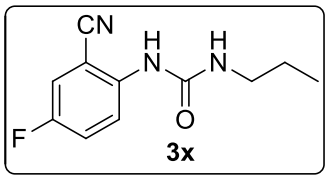
1-benzyl-3-(2-cyano-4-fluorophenyl)urea (3v)

Yield: 204 mg, 76 %; MP. 210 °C; White solid; ^{1}H-NMR (400 MHz, DMSO-d_6): δ ppm: 4.315-4.329 (d, 2H, -CH_2-, J = 5.6 Hz), 7.244-7.404 (m, 6H, Ar), 7.473-7.525 (m, 1H, Ar), 7.681-7.708 (m, 1H, Ar), 7.997-8.034 (m, 1H, -NH-), 8.609 (s, 1H, -NH-); ^{13}C- NMR (400 MHz, DMSO-d_6): δ ppm: 48.024, 107.830, 120.993, 123.815, 124.077, 126.344, 126.568, 128.514, 128.582, 131.939, 132.308, 133.418, 144.557, 144.713, 159.745, 160.212, 162.615; HRMS: m/z calculated for [$C_{15}H_{12}FN_3O$ + H^+] = 270.1037: found = 270.1039.



1-(2-cyanophenyl)-3-propylurea (3w)

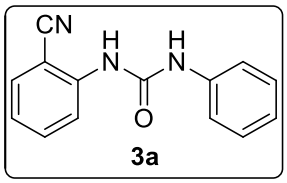
Yield: 154 mg, 76 %; MP. 199 °C; White solid; ^{1}H-NMR (400 MHz, DMSO-d_6): δ ppm: 0.853-0.888 (t, 3H, -CH_3, J = 7.2 Hz), 1.412-1.462 (m, 2H, -CH_2-), 3.037-3.051 (d, 2H, -CH_2-, J = 5.6 Hz), 6.968 (s, 1H, Ar), 7.041-7.076 (t, 1H, Ar, J = 6.8 Hz), 7.525-7.562 (t, 1H, Ar, J = 7.6 Hz), 7.637-7.655 (d, 1H, Ar, J = 7.2 Hz), 8.039-8.059 (d, 1H, -NH-, J = 8.0 Hz), 8.412 (s, 1H, -NH-); ^{13}C- NMR (400 MHz, DMSO-d_6): δ ppm: 11.805, 23.149, 41.401, 101.216, 117.503, 121.005, 122.474, 133.390, 134.266, 143.324, 154.911; HRMS: m/z calculated for [$C_{11}H_{13}N_3O$ + H^+] = 204.1131: found = 204.1136.



1-(2-cyano-4-fluorophenyl)-3-propylurea (3x)

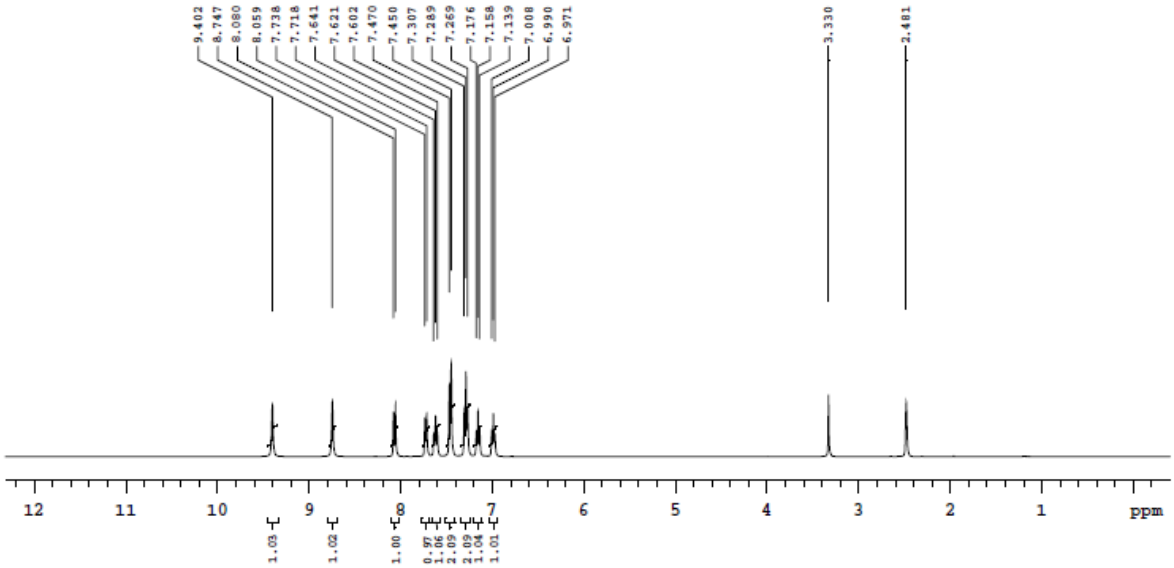
Yield: 164 mg, 74 %; MP. 204 °C; White solid; ^{1}H-NMR (400 MHz, DMSO-d_6): δ ppm: 0.863-0.900 (t, 3H, -CH_3, J = 7.6 Hz), 1.423-1.476 (m, 2H, -CH_2-), 3.032-3.079 (m, 2H, -CH_2-), 6.913 (s, 1H, Ar), 7.478-7.499 (t, 1H, Ar, J = 2.4 Hz), 7.665-7.692 (m, 1H, Ar), 7.987-8.022 (m, 1H, -NH-), 8.465 (s, 1H, -NH-); ^{13}C- NMR (400 MHz, DMSO-d_6): δ ppm: 16.395, 27.787, 46.059, 107.392, 121.042, 123.776, 124.029, 126.354, 126.578, 128.271, 144.762, 159.628, 160.046, 162.430; HRMS: m/z calculated for [$C_{11}H_{12}FN_3O$ + H^+] = 222.1042: found = 222.1047.

4. ^{1}H-NMR, ^{13}C-NMR and Mass Spectra

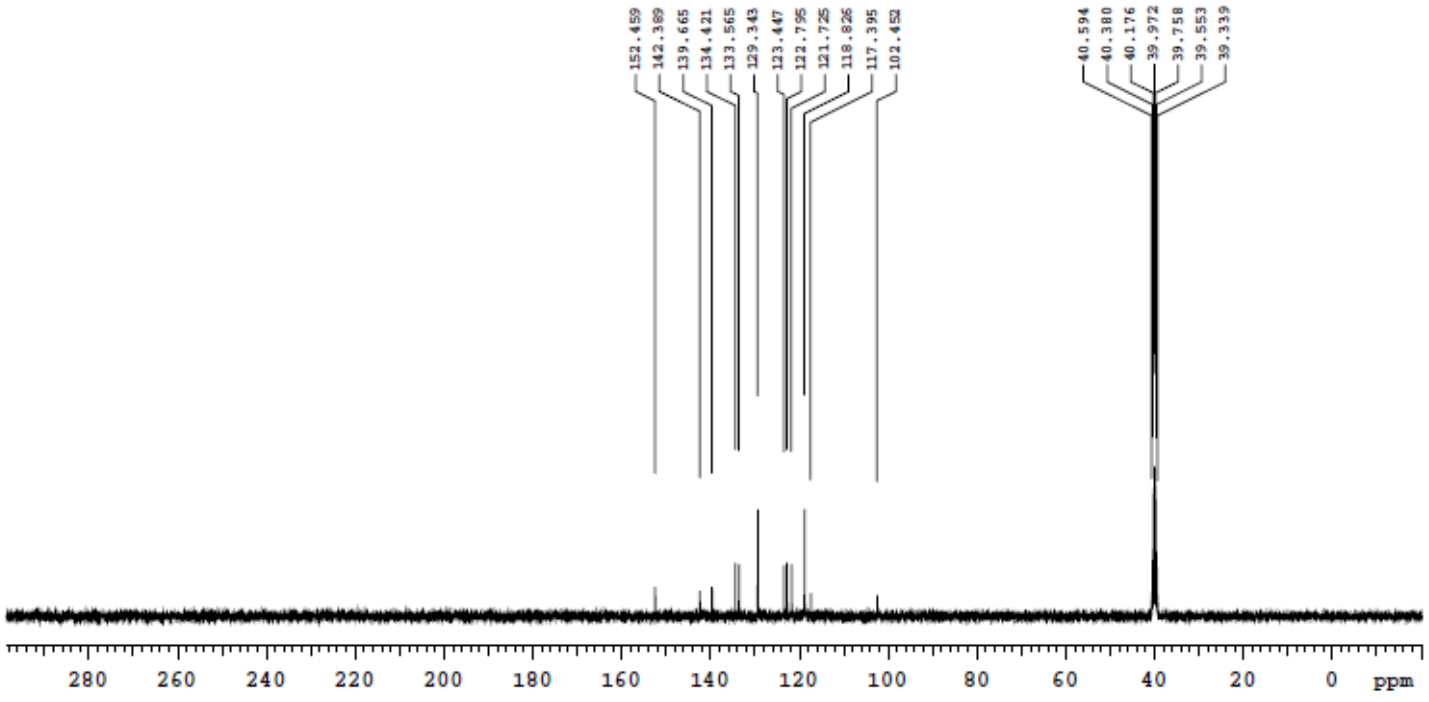


3a

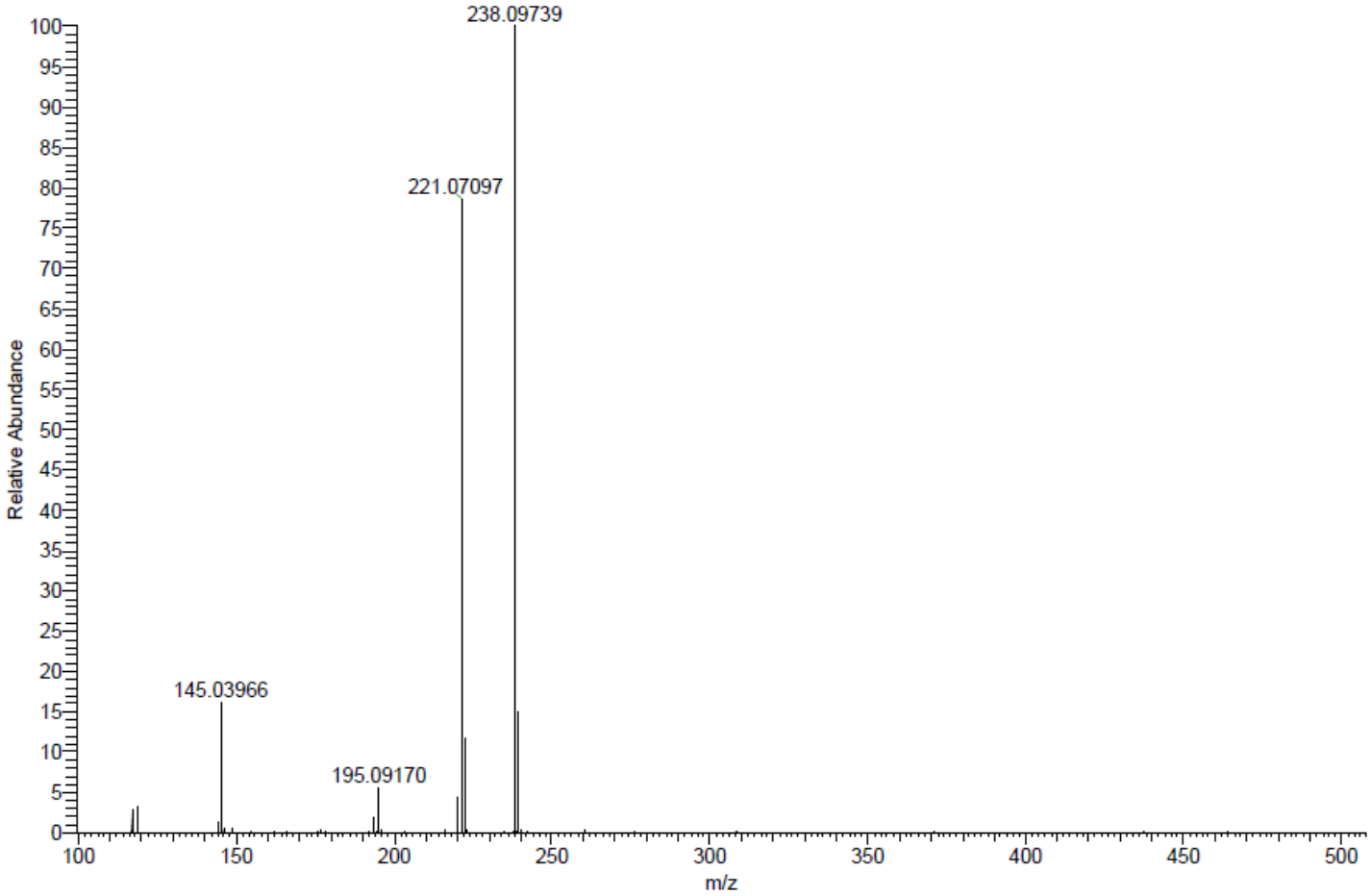
^{1}H-NMR of 3a:



^{13}C-NMR of 3a:



HRMS of 3a:


238.09739
221.07097
145.03966
195.09170
Relative Abundance
m/z
100
95
90
85
80
75
70
65
60
55
50
45
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35
30
25
20
15
10
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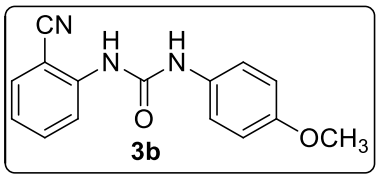
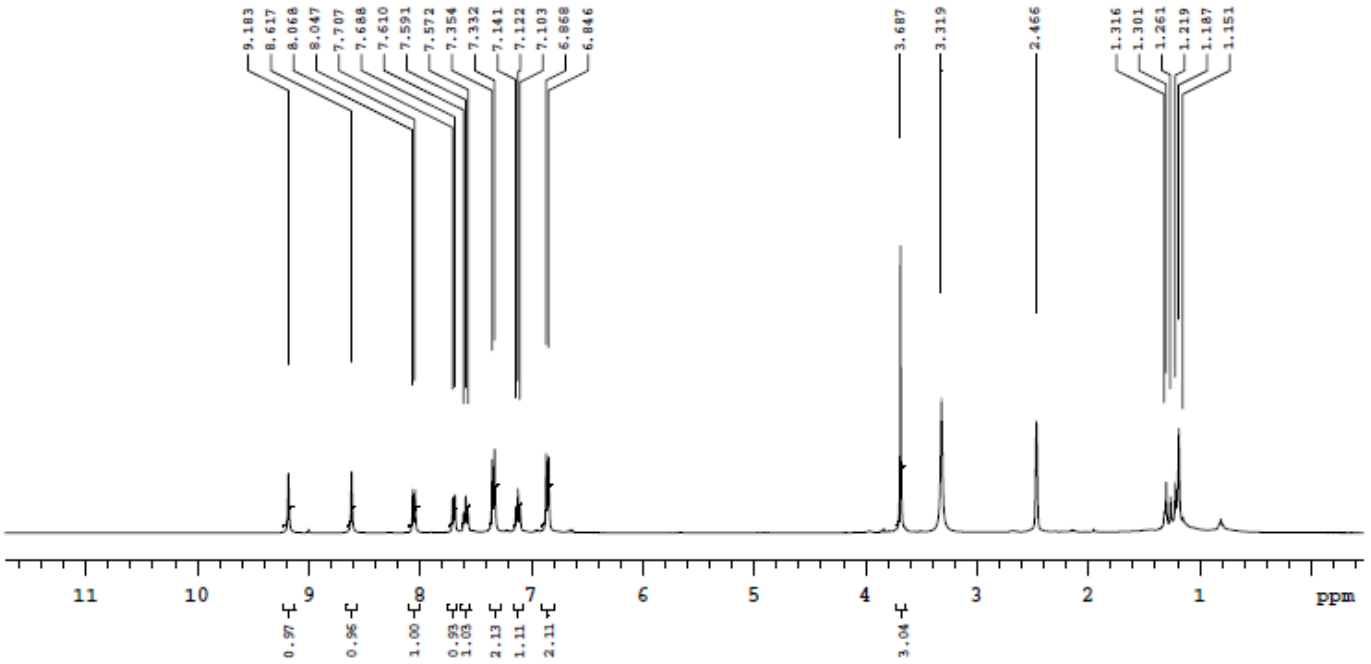
0
100
150
200
250
300
350
400
450
500

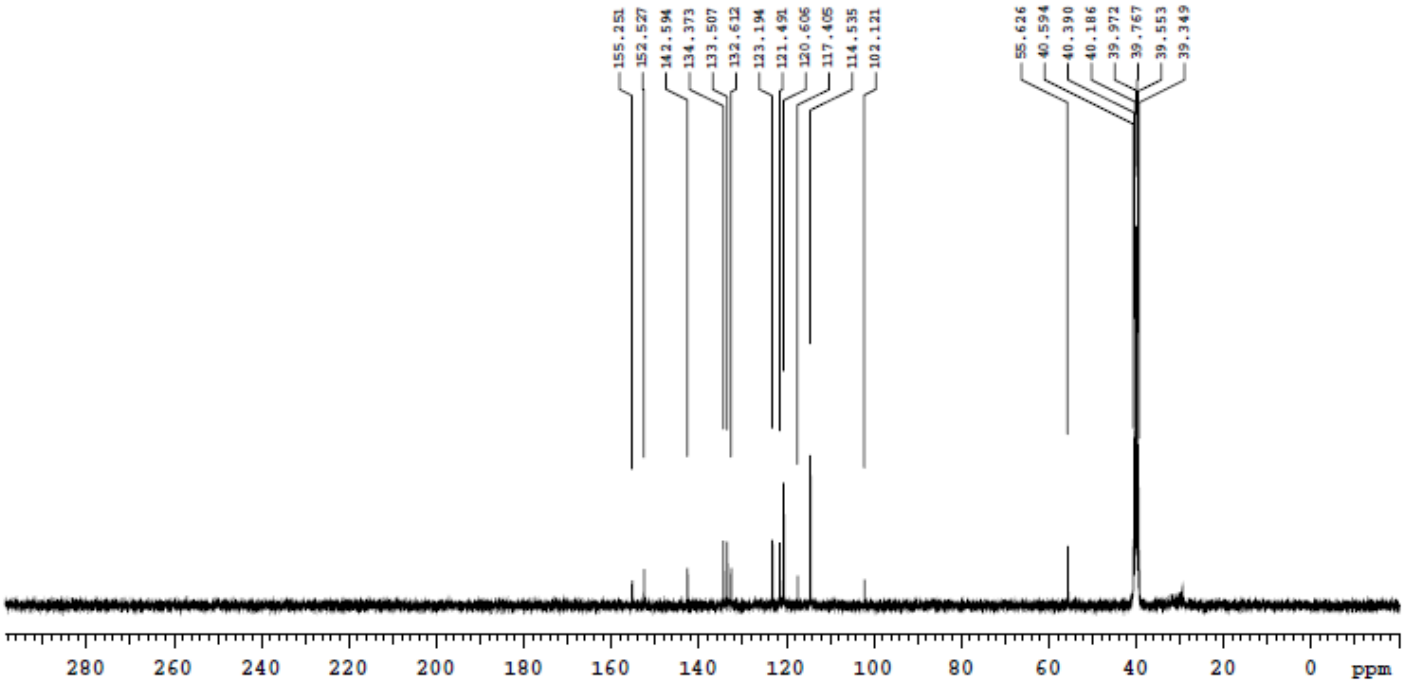


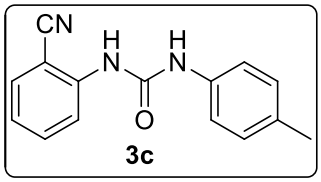
3b

[1]H-NMR of 3b:

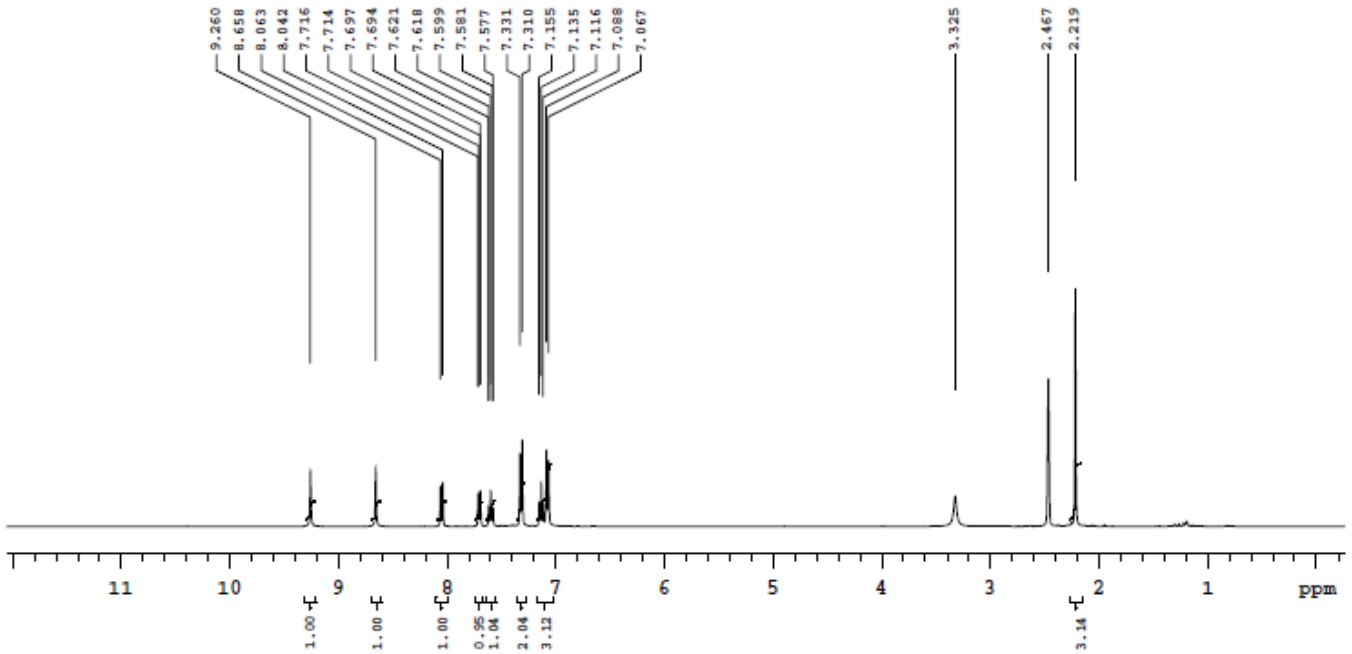


[13]C-NMR of 3b:

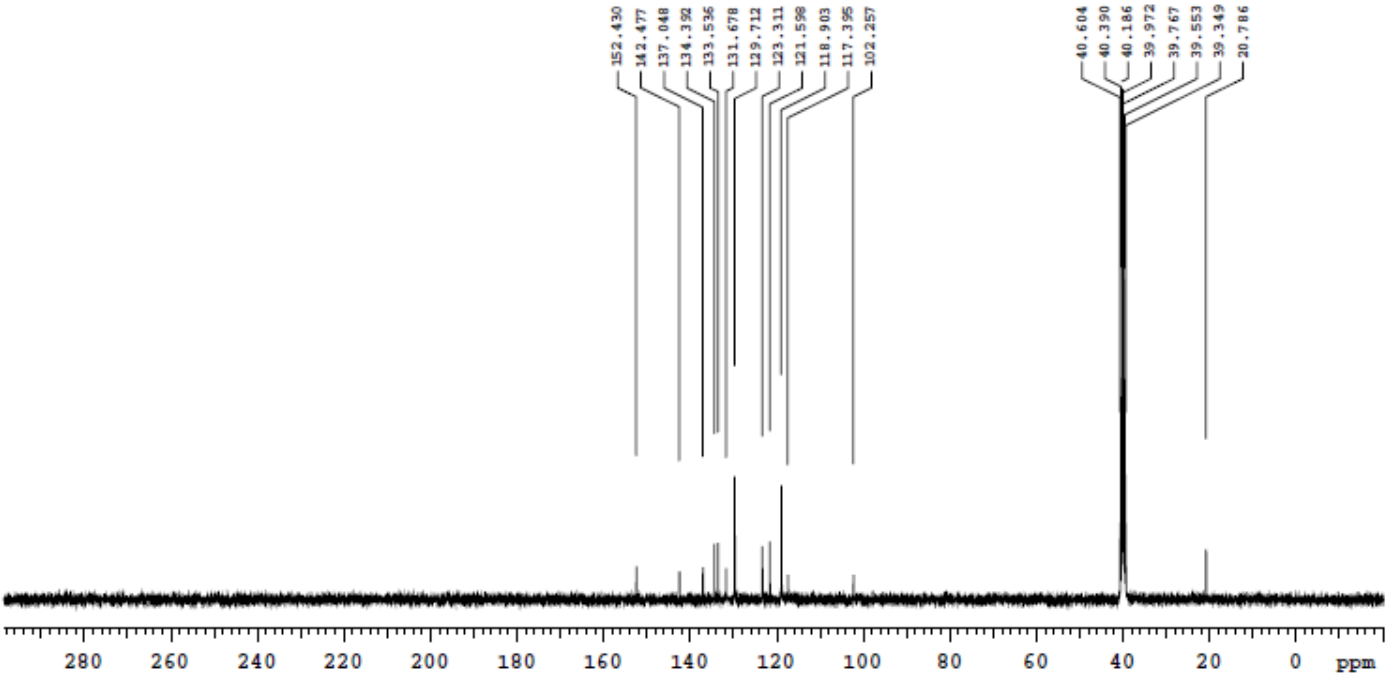




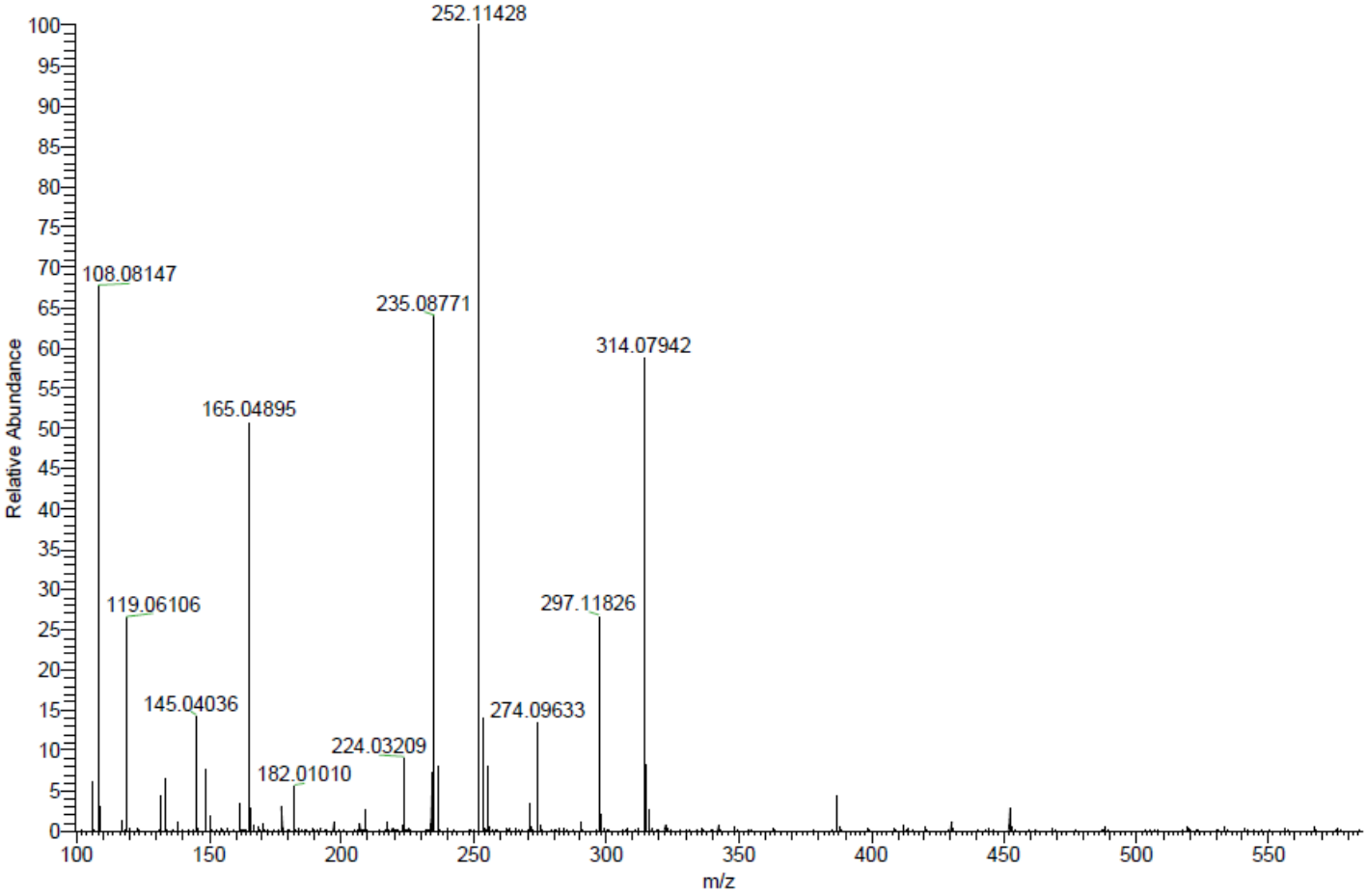
[1]H-NMR of 3c:



[13]C-NMR of 3c:



HRMS of 3c:


252.11428
108.08147
235.08771
314.07942
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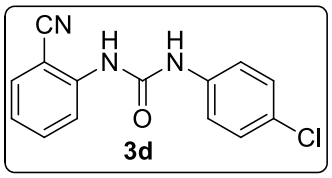
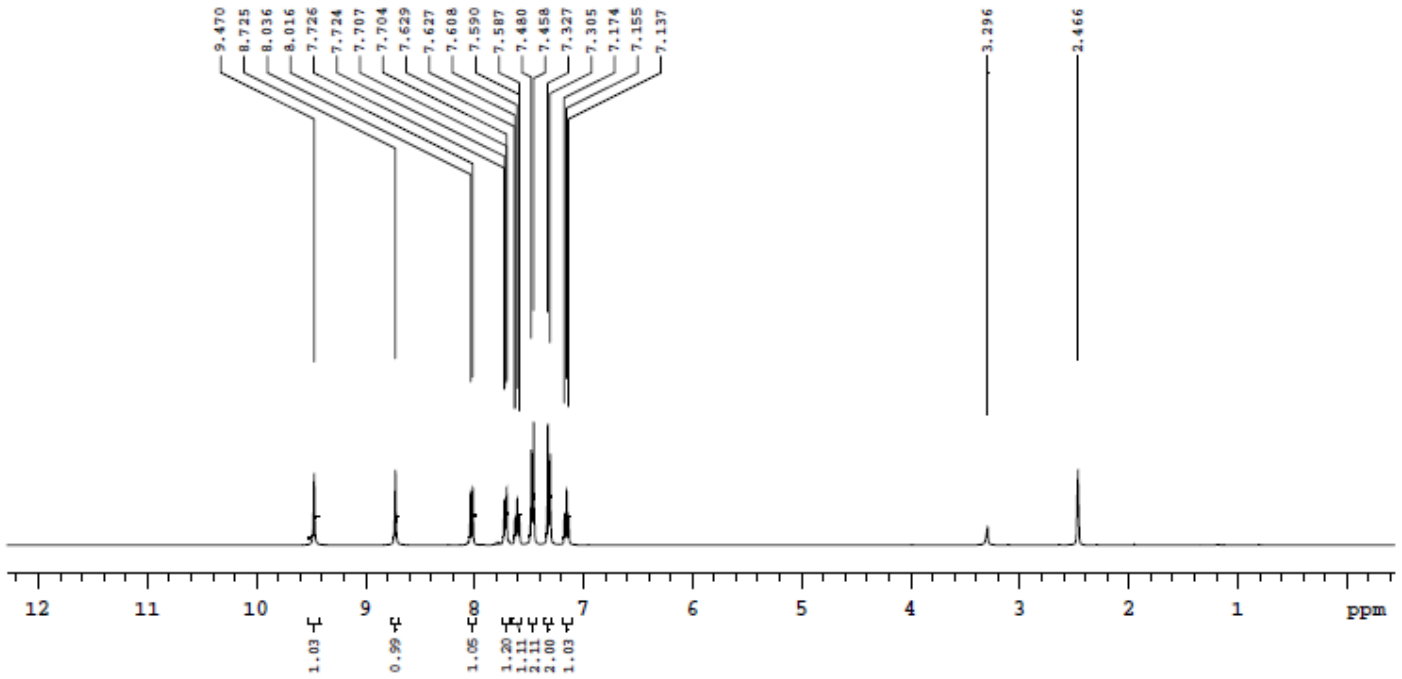
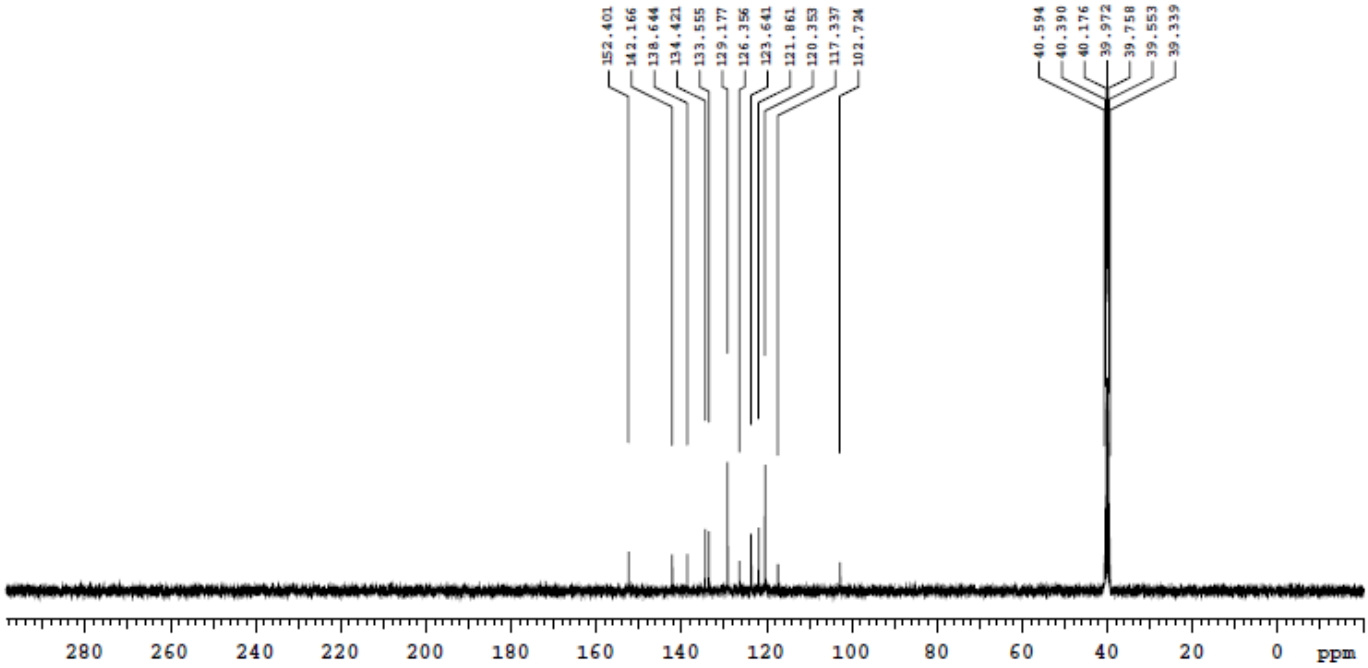
119.06106
297.11826
145.04036
274.09633
224.03209
182.01010
Relative Abundance
m/z



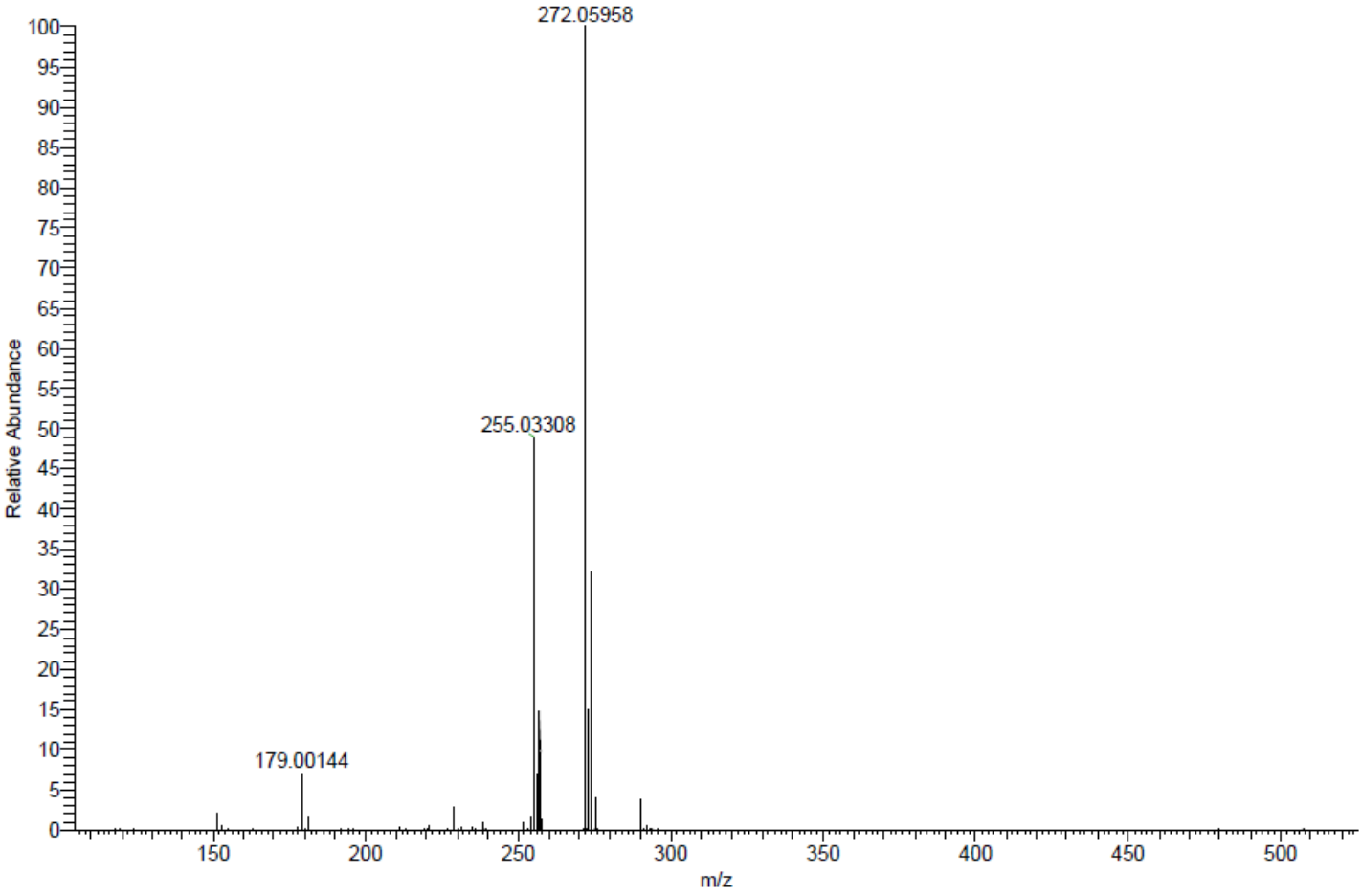
[1]H-NMR of 3d:



[13]C-NMR of 3d:



HRMS of 3d:


272.05958
255.03308
179.00144
Relative Abundance
m/z
100
95
90
85
80
75
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65
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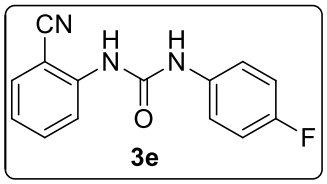
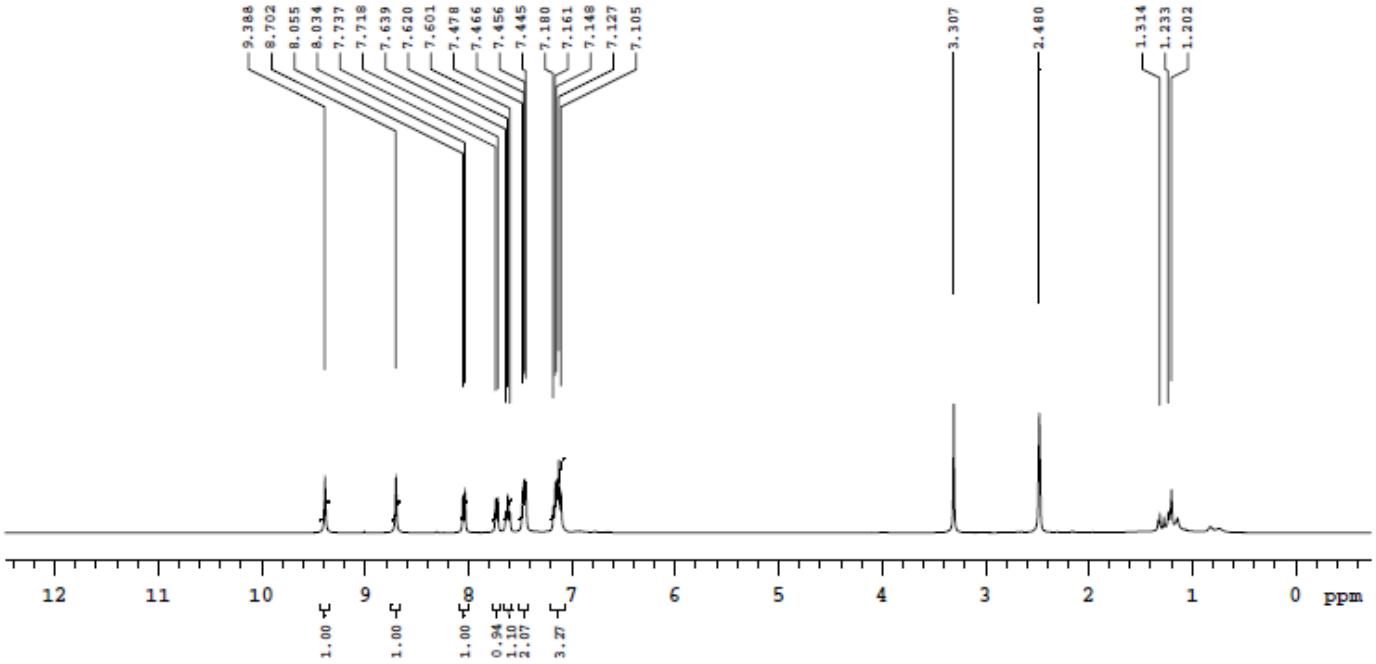
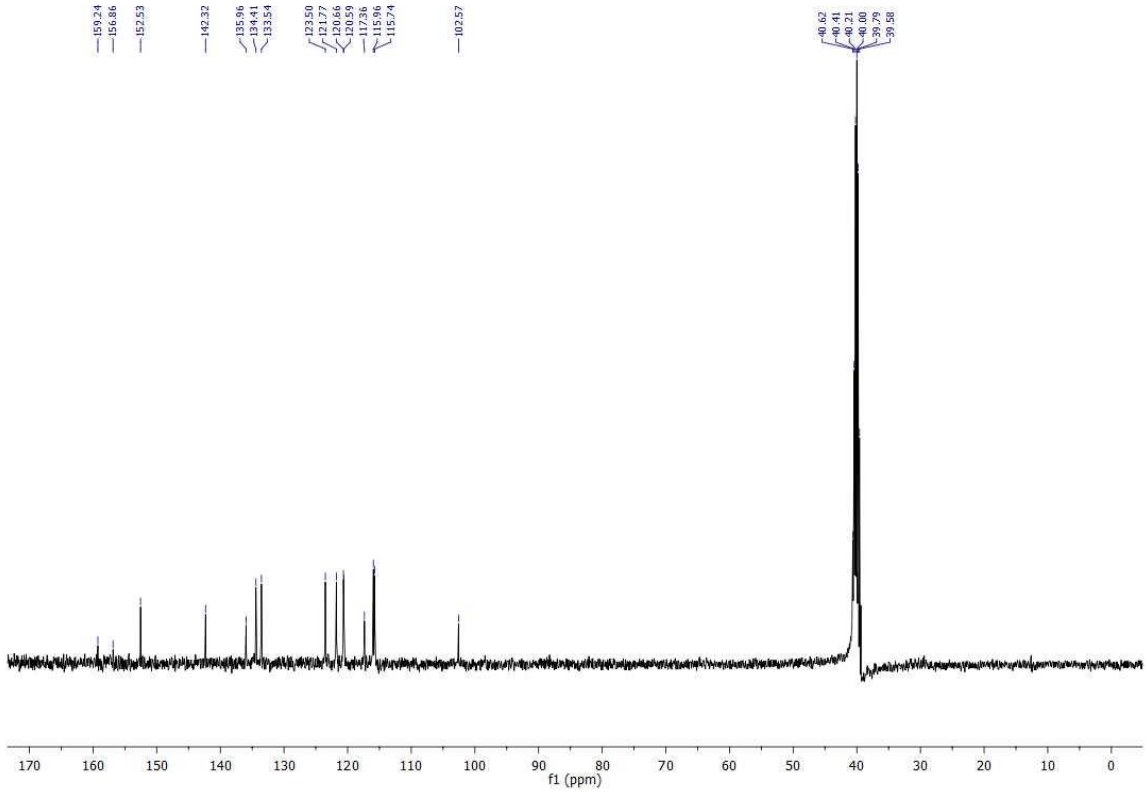
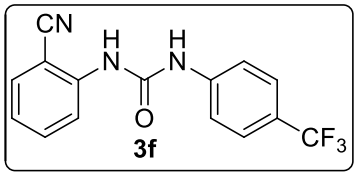


[1]H-NMR of 3e:

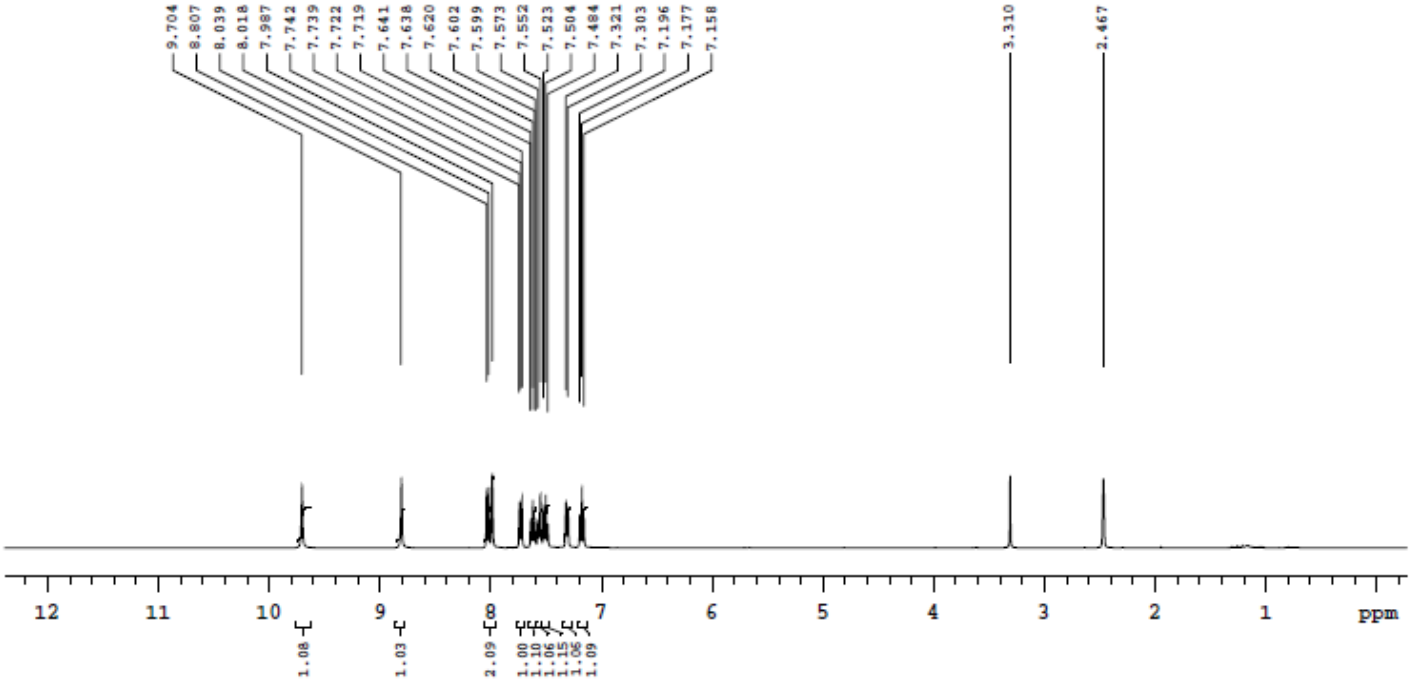


[13]C-NMR of 3e:

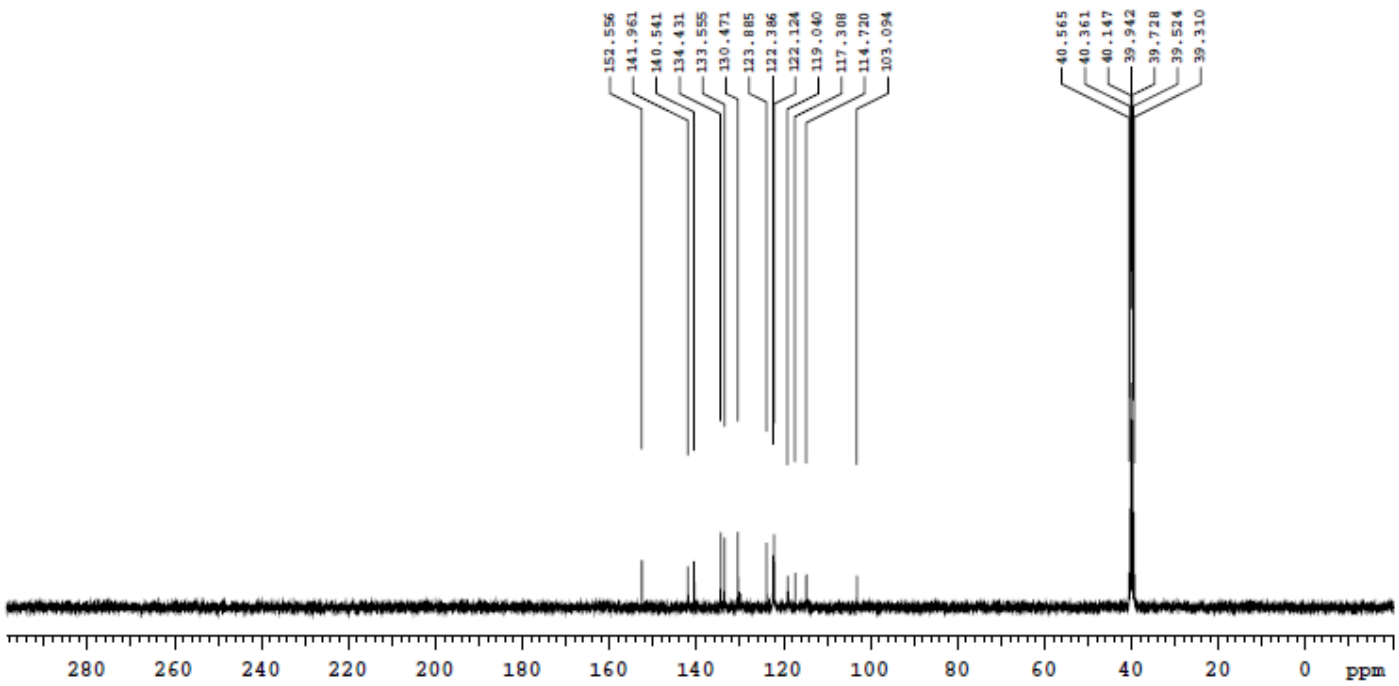




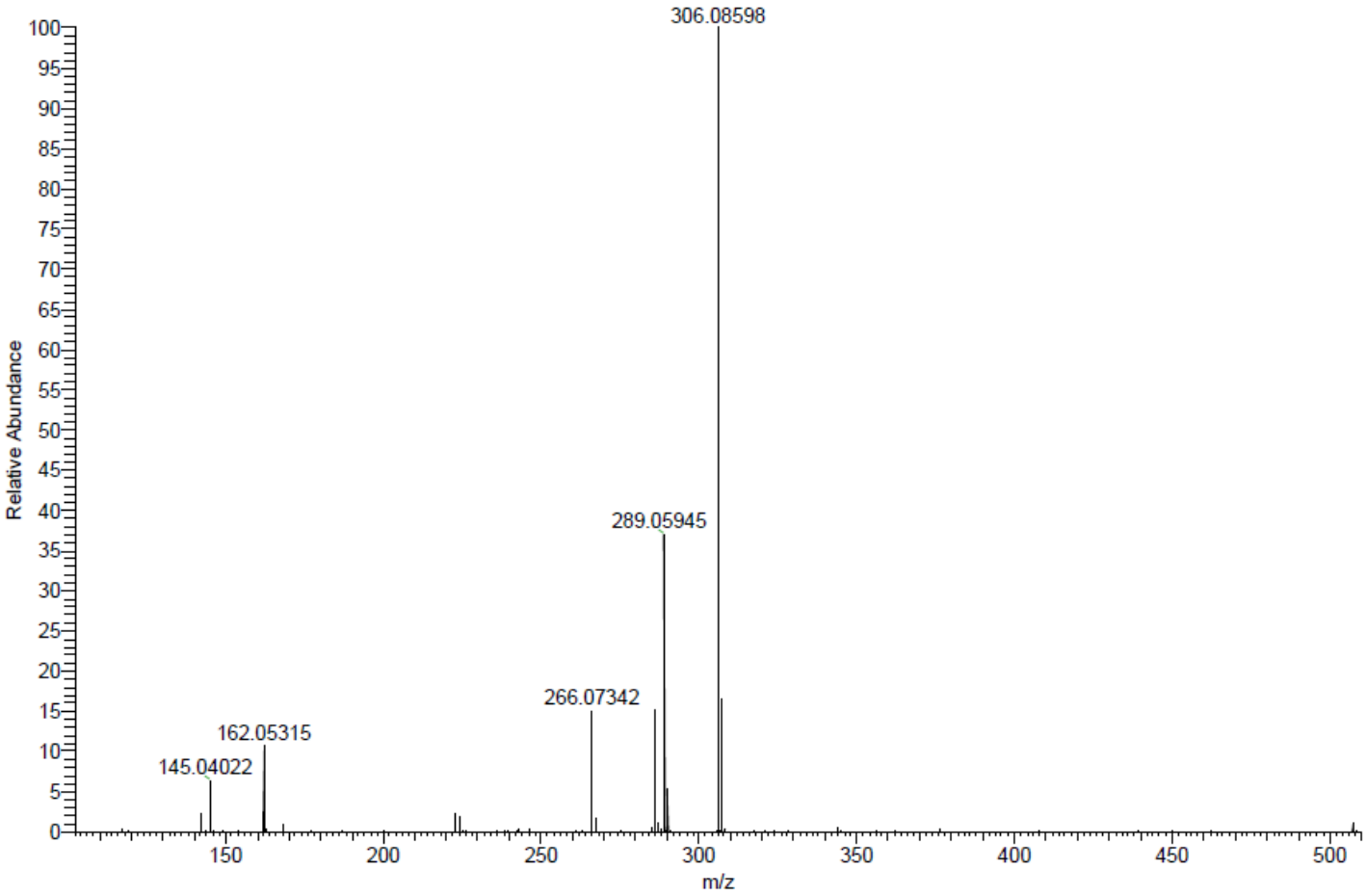
[1]H-NMR of 3f:



[13]C-NMR of 3f:



HRMS of 3f:


306.08598
289.05945
266.07342
162.05315
145.04022
Relative Abundance
m/z
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95
90
85
80
75
70
65
60
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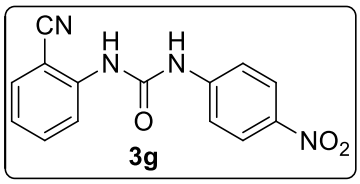
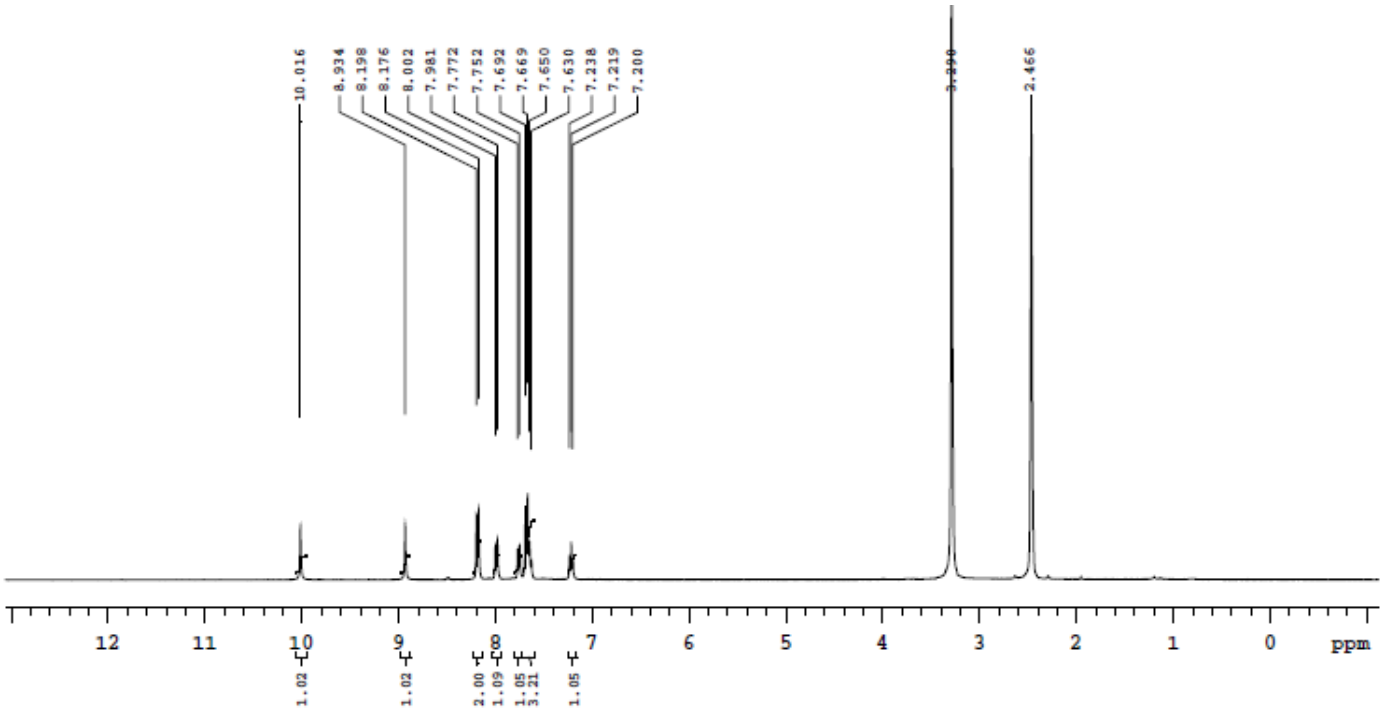
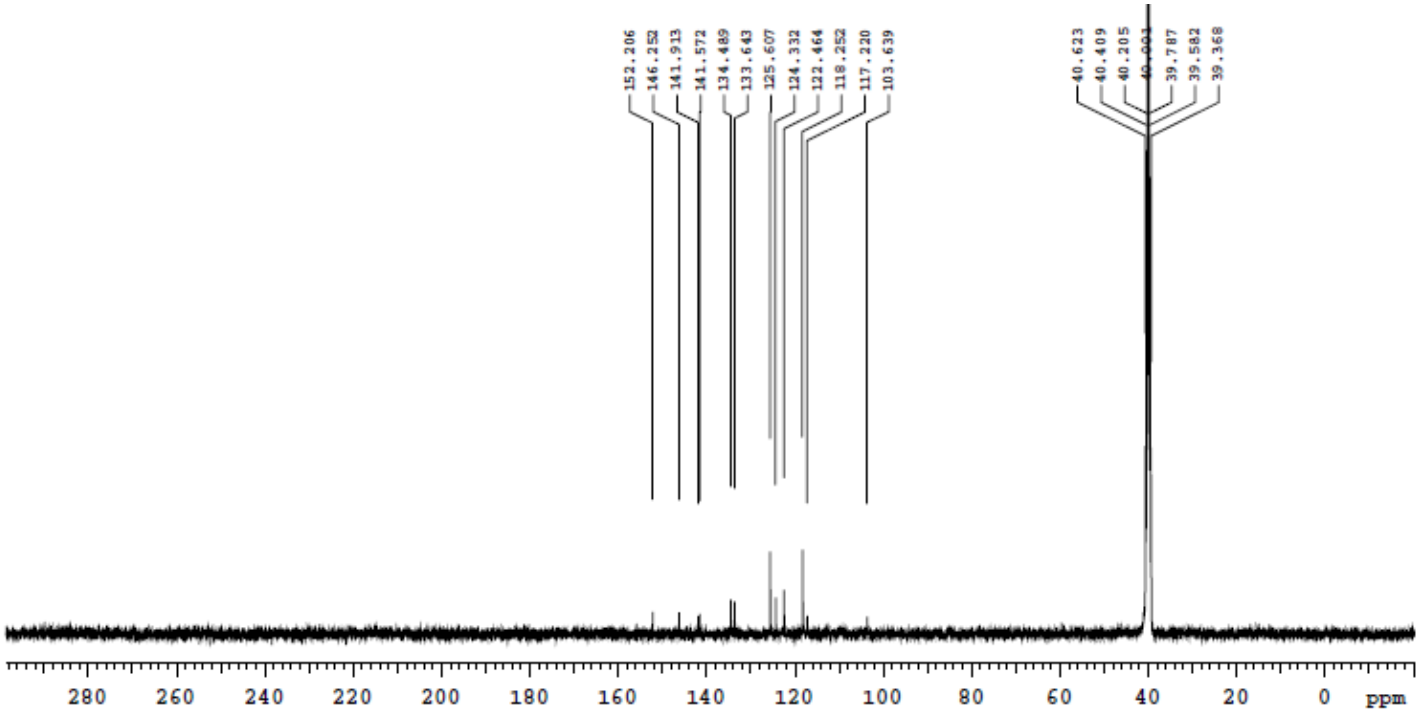
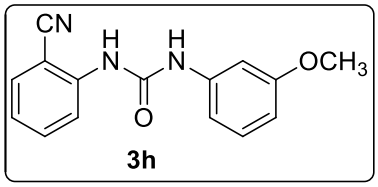


[1]H-NMR of 3g:



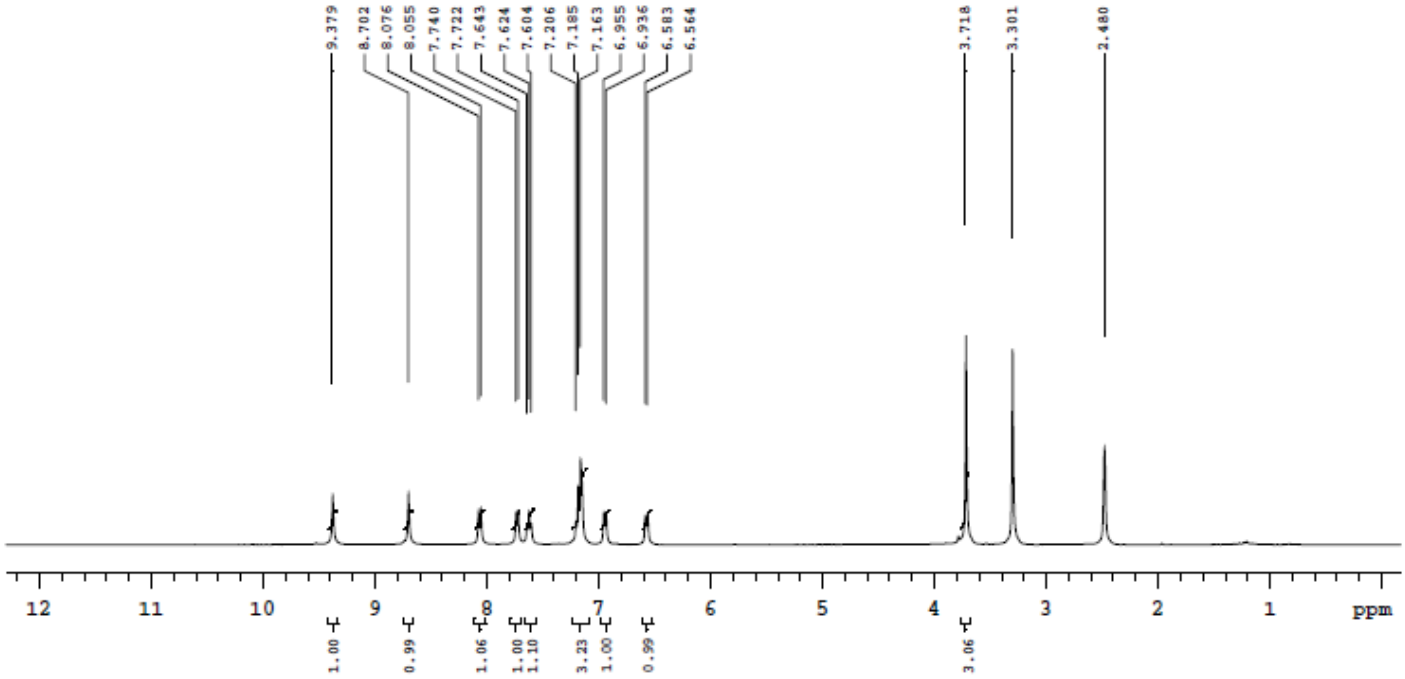
[13]C-NMR of 3g:



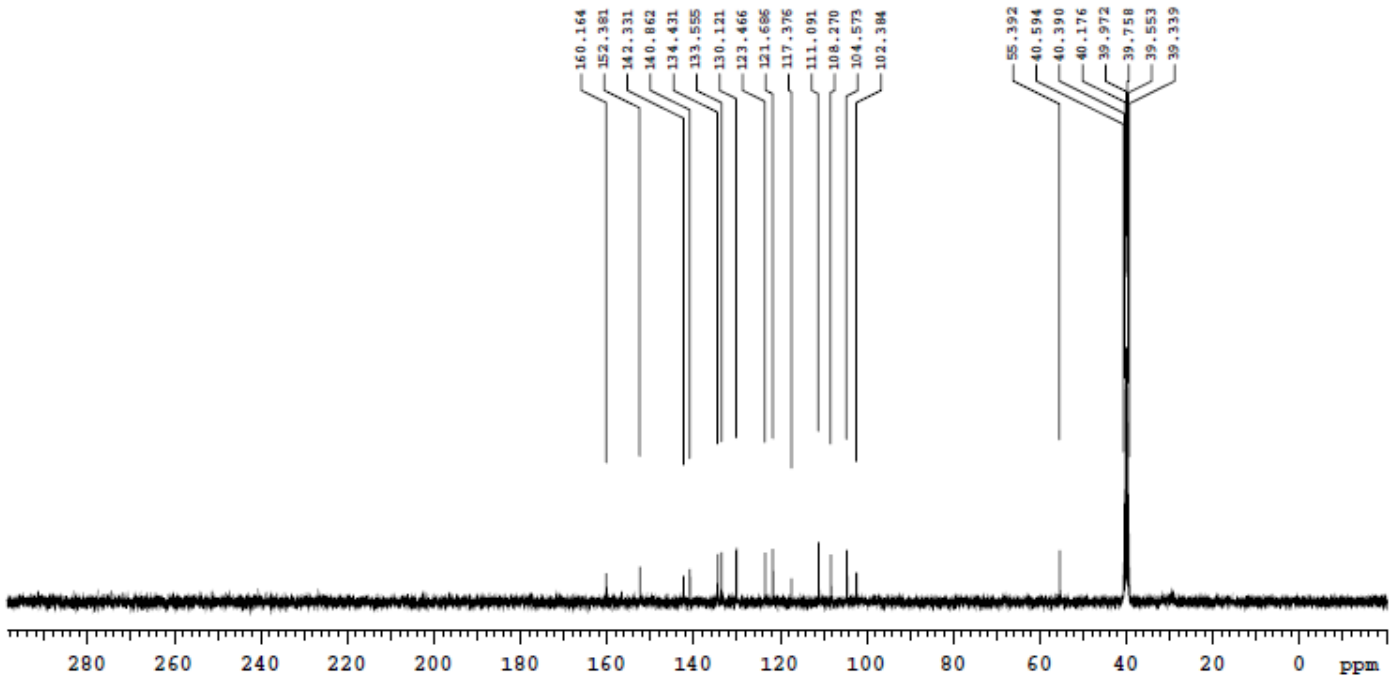


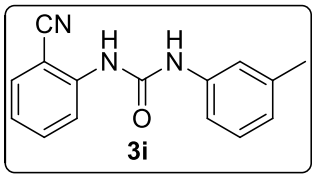
3h

[1]H-NMR of 3h:



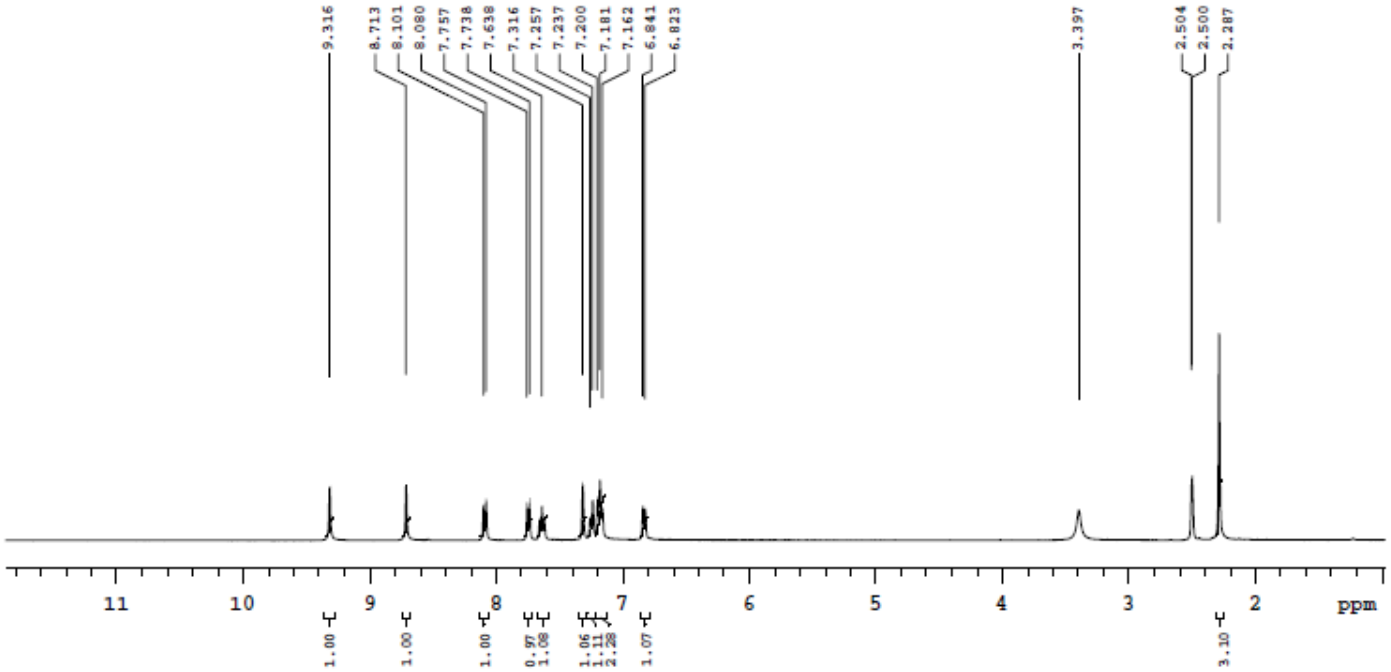
[13]C-NMR of 3h:



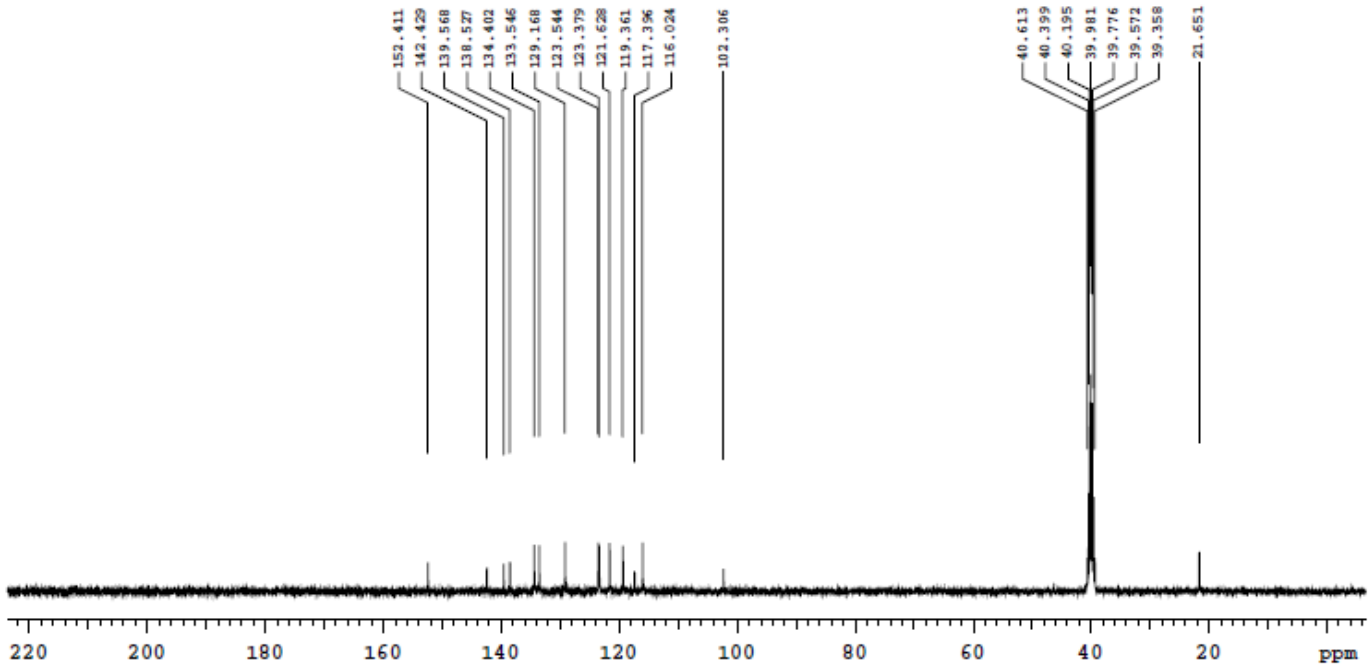


3i

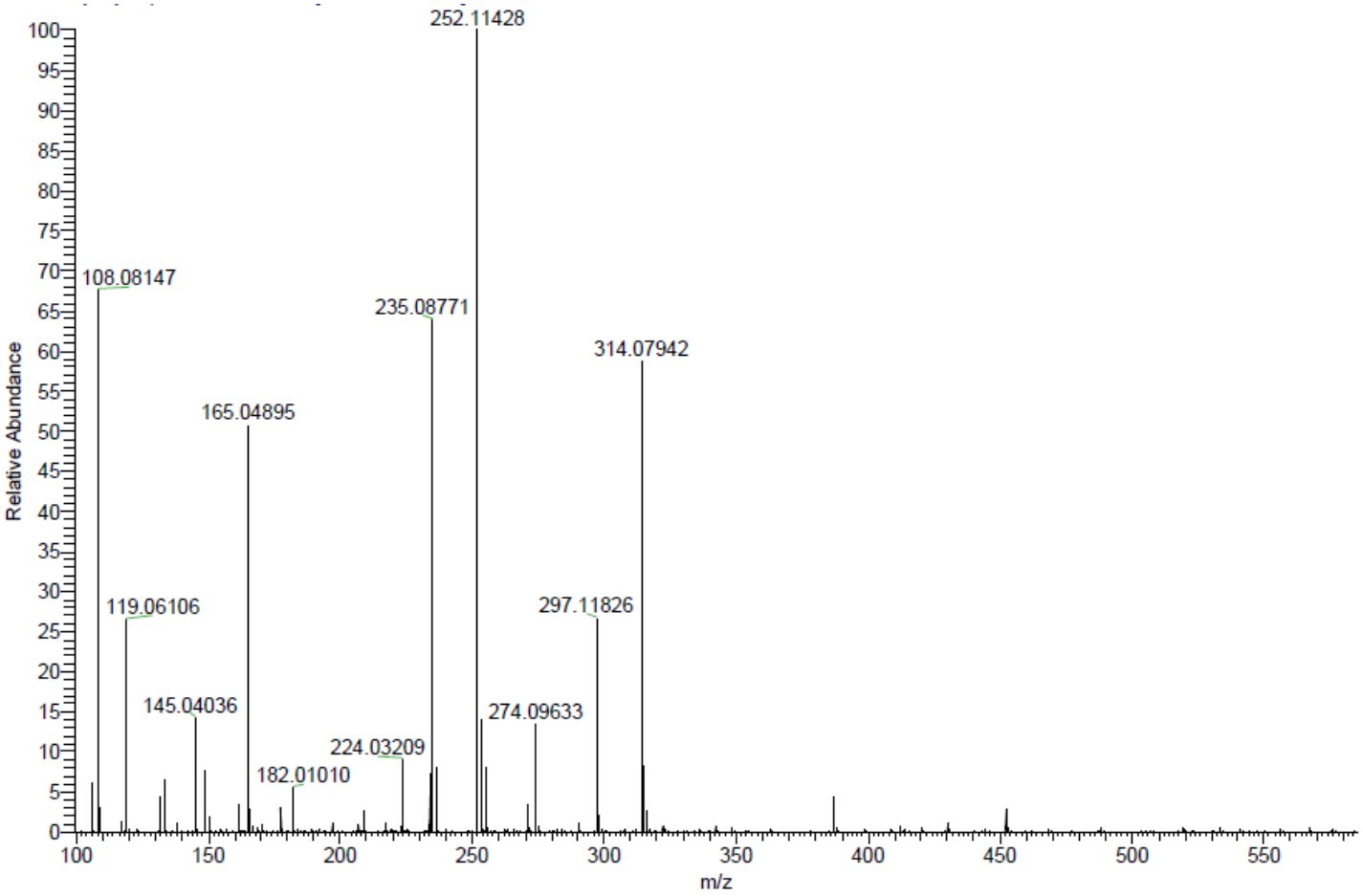
[1]H-NMR of 3i:

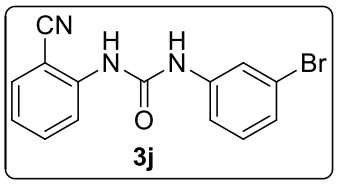


[13]C-NMR of 3i:

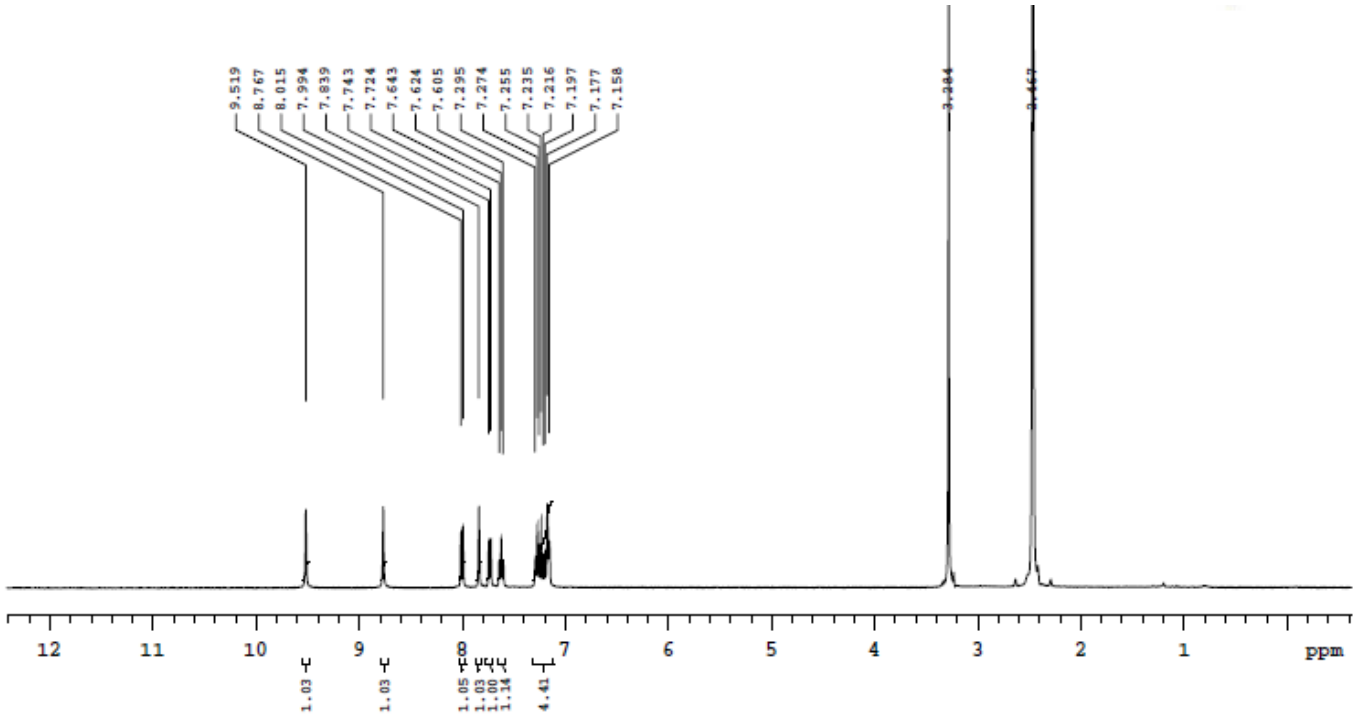


HRMS of 3i:

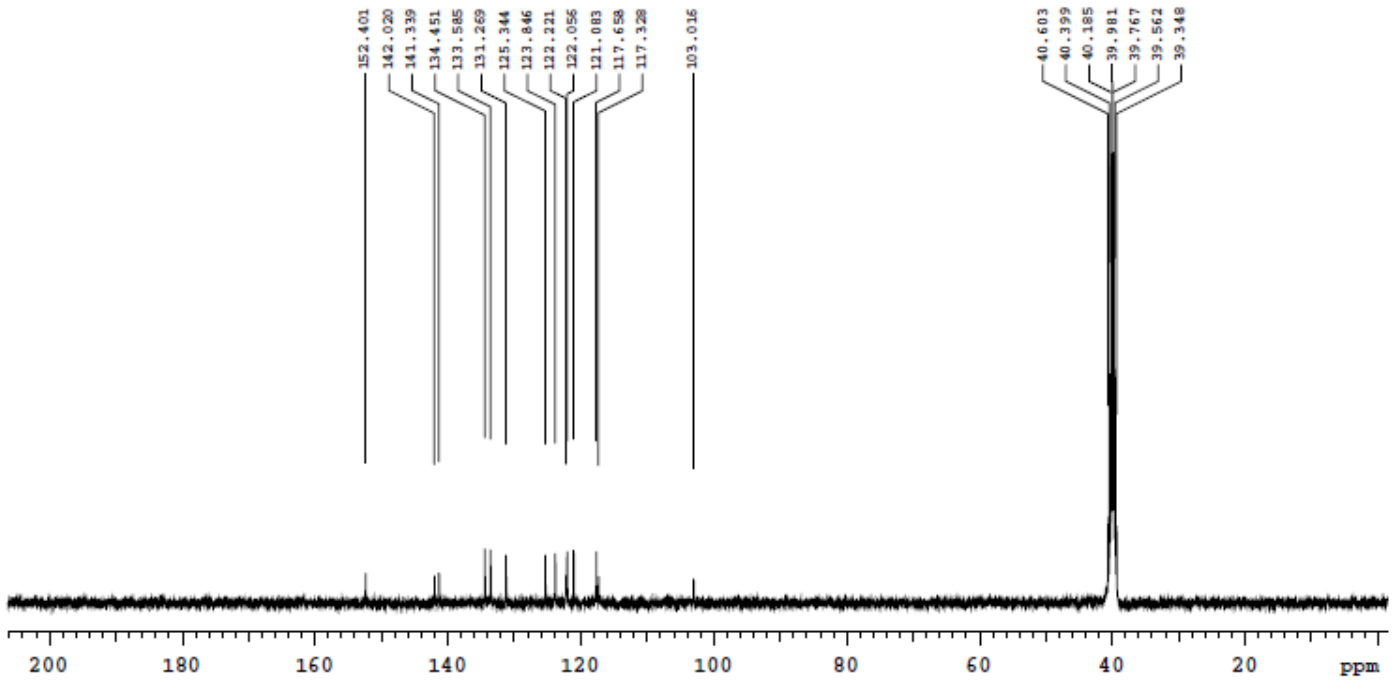

252.11428
108.08147
235.08771
314.07942
165.04895
119.06106
297.11826
145.04036
274.09633
224.03209
182.01010
Relative Abundance
m/z

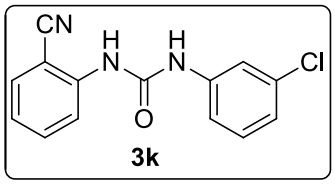


[1]H-NMR of 3j:

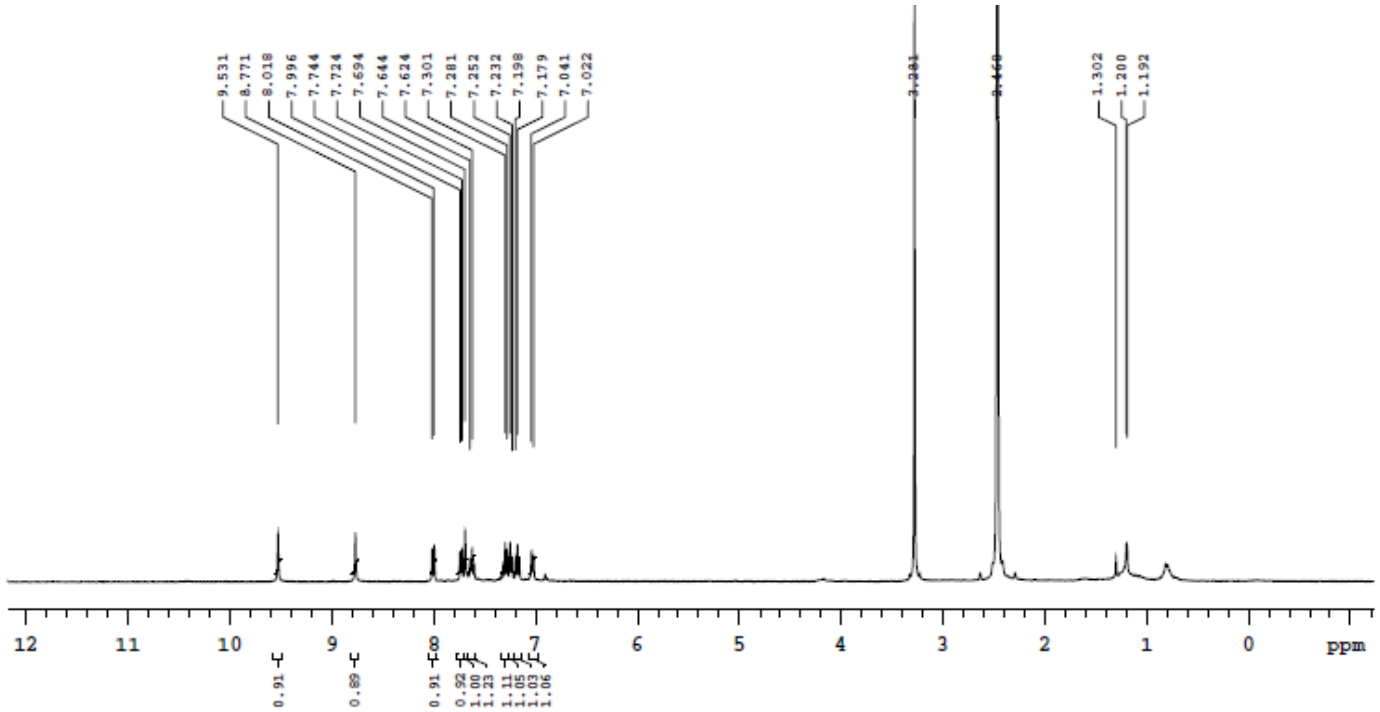


[13]C-NMR of 3j:

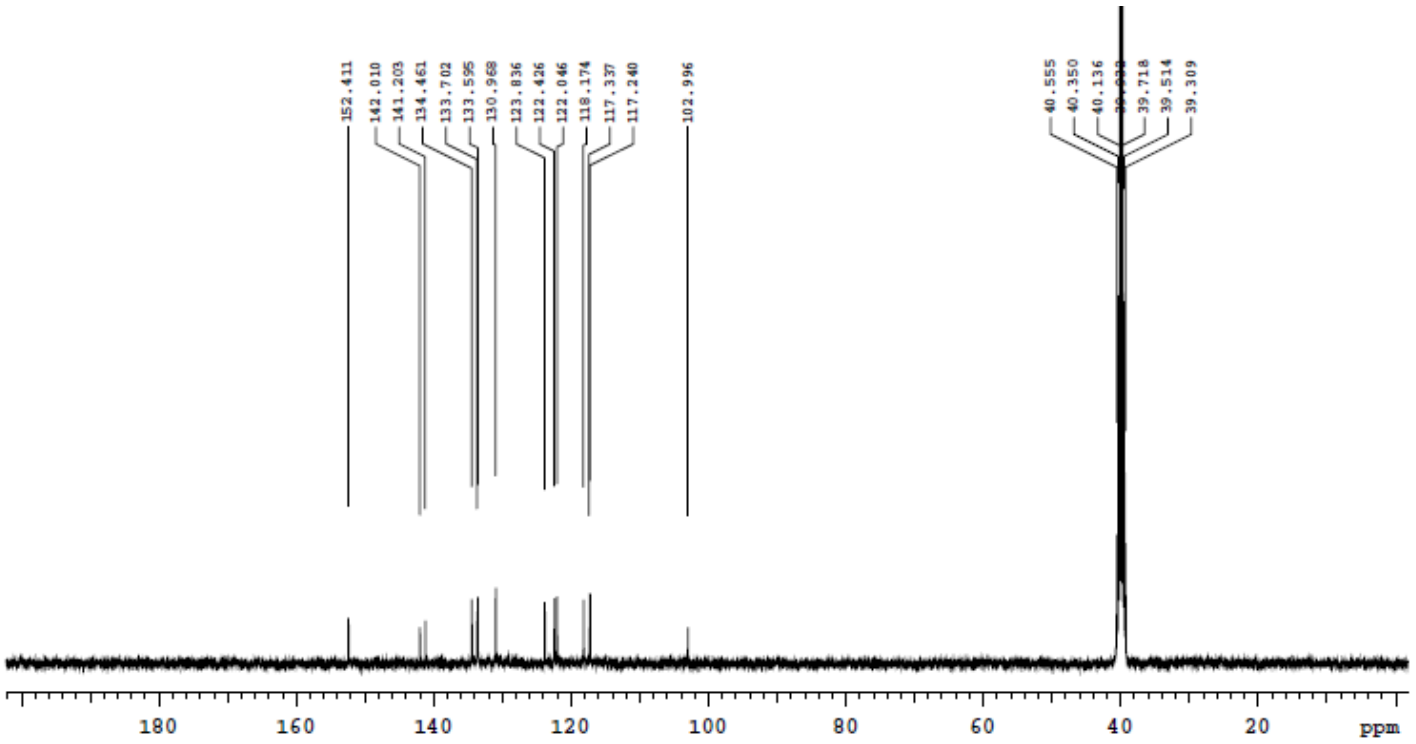




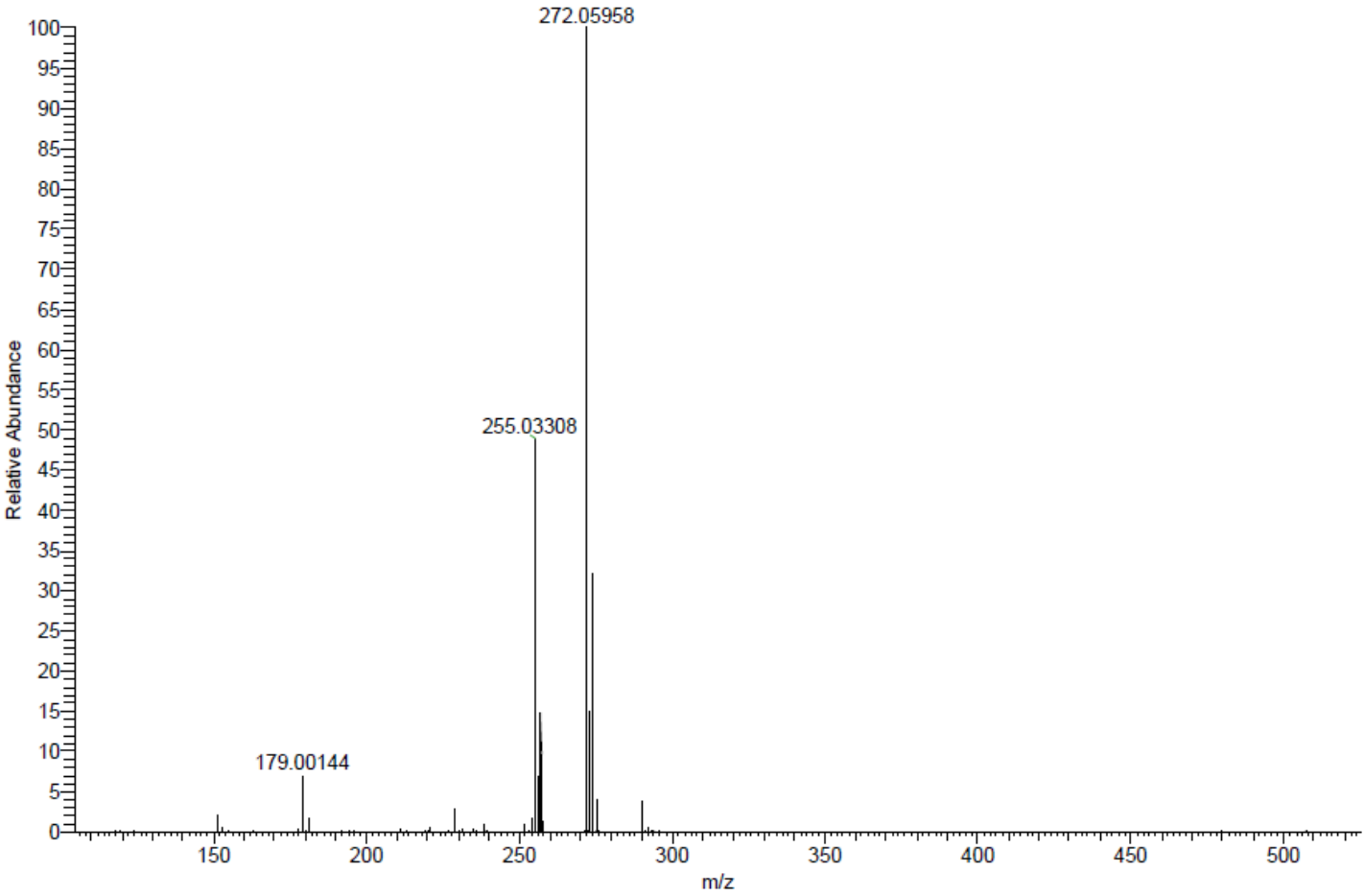
[1]H-NMR of 3k:

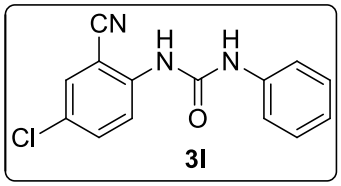


[13]C-NMR of 3k:



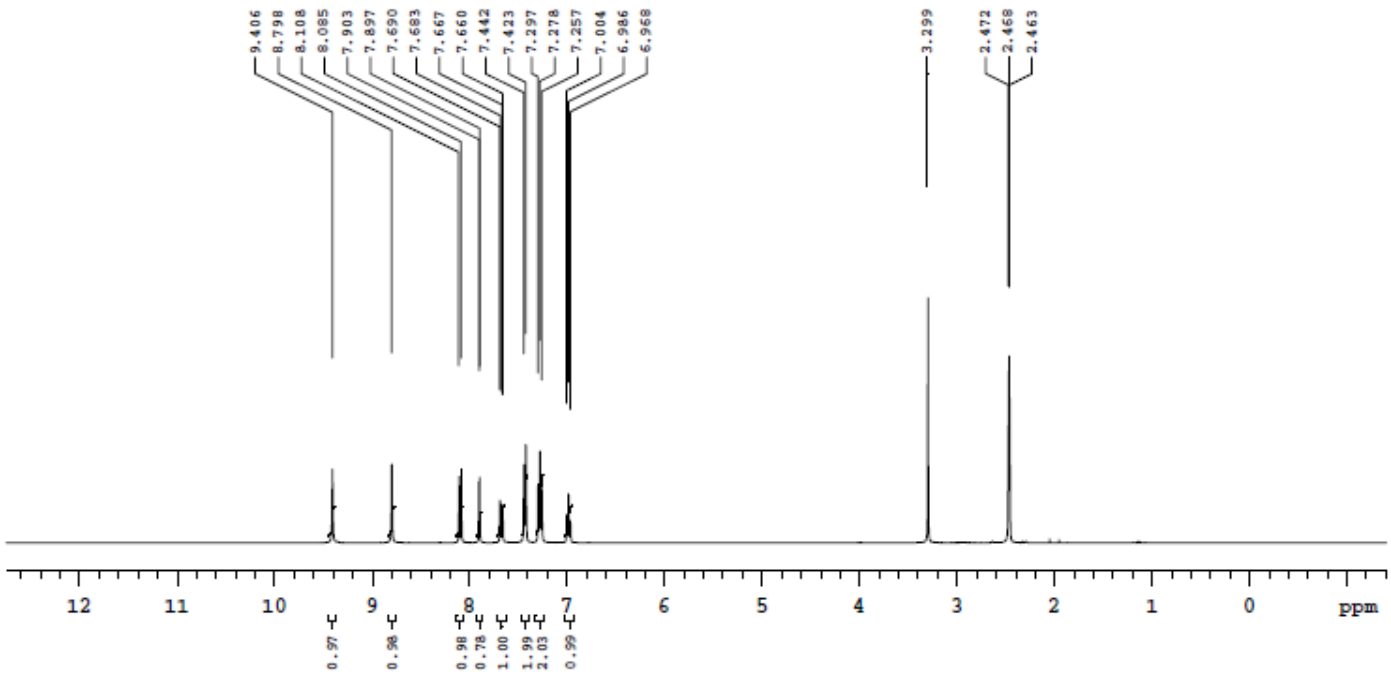
HRMS of 3k:


272.05958
255.03308
179.00144
Relative Abundance
m/z
100
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0
150
200
250
300
350
400
450
500

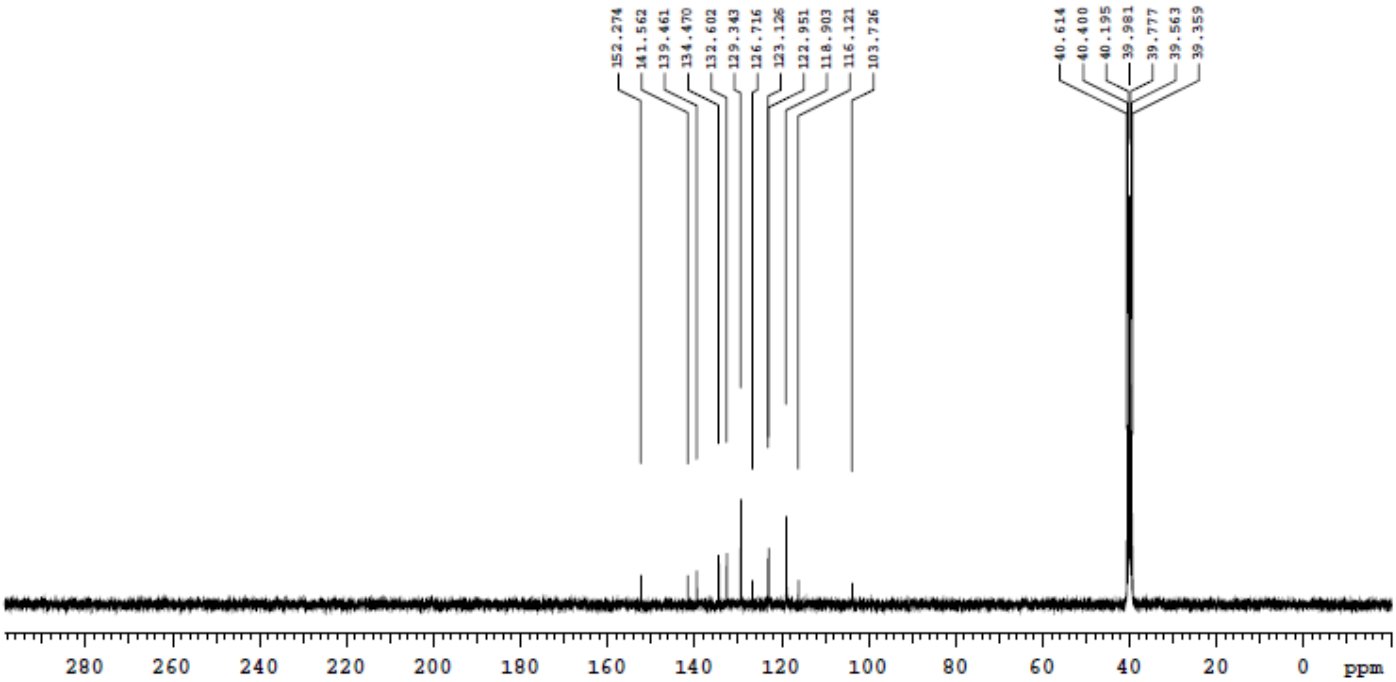


3l

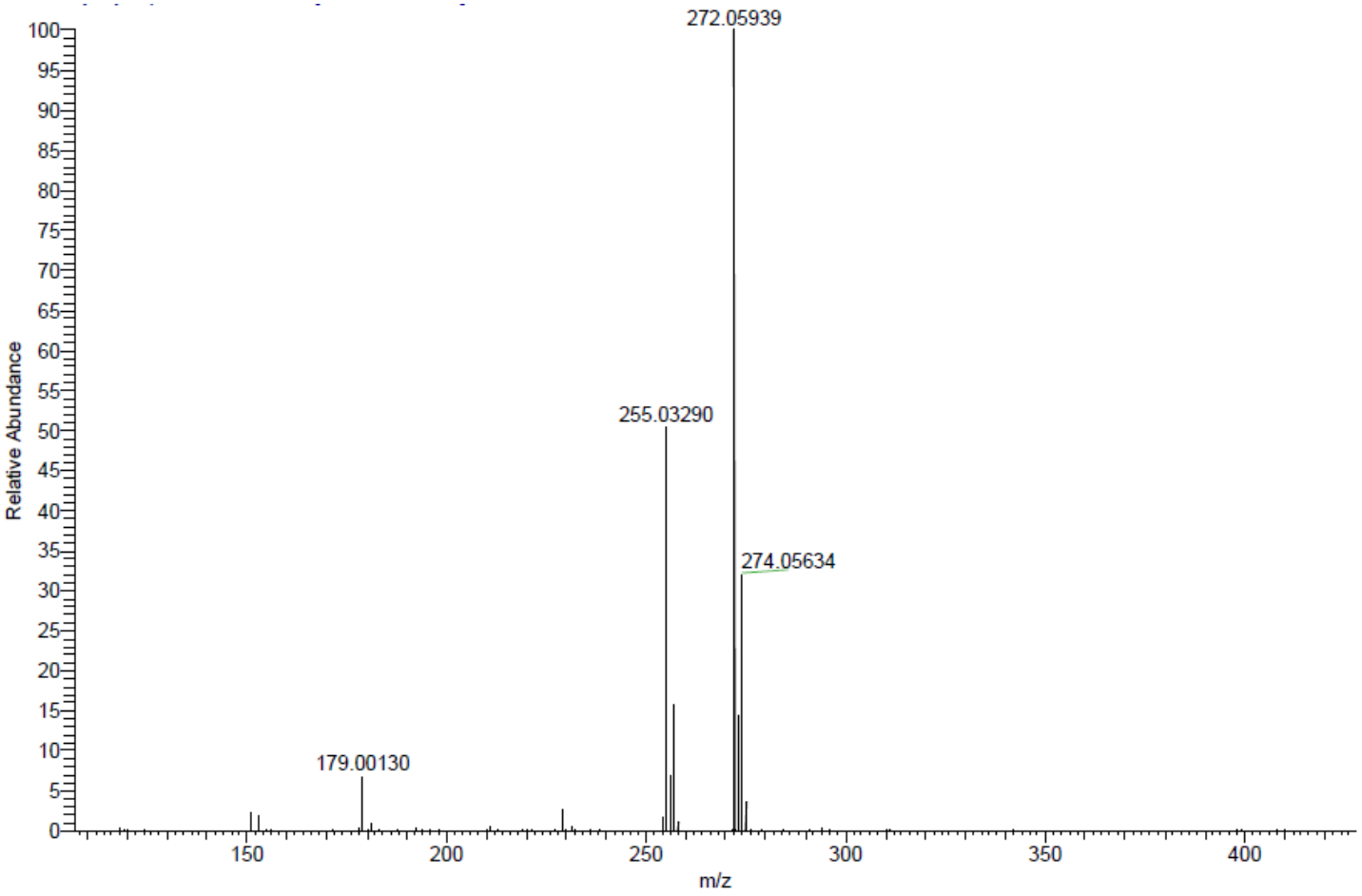
[1]H-NMR of 3l:

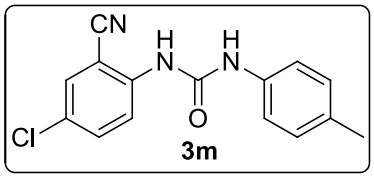


[13]C-NMR of 3l:

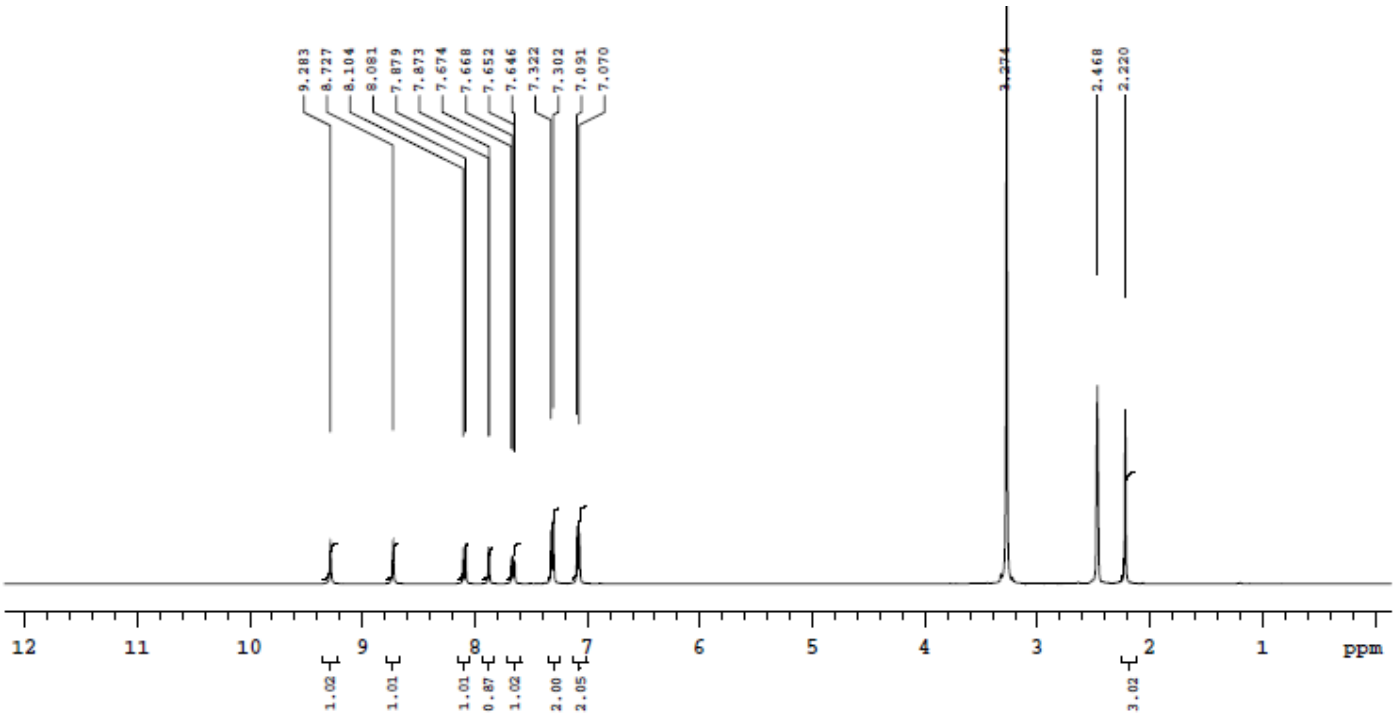


HRMS of 3l:

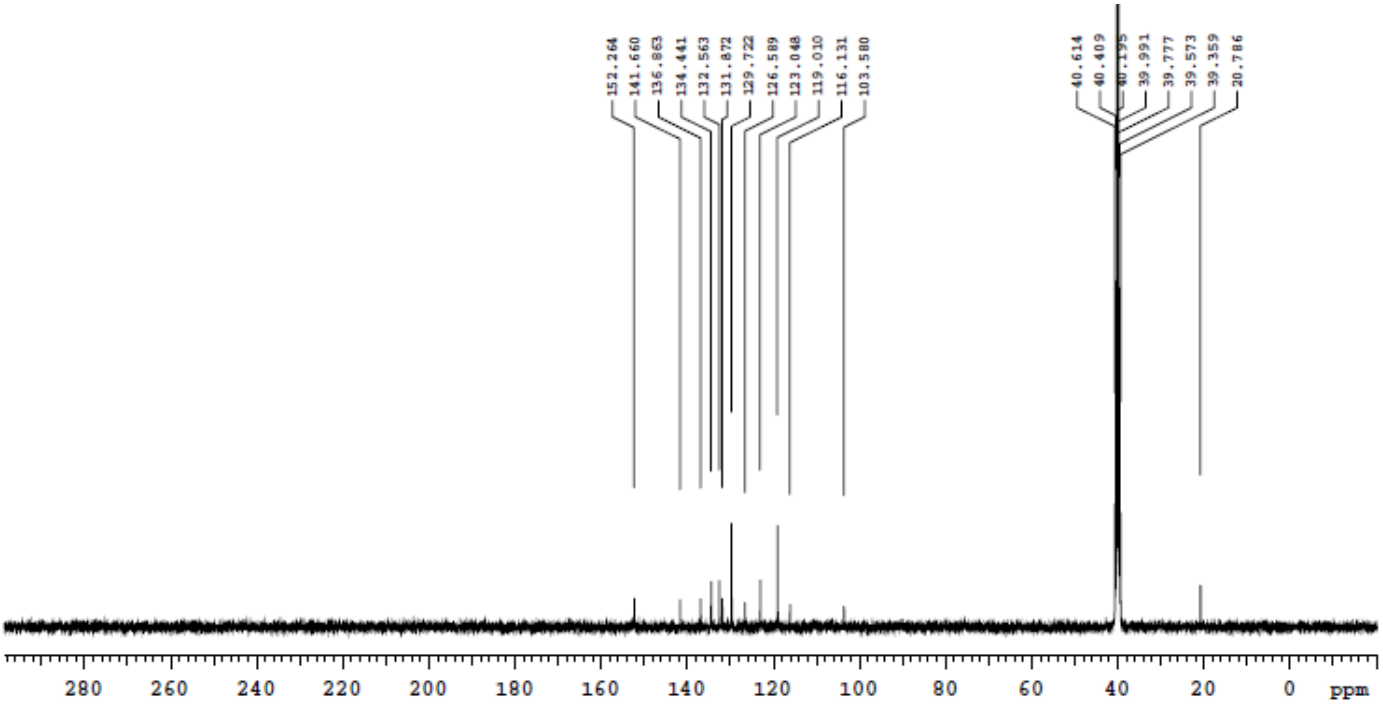

272.05939
255.03290
274.05634
179.00130
Relative Abundance
m/z
100
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0
150
200
250
300
350
400

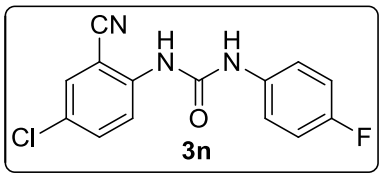


[1]H-NMR of 3m:

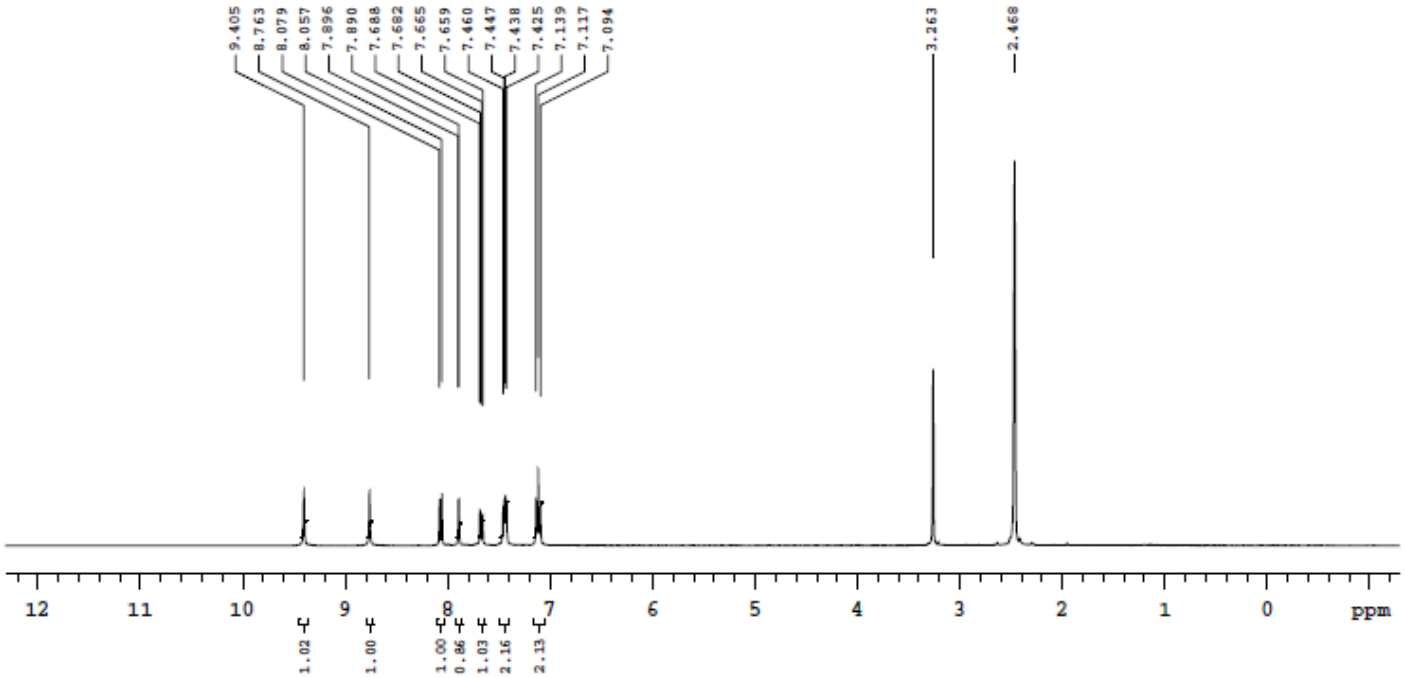


[13]C-NMR of 3m:

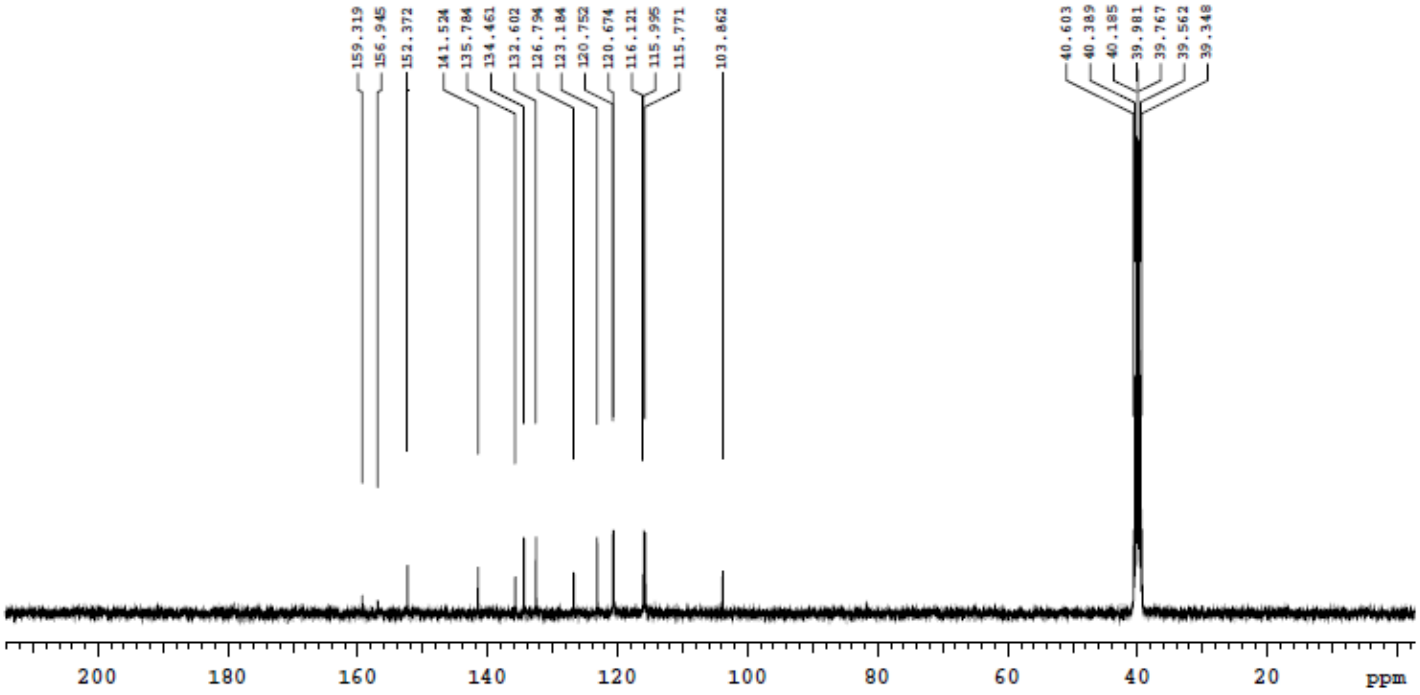




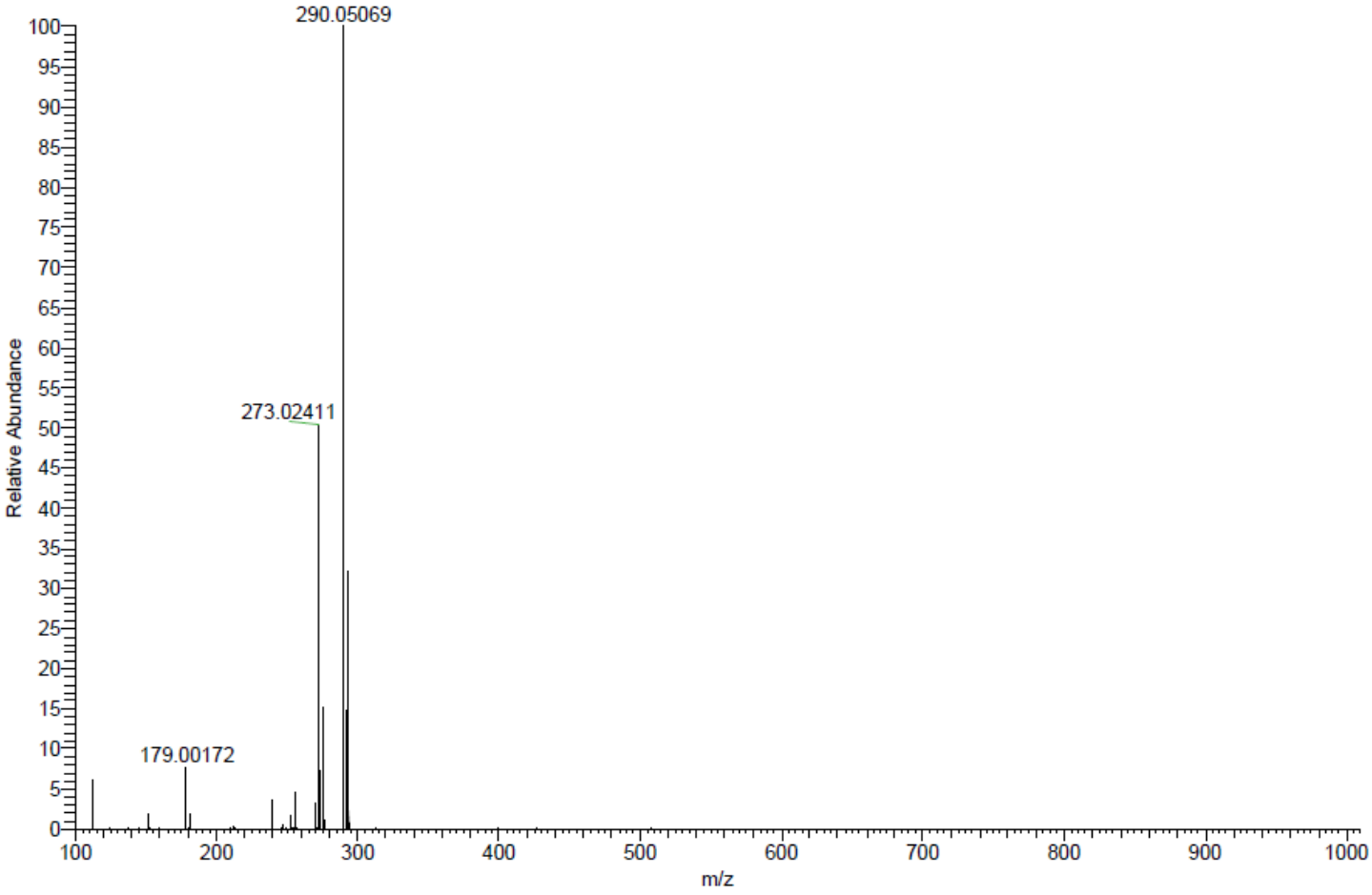
[1]H-NMR of 3n:



[13]C-NMR of 3n:



HRMS of 3n:


290.05069
273.02411
179.00172
Relative Abundance
m/z
100
95
90
85
80
75
70
65
60
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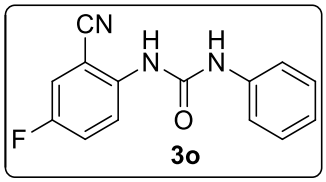
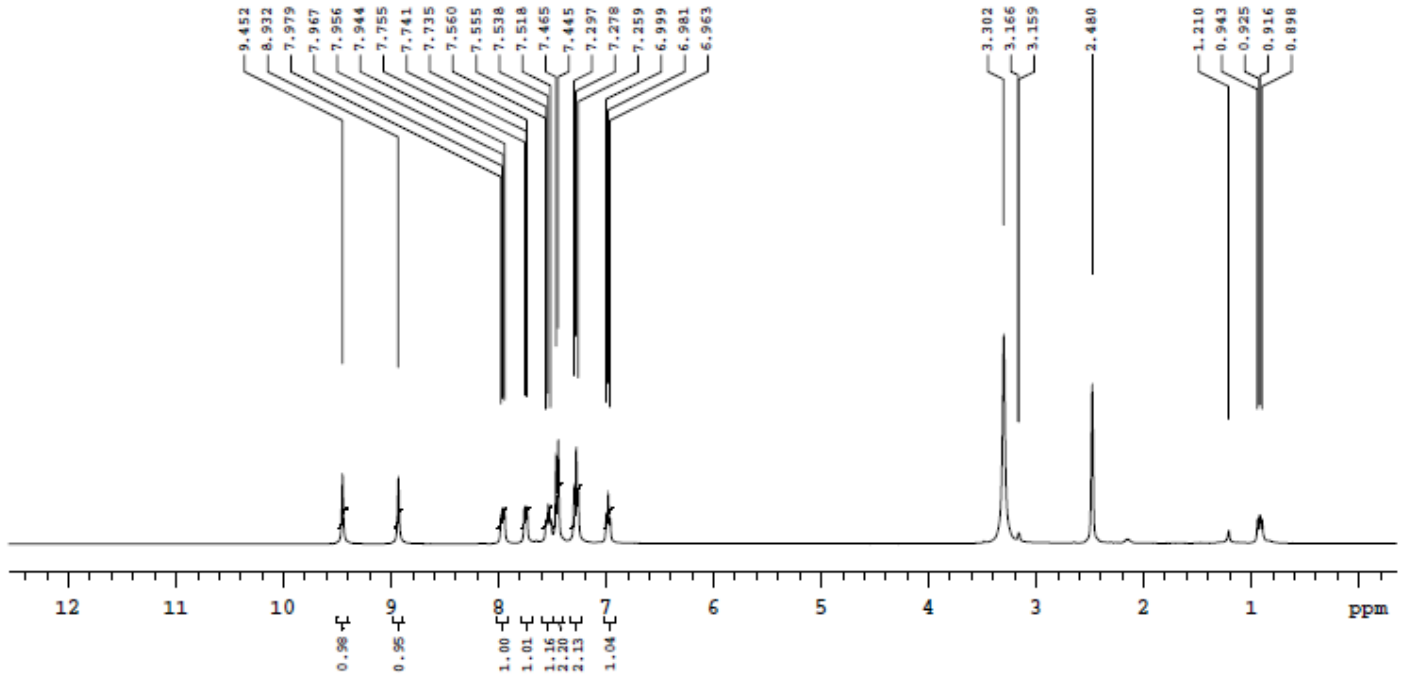
500
600
700
800
900
1000

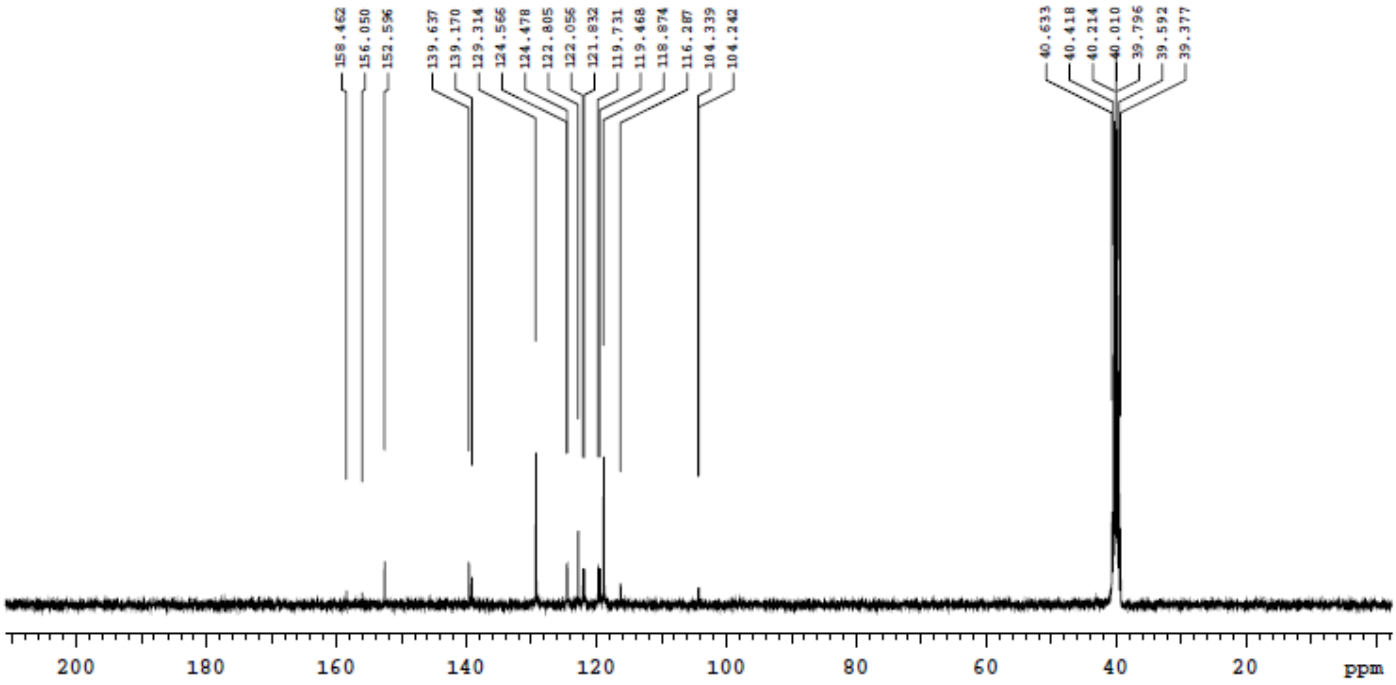


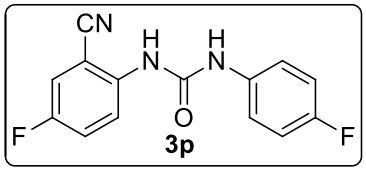
3o

[1]H-NMR of 3o:

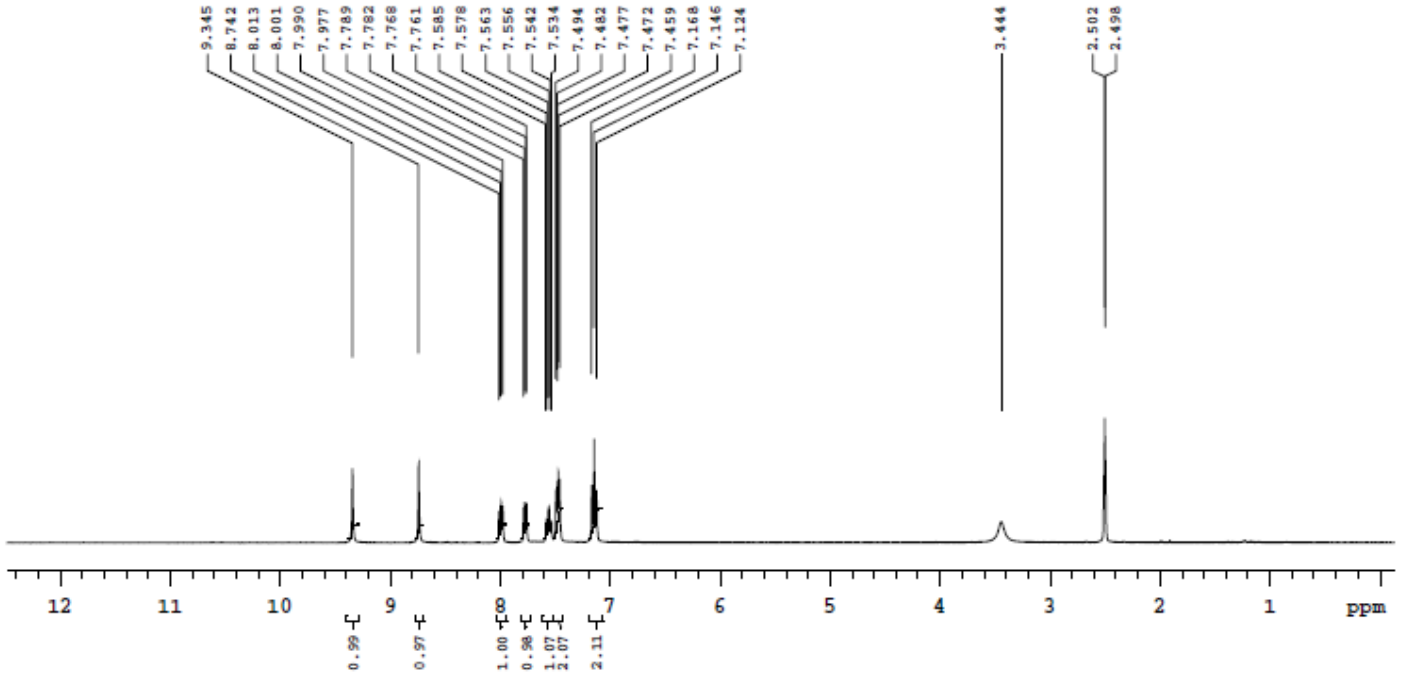


[13]C-NMR of 3o:

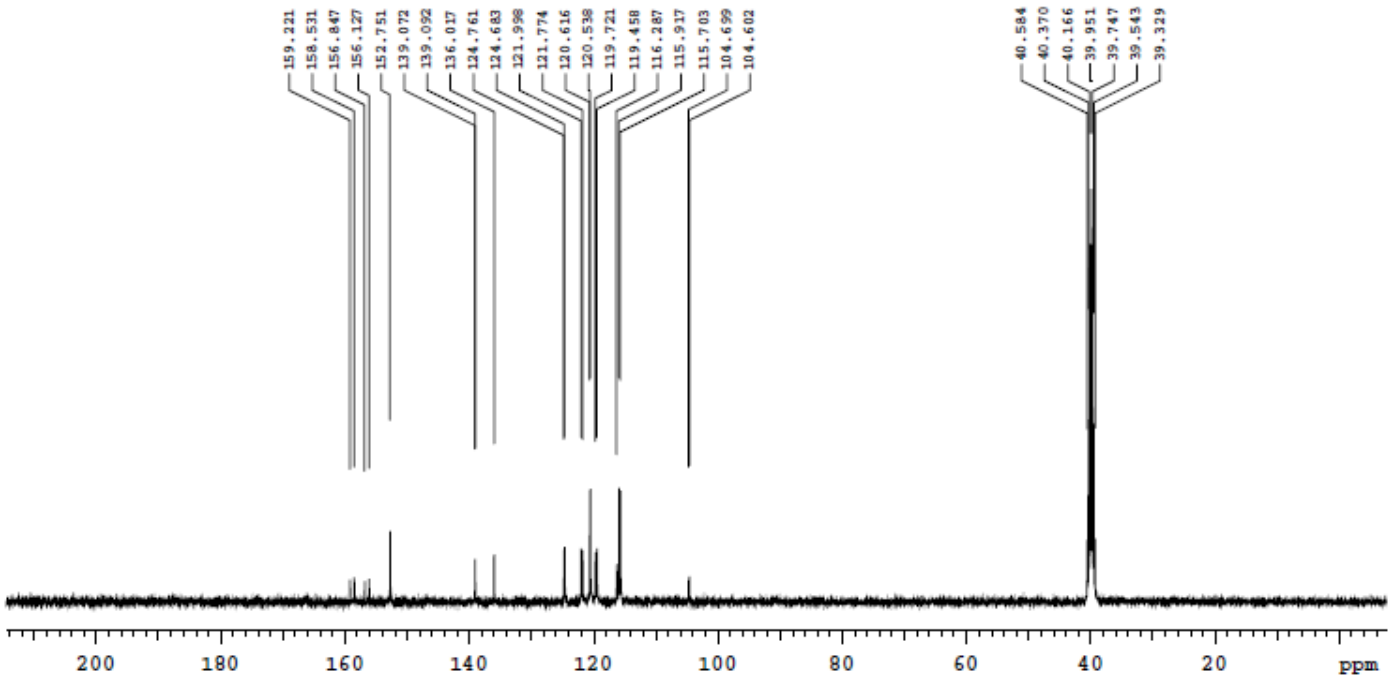




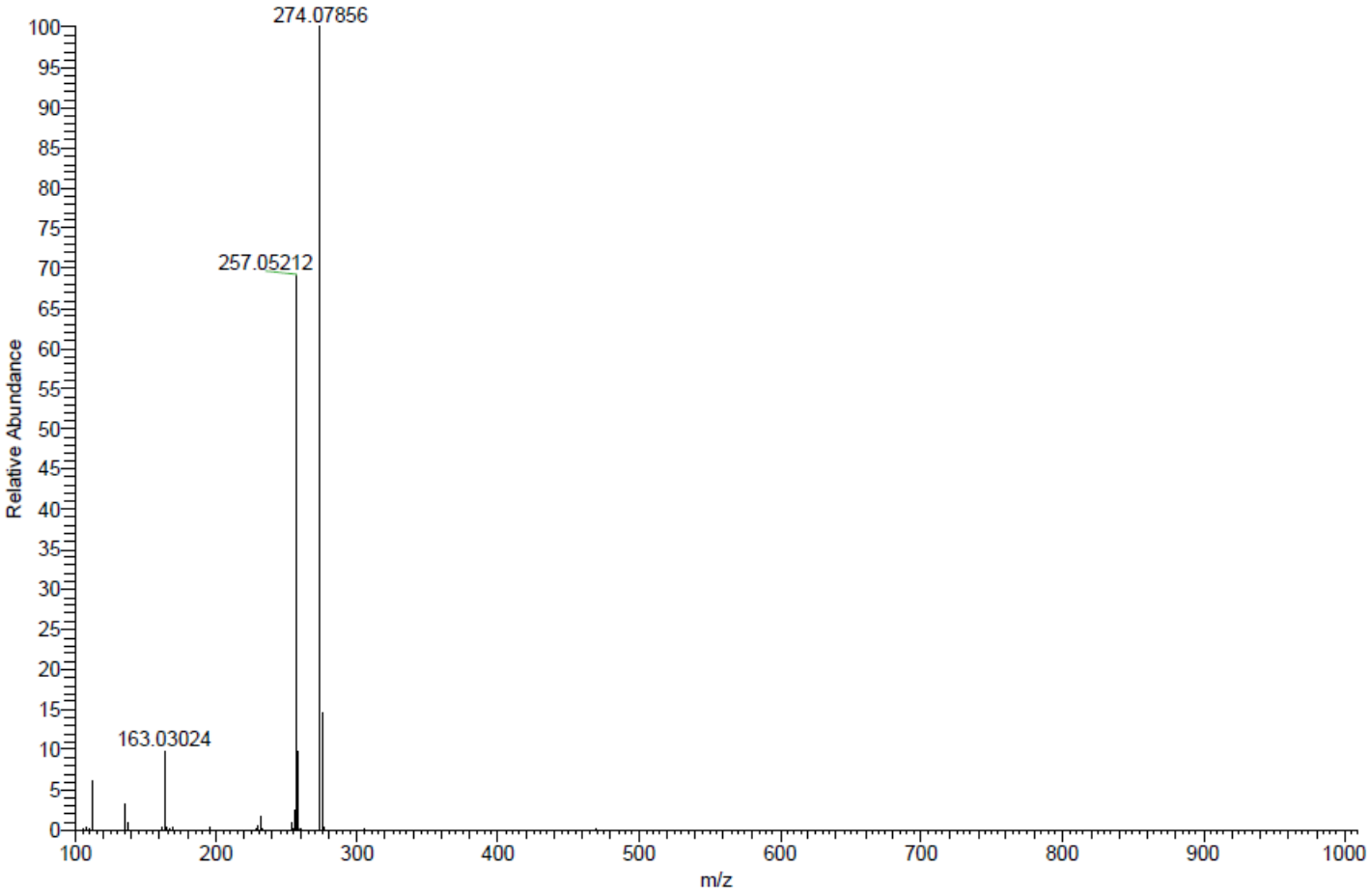
[1]H-NMR of 3p:



[13]C-NMR of 3p:



HRMS of 3p:


274.07856
257.05212
163.03024
Relative Abundance
m/z
100
95
90
85
80
75
70
65
60
55
50
45
40
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30
25
20
15
10
5
0
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300
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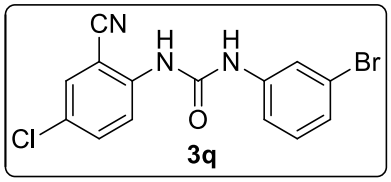
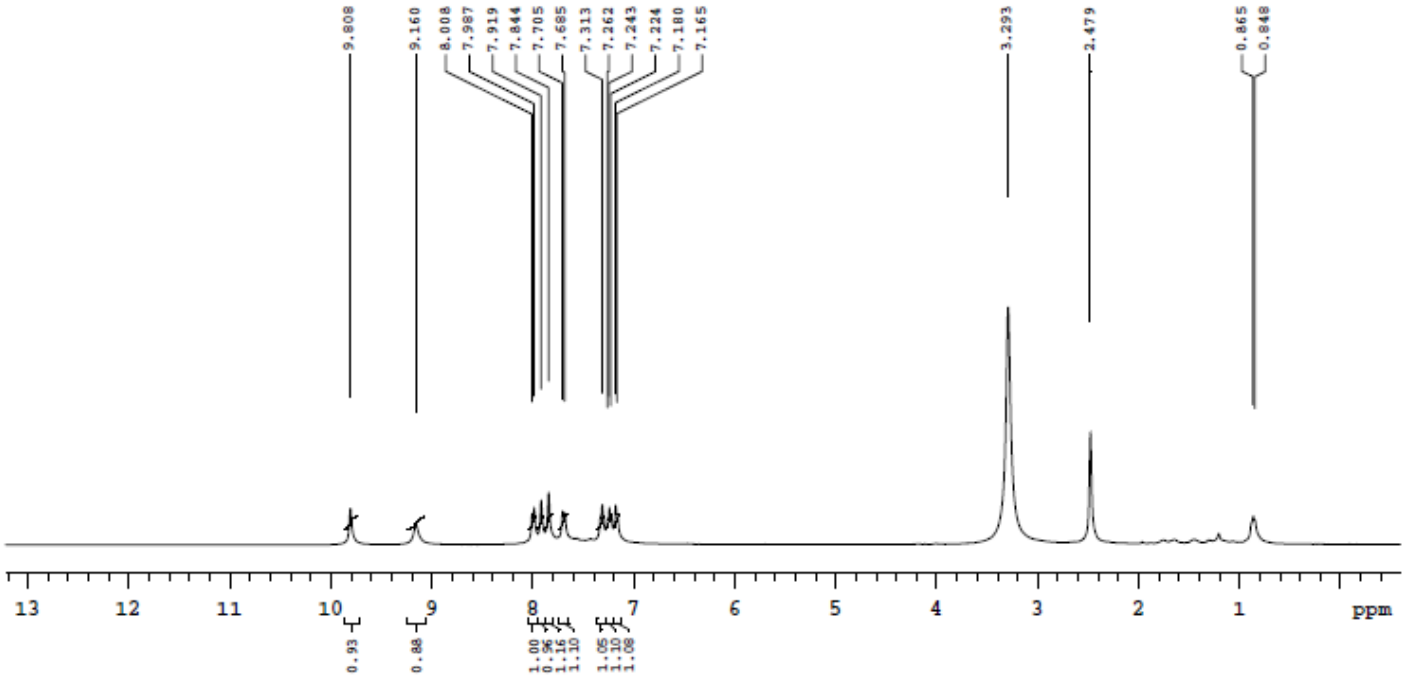
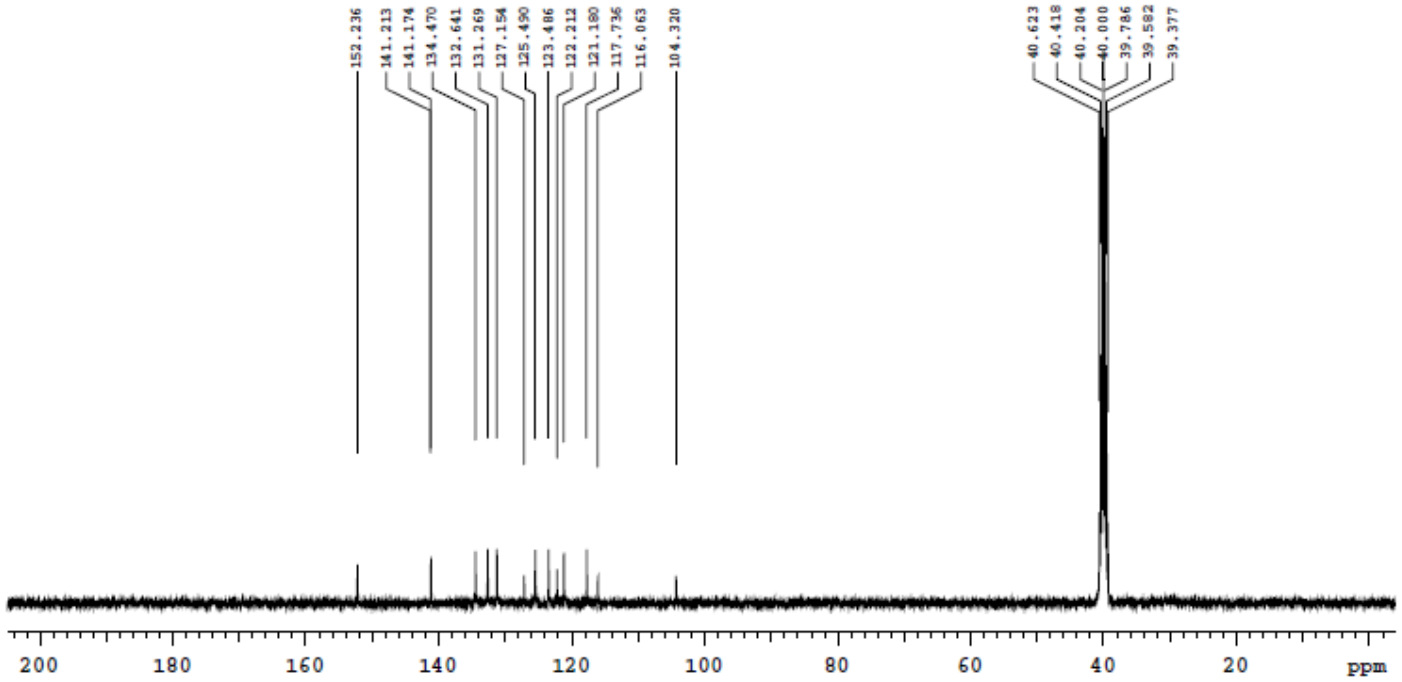
500
600
700
800
900
1000



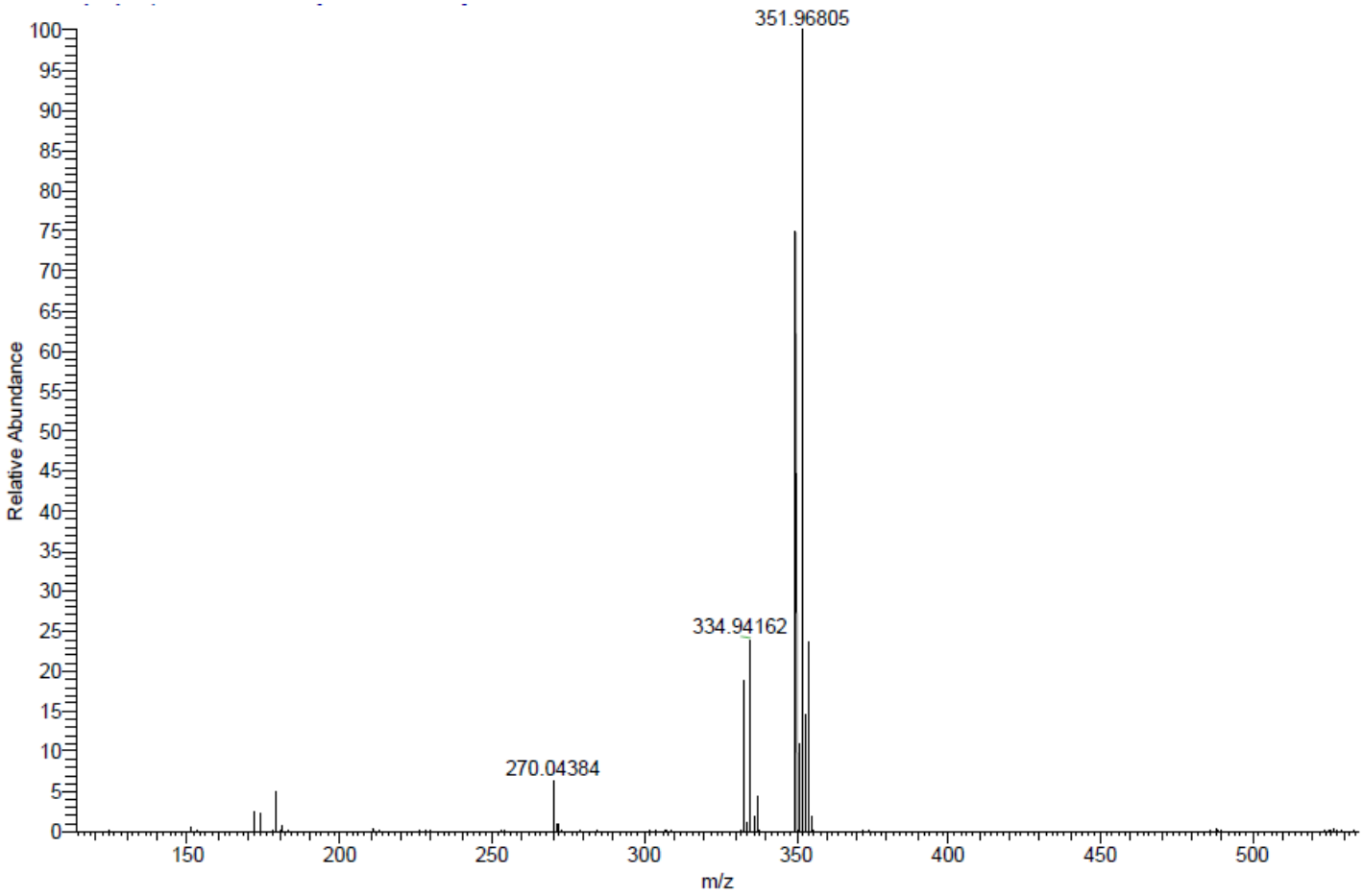
[1]H-NMR of 3q:



[13]C-NMR of 3q:



HRMS of 3q:


351.96805
334.94162
270.04384
Relative Abundance
m/z
100
95
90
85
80
75
70
65
60
55
50
45
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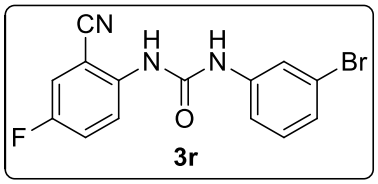
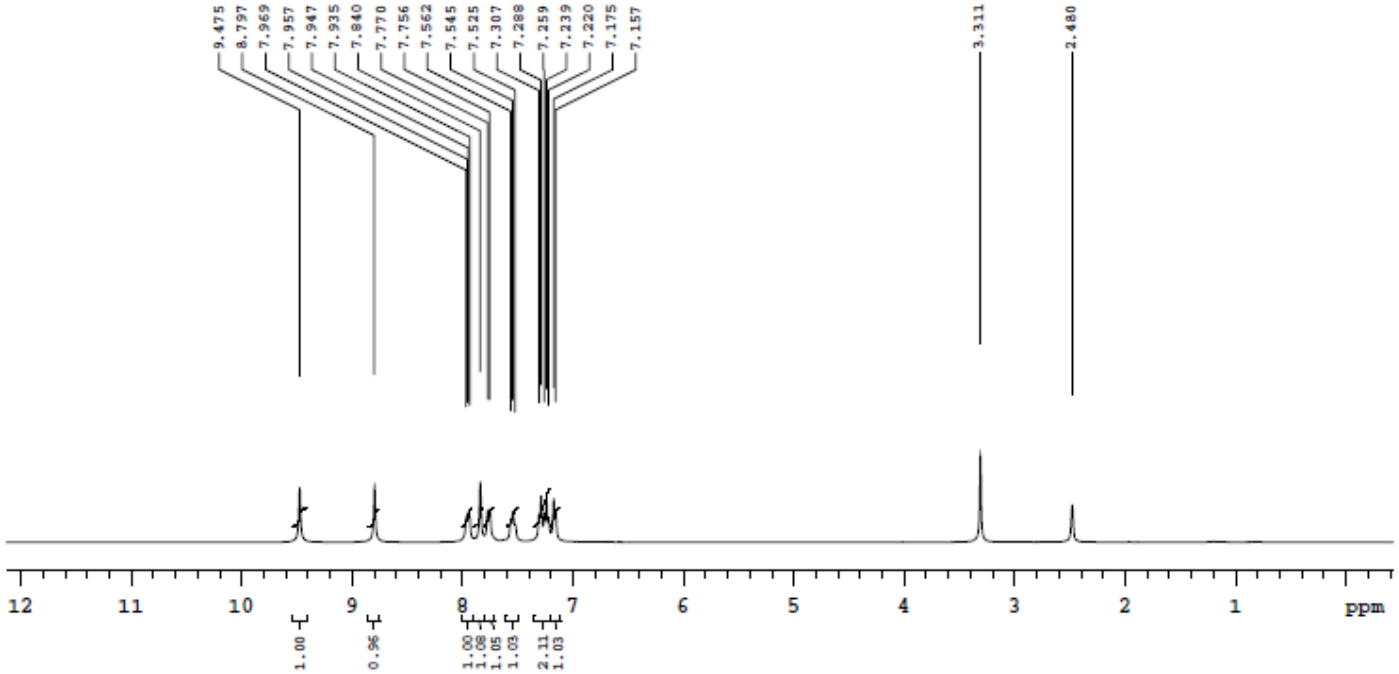
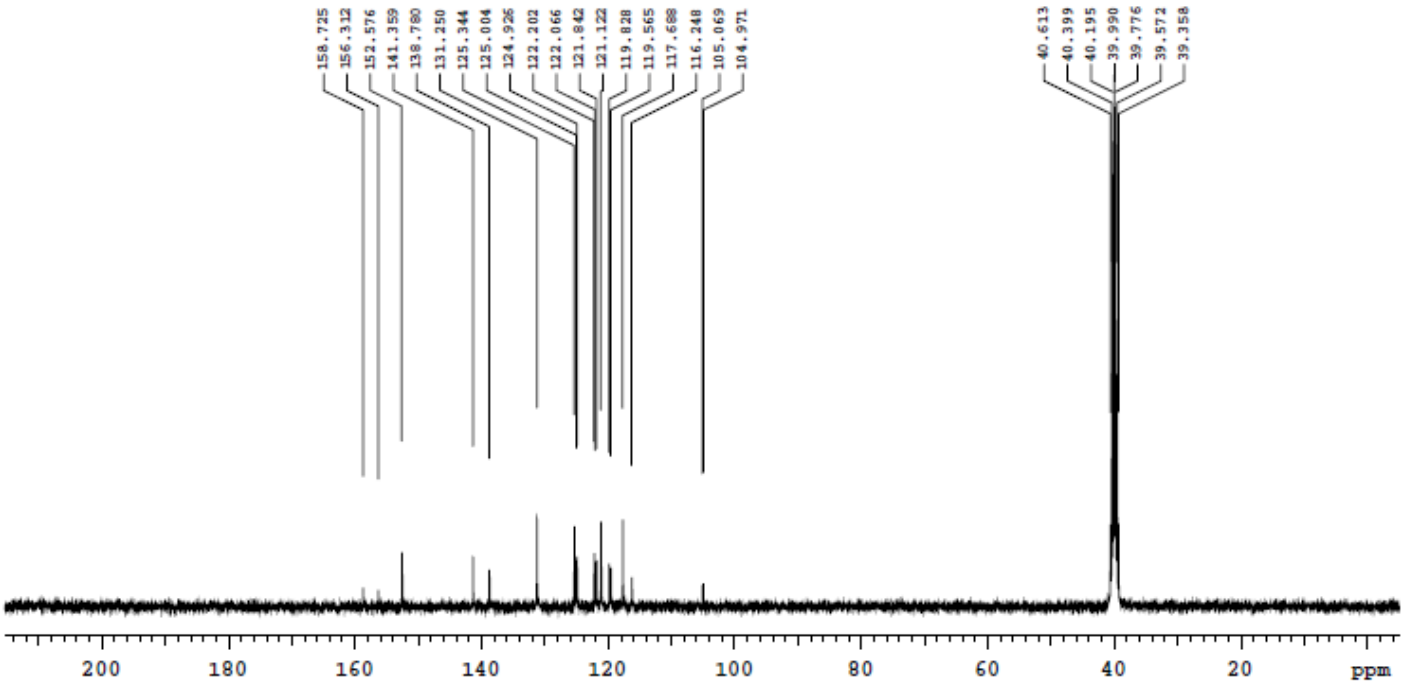
35
30
25
20
15
10
5
0
150
200
250
300
350
400
450
500



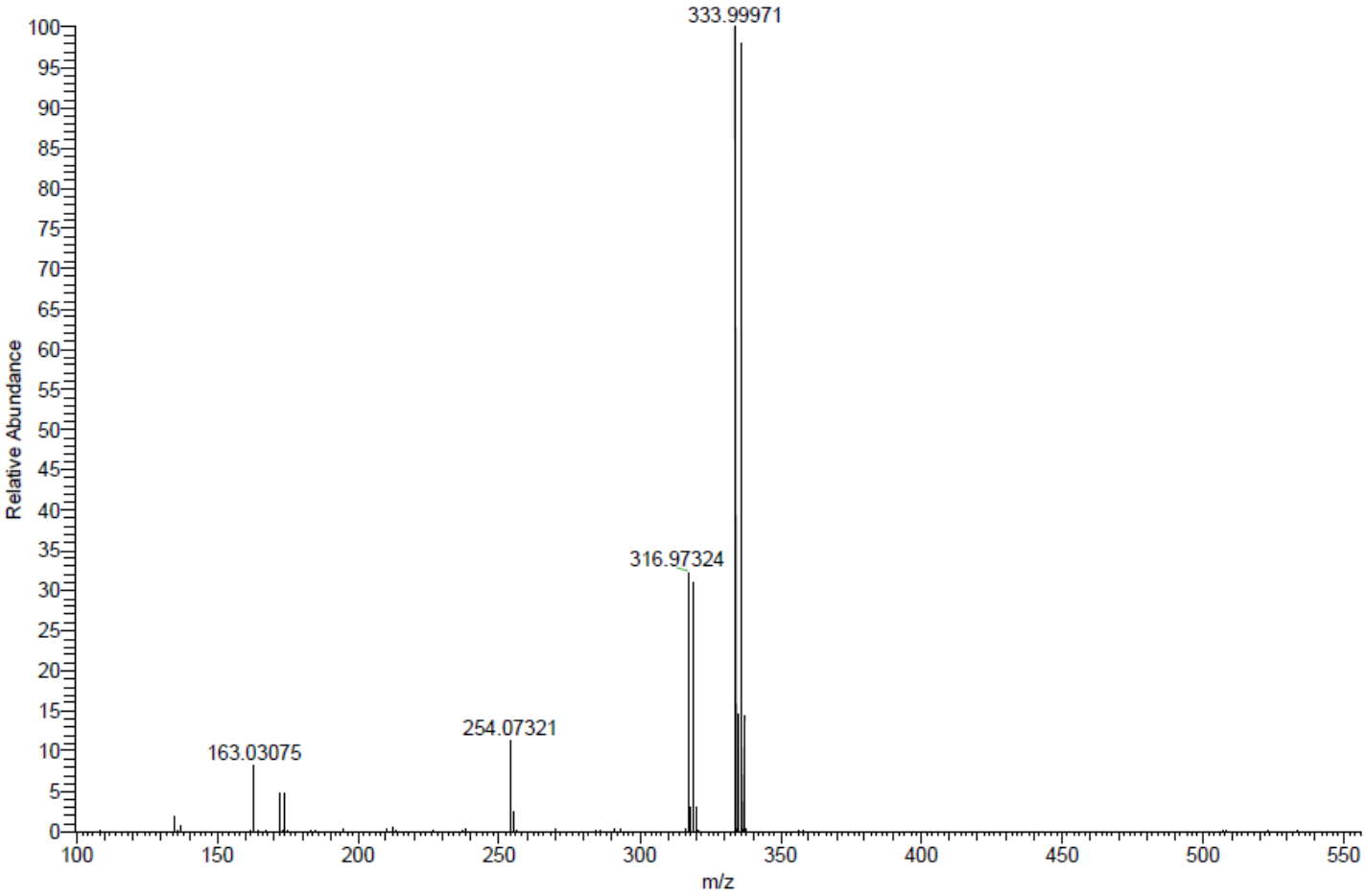
[1]H-NMR of 3r:



[13]C-NMR of 3r:



HRMS of 3r:


333.99971
316.97324
254.07321
163.03075
Relative Abundance
m/z
100
95
90
85
80
75
70
65
60
55
50
45
40
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20
15
10
5
0
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200
250
300
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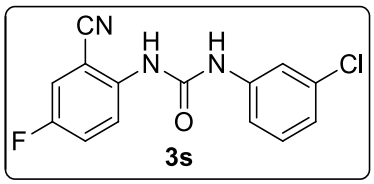
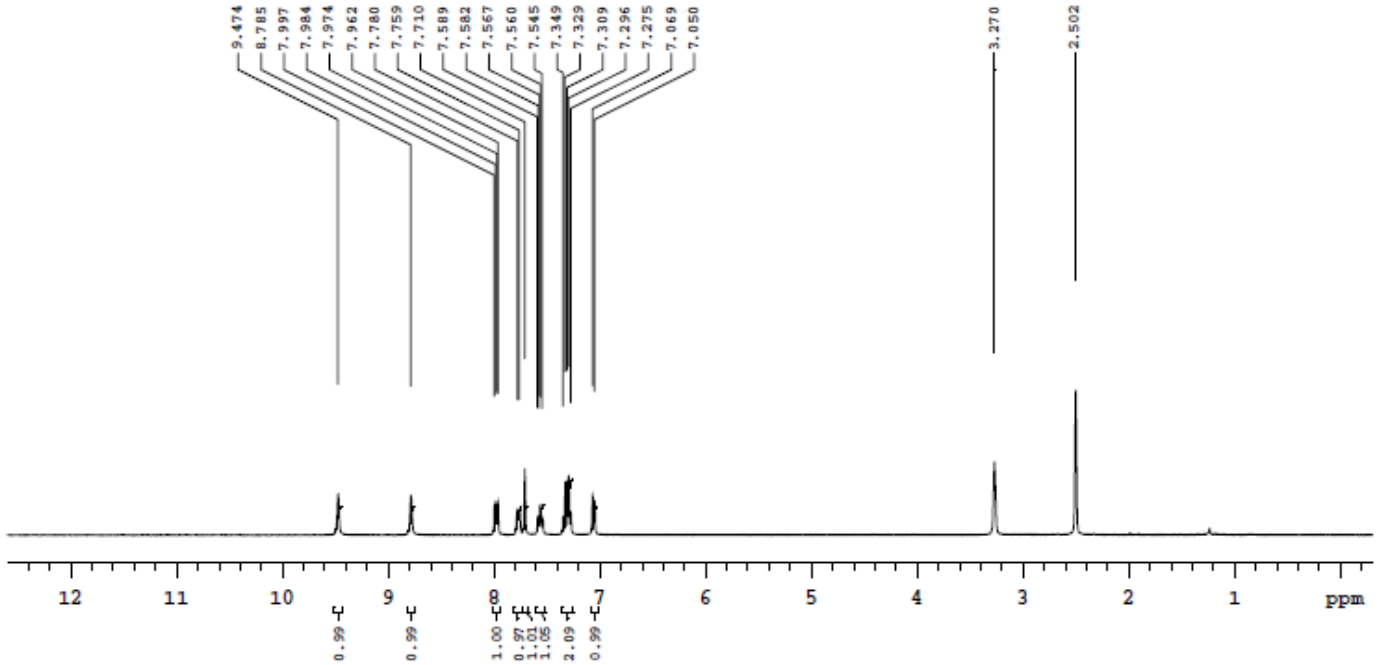
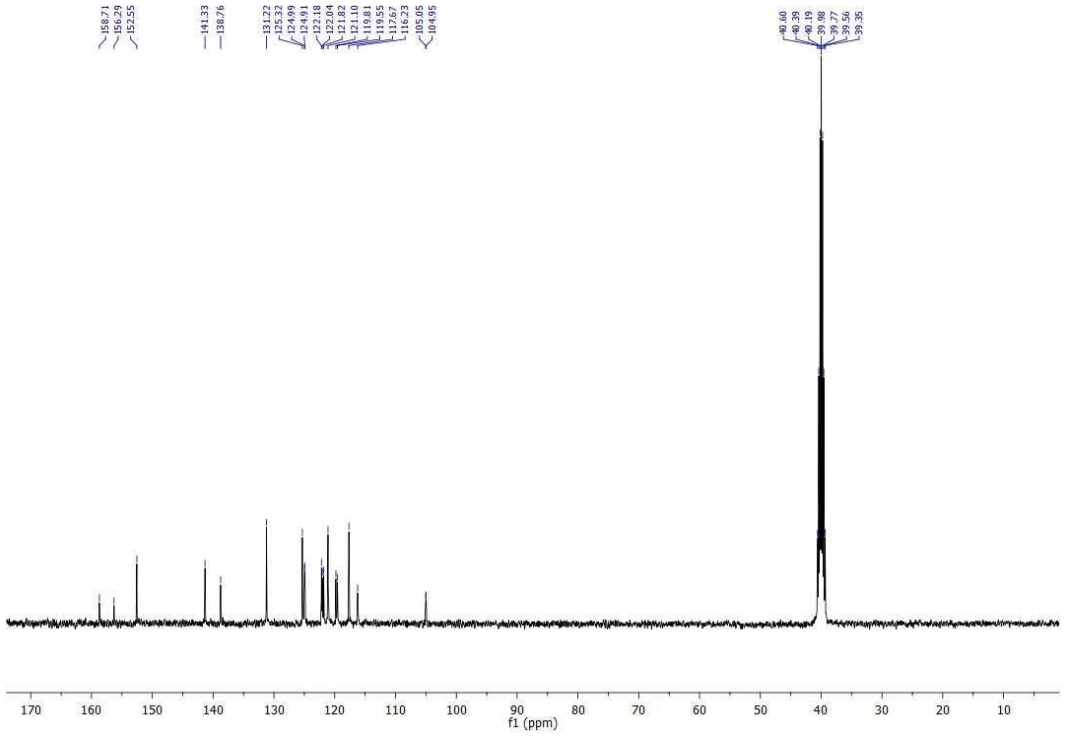
400
450
500
550



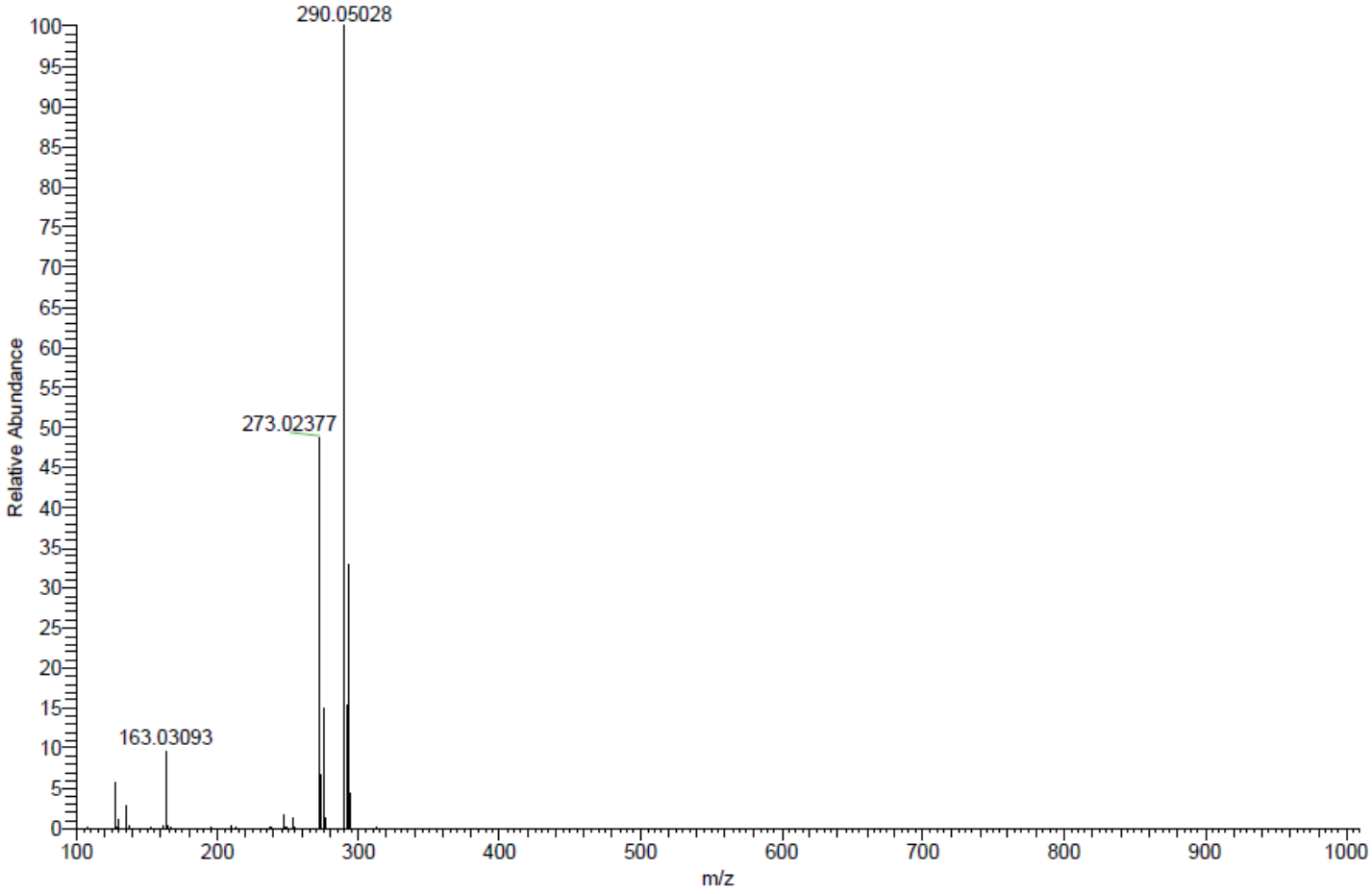
[1]H-NMR of 3s:



[13]C-NMR of 3s:



HRMS of 3s:


290.05028
273.02377
163.03093
Relative Abundance
m/z
100
95
90
85
80
75
70
65
60
55
50
45
40
35
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25
20
15
10
5
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300
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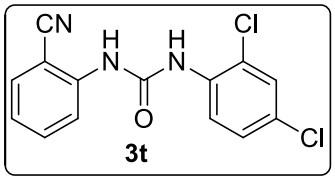
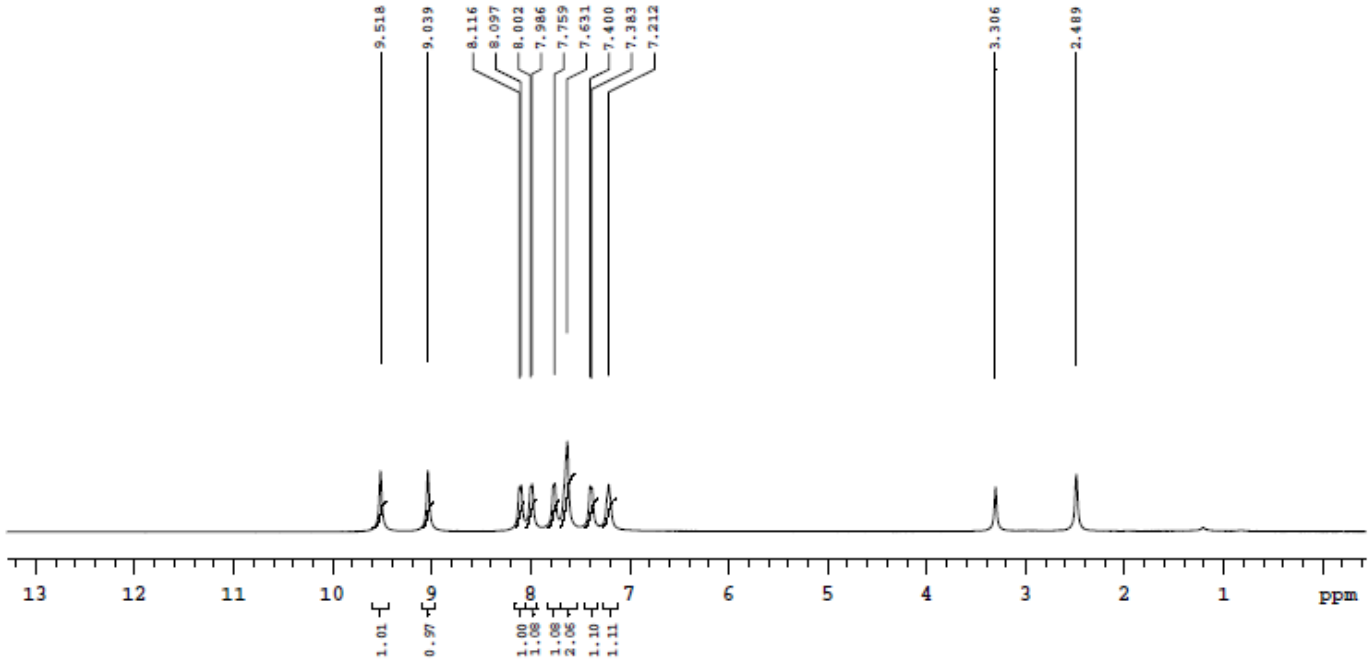
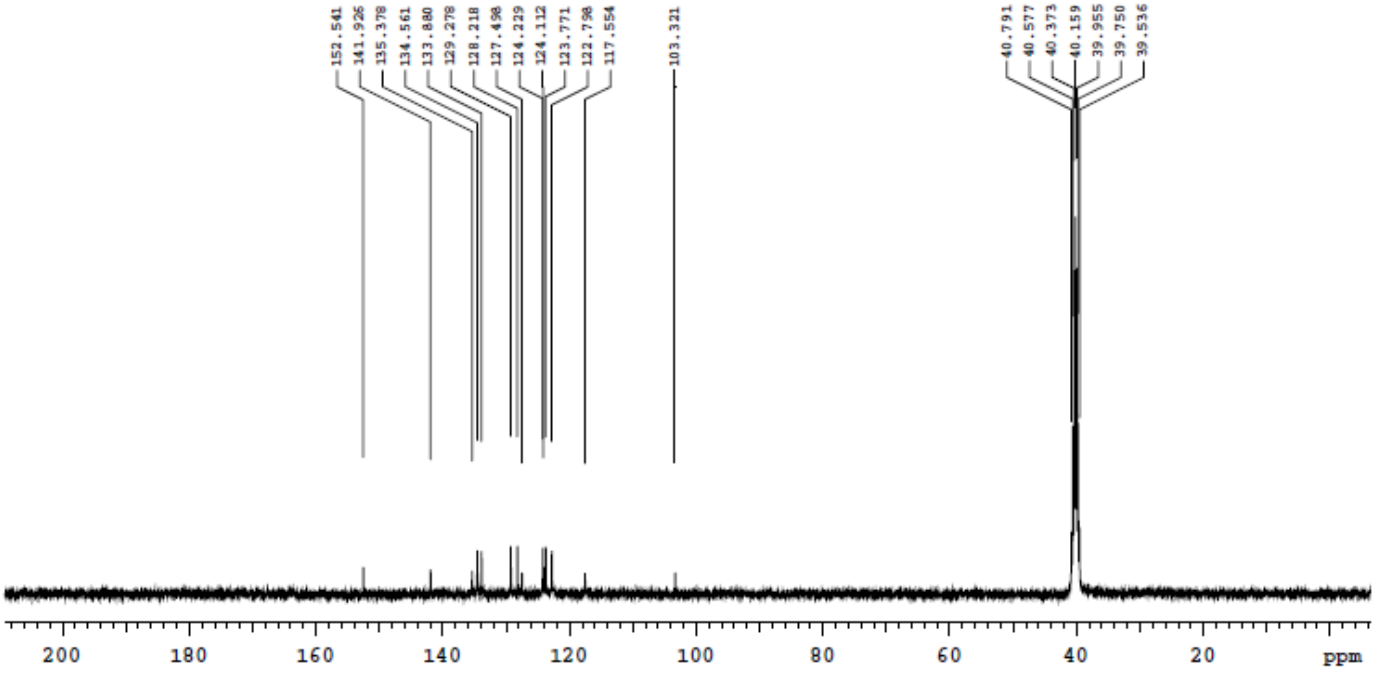
700
800
900
1000



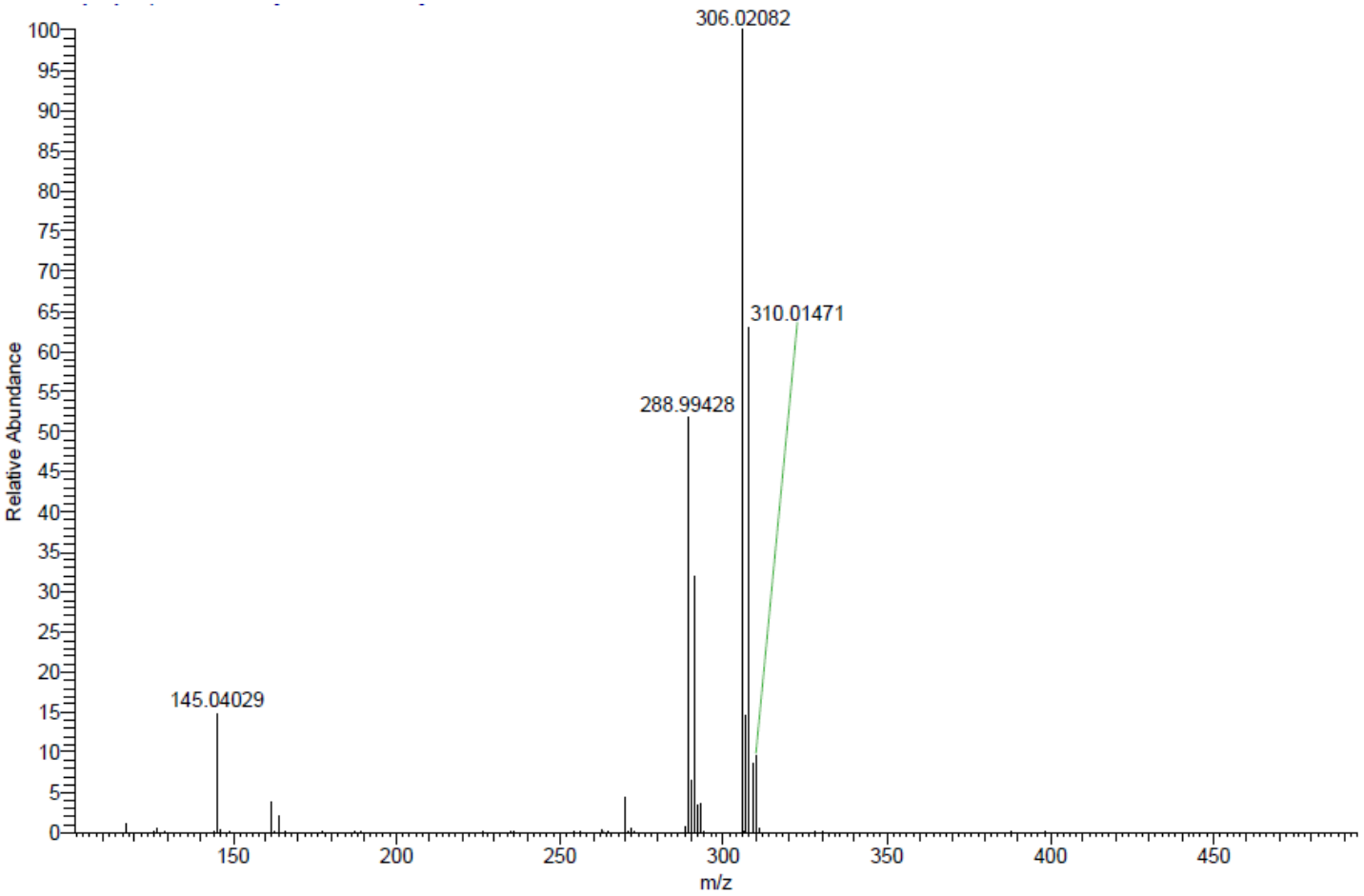
[1]H-NMR of 3t:



[13]C-NMR of 3t:



HRMS of 3t:


306.02082
310.01471
288.99428
145.04029
Relative Abundance
m/z
100
95
90
85
80
75
70
65
60
55
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40
35
30
25
20
15
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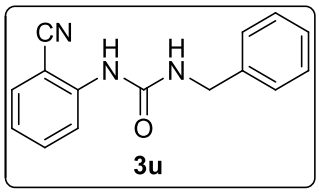
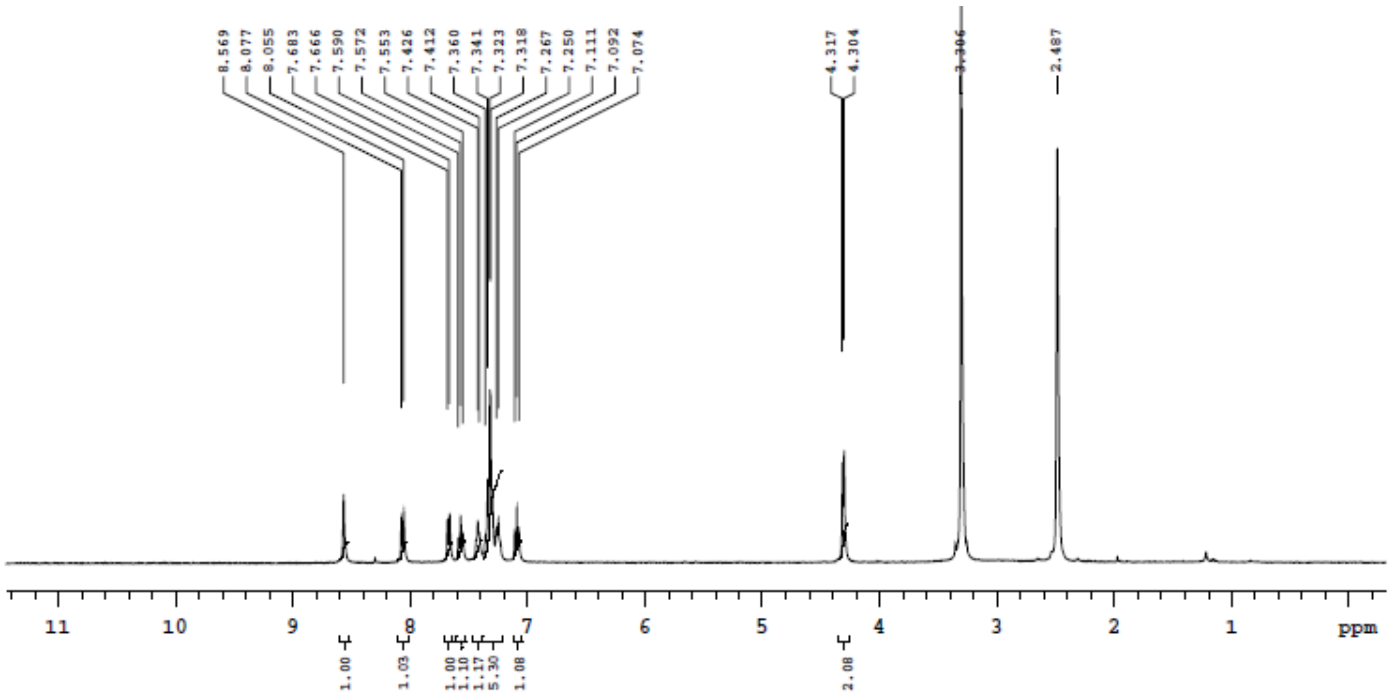
5
0
150
200
250
300
350
400
450

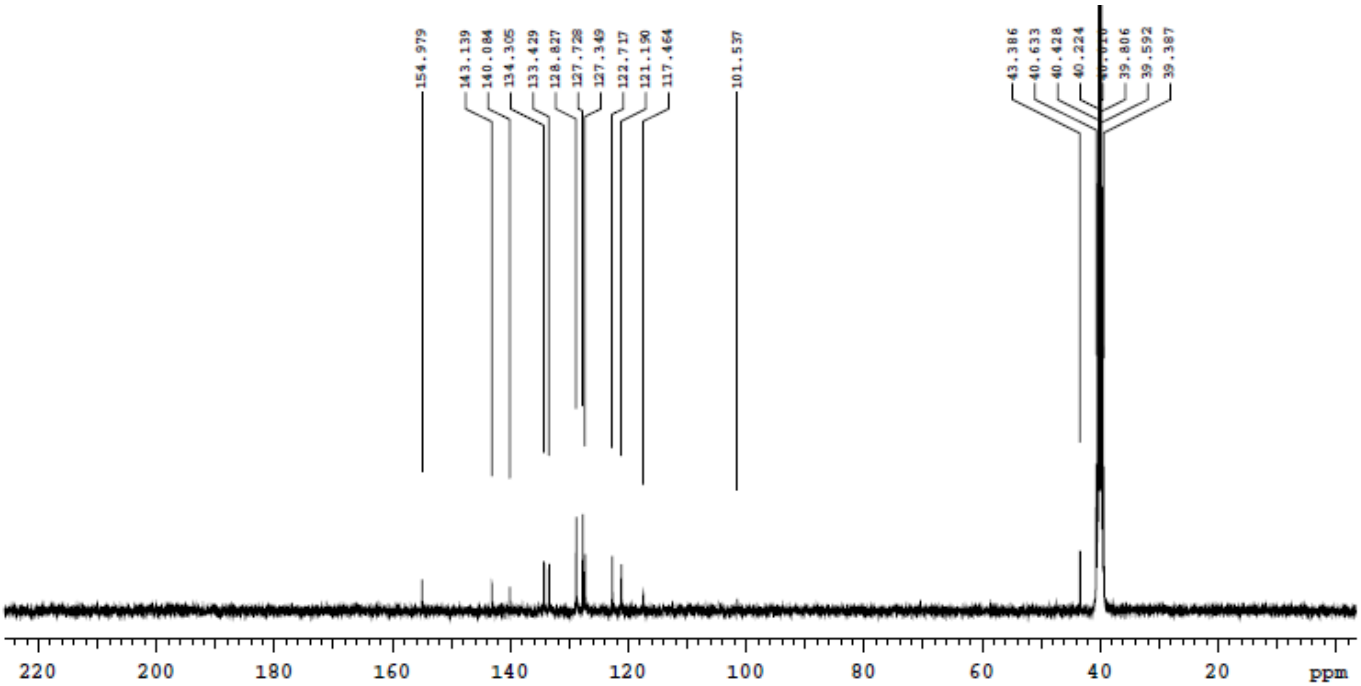


3u

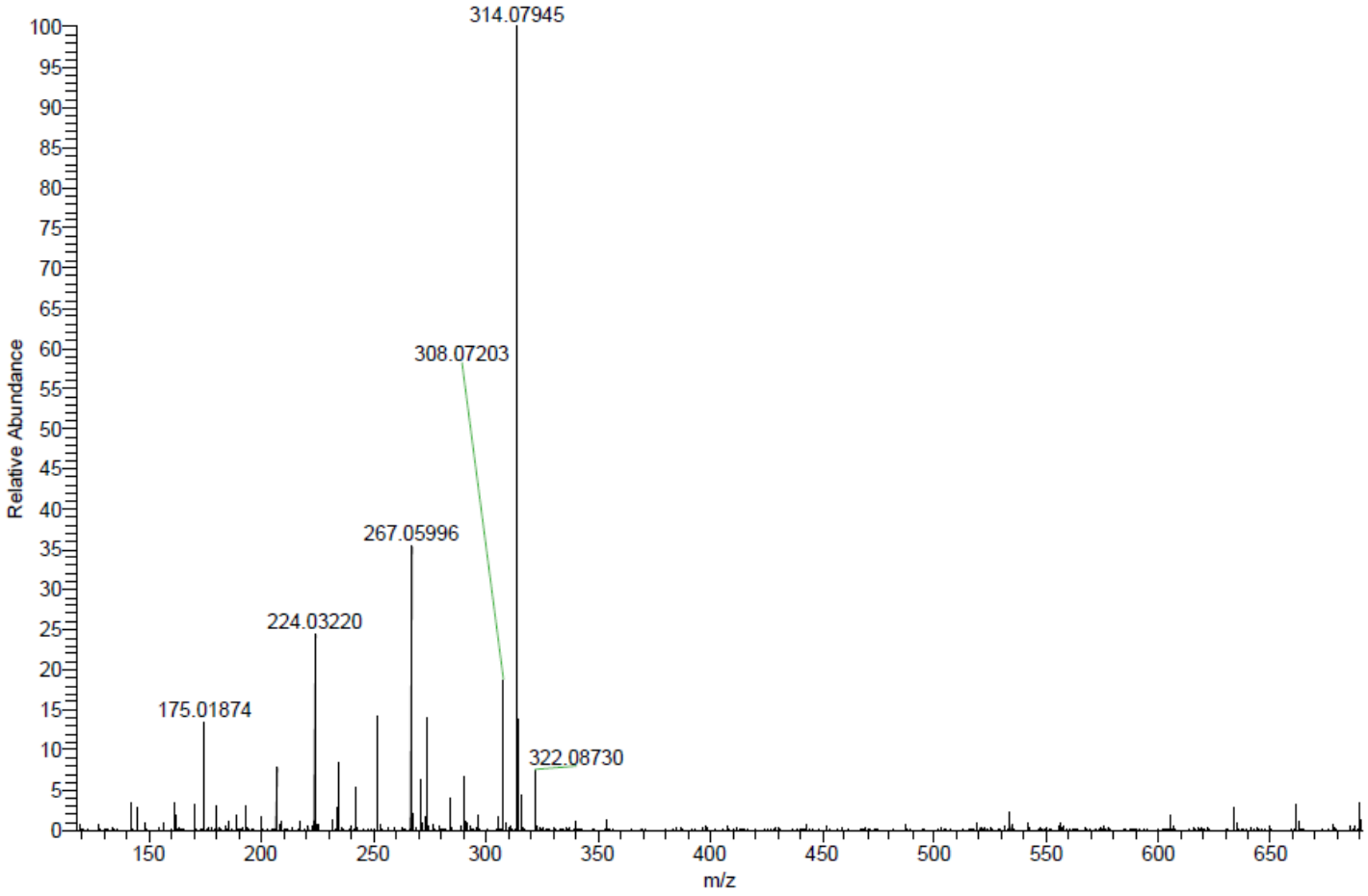
[1]H-NMR of 3u:

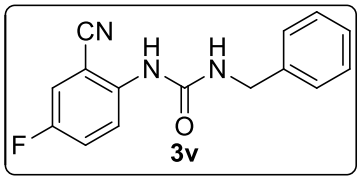


[13]C-NMR of 3u:

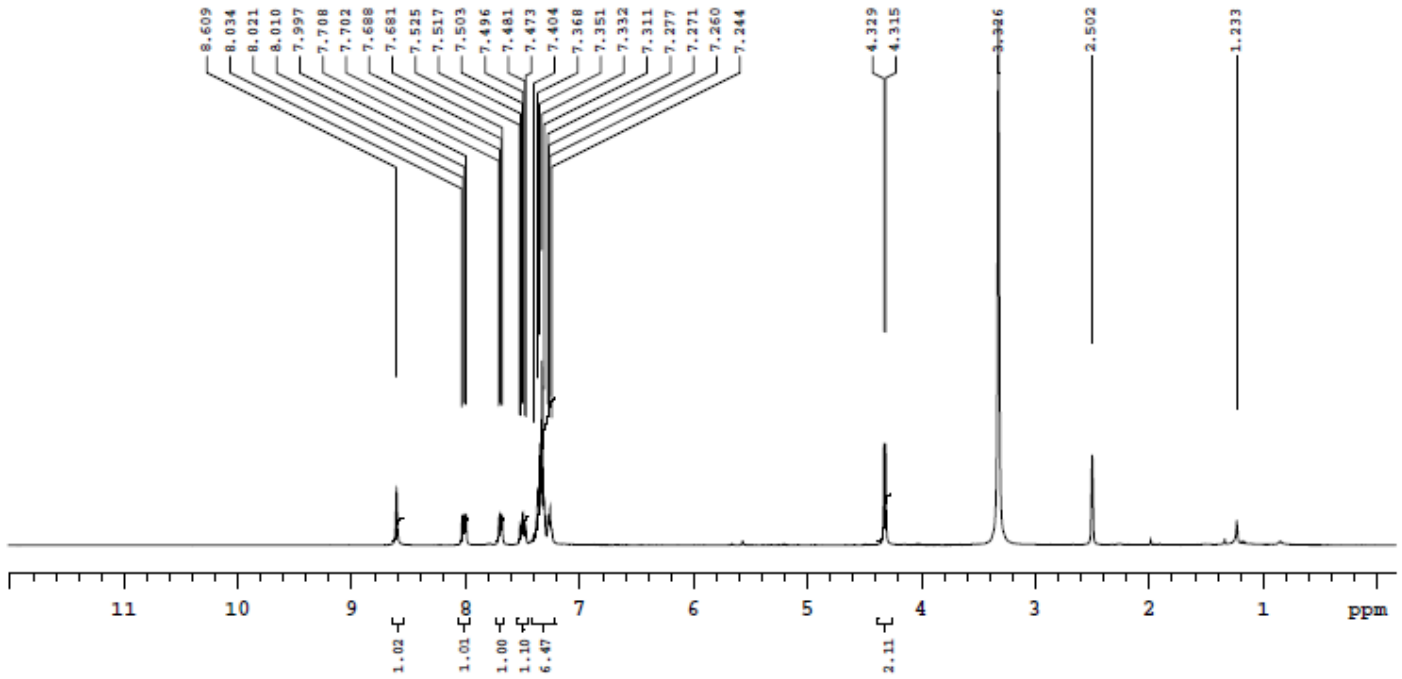


HRMS of 3u:

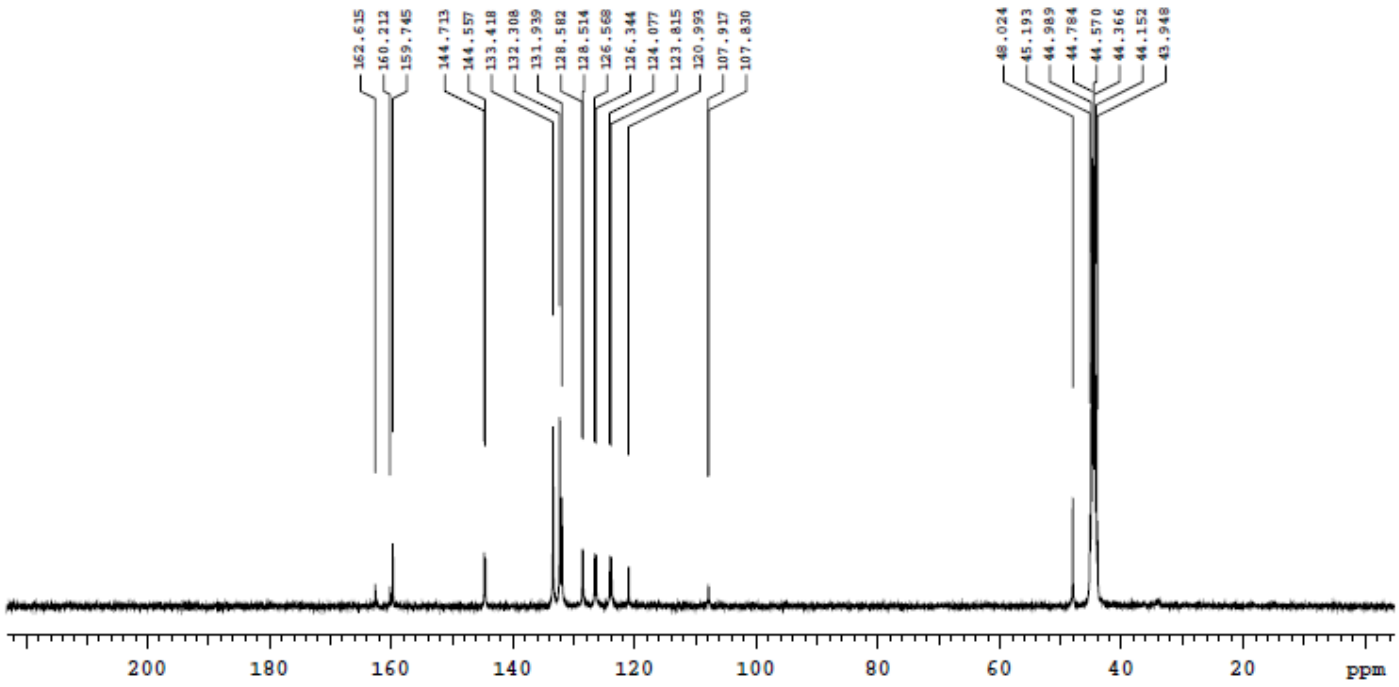

314.07945
308.07203
267.05996
224.03220
175.01874
322.08730
Relative Abundance
m/z



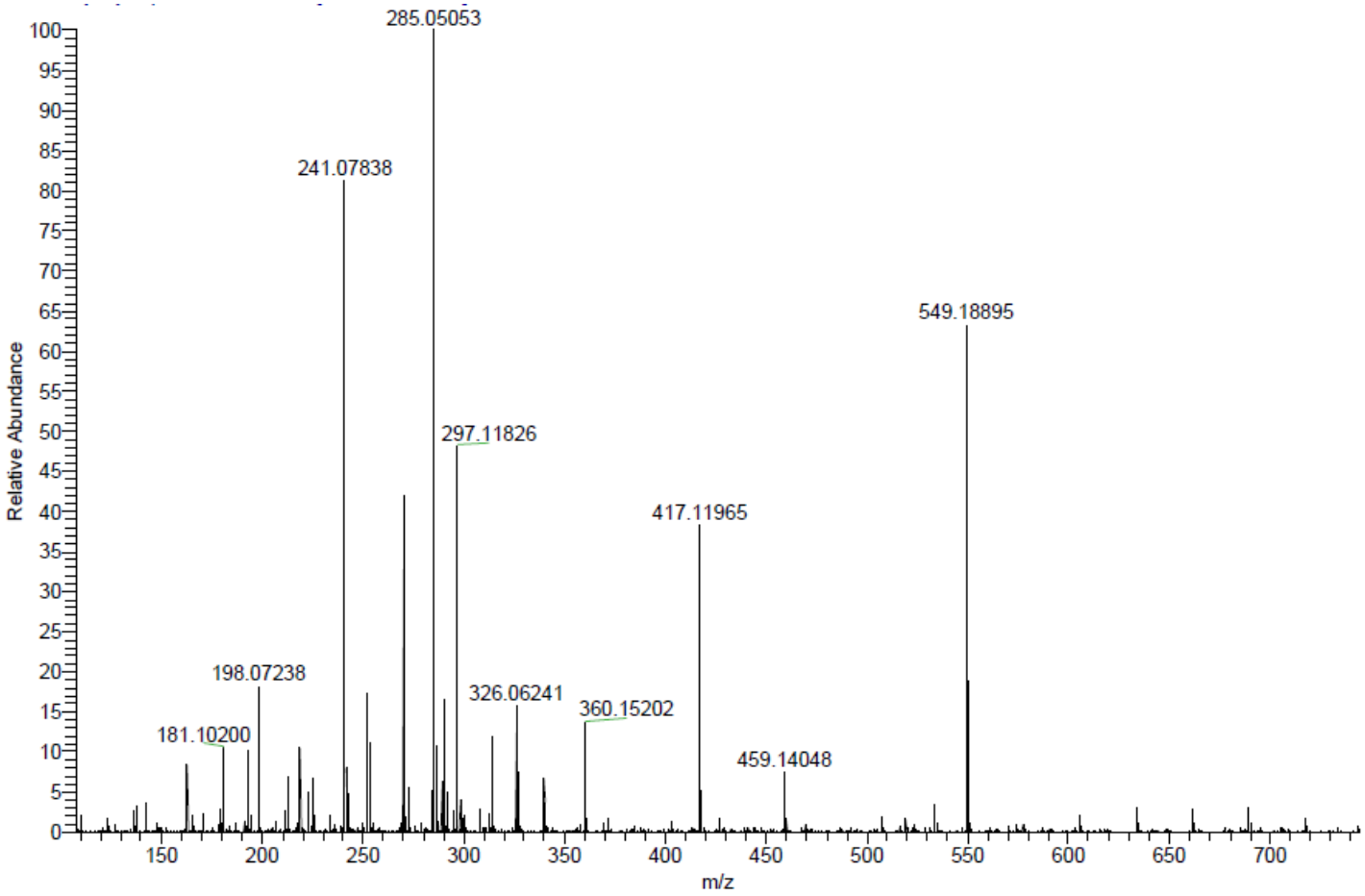
[1]H-NMR of 3v:

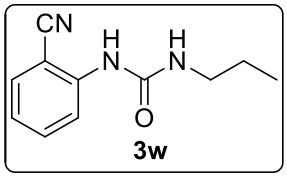


[13]C-NMR of 3v:

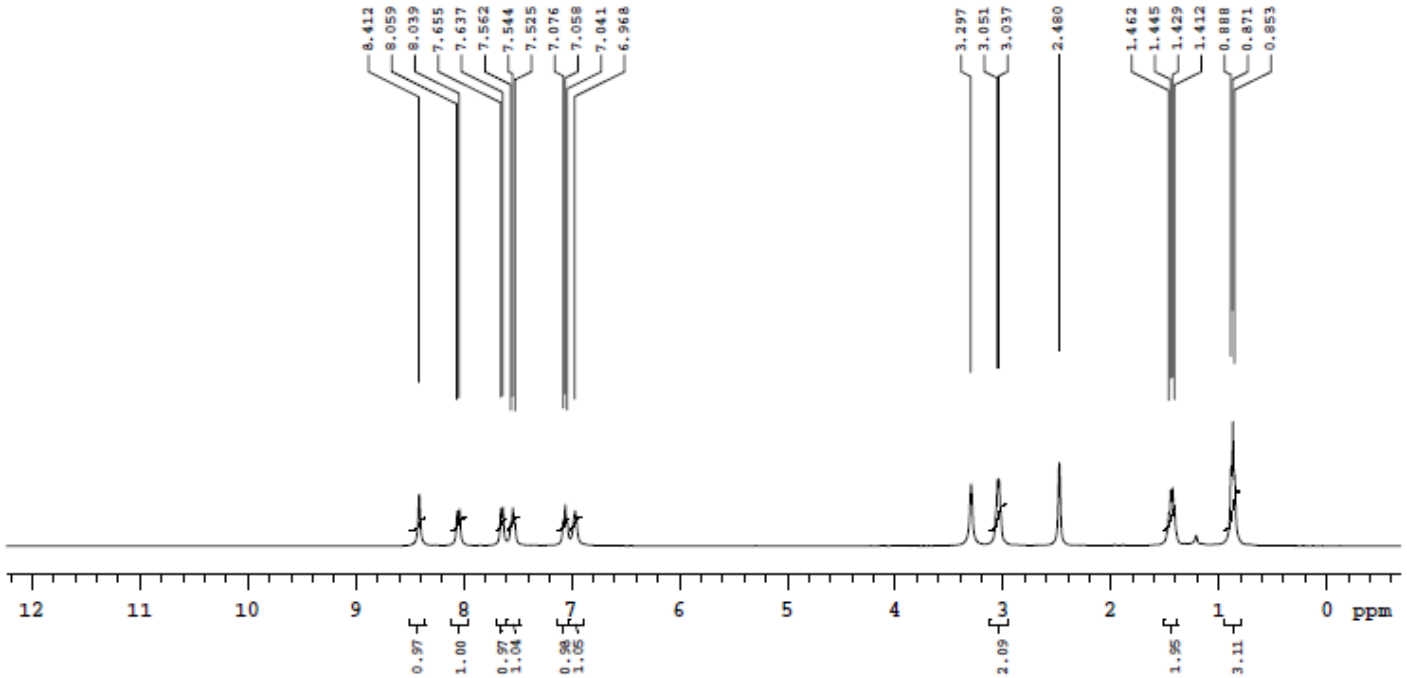


HRMS of 3v:

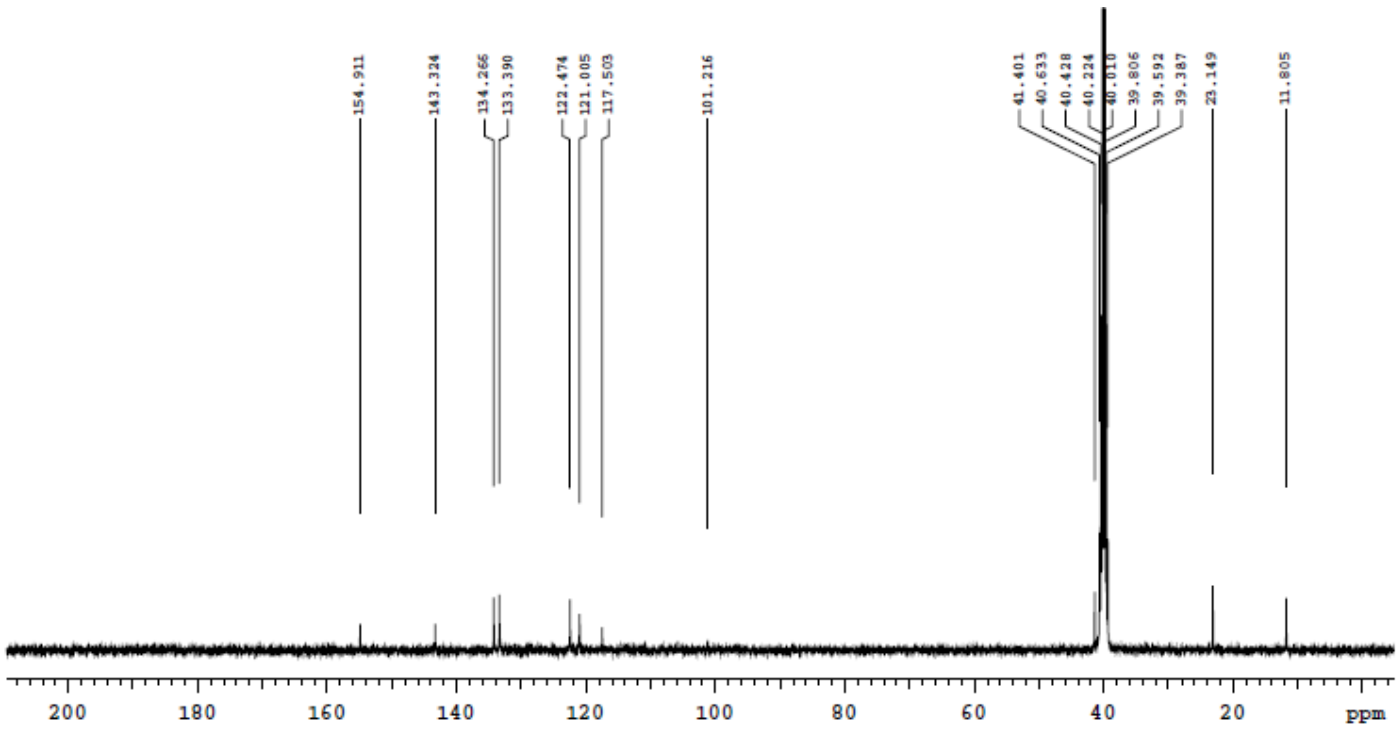

285.05053
241.07838
549.18895
297.11826
417.11965
198.07238
326.06241
360.15202
181.10200
459.14048
Relative Abundance
m/z

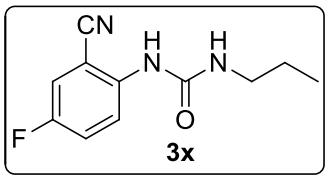


[1]H-NMR of 3w:



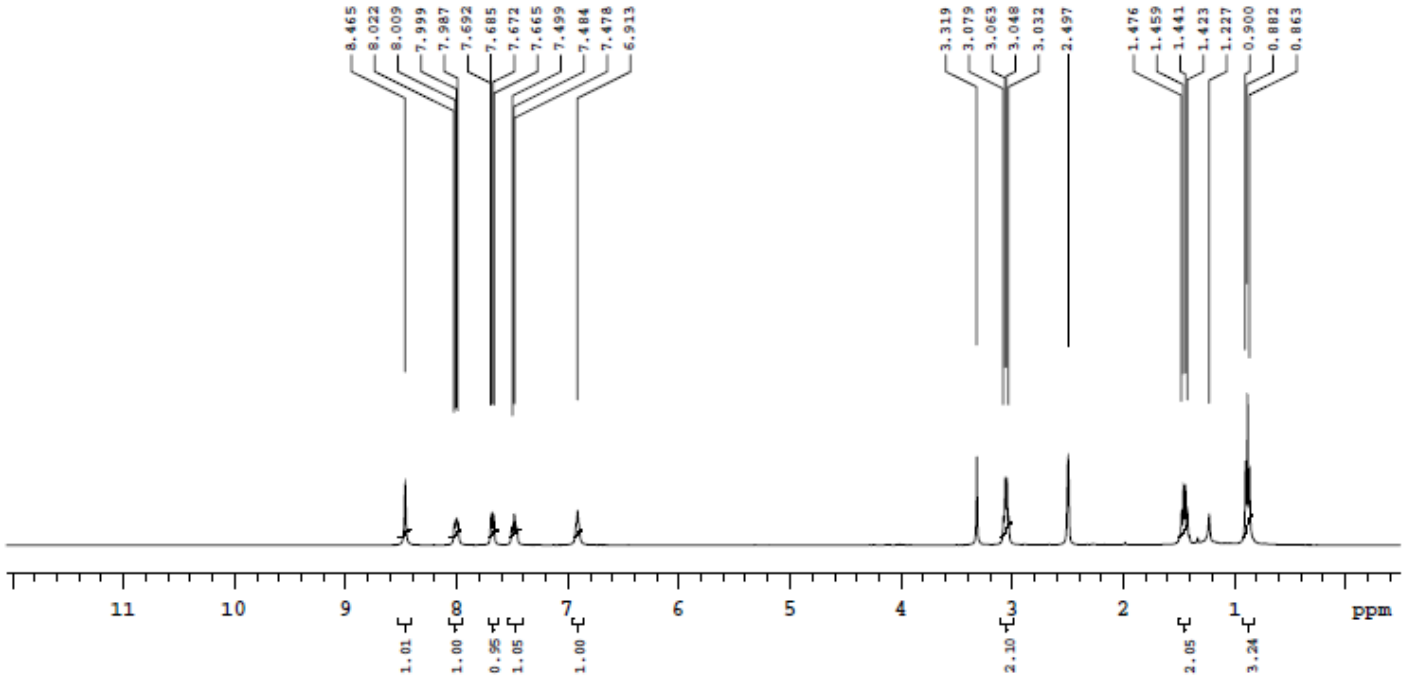
[13]C-NMR of 3w:



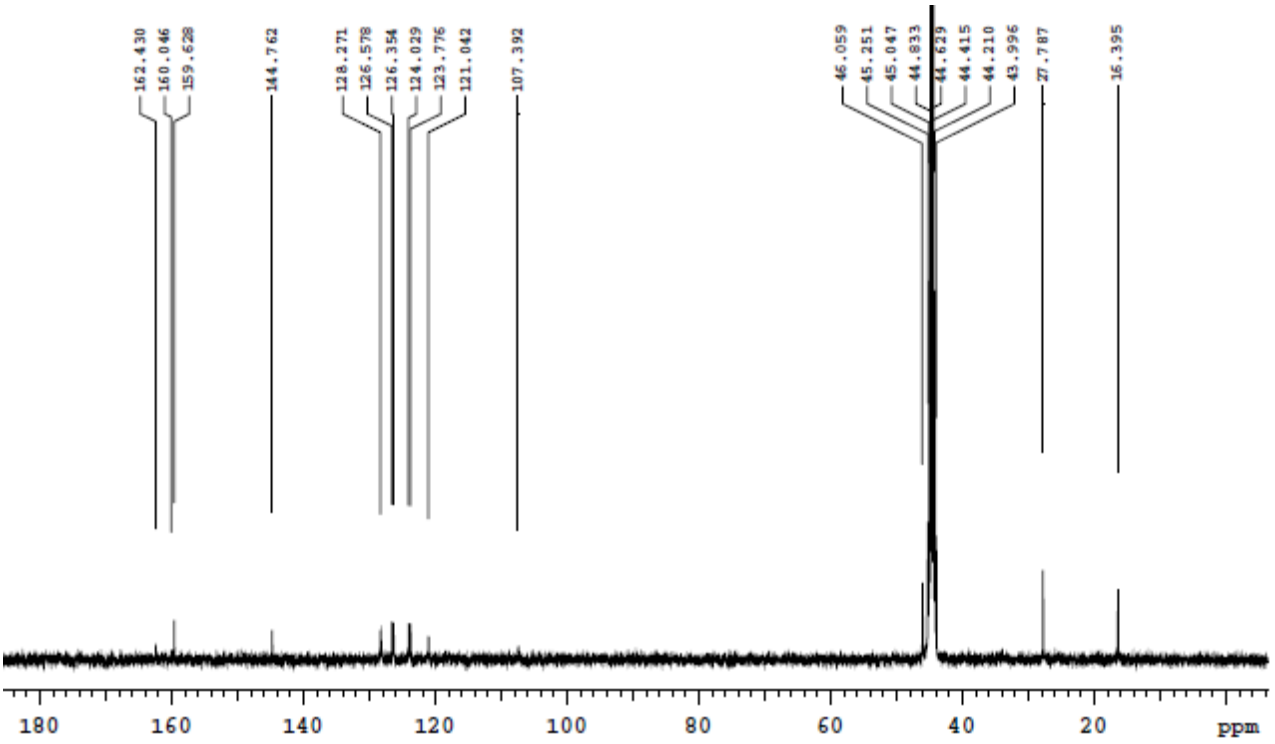


3x

[1]H-NMR of 3w:



[13]C-NMR of 3w:



5. Crystal analysis

Single crystal X-ray diffraction studies

The crystals of the compound were obtained using the slow evaporation method, defect free single crystals of appropriate dimensions were chosen for X-ray diffraction studies. X-ray intensity data of the compounds were collected using Rigaku XtaLAB Mini diffractometer with X-ray generator operating at 50 kV, 12 mA and MoK_{α} radiation. Data were collected with χ fixed at 54°, for different settings of φ (0° and 360°), keeping the scan width of 0.5° with exposure time of 4 s and the sample to detector distance was fixed to 50 mm. The complete intensity data sets were processed using *CRYSTAL CLEAR* [1]. The data sets were indexed with monoclinic crystal system, with *P*21/*c* space group. The crystal structures were solved by direct method and refined by full-matrix least squares method on F^2 using *SHELXS* and *SHELXL* programs [2-3]. All the non-hydrogen atoms were refined anisotropically and the hydrogen atoms were positioned geometrically. After several cycles of refinement, the final difference Fourier map showed peaks of no chemical significance and the residuals were saturated to accepted values. Total 163 parameters were refined with 2575 independent reflections of 5122 overall reflections. Final residual value is coverged to 0.0399. The geometrical calculations were carried out using the program *PLATON* [4]. The molecular and packing diagrams were generated using the software *MERCURY* [5].

References:

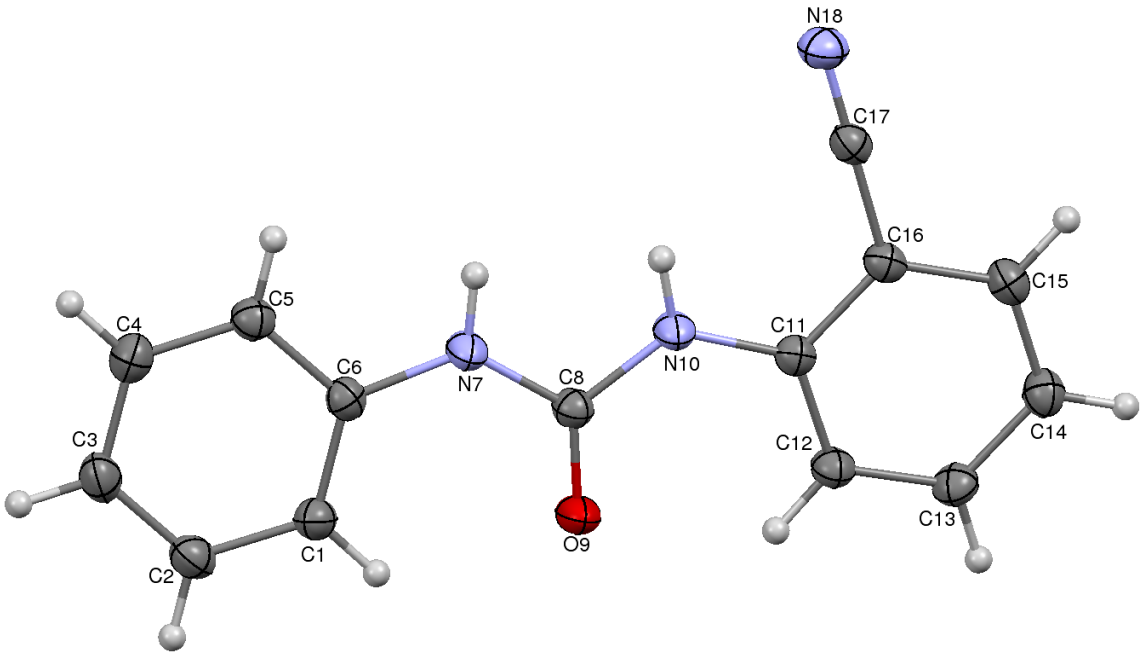
1. Rigaku, Crystal Clear, 2011.

2. G. M. Sheldrick, Crystal structure refinement with SHELXL. Acta Cryst. C71 (2015) 3-8. https://doi.org/10.1107/S2053229614024218.

3. G. M. Sheldrick, Phase annealing in SHELX-90: direct methods for larger structures. Acta Cryst. A 46(6) (1990) 467-473. https://doi.org/10.1107/S0108767390000277

4. A. L. Spek, PLATON, an integrated tool for the analysis of the results of a single crystal structure determination, Acta. Cryst. A. 46 (1990) 34.

5. C. F. Macrae, I. J. Bruno, J. A. Chisholm, P. R. Edgington, P. McCabe, E. Pidcock, L. M. Rodriguez, R. Taylor, J. van de Streek, P. A. Wood, Mercury CSD 2.0-new features for the visualization and investigation of crystal structures, J. Appl. Cryst 41 (2008) 466-470.



Crystal Structure of 1-(2-cyanophenyl)-3-phenylurea (3a):